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Chemistry of dioxine-annelated cycloheptatriene endoperoxides and their conversion into tropolone derivatives: an unusual non-benzenoid singlet oxygen source

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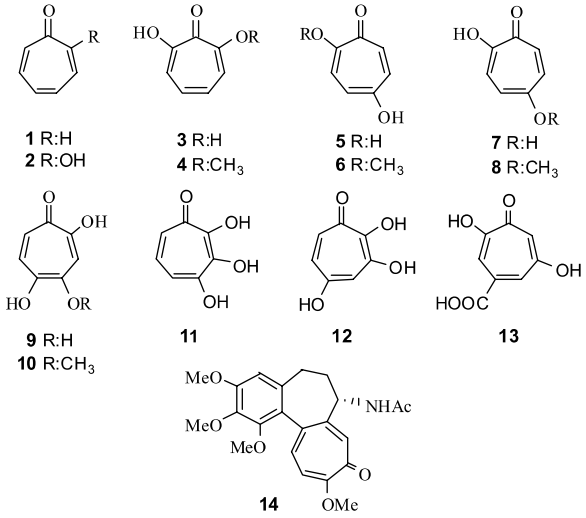
Abstract—The chemistry of two bicyclic endoperoxides, obtained by photooxygenation of 2,3-dihydro-7*H*-cyclohepta[1,4]dioxine and 2,3-dihydro-7*H*-cyclohepta[*b*][1,4]dioxin-7-one was investigated with the aim of synthesizing the respective tropolone derivatives. The reaction of these endoperoxides with base, thiourea and their thermolysis provided the desired tropolone derivatives in high yield. On the other hand, the thermolysis of the endoperoxide derived from 2,3-dihydro-7*H*-cyclohepta[*b*][1,4]dioxin-7-one underwent an unprecedented route and formed parent molecule and singlet oxygen instead of the expected troponoids. The formation mechanisms of all products are discussed.

1. Introduction

Tropone (**1**) and tropolone (**2**) have fascinated organic chemists for well over 50 years. The most significant reason for the interest in ring system tropones is that they represent the key structural element in a wide range of natural products, many of which **3**–**14** display interesting biological activity[1] such as the inhibitor activity of inositol monophosphatase,[2] antibiotic,[3] antitumor,[3a,4] antibacterial activity,[5] and lipoxygenase inhibitor activity.[6]



The synthesis of substituted tropone as well as tropolones continues to be a considerable synthetic challenge. Recently, renewed interest in the ability of colchicine **14** to inhibit tubulin polymerisation has been complemented by special new approaches to tropolone structures.[7] A number of syntheses of tropolone derivatives have been developed.[8] Although the tropones can be oxidized to the tropolones, those approaches suffer from regiochemical control problems when the substituted tropones are used as starting materials. In connection with the development of new synthetic strategies to tropolones, we recently studied the applicability of bicyclic endoperoxides derived by the cycloaddition of singlet oxygen[9] to the appropriate cyclic dienes and subsequently synthesized a new isomer of stipitatic acid **13**[10] and some benzotroponoid systems.[11]

In this paper, we report on the synthesis of new and possible bioactive tropolones via photooxygenation of oxygen-functionalized cycloheptatriene derivatives.

2. Results and discussion

The starting materials **16** and **18** were synthesized as reported in the literature. The thermolysis of tropone

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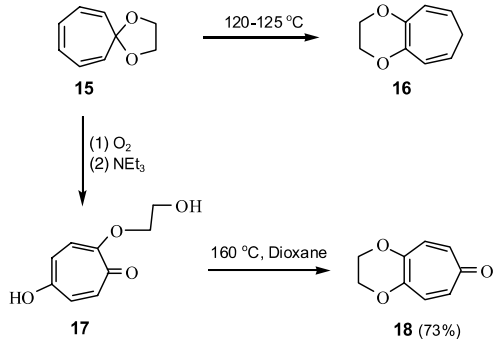
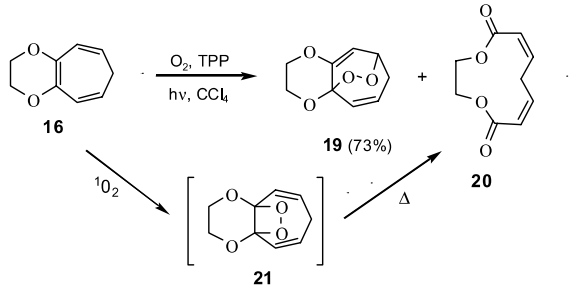
ethylene ketal **15**[12] provided the cycloheptatriene derivative **16**.[13] The photooxygenation of **15**, followed by the reaction of the formed bicyclic endoperoxide with NEt_3 gave the tropolone derivative **17**.[14] The thermolysis of **17** in dioxane resulted in the formation of the starting material **18** (Scheme 1).



Scheme 1.

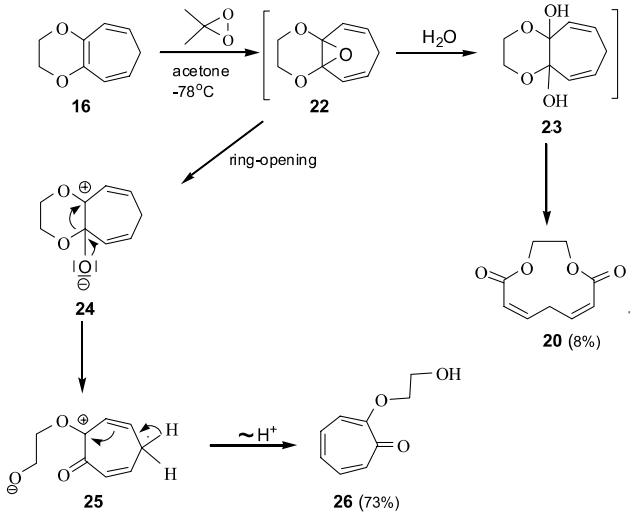
The tetraphenylporphyrin-sensitized photooxygenation of **16** produced the tricyclic endoperoxide **19** in 73% yield (Scheme 2). The sensitized photooxygenation of electron-rich olefins constitutes an effective means of preparing 1,2-dioxetanes through [2+2] cycloaddition.[15] During the photooxygenation reaction of **16** we expected a large amount of dioxetane **21**. Careful inspection of the reaction mixture showed the formation of dilactone **20** in trace amounts, which is a secondary product formed by the cleavage of the initially formed dioxetane **21**. The structural assignments of the products were performed from ^1H and ^{13}C NMR spectra.



