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THE OXYMERCURATION–DEMERCURATION OF CARYOPHYLLENES

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The oxymercuration–demercuration of caryophyllene (I) at a molar ratio of olefin to mercury salt of 1:2 has been performed. Using various chromatographic methods, the following substances have been isolated from the crude product: clovene (II), 1%; caryophyllane 4,8-α-oxide (III), 52%; 9-epicaryophyllane 4,8-β-oxide (IV), 11%; caryolan-1-ol (V), 5.3%; dihydrocaryophyllen-4α-ol (VI), 11%; caryophyllan-4-ol 5,8-oxide (VII), 6.5%; the symmetrical mercury derivative of the 9-epi-4,8-β-oxide (VIII), 2.1%; and an unknown hydrocarbon, A, 1%. The structure of the oxide (IV) has been established by x-ray structural analysis.

Oxymercuration followed reductive demercuration is a simple method for hydrating olefins [1]. Under the action of mercury(II) salts, as a rule, di- and triolefins cyclize [2]. Cases are known of cyclization with the participation of the oxygen atom and the formation of intracyclic ethers as, for example, in the case of α-humulene [3] and of Δ³-carene [4].

According to literature, the oxymercuration–demercuration of caryophyllene (I) at a molar ratio of olefin to mercury salt of 1:1 leads to caryolan-1-ol (V) with a yield of 61% [5], while the same reaction at a ratio of 1:2 gives caryophyllane 4,8-α-oxide (III) with a yield of 83% [6]. It appears unlikely that the ratio of the reactants would affect the direction of cyclization in this way. In the present paper we give the results of a more detailed study of the reaction of caryophyllene with mercury(II) acetate.

The reaction was carried out at room temperature by a standard procedure [1], and the mixture of products was separated into hydrocarbon, ether, and alcohol fractions (Table 1).
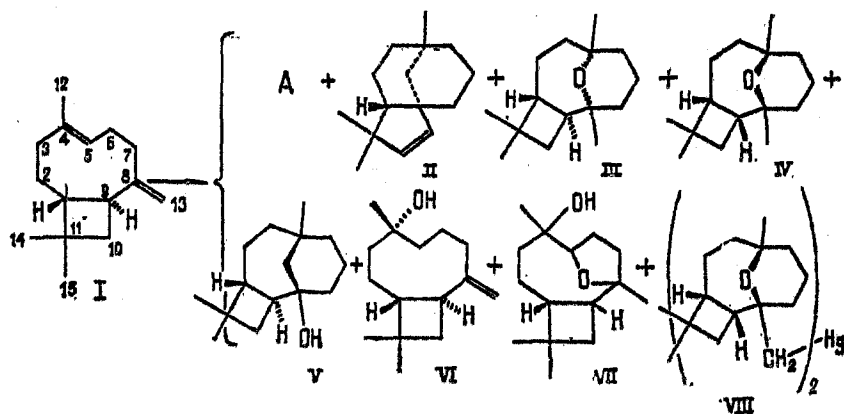
The hydrocarbon fraction was a mixture of unchanged caryophyllene, clovene (II), and a hydrocarbon A. According to ^{1}H NMR, ^{13}C NMR, IR spectroscopy, and mass spectrometry, the last-mentioned compound was a tricyclic sesquiterpene hydrocarbon, and its structure is currently being studied. The yield of this product can be increased considerably by performing the reaction in the presence of sodium acetate.

The ether fraction was chromatographically homogeneous (according to thin-layer chromatography (TLC)) but analytical gas–liquid chromatography (GLC) showed the presence of two components in a ratio of 83:17. The individual compounds were isolated with the aid of preparative GLC. The main product was identified from its spectral characteristics as caryophyllane 4,8-α-oxide (III) [6]. The minor product had mp 54.5–55.5°C. The mass of the molecular ion in the mass spectrum of this compound was 222, which corresponds to the composition $C_{15}H_{26}O$. The molecule of this ether contains two geminal methyl groups ([1]H

NMR: 0.93 ppm, 6 H) and two $CH_3-\overset{|}{\underset{|}{C}}-OR$ fragments (1.10 ppm, 3 H; 1.14 ppm, 3 H). The

oxygen atom links two tertiary carbon atoms (^{13}C NMR: 74.4 ppm, singlet, 75.9 pp, singlet) and forms the ether system of tetrahydropyran (IR: 1062 cm^{-1}). These facts are in harmony with the structure of a caryophyllane 4,8-oxide but differ from the characteristics of the known α-oxide (III) and β-oxide (IX) [6]. It was established by x-ray structural analysis that the minor product in the ether fraction was 9-epicaryophyllane 4,8-β-oxide (IV). The structure of one of the two crystallographically independent molecules of the oxide (IV) is shown in Fig. 1.

