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Unusual Oxidation Reactions of 7α-Methyl- and 7α-Phenylcholest-5-ene-3β,7β-diol

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Summary. Ozonation of 7α-methyl (or 7α-phenyl) cholest-5-ene-3β,7β-diol 3-*TBDMS* ether afforded the corresponding 5β,6β-epoxy derivatives. The same product was formed by *MCPBA* oxidation. The reaction of 7α-phenylcholest-5-ene-3β,7β-diol with CrO_3 yielded 3,7-dioxo-6,7-*seco*-7-phenylcholest-4-ene-5-carboxaldehyde. An analogous B-*seco* aldehyde was obtained from 7α-methylcholest-5-ene-3β,7β-diol in addition to 7-methylcholesta-4,6-dien-3-one. *Jones* oxidation of 7α-phenylcholest-5-ene-3β,7β-diol or B-*seco*-aldehyde gave 3,7-dioxo-6,7-*seco*-7-phenylcholest-4-en-6-oic acid isolated as its methyl ester upon treatment with diazomethane.

Keywords: Steroids; Ozonization; CrO_3 oxidation; Epoxidation; B-*seco* steroids.

Ungewöhnliche Oxidation von 7α-Methyl- und 7α-Phenylcholest-3-en-3β,7β-diol

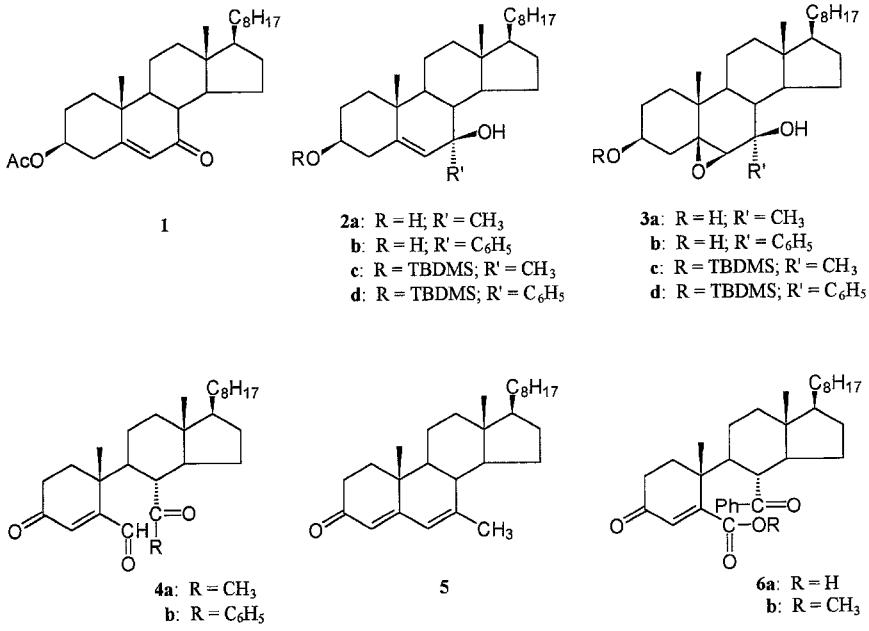
Zusammenfassung. Ozonolyse von 7α-Methyl- bzw. 7α-Phenyl-cholest-3-en-3β,7β-diol-3-*TBDMS*-ether ergab die entsprechenden 5β,6β-Epoxy-Derivate. *MCPBA*-Oxidation führte zum gleichen Ergebnis. Bei der Reaktion von 7α-Phenyl-cholest-5-en-3β,7β-diol mit CrO_3 wurde 3,7-Dioxo-6,7-*seco*-7-phenyl-cholest-4-en-5-carbaldehyd gebildet. Einen analogen B-*seco*-Aldehyd erhält man neben 7-Methyl-cholesta-4,6-dien-3-on auch aus 7α-Methyl-cholest-5-en-3β,7β-diol. Durch *Jones*-Oxidation von 7α-Phenyl-cholest-5-en-3β,7β-diol oder B-*seco*-Aldehyd erhält man 3,7-Dioxo-6,7-*seco*-7-phenyl-cholest-4-en-6-carbonsäure, die nach Behandlung mit Diazomethan als ihr Methylester isoliert wurde.

