Photoinduced Molecular Transformations. Part 106.[1] Intramolecular Addition *vs* β-Scission of Oxyl Radicals Generated from *A*-Homo-5α-cholest-1-en-4α- and -4β-ol Hypoiodites and 4-Methyl-*A*-homo-5α-cholest-1-en-4α- and -4β-ol Hypoiodites

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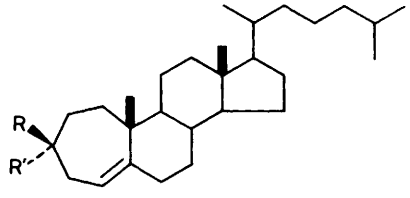
Photoinduced reaction of *A*-homo-5α-cholest-1-en-4α-ol hypoiodite or the corresponding 4β-methyl derivative resulted in the formation of the two formates or the two corresponding acetates which arose from successive reactions of the radical intermediates generated from β-scission of the corresponding alkoxyl radicals. The photoinduced reactions of the hypoiodites of the isomeric 4β-ol or its 4α-methyl derivative, on the other hand, respectively gave 1β,4β-epoxy-2α-iodo-*A*-homo-5α-cholestane or its 4α-methyl derivative produced by intramolecular radical addition of the 4β-alkoxyl radicals with accompanying formation of the two formates or the corresponding acetates identical with those obtained from the 4α-series. Thus, unlike the corresponding reactions of *A*-homocholest-4a-en-3-ols and *B*-homocholest-5-en-7a-ols, the β-scission is a predominant process over the intramolecular radical addition in the alkoxyl radicals derived from *A*-homocholest-1-en-4α-ols. The paths which led to all the products are discussed on the basis of an ^{18}O labelling experiment carried out for the formation of 2α-iodomethyl-*A*-nor-5α-cholestan-1α-ol formate from *A*-homo-5α-cholest-1-en-4α-ol.

In previous papers,[2,3] we reported the photoinduced reactions of the hypoiodites of several steroidal seven-membered cyclic homoallyl alcohols such as *A*-homocholest-4a-en-3-ols (**1**)–(**4**) and *B*-homocholest-5-en-7a-ols (**9**) and (**10**), in the presence of mercury(II) oxide and iodine (Schemes 1 and 2). We found that



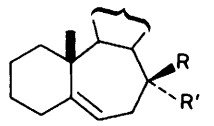
(**1**) R = OH, R' = H
(**2**) R = OH, R' = Me
(**3**) R = H, R' = OH
(**4**) R = Me, R = OH

(**5**) R = H
(**7**) R = Me

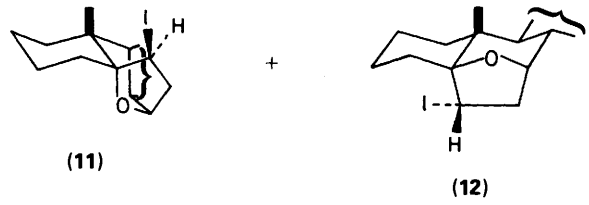
(**6**) R = H
(**8**) R = Me

Scheme 1. *Reagents and conditions:* i, $HgO–I_2$, benzene; ii, *hν*.

intramolecular radical addition of the alkoxyl radicals to the double bond to form oxabicyclic compounds (**5**)–(**8**), (**11**), and (**12**) takes place in the alkoxyl radicals generated from these



(**9**) R = OH, R' = H
(**10**) R = H, R' = OH



(**11**)

(**12**)

Scheme 2. *Reagents and conditions:* i, $HgO–I_2$, benzene; ii, *hν*.

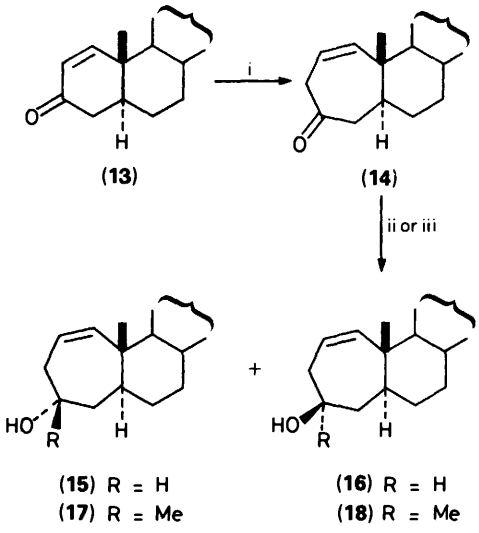
homoallyl alcohols in preference to β-scission which leads to secosteroids. The exclusive intramolecular radical addition of homoallylic alkoxyl radicals was also observed in those generated from simple six-membered alcohols, *viz.* cyclohex-3-enols.[4] This intramolecular addition found with homoallylic alkoxyl radicals, which are considered to be susceptible to β-scission, is potentially useful in synthesis.

In view of the few experimental results accumulated for the behaviour of alkoxyl radicals with regard to intramolecular addition *versus* β-scission when compared with studies on intramolecular hydrogen abstraction *versus* β-scission,[5–7] a further study seemed worthwhile in order to widen our knowledge of the behaviour of the alkoxyl radicals with regard to the addition *versus* cleavage. The steroidal homoallylic

system may be an appropriate substrate for this study. We have therefore investigated the photoinduced reactions of the hypoiodites of *A*-homo-5α-cholest-1-en-4-ols (**15**)–(**18**) in the presence of mercury(II) oxide and iodine. The results are reported in this paper.

Results

Preparation of A-*Homo-5α-cholest-1-en-4-ols* (*Scheme* 3).—Four seven-membered cyclic homoallyl alcohols (**15**)–(**18**)



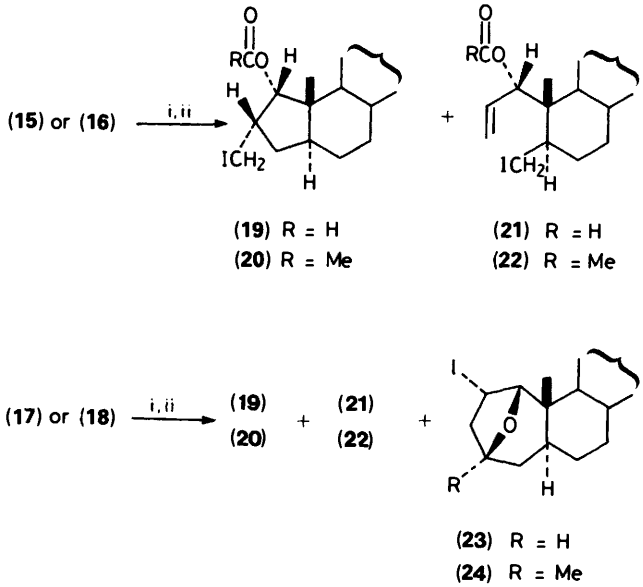
Scheme 3. *Reagents and conditions:* i, $AlCl_3$–(1:1) Et_2O–benzene, CH_2N_2; ii, $LiAlH_4$, Et_2O; iii, MeLi, Et_2O.

