Erythristemine, a New Alkaloid from *Erythrina lysistemon:* a Spectroscopic and Crystallographic Study

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Summary The constitution and absolute configuration of erythristemine have been determined by spectroscopic and *X*-ray crystallographic methods.

DURING the course of studies on Erythrina alkaloid biogenesis,[1] we attempted to extract erythraline (I) from the previously unexamined *E. lysistemon*.[2] Chromatography of the alkaloidal extract (from 5 kg. of dried leaves) over alumina (Grade III) gave 300 mg. of a non-polar alkaloid fraction. Further purification by column chromatography gave crystalline erythristemine (120 mg.), m.p. 127—129° $[\alpha]_D^{22}$ + 189° (*c* 0·4 in $CHCl_3$). The assignment of the

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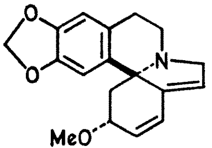
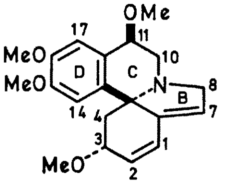
structure of erythristemine as (II) with the absolute stereochemistry as in (II) and (III) is based on the following evidence.

The molecular formula ($C_{20}H_{25}NO_4$) was established by microanalysis and by mass spectrometry (Found M^+ 343·1789; $C_{20}H_{25}NO_4$ requires 343·1783). The i.r. spectrum (ν_{max} 1610 cm^{-1}) showed no evidence for hydroxyl or carbonyl functions, and the u.v spectrum [λ_{max} (EtOH) 283 (ϵ 3100), 235 nm (ϵ 20,000)] was almost identical to that of erythraline.[3] The mass spectrum showed identical significant ions at m/e 343 (M^+), 328, 312, 311 (100%) 310, 296, and 280. The fragmentation pattern was consistent with an aromatic *Erythrina* alkaloid having a 1,6-diene system,[4] and an additional oxygen function on either of rings C or D.

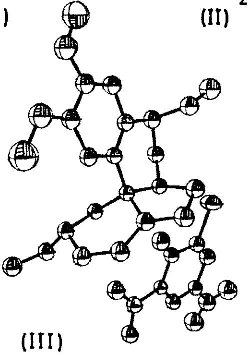
If the presence of the erythrinan carbon skeleton is assumed, it is possible to interpret the n.m.r. spectrum completely with the aid of decoupling and INDOR[5] type experiments. Thus in hexadeuteriobenzene solution, two aromatic proton singlets occurred at τ 2·91 (14-H) and 3·07 (17-H),[1a] and methoxy-group singlets at τ 6·57 (6H), 6·79 (3H), and 6·98 (3H). On irradiation at τ 5·95 the double doublet at τ 7·51 and the triplet at τ 7·92 each collapsed to a doublet. This ABX system was shown to be in ring A of the structure (II), as irradiation at τ 5·94 also reduced the fine structure apparent at τ 3·68, the lower half of the olefinic multiplet. These results are consistent with a pseudo-axial proton at C-3 (τ 5·94) coupled with 4a-H (τ 7·92, $J_{3,4a}$ 10·5 Hz) and with 4e-H (τ 7·51, $J_{3,4e}$ 5·5 Hz), the geminal coupling being 10·5 Hz.[1a] In addition, 2-H must absorb at τ 3·68 ($J_{2,3}$ 2 Hz) and 1-H at τ 4·12 ($J_{1,2}$ 10 Hz). The methoxy-group at C-3 is therefore pseudo-equatorial, as in other *Erythrina* alkaloids.[1a,6] Expansion of the double doublet at τ 7·51 and the triplet at τ 7·92 on a 100 Hz sweep revealed fine splitting of the former. Irradiation at τ 4·62 (7-H) reduced this to a small doublet splitting (J 1—1·5 Hz) which was removed by irradiation at τ 4·12 (1-H). The coupling initially removed had $J_{4a,7}$ 1—1·5 Hz.



(I)



(II)



(III)

Irradiation at τ 4·62 (7-H) caused the collapse of the doublets at τ 6·26 and 6·4 (J 2·5 Hz) to two lines (upper half of an AB quartet, $J_{A,B}$ 15 Hz, 8-H). The INDOR technique was used to identify the other half of the quartet. By using responses from the near singlet at τ 4·62 (7-H), the main peak of the other half was located at τ 6·12 and using one side of the signal at τ 6·26, the fourth peak was located at τ 5·95.

Irradiation of the aromatic signal at τ 3·07 (17-H) caused a slight narrowing of the signal at τ 6·06 which suggested that this was the proton at C-11. The protons at C-10 and C-11 were obscured to some extent by the *O*-methyl signals, but assignments could be made using the INDOR technique. Using the peak at τ 6·06 (11-H) as the observing transition, responses were obtained from eight other peaks. This is consistent with observing from the central line of the X-band of an ABX system having $J_{AX} = J_{BX}$.[7] The separations of the responses gave $J_{AX} = J_{BX} = 4$ Hz and $J_{AB} = 14$ Hz. This suggests a three-spin system in a six-membered ring having one geminal coupling (14 Hz), one pseudo-axial/pseudo-equatorial coupling, and one di-pseudo-equatorial coupling (4 Hz). The chemical shift of the low-field member of this group is consistent with a proton attached to a carbon bearing both methoxy- and aryl (or nitrogen) groups. It follows that there must be a methoxy-group in ring C and that this must be at C-11.

The configuration of C-11 could not be determined as the conformation of ring C was unknown. In order to resolve this point, and to confirm the constitution, erythristemine was converted into its 2-bromo-4,6-dinitrophenolate salt, (m.p. 144—148°), and its crystal structure determined.

Crystals were grown from ethanol as thin hexagonal plates in the monoclinic space group $P2_1, a = 7·99$, $b = 16·15$, $c = 10·54$ Å, $\beta = 97·48°$, $D_m = 1·49$ g. cm.$^{-3}$, $D_c = 1·49$ g. cm.$^{-3}$ for $Z = 2$.

Intensity data for 2087 independent reflections were measured using Cu-K_α radiation. The structure was solved by the standard heavy-atom procedure and has been refined, the current value of R being 0·11. The structure is shown in (III). The absolute configuration shown in (III), deduced from anomalous scattering of Cu radiation by bromine, matches that deduced for dihydro-β-erythroidine hydrobromide[8] by anomalous scattering and for the aromatic *Erythrina* alkaloids by chemical studies.[1a,6]

The use of 2-bromo-4,6-dinitrophenol for the preparation of a heavy-atom derivative is, we believe, novel and may be applicable in other cases. In this instance, very suitable crystals were grown with ease.

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