SUPERACID CYCLIZATION OF ESTERS OF SOME BISHOMOISOPRENOID ACIDS

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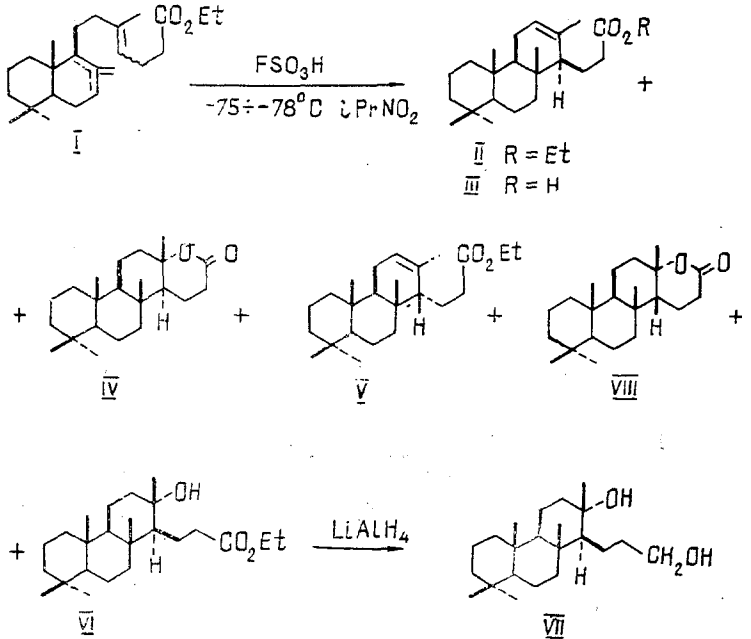
It is shown that on the superacid cyclization of esters of bishomobicyclogeranylgeranic and E,E-bishomofarnesic acids fully cyclized hydroxyesters are formed in good yield, while on the interaction of esters of 6-hydroxy- and 6-acyloxy-15-bishomobicyclogeranylgeranic acids with a superacid no carbocyclization takes place.

We have shown previously [1] that on the superacid cyclization of homo- and bishomoisoprenoid acids the corresponding γ- and δ-lactones are formed in good yield. For comparison, it was of interest to investigate the behavior of esters of the above-mentioned aicds in a superacid medium. In the present communication we give the results of the superacid cyclization of esters of bishomobicyclogeranylgeranic acids, including those with hydroxy and acyloxy groups at C-6, and of bishomofarnesic acid.

Initially, as the substrate we used a readily available mixture of esters of isomeric bishomobicyclogeranylgeranic acids (I) obtained by a procedure described previously [2].

The superacid cyclization of the ester mixture (I) in 2-nitropropane led to a mixture of products, which was separated by chromatography on a column of silica gel into three fractions. The least polar of them consisted of a mixture (3:1) of two substances (according to GLC). Rechromatography of this fraction on silica gel impregnated with silver nitrate [3] permitted the isolation of only the predominating component (II) in the pure form (Scheme 1). Its structure followed from its spectral characteristics (see the Experimental part). The β-orientation of the side-chain of the ester under investigation at C-14 was shown by the fact that the acid (II) obtained by its alkaline saponification was cyclized by fluorosulfonic acid into the known lactone (IV) [2]. The second component of this fraction apparently consisted of the epimeric ester (V), since the initial mixture of estes (I) also contained the ester with the 13Z-configuration (see [2]), although its structure had not been definitively shown.



Scheme 1

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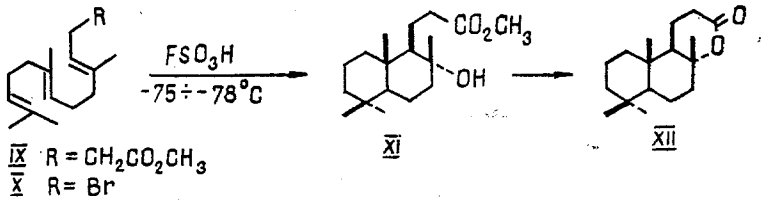
The second fraction with respect to polarity eluted from the silica gel column was crystallized from petroleum ether, giving the crystalline hydroxyester (VI) (scheme 1). Its structure followed from its spectral characteristics (see the Experimental part). The structure and stereochemistry of the hydroxyester (VI) were definitively confirmed by the fact that its hydride reduction led to the known diol (VII) [2].

The most polar fraction eluted from the column consisted of a mixture (~4:1) of the known lactones (IV) and (VIII). They were identified by comparison with authentic specimens [2].

Thus, on the superacid cyclization of a mixture of isomeric esters of bishomobicyclogeranylgeranic acid (I), a mixture of substances with bishomoagathane structures containing the unsaturated esters (II) and (III), the hydroxyester (VI) and the δ-lactones (IV) and (VIII) was formed, i.e., the reaction was structurally selective. It is possible that lactones (IV) and (VIII) were products of the intramolecular transesterification of the hydroxyester (VI) and of its epimer, the latter of which we did not observe among the reaction products.

