Synthesis of 1-hydroperoxy-1′-alkoxyperoxides by the iodine-catalyzed reactions of geminal bishydroperoxides with acetals or enol ethers†

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Received 9th June 2008, Accepted 1st September 2008
First published as an Advance Article on the web 20th October 2008
DOI: 10.1039/b809661a

It was found that iodine-catalyzed reactions of geminal bishydroperoxides with acetals proceed with the replacement of only one alkoxy group by the peroxide group to give previously unknown structures of 1-hydroperoxy-1′-alkoxyperoxides in yields up to 64%. The same compounds are formed in the iodine-catalyzed reactions of geminal bishydroperoxides with enol ethers. The nature of the solvent has a decisive influence on the formation of 1-hydroperoxy-1′-alkoxyperoxides. In the series of Et_2O, THF, EtOH, $CHCl_3$, CH_3CN, and hexane, the best results were obtained with the use of Et_2O or THF as the solvent.

Introduction

In the last decade, organic peroxides have attracted great attention of chemists and researchers engaged in drug design due to their high antimalarial[1–3] and antitumor[4] activities. Tetraoxanes, ozonides, and trioxanes having activity[5] comparable to or higher than the activity of artemisinin, which is the natural peroxide used for the treatment of malaria, have been synthesized.

Organic peroxides hold a leading position as radical polymerization initiators in the industrial synthesis of such polymer materials as polyacrylates, polystyrene, styrene-containing resins, and high-pressure polyethylene and have found use as cross-linking reagents.

Geminal bishydroperoxides belong to a relatively new and important class of organic peroxides. In the last two decades, there has been considerable progress in the development of methods for the preparation and the use of these compounds.[6–8] Geminal bishydroperoxides containing six or more carbon atoms are the key compounds in the synthesis of a wide range of cyclic peroxides[1–5] having antimalarial and antitumor activities and can be used as oxidants[9] or radical polymerization initiators.[10] The easily accessible (unlike its high-molecular-weight analogs) geminal bishydroperoxide methyl ethyl ketone peroxide (MEKPO) is widely used in the manufacturing process of acrylic resins, as a hardening agent for fiberglass reinforced plastics, and as a curing agent for unsaturated polyester resins.[11]

In the present study, we report a new transformation of geminal bishydroperoxides, to be more precise, the iodine-catalyzed reaction with acetals and enol ethers giving rise to previously unknown structures of 1-hydroperoxy-1′-alkoxyperoxides. The distinguishing feature of this reaction is that only one alkoxy group of acetals is replaced by the peroxide group under the conditions used. This result is unexpected and differs from the results obtained in our earlier studies, where the boron trifluoride-catalyzed reaction of gem-bishydroperoxides and related 1,1′-dihydroperoxyperoxides with acetals in diethyl ether has been demonstrated to proceed with the replacement of both alkoxy groups accompanied by the formation of cyclic products, such as tetraoxanes[12] and hexaoxonanes[13] (Scheme 1).

An idea of combining iodine with hydroperoxides or hydrogen peroxide proved to be successful. In recent years, this idea has been advantageously realized in the synthesis of peroxides from carbonyl compounds[8] and alkenes.[14] The I_2-H_2O_2 system reveals versatile reactivities. Thus, depending on the reaction conditions, hydrogen peroxide involved in this system can act not only as the reagent for the formation of the C–O–O fragment but also as an activator for iodine in iodoalkoxylation of alkenes[15] and iodination of arenes,[16] ketones,[17] and alkynes.[18] This system was also used for the Baeyer–Villiger oxidation of ketones to lactones.[19]

The transformation of bishydroperoxides, acetals, and enol ethers discovered in the present study is a new step in the development of methods for the synthesis of compounds containing the monoperoxyacetal fragment, which is of importance for the antimalarial activity of artemisinin and ozonides. 1-Hydroperoxy-1′-alkoxyperoxides are of interest as intermediates in the synthesis of structurally more complex peroxides because they contain the following two active centers, whose reactivity is well known: the nucleophilic bishydroperoxide center (containing the free hydroperoxide group)[3,20] and the "latent" electrophilic monoperoxyacetal center.[21] In addition, it is known that compounds containing the monoperoxyketal fragment are convenient radical reaction initiators.[22]

Results and discussion

Peroxides **3c-f**, **4a-e**, **5a-c**, and **6a**,**d** were synthesized at 20–25 °C by the addition of iodine as the reaction catalyst to a solution of geminal bishydroperoxide **1a-d** and acetal **2a-f**. The reaction mixture was kept for 24 h (Scheme 2).

