COMPOSITION OF THE NEUTRAL FRACTION OF THE OLEORESIN OF PINUS SIBIRICA

III. Structure of the Sesquiterpene Hydrocarbon D-γ-Muurolene

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Earlier, in a study of the composition of the sesquiterpene hydrocarbons of the oleoresin of Pinus sibirica R. Mayr (Siberian stone pine) [1], we isolated the hydrocarbon D-muurolene. The IR spectra of chromatographic fractions of muurolene differed slightly with respect to the intensity of the bands of the exomethylene double bond, which was explained by the presence of an impurity.

In a further study of the muurolene fractions obtained from the oleoresin of Pinus sibirica [1], we separated them on silica gel impregnated with silver nitrate [2, 3] into three individual hydrocarbons: muurolene-1, muurolene-2, and muurolene-3, [1, 4, 5].

The object of the present work was to show the structure of muurolene-3. The IR spectrum of this hydrocarbon has bands at 890, 1655 cm^{-1} (exomethylene double bond); 837, 1680 cm^{-1} (trisubstituted double bond); 1380, 1395 cm^{-1} (isopropyl group). In the UV spectrum, there is no absorption in the 200-400 mμ region. In the mass spectrum of the hydrocarbon, the fragment with m/e 161 (M − 43) shows the presence of an isopropyl group.

The exhaustive hydrogenation and perbenzoic acid titration of muurolene-3 confirmed the presence of two double bonds in it. The determination of methylene double bonds by Naves's method [6] showed that the amount of formaldehyde liberated corresponded to one methylene group. Muurolene-3 can be included among the hydrocarbons of the cadinene type, since on dehydrogenation it gave 1, 6-dimethyl-4-isopropylnaphthalene [7-10].

It is known [5, 8-10] that cadinene hydrocarbons have a trans-linkage of the rings and differ from one another by the position of the double bonds at C_1 and C_6.

According to Westfeld [5], D-ε-muurolene differs from ε-cadinene by a cis-linkage of the rings while having the analogous position of the double bond. Consequently, it may be expected that, in addition to the cadinene series, hydrocarbons of a muurolene series with cis-linkage of the rings exist.

On the basis of what has been said above, we can put forward for muurolene-3 three structures, (I), (II), and (III), containing a trisubstituted double bond and an exomethylene double bond.

To establish the position of the double bonds in muurolene-3, we used the method which has been employed repeatedly in the study of the structure of the cadinenes, of introducing a methyl group at the position of the trisubstituted double bond [8, 11-15]. The formation of the corresponding trimethylisopropylnaphthalene unambiguously determines the position of both bonds.

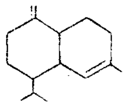
When murrolene-3 was oxidized with the calculated amount of perbenzoic acid, we obtained a monoepoxide (IV). The IR spectrum of the latter still contained the absorption bands of the exomethylene double bonds and bands appeared at 865 and 917 cm^{-1} (epoxide group). The reduction of the monoepoxide with lithium aluminum hydride gave a secondary alcohol with absorption bands in the IR spectrum at 1122 and 3612 cm^{-1}. Oxidation of the alcohol with chromic anhydride gave a ketone with an absorption band at 1715 cm^{-1} (keto group in a six-membered ring). On treatment with methylmagnesium iodide, the liquid ketone was converted into a tertiary alcohol, from which by direct dehydrogenation we isolated 1, 5, 6-trimethyl-4-isopropylnaphthalene [14].

The production of 1, 5, 6-trimethyl-4-isopropylnaphthalene shows that the trisubstituted double bond in muurolene-3 is located between the 5th and 6th carbon atoms and the exomethylene group can be only at C_1 (I).

Since the arrangement of the double bond in muurolene-3 is analogous to that of γ-cadinene [8], we have called the new hydrocarbon D-γ-muurolene. In view of the fact that the muurolene series has a cis-linkage of the rings [5], the absolute configuration of D-γ-muurolene can be represented by formula (VIII).

Experimental

Isolation of the muurolenes. The sesquiterpene hydrocarbons isolated from the oleoresin by the usual method [1] were fractionated in a column with 70 theoretical plates. The muurolene fractions, which were selected in accordance with their physicochemical constants and the results of thin-layer and gas-liquid chromatography, were separated on silica gel impregnated with silver nitrate (10%) at a ratio of 1:30. Elution was carried out with petroleum ether con-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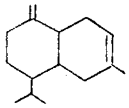
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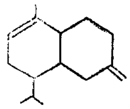
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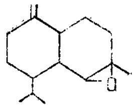
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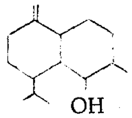
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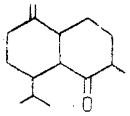
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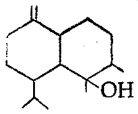
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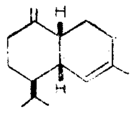
VIII

