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Photooxygenation of an Enol Ether: Synthesis of exo- and endo-3,4-Dioxa-2,5-dimethoxy-7,8-benzo[4.2.2.$0^{2,5}$]deca-7,9-diene and its Chemical Transformations

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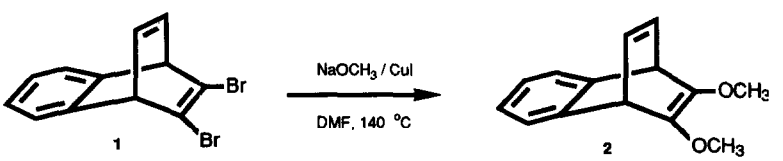
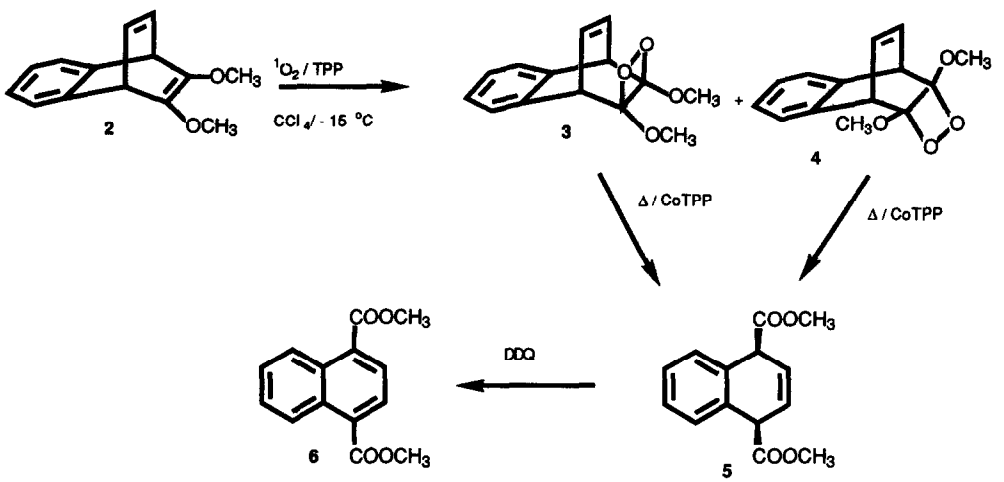
Abstract: The reaction of singlet oxygen with 2 afforded two isomeric dioxetanes 3 and 4 which were decomposed upon heating to the expected dihydronaphthalene derivative 5. Photooxygenation of 2 in the presence of thiourea resulted in the formation of diketone 8 and ketal 7 ; the later presumably derived from incorporation of the solvent molecule.

The cycloaddition of singlet oxygen to electron-rich olefins such as enol ethers and enamines is a general route for the preparation of dioxetanes[1]. In 1970, Bartlett and Schaap showed that cis-3,4-diethoxy-1,2-dioxetane could be prepared in high yield via the reaction of singlet oxygen with cis-diethoxyethylene[2]. Alkenes with readily abstractable allylic hydrogen atoms generally undergo the ene reaction to yield allylic hydroperoxide instead of dioxetanes[1-3]. Therefore, 1,2-addition of singlet oxygen to electron-rich olefins competes ineffectively with the other reaction modes, ene reaction and 1,4-cycloaddition. Bicyclic systems such as norbornene, barrelene etc. are ideal compounds to generate dioxetanes because the required allylic shift is geometrically impossible. The characteristic reaction of dioxetanes is the chemiluminescent thermal decomposition to two carbonyl fragments. Therefore, dioxetanes become obvious synthetic targets for the synthesis of the unusual compounds with definitive stereochemistry. In this paper, we describe the synthesis of two dioxetanes derived from 2,3-dimethoxybenzobarrelene **2** and their chemical transformations.



Scheme 1

The starting material dimethoxybenzobarrelene **2** was synthesized by copper-promoted nucleophilic substitution by methoxide[4] ion of dibromobenzobarrelene[5] **1** in a yield of 80 % as shown

