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Cobalt catalyzed autoxidation of monoterpenes in acetic acid and acetonitrile solutions

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Abstract

Oxidation of limonene, α-pinene and β-pinene with dioxygen in acetic acid and acetonitrile solutions containing catalytic amounts of $CoCl_2$ has been studied. Limonene and α-pinene give both allylic oxidation and epoxidation products in a molar ratio of near 1/1, with chemoselectivities for corresponding products being higher in acetonitrile than those in acetic acid. On the other hand, oxidation of β-pinene leads essentially to allylic products, i.e. highly valuable pinocarveol, pinocarvone, myrtenol and myrtenal. In acetic acid, a combined selectivity for these products does not exceed 40% due to the concomitant substrate isomerization and acetic acid addition, while in acetonitrile, good selectivities of up to 85% at a 40–50% substrate conversion have been achieved.

Keywords: β-Pinene; α-Pinene; Limonene; Cobalt catalysts; Oxidation

1. Introduction

Monoterpenes are low-priced naturally occurring products widely used in flavor and fragrance industry, which is known to be essentially based on chemistry of terpenes [1–4].

Terpenic aldehydes, alcohols and esters often show valuable organoleptic properties as well as biological and phytosanitary activities. We have recently been involved in metal and heteropoly acid catalyzed oxyfunctionalization of some monoterpenes [5–11]. We reported selective $PdCl_2/CuCl_2$ catalyzed oxidations of limonene [5] and myrcene [11] with dioxygen, however failed to extend this method to bicyclic monoterpenes due to their skeletal rearrangements promoted by $CuCl_2$ [5]. Then, we developed $CuCl_2$-free systems for the selective oxidation of β-pinene and camphene into allylic and glycol derivatives, respectively, using H_2O_2 as final oxidant and $Pd(OAc)_2$ as catalyst [6]. An alternative $Pd(OAc)_2/LiNO_3$ catalytic system promoted a tandem oxidative coupling-oxidation of camphene with dioxygen [9]. The present work describes a $CoCl_2$ catalyzed oxidation of limonene, α-pinene and β-pinene with dioxygen in acetic acid and acetonitrile solutions. Autoxidation of alkylbenzenes and alkanes by cobalt catalyzed homolytic processes has been extensively studied because of their industrial importance [12,13]. Surprisingly, autoxidation of alkenes in the presence of cobalt complexes has attracted much less attention [12–16]. These reactions involve radical

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intermediates and a competition between the abstraction of the allylic hydrogen to give allylic oxidation products and the addition of the alkylperoxy radical to the double bond resulting in epoxide products is usually expected [12].

Some reports on the autoxidation of a number of monoterpenes including α-pinene [17–25], limonene [22] and β-pinene [22], in the presence of cobalt complexes, have previously been published. Most of the studies with α-pinene were performed under solvent-free conditions, with α-pinene oxide, verbenone and verbenol being main reaction products. The autoxidation of limonene and β-pinene has been studied in acetic acid solutions of $Co(OAc)_2$/NaBr [22]. Both substrates gave complex mixtures of oxygenated derivatives with a very low selectivity for allylic oxidation products. Thus, myrtenal, pinocarveol and pinocarvone were obtained from β-pinene in a 15, 8 and 6% selectivity, respectively.

We wish to report here a comparative study on the $CoCl_2$ catalyzed autoxidation of limonene, α-pinene and β-pinene in acetic acid versus acetonitrile solutions. The effect of the structure of monoterpene on the ratio between allylic oxidation and epoxidation products is discussed. A novel selective oxidation of β-pinene into valuable allylic derivatives has been developed.

