TRANSFORMED STEROIDS.

132. SYNTHESIS OF NATURAL CHIOGRALACTONE

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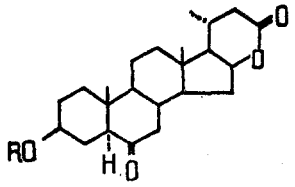
A seven-stage stereospecific synthesis of the natural phytosteroid "chiogralactone" has been effected from the readily available 3β,16α-diacetoxypregn-5-en-20-one. The scheme of the synthesis includes the Reformatskii reaction with this 20-ketone, the hydrogenation of the δ-lactone formed to the 21α(CH_3) saturated lactone, the opening of the ring and the saponification of the 3-acetoxy group, the conversion of the latter into the 3,16α-ditosylate, and the alkaline treatment of the ditosylate, leading to a 3,5α-cyclosteroid with a δ-lactone ring and the α(H) configuration of the C(16) center. This is the key stage of the synthesis. Subsequent transformations — the oxidation of the 6-hydroxy group to a 6-keto group, the opening of the cyclopropane ring, and saponification of the 3-acetoxy group — led to the 23 → 16 lactone of 3β, 16β-dihydroxy-6-oxo-24-nor-5α-cholan-23-oic acid, which was identical, according to literature characteristics, with "chiogralactone." Another way of approach to its 3,6-dihydroxy analog was studied on the basis of 5,6α:16,17α-diepoxysteroids. It was shown that on both Pd and Pt catalysts hydrogenolysis takes place primarily of the 16,17α-oxide ring.

The only known representative of natural steroid 23 → 16 lactones, chiogralactone, $C_{23}H_{34}O_4$, was isolated from the plant *Chionographis japonica* M. by Japanese chemists, who showed that it is the 23 → 16 lactone of 3β,16β-dihydroxy-6-oxo-24-nor-5α-cholan-23-oic acid (Ia) [1-3].



Ia R=H, mp. 238-240°C

Ib R=Ac, mp. 228-230°C

There is information on its biological activity with respect to animals and plants. At the same time, it is known that, as a rule, steroid lactones of very diverse structures exhibit an appreciable biological action [4-7]. This induced us to undertake the synthesis of (I) with the aim of an all-sided biological study.

It appeared promising to use for this purpose the steroid triene (II) synthesized previously [8] and to convert it by treatment with m-chloroperbenzoic acid (CPBA) into the diepoxide (III), which on hydrolysis was to give [9] a 6,16-dihydroxy-23-alkoxycarbonyl steroid — a precursor of (I). The results of a study of the hydrogenation of the diepoxide (III) under various conditions showed that the reaction took place ambiguously. On hydrogenation over 10% Pd/C at 20°C, the main product was the allyl alcohol (IVa), arising as the result of the reduction of the 16α,17α-epoxide grouping alone by the mechanism of a 1,4-addition of hydrogen [9]. The exhaustive hydrogenation of (IV) over PtO_2 in AcOH formed the saturated ethoxycarbonyl diacetate (V), which, however, did not lactonize on subsequent treatment.

