Tetrahedron Letters No. 33, pp.3093-3096, 1971. Pergamon Press. Printed in Great Britain.

CORUNNINE AND PONTEVEDRINE, TWO NEW APORPHINE ALKALOIDS FROM GLAUCIUM FLAVUM CR. VAR. VESTITUM.

I. Ribas, J. Sueiras and L. Castedo.

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

(Received in UK 28 June 1971; accepted in UK for publication 14 July 1971)

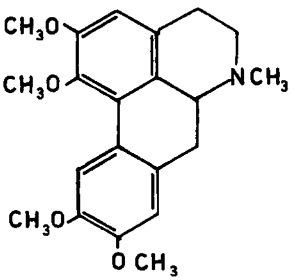
In the course of our studies of Spanish Papaveraceae, two novel highly coloured, weakly basic alkaloids have been isolated from Glaucium Flavum Cr. var. Vestitum. They are present in only very small amounts, along with small quantities of the closely related yellow alkaloid (IV) (1) and colourless alkaloids, and large amounts of Glaucine (I) (1). We have named them Corunnine and Pontevedrine and propose structures (II) and (III), respectively, on the following evidence. To our knowledge, Pontevedrine (III) represents the first example of a 5,7-dioxo-aporphine (2).

Corunnine (II) crystallized from ethanol as violet needles, M.P., 255-57°C and gave a molecular ion peak at m/e 351, confirming the molecular formula $C_{20}H_{17}O_5N$ assigned on the basis of elementary analysis. It is little soluble in the common organic solvents and insoluble in aqueous alkali, and it gave a positive ferric chloride test. Corunnine is green in neutral or basic solution and redish in acid solution. Its UV spectrum in ethanol or aqueous ethanolic alkali showed the following absorption: $\lambda_{max.}$ (log ϵ) 258 (4,13), 325 (4,32), 400 (3,54)440 (sh, 3,42) and 630 nm (3,35). On addition of acid, a hypsochromic shift of the absorption bands from those observed in ethanol resulted; a similar shift is known in the case of the alkaloid PO-3 (3). In acid solution, the UV spectrum of Corunnine is close to that of yellow alkaloid (IV) (by direct comparison) and showed the following absorption: $\lambda_{max.}$ (log ϵ) 256 (4,23), 295 (4,14), 385 nm (3,75)

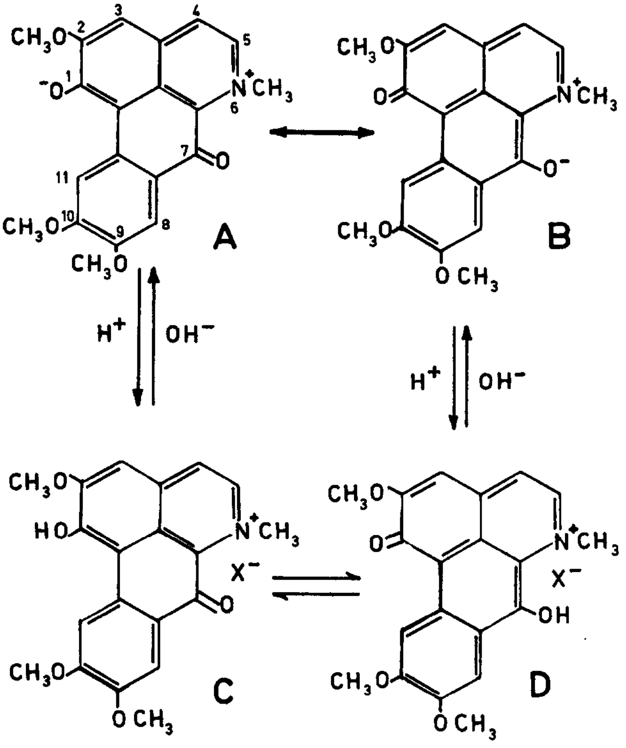
In the region of C=O, C=C and C=$\overset{+}{N}$ stretching frequencies, the IR spectrum (BrK) of Corunnine only revealed two bands at 1620 (w) and 1567 cm^{-1} (m). Owing to its low solubility, its NMR spectrum could be only obtained in TFA and it revealed three aromatic methoxy groups at δ 4,55 (6H) and 4,80 (3H), one sp^2 $\overset{+}{N}$-Me group at 5,36, one AB quartet (J=6 cps, δ A=8,75 and δ B=8,95) assigned to non-equivalent protons dessignated as H-4 and H-5 (II) and three aromatic one proton singlets at δ 7,93, 8,33 and 9,30.