2. Results and discussion

Oxidation of limonene (**1**), α-pinene (**2**) and β-pinene (**3**) was performed in two solvents: acetic acid and acetonitrile. In most experiments, $CoCl_2$ alone was applied as catalyst without the addition of bromide ions, which are usually used as auxiliary hydrogen abstraction agents in cobalt catalyzed oxidation processes. The results are presented in Tables 1–3. Limonene and α-pinene undergo a very slow conversion in both solvents in the absence of cobalt catalyst (Tables 1 and 2, runs 1 and 5). In acetic acid, the products of substrate isomerization are mainly detected, while in acetonitrile, a slow autoxidation occurs resulting in corresponding epoxides and allylic oxidation products in approximately equal amounts. $CoCl_2$ effectively catalyzes the autoxidation of limonene and α-pinene producing a wide variety of oxygenated derivatives, with the molar ratio between allylic oxidation products and the products originating from epoxides being of near 1/1 (1.3/1.0–1.0/1.3). The product distribution for both substrates strongly depends on the solvent nature. Chemoselectivities for corresponding epoxides are considerably higher in acetonitrile compared to acetic acid.

Limonene forms in acetonitrile three main products: limonene oxide (**4**) (*cis*/*trans* ≈ 1/1), carvone (**5**) and

Table 1
Oxidation of limonene (**1**) catalyzed by $CoCl_2$[a]

Run	[$CoCl_2$] (mol%)	Conversion (%)	Product selectivity (%)				S_{allyl}[c] (%)	S_{epoxi}[d] (%)	S_{allyl}/S_{epoxi} (%)
			4	Glycol[b]	**5**	**6**			
Solvent: acetic acid									
1[e]	0	5							
2	0.5	36	7	34	23	17	40	41	1.0/1.0
3	1.0	40	3	42	25	18	43	45	1.0/1.0
4	2.0	35	5	38	24	21	45	43	1.0/1.0
Solvent: acetonitrile									
5	0	9	29		13	19	32	29	1.1/1.0
6	0.5	41	43		17	20	37	43	1.0/1.2
7	1.0	43	37		20	23	43	37	1.2/1.0
8	2.0	30	35		18	20	38	35	1.1/1.0

[a] [Limonene] = 1.0 M, 60 °C, reaction time 4 h. Conversion and selectivity were determined by GC; 20–25% (based on reacted substrate) of unidentified products were also formed.
[b] Mixture of limonene glycol and its acetates.
[c] Selectivity for allylic oxidation products (**5** and **6**).
[d] Selectivity for epoxidation products (**4** and glycol derivatives).
[e] Products of limonene isomerization were mainly formed.

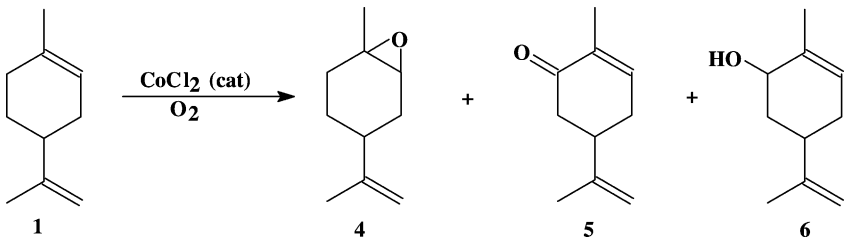
Table 2
Oxidation of α-pinene (**2**) catalyzed by $CoCl_2$[a]

Run	[$CoCl_2$] (mol%)	Time (h)	Conversion (%)	Product selectivity (%)								S_{allyl}[c] (%)	S_{epoxi}[d] (%)	S_{allyl}/S_{epoxi} (%)
				Epoxidation					Allylic oxidation					
				6	**7**	**8**	**9**	Glycol[b]	**10**	**11**	**12**			
Solvent: acetic acid														
1	0	3	2											
2	0.5	3	19	9	7	16		18	20		17	37	50	1.0/1.3
3	1.0	3	21	8	5	14		20	19		18	37	47	1.0/1.3
4	2.0	3	22	10	5	15		17	19		20	39	47	1.0/1.2
Solvent: acetonitrile														
5	0	6	16		31		8		14	31		45	39	1.1/1.0
6	0.5	6	48		30	1	8		25	23		48	39	1.2/1.0
7	1.0	6	55		29	3	5		26	23		49	37	1.3/1.0
8	2.0	6	50		24	6	5		25	22		47	35	1.3/1.0
9[e]	2.0	3	50	4	26	5	8		26	23		49	43	1.1/1.0

