Tandem Carbon-Radical Peroxidation–Addition to Carbonyl Groups Reaction. A New Synthesis of Steroidal β-Peroxy Lactones

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A mild and efficient synthesis of β-peroxy lactones by alkoxy radical β-fragmentation reaction of γ-hydroxy carbonyl compounds is described. Steroidal models 5-hydroxy-4-nor-3-oxa-5α-cholestan-2-one (**1**), 5-hydroxy-5α-cholestan-2-one (**2**), and 5,17β-dihydroxy-4-nor-5α-androstan-2-one 17-acetate (**3**) were synthesized to test the present methodology. These substrates are subjected to photolysis with visible light in the presence of (diacetoxyiodo)benzene, lead tetraacetate, or HgO, I_2, and molecular oxygen to generate the corresponding alkoxy radical. The fragmentation of this radical results in the carbon radical which is trapped by molecular oxygen in the key step to generate a peroxy radical. Intramolecular addition of this peroxy radical to the carbonyl group present in the molecule is followed by β-fragmentation to yield the peroxy lactone radical. Subsequent trapping of this radical results in stable peroxy lactone. In all cases, regiospecific β-fragmentations and stereoselective peroxidation at C-10 radical were observed. This operationally simple multistep radical procedure permitted us to synthesize steroidal β-peroxy lactones **8**, **12**, and **15** in moderate to good yields.

In recent years we have witnessed a remarkable upsurge of the interest among synthetic organic chemists in carbon-centered radical chemistry[1] as well as its synthetic applications in utilizing the alkoxy radicals.[2] Particular attention has been paid to the β-fragmentation of alkoxy radicals and its application to the synthesis of a great variety of products.[3] Previous papers from this laboratory described the synthesis of medium-sized ring lactones[4] and ketones[5] via β-fragmentation of alkoxy radicals generated by photolysis of hemiacetals and tertiary alcohols, respectively, in the presence of a hypervalent organoiodine reagent. When the β-fragmentation reaction is performed under oxygen atmosphere the intermediate C-radical could be peroxidated, yielding a peroxy radical. The latter could be trapped by a conveniently positioned carbon–carbon double bond to give dioxolanes.[6] While the addition of peroxy radicals to olefins has received considerable interest[7] due to its biological importance,[8] relatively little attention has been paid to the addition of peroxy radicals to carbon–oxygen double bonds and its synthetic applications.[9] In continuation of our studies on these synthetic utilities of the β-fragmentation reactions of alkoxy radicals[10] we envisaged that the synthesis of the β-peroxy lactones from hydroxy compounds could be accomplished with suitably positioned carbonyl groups, such as the lactol **1** and

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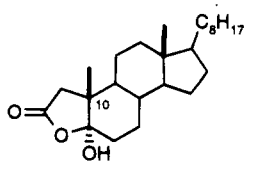

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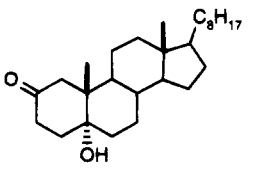

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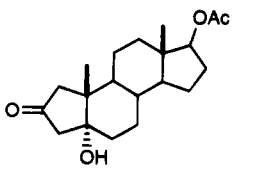

3

hydroxy ketones **2** and **3**, if the photolysis is performed under the oxygen atmosphere. The alkoxy radical such as I (Scheme 1), generated by photolysis of the corresponding hydroxyl compounds **1**–**3** by treatment with (diacetoxyiodo)benzene (DIB) and iodine under irradiation with visible light undergoes β-fragmentation to provide the carbon radical II. Subsequently, these radicals would evolve into medium-sized ring olefinic products or generate a peroxy radical III, by trapping molecular oxygen. The peroxy radical thus generated could then add to the carbonyl group to give peroxyhemiacetal radical IV, which would yield the desired β-peroxy lactone, via the intermediate V. In this paper we present the full account of this β-fragmentation–peroxidation–addition–β-fragmentation sequence and its application to the synthesis of β-peroxy lactones.[11] The C-10 stereochemistry of this stereoselective oxygen addition to the C-10 radical is also investigated and determined.

Results and Discussion

Synthesis of Hydroxy Carbonyl Compounds 1–3. 5-Hydroxy-4-nor-3-oxa-5α-cholestan-2-one (**1**) was prepared from 4-cholestan-3-one as previously described.[12] The β-keto carboxylic acid **1** is in the ring-chain tautomeric equilibrium[13] predominantly in the cyclic hemiacetal form, as evidenced by its spectroscopic data. In fact, its IR spectrum shows an absorption for a hydroxyl function at 3580 cm^{-1}, and its ^{13}C NMR spectrum presents a singlet (DEPT experiment) at δ 108.56 corresponding to the hemiacetal group at C-5 and no signal for a free ketone group in the δ 190–220 region.

For the synthesis of 5-hydroxy-5α-cholestan-2-one (**2**), 4-cholesten-3-one was also used as the starting material, essentially following a previously reported procedure.[14]

5,17β-Dihydroxy-4-nor-5α-androstan-2-one 17-acetate (**3**) (Scheme 2) was synthesized from 17β-hydroxy-4-nor-

Scheme 1

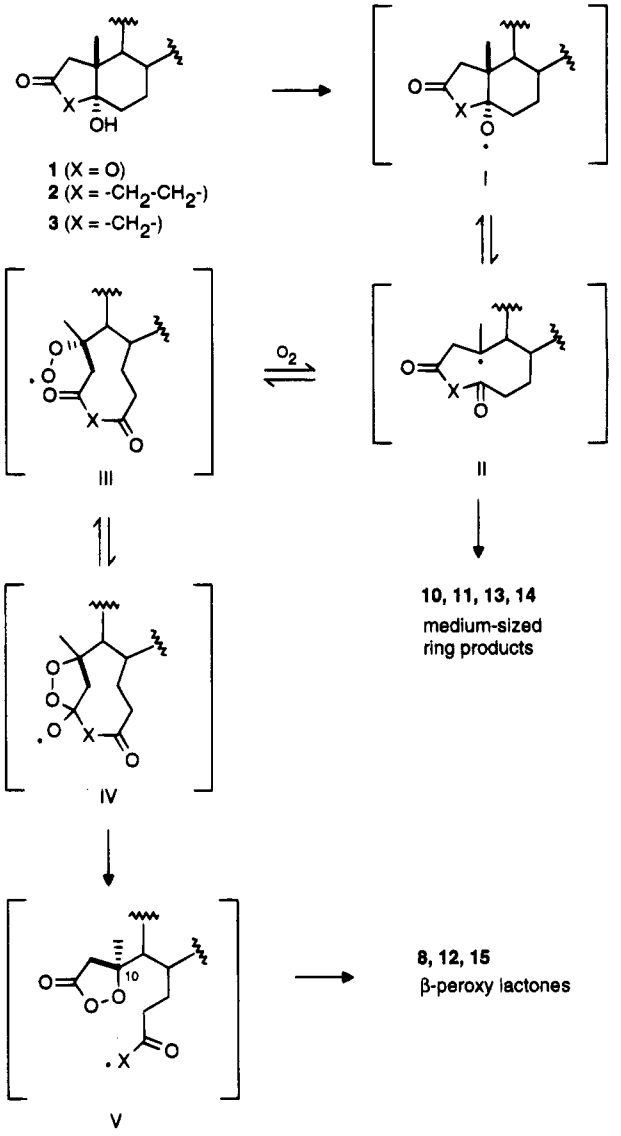

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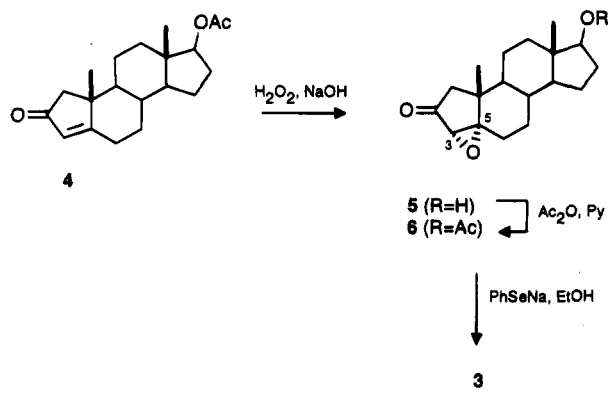
Table 1.[a] β-Fragmentation of γ-Hydroxy Carbonyl Compounds 1–3