chosen for the present study were prepared from *A*-homo-5α-cholest-1-en-4-one (**14**). The β,γ-unsaturated ketone (**14**) has been synthesized by Meakins and Morris[8] from 5α-cholestan-3-one through ring expansion to *A*-homo-5α-cholestan-4-one followed by bromination, dehydrobromination, and a base- or acid-catalysed isomerization to the β,γ-isomer (**14**) (9% overall yield). We prepared this ketone (**14**) through a ring expansion of cholest-1-en-3-one (**13**) with diazomethane in the presence of a Lewis acid.[9] We found that the original procedure used by Johnson *et al.* (dichloromethane–BF_3)[9] gave only a 12% yield of the desired 7-membered ketone (**14**) with the accompanying formation of several products including an 8-membered cyclic ketone and a 7-membered α,β-unsaturated ketone. After several experiments under a variety of conditions, we found that the procedure for the ring expansion used by Müller *et al.* [(1:1) benzene–diethyl ether, $AlCl_3$][10] gave the best yield of the desired ketone (**14**) (35%).

Reduction of cyclic ketone (**14**) with lithium aluminium hydride in diethyl ether at room temperature gave *A*-homo-5α-cholest-1-en-4α-ol (**15**) and its 4β-epimer (**16**) in 29 and 39% yields, respectively. The two isomeric alcohols (**15**) and (**16**) were readily separated by preparative TLC (PLC). The configurations of the 4-hydroxy groups were deduced by means of ^1H NMR spectroscopy. Molecular models of the two alcohols (**15**) and (**16**) indicated that the 4β-hydrogen of the 4α-ol (**15**) and 4α-hydrogen of the 4β-ol (**16**) would occupy a *pseudo*-equatorial and a *pseudo*-axial position, respectively. The signal of the 4-hydrogens of alcohols (**15**) and (**16**), respectively, appeared as multiplets at δ 3.98 ($w_{\frac{1}{2}}$ 14 Hz) and at δ 3.62 ($w_{\frac{1}{2}}$ 21 Hz). These chemical shifts and the half bandwidths of the two isomeric alcohols allowed us to assign the 4α-configuration to the hydroxyl groups of the alcohol (**15**) and the 4β-configuration to the hydroxyl groups of the alcohol (**16**).

The reaction of the β,γ-unsaturated ketone (**14**) with methyllithium in diethyl ether in an atmosphere of nitrogen gave two 4-methyl alcohols (**17**) and (**18**) in 15 and 40% yield. The two isomers were separated readily by means of PLC. Predominant alcohol (**18**) was assigned to be the 4β-ol since the nucleophile may approach predominantly from the α-face of the *A*-homoketone (**14**).

Products of Irradiation of A-*Homo-5α-cholest-1-en-4-ols* (**15**) *and* (**16**) *in the Presence of Mercury*(II) *Oxide and Iodine* (*Schemes* 4 *and* 5).—Irradiation of the 4α-ol (**15**) in benzene containing mercury(II) oxide and iodine (each 3 mol equiv.) with a 100-W high-pressure mercury arc for 2 h under nitrogen[2,3] gave a mixture of products from which two amorphous products (**19**) and (**21**) were isolated by means of PLC (Scheme 4).



Scheme 4. *Reagents and conditions:* i, HgO–I_2, benzene; ii, *hv*.

The molecular formula of product (**19**) (11% yield) was established as $C_{28}H_{47}IO_2$ by high-resolution mass spectrometry. The IR spectrum showed the presence of a formoxy group. This was confirmed by the ^1H NMR spectrum which exhibited a one-proton singlet at δ 8.15 assignable to the formyl proton. The ^1H NMR spectrum also exhibited a double doublet at δ 3.08 (A part of ABX) with *J* 9.20 and 8.24 Hz, a double doublet at δ 3.15 (B part of ABX) with *J* 9.20 and 8.20 Hz, and a multiplet at δ 2.78 (X part of ABX) which were assignable to a group CH–CH_2I. There was also a doublet at δ 5.17 (*J* 4.96 Hz) assignable to a proton attached to a carbon having an OCHO substituent.

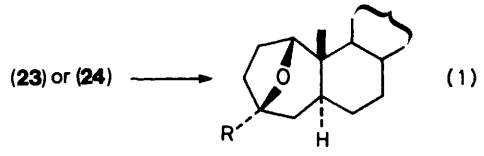
NOE measurements indicated that irradiation of signal ascribable to the 19-H caused an enhancement of the signal area at δ 5.17, and irradiation of the signal at δ 5.17 resulted in enhancement of the signal area at δ 2.78. These spectral results, as well as consideration of pathways for the formation of the product (*vide infra*), suggested that the structure was 2α-iodomethyl-*A*-nor-5α-cholestan-1α-yl formate (**19**).

High-resolution mass spectrometry indicated that the molecular formula of product (**21**) was $C_{28}H_{47}IO_2$. The IR and the ^1H NMR spectra indicated the presence of a formoxy group. The ^1H NMR spectrum also exhibited a one-proton doublet at δ 5.58 (*J* 6.66 Hz) assignable to a hydrogen attached to the carbon carrying an OCHO group, and a series of signals ascribable to a terminal vinyl group and a non-equivalent methylene group carrying an iodine atom (see Experimental section). These spectral results, in conjunction with the possible pathways[7a] of formation of the product (*vide infra*), suggested

that the structure of formate (**21**) was 4-iodo-3,4-seco-5α-cholest-2-en-1-yl formate.

Photolysis of the 4β-isomer (**16**) in benzene containing mercury (II) oxide and iodine under the above experimental conditions for 2 h afforded a product mixture from which five-membered formate (**19**) and olefinic formate (**21**) were obtained in 15 and 9% yield. In addition to these products derived from β-scission, a third crystalline product (**23**) was obtained in 5.3% yield. It contained an iodine atom and the molecular formula, $C_{28}H_{47}IO$, was determined by high-resolution mass spectrometry. Its IR spectrum showed the absence of both carbonyl and hydroxy groups in the molecule. The 400 MHz ^1H NMR spectrum (for details of the analysis, see Experimental section) exhibited a 1 H doublet at δ 3.95, a 1 H signal (ddd) at δ 4.05, and a 1 H signal (ddd) at δ 4.31. NOE measurements then indicated that irradiation of the signal at δ 4.05 (2-H_β) resulted in an enhancement of the signal area at δ 2.60 (3-H_β), and that irradiation of the signal at δ 4.31 (4-H_α) caused enhancements of the signal areas at δ 2.04 (3-H_α) and 1.10 (4a-H_α). On the basis of the coupling patterns and the results of the NOE experiments, these signals are respectively assigned to protons attached to carbons carrying an ethereal oxygen, and iodine, and an ethereal oxygen of 1β,4β-epoxy-2α-iodo-*A*-homo-5α-cholestane produced by an intramolecular addition of the 4β-alkoxyl radical to the double bond.