[a] [α-Pinene] = 1.0 M, 60 °C. Conversion and selectivity were determined by GC; 10–15% (based on reacted substrate) of unidentified products were also formed.
[b] Mixture of α-pinene glycol and its acetates.
[c] Selectivity for allylic oxidation products (**10**–**12**).
[d] Selectivity for epoxidation products (**6**–**9** and glycol derivatives).
[e] [NaBr] = 8 mol%.

carveol (**6**) (≈80% *cis*) in ca. 40, 20 and 20% selectivities (Scheme 1, Table 1, runs 6 and 7). An approximately 40% conversion is achieved for 4 h at 60 °C. After 40–50% substrate conversion, the reaction rates and product selectivities significantly decrease for all substrates studied due to the further oxidation of the primarily formed compounds. In acetic acid, epoxide **4** undergoes ring opening giving a mixture of limonene glycol and its acetates. Only small amounts of **4** were detected in reaction solutions (Table 1, runs 2–4). The *endo* cyclic double bond of limonene is much more sensitive to epoxidation: epoxide resulting from the oxidation of the terminal *exo* double bond is detected in 7–10 times lower concentrations than epoxide **4**.

The cobalt catalyzed oxidation of α-pinene results in carveol (**6**), α-pinene oxide (**7**), α-campholene aldehyde (**8**), 3-pinen-2-ol (**9**), verbenone (**10**) and *trans*-verbenol (**11**) or its acetate (**12**), along with some unidentified products (10–15% based on reacted substrate) (Scheme 2). In acetic acid, epoxide **7** is essentially transformed into a mixture of corresponding glycol and its acetates (Table 2, runs 2–4). Products **6**, **8** and **9** more likely result from the skeletal rearrangement of epoxide **7** under the reaction conditions [24], thus these products are referred in Table 2 as epoxidation products. Expectedly, in acetic acid solutions, primarily formed **7** is much more susceptible to ring cleavage and rearrangements.



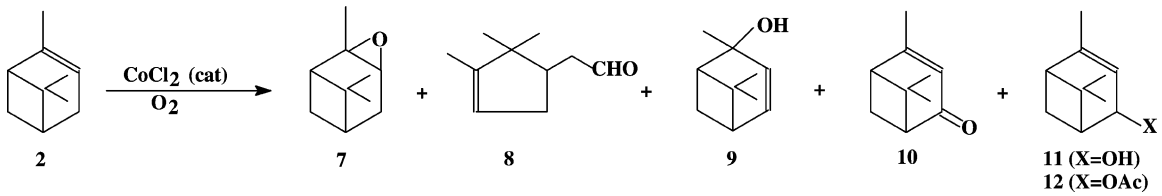
Scheme 1.

Table 3
Oxidation of β-pinene (**3**) catalyzed by $CoCl_2$[a]

Run	[$CoCl_2$] (mol%)	Time (h)	Conversion (%)	Product selectivity (%)						S_{allyl}[b] (%)
				Isomerization[c]	Isomerization/solvent addition[d]	Allylic oxidation				
						13	**14**	**15**	**16**	
Solvent: acetic acid										
1	0	4	25	60	40					0
2	0.5	4	58	25	30	5	8	10	10	33
3	2.0	5	65	15	25	6	7	12	15	40
Solvent: acetonitrile										
4	0	7	15			12	16	29	25	82
5	0.25	5	25			11	20	24	26	81
		8	40			12	15	23	27	77
6	0.5	4	23			11	19	25	27	82
		7	40			12	20	22	28	82
7	1.0	8	42			13	17	23	27	80
8	2.0	5	47			17	16	23	24	80
9[e]	1.0	4	39			17	19	25	24	85
		5.5	51			16	15	19	23	73
10[f]	0.67	2	31			17	19	22	24	82
		5	50			18	21	13	22	74

[a] [β-Pinene] = 1.0 M, 60 °C. Conversion and selectivity were determined by GC; 15–25% (based on reacted substrate) of unidentified products were also formed.
[b] Selectivity for allylic oxidation products (**13**–**16**).
[c] Mainly α-pinene and limonene.
[d] α-Terpenyl acetate, bornyl acetate and fenchyl acetate (≈2/1/1).
[e] [β-Pinene] = 2.0 M.
[f] [β-Pinene] = 3.0 M.

