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STRUCTURE OF ERYSOPHORINE: A NEW QUATERNARY ALKALOID OF *ERYTHRINA ARBORESCENS**

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Key Word Index—*Erythrina arborescens*; Leguminosae; quaternary indole-eryso alkaloid, erysophorine.

Abstract—Isolation and structure elucidation of a new quaternary indole-eryso alkaloid, named erysophorine, from seeds of *Erythrina arborescens* are reported. An indole-erythrina alkaloid, such as erysophorine, has not been encountered before in nature or prepared synthetically.

INTRODUCTION

IN A PREVIOUS paper,[1] the occurrence of a new erythrina alkaloid, erythrascine, ten previously known erythrina bases, together with hypaphorine and a partially characterized tetrahydro-isoquinoline alkaloid has been reported in seeds of *Erythrina arborescens* Roxb. of Indian origin. Further investigation of the water-soluble alkaloid fraction of the seed extracts revealed the presence of a complex mixture of quaternary alkaloids. Preparative layer chromatography of this mixture afforded a new indole-erythrina alkaloid, which we named erysophorine. In this paper, we set out evidence for the structure of erysophorine as (**1**).

RESULTS AND DISCUSSION

The water-soluble bases were isolated as their reineckate salts, precipitated at two pH levels (*ca* 8 and 2), according to previously described procedures.[2,3] Erysophorine (**1**) was hydrolysed when an EtOH-soln of its reineckate salt was passed over De-Acidite FF (HO^-) resin column.[2] The quaternary alkaloids were therefore isolated as their chlorides by exchanging EtOH-solns of their reineckate salts with Amberlite IRA-400 (Cl^-). Subsequently, PLC of the mixture of quaternary chlorides afforded two quaternary alkaloids as homogeneous entities. Erysophorine, the major quaternary alkaloid, crystallized from acetone–methanol as a brown microcrystalline solid which decomposed, without melting, above 260°. The molecular formula, $C_{32}H_{38}N_3O_4Cl$, of erysophorine chloride was established from elemental analyses and from the integrals of the proton signals (38H ± 1H in DMSO–d_6). Erysophorine, as such, did not respond to an Ehrlich test for α- or β-unsubstituted indoles. The acid hydrolysed product, on the other hand, showed a positive Ehrlich test. This is presumably due to the attachment of the bulky ester function which blocks

* Part V in the series "*Erythrina* Alkaloids". For Part IV see ref. 1.

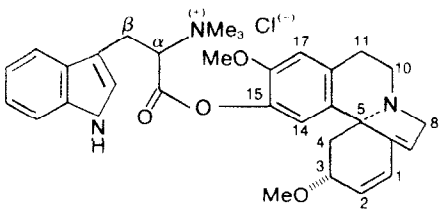
[1] GHOSAL, S., CHAKRABORTI, A. and SRIVASTAVA, R. S. (1972) *Phytochemistry* **11**, 2101.

[2] GHOSAL, S., BANERJEE, P. K. and BANERJEE, S. K. (1970) *Phytochemistry* **9**, 429.

[3] GHOSAL, S., DUTTA, S. K. and BHATTACHARYA, S. K. (1972) *J. Pharm. Sci.* **61**, 1274.

the free α-position of the indole ring of erysophorine. The UV absorption spectrum of erysophorine is strikingly similar to that of an equimolecular mixture of hypaphorine[1,3] and erysovine.[1,3] The IR spectrum of the alkaloid exhibited major bands at ν 3400 (br., NH), 1768 (phenol ester), 1612 (indole ring), 1585, 1502, 1285, 1092 cm^{-1} (spiroamine ring). Erysophorine did not exhibit a M^+ in its MS, but significant fragment ion peaks appeared corresponding to the 1,6-diene aromatic erythrina[4] and carboxylated indole-3-alkylamine moieties present. The 60 MHz PMR spectrum of the alkaloid in D_2O provided further information on its structure. Thus, the quaternary N,N,N-trimethyl signal appeared as the most intense peak at δ 3·15 (9H, s), followed by two methoxy group singlets at δ 3·45 (3H, s) and 3·65 (3H, s). The olefinic (C_1, C_2, C_7 of spiroamine), aromatic (C_{14}, C_{17}), and indole ring protons appeared as a 10-proton group of signals between δ 5·85–7·6. In addition, the methine (C_3, α-CH) and methylene (C_4, C_8, C_{10}, C_{11}, β-CH_2) protons absorbed as a 12-proton group of signals between δ 1·98–4·45.

The further chemistry of erysophorine, in particular, the hydrolysis of the alkaloid with dilute HCl to give hypahorine[1,3] and erysovine,[1,3] is readily explicable in terms of the formula (**1**) for erysophorine.



(1)

The phenolic erythrina (eryso) alkaloids which are usually present in a water-soluble bound form, their phenol groups are, for the most part, esterified with sulphoacetic acid as in erysothiovine and erysothiopine, and more rarely bound to glucose, as in glucoerysodine. This study is the first demonstration of the occurrence of an eryso alkaloid involved in an ester linkage with the indole base, hypaphorine. Hypaphorine occurs ubiquitously in *Erythrina* species although its role, if any, in the biogenesis of erythrina alkaloids is as yet unknown. It is however, well established[5] that for the phenolic oxidative coupling of the precursor (N-*nor*-protosinimenine) of erythrina bases, O(7)-substitution of the benzylisoquinoline compound is a key step. In view of this fact, the natural occurrence of the ester alkaloid (**1**) seems to be biogenetically significant as it may account for the co-occurrence of hypaphorine with erythrina alkaloids. In erysophorine, the point of hypaphorine ester linkage, located at O(15) of the erysovine moiety, is equivalent to O(7)-position of the benzylisoquinoline precursor. Further investigation is necessary to establish this role of hypaphorine in the biogenesis of erythrina alkaloids.

