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REMOTE HALOGENATION: SOME MODEL STUDIES AND SPECIFIC DEGRADATION OF THE CHOLESTEROL, SITOSTEROL, AND CAMPESTEROL SIDE CHAIN

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Abstract - 1) Two high-yield procedures for the conversion of **1** to **4** are reported. 2) **11** was degraded to **34** in good overall yield via **17**, **20**, **26**, **31**, **29**, and **30**. Similarly, **34** was obtained from **12** and **13**.

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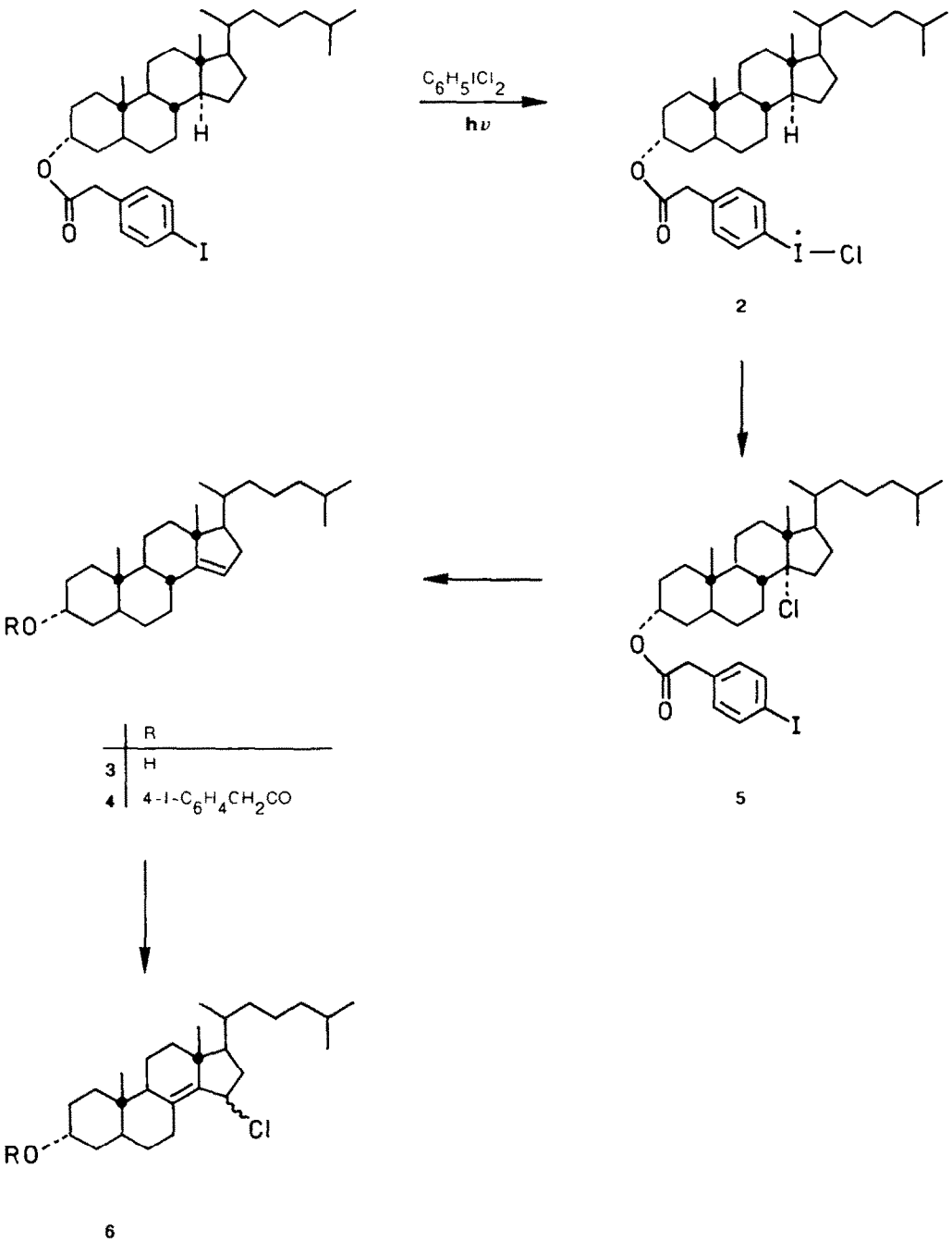
Remote functionalization was introduced by Breslow [1] and by Baldwin [2] as a powerful new tool for the regioselective functionalization of tertiary hydrocarbon centers in the steroid nucleus. Usually, a reagent, catalyst or template group is complexed or covalently linked to a position of the substrate far away from the reaction site. Site-specificity is governed by proximity effects. For example, reaction of **1** with a chlorinating agent such as iodobenzene dichloride under free radical conditions followed by KOH treatment leads to the olefin **3** in up to 55% yield. [3] It is assumed that first intermediate **2** is formed. For geometrical reasons 14α-H is the only tertiary hydrogen that can be intramolecularly abstracted by the radical grouping of **2**. A carbon radical is formed which reacts in the last step of the chain reaction to produce **5**. In this particular case due to its instability **5** was neither isolated nor identified but was immediately transferred into **3**. These so-called template-controlled radical-relay chlorinations have found a number of elegant synthetic applications. [3,4]
In this paper we report some new results on remote chlorination of model compound **1** and detail an efficient side-chain degradation of sterols **11**, **12**, and **13** in which remote chlorination is one of the key steps. [5]