Thus, among the products of the cyclization of the mixture of esters (I) there were not only unsaturated tricyclic compounds but also the products of their hydration and subsequent transformation.



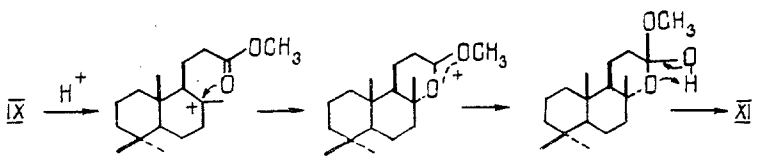
Scheme 2

In order to elucidate the course of the reaction in the superacid cyclization of aliphatic bishomoesters, we investigated the process of cyclization of an ester of E,E-bishomofarnesic acid (IX) (scheme 2), which was synthesized from E,E-farnesyl bromide (X). The latter reacted with malonic ester under conditions of phase-transfer catalysis [4], giving the corresponding diester, which, on subsequent alkaline saponification, decarboxylation, and methylation with diazomethane was converted into the methyl ester of E,E-bishomofarnesic acid (IX), the structure of which was confirmed by its spectral characteristics.

The superacid cyclization of the methyl ester (IX) in 2-nitropropane at −75 to −78°C with a ratio of the substrate to the cyclizing agent of 1:5 and a reaction time of 40 min led to a single reaction product – the hydroxyester (IX) (yield 75%), the structure and stereochemistry of which followed from the totality of its spectral characteristics and from its alkaline saponification into (±)-ambrenolide (XII), which was identified by comparison with a specimen of it that we had obtained previously [1]. On the basis of these facts the product of the cyclization of ester (IX) was ascribed the structure and stereochemistry represented by formula (XI).

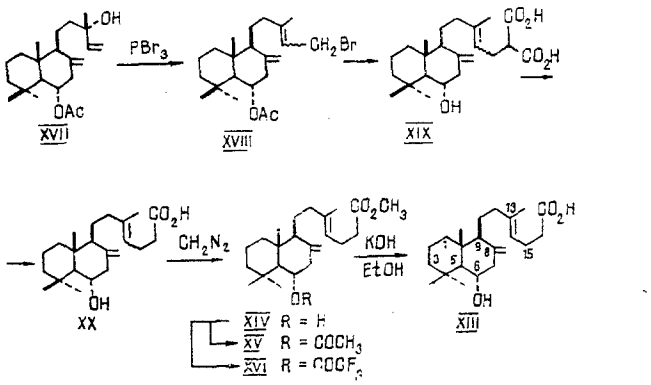
Thus, on the superacid cyclization of the aliphatic bishomoisoprenoid ester (IX) the fully cyclized bifunctionalized hydroxyester (XI) was formed. The reaction was structurally selective and stereospecific. The formation of the hydroxyester may be represented by Scheme 3.

In view of the favorable results that we obtained above, with the aim of synthesizing 15-bishomoisoagathane compounds with functional groups at C-6, C-13, and C-16 that could serve as the initial substances for passage to polyfunctionalized cheilanthane sesterterpenoids, we



Scheme 3

have made a detailed study of the superacid cyclization of (13E)-6α-hydroxy-15-bishomobicyclogeranylgeranic acid (XIII) and its esters (XIV-XVI), which we synthesized from the readily accessible labdane diterpenoid larixyl acetate (XVII) [5] by Scheme 4.

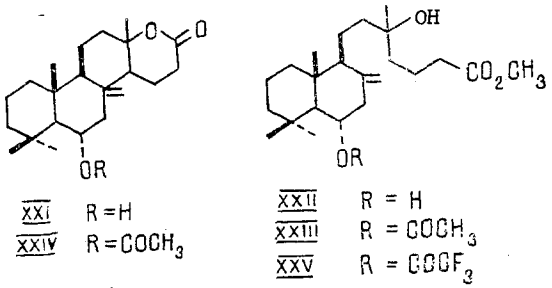


Scheme 4

The mixture of isomeric acetoxybromides (XVIII) obtained from larixyl acetate (XVII) by the procedure of [6] was converted by reaction with malonic ester in the presence of a phase-transfer catalyst [4] into a mixture of diesters, which was saponified by alkali without purification to the mixture of hydroxyadiacids (XIX), and these were decarboxylated by boiling in pyridine to form the mixture of hydroxyacids (XX). The latter was methylated with diazomethane. By crystallizing the resulting mixture of hydroxydiesters we isolated the predominating (13E)-hydroxyester (XIV). Its yield, calculated on the larixyl acetate (XVII), amounted to ~33%. It was impossible to isolate the 13Z-hydroxyester in the pure form. The structure of the hydroxyester (XIV) was confirmed by the results of elementary analysis and of IR and PMR spectroscopy (see the Experimental part).