Introduction

5α-Reductase is the enzyme which catalyzes the conversion of testosterone to dihydro-testosterone, the more potent androgen involved in the development of benign prostatic hyperplasia and other androgen dependent diseases [1, 2]. Two isozymes of 5α-reductase are present in humans [3], and the 7-substituted 6-aza-cholestane derivatives (likewise 7-alkyl 4-azacholestanes) have been found to be selective inhibitors of human type 1 enzyme [4, 5]. Due to its location in the skin, a type 1 selective inhibitor could be useful in treating acne, alopecia, and hirsutism. The synthesis of 6-azacholest-4-en-3-one and its 7-methyl derivatives by multi-step transformations of cholesterol has recently been described [5]. As precursors of these 6-azasteroids and other 6-heterosteroids [6], suitably substituted B-*seco* compounds can be employed. The goal of this investigation was to elaborate a simple and efficient route to B-*seco* precursors of 7-methyl- and 7-phenyl-6-azacholestanes.

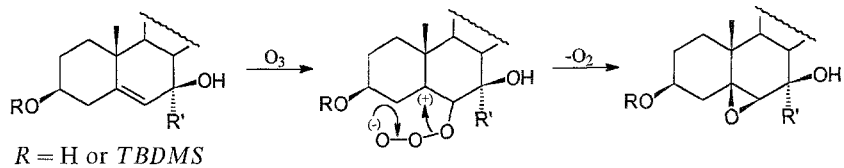
Results and Discussion

The starting material for the present work was 3β-acetoxycholest-5-en-7-one. This compound was treated with methylmagnesium iodide or phenylmagnesium bromide in ether at room temperature [7, 8]. The ^{1}H NMR analysis of the crude reaction products showed in both cases a large excess of a single stereoisomer, but there was no proof for its configuration at C-7. According to the approach vector analysis method, the stereochemistry of the nucleophilic addition to Δ^5-7-ones is controlled by the *quasi*-axial β-hydrogen at C-8 [9]. This suggests that the *Grignard* reagents approach from the α-side. Additional support for the 7α-methyl (or phenyl) structure of the products stems from studies on their dehydration described in the literature (no dehydration to the 5,7-diene was observed) [8].



Scheme 1

In order to cleave the double bond in the ring B, the compounds **2c** and **2d** were subjected to ozonization. The crude reaction products were treated with dimethyl sulfide, but TLC control did not show any change in the composition of the reaction mixtures after addition of the reducing agent. The spectroscopic analysis (MS, ^{13}C NMR, ^{1}H NMR, IR) of the main product of both reaction suggested the presence of an ether moiety in ring B (the molecular weight was higher by 16 units as compared with the starting material; no change in carbon atom number, no carbonyl groups, no olefinic protons, one proton singlet in the ether resonance region). The lack of acetal carbon atoms (^{13}C NMR) and the retention of a hydroxyl group pointed to an epoxidation of the allylic alcohols **2c** and **2d** with ozone, a reaction known as "partial cleavage" and sometimes observed with highly hindered alkenes [10]. However, on the basis of the spectroscopic data it was difficult to draw a definite conclusion on the epoxide configuration.