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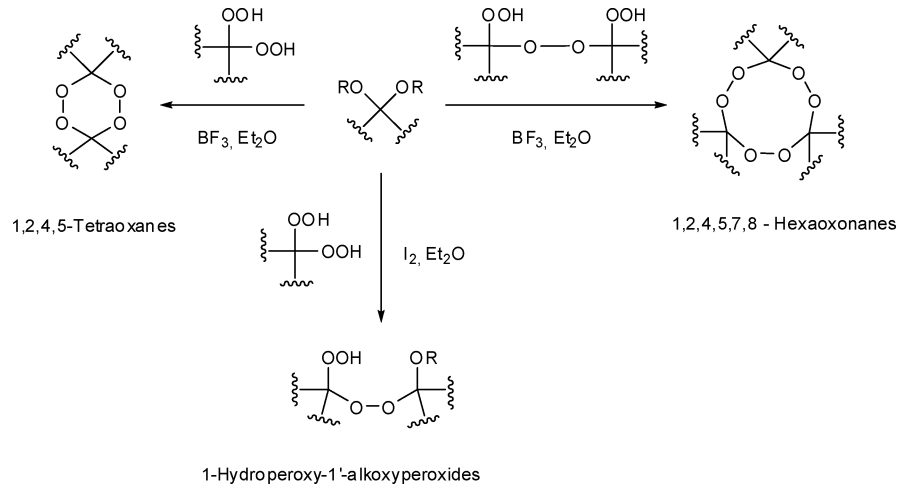
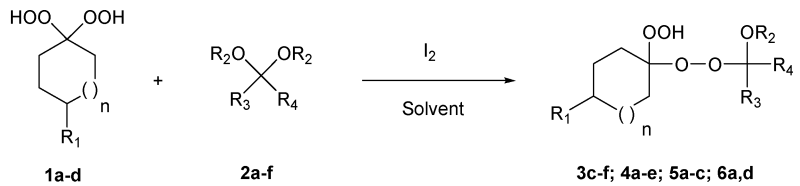
† Electronic supplementary information (ESI) available: ^1H and ^{13}C NMR spectra for peroxides **3c-f**, **4a-e**, **5a-c**, **6a,d**. CCDC reference number 689447]. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b809661a



Scheme 1 Boron trifluoride- and iodine-catalyzed reactions of acetals with bis- and dihydroperoxides.



1a-d **2a-f** **3c-f; 4a-e; 5a-c; 6a,d**

1a: n = 1, R_1 = H
1b: n = 1, R_1 = Me
1c: n = 2, R_1 = H
1d: n = 7, R_1 = H

2a: R_3 = Me; R_4 = Me ; R_2 = Me
2b: R_3 = Me; R_4 = C_7H_{15} ; R_2 = Me
2c: R_3, R_4 = -$(CH_2)_4$- ; R_2 = Et
2d: R_3, R_4 = -$(CH_2)_5$- ; R_2 = Me
2e: R_3, R_4 = -$(CH_2)_6$- ; R_2 = Me
2f: R_3, R_4 = -$(CH_2)_6$- ; R_2 = Et

3c: n = 1, R_1 = H; R_3, R_4 = -$(CH_2)_4$- ; R_2 = Et
3d: n = 1, R_1 = H; R_3, R_4 = -$(CH_2)_5$- ; R_2 = Me
3e: n = 1, R_1 = H; R_3, R_4 = -$(CH_2)_6$- ; R_2 = Me
3f: n = 1, R_1 = H; R_3, R_4 = -$(CH_2)_6$- ; R_2 = Et
4a: n = 1, R_1 = Me; R_3 = Me; R_4 = Me ; R_2 = Me
4b: n = 1, R_1 = Me; R_3 = Me; R_4 = C_7H_{15} ; R_2 = Me
4c: n = 1, R_1 = Me; R_3, R_4 = -$(CH_2)_4$- ; R_2 = Et
4d: n = 1, R_1 = Me; R_3, R_4 = -$(CH_2)_5$- ; R_2 = Me
4e: n = 1, R_1 = Me; R_3, R_4 = -$(CH_2)_6$- ; R_2 = Me
5a: n = 2, R_1 = H; R_3 = Me; R_4 = Me ; R_2 = Me
5b: n = 2, R_1 = H; R_3 = Me; R_4 = C_7H_{15} ; R_2 = Me
5c: n = 2, R_1 = H; R_3, R_4 = -$(CH_2)_4$- ; R_2 = Et
6a: n = 7, R_1 = H; R_3 = Me; R_4 = Me ; R_2 = Me
6d: n = 7, R_1 = H; R_3, R_4 = -$(CH_2)_5$- ; R_2 = Me

Scheme 2 Synthesis of peroxides **3–6** by the iodine-catalyzed reaction of geminal bishydroperoxides **1** with acetals **2**. Using the synthesis of peroxide **4e** as an example, the optimal conditions of this reaction, such as the ratio of **1b**, **2e**, and iodine, the reaction time, and the nature of the solvent, were found (Table 1).

