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An Intramolecular Substitution of Hydroperoxy-endoperoxide to a Bis-endoperoxide

Nurhan (Horasan) Kishali,* Ertan Sahin,[†] and Yunus Kara*

Department of Chemistry, Faculty of Arts and Sciences, Atatürk University,
25240 Erzurum, Turkey

nhorasan@atauni.edu.tr; yukara@atauni.edu.tr

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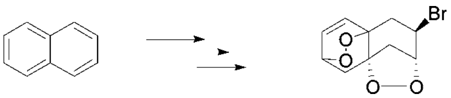
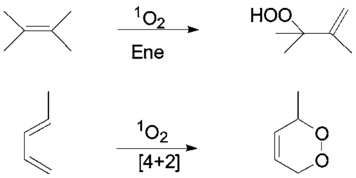
ABSTRACT



A new and stereospecific synthesis for bis-endoperoxide has been developed starting from tetrahydronaphthalene. Photooxygenation of tetrahydronaphthalene resulted in the formation of hydroperoxy-endoperoxide. The bromination reaction of hydroperoxy-endoperoxide gave bis-endoperoxide, whose exact configuration has been determined by X-ray analysis. The lowest-energy conformer of bis-endoperoxide is the boat-chair form.

Singlet molecular oxygen was first observed in 1924.[1] It has been reported that the main reactions of singlet oxygen are cycloaddition and ene-reaction. The 1,4-cycloaddition of singlet oxygen to a cyclic diene results in the formation of bicyclicendoperoxide.

Scheme 1



The ene-reaction of singlet oxygen with olefins containing allylic hydrogens results in the formation of unsaturated hydroperoxide.

1,4-Epiperoxides (endoperoxides) serve as key substances in a variety of chemical[2] and biological[2,3] transformations. The O−O bond undergoes either homolytic or hetereolytic cleavage, depending on reaction conditions. Although approximately 4,000 endoperoxides have been reported in the literature, only a few examples have bis-endoperoxide structures[4] (Figure 1).

The preparation of these bis-endoperoxides is based completely on cycloaddition of singlet oxygen to the corresponding diene moiety (Figure 1). To the best of our knowledge, we present for the first time a unique example describing a preparation of a new bis-endoperoxide via hydroperoxide rearrangement.

Our starting material was tetrahydronaphthalene **5**, synthesized by metal-ammonia reduction.[5] Tetraphenylporphyrin

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[†] To whom inquires concerning the X-ray structure should be directed.

(1) Frimer, A. A. *Singlet $^1O_2$, Reaction Modes and Products*; CRC Press: Boca Raton, FL, 1985; Vol. II, Part 1; Vol. III, Part 2. Patai, S. *The Chemistry of Functional Groups, Peroxides*; Wiley: New York, 1983. Wasserman, H. H., Murray, W. M. *Singlet Oxygen*; Academic Press: New York, 1979.

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10.1021/ol060272s CCC: $33.50

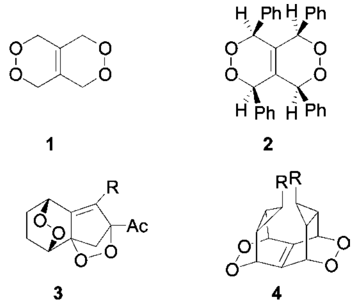
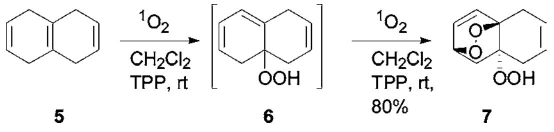


Figure 1. Bis-endoperoxides

(TPP)-sensitized photooxygenation of tetrahydronaphthalene in methylene chloride at room-temperature resulted in the formation of the tricyclic compound **7**. The reaction mixture was chromatographed on a neutral Al_2O_3 column with hexane/ethyl acetate (4:1) as an eluent to obtain endoperoxide **7** as a sole product (80% yield). This reaction is similar to the addition of singlet oxygen to 1,4-cyclohexadiene.[6] Singlet oxygen undergoes an ene-reaction with **5** to afford reactive diene **6**, and the conjugated diene unit **6** can be easily trapped by singlet oxygen.

Scheme 2



Since the hydroperoxide **6** has no plane of symmetry, singlet oxygen approaches the diene unit in **6** preferentially from the sterically less crowded face of the molecule.

The structure of **7** was assigned by ^1H and ^{13}C NMR. There are five distinct AB-systems in the ^1H NMR spectrum, which are four olefinic and six methylenic protons.

