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TRANSFORMATIONS OF (–)-α-PINENE PEROXIDE OZONOLYSIS PRODUCTS BY HYDRAZINES OF HCl AND H_2SO_4

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The reactivities of hydrazines of HCl and H_2SO_4 for (–)-α-pinene peroxide ozonolysis products were studied. It was shown that these reagents were less effective and selective than semicarbazide hydrochloride for transformations into cis*-pinonic acid and its esters.*

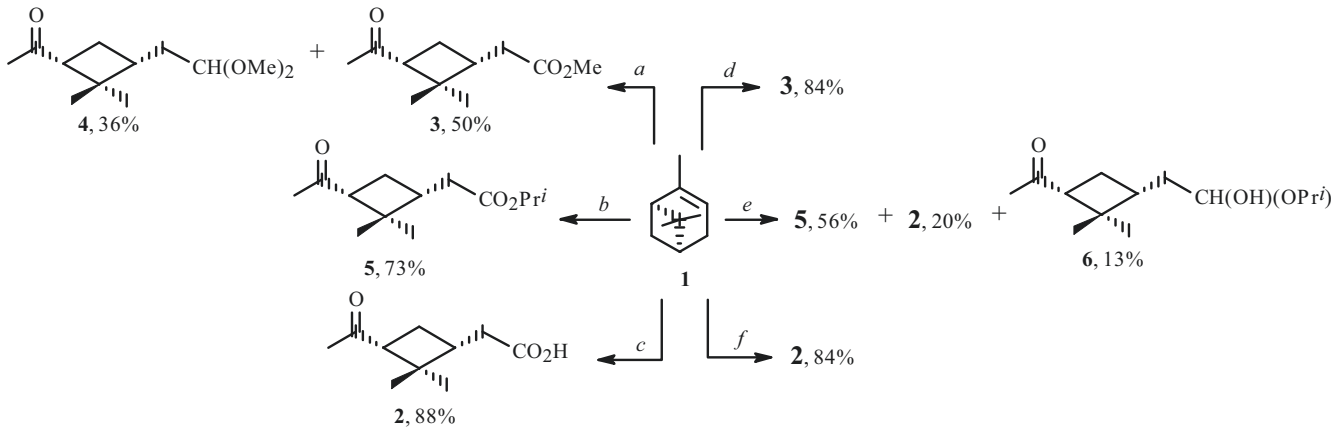
Keywords: (–)-α-pinene, peroxide and non-peroxide ozonolysis products, hydrazine sulfate, hydrazine hydrochloride.

The use of chiral building blocks for targeted synthesis of biologically active compounds is an important and promising thrust in organic chemistry. α-Pinene (**1**), which is isolated from resin and turpentine of various *Pinus* species, is an available source of such molecules owing to its native optical activity.

Hydrazine derivatives (2,4-dinitrophenylhydrazine, semicarbazide, and phenylhydrazine, semicarbazide, and thiosemicarbazide hydrochlorides) are effective reductants for peroxide ozonolysis products of olefins and their derivatives. Thus, *cis*-pinonic acid (**2**) [1] and its methyl [2] and isopropyl [3] esters and disemicarbazone [4] were produced from α-pinene using these reagents.

In continuation of research in this area, we studied the reactivities of hydrazine hydrochloride and sulfate toward peroxide ozonolysis products of **1**.

Hydrazine hydrochloride formed intermediate peroxides from **1** that were converted depending on the solvent into methyl (**3**) or isopropyl (**5**) ketoesters or into ketoacid **2**, like previously used semicarbazide hydrochloride [1–3]. Hydrazine hydrochloride was noted to be less reactive and selective than semicarbazide hydrochloride. The peroxides were completely reduced in alcohols after 1–3 weeks whereas four days were required to convert them into ketoacid **2** in AcOH–CH_2Cl_2. Furthermore, a mixture of ketoester **3** and ketoacetal **4** was formed if the reaction was carried out in MeOH.