The formation from caryophyllene itself of derivatives with the cis linkage of the butane fragment has not been observed previously, but such compounds are found in nature: 9-Epicaryophyllene α-oxide and 2-epicaryolane-1,9-diol have been isolated from *Senecio crassissimus* Humb. [7], and the alcohol koraiol from the oleorein from *Pinus pumila* (Pall.) Rgl. and *Pinus koraiensis* Sieb et Zucc. [8].

In the reaction of caryophyllene that was being studied, in addition to the α-oxide (III) it would have been possible to expect the formation of the β-oxide (IX). We synthesized the pure oxide (IX) by the cyclization of 4,5-dihydrocaryophyllen-4β-ol (X), which was obtained by the reduction of caryophyllene α-oxide (XI) with lithium in ethylenediamine.
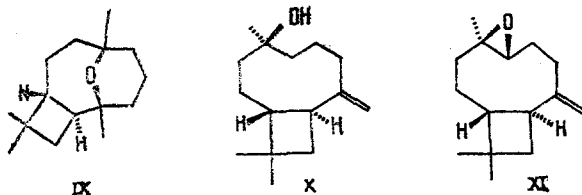
^{1}H NMR spectroscopy is unsuitable for the analysis of the mixture of ethers (III) and (IX), since the signals of the protons of the methyl groups in the spectra of these compounds have similar values of the chemical shifts. GLC using capillary columns likewise does not give satisfactory results because of the small difference in the retention times.

Ratio of caryo-phyllene to mercury salt	Solvent	Deg. of con-version of the caryophyllene, %	Yields of products,* %							
			hydrocarbon fraction		ether fraction		alcohol fraction			
			A	II	III	IV	V	VI	VII	VIII
1:2	THF —H₂O	99.9	1	1	52	11	5,3	11	6,5	2,1
1:1	THF —H₂O	58	+†	+	52	10	7,0	12	5,1	+
1:2	Acetone —H₂O	99	+	+	63	5	11	4,0	5,2	+
1:2	THF ; H₂O NaOAc	84	29	—	38	5	1,5	—	19	+

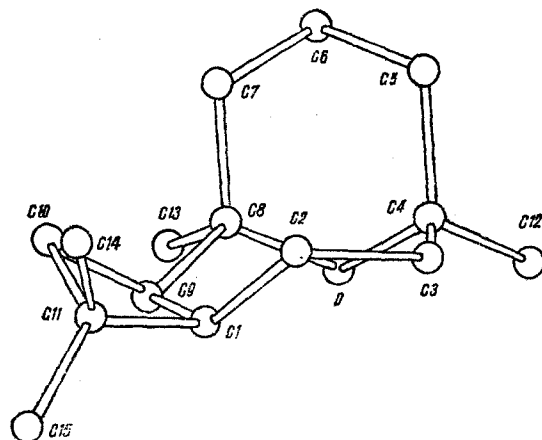*Calculated on the caryophyllene that had reacted.
†Yield of product less than 1%.

Fig. 1. Structure of one of the two crystallographically independent mole-cules of 9-epicaryophyllane 4,8-β-oxide according to the results of x-ray struc-tural analysis.

TABLE 2. Chemical Shifts of the Protons in the ^{1}H NMR Spectra and Specific Rotations of Some Cyclic Ethers of the Caryophyllene Series

Chemical shifts, δ,scale	VII	XII	XIII	XIV	XV
2CH₃(C-11)	0,94*	0,95 0,97	0,95 0,96	0,98	1,02
CH₃(C-4)	1,30	1,00	1,32	1,31	1,20
H(C-5)	4,01	3,99	3,95	3,93	3,55
$[\alpha]_D$	+55,3°	—49°	—62°	—2,6°	

*In ppm relative to TMS for solutions in CDCl₃.

To study the composition of the mixture it is possible to use difference in the IR spectra and the Raman spectra of these isomers.

For the quantitative evaluation of the amounts of the oxides (III) and (IX) in the reaction products we used absorption bands in their IR spectra: at 824 cm^{-1} for the oxide (III) and at 841 cm^{-1} for the oxide (IX). It was established by special experiments that the lower limit of detection of (IX) in (III) was 3%. No β-oxide could be detected in the sample of the α-oxide (III) obtained in the oxymercuration-demercuration of caryophyllene. At the same time, in the Raman spectrum of this specimen the bands at 263, 535, 600, and 735 cm^{-1} were appreciably broadened, apparently because of the presence of a small amount

of the β-oxide (IX), which has strong bands at 259, 540, 589, and 743 cm^{-1}. Thus the α-oxide (III) formed in the reaction contained not more than 3% of the β-oxide (IX).

