Fragmentation of Alkoxy Radicals: Tandem β-Fragmentation–Cycloperoxyiodination Reaction

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Received March 22, 1994®

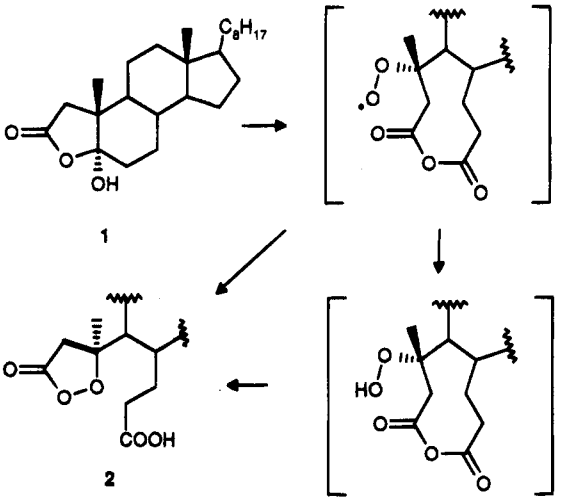
The steroidal alcohols 2-cholesten-5α-ol (**3**), 3-phenyl-2-cholesten-5α-ol (**4**), and 3α*H*-2′-oxofuro-[2,3]cholestan-5α-ol (**5**) were prepared in order to test a new tandem β-fragmentation–cycloperoxyiodination reaction. The alkoxy radicals generated by irradiation of these alcohols with visible light in the presence of (diacetoxyiodo)benzene, I_2, and molecular oxygen undergo a β-fragmentation reaction with subsequent peroxidation of the C-radical formed. This peroxy radical is added to conveniently positioned double bonds to give 10-membered cyclic ketones possessing a 1,2-dioxolane group.

During the past several years, a resurgence in carbon-centered radical chemistry has been accompanied by an increased interest in alkoxy radicals.[1] The principal studies have been related to the β-fragmentation reaction and subsequent transformations of the C-radicals formed during this process.[2]

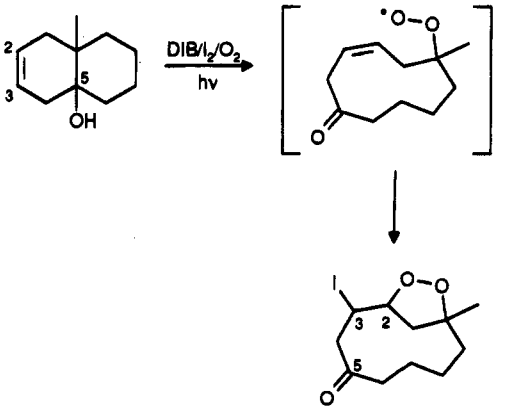
We have recently reported that the β-fragmentation reaction of alkoxy radicals generated by treatment of tertiary alcohols, hemiacetals, or lactols (e.g., **1**) with (diacetoxyiodo)benzene (DIB) and I_2 under irradiation with visible light leads, in the presence of O_2, to peroxidation of the initially produced C-radical by trapping molecular oxygen.[3] The resulting peroxy radical or its corresponding hydroperoxide reacts with suitably positioned carbonyl groups yielding β-peroxy lactones (e.g., **2**) in good yields (Scheme 1).[3a,c]

In a continuation of these studies, we envisioned that highly functionalized medium-sized cyclic ketones might be accessible from homoallylic alcohols using conveniently positioned double bonds to trap intramolecularly the peroxy radical intermediate formed (Scheme 2). Intramolecular addition of peroxy radicals to C—C double bonds to give internal endoperoxides (1,2-dioxolanes) is a very important reaction and the key step in the biosynthesis of prostaglandins and thromboxanes.[4] Synthetic applications of this reaction have also been developed.[5]

Scheme 1



Scheme 2



In this paper we describe the preparation of steroidal alcohols **3**–**5**. These alcohols on treatment with DIB and I_2 under an O_2 atmosphere and irradiation with visible

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® Abstract published in *Advance ACS Abstracts,* July 1, 1994.

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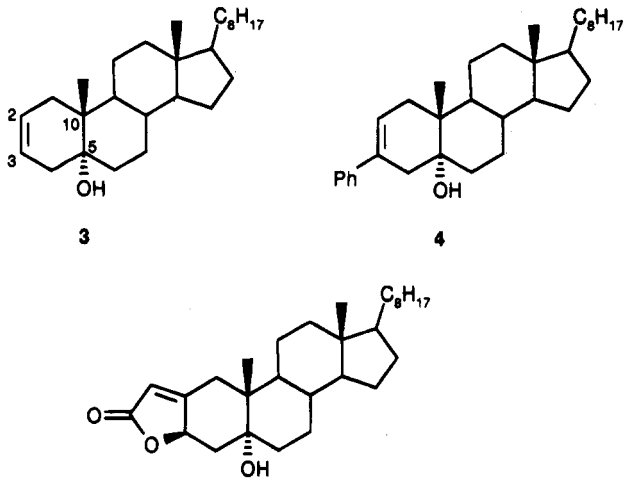
light gave a new tandem β-fragmentation–cycloperoxyiodination reaction to afford cyclic epidioxy ketones in moderate yields. Preliminary experiments to ascertain the feasibility of this approach have been reported earlier.[3b]

Results and Discussion

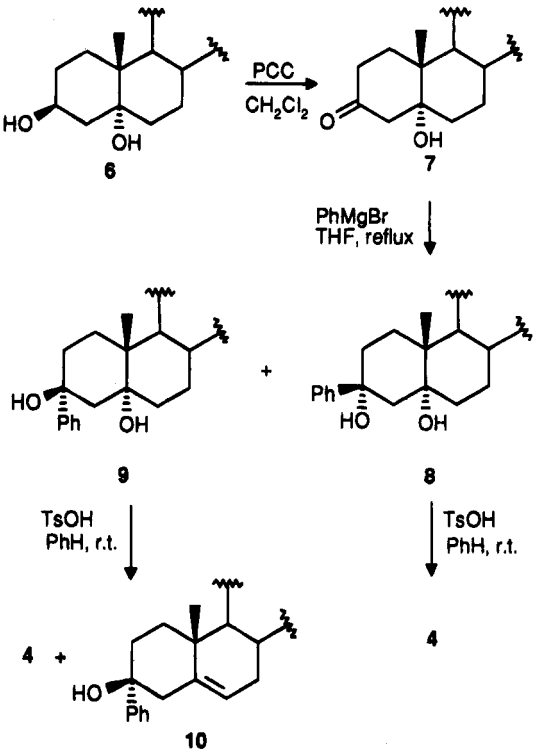
Synthesis of Substrates 3–5. Alcohol **3** was prepared from cholesterol essentially following a previously reported procedure.[6] The phenyl-substituted analog **4** was synthesized starting from known diol **6**.[6] Oxidation



of **6** with PCC afforded ketone **7** (Scheme 3), which was treated with PhMgBr to yield a mixture of alcohols **8** (31%) and **9** (58%). The C_3 stereochemistry of these alcohols was initially determined by considering the possibility of hydrogen bonding of the 1,3 diol system, the position of the C_{10} methyl group in the ^1H NMR spectrum as calculated by the method of Zürcher,[7] and mechanistic properties.[8] The stereochemistry of alcohol **8** was unequivocally confirmed (*vide infra*) by $LiAlH_4$ reduction of epoxide **25** (Scheme 6).

Regioselective dehydration of diol **8** was readily accomplished by acid treatment giving homoallylic alcohol **4** as a single product in 70% yield. However, less regioselectivity was observed in the acid treatment of the

Scheme 3



diastereoisomeric diol **9**, and a mixture of compounds **4** (10%) and **10** (30%) was obtained. These results also support the C_3 stereochemistry assigned to compounds **8** and **9**. In the case of diol **8**, the elimination of the axial alcohol at C_3 is faster than that at C_5, while in compound **9** the axial alcohol at C_5 dehydrates preferentially to the equatorial alcohol at C_3.

The synthesis of lactone **5** from cholest-2-en-5α-ol (**3**) is outlined in Scheme 4. Epoxidation of **3** with *m*-CPBA gave a single epoxide **11** in 96% yield, which was treated with allylmagnesium bromide to give diol **12** (71%). Acetylation of the secondary alcohol on C_3 with acetic anhydride in pyridine followed by oxidation of the resulting acetate **13** with HIO_4–$RuCl_3$ furnished acid **14**.[9] Purification of **14** was accomplished by methylation with ethereal CH_2N_2 and chromatography of the resulting methyl ester **15** (67% from **13**). Ester **15** was hydrolyzed with 5% aqueous KOH affording acid **16**. Reaction conditions initially explored for the lactonization of **16** utilized perchloric acid or TsOH. Although the lactones were obtained, yields were poor since concomitant dehydration of the 5α-hydroxyl group occurred. An improvement in the lactonization reaction, however, was accomplished by using Mitsunobu conditions giving the expected (3*S*)-lactone **17** (59%) along with (3*R*)-lactone **18** (31%) in which the stereochemistry at C-3 was retained.[10]

Assignment of the C_3 stereochemistry of these lactones was realized by NOE difference experiments. In the case of lactone **17**, irradiation of the signal for the C_{10} methyl group resulted in the clear enhancement (7%) of the 1′α-H proton signal at δ 2.64 (dd, J = 17.6, 13 Hz). This result is also consistent with a chair conformation of the steroidal ring A. The simulated shape of the C_3 proton signal using coupling constants obtained by molecular modeling also supported the proposed stereochemistry.[11]