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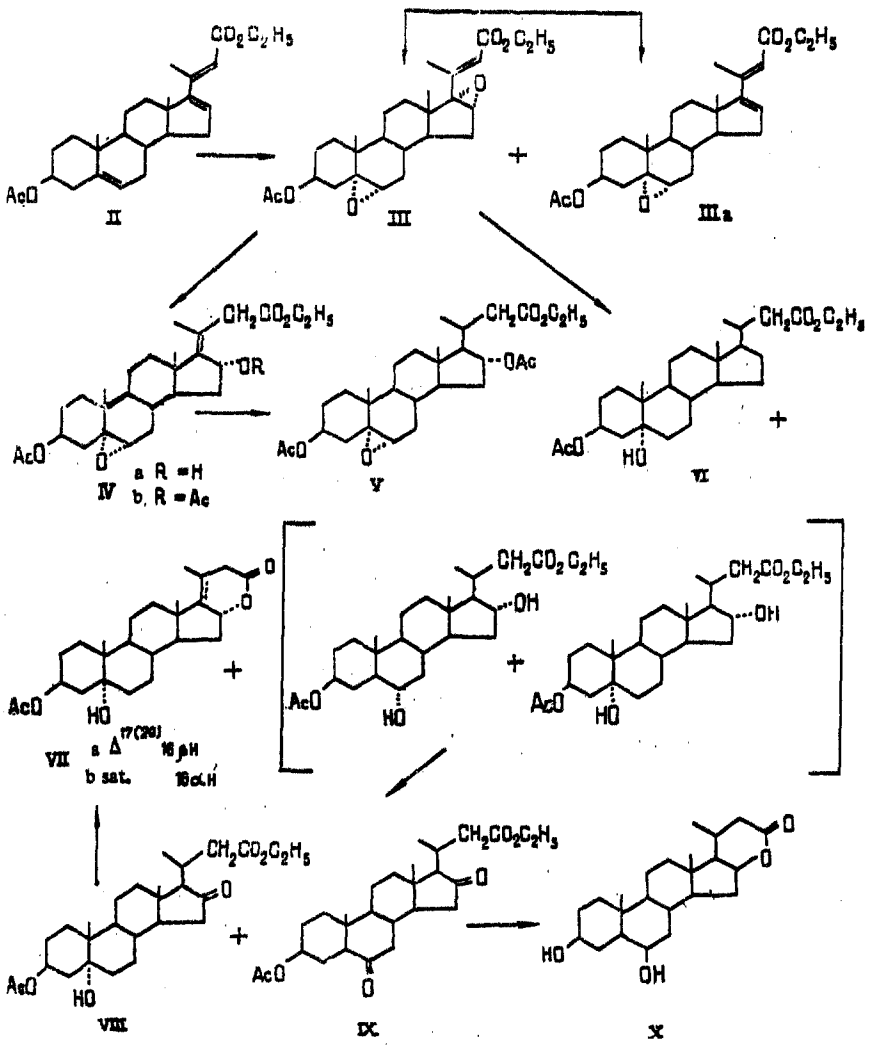
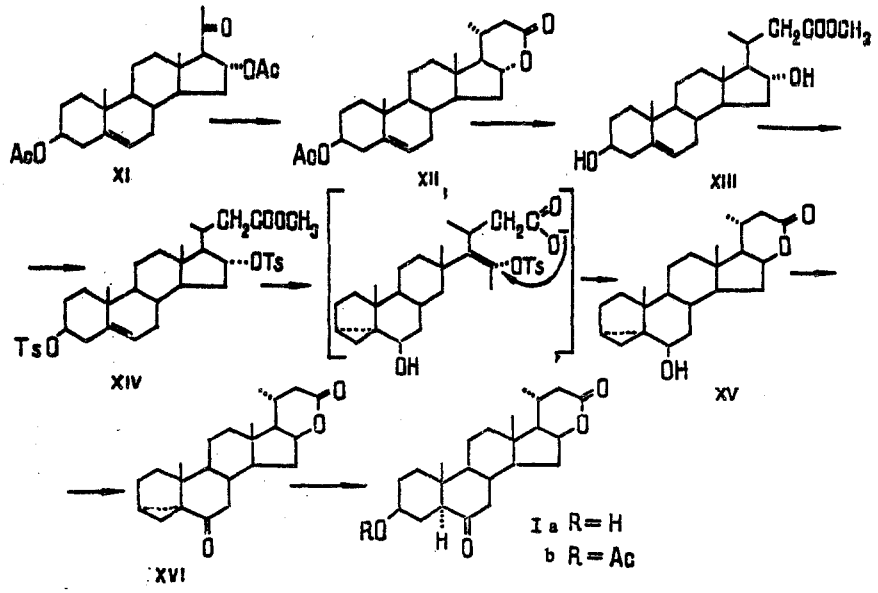


