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Journal of Organometallic Chemistry 690 (2005) 2996–3003
Journal of Organometallic Chemistry
www.elsevier.com/locate/jorganchem

Palladium catalyzed oxidation of monoterpenes: NMR study of palladium(II)–monoterpene interactions

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Received 5 January 2005; revised 11 March 2005; accepted 16 March 2005
Available online 26 April 2005

Abstract

Reactions of the monoterpenes β-pinene, limonene and myrcene with Pd(II) complexes in acetic acid solutions were studied by ^{1}H NMR spectroscopy. Various π-allyl palladium complexes were detected in situ and their interaction with $CuCl_2$ has been investigated. The results clarify the mechanism of allylic oxidation of these substrates mediated by Pd(II)/Cu(II)-based catalytic systems. Originally introduced to regenerate reduced palladium species, $CuCl_2$ has been shown to play an important role in the formation and/or decomposition of key reaction intermediates – π-allyl palladium complexes. β-Pinene and myrcene readily react with $Pd(OAc)_2$ giving corresponding π-allyls, with two complexes acyclic and cyclic being formed from myrcene. On the other hand, the formation of π-allyl complexes from limonene occurs at a significant rate only in the presence of $CuCl_2$. NMR observations, including selective paramagnetic enhancement of spin-lattice relaxation, indicate that π-allyl palladium intermediates specifically interact with Cu(II) ions in the reaction solutions. Such interaction probably involves Cu(II) bonding to Pd(II) via bridging ligands, and seems to be responsible for the accelerative effect of $CuCl_2$ in the palladium catalyzed oxidation of the monoterpenes. Indeed, most of these reactions do not occur at all in the absence of $CuCl_2$.

Keywords: Palladium; Oxidation; Limonene; β-Pinene; Myrcene

1. Introduction

Palladium catalyzed oxidations represent a commercially valuable pathway to oxygenated products from olefins and dioxygen, the most abundant and cheapest oxidant [1–5]. However, their applications to natural product synthesis are rather scare. Sufficiently abundant monoterpenes are particularly important precursors of oxygenated materials of interest to the flavor and fragrance industry, which is essentially based on the chemistry of terpenes [6–9]. For several years, we have been interested in palladium mediated oxidative transformations of monoterpenes, such as limonene, β-pinene, camphene and myrcene [10–16]. We have reported efficient and selective oxidations of limonene and β-pinene into allylic acetates in $PdCl_2$(cat)/$CuCl_2$(cat)/O_2 and $Pd(OAc)_2$(cat)/H_2O_2 systems, respectively [10,11]. A conventional Wacker catalyst ($PdCl_2$/$CuCl_2$) has been used to promote a novel oxidative cyclization of myrcene giving new acetates with a cyclopentane skeleton [13]. Recently, we have developed a chloride-free multi-component catalytic combination $Pd(OAc)_2$/benzoquinone/Cu or Mn acetates for the aerobic oxidation of limonene [15]. A good control of chemo- and regioselectivities in the allylic oxidation of limonene has been achieved through the addition of *p*-toluenesulfonic acid.

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doi:10.1016/j.jorganchem.2005.03.026

The products of the oxidation of limonene, β-pinene and myrcene reported in the works cited above seem to arise via the intermediate formation of π-allyl palladium complexes, with $CuCl_2$ (if any) having behavior far exceeding that of a simple reoxidation agent. We have supposed that one of the specific functions of $CuCl_2$ is to assist at the decomposition of the π-allyl intermediates due to the formation of bridging Pd–Cl–Cu complexes, but no spectroscopic studies to support this hypothesis have been carried out so far.

In the case of camphene, the only allylic hydrogen is at a bridgehead position and not easily abstracted, so allylic oxidation products are not expected. Indeed, the oxidation of camphene with hydrogen peroxide catalyzed by $Pd(OAc)_2$ resulted in glycol derivatives [11], whereas a $Pd(II)/NO_n^-(n = 2, 3)$ catalytic system promoted its oxidative coupling [12,14]. We have recently studied by in situ NMR the interaction of camphene with palladium(II) complexes and obtained evidence for the formation of σ-vinyl palladium hydride intermediates [16].