As can be seen from Table 1, the nature of the solvent has a decisive influence on the condensation of bishydroperoxide **1b** with acetal **2e**. The best results were obtained with the use of diethyl ether as the solvent (runs 7–13). The reactions in tetrahydrofuran (runs 5 and 6) are somewhat less efficient. In chloroform, hexane, acetonitrile, and methanol (runs 1–4), the yields of the target peroxide are 2–5 times lower (10–34%) than those achieved in diethyl ether (60%). The reaction time is an important factor. For example, the reaction is completed in 24 h at 20 °C; after 1 h the conversion of the reagents is *ca.* 25%. An increase in the time of storage of the reaction mixture to 48 h has virtually no effect on the results.

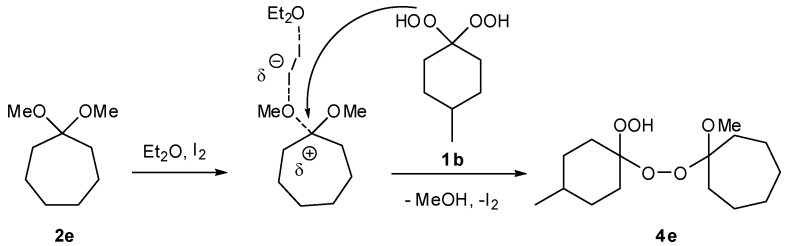
The optimal iodine-to-acetal **2e** ratio is evidently close to 0.4. A decrease (runs 7–9) or an increase (runs 14 and 15) in this ratio has a negative effect on the yield of peroxide **4e**.

An attempt to prepare peroxide **4e** directly from cycloheptanone and, by this means, to eliminate the additional step involving the synthesis of 1,1-dimethoxycycloheptane **2e** failed. The reaction of bishydroperoxide **1b** with cycloheptanone in MeOH (run 16) and in a MeOH-Et_2O mixture (run 17) affords peroxide **4e** in low yield (6–8%). Hence, this procedure is unsuitable for the preparative synthesis because it produces the target peroxide **4e** in low yield.

Diethyl ether not only serves as the solvent but, judging from the results, is also involved in the chemical reaction acting as an activator for iodine. Other tested solvents exhibit this property to a lesser extent (tetrahydrofuran), if at all.

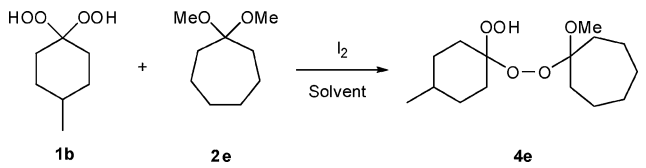
The reaction giving rise to peroxide **4e** proceeds through the iodine-catalyzed replacement of the methoxy group in acetal (Scheme 3).

Initially, iodine, which exists apparently as a complex with diethyl ether (or tetrahydrofuran)[23] where it behaves as a Lewis acid, reacts with the methoxyl group of acetal **2e**. Then geminal bishydroperoxide attacks the electrophilic center that is formed at the quaternary carbon atom. Finally, methanol is eliminated to give the target peroxide **4e**. The reaction stops with the monosubstitution stage presumably as the result of steric strain arising from 1,2,4,5-tetraoxane (disubstitution product) forming.



Scheme 3 Iodine-catalyzed reaction of acetal **2e** with bishydroperoxide **1b** in diethyl ether.

Table 1 Influence of the molar ratio of the reagents, the reaction time, and the nature of the solvent on the yield of **4e**[a]



1b **2e** **4e**

Run	Solvent	Molar ratio I_2/**2e**	Molar ratio **1b**/**2e**	Yield of **4e**,%[b]
1	$CHCl_3$	0.4	1	10[c]
2	Hexane	0.4	1	34[c]
3	MeOH	0.5	1	16[c]
4	CH_3CN	0.5	1	10[c]
5	THF	0.5	1	44
6	THF	1.1	1	31
7	Et_2O	0.1	1	21
8	Et_2O	0.2	1	37
9	Et_2O	0.4	1	49
10	Et_2O	0.4	0.8	44
11	Et_2O	0.4	1.2	60
12	Et_2O	0.4	1.2	21[d]
13	Et_2O	0.4	1.2	59[e]
14	Et_2O	1.1	1.2	24
15	Et_2O	1.1	0.8	24
16	MeOH[f]	0.5	1	8[c]
17	MeOH-Et_2O[g]	0.5	1	6

