2,3-Dioxabicyclo[2.2.2]oct-7-en-5-one: Synthesis and Reactions of the Keto Endoperoxide of Phenol

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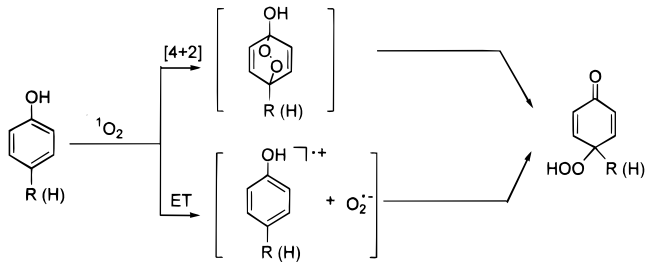
The photooxygenation of 1,4-cyclohexadiene (**3**) affords the diastereomeric hydroperoxy endoperoxides *exo*-**4** and *endo*-**4** and the diastereomeric hydroperoxides *trans*-**5** and *cis*-**5** in a ratio of 87:9:3.5:0.5. Selective reduction of hydroperoxide group in the endoperoxides *exo*-**4** and *endo*-**4** in the presence of titanium tetraisopropoxide−diethyl sulfide gave the corresponding hydroxy endoperoxides *exo*-**7** and *endo*-**7**, which on PCC oxidation leads to the phenol-derived keto endoperoxide **2**. The triphenylphosphine deoxygenation of the keto endoperoxide **2** produces a 9:1 mixture of 1,2- and 1,4-dihydroxybenzenes **10** and **11**, while the CoTPP-catalyzed rearrangement affords the bisepoxide **12**, malealdehyde (**13**), and β-lactone **14**. The mechanisms of these transformations are presented.

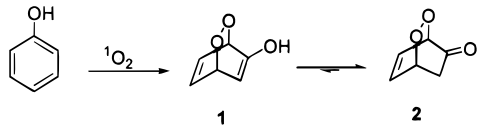
Introduction

Singlet oxygen ($^1O_2$) is an effective electrophilic oxidant for a variety of electron-rich organic compounds.[1] Among these, phenols are of interest because these ubiquitous organic substances (found in natural waters, drinking water, and wastewater) are rapidly oxidized by singlet oxygen. Moreover, phenols occur numerously as anthropogenic pollutants (e.g., industrial solvents, coal- and petroleum-derived wastes, detergent metabolites, pesticides, and antioxidants), but also in natural products[2] (e.g., amino acids, vitamins, lignin, and humic substances). Previous studies have shown that in the dye-sensitized photooxygenation of phenols,[3] the singlet oxygen produces hydroperoxides (Scheme 1); however, the parent phenol does not undergo this reaction because it physically quenches singlet oxygen efficiently.[2,4] In contrast, the more electron-rich derivatives (catechol and methoxybenzenes, such as 1,2,3,4-tetramethoxybenzene) do react chemically with singlet oxygen.[1e,5] Plausible mechanisms are [$_\pi4_s + {}_\pi2_s$] cycloaddition of the singlet oxygen to the phenol and subsequent ring-opening of the labile endoperoxide to its hydroperoxide, or electron-transfer (ET) between singlet oxygen and phenol to afford the hydroperoxide by way of the superoxide ion and the phenol radical cation (Scheme 1).[6]

Scheme 1



Scheme 2



As already stated above, the endoperoxide or its ring-opened hydroperoxide (Scheme 1, R = H) of the parent phenol is to date not known, nor is its regioisomeric endoperoxide **1** (Scheme 2), which may exist as its tautomeric endoperoxide **2**. Since the later is not directly accessible through photooxygenation of the parent phenol, in this paper we describe the indirect synthesis of the hitherto unknown endoperoxide **2** and its chemistry. We demonstrate that an effective methodology involves 1,4-cyclohexadiene, which allows the introduction of the three oxygen functionalities at the required positions and further functionalization.

Results and Discussion

Preparation of the Keto Endoperoxide 2. Tetraphenylporphine(TPP)-sensitized photooxygenation of 1,4-

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(1) (a) Saito, I.; Matsuura, T. *In Singlet Oxygen*; Wasserman, H. H.; Murray, R. W. Eds.; Academic: New York, 1979. (b) Adam, W.; Prein, M. *Acc. Chem. Res.* **1996**, *29*, 275. (c) Adam, W.; Prein, M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 477. (d) Balci, M. *Chem. Rev.* **1981**, *81*, 91. (e) Frimer, A. A. Ed. *Singlet Oxygen*; CRC Press: Boca Raton, FL, 1985. (f) Frimer, A. A. *The Chemistry of Peroxides*; John Wiley: Chichester, 1983, 201.
(2) Tratnyek, P. G.; Holgne, *J. Environ. Sci. Technol.* **1991**, *25*, 1596.
(3) (a) Matsuura, T.; Omura, K.; Nakashima, R. *Bull. Chem. Soc. Jpn.* **1965**, *38*, 1358. (b) Matsuura, T.; Nishinaga, A.; Yoshimura, N.; Arai, T.; Omura, K.; Matsushima, H.; Kato, S.; Saito, I. *Tetrahedron Lett.* **1969**, 1673. (c) Saito, I.; Kato, S.; Matsuura, T. *Tetrahedron Lett.* **1970**, 4987.
(4) Yamaguchi, K.; Ikeda, Y.; Fueno, T. *Tetrahedron* **1985**, *46*, 2099.
(5) Thomas, M. J.; Foote, C. S. *Photochem. Photobiol.* **1978**, *27*, 325.
(6) Foote, S. C.; Jensen, F. *Photochem. Photobiol.* **1987**, *46*, 325.

