

Hydroxylamine Reactions with Peroxide Products of Alkenes Ozonolysis

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Abstract—Reactions were studied of peroxide ozonolysis products obtained from linear and cyclic alkenes with hydroxylamine prepared *in situ* from NH₂OH·HCl by hydrogen chloride neutralization with sodium acetate. A one-pot reactions sequence was performed: alkene oxidation with ozone → reduction to a carbonyl compound with hydroxylamine → condensation of the carbonyl compound with hydroxylamine providing a possibility of direct transformation of alkenes in keto- and aldoximes excluding the stage of preparation and isolation of the carbonyl compound.

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Ozonolysis splitting is one of efficient and environmentally friendly oxidation methods widely utilized both in the industry and in the fine organic synthesis. Ozonolysis reaction and subsequent transformations of the formed peroxide compounds are well explored, and the reducers like Me₂S, PPh₃, NaBH₄ are now traditional and are actively applied in converting alkene substrates in carbonyl compounds and alcohols [1]. Yet the application of *N*-containing compounds both directly at the ozonation and in further treatments of the arising peroxides is a topical issue. The use of hydroxylamine hydrochloride for treating the peroxide products of olefins ozonolysis was formerly limited to several examples, all reactions were carried out in MeOH, and depending on the substrate nature the resulting substances were aldehydes [2], aldoxime [3], or ester [1]. It was found later that the use of NH₂OH·HCl in ozonolysis–reduction reactions depending on the applied solvent afforded carboxylic acids [4, 5] or esters [6, 7] forming either in an individual state or in mixtures with oximes or nitriles and resulting from the sequence of

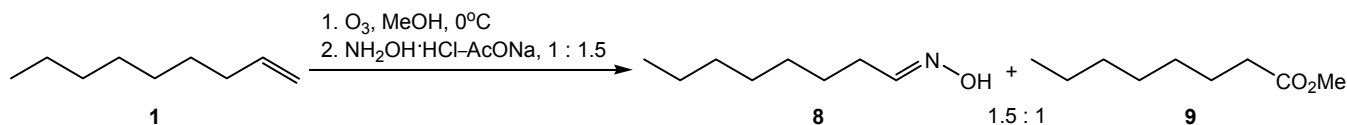
transformations aldehyde → aldoxime → nitrile → carboxylic acid/ester.

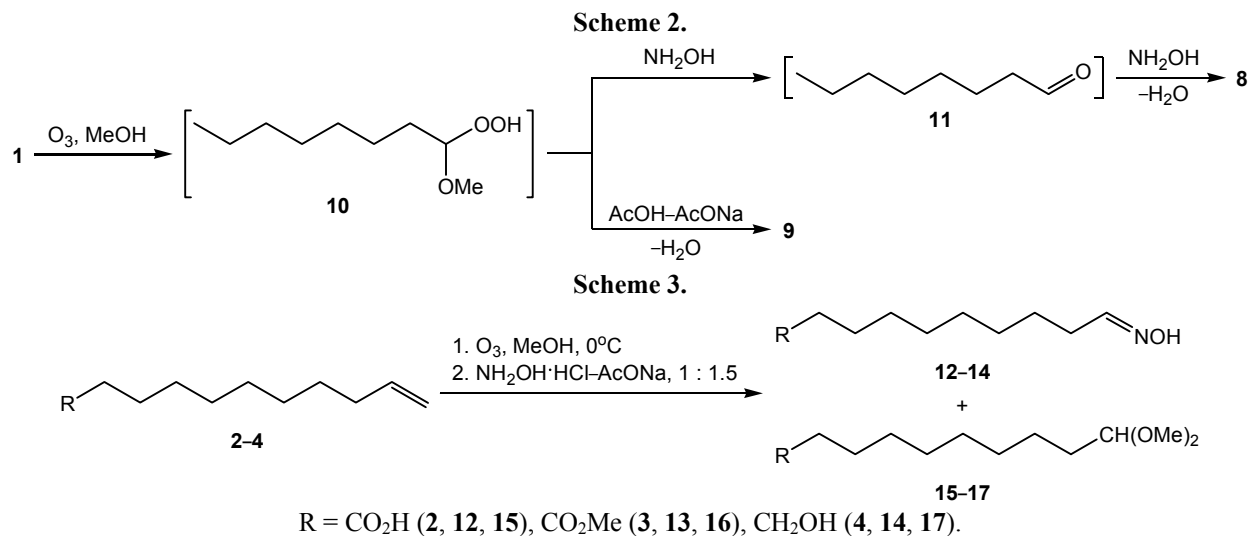
The goal of this study is the investigation of the reaction of peroxide alkene ozonolysis products with hydroxylamine proper obtained *in situ* by neutralizing the hydrogen chloride with sodium acetate. We selected as initial compound alkenes with a terminal double bond monosubstituted non-1-ene **1**, undec-10-enoic acid **2**, its methyl ester **3**, and 10-undecen-1-ol **4**, and also optically active trisubstituted alkenes: (–)- α -pinene **5**, (+)-3-carene **6**, (S)-(-)-limonene **7**.

