Photoinduced Molecular Transformations. Part 136.[1] Reactions of Alkoxyl Radicals generated from Hypoiodites of 3β-Hydroxy-7-oxo-Δ⁵-Steroids. Synthesis of Some Functionalized Oxasteroids

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The synthesis of several unsaturated 3-oxasteroids and 4a-homo-4-oxasteroids of cholestane series functionalized at their B-ring is described; 3β-hydroxycholest-5-en-7-one and its 4,4-dimethyl derivative were transformed into 3-oxacholest-5-en-7-one and its 4,4-dimethyl derivative in two or three steps involving a regioselective β-scission of the corresponding alkoxyl radicals (generated by irradiating their hypoiodites in benzene) as the key step. The formation of 2-iodo-7-oxo-4-nor-2,3-secocholest-5-en-3-yl formate by irradiation of the hypoiodite of 3β-hydroxycholest-5-en-7-one was accompanied by the formation of a product arising from a new ring contraction of the A-ring. The ring-contraction mechanism is discussed.

The replacement of one or more carbon atoms of a steroid molecule brings about significant modifications to its biological activity. A number of investigations have therefore been carried out on both the total and partial syntheses of heterosteroids and their biological activities.[2,3]

In previous papers of this series we have reported on the partial[3–8] and total[9] syntheses of various mono- and di-heterosteroids. The partial synthesis involved a carbonyl group of saturated steroidal ketones, or a hydroxymethylene group of saturated steroidal alcohols of cholestane, as well as an androstane series by use of heteroatoms (N, O, S, Se and Te). The key step in these transformations was a β-scission of the alkoxyl radicals generated from steroidal alcohols or lactols derived from cyclic ketones *via* irradiation of their hypoiodites [prepared *in situ* with mercury(II) oxide and iodine] to give the corresponding secosteroidal iodoformates, from which the heterosteroids were derived.

In this paper we report on the synthesis of some *unsaturated* 3-oxasteroids and 4a-homo-4-oxasteroids of the cholestane series functionalized at their B-ring. This work was carried out as a re-investigation and extension of early work in this series undertaken by one of us.[10]

Results

Synthesis of 3-*Oxacholest*-5-*en*-7-*one* **9** *and its* 4,4-*Dimethyl Derivative* **10**.—One of us reported that the irradiation of the hypoiodite of 3β-hydroxycholest-5-en-7-one **1**, prepared *in situ* with mercury(II) oxide and iodine, gave 2-iodo-7-oxo-4-nor-2,3-secocholest-5-en-3-yl formate **4**, together with 5ζ-iodomethyl-4-norcholestane-3,7-dione and cholesta-3,5-dien-7-one.[10] Repetition of this reaction to obtain secosteroid **4** as a precursor for the synthesis of 3-oxacholest-5-en-7-one **9** gave crystalline secosteroid **4** (40%) in better yield than that previously reported,[10] along with accompanying formation of a new crystalline product **3** in 8% yield. No 5ζ-iodomethyl-4-norcholestane-3,7-dione or cholesta-3,5-dien-7-one obtained in the previous experiment[10] was found in the product mixture. Although the reason for this is obscure, the previously reported products might be secondary products formed during chromatographic separation.

Crystalline product **3** contained iodine. Combustion analysis and mass spectrometry indicated that it had the molecular formula of $C_{27}H_{42}I_2O_2$. The IR spectrum showed two bands at 1710 and 1743 cm^{-1} that are assignable to the carbonyl groups of fused cyclohexane and cyclopentane rings. The ^1H NMR spectrum exhibited two singlets (each 3 H) at δ 0.69 and 1.40 that are assignable to 18-H_3 and 19-H_3. It also exhibited a double doublet at δ 3.37 with *J* 12.5 and 11.0 Hz, an AB quartet at δ 3.64 and 3.75 with *J* 10.7 Hz, and a 1 H singlet at δ 4.83. These signals are assignable to 8β-H, a CH_2I group attached to a tertiary carbon and a CHI group flanked by a carbonyl group, based on their chemical shifts and coupling constants. A nuclear Overhauser enhancement (NOE) measurement indicated that irradiation of the 19-H_3 signal resulted in enhancement of the double doublet at δ 3.37 and the AB quartet, but no enhancement of the singlet at δ 4.83.

These IR and NMR results can be safely accommodated by the structure, 6β-iodo-5-iodomethyl-4-nor-5β-cholestane-3,7-dione for compound **3**.