Model studies

To a solution of **1** in CH_2Cl_2 which was irradiated with a sunlamp at -50 to -30°C (argon atmosphere) a solution of iodobenzene dichloride was added dropwise. When the reaction was finished (after about 11 min) usual work-up and chromatography gave **4** (80%), and traces of **6**. Notable features of this experiment are that (i) the yield is much higher than that reported by Breslow and coworkers, [3] (ii) base treatment is unnecessary to obtain an olefin, (iii) the ester group which protects the 3-OH function is retained under these experimental conditions. There remains, however, one disadvantage, namely



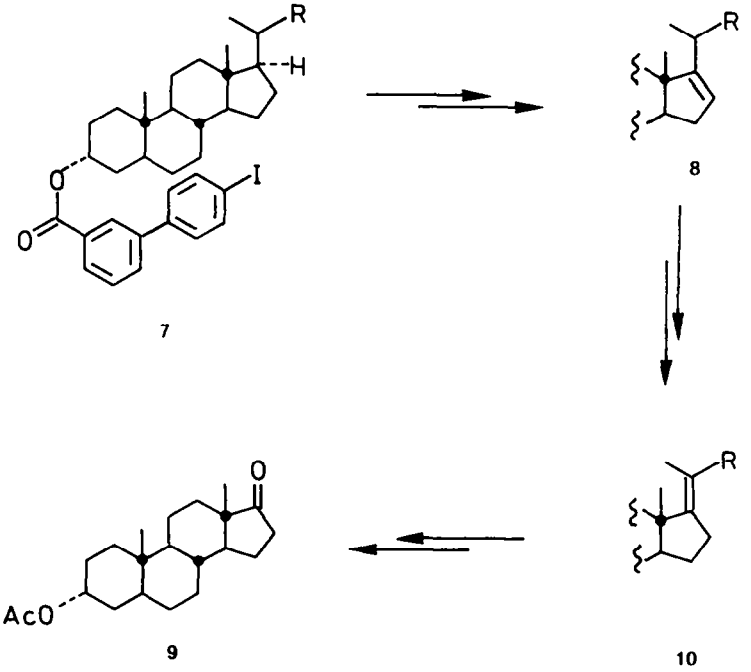
that iodobenzene has to be prepared in a separate step. We tried, therefore, to find simpler chlorinating reagents for the radical relay reaction. tert-Butyl hypochlorite, trichloromethanesulfonyl chloride, and iodine trichloride were tried without success. [6] The use of sulfuryl dichloride will be described below. Cl_2 in the presence of complexing solvents such as diphenyl ether, diethyl ether, dioxane, quinoline, thiophene, bis(tert-butyl)sulfide, or sulfur dichloride was too unselective. [6] On the other hand, in agreement with Russell's classical work, [7] when **1** was submitted to the radical relay chlorination with Cl_2 in carbon disulfide at -60°C under very carefully controlled conditions (see Experimental) **4** was obtained in excellent yield (77%) along with a small amount of allyl chloride **6**.