The products of ozonation in methanol (0°C) of non-1-ene **1** when treated with molar 3.5-excess of the mixture NH₂OH·HCl–AcONa, 1 : 1.5, afforded a mixture of oxime **8** and ester **9**, 1.5 : 1 (Scheme 1).

It is known [1, 8] that zwitter-ions are stabilized in methanol owing to the formation of methoxyhydroperoxides. The formation under these conditions of oxime **8** is logically understood as the reduction of the intermediate peroxide **10** to aldehyde **11**, whose condensation with

Scheme 1.



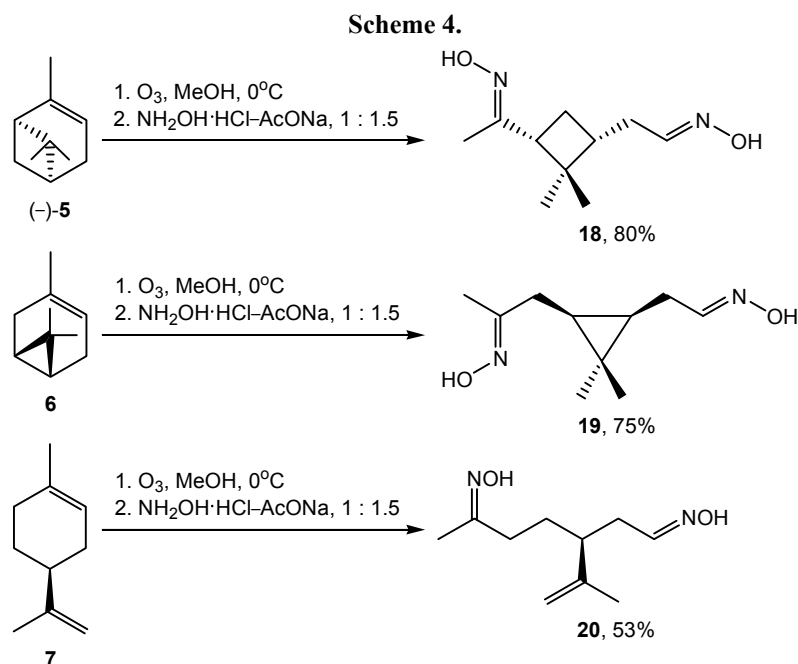


hydroxylamine provides aldoxime **8**. The formation of ester **9** may be evidently due to the sensitivity of hydroperoxide **10** to pH of the environment and its dehydration under the conditions of the acetate buffer formation (Scheme 2).

The presence of substituents in the substrate molecule somewhat changes the transformation process of the peroxide products. For instance, at treating with NH₂OH the ozonolysis products of undec-10-enoic acid **2**, its methyl ester **3**, and 10-undecen-1-ol **4** were reduced into the corresponding aldehydes which were isolated as a mixture of condensation

products: oximes **12–14** and acetals **15–17** with the prevalence of the latter (**12–15** 1 : 1.7, **13–16** 1 : 1.5, **14–17** 1 : 2) (Scheme 3).

The presence of functional groups essentially affects the structure of intermediate peroxides and consequently the structure of final reaction products. When a proton-donor is present in the alkene molecule, it takes part in zwitter-ion stabilization [9]. Apparently, the peroxides formed from alkenes **2–4** are less prone to dehydration, therefore under the reaction conditions they are reduced to aldehydes that further are transformed in oximes **12–14** and acetals **15–17**.



