INVESTIGATION OF THE PRODUCTS OF THE OZONOLYSIS OF NEOABIENOLS

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The ozonolysis of a mixture of 13Z- and 13E-neoabienols (I and III) leads, depending on the conditions, either to 8α-hydroxy-14,15-bis-norlabd-11-en-13-one (IV) or to 8α-hydroxdriman-11-oic acid (VI) or to driman-8α,11-diol (VII). Compound (IV) undergoes hydrogenation smoothly with the formation of a mixture of 8α-hydroxy-14,15-bisnorlabdan-13-one (X) and "sclareol oxide" (XI).

Neoabienol, which is labda-11,13Z-dien-8α-ol (I) was first isolated from the high-boiling neutral fraction of the oleoresin of the Siberian fir [1]. Later, [2, 3], the hypothesis was expressed, and has recently received conformation [4], that neoabienol (I) is product of the rearrangement of cis-abienol (II) — the main component of this fraction of Siberian fir oleoresin. It has also been shown that neoabienol must in actual fact consist of a mixture of 13E- and 13Z-neoabienols (I) and (III) [3].

In view of the availability of a mixture of the neoabienols (I) and (III) (Siberian fir oleoresin is obtained on the industrial scale [4]), and the peculiar nature of their chemical structures, suggesting the probable possibility of their use as the starting materials for obtaining valuable norlabdane and drimane compounds, we have undertaken a detailed investigation of the ozonolysis of the mixture of neoabienols (I) and (III), and its results are given in the present communication.

It was found that the nature of the products of the ozonization of the neobienols (I) and (III) depended substantially on the conditions of performing the reaction and, above all, on the amount of oxidant and the method of decomposing the ozonide or the peroxide ozonization products. Thus, when one molar equivalent of ozone was used in ozonization at −60 to −70°C in ethyl acetate in the presence of pyridine or in methanol with the subsequent decomposition of the peroxide reaction products by dimethyl sulfide, the only neutral reaction product, formed with a yield of 70%, was a substance with the composition $C_{18}H_{30}O_2$. Its IR spectrum contained bands characteristic for a conjugated trans-disubstituted double bond (930, 980, 1613 cm^{-1}), a hydroxy group (1120, 3450, 3587 cm^{-1}), and a conjugated keto group (1683 and 1691 cm^{-1}), while its PMR spectra contained singlet signals of three methyl groups at quaternary carbon atoms, of a methyl group at a carbinol carbon atom (1.17 ppm), and of a methyl ketone group (2.13 ppm), a one-proton doublet (5.96 ppm), and a one-proton doublet of doublets at 6.66 ppm (trans-located vinyl protons at a disubstituted double bond).

These facts led to the structure of 8α-hydroxy-14,15-bisnorlabd-11-en-13-one (IV) for the substance under investigation. This substance was first isolated from the oleoresin of the Siberian fir [5] although it is likewise not a native component and consists of the product of the autooxidation of the neoabienols [1, 3]. The hydroxy ketone (IV) was identified by its comparison with an authentic sample that we had obtained previously [3]. In addition to the hydroxy ketone (IV), a small amount of an acid fraction was isolated. Thus, on the use of 1 molar equivalent of ozone the ozonolysis of the mixture of neoabienols (I) and (III) takes place selectively, regardless of the solvent used and the method of decomposing the ozonization products: it is mainly only the double bond of the neoabienols at C-13 that undergoes cleavage. However, the degree of selectivity of the process depends on the temperature at which it is performed. Thus, when the mixture of neoabienols was ozonized in methanol at 0°C and the peroxide reaction products were reduced with dimethyl sulfide, the yield of the hydroxy ketone (IV) fell to 55%. Monitoring of the course of ozonization by TLC showed after 5-10 min the double bond of the neoabienols at C-13 had

