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# Steroidal Analogue of Deoxyvernolepin. Synthesis of δ-Lactone Key Intermediate

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Sesquiterpene lactones of elemanolide type vernolepin *1* and deoxyvernolepin *2* exhibit a pronounced antitumor activity against the Walker intramuscular carcinosarcoma 256 and CCRF — CEM human lymphoblastic leukemia cells in culture and were therefore, subjects of many partial and total syntheses.

The synthesis of the steroidal analogue of deoxyvernolepin *3*, i. e., its key intermediate, δ-lactone 28-hydroxy-2-oxa-5α,10α--cholest-6-en-3-one *4* starting from cholesterol is the subject of this report.

Known reactions, as well as modified ones, were used in the synthesis. A new reaction for the preparation of dimethyl acetals with pyridinium chlorochromate and methanol was also developed. It was found that the acetalization reaction using pyridinium chlorochromate and methanol could be performed without affecting an acid-sensitive functional groups such as the oxirane ring.

During the last 30 years more than 800 sesquiterpene lactones have been isolated and identified from various plant species of *Compositae* and *Umbelliferae*, as well as from *Lauraceae, Burserceae, Magnoliaceae* and *Hepaticeae*.[1,2]

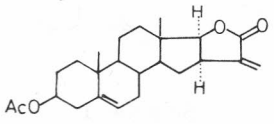
It was found that the pronounced actineoplastic (antitumor) activity *in vitro*, seldom *in vivo*, of sesquiterpene lactones is due to the α-ethylene-γ- and/or δ-lactone ring and the stereochemistry of epoxide, hydroxy and other functional groups in their molecule.[2–7]

Bis-α-methylene sesquiterpene lactones of elemanolide type vernolepin *1*[3,5–10] and deoxyvernolepin *2*[11–13] (Figure 1) exhibit a pronounced antitumor activity against the Walker intramuscular carcinosarcoma 256[8] and CCRF — CEM human lymphoblastic leukemia cells in culture[12] and were, therefore, subjects of many partial and total syntheses.[11,13–22]

These facts encouraged us to synthesize the steroidal analogue of deoxyvernolepin *3*, i. e., its δ-lactone key intermediate, 28-hydroxy-2-oxa--5α,10α-cholest-6-en-3-one *4*, starting from cholesterol*.

* Part of Ph. D. thesis of B. Š.

* The steroidal γ-lactone *5* which exhibits antitumor activity against *HeLa* cells has been synthesized recently.[23]

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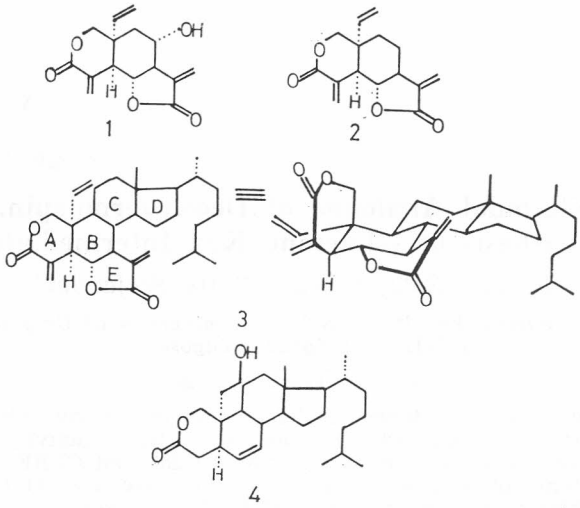


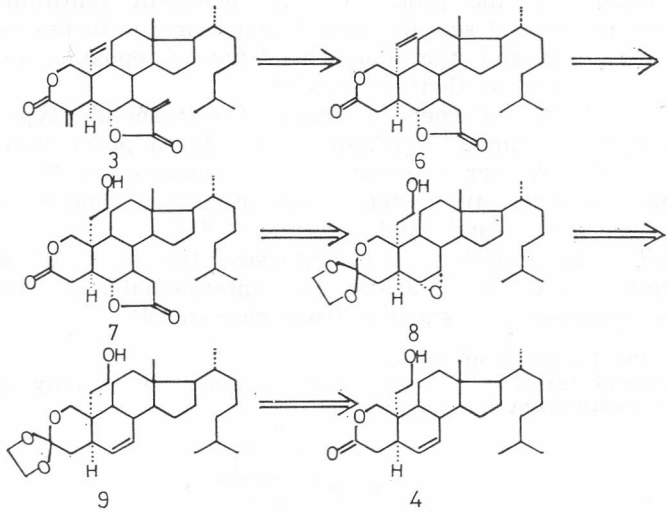

Retrosynthetic analysis of steroidal dilactone *3* (Scheme 1) points to the need for the following transformations of the cholesterol framework:

— simultaneous introduction of exocyclic double bonds into α-position of the γ- and δ-lactone rings,[24]

— synthesis of the γ-lactone ring (ring E) by the opening of the 6α,7α--epoxide ring with a suitable nucleophile,

— synthesis of the δ-lactone ring (ring A) by ozonolysis of $\Delta^2$-double bond and subsequent acification of the obtained product and

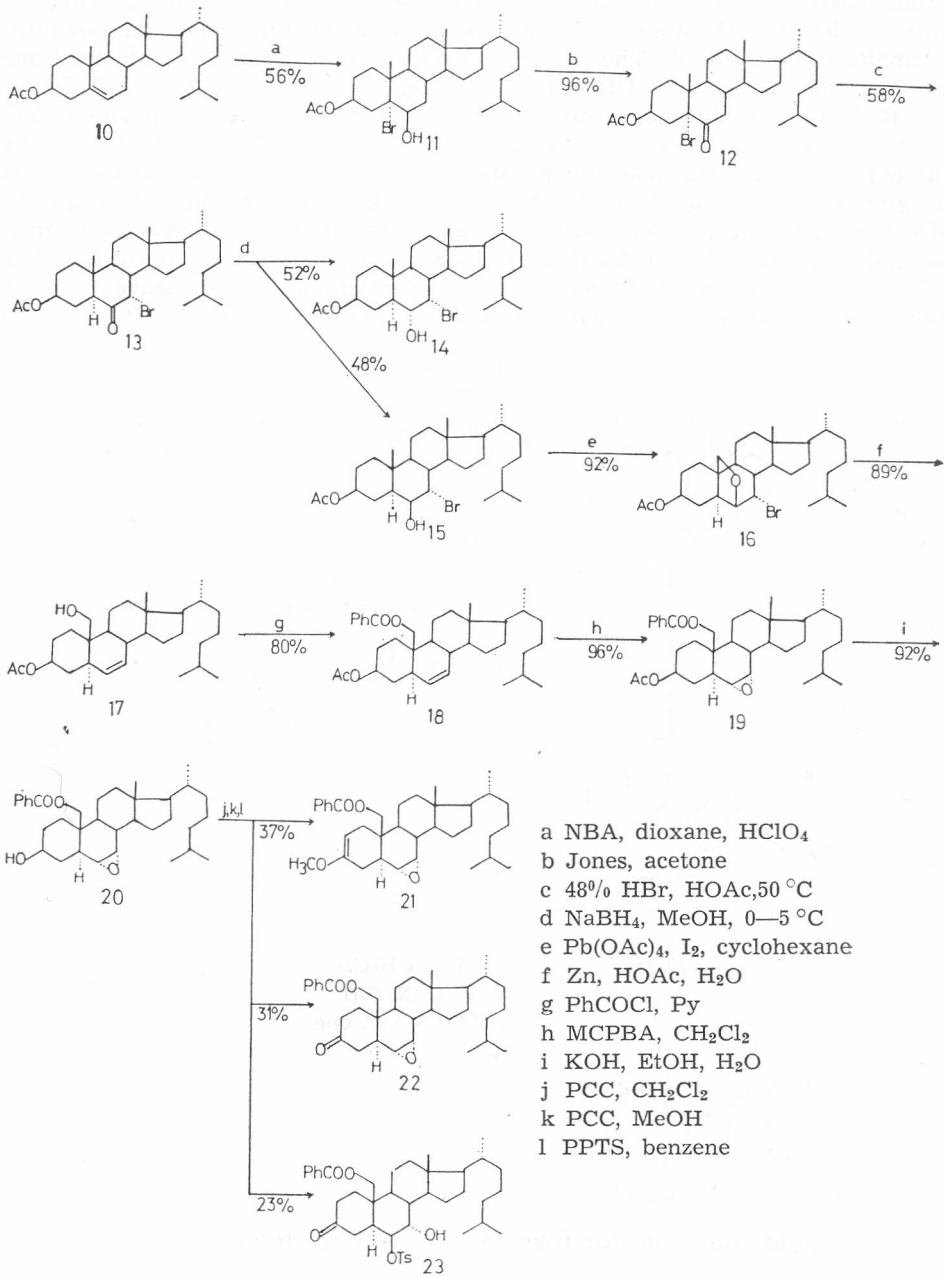
— conversion of primary alcohol into terminal double bond (the vinyl group) *via* the corresponding arylselenyl derivative.




