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Studies Towards the Synthesis of Polyoxygenated Steroids[1]. Reaction of Some Tri- and Tetra-Substituted Monoene Steroids with RuO_4

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Abstract.- The course of the reaction of ruthenium tetroxide with some tri- and tetra-substituted nuclear monoene steroids, namely Δ^4, Δ^5, Δ^7 and $\Delta^{8(14)}$-steroids, has been investigated in acetone-water or carbon tetrachloride as solvent systems using stoichiometric amounts of the oxidant. In contrast with results previously reported for RuO_4 oxidations, we found that trisubstituted double bonds gave α-hydroxy ketones and/or 1,2-diols rather than the expected products deriving from the scission of the carbon-carbon double bond. Scission of the double bond indeed occurs when fully substituted steroidal alkenes are oxidized. Only in the case of the $\Delta^{8(14)}$-steroid, an allylic oxidation product wa obtained in addition to the scission product. The change in the solvent system seems to profoundly affect the course of the reaction.

Since its introduction in 1953 as an organic oxidant by Djerassi and Engle[2], ruthenium tetroxide has been employed to oxidize a variety of compounds such as alcohols, ethers, carbohydrates, alkynes, sulfur compounds, and cyclic amines and for the cleavage of olefins, aromatic rings, conjugated ketones, enolethers and enamines[3-7]. Ruthenium tetroxide is usually produced in situ from ruthenium dioxide and sodium metaperiodate in aqueous acetone solution[8] or in a two-phase system of carbon tetrachloride-water[9]. Addition of acetonitrile to the carbon tetrachloride-water system is reported to improve the procedure for ruthenium tetroxide catalyzed oxidation[10].

There are few reports on the oxidative cleavage of alkenes with stoichiometric amounts of ruthenium tetroxide in absence of a secondary oxidant[11-14] possibly because the yields are low[11,12]. Instead, the reaction has been usually conducted with catalytic amounts of ruthenium

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Dedicated to professor Carl Djerassi on the occasion of his 70th birthday.

tetroxide in the presence of a cooxidant such as sodium metaperiodate[8,10,15-22] that continuously regenerates RuO_4 from RuO_2. Isolated carbon-carbon double bonds are reported[3,4,7] to react with ruthenium tetroxide to give only cleavage products that is aldehydes and ketones or carboxylic acids.

In this paper we report the results of a study aimed at the clarification of the reactivity of a number of nuclear steroidal alkenes towards ruthenium tetroxide and, eventually, at the collection of data which could throw light on the mechanism of this oxidation reaction.

Our research started from the fortuitous observation that cholest-5-en-3β-yl acetate, when treated in acetone-water with a stoichiometric amount of RuO_4 in the absence of a cooxidant, did not give the expected 5,6-secosterol while afforded a mixture of the known 3β-acetoxy-5-hydroxy-5α-cholestan-6-one[23] **7** and 5α-cholestane-3β,5,6α-triol 3-acetate[24] **8**, in the approximate ratio of 2:1 (**7**: 60% yield; **8**: 32% yield) (Table 1, entry 3). Compounds **7** and **8** were characterized by ^1H- and ^{13}C-NMR data[23] and comparison with authentic specimens. The observed stereochemistry at C-5 in **7** and at C-5/C-6 in **8** requires a syn attach of the reagent from the less hindered α face of the molecule.

This unexpected result prompted us to extend our oxidation procedure, with acetone-water-RuO_4 system to some other easily available trisubstituted steroidal alkenes such as cholest-4-en-3β-yl acetate (entry 1), androst-4-ene-3β,17β-diol diacetate (entry 2), 5α-cholest-7-en-3β-yl acetate (entry 5) and its 6α-acetossiderivative 5α-cholest-7-ene-3β,6α-diol diacetate (entry 6), synthesized from 7-dehydrocholesterol by hydroboration with the BH_3-THF complex followed by treatment with alkaline hydrogen peroxide and then with Ac_2O-pyridine[25].

Cholest-4-en-3β-yl acetate and androst-4-ene-3β,17β-diol diacetate showed very similar chemical behaviour towards RuO_4 oxidation giving the 5α-hydroxy-4-ketosterol derivatives, **1** (72% yield) and **4** (50% yield), respectively, as the major reaction products which were accompanied by minor amounts of the corresponding 4α,5α- and 4β,5β-dihydroxyderivatives: **2** (11% yield) and **3** (5% yield) from cholest-4-en-3β-yl acetate and **5** (32% yield) and **6** (6% yield) from the androstene substrate. In both the reactions the 4α,5α-isomer predominate over the 4β,5β one. The α-hydroxy ketone **1** and diols **2** and **3** were identified on comparison of their spectral properties (see experimental) with those reported in literature[26] and through additional spectral data. Compounds **2** and **3** have previuosly been synthesized from cholest-4-en-3β-yl acetate by treatment with osmium tetroxide[26]; 1,2-ketol **1** has been synthesized by chromium trioxide-pyridine oxidation of diol **2**[26].

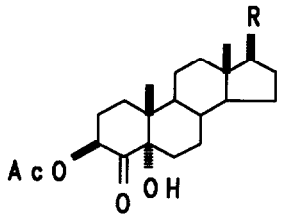
The mass spectra of 5-hydroxysteroids **1-6** revealed the characteristic breakdown of ring A and the loss of atoms C-1 to C-4[27].

When the reaction was performed on 5α-cholest-7-en-3β-yl acetate (entry 5) the hitherto unknown 3β-acetoxy-8α-hydroxy-5α-cholestan-7-one

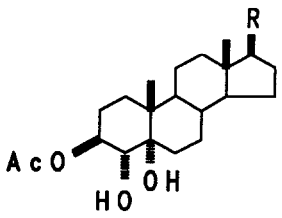
Table 1. RuO_4 oxidation of some steroidal alkenes in acetone-water.

Entry	Substrate	Products	Reaction time (min)	Yield[a] (%)
1	Cholest-4-en-3β-yl acetate	1	5	72
		2		11
		3		5
2	Androst-4-ene-3β,17β-diol diacetate	4	10	50
		5		32
		6		6
3	Cholest-5-en-3β-yl acetate	7	120	60
		8		32
4	3β-Acetoxy-6-methylpregn-5-en-20-one	9	10	100
5	5α-Cholest-7-en-3β-yl acetate	12	5	34
		13		33
6	5α-Cholest-7-ene-3β,6α-diol diacetate	14	30	49
7	5α-Cholest-8(14)-ene-3β, 7α-diol diacetate	15	20	44
		16		35

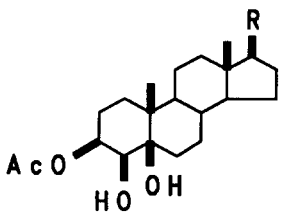
a. Yields are for isolated products.



