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THE ACID CATALYSED HYDRATION OF 1-ISOPROPYL-4- METHYLENEBICICLO [3.1.0] HEXANE (SABINENE). THE SYNTHESIS OF THE TERPINEN-4-OL

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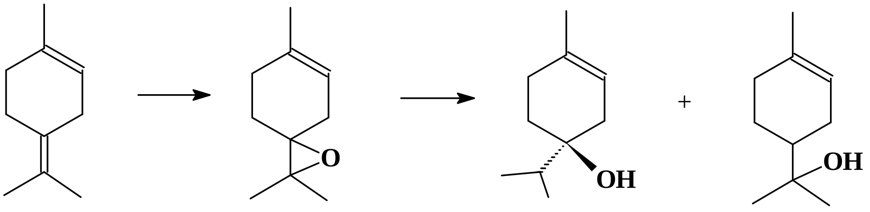
ABSTRACT. The acid catalysed hydration of (+)-sabinene, using various acids in aqueous acetone at 30^{0}C for 50 hours, gave (+)-terpinen-4-ol as a main product (80%), α- and γ-terpinene (about 15%), p-cymene (6-10%) together with trace quantities of unidentified materials.

INTRODUCTION

Terpinen-4-ol (**3**), was identified by Wallach [1], as the one present in majoram oil from *Origanum majorana L*. This alcohol is a constituent of numerous essential oils and occurs in the dextro modification: $[\alpha]_D$ $+17^0$ (homo.). It is used as an important additive in the perfume industry. Because of its importance, several syntheses of this compound has been reported [2-4]. Terpinen-4-ol can be prepared from terpinolene, α-thujene and sabinene. The manufacture of this alcohol utilizes a novel method using a terpinolene (**1**) as a starting material [5-7].

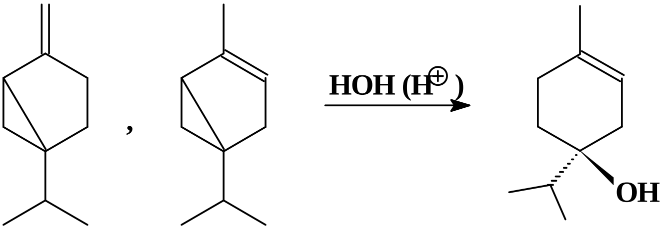


1 2 3 4

Terpinolene is epoxidized with peracetic acid in methylene chloride to give 94% 4,8-epoxy terpinolene (**2**). Lithium aluminium hydride reduction of the epoxide produces simultaneously terpinen-4-ol (**3**) and α-terpineol (**4**), the former constituting 60% of the alcohol mixture. By this method, only the racemic terpinen-4-ol is obtained.

A modification of this method consists in treating the epoxide with aq. 40% Me$_2$NH at 140^{0}C, followed by hydrogenation of the exocyclic double bond to give terpinen-4-ol in 50% yield [5]. Another method performed in the synthesis of the terpinen-4-ol starts from sabinene (**5**) and α-thujene (**6**) [3]. The acid catalysed hydration of the two byciclic olefins affords terpinen-4-ol. A variety of acids can be used, the most notable being sulphuric, benzene sulphonic, formic and oxalic acids. Sabinene is hydrated more rapidly than α-thujene by a factor of 20:8 at 45^{0}C and appears to be the most suitable raw material for the alcohol production. [4].

By hydrogenation and hydroboration, Brown [8] has suggested that sabinene is stabilised by greater conjugation between the double bond and the cyclopropane ring.



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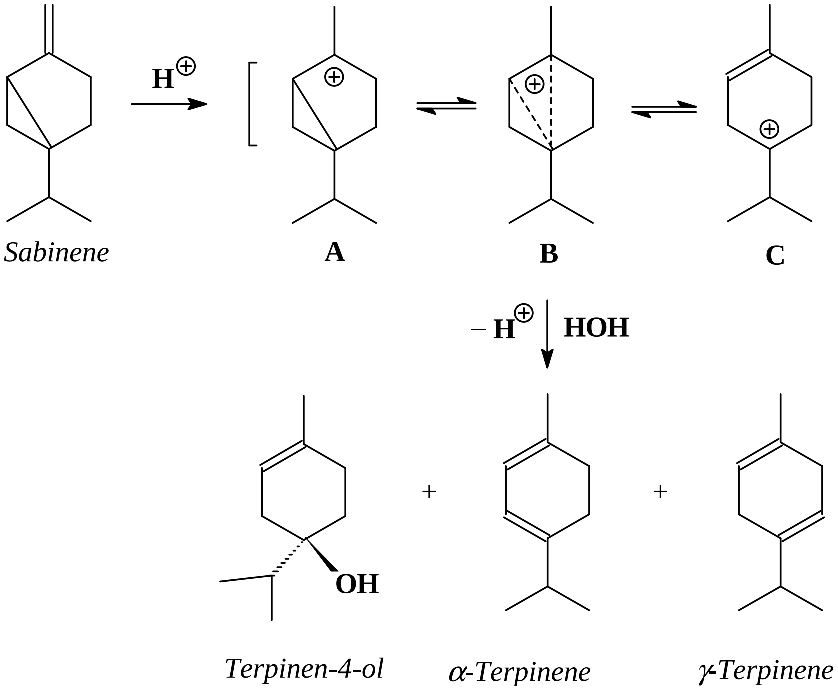
Tolstikov [2] has studied the hydration of sabinene (95% purity) in water and 2-5% H_2SO_4 for 50 hours at 25^{0}C to obtain terpinen-4-ol in 65% isolated yield. Norin et all [3] were also prepared terpinen-4-ol in 70% yield (glc analysis), by hydration of sabinene in aqueous dioxane (75%), using perchloric acid as catalyst.