The alcohol fraction contained not less than ten compounds (according to TLC), and with the aid of column chromatography the four main components were isolated: (V), (VI), (VII), and (VIII).

The crystalline alcohol (V) was identified by its physicochemical constants and spectral characteristics as caryolan-1-ol [9].

Compound (VI), with mp 89–90°C, was a tertiary alcohol (3624 cm^{-1}; ^{13}C NMR: 78.8 ppm, singlet), the molecule of which contained an exocyclic double bond (3087, 1641, 898 cm^{-1}; ^{1}H NMR: 4.66 ppm, 2 H; ^{13}C NMR: 141.6 ppm, singlet, 103.9 ppm, triplet). The cyclization of this alcohol led to the 4,8-α-oxide (III). Thus, alcohol (VI) is 4,5-dihydrocaryophyllen-4α-ol. The cyclization of the crude product (VI) (not purified by crystallization) gave the α-oxide (III) not contaminated with the β-oxide (IX) (according to the IR spectrum), i.e., the reaction forms only one of the two epimeric dihydrocaryophyllenols, namely the α-alcohol (VI).

When caryophyllene was hydrated in chloroacetic acids, Japanese authors obtained a dihydrocaryophyllen-4-ol [10], which was similar in spectral characteristics and specific rotation to the β-alcohol (X) and is therefore 4,5-dihydrocaryophyllen-4β-ol.

Alcohol (VII) (3622 cm^{-1}) had mp 82–83°C. The ^{1}H NMR spectrum of this compound contained the signals of the protons of two geminal methyl groups (0.96 ppm, 6 H), of two

fragments $\mathrm{CH_3}$—$\overset{|}{\underset{|}{\mathrm{C}}}$—OR (1.07 ppm and 1.30 ppm, 3 H each) and of a H—$\overset{|}{\underset{|}{\mathrm{C}}}$—OR group (4.01 ppm,

1 H, triplet, J = 7 Hz). The ^{13}C NMR spectrum showed three weak-field signals: 75.5 ppm (singlet), 84.6 ppm (singlet), and 85.1 ppm (doublet). An intense absorption band at 1076 cm^{-1} in the IR spectrum is characteristic of cyclic ethers of the tetrahydrofuran series.

The mass of the molecular ion was 238, which corresponds to the empirical formula $C_{15}H_{26}O_2$. This alcohol is tertiary, since it was not acetylated by acetic anhydride in pyridine and, moreover, in the ^{1}H NMR spectrum of the p-nitrobenzoate a weak-field triplet was observed at 4.51 ppm, i.e., the downfield shift amounted to 0.5 ppm as compared with 1.5 ppm for the p-nitrobenzoates of secondary alcohols. On the basis of these facts the structure of caryophyllan-4-ol 5,8-oxide is suggested for compound (VII).

A comparison of the ^{1}H NMR spectrum of this compound with the spectra of the series of caryophyllanediol oxides (XII), (XIII), (XIV), and (XV) (Table 2) obtained from epoxides and epoxydiols of caryophyllene and isocaryophyllene [11] confirmed that in the molecule of the alcohol (VII) the oxygen bridge actually links carbon atoms C-5 and C-8, and the hydroxy group is tertiary and is located at the C-4 atom (as in compounds (XII-XIV)). Furthermore, the methyl group at C-4 and the 5,8-oxygen bridge are present in the cis position relative to one another (as in compounds (XIII) and (XIV)).
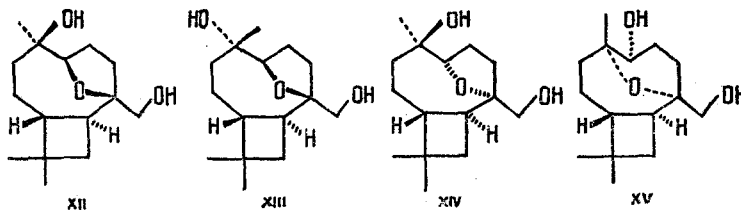

A comparison of the specific rotations of the alcohols (VII), (XIII), and (XIV) (Table 2) does not permit a choice to be made between the two possible structures (VII.1) and (VII.2). The large shift of the specific rotation to the right in compound (VII) as compared with (XIII) and (XIV) cannot be due only to the replacement of a hydromethyl group by a methyl group at C-8. It is possible that in the molecule of the alcohol (VII) the nonane and butane rings have a cis linkage, since inversion of the configuration at C-9 gives a change in the specific rotation to the right. For the 4,8-β-oxide (IX), $[\alpha]_D$ − 73°, and for the 9-epi-4,8-β-oxide (IV) the figure is −30°; for caryophyllene α-oxide (XI) it is

−68° and for 9-epicaryophyllene α-oxide it is +8° [12].

