THE ACTIVITY OF SILICA IMMOBILIZED PALLADIUM N-HETEROCYCLIC CARBENE COMPLEXES TOWARD MIZOROKI-HECK REACTION AND THEIR CHARACTERIZATION

A Thesis Submitted to
the Graduate School of Engineering and Sciences of
İzmir Institute of Technology
in Partial Fulfilment of the Requirements for the Degree of

MASTER OF SCIENCE

in Chemistry

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August 2005
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ACKNOWLEDGEMENTS

There are so many people who have affected me during my thesis study and I would like to thank every one of them.

In my life, I know a few people that know how to inspire, encourage and give self-confidence to their students, one of them is my advisor, Professor Levent ARTOK. He always guided me during my professional and personal life. I am grateful to him for giving me the chance to work with him during this study and I feel very privileged to be part of his group. I think that he is the only person that can be studied in his topic in IYTE and I can’t imagine what IYTE would have been without him and his studies.

I also wish to thank to Professor Bekir Çetinkaya for suggestions and fruitful discussions as well as his intensity as a teacher and a scientist that really turned me on to chemistry when I was in Ege University.

I would also like to thank Rsch. Asst. Hayati Türkmen for the syntheses of Pd-N-Heterocyclic carbene complexes and for his valuable friendship. I wish to thank the entire Organic group (past and present) for a memorable two years and Mr. Erhan Özkal for his assistance in experiments.

I would also like to thank to Scientific and Technical Research Council of Turkey (TBAG-2311-103T051), IZTECH (2002-IYTE-36 and 2005-IYTE-18) and Ege University (03/BIL/015) Scientific Research Project Offices for financial support for this study. I thank Prof. Orhan Büyükgüngör of Ondokuz Mayıs University for X-ray analysis, Chaoying Ni of the Department of Materials Science and Engineering, University of Delaware for TEM analyses, Prof. Devrim Balköse of the Department of Chemical Engineering for her guidance in the synthesis of the amorphous silica, Mr. Sinan Yılmaz for AAS analyses, the Enviromental Research Center for GC-MS analyses, and the Department of Chemical Engineering for BET analyses.

Especially, I wish to thank ALL of my family for the support and understanding they have given. Every one feels that their family is great but I am very lucky to a member of this great family.

ABSTRACT

C-C bond formation reactions are among the important processes in chemistry. A palladium-catalyzed reaction, commonly known as the Mizoroki-Heck (M-H) reaction, is a powerful method in construction of C-C coupling of olefins with aryl and vinyl halides.

This thesis describes, mainly development and applications of novel silica anchored saturated molecular Pd-N-heterocyclic carbene (Pd-NHC) catalysts toward the M-H reactions of aryl halides.

Characterization of the novel Pd-NHC complexes were performed using elemental analysis, NMR and X-ray crystallography techniques. The synthesized complexes were anchored over an amorphous silica surface through their triethoxy silane groups.

On the basis of the results, the silica supported saturated Pd-NHCs were found to be highly active catalyst precursors for Mizoroki-Heck reactions of iodo- and bromoarenes with styrene and butyl acrylate olefins, when reactions were performed at 140 °C in the presence of 1.5 molar equivalent Na_2CO_3 base. The catalyst preserved its original activity for 4-iodoanisole, 4-bromoacetophenone, 4-iodoacetophenone, iodobenzene and 4-iodotoluene reagents at least for 8 uses when Pd concentration, with respect to the aryl halide, was 0.5% in the reaction medium.

The catalyst afforded high turnover numbers, 10^4-10^5. The higher turnover frequencies were realized at the lower Pd concentrations. The AAS analyses revealed the presence of dissolved Pd species within the reaction medium at the early stages of reaction. Along with this finding, determination of Pd agglomerates onto silica surface by TEM examination indicates that the catalyst acted as a Pd reservoir and reactions were catalyzed homogeneously. In the course of reaction, Pd is liberalized to the solution involved with the reaction cycle and deposited onto silica surface to lead to form less active Pd agglomerates. That no trace of dissolved Pd was detected at the end of reaction by AAS is a positive finding for the purity of product.

ÖZET

C-C bağ oluşturan tepkimeler, kimyada yer alan proseslerin en önemlilerinden biridir. Yaygın olarak Mizoroki-Heck (M-H) tepkimesi olarak bilinen paladyum katalizli tepkime aril ve vinil halojenlerin olefinler ile C-C kenetlenmesinin oluşumunda etkili bir metotdur.

Bu tezde; yeni sentezlenen doymuş ve moleküler yapılı, Pd-N-Heterohalkalı karben (Pd-NHK) komplekslerin trialkoksi silan grupları aracılığı ile silika yüzeyine bağlanarak aril halojenürlerin M-H tepkimesinde katalizör olarak uygulamaları araştırılmıştır .

Yeni sentezlenen Pd-NHK komplekslerin karakterizasyonu elementel analiz, NMR ve X-ray kristallografi teknikleri kullanılarak yapılmıştır.

Alınan sonuçlar neticesinde, silikaya bağlı doymuş Pd-NHK' lerin 140ºC de 1,5 molar eşdeğer Na_2CO_3 bazı varlığında iyodo- ve bromoarenlerin stiren ve butil akrilat ile M-H tepkimesinde yüksek aktiviteye sahip oldukları bulunmuştur. Katalizör, reaksiyon ortamı aril halojenüre göre %0,5 Pd derişimi içerdiğinde 4-iyodoanisol, 4-bromoasetofenon, 4-iyodoasetofenon, iyodobenzen ve 4-iyodotoluen için en az 8 kullanım boyunca aktivitesini korumuştur.

Katalizör yüksek döngü sayılarına (10^4-10^5, TON) ulaşabilmiştir. Daha düşük Pd derişimleriyle daha yüksek döngü çokluğu (TOF) sağlanmıştır. AAS ile yapılan analizler sonucu reaksiyonun ilk zamanlarında çözeltiye silika yüzeyinden bir miktar Pd çözündüğü saptanmıştır. Bu bulgu ile birlikte kullanılmış katalizör yüzeyinde, geçirimli elektron mikroskop (TEM) analizleri sonucu, kümelenmiş Pd taneciklerinin gözlenmesi tepkimelerin homojen katalizli olarak gerçekleştiği fikrini vermektedir. Tepkime sırasında katalizör çözeltiye çözünebilen Pd vermektedir. Bu çözünmüş Pd reaksiyon döngüsünde katalizör işlevi görmekte ve tepkime sonunda silika yüzeyinde katalitik aktivitesi daha düşük bir yapıya sahip Pd kümelerine dönüşmektedir. Tepkime sonunda çözelti ortamında paladyuma rastlanmaması ürün saflığı açısından olumlu bir sonuçtur.

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CHAPTER 1

INTRODUCTION

The Mizoroki-Heck (M-H) reaction is a powerful method in construction of C-C coupling of olefins with aryl and vinyl halides (de Meijer and Meyer 1994, Cabri and Candiani 1998, Crisp 1998, Genet and Savignac 1999, Amatore and Jutand 1999, Tsuji 2000, Beletskaya and Cheprakov 2000, Witcombe and Hii 2001, Negishi 2002). This palladium-catalyzed reaction tolerates a broad range of functional groups and is also insensitive to the presence of moisture. Although there are some industrial applications for the process (Zapf and Beller 2002, de Veries et al. 2001), the process awaits to become more cost effective and environmentally benign for wider industrial applicability. To fulfill these criteria, it is essential to reduce the use of expensive Pd as well as its associated ligand and to shift the process to less expensive substrates. It is unfortunate that the activity and cost of the aryl halide substrate parallels in their dependence on the halide type associated with in the order of –I> -Br> -Cl.

Researchers have used a variety of ligand types to promote the catalytic activity of Pd; rather high turnover numbers (TONs) were realized with traditionally used phosphines (Spencer 1984, Böhm and Herrmann 2000) and even deactivated chloroarenes (Böhm and Herrmann 2000, Littke and Fu 1999, Shaughneessy et al. 1999, Ehrentraut et al. 2000, Littke and Fu 2001) were successfully subjected to the M-H reaction using bulky phosphines. However, phosphines are oxidizable, difficult to handle, toxic, and those with alkyl groups and relatively complex sites are generally expensive. Recently, palladacycles (Herrmann et al. 1995, Herrmann et al. 1997, Böhm and Herrmann 2001, Muňoz et al. 2001, Loch et al. 2002, Peris et al. 2001, Eberhard 2004, Frech et al. 2005, Takenaka and Uozumi 2004, Bergbreiter 2005, Beletskaya and Cheprakov 2004, Lee et al. 2004) and carbene ligated Pd complexes (Herrmann and Köcher 1997, Calò et al. 2000, Selvakumar et al. 2002, Viciu et al. 2003, Weskamp et al. 2000, Bourissou et al. 2000, Herrmann 2002, Weskamp et al. 1999) were shown to be highly active coupling catalysts and have been proposed as alternatives to their phosphinated counterparts. Ligand free simple palladium compounds (Reetz et al. 1998, Gruber et al. 2001, Yao et al. 2003, de Vries et al. 2003, Schmidt and Smirnov 2003, Bahattacharya et al. 2005, Reetz and de Vries 2004) and palladium colloids (Reetz and de Vries 2004, Biffis et al. 2001, de Vries et al. 2002, Calò et al. 2003) also exhibited remarkable activities and these Pd structures have been considered to act as reservoirs of Pd(0) catalytic active species (de Vries at al. 2003).

One strategy for reducing costs associated with the use of Pd and to avoid the contamination of products with palladium and ligand species is to recover the palladium after the reaction and reuse it for subsequent cycles. In this regard, many reports proposed techniques that involved the use of supported Pd (Koehler and Djakovitch 1999, Djakovitch et al**.** 1999, Köhler and Wagner 2001, Djakovitch and Köhler 2001, Dams et al. 2002, Corma et al. 2003, Pröckl et al. 2004, Okumura et al. 2005, Wagner et al 2000, Iyer 2000, Augustine and O'Leary 1992, Hagiwara et al. 2001, Heidenreich et al. 2002a, Heidenreich et al. 2002b, Köhler et al. 2002, Xie et al. 2004, Mehnert and Ying 1997, Mehnert et al. 1998, Li et al. 2004, Li et al. 2005, Zhao et al. 2002, Bennur et al. 2002, Ramchandani et al. 1997, Srivastava et al. 2003, Choudary et al. 2002), stabilized Pd nanoparticles (Yeung and Crooks 2001, Rahim et al. 2001, Le Bars et al. 1999, Reetz and Westermann 2000, Luo et al. 2005, Chandrasekhar et al. 2002, Datta et al. 2003, Okamoto et al. 2005, Calò et al. 2004, Papp et al. 2005, Zhou et al. 2002, Zhao et al. 2003, Shimizu et al. 2004), immobilized Pd complexes (Buchmeiser and Wurst 1999, Schwarz et al. 2000, Silberg et al. 2001, Chandrasekhar and Atrimoolam 2004, Yang and Luh 2003, Buchmeiser et al. 2003, Lin et al. 2003, Steel and Teasdale 2004, Yu et al. 2004, Phan et al. 2004, Luo et al. 2005,Schönfelder et al. 2005, Augustine and O'Leary 1992, Clark et al. 2000, Fujita et al. 2002,Venkatesan and Singh 2003, Gürbüz et al. 2003, Chanthayenonth and Alper 2003, Arellano et al. 2004, Tsai et al. 2004, Horniakova et al. 2004, Poyatos et al. 2003, Hardy et al. 2004, Ooe et al. 2004), Pd dispersed within ionic phases on silica (Fujita et al. 2002, Hagiwara et al. 2004) and Pd dispersed within ionic liquids (Calò et al. 2003, Park and Alper 2003, Xiao et al. 2004, Liu et al. 2004, Mo et al. 2005, Cassol et al. 2005). Nonetheless, most of these studies were mainly interested in the reuse of catalysts and only a few were tested for their TON limits (Pröckl et al. 2004, Rahim et al. 2001, Okamoto et al. 2005, Buchmeiser and Wurst 1999, Silberg etal. 2001, Horniakova et al. 2004, Hagiwara et al. 2004), whereby TONs $>10^4$ should be achieved to be competitive with homogeneous ones (Farina 2004).

The total TONs that can be achieved for the most reusable Pd catalysts are unknown and, in fact, it may not be practical to determine as it may require that the catalyst be run for hundreds of experimental cycles to reach their limits. In this regard, Schwarz et al. demonstrated that a polymer supported N-heterocyclic dicarbene chelate complex of palladium was recyclable up to 15 times for the M-H reaction of 4-bromoacetophenone with styrene with a Pd concentration of 0.15%, while its activity gradually decreased after the fourth use when the Pd concentration was 0.02% in the reaction medium (Schwarz et al. 2000). The TON issue for the Pd catalyzed M-H reactions was addressed in a recent review by Farina (Farina 2004).

N-heterocyclic carbenes (NHC) are considered as substitutes to commonly used phosphane ligands for palladium catalyzed coupling reactions, because they resemble organophosphanes due to their strong σ-donating character (Herrmann and Köcher 1997, Calò et al. 2000, Selvakumar et al. 2002, Viciu et al. 2003, Weskamp et al. 2000, Bourissou et al. 2000, Herrmann 2002, Weskamp et al. 1999). After all, they are easily accessible, non-toxic and exhibit high thermal stability as compared to phosphanes.

There are a few studies that tested immobilized unsaturated Pd-NHC complexes in M-H reactions as follows: the study using polymer supported Pd-NHCs by Schwarz et al. as described above (Schwarz et al. 2000), a clay immobilized pincer type Pd-NHC (Poyatos et al. 2003), and polymer supported Pd NHCs were reported to be reusable catalyst for iodoarenes (Steel and Teasdale 2004, Schönfelder et al. 2005).

According to the proposed reaction mechanism, oxidative Pd addition to haloarenes is believed to be the rate determining step and the activity of the catalyst is related to the electron density on palladium. Hence, we preferred to use saturated NHCs for their stronger electron donor ligand property compared to their unsaturated counterparts (Gürbüz et al. 2004, Özdemir et al. 2004). We report, for the first time, our results on the activity of anchored saturated molecular Pd-NHC catalysts towards M-H reactions of aryl halides.

CHAPTER 2

CATALYSIS

2.1. The Concept of Catalysis

The concept of catalysis as a method of controlling the rate and direction of a chemical reaction has captured the imagination of scientists and technologists since Berzelius in 1835 coordinated a number of disparate observations on chemical transformations by attributing them to a “catalytic force” and coined the term *catalysis* to refer to the “decomposition of bodies” by the force (Satterfield 1991). At about the same time Mitscherlich introduced the term contact action for a similar group of phenomena. Ideas of what constitutes a catalyst and the mechanism of catalytic activity have since undergone continuous refinement, spurred by the enormous industrial importance of catalysts as illustrated by the variety of catalytic processes characteristic of modern petroleum refineries and of the chemical industries. Most of these processes involve solid catalysts, and an understanding of catalysis from both the theoretical and practical point of view is essential to chemists and chemical engineers.

In practice catalysis is primarily a technology that draws on many fields such as organic chemistry, surface chemistry, chemical kinetics, thermodynamics, solid-state physics, ceramics, and physical metallurgy. No unified theory of catalysis exists, and there are frequently several alternative, and not necessarily mutually exclusive, theoretical explanations for any given set of facts (Satterfield 1991).

2.2. Catalytic Functions

There are three important catalytic functions: activity, selectivity, and deactivation. It is difficult to answer which is the important since each application has its own set of specific needs.

The *activity* of a catalyst refers to the rate at which it causes the reaction to proceed to chemical equilibrium. The rate of reaction depends on pressure, temperature, concentration of reactants and products, and other variables.

The *selectivity* of a catalyst is a measure of the extent to which the catalyst accelerates the reaction to form one or more of the desired products, which are usually intermediates, instead of those formed by reaction to the overall state of lowest free energy. The selectivity usually varies with pressure, temperature, reactant composition, and extent of conversion, as well as with the nature of the catalysts.

A catalyst may be useful for either its activity or its selectivity or both. If a variety of products are possible, selectivity is usually the more important. Activity can usually be stepped up by raising the temperature, although frequently increased temperature shortens the life of the catalyst or increases undesirable reactions that may be catalytic or thermal, both. A higher temperature may also decrease the maximum conversion obtainable if the reaction is exothermic and is limited in extent by thermodynamic equilibrium.

A catalyst may lose its activity or its selectivity for a wide variety of reasons. The loses may be grouped loosely into

1. Poisoning
2. Fouling
3. Reduction of active area by sintering or migration
4. Loss of active species

A somewhat amorphous catalyst may crystallize, or a compound active in one crystal habit may be converted into a less active crystalline form. A supported metal catalyst may be reduced in activity or selectivity by becoming alloyed with a metallic impurity or by reaction with the support; for example a nickel/alumina catalyst may be converted to a nickel aluminate (Satterfield 1991).

2.3. Organization of Catalysis

Catalysis can de divided into two main groups: a homogeneous catalysis occurs when the catalyst and the reactants are both in the same phase, either gas or liquid (Satterfield 1991); in heterogeneous systems the reactants and catalyst exist in different phases. Most commonly, solid catalysts are used with gaseous or liquid reactants, sometimes both.

Heterogeneous catalysts have an advantage that at the end of reaction the catalyst can be removed by simple filtration. In principle the product is un-contaminated with a transition metal or ligand and allows the catalyst to be recycled into the next reaction. While the distinction between homogeneous and heterogeneous catalysis seems well-defined, in many cases there may be leaching of the transition metal into solution (Ian et al. 2001).

From an industrial point of view, catalysts not soluble in the same phase as the organic reactant have the inherent advantage of easy separation and very often also of better handling properties, but homogeneous catalysts are better defined and understood (for a short comparison see Table 2.1.) (Hans-Ulrich et al. 2001).

Table 2.1. Strong and weak points of heterogeneous and homogeneous catalysts

	Homogeneous	**Heterogeneous**
Strong points	Defined on molecular level (close to organic chemistry) Scope, variability (design?) Preparation	Separation, recovery, recycling Stability, handling Many (hydrogenation) catalysts commercially available
Weak points	Sensitivity (handling, stability) Activity, productivity (of many literature procedures) Separation	Characterization (understanding on points molecular level) Preparation (needs special know-how), reproducibility Diffusion to and within catalyst

2.4. Transition Metals as Catalysts

Transition metals (of which there are 64) occupy the middle portion of the periodic table; they can be defined as metallic elements that have valence electrons in two shells instead of one. These metals are suitable as catalyst because of their ability to change oxidation states during a catalytic cycle and the formation of lower-energy intermediates leading to a reduction of the activation barrier of the catalytic reactions.

One of the most common uses of a transition metal is in the antipollution devices in automobiles; platinum or palladium is used as a heterogeneous catalyst in these systems. The catalytic converter combines carbon monoxide and unburned fuel from a car’s exhaust with oxygen from the air to form carbon dioxide and water vapor. Many of the important transition metals in heterogeneous catalysis are found among the "late transition metals" such as Ru, Co, Rh, Ni, Pd and Pt. The complexes formed by transition metals with ligands allow their catalytic properties to be fine-tuned.

Organometallic chemistry, the chemistry of compounds containing metal-carbon bonds, is one of the most interesting and certainly most rapidly growing areas of chemical research. It encompasses a wide variety of chemical compounds and their reactions: compounds containing both sigma (σ) and pi (π) bonds between metal atoms and carbon; many cluster compounds, containing one or more metal-metal bonds; molecules of structural types unusual or unknown in organic chemistry; and reactions that in some cases bear similarities to known organic reactions and in other cases are dramatically different. Aside from their instrinsically interesting nature, many organometallic compounds form useful catalysts and consequently are of significant industrial interest.

The first organometallic compound to be reported was synthesized in 1827 by Zeise, who obtained yellow needle-like crystals after refluxing a mixture of $PtCl_4$ and $PtCl_2$ in ethanol, followed by addition of KCl solution.

The first compound containing carbon monoxide as a ligand was another platinum-chloro complex, reported in 1867. In 1890, Mond reported the preparation of $Ni(CO)_4$, a compound that became commercially useful for the purification of nickel.

Reactions between magnesium and alkyl halides performed by Barbier in 1898 and 1899 and subsequently by Grignard, led to the synthesis of alkyl magnesium complex now known as Grignard reagents.

From the discovery of Zeise's salt in 1827 to approximately 1950, organometallic chemistry developed rather slowly.

Transition metals are normally expensive, and sometimes toxic, it is important that they can be used in sub-stoichiometric amounts. A nicely engineered solution is exemplified in the commercially important Wacker process, which was discovered in 1959 by German chemists (Figure 2.1.) (Bäckvall et al. 1979).

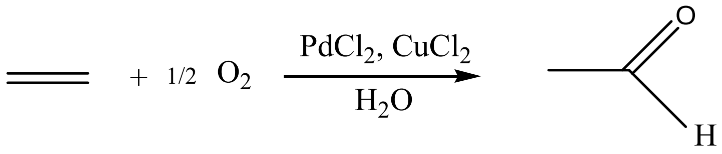


Figure 2.1. Palladium-catalyzed oxidation of an olefin, the Wacker process.

Here, palladium dichloride is used as the catalyst and is regenerated after each cycle with help of catalytic amounts of copper, which in turn is reoxidized by cheap and environmentally friendly oxygen gas.

The very versatile vinylic substitution reaction, the Heck coupling, employing aryl iodides, was developed around a decade later (Figure 2.2.) (Heck and Nolley 1972).

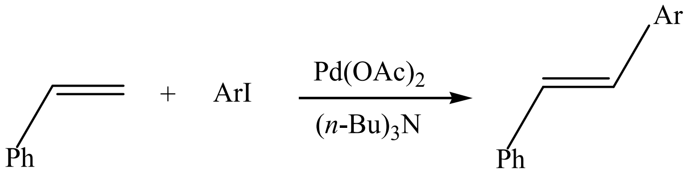


Figure 2.2. Palladium-catalyzed arylation of an olefin

2.4.1. Catalytic Properties

The extended possibility for coordination of ligands as a result of access to partially filled d-orbitals make transition metals, especially the late, more versatile than the main group metals in a catalytic sense. This partial occupation of the d-orbitals also results in new features such as simultaneous electron-accepting and electron-donating characteristics. The interaction with ligands such as olefins (Van Houten 2002), carbon monoxide, arenes, isocyanides, alkynes, nitric oxide etc, which have the same kind of acceptor/donor capabilities, gives rise to a situation where both ‘bonding’ and ‘backbonding’ are possible.

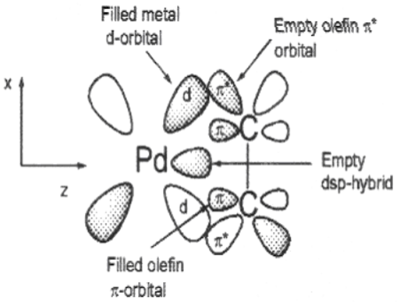


Figure 2.3. Ethene coordinating palladium in η^2-mode, according to the Dewar–Chatt–Duncanson π-bond model (Source: Van Houten 2002).

A ‘bonding’ interaction (Figure 2.3.) develops between the filled olefin π-orbital and the spd hybrid on the metal, whereas ‘backbonding’ occurs between the empty olefin antibonding orbital and the filled d_{xz} orbital on the metal. The ‘bonding’ interaction is classified as a σ-bond, since it is symmetric when rotated around the z-axis. Accordingly, the ‘backbonding’ interaction is defined as a π-bond (anti-symmetric). In combination with the 18-electron rule, this bonding situation opens up very rich coordination chemistry where the electron density (changes in the HOMO and LUMO levels) on the metal can be easily varied by the judicious choice of ligands. The reactivity and selectivity of the transition metal complex, employed as a homogeneous catalyst, can therefore be fine-tuned.

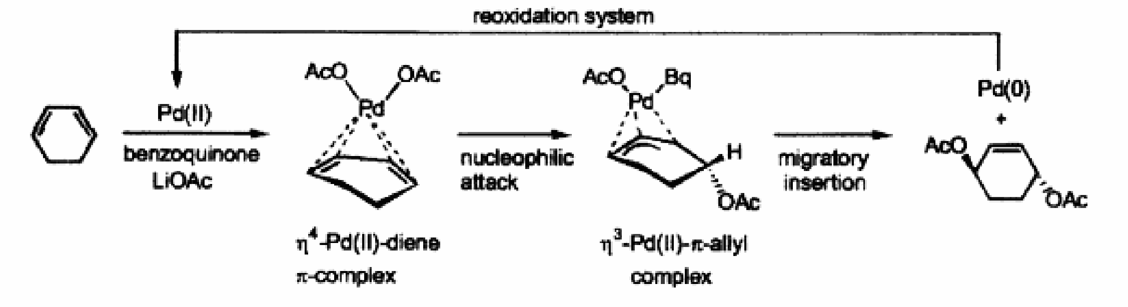


Figure 2.4. Coordination to electrophilic palladium facilitates subsequent nucleophilic attack on the diene by acetate anion (Source: Bäckvall et al. 1984).

Since nearly every organic functional group is potentially capable of coordination to transition metals, there is a good probability of finding a suitable catalyst for the desired transformation. Transition metals can reverse the polarity (i.e. electron density) of coordinated functional groups introduce a complementary reactivity (Figure 2.4.) (Bäckvall et al. 1984).

2.5. Palladium as a Catalyst

There are probably hundreds of Pd-catalyzed processes in operation for the production of fine chemicals and of biologically active ingredients. The catalytic profile of Pd catalysts differs significantly from Pt, Rh, Ru, Ni, or Cu in the following properties:

- Palladium is the most versatile and the most widely applied metal for catalytic organic synthesis and the manufacture of fine chemicals.
- The catalytic behavior of Pd catalysts can be tuned by adding organic or inorganic modifiers (Hans-Ulrich et al. 2001).
- Palladium strongly favors the 0 and +2 oxidation states as they are separated by a relatively narrow energy gap. This feature impends to the palladium to undergo one-electron or radical process and makes palladium a fairly selective catalyst, possibly through the minimization of unwanted side reactions.
- Palladium has comparatively high electronegativity that allows relatively non-polar Pd-C bonds and display low reactivity to polar functional groups, such as ketones, esters, amides, nitro compounds. This quality constitutes a desirable complement to e.g. the Grignard reagents and organolithium compounds that are very reactive to various carbonyl groups.
- Palladium has an impressive functional group tolerance, i.e. chemoselectivity, which makes Pd-catalysis applicable to a large number of different substrates such as carbonyl and hydroxyl groups. Pd-catalyzed reactions can be carried out without protection of these functional groups.
- Palladium complexes are usually easy to handle, relatively nontoxic and mostly insensitive to oxygen, moisture and acid.
- Palladium is rare but less expensive than rhodium, iridium, osmium or platinum. The fact that a number of industrial processes (more than ten at least) based on Pd catalyzed reactions have been developed and are now operated reflects these advantages of using Pd catalyst commercially (Tsuji 2000).

Palladium catalysis is being developed into two major directions: towards complex synthesis where selectivity is the major issue, while the efficiency of catalysts may be completely neglected as the value of compounds being synthesized by far exceeds the cost of catalyst; and towards common organic preparations with the perspective of industrial applications, in which catalyst efficiency often becomes the major issue.

A broad application of palladium catalysts for organic synthesis, including reactions of industrial importance, such as ethylene chemistry is presented in Figure 2.5 (Murahashi and Davies 1996).

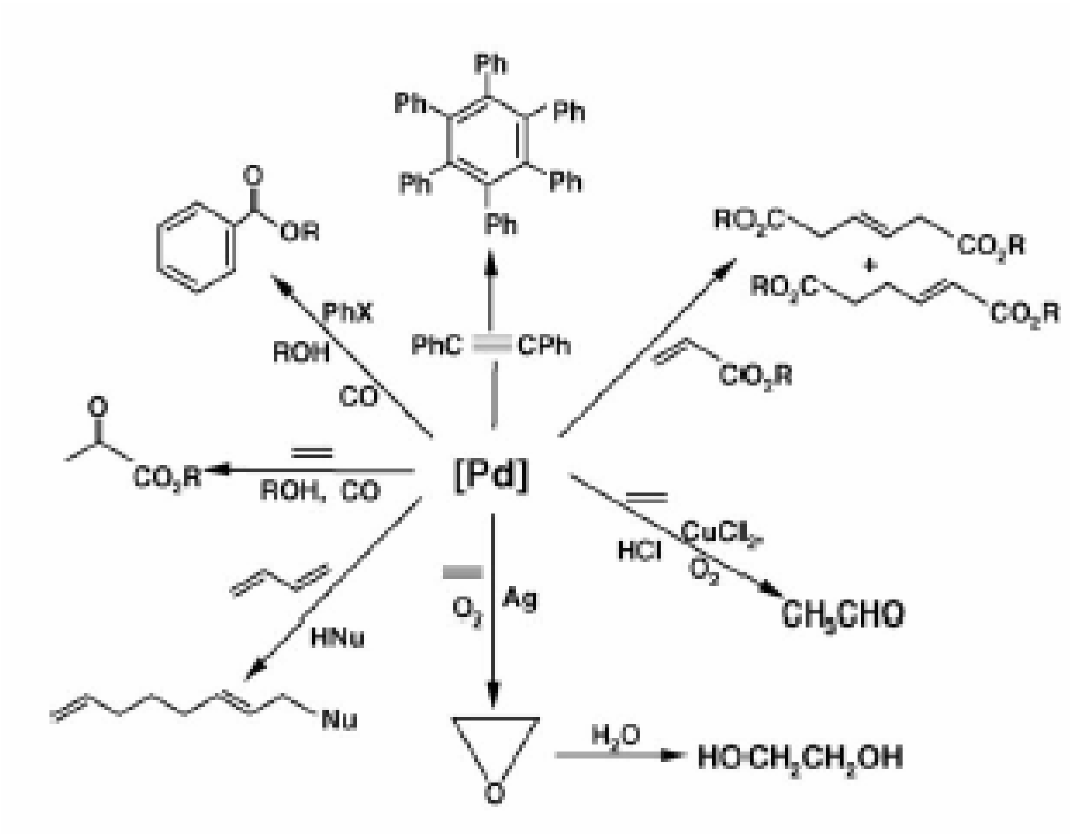


Figure 2.5. Palladium catalyzed organic reactions (Murahashi and Davies 1996).

Over 90 organic reactions are catalyzed with palladium, although most of them are not commercialized. The Wacker process, which delivers several million tons of acetaldehyde per year (converted mainly into acetic acid) is one of the simplest and most spectacular industrial applications of palladium catalysts although recently this process has been replaced by methanol carbonylation. For about 50 years palladium compounds have been used as active and selective catalysts for reactions of many rather complicated substrates providing new useful synthetic organic products. Among those processes, palladium-catalyzed reactions with aryl halides as substrates are of particular importance (Figure 2.6.) (Herrmann et al. 2003).

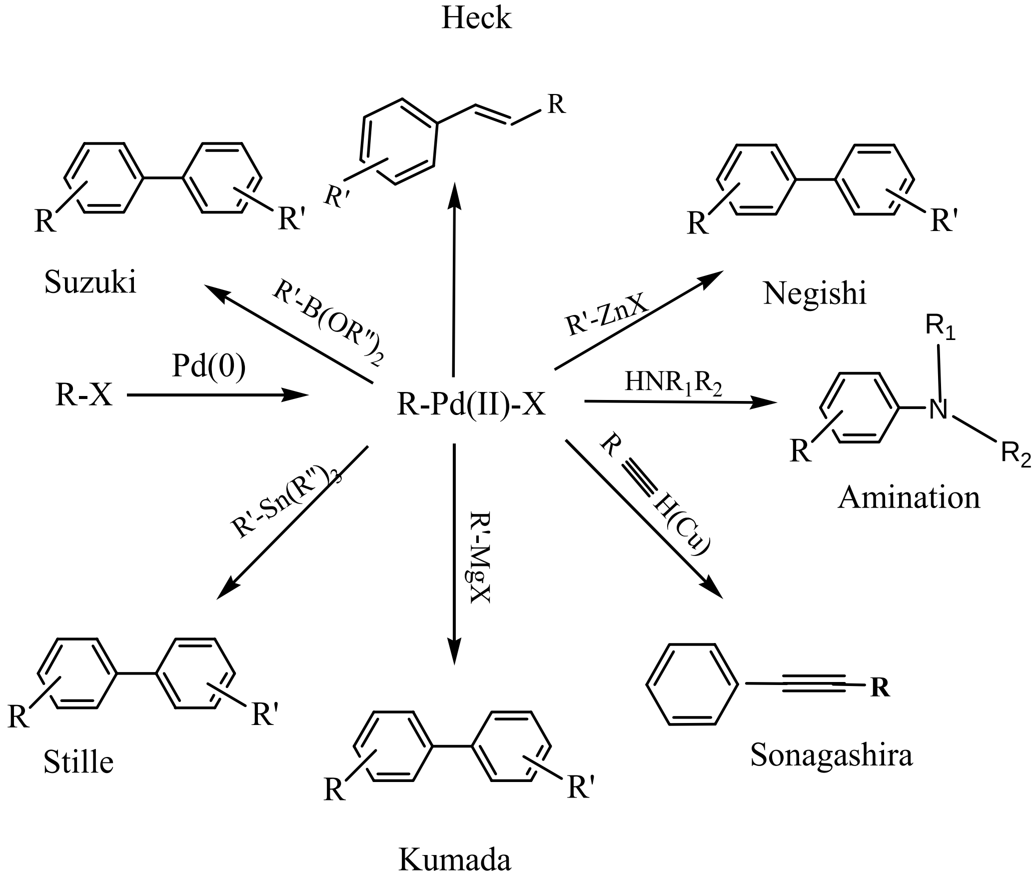


Figure 2.6. Principle of palladium catalyzed cross-coupling reactions.

Depending on the reaction conditions, aryl halides can be transformed into carboxylic acids, esters, or amides in a one stage carbonylation process. Olefination of aryl halides, the so-called Heck reaction. (Cornils and Herrmann 1996, Miyaura and Suzuki 1995, Remmele et al. 2003, Heck 1979), produces functionalized olefins. In the Suzuki reaction bi-phenyl derivatives are obtained, and in the Sonogashira process phenylated alkynes are formed (Malleron et al. 1997).

During the past 15 years palladium chemistry has become an extremely active part of coordination and organometallic chemistry related to broadly understood catalysis: homogeneous, heterogeneous, and, recently, nanocatalysis (Trzeciak and Ziölkowski 2005).

CHAPTER 3

RECYCLABLE CATALYTIC SYSTEMS

Homogeneous catalysis has a fatal drawback in that the catalyst is used only for a single run. None of the catalysts used for truly homogeneous processes can be recovered from the reaction mixtures in a reactive form suitable for immediate re-use. Thus, the cost of the catalyst, which is often quite high, adds to the cost of the product. This can be appropriate only for very complex and expensive products (e.g. chiral compounds with high enantiomerism), but is prohibitive for the application of such processes to the vast majority of other chemicals (Murahashi and Davies 1996).

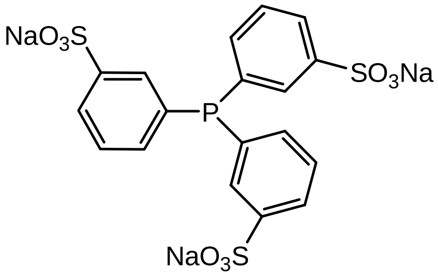
The heterogeneous processes, However, for which catalyst recovery and continuous-flow operation are inherent, are often hopeless in areas where selectivity is the major issue. It is obvious that combining what is good in each of the types of catalysis while leaving behind what is deficient must be an appealing challenge. It should be added that increasing catalytic efficiency (the yield of product per load of catalyst) is an approach that is roughly equivalent to recycling. Indeed, any method of recycling can not have an absolute recovery, and some of the catalyst is still lost at each cycle. For example, increasing the efficiency (turnover number) by 100 times (going from 5mol% of catalyst load to 0.05mol%) in a non-recyclable process is equivalent to having a recyclable catalyst with total recovery 99% (summed up for a whole lifetime of a recycled catalyst), which is an enviable value rarely achieved in real processes. The application of novel rigid complexes and of some phosphine-free systems in aqueous homogeneous or solubilized media affords turnover number exceeding 50,000-100,000. Such efficiency in a single run already by far exceeds values those achievable from any real recycling procedure (Murahashi and Davies 1996).

There are two main approaches for the design of recyclable catalysts: running the process in a biphasic (liquid-liquid or liquid-solid) system in which the catalysts are physically bound to one of the phases; and chemically binding the catalyst to the carrier molecule possesing specific physical properties, which enables the seperation of the whole unit by methods applicable to the carrier. Both approaches have been applied already to palladium catalysis.

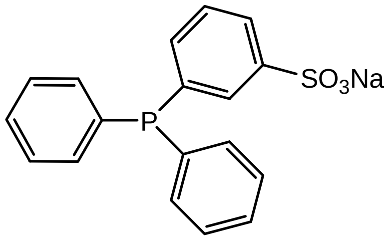
3.1. Liquid-liquid biphasic catalysis

Liquid-liquid biphasic catalysis relies on catalyst held in one of the phases, while the products accumulate in the other phase. After the reaction the phases are separated, either directly or, in the case of systems prone to emulsification, by applying various technical tricks such as passing the reaction mixture through semi-permeable membranes that allow only one phase to pass through. The simplest and most obvious example of such systems uses water as the catalyst-containing phase, although there are non-aqueous biphasic systems (Murahashi and Davies 1996).

In order to make the recycling truly efficient, it is important not to allow the palladium to be reduced to metal and to have it quantitatively bound to a complex with such a high solubility in its own phase that any leaching to the other phase can be neglected. In order to achieve this, highly hydrophilic ligands need to employed, the most important of which has been, and stil is, tris(*m*-sulfonatophenyl)phosphine used as its trisodium salt (TPPTS).



TPPTS



TPPMS

Both TPPTS and TPPMS ligands are quite popular as water-soluble analogs of PPh_3 in phosphine-mediated reactions in aqueous media for reasons that have nothing to do with recycling. The use of aqueous or organic solvents apparently solves no environmental or safety problems, such media are required for applying the catalytic reactions towards highly hydrophilic molecules, e.g. for modification of natural compounds and their analogs, which may be incompatible with organic solvents due to poor solubility or destruction of inherent conformations (Murahashi and Davies 1996).

3.2. Immobilized catalysts

Immobilization of palladium catalysts on *polymeric resins* so far has not produced any spectacular results. The problems here are manifold, including low thermal stability of the polymers that are usually employed for such purposes (mostly various linear and cross-linked polyolefins), which leads to the fast degradation of expensive catalyst and prevents recycling, as well as very low rates due to both the limited diffusion of reactants in polymers and the low concentration of catalytic centers that are bound only to end-cap residues. Several attempts to enhance the stability of supports and to increase the load of palladium per molecule of polymer by introducing the ligating molecules inside the polymeric molecule were made recently (Murahashi and Davies 1996). For example, a resin containing 1,10-phenanthroline units was developed and used as a support for palladium in Heck arylation of acrylamide to give cinnamamides, which can be converted further to acryl acetic aldehydes (Zhuangyu et al. 1991).

A new class of macromolecules, *dendrimers*, based on 1,4diaminobutane (DAB) bearing peripheral amino groups was derivatized with diphenylphosphine (PPh_2) to give a macromolecule with 16 chelating diphosphine units, DAB-*dend*-$[N(CH_2PPh_2)_2]_{16}$, which can bind transition metals (e.g. palladium, nickel, rhodium) to give complexes (Reetz et al. 1997).

Like other macromolecules, dendrimers can be precipitated from solutions by the addition of weakly interacting solvents, making them useful for recycling purposes (Murahashi and Davies 1996). A very strong advantage of dendrimeric support over other kinds of organic polymers is a full exposure of catalytic centers to the environment. Because the whole macromolecule is inside the particle, diffusion limitations are not important.

Dendrimeric catalyst DAB-*dend*-$[N(CH_2PPh_2)_2PdMe_2]_{16}$ showed about three times higher catalytic activity than parent complex *n*-$PrN(CH_2PPh_2)_2PdMe_2$ in the Heck arylation of stilbene with bromobenzene carried out in DMF at 130ºC in the presence of NaOAc as base, due to the higher stability of the former. Indeed, the deactivation of palladium catalyst in catalytic reactions is due to the formation of large metallic particles, the process initiated by encounters of Pd (0) species. It is evident that the encounter rate is much higher for small molecules than for macromolecules, due to both diffusional and entropic considerations (Murahashi and Davies 1996).

Advances in the chemistry of materials led to the discovery of a number of new types of regularly structured inorganic polymer with fascinating properties, including high thermal stability, reproducible three-dimensional structure and availability of reactive groups for modification with organic residues. Unlike such conventional solid supports as charcoal, silica (this support will be fully discussed in 3.3), alumina, etc, which are charged by reagents or catalysts using simple impregnation and drying procedures that rely on physical absorption, which is very hard to control, novel materials are modified via more predictable processes such as ion exchange or chemical bonding.

Thus, a well known very cheap natural ion exchanger, *montmorillonite clay*, can be charged by Pd(II) and Cu(II)to provide a recyclable catalyst for Heck arylations with aryl bromides (Ramchandani et al. 1997).

Novel materials used for the construction of solid recyclables are the *mesoporous molecular sieves*. Such materials provide an ingenious link between microstructures formed by surfactants and silicate frameworks. The composition and morphology of these materials are easily adjustable; e.g. pores size can be varied continuously over a broad range of values. Catalytically active sites can be added either during the preparation of the material or later. The first report on the use of such material grafted with palladium for Heck reaction has been tested on 4-bromoacetophenone and some other bromoarenes with butyl acrylate, the catalyst showed high activity, although the lifetime of the catalyst was limited due to agglomeration of palladium and the formation of large polydispersed particles (Mehnert and Ying 1997).

3.3 Catalyst Support: Silica

The early concept of a support or a carrier was of an inert substance that provided a means of spreading out an expensive catalyst ingredient such as platinum for its most extensive use, or a means of improving the mechanical strength of an inherently weak catalyst. However, the carrier may actually contribute catalytic activity, depending on the reaction and the reaction conditions, and it may react to some extent with other catalyst ingredients during the manufacture process. It can also help to stabilize the catalytically active structure.

The selection of a carrier is based on its having certain desirable characteristics. In addition to possible chemical effects, certain physical properties are important (Satterfield 1991):

1. Inertness to undesired reactions
2. Desirable mechanical properties, including attrition resistance, hardness, and comprehensive strength
3. Stability under reaction and regeneration conditions
4. Surface area (High surface area is usually, but not always, desirable)
5. Porosity, including average pore size and pore-size distribution (high area implies fine pores but relatively small pores, such as < 2 nm may become plugged in catalyst especially if high loadings are sought)
6. Low cost

The first report on the preparation of coherent expanded aerogels was published by Kistler in 1931. He clearly showed that the inorganic gel, when dehydrated under normal conditions, collapses into a powder as a result of the disruption in the pore structure of the gel. However, when the gel was dehydrated under super-critical conditions of temperature and pressure, the liquid-vapor boundary within the pores of the gel no longer existed and the gels did not collapse on drying. Kistler described the formation of gels of silica, alumina, ferric oxide, stannic oxide, tungstic oxide, nickel oxide, and several organic materials (Gesser and Goswami 1989). Silica gel chemistry is performed either with an inorganic precursor, like ‘‘water-glass’’ or with organic precursors such as silicon alkoxides, tetraethoxysilane (TEOS) of formula $Si(OC_2H_5)_4$ or tetramethoxysilane (TMOS) of formula $Si(OCH_3)_4$, which are usually engaged as monomers, but partially condensed silica or prepolymers (oligomers) are sometimes also used (Crudden and Allen 2004). Silica gel is most commonly prepared by hydrolyzing an acid, generally hydrochloric acid, with a solution of “water glass” which consists of ortosilicates (Na_4SiO_4), metasilicates (Na_2SiO_3), and related compounds. It was then allowed to set and washed until the chloride was removed. As the pH is lowered, a polymerization and a condensation process takes place, which can be visualized starting with silisic acid [$Si(OH)_4$]. This polymerized with condensation of silane groups (SiOH) to form an ill-defined polymer in which the primary bonds are the siloxane type (Si-O-Si). This precipitates as a gel or as a colloid, the properties of which depend on mixing procedures, the presence of electrolytes, temperature, aging, etc. By proper control, a hydrogel consisting of small micelles that are roughly spherical is obtained. During drying, the micelles do not coalesce appreciably, particularly if the liquid is removed at above critical temperatures and pressures. Under these conditions, no interface forms that could otherwise collapse the structure by the forces of surface tension. The tiny size of the micelles and use of procedures to prevent coalescence leads to a product of high surface area. Commercial material usually has a high area, as high as about 700 m^2/g. The average pore diameter correspondingly very low typically in the range of 2.5 to 5 nm (these pores are however considerably larger than those in zeolites and are substantially greater than the most reactant molecules of interest.)

By varying the manufacturing and aging procedures, silica gels can be made with considerably larger pore diameter and correspondingly lower surface area, perhaps as low as about 100 m^2/g. Silica gel is generally inert. The final dry product should be referred to strictly as a xerogel or porous silica, but the term *silica gel* is in common usage. At ambient temperature the surface consists of a layer of silanol groups (SiOH) plus the physically adsorbed water. Most of the water is removed upon drying in air at 150 to 200 °C. Silanol groups are left on the surface, and these are progressively lost with increased temperature. Some siloxane groups may also be present on the surface (Satterfiled 1991).

A basic knowledge of the surface structure is of great help in understanding the adsorption behavior and the chemical reactivity of silica in a variety of processes. With respect to the surface of crystalline silica, it was assumed that all of the hydroxyl groups exist as a free or isolated hydroxyl groups (Figure 3.1.). In contrast, the surface structure of amorphous silica is highly disordered and such a regular arrangement of hydroxyl groups cannot be expected (Unger 1988).

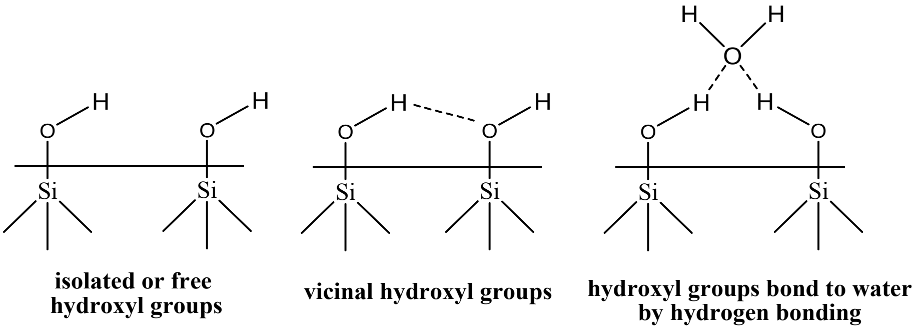
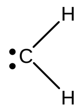


Figure 3.1. Arrangement of hydroxyl groups on a silica surface.

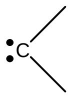
CHAPTER 4

CARBENES

Carbenes **1 and 2** are neutral compounds featuring a divalent carbon atom with only six electrons in its valence shell (Bourissou et al. 2000).

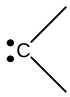


1



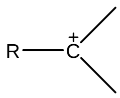
2

Carbene **2** could be regarded as bases conjugate to carbonium ions, **3**. However, in the presence of other molecules they react as electrophilic reagents, attacking nucleophilic centers (Chinoporos 1962).



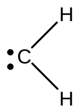
2

congugate to

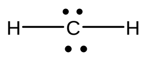


3

Considering a prototype carbene –C:–, the carbon atom can be either linear **4** or bent **1**, each geometry describable by a certain degree of hybridization.



1



4

The linear geometry implies a sp-hybridized carbene center with two nonbonding degenerate orbitals (p_x and p_y). Bending the molecule breaks this degeneracy and the carbon atom adopts an sp^2-type hybridization: the p_y orbital remains almost unchanged (it is usually called p_π), while the orbital that starts as pure p_x orbital is stabilized since it acquires some s character (it is therefore called σ) (Figure 4.1).

