

## AROSINE AND AROSININE, TWO NEW QUATERNARY OXOAPORPHINE ALKALOIDS

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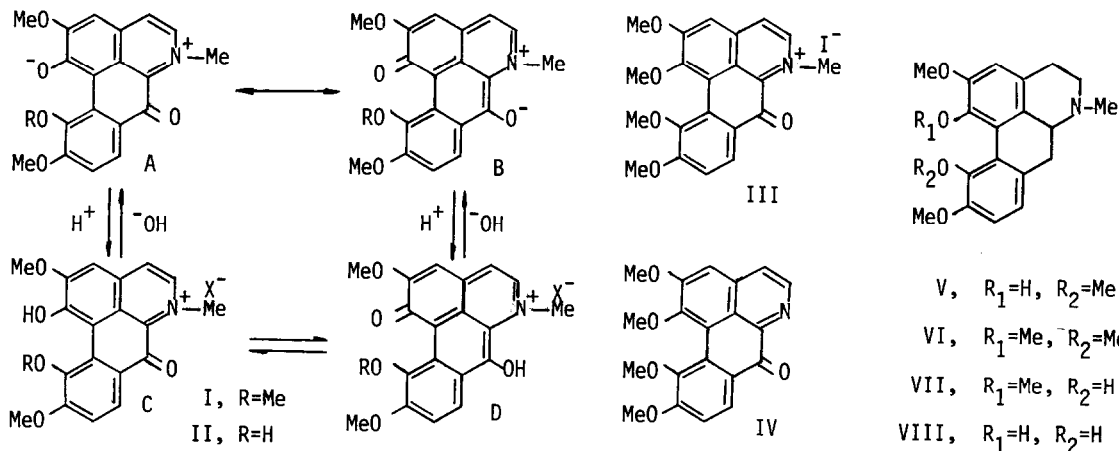
SUMMARY. Structure of (I) and (II) were deduced from spectral data, chemical evidence and synthesis.

Further to our study on the alkaloids from the roots of *Glaucium flavum* Cr. var. *vestitum* (1), we can now report the isolation of two new alkaloids, namely arosine (I) and arosinine (II), which represent the two first examples of a 1,2,10,11-tetrasubstituted quaternary oxoaporphine (2). They are highly coloured compounds, obtained only in small amounts from the plant and their structures assigned on the bases of the following evidence.

Arosine (I) was isolated as dark green prisms (EtOAc/CHCl<sub>3</sub>), mp 245-8°C(dec.). It is green in neutral or basic solution and yellow upon addition of acid. High resolution mass spectrometry and elemental analysis established its molecular formula as C<sub>20</sub>H<sub>17</sub>NO<sub>5</sub> (M<sup>+</sup> 351.1113; calculated 351.1107). The IR spectrum shows  $\nu_{\text{max}}^{\text{KBr}}$  3400-3650 (OH), 1625 weak (highly conjugated carbonyl) and 1580 cm<sup>-1</sup> strong, and its UV spectrum in ethanol or basic solution exhibits the following absorptions:  $\lambda_{\text{max}}^{\text{EtOH}}$  (log.ε) 238(4.47), 314(4.40), 410(3.78) and 610(3.60). On addition of acid a very strong hypsochromic shift of the absorption bands was observed which then appeared at  $\lambda_{\text{max}}^{\text{EtOH/HCl}}$  (log.ε) 221(4.50), 253(4.57), 282(sh,4.41), 383(3.95) and 430 nm(sh,3.60), being now very similar to both the oxoaporphine (IV)(in acid solution) and the methiodide (III) by direct comparison. This suggests the presence of a tetrasubstituted oxoaporphine skeleton in arosine(I). This was confirmed by its pmr (CDCl<sub>3</sub>/TFA-d<sub>1</sub>) which shows three aromatic methoxy groups at δ 3.87, 4.11 and 4.21 (at C-2, C-10 and C-11), one quaternary  $\overset{+}{\text{N}}$ -Me group at 4.71 (s,3H), one aromatic proton singlet at 7.46 (H-3) and two AB quartets [J=9 Hz, δ<sub>A</sub>=8.33 and δ<sub>B</sub>=7.28 (H-8 and H-9) and J=6.5 Hz, δ<sub>A</sub>=8.45 and δ<sub>B</sub>=8.27 ppm (H-5 and H-4)]. Reduction of arosine (I) with Zn in HOAc/HCl under reflux for one day afforded corydine (V) (3) in 75% yield which unambiguously establishes the 1,2,10,11-tetraoxygenated pattern and the placement of the three methoxy groups at C-2, C-10 and C-11 in arosine (I).