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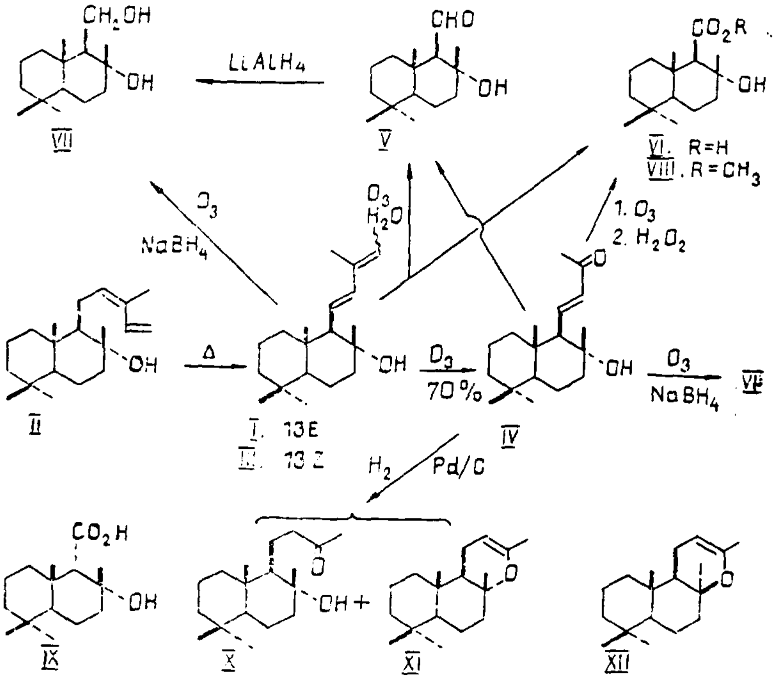
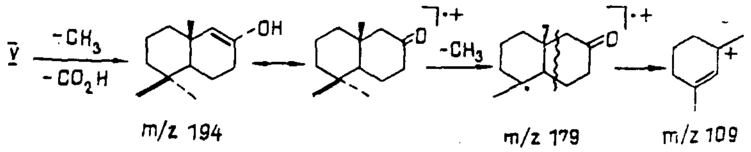
reacted completely and only then did the disubstituted double bond at C-11 take part in the reaction. The latter bond is fairly resistant to the action of ozone and reacts with difficulty, its cleavage requiring a large excess of ozone, while the breakthrough of ozone through the solution does not coincide with the completion of the reaction, and its course was followed by TLC.

On the exhaustive ozonization of the mixture of neoabienols (I) and (III) in hexane at −60 to −70°C (monitoring by TLC) and decomposition of the ozonide by heating with water, the reaction product consisted of neutral (~60%) and acid (~25%) fractions. According to TLC, the liquid neutral fraction consisted of an individual compound which was extremely unstable and rapidly changed on storage. For this reason, it was impossible to obtain a satisfactory elementary analysis for it, and it was characterized only spectrally. Its IR spectrum contained bands characteristic for a tertiary hydroxy group and an aldehyde group, and its PMR spectrum the signals of three methyl groups at quaternary carbon atoms, of one at a carbinol carbon atom, and of an aldehydic proton. On the basis of these facts, the structure of 8-hydroxydriman-11-al (V) was assigned to the product under investigation.



The acid fraction of the ozonolysis product consisted of a crystalline substance with mp 178-179.5°C. In its IR spectrum there were the maxima of carboxy and hydroxy groups, and in its PMR spectrum the signals of three methyl groups at quaternary carbons and of one at a carbinol carbon atom, and in a fairly weak field, a broadened signal of the carboxylic proton at 6.08 ppm and a signal of a C-9 proton at 2.35 ppm. The above-mentioned spectral characteristics, and also the results of a elementary analysis led to the structure of 8-hydroxydriman-11-oic acid (VI) for the compound under investigation. This structure was confirmed by its mass spectrum which contained the peaks of the molecular ion with m/z 254, and also intense peaks of ion with m/z 236 (M − H_2O), 221 [M − (H_2O + CH_3)], 194 [M − (CH_3 + CO_2H)], 179 [M − (2CH_3 + CO_2H)] and 109 (100% intensity). The formation of the last three ions may take place by the following scheme:



The hydroxy acid (VI) became the main reaction product (yield 71%) when ozonization was performed in hexane followed by the oxidative cleavage of the ozonide with dihydrogen peroxide. When the hydroxy acid (VI) was reduced with lithium tetrahydroaluminate, the known drimane-8α,11-diol (VII) [6, 7] was obtained.

