Chemistry of the Benzotropone Endoperoxides and Their Conversion into Tropolone Derivatives: Unusual Endoperoxide Rearrangements

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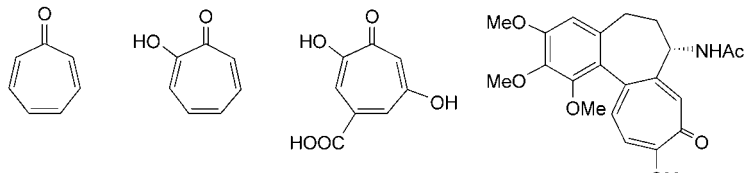
The chemistry of two bicyclic endoperoxides, obtained by photooxygenation of 2,3-benzotropone (= 5*H*-benzocyclohepten-5-one; **5**) and of its ethyl carboxylate derivative **15**, was investigated with the aim of synthesizing the respective benzotropolone derivatives. The reaction of the endoperoxide **10** derived from **5** with thiourea gave the desired benzotropolone, *i.e.*, 6-hydroxy-5*H*-benzocyclohepten-5-one (**11**), in high yield (*Scheme 1*). On the other hand, the endoperoxide **16** derived from the ethyl carboxylate derivative **15** underwent an unprecedented transformation yielding mainly the ring-contracted lactones **28** and **29** besides the expected substituted benzotropolone derivative **27** (*Scheme 5*). However, the thermolysis reaction of the same endoperoxide **16** resulted in the formation of four rearranged compounds with different skeletons (*Scheme 3*). The formation mechanism of all products is discussed (*Schemes 4* and *6*).

Introduction. – Tropone (= cyclohepta-2,4,6-trien-1-one; **1**) and tropolone (= 2-hydroxycyclohepta-2,4,6-trien-1-one; **2**) have fascinated organic chemists for well over 50 years. The most significant reason for the interest in the tropone ring system is that it represents the key structural element in a wide range of natural products, many of which display interesting biological activity [1]. The synthesis of substituted tropones as well as tropolones continues to be a considerable synthetic challenge. A recent renewed interest in the ability of colchicine **4** to inhibit tubulin polymerization has been complemented by elegant new approaches to tropolone structures [2].

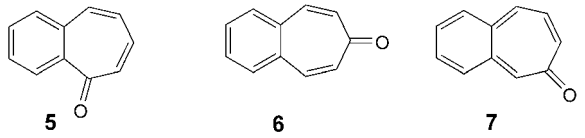


1 **2** **3** **4**

Although tropones can be oxidized to tropolones, this approach suffers from regiochemical control when substituted tropones are used as starting materials. A number of syntheses of tropolone derivatives have been developed [3]. In this connection, we recently studied the applicability of bicyclic endoperoxides derived by the cycloaddition of singlet oxygen [4] to the appropriate cyclic dienes and synthesized a new isomer of stipitatic acid (= 3,6-dihydroxy-5-oxocyclohepta-1,3,6-triene-1-carboxylic acid; **3**) [5]. In this paper, we report the synthesis of some benzotropones and their

photooxygenation and conversions to benzotropolones and unusual rearrangement products.

Results and Discussion. – *Synthesis of Endoperoxides* **10** *and* **16**. Three benzotropones can be formulated, namely 2,3-benzotropone (**5**), 4,5-benzotropone (**6**), and 3,4-benzotropone (**7**). Theoretical calculations [6] predict strong stabilization by π-electron delocalization for **5** and **6**. On the other hand, 3,4-benzotropone (**7**) is only weakly stabilized by π-electron delocalization since it possesses a quinodimethane-based structure. There are plenty of methods [7] known for the preparation of 2,3- and 4,5-benzotropone (**5** and **6**, resp.). In previous reports [7a,b], we have reported on an alternative synthetic way for benzotropone derivatives by oxidation of bromobenzocycloheptenes with different oxidizing reagents.



5 **6** **7**

First of all, we concentrated on the synthesis of benzotropolone **11** *via* endoperoxide **10**, whereby **5** was prepared by *Collington*'s method [8] starting from commercially available benzosuberone (=6,7,8,9-tetrahydro-5*H*-benzocyclohepten-5-one; **8**) (*Scheme 1*). The cycloaddition of singlet oxygen to a conjugated diene provides an excellent opportunity to introduce two O-functionalities in the 1,4-positions of 1,3-dienes [4]. In a recent study [5], we showed that cleavage of the O–O bond of a bicyclic endoperoxide obtained by the photooxygenation of a cycloheptatriene derivative resulted in the formation of tropolone derivatives. Furthermore, *Oda* and *Kitahara* [9] succeeded in the synthesis of tropolone by treatment of tropone endoperoxide with Et_3N. Thus, the bicyclic endoperoxide **10** was synthesized by tetraphenylporphyrine (TPP)-sensitized photooxygenation of **5** in 74% yield. The structural assignment was established by ^{1}H- and ^{13}C-NMR spectra. The reaction of endoperoxide **10** with thiourea gave the desired tropolone **11** [10] in quantitative yield (*Scheme 1*).

