Photoinduced Molecular Transformations. Part 106.[1] The Formation of Cyclic Anhydrides *via* Regioselective β-Scission of Alkoxyl Radicals generated from 5- and 6-Membered α-Hydroxy Cyclic Ketones.

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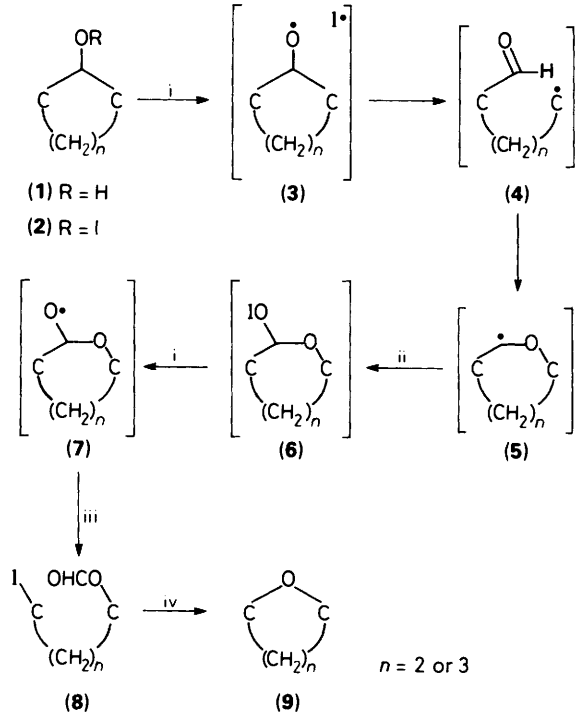
The irradiation of the hypoiodites of 5- or 6-membered cyclic α-ketols in benzene containing mercury(II) oxide and iodine (each 3 equiv.) resulted in the formation of the corresponding cyclic anhydrides arising from the insertion of an oxygen. A novel formation of a methylenedioxy group arising from an intramolecular hydrogen abstraction, on the other hand, was found when a steroidal α,α-dimethoxy alcohol hypoiodite was irradiated in benzene. An ^{18}O labelling study of the formation of the cyclic anhydride on photolyses of 17β-hydroxy-4β-methoxy-5α-androstan-16-one hypoiodite generated *in situ* by an excess of mercury(II) oxide and iodine in benzene indicated that the heavy oxygen of Hg ^{18}O is incorporated as the ring oxygen of the anhydride. On the basis of this result, a pathway involving a regioselective β-scission of the alkoxyl radical is proposed as leading to formation of the cyclic anhydride.

In our previous papers in this series, we have reported that the irradiation of the hypoiodites (**2**) generated *in situ* by the reaction of steroidal 5- and 6-membered cyclic alcohols (**1**) with an excess of mercury(II) oxide and iodine in benzene give novel formates (**8**) arising from the successive reactions triggered by a β-scission of the corresponding alkoxyl radicals (**3**) as outlined in Scheme 1.[2,3] These formates can readily be cyclized to oxasteroids (**9**) by the treatment with sodium borohydride or methyl-lithium. We have shown that this two-step process can be applied to the general transformation of hydroxy steroids (**1**) into oxasteroids (**9**) with the oxygen-containing ring of the same size as that of the starting ring.



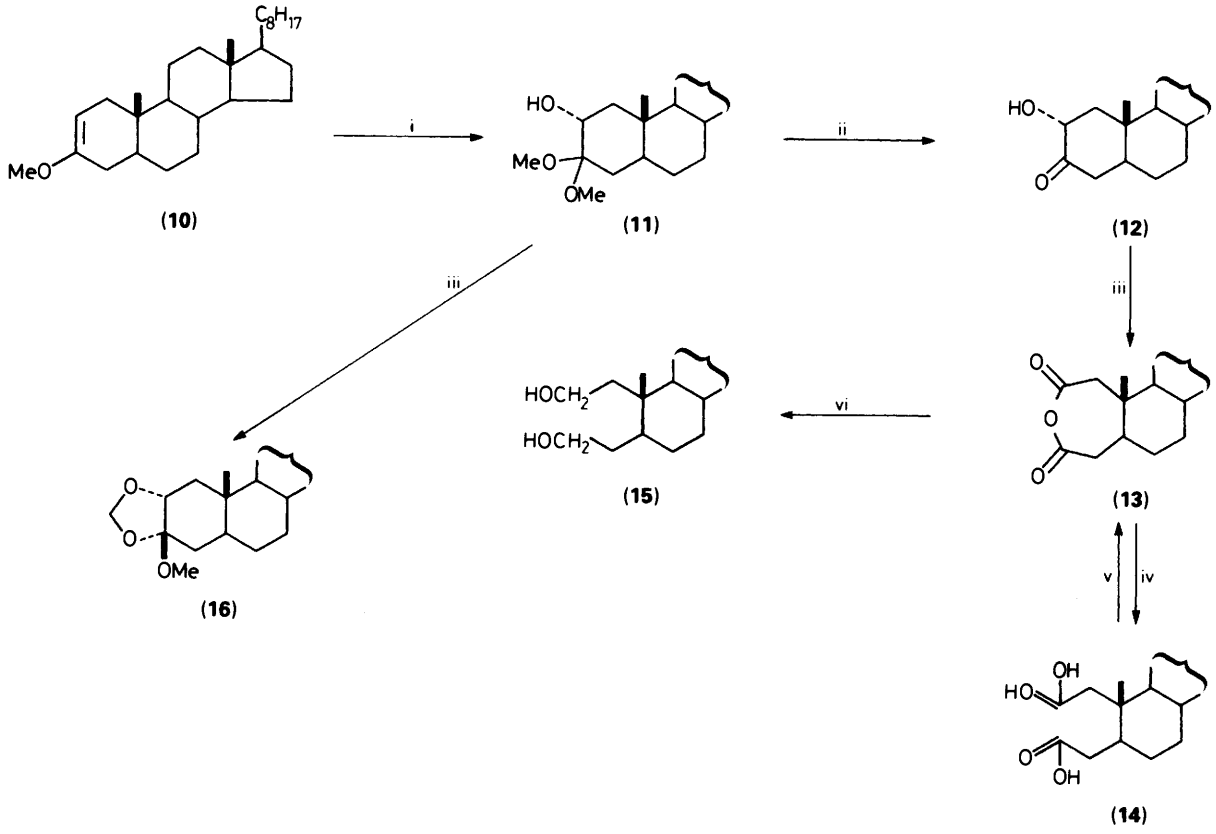
Scheme 1. *Reagents and conditions:* i, $HgO–I_2$ (each 3 equiv.), *hν*, benzene, room temp; ii, ^-OI or −e, I_2O; iii, I_2; iv, $NaBH_4$, THF, reflux or MeLi, diethyl ether, −78 °C.