The combination of facts given above led unambiguously to structure (VI) for the hydroxy acid under investigation. Its constants coincided with those given for it in [8]. The constants of their methyl esters (VIII) also coincided.

It must be mentioned that the formation of a hydroxy acid with the structure (VI) by the ozonization of 13Z-neoabienol (I) was described in [1]. However, the melting point of this substance (143-144°C) differed substantially from the melting point of the acid that we have isolated (178-179.5°C). The mass spectra of these substances also differed, namely by the most intensive peaks of different ions in them. In particular, in the spectrum of the hydroxy acid that we had obtained there was the peak of the molecular ion (with an intensity of ~14%) which was almost absent (intensity <1%) in the spectrum of the hydroxy acid (VI) given in [1] and, moreover, in the first spectrum the peak of the ion with m/z 107 had an intensity of 100%, while in the second spectrum the 100% peak was that of an ion with m/z 109. In view of this, we ozonized the hydroxy ketone (IV) under the conditions given in [1]. The main reaction product (with a yield of ~42%) in this case, as well, proved to be the hydroxy acid (VI) with mp 178-179°C. Furthermore, another product was formed, in a yield of 9%, which did not crystallize and, because of the lack of substance, could not be strictly identified; however, judging from its PMR spectrum, which contained the singlet signals of three methyl groups at quaternary atoms and of a methyl group at a carbinol atom and singlet signals of a proton at 2.01 ppm and of the proton of a carboxy group at 12.27 ppm, it apparently consisted of the epimer (IX) of the hydroxy acid (VI) at C-9.

In view of the instability of the hydroxy aldehyde (V), to determine the total yield of substances (V) and (VI) the product of exhaustive ozonization of the mixture of neoabienols (I) and (III) was subsequently decomposed and, without separation into acidic and neutral fractions, was reduced with lithium tetrahydroaluminate to the diol (VII), and the yield of the latter was determined. On ozonization in ethyl acetate and in methylene chloride in the presence of pyridine it amounted to 44.5 and 46.7%, respectively, while on ozonization in methanol followed by reduction of the peroxide compounds with dimethyl sulfide it amounted to 47%. The reason for the relatively low yield of the diol (VII) is apparently the fact that the hydroxy aldehyde (V) is not oxidized to the hydroxy acid (VI), but is also decomposed with the formation of other products. In actual fact, if the mixture of neoabienols (I) and (III) was exhaustively ozonized in methanol at −75 to −78°C and the peroxide ozonization products were reduced immediately by sodium tetrahydroborate, the yield of the diol (VII) amounted to 74%. This method of ozonizing the mixture of neoabienols (I) and (III) is preferable in the production of the drimanediol (VII) − the main starting compound for the synthesis of natural drimane sesquiterpenoids. It must be mentioned that the yield of diol (VII) is affected by the temperature at which ozonization is performed. With a rise in the temperature it fell, and amounted to 65% at −40 to −45°C and to 60% at −20 to −25°C.

We also investigated the products of the ozonization of the hydroxy ketone (IV). As in the case of the neoabienols (I) and (III), their nature depended substantially on the conditions of performing the reaction. Thus, on itz ozonization in methanol and the decomposition of the peroxides with dimethyl sulfide, ~77% of the hydroxy aldehyde (V) and ~20% of the hydroxy acid (VI) were formed, while on ozonization in ethyl acetate in the presence of pyridine the yields were 60-65% and ~30%, respectively. When the reaction was performed in hexane and the ozonide was decomposed with hydrogen peroxide, the reaction product was the hydroxy acid (VI) (yield 74%). Finally, the ozonization of the hydroxy ketone (IV) in methanol with subsequent reduction of the peroxides by sodium tetrahydroborate led smoothly to drimane-8α,11-diol (VII) (69%). The existence of a definite parallelism in the yields of the individual products on ozonization under identical reaction conditions of a mixture of neoabienols (I) and (III) and of the hydroxy ketone (IV) is an additional indication of the fact that in the neoabienols the bond at C-13 is cleaved first, and then that at C-11.

