ISSN 1070-4280, Russian Journal of Organic Chemistry, 2013, Vol. 49, No. 10, pp. 1415–1419. © Pleiades Publishing, Ltd., 2013.
Original Russian Text © G.Yu. Ishmuratov, Yu.V. Legostaeva, L.R. Garifullina, L.P. Botsman, R.R. Muslukhov, G.A. Tolstikov, 2013, published in Zhurnal Organicheskoi Khimii, 2013, Vol. 49, No. 10, pp. 1439–1442.

Transformations of Peroxide Olefin Ozonolysis Products in Methanol in the Presence of Water

G. Yu. Ishmuratov[a], **Yu. V. Legostaeva**[a], **L. R. Garifullina**[a], **L. P. Botsman**[a],
R. R. Muslukhov[a], and **G. A. Tolstikov**[†b]

[a] *Institute of Organic Chemistry, Ufa Research Center, Russian Academy of Sciences,*
pr. Oktyabrya 71, Ufa, 450054 Bashkortostan, Russia
e-mail: insect@anrb.ru

[b] *Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch, Russian Academy of Sciences,*
pr. Akademika Lavrent'eva 9, Novosibirsk, 630090 Russia

Received May 15, 2013

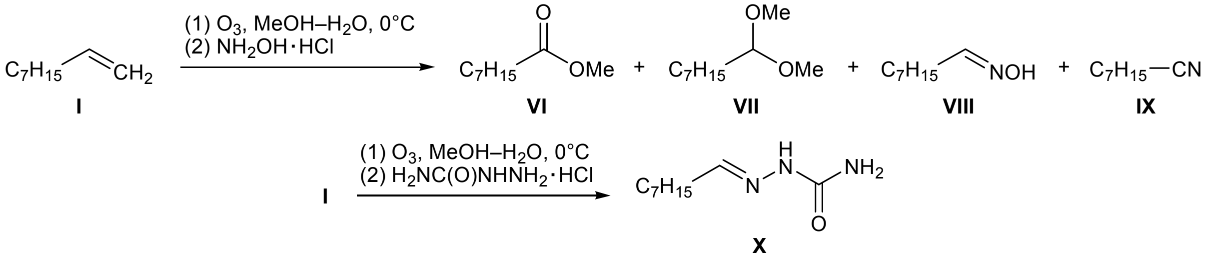
Abstract—Transformations of peroxide products of ozonolysis of various olefins with different degrees of substitution at the double bond by the action of hydroxylamine and semicarbazide hydrochloride in methanol in the presence of water as co-solvent were studied.

DOI: 10.1134/S1070428013100023

We previously showed [1–4] that hydroxylamine and semicarbazide hydrochlorides are the most efficient nitrogen-containing organic reducing agents toward peroxide products of olefin ozonolysis in methyl or isopropyl alcohol; as a result, the corresponding carbonyl compounds and their derivatives are formed. The structure of peroxide ozonolysis products and products of their further transformation is determined by the conditions of ozonolysis, primarily by the solvent nature [1]. We found [4] that ozonolysis of olefins in the system isopropyl alcohol–water, followed by treatment of peroxide products with semicarbazide or hydroxylamine hydrochloride, gives mainly mixtures of isopropyl esters and carboxylic acids whose ratio depends on the substrate structure and is likely to be established at the stage of formation of isopropoxy or hydroxy hydroperoxides. In continuation of studies in this line, in the present work we examined transformations of peroxide products of ozonolysis of olefins with different degrees of substitution at the double bond by the action of the same reagents in methanol containing water as co-solvent. As substrates we used non-1-ene (**I**), cyclooctene (**II**), 1,5-dimethylcycloocta-1,5-diene (**III**), Δ^3-carene (**IV**, *ee* 100%), and (–)-α-pinene (**V**, *ee* 86%).