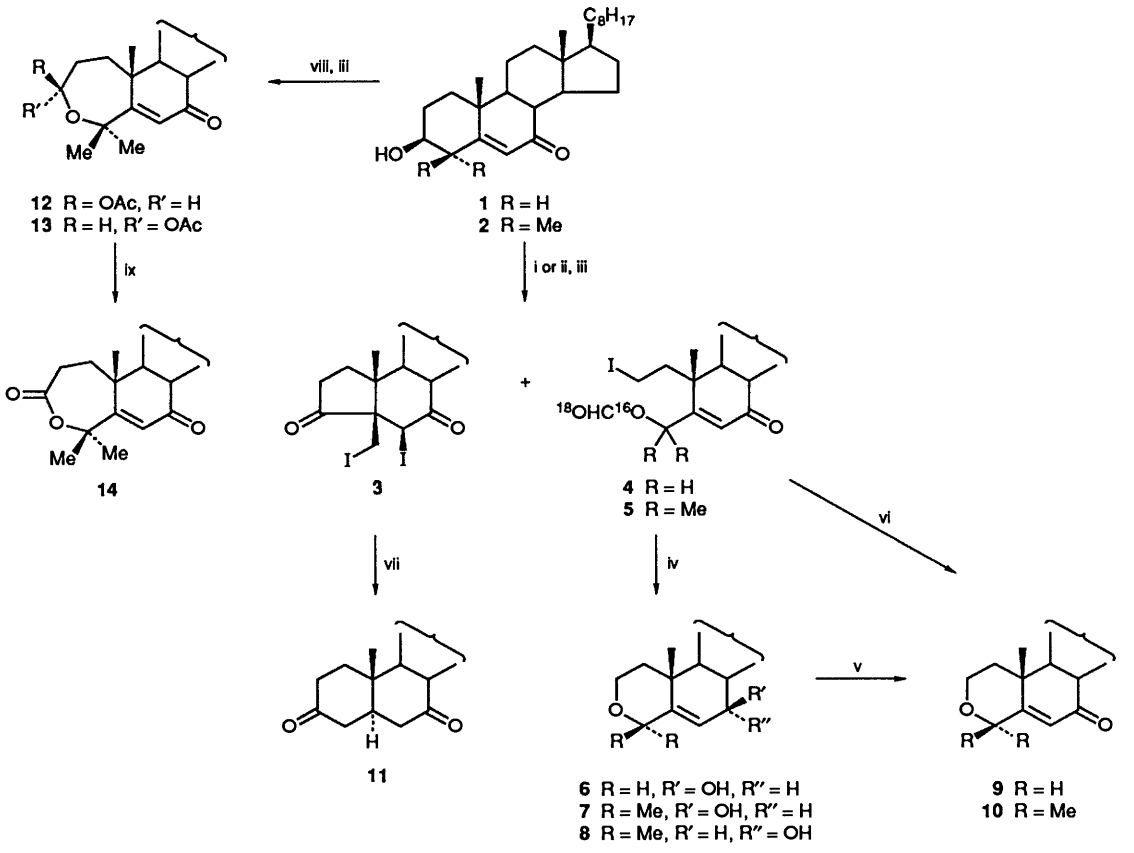
This structure was further confirmed by the following reaction: a reduction of product **3** with tributyltin hydride in the presence of azoisobutyronitrile (AIBN) in benzene under irradiation gave 5α-cholestane-3,7-dione **11**[11] in 73% yield (Scheme 1). The pathway for the formation of dione **11** clearly involves an intramolecular addition of a carbon-centred radical **A** generated from diiodide **3**, which gives rise to an alkoxyl radical **B**, followed by selective β-scission of the resulting cyclopropane ring to a cyclohexyl radical **C**,[12] and a final hydrogen abstraction to afford product **11**, as outlined in Scheme 2.

Treatment of iodo formate **4** with sodium borohydride[3–5] in ethanol under reflux afforded 3-oxacholest-5-en-7β-ol **6** as a single product in 70% yield.

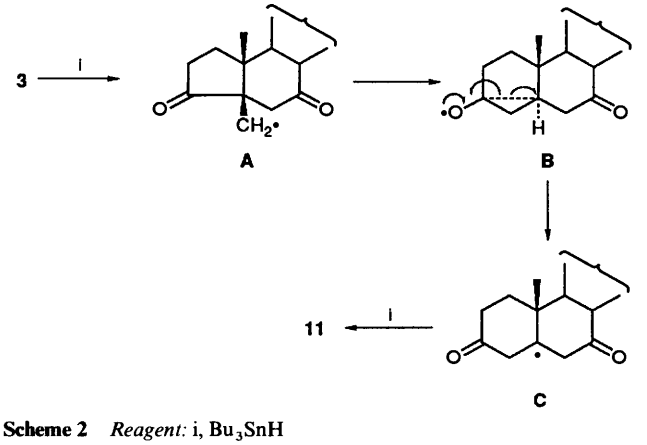
A similar cyclization of 4,4-dimethyl-4-hydroxy-2-iodo-3-nor-2,4-secocholest-5-ene formate **5** with sodium borohydride gave a 1:4 mixture of 4,4-dimethyl-3-oxacholest-5-en-7α-ol and -7β-ol **7** and **8** in 58% combined yield. The epimeric ratio was determined by means of ^1H NMR spectroscopy.

