Periodate Oxidation of the Salsoloside (II). The glycoside (100 mg) was oxidized in 30 ml of 1% sodium periodate solution. After hydrolysis, no free sugars were detected among the oxidation products.

SUMMARY

New triterpene glycosides — salsolosides C and D, which form a pair of bisdesmosidic glycosides — have been isolated from the epigeal part of *Salsola micranthera* Botsch. (family Chenopodiaceae).

Salsoloside C has the structure of oleanolic acid 28-O-β-D-glucopyranoside 3-O-[O-β-D-xylopyranosyl-(1 → 4)-β-D-glucuronopyranoside], and salsoloside D is hederagenin 28-O-β-D-glucopyranoside 3-O-[O-β-D-xylopyranosyl-(1 → 4)-β-D-glucuronopyranoside].

LITERATURE CITED

1. Ch. Annaev, M. Isamukhamedova, and N. K. Abubakirov, Khim. Prir. Soedin., 202 (1983).
2. T. T. Gorovits, Khim. Prir. Soedin., 263 (1970).
3. S. Kasprzyk and Z. Wojeichowski, Phytochemistry, 6, 69 (1967).
4. M. Patkhullaeva, L. G. Mzhel'skaya, and N. K. Abubakirov, Khim. Prir. Soedin., 466 (1972).
5. S. Hakomori, J. Biochem. (Tokyo), 55, 205 (1964).
6. T. G. Bonner, Chem. Ind. (London), 345 (1960).
7. W. Klyne, Biochem. J., 47, xli (1950).
8. J. M. Van der Veen, J. Org. Chem., 28, 564 (1963).
9. Ch. Annaev, M. Isamukhamedova, and N. K. Abubakirov, Khim. Prir. Soedin., 169 (1982).

TRANSFORMED STEROIDS.

133. SYNTHESIS OF 20-DEOXYSTEROIDS WITH A TETRAHYDROPYRAN RING E

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The synthesis of 20-deoxy compounds — the precursors of the steroid pyranols and pyranones synthesized by the authors previously — has been effected from a steroid 20-ketotetrahydropyran by the hydrogenolysis of the corresponding ethylene dithioketal with Raney nickel. The ^{1}H and ^{13}C NMR spectra have been studied in detail. Transformations of rings A and B via the epoxide or the 3,5α-cyclosteroid have led to 3-acetoxy-16β,23-epoxy-5αH-21,24-dinorchol-5-en-6-one and 3-acetoxy-5α-hydroxy-16β,23-epoxy-21,24-dinorchol-5-en-6-one.

It is proposed [1] to correlate the degree of the inhibitory action of steroid aglycones on Na^+,K^+-dependent ATPase with the position in space of the 23-carbonyl group. At the same time, we have shown previously [2] that a number of steroids bearing a carbonyl group in a different position or having a hydroxy or acetate function in place of it also exhibit ATPase-inhibiting properties. This induced us to undertake the synthesis of steroid E-tetrahydropyrans having no oxygen functions in ring E.

The initial compound for this purpose was the 20-ketotetrahydropyran (I) [3], the carbonyl group in which can be eliminated either through the tosylhydrazone by reduction with $NaBH_4$ [4] or by desulfurizing the corresponding ethylene dithioketal [5]. The reduction of the tosylhydrazone (Ia) took place with low yield and led only to a mixture of products. The ethylene dithioketal (II) was obtained with high yield by treating (I) with ethanedithiol in the presence of perchloric acid. The prolonged boiling of (II) in absolute ethanol in the presence of Raney nickel previously saturated with hydrogen led, again with a high yield, to the 20-deoxy compound (III). The tetrahydropyranyl steroid (III) is the parent compound of

