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ALKOXYLATION AND HYDRATION OF CAMPHÈNE IN THE PRESENCE OF ACID CATALYSTS

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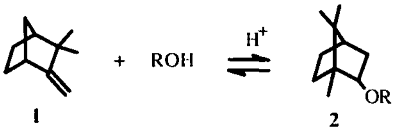
The alkoxylation of camphene in the presence of various acid catalysts is studied. Alkylisobornyl ethers are obtained in high yields if the heteropolyacids $H_4SiW_{12}O_{40}$ *and* $H_3PW_{12}O_{40}$ *are used as the catalysts. The mechanism of the acid-catalyzed hydration of camphene in aqueous-alcohol solutions is examined.*

Monoterpenes extracted from conifers are widely used in the synthesis of fragrances. They provide a wide range of compounds upon which perfumes, colognes, creams, cosmetics, medicines, and other biologically active preparations are based [1]. In particular, several monoterpene esters and ethers that are produced by acid-catalyzed reaction of monoterpenes with carboxylic acids or alcohols, respectively, can be used as fragrances [2-6]. Patents have been issued for the preparation of several alkylisobornyl ethers by alkoxylation of camphene [7-10].

The acid-catalyzed reaction of camphene with simple aliphatic alcohols is also interesting as an intermediate step in the synthesis of camphor [11, 12]. The alkylisobornyl ether that is formed by alkoxylation of camphene was oxidized without prior purification to camphor by a mixture of H_2SO_4 and HNO_3. Sulfuric acid was suggested as the acid catalyst for the alkoxylation of camphene [11]. A cation-exchange resin in the H-form was also used for this purpose [12]. The use of H-mordenite zeolite as the catalyst produces pseudoborneol ether in addition to isoborneol ether [13]. The synthesis of camphor, including the alkoxylation of camphene, would evidently be of practical interest if the conditions for oxidizing alkylisobornyl ethers that satisfy current economic and industrial requirements could be developed.

The present work reports results from a study of the reaction of camphene with C_1-C_4 alcohols in the presence of various acid catalysts such as H_2SO_4, H_3PO_4, HNO_3, *p*-toluenesulfonic acid, and the heteropolyacids (HPA) $H_4SiW_{12}O_{40}$ and $H_3SiW_{12}O_{40}$. The structure, properties, and application of HPA, methods for synthesizing them, and several reactions catalyzed by them have been reviewed [14-18]. The acid-catalyzed hydration of terpenes using HPA has been investigated [19, 20]. We have previously studied the homogeneous hydration of camphene that is catalyzed by HPA SiW_{12} and PW_{12} [21].

We found that the reaction of camphene (**1**) and methyl and ethyl alcohols in the presence of HPAs SiW_{12} and PW_{12} and H_2SO_4 gives the corresponding methylisobornyl and ethylisobornyl ethers (**2**) in yields of 86-92% (Table 1).



R = CH_3, C_2H_5

These ethers are practically the only products. HPA acts as a better catalyst than H_2SO_4. Table 1 shows that the concentration of H_2SO_4 must be 17 times that of HPA in order to achieve the maximum yield of methylisobornyl ether. Use of *p*-toluenesulfonic acid as the catalyst gave unsatisfactory results. For example, the conversion of camphene by methanol was <3%.

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TABLE 1. Alkoxylation of Camphene in the Presence of Acid Catalysts at 65°C (3 h, $m_{0\,\mathrm{camph}} = 0.2$, $m_{\mathrm{alc}} = 10-13$)