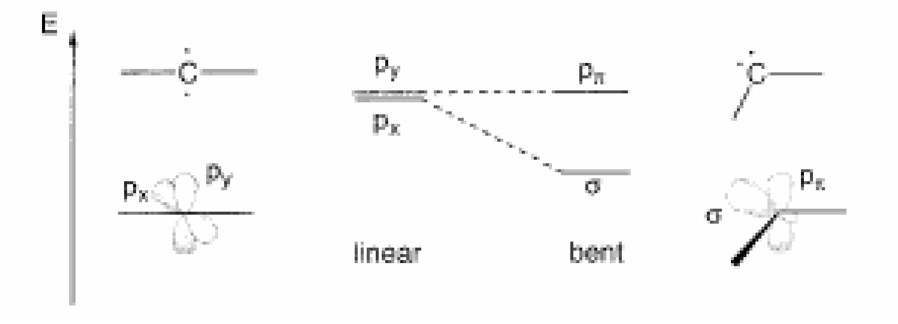


Figure 4.1. Relationship between the carbene bond angle and the nature of the frontier orbitals (Bourissou et al. 2000).

The linear geometry is an extreme case; most carbenes are bent and their frontier orbitals will be systematically called σ and p_{π}.

As depicted in Figure 4.2, four electronic configurations can be envisaged. The two nonbonding electrons can be in two different orbitals with parallel spins (triplet state); hence, the molecule is correctly described by the $\sigma^1 p_{\pi}{}^1$ configuration ($^3B_1$ state).

In contrast, for singlet carbenes, the two nonbonding electrons can be paired in the same σ or p_{π} orbital. Therefore, there are two different $^1A_1$ states, the σ^2 being generally more stable than the $p\pi^2$. Last, an excited singlet state with $\sigma^1 p_{\pi}{}^1$ configuration can also be envisaged ($^1B_1$ state).

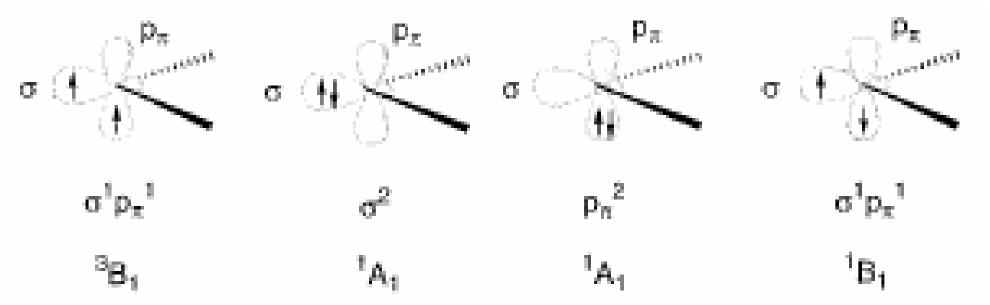


Figure 4.2. Electronic configurations of carbenes (Bourissou et al. 2000).

The ground-state spin multiplicity is a fundamental feature of carbenes that dictates their reactivity. Indeed, singlet carbenes feature a filled and a vacant orbital, and therefore, they should possess an ambiphilic character. On the other hand, triplet carbenes have two singly occupied orbitals and are generally regarded as diradicals.

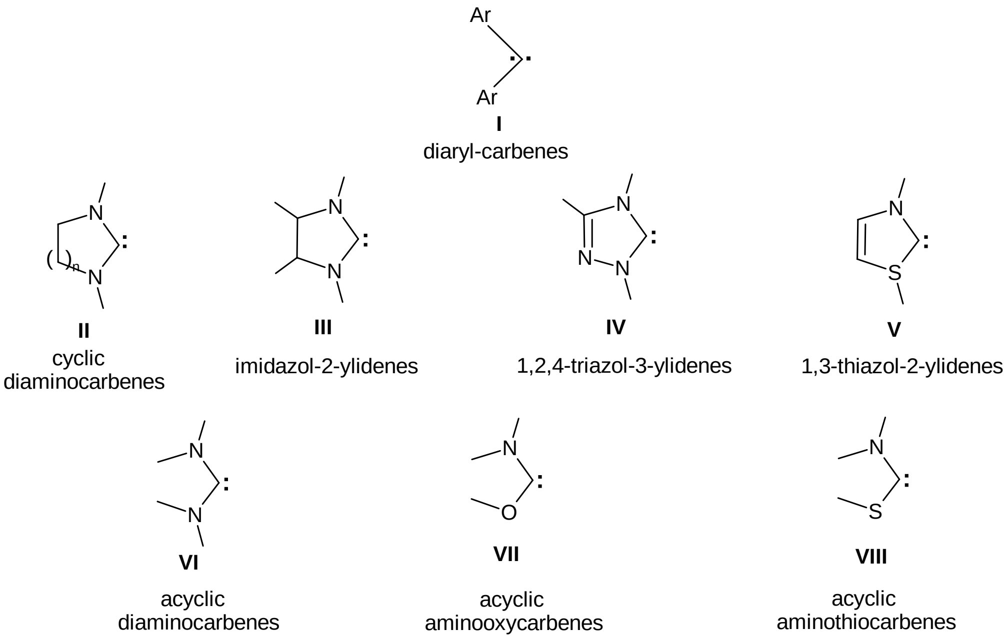


Figure 4.3. Triplet carbenes I and singlet carbenes II-VIII.

The influence of the substituents on the carbene ground-state multiplicity can be easily analyzed in terms of electronic and steric effects (Bourissou et al. 2000).

a) Electronic Effects

σ-electron-withdrawing substituents favor the singlet versus the triplet state. Substituents interacting with the carbene center can be classified into two types, namely X (for π-electron-donating groups such as -F, -Cl, -Br, -I, -NR$_2$, -PR$_2$, -OR, -SR, -SR$_3$, ...) and Z (for π-electron-withdrawing groups such as -COR, -CN, CF$_3$, -BR$_2$, -SiR$_3$, -PR$_3^+$, ...). Therefore, the singlet carbenes can be classified according to their substituents: the highly bent (X,X)-carbenes and the linear or quasi-linear (Z,Z)- and (X,Z)-carbenes.

b) Steric Effects

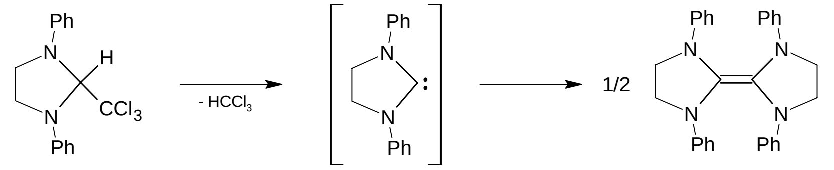
Bulky substituents clearly kinetically stabilize all types of carbenes. Moreover, if electronic effects are negligible, the steric effects may also dictate the ground-state spin multiplicity. Increasing the steric bulk of carbene substituents broadens the carbene bond angle and therefore favors the triplet state.

4.1. Stable Singlet Carbenes

The singlet carbenes have been classified as (X,X)-carbenes which are aminocarbenes, (Z,Z)-carbenes which are diborylcarbenes, and (X,Z)-carbenes Phosphinosilyl- and Phosphinophosphoniocarbenes.

4.1.1. Aminocarbenes

In the early 1960s, Wanzlick realized that the stability of carbenes could be dramatically enhanced by the presence of amino substituents and tried to prepare the 1,3-diphenylimidazolidin-2-ylidene **6a** from **5** by thermal elimination of chloroform (Eq. 4.1) (Wanzlick and Kleiner 1961).

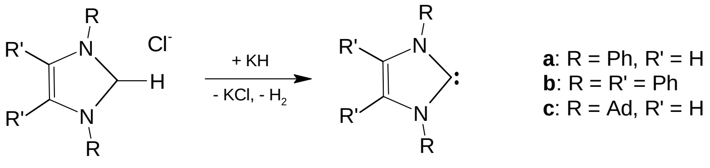


(4.1)

5 **6a** **(6a)$_2$**

At that time, only the dimeric electron-rich olefin (6a)$_2$ was isolated and cross-coupling experiments did not support an equilibrium between (6a)$_2$ and two-carbene units (Winberg et al. 1965).

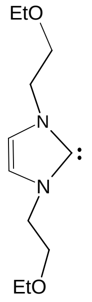
In 1970, Wanzlick and co-workers demonstrated that imidazolium salts **7a,b** could be deprotonated by potassium *tert*-butoxide to afford the corresponding imidazol-2-ylidenes **8a,b** which were trapped but not isolated. Following this principle, almost two decades later Arduengo *et al.* prepared "A Stable Crystalline Carbene" (Arduengo et al. 1991). **8c** was obtained in near quantitative yield by deprotonation of the 1,3-di-1-adamantylimidazolium chloride **7c** with sodium or potassium hydride in the presence of catalytic amounts of either KOBu^t or the dimethylsulfoxide anion (Eq. 4.2).



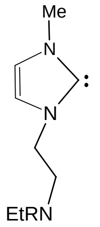
(4.2)

7a-c **8a-c**

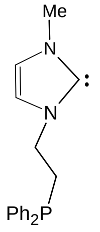
Herrmann and co-workers showed that the deprotonation occurs much faster with liquid ammonia as the solvent (homogeneous phase), and oxygen, nitrogen, and phosphorus *N*-functionalized **8d-f** as well as chiral **8g** and bis-imidazol-2-ylidenes **8h** have been prepared following this procedure.



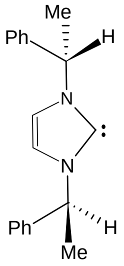
8d



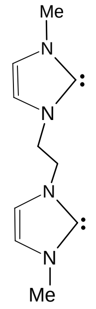
8e



8f

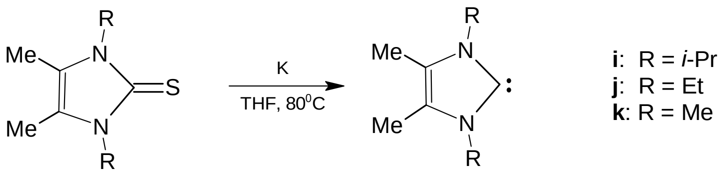


8g



8h

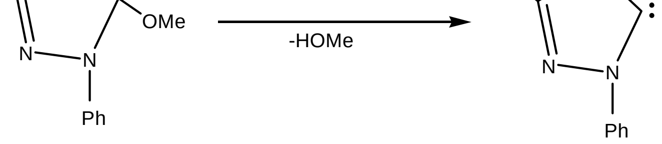
In 1993, Kuhn and co-workers developed a new and versatile approach to the alkyl-substituted *N*-heterocyclic carbenes **8i-k**. This original synthetic strategy relied on the reduction of imidazol-2-thiones 9**i-k** with potassium in boiling THF (Eq. 4.3).



9i-k **8i-k**

(4.3)

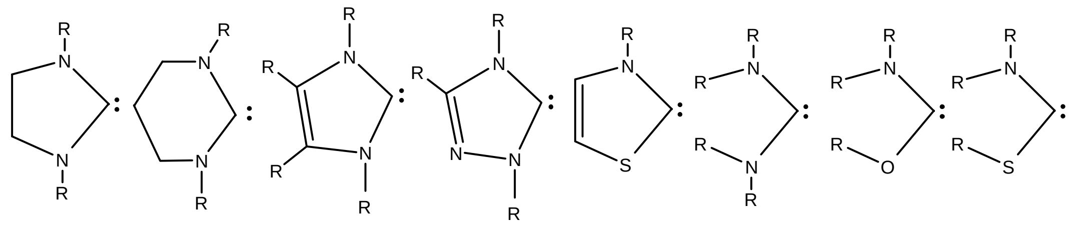
Enders et al. reported in 1995 that the 1,2,4-triazol-5-ylidene **11a** could be obtained in quantitative yield from the corresponding 5-methoxy-1,3,4- triphenyl-4,5-dihydro-1*H*-1,2,4-triazole **10** by thermal elimination (80 °C) of methanol in vacuo (0.1 mbar) (eq 4.4). Compound **11a** became the first carbene to be commercially available (Enders et al. 1995).



10 **11a**

(4.4)

Following these synthetic routes, a number of stable aminocarbenes have been isolated: imidazolidin-2-ylidenes **6**, tetrahydropyrimid-2-ylidene **6**a, imidazol-2-ylidenes **8**, 1,2,4-triazol-5-ylidenes **11**, 1,3-thiazol-2-ylidenes **12**, as well as acyclic diamino- **13**, aminooxy- **14**, and aminothiocarbenes **15** (Figure 4.4). For all of these compounds, the carbene center bears two π-donor substituents, of which at least one is an amino group. The superior π-donor ability and therefore the superior stabilizing effect of amino versus alkoxy groups has been evidenced experimentally (Bourissou et al. 2000).

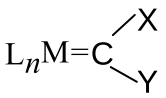


6 **6’** **8** **11** **12** **13** **14** **15**

Figure 4.4. Isolated stable aminocarbenes

4.2. Transition metal-Carbene complexes

The term metal-carbene complexes **16** refers here to compounds of the general type in which a carbene, :CXY, is coordinated to a metal atom, **M,** and **L,** simply represents the various other coordinated ligands.



$L_nM{=}C(X)(Y)$

16

The carbene *ligand* is usually bound terminally, but is also found as a bridging moiety. Complexes are usually neutral, but cationic species are also known and anionic ones have been postulated as reaction intermediates. For cationic and anionic complexes, an alternative symbolism is to regard these compounds as transition metal substituted carbonium ions or carbanions. Likewise neutral carbene complexes may be alternatively regarded as transition metal ylides, like the Wittig (e.g.**,** Ph_3-PCH_2) and related reagents. The carbene may be considered as a “soft” ligand, being normally found in complexes in which the metal is in a low oxidation state, but Rh(III) and Pt(IV) compounds have been described; the carbene ligand is classed as a neutral species.

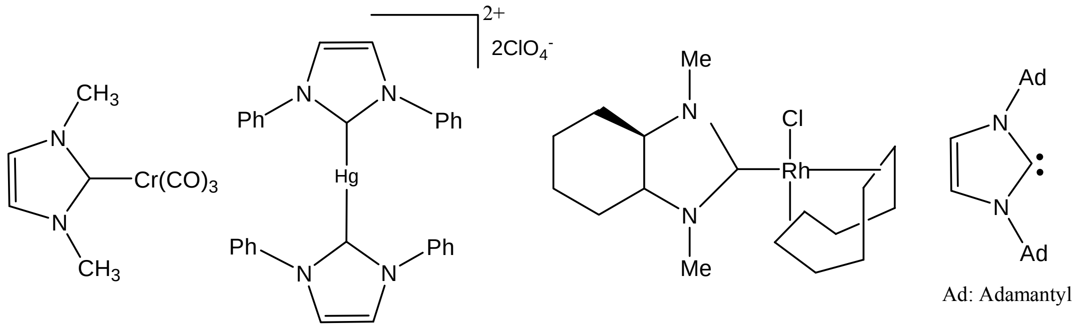
Stable carbene complexes have been prepared only when either **X** or **Y** (or both) is an element other than carbon (a heteroatom), commonly O, S, or N; and ***n*** interaction between the carbene carbon (C_{carb}) and **X** or Y is an important factor in stabilizing the complexes.

The free carbene ***:CXY*** is thus classified as a nucleophilic carbene. As will be seen, C_{carb} may be regarded in valence-bond language as a sp^2 C. However, the term carbene complex does not include alkenyl- or alkynyl-metal compounds and related species, in which a carbon ligand atom is formally doubly bonded to **X** or **Y.**

Although the first carbene complexes were evidently prepared in 1915**,** they were not recognized as such until 1962, and the current interest started with the preparation of (OC)$_5$WC(OMe)Ph, the first carbene complex to be so formulated (Jardin et al. 1972).

4.3. NHC Complexes of Transition Metals

The use of *N*-heterocyclic carbenes (NHC's) as ligands for transition metal complexes was described 36 years ago by Öfele and Wanzlick who prepared compounds **17** and **18**. With the notable exception of Lappert's extensive studies into the chemistry of late transition metal carbene complexes such as **19**, little attention was paid to these species until the 1991 report of Arduengo et al. describing the isolation and crystallization of a free carbene **20** (Figure 4.5) (Crudden and Allen 2004).



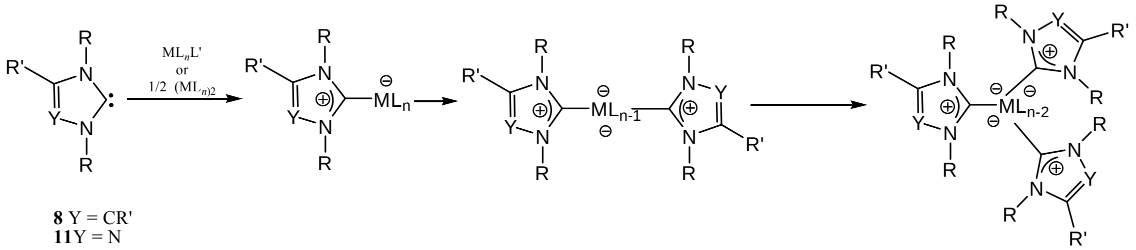
17 **18** **19** **20**

Figure 4.5. An early example of NHC–complexes and Arduengo's isolated free carbene.

4.3.1. Synthesis of N-Heterocyclic Carbene Complexes

Transition metal complexes of N-heterocyclic carbenes are accessible by six different routes (eq 4.5-4.10).

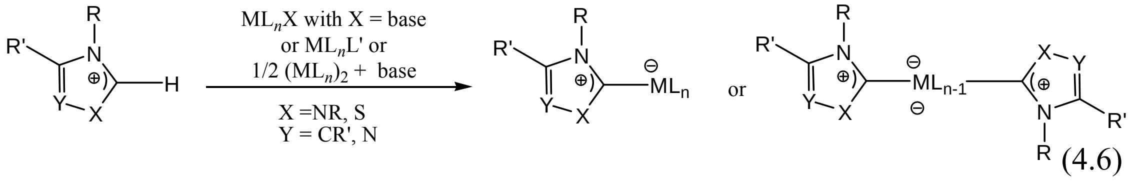
a) Imidazol-2-ylidenes **8** and triazol-2-ylidenes **11** react with a broad variety of organometallic precursors ML_nL' to afford the corresponding complexes after replacement of a two-electron donor. (eq. 4.5)



8 Y = CR'
11Y = N

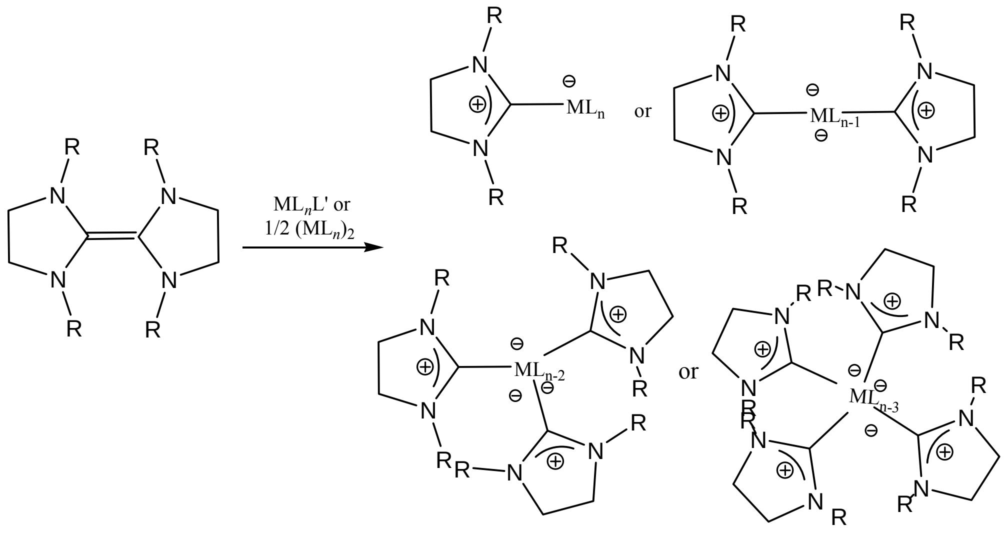
(4.5)

b) N-Heterocyclic carbene complexes can also be obtained by deprotonation of the corresponding azolium salts in the presence of organometallic fragments ML_nX or ML_nL' (eq. 4.6). A basic ligand X (such as hydride, alkoxide, or acetate) of a ML_nX complex can deprotonate the azolium salt, or alternatively, an organic base (such as triethylamine) can be used with ML_nL' or $(ML_n)_2$ fragments. This synthetic strategy was recognized as early as 1968 by Öfele, and because of the broad variety of CH-acidic heteroaromatic compounds, it is much more general than the previous method starting from isolated carbenes.

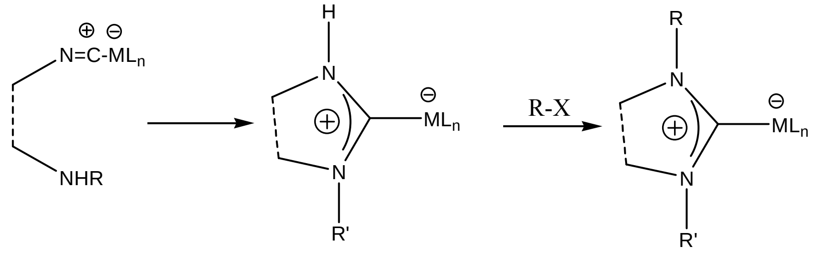


(4.6)

c) Imidazolidin-2-ylidene complexes are accessible by reaction of the corresponding electron-rich olefin dimers with mononuclear or bridged dinuclear organometallic fragments (eq. 4.7).



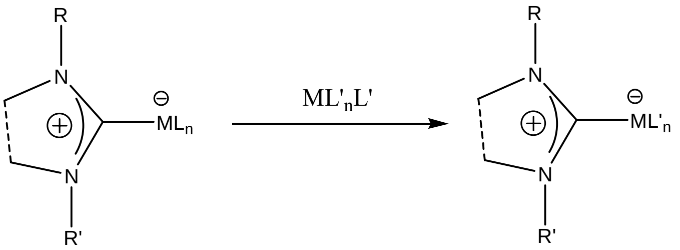
d) Complexes of acyclic as well as cyclic diheteroatomsubstituted carbenes can be generated by transforming other C-bound ligands (eq. 4.8).



(4.7)

(4.8)

e) Carbene transfer reactions between transition metals have been recently reported (eq. 4.9). So far, this promising strategy has allowed the preparation of groups 9 and 10 metal-imidazolidin-2-ylidene complexes from the corresponding group 6 metal complexes. Complex preparation by transfer of imidazolin-2-ylidene ligands from silver(I) (eq. 4.10). In this thesis, this route is followed to synthesize Pd(NHC) complexes.



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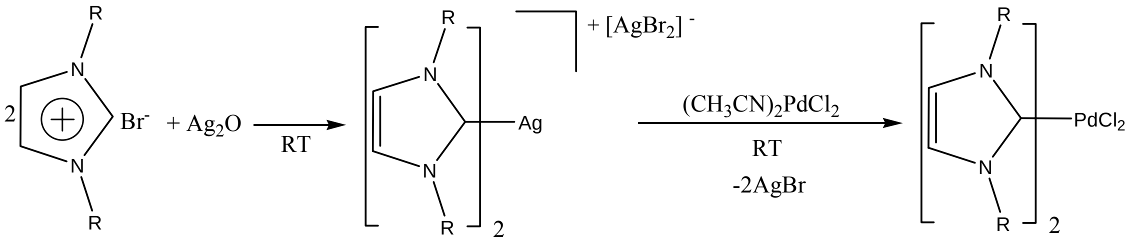
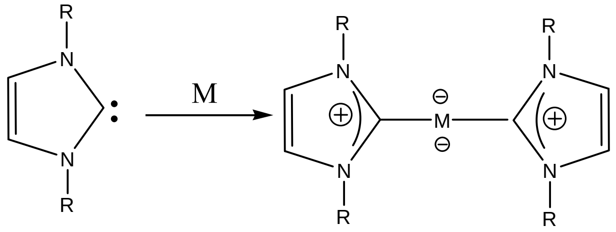


(4.10)

f) Two-coordinate homoleptic metal carbene complexes have been obtained by co-condensation of group 10 metal vapor with imidazol-2-ylidenes **8** (eq. 4.11).



8

(4.11)

4.3.2. Electronic Properties of NHC Complexes

Carbene complexes have been divided into two types according to the nature of the formal metal-carbon double bond (Figure 4.6). The metal-carbon bond of Fischer type carbene complexes is a donor-acceptor bond and formally results from the superposition of carbene to metal σ-donation and metal to carbene π-backdonation (Figure 4.6a). In contrast, the metal-carbene bond of Schrock-type complexes is essentially covalent and formally results from the interaction of a triplet carbene with a triplet metal fragment (Figure 4.6b).

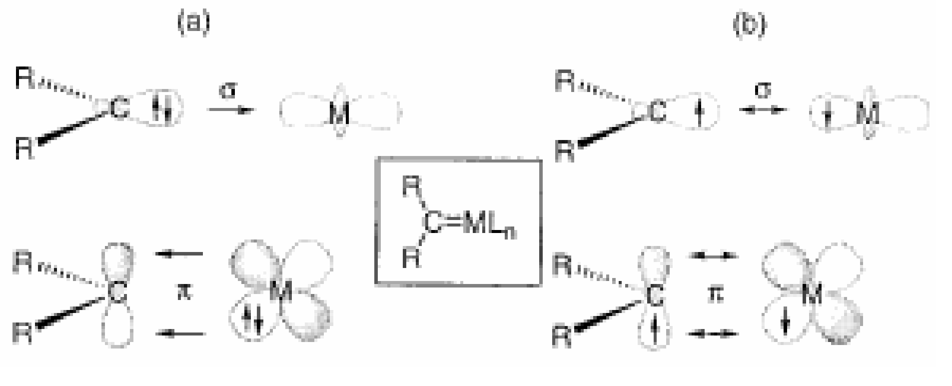
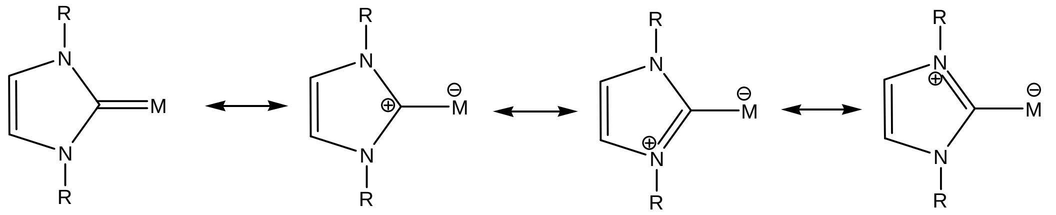


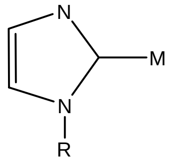
Figure 4.6. Schematic representations of (a) donor-acceptor bonding in Fischer carbene complexes and (b) covalent bonding in Schrock carbene complexes Bourissou et al. 2000.

Due to the presence of two σ-donor substituents at the carbene center, the N-heterocyclic carbene complexes may be classified, at a first glance, as Fischer-type compounds. However, in contrast to usual Fischer-type complexes, N-heterocyclic carbenes and especially imidazol-2-ylidenes **8** and imidazolidin-2-ylidenes **6** bind to transition metals only through σ-donation, π-backbonding being negligible (Bourissou et al. 2000).

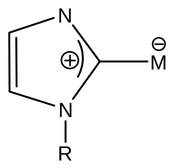
Electron-rich carbenes complexed to metals are good σ-donors and very poor π-acceptors because the proximal nitrogen atoms preferentially donate electron density into the empty orbital on the carbon atom. Thus, of the valence bond representations **21** to **26** (shown for the particular case of imidazolylidene complexes) contributing forms **23** and **24** are probably the most important, and **21** is the least. Most researchers represent complexes of electron-rich carbenes using diagrams like **25**. This is less accurate than representations like **26**, for instance, but diagrams in the style of **25** are preferred, presumably because they avoid complications regarding the actual charge of the complex (Perry and Burgess 2003).



21 **22** **23** **24**



25
conventional representation



26
more accurate representation

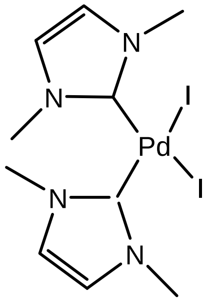
The ratio of σ-donation to π-backdonation for $Fe(CO)_4$-bonded heteroatom-substituted carbenes increases in the order; $:C(OR)R < :C(NR_2)R < :C(NR_2)_2 \approx$ imidazolidin-2-ylidenes ≈ imidazol-2-ylidenes (Bourissou et al. 2000).

4.3.3. Applications of NHC's

The application of *N*-heterocyclic carbenes as ligands for transition metals has led to significant advances in several important catalytic reactions, most notably the metathesis of olefins (Scholl et al. 1999a, Scholl et al. 1999b, Sanford et al. 2001, Trnka et al. 2003, Day and Grubbs 2003, Love et al. 2003, Seider et al. 2001) and Pd-catalyzed coupling reactions (Weskamp et al. 1998, Herrmann 2002, Weskamp et al. 1999, Ackerrmann et al. 1999, Herrmann et al. 1995, Herrmann et al. 2003, Herrmann et al. 1998, Gstöttmayr et al. 2002, Altenhoff et al. 2003, Zhang et al. 1999, Fürstner and Leitner 2001, Eckhardt and Fu 2003, Frisch et al. 2003, Stauffer et al. 2000, Viciu et al. 2000, Cheng and Trudell 2001, Huang et al. 1999, Gradel et al. 2001).

Carbene complexes are also superior to their phosphine analogs in many Pd-catalyzed coupling reactions, and special attention has been given to the Mizoroki–Heck and Suzuki–Miyaura reactions (Weskamp et al. 1998, Herrmann 2002, Weskamp et al. 1999, Ackerrmann et al. 1999, Herrmann et al. 1995, Herrmann et al. 2003, Herrmann et al. 1998, Gstöttmayr et al. 2002, Altenhoff et al. 2003, Zhang et al. 1999, Fürstner and Leitner 2001, Eckhardt and Fu 2003, Frisch et al. 2003, Stauffer et al. 2000, Viciu et al. 2000, Cheng and Trudell 2001, Huang et al. 1999, Gradel et al. 2001). The ability of NHC's to stabilize low valent Pd species is likely responsible for the enhanced activity observed in these cases.

The first report of the use of an NHC-ligated complex in a coupling reaction was the application of complexes **27** and **28** in the Mizoroki–Heck reaction by Herrmann in 1995 (Herrmann et al. 1995). It is believed that the carbene ligands enhance oxidative addition of the aryl halide because their strong sigma-donating abilities make the metal more electron rich. NHC ligands should also promote reductive elimination in the more highly substituted complexes formed at the end of the catalytic cycles because of their greater steric hindrance.



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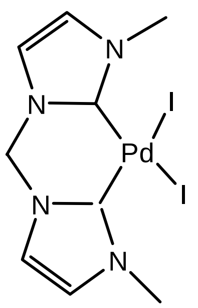

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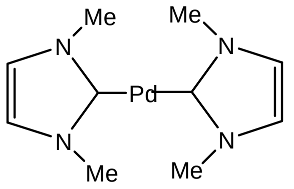
N-Heterocyclic carbenes have been employed in a wide variety of reactions including polymerization, hydrogenation, hydrosilylation hydroboration], hydroformylation, allylic substitution, and methenylation. Recent reports have begun to document the preparation of *N*-heterocyclic carbene complexes anchored to solid or reusable supports by virtue of the NHC ligand.

Despite the fact that NHC's generally confer greater thermal and oxidative stability on their metal complexes than the corresponding phosphines, presumably because of decreased ligand lability, it is still important to be aware of the potential decomposition pathways available to NHC ligands. This is especially crucial in cases where the kinetic stability of the metal–ligand bond is important, for example chiral NHC's for asymmetric catalysis, or supported versions of NHC complexes (Crudden and Allen 2004).



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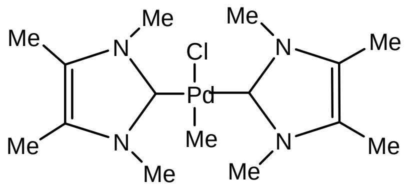

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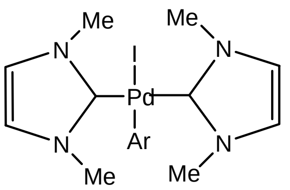

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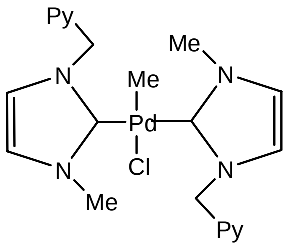
Ar : p-$NO_2C_6H_4$



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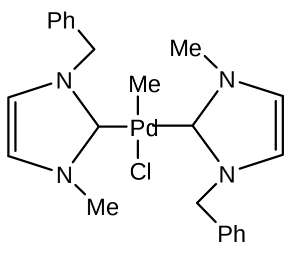

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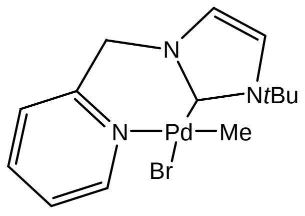

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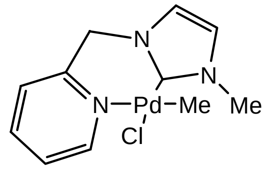

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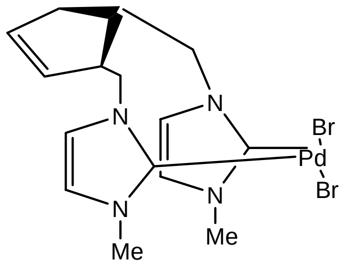

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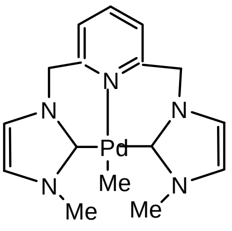

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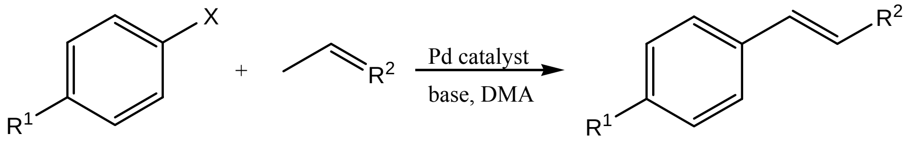
Complex **34** was shown to be a highly active catalyst for the Mizoroki–Heck reaction between iodobenzene and methyl acrylate, giving almost 3 million turnovers and a turnover rate of >75,000h^{-1} under optimized conditions (140ºC, dimethylacetamide (DMA) as solvent, see Table 4.1) (Tulloch 2000).

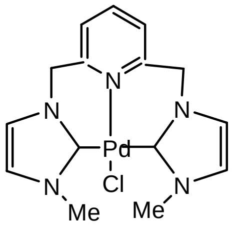
Table 4.1. Reactivity of Pd–NHC complexes in the Mizoroki–Heck reaction.



Reaction A: R^1 : $COCH_3$ X : Br R^2 : CO_2Bu
Reaction B: R^1 : H X : I R^2 : Ph

Entry	**Catalyst**	**Reaction**	**Conditions / Additives**	**TON[a] (TOF)[b]**
1	27	A	100ºC	>200
2	28	A	100ºC	>200
3	29	A	125ºC	250,000 (15,000[c])
4	30	A	120ºC	18,000 (1,000)
5	31	A	120ºC	50,000
6	32	A	120ºC/Pr_4NBr	1,700,000 (14,166)
7	33	A	120ºC/Pr_4NBr and $NH_2NH_2.H_2O$	980,000 (10,000)
8	34	B[d]	140C	2,858,000 (75,000)
9	35	A	120ºC	610,000 (5,080)
10	36	A	120ºC/Pr_4NBr and $NH_2NH_2.H_2O$	970,000 (10,430)
11	37	A	120ºC/Pr_4NBr	34,330 (1,720)
12	38	A	120ºC/$NH_2NH_2.H_2O$	40,160 (1,980)
13	39	A	160ºC in air	330,000 (16,500) (85,000)[e]
14	40	A	120ºC/Pr_4NBr	660,000 (10,000)
15	41	A	120ºC/$NH_2NH_2.H_2O$	44,000 (1,000)

[a] TON: turnover number (moles product/moles catalyst). [b] TOF: turnover frequency (TON/hr). [c] Generated in situ from $Pd(dba)_2$ and free carbene. [d] 4-Bromoanisole was used in the calculation of turnover frequency while 4-bromoacetophenone was cited for the turnover number. [e] Methyl acrylate was employed as the olefin. [f] Under argon.



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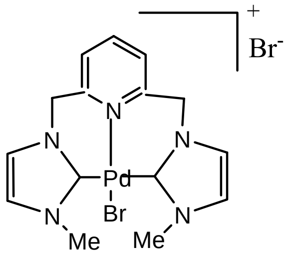

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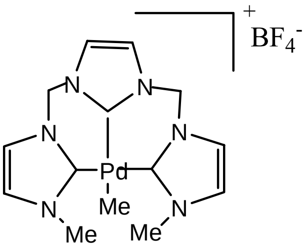

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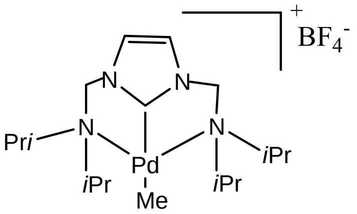

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CHAPTER 5

THE MIZOROKI-HECK REACTION

The palladium-catalyzed arylation of an alkene with an organic halide was first reported by Mizoroki and Heck in the early 1970s (Mizoroki et al. 1971, Heck and Nolley 1972).

The classical Heck reaction involves bond formation between two sp^2 carbon centers by an overall substitution of a C-H bond of an alkene by R^1 from the R^1X substrate (where R^1=aryl or vinyl; X=I, Br; R^2 = electron withdrawing or releasing group) under basic conditions. The transformation has since become known as the Heck reaction (Figure 5.1.).

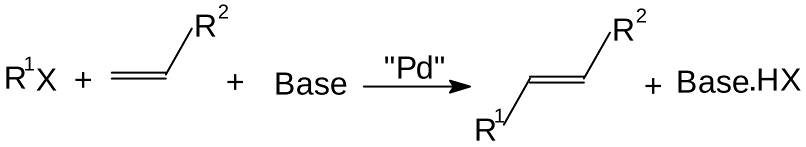


Figure 5.1. The Mizoroki-Heck Reaction

Since its discovery, the methodology has been found to be highly versatile and applicable to a wide range of aryl species Ar-X, where X = Cl, Br, I, OTf, OTs and N_2^+ (Whitcombe 2001).

Advantage of this reaction is not limited to activated alkenes. The substrate can be a simple olefin (with ethylene being the most reactive one), or it can contain a variety of functional groups, such as ester, ether, carboxyl, phenolic, or cyano groups (Shibasaki and Vogl 1999).

Despite the many benefits associated with these reactions including to tolerance of water and other functional groups in the substrate, interest in the reaction has been sporadic, largely due to the problems of regiocontrol in the case of unsymmetrical alkene substrates leading to low product yields and large volumes of waste, and an incomplete understanding of the reaction mechanism (Clark et al. 2000).

The reaction constitutes a powerful and versatile method for the synthesis of polyfunctional compounds, e.g., dienes, cinnamic esters, and other variously substituted olefinic compounds, which are primarily applied as dyes, UV absorbers, and intermediates for pharmaceuticals, agrochemicals, and fragrances (Dams et al. 2002).

The reaction is also useful in polymerization chemistry, giving access to conjugated polymers applicable, e.g., as new materials for optoelectronic devices (Beletskaya 2000).

The reaction can be catalyzed by palladium complexes with or without phosphine ligands (phosphine-assisted vs. phosphine-free catalysis). These reactions are generally catalyzed by soluble Pd complexes with phosphine ligands. However, homogeneous catalysts are generally connected with the problem of separation and wasted inorganics. In addition, the phosphine ligands and Pd precursors are usually difficult to handle because of their air-sensitive nature and are too difficult to reuse after the reaction. The stability of the Pd catalyst is also important for large-scale industrial application of the coupling reactions. It is generally assumed that the deactivation of the Pd complex occurs via aggregation of palladium intermediates to clusters and further to inactive large metallic particles (Pd black). To overcome these problems, it is highly desirable to develop phosphine-free heterogeneous catalysts having a high stability and recyclability (Shimizu et al. 2004).

The most common ones are; polymer-supported Pd complexes were used for the activation of aryl iodides by several groups. For the conversion of aryl chlorides and bromides, Pd on carbon, on metal oxides and zeolites were found to be suitable catalysts. Stabilized Pd colloids can catalyze the Heck reaction of aryl iodides (and partially bromides) (Köhler et al. 2001).

5.1. The Catalytic Cycle

The general mechanism for the Heck reaction has been widely accepted for many years; however, numerous recent and ongoing studies are revealing subtle mechanistic details of this transformation. Recent reviews on this topic provide a thorough discussion of mechanistic investigations of the Heck cyclization (Dounay and Overman 2003).

The mechanism outlined in Figure 5.2., provides a general description of the steps required for catalytic olefination: *The Heck Reaction* involves preactivation step **A** which includes the reduction of Pd(II) complexes to catalytically active Pd(0) species.

Thereafter, oxidation addition **B** of a Pd(0) catalyst to afford σ-aryl palladium(II) complexes. Coordination of an alkene and subsequent C-C bond formation by syn addition provide σ-alkyl palladium(II) intermediates which readily undergoes β-hydride elimination **E** to release the alkene Heck product. In order for the cycle to continue, a base is required for conversion of hydridopalladium(II) complex [HPdXL$_2$] to the active Pd(0) catalyst. Below, each of the steps is described more thoroughly to present the key issues that control the reactivity and selectivity of the palladium species, in the overall process.

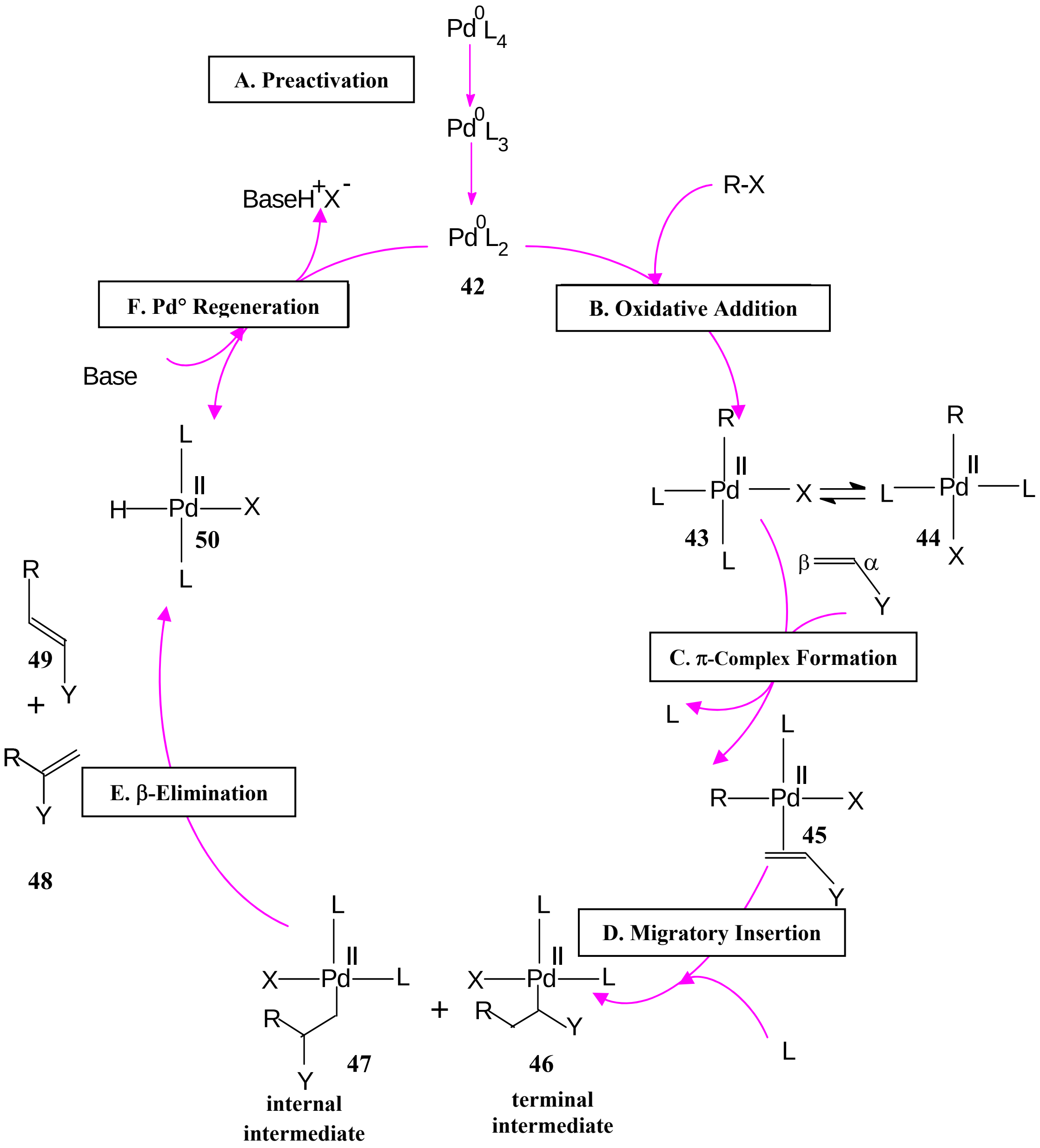


Figure 5.2. The Mechanism of the Classical Heck Cycle

5.1.1. Preactivation (A):

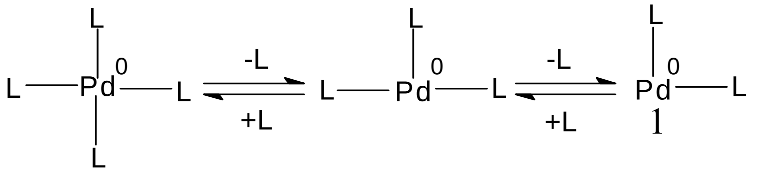
Palladium salts [e.g. $Pd(OAc)_2$, $PdCl_2$] alone can be used, although the addition of certain ligands (L) is often found to improve the efficiency of the reaction. The palladium catalytic precursor has been postulated as a coordinatively unsaturated 14-electron species (PdL_2) (Whitcombe 2001).

The entry into the catalytic cycle includes the reduction of Pd(II) complexes to Pd(0) and the generation of active species through multiple ligand exchange equilibria. The preactivation has been extensively studied by Amartore and Jutand et al. for phosphine-assisted systems (Beletskaya 2000).

The primary reduction of Pd(II) to Pd(0) is most likely accomplished by phosphine in the phosphine-assisted catalytic cycle. The reduction is assisted by hard nucleophile, of which the most common are hydroxides and alkoxide ions, water, and water and acetate ion, though in special cases even fluoride in the presence of water can play the role (Beletskaya 2000).

In phosphine–free systems, the primary reduction of Pd(II) can be effected by amines, if these are used as base or olefin. It is interesting to note that neither Et_3N nor olefin have any detectable influence on the reduction rate in the presence of phosphine. In the absence of phosphine, olefins are oxidized by Pd(II) via the first run turn of a Wacker-type catalytic cycle. This process may be a yield-decreasing factor in the reactions with high initial loads of palladium salts in phosphine-free systems if the olefin is taken in an equimolar amount with respect to the electrophilic substrate.

Indirect evidence tells that Pd(II) → Pd(0) reduction can also be affected by quaternary ammonium and phosphonium salts, possibly initiated by oxidative addition to C-P or C-N bonds. Thus, Herrmann reported that the addition of TBABr eliminated the induction period in the reaction catalyzed by Pd carbene complex. To enter the catalytic cycle through the oxidative addition, palladium(0) species must have a proper coordination shell. No more than two strongly bound ligands are allowed. This requirement places a serious restriction on the choice of ligands and their concentration in the reaction mixture.



$$L_4Pd^0 \xrightleftharpoons[+L]{-L} L_3Pd^0 \xrightleftharpoons[+L]{-L} L_2Pd^0 \quad (5.1)$$

The active palladium(0) 14-electron complex is assumed to be in equilibrium with the 18-electron palladium(0) species coordinating four ligands (Eq. 5.1.)

5.1.2. Oxidative Addition (B):

The oxidative addition of Ar-X to palladium(0) species has been the most well studied step of the Heck reaction as it is a common initiation stage for many palladium-catalyzed reactions involving aryl halide substrates (Whitcombe 2001).

