

## ORGANOMETALLIC CATALYSIS: SOME CONTRIBUTIONS TO ORGANIC SYNTHESIS#

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In the present paper some general aspects of metal complex catalysis and its applications for oxyfunctionalization of various olefins, including naturally occurring ones, via selective oxidation, hydroformylation and alkoxy-carbonylation are discussed.

Keywords: catalysis; metal complexes; olefins.

## INTRODUCTION

Synthetic chemicals are extremely important in all fields of our life and their cheap production in large amounts is necessary for the successful economic growth of modern civilization. Catalysis offers the unique possibility of fast and selective synthesis of desired chemical molecules without consumption of extra amounts of energy and theoretically without the consumption of catalyst itself. Presently, most of industrial chemical processes are based on catalysis. The steady replacement of classical stoichiometric methodologies with cleaner catalytic alternatives is also promoted by a growing environmental awareness and an increasing pressure on chemical industry to reduce a waste production. The amounts of waste (undesired products) produced per kilogram of product, designated as E factor, are especially high in the manufacture of fine chemicals (up to 100 kg), while oil refining and bulk chemicals industry usually produce ca. 0.1 and 1-5 kg of by-products, respectively, per kilogram of product<sup>1,2</sup>. This situation is partly due to the use of multi-step syntheses in fine chemistry but also due to the predominant utilization of stoichiometric rather than catalytic methods. On the other hand, most of modern petrochemical technologies are one-step catalytic processes with high atom utilization<sup>1,2</sup>.

Transition metals have become an important instrument in organic synthesis due to their ability to activate organic substrates and promote various interactions between them<sup>3</sup>. A rapid progress in the study of organometallic and coordination compounds has led to the development and successful industrial application of a number of catalytic processes based on use of these compounds as catalysts<sup>4,6</sup>. The major advantage of organometallic catalysis that has led to its widespread adoption by industry is selectivity, the ability to produce pure products in high yield. The main reasons why transition metals contribute so essentially in catalysis are the follows<sup>4</sup>: a) bonding ability: the ability to form both  $\pi$ - and  $\sigma$ -bonds with other moieties; b) wide choice of ligands: transition elements readily form chemical bonds with almost every other element and almost any organic molecule; c) ligand effects: a ligand can influence the behavior of a transition metal catalyst by varying the steric or electronic environment at the active site; d) variability of oxidation state and co-ordination number; e) ability to readily interchanges between oxidation states during a catalytic reaction: transition metals can be readily involved in redox processes.

The mechanism of catalytic reactions promoted by transition metal complexes can be rationalized as a sequence of stoichiometric steps linked in a cyclic way thus forming a catalytic cycle. First, the formation of an organometallic compound occurs via the coordination or addition of substrate(s) to a metal center. That is followed by a series of intramolecular transformations of the activated substrate(s), which can involve also external groups and substrate(s), and the decomposition of the organometallic compound to give reaction products. Generally, metal complexes are changed as a result of such transformations and their regeneration is necessary to complete a catalytic cycle. Stoichiometric transformations involved in a catalytic process are the fundamental reactions of coordination and organometallic chemistry: ligand coordination, oxidative addition, insertion, isomerization, reductive elimination, etc.

No doubt much of the interest arises from the potential commercial importance of these reactions and for this reason, most of the earlier works were concerned with the preparative aspects of organometallic catalysis. However, during the last 30 years a considerable number of mechanistic works, including studies of the organometallic chemistry involved in catalytic reactions, appeared in the literature.

## PALLADIUM CATALYZED OXIDATION OF OLEFINS

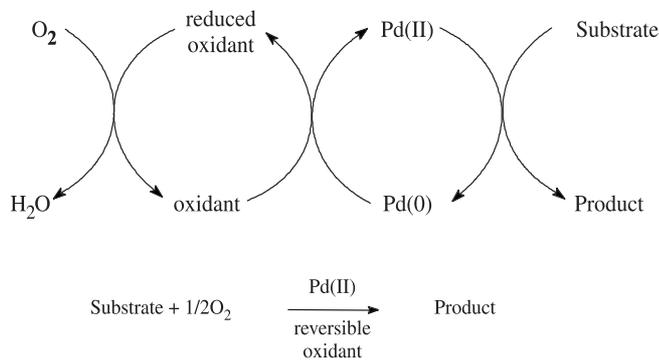
In the middle of the 1950s, a special interest of organic chemists to palladium arose. One of the events that stimulated the development of the palladium organic chemistry was the discovery of a Wacker process in 1956 by a German research team<sup>7</sup> and its further industrial application. Presently about 1.5 million tones of acetaldehyde per year are produced from ethylene and oxygen using PdCl<sub>2</sub>/CuCl<sub>2</sub> as the catalyst. In 1894, Phillips reported<sup>8</sup> that aqueous palladium chloride was reduced to palladium metal by ethylene. A great contribution of the Wacker group was the invention of the catalytic process by the addition of copper(II) chloride to re-oxidize palladium thus allowing the use of the noble metal in catalytic amounts. Reduced copper complexes are readily re-oxidized by dioxygen.

