

DECOMPOSITION OF OZONOLYSIS PEROXIDE PRODUCTS OF (+)- α - AND (+)- β -PINENES IN METHANOL BY Fe(III) SALTS

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The reaction of ozonolysis peroxide products of (+)- α and (+)- β -pinenes with Fe(III) salts in MeOH was studied. It was found that decomposition of methoxyhydroperoxides obtained via ozonolysis of (+)- β -pinene using $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ occurred at room temperature with formation of nopinone and its 3-chloro derivative; under reflux, nopinone and *p*-isopropylphenol. Replacing $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ by $\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ produced the single product nopinone. Decomposition of peroxide compounds obtained via ozonolysis of (+)- α -pinene using $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ gave a mixture of (1*S*,3*S*)-3-acetyl-2,2-dimethyl-1-(2,2-dimethoxyethyl)cyclobutane and [(1*S*,3*S*)-3-acetyl-2,2-dimethylcyclobutyl]acetate.

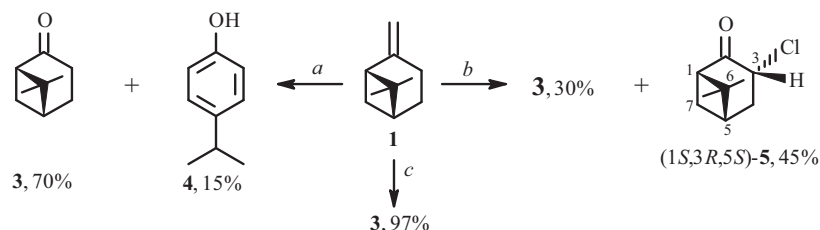
Keywords: (+)- α - and (+)- β -pinenes, ozonolysis, MeOH, FeCl_3 , $\text{Fe}(\text{NO}_3)_3$.

Ozonolysis of olefins is widely used in synthetic organic chemistry [1, 2]. Ozonolysis of readily available chiral monoterpenes is especially significant because it enables various α,ω -bifunctional compounds to be prepared. These are interesting as intermediates in the synthesis of low-molecular-weight bioregulators [3].

The structures of ozonolysis products are determined by a combination of several factors such as the reaction temperature, solvent, substrate structure, and the reagents used to work up the intermediate peroxide compounds. The reagents used most frequently to decompose the ozonolysis peroxide products are Me_2S , Zn/AcOH , $\text{H}_2/\text{Pd}-\text{CaCO}_3-\text{PbO}$, PPh_3 , and $\text{H}_2\text{O}_2/\text{SeO}_2$.

It was shown earlier that a halogen atom or double bond may be introduced or a dimeric product may be obtained through the action of salts of redox-active metals on the ozonolysis peroxide products [4]. However, such data are sparse. Nevertheless, the application of this method to natural monoterpenes could expand their synthetic capabilities.

Therefore, our goal was to study ozonolysis of (+)- β - (**1**) and (+)- α -pinene (**2**) in MeOH with subsequent decomposition of the peroxide products by Fe(III) salts. Ozonolysis of **1** in MeOH at 0°C with subsequent work up of the peroxide products from ozonolytic cleavage of the double bond by $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ solution (1 M) in MeOH under reflux gave nopinone (**3**) and *p*-isopropylphenol (**4**), which were separated by column chromatography over SiO_2 .

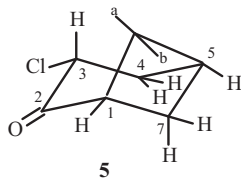


a. 1) O_3/MeOH , 2) $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 60°C; b. 1) O_3/MeOH , 2) $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$; c. 1) O_3/MeOH , 2) $\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$

Decomposition of the products from ozonolytic cleavage of **1** by $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ at room temperature produced a mixture of **3** and (1*S*,3*R*,5*S*)-3-chloro-6,6-dimethylbicyclo[3.1.1]heptan-2-one (**5**) in yields of 30 and 45%, respectively. The structure of **5** was established using spectral methods. All protons and C atoms were assigned based on two-dimensional CH-corr and $^1\text{H}-^1\text{H}$ -COSY-90 spectra. The SSCC of the proton on the C atom bound to the Cl atom ($^3J_{3-4} = 8.9$ and 1.7 Hz) indicated that a single isomer was obtained at the newly formed asymmetric center with the equatorial orientation of the Cl atom. The C-5

