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STRUCTURE AND STEREOCHEMISTRY OF COCCUTRINE, A NEW *ERYTHRINA* ALKALOID FROM *COCCULUS TRILOBUS* D C.

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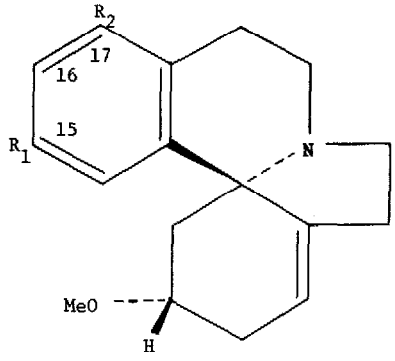
Several alkaloids from *Cocculus trilobus* D C. have been isolated previously by Tomita and others.[1] We here report on the isolation and structural characterization of two *Erythrina* alkaloids from this same plant.

Coccutrine, a new alkaloid, was isolated in the form of colorless needles from the phenolic fraction by careful silica gel chromatography and fractional crystallization. Coccutrine (I), $C_{18}H_{23}O_3N$, m.p. 263-265°, $[\alpha]_D$ +232° (MeOH); PMR (pyridine-d_5) : δ 3.11 (3H, s., OCH_3), 3.73 (3H, s., OCH_3), 5.47 (1H, m. , olefinic-H), 6.7-6.8 (2H, m., aromatic-H). Methylation of (I) with diazomethane afforded O-methylcoccutrine (II) as a colorless oil; PMR ($CDCl_3$): δ 3.28 (3H, s., OCH_3), 3.78 (3H, s., OCH_3), 3.83 (3H, s., OCH_3), 5.58 (1H, m. , olefinic-H), 6.28 (1H, d., J = 2.5 Hz, aromatic-H), 6.37 (1H, d., J = 2.5 Hz, aromatic-H). These data suggested the presence in (I) of two methoxyl groups, one phenolic hydroxyl group, one trisubstituted double bond, and two aromatic protons which are situated meta to each other. Lack of any signal due to an NH or an N-methyl group in the PMR spectra of (I) and (II) led us to conclude that (I) must be a tetracyclic alkaloid.

Information relating to the skeletal structure of (I) was obtained from its mass spectrum which showed fragmentation peaks at m/e 301(M^+), 243, 242, and 226. The base peak at m/e 243 (M-58) arises from a *retro* Diels-Alder type fragmentation of the substituted cyclohexene ring and it is a diagnostically important peak for aromatic *Erythrina* alkaloids.[2,3] On the basis of these data coccutrine may be assigned structure (I) with only the positions of the aromatic -OH and -OMe groups remaining to be established. The total structure and relative stereochemistry were defined unequivocally by a single crystal x-ray analysis (*vide infra*).



(I) R_1 = OH, R_2 = OMe

(II) R_1 = R_2 = OMe

(III) R_1 = OH, R_2 = H

A second *Erythrina* alkaloid was isolated from the mother liquor of coccutrine as colorless needles, $C_{17}H_{21}O_2N$, m.p. 205-207°, $[\alpha]_D$ +232° (MeOH); PMR ($CDCl_3$) : δ 3.24 (3H, s., OCH_3), 5.64 (1H, broad s., olefinic-H), 6.62 (1H, d., J = 3.0 Hz, aromatic-H), 6.66 (1H, d.d., J = 8.0, 3.0 Hz, aromatic-H), 7.01 (1H, d., J = 8.0 Hz, aromatic-H). These data closely resemble those reported for cocculine (III) which was isolated from *Cocculus laurifolius* D C. by Yunusov *et al.* [4] Direct comparison of cocculine with the alkaloid isolated by us could not be made as an authentic sample of cocculine was not available from the Soviet group. The identity of these two alkaloids was established, however, by a single crystal x-ray analysis of (III).

Crystals of (I) and (III) belong to the orthorhombic system, space group $P2_12_12_1$, with a = 10.69(1), b = 16.65(1), c = 8.80(1) Å, Z = 4, for (I), and a = 10.51(1), b = 15.87(1), c = 8.95(1) Å, Z = 4, for (III). Three-dimensional x-ray intensity data were recorded on an Enraf-Nonius CAD 3 automated diffractometer (Ni-filtered Cu-K_α radiation, λ = 1.542 Å ; 3° take-off angle) by the θ-2θ scanning technique. Both crystal structures were solved by direct non-centrosymmetric phase-determining procedures by use of MULTAN.[5] Atomic positional and thermal parameters (anisotropic C,N,O; isotropic H) were refined by full-matrix least-squares calculations to R 0.062 [1360 statistically significant reflections (I)] and 0.078 [965 reflections (III)]. The relative stereochemistry derived from these studies is depicted in (I) and (III) to conform with the absolute stereochemistry of other aromatic *Erythrina* alkaloids.[3,6,7]

From the viewpoint of aromatic *Erythrina* alkaloid biosynthesis,lack of an oxygenated function at C-16 in the benzene rings of (I) and (III) is unusual. It is now accepted that aromatic *Erythrina* alkaloids are biogenetically derived from suitably oxidized benzyltetrahydroisoquinoline precursors.[3,8] Accordingly, all aromatic *Erythrina* alkaloids from *Erythrina* species (*Leguminosae*) have been found to bear an oxygenated function at C-16. In contrast, alkaloids possessing the same *Erythrina* skeleton but lacking an oxygenated function at C-16 have been found only in plants of *Cocculus* species (*Menispermaceae*).

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References and Footnotes

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