We then turned our attention to the synthesis of a substituted benzotropolone *via* endoperoxide **16**. First, we synthesized the substituted benzotropone derivative **15** starting from naphthalene (*Scheme 2*). The Rh^{II}-catalyzed cyclopropanation of 1,4-dihydronaphthalene was performed with ethyl diazoacetate to give the corresponding cyclopropane derivative[1]). Bromination of the latter with *N*-bromosuccinimide (NBS) followed by reductive debromination with Zn produced the ring-enlarged product **13**[2]). The base-catalyzed isomerization of **13** resulted in the formation of **14**. The benzocycloheptene derivatives **13** and **14** were oxidized with CrO_3/pyridine to benzotropone derivative **15**. These transformations represent the first and efficient synthesis of **15**. The latter was submitted to the usual photooxygenation reaction with

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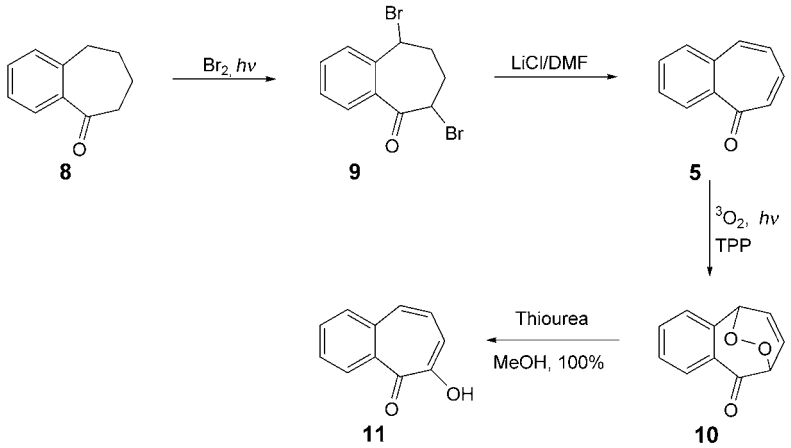
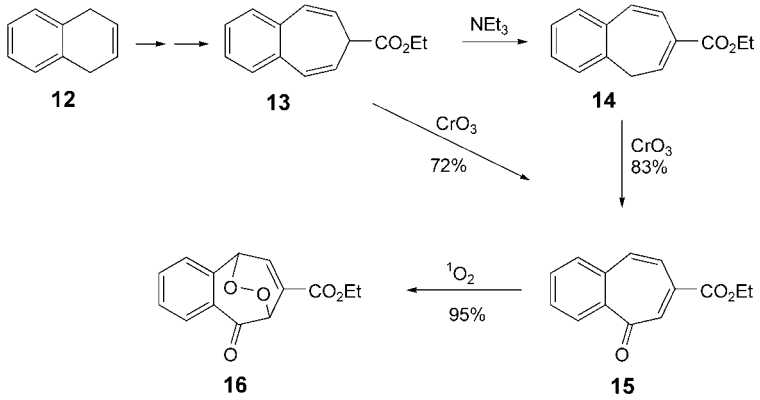
[1]) For the methyl ester derivative, see [11].

[2]) Benzocycloheptenecarboxylate **13** was obtained as by-product by Rh^{II}-catalyzed cyclopropanation of naphthalene with ethyl diazoacetate [12].

Scheme 1



Scheme 2



TPP as sensitizer in CCl_4 at 10°[3]). After 20 h, ^{1}H-NMR analysis indicated complete consumption of **15** and formation of endoperoxide **16** in high yield (*Scheme 2*).

For the further conversion of endoperoxide **16** to benzotropolone and benzostipitatic acid derivatives, we studied the chemistry of endoperoxide **16** in more detail (see below).

Thermolysis of Endoperoxide **16**. When endoperoxide **16** was heated to 131° for 24 h, the products **17**–**20** were isolated after chromatography, *i.e.*, the two benzofuranone derivatives **17** and **19**, a naphthalene derivative **20** [14], and a tricyclic acetal **18** (*Scheme 3*). Full characterization of all formed products was accomplished by means of NMR techniques (COSY, DEPT, HMQC, and HMBC) and elemental analyses.

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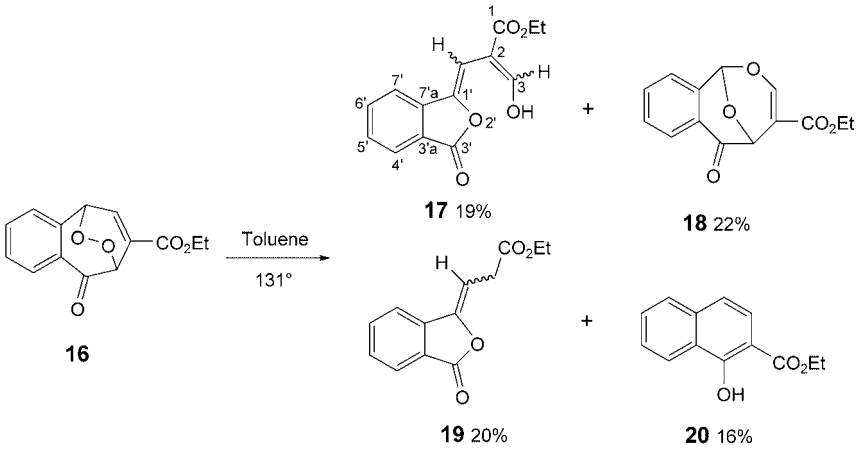
[3]) For recent publications on photooxygenation of some substituted tropone derivatives, see [13].

