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COMPOSITION OF THE NEUTRAL FRACTION FROM THE OLEORESIN OF PINUS SIBIRICA

VI. Isocembrene and Isocembrol

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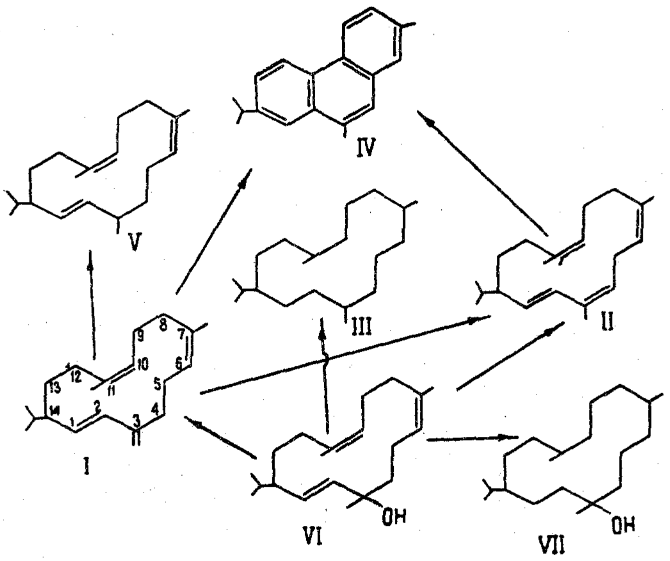
Continuing our study [1–3] of the neutral fraction of the oleoresin of Pinus sibirica R. Mayr (Siberian pine), we have isolated two more new compounds with 14-membered rings (a hydrocarbon $C_{20}H_{32}$ and an alcohol $C_{20}H_{34}O$), which we have called isocembrene (I) and isocembrol (VI).

Isocembrene has four double bonds. In the IR spectrum of the compound, bands at 890, 1655, and 3085 cm^{-1} relate to an exomethylenic bond, at 840 and 1665 cm^{-1} to a trisubstituted double bond, and at 970 cm^{-1} to a trans-disubstituted double bond. The exomethylenic double bond is confirmed by ozonization [4]. The UV spectrum has an absorption maxium at 238 mμ (log ε 4.3) showing the conjugation of double bonds.

On chromatography on alumina impregnated with silver nitrate, isocembrene isomerizes into cembrene (II).

Exhaustive hydrogenation of isocembrene on platinum oxide in acetic acid leads to the production of octahydrocembrene (III).



Dehydrogenation of (I) with selenium forms 7-isopropyl-2, 9-dimethylphenanthrene (IV). Consequently, the hydrocarbon that we isolated is a near isomer of cembrene (II) and differs from the latter only by the presence of an exomethylenic double bond. To confirm this, we hydrogenated isocembrene over $Pd/CaCO_3$ (with the calculated consumption of hydrogen for one double bond). This gave a mixture of products of which the main one was a hydrocarbon $C_{20}H_{34}$. Its IR spectrum lacks the bands characteristic for an exomethylenic double bond. The constants of this compound are identical with those of the hydrocarbon (V) obtained by the hydrogenation of cembrene (II) with lithium in liquid ammonia [5]. Thus, isocembrene has the structure (I).

The alcohol $C_{20}H_{34}O$ with a structure relating to that of isocembrene—isocembrol (VI)—is an isomer of cembrol [3]. It was isolated by chromatography of the oxygen-containing neutral fraction of the oleoresin of the pine, and its IR spectrum has the bands of a trans-disubstituted double bond (970 cm^{-1}) and a trisubstituted double bond (840, 1665 cm^{-1}) and bands of a tertiary hydroxyl (1140, 3615 cm^{-1}). The UV spectrum has no absorption maximum in the 220–400-mμ region. The consumption of hydrogen on hydrogenation corresponds to three double bonds.

When treated with p-nitrobenzyl chloride, thionyl chloride, and acetic acid, isocembrol is readily dehydrated to cembrene (II). Dehydration was also observed when the isolated alcohol was purified on silica gel containing silver, but in this case isocembrene (I) was formed with a yield of 60%.

It is interesting to note that when isocembrol was hydrogenated in acetic acid, dehydration took place with the formation of octahydrocembrene (III), which was isolated as the main product (82%) in one of the experiments.

Formation, by dehydration of isocembrol, of two hydrocarbons—(I) and (II)—with characteristic maxima in the UV region unambiguously leads to structure (VI). The NMR spectrum of isocembrol confirms this structure. In the strong-field region there is a signal with a center at 0.85 ppm corresponding to an isopropyl group. A signal at 1.31 ppm relates to a methyl group at C-3. Signals at 1.52 and 1.62 ppm belong to methyls on a trisubstituted double bond. In the weak-field region there is a doublet with a center at 5.75 ppm (J = 17 Hz) of one of the protons of a trans-disubstituted double bond [5–8].