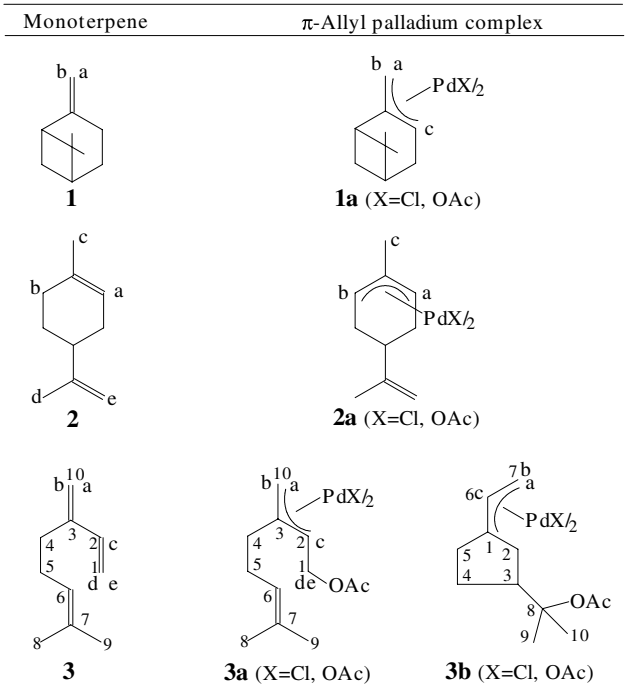
This paper reports NMR studies of the reactions between other monoterpenes, i.e., β-pinene, limonene and myrcene, and Pd(II) complexes in acetic acid solutions. We have detected the formation of various π-allyl palladium complexes and investigated their interaction with $CuCl_2$. The results clarify the mechanism of allylic oxidation of these substrates mediated by Pd(II)/Cu(II)-based catalytic systems.

2. Experimental

All reagents were purchased from commercial sources and used as received, unless otherwise indicated. Myrcene was purchased from Aldrich and distilled before use. The reactions were carried out in a stirred glass reactor and followed by measuring the dioxygen uptake (if any) and/or by gas chromatography (GC) (Shimadzu 17A, Carbowax 20 M). NMR spectra were recorded at 25 °C using a Bruker DRX-400 *AVANCE* spectrometer operating at 400 MHz. Chemical shifts are referenced to tetramethylsilane as internal standard. In NMR standard experiments, concentrations of monoterpenes and $Pd(OAc)_2$ were 20 and 10 mM, respectively. CD_3COOD (99.5 atom% D) was used as a solvent in NMR experiments. T_1 measurements used a standard inversion-recovery method with 20 s relaxation delays.

3. Results and discussion

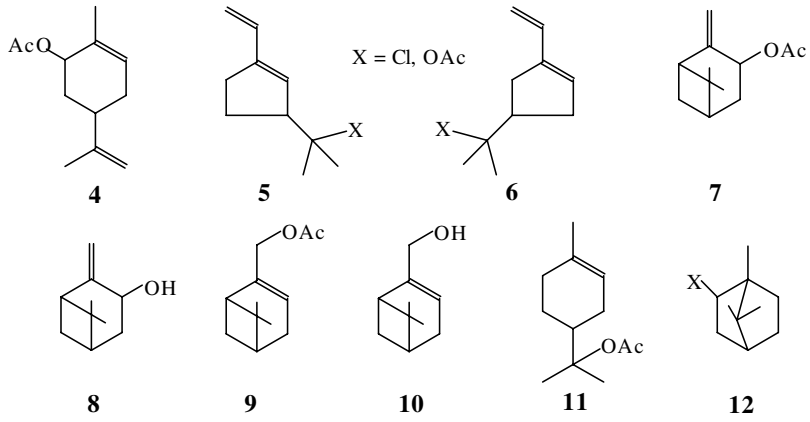
In acetic acid solutions, all three monoterpenes studied, i.e., β-pinene (**1**), limonene (**2**) and myrcene (**3**) (Scheme 1) undergo a palladium catalyzed oxidation by dioxygen. The main products formed in these reactions



Scheme 1.

are shown in Scheme 2. With a $PdCl_2/CuCl_2$ catalytic system, limonene gives mainly carveyl acetate **4** with up to 90% selectivity [10], whereas myrcene selectively forms the products of oxidative cyclization **5** and **6** [13]. It has been suggested that all these compounds originate from corresponding π-allyl palladium complexes. On the other hand, a palladium catalyzed oxidation of β-pinene in acetic acid solutions containing $CuCl_2$ is strongly complicated by its skeletal rearrangement accompanied by the addition of nucleophiles present in the solutions [10]. A combined selectivity of only 15% for allylic oxidation products **7**–**10** has been detected after 22 h of the reaction ([β-pinene] = 0.25 M, $[Pd(OAc)_2]$ = 0.01 M, $[CuCl_2]$ = 0.02 M, [LiCl] = 0.05 M, 25 °C). Main products are α-terpenyl acetate **11** and bornyl derivatives **12**, arising from the nucleophilic attack by acetate or chloride ions on the carbonium ions formed by the protonation of original β-pinene. A selective allylic oxidation of β-pinene was achieved in a $CuCl_2$-free system, using $Pd(OAc)_2$ as catalyst and hydrogen peroxide as both a final oxidant and reoxidant for reduced palladium species [11]. Pinocarveol **8** and myrtenol **10**, along with their acetates **7** and **9**, were obtained with 75% combined selectivity.