The hydroxy ketone (IV) could serve as the initial compound for the synthesis of 8α-hydroxy-14,15-bisnorlabdan-13-one (X), an important intermediate in obtaining valuable perfume substances with the odor of ambergris [9]. However, when the hydroxy ketone (IV) was hydrogenated over platinum in ethyl acetate, according to [5], compounds (X), (XI), and (XII) were formed. In view of the mild conditions of hydrogenation, the formation of the oxide (XII) epimeric at C-8 is unexpected and difficult to explain. In view of this, we performed the hydrogenation of the hydroxy ketone (IV) in ethanol over palladium on carbon. The reaction product consisted only of "sclareol oxide" (XI) (yield 78%) and the hydroxy ketone (14%).

The successful performance of the transformation (I) + (III) → (IV) → (X) + (XI) shows that the readily available neoabienols (I) and (III) may serve as the starting material for obtaining valuable perfume substances of the 14,15-bisnorlabdane and bicyclohomofarnesane series. Furthermore, we have shown that the ozonization of the mixture of neoabienols (I) and (III) is an effective route to drimane sesquiterpenoids.

EXPERIMENTAL

For the general part, see [10]. The productivity of the ozonizer was 1.6 g of ozone per hour, the rate of feed of the ozone-oxygen mixture 1.5 liters/min, and the concentration of ozone 0.3% by weight. Mass spectra were taken on a MKh-1320 spectrometer with a glass system for introducing the sample into the ion source at an ionizing energy of 70 eV.

Production of 8α-Hydroxy-14,15-bisnorlabd-11-en-13-one (IV). a) At −65 to −70°C a mixture of ozone and oxygen in an amount corresponding to one molar equivalent of ozone (6 min) was passed through a solution of 100 mg of the mixture of neoabienols (I) and (III) in 10 ml of dry ethyl acetate and 0.1 ml of dry pyridine. The reaction mixture was purged with nitrogen for 5 min and was left to assume room temperature after which 20 ml of a 10% solution of H_2SO_4 was added to it. The mixture was extracted with ether (3 × 20 ml), the extract was washed with 20 ml of saturated $NaHCO_3$ solution and with water (3 × 15 ml), dried with anhydrous Na_2SO_4, and filtered, the solvent was distilled off, and the residue was chromatographed on a column containing 3 g of SiO_2 (100/160 μm deactivated by the addition of 10% of water). Petroleum ether—ethyl acetate (9:1) eluted 68 mg (71%) of 8α-hydroxy-14,15-bisnorlabd-11-en-13-one (XII), mp 126-127°C (from petroleum ether). IR spectraum (cm^{-1}): 930, 980, 1613 (trans-disubstituted conjugated double bond); 1120, 3450 (band), 3587 (OH); 1683, 1691 (conjugated keto group). PMR spectrum (ppm): 0.80 (3H, s), 0.86 (3H, s) $[C_4 - (CH_3)_2]$, 0.97 (3H, s, $C_{10} - CH_3$), 1.17 (3H, s, $C_8 - CH_3$), 2.13 (3H, s, CH_3CO—), 5.96 (1H, d, J = 15 Hz, $C_{12} - H$), 6.66 (1H, dd, J_1 = 15 Hz, J_2 = 10 Hz, $C_{11} - H$). According to the literature [5]: mp 126°C. The hydroxy ketone (IV) was identical with an authentic sample that we had obtained previously [3].

