Oxidative fragmentations of 5-hydroxy-1-oxo-5α-cholestan-3β-yl acetate

NATALIJA M. KRSTIČ, MIRA S. BJELAKOVIĆ, LJUBINKA B. LORENČ and VLADIMIR D. PAVLOVIĆ

aCenter for Chemistry, ICTM, P. O. Box 473, 11001 Belgrade and bFaculty of Chemistry, University of Belgrade, Studentski trg 12-16, P. O. Box 158, 11001 Belgrade, Serbia and Montenegro

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Abstract: 5-Hydroxy-1-oxo-5α-cholestan-3β-yl acetate (11) was prepared in 5 steps starting from (E)-3β-acetoxy-5,10-seco-1(10)-cholesten-5-one (6). Treatment of the 1-oxo-5-hydroxy derivative 11 with lead tetraacetate (LTA) (under thermal or hypoidote conditions) or with mercuric oxide/iodine (HgO/I2) reagent resulted in the oxidative β-fragmentation of the C(5)–C(10) bond affording 1,5-dioxo-5,10-secocholest-10(19)-en-3β-yl acetate (12), in different yields, depending on the reagent. Also the stereochemistry of the 1,6-cyclization product 13, formed by transannular cyclization of the 1,5-diketone 12 on silica gel, is discussed in this work.

Keywords: 5-Hydroxy-1-oxo-5α-cholestan-3β-yl acetate, 1,5-dioxo-5,10-secocholest-10(19)-en-3β-yl acetate, β-fragmentation, transannular cyclization.

INTRODUCTION

It is well known that the alkoxy radical i (generated by the oxidation of the 5-hydroxy steroids 1 and 2 with lead tetraacetate (LTA) under thermal or photolytic conditions or with hypoidote-forming reagents) readily undergoes β-fragmentation involving scission of the C(5)–C(10) bond, to afford, via the C(10)-radical intermediate ii, the diastereomeric (Z)- and (E)-1(10)-unsaturated 5,10-secocholesten-5-ketones 3 and 4 in different proportions and, depending on the oxidant used, in high yield (Scheme 1).1–3

The direction of β-fragmentation in 1 and 2 to give exclusively the 5,10-secoketones 3 and 4 was explained by the stability of the tertiary C-radical intermediate ii, due to the presence of the angular Me(19) group at the C(10)-radical center.

In accordance with such an explanation, it was anticipated that other 5-hydroxy steroids with similar structures and with the same reagents should react in the same way. However, when LTA oxidations (thermal and hypoidote) of the 5-hydroxy-8,9-seco-8,9-diketone 5, a
substrate with a polar oxo-group located at the α-position to the corresponding C(10)-radical center (type ii), were performed under similar experimental conditions, the only obtained product was an unresolvable mixture of the 7-, 11- and 14-acetoxy derivatives arising from the competing acetoxylation of the α-positions next to the C(8)- and C(9)-oxo groups.

On the other hand, when the oxidative fragmentation of the C(5)–C(10) bond in compound 5 was attempted with HgO/I₂ reagent, practically all the starting material remained unchanged (recovery being ≈ 82 %, while the rest was an unresolvable mixture) (Scheme 2).

The resistance of compound 5 to undergo oxidative β-fragmentation of its C(5)–C(10) bond was explained by strong hydrogen bonding between the 5-OH group and the 9-oxo
function. As a consequence of this interaction, the formation of the alkoxy radical was suppressed.

RESULTS AND DISCUSSION

In order to obtain more information concerning the influence of an oxo-group in the α-position to the C(10) on the oxidative fragmentation of the C(5)–C(10) bond, in the present work the possibility of inducing oxidative β-fragmentation of 5-hydroxy-1-oxo-5α-cholestan-3β-yl acetate (11) was investigated.