Scheme 1

The structure of (V) was confirmed by IR, mass, and PMR spectra, and also by a comparison with the compounds described previously [10]. When (III) was hydrogenated under more severe conditions over PtO_2 in AcOH at 50°C under a pressure of 10-15 atm, a whole range of hydrogenolysis products was formed. Under these conditions, apparently, the 5,6-oxide ring was reduced first, since all the products isolated contained a 5α-hydroxy or a 6-hydroxy group the position of which was determined by its capacity for undergoing acetylation under mild conditions. In the side chain, either complete hydrogenolysis of the 16,17-oxide group, as a result of which a 16,17-deoxy ethoxycarbonyl derivative (VI) was formed, or there was partial 1,4-addition to the allyl oxide, the 16α-allyl alcohol either lactonizing to (VIIa) or being saturated at the $\Delta^{17(20)}$ bond. In the latter case, a mixture of diols isomeric with respect to the position of the OH group in ring B was formed, and after its oxidation with CrO_3 in pyridine the 5α-hydroxy-16-ketone (VIII) and the 6,16-diketone (IX) were isolated and characterized. The reduction of the latter with $NaBH_4$ and cyclization in acid medium by the method described by Iwasaki [3] led to the 3,6-dihydroxylactone (X), corresponding in its PMR spectrum and melting point to the corresponding derivative of chiogralactone [3].

However, the negligibly small yield of (X) impelled us to seek a different route for the synthesis of (I). It has been shown previously [10] that the application of the Reformatskii reaction to the readily available 3β,16α-diacetoxypregn-5-en-20-one (XI) [11] leads to a $\Delta^{20(22)}$-δ-lactone the hydrogenation of which over PtO_2 in AcOH with the strictly stoichiometric amount of hydrogen forms a Δ^5-steroid with a saturated lactone ring (XII) having the β(H) configuration at C(16), opposite to that of compound (I), but the natural

α(CH_3) configuration at C(20). The reversal of the configuration at C(16) and the simultaneous introduction of a 5α(H)-6-keto grouping was effected in the following way. The prolonged exposure of (XII) in a mixture of $CHCl_3$, CH_3OH, and HCl led to the liberation of the 3-hydroxy group and to the cleavage of the δ-lactone ring. The methoxycarbonyl diol formed (XIII) was converted by treatment with p-toluenesulfonyl chloride in pyridine at +4°C for 48 h into a mixture of tosylates the main component of which was the 3β,16α-ditosylate (XIV). This structure was shown by its fragmentation on mass spectrometry (presence of fragments with masses corresponding to M − 2 × TsOH, and TsOH).



Scheme 2

The PMR spectrum shows the chemical shifts of protons corresponding in magnitude and position to OCH_3, 21-CH_3, and $CH_3C_6H_4SO_2$– groups. Boiling the ditosylate (XIV) in an alkaline medium ($KHCO_3$ in acetone) led simultaneously to the usual transformation of rings A/B into a i-steroid and to the cyclization of the side chain into a δ-lactone with the α(H) configuration of the C(16) center. The latter was due to the formation in the alkaline medium of the free C(23) acid the anion of which attacks the C(16)-OTs group from the β region nucleophilically [12].

Thus, the 6-hydroxy-i-steroid (XV) was obtained from its structure and its stereochemistry at C(16) being confirmed by the mass spectrum and CD spectrum, which showed a negative Cotton effect (CE) [10]:

Steroid	CD characteristics	
	Δε	λ_{max}, nm
VIIa	+1,31	218
VIIb	−10,7	197
XV	−2,15	210
	−1,37	217
Ib	−0,554	290
	−0,56	297

The oxidation of the 6β-hydroxy group of (XV) with CrO_3 in pyridine gave the 6-ketolactone (XVI). In an attempt to pass to the 6-ketosteroid (XVI) without passing through the 6-hydroxysteroid by the direct treatment of the (XIV) with DMSO and NaOAc, as described by Cambie et al. [13], it was found that the reaction took place ambiguously with the formation of a range of products among which (XVI) was present according to TLC. The opening of the 3,5α-cyclopropane ring in the latter by treatment with concentrated H_2SO_4 in AcOH gave a quantitative yield of the 3-acetate(Ib), coinciding in melting point (228-230°C) and ORD indices with those given in the literature for chiogralactone acetate [3].

The PMR spectrum contained the signal of the 21-CH_3 group in the form of a doublet at δ 1.14 ppm with an SSCC of 6.5 Hz, confirming the natural α configuration at C(21). The 16β(O) configuration in ring E was confirmed by a comparison of the CD spectra of saturated

δ-lactones [10]. The trans linkage of rings A/B in (I) was confirmed both by ORD [3] and by CD, a negative CD being present in the region of the n→π* transition of the carbonyl group (λ_{max} 290 nm) [14]. The saponification of (Ib) under conditions given in the literature [2] led to chiogralactone (Ia), mp 238-240°C. Thus, by the second scheme chiogralactone was synthesized with a yield of 11%, starting from (XII).

