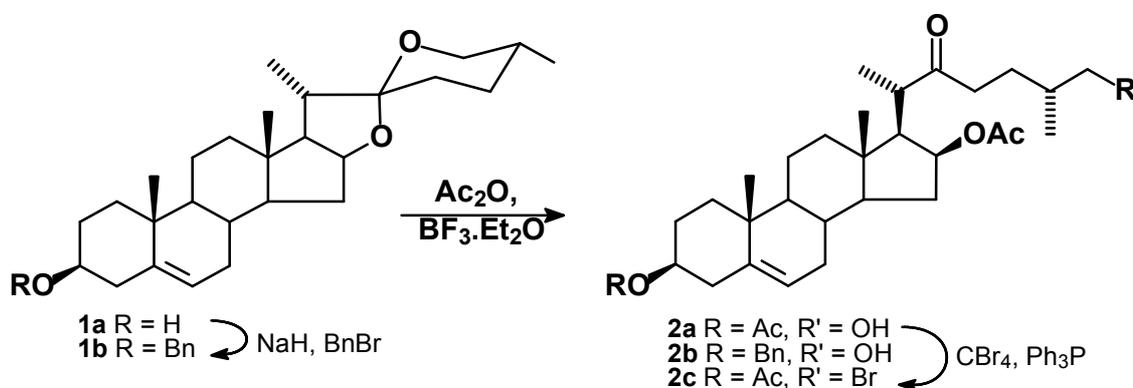


Unexpected fragmentation of 16 β -acetoxy-22-oxocholestanes on the action of methylenetriphenylphosphorane

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Starting ketones **2a,b** were obtained from diosgenin **1a** and its benzyl ether **1b** using acetylation of spirostane.¹ Ketone **2c** was synthesized from **2a** by the substitution of hydroxyl group for Br by the action of CBr₄-Ph₃P reagent.



Experimental

General

NMR spectra were recorded on a Bruker AM-300 (300.13 MHz for ¹H and 75.47 MHz for ¹³C) or Bruker AVANCE-500 (500.13 MHz and 125.77 MHz for ¹³C) spectrometers, using TMS as an internal standard. IR spectra in Nujol were recorded on IR Prestige-21 Fourier Transform Shimadzu spectrophotometer. Mass spectra were measured

with Thermo Finnigan MAT 95XP apparatus, the temperature of the ionizing chamber was kept at 200°C, the temperature of the sample injection was 50-270°C, the temperature was raised at the rate of 22°C min⁻¹. Optical rotations were determined on a Perkin–Elmer-341 polarimeter. The reaction course was monitored by TLC on “Sorbfil” plates (Russia) with visualization of the spots by spraying with ethanol solution of anisaldehyde acidified with sulfuric acid and subsequent heating at 120-150°C. The products were isolated by column chromatography on silica gel (30-60 g of adsorbent per 1 g of compound); freshly distilled solvents were used as eluents.

(25*R*)-3β-(Benzyloxy)spirost-5-ene (1b). The solution of diosgenin **1a** (500 mg, 1.19 mmol) in mixture DMF-THF (2:1, 12 ml) was added dropwise under argon to a stirred suspension of NaH (0.14 g, 3.57 mmol) in anhydrous THF (5 ml) and the mixture was stirred 1 h at 50°C. Then BnBr (0.61 g, 3.57 mmol) was added to the reaction mixture and the stirring continued 24 h at 100°C. The cooled mixture was quenched with H₂O (1 ml), THF was evaporated, the residue was acidified with HCl solution and extracted with CHCl₃ (5×10 ml). The extract was washed with brine, dried over Na₂SO₄, and concentrated under vacuum. The crude product was purified by column chromatography on SiO₂ using benzene as the eluent to obtain colorless crystals **1b** (0.51 g, 85%). Mp 111-112°C. [α]_D²⁰ -105.3 (*c* 1.0, CHCl₃); *R*_f (EtOAc/petroleum ether, 1:9) 0.37; IR (Nujol, ν_{\max} , cm⁻¹): 2926, 2910, 2360, 1541, 1507, 14556, 1375, 1259, 1097, 1073, 1100, 980, 897, 827, 724 cm⁻¹; δ_{H} (300 MHz, CDCl₃) 0.79 (3H, s, CH₃), 0.80 (3H, d, CH₃, *J* 6.1 Hz), 0.98 (3H, d, CH₃, *J* 6.8 Hz), 1.04 (3H, s, CH₃), 2.29 (1H, m) and 2.41-2.46 (1H, m, H-15), 3.28 (1H, m, H-3), 3.39 (1H, t, H-26, *J* 10.8 Hz) and 3.47 (1H, m, H-26), 4.41 (1H, q, H-16, *J* 7.5 Hz), 4.57 (2H, s, OCH₂), 5.35 (1H, d, H-6, *J* 5.1 Hz), 7.26-7.53 (5H, m, Ph). ¹³C NMR (75.47 MHz, CDCl₃, δ): 14.48 (CH₃), 16.22 (CH₃), 17.09 (CH₃), 19.33 (CH₃), 20.75 (C-11), 28.32 (C-2), 28.71 (C-24), 30.21 (C-25), 31.32 (C-24), 31.35 (C-8), 31.75 (C-7),