The preparation of 2-iodo-3,3-dimethyl-7-oxo-4-nor-2,3-secocholest-5-en-3-yl formate **5** was also carried out with a labelled mercury(II) oxide (47% $Hg^{18}O$) and iodine. The EI mass spectrum of iodo formate **5** exhibited a molecular ion at *m/z* 572 (15.1%), thereby indicating the incorporation of an ^{18}O atom into the molecule. The iodo formate **5** was then transformed into 3-oxasteroid **6** on treatment with sodium borohydride. Mass spectrometric analysis of 3-oxasteroid **6** indicated that no heavy oxygen was incorporated in the molecule.

These experiments once again confirmed our previously reported results:[4] a heavy oxygen of $Hg^{18}O$ is incorporated in the formyl oxygen of iodo secosteroid **5**.



Scheme 1 *Reagents and conditions:* i, $HgO–I_2$–benzene; ii, $Hg^{18}O–I_2$–benzene; iii, *hv*; iv, $NaBH_4$–EtOH, reflux; v, PCC–CH_2Cl_2; vi, aq. NaOH; vii, Bu_3SnH–AIBN–*hv*–benzene; viii, $Pb(OAc)_4–I_2$–benzene; ix, PCC–CH_2Cl_2



Scheme 2 *Reagent:* i, Bu_3SnH

Oxidation of either 7β-hydroxy-3-oxasteroid **6** or a mixture of 7α- and 7β-hydroxy steroids with pyridinium chlorochromate (PCC) in dichloromethane at room temperature gave 3-oxacholest-5-en-7-one **9** (90%) or 4,4-dimethyl-3-oxacholest-5-en-7-one **10** (83%).

Direct cyclization of iodo formates **4** or **5** to oxasteroids **9** or **10** was also achieved by treatment of iodo formate **4** or **5** with a 2 mol dm^{-3} solution of sodium hydroxide in tetrahydrofuran (THF) at room temperature in 82 and 88% yield.

Synthesis of 4a,4a-*Dimethyl*-4a-*homo*-4-*oxacholest*-5-*ene*-3,7-*dione* **14**.—In a previous paper[13] we reported that β-scission of the hypoiodites of steroidal cyclic homoallyl alcohols, generated *in situ* with *lead tetraacetate and iodine* in benzene, resulted in unprecedented formation of the corresponding lactol acetates in good yield. These products differed considerably from those of the above mentioned β-scission using mercury(II) oxide and iodine as the reagents for generating the hypoiodites. They also differed from those in the oxidation of the steroidal homoallyl alcohols with lead tetraacetate alone.

Since the reaction can be useful in syntheses, we carried out the β-scission of 3β-ols **1** and **2** by using a lead tetraacetate–iodine reagent. Irradiation of the hypoiodite of 3β-ol **2**, prepared *in situ* with lead tetraacetate and iodine (each 3 mol equiv.) in benzene, thus gave a 1.5:1 mixture of 3α- and 3β-acetoxy-4a,4a-dimethyl-4a-homo-4-oxacholest-5-en-7-one **12** and **13** as virtually exclusive products in 95% yield. The structures and the ratio of the two epimers were determined by spectral analyses. A similar reaction with 3β-ol **1**, however, resulted in an intractable mixture, presumably due to further oxidation of the allylic methylene group with lead tetraacetate during the reaction.

Oxidation of the lactol acetates **12** and **13** with PCC in dichloromethane at room temperature[13] gave the corresponding lactone **14**, functionalized in ring B, in 55% yield.

Discussion

The foregoing experiments showed that *unsaturated* oxasteroids can be prepared from unsaturated hydroxysteroids by a process involving regioselective β-scission of the corresponding alkoxyl radicals, which we previously reported.[3–5] These functionalised oxasteroids can be useful with regard to their further transformations into potentially biologically active compounds.