EXPERIMENTAL

Melting points were determined on a Kofler block, and IR spectra were measured on a UR-20 spectrometer and UV spectra on a Unicam SP-700 in C_2H_5OH. Mass spectra were recorded on a Varian CH-6 MAT mass spectrometer with direct introduction of the samples into the ion source at an ionizing voltage of 70 V. PMR spectra were measured on Tesla BS 497 instrument and a Bruker M-250 instrument with a working frequency of 250 MHz (internal standard TMS) in $CDCl_3$. CD and ORD spectra were recorded on a Spectropol-1 instrument and a Jobin Yvon Dichrographe-3 at 20°C using a concentration of 1 mg/1 ml in CH_3CN with a path length of the cell of 0.1 cm. Silica gel 5/40 μm (+ 13% of gypsum) was used for TLC. Mixtures were separated in columns containing SiO_2 40/100 μm in an atmosphere of N_2.

Ethyl 3β-Acetoxy-5,6α:16,17α-diepoxy-24-norchol-20(22)-en-23-oate (III). A. A solution of 1.28 g (2.9 mmole) of (II) [8] in 30 ml of CH_2Cl_2 was treated with 2.0 g (11.6 mmole) of CPBA in 20 ml of CH_2Cl_2. After 20 h at 20°C, the reaction mixture was treated successively with solutions of Na_2SO_3 and of $KHCO_3$ and with water. Then it was extracted with CH_2Cl_2, and the extract was dried with $MgSO_4$ and evaporated. Chromatography of the residue in the heptane–ether (2:1) system yielded 600 mg of the diepoxide (III), mp 196-198°C (from heptane–ether).

IR spectrum (ν, cm^{-1}); 1240, 1650, 1730 (KBr). UV spectrum (λ_{max}, nm): 217 (ε 14,200). Mol. wt. 458 calculated as $C_{27}H_{38}O_6$. Mass spectrum (*m/z*): 458 (M), 443 (M−15), 413 (M−45), 385 (M−73), 352, 343, 337. PMR spectrum (δ, ppm): 0.66 s (3 H, 18-CH_3); 1.0 s (3 H, 19-CH_3); 1.18 t (J = 6.5 Hz, 3 H, OCH_2CH_3); 1.91 s (3 H, acetate); 2.01 s (3 H, 21-CH_3); 2.8 m (1 H, 6-H); 3.51 s (1 H, 16-H); 4.1 q (J = 6.5 Hz, 2 H, OCH_2CH_3); 4.8 m (1 H, 3-H); 5.7 (1 H, 22-H).

B. A solution of 980 mg (2.2 mmole) of (II) in 45 ml of CH_2Cl_2 was treated with 780 mg (4.45 mmole) of CPBA in 30 ml of CH_2Cl_2. After working up similar to that described above and chromatography in the ether–heptane (1:2) system, 230 mg of the diepoxide (III) and 110 mg of the monoepoxide (IIIa) with R_f 0.64 (ether–heptane (3:1)) were obtained.

IR spectrum (ν, cm^{-1}): 1250, 1610, 1710, 1730 (KBr). UV spectrum (λ_{max}, nm); 272 (ε 10,500). Mol. wt. 442 calculated as $C_{27}H_{38}O_5$. Mass spectrum (m/z): 442 (M), 427 (M − 15). The additional oxidation of 410 mg of (IIIa) in 20 ml of CH_2Cl_2 with 160 mg of CPBA and working up similar to that described above gave 220 mg of the diepoxide (III).