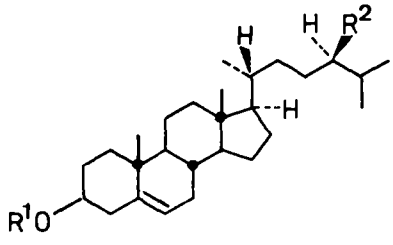
Under these experimental conditions evidence for the intermediate formation of chloro compound **5** was obtained for the first time. A ^{1}H NMR spectrum taken at the end of the chlorination reaction at -50°C did not show the olefinic proton signal of **4**. This signal slowly appeared at room temperature and under the conditions of the working-up procedure.

4-Androstene-3,17-dione (**34**) from Cholesterol (**11**), ß-Sitosterol (**12**) and Campesterol (**13**) by Chemical Degradation.

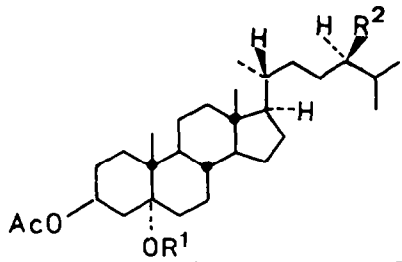
For many years diosgenin, deoxycholic acid, and stigmasterol served as the most important raw materials for the partial synthesis of steroid hormones. [8] Recently, economic processes have been developed for the microbial conversion of abundant naturally occurring sterols such as cholesterol (**11**), ß-sitosterol (**12**), and campesterol (**13**) into useful steroid hormone intermediates such as 4-androstene-3,17-dione (**34**). [9,10] An analogous degradation of the saturated hydrocarbon side chain by conventional chemical methods can be accomplished only with unacceptably low yields even after protection of the Δ^5 double bond. [11] We have now developed an efficient chemical method for this degradation which is based on the remote halogenation methodology. One of the main problems is, of course, to preserve the Δ^5 double bond or an equivalent of it throughout the degradation procedure. Site-specific introduction of a Δ^{16} double bond into saturated steroids has been achieved by Breslow [3] and Baldwin, [2] respectively, using remote functionalization processes with the "reagent" group attached either to the 3- or the 7-position. For example, **7** was transformed into **8** by the Breslow group. **10** was obtained from **8** in three steps and could in turn be degraded to androsterone acetate (**9**).[3]

We reasoned that compounds **20**, **21** and **22**, respectively, would be very useful intermediates in the desired degradation of sterols **11**, **12** and **13**. By moving the p-iodophenylacetate attachment from C-3 as in **1** to C-5 displaces the position of attack from 14-H (as discussed above, see **2**) to 17-H as desired. [12] Furthermore, the functional group at C-5 serves as a protective group for the Δ^5 double bond.

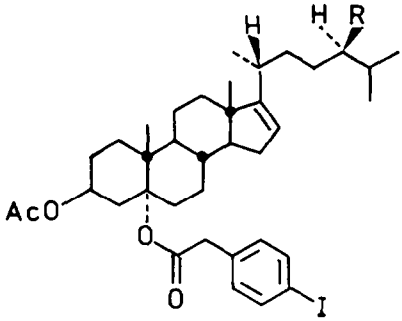




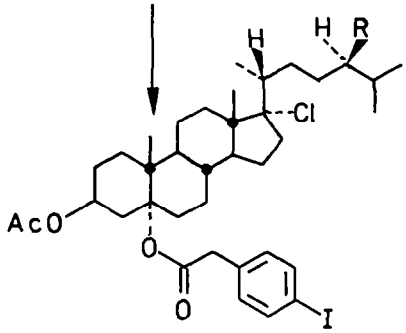
	R^1	R^2
11	H	H
12	H	Et
13	H	Me
14	Ac	H
15	Ac	Et
16	Ac	Me



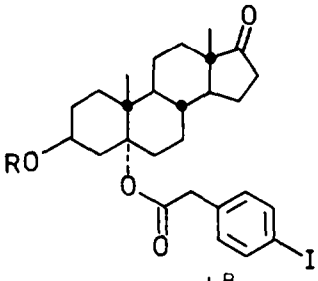
	R^1	R^2
17	H	H
18	H	Et
19	H	Me
20	4-I-$C_6H_4CH_2CO$	H
21	4-I-$C_6H_4CH_2CO$	Et
22	4-I-$C_6H_4CH_2CO$	Me