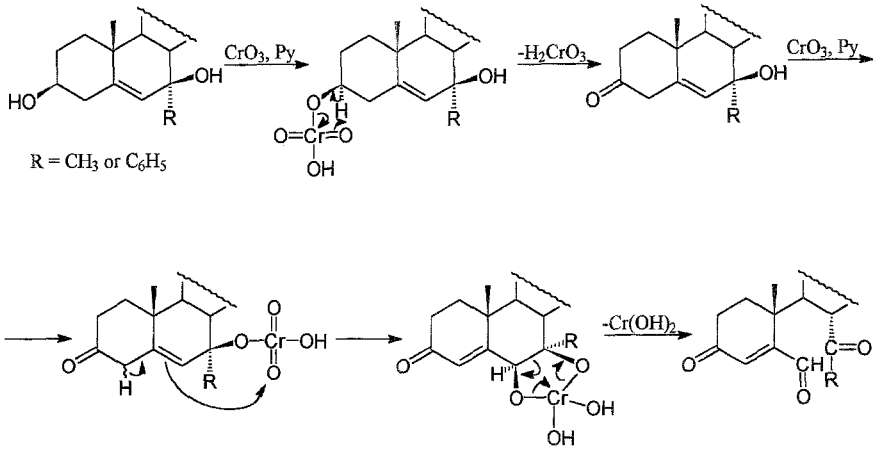


R = H or *TBDMS*
R' = CH_3 or C_6H_5

Scheme 2

The tentative mechanism of the reaction (Scheme 2) involves an electrophilic ozone attack to give a σ complex with a formation of the more stable carbonium ion, followed by loss of molecular oxygen. An inspection of *Dreiding* stereo models shows that the β side of the 7α-substituted Δ^5-steroids is less hindered; thus, the β-epoxide should preferentially by formed. However, the structure of this unusual ozonization product, particularly its stereochemistry, needed further confirmation. For this reason, epoxidation reactions of allylic alcohols **2c** and **2d** with *MCPBA* were performed. The products of epoxidation proved to be identical with the corresponding ozonization products. Since it is well established that the stereochemistry of the epoxidation of allylic alcohols with peracids is controlled by a hydroxy group which forms a hydrogen bond with the reagent [11], the epoxide ring configuration in both compounds **3c** and **3d** is β.

The failure of the double bond ozonolysis in the allylic alcohols **2a–d** prompted us to undertake further attempts towards a ring B cleavage in these compounds. In some experiments, **2a** and **2b** were subjected to CrO_3 oxidation in pyridine (*Sarrett* reagent). This very mild reagent unexpectedly led to the formation of the desired B-*seco* products. The oxidation of 7α-phenylcholest-5-ene-3β,7β-diol (**2b**) afforded B-*seco* aldehyde **4b** in relatively high yield. The oxidation with CrO_3/pyridine in dichloromethane worked even better and the same product was obtained. The analogous aldehyde **4a** was formed in addition to dienone **5** as the oxidation product of 7α-methyl allylic alcohol **2a** with both CrO_3 based reagents. Compound **5** has been obtained previously from **2a** by *Oppenauer* oxidation [12, 13]. The ratio of products **4a**:**5** was 59:41 but may be slightly changed by varying the reaction conditions. The tentative mechanism of the reaction is shown in Scheme 3.



R = CH_3 or C_6H_5

Scheme 3

The B-*seco* aldehyde **4a** underwent slow epimerization at C-8 upon storing in solution or without solvent. No similar epimerization was observed in the case of compound **4b**, presumably due to a lower acidity of 8β-H (α protons of alkyl aryl ketones are less acidic than those of dialkyl ketones). The B-*seco* aldehydes **4a** and **4b** were subjected to *Jones* oxidation followed by treatment of the crude acidic products with diazomethane. The procedure worked well for **4b** but failed in the case of **4a** due to the isomerization process. The methyl ester **6b** obtained proved to be identical with the product of direct oxidation of 7α-phenylcholest-5-ene-3β,7β-diol (**2b**) subjected to the same procedure. The latter reaction is of synthetic interest due to its rather good yield (41%).

Further studies on the conversion of B-*seco* compounds into 6-azasteroids are in progress.

Experimental

Melting points were determined on a Kofler apparatus of the Boetius type and are uncorrected. NMR spectra were recorded with a Bruker AC 200 F spectrometer using $CDCl_3$ solutions with *TMS* as internal standard. Infrared spectra were recorded on a Specord 75 IR as chloroform solutions. Mass spectra were obtained at 70 eV with an AMD-604 spectrometer. The reaction products were isolated by column chromatography performed on silica gel 70–230 or 230–400 mesh ASTM (Merck). Thin layer chromatograms were developed on aluminum TLC sheets precoated with silica gel F_{254} and visualized with 50% sulfuric acid after heating. All solvents were dried and freshly distilled prior to use. Compounds **2a** (m.p.: 162–164 °C; Ref. [7, 8]: m.p.: 164–165 °C) and **2b** (m.p.: 148–150 °C; Ref. [8]: m.p.: 151–152 °C) were obtained from 7-oxo-cholesteryl acetate (**1**) by reaction with methyl or phenyl magnesium halides, respectively, according to the procedures described in the literature.