The formation of secosteroid **4** is accompanied by the formation of a 4-norsteroid **3** arising from a new ring contraction of ring A of the steroid in the photoreaction of the hypoiodite of 3β-hydroxycholest-5-en-7-one **1**, while secosteroid **5** is formed with no accompanying formation of the corresponding 4-norsteroid in the photoreaction of the hypoiodite of the 4,4-dimethyl derivative **2**.

On the other hand, an insertion of oxygen between C-3 and C-4 of the steroidal skeleton, giving 4a-homo-4-oxasteroids **12** and **13**, is an exclusive reaction when the hypoiodite is generated with a lead tetraacetate–iodine reagent.

All of the pathways which reasonably explain the formation of these varied products are outlined in Scheme 3. All of products **3**, **4**, **5**, **12** and **13** are formed from an allyl radical intermediate **F** derived from β-scission of alkoxyl radical **E**, itself derived from the putative hypoiodite **D**. Allyl radical **F** generated from 3β-ol **1** traps iodine at the less hindered C-4 end to give an iodo secosteroid **G**, from which a radical species (perhaps an alkoxyl radical) abstracts the formyl hydrogen to give an acyl radicals **H**. Intramolecular radical cyclization of species **H** affords a five-membered ketone **3** *via* radical intermediate **I**. Since, however, iodo secosteroids of type **G** have never been isolated in the photoreaction of the hypoiodites of 3β-hydroxy-Δ^5-steroids under the same conditions as those reported in the present study,[14] the possible formation of diiodide **3** *via* intermediates **G′**, **H′** and **I′** should not be excluded.

There are some intermolecular versions of the photoinduced radical additions of aldehydes to cyclohexenones or α,β-unsaturated carboxylic acids esters.[15] For example, Cerfontain and Noort[15b] reported that 4-oxoalkanoic acid esters are formed by the benzophenone-initiated photochemical addition of aldehydes to α,β-unsaturated carboxylic acid esters.

The pathway leading to the formation of secosteroids **4** and **5** has already been studied by us.[4] The pathway, which involves successive intermediates **J**, **K**, **L**, **M** and **N**, has been established on the basis of our ^{18}O-labelling experiment. The present work was carried out on 3β-ol **2**, and again indicated that ^{18}O of the reagent $I_2{}^{18}O$ is incorporated into the formyl oxygen of secosteroid **5**, thus confirming the pathway outlined in Scheme 3.

No 4-norsteroid corresponding to 4-norsteroid **3** is formed in the photoreaction of the hypoiodite of 4,4-dimethyl steroid **2**. The preference for intramolecular cyclization of the C-4 terminus of allyl radical **F** with the carbonyl oxygen to give intermediate **L** over intermolecular combination of the C-4 terminus with an iodine atom in the 4,4-dimethyl derivative **2** is presumably due to hindrance due to the two methyl groups.[16]

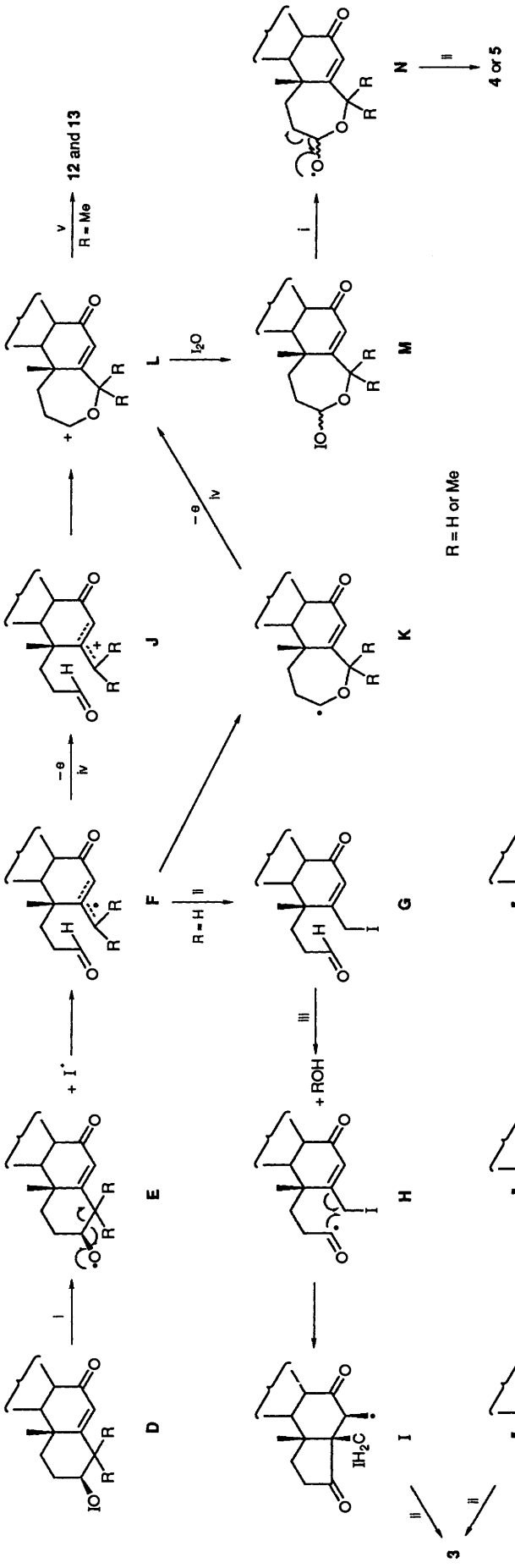
Products **12** and **13** in the photoreaction of the hypoiodite of 3β-ol **2** with a lead tetraacetate–iodine reagent are formed

