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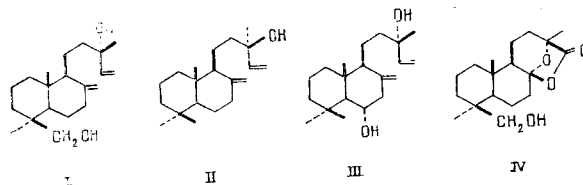
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The structure of the products of the ozonization of epitorulosol [13S-labda-8(20),14-diene-13,19-diol] (I) has been established. Compound (I) (1 g) was ozonized at -30°C in 100 ml of absolute CH_3OH until saturation. The O_3 was driven off by nitrogen, 1 ml of $(\text{CH}_3)_2\text{S}$ was added at -10°C , and the mixture was stirred for 1 h each at -10 , 0 , and 20°C and was worked up, and the product (1.13 g) was chromatographed on a column containing 45 g of silica gel. The following were eluted in the order of increasing polarity: 420 mg of 19-hydroxy-8,13;8,14-diepoxy-13S-15,20-bisnorlabdan-14-one (II), mp $141.5-142.5^{\circ}\text{C}$ (from petroleum ether), $[\alpha]_{\text{D}}^{23} -63^{\circ}$ (c 3.1); 255 mg of 8,13;8,14-diepoxy-13S-15,20-bisnorlabdane-14,19-diol (III), characterized in the form of the diacetate (IV) with mp $100-107^{\circ}\text{C}$ (from petroleum ether); and 117 mg of 19-hydroxy-14,15,20-trisnorlabdane-8,13-dione (V), mp $82-83^{\circ}\text{C}$ [from petroleum ether-diethyl ether (1:1)], $[\alpha]_{\text{D}}^{26} -40^{\circ}$ (c 1.7). The same products but in different ratios were formed on the ozonization of (I) in CH_2Cl_2 -Py or in hexane followed by decomposition of the ozonide by heating with H_2O . The $[\alpha]_{\text{D}}$ values were measured in CHCl_3 . Details of the IR and PMR spectra are given.

Continuing studies of the ozonolytic cleavage of labdanoids, we have investigated the products of the ozonolysis of epitorulosol (I).

Epitorulosol was first detected among the extractive substances of the bark of *Pinus contorta* Dougl. by Rowe and Scroggins, who established its structure [1]. The stereochemistry of this compound was elucidated later [2, 3]. Subsequently, compound (I) was found in the oleoresin of *Pinus banksiana* [4] and also in the oleoresins of some species of larch [5-7], and is a relatively accessible substance.

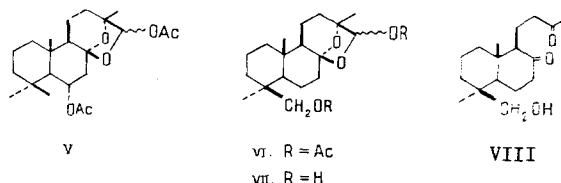
On the ozonization of epitorulosol in absolute methanol at -30°C followed by the treatment of the ozonization product with dimethyl sulfide, a mixture of three substances was obtained which were separated by column chromatography on silica gel. The predominating, least polar, compound, with the composition $\text{C}_{18}\text{H}_{28}\text{O}_4$, contained in its molecule, judging from the results of the IR spectroscopy, primary hydroxy, γ -lactone, and ketal groups. Its PMR spectrum contained the signals of AB systems belonging to a hydroxymethyl group at C-4 and also singlet signals of three methyl groups at quaternary carbon atoms. On the basis of these facts and the results of their comparison with the spectral characteristics of the products of the ozonization of manool (II) [8, 9] and larixol (III) [10], and also in view of the fact that under the ozonolysis conditions used a hydroxy group at C-19 should remain unchanged, the product under investigation was ascribed the structure and stereochemistry shown in formula (IV) (19-hydroxy-8,13;8,14-diepoxy-13S-15,20-bisnorlabdan-14-one).



The substance next in polarity eluted from the column proved to be sparingly soluble in the majority of organic solvents for hydroxy compounds. It was therefore acetylated with a mixture of acetic anhydride and pyridine and the subsequent work on its identification was

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carried out with the acetylation product, having the composition $C_{22}H_{34}O_6$. According to its spectral characteristics, its molecule contained a ketal group and two acetoxy groups. One of the acetoxy groups was present at C-19, as was shown by the presence in the PMR spectrum of the signals of an AB system at 3.77 and 4.23 ppm, and a second one at a carbon atom next to the oxygen of the ketal group, as was shown by the position of maximum in the IR spectrum at 1760 cm^{-1} and by the presence of a singlet one-proton signal at 5.88 ppm in the PMR spectrum. The combination of the characteristics given and the closeness of some of them to those for the diacetoxycetal (V) obtained from (III) [10] permitted the compound under investigation to be assigned the structure of the diacetate of 8,13;8,14-diepoxy-13S-15,20-bisnorlabdane-14,19-diol (IV) and, consequently, the second product of the ozonolysis of epitorulosol was 8,13;8,14-diepoxy-13S-15,20-bisnorlabdane-14,19-diol (VII).



