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Palladium-catalyzed oxidation of monoterpenes: Highly selective syntheses of allylic ethers from limonene

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Abstract

Selective oxidation of limonene (**1**) with benzoquinone in the solutions of various alcohols (methanol, ethanol and 2-propanol) containing catalytic amounts of palladium(II) complexes and *p*-toluenesulfonic acid has been carried out. Two isomeric allylic ethers have been characterized as major products in each alcohol, showing that they arise from either exo- or endocyclic η^3-allyl intermediates formed by the reaction of palladium catalysts with the endocyclic C=C bond of limonene. A good control of regioselectivity was achieved through the appropriate choice of the ligand on palladium and reaction conditions. Allylic ethers **2a–c** with two exocyclic double bonds are main reaction products in chloride-free catalytic systems, while carveol derivatives **3a–c** are formed when palladium chloride is used as the catalyst. *p*-Toluenesulfonic acid exerts a great accelerative and catalyst stabilizing effect in these reactions. Monoterpenic ethers **2a–c** and **3a–c** have mild scents of flower or fruit and can be useful as components of synthetic fragrances. These compounds were obtained in 80–97% chemoselectivity each at a limonene conversion of 95–98% under appropriate conditions.

Keywords: Palladium; Limonene; Allylic oxidation; Benzoquinone

1. Introduction

Palladium-catalyzed allylic oxidations of olefins to allylic alcohols or acetates have been developed into useful synthetic methods, however their applications to natural terpenic olefins are rather scarce. Naturally occurring terpenes are available and inexpensive materials widely used in pharmaceutical, perfume and flavor industries [1–4]. Monoterpenic alcohols and esters often show valuable organoleptic properties and form the largest group of modern fragrance ingredients. For several years, we have been interested in catalytic transformations of various monoterpenes, including limonene, which occurs in citrus oils and is particularly very important precursor of valuable oxygenated products [5–12]. A palladium-catalyzed oxidation of limonene using $CuCl_2$ or benzoquinone (BQ) as stoichiometric oxidants was found to result in carvone or carveol derivatives as main products [13–15]. In previous works, we reported an efficient and selective $PdCl_2/CuCl_2$ catalyzed oxidation of limonene with dioxygen into carveyl acetate in acetic acid solutions [5] and studied its mechanism [6]. This system has been recently modified by use of *t*-butyl hydroperoxide as a final oxidant [16]. A chloride-free $Pd(OAc)_2/LiNO_3$ catalytic combination was also applied to the aerobic oxidation of limonene but no promising results were obtained [5].

Some reports on the cobalt-catalyzed autoxidation of limonene were also reported [10,11,17]. In acetic acid solutions, the reaction gave a complex mixture of oxygenated products [10,17], while in acetonitrile, three main products, i.e., limonene oxide, carvone and carveol, were obtained in a combined selectivity of near 80% [10]. A similar selectivity was achieved under solvent free conditions with a heterogeneous sol–gel Co/SiO_2 catalyst [11].

Organic oxidations with palladium complexes can be made catalytic with the use of reversible co-oxidants for the re-oxidation of Pd(0), with $CuCl_2$ being the most convenient one (Wacker-type catalyst) [18]. However, the systems with $CuCl_2$ and chloride ions often suffer from serious corrosion problems and promote the formation of chlorinated side products. Benzoquinone also readily re-oxidizes Pd(0) during the catalytic cycle. Although the oxidation of hydroquinone (HQ) back to benzoquinone by dioxygen is a slow reaction, the use of BQ as the oxidant in palladium-catalyzed oxidations of organic sub-

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strates represents a valuable chloride-free synthetic alternative. HQ can be, in principle, re-cycled by catalytic oxidation with dioxygen. For example, we have recently developed a chloride-free multi-component catalytic combination $Pd(OAc)_2$/BQ/(Cu or Mn acetates) for the aerobic allylic oxidation of limonene in acetic acid solutions [12].

The scope of palladium-catalyzed allylic oxidations of olefins can be extended by the use of alcohols as nucleophiles. The aim of the present work was to investigate the catalytic oxidation of limonene in the solutions of various alcohols (methanol, ethanol, 2-propanol and *t*-butanol) We developed selective methods for the synthesis of a series of allylic ethers from limonene, which are potentially useful as fragrance ingredients, employing a Pd(II)/*p*-toluenesulfonic acid catalytic system. We also attempted to create a multi-component catalyst based on $Pd(OAc)_2$ and BQ for the aerobic oxidation of limonene.

