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Methoxynepetaefolin, A New Labdane Diterpene from Leonotis nepetaefolia

P. S. Manchand*

Department of Chemistry
Harvard University
Cambridge, Massachusetts 02138

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Our recent studies[1,2] on the constituents of the tropical plant Leonotis nepetaefolia R. Br (Labiatae) have resulted in the isolation and structural elucidation of a number of new labdane diterpenes of which nepetaefolin (I) is the most abundant. This communication reports the isolation of an additional but biogenetically interesting labdane diterpene, methoxynepetaefolin (II), as a minor constituent of L. nepetaefolia.

Methoxynepetaefolin has the molecular formula $C_{23}H_{32}O_8$ (M^+ 436.1985), mp 275-278°, $\{\alpha\}_D^{26}$ -35.8° (C 1.2, $CHCl_3$), $\nu_{max}^{CHCl_3}$ 1737 (OAc), 1725 (δ-lactone) and 1031 cm^{-1} (OMe).

The n.m.r. spectrum ($CDCl_3$)[3] of methoxynepetaefolin revealed a close structural similarity to that of nepetaefolin. Thus, two sharp 3H singlets at 1.16 and 2.02 are attributed to methyl and acetate groups at C_4 and C_6 respectively; absorption due to the methine proton at C_6 appeared as overlapping triplets centred at 5.20. Three AB quartets were discernible: the first of these, at 2.30 and 2.62 (J = 3.5 Hz), is due to the protons of the terminal epoxide at C_8; the second, at 3.53 and 3.78 (J = 8 Hz), represents absorption due to the methylene protons on C_{16}; the third, at 4.00 and 5.10 (J = 11 Hz), is indicative of the methylene protons on C_{20} which form part of the δ-lactone system. A pair of doublets at 4.96 and 5.02 (J = 6 and 3 Hz) are attributed to the X part of an ABX system, these absorptions are therefore ascribed to the proton on C_{15}. Absorption due to the methoxyl group appeared as a sharp singlet at 3.38.

No structurally diagnostic features of any significance could be obtained from the mass spectrum[4] of methoxynepetaefolin; the main peaks present were at m/e 405 ($M-OCH_3$), 376 ($M-CH_3CO_2H$) and 361 ($M-CH_3CO_2H - CH_3$).

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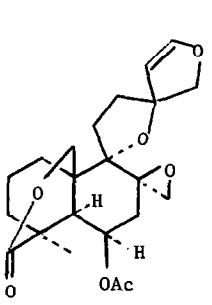
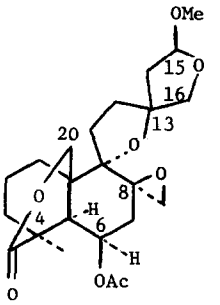
*Present address: Chemical Research Department, Hoffmann-La Roche Inc., Nutley, New Jersey 07110.



(I)



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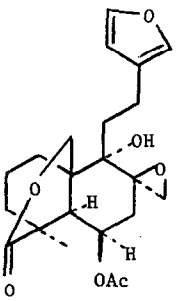

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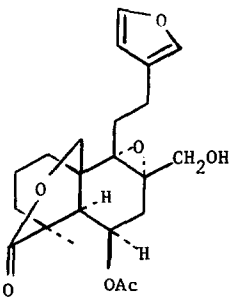

(IV)

The above spectral evidence leads to structure (II) for methoxynepetaefolin. Confirmation of this structure was provided by its conversion to a mixture of nepetaefuran[2] (III) and isonepetaefuran (IV) when treated with 1% methanolic sulfuric acid at room temperature for 3 hr. The stereochemistry associated with centres C_{13} and C_{15} was not determined.

Biogenetically the methoxyl group in methoxynepetaefolin is most likely formed by C_1 methylation (S-methionine?) of the corresponding hemi-acetal. Compounds containing the hemi-acetal[5] and γ-lactone[6] functions at C_{15} in premarrubiin[7] have recently been isolated.

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References

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3. Determined on a Varian HA-100 spectrometer with T.M.S. as internal standard. Chemical shifts are expressed in δ-values.

4. Mass spectral data were obtained from an AEI MS-9 double focusing instrument.

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