Scheme 3



It is well established that thermolysis of endoperoxides generally results in formation of bis-epoxides [4][15]. Actually, no trace of any epoxide was detected. The formation of the observed products can be rationalized by the following mechanism. An initial cleavage of the peroxide linkage to diradical **21** followed by rearrangement to **22** (*Path a*) and collapse of the radicals in **22** form the intermediate **23** (*Scheme 4*). This intermediate **23** either forms the extended conjugated system **17** or undergoes double-bond isomerization at the given temperature and decarbonylation to yield **19** [16]. On the other hand, the primarily formed diradical **21** undergoes C–C cleavage to give a new diradical **24** (*Path b*), which in turn rearranges to the tricyclic acetal **18**[4]). A bis-epoxide **25** as an intermediate should also be considered in the formation of cyclic acetal **18**, the latter being obtained *via* ring opening of the former to the corresponding cyclic carbonyl ylide substructure **26** (*Path c*) and a subsequent thermally allowed [1*s*,4*s*]-sigmatropic O-shift[5]). The formation of naphthalene derivative **20** can be rationalized by the loss of CO_2 in a *retro-Diels–Alder* reaction of an intermediate like **33** (see below, *Scheme 6*).

Thiourea Reaction of Endoperoxide **16**. For the synthesis of a tropolone derivative, bicyclic endoperoxide **16** was treated with thiourea in MeOH at room temperature. After chromatography, the desired benzotropolone **27** was obtained in 32% yield, besides the two isomeric lactones **28** and **29** in 26 and 19% yield, respectively (*Scheme 5*).

The formation of **27** by H_2O elimination from the initially formed diol **30** is straightforward (*Scheme 6*). However, the formation of bicyclic lactones **28** and **29** is unusual in endoperoxide chemistry. We assume that thiourea acts in this reaction as a reducing reagent of the peroxide linkage as well as as a base[6]). Probably, thiourea catalyzes the endoperoxide rearrangement to form the keto alkoxide **31**, which then

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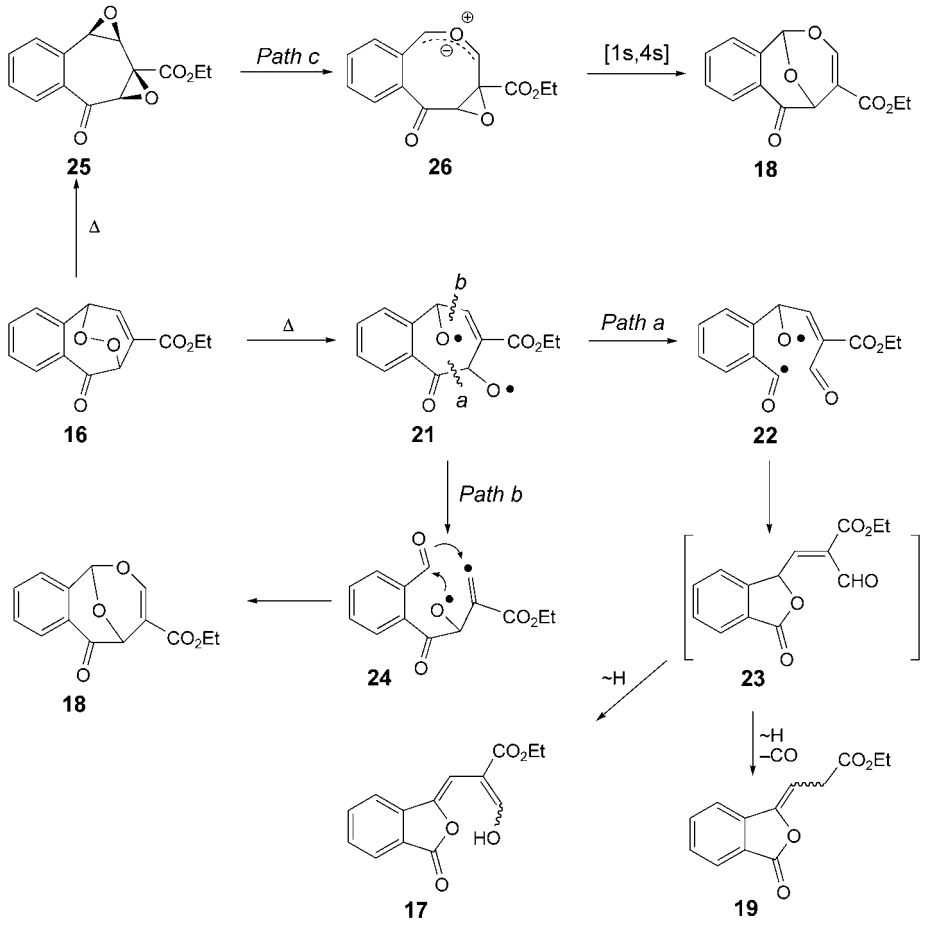
[4]) For a similar decomposition of endoperoxides, see [17].

