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PREPEREGRININE, A PREFURANIC LABDANE DITERPENE FROM *MARRUBIUM FRIWALDSKYANUM*

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Key Word Index—*Marrubium friwaldskyanum*, Labiatae, diterpenoids, furanic and prefuranic labdane derivatives, peregrinine, preperegrinine

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Abstract—From the aerial part of *Marrubium friwaldskyanum* the previously known diterpenoid peregrinine and its new prefuranic derivative, preperegrinine, have been isolated The known compound 5,6-dihydroxy-7,4′-dimethoxyflavone has also been found in the same source

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In our search for new natural diterpenoids in the Labiatae plants belonging to the genus *Marrubium* [1], we have examined the aerial part of *M friwaldskyanum* Boiss From this plant two diterpenes have been isolated, one of which is the previously known peregrinine (**1**) [2, 3] and the other is a new substance, whose structure was established as the 13*R*-prefuranic derivative of peregrinine (**2**) In addition, the previously known 5,6-dihydroxy-7,4′-dimethoxyflavone [4, 5] has also been isolated from the same plant

Preperegrinine (**2**) has a molecular formula $C_{20}H_{26}O_5$ and its IR spectrum showed γ-lactone (1780 cm^{-1}), ketone (1715 cm^{-1}) and enol-ether (3100, 1615 cm^{-1}) absorptions and no hydroxyl bands The ^1H NMR spectrum of the new diterpenoid showed signals in complete agreement with a structure such as **2** δ 6 48 (1H, *d*, $J_{15,14}$ = 2 5 Hz, H-15), 5 14 (1H, *d*, $J_{14,15}$ = 2 5 Hz, H-14), 4 56 (1H, *ddd*, $J_{6\alpha,5\alpha} = J_{6\alpha\ 7\alpha}$ = 5 Hz, $J_{6\alpha\ 7\beta}$ = 1 5 Hz, H-6α), 4 45 and 4 10 (an AB system, J_{AB} = 10 Hz, 2H-16), 2 60 (1H, *dd*, $J_{5\alpha,6\alpha}$ = 5 Hz, $^4J_{5\alpha,20}$ = 1 Hz, H-5α), 1 45 (3H, *s*, 3H-18), 0 91 (3H, *d*, $^4J_{20,5\alpha}$ = 1 Hz, 3H-20) and 0 91 (3H, *d*, $J_{17,8}$ = 6 Hz, 3H-17) On the other hand, the above conclusion was confirmed by the ready conversion of preperegrinine (**2**) into peregrinine (**1**) [2, 3] by mild acidic reagents, thus establishing the structure and absolute configuration depicted in **2** for the new diterpenoid

Finally, the 13*R*-configuration assigned to preperegrinine (**2**) was supported by NOE experiments [6, 7] When the C-17 methyl signal (δ 0 91) was irradiated, it gave a clear Overhauser effect on the low-field signal (δ 4 45) of the AB system of the C-16 protons, whereas no NOE was observed on the C-14 proton This behaviour clearly established [6, 7] as *R* the configuration of the C-13 centre of preperegrinine, which is thus 9α, 13*R*, 15,16-diepoxy-3-oxo-labd-14-en-19,6β-olide (**2**)

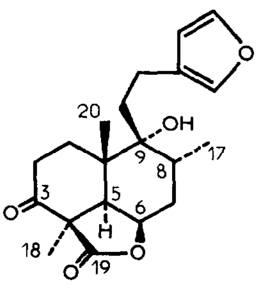
EXPERIMENTAL

For general details on experimental, see refs [1, 7] Plant materials were collected in June 1982, in the Botanic Garden of the University of Palermo, Italy, and voucher specimens were deposited in the Herbarium of this Centre

Extraction and isolation of the compounds Dried and finely powdered *Marrubium friwaldskyanum* Boiss aerial parts (650 g) were extracted with Me_2CO (4 l × 3) at room temp for 3 days The extracts were evapd to dryness under red pres and low temp (24°) The residue (32 g) was chromatographed on a silica gel (Merck, No 7734, deactivated with 15% H_2O) column (700 g) Elution with $CHCl_3$ gave in order of elution, preperegrinine (**2**, 400 mg), peregrinine (**1**, 200 mg) and 5,6-dihydroxy-7,4′-dimethoxyflavone (60 mg) The previously known compounds (peregrinine and 5,6-dihydroxy-7,4′-dimethoxyflavone) were identified by their physical (mp, $[\alpha]_D$) and spectroscopic (IR, UV, ^1H NMR, mass spectra) data and by comparison (mmp, TLC) with authentic samples