Irradiation of the 1β,4β-epoxide (**23**) in benzene containing tributyltin hydride and azoisobutyronitrile (AIBN) resulted in the removal of the iodine atom to give crystalline 1β,4β-epoxy-*A*-homo-5α-cholestane (**25**) in 82% yield (Scheme 5). ^1H NMR spectrum exhibited broad doublets at δ 3.99 (*J* 7.0 Hz) and at δ 4.32 (*J* 6.6 Hz) assignable to the 1-H_α and 4-H_α.



(**25**) R = H
(**26**) R = Me

Scheme 5. *Reagents and conditions:* Bu_3SnH–AIBN, *hv*, benzene.

Products of Irradiation of 4-*Methyl*-A-*homo*-5α-*cholest*-1-*en*-4α- *and* -4β-*ol*, (**17**) *and* (**18**), *in the Presence of Mercury*(II) *Oxide and Iodine* (*Scheme* 4).—The photolysis of the hypoiodites of the 4-methyl derivatives (**17**) and (**18**) of *A*-homo-5α-cholest-1-en-4α- and -4β-ol, (**15**) and (**16**), was then undertaken in order to examine the effects of the methyl substitution at C-4.

Irradiation of the 4β-methyl derivative (**17**) in benzene containing iodine and mercury(II) oxide under conditions similar to the case of 4α-ol (**15**) for 2 h gave a product mixture, from which two products (**20**) and (**22**) were obtained by PLC in 15 and 21% yield (Scheme 4). An amorphous product (**20**) had the molecular formula $C_{29}H_{49}IO_2$ by means of high-resolution mass spectrometry. The IR spectrum exhibited a band at 1 737 cm^{-1} assignable to the OAc group. The ^1H NMR spectrum exhibited a 3 H singlet at δ 2.08 assignable to the OAc. It also exhibited a one-proton multiplet centred at δ 2.76 ($w_{\frac{1}{2}}$ 22 Hz), a double doublet at δ 3.03 (A part of ABX system) with *J* 9.16 and 8.79 Hz, a double doublet at δ 3.16 (B part of ABX system) with *J* 9.16 and 7.33 Hz, and a doublet at δ 5.11 with *J* 5.13 Hz. These spectral results, in conjunction with the possible formation pathways,[7a] indicated that the product (**20**) was an acetate corresponding to the formate (**19**). The above signals are attributable to the 2-H_β, the protons of the CH_2I, and the 1-H_β, respectively.

The molecular formula of the other amorphous product (**22**) was confirmed to be $C_{29}H_{49}IO_2$ by means of high-resolution mass spectrometry. The IR spectrum exhibited a band at 1 744 cm^{-1} assignable to the OAc group. Apart from the presence of a singlet at δ 2.09 ascribable to the OAc and the absence of a singlet ascribable to an OCHO, the ^1H NMR spectrum of product (**22**) exhibited a series of signals parallel to those in the ^1H NMR spectrum of product (**21**) (see Experimental section). These spectral results indicated that the product was 4-iodo-3,4-seco-5α-cholest-2-en-1-yl acetate (**22**). Similar irradiation of the 4α-methyl derivative (**18**) produced a mixture of products from which the acetate (**20**), seco acetate (**22**), and a new product (**24**) were obtained in 4, 9, and 19% yield, respectively. Crystalline product (**24**) had the molecular formula $C_{29}H_{49}IO$ by means of FI high-resolution mass spectrometry. The NMR spectrum showed a 1 H doublet at δ 3.98 with *J* 6.23 Hz and a 1 H signal (ddd) at δ 4.15 with *J* 9.53, 9.16, and 6.23 Hz, assignable to a methine proton attached to the carbon carrying an ethereal oxygen and a methine proton attached to the carbon carrying an iodine atom, respectively. These results indicated that the structure was 2α-iodo-4α-methyl-1β,4-epoxy-*A*-homo-5α-cholestane (**24**) formed by an intramolecular addition of the 4β-alkoxyl radical.

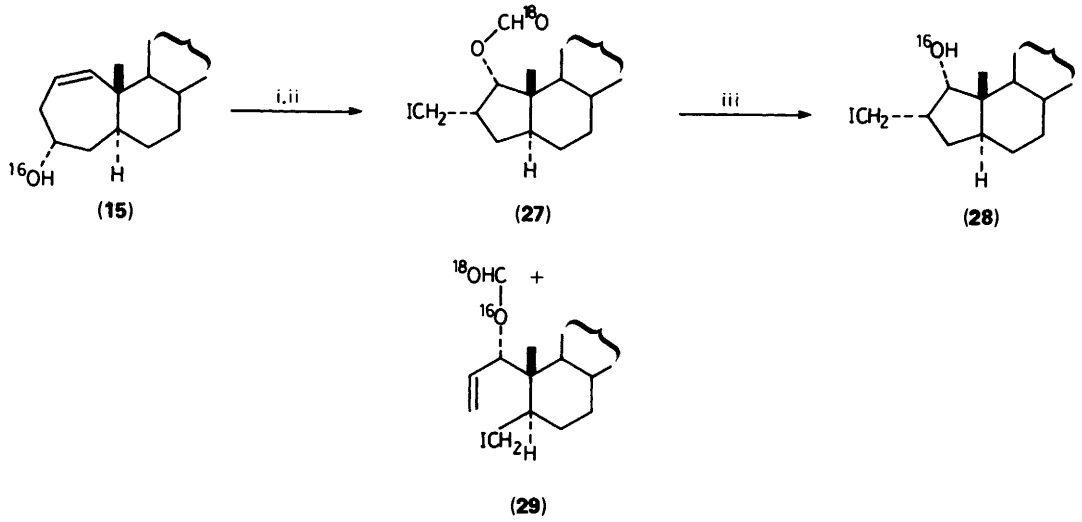
Removal of the iodine atom from the iodocholestane (**24**) was achieved with tributyltin hydride and AIBN in benzene under the conditions similar to the case of epoxyiodocholestane (**23**) to give crystalline 1β,4-epoxy-4α-methyl-*A*-homo-5α-cholestane (**26**) in 83% yield. The oxasteroid (**26**) gave expected spectral results.