Scheme 1

The synthesis should envisage an intermediate with *cis*-5α,10α-fused A and B rings because the nucleophilic attack on the 6α,7α-epoxide ring of the cholestane (5α,10β-) derivative yields the inappropriate *trans*-6β,7α--diaxial product.[28,29] It was expected that the regiospecific β-attack of the nucleophile (dilithio acetate,[16,18,19] *t*-butyl dilithioacetoacetate[20] or some other

Chart I



appropriate nucleophile) on the C-7 carbon atom of compound *8* should give *trans*-γ-lactone upon acidification.

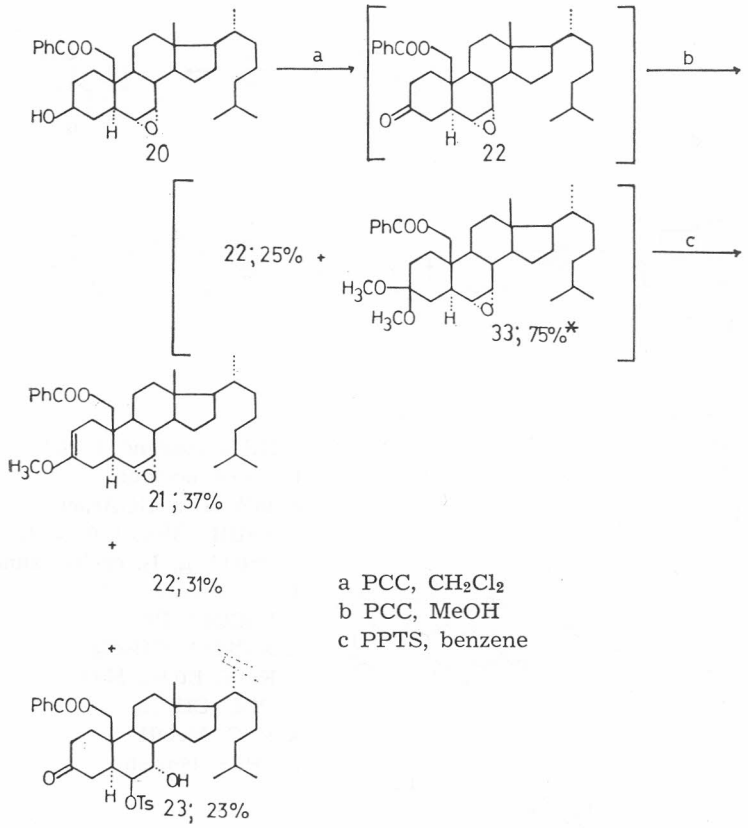
In this report, beside the δ-lactone *4*, the synthesis of 2-oxa-5α,10α--cholest-6,19-dien-3-one *29 via* the corresponding selenide *28* is described (Chart III).

Cholesteryl acetate *10* was treated with HOBr in dioxane solution and bromohydrin *11* was obtained in 56% yield[30] (Chart I). Bromohydrin *11* was oxidized with Jones reagent in acetone yielding the corresponding bromoketone *12* (96%). The latter compound was further transformed into its 7α-isomer with 48% HBr in acetic acid[31] in 58% yield.

Reduction of bromoketone *13* with sodium borohydride in methanol[32] gave 7α-bromo-5α-cholestan-3β,6β-diol 3-monoacetate *15* (48%), which was further cyclized with lead tetraacetate and iodine in cyclohexane solution to give 6β,19-epoxide *16* (92%).[30,33-36] The 6β,19-epoxide ring cleavage was effected with zinc in acetic acid and water (89%) and the obtained primary alcohol *17* protected by esterification with benzoyl chloride in pyridine (80%).

The epoxidation of *18* with *m*-chloroperoxybenzoic acid gave only the 6α,7α-epoxide *19* (96%) which was further hydrolized into 6α,7α-epoxy-5α-

Chart II




a PCC, $CH_2Cl_2$
b PCC, MeOH
c PPTS, benzene

* The yield was estimated from the $^1H$ NMR spectrum.

-cholestan-3β,19-diol 19-monobenzoate *20* under mild conditions (0.1 M KOH, $H_2O$) in 92% yield.

Synthesis of enol ether *21* was accomplished *via* the intermediate dimethyl acetal *33* (Chart II).

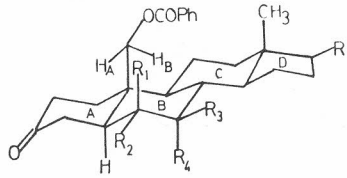
The intermediate compound *33* was prepared from alcohol *20*, which was oxidized with pyridinium chlorochromate (PCC) into the corresponding ketone *22*. The latter compound was dissolved in hot methanol together with »black gum«[37] and 3,3-dimethyl acetal *33* was obtained in 75% yield*, according to $^1H$ NMR spectrum (not isolated).

In order to establish the reaction mechanism of this facile route for the preparation of dimethyl acetals[39] from alcohols or ketones, we treated the previously prepared 6α,7α-epoxy-19-benzoyloxy-5α-cholestan-3-one *22* with boiling methanol in the presence of pyridinium ion (originated from $PyH^+Cl^-$ or pyridinium *p*-toluenesulphonate (PPTS)), but without success. However, when the same ketone was treated with methanol and PCC as catalyst, dimethyl acetal *33* was obtained in almost the same yield as in the case when the intermediate ketone was not isolated. Thus we presume that the $Cr^{4+}$ ion takes part in this reaction**.

This new method for the preparation of dimethyl acetals directly from alcohols, without isolation of intermediate ketones was presented in our previous paper.[38]

The mixture of *22* and *33*, which could not be separated on a silica gel column, was treated with PPTS in boiling benzene[13,39] to give the expected enol ether *21* (37%), ketone *22* (31%) and 7α-hydroxy-6β-*p*-toluenesulphonyloxy-19-benzoyloxy-5α-cholestan-3-one *23* (23%), a product of nucleophilic attack of tosyloxy anion on the C-6 carbon atom of 6α,7α-epoxide ring (Chart II).

Inspection of Dreiding models and the $^1H$ NMR data of *22*, *23* and *34* (Figure 2) point to chair conformation of the B ring of *p*-toluenesulphonate *23* in spite of the 10β-position of the bulky —$CH_2OCOPh$ group.




| | | | |
|---|---|---|---|
| *34* | $R_1=R_2=R_3=R_4=H$ | 2H-19 | δ 4.72, s[40] |
| *22* | $R_1=R_3=H$ | H-6 | δ 2.84, d, $J_{6,7}=4$ Hz |
| | $R_2+R_4=O$ | H-7 | δ 3.16, dd, $J_{7,6}=4$ Hz, $J_{7,8}=2.5$ Hz |
| *23* | $R_1$=OTs | 2H-19 | δ 4.49 and δ 4.71, AB syst., $J=12$ Hz |
| | | H-6 | δ 4.36, dd, $J_{6,5}=3.75$ Hz, $J_{6,7}=2$ Hz |
| | $R_2=R_3=H$ | H-7 | δ 3.91, m, $W_{1/2}=7.5$ Hz |
| | $R_4$=OH | 2H-19 | δ 4.53 and δ 4.63, AB syst., $J=13$ Hz |
| | $R=C_8H_{17}$ | | |

Figure 2

* See experimental part. It is not clear what are the reduction products of the $Cr^{6+}$ ion in these reactions; several authors proposed that $Cr^{4+}$ might be one. For further information see. G. Piancatelli and M. D'Aruia, *Synthesis*, (1982) 245 and references therein.