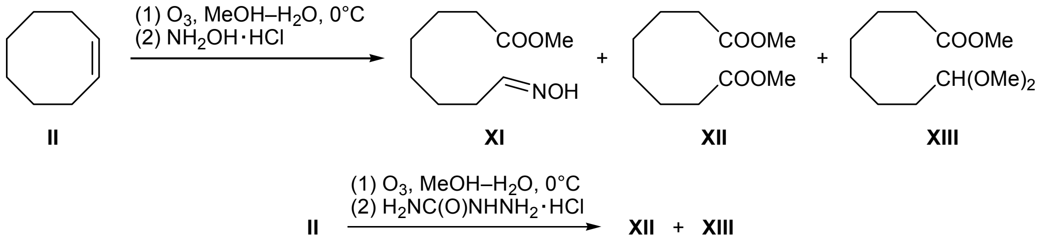
Ozonolysis of non-1-ene (**I**) in methanol–water at 0°C, followed by treatment with hydroxylamine hydrochloride, gave a mixture of products, the major of which being methyl octanoate **VI**. From the reaction mixture we also isolated small amounts of dimethyl acetal **VII**, octanal oxime **VIII** and octanenitrile (**IX**). Under analogous conditions, ozonolysis of **I** and subsequent treatment with semicarbazide hydrochloride resulted in the formation of octanal semicarbazone (**X**)

Scheme 1.

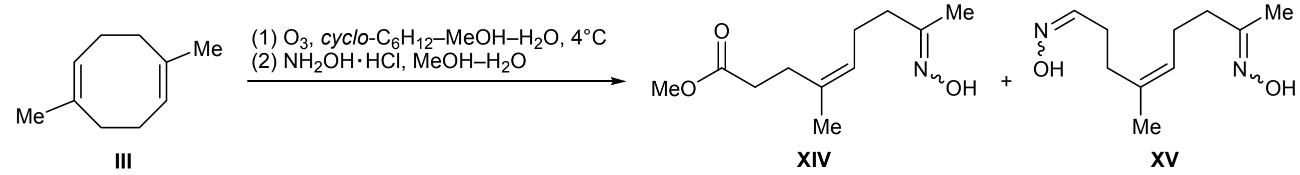


[†] Deceased.

Scheme 2.



Scheme 3.



(Scheme 1). The reduction with hydroxylamine hydrochloride of peroxide ozonolysis products derived from cyclooctene (**II**) afforded methyl 8-hydroxyiminooctanoate (**XI**), dimethyl octanedioate (**XII**), and methyl 8,8-dimethoxyoctanoate (**XIII**). Compounds **XII** and **XIII** were obtained when peroxide products of ozonolysis of cyclooctene (**II**) in MeOH–H_2O were treated with semicarbazide hydrochloride (Scheme 2).

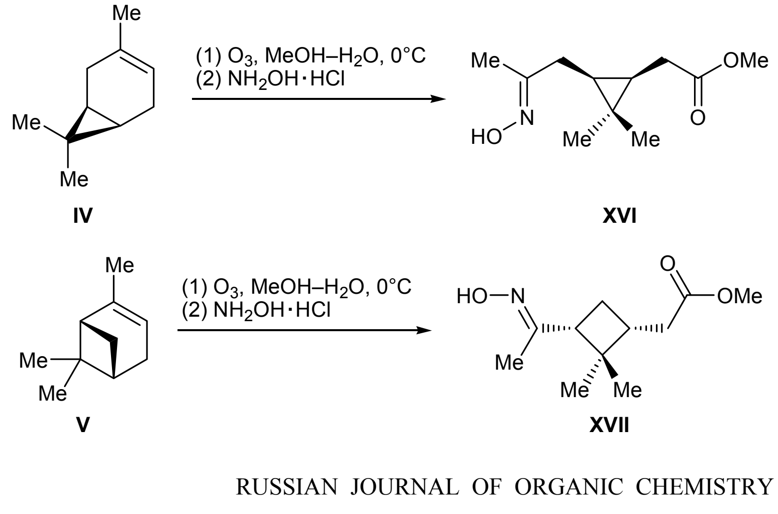
The ozonolysis of 1,5-dimethylcycloocta-1,5-diene (**III**) was carried out in a mixture of cyclohexane with methanol, and the subsequent treatment of peroxide products with hydroxylamine hydrochloride in MeOH–H_2O led to a mixture of *syn*/*anti*-oxime **XIV** (1 : 1) and *syn*/*anti*-dioxime **XV** (1 : 1) which were isolated by column chromatography (Scheme 3). When the peroxide ozonolysis products derived from **III** were treated with semicarbazide hydrochloride, an intractable mixture of unidentifiable compounds was obtained.