The Oxygen-18 *Labelling Study* (*Scheme* 6).—In order to determine whether the oxygens of the –OCHO group of formates [(**19**) and (**20**)] and vinyl formates [(**21**) and (**22**)] are derived from the hydroxy group of the *A*-homoalcohols (**15**)–(**18**) or from the HgO, an ^{18}O labelling study was carried out for the formation of formate (**19**) from *A*-homoalcohol (**15**). The ^{18}O labelling experiment was carried out by irradiating a solution of the hypoiodite of *A*-homoalcohol (**15**) prepared *in situ* from the alcohol with an excess of $Hg^{18}O$ (^{18}O, 88 atom%) and iodine in dry benzene under the conditions described above. The extent of the incorporation of ^{18}O into the formate (**27**) and the corresponding alcohol (**28**) obtained by treatment with $NaBH_4$ were analysed by mass spectrometry. The molecular ion in the mass spectrum of formate (**27**) indicated that only one ^{18}O atom was incorporated in the formate. The mass spectrum of alcohol (**28**) showed that none of the ^{18}O atom was incorporated in the hydroxy group. It was thus clear that the ^{18}O atom in formate (**27**) is incorporated in the formyl carbonyl group.

Discussion

The foregoing experiments showed that, in contrast to the reaction of alkoxyl radicals generated from *A*-homocholest-4a-en-3-ols and *B*-homocholest-5-en-7a-ols reported previously,[2,3] the primary reactions of the alkoxyl radicals generated from *A*-homo-5α-cholest-1-en-4α-ol and its 4β-methyl derivative are β-scissions. The above experiments also revealed that a β-scission and an intramolecular addition take place competitively in the reaction of alkoxyl radicals generated from isomeric *A*-homo-5α-cholest-1-en-4β-ol and its 4α-methyl derivative.

The experiments also showed that, in contrast to the photoinduced reaction of *B*-homocholest-5-en-7a-ol in the presence of mercury(II) oxide and iodine,[2] no oxabicyclic compounds without an iodine atom were formed. The results with regard to the addition are thus parallel with those observed in the photoreaction of the ring-*A*-alcohol hypoiodites previously reported by us.[3]



Scheme 6. *Reagents and conditions:* i, $Hg^{18}O$–I_2, benzene; ii, *hv*; iii, $NaBH_4$, THF–MeOH, room temp.

Scheme 7 outlines the probable genesis of all the products (**19**)–(**24**), (**27**) and (**28**) which accounts for the foregoing labelling results. Thus, a β-scission of alkoxyl radicals (**A**) generated from the 4α-ol and its 4β-methyl derivative affords an allylic radical intermediate (**C**). An intramolecular combination of the allylic radical with the carbonyl oxygen to give another intermediate radical (**F**) followed by the reaction with IO· or I_2O (after one-electron oxidation) affords a second hypoiodite (**G**).[7a] A second β-scission of the alkoxyl radical (**H**) generated from the hypoiodite (**G**) gives a carbon-centred radical (**K'**).[7a] The intermediate radical (**K'**) will either abstract iodine to give products (**21**), (**22**), and (**29**) or will combine intramolecularly with the double bond to give a species (**L**) which reacts with iodine to afford products (**19**), (**20**), and (**27**). We outline two other possible pathways, which lead to lactol alkoxyl radicals (**I**) and (**J**) which correspond to the alkoxyl radical (**H**) in Scheme 7. The results of our ^{18}O labelling study, however, exclude these pathways.

The alkoxyl radicals (**B**) generated from the 4β-ol and its 4α-methyl derivative, on the other hand, react in two directions; a β-scission to give the allylic radical (**C**), which is identical with the one generated from the alkoxyl radical (**A**), and an intramolecular radical addition to give epoxy steroids (**23**) or (**24**).

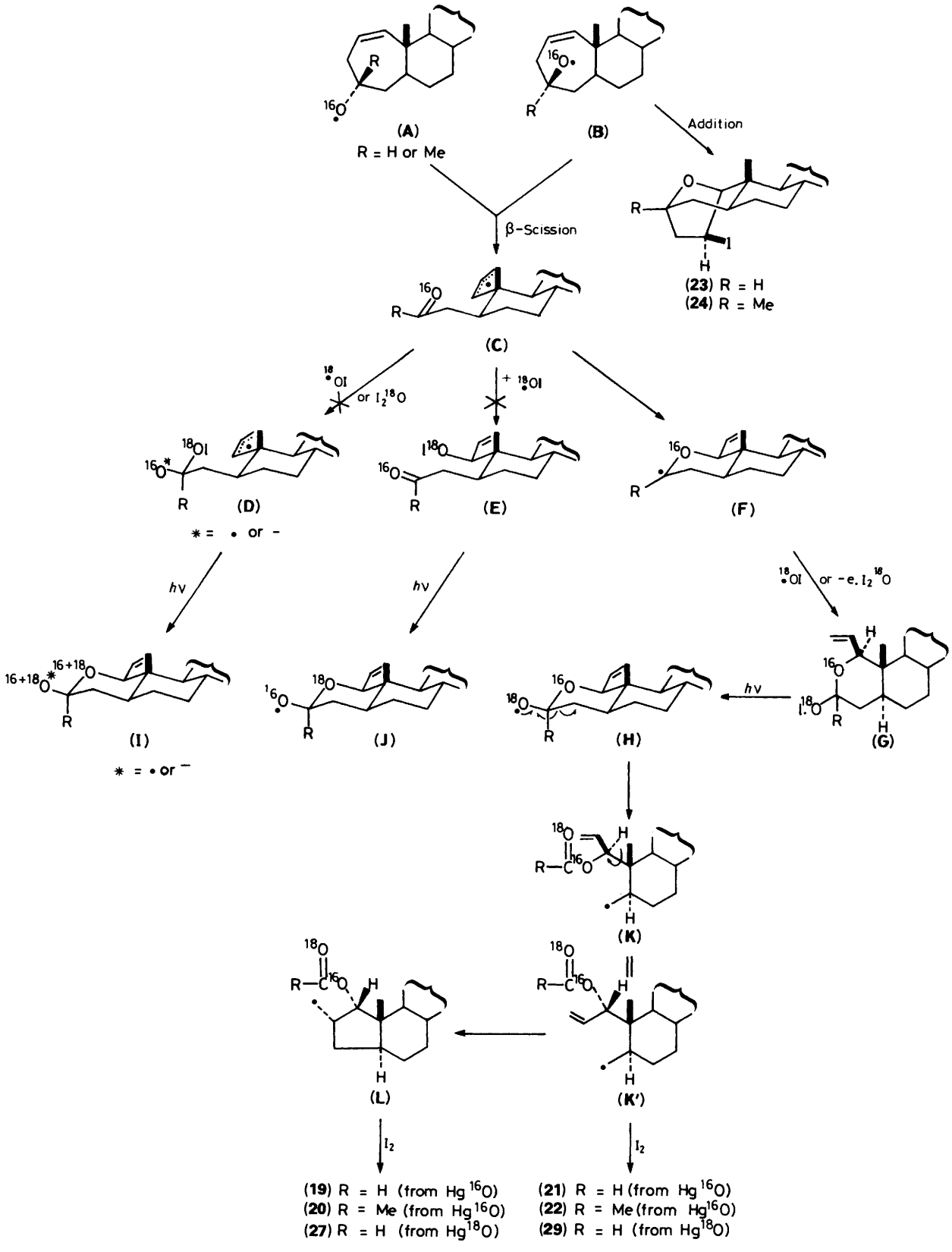
The observed total absence of any product arising from intramolecular radical addition in the reaction of *A*-homo-5α-cholest-1-en-4α-ols (**15**) and (**17**) is explained by a greater strain introduced into the transition state in the addition rather than a hindrance owing to a *quasi*-1,3-diaxial interaction between the incoming iodine and the 10β-methyl group when the intramolecular addition of alkoxyl radical takes place from the α-face.