its 4,4-dimethylation with iodomethane–potassium *tert*-butoxide, followed by allylic oxidation with *tert*-butyl chromate) in ethanol (40 cm^3) was reduced with sodium borohydride (94 mg, 1.5 mol equiv.) at 0 °C to give a crude 3β-ol **2** (703 mg). The product was purified by PLC [(2:1) hexane–ethyl acetate] to give a pure 3β-ol **2** (602 mg, 86%), m.p. 144–146 °C (from hexane) [lit.,[17] 153 °C (from MeOH)]; ν_{max}/cm^{-1} 3390 (OH) and 1661 and 1608 (C=CC=O); δ(90 MHz) 0.69 (3 H, s, 18-H_3), 1.14 (3 H, s, 19-H_3), 1.23 and 1.25 (each 3 H, each s, 4,4-dimethyl), 3.2–3.5 (1 H, m, 3-H) and 5.94 (1 H, s, 6-H).

Photoreaction of the Hypoiodite of 7-Oxocholesterol **1** *in Benzene containing an Excess of Mercury*(II) *Oxide and Iodine.*—A solution of 7-oxocholest-5-en-3β-ol **1** (1.00 g, 2.5 mmol) in benzene (150 cm^3) containing red mercury(II) oxide (1.62 g, 7.5 mmol) and iodine (1.91 g, 7.5 mmol) in a Pyrex vessel was irradiated with a 100 W mercury arc for 8.5 h. The solution was then filtered through Celite; the filtrate was washed successively with a 5% aq. sodium thiosulfate, water and brine, and was then dried over anhydrous sodium sulfate. Evaporation of the solvent gave an oily mixture of products, which was subjected to column chromatography. Elution with benzene gave two fractions. Elution was continued with chloroform to a third fraction (40 mg), and finally with diethyl ether to give a fourth (391 mg) fraction. The first fraction (203 mg) was subjected to PLC [(4:1) hexane–ethyl acetate] to give *diiodo diketone* **3** (131 mg, 8%), m.p. 164–165 °C (from MeOH) (Found: C, 49.6; H, 6.5; I, 38.8. $C_{27}H_{42}I_2O_2$ requires C, 49.69; H, 6.44; I, 38.95%); ν_{max}/cm^{-1} 1743 (5-membered ring C=O) and 1710 (6-membered ring C=O); δ(400 MHz) 0.69 (3 H, s, 18-H_3), 1.40 (3 H, s, 19-H_3) and 3.37 (1 H, dd, *J* 12.5 and 11.0, 8β-H), 3.64 and 3.75 (each 1 H, each d, *J* 10.7, CH_2I) and 4.83 (1 H, s, 6α-H); *m/z* 525 [$(M - I)^+$, 22.7%] and 398 [$(M - 2I)^+$, 100].

The second fraction (543 mg) was iodo formate **4** (40%), m.p. 99–100 °C (lit.,[10] 99–100 °C); ν_{max}/cm^{-1} 1735 (CHO), 1675 and 1637 (C=CC=O), and 1159 (C–O); δ(90 MHz) 0.68 (3 H, s, 18-H_3), 1.21 (3 H, s, 19-H_3), 2.7–3.2 (2 H, m, 2-H_2), 4.80 (2 H, s, CH_2O), 6.02 (1 H, s, 6-H) and 8.14 (1 H, s, OCHO); *m/z* 542 (M^+, 9.9%), 527 [(M − Me) 3.8], 497 [(M − OCHO), 2.7], 415 [$(M - I)^+$, 48] and 341 (100).