Expt. No.	Reagent	Catalyst	m_{cat}, M	Products, mass %		
				camphene	ether	others
1	Methanol	n-CH_3PhSO_3H	0.1	97.5	2.5	-
2	Methanol	H_2SO_4	0.4	30.0	68.0	2.0
3	Methanol	H_2SO_4	1.7	8.0	90.0	2.0
4	Methanol	PW_{12}	0.1	7.5	92.5	Tr.
5	Methanol	SiW_{12}	0.1	8.0	92.0	Tr.
6	Ethanol	H_2SO_4	1.7	14.0	86.0	-
7	Ethanol	PW_{12}	0.1	13.0	87.0	-
8	Ethanol	SiW_{12}	0.1	13.5	86.5	-
9	Isopropanol	H_2SO_4	1.7	40.0	60.0	-
10	Isopropanol	PW_{12}	0.1	21.0	79.0	-
11	Isopropanol	SiW_{12}	0.1	22.0	78.0	-
12	Tert-butanol	PW_{12}	0.1	49.0	51.0	-
13	Tert-butanol	SiW_{12}	0.1	47.5	52.5	-
14	Tert-butanol	H_2SO_4	1.7	Ether not formed	Ether not formed	Ether not formed
15	Tert-butanol	H_3PO_4	2.0	Ether not formed	Ether not formed	Ether not formed
16	Tert-butanol	HNO_3	1.5	Ether not formed	Ether not formed	Ether not formed

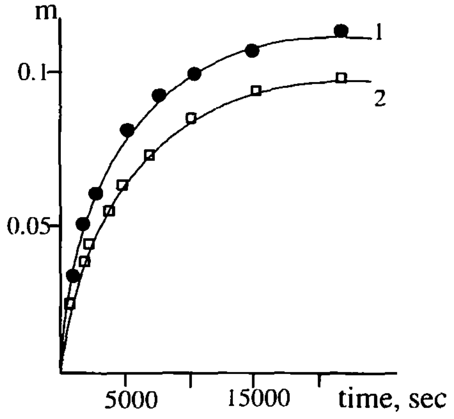


Fig. 1

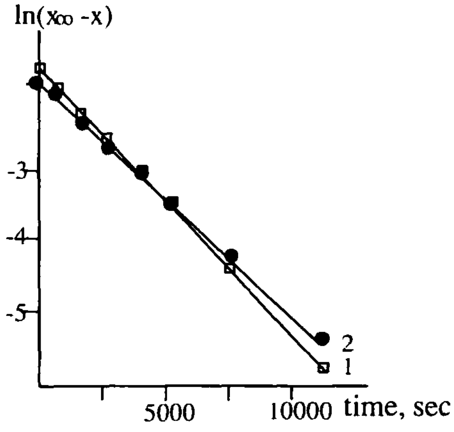


Fig. 2

Fig. 1. Accumulation of isopropylbornyl ether formed during the reaction of camphene with isopropanol in the presence of acid catalysts at 65°C: HPA (1) and H_2SO_4 (2).

Fig. 2. Plot of Eq. (3) for the reaction of camphene with isopropanol in the presence of acid catalysts at 65°C: HPA (1) and H_2SO_4 (2).

The reaction of camphene and isopropanol also produces exclusively isopropylisobornyl ether. However, the yield was much higher in the presence of HPA than in the case when H_2SO_4 was used as the catalyst (Table 1). The different catalytic properties of HPA and H_2SO_4 is clearly evident in the reaction of camphene with t-butyl alcohol. Whereas the ether is formed in moderate yields in the presence of HPA, ether is not formed at all with H_2SO_4 and other mineral-acid catalysts under comparable conditions (Table 1).

The alkoxylation of camphene is reversible, according to kinetic data obtained for the reaction of camphene with isopropanol (Figs. 1 and 2).

TABLE 2. Rate Constants and Equilibrium Constants for the Reaction of Camphene with Isopropanol in the Presence of Acid Catalysts at 65°C (m_{alc} = 13, $m_{0\ camph}$ = 0.2)

Expt. No.	Catalyst	m_{cat}	$(K_1+K_{-1}) \times 10^4$, sec^{-1}	$K_1 \times 10^4$, sec^{-1}	$K_1 \times 10^4$, sec^{-1}	K
1	SiW_{12}	0.1	3.1 ± 0.2	2.5 ± 0.3	0.62 ± 0.04	3.7 ± 0.3
2	H_2SO_4	1.7	2.05 ± 0.11	1.30 ±0.09	0.76 ± 0.03	1.7 ± 0.1