2. Experimental

All reagents were purchased from commercial sources and used as received, unless otherwise indicated. Benzoquinone was purified by column chromatography (silica).

The reactions were carried out in a glass reactor equipped with a magnetic stirrer and followed by measuring the dioxygen uptake (if any) and by gas chromatography (GC) using a Shimadzu 17 instrument fitted with a Carbowax 20 m capillary column and a flame ionization detector. The solution of the palladium complex, benzoquinone and *p*-toluenesulfonic acid, if any, was stirred at the reaction temperature and an air or oxygen pressure of 1 atm for 15 min. Then, limonene was added and the mixture was stirred. Products were identified by GC/MS (Hewlett-Packard MSD 5890/Series II, 70 eV). Ethers **2a–c** and **3a–c** were isolated by column chromatography (silica) using mixtures of hexane and CH_2Cl_2 as eluents and identified (including stereochemistry) by GC/MS and ^1H and ^{13}C NMR spectroscopy (Bruker DRX-400, tetramethylsilane, $CDCl_3$, COSY, HMQC, DEPT and NOESY experiments).

2-*Methoxy-p-mentha*-1(7),8-*diene* (*trans*) (**2a**) (light yellow oil): MS (*m/z*/rel.int.): 166/2 $[M]^+$, 151/5 $[M-CH_3]^+$, 134/100 $[M-CH_3OH]^+$, 123/50, 119/75, 105/35, 97/35, 93/40, 92/30, 91/70, 79/30, 67/25, 55/30, 45/35. Compound described by El Firdoussi et al. [15]. For NMR data see Table 1.

2-*Ethoxy-p-mentha*-1(7),8-*diene* (*trans*) (**2b**) (light yellow oil): MS (*m/z*/rel.int.): 180/1 $[M]^+$, 165/5 $[M-CH_3]^+$, 151/5 $[M-C_2H_5]^+$, 134/100 $[M-C_2H_5OH]^+$, 119/75, 105/30, 93/55, 92/35, 91/70, 83/35, 79/30, 55/40. For NMR data see Table 1.

2-*Isopropoxy-p-mentha*-1(7),8-*diene* (*trans*) (**2c**) (new compound) (light yellow oil): MS (*m/z*/rel.int.): 194/1 $[M]^+$, 179/1 $[M-CH_3]^+$, 165/1 $[M-C_2H_5]^+$, 151/10 $[M-C_3H_7]^+$, 134/100 $[M-C_3H_7OH]^+$, 119/45, 109/100, 107/45, 93/50, 91/49, 79/35, 55/35. For NMR data see Table 1.

2-*Methoxy-p-mentha*-1(6),8-*diene* (*trans*) (**3a**) (light yellow oil): MS (*m/z*/rel.int.): 166/14 $[M]^+$, 151/25 $[M-CH_3]^+$, 134/22 $[M-CH_3OH]^+$, 123/100, 119/57, 98/68, 93/39, 91/79, 83/67, 79/38, 77/43, 55/58. Compound described by El Firdoussi et al. [15]. For NMR data see Table 2.

2-*Ethoxy-p-mentha*-1(6),8-*diene* (*trans*) (**3b**) (light yellow oil): MS (*m/z*/rel.int.): 180/36 $[M]^+$, 165/20 $[M-CH_3]^+$, 151/33 $[M-C_2H_5]^+$, 137/95, 134/16 $[M-C_2H_5OH]^+$, 119/52, 112/46, 109/59, 93/54, 91/56, 84/100, 83/46, 55/72. For NMR data see Table 2.

2-*Isopropoxy-p-mentha*-1(6),8-*diene* (*trans*) (**3c**) (light yellow oil): MS (*m/z*/rel.int.): 194/2 $[M]^+$, 179/1 $[M-CH_3]^+$, 134/5 $[M-C_3H_7OH]^+$, 119/23, 109/93, 93/35, 91/35, 84/100, 83/30, 55/44. For NMR data see Table 2.

3. Results and discussion

The data on the palladium-catalyzed oxidation of limonene by benzoquinone in various alcohols are collected in Table 3. In the solutions of methanol, ethanol or 2-propanol containing BQ and catalytic amounts of $Pd(OAc)_2$ limonene is oxidized at a very low rate, with only 5–8% conversions being observed after 6-h reactions (Fig. 1). It is known that the addition of small amounts of strong acids benefits the oxidations with Pd/BQ systems favoring a BQ-mediated re-oxidation of Pd(0), thus preventing its precipitation, and sometimes increasing the reaction rate [15,19,20]. Indeed, introducing 10 mol% (0.02 M) of *p*-toluenesulfonic acid (PTSA) significantly accelerated the reaction rates: even at 25 °C nearly complete conversion of limonene was observed in methanol for 6 h, in ethanol for 8 h and in 2-propanol in 12 h (runs 1, 7 and 12). The effect of the PTSA on the oxidation of limonene is illustrated by Fig. 1.