For the introduction of an oxygen function at the C(1)-position, the ten-membered ring containing (E)-3β-acetoxo-5,10-seco-1(10)-cholesten-5-one (6) was required. This compound was prepared from cholestane-3β,5α-diol 3-acetate according to the procedure given in Ref. 3. Substrate 11 was then synthesized in 5 steps, as shown in Scheme 3.

UV irradiation of 6 in acetone solution with a high pressure mercury lamp (TQ 150 Z2) afforded a photoproduct (Paterno-Büchi reaction) with an oxetane structure, i.e. 1α,5-epoxy-5α-cholestan-3β-yl acetate (7) in 36.5 % yield. Treatment of the oxetane derivative 7 with hydroiodic acid in glacial acetic acid at 5 ºC resulted in the opening of the four-membered ether ring and the formation of cholest-5-en-1α,3β-diol 3-acetate (8) in high yield (78.0 %).5 The epoxy derivative 9 was prepared by m-chloroperbenzoic acid (MCPBA) oxidation of 8 (in 83.5 % yield).6 This product under conditions of catalytic hydrogenation (performed over PtO2 in acetic acid solution) gave 5α-cholestan-1α,3β,5-triol 3-acetate (10)(7) (35.7 %). Jones oxidation of the triol-monoacetate 10 in acetone solution at −5 ºC afforded the 5-hydroxy-1-oxo-5α-cholestan-3β-yl acetate (11) in 78.6 % yield.

Oxidations of alcohol 11 were performed with hypoiodite-forming reagents and LTA (thermal) under conditions similar to those previously applied to compounds 1, 2 and 5.1–4

The HgO/I2 version of the hypoiodite reaction of 11 performed with an excess of oxidant in CCl₄ solution by irradiation with a 15 W-lamp at 220 V at room temperature for
90 min in the presence of air gave, besides starting material 11 (20 %), an unresolvable complex mixture from which not one product with a defined structure could be isolated. The same results were obtained when the reaction was performed under O₂. However, when the above irradiation was performed under Ar, the resulting mixture of reaction products, after separation by column chromatography on silica gel, gave the 1,5-dioxo-5,10-secocholest-10(19)-en-3β-yl acetate (12) (38 %), the starting compound 11 (27 %) and the cyclization product 13 (28 %) (Scheme 4).

The structure of the product 12 was deduced from its analytical and spectral data (IR, ¹H-NMR, ¹³C-NMR, MS). In the IR spectrum, the absorption of the 1-oxo group migrates from 1716 to 1670 cm⁻¹, indicating an αβ-unsaturated carbonyl, and the absorption for the original 5α-hydroxyl group was missing and instead a new absorption at 1701 cm⁻¹ for the 5-oxo group appeared. In the ¹³C-NMR spectrum, a new singlet appeared at 207.7 ppm for C(5). The presence of the exocyclic methyldiene group CH₂=C(10) was evident from the IR spectrum (absorptions at 3100 and 1620 cm⁻¹) and confirmed by ¹H- and ¹³C-NMR data. Instead of the signal for the Me(19) group, the ¹H-NMR spectrum showed a pair of singlets at 5.83 and 6.15 ppm, and the ¹³C-NMR spectrum showed a triplet at 124.6 ppm for C(19) and a singlet at 155.0 ppm for C(10). Also, in the ¹³C-NMR spectrum, a singlet at 199.4 ppm for C(1) in the 1,5-diketone 12 was situated upfield when compared to the resonance at 209.4 ppm for C(1) in compound 11, indicating the influence of the exocyclic methyldiene group in the α-position.
Compound 13 is a secondary reaction product, formed by intramolecular 1,6-cyclization of the 1,5-diketone 12. This was confirmed by prolonged stirring (24 hours) of compound 12 with SiO₂ in toluene solution which afforded, besides the starting material, only one product, i.e. compound 13 (Scheme 5).