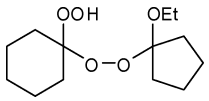
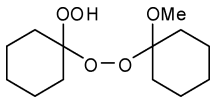
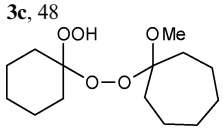
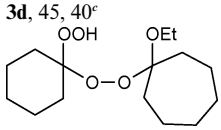
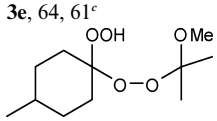
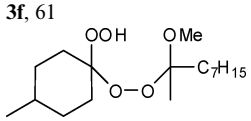
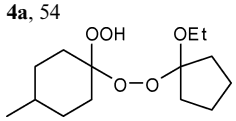
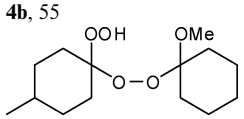
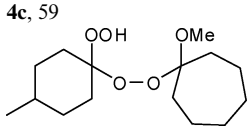
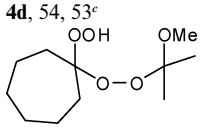
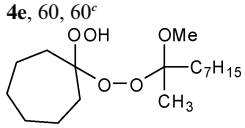
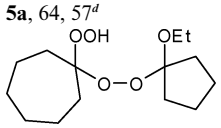
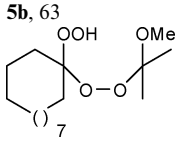
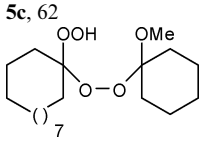
[a] Reaction conditions: I_2 (0.13–0.35 g, 0.5–1.38 mmol) was added to a solution of bishydroperoxide **1b** (0.16–0.24 g, 1.00–1.50 mmol), and acetal **2e** (0.2 g, 1.25 mmol) in Et_2O, THF, MeOH, $CHCl_3$, CH_3CN, or hexane (4 mL), and the reaction mixture was kept for 24 h. [b] The yield based on the isolated product. [c] Iodocycloheptanone as the by-product; the yield was 23% (run 1), 30% (run 2), 29% (run 3), 18% (run 4), and 17% (run 16). [d] The reaction time was 1 h. [e] The reaction time was 48 h. [f] The reaction of **1b** with cycloheptanone in MeOH (4 mL). [g] The reaction of **1b** with cycloheptanone in MeOH (2 mL) + Et_2O (2 mL).

Taking into account the conditions used for the synthesis of **4e** (Table 1), we prepared peroxides **3–6** in yields from 45 to 64% by the reaction of cyclic bishydroperoxides **1** (C_6, C_7, and C_{12}) with acetals generated from cyclic ketones **2c-f** (C_5, C_6, and C_7) and linear ketones **2a** and **2b** (acetone and methyl heptyl ketone) (Table 2).

It should be noted that the yield of peroxides depends only slightly on the structures of the reagents, due to which the results of application of this reaction to other structurally similar compounds are predictable.

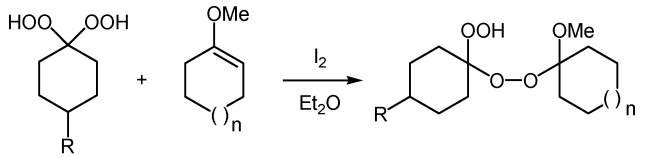
The reactions with the use of enol ethers **7** and **8** instead of related acetals **2d** and **2e** afford the target peroxides **3d**,**e**, **4d**,**e**, and **6d** in the same yields (Table 2, Scheme 4).

Table 2 Structures and yields of peroxides **3–6**[a]

Run	Structures of **3–6**, yield%.[b]	Run	Structures of **3–6**, yield%.[b]
1		2	
	3c, 48		**3d**, 45, 40[c]
3		4	
	3e, 64, 61[c]		**3f**, 61
5		6	
	4a, 54		**4b**, 55
7		8	
	4c, 59		**4d**, 54, 53[c]
9		10	
	4e, 60, 60[c]		**5a**, 64, 57[d]
11		12	
	5b, 63		**5c**, 62
13		14	
	6a, 51, 57[d]		**6d**, 50, 53[c], 59[d]

[a] **Reaction conditions:** I_2 (0.13 g, 0.5 mmol; 0.4 mol/1 mol **2**) was added to a solution of bishydroperoxide **1** (1.5 mmol; 1.2 mol/1 mol **2**) and acetal **2** (1.25 mmol) in Et_2O (4 mL), and the reaction mixture was kept for 24 h. [b] The yield based on the isolated product. [c] The yield in the reaction with 1-methoxycyclohexene and 1-methoxycycloheptene under the same reaction conditions. [d] The yield in the reaction with the use of THF as the solvent.

The reaction of bishydroperoxides with enol ethers is probably catalyzed by HI formed in a little amount as the result of interaction of iodine and bishydroperoxide.



Scheme 4 Iodine-catalyzed synthesis of peroxides **3d**,**e**, **4d**,**e**, and **6d** from bishydroperoxides **1a**, **b**, **d** and enol ethers **7** and **8**.