Formerly at the use of hydroxylamine hydrochloride for processing peroxides obtained by ozonation of (–)- α -pinene **5** and (+)-3-carene **6** in methanol we isolated in a good yield bifunctional derivatives containing an ester and a ketoxime groups [10]. At the reduction of peroxides prepared from monoterpenes **5–7** in the same conditions with hydroxylamine proper we isolated optically active dioximes **18–20** (Scheme 4).

Ald- and ketoximes are valuable intermediate products of the synthetic organic chemistry widely used in the chemical industry [11], and they are traditionally prepared by treating aldehydes and ketones with mineral salts of hydroxylamine (for instance, $\text{NH}_2\text{OH}\cdot\text{HCl}$ or $\text{NH}_2\text{OH}\cdot\text{H}_2\text{SO}_4$) [12, 13]. In this case at the treating ozonolysis products with hydroxylamine generated *in situ* from the hydrochloride a one-pot sequence is performed: alkene oxidation with ozone \rightarrow reduction to a carbonyl compound with hydroxylamine \rightarrow condensation of the carbonyl compound with hydroxylamine providing a possibility of direct transformation of alkenes in keto- and aldioximes excluding the stage of preparation and isolation of the carbonyl compound.

Thus at treating with hydroxylamine the peroxide ozonolysis products obtained from linear and cyclic alkenes the reduction prevailingly furnished aldehydes/ ketones isolated depending on the substrate as keto- and aldioximes or acetals.

EXPERIMENTAL

IR spectra were recorded on a spectrophotometer IR Prestige-21 (Fourier Transform Spectrophotometer – Shimadzu). NMR spectra were registered on a high resolution spectrometer Bruker Avance III 500 [operating frequencies 500 (^1H), 125.76 (^{13}C) MHz] in CDCl_3 , internal reference TMS. GLC was performed on a chromatograph Chrom-5 [column 1.2 m long, stationary phase SE-30 (5%) on the carrier Chromaton N-AW-DMCS (0.16–0.20 mm), working temperature 50–300°C], carrier gas helium. The optical rotation was measured on a polarimeter Perkin Elmer 241-MC. Mass spectra were taken on an instrument LCMS-2010 EV (Shimadzu) (injection sample admission, eluent acetonitrile–water, 95 : 5, flow rate 0.1 mL/min) in the mode of positive and negative ions registration at the capillary potential 4.5 and –3.5 kV. Interface (CIAP) temperature 250°C, oven temperature 200°C, vaporizer temperature 230°C. Flow rate of nebulizing gas (nitrogen)

1.5 (Electrospray ionization) and 2.5 (CIAP) L/min. Elemental analysis was carried out on a CHNS-analyzer Euro EA 3000. TLC monitoring was performed on SiO_2 Sorbfil (Russia). In column chromatography SiO_2 (70–230) Lancaster (England) was used. Ozonizer capacity was 40 mmol O_3/h .

Alkenes ozonolysis and treatment of the reaction mixture with hydroxylamine. General procedure.

Through a solution of 10.0 mmol of alkene in 25 mL of anhydrous methanol at 0°C was bubbled ozone-oxygen mixture till 10 mmol of ozone was consumed. The reaction mixture was flushed with argon. At 0°C a mixture of 2.44 g (35.0 mmol) of $\text{NH}_2\text{OH}\cdot\text{HCl}$ and 4.10 g (50 mmol) of AcONa was added to the ozonolysis products and stirring was continued till peroxides disappearance (negative iodine-starch test). The solvent was distilled off, the residue was dissolved in CHCl_3 (150 mL), washed with brine (4 \times 35 mL), dried with Na_2SO_4 , and evaporated.

Ozonolysis of non-1-ene (1). After chromatographing of 0.96 g of reaction mixture (petroleum ether–methyl *tert*-butyl ether, 10 : 1 \rightarrow 1 : 2) we obtained 0.37 g (23%) of methyl octanoate **9** [14] and 0.56 g (39%) of (1*E*)-octanal oxime **8** (mp 57–58°C) [7].