7α-Phenylcholest-5-ene-3β,7β-diol 3-TBDMS ether (**2d**)

To a solution of 7α-phenyl diol **2b** (200 mg; 0.42 mmol) in anhydrous *DMF* (1.32 ml), imidazole (75.7 mg; 1.24 mmol) and *t*-butyldimethylsilyl chloride (70.9 mg; 0.47 mmol) were added. The reaction mixture was magnetically stirred at room temperature for 16 hours, diluted with water, and extracted three times with chloroform. The combined extracts were dried ($MgSO_4$) and evaporated *in vacuo*. The crude product was purified by silica gel column chromatography. Elution with benzene afforded *TBDMS* ether **2d** (208.8 mg; 84.3%); m.p.: 56–58 °C (hexane-methylene chloride); IR ($CHCl_3$): $\nu = 3582$ (weak), 1259, 1095, 1012, 835, 699 cm^{-1}; ^1H NMR: $\delta = 7.48$–7.52 (m, 2H, *o*-Ar-H), 7.28–7.38 (m, 3H, *m*-, *p*-Ar-H), 5.16 (d, $J = 1.2$ Hz, 1H, 6-H), 3.60 (m, 1H, 3α-H), 1.15 (s, 3H, 19-H), 0.88 (s, 9H, *t*-Bu-Si), 0.82–0.85 (m, 9H, 21-H, 26-H and 27-H), 0.67 (s, 3H, 18-H), 0.06 and 0.07 (2 × s, 6H, Me-Si) ppm; ^{13}C NMR: $\delta = 143.6$ (C), 141.4 (C), 129.6 (CH), 127.5 (2 × CH), 127.3 (2 × CH), 126.6 (CH), 77.8 (C), 72.5 (CH), 54.3 (CH), 50.1 (CH), 45.4 (CH), 44.5 (CH), 43.0 (C), 42.3 (CH_2), 39.4 (CH_2), 38.5 (CH_2), 37.3 (CH_2), 37.1 (C), 36.1 (CH_2), 35.6 (CH), 32.0 (CH_2), 28.3 (CH_2), 28.0 (CH), 26.7 (CH_2), 25.9 (3 × CH_3), 23.9 (CH_2), 22.8 (CH_3), 22.5 (CH_3), 20.8 (CH_2), 19.0 (CH_3), 18.8 (CH_3), 18.2 (C), 12.1 (CH_3), 1.0 (CH_3), −4.6 (CH_3) ppm.

The silylation of diol **2a** was performed in a similar manner to afford 7α-methylcholest-5-ene-3β,7β-diol 3-*TBDMS* ether (**2c**). M.p.: 43–45 °C (methanol); IR ($CHCl_3$): $\nu = 3599$, 3425, 1258, 1094 cm^{-1}; ^1H NMR: $\delta = 5.16$ (d, $J = 1.4$ Hz, 1H, 6-H), 3.48 (m, 1H, 3α-H), 1.16 (s, 3H, 7α-Me), 1.04 (s, 3H, 19-H), 0.93 (d, $J = 6.5$ Hz, 3H, 21-H), 0.89 and 0.87 (s and d overlapped, 15H, *t*-Bu-Si, 26-H and 27-H), 0.69 (s, 3H, 18-H), 0.06 (s, 6H, Me-Si) ppm.

*5β,6β-Epoxy-7α-phenylcholestane-3β,7β-diol 3-TBDMS ether (***3d***) by ozonization of* **2d**

Compound **2d** (208.8 mg; 0.35 mmol) was dissolved in 18 ml of chloroform-ethyl acetate (2:1). The solution was cooled to −70 °C in a dry ice-acetone bath, and a slow stream of ozone was passed

through (about 1.5 mg/min). When TLC control indicated the disappearance of the starting material, the excess ozone was blown out with oxygen and a drop of dimethyl sulfide was added. The crude product obtained by removal of solvents under reduced pressure was purified by silica gel column chromatography. An oily epoxide **3d** (127.4 mg; 59.4%) was eluted with a benzene-ether (99.5:0.5) mixture; IR ($CHCl_3$): $\nu = 3573$ (weak), 1259, 1102, 838, 699 cm^{-1}; ^1H NMR: $\delta = 7.49$–7.54 (m, 2H, *o*-Ar-H), 7.32–7.42 (m, 3H, *m*-, *p*-Ar-H), 3.83 (m, 1H, 3α-H), 3.02 (s, 1H, 6α-H), 1.11 (s, 3H, 19-H), 0.80–0.90 (m, 18H, *t*-Bu-Si, 21-H, 26-H and 27-H), 0.65 (s, 3H, 18-H), 0.06 and 0.07 (2 × s, 6H, Me-Si) ppm; ^{13}C NMR: $\delta = 140.5$ (C), 127.7 (2 × CH), 127.4 (CH), 127.0 (2 × CH), 78.0 (C), 71.9 (CH), 70.1 (CH), 68.2 (C), 54.3 (CH), 49.3 (CH), 45.7 (CH), 43.1 (C), 42.7 (CH_2), 42.0 (CH), 39.4 (CH_2), 38.5 (CH_2), 37.0 (CH_2), 36.1 (CH_2), 35.6 (CH), 34.3 (C), 31.5 (CH_2), 28.4 (CH_2), 28.0 (CH), 27.5 (CH_2), 25.8 (3 × CH_3), 23.9 (CH_2), 22.8 (CH_3), 22.5 (CH_3), 21.7 (CH_2), 18.8 (CH_3), 18.2 (C), 17.8 (CH_3), 12.1 (CH_3), −4.58 (CH_3), −4.64 (CH_3) ppm.