entry	substrate	reagents[b] (mmol)	solvent	P (atm)	time (h)	products (yield, %)
1	**1**	LTA (3), I_2 (1)	Cy[c]	Ar (1)	1	**7** (9)
2	**1**	DIB (1.5), I_2 (1)	Cy	Ar (1)	3	**7** (11), **1** (60)
3	**1**	LTA (3), I_2 (1)	Cy[c]	air (1)	1.5	**8** (35)
4	**1**	LTA (3), I_2 (1)	Cy	air (1)	2	**9**[d] (77)
5	**1**	DIB (1.5), I_2 (1)	Cy	air (1)	3	**9**[d] (81)
6	**1**	DIB (1.5), I_2 (0,1)	Cy	air (1)	3	**9**[d] (50), **1** (21)
7	**1**	DIB (1.5), I_2 (1)	Cy	O_2 (10)	0.75	**9**[d] (46)
8	**2**	DIB (2), I_2 (1.3)	CCl_4	Ar (1)	0.3	**10-*E*** (14), **10-*Z*** (17), **11** (38)
9	**2**	HgO (5.5), I_2 (2)	CCl_4	Ar (1)	7	**10-*E*** (10), **10-*Z*** (46), **11** (42)
10	**2**	DIB (3), I_2 (1)	CCl_4	air (1)	2	**10-*Z*** (9), **11** (9), **12** (45)
11	**2**	DIB (2), I_2 (1)	CCl_4	O_2 (5)	0.5	**12** (42)
12	**2**	DIB (1.5), I_2 (1)	CCl_4	O_2 (10)	0.75	**12** (23)
13	**2**	HgO (4), I_2 (2)	CCl_4	air (1)	2	**10-*E*** (10), **10-*Z*** (20), **11** (15), **12** (40)
14	**2**	HgO (4), I_2 (2)	CCl_4	O_2 (5)	2	**12** (49)
15	**3**	DIB (1.5), I_2 (1)	Cy	Ar (1)	5	**13** (48), **14** (17)
16	**3**	DIB (1.5), I_2 (1)	Cy	air (1)	3.5	**13** (9), **15** (43), **16** (12)
17	**3**	DIB (1.5), I_2 (1)	CCl_4	O_2 (1)	2	**13** (8), **15** (16), **16** (16)
18	**3**	DIB (1.5), I_2 (1)	Cy	O2 (3)	5.5	**15** (17), **16** (16), **17** (23)
19	**3**	HgO (5), I_2 (1)	Cy	air (1)	9	**13** (16), **14** (14), **15** (39), **16** (16)
20	**3**	HgO (5), I_2 (1)	Cy	O2 (1)	9	**13** (13), **14** (10), **15** (20), **16** (9), **17** (8)

[a] All reactions were irradiated with two 100 W tungsten-filament lamps at 40–45 °C; those under pressure were made in a borosilicate Griffin-Worden pressure vessel (Kontes K-767100). [b] Per mmol of substrate. [c] Reaction made at reflux. [d] The crude reaction mixture was treated with ethereal diazomethane at room temperature. LTA = lead tetraacetate; DIB = (diacetoxyiodo)benzene.

Scheme 2



5α-androst-3-en-2-one 17-acetate (**4**), which was prepared from testosterone as previously described.[12,15] Treatment of the enone **4** with 30% hydrogen peroxide under basic conditions[16] yielded epoxide **5**. This compound upon treatment with Ac_2O/pyridine gave the acetate **6**. Cleavage of the oxirane ring was then achieved[17] with sodium phenylselenide in ethanol,[18] affording the desired hydroxy ketone **3** in good yield, together with minor amounts of the enone **4** that could be recycled to **3**. Compound **3** presents in its IR spectrum absorptions at 3604 and 1736 cm^{-1} for hydroxyl and carbonyl groups, respectively, and in its ^{13}C NMR a singlet at δ 79.50 corresponding to the C-5.

Photolysis of Hydroxy Carbonyl Compounds 1–3. Photolysis of lactol **1** under different conditions is summarized in Table 1. When the reaction was performed under argon (entries 1 and 2) iodo ketone **7** (Scheme 3) was obtained by oxidative decarboxylation[19] of the tautomeric keto acid **1a**. However, when the photolysis was conducted with air or under oxygen pressure (entries 3–7) peroxy lactone **8** was formed.

A plausible radical-chain mechanism for the formation of iodo ketone **7** and peroxy lactone **8** is shown in Scheme 3. Lactol **1** is in equilibrium with its tautomeric keto acid **1a**. On treatment with DIB–I_2[20] or LTA–I_2,[21] **1a** generates acyloxy radical VI which can lose CO_2 forming the intermediate VII. The latter may trap an iodine atom yielding the iodo ketone **7**. Tautomeric cyclic keto acid **1** may also generate the alkoxy radical VIII, which undergoes β-fragmentation to the carbon radical IX. Under inert atmosphere, intermediate IX probably reverts quickly to VIII and then to VI, as no medium-sized ring anhydride derivatives from IX were isolated. In the presence of oxygen, however, radical IX can be peroxidized to X. This peroxy radical is added to the carbonyl group at C-2 to give XI, which undergoes β-fragmentation to yield peroxy lactone **8** via the carboxy radical XII. Interestingly, the intermediate carboxy radical XII did not decarboxylate, but was stabilized by trapping a hydrogen atom from the reaction medium to produce the β-peroxy lactone **8**. Usually, the crude residue containing the acid **8** was methylated to ester **9** to facilitate purification. The best yield for compound **9** was obtained with DIB–I_2 under air atmosphere (entry 5), while increasing oxygen pressure led to lower yield (entry 7).

Iodo ketone **7** shows in its ^1H NMR spectrum an AB system corresponding to protons at C-1[22] appearing at δ 2.97 and 3.66. The ^{13}C NMR spectrum shows a singlet at δ 211.62 for C-5 (carbonyl function) and a triplet at δ 12.67 for the iodomethylene group. Peroxy lactone **8** presents in its IR spectrum two carboxyl stretches

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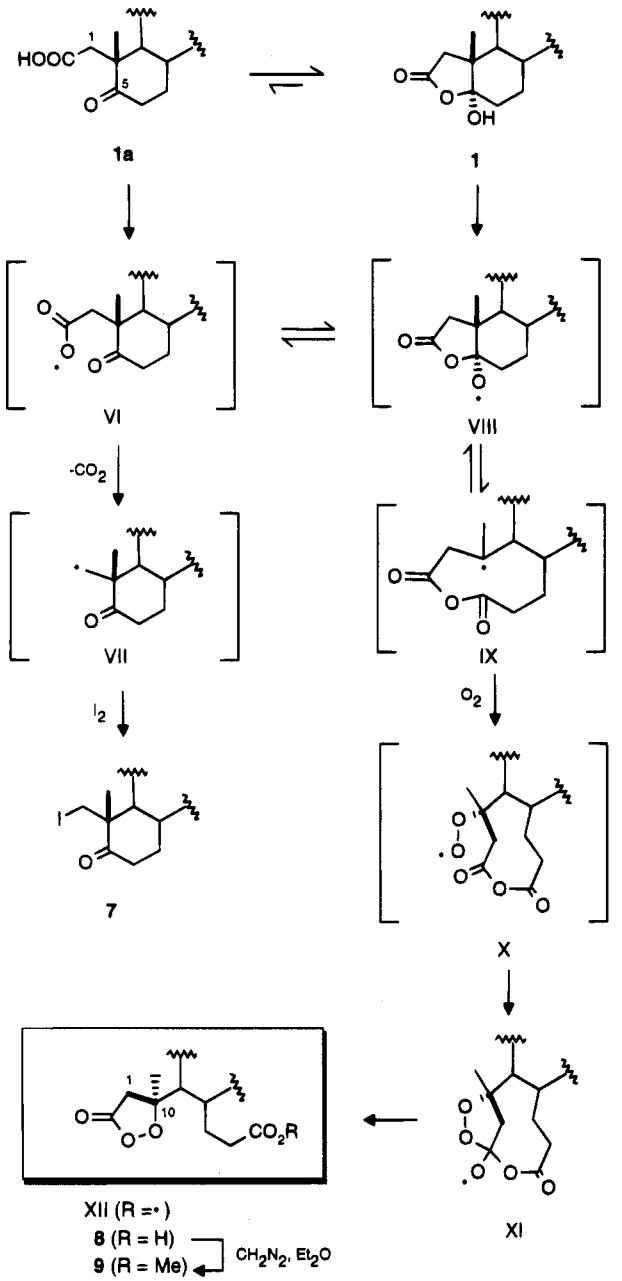
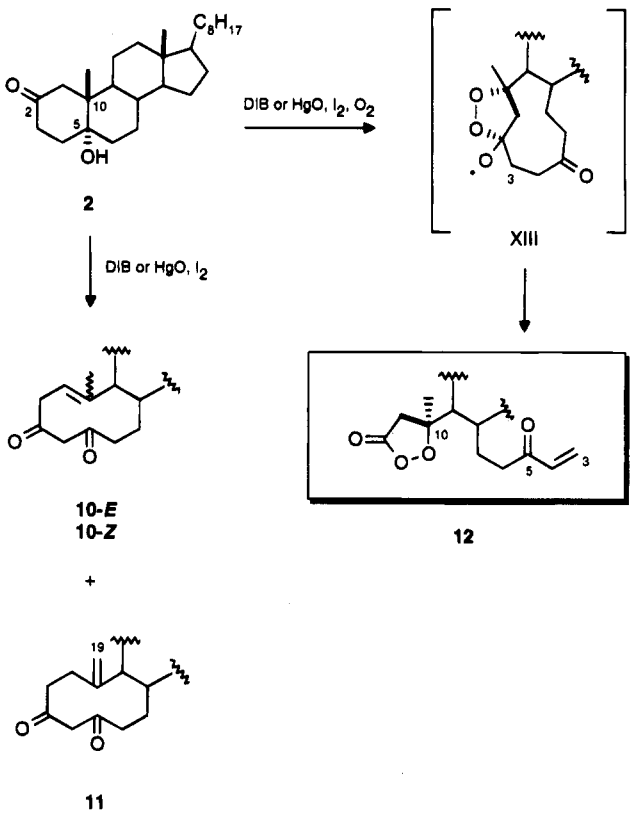
Scheme 3



Scheme 4



characteristic of a β-peroxy lactone and an ester function, respectively, at 1795 and 1700 cm^{-1}. The ^1H NMR spectrum shows an AB system at δ 3.02, 2.84 corresponding to protons at C-1. The signals for C-2 and C-10 appear at δ 175.84 and 91.84, respectively, as two singlets in the ^{13}C NMR spectrum (DEPT experiment).

