Synthesis of 1,1⁻-bishydroperoxydi(cycloalkyl) peroxides by homocoupling of 11—15-membered *gem*-bis(hydroperoxy)cycloalkanes in the presence of boron trifluoride*

A. O. Terent 'ev,^a* A. V. Kutkin,^a M. M. Platonov,^a Z. A. Starikova,^b Yu. N. Ogibin,^a and G. I. Nikishin^a

 ^aN. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 47 Leninsky prosp., 119991 Moscow, Russian Federation. Fax: +7 (095) 135 5328. E-mail: alterex@yandex.ru
^bA. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 28 ul. Vavilova, 119991 Moscow, Russian Federation. Fax: +7 (095) 135 5085

A procedure was developed for the synthesis of 1,1'-bishydroperoxydi(C_{11} - C_{15} -cycloalkyl) peroxides based on homocoupling of geminal 11–15-membered bis(hydroperoxy)cycloalkanes in the presence of BF₃·OEt₂.

Key words: 1,1'-bishydroxyperoxydi(cycloalkyl) peroxides, *gem*-bis(hydroxyperoxy)cyclo-alkanes, boron trifluoride diethyl etherate.

1,1 -Bishydroxyperoxydi(cycloalkyl) peroxides (1) are of interest as intermediates in the synthesis of macrocyclic lactones, hydrocarbons, ^{1,2} and difficultly accessible nonsymmetrical tetroxanes.³



Peroxides 1 with five- and six-membered rings (n = 4and 5 (1a)) are readily accessible. They can rapidly (in 1-2 h) be prepared in high yields (70-90%) by just mixing the corresponding cycloalkanones or their solutions in carboxylic acids or acetonitrile with 30-90% aqueous H₂O₂ in the presence of perchloric, hydrochloric, or nitric acid.^{1,3-6} No studies aimed at synthesizing peroxide 1b (n = 10) from cycloundecanone have been carried out. Under these conditions, the reactions of cyclododecanone and cyclotridecanone afford 12- and 13-membered gem-bis(hydroxyperoxy)cycloalkanes, respectively, as the major products, whereas the corresponding peroxides 1c,d (n = 11 and 12, respectively) are formed as minor products.^{7,8} Peroxide 1c (n = 11) could be synthesized in high yield only by perchloric acid-catalyzed homocoupling of bis(hydroxyperoxy)cyclododecane in

* Dedicated to Academician N. K. Kochetkov on the occasion of his 90th birthday.

propionic acid.⁹ The major portion of peroxide 1c produced in this reaction precipitates, due to which its subsequent transformation into symmetrical dispiro-1,2,4,5tetroxane 2 (n = 11) is almost completely suppressed.



However, prolonged storage of the reaction mixture at low temperature (0 °C, 16 h) is required for the efficient transformation of the starting bis(hydroxyperoxy)cyclododecane into peroxide **1c** and complete precipitation of the latter from the reaction mixture. Yet another drawback of this method is low purity of peroxide **1c** that precipitates from the propionic acid solution due to which repeated recrystallization is required to purify **1c** from byproducts.

In the present work, we report on a modified method for the synthesis of 1,1'-bishydroxyperoxydi(cycloalkyl) peroxides **1** from *gem*-bis(hydroxyperoxy)cycloalkanes devoid of the above drawbacks. Derivatives of $C_{11}-C_{15}$ -cycloalkanes can easily be prepared according to a simple and convenient procedure that we have developed for their preparation by BF₃-catalyzed condensation of the corresponding cycloalkanone ketals with hydrogen peroxide.^{10,11} The proposed modified method is based on homocoupling of *gem*-bis(hydroxyperoxy)cyclo-

Published in Russian in Izvestiya Akademii Nauk. Seriya Khimicheskaya, No. 5, pp. 1182-1185, May, 2005.

1066-5285/05/5405-1214 © 2005 Springer Science+Business Media, Inc.