Hydrogenation of the Diepoxide (III). A. The hydrogenation of 200 mg of (III) was carried out in 25 ml of AcOH over 20 mg of 10% Pd/C until the absorption of H_2 ceased (35 ml). Then the catalyst was filtered off, the filtrate was diluted with water and extracted with ether, and the extracts were washed with $NaHCO_3$ solution and with water, dried with $MgSO_4$, and evaporated. The residue (200 mg) was separated by chromatography on a column in the heptane–ether (3:1) and (1:1) and ether systems. This led to the isolation of 100 mg of ethyl 3-acetoxy-16α-hydroxy-5,6α-epoxy-24-norchol-17(20)-en-23-oate (IVa), R_f 0.5 (ether). IR spectrum (ν, cm^{-1}): 1040, 1640, 1725, 3600, 3675 (in $CHCl_3$). Mol. wt. 460 calculated as $C_{27}H_{40}O_6$. Mass spectrum (m/z): 460 (M), 442 (M − 18), 427 (M − 18 − 15), 415, 400 (M − 60), 382 (M − 2 × 60), 354, 289.

The acetylation of 100 mg of (IVa) led to 90 mg of ethyl 3,16α-diacetoxy-5,6α-epoxy-24-norchol-17(20)-en-23-oate (IVb), R_f 0.7 (ether). IR spectrum (ν, cm^{-1}): 1255, 1730 (in $CHCl_3$). Mol. wt. 502 calculated as $C_{29}H_{42}O_7$. Mass spectrum, (m/z): 502 (M), 460 (M − 42), 445 (M − 42 − 15), 442 (M − 60), 427 (M − 60 − 15), 399 (M − 42 − 15 − 46), 382, 349, 303. PMR spectrum (δ, ppm): 0.78, 0.96, 0.97 s (18-CH_3, 19-CH_3); 1.18 t (J = 6.5 Hz, 3 H, OCH_2CH_3); 1.58 (3 H, 21-CH_3); 1.95 s (6 H, acetate groups); 2.8 m (1 H, 6-H); 4.05 q (J = 6.5 Hz, 2 H,

OCH_2CH_3); 4.50 m (1 H, 3-H); 5.26 m (1 H, 16-H).

The hydrogenation of 90 mg of the allyl acetate (IVb) was carried out in 8 ml of AcOH over 20 mg of PtO_2 until the absorption of H_3 ceased (16 h). After the usual working up it was possible to isolate by chromatography in ether: two isomeric 3,16-diacetates of ethyl 3,16α-dihydroxy-5,6α-epoxy-24-norcholan-23-oate (V), R_f 0.47 [ether–hexane (5:1)]. IR spectrum (ν, cm^{-1}); 1040, 1250, 1725 (in $CHCl_3$). Molecular weight, calculated as $C_{29}H_{44}O_7$, 504. Mass spectrum (m/z): 444 (M − 60), 426, 384, 366, 329, 311. PMR spectrum (δ, ppm): 0.7 s (3 H, 18-CH_3); 0.84 s (3 H, 19-CH_3); 1.18 t (3 H, J = 6.5 Hz, OCH_2CH_3); 1.10 d (3 H, J = 6.5 Hz, 20-CH_3); 1.99, 2.03 s (6 H, acetates); 3.13 m, (1 H, 6-H); 4.04 q (J = 6.5 Hz, 2 H, OCH_2CH_3); 5.04 m, 5.55 m, (2 H, 3-H, 16-H); and compound (VI), R_f 0.24 (ether–hexane (5:1)). IR spectrum (ν, cm^{-1}): 1040, 1250, 1725 (in $CHCl_3$). Molecular weight, calculated as $C_{29}H_{44}O_7$, 504. Mass spectrum (m/z): 444 (M − 60), 426, 417, 384, 374, 366, 347, 329, 311. PMR spectrum (δ, ppm): 0.69 s (3 H, 18-CH_3); 0.83 s (3 H, 19-CH_3); 1.17 d (J = 6.5 Hz, 3 H, 21-CH_3); 1.18 t (J = 6.5 Hz, 3 H, OCH_2CH_3); 1.99; 2.03 s (6 H, acetates); 3.13 m (1 H, 6-H); 4.04 q (J = 6.5 Hz, 2 H, OCH_2CH_3); 5.04, 5.55 m (2 H, 3-H, 16-H); 15 mg each.