In this paper we report further results in this area; results on the photoinduced reactions of the hypoiodites of 5- or 6-membered cyclic α-oxo and α,α′-dialkoxy alcohols. This study was carried out to widen our knowledge of the effect of neighbouring substituents on the β-scission of the alkoxyl radicals generated from hypoiodites of cyclic alcohols. As described below, we found that cyclic anhydrides are the products of the photoinduced reactions of the cyclic α-ketol hypoiodites while a novel formation of a methylenedioxy group arising from an intramolecular hydrogen abstraction was found when a steroidal α,α′-dimethoxy alcohol hypoiodite is irradiated in benzene.

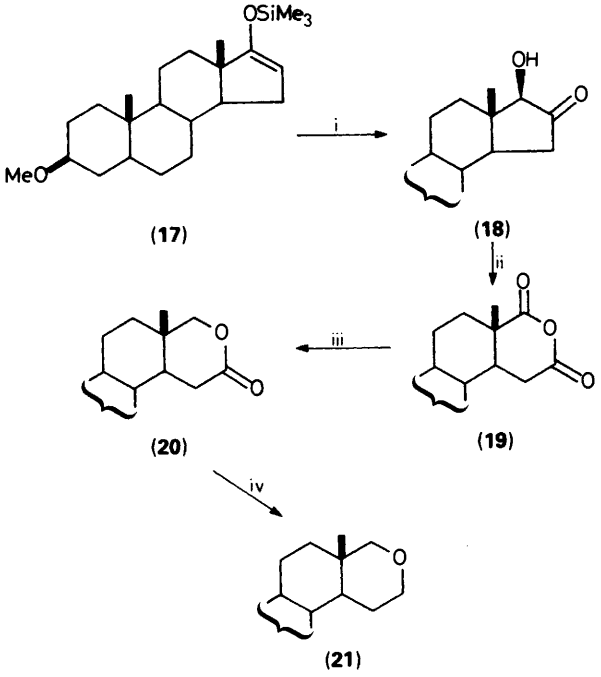
Results

Products of the Photoinduced Reactions of Cyclic α-Ketol Hypoiodites.—2α-Hydroxy-5α-cholestan-3-one (**12**), 17β-hydroxy-3β-methoxy-5α-androstan-16-one (**18**) and a mixture of 3-*exo*- and 3-*endo*-hydroxy camphors (**24**) and (**25**) were chosen as the model of α-ketols. The authentic 2α-hydroxy-5α-cholestan-3-one (**12**)[4] for the present study was prepared without ketol rearrangements by an acidic hydrolysis of 3,3-dimethoxy-5α-cholestan-2α-ol (**11**) which was prepared by an epoxidation of 3-methoxy-5α-cholest-2-ene (**10**)[5] according to the procedure of Frimer[6] as outlined in Scheme 2. The structure was proved by its independent synthesis by stereoselective hydrolysis of 2α-bromo-5α-cholestan-3-one[7] and by the ^1H NMR spectrum.

17β-Hydroxy-3β-methoxy-5α-androstan-16-one (**18**) was prepared in a 16% yield by means of peracid epoxidation[8] of the trimethylsilyl enol ether (**17**)[9] of 3β-methoxy-5α-androstan-17-one which was prepared by methylation[10] of a commercially available epiandrosterone (Scheme 3). The structure of the α-hydroxy ketone (**18**) that resulted from a ketol rearrangement[7,11,12] of an initially-formed 16α-hydroxy-3β-methoxy-5α-androstan-17-one[13] under the experimental conditions, was proved by the ^1H NMR spectrum; it exhibited a singlet at δ 3.75 assignable to the 17-H. The configuration of the 17-hyd-



Scheme 2. Reagents and conditions: i, MCPBA, MeOH, 0 °C; ii, 2M HCl, THF, 0 °C; iii, HgO, I_2 (each 3 equiv.), benzene, *hv*; iv, 2M NaOH, room temp; v, DCC, dioxane, room temp; vi, $NaBH_4$, THF, room temp.