Since that discovery, palladium has been introducing to modern chemistry resulting in important changes in organic synthesis. Due to a great number of the developed oxidative processes promoted by palladium complexes, this element has become one the most frequently used in organic transformations transition metals. Stoichiometric in palladium reactions may be incorporated into catalytic processes using reversible oxidants. Scheme 1 represents a catalytic cycle for the oxidation of organic substrate, e.g., olefin, by dioxygen promoted by a two-component catalytic system "palladium/

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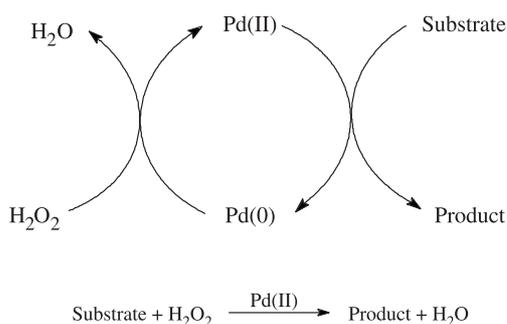
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reversible oxidant". Complexes of Cu(II), Fe(II), heteropoly acids and benzoquinone are commonly used as reversible oxidants in these systems. In the case of benzoquinone, the re-oxidation of its reduced form, i.e. hydroquinone, is a slow reaction, which can be accelerated by the addition on a third component into the catalytic system, e.g., some cobalt complexes or heteropoly acids<sup>9-11</sup>.



**Scheme 1.** Palladium catalyzed oxidation with dioxygen

An alternative final oxidant for palladium catalyzed organic oxidations is hydrogen peroxide: a cheap and environmentally friendly reagent, with water being formed as the only by-product (Scheme 2). There are relatively little information in the literature concerning the use of hydrogen peroxide as a palladium re-oxidant in Wacker-type processes<sup>12,13</sup>. The introduction of benzoquinone exerts a beneficial effect in these systems<sup>14,15</sup>, probably due to the formation of palladium-benzoquinone complexes.

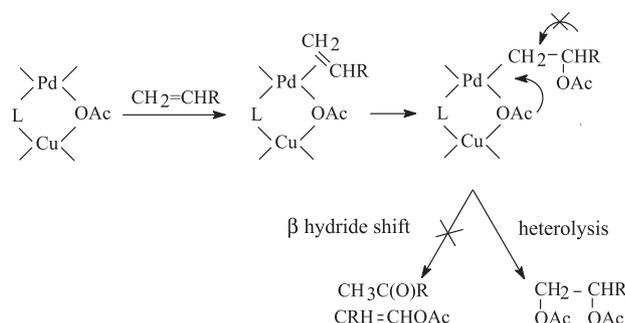


**Scheme 2.** Palladium catalyzed oxidation with hydrogen peroxide

In multi-component catalytic systems, re-oxidants frequently interfere in the mechanism of the olefin oxidation and can even change a product distribution. It is especially probable for coordinating re-oxidants. Re-oxidants are originally introduced to palladium-based catalytic systems to simply re-oxidize the reduced palladium species and, according to Scheme 1, should not influence the step of the palladium-olefin interaction, which determines a product nature. However, there were published some observations showing that such an influence cannot be disregarded.

The main products of  $\alpha$ -olefin oxidation by Pd(II) salts in water and acetic acid solutions are carbonyl compounds and vinyl ethers, respectively. In 1964, Clement *et al.*<sup>16</sup> found that the introduction of CuCl<sub>2</sub> (as re-oxidant) in high concentrations completely changed the reaction route: glycol derivatives (acetates and chlorohydrines) were mainly formed. M. Tamura<sup>17</sup> observed that the use of LiNO<sub>3</sub> for the reoxidation of palladium in acetic acid also led to the formation of

exclusively glycol acetates from  $\alpha$ -olefins. Later, some other examples of such a behavior were reported<sup>18,19</sup>. All early explanations of the influence of copper chloride on the reaction mechanism were based only on the analysis of the product composition<sup>19</sup>. We clarified a nature of this effect by the detailed kinetic and spectroscopic study of propylene oxidation in the PdCl<sub>2</sub>/CuCl<sub>2</sub>/HOAc system using UV-VIS, EPR and NMR spectroscopy<sup>20</sup>. Under the reaction conditions, the heteronuclear bridging Pd-Cu complexes and adducts between  $\pi$ -olefin palladium complexes and copper(II) ions have been detected (Scheme 3). Due to the insertion of olefin into the Pd-O bond a  $\sigma$ -organopalladium intermediate is formed. The presence of copper in this intermediate favors its decomposition *not via a  $\beta$ -hydride shift*, which would lead to acetone, *but via a heterolysis of the Pd-C bond* (much less common for alkyl palladium compounds with  $\beta$ -hydrogens) resulting in a highly valuable glycol acetate.