The formation of peroxy lactone **8** is remarkable. There are few syntheses of these interesting compounds, used by Adam *et al.*[23] for studies on the reactivity of oxygen diradicals.[24] It is also interesting to note that the peroxy lactone was obtained as a single stereoisomer of the two possible C-10 epimers, where oxygen attack occurs exclusively at the β-face of the molecule. The stereochemistry of C-10 of compound **8** was determined by comparison with that of a suitable derivative (*vide infra*).

The formation of the peroxy lactone **8** from lactol **1** encouraged us to study the photolysis under oxygen of structurally related compounds such as hydroxy ketones **2** and **3**. Thus, photolysis of compound **2** with DIB–I_2 or HgO–I_2[25] under several conditions is summarized in Table 1. When the photolysis was performed under inert atmosphere (entries 8 and 9), the expected ring expansion[4–6,26] took place and a mixture of olefinic compounds **10** and **11** was formed by stabilization of the generated C-10 radical (Scheme 4). However, when the reaction was conducted under oxygen (entries 10–14) the peroxy lactone **12** was obtained. The best results were obtained with air or under oxygen pressure (5 atm or less). As expected, in the presence of oxygen a peroxy radical intermediate was formed which added to the carbonyl group, generating a peroxyhemiacetyl radical XIII and then a second β-fragmentation reaction took place yielding a C-radical at C-3 which lost a hydrogen atom to give a double bond conjugated with the carbonyl group at C-5. Also in this case only a single isomer of peroxy lactone **12** was formed (*vide infra*).

Olefin **10-*E*** presented in its IR spectrum two stretches at 1700 and 1690 cm^{-1} due to the carbonyl groups and in its UV spectrum showed an absorption maximum at λ = 237 nm (ϵ = 8500). In the ^1H NMR spectrum a singlet appeared at δ 5.88 due to the C-1 proton and a broad singlet at δ 1.91 for 10-Me, and the ^{13}C NMR spectrum presented two singlets at δ 203.08 and 212.21 for C-2 and C-5 carbonyl functions, but not those corre-

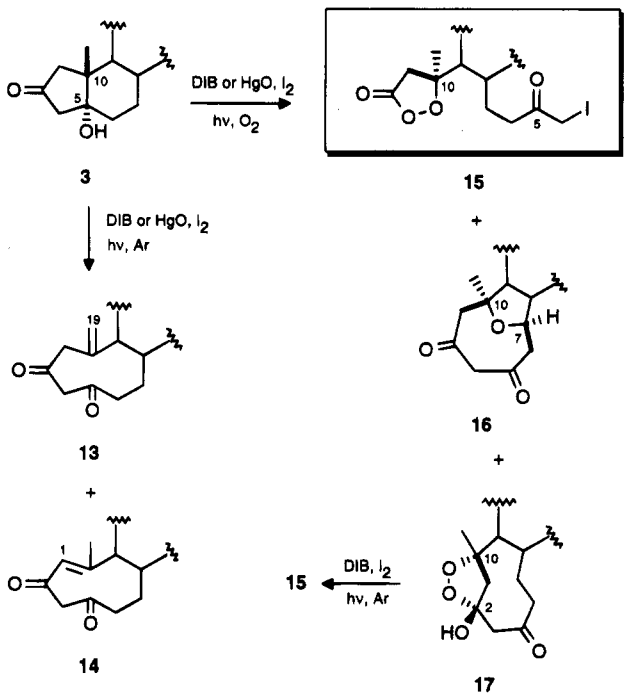
(23) (a) Adam, W.; Rojas, C. I. *Synthesis* **1972**, 616. (b) Greene, F. D.; Adam, W.; Knudsen, G. A. *J. Org. Chem.* **1966**, *31*, 2087.

(24) Adam, W. *Acc. Chem. Res.* **1979**, *12*, 290 and references cited therein.

(25) (a) Suginome, H.; Yamada, S. *Tetrahedron* **1987**, *43*, 3371. (b) Suginome, H.; Yamada, S. *J. Org. Chem.* **1984**, *49*, 3753. (c) Akhtar, M.; Barton, D. H. R. *J. Am. Chem. Soc.* **1964**, *86*, 1528.

(26) For previous works on alkoxy radical β-fragmentation of 5-hydroxycholestane derivatives see: (a) Mihailovic, M. Lj.; Lorenc, Lj.; Gasic, M.; Rogic, M.; Melera, A.; Stefanovic, M. *Tetrahedron* **1966**, *22*, 2345. (b) Mez, H.-C.; Rist, G.; Ermer, O.; Lorenc, Lj.; Kalvoda, J.; Mihailovic, M. Lj. *Helv. Chim. Acta* **1976**, *59*, 1273.

Scheme 5



sponding to the olefinic carbons.[27] The isomer **10-Z** presented analogous spectroscopic data to **10-E**, the main differences appearing in its ^{1}H NMR spectrum, the signals for 1-H and 10-Me thus being shifted 0.04 and −0.15 ppm, respectively. The ^{1}H NMR experiment of diketone **11** showed a broad singlet at δ 5.04 integrating for the two protons at C-19, and its ^{13}C NMR spectrum presented a singlet (δ 145.95) and a triplet (δ 114.80) for olefinic carbons C-10 and C-19, respectively. Peroxy lactone **12** presented in its IR spectrum the characteristic signal of a peroxy lactone carbonyl group at 1800 cm^{-1} and in its ^{1}H NMR spectrum three doublets of doublets at δ 6.34, 6.29, and 5.84, corresponding to C-4, *trans* C-3, and *cis* C-3 protons, respectively.

Photolysis of hydroxy ketone **3** under several conditions is also shown in Table 1. Under inert atmosphere (entry 15) ring expansion products **13** and **14** were obtained (Scheme 5). In the presence of oxygen (entries 16−20) β-peroxy lactone **15** was formed. Nevertheless, the reaction was more complex than in the case of the hydroxy ketone **2** and two new compounds were formed, the tetrahydrofuran derivative **16** (entries 16−20) and in some experiments the peroxyhemiacetal **17** (entries 18 and 20). It is noteworthy that in the photolysis under air the peroxyhemiacetal **17** (entries 16 and 19) was not isolated, while the peroxy lactone **15** reached maximum yields. When more oxygen pressure was applied (entries 17, 18, and 20) the yields of **15** diminished notably. In the case of the tetrahydrofuran derivative **16**, the changes in oxygen pressure had little influence on its final yield.

Diketone **13** presented in its ^{1}H NMR experiment two singlets at δ 5.19 and 5.16 due to the 19-H$_2$ and the corresponding olefinic carbons at δ 145.60 (singlet, C-10) and 118.14 (triplet, C-19) in its ^{13}C NMR spectrum.

The spectroscopic data for product **14** resembled those of olefin **10−Z**. Its UV spectrum thus showed an absorption maximum at λ = 240 nm (ε = 4610). In the ^{1}H NMR experiment a doublet at δ 5.91 corresponding to the 1-H was observed, while the 10-Me signal was a doublet at δ 1.76. Although, due to the slow conformational equilibrium of the nine-membered ring, the ^{13}C NMR spectrum showed no signals for the carbonylic or olefinic carbons,[27] its molecular composition ($C_{20}H_{28}O_4$) was, however, in agreement with an accurate mass spectrometric measurement.

Peroxy lactone **15** showed analogous spectroscopic data to those of compounds **8** and **12**. The main difference came from the iodomethylene group, that is observed as an AB system at δ 3.80, 3.82 in the ^{1}H NMR spectrum, and a triplet at δ 5.93 corresponding to C-3, in the ^{13}C NMR spectrum.

Tetrahydrofuran derivative **16** presented in its ^{1}H NMR spectrum in $CDCl_3$ several overlapping signals, but was better resolved when executed in C_6D_6. A doublet of doublets of doublets at δ 3.66 corresponded to the 7-H coupled to one of the protons at C-6 (δ 2.77, dd). Two AB systems at δ 3.90, 3.09 and at δ 2.36, 2.08 corresponded to the 3-H$_2$ and 1-H$_2$ systems, respectively. Its ^{13}C NMR spectrum presents three singlet signals at δ 202.62, 201.99, and 171.17 for the carbonyl functions. Carbons C-10 and C-7 in the tetrahydrofuran ring appeared at δ 83.16 (singlet) and 77.13 (doublet), respectively.