The oxidative addition proceeds as a concerted process in which C-X bond rupture is more or less perfectly synchronized with the formation of M-C and M-X bonds. Unlike stepwise addition-elimination mechanisms of nucleophilic aromatic or vinylic substitution in which the addition to the unsaturated system is the primary and often rate-limiting stage while the rupture of C-X bond is fast, the oxidative addition is much less sensitive to the substituents in the unsaturated system but much more sensitive to the nature of nucleophile and the strength of C-X and M-X bonds (Beletskaya 2000).

The order of bond strengths for aryl halides is: Ar-Cl>Ar-Br>Ar-I. This trend is also reflected in the ability of aryl halides to undergo oxidative addition with palladium (0) complexes: Ar-Cl<<Ar-Br<ArOTf<<Ar-I. Electron-donating substituents on the aryl group also make the oxidative addition more difficult and, as a result, electron-poor aryl halides are often referred to as ‘activated’, and electron rich aryl groups as ‘deactivated’.

There are a number of advantages in developing procedures to efficiently utilize aryl bromides and the synthetically more challenging aryl chlorides:

a) aryl iodides are often more expensive than either aryl bromides or chlorides and are less desirable in terms of atom economy;
b) aryl chlorides are more widely available,
c) aryl chlorides are more robust and can tolerate a wider range of reaction protocols.

One of the biggest challenges for Heck chemistry is the development of an efficient system that can achieve high turnovers for deactivated aryl halides such as 4-chloroanisole (Whitcombe 2001).

In phosphine-assisted catalysis, C-P bonds of phosphine ligand can compete for Pd(0) with less reactive substrates, leading both to the scrambling of substituents in product and to the depletion and deactivation of catalyst (Beletskaya 2000).

Triarylphosphine ligands have traditionally been used in the Heck reaction to promote the lifetime of the catalyst, temperatures above 120ºC, however, often lead to competitive degradation of the palladium catalyst and the formation of unwanted by-products through thermally-activated P-C bond cleavage of a coordinated phosphine ligand (Whitcombe 2001).

In most cases except for the complexes with chelating ligands, the isolable product of the oxidative addition possesses *trans*-geometry, though it is obvious that *cis*-complex must be formed first. Moreover, it is *cis*-complex which enters the next stage of the catalytic cycle.

Recent studies explicitly revealed both the formation of *cis*-adduct and *cis*-*trans* isomerization. The latter process can proceed by several independent routes, both through dissociation-isomerization-addition and through association-pseudorotation-dissociation.

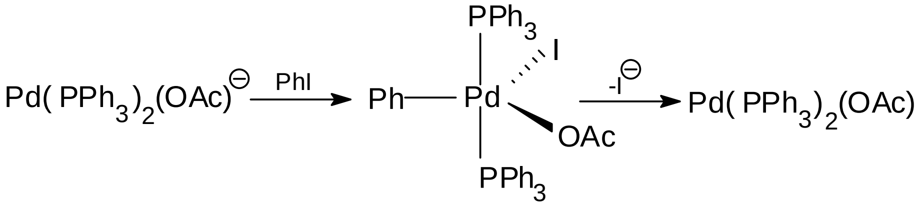


Figure 5.3. Oxidative Addition via Pentacoordinated Palladium Species

The availability of the latter route involving five-coordinate complexes (Figure 5.3.) is of prime importance for complexes with strongly bonded undissociating ligands, which otherwise would be unable to participate in the Heck reaction (Beletskaya 2000).

P-C bond cleavage was also seen as a contributing factor to the decomposition of the catalytic species by creating unstable subcoordinated palladium complexes that eventually precipitated out of solution as palladium Black (Beletskaya 2000).

5.1.3. Migratory Insertion (C & D):

Migratory insertion is the product-forming step of the Heck cycle, in which a new C-C bond is formed. It is this step which is most likely responsible for regio- and stereodiscrimination as well as substrate selectivity (Beletskaya 2000).

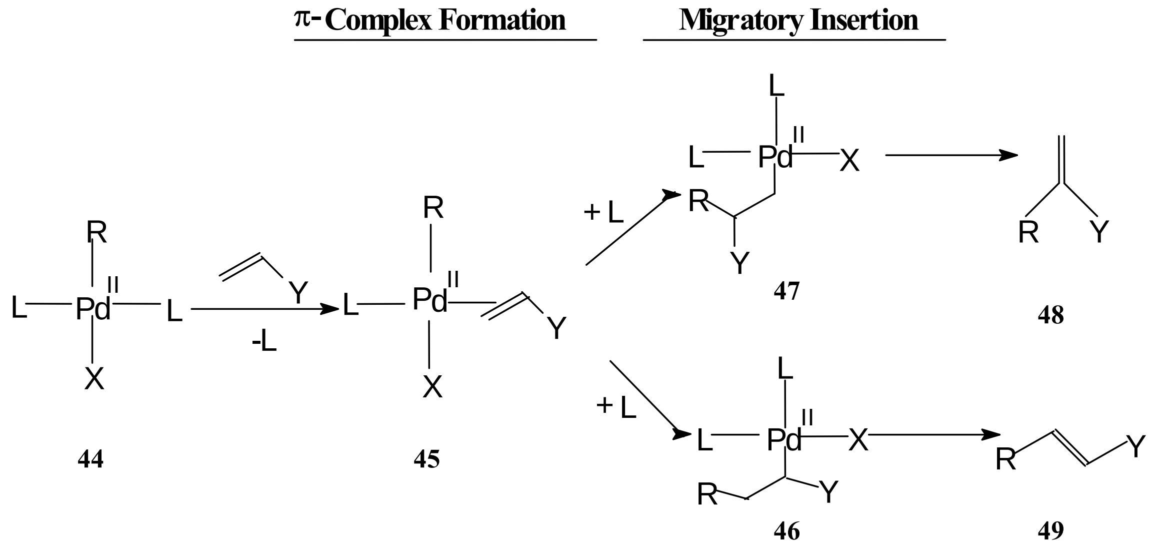


Figure 5.4. Internal and Terminal Insertion in the Heck Reaction.

It is assumed that one ligand (neutral or anionic) coordinating to the palladium dissociates to generate a free coordination site on the unsaturated Pd(II) species. Thus, a syn migratory insertion follows π-coordination of an alkene to palladium to form a new carbon-carbon bond in a presumably concerted fashion (Figure 5.4.).

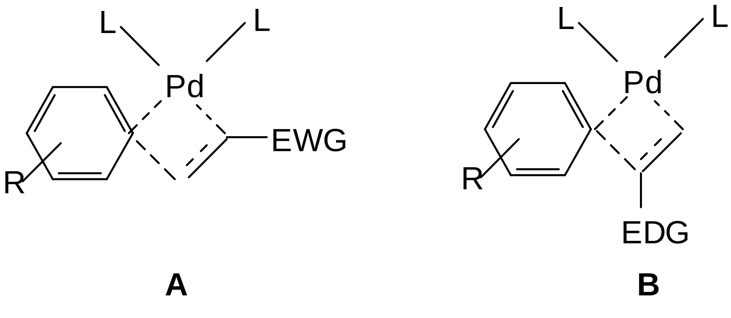


Figure 5.5. Electronic effect directing the olefin in the migratory insertion. **A**) Electron withdrawing group favoring the terminal insertion **B**) Electron donating group promoting the internal insertion.

The outcome of the two modes of insertion according to the claimed view with neutral intermediates, i.e. the internal **47** (formed by σ-attack) or terminal **46** (formed by β-attack) σ-intermediates, is governed by a delicate balance between electronic (Figure 5.5.) and steric parameters which in turn are affected by the Pd(II) complex, the olefin and the properties of solvent. (Cabri and Candiani 1995, Heck 1971).

5.1.4. β-Elimination (E):

β-hydride elimination is the transfer of a hydride from the β-position of the ligand to metal center. The mechanism involves a four-centered transition state in which the hydride transferred to the metal (Figure 5.6.)

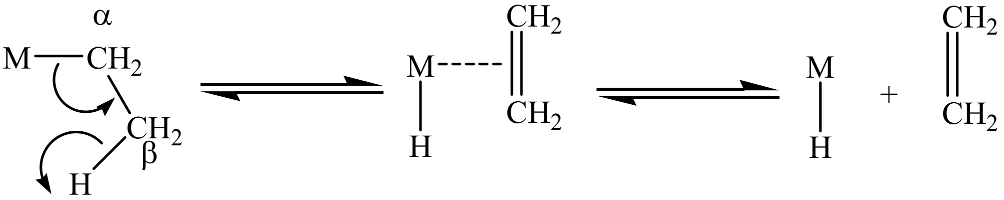


Figure 5.6. Mechanism of β-hydride elimination

The β-hydride elimination is the step yielding the final product of the Heck-reaction. An additional concern arises from potential reversibility of the *β*-hydride elimination step, which introduces the possibility that the hydridopalladium(II) species produced initially upon *β*-hydride elimination could re-add across the initially generated double bond. Depending upon the regio- and stereochemistry of this hydropalladation step, subsequent *β*-hydride elimination could regenerate either the initial Heck product or a regioisomer. The use of low reaction temperatures or additives such as silver salts has been shown to minimize this type of alkene isomerization in several cases (Dounay and Overman 2003).

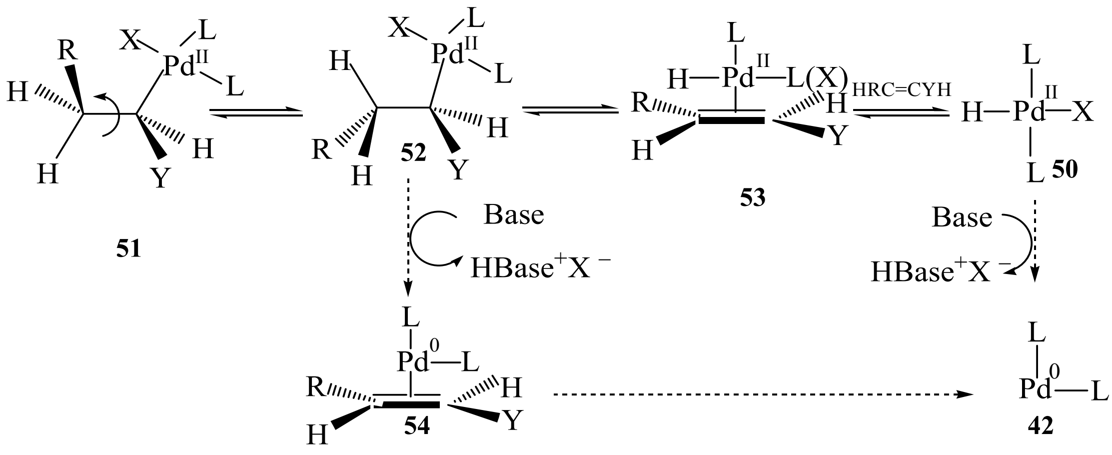


Figure 5.7. The base promoted vs. the classical elimination mechanism

For this process to occur, through stereoselective elimination, the alkyl palladium species **51** has to undergo an internal rotation to align the β-hydride syn to the palladium centre **52** (Figure 5.7.). The elimination will then result in a reconstituted alkene **48** and **49** and a Palladium hydride species **50**. Furthermore, if the dissociation of the olefin to the Pd (II)-hydride complex **53** is slow, re-addition to the double bond might occur, resulting in the formation of a double-bond isomer (Spencer 1982, Larock et al. 1989).

5.1.5. Pd(0) Regeneration (F):

Pd(0) regeneration process can also be called as the reductive elimination process since Pd(II) species is reduced to Pd(0). Reductive elimination is a unimolecular decomposition pathway and the reverse of oxidative addition.

By reductive elimination, both the coordination number and the formal oxidation state of the metal M(n+2) are reduced by two units to generate M(n) (Tsuji 1995).

In the Pd(0) regeneration process, the presence of base will scavenge the readdition by removing HX from the palladium(II)-complex **50**, producing the reduced $Pd(0)L_2$-species **42**. Typical bases are trialkylamines (Et_3N, Pr_2NEt, etc.) or inorganic salts (AcONa, HCO_3, etc.); however, good results were sometimes obtained with either Proton Sponge or TUI) or Ag(I) salts (Dounay and Overman 2003).

The re-formed active Pd(0) catalyst can then activate another R-X and initiate the next catalytic cycle (Deeth et al. 1998).

5.2. Experimental Conditions

The development of efficient, enantioselective Heck reaction conditions for a particular substrate generally requires optimization of a variety of reaction parameters (Dounay and Overman 2003).

The reaction intermediates and their associated reactivities are intimately associated with the chosen catalyst, substrates, additives and reaction conditions (Whitcombe 2001).

Much work has focused on improving the efficiency and scope of the reaction by tailoring the Pd catalyst and by varying reaction conditions (solvent, temperature, base, additives).

The first use of Pd-phosphine complexes for vinylic hydrogen substitution reactions was by Dieck and Heck in 1974. Although the catalysts are frequently generated in situ [e.g., from $Pd(OAc)_2$ and a monodentate tertiary phosphine] (Biffis et al. 2001).

5.2.1. Effect of Pd Catalysts

A variety of Pd(II) and Pd(0) complexes serve as effective precatalysts to the active Pd(0) catalyst (Dounay and Overman 2003).

The Heck reaction is generally catalyzed in solution by palladium species generated from either Pd(0) compounds, such as $[Pd(PPh_3)_4]$ and $[Pd_2(dba)_3]$, or Pd(II) salts, such as the acetate and the chloride (Biffis et al. 2001).

Recent studies by Amatore and Jutand have demonstrated that 2.0 equiv of diphosphine ligand is required per equivalent of Pd when $Pd(OAc)_2$ is used as a precatalyst, because 1 equiv of ligand is consumed in the reduction of the Pd(II) precatalyst to the Pd(0) catalyst species. Although most mechanisms written for the Heck reaction indicate the active Pd(0) diphosphine catalyst in a generic representation and omit altogether the ligands derived from the palladium precatalyst, these “spectator” ligands can play a significant role in the Heck reaction. Dibenzylideneacetone (dba) can also play a role. For example, Amatore and Jutand have shown that mixtures of $Pd(dba)_2$ and BINAP afford Pd(dba)(BINAP), which is sluggish in oxidative addition reactions with PhI. Likewise, Pregosin and co-workers have shown that Pd(dba)(MeO-BIPHEP) undergoes oxidative addition to aryl triflates and halides more sluggishly than the Pd(0) catalyst generated by reduction of $PdCl_2$(MeOBIPHEP) with $NaBH_4$. A variety of chiral phosphine ligands have been used to effect asymmetric Heck reactions (Figure 5.8). BINAP **57** has been employed most widely to date. Oxidative addition is favored by basic ligands and by bidentate ligands having a small bite angle (Dounay and Overman 2003).

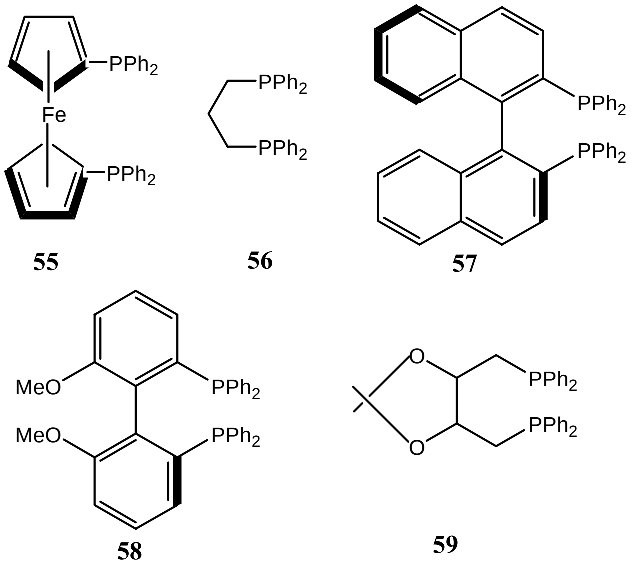


Figure 5.8. Common bidentate ligands: dppf **55**, dppp **56**, (S)-BINAP **57**, BIHEP **58** and DIOP **59**.

Amatore et al. found the opposite in a comparative study of DIOP **59**, dppf **55**, and BINAP **57**; BINAP having the smallest bite angle gave the slowest oxidative addition. This study, however, was complicated by the presence of dba from $Pd(dba)_2$ precursor. Amatore has shown that for monodentate phosphines the presence of labile ligands such as dba, halide ligands, and acetate can change the kinetics of the reaction by coordination to the low valent palladium intermediates.

Since reductive elimination is in fact the reverse reaction of oxidative addition, ligand effects will often be opposite for this reaction. By comparing the elimination rates using dppp, dppf, and dpp-ruthenocene, they showed that the reaction became faster with increasing bite angle. Hayashi et al. found in a systematic study that dppf, a diphosphine with a large P-Pd-P bite angle of 96° in (dppf)$PdCl_2$, induced the highest activity and selectivity of a range of diphosphine ligands (dppe, dppp, dppb, and dppf). Furthermore, comparison of different diphosphines revealed an increase of selectivity with an increasing bite angle (Piet et al. 2000).

Table 5.1. Bite angles of some of the ligands

LIGAND	BITE ANGLE
Dppp	91.0°
BINAP	92.7°
Dppf	96°
Dppb	98°
Dppe	85°

Palladium(II) complexes of the $PdCl_2P_2$ type are convenient catalysts precursors of Heck and carbonylation reactions. Depending on the steric properties of the coordinated phosphorus ligand (P), the complexes have *cis* (e.g. for P = $P(OPh)_3$, $P(OMe)_3$) or *trans* (e.g. for P = PPh_3, PCy_3) structures.

Palladium acetate ($Pd(OAc)_2$) and dichloride ($PdCl_2$) with the addition of TPPTS (TPPTS = $P(m\text{-}C_6H_4SO_3Na)_3$), are very active catalysts in the Heck reaction of iodobenzene with butyl acrylate in a two-phase system (toluene–ethylene glycol) (Trzeciak and Ziolkowski 2005).

A cyclometallated complex formed in the reaction of $Pd(OAc)_2$ with sterically demanding tri-*ortho*-tolyl phosphine (Figure 5.9.) has been developed by Herrmann and applied very successfully to Heck reactions of activated and non-activated olefins (Böhm and Herrmann 2000).

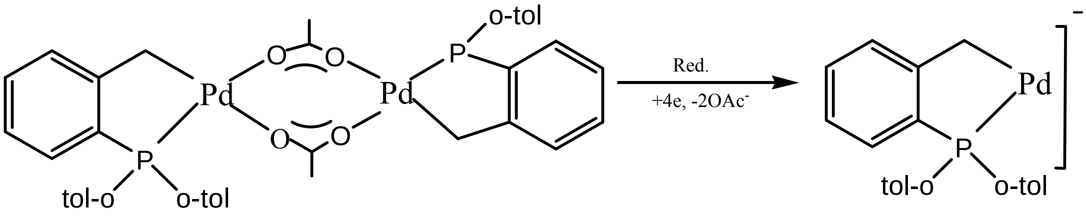


Figure 5.9. The pattern of palladacycle reduction to Pd(0) ionic complex

A benzothiazole carbene complex of Pd(II) (Figure 5.10. (a)) has been found to be an efficient Heck reaction catalyst in the synthesis of cinnamates.

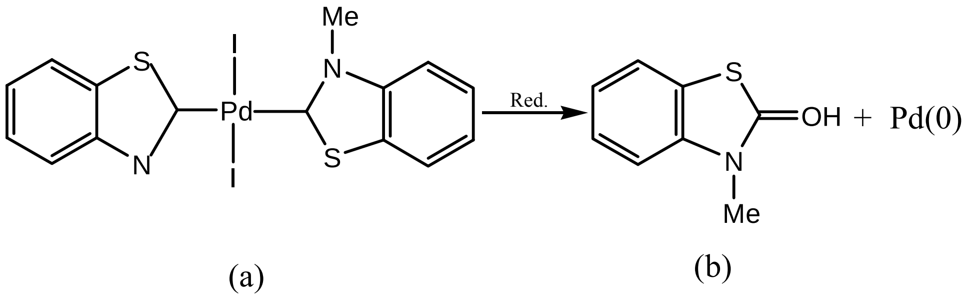
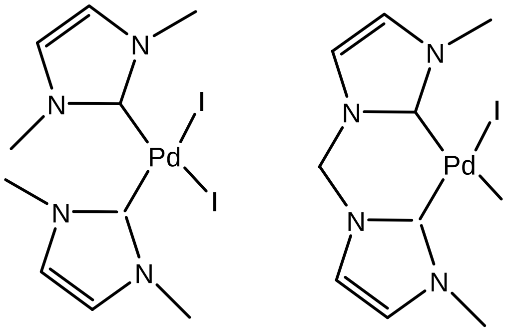


Figure 5.10. Palladium(II) carbene complex reduction to Pd(0) colloid.

The family of phosphine-free catalysts also includes palladium complexes with *N*-heterocyclic carbenes, such as imidazol-2-ylidenes, which are regarded as ligands alternative to phosphanes (Böhm and Herrmann 2000).

Because of their convenient preparation from palladium(II) acetate and the corresponding imidazolium salts, palladium(II) complexes were first examined as potential catalysts for the Mizoroki-Heck reaction by Herrmann et al. In this work, the first Heck coupling of aryl bromides and aryl chlorides was communicated: Complexes 27 and 28 (Figure 5.11) are active upon smooth reduction with formiate or hydrazine, thus generating the active Pd(0) species (Herrmann et al. 2003).



27 **28**

Figure 5.11. Pd complexes with monodentate and bidentate NHC ligands.

These catalysts are exceptionally stable toward heat, oxygen, and moisture; moreover, carbene dissociation has never been detected. All these properties make these palladium-carbene complexes suitable for the Heck reaction, particularly for the activation of chloro arenes

High efficiencies in Heck reactions of aryl bromides were reported by the Nolan group who used palladium in the presence of C,P-chelating NHC ligands derived from the sterically demanding imidazolium salt (Figure 5.12). A catalyst loading of 0.5 mol% based on palladium was sufficient to obtain good yields. Cesium carbonate turned out to be the most efficient base, much better than $KOtC_4H_9$, NaOAc and K_2CO_3 (Herrmann et al. 2003).

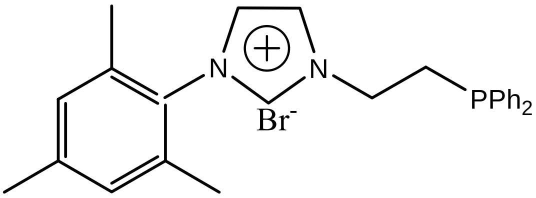


Figure 5.12. Precursor of a C-P-chelating NHC ligand.

Pd complexes with pyridine or carbonyl donors containing carbene ligands show high activity and stability in the Heck, Suzuki and Sonogashira coupling reactions (McGuiness and Cavell 2000).

Highly efficient, recyclable Pd(II) catalysts obtained in the reaction of Pd(cod)Cl(Me) with bis-imidazole ligands were used in the Heck reaction (Park and Alper 2003). Bis-carbene pincer complexes of Pd(II) immobilized on K-10 montmorillonite catalyzed Heck coupling of phenyl halides with (Poyatos et al. 2003, Herrmann et al. 2003).

Identification of Pd(0) colloids in catalytically active systems obtained from different palladium precursors makes it possible to propose a new interpretation of phosphine-free systems in which the appearance of nanoparticles is consistent with the demonstrated catalytic activity. However, it is not definitely certain if soluble palladium colloids are true catalysts or just only the source of Pd(0) species which play an important role in catalysis.

In a Heck reaction catalyzed with Pd(0) nanoparticles formed from $Pd(OAc)_2$ the best yield of products is obtained at rather low concentrations of palladium, counter acting agglomeration.

The first experiments with a specially prepared Pd(0) colloid as the catalyst in the Heck reaction of unactivated aryl bromides gave a low yield of products. It has been proven experimentally that $Pd(OAc)_2$, $PdCl_2$, or $Pd(NO_3)_2$, catalyst precursors in the Heck coupling reactions, form Pd(0) nanoparticles during warming in THF in the presence of an excess of tetraalkylammonium carboxylates, $[R_4N]^+[RCO_2]^-$, which act as a reducing and stabilizing agents (Herrmann et al. 2003).

5.2.2. Additives

Additives play a critical role in many asymmetric Heck reactions. Silver(I) additives have been used to increase the reaction rates in Heck reactions of unsaturated halides, prevent deactivation of the palladium catalyst, minimize alkene isomerization of the Heck products, and dramatically enhance enantioselectivity.

Although a variety of silver salts have been used as additives in Heck reactions of Halide precursors, the most common and effective reagents are Ag_2CO_3, Ag_3PO_4, and silver-exchanged zeolite. Thallium salts (Tl_2CO_3, TlOAc, and $TlNO_3$) have also been used as halide scavengers in Heck reactions, but the high toxicity associated with these reagents makes them a less attractive alternative to silver salts.

Shibasaki and co-workers have reported that the addition of tertiary alcohols such as pinacol or *tert*butyl alcohol accelerated the Heck cyclizations of vinyl triflates in 1,2-dichloroethane (DCE); potassium acetate produced similar rate enhancements (Dounay and Overman 2003).

5.2.3. Solvents and Temperature

Solvent polarity has been shown to affect the Heck reaction. The most useful are polar aprotic solvents having an ability to additionally support palladium complexes by weak coordination, such as CH_3CN, THF, *N*,*N*-dimethylacetamide (DMA), *N*,*N*-dimethylformamide (DMF), and 1-methyl-2-pyrrolidinone (NMP) are typically used, although benzene, toluene, and DCE are preferred in some cases (Beletskaya 2000, Dounay and Overman 2003).

Molten Salts. The use of molten salts as media (the so-called nonaqueous ionic liquids) allows for both easy recycling of catalytic system (e.g. due to temperature-dependent miscibility with nonpolar solvents and water) and possible activation of catalysts. Molten salts are highly polar, thus facilitating the cationic mechanism of Heck reactions, can contribute to the stabilization of underligated Pd(0) species by forming anionic complexes with halide ions. The following molten salts were used: tetranbutylammonium bromide (n-Bu_4NBr), Ph_3MePCl, Ph_3MePBr, n-Bu_3-n-$C_{16}H_{33}NBr$, and 1-methyl-3-propylimidazolium bromide. The simplest the salt of the series n-Bu_4NBr performed the best and thus was recommended as a basic choice for such media (Beletskaya 2000).

The application of molten salts was first reported by Kaufmann (Kaufmann et al. 1996) and has been significantly developed by Herrmann (Herrmann and Böhm, 1999, Böhm and Herrmann 2000).

Molten salts have a number of advantages over conventional molecular solvents, the first as being conventional solvents e.g. DMF and NMP, are not required. Secondly, the volatile components of the reaction are removed by distillation, and so, the entire catalyst-containing melt can therefore be recycled for further use. Finally, as the reagents and products are distilled off, any enviromental issues associated with metal leaching can be circumvented (Whitcombe 2001).

Further development of the ionic melt protocol involves the use of salts which are liquid even at room temperature and immiscible both with water and hydrocarbons: 1-butyl-3-methyl-imidazolium (bmim), 1-pentyl-3-methylimidazolium (pmim), and 1-hexyl-pyridinium (C_6py) cations and Cl^-, BF_4^-, or PF_6^- as counteranions.

The addition of PPh_3 retards the reaction system. Imıdazolium salts were inefficient in the absence of phosphine ligands at temperatures below 100ºC, possibly due to the formation of carbene complexes, which release catalytically active palladium only at higher temperatures. However, in the presence of PPh_3, the system based on (bmim)PF_6 salt and Et_3N as base gave quantitative yields at 100ºC (Beletskaya 2000).

Unfortunately, imidazolium salt melts were independently shown by several researchers to be ineffective for processing chloroarenes. Still, ionic melts of imidazolium salts can be positioned as one of the best recyclable systems for processing bromoarenes, even for unreactive ones as 4-bromoanisole. At 140ºC the conversion reaches 94% (TOF=2.6h^{-1}) in (bmim)-PF_6 in the presence of Et_3N. The yield may be slightly improved by the addition of such ligands as Ph_3P,o-tol_3P, dppf, and Ph_3As, though $(PhO)_3P$, dppe, and Ph_3Sb gave poor results (Beletskaya 2000).

5.2.4. Bases

A base is required in Heck reactions to neutralize the acid (HX) that is produced when the hydridopalladium(II) species is reduced to regenerate the active Pd(0) catalyst. A stoichiometric amount of base is needed, but in practice, 3-5 molar equivalents are often used. A variety of inorganic bases have been used in Heck reactions, K_2CO_3 and $CaCO_3$ were the most reported frequently. Tertiary amine bases such as Et_3N, i-Pr_2NEt, a Proton Sponge and 1,2,2,6,6-pentamethylpiperidine (PMP) are also commonly employed. Among these, the extremely hindered base PMP has become a favorite choice for asymmetric Heck cyclizations (Dounay and Overman 2003).

The reaction in the presence of inorganic bases such as NaOAc gave the mixture of internal and terminal olefins with a ratio equal to the ratio of the number of protons at the respective sites, which has been interpreted as a result of conventional base-independent syn-elimination. The reaction in the presence of amine base yielded almost exclusively the internal product. Indeed, the stronger base can switch the process to base-catalyzed elimination, giving a more stable internal olefin.

In conclusion, as if base-catalyzed elimination can indeed occur, a base would have a strong influence both on the reactivity and stereochemistry of Heck reaction (Beletskaya 2000).

5.2.5. Effect of Pressure and Microwave Heating

Additional improvement of Heck procedures can be sought in ultra fast heating and pressure effects. Very fast heating by means of microwaves leads to shortening of the reaction time, while the yields and selectivity do not greatly differ from the same reactions carried out using conventional heating.

No specific effects belonging to any particular type of reaction were noted. Most probably the influence of microwave heating is associated with direct and uniform input of energy to the reaction media. Heck reactions are very well-known to run better at higher temperatures, naturally if reagents, products, and catalyst can survive such a harsh treatment. In conventional heating the energy is transferred by heat transfer through the walls of the reaction vessel and further on through convection causing nonuniform distribution of heat. Local overheating at the walls leads to decomposition of catalyst. Uniform deployment of heat directly to the reacting molecules by means of absorption of microwave energy by a polar solvent effectively affords higher temperatures than those achievable through conventional heating.

Microwave-promoted Heck reactions showed that common substrates like *p*-iodoanisole and methyl acrylate, which under standard conditions need several hours for reasonable conversions, can be carried out in just a few minutes if DMF is used as a solvent and microwave irradiation is applied (Shibasaki and Vogl 1999, Larhed and Hallberg 1996).

High pressure can also have a beneficial effect on Heck reactions. The key steps of the Heck cycles, oxidative addition and migratory insertions have a negative activation volume and thus are likely to be accelerated by pressure. On the other hand, PdH elimination can be retarded by high pressure, which may lead to a change of the product distribution.

The increase of oxidative addition with pressure rate makes it possible to perform reactions with substrates, practically unreactive under normal pressure, e.g., to perform differential Heck reaction by substituting a better leaving group (nonaflate) at normal pressure and poorer leaving group (chlorine) at high pressure as well as to use bromoderivatives in place of iododerivatives (Beletskaya 2000).

5.3. Recycled Heck Reaction

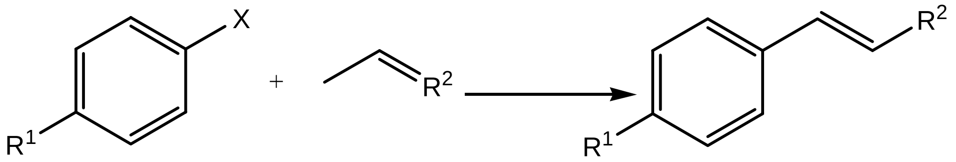
The problems associated with the need and handling of sensitive ligands, and the difficulty of catalyst separation, recovery and recycling of the expensive Pd have led to the development of immobilized homogeneous catalyst systems. Successful methods include supporting Pd complexes on polymers, the anchoring of Pd complexes to various solids such as modified silicas or layered double hydroxide, and ion-exchange of Pd^{2+} into suitable solid materials. Furthermore, there has been a search for suitable supported heterogeneous Pd catalysts. In fact, heterogeneous Pd catalyst systems were found to be highly effective. In addition, to stabilized colloidal palladium and palladium nanoparticles numerous reports have shown the utility of various supported palladium catalysts. Commercial Pd-on-active carbon was studied most along with Pd supported on mesoporous MCM-41, molecular sieves, oxides, layered double hydroxide, zeolites and $Pd(OH)_2/C$. The application of heterogeneous Ni, Cu and Co, and Ru catalysts was also reported. An interesting new approach is the use of bifunctional heterogeneous systems composed of both Pd and basic sites such as basic zeolites and alkali-exchanged sepolites. Recent results show that the Heck coupling of chloroarenes can be induced by Pd-on-carbon, Pd nanoparticles deposited on layered double hydroxide or solid Pd catalysts having highly dispersed Pd^{2+} species to give the corresponding vinylarenes in high yields under appropriate reaction conditions (Papp et al. 2004).

An important consideration in developing insoluble heterogeneous catalytic systems for the Heck reaction is the solubility of the Base. HX salt. An insoluble salt will smoother the surface of the catalyst and the reaction therefore needs to be carried out in a solvent that can solubilise this by-product, removing it from the vicinity of the metal surface (Whitcombe 2001).

Palladium on carbon proved to be active for Heck coupling under several different conditions. A selection of the results obtained with this kind of catalyst is presented in Table 5.2. One of the most interesting results is the relatively high yield in stilbene from the reaction of chlorobenzene with styrene reported by Julia et al. (Table 5.2, nos. 1-4). In pure methanol at 120ºC (the reaction was carried out in an autoclave under pressure) stilbene was afforded in 62% yield (82% conversion of styrene), without any added phosphine. In this connection the authors showed that under these conditions added triphenylphosphine was an inhibitor rather than a promoter.

Palladium on carbon was also employed by Beller and Külhein as the catalyst for the reported first HETHR involving 4-methoxyphenyldiazonium (*p*-anisidyldiazonium) tetrafluoborate (Table 5.2, no. 5). According to them, this could be the Alternative route to classical condensation for the synthesis of substituted cinnamic esters, which are industrially important UV absorbers (Biffis et al. 2001).

Table 5.2. Heck reactions of aryl bromides and chlorides using Pd/C and inorganic oxides



Entry	ArX	Alkene	Catalyst	Conditions	Yield [%][a]
1	chlorobenzene	styrene	Pd/C	0.5wt%Pd, CH_3OH, Na_2CO_3, 120°C, 4h	62
2	chlorobenzene	styrene	Pd/C	0.5wt%Pd, ethylene glycol, Na_2CO_3, 120°C, 4h	55
3	chlorobenzene	styrene	Pd/C	0.5wt%Pd, ethylene glycol/CH_3OH, Na_2CO_3, 100°C, 24h	46
4	iodobenzene	Methyl acrylate	Pd/C	0.5wt%Pd, CH_3OH, Na_2CO_3, 150°°C, 4h	70
5	p-anisidyl diazonium tetrafluoroborate	Ethyl acrylate	Pd/C	0.5wt%Pd, C_2H_5OH, 40-60°C	98
6	chlorobenzene	styrene	Pd/MgO	0.25 wt % Pd, Na_2CO_3, 150°C, 5h	32
7	4-nitrochloro benzene	vinylbutylether	Pd/C	5 wt % Pd, Dioxane NEt_3, 100°C, 4h	77
8	4-nitrochloro benzene	vinylbutylether	Pd/Al_2O_3	6.06 wt % Pd, Dioxane, NEt_3, 100°C, 4h	71
9	4-nitrochloro benzene	vinylbutylether	Pd/SiO_2	1.22 wt % Pd, Dioxane, NEt_3, 100°C, 4h	51

[a] Yield of *trans* isomer given only

The first paper on heterogeneous Heck catalysis over palladium supported onto an inorganic oxide was published by Kaneda et al. in 1990 [41]. They reported thereby the activation of chlorobenzene in the coupling with styrene in methanol at 150°C (Table 5.2, no.6) using Na_2CO_3 as the base (Biffis et al. 2001).

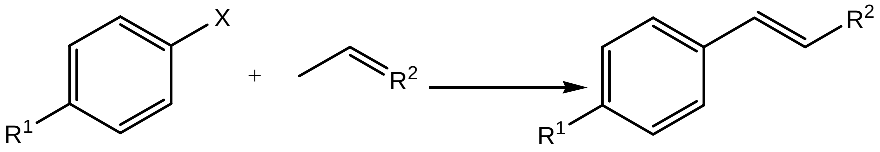
The difference yield in between Pd-MgO and Pd-C could be due to the instrinc character of the solid support. The basic MgO support can donate electrons to the palladium particles creating an electron-rich environment, which is favorable during the oxidative addition of the aryl halide. Pd-C is more acidic and its electron–donating character is therefore minimized (Whitcombe 2001).

Augustine and O'Leary initially found that whereas Pd/γ-Al_2O_3 was practically as active as Pd/C, Pd/SiO_2 was somewhat less efficient (Table 5.2, nos. 7-9). Support effects were observed only in the coupling of 4-nitrobenzoylchloride that was relatively slow over Pd/MgO in comparison with both Pd/SiO_2 and Pd/Al_2O_3. By contrast, for 4-bromotoluene and bromobenzene the support nature did not affect the coupling rates (Biffis et al. 2001).

Particles >10 nm in diameter are generally described as colloids and those <10 nm in diameter as clusters. Colloids and clusters differ from insoluble heterogeneous catalysts in that, while catalysis takes place on the surface of the dispersed metal particles, the colloid or cluster can be soluble. Pd sols are usually prepared either by chemical reduction of a palladium salt or electrochemical dispersion of palladium metal in the presence of a stabilizer. The stabilizer, e.g. a polymer, tetraalkylammonium salt or surfactant, forms a protective shell around the metal particles, preventing agglomeration and formation of an insoluble precipitate, i.e. palladium black.

Representative examples of aryl bromides and chlorides that have been successfully transformed are given in Table 5.3 (Whitcombe 2001). Excellent conversions can be achieved with activated aryl bromides using three types of stabilizers shown (Table 5.3; entry 1 (Reetz and Lohmer 1996) and entries 3-5 (Beller et al. 1996)). The propylene carbonate stabilized Pd sols could activate chlorobenzene, giving a reasonable conversion of 55% (Table 5.3; entry 2) (Reetz and Lohmer 1996), but the block copolymer micelle system and tetraoctylammonium bromide stabilized sol could not convert electron rich aryl bromides or activated aryl chlorides (Table 5.3; entry 4 (Beller et al. 1996) and entries 6-7 (Klingelhofer 1997).

Table 5.3. Heck reactions of aryl bromides and chlorides using Pd sols.



Entry	R^1	X	R^2	Stabilizer	Conditions	Conv. [%]
1	NO_2	Br	Ph	Propyl.carbonate[a]	3.5mol%Pd, 130 °C, 5h	100
2	H	Cl	Ph	Propyl.carbonate[a]	3.5mol% Pd, 155°C,65h	55
3	COMe	Br	$CO_2{}^n$Bu	$(C_8H_{17})_4NBr$[b]	0.05 mol % Pd, 140 °C	97
4	COMe	Cl	Ph	$(C_8H_{17})_4NBr$[b]	1 mol % Pd, 140 °C	<5
5	NO_2	Br	Ph	PS-*b*-P4VP[b]	0.05 mol % Pd, 140 °C, 24h	92
6	Me	Br	Ph	PS-*b*-P4VP[b]	0.05mol %Pd, 140°C, 72h	7
7	COMe	Cl	Ph	PS-*b*-P4VP[b]	0.05 mol % Pd,140^{0}C, 72h	0

[a] Electrochemical reduction. [b]Chemical reduction; PS-*b*-P4VP= block copolymer, polystyrene-*b*-poly-4-vinylpyridine

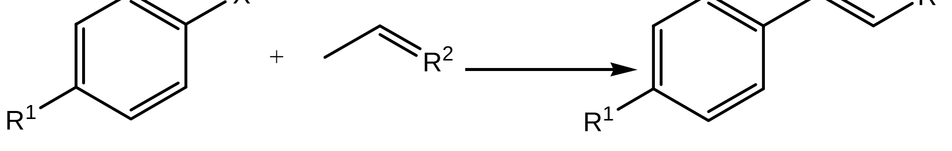
Mesoporous zeolites and other mesoporous support e.g. MCM-41, possess pores large enough for movement of larger molecules. On the other hand, binding of catalysts to such supports cannot be based on physical absorption (trapping) but require chemical bonding or the deposition of active metal (Beletskaya 2000).

Ying and co-workers prepared and tested some palladium catalysts supported onto a niobium modified mesoporous silicalite (Nb-MCM-41). The performance of the non silanized catalyst is illustrated by the data in Table 5.4 (nos. 1–7) (Augustine and O'Leary 1995). The catalyst is very effective for the coupling of bromoaryls with *para*-electron withdrawing ring substituents ($–NO_2$, $–COCH_3$), but not so much with bromobenzene. Only small amounts of coupling products were observed with chlorobenzene.

Djakovitch and Köhler have studied a series of palladium catalysts obtained by ion-exchanging Na- or H-zeolites (Mordenite, Y) with $[Pd(NH_3)_4]Cl_2$ (Table 5.4, nos. 8–19) (Djakovitch and Köhler 1999). The exchanged materials were calcined in O_2 at 500 °C and then used as such or after reduction of Pd(II) to Pd(0) under H_2 at 350 °C. The performances of the reduced and unreduced catalysts in terms of yields and product distribution were similar for the Heck reaction of styrene with 4-substituted bromobenzenes (nitro, acetyl and fluoro derivatives). These catalysts, however, were not particularly active: reaction times exceeding 24 h were required for complete reaction (Biffis et al. 2001).

By using $[Pd(NH_3)_4]^{2+}$-containing zeolite, 4-bromoanisole can be coupled with styrene in good yield (entry 20). In addition, the activated aryl chloride, 4-chlorobenzophenone, gives reasonable yields without the use of promoter (entry 21) but the yield increases on addition of $n-Bu_4NCl$ (entry 22). In both examples, a high temperatures of 170°C is required (Djakovitch and Köhler 2001).

Table 5.4. Heck reactions over palladium supported by molecular sieves.

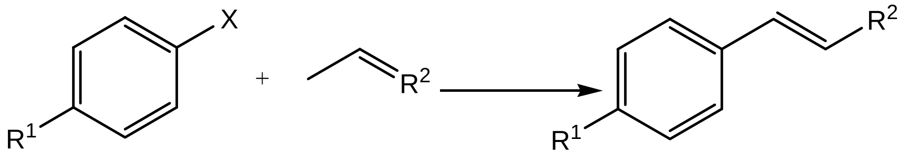


Entry	**R^1**	**X**	**R^2**	**Catalyst**	**Yield [%]^d**
1	H	Br	Ph	Pd/Nb-MCM-41	32 (48h)^a
2	H	Br	$CO_2{}^n Bu$	Pd/Nb-MCM-41	62 (48h)^a
3	H	Cl	$CO_2{}^n Bu$	Pd/Nb-MCM-41	6.4 (32h)^a
4	NO_2	Br	Ph	Pd/Nb-MCM-41	97 (0.33h)^a
5	COMe	Br	Ph	Pd/Nb-MCM-41	97 (0.75h)^a
6	NO_2	Br	$CO_2{}^n Bu$	Pd/Nb-MCM-41	99 (0.25h)^a
7	COMe	Br	$CO_2{}^n Bu$	Pd/Nb-MCM-41	99 (0.4h)^a
8	H	F	Ph	Pd(0)/Na-Mor	89^b
9	NO_2	Br	Ph	Pd(0)/Na-Mor	96^b
10	COMe	Br	Ph	Pd(0)/Na-Mor	86^b
11	H	Br	Ph	Pd(0)/Na-Mor	32^b
12	H	F	Ph	Pd(II)/Na-Mor	92^b
13	NO_2	Br	Ph	Pd(II)/Na-Mor	94^b
14	COMe	Br	Ph	Pd(II)/Na-Mor	86^b
15	H	Br	Ph	Pd(II)/Na-Mor	72^b
16	H	F	Ph	Pd(II)/H-Mor	91^b
17	H	F	Ph	Pd(II)/HY	92^b
18	H	F	Ph	Pd(II)/HY	93^b
19	H	F	Ph	Pd(II)/HY	92^b
20	OMe	Br	Ph	Pd(II)/NaY	81^c
21	COPh	Cl	Ph	Pd(II)/NaY	44^c
22	COPh	Cl	Ph	Pd(II)/NaY	59^{c,e}

[a] DMA, NEt_3, 170ºC, [b] 7 wt % Pd,DMA, NaOAc, 20h, 140ºC, [c] 0.1 mol % Pd, 20h, 140-170°C, [d] Yield of *trans* isomer given only [e] n-Bu_4NCl is added.

The surface silanized material (Pd-TMS11) which was formed through vapour deposition of palladium into a mesoporous material was tested for its ability to couple aryl halides with either styrene or n-butyl acrylate (Mehnert et al. 1998).

Table 5.5. Heck reactions over surface modified catalyst



Entry	R^1	X	R^2	Catalyst	Conditions	Con.
1	COMe	Br	$CO_2{}^n$Bu	Pd-TSM11	0.02mol%Pd, 120 °C,1h	100
2	H	Br	$CO_2{}^n$Bu	Pd-TSM11	0.1mol%Pd, 170 °C,48h	67
3	H	Cl	$CO_2{}^n$Bu	Pd-TSM11	0.1mol%Pd, 170 °C, 32h	16

Very good conversions were obtained for activated aryl bromides where TONs of 5000 were achieved (Table 5.5; entry 1). Harsh conditions (170°C, 48h) were necessary to convert bromobenzene to cinnamic ester (Table 5.5; entry 2). Even at 170°C, however, chlorobenzene remained essentially inactive (entry 3) (Whitcombe 2001).

Polymeric materials have been relatively widely used for the immobilization of homogenous Heck catalysts onto a solid support. Zhuangyu and co-workers reported on the preparation of palladium catalysts supported onto modified polystyrene resins. This kind of catalysts were as active as [$Pd(OAc)_2$] in a number of Heck couplings of iodobenzene with styrene at 100-130ºC in 4-5h. They also found that the catalysts underwent severe metal leaching (up to 74% of the metal was released into the liquid phase after three runs), which limited the catalyst lifetime. This was attributed to the metal coordination of NBu_3 that stabilized palladium in solution (Biffis et al 2001).

Palladium complexes of NHCs are convenient and cost efficient to prepare and have the potential for modification into polymer-supported reagents. The polymer-supported catalyst does not display induction periods, and is not influenced by the addition of promoters such as n-Bu_4NBr and PPh_4Cl. Excellent conversions can be achieved for activated aryl bromides but aryl chlorides can not be induced to react, even under forcing conditions (Whitcombe 2001).

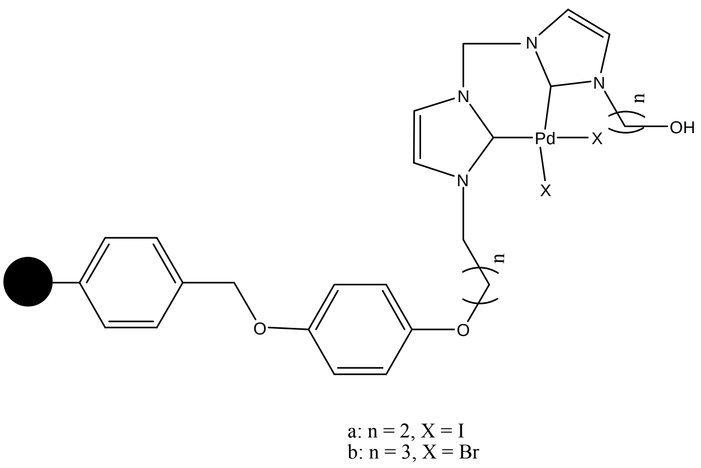


Figure 5.13. Polymer-supported NHC complexes of palladium according to Hermann et.al.

5.4. Fine Chemical Synthesis by Heck Reaction

Palladium catalyzed C-C bond formation (the Heck reaction) is one of the most versatile and useful tools in modern organic chemistry. The recent applications of Heck reactions include the manufacture of Novartis' Prosulfuron™—an agrochemical, octyl-*p*-methoxycinnamate—a sun-screen agent, Albemarle's Naproxen—an antibiotic and Singulair—an anti-asthma drug (Srivastava et al. 2003).