Experimental

M.p.s were determined with a Yanagimoto micro m.p. apparatus and are uncorrected. IR spectra were determined for Nujol mulls with a Hitachi 285 spectrophotometer unless stated otherwise. ^1H NMR spectra were determined in $CDCl_3$ ($SiMe_4$ as internal reference) with a JEOL GX-270 (Faculty of Pharmaceutical Sciences) or a Bruker MSL-400 spectrometer. High- and low-resolution mass spectra were recorded with a JMS-OISG-2 spectrometer at the Faculty of Agriculture of this University. TLC was carried out on Merck Silica gel Art. 7749. The yields described are based on the converted starting materials. Light petroleum refers to the fraction boiling in the range 30–70 °C.

Synthesis of A-*Homo-5α-Cholest-1-en-4-one* (**14**).—To a shaken suspension of methyl(nitroso)urea (5 g) in diethyl ether (40 ml) was slowly added aq. 40% sodium hydroxide (50 ml). The organic layer containing diazomethane was separated, dried over KOH pellets, and added to a stirred suspension of cholest-1-en-3-one (**13**) (5.0 g) and powdered $AlCl_3$ (80 mg) in a mixed solvent (80 ml) of benzene and diethyl ether (1:1) in the course of 30 min while the solution was cooled in an ice–salt-bath. The solution was stirred for 3 h and active carbon was added to the solution. The mixture was then filtered through a pad of powdered $MgSO_4$. Removal of the solvent left an oily product, which was subjected to column chromatography (silica gel, 350 g). Elution with (6:1) benzene–dichloromethane gave *A*-homo-5α-cholest-1-en-one (**14**) (0.66 g, 35%) as the first fraction and then recovered starting ketone (3.11 g, 62% recovery). The 7-membered ketone was recrystallized from methanol–acetone, m.p. 99–102 °C (lit.,[8] 94–95 °C); ν_{max}(Nujol) 1 717 cm^{-1} (C=O); δ(270 MHz) 0.67 (3 H, s, 18-H_3), 0.90 (3 H, s, 19-H_3), 2.20 (1 H, dd, *J* 2.20 and 18.32 Hz, 4a-H_α), 2.63 (1 H, dd, *J* 12.09 and 18.32 Hz, 4a-H_β), 2.77 (1 H, dd, *J* 8.79 and 14.65 Hz, 3-H_β), 3.60 (1 H, dt, *J* 3.30 and 14.65 Hz, 3-H_α), 5.34 (1 H, ddd, *J* 12.09, 8.79, and 3.30 Hz, 2-H), and 5.72 (1 H, dd, *J* 3.30 and 12.09 Hz, 1-H); *m/z* (FDMS) 309 (M^+, 100%).

Reduction of A-*Homo-5α-Cholest-1-en-4-one* (**14**) *with Lithium Aluminium Hydride.*—A mixture of *A*-homo-5α-cholest-1-en-4-one (**14**) (670 mg) and $LiAlH_4$ (125 mg) in dry diethyl ether (25 ml) was stirred under nitrogen for 2 h. The excess of $LiAlH_4$ was decomposed by the addition of a small volume of water and the mixture was filtered through a pad of $MgSO_4$. The filtrate was washed successively with dil. HCl, water, and saturated brine, and dried over anhydrous Na_2SO_4. Removal of the solvent gave an oily product (680 mg), which was subjected to preparative TLC with a 1:1 benzene–dichloromethane mixture. Development (×2) of the plate gave two fractions. The more mobile fraction (R_f 0.4) (195 mg, 29%) was *compound* (**15**). It was recrystallized from methanol–water to give a specimen for analysis, m.p. 102–104 °C (Found: C, 83.8; H, 12.1. $C_{28}H_{48}O$ requires C, 83.93; H, 12.08%); ν_{max} 3 300 cm^{-1} (OH); δ(270 MHz) 0.67 (3 H, s, 18-H_3), 0.92 (3 H, s, 19-H_3), 3.98 (1 H, m, 4-H_β), 5.43 (1 H, dt, *J* 12.09, 6.59, and 6.59 Hz, 2-H), and 5.82 (1 H,



Scheme 7.

d, *J* 12.09 Hz, 1-H); *m/z* (FDMS) 400 (M^+, 100%) and 383 [$(M - OH)^+$, 5.5].

The less mobile fraction (R_f 0.3) (260 mg, 39%) was A-*homo*-5α-*cholest*-1-*en*-4β-*ol* (**16**). The 4β-ol was recrystallized from aq. methanol to give a specimen for analysis, m.p. 121–123 °C (Found: C, 83.8; H, 12.3%); ν_{max} 3 320 cm^{-1} (OH); δ(270 MHz) 0.67 (3 H, s, 18-H_3), 0.98 (3 H, s, 19-H_3), 3.62 (1 H, m, 4-H_α), 5.48 (1 H, ddd, *J* 12.09, 8.79, and 5.13 Hz, 2-H), and 5.79 (1 H,

dd, *J* 12.09 and 2.20 Hz, 1-H); *m/z* (FDMS) 400 (M^+, 100) and 383 [$(M - OH)^+$, 4.5].