A main reaction is an allylic oxidation giving isomeric ethers **2a–c** and **3a–c** with a combined selectivity of 90–98% depending on the solvent (Schemes 1 and 2). It is remarkable a strong preference in all alcohols for the formation of allylic ethers **2a–c** containing two exocyclic double bonds. For example, in methanol, ether **2a** is formed almost exclusively with a chemoselectivity of 95%. In ethanol and 2-propanol, the amount of corresponding ethers **2b** and **c** reach 90–96% of the total amount of both isomers **2** and **3**. In the absence of PTSA, the reaction

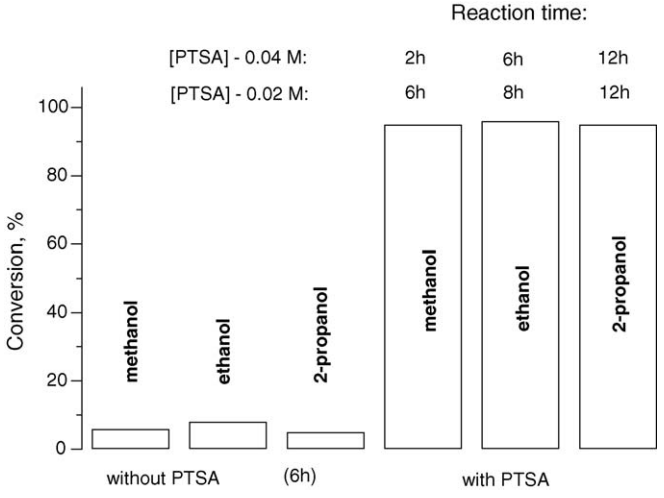


Fig. 1. Effect of *p*-toluenesulfonic acid (PTSA) on the palladium-catalyzed oxidation of limonene in the solutions of various alcohols. Reaction conditions: [Limonene] = 0.20 M, [Pd] = 0.01 M, [BQ] = 0.40 M, 25 °C (PTSA: *p*-toluenesulfonic acid).

Table 1
NMR data for products **2a–c** (carbon numbering is given in Scheme 1)