Scheme 1



n = 5 (**a**), 10 (**b**), 11 (**c**), 12 (**d**), 14 (**e**)

Reagents and conditions: Et₂O, BF₃·OEt₂ (0.5-1.0 equiv.), 20 °C, 1-12 h.

alkanes in the presence of BF_3 and the use of diethyl ether as the solvent. *gem*-Bis(hydroxyperoxy)cycloalkanes **3a**-e were used as the starting substrates (Scheme 1).

Homocoupling of bis(hydroxyperoxides) 3a,b, bis(hydroperoxides) 3c,e, and bis(hydroperoxide) 3dwas carried out at room temperature, 0-20 °C, and -20-20 °C, respectively, with the use of 0.5-1.0 equiv. of BF₃•OEt₂. Under these conditions, complete conversion of bis(hydroperoxides) 3a-e occurred (TLC control) to give 1,1'-bishydroxyperoxydi(cycloalkyl) peroxides 1a-e in 1-2 h (in the case of 3b, in 12 h) (Table 1). In the presence of a smaller amount of the catalyst (0.1 equiv.), the homocoupling of bis(hydroperoxides) occurred much more slowly and their complete conversion was not achieved.

Taking into account that homocoupling of bis(hydroperoxide) **3a** affords considerable amount of tetroxane **2a**, the substantial difference in the yields of peroxides **1a** and **1b—e** is probably associated primarily with the competitive conversion of **1a** into **2a**. Apparently, product **1a** only partially precipitates from the ethereal solution, as a con-

Table 1. Homocoupling of *gem*-bis(hydroxyperoxy)cycloalkanes 3a-e in the presence of BF₃·OEt₂

Bis(hydro per- oxide)	o- Amount of $BF_3 \cdot OEt_2$ (equiv.)	τ/h	T∕°C	Bishydroxyperoxy- di(cycloalkyl) per- oxide (yield (%))
3 a	0.5	1	20	1a (36)*
3b	0.5	12	20	1b (64)
3c	1.0	2	0-20	1c (86)
3d	0.6	2	-20 - 20	1d (64)
3e	0.65	2	0-20	1e (84)

* Tetroxane **2a** (45% yield) and cyclohexanone (7% yield) were also produced.

sequence of which it is involved in intramolecular condensation giving rise to tetroxane **2a**. Because of lower solubility of peroxides **3b**—**e** in diethyl ether, their transformation into the corresponding tetroxanes was not observed. Due to this fact, as well as due to better solubility of other by-products in diethyl ether, high-purity target products **3b**—**e** (the purity was higher than 90%) precipitate from diethyl ether, which obviates the necessity to purify these products by recrystallization.

The structures and compositions of the products were confirmed by NMR spectroscopy and elemental analysis. The structure of 1,1'-bishydroperoxydi(cyclododecyl) peroxide (1c) was established by X-ray diffraction analysis (Fig. 1). In the present study, peroxides **1b**,**e** were characterized for the first time. These compounds, like analogs **1c**,**d**, are sufficiently stable. They do not decompose at room temperature, nor they detonate upon impact and friction.

The molecule of peroxide **1c** (see Fig. 1) (**I** is the monoclinic modification) has a bent structure. The dihedral angle between the mean planes of the rings is 93.3° . The angle between the C(1)...C(7) and C(13)...C(21) lines is 126.3° .

The hydroperoxide groups are tightened together by the O(6)-H(6(O))...O(3) and O(4)-H(4(O))...O(5) hydrogen bonds (the parameters of the hydrogen bonds: the O...O and O...H distances and the O-H...O angle are, respectively, 2.810(3), 2.14 Å, 139° and 2.802(3), 2.13 Å, 140°).

The (C)O(1)–O(2(C)) and O–O(H) bond lengths (1.487(2) and 1.461(1), 1.457(3) Å) are close to the standard values¹² (1.482 and 1.464 Å for the O–O bonds characterized by the torsion angles of 70–85° and those close to 180°, respectively). In structure I, the C(1)–O(1)–O(2)–C(13), C(1)–O(3)–O(4)–H(4(O)), and C(13)–O(5)–O(6)–H(6(O)) torsion angles are



Fig. 1. Molecular structure of 1,1'-bishydroxyperoxydi(cyclododecyl) peroxide (1c) (modification I).