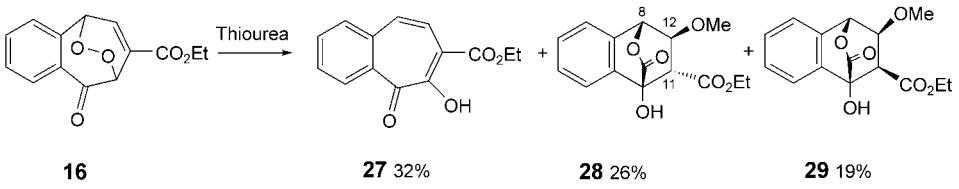
[5]) For similar transformations, see [18].

[6]) Recently, we have noticed that thiourea can initiate peroxide rearrangement as a base [19].

Scheme 4



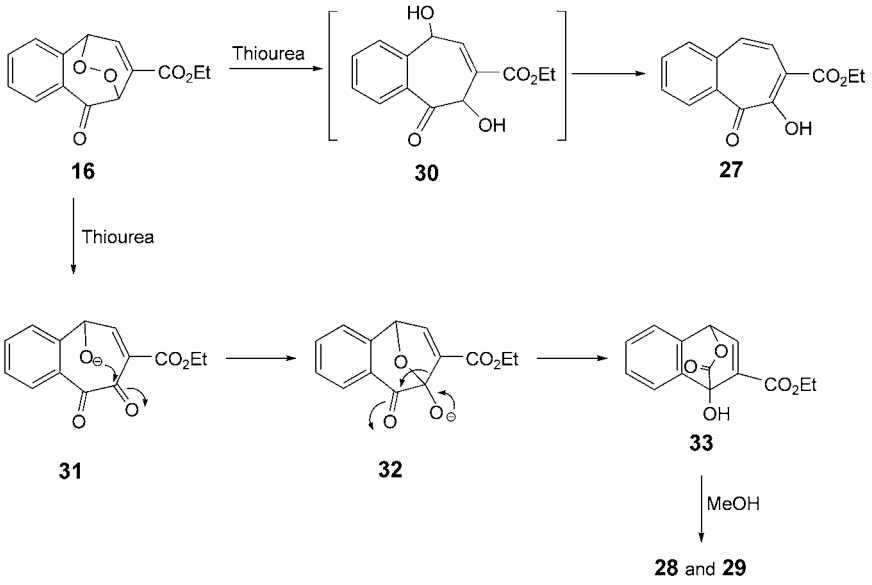
Scheme 5



rapidly cyclizes to the cyclic ether **32** (*Scheme 6*). Recently, we have demonstrated that the seven-membered ring endoperoxides have tendency to form cyclic ethers upon base treatment[7]). Intermediate **32** is an ideal system for a benzilic acid type rearrangement

[7]) We have demonstrated that benzocycloheptene endoperoxides can form cyclic ethers as intermediates [20].

Scheme 6



(→**33**). The ring strain in the molecule **33** can partially be released by addition of MeOH to the activated C=C bond yielding the isomeric methoxy derivatives **28** and **29**.

The configuration of the isomers **28** and **29** was determined by the coupling constants: $J(11,12) = 3.1$ Hz for **28** is typical for the *trans*-positioned MeO and COOEt groups, whereas $J(11,12) = 9.7$ for **29** establishes the corresponding *cis* configuration. Furthermore, the small coupling observed between the bridgehead H–C(8) and H–C(12) ($^3J(8,12) = 1.7$ and 1.8, resp.) confirms the *exo*-orientation of the MeO substituent with respect to the carbonyloxy branch.

Conclusions. – We developed a short and efficient synthesis for the bicyclic endoperoxides **10** and **16**. Thiourea reduction of endoperoxide **10** resulted in the formation of the corresponding benzotropolone **11** in quantitative yield upon treatment with thiourea, whereas the thiourea reaction of **16** produced mainly unusual rearrangement products **28** and **29** beside the desired benzotropolone derivative **27**.

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Experimental Part

General. All substances reported in this paper are in their racemic form. TLC: *Merck* 0.2 mm silica gel *60* F_{254} anal. aluminium plates. Column chromatography (CC): silica gel (60-mesh, *Merck*). M.p.: uncorrected. IR Spectra: soln. in 0.1-mm cells or KBr pellets; in cm^{-1}. ^1H- and ^{13}C-NMR Spectra: 400(100)- and 200(50)-MHz spectrometers; apparent splittings are given in all cases; δ in ppm, J in Hz. MS: in m/z (rel. %).