The isolation of tetrahydrofuran **16** is also noteworthy. We have obtained similar cyclic ethers in the photolysis of other substrates in the presence of oxygen and reported a possible mechanism which involves reduction of the intermediate peroxyradical to an alkoxy radical, followed by hydrogen transfer from C-7 to the alkoxy radical and cyclization.[5a,6b,10c,k]

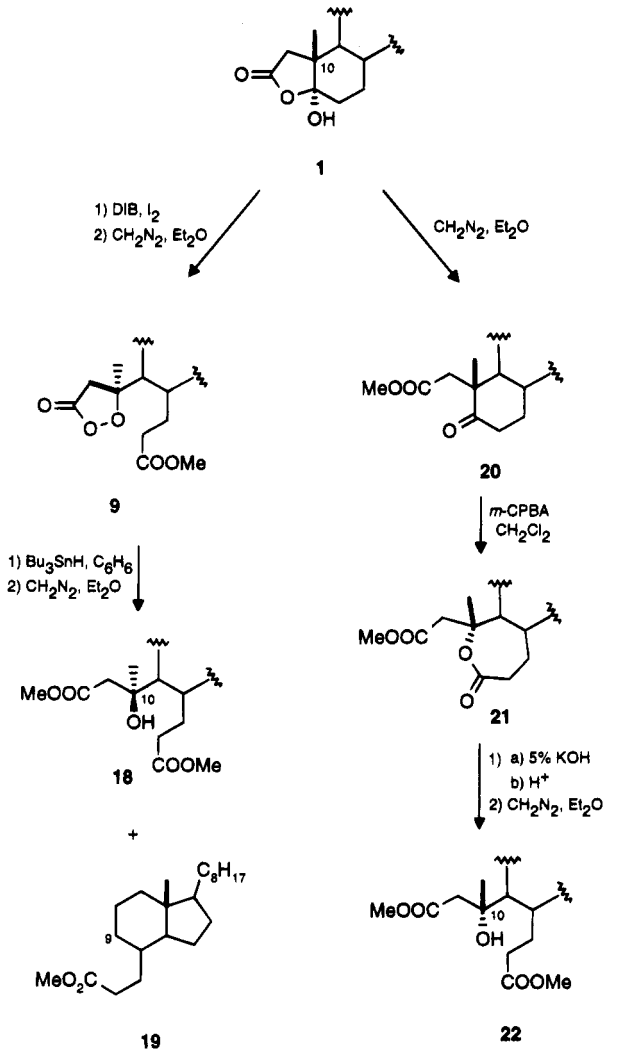
The peroxyhemiacetal **17** showed in its IR spectrum two stretches at 3530 and 1720 cm^{-1} corresponding to the hemiacetal hydroxyl and the carbonyl group, respectively, while in its ^{13}C NMR spectrum two singlets at δ 106.14 and 91.10 are due to the C-2 and C-10, respectively.

The formation opf peroxyhemiacetal **17** deserves special interest since it supports the proposed mechanism for the formation of peroxy lactones **8**, **12**, and **15**. In effect photolysis of **17** with DIB-I$_2$, under argon atmosphere, yielded peroxy lactone **15** in almost quantitative yield.

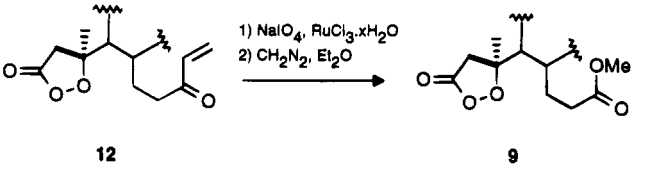
Stereochemistry of β-Peroxy Lactones 9, 12, and 15. Although in each example two possible isomers at C-10 can be expected from the radical dioxygen attack, only one compound could be detected by careful chromatography and ^{1}H NMR and ^{13}C NMR spectroscopy. The stereochemistry of the peroxy lactone **9** was determined by comparing hydroxy compound **18**, synthesized from **9**, and the C-10 isomeric product **22**, both obtained stereoselectively from lactol **1** (Scheme 6). Compound **18** was synthesized as follows: reduction of the peroxy lactone group on **9** was executed with tributyltin hydride−AIBN and subsequent methylation, producing the hydroxy diester **18** together with the ester **19**. We presume that in the reaction mixture the peroxy lactone group of **9** undergoes homolytic cleavage to give a carboxy and an alkoxy radical, which are subsequently reduced by tributyltin hydride to a carboxy and a hydroxy function, respectively, no decarboxylation being observed. Alternatively, the alkoxy radical at C-10 may evolve by β-fragmentation producing a new radical at C-9, that is reduced with excess of Bu_3SnH to give the ester **19**. The detailed account of these reduction experiments of peroxy

(27) In the ^{13}C NMR spectra of olefins **10-E**, **11**, and **14** some carbons could not be observed or were observed as badly-resolved broad signals due to the slow conformational equilibrium of the medium-sized rings.

Scheme 6



Scheme 7



lactones and other aspects of their reactivity will be published elsewhere.

The ^{13}C NMR spectrum of the hydroxy diester **18** showed a singlet at δ 74.43 for C-10, while the methyl group at C-10 appeared at δ 28.17. The structure of the ester **19** was also established by its spectroscopic data (see Experimental Section).

For the synthesis of compound **22** the lactol **1** was treated with ethereal diazomethane to afford methyl ester derivative **20**. Baeyer–Villiger rearrangement of **20** proceeded regio and stereoselectively to give lactone **21**, which was hydrolyzed with 5% KOH MeOH–H_2O. The resulting hydroxy acid was not isolated, but the crude reaction mixture was treated with ethereal diazomethane yielding diester **22**. The spectroscopic data for **22** are analogous but different from those of its C-10 isomer **18**. The main differences appear in the ^{13}C NMR spectrum, where the signals for 10-Me and C-10 are shifted +7.18 and −0.44 ppm, respectively. Since compound **22** possesses an *R*-configuration at C-10, compound **18**, and hence peroxy lactone **9**, must have a 10*S*-configuration.

In the case of peroxy lactone **12**, degradative oxidation of the double bond by treatment with ruthenium tetraoxide,[28] followed by methylation with ethereal diazomethane of the crude acid **8** gave peroxy lactone **9** (Scheme 7). This indicates that in both examples the molecular oxygen in the intermediate C-10 radical such as IX (Scheme 3) enters, stereoselectively, through the β-face in the steroidal framework. Presumably, an analogous mechanism operates in the formation of the β-peroxy lactone **15**.

In conclusion, our approach allows a stereoselective, one-step synthesis of steroidal β-peroxy lactones in moderate to excellent yields from easily available hydroxy carbonyl compounds, using molecular oxygen as the source of the peroxy group.

Experimental Section

General. Melting points were determined with a hot-stage apparatus and are uncorrected. Optical rotation measurements were recorded at room temperature in $CHCl_3$. IR spectra were recorded in $CHCl_3$ solutions. UV spectra were recorded in EtOH. NMR spectra were determined at 200 or 400 MHz for ^1H and 50.3 MHz for ^{13}C for $CDCl_3$ solutions unless otherwise stated in the presence of TMS as internal standard. Mass spectra were determined at 70 eV unless otherwise specified. 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 Chromatotron for centrifugally assisted chromatography. Commercial reagents and solvents were analytical grade or were purified by standard procedures prior to use.[29] All reactions involving air- or moisture-sensitive materials were carried out under an argon atmosphere. 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.

5-Hydroxy-4-nor-3-oxa-5α-cholestan-2-one (1). Compound **1** was prepared from cholest-4-en-3-one[12] in 28% overall yield: mp 166–167 °C (from acetone-*n*-hexane); $[\alpha]_D = +30°$ ($c = 0.24$) (lit.[12] mp 166.5–167.5 °C; $[\alpha]_D = +29.8°$).

5-Hydroxy-5α-cholestan-2-one (2). Compound **2** was prepared from cholest-4-en-3-one[14] in 18% overall yield: mp 182–184 °C (from EtOAc–*n*-hexane); $[\alpha]_D = +28°$ ($c = 0.46$) (lit.[14e] mp 181.5–182.5 °C; $[\alpha]_D = +29.2°$).

17β-Hydroxy-4-norandrost-3-en-2-one Acetate (4). Compound **4** was obtained from testosterone[12,15] in 30% overall yield: mp 122–124.5 °C (from *n*-hexane); $[\alpha]_D = -21°$ ($c = 0.222$); IR 1719, 1698, 1681, 1620 cm^{-1}; UV (0.5 cm) $\lambda_{max} = 228$ nm ($\epsilon = 12930$); ^1H NMR 0.79 (3H, s), 1.12 (3H, s), 1.99 (3H, s), 4.54 (1H, dd, $J = 7.6$, 9.0 Hz), 5.73 (1H, d, $J = 1.4$ Hz); ^{13}C NMR 12.10 (q), 19.95 (q), 21.10 (q), 23.02 (t), 23.44 (t), 27.37 (t), 27.41 (t), 32.06 (t), 35.37 (d), 36.50 (t), 42.87 (s), 46.02 (s), 49.92 (d), 50.57 (t), 53.57 (d), 82.32 (d), 125.45 (d), 171.04 (s), 188.84 (s), 208.17 (s); MS *m/z* (rel intensity) 316 (M^+, 46), 288 (100), 256 (15), 228 (86); HRMS calcd for $C_{20}H_{28}O_3$ 316.20383, found 316.20345.