Carbon atom	Hydrogen atom	$\delta(^1H)$ (ppm)[a]		
		2a	**2b**	**2c**
1				
2	2	3.73 (t), $^3J_{2-3eq} = {}^3J_{2-3ax} = 2.9$	3.87 (t), $^3J_{2-3eq} = {}^3J_{2-3ax} = 3.0$	3.98 (t), $^3J_{2-3eq} = {}^3J_{2-3ax} = 3.0$
3	3ax	1.46 (td), $^2J = {}^3J_{3ax-4} = 13.1$, $^3J_{3ax-2} = 2.9$	1.46 (td), $^2J = {}^3J_{3ax-4} = 12.8$, $^3J_{3ax-2} = 3.0$	1.46 (td), $^2J = 13.2$, $^3J_{3ax-4} = 12.4$, $^3J_{3ax-2} = 3.0$
	3eq	2.01–2.06 (m)	2.06 (dq), $^2J = 12.8$, $^3J_{3eq-4} = 3.0$, $^4J_{3eq-5} = {}^3J_{3aq-2} = 3.0$	1.98 (dq), $^2J = 13.2$, $^3J_{3eq-4} = 3.0$, $^4J_{3eq-5} = {}^3J_{3aq-2} = 3.0$
4	4	2.47 (tt), $^3J_{4-3ax} = 13.1$, $^3J_{4-5ax} = 13.1$, $^3J_{4-3eq} = {}^3J_{4-5eq} = 3.2$	2.52 (tt), $^3J_{4-3ax} = 12.8$, $^3J_{4-5ax} = 12.8$, $^3J_{4-3eq} = 3.0$, $^3J_{4-5eq} = 3.3$	2.52 (tt), $^3J_{4-3ax} = 12.4$, $^3J_{4-5ax} = 12.4$, $^3J_{4-3eq} = 3.0$, $^3J_{4-5eq} = 3.4$
5	5ax	1.26 (qd), $^2J = {}^3J_{5ax-4} = 13.1$, $^3J_{5ax-6ax} = 13.5$, $^3J_{5ax-6eq} = 4.6$	1.28 (qd), $^2J = {}^3J_{5ax-4} = 12.8$, $^3J_{5ax-6ax} = 13.0$, $^3J_{5ax-6eq} = 3.6$	1.24 (qd), $^2J = {}^3J_{5ax-6ax} = 12.8$, $^3J_{5ax-4} = 12.4$, $^3J_{5ax-6eq} = 4.3$
	5eq	1.83–1.86 (br.d)	1.86 (dm), $^2J = 12.8$	1.85 (dm), $^2J = 12.8$
6	6ax	2.27 (dt), $^2J = 13.5$, $^3J_{6ax-5ax} = 13.5$, $^3J_{6ax-5eq} = 4.0$	2.29–2.33 (m)	2.34 (dtt), $^2J = 13.0$, $^3J_{6ax-5ax} = 12.8$, $^3J_{6ax-5eq} = 4.6$, $^4J_{6ax-10} = 1.7$
	6eq	2.18 (dt), $^2J = 13.5$, $^3J_{6eq-5ax} = 3.2$, $^3J_{6eq-5eq} = 3.2$	2.17 (dt), $^2J = 13.4$, $^3J_{6eq-5ax} = 3.6$, $^3J_{6eq-5eq} = 3.6$	2.14 (dt), $^2J = 13.0$, $^3J_{6eq-5ax} = 3.8$, $^3J_{6eq-5eq} = 3.8$
7	7	4.83 (t, 1H), $^4J_{10-6} = 1.5$, 4.89 (t, 1H), $^4J_{10-6} = 1.9$	4.80 (t, 1H), $^4J_{10-6} = 1.8$, 4.85 (t, 1H), $^4J_{10-6} = 1.8$	4.78 (t, 1H), $^4J_{10-6} = 1.7$, 4.82 (t, 1H), $^4J_{10-6} = 1.7$
8				
9	9	4.69 (br. s, 2H)	4.70 (t, 2H), $^4J_{8-9} = 0.8$	4.68 (t, 2H), $^4J_{8-9} = 1.2$
10	10	1.71 (s, 3H)	1.72 (br. t, 3H)	1.71 (t, 3H), $^4J_{9-8} = 1.2$
OCH_3 (**2a**), OCH_2CH_3 (**2b**), $OCH(CH_3)_2$(**2c**)				
CH_3		3.20 (s, 3H)	1.19 (t, 3H), $^3J = 7.0$	1.10 (d, 3H), $^3J = 6.1$, 1.13 (d, 3H), $^3J = 6.1$
CH_2			3.29 (qd, 1H), $^2J = 9.6$, $^3J = 7.0$, 3.43 (qd, 1H), $^2J = 9.6$, $^3J = 7.0$	
CH				3.57 (heptet, 1H), $^3J = 6.1$

Carbon atom	Hydrogen atom	$\delta(^{13}C)$ (ppm)		
		2a	**2b**	**2c**
1		146.96	148.01	148.65
2	2	81.17	79.05	76.03
3	3ax	38.12	38.28	38.50
	3eq			
4	4	38.63	38.60	38.52
5	5ax	32.72	32.97	33.09
	5eq			
6	6ax	30.20	30.43	30.52
	6eq			
7	7	111.38	110.62	110.24
8		149.65	149.82	149.89
9	9	108.66	108.60	108.57
10	10	20.88	20.98	21.02
OCH_3 (**2a**), OCH_2CH_3 (**2b**), $OCH(CH_3)_2$(**2c**)				
CH_3		55.27	15.39	21.16, 23.37
CH_2			62.64	
CH				67.03

[a] Resonance multiplicities and coupling constants (Hz): (s) singlet, (d) doublet, (t) triplet, (td) triplet of doublets, (tt) triplet of triplets, (qd) quartet of doublets, (dt) doublet of triplets, (dtt) doublet of triplets of triplets, (m) multiplet and (br) broadened.