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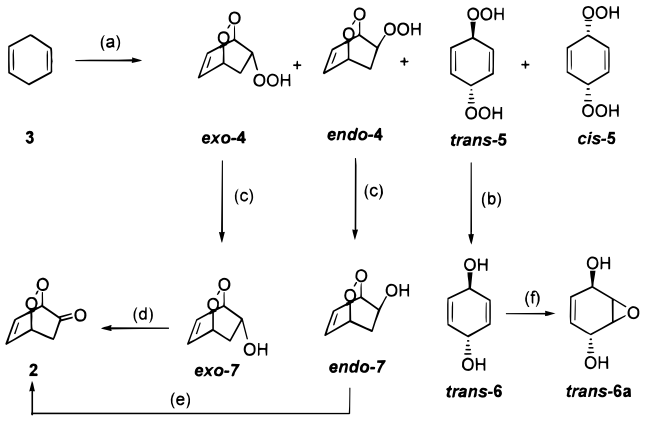
Scheme 3[a]



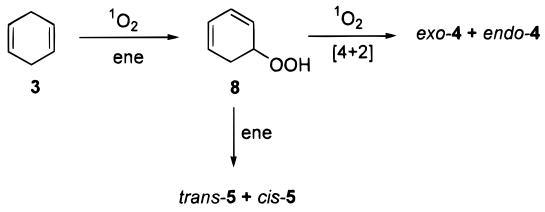
[a] Reagents: (a) O_2, TPP, *hv*, chloroform; product composition: *exo*-**4** (87%), *endo*-**4** (9%), *trans*-**5** (3.5%), *cis*-**5** (0.5%); (b) PPh_3, 20 °C, yield 75%; (c) Et_2S (1.2 equiv), Ti(O*i*-Pr)$_4$ (5 mol %), CH_2Cl_2, 5 °C, 4 Å molecular sieves, yield 96%; (d) PCC, CH_2Cl_2, ca. 20 °C, yield 52%; (e) PCC, CH_2Cl_2, ca. 20 °C, yield 48%; (f) *m*-CPBA (1 equiv), CH_2Cl_2, rt, (70% conversion).

cyclohexadiene (**3**) at −20 °C in chloroform solution gave the two known endoperoxides *exo*-**4** and *endo*-**4**,[7] and additionally the two labile bishydroperoxides *trans*-**5** and *cis*-**5** (*Caution! explosive*). These products were separated by silica gel column chromatography at low temperature (Scheme 3). A pure sample of the bishydroperoxide *trans*-**5**, which eluted together *exo*-**4** and *cis*-**5**, was obtained by means of several crystallizations. All attempts to isolate the bishydroperoxide *cis*-**5** failed because it was thermally too labile for isolation and decomposed immediately.

The structural assignment of the bishydroperoxide *trans*-**5** rests on its spectral and chemical data. Thus, the elemental analysis confirmed the empirical formula $C_6H_8O_4$, while the cyclohexadienyl hydroperoxide structure was established by its 250 MHz ^{1}H NMR and 63 MHz ^{13}C NMR and IR spectra. The ^{1}H NMR spectrum displayed a broad singlet at δ 10.75, which was assigned to the hydroperoxide proton. Olefinic and aliphatic protons comprise two separate multiplets at δ 6.17 and 4.73, while the IR band at 3381 cm^{-1} discloses the −OOH functionality. The suggested structure is in good accord with the ^{13}C NMR spectrum (one sp^2 and one sp^3 carbon atom). For chemical confirmation, the hydroperoxide group in *trans*-**5** was reduced with triphenylphosphine[1d] to the *trans*-**6** diol, whose symmetry is evident by the expected two-line ^{13}C NMR resonances. To support the correct configuration of the alcohol and peroxide functionalities in **5** and **6**, *trans*-**6** diol was treated with 1 mol of *m*-CPBA at 0 °C. The obtained mono-epoxide showed an asymmetric structure (six lines in the ^{13}C NMR) which indicates clearly the trans configuration of the starting material.

The formation of the diastereomeric endoperoxides *exo*-**4** and *endo*-**4**, as well as the diastereomeric hydroperoxides *trans*-**5** and *cis*-**5**, is outlined in Scheme 4. The first ene reaction of singlet oxygen leads to the monohydroperoxide **8**, which reacts subsequently with another singlet-oxygen molecule by a [4 + 2] cycloaddition to the

Scheme 4



endoperoxides *exo*-**4** and *endo*-**4**. Alternatively, a second ene reaction of the monohydroperoxide **8** affords the bishydroperoxides *trans*-**5** and *cis*-**5**.

The hydroperoxy-functionalized endoperoxides *exo*-**4** and *endo*-**4** are suitable substrates for the synthesis of the phenol-derived endoperoxide **2** since the two oxygen functionalities are regiomerically properly located in the six-membered ring as desired for the synthesis of the phenol endoperoxide. Reduction of the hydroperoxide group in the endoperoxides *endo*- and *exo*-**4** and subsequent oxidation should afford the desired phenol endoperoxide **2** (Scheme 2). However, it is well-known that both hydroperoxides and endoperoxides are highly susceptible to reductive cleavage by a variety of reductants.[1f] Moreover, since in the present case *exo*-**4** and *endo*-**4** possess both endoperoxide and hydroperoxide linkages, a selective reduction was required for the preservation of the endoperoxide functionality. This selective reduction was achieved by using titanium tetraisopropoxide in the presence of diethyl sulfide as reductant, which gave the desired hydroxy endoperoxides *exo*-**7** and *endo*-**7** (Scheme 3, step c).