The structures of peroxides **3–6** were established by NMR spectroscopy and elemental analysis. The ^{13}C NMR spectra of peroxides show signals at 105–117 ppm characteristic of monoperoxyacetal and bisperoxide fragments. The signals for the protons of the OOH groups in the ^{1}H NMR spectra are observed at 9.7–10.2 ppm, which is consistent with the spectra of structurally related 1,1-bishydroperoxycycloalkanes and 1,1′-dihydroperoxy(dicycloalkyl)peroxides.[7,8,13] Compounds **4a-e** were synthesized as mixtures of diastereomers. The ^{1}H NMR spectra show twice the number of signals for the protons of the OOH groups, and the ^{13}C NMR spectra have twice the number of signals with similar chemical shifts.

The molecular structure of **6d** (CCDC 689447) drawn with ORTEP-III[24] is presented in Fig. 1.

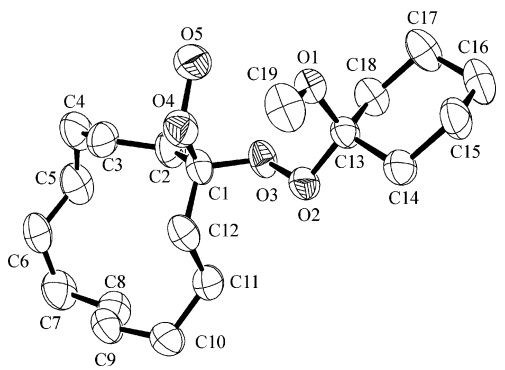


Fig. 1 Molecular structure of **6d**.

All bond lengths and bond angles in **6d** have typical values and are comparable with those observed in two related compounds, 1,1-bis(hydroperoxy)cyclododecane[25] and 1,1′-dihydroperoxy-1,1′-bis(cyclododecyl)peroxide.[26] The hydroxy group is involved in intramolecular O5-H5 ··· O1 hydrogen bonding (D ··· A, H ··· A, and D–H ··· A are 2.763(4) Å, 2.08 Å, and 141 °, respectively). In the crystal, there are no intermolecular H ··· O contacts shorter than 2.75 Å. Hence, the crystal packing is typical of branched hydrocarbons, with hydrophobic space-filling contacts reflecting the simple close packing of hydrophobic molecules.[27]

The removal of iodine is one of the difficulties in preparing analytically pure compounds **3–6**. We found that it is convenient to perform isolation in the following way. After completion of the reaction, hexane and an aqueous $Na_2S_2O_3$ solution were added to the reaction mixture, and the mixture was stirred until the organic layer became almost colorless, after which peroxides were easily isolated by column chromatography. During this work-up of the reaction mixture, almost no reduction of the target peroxides occurred. After chromatographic purification and drying *in vacuo* (10–20 Torr), the products contained a few weight percents of iodine, but they were visually colorless. Apparently, peroxides and iodine form rather strong complexes, in which the iodine molecule is coordinated by the hydroperoxide and alkoxy groups. Similar complexes of iodine with ethers were documented.[23] The complete removal of residual iodine (determined by elemental analysis) was achieved after storage of peroxides under a vacuum of ~ 0.1–0.5 Torr for one hour.

Conclusions

Previously unknown 1-hydroperoxy-1′-alkoxyperoxides were synthesized in 45–64% yield by the iodine-catalyzed reaction of geminal bishydroperoxides with acetals and enol ethers. The nature of the solvent has a decisive influence on the yield of the target peroxides. Good results were obtained in the reactions performed in Et_2O and THF. Under the optimal conditions, no replacement of the second alkoxy group giving rise to cyclic peroxides was observed. 1-Hydroperoxy-1′-alkoxyperoxides can easily be isolated from the reaction mixture by column chromatography.

Experimental

The NMR spectra were recorded on Bruker AC-200 (200.13 MHz for ^{1}H) and Bruker AM-300 (75.4 MHz for ^{13}C) spectrometers in $CDCl_3$. The TLC analysis was carried out on Silufol UV-254 chromatographic plates. Flash chromatography was performed on silica gel L 40/100 μm. Melting points were determined on a Kofler hot stage. MeOH, Et_2O, CH_3CN, $CHCl_3$, hexane, I_2, $Na_2S_2O_3$, and $MgSO_4$ of high-purity grade were home made. Geminal bishydroperoxides were synthesized according to the procedures described earlier.[7,8] Acetals and enol ethers were prepared according to a known procedure.[28]

Determination of the influence of the molar ratio of the reagents, the reaction time, and the nature of the solvent on the yield of 4e (Table 1, runs 1–15)