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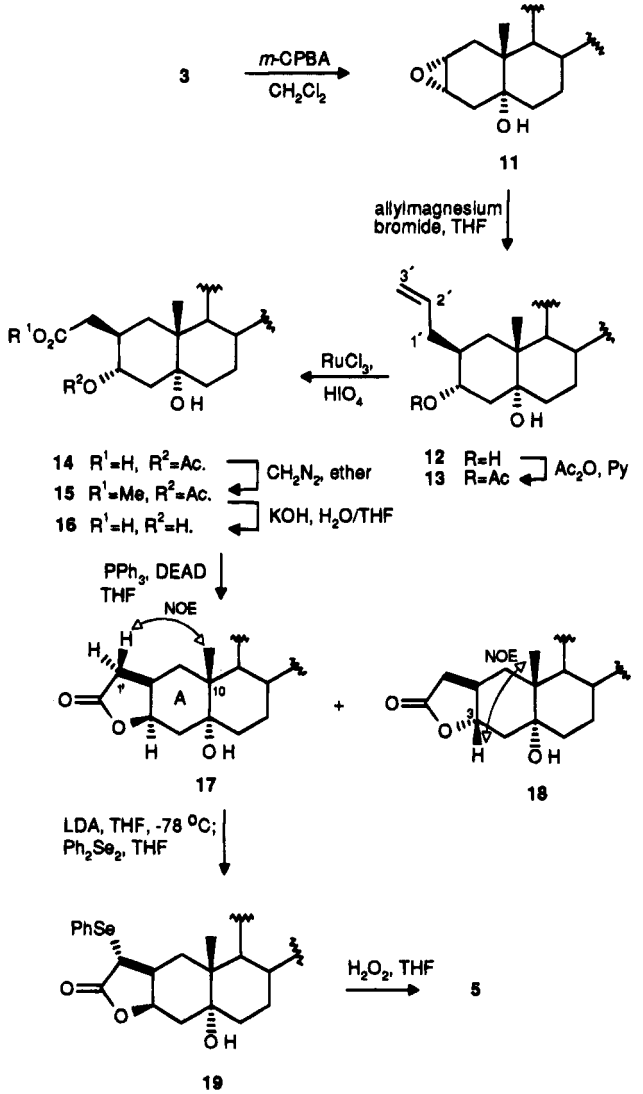
Table 1[a]

entry	substrate	reagents (mmol)	P (atm)	time (h)	products (yield, %)
1	**3**	DIB/I_2 (3/1.3)	Ar (1)	4	**20** (83)
2	**3**	DIB/I_2 (2/2)	air (1)	2	**20** (44)
3	**3**	DIB/I_2 (2/2)	O_2 (2)	1.75	**20** (23), **21** (40), **22** (11)
4	**3**	DIB/I_2 (2/2)	O_2 (5)	2	**20** (15), **21** (43), **22** (15)
5	**3**	DIB/I_2 (3/1.5)	O_2 (10)	3.5	**20** (25), **21** (16), **22** (8)
6	**3**	DIB/I_2 (2/2)	O_2 (2)	1.75	**20** (20), **23** (50)[b]
7	**4**	DIB/I_2 (2.8/1)	Ar (1)	4	**24** (23)
8	**4**	DIB/I_2 (3.5/1)	O_2 (5)	1.5	**25** (56), **26** (13)
9	**4**	DIB/I_2 (2.6/1)	O_2 (10)	2	**25** (47), **26** (18)
10	**5**	DIB/I_2 (1.6/1.6)	O_2 (2.5)	1	**28** (12), **29** (20), **5** (32)
11	**5**	DIB/I_2 (2.6/1.3)	O_2 (5)	0.75	**27** (3), **28** (2), **29** (24), **5** (47)
12	**5**	HgO/I_2 (4/1)	O_2 (5)	2	**27** (2), **28** (2), **29** (14)

[a] All reactions were run in cyclohexane (0.2 mmol in 15 mL) at 40–45 °C under irradiation with two 100-W tungsten-filament lamps; those under pressure were performed in a borosilicate Griffin–Worden pressure vessel (Kontes K-767100). [b] The crude reaction mixture was treated with silica gel Merck 60 PF_{254} in *n*-hexane at room temperature for 5.5 h. DIB = (diacetoxyiodo)benzene.

Scheme 4



The steroidal ring A in compound **18** must adopt a *twist* conformation in order to accommodate the *trans*-lactone. The *trans*-stereochemistry of lactone **18** was apparent from the NOE observed between the C_{10} methyl group and the 3β-H at δ 4.39. No other signals in the δ 2–5 region of the spectrum showed an enhancement. The simulated signal of the 3β-H was also consistent with the shape of the observed signal at δ 4.39.[11]

(11) Programs PCMODEL (Serena Software) and RACCOON (P. Schatz, University of Wisconsin) were utilized to obtain the coupling constants and simulation of the ^{1}H NMR signals, respectively.

The large amount of the anomalous (3*R*)-lactone (**18**, 31%) obtained in the Mitsunobu lactonization reaction deserves some comments. Variable amounts of retention products have been observed in the Mitsunobu reaction when weak acids are employed, and the reaction proceeds to some degree *via* an (acyloxy)phosphonium ion pair.[12]

Deprotonation of lactone **17** using LDA and reaction of the lithium enolate with diphenyl diselenide gave the phenylselenium derivative **19**. The phenylseleno group is introduced on the less hindered α-side of the molecule. Subsequently, **19** underwent oxidative *syn*-elimination with hydrogen peroxide at 0 °C to give the desired α,β-unsaturated lactone **5** (67% from **17**).

Tandem β-Fragmentation–Cycloperoxyiodination Reaction. The ring expansion reaction of homoallylic alcohols **3–5** to give polyfunctionalized decalones was effected by an alkoxy radical promoted β-fragmentation.[13] Alcohol **3** was treated with DIB-I_2 under irradiation with two 100-W tungsten-filament lamps under the conditions summarized in Table 1.

When the reaction was performed under argon (entry 1) dienone **20** was obtained in good yield; under air a lower yield of **20** was obtained but the formation of the desired cyclic peroxides was not observed (entry 2) (Scheme 5). However, under O_2 pressure homoallylic alcohol **3** underwent a tandem β-fragmentation–cycloperoxyiodination reaction to give two isomeric epidioxy iodides **21** and **22** (entries 3 and 4). Increased oxygen pressure led to clearly inferior results (entry 5). Although some decomposition was observed both compounds could be purified by chromatography on deactivated silica gel. When the crude reaction mixture was adsorbed on deactivated silica gel for 5.5 h enone **23** was obtained (entry 6). Pure iodides **21** and **22** were also transformed into enone **23** when submitted separately to this treatment, indicating that they are isomers at C_3. The more abundant and also more stable epidioxy iodide **21** is a crystalline solid whose spectroscopic data are in accord with the proposed structure. The ^{1}H NMR spectrum showed a doublet and a triplet at δ 4.86 (C_3-H) and 5.01 (C_2-H), respectively. The ^{13}C NMR spectrum and DEPT

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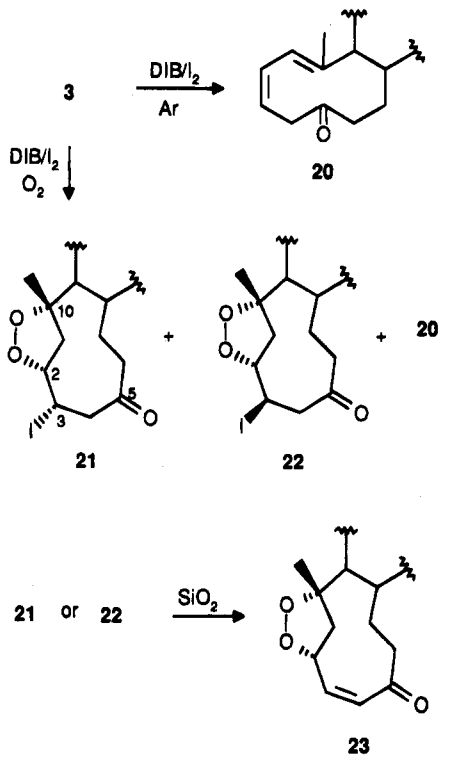
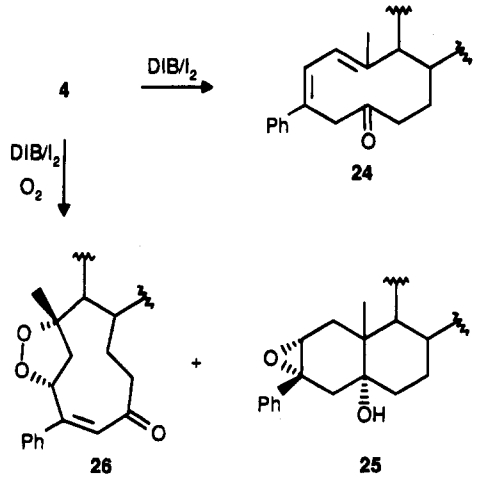
Scheme 5



Scheme 6

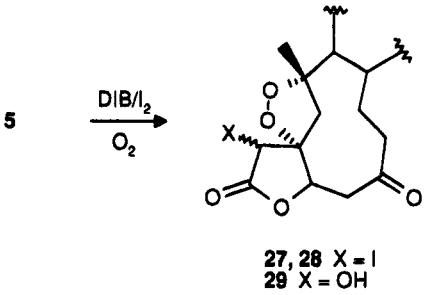


experiments showed the two peroxy carbons at δ 92.23 (C_{10}) and 85.65 (C_2). Its stereochemistry was determined by single-crystal X-ray analysis. Due to extensive decomposition, three crystals were used for data collection. Attempts to reduce the epidioxy bridge in either **21** or **22** with samarium(II) iodide, thiourea, or triphenylphosphine led to mixtures that were not studied further.