b) At −65 to −70°C, a mixture of ozone and oxygen in an amount corresponding to one molar equivalent of ozone was passed through a solution of 100 mg of the mixture of neoabienols (I) and (III) in 10 ml of methanol, and then the solution was purged with nitrogen (5 min) and was heated to −10°C, 0.1 ml of dimethyl sulfide was added, and the reaction mixture was stirred for 30 min each at the same temperature and at 0 and 20°C. The solvent was distilled off under a reduced pressure of nitrogen, the residue was treated with 25 ml of water and was extracted with ether (3 × 20 ml), and the extract was washed with water (3 × 20 ml) and with saturated $NaHCO_3$ solution and was dried with anhydrous Na_2SO_4, and filtered, and the solvent was distilled off. The residue (80 mg) was chromatographed on a column containing 3 g of SiO_2. Petroleum ether—ethyl acetate (9:1) eluted 66 mg (70%) of the hydroxy ketone (IV), mp 126-127°C identical with an authentic sample.

c) The mixture of neoabienols (I) and (III) (100 mg) was ozonized as described in paragraph b) but at 0°C, and the products were worked up as described above. This gave 52 mg (55%) of the hydroxy ketone (IV) and 9 mg of an acid fraction which was not investigated further.

Production of a Mixture of 8α-Hydroxydriman-11-al (V) and 8α-Hydroxydriman-11-oil acid (VI). a) From a Mixture of the Neoabienols (I) and (III). At −65 to −79°C, a mixture of ozone and oxygen was passed through a solution of 100 mg of the mixture of neoabienols (I) and (III) in 10 ml of hexane until the ozone broke through. The reaction mixture was purged with nitrogen (5 min), left to assume room temperature, treated with 20 ml of water, kept at room temperature for 1 h, and heated at 70°C for 2 h. Then it was cooled, another 20 ml of water was added to it, and it was extracted three times with ether. The extract was washed with 1% KOH solution and with water, was dried with anhydrous Na_2SO_4 and filtered, and the solvent was distilled off. This gave 49 mg (60%) of the liquid 8α-hydroxydriman-11-al (V), an individual substance according to TLC, which rapidly changed on storage. IR spectrum (cm^{-1}): 1135, 3460, 3550, 3615 (OH); 1718, 2750 (CHO). PMR spectrum (ppm): 0.80 (3H, s), 0.87 (3H, s), $[C_4 - (CH_3)_2]$, 1.08 (3H, s, $C_{10} - CH_3$), 1.30 (3H, s, $C_8 - CH_3$), 9.95 (1H, br.s, CHO).

The alkaline extract was acidified with H_2SO_4 and extracted with ether (2 × 20 ml), the extract was washed with water (2 × 20 ml), dried over anhydrous Na_2SO_4, and filtered, and the solvent was distilled off. This gave 21 mg (25%) of an acid fraction which crystallized on standing, mp 178-179.5°C [from petroleum ether—diether (1:1)], $[\alpha]_D^{18}$ +7° (c 2.33; $CHCl_3$). IR spectrum (cm^{-1}): 1135, 1720, 3300-3600 (broad band) (OH and CO_2H). PMR spectrum (ppm): 0.81 (3H, s), 0.86 (3H, s) $[C_4(CH_3)_2]$, 1.10 (3H, s, $C_{10} - CH_3$), 1.35 (3H, s, $C_8 - CH_3$), 2.35 (1H, s, $C_9 - H$), 6.08 (1H, br.s, COOH). Mass spectrum, m/z (%): 254 (M^+, 14), 237(11), 236(69), 220(5), 221(33), 208(13), 197(6), 195(5), 194(11), 193(9), 192(8), 180(6), 179(38), 178(4), 177(25), 176(9), 175(15), 166(3), 165(14), 161(9), 152(5), 151(19), 150(7), 149(8), 147(4), 141(7), 139(7), 137(35), 136(23), 135(15), 134(4), 133(6), 131(5), 130(43), 127(12), 126(3), 125(12), 124(22), 123(50), 122(9), 121(26), 120(4), 119(6), 115(3), 113(11), 112(29), 111(15), 110(18), 109(100), 108(11) 107(23), 106(3), 105(13), 105(13), 96(6), 95(33), 94(14), 93(79), 92(24), 91(18), 85(13), 89(11), 83(26), 82(26), 81(89), 80(7), 79(26), 78(4), 77(14).