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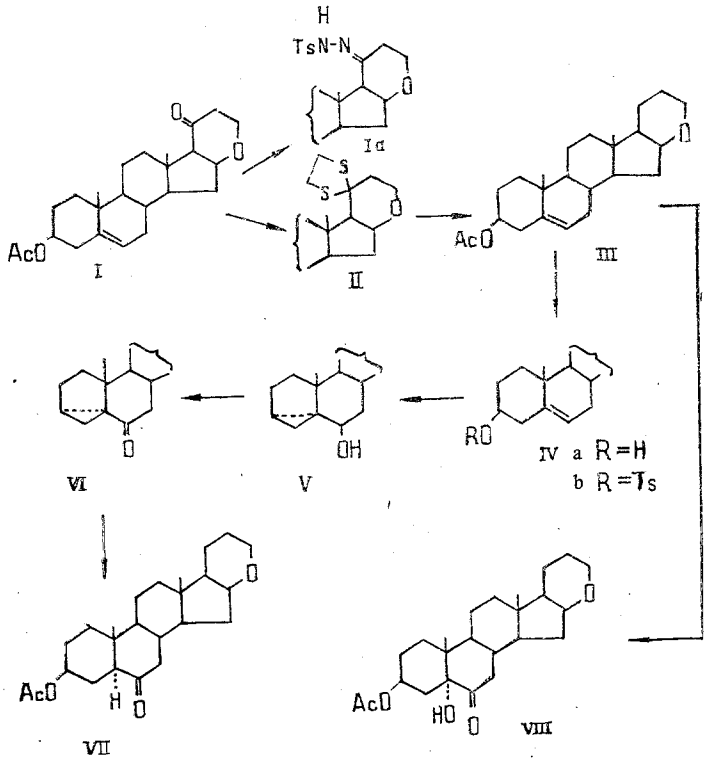
a homologous series of substituted pyrones and pyranols which have been synthesized previously and we therefore studied its physicochemical properties, including its ^{1}H and ^{13}C NMR spectra, in detail. To study the influence of the addition of tetrahydropyran ring E on the conformation of the steroid skeleton, the results of these spectra (III) were compared with those for acetate of 3β-hydroxyandrost-5-en-17-one. The close values of the chemical shifts (CSs) (δ, ppm) of these compounds permitted the conclusion that the introduction of the tetrahydropyran ring E into the steroid molecule does not lead to appreciable deformations of rings A, B, and C. The small effect of ring E in relation to the CSs of C^{12} and C^{14} confirms its 17(20)β-16-(O)β orientation [6]. In its turn, the influence of steroid skeleton on the CSs of the carbon atoms of the tetrahydropyran ring led to a displacement of the C^{16}, C^{17}, C^{20}, C^{22}, and C^{23} signals by +9.8, +22.0, −4.1, −3.5, and −1.7 ppm, respectively, relative to tetrahydropyran [7].



The transformations of rings A/B in (III) was carried out by two methods. The first of them consisted in the saponification of the 3-acetoxy group, the tosylation of (IVa) with passage to (IVb), the conversion of the latter by boiling with $KHCO_3$ in acetone into the 6-hydroxy-3,5α-cyclosteroid (V), and subsequent oxidation to the 6-ketone (VI). The opening of the cyclopropane ring in acetic and sulfuric acids led to the 3β-acetoxy-5α(H)-6-ketosteroid (VII). In the PMR spectrum of (VII), the CS from the 19-CH_3 group (δ 19-CH_3, ppm) is in a higher field than the CS of the 6-deoxy compound (III), which agrees with information in the literature [9].

The 5α-hydroxy analog (VIII) was obtained by a method described previously via the 5,6α-epoxide and its hydrolysis, and oxidation with the complex CrO_3•Py. The CD spectra of (VII) [λ_{max} 297 nm, Δε −1.67; λ_{max} 291 nm, Δε −1.59] and of (VIII) [λ_{max} 316 nm, Δε −1.67; λ_{max} 307 nm, Δε −1.75] confirm the trans-linkage of rings A/B [9, 10].

Compounds (III), (VII), and (VIII) have been sent for biological trials.