17β-Hydroxy-3α,5-epoxy-4-nor-5α-androstan-2-one (5). Compound **4** (516 mg, 1.88 mmol) in methanol (35 mL), cooled to 0 °C, was treated with 30% hydrogen peroxide (3.8 mL) and a 4 N NaOH aqueous solution (3.2 mL). After stirring for 8 h at 0 °C, the mixture was poured into water (100 mL), acidified with 4 N HCl aqueous solution (1.5 mL), and extracted with CH_2Cl_2 (3 × 50 mL). The organic phase was washed with H_2O (2 × 20 mL), dried (Na_2SO_4), and evaporated. Chromatotron chromatography of the residue (*n*-hexane–EtOAc, 70:30) gave **5** (375 mg, 75%): mp 143–146 °C (from EtOAc); $[\alpha]_D = +101°$

(28) (a) Carlsen, P. H. J.; Katsuki, T.; Martín, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936. (b) Nuñez, M. T.; Martín, V. S. *J. Org. Chem.* **1990**, *55*, 1928.

(29) Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon Press: New York, 1988.

(c = 0.182); IR 3613, 1747 cm^{-1}; ^{1}H NMR 0.77 (3H, s), 1.17 (3H, s), 2.07 (1H, d, J = 17.5 Hz), 2.15 (1H, d, J = 17.5 Hz), 3.14 (1H, s), 3.64 (1H, t, J = 7.9 Hz); ^{13}C NMR 11.14 (q), 15.5 (q), 21.89 (t), 23.29 (t), 25.11 (t), 29.50 (t), 30.18 (t), 35.16 (d), 36.19 (t), 41.07 (s), 43.09 (s), 44.95 (t), 50.26 (d), 50.35 (d), 62.07 (d), 73.82 (s), 81.37 (d), 210.58 (s); MS m/z (rel intensity) 290 (M$^+$, 21), 275 (8), 272 (87), 257 (27), 254 (12), 243 (44), 233 (34), 218 (100), 173 (47); HRMS calcd for $C_{18}H_{26}O_3$ 290.18819, found 290.18839.

17β-Hydroxy-3α,5-epoxy-4-nor-5α-androstan-2-one Acetate (6). Epoxide **5** (316 mg, 1.09 mmol) in pyridine (10 mL) was treated with Ac_2O (5 mL) at rt for 8 h. The mixture was poured into 5% HCl (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The organic phase was washed with 5% HCl (3 × 15 mL) and water (3 × 15 mL), dried, and evaporated. Chromatotron chromatography (n-hexane–EtOAc, 75:25) gave acetate **6** (335 mg, 93%): mp 141–142 °C (from n-hexane); $[\alpha]_D$ = +91° (c = 0.26); IR 1753, 1728 cm^{-1}; ^{1}H NMR 0.82 (3H, s), 1.18 (3H, s), 2.04 (3H, s), 2.07 (1H, d, J = 17.6 Hz), 2.15 (1H, d, J = 17.6 Hz), 3.16 (1H, s), 4.58 (1H, dd, J = 7.5, 9.0 Hz); ^{13}C NMR 12.09 (q), 15.50 (q), 21.09 (q), 21.75 (t), 23.45 (t), 25.09 (t), 27.41 (t), 29.49 (t), 34.91 (d), 36.36 (t), 41.01 (s), 42.68 (s), 44.94 (t), 50.00 (d), 50.16 (d), 62.08 (d), 73.64 (s), 82.33 (d), 171.02 (s), 210.17 (s); MS m/z (rel intensity) 332 (M$^+$, 7), 314 (19), 299 (3), 272 (16), 260 (19), 257 (7), 254 (26); HRMS calcd for $C_{20}H_{28}O_4$ 332.19876, found 332.19835.

5,17β-Dihydroxy-4-nor-5α-androstan-2-one 17-Acetate (3). Diphenyl diselenide (451 mg, 1.45 mmol) in ethanol (7.2 mL) and acetic acid (30 μL, 0.53 mmol) was treated with $NaBH_4$, added in little portions until disappearance of the yellow color was observed (135 mg, 3.57 mmol). This solution was added dropwise under Ar to a solution of epoxy acetate **6** (300 mg, 0.9 mmol) in ethanol (19 mL), previously cooled to 4 °C with a water–ice bath. Once the addition was over, stirring continued for 10 min. Then the mixture was poured into brine (100 mL) and extracted with CH_2Cl_2 (3 × 25 mL). The residue was purified by chromatotron chromatography (n-hexane–EtOAc, 80:20), giving the hydroxy acetate **3** (186 mg, 62%) and the enone **4** (96 mg, 34%). Compound **3**: mp 169–171 °C (from n-hexane–EtOAc); $[\alpha]_D$ = −65° (c = 0.372); IR 3604, 1736 cm^{-1}; ^{1}H NMR 0.80 (3H, s), 1.09 (3H, s), 2.03 (3H, s), 2.09 (1H, d, J = 18.7 Hz), 2.30 (1H, d, J = 18.3 Hz), 2.38 (1H, d, J = 18.3 Hz), 2.74 (1H, d, J = 18.7 Hz), 4.55 (1H, dd, J = 7.4, 8.9 Hz); ^{13}C NMR 12.17 (q), 13.16 (q), 21.12 (q), 22.14 (t), 23.44 (t), 27.55 (t), 28.14 (t), 31.94 (t), 34.95 (d), 36.70 (t), 42.62 (s), 46.05 (s), 47.84 (d), 47.89 (t), 49.16 (t), 50.51 (d), 79.50 (s), 82.49 (d), 171.17 (s), 217.54 (s); MS m/z (rel intensity) 334 (M$^+$, 8), 316 (3), 274 (86), 256 (9); HRMS calcd for $C_{20}H_{30}O_4$ 334.21441, found 334.21487.

Photolysis of 5-Hydroxy-4-nor-3-oxa-5α-cholestan-2-one (1). Method A. To a solution of lactol **1** (100 mg, 0.26 mmol) in cyclohexane (20 mL) were added LTA (340 mg, 0.77 mmol) and I_2 (65 mg, 0.26 mmol). The solution was deoxygenated by several cycles of pumping at −196 °C followed by filling with Ar at rt and then was irradiated with 2 × 100 W tungsten-filament lamps for 1 h at reflux temperature. The solution was allowed to reach rt, poured into 5% $Na_2S_2O_3$ aqueous solution (25 mL), and extracted with CH_2Cl_2 (3 × 10 mL). The organic layer was washed with brine (15 mL), dried (Na_2SO_4), and evaporated under vacuum. Column chromatography of the residue (C_6H_6) gave 1-iodo-2,3,4-trinor-1,2-secocholestan-5-one (**7**) (11 mg, 9%): amorphous; IR 1700 cm^{-1}; ^{1}H NMR 0.70 (3H, s), 0.84 (6H, d, J = 6.4 Hz), 1.19 (3H, s), 2.97 (1H, d, J = 9.9 Hz), 3.66 (1H, d, J = 9.9 Hz); ^{13}C NMR 11.89 (q), 12.67 (t), 18.61 (q), 19.23 (q), 21.13 (t), 22.55 (q), 22.79 (q), 23.75 (t), 24.23 (t), 28.01 (d), 28.05 (t), 30.44 (t), 35.16 (d), 35.68 (d), 36.09 (t), 37.56 (t), 39.05 (t), 39.48 (t), 42.43 (s), 48.88 (d), 50.25 (s), 55.42 (d), 55.89 (d), 211.62 (s); MS m/z (rel intensity) 472 (M$^+$, 23), 345 (77), 327 (100), 219 (27), 215 (45), 201 (36), 191 (27), 161 (45); HRMS calcd for $C_{24}H_{41}OI$ 472.2204, found 472.2203. The photolysis was also performed under Ar with DIB/I_2 at 40–45 °C (Table 1, entry 2).