The structure of 13 was deduced from its analytical and spectral data (IR, ¹H-NMR, ¹³C-NMR, MS). In the IR spectrum, the absorption of the 1-oxo group was replaced by a new absorption at 3483 cm⁻¹ of the 1-hydroxy group. The IR band at 1643 cm⁻¹ indicates that the exocyclic methyldiene group still existed, which was confirmed by ¹H- and ¹³C-NMR data. Its ¹H-NMR spectrum contained a pair of singlets at 4.86 and 5.00 ppm of the CH₂=C(10) group. Also, the ¹³C-NMR spectrum contained the following characteristic signals: a triplet at 105.4 ppm of the C(19), a singlet at 74.0 ppm of the C(1) and a doublet at 56.0 ppm of the C(6). The cis-1β,6β-stereochemistry for the cyclization product 13 was deduced from its ¹H-NMR spectral characteristics. The signal for the Hβ–C(6) (due to the deshielding influence by the 5-carbonyl group), was shifted downfield and appeared at 2.88 ppm as a fine doublet of doublets, indicating a dihedral angle of about 60º (J = 5.5 Hz) between the Hβ–C(6) and Hβ–C(7) and 180º (J = 13.5 Hz) between the Hβ–C(6) and H₂C(7), and the “W” arrangement of the Hβ–C(6)–C(5)–C(4)–Hβ (J = 1.8 Hz), which is present only in the 1β,6β-isomer.

The LTA version of the hypoiodite reaction° of 11 was carried out with a large excess of oxidant in benzene solution by irradiation with a 15 W-lamp at 220 V at room temperature for 30 min, i.e., until 11 had been completely consumed. The resulting mixture was separated by column chromatography (silica gel), affording the previously described compound 12 in a very good yield of 73 % and the cyclization product 13 in a 10 % yield (Scheme 4).

The thermal LTA oxidation of 11 was carried out with an excess of oxidant in the presence of CaCO₃ in boiling benzene for 48 h (practically, the reaction mixture was not changed after 4 h). After separation by chromatography on silica gel, the reaction mixture gave 1,5-dioxo-5,10-secocholeste-10(19)-en-3β-yl acetate (12) (18 %), the starting compound 11 (43 %) and the cyclization product 13 (7 %) (Scheme 4).

From the above results it follows that the described oxidations of 5-hydroxy-1-oxo-5α-cholestan-3β-yl acetate (11) proceed (exclusively with HgO/I₂ and LTA/I₂ under Ar) as
expected via the C(10)-centered radical C (Scheme 6) which is formed according to the generally accepted mechanism,\textsuperscript{8,9} i.e., the homolysis of the O–I bond in the primarily formed species A is followed by fragmentation of the C(5)–C(10) bond in the thus obtained alkoxy radical B. The radical C is then stabilized by elimination of a H-atom from the Me(19) to give the 10-methylidene seco ketone 12.

Scheme 6.

The formation of the cyclization product 13 may be explained by an acid-catalyzed intramolecular aldol reaction in compound 12 during the chromatography on SiO\textsubscript{2} (Scheme 7).

Scheme 7.
EXPERIMENTAL

General.

Prep. column chromatography: silica gel Merck 0.063–0.200 mm. TLC: control of reaction and separation of products on silica gel 60 F254 (Merck) with benzene/EtOAc 9:1, 8:2 and 7:3, detection with 50 % aq. H2SO4 soln. Mps. uncorrected. IR spectra: Perkin-Elmer-337 spectrophotometer; ν in cm⁻¹. NMR spectra: Varian Gemini 200 (1H at 200 MHz, 13C at 50 MHz); CDC13 soln. at r.t., TMS as internal standard; chemical shifts in ppm as δ values. J in Hz. Mass spectra: Finnigan-MAT 8230.