**Scheme 3.** Palladium-copper catalyzed oxidation of olefins with dioxygen into glycol derivatives

Some oxygen-containing re-oxidants may also serve as oxygen sources for the product formation. If the reduced form of the re-oxidant can be re-oxidized back by dioxygen, then this re-oxidant acts as the agent of oxygen transfer from dioxygen to olefin. Nitrite and nitrate anions are among such re-oxidants. Pd(II)/NO<sub>3</sub><sup>-</sup> catalytic systems in some cases offer valuable alternatives to the Wacker catalyst<sup>21-31</sup>. Products in these systems are formed as a result of the interaction between re-oxidant and olefin both coordinated on palladium. Thus, studies of the mechanisms of stoichiometric reactions of olefin oxidation by palladium complexes with nitro and nitrate ligands are of a great interest for the elucidation of the mechanisms of catalytic reactions.

We synthesized a series of nitro and nitrate palladium(II) complexes with a generalized formula Pd(NO<sub>n</sub>)<sub>m</sub>Cl<sub>2-m</sub>(CH<sub>3</sub>CN)<sub>2</sub>, where n=2, 3; m=0, 1, 2; and studied their reactivity in the oxidation of various olefins<sup>24-26, 29-31</sup>. The interaction of olefins with these complexes depends on the olefin nature, number of N-containing ligands on palladium and solvent. The interaction with acyclic olefins can result in aldehydes, ketones, 1,1-disubstituted alkanes, glycol derivatives and vinyl ethers<sup>24,30</sup>. For cyclic olefins and methylenecycloalkanes, the product nature is much more variable since their oxidation by palladium can be accompanied by skeletal rearrangements resulting in the formation of ring-expanded, ring contracted or ring-opened products<sup>25,26,29,31</sup>.

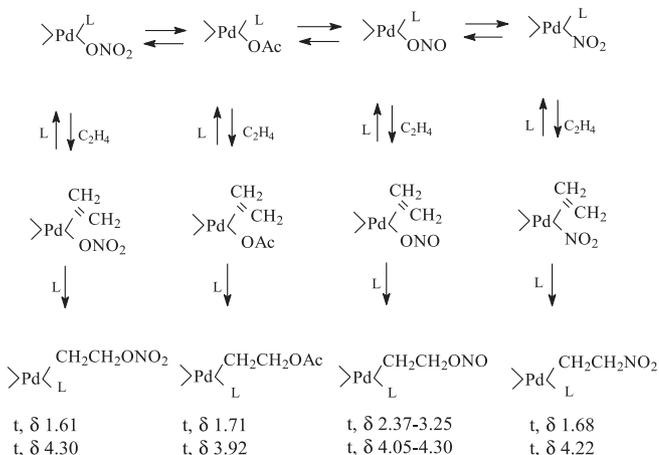
We studied the mechanism of these reactions by NMR and IR spectroscopy *in situ*. The reactions were performed directly in NMR tubes at low temperatures (down to 250K) in order to stabilize organopalladium intermediates and in special cells of IR spectrometers. Simultaneously with the registration of <sup>1</sup>H and <sup>13</sup>C NMR spectra during the olefin transformation into reaction products, the changes in nitrogen-containing fragments were monitored by IR

spectroscopy. Various organopalladium compounds with the dynamics characteristic for intermediates have been detected and monitored *in situ*, mostly for the first time, and their structure and reactivity have been studied. Based on obtained data the detailed mechanisms of various processes were suggested.

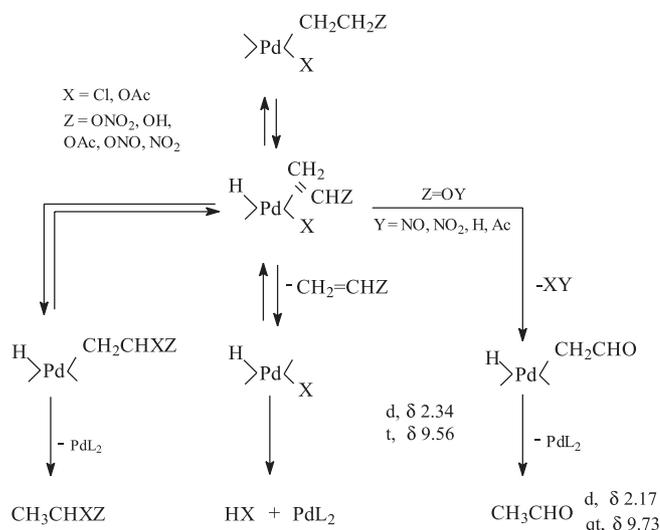
Even in the case of the most simple olefin, i.e., ethylene, a great variety of products can be formed: the products of *1,1-addition* (acetaldehyde and 1,1-disubstituted ethanes) and *1,2-addition* (glycol monoacetate) to the double bond as well as *vinyl derivatives* (vinyl acetate and nitroethylene). The study of the organometallic chemistry involved allowed us to generalize the mechanism of the formation of all these products<sup>24</sup>. The key reaction intermediates -  $\sigma$ -organopalladium compounds formed via the insertion of coordinated ethylene into Pd-O or Pd-N bonds - have been observed *in situ* by both NMR and IV (Scheme 4). The nature of oxidation products is determined in the step of the decomposition of these  $\sigma$ -alkyl palladium complexes. Scheme 5 shows the reaction routes leading to 1,1-addition products and vinyl ethers. In particular, for the first time we registered the organometallic precursor of acetaldehyde (Pd-CH<sub>2</sub>-CHO), which is, in fact, the intermediate of the  $\beta$ -hydride shift (later, we observed similar species for other olefins). Various intermediates responsible for the formation of glycol monoacetate have also been detected, e.g., the product of the acetoxylation of ethylene and the palladium complex with a hydroxyalkyl ligand and coordinated acetyl nitrite (or nitrate) shown in Scheme 6. The decomposition of the latter via a heterolysis of the Pd-C bond under the action of the coordinated acetyl nitrite (nitrate) gives glycol monoacetate and a nitrosyl palladium complex. In the absence of N-ligand, the palladium-hydroxyalkyl intermediate decomposes via the  $\beta$ -hydride shift resulting in acetaldehyde. Thus, it was understood the beneficial effect of nitrate ions, originally used as re-oxidants for the reduced palladium species, on the nature of the product of olefin oxidation by dioxygen catalyzed by Pd(II).