Table 2
NMR data for products **3a–c** (carbon numbering is given in Scheme 2)

Carbon atom	Hydrogen atom	$\delta(^1H)$ (ppm)[a]		
		3a	**3b**	**3c**
1				
2	2	3.43 (br. t), $^3J_{2–3ax} = 3.8$	3.54 (br. t), $^3J_{2–3ax} = 3.8$	3.70 (br. t), $^3J_{2–3ax} = 3.6$
3	3ax	1.31 (td), $^2J = {}^3J_{3ax–4} = 13.3$, $^3J_{3ax–2} = 3.8$	1.32 (td), $^2J = {}^3J_{3ax–4} = 13.2$, $^3J_{3ax–2} = 3.8$	1.40 (td), $^2J = {}^3J_{3ax–4} = 13.1$, $^3J_{3ax–2} = 3.6$
	3eq	2.00–2.03 (m)	1.96–2.00 (m)	1.95–2.00 (m)
4	4	2.22–2.28 (m), $^3J_{4–3ax} = 13.3$	2.26–2.32 (m), $^3J_{4–3ax} = 13.2$	2.36–2.41 (m), $^3J_{4–3ax} = 13.1$
5	5ax	2.04–2.11 (m)	2.06–2.13 (m)	2.10–2.16 (m)
	5eq	1.73–1.78 (m)	1.72–1.77 (m)	1.81–1.86 (m)
6	6	5.52–5.53 (m)	5.51–5.53 (m)	5.59–5.60 (m)
7	7	1.69 (s, 3H)	1.67 (s, 3H)	1.75 (s, 3H)
8				
9	9	4.66 (br.s, 2H)	4.66 (br.s, 2H)	4.73 (br.s, 2H)
10	10	1.71 (s, 3H)	1.70 (s, 3H)	1.76 (s, 3H)
$–OCH_3$ (**3a**), $–OCH_2CH_3$ (**3b**), $–OCH(CH_3)_2$ (**3c**)				
CH_3		3.32 (s, 3H)	1.15 (t, 3H), $^3J = 7.0$	1.18 (m, 6H)
CH_2			3.34–3.40 (m, 1H), 3.58–3.64 (m, 1H)	
CH				3.64–3.66 (m, 1H)

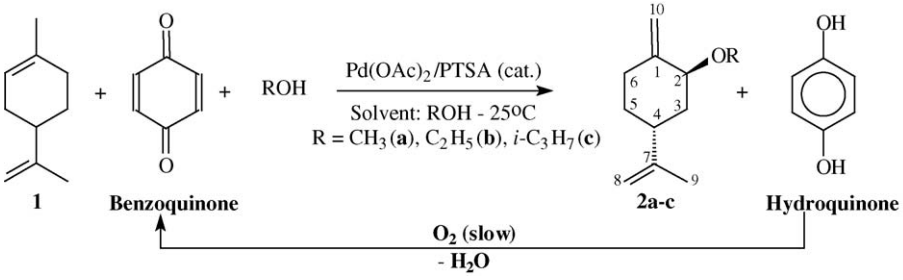
Carbon atom	Hydrogen atom	$\delta(^{13}C)$ (ppm)		
		3a	**3b**	**3c**
1		133.09	132.19	133.21
2	2	77.22	74.96	73.18
3	3ax	30.67	31.12	32.80
	3eq			
4	4	34.91	34.48	34.87
5	5ax	30.60	30.12	30.50
	5eq			
6	6	125.03	124.48	125.04
7	7	20.38	19.91	21.56
8		149.68	148.81	149.94
9	9	108.18	107.60	108.02
10	10	20.52	19.96	23.45
$–OCH_3$ (**3a**), $–OCH_2CH_3$ (**3b**), $–OCH(CH_3)_2$ (**3c**)				
CH_3		56.64	14.77	20.36, 20.42
CH_2			63.80	
CH				69.59

[a] Resonance multiplicities and coupling constants (Hz): (s) singlet, t (triplet), (td) triplet of doublets, (m) multiplet and (br) broadened.

Table 3
Oxidation of limonene (**1**) catalyzed by palladium complexes in various alcohols[a]