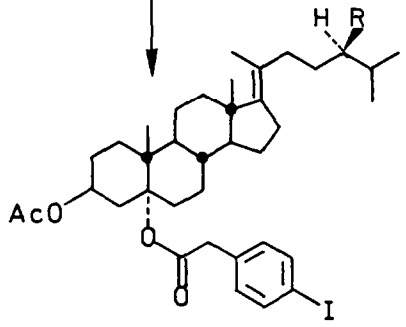
	R
23	H
24	Et
25	Me



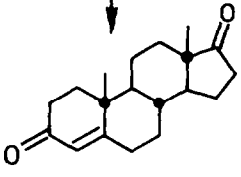
	R
26	H
27	Et
28	Me



	R
29	Ac
30	H



	R
31	H
32	Et
33	Me



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Accordingly, acetates **14** and **15/16** (obtained from a commercial 6:4 mixture of **12** and **13**) were transformed to the 5α -hydroxy compounds **17** and **18/19**, respectively, in an overall yield of 74% by sensitized photooxygenation [13] followed by catalytic hydrogenation of the intermediate (5α -hydroperoxy-7-ene) allylic hydroperoxides. Because of its simplicity, this method for the conversion of Δ^5-unsaturated into 5α-hydroxy steroids compares favourably with the standard procedure via the 5α,6α-epoxide. [14] Esterification of the tertiary OH-group in **17** and **18/19**, respectively, caused more difficulties than anticipated. After much experimentation it was found that a modification of the Oppenauer method [15] (refluxing a toluene solution of the alcohol with a 3-fold excess of 4-iodophenylacetyl chloride and calciumhydride in the presence of a catalytical amount of tetra-n-butylammonium iodide) gave the desired esters **20** and **21/22** in about 80% yield. Irradiation of a CCl_4 solution of **20** in the presence of sulfuryl chloride and azobis (isobutyronitrile) at -10°C with UV light (Philips HPK 125, pyrex filter) for 150 min or of a $CHCl_3$ solution of **20** and freshly prepared iodobenzene dichloride at 20°C with a 300 W sun lamp for 5 min furnished the desired 17α -chloro compound **26**. After chromatographic separation the somewhat unstable **26** was obtained in 53% yield. When **26** was heated in pyridine solution only the 16-olefin **23** was formed. This finding is consistent with Breslow's report [3] that the 17-chloro compounds obtained from **7** (with various R-groups) react with hot alkali exclusively to olefins **8**. As already discussed, from these olefins the side chain can be degraded only in a sequence of several steps. To our delight, we found that treatment of **26** with 1,5-diazabicyclo [5.4.0]-undecene-5 (DBU) at 90°C gave a 4:1 mixture of the desired 17(20)-olefin **31** [16] and of **23** [18]. When the chlorination and the elimination step were performed without purification of the intermediate **26** the overall yield of the 4:1 mixture of **31** and **23** was 64%. Simple ozonolysis of this mixture of olefins in CH_2Cl_2/methanol solution followed by trimethylphosphite workup gave 17-ketone **29** quantitatively (based on **31**). By the same sequence of reactions the mixture of **21** and **22** was degraded to **29**. Heating of a THF solution of **29** with aqueous 0.15 molar lithium hydroxide [19] under reflux for 4h furnished **30** by clean hydrolysis of the acetate group at C-3 in 86% yield. Finally, pyridinium chlorochromate oxidation [20] and brief treatment of the resulting 3-ketone in THF solution with 0.15 molar aqueous lithium hydroxide at 20°C provided **34** in quantitative yield.

In conclusion, sterols **11**, **12**, and **13** can be chemically degraded to **34** in good yield by a simple sequence of reactions.

EXPERIMENTAL

General

Usual work-up means partioning the reaction mixture between water and an organic solvent (given in parenthesis), drying the combined organic solutions over Na_2SO_4 and removal of solvent by distillation in vacuo using a rotatory evaporator. The instrumentation used was: ^{1}H NMR: WP 80 (Bruker); WH-250 (Bruker); IR: Perkin Elmer 257 and 681; MS: MAT-731 and MAT-CH-5 (Varian); LC: Medium pressure chromatography using 31.0 cm x 2.5 cm glass tubes, silica gel 60 Merck (40-63 µm), Duramat pump (CfG).