As shown in [4], the reduction of peroxide ozonolysis products obtained from Δ^3-carene (**IV**) and α-pinene (**V**) in methanol with hydroxylamine hydrochloride gives in high yield the corresponding hydroxyimino esters with *trans* configuration of the oxime C=N bond. When the ozonolysis of **IV** and **V** was carried out in methanol in the presence of water, the products were the same hydroxyimino esters **XVI** and **XVII**, but their yields were lower (Scheme 4).

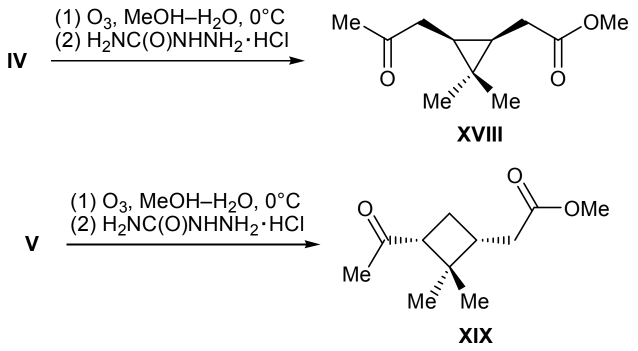
The transformation of peroxide products of ozonolysis monoterpenes **IV** and **V** in methanol by the action semicarbazide hydrochloride afforded the corresponding keto esters **XVIII** and **XIX** [4]. The same compounds were obtained, though in lower yields, using the system methanol–water, other conditions being equal (Scheme 5).

Thus the results of the present study showed that hydroxylamine and semicarbazide hydrochlorides effectively reduce peroxide products of olefin ozonolysis

Scheme 4.



Scheme 5.



in aqueous methanol to the corresponding carbonyl compounds and their derivatives. Under these conditions, the peroxide ozonolysis products are likely to be methoxy hydroperoxides, whereas no hydroxy hydroperoxides are formed. This follows from the predominant formation of methyl esters after treatment with semicarbazide or hydroxylamine hydrochloride. Lower yields of the final products as compared to the reactions in methanol should be noted.

EXPERIMENTAL

The IR spectra were recorded on a Shimadzu IR Prestige-21 instrument. The ^{1}H and ^{13}C NMR spectra were measured on a Bruker AM-300 spectrometer at 300 and 75 MHz, respectively, using $CDCl_3$ as solvent and tetramethylsilane as internal reference. Signals in the ^{1}H NMR spectra were assigned, and spin–spin coupling constants were determined, with the aid of double resonance and two-dimensional homonuclear shift correlation techniques (COSY H–H). The ^{13}C NMR spectra were recorded with broad-band decoupling from protons and J modulation (JMOD). GLC analysis was performed using Chrom-5 [1.2-m column packed with SE-30 (5%) on Chromaton N-AW-DMCS (0.16–0.20 mm); oven temperature 50–300°C] and Chrom-41 instruments (2.4-m column packed with PEG-6000; oven temperature 50–200°C); carrier gas helium. Sorbfil silica gel (Russia) was used for TLC analyses (hexane–*tert*-butyl methyl ether, 2:1). Column chromatography was performed on silica gel (70–230 μm; Lancaster, England) using the same solvent system as eluent. The optical rotations were measured on a Perkin Elmer 241-MC polarimeter. The elemental compositions of all isolated compounds were consistent with the calculated values. The ozonizer efficiency was 40 mmol of ozone per hour.