Method B. To a solution of lactol **1** (1 g, 2.56 mmol) in cyclohexane (150 mL) were added LTA (3.4 g, 7.7 mmol) and I_2 (650 mg, 2.6 mmol), and the mixture was irradiated at 40 °C with 2 × 100 W tungsten-filament lamps for 3 h, under atmosphere of dry air. Workup as before and column chromatography (C_6H_6–EtOAc, 1:1) afforded peroxy lactone acid **8** (375 mg, 35%): mp 99–101 °C (from acetone–n-hexane); $[\alpha]_D$ = −4° (c = 0.21); IR 3500–2400, 1795, 1700 cm^{-1}; ^{1}H NMR 0.65 (3H, s), 0.83 (6H, d, J = 6.6 Hz), 0.86 (3H, d, J = 6.8 Hz), 1.42 (3H, s), 2.84 (1H, d, J = 16.6 Hz), 3.02 (1H, d, J = 16.6 Hz); ^{13}C NMR 11.99 (q), 18.76 (q), 20.03 (q), 22.70 (t), 22.73 (q), 22.97 (q), 23.94 (t), 24.59 (t), 25.45 (t), 27.81 (t), 28.18 (d), 28.66 (t), 35.88 (d), 36.09 (d), 36.17 (t), 39.16 (t), 39.66 (t), 42.60 (s), 44.44 (t), 46.71 (d), 52.49 (d), 56.33 (d), 91.84 (s), 175.84 (s), 179.65 (s); MS m/z (rel intensity) 422 (M$^+$, 12), 404 (M$^+$-H_2O, 14), 378 (3), 363 (100), 321 (6), 320 (40), 247 (59), 207 (92); HRMS calcd for $C_{25}H_{40}O_4$ 404.2924, found 404.2897. Conducting the photolysis as before and then treating the crude residue containing acid **8** with ethereal CH_2N_2, followed by column chromatography (n-hexane–EtOAc, 95:5), gave methyl ester **9** in 77% yield: mp 67–69 °C (from acetone–n-hexane), $[\alpha]_D$ = −2° (c = 0.29); IR 1795, 1730 cm^{-1}; ^{1}H NMR 0.65 (3H, s), 0.83 (6H, d, J = 6.6 Hz), 0.86 (3H, d, J = 6.6 Hz), 1.42 (3H, s), 2.84 (1H, d, J = 16.6 Hz), 3.02 (1H, d, J = 16.6 Hz), 3.63 (3H, s); ^{13}C NMR 11.97 (q), 18.74 (q), 19.76 (q), 22.62 (t), 22.67 (q), 22.93 (q), 23.92 (t), 24.58 (t), 25.54 (t), 27.78 (t), 28.15 (d), 28.58 (t), 35.86 (d), 36.14 (d), 36.19 (t), 39.14 (t), 39.63 (t), 42.57 (s), 44.64 (t), 46.75 (d), 51.88 (q), 52.48 (d), 56.33 (d), 91.74 (s), 174.07 (s), 175.78 (s); MS m/z (rel intensity) 436 (M$^+$, 13), 392 (6), 377 (69), 335 (70), 303 (56), 247 (100), 221 (99); HRMS calcd for $C_{26}H_{44}O_5$ 436.3189, found 436.3195. Photolysis was also performed with DIB/I_2 under air (Table 1, entries 5, 6) and under O_2 atmosphere (entry 7).

Photolysis of 5-Hydroxy-5α-cholestan-2-one (2). Method A. A solution of ketone **2** (58 mg, 0.14 mmol) in CCl_4 (10 mL) containing DIB (90 mg, 0.28 mmol) and I_2 (45 mg, 0.18 mmol) was irradiated with 2 × 100 W tungsten-filament lamps for 20 min, at room temperature and under Ar. The reaction mixture was then poured into 10% $Na_2S_2O_3$ aqueous solution (15 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The organic layer was washed with brine (5 mL), dried (Na_2SO_4), and evaporated. Chromatotron chromatography (n-hexane–EtOAc, 95:5) afforded enones **10-*E*** (8 mg, 14%) and **10-*Z*** (10 mg, 17%) and olefin **11** (22 mg, 38%). Compound **10-*E***: amorphous; $[\alpha]_D$ = +33° (c = 0.12); IR 1700, 1690 cm^{-1}; UV (0.1 cm) λ_{max} = 237 nm (ϵ = 8500); ^{1}H NMR 0.73 (3H, s), 0.87 (6H, d, J = 6.5 Hz), 0.90 (3H, d, J = 5.8 Hz), 1.91 (3H, s), 5.88 (1H, s); ^{13}C NMR 12.01 (q), 18.65 (q), 22.53 (q), 22.79 (q), 23.79 (t), 24.85 (t), 27.78 (t), 27.99 (d), 35.69 (d), 36.08 (t), 38.05 (t), 39.46 (t), 42.05 (s), 44.39 (t), 56.17 (d), 203.08 (s), 212.21 (s), only 16 well-defined signals were observed;[27] MS m/z (rel intensity) 400 (M$^+$, 78), 385 (29), 382 (46), 367 (19); HRMS calcd for $C_{27}H_{44}O_2$ 400.33413, found 400.33555. Compound **10-*Z***: mp 107–108 °C (from EtOAc–n-hexane); $[\alpha]_D$ = +50° (c = 0.30); IR 1700, 1680, 1620 cm^{-1}; UV (0.1 cm) λ_{max} = 237 nm (ϵ = 2500); ^{1}H NMR 0.70 (3H, s), 0.87 (6H, d, J = 7 Hz), 0.91 (3H, d, J = 6.6 Hz), 1.76 (3H, d, J = 1 Hz), 5.92 (1H, d, J = 1 Hz); ^{13}C NMR 11.88 (q), 18.61 (q), 18.76 (q), 22.55 (q), 22.79 (q), 23.69 (t), 24.25 (t), 24.54 (t), 26.39 (t), 27.83 (t), 27.99 (d), 35.67 (d), 36.05 (t), 37.19 (d), 37.40 (t), 37.95 (t), 38.94 (t), 39.47 (t), 39.73 (t), 42.79 (s), 43.13 (d), 50.29 (d), 55.98 (d), 128.18 (d), 151.47 (s), 205.53 (s), 213.20 (s); MS m/z (rel intensity) 400 (M$^+$, 63), 385 (56), 382 (63), 367 (29); HRMS calcd for $C_{27}H_{44}O_2$ 400.33413, found 400.33233. Compound **11**: amorphous; $[\alpha]_D$ = −51° (c = 0.14); IR 1710, 1705 cm^{-1}; ^{1}H NMR 0.71 (3H, s), 0.87 (6H, d, J = 6.2 Hz), 0.89 (3H, d, J = 5.8 Hz), 5.04 (2H, s); ^{13}C NMR 11.95 (q), 18.61 (q), 22.53 (q), 22.79 (q), 23.77 (t), 24.30 (t), 27.90 (t), 27.97 (d), 35.69 (d), 36.07 (t), 36.77 (t), 37.07 (d), 39.46 (t), 39.62 (t), 42.89 (s), 56.09 (d), 114.80 (t), 145.95 (s), 208.53 (s), 211.56 (s), only 20 well-defined signals were observed;[27] MS m/z (rel intensity) 400 (M$^+$, 38), 385 (21), 382 (100), 367 (13); HRMS calcd for $C_{27}H_{44}O_2$ 400.33413, found 400.33256. The photolysis was also performed under Ar with HgO/I_2 (Table 1, entry 9).

Method B. A solution of ketone **2** (40 mg, 0.1 mmol) in CCl_4 (14 mL), containing DIB (64 mg, 0.1 mmol) and I_2 (25 mg, 0.1 mmol), was irradiated as before at rt and allowing the entrance of dry air for 2 h. Usual workup and chromatotron chromatography (n-hexane–EtOAc, 90:10) afforded diketones **10-*Z*** (3.5 mg, 9%) and **11** (3.5 mg, 9%), and **12** (18 mg, 45%).

Peroxy lactone **12**: amorphous; $[\alpha]_D = +4°$ ($c = 0.14$); IR 1800, 1715 cm^{-1}; ^1H NMR 0.69 (3H, s), 0.88 (6H, d, $J = 6.7$ Hz), 0.91 (3H, d, $J = 7.9$ Hz), 1.47 (3H, s), 2.84 (1H, d, $J = 16.6$ Hz), 3.0 (1H, d, $J = 16.6$ Hz), 5.84 (1H, dd, $J = 2.1$, 9.5 Hz), 6.29 (1H, dd, $J = 17.6$, 2.1 Hz), 6.34 (1H, dd, $J = 17.6$, 9.5 Hz); ^{13}C NMR 11.77 (q), 18.54 (q), 19.90 (q), 22.51 (q), 22.63 (t), 22.77 (q), 23.69 (t), 24.01 (t), 24.45 (t), 27.60 (t), 27.96 (d), 33.63 (t), 35.63 (d), 35.94 (t), 35.94 (d), 38.98 (t), 39.42 (t), 42.36 (s), 43.98 (t), 46.40 (d), 52.42 (d), 56.11 (d), 91.74 (s), 128.36 (t), 136.30 (d), 175.57 (s), 200.26 (s); MS m/z 15 eV (rel intensity) 416 ($M^+ - O$, 3), 398 (11); HRMS calcd for $C_{27}H_{44}O_3$ 416.32902, found 416.32917. Photolysis was also performed with DIB/I_2 under O_2 pressure (Table 1, entries 11 and 12), with HgO/I_2 under air (entry 13), and under O_2 pressure (entry 14).

