Synthesis of Compounds (IV) and (V). To a solution of the sodium thiolate obtained from 0.0086 g-atom of Na and 0.89 mole of RSH (R = Et, n-Bu) were added 0.0089 mole of β-3,4-epithiocarane (II) and 2 ml of DMSO. The reaction mixture was stirred at room temperature for 15 h and was then diluted with 100 ml of water and extracted with ether (5 × 50 ml); the extracts were washed with NaCl and dried with Na_2SO_4. The products were isolated by chromatography on silica gel (hexane).

Synthesis of Compound (VI). To the solution of sodium ethanolate obtained from 0.28 g (0.012 g/atom) of Na and 10 ml of absolute ethanol were added 1.68 g (0.015 mole) of PhSH, 2.0 g (0.012 mole) of β-3,4-epithiocarane (II), and 2 ml of DMSO. The reaction mixture was stirred at room temperature for 40 h and was then diluted with water and extracted with ether (5 × 50 ml), and the extracts were washed with aqueous NH_4Cl and dried with Na_2SO_4. The product was isolated by chromatography on silica gel (hexane) and was additionally purified by recrystallization from acetone.

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SYNTHESIS OF 12-DEOXYSCALAROLACTONE AND 12-DEOXYSCALARADIAL

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12-Deoxyscalarolactone and 12-deoxyscalaradial and substances related to them have been synthesized from methyl scalar-16-en-19-oate.

As is known [1], marine organisms serve as a source of scalarane sesterterpenoids. A whole series of scalaranoids functionalized at C-12, C-19, and C-20 has been isolated from them, and some of these possess biological activity. However, these compounds have hitherto remained little-studied, since the amount of them in marine organisms is, as a rule, low and the syntheses of them that have been described involve many stages and are inefficient [2-4].

Having developed a convenient and highly effective route for obtaining compound (I) [5], as a consequence of which it has become relatively accessible, we decided to use it as a basis for the synthesis of two analogues of the natural scalaranoids – 12-deoxyscalarolactone (II) and 12-deoxyscalaradial (III) (see scheme on following page).

The reaction of the ester (I) with selenium dioxide gave a complex mixture of substances difficult to separate. The product of the reduction of the ester (I), which has also been obtained by the superacid cyclization of aliphatic or bicyclic sesterterpene alcohols [6, 7], reacted with selenium dioxide more smoothly. From the reaction product, by careful chromatography on silica gel, it was possible to isolate compounds (III)-(VI) in order of increasing polarity.

The structure of the crystalline hydroxy ether (III) was shown by spectral methods. Its IR spectrum contained the maxima of primary hydroxyl and ether groups and of a trisubstituted double bond, and its PMR spectrum contained the signals of five methyl groups

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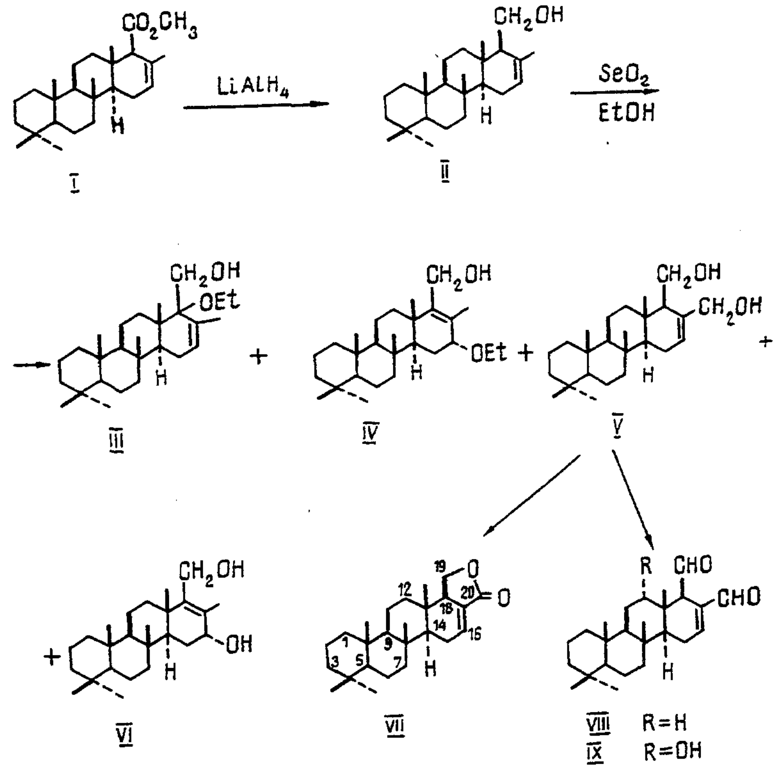