The crystalline product (VIII) (mp 128-130°C) was sparingly soluble in organic solvents. A group of ions in the mass spectrum of this compound (m/z, 416, 418, 419, 420, 421, 422, 424 with intensities corresponding to the natural proportions of the mercury isotopes ^{196}Hg, ^{198}Hg, ^{199}Hg, ^{200}Hg, ^{201}Hg, ^{202}Hg, and ^{204}Hg) belong to the $C_{15}H_{24}OHg$ fragment.

The IR spectrum of compound (VIII) is similar to that of the oxide (IV) in the 1400-900 cm^{-1} region; in the ^{1}H NMR spectrum there are the signals of the protons on three methyl groups (0.92 ppm, 3 H, and 1.13 ppm, 6 H) and of one methylene group of the

$-\overset{|}{\underset{|}{C}}-CH_2-Hg-R$ fragment (2.08 ppm, 2 H). The treatment of this mercury derivative with

lithium tetrahydroaluminate did not give the product of the reductive substitution of mercury by hydrogen but led to the elimination of the mercury residue [13] with the formation of the crystalline alcohol (XVI) (3613 cm^{-1}) having mp 109-112°C the molecule of which contains an exocyclic double bond (3086, 1648, 894 cm^{-1}; ^{1}H NMR; 4.82 pp, doublet J = 1 Hz, 1 H, 4.90 ppm, doublet, J = 1 Hz, 1 H) and three methyl groups (^{1}H NMR: 0.89 ppm, 3 H; 1.04 ppm, 3 H; 1.15 ppm, 3 H). This permits the proposal for compound (VIII) of the structure of the symmetrical mercury derivative of the 9-epi-oxide (IV), and for the alcohol (XVI) the structure of 9-epi-4,5-dihydrocaryophyllen-4β-ol.

VII.1   VII.2   XVI
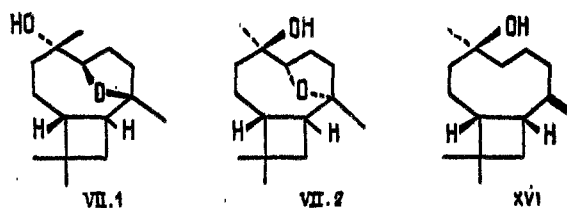
At ratio of the reactants of 1:1, the same set of reaction products was obtained as at a ratio of 1:2 (see Table 1). Thus, the main direction of cyclization in both cases is the formation of 4,8-oxides, and caryolan-1-ol (V) is not formed with a high yield at a 1:1 ratio, as reported by Misra and Chandra [5].

The replacement of tetrahydrofuran by acetone somewhat changed the ratio of the yields of the products (see Table 1). When the reaction was performed in the presence of sodium acetate, part of the caryophyllene isomerized into hydrocarbon A, the yield of alcohol (VII) rose, the yields of the oxides (III) and (IV) and of caryolan-1-ol (V) fell, while the α-alcohol (VI) was not formed.

EXPERIMENTAL

^{1}H NMR spectra (δ scale, HMDS) were recorded on Varian HA 56/60A (60 MHz) and Varian HA-100 (100 MHz) instruments for solutions in CCl$_4$, ^{13}C NMR spectra on a Bruker-Physik AG HX-90 (22.63 MHz) instrument for solutions in deuterochloroform, mass spectra on a MS-902 instrument with a glass inlet system, and IR spectra on a UR-20 instrument using 1% solutions in CCl$_4$. The IR spectra of the oxides (III) and (IX) for the purposes of estimating their quantitative amounts in the mixture were recorded on a Specord IR-75 spectrometer (c = 2-10% in hexane, d = 0.27 mm). The Raman spectra of the pure liquids were recorded on a Coderg PH-1 spectrometer with a helium-neon laser, λ_{exc} = 6328 Å). Analytical GLC was performed on a Chrom-41 instrument with 3.5 m × 3 mm column containing 10% of the stationary phase Tween-65 on Celite C-22 (0.16-0.20 mm) with nitrogen as the carrier gas at a rate of flow of 30 ml/min with the temperature of the thermostat being raised from 120 to 165°C at the rate of 2°C per minute. Preparative GLC was carried out on a Pye 405 instrument with a 5m × 6 mm column containing 12% of the stationary phase Tween-65 on Celite C-22 (0.20-0.25 mm) with helium as the carrier gas at a rate of flow of 150 ml/min and at a temperature of 169°C. Optical rotations were measured on a Zeiss polarimeter for solutions in CHCl$_3$ and pure liquids.