The structures of the hydroxy endoperoxides *exo*-**7** and *endo*-**7** were assigned by spectroscopic and chemical methods. For instance, a peroxide test with KI/HOAc confirmed that the endoperoxide linkage was preserved. The most conspicuous features in the ^{1}H NMR spectra of the hydroxy endoperoxides *exo*-**7** and *endo*-**7** are two distinct AB systems which correspond to two olefinic and two methylenic protons. The olefinic protons of *exo*-**7** at δ 6.44−6.71 show further splitting with the adjacent bridgehead protons. The methylenic protons appear as an AB system at δ 2.50 and 1.24 and are definitive for the proposed alcohol structure. The proposed structures are also in agreement with the ^{13}C NMR spectral data.

For the oxidation of the alcohols *exo*-**7** and *endo*-**7** to the keto derivative **2**, several chromate reagents[8−10] were tried, but the best yield (52% for the conversion of *exo*-**7** and 48% for *endo*-**7**) was obtained with pyridinium chlorochromate (PCC)[11] as oxidant (Scheme 3, steps d and e). The structure assignment of the keto endoperoxide **2** is based on its analytical and spectral data. The elemental analysis revealed the emprical formula $C_6H_6O_3$, while the ^{13}C NMR spectrum displayed the expected six carbon resonances. The IR band at 1748 cm^{-1} indicates the presence of the carbonyl group.

Transformations of the Keto Endoperoxide 2. The keto endoperoxide **2** persists at room temperature (ca. 25 °C) and does not decompose to phenol and oxygen under these conditions. Upon heating at 90−95 °C for 24 h, only 20% of the keto endoperoxide **2** was decom-

(7) (a) Seçen, H.; Salamci, E.; Sütbeyaz, Y.; Balci M. *Synlett* **1993**, 609. (b) Seçen, H.; Salamci, E.; Sütbeyaz, Y.; Balci, M. *J. Org. Chem.* **1997**, *62*, 2453. (c) Seçen, H.; Salamci, E.; Sütbeyaz, Y.; Balci M. *Synth. Commun.* **1997**, *27*, 2223.

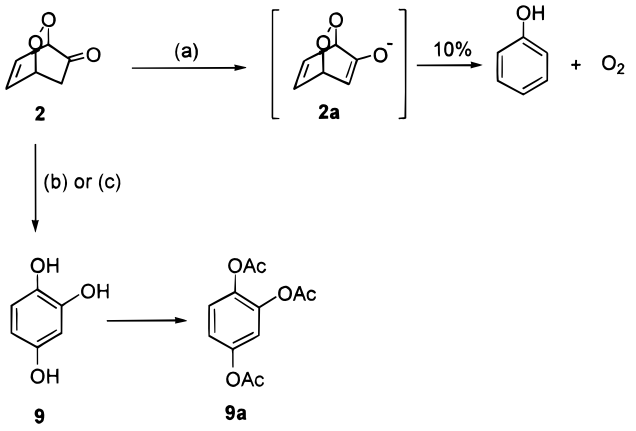
(8) Srimivason, R.; Stanley, P.; Balasubramanian, K. *Synth. Commun.* **1997**, *27*, 2057.

(9) Zhang, G.-S.; Shi, Q.-Z.; Chen, M.-F., Cai, K. *Synth. Commun.* **1997**, *27*, 3691.

(10) Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, 399.

(11) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.

Scheme 5[a]



[a] Reagents: (a) *t*-BuOK (1.0 equiv), DMF, 10 °C, HCl/H_2O; (b) NEt_3, Ac_2O $CHCl_3$, −60 °C, 2 h and 20 °C, 10 h, yield 60%; (c) *t*-BuOK (1.0 equiv), THF, rt, HCl/H_2O, yield 70%.

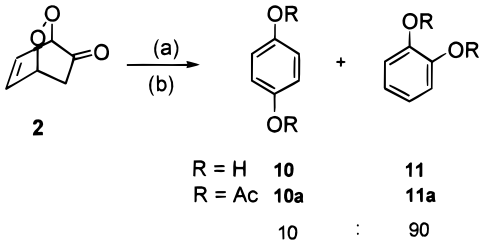
posed and formed polymeric materials; however, when endoperoxide **2** was treated with potassium *tert*-butoxide in DMF at 10 °C (Scheme 5, step a), phenol was the only isolable product. Thus, the labile phenolate endoperoxide **2a** must have been generated in situ as an intermediate, which readily released O_2.[12] Presumably, the released oxygen is again in the singlet state. To determine the electronic nature of the released oxygen we have carried the thermolysis as well as the base-promoted reaction of **2** in the presence of tetramethylethylene, which acts as singlet oxygen trapping agent. We were not able to detect any reaction (ene-reaction) between the generated oxygen and tetramethylethylene. But, these results do not exclude the formation of the singlet oxygen. It is well-known that phenols are capable of quenching singlet oxygen. Therefore, we assume that the generated singlet oxygen may be quenched by the formed phenols.[13]

Potassium *tert*-butoxide and triethylamine (Scheme 5, step a) abstract the bridgehead protons[14] of the keto endoperoxide **2** to form 1,2,4-benzenetriol (**9**),[15a−c] which was treated with acetic anhydride to afford the known 1,2,4-triacetoxybenzene **9a** (Scheme 5).[15d]

The triphenylphosphine deoxygenation[1d] of the keto endoperoxide **2** in $CHCl_3$ led to a mixture of 1,2- and 1,4-dihydroxybenzenes **10** and **11**, which were confirmed by comparison with authentic sample (Scheme 6, step a), e.g., no melting-point depression. Presumably, the reaction mechanism involves triphenylphosphine oxide elimination to give the corresponding epoxy enones, which can easily afford the two hydroxybenzenes **10** and **11**. For the characterization, **10** and **11** were converted to the diacetates **10a** and **11a** (Scheme 6, step b).