Compounds (VI) and (VII) apparently form a mixture of epimers at C-14, since the diacetoxycetal (VII) melted diffusely even after having been repeatedly recrystallized.

The last compound eluted from the column was a hydroxycarbonyl compound with the composition $C_{17}H_{28}O_3$. Judging from its spectral characteristics, its molecule contained a primary hydroxy and two keto groups one of which was a methyl ketone group, while the other was present in a six-membered ring. On this basis, the product under investigation was ascribed to the structure of 19-hydroxy-14,15,20-bisnorlabdane-8,13-dione (VIII).

Compounds (IV), (VII), and (VIII) were also formed on the ozonization of epitorulosol in a mixture of methylene chloride and pyridine or in hexane followed by the decomposition of the ozonide by heating with water. In both cases, the quantitative compositions of the ozonization products were fairly close to one another and differed from that which was obtained when ozonization was carried out in methanol and the ozonide was decomposed with dimethyl sulfide. In the latter case, the hydroxylactone (IV) predominated in the mixture of substances (IV), (VII), and (VIII), while in the other two cases the yield of this substance was the lowest.

EXPERIMENTAL

Melting points were determined on a Boëtius instrument. Specific rotations were measured in chloroform on a Polamat S polarimeter. IR spectra were taken in carbon tetrachloride on a Specord-71-IR spectrophotometer. PMR spectra were recorded in carbon tetrachloride on a Tesla BS-467 instrument (60 MHz) with TMS as internal standard (the signals are given on the δ scale).

Ozonization of Epitorulosol. Method A. A current of ozonized oxygen was passed at -30°C through a solution of 1 g (3.3 mmole) of epitorulosol in 100 ml of absolute methanol until the appearance of a permanent blue coloration of the solution. The excess of ozone was displaced from the solution with nitrogen and the reaction mixture was left to warm up to -10°C , after which 1 ml of dimethyl sulfide was added to it and it was stirred for 1 h each at -10 , 0, and 20°C . The solvent was distilled off in vacuum, the residue was extracted with ether, the extract was washed with water, with sodium bicarbonate solution, and again with water and was dried with sodium sulfate and filtered, and the solvent was distilled off in vacuum. The residue (1.13 g) was chromatographed on a column containing 45 g of type L 40/100 μ silica gel that had been deactivated by the addition of 10% of water. Petroleum ether-diethyl ether (8:2) eluted 420 mg (41.6%) of crystalline 19-hydroxy-8,13;8,14-diepoxy-13S-15,20-bisnorlabdane-14-one (IV), mp $141.5\text{--}142.5^\circ\text{C}$ (from petroleum ether). $[\alpha]_D^{23} -63^\circ$ (c 3.1). Found, %: C 70.39; H 9.03. $C_{18}H_{28}O_4$. Calculated, %: C 70.13; H 9.09. IR spectrum (cm^{-1}): 1110, 1130 (C-O-C), 1790 (γ -lactone), 1010, 3540, 3630 (OH group); PMR spectrum (ppm): 0.90 (s, 3H, 10- CH_3), 0.96 (s, 3H, 4- CH_3), 1.32 (s, 3H, 13- CH_3), 3.36 (d, 1H, J = 3.66 (d, 1H, J = 11 Hz) (AB system, 2 H-19). The same solvent mixture eluted from the column 255 mg (25%) of crystalline 8,13;8,14-diepoxy-13S-15,20-bisnorlabdane-14,19-diol (VII), sparingly soluble in organic solvents. Part of it (80 Mg) was dissolved in 1.5 ml of pyridine, and this solution was treated with 0.4 ml of acetic anhydride and kept at room temperature for 15 h, after which it was worked up in the usual way. The residue (90 mg) was recrystallized three times

from petroleum ether, giving the diacetate of 8,13;8,14-diepoxy-13S-14,15-bisnorlabdane-14,19-diol (VI), mp 100-107°C. Found, %: C 66.75; H 8.55. $C_{22}H_{34}O_6$. Calculated, %: C 66.98; H 8.69. IR spectrum (cm^{-1}): 1040, 1060, 1130 (ketal group), 1230, 1730, 1760 (two acetoxy groups); PMR spectrum (ppm): 0.90 (s, 3H, 10-CH₃); 1.03 (s, 6H, 4- and 13-CH₃); 1.95 (s, 3H); 2.06 (s, 3H) (two OAc groups); 3.77 (d, 1H, J = 11 Hz); 4.23 (d, 1H, J = 11 Hz) (AB system, 2 H-19); 5.88 (s, 1H, H-14).