Preperegrinine (**2**) A syrup, $[\alpha]_D^{19}$ −41 7° ($CHCl_3$, *c* 0 276), IR ν_{max}^{NaCl} cm^{-1} 3100, 3020, 2980, 2940, 2880, 1780, 1715, 1615, 1460, 1395, 1375, 1335, 1300, 1145, 1125, 1070, 990, 945, 900, 885, 860, 830, 805, 750, 665, ^1H NMR (80 MHz, $CDCl_3$) see discussion of results, EIMS (direct inlet) 75 eV, *m/z* (rel int) 346 $[M]^+$ (20), 331 (1), 328 (2), 317 (2), 302 (4), 274 (3), 265 (17), 247 (4), 224 (16), 223 (13), 205 (28), 195 (6), 189 (7), 177 (19), 165 (10), 152 (18), 149 (22), 135 (18), 123 (76), 109 (26), 96 (24), 95 (70), 93 (24), 85 (41), 83 (85), 82 (60), 81 (100), 79 (20), 77 (15), 69 (18), 67 (30), 59 (26), 55 (36), 53 (31), 47 (22), 43 (84), 41 (60) $C_{20}H_{26}O_5$ MW 346

Peregrinine (**1**) *from preperegrinine* (**2**) A suspension of preperegrinine (**2**, 60 mg), CH_2Cl_2 (10 ml) and Amberlite IR-120 (H^+ form, 100 mg) was stirred at room temp for 1 hr The soln was



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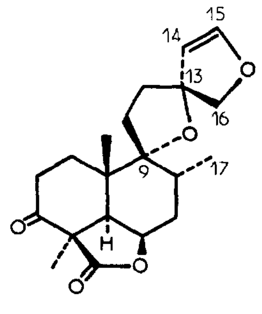

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filtered and the solvent removed After prep TLC purification it yielded a compound (43 mg), mp 174–176° (from EtOAc–*n*-hexane), $[\alpha]_D^{19}$ + 52 0°(MeOH, *c* 0 74), which was identical with natural peregrinine (**1**) [lit [3] mp 172–173°, $[\alpha]_D$ + 48° (MeOH, *c* 1 0)] This identity was also confirmed by mmp, TLC and spectroscopic (IR, ^{1}H NMR, mass spectra) data

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STRUCTURE ANALYSIS OF RIMUENE BY ^{13}C NMR SPECTROSCOPY*

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Key Word Index—*Richea continentis*, Epacridaceae, diterpenoids, rimuene, ^{13}C NMR spectra

Abstract—A diterpenoid forming the major component of the hydrocarbon fraction of the epicuticular wax of *Richea continentis* from Baw Baw Alpine Reserve is shown to be rimuene

INTRODUCTION

In a survey of alkane distribution in the leaf epicuticular wax of Epacridaceae [1], a strong unexpected peak was observed on the gas chromatogram of the hydrocarbon fraction of the wax of *Richea continentis* B L Burtt from the Baw Baw Alpine Reserve (but not in similar material from the Kosciusko National Park) It formed 41–43 % of the hydrocarbon fraction, while the major alkane, hentriacontane, was present to the extent of 21–25 % The present structure analysis shows this component to be rimuene (**1**), first isolated from *Dacrydium cupressinum* Lamb (Podocarpaceae) [2] and later found in a number of other gymnosperms However, there is only one report of rimuene having been found in a dicotyledon (*Cinnamomum cassia*, Lauraceae [3])

RESULTS AND DISCUSSION

Combined GC/MS of the hydrocarbon fraction gave a very simple mass spectrum for the unknown 272 (20), 257 (100), 80 (70), which according to mass spectra catalogues [4, 5] is characteristic of rimuene However, it is known in terpene chemistry that identical mass spectra may sometimes be obtained from different compounds, e g the triterpenes of the ursane and oleanane series Therefore it was considered necessary to isolate the compound and to verify its identity by the ^{13}C NMR spectrum

The ^{13}C NMR shifts and multiplicities for olefinic carbons in the hydrocarbon were identical with those reported [6] for rimuene (**1**) [δ 111 6 (CH_2), 116 0 (CH), 145 6 (C), 146 6 (CH)] Because of the unavailability of the ^{13}C NMR shifts for the saturated carbons of rimuene, the identification of the unknown was achieved by a comparison of the ^{13}C NMR shifts of the unknown with those reported [7] for *ent*-5,15-rosadiene (**2**) (Table 1) The diene **2** differs from rimuene in having an enantiomeric nucleus and an inverted relative configuration at C-13, displaying the equatorial vinyl group Thus the ^{13}C NMR

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