(−)-Caryophyllene was isolated from the wastes of oil of cloves (*Eugenia caryophyllata*) by chromatography on silica gel, and the purified product had $[\alpha]_D^{19}$ − 8.85° (d_4^{20} = 0.9025).

The oxymercuration—demercuration reaction was carried out by a standard procedure [1]. The mercuration stage took 4 h at room temperature.

The reduction of the organomercury compounds was performed at 40-45°C by the addition first of a 3 N aqueous solution of NaOH (3.6 ml of solution per 1 g of mercury salt) and then of a solution of NaBH$_4$ in 3 N aqueous solution of NaOH (3.6 ml of solution containing 0.08 g of tetrahydroborate per 1 g of mercury salt). The reaction mixture was stirred for 1 h after the addition of the reducing agent and then the aqueous layer was saturated with sodium chloride and extracted with ether. The reaction products were separated with the aid of adsorption column chromatography under pressure [14] on Chemapol silica gel (0.040-0.100 mm). The eluent was petroleum ether (bp 40-70°C) with increasing proportions (from 0 to 100%) of diethyl ether.

The Oxymercuration—Demercuration of Caryophyllene at a Ratio of Olefin to Mercury Salt of 1:2. The reaction of 10.0 g (49 mmole) of caryophyllene and 31.2 g of Hg(AcO)$_2$ (98 mmole) in 150 ml of anhydrous tetrahydrofuran (THF) gave 10.7 g of a crude product; when this was chromatographed, petroleum ether eluted 0.21 g of hydrocarbons; petroleum ether containing 3% of diethyl ether eluted 6.88 g of a mixture of the ethers (III) and (IV) in a ratio of 83:17 (according to GLC); and diethyl ether eluted 3.33 g of a mixture of alcohols. The hydrocarbon fraction yielded 0.010 g of caryophyllene, 0.090 g of hydrocarbon A, and 0.110 g of clovene (II), the IR and ^{1}H NMR spectra of which coincided with those given in the literature [15]. From the ether fraction the oxides (III) and (IV) were isolated by preparative GLC. Chromatography of the alcohol fraction yielded 0.58 g of caryolan-1-ol (mp 93.5-94.5°C (from hexane), $[\alpha]_D^{18}$ —7.94° (c 2.36), the IR spectrum coinciding with that given in the literature [9]), and 1.15 g, 0.76 g, and 0.32 g of substances (VI), (VII), and (VIII), respectively.

Hydrocarbon A. $[\alpha]_D^{19}$ + 146.3° $\left(d_4^{19} = 0.924\right)$. IR spectrum, cm^{-1}: 3030, 1652, 1462, 1370, 1290, 1267, 1222, 1136, 1121, 1035, 892. ^{1}H NMR: 0.90 (s, 6 H); 0.96 (s, 3 H); 5.43 (t, J = 6 Hz, 1 H). ^{13}C NMR: 142.1 (s), 126.7 (d); M$^+$ 204 (C$_{15}$H$_{24}$).

Caryophyllane 4,8-α-Oxide (III). $[\alpha]_D^{19}$ —33.25° (c 4.33). IR spectrum (in CCl$_4$), cm^{-1}: 1220, 1194, 1111, 1069, 1033, 1023, 980; (in the pure form): 981, 903, 886, 872, 858, 834, 812, 670, 640; (in hexane): 985, 974, 952, 892, 878, 862, 849, 824, 812, 802. Raman spectrum, cm^{-1}: 735, 706, 600, 535, 263. ^{1}H NMR: 0.92 (s, 3 H); 0.97 (s, 6 H); 1.04 (s, 3 H); ^{13}C NMR: 73.8 (s), 72.6 (s); M$^+$ 222 (C$_{15}$H$_{26}$O).

9-Epicaryophyllane 4,8-β-Oxide (IV). mp 54.5-55.5°C (from hexane, $[\alpha]_D^{21}$ —32.2° (c 2.83) . IR spectrum (in CCl$_4$), cm^{-1}: 1340, 1285, 1220, 1197, 1120, 1100, 1062, 1015, 990; (0.25% in KBr): 1016, 993, 982, 949, 935, 907, 896, 874, 858, 837, 820, 788, 752, 696, 624, 586, 527, 464, 426 cm^{-1}. ^{1}H NMR: 0.93 (s, 6 H); 1.10 (s, 3 H); 1.14 (s, 3 H); M$^+$ 222 (C$_{15}$H$_{26}$O).