a–c: $NH_2NH_2 \cdot HCl$; *d–f*: $NH_2NH_2 \cdot H_2SO_4$; *a*, *d*: O_3–MeOH, 0°C, 1 week; *b*, *e*: O_3–Pr^iOH, 0°C, 3 week; *c*, *f*: O_3–AcOH–CH_2Cl_2, 0°C, 4 days

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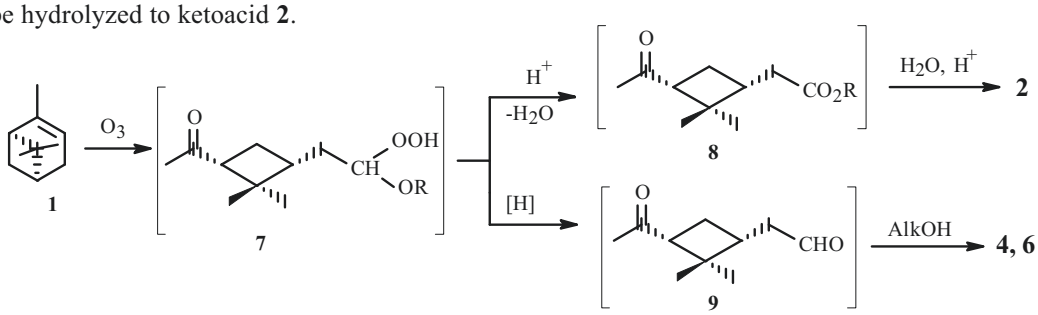
Changing the acid did not significantly alter the behavior of the hydrazine-based reductants. The main products for hydrazine sulfate were esters **3** or **5**, depending on the solvent, or carboxylic acid **2**. Also, ketoacid **2** and ketohemiacetal **6** were obtained via work up of the peroxide ozonolysis products of **1** in *i*-PrOH.

cis-Pinonic ketoacid **2** was obtained in high yields and is a key compound in the synthesis of the pheromone of the citrus mealy bug *Planococcus citri* (Risso), a hazardous citrus pest [4].

The formation of both carbonyl and carboxylic derivatives could be explained by competing transformations of hydroperoxides **7**, i.e., reduction to ketoaldehyde **9**, which was isolated as acetals **4** and **6**, or dehydration to esters **8**, which could in turn be hydrolyzed to ketoacid **2**.



R = Me, Pr^i, Ac; Alk = Me, Pr^i

Thus, hydrazine hydrochloride or sulfate transformed peroxide ozonolysis products of **1** into the corresponding ketoacid or its esters, depending on the solvent. However, these reagents were less reducing and selective than semicarbazide hydrochloride.

EXPERIMENTAL

General comments were published [2]. Equipment at the Khimiya Center for Collective Use and α-pinene (Acros Organics, 97% pure) were used. Elemental analyses of all compounds agreed with those calculated. The ozonator output was 40 mmol O_3/h.

General Method for Ozonolysis of (–)-α-Pinene (1). An O_3/O_2 mixture was bubbled through a solution of **1** (1 g, 7.35 mmol) in MeOH or *i*-PrOH (25 mL) or a mixture of AcOH (4.2 mL) and CH_2Cl_2 (20 mL) at 0°C until 8 mmol of O_3 were absorbed. The reaction mixture was purged with Ar, stirred, treated at the same temperature with reductant [25.7 mmol; $NH_2NH_2 \cdot H_2SO_4$ (3.34 g) or $NH_2NH_2 \cdot HCl$ (1.76 g)], and stirred at room temperature until the peroxide disappeared (monitored using I_2–starch). The solvent was distilled off. The residue was dissolved in $CHCl_3$ (150 mL), washed with H_2O (4 × 15 mL), dried over Na_2SO_4, and evaporated.

Work up of Peroxide Ozonolysis Products of 1 by $NH_2NH_2 \cdot HCl$. Ozonolysis in MeOH. Chromatography (SiO_2, hexane, hexane–MTBE, 10:1→1:1) of the residue (1.6 g) produced ketoester **3** (0.72 g, 50%) and ketoacetal **4** (0.57 g, 36%).

