DITERPENOIDS FROM MARRUBIUM PEREGRINUM. I.

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Some years ago, British workers conclusively showed the structure [1, 2] and the stereochemistry [3] of marrubiin, a bitter diterpenoid isolated from Marrubium vulgare L., and later from Leonotis leonurus R. Br. [4]. We have set ourselves the task of making a detailed study of compounds from related plants.

In the epigeal part of Marrubium peregrinum L., collected in the flowering period, we have detected new diterpenoids and a number of other compounds whose presence in this plant may be of interest from the biogenetic point of view.

Exhaustive extraction with petroleum ether with subsequent chromatographic separation of the extract on alumina gave a crystalline substance. From the results of analysis, this is a new bicyclic diterpene alcohol $C_{20}H_{36}O_2$, which we have called peregrinol.

From its composition and physical properties, peregrinol is very similar to the episclareol from Salvia sclarea L. [5]. However, a mixed melting point test of these substances and their IR spectra show that their structures differ. The molecule of the new diterpene contains two active hydrogen atoms. The IR spectrum exhibits clear bands of hydroxy groups and no bands of other oxygen functions. Consequently, peregrinol is a diol. The frequencies at 1670 and 820 cm^{-1} indicate the presence of a $> C{=}CH$ bond in it. Peregrinol is transparent in the UV region.

In the total acetone extract another crystalline substance was found. From the results of elementary and spectroscopic analysis, this is a diterpene hydroxylactone $C_{20}H_{25}O_5$ which we have called peregrinin.

Peregrinin was studied in comparison with marrubiin from a local sample of Marrubium vulgare L. It is characteristic that the UV spectra of both substances proved to be identical and their IR spectra were similar. Bands of hydroxy groups, a γ-lactone, and furan were found in both cases. However, peregrinin, unlike marrubiin, contains another strong and sharp band at 1710 cm^{-1} corresponding to a keto group.

Besides the two diterpenes mentioned, we have isolated from the same plant a colorless crystalline substance with mp 161°–162° C with the composition $C_{19}H_{18}O_6$. In addition, β-sitosterol was found in the extracts.

Experimental

The IR spectra were taken on a UR-10 instrument and the UV spectra on an SF-4 spectrophotometer. The specific rotations were measured on an ORD/UV-5 polarimeter of the Japan Spectroscopic Co. Ltd. The melting points were determined on a Kofler block.

Isolation of peregrinol. 3.2 g of the air-dry epigeal part of the plant was exhaustively extracted with petroleum ether. This gave a total of 42.3 g of product. The plant waxes were eliminated with methanol. The residue (12.5 g) was chromatographed on 350 g of alumina (activity grade III) with subsequent elution by petroleum ether, benzene, and diethyl ether.

The benzene fraction afforded a crystalline substance with mp 138° C (from ether). Yield 1 g. A mixture with authentic β-sitosterol gave no depression of the melting point, and their IR spectra were identical.

The diethyl ether fraction contained 0.66 g of peregrinol. Crystallization from diethyl ether gave colorless prisms with mp 130°–130.5° C; $[\alpha]^{25}_{D}$ +10.1° (c 0.5; chloroform). IR spectra: 3625 (OH), 1370 and 1385 (gem-dimethyl groups), 1670 and 825 ($> O{=}CH-$) cm^{-1}. The substance was transparent in UV light.

Found, %: C 77.84; H 11.63; H_{act} 0.68; mol. wt. 308 (mass spectrometry). $C_{20}H_{36}O_2$. Calculated, %: C 77.86; H 11.76; $2H_{act}$ 0.65; mol. wt. 308.49.

Isolation of peregrinin. The plant was subjected to further exhaustive extraction with acetone. The concentrate evaporated to dryness was repeatedly treated with diethyl ether. The dilute ethereal solution was washed with 5% sodium carbonate solution. After the ethereal layer had been washed with water, the neutral fraction was dried and concentrated. The crystals of crude peregrinin which deposited (1.6 g) were separated off.

The substance (0.5 g) was transferred to a column of 15 g of alumina (activity grade III). Elution with a mixture of benzene and 5% of ether gave pure peregrinin in the form of colorless plates with mp 173° C (from benzene), $[\alpha]^{27}_{D}$ +43.4° (c 0.5; methanol). The substance has a very bitter taste and solutions of it are unstable on storage.

IR spectrum: 3600 (OH), 1780 (γ-lactone), 1710 (keto group), 1506 (furan) cm^{-1}. UV spectrum: λ_{max} (in alcohol) 214 mμ (log ε 3.78).

Found, %: C 69.13; H 7.53; H_{act} 0.28. Calculated for $C_{20}H_{26}O_5$, %: C 69.34; H 7.57; H_{act} 0.28.

After the isolation of the peregrinin from the total product, the mother liquors were twice chromatographed on alumina (activity grade III). On elution with diethyl ether for the first time, a mixture of β-sitosterol and a substance strongly fluorescing in UV light were eluted, these being separated on rechromatography. Obtained in the pure state were large colorless polyhedra crystallizing from alcohol, mp 161°-162° C $[\alpha]_D^{22}$ ±0° (c 9.8; chloroform). IR spectrum: 2820, 1643, 1633, 1516 cm^{-1}. UV spectrum: λ_{max} (in alcohol) 216, 265, and 320 mμ (log ε 4.53, 4.23, and 4.50).

Found, %: C 66.85; H 5.28. Calculated for $C_{19}H_{18}O_6$, %: C 66.66; H 5.30.

The combined sodium carbonate solutions remaining after the ethereal wash were acidified with dilute sulphuric acid. The acid solution was repeatedly treated with ether, and the ether was clarified on a column of activated carbon. After the ether had been distilled off a solidifying mixture of acids with a sharp smell remained. The acids have not yet been investigated.

The IR spectra were taken by S. F. Manol and the UV spectra by V. I. Kuz'minov, and the analyses were performed by R. S. Shish.

Summary

Two new diterpenoids have been isolated from Marrubium peregrinum L.: a bicyclic diol $C_{20}H_{36}O_2$, peregrinol – and a hydroxyketolactone $C_{20}H_{25}O_5$, peregrinin. A substance $C_{19}H_{18}O_6$ has been obtained as a by-product.

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