Irradiation of A-*Homo*-5α-*cholest*-1-*en*-4α-*ol* (**15**) *in the Presence of Mercury*(II) *Oxide and Iodine.*—A solution of the 4α-ol (**15**) (100 mg, 0.25 mmol) in benzene (15 ml) containing red mercury(II) oxide (162 mg, 0.75 mmol) and iodine (190 mg, 0.75 mmol) was irradiated through a Pyrex filter for 2 h with a 100-W high-pressure Hg arc (Ushio) under nitrogen. The solution was then filtered and the filtrate was washed successively with aq. $Na_2S_2O_3$ and water, and dried over anhydrous Na_2SO_4. Evaporation of the solvent left a product (112 mg), which was subjected to PLC with (3:1) hexane–benzene to yield four fractions (A–D) in order of their mobility on TLC. Fraction A (R_f 0.7) (15 mg, 11%) was 2α-*iodomethyl*-A-*nor*-5α-*cholestan*-1α-*yl formate* (**19**) [Found: *m/z* (EI-HR-MS) 542.2641. $C_{28}H_{47}IO_2$ requires *M*, 542.2621]; ν_{max}(neat) 1 720 (HC=O) and 1 170 cm^{-1} (formoxy C–O); δ(400 MHz) 0.65 (3 H, s, 18-H_3), 0.78 (3 H, s, 19-H_3), 2.78 (1 H, m, $w_{\frac{1}{2}}$ 24, Hz, 2-H_β), 3.08 (1 H, dd, *J* 9.20 and 8.24 Hz, C*H*HI), 3.15 (1 H, d, *J* 9.20 and 8.20 Hz, CH*H*I), 5.17 (1 H, d, *J* 4.96 Hz, 1-H_β), and 8.15 (1 H, s, OCHO); *m/z* (FDMS)$^+$, 542 (100%), 497 [$(M - OCHO)^+$, 10], 416 [$(M - I + H)^+$, 41], and 414 [$(M - HI)^+$, 23].

Fraction B (R_f 0.6) (21 mg, 15.5%) was 4-*iodo*-3,4-*seco*-5α-*cholest*-2-*en*-1α-*yl formate* (**21**) [Found: *m/z* (EI-HR-MS) 542.2630. $C_{28}H_{47}IO_2$ requires *M*, 542.2621]; ν_{max}(neat) 1 729 (OCHO), 1 167 (formate C–O), 992, and 930 cm^{-1}; δ(400 MHz) 0.65 (3 H, s, 18-H_3), 0.82 (3 H, s, 19-H_3), 3.75 (1 H, dd, *J* 9.76 and 1.37 Hz, C*H*HI), 5.29 (1 H, d, *J* 17.44 Hz, 3-H), 5.31 (1 H, d, *J* 10.56 Hz, 3-H), 5.68 (1 H, d, *J* 6.66 Hz, 1-H_β), 5.88 (1 H, ddd, *J* 16.90, 10.76, and 6.66 Hz, 2-H), and 8.14 (1 H, s, OCHO); *m/z* (FDMS) 542 (M^+, 18.7%), 497 [$(M - OCHO)^+$, 11.4], and 457 [$(M - CH_2{=}CHOCHO)^+$, 100].

Fraction C (R_f 0.4) (13 mg) was an intractable mixture and the most polar fraction, D (R_f 0.1) (19 mg, 19%) was recovered starting material.

Irradiation of A-*Homo*-5α-*cholest*-1-*en*-4β-*ol* (**16**) *in the Presence of Mercury*(II) *Oxide and Iodine.*—A solution of the 4β-ol (100 mg, 0.25 mmol) in benzene containing red mercury(II) oxide and iodine was irradiated under the same conditions as in the case of the 4α-ol above. The solution was worked up as in the case of the 4α-ol to give five fractions (A–E) in order of their mobility on TLC plates. Fractions A (20 mg, 15%) and B (12 mg, 9%) were 2α-iodomethyl-*A*-nor-5α-cholestan-1α-yl formate (**19**) and 4-iodo(3,4-seco-5α-cholest-2-en-1α-yl formate (**21**) respectively.

Fraction C (R_f 0.5) (7 mg, 5.3%) was 1β,4-*epoxy*-2α-*iodo*-A-*homo*-5α-*cholestane* (**23**). It was recrystallized from methanol to give a specimen for analysis, m.p. 85–87 °C (Found: C, 64.0; H, 9.1. $C_{28}H_{47}IO$ requires C, 63.87; and H, 9.00%); ν_{max}(Nujol) 1 153, 1 020, and 1 006 cm^{-1}; δ(400 MHz) 0.66 (3 H, s, 18-H_3), 1.04 (3 H, s, 19-H_3), 1.10 [1 H, br dd, *J*(4a-H_α–4-H_α) < 0.5, *J*(4a-H_α–4a-H_β) 12.2, and *J*(4a-H_α–5-H_α) 4.2 Hz, 4a-H_α], 1.65 [1 H, dt, *J*(4a-H_β–4a-H_α) 12.2, *J*(4a-H_β–5-H_α) 12.2, and *J*(4a-H_β–4-H_α) 3.4 Hz, 4a-H_β], 2.04 [1 H, ddd, *J*(3-H_α–3-H_β) 12.2, *J*(3-H_α–2-H_β) 7.3, and *J*(3-H_α–4-H_α) 0.98 Hz, 3-H_α], 2.60 [1 H, ddd, *J*(3-H_β–3-H_α) 12.2, *J*(3-H_β–2-H_β) 11.3, and *J*(3-H_β–4-H_α) 7.3 Hz, 3-H_β], 3.95 (1 H, d, *J* 6.3 Hz, 1-H_α), 4.05 [1 H, ddd, *J*(2-H_β–3-H_β) 11.3, *J*(2-H_β–3-H_α) 7.3, and *J*(2-H_β–1-H_α) 6.3 Hz, 2-H_β], and 4.31 [1 H, ddd, *J*(4-H_α–3-H_β) 7.3, *J*(4-H_α–4a-H_β) 3.41, *J*(4-H_α–3-H_α) 0.98, and *J*(4-H_α–4a-H_α) < 0.5 Hz, 4-H_α]; *m/z* (FDMS) 527 [$(M + H)^+$, 21%] 526 (M^+, 13), and 399 [$(M - I)^+$, 100].

Fraction D (R_f 0.4) (3 mg) was an unidentified mixture. Fraction E (R_f 0.1) (14 mg, 14%) was the recovered starting material.