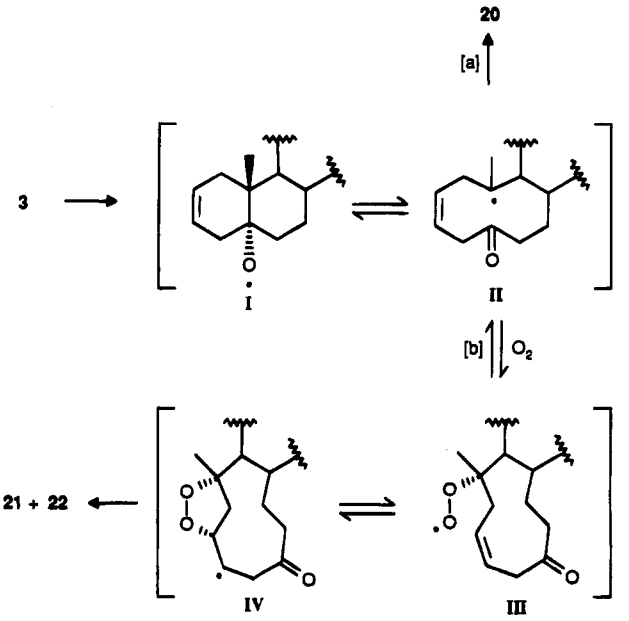
Homoallylic alcohol **4** was prepared in order to increase the nucleophilic character of the olefin and to permit the stabilization of the intermediate radical at C_3. In this case, when the β-fragmentation reaction was performed with exclusion of O_2, 10-membered dienone **24** (23%) was the only product that could be isolated from the complex reaction mixture (entry 7). Nevertheless, under O_2 (5 or 10 atm) the reaction proceeded smoothly to give compounds **25** and **26** (entries 8 and 9). Epidioxide **26** was obtained in low yield, the major product being epoxide **25** (Scheme 6).

Several experiments were performed to study the formation of epoxide **25**. Although the reactive species

Scheme 7



Scheme 8



involved in the epoxidation is not known, all reagents and irradiation are necessary for the reaction to take place. Hypervalent iodine reagents, catalyzed by transition metal complexes, have been previously used for the epoxidation of activated olefins,[14] but to our knowledge this is the first case of epoxidation of a simple olefin under these conditions. The low electrophilicity of this unknown species probably hinders the formation of any epoxide in the case of olefin **3**.

Lastly, we examined the reaction of α,β-unsaturated lactone **5** under the conditions shown in Table 1 (entries 10–12). Under 2.5 atm of oxygen we obtained a mixture of epidioxides **27–29** with a global yield of 32% (Scheme 7). When the pressure of oxygen was increased (entry 11) or the oxidizing agent changed to HgO (entry 12) no improvement of the epidioxides yield was observed.

A plausible mechanism for the formation of these peroxy derivatives, applied to the photolysis of model **3**, is shown in Scheme 8. The alkoxy radical I initially formed undergoes β-fragmentation producing a C_{10} radical II. The other possible fragmentations through C_4–C_5 or C_5–C_6 were not observed. Under Ar (path a), radical II was stabilized by elimination to give diene **20**. Notwithstanding, under an oxygen atmosphere the radical II was stereoselectively peroxidated with inversion of configuration. The formed peroxy radical III attacked the double bond to generate the C_3 radical which was stabilized by trapping an iodine atom from the medium in a nonstereoselective manner to yield a mixture of **21** and **22**.

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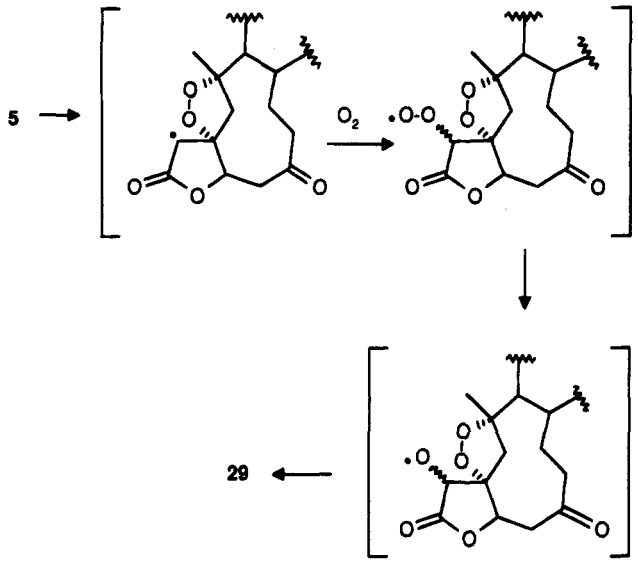
Scheme 9



The stereoselectivity observed in the peroxidation of radical I may be due not only to steric hindrance but also to the fact that the equilibrium between I and IV is directed kinetically or thermodynamically to the formation of isomers **21** and **22**. We cannot discard, taking into account the overall reaction yield, 74%, that small amounts of an unstable isomeric epidioxide could be formed and decomposed during the process.

Formation of alcohol **29** during the photolysis of **5** could be explained through the mechanism shown in Scheme 9. The peroxy radical intermediate underwent a homolytic cleavage or a reduction to the alkoxy radical which led to the alcohol **29**. Because of the relative weakness of the peroxide bond the catalyzed homolysis of the peroxy radical to give the alkoxy radical is a very easy process and, due to its biological importance, a well-documented one.[15] In our case this homolytic reaction may be catalyzed by radical species or traces of metal ions in the medium.

Experimental Section

General. Melting points were determined with a Kofler hot-stage apparatus and are uncorrected. Optical rotation measurements were recorded at room temperature in $CHCl_3$ on a Perkin-Elmer 141 or 142 polarimeter. IR spectra were recorded on a Perkin-Elmer 1605/FTIR spectrometer in $CHCl_3$ solutions. UV spectra were obtained with a Perkin-Elmer 550SE spectrometer. ^1H NMR spectra (δ) were determined with a Bruker WP200SY (200 MHz) or AMX 400 (400 MHz) spectrometer while ^{13}C NMR spectra (δ) were recorded with a Bruker WP 200 SY (50.3 MHz) spectrometer with Me_4Si as internal standard. Low-resolution mass spectra were determined with a Hewlett-Packard 5930A or VG Micromass ZAB-2F spectrometer and high-resolution mass spectra on a VG Micromass ZAB-2F spectrometer. Merck silica gel 60 PF_{254} and 60 (0.063–0.2 mm) were used for preparative thin-layer chromatography (TLC) and column chromatography, respectively. Circular layers of 1 mm of Merck silica gel 60 PF_{254} were used on a Harrison Chromatotron for centrifugally assisted chromatography. Commercial reagents and solvents were analytical grade or were purified by standard procedures prior to use.[16] The spray reagent for TLC was vanillin (1 g) in H_2SO_4–EtOH (4:1; 200 mL). (Diacetoxyiodo)benzene (DIB) 98% was purchased from Aldrich.

5α-Hydroxycholestan-3-one (7). Cholestane-3β,5α-diol (**6**) (269 mg, 0.67 mmol) in CH_2Cl_2 (100 mL) was treated with PCC (211 mg, 0.98 mmol) and stirred at rt for 24 h. The mixture was evaporated under vacuum, and after column chromatography through silica gel (*n*-hexane–EtOAc, 85:15), **7** was obtained (233 mg, 0.58 mmol, 87%): mp 211–213 °C (from acetone); $[\alpha]_D$ + 40.6° ($CHCl_3$, c = 0.32): IR 3540, 1700 cm^{-1}; ^1H NMR 0.68 (3H, s), 0.86 (6H, d, J = 6.62 Hz), 0.90 (3H, d, J = 8.52 Hz), 1.17 (3H, s), 2.11, (1H, d, J = 15.1 Hz), 2.86 (1H, d, J = 15.1 Hz); ^{13}C NMR 12.24, 15.94, 18.82, 21.62, 22.72, 22.97, 24.04, 24.33, 26.37, 28.16, 28.40, 32.84, 34.57, 35.02, 35.97, 36.32, 38.06, 39.33, 39.67, 40.08, 42.82, 46.09, 51.99, 56.14, 56.42, 77.68, 211.27 MS *m/z* (rel intensity) 402 (M^+, 15), 384 (100), 369 (28), 387 (7), 332 (36); HRMS calcd for $C_{27}H_{46}O_2$ 402.3498, found 402.3500.