Experimental

The melting points were determined on a Kofler block. The angles of rotation were measured in chloroform. The IR spectra were recorded on a UR-10 instrument in CCl_4, the UV spectra on an SF-4 instrument, and the NMR spectra on a JNM-4H-100 instrument in CCl_4 with tetramethylsilane as internal standard. The masses of the compounds were determined on an MKh-1303 instrument.

The diterpene compounds (200 g) isolated from the pine oleoresin by the method described previously [1] were separated on alkaline alumina (activity grade I–II, 1 : 15). Petroleum ether eluted the hydrocarbons (70 g), and ethanol, the oxygen-containing compounds (100 g).

Isocembrene (I). The hydrocarbon fraction was chromatographed on columns of silica gel impregnated with silver nitrate [9, 10]. The components were eluted successively with petroleum ether, mixtures of petroleum ether and benzene (with a gradual increase in the amount of benzene in the mixture from 5 to 90%), and with benzene. The benzene eluted isocembrene with n_D^{20} 1.5230, $[\alpha]_D^{20}$ +60.3° (c 2.6). Found, %: C 87.88; H 12.12; mol. wt. 272 (mass spectrometry). Calculated for $C_{20}H_{32}$, %: C 88.16; H 11.84; mol. wt. 272.

Dehydrogenation of isocembrene. Isocembrene (1 g) and selenium (1.5 g) were kept at 300–320° C for 6 hr. Chromatography on alumina yielded a hydrocarbon (0.65 g) with mp 75–76° C (picrate with mp 132–133° C). A mixture of the aromatic hydrocarbon with 7-isopropyl-2, 9-dimethylphenanthrene (mp 77–77.5° C) gave no depression of the melting point.

Hydrogenation of isocembrene. A) Isocembrene (200 mg) was hydrogenated in glacial acetic acid in the presence of 20 mg of platinum oxide. The consumption of hydrogen—63 ml (0° C, 760 mm)—corresponded to four double bonds (theoretical 65.6 ml). The saturated hydrocarbon was purified by chromatography on alumina containing 10% of $AgNO_3$ (1 : 100). Elution with petroleum ether yielded substance (III)—100 mg, n_D^{22} 1.4740; $[\alpha]_D^{22}$ +1.8° (c 0.54); mol. wt. 280 (mass spectrometry).

When a mixture (1 : 1) of the saturated hydrocarbon (III) and an authentic sample of octahydrocembrene was subjected to gas-liquid chromatography, a single peak* was found (retention time 21.6 min).

B) Isocembrene (1.0 g) was hydrogenated in ethyl acetate over $Pd/CaCO_3$ (0.1 g) for 1.5 hr. The consumption of hydrogen—82 ml (0° C, 760 mm)—corresponded to one double bond. The mixture of products, which, according to gas-liquid chromatography,** contained four components in a ratio of 1 : 4 : 12 : 5 with residence times of 5.69, 6.95, 9.06, and 12.64 min, was separated on Al_2O_3 plus 10% of $AgNO_3$ (1 : 100). They were eluted with petroleum ether and mixtures of petroleum ether and benzene (with concentrations of benzene in the mixture gradually increasing from 1 to 10%). A 97 : 3 mixture of petroleum ether and benzene yielded a hydrocarbon (0.03 g) with n_D^{20} 1.4760; $[\alpha]_D^{20}$ +24° (c 0.2); mol. wt. 278 (mass spectrometry); and a 95 : 5 mixture of petroleum ether and benzene eluted a hydrocarbon (0.15 g) with n_D^{20} 1.4940; $[\alpha]_D^{20}$ +28.6° (c 0.35); mol. wt. 276 (mass spectrometry). A 93 : 7 mixture eluted a hydrocarbon (V) (0.6 g), n_D^{20} 1.4990; $[\alpha]_D^{20}$ +43° (c 0.86); mol. wt. 274 (mass spectrometry). Literature data for the hydrocarbon (V)—$[\alpha]_D^{20}$ +40°; mol. wt. 274 [5].

Quantitative determination of the methylene double bonds [4]. In solution in propionic acid (3 ml), isocembrene (2.5 mg) was ozonized at −20° C for 2 min (the amount of ozone in the current of oxygen was 5.88 mg/min). The amount of formaldehyde isolated (0.25 ml) corresponded to one methylene double bond (theoretical 0.27 mg).

Isomerization of isocembrene (I) into cembrene (II). Isocembrene (200 mg) was transferred to a column of Al_2O_3 + 10% of $AgNO_3$ and was left for 3 days. Elution with petroleum ether containing 10% of benzene yielded 140 mg of cembrene [5]. No depression of the temperature with an authentic sample of cembrene was observed. The UV spectra were identical.