Eisenstadt and coworkers mention a multi-ton scale process for octyl *p*-methoxy cinnamate, the most common UV-B sunscreen, starting from 4-bromoanisol and using a Pd/C catalyst. Because of the high cost of bromoanisole, this synthesis is only commercially competitive if the recycling of the bromine and the bromination of anisole are part of this overall process. (Figure 5.14).

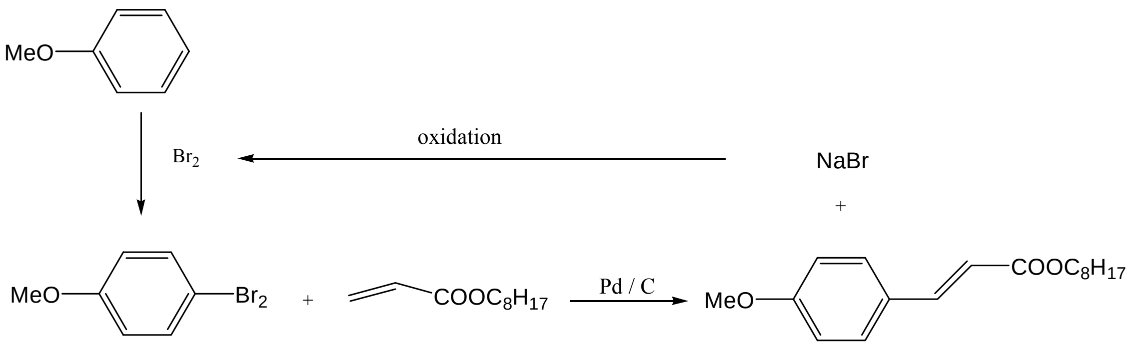


Figure 5.14. Production process for octyl methoxy cinnamate

An interesting combination of a homogeneous and heterogeneous approach is the production process developed for an intermediate of the Prosulfuron® sulfonylurea herbicide of Novartis/Syngenta, as shown in Figure 5.15 (Baumeister et al. 1997).

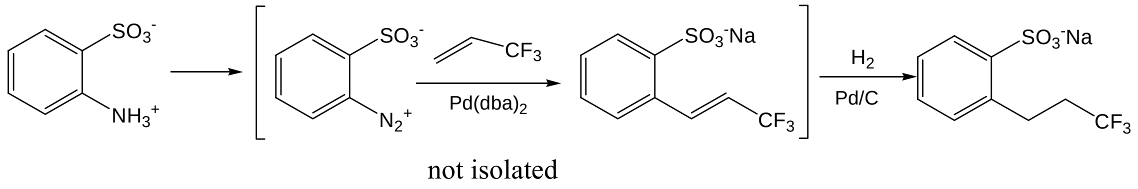


Figure 5.15. Production process for an intermediate of the Parasulfon® herbicide.

While the Matsuda Heck reaction is catalyzed by a homogeneous Pd catalyst, the Subsequent hydrogenation is carried out in the same reactor with Pd/C catalysts prepared in situ by adding active carbon to the reaction mixture. The overall yield is around 93%, but the catalyst activity and productivity are relatively low.

CHAPTER 6

EXPERIMENTAL STUDY

6.1. Synthesis of Amorphous Silica

A 3 N, 500 mL solution of H_2SO_4 was added sodium silicate solution (5% NaOH, 13.5% SiO_2, Riedel-de Haën) at a flow rate of 10 mL min^{-1} by means of a peristaltic pump until a PH of 3.65 was attained. Gelation occurred in 5 minutes after addition of the silicate solution was completed. The synthesized silica was washed with water until the solution conductivity showed no change.

Specific surface area of the pure support material was measured using a static process by means of a Micromeritics ASAP 2010 instrument using nitrogen at 77 K. The specific surface area was calculated by the BET method and average pore diameter and pore size distribution were calculated from the adsorption branch of the isotherm using the Barrett, Joyner and Helenda (BJH) method. The sample was degassed 3h at 423 K. The BET surface area was 549 m^2/g; the single point total pore volume was 0.838 cm^3/g. The pore diameter based on the maximum of the BJH size of silica was 61 Å.

6.2. Syntheses of Palladium N-Heterocyclic Carbene Complexes

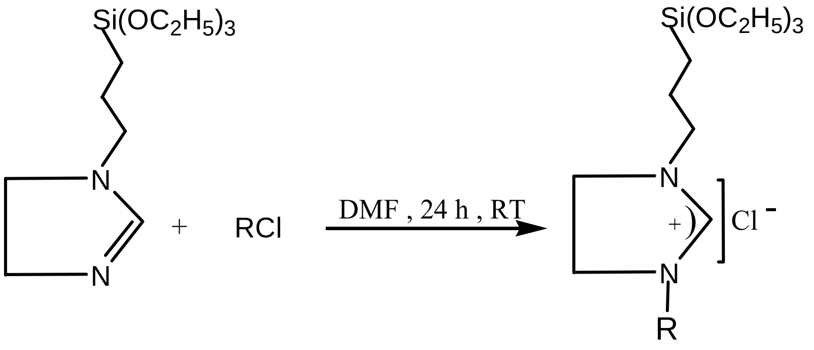
Syntheses of 1-(benzyl or 2,4,6-trimethylbenzyl)-3-(propyltriethoxysilane) imidazolidinium chloride salts **60** and **61,** bis[1-(benzyl)-3-(propyltriethoxysilane) imidazolidin-2-ylidene]dichloropalladium(II) complex **62** and bis[1-(2,4,6-trimethyl benzyl)-3-(propyltriethoxysilane)imidazolidin-2-ylidene]dichloropalladium(II) complex **63** were performed in Prof. Dr. Bekir Çetinkaya's laboratories of the chemistry Department of Ege University.

All the materials were used directly without further purification. 1-(3-triethoxysilylpropyl)-2-imidazoline (imeo) was obtained from Fluka. Diethyl ether (J. T. Baker) was distilled under nitrogen from sodium benzophenone ketyl just before use.

DMF (J. T. Baker) was dried over molecular sieve 4A. All synthesis of the 1,3-dialkylimidazolidininum salts **60**, **61** and the Pd(NHC) complexes **62, 63** (Figure 6.1. and 6.2.) were performed under a nitrogen atmosphere with the use of standard Schlenk techniques.

6.2.1. Synthesis of 1-(benzyl or 2,4,6-trimethylbenzyl)-3-(propyl triethoxysilane) imidazolinium chloride (60 and 61)

The preparation of the imidazolinium salts were readily accomplished by the quarternization of 1-(3-triethoxysilylpropyl)-2-imidazoline (imeo). To a 5 mL of DMF solution of imeo (3.99 g, 14.78 mmol) was added 14.79 mmol of benzyl or 2,4,6-trimethylbenzyl chloride and the resulting mixture was stirred at room temperature (RT) for 24 h. Diethyl ether (20 mL) was added to obtain a white crystalline solid. The product was filtered, washed with Et_2O (2 × 15 mL) and dried under vacuum. The salt was colorless, hygroscopic and freely soluble in $CHCl_3$, but insoluble in hexane or diethyl ether. The structural characterizations for this sample are given (Çetinkaya et al. 2002).



imeo

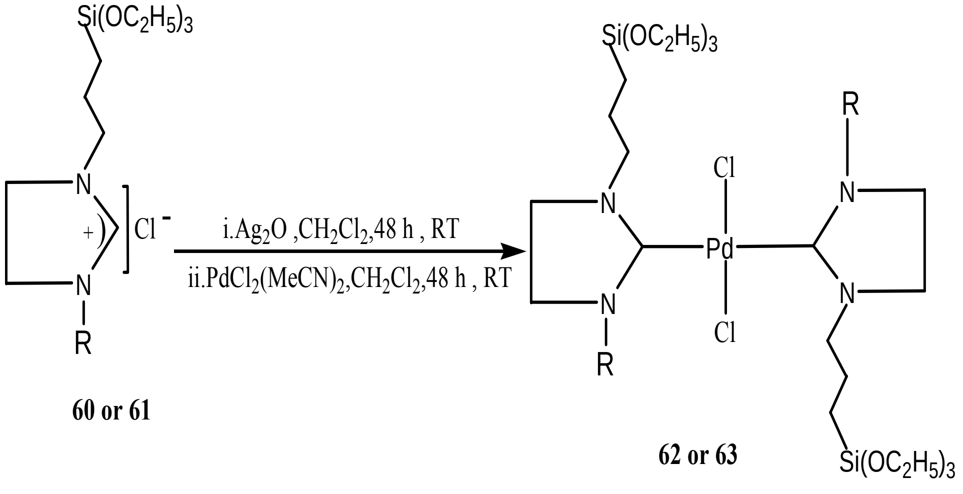
60 or 61

R: $PhCH_2$ **60**, 2,4,6-$(CH_3)_3PhCH_2$ **61**

Figure 6.1. Syntheses of imidazolinium salts 60 and 61.

6.2.2. Syntheses of bis[1-(benzyl)-3-(propyltriethoxysilane)imidazolidin-2-ylidene]dichloropalladium-II complex (62) and bis[1-(2,4,6-trimethylbenzyl)-3-(propyltriethoxysilane)imidazolidin-2-ylidene]di chloropalladium-II complex (63)

To a CH_2Cl_2 (10 mL) solution of the 1.0 mmol corresponding imidazolinium salt synthesized, 0.5 mmol Ag_2O was added. After stirring the mixture for 48 h at RT, 0.13 g (0.53 mmol) of $PdCl_2(CH_3CN)_2$ was added and it was further stirred for 48 h at RT. The precipitated AgCl was separated from the mixture by filtration. The complex was recrystallized from ether, giving 62 % yield. Analytical calculation for $C_{38}H_{64}Cl_2N_4PdSi_2$; C: 50.36%, H: 7.12%, N: 6.18%; found C: 48.8%, H: 6.8%, N: 6.1% for the benzyl substituted complex **62**. The structural elucidation of the complex was established through X-ray crystallography technique (Figure 6.3). The characterization of the 2,4,6-trimethylbenzyl substituted complex **63** is given elsewhere (Gürbüz et al. 2004).



60 or 61

62 or 63

R: $PhCH_2$ **(60, 62)**, 2,4,6-$(CH_3)_3PhCH_2$ **(61, 63)**

Figure 6.2. Syntheses of Pd(NHC) complexes 62 and 63.

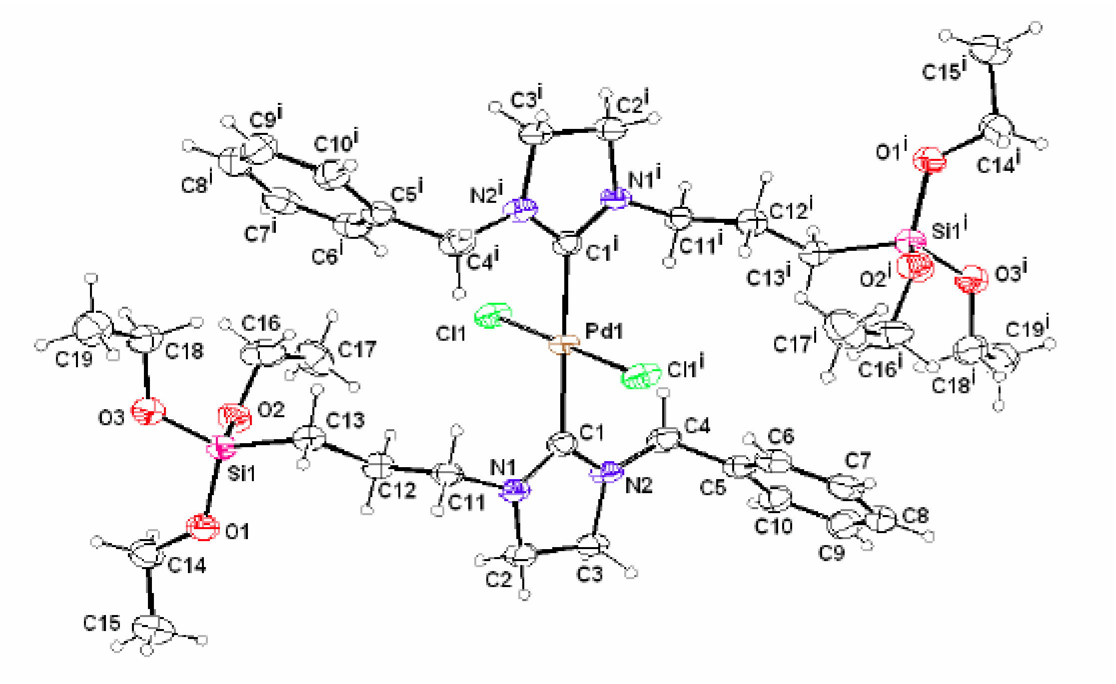


Figure 6.3. X-ray structure of complex **62**.

6.3. Anchoring of Pd(NHC) complex

Immobilization of PdNHC (Figure 6.4, Cat. 62 or Cat. 63).), which reserve as much possible as the coordination sphere of the metal. This was achieved by mainly direct anchoring of the homogeneous catalyst onto an inorganic support, amorphous silica.

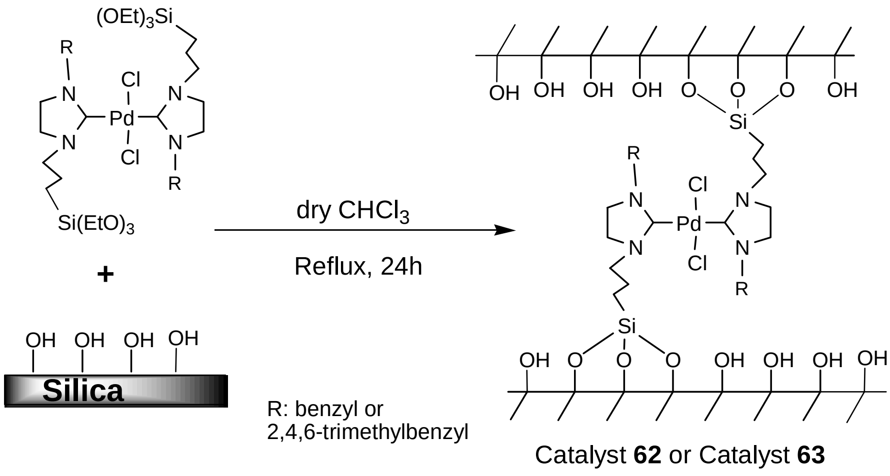


Figure 6.4. Immobilization of Homogeneous Catalyst.

Direct anchoring to an inorganic support (Amorphous Silica) is achieved via formation of covalent bonds between the solid (silanol groups -Si-OH) and Pd(NHC) complex that has appropriate groups (-Si(OEt)$_3$) at a position remote to the metal center.

Preparation of heterogenized materials of complexes bearing a triethoxy silylpropyl group were carried out, by controlled hydrolysis of Si-OEt bonds and reaction with the free silanol (Si-OH) on the surface of Amorphous Silica (Figure 6.4).

Reaction was carried out in a three-necked round-bottomed flask equipped with a reflux condenser and a dropping funnel under inert atmosphere (Ar or N_2). A dry $CHCl_3$ solution (20 mL/g silica) (Riedel-de Haën, extra pure) (refluxed over $CaCl_2$) which contained Pd-NHC complex in an amount furnishing 0.2 or 1 wt% Pd with respect to the silica amount was added drop wise to the amorphous silica which was evacuated overnight at 120 °C previous to the anchoring process (Figure 6.4). The resulting suspension was refluxed for 24 h while being magnetically stirred. After filtration, it was washed with CH_2Cl_2 (Merck, 99 %).

6.4. Characterization of the Catalysts by means of AAS, Elemental Analysis and TEM Analysis techniques

6.4.1. AAS

The palladium content of the catalyst was determined by atomic absorption spectroscopy (Solaar AA Spectrometer Thermo Elemental). The dissolved samples were prepared according to the microwave digestion method, which is summarized below.

A mixture of 3 mL concentrated HNO_3 (Merck, 65%), 2 mL concentrated HF (Merck, 40 %), and 1 mL $HClO_4$ (Riedel-de Haën, 65 %) were added over 20mg of a catalyst and these mixtures were heated in the Ethos Plus Microwave Labstation furnace according to the following heating program:

Step	Time (min)	Temperature (^oC)	Microwave Power(W)
1	4	120	500
2	4	150	550
3	5	180	550
4	17	180	600

At the end of this program, the digested samples were diluted to 50 mL. Standard solutions (0.5, 1, 2, 3, 4 ppm) were prepared from standard stock solution (0.5 mol/L) of 1000 ppm palladium(II)nitrate (Merck) in nitric acid for AAS analysis.

The immobilization of Pd-NHC complex by refluxing with silica particles in a ratio of 0.2 or 1 wt% Pd respect to the silica amount for 24 h gave the modified silica product Pd(NHC)-Silica shown in Scheme 6.3. Palladium analyses were performed on these samples and showed a palladium loading of 0.013 mmol Pd/g silica and 0.066 mmol Pd/g silica for catalyst **63**, respectively; 0.07 mmol Pd/g silica for catalyst **62**.

6.4.2. Elemental Analysis

Elemental analyses were performed by the TUBITAK ATAL Laboratories by using LECO CHNS-932 instrument. Samples were prepared by drying at 100 ^oC in an oil bath under vacuum for 2 days

Elemental analyses revealed the presence of C and N for all the modified and unmodified materials Table 6.1.

Table 6.1. Elemental analysis results of synthesized materials.

Material	C % (w/w)	N % (w/w)	C /N ratio
Pd-NHC-Silica **(Cat. 62)**	2.54	0.46	0.179
Pd(NHC) complex **62**	48.75	6.07	0.125

6.4.3. TEM

TEM observations were performed by Department of Materials Science and Engineering, University of Delaware by utilizing a Technai $G^2$12 transmission electron microscope operated at 120 kV.

6.5. General Procedure for the Heck Reactions

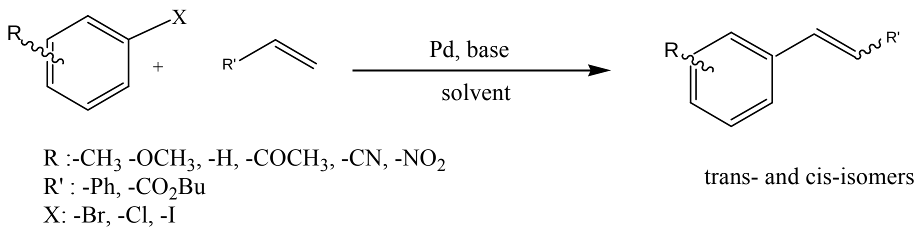


Figure 6.5. Reaction conditions; aryl halide:olefin (styrene or butyl acrylate):base:internal standard (1:1.2:1.5:0.625 mmol), DMF, 140 °C.

Prior to use, the immobilized catalyst was dried under vacuum for 2h at 110 °C. For the Heck reactions (Figure 6.5.), aryl halide: olefin (styrene, Fluka, >99 % or butyl acrylate, Merck, >99%): base: internal standard (hexadecane, Merck, >99%) (1:1.2:1.5:0.625 mmol) and prescribed amount of solvent (DMF, Lachema) were introduced into a 3-necked round bottomed flask which contained predried catalysts and equipped with a condenser and a septum. The reactor was then placed in a preheated oil bath at 140 °C with vigorous stirring. Small amount of samples were periodically withdrawn by syringe during the reaction, diluted in CH_2Cl_2 and analyzed by GC. The conversions were calculated based on hexadecane as internal standard. The course of the reaction was followed until no further increase in the formation of *trans*-coupling product is observed. After cooling to the room temperature the catalyst was recovered by filtering through a membrane filter with 0.2 μm porosity.

All products are known compounds and were isolated by column chromatography on silica gel and analyzed by means of GC, GC/MS, ^1H NMR and ^{13}C NMR techniques.

In order to remove adsorbed organic substrates and bases, the catalyst used was first washed with CH_2Cl_2 and then with CH_3OH (Riedel-de Haën, 99.7 %) for $NaOAc.3H_2O$ or with ultra pure water for other bases after the reaction. For the recycling studies, the recovered catalyst was dried at 110 °C under vacuum for at least 2 h and reused without further treatment. A small sample of the reaction mixture was collected for GC analysis and the remaining reaction mixture was reserved for Pd analysis.

6.6. Characterization of Reaction Products

6.6.1. GC Method

The samples were analyzed by GC/MS (HP GC/MS 6890/5973N on a HP-5MS (30 m, 0.25 mm capillary column (%5 phenylmethylsiloxane) with 0.25 μm film thickness) and GC (HP 6890N on a 30 m, 0.25 mm capillary column (5 % Dimethylsiloxane, 95 % phenyldimethylsiloxane) with a 0.25 μm film thickness and a FID detector).

The GC and GC/MS programs applied throughout the analysis was as follows: the column temperature was 40 ºC at the beginning of the program and it was heated with a rate of 10 ºC / min up to 250 ºC, then it was kept at this temperature for 3 min. Throughout the analysis the injector and detector temperatures were kept constant at 280 ºC and 300 ºC, respectively. The analysis was performed on a split mode with a split ratio of 1/50.

6.6.1.1. Calculation of Reactant and Product Amount on GC

For the calculation of amount of reactant and products, initially response factor of each reactant and product for the set temperature program of GC was determined. Hexadecane was used as an internal standard. The amount of internal standard does not change throughout the reaction, so the response factor of each compound was determined according to the amounts and areas under the peaks of internal standard and standard compound of interest. For the determination of the response factor of a compound, a known amount of standard compound together with a known amount of internal standard dissolved in the reaction solvent and diluted with dichloromethane, and then the solution was injected to GC. After the analysis is completed according to the set temperature program, equation (6.1) is used for the determination of response factor. Since we did not have the standard compounds of cis and 1,1-diarylethylene derivatives, R.F. of the *trans* product was used for the calculation of the amount of them.

$$\text{R.F.} = \left(\frac{\text{internal standard area}}{\text{compound area}}\right) \times \left(\frac{\text{compound amount}}{\text{internal standard amount}}\right) \qquad (6.1.)$$

In order to calculate the amount of both reactant and products at any time of reaction, aliquots of reaction sample were taken from the reaction flask at that time were injected to GC. At the end of GC analysis, taking the amount of hexadecane and the area under the hexadecane peak into account, equation (6.2) was used in order to calculate the amount of the reactant and products at that time.

$$\text{amount of compound} = \left(\frac{\text{internal standard amount}}{\text{internal standard area}}\right) \times \text{R.F.} \times \text{compound area} \qquad (6.2.)$$

6.6.1.2. Calculation of Reactant Conversion, Product Yield and Recovery

Reactant conversion at any time is calculated using equation 6.3:

$$(\text{Reactant Conversion})_t \ \% = \frac{\left((\text{Reactant})_i - (\text{Reactant})_t\right)}{(\text{Reactant})_i} \times 100 \qquad (6.3.)$$

where $(\text{reactant})_i$ is the weight of reactant at the beginning of the reaction and $(\text{reactant})_t$ is the weight of reactant at time t.

Product yield of a molecule was calculated according to the following equation (6.4):

$$\text{Product Yield} = \frac{\text{moles of product}_t}{\text{initial moles of aryl halide}} \qquad (6.4.)$$

6.6.2. Purification of the Products

Various types of products were purified by using column chromatography or crystallization techniques in this study.

The reaction mixture, which contained styrene or cinnamate derivatives were separated from catalyst by filtration. Then the organic phase was evaporated, and then, was dissolved in ethyl acetate and extracted with water for three times. The organic phase was dried over sodium sulphate and solvent was removed by using evaporator. The product was purified by using column chromatography (diameter of column 1.5 cm) on silica gel (Merck, Silica Gel 60) with a 0.63mm-0.200mm (20 g) or 0.40mm-0.63mm (35 g) for styrene and cinnamate derivatives, respectively.

The purity of products were determined by means of NMR, GC-MS and GC techniques.

All products are known compounds and products were determined by ^{1}H NMR, ^{13}C NMR (Varian AS Mercury + 400 MHz spectrometer). The values are represented below and coupling constant (*J*) are given in Hz.

4-Nitro-*trans*-stilbene: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.21 (d, 2H, *J*=9.2 Hz), 7.61 (d, 2H, *J*=9.2 Hz), 7.52 (d, 2H, *J*=7.2 Hz), 7.28-7.42 (m, 3H), 7.24 (d, 1H, *J*=16 Hz), 7.12 (d, 1H, *J*=16.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 147.15, 143.86, 136.37, 133.51, 129.07, 129.03, 127.20, 126.96, 126.47, 124.31; MS: 225 (M^+), 178.

4-Acetyl-*trans*-stilbene: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.92 (d, 2H, *J*=8.0 Hz), 7.55 (d, 2H, *J*=8.0 Hz), 7.50 (d, 2H, *J*=8.0 Hz), 7.24-7.38 (m, 3H), 7.19 (d, 1H, *J*=16.4 Hz), 7.04 (d, 1H, *J*=16.4 Hz), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 196.62, 142.10, 136.91, 136.28, 131.67, 129.03, 128.95, 128.47, 127.68, 127.01, 126.66, 26.59; MS: 222 (M^+), 207, 178.

4-Methoxy-*trans*-stilbene: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.37 (d, 2H, *J*=7.2 Hz), 7.33 (d, 2H, *J*=8.4 Hz), 7.23 (t, 2H, *J*=7.2 Hz), 7.12 (t, 1H, *J*=6.8 Hz), 6.95 (d, 1H, *J*=16.0 Hz), 6.85 (d, 1H, *J*=16.4 Hz), 6.78 (d, 2H, *J*=8.4 Hz), 3.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.44, 137.80, 130.29, 128.68, 128.39, 127.79, 127.23, 126.77, 126.37, 114.22, 55.19; MS: 210 (M^+), 165.

2-Methoxy-*trans*-stilbene: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.46 (d, 1H, *J*=8.0 Hz), 7.40 (d, 2H, *J*=7.2 Hz), 7.35 (d, 1H, *J*=16.8 Hz), 7.21 (t, 2H, *J*=7.6 Hz), 7.06-7.13 (m, 2H), 6.97 (d, 1H, *J*=16.4 Hz), 6.83 (t, 1H, *J*=7.6 Hz), 6.74 (d, 1H, *J*=8.0 Hz), 3.76 (s, 3H), ^{13}C NMR (100 MHz, $CDCl_3$) δ: 157.21, 138.33, 129.33, 128.84, 127.57, 126.88, 126.81, 126.69, 123.87, 121.04, 111.13, 55.60; MS: 210 (M^+).

4-Methyl-*trans*-stilbene: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.38 (d, 2H, *J*=8.4 Hz), 7.29 (d, 2H, *J*=8.0 Hz), 7.23 (t, 2H, *J*=7.6 Hz), 7.12 (t, 1H, *J*=6.4 Hz), 7.043 (d, 2H, *J*=8.0 Hz), 6.97 (d, 1H, *J*=16.5 Hz), 6.93 (d, 1H, *J*=16.3 Hz), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 137.71, 137.33, 134.78, 129.49, 128.84, 128.73, 127.93, 127.48, 126.62, 126.56, 21.46; MS: 194 (M^+), 179, 178.

***trans*-3-Styrylpyridine:** ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.62 (s, 1H), 8.38 (d, 1H, *J*=4.8 Hz), 7.70 (d, 1H, *J*=8.4 Hz), 7.40 (d, 2H, *J*=7.2 Hz), 7.26 (t, 2H, *J*=7.2 Hz), 7.12-7.20 (m, 2H), 7.05 (d, 1H, *J*=16.4 Hz), 6.95 (d, 1H, *J*=16.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 148.69, 148.63, 136.78, 133.04, 132.55, 130.98, 128.87, 128.30, 126.80, 125.04, 123.48; MS: 181 (M^+).

***trans*-4-Nitrocinnamic acid butyl ester:** ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.24 (d, 2H, *J*=8.8 Hz), 7.65-7.71 (m, 3H), 6.55 (d, 1H, *J*=16 Hz), 4.23 (t, 2H, *J*=6.8 Hz), 1.68 (quint, 2H, *J*=7.6 Hz), 1.43 (sixet, 2H, *J*=7.6 Hz), 0.96 (t, 3H, *J*=7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.3, 148.72, 141.76, 140.84, 128.82, 124.36, 122.86, 65.10, 30.91, 19.38, 13.9; MS: 249 (M^+), 194; 176; 130.

***trans*-4-Acetylcinnamic acid butyl ester:** ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.93 (d, 2H, *J*=8.8 Hz), 7.64 (d, 1H, *J*=16 Hz), 7.58 (d, 2H, *J*=8.4 Hz), 6.47 (d, 1H, *J*=16 Hz), 4.19 (t, 2H, *J*=7.2 Hz), 2.57 (s, 3H), 1.70 (quint, 2H, *J*=7.2 Hz), 1.42 (sixet, 2H, *J*=7.2 Hz), 0.96 (t, 3H, *J*=7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 196.34, 166.23, 143.04, 138.98, 138.24, 128.99, 128.21, 121.07, 64.62, 31.02, 26.63, 19.41, 13.98. MS: 246 (M^+), 231, 190, 175, 131, 115.

***trans*-3-(3-Pyridinyl)acrylic acid butyl ester:** ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.72 (s, 1H), 8.60 (m, 1H), 7.82 (d, 1H, *J*=8.4 Hz), 7.64 (d, 1H, *J*=16 Hz), 7.31 (m, 1H), 6.49 (d, 1H, J=16.4 Hz), 4.2 (t, 2H, *J*=6.6 Hz), 1.67 (quint, 2H, *J*=7.2 Hz), 1.41 (sixet, 2H, *J*=7.2 Hz), 0.94 (t, 3H, *J*=7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.55, 150.91, 149.67, 140.89, 134.56, 130.57, 123.98, 120.85, 64.90, 30.93, 21.17, 19.37, 13.90; MS: 205 (M^+), 190: 176; 150; 132; 121; 104; 77.

***trans*-4-methyl-cinnamic acid butyl ester:** ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.66 (d, 1H, *J*=16 Hz), 7.42 (d, 2H, *J*=8.4 Hz), 7.19 (d, 2H, *J*=8.4 Hz), 6.39 (d, 1H, *J*=16 Hz), 4.20 (t, 2H, *J*=6.4 Hz), 2.37 (s, 3H), 1.68 (quint, 2H, *J*=6 Hz), 1.45 (sixet, 2H, *J*=7.2 Hz), 0.97 (t, 3H, *J*=7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.49, 144.75, 140.80, 132.01, 129.81, 128.25, 117.47, 64.54, 31.04, 21.65, 19.43, 13.95; MS: 218 (M^+), 162, 145, 115, 91.

***trans*-cinnamic acid butyl ester:** ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.69 (d, 1H, *J*=16 Hz), 7.52 (m, 2H), 7.38 (m, 3H), 6.44 (d, 1H, *J*=16 Hz), 4.22 (t, 2H, *J*=6.8 Hz), 1.71 (quint, 2H, *J*=7.2 Hz), 1.44 (sixet, 2H, *J*=7.2 Hz), 0.97 (t, 3H, *J*=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.27, 144.73, 134.75, 130.40, 129.08, 128.26, 118.57, 64.63, 31.02, 19.42, 13.45; MS: 204 (M^+) 148, 131, 103, 77.

***trans*-3-(2-Naphthyl)-propenoic acid butyl ester:** ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.93-7.49 (m, 8H), 6.56 (d, 1H, *J*=16 Hz), 1.71 (quint, 2H, *J*=7.2 Hz), 1.44 (sixet, 2H, *J*=7.2 Hz), 0.97 (t, 3H, *J*=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.35, 144.80, 134.45, 133.55, 132.25, 130.04, 128.89, 128.78, 128, 127.40, 126.91, 123.77, 118.74, 64.67, 31.07, 19.46, 13.98; MS: 254 (M^+), 198, 181, 152.

***trans*-4-Cyanocinnamic acid butyl ester:** ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.70 (d, 2H, *J*=8 Hz), 7.68 (d, 1H, *J*=16.2 Hz), 7.63 (d, 2H, *J*=8.2 Hz), 6.54 (d, 1H, *J*=16 Hz), 4.25 (t, 2H, *J*=6.7 Hz), 1.72 (quint, 2H, *J*=7.2 Hz), 1.44 (sixet, 2H, *J*=7.4 Hz), 0.99 (t, 3H, *J*=7.4 Hz); MS: 229 (M^+), 173, 156, 128.

6.7. Leaching Test

The Pd lost of the catalyst of the each reaction was evaluated by digesting the filtrate after each reaction. The filtrate was digested in Teflon vessels in the presence of H_2O_2 (Merck, 99 %) and HNO_3 (conc.) after all the organic solvent was completely evaporated for AAS analysis. The Pd content in the digested residue was determined by using AAS as described before.

Table 6.2. Purification of coupling products by column chromatography.

Product	**Gradient Elution**	**Melting Point (ºC)**	**Appearance**	**Purity**
4-Nitro-*trans*-stilbene	Hexane:DCM (2:1)	156-157	Yellow plates	> 99%
4-Acetyl-*trans*-stilbene	Hexane:DCM (4:1)	138.7-144.8	White plates	> 99%
4-Methoxy-*trans*-stilbene	Hexane:DCM (4:1)	135.4-137.1	Pale yellow plates	> 99%
2-Methoxy-*trans*-stilbene	Hexane:DCM (9:1)	59.5-65.5	Pale yellow	
4-Methyl-*trans*-stilbene	Hexane	117-118	White plates	> 99%
trans-3-Styrylpyridine	Hexane:ether (2:3)	78.6-81.6	Pale yellow	> 99%
trans-4-Nitrocinnamic acid butyl ester	Hexane	59.6-64.4	Yellow plates	97.3%
trans-4-Acetylcinnamic acid butyl ester	Hexane:ethyl acetate (gradient elution, 8:2 and 6:4)	Oily	Colorless	99.1%
trans-4-methyl-cinnamic acid butyl ester	Hexane:ethyl acetate (12:1)	Oily	Colorless	97%
trans-3-(2-Naphthyl)-propenoic acid butyl ester	Hexane:ethyl acetate (11:1)	56.6-64	White plates	98.9%
trans-3-(3-Pyridinyl)acrylic acid butyl ester	Hexane:ethyl acetate (2:1)	Oily	Colorless	99.1%
trans-cinnamic acid butyl ester	Hexane:DCM (7:3)	Oily	Pale yellow	98.7%

CHAPTER 7

RESULTS AND DISCUSSIONS

In this study, the amorphous silica supported Pd-NHC complexes synthesized were tested for their activities in the Heck coupling reactions. The Heck coupling reactions were carried out for different aryl halide types. Recycling studies were performed as well.

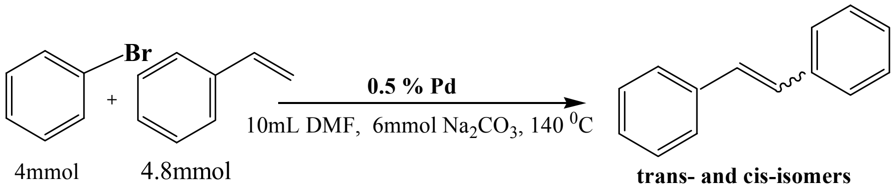
7.1. Heck Coupling Reactions

The catalytic activity of the saturated Pd-NHC complexes **62** and **63** immobilized, were studied in the arylation reaction of olefins. The catalytic activity of these materials was investigated, in detail, with activated (electron poor), non- and deactivated (electron neutral and electron rich) aryl halides and styrene or butyl acrylate as the vinylic substrates. Reusability studies were also performed for all catalysts.

At the beginning of our study, the catalytic activity of all catalysts were tested with 14 aryl halides that have different activities. Since the strength of the sp^2-carbon-halogen bond mainly determines the reactivity difference in carbon-carbon bond formation reactions, the rate determining step is considered to be the oxidative addition of palladium into a carbon–halogen bond.

The first trials were performed to determine the optimal base type for the coupling reaction of bromobenzene with styrene over the catalyst **63** (0.066 mmol Pd/g silica) with a Pd concentration of 0.5% in DMF solvent at 140°C. Catalyst **63** demonstrated very low activity with NaOAc and Cs_2CO_3 (Table 7.1). Na_2CO_3 was somewhat more effective than K_3PO_4.

Table 7.1. The effect of base on the Mizoroki-Heck Reactions of bromobenzene with styrene via catalyst **63**

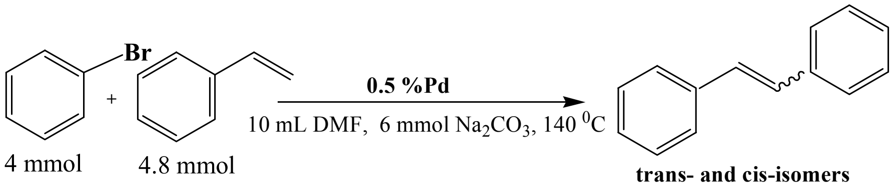


Entry	**Base**	**Time(h)**	**Conversion%**	**Yield% trans**
1	CH_3CO_2Na	14	40	25
2	Na_2CO_3	7	87	78
3	Cs_2CO_3	18	46	12
4	K_3PO_4	14	> 99	70

The catalysts were tested for their reusability involving the reactions of bromoarenes and iodoarenes with styrene for 10 cycles under the conditions given above, in the presence of Na_2CO_3 as a base. For each cycle, the amounts of solvent and reagents were adjusted depending on the amount of catalyst that had been recovered from the previous run. The reaction time given for each cycle represents the period of time for attaining the maximum amounts of *trans*-coupling products, that is usually 90-96% for 4-bromoacetophenone and 76-85% for iodoarenes. The conversion and yield values are shown above the bars for those reactions yielded less amount of *trans*-coupling product.

Both catalysts, **62** and **63** revealed comparable activities for the reaction of bromobenzene, affording 78 and 74% of the *trans*-coupling product after 7 h, respectively. However, their activities were remarkably reduced during subsequent uses; the coupling product formation achieved was 59 and only 6% for the second and third uses, respectively, when catalyst **62** was used. Product formation was only 26% for the second use with the catalyst **63** (Table 7.2).

Table 7.2. Reusability test of catalysts **62** and **63** for Mizoroki-Heck Reactions of bromobenzene and styrene[a]



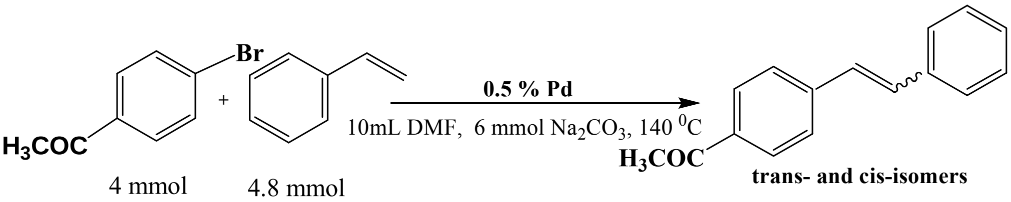
Entry	**Recycle**	**Catalyst**	**Time(h)**	**Conversion%**	**Yield% trans**	**TON[b]**	**TOF[b] h^{-1}**
1	1	62	7	87	74	148	21
2	2	62	19	76	58	116	6
3	3	62	20	19	6	12	1
4	1	63	7	87	78	156	22
5	2	63	33	72	26	52	2
6	1	63[c]	10.5	93	82	164	16
7	2	63[c]	8.5	31	19	38	4
8	1	63[d]	8.3	95	84	168	20
9	2	63[d]	22.5	27	15	30	1

[a]Catalyst **62** contained 0.07 mmol Pd/g silica, catalyst **63** contained 0.066mmol Pd/g silica silica. [b]TON=[*trans*-yield]/[Pd], TOF=TON/h [c]Bu_4NBr (20% with respect to the aryl halide) is added. [d]PPh_3 (2 molar equivalent of Pd) is added.

The effect of $(Bu)_4NBr$ (20% with respect to the aryl halide) and PPh_3 (2 molar equivalent of Pd) additives was examined for reaction efficiency. Their effect was negligible for the conversion of bromobenzene. In the second use, addition of PPh_3 deactivated the catalyst (Table 7.2, entries 6-9).

The catalyst had longer durability for the reaction involving 4-bromoacetophenone and the activity of catalyst **63** was somewhat better than catalyst **62**. Nevertheless, longer reaction times were required for each subsequent cycle to attain the *trans*-coupling product at yields greater than 90%. While the coupling product formation achieved was 95% after 2 h for the reaction of 4-bromoacetophenone with styrene during its first use, it took, however, 28.5 h to obtain 64% product yield when the catalysts had been used for the eight time, indicating that the catalyst underwent gradual deactivation at each cycle (Table 7.3).

Table 7.3. Reusability test of catalysts **62** and **63** for Mizoroki-Heck Reactions of 4-bromoacetophenone and styrene[a]



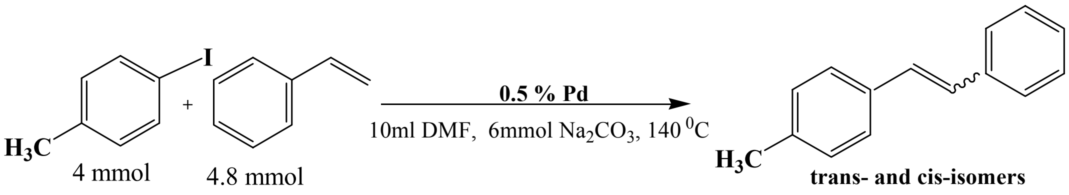
Entry	Recycle	Catalyst	Time(h)	Conversion%	Yield% trans	TON[b]	TOF[b] h^{-1}
1	1	62	3	98	92	184	61
2	2	62	4	100	90	180	45
3	3	62	7	> 99	91	182	26
4	4	62	7	97	95	190	27
5	5	62	8.6	>99	95	190	22
6	1	63	2	> 99	95	190	95
7	2	63	3	> 99	95	190	63
8	3	63	3.5-4	> 99	96	192	48-55
9	4	63	4.7	> 99	96	192	41
10	5	63	7.3	97	93	186	25
11	6	63	11.2	91	83	166	15
12	7	63	18	97	93	186	10
13	8	63	28.5	79	65	130	5

[a]Catalyst **62** contained 0.07 mmol Pd/g silica, catalyst **63** contained 0.066mmol Pd/g silica. [b]TON=[*trans*-yield]/[Pd], TOF=TON/h

Reaction trend of iodoarenes were similar also with 4-bromoacetophenone; the activity of catalyst **63** gradually decreased with each use, requiring longer reaction periods to achieve high yields.

The catalyst appeared to be reusable for 10 cycles for the reaction of 4-iodotoluene, albeit the reaction period was doubled in order to obtain high product formation when going from the first use to the tenth use (Table 7.4).

Table 7.4. Reusability test of catalyst **63** for the Mizoroki-Heck Reactions of 4-iodotoluene and styrene[a]



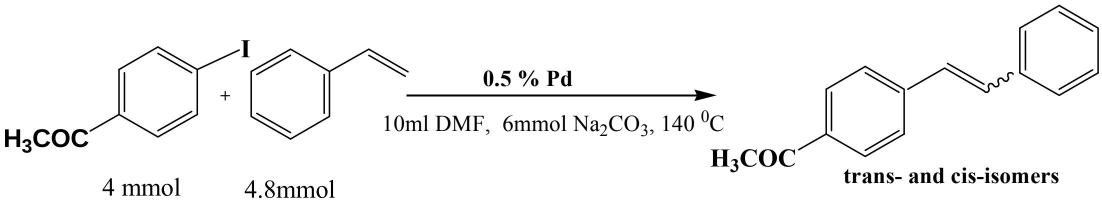
Entry	Recycle	Time(h)	Conversion%	Yield% trans	TON[b]	TOF[b] h^{-1}
1	1	7.3	96	87	174	24
2	2	6.8	96	85	170	25
3	3	6.6	97	88	176	27
4	4	7.5	95	91	182	24
5	5	8	97	89	178	22
6	6	7.4	98	88	176	24
7	7	10.5	97	88	176	17
8	8	11.5	97	88	176	15
9	9	11.3	98	90	180	16
10	10	14.3	97	86	172	12

[a]The catalyst contained 0.066 mmol Pd/g silica. [b]TON=[*trans*-yield]/[Pd], TOF=TON/h.

The coupling product formation was 83% after 7.75 h for the reaction of 4-iodoacetophenone with styrene during its first use, it took, however, the product formations diminished to 19% for the tenth use of the catalyst (Table 7.5, entries 1-10).

The effect of PPh_3 (2 molar equivalent of Pd) additive was also examined for 4-iodoacetophenone. Its effect was negligible for the conversion of bromobenzene, however, the presence of phosphine lowered the reaction rate of 4-iodoacetophenone, yielding 83% of the *trans*-coupling product at 15 h, while it took 7.75 h to obtain a comparable amount of product in the absence of PPh_3 (Table 7.5, Entries 1, 11). This may be due to different mechanistic behaviors of the catalyst with iodo- and bromoarenes [7d].

Table 7.5 Reusability test of catalyst **63** for the Mizoroki-Heck Reactions of 4-iodoacetophenone and styrene[a]

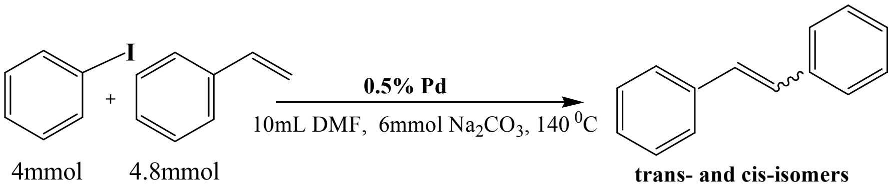


Entry	Recycle	Time(h)	Conversion%	Yield% trans	TON[b]	TOF[b] h^{-1}
1	1	7.8	98	83	166	21
2	2	8.9	99	83	166	19
3	3	7.8	96	74	148	17
4	4	10	96	85	170	17
5	5	14	96	82	164	12
6	6	12.7	100	90	180	14
7	7	10	96	93	186	19
8	8	9.8	98	90	180	18
9	9	18.7	97	83	166	9
10	10	23	35	19	38	2
11	1	15	96	83[c]	166	11

[a]The catalyst contained 0.066 mmol Pd/g silica. [b]TON=[*trans*-yield]/[Pd], TOF=TON/h [c]1mmol aryl halide, 4 mL DMF, PPH_3 (2 molar equivalent of Pd) is added.

The coupling product formation was 82% after 9.7 h for the reaction of 4-iodobenzene with styrene during its first use, although, the reaction period required 24 h to 73% product formation for the eighth use of the catalyst (Table 7.6, entries 1-8).

Table 7.6. Reusability test of catalyst **63** for the Mizoroki-Heck Reactions of iodobenzene and styrene[a]

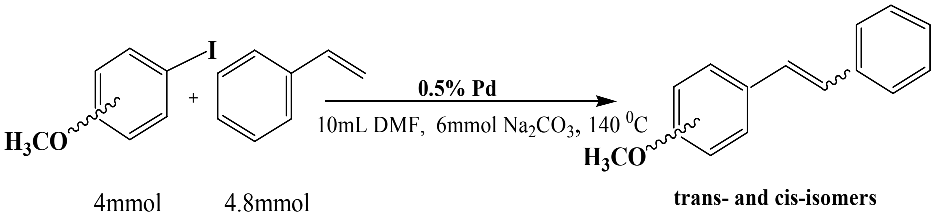


Entry	Recycle	Time(h)	Conversion%	Yield% trans	TON[b]	TOF[b] h^{-1}
1	1	9.7	94	82	164	17
2	2	8	97	97	194	24
3	3	8.4	95	80	160	19
4	4	10.4	99	85	170	16
5	5	9.5	99	86.5	173	18
6	6	16.7	87	75	150	9
7	7	19.5	91	73	146	8
8	8	24	92	73	146	6

[a]The catalyst contained 0.066 mmol Pd/g silica. [b]TON=[*trans*-yield]/[Pd], TOF=TON/h

The coupling product formation was 83% after 6 h for the reaction of 4-iodoanisole with styrene during its first use, although, the reaction rate and product formation decreased after the seventh run. (Table 7.7, entries 1-8).