taining increasing amounts of benzene. Fractions of 10 ml were collected, and the course of the separation was followed by thin-layer chromatography [silica gel + 16% of $AgNO_3$; solvent, petroleum ether–benzene (1 : 1); spots revealed by $SbCl_3$ in chloroform]. Petroleum ether with the addition of up to 5% of benzene eluted muurolene-1 with n_D^{20} 1.5074 and $[\alpha]_D^{20}$ + 75°; with up to 7% of benzene muurolene-2 was eluted with n_D^{20} 1.5044 and $[\alpha]_D^{20}$ −2.5°; with up to 15% of benzene muurolene-3 was eluted with n_D^{20} 1.5048 and $[\alpha]_D^{20}$ +5.0°. The individuality of the hydrocarbons was checked by gas-liquid chromatography ["Khrom-1" chromatograph with flame ionization detector; carrier gas nitrogen (24 ml/min); stainless steel column 170 × 0.6 cm; stationary phase 1, 2, 3-tris-(2-cyanoethoxy)-propane (16.7%); support INZ-600 (280–400 μ); 150° C].

Production of the dihydrochloride. D-γ-Muurolene (200 mg) in absolute diethyl ether (5 ml) was saturated at −5° C with dry hydrogen chloride for 5 hr. A dihydrochloride with mp 85° C (from ethyl acetate) was isolated.

Hydrogenation of D-γ-muurolene. D-γ-Muurolene (115.6 mg) was hydrogenated in the presence of an Adams catalyst in glacial acetic acid, 27.9 ml (0° C, 760 mm) of hydrogen being absorbed, which corresponded to 2.18 double bonds (theoretical consumption of hydrogen for two double bonds is 25.3 ml).

Dehydrogenation of D-γ-muurolene. D-γ-Muurolene (200 mg) was heated with selenium (80 mg) at 290° C for 2 hr. The dehydrogenation product was chromatographed on alkaline alumina (activity grades I and II). The picrate of the dehydrogenation product, after four recrystallizations from alcohol, had mp 113° C. When it was mixed with an authentic sample of 1, 6-dimethyl-4-isopropylnaphthalene picrate, no depression of the melting point was found.

Titration with perbenzoic acid. D-γ-Muurolene (278.9 mg) was oxidized with perbenzoic acid (500 mg) in chloroform (20 ml) at 0° C. The excess of acid was back-titrated with a 0.1 N solution of $Na_2S_2O_3$. The consumption of acid (379.5 mg) corresponded to 1.94 double bonds (theoretical consumption of acid for two double bonds is 384.8 mg).

Quantitative determination of the methylene double bond by Naves's method [6]. D-γ-Muurolene (2.4 mg) in propionic acid (3 ml) was ozonized at −20° C for 30 sec. The amount of formaldehyde liberated (0.39 mg) corresponded to 1.1 methylene double bond (theoretical amount of formaldehyde for one methylene double bond is 0.35 mg).

Production of 1, 5, 6-trimethyl-4-isopropylnaphthalene. D-γ-Muurolene (1180 mg) in chloroform (30 ml) was oxidized with perbenzoic acid (798 mg) in chloroform at 10° C for 27 hr. The chloroform solution was washed with a 3% solution of alkali and with water and was dried over anhydrous sodium sulfate. The monoepoxide (IV), purified by preparative thin-layer chromatography on neutral alumina [activity grade III, solvent petroleum ether–benzene (4 : 1)], had bp 160° C (5 mm); n_D^{26} 1.4950.

Found, %: C 81.86; H 10.94. Calculated for $C_{15}H_{24}O$, %: C 81.81; H 10.90.

A mixture of the monoepoxide of D-γ-muurolene (730 mg) and lithium aluminum hydride (460 mg) in absolute ether (50 ml) was boiled for 2 hr. The alcohol (V), isolated by the usual method, was purified by preparative thin-layer chromatography on neutral alumina [activity grades III and IV, solvent petroleum ether–benzene (1 : 1)], n_D^{22} 1.5010. The alcohol (V) (520 mg) was oxidized with chromic anhydride (500 mg) in glacial acetic acid (20 ml) with the addition of water (1 ml) at room temperature for 42 hr. The ketone (VI) isolated (370 mg) had n_D^{22} 1.4990. A Grignard reagent (0.6 g of Mg + 3.5 g of CH_3I in 70 ml of absolute ether) was added to a solution of the ketone (VI) (250 mg) in absolute ether (30 ml). The solution was stirred at room temperature for 1 hr and was boiled for 3 hr. The excess of reagent was decomposed with a solution of ammonium chloride. The resulting alcohol (VII) (300 mg) was dehydrogenated with selenium (372 mg) at 300° C for 11 hr. The dehydrogenation product (120 mg) was chromatographed on alkaline alumina (activity grades I and II). The picrate of the dehydrogenation product had mp 103° C; styphnate, mp 131° C. Literature data: 1, 5, 6-trimethyl-4-isopropylnaphthalene, mp 102.5°–103° C; styphnate, mp 130°–131° C [14].

Summary

Three sesquiterpene hydrocarbons, muurolene-1, muurolene-2, and muurolene-3, have been isolated from the oleoresin of Pinus sibirica R. Mayr.

Muurolene-3 is D-γ-muurolene and has the structure (VIII).

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