3β-Phenyl-3α,5α-cholestanediol (8) and 3α-Phenyl-3β,5α-cholestanediol (9). To a solution of **7** (230 mg, 0.57 mmol) in dry Et_2O (4 mL) was added dropwise and under Ar a solution of PhMgBr in Et_2O (4 mL, 5.6 mmol). During the addition reflux temperature was reached, and once the addition was finished, stirring continued for 30 min. Then the solution was cooled to rt and H_2O (5 mL) was slowly added. The mixture was poured into saturated aqueous NH_4Cl and extracted with Et_2O. The organic layer was washed successively with H_2O and brine, dried (Na_2SO_4), and evaporated. Chromatotron chromatography (*n*-hexane–EtOAc, 90:10) gave **8** (97 mg, 0.2 mmol, 36%) and **9** (159 mg, 0.33 mmol, 58%). Compound **8**: mp 213–215 °C (from EtOAc–MeOH); $[\alpha]_D$ +10° ($CHCl_3$, c = 0.3); IR 3460, 3450 cm^{-1}; ^1H NMR 0.68 (3H, s), 0.86 (6H, d, J = 6.5 Hz), 0.91 (3H, d, J = 6.5 Hz), 1.06 (3H, s), 3.85 (2H, br), 7.2–7.5 (5H, m); ^{13}C NMR 12.36, 16.28, 18.85, 21.34, 22.73, 22.99, 24.08, 24.25, 25.71, 28.18, 28.41 (2×), 34.22, 35.02, 35.50, 36.01, 36.36, 39.33, 39.69, 40.24, 42.94, 45.54, 45.77, 56.35, 56.45, 74.88, 75.60, 124.58, 126.89, 128.37, 148.71; MS *m/z* (rel intensity) 480 (M^+, 4), 462 (7), 444 (11), 429 (3); HRMS calcd for $C_{33}H_{52}O_2$ 480.3967, found 480.4001. Compound **9**: mp 143–144 °C (from *n*-hexane); $[\alpha]_D$ +47° ($CHCl_3$, c = 0.48); IR 3606, 3470 cm^{-1}; ^1H NMR 0.66 (3H, s), 0.86 (6H, d, J = 6.5 Hz), 0.91 (3H, d, J = 6.5 Hz), 0.99 (3H, s), 2.39 (1H, d, J = 15 Hz), 3.75 (2H, OH, br), 7.2–7.5 (5H, m); ^{13}C NMR 12.06, 16.81, 18.73, 21.59, 22.55, 22.77, 23.83, 24.23, 27.17, 28.01, 28.21, 28.67, 33.46, 34.78, 35.74, 35.92, 36.24, 39.57, 40.04, 40.15, 42.61, 43.44, 43.68, 56.30, 56.83, 75.08, 75.67, 124.48, 126.61, 128.23, 148.7; MS *m/z* (rel intensity) 480 (M^+, 17), 462 (28), 447 (2), 444 (27), 429 (3); HRMS calcd for $C_{33}H_{52}O_2$, 480.3967, found 480.3972.

3-Phenyl-2-cholesten-5α-ol (4). To a solution of diol **8** (31 mg, 0.06 mmol) in dry C_6H_6 (20 mL) was added a catalytic amount of TsOH, and the mixture was allowed to react for 5 days at rt. Then the solution was poured into 20% aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic layer was washed with brine, dried (Na_2SO_4), and evaporated. Chromatotron chromatography (*n*-hexane–EtOAc, 85:15) gave **4** (20.3 mg, 0.04 mmol, 70%): mp 134.5–136 °C (from acetone); $[\alpha]_D$ +52.5° ($CHCl_3$, c = 0.16); IR 3580, 1595 cm^{-1}; ^1H NMR 0.68 (3H, s), 0.86 (6H, d, J = 6.5 Hz), 0.91 (3H, d, J = 6.3 Hz), 0.92 (3H, s), 2.3 (1H, d, J = 18 Hz), 2.57 (1H, m), 6.15 (1H, m), 7.2–7.4 (5H, m); ^{13}C NMR 12.07, 16.60, 18.76, 21.21, 22.56, 22.80, 23.95, 24.21, 26.73, 28.03, 28.25, 33.69, 35.31, 35.86, 36.12, 36.27, 38.23, 39.59, 40.08 (2×), 42.65, 45.96, 56.20, 56.40, 72.54, 123.60, 125.06, 126.86, 128.28, 132.96, 141.5; MS *m/z* (rel intensity) 462 (M^+, <1), 444 (100), 429 (5); HRMS calcd for $C_{33}H_{50}O$ 462.3861, found 462.3879.

3α-Phenylcholest-5-en-3β-ol (10). To a solution of **9** (37 mg, 0.08 mmol) in dry C_6H_6 (3 mL) was added a catalytic amount of TsOH. The mixture was stirred at rt for 5 days, poured into 20% aqueous $NaHCO_3$, and extracted with EtOAc. The organic layer was washed with H_2O and brine, dried (Na_2SO_4), and evaporated. Chromatotron chromatography (*n*-hexane–EtOAc, 95:5) gave **4** (4 mg, 0.01 mmol, 10%), **10** (12 mg, 0.03 mmol, 33%), and a mixture of dienes (10 mg, 0.02 mmol, 30%), as well as starting material **9** (9 mg, 0.02 mmol, 25%). Compound **10**: amorphous; $[\alpha]_D$ +49.7° ($CHCl_3$, c = 0.31); IR 3590 cm^{-1}; ^1H NMR 0.66 (3H, s), 0.85 (6H, d, J = 6.2

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Hz), 0.88 (3H, d, J = 5.7 Hz), 1.01 (3H, s), 3.1 (1H, brd, J = 17 Hz), 6.45 (1H, m), 7.2–7.4 (5H, m); ^{13}C NMR 12.15, 16.17, 18.64, 22.13, 22.51, 22.72, 23.84, 24.13, 27.98, 28.22, 28.77, 32.66, 34.11, 34.57, 35.75, 36.18, 36.96, 39.35, 39.53, 39.96, 42.65, 44.44, 56.24, 56.76, 73.35, 122.05, 124.89, 126.79, 128.22, 132.81, 141.3; MS m/z (rel intensity) 462 (M^+, 2), 447 (3), 444 (100), 429 (4); HRMS calcd for $C_{33}H_{50}O$ 462.386 17, found 462.386 05.

2α,3α-Epoxycholestan-5α-ol (11). To a solution of **3** (550 mg, 1.42 mmol) in CH_2Cl_2 (15 mL) at 0 °C was added *m*-CPBA (284 mg, 1.8 mmol). The reaction was allowed to reach rt and was stirred for 2 h. It was then poured into 1% aqueous NaOH and extracted with CH_2Cl_2. The organic layer was successively washed with H_2O and brine, dried (Na_2SO_4), and evaporated under reduced pressure. Chromatotron chromatography (*n*-hexane–EtOAc, 95:5) gave **11** (552 mg, 1.37 mmol, 96%): mp 143–144 °C (from MeOH–EtOAc); $[\alpha]_D$ +20.8° ($CHCl_3$, c = 0.6); IR 3460 cm^{-1}; ^{1}H NMR 0.64 (3H, s), 0.86 (6H, d, J = 7.1 Hz), 0.89 (3H, d, J = 6.9 Hz), 0.91 (3H, s), 3.35 (2H, m), 3.46 (1H, OH); ^{13}C NMR 12.08, 17.50, 18.80, 20.89, 22.69, 22.95, 24.02, 24.29, 26.04, 28.12, 28.35, 33.89, 34.12, 34.27, 35.65, 35.95, 36.29, 38.37, 39.64, 39.99, 42.55, 46.06, 52.24, 54.11, 56.01, 56.35, 72.33; MS m/z (rel intensity) 402 (M^+, 10), 387 (5), 384 (98), 369 (48); HRMS calcd for $C_{27}H_{46}O_2$ 402.3498, found 402.3485.

2β-(2′-Propenyl)cholestane-3α,5α-diol (12). In a dry 100-mL round-bottom flask were placed Mg (1.18 g, 40 mmol) and a catalytic amount of I_2 (2 mg). Dry Et_2O was added (10 mL), and then a solution of allyl bromide (2 mL, 2.8 g, 20 mmol) in dry Et_2O (30 mL) was slowly dripped under Ar. During the addition, the reaction mixture reached reflux temperature. Once the addition was finished, stirring was continued for 30 min. Then the mixture was left overnight under Ar, and the resulting supernatant solution was separated from the precipitate and kept under Ar in a flask. From this allylmagnesium bromide solution in Et_2O was taken 20 mL (10 mmol) and added dropwise to epoxide **11** (1.48 g, 3.68 mmol) in anhydrous Et_2O (10 mL) at rt. After 30 min of stirring, the reaction mixture was poured into 5% aqueous HCl and extracted with Et_2O. The organic layer was dried (Na_2SO_4) and concentrated, and the residue was purified by column chromatography (*n*-hexane–EtOAc, 80:20), yielding **12** (1.17 g, 2.6 mmol, 73%): mp 160.7–161.9 °C (from MeOH); $[\alpha]_D$ +13.8° ($CHCl_3$, c = 0.25); IR 3600, 3460, 1630 cm^{-1}; ^{1}H NMR 0.65 (3H, s), 0.86 (6H, d, J = 6.8 Hz), 0.89 (3H, d, J = 7.0 Hz), 0.99 (3H, s), 2.17 (2H, m), 3.58 (2H, OH), 3.86 (1H, m), 4.97 (1H, dd, J = 6.6, 1.8 Hz), 5.04 (1H, s), 5.77 (1H, m); ^{13}C NMR 12.16, 18.60, 18.72, 20.94, 22.52, 22.78, 23.86, 23.98, 25.16, 27.95, 28.22, 32.45, 33.68, 34.21, 35.79, 36.14, 39.30, 39.46, 39.46, 39.51, 40.07, 41.15, 42.74, 46.57, 55.94, 56.21, 70.89, 75.52, 115.81, 138.21; MS m/z (rel intensity) 426 ($M^+ - H_2O$, 14), 411 (12), 408 (6); HRMS calcd for $C_{30}H_{50}O$ 426.386 17, found 426.388 37.