Substitution of acetic acid for acetonitrile significantly improves chemoselectivities. As high as ca. 80% combined selectivity for three main products detected in approximately equal amounts, i.e. epoxide **7**, verbenone **10** and *trans*-verbenol **11**, has been achieved at a 50–55% substrate conversion (Table 2, runs 6–8). As can be seen from Table 2, the relative amounts of the allylic oxidation products are slightly higher in acetonitrile than in acetic acid. However, as mentioned above, the cobalt catalyzed both epoxidation and allylic oxidation of limonene as well as α-pinene occur at comparable rates under the conditions used. Increasing the catalyst concentration within the range of 0.5–2 mol% produces almost no effect on the reaction rate and slightly decreases the product selectivities in the oxidation of both limonene and α-pinene (Tables 1 and 2).



Scheme 2.

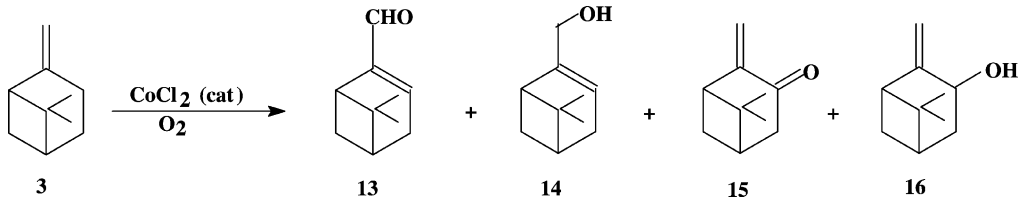
In autoxidation reactions of alkenes, a free radical chain mechanism is proposed which involves the formation of allylic hydroperoxides that typically decompose to several products [13]. The role of metal is generally explained in terms of catalysis of the decomposition of the allylic hydroperoxide intermediate which facilitates the initiation of the free radical chain mechanism. Metal bromides are frequently added as promoters in cobalt catalyzed oxidations of hydrocarbons. The mechanism involves a hydrogen abstraction by bromine atom as a chain transfer agent thus initiating the autoxidation sequence [12]. The addition of NaBr to the $CoCl_2$ system (Br/Co = 4; Table 2, run 9) really accelerates the α-pinene oxidation: the reaction time to reach a 50% conversion decreases from 6 to 3 h, with no significant decrease in product selectivity being observed (Table 2, run 9 versus run 8).

We have observed a strong effect of monoterpene structure on the product nature studying the oxidation of β-pinene (**3**). An unexpectedly high combined selectivity of up to 85% for allylic oxidation products, i.e. myrtenal (**13**), myrtenol (**14**), pinocarvone (**15**) and *trans*-pinocarveol (**16**), has been achieved, with neither epoxide nor corresponding glycol derivatives being detected in the reaction solutions (Scheme 3).

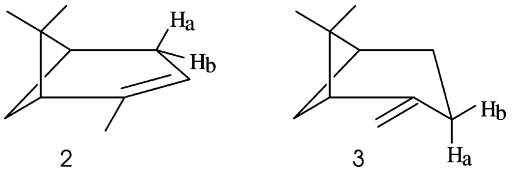
In the cobalt catalyzed oxidation of β-pinene, the effect of a solvent nature on selectivity is particularly noticeable (Table 3). The reaction in acetic acid was found not to be synthetically valuable because of low selectivities for the oxidation products. Oxidation is strongly complicated by acid catalyzed skeletal isomerization mainly into α-pinene and limonene as well as isomerization accompanied by a solvent addition giving α-terpenyl, bornyl and fenchyl acetates (≈2/1/1). These transformations rapidly occur even in the absence of $CoCl_2$ resulting in a 25% conversion of β-pinene for 4 h (Table 3, run 1). $CoCl_2$ accelerates the reaction and an oxygen consumption is observed, however, a combined selectivity for oxidation products does not exceed 40% (Table 3, runs 2 and 3).