In order to obtain 5β,6β-epoxy-7α-phenylcholestane-3β,7β-diol (**3b**), compound **3d** (104.9 mg; 0.17 mmol) was dissolved in 1 ml of *THF*, treated with a 1 *M* solution of tetrabutylammonium fluoride in *THF* (1 ml), and allowed to stand overnight. The reaction mixture was diluted with benzene, washed with water, dried ($MgSO_4$), and evaporated *in vacuo*. The crude product **3b** was crystallized from hexane-methylene chloride, Yield: 59.7 mg (70%); m.p.: 141–142 °C; IR ($CHCl_3$): $\nu = 3585$, 3420, 945, 699 cm^{-1}; ^1H NMR: $\delta = 7.48$–7.52 (m, 2H, *o*-Ar-H), 7.28–7.41 (m, 3H, *m*-, *p*-Ar-H), 3.91 (m, 1H, 3α-H), 3.04 (s, 1H, 6α-H), 1.13 (s, 3H, 19-H), 0.80–0.86 (m, 9H, 21-H, 26-H and 27-H), 0.66 (s, 3H, 18-H) ppm; MS: $m/z = 494$ (M^+, 12%), 476 (20%), 387 (20%), 371 (23%), 354 (100%), 105 (79%).

Ozonization of **2c** was performed in the same manner as described above for **2d** to afford 5β,6β-epoxy-7α-methylcholestane-3β,7β-diol 3-*TBDMS* ether (**3c**) in 51% yield. IR ($CHCl_3$): $\nu = 3570$ (weak), 1253, 1105 cm^{-1}; ^1H NMR: $\delta = 3.61$ (m, 1H, 3α-H), 2.86 (s, 1H, 6α-H), 1.18 (s, 3H, 7α-Me), 1.00 (s, 3H, 19-H), 0.84–0.92 (m, 18H, *t*-Bu-Si, 21-H, 26-H and 27-H), 0.66 (s, 3H, 18-H), 0.053 and 0.048 (2 × s, 6H, Me-Si) ppm; ^{13}C NMR: $\delta = 73.0$ (C), 72.4 (CH), 70.0 (CH), 67.5 (C), 55.2 (CH), 50.4 (CH), 48.5 (CH), 43.0 (C), 42.3 (CH_2), 40.6 (CH), 39.6 (CH_2), 39.5 (CH_2), 37.4 (CH_2), 36.2 (CH_2), 35.7 (CH), 34.4 (C), 31.2 (CH_2), 28.5 (CH_2), 28.0 (CH), 26.9 (CH_2), 25.8 (3 × CH_3), 23.8 (CH_2), 22.8 (CH_3), 22.7 (CH_2), 22.6 (CH_3), 18.8 (CH_3), 18.3 (CH_3), 18.1 (C), 17.3 (CH_3), 11.8 (CH_3), −4.6 (CH_3), −4.7 (CH_3) ppm; MS: $m/z = 546$ (M^+, 2%), 515 (5%), 489 (100%), 471 (49%), 397 (52%).