Treatment of peroxide ozonolysis products of olefins I, II, IV, and V with hydroxylamine hydrochloride (*general procedure*). An ozone–oxygen mixture (1 mol of O_3 per mole of double bond) was bubbled at 0°C through a solution of 10.0 mmol of olefin **I**, **II**, **IV**, or **V** in a mixture of 30 ml of distilled methanol and 1.66 ml of water. The mixture was purged with argon, 2.4 g (35.0 mmol) of hydroxylamine hydrochloride was added under stirring at 0°C, and the mixture was stirred at room temperature until peroxide compounds disappeared according to iodine–starch test. The solvent was distilled off, the residue was dissolved in 50 ml of chloroform, and the solution was washed with brine (4×25 ml), dried over Na_2SO_4, and evaporated.

Ozonolysis of non-1-ene (I). The residue, 1.32 g, was subjected to chromatography to isolate 0.95 g (60%) of ester **VI** (R_f 0.59), 0.10 g (6%) of 1,1-dimethoxyoctane (**VII**, R_f 0.67), 0.06 g (4%) of oxime **VIII** (R_f 0.53), and 0.04 g (3%) of nitrile **IX**. The IR and NMR spectra of **VI**–**VIII** were identical to those reported in [3, 5].

Octanenitrile (IX). R_f 0.26. IR spectrum (KBr): ν 2245 cm^{-1} (CN). ^{1}H NMR spectrum, δ, ppm: 0.88 t (3H, CH_3, J = 6.7 Hz), 1.18–1.38 m (6H, 4-H, 5-H, 6-H), 1.40–1.50 m (2H, 7-H), 1.54–1.62 m (2H, 3-H), 2.25 t (2H, 2-H, J = 7.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 13.89 q (C^8), 16.94 t (C^2), 22.46 t (C^7), 24.91 t (C^3), 28.86 t (C^5), 29.22 t (C^4), 31.58 t (C^6), 119.68 s (CN).

Ozonolysis of cyclooctene (II). The residue, 1.12 g, was subjected to chromatography to isolate 0.56 g (30%) of hydroxyimino ester **XI**, 0.32 g (15%) of diester **XII**, and 0.15 g (7%) of methyl 8,8-dimethoxyoctanoate (**XIII**).

Methyl (8*Z*)-8-(hydroxyimino)octanoate (XI). R_f 0.41. IR spectrum (KBr), ν, cm^{-1}: 3260 (NOH), 1735 (C=O), 1662 (C=N). ^{1}H NMR spectrum, δ, ppm: 1.22–1.44 m (8H, 3-H, 4-H, 5-H, 6-H), 1.52–1.70 m (2H, 2-H), 2.19 m (2H, 7-H), 3.65 s (3H, OCH_3), 7.40 t

(1H, 8-H), 9.75 s (OH). ^{13}C NMR spectrum, δ_C, ppm: 24.70 t (C^3), 26.31 t (C^6), 28.20 t (C^5), 28.71 t (C^4), 28.95 t (C^7), 33.97 t (C^2), 51.50 q (OCH_3), 151.97 d (C^8), 174.25 s (C=O).

Dimethyl octanedioate (XII). R_f 0.42. The IR and NMR spectra of diester **XII** were identical to those given in [2].

Methyl 8,8-dimethoxyoctanoate (XIII). R_f 0.52. IR spectrum (KBr), ν, cm^{-1}: 1735 (C=O), 1080 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 1.22–1.44 m (8H, 3-H, 4-H, 5-H, 6-H), 1.52–1.70 m (2H, 7-H), 2.25 m (2H, CH_2COOCH_3), 3.30 s (6H, 8-OCH_3), 3.65 s (3H, OCH_3), 4.24 t (1H, 8-H). ^{13}C NMR spectrum, δ_C, ppm: 24.70 t (C^3, C^6), 28.73 t (C^4), 29.06 t (C^5), 32.40 t (C^7), 33.96 t (C^2), 51.49 q ($COO\mathbf{C}H_3$), 52.60 q (8-OCH_3), 104.46 d (C^8), 174.20 s (C=O).