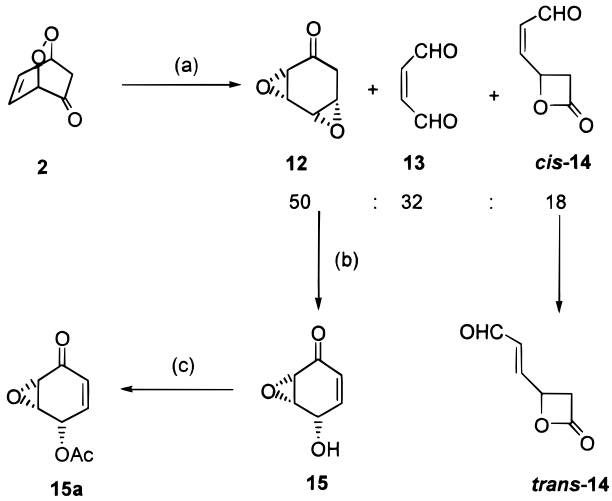
Endoperoxide **2** was submitted to the cobalt *meso*-tetraphenylporphine (CoTPP) complex[16] which catalyzed

Scheme 6[a]



[a] Reagents: (a) Ph_3P (1.0 equiv), $CHCl_3$, 0 °C, 30 min; (b) pyridine, Ac_2O, $CHCl_3$, 20 °C, 10 h, yield 70%.

Scheme 7[a]



[a] Reagents: (a) CoTPP 2 mol %, CH_2Cl_2, 20 °C, 2 h; (b) SiO_2, hexane/EtOAc, 20 °C; (c) pyridine, Ac_2O, $CHCl_3$, 20 °C, 4 h, yield 80%.

the rearrangement to the three products **12**−**14** in a ratio of 50:32:18, as confirmed by 200 MHz ^{1}H NMR spectroscopy (Scheme 7, step a). The resulting mixture was chromatographed on a silica gel from which only the rearranged product **15** was isolated (Scheme 7, step b). SiO_2 is responsible for the isomerization of the keto bisepoxide **12** (it persists in solution) to the epoxyenone **15**, whose structure was elucidated on the basis of NMR analysis and chemical transformation.[17]

Thus, acetylation with acetic anhydride in the presence of pyridine gave the corresponding acetate **15a** (Scheme 7, step c), for which the acetoxy functionality was confirmed by the IR band at 1758 cm^{-1}. The structure of the labile β-lactone **14**, which decomposes during silica gel chromatography, was determined by means of NMR data. However, low-temperature flash-chromatography allowed us to isolate *trans*-**14** in a purity of 80%. The aldehyde proton gives a doublet at δ 9.55, the olefinic protons display an AB system, and its large coupling constant (J = 16.0 Hz) clearly manifests the trans configuration of the double bond. Furthermore, the coupling constants of $^3J_{cis}$ = 6.3 Hz and $^3J_{trans}$ = 4.5 Hz and the geminal coupling constant (^2J = 16.4 Hz) support the presence of the four-membered ring. The ^{1}H NMR data of the *cis*-**14** has been extracted from the reaction

(12) (a) Noh, T.; Yang, N. C. *J. Am. Chem. Soc.* **1991**, *113*, 9412. (b) Schafer-Ridder, M.; Brocker, U.; Vogel, E. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 228.

(13) (a) Thomas, M. J.; Foote, C. S. *Photochem. Photobiol.* **1978**, *27*, 683. (b) Foote, C. S.; Thomas, M. J.; Ching, T.-J. *J. Photochem.* **1976**, *5*, 172. (c) Foote, C. S.; Ching, T.-J.; Geller, G. G. *Photochem. Photobiol.* **1974**, *20*, 511. (d) Saito, I.; Imuta, M.; Matsuura, T. *Tetrahedron* **1972**, *28*, 5307.

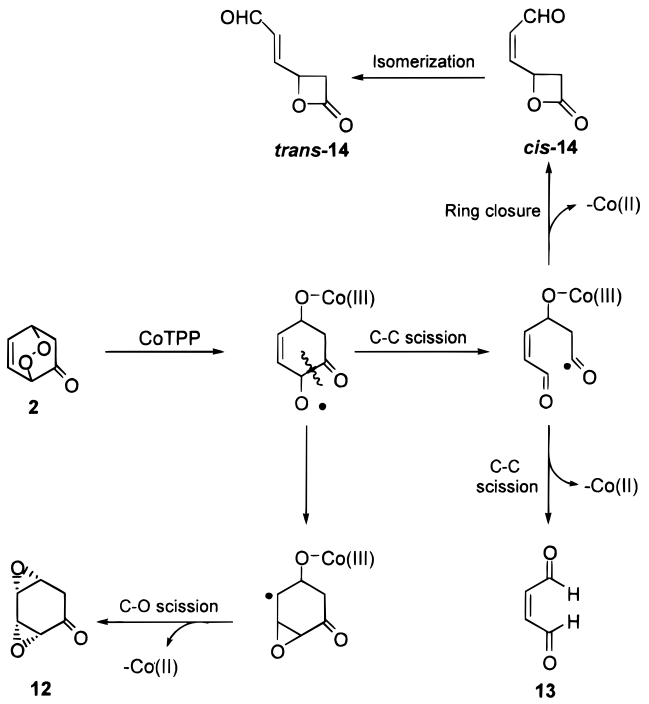
(14) Kornblum, N.; De La Mare, H. E. *J. Am. Chem. Soc.* **1951**, *73*, 880.