Dihydrocaryophyllen-4α-ol (VI). mp 89-90°C (from hexane); $[\alpha]_D^{19}$ + 46.5° (c 2.03). IR spectrum, cm^{-1}: 3624, 3087, 1641, 1473, 1453, 1380, 1192, 1136, 1109, 1093, 1078, 898. ^{1}H NMR: 0.98 (s, 6 H); 1.08 (s, 3 H); 4.66 (broad signal, 2 H). ^{13}C NMR: 31.4 (q); 32.2 (t); 33.8 (t); 37.2 (q); 37.6 (q); 40.4 (s); 42.3 (t); 43.9 (t); 44.8 (t); 46.0 (t); 48.6 (d); 57.5 (d); 78.8 (s); 103.9 (t); 141.6 (s); M$^+$ 222 (C$_{15}$H$_{26}$O).

Caryophyllan-4-ol 5,8-Oxide (VII). mp 82-83°C (from CCl$_4$), $[\alpha]_D^{19}$ + 56.3° (c 1.47). IR spectrum, cm^{-1}: 3622, 1471, 1389, 1377, 1303, 1127, 1111, 1076, 1049, 938, 884. ^{1}H NMR: 0.93 (s, 6 H); 1.00 (s, 3 H); 1.19 (s, 3 H); 3.84 (t, J = 7 Hz, 1 H). ^{1}H NMR (CDCl$_3$) (ppm): 0.94 (s, 6 H); 1.04 (s, 3H); 1.30 (s, 3 H); 4.01 (t, J = 7 Hz, 1 H). ^{13}C NMR; 20.7 (q); 25.4 (q); 25.6 (t); 26.5 (t); 27.2 (q); 30.0 (q); 32.0 (t); 34.1 (s); 36.3 (t); 38.9 (t); 47.7 (d); 48.6 (d); 75.5 (s); 84.6 (s); 85.1 (d); M$^+$ 238 (C$_{15}$H$_{26}$O$_2$).

Compound (VIII). mp 128-130°C (from acetone—hexane). IR spectrum (in CHCl$_3$), cm^{-1}: 1340, 1285, 1260, 1128, 1098, 1063, 1030, 1011, 990. ^{1}H NMR (CDCl$_3$): 0.92 (s, 3 H); 1.13 (s, 6 H); 2.08 (s, 2H).

Cyclization of the α-Alcohol (VI). A solution of 84 mg (0.315 mmole) of the alcohol (VI) in 3 ml of THF was added to a solution of 84 mg (0.330 mmole) of Hg(AcO)₂ in 6 ml of aqueous THF (1:1). After being stirred at room temperature for 30 min, the reaction mixture was worked up in the usual way. Chromatography of the crude product yielded 40 mg of the oxide (III).

Cyclization of the Alcohol (VI) (crude product). From 280 mg of the alcohol was obtained 150 mg of the oxide (III) containing none of the oxide (IX) as impurity (according to IR spectroscopy).

Benzoylation of the Alcohol (VII). A mixture of 70 mg (0.29 mmole) of the alcohol (VII) and 120 mg (0.70 mmole) of p-nitrobenzoyl chloride in 3 ml of pyridine was heated at 80°C for 16 h. By chromatography, 50 mg of the benzoate was isolated with ^{1}N NMR (CDCl₃), ppm: 0.96 (s, 6H); 1.12 (s, 3 H); 1.78 (s, 3 H); 4.51 (t, J = 12 Hz, 1 H); 8.15 (4 H).

Reduction of Compound (VIII). A mixture of 25 mg of compound (VIII) with 10 mg of LiAlH₄ in 2.5 ml of dry ether was heated for 5 min. After the excess of reducing agent had been decomposed with moist ether, the ethereal solution had been washed with water and dried over anhydrous sodium sulfate, and the solvent had been driven off, 10 mg of the alcohol (XVI) was obtained: mp 109-112° (from hexane), $[\alpha]_D^{20} + 23.4°$ (c 1.28). IR spectrum, cm⁻¹: 3613, 3086, 1648, 1457, 1375, 1340, 1260, 1223, 1192, 1100, 1063, 992, 950, 940, 894 cm⁻¹.

^{1}H NMR spectrum: 0.89 (s, 3 H); 1.04 (s, 3 H); 1.15 (s, 3 H); 4.82 (d, J = 1 Hz, 1 H); 4.90 (d, J = 1 Hz, 1 H).