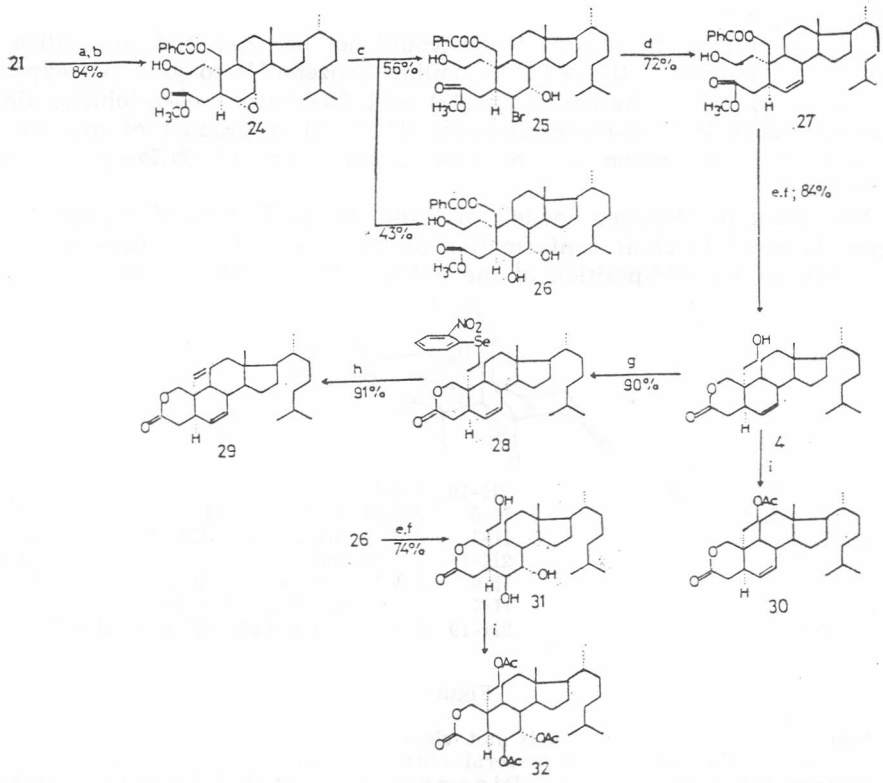
** Analogous results were obtained with 5α-cholest-3-one, 6β,19-epoxy-5α-cholestan-3-one and cholest-5-en-3-one.

Coupling constants of $J_{6,5} = 3.75$ Hz and $J_{6,7} = 2$ Hz are in agreement with the proposed conformation.

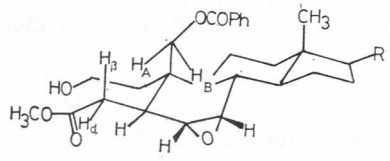
Methylene 2H-19 protons of keto-benzoate *34* appear as a singlet at δ 4.72[40] as a consequence of the diamagnetic anisotropic effect of the 3-keto group (chemical shift of methylene R—$CH_2$OCOPh protons in δ 4.20[41]).[42a-f] However, one of the H-19 protons of 6α,7α-epoxy-19-benzoyloxy-5α-cholestan--3-one *22* is shifted to upper field. Thus the chemical shifts of δ 4.71 for $H_A$-19 and δ 4.49 for $H_B$-19 are assigned. Both methylene protons of tosylate *23* are shifted to the upper field and their chemical shifts are $H_A$-19 δ 4.63 and $H_B$-9 δ 4.53.

Ozonolysis of the enol ether *21* at —78 °C in dichloromethane-methanol solution and subsequent reduction with sodium borohydride of intermediate hydroperoxide gave methyl-6α,7α-epoxy-2-hydroxy-19-benzoyloxy-2,3-seco-5α--cholestan-3-oate *24* (84%; Chart III). The 6α,7α-epoxide ring was treated with 48% hydrobromic acid in dioxane to give bromohydrin *25* (56%) and triol *26* (43%). Surprisingly the chair conformation was established for compound *25* on the basis of the $^1$H NMR data (Figure 3).

Chart III

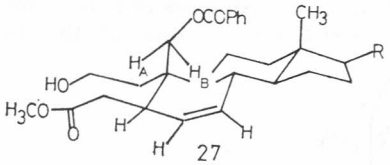



a $O_3$, $CH_2Cl_2$, MeOH, —78 °C; b $NaBH_4$, —20 °C, HOAc; c 48% HBr, dioksan, $H_2O$; d Zn, HOAc, $H_2O$; e KOH, MeOH, $H_2O$; f conc. HCl; g o-$O_2NC_6H_4SeCN$, THF, *n*-$Bu_3P$; h 30% $H_2O_2$, THF; i $Ac_2O$, Py.



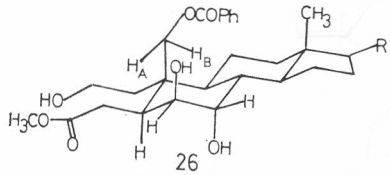
24

H-4α and H-5
δ 2.41, $B_2$ of $AB_2$, $J_{gem} = J_{4\alpha,5} = 11.20$ Hz
H-4β
δ 2.75, A of $AB_2$, $J_{gem} = J_{4\beta,5} = 11.20$ Hz
H-6
δ 2.98, d, $J_{6,7} = 4$ Hz
H-7
δ 3.10, dd, $J_{7,6} = 4$ Hz $J_{7,8} = 1.8$ Hz
2H-19
δ 4.24 and δ 4.14, AB syst., $J = 12$ Hz



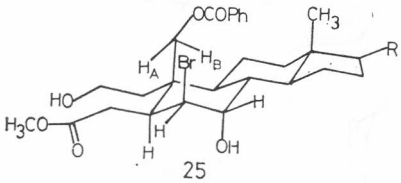
27

2H-4
δ 2.81, m, $W_{1/2} = 20$ Hz
H-6 and H-7
δ 5.34 and δ 5.56, AB syst., $J = 11.30$ Hz
2H-19
δ 4.35 and δ 4.23, AB syst., $J = 12$ Hz



26

2H-2, H-6 and H-7
δ 3.73, m, $W_{1/2} = 15$ Hz
2H-4 and H-5
δ 2.32, m, $W_{1/2} = 25$ Hz
2H-19
δ 4.68 and δ 4.47, AB syst., $J = 12$ Hz



25

2H-4 and H-5
δ 2.64, s
H-6
δ 4.40, m, $W_{1/2} = 5$ Hz
H-7
δ 4.06, m, $W_{1/2} = 7.5$ Hz
2H-19
δ 4.82 and δ 4.46, AB syst., $J = 12$ Hz

Figure 3

Shold the B ring of *25* exist in one of the two possible boat conformations (bot unfavourable because of strong 1,2-diequatorial interaction of the 6β-bromine atom and 7α-hydroxy group), the H-7 proton will appear as dd with $J \approx 10$—12 Hz, or as a singlet. However, $W_{1/2} = 7.5$ Hz was found for the H-7 proton, which together with a great downfield shift of both H-19 protons* (Table I) confirms the proposed conformation of the B ring.

Finally, the δ-lactone *4* was prepared from bromohydrin *25* by reductive introduction of the $\Delta^6$-double bond with zinc in acetic acid and water (72%),

TABLE I

| | | $H_A$ | $H_B$ | |
|---|---|---|---|---|
| *24* | 2H-19 | δ 4.24 | δ 4.14 | $\Delta\nu_{AB} = 8.0$ Hz |
| *27* | 2H-19 | δ 4.35 | δ 4.23 | $\Delta\nu_{AB} = 9.6$ Hz |
| *26* | 2H-19 | δ 4.68 | δ 4.47 | $\Delta\nu_{AB} = 16.8$ Hz |
| *25* | 2H-19 | δ 4.82 | δ 4.46 | $\Delta\nu_{AB} = 28.8$ Hz |

* Characteristic influence of axial 6β-substituents.[42e,42f]

alkaline hydrolysis and subsequent acidification with concentrated hydrochloric acid without isolation of the intermediate compound (84%; Chart III).