Removal of Iodine from 1β,4-*Epoxy*-2α-*iodo*-A-*homo*-5α-*cholestane* (**23**).—A solution of iodide (**23**) (8 mg) in dry benzene (2 ml) containing AIBN (0.5 mg) in a Pyrex vessel was flushed with nitrogen gas. To this stirred solution was added Bu_3SnH (0.01 ml, Aldrich Inc.) and the solution was irradiated for 30 min with a 100 W high-pressure Hg arc at room temperature. The solvent was then evaporated off to give a product, which was dissolved in diethyl ether (2 ml). To this solution was added 2M aq. potassium fluoride[5] (0.3 ml) and the solution was stirred for 30 min at room temperature, washed with saturated brine (2 ml × 2), and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a crystalline product, which was purified by PLC with benzene. A band with R_f 0.4 gave a *crystalline ether* (**25**) (5.5 mg). Recrystallization from methanol gave a sample for analysis as needles (5 mg, 82%), m.p. 101–102 °C (Found: C, 83.85; H, 12.35. $C_{28}H_{48}O$ requires C, 83.93; H, 12.08%); ν_{max}(Nujol) 1 048, 1 036, and 1 021 cm^{-1}; δ(270 MHz) 0.64 (3 H, s, 18-H_3), 1.00 (3 H, s, 19-H_3), 3.99 (1 H, d, *J* 7.0 Hz, 1-H_α), and 4.32 (1 H, br d, *J* 6.6 Hz, 4-H_α); *m/z* (FDMS) 400 (M^+, 100%) and 401 [$(M + H)^+$, 37].

Preparation of 4β-*Methyl*-A-*homo*-5α-*cholest*-1-*en*-4α-*ol* (**17**) *and its* 4β-*Isomer* (**18**).—To an ice-cooled solution of *A*-homo-5α-cholest-1-en-4-one (**14**) (400 mg, 1 mmol) in diethyl ether (12 ml) under nitrogen was added 1.5M methyl-lithium in diethyl ether (50 ml, 74 mmol) during 30 min. The solution was stirred at room temperature for 15 h and then cooled in an ice-bath, and ammonium chloride (1 g) and water (20 ml) were added. The two-layer solution was transferred to a separatory funnel and was neutralized with dil. hydrochloric acid. The organic layer was washed successively with aq. 1% $Na_2S_2O_3$ (30 ml), water (30 ml × 2), and saturated brine (30 ml). Evaporation of the solvent gave an oily product (452 mg), which was subjected to PLC with benzene to yield three fractions in order of their mobility on TLC plates.

Fraction A (R_f 0.6) was unchanged starting ketone (73 mg, 18% recovery). Fraction B (R_f 0.5) was further purified by PLC with (3:1) benzene–hexane to give an oily product (89 mg). Recrystallization from methanol gave an analytically pure sample of 4β-*methyl*-A-*homo*-5α-*cholest*-1-*en*-4α-*ol* (**17**) (51 mg, 15%), m.p. 122–124 °C (Found: C, 83.7; H, 12.1. $C_{29}H_{50}O$ requires C, 83.99; H, 12.15%); ν_{max}(Nujol) 3 368 cm^{-1} (OH); δ(270 MHz) 0.67 (3 H, s, 18-H_3), 0.95 (3 H, s, 19-H_3), 1.23 (3 H, s, 4-Me_β), 5.45 (1 H, ddd, *J* 11.91, 8.79, and 4.76 Hz, 2-H), and 5.88 (1 H, dd, *J* 11.19 and 2.20 Hz, 1-H); *m/z* (FDMS) 414 (M^+, 100%) and 397 [$(M - OH)^+$, 11.9].

Fraction C (R_f 0.2) was recrystallized from methanol to give crystals of 4α-*methyl*-A-*homo*-5α-*cholest*-1-*en*-4β-*ol* (**18**), m.p. 143–144.5 °C (Found: C, 84.06; H, 12.17%); ν_{max}(Nujol) 3 320 cm^{-1} (OH); δ(270 MHz) 0.67 (3 H, s, 18-H_3), 0.98 (3 H, s, 19-H_3), 1.23 (3 H, s, 4-Me_α), 5.44 (1 H, ddd, *J* 11.96, 7.96, and 5.86 Hz, 2-H), and 5.71 (1 H, dd, *J* 11.73 and 1.46 Hz, 1-H); *m/z* (FDMS) 414 (M^+, 100%) and 397 [$(M - OH)^+$, 7.4%].

Irradiation of 4β-*Methyl*-A-*homo*-5α-*cholest*-1-*en*-4α-*ol* (**17**) *in the Presence of Mercury*(II) *Oxide and Iodine.*—A solution of the 4α-ol (70 mg, 0.169 mmol) in benzene (15 ml) was irradiated under the same conditions as was the 4α-ol (**15**). The same work-up as in the case of 4α-ol (**15**) gave a product mixture (92 mg), which was subjected to PLC with (3:1) hexane–benzene to give four fractions in the order of their mobility. Fraction A (R_f 0.9) (14 mg, 15%) was 2α-*iodomethyl*-A-*nor*-5α-*cholestan*-1α-*yl acetate* (**20**) [Found: *m/z* (FD-HR-MS) 556.2781. $C_{29}H_{49}IO_2$ requires *M*, 556.2775]; ν_{max}(neat) 1 732 (OAc) and 1 241 cm^{-1}; δ(270 MHz) 0.64 (3 H, s, 18-H_3), 0.75 (3 H, s, 19-H_3), 2.08 (3 H, s, OAc), 2.76 (1 H, m, 2-H_β), 3.03 (1 H, dd, *J* 9.16 and 8.79 Hz, C*H*HI), 3.16 (1 H, *J* 9.16 and 7.33 Hz, CH*H*I), and 5.11 (1 H, d, *J* 5.13 Hz, 1-H_β); *m/z* (FDMS) 556 (M^+, 41.5%), 497 [$(M - OAc)^+$, 12], 429 [$(M - I)^+$, 19], and 428 [$(M - HI)^+$, 47].

Fraction B (R_f 0.8) (19 mg, 20%) was 4-*iodo*-3,4-*seco*-5α-*cholest*-2-*en*-1α-*yl acetate* (**22**) [Found: *m/z* (EI-HR-MS) 556.2746. $C_{29}H_{49}IO$ requires *M*, 556.2775]; ν_{max}(neat) 1 744 (OAc), 1 236, 990, and 930 cm^{-1}; δ(270 MHz) 0.65 (3 H, s, 18-H_3), 0.79 (3 H, s, 19-H_3), 2.09 (3 H, s, OAc), 2.76 (1 H, t, *J* 9.89 Hz, C*H*HI), 3.79 (1 H, dd, *J* 9.89 and 1.46 Hz, CH*H*I), 5.24 (1 H, d, *J* 16.85 Hz, C=C*H*H), 5.27 (1 H, d, *J* 10.63 Hz, C=CH*H*), 5.55 (1 H, d, *J* 6.32 Hz, 1-H_α), and 5.86 (1 H, ddd, *J* 16.85, 10.62, and 6.23 Hz, 2-H); *m/z* (FDMS) 542 (M^+, 44%) and 457 [$(M - CH_2{=}CHCHOAc)^+$, 100].