5α-EpOxy-5t-cholestan-3β-yl acetate (7)5

A stirred solution of (E)-5α-oxo-5,10-secocholest-1(10)-en-3β-yl acetate (6) (2 g) in acetonitrile (200 ml) was irradiated with a high pressure mercury lamp TQ 150 Z2 (Hansa) at room temperature for 6 h, evaporated to dryness and the oily residue (2.16 g) chromatographed on silica gel (100 g). Elution with toluene-EtOAc (98:2) gave the unchanged (E)-secoketone 6 (0.36 g, 18 %). Further elution with the same eluent gave 1α,5α-epoxy-5α-seco-3β-yl acetate (7) (0.73 g, 36.5 %) as a white solid, m.p. 101–102 °C (from acetonitrile). [α]D = +202±2 (c = 1.0), IR (CH2Cl2): 1732, 1238, 1025. 1H-NMR: 0.85 (s, 3H, CH(18)), 0.88 (d, 6H, CH₂(26), CH₂(27)), 0.92 (d, 3H, CH₃(21)), 2.07 (s, 3H, AcO), 2.41 (dd, J = 9.8, 14.8, 1H, H₃-CH(4)), 2.71 (m, 1H, H₂-CH(2)), 3.99 (d, J = 5.8, 1H, H-CH(1)), 5.24 (m, 1H, H-CH(3)). 13C-NMR: 170.7 (s, OCOCH₃), 88.6 (s, C(5)), 83.2 (d, C(1)), 66.7 (d, C(3)), 56.1 (d, C(14), C(17)), 47.0 (d, C(9)), 45.4 (s, C(10)), 42.4 (s, C(13)), 39.8 (t, C(12)), 39.5 (t, C(24)), 38.6 (s, C(4)), 36.1 (t, C(22)), 35.8 (d, C(20)), 34.1 (d, C(8)), 31.5 (s, C(2)), 31.0 (t, C(6)), 28.1 (t, C(16)), 28.0 (d, C(25)), 27.8 (t, C(7)), 24.4 (t, C(15)), 22.8 (t, C(23)), 23.1 (t, C(11)), 22.8 (q, C(27)), 22.5 (q, C(26)), 21.3 (q, OOCCH₃), 18.7 (q, C(21)), 11.8 (q, C(18)), 11.7 (q, C(19)). MS: m/z = 444 (M⁺). Anal. calcd. for C₂₉H₄₈O₃ (444.696): C 78.33, H 10.88; found: C 78.18, H 10.87.

Cholest-5-en-3β-diol 3-acetate (8)5

The oxetane derivative 7 (2.30 g) was dissolved in glacial AcOH (47 ml) and cooled to 5 °C. To this semi-solid solution, a cooled solution of hydroiodic acid (0.98 ml 57 % HI) in glacial AcOH (30.5 ml) was added portionwise. The resulting mixture was left at 5 °C for 30 min, diluted with H₂O and extracted with Et₂O. The ethereal extract was washed with H₂O, saturated aq. NaHCO₃ and H₂O, dried over Na₂SO₄ and evaporated to dryness, leaving a crystalline solid (2.4 g) which was chromatographed on SiO₂ (100 g). Elution with toluene-EtOAc (95:5) gave cholest-5-en-3α,3β-diol 3-acetate (8) (1.30 g, 78 %), m.p. 166–168 °C (from acetonitrile). [α]D = –41 (c = 0.7), IR (KBr): 3450, 3020, 1730, 1275, 1040. 1H-NMR: 0.68 (s, 3H, CH₃(18)), 0.86 (d, 6H, CH₂(26), CH₂(27)), 0.91 (d, 3H, CH₃(21)), 1.04 (s, 3H, CH₃(19)), 2.03 (s, 3H, AcO), 3.38 (brs, 1H, H-CH(1)), 3.03 (heptet, 1H, H-CH(3)), 5.61 (d, J = 5.2, 1H, H-CH(6)). 13C-NMR: 170.6 (s, OCOCH₃), 136.2 (s, C(5)), 126.5 (d, C(6)), 72.5 (d, C(1)), 69.5 (d, C(3)), 56.5 (d, C(17)), 56.0 (d, C(14)), 42.2 (s, C(13)), 41.7 (s, C(10)), 41.4 (d, C(9)), 39.4 (2t, C(12), C(24)), 37.2 (t, C(2)), 36.1 (t, C(22)), 35.7 (d, C(20)), 34.4 (t, C(4)), 31.7 (d, C(8)), 31.7 (t, C(7)), 28.1 (t, C(16)), 28.0 (d, C(25)), 24.3 (t, C(15)), 23.8 (t, C(23)), 22.8 (q, C(27)), 22.5 (q, C(26)), 21.3 (q, OOCCH₃), 20.1 (t, C(11)), 19.3 (q, C(21)), 18.7 (q, C(19)), 11.8 (q, C(18)). MS: m/z = 384 (M⁺ – 60, 99 %). Anal. calcd. for C₂₉H₄₈O₃ (444.696): C 78.33, H 10.88; found: C 78.31, H 10.69.