Ozonolysis of 3-carene (IV). The residue, 1.50 g, was subjected to chromatography to isolate 1.36 g (64%) of methyl {(1*R*,3*S*)-3-[(2*E*)-2-(hydroxyimino)-propyl]-2,2-dimethylcyclopropyl}acetate (**XVI**), R_f 0.29, $[\alpha]_D^{23}$ = –5° (*c* = 0.23, CH_2Cl_2). The IR and NMR spectra of compound **XVI** were identical to those given in [4].

Ozonolysis of α-pinene (V). The residue, 1.45 g, was subjected to chromatography to isolate 1.34 g (63%) of methyl {(1*R*,3*R*)-3-[(1*E*)-hydroxyimino-ethyl]-2,2-dimethylcyclobutyl}acetate (**XVII**), R_f 0.33, $[\alpha]_D^{23}$ = –3.7° (*c* = 0.93, CH_2Cl_2). The IR and NMR spectra of **XVII** were identical to those given in [4].

Ozonolysis of 1,5-dimethylcycloocta-1,5-diene (III). An ozone–oxygen mixture was bubbled at 4°C through a solution of 1.50 g (11.0 mmol) of compound **III** in a mixture of 13.5 ml of cyclohexane and 0.8 ml of anhydrous methanol until 10.0 mmol of ozone was absorbed. The mixture was purged with argon, a solution of 2.41 g (35 mmol) of hydroxylamine hydrochloride in a mixture of 45.3 ml of methanol and 20 ml of water was added at 0°C, and the mixture was stirred at room temperature until peroxide compounds disappeared according to iodine–starch test. The mixture was evaporated, the residue was dissolved in 50 ml of chloroform, the solution was washed with water (4× 25 ml), dried over Na_2SO_4, and evaporated, and the residue, 2.10 g, was subjected to chromatography to isolate 1.49 g (70%) of hydroxyimino ester **XIV** and 0.50 g (25%) of dioxime **XV**.

Methyl (4*Z*,8*Z*)-8-hydroxyimino-4-methylnon-4-enoate (XIV). R_f 0.66. IR spectrum (KBr), ν, cm^{-1}: 3260 (NOH), 1735 (C=O), 1662 (C=N). ^{1}H NMR spectrum, δ, ppm: 1.66 s (3H, 4-CH_3), 1.78 s (3H, C^9H_3), 1.90–2.20 m (6H, 2-H, 3-H, 6-H), 2.20–2.35 m (2H, 7-H), 3.50 s (3H, OCH_3), 5.03 t (1H, 5-H, ^3J = 6.9 Hz), 8.00 br.s (1H, OH). ^{13}C NMR spectrum, δ_C, ppm: 13.35 q (C^9), 23.06 q (4-CH_3), 24.40 t (C^6), 32.24 t (C^3), 35.68 t (C^2), 43.53 t (C^7), 51.58 q (OCH_3), 124.63 d (C^5), 134.36 s (C^4), 157.85 s (C^8), 173.67 s (C=O).

(1*Z*,4*Z*,8*Z*)-8-Hydroxyimino-4-methylnon-4-enal oxime (XV). R_f 0.56. IR spectrum (KBr), ν, cm^{-1}: 3260 (NOH), 1662 (C=N). ^{1}H NMR spectrum, δ, ppm: 1.65 s (3H, 4-CH_3), 1.77 s (3H, C^9H_3), 2.10–2.21 m (4H, 3-H, 6-H), 2.27–2.33 m (2H, 2-H), 2.35–2.40 m (2H, 7-H), 5.09 t (1H, 5-H, ^3J = 6.7 Hz), 7.30 t (1H, 1-H, ^3J = 5.0 Hz), 8.20 br.s (2H, NOH). ^{13}C NMR spectrum, δ_C, ppm: 13.74 q (C^9), 22.69 q (4-CH_3), 24.72 t (C^6), 32.66 t (C^3), 35.72 t (C^2), 43.75 t (C^7), 124.60 d (C^5), 134.43 s (C^4), 151.35 d (C^1), 158.20 s (C^8).