Corunnine monoperchlorate has been obtained and crystallized from an acid solution of ethanol/40%aqueous perchloric acid (7/1) as purple needles, M.P., 293-95° C, which gave satisfactory combustion analysis; in attempting to crystallize Corunnine monoperchlorate from aqueous ethanol, the free base resulted. As in the case of the free base, Corunnine monoperchlorate only revealed bands at 1640 (w) and 1598 cm^{-1} (m) in this region of the IR spectrum (BrK).

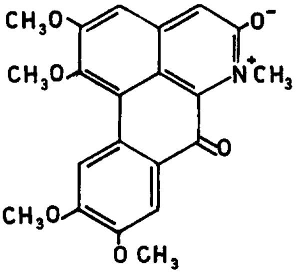
Since it has recently been determined (3) that only 7-Oxo-dibenzo-(de,g)-quinoline derivatives which carry a phenol group on C-1 or C-11 are green coloured compounds if they also have a zwitterionic structure, the aforemetioned data strongly suggest that Corunnine possesses a mesomeric and zwitterionic structure (II, A$\leftrightarrow$B). Tautomeric forms (II, C$\rightleftarrows$D) are ascribed to Corunnine in acid solution.



I



II



III

Pontevedrine(III) crystallized from ethanol/chloroform (1/1) as red needles which melted at 269-71° C, analyzed for $C_{21}H_{19}O_6N$, was insoluble in aqueous alkali and gave a positive ferric chloride test. Mass spectrometry confirmed the molecular weight as 381. Pontevedrine showed bands in the IR spectrum (BrK) at 1660 (s) (conjugated Carbonyl group), 1615 (w) and 1590 cm^{-1}, ($C{=}C$ and $C{=}N^{+}$ groups). Its UV spectrum in ethanol showed the following absortion: λ_{max} (log ϵ) 245 (4,59),312 (4,28), 325 (4,39) and 470 nm (4,01);on addition of acid or alkali to the ethanolic solution, no shift of these maxima has been observed. The NMR spectrum ($CDCl_3$) revealed four aromatic methoxy groups at δ 3,96 (3H), 4,00 (3H), and 4,10 (6H), one weakly basic N-Me group at δ 3,50 and four aromatic one proton singlets at δ 6,96, 7,00, 7,70 and 8,80. The above data suggest a rather zwitterionic structure (III) for Pontevedrine.

Further support for structures (II) and (III) of Corunnine and Pontevedrine was obtained both by their synthesis from Glaucine(I) as well as from yellow alkaloid (IV). Glaucine (I) has been isolated from Glaucium Flavum Cr. var. Vestitum and the yellow alkaloid (IV) obtained from Glaucine (I) and chromic acid in pyridine oxidation (4). A total synthesis of (IV) is known (5).

Since it has been suggested that Liriodenine type of alkaloids are probably derived from co-ocurring aporphine in the plant (5), we decided to reinvestigate the chromic acid in pyridine oxidation of Glaucine which is known to give (IV) (4) We have thus found that treatment of Glaucine (I) with a large excess of CrO_3 -Pyridine complex in dichloromethane (6) at O °C during 45 min. afforded a mixture in low yield of Dehydroglaucine (VII), Corunnine (II), Pontevedrine (III) and yellow alkaloid (IV), separable by Alumina chromatography (Act.III). The faster moving component (t.l.c.) was identified as Dehydroglaucine (VII) [IR,NMR, UV and M.P.(1,7)] and the major component of the reaction product was the yellow alkaloid (IV) [IR, UV. NMR and M.P.(1,8)]. Corunnine (II) and Pontevedrine (III) were only present in small amounts and their identity was proved by direct comparison (IR, t.l.c., UV and mixed M.P.) with the corresponding natural materials.

In attemting to prepare the N-Methyl quaternary salt (V) as a possible synthetic intermediate to (III), we have unexpectedly found that (IV) was converted almost quantitatively to Corunnine (II) (Fig. 1).