Scheme 2.

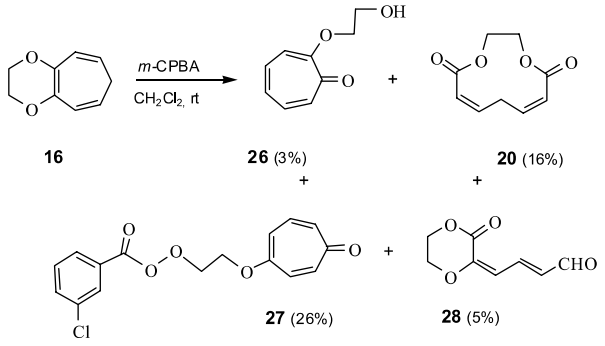
On the other hand, the oxidation of **16** with 3,3-dimethyldioxirane (DMD)[16] in acetone at −78 °C followed by column chromatography gave tropone derivative **26** as the major product as well as dilactone **20** in only 8% yield (Scheme 3). The formation of those products can be rationalized by the following mechanism. The initially formed monoepoxide **22** can undergo two different reactions; (i) forming the diol **23** by the opening of epoxide **22** with water to produce dilactone **20**, and (ii) opening of epoxide **22** to stable oxy-cation **24**, which can be rearranged through the intermediate **25** to the stable tropone **26**[13b] (Scheme 3).

For the further conversion of cycloheptatriene derivative **16** to tropolone derivatives, it was oxidized with *m*-chloroperbenzoic acid (*m*-CPBA). The reaction of **16** with



Scheme 3.

m-CPBA at room temperature in an ultrasonic bath gave four products; two tropolone derivatives **26**[13] and **27**, where *m*-CPBA was incorporated into the molecule, dilactone **20** and an unusual rearranged product **28** in yields of 3, 26, 16 and 5% yields, respectively (Scheme 4). Full characterization of all of the formed products was accomplished by means of detailed NMR analysis.

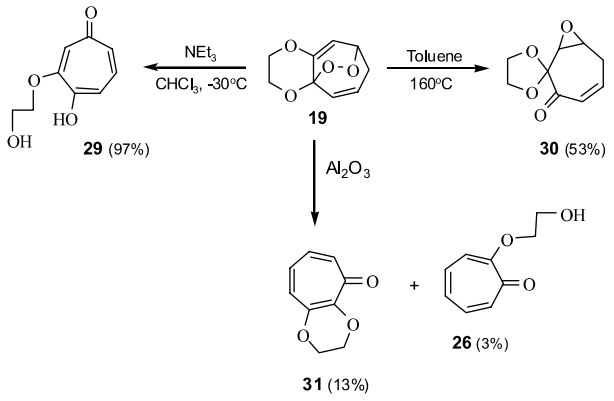


Scheme 4.

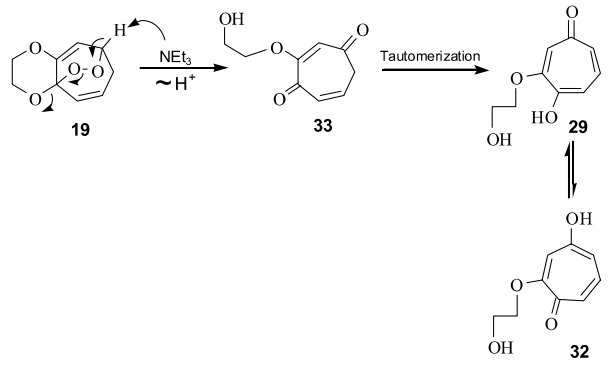
Base-catalyzed decomposition of unsaturated bicyclic peroxides generally results in the formation of hydroxy ketones.[9,17] Application of this reaction to the cycloheptatriene endoperoxides opens up an entry to the synthesis of troponoid compounds.[8g,10,11]

Treatment of endoperoxide **19** with a catalytic amount of triethylamine in dichloromethane at −30 °C provided a new tri-oxygenated tropolone **29** as the sole product in 97% yield (Scheme 5). The unsymmetrical tropolone derivative **29** can be in equilibrium with its tautomer **32** (Scheme 6). In order to determine, which is the most stable tautomer we undertook some AM1 calculations. The results show that the tautomer **29** has 0.48 kcal/mol lower heat of formation than the tautomer **32**. Therefore, the structure was tentatively assigned as **29**.

For the conversion of **19** to **29** we propose the mechanism depicted in Scheme 6. The abstraction of the bridgehead proton in **19** by the amine catalyst with the concomitant



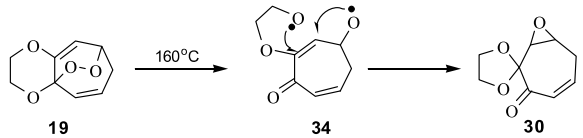
Scheme 5.



Scheme 6.