(15) (a) Callaghan, P. D.; Gibson, M. S. *J. Chem. Soc.* (*C*) **1970**, 2106. (b) Kurien, K. C. Robins, P. A. *J. Chem. Soc.* (*B*) **1970**, 855. (c) Luijkx, G. A. C.; Rantwijk, F.; Bekkum, H. *Recl. Trav. Chim. Pays-Bas* **1991**, *110*, 343. (d) Gent, P. A.; Gigg, R. *J. Chem. Soc.* (*C*) **1970**, 2253.

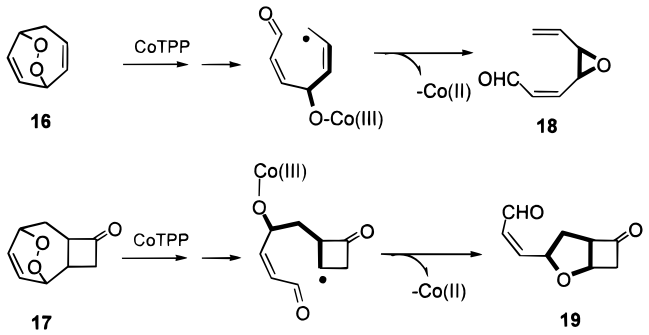
(16) (a) Boyd, J. D.; Foote, C. S.; Imagawa, D. K. *J. Am. Chem. Soc.* **1980,** *102*, 3641. (b) Sütbeyaz, Y.; Seçen, H.; Balci, M. *J. Org. Chem.* **1988**, *53*, 2312.

(17) For similar rearrangement see: Block, O.; Klein, G.; Altenbach, H.-J.; Brauer, D. *J. Org. Chem.* **2000**, *65*, 716.

Scheme 8



Scheme 9



mixture. Especially, the determined coupling constant between the olefinic protons (J_3 = 11.0 Hz) indicates clearly the cis configuration. The spectral data of the dialdehyde **13** are in agreement with the reported ones.[18a−c]

The mechanism of the CoTPP-catalyzed decomposition of the keto endoperoxide **2** involves radical pathways (Scheme 9).[16] The alkoxyl radical that results from electron transfer between the Co(ll) complex and the endoperoxide **2** serves as a key intermediate (Scheme 8). By scission of the C−C bond, the acyl radical is generated, which on cyclization produces the *β*-lactone **14** with cis configuration. The double bond in the *β*-lactone *cis*-**14** isomerizes partly to the *trans*-**14** under the reaction conditions. The scission of another C−C bond in the acyl radical forms malealdehyde **13** and radicals collapse into the double bond to give bisepoxide **12**. Related CoTPP-catalyzed decompositions have recently been observed, e.g., for the cycloheptatriene endoperoxide **16**[19] and cyclobutanone-annelated cycloheptadiene endoperoxide **17**,[20] which give the corresponding radical-cyclization products **18** and **19**.

In conclusion, a short and convenient method for the synthesis of the keto endoperoxide **2** has been developed starting from cyclohexa-1,2-diene. Upon base treatment, it decomposes readily through its tautomeric enolate **2a** to generate dioxygen and phenol. Furthermore, the chemistry of this hitherto unknown keto endoperoxide **2** was explored.

Experimental Section

Melting points were determined on a capillary melting point apparatus. IR spectra were obtained from films on NaCl plates for liquids or KBr pellets for solids on an infrared recording spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on 200, 250 (50, 62.5) MHz NMR spectrometers and are reported in δ units with $SiMe_4$ as internal standard. The column chromatography was performed on silica gel (60 mesh) and florisil (60−100 mesh).

Photooxygenation of 1,4-Cyclohexadiene (3). A sample of 2.00 g (24.98 mmol) of the olefine **3** and 30 mg of *meso*-tetraphenylporphine in 80 mL of chloroform were photolyzed for 24 h at −20 °C with a 150-W sodium lamp while a slow stream of oxygen gas was passed through the solution. After removal of the solvent (25 °C, 15 Torr), the mixture was chromatographed on silica gel (100 g) at −20 °C by elution with hexanes−Et_2O (3:2) to afford 2.82 g of products *exo*-**4**, *trans*-**5**, and *cis*-**5** and 0.27 g of (1.87 mmol, 7.5%) *endo*-**4**. The mixture of *exo*-**4**, *trans*-**5**, and *cis*-**5** was recrystallized from chloroform−hexane (4:1) to give 110 mg (0.76 mmol, 3%) of the bishydroperoxide *trans*-**5**. The filtrate was diluted with hexane and kept in the freezer, and 2.48 g (17.22 mmol, 69%) of *exo*-**4** was crystallized.

***exo*-2,3-Dioxabicyclo[2.2.2]oct-7-en-5-yl Hydroperoxide (*exo*-4).**[7b] Colorless powder from chloroform−hexane (3:2), mp 53−54 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.43 (br s, 1H), 6.75 (ddd, J = 11.3, 6.2, 1.5 Hz, 1H), 6.60−6.54 (m, 1H), 5.09−5.04 (m, 1H), 4.74−4.65 (m, 2H), 2.52 (ddd, J = 14.0, 8.5, 3.9 Hz, 1H), 1.19 (dm, J = 14.0 Hz, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 133.8, 129.0, 74.7, 70.7, 70.5, 29.3; IR (KBr, cm^{-1}) 3352, 2943, 1379, 1335, 1275, 1216, 1065, 1009, 971.

***endo*-2,3-Dioxabicyclo[2.2.2]oct-7-en-5-yl Hydroperoxide (*endo*-4).**[7b] Colorless powder from chloroform−hexane (3:2), mp 92−93 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.82 (br.s, 1H), 6.74 (ddd, J = 8.2, 5.8, 1.5 Hz, 1H), 6.63 (ddd, J = 8.2, 6.4, 1.8 Hz, 1H), 5.46 (dq, J = 6.4, 1.8 Hz, 1H), 4.64 (m, 1H), 4.21 (ddd, J = 10.0, 3.9, 1.8 Hz, 1H), 1.96 (ddd, J = 14.3, 10.0, 2.4 Hz, 1H), 1.83 (dt, J = 14.3, 3.6 Hz, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 134.9, 130.0, 77.4, 72.4, 70.8, 27.3; IR (KBr, cm^{-1}) 3321, 2926, 1424, 1374, 1069, 992, 915. Anal. Calcd for $C_6H_8O_4$: C, 50.03; H, 5.55. Found: C, 49.85, H, 5.56.