Reduction of Caryophyllene α-Oxide (XI). A mixture of 2.22 g (10 mmole) of the oxide (XI) with mp 61-62°C and $[\alpha]_D^{21} -67.5°$ (c 1.92) ((XI) was obtained by the reaction of caryophyllene with a peracid [16]), 15 ml of hexane, 7 ml of anhydrous ethylenediamine, and 0.28 g of lithium (0.4 g-atom) was heated at 60-70°C with vigorous stirring for 2 h. After cooling to room temperature, 20 ml of water was carefully added to the reaction mixture. The layer of hexane was separated off and the aqueous layer was extracted with a mixture of ether and hexane (1:1). The organic extracts were combined and dried over anhydrous magnesium sulfate. Elimination of the solvent yielded 2.10 g of crude product, the chromatography of which gave 0.75 g of the β-alcohol (X) with mp 88-89°C (from hexane, $[\alpha]_D^{24} -7.5°$ (c 3.22). IR spectrum, cm⁻¹: 3624, 3085, 1642, 1496, 1460, 1377, 1295, 1271, 1119, 963, 936, 899, 874 cm⁻¹. ^{1}H NMR: 0.99 (s, 6 H); 1.11 (s, 3 H); 4.76 (s, 2 H).

Cyclization of the β-Alcohol (X). As described for the α-alcohol, 220 mg (1 mmole) of the alcohol (X) yielded 120 mg of the β-oxide (IX), $[\alpha]_D^{20} -71.7°$ (c 2.05). IR spectrum (in CCl₄), cm⁻¹: 1468, 1455, 1392, 1377, 1289, 1240, 1218, 1122, 1102, 1081, 1062, 1013, 997, 946, 902 cm⁻¹; (in the pure state): 948, 907, 864, 851, 827, 794, 763, 745, 670, 581; (in hexane): 987, 968, 898, 856, 841, 817. Raman spectrum, cm⁻¹: 760, 743, 614, 589, 540, 259. ^{1}H NMR: 0.94 (s, 3 H); 0.97 (s, 6 H); 1.03 (s, 3 H).

Oxymercuration—Demercuration of Caryophyllene at a Ratio of 1:1. From 2.04 g (10 mmole) of caryophyllene and 3.19 g (10 mmole) of Hg(AcO)₂ was obtained 2.12 g of a crude product the chromatography of which yielded 0.84 g of caryophyllene, 0.80 g of a mixture of the ethers (III) and (IV) (84:16, according to GLC), 0.090 g of caryolan-1-ol (V), 0.154 g of the α-alcohol (VI), and 0.071 g of the alcohol (VII). Products A, (II), and (VII) were formed with yields of less than 1%.

Oxymercuration—Demercuration of Caryophyllene in Aqueous Acetone. A mixture of 1.02 g (5 mmole) of caryophyllene and 3.19 g (10 mmole) of Hg(AcO)₂ in 40 ml of aqueous acetone (1:3) was stirred at room temperature for 2 h. After elimination of the solvent in vacuum and reduction, 0.010 g of caryophyllene, 0.760 g of a mixture of the ethers (III) and (IV) (93:7 according to GLC), 0.120 g of caryolan-1-ol (V), 0.044 g of the alcohol (VI), and 0.061 g of the alcohol (VII) were isolated. Products A, (II), and (VIII) were formed with yields of less than 1%.

Oxymercuration—Demercuration of Caryophyllene in the Presence of Sodium Acetate. The reaction of 2.04 g (10 mmole) of caryophyllene and 6.40 g (10 mmole) of Hg(AcO)₂ in

TABLE 3. Coordinates of the Atoms ($\times 10^4$ and 10^3 for H) of the Two Crystallographically Independent Molecules of 9-Epicaryophyllane 4,8-β-Oxide (IV)*