The applications of the Pd(II)/NO<sub>3</sub><sup>-</sup> catalytic systems have been extended in our further works to small ring cycloalkenes and methylenecycloalkanes<sup>25,26</sup> as well as to monoterpenes<sup>29,30</sup>.

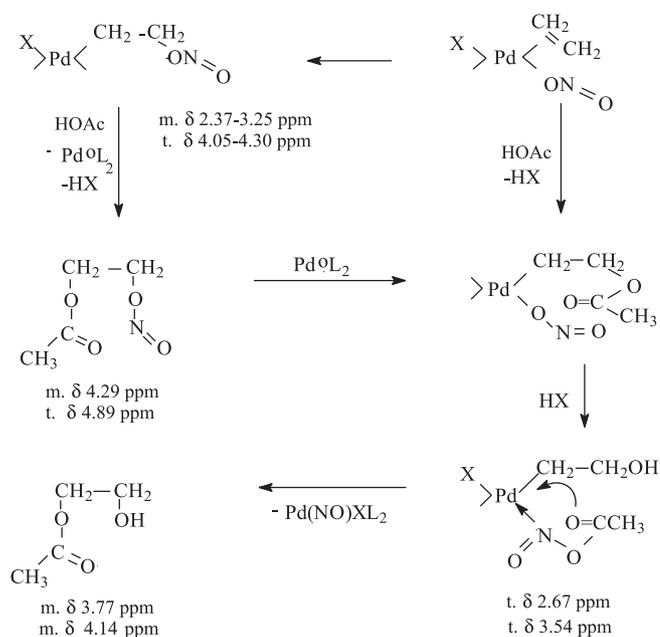
Then we tried to develop a heterogeneous version of the Pd(II)/NO<sub>3</sub><sup>-</sup> catalytic system, which showed a high activity in the oxidation of various olefins, in order to facilitate the step of the catalyst separation from reaction products. We have developed the oxidative acetoxylation of propylene into glycol acetate over Pd, Pd-Pt, and Pt-Rh catalysts supported on carbon, SiO<sub>2</sub>, and TiO<sub>2</sub> in acetic acid



**Scheme 4.** Formation of  $\sigma$ -organopalladium intermediates at ethylene oxidation



**Scheme 5.** Palladium catalyzed ethylene oxidation



**Scheme 6.** Palladium catalyzed ethylene oxidation

solutions of nitric acid<sup>27,28,32</sup>. Palladium catalysts on carbon exhibit a high activity and an ca. 90% selectivity, while monometallic platinum and rhodium catalysts show no activity. Propylene oxidation proceeds both on the catalyst surface and in the solution due to the palladium leaching. After the reaction, the catalyst can be regenerated at mild conditions. The treatment of the suspension with hydrogen results in the reduction of the dissolved palladium(II) complexes and the deposition of the palladium metal back on the support. After filtration, the catalyst can be used again for propylene oxidation.

We supposed that the addition of components that serve as hydrogen activators, such as platinum or rhodium, could improve the efficiency of the reductive regeneration and catalyst stability. Indeed, Pd-Pt/C catalysts show a high activity for 15 oxidation-regeneration cycles, while the activity of Pd/C and Pd-Rh/C catalysts is maintained only for 3-4 cycles. This work has become a basis for a new technology, which we developed and patented for the synthesis of propylene oxide<sup>32,33</sup>.

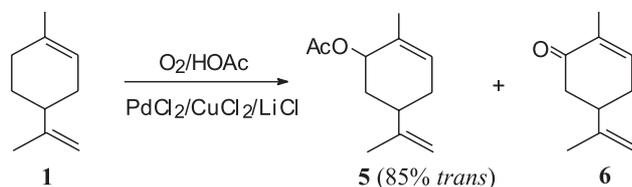
Propylene oxide is a key intermediate in the production of polyurethanes and polyesters and currently produced by non-catalytic methods via chlorohydrin or by propylene epoxidation with hydroperoxide, both suffering from heavy waste problems. We developed a new process<sup>27,33</sup> for the propylene oxide synthesis from propylene and dioxygen in two steps: 1) oxidation of propylene into propylene glycol monoacetate using Pd, Pd-Pt and Pd-Rh supported catalysts and 2) cracking of propylene glycol monoacetate into propylene oxide and acetic acid (which is recycled) in a flow reactor containing a melt of potassium acetate as catalyst.