32.00 (C-15), 36.92 (C-1), 37.10 (C-10), 38.22 (C-4), 39.02 (C-23), 39.68 (C-13), 40.15 (C-12), 41.49 (C-20), 49.98 (C-9), 56.42 (C-14), 61.99 (C-17), 66.73 (C-26), 69.84 (OCH₂), 78.41 (C-3), 80.72 (C-16), 109.25 (C-22), 121.24 (C-6), 127.33, 127.47, 128.26 and 138.90 (Ph), 140.84 (C-5); MS (EI, *m/z*): 504 (4 *M*⁺), 398 (18), 328 (5), 284 (53), 269 (26), 255 (22), 139 (100), 91 (72), 69 (12%).

Reaction of compound 1b with Ac₂O. Solution of **1b** (200 mg, 0.39 mmol) and Ac₂O (0.34 ml, 3.55 mmol) in anhydrous CH₂Cl₂ (2 ml) was cooled to 0°C under argon, then a mixture and BF₃·Et₂O (0.34 ml, 2.78 mmol) was added dropwise. The mixture was stirred at this temperature 20 min (TLC) and was poured into cold water and extracted with CH₂Cl₂ (3×10 ml). The extract was washed with saturated solution of NaHCO₃, dried with Na₂SO₄ and concentrated in vacuum. The residue was purified by column chromatography producing compounds **2b** (100 mg, 44%) and **2a** (30 mg, 13%). **(25R)-3β,16β-Diacetoxy-26-hydroxycholest-5-en-22-one (2a).** Spectral characteristics and the optical rotation of compound **2a** are identical with published data.¹ MS (EI, *m/z*): 516 (0.1 *M*⁺), 498 (88 [*M*-H₂O]⁺), 456 (35 [*M*-AcOH]⁺), 438 (74), 423 (25), 378 (30), 282 (37), 253 (50), 145 (40), 124 (100), 69 (36), 43 (42%). **(25R)-16β-Acetoxy-3β-benzyloxy-26-hydroxycholest-5-en-22-one (2b):** mp 164-165°C; [α]_D²⁰ +2.3 (*c* 1.0, CHCl₃); *R*_f (EtOAc/petroleum ether, 3:7) 0.10; IR (Nujol, *v*_{max}, cm⁻¹): 3546, 2962, 2903, 2891, 2850, 1735, 1715, 1707, 1455, 1375, 1242, 1110, 1029, 740, 690; ¹H NMR (300 MHz, CDCl₃, δ): 0.86 (3H, s, CH₃), 0.91 (3H, d, CH₃, *J* 6.9 Hz), 1.01 (3H, s, CH₃), 1.15 (3H, d, CH₃, *J* 7.1 Hz), 1.96 (3H, s, CH₃CO), 2.30 (2H, m, H-23), 2.40 (1H, m, H-23), 2.96 (1H, dq, H-20, *J* 7.0 and 3.8 Hz), 3.42 (2H, d, *J* 5.8 Hz), 3.28 (1H, m, H-3), 4.57 (2H, s, OCH₂), 4.98 (1H, m, H-16), 5.33 (1H, d, H-6, *J* 4.8 Hz), 7.34 (5H, m, Ph); ¹³C NMR (75.47 MHz, CDCl₃, δ): 13.27 (CH₃), 16.68 (CH₃), 16.88 (CH₃), 19.41 (CH₃), 20.81 (C-11), 21.17 (CH₃CO), 21.36 (CH₃CO), 26.27 (C-24), 28.46 (C-2), 31.35 (C-8), 31.69 (C-7), 34.88 (C-15), 35.51 (C-25), 36.11 (C-10), 36.91 (C-1), 37.20 (C-4), 38.56 (C-23), 39.16 (C-12),

