STRUCTURE AND PARTIAL SYNTHESIS OF EPERUOL

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ABSTRACT.—This paper reports the isolation and structural elucidation of eperuol, a new alcohol from the neutral fractions of *E. purpurea*.

In previous publications (1,2) we reported on the major constituents present in the trunk resin of *Eperua purpurea* Benth. Lately, an examination of the minor components of the neutral fraction was conducted to identify three new natural ketones (3). In this paper we wish to report the isolation and structural elucidation of a new alcohol from the neutrals of *E. purpurea*.

DISCUSSION

Repeated chromatography of the most polar fraction from the neutrals led to the isolation of a crystalline compound, mp, 94-5°, $[\alpha]^{25}D-24.6°$, whose ir indicates it to be an alcohol that probably bears a trisubstituted double-bond in its structure (3550 and 910 cm^{-1}). Elemental analyses indicated the molecular formula $C_{18}H_{30}O$, confirmed by the molecular ion in the mass spectrum at *m/z* 262. Microhydrogenation experiments indicated the uptake of 1 M hydrogen. The pmr spectrum shows four singlets at high field (0.83, 0.85, 0.90, and 1.18 ppm, 3H each), suggesting a terpenoidal nature, and an unresolved multiplet at 5.48 ppm (1H), which corroborates the presence of a trisubstituted double-bond in the structure. The absence of signals attributable to protons on carbons bearing oxygen, together with the impossibility of acetylation under mild conditions, demonstrate that the product is a tertiary alcohol. In addition, by comparison with labdanolic acid, **1** (4), the signal at 1.18 ppm is assigned to a methyl group geminal with the hydroxyl group (1.20 ppm in labdanolic acid). All this information indicates that the product should be a tricyclic, monounsaturated, diterpenoidal tertiary alcohol.

The fragmentation of the molecule under electron impact allows us to propose a structure for the compound. In effect, together with the expected $M^{\cdot+}$-15 and $M^{\cdot+}$-18 fragments (*m/z* 247, 7% and 244, 25%, respectively), the spectrum shows two relatively abundant ions at *m/z* 138 (17%) and *m/z* 124 (37%), which—accompanied by others very important at *m/z* 120 (100%), 109 (95%), and 105 (60%)—are sufficient evidence for a diterpenoidal structure with a C-7 C-8 double-bond (5) as in cativic acid, **2**. Eperuol should contain rings A and B of cativic acid, plus another ring to account for the remaining unsaturation. The compound is then assigned structure **3**, which is compatible with all the spectral information and explains the fragmentation observed (figure 1). The hydroxyl and methyl groups are placed at C-13 because it is biogenetically, the most favored position, considering that the alcohol is probably derived from ketone **4**.

Hydrogenation of eperuol yields a solid, $C_{18}H_{32}O$, mp, 77-9° $[\alpha]^{25}D+10.8°$, evincing the typical change of rotation (from − to +) shown by cativic acid (6), where hydrogenation is stereospecific, occurring through β-addition, thus giving support for the stereochemistry of rings A and B, leaving only the configuration of C-13 unknown. Evidence for the configuration at the latter carbon is turned out by the pmr spectrum of the benzoyl derivative of eperuol. Hence, the methyl geminal to the benzoate group appears at 1.53 ppm, while the other methyl groups show at 1.22, 0.80, and 0.70 ppm.