B. The hydrogenation of 2.4 g of (III) was carried out in 60 ml of AcOH over 60 mg of PtO_2 at 50°C and a pressure of 10-15 atm for 14 h. After a working up similar to that described above and chromatographic separation in the ether–hexane (1:2) and (1:1) and ether systems, the following products were obtained:

1) 440 mg of ethyl 3β-acetoxy-5α-hydroxy-24-norcholan-23-oate (VI), mp 164-166°C (from ether–hexane). Molecular weight 448 calculated as $C_{27}H_{44}O_5$. Found, %: C 72.05, H 9.57. Calculated, %: C 72.28, H 9.89. Mass spectrum (m/z): 448 (M), 430 (m − 18), 370 (M − 60 − 18), 355 (M − 18 − 60 − 15). IR spectrum (ν, cm^{-1}): 1260, 1730, 3460, 3600 (in $CHCl_3$). PMR spectrum (δ, ppm): 0.70 s (3 H, 18-CH_3), 0.93 d (3 H, J = 6.5 Hz, 21-CH_3), 1.0 s ₉3 H, 19-CH_3), 1.2 t (3 H, J = 7 Hz, OCH_2CH_3); 2.01 s (3 H, acetate); 4.14 q (H, J = 7 Hz, OCH_2CH_3); 5.17 m (1 H, 3-H). When the product was subjected to acetylation with Ac_2O in pyridine at 20°C, it underwent no change;

2) 300 mg of 3β-acetoxy-5α,16α-dihydroxy-24-norchol-17(20)-en-23-oic acid δ-lactone (VIIa). R_f 0.68 (ether). IR spectrum (ν, cm^{-1}): 1250, 1725, 3590 (in $CHCl_3$). Molecular weight 416, calculated as $C_{25}H_{36}O_5$. Mass spectrum, (m/z): 416 (M), 398 (M − 18), 356 (M − 60), 338 (M − 60 − 18), 323 (M − 60 − 18 − 15), 304. PMR spectrum (δ, ppm): 0.96, 1.04 s (6 H, 18-CH_3, 19-CH_3); 1.72 s (3 H, 21-CH_3); 2.01 s (3 H, acetate); 4.56 m (1 H, 16-H); 5.17 m (1 H, 3-H);

3) 290 mg of a mixture of diols which was separated after oxidation with CrO_3 in pyridine.

At 0°C, with stirring, a solution of 230 mg of the mixture od diols in 10 ml of pyridine was added to the CrO_3·Py complex obtained from 400 mg of CrO_3 and 15 ml of pyridine (2 h, 0-5°C). Stirring was continued at 0°C for 2 h and the reaction mixture was left at 20°C for 18 h. After treatment with a solution of $NaHCO_3$, extraction with ether, and drying with $MgSO_4$, the solvent was evaporated off. The residue (180 mg) was separated by chromatography in the ether–heptane (1:2) and (1:1) systems. This gave:

1. 90 mg of ethyl 3β-acetoxy-5α-hydroxy-16-oxo-24-norcholan-23-oate (XIII), R_f 0.53 (ether–hexane (4:1)). IR spectrum (ν, cm^{-1}): 1025, 1250, 1725, 3600 (in $CHCl_3$). Molecular weight, calculated as $C_{27}H_{42}O_6$, 462. Mass spectrum, (m/z): 462 (M), 447 (M − 15), 402 (M − 60), 401 (M − 15 − 46), 339;

2) 40 mg of ethyl 3-acetoxy-6,16-dioxo-24-norcholan-23-oate (IX), R_f 0.33 [ether–hexane (4:1)]. IR spectrum (ν, cm^{-1}): 1025, 1250, 1752 (in $CHCl_3$). Molecular weight, calculated as $C_{27}H_{40}O_6$, 460. Mass spectrum, (m/z): 460 (M), 445 (M − 15), 399 (M − 15 − 46), 357.

3β-Acetoxy-5α,16β-dihydroxy-24-norcholan-23-oic Acid δ-Lactone (VIIb). A solution of 85 mg of (VIII) in 6 ml of CH_3OH was treated with 300 mg of $NaBH_4$ in 4 ml of CH_3OH, and the mixture was stirred at 20°C for 3 h. After the usual working up, the product was saponified by being boiled in a mixture of 1 g of K_2CO_3, 6 ml of CH_3OH, and 4 ml of water for 1 h, and then the solvent was evaporated off, the residue was acidified with HCl to pH 1 and extracted with EtOAc, and the extracts were washed with $NaHCO_3$ solution and with water, dried with

$MgSO_4$, and evaporated. The residue (15 mg) was acetylated in 1 ml of pyridine and 0.1 ml of Ac_2O; after the usual working up, 10 mg of the lactone (VIIb) was obtained with R_f 0.29 (ether).