Run	[Pd]	PTSA (M)	Temp. (°C)	Time (h)	Conversion (%)	Product selectivity			
						Oxidation		Others[b]	**2** + **3**
						2	**3**		
Solvent: methanol									
1	$Pd(OAc)_2$	0.02	25	2, 6	80, 98	98, 95		2, 5	98, 95
2	$Pd(OAc)_2$	0.04	25	2, 3	94, 98	97, 97		3, 3	97, 97
3	$Pd(OAc)_2$	0.06	25	5	97	90		10	90
4	Na_2PdCl_4	0.02	60	2, 5	78, 97	2, 3	84, 82	14, 15	86, 85
5	Na_2PdCl_4	0.02	80	4	99	6	55	39	61
6	$Pd(acac)_2$	0.06	25	1, 20	28, 98	95, 95		5, 5	95, 95
Solvent: ethanol									
7	$Pd(OAc)_2$	0.02	25	2, 8	47, 98	88, 87	4, 4	8, 9	92, 91
8	$Pd(OAc)_2$	0.04	25	2, 6	78, 96	89, 88	5, 4	6, 8	94, 92
9	$Pd(OAc)_2$	0.06	25	5	95	80	3	17	83
10	Na_2PdCl_4	0.02	60	2, 6	67, 98	2, 3	86, 82	12, 15	88, 85
11	Na_2PdCl_4	0.06	80	4	93	4	44	52	48
Solvent: 2-propanol									
12	$Pd(OAc)_2$	0.02	25	2, 12	22, 95	80, 80	13, 10	7, 10	93, 90
13	$Pd(OAc)_2$	0.04	25	2, 12	20, 95	80, 77	12, 13	8, 10	92, 90
14	$Pd(OAc)_2$	0.06	25	12	96	73	8	19	81
15	Na_2PdCl_4	0.02	60	2, 6, 9	41, 86, 98	1, 1, 1	93, 92, 92	6, 7, 7	94, 93, 93
16	Na_2PdCl_4	0.04	60	2, 6, 24	30, 50, 99	3, 3, 3	77, 75, 74	20, 22, 23	80, 78, 77

[a] [Limonene] = 0.20 M, [Pd] = 0.01 M, [BQ] = 0.40 M, conversion and selectivity were determined by GC. BQ: benzoquinone; PTSA: *p*-toluenesulfonic acid.
[b] Mainly, the products of the alcohol addition to the exocyclic double bond (α-terpenol methyl ether) and isomers of limonene (mainly α-terpinolene and γ-terpinene).

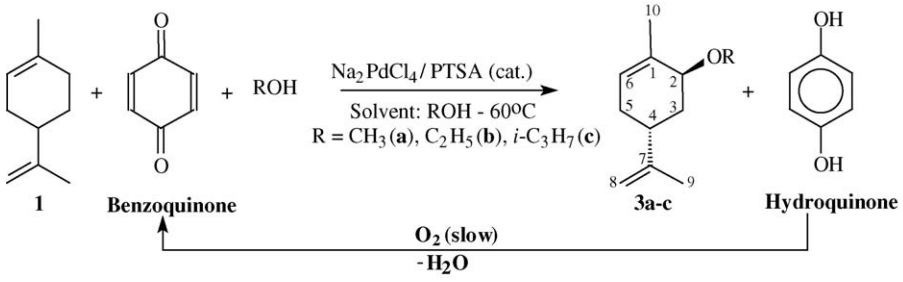


Scheme 1.

is very slow, as mentioned above, and leads almost exclusively to allylic ethers **2a**–**c**. In a blank reaction, with no $Pd(OAc)_2$ added, limonene as expected undergoes no oxidation.

We have previously observed the important effect of PTSA on the rate and regioselectivity of the allylic oxidation of limonene in acetic acid solutions, with the exclusive formation of allylic acetate analogous to the products **2** being detected under optimized conditions. We isolated ethers **2a**–**c** and found that they have mild scents with a flower or fruit tinge and, thus, can be useful as components of synthetic fragrances. Their complete characterization by GC/MS and NMR is presented in Experimental and in Table 1. The values observed for coupling constants show that these compounds have mainly a *trans* configuration (*trans*/*cis* ≈ 90/10).

The amounts of PTSA added are also very important to control the reaction rate and selectivity. In the attempts to accel-



Scheme 2.

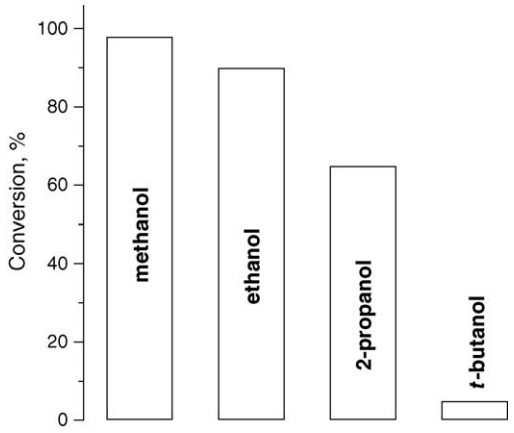


Fig. 2. Solvent effect on the palladium-catalyzed oxidation of limonene. Reaction conditions: [Limonene] = 0.20 M, [Pd] = 0.01 M, [PTSA] = 0.02 M, [BQ] = 0.40 M, 25 °C, 6 h (PTSA: *p*-toluenesulfonic acid).