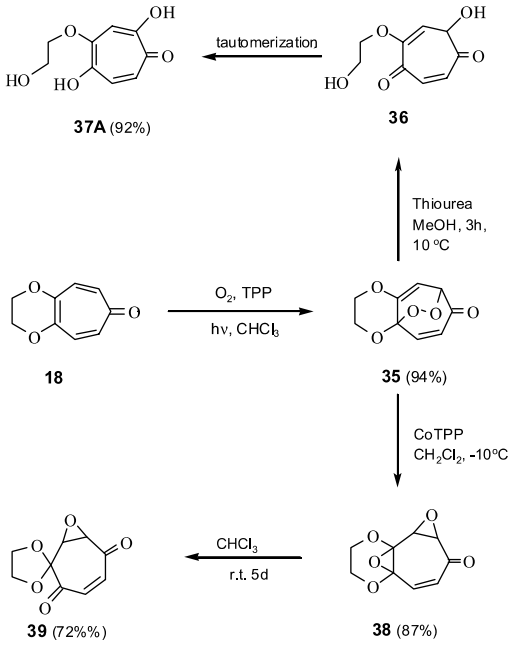
cleavage of O–O bond followed by ring opening can generate the unsaturated alkoxydiketone **33**, which could then afford substituted tropolone **29** by tautomerization (Scheme 6). Furthermore, we noticed that the endoperoxide **19** was partly rearranged during column chromatography on aluminum oxide to give troponoids **31** and **26** in 13 and 3% yields, respectively (Scheme 5).

Thermal decomposition of endoperoxides generally results in the formation of bisepoxides.[9,18] When endoperoxide **19** was heated to 160 °C in toluene in a sealed tube for 6 h, the epoxyketal **30** was isolated after chromatography on a florisil column in 53% yield (Scheme 5). Full characterization of the product was accomplished by means of ^{1}H and ^{13}C NMR spectra. No trace of any bisepoxide was detected. The formation of this product can be rationalized by the following mechanism. An initial cleavage of the peroxide linkage to diradical **34**, followed by rearrangement forms the product **30** (Scheme 7).



Scheme 7.

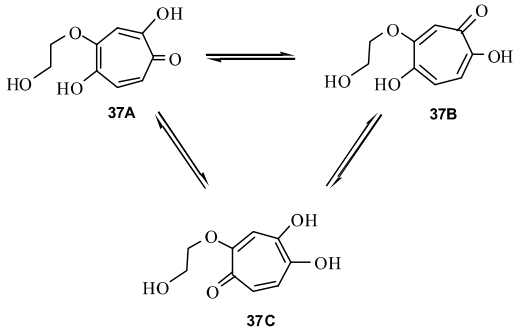
The tetraphenylporphyrin-sensitized photooxygenation of the cycloheptatriene derivative **18** produced only tricyclic endoperoxide **35** in 94% yield (Scheme 8). The expected [2+2] cycloaddition product was unformed, which may be



Scheme 8.

attributed to the reduced electron density caused by the carbonyl group.

It is well established that thiourea reduces the oxygen–oxygen bond to give a diol.[9] Recently, we showed that the substituted cycloheptatriene endoperoxide can easily form troponoid systems upon treatment with thiourea.[10,11a] Therefore, the bicyclic endoperoxide **35** was reacted with thiourea in methanol at 10 °C and the desired tetraoxygenated tropolone **37** was obtained in 94% yield (Scheme 8). The structure of **37** was characterized by its ^{1}H NMR spectrum. Vicinal olefinic protons (H_5 and H_6) of **37** resonate as an AB-system. The A-part of the AB-system appears at δ 7.08 ppm as a doublet ($J=11.3$ Hz) and the B-part at δ 6.95 ppm again as doublet, whereas the olefinic proton H_3 resonates at δ 7.04 ppm as a singlet. Its nine-line ^{13}C NMR spectrum supports the suggested unsymmetrical structure. For this compound, three different tautomers (**37A**, **37B** and **37C**) can be written (Scheme 9).



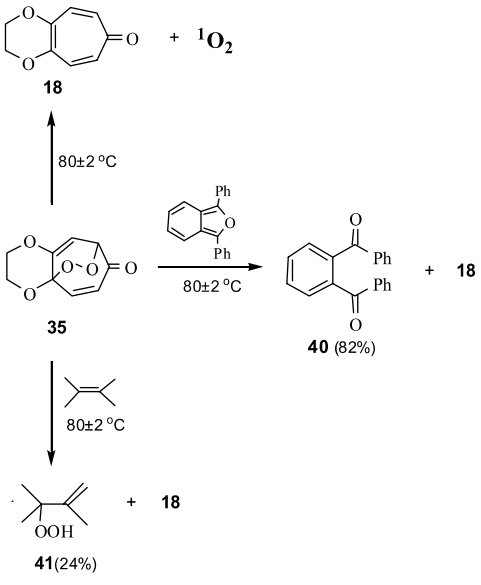
Scheme 9.

In order to find the most stable tautomer we carried out AM1 calculations for the three possible tautomers and found that the isomer **37A** is thermodynamically about 2.76 and 5.96 kcal/mol more stable than the isomers and **37C** and

37B, respectively. Therefore, the structure **37A** was assigned tentatively.

Foote et al.[19] and our group[20] have reported that cobalt *meso*-tetraphenylporphyrin (CoTPP) promotes the rearrangement of the bicyclic endoperoxides to the corresponding bis-epoxide with *syn*-configuration. In addition to this previously observed reaction of CoTPP we further demonstrated that some bicyclic endoperoxides derived from cycloheptatriene can be converted into tropolone derivatives upon treatment with CoTPP.[10] For that reason, endoperoxide **35** was treated with a catalytic amount of CoTPP at a low temperature. The corresponding bisepoxide **38** was isolated in 87% yield (Scheme 8). It was noticed that the bis-epoxide **38** was unstable at room temperature and was rearranged smoothly to epoxyketal **39** by way of standing at room temperature over a period of 5 days.