at quaternary atoms, of one at a double bond, and of a vinyl proton. The spectral characteristics mentioned, together with the results of elementary analysis, led to structure (III) for the crystalline hydroxy ether. The spectral characteristics of the hydroxy ether (IV) were close to those for the hydroxy ether (III). According to these characteristics, they contained the same functional groups and were allyl isomers, the difference between them consisting in the fact that in the hydroxy ether (IV) the double bond was tetrasubstituted and occupied the $\Delta^{17(18)}$ position and the hydroxyethyl group was located at C-16.

The diol (V) was identified on the basis of the identity of its IR and PMR spectra with those of the corresponding racemic diol (V) described in [4].

The last compound eluted from the column was the diol (VI), isomeric with diol (V). Its molecule contained one primary and one secondary hydroxy group. In its PMR spectrum there were the signals of five methyl groups at quaternary carbon atoms and of one methyl group at a double bond, a multiplet signal of the two protons of the hydroxymethyl group and also a broadened singlet of one proton linked with a carbinol carbon atom. Judging from the width of the signal of the carbinol proton at its half-height (7 Hz), the second hydroxy group of the diol under investigation was pseudoaxial, which agreed well with the results obtained for isoagathane compounds of similar structure [8]. On the basis of the facts mentioned, it was ascribed the structure and stereochemistry shown by formula (VI).

Oxidation of the diol (V) with manganese dioxide gave a 75% yield of scalarolactone (VII). Its IR spectrum contained bands characteristic for an α,β-unsaturated γ-lactone, and its PMR spectrum the signals of five methyl groups at quaternary carbon atoms, two one-proton triplets at 4.05 and 4.39 ppm, and a one-proton multiplet at 2.76 ppm belonging to an ABX system. The appearance of the signal of a vinyl proton at 6.85 ppm showed that it was in the β-position with respect to the carboxy group. On the basis of the spectral characteristics given and the results of elementary analysis, structure (VII) was ascribed to the lactone under investigation.

Oxidation of the glycol (V) with Swern's reagent [9] led in good yield to the dialdehyde (VII) — 12-deoxyscalaradial (VIII), an analogue of the natural scalarane hydroxy aldehyde (IX) [10]. Its structure was shown by spectral characteristics, which agreed well with those for its racemic form [4].

TABLE 1. Chromatographic Separation of the Product of the Oxidation of the Alcohol (II) with Selenium Dioxide

Frac Fraction No.	Solvent on the column	Weight of the fraction, mg	Composition of the fraction according to TLC and GLC
1	Pet. ether—ethyl acetate (49:1)	60	Hydroxy ether III
2		26	Mixture (1:1) of the hydroxy ethers (III) and (IV)
3		112	Hydroxy ether (IV)
4	Pet. ether—ethyl acetate (17:3)	130	Diol (V)
5	Pet. ether—ethyl acetate (4:1)	79	Diol (VI)

Thus, as a result of the investigations performed we have succeeded in synthesizing 12-deoxyscalaralactone (VII) and 12-deoxyscalaradial (VIII) — two analogues of natural scalarane sesterterpenoids — and also of substances related to them, (III)-(VI).

EXPERIMENTAL

Melting points were determined on a Boëtius heated stage. Specific rotations were measured in $CHCl_3$ on a SM polarimeter. IR spectra were taken on a Specord 24 IR instrument in CCl_4, and PMR spectra on Tesla BS-476 (60 MHz) and Bruker AC-80 (80 MHz) spectrometers in CCl_4. The internal standard was tetramethylsilane, and the signals are given in the δ scale. Mass spectra were recorded on a MKh-1320 spectrometer with a system for the direct introduction of the substance into the ion source at an ionizing energy of 70 eV. GLC analysis was conducted on a Chrom-5 chromatograph with a flame-ionization detector in a 3 × 1500 mm column containing the stationary phase SE-30 (5%) on Chromaton N-AW-DMCS.