$CuCl_2$, originally introduced to regenerate palladium, plays a key role in the oxidation of limonene and myrcene. Both reactions are accelerated by increased Cu(II) concentration, with an approximately first order rate dependence being observed. Moreover, substitution of $CuCl_2$ by other conventional reoxidants dramatically affects the oxidation reactions. Although nitrate ions readily oxidize reduced palladium species in acetic acid



Scheme 2.

solutions and are reoxidized back by dioxygen, neither significant oxygen consumption nor the formation of oxidation products from myrcene have been observed in the presence of $Pd(OAc)_2/LiNO_3$, $Pd(OAc_2)/Cu(NO_3)_2$ or $Pd(OAc_2)$/benzoquinone catalytic combinations [13]. The $Pd(II)/NO_3^-$ system also showed a very low activity in the oxidation of limonene and β-pinene [12]. In the case of β-pinene, a reasonable selectivity of ca. 50% for oxidation products **8** and **10** was obtained only in chloroform solutions, whereas in acetic acid the concomitant acid-catalyzed isomerization/nucleophilic addition reactions predominated.

We studied the interaction of β-pinene, limonene and myrcene with palladium complexes in the absence and in the presence of Cu(II) ions in deuteriated acetic acid. Solutions of monoterpene (1 equiv.) and $Pd(OAc)_2$ (0.5 equiv.) were monitored by ^1H NMR for 3–7 h. Then, $CuCl_2$ (0.125 equiv.) was introduced into the system and the spin-lattice relaxation times of the hydrogen nuclei of the substrates and of the reaction intermediates were measured. It has been observed that the addition of $Pd(OAc)_2$ to the solution of monoterpenes leads to the appearance of various new signals in the NMR spectra. The analysis of the changes in their intensities, chemical shifts and relaxation times induced by Cu(II) permitted us to clarify the mechanism of the Pd(II)/Cu(II) catalyzed allylic oxidation of these monoterpenes and to understand their different reactivities.

The addition of $Pd(OAc)_2$ to the acetic acid solution of β-pinene resulted in no detectable changes in chemical shifts, widths and relative intensities of its ^1H NMR signals, even after 7 h (Table 1). Thus, no π-olefin palladium complex is formed in significant concentrations from β-pinene during the reaction. On the other hand, some signals attributed to π-allyl palladium complex **1a** (Scheme 1, Table 1) appear in the spectrum: two singlets at 1.00 and 1.38 ppm from methyl groups and three broadened signals from allylic hydrogens (singlets at 2.95 and 3.72 ppm and doublet at 4.11 ppm). The intensities of these signals slowly increase with reaction time. After 1.5 h and then 5 h, 10% and 35% of β-pinene, respectively, was converted into π-allyl complex **1a**. After ca. 7 h, equimolar amounts of **1a**, based on $Pd(OAc)_2$ added, were detected in the reaction solution (**1/1a** ≈ 1/1). The spectral characteristics of complex **1a** are in agreement with those previously reported for related complexes [17–19]. Measurements of spin-lattice relaxation times (T_1) of the hydrogens of **1** and **1a** provide additional evidence for the signal attribution. The values of T_1 obtained for the hydrogens of **1a** were much shorter (by ca. 10 times) than those of the hydrogens of β-pinene, which is fully consistent with much higher molecular weight of **1a** and its consequent, much faster relaxation (Table 2).

The addition of $CuCl_2$ (0.125 equiv.) and LiCl (1 equiv.) had no detectable effect on the signals of β-pinene, however the signals of **1a** became much broader, especially those of allylic hydrogens H_a, H_b and H_c. In addition, significant shielding (12–36 Hz) of the signals of **1a** was observed in the presence of paramagnetic Cu(II), with the changes in chemical shifts of the allylic hydrogens being greater than those of the methyl groups (Table 1). Moreover, a specific paramagnetic relaxation enhancement of the hydrogens of π-allyl palladium complex **1a** occurs in the presence of Cu(II), i.e., the allylic hydrogens relax much faster (by 4–8 times) than other hydrogens of the molecule. For example, the value of T_1 or H_a is ca. 8 times shorter than those of the methyl groups. As can be seen from Table 2, the introduction of Cu(II) results as expected in somewhat faster relaxation of all nuclei in the solution: T_1 of the hydrogens of β-pinene and of the methyl hydrogens of **1a** becomes 3–4 times shorter than in the absence of $CuCl_2$. However, the allylic hydrogens of **1a** relax up to 14 times faster in the presence of $CuCl_2$, a much greater increase.