5α-EpOxy-5t-cholestan-1α,3β-diol 3-acetate (9)6

A solution of 8 (1.00 g) in CH₂Cl₂ (25 ml) was treated with 85 % m-chloroperoxybenzoic acid (500 mg in 25 ml CH₂Cl₂) at room temperature for 1 h. After the usual work-up, the obtained residue (0.980 g, 96.4 %) was recrystallized from acetone to give 5α,5α-DiOxy-5t-cholestan-1α,3β-diol 3-acetate (9) (0.865 g, 83.5 %), m.p. 156 °C. [α]D = –11.0 (c = 1.09), IR (KBr): 3450, 3030, 1730, 1710, 1275, 1042. 1H-NMR: 0.62 (s, 3H, CH₃(18)), 0.86 (d, 6H, CH₂(26), CH₂(27)), 0.89 (d, 3H, CH₃(21)), 1.10 (s, 3H, CH₃(19)), 2.02 (s, 3H, AcO), 2.32 (d, J = 4.8, 1H, H-CH(6)), 3.30 (brs, 1H, H-CH(3)). 13C-NMR: 170.1 (s, OCOCH₃), 72.8 (d, C(3)), 67.6 (d, C(11)), 64.0 (s, C(5)), 56.7 (d, C(17)), 56.5 (d, C(6)), 55.8 (d, C(14)), 42.3 (2s, C(10), C(13)), 39.4 (t, C(24)), 39.0 (t, C(12)), 36.6 (d, C(9)), 36.1 (d, C(20)), 35.7 (t, C(4)), 35.6 (t, C(2)),

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34.7 (t, C(22)), 29.8 (d, C(8)), 28.6 (t, C(16)), 28.0 (d, C(25)), 27.9 (t, C(7)), 24.1 (t, C(15)), 23.8 (t, C(23)), 22.8 (q, C(27)), 22.5 (q, C(26)), 21.2 (q, OCHOCH3), 19.7 (t, C(11)), 18.6 (q, C(21)), 16.5 (q, C(19)), 11.8 (q, C(18)). Anal. calcd. for C29H40O7 (460.699): C 75.61, H 10.50; found: C 74.43, H 10.68. CI-MS: m/z = 461 (M+ + 1).