Reduction of the (+)-Scalarane Ester (I). A solution of 600 mg of the ester (I) in 20 ml of absolute ether was treated with 200 mg of $LiAlH_4$, and the mixture was boiled under reflux for 0.5 h. The excess of hydride was decomposed with ethyl acetate, and the mixture was acidified with 10% sulfuric acid solution and was worked up in the usual way. This gave 480 mg of the alcohol (II): mp 165-166.5°C (from petroleum ether): 31.7° (c 2.3) [sic]. IR spectrum (cm^{-1}): 1040, 3435, 3600 (OH groups). PMR spectrum (ppm): 0.80 (s, 3H, CH_3 at C-10), 0.83 (s, 6H, CH_3 at C-4), 0.93 (s, 6H, CH_3 at C-8 and C-13), 1.58 (s, 3H, CH_3 at C-17), 3.50 (m, 2H, CH_2—O—), 5.41 (m, 1H, H at C-16). The product was identified by comparison with a sample that we had obtained previously [6].

Oxidation of the Alcohol (II) with Selenium Dioxide. A solution of 450 mg of the alcohol (II) in 4 ml of ethanol was heated with 70 mg of SeO_2, and the mixture was boiled under reflux for 1 h and was then worked up as described in [11], and the product was chromatographed on a column containing 9 g of SiO_2. The results of the separation are given in Table 1.

Hydroxy Ether (III). Fraction 1 was recrystallized from petroleum ether, giving 33 mg of the hydroxy ether (III): mp 64-65°C, $[\alpha]_D^{21}$ −47.2° (c 2.0). IR spectrum (cm^{-1}): 1072, 3435 (band), 3612 (OH), 1124 ($COCH_2CH_3$), 1672 ($>C=C<_H$). PMR spectrum (ppm): 0.87 (s, 9H), 0.93 (s, 3H), 0.97 (s, 3H), (5 CH_3 at C-4, C-8, C-10, and C-13), 1.28 (t, J = 5 Hz, 3H, CH_3CH_2O), 1.76 (s, 3H, CH_3 at C-17), 3.45 (m, 2H, OCH_2CH_3), 4.15 (br. s., 2H, H_2 at C-19), 5.43 (br. s., 1H, H at C-16). Found, %: C 80.22; H 11.67. $C_{27}H_{46}O_2$. Calculated, %: C 80.54; H 11.52.

Hydroxy Ether (IV). Fraction 3, a colorless viscous liquid, consisted of the hydroxy ether (IV): $[\alpha]_D^{23}$ −39.4° (c 2.2). IR spectrum, (cm^{-1}): 1078, 3435 (band), 3600 (OH-group), 1120 ($COCH_2CH_3$), 1347, 1376 [$C(CH_3)_2$]. PMR spectrum (ppm): 0.85 (c, 3H), 0.92 (c, 9H), and 0.98 (c, 3H) (5 CH_3 at C-4, C-8, C-10, and C-13), 1.28 (t, J = 5 Hz, 3H, CH_3CH_2O), 1.75 (s, 3H, CH_3 at C-17), 3.51 (m, 2H, OCH_2CH_3), 3.78 (br. s., 1H, H at C-16), 3.92 (br. s., 2H, H_2 at C-19). Found, %: C 80.92; H 11.46. $C_{27}H_{46}O_2$. Calculated, %: C 80.54; H 11.52.

Diol (V). Fraction 4 (see Table 1) was recrystallized from diethyl ether, giving 87 mg of the diol (V), mp 202-203.5°C: $[\alpha]_D^{24}$ +163° (c 1.3). IR spectrum (cm^{-1}): 1040, 1072, 3400 (band), 3645 (OH group), 838, 1640 ($>C=C<_H$), 1345, 1376 [$C(CH_3)_2$]. PMR spectrum

($CDCl_3$, ppm): 0.79 (s, 3H), 0.81 (s, 9H), and 0.92 (s, 3H) (5 CH_3 at C-4, C-8, C-10, and C-13), 3.83-4.50 (m, 4H, $2H_2$ at C-19 and C-20), 5.78 (m, 1H, H at C-16). Found, %: C 79.78; H 11.42. $C_{25}H_{42}O_2$. Calculated, %: C 80.16; H 11.30.