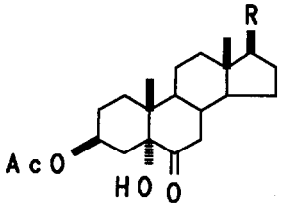
1 R = C_8H_{17}
4 R = OAc



2 R = C_8H_{17}
5 R = OAc



3 R = C_8H_{17}
6 R = OAc



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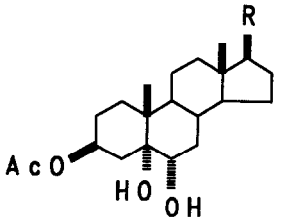
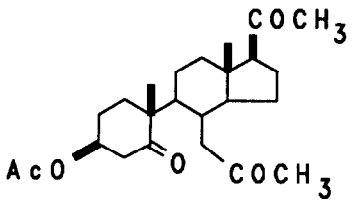


8 R = C_8H_{17}



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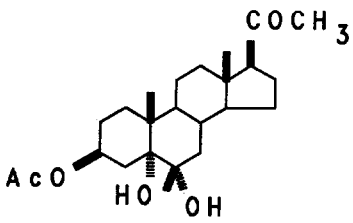

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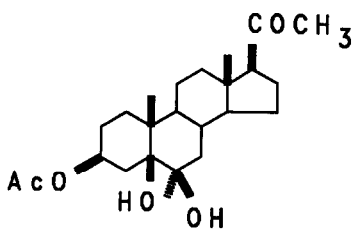

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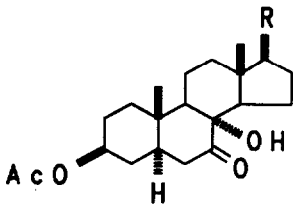

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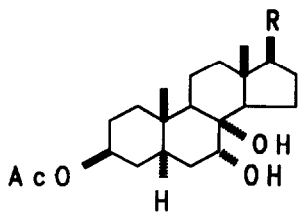
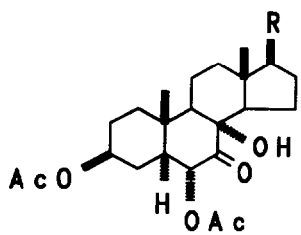
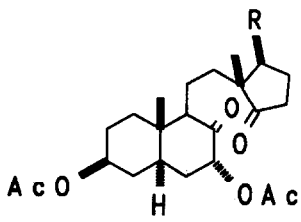


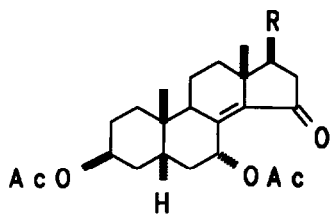
13 R = C_8H_{17}



14 R = C_8H_{17}



15 R = C_8H_{17}



16 R = C_8H_{17}

12 (34% yield) and 5α-cholestane-3β,7α,8α-triol 3-acetate **13** (33% yield) were obtained. The structure of these compounds was deduced from spectral analyses. The ^{13}C-NMR spectrum of **12** included signals for a ketonic carbonyl group at δ 210.51 (C-7) and an oxygen-bearing fully substituted carbon at δ 78.74 (C-8) while lacked resonances pertinent to the Δ^7 double bond. The presence of a hydroxyl group in the molecule was inferred from the IR spectrum (ν_{max}= 3474 cm^{-1}). These data indicated that the Δ^7 carbon-carbon double bond had been transformed, on reaction with RuO_4, into an α-ketol group. The C8-OH group is α-oriented as expected by the attack of RuO_4 on the Δ^7-double bond from the less hindered α face of the molecule. The unnatural stereochemistry at C-8 was also supported by the chemical shift value of the H-5 proton which resonated largely deshielded at δ 3.08 due to the vicinity in the space with the C-8 hydroxyl group, as judged from the examination of the Dreiding model of the molecule. A strong pyridine-induced shift of H-5 ($\Delta\delta$= 0.51 ppm)[28] reinforced the above conclusion. In addition, a nOe effect was seen in the H-5 proton when the OH-8 proton was irradiated.

Diol **13** had ^{1}H- and ^{13}C-NMR spectra strongly reminiscent of those of compound **12** except for the resonaces pertinent to the C-7 hydroxymethine grouping (^{1}H-NMR: δ 4.13, dd, H_β-7; ^{13}C-NMR: 69.95, d, C-7) which replaces

the C-7 keto group present in **12**. The relationship between **12** and **13** was finally proved by chromium trioxide-pyridine oxidation of **13** to **12**.

Interestingly, when the time of this reaction was prolonged to 55 min., the yield of the α-hydroxy ketone **12** increased to 56%, and that of the diol **13** decreased to 12% while the overall yield in the oxidation products, α-ketol plus 1,2-diol, remained virtually constant.

Using 5α-cholest-7-ene-3β,6α-diol diacetate as a substrate (entry 6), the hitherto unknown 3β,6α-diacetoxy-8α-hydroxy-5α-cholestan-7-one **14** was obtained in 49% yield while no trace of the corresponding 7α,8α-diol was detected. The stereostructure of compound **14** was established through spectroscopic analyses taking into account the strong similarity of the ^{1}H- and ^{13}C-NMR spectra (see experimental) of **14** with those of **12**. Compound **14** has never been synthesized before.

Even more interesting was the result of the RuO_4 oxidation when a Δ^5 fully substituted steroidal alkene, namely 3β-acetoxy-6-methylpregn-5-en-20-one, was used as substrate. In this case the hitherto unknown 5,6-secosterol **9**, deriving from the scission of the Δ^5 double bond, was obtained as the sole product (100% yield). No trace of the 5α,6α- and 5β,6β-diols, **10** and **11**, respectively, was found (HPLC analysis).

The following spectral evidences are in agreement with the proposed structure **9** for this compound. The mass spectrum of **9** contained a molecular ion peak at m/z 404 which suggested a molecular formula of $C_{24}H_{36}O_5$ for this compound. The ^{13}C-NMR spectrum displayed three ketonic carbonyl resonances at δ 216.20, 209.49 and 209.08 while the ^{1}H-NMR spectrum showed signals for three $-COCH_3$ groups at δ 2.10, 2.00 and 1.98. The IR absorption band at 1718 cm^{-1} further supported the presence of ketonic functionalities in the molecule. Compound **9** has never been synthesized before.

With this result at hand and with the aim of gaining further insight into the reactivity of tetrasubstituted steroidal alkenes, a $\Delta^{8(14)}$-substrate was chosen as the next candidate to be subjected to the RuO_4 oxidation. The reaction performed on 5α-cholest-8(14)-ene-3β,7α-diol diacetate, synthesized from 5α-cholest-7-en-3β-ol according to Fieser and Ourisson[29], gave two major products. The most abundant product (44% yield) was identified as the 8,14-secosterol **15** confirming that tetrasubstituted alkenes seem to prefer the scission of the carbon-carbon double bond. In agreement with the proposed structure the ^{13}C-NMR spectrum of **15** showed two newly created carbonyl resonances at δ 206.81 and 224.76 for carbons C-8 and C-14, while its mass spectrum displayed a molecular ion peak at m/z 518 which supported a $C_{31}H_{50}O_6$ molecular formula for this compound.