In presence of a small concentration of paramagnetic ions, the spin-lattice relaxation is known to be often dominated by pairwise electron–nuclear dipole–dipole

Table 1
NMR data for β-pinene (**1**) and π-allyl palladium complex **1a**

	β-Pinene (**1**) $\delta(^1H)$[b]				π-Allyl palladium complex **1a** $\delta(^1H)$[b]				
	H_a	H_b	CH_3	CH_3	H_a	H_b	H_c	CH_3	CH_3
1[a]	4.61 (br.s)	4.55 (br.s)	0.72 (s)	1.23 (s)					
1 + 0.5 equiv. $Pd(OAc)_2$[a]	4.61 (br.s)	4.55 (br.s)	0.72 (s)	1.23 (s)	2.95 (br.s)	3.72 (br.s)	4.11 (br.d)	1.00 (s)	1.38 (s)
1 + 0.5 equiv. $Pd(OAc)_2$ + 0.125 equiv. $CuCl_2$ + 1 equiv. LiCl[a]	4.61 (br.s)	4.55 (br.s)	0.72 (s)	1.23 (s)	2.86 (br.s)	3.63 (br.s)	4.05 (br.d)	0.95 (s)	1.35 (s)
$\Delta\delta$[c] (Hz)	0	0	0	0	36	36	24	20	12

[a] [β-pinene] = 20 mM, 25 °C, solvent: CD_3COOD.
[b] Resonance multiplicities in parentheses: (s) singlet, (d) doublet, (br) broadened.
[c] Chemical shift changes induced by the addition of $Pd(OAc)_2$ and/or $CuCl_2$/LiCl.

Table 2
Relaxation times (T_1) for the protons of β-pinene (**1**) and π-allyl palladium complex **1a** in the absence and in the presence of Cu^{2+}

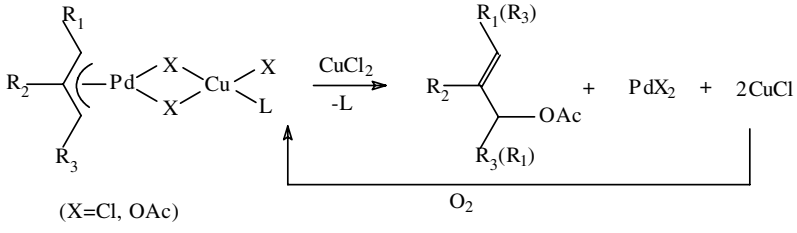
	β-Pinene (**1**) T_1 (s) of proton(s)				π-Allyl palladium complex **1a** T_1 (s) of proton(s)				
	H_a	H_b	CH_3	CH_3	H_a	H_b	H_c	CH_3	CH_3
In the absence of Cu^{2+}[a]	3.87	3.62	2.48	2.34	0.22	0.41	0.27	0.55	0.54
In the presence of Cu^{2+}[b]	0.86	0.90	0.70	0.68	0.02	0.03	0.04	0.15	0.16
Increase factor $T_1/T_{1(Cu)}$[c]	4.5	4.0	3.5	3.4	11.0	14.0	6.8	3.7	3.4

[a] [β-pinene] = 20 mM, [$Pd(OAc)_2$] = 10 mM, 25 °C, solvent: CD_3COOD.
[b] [β-pinene] = 20 mM, [$Pd(OAc)_2$] = 10 mM, [$CuCl_2$] = 2.5 mM, [LiCl] = 20 mM, 25 °C, solvent: CD_3COOD.
[c] Ratio between the relaxation times in the absence and in the presence of Cu^{2+}.

interactions between an unpaired spin of the paramagnetic center and the magnetic moment of a resonant nucleus. Therefore, the relaxation time may be used with care as a measure of its distance from the paramagnetic center. The larger the distance, the weaker the paramagnetic contribution to the relaxation. Thus, a specific paramagnetic relaxation (Table 2) as well as paramagnetic shifts (Table 1) of the signals of **1a** indicate a specific interaction between π-allyl complex **1a** and Cu(II) ions, with the latter being spatially more proximate to the allylic hydrogens of the molecule. It is reasonable to suggest that such interaction is realized via the formation of bimetallic π-allyl palladium–copper complexes with bridging acetate or, more probably, chloride ligands X as shown in Scheme 3.

It is worthwhile to emphasize the importance of chloride ions in the formation of such bimetallic complexes. When only $CuCl_2$, without LiCl, was added to the mixture of **1** and **1a** in acetic acid, the signals of π-allyl complex **1a** first broadened but then became thinner before rapidly returning to their original widths. Simultaneously, the yellow-brown solution (a color of $Pd(OAc)_2$ and anhydrous $CuCl_2$) changed to green (a color of $Cu(OAc)_2$), which indicated a substitution of chloride ligands on Cu(II) by acetate groups due to a ligand exchange with Pd(II). The addition of LiCl to this solution turned it back to brown, with the signals of π-allyl complex **1a** becoming broadened again because of the specific interaction with paramagnetic Cu(II) ions.

The allylic oxidation of β-pinene, as well as its isomerization, is slow at room temperature, with only trace amounts of oxidation products **7** and **9** being formed during the NMR experiments. At higher temperatures, a conversion of β-pinene begins; however, as mentioned above, the acid-catalyzed isomerization of β-pinene accompanied by the nucleophilic addition of chloride and acetate groups occurs faster than its palladium catalyzed oxidation.