***trans*-4-Hydroperoxycyclohexa-2,5-dien-1-yl Hydroperoxide (*trans*-5).** Colorless plates from chloroform−hexane, decomposition above 40 °C without melting; ^{1}H NMR (200 MHz, CD_3COCD_3) δ 10.75 (br. s, 2H), 6.17 (m, 4H), 4.73 (m, 2H); ^{13}C NMR (50 MHz, CD_3COCD_3) δ 131.9, 77.3; IR (KBr, cm^{-1}) 3381, 2786, 1397, 1279, 1013, 903. Anal. Calcd for $C_6H_8O_4$: C, 50.03; H, 5.55. Found: C, 49.76, H, 5.72.

***trans*-2,5-Cyclohexadiene-1,4-diol (*trans*-6).**[21] To a stirred solution of 200 mg (1.38 mmol) of hydroperoxide *trans*-**5** in 50 mL of dichloromethane was added 0.73 g (2.76 mmol) of triphenylphosphine at 20 °C and stirred for 20 min. After removal of the solvent (ca. 20 °C and 15 Torr), the mixture was dissolved in hot chloroform and kept in the freezer, and 100 mg (1.04 mmol, 75%) of diol **6** as colorless plates was crystallized, mp 138−139 °C; ^{1}H NMR (200 MHz, CD_3COCD_3) δ 5.93 (m, 4H), 4.31 (m, 2H), 3.89 (m, 2H); ^{13}C NMR (50 MHz, CD_3COCD_3) δ 133.3, 64.3; IR (KBr, cm^{-1}) 3336, 3285, 2902, 1446, 1421, 1268, 1063, 1038, 961.

(18) (a) Adam, W.; Erden, I. *J. Am. Chem. Soc.* **1979**, *101*, 5692. (b) Chipman, D. M.; Chauhan, S. M.-S.; George, M. V. *J. Org. Chem.* **1980**, *45*, 3187. (c) Adger, B. M.; Barrett, C.; Brennan, J.; McKervey, M. A.; Murray, R. W. *J. Chem. Soc., Chem. Commun.* **1991**, 1553.
(19) Balci, M.; Sütbeyaz, Y. *Tetrahedron Lett.* **1983**, *24*, 4135.
(20) Şengül, M. E.; Şimşek, N.; Balci, M. *Eur. J. Org. Chem.* **2000**, 1359.
(21) Pan, X.-M.; Schuchmann, M. N.; von Sonntag, C. *J. Chem. Soc., Perkin Trans. 2* **1993**, 289.

Epoxidation of *trans*-6 diol. To a stirred solution of *trans*-**6** diol (50 mg, 0.44 mmol) in 10 mL of CH_2CI_2 at room temperature was added 83 mg (0.48 mmol) of *m*-CPBA, and the resulting mixture was stirred for 24 h. The precipitate was removed by filtration, and the solvent was removed under reduced pressure. The 200 MHz ^{1}H and 50 MHz ^{13}C NMR analyses indicated 70% conversion of diol to mono-epoxide *trans*-**6a**. ^{1}H NMR (200 MHz, CD_3COCD_3) δ 5.65 (ddd, J = 8.2, 6.1, 1.8 Hz, A-part of the AB-system, 1H), 5.5 (dm, J = 8.2, B-part of the AB-system, 1H), 4.4 (m, 1H), 4.25 (m, 1H), 3.25 (m, 1H), 3.2 (m, 1H). ^{13}C NMR (50 MHz, CD_3COCD_3) δ 131.29, 128.98, 59.37, 57.57, 56.78, 56.12.

***exo*-2,3-Dioxabicyclo[2.2.2]oct-7-en-5-ol (*exo*-7).** To a stirred solution of 270 mg (1.87 mmol) of hydroperoxide *exo*-**4** and 2 g of molecular sieves (4°) in 10 mL of dichloromethane at 5 °C were added 200 mg (2.22 mmol) of Et_2S and 26.0 mg (0.09 mmol) of titanium tetraisopropoxide. Five minutes later, the reaction was stopped by the addition of 40 μL of water, and the solids were removed by filtration. After removal of the solvent (ca. 20 °C and 15 Torr), the mixture was loaded on a short silica gel column (20 g), and elution with Et_2O−hexane (4:1) gave 220 mg (1.71 mmol; 92%) of *exo*-**7**, which was recrystallized from Et_2O−hexane, colorless prisms, mp 106−107 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.71 (ddd, J = 8.2, 6.1, 1.8 Hz, 1H), 6.48−6.42 (m, 1H), 4.64−4.55 (m, 2H), 4.28−4.20 (m, 1H), 2.50 (ddd, J = 14.0, 7.9, 3.6 Hz, 1H), 1.75 (br d, 1H), 1.24 (dm, J = 14.0, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 134.8, 129.0, 73.0, 70.8, 62.5, 35.0; IR (KBr, cm^{-1}) 3424, 2936, 1337, 1319, 1282, 1077, 1012, 970. Anal. Calcd for $C_6H_8O_3$: C, 56.02; H, 6.24. Found: C, 55.93, H, 6.00.