126.3, 91.9, and 92.3°, respectively. The C–O bond lengths (1.430(3) and 1.423(3) Å) and the bond angles at the C(1) and C(13) atoms are consistent with the geometric parameters typical of C_{sp3} –OH units. The geometric characteristics of the C–C bonds in the rings also have standard values.

The structure of the triclinic polymorph of peroxide **1c** (II) has been described earlier.¹³ In this modification, the molecule has the same structure as that observed in the monoclinic modification and similar geometric parameters. Slight differences are observed in the dihedral angle between the mean planes of the rings (94.8°) and the angle between the C(1)...C(7) and C(13)...C(21) lines (119.9°). In addition, the hydrogen bond network in structure II differs from that observed in I. The O...H distances in II differ in length (H(4(O))...O(5), 2.06 Å;



Fig. 2. Dimeric pseudocentrosymmetric fragments of peroxide 1c (modification I).

H(6(O))...O(5), 2.29 Å), and the H(6(O)) atom forms the rather strong H(6(O))...O(4) intermolecular hydrogen bond (2.23 Å), resulting in the formation of centrosymmetric dimers. In structure I, the corresponding distance is substantially longer (2.64 Å). Nevertheless, structure I also contains dimeric pseudocentrosymmetric fragments (Fig. 2).

Both structures are identical in the character of molecular packing, which is determined by intermolecular C...H and H...H van der Waals interactions between the dimers (or pseudodimers), which have a shape similar to a flattened sphere (the diameters are 18.8, 14.8, and 5.7 Å) and a hydrophobic outer surface.

To summarize, we developed a convenient procedure for the synthesis of 1,1'-bishydroxyperoxydi(C_{11} - C_{15} -cycloalkyl) peroxides. The method allows one to prepare these compounds rapidly and in high yields (64-86%) and does not require laborious purification of the target products.

Experimental

The NMR spectra were recorded on Bruker WM-250 and Bruker AM-300 spectrometers ($CDCl_3$ as the solvent). The TLC analysis was carried out on Silufol UV-254 plates. Column chromatography was performed on silica gel (Merck, 63–200 mesh). The melting points were measured on a Kofler hot-stage apparatus.

Commercial cyclohexanone, cycloundecanone, cyclododecanone, cyclotridecanone, cyclopentadecanone, trimethyl orthoformate, and boron trifluoride diethyl etherate (Acros) were used. Methanol, diethyl ether, a 35% aqueous hydrogen peroxide solution, and sodium hydroxide were used without additional purification. The starting 1,1-bis(hydroxyperoxy)cyclohexane (**3a**) and 1,1-bis(hydroxyperoxy)cyclododecane (**3c**) were synthesized by condensation of the corresponding cycloalkanone ketals with H_2O_2 according to a procedure described earlier.^{10,11} gem-Bis(hydroperoxides) **3b,d,e** were prepared analogously. Complete X-ray diffraction data for 1,1'-bishydroxyperoxydi(cyclododecyl) peroxide (1c) were deposited with the Cambridge Structural Database (CSDB).

1,1-Dihydroperoxycycloundecane (3b). The yield was 92%. M.p. 80–82 °C (diethyl ether). Found (%): C, 60.42; H, 10.10. $C_{11}H_{22}O_4$. Calculated (%): C, 60.52; H, 10.16. ¹H NMR (250.13 MHz), δ : 1.28–1.63 (m, 16 H, CH₂); 1.70–1.88 (m, 4 H, CH₂); 9.30–9.49 (br.s, 2 H, OOH). ¹³C NMR (62.9 MHz), δ : 21.3, 25.4, 26.3, 26.9, 27.7 (CH₂); 115.4 (C).