A sample of the hydroxy acid (VI) (20 mg) was methylated with an excess of an ethereal solution of diazomethane and the product was worked up in the usual way to give 16 mg of the ester (VIII), mp 84-85°C (from petroleum ether). According to the literature [8]: mp 84.5-85.5°C.

b) From the Hydroxy Ketone (IV). 1. At −65 to −70°C, a mixture of ozone and oxygen was passed through a solution of 100 mg of the hydroxy ketone (IV) in 10 ml of ethyl acetate and 0.1 ml of pyridine until the initial hydroxy ketone had disappeared (monitoring by TLC) (45 min). Nitrogen was passed through the reaction mixture (5 min), it was diluted with 20 ml of 10% H_2SO_4 solution and extracted with ether (3 × 20 ml), and the extract was separated into neutral and acid fractions as described in paragraph a). This gave 58 mg (70%) of the hydroxy aldehyde (V) and 25 mg (20%) of the hydroxy acid (VI) which were identified chromatographically and by spectral comparison with authentic samples.

2. At −65 to −70°C, a mixture of ozone and oxygen was bubbled through a solution of 68 mg of the hydroxy ketone (IV) in 6 ml of dry methanol until the reaction was complete (monitoring by TLC) (20 min). The reaction mixture was purged with nitrogen (5 min), 0.1 ml of dimethyl sulfide was added, and the mixture was allowed to assume room temperature and was stirred for another 2 h, after which the methanol was distilled off under a reduced pressure of nitrogen, the residue was heated with 20 ml of 10% H_2SO_4 solution and was extracted with ether (3 × 25 ml), and the extract was separated into neutral and acid fractions as described above, giving 44 mg (77%) of the hydroxy aldehyde (V) and 14 mg (22%) of the hydroxy acid (VI).

Production of 8α-Hydroxydriman-11-oil Acid (VI). a) From the Mixture of Neoabienols (I) and (III). At −65 to −70°C, a mixture of ozone and oxygen was passed through a solution of 100 mg of the mixture of neoabienols (I) and (III) in 10 ml of hexane until the reaction the complete (monitoring by TLC), and then the ozone was displaced by nitrogen and the reaction mixture was allowed to assume room temperature. The hexane was distilled off under a reduced pressure of nitrogen at room temperature, the residue was treated with 20 ml of 10% H_2O_2, and the mixture was stirred at room temperature for 16 h or was heated at 70°C for 5 h. The resulting reaction mixture was extracted with ether and was separated in the usual way into acid and neutral fractions. This gave 64 mg (73%) of the hydroxy acid (VI) and 21 mg of a neutral fraction consisting of a complex mixture of substances which was not investigated further.

b. From the Hydroxy Ketone (IV). A solution of 100 mg of the hydroxy ketone in 10 ml of hexane was ozonized at −65 to −70°C until the reaction was complete (45 min) and the products were then worked up as described in paragraph a). This yielded 67 mg (74%) of the hydroxy acid (VI) and 22 mg of a mixture of neutral substances which was not investigated further.