The reaction rate was determined by changing the ether concentration expressed in molality. The ether concentration at given time points was found by GLC using standards. The experimental data are described well by the kinetic equation for a first-order reversible reaction (direct reaction is pseudo-first order):

$$dx/dt = K_1(m_0 - x) - K_{-1}x, \qquad (1)$$

after certain transformations

$$dx/dt = (K_1 + K_{-1})(x_\infty - x), \qquad (2)$$

where m_0 is the starting camphene concentration and x and x_∞ are the ether concentrations at an arbitrary time point and at equilibrium.

The overall constant $(K_1 + K_{-1})$ was found by extrapolation according to (Fig. 2):

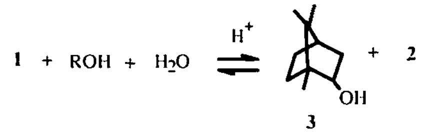
$$\ln(x_\infty - x) = (K_1 + K_{-1})\,t, \qquad (3)$$

The kinetic data obtained in the presence of HPA and H_2SO_4 in addition to the equilibrium concentration constants are given in Table 2.

The overall rate constant $(K_1 + K_{-1})$ refers to a single catalyst concentration (1 mol/kg) and is found from the ratio $(K_1 + K_{-1})/m_{cat}$, where m_{cat} is the catalyst concentration for HPA and H_2SO_4, $(3.1 \pm 0.2)\times10^{-3}$ and $(1.21 \pm 0.08)\times10^{-4}$ mol/kg·sec, respectively. Thus, equilibrium with HPA is reached 20 times faster that with H_2SO_4. A second feature is that the equilibrium concentration of ether is much higher in the reaction with HPA than with H_2SO_4 (Fig. 1, Table 2).

We also studied the reaction of camphene in a mixed alcohol—water (4:1) solvent. The ratio of components was dictated by the solubility of camphene. Our task was to determine the feasibility of using the aqueous alcohol solution for direct hydration of camphene in a homogeneous reaction. Camphene was also hydrated in neat dioxane for comparison.

As expected, isoborneol (3) in addition to alkylisobornyl ethers (2) formed in aqueous alcohol media:



The product ratio depends on the nature of the alcohol and catalyst. As the number of C atoms in the alcohol alkyl group increases, the conversion of camphene decreases and the amount of isoborneol in the reaction mixture increases in inverse sequence (Table 3).

The reaction of camphene occurring in aqueous alcohol media is presented in Fig. 3.

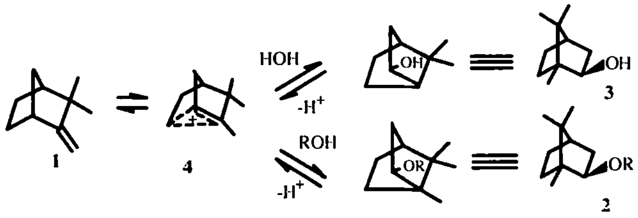


Fig. 3. Acid-catalyzed reaction of camphene in aqueous alcohol media.

TABLE 3. Products from Acid-Catalyzed Reaction of Camphene in Aqueous-Alcohol Media at 65°C (3 h) ($m_{0\,\mathrm{camph}} = 0.2$, $m_{\mathrm{water}} = 10.5$, $m_{\mathrm{alc}} = 10\text{-}13$, $V_{\mathrm{wate}}:V_{\mathrm{soln}} = 1:4$)

Expt. No.	Reagent	Catalyst	m_{cat}	Products, mass %			
				camphene	isoborneol	ether	others
1	Methanol—	H_2SO_4	1.7	5.0	3.5	91.0	-
2	water	SiW_{12}	0.1	9.0	8.5	82.0	-
3	Ethanol—	H_2SO_4	1.7	17.5	16.0	66.5	-
4	water	SiW_{12}	0.1	22.0	28.0	50.0	-
5	Isopropanol—	H_2SO_4	1.7	42.5	26.5	30.0	-
6	water	SiW_{12}	0.1	35.5	45.0	19.5	-
7	Dioxane—	H_2SO_4	1.7	87.0	10.0	-	3.0
8	water	SiW_{12}	0.1	60.0	40.0	-	Tr.