5a-Cholesterol-1α,3β,5-triol 3-acetate (10)²

A solution of 9 (1.8 g) in AcOH–EtOH (10:1, 110 ml) was hydrogenated over PtO2 (180 mg) in a Parr hydrogenator at room temperature and 3 atm pressure, for 13 h. After removal of the catalyst and solvent, the residue was chromatographed on SiO2 (120 g). Elution with toluene–EtOAc (95:5) afforded the unchanged starting compound 9 (0.86 g, 44.0 %). Elution with toluene–EtOAc (90:10) gave 5a-cholesterol-1α,3β,5-triol 3-acetate (10) (0.70 g, 35.7 %), m.p. 178–179 ºC (from acetone). IR (KBr): 3368, 1737, 1467, 1374, 1247.1H-NMR: 0.66 (s, 3H, CH3(18)), 0.85 (d, 6H, CH2(26), CH2(27)), 0.92 (d, 3H, CH3(21)), 0.94 (s, 3H, CH3(19)), 2.03 (s, 3H, AcO), 2.99 (s, 1H, OH–C(5)), 3.82 (m, 2H, H–C(1) and OH–C(5)), 5.41 (heptet, 1H, H–C(3)). 13C-NMR: 170.8 (s, OCOCH3), 77.3 (s, C(5)), 74.0 (d, C(3)), 67.8 (d, C(11)), 56.2 (d, C(17)), 56.0 (d, C(14)), 42.7 (s, C(13)), 41.4 (s, C(10)), 39.1 (d, C(9)), 39.4 (t, C(24)), 36.1 (t, C(4)), 35.8 (d, C(20)), 35.1 (t, C(22)), 34.7 (t, C(6)), 34.6 (d, C(8)), 29.6 (t, C(2)), 28.2 (t, C(16)), 28.0 (d, C(25)), 25.6 (t, C(7)), 24.1 (t, C(15)), 23.9 (t, C(23)), 22.8 (q, C(27)), 22.5 (q, C(26)), 21.4 (q, OCHOCH3). To a cooled (–5 ºC) solution of 11 (1.26 g) in acetonitrile (165 ml), a slight excess of Killiani’s chromic anhydride solution was added with constant stirring. After 20 min ice-cold H2O was added, the precipitate was filtered off, washed thoroughly with H2O and air-dried to give a residue (1.2 g, 95.7 %), which was chromatographed on SiO2 (40 g). Elution with toluene–EtOAc (95:5) afforded 5-hydroxy-1-oxo-5α-cholesterol-3β-yl acetate (11) which was recrystallized from acetone (0.98 g, 78.6 %), m.p. 138.5–140 °C. IR (KBr): 3494, 3454, 1716, 1377, 1245, 1032. 1H-NMR: 0.66 (s, 3H, CH3(18)), 0.85 (d, 6H, CH2(26), CH2(27)), 0.88 (d, 3H, CH3(21)), 1.28 (s, 3H, CH3(19)), 2.04 (s, 3H, AcO), 2.62 (dd, J = 6.8, 13.4, 1H, H2–C(4)), 2.81 (dd, J = 10.8, 12.8, 1H, H2–C(2)), 5.30 (m, H–C(3)). 13C-NMR: 209.4 (s, C(1)), 170.2 (s, OCOCH3), 76.0 (s, C(5)), 69.2 (d, C(3)), 56.2 (d, C(17)), 55.8 (d, C(14)), 53.8 (s, C(10)), 43.1 (t, C(2)), 42.7 (s, C(13)), 41.0 (d, C(9)), 39.8 (t, C(12)), 39.4 (t, C(24)), 39.2 (t, C(4)), 36.1 (d, C(22)), 35.8 (d, C(20)), 34.9 (d, C(8)), 33.6 (t, C(6)), 30.8 (t, C(16)), 27.9 (d, C(25)), 24.9 (t, C(7)), 24.0 (t, C(15)), 23.9 (t, C(23)), 22.8 (t, C(11)), 22.8 (q, C(27)), 22.5 (q, C(26)), 21.2 (q, OCHOCH3), 18.5 (q, C(21)), 16.4 (q, C(19)), 12.3 (q, C(18)). MS: m/z = 445 (M+–1), 435 (M+–2), 401 (M+–39), 383 (M+–50–17).

Oxidation of 5-hydroxy-1-oxo-5α-cholesterol-3β-yl acetate (11)