5α-Cholest-14-ene-3α-yl 4-iodophenylacetate (4).

a) A solution of **1** (50 mg, 0.08 mmol) in absolute CH_2Cl_2 (8 ml) was deoxygenated with argon (30 min). Then, under argon at -50 to -30°C, the solution was exposed to the light of a sun lamp (Osram Ultra-Vitralux, placed in 5 cm distance of the reaction flask) for 13 min. During this time, a solution of iodobenzene dichloride (49.0 mg, 0.18 mmol) in absolute CH_2Cl_2 (30 ml) was added dropwise. After additional irradiation for 2 min the solvent was evaporated. LC (petroleum ether-ethyl acetate 150:1) furnished **4** (40.2 mg, 80%) and traces (tlc) of **6**.

b) To a 0.6 molar solution of Cl_2 in CCl_4 (0.79 ml) was added precooled (-60°C) CS_2 (40 ml). This mixture was added dropwise within 1.5 min to an irradiated solution (sun lamp) of **1** (200 mg, 0.32 mmol) in CS_2 (25 ml) at -60°C. Irradiation was continued for 2 min. The solvent was evaporated, and the residue taken up in ether (20 ml). The solution was washed with 10% $NaHSO_3$ solution and satura -

ted $NaHCO_3$ solution (2x2 ml) before drying and solvent evaporation. The very difficult separation of **1**, **4**, and **6** and other by-products was performed by (i) LC (silica gel (170 g), petroleum ether-ethyl acetate 150:1) and (ii) LC (silica gel impregnated with 10% $AgNO_3$ (100 g), petroleum ether-ethyl acetate 150:1, then 20:1) and gave **4** (154.4 mg, 77%), **1** (21 mg, 10%), and **6** (2 mg, 1%).

c) **1** (50 mg, 0.79 mmol) was chlorinated as described under b). Part of the reaction mixture was diluted with precooled $CDCl_3$ (-50°C). The ^1H NMR spectrum (80 MHz) at -50°C featured a 0:1 ratio of integrals around δ = 5.2 (olefinic H) and 5.0 (3ß-H). When the reaction mixture (without working-up) was allowed to stand at room temperature for 15 h, this ratio was 1:4.6. Similarly, 50 mg of **1** were chlorinated as described under b), and ^1H NMR spectra were taken after each step of the working-up and purification procedure (see above). The ratio of the integrals at δ = 5.2 and 5.0 became gradually larger and was 1:1 at the end of the isolation procedure. The isolated yield of **4** was 70% in this experiment.

M.p. of **4**: 83-85°C (from ethanol).- ^1H NMR (80 MHz, $CDCl_3$): δ = 0.80 - 0.91 (methyl signals), 3.54 (s, $-CO-CH_2-Ar$), 5.03 (m, $W_{1/2}$ = 7Hz, 3ß-H), 5.20 (m, $W_{1/2}$ = 5.5 Hz, 15-H), 7.05 and 7.66 aromatic H's). - IR: 1725 cm^{-1} (CO).- MS: m/z (%)= 630 (10, M^+), 255 (100).- (Found C 66.74, H 8.17. Calc for $C_{35}H_{51}O_2I$ (630.7): C 66.65, H 8.15).

15ξ-Chloro-5α-cholest-8(14)-ene-3α-yl 4-iodophenylacetate (6).

A solution of **4** (50 mg, 0.79 mmol) in absolute CH_2Cl_2 (10 ml) was deoxygenated with argon (30 min). Then, at -30°C the solution was exposed to the light of a sun lamp (see above). Within 4 min iodobenzene dichloride (28.5 mg, 0.10 mmol) was added and photolysis continued for 4 min. Work-up (CH_2Cl_2) and LC (petroleum ether - ethyl acetate 50:1) provided **6** (41.3 mg, 80%).- M.p. 146-148°C (from ethanol).- IR (CCl_4): 1725 cm^{-1} (CO).- ^1H NMR (80 MHz, $CDCl_3$): δ = 0.86-0.93 (methyl signals), 3.58 (s, $-CO-CH_2-Ar$), 4.60 (X-part of an ABX system, $J_{AX} + J_{BX}$ = 10.7 Hz, 15-H), 5.02 (m, $W_{1/2}$ = 7 Hz, 3ß-H), 7.05 and 7.66 (aromatic H's).- MS: m/z (%) = 664 (1, M^+), 57 (100).- Found 664.2582 (MS). Calc for $C_{35}H_{50}O_2ClI$: 664.2541).