RESULTS AND DISCUSSION

In the present paper, we wish to report some results in the acid catalysed hydration of (+)-sabinene (75% purity). In our investigation, the hydration was performed in aqueous acetone (75%) using various acids: sulphuric acid, $HClO_4$, p-TsOH, HPA (heteropoly acids). The reaction was monitored by GC-MS analysis using 20m methylsilicone capillary column. The reaction conditions and product composition are shown in Table 1.

The best results were obtained using sulphuric acid as catalyst. Thus, sabinene (75% purity) reacts in acetone-water solution and 0.02M H_2SO_4 at 30^{0}C for 50 hours to give terpinen-4-ol in 80% yield (determined by GC-MS analysis), 12% γ-terpinene and 6% p-cymene respectively, with a conversion of 95% (see Table 1, run 2).

α-Terpinene was detected in very small amount, only 3%. Increasing the concentration of sulphuric acid (see Table 1, run 5) the yield of the terpinen-4-ol decreased, but increased slowly the yield of γ-terpinene (from 12% to 18%) and α-terpinene.These olefins are probably obtained by the dehydration of the terpinen-4-ol, formed during this reaction.



Scheme 1

Table 1.

Reaction conditions for hydration of sabinene[a]

Run	Catalyst	GC peak area%		Conversion %[d]		
	conc. (M)	terpinen-4-ol	γ-Terpinene	p-cymene		Others[b]
1	0.01 H_2SO_4	53.3	7.5	3.4	35.8	86
2	0.02 H_2SO_4	76.2	12.4	6.6	24.8	95
3	0.03 H_2SO_4	50.7	16.7	9.5	23.1	84
4	0.05 H_2SO_4	41.4	18.6	10.4	29.6	80
5	0.02 $HClO_4$	42.2	14.5	7.8	35.5	81
6	0.04 $HClO_4$	46.7	17.6	7.9	27.8	84
7	0.02 pTsOH	31.2	9.4	6.3	53.1	85
8	0.02 W-HPA[c]	32.3	4.2	3.2	60.3	89

[a] All experiments were performed in aqueous acetone (75%), at 30^0C, for 50 h.

[b] Others consisted of unreacted sabinene and unidentified products.

[c] $(NH_4)_5H_4[PMo_6V_6O_{40}]$

[d] Reported to (+)-sabinene 75%

As shown in Scheme 1, three ions in equilibrium (two carbenium ions **A**, **C** and a carbonium ion **B**) can be obtained by the protonation of the sabinene. The hydration of (+) sabinene takes place with a high retention of configuration at C_1. The terpinen-4-ol produced from optically active sabinene has been shown to retain 80% of the optical activity of the starting material [3]. The stereospecificity in the formation of (+)-terpinen-4-ol is in complete agreement with the carbonium ion **B**, which is the main intermediate in this rearrangement. Thus, there must be extensive charge delocalisation in the rearrangement, and a classical charge-localised ion (**A** or **C**) can be ruled out as a main product-determining intermediate. However, some racemic alcohol is also formed, which thus would suggest that the classical charge-localised ion **C** is also involved in this reaction. Ring opening could also take place to give the ion **C,** which can be lose a proton to lead to the observed olefins, but there is no evidence to support this route [9].

The kinetic study of the hydration of sabinene will be the topic of a next paper.

EXPERIMENTAL

Gas chromatography-mass spectroscopy (GC-MS) coupling analyses were performed on a Hewlett-Packard 5890 (GCL)-5972 (MSD) using a HP-5MS 20m x 0.25 x 0.25μm capillary. (+)-Sabinene, (+)-terpinen-4-ol and terpinolene were purchased from Aldrich. TLC was performed with Merck Kiselgel 60F 254, using petroleum ether:ether 5:2 as eluent.

Acid-catalysed hydration.

To a stirred solution of (+)-Sabinene (0.1 mol, 75% chemical purity, $[\alpha]_D=+78^0$, c=1,$CHCl_3$) in 120 ml acetone, 20 ml H_2O (2%H_2SO_4) was dropwise added for 30 min., and the solution was then stirred at 30^0C for 50 hours. The reaction mixture was neutralized with 1M $NaHCO_3$, then the solvent removed by distillation. The residual liquid was extracted with ether, dried on $MgSO_4$, filtered and final reaction product was analyzed by GC-MS (see Table 1). The pure terpinen-4-ol was obtained by vacuum distillation at 85-87^0C/14mmHg (59% isolated yield reported to starting material).

Dehydration of terpinen-4-ol.

Terpinen-4-ol (1g) in 30ml benzene and p-toluenesulphonic acid (0,1g) were refluxed for 1 hour, and the water resulted in the reaction was removed using a Dean-Stark trap. The reaction mixture was diluted with water, neutralized with 1M $NaHCO_3$, extracted with ether, dried on $MgSO_4$, then analyzed by GC-MS. γ-Terpinene (67%), α-terpinene (25%) and p-cymene (8%) were obtained.

The terpinen-4-ol (1g) was also dehydrated with 30% H_2SO_4 (20ml) at 100^0C for 0,5 hours to give γ-terpinene (52%), α-terpinene (15%) and p-cymene (30%) respectively.

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