The third and fourth fractions comprised intractable mixtures



Scheme 3 *Reagents and conditions:* i, *hν*; ii, I_2; iii, $RO^{\cdot}$; iv, Hg^{2+}; v, AcOH

in THF (15 cm^3) was added sodium borohydride (170 mg). The solution was heated under reflux for 2.5 h. After evaporation of the solvent, the product was dissolved in diethyl ether and the solution was washed successively with water and brine, and dried over anhydrous sodium sulfate. Evaporation of the solvent gave crude oxasteroid **6** (164 mg), which was subjected to PLC [(1:1) hexane–ethyl acetate] to give pure 3-*oxasteroid* **6** (101 mg, 70%), m.p. 137.5–139.0 °C (from hexane) (Found: M^+, 388.3322. $C_{26}H_{44}O_2$ requires *M*, 388.3341); ν_{max}/cm^{-1} 3370 (OH), 1071 and 1092 (C–O); δ(400 MHz) 0.71 (3 H, s, 18-H_3), 1.16 (3 H, s, 19-H_3), 3.7–4.2 (5 H, m, 2- and 4-H_2 and 7α-H) and 5.38 (1 H, d, *J* 1.5, 6-H); *m/z* 388 (M^+, 41%), 373 [$(M - Me)^+$, 53), 355 [$(M - Me - H_2O)^+$, 14] and 110 (100).

Preparation of 3-*Oxacholest-5-en-7-one* **9** *by Oxidation of* 3-*Oxacholest-5-en-7β-ol* **6** *with PCC.*—To a solution of hydroxy oxasteroid **6** (30 mg) in dichloromethane (5 cm^3) were added Celite (20 mg) and PCC (20 mg) and the solution was stirred for 3 h at room temperature. Removal of the solvent gave a product, which was dissolved in diethyl ether. The solution was worked up in the usual manner to give a crude oily oxasteroid (31 mg). Purification of this by PLC [(3:7) hexane–ethyl acetate] gave 3-*oxacholest-5-en-7-one* **9** (27 mg, 90%), m.p. 105–106.5 °C (from MeOH) (Found: C, 80.8; H, 11.0. $C_{26}H_{42}O_2$ requires C, 80.83; H, 10.88%); ν_{max}/cm^{-1} 1668 (C=CC=O) and 1106 (C–O); δ(400 MHz) 0.69 (3 H, s, 18-H_3), 1.29 (3 H, s, 19-H_3), 3.7–3.9 (1 H, m, 2β-H), 3.9–4.0 (1 H, m, 2α-H), 4.08 (1 H, d, *J* 14.2, 4β-H), 4.26 (1 H, dd, *J* 4.1 and 1.5, 4α-H) and 5.67 (1 H, s, 6-H); *m/z* 386 (M^+, 100%), 371 [$(M - Me)^+$, 12], 355 (21), 273 (33) and 178 (100).

Preparation of 3-*Oxacholest-5-en-7-one* **9** *from* 2-*Iodo-7-oxo-4-nor-2,3-secocholest-5-en-3-yl Formate* **4** *with Sodium Hydroxide.*—To a solution of secosteroid **4** (535 mg) in THF (15 cm^3) was added 2 mol dm^{-3} sodium hydroxide (1.7 cm^3). This solution was stirred for 3 h at room temperature. Removal of the solvent gave a product, which was dissolved in diethyl ether. The solution was worked up in the usual manner to give crude oxasteroid **9**, which was then recrystallized from methanol to give pure oxasteroid **9** (311 mg, 82%), identical with the specimen obtained by the oxidation of 7β-ol **6**.

Preparation of 4,4-*Dimethyl*-3-*oxacholest-5-en-7α- and -7β-ol* **7** *and* **8** *from* 2-*Iodo*-3,3-*dimethyl*-7-*oxo*-4-*nor*-2,3-*secocholest-5-en*-3-*yl Formate* **5** *with Sodium Borohydride.*—To a solution of iodo formate **5** (450 mg, 0.79 mmol) in THF (45 cm^3) was added sodium borohydride (450 mg). The solution was heated under reflux for 1 h under nitrogen. Removal of the solvent produced a residue, which was worked up to give a product (401 mg), as in the case of the preparation of oxasteroid **6**. This crude product was subjected to PLC [(2:1) hexane–ethyl acetate] to give a *mixture of* 7a- and 7β-*ol* **7** and **8** (190 mg, 58%) as a glass (Found: M^+, 416.3664. $C_{28}H_{48}O_2$ requires *M*, 416.3653); ν_{max}(neat)/cm^{-1} 3368 (OH) and 1095 (C–O); δ(400 MHz) 0.69 (3 H, s, 18-H_3 of **8**), 0.70 (3 H, s, 18-H_3 of **7**), 1.26 (3 H, s, 19-H_3 of **7**), 1.37 (3 H, s, 19-H_3 of **8**), 1.35 and 1.39 (each 3 H, each s, 4,4-dimethyl of **7** and **8**), 3.7–3.8 (1 H, m, 7-H of **7** and **8**), 3.8–4.0 (2 H, m, 2-H_2 of **7** and **8**), 5.62 (1 H, d, *J* 2.9, 6-H of **7**) and 5.89 (1 H, d, *J* 4.9, 6-H of **8**); *m/z* 416 (M^+, 0.6%), 401 [$(M - Me)^+$, 45], 383 [$(M - Me - H_2O)^+$, 12], 330 (71) and 43 (100).

