Phenol Oxidation. A Model for the Biosynthesis of the *Erythrina* Alkaloids

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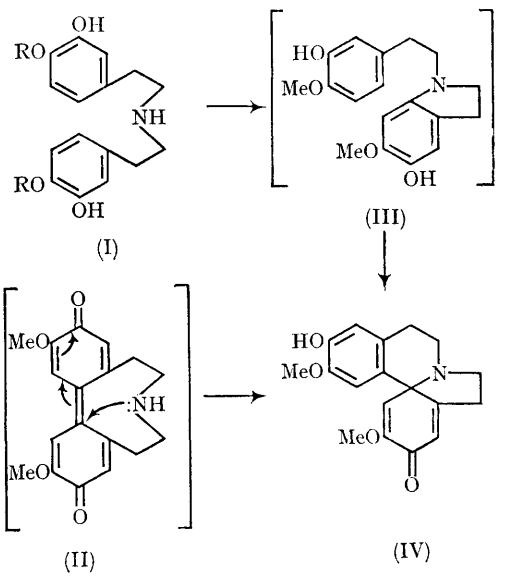
OCCUPYING an attractive position as a hypothetical intermediate in the biosynthesis of both benzylisoquinoline and *Erythrina* alkaloids[1,2] is the symmetrical tyrosine-derived amine (I; R = H).[3] Thus, oxidation of (I) could lead either *via* diphenoquinone (II)[4] or dihydroindole (III)[5] to the tetracyclic "erythrinadienone" (IV). Further conversion of (IV) into the aromatic alkaloids *e.g.*, erysodine (V)[1] would involve unexceptional reduction and rearrangement of the A/B ring system.

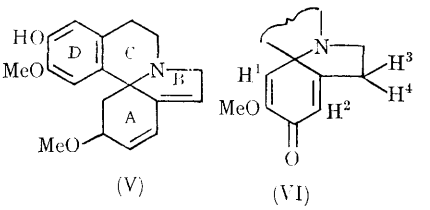
We now provide a laboratory analogy for such intervention of (I) and (IV) by a one-step synthesis of the *Erythrina* skeleton. Although oxidation of (I; R = H) under a wide variety of conditions afforded only polymeric product, the desired coupling reaction was effected when the dimethyl ether[3,6] (I; R = Me) was oxidised with alkaline potassium ferricyanide. The major product, formed in 35% yield, can be assigned the constitution (IV) on the basis of the following evidence. Mass-spectral data verified the formula $C_{18}H_{19}O_4N$



and the infrared [ν_{max}($CHCl_3$) 3500, 1690, 1665, 1630, 1595 cm.$^{-1}$] and ultraviolet (λ_{max} 242, 283 mμ) spectra were in accord with an aromatic-dienone structure.

The n.m.r. spectrum ($CDCl_3$) revealed two singlet aromatic protons (τ 3·36, 3·62), olefinic protons (see VI) (H^1; τ 3·99; singlet) and (H^2; τ 3·72; triplet, J = 1·5 c./sec.; allylic spin-coupling with H^3, H^4), one phenolic proton (τ 3·79; exchanged with D_2O), methyl singlets (τ 6·28, 6·38) and broad CH_2-multiplets (8H; τ 6·5—7·8; ring B/C protons), unambiguously confirming structure (IV).

Although a distinction between the intermediacy of (II) or (III) in this simple oxidative coupling has yet to be made, the biochemical roles of (I) and (IV) are now being subjected to radiochemical test in *Erythrina* species.



(V) (VI)

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[1] For structural studies see V. Boekelheide and V. Prelog in "Progress in Organic Chemistry" Ed. J. W. Cook, Vol. III, Butterworths, London, 1955, Ch. 5; V. Boekelheide and M. Y. Chang, *J. Org. Chem.*, 1964, **29**, 1303.

[2] For previous synthetic work see, *e.g.*, B. Belleau, *J. Amer. Chem. Soc.*, 1953, **75**, 5765; A. J. Manson and K. Wiesner, *Chem. and Ind.*, 1953, 1041; V. Prelog, A. Langemann, O. Rodig, and M. Ternbah, *Helv. Chim. Acta*, 1959, **42**, 1301; A. Mondon, *Tetrahedron*, 1963, **19**, 911 (and earlier papers); J. Blake, J. R. Tretter, and H. Rapoport, *J. Amer. Chem. Soc.*, 1965, **87**, 1398.

[3] The preparations of (I; R = H) and (I; R = Me) follow conventional procedure and will be described in a full paper together with their analytical and spectroscopic data.

[4] D. H. R. Barton and T. Cohen, "Festschrift A. Stoll", Birkhauser, Basle, 1957, p. 117.

[5] *Cf.* Sir Robert Robinson, "The Structural Relationships of Natural Products", Clarendon, Oxford, 1955; R. H. F. Manske, "The Alkaloids", Vol. VII, Academic Press, New York, 1960, Ch. 11. For a pertinent laboratory analogy see J. D. Bu'Lock and J. Harley-Mason, *J. Chem. Soc.*, 1951, 2248.

[6] The influence of methylation pattern on phenol oxidation has been noted previously in synthesis and biosynthesis. See A. I. Scott, *Quart. Rev.*, 1965, **19**, 1.