*(1*RS*,9*SR*)-10,11-Dioxatricyclo[7.2.2.0^{2,7}]trideca-2,4,6,12-tetraen-8-one* (= *(1*RS*,4*SR*)-1,4-Etheno-1*H*-2,3-benzodioxepin-5(4*H*)-one*; **10**). A soln. of 2,3-benzotropone (= 5*H*-benzocyclohepten-5-one; **5**) 1.35 g,

8.63 mmol) and 5,10,15,20-tetraphenylporphyrin (10 mg) in CCl_4 (50 ml) was irradiated with a projection lamp (500 W), while a slow stream of dry O_2 was passed through the soln. at r.t. After 18 h, the solvent was evaporated at 20° and the residue filtered through silica gel (30 g) eluting with hexane/AcOEt 95:5 pure **10** (1.2 g, 74%). Yellow wax. IR (liq.): 3068*w*, 3025*w*, 2971*w*, 1697*s*, 1605*m*, 1458*w*, 1362*w*, 1285*s*, 1227*m*, 977*m*, 931*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 8.08 (*m*, H–C(6)); 7.59–7.26 (*m*, 3 arom. H); 7.14 (br. *dd*, *J*(12,13) = 9.1, *J*(1,12) = 7.1, H–C(12)); 6.42 (br. *dd*, *J*(12,13) = 9.1, *J*(9,13) = 7.3, H–C(13)); 5.42 (br. *d*, *J*(9,13) = 7.3, H–C(9)); 5.18 (br. *d*, *J*(1,12) = 7.1, H–C(1)). ^{13}C-NMR (50 MHz, $CDCl_3$): 194.9; 141.8; 141.0; 135.8; 133.9; 132.6; 131.8; 130.2; 124.5; 87.4; 84.5. Anal. calc. for $C_{11}H_8O_3$: C 70.21, H 4.29; found: C 70.38, H 4.18.

*6-Hydroxy-5*H*-benzocyclohepten-5-one* (**11**). To a soln. of **10** (500 mg, 2.66 mmol) in MeOH (18 ml) at 0°, a soln. of thiourea (210 mg, 2.76 mmol) in MeOH (5 ml) was added dropwise in 10 min. The soln. was stirred in the ice bath for 30 min and at r.t. for additional 3 h. After evaporation ^{1}H-NMR analysis indicated the formation of **11** (457 mg, 100%), which was crystallized from CH_2Cl_2/hexane. M.p. 81–82° ([11]: m.p 85–86°). IR (KBr): 3460*m*, 3183*w*, 1643*w*, 1593*m*, 1555*m*, 1485*m*, 1428*m*, 1354*w*, 1235*s*, 1066*w*. ^{1}H-NMR (200 MHz, $CDCl_3$): 8.89 (br. *d*, *J*(3,4) = 7.4, H–C(4)); 8.70 (*m*, OH); 7.80–7.63 (*m*, 3 arom. H); 7.36 (br. *d*, *A* of *AB*, *J*(8,9) = 11.6, H–C(9)); 7.20 (br. *d*, *A* of *AB*, *J*(7,8) = 9.4, H–C(7)); 6.92 ('*dd*', *B* of *AB*, *J*(8,9) = 11.6, *J*(7,8) = 9.4, H–C(8)). ^{13}C-NMR (50 MHz, $CDCl_3$): 182.7; 159.0; 140.2; 136.0; 135.2; 134.8 (2 C); 133.1; 131.4; 128.7; 116.4. EI-MS (70 eV): 172 (100, M^+), 144 (74), 116 and 115 (83), 89 (14), 63 (10). Anal. calc. for $C_{11}H_8O_2$: C 76.73, H 4.68; found: C 77.03, H 4.64.

*Ethyl 5-Oxo-5*H*-benzocycloheptene-7-carboxylate* (**15**). A soln. of CrO_3 (4.23 g, 42.3 mmol) in pyridine/CH_2Cl_2 1:1 (42 ml) was cooled to 0°. Then ethyl 7*H*-benzocycloheptene-7-carboxylate (**13**; 1.4 g, 6.53 mmol) in CH_2Cl_2 (19 ml) was added dropwise. The mixture was stirred at 0° for 2 h and r.t. for 25 h, and the solvent was evaporated. The residue was filtered over silica gel (10 g) with hexane/AcOEt 95:5: pure **15** (1.07 g, 72%), which was crystallized from CH_2Cl_2/hexane. Pale yellow crystals. M.p. 81–82°. IR (KBr): 3061*w*, 2976*m*, 2915*w*, 1715*s*, 1576*s*, 1469*m*, 1330*m*, 1246*s*, 1130*m*, 1046*m*, 946*w*, 792*m*, 707*w*. ^{1}H-NMR (200 MHz, $CDCl_3$): 8.40 (*m*, H–C(4)); 7.76–7.61 (*m*, 3 arom. H, H–C(6)); 7.36 (br. *d*, *A* of *AB*, *J*(8,9) = 12.0, H–C(9)); 7.29 (*dd*, *B* of *AB*, *J*(8,9) = 12.0, *J*(6,8) = 1.8, H–C(8)); 4.37 (*q*, *J* = 7.2, CH_2O); 1.39 (*t*, *J* = 7.2, Me). ^{13}C-NMR (50 MHz, $CDCl_3$): 190.1; 168.6; 141.2; 140.1; 134.0; 137.7 (2 C); 135.6; 134.7; 132.7; 132.6; 126.9; 64.3; 16.1. Anal. calc. for $C_{14}H_{12}O_3$: C 73.67, H 5.30; found: C 73.56, H 5.23.