*5β,6β-Epoxy-7α-phenylcholestane-3β,7β-diol 3-TBDMS ether (**3d**) by MCPBA oxidation of **2d***

To a solution of compound **2d** (98.8 mg; 0.17 mmol) in 8 ml of chloroform, *m*-chloroperoxybenzoic acid (111.7 mg; 0.65 mmol) was added. The reaction mixture was stirred for 1 h, diluted with benzene, and washed twice with 5% sodium carbonate solution and water. The organic layer was dried ($MgSO_4$) and evaporated *in vacuo*. The oily residue was purified by silica gel chromatography. Elution with a benzene-ether (99.5:0.5) mixture afforded epoxide **3d** (30.8 mg; 30.4%), identical in all aspects with compound **3d** obtained by ozonization.

A similar oxidation of 7α-methyl compound **2c** with *m*-chloroperoxybenzoic acid afforded the corresponding 5β,6β-epoxy derivative. Epoxide **3c** obtained was identical in all respects with **3c**.

*3,7-Dioxo-6,7-seco-7-phenylcholest-4-ene-5-carboxaldehyde (**4b**) by oxidation of diol **2b***

a) Oxidation with CrO_3-pyridine in methylene chloride

To a vigorously stirred mixture of methylene chloride (25 ml) and pyridine (7.5 ml), chromic anhydride (932 mg; 9.32 mmol) was carefully added. The stirring was continued for 30 minutes; then, a solution of **2b** (310.8 mg; 0.65 mmol) in methylene chloride was added. The reaction was completed in about 12 h and quenched with water. The reaction mixture was washed with 5% aqueous sulfuric acid; the organic layer was separated, dried ($MgSO_4$), and evaporated *in vacuo*. The crude product was subjected to silica gel column chromatography. Elution with a benzene-ether (99:1) mixture afforded B-*seco* aldehyde **4b**

(147.5 mg; 46.3%). M.p.: 153–155 °C (hexane-methylene chloride); IR ($CHCl_3$): $\nu = 2720$ (weak), 1700, 1681, 1598 (weak), 1105, 697 cm^{-1}; ^1H NMR: $\delta = 9.68$ (s, 1H, CHO), 8.02 (d, $J = 6.9$ Hz, 2H, *o*-Ar-H), 7.40–7.65 (m, 3H, *m*-, *p*-Ar-H), 6.37 (s, 1H, 4-H), 3.56 and 3.12 (t, $J = 10.7$ Hz and m, 2 × 1H, 2-H), 1.12 (s, 3H, 19-H), 0.82–0.91 (m, 9H, 21-H, 26-H and 27-H), 0.78 (s, 3H, 18-H) ppm; ^{13}C NMR: $\delta = 203.1$ (C), 199.7 (C), 194 (CH), 160.7 (C), 137.8 (C), 137.7 (CH), 133.2 (CH), 128.9 (2 × CH), 128.3 (2 × CH), 54.8 (CH), 54.3 (CH), 43.7 (CH), 43.1 (CH), 42.3 (C), 40.8 (C), 39.4* (CH_2), 38.8 (CH_2), 35.9 (CH_2), 35.7 (CH), 34.4 (CH_2), 30.0 (CH_2), 27.9 (CH), 27.8 (CH_2), 25.3 (CH_3), 25.0* (CH_2), 23.7 (CH_2), 22.8 (CH_3), 22.5 (CH_3), 18.5 (CH_3), 11.6 (CH_3) ppm (*: one of these signals stands for two carbon atoms); MS: $m/z = 490$ (M^+, 33%), 353 (24%), 105 (100%).

b) Sarrett oxidation

Sarrett reagent was prepared by portionwise addition of chromic anhydride (861 mg; 8.61 mmol) to pyridine (6.9 ml). The reagent was stirred for 30 minutes; then, a solution of diol **2b** (287 mg; 0.6 mmol) in pyridine (1 ml) was added. The reaction mixture was allowed to stand for 12 h, poured into iced 5% aqueous sulfuric acid, and extracted twice with chloroform. The extract was washed with water, dried ($MgSO_4$), and evaporated *in vacuo*. The crude product **4b** was purified by silica gel column chromatography as described in section *a*. Yield: 132.4 mg (45%).

Analogous CrO_3-pyridine oxidations of 7α-methyl diol **2a** yielded the corresponding B-*seco* aldehyde **4a** in addition to 7-methylcholesta-4,6-dien-3-one (**5**).