The 13E-configuration of the hydroxyester (XIV) followed from the fact that when tertiary allyl alcohols are brominated with phosphorus tribromide the trans-bromide predomiantes [7], and it was confirmed by the subsequent transformations of compound (XIV).

The other substances required for cyclization were synthesized from the hydroxyester (XIV): the 6α-acetoxyester (XV) – by its acetylation with a mixture of acetic anhydride and pyridine under standard conditions; and its 6α-trifluoroacetoxy analog (XVI) by acylation with trifluoroacetic anhydride in pyridine at −30°C. it was impossible to obtain the diester (XVI) at a higher temperature because of the resinification of the reaction products. The hydroxyacid (XIII) was obtained by the alkaline saponification of the hydroxyester (XIV). The structures of compounds (XIII–XVI) were confirmed by their IR and PMR spectra.



On interaction of the hydroxyacid (XIII) with fluorosulfonic acid, the sole reaction product proved to be the bicarbocyclic 6α-hydroxy-δ-lactone (XXI), the structure of which followed from its spectral characteristics (see the Experimental part). Thus, in the reaction of hydroxyacid (XIII) with fluorosulfonic acid only the protonation of the double bond in the side-chain had taken place, with the subsequent closure of the δ-lactone ring. The double bond in ring B did not react. The reason for this is, apparently, that the fluorosulfonic acid initially protonated the hydroxy group at C-6 with the formation of an oxonium cation that then prevented the protonation of the exocyclic double bond, since this would have given rise to a carbocationic center at C-8 located in a 1,4-position with respect to the oxonium cation.

The presence of two close positively charged centers in a molecule is energetically unfavorable because of their mutual repulsion, and this prevented the protonation of the exocyclic double bond. We may note that attention has previously been drawn to this factor by Barkhash et al. [8].

A similar situation arose in the reaction of the hydroxyester (XIV) with fluorosulfonic acid. Here, the reaction product was a mixture of the hydroxylactone (XXI) and the hydroxyester (XXII). The structure of the latter followed from its spectral characteristics (see the Experimental).

We also investigated the reactions of the esters (XV) and (XVI) with fluorosulfonic acid, considering that on the introduction of an acyl group and, in particular, the electronegative trifluoroacetyl group, the ester oxygen would be protonated with greater difficulty than the exocyclic double bond.

However, the interaction of the acetoxyester (XV) with fluorosulfonic acid formed a mixture (3:1) of the hydroxyester (XXIII) and the acetoxy-δ-lactone (XXIV). Their structures were shown spectrally and, in particular, by a comparison of their spectral characteristics with those of the corresponding dihydroxyester (XXII) and hydroxylactone (XXI). The trifluoroacetoxy ester (XVI) reacted with fluorosulfonic acid to form the hydroxydiester (XXV); i.e., in this case only hydration of the double bond in the side-chain had taken place. The structure of compound (XXV) followed from its spectral characteristics and from the formation of the hydroxylactone (XXI) on its saponification and lactonization.

It follows from the facts given above that, in the reactions of 6α-hydroxy- or 6α-acyloxy-(13E)-15-bishomobicyclogeranylgeranic acids and their esters with a superacid, hydration of the double bond in the side-chain occurs, with the formation of hydroxyesters or δ-lactones, while there is no protonation of the homoallyl double bond in ring B and, consequently, no tricarbocyclic compounds are formed. Thus, it is impossible to obtain by this method tricyclic synthons functionalized at C-6 and suitable for the synthesis of natural cheilanthane sesterterpenoids.

EXPERIMENTAL

Melting points were determined on a Boëtius heated stage. Specific rotations were measured in $CHCl_3$ on a SM polarimeter. IR spectra were recorded on a Specord 74 IR instrument in CCl_4, and PMR spectra on Tesla BS-476 (60 MHz) and Bruker AC-80 (80 Mz) spectrometers in CCl_4. The signals are given on the δ scale, with tetramethylsilane as internal standard. GLC analysis was conducted on a Chrom-5 chromatograph with a flame-ionization detector and a 3 × 1500 mm glass column containing as the stationary phase 5% of SE-30 on Chromaton N-AW-DCMS, with the carrier gas helium at the rate of 45 ml/min, t_{col} 210°C, $t_{evaporator}$ 250°C.