Scheme 3.

Differently from β-pinene, limonene (**2**) reacts very slowly with $Pd(OAc)_2$ in acetic acid solutions at room temperature. Only trace amounts of π-allyl complex **2a** (Scheme 1) were detected by ^1H NMR after a 5-h reaction (two singlets at 1.65 and 1.73 ppm from methyl groups and triplet at 4.75 ppm from two allylic hydrogens). It should be mentioned that NMR study of the interaction between limonene and Pd(II) complexes is complicated by a partial signal overlap in the region of 4.7–4.8 ppm between the signals from allylic hydrogens H_a and H_b of complex **2a** and the signals from terminal vinylic hydrogens H_e of limonene and those from its oxidation product **4** as well as from vinylic hydrogens of **2a** itself (Table 3). The spectral characteristics of complex **2a** agree with those previously reported for related complexes [18,20]. As in the case of β-pinene, the addition of $Pd(OAc)_2$ resulted in no detectable changes in chemical shifts, widths and relative intensities of ^1H NMR signals of limonene, even in the presence of $CuCl_2$. Thus, in acetic acid solutions, the π-olefin palladium complex, which should be a short-lived intermediate, is not formed from limonene in measurable concentrations.

The addition of $CuCl_2$ (0.125 equiv.) and LiCl (1 equiv.) dramatically accelerates the formation of both π-allyl complex **2a** and oxidation product **4** from limonene. Within a few minutes at room temperature, the concentrations of **2a** and **4** in the solution reach 35% and 7% of the initial concentration of limonene, respectively. Thus, a significant fraction of the Pd(II) ions present in the solution is rapidly converted to allylic complex **2a** (initial molar ratio limonene/Pd(II) = 2). Due to the partial signal overlapping mentioned above, the times of the spin-lattice relaxation of the hydrogens of **2a** were determined in this case from the null points through which their relatively sharp resonances pass as they recover from their inversion. The values of T_1 obtained for the hydrogens of **2a** are, as expected, much shorter than those of limonene (Table 3). A specific interaction of Cu(II) ions with π-allyl complex **2a** was confirmed as previously by the substantial and specific added relaxation enhancement they induce. In the presence of $CuCl_2$, the T_1 values of the hydrogens of limonene generally become 4–8 times shorter, but those of **2a** decrease ca. 20 times. This is most probably induced by the binding of Cu(II) to Pd(II) via bridging ligands (Table 3). The decomposition of these complexes occurs even at room temperature, giving carveyl acetate **4** in the presence of $CuCl_2$.

Thus, the formation of the π-allyl palladium complex from limonene in acetic acid solutions proceeds at a significant rate only in the presence of $CuCl_2$. On the other hand, β-pinene readily forms the corresponding π-allyl complex without the assistance of $CuCl_2$; though even in this case $CuCl_2$ also accelerates the process. This effect can be explained by the participation in these processes of bimetallic Pd–Cu complexes formed in the reaction solutions. We have previously reported the spectroscopic data obtained during the study of a related Wacker oxidation of propylene, which indicate the formation of heterometallic Pd–Cu species in acetic acid solutions [21]. It is known that π-allyl palladium complexes are formed from olefins via the intermediate formation of π-olefin complexes. Then a formal oxidative addition of the olefin molecule to palladium(II) occurs giving palladium(IV) hydride intermediates. The presence of electrophilic Cu(II) ions bound to palladium via bridging ligands should favor the olefin coordination to the palladium atom bearing now a more positive partial charge. Moreover, $CuCl_2$ can be also involved in the oxidative decomposition of the palladium(IV) hydrides resulting in π-allyl complexes [18].

The paramagnetic relaxation enhancements show that both the π-allyl complexes, **1a** and **2a**, specifically interact with Cu(II) ions, most probably, via the formation of bimetallic π-allyl Pd–Cu complexes with bridging chloride (or acetate) ligands. The decomposition of these complexes results in the products of the allylic oxidation of limonene and β-pinene as shown in Scheme 3. There is in fact a large difference in the reactivity of complexes **1a** and **2a** in the presence of $CuCl_2$, with the latter complex, formed from limonene, being much more reactive towards a nucleophilic attack by acetate group leading

Table 3
NMR data for limonene (**2**) and π-allyl palladium complex **2a**: chemical shifts (δ) and relaxation times (T_1)

	Limonene (**2**)				π-Allyl palladium complex **2a**	
	H_a	H_e	$CH_{3(c)}$	$CH_{3(d)}$	H_a and H_b	$CH_{3(c)}$
$\delta(^1H)$[a]	5.40 (br.s)	4.70 (s)	1.65 (s)	1.73 (s)	4.75 (t, $^3J = 6.4$)	1.68 (s)
T_1 (s)[b] in the absence of Cu^{2+}	3.14	1.44	1.81	1.95	1.00[e]	1.18[e]
$T_{1(Cu)}$ (s)[c] in the presence of Cu^{2+}	0.39	0.32	0.32	0.29	0.05[e]	0. 05[e]
Increase factor $T_1/T_{1(Cu)}$[d]	8.0	4.5	5.6	6.7	20.0	23.6