Table 7.7. Reusability test of catalyst **63** for the Mizoroki-Heck Reactions of 4-iodoanisole and styrene[a]



Entry	Recycle	Time(h)	Conversion%	Yield% trans	TON[b]	TOF[b] h^{-1}
1	1	6	98	83	166	28
2	2	7.4	98	85	170	23
3	3	12.2	92	83	166	14
4	4	10	97	95	190	19
5	5	8.7	98	86	172	20
6	6	14.8	98	86	172	12
7	7	11	96	83	166	15
8	8	21	24	20	40	2

[a]The catalyst contained 0.066 mmol Pd/g silica. [bc]TON=[*trans*-yield]/[Pd], TOF=TON/h

a) TEM Analysis

TEM analyses revealed the presence of Pd particles on the silica support of the used catalysts which were recovered after the first and eight runs with 4-bromoacetophenone and styrene (Figure 7.1). After its first use, the Pd agglomerates were considerably large, extending to diameters as large as 90 nm, with an average size of 53 nm. Nevertheless, the catalyst after the eight run contained a higher quantity of particles with smaller average size (9 nm), and the particles were located less distant with respect to each other on the silica when compared to those of the former catalyst.

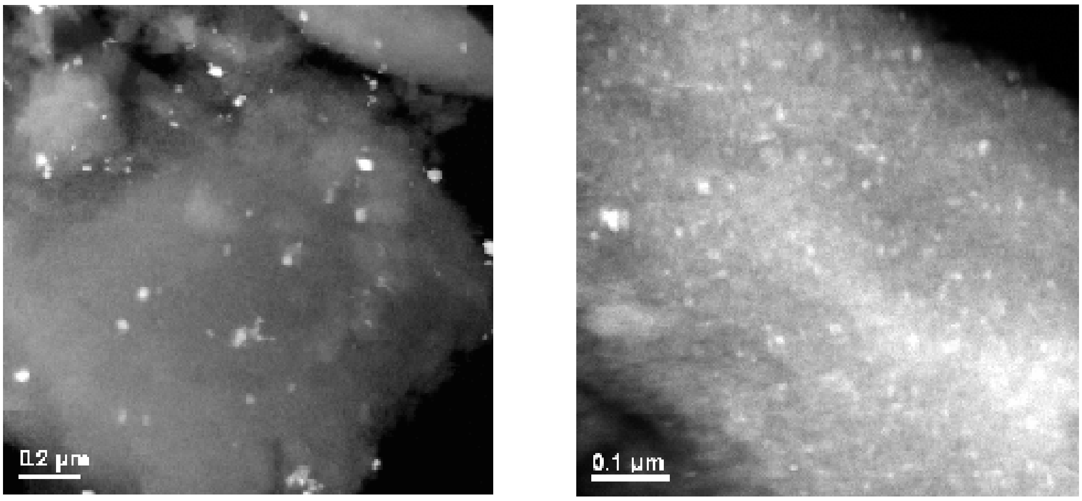


Figure 7.1. The TEM micrographs of catalyst 2 recovered from the reaction of 4-bromoacetophenone with styrene after the first run (left figure) and eight run (right figure).

On the basis of these observations, it can be commented that the catalyst acted as a Pd reservoir rather than a true heterogeneous catalyst, so that Pd was released gradually from the complex anchored onto the silica surface, inserted into the catalyst cycle and finally deposited back on the silica surface, at the end of the reaction, to form aggregates that are more reluctant to donate active Pd species to the reaction system, leading to the reduction of an effective source of the active Pd for subsequent uses, i.e., the used catalyst would deliver less amounts of active Pd species to the reaction solution during the next run (Figure 7.2). Various supported Pd catalysts (de Vries et al. 2002, Zhao et al. 2002, Reetz and Westermann 2000, Cassol et al. 2005), some pincer complexes (Takenaka and Uozumi 2004, de Vries et al. 2003, Yu et al. 2004), palladacycles (Munoz et al. 2001, de Vries et al. 2003), and simple Pd compounds (Reetz et al. 1998, Gruber et al. 2001, Yao et al. 2003, de Vries et al. 2003, Schmidt et al. 2003, Reetz and de Vries 2004), were also shown to act as Pd reservoirs when used for M-H reactions.

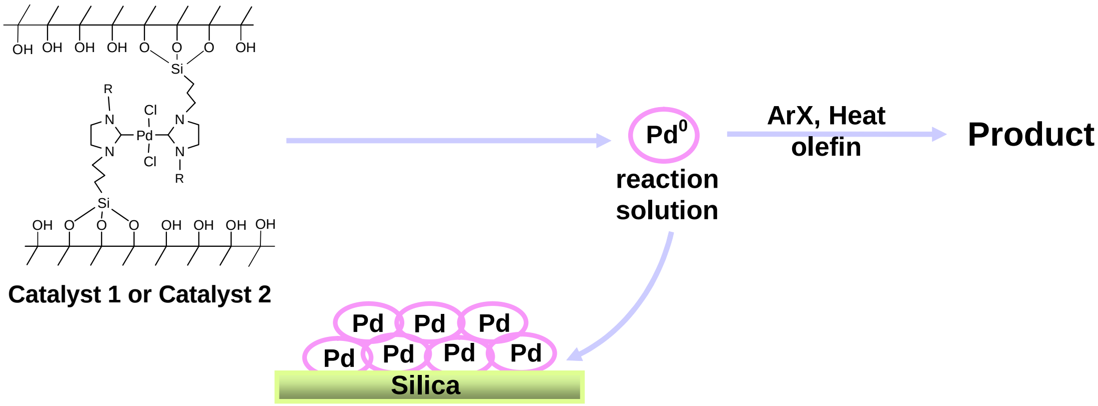
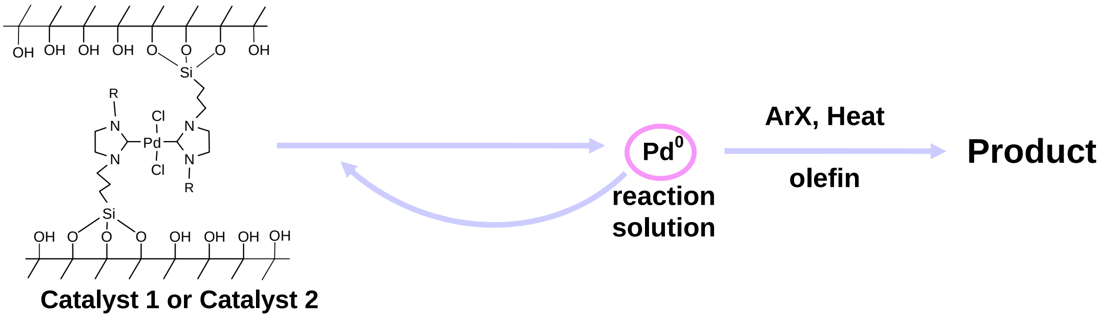


Figure 7.2. A schematic representation for Pd leaching from the catalyst and Pd agglomeration

b) Heterogeneity Test

The leaching of active species from heterogeneous catalysts into solution is a crucial question in order to identify whether the active centers are immobilized to the inorganic support or whether they are dissolved palladium complexes in the homogeneous solution. In related precedents, it has been found (Beletskaya and Cheprakov 2000) that the use of polar solvents and particularly DMF causes the partial leaching of Pd metal from the solid to the solution.

Atomic Absorption Spectrometry (AAS) analyses revealed no detectible amount of Pd within the filtrates after the reactions. However, a significant amount of Pd was determined in a solution recovered upon hot filtration; the reaction of 2 mmol 4-bromoacetophenone with styrene which had been performed under standard conditions was recovered upon hot filtration under dry N_2 atmosphere after 15 minutes of reaction, where the conversion and *trans*-yield formation were 16 and 9%, respectively.



Further AAS analysis revealed the presence of 3.6 ppm Pd in the solution, this being about 3.4% of the Pd charged initially. Moreover, the reaction proceeded to give a 39% conversion and to yield 34% of the *trans*-coupling product when base was added to the filtrate and heated for 3.75 h. Though these results do not rule out the possibility that the anchored complex might have been involved in the reaction in a heterogeneous way, it can reasonably be stated that the catalyst released Pd species into the solution that were capable of catalyzing the reaction. As a result, the catalyst was precursor to homogeneous catalysis.

The sterically congested 2-iodoanisole required comparatively longer reaction times (Table 7.8, Entry 6).

The M-H reactions were also performed at low Pd concentrations. However, a lower Pd-loaded immobilized catalyst (0.013 mmol/g silica) was used in these experiments unless otherwise stated, because it would not be practical to weigh very small amounts of catalyst when the former higher Pd-loaded catalyst was used at low Pd concentrations. The overall silica content of each reaction medium was completed to overall 300 mg upon addition of silica that contained no Pd originally. This enabled us to recover the catalyst more effectively, otherwise it would have been impractical to recover very little amounts of catalyst used for the studies at low catalyst concentrations.

As can be seen in Table 7.8, catalyst **63** showed higher activities when used also in lower proportions for the M-H reactions with styrene. The use of a ten fold lower Pd concentration, 0.05%, interestingly afforded the reaction of 4-iodoanisole at a comparable rate as compared with using 0.5% Pd (Table 7.8, Entries 1, 3).

Very high TONs and turnover frequencies (TOF), which were calculated on the basis of *trans*-coupling product formation, were calculated for iodo- and bromoarenes.

Table 7.8 The M-H Reactions of aryl halides with styrene over the catalyst **63**.[a]

Entry	**Aryl halide**	**Pd%**	**Time(h)**	**Conversion %**	**Yield% (*trans*-)**	**TON[b]**	**TOF,[b] h^{-1}**
1	4-$CH_3OC_6H_4I^{c}$	$5x10^{-1}$	6	98	83	166	28
2	4-$CH_3OC_6H_4I$	$5x10^{-2}$	5.3	> 99	82	1,640	309
3	4-$CH_3OC_6H_4I^{d}$	$5x10^{-3}$	14.5	100	82	16,400	1,131
4	4-$CH_3OC_6H_4I^{d,e}$	$5x10^{-3}$	22	50	44	8,800	400
5	4-$CH_3OC_6H_4I^{f}$	$5x10^{-4}$	24	94	83	166,000	6,917
6	2-$CH_3OC_6H_4I^{c,i}$	$5x10^{-1}$	23	96	90	180	8
8	4-$CH_3COC_6H_4Br^{c}$	$5x10^{-1}$	2	> 99	95	190	85
9	4-$CH_3COC_6H_4Br^{g,}$	$5x10^{-3}$	16.5	> 99	95	19,000	1,152
10	4-$CH_3COC_6H_4Br^{f}$	$5x10^{-3}$	15	99	93	18,600	1,240
11	4-$CH_3COC_6H_4Br^{e,f}$	$5x10^{-3}$	38	54	48	9,600	253
12	4-$CH_3COC_6H_4Brf$	$1x10^{-3}$	37	77	66	66,000	1,784
13	4-$CH_3COC_6H_4Br^{h}$	$5x10^{-4}$	12	3	0	–	–
14	4-$NO_2C_6H_4Br^{d}$	$5x10^{-3}$	22	93	78	15,600	709
15	3-BrC_6H_5N	$5x10^{-2}$	16	> 99	87	1,740	109
16	3-BrC_6H_5N	$1x10^{-2}$	35	82	60	6,000	171
17	3-$BrC_6H_5N^{d}$	$5x10^{-3}$	40.5	37	24	4,800	119
18	C_6H_5Br	$5x10^{-1}$	7	87	78	156	22
19	C_6H_5Br	$5x10^{-2}$	15	84	59	1,180	79
20	C_6H_5Br	$1x10^{-2}$	8	57	28	2,800	350
21	$C_6H_5Br^{f}$	$5x10^{-3}$	23	21	14.5	2,900	126
22	4-$CH_3C_6H_4Br^{c}$	$5x10^{-1}$	10.7	69	63	126	12
23	4-$CH_3C_6H_4Br$	$5x10^{-2}$	15	73	64	1,280	85
24	4-$CH_3C_6H_4Br$	$1x10^{-2}$	9	35	29	2,900	322
25	4-$CH_3OC_6H_4Br^{j}$	$5x10^{-1}$	5	23	19	38	7.6
26	4-$CH_3OC_6H_4Br$	$5x10^{-2}$	6	15	14	280	47
27	4-$CH_3COC_6H_4Cl^{c,j}$	$5x10^{-1}$	19	28	15	30	2
28	C_6H_5I	$5x10^{-1}$	9.7	94	82	164	17
29	$C_6H_5I^{d}$	$5x10^{-3}$	15.7	77	69	13,800	879

[a][Styrene]/[aryl halide] = 1.2, [Na_2CO_3]/[aryl halide] = 1.5, with hexadecane as an internal standard, 140°C, under inert atmosphere, the catalyst contained 0.013 mmol Pd/g silica, sufficient amount of silica was added to the reaction medium to contain 300 mg of silica overall, 4 mmol aryl halide, 10 mL DMF. [b]TON=[*trans*-

yield]/[Pd], TOF=TON/h. [c]The catalyst contained 0.066 mmol Pd/g silica, with no additional silica [d]6.67 mmol aryl halide. [e]second use. [f]20 mmol aryl halide, 15 mL DMF. [g]33 mmol aryl halide, 20 mL DMF. [h]40mmol aryl halide, 20mL DMF. [i]2mmol aryl halide, 5mL DMF. [j]1mmol aryl halide, 5mL DMF.

Higher TOF values were obtained at lower catalyst concentrations because of direction of an equilibrium between a higher order Pd species, i.e. the Pd cluster and a lower-order species, i.e. such as the monomeric or dimeric catalyst species. According to Le Chatelier principle, the equilibrium shifts towards the lower order species at lower Pd concentrations. Low Pd concentrations supress the formation of Pd black and keep all the metal available for catalysis (Figure 7.3). TON values were as high as 166,000 and 19,000, and TOF values of ≈ 6900 h^{-1} and ≈ 1200 h^{-1} were obtained with excellent yield of *trans*-coupling products from the reactions of 4-iodoanisole and 4-bromoacetophenone with styrene, respectively, and a good yield (66%) was obtained at a very high TON value (66,000) for the reaction using 4-bromoacetophenone (Table 7.8, Entries 1-5 and Table 7.8, Entries 8-13), whereas the total TON and TOF values were only 1238 and ≈ 16 for 4-iodoanisole, and 1422 and 18 h^{-1} for 4-bromoacetophenone after eight consecutive runs that were conducted, respectively.

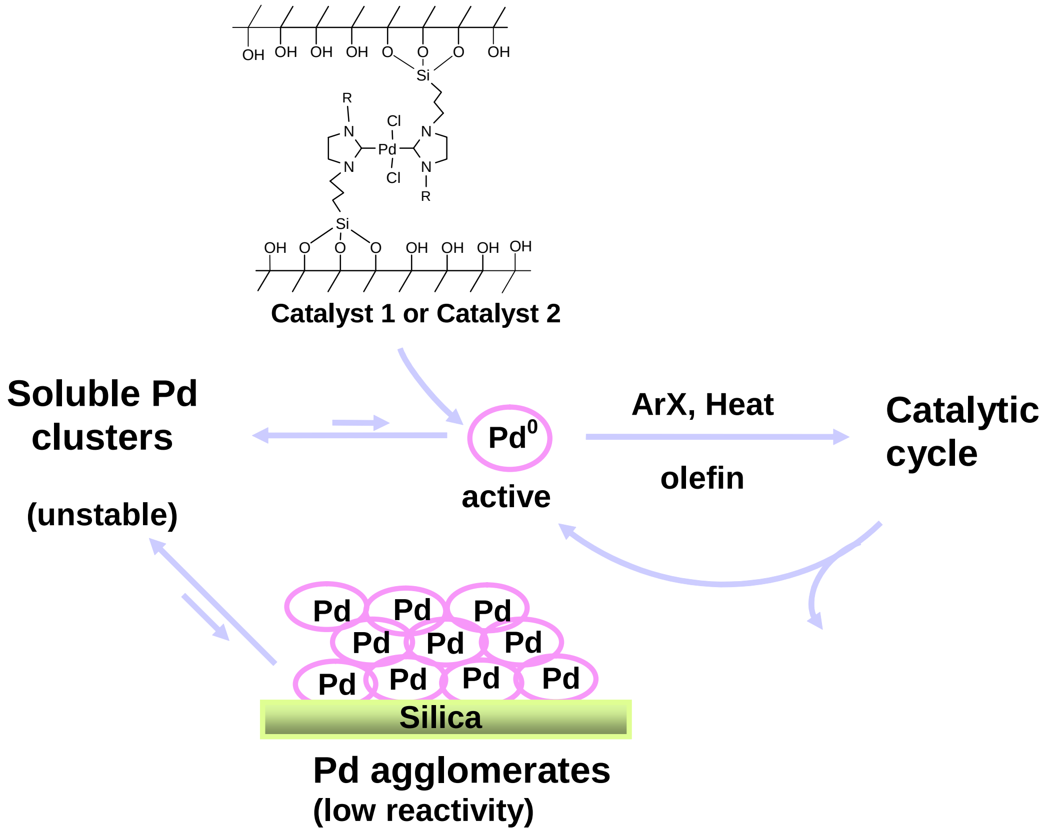


Figure 7.3. A schematic representation for overall behaviour of Pd during M-H reaction

Varying the Pd loading level on the silica and adding silica, which originally contained no Pd, to the reaction medium appeared to have no effect on the reaction efficiency (compare the Entries 9 and 10 in Table 7.8). Both the lower and higher Pd loaded catalysts (0.0133 and 0.066 mmol Pd/g silica, respectively) gave comparable yield formation in comparable reaction times when the reactions were performed at a Pd concentration of 0.005%.

Catalyst **63** which was subjected to the M-H reaction of 4-bromoacetophenone at a Pd concentration of 0.005% showed reduced activity during second use of the catalyst, giving 48% of the *trans*-coupling product after 38 h of reaction time (Table 7.8, Entry 11). Product was not formed when ten fold lower Pd concentration, 0.0005%, was used (Table 7.8, Entry 13).

Another activated aryl bromide, 4-bromonitrobenzene afforded relatively lower *trans*-coupling products at a Pd concentration of 0.005%, giving rise of 78% *trans*-coupling product with TON value of 15,600 (Table 7.8, Entry 14).

As a model molecule to hetero-aryl halide compounds, 3-bromopyridine was also converted effectively, yielding 87 and 60% *trans*-coupling products for Pd concentrations of 0.05 and 0.01%, respectively (Table 7.8, Entries 15, 16). Concentration of 0.005% Pd gave 24% yield (Table 7.8, Entry 17).

Non-activated bromoarenes, bromobenzene, and 4-bromotoluene gave moderate to high coupling yields at Pd concentrations of 0.5 and 0.05% (Table 7.8, Entries 18-19, 22-23). The use of 5 fold lower Pd concentration, 0.01%, the product formation was reduced to 29% with 4-bromotoluene (Table 7.8, Entry 24).

Catalyst **63** was, however, was low in its activity toward the M-H reactions of 4-bromoanisole and 4-chloroacetophenone (Table 7.8, Entries 25-27).

Nevertheless, it should be noted that *trans*-coupling formation was approximately comparable and ceased between the fifth and sixth h of reaction of 4-bromoanisole for Pd concentrations of both 0.5 and 0.05%, respectively.

That the variation of Pd concentration had no effect on the reaction kinetic of 4-bromoanisole and that the catalyst was deactivated at the early stages of the reactions may be explained by the fact that the formation of inactive Pd agglomeration is favored when the active Pd species have difficulty in oxidative addition to inactive aryl halide amounts and the increase of Pd concentration favors the equilibrium on the side of Pd agglomerates more than for the reaction cycle. It should also be noted that the catalyst turned dark over a shorter period of reaction when less active aryl halides were present compared with activated aryl halides. This observation also implies that the Pd precipitated on the silica more readily with the less active aryl halide types.

1,1-Diarylethylene type isomer was the major isomeric by-product of the M-H reactions when styrene was used as an olefin source. Its formation varied between 3-6% with bromoarenes, while iodoarenes gave rise higher amount of this isomeric product, 6-15%. C*is*-coupling isomer formation was generally <1%.

The reactions with low Pd amounts were performed also with butyl acrylate as an olefin reagent. As expected, the catalyst was more active with this olefin, giving extremely high TONs with activated aryl bromides (Table 7.9). The reaction was more selective to trans-coupling product with acrylate reagent than with styrene (total isomeric products are usually < 1%). The higher TOF values with the lower catalyst amounts were also a characteristic trend for the coupling reaction of this reagent with aryl halides.

Catalyst **63** gave high coupling product formation with extremely high TONs for all the activated aryl bromides employed, being as high as 700,000 and 840,000 for 4-nitrobromobenzene and 4-bromoacetophenone, respectively (Table 7.9, Entries 1-9).

However, the catalyst was sensitive to air under reaction conditions; the *trans*-coupling product formation was 63% after 9 h of reaction of 4-bromoacetophenone under air, vs. 95% in 6.8 h under inert atmosphere (Table 7.9, entry 2, 3).

For butyl acrylate, the catalyst was ineffective during second use under low Pd concentrations (Table 7.9, Entry 5).

Catalyst **63** was also very active for the reactions involving either 3-bromopyridine or 2-bromonaphthalene, yielding very high coupling products with low Pd concentrations such as 0.0005% (Table 7.9, Entries 12-14).

A moderate coupling product formation was obtained for Pd-catalyzed M-H reaction involving bromobenzene and 4-bromotoluene (Table 7.9, Entries 15-20).

The sterically congested 2-bromoacetophenone required 91% yield with 0.005% Pd concentration; however, the use of 25 fold lower Pd concentration gave 7% yield (Table 7.9, Entry21-22).

Table 7.9 The M-H Reactions of aryl halides with butyl acrylate over the catalyst **63**[a]

Entry	**Aryl halide**	**Pd%**	**Time (h)**	**Conversion %**	**Yield% (*trans*-)**	**TON**[b]	**TOF**[b] **h^{-1}**
1	$4\text{-}CH_3COC_6H_4Br$[c]	$5x10^{-3}$	2.5	100	98	19,600	7,840
2	$4\text{-}CH_3COC_6H_4Br$[d]	$5x10^{-4}$	6.8	97	95	190,000	27,941
3	$4\text{-}CH_3COC_6H_4Br$[d,e]	$5x10^{-4}$	9	69	63	126,000	14,000
4	$4\text{-}CH_3COC_6H_4Br$[d]	$2x10^{-4}$	12	73	68	340,000	28,333
5	$4\text{-}CH_3COC_6H_4Br$[d,f]	$2x10^{-4}$	28	30	12	60,000	2,143
6	$4\text{-}CH_3COC_6H_4Br$[g]	$1x10^{-4}$	28	87	84	840,000	30,000
7	$4\text{-}NO_2C_6H_4Br$[h]	$5x10^{-4}$	24	77	74	148,000	6,167
8	$4\text{-}NO_2C_6H_4Br$[d]	$2x10^{-4}$	24	78	71	355,000	14,792
9	$4\text{-}NO_2C_6H_4Br$[d]	$1x10^{-4}$	25	77	70	700,000	28,000
10	$4\text{-}CNC_6H_4Br$[d]	$5x10^{-4}$	22	97	81	162,000	7,364
11	$4\text{-}CNC_6H_4Br$[d]	$2x10^{-4}$	24	88	66	330,000	13,750
12	$3\text{-}BrC_6H_5N$[i]	$1x10^{-2}$	16	99	98	9,800	613
13	$3\text{-}BrC_6H_5N$[c]	$5x10^{-3}$	28	81	80	16,000	571
14	2-Bromonaphthalene[c]	$5x10^{-3}$	20	97	94	18,000	940
15	C_6H_5Br[i]	$5x10^{-2}$	7.8	74	64	1,280	164
16	C_6H_5Br[i]	$1x10^{-2}$	9	64	54	5,400	600
17	C_6H_5Br[c]	$5x10^{-3}$	20	39	31	6,200	310
18	C_6H_5Br[d]	$5x10^{-4}$	17.5	25	11	22,000	1,257
19	$4\text{-}CH_3C_6H_4Br$[i]	$5x10^{-2}$	11	52	48	960	82
20	$4\text{-}CH_3C_6H_4Br$[i]	$1x10^{-2}$	16	20	17	1,700	106
21	$2\text{-}CH_3COC_6H_4Br$[c]	$5x10^{-3}$	29	92	91	18,200	628
22	$2\text{-}CH_3COC_6H_4Br$[c]	$2x10^{-4}$	27	20	7	35,000	1296

[a][butyl acrylate]/[aryl halide] = 1.2; [Na_2CO_3]/[aryl halide] = 1.5, with 0.013 mmol Pd/g silica, under Ar, sufficient amount of silica was added to the reaction medium to contain 300 mg of silica overall; [b]TON=[*trans*- yield]/[Pd], TOF=TON/h; [c]6.67 mmol aryl halide, 10 mL DMF; [d]20 mmol aryl halide, 15 mL DMF; [e]under air; [f]second use; [g]40 mmol, 20 mL DMF; [h]10 mmol aryl halide, 10 mL DMF; [i]4 mmol, 10 mL DMF.

CHAPTER 8

CONCLUSION

Silica anchored saturated Palladium-N-heterocyclic carbene complexes were tested for their activity in M-H reactions of aryl halides.

The activity of catalyst diminished with each subsequent reuse of the catalyst at Pd concentration of 0.5%. However, it allowed very high TONs for aryl bromides and aryl iodides to be obtained.

The higher TOF values were realized at lower Pd concentrations.

The effective recovery of both Pd and ligand after the reaction along with high TON activities provided are of the advantages of the catalyst.

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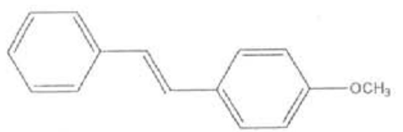
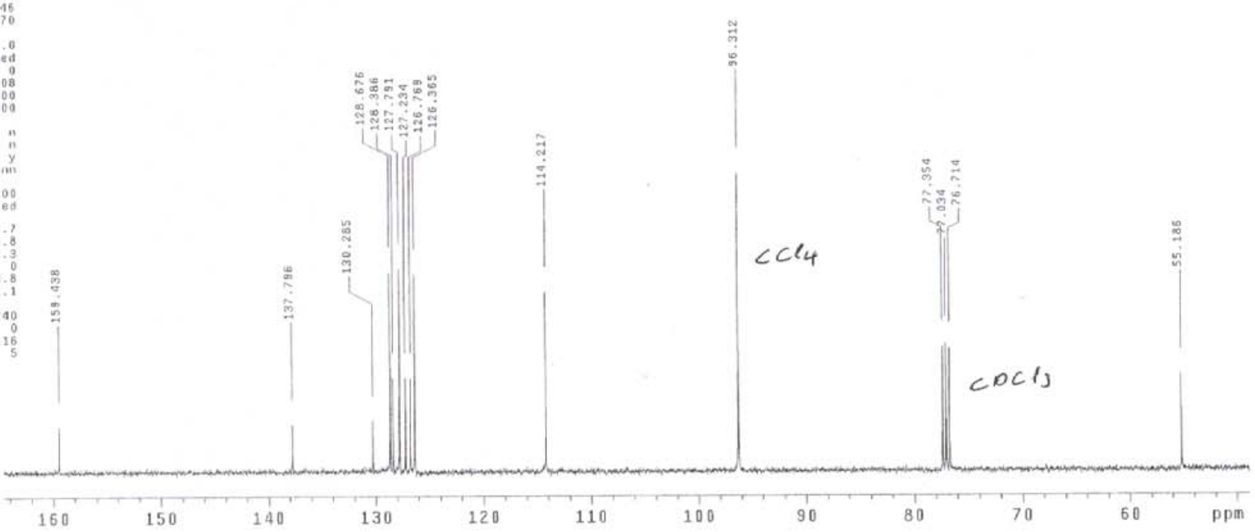
APPENDIX A

^{13}C NMR AND ^{1}H NMR of MIZOROKI-HECK COUPLING PRODUCTS

Figure A.1. ^{13}C NMR of 4-methoxy-trans-stilbene



4-methoxy-trans-stilbene



```
41anisol

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np            60270
fb            13800
bs               64
d1            1.000
nt             2000
ct             2000
     TRANSMITTER
tn              C13
sfrq        100.561
tof          1553.6
tpwr             60
pw            8.750
      DECOUPLER
dn               H1
dof               0
dm              yyy
dmm               w
dpwr             46
dmf           12270
       SPECIAL
temp           30.0
gain       not used
spin              0
hst           0.008
pw90         17.500
alfa         20.000
        FLAGS
il                n
in                n
dp                y
hs               nn
     PROCESSING
lb             1.00
fn         not used
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rp             83.8
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vs              116
th                5
ai   no   ph
```

Figure A.2. ^{1}H NMR of 4-methoxy-trans-stilbene

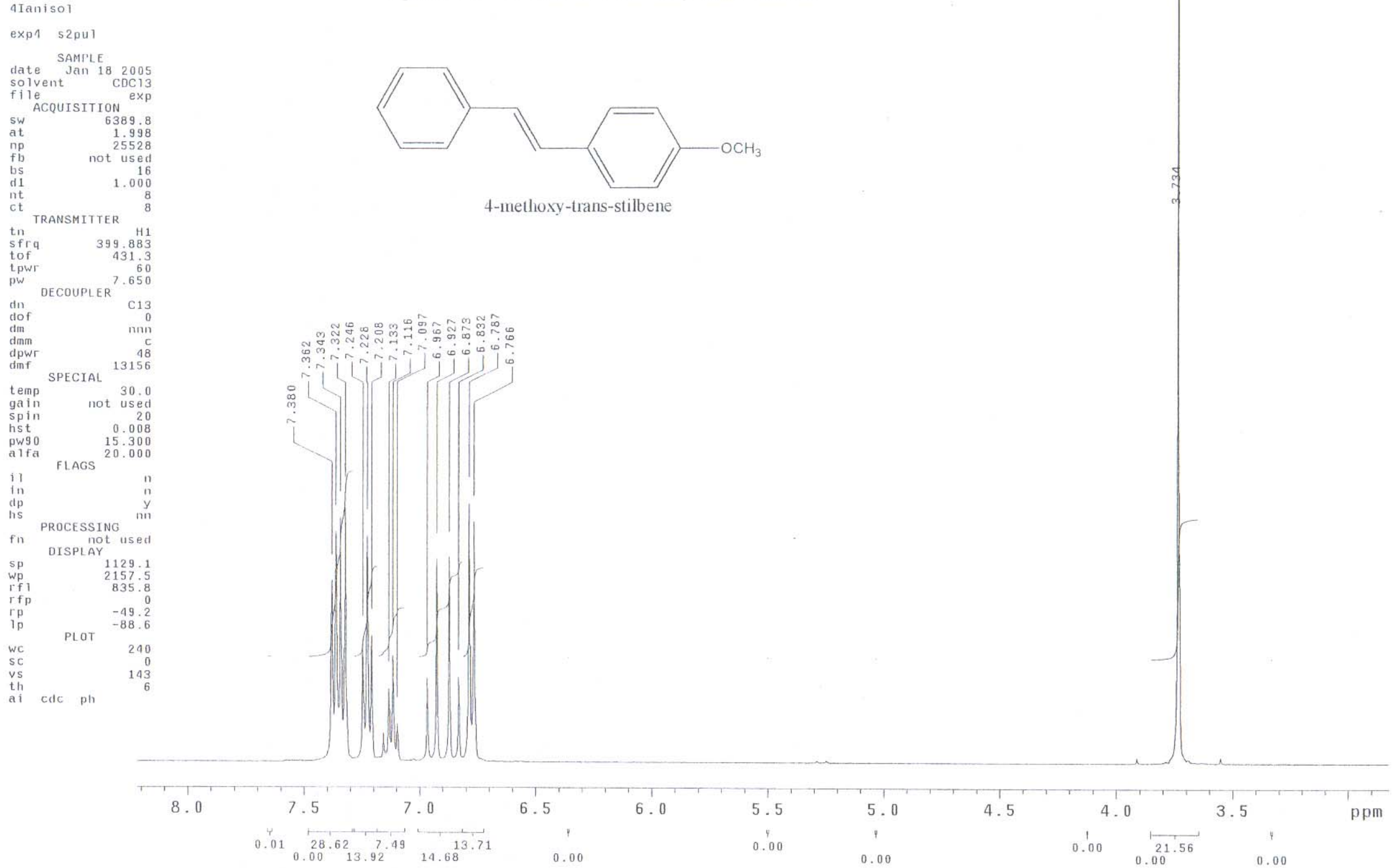

Figure A.3. ^{13}C NMR of 2-methoxy-trans-stilbene

```
2Ianisol

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file            exp
    ACQUISITION
sw          25125.6
at            1.199
np            60270
fb            13800
bs               64
d1            1.000
nt             2000
ct             2000
    TRANSMITTER
tn              C13
sfrq        100.561
tof          1553.6
tpwr             60
pw            8.750
     DECOUPLER
dn               H1
dof               0
dm              yyy
dmm               w
dpwr             46
dmf           12270
      SPECIAL
temp           30.0
gain       not used
spin              0
hst           0.008
pw90         17.500
alfa         20.000
       FLAGS
il                n
in                n
dp                y
hs               nn
     PROCESSING
lb             1.00
fn         not used
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sp           5233.0
wp          10994.0
rfl          1502.3
rfp               0
rp            107 7
lp           -356.6
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sc                0
vs               65
th                7
ai   no   ph
```

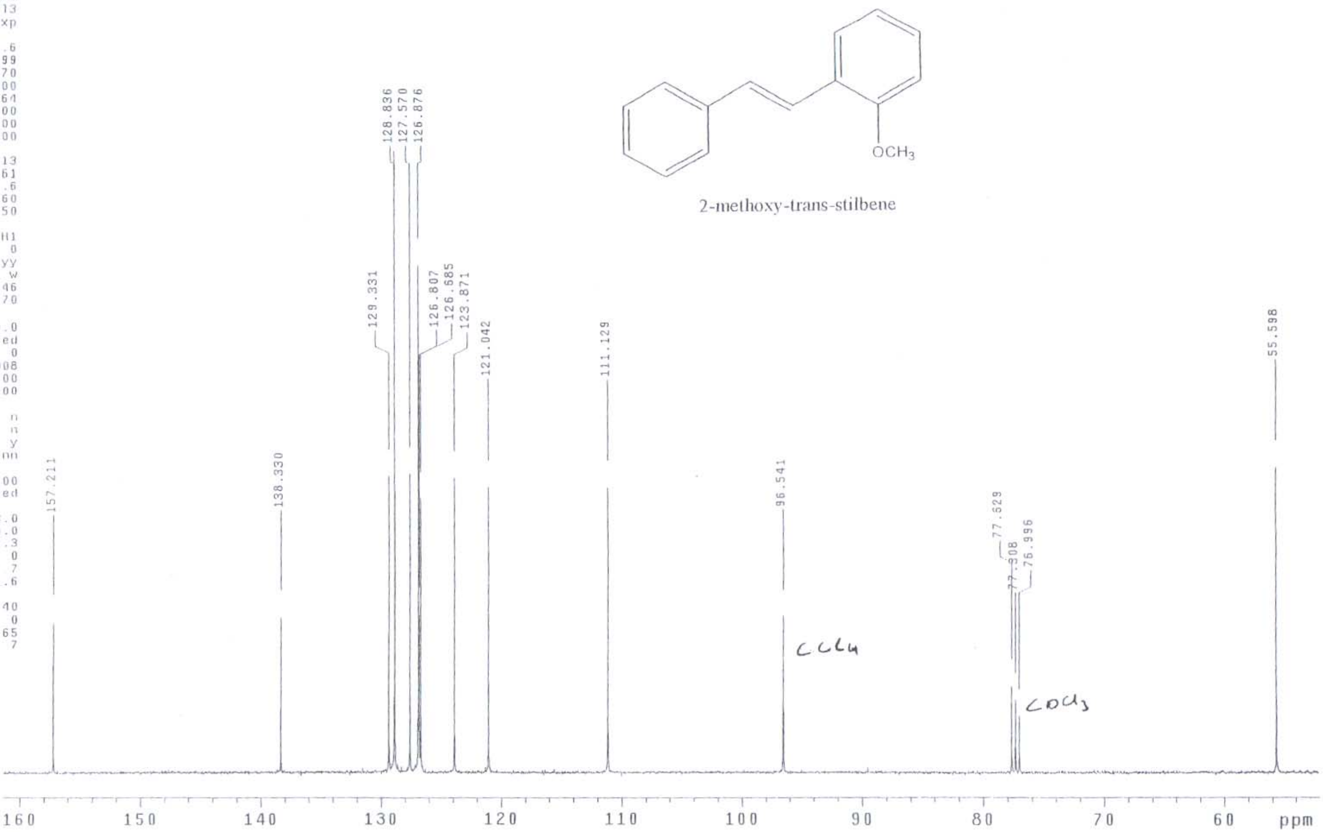


Figure A.4. ^{1}H NMR of 2-methoxy-trans-stilbene

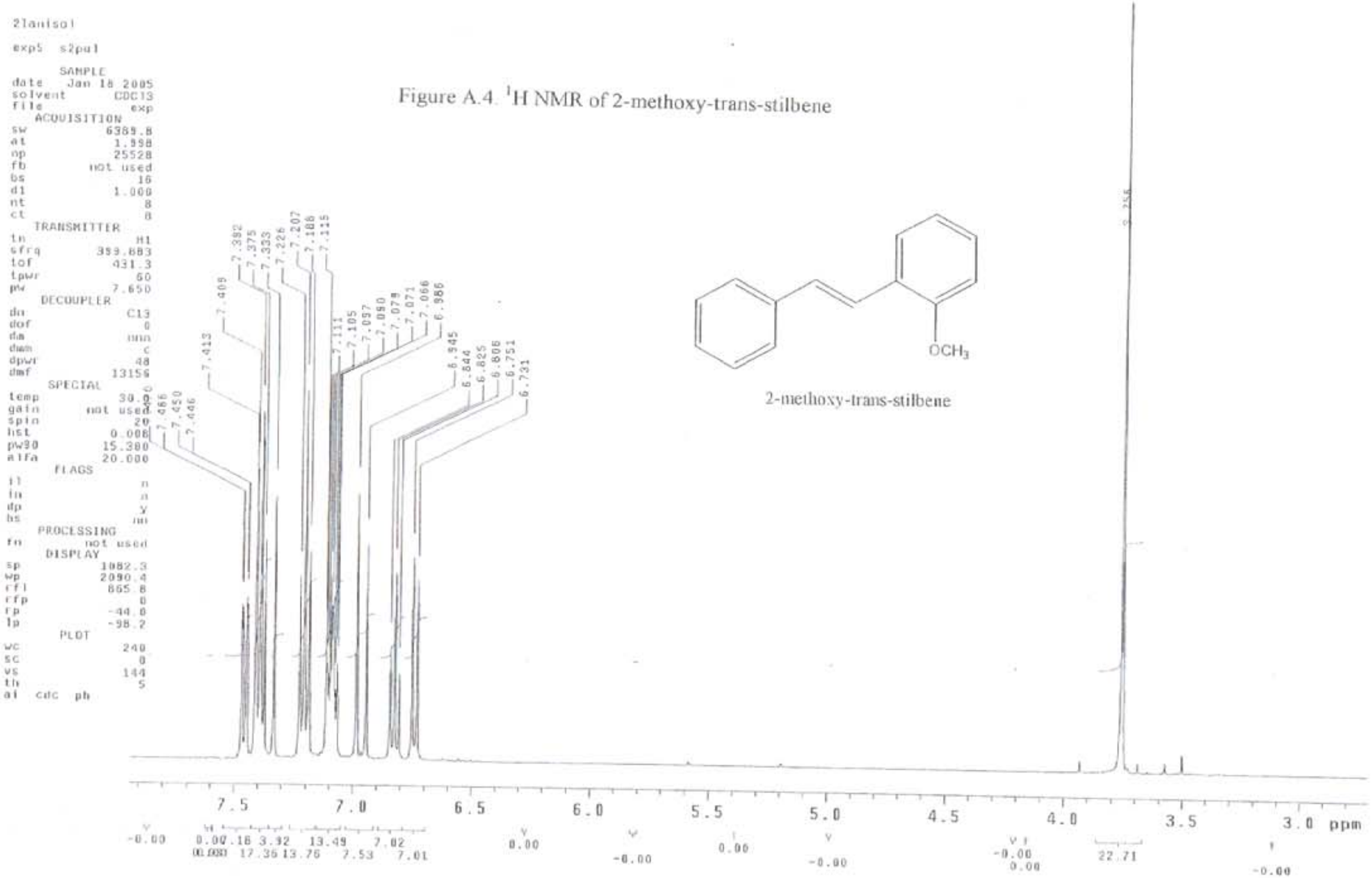
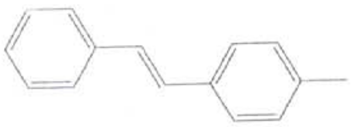


Figure A.5. ^{13}C NMR of 4-methyl-trans-stilbene



4-methyl-trans-stilbene

```
met-stb

exp31  s2pul

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date    Jan 22 2005
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file            exp
     ACQUISITION
sw          25125.6
at            1.199
np            60270
fb            13800
bs               64
d1            2.000
nt            10000
ct            10000
     TRANSMITTER
tn              C13
sfrq        100.561
tof          1553.6
tpwr             60
pw            8.750
      DECOUPLER
dn               H1
dof               0
dm              yyy
dmm               w
dpwr             46
dmf           12270
       SPECIAL
temp           30.0
gain       not used
spin              0
hst           0.008
pw90         17.500
alfa         20.000
        FLAGS
il                n
in                n
dp                y
hs               nn
      PROCESSING
lb             1.00
fn         not used
       DISPLAY
sp          -1501.5
wp          25124.9
rfl          1502.3
rfp               0
rp             88.0
lp           -319.4
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wc              240
sc                0
vs               87
th                2
ai   no  ph
```

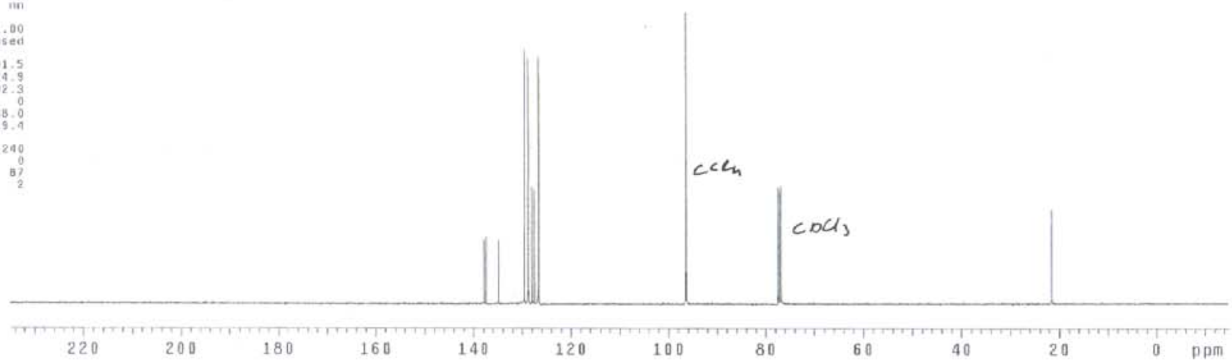
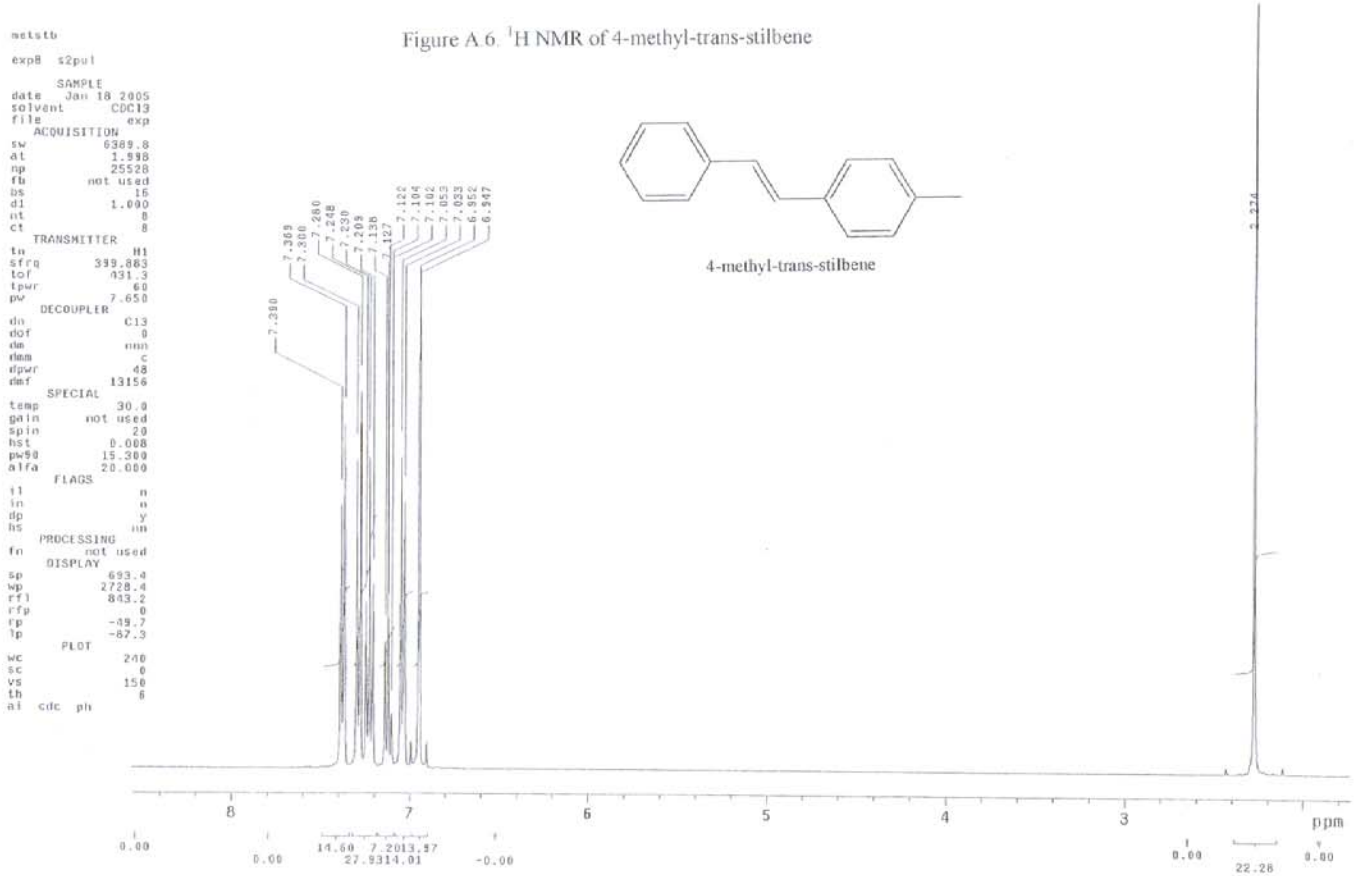
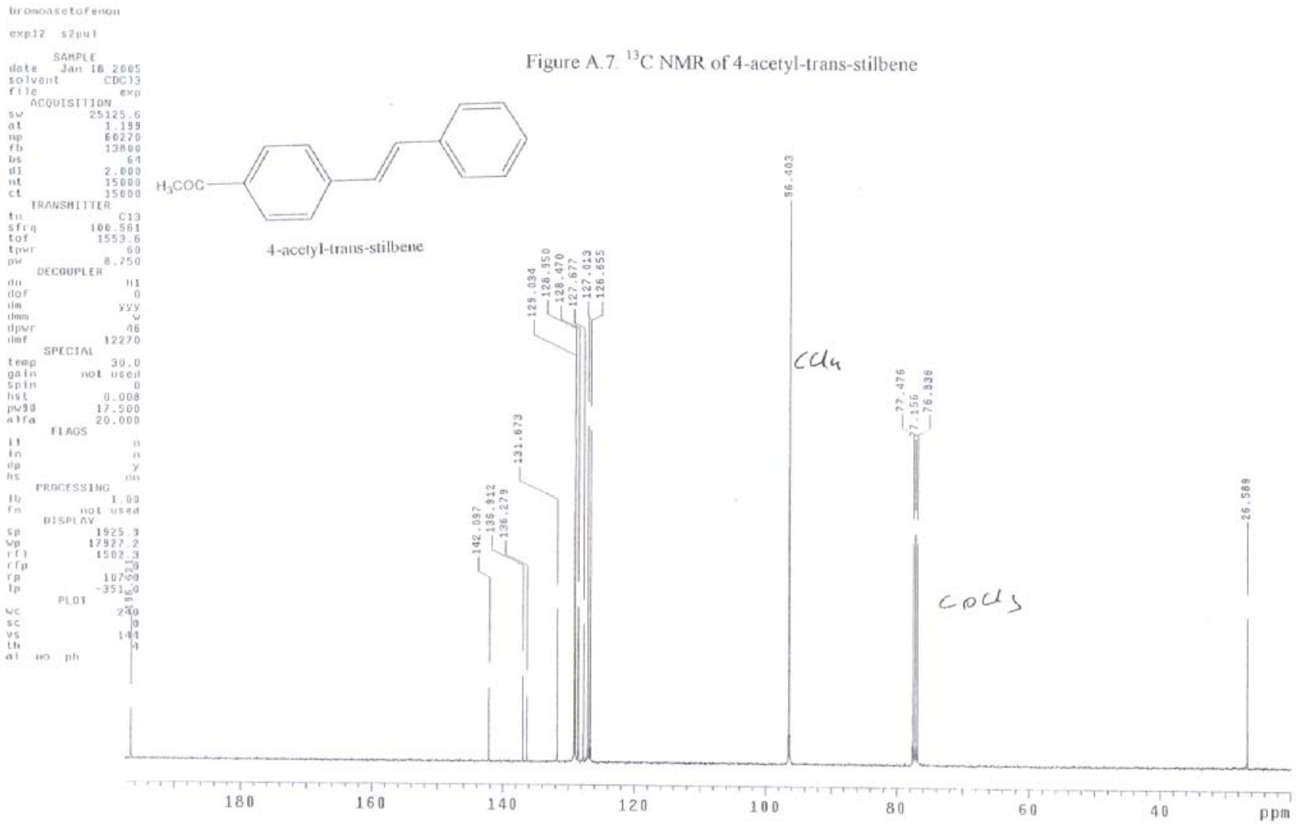