Iodine (0.13–0.35 g, 0.5–1.38 mmol) was added to a solution of bishydroperoxide **1b** (0.16–0.24 g, 1.00–1.5 mmol) and acetal **2e** (0.2 g, 1.25 mmol) in Et_2O, THF, MeOH, $CHCl_3$, CH_3CN, or hexane (4 mL). The reaction mixture was kept at 20–25 °C for 1, 24, or 48 h. Then hexane (30 mL) and a 2–5% $Na_2S_2O_3$ solution were added. The mixture was stirred until it became almost colorless and then was washed with water (3 × 5 ml). The organic layer was dried with $MgSO_4$ and filtered. The filtrate was concentrated to the volume of approximately 1 mL. Peroxide **4e** was isolated by silica gel column chromatography using gradient elution in a hexane–diethyl ether mixture, the ratio being changed from 20:1 to 7:1 (v/v).

The reactions of **1b** with cycloheptanone in MeOH (4 mL; run 16) and a MeOH + Et_2O mixture (2 mL + 2 mL; run 17) were carried out analogously for 24 h.

General procedure for the synthesis of peroxides 3–6 (Table 2)

Iodine (0.13 g, 0.5 mmol; 0.4 mol/1 mol **2a-f**) was added to a solution of bishydroperoxide **1a-d** (1.5 mmol; 1.2 mol/1 mol **2a-f**) and acetal **2a-f** (1.25 mmol) in Et_2O or THF (4 mL). The reaction

mixture was kept for 24 h. Then the reaction mixture was worked up and the target peroxides were isolated as described above.

Compounds **3d**,**e** **4d**,**e**, and **6d** were synthesized analogously with the use of 1-methoxycyclohexene **7** and 1-methoxycycloheptene **8**.

1-(1-Ethoxycyclopentylperoxy)-1-hydroperoxycyclohexane, 3c. Oil. R_f 0.30 (hexane:EtOAc, 20:1). Calcd for $C_{13}H_{24}O_5$: C, 59.98; H, 9.29. Found: C, 59.67; H, 9.64. ν_{max}/cm^{-1} (CCl_4) 3365br (OOH). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.22 (t, 3H, CH_3, J = 7.3 Hz), 1.33–1.83 (m, 16H, CH_2), 1.99–2.10 (m, 2H, CH_2), 3.68 (q, 2H, CH_2, J = 7.3 Hz), 9.73 (s, 1H, OOH). ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 14.8 (CH_3), 22.5, 23.3, 25.4, 29.9, 33.9 (CH_2), 59.5 (OCH_2) 109.1 (COOH), 117.3 (COEt).

1-Hydroperoxy-1-(1-methoxycyclohexylperoxy)cyclohexane, 3d. Oil. R_f 0.33 (hexane:EtOAc, 20:1). Calcd for $C_{13}H_{24}O_5$: C, 59.98; H, 9.29. Found: C, 59.75; H, 9.53. ν_{max}/cm^{-1} (CCl_4) 3360br (OOH). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.35–1.91 (m, 20H, CH_2), 3.38 (s, 3H, CH_3), 10.0 (s, 1H, OOH). ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 22.5, 22.7, 25.3, 25.5, 29.9, 31.7 (CH_2), 49.2 (OCH_3) 106.1, 109.30 (C).

1-[(1-methoxycycloheptyl)peroxy]cyclohexyl hydroperoxide, 3e. Oil. R_f 0.52 (hexane:EtOAc, 5:1). Calcd for $C_{14}H_{26}O_5$: C, 61.29; H, 9.55. Found: C, 61.43; H, 9.36. ν_{max}/cm^{-1} (CCl_4) 3360br (OOH). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.33–1.93 (m, 22H, CH_2), 3.35 (s, 3H, CH_3), 9.89 (s, 1H, OOH). ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 22.2, 22.5, 25.4, 29.6, 29.8, 34.6, 35.1 (CH_2), 49.6 (OCH_3) 109.3 (COOH), 111.0 (COEt).

1-Ethoxy-1-(1-hydroperoxycyclohexylperoxy)cycloheptane, 3f. Oil. R_f 0.57 (hexane:EtOAc, 5:1). Calcd for $C_{15}H_{28}O_5$: C, 62.47; H, 9.79. Found: C, 62.58; H, 9.57. ν_{max}/cm^{-1} (CCl_4) 3355br (OOH). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.25 (t, 3H, CH_3, J = 7.3 Hz), 1.32–1.98 (m, 22H, CH_2), 3.67 (q, 2H, CH_2, J = 7.3 Hz), 9.83 (s, 1H, OOH). ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 14.7 (CH_3), 22.3, 22.5, 25.5, 29.7, 29.9, 35.7 (CH_2), 57.4 (OCH_2) 109.1 (COOH), 111.0 (COEt).