5α-Stigmastane-3ß,5-diol 3-acetate (18) and 5α-Campestane-3ß,5-diol 3-acetate (19).

Commercial sitosterol (Aldrich, 6:4 mixture of ß-sitosterol (**12**) and campesterol (**13**), ratio determined by GC) was acetylated (acetic anhydride-pyridine) to give a mixture of **15** and **16**. A solution of **15**/**16** (210.5 mg, 0.5 mmol) in CH_2Cl_2 (700 ml) and dry pyridine (10 ml) was irradiated with a 1000 W halogen lamp (Osram Studio SLV 1000) while oxygen was continously bubbled through the solution. After 14 h at 15°C, the solvent was removed at 25°C. The residue in ethyl acetate (200 ml) containing Pt (20 mg PtO_2, H_2O) was stirred under H_2 at room temperature and atmospheric pressure. After 10 h, the mixture was filtered and the solvent evaporated. LC (petroleum ether - ethyl acetate 5:1) furnished a mixture of **18** and **19** (137.8 mg, 63%). In some runs, the ^1H NMR spectrum of the products still showed olefinic proton signals and the hydrogenation reaction had to be repeated at this stage.

^1H NMR (80 MHz, $CDCl_3$): δ = 0.66 (s, CH_3-18), 1.00 (s, CH_3-19), 2.00 (s, 3ß-OAc), 4.92-5.48 (m, 3α-H).- MS: m/z (%) = 474 (2, M^+ of **18**, $C_{31}H_{54}O_3$), 460 (1, M^+ of **19**, $C_{30}H_{52}O_3$), 396 (100).

5α-Cholestane-3ß,5-diol 3-acetate (17).

The same procedure as described above was used. Yield: 76%, m.p. 185°C (from acetone), lit.[14] m.p. 185°C.

5α-Stigmastane-3β,5-diol 3-acetate 5-(4-iodophenyl)acetate (**21**) and 5α-Campestane-3β,5-diol 3-acetate 5-(4-iodophenyl)acetate (**22**).

To a mixture of **18/19** (100 mg, 0.21 mmol), calcium hydride (50 mg, 1.2 mmol), tetra-n-butylammonium iodide (catalytic amount), and absolute toluene (5 ml) a solution of freshly distilled 4-iodophenylacetyl chloride (177 mg, 0.63 mmol) in absolute toluene (1.5 ml) was added. The reaction mixture was then stirred at reflux temperature. Over a period of 28 h portions of 4-iodophenylacetyl chloride and calcium hydride were added (1. 4-iodophenylacetyl chloride (177 mg, 0.63 mmol) in toluene (1.5 ml) and calcium hydride (40 mg, 1 mmol), 2. 4-iodophenylacetyl chloride (118 mg, 0.42 mmol) in toluene (1 ml) and calcium hydride (30 mg, 0.7 mmol), 3. 4-iodophenylacetyl chloride (57 mg, 0.2 mmol) in toluene (0.5 ml)). After 30 h the mixture was cooled to room temperature and poured into ice-cooled 5% $NaHCO_3$ solution. After stirring for 30 min work-up (CH_2Cl_2) and LC (petroleum ether-ethyl acetate 5:1) furnished a mixture of **21** and **22** (121 mg, 80%).- ^1H NMR (80 MHz, $CDCl_3$): δ = 0.60 (s, CH_3-18), 0.97 (s, CH_3-19), 2.00 (s, 3β-OAc), 3.51, 3.62 (AB system $|J_{AB}|$ = 16 Hz, -$COCH_2$-Ar), 4.55-5.03 (m, 3α-H), 7.05, 7.65 (aromatic H's).- MS: no molecular ion, 492 (1), 462 (2), 397 (12), 396 (18), 383 (10), 382 (15), 262 (79), 229 (42), 217 (100).

5α-Cholestane-3β,5-diol 3-acetate 5-(4-iodophenyl) acetate (**20**).

Esterification of **11**, as described above for the preparation of **21/22**, gave **20** in 74% yield; m.p. 170°C (from petroleum ether).- ^1H NMR (80 MHz, $CDCl_3$): δ = 0.59 (s, CH_3-18); 0.92 (s, CH_3-19); 2.00 (s, 3β-OAc); 3.62, 3.51 (AB system, $|J_{AB}|$ = 16 Hz, -CO-CH_2Ar); 4.48-5.00 (m, 3α-H); 7.06, 7.68 (aromatic H's).- MS: m/z (%)= 688 (0.03, M^+), 369 (94), 368 (100), 262 (51), 217 (61).- (Found C 64.30, H 8.10. Calc for $C_{37}H_{55}O_4I$ (690.7): C 64.34, H 8.03).