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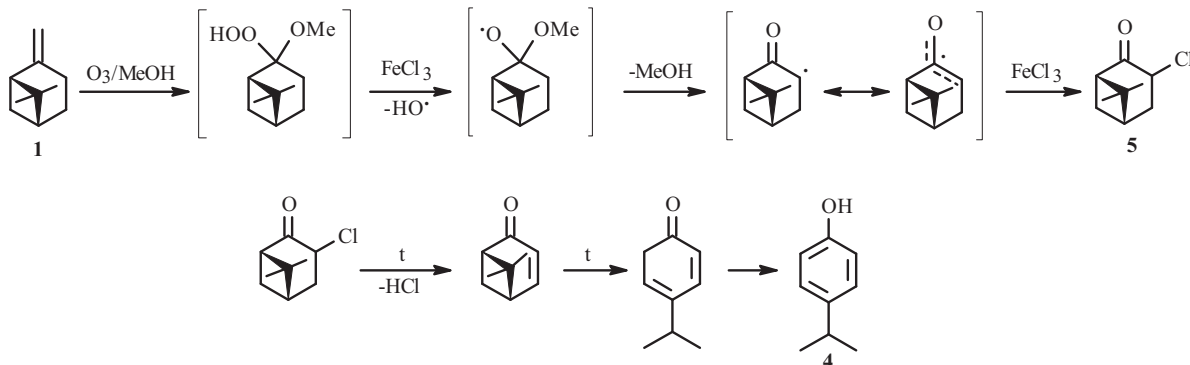
and C-1 protons were equatorial because they had small SSCC with the C-7 protons. The conformation was shifted in favor of a chair-shaped hexane ring with axial placement of the C-1–C-6 bond of the cyclobutane moiety.



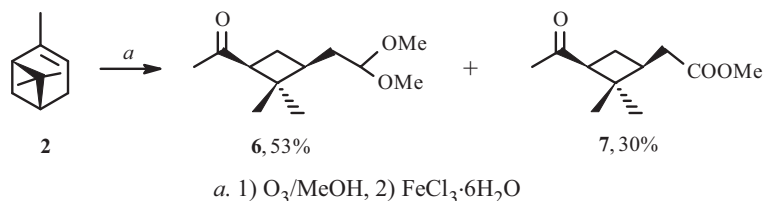
Work up of the ozonolysis peroxide products of **1** by $\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ in MeOH gave **3** in 97% yield.

Ketone **3** was not an intermediate on the pathway to **5**. Chloro-derivative **5** was not formed by heating **3** with $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ under conditions identical to those for decomposition of the peroxides.

We propose that compounds **4** and **5** were formed through the following mechanism:



Decomposition of the ozonolysis peroxide products of **2** by $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ both at room temperature and with heating produced a mixture of (1*S*,3*S*)-3-acetyl-2,2-dimethyl-1-(2,2-dimethoxyethyl)cyclobutane (**6**) and methyl [(1*S*,3*S*)-3-acetyl-2,2-dimethylcyclobutyl]acetate (**7**) in a 5:3 ratio. Formation of the methoxycarbonyl group could be explained by dehydration of the methoxyhydroperoxide intermediate in acidic medium [5] that was obviously caused by adding $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ to the reaction mixture after ozonolysis. Production of **7** by ozonolysis of (+)- α -pinene in MeOH with subsequent work up of the methoxyhydroperoxides under acidic conditions was reported earlier [6].



Thus, decomposition of ozonolysis peroxide products of **1** and **2** by Fe(III) salts is a convenient method for synthesizing synthons that are important in practice for chiral low-molecular-weight bioregulators.

EXPERIMENTAL

PMR and ^{13}C NMR spectra were taken in CDCl_3 on a Bruker AM-300 spectrometer (operating frequency 300 and 75.46 MHz, respectively). Chemical shifts are given relative to TMS. IR spectra were recorded in thin layers on a Specord M-80 instrument in the range 400–4000 cm^{-1} . GC was performed in a Chrom-5 chromatograph [column 1200 \times 3 mm, stationary phase silicone SE-30, 5% on Chromaton N-AW-DMCS (0.16–0.20 mm), operating temperature 50–300°C] with He carrier gas. Optical rotation angles were measured on a Perkin–Elmer 241 MS instrument. Optical purities of products agreed with those of the starting compounds.