1-Hydroperoxy-1-(2-methoxypropan-2-ylperoxy)-4-methylcyclohexane (mixture of isomers), 4a. Oil. R_f 0.38 (hexane:EtOAc, 20:1). Calcd for $C_{11}H_{22}O_5$: C, 56.39; H, 9.46. Found: C, 56.53; H, 9.31. ν_{max}/cm^{-1} (CCl_4) 3340br (OOH). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 0.85–0.92 (m, 3H, CH_3), 1.14–1.65 (m, 13H, CH, CH_2, CH_3), 2.10–2.21 (m, 2H, CH_2), 3.37, 3,39 (s, 3H, CH_3), 10.01, 10.05 (s, 1H, OOH). ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 21.4, 21.6, 22.89, 22.94, 29.3, 29.4, 30.7, 30.8 (CH_3, CH_2, CH), 50.4, 50.5 (OCH_3) 106.0, 109.4, 109.5 (C).

1-Hydroperoxy-1-(2-methoxynonan-2-ylperoxy)-4-methylcyclohexane (the mixture of isomers), 4b. Oil. R_f 0.45 (hexane:EtOAc, 20:1). Calcd for $C_{17}H_{34}O_5$: C, 64.12; H, 10.76. Found: C, 64.33; H, 10.54. ν_{max}/cm^{-1} (CCl_4) 3355br (OOH). ^{1}H NMR (200.13 MHz, $CDCl_3$), δ: 0.77–0.92 (m, 6H, CH_3), 1.11–1.75 (m, 22H, CH, CH_2, CH_3), 2.06–2.21 (m, 2H, CH_2), 3.33, 3.36 (s, 3H, CH_3), 9.97, 10.02 (s, 1H, OOH). ^{13}C NMR (50.32 MHz, $CDCl_3$), δ: 14.0 (CH_3), 19.6, 19.7, 21.4, 21.5, 22.6, 24.2, 29.0, 29.1, 29.2, 29.4, 29.6, 29.8, 30.6, 30.7, 30.9, 31.7, 35.6, 35.7 (CH_3, CH_2, CH), 50.0, 50.1 (OCH_3) 107.86, 107.91, 109.19, 109.30 (C).

1-(1-Ethoxycyclopentylperoxy)-1-hydroperoxy-4-methylcyclohexane, 4c. Oil. R_f 0.32 (hexane:EtOAc, 20:1). Calcd for $C_{14}H_{26}O_5$: C, 61.29; H, 9.55. Found: C, 61.45; H, 9.72. ν_{max}/cm^{-1} (CCl_4) 3385br (OOH). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 0.87–0.95 (m, 3H, CH_3), 1.15–1.89 (m, 16H, CH, CH_2, CH_3), 2.05–2.22 (m, 4H, CH_2), 3.69–3.80 (m, 2H, CH_2), 9.84, 9.89 (s, 1H, OOH). ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 14.8, 14.9 (CH_3), 21.4, 21.5, 23.38, 23.44, 29.4, 29.6, 30.7, 30.9, 31.7, 31.8, 34.0 (CH_2), 59.5, 59.7 (OCH_2) 109.2, 109.3 (COOH), 117.4, 117.5 (COEt).

1-Hydroperoxy-1-(1-methoxycyclohexylperoxy)-4-methylcyclohexane (mixture of isomers), 4d. Oil. R_f 0.57 (hexane:EtOAc, 5:1). Calcd for $C_{14}H_{26}O_5$: C, 61.29; H, 9.55. Found: C, 61.42; H, 9.37. ν_{max}/cm^{-1} (CCl_4) 3330br (OOH). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 0.82–0.89 (m, 3H, CH_3), 1.09–1.83 (m, 17H, CH, CH_2), 2.05–2.19 (m, 2H, CH_2), 3.32, 3.34 (s, 3H, CH_3), 9.89, 9.98 (s, 1H, OOH). ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 21.3, 21.4, 22.6, 22.7, 25.2, 25.3, 29.2, 29.4, 30.6, 30.8, 31.6, 31.7 (CH_3, CH_2, CH), 49.1, 49.2 (OCH_3) 106.05, 106.10, 109.1, 109.2 (C).

1-(1-Hydroperoxy-4-methylcyclohexylperoxy)-1-methoxycycloheptane, 4e. Oil. R_f 0.60 (hexane:EtOAc, 5:1). Calcd for $C_{15}H_{28}O_5$: C, 62.47; H, 9.79. Found: C, 62.15; H, 9.71. ν_{max}/cm^{-1} (CCl_4) 3335br (OOH). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 0.85–0.94 (m, 3H, CH_3), 1.11–1.65 (m, 15H, CH, CH_2), 1.85–2.01 (m, 4H, CH_2), 2.10–2.20 (m, 2H, CH_2), 3.36, 3.38(s, 3H, CH_3), 9.96, 10.03 (s, 1H, OOH). ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 21.4, 21.5, 22.2, 22.3, 29.3, 29.4, 29.6, 29.8, 30.7, 30.8, 31.7, 31.8 (CH_3, CH_2, CH), 49.6, 49.7 (OCH_3) 109.3, 109.4, 111.0, 111.3 (C).