Atom	x	y	z	Atom	x	y	z
O	3344(2)	2705(0)	4801(1)	1H5	208	—136	524
	2210(2)	6633(6)	8378(1)		383	266	895
C1	1161(2)	3914(8)	4019(2)	2H5	300	—155	590
	3166(3)	7515(9)	10282(2)		343	290	797
C2	0849(3)	2334(9)	4628(2)	1H6	438	—087	489
	4013(3)	6065(9)	9965(2)		211	086	857
C3	1586(3)	2627(9)	5369(2)	2H6	348	—320	469
	4164(3)	6551(9)	9139(2)		157	275	814
C4	2767(4)	1748(9)	5389(2)	1H7	221	—086	389
	3268(3)	5742(9)	8542(2)		225	285	987
C5	2809(4)	—0739(9)	5364(2)	2H7	339	—117	346
	3240(4)	3253(9)	8497(2)		114	239	949
C6	3458(4)	—1560(9)	4727(2)	H9	260	487	352
	2093(4)	2365(9)	8597(2)		149	875	1004
C7	2949(3)	—0518(9)	3989(2)	1H10	147	297	235
	1754(3)	3298(9)	9343(2)		115	642	1106
C8	3136(3)	1956(8)	4020(2)	2H10	143	067	287
	1611(3)	5758(9)	9281(2)		193	441	1076
C9	2214(3)	3350(8)	3618(2)	1H12	345	435	617
	1937(3)	7050(8)	10003(2)		428	614	762
C10	1473(3)	2471(9)	2930(2)	2H12	296	206	658
	1770(3)	6035(9)	10797(2)		293	616	738
C11	0490(3)	3734(9)	3212(2)	3H12	411	209	615
	2885(3)	7076(9)	11120(2)		352	854	781
C12	3415(3)	2578(9)	6107(2)	1H13	437	412	366
	3482(3)	6723(9)	7777(2)		—017	573	940
C13	4208(3)	2454(10)	3679(2)	2H13	486	111	393
	0414(3)	6268(9)	9012(2)		030	823	892
C 4	—0606(3)	2531(10)	3156(2)	3H13	418	236	309
	3629(3)	5596(11)	11617(2)		018	520	849
C15	0339(3)	5949(9)	2840(2)	1H14	—121	328	344
	2709(4)	9225(10)	11522(2)		336	500	1213
H1	113	563	422	2H14	—093	231	261
	343	916	1016		444	627	1181
1H2	011	263	478	3H14	—056	100	341
	475	620	1026		379	415	1137
2H2	081	068	445	1H15	123	673	288
	395	460	1007		240	912	1197
1H3	162	430	550	2H15	—013	671	315
	432	838	902		230	1027	1124
2H3	124	191	571	3H15	007	572	225
	478	582	901		356	983	1165

*The first line gives the coordinates of the atom in one molecule, and the second line gives the coordinates of the atom in the other molecule.

40 ml of anhydrous THF (1:1) was performed in the presence of 0.54 g of NaOAc·3H$_2$O (4 mmole). The crude product yielded 0.32 g of caryophyllene, 0.50 g of hydrocarbon A, 0.81 g of a mixture of the ethers (III) and (IV) (89:11 according to GLC), 0.028 g of caryolan-1-ol (V), and 0.38 of the alcohol (VII). The yield of (VIII) was less than 1%. No clovene (II) or the alcohol (VI) was formed.

X-Ray Structural Analysis. The x-ray structural experiment was performed on a Syntex P2$_1$ diffractometer at a temperature of the crystal of —105°C, using Mo radiation with a graphite monochromator. The crystallographic characteristics of 9-epicaryophyllane 4,8-β-oxide (IV): a=12.252 (3), b=6.168 (2), c=17.704 (6) Å, β=95.24 (2)°, z=4, sp. gr. P2$_1$. The intensities of 2601 reflections of a crystal with dimensions of 0.5 × 0.5 × 0.7 mm^3 were measured by the 2Θ:Θ scanning method in the 2Θ < 50° region. In the calculations 2382 reflections with I > 2σ were used. The structure was interpreted by the direct method using the MULTAN-XTL program. The hydrogen atoms found from a difference synthesis took no part in the full-matrix anisotropic approximation by the method of least squares. The final values of the R factors were: R = 0.050, R$_w$ = 0.046, W = σ$_F^2$. The coordinates of the atoms of the molecules are given in Table 3.

The crystal of the oxide (VI) is constructed of two crystallographically independent molecules differing slightly from one another (the structure of one of them is shown in Fig. 1). In the butane ring, which is cis-linked to the remainder of the molecule, the mean length of the C—C bond is 1.567 Å, and the mean torsional angle is 16°. The epoxide ring between the C-4 and C-8 atoms forms seven- and six-membered rings in the molecule, which have the chair and distorted boat conformations, respectively. The mean length of a C—O bond is 1.45 Å and the mean C—O—C valence angle is 120.1°. The intermolecular contacts in the crystal are the usual ones.

SUMMARY

1. The products of the oxymercuration—demercuration reaction of caryophyllene under various conditions have been studied.

2. It has been shown that the direction of cyclization does not depend on the ratio of the reactants in the standard procedure for performing the reaction.

3. A compound with the cis linkage of butane and nonane rings has been synthesized from caryophyllene. The structure of 9-epicaryophyllane 4,8-β-oxide has been established for it by x-ray structural analysis.

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