Fraction C (R_f 0.7) (8 mg) and fraction D (R_f 0.4) (5 mg) were both unidentified mixtures. Faction E (R_f 0.2) (12 mg, 17%) was recovered starting material.

Irradiation of 4α-*Methyl*-A-*homo*-5α-*cholest*-1-*en*-4β-*ol* (**18**) *in the Presence of Mercury*(II) *Oxide and Iodine*.—A solution of the 4β-ol (95 mg, 0.23 mmol) in benzene (15 ml) containing red mercury(II) oxide (154 mg, 0.70 mmol) and iodine (180 mg, 0.71 mmol) was subjected to hypoiodite photolysis as in the case of the 4α-ol. The product (108 mg) was subjected to PLC with (1:3) benzene–hexane to give five fractions in order of their mobility. Fraction A (5 mg) (3.8%) was 2α-iodomethyl-*A*-nor-5α-cholestan-1α-yl acetate (**20**), identical with a specimen obtained from the 4α-ol (**17**). Fraction C (R_f 0.85) (24 mg, 19.4%) was 1β,4-*epoxy*-2α-*iodo*-4α-*methyl*-A-*homo*-5α-*cholestane* (**24**), m.p. 87–88.5 °C (after recrystallization from methanol–ethanol) [Found: *m/z* (FI-HR-MS) 540.2856. $C_{29}H_{49}IO$ requires *M*, 540.2828]; ν_{max}(neat) 1 167, 1 119, 1 054, and 989 cm^{-1}; δ(270 MHz) 0.65 (3 H, s, 18-H_3), 1.01 (3 H, s, 19-H_3), 1.31 (3 H, s, 4-Me_α), 3.98 (1 H, d, *J* 6.23 Hz, 1-H_α) and 4.15 (1 H, ddd, *J* 9.53, 9.16, and 6.23 Hz, 2-H_β); *m/z* (FDMS) 540 (M^+, 50%) and 413 [$(M - I)^+$, 100]. Fraction D (R_f 0.4) (3 mg) was an unidentified mixture. Fraction E (R_f 0.1) (14 mg, 14.7%) was recovered starting material.

Removal of Iodine from 1β,4-*Epoxy*-2α-*iodo*-4α-*methyl*-A-*homo*-5α-*cholestane* (**24**).—A solution of the iodide (10 mg) in dry benzene (2 ml) containing AIBN (0.5 mg) was placed in a Pyrex vessel. The solution was flushed with nitrogen. Bu_3SnH (0.01 ml) was added to the solution, which was then irradiated with a 100 W high-pressure Hg arc for 30 min. The solution was then worked up as in the case of 1β,4-epoxy-2α-iodo-*A*-homo-5α-cholestane (**23**) to yield a product, which was purified by PLC (benzene) to give crystals of 1β,4-*epoxy*-4α-*methyl*-A-*homo*-5α-*cholestane* (**26**) (8 mg). Recrystallization from methanol gave needles (6.5 mg, 83%), m.p. 116–117 °C (Found: C, 83.9; H, 12.1. $C_{29}H_{50}O$ requires C, 83.99; H, 12.15%); ν_{max}(Nujol) 1 028 and 1 012 cm^{-1}; δ(270 MHz) 0.64 (3 H, s, 18-H_3), 0.97 (3 H, s, 19-H_3), 1.28 (3 H, s, 4-Me_α), and 4.00 (1 H, d, *J* 7.0 Hz, 1-H_α); *m/z* (FDMS) 414 (M^+, 100%) and 415 [$(M + H)^+$, 38].

Mercury(II) [^{18}O]*oxide* (88 *atom*% ^{18}O).—This labelled mercury(II) oxide was prepared by the reaction of red mercury(II) chloride in [^{18}O]water (Merck Sharp and Dohme Canada Ltd., 97 atom% ^{18}O) with sodium hydroxide–[^{18}O]water as described in our previous paper.[6a]

The ^{18}*O Labelling Experiments*.—A solution of the 4α-ol (**15**) (30 mg, 0.075 mmol) in benzene (4 ml) containing $Hg^{18}O$ (88 atom%; 49 mg, 0.125 mmol) and I_2 (57 mg, 0.125 mmol) was irradiated as described above. Separation of product mixture by PLC in the same manner as noted above gave formate (**27**) (12.5 mg), vinyl formate (**29**) (5 mg), and the starting alcohol (1.5 mg recovery). FD-MS (JEOL JMS-HS 110) for formate (**27**): *m/z* 544 (M^+, 100%), 542 (M^+, 93.5), 497 [$(M - OCHO)^+$, 17.8], 417 [$(M - I)^+$, <0.01], and 415 [$(M - I)^+$, 4.0]. For the seco formate (**28**): *m/z* 544 (3.6%), 542 (9.8), 497 [$(M - OCHO)^+$, 14.6], and 457 [$(M - OHCOCHCH{=}CH_2)^+$, 100].

To a solution of the [^{18}O]formate (**27**) (10 mg) in THF (0.5 ml) and methanol (1 ml) was added $NaBH_4$ (5 mg) at room temperature. The solution was stirred for 1 h, more $NaBH_4$ (5 mg) was added, and the solution was stirred for another hour. After the solvent was removed, water (2 ml) was added and the mixture was extracted with dichloromethane (2 ml × 2). The combined extracts were dried over anhydrous Na_2SO_4. Removal of the solvent left a residue (10 mg), which was subjected to PLC with a (1:3) mixture of benzene and hexane to give 2α-iodomethyl-*A*-nor-5α-cholestan-1α-ol (**28**) (6 mg, 63%), which was recrystallized from light petroleum to give *crystals*, m.p. 78–81 °C (Found: C, 63.1; H, 9.5; I, 24.6. $C_{27}H_{47}IO$ requires C, 63.02; H, 9.21; I, 24.66%); ν_{max}(neat) 3 480 cm^{-1} (OH); δ(270 MHz) 0.66 (3 H, s, 18-Me_3), 0.69 (3 H, s, 19-Me_3), 2.61 (1 H, m, 2-H_β), 3.24 (1 H, dd, *J* 6.4 and 8.8 Hz, C*H*HI), 3.32 (1 H, dd, *J* 8.8 and 10.5 Hz, CH*H*I), and 3.84 (1 H, t, *J* 4.5 Hz, 1-H_β); *m/z* (FD-MS) 516 (<0.01%), 514 (M^+, 11.8), 513 [$(M - I)^+$, 15.4], 497 [$(M - OH)^+$, 29.6], 389 [$(M - I)^+$, 4.9] and 387 [$(M - I)^+$, 71.7].

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