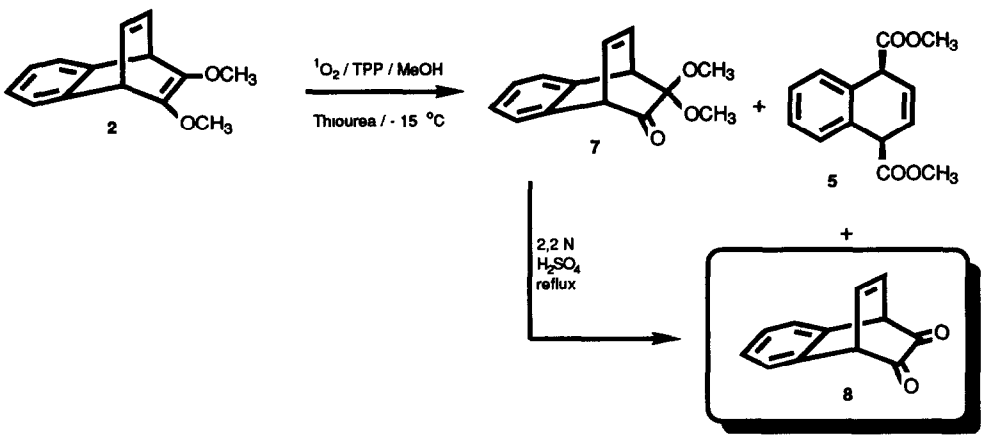


Scheme 2

in scheme 1. The structure of **2** was established unambiguously on the basis of ^{1}H-NMR spectra. The observed AA'BB' system (aromatic protons) and AA'XX' system (olefinic and bridgehead protons) are in agreement with the proposed symmetrical structure.

The photooxygenation[6] of the enol ether **2** in aprotic solvent (carbon tetrachloride) using tetraphenylporphyrine as sensitizer at -15 °C gave three products, the dioxetanes **3**, **4** and dihydronaphthalene derivative **5** in a ratio of 5:2:2, respectively (Scheme 2). The isomeric dioxetanes could not be separated due to the instability of these formed products on column material. The dioxetanes have been characterized by means of their ^{1}H-NMR data and chemical transformations. We assume that the major product **3** has the exo-configuration. Numerous experimental and theoretical studies have shown that the reactivity of the double bond in this kind of systems is characterized by a pronounced preference for exo-attack[7]. Subsequently, cleavage of the weak oxygen-oxygen bond on warm-up to room temperature (partly at lower temperatures) afforded the expected 1,4-cis-carbomethoxy-1,4-dihydro-naphthalene **5**[8]. The ^{1}H-NMR of **5** shows two distinct AA'BB' system as expected from the symmetrical structure. For further characterization we converted this dihydronaphthalene derivative **5** into the corresponding 1,4-carbomethoxynaphthalene **6** upon oxidation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone. On the other hand, both dioxetanes **3** and **4** were treated with Cobalt-(II)-tetraphenyl porpyrine[9] at low temperature and we isolated again **5** as the sole product nearly in quantitative yield. This synthetic method is a stereospecific way leading to the cis-1,4-dihydro-1,4-disubstituted naphthalene derivatives.

It is well established that thiourea reduces only the oxygen-oxygen bond and thus preserves most other functional groups in the molecule[10]. Therefore, we carried out the photooxygenation reaction in the presence of thiourea in methanol at -15 °C and obtained a reaction mixture consisting of **5**, **7**, and **8** in a yield of 15, 45 and 19 %, respectively (Scheme 3). Dihydronaphthalene **5** is probably formed directly from thermolysis of the formed dioxetanes **3** and **4** as described above. Diketone **8** is the expected product in this reaction.