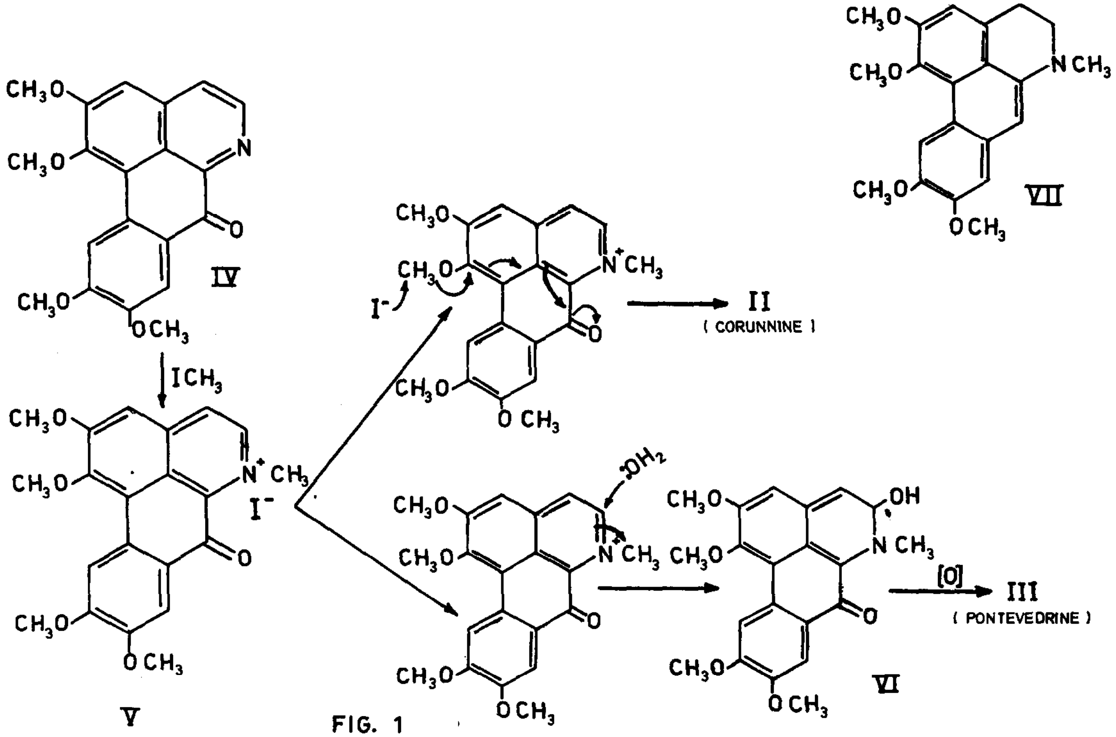


FIG. 1

Thus, treatment of (IV) with excess of methyl Iodide in dry benzene for several hours under reflux afforded Corunnine (II) which was purified by filtration over Alumina (act. III). When the experiment was repeated in commercial acetone, reaction between (IV) and methyl Iodide gave a reaction product which contained Corunnine (II) and small amounts of Pontevedrine (III), which were isolated by alumina chromatography. Shorter reaction times led us to the isolation of an appreciable amount of quaternary salt (V) by Alumina chromatography of the reaction product; subsequent boiling of an acetonic solution of (V) afforded Corunnine (II) as the only reaction product. In vew of these findings and from t.l.c. evidence (the reactions were followed by t.l.c.), the formation of Corunnine (II) and Pontevedrine (III) may be regarded as proceeding in the following manner: initial quaternization of (IV) with methyl Iodide leads to (V) which either is demethylated to (II) (main reaction) or can react with water to give (VI) which can be oxidized to (III) by the Iodine resulting from the partial decomposition of the methyl Iodide during the heating.

The above chemical evidence fully proves that the carbon skeleton of Corunnine (II) and Pontevedrine (III) must be that of a 1,2,9,10-tetraoxygenated aporphine.

The possibility of (II) and (III) being artefacts derived from co-ocurring aporphines by air oxidation during the isolation has been rejected since a rapid extraction of alkaloids from fresh plant showed the presence (t.l.c.) of (II) and (III) in the crude extract. Further studies on this point and unambigous synthetic work to confirm the proposed structures (II) and (III) for Corunnine and Pontevedrine, respectively, are in progress.

Acknowledgments.

We thank "Fundación Barrié de la Maza" for its finnantial support and to Mr. G.C. Crawley (University Chemical Laboratory, Cambridge) for the mass spectra.

References

NMR spectra were obtained on a JEOL miNiMaR-60 spectrometer.

1.- Kiryakov KH. G. and Panov P., Dokl. Bolg. Acad. Nauk.,**22** **(9)**, 1019 (1969); Chem. Abstr.**72**,51776B (1970).

2.- Glick M.D., Cook R.E., Cava, M.P., Srinivasan M., Kunitomo J. and DaRocha A.I., Chem. Comm., 1217 (1969).

3.- Preininger V., Hrbek jun.J., Samek Z and Šantavý F., Arch. Pharmaz.**302**,808 (1969).
4.- Tomita M., Yang T.-H., Furukawa H. and Yang H.-M., J. Pharm. Soc. Japan,**82**, 1574 (1962); Chem.Abstr.,**58** 14012 (1963).

5.- Cohen J., Von Lagenthal W. and Taylor W.I., J. Org. Chem., **26**, 4143 (1961).

6.- Ratcliffe R. and Rodehorst R., J. Org. Chem.,**35**, 4000 (1970).

7.- Kiryakov H.G., Chem. and Ind., **51**, 1807 (1968).

8.- Buchanan M.A., and Dickey E.E., J. Org. Chem.,**25**, 1389 (1960).