An analogous reaction scheme was applied to the synthesis of δ-lactone *31* from triol *26*.

Introduction of the vinyl group to the 10α-position of the lactone *4* was performed with *o*-nitrophenyl selenocyanate and tri-*n*-butylphosphine in THF[26,27] and the obtained yellow 28-*o*-nitrophenylseleno-2-oxa-5α,10α-cholest--6-en-3-one *28* (90%) was treated with 30% hydrogen peroxide to give 2-oxa--5α,10α-cholest-6,19-dien-3-one *29* in 91% yield.

Inspection of Dreiding models suggested that the synthesized δ-lactones *4, 28, 29, 31,* and acetates *30* and *32* may exist *i. e.* in one of the two

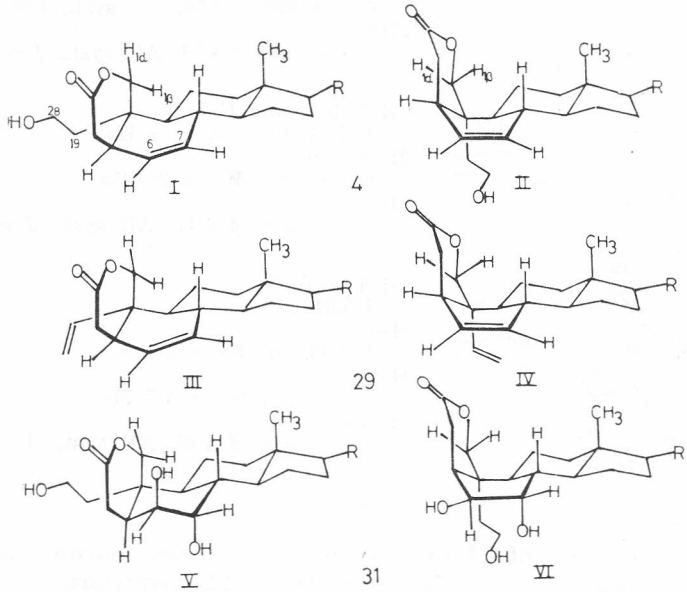



Figure 4

conformations* shown in Figure 4. Analysis of the $^1$H NMR data of the obtained lactones (Table II) indicates that conformations I, III and V of *4, 29* and *31,* respectively, can be found in $CDCl_3$ or acetone-$d_6$ solutions. Distorted chair conformation of the δ-lactone ring is proposed on the basis of the great downfield shift of H-1β protons (δ 4.37, δ 4.39 and δ 4.89) caused by the diamagnetic anisotropic effect of the carbonyl group of the lactone ring on H-1β proton.

The great downfield shift of the H-1β proton of δ-lactone *31* (δ 4.89) is indicative of an additional effect of the axial 6β-hydroxy group.

The half-chair conformation of the B ring of *4, 28* and *29* is proposed on the basis of $J_{6,7} = 10$ Hz, $J_{6,5} = 1.2$ Hz and $J_{6,8} = 1$ Hz. In the case of the boat conformation of the B ring (structures II and IV; Figure 4) the coupling constant $J_{6,5} \approx 8$—10 Hz should be found.

* Twisted congormations could also be taken into consideration.

| | | | | | | |
|---|---|---|---|---|---|---|
| | 3.83<br>B of AB, $J$=12 | 3.84<br>B of AB, $J$=12 | 3.86, dd<br>$J_{gem}$=11.25, $J$=2.5 | 4.01, dd<br>$J_{gem}$=11.25, $J$=2.5 | 3.84<br>B of AB, $J$=12 | |
| H-1β | 4.37<br>A of AB, $J$=12 | 4.39<br>A of AB, $J$=12 | 4.89<br>$J_{gem}$ = 11.25 | 4.76<br>$J_{gem}$=11.25 | 4.41<br>A of AB, $J$=12 | 4.39, s |
| H-4 | 2.80, m, $W_{1/2}$=25 | 2.78, m, $W_{1/2}$=25 | 2.81, m, $W_{1/2}$=26.25 | 2.86, m, $W_{1/2}$=41.25 | 2.83, m, $W_{1/2}$=28.75 | |
| H-5 | 2.29, m, $W_{1/2}$=31.25 | 2.32, m, $W_{1/2}$=31.25 | 2.36, m, $W_{1/2}$=15 | 2.31, m, $W_{1/2}$=10 | 2.33, m, $W_{1/2}$=26.25 | 2.56, m, $W_{1/2}$=50 |
| H-6 | 5.43, ddd, $J_{6,7}$=10<br>$J_{6,5}$=1.2, $J_{6,8}$=1 | 5.43, ddd, $J_{6,7}$=10<br>$J_{6,5}$=1.2, $J_{6,8}$=1 | | 5.05, t, $J$=3.25 | 5.48, ddd, $J_{6,7}$=10<br>$J_{6,5}$=1.2, $J_{6,8}$=1 | 5.48, ddd, $J_{6,7}$=10<br>$J_{6,5}$=1.2, $J_{6,8}$=1 |
| H-7 | 5.73, d, $J_{7,6}$=10 | 5.73, d, $J_{7,6}$=10 | 3.74, m, $W_{1/2}$=12.5 | 4.86, m, $W_{1/2}$=5.5 | 5.82, d, $J_{7,6}$=10 | 5.66, d, $J_{7,6}$=10 |
| H-18 | 0.71, s | 0.73, s | 0.71, s | 0.69, s | 0.74, s | 0.71, s |
| H-19 | 1.73, t, $J$=7.5 | 1.83, t, $J$=7.5 | — | — | — | 5.68, dd<br>$J_{19,28A}$=15<br>$J_{19,28B}$=10 |
| H-26 and H-27 | 0.86, d, $J$=6 | 0.89, d, J=6 | 0.86, d, $J$=6 | 0.86, d, J=6 | 0.86, d, $J$=6 | 0.88, d, $J$=6 |
| H-28 | 3.80, t, $J$=7.5 | 4.14, t, $J$=7.5 | 3.64, t, $J$=7.5 | 4.18, t $J$=7.5 | 4.18, m, $W_{1/2}$=28.75 | — |
| —OCOCH$_3$ | — | 2.07 | — | 2.06, 2.08, 2.11 | — | — |
| H-28$_A$ | — | — | — | — | — | 5.43, dd<br>$J_{28A,19}$=15<br>$J_{28A,28B}$=2.5 |
| H-28$_B$ | — | — | — | — | — | 5.14, dd<br>$J_{82B,19}$=10<br>$J_{28B,28A}$=2.5 |

[a] Chemical shifts expressed in terms of ppm (δ) values and coupling constants ($J$) in Hz.
[b] $CDCl_3$
[c] acetone-$d_6$

## EXPERIMENTAL

Melting points were taken on the Boetius PHMK apparatus and were not corrected. IR spectra were recorded (KBr pellets or film) on a Perkin-Elmer spectrophotometer, model 457. $^1$H NMR spectra were recorded on a Varian FT-80A spectrometer in $CDCl_3$ and acetone-$d_6$ using tetramethylsilane as internal standard. Chemical shifts were expressed in terms of ppm ($\delta$) values and coupling constants ($J$) in Hz. $^{13}$C NMR spectra were recorded on a Varian FT-80A spectrometer at 20 MHz in $CDCl_3$ and acetone-$d_6$.

*5α-Bromo-5α-cholestan-3β,6β-diol 3-monoacetate* 11

Bromohydrin *11* was synthesized from cholesterol according to the known procedure of Kalvoda *et al.*[30] (38 g, 56% m. p. 172—174 °C).