After the dihydroxyketal (VII), the same mixture of solvents eluted from the column 117 mg (12.7%) of crystalline 19-hydroxy-14,15,20-trisnorlabdane-8,13-diol (VIII), mp 82-83°C [from petroleum ether-diethyl ether (1:1)]. $[\alpha]_D^{26} -40^\circ$ (c 1.7). Found, %: C 72.66; H 9.59. $C_{17}H_{28}O_3$. Calculated, %: C 72.85; H 10.00. IR spectrum (cm^{-1}): 1110, 3620, 3635 (OH group), 1170, 1705 (C=O group).

PMR spectrum (ppm): 0.68 (s, 3H, 10-CH₃); 1.01 (s, 3H, 4-CH₃); 2.02 (s, 3H, OAc); 3.33 (d, 1H, J = 10 Hz); 3.66 (d, 1H, J = 10 Hz) (AB system, 2 H-19).

Method B. A current of ozonized oxygen was passed at -65 to -70°C through a solution of 100 mg of (I) in 10 ml of dry methylene chloride and 0.1 ml of dry pyridine until ozone broke through to the outlet from the reaction flask (10 min). The reaction mixture was allowed to assume room temperature and was washed with a 10% solution of sulfuric acid, with water, with sodium bicarbonate solution, and with water again and was dried over anhydrous sodium sulfate and filtered, and the solvent was distilled off in vacuum. The residue (110 mg) was chromatographed as described in the preceding experiment, leading to the isolation of 19 mg (18.8%) of the hydroxylactone (IV), 40 mg (39.6%) of the dihydroxyketone (VII), and 28 mg (30.4%) of the hydroxydiketone (VIII).

Method C. A current of ozonized oxygen was passed at 22°C through a solution of 100 mg of (I) in 10 ml of hexane until ozone broke through (10 min). The excess of ozone was driven off by the passage of dry nitrogen through the solution, and then 10 ml of water was added to it and then the reaction mixture was heated at 70°C for 1 h. The organic layer was separated off, dried with anhydrous sodium sulfate, and filtered, and the solvent was distilled off. The residue (98 mg) was chromatographed on a column of silica gel, with the isolation of 20 mg (19.8%) of the hydroxylactone (IV), 35 mg (34.7%) of the dihydroxyketal (VII), and 36 mg (39.1%) of the hydroxydiketone (VIII).

CONCLUSION

It has been established that the ozonization of epitorulosol forms 19-hydroxy-8,13;8,14-diepoxy-13S-15,20-bisnorlabdan-14-one, 8,13;8,14-diepoxy-13S-15,20-bisnorlabdane-14,19-diol, and 19-hydroxy-14,15,20-trisnorlabdane-8,13-dione.

LITERATURE CITED

1. J. W. Rowe and J. H. Scroggins, *J. Org. Chem.*, **29**, 1554 (1964).
2. L. J. Gough, *Chem. Ind. (London)*, 2059 (1964).
3. J. W. Rowe and G. W. Schaffer, *Tetrahedron Lett.*, 2633 (1965).
4. C. L. Bower and J. W. Rowe, *Phytochemistry*, **6**, 151 (1967).
5. E. N. Shmidt, A. I. Rezvukhin, and V. A. Pentegova, *Khim. Prir. Soedin.*, 61 (1967).
6. J. S. Mills, *Phytochemistry*, **12**, 2407 (1973).
7. E. N. Shmidt, L. E. Chupakhina, and V. A. Pentegova, *Izv. Sibirsk. Otd. Akad. Nauk SSSR, Ser. Khim.*, Issue No. 12, Series No. 5, 173 (1975).
8. R. C. Cambie, K. H. Joblin, and A. F. Preston, *Austr. J. Chem.*, **24**, 2365 (1971).
9. P. K. Grant and H. T. L. Liao, *Austr. J. Chem.*, **31**, 1791 (1978).
10. P. F. Vlad, A. N. Kyl'chik, E. N. Shmidt, M. N. Koltsa, V. N. Odinov, and V. A. Pentegova, *Khim. Prir. Soedin.*, 577 (1986).