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CATALINE, A NEW APORPHINE ALKALOID FROM GLAUCIUM FLAVUM Cr. VAR. VESTITUM.

I. Ribas, J. Sueiras and L. Castedo

Laboratorio del Departamento de Quimica Orgánica de la Facultad de Ciencias
y del Patronato "Juan de la Cierva" del C.S.I.C.
Santiago de Compostela, Spain

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In the study of alkaloids from Glaucium Flavum Cr. var. Vestitum, the isolation and characterization of two new aporphine alkaloids, corunnine and pontevedrine was recently reported (1).

We further examined alkaloidal components of the above plant and could isolate a new non-phenolic aporphine alcaloid, namely cataline (I) (2), in addition to the known aporphine alkaloids thalicmidine (II) (3) and dehydroglaucine (IX) (1, 6). They were obtained only in small amounts from the plant. To our knowledge, the isolation of thalicmidine from Glaucium Flavum Cr. var. Vestitum represents the first time this alkaloid has been found in the Papaveraceae.

Recently, Kunitomo and coworkers reported the isolation of sterporphine from Stephania Sasakii HAYATA, the first aporphine found to be hydroxylated at C–4 (4). In this paper, chemical transformations of cataline (I) are described, and these, together with physical evidence, led us to establish structure (I) for the new alkaloid, which is the second example of a 4–hydroxylated aporphine.

Cataline (I) was obtained as colourless crystals, m.p. 183°C, $[\alpha]_D$ + 166° ($CHCl_3$) and gave a molecular ion peak at m/e 371, confirming the molecular formula $C_{21}H_{25}O_5N$ assigned on the basis of elementary analysis. The UV spectrum exhibited $\lambda^{EtOH}_{max.}$ 303 and 282 mμ (log. ε 4,14 and 4,14) characteristic of a 1, 2, 9, 10–tetrasubstituted aporphine. The IR spectrum ($CHCl_3$) of the alkaloid showed absorption due to intramolecularly hydrogen–bonded hydroxyl (at 3520 cm^{-1}) and its NMR spectrum ($CDCl_3$) revealed an N–Methyl group (at 2,78 δ), four aromatic methoxy groups [at δ3,88 (3H), 4,20(3H) and 4,27 (6H)], three aromatic one proton singlets (at δ 7,10, 7,23 and 8,40) and one proton (at 4,83 δ) which appears as a poorly resolved triplet (half band width 4 cps). The total proton integration between δ 2 and 9 accounted for 25 protons (for $C_{21}H_{25}O_5N$).

O–acetylation of cataline (I) with acetic anhydride and pyridine at 0°C for three days gave a monoacetate (III), m.p. 91–92°C which showed absorption in the IR spectrum ($CHCl_3$) at 1715 cm^{-1} (acetoxy group). Its NMR spectrum was readily interpretable in accord with structure (III) and it showed an acetoxy group (at 2,30δ), an N–Methyl group (at 2,67δ), four methoxy groups [at δ 3,87 (3H) and 4,10 (9H)], three aromatic unsplit protons (at δ 6,95, 7,00 and 8,20) and a poorly resolved one proton triplet (at 6,03 δ; half band width 4 cps) which establishes the existence of a secondary hydroxyl group in cataline(I).

In the mass spectrum of cataline (I), peaks are observed at m/e 370 (M–1, a), 356 (b), 340 (c) and 328 (d) in addition to the molecular ion peak. The presence of the strong peak (d), derived from the molecular ion by retro–Diels–Alder type fragmentation, strongly suggests that the hydroxyl group must be situated at the C–4 position. Similar spectroscopic evidence was presented by Kunitomo and coworkers in the case of sterporphine (4).

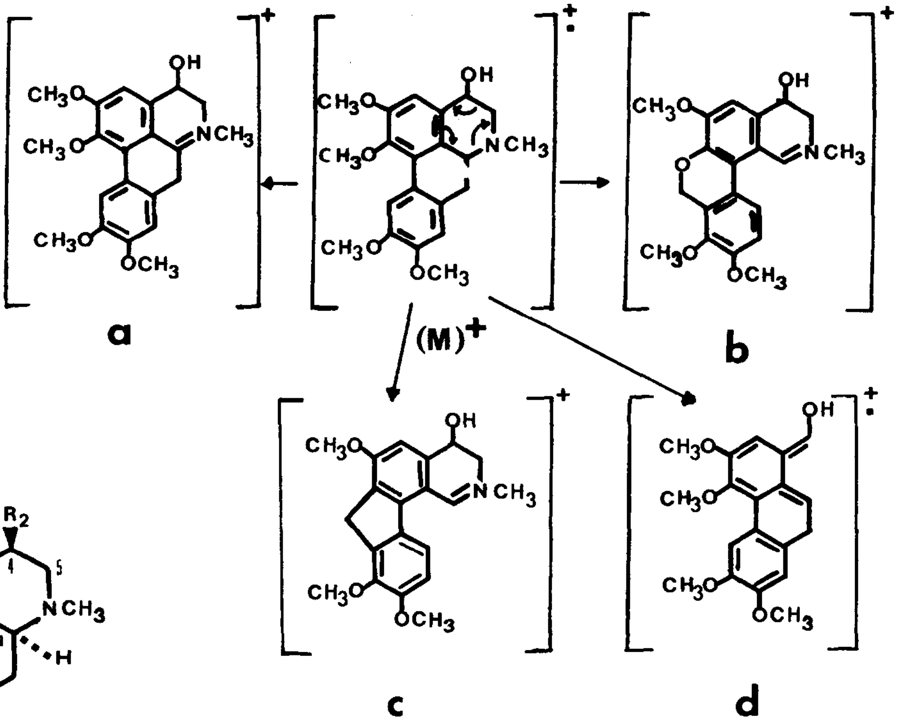
Since the IR spectrum of cataline (I) shows the presence of an intramolecularly hydrogen–bonded hydroxyl and the proton at C–4 appears in the NMR spectrum of cataline (I) and its monoacetate (III) as a poorly resolved triplet (half band width 4 cps), which is an indication that the dihedral angle is small between the C–4 proton and the vicinal protons at C–5, examination of Dreiding models of 4–hydroxy–aporphines clearly shows that the relative configuration of cataline at C–4 and C–6a must be as shown in Fig. (I).