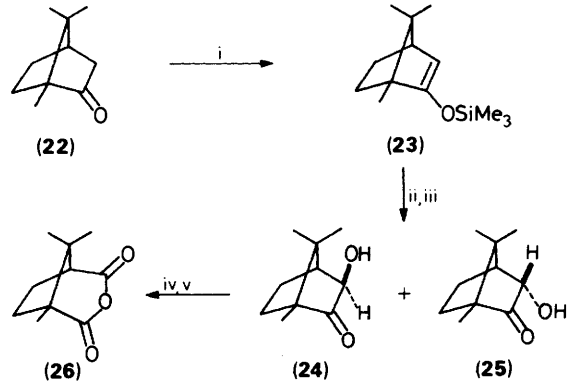


Scheme 3. *Reagents and conditions:* i, MCPBA, MeOH, 0 °C and then 2M NaOH, room temp, ii, HgO, I_2 (each 3 equiv.), benzene, *hv*; iii, $NaBH_4$, THF, 0 °C; iv, $LiAlH_4$, BF_3·Et_2O.

roxyl group is assigned as β on the basis of the result of the ketol rearrangement of 3β, 16α-hydroxy-5α-androstan-17-one.[11]

A 1:1 mixture of 3-*exo*- and 3-*endo*-camphors[14] (**24**) and (**25**) were prepared by oxidation of the trimethylsilyl enol ether (**23**) of (+)-camphor (**22**) with *m*-chloroperbenzoic acid (MCPBA), followed by treatment of the crude product with aqueous sodium hydroxide (Scheme 4).[8]

The photolysis of the hypoiodite of 2α-hydroxy-5α-cholestan-3-one (**12**), prepared *in situ* with 3 molar equivalents each of



Scheme 4. *Reagents and conditions:* i, LDA, THF, Me_3SiCl; ii, MCPBA, Hexane; iii, NaOH, H_2O; iv, HgO, I_2 (each 3 equiv.), benzene; v, *hv*.

mercury(II) oxide and iodine in benzene in a Pyrex vessel as described in the previous papers[2] gave a major product (**13**). The IR spectrum of the amorphous product (**13**), which was rather difficult to purify, exhibited intense absorption bands which were assigned to a cyclic anhydride group. The cyclic anhydride was identified by converting it into the known dibasic acid (**14**)[4,15] by basic hydrolysis and recyclization to the

original anhydride with DCC according to the procedure of Doorenbos.[15] Moreover, reduction of product (**13**) with an excess of sodium borohydride gave 2,3-seco-5α-cholestane-2,3-diol (**15**).[16] These results established that product (**13**) was 4a-homo-3-oxa-5α-cholestane-2,4-dione[15,16,*] (Scheme 2).

A similar photolysis of the hypoiodite of 17β-hydroxy-3β-methoxy-5α-androstan-16-one (**18**) in benzene in the presence of an excess of mercury(II) oxide and iodine gave 3β-methoxy-17α-homo-17-oxa-5α-androstane-16,17a-dione (**19**). Its IR spectrum exhibited intense absorption bands at 1 761 and 1 806 cm^{-1} which were assigned to the anhydride group. The structure was further proved by transforming it into the corresponding lactone (**20**) by regioselective reduction with $NaBH_4$.[17] The structure of the lactone was proved to be 3β-methoxy-17a-homo-17-oxa-5α-androstan-16-one by comparison of the ^1H NMR spectrum with that of 17a-homo-17-oxa-5α-androstan-16-one.[2] A further reduction of the lactone (**20**) with $LiALH_4$ and BF_3–diethyl ether gave 3β-methoxy-17a-homo-17-oxa-5α-androstane (**21**).

Irradiation of hypoiodites of a 1:1 mixture of 3-*exo*- and 3-*endo*-camphors (**24**) and (**25**) in benzene under the same conditions as above gave similarly camphoric acid anhydride (**26**)[18] in a 38% yield (Scheme 4).

The Product of the Photolysis of the Hypoiodite of Steroidal α,α′-Dimethoxy Cyclic Alcohol in the presence of Mercury(II) Oxide and Iodine.—One of the present authors previously reported that no β-scission reaction takes place when the hypoiodite of a steroidal 6-membered α-acetoxy alcohol in benzene was irradiated under experimental conditions similar to those of the present experiment.[19] Irradiation of the hypoiodite of 3,3-dimethoxy-5α-cholestan-2α-ol (**11**) in benzene containing mercury(II) oxide and iodine (each 3 equiv.) gave a crystalline compound (**16**) almost exclusively although a large amount of the starting alcohol was recovered unchanged. Mass spectrometry established the molecular formula of the product to be $C_{29}H_{50}O_3$. The product (**16**) exhibited no absorption bands due to hydroxy and carbonyl groups in the IR spectrum. The ^1H NMR spectrum of the product (**16**) exhibited a 3 proton singlet at δ 3.30, a 1 proton doublet of doublets at δ 4.08 with *J* 6.83 and 10.25 Hz, and a 2 proton AB quartet at δ 5.10 and 5.14 with *J* 1.0 Hz. These signals were assignable to the methoxy group, the proton attached to the carbon having an oxygen atom and protons of the methylendioxy group. On the basis of these spectral results together with mechanistic considerations the structure was assigned as 3α-methoxy-2α,3β-methylenedioxy-5α-cholestane (**16**). The assigned structure was also supported by the EI mass spectrum which exhibited an ion at *m/z* 130 as the base peak. The probable structure and the genesis are outlined in Figure 1.

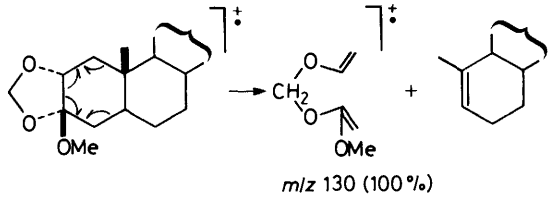


Figure 1.