Superacid Cyclization of the Mixture of Ethyl Esters (I). With stirring, a solution of 5 g of the mixture of isomeric esters (I) [2] in 20 ml of 2-nitropropane cooled to −65°C was added to a solution of 1.67 g of fluorosulfonic acid in 6 ml of 2-nitropropane cooled to −(75-78)°C. The reaction mixture was stirred for 5 min, and then it was frozen with liquid nitrogen and on thawing it was poured into a 20% solution of KOH. The mixture was worked up in the usual way, to give 4.84 g of reaction product, which was chromatographed on a column containing 100 g of SiO_2. A mixture of petroleum ether and ethyl acetate (19:1) eluted fraction 1 (1.64 g), which consisted of a mixture (~3:1) of the unsaturated esters (II) and (V). A 9:1 mixture of the same solvents eluted the crystalline fraction 2 (1.75 g). Then a 17:3 mixture of the same solvents eluted crystalline fraction 3 (0.68 g).

Ethyl Bishomoagath-12-en-17-oate (II). Fraction 1 (1.64 g) was rechromatographed on a column containing 20 g of $SiO_2/AgNO_3$. A mixture of petroleum ether and ethyl acetate (99:1) eluted 1.12 g of a mixture of the esters (II) and (V). Then the same solvent eluted 0.46 g of ethyl bishomoagath-12-en-17-oate (II) as a colorless viscous liquid: $[\alpha]_D^{22}$ −10.2° (c 1.2). IR spectrum (cm^{-1}): 1725 ($CO_2C_2H_5$), 840, 1660 (>C=C<$_H$), 1362, 1375 [$C(CH_3)_2$], PMR spectrum (ppm): 0.84 (s, 3H), 0.87 (s, 6H), 0.94 (s, 3H) ($4CH_3$ at C-4, C-8 and C-10), 1.25 (t, J = 7 Hz, 3H, $\underline{CH_3}CH_2O$−), 1.56 (s, 3H, CH_3 at C-13), 4.10 (q; J = 7 Hz, 2H, $O\underline{CH_2}CH_3$), 5.38 (br.s, 1H, H at C-12). Found %: C 79.88; H 11.27. $C_{24}H_{40}O_2$. Calculated %: C 79.94; H 11.18.

The Hydroxyester (VI). Fraction 2 (1.75 g), was crystallized from petroleum ether, to give 0.8 g of an individual compound (VI): mp 220-222°C; $[\alpha]_D^{22}$ −12.4° (c 1.7). IR spectrum (cm^{-1}): 1720 ($CO_2CH_2CH_3$), 1155, 3470, 3600 (OH group), 1362, 1373 [$C(CH_3)_2$]. PMR spectrum (ppm): 0.81 (s, 3H), 0.87 (s, 6H), 0.93 (s, 3H) (4 CH_3 at C-4, C-8 and C-10), 1.14 (s, 3H,

CH_3 at C-13), 1.28 (t, J = 7 Hz, 3H, $\underline{CH_3}CH_2O$–), 4.07 (s, J = 7 Hz, 2H, $\underline{CH_2}CH_3$). Found %: C 75.92; H 11.33. $C_{24}H_{40}O_3$. Calculated %: C 76.14; H 11.18.

Reduction of the Hydroxyester (VI). A solution of 65 mg of the hydroxyester (VI) in 5 ml of abs. THF was treated with 55 mg of $LiAlH_4$, and the reaction mixture was boiled under reflux for 30 min. Then it was worked up in the usual way, to give 47 mg (86%) of the diol (VII): mp 165-167°C (from diethyl ether), identical in its chromatographic and spectral properties with an authentic specimen [2].

Lactone (IV). a) Fraction 2 (0.68 g) was recrystallized from petroleum ether, giving 0.36 g of the lactone (IV): mp 132-133°C, identical with an authentic specimen [2].

b) A solution of 40 mg of the ester (II) in 0.5 ml of ethanol was treated with 2 ml of 10% caustic soda solution, and the mixture was boiled under reflux for 1 h. It was then worked up, giving 28 mg of the acid (III). This was dissolved in 0.5 ml of 2-nitropropane and the solution was cooled to −65°C and was added to a solution of 45 mg of FSO_3H in 0.8 ml of 2-nitropropane cooled to the same temperature. The reaction mixture was stirred for 15 min, and to it was added 3 ml of a 20% solution of KOH. The mixture was worked up in the usual way, to give 20 mg of the crystalline lactone (IV): mp 131-132.5°C (from petroleum ether), identical with an authentic specimen [2].