The second product (35% yield) was found to be the product of allylic oxidation at C-15 (**16**). Its structure was established on the basis of the following spectral evidences. The ^{13}C-NMR spectrum of **16** showed resonances attributable to the $\Delta^{8(14)}$ double bond at δ 146.12 and 141.70, and included a signal at δ 206.99 for an α,β-unsaturated carbonyl

group at C-15[30] which was also supported by UV absorption at 249 nm (ϵ= 13180)[31] and IR band at 1718 cm^{-1}. The remainder of the spectral data are in agreement with the proposed structure. Compounds **15** and **16** have never been synthesized before.

It is to be noted that the sole example of allylic RuO_4 oxidation so far reported in literature concerns lanost-8-en-3β-yl acetate, a molecule including a tetrasubstituted double bond in the structure. This product on RuO_4 oxidation gave, along with the expected 8,9-secoderivative, an enedione product deriving from the oxidation both at C-7 and C-11 positions[14].

All the reactions described above were also performed using carbon tetrachloride as solvent system. Interestingly, it was found that the change in the solvent markedly affected the course of the reaction as far as type and yield of the products is concerned, except in the case of 5α-cholest-8(14)-ene-3β,7α-diol diacetate which afforded the same derivatives **15** and **16** approximately with the same yields (Table 1).

Particularly, when referring to the oxidation of the cholest-4-en-3β-yl acetate, no trace of the α-ketol **1** (the major product obtained from the oxidation in acetone-water) was found, while 4α,5α- and 4β,5β-diols, **2** and **3** respectively, were obtained in 70% and 10% yields, respectively.

Similar results were obtained in the reaction on the androst-4-ene-3β,17β-diol diacetate. Compound **5** and **6** were obtained in 50% and 20% yields, respectively.

Likewise, the reaction performed on 5α-cholest-7-en-3β-yl acetate gave the 7α,8α-diol **13** in 55% yield while the α-hydroxy ketone **12** was obtained at all.

When cholest-5-en-3β-yl acetate was oxidized, the 5α,6α-diol **8** was obtained as the major product (60% yield); however, a little amount of α-ketol **7** (10% yield) was detected in this case.

The reaction on the 3β-acetoxy-6-methylpregn-5-en-20-one in carbon tetrachloride also diverged from that achieved in acetone-water. The 8,14-secosterol **9** was still obtained but only with 21% yield. This product was accompanied by little amounts of the 5α,6α- and 5β,6β-diols, **10** (6% yield) and **11** (7% yield), respectively. The structures of these compounds were deduced from interpretation of spectral data and finally confirmed by $Pb(OAc)_4$ scission of the 5,6-diol system to give the 5,6-secosterol **9**. In particular, the mass spectra of compounds **10** and **11** showed a common molecular ion peak at m/z 406 compatible with a $C_{24}H_{38}O_5$ molecular formula which indicated the presence of two more oxygen atoms in both the molecules. Chemical shift value and shape of the seven-line multiplet at δ 5.18 in the ^{1}H-NMR spectrum of **10** suggested it to be the normal 3α-H proton of an A/B trans 3β-acetoxysteroid having an oxygenated function linked at C-5 with the α-configuration[32,33]. The absence of the Δ^5 double bond was indicated by the chemical shift value of the signal for the 6_β-methyl group protons which resonated at δ 1.28 (in the 3β-acetoxy-6-

methylpregn-5-en-20-one these protons resonated at δ 1.62). This value well agreed with that expected for a methyl group geminal to oxygen. These data indicated that dihydroxylation at C-5 and C-6 had taken place during the reaction. The α-configuration at C-6 was assumed considering a syn attack of the reagent from the α face of the molecule.

Similar reasonings were applied to compound **11**. The only noticeable difference between the proton spectra of **10** and **11** was in the shape of the signal for the 3α-H proton which in **11** resonated as a broad singlet at δ 5.20. This observation indicated that a cis junction between rings A and B[34] was present in compound **11**. These data and the absence of the Δ^5 double bond (the protons of 6_α-methyl group resonated at δ 1.14 or 1.12) suggested that compound **11** was the 5β,6β-dihydroxy isomer of **10**.

In summary, ruthenium tetroxide oxidation of steroidal trisubstituted olefines provides a simple procedure for obtaining α-hydroxy ketones when the reaction is performed in acetone-water while furnishes mainly vicinal diols if the reaction is conducted in carbon tetrachloride. In the same conditions fully substituted steroidal alkenes give scission products. In one case an allylic oxidation product has been found.

REACTION MECHANISM CONSIDERATION

Little is known about the mechanism of the reaction of RuO_4 with double bonds. Kinetic studies indicated that the oxidation of the double bond proceeds via a cyclic ruthenium (VI) intermediate, which successively undergoes to oxidative cleavage to generate carbonyl compounds[35,7]. Our results concerning the oxidation of trisubstituted steroidal alkenes can be explained assuming that the initially formed cyclic ruthenium diester may undergo hydrolysis to an acyclic monoester derivative which in turn may undergo further scission to the 1,2-diol or an oxidative decomposition to give the α-ketol, as proposed for the mechanism of the permanganate oxidation of alkenes[36].

EXPERIMENTAL

^{1}H- and ^{13}C-NMR spectra were recorded on Bruker WM 270 and 400 spectrometers in $CDCl_3$ or pyridine-d_5 solutions. Proton chemical shifts were referenced to the residual $CHCl_3$ and pyridine signals (7.26 and 8.71 ppm, respectively). ^{13}C-NMR chemical shifts were referenced to the solvents ($CDCl_3$: 77.0 ppm; C_5D_5N: 149.9). The multiplicity of ^{13}C-NMR resonances was determined by DEPT experiments[38], which were performed

using polarization transfer pulses of 90° and 135°, obtaining in the first case only signals for CH groups and in the second case positive signals for CH and CH_3 and negative signals for CH_2 groups. The ^1H-^1H shift correlation experiments were performed with a COSY 45 sequence[39,40]. High-resolution electron impact mass spectra (HREIMS) were recorded on a Kratos Analytical Instruments AEI MS 902 spectrometer. Electron impact mass spectra (EIMS) were recorded on a TRIO 2000 mass spectrometer. FAB mass spectra were recorded on a Kratos MS 50 mass spectrometer equipped with a Kratos FAB source. Fourier transform IR spectra (FTIR) were obtained with a Perkin-Elmer 1760-X FT-ir spectrophotometer. Ultraviolet (UV) spectra were recorded with a Perkin-Elmer Model 550S spectrophotometer in CH_3OH solutions. High performance liquid chromatographies (HPLC) were performed using a Varian 2510 pump equipped with a Waters dual cell refractometer using Hibar LiChrosorb Si-60 (250 x 10 and 250 x 4 mm) and Hibar Superspher RP-18 (250 x 4 mm) columns. Melting points were determined on a Reichert Termovar type 300429 Kofler hot stage melting apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer Model 141 polarimeter in $CHCl_3$ solutions. Column chromatography was carried out on Merck silica gel 40 (70-230 mesh) and 60 (230-400 mesh). Thin-layer chromatography (TLC) analyses were performed on precoated silica gel F_{254} plates (0.25 thick, Merck).