Methyl [(1*R*,3*R*)-3-Acetyl-2,2-dimethylcyclobutyl]acetate (3). R_f 0.44, $[\alpha]_D^{23}$ –24.8° (*c* 0.73, CH_2Cl_2). The IR and NMR spectra were identical to those published earlier [2].

1-[(1*R*,3*R*)-3-(2,2-Dimethoxyethyl)-2,2-dimethylcyclobutyl]ethanone (4). 1.14 g (72%), R_f 0.40. IR and NMR spectra were identical to those published earlier [5].

Ozonolysis in *i*-PrOH. Chromatography (SiO_2, hexane–MTBE, 10:1→1:1) of the residue (1.3 g) produced ketoisopropyl ester **5** (1.20 g, 73%).

Isopropyl [(1*S*,3*S*)-3-Acetyl-2,2-dimethylcyclobutyl]acetate (5). R_f 0.62. IR and NMR spectra were identical to those published earlier [3].

Ozonolysis in CH_2Cl_2–AcOH. Chromatography (SiO_2, hexane–MTBE, 10:1→1:1) of the residue (1.30 g) produced ketoacid **2** (1.19 g, 88%).

[(1*R*,3*R*)-3-Acetyl-2,2-dimethylcyclobutyl]acetic Acid (2). R_f 0.21 (hexane–MTBE, 4:1), $[\alpha]_D^{20}$ –40.0° (CH_2Cl_2, 0.8164). IR and NMR spectra were identical to those published earlier [1].

Work up of Peroxide Ozonolysis Products of 1 by $NH_2NH_2 \cdot H_2SO_4$. Ozonolysis in MeOH. Chromatography (SiO_2, hexane, hexane–MTBE, 10:1→1:1) of the residue (1.40 g) produced ketoester **3** (1.22 g, 84%).

Ozonolysis in *i*-PrOH. Chromatography (SiO_2, hexane–MTBE, 10:1→1:1) of the residue (1.70 g) produced ketoisopropyl ester **5** (0.90 g, 56%), ketoacid **2** (0.13 g, 20%), and hemiacetal **6** (0.11 g, 13%).

1-[3-(2-Hydroxy-2-isopropoxyethyl)-2,2-dimethylcyclobutyl]ethanone (6). R_f 0.37. IR spectrum (KBr, ν, cm^{-1}): 1110 (C–O–C), 3392 (OH). ^1H NMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.82 (3H, s, $C^{cis}H_3$), 1.23 (6H, d, $2CH_3$), 1.32 (3H, s, $C^{trans}H_3$), 1.83–2.05 (1H, m, H-4), 2.08 (3H, s, $CH_3C(O)$), 2.15 (2H, m, $C\underline{H}_2CH$), 2.25–2.35 (1H, m, H-1), 2.90 (1H, m, H-3), 4.02 (1H, m, $C\underline{H}(CH_3)_2$), 4.9 (1H, m, $C\underline{H}OH$), 5.7 (1H, br.s, OH). ^{13}C NMR spectrum (75.47, $CDCl_3$, δ, ppm): 22.12 (q, CH_3), 23.23 (q, CH_3), 24.77 (q, $2CH_3$), 29.98 (t, C-4), 30.16 (q, $\underline{C}H_3C(O)$), 38.09 (t, CH_2), 38.37 (d, C-3), 43.16 (s, C-2), 53.79 (d, C-1), 67.54 (d, $\underline{C}H(CH_3)_2$), 103.45 (d, $\underline{C}H(OH)OCH(CH_3)_2$), 208.03 (s, C=O).

Ozonolysis in CH_2Cl_2–AcOH. Chromatography (SiO_2, hexane–MTBE, 10:1→1:1) of the residue (1.35 g) produced ketoacid **2** (1.13 g, 84%).

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