Ozonolysis of undec-10-enoic acid (2). After chromatographing of 1.91 g of reaction mixture (petroleum ether–methyl *tert*-butyl ether, 10 : 1 \rightarrow 1 : 1, MeOH) we obtained a mixture of 0.71 g (35%) of oximacid **12** and 1.2 g (58%) of acid **15**.

(10*E*)-10-(Hydroxyimino)decanoic acid (12). Oily substance, R_f 0.22 (petroleum ether–ethyl acetate, 1 : 2). Mass spectrum, m/z (I_{rel} , %): [$M + \text{H}$] $^+$ 202 (28.5). IR and NMR spectra are identical to the published data [15].

10,10-Dimethoxydecanoic acid (15). Oily substance, R_f 0.27 (petroleum ether–ethyl acetate, 1 : 2). IR spectrum (KBr), ν , cm^{-1} : 2853 (O–CH₃). ^1H NMR spectrum, δ , ppm: 1.20–1.70 m (14H, C^{3-9}H_2), 2.25–2.32 m (2H, C^2H_2), 3.45 s (6H, 2OCH₃), 3.95 t (1H, C^{10}H , J 6.6 Hz), 9.75 br.s (1H, CO₂H). ^{13}C NMR spectrum, δ , ppm: 24.58 t (C^8H_2), 24.80 t (C^7H_2), 25.70 t (C^6H_2), 26.22 t (C^5H_2), 27.45 t (C^4H_2), 29.34 t (C^3H_2), 31.24 t (C^9H_2), 34.01 t (C^2H_2), 55.84 q (2OCH₃), 108.83 d (C^{10}H), 179.70 s (CO₂H). Found, %: C 61.85; H 10.08. $\text{C}_{12}\text{H}_{24}\text{O}_4$. Calculated, %: C 62.04; H 10.41.

Ozonolysis of methyl undec-10-enoate (3). After chromatographing of 2.10 g of reaction mixture

(petroleum ether–methyl *tert*-butyl ether, 10 : 1→1 : 1, MeOH) we obtained 0.82 g (38%) of compound **13** and 1.23 g (55%) of compound **16**.

Methyl (10*E*)-10-(hydroxyimino)decanoate (13). Oily substance, R_f 0.33 (petroleum ether–ethyl acetate, 1 : 2). Mass spectrum, m/z (I_{rel} , %): $[M + H]^+$ 216 (100). IR and NMR spectra are identical to the published data [16].

Methyl 10,10-dimethoxydecanoate (16). Oily substance, R_f 0.39 (petroleum ether–ethyl acetate, 1 : 2). IR spectrum (KBr), ν , cm^{-1} : 2856 (O–CH₃), 1730 (CO₂CH₃). ¹H NMR spectrum, δ , ppm: 1.20–1.60 m (14H, C^{3–9}H₂), 2.24 t (2H, C²H₂, J 7.5 Hz), 3.61 s (6H, 2OCH₃), 3.82 s (3H, CO₂CH₃), 3.93 t (1H, C¹⁰H, J 6.5 Hz). ¹³C NMR spectrum, δ , ppm: 24.78 t (C³H₂), 27.49 t (C⁴H₂), 28.80 t (C⁵H₂), 28.90 t (C⁶H₂), 29.26 t (C⁷H₂), 29.44 t (C⁸H₂), 32.50 t (C⁹H₂), 33.80 t (C²H₂), 51.18 q (CO₂CH₃), 51.38 q (2OCH₃), 108.67 d (C¹⁰H), 174.33 s (CO₂CH₃). Found, %: C 64.01; H 10.20. C₁₃H₂₆O₄. Calculated, %: C 63.38; H 10.64.

Ozonolysis of 10-undecen-1-ol (4). After chromatographing of 1.92 g of reaction mixture (petroleum ether–methyl *tert*-butyl ether, 10 : 1→1 : 1, MeOH) we obtained 0.63 g (34%) of oxime **14** and 1.2 g (55%) of compound **17**.