Treatment of peroxide ozonolysis products of olefins I, II, IV, and V with semicarbazide hydrochloride (*general procedure*). An ozone–oxygen mixture (1 mol of O_3 per mole of double bond) was passed at 0°C through a solution of 10.0 mmol of olefin **I**, **II**, **IV**, or **V** in a mixture of 30 ml of distilled methanol and 1.66 ml of water. The mixture was purged with argon, 3.90 g (35.0 mmol) of semicarbazide hydrochloride was added at 0°C under stirring, and the mixture was stirred at room temperature until peroxide compounds disappeared according to iodine–starch test. The solvent was distilled off, the residue was dissolved in 50 ml of chloroform, and the solution was washed with brine (4×25 ml), dried over Na_2SO_4, and evaporated.

Ozonolysis of non-1-ene (I). The residue, 0.94 g, was subjected to chromatography to isolate 0.85 g (45%) of octanal semicarbazone (**X**), R_f 0.11, mp 99–100°C [6]. The IR and NMR spectra of **X** were identical to those given in [7].

Ozonolysis of cyclooctene (II). The residue, 1.20 g, was subjected to chromatography to isolate 1.00 g (50%) of dimethyl octanedioate (**XII**) and 0.10 g (5%) of methyl 8,8-dimethoxyoctanoate (**XIII**) whose IR and NMR spectra were identical to those given above.

Ozonolysis of 3-carene (IV). The residue, 1.47 g, was subjected to chromatography to isolate 1.29 g (65%) of methyl [(1*R*,3*S*)-2,2-dimethyl-3-(2-oxo-propyl)cyclopropyl]acetate (**XVIII**), R_f 0.36, $[\alpha]_D^{20}$ =

–21° ($c = 0.009$, CH_2Cl_2). The IR and NMR spectra of **XVIII** were identical to those given in [4].

Ozonolysis of α-pinene (V). The residue, 1.53 g, was subjected to chromatography to isolate 1.37 g (69%) of methyl [(1*R*,3*R*)-3-acetyl-2,2-dimethylcyclobutyl]acetate (**XIX**), R_f 0.44, $[\alpha]_D^{23} = -24.8°$ ($c = 0.73$, CH_2Cl_2). The IR and NMR spectra of **XIX** were identical to those given in [4].

REFERENCES

1. Ishmuratov, G.Yu., Legostaeva, Yu.V., Botsman, L.P., and Tolstikov, G.A., *Russ. J. Org. Chem.*, 2010, vol. 46, p. 1593.
2. Ishmuratov, G.Yu., Shayakhmetova, A.Kh., Yakovleva, M.P., Legostaeva, Yu.V., Shitikova, O.V., Galkin, E.G., and Tolstikov, G.A., *Russ. J. Org. Chem.*, 2007, vol. 43, p. 1114.
3. Ishmuratov, G.Yu., Legostaeva, Yu.V., Botsman, L.P., Muslukhov, R.R., Yakovleva, M.P., and Talipov, R.F., *Vestn. Bash. Gos. Univ.*, 2009, no. 1, p. 27.
4. Ishmuratov, G.Yu., Legostaeva, Yu.V., Botsman, L.P., Yakovleva, M.P., Shakhanova, O.O., Muslukhov, R.R., and Tolstikov, G.A., *Khim. Prirodn. Soedin.*, 2009, no. 3, p. 272.
5. Ishmuratov, G.Yu., Legostaeva, Yu.V., Garifullina, L.R., Botsman, L.P., Idrisova, Z.I., Muslukhov, R.R., Ishmuratova, N.M., and Tolstikov, G.A., *Russ. J. Org. Chem.*, 2013, vol. 49, p. 1409.
6. Tietze, L.-F. and Eicher, T., *Reactions and Syntheses in the Organic Chemistry Laboratory*, Weinheim: Wiley–VCH, 2007, 2nd ed.
7. Ishmuratov, G.Yu., Legostaeva, Yu.V., Botsman, L.P., Nasibullina, G.V., Garifullina, L.R., Muslukhov, R.R., and Tolstikov, G.A., *Russ. J. Org. Chem.*, 2012, vol. 48, p. 1272.