Diol (VI). Fraction 5 was recrystallized from diethyl ether, giving 32 mg of the diol (VI): mp 190-192°C; $[\alpha]_D^{24}$ 34.3° (c 2.9). IR spectrum (cm^{-1}): 1034, 3380 (band), 3588 (OH group), 1360, 1372 $[C(CH_3)_2]$. PMR spectrum ($CDCl_3$, ppm): 0.87 (s, 9H), 0.93 (s, 3H), and 0.98 (s, 3H) (5 CH_3 at C-4, C-8, C-10, and C-13), 1.86 (s, 3H, CH_3 at C-17), 3.75 (m, 2H, H_2 at C-19), 4.13 (br. s., 1H, $H_{1/2}$ = 7 Hz, H at C-16). Mass spectrum, m/z (intensity, %): 374 (M^+, 2), 359 ($M - CH_3$, 28), 314(20), 342 (8), 269(18), 255(33), 241(20), 142(33), 127(44), 69(100). Found, %: C 80.54; H 11.22. $C_{25}H_{42}O_2$. Calculated, %: C 80.16; H 11.30.

12-Deoxyscalarolactone (VII). A solution of 40 mg of the diol (V) in 8 ml of CH_2Cl_2 was treated with 1.8 g of manganese dioxide, and the mixture was stirred at the ordinary temperature for 6 h. The oxidant was filtered off, and the solvent was distilled off. This gave 38 mg of reaction product, which was chromatographed on a column containing 0.8 g of SiO_2. A mixture of petroleum ether and ethyl acetate (9:1) eluted 30 mg (75%) of 12-deoxyscalarolactone (VII): mp 196-198°C (from petroleum ether); $[\alpha]_D^{23}$ −49° (c 2.0). IR spectrum (cm^{-1}): 1690, 1768 (α,β-unsaturated γ-lactone), 1360, 1382 $[C(CH_3)_2]$. PMR spectrum ($CDCl_3$, ppm): 0.69 (s, 3H), 0.78 (s, 3H), 0.86 (s, 3H), 0.89 (s, 3H) and 0.95 (s, 3H) (5 CH_3 at C-4, C-8, C-10, and C-13), 2.24 (m, 2H, H_2 at C-15), 2.76 (m, 1H), 4.05 (t, J = 9 Hz, 1H), and 4.39 (t, J = 9 Hz, 1H) (ABX three-proton system $CH{-}CH_2O{-}$), 6.85 (dd, J_1 = 3 Hz; J_2 = 7 Hz, H at C-16). Found, %: C 80.84; H 10.26. $C_{25}H_{38}O_2$. Calculated, %: C 81.03; H 10.34.

12-Deoxyscalaradial (VIII). With stirring at −60 to −62°C a solution of 100 mg of DMSO in 0.3 ml of CH_2Cl_2 was added to a solution of 90 mg of oxalyl chloride in 1.5 ml of dry CH_2Cl_2. The mixture was stirred at the same temperature for 5 min, and 50 mg of the diol (V) in 0.3 ml of CH_2Cl_2 was added to it. The reaction mixture was stirred at the same temperature for 45 min and, with continued stirring, 270 mg of triethylamine was added to it, and it was kept at −60°C for 10 min, after which the temperature was gradually raised to that of the room. Then it was diluted with 30 ml of ether and was worked up in the usual way. The reaction product (47 mg) was chromatographed on a column containing 0.8 g of SiO_2.

A mixture of petroleum ether and ethyl acetate (9:1) eluted 24 mg (48.5%) of 12-deoxyscalaradial (VIII): mp 174-175.5°C (from petroleum ether); $[\alpha]_D^{23}$ −135.6° (c 0.9). IR spectrum (cm^{-1}): 1642, 1673 (conjugated CHO), 1715, 2726 (CHO). PMR spectrum ($CDCl_3$, ppm): 0.81 (s, 3H), 0.85 (s, 3H), 0.89 (s, 3H), 0.92 (s, 3H), and 0.96 (s, 3H) (5 CH_3 at C-4, C-8, C-10, and C-13), 2.34 (m, 2H, H_2 at C-15), 3.49 (m, 1H, H at C-18), 7.19 (m, 1H, H at C-16), 9.46 (d, J = 5 Hz, 1H, CHO at C-17), and 9.58 (s, 1H, CHO at C-18). Mass spectrum, m/z (intensity, %): 370 (M^+, 8), 342 (M − CO, 64), 326(23), 238(42), 192(17), 191(64), 172(91), 137(55), 123(100), 69(74). Found, %: C 80.77; H 10.26. $C_{25}H_{38}O_2$. Calculated, %: C 81.03; H 10.34. The spectra were identical with those given in [4].

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