(i) Hyposidote mercuric oxide/iodine oxidation. A stirred suspension of 11 (100 mg, 0.217 mmol), yellow HgO (325 mg, 1.5 mmol) and I2 (437 mg, 1.7 mmol) in CH2Cl2 (30 ml) was irradiated with a 15 W (220 V) fluorescent lamp for 90 min without heating. All the time argon was introduced through the reaction mixture. The solid was removed by filtration, washed with Et2O, and filtrate washed successively with water, 10 %aq. Na2SO4, saturated NaHCO3 and water, dried over Na2SO4 and evaporated to dryness. The resulting mixture (111 mg) was chromatographed on silica gel (10 g). Elution with toluene–EtOAc (99:1, 98.2:97.3) afforded a complex mixture (11 mg) which was not further investigated. Toluene–EtOAc (96:4) eluted 1,5-dioxy-5,10-secocholestan-10(19)-en-3β-yl acetate 12 which was recrystallized from acetonemethanol (38 mg, 38 %), m.p. 157–158 °C. IR (KBr): 1735, 1701, 1672, 1620, 1251, 1032. 1H-NMR: 0.74 (s, 3H, CH3(18)), 0.86 (d, 6H, CH2(26), CH2(27)), 0.90 (d, 3H, CH3(21)), 2.05 (s, 3H, AcO), 2.44 (m, 2H, H2–C(6)), 2.65 (dd, J = 3.5, 15.7, 1H, H–C(4)), 2.95 (dd, J = 11.4, 1H, H–C(4)), 3.00 (ABq, J = 3.6, 2H, H2–C(2)), 5.60 (m, H–C(3)), 5.83 and 6.15 (2s, 2H, H2–C(2)), 13C-NMR: 207.7 (s, C(3)), 199.4 (s, C(1)), 169.8 (s, OCHOCH3), 155.0 (s, C(10)), 124.6 (t, C(19)), 68.8 (d, C(3)), 56.1 (d, C(17)), 54.2 (d, C(14)), 46.5 (t, C(4)), 44.5 (d, C(9)), 43.1 (t, C(2)), 42.5 (s, C(13)), 41.8 (t, C(22)), 39.7 (t, C(24)), 39.5 (t, C(6)), 38.3 (d, C(8)), 36.0 (t, C(22)), 35.7 (t, C(20)), 33.4 (t, C(7)), 28.0 (d, C(25)), 27.8 (t, C(16)), 26.8 (t, C(15)), 24.9 (t, C(11)), 23.8 (t, C(23)), 22.8 (q, C(27)), 22.5 (q, C(26)), 21.1 (q, OCHOCH3), 18.6 (q, C(21)), 11.8 (q, C(18)). CI-MS: m/z = 459 (M+ + 1).
Further elution with the same eluent afforded the starting compound 11 (27 mg, 27 %).

Further elution with toluene–EtOAc (95:5) gave compound 13 (28 mg, 28 %). Oil. IR (KBr): 3483, 1732, 1709, 1643, 1269, 1028. 1H-NMR: 0.67 (s, 3H, CH3(18)), 0.85 (d, 6H, CH3(26), CH3(27)), 3.89 (m, 4H, CH2(2), CH2(4)), 2.88 (fdd, J = 1.8, 13.5, 1H, H–C(6)), 4.86 and 5.00 (2fs, J = 1.6, 2H, H–C(19)), 5.38 (heptet, 1H, H–C(3)). 13C-NMR: 206.2 (s, C(5)), 170.2 (s, OCOCH3), 154.3 (s, C(10)), 105.4 (t, C(19)), 74.0 (s, C(1)), 69.2 (d, C(3)), 56.7 (d, C(17)), 56.0 (2d, C(6), C(14)), 46.5 (t, C(4)), 42.8 (s, C(13)), 42.3 (d, C(9)), 41.1 (d, C(8)), 40.4 (t, C(22)), 39.4 (t, C(12)), 39.3 (t, C(24)), 36.1 (t, C(22)), 35.8 (d, C(20)), 29.7 (t, C(7)), 28.2 (t, C(16)), 28.0 (d, C(25)), 25.3 (t, C(15)), 24.8 (t, C(11)), 23.8 (t, C(23)), 22.8 (q, C(27)), 22.5 (q, C(26)), 21.2 (q, OCOCH3), 18.6 (q, C(21)), 12.0 (q, C(18)).