RuO_4 OXIDATION IN ACETONE-WATER. GENERAL PROCEDURE.

Oxidation of cholest-5-en-3β-yl acetate. Synthesis of 3β-acetoxy-5-hydroxy-5α-cholestan-6-one (7) and 5α-cholestane-3β,5,6α-triol 3-acetate (8) (entry 3).

To a suspension of sodium metaperiodate (130 mg, 0.608 mmol) in acetone-water (5:1, 24 mL), $RuO_2 \cdot 2H_2O$ (18 mg, 0.106 mmol) was added. The mixture was vigorously stirred at room temperature until it became yellow (1 h) and then centrifuged. The supernatant was recovered and added to a solution of cholesteryl acetate (30 mg, 0.07 mmol) in 10 mL of acetone under stirring at room temperature and the reaction was monitored by TLC. When the reaction was complete (120 min), 2-propanol was added to reduce RuO_4 excess and the mixture centrifuged again. The supernatant was recovered and taken to dryness. The residue was fractionated by HPLC (n-hexane-ethyl acetate, 8:2) to give **7** (18 mg, 60% yield) and **8** (9.6 mg, 32% yield).

7: m.p. 240-242°C (CH_3OH) [lit.[23], 232-233°C (CH_3OH)]; $[\alpha]_D$=-54.3 (c= 0.7,$CHCl_3$); FTIR (film) ν_{max} 3387, 1734 and 1714 cm^{-1}; ^1H-NMR ($CDCl_3$, 270 MHz) δ 5.01 (1H, m, H_α-3), 2.75 (1H, dd, J=13.2 and 13.2 Hz, H-7), 1.97 (3H, s, acetate), 0.87 (3H, d, J=6.6 Hz, H_3-21), 0.84 (6H, d, J=6.6 Hz, H_3-26 and H_3-27), 0.78 (3H, s, H_3-19), 0.62 (3H, s, H_3-18); ^{13}C-NMR

($CDCl_3$, 67.9 MHz) δ 212.53 (C-6), 171.03 ($CH_3\underline{C}O$), 80.18 (C-5), 70.80 (C-3), 56.24 (C-17 and C-14), 44.21 (C-9), 43.10 (C-13 or C-10), 42.47 (C-10 or C-14), 41.71 (C-7), 39.58 (C-24 or C-12), 39.43 (C-12 or C-24), 37.33 (C-8), 36.09 (C-22), 35.73 (C-20), 32.25 (C-4), 29.51 (C-1), 28.06 (C-16), 27.96 (C-25), 26.25 (C-2), 23.91 (C-23 and C-15), 22.76 (C-26 and C-27), 22.52 ($\underline{C}H_3CO$), 21.33 (C-11), 18.60 (C-21), 13.85 (C-19), 11.98 (C-18); EIMS m/z 460 M^+, 400 (M^+-CH_3COOH, base peak), 382 ($M^+-CH_3COOH-H_2O$), 367 ($M^+-CH_3COOH-H_2O-CH_3$).

8: m.p. 171-173°C (CH_3OH) [lit.[24], 170.5-171.5°C (CH_3OH)]; $[\alpha]_D$=+6.1 (c=0.3, $CHCl_3$); FTIR (film) ν_{max} 3457 and 1735 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 5.07 (1H, m, H_α-3), 3.65 (1H, dd, J=11.0 and 5.5 Hz, H_β-6), 2.24 (1H, dd, J=11.5 and 3.8 Hz, H_{eq}-4), 2.00 (3H, s, acetate), 0.95 (3H, s, H_3-19), 0.88 (3H, d, J=6.6 Hz, H_3-21), 0.85 (6H, d, J=6.6 Hz, H_3-26 and H_3-27), 0.63 (3H, s, H_3-18); ^{13}C-NMR ($CDCl_3$, 67.9 MHz) δ 170.97 ($CH_3\underline{C}O$), 71.47 (C-3), 76.52 (C-5), 70.63 (C-6), 56.19 (C-17), 55.77 (C-14), 44.23 (C-9), 42.65 (C-13), 39.81 (C-12), 39.48 (C-24), 39.19 (C-10), 36.13 (C-22), 35.78 (C-20), 34.99 (C-7), 34.32 (C-4), 33.62 (C-8), 30.84 (C-1), 28.20 (C-16), 27.97 (C-25), 26.62 (C-2), 24.11 (C-15 or C-23), 23.86 (C-23 or C-15), 22.79 (C-27), 22.53 (C-26), 21.44 ($\underline{C}H_3CO$), 21.08 (C-11), 18.63 (C-21), 15.42 (C-19), 12.04 (C-18); EIMS m/z 462 M^+, 444 (M^+-H_2O), 426 (M^+-2H_2O), 402 (M^+-CH_3COOH), 384 ($M^+-CH_3COOH-H_2O$), 366 ($M^+-CH_3COOH-2H_2O$), 43 (base peak).

3β-Acetoxy-5-hydroxy-5α-cholestan-4-one (1), 5α-cholestane-3β,4α,5-triol 3-acetate (2) and 5β-cholestane-3β,4β,5-triol 3-acetate (3) (entry 1).

Following the general procedure described above, 30 mg of cholest-4-en-3β-yl acetate dissolved in 10 mL of acetone were oxidized in 5 min to give a mixture of α-hydroxy ketone **1** (22 mg, 72% yield) and diols **2** and **3** which were separated by silica gel column chromatography using n-hexane-ethyl acetate mixtures as eluent. n-Hexane-ethyl acetate (95:5) eluted 22 mg (72% yield) of compound **1**; diols **2** (3.6 mg, 11%) and **3** (1.8 mg, 5%) were eluted with n-hexane-ethyl acetate, (8:2). Attempts to crystallize compound **3** were unsuccessfull.

