UDC 547.913

CORRELATION OF PEREGRINOL WITH SCLAREOL III.

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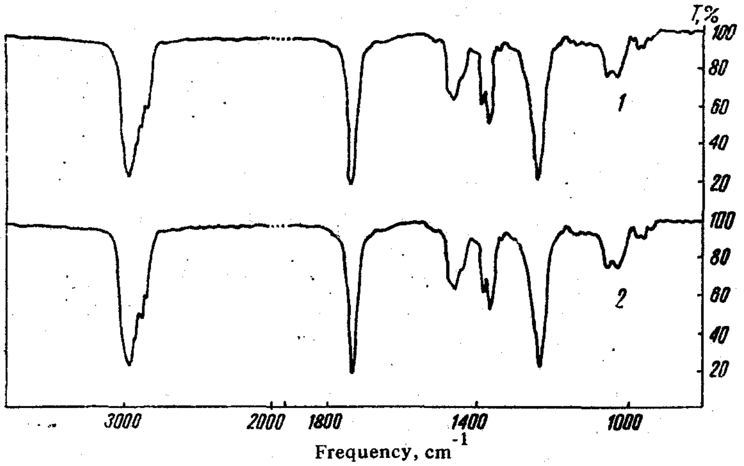
Khimiya Prirodnykh Soedinenii, Vol. 3, No. 5, pp. 301–303, 1967

On the basis of chemical and spectroscopic data, the diterpene alcohol peregrinol, isolated from Marrubium peregrinum, has been assigned the structure of 13-labdene-9, 15-diol [1].

To confirm the labdane skeleton of peregrinol (I) and to establish the stereochemistry of the linkage of the A and B rings, a correlation of it with sclareol [2], a diterpenoid of the labdane group with a known configuration at the asymmetric carbon centers, has been carried out.

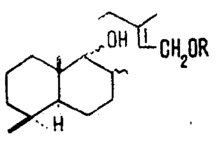


IR spectra of 15-acetoxysclarene from sclareol (1), and from peregrinol (2) (UR-10 spectrometer, 6% solution in CCl_4).

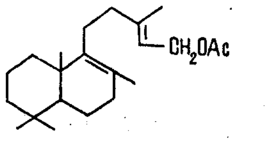
Peregrinol acetate (II) was dehydrated with thionyl chloride in pyridine to give the unsaturated product III. When the latter was hydrogenated in the presence of platinum oxide in acetic acid, a mixture of two substances was formed, a saturated acetate of a primary alcohol IV and an unsaturated hydrocarbon V which were identical with the hydrogenation products of the acetate of the primary alcohol VI obtained from sclareol by Ohloff's method [3]. The figure gives for comparison the spectra of the acetates from peregrinol and sclareol (IV).

When IV was saponified, identical alcohols VII were again isolated, being characterized additionally in the form of the p-nitrobenzoates.

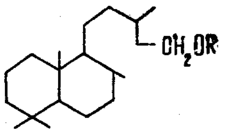
Taking into account the fact that the chemical transformations carried out do not affect the stereochemical linkage of the ring, it can be said that peregrinol is a diterpenoid of the labdane group with a normal translinkage of the A and B rings and, consequently, can be represented by the partial stereochemical formula I.



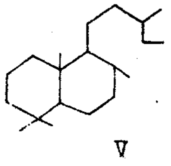
I R=H II R=Ac



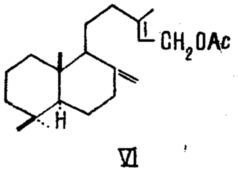
III



IV R=Ac VII R=H



V



VI

Experimental

Dehydration of (II). With cooling to 0° C, 1 ml of thionyl chloride was added in drops to 240 mg of peregrinol acetate [1] in 3 ml of dry pyridine. After 20 min, ice was added and the reaction products were extracted with ether. The ethereal extracts were washed with water, 5% hydrochloric acid, and water again, and were dried with sodium sulfate and distilled. The residue (an oil) was chromatographed on 5 g of silica gel. As in the two following cases, the fractions were monitored by thin-layer chromatography on silica gel and by IR spectrometry. A yellow oil, III, (230 mg) was obtained.

Found, %: C 79.20; H 10.99. Calculated for $C_{22}H_{36}O_2$, %: C 79.46; H 10.91.

Hydrogenation of III. A solution of 230 mg of dehydrated peregrinol acetate in 10 ml of glacial acetic acid containing n-hexane was saturated with hydrogen in the presence of Adams platinum oxide. The amount of hydrogen absorbed was 2.5 mole/mole. The reaction products were extracted with ether in the usual way and chromatographed on 5 g of silica gel. Petroleum ether eluted 60 mg of substance V.

Found, %: C 86.38; H 13.96. Calculated for $C_{20}H_{38}$, %: C 86.26; H 13.74.

Benzene eluted 130 mg of IV as a barely yellowish oil (bp 135°–136° C/0.4 mm); $[\alpha]_D^{18}$ +37° (c 5.5; chloroform); n_D^{18} 1.4922; IR spectrum (UR-10 spectrometer) 1735, 1240 cm^{-1} (acetate), the region of OH groups and double bonds being transparent.

Found, %: 78.47; H 11.67. Calculated for $C_{22}H_{40}O_2$, %: C 78.51; H 11.98.

Hydrogenation of VI. 510 mg of the acetate of the primary alcohol sclareol prepared by Ohloff's method [3] was hydrogenated under the same conditions as III. It absorbed 2.6 mole/mole of hydrogen. The mixture obtained was separated by chromatography. The identity of the substance eluted by petroleum ether (150 mg) with the hydrocarbon V was shown by a comparison of the results of chromatography, elemental analysis, and IR spectrometry. In the same way, the benzene fraction (250 mg) was shown to be identical with IV.

Saponification of the acetates. 100 mg of one of the acetates IV was heated with 10% methanolic caustic potash solution. The mixture was left for 12 hr and then the solvent was distilled off in vacuum, water was added and the product was extracted with ether. The ethereal extracts were washed with water to neutrality and dried, and the ether was distilled off. The residue was chromatographed. 60 mg of colorless oil was isolated in each case. The tetrahydroacetate of the primary alcohol sclareol (IV) yielded the alcohol VII.

Found, %: C 81.55; H 12.83. Calculated for $C_{20}H_{38}O$, %: C 81.58; H 13.01.

The tetrahydroacetate of peregrinol (IV) also gave the primary alcohol VII. The IR spectra were identical.

Found, %: C 82.19; H 12.94. Calculated for $C_{20}H_{38}O$, %: C 81.58; H 13.01.

Preparation of the p-nitrobenzoates. 50 mg of the oil VII from sclareol or peregrinol was dissolved in dry pyridine (2 ml). An excess (120 mg) of p-nitrobenzoyl chloride was added. The mixture was heated on the oil bath for 15 min. After the usual isolation and purification, yellow-green liquids were obtained in each case which were identical with one another according to chromatographic data and IR spectrometry.

The analyses were carried out by R. S. Shish, and the IR spectra were recorded by S. F. Manole.

Summary

A correlation of peregrinol with sclareol has confirmed the structure of the hydrocarbon skeleton of the former and its stereochemistry at the C-5 and C-10 asymmetric centers.

REFERENCES

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2. W. Klyne, J. Chem. Soc., 3072, 1953.
3. G. Ohloff, Ann., **617**, 134, 1958.

11 July 1966

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