EXPERIMENTAL

Melting points were determined on a Kofler block. IR spectra were taken on a UR-20 instrument in KBr or $CHCl_3$, NMR spectra on a Tesla-BS497HA-100 spectrometer, and ^{13}C NMR spectra on a Bruker M-250 spectrometer with a working frequency of 62.89 MHz in $CDCl_3$, chemical

shifts (CSs) ±0.03 ppm being measured relative to TMS as internal standard. CD spectra were taken on a Jobin Yvon Dichrographe-3 instrument in CH_3CN, concentration 1 mg/ml, 20-23°C, cell length 0.1 cm.

The mixtures were separated on columns of SiO_2 (40/100 μ) under a pressure of nitrogen. For TLC we used plates with SiO_2 (5/40 μ + 13% of gypsum).

3β-Acetoxy-16β,23-epoxy-21,24-dinorchol-5-ene (III). A solution of 1.1 g of (I) in 20 ml of ethane-1,2-diol was treated with three drops of 68% $HClO_4$ and the mixture was stirred at 20°C for 20 h. Then it was diluted with ether and was washed successively with 2N NaOH (until the odor had disappeared) and with water and was dried with $MgSO_4$. After evaporation, 1 g (yield 76%) of the dithioketal (II) was obtained with R_f 0.5 [ether–heptane (1:1)]. IR spectrum ($\nu_{max}^{CHCl_3}$, cm^{-1}): 1030, 1260, 1730. $C_{26}H_{38}O_3S_2$. Mass spectrum (m/z): 402 ($M^+ - 60$), 374, 341, 309 ($M^+ - 60-93$).

Without additional purification, a solution of 980 mg of (II) in 20 ml of absolute dioxane was boiled for 20 h with 10 g of Raney nickel that had previously been saturated with H_2. After the end of the reaction (TLC), the mixture was filtered hot through Celite, the solvent was evaporated off, with cyclohexane, and after crystallization of the residue from hexane–ether, 530 mg (66.6%) of (III) was obtained with mp 167-171°C. IR spectra ($\nu_{max}^{CHCl_3}$, cm^{-1}): 1260, 1725. $C_{24}H_{36}O_3$. Mass spectrum (m/z): 372 (M^+), 312 ($M^+ - 60$), 297 ($M^+ - 60-15$). PMR spectrum (δ, ppm): 0.91 s, 1.06 s (6 H, 18-CH_3, 19-CH_3); 2.02 s (3 H, acetate); 3.38 m (1 H, 16-H); 3.93 m (2 H, OCH_2); 4.60 m (1 H, 3-H); 5.40 m (1 H, 6-H). ^{13}C NMR spectrum ($J_{^{13}C-H}$, Hz): C^1–37.1 (126); C^2–27.9 (128); C^3 – 73.9 (148); C^4 – 38.2 (128); C^5 – 139.8; C^6 – 122.4 (153); C^7 – 32.0 (124); C^8 – 31.5 (126); C^9 – 50.7 (120); C^{10} – 36.9; C^{11} – 20.5 (122); C^{12} – 38.0 (129); C^{13} – 42.3; C^{14} – 53.6 (119); C^{15} – 34.4 (126); C^{16} – 77.8 (147); C^{17} – 48.6 (125); C^{18} – 15.2 (125); C^{19} – 19.3; C^{20} – 19.5 (126); C^{22} – 23.1 (126); C^{23} – 66.3 (136; 144); 3-OAc – 21.3 (129).

Synthesis of the Tosylhydrazone (Ia). A mixture consisting of 300 mg of (I), 450 mg of tosylhydrazine, and glacial AcOH was kept at 20°C for 48 h. Then it was treated with water and extracted with EtOAc, and the extract was washed with $KHCO_3$ solution and with water, dried with $MgSO_4$, and evaporated. Crystallization of the residue from absolute CH_3OH yielded 370 mg (86%) of (Ia) with mp 211.5-212.5°C. Mass spectrum (m/z): 494 ($M^+ - 60$).