*An ^{18}O Labelling Experiment of the Formation of Anhydride (**19**) in the Photolysis of 17β-Hydroxy-3β-methoxy-5α-androstan-16-one hypoiodite.*—In order to confirm the pathway which led to the anhydride (**19**), an ^{18}O labelling experiment was performed by irradiating a solution of the hypoiodite, prepared *in situ* from the α-ketol (**18**) with an excess of $Hg^{18}O$ (^{18}O, 88 atom %) and iodine in dry benzene under the conditions described above. The anhydride (**19**) was first transformed into 3β-methoxy-17a-homo-17-oxa-5α-androstan-16-one (**20**) with $NaBH_4$ and then into 3β-methoxy-17a-homo-17-oxa-5α-androstane (**21**) with $LiAlH_4$–BF_3·OEt_2. The extent of the incorporation of ^{18}O into the lactone (**20**) and cyclic ether (**21**) was analyzed by means of mass spectrometry. The molecular ion in the mass spectrum of lactone (**20**) indicated that only one ^{18}O atom was incorporated in the lactone (**20**). The molecular ion in the mass spectrum of the cyclic ether (**21**) indicates that 30% of ^{18}O was incorporated as the ring oxygen.

Discussion

The foregoing experiments indicated that the alkoxyl radicals generated from the 5- or 6-membered cyclic α-ketols fragment at their C–C bonds between the carbon having alkoxyl radical and the carbonyl group and an oxygen is inserted to give cyclic anhydrides. Our experiments also disclosed that the alkoxyl radical generated from a 6-membered cyclic alcohol having *gem* dimethoxy groups does not fragment but abstracts a hydrogen of the methoxy group attached to the α-carbon.

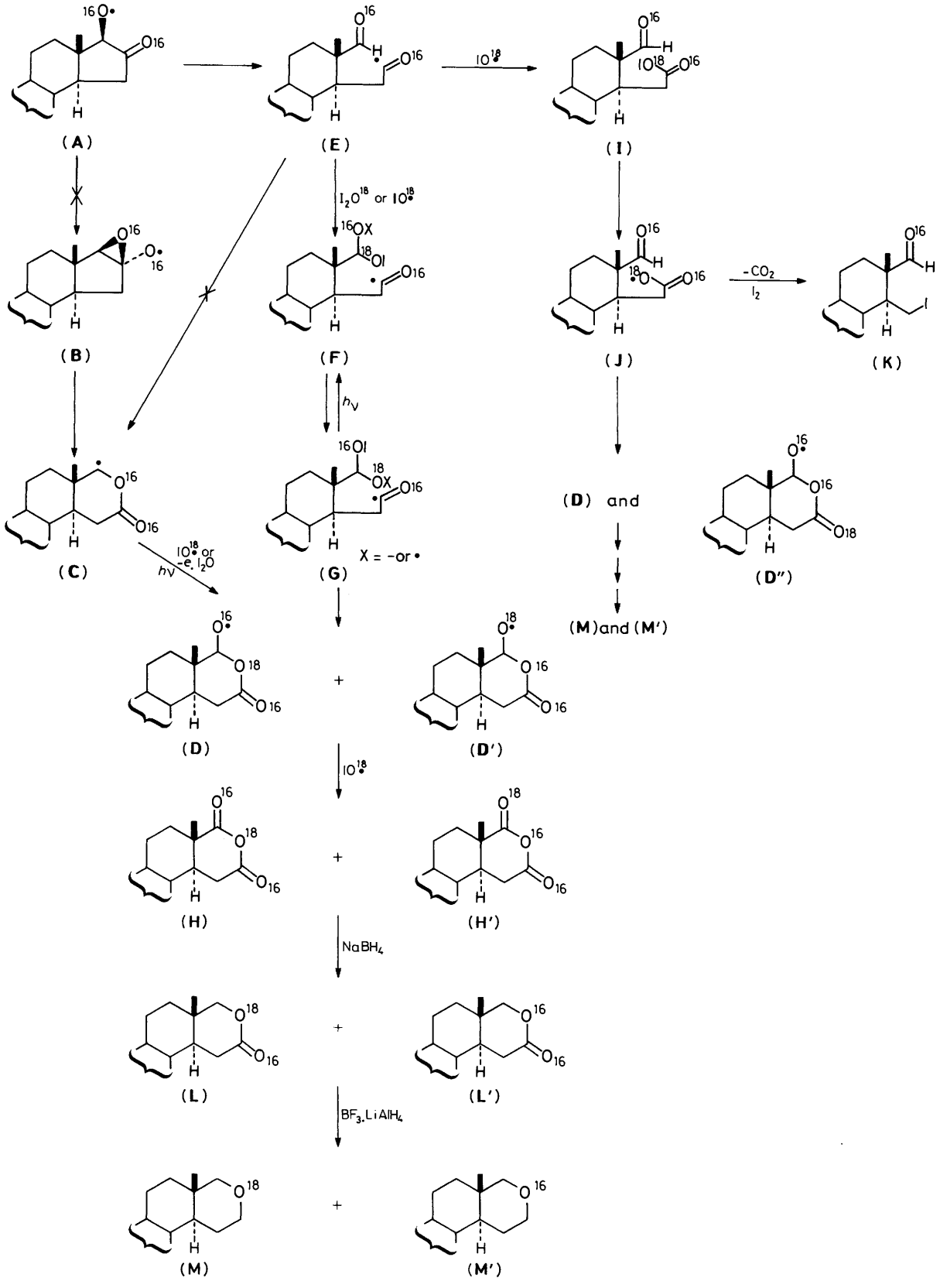
Several pathways can be considered for the formation of the cyclic anhydrides (**13**) and (**19**) on the basis of our knowledge of the photolysis of the hypoiodites generated with mercury(II) oxide and iodine.[2,3,20] Probable pathways leading to the anhydride (**19**) are outlined in Scheme 5. The result of the above ^{18}O labelling study suggests that the anhydride (**19**) is formed through the reaction of an intermediate (**E**), generated from a regioselective β-scission of the alkoxyl radical (**A**), with I_2O or $^{\bullet}OI$.

