The structure of peregrinol, a diterpenoid from *Marrubium peregrinum*. II

L. A. Selev, D. P. Popa, L. Doleish, and G. V. Lazur'evskii

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We have previously [1] described a diterpenoid isolated from *M. peregrinum* L., peregrinol C_{20}H_{36}O_{2}, a bicyclic diterpene diol with a trisubstituted double bond.

In the present communication we give information permitting structure (I) to be assigned to peregrinol.

The hydrogenation of substance (I) in acetic acid on platinum took place with the absorption of 1.8 mole of hydrogen and with the formation of dihydroperegrinol C_{20}H_{36}O_{2} (II) and a hydrogenolysis product of peregrinol C_{20}H_{36}O (III). When (I) was hydrogenated in alcohol in the presence of palladium on strontium carbonate, less of the peregrinol underwent hydrogenolysis (1.2 mole of hydrogen was absorbed) and the main reaction product was dihydroperegrinol.

The ease of hydrogenolysis of peregrinol makes it possible to assume that its molecule contains at least one allyl hydroxy group:

\[
\text{IV} \quad \text{II, III, IV, VI, VII, VIII} \quad \text{IX}
\]

\[
\begin{align*}
\text{I} & \quad \text{R}=\text{H}; \\
\text{II} & \quad \text{R}=\text{CH}_{2}\text{OH}, \text{R}_{1} = \text{R}_{2} = \text{H}; \\
\text{III} & \quad \text{R}=\text{CH}_{3}, \text{R}_{1} = \text{R}_{2} = \text{H}; \\
\text{IV} & \quad \text{R}=\text{CH}_{2}\text{OH}, \text{R}_{1} = \text{R}_{2} = \text{OH}; \\
\text{V} & \quad \text{R}=\text{COCH}_{3}; \\
\text{VI} & \quad \text{R}=\text{COOH}, \text{R}_{1} = \text{R}_{2} = \text{H}; \\
\text{VII} & \quad \text{R}=\text{COOCH}_{3}, \text{R}_{1} = \text{R}_{2} = \text{H}; \\
\text{VIII} & \quad \text{R}=\text{CH}_{2}\text{OTs}, \text{R}_{1} = \text{R}_{2} = \text{H}.
\end{align*}
\]

The hydroxylation of peregrinol with osmic acid gave a tetrol (IV), which consumed two equivalents of periodic acid on oxidation. This means that only one of the two hydroxy groups is present in the allyl position.

The reaction of (I) with acetic anhydride in pyridine gave a monoacetate C_{22}H_{36}O_{5} (V). The oxidation of dihydroperegrinol with chromic acid [2, 3] led to a hydroxy acid C_{20}H_{36}O_{3} (VI) with the same number of carbon atoms. The methylation of the latter with diazomethane gave the methyl ester (VII). It can be seen from these facts that one hydroxy group in peregrinol is primary and the other is tertiary.

The tosylation of dihydroperegrinol and subsequent reduction of the tosylate (VIII) with lithium aluminum hydride gave the hydrogenolysis product of peregrinol (III), it may be assumed that the allyl hydroxyl is primary.

The structure of peregrinol (I) was confirmed by a study of the mass spectra taken on a MKh-1305 instrument with an ionization energy of 90 eV and an ionization temperature in the chamber of 150° C.

Mass spectrum of peregrinol.
In the spectrum of peregrinol (figure), the molecular ion at mass 309 has a low intensity. The ionized molecule very readily loses a molecule of water forming an ion with mass 290 m/e. If it is assumed that in the elimination of water the hydroxy group is split off from position 15 (cf. the appearance of ion D below), structure A (scheme 2) may be assigned to this particle with mass 290. Ion B with mass 222 evidently arises by the splitting of the molecule in the allyl position of the 11,12 carbon–carbon bond with the transfer of a hydrogen atom. The fragment with mass 209 denoted by C in the scheme splits off a molecule of water (metastable transition at 174.5) and is converted into the ion C −18 with mass 191.

The main peak in the spectrum is formed by ion D with mass 151, which (metastable transition at 78.7) arises from ion A by the elimination of a particle with mass 189. This is analogous to the fragmentation of grindelane (IX) [5] which also forms the ion M − 189 as the main peak in the mass spectrum.

Ion D, in contrast to fragment C, does not lose a molecule of water; the conjugation of an oxonium ion with a secondary double bond evidently promotes the stabilization of ion D. The ions with masses 123 and 109 may be represented by structures E and F [4, 5].

The mass-spectroscopic fragmentation of the ester (VII) is similar to that of peregrinol (I). Here the molecular ion is represented by a comparatively intense peak at mass 338. In the spectrum of the ester, the M − 18 ion has a very low intensity, which once again confirms the presence of a tertiary hydroxy group in position 9 in ion A.

Ion B is not found in the spectrum of the ester, since in this case there is no double bond. On the other hand, the fragments C, C −18, and E with masses 209, 291, and 123 are preserved. Very intense peaks in the central part of the spectrum are due to fragments of types D (199 m/e) and D−32 (167 m/e).

The loss of methanol by ion D shows the presence of a metastable transition at 140.2. Structure G may be assigned to the fragment with mass 186. Although there is no metastable transition in the spectrum, it can be stated with confidence that the ion G loses a molecule of methanol to form the ion G − 32 with mass 154. Similarly, the ion G in the spectrum of peregrinol has mass 183.

The mass spectra of peregrinane (from peregrinol) and of sclarane (from sclareol) are also similar. Their molecular peak is at 278 m/e, and they have characteristic peaks at M−15, 123 m/e (E) and 109 m/e.

Thus, the mass-spectrometric fragmentation of peregrinol and the ester (VII) confirm the structure (I), including the position of the tertiary hydroxy group on C − 9. The latter is further confirmed by the results of the NMR spectra (taken in a Varian-100 instrument in CDCl₃ solution), according to which the molecule of peregrinol contains one secondary methyl group (doublet at 0.91 ppm, J = 6 Hz) and four tertiary methyl groups (three singlets at 0.97, 0.90, and 0.88 ppm and a singlet at 1.68 ppm due to a methyl group on a double bond).

If one takes into account the fact that the IR spectra of peregrinol and its derivatives are very similar to the spectra of some sclareol derivatives, peregrinol may with confidence be assigned the structure 13-labdene-9,15-diol(I). At the moment we are carrying out a correlation of peregrinol with sclareol. This part of the investigation, and also the chemical proof of the position of the tertiary hydroxy group, will be published in a subsequent paper.