As described above with ethyl 5*H*-benzocycloheptene-7-carboxylate (**14**; 0.66 g, 3.08 mmol) in CH_2Cl_2 (9 ml): 583 mg (83%) of **15**.

*Ethyl (1*RS*,9*SR*)-8-Oxo-10,11-dioxatricyclo[7.2.2.0^{2,7}]trideca-2,4,6,12-tetraene-13-carboxylate = Ethyl (1*RS*,4*SR*)-4,5-Dihydro-5-oxo-1,4-etheno-1 H-2,3-benzodioxepin-10-carboxylate*; (**16**). A soln. of **15** (1.5 g, 6.57 mmol) and 5,10,15,20-tetraphenylporphyrin (10 mg) in CCl_4 (50 ml) was irradiated with a projection lamp (500 W) while a slow stream of dry O_2 was passed through the soln. at r.t. After 20 h, the solvent was evaporated at 20° and the residue crystallized from Et_2O/hexane 1:1: **16** (1.62 g, 95%). Pale yellow crystals. M.p. 127–128°. IR (KBr): 3093*w*, 2984*m*, 2942*w*, 2904*w*, 1703*s*, 1596*m*, 1465*m*, 1375*m*, 1266*s*, 1090*m*, 1017*m*, 964*m*, 938*m*, 892*w*, 865*w*, 810*w*, 760*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 8.13 (*m*, H–C(6)); 8.00 ('*dd*', *A* of *AX*, *J*(1,12) = 7.6, *J*(9,12) = 1.4, H–C(12)); 7.63–7.33 (*m*, 3 arom. H); 5.83 (*t*, *J*(9,12) = *J*(1,9) = 1.4, H–C(9)); 5.65 (*dd*, *X* of *AX*, *J*(1,12) = 7.6, *J*(1,9) = 1.4, H–C(1)); 4.31 (*q*, *J* = 7.1, CH_2O); 1.37 (*t*, *J* = 7.1, Me). ^{13}C-NMR (50 MHz, $CDCl_3$): 192.9; 164.3; 146.6; 140.8; 135.8; 133.9; 132.8; 132.2; 130.2; 130.0; 86.4; 83.5; 63.8; 16.0. EI-MS (70 eV): 260 (12, M^+), 214 (35), 146 (100), 133 (42), 105 (28), 77 (47), 51 (23). Anal. calc. for $C_{14}H_{12}O_5$: C 64.61, H 4.65; found: C 64.20, H 4.59.

Thermolyses of **16**. A soln. of **16** (500 mg, 1.92 mmol) in toluene (10 ml) in a sealed tube was heated at 131° for 24 h. Then the solvent was evaported and the residue subjected to CC (silica gel (60 g), hexane/AcOEt 95:5 and 50:50): increasing by polar **20** (66 mg, 16%), **18** (110 mg, 22%), **19** (89 mg, 20%), and **17** (95 mg, 19%).

Ethyl 1-Hydroxynaphthalene-2-carboxylate (**20**): Recrystallization from CH_2Cl_2/hexane gave pale yellow crystals. M.p. 43–44° [14a]: 40.5–41°; [14b]: 47–48°). IR (KBr): 3441*w*, 3048*w*, 2979*w*, 2921*w*, 1651*s*, 1593*m*, 1470*m*, 1412*m*, 1335*m*, 1258*s*, 1162*m*, 1085*w*, 1023*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 12.08 (*m*, OH); 8.42 (br. *d*, *J* = 8.3, H–C(8)); 7.81–7.48 (*m*, 4 arom. H); 7.28 (br. *d*, *J*(3,4) = 8.8, H–C(4)); 4.46 (*q*, *J* = 7.2, CH_2O); 1.44 (*t*, *J* = 7.2, Me). ^{13}C-NMR (100 MHz, $CDCl_3$): 173.1; 163.0; 139.2; 131.3; 129.4; 127.7; 126.8; 126.3; 125.9; 120.5; 107.8; 63.4; 16.3. EI-MS (70 eV): 216 (68, M^+), 170 (100), 142 (22), 114 (83), 88 (14), 63 (15).

*Ethyl (1*RS*,9*RS*)-8-Oxo-12,13-dioxatricyclo[7.3.1.0^{2,7}]trideca-2,4,6,10-tetraene-10-carboxylate* (= *Ethyl (1*RS*,5*RS*)-5,6-Dihydro-6-oxo-1,5-epoxy-1*H*-2-benzoxocin-4-carboxylate*; **18**): Recrystallization from Et_2O/hexane gave pale yellow crystals. M.p. 81–82°. IR (KBr): 3068*w*, 2998*w*, 1716*s*, 1624*m*, 1601*m*, 1393*m*, 1374*m*, 1297*m*, 1235*m*, 1177*m*, 1131*m*, 1104*m*, 965*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.99 (*dd*, *J*(5,6) = 7.6, *J*(4,6) = 1.1, H–C(6)); 7.61 (*dt*, *J*(4,5) = *J*(3,4) = 7.6, *J*(4,6) = 1.1, H–C(4)); 7.50 (*s*, H–C(11)); 7.48 (*dt*, *J*(4,5) =