Anhydride (**19**) can be formed either through an intermediate (**F**) or through another intermediate (**I**). (**F**) and (**I**) are formed either through the reaction of the formyl carbon of (**E**) with I_2O or $^{\bullet}OI$[3] or through a radical combination between the carbonyl radical of (**E**) and $^{\bullet}OI$. Scrambling of ^{16}O and ^{18}O in the cyclization of (**D**) and (**D′**) from (**F**) may take place through intermediate (**G**) that is interconvertible with (**F**). Alternatively, the cyclization of radical (**J**) generated from (**I**) may give (**D**), and (**D″**) in which ^{16}O and ^{18}O are scrambled at their ring oxygen. The extent of the incorporation of the ^{18}O into the ring oxygen of oxasteroids (**M**) and (**M′**), proved by the above ^{18}O labelling study, is consistent with this path. It is worth noting that no products arising from the fragmentation of the C(13)–C(17) bond of the alkoxyl radical (**A**) or of the C(13)–C(17a) bond of hypothetical precursors (**D**), (**D′**), and (**D″**) were obtained. Of these paths, the path through (**I**) seems less probable since intermediate (**J**) would give a product (**K**) by a loss of CO_2 rather than (**D**) and (**D″**) by cyclization.

Other hypothetical paths to anhydride (**19**) involve intermediate (**C**) through either species (**B**) or (**E**). These paths are, however, excluded on the basis of the results of the above ^{18}O labelling experiments.

The product (**16**) of the photolysis of the hypoiodite of alcohol (**10**) is apparently formed by an intramolecular hydrogen abstraction from the 3β-methoxy group through a favoured 6-membered transition state (**N**) (Scheme 6) by the 2α-alkoxyl radical. The analogous formation of a methylenedioxy group *via* an intramolecular hydrogen abstraction from a methoxy group by an alkoxyl radical generated from steroidal α-methoxy alcohols with lead tetra-acetate has previously been reported by Morand and Kaufman[22] although the mode of the reported reaction[22] is not exactly same as ours. The intramolecular hydrogen abstraction is thus apparently faster than β-scission in the α-dimethoxy alkoxyl radical (**N**) as we

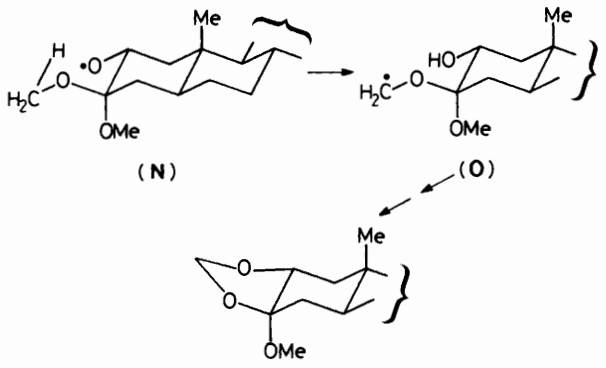
* Nomenclature according to 1989 I.U.P.A.C. recommendations: *Pure Appl. Chem.*, 1989, **61**, 1783.



Scheme 5.

have already found in the alkoxyl radical generated from the α-acetoxy alcohol[19] owing to appropriate geometry for the intramolecular hydrogen abstraction.

The formation of 5- and 6-membered cyclic anhydrides involving a new type of insertion of oxygen into the ring performed by an α-oxo alkoxyl radical at room temperature



(16)

Scheme 6.

may be of potential utility for the synthesis of oxasteroids and related molecules.

Experimental

For the instruments and the general procedure for the hypoiodite photolysis described in this work see reference 2.

Preparation of 3,3-*Dimethoxy*-5*a*-*cholestan*-2α-*ol* (**11**).—To 3-methoxy-5α-cholest-2-ene (1 g, 2.5 mmol) in methanol–dichloromethane (1:1) (15 ml) MCPBA (615 mg) in methanol (5 ml) was added at 0 °C. After the solution had been stirred for 1.5 h, the solvent was removed by a rotary evaporator. The residue was dissolved in diethyl ether and washed with 5% sodium thiosulphate solution, 5% sodium hydrogen carbonate solution, water and saturated brine successively and dried (Na_2SO_4). The usual work-up of the solution gave a crude 2α-ol (**11**) (1.09 g) which was recrystallized from methanol–acetone (878 mg, 78%), m.p. 123–125 °C (Found: C, 77.65; H, 11.65. $C_{29}H_{52}O_3$ requires C, 77.62; H, 11.68%); ν_{max}(Nujol) 3 447 cm^{-1} (OH); δ (270 MHz) 0.64 (3 H, s, 18-H), 0.82 (3 H, s, 19-H), 3.45 (3 H, s, OMe), 3.49 (3 H, s, OMe), and 3.75 (1 H, m, 2β-H); *m*/*z* 448 (M^+, 27%) and 127 (100).