17-Chloro-5α-cholestane-3β,5-diol 3-acetate 5-(4-iodophenyl) acetate (**26**).

a) A solution of 20 (80.1 mg, 0.12 mmol), azobis(isobutyronitrile) (59 mg), SO_2Cl_2 (117.5 mg, 0.87 mmol) in dry CCl_4 was deoxygenated with a stream of argon and at -10°C exposed to UV-light (Philips HPK 125, pyrex filter) for 150 min. After addition of CH_2Cl_2 the organic solution was washed with ice-cold 5% $Na_2S_2O_3$ solution, ice-cold 5% $NaHCO_3$ solution and ice-cold water. Drying, solvent evaporation (at 20°C), and LC (petroleum ether-ethyl acetate 10:1) provided **26** (49.9 mg, 59%).
b) A solution of **20** (96 mg, 0.14 mmol) and freshly prepared iodobenzene dichloride (163.8 mg, 0.60 mmol) in $CHCl_3$ (100 ml spectrophotometric grade) was deoxygenated with a stream of argon. Photolysis was carried out at 20°C using a 300 W sun lamp (Osram Ultra-Vitralux) placed in 5 cm distance of the reaction flask. At the appearence of a slight pink colour the reaction stopped. Working up and LC as described above furnished **26** (58.4 mg, 58%). M.p. 162°C (from CH_2Cl_2-petroleum ether).- ^1H NMR (80 MHz, $CDCl_3$): δ = 0.70 (s, CH_3-18), 0.88 (s, CH_3-19), 1.93 (s, 3β-OAc), 3.50 (narrow m, -CO-CH_2Ar), 4.38-4.93 (m, 3α-H), 7.00, 7.68 (aromatic H's).- MS: m/z (%)= 688 (4, $C_{37}H_{54}O_4ClI$-HCl $^+$), 673 (7), 603 (12), 575 (35), 351 (77), 313 (70), 281 (25), 262 (25), 53 (100), 217 (40).

5α-Cholest-16-ene-3β,5-diol 3-acetate 5-(4-iodophenyl)acetate (**23**).

Using the iodobenzene dichloride procedure described above **20** (13.3 mg, 0.02 mmol) was transformed into **26**. After working-up dry pyridine (100 µl) was added and the mixture stirred under argon at 135°C for 45 min. LC(Merck LiChroprep RP-8, methanol-water 100:1) gave **23** (11.5 mg, 87%, based on **20**).- M.p. 124-126°C (from acetone-water).- ^1H NMR (250 MHz, $CDCl_3$): δ = 0.65 (s, CH_3-18), 0.81 (d, J = 8Hz, CH_3-26 and CH_3-27), 0.94 (s, CH_3-19), 2.00 (s, 3β-OAc), 3.60 (narrow m, -CO-CH_2Ar), 4.82 (m, 3α-H), 7.17, 7.79 (aromatic H's).- MS: m/z(%) = 688 (6, M^+), 253 (100).- (Found 688.2957 (MS). Calc for $C_{37}H_{53}O_4I$: 688.2974).

Preparation of a 4:1 mixture of **31** and **23** from **20**.

In three runs 49.8 mg (0.07 mmol), 18.6 mg (0.03 mmol), and 10.0 mg (0.01 mmol) of **20** were transformed into **26** (iodobenzene dichloride procedure). After work-up the products were combined and treated with DBU (142 µl). The resulting mixture was stirred under argon for 150 min at 90°C. Aqueous work-up ($CHCl_3$) and LC (petroleum ether-ethyl acetate 10:1) furnished a 4:1 mixture (^{1}H NMR, integration of 3α-H and 16-H signals at δ =4.83 and δ = 5.25, respectively) of **31** and **23** (49.9 mg, 64 %, based on **20**).

5α-Cholest-17(20)-ene-3β,5-diol 3-acetate 5-(4-iodophenyl)acetate (**31**).