3-Acetate of 2β-(2′-Propenyl)cholestane-3α,5α-diol (13). A solution of diol **12** (1.05 g, 2.3 mmol) in dry C_5H_5N (1 mL) was treated with Ac_2O and stirred at rt for 3 h, and then it was poured into 10% aqueous HCl and extracted with CH_2Cl_2. The organic layer was washed with H_2O and brine, dried (Na_2SO_4), and concentrated. The white residue was identified by ^{1}H NMR as the 3α-acetate **13** (1.08 g, 2.2 mmol, 95%): mp 111.9–113.7 °C (from MeOH); $[\alpha]_D$ +44.3° ($CHCl_3$, c = 0.38); IR 3570, 1720 cm^{-1}; ^{1}H NMR 0.66 (3H, s), 0.86 (6H, d, J = 6.9 Hz), 0.89 (3H, d, J = 6.7 Hz), 0.98 (3H, s), 2.05 (3H, s), 2.17 (1H, dd, J = 6, 15 Hz), 4.98 (2H, m), 5.02 (1H, s), 5.77 (1H, m); ^{13}C NMR 12.14, 18.61, 19.51, 20.99, 21.33, 22.51, 22.77, 23.85, 24.00, 25.65, 27.93, 28.20, 34.06, 34.53, 35.38, 35.77, 36.12, 36.69, 38.05, 38.86, 38.86, 39.45, 40.07, 42.73, 47.29, 55.96, 56.23, 73.37, 74.30, 116.22, 136.90, 169.74; MS m/z (rel intensity) 468 ($M^+ - H_2O$, 6), 426 (12), 408 (100), 393 (17), 332 (99); HRMS calcd for $C_{32}H_{52}O_2$ 468.396 73, found 468.397 63.

3-Acetate of 2β-(Carbomethoxymethyl)cholestane-3α,5α-diol (15). Acetate **13** (1 g, 2.0 mmol) in CCl_4–MeCN–H_2O, 1:1:2 (16 mL), was treated with HIO_4 (1.86 g, 8.2 mmol) and $RuCl_3$ (16 mg, 0.02 mmol). The reaction mixture was vigorously stirred for 1 h, and then Et_2O was added (10 mL) and the stirring continued for 10 min. Afterwards, the organic layer was separated and the aqueous layer extracted with Et_2O. The organic layers were combined, dried (Na_2SO_4), and evaporated as described previously. A very polar product was obtained and identified as the 3-acetate **14**: mp 178.8–180.4 °C (from EtOAc); $[\alpha]_D$ +75.3° ($CHCl_3$, c = 0.19); IR 3570, 1728, 1707 cm^{-1}; ^{1}H NMR 0.66 (3H, s), 0.87 (6H, d, J = 6.6 Hz), 0.90 (3H, d, J = 6.4 Hz), 0.99 (3H, s), 2.05 (3H, s), 2.5 (1H, dd, J = 6.7, 15 Hz), 2.79 (1H, m), 4.92 (1H, m); ^{13}C NMR 12.12, 18.60, 20.12, 21.03, 21.13, 22.51, 22.77, 23.84, 23.99, 25.76, 27.94, 28.18, 33.35, 34.37, 34.59, 35.75, 36.10, 37.51, 38.68, 39.23, 39.44, 39.88, 39.97, 42.70, 47.72, 55.87, 56.18, 72.90, 74.84, 170.29, 177.97; MS m/z (rel intensity) 486 ($M^+ - H_2O$, 1), 444 (2), 426 (30), 411 (9); HRMS calcd for $C_{31}H_{50}O_4$ 486.370 91, found 402.370 79. The crude acid **14** was dissolved in Et_2O and treated with ethereal CH_2N_2 at 0 °C. After 30 min the mixture was concentrated under vacuum; chromatotron chromatography (*n*-hexane–EtOAc, 90:10) afforded the 3-acetate **15** (0.72 g, 1.4 mmol, 67% from acetate **13**): mp 145.7–146.3 °C (from EtOAc); $[\alpha]_D$ +68° ($CHCl_3$, c = 0.4); IR 3581, 1728 cm^{-1}; ^{1}H NMR 0.64 (3H, s), 0.85 (6H, d, J = 6.6 Hz), 0.89 (3H, d, J = 6.5 Hz), 0.97 (3H, s), 2.03 (3H, s), 2.45 (1H, dd, J = 7, 15 Hz), 2.72 (1H, m), 3.67 (3H, s), 4.92 (1H, m); ^{13}C NMR 12.15, 18.63, 19.98, 21.04, 21.21, 22.53, 22.79, 23.87, 24.02, 25.76, 27.98, 28.20, 33.65, 34.34, 34.61, 35.79, 36.14, 37.07, 38.77, 39.33, 39.33, 39.48, 40.03, 42.75, 47.64, 51.56, 55.95, 56.23, 72.95, 74.50, 170.01, 172.92; MS m/z (rel intensity (458 M^+ – AcOH, 4), 440 (22), 425 (6); HRMS calcd for $C_{30}H_{50}O_3$ 458.376 00, found 458.377 84.

2β-Carboxymethylcholestane-3α,5α-diol (16). A solution of methyl ester **15** (0.72 g, 1.38 mmol) in THF (10 mL) was treated with a 5% aqueous solution of KOH (20 mL). The reaction mixture was stirred at rt for 24 h and then poured into 10% aqueous HCl and extracted with EtOAc. The organic layer was washed with H_2O and brine, dried (Na_2SO_4), and evaporated, affording **16** (0.63 g, 1.36 mmol, 98%): IR 3600, 3510, 1711 cm^{-1}; ^{1}H NMR 0.66 (3H, s), 0.87 (6H, d, J = 6.7 Hz), 0.9 (3H, d, J = 6.8 Hz), 0.98 (3H, s), 3.91 (1H, m); MS m/z (rel intensity) 444 ($M^+ - H_2O$, 10), 426 (64), 411 (40); HRMS calcd for $C_{29}H_{48}O_3$ 444.360 33, found 444.361 03.

(2α,3α)*H*-Dihydro-2′(3′*H*)-oxofuro[4′5′:2,3]cholestan-5α-ol (17) and (2α,3β)*H*-Dihydro-2′(3′*H*)-oxofuro[4′,5′:2,3]-cholestan-5α-ol (18). To a solution of acid **16** (0.5 g, 1.08 mmol) and Ph_3P (0.80 g, 3 mmol) in THF (20 mL) was added dropwise, at rt and under Ar, a solution of DEAD (0.25 mL, 1.5 mmol) in dry THF (3 mL). The solution was stirred for 10 min and afterwards concentrated under vacuum. Chromatotron chromatography (*n*-hexane–EtOAc, 80:20) gave the title lactones **17** (0.28 g, 0.63 mmol, 59%) and **18** (0.15 g, 0.3 mmol, 31%). Lactone **17**: mp 194–196 °C (from MeOH); $[\alpha]_D$ +10° ($CHCl_3$, c = 0.24); IR 3609, 1761 cm^{-1}; ^{1}H NMR 0.66 (3H, s), 0.86 (6H, d, J = 6.6 Hz), 0.89 (3H, d, J = 6.4 Hz), 1.10 (3H, s), 2.64 (1H, dd, J = 17.6, 13 Hz), 2.51 (1H, dd, J = 17.7, 9.6 Hz), 2.83 (1H, m), 4.95 (1H, m); ^{13}C NMR 12.07, 18.59, 19.31, 21.14, 22.49, 22.75, 23.78, 23.97, 25.53, 27.92, 28.12, 32.75, 33.31, 34.02, 34.02, 34.12, 35.69, 36.08, 38.04, 38.69, 39.43, 39.92, 42.61, 47.24, 55.85, 56.17, 74.49, 78.45, 177.23; MS m/z (rel intensity) 444 (M^+, 4), 426 (52), 411 (21); HRMS calcd for $C_{29}H_{48}O_3$ 444.360 35, found 444.359 45. Lactone **18**: amorphous; $[\alpha]_D$ +41.6° ($CHCl_3$, c = 0.48); IR 3601, 1770 cm^{-1}; ^{1}H NMR 0.67 (3H, s), 0.87 (6H, d, J = 6.8 Hz), 0.90 (3H, d, J = 6.8 Hz), 1.01 (3H, s), 1.79 (1H, dd, J = 14.4, 8.4 Hz), 1.90 (1H, dd, J = 13.2, 8.4 Hz), 1.99 (1H, brd, J = 12.8 Hz), 2.07 (1H, dd, J = 16, 13.6 Hz), 2.24 (1H, dd, J = 14.4, 8.4 Hz), 2.53 (1H, dd, J = 16, 6.8 Hz), 3.1 (1H, m), 4.39 (1H, m); ^{13}C NMR 12.12, 18.57, 21.13, 21.44, 22.49, 22.75, 23.93, 25.76, 23.77, 27.89, 28.15, 34.68, 35.69, 35.69, 36.06, 36.28, 37.22, 38.36, 39.40, 39.94, 40.06, 40.30, 42.75, 48.92, 55.71, 56.12, 75.97, 79.31, 177.48; MS m/z (rel intensity) 444 (M^+, 5), 426 (47), 411 (25), 332 (5); HRMS calcd for $C_{29}H_{48}O_3$ 444.360 35, found 444.359 96.