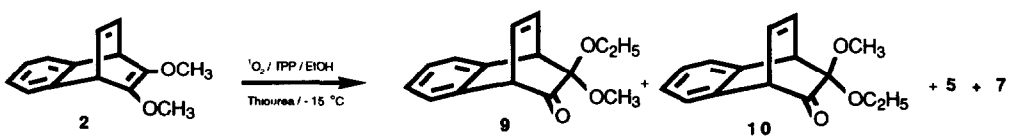


Scheme 3

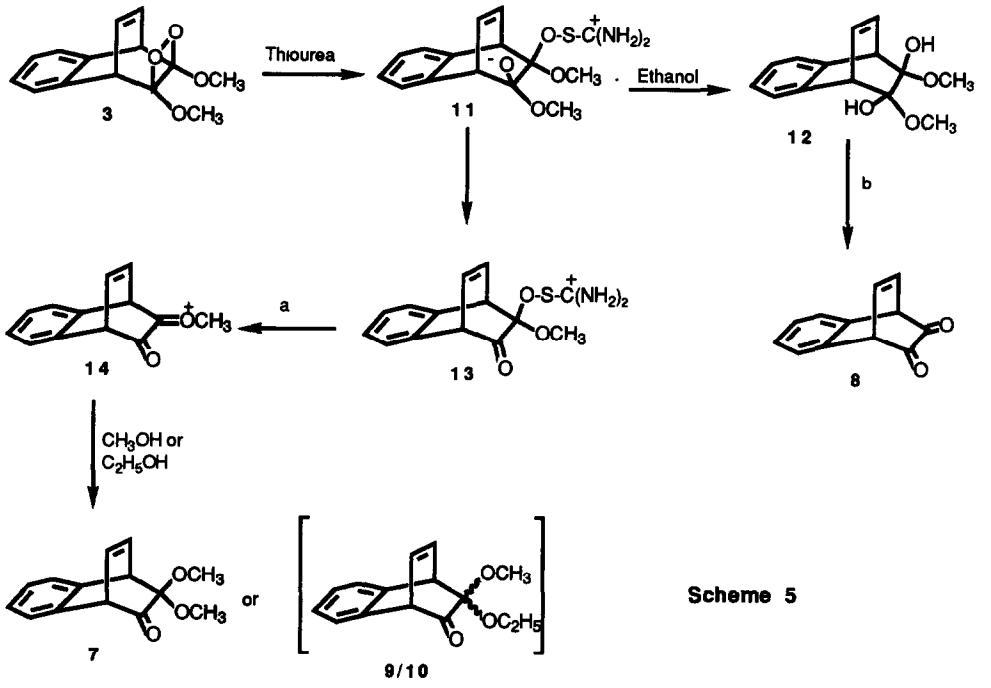
We have been able to isolate all three products by careful silica gel column chromatography. The ^{1}H- and ^{13}C-NMR spectra of **8**[11] were highly symmetrical according to the symmetry in the molecule. The ^{1}H-NMR spectrum consists of a singlet (aromatic protons) and an AA'BB' system arising from the bridgehead and double bond protons. A six-line ^{13}C-NMR spectrum is in good agreement with the proposed structure. The diketone **8** was also obtained in pure state from the hydrolysis of **7** in an acidified water solution in a yield of 90%.

Dimethoxyketal **7** has been characterized by means of spectral data. The aromatic protons of **7** resonate at δ 7.2-7.4 ppm as multiplet due to the asymmetry in the molecule. Bridgehead protons and olefinic protons resonate as multiplets at δ 4.25 and δ 6.60, respectively. Two distinct methyl resonances at δ 3.20 and 3.40 ppm are good indication of an asymmetrical structure. On the other hand, the 14 line ^{13}C-NMR spectrum supports strongly the proposed structure.

The formation of **7** during this photooxygenation reaction is unexpected but in view of the formation mechanism is interesting. This ketal can be formed by ketalization of the formed diketone **8** in methanol. However, stability of **8** in methanol indicates that the ketalization mechanism is out of the question. For clarification of the reaction mechanism one should know whether both methoxyl groups in **7** are arising from the same molecule by a possible methoxyl shift or one of them is incorporated by solvent molecule. For that, we carried out photooxygenation reaction in ethanol instead of methanol. Careful examination of the reaction mixture indicated clearly the formation of an isomeric mixture consisting of **9** and **10** besides **5** and **8** (Scheme 4). We were not able to detect any trace of **7**. The molecules **9** and **10** contain exactly one methoxyl and one ethoxyl group.



Scheme 4



Scheme 5

On the basis of the ethanol reaction we can conclude that the second methoxyl group in **7** is incorporated by solvent molecule. For the formation of **7** and **8** we suggest the following reaction mechanism as depicted on scheme 5. Photooxygenation of **2** formS the corresponding dioxetanes **3** and **4** initially. Subsequent heterolytic cleavage of the peroxide linkage in dioxetanes **3** and **4** supported by thiourea affords the intermediate **11**[12] which can undergo two different routes. Following route **a** can form an ionic species, such as **14** which can be intercepted by methanol (or ethanol) to give isomeric solvent-incorporated products **7** or **9/10**. By the second cleavage route of the intermediate **11** (route **b**), diketone **8** can be formed from the corresponding hemiketal **12**.

Experimental Section

General: Melting points were determined on a Thomas-Hoover capillary melting point apparatus. Solvents were concentrated at reduced pressure. Infrared spectra were obtained from films on NaCl plates for liquids or from solution in 0.1 mm cells or KBr pellets for solids on a Perkin-Elmer 337 Infrared recording spectrophotometer. The ^{1}H-NMR spectra were recorded on an EM 360 Varian, Varian 200 and Brucker WM 300 MHz spectrometer and are reported in δ units with $(CH_3)_4Si$ as internal standard. Apparent splittings are given in all cases. All column chromatography was performed on silica gel (60-mesh, Merck). TLC was carried out on Merck 0.2 mm silica gel 60 F_{254} analytical alumina plates.