It is well known that benzenoid aromatic hydrocarbons such as anthracene, rubrene, tetracene, and substituted naphthalanes[21] undergo photosensitized autoxidation to form bicyclic endoperoxides. These peroxides undergo dissociation on heating to regenerate singlet oxygen and the parent aromatic compounds. The ease of oxygen release from these systems depends on the polycyclic aromatic system and the nature of the substituents. During the thermal reaction of endoperoxide **35** we observed that it loses oxygen and forms the parent tropone **18** as the sole product (Scheme 10). In order to test whether the formed oxygen is singlet or molecular oxygen, the thermolysis reaction of endoperoxide **35** was carried out in the presence of the known singlet oxygen acceptors, such as 1,3-diphenylisobenzofuran (DBI)[22] and tetramethylethylene. The decomposition of **35** in the presence of tetramethylethylene gave the ene-product **41**, whereas the DBI formed **40** as the trapping product.



Scheme 10.

3. Conclusions

In conclusion, we synthesized two bicyclic endoperoxides by the photooxygenation reaction of two different dioxine-annelated cycloheptatrienes. The reaction of these endoperoxides with base, thiourea and their thermolysis provided an entry to the synthesis of new tropolone derivatives in high yield. Furthermore, we have studied their oxidation and thermal reactions. The tricyclic endoperoxide **35** obtained by the photooxygenation of **18** showed an unprecedented behavior and produced singlet oxygen and the parent tropone upon thermolysis. To the best of our knowledge it is the first report where a non-benzonoid system generative singlet oxygen. The results described here should lead to the synthesis of new tropon and tropolone derivatives upon photooxygenation of highly oxygenated cycloheptatriene derivatives.

4. Experimental

4.1. General

Melting points are uncorrected. Infrared spectra were obtained from solution in 0.1 mm cells or KBr pellets on a regular instrument. The ^1H and ^{13}C NMR spectra were recorded on 200 (50) MHz spectrometers. Apparent splittings are given in all cases. 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 aluminum plates. All substances reported in this paper are in their racemic form.

4.1.1. Synthesis of 2,3-dihydro-7*H*-cyclohepta[1,4]-dioxine (16). The tropone ethylene ketal **15**[12] (3.0 g, 0.02 mol) was dissolved in cyclohexane (3 mL) and heated to 123±2 °C for 16 days in a sealed tube. After evaporation of the solvent the residue was distilled to give **16**[13] (2.04 g, 68%, pale yellow liquid). ^1H NMR (200 MHz, $CDCl_3$): δ 5.99 (d, A-part of, AX system, $J_{5,6}=J_{8,9}=9.8$ Hz, 2H, H_5 and H_9), 5.27 (dt, X-part of, AX system, $J_{5,6}=J_{8,9}=9.8$ Hz, $J_{6,7}=J_{8,7}=6.9$ Hz, 2H, H_6 and H_8), 4.16 (s, 4H, OCH_2), 2.33 (t, $J_{6,7}=J_{8,7}=6.9$ Hz, 2H, H_7). ^{13}C NMR (50 MHz, $CDCl_3$): δ 139.1, 123.4, 118.5, 64.4, 28.0.

4.1.2. Synthesis of 2,3-dihydro-cyclohepta[1,4]dioxin-7-one (18). Tropolone **17**[14] (300 mg, 1.65 mmol) was dissolved in dioxane (5 mL) and heated to 160 °C for 48 h in a sealed tube. After evaporation of the solvent the residue was filtered through silica gel column (30 g) eluting with *n*-hexane–ethyl acetate (6/4) to give **18**[14a] (197 mg, 73%, pale yellow crystals), mp 150–151 °C from methylene chloride/*n*-hexane 1:1 (lit. mp 151–152 °C).[14a] ^1H NMR (200 MHz, $CDCl_3$): δ 7.03 (AA′ part of AA′BB′ system, 2H, H_5 and H_9), 6.82 (BB′ part of AA′BB′ system, 2H, H_6 and H_8), 4.24 (s, 4H, OCH_2). ^{13}C NMR (50 MHz, $CDCl_3$): δ 187.2, 146.4, 136.1, 135.4, 65.8.

4.1.3. Photooxygenation of 2,3-dihydro-7*H*-cyclohepta[1,4]dioxine (16). The cycloheptatriene derivative **16**[13a] (1.0 g, 6.67 mmol) and tetraphenylporphyrin (10 mg) were dissolved in 200 mL of CCl_4. The solution was then irradiated with a projection lamp (500 W) while a slow stream of dry oxygen was passed through the solution at 10 °C. After 1.5 h, the solvent was evaporated (20 °C). The crystallization of the residue from CH_2Cl_2–ether (1/4) provided endoperoxide **19** as colorless crystals (886 mg,

73%, mp 97–98 °C). *(4aR(S),8S(R))-2,3,7,8-Tetrahydro-4a,8-epidioxycyclohepta[b][1,4]-dioxine* (**19**): ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.95 (ddd, A-part of AB system. $J_{5,6}=12.2$ Hz, $J_{5,7}=3.0$ Hz, $J_{5,7'}=1.8$ Hz, 1H, H_5), 5.65 (bddd, B-part of AB system, $J_{5,6}=12.2$ Hz, $J_{6,7}=4.7$ Hz, $J_{6,7'}=3.8$ Hz, 1H, H_6), 5.39 (d, $J_{8,9}=7.7$ Hz, 1H, H_9), 4.87 (m, 1H, H_8), 4.34–3.79 (m, 4H, OCH_2), 2.89 (br d, A-part of AB system, $J_{7,7'}=19.5$ Hz, 1H, H_7), 2.35 (br d, B-part of AB system, $J_{7,7'}=19.5$ Hz, 1H, $H_{7'}$). ^{13}C NMR (50 MHz, $CDCl_3$): δ 155.3, 133.7, 130.6, 101.0, 99.6, 79.4, 68.3, 63.6, 38.0. MS (EI, 70) *m/z* 182 (M^+, 10), 164 (8), 154 (6), 139 (12), 125 (66), 112 (96), 81 (100), 68 (74). Anal. Calcd for $C_9H_{10}O_4$: C, 59.34; H, 5.53. Found: C, 59.20; H, 5.46.