3′-(Phenylseleno)-(2α,3α)*H*-dihydro-2′(3′*H*)-oxofuro-[4′,5′:2,3]cholestan-5α-ol (19). To a solution of lactone **17** (91 mg, 0.2 mmol) in dry THF (1 mL) was added dropwise a 1.18 M solution of LDA in THF (0.44 mL, 0.5 mmol), at −78 °C and under Ar. The solution was stirred for 30 min at −78 °C, and then $(PhSe)_2$ (94 mg, 0.3 mmol) in dry THF (1 mL) was added slowly. The stirring was continued for 3 h, and

then the reaction mixture was poured into iced H_2O, acidulated with $NaHSO_3$, and extracted with EtOAc. The organic layer was washed with H_2O and brine, dried (Na_2SO_4), and evaporated. Chromatotron chromatography of the residue (*n*-hexane–EtOAc, 90:10) gave lactone **19** (98 mg, 0.16 mmol, 80%), as well as the starting lactone **17** (14 mg, 0.03 mmol, 15%). Compound **19**: amorphous; ^{1}H NMR 0.64 (3H, s), 0.87 (6H, d, J = 6.6 Hz), 0.90 (3H, d, J = 6.6 Hz), 1.01 (3H, s), 2.60 (1H, m), 3.92 (1H, d, J = 13 Hz), 4.81 (1H, m), 7.26–7.36 (3H, m), 7.65–7.70 (2H, m); ^{13}C NMR 12.10, 18.62, 19.24, 21.19, 22.51, 22.77, 23.79, 23.97, 25.49, 27.95, 28.12, 31.99, 33.93, 34.01, 35.71, 36.09, 38.31, 38.60, 39.37, 39.45, 39.89, 42.63, 43.99, 47.31, 55.82, 56.16, 74.83, 77.36, 128.96, 129.3, 136.4, 136.4, 175.83; MS *m/z* (rel intensity) 600 (M^+, 11), 442 (9), 427 (11), 424 (70), 409 (17).

3α*H*-2′-Oxofuro[2,3]cholestan-5α-ol (5). Lactone **19** (98 mg, 0.16 mmol) in THF (4 mL) was treated with 30% H_2O_2 (0.2 mL) and HOAc (0.05 mL). The mixture was stirred at 0 °C for 2 h and then poured into H_2O and extracted with EtOAc. The organic layer was washed with brine, dried (Na_2SO_4), and concentrated. Chromatotron chromatography (*n*-hexane–EtOAc, 80:20) gave lactone **5** (60 mg, 0.13 mmol, 83%): mp 208–210 °C (from MeOH); $[\alpha]_D$ −94.53° ($CHCl_3$, c = 0.13); IR 3650, 1740, 1640 cm^{-1}; ^{1}H NMR 0.65 (3H, s), 0.87 (3H, s), 0.85 (6H, d, J = 6.7 Hz), 0.90 (3H, d, J = 6.6 Hz), 2.23 (1H, dd, J = 7.2, 13 Hz), 2.47 (2H, J = 13 Hz), 2.53 (2H, J = 13 Hz), 5.20 (1H, m), 5.75 (1H, s); ^{13}C NMR 11.93, 16.20, 18.58, 21.25, 22.47, 22.73, 23.76, 24.07, 25.73, 27.90, 28.11, 33.90, 34.79, 35.53, 35.67, 36.05, 39.40, 39.64, 42.41, 42.46, 43.09, 45.82, 55.83, 56.12, 74.37, 80.19, 114.37, 171.84, 174.04; MS *m/z* (rel intensity) 442 (M^+, 13), 424 (90), 409 (22); HRMS calcd for $C_{29}H_{46}O_3$ 442.344 70, found 442.344 87.

Photolysis of 2-Cholesten-5α-ol (3) under Argon. A solution of alcohol **3** (150 mg, 0.39 mmol) in dry cyclohexane (12 mL) was treated with I_2 (128 mg, 0.5 mmol) and DIB (375 mg, 1.16 mmol). After careful deoxygenation by several cycles of pumping followed by filling with Ar, the mixture was irradiated with two 100-W tungsten-filament lamps at 40 °C for 4 h and then poured into 10% aqueous $Na_2S_2O_3$ and extracted with CH_2Cl_2. The organic layer was washed with H_2O and brine, dried (Na_2SO_4), and concentrated under reduced pressure. Chromatotron chromatography of the residue (*n*-hexane–EtOAc, 97:3) gave 5,10-secocholesta-1(10),2-dien-5-one (**20**) (124 mg, 0.32 mmol, 83%): mp 92.5–94.5 °C (from MeOH); $[\alpha]_D$ −247.5° ($CHCl_3$, c = 0.24); IR 1700 cm^{-1}; UV (EtOH) λ_{max} 218 nm (ϵ = 6030); ^{1}H NMR 0.68 (3H, s), 0.86 (6H, d, J = 6.2 Hz), 0.89 (3H, d, J = 6 Hz), 1.7 (3H, s), 3.88 (1H, dd, J = 10.2, 14.7 Hz), 5.59 (1H, m), 5.8 (1H, dddd, J = 5.7, 10.2, 10.7, 1.4 Hz), 5.94 (1H, m); ^{13}C NMR 11.89, 18.79, 18.79, 22.70, 22.94, 23.83, 24.16, 25.20, 27.03, 28.06, 28.15, 35.78, 36.24, 36.73, 39.35, 39.40, 39.58, 39.66, 42.58, 42.80, 49.96, 55.94, 122.43, 125.92, 129.81, 144.06, 214.28; MS *m/z* (rel intensity) 384 (M^+, 78), 369 (14), 355 (5), 330 (38), 314 (11); HRMS calcd for $C_{27}H_{44}O$ 384.3392, found 384.3365.

Photolysis of 2-Cholesten-5α-ol (3) under Air. A solution of compound **3** (100 mg, 0.26 mmol) in dry cyclohexane (20 mL) containing I_2 (132 mg, 0.5 mmol) and DIB (167 mg, 0.52 mmol) was irradiated with two 100-W tungsten-filament lamps at 40 °C, allowing the entrance of dry air. After 2 h the reaction mixture was extracted, dried (Na_2SO_4), and evaporated as before. Purification of the residue by chromatotron chromatography afforded product **20** (44 mg, 0.11 mmol, 44%).

Photolysis of 2-Cholesten-5α-ol (3) under Oxygen Pressure. (a) Photolysis under 2 atm. Compound **3** (100 mg, 0.26 mmol), DIB (167 mg, 0.52 mmol), and I_2 (132 mg, 0.52 mmol) in dry cyclohexane (20 mL) were placed in a borosilicate Griffin–Worden pressure vessel (Kontes K-767100). O_2 pressure was applied (2 atm), and the solution was irradiated with two 100-W tungsten-filament lamps at 40 °C for 1.75 h. Workup as described previously, followed by chromatotron chromatography, afforded diene **20** (23 mg, 0.06 mmol, 23%), 2α,10α-epidioxy-3α-iodo-5,10-secocholestan-5-one (**21**) (56 mg, 0.1 mmol, 40%), and 2α,10α-epidioxy-3β-iodo-5,10-secocholestan-5-one (**22**) (15 mg, 0.03 mmol, 11%; global yield of peroxy compounds 51%). Compound **21**: mp 125–127 °C (from MeOH); $[\alpha]_D$ −88.5° ($CHCl_3$, c = 0.4); IR 1700 cm^{-1}; ^{1}H NMR 0.64 (3H, s), 0.86 (6H, d, J = 6.5 Hz), 0.87 (3H, d, J = 6.3 Hz), 1.31 (3H, s), 2.15 (2H, d, J = 7.3 Hz), 2.54 (1H, d, J = 16.8 Hz), 4.13 (1H, dd, J = 12, 16.8 Hz), 4.86 (1H, d, J = 12 Hz), 5.01 (1H, t, J = 7.3 Hz); ^{13}C NMR 11.99, 18.75, 22.70, 22.96, 23.97, 24.86, 26.50, 26.75, 26.95, 27.89, 27.98, 28.15, 35.34, 35.95, 36.21, 39.64, 40.0, 42.38, 43.40, 44.81, 46.40, 46.94, 55.92, 57.80, 85.65, 92.23, 211.5; MS *m/z* (rel intensity) 544 (M^+, 1), 526 (<1), 417 (6), 399 (5), 384 (14), 371 (7), 369 (3); HRMS calcd for $C_{27}H_{45}O_3I$ 544.2415, found 544.2391. X-ray analysis: $C_{27}H_{45}O_3I$, orthorhombic, space groups $P2_12_12_1$, Z = 4, a = 10.076(3) Å, b = 10.166(2) Å, c = 26.626(4) Å. The data were measured on a Philips PW-1100 four-circle automatic diffractometer operating with Cu Kα radiation (λ = 1.5418 Å) monochromated by graphite. The orientation matrix of the crystal was calculated from the angular setting of 25 randomly distributed reflections found in the range 10° < θ > 25°. The structure was solved by means of direct methods and refined with isotropic and then anisotropic thermal factors, for the non-hydrogen atoms, by the full-matrix least-squares procedure. Most of the hydrogen atoms (64% of the total) were located on successive Fourier-difference maps and introduced with a fixed isotropic thermal factor equal to that of the bonded carbon. The others were imposed at their theoretical places. An important decomposition was found during the data collection, and the crystal lifetime is about 3 h, the crystal turning brown upon I_2 release. Three crystals were used in the data collection. A very high-speed recording technique was adopted: no background measurements during the data collection and a 15-s scanning time per reflection. The background was evaluated *a posteriori* from an extrapolated curve of stationary counts (time = 30 s) obtained at different θ angles. The intensities, measured up to θ = 68°, were merged and averaged after scaling as usual with an overall R_{symm} = 9.7% for 4724 measured reflections. The final agreement factor was R = 9.1% for 2172 reflections observed above for 2σ background level. Compound **22**: amorphous, $[\alpha]_D$ +31° ($CHCl_3$, c = 0.33); IR 1710 cm^{-1}; ^{1}H NMR 0.78 (3H, s), 0.87 (6H, d, J = 6.5 Hz), 0.92 (3H, d, J = 6.4 Hz), 1.35 (3H, s), 2.43 (1H, dd, J = 8.6, 13.2 Hz), 2.66 (1H, dd, J = 3.8, 13.2 Hz), 2.91 (1H, dd, J = 3.6, 16.6 Hz), 3.62 (1H, dd, J = 12, 16.6 Hz), 4.85 (1H, ddd, J = 3.4, 8.6, 3.8 Hz), 4.97 (1H, ddd, J = 12, 3.6, 3.4 Hz); ^{13}C NMR 12.11, 18.85, 22.72, 22.98, 24.0, 24.94, 27.03, 27.24, 27.48, 27.79, 28.17, 32.58, 35.98, 36.24, 36.8, 39.28, 39.66, 41.18, 42.36, 44.77, 49.88, 49.88, 55.94, 57.70, 83.29, 91.48, 207.45; MS *m/z* (rel intensity) 544 (M^+, 1), 528 (3), 526 (1), 417 (12), 416 (12), 402 (6), 401 (20), 400 (43), 399 (20), 398 (13), 384 (10); HRMS calcd for $C_{27}H_{45}O_3I$ 528.246 43, found 528.243 85.