3β-Acetoxy-16β,23-epoxy-21,24-dinor-5α-cholan-6-one (VII). A solution of 530 mg of (III) in 50 ml of CH_3OH was treated with 1 ml of a 10% solution of K_2CO_3 in CH_3OH–water (1:1), and the mixture was left at 20°C for 18 h. Then it was neutralized with 2% HCl, the solvent was evaporated off, the residue was extracted with $CHCl_3$, and the extract was dried with $MgSO_4$ and evaporated, which led to 470 mg (99%) of the 3-hydroxy compound (IVa), R_f 0.63 (ether). IR spectrum (ν_{max}^{KBr}, cm^{-1}): 3460. $C_{22}H_{34}O_2$. Mass spectrum (m/z): 330 (M^+), 312 ($M^+ - 18$), 297 ($M^+ - 18-15$). With cooling, 560 mg of TsCl was added to a solution of 470 mg of (IVa) in 6 ml of pyridine, and the mixture was left at +4°C for 48 h. Then it was diluted with water and extracted with $CHCl_3$, and the extract was washed with 2% HCl to pH 7, the solvent was evaporated off, and the residue was washed with a mixture of methanol and hexane. This gave 590 mg (88%) of (IVb) R_f 0.89 (ether). IR spectrum ($\nu_{max}^{CHCl_3}$, cm^{-1}): 1180, 1190, 1600. $C_{29}H_{40}O_4S$. Mass spectrum (m/z): 312 ($M^+ - 172$), 172.

A solution of 550 mg of (IVb) in 50 ml of acetone was treated with 350 mg of $KHCO_3$ and 6 ml of water. The mixture was boiled for 6 h (TLC), the solvent was evaporated off partially, the residue was extracted with EtOAc, and the extract was washed with water to pH 7 and dried with $MgSO_4$. After the solvent had been evaporated off and the residue had been subjected to chromatographic purification on SiO_2 with elution by the ether–hexane (3:1) system, 270 mg (72%) of (V) was isolated with R_f 0.50 [ether–hexane (4:1)]. IR spectrum ($\nu_{max}^{CHCl_3}$, cm^{-1}): 1380, 3610. $C_{22}H_{34}O_2$. Mass spectrum (m/z): 330 (M^+), 315 ($M^+ - 15$), 297 ($M^+ - 15-18$).

Without additional purification (V) was oxidized with the CrO_3•Py complex. To a mixture of 550 mg of dry CrO_3 and 7 ml of pyridine (after it had been stirred at 0°C for 3 h) was added 250 mg of (V) in 5 ml of pyridine, and stirring was carried out at 20°C for another 2 h and the mixture was then left at 20°C for 18 h. After this, it was diluted with water and extracted with EtOAc. The extract was washed with $KHCO_3$ solution, with 2% HCl, and with water to pH 7. After drying with $MgSO_4$, evaporation of the solvent, and chromatographic purification on SiO_2 in the ether–hexane (1:3) system, 180 mg (72%) of (VI) was obtained with R_f 0.71 [ether–hexane (4:1)]. $C_{22}H_{32}O_2$, mass spectrum (m/z): 328 (M^+), 310 ($M^+ - 18$), 295 ($M^+ - 18-15$).

A solution of 140 mg of (VI) in 14 ml of AcOH (glacial) was treated with 0.4 ml of concentrated H_2SO_4 and the mixture was left at 20°C for 18 h. Then it was diluted with water and extracted with EtOAc and the extract was washed with water and dried with $MgSO_4$; after evaporation of the solvents and recrystallization of the residue from ether, 120 mg (70%) of the 3-acetate 6-ketone (VII) was obtained with mp 195-197°C. IR spectrum (ν_{max}^{KBr}, cm^{-1}): 1240, 1708, 1735. $C_{24}H_{36}O_4$. Mass spectrum (m/z): 388 (M^+), 328 ($M^+ - 60$), 313 ($M^+ - 60-15$). PMR spectrum (δ, ppm): 0.8 s (3 H, 19-CH_3); 0.89 s (3 H, 18-CH_3); 2.02 s (3 H, acetate); 3.34 m (1 H, 16-H); 3.82-3.99 m (2 H, OCH_2); 4.69 m (1 H, 3-H).