Synthesis of Methyl E,E-Bishomofarnesate (IX). With stirring, a solution of 2.8 g of E,E-farnesyl bromide (X) in 0.5 ml of DMFA, 0.9 ml of acetone, and 45 mg of benzyltriethylammonium chloride were added to a suspension of 0.7 g of K_2CO_3 in 0.6 ml of malonic ester. The mixture was stirred at 75-78°C for 8 h and was worked up in the usual way, and then the reaction product (2.6 g) was boiled with a solution of 0.5 g of KOH in 10 ml of ethanol for 2 h. After the usual working up, the new reaction product (2.1 g) was dissolved in 10 ml of dry pyridine, and the solution was boiled under reflux for 5 h. Then it was diluted with water (30 ml), acidified with 10% H_2SO_4, and worked up in the usual way. This gave 1.78 g of an acid, which was methylated with an excess of CH_2N_2. The reaction product after working up was chromatographed on a column containing 45 g of silica gel. Petroleum ether–ethyl acetate (9:1) eluted 1.53 g of methyl E,E-bishomofarnesate (IX), as a colorless viscous liquid. IR spectrum (cm^{-1}): 1730 (CO_2CH_3); 837, 1656 (>C=C<$_H$). PMR spectrum (ppm): 1.61 (s, 9 H, 3 CH_3 at C-9 and C-13); 1.67 (s, 3 H, CH_3 at C-5); 3.62 (s, 3 H, CO_2CH_3); 5.07 (br. s, 3 H, vinyl protons at C-4, C-8, and C-12). The product was identified by comparison with a spefimen that we had obtained earlier [1].

Superacid Cyclization of Methyl E,E-Bishomofarnesate (IX). A solution of 175 mg of FSO_3H in 2 ml of 2-nitropropane cooled to −(75-78)°C was added to a solution of 100 mg of methyl E,E-bishomofarnesate (IX) cooled to the same temperature, and the mixture was stirred at this temperature for 40 min. Then 3 ml of 20% KOH solution was added to the reaction mixture, and, after the usual working up, the reaction product (92 mg) was chromatographed on a column containing 2 g of SiO_2. Petroleum ether eluted 8 mg of a mixture of feebly polar substances. A mixture of petroleum ether and ethyl acetate (9:1) eluted 80 mg of the hydroxyester (XI). IR spectrum (cm^{-1}): 1730 (CO_2CH_3), 1020, 3484 (band), 3600 (OH group). PMR spectrum (ppm): 0.88 (s, 3H, CH_3), 0.97 (s, 3H) and 1.02 (s, 3H) (CH_3 at C-4 and C-10), 1.27 (s, 3H, CH_3 at C-8), 2.25 (br.s, 1H, OH), 3.62 (s, 3H, CO_2CH_3). Found, %: C 72.77; H 10.98. $C_{18}H_{32}O_3$. Calculated, %: C 72.93; H 10.88.

(±)-Ambrenolide (XII). A solution of 40 mg of the hydroxyester (XI) in 1 ml of ethanol was treated with 3 ml of a 20% alcoholic solution of KOH, and the mixture was boiled under reflux for 3 h. The mixture was worked up in the usual way, the reaction product (32 mg) was dissolved in 4 ml of toluene, and the solution was boiled in a Dean–Stark apparatus for 4 h. After the usual working up, 28 mg of reaction product was obtained, and this was chromatographed on a column containing 0.4 g of SiO_2. A mixture of petroleum and ethyl acetate (4:1) eluted 21 mg of (±)-ambrenolide (XII), mp 129-131.5°C (from petroleum ether), identical with an authentic specimen [1].

Synthesis of Methyl (13E)-6α-Hydroxy-15-bishomolabd-8(19),13-dienoate (XIV). A solution of larixyl acetate (XVII) [5] in 100 ml of abs. ether was treated with 4.5 ml of dry pyridine, and, with stirring at −5 to −7°C, a solution of 14.3 g of phosphorus tribromide in 40 ml of absolute ether was added dropwise. The reaction mixture was stirred at the same temperature for 2 h, and then at 0°C for 4 h, and it was left to stand at room temperature for 15 h. The excess of PBr_3 was decomposed with ice, and the mixture was diluted with water

(150 ml) and was worked up in the usual way. This gave 11.5 g of the mixture of acetoxybromides (XVIII), which was used without purification for the following stage.

With stirring, a solution of 11.4 g of the acetoxybromides (XVIII) obtained above in 2 ml of DMFA, 5.8 ml of acetone, and 0.3 g of benzyltriethylammonium chloride were added to a suspension of 5 g of K_2CO_3 in 4 ml of malonic ester. The mixture was stirred at 70-75°C for 4 h and was worked up in the usual way, and the reaction product (12.5 g) was boiled with 150 ml of a 10% alcoholic solution of KOH for 2 h. After the usual working up procedure, 3 g of a neutral fraction, which we did not investigate, and 6.6 g of an acid fraction were obtained.