EXPERIMENTAL

General. M.ps. were uncorrected. UV spectra were determined in 95% EtOH and IR spectra in KBr pellets or mineral oil and only the major bands are quoted. PMR spectra were measured in a 60 MHz instrument in DMSO-d_6, $CDCl_3$ or D_2O using TMS or CH_3CN as an internal standard. MS were recorded at 70 eV using a probe. Silica gel G was used for analytical and preparative TLC. The plant material was supplied by Messrs United Chemical and Allied Products, Calcutta.

[4] BOAR, R. B. and WIDDOWSON, D. A. (1970) *J. Chem. Soc. (B)* 1591.
[5] BARTON, D. H. R., JAMES, R., KIRBY, G. W., TURNER, D. W. and WIDDOWSON, D. A. (1968) *J. Chem. Soc. (C)* 1529.

Extraction of Erythrina arborescens. Dried and finely ground seeds (4·8 kg) were continuously extracted first with light petroleum (60–80°) then with EtOH (36 hr, each). The EtOH extract was concentrated to a viscous slurry and then extracted with 2 N HCl to separate the alkaloids from the fatty matter. The acidic aq. soln was extracted with $CHCl_3$ when several weak bases were separated as $CHCl_3$-soluble hydrochlorides.[1] The clarified acidic aq. soln was again extracted with $CHCl_3$ at two pH levels (*ca* 4 and 9) to yield a further quantity of weak and moderately strong bases.[1,3] The H_2O-soluble alkaloids were precipitated as reineckate salts at two pH levels (*ca* 8 and 2). The reineckate salts, precipitated under basic condition, were dissolved in EtOH and the soln was mechanically stirred with Amberlite IRA-400 (Cl^-) resin for 8 hr. The pale brown EtOH soln was filtered and the solvent was evaporated under red. pres. The residue, obtained as a brown gum (0·47 g), showed three major Dragendorff-positive spots, R_f 0·18, 0·42, 0·73 (*n*-BuOH–HOAc–H_2O, 4:1:2). The most polar component (R_f 0·18) gradually suffered autoxidation. The other two components (R_f 0·42 and 0·73) were separated by PLC using the same solvent system.

Isolation of erysophorine (**1**). The mixture of quaternary chlorides was dissolved in EtOH and subjected to PLC on 2 mm layers. The two major Dragendorff-positive bands, R_f 0·4 and 0·7, were removed and eluted with MeOH. The residue from the R_f zone 0·7 was obtained as an amorphous solid (122 mg). The alkaloid was again dissolved in EtOH and passed over a column of Amberlite IRA-400 (Cl^-). The residue from the EtOH eluate finally crystallized from Me_2CO–MeOH as brown micro crystals (58 mg) which decomposed, without melting, above 260°; UV: λ_{max}^{EtOH} 222 (log ϵ, 4·38), 230 sh (4·24), 284 (3·82), 292–294 nm (3·76); UV of equimolecular mixture of hypaphorine and erysovine: λ_{max}^{EtOH} 220–222, 230–235 sh, 284, 290–295 nm; PMR (D_2O): δ 1·98 (1H, *d*, *J* 10 Hz, C_4-H), 2·44 (1H, *d*, *J* 5 Hz, C_4-H), 3·15 (9H, *s*, $N^{(+)}Me_3$), 3·45 (3H, *s*, C_3–OMe), 3·58 (4H, *m*, β–CH_2–, C_8–CH_2–), 3·65 (3H, *s*, C_{16}–OMe), 3·94 (4H, C_{10} and C_{11}–CH_2–), 4·06 (1H, *m*, C_3–H), 4·45 (1H, *m*, Cα–H), 5·85 (1H, *br. s*, C_7–H), 6·10 (1H, *d*, *J* 10 Hz, C_1–H), 6·68 (1H, *m*, C_2–H), 6·8–7·6 (7H, complex multiplet, C_{14}–H, C_{17}–H, and protons on the indole ring); MS: significant fragment ion peaks at *m/e* 298 (24%), 283 (8), 267 (42), 246 (12), 240 (7), 218 (3), 217 (4), 215 (4), 214 (5), 170 (14), 130 (100), 102 (16). (Found: C, 67·4; H, 7·2; N, 7·4. $C_{32}H_{38}N_3O_4Cl$ requires: C, 68·1; H, 6·7; N, 7·8%).

Hydrolysis of erysophorine. Erysophorine (42 mg) was hydrolyzed with 6N HCl (10 ml) for 30 min at 100°. The reaction was cooled, made alkaline (NH_4OH), and extracted with Et_2O. The organic layer, after the usual processing, afforded a brown solid which crystallized from EtOH as needles (11 mg), m.p. 174–176°. The m.p., mixed m.p., R_f value, and IR absorption spectrum of the compound were identical with those of erysovine.[1,3] The alkaline aq. layer, after separation of erysovine, was acidified (pH ~2) and treated with a saturated aq. soln of ammonium reineckate. An EtOH soln of the reineckate salt on treatment with Amberlite IRA-400 (Cl^-) gave hypaphorine-HCl (6 mg), m.p. 234–236°. The m.p., mixed m.p., R_f value and UV spectrum of the compound were identical with those of hypaphorine-HCl.

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