3β-Acetoxy-5α-hydroxy-16β,23-epoxy-21,24-dinorcholan-6-one (VIII). A solution of 140 mg of (III) in 10 ml of CH_2Cl_2 was treated with 210 mg of chloroperbenzoic acid. After 24 h, the mixture was treated successively with 10% Na_2SO_3 solution, $NaHCO_3$, water, and NaCl and was extracted with $CHCl_3$, and the extract was dried with $MgSO_4$ and evaporated. The residue was dissolved in 5 ml of dioxane, and the solution was treated with 0.09 ml of 68% $HClO_4$ solution and 0.09 ml of water. After 1.5 h, water was added and the mixture was extracted with EtOAc and the extract was dried with $MgSO_4$ and evaporated. The resulting diol (140 mg) was oxidized in 3 ml of pyridine with a mixture of 250 mg of CrO_3 and 4 ml of pyridine under the conditions described for (IVb). After treatment with water and extraction with EtOAc and treatment of the mixture so obtained by chromatography on a column of SiO_2 with the ether–heptane (1.5:1) system, 50 mg of (VIII) was isolated with mp 215-217°C (from hexane–ether). IR spectrum ($\nu_{max}^{CHCl_3}$, cm^{-1}): 1280, 1710, 1720, 3580. $C_{24}H_{36}O_5$. Mass spectrum (m/z): 404 (M^+), 344 ($M^+ - 60$), 329 ($M^+ - 60-15$), 326 ($M^+ - 60-18$). PMR spectrum (δ, ppm): 0.82, 0.84 s (6 H, 18-CH_3, 19-CH_3); 1.98 s (3 H, acetate); 3.33 m (1 H, 16-H); 3.84 m (2 H, OCH_2); 5.04 m (1 H, 3-H).

SUMMARY

The synthesis of 3-acetoxy-16β,23-epoxy-5αH-21,24-dinorchol-5-en-6-one and of 3-acetoxy-5α-hydroxy-16β,23-epoxy-21,24-dinorcholan-6-one — 20-deoxysteroids with a tetrahydropyran rings E — has been effected and their physicochemical properties have been studied.

LITERATURE CITED

1. D. C. Rohrer, D. F. Fullerton, K. Yoshioka, A. H. From, and K. Ahmed, ACS Symp. Ser., No. 112, 259 (1979).
2. A. V. Kamernitskii, I. G. Reshetova, N. M. Mirsalikhova, and F. T. Umarova, Biokhimiya, 47, No. 6, 957 (1982).
3. A. A. Akhrem, A. V. Kamernitskii, I. G. Reshetova, and K. Yu. Chernyuk, Izv. Akad. Nauk SSSR, Ser. Khim., 1633 (1973).
4. R. O. Hutchins and N. R. Natale, J. Org. Chem., 43, 2299 (1978).
5. G. R. Pettit and W. J. Bowyer, J. Org. Chem., 25, 84 (1960).
6. I. W. Blunt and I. B. Stothers, Org. Magn. Reson., 9, 439 (1977).
7. I. B. Lambert, D. S. Netzel, H. Sun, and K. K. Lilianstrom, J. Am. Chem. Soc., 98, 3778 (1976).
8. A. V. Kamernitskii, V. G. Levi, and I. G. Reshetova, Izv. Akad. Nauk SSSR, Ser. Khim., 887 (1981).
9. G. Cleve and G. A. Hoyer, Tetrahedron, 28, 2637 (1972).
10. J. R. Bull and P. R. Enslin, Tetrahedron, 26, 1525 (1970).