(10*E*)-10-Hydroxydecanal oxime (14). Oily substance, R_f 0.17 (petroleum ether–ethyl acetate, 1 : 2). IR spectrum (KBr), ν , cm^{-1} : 1600 (C=N). ¹H NMR spectrum, δ , ppm: 1.20–1.43 m (12H, C^{3–8}H₂), 1.52–1.56 m (2H, C⁹H₂), 2.13–2.20 m (2H, C²H₂), 3.60–3.65 m (2H, C¹⁰H₂), 5.25 br.s (1H, OH), 6.65 br.s (1H, NOH), 7.35 t (1H, C¹H, J 6.2 Hz). ¹³C NMR spectrum, δ , ppm: 25.80 t (C⁸H₂), 26.46 t (C⁷H₂), 27.53 t (C⁶H₂), 28.98 t (C⁵H₂), 29.03 t (C⁴H₂), 29.21 t (C²H₂), 29.34 t (C³H₂), 31.53 t (C⁹H₂), 62.89 t (C¹⁰H₂), 152.22 d (C¹H). Mass spectrum, m/z (I_{rel} , %): $[M + H]^+$ 188 (100). Found, %: C 64.28; H 11.84; N 7.21. C₁₀H₂₁NO₂. Calculated, %: C 64.13; H 11.30; N 7.48.

10,10-Dimethoxydecan-1-ol (17). Oily substance, R_f 0.23 (petroleum ether–ethyl acetate, 1 : 2). IR spectrum (KBr), ν , cm^{-1} : 3500 (OH), 2855 (O–CH₃). ¹H NMR spectrum, δ , ppm: 1.20–1.43 m (14H, C^{2–8}H₂), 1.49–1.53 m (2H, C⁹H₂), 3.15 br.s (1H, OH), 3.43 s (6H, 2CH₃), 3.50–3.55 m (2H, C¹H₂), 4.65 t (1H, C¹⁰H, J 6.6 Hz). ¹³C NMR spectrum, δ , ppm: 25.60 t (C⁸H₂), 26.00 t (C⁷H₂), 28.89 t (C⁵H₂), 29.14 t (C⁶H₂), 29.21 t (C³H₂), 29.26 t (C⁴H₂), 32.53 t (C²H₂), 34.04 t (C⁹H₂), 55.85 q (2OCH₃), 62.84 t (C¹H₂),

108.74 d (C¹⁰H). Found, %: C 66.72; H 12.30. C₁₂H₂₆O₃. Calculated, %: C 66.01; H 12.00.

Ozonolysis of (–)- α -pinene (5). After chromatographing of 1.97 g of reaction mixture (petroleum ether–methyl *tert*-butyl ether, 10 : 1→1 : 1, MeOH) we obtained 1.58 g (80%) of oxime **18**.

(1*E*)-{(1*R*,3*R*)-3-[(1*E*)-*N*-Hydroxyethanimidoyl]-2,2-dimethylcyclobutyl}acetaldehyde oxime (18) [4]. Oily substance, R_f 0.61 (petroleum ether–ethyl acetate, 1 : 1). $[\alpha]_D^{20}$ -8° (c 1.64, CHCl₃). IR spectrum (KBr), ν , cm^{-1} : 1601 (C=N). ¹H NMR spectrum, δ , ppm: 0.89, 1.22 s (6H, 2CH₃), 1.82 s (3H, CH₃C=N), 1.90–2.04 m (2H, CH₂), 2.08 m (1H, CH), 2.13–2.25 m (2H, CH₂CH=N), 2.61 m (1H, CHC=N), 7.35 m (1H, CH₂CH=N), 8.70–9.30 br.s (2H, 2NOH). ¹³C NMR spectrum, δ , ppm: 14.50 q (CH₃C=N), 17.02 q (CH₃C), 24.60 t (CHCH₂CH), 30.27 t (CH₂CH=N), 30.39 q (CH₃C), 39.67 s (C), 42.81 d (CH), 47.97 d (CHC=N), 151.33 d (CH=N), 157.98 s (C=N). Mass spectrum, m/z (I_{rel} , %): $[M + H]^+$ 199 (100). Found, %: C 60.12; H 9.13; N 14.25. C₁₀H₁₈N₂O₂. Calculated, %: C 60.58; H 9.15; N 14.13.