1-Hydroperoxy-1-(2-methoxypropan-2-ylperoxy)cycloheptane, 5a. White crystals. Mp 17–19 °C (hexane). R_f 0.37 (hexane:EtOAc, 20:1). Calcd for $C_{11}H_{22}O_5$: C, 56.39; H, 9.46. Found: C, 56.44; H, 9.61. ν_{max}/cm^{-1} (CCl_4) 3340br (OOH). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.25–1.60 (m, 14H, CH_2, CH_3), 1.85–1.95 (m, 4H, CH_2), 3.36 (s, 3H, CH_3), 10.08 (s, 1H, OOH). ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 22.8 (CH_3), 22.9, 30.0, 32.6 (CH_2), 50.4 (OCH_3), 105.6, 114.7 (C).

1-Hydroperoxy-1-(2-methoxynonan-2-ylperoxy)cycloheptane, 5b. Oil. R_f 0.45 (hexane:EtOAc, 20:1). Calcd for $C_{17}H_{34}O_5$: C, 64.12; H, 10.76. Found: C, 64.29; H, 10.91. ν_{max}/cm^{-1} (CCl_4) 3335br (OOH). ^{1}H NMR (200.13 MHz, $CDCl_3$), δ: 0.89 (t, 3H, CH_3, J = 7 Hz), 1.21–2.00 (m, 27H, CH, CH_2, CH_3), 3.39 (s, 3H, OCH_3), 10.11 (s, 1H, OOH). ^{13}C NMR (50.32 MHz, $CDCl_3$), δ: 14.0 (CH_3), 19.8, 22.6, 22.9, 24.2, 29.1, 29.7, 29.9, 31.7, 32.6, 35.8 (CH_3, CH_2), 50.1 (OCH_3) 108.1, 114.5 (C).

1-(1-Ethoxycyclopentylperoxy)-1-hydroperoxycycloheptane, 5c. Oil. R_f 0.32 (hexane:EtOAc, 20:1). Calcd for $C_{14}H_{26}O_5$: C, 61.29; H, 9.55. Found: C, 61.41; H, 9.68. ν_{max}/cm^{-1} (CCl_4) 3325br (OOH). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.23 (t, 3H, CH_3, J = 7.3 Hz), 1.47 –1.98 (m, 18H, CH_2), 2.00–2.11 (m, 2H, CH_2), 3.70 (q, 2H, CH_2, J = 7.3 Hz), 9.94 (s, 1H, OOH). ^{13}C NMR (50.32 MHz, $CDCl_3$), δ: 14.8 (CH_3), 22.8, 23.3, 29.9, 32.7, 34.0 (CH_2), 59.6 (OCH_2), 114.3, 117.4 (C).

1-Hydroperoxy-1-(2-methoxypropan-2-ylperoxy)cyclododecane, 6a. White crystals. Mp 77–78 °C (hexane). R_f 0.42 (hexane:EtOAc, 20:1). Calcd for $C_{16}H_{32}O_5$: C, 63.13; H, 10.60. Found: C, 63.01; H, 10.47. ν_{max}/cm^{-1} (CCl_4) 3360br (OOH). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.21 –1.75 (m, 28H, CH_2,CH_3), 3.42 (s,

3H, CH_3), 10.18 (s, 1H, OOH). ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 19.3, 21.8, 22.1, 22.9, 25.9, 26.1, 26.3 (CH_2), 50.5 (OCH_3) 105.9, 113.8 (C).

1-Hydroperoxy-1-(1-methoxycyclohexylperoxy)cyclododecane, 6d. White crystals. Mp 85–87 °C (hexane). R_f 0.38 (hexane:EtOAc, 20:1). Calcd for $C_{19}H_{36}O_5$: C, 66.24; H, 10.53. Found: C, 66.57; H, 10.83. ν_{max}/cm ^{1} (CCl_4) 3330br (OOH). ^1H NMR (300.13 MHz, $CDCl_3$), δ: 1.25 –1.92 (m, 32H, CH_2), 3.38 (s, 3H, OCH_3), 10.14 (s, 1H, OOH). ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 19.4, 21.9, 22.1, 22.8, 25.3, 25.9, 26.2, 26.3, 31.7 (CH_2), 49.4 (OCH_3) 106.2, 113.5 (C).

Acknowledgements

This work is supported by the Program for Support of Leading Scientific Schools of the Russian Federation (Grant NSh 2942.2008.3) and the Grant of the President of the Russian Federation (No. MK-3515.2007.3).

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