The acid fraction (6.6 g) was dissolved in 50 ml of dry pyridine, and the solution was boiled under reflux for 3 h; then it was cooled and was worked up in the usual way, to give 5.7 g of a mixture of hydroxyacids. Crystallization from petroleum ether yielded 3.2 g of methyl (13E)-6α-hydroxy-15-bishomolabd-8(19),13-dien-17-oate (XIV); mp 50-52°C; $[\alpha]_D^{25}$ + 42.2° (c 2.9). IR spectrum (cm^{-1}): 1730 (CO_2CH_3), 1050, 3460 (band), 3590 (OH group), 890, 1635 (>C=CH_2), 840 (>C=C<$_H$). PMR spectrum (ppm, 0.69 (s, 3H, CH_3 at C-10), 0.96 (s, 3H) and 1.10 (s, 3H) ($2CH_3$ groups at C-4), 1.58 (s, 3H, CH_3 at C-13), 2.55 (m, 1H, H at C-6), 3.63 (s, 3H, CO_2CH_3), 4.65 (m, 1H) and 4.83 (m, 1H) (>C=CH_3), 5.05 (m, 1H, >C=C<$_H$). Found, %: C 76.42; H 10.48. $C_{23}H_{38}O_3$. Calculated, %: C 76.20; H 10.56.

Methyl (13E)-6α-Acetoxy-15-bishomolabd-8(19),13-dien-17-oate (XV). A solution of 1.5 g of the ester (XIV) in 10 ml of dry pyridine was treated with 1 ml of acetic anhydride, and the mixture was left to stand at room temperature for 20 h. Then it was worked up in the usual way, and gave 1.46 g of the diester (XV) in the form of a colorless liquid: $[\alpha]_D^{23}$ + 16.7° (c 1.3). IR spectrum (cm^{-1}): 1710, 1235 ($OCOCH_3$), 1730 (CO_2CH_3), 890, 1640 (>C=CH_2), 840, >C=C<$_H$), PMR spectrum (ppm): 0.72 (s, 3H, CH_3 at C-10), 0.85 (s, 3H) and 0.98 (s, 3H), $2CH_3$ groups at C-4), 1.59 (s, 3H, CH_3 at C-13), 1,.93 (c, 3H, $OCOCH_3$), 2.51 (m, 1H, H at C-6), 3.63 (s, 3H, CO_2CH_3), 4.53 (m, 1H) and 4.84 (m, 1H) (>C=CH_2), 5.03 (m, 1H, >C=C<$_H$). Found, %: C 73.97; H 10.12. $C_{25}H_{40}O_4$. Calculated, %: C 74.22; H 9.96.

(13E)-6α-hydroxy-15-Bishomolabd-8(19),13-dien-17-oic Acid (XIII). To 3.05 g of the hydroxyester (XIV) was added 30 ml of 10% alcoholic KOH, and the mixture was boiled under reflux for 3 h. Working up in the usual way led to 2.79 g of reaction product, which was chromatographed on a column containing 80 g of SiO_2. A 3:1 mixture of petroleum ether and ethyl acetate eluted 2.33 g of the hydroxyacid (XIII): mp 95.5-97°C (from pet. ether): $[\alpha]_D^{24}$ + 102° (c 1.6). IR spectrum (cm^{-1}): 1730 (CO_2H group), 1050, 3100-3540, 3600 (OH group 890, 1640 (>C=H_2). Found, %: C 75.58; H 10.35. $C_{22}H_{36}O_3$. Calculated, %: C 75.82; H 10.41.

Methyl (13E)-6αs-Trifluoroacetoxy-15-bishomolabd-8(19),13-dien-17-oate (XVI). At −30°C, 2 ml of trifluoroacetic anhydride was added to a solution of 2 g of the hydroxyester (XIV) in 14 ml of dry pyridine, and the mixture was stirred at the same temperature for 15 min and was then worked up in the usual way. The reaction product (2.1 g) was chromatographed on a column containing 35 g of SiO_2. Petroleum ether–ethyl acetate (19:1) eluted 1.8 g of the diester (XVI) in the form of a colorless viscous liquid, $[\alpha]_D^{25}$ + 11° (c 1.9). IR spectrum (cm^{-1}): 1220, 1770 ($OCOCF_3$), 1733 (CO_2CH_3), 890, 1640 (>C=CH_2), 848 (>C=C<$_H$). PMR spectrum (ppm): 0.77 (s, 3H, CH_3 at C-10), 0.88 (s, 3H) and 0.98 (s, 3H) ($2CH_3$ groups at C-4), 1.51 (s, 3H, CH_3 at C-13), 2.785 (m, 1H, at C-6), 3.59 (s, 3H, CO_2CH_3), 4.73 (m, 1H) and 4.88 (m, 1H) (>C=CH_2), 5.02 (m, 1H, >C=C<$_H$). Found, %: C 65.42; H 8.94. $C_{25}H_{40}F_3O_4$. Calculated, %: C 65.05; H 8.73.