*5α-Bromo-3β-acetoxy-5α-cholestan-6-one* 12

Bromohydrin *11* was dissolved in acetone and oxidized with Jones reagent. After the usual work-up procedure, bromoketone *12* (36.5 g, 96%; m. p. 158—160 °C (EtOH)) was obtained.

*7α-Bromo-3β-acetoxy-5α-cholectan-6-one* 13

Isomerization of 5α-bromo-6-ketone *12* into 7α-bromo isomer *13* was performed with 48% hydrobromic acid in acetic acid according to Heilbron *et. al.*[31] (20.8 g, 58%; m. p. 142—145 ° (EtOH)).

*7α-Bromo-5-α-cholestan-3β,6β-diol 3-monoacetate* 15

7α-Bromoketone *13* was reduced with sodium borohydride in methanol solution at 0—5 °C. After work-up and separation on a silica gel column bromohydrin *15* was obtained (14 g, 48%; m. p. 179—180 °C (EtOH)) together with its epimer, 7α-bromo-5α-cholestan-3β,6α-diol 3-monoacetate *14* (15 g, 52%; m. p. 162—163 °C (EtOH)).

*7α-Bromo-6β,19-epoxy-5α-cholestan-3β-ol 3-acetate* 16

A suspension of lead tetraacetate (76 g; 0.171 mole) and calcium carbonate (34 g) in cyclohexane (1666 ml) were stirred at reflux for 20 min. Upon addition of bromohydrin *15* (15 g; 0.029 mole) and iodine (16.5 g; 0.065 mole) the reaction mixture was irradiated with a Wolfram lamp (500 W) for 40 minutes. The cooled reaction mixture was filtered through celite, the filtrate was diluted with ether and washed with 10% sodium tiosulphate and water and dried over anhydrous magnesium sulphate. Magnesium sulphate was filtered off, the filtrate evaporated *in vacuo* and the residue crystallized from methanol and ether to give *7α-bromo-6β,19-epoxy-5α-cholestan-3β-ol 3-acetate* 16, 13.7 g (92%), m. p. 126—128 °C (MeOH/ether), lit.[33] m. p. 129—130 °C; $[\alpha]_D^{20} = -62.30°$ (c = 1.00, chl.); IR (KBr): $\nu$ 1740, 1245, 1235, 1197, 1038, 1022, 970, 962, 936, 922, 905 cm$^{-1}$; $^1$H NMR ($CDCl_3$): $\delta$ 0.75 (3H, s, H-18), 0.88 (6H, d, $J = 6$ Hz, H-26 and H-27), 0.93 (3H, d, $J = 6$ Hz, H-21), 2.05 (3H, s, —$OCOCH_3$), 2.56 (1H, dd, $J_{8.7} = 4$ Hz, $J_{8.9} = 12$ Hz, H-8), 3.69 and 3.87 (2H, AB system, $J = 8.8$ Hz, H-19), 4.09 (2H, m, $W_{1/2} = 17.5$ Hz, H-6 and H-7), 4.73 (1H, m, $W_{1/2} = 25$ Hz, H-3).

*5α-Cholest-6-en-3β,19-diol 3-monoacetate* 17

Powdered zinc (91 g) was added to a solution of 6β,19-epoxide *16* (13.6 g; 0.026 mole) in glacial acetic acid (456 ml) and water (20 ml) at 45—50 °C while the reaction mixture was vigorously stirred. After 40 min the reaction mixture was colled to room temperature, inorganic material filtered off and the filtrate evaporated *in vacuo*. The obtained oily residue was dissolved in the mixture of ether and chloroform (5 : 1) and washed with a saturated solution of sodium bicarbonate and water. The dried solution was evaporated *in vacuo* and the residue crystallized from a mixture of methanol and chloroform to give *5α-cholest-6-en-3β,19-diol 3-monoacetate 17*, 10.4 g (89%), m. p. 147—149 °C (MeOH/$CHCl_3$), lit.[33] m. p. 102—103 °C; $[\alpha]_D^{15} = -94.94°$ (c = 1.12, chl); IR (KBr): $\nu$ 3520, 3040, 1650, 1265, 1055, 1045, 1029,

995, 985 $cm^{-1}$ $^1H$ NMR ($CDCl_3$): $\delta$ 0.73 (3H, s, H-18), 0.87 (6H, d, $J = 6$ Hz, H-26 and H-27), 0.90 (3H, d, $J = 6$ Hz, H-21), 2.03 (3H, s, —$OCOCH_3$), 3.85 (2H, s, H-19), 4.75 (1H, m, $W_{1/2} = 30$ Hz, H-3), 5.24 and 5.51 (2H, AB system, $J = 10$ Hz, H-16 and H-7).

*Anal.* $C_{29}H_{48}O_3$ (444.72) calc'd: C 78.33; H 10.88%
found: C 78.01; H 10.74%.

*5α-Cholest-6-en-3β,19-diol 3-acetate 19-benzoate* 18

Monoacetate *17* (10.4 g; 0.023 mole), dissolved in pyridine (48 ml), was treated with benzoyl chloride (10.4 ml; 0.09 mole) at room temperature. After the usual work-up the obtained oily residue crystallized from methanol to give *5α-cholest-6-en-3β,19-diol 3-acetate 19-benzoate 18*, 10.1 g (80%), m. p. 126—128 °C (MeOH); $[\alpha]_D^{17} = -58.15°$ (c = 0.92, chl.); IR (KBr): $\nu$ 3030, 1745, 1730, 1650, 1620, 1600, 1275, 1240, 1180, 1115, 1073, 1055, 1030, 715 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$ 0.65 (3H, s, H-18), 0.86 (6H, d, $J = 6$ Hz, H-26 and H-27), 0.93 (3H, d, $J = 6$ Hz, H-21), 2.05 (3H, s, —$OCOCH_3$), 4.46 and 4.68 (2H, AB system, $J = 12$ Hz, H-19), 4.80 (1H, m, $W_{1/2} = 30$ Hz, H-3), 5.28 and 5.56 (2H, AB system, $J = 10$ Hz, H-6 and H-7), 7.28—8.05 (5H, arom.).

*Anal.* $C_{36}H_{52}O_4$ (548.81) calc'd.: C 78.79; H 9.55%
found: C 79.04; H 9.57%.

*6α,7α-Epoxy-5α-cholestan-3β,19-diol 3-acetate 19-benzoate* 19

10.1 g (0.018 mole) of *18*, dissolved in dichloromethane (163 ml), was treated with *m*-chloroperoxybenzoic acid (4.2 g; 0.024 mole). The reaction mixture was left overnight, washed with a saturated solution of sodium bicarbonate and water. The dried organic solution was evaporated *in vacuo* and the obtained residue crystallized from methanol to give *6α,7α-epoxy-5α-cholestan-3β,19-diol 3-acetate 19-benzoate 19*, 10 g (96%), m. p. 110—112 °C (MeOH); $[\alpha]_D^{16} = -18.24°$ (c = 1.17, chl.); IR (KBr): $\nu$ 3050, 1730, 1595, 1582, 1262, 1245, 1180, 1105, 1074, 1050, 1025, 725 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$ 0.64 (3H, s, H-18), 0.87 (6H, d, $J = 6$ Hz, H-26 and H-27), 0.91 (3H, d, $J = 6$ Hz, H-21), 2.05 (3H, s, —$OCOCH_3$), 2.83 (1H, d, $J_{6.7} = 4$ Hz, H-6), 3.11 (1H, dd, $J_{7.6} = 4$ Hz, $J_{7.8} = 2.5$ Hz, H-7), 4.37 and 4.64 (2H, AB system, $J = 12$ Hz, H-19), 4.76 (1H, m, $W_{1/2} = 30$ Hz, H-3), 7.28—8.10 (5H, arom.).

*Anal.* $C_{36}H_{52}H_5$ (564.81) calc'd.: C 76.55; H 9.28%
found: C 76.90; H 9.33%.