***endo*-2,3-Dioxabicyclo[2.2.2]oct-7-en-5-ol (*endo*-7).** To a stirred solution of 190 mg (1.31 mmol) of hydroperoxide *endo*-**4** and 1 g of molecular sieves (4°) in 10 mL of dichloromethane at 5 °C were added 142 mg (1.57 mmol) of Et_2S and 19.0 mg (0.065 mmol) of titanium tetraisopropoxide. The reaction was stopped by the addition of 30 μL of water and 5 min later, the solid material was removed by filtration. After evaporation of the solvent (20 °C and 15 Torr), the mixture was loaded on a short silica gel column (20 g) and elution with Et_2O−hexane (4:1) gave 160 mg (1.25 mmol, 95%) of solid *endo*-**7**, which was recrystallized from Et_2O−hexane, colorless needles, mp 91−92 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.72−6.60 (m, 2H), 4.46 (m, 1H), 4.55 (m, 1H), 3.85 (m, 1H), 2.80 (br. d, 1H), 2.04 (ddd, J = 14.3, 9.4, 2.1 Hz, 1H), 1.91 (dt, J = 14.3, 3.3 Hz, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 135.5, 131.4, 78.3, 72.7, 65.0, 33.8; IR (KBr, cm^{-1}) 3213, 2922, 1432, 1390, 1291, 1256, 1086, 998. Anal. Calcd for $C_6H_8O_3$: C, 56.02; H, 6.24. Found: C, 56.30, H, 6.14.

2,3-Dioxabicyclo[2.2.2]oct-7-en-5-one (2). To a stirred solution of 250 mg (1.95 mmol) of alcohol *exo*-**7** in 75 mL of dichloromethane was added 0.47 g (2.61 mmol) of pyridine chlorochromate (PCC) at room temperature (ca. 25 °C). The resulting mixture was stirred for 3 h and diluted with 50 mL of Et_2O, and the solid material was removed by filtration. After evaporation of the solvent (20 °C and 15 Torr), the residue was chromatographed on a silica gel (20 g) by elution with hexanes−Et_2O (1:4). The first fraction gave 100 mg (0.75 mmol, 52% based on converted starting material) of the keto endoperoxide **2** as a light yellow oil and 50 mg of unreacted alcohol *exo*-**7**.^{1}H NMR (200 MHz, $CDCl_3$) δ 6.95 (dm, J = 8.3 Hz, 1H), 6.70 (dm, J =8.3 Hz, 1H), 5.17−5.10 (m, 1H), 4.61 (dm, J = 6.5 Hz, 1H), 2.80 (dd, J = 18.1, 3.2 Hz, 1H), 2.34 (dd, J = 18.1, 2.4 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 201.0, 140.3, 129.7, 81.7, 75.6, 38.5; IR (film, cm^{-1}) 3072, 2989, 2931, 1748, 1396, 1354, 1307, 1178, 1020, 967. Anal. Calcd for $C_6H_6O_3$: C, 57.17; H, 4.76. Found: C, 56.75, H, 5.02.

2,3-Dioxabicyclo[2.2.2]oct-7-en-5-one (2) from *endo*-Alcohol 7. To a stirred solution of 55 mg (0.43 mmol) of alcohol *endo*-**7** in 15 mL of dichloromethane was added 0.1 g (0.55 mmol) of pyridine chlorocromate (PCC) at room temperature (ca. 25 °C). The reaction was carried out as described above. Chromatography on a silica gel (5 g) gave as the first fraction 17 mg (48%) of **2** based on converted starting material.

The Reaction of Keto Endoperoxide 2 with Potassium *tert*-Butoxide in DMF. To a stirred solution of 160 mg (1.26 mmol) of the keto endoperoxide **2** in 15 mL of DMF at 10 °C was added within 10 min 141 mg (1.26 mmol) of potassium *tert*-butoxide in 10 mL of DMF. The resulting mixture was stirred for 1.5 h and hydrolyzed with 5 mL HCl (5 N). The solution was extracted with Et_2O (2 × 100 mL) and dried over $MgSO_4$. After evaporation of the solvent (20 °C and 15 Torr), the residue was chromatographed on a silica gel column (15 g) by elution with hexanes−Et_2O (1:1). The first fraction gave 12.0 mg (0.12 mmol, 10%) of phenol.

2,4-Bis(acetyloxy)phenyl Acetate (9a).[15d] To a stirred solution of 0.30 g (2.34 mmol) of the keto endoperoxide **2** in 50 mL of chloroform at −60 °C were added within 2 h 470 mg (4.68 mmol) of NEt_3 and 3 mL of acetic anhydride. The mixture was allowed to reach room temperature (ca. 25 °C), and at this temperature the solution was stirred for 10 h. The mixture was poured into 50 mL of a saturated aqueous $NaHCO_3$ solution. The aqueous organic layer was extracted with Et_2O (2 × 100 mL), and the combined organic layers were dried over $CaCl_2$. Evaporation of the solvent (20 °C and 15 Torr) gave 0.35 g (1.38 mmol, 60%) of product **9a**, which was recrystallized from hexane, colorless plates, mp 100−101 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.19−6.97 (m, 3H), 2.27 (s, 9H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 168.8, 168.1, 167.8, 148.1, 142.2, 139.6, 123.5, 119.4, 117.1, 21.0, 20.6 (2C); IR (KBr, cm^{-1}) 3108, 2948, 1765, 1609, 1498, 1425, 1372, 1270, 1180, 1098, 1045, 962.