2α-*Hydroxy*-5α-*cholestan*-3-*one* (**12**).—To 3,3-dimethoxy-5α-cholestan-2α-ol (**11**) (255 mg, 0.57 mmol) in THF (5 ml) 2M hydrochloric acid (0.5 ml) was added dropwise at 0 °C. The solution was stirred for 6 h at room temperature and THF was evaporated under reduced pressure. The remaining aqueous solution was extracted with diethyl ether. The organic layer was worked up by the usual method to give crystals which were recrystallized from acetone to yield ketone (**12**) (168 mg, 74%), m.p. 144–146 °C, (lit.,[4a] m.p. 125–127 °C; lit.,[4b] m.p. 126–128 °C; lit.,[4c] m.p. 160–162 °C); δ(200 MHz) 0.67 (3 H, s, 18-H), 1.09 (3 H, s, 19-H), 3.51 (1 H, d, *J* 3.42 Hz, OH), and 4.25 (1 H, ddd, *J* 3.42, 6.84 and 11.23 Hz, 2β-H); ν_{max}(Nujol) 3 447 (OH), and 1 721 cm^{-1} (C=O); *m*/*z* 402 (M^+, 83%), 247 [(M − D-ring)$^+$, 100] and 248 (81).

Irradiation of the Hypoiodite of 2α-*Hydroxy*-5α-*cholestan*-3-*one* (**12**) *in the Presence of Mercury*(II) *Oxide and Iodine*.—The alcohol (**12**) (203 mg, 0.5 mmol) in dry benzene (35 ml) containing mercury(II) oxide (328 mg, 1.5 mmol) in a Pyrex vessel was flushed with nitrogen and was irradiated with a 100-W high pressure Hg arc for 5 h. The solution was filtered and the filtrate was washed with 5% aqueous sodium thiosulphate and water successively and dried (Na_2SO_4). The solution was worked up as usual to yield crude anhydride (**13**) (237 mg) as an amorphous solid which was immediately subjected to reduction with sodium borohydride (Found: *m*/*z* 416.3260. $C_{27}H_{44}O_3$ requires *M* 416.3288); ν_{max}(Nujol) 1 811 and 1 752 (anhydride group) and 1 045 cm^{-1}; δ(100 MHz) 0.66 (3 H, s, 18-H) and 1.00 (3 H, s, 19-H); *m*/*z* 416 (M^+, 24%) and 43 (100).

Basic Hydrolysis of Anhydride (**13**) *to Diacid* (**14**) *and Regeneration of Anhydride* (**13**) *with DCC*.—Crude anhydride (**13**) (237 mg) was dissolved in 2M aqueous sodium hydroxide and the solution was stirred for 7 h at room temperature. The solution was filtered and the filtrate was extracted with diethyl ether. The aqueous solution was then neutralized with 2M hydrochloric acid and extracted with dichloromethane. The organic layer was washed with water and dried (Na_2SO_4). Removal of the solvent gave crude diacid (**14**) which was recrystallized from acetone, m.p. 192–195 °C. (lit.,[12] 195–196 °C). ν_{max}(Nujol) 3 400 (OH), 1 705 (C=O), and 1 204 cm^{-1}; δ(270 MHz) 0.65 (3 H, s, 18-H) and 0.85 (3 H, s, 19-H); *m*/*z* 434 (M^+, 1.1), 416 [(M − H_2O)$^+$, 5.0], 388 (4.6), and 374 (100).

Dicyclohexylcarbodi-imide (DCC) (22 mg, 0.11 mmol) was added to a solution of dibasic acid (**14**) (47 mg, 0.11 mmol) in dioxane (5 ml). The solution was stirred at room temperature overnight and then filtered. Evaporation of the solvent gave cyclic anhydride (39 mg, 85%) which was recrystallized from methanol-acetone, m.p. 140–142 °C (lit.,[12] m.p. 140–141 °C).

Reduction of 4a-*Homo*-3-*oxa*-5α-*cholestane*-2,4-*dione* (**13**).—Crude cyclic anhydride (**13**) (108 mg, 0.26 mmol) obtained as above in THF (3 ml) was added to $NaBH_4$ (12 mg) in THF (2 ml) at 0 °C. The solution was stirred for 1 h at room temperature and excess $NaBH_4$ was then decomposed with 2M hydrochloric acid. The solution was extracted with diethyl ether and the organic layer was worked up as usual to give a crude diol (**15**) which was purified by means of preparative TLC with ethyl acetate–hexane (4:1) as eluant, m.p. 154–156 °C (lit.,[13] 156–157 °C) (25 mg), ν_{max}(Nujol) 3 320 (OH), 1 217 (C–O), and 1 042 and 1 019 cm^{-1}; δ(90 MHz), 0.65 (3 H, s, 18-H), 0.90 (3 H, s, 19-H), and 3.45–3.86 (4 H, m, CH_2OH); *m*/*z* 406 (M^+, 2.8) and 361 (100%).

Irradiation of the Hypoiodite of 3,3-*Dimethoxy*-5a-*cholestan*-2α-*ol* (**11**).—The 2α-ol (**11**) (203 mg, 0.45 mmol) in a benzene–pyridine (50:1) containing mercury(II) oxide (196 mg, 0.90 mmol) was flushed with a nitrogen and irradiated with a 100-W high pressure Hg arc through a Pyrex-filter for 9.5 h under an atmosphere of nitrogen. The solution was then filtered and the filtrate was worked up in a usual manner to give products which were subjected to preparative TLC with benzene–diethyl ether (2:1). Two fractions were obtained. The less mobile fraction (123 mg, 61%) was unchanged starting material. The more mobile fraction (46 mg, 23%) was 3α-methoxy-2α,3β-methylenedioxy-5α-cholestane (**16**) (Found: C, 77.85; H, 11.10. $C_{29}H_{50}O_3$ requires C, 77.97; H, 11.28%); ν_{max}(Nujol) 1 108 cm^{-1} (C–O); *m*/*z* 446 (M^+, 86%) and 130 (100); δ(200 MHz) 0.64 (3 H, s, 18-H), 0.79 (3 H, s, 19-H), 3.30 (3 H, s, OMe), 4.08 (1 H, dd, *J* 6.83 and 10.25 Hz, 2β-H), and 5.10 and 5.14 (each 1 H, each d, *J* 1.0 Hz, OCH_2O).