Using acetonitrile as a solvent permits to avoid the concomitant rearrangement of β-pinene and to attain 75–85% selectivities for allylic oxidation products, which should be considered rather high for the reaction involving free radicals (Table 3, runs 5–10). In the only work found in the literature which describes the cobalt catalyzed oxidation of β-pinene, a less than 30% combined selectivity for allylic products has been reported [22]. Even a $Pd(OAc)_2$ catalyzed oxidation of β-pinene developed in our previous work offers an ca. 75% total selectivity for oxygenated allylic derivatives [6]. Oxidation of β-pinene has been performed at different concentrations of the catalyst and substrate. A 40–50% conversion has been achieved for 5–7 h, after which the reaction rate and selectivity significantly decrease. Differently from what has been observed for α-pinene, the addition of NaBr in various proportions to $CoCl_2$ (Br/Co = 2–8) noticeably influences neither the product selectivities nor substrate conversion.

A strong preference exhibited by β-pinene compared to α-pinene for allylic oxidation over epoxidation can be explained by different reactivity of the allylic hydrogens toward the abstraction. It seems that the allylic hydrogen abstraction is promoted by overlapping between the olefinic π-orbital and the developing π-orbital containing an unpaired electron in the transition state [23]. The molecule of α-pinene is a rigid structure in which the four-membered ring is puckered and five carbons of the six-membered ring (including olefinic carbons) are approximately in the same plane, with two secondary allylic hydrogens (H_a and H_b) being at ca. 45° angle to this plane (Scheme 4) [4,23]. Thus, orbital overlapping cannot contribute to the additional stabilization of the allylic radical formed to promote the hydrogen abstraction. According with the composition of the detected



Scheme 3.



Scheme 4.

products, the allylic oxidation of α-pinene and the double bond attack (which leads to epoxidation) occur at comparable rates.

On the other hand, β-pinene preferably adopts a pseudo-chair conformation [4], in which allylic hydrogen H_a is approximately orthogonal to the double bond and would be the best candidate for abstraction (Scheme 4). Thus, a so-called "cyclic activation", which is an enhanced reactivity of cyclic allylic hydrogens compared to acyclic ones due to the initial arrangement of the molecule similar to the transition state in the course of the hydrogen abstraction [23], is successfully realized in β-pinene. The favorable for π–p interaction structure of the allylic radical formed from β-pinene makes the allylic oxidation become a major reaction. The formation of the *trans* isomer of pinocarveol **16** originating from the H_a abstraction supports these arguments. In addition, the approach of the abstracting radical from the less crowded "bottom" face of the β-pinene molecule should make the abstraction of H_a kinetically preferred compared to that of H_b. Further isomerization of the primarily formed allylic radical gives smaller amounts of myrtenyl derivatives, i.e. **13** and **14**. In the case of β-pinene, the allylic oxidation becomes so favorable that epoxide and epoxide derived products are not detected at all.

3. Conclusions

In summary, a selective $CoCl_2$ catalyzed oxidation of β-pinene, which is readily available natural raw material, by dioxygen in acetonitrile solutions has been developed. The reaction results in highly valuable allylic oxygenated derivatives: pinocarveol, pinocarvone, myrtenol and myrtenal. Limonene and α-pinene give both allylic oxidation and epoxidation products in a molar ratio of near 1/1, with chemoselectivities being higher in acetonitrile that those in acetic acid.

4. Experimental

All reagents were purchased from commercial sources and used as received, unless otherwise indicated. Monoterpenes were distilled before use. Glacial acetic acid and acetonitrile were used as solvents. Reactions were carried out in a glass reactor equipped with a magnetic stirrer, a sampling system and connected to a gas burette to monitor the oxygen uptake. In a typical run, the solution of $CoCl_2$ (0.0025–0.02 M) in acetic acid or in acetonitrile was stirred at the reaction temperature and oxygen pressure of 0.1 MPa for 15 min. Then, monoterpene was added. Reactions were followed by measuring the dioxygen uptake and by gas chromatography (GC) (Shimadzu 17 instrument, Carbowax 20 M capillary column). Reaction products were separated by column chromatography (silica) using mixtures of hexane, CH_2Cl_2 and methanol as eluents and then identified by GC/MS (Hewlett-Packard MSD 5890/Series II, 70 eV) by comparison with the authentic samples.

Acknowledgements

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