The hydroperoxide proton resonated at δ 7.60 ppm. Although double resonance experiments and 10 line in ^{13}C NMR support the structure, we were not sure of the exact configuration on the basis of spectral data. The exact configuration of **7** was determined by further chemical reactions and X-ray crystal analysis of bis-endoperoxide **8** (Figure 2).[8,9] To test the behavior of a hydroperoxide-endoperoxide in the bicyclic system and confirm the product distribution, we decided to perform the bromination of endoperoxide **7**. It has been reported that interesting compounds are formed in the bromination reaction of bicyclic systems.[7] In the reaction, unexpected compounds are formed depending on functional groups. The bromination of endoperoxide **7** in CH_2Cl_2 gave a very interesting sole product. ^1H and ^{13}C NMR spectroscopic data confirmed the addition of bromine to the double bond. In fact, we supposed that the bromine would add to the double bond to give a dibromide. However, ^1H NMR spectra interestingly showed only one CH-Br proton and two CH-O protons. In addition, four different carbon signals that are adjacent to oxygen appeared at ^{13}C NMR. In this case, we assume that hydroperoxide oxygen is conjoined with the ring. These results showed that hydroperoxide oxygen attacks from the backside of the bromonium ion and opens it to form the bis-endoperoxide (Scheme 3). Although all NMR spectral data support the proposed structure, to gain more insight about the crystal structure of the compound **8**, we decided to confirm its exact structure by single-crystal X-ray diffraction techniques.[9] The molecular structure along with the atom-numbering scheme is depicted in Figure 2.

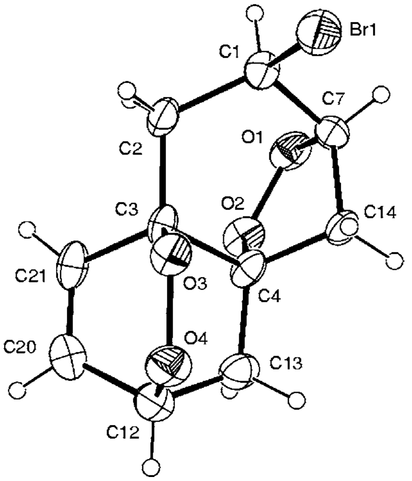
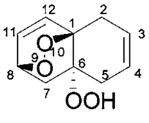
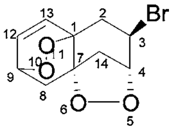


Figure 2. Molecular structure of compound **8** along with the labeling atoms. Thermal ellipsoids of non-hydrogen atoms are drawn at the 40% probability level.



7



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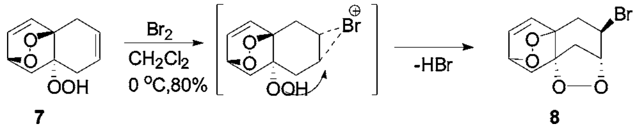
[7] (a) Kishali, H. N.; Kara, Y.; Azizoglu, A.; Balci, M. *Tetrahedron* **2003**, *59*, 3691. (b) Dastan, A.; Taskesenligil, Y.; Tümer. F.; Balci, M. *Tetrahedron* **1996**, *52*, 14005. (c) Altundas, A.; Dastan, A.; McKee, M.; Balci, M. *Tetrahedron* **2000**, *56*, 6115.

[8] **Spectral Data of 7.** ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 7.64 (s, OOH), 6.72 (dd, A part of $AB_{olefinic}$ system, 1H, H_{12}, $J = 8.4, 6.2$ Hz), 6.25 (dd, B part of $AB_{olefinic}$ system 1H, H_{11}, $J = 8.4, 1.5$ Hz), 5.68−5.61 (m, 2H, H_3, H_4,), 4.76 (m, 1H, H_8), 2.88 (dd, A part of AB system, 1H, H_{5a}, $J = 18.8, 5.1$ Hz), 2.48 (m, B part of AB system, 1H, H_{5b}), 2.59−2.36 (m, 2H, H_{2a}, H_{2b}), 2.14 (dd, A part of AB system, 1H, H_{7a}, $J = 13.5, 4.0$ Hz), 2.02 (dd, B part of AB system, 1H, H_{7b}, $J = 13.9, 1.6$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 134.16, 132.83, 124.47, 122.75, 79.24, 75.09, 71.99, 37.17, 32.62, 30.05. IR ($CHCl_3$, cm^{-1}): 3400, 3033, 2936, 2902, 1662, 1417, 1374, 1237, 1092, 851. $C_{12}H_{18}O_6$ (258.1): calcd C 55.81, H 7.02; found C 55.71, H 7.08. Mp: 103−104 °C.