[a] Resonance multiplicities and coupling constants (Hz) in parentheses: (s) singlet, (t) triplet, (br) broadened.
[b] [Limonene] = 20 mM, $[Pd(OAc)_2]$ = 10 mM, 25 °C, solvent: CD_3COOD.
[c] [Limonene] = 20 mM, $[Pd(OAc)_2]$ = 10 mM, $[CuCl_2]$ = 2.5 mM, [LiCl] = 20 mM, 25 °C, solvent: CD_3COOD.
[d] Ratio between the relaxation times in the absence and in the presence of Cu^{2+}.
[e] Determined from the null points through which the resonances pass as they recover from their inversion.

to carveyl acetate **4**, i.e., a net allylic oxidation. The presence of electrophilic Cu(II) ions bound to palladium in π-allylic intermediates should render them more susceptible to such attack.

A high stability of the π-allyl complexes formed from β-pinene, even in the presence of Cu(II) ions, seems to be responsible for the low selectivity obtained in the oxidation of β-pinene. In acetic acid solutions, especially in those containing chloride ions, this substrate undergoes a double-bond protonation followed by isomerization or nucleophilic addition that is much faster than the allylic oxidation. A selective allylic oxidation of β-pinene has been realized only in a chloride-free system, using $Pd(OAc)_2$ as a catalyst [11]. This result is completely consistent with the expected relative reactivities of π-allyl palladium chlorides and π-allyl palladium acetates, with the latter being much more prone to collapse to allylically substituted systems [18]. Thus, under such conditions, the allylic oxidation of β-pinene successfully competes with its protonation. On the other hand, we have failed to develop a selective oxidation of limonene in the $CuCl_2$ free systems, i.e., $Pd(OAc)_2$(cat)/$LiNO_3$-(cat)/O_2 and $Pd(OAc)_2$(cat)/H_2O_2, which can now be explained by a key role of $CuCl_2$ in the formation of π-allyl palladium complexes from limonene and also in their decomposition.

The other monoterpene studied, myrcene (**3**), readily reacts with Pd(II) complexes in acetic acid solution even at room temperature, giving the acyclic and cyclic π-allyl–palladium complexes **3a**and **3b** (Scheme 1). Spectral characteristics of these compounds, consistent with those of related complexes [22–24], are presented in Tables 4 and 5. The intensities of the signals of **3a** and **3b** slowly increase with reaction time and, at 4 h, correspond to ca. 40% conversion of myrcene, which is slightly less then an equimolar proportion based on palladium added (initial ratio **3**/Pd≈2/1). The values of T_1 obtained for the hydrogens of **3a** and **3b** are, as expected, much shorter (by 5–10 times) than T_1 for the hydrogens of myrcene itself. The cyclic complex **3b**, which seems to be a precursor of substituted cyclopentenes **5** and **6**, predominates in the reaction of myrcene with $Pd(OAc)_2$(**3a**/**3b** = 1/2).

It is interesting that the addition of LiCl (1 equiv.) leads to a further increase in the relative amounts of the cyclic complex **3b** (**3a**/**3b** ≈ 1/5). We also note that in the absence of chloride ions, the signals of all allylic hydrogens in both allylic complexes **3a** and **3b**, as well as hydrogens H_e and H_d in **3a** are slightly broadened and become well resolved only after the addition of LiCl. No products of the oxidation of myrcene appear in detectable concentrations in the absence of $CuCl_2$.

Next, we studied the interaction of these intermediates with $CuCl_2$. The addition of $CuCl_2$ (0.125 equiv.) immediately results in significant broadening the signals of π-allyl complexes **3a** and **3b** but not the signals of myrcene

Table 4
NMR data for myrcene (**3**) and π-allyl palladium complex **3a**: chemical shifts (*δ*)nd relaxation times (T_1)