*6α,7α-Epoxy-5α-cholestan-3β,19-diol 19-monobenzoate* 20

A solution of potassium hydroxide in water (1 g KOH in 2.7 ml $H_2O$) was added to the stirred solution of *19* (10 g; 0.018 mole) in ethanol (259 ml) at room temperature. After 90 min, the reaction mixture was poured into cold water and acidified with diluted hydrochloric acid. The precipitate was filtered off, washed well with water and crystallized from methanol to give *6α,7α-epoxy-5α-cholestan-3β,19-diol 19-monobenzoate 20*, 8.5 g (92%), m. p. 107—109 °C (MeOH); $[\alpha]_D^{18} = -13.09°$ (c = 1.12, chl.); IR (KBr): $\nu$ 3350, 1730, 1610, 1595, 1180, 1115, 1075, 1032, 719 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$ 0.63 (3H, s, H-18), 0.85 (6H, d, $J = 6$ Hz, H-26 and H-27), 0.88 (3H, d, $J = 6$ Hz, H-21), 2.83 (1H, d, $J_{6.7} = 4$ Hz, H-6), 3.13 (1H, dd, $J_{7.6} = 4$ Hz, $J_{7.8} = 2.5$ Hz, H-7), 3.70 (1H, m, $W_{1/2} = 18$ Hz, H-3), 4.36 and 4.60 (2H, AB system, $J = 12$ Hz, H-19), 7.28—8.08 (5H, arom.).

*Anal.* $C_{34}H_{50}O_4$ (522.81) calc'd.: C 78.12; H 9.64%
found: C 77.84; H 9.45%.

*3-Methoxy-6α,7α-epoxy-5α-cholest-2-en-19-ol 19-benzoate* 21

To a solution of alcohol *20* (8.5 g; 0.016 mole) in dichloromethane (223 ml) pyridinium chlorochromate (12.6 g; 0.058 mole) was added in small portions. The reaction was mechanically stirred for four hours at room temperature. After the oxidation was finished (TLC), the supernatant was poured off and the precipitate washed with dry ether (3 × 100 ml). The combined solutions were left at room temperature for 45 min, the precipitate was filtered off and the filtrate evaporated

*in vacuo*. The obtained brown-reddish oil was dissolved in methanol (100 ml) and solution refluxed for 20 minutes. The resulting green-coloured the solution was evaporated *in vacuo* and the oily residue eluted with benzene through a short silica gel column. The obtained colourless oil was dissolved in dry benzene (223 ml), pyridinium *p*-toluenesulphonate was added (0.95 g; 0.004 mole) and the reaction mixture refluxed for 30 minutes. The cooled reaction mixture was twice washed with water, dried over anhydrous magnesium sulphate and evaporated *in vacuo*. After separation on a silica gel column enol ether *21*, ketone *22* and *p*-toluenesulphonate *23* were isolated. *3-methoxy-6α,7α-epoxy-5α-cholest-2-en-19-ol 19-benzoate 21*, 3.2 g (37%), oil; $[\alpha]_D^{18} = +24.44°$ (c = 0.71, chl.); IR (KBr): $\nu$ 3055, 1718, 1665, 1600, 1582, 1270, 1213, 1180, 1110, 1070, 1028, 712 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$ 0.61 (3H, s, H-18), 0.86 (6H, d, $J = 6$ Hz, H-26 and H-27), 0.90 (3H, s, $J = 6$ Hz, H-21), 2.95 (2H, d, $J_{6,7} = 4$ Hz, H-6), 3.13 (1H, dd, $J_{7,6} = 4$ Hz, $J_{7,8} = 2.5$ Hz, H-7), 3.50 (3H, s, —$OCH_3$), 4.30 and 4.40 (2H, AB system, $J = 12$ Hz, H-19), 4.58 (1H, d, $J_{2,1\alpha} = 3.5$ Hz, H-2), 7.28—8.08 (5H, arom.).

*Anal.* $C_{35}H_{50}O_4$ (534.81) calc'd.: C 78.61; H 9.42%
found: C 78.01; H 9.69%.

*6α,7α-epoxy-19-benzoyloxy-5α-cholestan-3-one 22*, 2.7 g (31%), oil; $[\alpha]_D^{23} = +14.71°$ (c = 0.64, chl.); IR (film): $\nu$ 3055, 1717, 1600, 1585, 1270, 1110, 1100, 1072, 1028, 715 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$ 0.69 (3H, s, H-18), 0.86 (6H, d, $J = 6$ Hz, H-26 and H-27), 0.88 (3H, d, $J = 6$ Hz, H-21), 2.84 (1H, d, $J_{6,7} = 4$ Hz, H-6), 3.16 (1H, dd, $J_{7,6} = 4$ Hz, $J_{7,8} = 2.5$ Hz, H-7), 4.49 and 4.71 (2H, AB system, $J = 12$ Hz, H-19), 7.27—8.08 (5H, arom.).

*7α-hydroxy-6β-p-toluenesulphonyloxy-19-benzoyloxy-5α-cholestan-3-one 23*, 2.5 g (23%), oil; $[\alpha]_D^{20.5} = +11.48°$ (c = 0.82, chl.); IR (film): $\nu$ 3500, 3060, 1715, 1600, 1585, 1271, 1191, 1179, 1112, 1099, 1072, 1023, 938, 715, 677 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$ 0.69 (3H, s, H-18), 0.86 (6H, d, $J = 6$ Hz, H-26 and H-27), 0.89 (3H, d, $J = 6$ Hz, H-21), 2.45 (3H, s, $CH_3$/TsO—), 3.91 (1H, m, $W_{1/2} = 7.5$ Hz, H-7), 4.36 (1H, dd, $J_{6,5} = 3.75$ Hz, $J_{6,7} = 2$ Hz, H-6), 4.53 and 4.63 (2H, AB system, $J = 13$ Hz, H-19), 7.33—8.04 (9H, arom.).

### *Methyl-6α,7α-epoxy-2-hydroxy-19-benzoyloxy-2,3-seco-5α--cholestan-3-oate* 24

Through a solution of enol ether *21* (0.05 g; $9 \times 10^{-5}$ mole) in dichloromethane (4.1 ml) and methanol (0.1 ml) ozone (~ 5%) was bubbled for 5 min at —78 °C. After the reaction was over (TLC), ozone was replaced by an argon atmosphere, the reaction mixture warmed to —20 °C and methanol (1 ml) added, followed by sodium borohydride (0.014 g; $3.70 \times 10^{-4}$ mole). After the reduction was completed, the reaction mixture was acidified with glacial acetic acid (—20 °C → 0 °C). The organic layer was washed with water, dried over anhydrous magnesium sulphate and evaporated *in vacuo* to give, *methyl-6α,7α-epoxy-2-hydroxy-19-benzoyloxy--2,3-seco-5α-cholestan-3-oate 24*, 0.044 g (84%), oil; $[\alpha]_D^{19} = —27.66°$ (c = 0.53, chl.); IR (KBr): $\nu$ 3440, 3055, 1735, 1718, 1660, 1582, 1270, 1177, 1110, 1070, 1028, 712 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$ 0.66 (3H, s, H-18), 0.88 (6H, d, $J = 6$ Hz, H-26 and H-27), 0.91 (3H, d, $J = 6$ Hz, H-21), 2.41 (2H, $B_2$ of $AB_2$ system, $J_{gem} = J_{4\alpha,5} = 11.2$ Hz, H-4α and H-5), 2.75 (1H, A of $AB_2$ system, $J_{gem} = J_{4\beta,5} = 11.2$ Hz, H-4β), 2.98 (1H, d, $J_{6,7} = 4$ Hz, H-6), 3.10 (1H, dd, $J_{7,6} = 4$ Hz, $J_{7,8} = 1.8$ Hz, H-7), 3.69 (2H, t, $J = 6$ Hz, H-2), 3.72 (3H, s, —$COOCH_3$), 4.14 and 4.24 (2H, AB system, $J = 12$ Hz, H-19), 7.29—8.06 (5H, arom.).