1: m.p. 187-190°C ($CHCl_3$-CH_3OH) [lit.[26], 192-195 °C ($CHCl_3$-CH_3OH)]; $[\alpha]_D$=+7.7 (c=1.2, $CHCl_3$) [lit.[26], $[\alpha]_D$=+5]; FTIR (film) ν_{max} 3452, 1743 and 1724 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 5.94 (1H, dd, J=11.9 and 7.5, H_α-3), 2.14 (3H, s, acetate), 0.90 (3H, d, J=6.2 Hz, H_3-21), 0.86 (6H, d, J=6.6 Hz, H_3-26 and H_3-27), 0.79 (3H, s, H_3-19), 0.64 (3H, s, H_3-18); ^{13}C-NMR ($CDCl_3$, 100.1 MHz) δ 206.56 (s), 170.23 (s), 80.60 (s), 73.88 (s), 56.36 (d), 55.86 (d), 45.35 (d), 44.07 (s), 42.69 (s), 40.02 (t), 39.53 (t), 36.19 (t), 35.78 (d), 34.44 (d), 29.34 (t), 28.20 (t), 27.99 (d), 27.84 (t), 26.77 (t), 25.08 (t), 24.07 (t), 23.89 (t), 22.76 (q), 22.52 (q), 21.50 (t), 20.73 (q), 18.67 (q), 15.13 (q), 12.08 (q); EIMS m/z 460 M^+, 400 (M^+-CH_3COOH), 372 (base peak), 357, 354, 332 (ring A fission and

loss of atoms C-1 to C-4).

2: m.p. 170-173°C ($CHCl_3$-CH_3OH) [lit.[26], 177-180°C ($CHCl_3$-CH_3OH)]; $[\alpha]_D$=+13.2 (c=0.7, $CHCl_3$) [lit.[26], $[\alpha]_D$=+22]; FTIR (film) ν_{max} 3450 and 1718 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 5.02 (1H, ddd, J= 11.5, 9.3 and 6.2 Hz, H_α-3), 3.62 (1H, d, J= 9.3 Hz, H_β-4), 2.09 (3H, s, acetate), 0.98 (3H,s, H_3-19), 0.90 (3H,d, J=6.6 Hz, H_3-21), 0.86 (6H, d, J=6.6 Hz, H_3-26 and H_3-27), 0.65 (3H, s, H_3-18); ^{13}C-NMR (pyridine-d_5, 100.1 MHz) δ 178.31 (s), 76.85 (d), 76.66 (s), 73.93 (d), 56.58 (d), 56.46 (d), 45.74 (d), 42.89 (s), 40.48 (t), 40.32 (s), 39.77 (t), 36.51 (t), 36.08 (d), 34.93 (d), 30.33 (t), 29.34 (t), 28.60 (t), 28.25 (d), 26.35 (t), 26.25 (t), 24.45 (t), 24.17 (t), 22.94 (q), 22.71 (q), 21.44 (t), 21.39 (q), 18.94 (q), 15.78 (q), 12.38 (q); EIMS m/z 444 (M^+-H_2O), 384 (M^+-CH_3COOH-H_2O), 332 (ring A fission and loss of atoms C-1 to C-4, base peak); FABMS m/z 463 $(M+H)^+$.

3: $[\alpha]_D$=+32 (c=0.1, $CHCl_3$) [lit.[26], $[\alpha]_D$=+55]; FTIR (film) ν_{max} 3446 and 1739 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 5.26 (1H, bs, H_α-3), 4.00 (1H, bd, J= 7.5 Hz, H_α-4), 2.12 (3H, s, acetate), 1.01 (3H, s, H_3-19), 0.90 (3H, d, J= 6.6 Hz, H_3-21), 0.86 (6H, d, J= 6.6 Hz, H_3-26 and H_3-27), 0.66 (3H, s, H_3-18); EIMS m/z 444 (M^+-H_2O), 384 (M^+-CH_3COOH-H_2O), 332 (ring A fission and loss of atoms C-1 to C-4, base peak); FABMS m/z 463 $(M+H)^+$.

3β,17β-Diacetoxy-5-hydroxy-5α-androstan-4-one (4), 5α-androstane-3β,4α,5, 17β-tetraol 3,17-diacetate (5) and 5β-androstane-3β,4β,5,17β-tetraol 3,17-diacetate (6) (entry 2).

Androst-4-ene-3β,17β-diol diacetate (30 mg) dissolved in 10 mL of acetone was oxidized as above in 10 min to give the α-hydroxy ketone **4** (15.7 mg, 50% yield) and diols **5** (10.3 mg, 32%) and **6** (2.0 mg, 6%). Pure compounds **4-6** were obtained by HPLC on a Hibar LiChrosorb Si-60 (250 x 10 mm) column eluted with n-hexane-ethyl acetate, (8:2). Compound **6** could not be induced to crystallize.

4: oil; $[\alpha]_D$=-12.7 (c=1.1, $CHCl_3$); FTIR (film) ν_{max} 3446, 1733 and 1724 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 5.93 (1H, dd, J=11.9 and 7.5 Hz, H_α-3), 4.60 (1H, dd, J=8.8 and 8.8 Hz, H-17), 2.14, 2.03 (3H each, s's, acetates), 0.80 (3H, s, H_3-19), 0.77 (3H, s, H_3-18); ^{13}C-NMR ($CDCl_3$, 67.9 MHz) δ 206.77 (s), 171.20 (s), 170.37 (s), 82.68 (d), 80.42 (s), 73.90 (d), 50.13 (d), 45.19 (d), 44.12 (s), 42.67 (s), 36.88 (t), 34.20 (d), 29.67 (t), 27.74 (t), 27.52 (t), 26.61 (t), 24.59 (t), 23.38 (t), 21.15 (q), 20.94 (t), 20.78 (q), 15.12 (q), 12.11 (q); EIMS m/z 406 M^+, 388 (M^+-H_2O), 360 (M^+-H_2O-28), 346 (M^+-CH_3COOH), 278 (ring A fission and loss of atoms C-1 to C-4), 83 (base peak); HRMS found m/z 406.2403 $C_{23}H_{34}O_6$ requires 406.2355.

5: m.p. 213-215 °C (CH_3OH); $[\alpha]_D$= +5.1 (c= 0.3, $CHCl_3$); FTIR (film) ν_{max} 3436 and 1735 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 5.01 (1H, ddd, J=11.5, 9.3 and 6.2, H_α-3), 4.58 (1H, dd, J=8.0 and 8.0 Hz, H-17), 3.63

(1H, d, J=9.3 Hz, H_β-4), 2.08, 2.03 (3H each, s's, acetates), 0.98 (3H, s, H_3-19), 0.78 (3H, s, H_3-18); ^{13}C-NMR ($CDCl_3$, 100.1 MHz) δ 172.29 (s), 171.18 (s),82.81 (d), 76.69 (d), 74.67 (d), 50.32 (d), 45.51 (d), 42.62 (s), 39.67 (s), 36.85 (t), 34.24 (d), 29.61 (t), 28.45 (t), 27.59 (t), 25.23 (t), 25.18 (t), 23.41 (t), 21.36 (q), 21.15 (q), 20.43 (t), 15.63 (q), 12.13 (q); EIMS m/z 330 (M^+-CH_3COOH-H_2O), 278 (ring A fission and loss of atoms C-1 to C-4, base peak); FABMS m/z 409 $(M+H)^+$; HRMS found m/z 408.2538 $C_{23}H_{36}O_6$ requires 408.2512.