(b) Photolysis under 5 atm. To a solution of **3** (100 mg, 0.26 mmol) in dry cyclohexane (20 mL), placed in a Griffin–Worden pressure vessel, were added DIB (167 mg, 0.52 mmol) and I_2 (132 mg, 0.52 mmol). O_2 pressure was applied (5 atm), and the solution was irradiated with two 100-W tungsten-filament lamps at 40 °C for 2 h. After the usual workup, chromatotron chromatography (*n*-hexane–EtOAc, 95:5) gave diene **20** (15 mg, 0.04 mmol, 15%) and peroxy derivatives **21** (60 mg, 0.11 mmol, 43%) and **22** (21 mg, 0.04 mmol, 15%; overall yield of peroxy compounds 58%).

(c) Photolysis under 10 atm. To a solution of **3** (100 mg, 0.26 mmol) in dry cyclohexane (20 mL) were added I_2 (99 mg, 0.39 mmol) and DIB (250 mg, 0.78 mmol). O_2 pressure was applied (10 atm), and the mixture was irradiated with two 100-W tungsten-filament lamps for 3.5 h, at 40 °C. Usual workup and chromatotron chromatography (*n*-hexane–EtOAc, 99:1) afforded diene **20** (25 mg, 0.06 mmol, 25%) and compounds **21** (23 mg, 0.04 mmol, 16%) and **22** (11 mg, 0.02 mmol, 8%, global yield of peroxy derivatives 24%).

2α,10α-Epidioxy-5,10-secocholest-3-en-5-one (23). (a) Dehalogenation of Peroxy Compounds 21 and 22. Compounds **21** (20 mg, 0.037 mmol) and **22** (20 mg, 0.037 mmol) were dissolved separately in hexane (8 mL) and mixed with deactivated silica gel, the latter being prepared by mixing silica gel Merck (60PF_{254} with $CaSO_4$) with distilled H_2O until formation of a slurry, which was dried (Na_2SO_4) with air and ground in a mortar. After 3 h, each portion of compound **21**

or **22** in silica gel was placed in a filter and extracted with CH_2Cl_2. The organic extracts were concentrated under reduced pressure. It was observed by TLC and ^1H NMR that both **21** and **22** had given the same product, 2α,10α-epidioxy-5,10-secocholest-3-en-5-one (**23**) (14 mg, 0.03 mmol, 93% for **21** and 13 mg, 0.03 mmol, 86% for **22**). Compound **23**: amorphous; $[\alpha]_D$ −58.5° ($CHCl_3$, c = 0.31); IR 1680 cm^{-1}; UV (EtOH) λ_{max} 219 nm (ϵ = 3386); ^1H NMR 0.57 (3H, s), 0.86 (6H, d, J = 6.7 Hz), 0.88 (3H, d, J = 6.5 Hz), 1.41 (3H, s), 5.03 (1H, br d), 5.68 (1H, dd, J = 17, 1.3 Hz), 7.02 (1H, d, J = 17 Hz); ^{13}C NMR 9.08, 16.13, 19.98, 20.24, 21.22, 24.47, 24.71, 25.44, 25.48, 28.22, 29.38, 32.90, 33.10, 33.51, 36.85, 36.91, 39.68, 40.90, 45.17, 46.21, 52.72, 55.96, 75.67, 88.92, 132.01, 133.06, 202.44; MS m/z (rel intensity) 416 (M^+, 10), 401 (12), 400 (22), 398 (18); HRMS calcd for $C_{27}H_{44}O_3$ 416.329 05, found 416.328 69.

(b) Photolysis of 3 under O_2 Pressure and Chromatography on Deactivated Silica Gel. To a solution of **3** (100 mg, 0.26 mmol) in dry cyclohexane (15 mL), placed in a Griffin−Worden pressure vessel as described previously, were added I_2 (130 mg, 0.51 mmol) and DIB (160 mg, 0.50 mmol). O_2 pressure (2 atm) was applied, and the reaction mixture was irradiated with two 100-W tungsten-filament lamps at 40 °C for 1.75 h. After the usual workup and evaporation, the residue was dissolved in CH_2Cl_2 and adsorbed in a chromatotron plate (silica gel Merck 60 PF_{254}). The plate had been previously deactivated by standing face down over a H_2O bath (60 °C) for 6 h and then 24 h at rt. Once the reaction mixture was adsorbed to the silica, it was left on the plate for 1 h (CH_2Cl_2 evaporated) and then eluted with n-hexane−EtOAc, 95:5. Diene **20** (20 mg, 0.05 mmol, 20%) and unsaturated ketone **23** (54 mg, 0.13 mmol, 50%) were obtained.

Photolysis of 3-Phenyl-2-cholesten-5α-ol (4) under Argon. To a solution of **4** (30 mg, 0.06 mmol) in dry cyclohexane (2 mL) were added I_2 (17 mg, 0.07 mmol) and DIB (22 mg, 0.07 mmol), and the mixture was irradiated with two 100-W tungsten-filament lamps for 1.5 h, at 40 °C and under Ar. Since there was some starting product left, more DIB was added (32 mg, 0.1 mmol) and the reaction continued for 2.5 h. A complex mixture of products was formed, as observed by TLC. After the usual workup, chromatotron chromatography (n-hexane−EtOAc, 99:1) yielded 3-phenyl-5,10-secocholesta-1(10),2-dien-5-one (**24**) (7 mg, 0.01 mmol, 23%): amorphous; IR 1690 cm^{-1}; ^1H NMR 0.70 (3H, s), 0.85 (3H, d, J = 6.8 Hz), 0.87 (3H, d, J = 7.3 Hz), 0.89 (3H, d, J = 7 Hz), 1.58 (3H, s), 3.09 (1H, d, J = 15.2 Hz), 4.14 (1H, d, J = 15.2 Hz), 5.84 (1H, m), 6.53 (1H, m), 7.44−7.25 (5H, m); MS m/z (rel intensity) 460 (M^+, 100), 445 (14); HRMS calcd for $C_{33}H_{48}O_2$ 460.370 50, found 460.371 27.

Photolysis of 3-Phenyl-2-cholesten-5α-ol (4) under Oxygen Pressure. (a) Photolysis under 10 atm. Compound **4** (17 mg, 0.03 mmol) in cyclohexane (7 mL) was treated with DIB (26 mg, 0.08 mmol) and I_2 (8 mg, 0.03 mmol) and irradiated with two 100-W tungsten-filament lamps at 45 °C under O_2 pressure (10 atm) for 2 h. After usual workup, chromatotron chromatography (n-hexane−EtOAc, 95:5) gave epoxide **25** (8.1 mg, 0.017 mmol, 47%) and 2α,10α-epidioxy-3-phenyl-5,10-secocholest-3-en-5-one (**26**) (3.3 mg, 0.007 mmol, 18%). Epoxide **25**: mp 130−132 °C (from n-hexane); $[\alpha]_D$ +40° ($CHCl_3$, c = 0.3); IR 3460 cm^{-1}; ^1H NMR 0.66 (3H, s), 0.86 (6H, d, J = 6.5 Hz), 0.90 (3H, d, J = 8.4 Hz), 1.02 (3H, s), 2.05 (1H, d, J = 15.7 Hz), 2.45 (1H, d, J = 15.7 Hz), 3.28 (1H, m), 3.88 (1H, OH), 7.26−7.36 (5H, m); ^{13}C NMR 11.97, 17.45, 18.67, 20.88, 22.55, 22.82, 23.89, 24.17, 25.99, 28.00, 28.23, 34.28, 34.73, 35.57, 35.83, 36.16, 37.64, 38.19, 39.50, 39.85, 42.44, 45.91, 55.90, 56.23, 61.55, 62.40, 72.30, 125.12, 127.81, 128.49, 140.49; MS m/z (rel intensity) 478 (M^+, 1), 460 (3), 445 (2); HRMS calcd for $C_{33}H_{50}O_2$ 478.3811, found 478.3842. Compound **26**: amorphous; $[\alpha]_D$ +30° ($CHCl_3$, c = 0.34); IR 1700 cm^{-1}; ^1H NMR 0.80 (3H, s), 0.87 (6H, d, J = 6.5 Hz), 0.93 (3H, d, J = 6.4 Hz), 1.37 (3H, s), 2.57 (1H, d, J = 17 Hz), 3.82 (1H, d, J = 17 Hz), 4.37 (1H, dd, J = 3.6, 8.7 Hz), 6.42 (1H, s), 7.3−7.5 (5H, m); ^{13}C NMR 11.89, 18.67, 22.54, 22.80, 23.82, 24.84, 26.67, 27.03, 27.62, 28.01, 33.12, 35.82, 36.06, 36.62, 38.94, 39.48, 42.20, 42.47, 45.57, 49.35, 55.76, 57.27, 87.10, 91.06, 124.99, 127.74, 128.62, 142.96, 212.14; MS m/z (rel intensity) 492 (M^+, 2), 476 (4), 474 (2), 459 (2); HRMS calcd for $C_{33}H_{48}O_3$ 492.366 22, found 492.360 77.