### *Methyl-6β-bromo-2,7α-dihydroxy-19-benzoyloxy-2,3-seco-5α--cholestan-3-oate* 25

A solution of epoxide *24* (1.60 g; $2.8 \times 10^{-3}$ mole) in dioxane (57 ml) and water (4.73 ml) was treated with 48% hydrobromic acid (4.70 ml) and stirred for 45 min at room temperature. The reaction mixture was diluted with water (20 ml), extracted with ether (3 × 40 ml) and the etheral solution washed with a saturated sodium bicarbonate solution and water. The dried solution was evaporated *in vacuo and* after separation on a silica gel column bromohydrin *25* and triol *26* were obtained, *methyl-6β-bromo-2,7α-dihydroxy-19-benzoyloxy-2,3-seco-5α-cholestan-3-*

*-oate 25,* 1.02 g (56%), m. p. 149—151 °C (chl./hexane); $[\alpha]_D^{20} = +11.07°$ (c = 0.85, chl.); IR (KBr): $\nu$ 3435, 3055, 1722, 1710, 1600, 1585, 1275, 1176, 1027, 712 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$ 0.75 (3H, s, H-18), 0.89 (6H, d, $J = 6$ Hz, H-26 and H-27), 0.93 (3H, d, $J = 6$ Hz, H-21), 2.64 (3H, s, H-4 and H-5), 3.71 (3H, s, —$COOCH_3$), 3.75 (2H, m, $W_{1/2} = 15$ Hz, H-2), 4.06 (1H, m, $W_{1/2} = 7.5$ Hz, H-7), 4.40 (1H, m, $W_{1/2} = 5$ Hz, H-6), 4.46 and 4.82 (2H, AB system, $J = 12$ Hz, H-19), 7.29—8.19 (5H, arom.).

*Anal.* $C_{35}H_{53}BrO_6$ (649.70) calc'd.: C 64.70; H 8.22%
found: C 64.80; H 7.88%

*methyl-2,6β,7α-trihydroxy-19-benzyloxy-2,3-seco-5α-cholestan-3-oate 26,* 0.71 g (43%), m. p. 177.5—179.5 °C (chl./hexane); $[\alpha]_D^{19} = 0°$ (c = 0.67, chl.); IR (KBr): $\nu$ 3450, 3330, 3245, 3055, 1732, 1690, 1600, 1582, 1277, 1240, 1180, 1168, 1029, 712 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$ 0.68 (3H, s, H-18), 0.87 (6H, d, $J = 12$ Hz, H-26 and H-27), 2.32 (3H, m, $W_{1/2} = 25$ Hz, H-4 and H-5), 3.67 (3H, s, —$COOCH_3$), 3.73 (4H, m, $W_{1/2} = 15$ Hz, H-2, H-6 and H-7), 4.47 and 4.68 (2H, AB system, $J = 12$ Hz, H-19), 7.28—8.11 (5H, arom.).

*Anal.* $C_{35}H_{54}O_7$ (586.81) calc'd.: C 71.64; H 9.28%
found: C 71.87; H 9.10%.

*Methyl-2-hydroxy-2,3-seco-5α-cholest-6-en-3-oate* 27

Powdered zinc (5.41 g) was added to a solution of bromohydrin *25* (1.02 g; $1.6 \times 10^{-3}$ mole) in glacial acetic acid (27 ml) and water (1.2 ml) at 45—50 °C while the reaction mixture was vigorously stirred. After 40 min the reaction mixture was cooled to room temperature, the inorganic material filtered off and the filtrate evaporated *in vacuo*. The obtained oily residue was dissolved in the mixture of ether and chloroform (5 : 1) and washed with saturated sodium bicarbonate solution and water. The dried solution was evaporated *in vacuo* and the residue eluted through a short silica gel column to give *methyl-2-hydroxy--2,3-seco-5α-cholest-6-en-3-oate 27,* 0.62 g (72%), oil; $[\alpha]_D^{23} = -68.05°$ (c = 1.15, chl.); IR (film): $\nu$ 3500, 3055, 3015, 1735, 1720, 1640, 1600, 1585, 1272, 1178, 1112, 1022, 978, 712 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$ 0.66 (3H, s, H-18), 0.86 (6H, d, $J = 6$ Hz, H-26 and H-27), 0.89 (3H, d, $J = 6$ Hz, H-21), 2.81 (2H, m, $W_{1/2} = 20$ Hz, H-4), 3.66 (3H, s, —$COOCH_3$), 3.71 (2H, m, $W_{1/2} = 15$ Hz, H-2), 4.23 and 4.35 (2H, AB system, $J = 12$ Hz, H-19), 5.34 and 5.56 (2H, AB system, $J = 11.3$ Hz, H-6 and H-7), 7.28—8.08 (5H, arom.).

*28-Hydroxy-2-oxa-5α,10α-cholest-6-en-3-one* 4

A solution of potassium hydroxide (0.2 g KOH in 2 ml $H_2O$) was added to a suspension of *27* (0.54 g; $9.8 \times 10^{-4}$ mole) in methanol (3 ml) and the reaction mixture was left on a steam bath for 15 min and acidified with concentrated hydrochloric acid. The obtained suspension was extracted with ether and chloroform (5 : 1), the separated organic solution washed with saturated sodium bicarbonate solution and water, dried over anhydrous magnesium sulphate and evaporated *in vacuo*. Crystallization from chloroform and hexane gave *28-hydroxy--2-oxa-5α,10α-cholest-6-en-3-one 4,* 0.34 g (84%), m. p. 102—103.5 °C (chl./hexane); $[\alpha]_D^{18} = -78.16°$ (c = 0.77, chl.); IR (KBr): $\nu$ 3440, 3010, 1735, 1650, 1060 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$ 0.71 (3H, s, H-18), 0.86 (6H, d, $J = 6$ Hz, H-26 and H-27), 0.92 (3H, d, $J = 6$ Hz, H-21), 1.73 (2H, t, $J = 7.5$ Hz, H-19), 2.29 (1H, m, $W_{1/2} = 25$ Hz, H-5), 2.80 (2H, m, $W_{1/2} = 31.25$ Hz, H-4), 3.80 (2H, d, $J = 7.5$ Hz, H-28), 3.83 and 4.37 (2H, AB system, $J = 12$ Hz, H-1), 5.43 (1H, ddd, $J_{6,7} = 10$ Hz, $J_{6,5} = 1.2$ Hz, $J_{6,8} = 1$ Hz, H-6), 5.73 (1H, d, $J_{7,6} = 10$ Hz, H-7); $^{13}C$ NMR ($CDCl_3$): $\delta$ 172.9 (C-3), 132.0 and 129.0 (C-6 and C-7), 71.5 (C-1), 58.4 (C-28), 36.1 (C-22), 35.7 (C-20), 28.1 (C-16), 28.0 (C-24), 23.8 (C-23), 22.5 and 22.6 (C-26 and C-27), 18.7 (C-21), 11.9 (C-18).

*Anal.* $C_{27}H_{44}O_3$ (416.64) calc'd: C 77.84; H 10.64%
found: C 78.10; H 10.54%.

Acetylation of *4* with acetic anhydride in pyridine gave *28-acetoxy-2--oxa-5α,10α-cholest-6-en-3-one 30,* oil; IR (film): $\nu$ 3010, 1755, 1737, 1660, 1232, 1065 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$ 0.73 (3H, s, H-18), 0.89 (6H, d, $J = 6$ Hz, H-26

and H-27), 0.93 (3H, d, $J = 6$ Hz, H-21), 1.83 (2H, t, $J = 7.5$ Hz, H-19), 2.07 (3H, s, —$OCOCH_3$), 2.32 (1H, m, $W_{1/2} = 25$ Hz, H-5), 2.78 (2H, m, $W_{1/2} = 31.25$ Hz, H-4), 3.84 and 4.39 (2H, AB system, $J = 12$ Hz, H-1), 4.14 (2H, t, $J = 7.5$ Hz, H-28), 5.43 (1H, ddd, $J_{6,7} = 10$ Hz, $J_{6,5} = 1.2$ Hz, $J_{6,8} = 1$ Hz, H-6), 5.73 (1H, d, $J_{7,6} = 10$ Hz, H-7).