6: $[\alpha]_D$=+15 (c=0.2, $CHCl_3$); FTIR (film) ν_{max} 3442 and 1733 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 5.26 (1H, bs, $W_{1/2}$=6.6 Hz, H_α-3), 4.59 (1H, dd, J=8.0 and 8.0 Hz, H-17), 3.99 (1H, bs, $W_{1/2}$=8.8 Hz, H_α-4), 2.12, 2.04 (3H each, s's, acetates), 1.02 (3H, s, H_3-19), 0.79 (3H, s, H_3-18); EIMS m/z 348 (M^+-CH_3COOH), 330 (M^+-CH_3COOH-H_2O), 288 (M^+-2CH_3COOH), 278 (ring A fission and loss of atoms C-1 to C-4, base peak); FABMS m/z 409 $(M+H)^+$.

3β-Acetoxy-6-methyl-5,6-secopregn-5-ene-5,6,20-trione (9) (entry 4).

3β-Acetoxy-6-methylpregn-5-en-20-one (30 mg) in 5 mL of acetone was oxidized in 10 min to give secosterol **9** (33 mg, 100% yield).

9: oil; $[\alpha]_D$= +96.2 (c=0.8, $CHCl_3$); FTIR (film) ν_{max} 1737 and 1718 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.35 (1H, bs, $W_{1/2}$= 8.0 Hz, H_α-3), 2.10, 2.00 and 1.98 (3H each, s's, 3x CH_3-CO), 1.00 (3H, s, H_3-19), 0.62 (3H, s, H_3-18); ^{13}C-NMR ($CDCl_3$, 100.1 MHz) δ 216.20 (s), 209.49 (s), 209.08 (s), 170.15 (s), 73.35 (d), 63.59 (d), 53.06 (d), 52.24 (s), 43.84 (s), 43.06 (t), 42.25 (t), 41.03 (d), 38.87 (t), 35.24 (d), 34.25 (t), 31.32 (q), 30.21 (q), 25.04 (t), 24.84 (t), 23.12 (t), 22.48 (t), 21.17 (q), 17.48 (q), 12.72 (q); EIMS m/z 404 M^+, 344 (M^+-CH_3COOH), 284 (M^+-2CH_3COOH), 43 (base peak); HRMS found m/z 404.2615 $C_{24}H_{36}O_5$ requires 404.2563.

3β-Acetoxy-8α-hydroxy-5α-cholestan-7-one (12) and 5α-cholestane-3β,7α,8α-triol 3-acetate (13) (entry 5).

A solution of 5α-cholest-7-en-3β-yl acetate (8.5 mg) in acetone (5 mL) was oxidized in 5 min with RuO_4. HPLC separation of the resulting reaction mixture on a Hibar LiChrosorb Si-60 (250 x 10 mm) column (eluent n-hexane-ethyl acetate, 78:22) gave α-hydroxy ketone **12** (3.1 mg, 34% yield) and diol **13** (3.0 mg, 33% yield).

12: m.p. 153-155 °C (CH_3OH); $[\alpha]_D$= -9.1 (c= 0.8, $CHCl_3$); FTIR (film) ν_{max} 3474 and 1718 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz; assignments based on a COSY-45 experiment) δ 4.75 (1H, m, H_α-3), 3.08 (1H, dddd, J= 11.5, 11.5, 6.6 and 3.8 Hz, H-5), 2.57 (1H, dd, J= 17.6 and 6.6 Hz, H_α-6), 2.02 (3H, s, acetate), 1.82 (m, overlapped to other signals, H_β-6), 0.89 (3H, d, J=6.6 Hz, H_3-21), 0.85 (6H, d, J=6.6 Hz, H_3-26 and H_3-27), 0.79 (3H, s, H_3-19 or H_3-18), 0.75 (3H, s, H_3-18 or H_3-19); ^{1}H-NMR (pyridine-d_5, 270 MHz) δ 6.74 (1H, s, OH-8), 4.91 (1H, m, H-3), 3.59 (1H, dddd, J= 10.8, 10.8, 6.4 and 3.8 Hz, H-5), 2.78 (1H, dd, J= 17.2 and 7.0 Hz, H_{eq}-6), 2.03

(3H, s, acetate), 1.00 (3H, s, H_3-19), 0.98 (3H, d, J= 6.6 Hz, H_3-21), 0.87 (6H, d, J= 6.6 Hz, H_3-26 and H_3-27), 0.82 (3H, s, H_3-18); ^{13}C-NMR ($CDCl_3$, 67.9 MHz) δ 210.51 (s), 170.54 (s), 78.74 (s), 72.86 (d), 58.78 (d), 57.25 (d), 56.58 (d), 43.40 (t), 42.79 (s), 39.54 (t), 39.47 (t), 38.90 (t), 36.52 (d), 35.90 (t), 35.80 (d), 35.52 (s), 33.20 (t), 27.97 (d), 27.60 (t), 27.10 (t), 23.76 (t), 22.80 (t), 22.52 (q), 22.52 (q), 21.36 (q), 19.39 (t), 18.64 (q), 14.89 (q), 13.25 (q); EIMS m/z 460 M^+, 442 (M^+-H_2O), 418 (M^+-CH_2CO), 400 (M^+-CH_3COOH), 385(M^+-CH_3COOH-CH_3), 382 (M^+-CH_3COOH-H_2O), 372 (M^+-CH_3COOH-CO), 315, 294, 273, 264, 55 (base peak); HRMS found m/z 460.3600 $C_{29}H_{48}O_4$ requires 460.3553.

13: amorphous powder; $[\alpha]_D$=-4.5 (c= 0.2, $CHCl_3$); FTIR (film) ν_{max} 3452 and 1737 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 4.73 (1H, m, H_α-3), 4.13 (1H, dd, J= 12.8 and 6.6 Hz, H_β-7), 2.64 (1H, dddd, J= 11.5, 11.5, 6.6 and 3.8 Hz, H-5), 2.01 (3H, s, acetate), 0.90 (3H, d, J= 6.2 Hz, H_3-21), 0.86 (6H, d, J= 6.6 Hz, H_3-26 and H_3-27), 0.83, 0.82 (3H each, s's, H_3-18 and H_3-19); ^{13}C-NMR ($CDCl_3$, 67.9 MHz) δ 170.57 (s), 78.41 (s), 73.34 (d), 69.95 (d), 61.72 (d), 56.64 (d), 54.79 (d), 43.11 (s), 40.18 (t), 40.00 (t), 39.46 (t), 37.90 (t), 35.86 (t), 35.66 (d), 35.53 (s), 35.37 (d), 33.16 (t), 27.96 (d), 27.47 (t), 27.15 (t), 23.95 (t), 23.82 (t), 22.75 (q), 22.70 (t), 22.51 (q), 21.38 (q), 18.66 (q), 15.45 (q), 11.93 (q); EIMS m/z 462 M^+, 444 (M^+-H_2O), 426 (M^+-$2H_2O$), 402 (M^+-CH_3COOH), 384 (M^+-CH_3COOH-H_2O), 366 (M^+-CH_3COOH-$2H_2O$), 108 (base peak); HRMS found m/z 462.3750 $C_{29}H_{50}O_4$ requires 462.3709.