Further support for structure (I) of arosine was obtained from its synthesis which was accomplished by a route previously proved for the 1,2,9,10-tetrasubstituted oxoaporphine analogue corunnine (4). Thus photochemical oxidation (eosine, O<sub>2</sub>) (5) of 0,0-dimethyl corytuberine (VI), prepared by methylation of isocorydine (VII), afforded the oxoaporphine (IV) (45% yield). When treated with excess methyl iodide in acetone at room temperature for several hours produced quantitatively the methiodide salt (III) as red prisms, mp 155-7°C (6) which by subsequent refluxing in dry acetone (diluted solution) gave arosine (I) 65% yield and 89% based on recovered (III) .

Arosinine (II) crystallized from (CHCl<sub>3</sub>/EtOH) as very dark green needles, mp 302-5°C(dec.). It is green in neutral or basic solution and red in acid solution. High resolution mass spectrometry and elemental analysis established its molecular formula as C<sub>19</sub>H<sub>15</sub>NO<sub>5</sub> (M<sup>+</sup> 337.0949; calculated 337.0950). It exhibits an IR  $\left[ \nu_{\text{max}}^{\text{KBr}} \right]$  3650-3300 (OH), 1645 weak (highly conjugated carbonyl) and 1590



cm<sup>-1</sup> medium], UV [ $\lambda_{\text{max}}^{\text{EtOH}}$  (log.  $\epsilon$ ) 244(4.58), 317(4.53), 413(4.01) and 590 nm (3.76);  $\lambda_{\text{max}}^{\text{EtOH/HCl}}$  (log.  $\epsilon$ ) 246(4.65), 292(sh, 4.42), 316(sh, 4.35), 391(3.99) and 480 nm (3.62)] and pmr spectra [(CDCl<sub>3</sub>/TFA-d<sub>1</sub>) ( $\delta$ ) 4.12 and 4.20(s, 3H each, ArOCH<sub>3</sub>), 4.71(s, 3H, N-CH<sub>3</sub>), 7.43(s, 1H, H-3), 8.12 and 7.22(AB quartet), J=9Hz, 2H, H-8 and H-9 and 8.41 and 8.24ppm(AB quartet, J=6.5Hz, H-5 and H-4)] suggestive of the quaternary oxoaporphine structure(II). Reduction of arosinine(II) with Zn in HOAc/HCl under reflux for two days produced corytuberine(VIII)(3) in 70% yield thus proving that arosinine(II) must be a 1,2,10,11-tetraoxygenated oxoaporphine with the two methoxy groups located at C-2 and C-10.

Further evidence for structure(II) of arosinine was obtained as follows. Heating of oxoaporphine (IV)(7) at 150°C (bath temperature) for 16 hours gave after preparative tlc arosine (I) and arosinine (II) 15% and 45% yield respectively based on recovered (IV). When arosine (I) was treated in the same way, arosinine(II) was obtained in an almost quantitative yield (8) which establishes that arosine (I) is the first stage of the above transformation.

Since it has been noted that only aporphine alkaloids carrying a phenolic group at C-1 or C-11 give rise to green oxidation products (9), we have treated corydine (V) with I<sub>2</sub>/NaOAc in dioxane under reflux for five hours, we thus obtained a complex mixture from which arosine (I) (30% yield) was separated by preparative tlc on silica gel.

Arosine (I) and arosinine (II) therefore can be represented by corresponding forms A, B, C and D, the latter two prevailing in acid solution.

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3. The identity was proved by direct comparison(tlc, UV and pmr) with an authentic sample.
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8. MeOH was detected (glc) in this reaction which suggests that water is the necessary nucleophile.
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