IR spectrum (ν, cm^{-1}): 1040, 1250, 1730, 3600 (in $CHCl_3$). Molecular weight, calculated as $C_{25}H_{38}O_5$, 418. Mass spectrum, (m/z): 418 (M), 400 (M − 18), 358 (M − 60), 356, 340, 325, 304, 289, 274, 127. PMR spectrum (δ, ppm): 0.89 s (3 H, 18-CH_3); 1.0 s (3 H, 19-CH_3); 1.15 d (J = 6.5 Hz, 3 H, 21-CH_3); 2.02 s (3 H, acetate); 4.17 m (1 H, 16-H); 4.81 m (1 H, 3-H).

3β,6β,16β-Trihydroxy-24-nor-5α-cholan-23-oic Acid δ-Lactone (X). The same sequence of reactions as described above (apart from acetylation) applied to 30 mg of the diketone (IX) yielded 5 mg of the dihydroxy lactone (X), mp 274-278°C (according to the literature: 278-280°C [2]). PMR (δ, ppm): 0.88 s (3 H, 18-CH_3); 1.05 s (3 H, 19-CH_3); 1.21 d (J = 6.5 Hz, 3 H, 21-CH_3); 2.48 m (2 H, OH); 3.72 m, 4.04 m, 4.90 m (3 H, OCH, 16-H).

Methyl 3β,16α-Dihydroxy-24-norchol-5-en-23-oate (XIII). The hydrogenation of 0.98 g of the $\Delta^{20(22)}$-lactone obtained from 5.0 g of the diacetate (XI) by the Reformatskii reaction using the method which we have described [10] was carried out over 50 mg of PtO_2 in 35 ml of AcOH until an equimolar amount of hydrogen (59 ml as compared with 55 ml theoretically) had been absorbed. After the usual working up, 0.95 g of (XII) was obtained with mp 177-180°C (from CH_3OH). A mixture consisting of 0.95 g of (XII), 36 ml of CH_3OH, 9 ml of $CHCl_3$, 3 ml of water, and 1.8 ml of concentrated HCl was kept at 20°C for 50 h. Then the solvent was partially evaporated off and the residue was washed with water and extracted with $CHCl_3$; the extracts were washed with $NaHCO_3$ solution, with water, and with NaCl solution, dried with $MgSO_4$, and evaporated. The residue (0.95 g) was recrystallized from a mixture of hexane and $CHCl_3$. This gave 570 mg of (XIII) with mp 164-167°C. IR spectrum (ν, cm^{-1}): 1725, 3600 (in $CHCl_3$). Molecular weight 390 calculated as $C_{24}H_{38}O_4$. Mass spectrum, (m/z): 390 (M), 372 (M − 18), 358 (M − 32), 340 (M − 32 − 18), 325 (M − 32 − 15).

16β-Hydroxy-6-oxo-3,5α-cyclo-24-norcholan-23-oic Acid (23 → 16)-δ-Lactone (XVI). A mixture consisting of 0.57 g of the diol (XIII), 0.60 g of toluenesulfonyl chloride, and 5 ml of pyridine was kept at +4°C for 48 h. Then it was diluted with water and extracted with $CHCl_3$. The extracts were washed with 2 N HCl to pH 7 and with water, and were dried with $MgSO_4$ and evaporated. The residue was washed with a mixture of CH_3OH and hexane. This gave 780 mg of a mixture of tosylates, 80 mg of which was separated on an 18 × 23 cm plate coated with SiO_2 in the benzene–acetone (9:1) system, with the isolation of 6 mg of the ditosylate (XIV).