The ^{1}H NMR spectral studies of the residue obtained after crystallization showed the presence of dilactone **20**, which was formed in about 1–2% (for spectral data see Section 4.1.4).

4.1.4. Oxidation of 16[13a] with 3,3-dimethyl-dioxirane (DMD) To a dioxirane–acetone solution (8.5 mL, 0.08 M) synthesized as described in the literature[16] was added a solution of **16** (100 mg, 0.67 mmol) in acetone (10 mL) over a period of 10 min at −78 °C. The reaction mixture was allowed to come to room temperature during 1 h. After additional stirring for 1 h at room temperature the solvent was evaporated and the residue was chromatographed on a silica gel (30 g) column eluting with *n*-hexane–ethyl acetate (9/1). The first fraction was identified as dilactone **20** (9 mg, 8%). *1,4-Dioxacycloundeca-6,9-diene-5,11-dione* (**20**): ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.15 (dt, A-part of AB system, $J_{6,7}=J_{9,10}=11.7$ Hz, $J_{7,8}=J_{8,9}=8.4$ Hz, 2H, H_7 and H_9), 5.89 (dt, B-part of AB system, $J_{6,7}=J_{9,10}=11.7$ Hz, $J_{6,8}=J_{10,8}=1.1$ Hz, 2H, H_6 and H_{10}), 4.48 (s, 4H, OCH_2), 3.45 (tt, $J_{7,8}=J_{8,9}=8.4$ Hz, $J_{6,8}=J_{10,8}=1.1$ Hz, 2H, Hg). ^{13}C NMR (50 MHz, $CDCl_3$): δ 169.0, 140.6, 125.0, 63.5, 31.4. IR (KBr, cm^{-1}): 3055, 3030, 2979, 2953, 2928, 1728, 1446, 1396, 1294, 1268, 1243, 1217, 1166, 1064, 911, 834. Anal. MS (EI, 70 eV) *m/z* 138 (M^+-CO_2, 6), 122 (8), 94 ($M^+-2\times CO_2$, 100), 82 (9). Anal. Calcd for $C_9H_{10}O_4$: C, 59.34; H, 5.53. Found: C, 59.31; H, 5.72.

The second fraction was identified as **26** (81 mg, 73%), mp 80–81 °C, (lit. mp[13] 83–84 °C). *2-(2-Hydroxyethoxy)-cyclohepta-2,4,6-trien-1-one* (**26**): [13] ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.34–7.05 (m, 5H, H_3, H_4, H_5, H_6 and H_7), 4.90 (m, 1H, OH), 4.15 (A_2-part of A_2B_2 system, 2H, OCH_2), 4.05 (B_2-part of A_2B_2 system, 2H, OCH_2). ^{13}C NMR ($CDCl_3$): δ 182.8, 166.9, 139.1, 139.0, 135.0, 130.6, 116.7, 73.2, 62.4. IR (KBr, cm^{-1}): 3361, 2953, 2876, 1626, 1603, 1568, 1475, 1290, 1279, 1209, 1094, 1024, 781, 723.

4.1.5. Oxidation of 16 with *m*-chloroperbenzoic acid (*m*-CPBA). To a solution of **16** (360 mg, 2.40 mmol) in methylene chloride (20 mL) was added Na_2CO_3 (1.27 g, 12 mmol) and *m*-CPBA (426 mg, 2.47 mmol). The resulting mixture was stirred for 4 h at room temperature in an ultrasound bath. The precipitate was filtered and the solvent evaporated to dryness. The residue was chromatographed on silica gel (100 g) eluting with *n*-hexane–ethyl acetate (8/2). The first fraction was identified as **27** (200 mg, 26%, mp 105–106 °C from methylene chloride–*n*-hexane 1/2). *2-[(5-Oxocyclohepta-1,3,6-trien-1-yl)oxy]ethyl 3-chlorobenzenecarboperoxoate* (**27**): ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.03 (m, 1H, $H_{2'}$), 7.92 (br d, $J_{5'6'}=7.6$ Hz, 1H, $H_{6'}$), 7.55 (br d, $J_{4',5'}=7.6$ Hz, 1H, $H_{4'}$), 7.40 (t, $J_{4',5'}=J_{5',6'}=7.6$ Hz, 1H, $H_{5'}$), 6.48 (bdd, A-part of AB system, $J_{6,7}=12.1$ Hz, $J_{2,7}=4.0$ Hz, 1H, H_7), 6.29 (dd, A-part of AB system, $J_{3,4}=11.4$ Hz, $J_{2,3}=5.1$ Hz, 1H, H_3), 6.04 (br d, B-part of AB system, $J_{3,4}=11.4$ Hz, 1H, H_4), 5.87 (d, B-part of AB system, $J_{6,7}=12.1$ Hz, 1H, H_6), 5.17 (br d, $J_{2,3}=5.1$ Hz, 1H, H_2). 4.52 (A_2-part of A_2B_2 system, 2H, OCH_2), 4.37 (B_2-part of A_2B_2 system, 2H, OCH_2). ^{13}C NMR (APT, 50 MHz, $CDCl_3$): δ 168.7, 164.7, 153.7, 141.3 (−)(C_7), 136.7, 135.8 (−), 132.5, 132.1 (−), 131.9 (−), 130.3 (−), 129.7 (−)(C_4), 128.0 (−)(C_3), 125.5 (−)(C_6), 99.3 (−)(C_2), 69.7 (OCH_2), 65.2 (OCH_2). IR (KBr film, cm^{-1}): 3029, 2978, 1753, 1707, 1429, 1417, 1325, 1255, 1198, 1094, 1059, 1024, 885. MS (EI, 70 eV) *m/z* 320 (M^+, 5), 232 (5), 183 (62), 139 (100), 111 (40), 75 (25%). Anal. Calcd for $C_{16}H_{13}ClO_5$: C, 59.92; H, 4.09. Found: C, 59.80; H, 4.06.