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*KhROM-2 chromatograph (Czechoslovakia); flame-ionization detector; column 3.4 m × 0.6 cm; packing: E-301 silicone elastomer (1%) on Chromosorb G (0.177–0.250 mm); carrier gas: nitrogen (0.8 atm. gauge); column temperature: 160° C.

**KhROM-1 chromatograph (Czechoslovakia); flame-ionization detector; column 1.7 m × 0.6 cm; packing: poly(ethylene glycol adipate) (20%) of Celite (0.160–0.252 mm); carrier gas: nitrogen (25 ml/min); column temperature: 200° C.

Isocembrol. The oxygen-containing compounds were separated on neutral alumina (activity grade II–III, 1 : 50). The fraction eluted by a mixture of petroleum ether and diethyl ether (1 : 1) was rechromatographed on silica gel (KSK, 140 μ, moisture content 20%). The isocembrol (VI) was eluted with a mixture of petroleum ether and benzene (70 : 30), forming a colorless oil with n_D^{20} 1.5035, $[\alpha]_D^{20}$ +80.1° (c 3.2). Found, %: C 82.70; H 11.69; mol. wt. 290 (mass spectrometry). Calculated for $C_{20}H_{34}O$, %: C 82.69; H 11.80.

Dehydration of isocembrol. A mixture of isocembrol (VI) (1.14 g) and p-nitrobenzoyl chloride (0.57 g) was heated without a solvent for 10 min. The reaction product was extracted with ether and was purified on alkaline alumina (activity grade I, 1 : 10). Petroleum ether eluted 0.63 g of cembrene (II) with mp 59–59.5° C; λ_{max} 245 mμ (log ε 3.86). No depression of the melting point was found with an authentic sample.

Dehydration of isocembrol on a sorbent. Isocembrol (0.5 g) was transferred to a column of silica gel (with 10% of $AgNO_3$). Diethyl ether eluted 0.3 g of a hydrocarbon which, after additional purification by means of thin-layer chromatography, had $[\alpha]_D^{20}$ +61.0°; n_D^{20} 1.5240; mol. wt. 272 (mass spectrometry). The IR spectrum of the hydrocarbon coincided completely with that of isocembrene (I).

Hydrogenation of isocembrol. A) Isocembrol (0.3 g) was hydrogenated in glacial acetic acid in the presence of platinum oxide (0.03 g) for 3 hr. The consumption of hydrogen (225 ml, 0° C, 760 mm) corresponded to three double bonds (theoretical 232.9 ml). The saturated alcohol (0.28 g) was purified by TLC on silica gel. This gave hexahydrocembrol with mp 91–92° C; $[\alpha]_D^{20}$ +2.4° (c 2.5). Found, %: C 80.96; H 13.51. Calculated for $C_{20}H_{40}O$, %: C 81.00; H 13.60.

B) The hydrogenation of isocembrol (0.5 g) under the same conditions for 10 hr led to the formation of a mixture of products the chromatography of which on SiO_2 (KSK, 140 μ, 1 : 100) gave as the main product (0.41 g) octahydrocembrene (III) with n_D^{22} 1.4738 and $[\alpha]_D^{22}$ +1.5° (c 0.41). The retention time of this product on GLC coincided with that of an authentic sample of octahydrocembrene.

Conclusions

1. From the neutral fraction of the oleoresin of Pinus sibirica R. Mayr have been isolated new macrocyclic diterpene compounds—isocembrene (I) and isocembrol (VI).

2. It has been shown that isocembrol is readily dehydrated into cembrene and isocembrene.

REFERENCES

1. V. A. Pentegova, O. Motl, and V. Herout, Coll. Czech. Chem. Comm., 26, 1362, 1961.
2. V. A. Pentegova and N. K. Kashtanova, KhPS [Chemistry of Natural Compounds], 1, 223, 1965.
3. A. I. Lisina, A. I. Rezvukhin, and V. A. Pentegova, KhPS [Chemistry of Natural Compounds], 1, 250, 1965.
4. J. R. Naves, Helv. Chim. Acta, 32, 1151, 1949.
5. W. G. Dauben, W. E. Thessen, and P. F. Resnik, J. Org. Chem., 30, 1693, 1965.
6. D. L. Roberts and R. L. Rowland, J. Org. Chem., 27, 3989, 1962.
7. R. L. Rowland and D. L. Roberts, J. Org. Chem., 28, 1165, 1963.
8. R. L. Rowland and D. L. Roberts, J. Org. Chem., 29, 16, 1964.
9. A. S. Gupta and Sukh Dev, J. Chrom., 12, 189, 1963.
10. H. Erdtman and L. Westfelt, Acta Chem. Scand., 17, 1826, 1963.

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