Production of Drimane-8α,11-diol (VII). a) From the Mixture of Neoabienols (I) and (III). 1. At −65 to −70°C a mixture of ozone and oxygen was bubbled through a solution of 118 mg of the mixture of neoabienols (I) and (III) in 11 ml of absolute methanol until the reaction was complete (breakthrough of ozone and monitoring by TLC), the ozone was displaced by nitrogen (5 min), and the mixture was left to assume room temperature. Then 100 mg of 74% $NaBH_4$ was added to it and the resulting mixture was stirred at room temperature for 1 h. The excess of hydride was decomposed by the addition of 20 ml of a 5% solution of hydrochloric acid, and the reaction mixture was extracted with ether (3 × 20 ml). The extract was washed with water (2 × 30 ml), with a 1% solution of KOH, again with water, to neutrality, and it was dried over Na_2SO_4 and filtered, and the solvent was distilled off in vacuum. The residue (103 mg) was chromatographed on a column containing 3 g of SiO_2. This gave 73 mg (74%) of drimane-8α,11-diol (VII) mp 121-122°C (from petroleum ether), $[\alpha]_D^{22}$ + 8.4° (c 2.4; $CHCl_3$). IR spectrum ($CHCl_3$, cm^{-1}): 1118, 1176, 3320 (strong band) (OH groups) PMR spectrum (ppm): 0.78 (6H, s), 0.88 (3H, s) (C_4- and C_{10}-CH_3), 1.25 (3H, s, C_8-CH_3), 3.80 (2H, d, J = 6 Hz, C_{11}-C_2), 4.68 (2H, br.s, OH groups). Found, %: C 75.14, H 11.73. $C_{15}H_{28}O_2$. Calculated, %: C 74.94, H 11.74. According to the literature: mp 119-120°C $[\alpha]_D$ +1.6° [6]; 127-128°C, $[\alpha]_D$ +4.2° [7].

2. At -60 to -70°C, an excess of a mixture of ozone and oxygen was passed through a solution of 100 mg of the mixture of neoabienols (I) and (III) in 10 ml of methylene chloride and 0.1 ml of dry pyridine until the hydroxy ketone (IV) had disappeared (according to TLC). The ozone was displaced by nitrogen. The reaction mixture was treated with 20 ml of 10% H_2SO_4 solution and extracted with diethyl ether (3 × 25 ml). The extract was washed with 10% H_2SO_4 (2 × 20 ml) and with water (3 × 20 ml), dried with Na_2SO_4, and filtered, and the solvent was evaporated off.

The residue (95 mg) was dissolved in 6 ml of absolute ether, and 56 mg of lithium tetrahydroaluminate was added. The mixture was boiled under reflux for 3 h. The excess of hydride was decomposed with ethyl acetate and the reaction mixture was acidified with 20 ml of 100% H_2SO_4 [sic] and extracted with ether, and the extract was washed with water (3 × 20 ml), dried with Na_2SO_4, and filtered, and the solvent was distilled off in vacuum. The product (64 mg) was chromatographed on a column containing 3 g of silica gel. The yield of drimane-8α,11-diol (VII) was 39 mg (46.7%).

3. The mixture of neoabienols (I) and (III) (98 mg) was dissolved in 10 ml of ethyl acetate and 0.1 ml of dry pyridine and was ozonized at -1 to +1°C as described in paragraph 2. After the working up of the ozonolysis product as described above, its reduction with lithium tetrahydroaluminate, and chromatography (see paragraph 2), 37.1 mg (44.5%) of drimane-8α,11-diol (VII) was obtained.

4. A solution of 114 mg of the mixture of neoabienols (I) and (III) in 10 ml of methanol was exhaustively ozonized at -60 to -70°C. The ozone was displaced by nitrogen, the temperature of the mixture was brought to -10°C, 0.1 ml of dimethyl sulfide was added, the solution was stirred for 20 min, the temperature was raised to 0°C and stirring was continued for another 20 min, and was then continued at room temperature for 30 min. The mixture was treated with 25 ml of water and was extracted with ether (3 × 20 ml), the extract was washed with water (3 × 20 ml), dried with Na_2SO_4, and filtered, and the solvent was distilled off. The residue (85 mg, a mixture of four substances of which two predominated according to TLC) was reduced by boiling under reflux with the solution of 51 mg of lithium tetrahydroaluminate in 5 ml of absolute ether for 3 h.