The second fraction was identified as dilactone **20** (70 mg, 16%). The elution of the column was continued with ethyl acetate–methanol (98/2) and as the third fraction; the aldehyde **28** was isolated (20 mg, 5%, imp. 128–129 °C from methylene chloride/*n*-hexane 1:1). *(2E,4E)-4-(3-Oxo-1,4-dioxan-2-ylidene)but-2-enal* (**28**): ^{1}H NMR (200 MHz, $CDCl_3$): δ 9.63 (d, $J_{1,2}=7.8$ Hz, 1H, H_1), 7.44 (dd, $J_{2,3}=15.6$ Hz, $J_{3,4}=11.7$ Hz, 1H, H_3), 6.73 (d, $J_{3,4}=11.7$ Hz, 1H, H_4), 6.33 (dd, $J_{2,3}=15.6$ Hz, $J_{1,2}=7.8$ Hz, 1H), 4.58 (AA'-part of $AA'BB'$ system, 2H, OCH_2), 4.33 (BB'-part of $AA'BB'$, 2H, OCH_2). ^{13}C NMR (APT) (50 MHz, $CDCl_3$): δ 195.1, 160.8, 147.1, 143.8, 136.3, 116.8, 68.6, 66.0. IR (KBr film, cm^{-1}): 3080, 2978, 2953, 2825, 1778, 1753, 1728, 1676, 1472, 1421, 1344, 1319, 1293, 1268, 1242, 1217, 1114, 1089. MS (EI, 70 eV) *m/z* 168 (M^+, 19), 139 (41), 110 (13), 96 (95), 83 (19), 68 (100%). The last fraction was identified as tropolone **26** (12 mg, 3%).

4.1.6. Reaction of the endoperoxide 19 with NEt_3. To a solution of endoperoxide **19** (200 mg, 1.10 mmol) in 10 mL of CH_2Cl_2 at −30 °C, one drop of freshly distilled triethylamine was added. The mixture was then stirred at −30 °C for 3.5 h and to the residue ether (10 mL) was added to precipitate the product. The formed product was separated by filtration and crystallized from hot water to give pure **29** (194 mg, 97%, mp 223–224 °C). *4-Hydroxy-3-(2-hydroxyethoxy)cyclohepta-2,4,6-trien-1-one* (**29**): ^{1}H NMR (200 MHz, CD_3OD) 7.32 (dd, A-part of AB system and A-part of AX system, $J_{5,6}=11.7$ Hz, $J_{6,7}=10.4$ Hz, 1H, H_6), 6.88 (d, $J_{2,7}=2.3$ Hz, 1H, H_2), 6.86 (d, B-part of AB system, $J_{5,6}=11.7$ Hz, 1H, H_5), 6.62 (dd, X-part of AX system, $J_{6,7}=10.4$ Hz, $J_{2,7}=2.3$ Hz, 1H, H_7), 4.09 (A_2-part of A_2B_2 system, 2H, OCH_2), 3.96 (B_2-part of A_2B_2 system, 2H, OCH_2). ^{13}C NMR (CD_3OD): 177.4, 173.4, 166.7, 141.8, 126.5, 119.5, 115.8, 74.2, 62.8. IR (KBr film, cm^{-1}): 3464, 3004, 2979, 2953, 2927, 2570, 1600, 1548, 1523, 1446, 1421, 1191, 1165, 936. MS (EI, 70 eV) *m/z* 182 (M^+, 12), 154 (18), 138 (3), 125 (66), 110 (100), 83 (17). Anal. Calcd for $C_9H_{10}O_4$: C, 59.34; H, 5.53. Found: C, 59.39; H, 5.63.

4.1.7. Reaction of endoperoxide 19 with Al_2O_3. A solution of endoperoxide **19** (200 mg, 1.10 mmol) in 5 mL of $CHCl_3$ was loaded to an aluminum oxide column

(30 g, neutral, activity 3) prepared with hexane, and the top of the column was closed for 30 min. After a total waiting time of 30 min, the top of the column was opened and elution was continued with *n*-hexane–ethyl acetate (4/6) to give **31** as pale yellow crystals (23 mg, 13%, mp 98 °C from methylenechloride–*n*-hexane (1/2). Later, the elution was continued with ethyl acetate and methanol (4:1) to give **26**[13] as pale yellow crystals (6 mg, 3%). *2,3-Dihydro-5H-cyclohepta[b][1,4]dioxin-5-one* (**31**): ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.95–6.84 (m, 3H, H_7, H_8 and H_9 (or H_6)), 6.61 (dd, $J=8.8$, 1.7 Hz, 1H, H_9 (or H_6)), 4.30 (br s, 4H, OCH_2). ^{13}C NMR ($CDCl_3$): δ 186.4, 155.9, 154.7, 139.4, 134.4, 128.3, 118.5, 65.9, 65.7. IR (KBr, cm^{-1}): 3055, 2978, 2927, 1651, 1548, 1472, 1425, 1293, 1217, 1191, 1089, 885, 808. MS (EI, 70 eV) *m/z*) 164 (M^+, 9), 136 (65), 80 (100), 52 (65%). Anal. Calcd for $C_9H_8O_3$: C, 65.85; H, 4.91. Found: C, 66.02; H, 4.95.