IR spectrum (ν, cm^{-1}): 1175, 1600, 1730 (in $CHCl_3$). Molecular weight, calculated as $C_{38}H_{50}O_8S_2$, 698. Mass spectrum (m/z): 354 (M − 2 × 172), 340, 172. PMR spectrum (δ, ppm): 0.7 s (3 H, 18-CH_3); 0.94 s (3 H, 19-CH_3); 1.13 d (J = 6.5 Hz, 3 H, 21-CH_3); 2.48 s (6 H, aryl 2 CH_3); 3.62 s (3 H, OCH_3); 4.35, 4.83 m (2 H, 3-H, 16-H), 5.28 m (1 H, 6-H); 7.33, 7.80, 2d (8 H, 2 × aryl H's).

The unpurified ditosylate (XIV) (680 mg) was boiled in a mixture of 22 ml of acetone, 1.18 g of $KHCO_3$, and 6 ml of water for 6 h. After cooling, the solution was partially evaporated, the residue was extracted with EtOAc, and the extracts were washed with water, dried with $MgSO_4$, and evaporated. Chromatography on SiO_2 in the ether–heptane (3:1) system yielded 170 mg of the 6β-hydroxy-3,5α-cyclolactone (XV), R_f 0.26 [benzene–acetone (9:1)].

IR spectrum (ν, cm^{-1}): 1710, 1740, 3600 (in $CHCl_3$). Molecular weight 358 calculated as $C_{23}H_{34}O_3$. Mass spectrum (m/z): 358 (M), 343 (M − 15), 340 (M − 18), 325 (M − 15 − 18). The hydroxysteroid (XV) (170 mg) was oxidized in 3 ml of pyridine at 0°C for 2 h and then at 20°C for 18 h with the CrO_3·Py complex prepared from 290 mg of CrO_3 and 2 ml of pyridine.

After the usual working up, chromatography of the residue (130 mg) with benzene–acetone (1:1) yielded 75 mg of the 6-ketone (XVI), mp 245-250°C (from ether). IR spectrum (ν, cm^{-1}): 1040, 1080, 1610, 1685, 1740 (in $CHCl_3$). Molecular weight, calculated as $C_{23}H_{32}O_3$, 356. Mass spectrum (m/z): 356 (M), 341 (M − 15), 338 (M − 18), 328 (M − 28). PMR spectrum (δ, ppm): 0.7 m, 2 H, 4-CH_2); 0.84 s (3 H, 18-CH_3); 1.03 s (3 H, 19-CH_3); 1.15 d, (J = 6.5 Hz, 3 H, 21-CH_3); 4.69 m (1 H, 16-H).

3β-Acetoxy-16β-hydroxy-6-oxo-24-nor-5α-cholan-23-oic Acid 23 → 16-δ-Lactone (Ib). A mixture consisting of 75 mg of (XVI), 6 ml of AcOH, and 0.15 ml of concentrated H_2SO_4 was kept at 20°C for 18 h and was then treated with water and extracted with EtOAc, and the extract was washed with $NaHCO_3$, dried with $MgSO_4$, and evaporated. Recrystallization of the residue from ether–acetone yielded 37 mg of the lactone (Ib) with mp 228-230°C (according to the literature, mp 228-230°C [2]). IR spectrum (ν, cm^{-1}): 1250, 1730 (in $CHCl_3$). Molecular weight 416 calculated as $C_{25}H_{36}O_5$. Mass spectrum (m/z): 356 (M − 60), 341 (M − 60 − 15), 338 (M − 60 − 18), 328 (M − 60 − 28). PMR spectrum (δ, ppm): 0.78 s (6 H, 18-CH_3, 19-CH_3); 1.13 d (J = 6.3 Hz, (3 H, 21-H_3); 2.04 s (3 H, acetate); 4.64 m (2 H, 6-H, 16-H). ORD: $[M]_{305}$ − 3580; $[M]_{277}$ − 646 (c 0.670; CH_3OH).

The saponification of 30 mg of (I) under the conditions given in the literature [2] led to 25 mg of (Ia), with mp 237.5-240°C (from acetone–hexane), coinciding in its constants with literature figures for chiogralactone [2].

SUMMARY

1. A stereospecific synthesis of the natural phytosteroid "chiogralactone" has been effected from the readily available 3β,16α-diacetoxypregn-5-en-20-one.

2. The hydrogenolysis of 5,6α:16,17α-diepoxysteroids has been studied and it has been shown that on Pd and Pt catalysts the 16,17α-oxide ring is reduced first.

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