$J(5,6) = 7.6$, $J(3,5) = 1.1$, H–C(5)); 7.36 (*dd*, $J(3,4) = 7.6$, $J(3,5) = 1.1$, H–C(3)); 6.30 (*s*, H–C(1)); 5.15 (*s*, H–C(9)); 4.13 (*q*, $J = 7.1$, CH_2O); 1.21 (*t*, $J = 7.1$, Me). ^{13}C-NMR (100 MHz, $CDCl_3$): 190.9 (C(8)); 164.1(*C*O_2Et); 152.0(C(11)); 136.5(C(7)); 135.0(C(4)); 130.9(C(5)); 127.1(C(2)); 127.0(C(6)); 126.8(C(3)); 104.5(C(10)); 93.8(C(1)); 71.7(C(9)); 61.0(CH_2O); 14.6 (Me). EI-MS (70 eV): 260 (5, M^+); 214 (18), 146 (100), 133 (52), 130 (22), 118 (15), 105 (37), 77 (72), 51 (41). Anal. calc. for $C_{14}H_{12}O_5$: C 64.61, H 4.65; found: C 64.93, H 4.71.

*Ethyl 3-[3-Oxoisobenzofuran-1(3*H*)-ylidene]propanoate* (**19**): Recrystallization from Et_2O/hexane gave pale yellow crystals. M.p. 48–49° ([16]: yellow oil). IR (KBr): 2991*m*, 1855*m*, 1786*s*, 1736*s*, 1601*w*, 1470*w*, 1408*w*, 1381*w*, 1274*s*, 1120*w*, 1027*m*, 912*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.91–7.50 (*m*, 4 arom. H); 5.82 (*t*, $J(2,3) = 7.4$, H–C(3)); 4.20 (*q*, $J = 7.1$, CH_2O); 3.53 (*d*, $J(2,3) = 7.4$, CH_2(2)); 1.31 (*t*, $J = 7.1$, Me). ^{13}C-NMR (50 MHz, $CDCl_3$): 172.7; 168.5; 149.0; 141.0; 136.5; 132.0; 127.4; 126.6; 122.2; 102.3; 63.2; 33.3; 16.2. EI-MS (70 eV): 202 (6, M^+), 159 (9), 132 (16), 104 (100), 77 (72), 91(16), 76(56), 50(26), 44(30). Anal. calc. for $C_{13}H_{12}O_3$: C 67.23, H 5.21; found: C 67.53, H 5.41.

*Ethyl 3-Hydroxy-2-{[3-oxoisobenzofuran-1(3*H*)-ylidene]methyl}prop-2-enoate* (**17**): Crystallization from CH_2Cl_2/Et_2O gave pale yellow crystals. M.p. 122–123°. IR (KBr): 3006*w*, 2910*w*, 1786*s*, 1670*s*, 1605*m*, 1478*w*, 1412*m*, 1293*m*, 1227*s*, 1139*m*, 1085*m*, 1023*m*, 973*m*, 873*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 12.56 (*d*, *J*(3,OH) = 12.8, OH); 8.32 (*d*, *J*(3,OH) = 12.8, H–C(3)); 7.83 (br. *d*, $J(4,5) = 7.7$, H–C(4′)); 7.65 (*m*, H–C(6′)); H–C(7′)); 7.43 (*m*, H–C(5′)); 6.22 (*s*, CH=C(1′)); 4.29 (*q*, $J = 7.1$, CH_2O); 1.33 (*t*, $J = 7.1$, Me). ^{13}C-NMR (100 MHz, $CDCl_3$): 171.2(C(1)); 169.5(C(3)); 167.2(C(3′)) 142.0(C(1′)); 140.8(C(3′a)); 134.8(C(7′)); 129.5(C(5′)); 125.9(C(4′)); 123.5(C(7′a)); 119.8(C(6′)); 101.4(C(2)); 99.1(*C*H=C(1′)); 61.8(CH_2O); 14.6(Me). EI-MS (70 eV): 188.1(5, $[M - CO_2Et]^+$), 159 (100), 131 (58), 103 (91), 77 (83), 63 (12), 55 (42), 50 (45%). Anal. calc. for $C_{14}H_{12}O_5$: C 64.61, H 4.65; found: C 64.48, H 4.73.

Reaction of **16** *with Thiourea*. To a soln. of **16** (500 mg, 1.92 mmol) in MeOH (20 ml) at 0°, a soln. of thiourea (146 mg, 1.92 mmol) in MeOH (5 ml) was added dropwise over 10 min. The soln. was stirred in an ice bath for 30 min and at r.t. for 3 h. The solvent was evaporated and the residue filtered through silica gel (80 g) with hexane/AcOEt 85:15: increasingly polar **27** (150 mg, 32%), **28** (146 mg, 26%), and **29** (106 mg, 19%).