Superacid Cyclization of the Hydroxyacid (XIII). A solution of 140 mg of FSO_3H in 0.6 ml of 2-nitropropane cooled to −80°C was added to a solution of 100 mg of the hydroxacid (I) cooled to the same temperature. The reaction mixture was stirred at this temperature for 20 min, and then 1.5 ml of a 20% solution of KOH was added to it and it was worked up in the usual way. The reaction product was separated into acid and neutral fractions. The amount of acid fraction, consisting, according to chromatographic results, of the initial hydroxyacid (I), was 34 mg. The neutral fraction (61 mg) consisted of the hydroxylactone (XXI), a colorless viscous liquid; $[\alpha]_D^{25}$ −11° (c 2.9). IR spectrum (cm^{-1}): 1738 (δ-lactone), 1030, 3400 (band) (OH group), 880, 1650 (>C=CH_2). PMR spectrum (ppm): 0.70 (s, 3H, CH_3 at C-10), 0.86 (s, 3H) and 1.11 (s, 3H) ($2CH_3$ at C-4), 1.33 (s, 3H, CH_3 at C-13), 2.41 (m, 1H, H at C-6), 4.53 (m, 1H), 4.82 (m, 1H) (>C=CH_2). Found, %: C 75.94; H 10.72. $C_{22}H_{38}O_3$. Calculated, %: C 76.20; H 10.56.

Superacid Cyclization of the Hydroxyester (XIV). A solution of 820 mg of FSO_3H in 1 ml of 2-nitropropane cooled to −80°C was added to a solution of 150 mg of the hydroxyester

(XIV) in 2.7 ml of 2-nitropropane cooled to the same temperature. The mixture was stirred at this temperature for 1 h and, after treatment with 5 ml of 20% KOH solution, it was worked up in the usual way. The reaction product (138 mg) was chromatographed on a column containing 4 g of SiO_2. A mixture of petroleum ether and ethyl acetate (7:3) eluted 72 mg of the dihydroxyester (XXII), $[\alpha]_D^{23}$ + 11.3° (c 1.8). IR spectrum (cm^{-1}): 1040, 3300 (band), 3580 (OH group), 1725 (CO_2CH_3), 890, 1640 (>C=CH_2). PMR spectrum (CCl_4 ppm): 0.86 (s, 3H, CH_3 at C-10), 0.95 (s, 3H) and 1.12 (s, 3H) ($2CH_3$ at C-4), 1.23 (s, 3H, CH_3 at C-13), 2.55 (m, 1H, H at C-6), 3.62 (s, 3H, CO_2CH_3), 4.55 (m, 1H) and 4.78 (m, 1H) (>C=CH_2). Found, %: C 72.32; H 10.74. $C_{23}H_{40}O_4$. Calculated, %: C 72.59; H 10.59.

Then a 13:7 mixture of the same solvents eluted 36 mg of the hydroxylacetone (XXI) from the column.

Superacid Cyclization of the Acetoxyester (XV). A solution of 390 mg of FSO_3H in 0.8 ml of 2-nitropropane cooled to −80°C was added to a solution of 120 mg of the acetoxyester (XV) in 1.6 ml of 2-nitropropane cooled to the same temperature. The reaction mixture was stirred at this temperature for 20 min, and then 3.5 ml of 20% KOH solution was added, and it was worked up in the usual way. The reaction product (114.7 mg) was chromatographed on a column containing 3 g of SiO_2. Petroleum ether–ethyl acetate (9:1) eluted 54 mg of the hydroxydiester (XXIII), a colorless viscous liquid: $[\alpha]_D^{24}$ − 23.2° (c 1.9). IR spectrum (cm^{-1}): 1230, 1720 ($OCOCH_3$), 1735 (CO_2CH_3), 1040, 3480 (band), 3600 (OH group), 880, 1640 (>C=CH_2). PMR spectrum (ppm): 0.75 (s, 3H, CH_3 at C-10), 0.88 (s, 6H, $2CH_3$ groups at C-4), 1.28 (s, 3H, CH_3 at C-13), 2.02 (s, 3H, $OCOCH_3$), 3.58 (s, 3H, CO_2CH_3), 4.95 (m, 1H) and 5.25 (m, 1H) (>C=CH_2). Found, %: C 71.27; H 10.14. $C_{25}H_{42}O_5$. Calculated, %: C 71.05; H 10.02.

Then a 4:1 mixture of the same solvents eluted from the column 25 mg of the acetoxylacetone (XXIV): IR spectrum (cm^{-1}): 1740 (δ-lactone), 1720, 1230 ($OCOCH_3$), 890, 1636 (>C=CH_2). PMR spectrum (ppm): 0.78 (s, 3H, CH_3 at C-10), 0.85 (s, 6H, $2CH_3$ groups at C-4), 1.23 (s, 3H, CH_3 at C-13), 2.03 (s, 3H, $OCOCH_3$), 2.57 (m, 1H, H at C-6), 4.90 (m, 1H) and 5.23 (m, 1H) (>C=CH_2). Found, %: C 73.72; H 9.94., $C_{24}H_{38}O_4$. Calculated, %: C 73.81; H 9.81.