Figure A.6. ^{1}H NMR of 4-methyl-trans-stilbene





```
bromoasetofenon

exp12  s2pul

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file            exp
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np            60270
fb            13800
bs               64
d1            2.000
nt            15000
ct            15000
    TRANSMITTER
tn              C13
sfrq        100.561
tof          1553.6
tpwr             60
pw            8.750
     DECOUPLER
dn               H1
dof               0
dm              yyy
dmm               w
dpwr             46
dmf           12270
      SPECIAL
temp           30.0
gain       not used
spin              0
hst           0.008
pw90         17.500
alfa         20.000
       FLAGS
il                n
in                n
dp                y
hs               nn
    PROCESSING
lb             1.00
fn         not used
      DISPLAY
sp           1925.3
wp          17927.2
rfl          1502.3
rfp               0
rp            107.0
lp           -351.0
       PLOT
wc              250
sc                0
vs              141
th                4
ai   no   ph
```

Figure A.7. ^{13}C NMR of 4-acetyl-trans-stilbene

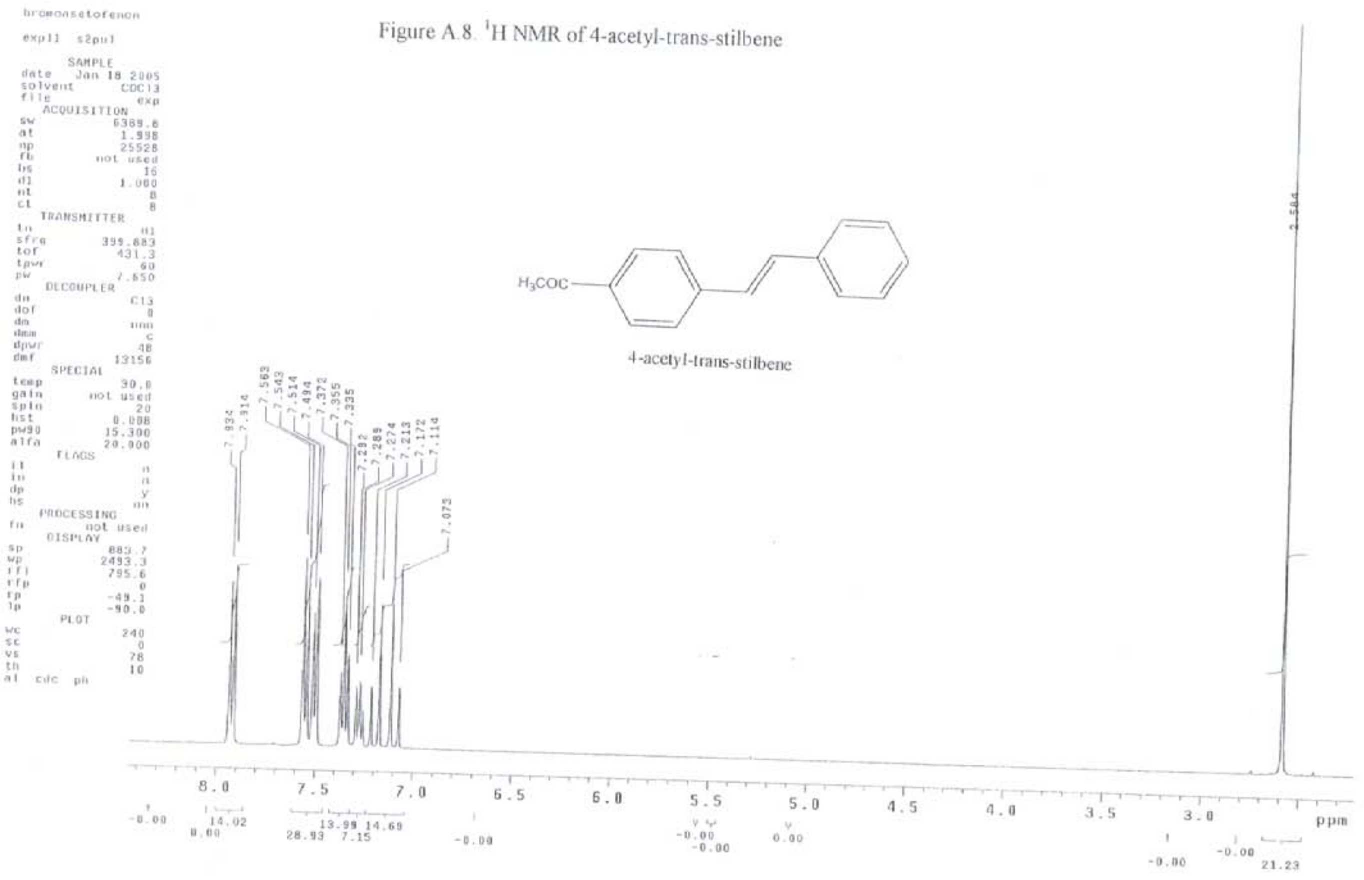

Figure A.8. ^{1}H NMR of 4-acetyl-trans-stilbene

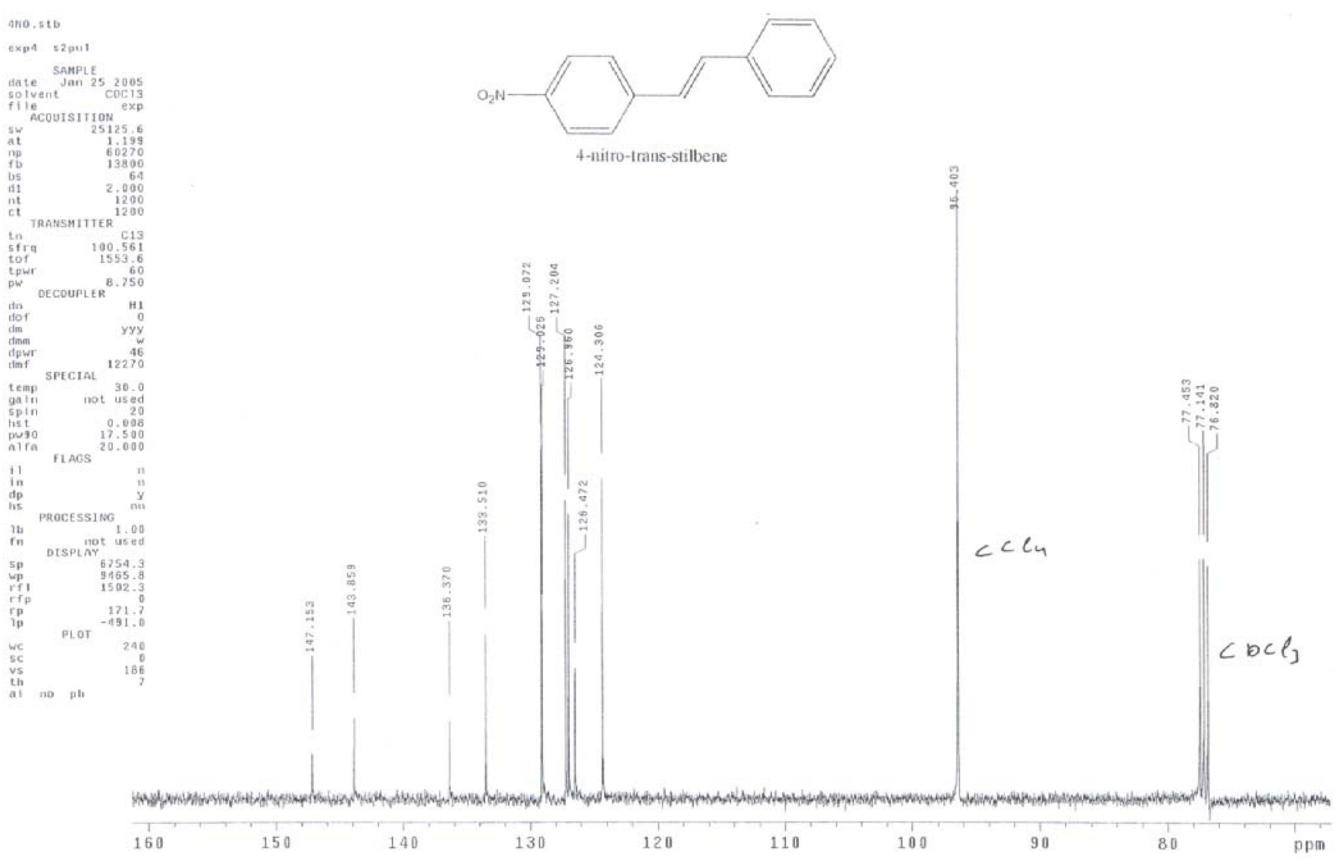

Figure A.9. ^{13}C NMR of 4-nitro-trans-stilbene

```
4NO.stb

exp4  s2pul

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solvent       CDC13
file            exp
     ACQUISITION
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at            1.199
np            60270
fb            13800
bs               64
d1            2.000
nt             1200
ct             1200
     TRANSMITTER
tn              C13
sfrq        100.561
tof          1553.6
tpwr             60
pw            8.750
      DECOUPLER
dn               H1
dof               0
dm              yyy
dmm               w
dpwr             46
dmf           12270
       SPECIAL
temp           30.0
gain       not used
spin             20
hst           0.008
pw90         17.500
alfa         20.000
        FLAGS
il                n
in                n
dp                y
hs               nn
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lb             1.00
fn         not used
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wp           9465.8
rfl          1502.3
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rp            171.7
lp           -491.0
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vs              186
th                7
ai   no   ph
```
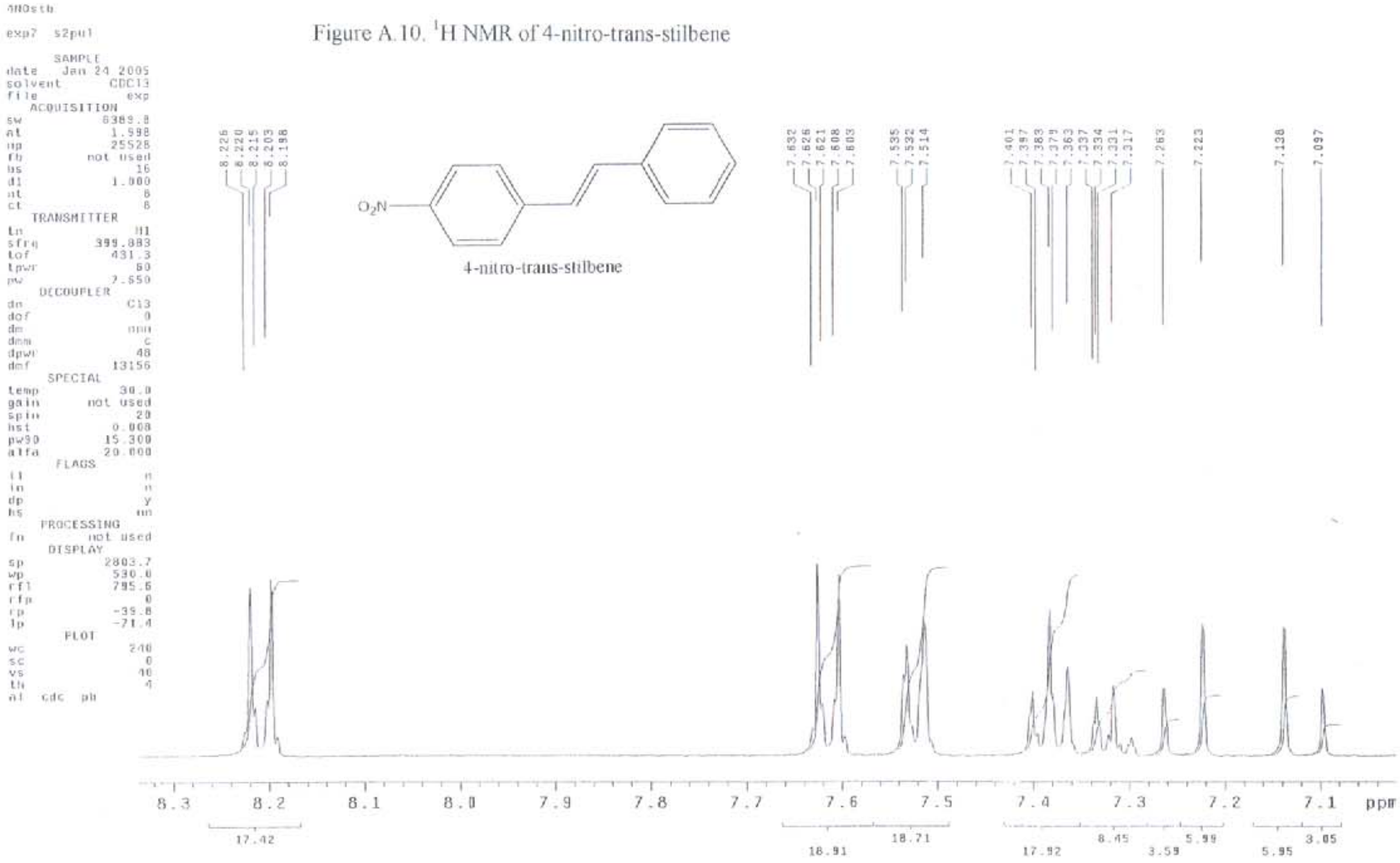

Figure A.10. ^{1}H NMR of 4-nitro-trans-stilbene



```
4NOstb

exp7  s2pul

        SAMPLE
date    Jan 24 2005
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file            exp
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at            1.998
np            25528
fb         not used
bs               16
d1            1.000
nt                8
ct                8
     TRANSMITTER
tn               H1
sfrq        399.883
tof           431.3
tpwr             60
pw            7.650
       DECOUPLER
dn              C13
dof               0
dm              nnn
dmm               c
dpwr             48
dmf           13156
        SPECIAL
temp           30.0
gain       not used
spin             20
hst           0.008
pw90         15.300
alfa         20.000
         FLAGS
il                n
in                n
dp                y
hs               nn
      PROCESSING
fn         not used
        DISPLAY
sp           2803.7
wp            530.0
rfl           795.6
rfp               0
rp            -35.8
lp            -71.4
          PLOT
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sc                0
vs               40
th                4
ai   cdc   ph
```

Figure A.11. ^{13}C NMR of trans-3-styrylpyridine

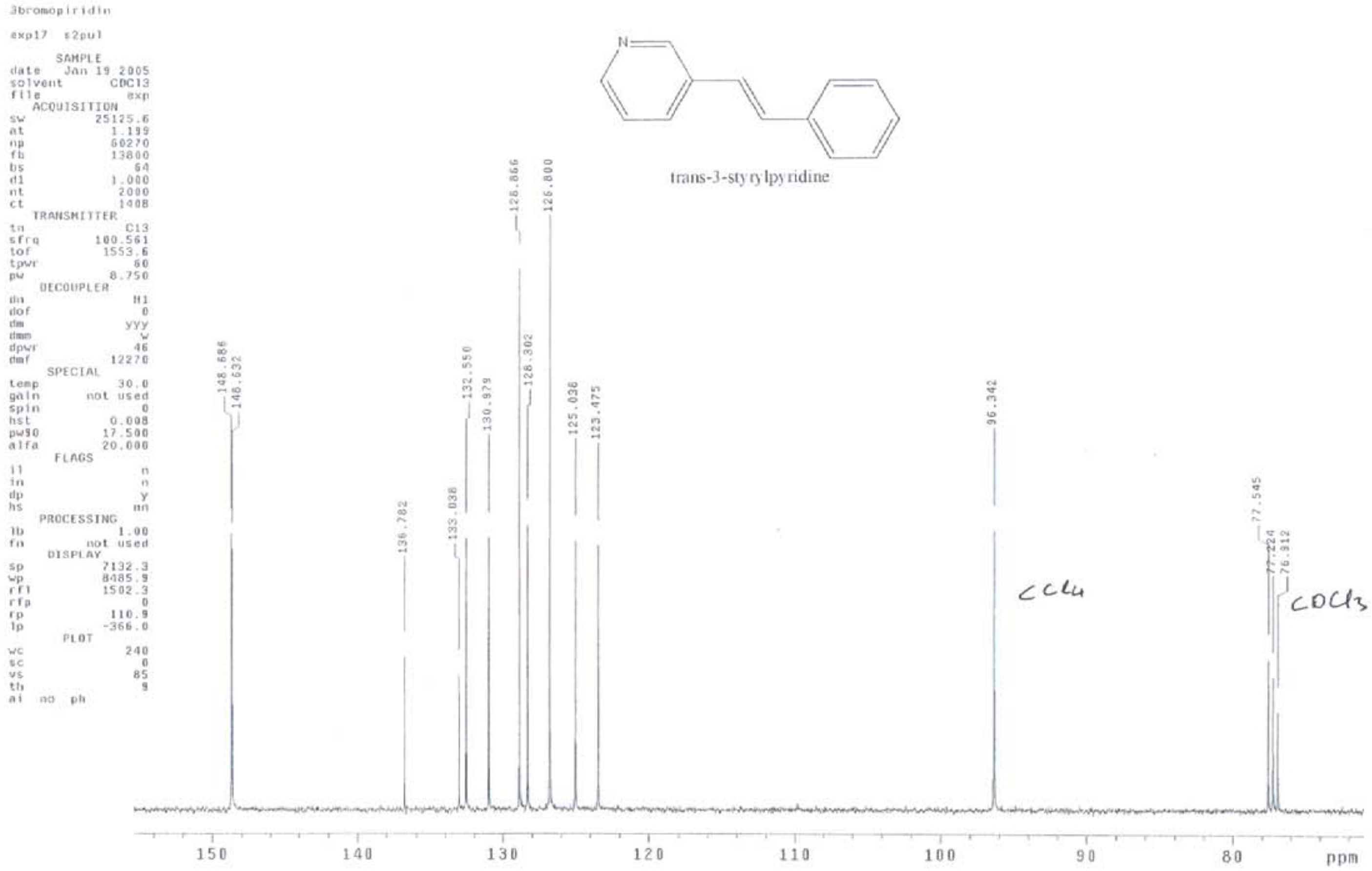
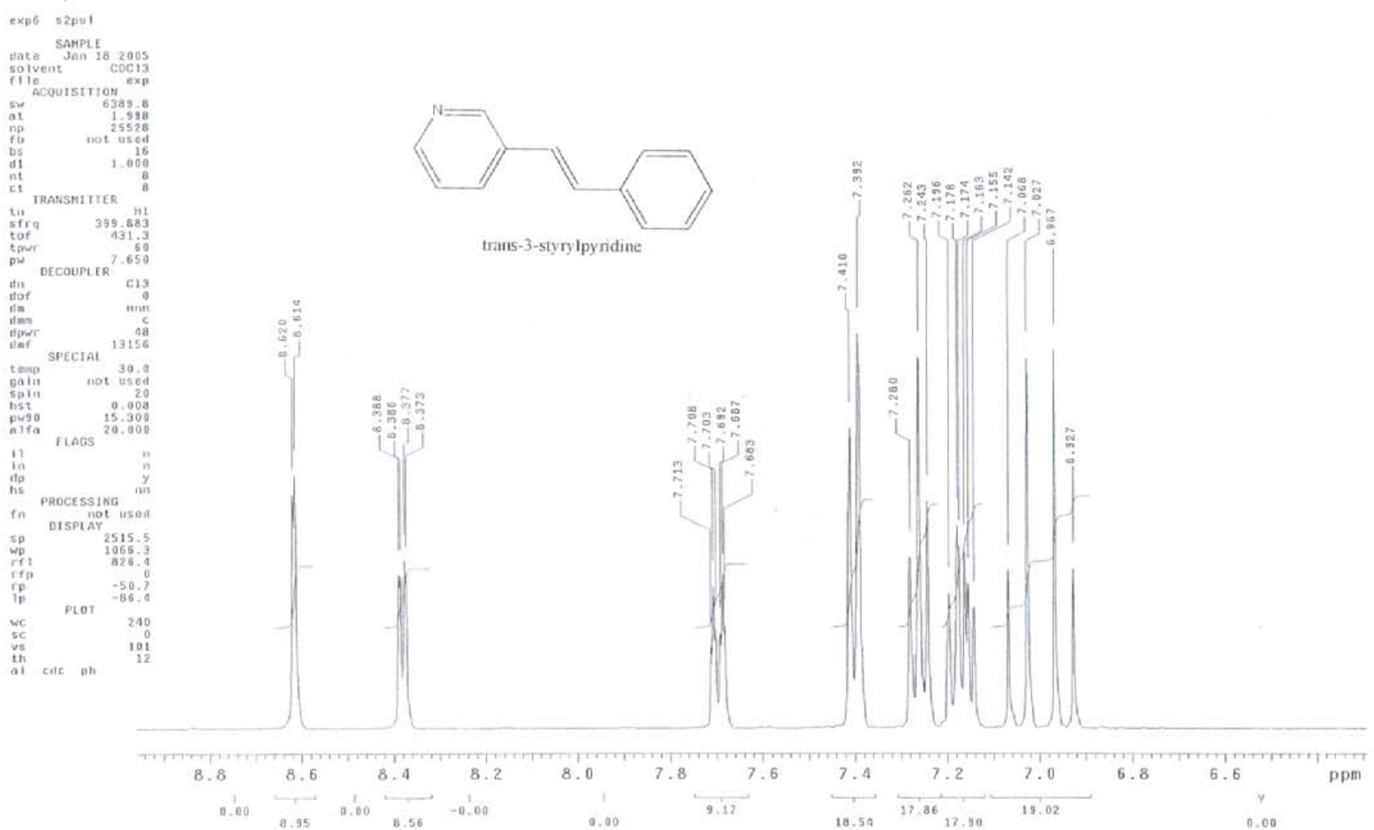


Figure A.12. ^{1}H NMR of trans-3-styrylpyridine



```
3 bromopiridin

exp6  s2pul

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np           25528
fb        not used
bs              16
d1           1.000
nt               8
ct               8
    TRANSMITTER
tn              H1
sfrq       399.883
tof          431.3
tpwr            60
pw           7.650
     DECOUPLER
dn             C13
dof              0
dm             nnn
dmm              c
dpwr            48
dmf          13156
      SPECIAL
temp          30.0
gain      not used
spin            20
hst          0.008
pw90        15.300
alfa        20.000
       FLAGS
il               n
in               n
dp               y
hs              nn
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fn        not used
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wp          1066.3
rfl          826.4
rfp              0
rp           -50.7
lp           -86.4
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wc             240
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vs             101
th              12
ai   cdc   ph
```
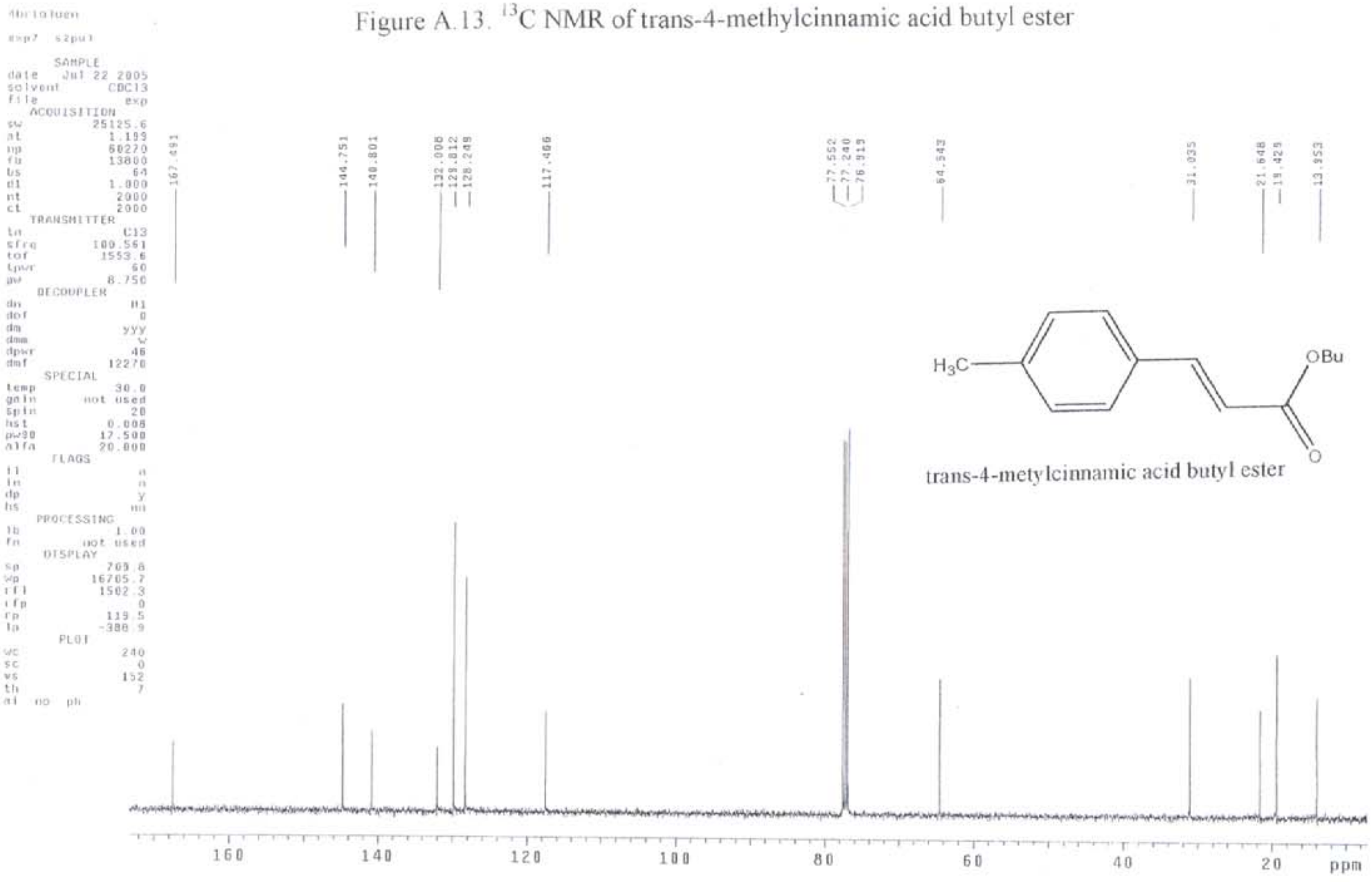

Figure A.13. ${}^{13}C$ NMR of trans-4-methylcinnamic acid butyl ester



```
4brtoluen

exp7  s2pul

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np            60270
fb            13800
bs               64
d1            1.000
nt             2000
ct             2000
     TRANSMITTER
tn              C13
sfrq        100.561
tof          1553.6
tpwr             60
pw            8.750
      DECOUPLER
dn               H1
dof               0
dm              yyy
dmm               w
dpwr             46
dmf           12270
       SPECIAL
temp           30.0
gain       not used
spin             20
hst           0.008
pw90         17.500
alfa         20.000
        FLAGS
il                n
in                n
dp                y
hs               nn
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sp            709.8
wp          16705.7
rfl          1502.3
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ai   no   ph
```
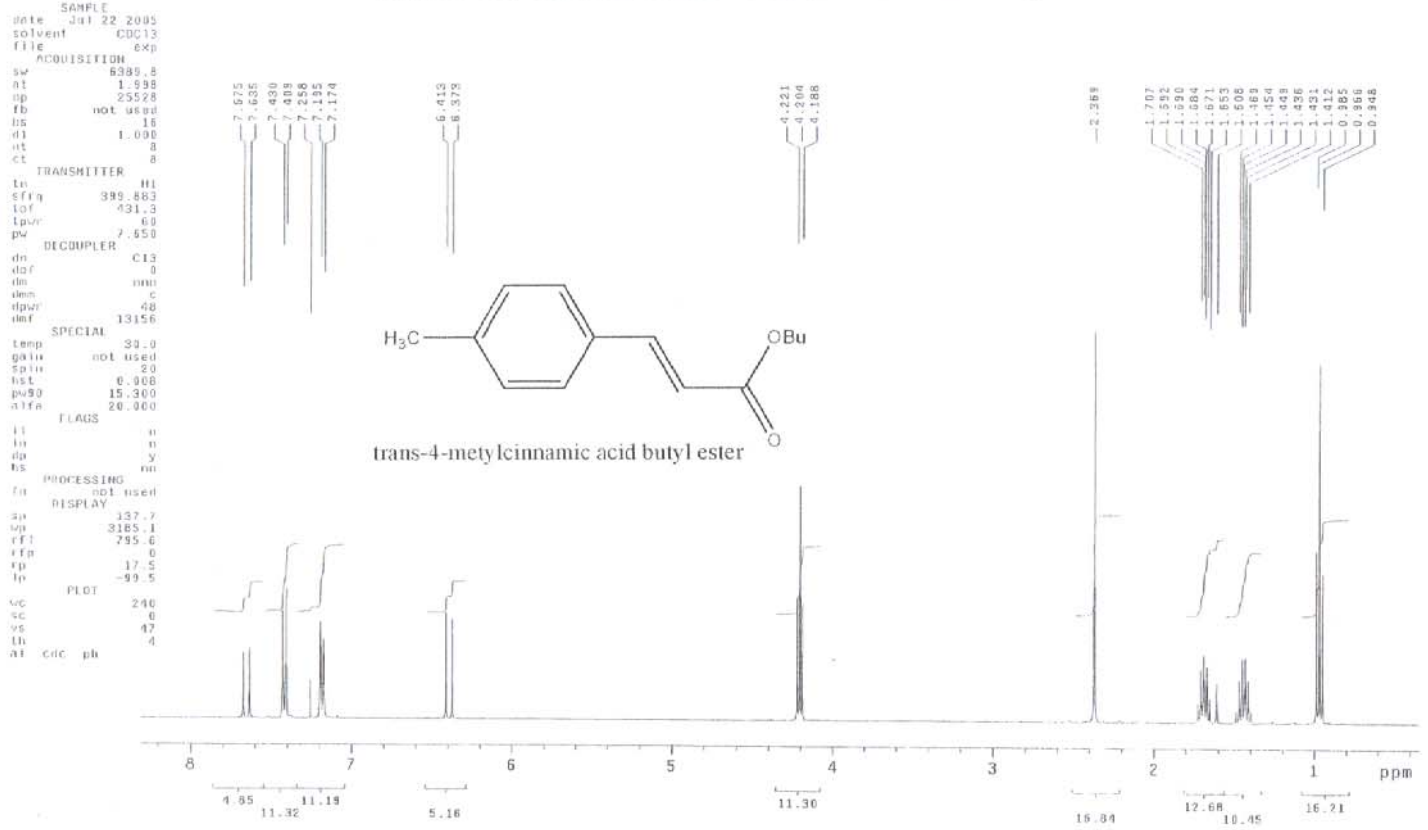

Figure A.14. ¹H NMR of trans-4-methylcinnamic acid butyl ester



```
48rtoluen

exp7  s2pul

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np           25528
fb        not used
bs              16
d1           1.000
nt               8
ct               8
     TRANSMITTER
tn              H1
sfrq       399.883
tof          431.3
tpwr            60
pw           7.650
      DECOUPLER
dn             C13
dof              0
dm             nnn
dmm              c
dpwr            48
dmf          13156
       SPECIAL
temp          30.0
gain      not used
spin            20
hst          0.008
pw90        15.300
alfa        20.000
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in               n
dp               y
hs              nn
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th               4
ai   cdc   ph
```

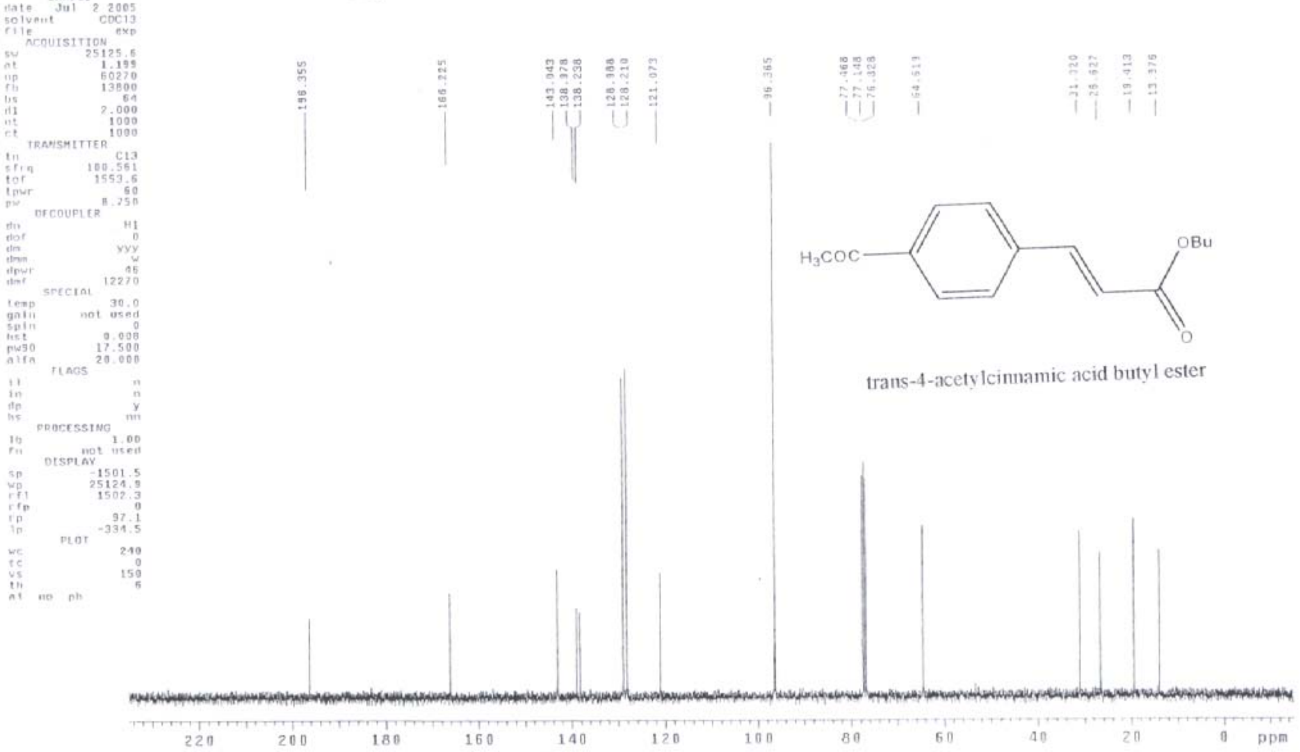
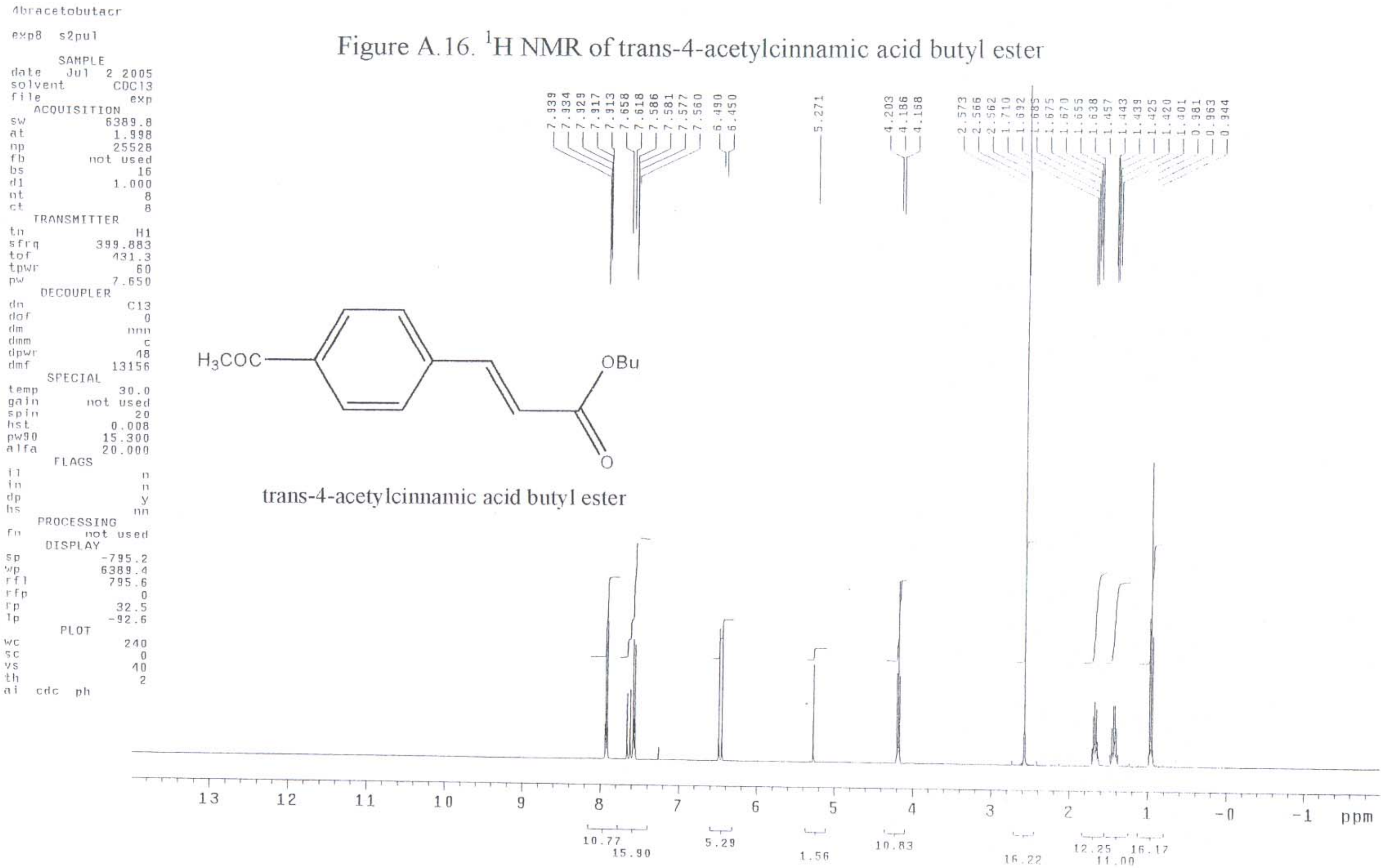


Figure A.15. ^{13}C NMR of trans-4-acetylcinnamic acid butyl ester

trans-4-acetylcinnamic acid butyl ester

Figure A.16. ^{1}H NMR of trans-4-acetylcinnamic acid butyl ester



```
4bracetobutacr

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np            25528
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bs               16
d1            1.000
nt                8
ct                8
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tn               H1
sfrq        399.883
tof           431.3
tpwr             60
pw            7.650
     DECOUPLER
dn              C13
dof               0
dm              nnn
dmm               c
dpwr             48
dmf           13156
      SPECIAL
temp           30.0
gain       not used
spin             20
hst           0.008
pw90         15.300
alfa         20.000
       FLAGS
il                n
in                n
dp                y
hs               nn
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fn         not used
     DISPLAY
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wp           6389.4
rfl           795.6
rfp               0
rp             32.5
lp            -92.6
        PLOT
wc              240
sc                0
vs               40
th                2
ai   cdc   ph
```
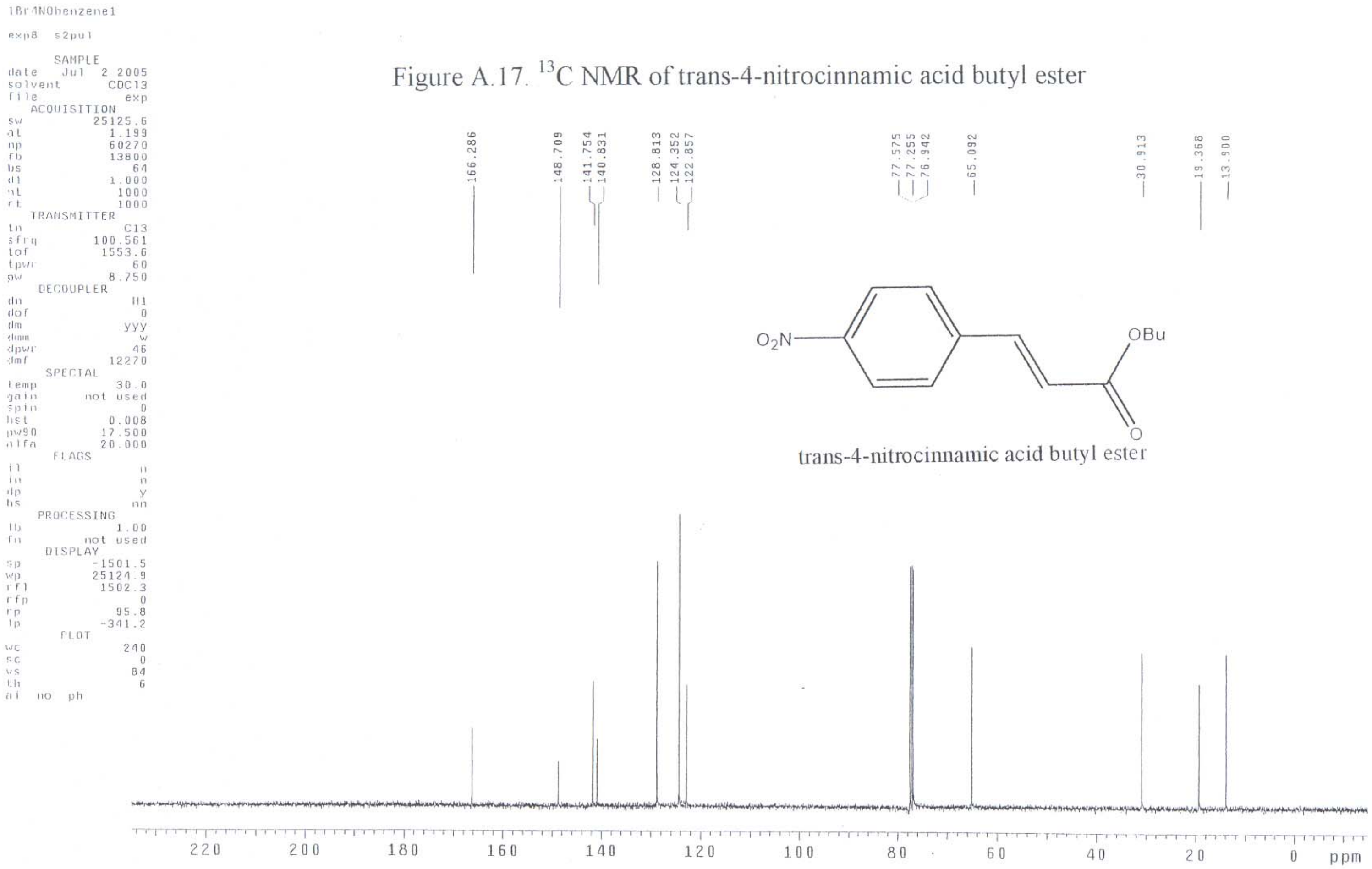