Preparation of 4,4-*Dimethyl*-3-*oxacholest-5-en-7-one* **10** *by Oxidation of a Mixture of* 7α- *and* 7β-*Hydroxy*-3-*oxacholest-5-enes* **7** *and* **8** *with PCC.*—A mixture of hydroxy oxasteroids **7** and **8** (190 mg), Celite (350 mg), and PCC (378 mg) in dichloromethane (10 cm^3) was stirred for 40 min at room temperature. The solution was then worked up in a way similar to the case of the oxidation of hydroxy oxasteroid **6**, to give crystalline oxasteroid **10** (187 mg). Recrystallization from methanol gave pure *oxasteroid* **10** (156 mg, 83%), m.p. 117.0–118.0 °C (Found: C, 81.0; H, 11.0. $C_{28}H_{46}O_2$ requires C, 81.16; H, 11.11%); ν_{max}/cm^{-1} 1666 and 1626 (C=CC=O) and 1088 and 1060 (C–C); δ(400 MHz) 0.70 (3 H, s, 18-H_3), 1.38, 1.39 and 1.41 (each 3 H, each s, 19-H_3 and 4,4-dimethyl), 3.84–3.90 (1 H, m, 2-H) and 5.73 (1 H, s, 6-H); *m/z* 414 (M^+, 22%) and 399 [$(M - Me)^+$, 100].

^{18}O-*Labelling Study of the Photoreaction of the Hypoiodite of* 3β-*Hydroxy*-4,4-*dimethylcholest-5-en-7-one* **2**.—A mixture of 3β-hydroxy-4,4-dimethylcholest-5-en-7-one **2** (502 mg) in benzene (72 cm^3) containing freshly prepared yellow $Hg^{18}O$ ($Hg^{18}O$ 48%; 810 mg, 3 mol equiv.) and iodine (955 mg, 3 mol equiv.) was irradiated under the same conditions as those in the above mentioned reaction with HgO. Work-up, as in the case of the photoreaction with HgO–I_2, gave 2-iodo-3,3-dimethyl-7-oxo-4-nor-2,3-secocholest-5-en-3-ylformate **5** (314 mg, 47%). The EI mass spectrum of iodo formate **5** exhibited a molecular ion at *m/z* 572 (15.1%) and peaks at *m/z* 570 (28.6) and 330 (100).

Iodo formate **5** (314 mg) was then subjected to treatment with sodium borohydride by the same procedure as mentioned above to give 4,4-dimethyl-3-oxacholest-5-en-7β-ol **6** (122 mg, 57%). The EI mass spectrum exhibited a molecular ion at *m/z* 416 (0.93%) and peaks at *m/z* 401 (85.3) and 330 (100).

Preparation of 4,4-*Dimethyl*-3-*oxacholest-5-en-7-one* **10** *from* 2-*Iodo*-3,3-*dimethyl*-7-*oxo*-4-*nor*-2,3-*secocholest-5-en*-3-*yl Formate* **5** *with Sodium Hydroxide.*—A solution of secosteroid **5** (22 mg) in THF (1 cm^3) containing 2 mol dm^{-3} sodium hydroxide (1 cm^3) was stirred for 5 h at room temperature. The solution was then worked up as in the case of oxasteroid **7** to give crude oxasteroid **10** (17 mg). Recrystallization from methanol gave pure oxasteroid **10** (14 mg, 88%), identical with the sample obtained by the oxidation of 7-ols **7** and **8**.