An analytical sample was obtained by careful chromatographic separation of a 4:1 mixture of **31** and **23** (petroleum ether-ethyl acetate 10:1).- M.p. 149-152°C (from acetone-water).- ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.73 (s, CH_3-18), 0.85 (d, J = 8Hz, CH_3-26, CH_3-27), 0.92 (s, CH_3-19), 2.00 (s, 3β-OAc), 3.54 and 3.61 (AB system, J_{AB} = 15Hz, -CO-CH_2-Ar), 4.83 (m, 3α-H), 7.18 and 7.80 (aromatic H's).- MS: m/z (%) = 688 (11, M^+), 281 (100).- (Found C 64.58, H 7.73. Calc for $C_{37}H_{53}O_4I$ (688.7): C 64.52, H 7.76).

Preparation of a 4:1 mixture of **32/33** and **24/25** from **21/22**.

A mixture of **21** and **22** was transformed into a 4:1 mixture (^{1}H NMR) of **32/33** and **24/25** in 53% overall yield using the procedure described for the preparation of **31/23** from **20**. ^{1}H NMR (80 MHz, $CDCl_3$): δ = 1.94 (s, 3β-OAc), 3.50 (narrow m, -CO-CH_2Ar), 4.70 (m, 3α-H), 5.25 (m, 16-H), 7.00 and 7.60 (aromatic H's).- MS: m/z (%) = 716 (1, M^+ of **32** and **24**, $C_{39}H_{57}O_4I$), 702 (1, M^+ of **33** and **25**, $C_{38}H_{55}O_4I$), 217 (100).

17-Oxo-5α-androstane-3β,5-diol 3-acetate 5-(4-iodophenyl)acetate (**29**).

A 4:1 mixture of **31** and **23** (26.7 mg, 0.04 mmol) dissolved in 1:1 CH_2Cl_2-methanol (absolute, 6 ml) was ozonized at -78°C. When a blue colour persisted, excess ozone was removed with a stream of oxygen. Trimethyl phosphite (0.33 ml) was added and the mixture stirred at room temperature for 90 min. Evaporation of the solvent and LC (petroleum ether-ethyl acetate 5:1) provided **29** (17.6 mg, 100%, based on **31**). - Using the same procedure, the above mixture of **32/33** and **24/25** was transformed into **29**.- M.p. 149°C (from petroleum ether).- ^{1}H NMR (80 MHz, $CDCl_3$): δ =0.73 (s, CH_3-18), 0.90 (s, CH_3-19), 1.93 (s, 3β-OAc), 3.50 (narrow m, -CO-CH_2Ar), 4.43-4.93 (m, 3α -H), 6.95 and 7.55 aromatic H's).- MS: m/z (%) = 592 (1, M^+), 81 (100).- (Found C 58.87, H 6.42. Calc for $C_{29}H_{37}O_5I$ (592.5): C 58.78, H 6.29).

4-Androstene-3,17-dione (**34**).

To a solution of **29** (13.1 mg, 0.02 mmol) in THF (1 ml) was added 0.15 molar aqueous LiOH (0.2 ml). The mixture was refluxed under argon for 4 h, then cooled to room temperature and neutralized by careful addition of dilute H_2SO_4. After work-up (CH_2Cl_2) pure **30** (10.5 mg, 86%) was obtained, ^{1}H NMR (80 MHz, $CDCl_3$): δ = 0.73 (s, CH_3-18), 0.87 (s, CH_3-19), 3.43 (narrow m, -CO-CH_2Ar), 3.59 (m, 3α -H), 6.94 and 7.56 (aromatic H's).- To a solution of the above sample of **30** (5.2 mg, 0.01 mmol) in dry CH_2Cl_2 (0.5 ml) was added pyridinium chlorochromate (4.0 mg, 0.02 mmol) and sodium acetate (1.5 mg). The mixture was stirred for 1 h at room temperature. Dry diethyl ether (1 ml) was added and the suspension filtered through a pad of silica gel (elution with ethyl acetate). The solvent was evaporated and the residue taken up in THF (0.5 ml) and 0.15 molar aqueous LiOH (0.1 ml). After 5 min at room temperature, water was added. Work-up (CH_2Cl_2) furnished pure **34** (2.8 mg, 100%).- M.p. 171°C (from CH_2Cl_2-petroleum ether). Mixed m.p. with an authentic sample: 171°C.

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