3β-*Methoxy*-5α-*androstan*-17-*one*.—This steroidal ether was prepared according to the published procedure.[10]

Preparation of the Trimethylsilyl Enol Ether (**17**) *of* 3β-*Methoxy*-5α-*androstan*-17-*one*.—To THF (3 ml) containing diisopropylamine (0.33 ml), butyl-lithium (1.55M hexane solution; 3.1 ml, 4.85 mmol) was added at −78 °C dropwise while stirring. The solution was stirred for half an hour at −78 °C. Trimethylsilyl chloride (0.42 ml, 3.88 mmol) was then added to this solution and the solution was stirred for 2 h at −78 °C and then the temperature of the solution was raised to room

temperature. After adding hexane (15 ml) to this solution, the solvent was removed under reduced pressure. To the residue, hexane was again added and after filtration the solvent was evaporated to yield colourless crystals of trimethylsilyl ether (**17**) (724 mg). This enol ether was used for the next step without further purification.

Preparation of 17β-*Hydroxy*-3β-*methoxy*-5α-*androstan*-16-*one* (**18**).—To hexane (3 ml) containing MCPBA (418 mg), trimethylsilyl enol ether (**17**) (724 mg) in hexane (18 ml) was added at 0 °C. The solution was stirred for 1 h. After the solution was filtered the solvent was evaporated to yield the crude epoxide as an oil which was dissolved in diethyl ether (10 ml). To this solution 2M aqueous sodium hydroxide (10 ml) was added and the solution was stirred for 48 h at room temperature. The organic layer was washed with water and then brine and dried (Na_2SO_4). After the removal of the solvent the residue was subjected to preparative TLC with hexane–ethyl acetate (3:1) as eluant to yield the α-hydroxy ketone (**18**) (99 mg). After recrystallization from acetone, colourless crystals of the ketone (**18**) melted at 186–188 °C (Found: C, 74.85: H, 10.1. $C_{20}H_{32}O_3$ requires C, 74.96; H, 10.06%); ν_{max}(Nujol) 3 387 (OH), 1 741 (C=O), and 1 076 cm^{-1}; δ(270 MHz) 0.71 (3 H, s, 18-H), 0.84 (3 H, s, 19-H), 3.13 (1 H, m, 3α-H), 3.35 (3 H, s, OMe), and 3.75 (1 H, s, 17α-H); *m/z* 320 (M^+, 35.8%) and 251 [(M − MeOH − D-ring)$^+$, 100].

Irradiation of the Hypoiodite of 17β-*Hydroxy*-3β-*methoxy*-5α-*androstan*-16-*one* (**18**) *in the Presence of Mercury*(II) *Oxide and Iodine*.—The α-ketol (**18**) (105 mg, 0.33 mg) in dry benzene (20 ml) containing mercury(II) oxide (214 mg, 0.99 mmol) and iodine (251 mg, 0.99 mmol) in a Pyrex vessel was flushed with nitrogen. The solution was irradiated with a 100-W high pressure Hg arc for 9 h. The solution was then worked up in the usual manner to yield a crude cyclic anhydride, 3β-methoxy-17-oxa-17a-homo-5α-androstan-16,17a-dione (**17**); ν_{max}(neat) 1 806 and 1 761 cm^{-1} (anhydride group); δ(270 MHz) 0.79 (3 H, s, 19-H), 1.19 (3 H, s, 18-H), 3.13 (1 H, M, 3α-H), and 3.34 (3 H, s, OMe).

Reduction of 3β-*Methoxy*-17a-*homo*-17-*oxa*-5α-*androstane*-16,17a-*dione* (**19**) *with Sodium Borohydride*.—To THF (2 ml) containing $NaBH_4$ (15 mg), a solution of the anhydride (**18**) (110 mg) in THF (2 ml) was added at 0 °C. The solution was stirred for 1 h and an excess of $NaBH_4$ was decomposed with a 2M hydrochloric acid. The solution was then extracted with diethyl ether. The organic layer was worked up by the usual method to give a crude lactone (**20**) which was purified by means of preparative TLC with hexane–ethyl acetate (3:1). Crystals of the lactone (37 mg, 35%) obtained were recrystallized from methanol–hexane to give a specimen for analysis, m.p. 145–148 °C (Found: *m/z* 320.2382. $C_{20}H_{32}O_3$ requires *M*, 320.2351); ν_{max} 1 724 cm^{-1} (C=O); δ(200 MHz) 0.80 (3 H, s, 19-H), 0.99 (3 H, s, 18-H), 2.09 (2 H, dd, *J* 12.7 and 18.8 Hz, 15β-H), 2.72 (1 H, dd, *J* 5.86 and 18.8 Hz, 15α-H), 3.07 (1 H, m, 3α-H), and 3.96 (1 H, d, *J* 10.7 Hz, 17a-H); *m/z* 320 (M^+, 19%) and 97 (100).

