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LUGUINE, A NEW BENZOPHENANTHRIDINE ALKALOID FROM GLAUCIUM FLAVUM CR. VAR. VESTITUM

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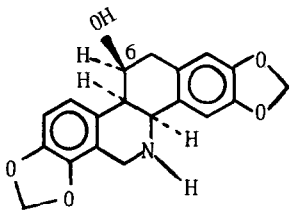
Previously (2,3), we have reported on the alkaloidal components isolated from the above-ground parts of *Glaucium flavum* Cr.var.*vestitum*. In addition to (-)-norchelidonine(I), protopine (major component), chelerythrine, chelirubine, sanguinarine, isoboldine and (+)-isocorydine described earlier from the roots of *Glaucium flavum* Cr.(4), norsanguinarine(IV)(5), oxysanguinarine (6), (+)-N-methyllindcarpine (7) and a new benzophenanthridine alkaloid, namely luguine(II), have now been isolated from the roots of *Glaucium flavum* Cr.var.*vestitum*. Norsanguinarine and oxysanguinarine have not previously been found in the *Glaucium* genus. The identification of the above known alkaloids was obtained from spectral and chemical evidence and by direct comparison with authentic samples.

In this communication, chemical transformations of luguine (II) are described and these, together with physical evidence, have led us to establish structure (II) for the new alkaloid, which is the first example of a 6-hydroxy benzophenanthridine alkaloid where ring C is aromatic.

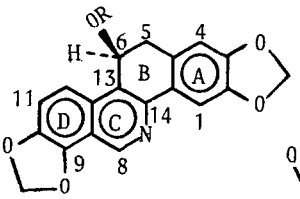
Luguine (II) was isolated as yellow crystals, mp 282-84°C (from ethylacetate), $[\alpha]_D^{20}$ +172° (c=0,05, dioxan) which analyzed for $C_{19}H_{13}O_5N$. Mass spectrometry confirmed the molecular ion as 335 and indicated the presence of a hydroxy group in luguine by showing a strong peak at m/e 317 (M^+-18, base peak). Its UV spectrum in dioxan or alkaline aqueous dioxan showed the following absorption: $\lambda_{max.}$ (log ε) 255(4,44), 334(4,36), 345(4,39) and 384(3,65). On addition of acid, a bathochromic shift of the absorption bands was observed which then appeared at $\lambda_{max.}^{0.1N\ HCl}$ in dioxan (log ε) 250(4,33), 269(4,29), 352(4,27), 362(4,30) and 458(3,80). The IR spectrum of the alkaloid (II) exhibited absorption (KBr) at 3400-3150 (OH) and 1650 cm^{-1} (C=N) and its pmr spectrum (80MHz, $CDCl_3$/TFA-d_1) revealed three aromatic one proton singlets [at δ 9,34, 7,35 and 6,87 (H8, H1 and H4, respectively)], one AB quartet [J=9Hz, δ_A=7,98 and δ_B=7,78 (H12 and H11)], two methylendioxy groups [at δ 6,40 and 6,03 (2H each, s)] and two broad signals [at δ 5,73 (1H, half band width 7Hz, H6) and 3,30 (2H, half band width 7Hz, H5)].

O-acetylation of luguine (II) with acetic anhydride in pyridine at room temperature for one day gave a monoacetate (III), mp 284°C, which showed absorption in the IR spectrum (KBr) at 1730 cm^{-1} (acetoxy group). Its pmr spectrum ($CDCl_3$) was readily interpretable in accord with structure (III) and it showed an acetoxy group (at δ 1,92), two methylendioxy groups [at δ 5,96 and 6,20 (2H each, s)], three aromatic one proton singlets [at δ 6,71, 7,97 and 9,29 (H4, H1 and H8, respectively)], one AB quartet [J=9Hz, δ_A=7,35 and δ_B=7,58 (H11 and H12)], a two proton doublet (at δ 3,20, J=3,5Hz, H5) and a one proton triplet (at δ 6,76, J=3,5Hz, H6) which establishes the existence of a secondary hydroxyl group in luguine (II).

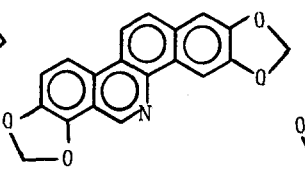
Direct evidence for the basic skeleton of luguine (II) was first obtained from its pmr spectrum which was identical to that of norsanguinarine(IV)(by direct comparison) after twelve



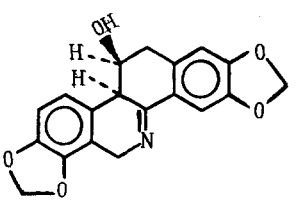
I



II, R=H
III, R=Ac



IV



V

hours at room temperature.This dehydration obtained on standing the pmr solution of the alkaloid (II) was achieved chemically by refluxing luguine (II) with $POCl_3/CHCl_3$ for six hours,affording norsanguinarine (IV) in 70% yield. When O-acetyl luguine (III) was treated with TFA at room temperature for 3 days, a quantitative yield of norsanguinarine (IV) was obtained.

All the above evidence strongly suggests that the structure of luguine must be that of a benzophenanthridine alkaloid in which the ring C is aromatic and hydroxylated at C-6 or C-5. This assignment was confirmed by the off-resonance C-13 nmr spectrum(DMSO-d_6)of luguine which showed only four aliphatic carbons [at 100,78, 102,62(each 1C,t,20-CH_2-O), 61,02(d, C6) and 36,13(t, C5)].

Finally,placement of the hydroxyl group in (+)-luguine at C-6 as well as the determination of its absolute configuration as shown in structure(II)were unambigously established from its chemical correlation with(-)-norchelidonine(I)as follows.Treatment of(-)-norchelidonine(I)with I_2/NaOAc in abs.EtOH under reflux for one day or with DDQ in dioxan at room temperature for 4 hours, afforded (+)-luguine(II) in 60 and 80% yield,respectively.However,when the dehydrogenation of norchelidonine (I) was carried out with 10% Pd/C in hot p-cymene for 5 hours, the reaction was accompanied by dehydration,giving a 60% yield of norsanguinarine(IV).Since the absolute configuration of (-)-norchelidonine(I)at C-6 is S(8),the following absolute configuration is proposed for(+)-luguine(II):(6S

(+)-Luguine(II)might represent an important intermediate to explain the biosynthetic origin of the completely aromatic benzophenanthridine alkaloids(9)such as norsanguinarine(IV),It is possible that (+)-luguine(II) is the result of a further transformation of (-)-norchelidonine(I) (present in a higher proportion in the plant), but, on the other hand, they may arise by separate biogenetic pathways from a common intermediate such as (V) derived from stylopine.

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