Superacid Cyclization of the Diester (XVI). A solution of 260 mg of FSO_3H in 0.5 ml of 2-nitropropane cooled to −80°C was added to a solution of 250 mg of the diester (XVI) in 5 ml of 2-nitropropane cooled to the same temperature. The mixture was stirred at this temperature for 1 h, and then 3 ml of 20% KOH was added to it and it was worked up in the usual way. The reaction product (237 mg) was chromatographed on a column containing 4 g of SiO_2. Petroleum ether–ethyl acetate (7:3) eluted 179 mg of the hydroxydiester (XXV) in the form of a colorless viscous liquid: $[\alpha]_D^{25}$ +11.1° (c 1.7). IR spectrum (cm^{-1}): 1730 (CO_2CH_3), 1210, 1764 ($OCOCF_3$) 1040, 3458, 3600 (OH group), 887, 1638 (>C=CH_2). PMR spectrum (ppm): 0.90 (s, 3H, CH_3 at C-10), 0.95 (s, 3H) and 1.03 (s, 3H) ($2CH_3$ groups at C-4), 1.30 (s, 3H CH_3 at C-13), 49.3 (m, 1H) and 5.26 (m, 1H) (>C=CH_2). Found, %: C 62.94; H 8.47. $C_{25}H_{30}F_3O_5$. Calculated, %: C 63.01, H 8.25.

Conversion of the Hydroxydiester (XXV) into the Hydroxylactone (XXI). A solution of 60 mg of the hydroxydiester (XXV) in 0.5 ml of ethanol was treated with 2 ml of a 10% solution of KOH, and the mixture was boiled under reflux for 2 h. After the usual working up procedure, the reaction product (43 mg) was dissolved in 2 ml of toluene, and this solution was boiled in a Dean–Stark apparatus for 3 h. Then the solvent was distilled off, to give 36 mg of the hydroxylacetone (XXI), identical in its chromatographic properties with the specimen obtained above.

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EXTRACTIVE SUBSTANCES OF THE BARK OF Picea obovata

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The chemical composition of a petroleum ether extract of the bark of the Siberian spruce has been studied. Extracts included saturated aliphatic alcohols and C_{16}–C_{24} acids – abietic, dehydroabietic, isopimaric, oleic, lineolic, and linolenic – alkyl ferulates, ketones, and alcohols of the serratene type, and also Δ^4-stigmasten-3-one. Onoceradienedione and onoceradienediol – precursors of the serratene triterpenoids – and also a saturated vicinal diol – triacontane-10,11-diol – have been isolated from the extractive substances of conifer in the native form for the first time.

Pices obovata Lebd. (Siberian spruce) is the most widespread species of all forest-forming dark-needled conifers of the taiga zone in the mountain-taiga belt, the area of which stretches from the north of Scandanavia to the shores of the Sea of Okhotsk [1]. The extractive substances of the bark of the Siberian spruce have scarcely been studied, although there is information in the literature on the composition of the bark of other species of spruce [2-4].

The present work was devoted to a study of the chemical comosition of an extract of the bark of the Siberian spruce growing in the Altai. The extract was obtained by treating the bark with petroleum ether (PE) (bp 70-100°C), and its yield amounted to 1-1.8%. The extract, consisting of a grease-like light brown product, was separated into acidic and neutral components by the usual method.

The acidic part of the extract was treated with diazomethane and the result ethyl esters were then analyzed by the GLC method. The main components of the acidic fraction were the C_{18}–C_{24} saturated fatty acids, among which lignoceric acid (14.6%) predomianted, unsaturated fatty acids – oleic (15%) and linoleic (8%), and resin acids – isopimaric (11%) and dehydropimaric and abietic (32.6%), and also alkyl ferulates, which are typical components of bark extracts from coniferous plants [2, 5].

The neutral part of the extract was separated into groups of substances and individual compounds by adsorption chromatography. A nonpolar fraction was deluted by PE (bp 40-70°C) and was analyzed by the GLC method. It was found to contain 29 components and consisted of n-alkanes (C_{16}–C_{28} and C_{17}–C_{31} [sic]) the amounts of the individual components of which ranged from 0.3 to 9.2%. With an increase in the polarity of the eluting system, fractions of esters, ketones, tertiary alcohols, primary alcohols, triterpene alcohols, β-sitosterol, and diols were isolated successively.

The ester fraction was saponified with alcoholic alkali, as a result of which neutral unsaponifiable substances and the sum of the "bound" acids were obtained, and the latter were analyzed by the GLC method in the form of their methyl esters. It was established that the "bound" acids consisted mainly of saturated fatty acids (C_{14}– $_{24}$) with a predominance of behenic (22%) and lignoceric (28%), and also unsaturated acids – oleic (6.6%), lineolic (11.5%), and linolenic (14%).

The composition of the neutral unsaponifiable substances obtained on the saponification of the esters was unusual. In addition to β-sitosterol and the total fatty alcohols – the usual components of extractive substances, in this fraction the main component (64%) was a

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