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OXIDATION OF SECONDARY TERPENE ALCOHOLS BY CHLORINE DIOXIDE

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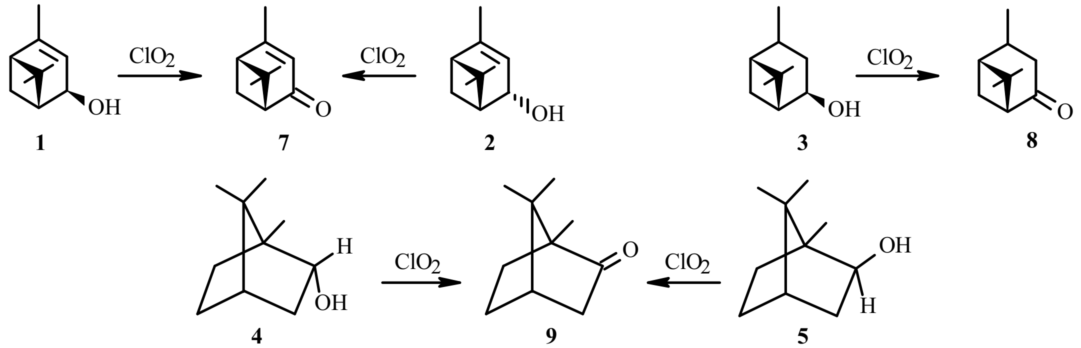
Secondary terpene alcohols cis- *and* trans-*verbenol,* neo-iso-*verbanol, borneol,* iso-*borneol, and menthol were oxidized by chlorine dioxide into the corresponding ketones. It was shown that the nature of the solvent and catalyst and the structure of the starting compound, including the stereochemistry of the hydroxyl, influenced the oxidation process.*

Key words: *cis*- and *trans*-verbenol, *neo*-*iso*-verbanol, borneol, *iso*-borneol, menthol, chlorine dioxide, oxidation, catalysts.

The search for new selective oxidants is a critical task for organic synthesis. Chlorine dioxide (ClO_2), which is an industrial compound and is used to bleach cellulose and purify drinking and wastewater, is of definite interest [1]. It was shown earlier that the use of ClO_2 in organic synthesis is convenient and promising using oxidation of sulfides, thiols, certain organoboron and organometallic compounds, terpene primary allyl alcohols and α,β-unsaturated aldehydes [2-7], and simple alcohols and phenols [8] as examples.

Herein we report oxidation by ClO_2 of secondary terpene alcohols *cis*- (**1**) and *trans*-verbenol (**2**), *neo*-*iso*-verbanol (**3**), borneol (**4**), *iso*-borneol (**5**), and menthol (**6**) in various solvents with or without catalysts.



It is known that C–H bonds of secondary C atoms located in the α-position to a double bond are most easily oxidized. This has been confirmed by ClO_2 oxidation of secondary allyl (**1**, **2**) and saturated (**3**-**5**) alcohols. Oxidation of **1** and **2** proceeds readily without a catalyst in EtOH or Py in 1.5-4 h at room temperature with 89-100% conversion and verbenone (**7**) content 68-79% according to GC (Table 1) whereas oxidation of **3** and **4** is best carried out with a catalyst (Table 2). Furthermore, the selectivity of camphor formation (97-100%) was much greater than that for verbenone formation (73-79%).

The best solvent for all substrates was Py. A significant amount of side products, including chloroderivatives, formed in CCl_4. Thus, oxidation of *trans*-verbenol with 65% conversion gave only 30% verbenone; camphor, 23 and 30% with 41 and 54% conversion of borneol and *iso*-borneol, respectively (Tables 1 and 2).

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TABLE 1. Oxidation of **1**-**3** by Chlorine Dioxide

Substrate	Solvent	T, °C	Time, h	Conversion, %	Content of **7** or **8**, GC, %	Selectivity, %
1	EtOH	20	1.5	100	73	73
	Py	20	2	100	79	79
2	CCl_4	30-35	3	65	30	46
	Py	20	4	89	68	76
	Py	50-55	3	100	78	78
3	EtOH	20	2	Poor	Trace	-
	EtOH	30-35	3	34	24	70
	Py	20	1	16	11	71

TABLE 2. Oxidation of **4** and **5** by Chlorine Dioxide at 20°C

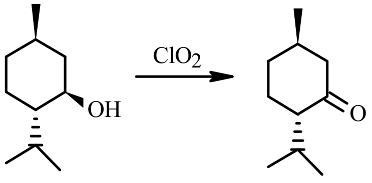
Substrate	Solvent	Catalyst	Time, h	Conversion, %	Content of **9**, GC, %	Selectivity, %
4	CCl_4	-	5	41	23	56
	Py	-	5	33	32	97
	Py	$ZrOCl_2$	5	100	100	100
5	CCl_4	-	5	54	30	56
	Py	-	2	56	55	98
	Py	-	5	100	98	98
	Py	$ZrOCl_2$	3	100	100	100

TABLE 3. Oxidation of **6** by Chlorine Dioxide in Py at 20°C

Catalyst	Time, h	Conversion, %
-	4	53
-	5	79
$ZrOCl_2$	1	42
$ZrOCl_2$	2	59
$ZrOCl_2$	3	100

In CCl_4: T = 20-50°C; time, 8 h; conversion, %; poor, no catalyst.