Carbon atom	Hydrogen atom	Myrcene (**3**)				π-Allyl palladium complex **3a**			
		$\delta(^1H)$[a]	T_1 (s)[b]	$T_{1(Cu)}$ (s)[c]	$T_{1(Cu)}$ (s)[d]	$\delta(^1H)$[a]	T_1 (s)[b]	$T_{1(Cu)}$ (s)[c]	$T_{1(Cu)}$ (s)[d]
1	H_d	5.25 (d, $^3J_{d-e}$ = 17.6)	2.73	2.84	1.67	4.48 (dd, $^3J_{d-c}$ = 5.2, $^3J_{d-e}$ = 12.6)	0.61	0.63	0.42
	H_e	5.04 (d, $^3J_{e-c}$10.8)	3.36	3.46	1.56	4.27 (dd, $^3J_{e-c}$ = 9.1, $^3J_{e-d}$ = 12.6)	0.48	0.43	0.40
2	H_c	6.38 (dd, $^3J_{c-d}$ = 17.6, $^3J_{c-e}$ = 10.8)	12.92	8.46	8.96	3.54 (dd, $^3J_{c-d}$ = 5.2, $^3J_{c-e}$ = 9.1)	0.94	0.99	0.96
4	H-4	2.17–2.25	2.80	2.97	2.17	1.80–1.86 (m)	0.78	0.79	n.d.[e]
5	H-5	2.17–2.25	2.80	2.97	2.17	2.20–2.40 (m)	n.d.[e]	n.d.[e]	n.d.[e]
6	H-6	5.16 (t, ^3J = 6.0)	3.08	3.06	1.90	5.33–5.38 (m)	1.20	1.33	0.96
8	H-8	1.60 (s)	5.25	4.98	3.17	1.64 (s)	1.34	1.36	1.20
9	H-9	1.68 (s)	2.85	2.94	2.04	1.71 (s)	1.59	1.54	1.57
10	H_a	5.00 (s)	3.30	3.39	2.43	2.82 (s)	0.47	0.49	0.61
	H_b	5.00 (s)	3.30	3.39	2.43	3.83 (s)	0.49	0.51	0.44

[a] Resonance multiplicities and coupling constants (Hz) in parentheses: (s) singlet, (d) doublet, (t) triplet, (dd) doublet of doublets, (m) multiplet.
[b] [Myrcene] = 20 mM, [$Pd(OAc)_2$] = 10 mM, [LiCl] = 20 mM, 25 °C, solvent: CD_3COOD.
[c] [Myrcene] = 20 mM, [$Pd(OAc)_2$] = 10 mM, [$CuCl_2$] = 2.5 mM, [LiCl] = 20 mM, 25 °C, solvent: CD_3COOD.
[d] More 2.5 mM of $CuCl_2$ were added to the solution.
[e] Not determined.

Table 5
NMR data for π-allyl palladium complex **3b**: chemical shifts (δ) and relaxation times (T_1)

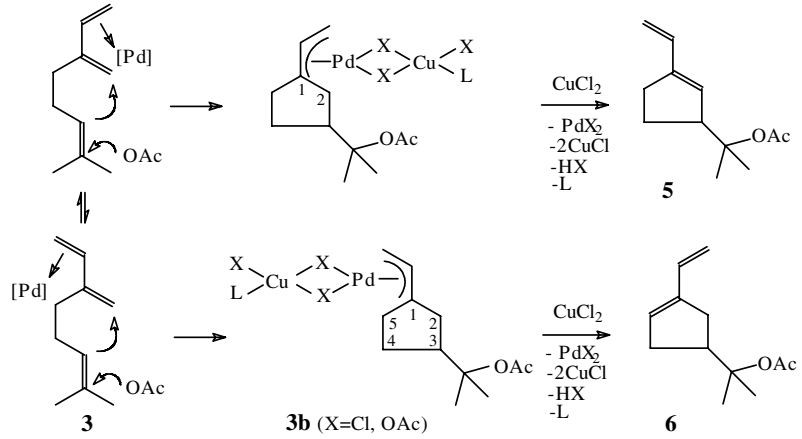
Carbon atom	Hydrogen atom	$\delta(^1H)$[a]	T_1 (s)[b]	$T_{1(Cu)}$ (s)[c]	$T_{1(Cu)}$ (s)[d]
2	H-2	2.30–2.40 (m)	0.63	0.59	0.69
3	H-3	2.50–2.60 (m)	0.56	0.78	0.61
4	H-4	2.30–2.40 (m)	0.63	0.59	0.69
5	H-5	2.30–2.40 (m)	0.63	0.59	0.69
6	H_c	5.33–5.38 (m)	1.20	1.33	0.96
7	H_a (1st isomer)	3.07 (d, $^3J_{a-c}$ = 12.4)	0.45	0.48	0.41
	H_a (2nd isomer)	3.05 (d, $^3J_{a-c}$ = 11.7)			
	H_b (1st isomer)	3.85 (d, $^3J_{b-c}$ = 7.4)	0.49	0.51	0.44
	H_b (2nd isomer)	3.89 (d, $^3J_{b-c}$ = 7.1)			
9	H-9	1.49 (br.s)	0.50	0.56	0.59
10	H-10	1.49 (br.s)	0.50	0.56	0.59

[a] Resonance multiplicities and coupling constants (Hz) in parentheses: (s) singlet, (d) doublet, (m) multiplet, (br) broadened.
[b] [Myrcene] = 20 mM, [$Pd(OAc)_2$] = 10 mM, [LiCl] = 20 mM, 25 °C, solvent: CD_3COOD.
[c] [Myrcene] = 20 mM, [$Pd(OAc)_2$] = 10 mM, [$CuCl_2$] = 2.5 mM, [LiCl] = 20 mM, 25 °C, solvent: CD_3COOD.
[d] More 2.5 mM of $CuCl_2$ were added to the solution.