### METAL COMPLEX CATALYZED FUNCTIONALIZATION OF NATURALLY OCCURRING OLEFINS

Selective functionalization of sufficiently abundant monoterpenes represents a promising route for the valorization of these cheap natural products. Some of their oxygenated derivatives (alcohols, aldehydes, ketones, allylic ethers, carboxylic acid esters) are commercially important materials for pharmaceutical, flavor, and perfumery industries as well as useful synthetic intermediates and chiral building blocks<sup>34,35</sup>. These compounds can be produced from olefins by metal catalyzed selective oxidation and carbonylation of their double bonds<sup>3-6,18,19</sup>. Because of its commercial importance the olefin oxidation by palladium(II) salts has received the most considerable attention, especially when such environmentally friendly and low-priced oxidants as dioxygen and hydrogen peroxide are involved<sup>18,19,36</sup>. Although these reactions have been developed into important synthetic methods, there is very little information in literature concerning their application to natural product synthesis. The other important pathways for the synthesis of oxygen-containing derivatives of monoterpenes are metal catalyzed carbonylation, i. e., alkoxycarbonylation and hydroformylation. We have, in recent years, been studying the selective oxidation and carbonylation of monoterpenes, such as limonene (**1**),  $\alpha$ -pinene (**2**),  $\beta$ -pinene (**3**) and camphene (**4**), via homogeneous catalysis by metal complexes. In the present paper, some recent results in this field are presented.

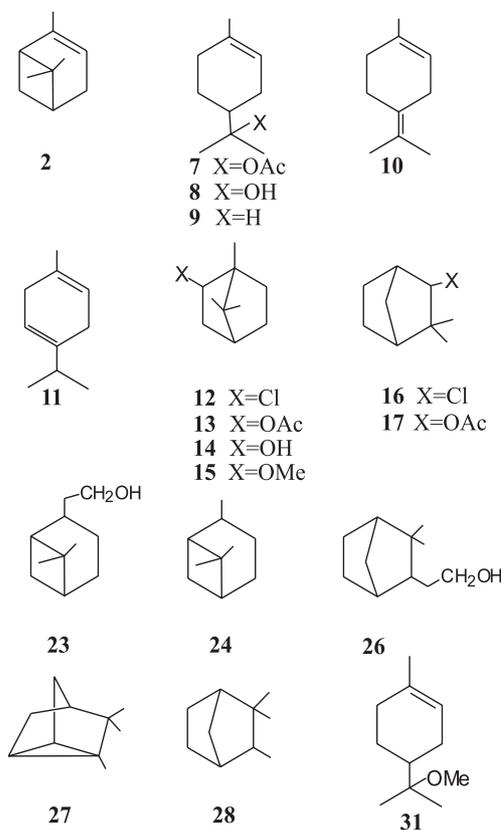
#### Palladium catalyzed oxidation of monoterpenes by dioxygen

We have investigated the use of the "Pd(II)+reversible re-oxidant (CuCl<sub>2</sub> or LiNO<sub>3</sub>)" catalytic systems for the oxidation of monoterpenes, such as limonene, camphene,  $\alpha$ -pinene and  $\beta$ -pinene, with dioxygen<sup>15,29,30,37</sup>. Acetic acid solutions of limonene (**1**) containing PdCl<sub>2</sub>, CuCl<sub>2</sub> and LiCl rapidly consumed dioxygen at 60–80 °C and 0.1 MPa<sup>37</sup>. Allylic oxidation of limonene into carveyl acetate (**5**, 85% *trans*) and carvone (**6**) was observed as a main reaction (Scheme 7), along with its isomerization into  $\alpha$ -terpinolene (**10**) and  $\gamma$ -terpinene (**11**) and an HOAc/H<sub>2</sub>O addition resulting in  $\alpha$ -terpenyl acetate (**7**) and  $\alpha$ -terpineol (**8**) (Scheme 8).



Scheme 7. Oxidation of limonene by dioxygen

Both addition and isomerization reactions are reversible, with no allylic oxidation of **7**, **8**, **10** and **9**, which contain no terminal



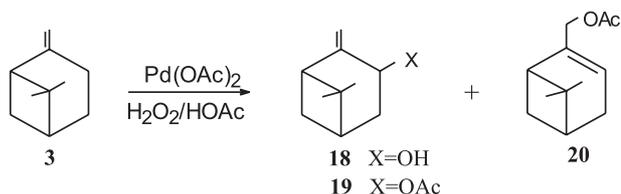
Scheme 8. Derivatives of monoterpenes

double bond, being observed. A  $\pi$ -allyl palladium complex was suggested as a reaction intermediate, with the coordination of the exocyclic double bond on the same palladium atom being of a critical importance for its reactivity: e.g., carvomenthene (**9**) undergoes no allylic oxidation even at high temperature<sup>37-39</sup>. The isomerization and addition equilibria are shifted towards the formation of **1** at higher conversions, thus, the selectivities for **5** and **6** rise significantly with the reaction time. Under the optimized conditions a 90% conversion and 96% combined selectivity for **5** and **6** were obtained. We have found that the rate of the allylic oxidation of limonene is the first order in copper concentration. This observation indicates that CuCl<sub>2</sub> has behavior far exceeding that of a simple re-oxidant. We have supposed that one of the specific functions of CuCl<sub>2</sub> is to assist at the decomposition of the  $\pi$ -allyl Pd intermediate due to the formation of bridging Pd-Cu complexes.