After the usual working up and chromatography (see paragraph 2), 44 mg (47%) of the drimanediol (VII) was isolated.

b) From 8α-Hydroxy-14,15-bisnorlabd-11-en-13-one (IV). The hydroxy ketone (IV) (100 mg) was dissolved in 10 ml of absolute methanol, and a current of an ozone-oxygen mixture was bubbled through at -65 to -70°C until the initial hydroxy ketone had disappeared (40 min, monitoring by TLC). The ozone was displaced by nitrogen (5 min) and the reaction mixture was left to assume room temperature; then 86 mg of 74% sodium tetrahydroborate was added and the mixture was stirred at 22°C for 1 h. The excess of hydride was decomposed by the addition of 20 ml of a 5% solution of hydrochloric acid, the product was extracted with ether (3 × 20 ml), and the extract was washed with water to neutrality and was worked up in the usual way to give 83 mg of reaction product which was chromatographed on a column containing 3 g of silica gel. A mixture of petroleum ether and diethyl ether (9:1) eluted 60 mg (69%) of drimane-8α,11-diol (VII).

Production of 8α-Hydroxy-14,15-bisnorlabdan-13-one (X) and "Sclareol Oxide" (XI). A solution of 100 mg of 8α-hydroxy-14,15-bisnorlabd-11-en-13-one (IV) in 3.5 ml of ethanol was treated with 36 mg of 10% Pd/C and, with stirring by a magnetic stirrer, a current of dry hydrogen was passed through the solution until hydrogenation was complete (3 h). The catalyst was filtered off and was washed with ethanol, and the solvent was distilled off in vacuum. The product (98 mg) was chromatographed on column containing 5 g of Al_2O_3 (activity grade III). Hexane eluted 73 mg (78% yield) of "sclareol oxide" (XI), mp 44-45°C (from petroleum ether), and then 14 mg (14%) of 8α-hydroxy-14,15-bisnorlabdan-13-one (X), mp 87-88°C (from petroleum ether). Compounds (X) and (XI) were identified by spectral and chromatographic comparison with authentic samples.

Ozonolysis of the Hydroxy Ketone (IV) by the Method of [1]. The hydroxy ketone (IV) (60 mg) was ozonized in 10 ml of methylene chloride and the product was worked up as described in [1]. This led to the isolation of 10 mg of a neutral fraction and 31 mg of an acid fraction. The latter, consisting, according to TLC, of two components, was chromatographed on a column containing 9 g of silica gel 100/250 μ deactivated by the addition of 10% of water. Petroleum ether–diethyl ether (4:1) eluted 5 mg of a product apparently consisting of the hydroxy acid (IX). PMR spectrum (ppm): 0.74 (3H, s), 0.91 (3H, s), 0.94 (3H, s), 0.91 (3H, s), 0.94 (3H, s) [C_4– and C_{10}–CH_3], 1.12 (3H, s) (C_8–CH_3), 2.03 (1H, s, C_9–H), 12.27 (1H, s, COOH).

Then the same solvent eluted 23 mg of 8αhydroxydriman-11-oil acid (VI) with mp 176-178°C.

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PRODUCTS OF THE OZONOLYSIS OF ISOABIENOL

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The ozonization of abienol in ethyl acetate in the presence of pyridine or in methanol followed by the reduction of the peroxides by methyl sulfide has given ambreinolide. On reduction of the peroxide products of the ozonolysis of isoabienol in methanol with potassium tetrahydroborate, the main reaction product was 15,16-bisnorlabdane-8,13,14-triol. Dimethyl sulfide first caused the rearrangement of the peroxide products of ozonization with the cleavage of the ordinary C-13–C-14 carbon bond, and then their reduction.

We [1] were the first to show that isoabienol (I) can be selectively oxidized with potassium permanganate to ambreinolide (II) – a valuable product for the perfumery industry [2]. With the discovery by Ekman et al. [3] of a readily available source of isoabienol, the question of its oxidation to ambreinolide has also acquired practical interest. A method for obtaining ambreinolide by the ozonization of isoabienol has been patented [4]. When ozonolysis was performed in absolute methanol at 0°C and the peroxides were

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