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PETALINE: A 7,8-DIOXYGENATED BENZYLISOQUINOLINE

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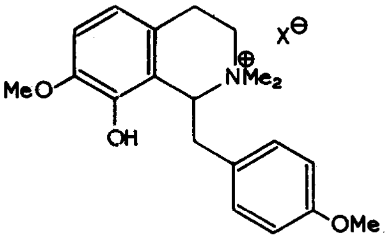
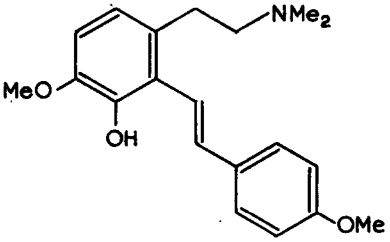
The presence of oxygen functions in the 6- and 7- positions is a characteristic feature not only of all the hitherto reported benzylisoquinoline alkaloids but also of all but one of the various groups of alkaloids which can be considered to be derived biogenetically from a benzylisoquinoline precursor. This exception is the cularine group of alkaloids and here a 7,8-dioxygenated benzylisoquinoline precursor has been suggested (1). We now present evidence that the quaternary alkaloid petaline (reassigned molecular formula $C_{20}H_{26}O_3N^+X^-$), which occurs in Leontice leontopetalum L. (2) has the structure I, making it the first simple benzylisoquinoline alkaloid having a 7,8-dioxygenation pattern.

Petaline, which was isolated as the reineckate as previously described (2), undergoes Hofmann degradation under exceptionally mild conditions, passage of an ethanolic solution of the reineckate or chloride through a column of Amberlite IRA-400 (OH) anion exchange resin being sufficient to produce the corresponding methine base (II), $C_{20}H_{25}O_3N$, molecular weight 327 (mass spectrum). This was identical in all respects with the previously described leonticine (2), which in view of the alkaline conditions used during the isolation procedure is therefore most likely an



I

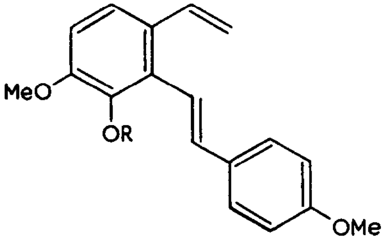


II

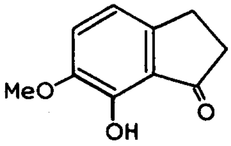
artefact rather than a second alkaloid of <u>L. leontopetalum.</u> We therefore propose to describe this compound as petaline methine rather than leonticine in future.

Petaline methine contains two methoxyl groups (analysis, n.m.r.) and a phenolic hydroxyl group [τ4.05, disappearing on deuteration, deep purple colouration with ferric chloride in methanol, ν_{max} (in CCl_4) 3540 cm^{-1} (in accord with a location <u>ortho</u> and weakly intramolecularly hydrogen bonded to a methoxyl group)]. Dilute aqueous sodium hydroxide gives a sparingly soluble sodium salt. The presence of a dimethylaminoethyl side chain in petaline methine was indicated by the appropriate n.m.r. peaks [multiplets (4H) at 7.0-7.6τ, singlet (6H) at 7.65τ] and by conversion of its methiodide, m.p. 169-171°, by anion exchange resin into the corresponding methohydroxide, which underwent Hofmann degradation on refluxing with ethanolic sodium ethoxide. This gave trimethylamine, which was characterised as its picrate, and a styrene, III (R=H.), mass spectrometric molecular weight 282, λ_{max} 269 mμ ($\Delta\varepsilon$ 13,000) (3) superposed on the spectrum of petaline methine (vide infra). The methylidine protons stood out clearly in the n.m.r. spectrum of the corresponding acetate (III, R=Ac) as 2 doublets (each 1H) at 4.5 τ (J=17c.p.s.) and 4.9 τ (J=10c.p.s.) each peak being further split into a doublet (J=ca.1.6c.p.s.).

The absence of a substituent *para* to the phenol group in petaline methine was indicated by a positive Gibbs test (4) (sharp maximum at 623 mμ, log ε ca.4.0) and this was confirmed as follows. The methine was converted into its amorphous *O*-methanesulphonyl derivative, which, without purification, was oxidised with potassium dichromate in 6*N*-aqueous sulphuric acid to give *p*-methoxybenzoic acid[*] and 3-methanesulphonoxy-4-methoxyphthalic acid. The latter, which was characterised as its anhydride, was identical (i.r. and mixed m.p.) with a sample synthesised by an unambiguous route via the indanone IV (5).



III



IV

These findings are accommodated by two alternative structures for petaline methine namely II and V. However, structure V was shown to be

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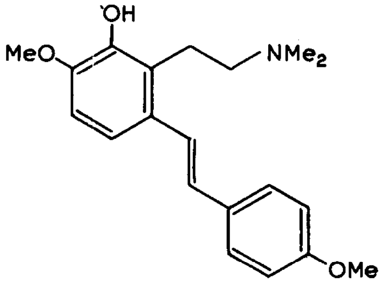
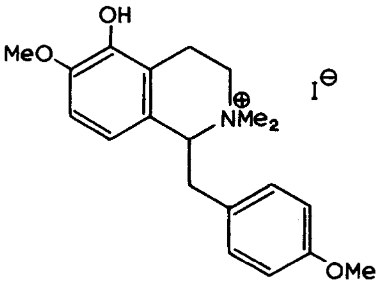
[*] The corresponding aldehyde was obtained by ozonolysis of petaline methine.

incorrect by the dissimilarity (m.p. and i.r.) of petaline methine (m.p. 123°) with a sample of the synthetic compound V (m.p. 173°) prepared in a straightforward manner via VI. The latter compound (VI) was easily differentiated from its isomer petaline iodide (I,X=iodide) since IRA-400 (OH) resin converted VI into the corresponding quaternary hydroxide. It follows therefore that the most probable structures for petaline and petaline methine are I and II respectively.

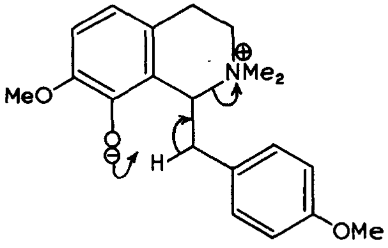


V



VI

The assignment of the hydroxyl group to the 8- position of petaline allows an explanation of the position of the long wavelength band (299 mµ, log ϵ 4.32) of petaline methine in terms of steric inhibition of stilbene resonance (6). (Cf. the isomeric stilbene V λ_{max} 317 mµ, log ϵ 4.37). It also accords well with the particular facility with which petaline undergoes Hofmann degradation since the phenolate anion will be appropriately located for intramolecular abstraction of the hydrogen atom β to the quaternary nitrogen atom (see VII).



VII

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References

1. R. H. F. Manske, J. Amer. Chem. Soc., 72, 55 (1950).
2. J. McShefferty, P. F. Nelson, J. L. Paterson, J. B. Stenlake and J. P. Todd, J. Pharm. Pharmacol., 8, 117 (1956).
3. Cf. A. I. Scott, Interpretation of the Ultraviolet Spectra of Natural Products, Pergamon Press, London (1964), pp. 97-100.
4. F. E. King, T. J. King and L. C. Manning, J. Chem. Soc., 563 (1957).
5. Cf. R. D. Haworth, W. H. Perkin and T. S. Stevens, Ibid., 1764 (1926).
6. H. Suzuki, Bull. Chem. Soc., Japan, 33, 406 (1960).