*6β,7α,28-Trihydroxy-2-oxa-5α,10α-cholestan-3-one* 31

δ-Lactone *31* was obtained in the same manner from triol *26* as *4* from *27*. *6β,7α,28-trihydroxy-2-oxa-5α,10α-cholestan-3-one 31*, 0.37 g, (74%), m. p. 193—195 °C (EtOAc); $[\alpha]_D^{19.5} = +17.35°$ (c = 0.70, chl.); IR (KBr): ν 3410, 1705, 1225, 1067, 1050, 1021, 986 $cm^{-1}$; $^1H$ NMR (acetone-$d_6$): δ 0.71 (3H, s, H-18), 0.86 (6H, d, $J = 6$ Hz, 2.81 (2H, m, $W_{1/2} = 26.85$ Hz, H-4), 3.64 (2H, d, $J = 7.5$ Hz, H-28), 3.74 (2H, d, $W_{1/2} = 12.5$ Hz, H-6 and H-7), 3.86 (1H, dd, $J_{gem} = 11.25$ Hz, $J = 2.5$ Hz, H-1α), 4.89 (1H, d, $J_{gem} = 11.25$ Hz, H-1β); $^{13}C$ NMR (aceton-$d_6$): δ 171.2 (C-3), 76.2 and 75.7 (C-6 and C-7), 71.4 (C-1), 57.2 (C-28), 36.7 (C-22), 35.9 (C-20), 24.1 (C-23), 23.1 and 22.8 (C-26 and C-27), 19.1 (C-21), 12.2 (C-18).

*Anal.* $C_{27}H_{46}O_5$ (450.66) calc'd: C 71.96; H 10.29%
found: C 72.46; H 10.53%.

Acetylation of *31* with acetic acid anhydride in pyridine gave *6β,7α,28-triacetoxy-2-oxa-5α,10α-cholestan-3-one 32*, oil; IR (KBr): ν 1755, 1735, 1265, 1234, 1210, 1060, 1032, 970 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 0.69 (3H, s, H-18), 0.86 (6H, d, $J = 6$ Hz, H-26 and H-27), 0.91 (3H, d, $J = 6$ Hz, H-21), 2.06 (3H, m, —$OCOCH_3$), 2.08 (3H, s, —$OCOCH_3$), 2.11 (3H, s, —$OCOCH_3$), 2.31 (1H, m, $W_{1/2} =$ Hz, H-5), 2.86 (2H, m, $W_{1/2} = 41.25$ Hz, H-4), 4.01 (1H, dd, $J_{gem} = 11.25$ Hz, $J = 2.5$ Hz, H-1α), 4.18 (2H, t, $J = 7.5$ Hz, H-28), 4.76 (1H, d, $J_{gem} = 11.25$ Hz, H-1β), 4.86 (1H, m, $W_{1/2} = 5.5$ Hz, H-7), 5.05 (1H, t, $J = 3.25$ Hz, H-6).

*28-o-nitrophenylseleno-2-oxa-5α,10α-cholest-6-en-3-one* 28

δ-Lactone *4* (0.15 g, $3.6 \times 10^{-4}$ mole) dissolved in dry tetrahydrofurane (2 ml) was treated with *o*-nitrophenyl selenocyanate (0.13 g; $5.7 \times 10^{-4}$ mole)[43] and tri-*n*-butylphosphine. When the reaction was over (determined by disappearance of the deep-red colour) the solution was evaporated *in vacuo* and the obtained oil was eluted through a short silica gel column. Crystallization from hexane afforded *28-o-nitrophenylseleno-2-oxa-5α,10α-cholest-6-en-3-one 28*, 0.18 g (90%), m. p. 105—106 °C (hexane); $[\alpha]_D^{20} = -15.55°$ (c = 0.86, acetone); IR KBr): ν 3010, 1750, 1720, 1690, 1582, 1560, 1503, 1335, 1297, 847, 782, 730 $cm^{-1}$; H NMR ($CDCl_3$): δ 0.74 (3H, s, H-18), 0.86 (6H, d, $J = 6$ Hz H-26 and H-27), 0.93 (3H, d, $J = 6$ Hz, H-21), 2.33 (1H, m, $W_{1/2} = 26.25$ Hz, H-5), 2.83 (4H, m, $W_{1/2} = 28.75$ Hz, H-4 and H-28), 3.84 and 4.41 (2H, AB system, $J = 12$ Hz, H-1), 5.48 (1H, ddd, $J_{6,7} = 10$ Hz, $J_{6,5} = 1.2$ Hz, $J_{6,8} = 1$ Hz, H-6), 5.82 (1H, d, $J_{7,6} = 10$ Hz, H-7).

*Anal.* $C_{33}H_{47}O_4NSe$ (600.70) calc'd.: C 65.98; H 7.89; N 2.33%
found: C 66.62; H 7.73; N 3.61%.

*2-Oxa-5α,10α-cholest-6,19-dien-3-one* 29

A solution of *28* (0.15 g; $2.5 \times 10^{-4}$ mole) in tetrahydrofurane (2 ml) was cooled to 0 °C and treated with 30% hydrogen peroxide (1 ml). The reaction mixture was left overnight at room temperature, extracted with ethyl acetate and washed with saturated sodium bicarbonate solution and water. The dried solution was evaporated *in vacuo* and the resulting oil crystallized from methanol to give *2-oxa-5α,10α-cholest-6,19-dien-3-one 29*, 0.091 g (91%), m. p. 84—85 °C (MeOH); $[\alpha]_D^{25} = -87.70°$ (c = 0.61, chl.); IR (KBr): ν 3070, 3010, 1750, 1725, 1712, 1690, 1627, 1280, 1205, 1181, 1147, 1052, 1031, 1007, 920, 729, 700 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 0.71 (3H, s, H-18), 0.88 (6H, d, $J = 6$ Hz, H-26 and H-27), 0.91 (3H, d, $J = 6$ Hz, H-21), 2.56 (3H, m, $W_{1/2} = 50$ Hz, H-4 and H-5), 4.39 (2H, s, H-1), 5.14 (1H, dd, $J_{28_B,19}=10$ Hz, $J_{28_B,28_A}=2.5$ Hz, H-28$_B$), 5.43 (1H, dd, $J_{28_A,19}=15$ Hz, $J_{28_A,28_B}=2.5$ Hz, H-28), 5.49 (1H, ddd, $J_{6,7} = 10$ Hz, $J_{6,5} = 1.2$ Hz $J_{6,8} = 1$ Hz, H-6), 5.66 (1H, d, $J_{6,7} = 10$ Hz, H-7), 5.68 (1H, dd, $J_{19,28_A} = 15$ Hz, $J_{19,28_B} = 10$ Hz, H-19).

*Anal.* $C_{27}H_{42}O_2$ (398.63) calc'd: C 18.35; H 10.62%
found: C 81.53; H 10.23%.

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## IZVOD

**Steroidni analozi deoksivernolepina. Sinteza δ-laktonskog ključnog intermedijera**

*Bogdan Šolaja i Milutin Stefanović*

Seskviterpenski laktoni elemanolidnog tipa vernolepin *1* i deoksivernolepin *2* pokazuju izraženu antitumorsku aktivnost protiv Walker-ovog intramuskularnog karcinosarkoma 256 i CCRF — CEM humanih limfoblastičnih ćelija leukemije u kulturi i stoga su bili predmet mnogih parcijalnih i totalnih sinteza.

Zbog značajnog aktineoplastičnog (antitumorskog) dejstva seksviterpenskih laktona sa α-metilenskom funkcijom na γ- i δ-laktonskom prstenu sintetizovan je polazeći od holesterola, steroidni analog deoksivernolepina *3*, odnosno ključni intermedijer u njegovoj sintezi 28-hidroksi-2-oksa-5α,10α-holest-6-en-3-on(4).

U sintezi su primenjene poznate reakcije, neke su modifikovane, a upotrebljena je i nova reakcija za dobivanje dimetil-acetala pomoću metanola i piridinijum-hlorohromata. Ovim reagensom mogu se reakcije acetalizacije vršiti u prisustvu osetljivih funkcionalnih grupa kao što je epoksidna grupa.