itself. This clearly indicates a specific interaction of Cu(II) ions with the allylic intermediates. Measuring spin-lattice relaxation times showed, to our surprise, no significant increase in the relaxation times of any nucleus present in the solutions, which the paramagnetic Cu(II) ions should induce. Indeed, as can be seen in Tables 4 and 5, the relaxation times of the hydrogens of **3a** and **3b** as well as of the myrcene itself are very similar in the absence and in the presence of $CuCl_2$. Moreover, when the ^1H NMR spectrum of the solution was re-measured after the T_1 experiment, all the previously broadened signals of **3a** and **3b** became well resolved and returned to their original widths. Simultaneously, a fast conversion of myrcene into **5** and **6** (as well as into some unidentified products) was observed even at room temperature, with the total amounts of these products approximately corresponding to the amounts of $CuCl_2$ added. The formation of the products **5** and **6** was monitored by the integrals of the signals from the vinylic hydrogens at 6.50–6.57 ppm (doublet of doublets) and 5.62–5.68 ppm (broadened signal) [13].

These results show that $CuCl_2$ interacts with π-allyl–palladium complexes of myrcene and promotes their fast decomposition to oxidation products. However, no paramagnetic enhancement of spin-lattice relaxation is observed here because, as a result of this reaction, all Cu(II) ions added are rapidly reduced to diamagnetic Cu(I) (the reaction mechanism is discussed below). The addition of extra amounts of $CuCl_2$ (more 0.125 equiv.) to the solution promoted a further conversion of myrcene with the formation of **5** and **6** in stoichiometric amounts relative to Cu(II). After initial broadening, the signals of the π-allylic intermediates rapidly returned to their original widths. All Cu(II) ions added were converted into Cu(I) because no significant decrease in spin-lattice relaxation times of the nuclei of either myrcene or π-allyl–palladium complexes was observed in this case (Tables 4 and 5).

So, once again, the accelerative effect of $CuCl_2$ on the decomposition of π-allyl–palladium complexes has been confirmed spectroscopically. The proposed pathway of myrcene oxidative cyclization is shown in Scheme 4.



Scheme 4.

First, two isomers of π-allyl complex **3b** are formed from *s-cis* and *s-trans* conformations of myrcene. It should be mentioned that, as in the case of β-pinene and limonene, the addition of Pd(II) ions, even together with $CuCl_2$, results in no detectable changes in ^1H NMR signals of myrcene. Thus, intermediate π-olefin palladium complexes formed from myrcene should be present during the reaction, albeit in non-detectable low concentrations. The π-allyl palladium intermediates decompose probably via *anti*-elimination [25] giving two isomers of substituted vinyl cyclopentene **5** and **6** and a palladium(II) hydride, with hydrogen being abstracted from carbons 2 or 5. As confirmed by the NMR study, a coordination of Pd(II) with Cu(II) in **3b** is crucial for the reactivity of this intermediate towards the decomposition. In the absence of $CuCl_2$, no appreciable reaction occurs under the conditions studied. Palladium hydride undergoes an intramolecular redox reaction resulting in a proton and Pd(0) complex, which is recycled by $CuCl_2$. The reduced Cu(I) species can be oxidized back to Cu(II) by dioxygen, thus keeping the catalytic system active. This occurs readily in a catalytic reactor under intense stirring, whereas it is strongly limited by an oxygen transfer process in the NMR tube. Thus, the palladium metal and Cu(I) ions are formed at the end of NMR experiments.

4. Conclusions

In summary, a specific function of $CuCl_2$ in the palladium catalyzed allylic oxidation of some monoterpenes has been clarified by in situ NMR. Originally, introduced to regenerate reduced palladium species, $CuCl_2$ was shown to play an important role in the formation and/or decomposition of key reaction intermediates – π-allyl palladium complexes. While β-pinene and myrcene readily react with $Pd(OAc)_2$ in acetic acid solutions giving stable π-allyls, the formation of corresponding complexes from limonene occurs at a significant rate at room temperature only in the presence of $CuCl_2$. The results of the NMR experiments, in particular selective paramagnetic relaxation enhancement, indicate that the π-allyl palladium intermediates specifically interact with paramagnetic Cu(II) ions in the reaction solutions. Such interaction probably involves Cu(II) bonding to Pd(II) via bridging ligands and seems to be responsible for the accelerative effect of $CuCl_2$ in the palladium catalyzed oxidation of the monoterpenes. Most of these reactions do not occur at all in the absence of $CuCl_2$.

Acknowledgments

We acknowledge the financial support from the CNPq and FAPEMIG (Brazil) and scholarships from CNPq (MJS and JAG). The authors thank Ivana Silva Lula for technical assistance in the NMR studies.

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