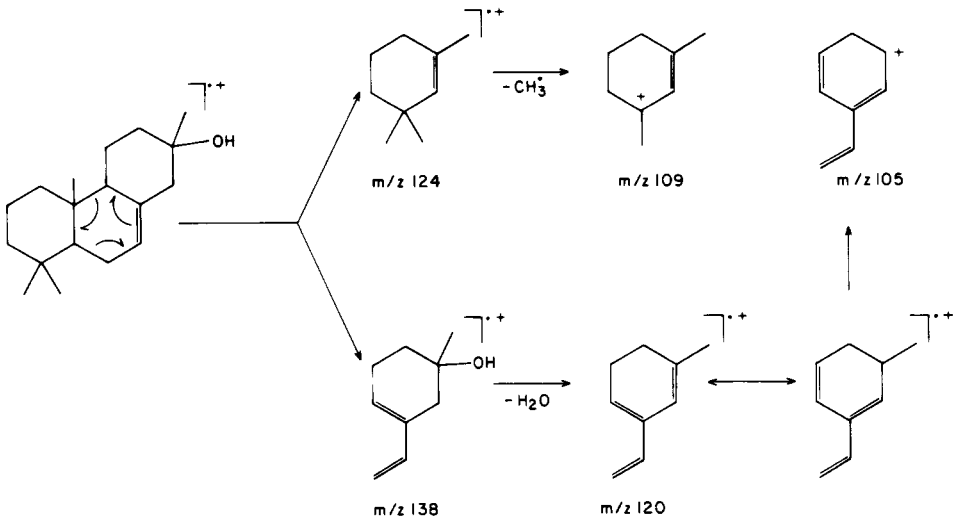
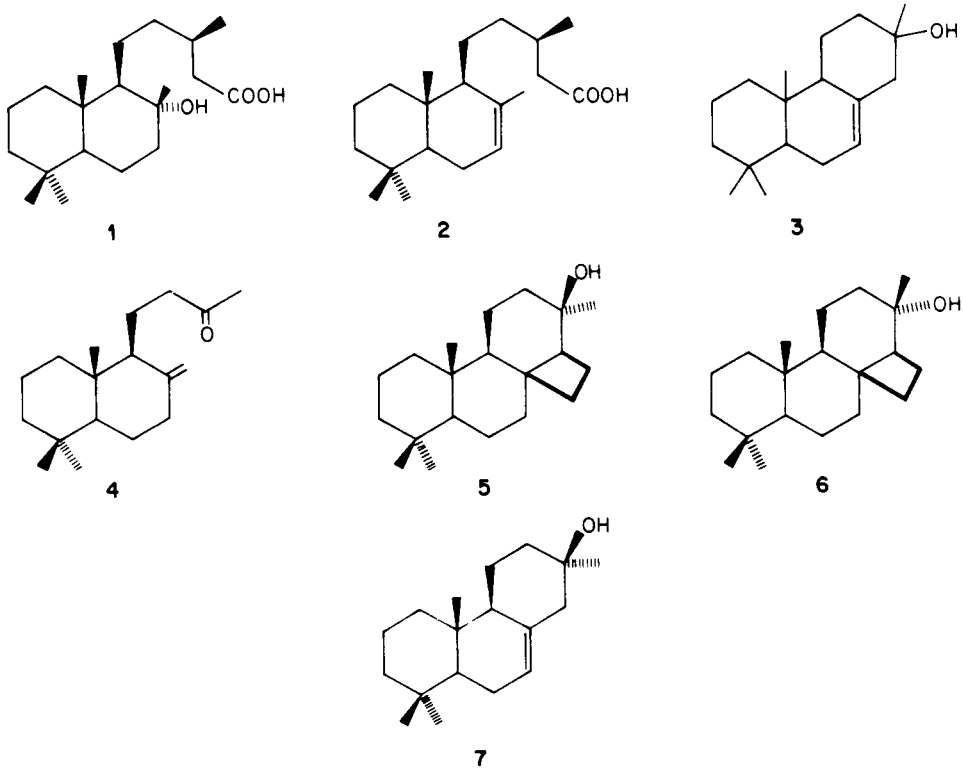


FIGURE 1. Fragmentation of eperuol under electron impact.