The reactions of  $\alpha$ -pinene (**2**) and  $\beta$ -pinene (**3**) under similar conditions result in a mixture of **5** (ca. 25%), **7** (ca. 25%), bornyl chloride (**12**) (ca. 30%), and fenchyl chloride (**16**) (ca. 15%)<sup>37</sup>. Camphene (**4**) also undergoes a skeletal rearrangement and an acetic acid/water addition resulting in bornyl acetate (**13**) and borneol (**14**) as major products<sup>15</sup>. The results obtained show that the application of the PdCl<sub>2</sub>-CuCl<sub>2</sub> system for the oxidation of bicyclic monoterpenes is limited, since CuCl<sub>2</sub>, acting as a Lewis acid, promotes undesirable non-oxidative skeletal isomerizations. We concentrated our efforts on developing a CuCl<sub>2</sub>-free catalyst. The activity of the Pd(OAc)<sub>2</sub>-LiNO<sub>3</sub> system has been studied<sup>15,37</sup>. Although nitrate ions readily re-oxidize reduced palladium species and are reoxidized back by dioxygen, no formation of oxidation products in significant amounts are observed for limonene,  $\alpha$ -pinene and  $\beta$ -pinene. In the case of camphene, however, highly selective oxidative processes occur in the presence of this catalytic system<sup>29,30</sup>.

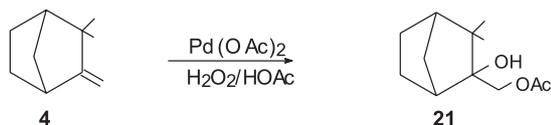
### Palladium catalyzed oxidation of monoterpenes by hydrogen peroxide

We have found that some monoterpenes can be selectively oxidized by  $H_2O_2$  using  $Pd(OAc)_2$  as the catalyst in  $HOAc/H_2O$  solutions in the absence of halogens and co-metals, with the olefin structure greatly influencing the product nature<sup>15</sup>.  $\beta$ -pinene gives the allylic oxidation products, *i.e.*, pinocarveol (**18**), pinocarveyl acetate (**19**), and myrtenyl acetate (**20**), with selectivity up to 75% at virtually complete conversion of **3** (Scheme 9). A competing skeletal isomerization and solvent addition yield various by-products, the major of them being **7**, along with **13**, **8**, and bornyl acetate (**17**).



Scheme 9. Oxidation of  $\beta$ -pinene by hydrogen peroxide

Camphene (**4**), which has the only and not easily abstractable allylic hydrogen at a bridgehead position, gives camphene glycol monoacetate **21** (Scheme 10) with ca. 90% selectivity at 80% substrate conversion. The introduction of benzoquinone (BQ) in catalytic amounts up to BQ/Pd=10 exerted a beneficial effect on the catalyst stability and selectivity. Product **21** was not detected at all if palladium acetate was excluded, therefore, its formation cannot be explained by a non palladium-centered epoxidation of camphene by the peroxyacetic acid generated *in situ* followed by ring opening of epoxide by acetic acid.



Scheme 10. Oxidation of camphene by hydrogen peroxide

The palladium catalyzed acetoxylation of  $\beta$ -pinene and camphene in aqueous acetic acid solutions containing hydrogen peroxide can

be seen as a nucleophilic attack by three nucleophiles, *i.e.*,  $H_2O_2$ ,  $H_2O$  and  $HOAc$ , on the olefin coordinated to palladium in a  $\pi$ - (for camphene) or  $\pi$ -allylic (for  $\beta$ -pinene) mode. The nature of reaction products depends strongly on the coordination mode, which, in turn, is determined by the olefin structure. The allylic derivatives of  $\beta$ -pinene **18-20** appear to be formed via the nucleophilic attack of the acetate group on a ( $\pi$ -allyl)-palladium intermediate, whereas glycol acetate **21** via hydroxy- or peroxy-palladation of olefin in a  $\pi$ -camphene-palladium complex (Scheme 11).