The stereochemical location of the hydroxyls also affected the oxidation. Compounds **1** and **5** with OH groups in the *exo*-position were oxidized faster than the corresponding epimers, i.e., the oxidation pathway was easier from the less sterically hindered side of the starting material. Menthol (**6**) was rather stable to oxidation by ClO_2. It was practically not oxidized in CCl_4 at room temperature or with heating to 50°C. The conversion was 79% in Py after 5 h (Table 3). The exclusive reaction product was menthone (**10**). Oxidation of **6** by Cr^{+6} compounds almost always produces a certain amount of *iso*-menthone [9]. However, treatment of the reaction mixture with dilute H_2SO_4 over 1 d produced an equilibrium mixture of menthone and *iso*-menthone (~70:30), which were isolated pure by chromatography over SiO_2 and characterized by spectral methods.



6 **10**

Catalysts had a favorable effect on oxidation by ClO_2. Thus, the time for oxidation of *iso*-borneol was halved and the conversion of borneol increased from 33% (without catalyst) to 100% in the presence of $ZrOCl_2$, which was used previously to accelerate the reaction of ClO_2 with propan-2-ol [10]. The yield of menthone (**10**) was quantitative at room temperature after 3 h in the presence of catalytic amounts of $ZrOCl_2$.

Next we studied the effect of the metal in certain acetylacetonates (Fe^{+2}, Cu^{+2}, Co^{+2}, VO^{+2}), which are widely used for hydroperoxide oxidation [11, 12], the amount of catalyst, and the duration of the oxidation of borneol. The oxidation was accelerated by acetylacetonates of Cu, Co, and VO. The yield of camphor reached 100%. Iron(II) acetylacetonate precipitated presumably as iron oxide, which inhibited the oxidation. According to the results, $VO(acac)_2$ was the most active catalyst for borneol oxidation. The yield of camphor was quantitative in 3 h using 1.5% catalyst. Increasing the amount of catalyst from 0.8 to 10% did not affect the conversion of **4** and the yield of camphor, which was almost 100% (Py solvent, 5 h).

The effect of the metal of the catalyst on borneol oxidation by ClO_2 (Py, 5 h, 10% catalyst) can be seen from the following data:

Catalyst	*Conversion, %*	*Content of **9**, GC, %*
-	33	32
$Fe(acac)_2$	9	6
$Cu(acac)_2$	45-49	45-48
$Co(acac)_2$	73-98	72-98
$VO(acac)_2$	100	100

Oxidation of borneol by ClO_2 in the presence of $VO(acac)_2$ (1.5%, Py solvent, T = 20°C) depended on time. The content of **9** was 38% after 1 h; 69%, after 2 h; 100%, after 3 h.

Thus, the results showed that the optimal conditions for oxidizing terpene alcohols **1-6** by ClO_2 were Py solvent, room temperature, catalytic amounts of $ZrOCl_2$ and VO or Co acetylacetonates. Cyclic allyl alcohols and alcohols with an *exo*-OH group were oxidized easier than saturated alcohols and those with an *endo*-OH group, respectively. ClO_2 was also a selective, mild, and convenient oxidant that can compete with certain traditional oxidants, particularly, hexavalent Cr compounds.

EXPERIMENTAL

GC was performed on a Kristall-2000M chromatograph with a flame-ionization detector, capillary column (60 m, 0.251 mm, HP-5MS phase, Ar carrier gas). Reaction products were identified by comparison with authentic compounds using GC and TLC. TLC was performed on Silufol and Sorbfil plates with elution by diethylether:heptane and vanillin developer in EtOH (3%). The concentration of ClO_2, which was supplied by OAO MBP Syktyvkar LPK as an aqueous solution of 5-7 g/L, was determined by iodometric titration by the literature method [13]. We used commercially available borneol, *iso*-borneol, menthol, and camphor that were purified by crystallization. *neo-iso*-Verbanol and *cis*-verbenol [14], *trans*-verbenol [15], and verbenone [16] were prepared as before. We used chemically pure solvents and freshly distilled Py. Metal acetylacetonates were prepared by the literature method [17].

General Method for Oxidizing Terpene Alcohols. Starting compound (0.5-1 g, **1-6**) was dissolved in solvent (10-15 mL) with or without catalyst, stirred, and treated with a stream of ClO_2 in air. The reaction was monitored by TLC. Solvent was distilled off. The mixture was diluted with diethylether, washed with H_2SO_4 (5-10%, if Py was used) and saturated NaCl solution, and dried over Na_2SO_4 or $MgSO_4$. The ether was removed. The mixture was analyzed by GC by comparison with known compounds (**7-10**). The yields of oxidation products were 82-91%.

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