4a: IR ($CHCl_3$): $\nu = 2716$ (weak), 1697 (broad), 1611, 1102 cm^{-1}; ^1H NMR: $\delta = 9.66$ (s, 1H, CHO), 6.41 (s, 1H, 4-H), 2.23 (s, 3H, 7-Me), 0.83–0.89 (m, 12H, 19-H, 21-H, 26-H and 27-H), 0.64 (s, 3H, 18-H) ppm; MS: $m/z = 482$ (M^+, 85%), 358 (21%), 292 (28%), 138 (100%); exact mass calcd. for $C_{28}H_{44}O_3$: 428.3290; found: 428.3269.

5: IR ($CHCl_3$): $\nu = 1651$, 1615 cm^{-1}; ^1H NMR: $\delta = 5.94$ (s, 1H, 4-H), 5.58 (s, 1H, 6-H), 1.93 (s, 3H, 7-Me), 1.08 (s, 3H, 19-H), 0.94 (d, $J = 6.5$ Hz, 3H, 21-H), 0.87 (d, $J = 6.9$ Hz, 6H, 26-H and 27-H), 0.77 (s, 3H, 18-H) ppm; ^{13}C NMR: $\delta = 199.7$ (C), 164.9 (C), 152.4 (C), 126.7 (CH), 121.1 (CH), 54.6 (CH), 53.3 (CH), 50.7 (CH), 45.0 (C), 41.7 (CH), 39.5 (CH_2), 39.3 (CH_2), 36.1 (CH_2), 35.7 (C), 35.5 (CH), 34.2 (CH_2), 34.0 (CH_2), 28.5 (CH_2), 28.0 (CH), 27.8 (CH_2), 25.6 (CH_3), 23.8 (CH_2), 22.8 (CH_3), 22.5 (CH_3), 20.8 (CH_2), 18.9 (CH_3), 16.4 (CH_3), 12.2 (CH_3) ppm.

*3,7-Dioxo-6,7-seco-7-phenylcholest-4-en-6-oic acid (**6a**) and its methyl ester (**6b**) by Jones oxidation of **2b** or **4b***

To a solution of diol **2b** (195.2 mg; 0.41 mmol) in acetone (26 ml), a *Jones* reagent prepared from 1.34 g of CrO_3, 3.8 ml of water, and 1.2 ml of sulfuric acid was added. The reaction mixture was stirred for 1 h, quenched with water, and extracted with chloroform. The extract was washed with water, dried ($MgSO_4$), and evaporated *in vacuo*. The crude B-*seco*-acid **6a** was treated with etheral diazomethane. Ether was removed *in vacuo*, and the residue was chromatographed on a silica gel column. Pure methyl ester **6b** was eluted with benzene-ether (99:1). Yield: 87.1 mg (41%); m.p.: 164–166 °C (hexane-methylene chloride); IR ($CHCl_3$): $\nu = 1723$, 1675, 1242 cm^{-1}; ^1H NMR: $\delta = 8.00$–8.05 (m, 2H, *o*-Ar-H), 7.45–7.65 (m, 3H, *m*-, *p*-Ar-H), 6.44 (s, 1H, 4-H), 3.83 (s, 3H, Me-OCO), 3.54 and 2.90 (t, $J = 10.7$ Hz and m, 2 × 1H, 2-H), 1.19 (s, 3H, 19-H), 0.77 (s, 3H, 18-H) ppm; ^{13}C NMR: $\delta = 203.1$ (C), 199.2 (C), 167.2 (C), 157.4 (C), 137.9 (C), 133.2 (CH), 131.5 (CH), 128.9 (2 × CH), 128.3 (2 × CH), 54.9 (CH), 54.5 (CH), 52.4 (CH_3), 45.1 (CH), 43.5 (CH), 42.3 (C), 41.5 (C), 39.4 (CH_2), 39.0 (CH_2), 36.0 (CH_2), 35.8 (CH), 34.0 (CH_2), 30.2 (CH_2), 28.0 (CH), 27.8 (CH_2), 26.4 (CH_3), 25.0 (CH_2), 24.5 (CH_2), 23.7 (CH_2), 22.8 (CH_3), 22.5 (CH_3), 18.6 (CH_3), 11.7 (CH_3) ppm; MS: $m/z = 520$ (M^+, 10%), 488 (7%), 353 (36%), 168 (49%), 105 (100%); exact mass calcd. for $C_{34}H_{48}O_4$: 520.3553; found: 520.3546.

A similar reaction of **4b** with *Jones* reagent followed by treatment with diazomethane afforded the same methyl ester **6b** in 42% yield.

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