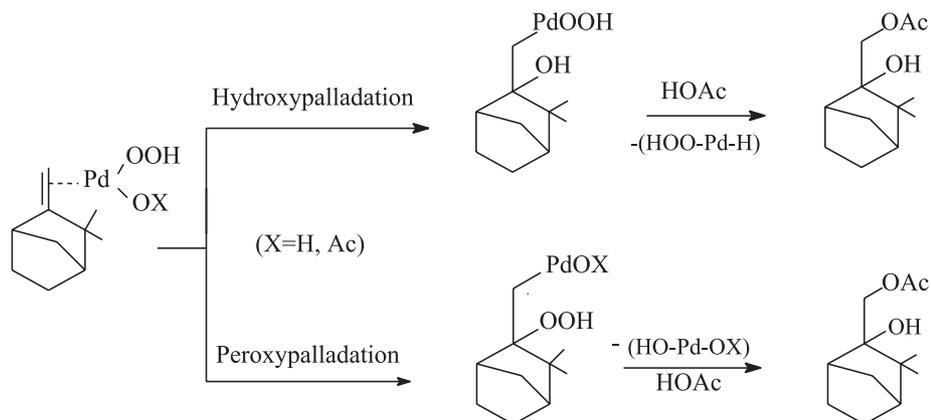
Without the oxidizable substrates hydrogen peroxide decomposes with palladium acetate, but this decomposition is fairly slow with respect to palladium-catalyzed oxidation of  $\beta$ -pinene and camphene. No selective oxidation of limonene and  $\alpha$ -pinene was observed under similar conditions<sup>15</sup>.

### Platinum/tin catalyzed hydroformylation of monoterpenes

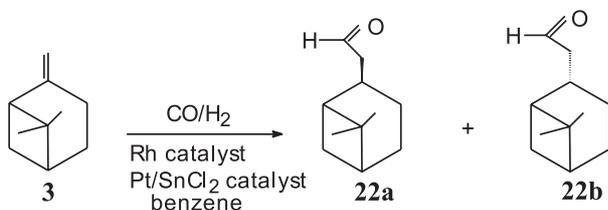
Hydroformylation represents a versatile method for the production of commercially important aldehydes and alcohols, which are difficult to obtain by conventional synthetic pathways. A number of monoterpenes<sup>40-42</sup> have been hydroformylated, in the presence of cobalt and rhodium complexes, which are most commonly used to catalyze this reaction in industrial processes. Most of the cobalt and rhodium catalysts promote a significant undesirable isomerization of  $\beta$ -pinene to  $\alpha$ -pinene. Among the alternative catalytic systems, those based on platinum/tin compositions are probably the most promising ones, as these systems allow high regioselectivity for the formation of linear aldehydes and are especially efficient in asymmetric reactions. However, their applications to monoterpenes are scarcer<sup>43-46</sup>.

We studied the hydroformylation of  $\beta$ -pinene (Scheme 12) using rhodium complexes and various phosphines and diphosphines as auxiliaries<sup>47</sup>. For all catalytic systems, a significant formation of  $\alpha$ -pinene **2** occurs, with the ratio between the *trans* and *cis* isomer of 10-formylpinane **22** depending on the auxiliary nature, temperature and Rh/P ratio. *Cis* isomer **22a** is preferentially formed in all promoted systems (60-85%).

In the presence of the  $PtCl_2P_2/SnCl_2/PPh_3$  systems ( $P=PPh_3$ ,  $P_2 = dppe$ ,  $dppp$ , and 1,4-bis(diphenylphosphino)butane ( $dppb$ )), hydroformylation of limonene (**1**),  $\beta$ -pinene (**3**), and camphene (**4**) proceeds regioselectively resulting exclusively in linear aldehydes (Schemes 12-14). The hydroformylation of **3** yields *trans*-isomer **22b** with a 98% diastereoisomeric excess (d.e.), while **1** and **4** give the diastereoisomeric mixtures of aldehydes **29** and **25** (d.e. of ca. 10 and



Scheme 11. Palladium catalyzed camphene oxidation



**Scheme 12.** Hydroformylation of  $\beta$ -pinene

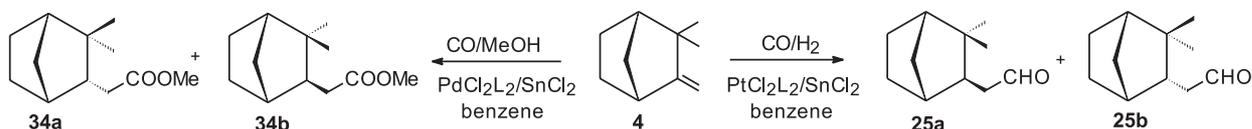
15%, respectively). Differently from most of the cobalt and rhodium catalysts, the isomerization of  $\beta$ - into  $\alpha$ -pinene is slow (1-5% on reacted **3**). Concurrent transformations of monoterpenes and primarily formed aldehydes occur: hydrogenation of substrates (into pinane (**24**), isocamphane (**28**), and **9**) and aldehydes (into alcohols **23** and **26**), substrate isomerizations which can be accompanied by a nucleophilic addition (giving **2**, tricyclene (**27**), **10-12**, and **16**), etc. Under optimized conditions, chemoselectivities for aldehydes of near 90% have been attained for all monoterpenes studied, however, d.e. for **25** is low in all systems with achiral ligands. Asymmetric hydroformylation of **4** in up to 60% d.e. has been achieved with  $\text{PtCl}_2(\text{PhCN})_2/\text{SnCl}_4/\text{diphosphine}$  catalysts containing chiral diphosphines such as (R)-(+)-binap (2,2'-bis(diphenylphosphino)-1,1'-binaphthyl)<sup>48</sup>.