Ozonolysis of 1. a. An O_3/O_2 mixture was bubbled through a solution of **1** (5 g, 37.7 mmol, *ee* 100%) in anhydrous MeOH (120 mL) until 37.7 mmol of O_2 were absorbed. The mixture was added dropwise to a refluxing solution of $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ (81.5 mL, 1 M) in MeOH, refluxed for 2 h, and cooled. The MeOH was evaporated at reduced pressure. The solid was treated with petroleum ether, washed with H_2O , and dried over Na_2SO_4 to afford crude product (4.5 g) from which chromatography

over SiO₂ (petroleum ether:EtOAc, 9:1) isolated nopinone (**3**) and 4-isopropylphenol (**4**). Yield of **3**, 3.5 g (70%), light-yellow oil; **4**, 0.8 g (15%), colorless crystals, mp 62°C.

The PMR and ¹³C NMR spectra of **3** were analogous to those reported [7]; for **4**, [8].

b. Compound **1** (5 g, 37.7 mmol) was ozonolyzed analogously to that described in **a**. The reaction mixture was added dropwise to a solution of FeCl₃·6H₂O (81.5 mL, 1 M) in MeOH at room temperature and worked up analogously to that described above to afford **3** and **5**. Yield of **3**, 1.5 g (30%); of **5**, 2.9 g (45%), colorless oil, [α]_D²⁰+73.5° (c 0.83, CH₂Cl₂).

For **5**, IR spectrum (ν, cm⁻¹): 735 (C–Cl), 1200, 1458, 1728 (C=O), 2872, 2953.

PMR spectrum (CDCl₃, δ, ppm, J/Hz): 0.8, 1.32 (6H, s, gem-CH₃), 2.0 (1H, d, ²J = 10.9, H_c-7), 2.25 (1H, ddd, ³J = 6.5, 5.3, 2.0, H-5), 2.30 (1H, ddd, ²J = 13.3, ³J = 8.9, 2.0, H_a-4), 2.65 (1H, ddd, ²J = 10.9, ³J = 5.6, 6.5, H_a-7), 2.70 (1H, ddd, ²J = 13.3, ³J = 5.3, 1.7, H_c-4), 2.75 (1H, d, J = 5.6, H-1), 4.22 (1H, dd, J = 8.9, 1.7, H-3).

¹³C NMR spectrum (CDCl₃, δ, ppm): 22.64 (CH₃), 25.50 (C-7), 25.81 (CH₃), 34.20 (C-4), 40.47 (C-5), 42.02 (C-6), 52.47 (C-3), 57.99 (C-1), 206.53 (C-2). C₉H₁₃ClO.

c. Compound **1** (2 g, 14.8 mmol) in anhydrous MeOH (50 mL) was ozonolyzed analogously to that in the preceding experiment. The reaction mixture was treated with a solution of Fe(NO₃)₃·9H₂O (32 mL, 1 M) in MeOH at room temperature and stirred for 1 h. The MeOH was distilled off. The solid was extracted with petroleum ether. The extract was dried over Na₂SO₄. The solvent was evaporated. Yield of **3**, 1.9 g (97%).

Ozonolysis of 2. An O₃/O₂ mixture was bubbled through a solution of **2** (3 g, 22.2 mmol, ee 51%) in anhydrous MeOH (72 mL) until 22.2 mmol of O₃ was absorbed. The resulting methoxyhydroperoxide was treated dropwise with a solution of FeCl₃·6H₂O (48 mL, 1 M) in MeOH at room temperature and stirred for 1 h. The MeOH was evaporated at reduced pressure. The solid was treated with petroleum ether, washed with H₂O, and dried over Na₂SO₄ to afford crude product (1.8 g) from which chromatography over SiO₂ (petroleum ether:EtOAc, 9:1) isolated **6**, yield 1.6 g (53%), [α]_D²⁰+30.9° (c 0.86, CHCl₃) and **7**, yield 1 g (30%), +20.9° (c 1.49, CH₂Cl₂). The spectral properties of **6** were identical to those published [9]; of **7**, [6].

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