Camphene (**1**) adds a proton, forming the nonclassic ion (**4**), which reacts with water or alcohol to form isoborneol (**3**) or alkylisobornyl ether (**2**), respectively. Steric effects occurring during the conversion of **4** into the products apparently cause the amount of isoborneol to increase as a function of the alcohol in the mixed solvent. Increasing the steric radius of the alkyl group hinders the formation of the ether, favoring the competitive reaction of the carbocation with water.

The data indicate that HPAs act differently as homogeneous catalysts than mineral acids. The high activity of HPAs is due to the fact that they are stronger Bronsted acids [18]. Furthermore, it has been noted [22-25] that HPAs are naturally capable of specifically coordinating to organic molecules and activating them, thereby influencing the course of acid-catalyzed reactions. In our opinion, this may explain the formation of *t*-butylisobornyl ether in the presence of HPA.

EXPERIMENTAL

Camphene was purified by double distillation to 99% purity. Solvents were dried according to the literature [26]. Technical heteropolyacids PW_{12} and SiW_{12} were obtained from the "Krasnyi Khimik" plant (St. Petersburg) and were heated in vacuum at 200-220°C for 2 h to remove completely water of hydration.

The alkoxylation and hydration of camphene was carried out in a reactor equipped with heating. The temperature in the reactor was held constant (±0.1°C) by circulating water from a thermostat. The reaction mixture was rapidly cooled a certain time after the start of the reaction. The reaction product were twice extracted with hexane. The combined extracts were neutralized by 10% Na_2CO_3, washed with water until the pH was 7, and dried over anhydrous $MgSO_4$. The excess of solvent was distilled off. The reaction products were analyzed by GLC.

Chromatography was performed on a Chrom 5 chromatograph with a flame-ionization detector and a stainless-steel column 3 m long filled with 15% PFMS-4 silicone oil on N-AW-DMSC chromaton (0.20-0.25 mm). The temperature of the thermostat was 110°C; of the vaporizer, 250°C. The He flow rate was 60 ml/min. The component contents were calculated using an internal standard of tridecane. The relative uncertainty of the analysis within a confidence level of 0.95 was ±2%. The average of five parallel experiments was used in the analysis.

The direct (K_1) and reverse (K_{-1}) rate constants for the alkoxylation of camphene in isopropanol and the equilibrium constant (K) were calculated as before [27].

Synthesis of Alkylisobornyl Ethers. A solution of $H_4SiW_{12}O_{40}$ (75 g) in the appropriate alcohol (250 ml) was treated with camphene (15 g) and heated to 65°C, at which temperature the reaction was carried out for 5 h. The mixture was cooled and extracted twice with hexane. The combined extract was neutralized with 10% Na_2CO_3, washed with water, and dried over anhydrous $MgSO_4$. The excess of solvent was distilled off at atmospheric pressure. Then the reaction mixture was vacuum distilled. Results: methylisobornyl ether, 92% yield, bp 77°C/15 mm, $n_d^{16} = 1.4664$ (in agreement with the literature [28]); ethylisobornyl ether, 86% yield, bp 115°C/50 mm, $n_d^{16} = 1.4598$ (the data obtained are in agreement with the literature [28]); isopropylisobornyl ether, yield 78%, bp 145°C/20 mm, $n_d^{16} = 1.4538$ (the data obtained are in agreement with the literature [9]); *t*-butylisobornyl ether, 52% yield, bp 173°C/20 mm, $n_d^{16} = 1.4768$ (no literature data).

The *t*-butylisobornyl ether was identified using elemental analysis and IR spectroscopy. The IR spectra were recorded on a Specord-75 IR instrument.

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