Figure A.17. ^{13}C NMR of trans-4-nitrocinnamic acid butyl ester



```
1Br4NObenzene1

exp8   s2pul

        SAMPLE
date    Jul  2 2005
solvent       CDC13
file            exp
     ACQUISITION
sw          25125.6
at            1.199
np            60270
fb            13800
bs               64
d1            1.000
nt             1000
ct             1000
     TRANSMITTER
tn              C13
sfrq        100.561
tof          1553.6
tpwr             60
pw            8.750
      DECOUPLER
dn               H1
dof               0
dm              yyy
dmm               w
dpwr             46
dmf           12270
       SPECIAL
temp           30.0
gain       not used
spin              0
hst           0.008
pw90         17.500
alfa         20.000
        FLAGS
il                n
in                n
dp                y
hs               nn
      PROCESSING
lb             1.00
fn         not used
       DISPLAY
sp          -1501.5
wp          25124.9
rfl          1502.3
rfp               0
rp             95.8
lp           -341.2
         PLOT
wc              240
sc                0
vs               84
th                6
ai   no   ph
```

trans-4-nitrocinnamic acid butyl ester

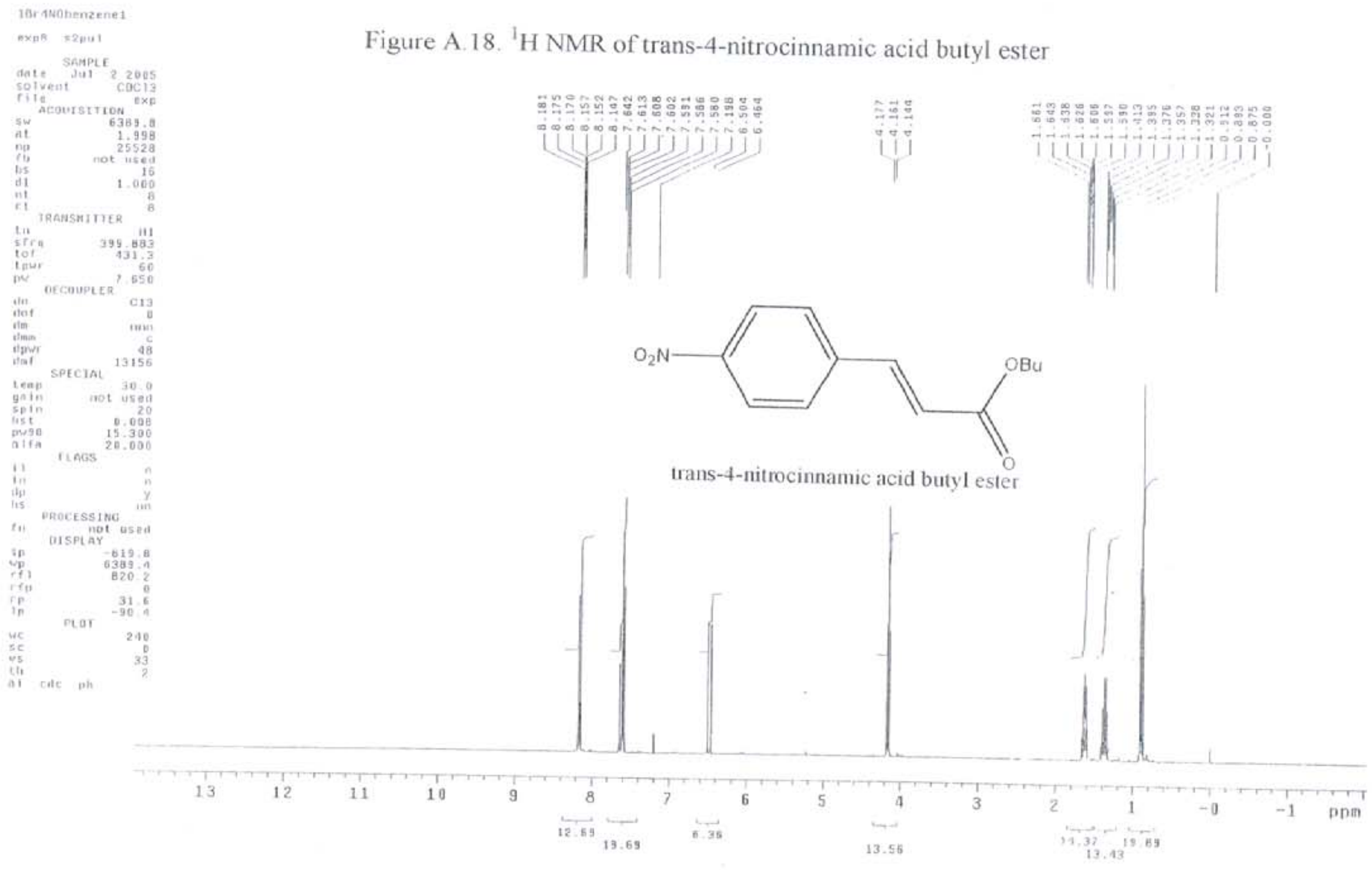
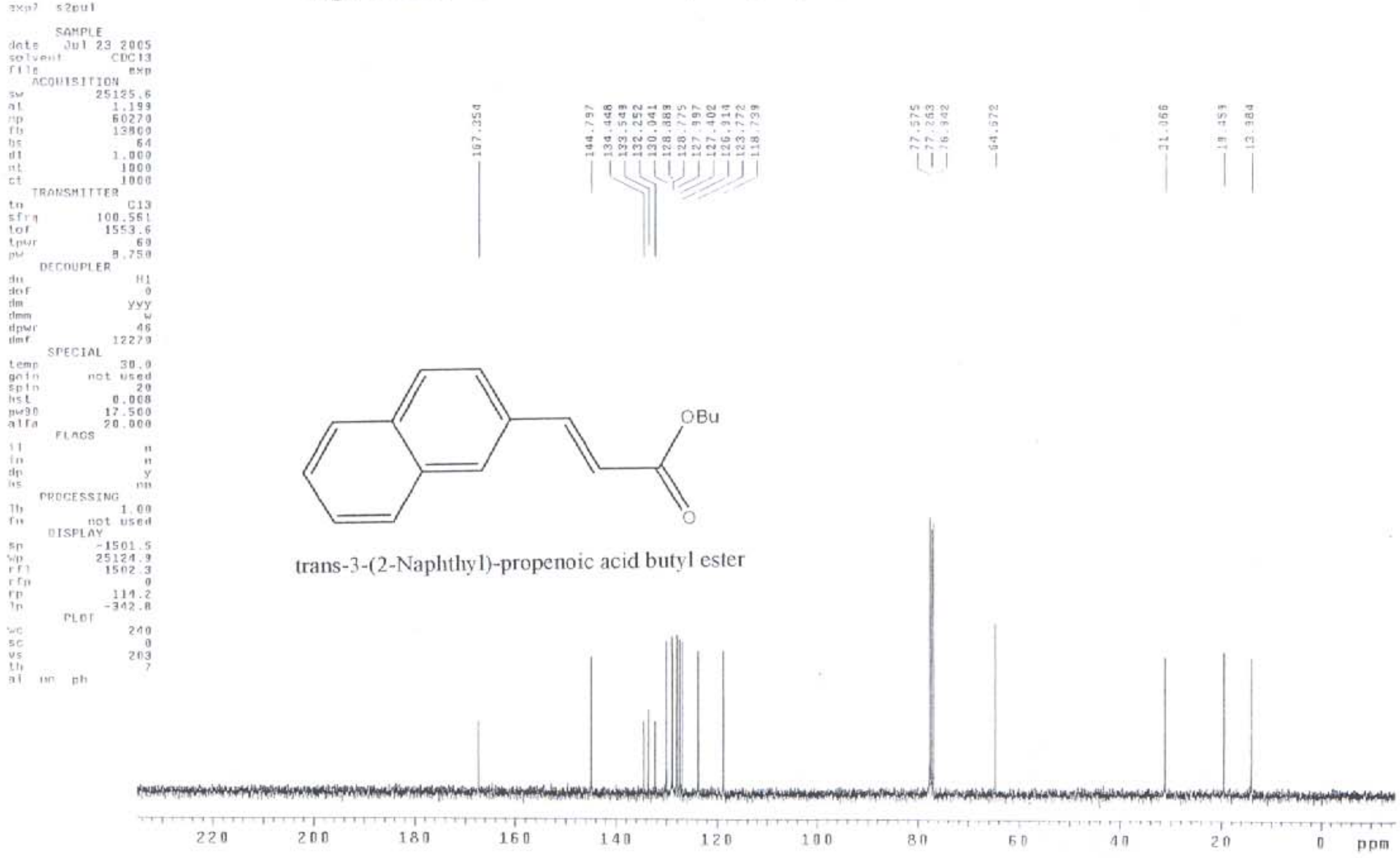


Figure A.18. ^{1}H NMR of trans-4-nitrocinnamic acid butyl ester

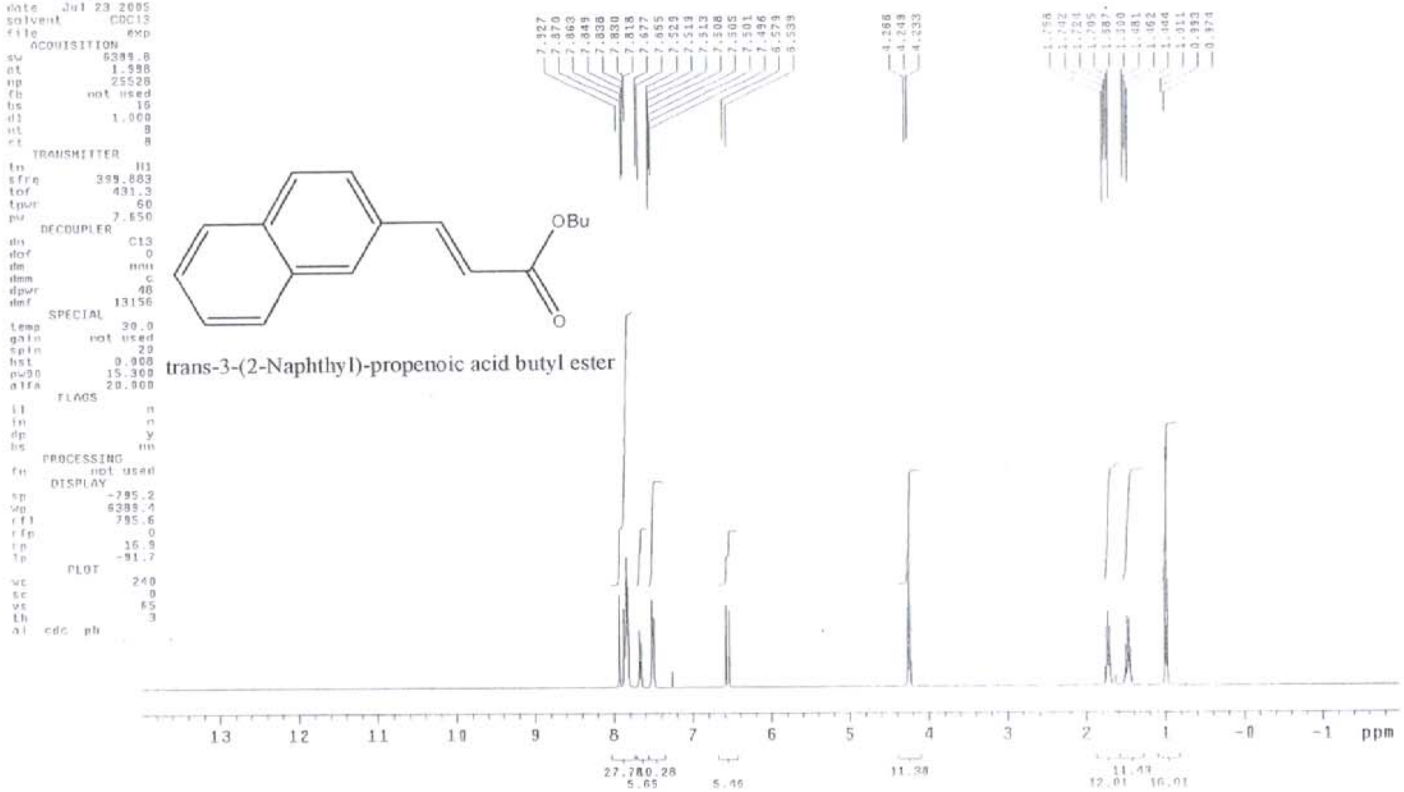
Figure A.19. ^{13}C NMR of trans-3-(2-Naphthyl)-propenoic acid butyl ester



trans-3-(2-Naphthyl)-propenoic acid butyl ester

```
2BrNapButAc

exp7  s2pul

      SAMPLE
date    Jul 23 2005
solvent       CDC13
file            exp
   ACQUISITION
sw          25125.6
at            1.199
np            60270
fb            13800
bs               64
d1            1.000
nt             1000
ct             1000
   TRANSMITTER
tn              C13
sfrq        100.561
tof          1553.6
tpwr             60
pw            8.750
    DECOUPLER
dn               H1
dof               0
dm              yyy
dmm               w
dpwr             46
dmf           12279
     SPECIAL
temp           30.0
gain       not used
spin             20
hst           0.008
pw90         17.500
alfa         20.000
      FLAGS
il                n
in                n
dp                y
hs               nn
   PROCESSING
lb             1.00
fn         not used
     DISPLAY
sp          -1501.5
wp          25124.9
rfl          1502.3
rfp               0
rp            114.2
lp           -342.8
       PLOT
wc              240
sc                0
vs              203
th                7
ai  nm  ph
```

Figure A.20. ^{1}H NMR of trans-3-(2-Naphthyl)-propenoic acid butyl ester



```
2BrNapButAc

exp7  s2pul

      SAMPLE
date   Jul 23 2005
solvent      CDCl3
file           exp
   ACQUISITION
sw          6389.8
at           1.998
np           25528
fb        not used
bs              16
d1           1.000
nt               8
ct               8
    TRANSMITTER
tn              H1
sfrq       399.883
tof          431.3
tpwr            60
pw           7.650
     DECOUPLER
dn             C13
dof              0
dm             nnn
dmm              c
dpwr            48
dmf          13156
      SPECIAL
temp          30.0
gain      not used
spin            20
hst          0.008
pw90        15.300
alfa        20.000
       FLAGS
il               n
in               n
dp               y
hs              nn
    PROCESSING
fn        not used
      DISPLAY
sp          -795.2
wp          6389.4
rfl          795.6
rfp              0
rp            16.9
lp           -91.7
        PLOT
wc             240
sc               0
vs              65
th               3
ai   cdc   ph
```

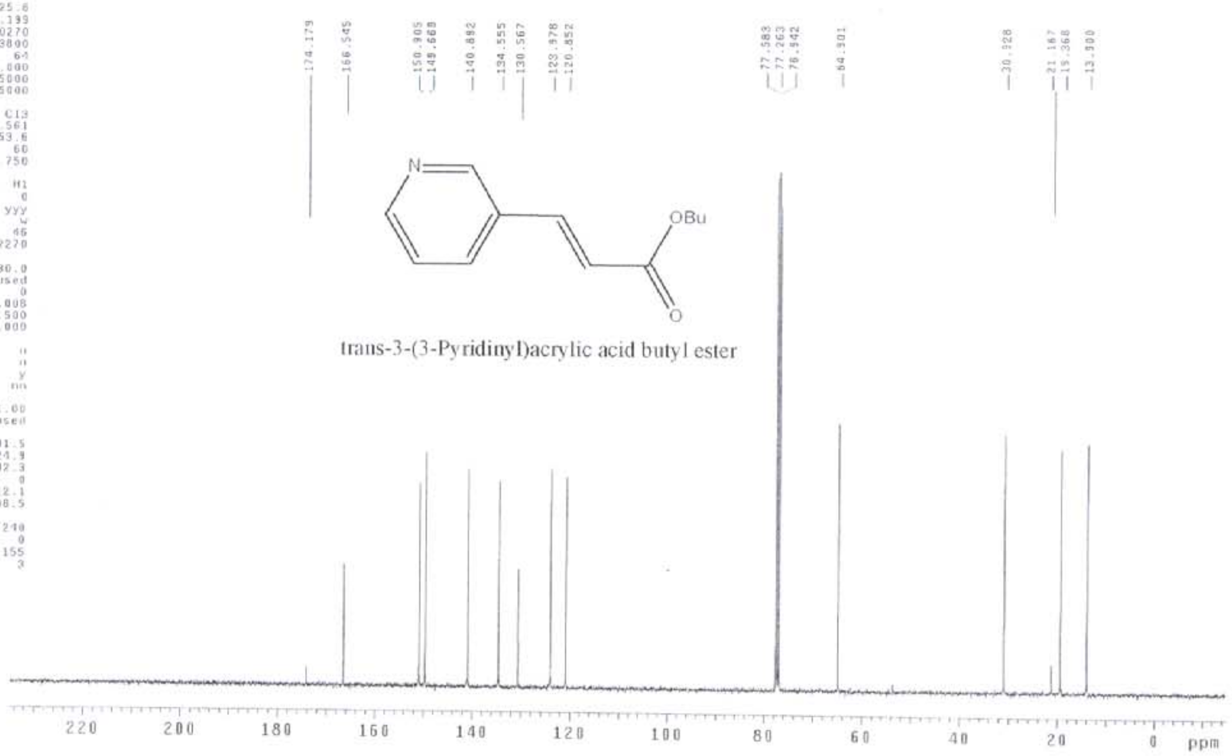


Figure A.21. ^{13}C NMR of trans-3-(3-Pyridinyl)acrylic acid butyl ester

```
3Brpridine

exp7  s2pul

      SAMPLE
date   Jul 22 2005
solvent      CDCl3
file           exp
   ACQUISITION
sw         25125.6
at           1.199
np           60270
fb           13800
bs              64
d1           2.000
nt            5000
ct            5000
   TRANSMITTER
tn             C13
sfrq       100.561
tof         1553.6
tpwr            60
pw           8.750
    DECOUPLER
dn              H1
dof              0
dm             yyy
dmm              w
dpwr            46
dmf          12270
     SPECIAL
temp          30.0
gain      not used
spin             0
hst          0.008
pw90        17.500
alfa        20.000
      FLAGS
il               n
in               n
dp               y
hs              nn
   PROCESSING
lb            1.00
fn        not used
     DISPLAY
sp         -1501.5
wp         25124.9
rfl         1502.3
rfp              0
rp           112.1
lp          -348.5
       PLOT
wc             240
sc               0
vs             155
th               3
ai   no   ph
```

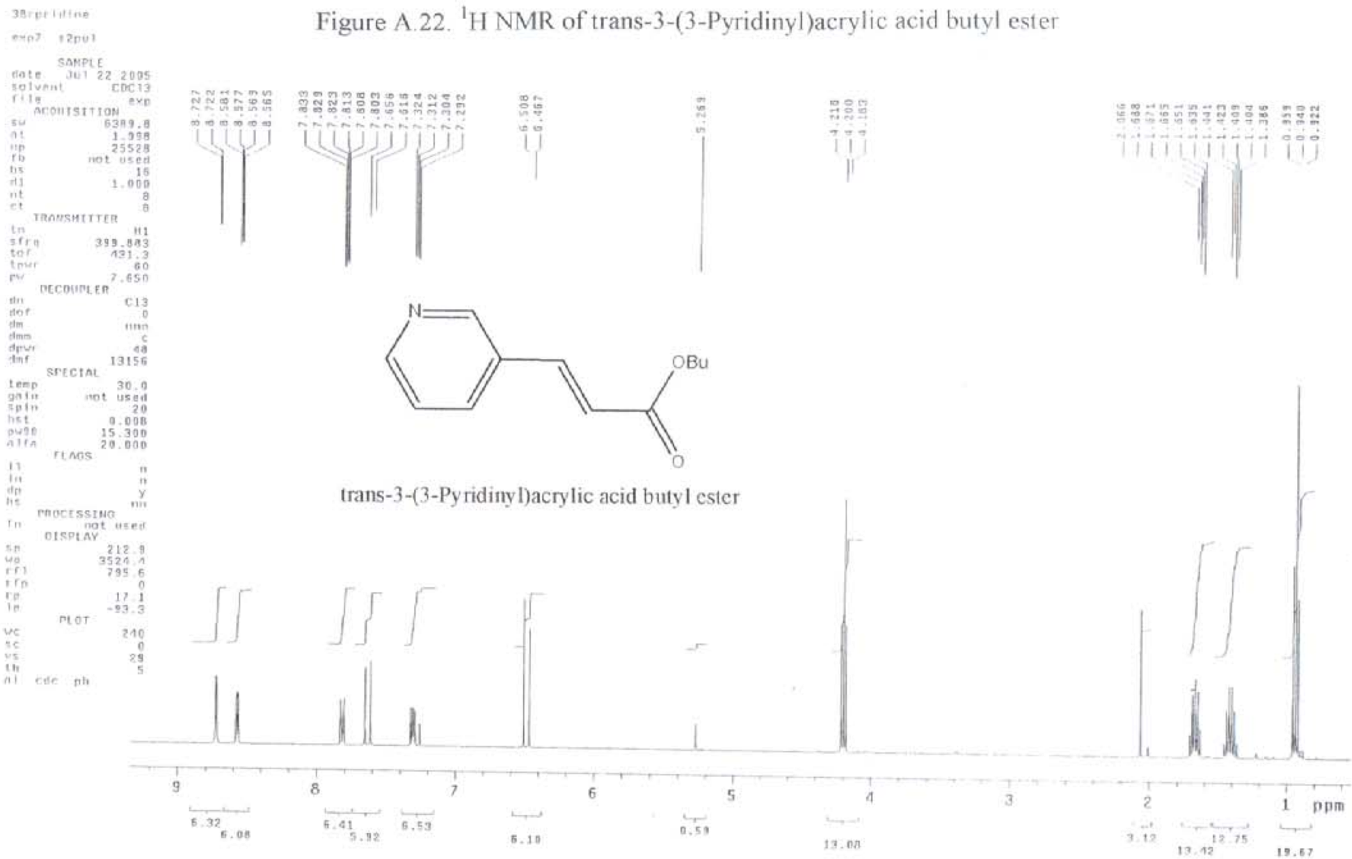
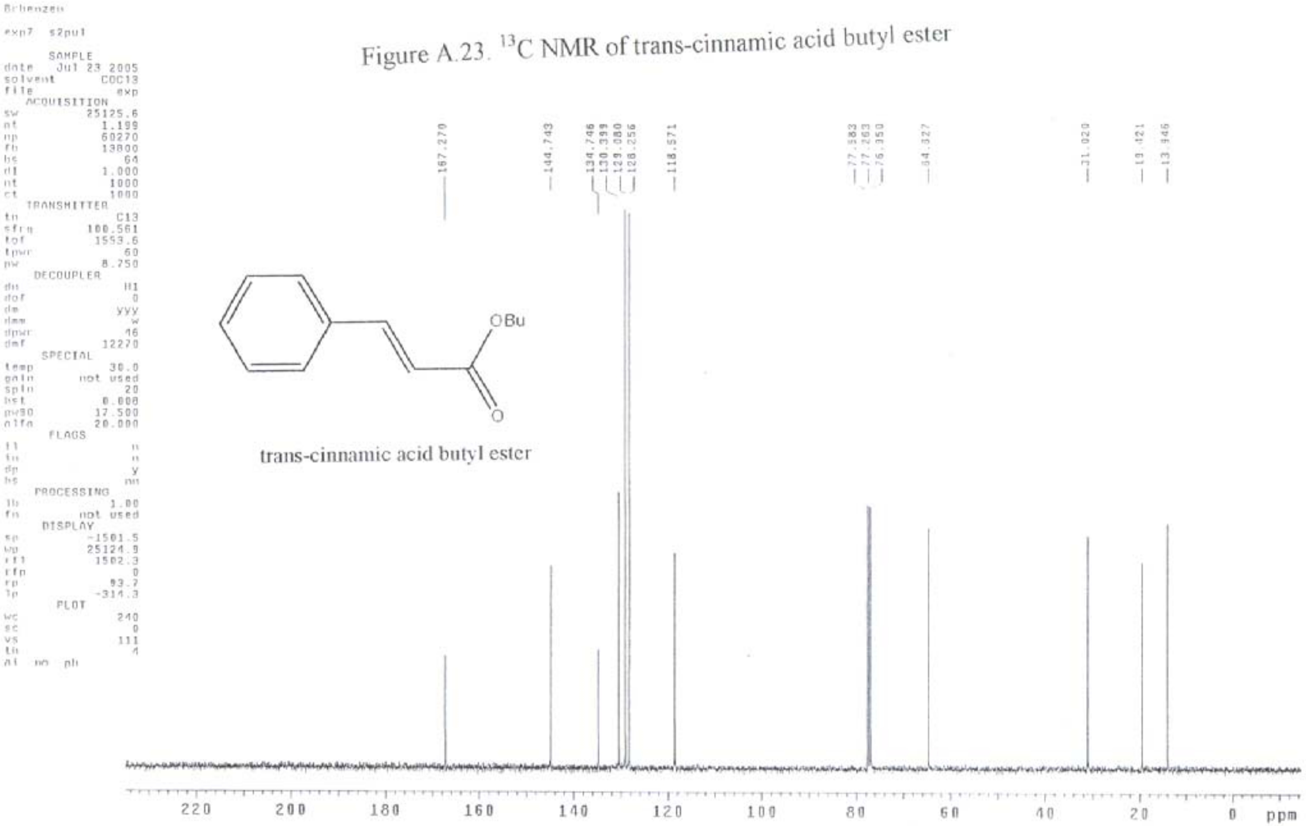


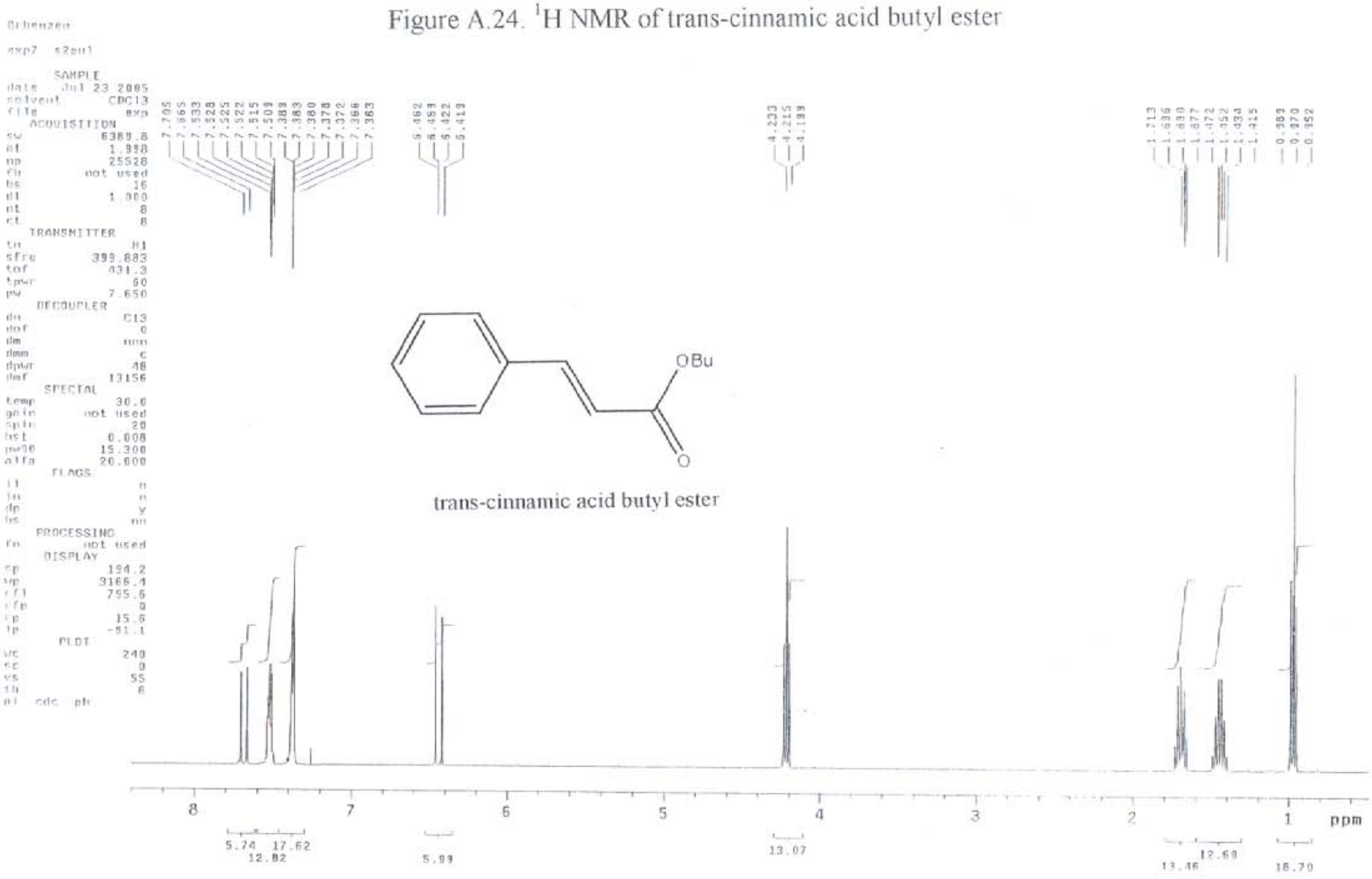
Figure A.22. ^{1}H NMR of trans-3-(3-Pyridinyl)acrylic acid butyl ester

Figure A.23. ^{13}C NMR of trans-cinnamic acid butyl ester



```
Brbenzen

exp7  s2pul

      SAMPLE
date    Jul 23 2005
solvent       CDCl3
file            exp
    ACQUISITION
sw          25125.6
at            1.199
np            60270
fb            13800
bs               64
d1            1.000
nt             1000
ct             1000
    TRANSMITTER
tn              C13
sfrq        100.561
tof          1553.6
tpwr             60
pw            8.750
     DECOUPLER
dn               H1
dof               0
dm              yyy
dmm               w
dpwr             46
dmf           12270
      SPECIAL
temp           30.0
gain       not used
spin             20
hst           0.008
pw90         17.500
alfa         20.000
       FLAGS
il                n
in                n
dp                y
hs               nn
     PROCESSING
lb             1.00
fn         not used
      DISPLAY
sp          -1501.5
wp          25124.9
rfl          1502.3
rfp               0
rp             93.7
lp           -314.3
        PLOT
wc              240
sc                0
vs              111
th                4
ai  no  ph
```

Figure A.24. ¹H NMR of trans-cinnamic acid butyl ester


trans-cinnamic acid butyl ester

APPENDIX B

MASS SPECTRUMS of MIZOROKI-HECK COUPLING PRODUCTS

Figure B.1. Mass Spectrum of trans-4-methoxystilbene

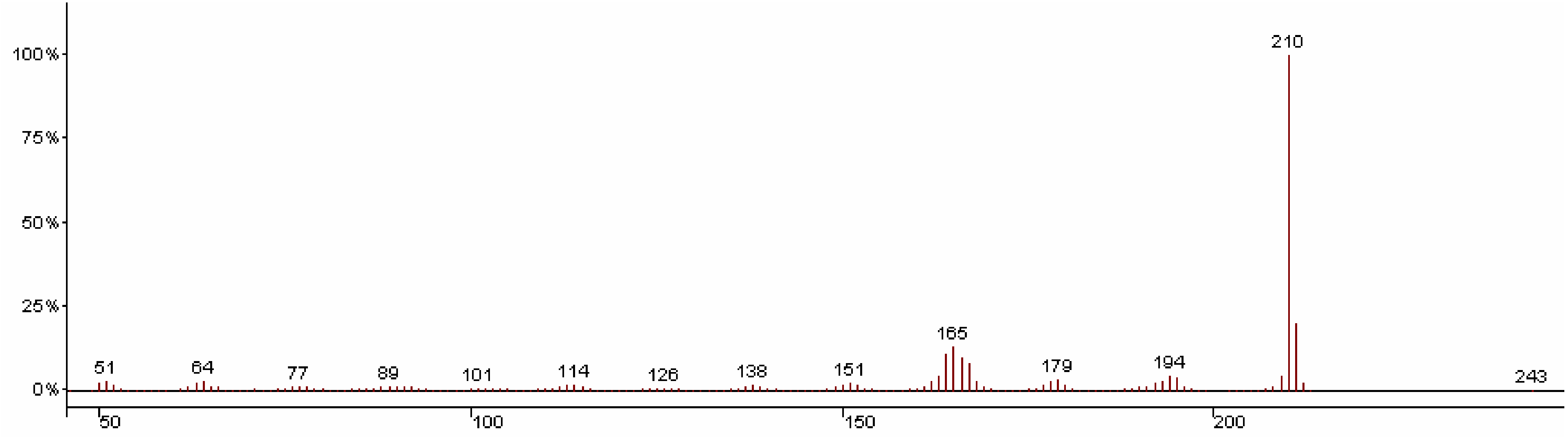


Figure B.2. Mass Spectrum of trans-2-methoxystilbene

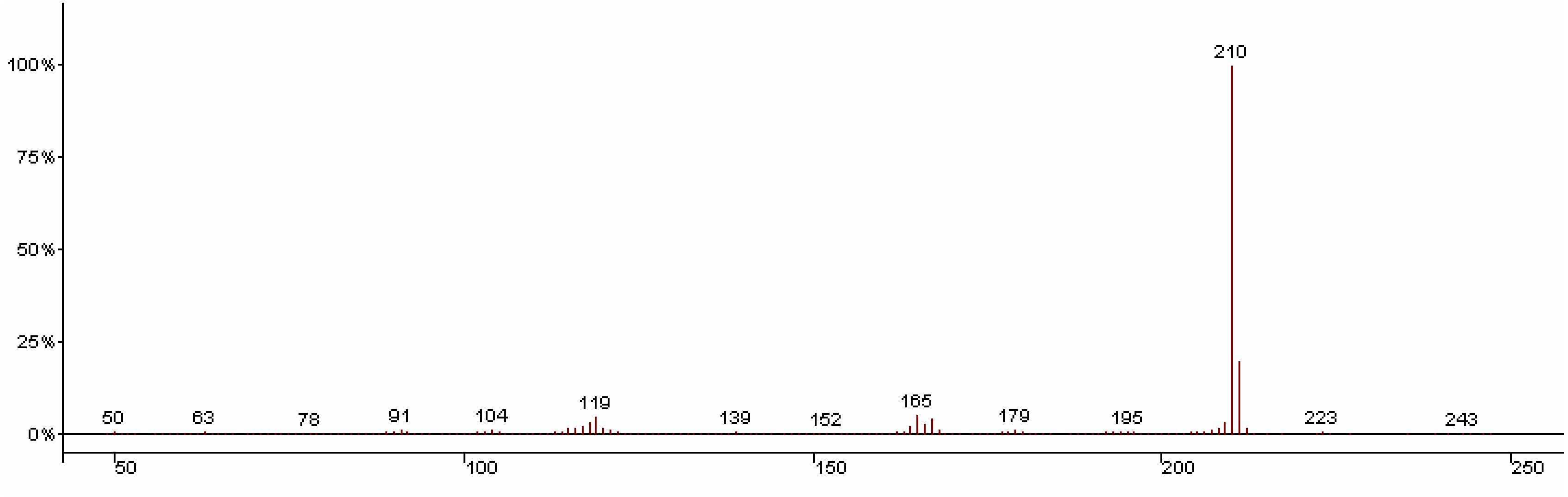


Figure B.3. Mass Spectrum of 3-Styrylpyridine

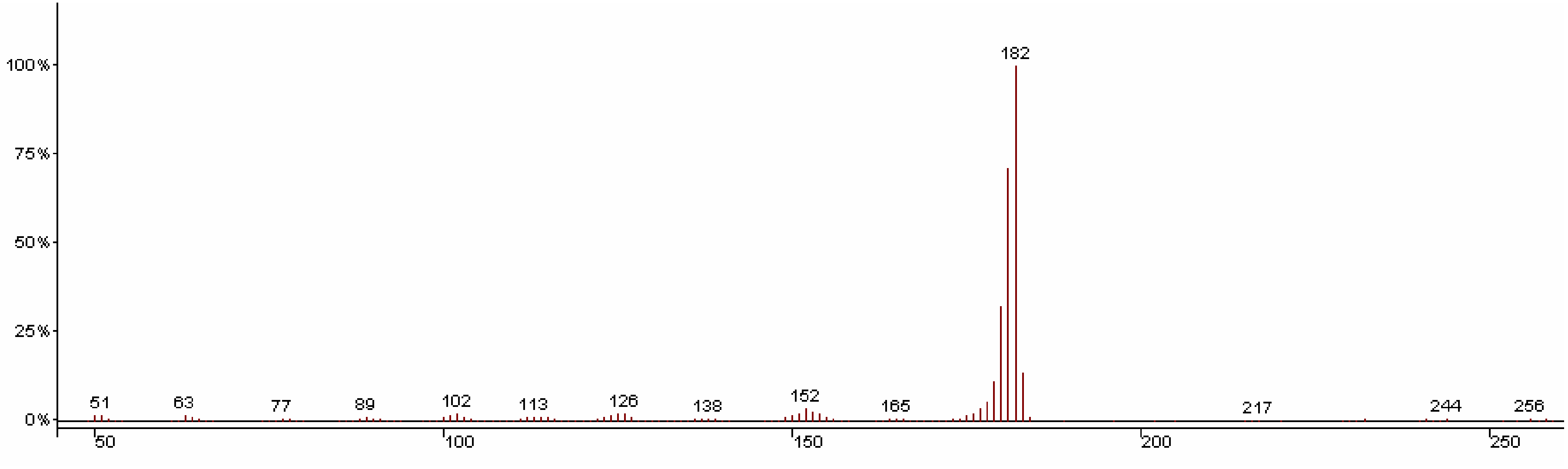


Figure B.4. Mass Spectrum of trans-4-Nitrostilbene

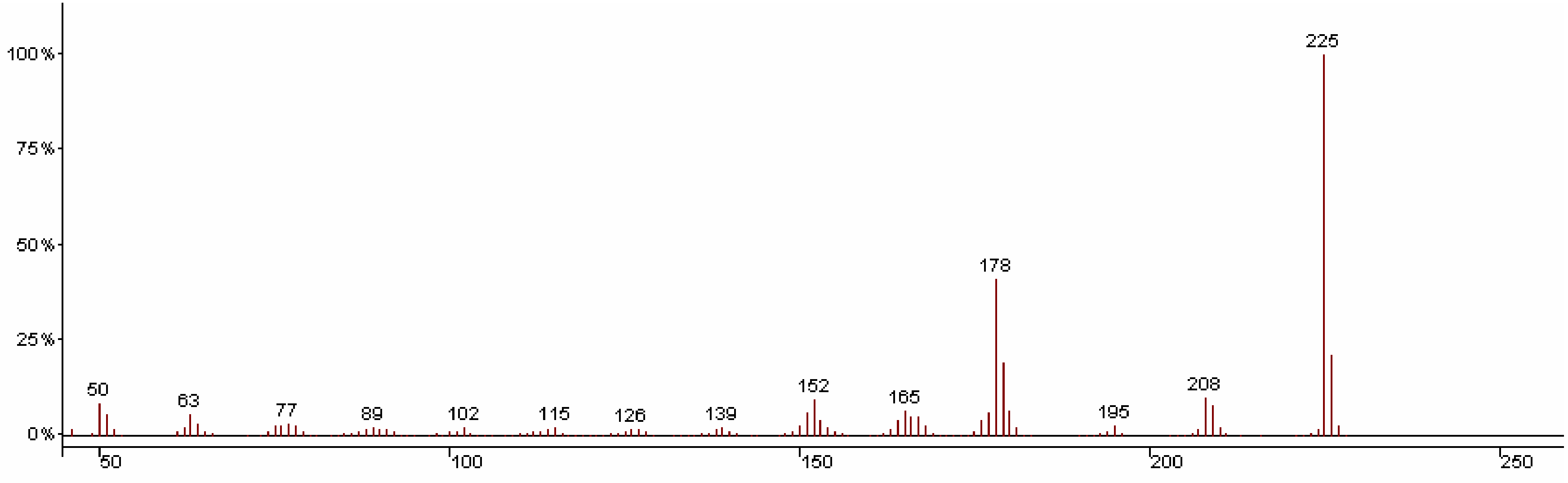


Figure B.5. Mass Spectrum of trans-4-Acetylstilbene

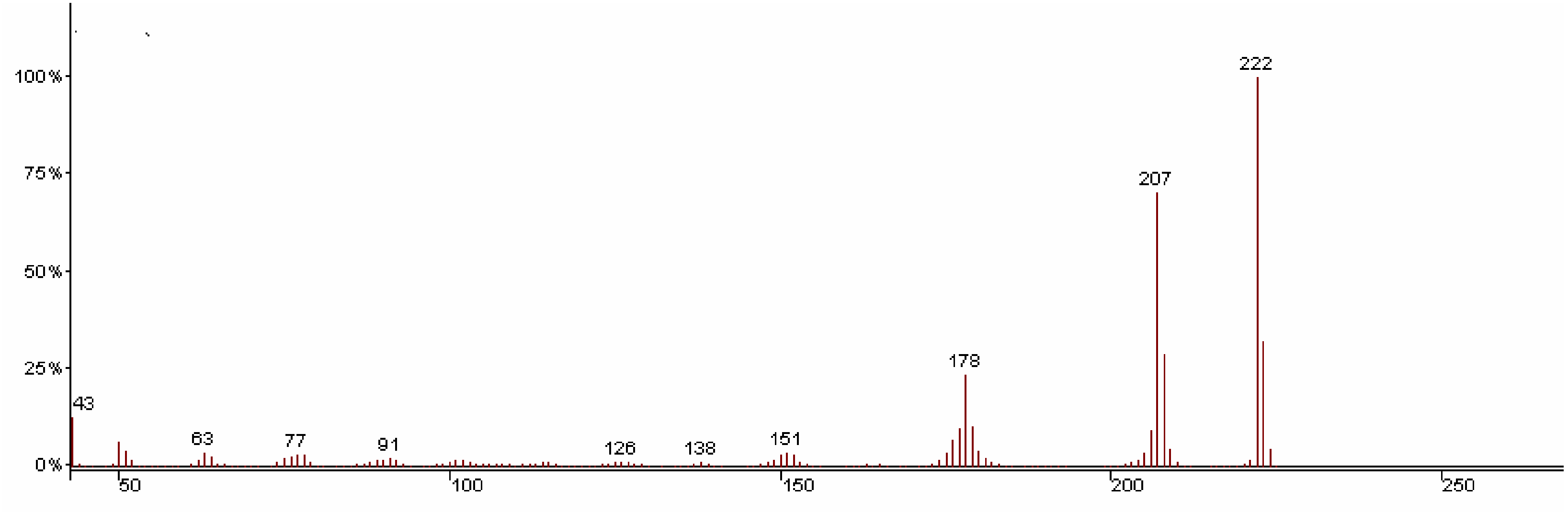


Figure B.6. Mass Spectrum of trans-4-methylstilbene

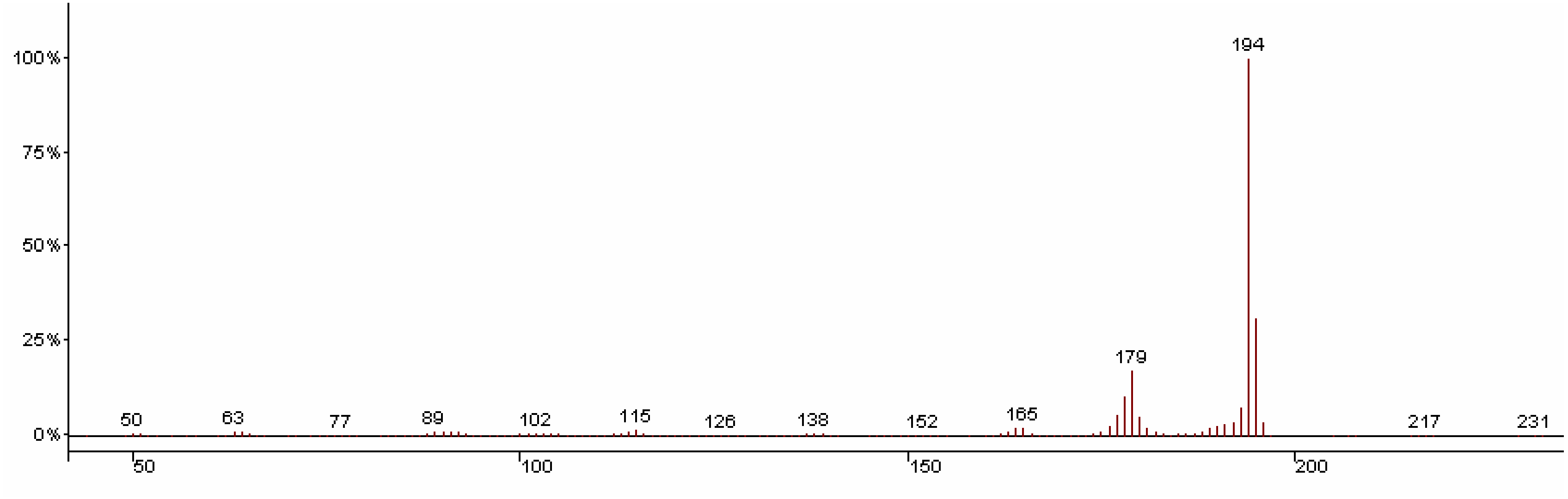
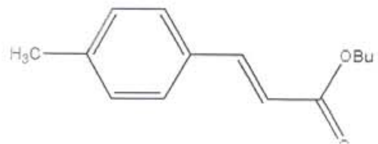


Figure B.7. Mass spectrum of trans-4-methylcinnamic acid butyl ester



trans-4-metylcinnamic acid butyl ester

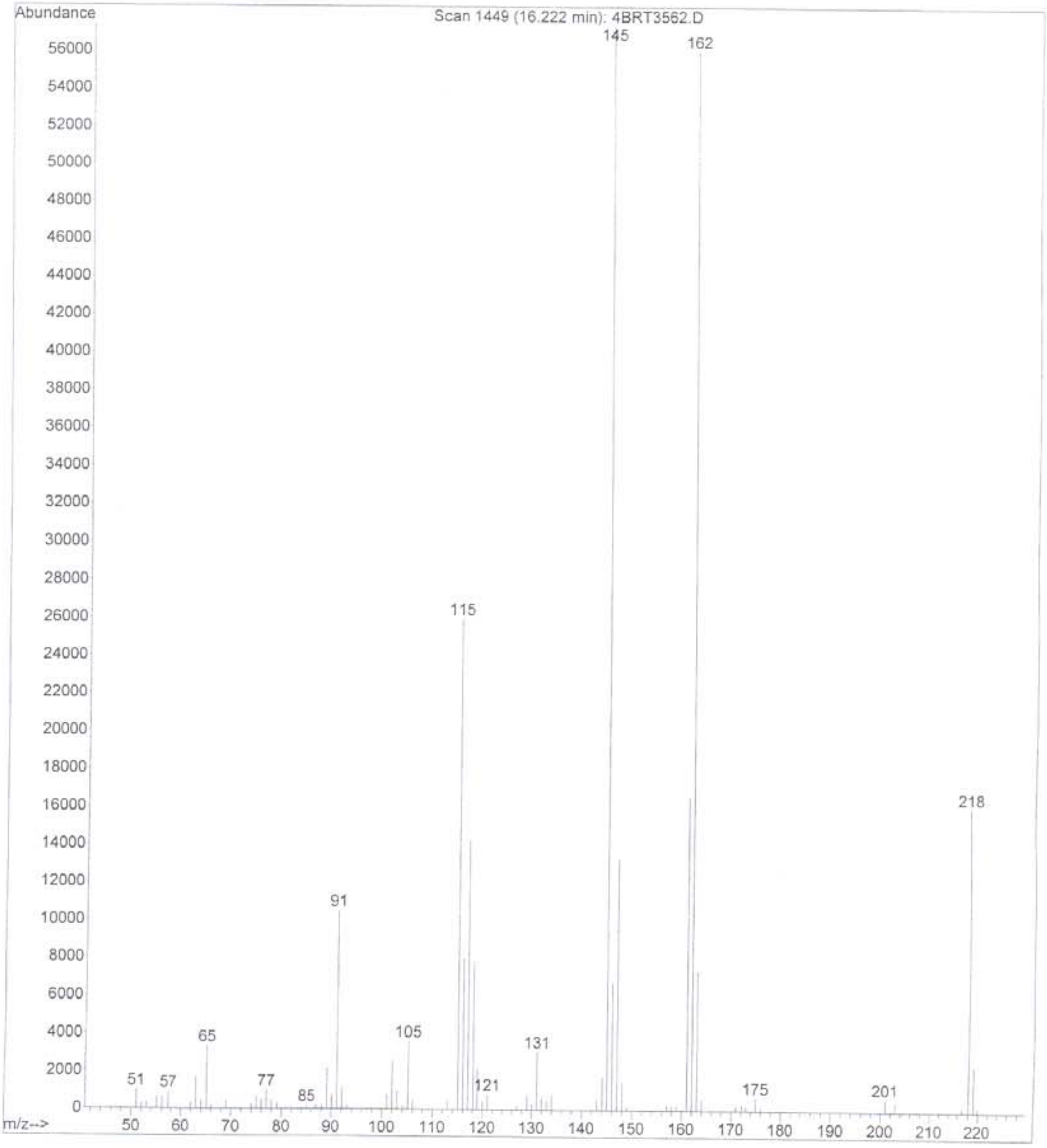
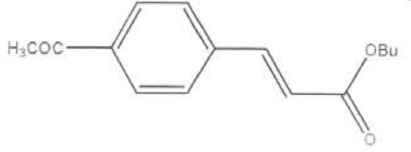