4.1.8. Thermolysis of endoperoxide 19. The endoperoxide **19** (160 mg, 0.88 mmol) was dissolved in toluene (5 mL) and heated to 160 °C for 6 h in a sealed tube. After evaporation of the solvent the residue was filtered through florisil column (30 g) eluting with *n*-hexane–ethyl acetate (4/1) to give **30** (85 mg, 53%, pale yellow crystals, mp 94–95 °C from ether/*n*-hexane 1:1). *(7R(S),8R(S))-7,8-Epoxy-1,4-dioxaspiro[4.6]undec-10-en-6-one* (**30**): ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.67 (m, 2H, H_{10} and H_{11}), 4.17–3.95 (m, 4H, OCH_2), 3.74 (d, A-part of AB system, $J_{7,8}=$ 4.8 Hz, 1H, H_7), 3.54 (dd, B-part of AB system, $J_{7,8}=$ 4.8 Hz, $J_{8,9}=4.5$ Hz, 1H, H_8), 3.02 (ddt, A-part of AB system, $J_{9,9'}=19.2$ Hz, $J_{8,9}=J_{9,10}=4.5$ Hz, $J_{9,11}=1.9$ Hz, 1H, H_9), 2.76 (br d, B-part of AB system, $J_{9,9'}=19.2$ Hz, 1H, $H_{9'}$). ^{13}C NMR ($CDCl_3$): δ 200.6, 129.6, 128.4, 107.5, 68.3, 67.4, 59.2, 54.8, 28.7. IR (KBr film): 3029, 2998, 2985, 2896, 2883, 2870, 1727, 1446, 1395, 1217, 1191, 1089, 1012, 961. MS (EI, 70 eV) *m/z* 183 (M^+, 1), 125 (19), 113 (43), 82 (69), 68 (56), 53 (100%). Anal. Calcd for $C_9H_{10}O_4$: C, 59.34; H, 5.53. Found: C, 59.14; H, 5.48.

4.1.9. Photooxygenation of 2,3-dihydro-7*H*-cyclohepta[*b*][1,4]dioxin-7-one (18). The reaction was carried out according to the above mentioned procedure (Section 4.1.2) by using 200 mg (1.22 mmol) of **18**[14] and TPP (10 mg) in 200 mL of chloroform. After 45 min irradiation, the solvent was evaporated and the ^{1}H NMR analysis of residue indicated the formation of the endoperoxide **35** as the sole product. The recrystallization of the residue from CH_2Cl_2–ether (1/3) gave the endoperoxide **35** as colorless crystals (225 mg, 94%, mp 106–107 °C). *(4aR(S),8R(S))-2,3-Dihydro-4a,8-epidioxycyclohepta[b][1,4]-dioxin-7(8H)-one* (**35**): ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.80 (d, A-part of AX system, $J_{5,6}=11.4$ Hz, 1H, H_5), 5.93, (dd, B-part of AX system, $J_{5,6}=11.4$ Hz, $J_{6,8}=1.9$ Hz, 1H, H_6), 5.52 (d, A-part of AX system, $J_{8,9}=8.1$ Hz, 1H, H_9), 5.00 (dd, X-part of AX system, $J_{8,9}=8.1$ Hz, $J_{6,8}=1.9$ Hz, 1H, H_8), 4.41–3.94 (m, 4H, OCH_2). ^{13}C NMR ($CDCl_3$): δ 195.4, 159.0, 147.5, 130.3, 102.6, 97.0, 89.12, 68.3, 64.5. IR (KBr, film): 3080, 3055, 2978, 2953, 2927, 1728, 1702, 1676, 1472, 1395, 1370, 1344, 1293, 1268, 1165, 1013, 859. MS (EI, 70 eV) *m/z* 196 (M^+, 2), 164 (M^+-O_2, 14), 137 (28), 83 (38), 69 (48), 54 (100%). Anal. Calcd for $C_9H_8O_5$: C, 55.11; H, 4.11. Found: C, 55.13; H, 4.18.

4.1.10. Reaction of endoperoxide 35 with thiourea. The endoperoxide **35** (100 mg, 0.51 mmol) was dissolved in CH_3OH (10 mL) at 10 °C. A solution of thiourea (53 mg, 0.69 mmol) in CH_3OH (3 mL) was added dropwise over 1 min, then the solution was stirred 3 h at room temperature. The residue was filtered and the solvent was reduced to half of its volume. After standing in freezer for one night, the formed crystals were characterized as tropolone **37A** (93 mg, 92%, pale yellow crystals, mp 185–186 °C from methanol). *2,5-Dihydroxy-4-(2-hydroxyethoxy)cyclohepta-2,4,6-trien-1-one* (**37**): ^{1}H NMR (200 MHz, CD_3OD): δ 7.08 (d, A-part of AB system. $J_{6,7}=11.3$ Hz, 1H, H_6), 7.04 (s, 1H, H_3), 6.95 (d, B-part of AB system, $J_{6,7}=1.3$ Hz, 1H, H_6), 4.20 (A_2-part of A_2B_2 system, 2H, OCH_2), 3.98 (B_2-part of A_2B_2 system, 2H, 2H, OCH_2). ^{13}C NMR (50 MHz, CD_3OD): 176.7, 162.2, 161.21, 154.3, 119.9, 117.6, 115.7, 74.4, 62.7. IR (KBr, cm^{-1}): 3423, 3269, 2436, 1603, 1549, 1472, 1425, 1263, 1197, 1078, 916, 870. MS (EI, 70 eV) *m/z* 199 (M^+, 5), 154 (10), 127 (52), 96 (16), 70 (24), 64 (100), 53 (39%). Anal. Calcd for $C_9H_{10}O_5$: C, 54.55; H, 5.09. Found: C 54.01 H: 5.60.