The signal at 1.22 ppm can only be ascribed to the angular methyl, influenced by an axial benzoate substituent at C-13, which falls close to the former due to the deformation produced by the double-bond. The examination of models indicates that an equatorial benzoate would not produce, in any case, such a large long-range effect on any of the methyl groups in the molecule. Confirmation for this conclusion is given by the dihydrobenzoate, whose pmr spectrum shows the angular methyl at 0.95 ppm. Additional support is obtained by comparing eperuol with alcohols **5** and **6** (7) where the



equatorial C-13 methyl group absorbs at 1.20 ppm, while the axial isomer absorbs at 1.08 ppm. We propose, for eperuol, the structure and absolute stereochemistry of 13α-methyl-13β-hydroxy-podocarp-7-ene, **7.**

Proof for the structure was obtained by synthesis of racemic dihydroeperuol, **8,** from racemic labda-8(20), 13-dien-15-oic acid **9,** through degradation to the enone **10,** hydrogenation of the enone, where addition is known to occur stereospecifically from the β-face (7), treatment of the saturated ketone with MeLi, and chromatographic separation of the mixture of racemic alcohols (figure 2). Racemic dihydroeperuol gave spectral data identical to dihydroeperuol.

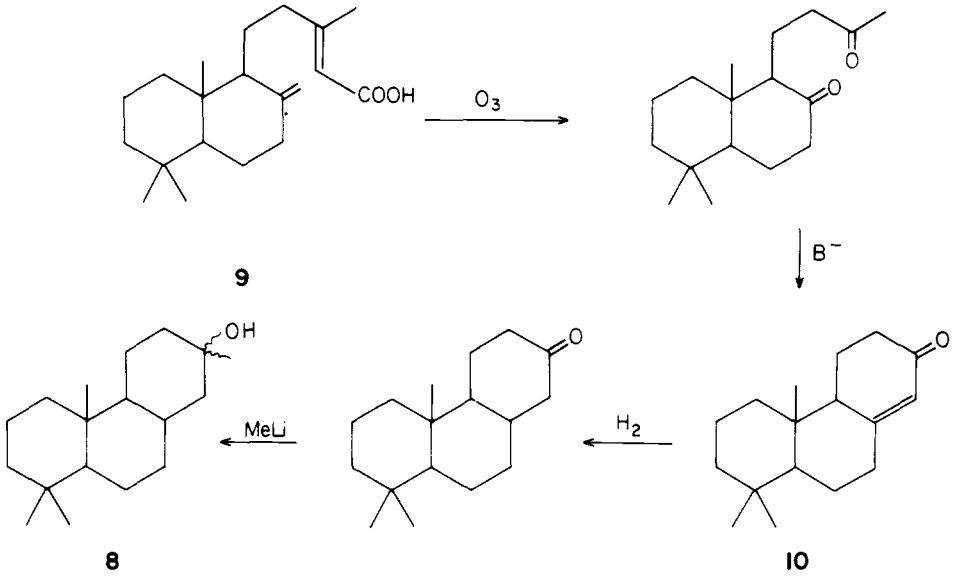


FIGURE 2. Synthetic scheme of dihydroeperuol.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The mp for each is uncorrected. Optical rotations were measured in a Zeiss polarimeter in EtOH solutions. The pmr spectra were recorded in $CDCl_3$ and CCl_4, with TMS as internal standard, at 90 MHz; ms were recorded at 70 eV.

ISOLATION.—The most polar fraction obtained from the chromatography of the neutrals of *E. purpurea* resin (see ref. 2 for details) was rechromatographed on silica using hexane with increasing amounts of Et_2O as eluent. The hexane-2% Et_2O fraction gave **7** (300 mg).

EPERUOL (13α-METHYL-13β-HYDROXY-PODOCARP-7-ENE) (**7**).—The solid obtained from the hexane-2% Et_2O fraction was recrystallized from hot hexane to yield white crystals, mp 97°, $[\alpha]^{25}D$ −24.6°($CHCl_3$) (c, 2.6).

Anal. calcd for $C_{18}H_{30}O$: C, 82.37; H, 11.52; O, 6.10. Found: C, 82.27; H, 11.45; O, 6.06.

It gave the following physical data: ν max (KBr) 3310, 2950, 2900, 2850, 2825, 1450, 1440, 1375, 850, cm^{-1}; pmr: δ 0.83, 0.85, 0.90, and 1.18 (4s, 3H each, quat. Me), 5.48 (m, 1H. C.7-H); *m/z* 262 ($M^{\cdot+}$), 247 ($M^{\cdot+}$-15), 244 ($M^{\cdot+}$-18), 138, 124, 120 (100%).