Photolysis of 5,17β-Dihydroxy-4-nor-5α-androstan-2-one 17-Acetate (3). Method A. To a carefully deoxygenated solution of hydroxy ketone **3** (33.4 mg, 0.1 mmol) in cyclohexane (13 mL) were added DIB (48 mg, 0.15 mmol) and I_2 (25 mg, 0.1 mmol). The mixture was irradiated with 2 × 100 W tungsten-filament lamps for 5 h at 45 °C under Ar. Usual workup and chromatotron chromatography (C_6H_6–EtOAc, 97:3) afforded the olefin **13** (16 mg, 48%) and the enone **14** (5.6 mg, 17%). Compound **13**: mp 126–127.5 °C (from EtOAc–*n*-hexane); $[\alpha]_D = +54°$ ($c = 0.094$); IR 1720, 1690 cm^{-1}; ^1H NMR 0.81 (3H, s), 2.02 (3H, s), 3.11 (1H, d, $J = 15.2$ Hz), 3.20 (1H, d, $J = 15.2$ Hz), 3.62 (1H, d, $J = 12.7$ Hz), 3.73 (1H, d, $J = 12.7$ Hz), 4.59 (1H, dd, $J = 7.4$, 8.9 Hz), 5.16 (1H, s), 5.19 (1H, s); ^{13}C NMR 12.05 (q), 21.10 (q), 23.75 (t), 26.18 (t), 27.24 (t), 29.14 (t), 36.50 (t), 37.75 (d), 42.86 (t), 42.91 (s), 48.77 (d), 50.04 (t), 51.54 (d), 53.51 (t), 82.28 (d), 118.14 (t), 145.60 (s), 171.06 (s), 201.20 (s), 205.24 (s); MS m/z (rel intensity) 332 (M^+, 6), 314 (2), 304 (5), 290 (8), 272 (9); HRMS calcd for $C_{20}H_{28}O_4$ 332.19876, found 332.19769. Compound **14**: mp 166–168 °C (from *n*-hexane); $[\alpha]_D = +42°$ ($c = 0.07$); IR 1720, 1680 cm^{-1}; UV (0.5 cm) $\lambda_{max} = 240$ nm, ($\epsilon = 4610$); ^1H NMR 0.84 (3H, s), 1.76 (3H, d, $J = 1.3$ Hz), 2.04 (3H, s), 3.71 (1H, d, $J = 13.8$ Hz), 3.79 (1H, d, $J = 13.8$ Hz), 4.65 (1H, dd, $J = 7.4$, 9.1 Hz), 5.91 (1H, d, $J = 1.3$ Hz); ^{13}C NMR 11.94 (q), 21.10 (q), 23.66 (t), 27.12 (t), 36.19 (t), 36.79 (d), 82.29 (d), only 7 well-defined signals were observed;[27] MS m/z (rel intensity) 332 (M^+, 3), 317 (2), 314 (7), 304 (10), 290 (11), 275 (15), 272 (10), 261 (50); HRMS calcd for $C_{20}H_{28}O_4$ 332.19876, found 332.19731.

Method B. Hydroxy ketone **3** (33.4 mg, 0.1 mmol) in cyclohexane (13 mL) was treated with DIB (48 mg, 0.15 mmol) and I_2 (25 mg, 0.1 mmol). The mixture was irradiated as previously at 45 °C for 3.5 h, allowing the entrance of dry air. After usual workup, chromatotron chromatography (*n*-hexane–EtOAc, 85:15) afforded dione **13** (3 mg, 9%), peroxy lactone **15** (21 mg, 43%), and epoxide **16** (4.2 mg, 12%). Compound **15**: amorphous; IR 1798, 1726 cm^{-1}; ^1H NMR 0.82 (3H, s), 1.47 (3H, s), 2.04 (3H, s), 2.87 (1H, d, $J = 16.6$ Hz), 3.03 (1H, d, $J = 16.6$ Hz), 3.80 (1H, d, $J = 9.6$ Hz), 3.82 (1H, d, $J = 9.6$ Hz), 4.60 (1H, dd, $J = 7.4$, 8.9 Hz); ^{13}C NMR 5.93 (t), 11.85 (q), 20.22 (q), 21.06 (q), 22.33 (t), 23.77 (t), 23.79 (t), 26.97 (t), 33.26 (t), 35.74 (d), 36.00 (t), 42.43 (s), 43.79 (t), 46.56 (d), 47.10 (d), 82.12 (d), 91.56 (s), 171.02 (s), 175.27 (s), 202.59 (s); MS m/z 15 eV (rel intensity) 474 ($M^+ - H_2O$, <1), 391 (2), 349 (2), 331 (5), 318 (16), 254 (100); HRMS calcd for $C_{16}H_{24}IO_3$ 391.07719, found 391.07603. Compound **16**: amorphous; IR 1719, 1691 cm^{-1}; ^1H NMR 0.74 (3H, s), 1.38 (3H, s), 2.05 (3H, s), 2.36 (1H, ddd, $J = 13.2$, 2.8, 0.8 Hz), 2.55 (1H, d, $J = 12.2$ Hz), 2.63 (1H, d, $J = 12.2$ Hz), 3.21 (1H, dd, $J = 10.4$, 1.2 Hz), 3.22 (1H, dd, $J = 13.2$, 4.8 Hz), 4.09 (1H, ddd, $J = 8.9$, 4.8, 2.8 Hz), 4.31 (1H, d, $J = 10.4$ Hz), 4.62 (1H, dd, $J = 7.8$, 8.9 Hz); ^1H NMR (C_6D_6) 0.71 (3H, s), 1.12 (3H, s), 1.66 (3H, s), 2.08 (1H, d, $J = 12.1$ Hz), 2.36 (1H, d, $J = 12.1$ Hz), 2.77 (1H, dd, $J = 13.2$, 4.9 Hz), 3.09 (1H, d, $J = 10.6$ Hz), 3.90 (1H, d, $J = 10.6$ Hz), 3.66 (1H, ddd, $J = 9.7$, 4.8, 2.0 Hz), 4.66 (1H, dd, $J = 7.4$, 9.0 Hz); ^{13}C NMR 12.42 (q), 20.62 (t), 21.11 (q), 23.36 (t), 27.36 (q), 27.66 (t), 36.16 (t), 44.59 (s), 44.75 (d), 48.37 (d), 50.36 (t), 52.54 (t), 57.84 (d), 60.25 (t), 77.13 (d), 81.35 (d), 83.16 (s), 171.17 (s), 201.99 (s), 202.62 (s); MS m/z (rel intensity) 348 (M^+, 21), 330 (1), 306 (12), 248 (16), 291 (2), 288 (4); HRMS calcd for $C_{20}H_{28}O_5$ 348.19367, found 348.19456. The photolysis was also performed under O_2 atmosphere (Table 1, entry 17).

Method C. A solution of hydroxy ketone **3** (33.4 mg, 0.1 mmol) in cyclohexane (13 mL) containing DIB (48 mg, 0.15 mmol) and I_2 (25 mg, 0.1 mmol) was placed in a borosilicate Griffin-Worden pressure vessel (Kontes K-767100) and irradiated at 45 °C for 5.5 h, under 3 atm O_2 pressure. Usual workup and chromatography (*n*-hexane–EtOAc, 85:15) yielded peroxy lactone **15** (8.4 mg, 17%), ether **16** (5.6 mg, 16%), and peroxyhemiacetal **17** (8.5 mg, 23%): compound **17**: amorphous; IR 3530, 1720 cm^{-1}; ^1H NMR 0.81 (3H, s), 1.50 (3H, s), 2.05 (3H, s), 2.24 (1H, d, $J = 13.6$ Hz), 2.91 (1H, d, $J = 13.6$ Hz), 3.07 (1H, s), 4.58 (1H, dd, $J = 8.9$, 7.6 Hz); ^{13}C NMR 11.96 (q), 21.15 (q), 24.21 (t), 25.76 (t), 26.91 (t), 27.90 (q), 28.29 (t), 36.37 (t), 37.61 (d), 42.45 (s), 44.15 (t), 50.32 (d), 50.41 (d), 50.54 (t), 56.07 (t), 82.31 (d), 91.10 (s), 106.14 (s), 171.17 (s), 210.23 (s); MS m/z (rel intensity) 366 (M^+, <1), 348 (1), 333 (7), 306 (1), 291 (2), 273 (7), 249 (8), 231 (15), 147 (100); HRMS calcd for $C_{20}H_{30}O_6$ 366.20422, found 366.20337. Photolysis was also performed with HgO/I_2 in the presence of air and O_2 (Table 1, entries 19 and 20).

Photolysis of Peroxyhemiacetal 17 under Argon. A solution of peroxyhemiacetal **17** (16 mg, 0.04 mmol) in cyclohexane (5 mL) was treated with DIB (21 mg, 0.06 mmol) and I_2 (11 mg, 0.04 mmol) and then irradiated with 2 × 100 W tungsten-filament lamps for 2 h, at 45 °C under Ar. Usual workup and chromatotron chromatography (*n*-hexane–EtOAc, 85:15) afforded peroxy lactone **15** (21.5 mg, 99%).