Chromium trioxide-pyridine oxidation of diol 13.

Compound **13** (4.7 mg) dissolved in 1 mL of pyridine was added to a solution of chromium trioxide (7.0 mg) in pyridine (1.0 mL) prepared as previously described[37]. The mixture was kept under stirring at room temperature for 20 h, then was diluted with water (0.5 mL) and extracted with ethyl ether (3 x 3 mL). The organic solution was washed with water, dried over Na_2SO_4 and evaporated. The residue was chromatographed on a Hibar LiChrosorb Si-60 (250 x 10 mm) column (eluent n-hexane-ethyl acetate, 78:22) to give 2.5 mg of ketone **12**.

3β,6α-Diacetoxy-8α-hydroxy-5α-cholestan-7-one (14) (entry 6).

Oxidation in 30 min of 30 mg of 5α-cholest-7-ene-3β,6α-diol diacetate in 10 mL of acetone gave the crude α-hydroxy ketone **14** which was purifid by HPLC on Hibar LiChrosorb Si-60 (250 x 10 mm) column (eluent n-hexane-ethyl acetate, 8:2). 15.5 Mg (49% yield) of pure **14** were obtained.

14: oil; $[\alpha]_D$= +36 (c= 0.3, $CHCl_3$); FTIR (film) ν_{max} 3452 and 1733 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 4.98 (1H, d, J= 12.1 Hz, H_β-6), 4.75 (1H, m, H_α-3), 3.10 (1H, ddd, J= 12.1, 12.1 and 3.2 Hz, H-5), 2.12, 2.02 (3H each, s's, acetates), 0.99 (3H, s, H_3-19), 0.88 (3H, d, J= 6.4 Hz, H_3-21), 0.86

(6H, d, J= 6.6 Hz, H_3-26 and H_3-27), 0.65 (3H, s, H_3-18); ^{13}C-NMR ($CDCl_3$, 100.1 MHz) δ 205.21 (s), 170.47 (s), 170.42 (s), 78.17 (s), 74.63 (d), 72.34 (d), 59.13 (d), 56.54 (d), 53.34 (d), 42.83 (s), 40.03 (d), 39.92 (t), 39.83 (t), 39.46 (t), 35.88 (t), 35.46 (d), 34.66 (s), 28.71 (t), 27.97 (d), 27.62 (t), 27.13 (t), 24.39 (t), 23.77 (t), 22.77 (q), 22.52 (q), 21.31 (q), 20.76 (d), 19.52 (t), 18.57 (q), 15.96 (q), 13.27 (q); EIMS m/z 518 M^+, 500 (M^+-H_2O), 490 (M^+-CO), 475 (M^+-CO-CH_3), 458 (M^+-CH_3COOH), 440 (M^+-CH_3COOH-H_2O), 430 (M^+-CH_3COOH-CO), 415 (M^+-CH_3COOH-CO-CH_3), 264 (base peak); HRMS found m/z 518.3618 $C_{31}H_{50}O_6$ requires 518.3607.

3β,7α-Diacetoxy-8(14)-seco-5α-cholest-8(14)-ene-8,14-dione (15) and 3β,7α-diacetoxy-5α-cholest-8(14)-en-15-one (16) (entry 7).

Following the general procedure described above, 14 mg of 5α-cholest-8(14)-ene-3β,7α-diol diacetate dissolved in 5 mL of acetone were oxidized in 20 min to give the 8,14-secosterol **15** (6.6 mg, 44% yield) and the α,β-unsaturated ketone **16** (5.0 mg, 35% yield). Separation of compounds **15** and **16** was achieved as follows. HPLC separation of the mixture of **15** and **16** on a Hibar LiChrosorb Si-60 (250 x 4 mm) column (eluent n-hexane-ethyl acetate, 8:2) gave 6.6 mg of diketone **15** and 8.3 mg of **16** still contaminated by other products. Final purification of **16** by HPLC on a Hibar Superspher RP-18 (250 x 4 mm) column eluted with CH_3OH-H_2O (95:5) gave 5 mg of the pure compound.

15: m.p. 135-137 °C (acetone); $[\alpha]_D$= -27.5 (c= 0.4,$CHCl_3$); FTIR (film) ν_{max} 1736 and 1723 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 4.78 (1H, bdd, J= 2.6 and 2.6 Hz, H_β-7), 4.75 (1H, m, H_α-3), 2.15 (3H, s, acetate), 2.02 (3H, s, acetate), 1.06 (3H, d, J= 6.6 Hz, H_3-21), 0.88 (6H, d, J= 6.6 Hz, H_3-26 and H_3-27), 0.85 (3H, s, H_3-19), 0.63 (3H, s, H_3-18); ^{13}C-NMR ($CDCl_3$, 100.1 MHz) δ 224.76 (s), 206.81 (s), 170.55 (s), 169.83 (s), 72.75 (d), 58.44 (d), 52.45 (s), 46.75 (d), 42.01 (s), 39.45 (t), 37.85 (t), 37.57 (d), 36.26 (t), 36.10 (t), 34.97 (t), 34.66 (t), 34.16 (d), 32.47 (t), 27.96 (d), 26.52 (t), 24.10 (t), 23.61 (t), 22.80 (q), 22.55 (q), 21.32 ($\underline{C}H_3CO$), 20.96 ($\underline{C}H_3CO$), 18.49 (q), 18.14 (q), 16.99 (t), 11.58 (q); EIMS m/z 518 M^+, 458 (M^+-CH_3COOH), 398 (M^+-$2CH_3COOH$), 97 (base peak); HRMS found m/z 518.3580 $C_{31}H_{50}O_6$ requires 518.3607.