(iii) Hypoiodite lead tetraacetate/iodine oxidation. A stirred suspension of LTA (450 mg, 0.91 mmol), I2 (94 mg, 0.37 mmol) and 11 (100 mg, 0.217 mmol), in dry benzene was irradiated with a 15 W (220 V) fluorescent lamp at room temperature for 30 min. All the time argon was introduced through the reaction mixture. The solid was removed by filtration, washed with Et2O and filtrate washed successively with water, 10 % aq. Na2S2O3, saturated NaHCO3 and water, dried over Na2SO4 and evaporated to dryness. The resulting mixture (141 mg) was chromatographed on silica gel. Elution with toluene–EtOAc (99:1, 98:2, 97:3) afforded a complex mixture (17 mg) which was not further investigated. Toluene–EtOAc (96:4) eluted the 1,5-dioxo compound 12 which was recrystallized from acetone/methanol (73 mg, 73 %), m.p. 157–158 ºC.

Further elution with toluene–EtOAc (95:5) gave compound 13 (10 mg, 10 %).

(iii) Thermal lead tetraacetate oxidation. A suspension of 11 (100 mg, 0.217 mmol), LTA (450 mg, 0.900 mmol) and anh. CaCO3 (95 mg, 0.960 mmol) in anh. benzene (15 ml) was heated under reflux with stirring for 48 h, after which time the starch-iodine test became negative. The cooled mixture was diluted with Et2O and filtrate washed successively with water, 10 % aq. Na2S2O3, saturated NaHCO3 and water, dried over Na2SO4 and evaporated to dryness. The resulting mixture (116 mg) was chromatographed on silica gel. Elution with toluene–EtOAc (99:1, 98:2, 97:3) afforded a complex mixture (15 mg, 15 %) which was not further investigated. Toluene–EtOAc (96:4) eluted the 1,5-dioxo compound 12 (18 mg, 18 %).

Further elution with same eluent afforded the starting compound 11 (43 mg, 43 %).

Elution with toluene–EtOAc (95:5) gave the cyclic compound 13 (7 mg, 7 %).

Cyclization of 1,5-dioxo-5,10-secocholest-10(19)-en-3β-yl acetate 12 on SiO2

1,5-Diketone 12 (40 mg) was stirred with SiO2 (Merck, 0.063–0.20 mm) in toluene (5 ml) for 24 h at room temperature. After removal of the SiO2 and solvent the residue was chromatographed on SiO2 (4 g). Elution with toluene–EtOAc (96:4) gave unchanged starting material 12 (18 mg, 45 %).

Further elution with toluene–EtOAc (95:5) afforded compound 13 (17.2 mg, 43 %).

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ОКСИДАТИВНЕ ФРАГМЕНТАЦИЈЕ
5-ХИДРОКСИ-1-ОКСО-5α-ХОЛЕСТАН-3β-ИЛ-АЦЕТАТА

НАТАЛИЈА М. КРСТИЋ, МИРА С. БЈЕЛАКОВИЋ, ЉУБИНИКА Б. ЛОРЕНЦ И ВЛАДИМИР Д. ПАВЛОВИЋ

Синтетизован је 5-хидрокси-1-оксо-5α-холестан-3β-ил-acetат (11) у 5 фаза похађај од (E)-3β-ацетокси-5,10-секо-1(10)-холестен-5-она (6). Дејством олуто-тетраацетата (LTA) (под термичним или хипоидитним условима), или меркур-оксид/йодног реагента (HgO/I2) на 1-оксо-5-хидрокси-дериват 11, врши се оксидативна β-фрагментација његове C(5)–C(10) везе, при чему се добија 1,5-диоксо-5,10-секохолест-10(19)-ен-3β-ил-ацетат (12), у различитим присуствима у зависности од употребљеног реагенца. Такође, дискутувана је стереохемија 1β,6β-циклизационог производа 13, насталог интразелекулском циклизацијом 1,5-диоксо-5,10-секо јединења 12 на силика гелу.

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