Under hydroformylation conditions limonene can be converted in one pot into bicyclic alcohol **30**, useful as perfume, employing the  $\text{PtCl}_2(\text{dppb})/\text{PPh}_3/\text{SnCl}_4$  bifunctional catalyst, which promotes both the hydroformylation of **1** and then the stereospecific intramolecular cyclization of menthene (**29**)<sup>45</sup>. At 130 °C, **30** becomes the dominant product (ca. 82% selectivity at 95% conversion). High selectivities for **29** can be attained at lower conversions. In the absence of either a platinum complex or  $\text{SnCl}_4$ , no cyclization of **29** is observed, thus the heterobimetallic platinum-tin species seems to be involved in this reaction.

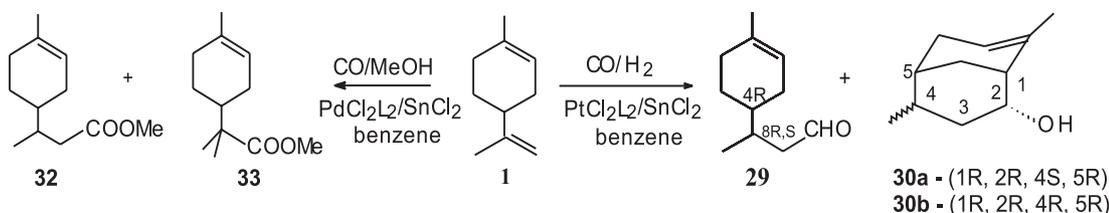
### Palladium/tin catalyzed alkoxy carbonylation of monoterpenes

Metal complex catalyzed alkoxy carbonylation represents another valuable route for the functionalization of monoterpenes which provides directly carboxylic acid derivatives. We used the  $\text{PdCl}_2\text{P}_2/\text{SnCl}_4/\text{PPh}_3$  systems as catalysts for alkoxy carbonylation of monoterpenes ( $\text{P}=\text{PPh}_3$ ,  $\text{P}_2 = \text{dppe}$ ,  $\text{dppp}$ ,  $\text{dppb}$ )<sup>49</sup>. Limonene gives mainly linear ester **32** (ca. 90%) along with **10**, **11** and methanol addition product **31**, while in the absence of  $\text{SnCl}_4$ , branched ester **33** is also formed (ca. 10%) (Scheme 14). The reaction of  $\beta$ -pinene yields exclusively the products of the Lewis acid catalyzed skeletal rearrangement/nucleophilic addition (**1**, **2**, **9-12**, **16**). No products of CO incorporation were observed. Camphene can be converted into linear ester **34** (**34a/34b**  $\approx$  1/1) with a 90% chemoselectivity and virtually 100% regioselectivity (linear/branched esters) (Scheme 13). Methyl bornyl ether **15** is the only major by-product.  $\text{SnCl}_4$  and  $\text{PdCl}_2(\text{PPh}_3)_2$  exhibit a strong synergetic effect on the camphene alkoxy carbonylation.  $\text{PdCl}_2(\text{PPh}_3)_2$  alone shows a very low catalytic activity promoting the predominant formation of thermodynamically more stable *exo* isomer **34b** (**34a/34b**  $\approx$  1/2).

It is surprising the difference in reactivity between camphene and  $\beta$ -pinene considering the similarity of these olefins. This difference could be related with the facility of  $\beta$ -pinene for the formation of  $\pi$ -allyl complexes with palladium(II), which are carbonylated at a much slower rate. The only allylic hydrogen in the molecule of camphene is at a tertiary carbon atom and not easily abstractable. So, the interaction of camphene with a palladium(II) hydride leads to the formation of a  $\pi$ -olefin complex followed by hydride addition. The stereochemistry of the ester is determined by the mode of camphene coordination to the palladium atom. In the presence of a sterically demanding  $\text{SnCl}_4$  ligand, the preferred coordination is through the less hindered "top" face of camphene resulting in ester **34a**. In the absence of  $\text{SnCl}_4$ , *exo* isomer **34b** is predominantly formed, which implicates the camphene coordination on the more crowded "bottom" face.



**Scheme 13.** Hydroformylation and alkoxy carbonylation of camphene



**Scheme 14.** Hydroformylation/cyclization and alkoxy carbonylation of limonene

## CONCLUSIONS

Organometallic catalysis offers excellent opportunities for organic synthesis, especially for the synthesis of fine chemicals. Transition metals have a very rich organic chemistry and promote a great number of organic transformations including unconventional ones. The exceptional specificity of their action and functional group tolerance

allow a flexibility in the choice of starting material and permit to develop environmentally benign catalytic processes with high atom utilization. The applications of organometallic catalysis was shown to be very promising routes for the selective oxyfunctionalization of low-priced naturally occurring monoterpenes, which are useful as substrates for the production of monoterpenoid flavors and fragrances. Various allylic acetates, alcohols, aldehydes, ketones and esters can

be obtained in good yields and in some cases with high stereoselectivity by catalytic oxidation, alkoxyacylation, hydroformylation, hydration<sup>50</sup> and acetoxylation<sup>50</sup> of limonene,  $\beta$ -pinene,  $\alpha$ -pinene and camphene.

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