*Ethyl 6-Hydroxy-5-oxo-5*H*-benzocycloheptene-7-carboxylate* (**27**): Crystallization from Et_2O/hexane gave dark yellow crystals. M.p. 84–85°. IR (KBr): 3521*w*, 3451*w*, 3251*m*, 2989*w*, 2935*w*, 1735*w*, 1689*m*, 1592*m*, 1546*m*, 1477*m*, 1380*m*, 1265*s*, 1234*s*, 1176*m*, 1137*s*, 1033*m*, 813*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 11.33 (br. *s*, OH); 8.56 (br. *d*, $J(3,4) = 8.3$, H–C(4)); 7.76–7.56 (*m*, 3 arom. H); 7.13 (*m*, H–C(8), H–C(9)); 4.44 (*q*, $J = 7.1$, CH_2O); 1.42 (*t*, $J = 7.1$, Me). ^{13}C-NMR (50 MHz, $CDCl_3$): 182.2(C(5)); 169.1(*C*O_2Et); 158.7(C(6)); 136.3(C(9a)); 132.2(C(2)); 131.6(C(1)); 130.1(C(4a)); 130.1(C(4)); 129.1(C(8)); 128.4(C(3)); 123.0(C(9)); 113.1(C(7)); 61.5(CH_2O); 13.1(Me). EI-MS (70 eV): 244 (5, M^+), 207 (22), 185 (37), 141 (15), 114 (46), 96 (27), 73 (28), 44 (100). Anal. calc. for $C_{14}H_{12}O_4$: C 68.85, H 4.95; found: C 68.75, H, 4.87.

Ethyl trans-*1-Hydroxy-12-methoxy-10-oxo-9-oxatricyclo[6.2.2.0^{2,7}]dodeca-2,4,6-triene-11-carboxylate* (= *Ethyl (1*RS,*4*SR,*9*SR,*10*SR*)-3,4-Dihydro-4-hydroxy-10-methoxy-3-oxo-1,4-ethano-1*H*-2-benzopyran-9-carboxylate*; **28**): Colorless wax. IR (liq.: 3453*w*, 2987*w*, 2941*w*, 2844*w*, 1766*s*, 1470*w*, 1370*w*, 1277*m*, 1197*m*, 1150*m*, 1100*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.50 (br. *d*, $J(3,4) = 7.5$, H–C(3)); 7.37 (*m*, H–C(4)); 7.30–7.25 (*m*, 2 arom. H); 5.64 (*d*, $J(8,12) = 1.7$, H–C(8)); 4.07 (*q*, $J = 7.2$, CH_2O); 3.81 (*dd*, $J(11,12) = 3.1$, $J(8,12) = 1.7$, H–C(12)); 3.39 (*s*, MeO); 2.89 (*d*, $J(11,12) = 3.1$, H–C(11)); 1.18 (*t*, $J = 7.2$, Me). ^{13}C-NMR (100 MHz, $CDCl_3$): 173.6(C(10)); 169.9(*C*O_2Et); 135.8(C(2)); 131.8(C(7)); 130.3(C(4)); 124.2(C(6)); 123.71(C(5)); 123.74(C(3)); 81.8(C(12)); 78.8(C(8)); 75.7(C(1)); 62.1(CH_2O); 57.5(MeO); 51.3(C(11)); 14.8(Me). EI-MS (70 eV): 217, 216 (24, $[M - CO_2 - MeO]^+$), 170 (8), 162 (22), 144 (100), 131 (35), 115 (34), 105 (24), 85 (50), 77 (17). Anal. calc. for $C_{15}H_{16}O_6$: C 61.64, H 5.52; found: C 61.23, H, 5.56.

Ethyl cis-*1-Hydroxy-12-methoxy-10-oxo-9-oxa-tricyclo[6.2.2.0^{2,7}]dodeca-2,4,6-triene-11-carboxylate* (= *Ethyl (1*RS,*4*SR,*9*RS,*10*SR*)-3,4-Dihydro-4-hydroxy-10-methoxy-3-oxo-1,4-ethano-1*H*-2-benzopyran-9-carboxylate*; **29**): Colorless wax. IR (liq.): 3468*m*, 2979*m*, 2937*m*, 2841*w*, 1774*s*, 1462*m*, 1374*m*, 1335*m*, 1285*w*, 1193*m*, 1112*m*, 1019*w*, 1016*w*, 996*w*, 931*w*. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.61–7.27 (*m*, 4 arom. H); 5.71 (*d*, $J(8,12) = 1.8$, H–C(8)); 4.23 (*q*, $J = 7.1$, CH_2O); 3.93 (*dd*, *A* of *AB*, $J(11,12) = 9.7$, $J(8,12) = 1.8$, H–C(12)); 3.52 (*s*, MeO); 3.25 (*d*, *B* of *AB*, $J(11,12) = 9.7$, H–C(11)); 1.28 (*t*, $J = 7.1$, Me). ^{13}C-NMR (50 MHz, $CDCl_3$): 174.6; 169.9; 140.0; 133.8; 132.1; 130.2; 126.1; 124.0; 79.9; 79.0; 76.3; 63.4; 60.1; 53.2; 16.0. Anal. calc. for $C_{15}H_{16}O_6$: C 61.64, H 5.52; found: C 61.38, H 5.55.

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