The Reaction of Keto Endoperoxide 2 with Potassium *tert*-Butoxide in THF. To a stirred solution of 50 mg (0.39 mmol) of the keto endoperoxide **2** in 10 mL of THF at room temperature was added 50 mg (0.4 mmol) of potassium *tert*-butoxide in 10 mL of THF. The resulting mixture was stirred for 3 h. The resulting mixture was hydrolyzed with 1 mL of HCl (5 N), and the solvent was evaporated. The residue was dissolved in 1 mL of acetic anhydride, and 1−2 drop of pyridine was added. The mixture was stirred for 6 h and poured into saturated $NaHCO_3$ solution and extracted with diethyl ether (2 × 20 mL). The organic layer was washed with water and dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed on a silica gel column (5 g) by elution with hexanes−Et_2O (7:3) giving 68 mg (0.27 mmol) of benzenetriacetate in 70% yield.

Deoxygenation of the Keto Endoperoxide 2 by Triphenylphospine. To a stirred solution of 0.45 g (3.57 mmol) of the keto endoperoxide **2** in 50 mL of chloroform at 0 °C was added within 30 min 0.93 g (3.57 mmol) of PPh_3; the triphenylphosphine oxide, a white solid precipitated. After evaporation of the solvent (20 °C and 15 Torr), the residue was redissolved in 10 mL of acetic anhydride containing 50 mg of pyridine and stirred at room temperature (ca. 25 °C) for 12 h. The mixture was poured into 50 mL of saturated aqueous $NaHCO_3$ solution, extracted with Et_2O (2 × 50 mL), and dried over $MgSO_4$. After removal of the solvent (20 °C, 15 Torr), the residue was chromatographed on silica gel (10 g) by eluting with hexane:EtOAc (4:1) to afford 0.48 g (2.49 mmol, 70%) of a 9:1 mixture of the diacetates **10a** and **11a**, identified by comparison ^{1}H NMR spectra and GC retention times with the authentic materials.

Decomposition of the Keto Endoperoxide 2 Catalyzed by the Cobalt Complex of *meso*-Tetraphenylporphine (CoTPP). To a stirred solution of 0.50 g (3.9 mmol) of the keto endoperoxide **2** in 50 mL of CH_2Cl_2 at room temperature (ca. 25 °C) was added 50 mg (0.078 mmol) of CoTPP. The resulting mixture was stirred for 3 h, and the solvent was removed (5 °C, 15 Torr). ^{1}H NMR analysis indicated that the products **12**−**14** were present in the mixture in a ratio of 50:32:18. The mixture was chromatographed on silica gel (30 g) by elution with hexane:EtOAc (1:1) to afford 150 mg (1.19 mmol, 30%) of the keto epoxy alcohol **15** as a brown oil.

***cis*-2-Butendial (13).**[18] ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.61 (AA′ part of AA′XX system, 2H), 6.68 (XX′ part of AA′XX′ system, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) 192.9, 142.0.

***syn*-5-Hydroxy-7-oxabicylo[4.1.0]hept-3-en-2-one (15).**[21] ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.51 (dt, J = 10.5, 2.8 Hz, 1H), 5.88 (dt, J = 10.5, 2.1 Hz, 1H), 4.66 (m, 1H), 3.83 (dd, J = 3.9, 2.1 Hz, 1H), 3.46 (dd, J = 3.9, 2.1 Hz, 1H), 2.80 (bs, 1H); ^{13}C

NMR (50 MHz, $CDCl_3$) δ 194.6, 147.3, 127.3, 66.9, 56.4, 55.5; IR (film, cm^{-1}) 3387, 2953, 1707, 1421, 1446, 1293, 1268, 1089, 1063.

***syn*-5-Oxa-7-oxabicylo[4.1.0]hept-3-en-2-yl Acetate (15a).** To a stirred solution of 100 mg (0.79 mmol) of **15** in 2 mL of acetic anhydride at room temperature (ca. 20 °C) was added a drop of pyridine, the resulting mixture was stirred for 4 h, and the solvent was evaporated (40 °C, 15 Torr). The residue was chromatographed on silica gel (30 g) by elution with hexane:EtOAc (4:1) to yield 85.0 mg (0.50 mmol, 80%) of acetate **15a** as a yellow oil and 20 mg unreacted **15**. ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.51 (dt, J = 10.5, 2.4 Hz, 1H), 5.96 (dt, J = 10.5, 2.1 Hz, 1H), 5.76 (dd, J = 5.0, 2.4 Hz, 1H), 3.85 (m, 1H), 3.44 (dd, J = 4.1, 2.1 Hz, 1H), 2.20 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 193.8, 171.7, 142.9, 128.7, 68.6, 54.3, 53.4, 22.6; IR (NaCl film, cm^{-1}) 3055, 2927, 1758, 1702, 1395, 1268, 1165, 1063, 910. Anal. Calcd for $C_8H_8O_4$: C, 57.17; H, 4.76. Found: C, 56.96, H, 4.93.

(*Z*)-3-(4-Oxooxetan-2-yl)prop-2-enal (14). ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.84 (d, J = 5.0 Hz, 1H), 6.58 (dd, J = 11.0, 7.0 Hz, 1H), 6.36 (dd, J = 11.0, 5.0 Hz, 1H), 5.66 (m, 1H), 3.62 (dd, J = 16.0, 6.4 Hz, 1H), 3.28 (dd, J = 16.0, 4.5 Hz, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 195.5, 168.7, 147.5, 146.9, 132.0, 68.7, 47.5.

(*E*)-3-(4-Oxooxetan-2-yl)prop-2-enal (14). ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.55 (d, J = 7.5 Hz, 1H), 6.81 (dd, J = 16.0, 6.0 Hz, 1H), 6.36 (dd, J = 16.0, 7.5 Hz, 1H), 5.11 (m, 1H), 3.78 (dd, J = 16.4, 6.3 Hz, 1H), 3.28 (dd, J = 16.4, 4.5 Hz, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 192.1, 167.8, 147.9, 133.1, 67.7, 44.6.

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