1,1-Dihydroperoxycyclotridecane (3d). The yield was 94%. M.p. 115–116.5 °C (diethyl ether). Found (%): C, 63.26; H, 10.53. $C_{13}H_{26}O_4$. Calculated (%): C, 63.38; H, 10.64. ¹H NMR (300.13 MHz), δ : 1.25–1.60 (m, 20 H, CH₂); 1.64–1.82 (m, 4 H, CH₂); 9.35–9.43 (br.s, 2 H, OOH). ¹³C NMR (75.47 MHz), δ : 20.8, 25.5, 25.6, 26.8, 27.3, 28.6 (CH₂); 115.1 (C).

1,1-Dihydroperoxycyclopentadecane (3e). The yield was 34%. M.p. 116–118 °C (diethyl ether). Found (%): C, 65.37; H, 10.78. $C_{15}H_{30}O_4$. Calculated (%): C, 65.66; H, 11.02. ¹H NMR (300.13 MHz), δ : 1.23–1.55 (m, 24 H, CH₂); 1.59–1.80 (m, 4 H, CH₂); 9.05–9.12 (br.s, 2 H, OOH). ¹³C NMR (75.47 MHz), δ : 21.8, 26.5, 26.6, 26.9, 27.5, 29.3 (CH₂); 115.1 (C).

Homocoupling of gem-bis(hydroperoxides) 3a,b in the presence of $BF_3 \cdot OEt_2$. Synthesis of 1,1⁻-bishydroxyperoxydi(cycloalkyl) peroxides 1a,b. Boron trifluoride diethyl etherate (0.5 equiv.) was added to a solution of gem-bis(hydroxyperoxy)cycloalkane 3 (2.3-3.4 mmol) in Et₂O (10-20 mL). The reaction mixture was stirred at room temperature for 1 h (in the case of **3b**, for 12 h), Et₂O (20 mL) was added, and the mixture was washed with water (4×5 mL). In the synthesis of compound **1b**, the reaction mixture was then washed with a 5% NaOH solution $(2 \times 5 \text{ mL})$ and water (5 mL), and the ethereal layer was dried (MgSO₄) and concentrated. In the synthesis of compound 1a, the ethereal layer was dried (MgSO₄) and concentrated, after which cyclohexanone, tetroxane 2a, and peroxide 1a were isolated by column chromatography (light petroleum-diethyl ether, 95 : 5, as the eluent) (see Table 1). Cyclohexanone and tetroxane 2a were identified by TLC using authentic samples. The residue prepared upon homocoupling of bis(hydroperoxide) 3b was crystallized from diethyl ether and peroxide 1b was obtained.

1,1'-Bishydroxyperoxydi(cyclohexyl) peroxide (1a).¹⁴ The yield was 36%. M.p. 80–81.5 °C (light petroleum) (*cf.* lit. data¹⁴: m.p. 81–82 °C). ¹H NMR (300.13 MHz), δ: 1.43–1.68 (m, 12 H, CH₂); 1.78–1.98 (m, 8 H, C–CH₂); 9.42–9.62 (br.s, 2 H, OOH). ¹³C NMR (75.47 MHz), δ: 22.6, 25.5, 29.9 (CH₂); 111.3 (C).

1,1'-Bishydroxyperoxydi(cycloundecyl) peroxide (1b). The yield was 64%. M.p. 111–113 °C (diethyl ether). Found (%): C, 65.58; H, 10.64. $C_{22}H_{42}O_6$. Calculated (%): C, 65.64; H, 10.52. ¹H NMR (300.13 MHz), δ : 1.22–1.52 (m, 16 H, CH₂); 1.56–1.78 (m, 4 H, CH₂); 9.23–9.32 (br.s, 2 H, OOH). ¹³C NMR (75.47 MHz), δ : 29.02, 27.5, 26.7, 26.5, 21.8 (CH₂); 114.6 (C).

Homocoupling of gem-bis(hydroperoxides) 3c-e in the presence of BF₃·OEt₂. Synthesis of 1,1 '-bishydroxyperoxydi(cycloalkyl) peroxides 1c-e (general procedure). Boron trifluoride diethyl etherate (0.6–1 equiv.) was added to a solution of gem-bis(hydroxyperoxy)cycloalkane 3 (1.8–2.2 mmol) in Et₂O (10 mL). The reaction mixture was stirred for 1 h, cooled to 0 °C (in the case of bis(hydroperoxide) **3d**, to -20 °C), and kept in the cold state for 1 h. Crystals of peroxides **1c**—**e** that precipitated were filtered off, washed with water (3×5 mL), and diethyl ether (2×2 mL) cooled to -20 °C, and evacuated at room temperature and at 0.1 Torr for 1 h.

