

## Ozonolysis of verbenone in aprotic solvents

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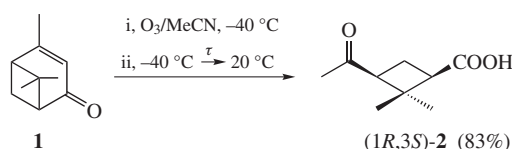
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The ozonolysis of verbenone in methylene chloride and acetonitrile at  $-60$  and  $0$  °C proceeds with cleavage of the double bond and neighbouring  $\sigma$ -bond to give (1*R*,3*S*)-acetyl-2,2-dimethylcyclobutane carboxylic acid. The mechanism of the reaction has been proposed.

The ozonolysis of olefins is widely used in synthetic organic chemistry because it allows one to introduce oxygen-containing substituents into a molecule for the synthesis of biologically active compounds.<sup>1</sup> However, the results of the reaction of a cycloolefin with ozone are not always identical, especially when in the substrate there are functional groups which can react with obtained peroxides leading to anomalous ozonolysis products. For instance, the ozonolysis of  $\alpha,\beta$ -unsaturated carbonyl compounds occurs with the additional cleavage of a neighbouring  $\sigma$ -bond to shorten a hydrocarbon chain.<sup>2,3</sup> The mechanism of enone ozonolysis depends on the structural environment of the reacting double bond and ozonolysis conditions.

This work is devoted to the study of the structure of peroxide products of verbenone ozonolysis in aprotic solvents, the dynamics of peroxide decomposition and the composition of the products with the aim to reveal the possible reaction mechanisms.

The ozonolysis of verbenone **1** in methylene chloride and acetonitrile gives (1*R*,3*S*)-3-acetyl-2,2-dimethylcyclobutane carboxylic acid **2** as the main product (Scheme 1).



Scheme 1

The reaction stoichiometry of verbenone **1** with ozone at different temperatures ( $0$ ,  $-40$  and  $-60$  °C) was determined according to a published method.<sup>4</sup> The data on the ozone quantity needed for the total verbenone conversion are presented in Table 1.

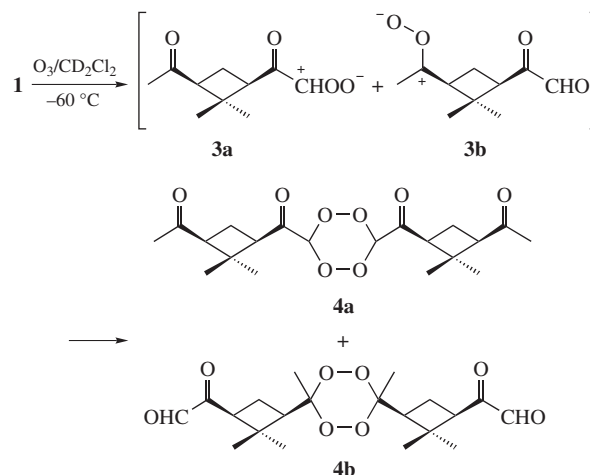
The stabilization of resulting carbonyl oxides depends on the reaction temperature. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of the products of the ozonolysis carried out in  $\text{CD}_2\text{Cl}_2$  at  $-60$  °C showed that the reaction results in the formation of carbonyl oxides **3a,b**, which are transformed into dimer peroxides **4a,b** (Scheme 2), that is the meaning by the signals of carbon atoms

**Table 1** Ozone consumed depending on the ozonolysis conditions of verbenone **1** (1 mmol).

Entry	$T/^\circ\text{C}$	Solvent	Consumed $\text{O}_3/\text{mmol}$	Yield of <b>2</b> (%)
1	$-60$	$\text{CH}_2\text{Cl}_2$	1.1–1.3	70
2	$-40$	MeCN	1.1–1.3	83
3	$0$	$\text{CH}_2\text{Cl}_2$	1.1–1.3	71
3	$0$	MeCN	1.5–1.7	57

of keto groups at 196.68, 201.39 and 201.49 ppm. The first signal corresponds to keto functions in peroxide **4b**, the other, to keto functions in dimer **4a**. The aldehyde group neighbouring with a keto group appears at 188.71 ppm. In the  $^{13}\text{C}$  NMR spectrum, two carbon atoms of an acetal fragment are also observed (98.42 ppm for **4a** and 109.97 ppm for **4b**).