Reduction of Peroxy Lactone 9 with Bu_3SnH. A solution of peroxy lactone **9** (80 mg, 0.183 mmol), tributyltin hydride (126 μl, 0.47 mmol), and a catalytic amount of AIBN in dry C_6H_6 (30 mL) was stirred under Ar at 40–45 °C for 48 h. Then further tributyltin hydride (189 μl, 0.70 mmol) and AIBN (catalytic amount) were added, and the reaction was continued for another 24 h. The reaction mixture was poured into water (15 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The organic layer was dried (Na_2SO_4) and evaporated in the usual way, and the residue in ether (5 mL) at 0 °C was treated with an ethereal solution of CH_2N_2 for 1 h. Evaporation under vacuum and chromatotron chromatography (*n*-hexane–EtOAc, 97:3) gave hydroxy diester **18** (48 mg, 58%) and ester **19** (11 mg, 17%). Hydroxy diester **18**: amorphous; IR 3600, 1720 cm^{-1}; ^1H NMR 0.66 (3H, s), 0.87 (6H, d, $J = 6.3$ Hz), 0.90 (3H, d, $J = 5.7$ Hz), 1.22 (3H, s), 2.44 (1H, d, $J = 15.1$ Hz), 2.65 (1H, d, $J = 15.1$ Hz), 3.41 (1H, s, OH), 3.64 (3H, s), 3.73 (3H, s); ^{13}C NMR 11.95 (q), 18.74 (q), 22.71 (q), 22.96 (q), 23.92 (t), 24.43 (t), 24.78 (t), 25.80 (t), 28.03 (t), 28.17 (t), 28.17 (q), 28.60 (d), 35.92 (d), 36.07 (d), 36.18 (t), 39.65 (t), 40.00 (t), 40.00 (t), 42.46 (s), 48.22 (d), 51.51 (q), 51.86 (q), 52.72 (d), 56.47 (d), 74.43 (s), 174.17 (s), 175.64 (s); MS m/z (rel intensity) 452 (M^+, 3), 434 (1), 419 (1), 403 (4), 389 (2), 336 (18), 304 (4), 117 (100); HRMS calcd for $C_{27}H_{48}O_5$ 452.3502, found 452.3483. Ester **19**: amorphous; IR 1725 cm^{-1}; ^1H NMR 0.66 (3H, s), 0.87 (6H, d, $J = 6.7$ Hz), 0.91 (3H, d, $J = 6.5$ Hz), 2.30 (2H, m), 3.66 (3H, s); ^{13}C NMR 11.98 (q), 18.87 (q), 22.27 (t), 22.71 (q), 22.96 (q), 23.98 (t), 24.71 (t), 27.87 (t), 28.17 (d), 30.15 (t), 31.68 (t), 32.05 (t), 35.90 (d), 36.13 (d), 36.36 (t), 39.68 (t), 40.22 (t), 43.17 (s), 51.59 (q), 55.56 (d), 56.60 (d), 174.89 (s); MS m/z (rel intensity) 336 (M^+, 20), 321 (1), 304 (2), 287 (3), 262 (8), 249 (8), 223 (7), 196 (17), 191 (6), 181 (72), 164 (16), 109 (100); HRMS calcd for $C_{22}H_{40}O_2$ 336.3028, found 336.3010.

Methyl 5-Oxo-3,4-dinor-2,3-secocholestan-2-oate (20). To a solution of lactol **1** (1.1 g, 2.7 mmol) in ether (40 mL) at 0 °C was added an ethereal solution of CH_2N_2 and stirred for 1 h. The reaction mixture was evaporated under vacuum and purified by column chromatography through silica gel (*n*-hexane–EtOAc, 95:5), yielding keto ester **20** (1.1 g, 96%): mp 45–49 °C (neat); $[\alpha]_D = +53°$ ($c = 0.36$); IR 1725, 1700 cm^{-1}; ^1H NMR 0.73 (3H, s), 0.86 (6H, d, $J = 6.9$ Hz), 0.91 (3H, d, $J = 6.5$ Hz), 1.17 (3H, s), 2.35 (1H, d, $J = 16.6$ Hz), 2.75 (1H, d, $J = 16.6$ Hz), 3.64 (3H, s); ^{13}C NMR 12.02 (q), 18.64 (q), 19.96 (q), 21.13 (t), 22.57 (q), 22.83 (q), 23.86 (t), 24.26 (t), 28.01 (d), 28.12 (t), 30.52 (t), 35.14 (d), 35.76 (d), 36.17 (t), 37.82 (t), 39.18 (t), 39.42 (t), 39.54 (t), 42.57 (s), 48.37 (d), 50.20 (s), 51.20 (q), 55.61 (d), 56.05 (d), 172.34 (s), 213.91 (s); MS m/z (rel intensity) 404 (M^+, 2), 389 (4), 386 (3), 372 (32), 357 (13), 331 (100); HRMS calcd for $C_{26}H_{44}O_3$ 404.3288, found 404.3278.

Lactone 21. To a solution of ketone **20** (1.1 g, 2.72 mmol) in dry chloroform (60 mL) was added *m*-CPBA (0.47 g, 2.72

mmol) in portions. The reaction mixture was stirred at room temperature for 36 h and then poured into water (60 mL) and extracted with CH_2Cl_2 (3 × 60 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ solution (3 × 30 mL), water (30 mL), dried (Na_2SO_4), and evaporated under vacuum. Column chromatography of the residue (*n*-hexane–EtOAc, 80:20) gave lactone **21** (1.03 g, 91%): mp 61–63 °C (neat); $[\alpha]_D$ = +62° (*c* = 0.23); IR 1710 cm^{-1}; ^1H NMR 0.71 (3H, s), 0.86 (6H, d, *J* = 6.3 Hz), 0.90 (3H, d, *J* = 6.6 Hz), 1.61 (3H, s), 2.68 (2H, s), 3.70 (3H, s); ^{13}C NMR 11.93 (q), 18.56 (q), 20.74 (q), 22.53 (q), 22.78 (q), 23.77 (t), 24.81 (t), 25.78 (t), 27.80 (t), 27.87 (t), 27.96 (d), 35.69 (t), 35.69 (d), 36.0 (t), 38.44 (d), 39.46 (t), 39.51 (t), 42.21 (s), 47.06 (t), 50.55 (d), 51.55 (q), 55.14 (d), 56.23 (d), 85.24 (s), 170.11 (s), 174.11 (s); MS *m/z* (rel intensity) 420 (M^+, 1), 405 (3), 370 (5), 347 (10), 319 (19), 315 (17), 304 (100); HRMS calcd for $C_{26}H_{44}O_4$ 420.3237, found 420.3224.

Hydroxy Diester 22. Lactone **21** (130 mg, 0.31 mmol) was treated with 5% KOH in methanol–water (9:1, 20 mL), and the reaction mixture was stirred at rt for 24 h and then poured into 10% aqueous HCl (20 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The organic layer was dried, and evaporated in the usual way. The residue was dissolved in ether (10 mL) and treated with an excess of ethereal CH_2N_2. After 1 h, the solution was evaporated under vacuum and the residue was purified by chromatotron chromatography (*n*-hexane–EtOAc, 90:10), giving hydroxy diester **22** (118 mg, 84%): mp 49–50 °C (neat); $[\alpha]_D$ = +12° (*c* = 0.23); IR 3500, 1720 cm^{-1}; ^1H NMR 0.66 (3H, s), 0.86 (6H, d, *J* = 6.7 Hz), 0.88 (3H, d, *J* = 6.3 Hz), 1.22 (3H, s), 2.42 (1H, d, *J* = 15.8 Hz), 2.57 (1H, d, *J* = 15.8 Hz), 3.64 (3H, s), 3.71 (3H, s), 3.81 (1H, OH); ^{13}C NMR 11.83 (q), 18.65 (q), 21.99 (q), 22.61 (q), 22.87 (q), 23.81 (t), 24.35 (t), 25.42 (t), 25.71 (t), 27.92 (t), 28.06 (d), 28.37 (t), 35.80 (d), 35.84 (d), 36.09 (t), 39.55 (t), 39.84 (t), 42.27 (s), 45.64 (t), 46.74 (d), 51.42 (q), 51.69 (q), 52.58 (d), 56.37 (d), 74.87 (s), 173.77 (s), 175.40 (s); MS *m/z* (rel intensity) 434 ($M^+ - H_2O$, 1), 419 (2), 403 (6), 389 (5), 378 (6), 360 (3), 347 (4), 336 (31), 304 (23), 293 (100); HRMS calcd for $C_{27}H_{46}O_4$ 434.3394, found 434.3428.

Degradative Oxidation of Peroxy Lactone 12. Peroxy lactone **12** (15 mg, 0.03 mmol) in CCl_4–CH_3CN–H_2O (1:1:1.5, 3 mL) was treated with $NaIO_4$ (35 mg, 0.16 mmol) and a catalytic amount of $RuCl_3 x H_2O$ (2 mg). After stirring at rt for 5 h, the reaction mixture was poured into water (10 mL) and extracted with EtOAc (3 × 5 mL). After drying and evaporating as usual, the residue was dissolved in ether (1 mL) and treated at 0 °C with etheral CH_2N_2. After 5 min, the solution was evaporated and purified by chromatography. The resulting product (10 mg, 66%) was identified as methyl ester **9**.

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Supporting Information Available: Copies of ^1H NMR and ^{13}C NMR spectra of compounds **3-22** (43 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.

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