4.1.11. CoTPP-catalyzed reaction of endoperoxide (35). To a magnetically stirred solution of endoperoxide **35** (100 mg, 0.51 mmol) in CH_2Cl_2 (10 mL) at −10 °C was added cobalt-*meso*-tetraphenylporphyrin (C0TPP) (20 mg) in portions. The mixture was stirred for 2 min. The solvent was then evaporated. The ^{1}H NMR spectral analysis of the residue indicated the formation of bisepoxide **38** (87 mg, 87%, colorless crystals from methylenechloride/ether 1:1, mp 105–106 °C). *2,3,(7aR(S)),(8aS(R))-Tetra-hydro-7H-(4aR(S)),8b(S(R))-epoxyoxireno[3,4]cyclohepta[1,2-b][1,4]dioxin-7-one* (**38**): ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.38 (d, A-part of AB system, $J_{5,6}=11.5$ Hz, 1H, H_5), 5.89 (dd, B-part of AB system, $J_{5,6}=11.5$ Hz, $J_{7a,6}=1.8$ Hz, 1H, H_6), 3.98 (m, 2H, OCH_2), 3.78 (d, A-part of AB system, $J_{7a,8a}=$ 4.3 Hz, 1H, H_{8a}), 3.74 (m, 2H, OCH_2), 3.68 (dd, B-part of AB system, $J_{7a,8a}=4.3$ Hz, $J_{7a,6}=1.8$ Hz, 1H, H7a). ^{13}C NMR (50 MHz, $CDCl_3$): δ 199.3, 132.1, 129.8, 86.1, 84.6, 64.3, 63.4, 61.6, 56.4. IR (KBr, cm^{-1}): 2961, 2899, 1641, 1449, 1410, 1317, 1171, 1101, 1032, 909. Anal. Calcd for $C_9H_8O_5$: C, 55.11; H, 4.11. Found: C, 55.20; H, 4.01.

4.1.12. The formation of 39 from 38. Bisepoxide **38** (40 mg, 0.20 mmol) was dissolved in 0.5 mL of $CDCl_3$ and its rearrangement was followed by the ^{1}H NMR spectroscopy. After 5 days, the bisepoxide was completely rearranged to epoxy ketal **39** at room temperature. The residue was recrystallized from methylene chloride–ether (2/1) to give pure **39** (29 mg, 72%, colorless crystals mp 97–98 °C). *(7S(R),8R(S))-7,8-Epoxy-1,4-dioxaspiro[4.6]undec-10-ene-6,9-dione* (**39**): ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.25 (d, A-part of AB system, $J_{10,11}=12.9$ Hz, 1H, H_{11}), 6.00 (dd, B-part of AB system, $J_{1,11}=12.9$ Hz, $J_{8,10}=1.8$ Hz, 1H, H_{10}), 4.28–3.98 (m, 4H, OCH_2), 4.01 (d, A-part of AB system, $J_{7,8}=5.0$ Hz, 1H, H_7), 3.88 (dd, B-part of AB system, $J_{7,8}=5.0$ Hz, $J_{8,10}=1.8$ Hz, 1H, H_8). ^{13}C NMR (50 MHz, $CDCl_3$): δ 197.7, 196.8, 140.1, 129.7, 106.3, 69.0, 67.9, 58.8, 58.1. IR (KBr, cm^{-1}): 2976, 2902, 1730, 1702, 1611, 1384, 1173, 1030, 950, 782. MS (EI, 70 eV) *m/z* 196 (M^+, 1), 167 (3), 140 (16), 126 (22), 114 (19), 99 (77), 86 (47), 69 (50), 54 (100%). Anal. Calcd for $C_9H_8O_5$: C, 55.11; H, 4.11. Found: C, 54.95; H, 4.05.

4.1.13. Thermolysis of endoperoxide 35. Endoperoxide **35** (104 mg, 0.53 mmol) was dissolved in toluene (10 mL) and heated to 80±2 °C for 2 days in a sealed tube. After evaporation of the solvent, the ^{1}H NMR spectrum of the residue showed the formation of **18** as the sole product in quantitative yield. (104 mg, 100%).

4.2. Thermolysis of endoperoxide 35 in the presence of DBI. Endoperoxide **35** (200 mg, 1.02 mmol) and 1,3-diphenyl-isobenzofuran (DBI) (551 mg, 2.04 mmol) were dissolved in anhydrous benzene (10 mL) and heated to 80± 2 °C for 2 days in a sealed tube. After evaporation of the solvent the residue was chromatographed on silica gel (20 g) eluting with *n*-hexane–ethyl acetate (9/1). The first fraction was identified as diketone **40** (240 mg, 82%).[21a] Further elution with hexane–ethyl acetate (1/1) gave the tropone **18** (150 mg, 90%) as the second product.

4.3. Thermolysis of endoperoxide in the presence of 2,3-dimethyl-but-2-ene. The endoperoxide **35** (200 mg, 1.02 mmol) and 2,3-dimethyl-but-2-ene (172 mg, 2.04 mmol) in 10 mL of anhydrous benzene was reacted in a sealed tube as described above. The ^{1}H NMR analysis of the residue showed the formation of the hydroperoxide **41**[21a] in 24% yield and tropone **18** in 90% yield.

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