2,3-Dimethoxybenzobarrelene 2: Freshly cut sodium (0.6g, 26 mmol) was added to 15 mL of absolute methanol under nitrogen. When the reaction was completed , the solution was diluted by dry DMF (15 mL). To the mixture was added CuI (0.25 g, 1.3 mmol) and a solution of 2,3-dibromobenzobarrelene **1** (0.4 g, 1.28 mmol) in 50 mL of dry DMF. After the mixture was refluxed for 12h at 110-120 ^oC (620 mm Hg) , was cooled to room temperature, added water (200 ml), extracted with ether (2X 200 mL), and dried ($MgSO_4$). Evaporation of the solvent and chromatography of the residue on a basic Al_2O_3 column eluting with ether-hexane(1:99) gave 2.3-dimethoxybenzobarrelene **2** (220 mg, 80%).

^{1}H-NMR (60 MHz, CCl_4, TMS) δ 7.20-6.60 (AA'BB' system for aromatic protons, 4H, and AA' part of AA'XX'-system, 2H), 4.26 (XX' part of AA'XX'-system, 2H), 3.60 (s, methoxyl protons, 6H); IR (CCl_4) 3080, 2990, 2970, 2840, 1470, 1320, 1290, 1180. Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59; O, 14.93. Found: C, 79.03; H, 6.33.

Photooxygenation of 2,3-dimethoxybenzobarrelene 2 in CCl_4: To a magnetically stirred solution of (400 mg, 1.87 mmol) 2,3-dimethoxybenzobarrelene **2** in 50 mL of CCl_4 was given ca.10 mg of tetraphenylporphyrine (TPP) as sensitizer. The solution was irradiated with a projector lamp (150 watt) at -15 °C while passing continously a slow stream of dry oxygen gas. The progress of the photooxygenation was monitored by ^{1}H-NMR until essentialy complete consumption of the starting material. The reaction was completed in 1h. ^{1}H-NMR spectrum showed the formation of 1,4-dihydrodicarbomethoxy-naphthalene **5**, exo-, and endo-dioxetanes **3** and **4** in a ratio of 2:5:2, respectively.. Removing of the solvent and chromatography of the residue on a silica gel column eluting with ethyl acetate-petroleum ether (1:99) gave cis-1.4-dicarbomethoxy-1,4-dihydronaphthalene **5** (450 mg, 97%).

1,4-Dihydro-1,4-dicarbomethoxy-naphthalene 5[8]: ^{1}H-NMR (200 MHz, $CDCl_3$), δ 7.32 (br. s, 4H), 6.20 (AA'-part of AA'XX'-system, olefinic protons, 2H), 4.46 (XX'-part of AA'XX'-system, aliphatic protons, 2H), 3.67 (s, 6H). IR (CCl_4) 3020, 2940, 2740, 1730, 1490, 1430, 1260, 1220, 1150, 1040.

exo-Dioxetane 3: ^{1}H-NMR (200 MHz, $CDCl_3$), δ 7.20-7.29, (m, 4H) , 6.75 (AA'-part of AA'XX'-system, olefinic protons, 2H), 4.20 (XX'-part of AA'XX'-system, bridgehead protons, 2H) 3.60 (s, 6H).

endo-Dioxetane 4: ^{1}H-NMR (200 MHz, $CDCl_3$), δ 7.25, (m, aromatic protons, 4H), 6.60 (AA'-Part of AA'XX'-system, olefinic protons, 2H), 4.20 (XX'-part of AA'XX'-system, bridgehead protons, 2H) 3.60 (s, 6H).

CoTPP-catalyzed photooxygenation of 2,3-dimethoxybenzobarrelene 2: The reaction was carried out as described above in the presence of 20 mg of Cobalt(II)-tetraphenylporphyrine. We obtained cis-1.4-dicarbomethoxy-1,4-dihydronaphthalene **5** as the sole product (96%).

1.4-Dicarbomethoxy-naphthalene 6: To a magnetically stirred solution of (280mg, 1.14 mmol) 1,4-dihydrodicarbomethoxynaphthalene **5** in 50 mL of benzene was added 0.26 g (1.14 mmol) dichlorodicyano-p-benzoquinone (DDQ). The reaction mixture was stirred at room temperature for 4h. After filtering of the precipitate, removing of the solvent and chromatography of the residue on a silica gel column eluting with benzene gave 1,4-dicarbomethoxynaphthalene **6** (139 mg, 54%). m.p 64-65 °C (recrystallized from CCl_4/ petroleum ether).