(b) Photolysis under 5 atm. A solution of **4** (40 mg, 0.09 mmol) in cyclohexane (10 mL) containing DIB (56 mg, 0.17 mmol) and I_2 (20 mg, 0.08 mmol) was irradiated with two 100-W tungsten-filament lamps at 40 °C under O_2 pressure (5 atm) for 45 min. As there was untransformed starting material, more DIB was added (50 mg, 0.16 mmol) and the photolysis continued for 45 min. After usual workup, chromatotron chromatography (n-hexane−EtOAc, 97:3) afforded epoxide **25** (23 mg, 0.05 mmol, 56%) and peroxy compound **26** (5.7 mg, 0.01 mmol, 13%).

2α,3α-Epoxy-3β-phenylcholestan-5α-ol (25). Compound **4** (5 mg, 0.01 mmol) in CH_2Cl_2 (2 mL) was treated with m-CPBA (9 mg, 0.06 mmol). The mixture was stirred at rt for 30 min and then poured into saturated aqueous $NaHCO_3$ solution and extracted with CH_2Cl_2. The organic layer was washed with H_2O and brine, dried (Na_2SO_4), and evaporated as usual. Chromatotron chromatography (n-hexane−EtOAc, 95:5) afforded epoxide **25** (4 mg, 0.008 mmol, 78%).

3β-Phenyl-3α,5α-cholestanediol (8). To a solution of epoxide **25** (40 mg, 0.08 mmol) in THF (10 mL) was added $LiAlH_4$ (20 mg, 0.5 mmol), and the mixture was refluxed for 8 h. The excess of $LiAlH_4$ was quenched with saturated aqueous Na_2SO_4, the solution filtered, and the organic phase concentrated under reduced pressure. Chromatotron chromatography (n-hexane−EtOAc, 95:5) afforded compound **8** (24 mg, 0.05 mmol, 60%).

Photolysis of 3α*H*-2′-Oxofuro[2,3]cholestan-5α-ol (5) under Argon. A solution of lactone **5** (10 mg, 0.23 mmol) in cyclohexane (10 mL) containing DIB (21 mg, 0.06 mmol) and I_2 (11 mg, 0.04 mmol), was irradiated with two 100-W tungsten-filament lamps for 30 min under Ar at 40 °C. Since the reaction was not complete, more DIB was added (21 mg, 0.23 mmol) and the photolysis continued for 1.5 h. After usual workup, chromatotron chromatography (n-hexane−EtOAc, 95:5) afforded starting compound **5** (3 mg, 30%) and a product which decomposed easily and could not be identified (3 mg).

Photolysis of 3α*H*-2′-Oxofuro[2,3]cholestan-5α-ol (5) under Oxygen Pressure. (a) Photolysis with DIB, I_2, and O_2 (5 atm). To a solution of lactone **5** (15 mg, 0.03 mmol) in cyclohexane (10 mL) were added I_2 (10 mg, 0.04 mmol) and DIB (25 mg, 0.08 mmol). The mixture was irradiated with two 100-W tungsten-filament lamps at 40 °C under O_2 pressure (5 atm) for 45 min. After usual workup and evaporation, chromatotron chromatography (n-hexane−EtOAc, 90:10) gave a 60:40 mixture of 2α,10α-epidioxy-3′ζ-iodo-3α*H*-2′(3′*H*)-oxofuro[4′,5′:2,3]-5,10-secocholestan-5-one (**27**) and 2α,10α-epidioxy-3′ζ-iodo-3α*H*-2′(3′*H*)-oxofuro[4′,5′:2,3]-5,10-secocholestan-5-one (**28**) (1 mg, 5%), as well as 2α,10α-epidioxy-3′ζ-hydroxy-3α*H*-2′(3′*H*)-oxofuro[4′,5′:2,3]-5,10-secocholestan-5-one (**29**) (4.0 mg, 0.008 mmol, 24%). A considerable amount of starting product **5** was also recovered (7 mg, 0.016 mmol, 47%). Compound **27**: amorphous; $[\alpha]_D$ −17° ($CHCl_3$, c = 0.19); IR 1780, 1703 cm^{-1}; ^1H NMR 0.67 (3H, s), 0.87 (6H, d, J = 6.6 Hz), 0.88 (3H, d, J = 6.3 Hz), 1.43 (3H, s), 3.82 (1H, dd, J = 11, 16 Hz), 4.43 (1H, s), 5.35 (1H, dd, J = 2, 11 Hz); ^{13}C NMR 11.83, 15.86, 18.61, 22.52, 22.78, 23.79, 24.86, 26.86, 27.64, 27.78, 27.99, 28.46, 33.92, 35.76, 36.03, 37.57, 39.46, 39.56, 42.21, 45.10, 47.27, 47.57, 55.69, 57.54, 81.23, 90.46, 92.67, 160.97, 210.15; MS m/z (rel intensity) 600 (M^+, 1), 473 (19), 472 (5), 457 (3), 456 (4), 428 (30); HRMS calcd for $C_{29}H_{45}O_5$ 473.326 70, found 473.3284. Compound **28**: amorphous; $[\alpha]_D$ −3.7° ($CHCl_3$, c = 0.4); IR 1780, 1702 cm^{-1}; ^1H NMR 0.64 (3H, s), 0.86 (6H, d, J = 6.6 Hz), 0.89 (3H, d, J = 6.4 Hz), 1.6 (3H, s), 3.83 (1H, dd, J = 11, 16.4 Hz), 5.04 (1H, s), 5.15 (1H, dd, J = 1.7, 11 Hz); ^{13}C NMR 9.21, 16.06, 19.95, 19.95, 20.26, 21.25, 22.48, 24.39, 25.27, 25.45, 26.15, 26.77, 30.97, 33.22, 33.48, 36.05, 36.91, 36.97, 39.64, 41.58, 42.32, 45.45, 53.08, 55.05, 79.59, 85.20, 90.01, 167.01, 207.41; MS m/z (rel intensity) 582 (M^+ − H_2O, 1), 473 (17), 457 (3), 456 (8), 428 (10); HRMS $C_{29}H_{45}O_5$ 473.326 70, found 473.326 01. Compound **29**: amorphous; $[\alpha]_D$ +50° ($CHCl_3$, c = 0.13); IR 3586, 1791, 1710 cm^{-1}; ^1H NMR 0.74 (3H, s), 0.87 (6H, d, J = 6.6 Hz), 0.91 (3H, d, J = 6.5 Hz), 1.44 (3H, s), 2.57 (1H, d, J = 13 Hz), 2.65 (1H, d, J = 13 Hz), 2.91 (1H, dd, J = 16.2, 3.4 Hz), 3.37 (1H, dd, J =

12, 16.2 Hz), 4.67 (1H, s), 5.11 (1H, dd, J = 3.4, 12 Hz); ^{13}C NMR 11.82, 18.63, 22.52, 22.78, 23.81, 24.91, 26.81, 26.81, 27.67, 27.99, 32.42, 35.78, 36.04, 36.81, 37.36, 39.04, 39.46, 42.01, 42.76, 45.06, 48.83, 55.67, 57.79, 69.23, 78.75, 91.21, 92.96, 172.07, 206.78; MS m/z (rel intensity) 490 (M^+, 9), 472 (3), 457 (3); HRMS calcd for $C_{29}H_{46}O_6$ 490.329 44, found 490.330 05.

(b) Photolysis with DIB, I_2, and O_2 (2.5 atm). A solution of lactone **5** (20 mg, 0.05 mmol) in cyclohexane (12 mL) containing DIB (25 mg, 0.08 mmol) and I_2 (20 mg, 0.08 mmol) was irradiated with two 100-W tungsten-filament lamps at 50 °C under O_2 pressure (2.5 atm) for 1 h. After usual workup, chromatotron chromatography (n-hexane–EtOAc, 90:10) gave peroxy compounds **28** (3.3 mg, 0.006 mmol, 12%) and **29** (4.4 mg, 0.01 mmol, 20%). Starting product **5** was also recovered (6.5 mg, 32%).

(c) Photolysis with HgO, I_2, and O_2 (5 atm). Lactone **5** (15 mg, 0.03 mmol) in CCl_4 (5 mL) was treated with HgO (25 mg, 0.12 mmol) and I_2 (10 mg, 0.04 mmol) and was irradiated at 40 °C with two 100-W tungsten-filament lamps and under O_2 pressure (5 atm) for 2 h. Workup as described previously and chromatotron chromatography (n-hexane–EtOAc, 90:10) gave a 1:1 mixture of iodoperoxy compounds **27** and **28** (0.8 mg, 0.001 mmol, 4%), as well as hydroxyperoxy derivative **29** (2.3 mg, 0.005 mmol, 14%).

Supplementary Material Available: ^{1}H NMR spectra of compounds **4**, **5**, **7–15**, **17–23**, and **25–29**, ^{1}H NMR of compounds **16** and **24**, and ORTEP drawing from the X-ray analysis of compound **21** (49 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information. The authors have deposited atomic coordinates for compound **21** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.