16: oil; $[\alpha]_D$= +32 (c= 0.5, $CHCl_3$); FTIR (film) ν_{max} 1734, 1718 and 1645 cm^{-1}; UV (CH_3OH) ν_{max} 249 nm (ϵ 13180); ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 6.68 (1H, bdd, J=2.6 and 2.6 Hz, H_β-7), 4.76 (1H, m, H_α-3), 2.03, 1.99 (3H each, s's, acetates), 0.99 (3H, d, J= 6.6 Hz, H_3-21), 0.96 (3H, s, H_3-18), 0.86 (6H, d, J= 6.6 Hz, H_3-26 and H_3-27), 0.72 (3H, s, H_3-19); ^{13}C-NMR ($CDCl_3$, 100.1 MHz) δ 206.99 (C-15), 170.52 ($CH_3\underline{C}O$), 169.70 ($CH_3\underline{C}O$), 146.12 (C-8), 141.70 (C-14), 73.06 (C-3), 65.71 (C-7), 51.27 (C-17), 45.12 (C-9), 42.68 (C-13), 41.26 (C-16), 39.31 (C-24), 38.50 (C-10), 37.50 (C-5), 36.46 (C-12), 36.20 (C-1), 35.76 (C-22), 34.62 (C-20), 33.66 (C-6), 33.17 (C-4), 27.96 (C-25), 27.16 (C-2), 23.90 (C-23), 22.76 (C-27), 22.50 (C-26), 21.37

($\underline{C}H_3CO$), 21.37 ($\underline{C}H_3CO$), 19.14 (C-21), 19.11 (C-11), 16.08 (C-18), 11.97 (C-19); EIMS m/z 500 M^+, 458 (M^+-CH_2CO, base peak), 440 (M^+-CH_3COOH), 398 ($M^+-CH_3COOH-CH_2CO$), 380 (M^+-2CH_3COOH); HRMS found m/z 500.3514 $C_{31}H_{48}O_5$ requires 500.3502.

RuO_4 OXIDATION IN CARBON TETRACHLORIDE. GENERAL PROCEDURE.

Oxidation of cholest-5-en-3β-yl acetate . Synthesis of 3β-acetoxy-5-hydroxy-5α-cholestan-6-one (7) and 5α-cholestane-3β,5,6α-triol 3-acetate (8)

A solution of sodium metaperiodate (258 mg, 1.2 mmol) in water (10 mL) was added to a suspension of $RuO_2 \cdot 2H_2O$ (60 mg, 0.351 mmol) in carbon tetrachloride (30 mL). The biphasic suspension was vigorously stirred at room temperature until the suspended black ruthenium dioxide dissolved (1 h). The yellow CCl_4 layer was separated and added over a 10 min period to a solution of 50 mg (0.117 mmol) of cholesteryl acetate in 10 mL of carbon tetrachloride under stirring at room temperature and the reaction was monitored by TLC. When the reaction was complete (60 min), 2-propanol was added to reduce RuO_4 and the black suspension was filtered through a Celite pad. The filtrate was concentrated to give a residue which was fractionated by HPLC on a Hibar LiChrosorb Si-60 (250x10 mm) column using n-hexane-ethyl acetate (8:2), as eluent to give compounds **7** (9.7 mg, 16% yield) and **8** (32.4 mg, 60% yield).

Oxidation of cholest-4-en-3β-yl acetate, androst-4-ene-3β,17β-diol diacetate, 3β-acetoxy-6-methylpregn-5-en-20-one, 5α-cholest-7-en-3β-yl acetate and 5α-cholest-8(14)-ene-3β,7α-diol diacetate in CCl_4 solution.

Cholest-4-en-3β-yl acetate (20 mg), dissolved in 10 mL of CCl_4 was oxidized (20 min) following the general procedure described above to give diols **2** and **3** in 70% and 10% yield, respectively.

Androst-4-ene-3β,17β-diol diacetate (30 mg) in 10 mL of CCl_4 gave on RuO_4 oxidation (15 min) diols **5** and **6** in 50% and 20% yield, respectively.

5α-Cholest-7-en-3β-yl acetate (31 mg) in 10 mL of CCl_4 was oxidized in 10 min to give diol **13** in 55% yield.

5α-Cholest-8(14)-ene-3β,7α-diol diacetate (15 mg) in 5 mL of CCl_4 was oxidized in 105 min to give compounds **15** and **16** in 38% and 34% yield, respectively.

3β-Acetoxy-6-methylpregn-5-en-20-one (27 mg) in CCl_4 (10 mL) was oxidized in 20 min to give a mixture (12.5 mg) of 5,6-secosterol **9**, and 5α,6α- and 5β,6β-diols **10** and **11**, respectively, which were separated by HPLC on a Hibar LiChrosorb Si-60 (250 x 4 mm) column using $CHCl_3$ as eluent. 8.3 Mg (21% yield) of **9**, 1.6 mg (6% yield) of **10**, and 2.0 mg (7% yield) of **11**, were obtained.

10: $[\alpha]_D$= +20.0 (c= 0.1, $CHCl_3$); FTIR (film) ν_{max} 3446, 1735 and 1702 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 5.18 (1H, m, H_α-3), 2.11, 2.03 (3H each, s's, H_3-21 and acetate), 1.28 (3H, s, 6_β-Me), 1.06 (3H, s, H_3-19), 0.62 (3H, s, H_3-18); EIMS m/z 406 M^+, 391 (M^+-CH_3), 388 (M^+-H_2O), 370 (M^+-$2H_2O$), 346 (M^+-CH_3COOH), 328 (M^+-CH_3COOH-H_2O), 310 (M^+-CH_3COOH-$2H_2O$), 193 (base peak); HRMS found m/z 406.2737 $C_{24}H_{38}O_5$ requires 406.2719.

11: $[\alpha]_D$= +48.0 (c= 0.2, $CHCl_3$); FTIR (film) ν_{max} 3446, 1735 and 1702 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 5.20 (1H, bs, $W_{1/2}$=8.8 Hz, H_α-3), 2.11 (6H, s, H_3-21 and acetate), 1.14, 1.12 (3H each, s's, 6_α-Me and H_3-19), 0.63 (3H, s, H_3-18); EIMS m/z 406 M^+, 391 (M^+-CH_3), 388 (M^+-H_2O), 373 (M^+-H_2O-CH_3), 370 (M^+-$2H_2O$), 346 (M^+-CH_3COOH), 328 (M^+-CH_3COOH-H_2O), 310 (M^+-CH_3COOH-$2H_2O$), 193 (base peak).

$Pb(OAc)_4$ oxidation of diols 10 and 11.

To a solution of **10** (1.2 mg) in CH_3COOH (1 mL), crystalline lead tetraacetate (1.5 mg) was added portionwise at room temperature. When the reaction was complete (30 min) two drops of ethylene glycol were added and the mixture was diluted with ice-water and extracted with $CHCl_3$. The organic layer was washed with aqueous $NaHCO_3$, dried (Na_2SO_4) and taken to dryness. The residue was chromatographed on a Hibar LiChrosorb Si-60 (250 x 4 mm) column using $CHCl_3$ as eluent to give 1.0 mg of a product which had spectral (^{1}H-NMR, IR, MS) and chromatographic properties identical to those exhibited by diketone **9**.

Following the same procedure, oxidation of 5β,6β-diol **11** (1.4 mg) with 2.0 mg of $Pb(OAc)_4$ gave 1.2 mg of diketone **9** .

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