^{1}H-NMR (60 MHz, CCl_4, TMS) δ 9.00 -8.66 (AA'-part of AA'XX'-system, 2H), 8.00 (s, 2H), 7.66-7.40 (XX'-part of AA'XX'-system, 2H), 4.00 (s, methoxyl protons, 6H).

Photooxygenation of 2,3-dimethoxybenzobarrelene in MeOH and in the presence of thiourea: To a magnetically stirred solution of (790mg, 3.69 mmol) 2,3-dimethoxybenzobarrelene in 60 mL of chloroform was given ca. 30 mg of tetraphenylporphyrine (TPP) as sensitizer and a solution of thiourea (280 mg, 3.69 mmol) in 30 mL of methanol. The solution was irradiated with a projector lamp (150 watt) at -15 °C while passing continously a slow stream of dry oxygen gas for 3 h. The sulphur precipitate was filtered. Removing of the solvent and chromatography of the residue on a silica gel column (80 g) eluting with chloroform gave three products.

The first fraction: **3,3-Dimethoxy-1,4-dihydro-1,4-ethenonaphthalen-2-one 7**: Colorless liquid; 200 mg, 23%; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.40-7.20 (m, aromatic protons, 4H), 6.60 (m, olefinic protons, 2H), 4.25 (m, bridgehead protons, 2H), 3.40 (s, methoxyl protons, 3H), 3.20 (s, methoxyl protons, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 195.85, 138.26, 136.01, 134.31, 130.18, 127.37, 126.95, 125.26, 124.81, 91.54, 57.48, 50.35, 49.61, 47.72 . IR (liquid) 3070, 2940, 2820, 1740, 1450, 1340, 1290, 1200, 1130, 1050. Anal. Calcd for $C_{14}H_{14}O_3$: C, 73.02; H, 6.13; O, 20.85. Found: C, 73.53; H, 6.28.

The second fraction:**1,4-Dihydro-1,4-ethenonaphthalen-2,3-dione 8**: 100 mg, 15%, m.p 75-76 °C, recrystallized from ether/hexane; ^{1}H-NMR (200 MHz, $CDCl_{13}$) δ 7.40 (s, aromatic protons, 4H), 6.79 (AA'-part of AA'XX'-system, 2H), 4.61 (XX'-part of AA'XX'-system). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 182.15, 134.35, 132.34, 129.79, 126.68, 56.32. IR(KBr) 3060, 2990, 1740, 1500, 1450, 1300, 1220, 1170, 1090, 1010.

The third fraction: **1,4-Dihydrodicarbomethoxy-naphthalene 5**: 60 mg, 6.6 %. Spectral data are given above.

Hydrolysis of 3,3-dimethoxy-1,4-dihydro-1,4-ethenonaphthalen-2-one 7. : 140 mg (0.6 mmol) of dimethoxyketone **7** in 20 mL of H_2SO_4 (2.2 N) was refluxed for 12 h. After cooling to the room temperature, organic layer was extracted with ether (2x50 ml) and collected ether phases were extracted with $NaHCO_3$ (2x25 mL) and with water and dried ($MgSO_4$). Evaporation of the solvent gave 1,4-dihydro-1,4-etheno-naphthalene-2,3-dione **8** (97 mg, 88 %) which was crystallized from ether/hexane.

Photooxygenation of 2,3-dimethoxybenzobarrelene in the presence of thiourea in ethanol: To a magnetically stirred solution of (500 mg, 2.33 mmol) 2,3-dimethoxybenzobarrelene **2** in 60 mL of choloroform was given ca. 30 mg of tetraphenylporphyrine (TPP) as sensitizer and a solution of thiourea (180 mg, 2.43 mmol) in 30 mL of ethanol. The solution was irradiated with a projector lamp (150 Watt) at room temperature while passing continously a slow stream of dry oxygen gas for 3 h. The precipitate was filtered. Removing of the solvent and chromatography of the residue on a silica gel column (80 g) eluting with chloroform gave a mixture consisting of **9** and **10** (2:3, 400 mg, 70%) and cis-1,4-dicarbomethoxy- 1,4-naphthalene (100mg, 17%).

^{1}H-NMR (200 MHz, $CDCl_3$) δ 7.25 (br. s, aromatic protons, 4H), 6.55 (t, olefinic protons, 2H), 4.2 (t, bridgehead protons, 2H), 3,4-3,8 (m, two q, methylene protons, 2H), 3.35 (s, methoxyl protons), 3.2 (s, methoxyl protons), 0.8-1.4 (two t, methyl protons, 3H).

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