erate the process, we doubled the PTSA concentration from 10 to 20 mol% (0.04 M) (cf. runs 1, 7, 12 and 2, 8, 13). This increased the reaction rate in methanol and ethanol (but not in 2-propanol) practically without the decrease in selectivity for **2**. Limonene conversions of ca. 95% with selectivities of 90–97% for the allylic oxidation products have been achieved for 2 h in methanol, 6 h in ethanol and 12 h in 2-propanol (Fig. 1). However, a further increase in the PTSA concentration (runs 3, 9 and 14) decreased the selectivity for the allylic oxidation at the expense of limonene isomerization and oligomerization as well as the formation of α-terpineol ethers. The latter are the products of the reversible addition of the alcohol to the limonene exocyclic double bond. In the case of ethanol and 2-propanol, the selectivity drops to ca. 80%. We ran the reaction in ethanol with another strong acid: perchloric acid, $HClO_4$, under the conditions indicated in Table 3 for runs 7 and 8. The systems with PTSA and $HClO_4$ at the same concentrations show similar reaction rates and selectivities, thus, a specific acid catalysis seems to operate in this reaction.

All these undesired transformations occurring with limonene are acid-catalyzed and proceed via a carbenium ion mechanism. The protonation of the exocyclic double bond originates a corresponding carbenium ion, which then undergoes a nucleophilic attack by alkoxy group to give the corresponding ethers of α-terpineol or, alternatively, can lose a proton resulting in the isomers of limonene, mainly α-terpinene and γ-terpinene. The carbenium ion can also react with another molecule of olefin present in the reaction solutions to give a C_{20} carbenium ion initiating the irreversible process of oligomerization.

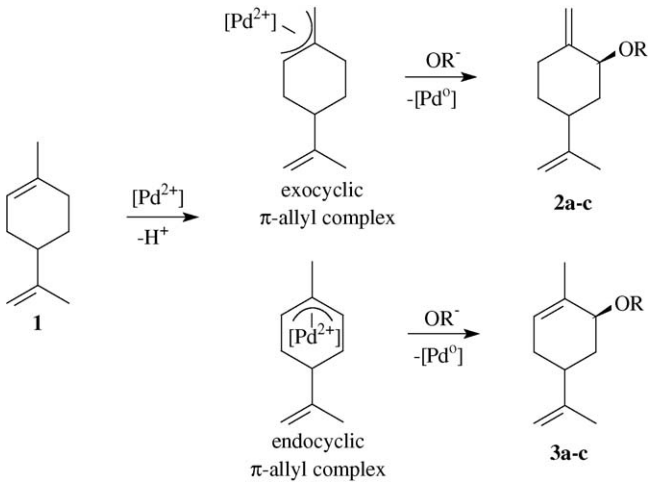
As it is illustrated by Fig. 2 and can be also seen in Table 3, the increase in a steric volume of the alkoxy group decreases the reaction rate. The reaction in methanol is faster than in ethanol and much faster than in a secondary alcohol, 2-propanol. We also tried to use a tertiary alcohol, *t*-butanol, as a solvent and a nucleophile in this reaction. A very low conversion of limonene (<5%) was observed in a 6 h reaction under the conditions shown in Fig. 2, while in methanol and ethanol limonene was almost completely converted for the same time.

$Pd(acac)_2$ can be also used as a catalyst instead of $Pd(OAc)_2$ (run 6 versus run 3). The reaction is also highly selective to methyl ether **2a** (selectivity of 95% at 98% conversion), however the reaction rate is much lower. The effect of the ligand on palladium in the allylic oxidation of limonene became much more pronounced when $Pd(OAc)_2$ was substituted by Na_2PdCl_4. In the presence of chloride ligands, the regioselectivity of allylic oxidation was completely switched. Other allylic ethers, i.e. carveyl derivatives **3a–c**, are formed as major oxidation products with very small amounts of **2a–c** being detected in these runs. Concurrent transformations of limonene, such as isomerization, oligomerization and solvent addition, can be minimized by the careful choice of the reaction variables, in particular, PTSA concentration. Under optimized conditions, as high as 85–93% chemoselectivities for the allylic oxidation were achieved at near complete limonene conversions for 5 h in methanol, 6 h in ethanol and 9 h in 2-propanol (runs 4, 10 and 15).

Compounds **3a–c** were isolated and completely characterized by GC/MS and NMR (experimental and Table 2). They also have pleasant scents and can be useful as components of synthetic perfumes. The values observed for coupling constants show that these compounds have mainly a *trans* configuration (*trans*/*cis* ≈ 90/10).