Reduction of Diiodo Ketone **3** *with Tributyltin Hydride.*—To a solution of diiodo ketone **3** (38 mg, 0.058 mmol) in benzene (3 cm^3) placed in a Pyrex tube were added tributyltin hydride (0.034 cm^3, 0.101 mmol) and AIBN (4 mg). The solution was flushed with nitrogen and was then irradiated with a 100 W high-pressure mercury arc for 30 min. The solvent was evaporated off to give a product, which was dissolved in diethyl ether. To the solution was added potassium fluoride (10 mg) and the mixture was stirred for 20 h. The solution was then filtered through Celite. The filtrate was washed successively with water, brine, and water, and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a product (63 mg), which was subjected to PLC [(3:1) hexane–ethyl acetate] to give crystals of diketone **11** (17 mg, 73%), m.p. 188–190 °C (from MeOH) (lit.,[11] 190 °C); ν_{max}/cm^{-1} 1705 (C=O); δ(400 MHz) 0.68 (3 H, s, 18-H_3) and 1.28 (3 H, s, 19-H_3); *m/z* 400 (M^+, 100%), 382 [$(M - H_2O)^+$, 30], 296 (46), 246 (78) and 192 (84).

Preparation of 3α- *and* 3β-*Acetoxy*-4a,4a-*dimethyl*-4a-*homo*-4-*oxacholest-5-en-7-one* **12** *and* **13** *from* 3-*Hydroxy*-4,4-*dimethylcholest-5-en-7-one* **2** *by the Insertion of Oxygen with Lead Tetraacetate–Iodine under Irradiation.*—To a solution of 3β-hydroxy-4,4-dimethylcholest-5-en-7-one **2** (100 mg, 0.23 mmol) in benzene (15 cm^3) were added lead tetraacetate (340 mg, 0.69 mmol) and iodine (175 mg, 0.69 mmol). The solution was flushed with nitrogen and was then irradiated for 1 h while being stirred. The filtered solution was washed successively with 5% aq. sodium thiosulfate, 5% aq. sodium hydrogen carbonate, water, and brine, and was then dried over anhydrous sodium sulfate. Evaporation of the solvent gave a purple-coloured oily mixture, which was subjected to PLC [(3:1) hexane–ethyl acetate] to give three fractions (A, B and C) in order of their

mobility on the TLC plate. Fractions A (9 mg) and C (10 mg) were intractable mixtures. Fraction B (108 mg, 95%) was a 1.5:1 *mixture of* 3α- *and* 3β-*acetoxy*-4a,4a-*dimethyl*-4a-*homo*-4-*oxacholest*-5-*en*-7-*one* **12** and **13** (Found: M^+, 486.3685. $C_{31}H_{50}O_4$ requires *M*, 486.3709); ν_{max}(neat)/cm^{-1} 1737 (OAc), 1667 and 1610 (C=CC=O) and 1025 (C–O); δ(400 MHz) 0.70 (3 H, s, 18-H_3), 2.06 and 2.08 (each 3 H, each s, OAc of 3α- and 3β-epimer), 5.77 and 5.88 (each 1 H, each s, 6-H of 3α- and 3β-epimer) and 5.88 and 6.04 (each 1 H, each dd, *J* 2.4 and 4.4, 3-H of 3α- and 3β-epimer); *m*/*z* 486 (M^+, 13.83%), 426 [$(M - AcOH)^+$, 43.34], 386 (58.5), 370 (52.4) and 43 (100).

4a,4a-*Dimethyl*-4a-*homo*-4-*oxacholest*-5-*ene*-3,7-*dione* **14** *by Oxidation of Lactol Acetates* **12** *and* **13** *with PCC*.—To a solution of the lactol acetates (52 mg, 0.11 mmol) in dichloromethane was added PCC (100 mg). The solution was stirred for 48 h at room temperature, and was then filtered through Celite, and the filtrate was evaporated to give a residue, which was dissolved in diethyl ether. The solution was then worked up in usual manner to give an oily product, which was subjected to PLC [(3:1) hexane–ethyl acetate], giving *lactone* **14** (26 mg, 55%), m.p. 167.5–169.0 °C (from MeOH) (Found: C, 78.5; H, 10.3 $C_{29}H_{46}O_3$ requires C, 78.68; H, 10.39%); ν_{max}/cm^{-1} 1733 (lactone C=O), 1669 and 1608 (C=CC=O) and 1116 (C–O); δ(270 MHz; JEOL J-FX270) 0.70 (3 H, s, 18-H_3), 1.43, 1.64 and 1.76 (each 3 H, each s, 4,4-dimethyl and 19-H_3) and 5.92 (1 H, s, 6-H); *m*/*z* 442 (M^+, 100%), 427 [$(M - Me)^+$, 4.9], 383 (13.7) and 369 (30.7).

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