[9] **Spectral Data of 8.** ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 6.74 (dd, A part of $AB_{olefinic}$ system, 1H, H_{12}, $J = 8.2, 6.2$ Hz), 6.23 (dd, B part of $AB_{olefinic}$ system 1H, H_{13}, $J = 8.2, 1.1$ Hz), 4.78 (m, 2H, $H_{4,9}$), 4.23 (m, 1H, H_3), 3.93 (d, A part of AB system, 1H, H_{8a}, $J = 12.4$ Hz), 3.03 (dd, A part of AB system, 1H, H_{14a}, $J = 17.2, 6.6$ Hz), 2.51 (m, 3H, $H_{8b,\ 14b,\ 2a}$), 1.82 (d, B part of AB system, 1H, H_{2b}, $J = 13.9$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 134.60, 133.60, 80.69, 79.91, 77.03, 72.10, 43.65, 43.00, 35.66, 34.59. IR ($CHCl_3$, cm^{-1}): 3430, 2936, 1703, 1661, 1436, 1414, 1367, 1012, 994, 884. Mp: 137−138 °C.

Scheme 3



Compound **8** ($C_{10}H_{11}BrO_4$) contains two six-membered cyclic arrangements of carbon atoms. Except for C7 and C8, each carbon atoms has a tetrahedral arrangement of atoms surrounding it. This arrangement is found in two main groups of conformers: the boat form ring A(C3/C4/C10/C9/C8/C7) with the puckering parameters[12] $Q_T = 0.790(13)$ Å, $\varphi_2 = 357.1(9)$, $\theta_2 = 90.5(9)$ and the chair form ring B(C1/C2/C3/C4/C5/C7), $Q_T = 0.631(12)$ Å, $\varphi_2 = 62(2)$, $\theta_2 = 150.7(11)$. As seen, the lowest-energy conformer of **8** is the boat-chair form. Two rings are connected at adjacent C3 and C4 atoms (fused ring structure). The six-membered cyclohexene ring with one double bond (C8 = C7 = 1.312(8) Å) has an endoperoxide bridge (O3−O4 = 1.490(8) Å) from pseudoequatorial to pseudoaxial position. Furthermore, ring C(C3/O3/O4/C9/C10/C4), $Q_T = 0.859(12)$ Å, $\varphi_2 = 116.2(8)$, $\theta_2 = 91.0(8)$, and D(C3/O3/O4/C9/C8/C7), $Q_T = 0.783(12)$ Å, $\varphi_2 = 301.5(9)$, $\theta_2 = 89.9(9)$ has the boat conformation. The whole ring A, C, and D system is geometrically symmetric (O4−C9−C10 = 107.4(6)°, C10−C9−C8 = 109.8(6)°, O4−C9−C8 = 107.9(6)°). Another bridged peroxide group (O1−O2 = 1.485(8) Å) forms five-membered ring E(O1/O2/C4/C5/C6), and it has an envelope conformation. O1/O2/C4/C6 atoms are coplanar and C15 atom projects out of the plane (deviating 0.671 Å from the plane). The puckering parameters of this ring are $Q = 0.437$ Å and $\varphi = 281.3°$ calculated according to Cremer and Pople.[11] In the cyclohexane ring bromine atom is trans to the endoperoxide (C1−Br = 1.967(7) Å).

In summary, a short and stereocontrolled approach to a new class of bis-endoperoxide started from tetrahydronaphthalene. Further work starting from bis-endoperoxide to investigate its chemical transformation reaction is currently in progress.

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Supporting Information Available: Synthetic procedure and spectroscopic characterization of compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) The molecular structure of the compound ($C_{10}H_{11}BrO_4$) was established by X-ray diffraction analysis. All data were calculated on a Rigaku R-AXIS RAPID IP diffractometer at 293 K using graphite-monocromated Mo Kα radiation ($\lambda = 0.71073$ Å) and oscillation scans technique. The structures were solved by direct methods (SHELXS-97)[10] and non-H atoms were refined by full-matrix least-squares method with anisotropic temperature factors. **Crystal data for compound 8**: $CH_{16}Br_2O_4$, crystal system, space group monoclinic, $P21$; unit cell dimensions $a = 8.2666$ (7), $b = 8.1952$ (8), $c = 8.3424$ (7) Å, $\beta = 117.88$ (2); volume 499.53 (8) Å^3; $Z = 4$; calculated density 4.707 mg/m^3; absorption coefficient 16.216 mm^{-1}; F (000) 688; crystal size 0.04 × 0.03 × 0.02 mm^3; θ range for data collection 2.4−30.5°; completeness to θ 30.5, 99.0%; refinement method full-matrix least-squares on F^2; data/parameters 2866/138; goodness-of-fit on F^2 1.297; final R indices [$I > 2\sigma(I)$] $R_1 = 0.094$, $wR_2 = 0.142$; $R_{int} = 0.078$; extinction coefficient 0.00; largest diff. peak and hole 0.92 and −0.52 e Å^{-3}.

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