41.96 (C-13), 43.56 (C-20), 50.00 (C-9), 54.07 (C-14), 55.15 (C-17), 67.55 (C-26), 70.03 (OCH₂), 75.76 (C-16), 78.53 (C-3), 121.26 (C-6), 127.46, 127.61, 128.39 and 139.08 (Ph), 140.95 (C-5), 169.85 (CH₃C=O), 213.67 (C=O); MS (EI, *m/z*): 564 (0.05 *M*⁺), 546 (13 [*M*-H₂O]⁺), 486 (44), 378 (34), 328 (26), 284 (52), 269 (49), 253 (47), 145 (30), 91 (100), 69 (48%); HRMS (EI): [*M*-H₂O]⁺, found 546.3695. C₃₆H₅₀O₄ requires 546.3709.

(25*R*)-26-Bromo-3β,16β-diacetoxycholest-5-en-22-one (2c). CBr₄ (0.23 g, 0.69 mmol) was added portionwise to a stirred solution of ketone **2a** (0.24 g, 0.46 mmol) and PPh₃ (0.18 g, 0.69 mmol) in anhydrous acetonitrile (5 ml). The reaction mixture was stirred for 4 h at room temperature then the precipitate was filtered off, CH₃CN was evaporated, and the residue was chromatographed affording bromide **2c** (0.23 g, 88%). Mp 201-202°C; [α]_D²⁰ +4.2 (*c* 1.0, CHCl₃); *R*_f (EtOAc/petroleum ether, 1:4) 0.28; IR (Nujol, ν_{\max} , cm⁻¹): 2952, 2932, 2902, 2889, 2853, 1733, 1728, 1708, 1456, 1377, 1362, 1250, 1109, 1041, 615 cm⁻¹; ¹H NMR (300 MHz, CDCl₃, δ): 0.86 (3H, s, CH₃), 1.01 (3H, d, CH₃, *J* 6.6 Hz), 1.02 (3H, s, CH₃), 1.15 (3H, d, CH₃, *J* 7.2 Hz), 1.96 (3H, s, CH₃CO), 2.02 (3H, s, CH₃CO), 2.33-2.42 (4H, m, CH), 2.62 (1H, m, H-23), 2.96 (1H, m, H-20), 3.35 (2H, m, CH₂Br), 4.60 (1H, m, H-3), 4.97 (1H, m, H-16), 5.36 (1H, d, H-6, *J* 3.7 Hz); ¹³C NMR (75.47 MHz, CDCl₃, δ): 13.73 (CH₃), 18.02 (CH₃), 19.33 (CH₃), 20.30 (C-11), 21.43 (CH₃CO), 27.69 (C-2), 31.21 (C-8), 31.88 (C-7), 33.11 (C-15), 36.05 (C-20), 36.68 (C-10), 36.96 (C-12), 38.03 (C-4), 38.15 (C-1), 41.47 (C-13), 50.01 (C-9), 54.75 (C-14), 58.94 (C-17), 73.74 (C-3), 82.72 (C-16), 121.94 (C-6), 139.83 (C-5), 170.59 (CH₃C=O), 181.32 (C=O); MS (EI, *m/z*): 518 (88 [*M*-AcOH]⁺), 438 (98), 378 (42), 281 (40), 253 (96), 145 (52), 124 (100), 69 (48%); HRMS (EI): [*M*-AcOH]⁺, found 518.2360. C₂₉H₄₃O₃Br requires 518.2390.

References

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