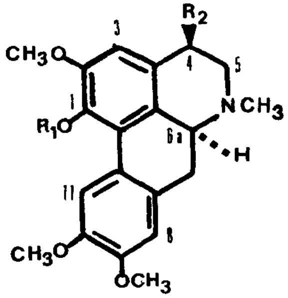
Catalytic hydrogenolysis of cataline (I) over 10 °/₀ palladium–charcoal in acetic acid containing a few drops of perchloric acid at 55°C under 4 atmosphere pressure for 4 hours yielded (+)–glaucine (IV). Identity was proved by direct comparison (t.l.c., UV and NMR) with authentic material. Since the absolute configuration of (+)–glaucine (IV) is (S) (5), provided that the transformation (I) to (IV) does not involve inversion at C–6a, the following absolute configuration is proposed for cataline: (4S: 6a S).

In attempting to dehydrate cataline (I), we have found that treatment of cataline (I) with aqueous sulphuric acid (1:1) for about 5 hours at 90°C afforded a mixture of didehydroglaucine (V), corunnine (VI) and traces of pontevedrine (VII) which was resolved by Alumina chromatography. The identity of corunnine and pontevedrine was established by direct comparison (UV, t.l.c.) with natural materials.

Didehydroglaucine (V) was obtained as an unstable yellowish froth and showed absorption bands in the UV spectrum at $\lambda_{max.}^{EtOH}$ 415, 405, 358, 265 and 243 mμ .On addition of an acid, a shift of the absorption bands was observed and they then appeared at $\lambda_{max.}$ 430, 283 and 255 mμ . The IR spectrum ($CHCl_3$)of the compound showed absorption at 1648 and 1610 cm^{-1} (C=C and benzene ring) and its NMR spectrum was readily interpretable in accord with structure (V); it showed an N–Me group (at 3,34 δ), four aromatic methoxyl groups [at δ 4,10 (3H), 4,21 (3H) and 4,28 (6H)], four unsplit protons (at δ 6,30, 6,77 and 7,15) and one AB quartet (J = 7,5 cps. δ_A= 5,90, δ_B= 6,60) assigned to non–equivalent protons designated as H–4 and H–5.

Since dehydroglaucine (IX) is difficult to reduce catalytically (6) we obtained further proof of didehydroglaucine by catalytic reduction of the compound over Adams catalyst in ethanol, which yielded dehydroglaucine (IX) identical in all respects with authentic material (1). We regard the formation of didehydroglaucine (V), corunnine (VI) and pontevedrine (VII) as due not only to the dehydrating action of the sulphuric acid but also to its oxidizing action. 4–5–dehydroglaucine has not yet been isolated.



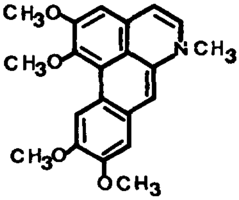


I, $R_1=CH_3$, $R_2=OH$

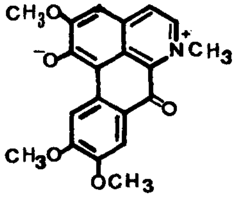
II, $R_1=H$, $R_2=H$

III, $R_1=CH_3$, $R_2=OAc$

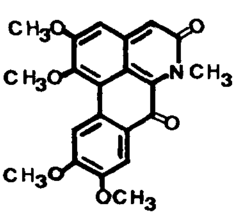
IV, $R_1=CH_3$, $R_2=H$



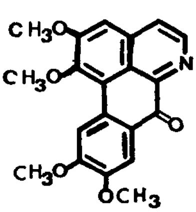
V



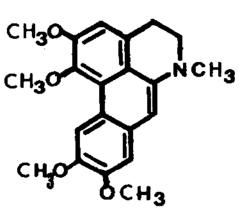
VI



VII



VIII



IX

Finnally, since free oxygen oxidation of cataline (I) and didehydroglaucine (V) in hot hexamethylphosphoramide under free radical conditions afforded a mixture of pontevedrine (VII) (main product), corunnine (VI) and traces of yellow compound (VIII) (1), further studies on this reaction and the action of different oxidizing agents on compounds (I) and (V) are in progress.

Acknowlegments

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References

NMR spectra were obtained on JEOL miNiMaR–60 spectrophotometer.

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