Ozonolysis of (+)-3-carene (6). After chromatographing of 1.57 g of reaction mixture (petroleum ether–methyl *tert*-butyl ether, 10 : 1→1 : 1, MeOH) we obtained 1.49 g (75 %) of oxime **19**.

(1*E*)-{(1*R*,3*S*)-3-[(2*E*)-2-(Hydroxyimino)propyl]-2,2-dimethylcyclopropyl}acetaldehyde oxime (19) [6]. Oily substance, R_f 0.44 (petroleum ether–ethyl acetate, 1 : 1). $[\alpha]_D^{20}$ -20° (c 0.08, CHCl₃). IR spectrum (KBr), ν , cm^{-1} : 1598 (C=N). ¹H NMR spectrum, δ , ppm: 0.76–0.94 m (2H, 2CH), 0.94, 0.99 s (6H, 2CH₃C), 1.94 s (3H, CH₃C=N), 2.13–2.25 m (8H, 4CH₂), 7.43 t (1H, CH₂CH=N). ¹³C NMR spectrum, δ , ppm: 13.64 q (CH₃C=N), 14.82 q (CH₃C), 14.94 q (CH₃C), 17.22 s (C), 21.12 d (CHCH₂C), 22.76 d (CHCH₂CH), 25.29 t (CH₂CH=N), 30.74 t (CH₂C=N), 151.16 d (CH=N), 158.46 s (C=N). Mass spectrum, m/z (I_{rel} , %): $[M + H]^+$ 199 (91). Found, %: C 60.39; H 9.38; N 14.19. C₁₀H₁₈N₂O₂. Calculated, %: C 60.58; H 9.15; N 14.13.

(1*E*,3*S*)-3-[(3*Z*)-3-(Hydroxyimino)butyl]-4-methylpent-4-enal oxime (20). Through a solution of 1.1 g (8.09 mmol) of (*S*)-(–)-limonene **7** in a mixture of 20 mL of cyclohexane and 0.6 mL of anhydrous methanol at 2°C was bubbled ozone-oxygen mixture till 7.4 mmol of ozone was consumed. The reaction mixture was flushed with argon. The cyclohexane

layer was decanted. At 0°C 20 mL of anhydrous methanol and a mixture of 1.79 g (25.72 mmol) of $\text{NH}_2\text{OH}\cdot\text{HCl}$ and 3.01 g (36.75 mmol) of AcONa was added, the reaction mixture was stirred at room temperature till peroxides disappearance (negative iodine-starch test). The solvent was distilled off, the residue was dissolved in CHCl_3 (150 mL), washed with brine (4×35 mL), dried with Na_2SO_4 , and evaporated. After chromatographing of 1.21 g of reaction mixture (petroleum ether–methyl *tert*-butyl ether, 10 : 1→1 : 1, MeOH) yield 0.77 g (53%). Oily substance, R_f 0.51 (petroleum ether–ethyl acetate, 1 : 1). IR spectrum (KBr), ν , cm^{-1} : 1610 (C=N). ^1H NMR spectrum, δ , ppm: 1.13–1.30 m (2H, CH_2), 1.65 s (3H, CH_3), 1.82 s (3H, CH_3), 2.00–2.18 m (4H, 2CH_2), 2.20–2.30 m (1H, CH), 4.60–4.90 m (2H, $\text{CH}_2=\text{C}$), 6.25–6.30 m (1H, $\text{CH}=\text{NOH}$), 8.20–8.90 br.s (2H, 2NOH). ^{13}C NMR spectrum, δ , ppm: 13.68 q ($\text{CH}_3\text{C}=\text{N}$), 18.20 q (CH_3CCH_2), 28.41 t (CH_2CHC), 33.00 t ($\text{CH}_2\text{CH}=\text{N}$), 33.41 t ($\text{CH}_2\text{C}=\text{N}$), 43.94 d (CH_3CCH), 113.20 t (C= CH_2), 145.26 s (C= CH_2), 150.62 d (CH=N), 158.59 s (C=N). Mass spectrum, m/z (I_{rel} , %): $[M + \text{H}]^+$ 199 (55.4). Found, %: C 60.20; H 8.98; N 14.21. $\text{C}_{10}\text{H}_{18}\text{N}_2\text{O}_2$. Calculated, %: C 60.58; H 9.15; N 14.13.

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