Figure B.8. Mass spectrum of trans-4-acetylcinnamic acid butyl ester



trans-4-acetylcinnamic acid butyl ester

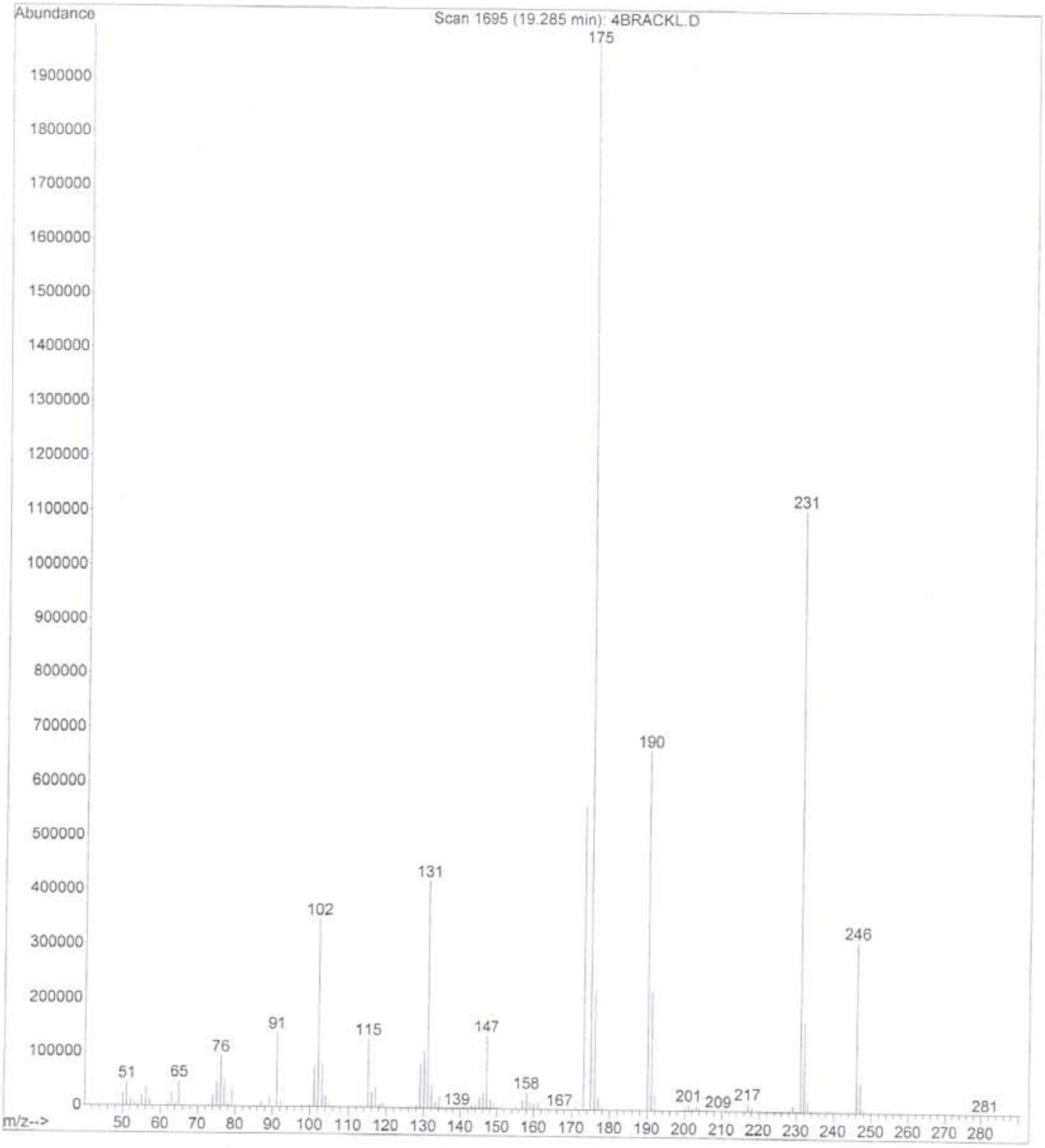
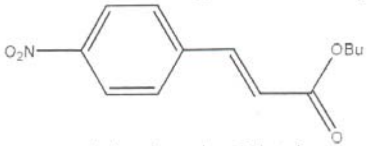


Figure B.9. Mass spectrum of trans-4-nitrocinnamic acid butyl ester



trans-4-nitrocinnamic acid butyl ester

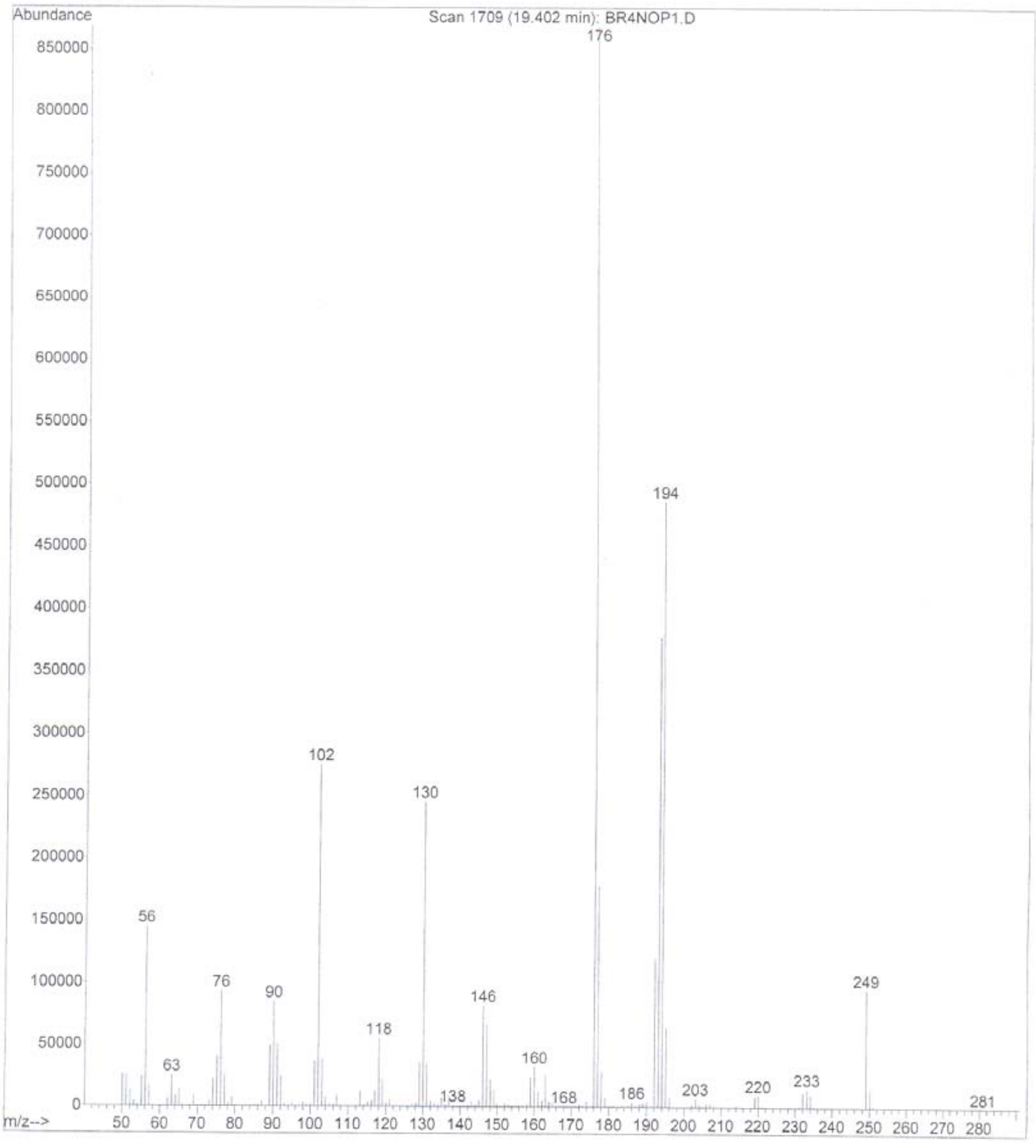
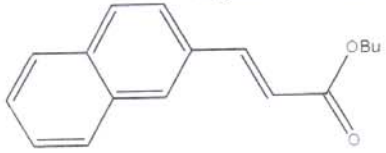


Figure B.10. Mass spectrum of trans-3-(2-Naphthyl)-propenoic acid butyl ester



trans-3-(2-Naphthyl)-propenoic acid butyl ester

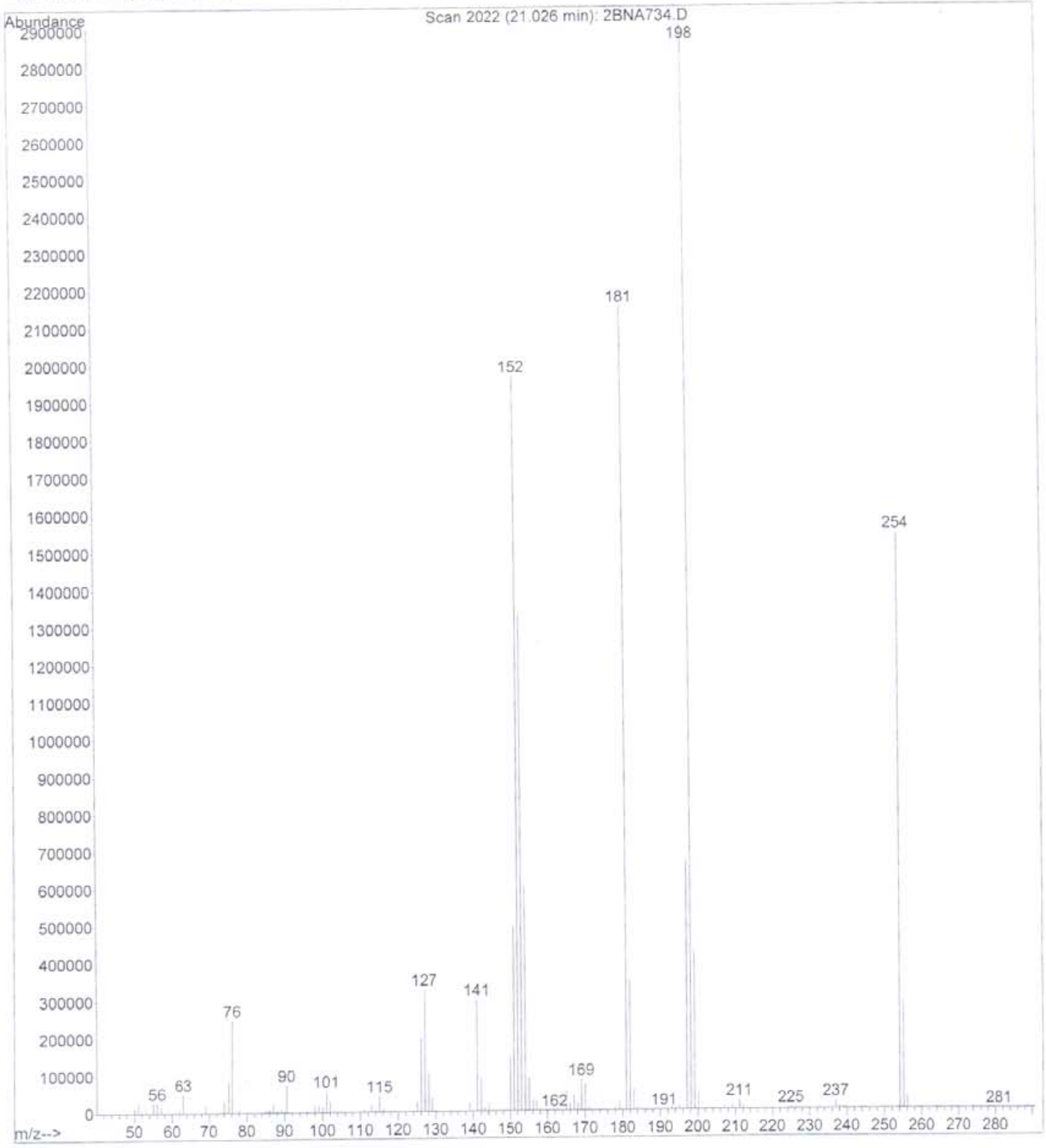
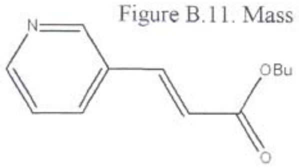


Figure B.11. Mass spectrum of trans-3-(3-Pyridinyl)acrylic acid butyl ester



trans-3-(3-Pyridinyl)acrylic acid butyl ester

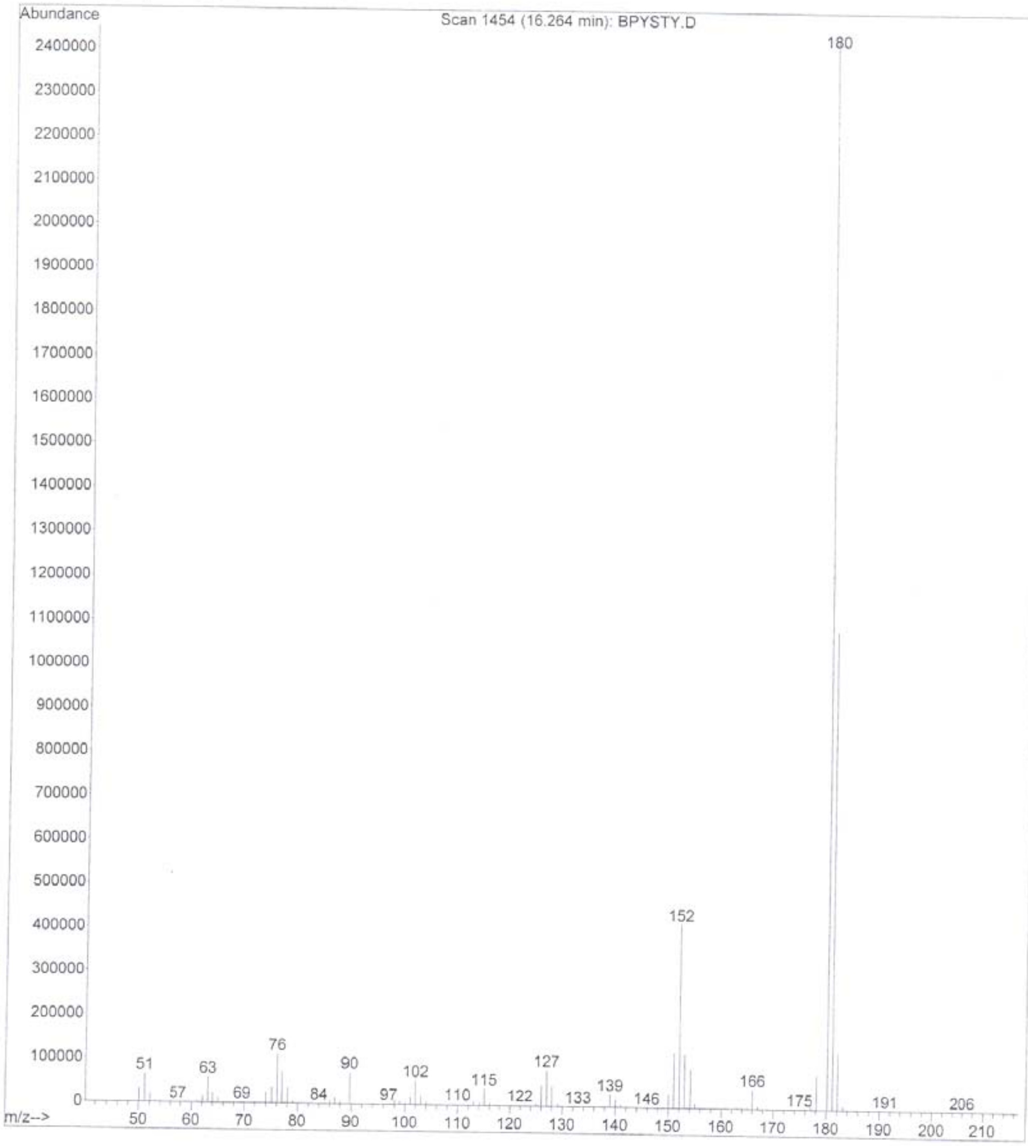
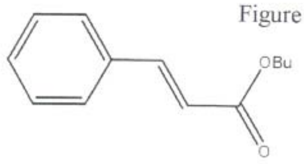
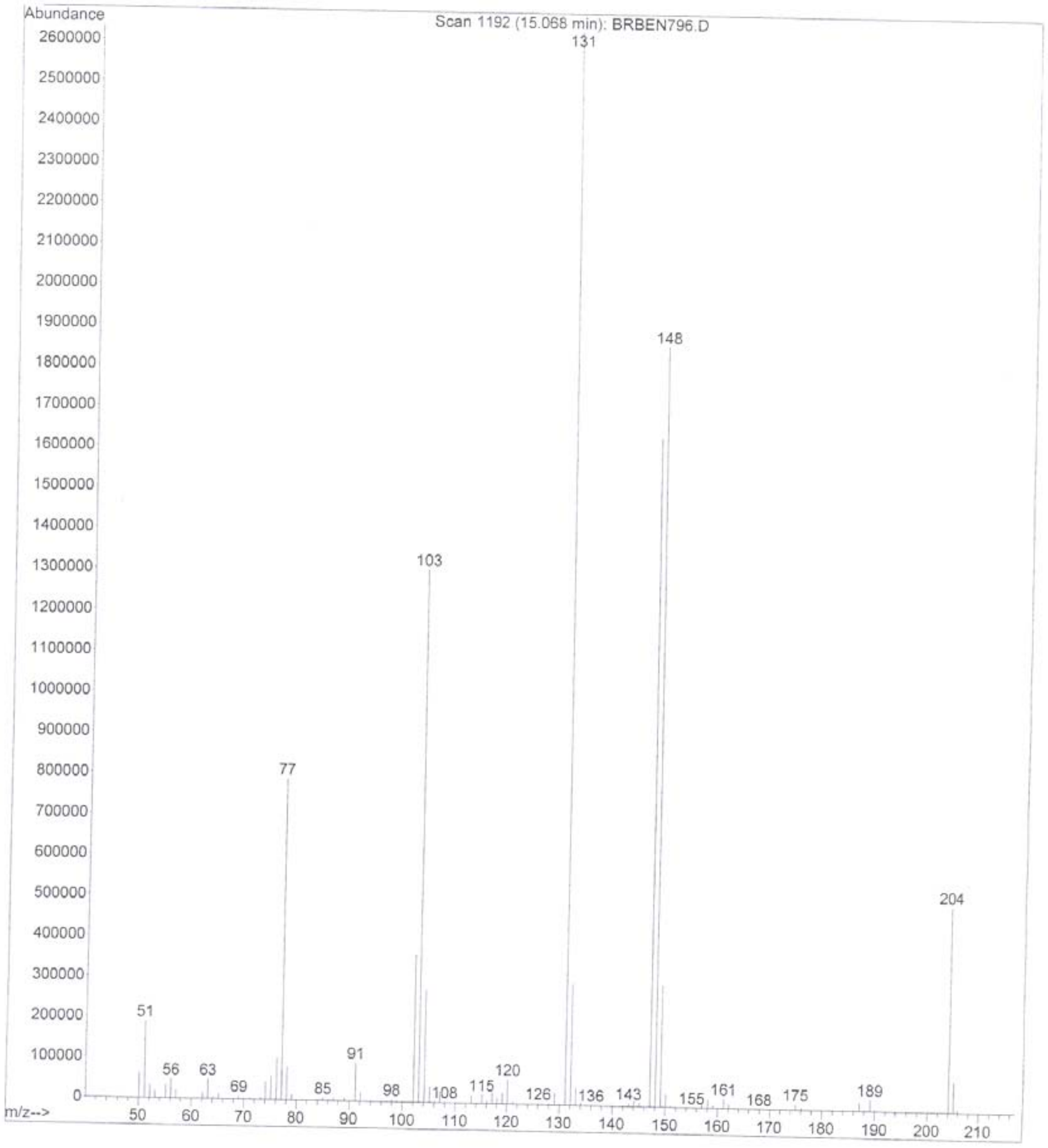


Figure B.12. Mass spectrum of trans-cinnamic acid butyl ester

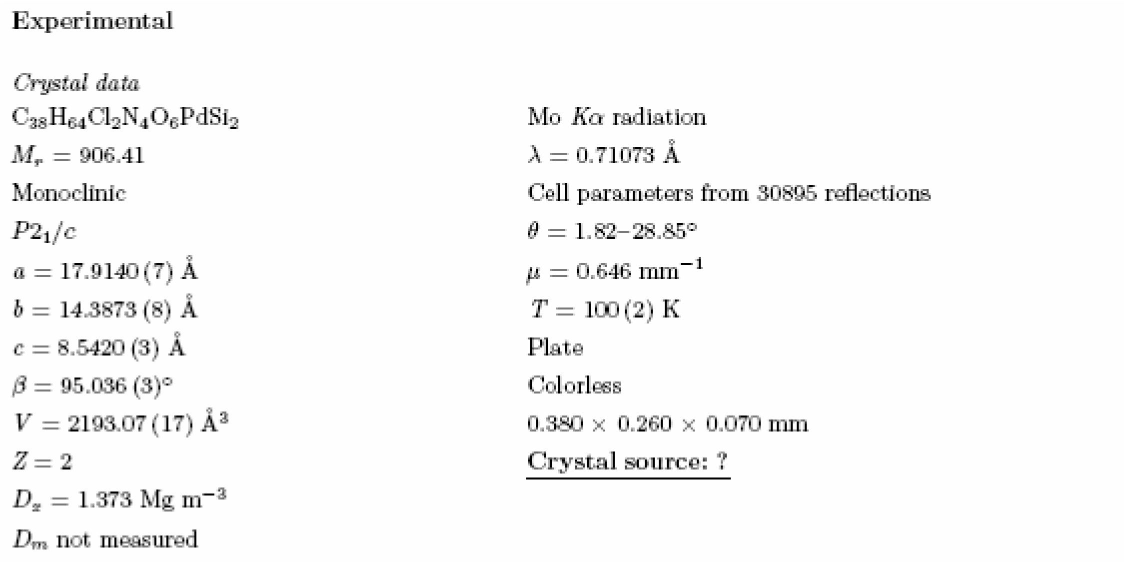


trans-cinnamic acid butyl ester



APPENDIX C

X-RAY CRYSTALLOGRAPHY DATA AND PARAMETERS



Experimental

Crystal data

$C_{38}H_{64}Cl_2N_4O_6PdSi_2$

$M_r = 906.41$

Monoclinic

$P2_1/c$

$a = 17.9140\,(7)$ Å

$b = 14.3873\,(8)$ Å

$c = 8.5420\,(3)$ Å

$\beta = 95.036\,(3)^\circ$

$V = 2193.07\,(17)$ Å^3

$Z = 2$

$D_x = 1.373$ Mg m^{-3}

D_m not measured

Mo $K\alpha$ radiation

$\lambda = 0.71073$ Å

Cell parameters from 30895 reflections

$\theta = 1.82–28.85^\circ$

$\mu = 0.646$ mm^{-1}

$T = 100\,(2)$ K

Plate

Colorless

0.380 × 0.260 × 0.070 mm

Crystal source: ?

Data collection

Stoe IPDS 2 diffractometer
ω scans rotation
Absorption correction:
by integration (X-RED32; Stoe & Cie, 2002)
$T_{\min} = 0.6857$, $T_{\max} = 0.8727$
30895 measured reflections
4315 independent reflections

3741 reflections with
$>2\text{sigma}(I)$
$R_{\text{int}} = 0.0838$
$\theta_{\max} = 26.00°$
$h = -22 \rightarrow 22$
$k = -17 \rightarrow 17$
$l = -10 \rightarrow 10$
every 0 reflections
frequency: 0 min
intensity decay: <2%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.0398$
$wR(F^2) = 0.1092$
$S = 1.030$
4315 reflections
242 parameters
H-atom parameters constrained
$w=1/[\sigma^2(F_o^2) + (0.0736P)^2 + 0.5678P]$
where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} = 0.000$
$\Delta\rho_{\max} = 1.089$ e Å^{-3}
$\Delta\rho_{\min} = -0.967$ e Å^{-3}
Extinction correction: *SHELXL*
Extinction coefficient: 0.0070 (8)
Scattering factors from *International Tables for Crystallography* (Vol. C)

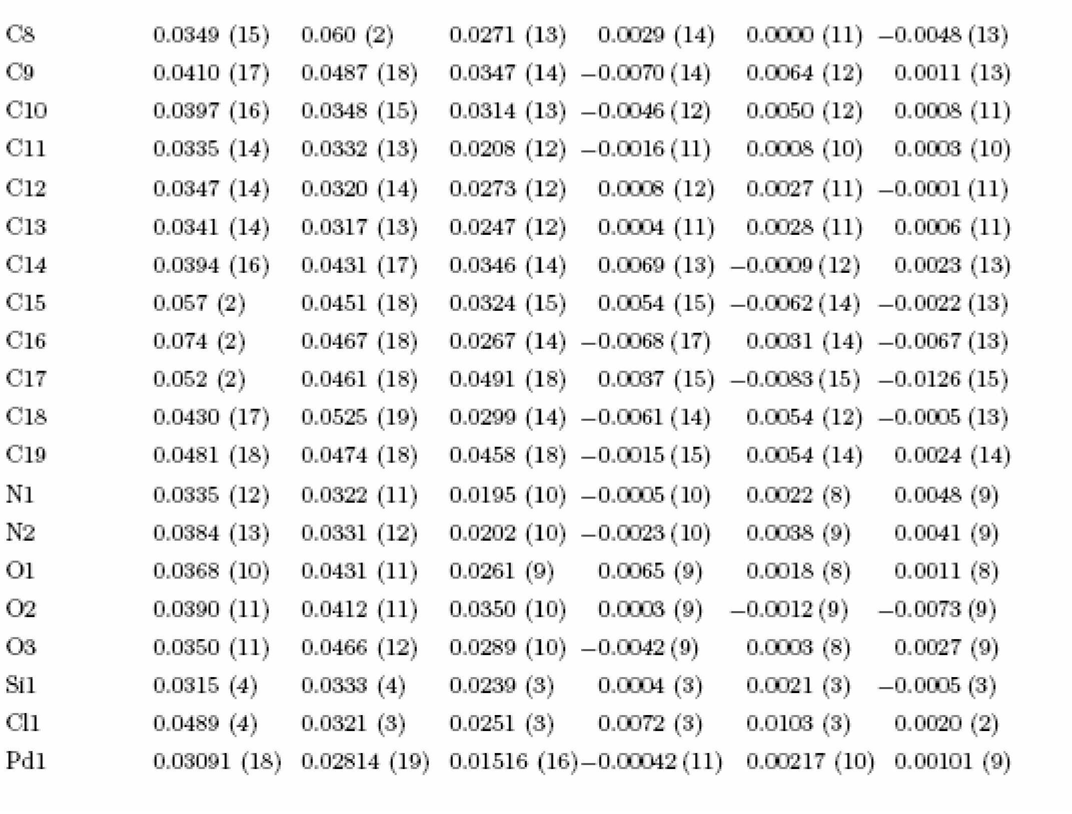
Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* ($\mathring{A}^2$)

$$U_{\mathrm{eq}} = (1/3)\Sigma_i\Sigma_j U^{ij}a^i a^j \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	U_{eq}
C1	0.48503 (15)	0.55940 (18)	0.2838 (3)	0.0271 (5)
C2	0.42833 (16)	0.5960 (2)	0.0359 (3)	0.0345 (6)
C3	0.50262 (16)	0.6476 (2)	0.0602 (3)	0.0306 (6)
C4	0.59240 (16)	0.6679 (2)	0.3066 (3)	0.0340 (6)
C5	0.66426 (16)	0.6494 (2)	0.2310 (3)	0.0309 (6)
C6	0.69408 (17)	0.5597 (2)	0.2269 (3)	0.0350 (6)
C7	0.75970 (17)	0.5435 (2)	0.1570 (3)	0.0385 (7)
C8	0.79707 (17)	0.6162 (2)	0.0909 (3)	0.0409 (7)
C9	0.76766 (18)	0.7050 (2)	0.0940 (3)	0.0413 (7)
C10	0.70193 (17)	0.7212 (2)	0.1634 (3)	0.0352 (6)
C11	0.36652 (15)	0.4787 (2)	0.2095 (3)	0.0292 (6)
C12	0.29852 (16)	0.5358 (2)	0.2436 (3)	0.0313 (6)
C13	0.23572 (16)	0.4758 (2)	0.3011 (3)	0.0302 (6)
C14	0.05196 (17)	0.6155 (2)	0.0723 (3)	0.0393 (7)
C15	0.0485 (2)	0.6298 (2)	−0.1026 (3)	0.0455 (8)
C16	0.1936 (2)	0.6525 (2)	0.5420 (3)	0.0491 (8)
C17	0.2417 (2)	0.7370 (2)	0.5473 (4)	0.0497 (8)
C18	0.09046 (18)	0.4366 (2)	0.5302 (3)	0.0417 (7)
C19	0.0499 (2)	0.3463 (3)	0.5344 (4)	0.0470 (8)
N1	0.42983 (13)	0.53652 (16)	0.1758 (2)	0.0284 (5)
N2	0.52749 (13)	0.62427 (16)	0.2246 (2)	0.0305 (5)
O1	0.11556 (11)	0.55937 (15)	0.1203 (2)	0.0354 (4)
O2	0.15620 (12)	0.63939 (15)	0.3887 (2)	0.0387 (5)
O3	0.08252 (12)	0.47568 (16)	0.3761 (2)	0.0370 (5)
Si1	0.14549 (4)	0.53883 (6)	0.30156 (8)	0.02961 (19)
Cl1	0.43387 (4)	0.61902 (5)	0.60579 (7)	0.03497 (18)
Pd1	1/2	1/2	1/2	0.02473 (12)

Table 2. *Anisotropic displacement parameters* ($\mathring{A}^2$)

	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C1	0.0301 (13)	0.0297 (13)	0.0218 (11)	0.0017 (10)	0.0040 (9)	−0.0031 (10)
C2	0.0386 (15)	0.0421 (16)	0.0228 (12)	0.0049 (12)	0.0023 (11)	0.0091 (11)
C3	0.0396 (15)	0.0329 (14)	0.0196 (12)	0.0032 (11)	0.0036 (10)	0.0052 (10)
C4	0.0436 (16)	0.0344 (14)	0.0244 (12)	−0.0077 (12)	0.0060 (11)	−0.0046 (11)
C5	0.0385 (15)	0.0343 (14)	0.0195 (11)	−0.0039 (12)	−0.0001 (10)	−0.0025 (10)
C6	0.0451 (16)	0.0353 (14)	0.0232 (12)	−0.0040 (12)	−0.0041 (11)	0.0006 (11)
C7	0.0443 (17)	0.0417 (17)	0.0278 (13)	0.0078 (13)	−0.0059 (12)	−0.0026 (12)



C8	0.0349 (15)	0.060 (2)	0.0271 (13)	0.0029 (14)	0.0000 (11)	−0.0048 (13)
C9	0.0410 (17)	0.0487 (18)	0.0347 (14)	−0.0070 (14)	0.0064 (12)	0.0011 (13)
C10	0.0397 (16)	0.0348 (15)	0.0314 (13)	−0.0046 (12)	0.0050 (12)	0.0008 (11)
C11	0.0335 (14)	0.0332 (13)	0.0208 (12)	−0.0016 (11)	0.0008 (10)	0.0003 (10)
C12	0.0347 (14)	0.0320 (14)	0.0273 (12)	0.0008 (12)	0.0027 (11)	−0.0001 (11)
C13	0.0341 (14)	0.0317 (13)	0.0247 (12)	0.0004 (11)	0.0028 (11)	0.0006 (11)
C14	0.0394 (16)	0.0431 (17)	0.0346 (14)	0.0069 (13)	−0.0009 (12)	0.0023 (13)
C15	0.057 (2)	0.0451 (18)	0.0324 (15)	0.0054 (15)	−0.0062 (14)	−0.0022 (13)
C16	0.074 (2)	0.0467 (18)	0.0267 (14)	−0.0068 (17)	0.0031 (14)	−0.0067 (13)
C17	0.052 (2)	0.0461 (18)	0.0491 (18)	0.0037 (15)	−0.0083 (15)	−0.0126 (15)
C18	0.0430 (17)	0.0525 (19)	0.0299 (14)	−0.0061 (14)	0.0054 (12)	−0.0005 (13)
C19	0.0481 (18)	0.0474 (18)	0.0458 (18)	−0.0015 (15)	0.0054 (14)	0.0024 (14)
N1	0.0335 (12)	0.0322 (11)	0.0195 (10)	−0.0005 (10)	0.0022 (8)	0.0048 (9)
N2	0.0384 (13)	0.0331 (12)	0.0202 (10)	−0.0023 (10)	0.0038 (9)	0.0041 (9)
O1	0.0368 (10)	0.0431 (11)	0.0261 (9)	0.0065 (9)	0.0018 (8)	0.0011 (8)
O2	0.0390 (11)	0.0412 (11)	0.0350 (10)	0.0003 (9)	−0.0012 (9)	−0.0073 (9)
O3	0.0350 (11)	0.0466 (12)	0.0289 (10)	−0.0042 (9)	0.0003 (8)	0.0027 (9)
Si1	0.0315 (4)	0.0333 (4)	0.0239 (3)	0.0004 (3)	0.0021 (3)	−0.0005 (3)
Cl1	0.0489 (4)	0.0321 (3)	0.0251 (3)	0.0072 (3)	0.0103 (3)	0.0020 (2)
Pd1	0.03091 (18)	0.02814 (19)	0.01516 (16)	−0.00042 (11)	0.00217 (10)	0.00101 (9)

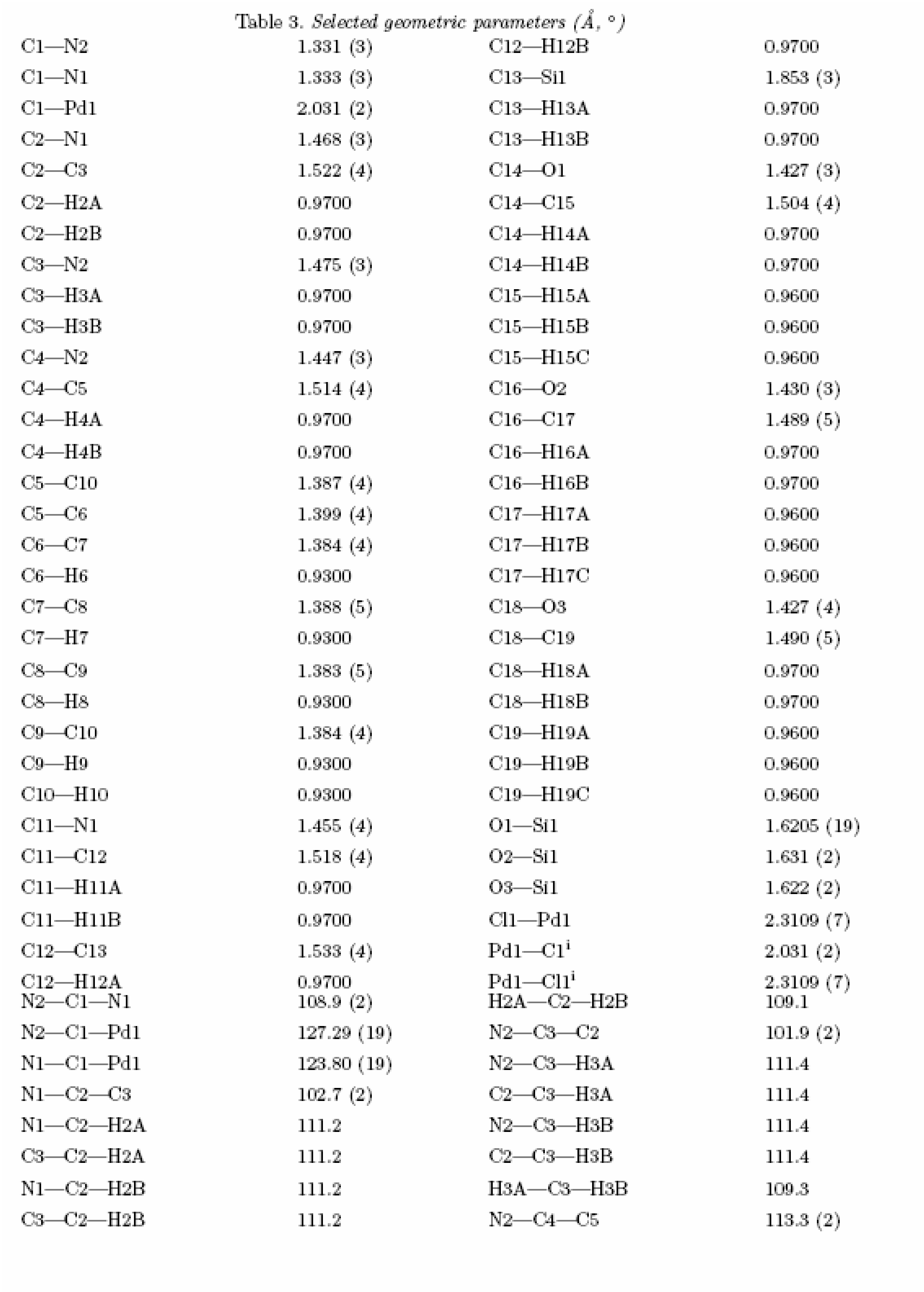
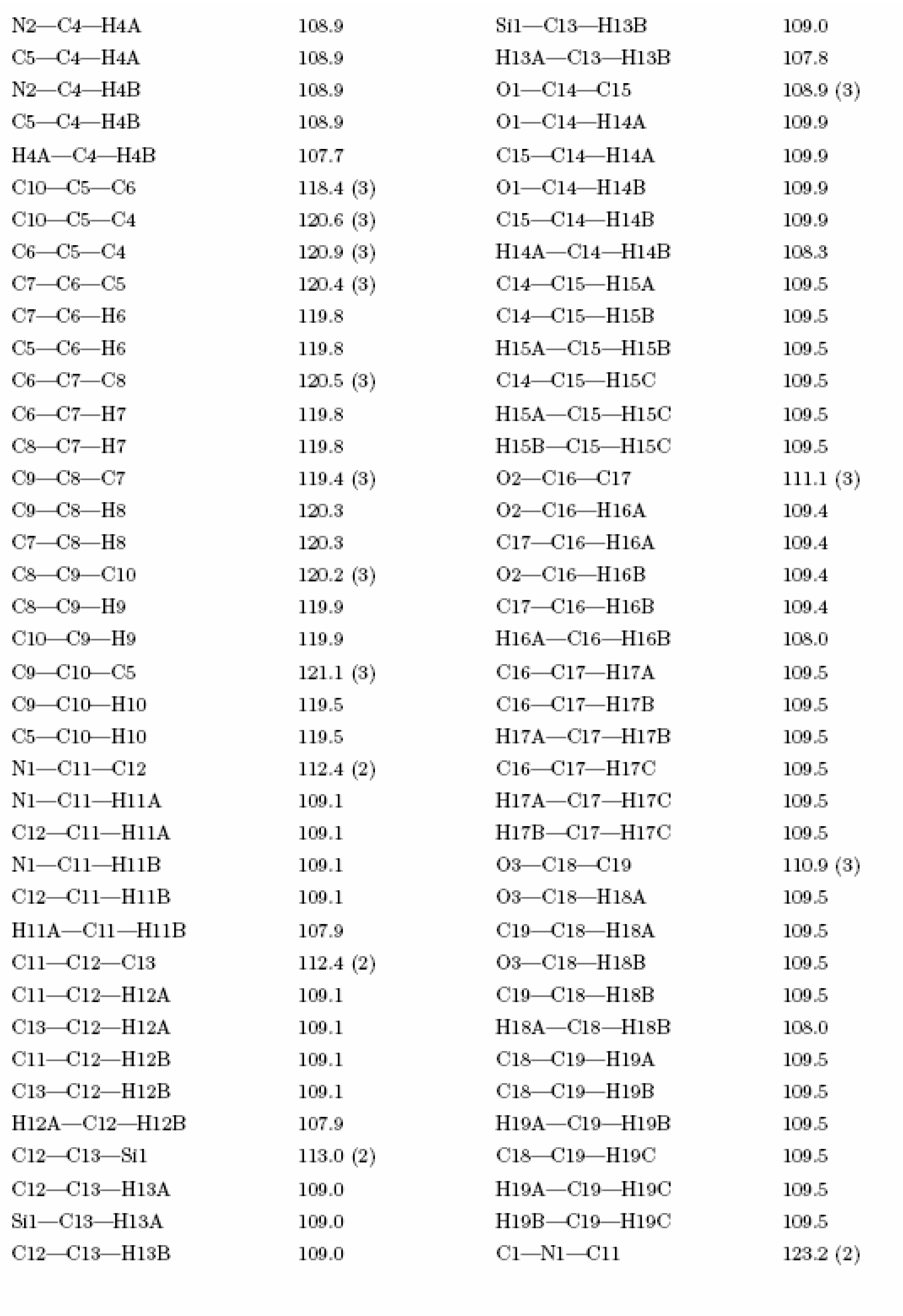


Table 3. *Selected geometric parameters (Å, °)*

C1—N2	1.331 (3)	C12—H12B	0.9700
C1—N1	1.333 (3)	C13—Si1	1.853 (3)
C1—Pd1	2.031 (2)	C13—H13A	0.9700
C2—N1	1.468 (3)	C13—H13B	0.9700
C2—C3	1.522 (4)	C14—O1	1.427 (3)
C2—H2A	0.9700	C14—C15	1.504 (4)
C2—H2B	0.9700	C14—H14A	0.9700
C3—N2	1.475 (3)	C14—H14B	0.9700
C3—H3A	0.9700	C15—H15A	0.9600
C3—H3B	0.9700	C15—H15B	0.9600
C4—N2	1.447 (3)	C15—H15C	0.9600
C4—C5	1.514 (4)	C16—O2	1.430 (3)
C4—H4A	0.9700	C16—C17	1.489 (5)
C4—H4B	0.9700	C16—H16A	0.9700
C5—C10	1.387 (4)	C16—H16B	0.9700
C5—C6	1.399 (4)	C17—H17A	0.9600
C6—C7	1.384 (4)	C17—H17B	0.9600
C6—H6	0.9300	C17—H17C	0.9600
C7—C8	1.388 (5)	C18—O3	1.427 (4)
C7—H7	0.9300	C18—C19	1.490 (5)
C8—C9	1.383 (5)	C18—H18A	0.9700
C8—H8	0.9300	C18—H18B	0.9700
C9—C10	1.384 (4)	C19—H19A	0.9600
C9—H9	0.9300	C19—H19B	0.9600
C10—H10	0.9300	C19—H19C	0.9600
C11—N1	1.455 (4)	O1—Si1	1.6205 (19)
C11—C12	1.518 (4)	O2—Si1	1.631 (2)
C11—H11A	0.9700	O3—Si1	1.622 (2)
C11—H11B	0.9700	Cl1—Pd1	2.3109 (7)
C12—C13	1.533 (4)	Pd1—C1^{i}	2.031 (2)
C12—H12A	0.9700	Pd1—Cl1^{i}	2.3109 (7)
N2—C1—N1	108.9 (2)	H2A—C2—H2B	109.1
N2—C1—Pd1	127.29 (19)	N2—C3—C2	101.9 (2)
N1—C1—Pd1	123.80 (19)	N2—C3—H3A	111.4
N1—C2—C3	102.7 (2)	C2—C3—H3A	111.4
N1—C2—H2A	111.2	N2—C3—H3B	111.4
C3—C2—H2A	111.2	C2—C3—H3B	111.4
N1—C2—H2B	111.2	H3A—C3—H3B	109.3
C3—C2—H2B	111.2	N2—C4—C5	113.3 (2)



N2—C4—H4A	108.9	Si1—C13—H13B	109.0
C5—C4—H4A	108.9	H13A—C13—H13B	107.8
N2—C4—H4B	108.9	O1—C14—C15	108.9 (3)
C5—C4—H4B	108.9	O1—C14—H14A	109.9
H4A—C4—H4B	107.7	C15—C14—H14A	109.9
C10—C5—C6	118.4 (3)	O1—C14—H14B	109.9
C10—C5—C4	120.6 (3)	C15—C14—H14B	109.9
C6—C5—C4	120.9 (3)	H14A—C14—H14B	108.3
C7—C6—C5	120.4 (3)	C14—C15—H15A	109.5
C7—C6—H6	119.8	C14—C15—H15B	109.5
C5—C6—H6	119.8	H15A—C15—H15B	109.5
C6—C7—C8	120.5 (3)	C14—C15—H15C	109.5
C6—C7—H7	119.8	H15A—C15—H15C	109.5
C8—C7—H7	119.8	H15B—C15—H15C	109.5
C9—C8—C7	119.4 (3)	O2—C16—C17	111.1 (3)
C9—C8—H8	120.3	O2—C16—H16A	109.4
C7—C8—H8	120.3	C17—C16—H16A	109.4
C8—C9—C10	120.2 (3)	O2—C16—H16B	109.4
C8—C9—H9	119.9	C17—C16—H16B	109.4
C10—C9—H9	119.9	H16A—C16—H16B	108.0
C9—C10—C5	121.1 (3)	C16—C17—H17A	109.5
C9—C10—H10	119.5	C16—C17—H17B	109.5
C5—C10—H10	119.5	H17A—C17—H17B	109.5
N1—C11—C12	112.4 (2)	C16—C17—H17C	109.5
N1—C11—H11A	109.1	H17A—C17—H17C	109.5
C12—C11—H11A	109.1	H17B—C17—H17C	109.5
N1—C11—H11B	109.1	O3—C18—C19	110.9 (3)
C12—C11—H11B	109.1	O3—C18—H18A	109.5
H11A—C11—H11B	107.9	C19—C18—H18A	109.5
C11—C12—C13	112.4 (2)	O3—C18—H18B	109.5
C11—C12—H12A	109.1	C19—C18—H18B	109.5
C13—C12—H12A	109.1	H18A—C18—H18B	108.0
C11—C12—H12B	109.1	C18—C19—H19A	109.5
C13—C12—H12B	109.1	C18—C19—H19B	109.5
H12A—C12—H12B	107.9	H19A—C19—H19B	109.5
C12—C13—Si1	113.0 (2)	C18—C19—H19C	109.5
C12—C13—H13A	109.0	H19A—C19—H19C	109.5
Si1—C13—H13A	109.0	H19B—C19—H19C	109.5
C12—C13—H13B	109.0	C1—N1—C11	123.2 (2)

C1—N1—C2	112.3 (2)	O3—Si1—O2	112.08 (12)
C11—N1—C2	122.4 (2)	O1—Si1—C13	107.62 (12)
C1—N2—C4	125.6 (2)	O3—Si1—C13	111.33 (13)
C1—N2—C3	112.7 (2)	O2—Si1—C13	111.53 (12)
C4—N2—C3	121.7 (2)	C1^{i}—Pd1—C1	180.000 (1)
C14—O1—Si1	124.50 (18)	C1^{i}—Pd1—Cl1^{i}	90.71 (7)
C16—O2—Si1	124.2 (2)	C1—Pd1—Cl1^{i}	89.29 (7)
C18—O3—Si1	124.52 (19)	C1^{i}—Pd1—Cl1	89.29 (7)
O1—Si1—O3	107.11 (11)	C1—Pd1—Cl1	90.71 (7)
O1—Si1—O2	106.86 (11)	Cl1^{i}—Pd1—Cl1	180.00 (3)
N1—C2—C3—N2	−11.4 (3)	Pd1—C1—N2—C3	176.63 (19)
N2—C4—C5—C10	113.9 (3)	C5—C4—N2—C1	117.5 (3)
N2—C4—C5—C6	−65.8 (3)	C5—C4—N2—C3	−61.2 (3)
C10—C5—C6—C7	0.1 (4)	C2—C3—N2—C1	8.9 (3)
C4—C5—C6—C7	179.8 (2)	C2—C3—N2—C4	−172.2 (2)
C5—C6—C7—C8	0.4 (4)	C15—C14—O1—Si1	171.7 (2)
C6—C7—C8—C9	−0.7 (4)	C17—C16—O2—Si1	138.9 (3)
C7—C8—C9—C10	0.5 (4)	C19—C18—O3—Si1	−148.0 (2)
C8—C9—C10—C5	0.0 (4)	C14—O1—Si1—O3	67.4 (3)
C6—C5—C10—C9	−0.3 (4)	C14—O1—Si1—O2	−52.8 (3)
C4—C5—C10—C9	−180.0 (3)	C14—O1—Si1—C13	−172.8 (2)
N1—C11—C12—C13	−172.1 (2)	C18—O3—Si1—O1	174.8 (2)
C11—C12—C13—Si1	−167.39 (18)	C18—O3—Si1—O2	−68.3 (3)
N2—C1—N1—C11	−169.9 (2)	C18—O3—Si1—C13	57.4 (3)
Pd1—C1—N1—C11	11.3 (4)	C16—O2—Si1—O1	−168.9 (2)
N2—C1—N1—C2	−6.3 (3)	C16—O2—Si1—O3	74.0 (3)
Pd1—C1—N1—C2	174.88 (19)	C16—O2—Si1—C13	−51.6 (3)
C12—C11—N1—C1	96.2 (3)	C12—C13—Si1—O1	67.5 (2)
C12—C11—N1—C2	−65.7 (3)	C12—C13—Si1—O3	−175.46 (17)
C3—C2—N1—C1	11.5 (3)	C12—C13—Si1—O2	−49.5 (2)
C3—C2—N1—C11	175.2 (2)	N2—C1—Pd1—Cl1^{i}	−93.5 (2)
N1—C1—N2—C4	179.1 (2)	N1—C1—Pd1—Cl1^{i}	85.0 (2)
Pd1—C1—N2—C4	−2.2 (4)	N2—C1—Pd1—Cl1	86.5 (2)
N1—C1—N2—C3	−2.1 (3)	N1—C1—Pd1—Cl1	−95.0 (2)

Symmetry codes: (i) $1-x, 1-y, 1-z$.