DI-HYDROEPERUOL (**8**).—Eperuol (75 mg) was hydrogenated at 40 psi H_2, using PtO_2 as catalyst, to yield an oil that, when purified by chromatography, afforded crystals, mp 77-9°, $[\alpha]^{25}D$ +10.8° ($CHCl_3$) (c, 2.0).

Anal. calcd for $C_{18}H_{32}O$: C, 81.75; H, 12.20; O, 6.05. Found: C, 81.70; H, 12.35; O, 5.92, *m/z* 264 ($M^{\cdot+}$), 249 ($M^{\cdot+}$-15), 246 ($M^{\cdot+}$-18), 123, 108 (100%).

EPERUYL-BENZOATE AND DIHYDROEPERUYL BENZOATE.—Eperuol (44 mg) was dissolved in dry pyridine; an excess BzOCl was added, and the mixture was left overnight at room temperature. The product was treated with HCl (15%) and extracted with Et_2O three times. The pooled ether extracts were washed three times with ammonia, dried, and evaporated to dryness to yield a thick oil that could not be

crystallized; pmr: δ 0.70, 0.80, 1.22, and 1.53 (4s, 3H each, quat. Me), 5.48 (m, 1H, C.7-H), 7.40 and 7.95 (2m, 5H, arom.), *m/z* 244 ($M^{\cdot+}$-BzOH, 100%), 229, 159, 120, 109, 108, 105. Dihydroeperuyl benzoate was prepared in the usual manner using Pd/C as catalyst; pmr: δ 0.70, 0.76, 0.95, and 1.53 (4s, 3H each, quat. Me), *m/z* 246 ($M^{\cdot+}$-BzOH, 100%), 245, 244, 231, 229, 123, 108, 105.

PODOCARP-8 (14)-EN-13-ONE (**10**).—Racemic **9** (10.8 g) was ozonized, cyclized, and dehydrated, following the procedures of reference (9), to yield the racemic enone **10** (5.8 g), mp 86-7° [Lit. (9) 89-90°], ν max (KBr) 1660, 1640, 880, cm^{-1}.

(±) DIHYDROEPERUOL (**8**).—To racemic **10** (1.75 g) dissolved in methanol (50 ml) was added 5% Pd/C (150 mg); the mixture shaken (4 h) under 40 psi H_2. The reaction mixture was filtered and the solvent removed to give a crystalline mass (1.72 g).

Part of the crude (500 mg) was dissolved in dry ether (6 ml), cooled in dry ice-acetone, and treated with 1.1 M MeLi solution (2 ml) for 1.5 h. The reaction complex was then hydrolyzed with aqueous NH_4Cl and extracted with ether three times. The pooled extracts were dried over Na_2SO_4, and the solvent was evaporated to give a white solid (400 mg). Chromatography over silica-gel, using hexane with increasing amounts of ether as eluent, allowed us to separate the racemic epimers. (±) Dihydroeperuol (112 mg) was further purified by fractional sublimation to give white crystals, mp 91-4°. *Anal.* calcd for $C_{18}H_{32}O$: C, 81.75; H, 12.20; O, 6.05. Found: C, 81.90; H, 12.0; O, 6.05; *m/z* 264 ($M^{\cdot+}$), 249 ($M^{\cdot+}$-15); 246 ($M^{\cdot+}$-18), 123, 108 (100%).

ACKNOWLEDGMENTS

This paper is a contribution of the Amazonas project of I.V.I.C. Partial financial support of CONICIT (Venezuela), the Organization of American States (OAS), and UNEP-UNESCO is hereby acknowledged.

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Received 30 April 1982

ERRATUM

Due to an oversight, the structures for the article "The Alkaloids of *Corydalis meifolia*" by D.S. Bhakuni and Rekha Chaturvedi [*J. Nat. Prod.*, **46**, 320 (1983)] were not printed. Therefore, this article has been reprinted in its entirety and appears on pages 466-470 of this issue.