π-Allyl palladium complexes are usually proposed as reaction intermediates in the palladium-catalyzed oxidation of limonene [5,12,15]. An abstraction of a hydrogen atom from the CH_3 group of limonene results in an exocyclic π-allyl complex and from the CH_2 group in an endocyclic π-allyl complex as depicted in Scheme 3. A subsequent nucleophilic attack of the alkoxy group affords ether **2** from the exocyclic complex and ether **3** from the endocyclic one. Near 90% of both ethers **2** and **3** have a *trans* configuration, therefore an external rather then coordinated on palladium nucleophile predominantly participate in this attack, which occurs on a less hindered face of the molecule of limonene.

Although the bulky benzoquinone behaves as a ligand in palladium systems [21], in the presence of strongly coordinating chloride ions mostly palladium complexes with less bulky chloride ligands seem to be involved in the reaction. This allows the



Scheme 3.

almost exclusive formation of the endocyclic π-allyls, which are more sterically demanding. Thus, in the presence of chloride ions, oxidation of limonene mainly results in carveyl derivatives **3**. In the chloride-free systems, the formation of the endocyclic π-allyls becomes so unfavorable that ethers **2** appear as predominant allylic oxidation products. The presence of PTSA, probably acting as another bulky coordinating molecule in the absence of chloride groups [12], makes an additional steric contribution favoring the formation of the exocyclic π-allyls. The chemoselectivities for the ethers **2a**–**c** reach 80–97% in the $Pd(OAc)_2$/PTSA/BQ system.

In should be noted that limonene is much more reactive in the chloride-free systems. For example, a 2-h reaction resulted in ca. 80% conversion of limonene with $Pd(OAc)_2$ at 25 °C but only at 60 °C with Na_2PdCl_4 (cf. runs 1 and 4). 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 [22].

In the runs described above, BQ was used in more than stoichiometric amounts relatively to limonene since its reduced form, hydroquinone, reacts with dioxygen at a very low rate. We attempted to create a catalytic system based on $Pd(OAc)_2$ and BQ for the oxidation of limonene by dioxygen in alcoholic solutions. Various compounds have been previously used to accelerate the re-oxidation of HQ and to develop Pd(II)/BQ-based catalytic systems for the oxidation of organic substrates with dioxygen: macrocyclic cobalt complexes [23], iron phthalocyanine [19], copper salts [24,25] and heteropoly compounds [26–28], with the latter compounds being the most promising ones. We tried to use $H_5[PMo_{10}V_2O_{40}]$ (0.2–2 mol%) in a $Pd(OAc)_2$ (5 mol%)/BQ (5 mol%) system for the aerobic oxidation of limonene in methanol (45 °C, O_2, 1 atm). Unfortunately, limonene was converted in a mixture of isomers and oligomers due to acid-catalyzed reactions, with a very low selectivity for the allylic oxidation being observed.

$Cu(OAc)_2$ was also tested as an oxygen-activating agent for the re-oxidation of HQ. Solutions of limonene (0.50 M), $Pd(OAc)_2$ (2 mol%), PTSA (4 mol%), $Cu(OAc)_2$ (2 mol%) and BQ (20 mol%) in methanol, ethanol and 2-propanol consume dioxygen very slowly at 25–70 °C. A palladium mirror was rapidly formed on the walls of the reaction vessel in all alcohols used, along with small amounts of the corresponding ether **2**. Studies on the development of the catalytic systems for the aerobic oxidation of limonene in alcoholic solutions are in progress in our laboratory.

4. Conclusions

The oxidation of limonene with benzoquinone in the solutions of methanol, ethanol and 2-propanol, containing catalytic amounts of palladium(II) complexes and *p*-toluenesulfonic acid, results in two isomeric allylic ethers in each alcohol. A good control of regioselectivity was achieved through the appropriate choice of the ligand on palladium and reaction conditions. Allylic ethers **2a**–**c** with two exocyclic double bonds are main reaction products in chloride-free catalytic systems, while carveol derivatives **3a**–**c** are formed when palladium chloride is used as the catalyst. *p*-Toluenesulfonic acid exerts a great accelerative and catalyst stabilizing effect in these reactions. Under appropriate conditions, monoterpenic ethers **2a**–**c** and **3a**–**c**, which have mild scents of flower or fruit and can be useful as components of synthetic fragrances, were obtained in 80–97 chemoselectivity each at 95–98% limonene conversions.

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