1,1[']-Bishydroxyperoxydi(cyclododecyl) peroxide (1c).^{9,12} The yield was 86%. M.p. 154–155.5 °C (CHCl₃) (*cf.* lit. data⁹: m.p. 151–152 °C). Found (%): C, 66.80; H, 10.43. $C_{24}H_{46}O_6$. Calculated (%): C, 66.94; H, 10.77. ¹H NMR (300.13 MHz), δ : 1.21–1.82 (m, 44 H, CH₂); 9.78 (s, 2 H, OOH). ¹³C NMR (75.47 MHz), δ : 19.40, 21.85, 22.12, 25.89, 26.20, 26.44 (CH₂); 115.38 (C).

1,1[^]-Bishydroxyperoxydi(cyclotridecyl) peroxide (1d).⁸ The yield was 64%. M.p. 127–128.5 °C (CHCl₃) (*cf.* lit. data⁸: m.p. 128–129 °C). ¹H NMR (300.13 MHz), δ: 1.20–1.78 (m, 48 H, CH₂); 9.35–9.42 (br.s, 2 H, OOH). ¹³C NMR (75.47 MHz), δ: 20.9, 25.2, 25.6, 26.5, 27.2, 28.6 (CH₂); 111.4 (C).

1,1'-Bishydroxyperoxydi(cyclopentadecyl) peroxide (1e). The yield was 84%. M.p. 113–115 °C (CHCl₃). Found (%): C, 70.32; H, 11.15. $C_{30}H_{58}O_6$. Calculated (%): C, 70.00; H, 11.36. ¹H NMR (300.13 MHz), δ : 1.20–1.78 (m, 56 H, CH₂); 9.60–9.65 (br.s, 2 H, OOH). ¹³C NMR (75.47 MHz), δ : 21.4, 25.3, 25.4, 25.5, 26.0, 26.2, 27.9 (CH₂); 115.6 (C).

X-ray diffraction study of 1,1[°]-bishydroxyperoxydi(cyclododecyl) peroxide (1c). Crystals of compound 1c ($C_{24}H_{46}O_6$) are monoclinic, M 430.61, at 213 K a = 10.398(8), b = 10.934(6), c = 21.726(15) Å, $\beta = 100.39(6)^\circ$, V = 2430(3) Å³, $d_{calc} =$ 1.177 g cm⁻³, $\mu = 0.082$ mm⁻¹, space group P2/n, Z = 4.

The intensities of 4676 independent reflections were measured on a four-circle Syntex P2₁ diffractometer (λ (MoK α) = 0.71073 Å, graphite monochromator, $\theta/2\theta$ scanning technique, $2\theta_{max} = 52^{\circ}$, data completeness was 89.6%). The equivalent reflections were merged to obtain 4290 independent reflections ($R_{int} = 0.0822$), which were used in subsequent calculations.

The structure was solved by direct methods. The nonhydrogen atoms were refined anisotropically by the full-matrix least-squares method against F^2 . The hydrogen atoms were placed in calculated positions and refined using a riding model. The final *R* factors were as follows: $R_1 = 0.0581$ (calculated against *F* for 2467 reflections with $I > 2\sigma(I)$), $wR_2 = 0.1306$ (calculated against F^2 for all 4290 reflections), 271 parameters were refined, GOOF = 1.029. All calculations were carried out with the use of the SHELXTL-97 program package.¹⁵

This study was financially supported by the Council on Grants of the President of the Russian Federation (Program for State Support of Leading Scientific Schools of the Russian Federation, Grants NSh 02121.2003.3 and NSh 1060.2003.3).

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Received February 11, 2005; in revised form April 15, 2005