In the  $^1\text{H}$  NMR spectrum of dimer peroxides **4a,b**, the signals of protons of the aldehyde groups are observed at 8.99 ppm, and the proton at carbon atom bound with two oxygens – at 4.95 ppm.



Scheme 2

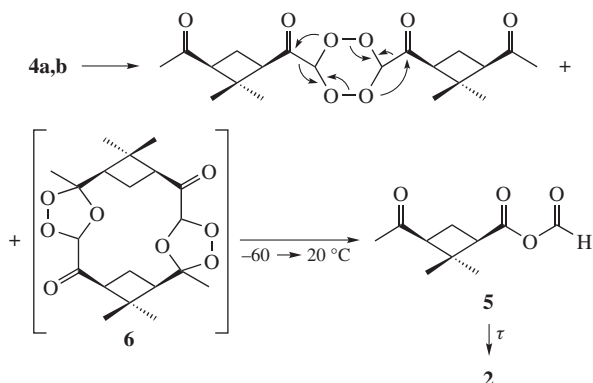
Dimer peroxides **4a,b** are unstable, that is testified by the decrease of their concentration at heating the reaction mass to room temperature.

After the ozonization, the concentration of dimers is practically equal to the concentration of initial verbenone **1**; at  $-40$  °C, it decreases by two times, and at room temperature they decompose completely (Table 2).

**Table 2** Peroxide concentration dependence on ozonization conditions (verbenone concentration is  $0.22 \text{ mol dm}^{-3}$ ).

Entry	$T/^\circ\text{C}$	Solvent	Peroxide concentration/ $\text{mol dm}^{-3}$	
			Ozonolysis temperature	$25^\circ\text{C}$
1	$-60$	$\text{CH}_2\text{Cl}_2$	0.21	0.05
2	$-40$	MeCN	0.11	0.05
		$\text{CH}_2\text{Cl}_2$	0.10	0.06
3	$0$	MeCN	0.06	0.06

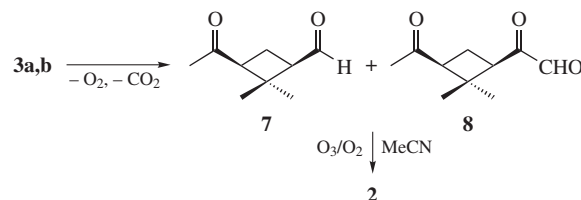
The increase in the temperature of compounds **4a,b** leads to the rearrangement into mixed anhydride **5**, which, according to spectral data, results from both peroxides. Probably, this rearrangement of peroxide **4b** occurs via dimer **6** (Scheme 3).



Scheme 3

The intermediate formation of anhydride **5** is confirmed by spectroscopic data. In the  $^{13}\text{C}$  NMR spectrum, the signal at 188.71 ppm disappears and the signals of carbon atoms of the anhydride fragment appear (156.67 and 169.84 ppm). The signal of the carbonyl atom of the acetyl fragment is observed at 206.51 ppm. On storage, compound **5** decomposes to acid **2**.

According to the results, the formation of dimer peroxides proceeds only at reduced temperatures. The ozonolysis in aprotic solvents at  $-20^\circ\text{C}$  occurs, probably, otherwise. The aldehyde groups of compounds **7** and **8** resulted from zwitterions of **3a,b** are oxidized by ozone with the formation of the single product – ketoacid **2** (Scheme 4). The possibility of such a transformation is described in the literature.<sup>5</sup> The reaction in aprotic solvents at  $-20^\circ\text{C}$  leads to the consumption of 1.5–1.7 mol of ozone per 1 mol of verbenone, that is conformed to the mechanism of aldehydes oxidation by ozone.<sup>6</sup>



Scheme 4

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