Reduction of 3β-*Methoxy*-17a-*homo*-17-*oxa*-5α-*androstan*-16-*one* (**20**) *with Lithium Aluminium Hydride–Boron Trifluoride–Diethyl Ether*.—To THF (2 ml) containing the lactone (**20**) (22 mg, 0.068 mmol) and BF_3–Et_2O complex (0.28 ml), lithium aluminium hydride (15 mg) in THF (2 ml) was added at 0 °C. The solution was stirred for 6 h at room temperature and then water and diethyl ether were added. The aqueous layer was extracted with diethyl ether. The combined organic layers were washed with saturated brine and then water and dried (Na_2SO_4). The usual work-up gave a residue which was subjected to preparative TLC with hexane–ethyl acetate (1:1) as eluant to give 3β-methoxy-17a-homo-17-oxa-5α-androstane (**21**) (5 mg, 24%), m.p. 83–85 °C (Found: *M*, 306.2554. $C_{20}H_{34}O_2$ requires M^+, 306.2558); ν_{max} 2 930, 1 123, and 1 095 cm^{-1}; δ(270 MHz) 0.79 (3 H, s, 19-H), 0.96 (3 H, s, 18-H), 2.95 and 3.37 (each 1 H, each d, *J* 10.81 Hz, 17aα- and 17aβ-H), 3.13 (1 H, m, 3α-H), 3.33 (1 H, ddd, *J* 10.50, 3.10, and <1 Hz, 16-H) 4.03 (1 H, ddd, *J* 10.50, 3.10, and 1 Hz, 16-H), and 3.34 (3 H, s, OMe); *m/z* 306 (M^+, 53%) and 274 (100).

Preparation of exo- *and* endo-3-*Hydroxycamphors* (**24**) *and* (**25**).—Butyl-lithium [34.5 ml (54.0 mmol) of 1.55M hexane solution] was dropwise added to a stirred solution of isopropylamine (4.5 ml, 32.4 mmol) in dry THF (5 ml) at −78 °C and the solution was stirred for 30 min. To this solution, (+)-camphor (4.10 g, 27.0 mmol) in THF (5 ml) was added dropwise and the solution was again stirred for 1 h. To this solution, trimethylsilyl chloride (6.8 mmol) was added. After the solution had been stirred for 2 h at −78 °C its temperature was raised to room temperature and water and diethyl ether were added. The separated organic layer was dried ($MgSO_4$) and the solvent evaporated to give an unstable colourless crystalline trimethylsilyl enol ether (**23**) (5.77 g, 99%), ν_{max}(neat) 1 620 cm^{-1} (C=C); δ(90 MHz) 0.18 (9 H, s, Me_3Si), 0.71 (3 H, s, 10-H), 0.87 (6 H, s, 8-H and 9-H), and 4.62 (1 H, d, *J* 3.3 Hz, 3-H).

To a solution of MCPBA (80%) (5.81 g, 27.0 mmol) in hexane (20 ml), trimethylsilyl enol ether (**23**) (5.77 g, 27.0 mmol) in hexane (6 ml) was added at 0 °C with stirring. The solution was stirred for 24 h at room temperature and then the solvent evaporated under reduced pressure to give a crude product. After the addition of diethyl ether (10 ml) and aqueous sodium hydroxide (2M; 10 ml) to the product, the solution was stirred for 48 h at room temperature. The separated aqueous layer was neutralized with 2M hydrochloric acid and extracted with diethyl ether. The combined ether layers were washed with water and brine and dried ($MgSO_4$). Evaporation of the solvent gave a residue which was subjected to a column chromatography (silica gel, 100 g). Elution with hexane–ethyl acetate (3:1) gave a 1:1 mixture of 3-hydroxycamphors (**24**) and (**25**) (300 mg, 7%), as colourless crystals; ν_{max}(Nujol) 3 433 (OH) and 1 741 cm^{-1} (C=O); δ(270 MHz) 3.76 (1 H, s, *exo* 3-H), 4.22 (1 H, d, *J* 4.76 Hz, *endo* 3-H) (lit.,[11] *exo* 3-H, 3.72, s; *endo* 3 H, 4.28, d, *J* 5 Hz).

Irradiation of the Hypoiodites of exo- *and* endo-3-*Hydroxycamphors* (**24**) *and* (**25**) *in Benzene in the Presence of Mercury*(II) *Oxide and Iodine*.—The 3-hydroxycamphors (**24**) and (**25**) (101 mg, 0.60 mmol) in benzene (25 ml) containing mercury(II) oxide (390 mg, 1.80 mmol) and iodine (465 mg, 1.80 mmol) were irradiated for 3 h under the conditions as described for the steroidal α-ketols. The crude product was subjected to preparative TLC with hexane–ethyl acetate (3:1) as eluant to give (+)-*cis*-camphoric anhydride (41 mg, 38%), m.p. 222–225 °C (from acetone) (lit.,[15] 220–221 °C). ν_{max}(Nujol) 1 801 (C=O) and 1 762 cm^{-1} (C=O); δ(90 MHz) 1.01 (3 H, s, 7-Me), 1.10 (3 H, s, 7-Me), 1.27 (3 H, s, 1-Me), 2.11 (4 H, m, 5-H and 6-H), and 2.83 (1 H, d, *J* 6.37 Hz, 4-H).

The ^{18}O *Labelling of the Anhydride* (**19**).—Irradiation of the hypoiodite of 17β-hydroxy-3β-methoxy-5α-androstan-16-one (**18**) (50 mg, 0.16 mmol) in the presence of mercury(II) [^{18}O] oxide (102 mg, 88 atom % ^{18}O) and iodine (118 mg) was performed under the same conditions as those described above. Mercury(II) [^{18}O]oxide was prepared as described previously.[3]

The Transformation of the Labelled Anhydride (**13**) *into the Lactone* (**20**) *as well as the Transformation of the Lactone* (**20**) *into the Oxasteroid* (**21**).—These transformations were carried

out as described for the reductions of the unlabelled anhydride (**13**) and lactone (**20**).

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