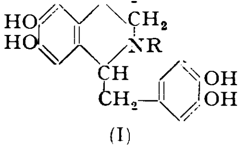
298. iso*Quinoline Alkaloids. Part I. The Oxidation of Tetrahydropapaveroline.*

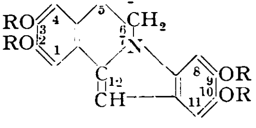
By John Harley-Mason.

Ferricyanide oxidation of tetrahydropapaveroline gives 5 : 6-dihydro-2 : 3 : 9 : 10-tetrahydroxydibenzo[*b*, *g*]pyrrocoline (II; R = H) which is readily further oxidised to the corresponding fully aromatic dibenzopyrrocoline (III; R = H).

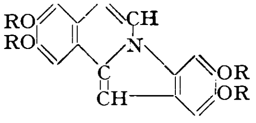
By oxidation of laudanosoline (I; R = Me) with chloranil Robinson and Sugasawa (*J.*, 1932, 789) obtained tetrahydro-2 : 3 : 9 : 10-tetrahydroxy-7-methyldibenzopyrrocolinium chloride (dehydrolaudanosoline), two hydrogen atoms being lost; two alkaloids derived from this structure have recently been described (Ewing, Hughes, Ritchie, and Taylor, *Nature*, 1952, **169**, 618). It was of interest in another connection to examine the oxidation of the corresponding unmethylated compound, tetrahydropapaveroline (I; R = H).



(I)

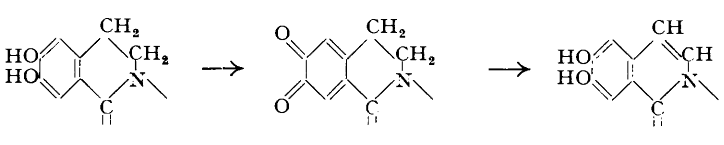


(II)



(III)

This was found to be oxidised very readily and conveniently by potassium ferricyanide with the loss of four hydrogen atoms giving 2 : 3 : 9 : 10-tetrahydroxy-5 : 6-dihydrodibenzo[*b*, *g*]pyrrocoline (II; R = H). The structure of this compound is shown by the identity of its almost colourless tetra-acetate (II; R = Ac) with the product obtained by Robinson and Sugasawa (*loc. cit.*) by the action of hot acetic anhydride on dehydrolaudanosoline, when demethylation and oxidation occur in addition to acetylation. It was found that (II; R = H) is very readily further oxidised; on exposure to air the material, originally pale yellow, very rapidly darkens, eventually becoming deep violet, and the same change occurs in ethyl acetate solution. Acetylation of the autoxidised material gave, after purification, a yellow tetra-acetate which contained less hydrogen than (II; R = Ac) and differed from it further in melting point and in exhibiting a strong bluish-green fluorescence in solution, whereas (II; R = Ac) fluoresces weakly violet. It was therefore formulated as 2 : 3 : 9 : 10-tetra-acetoxydibenzo[*b*, *g*]pyrrocoline (III; R = Ac). This was confirmed by the fact that the same product was obtained, though in very small yield, by ferricyanide oxidation of papaveroline and acetylation of the product.



This very ready aromatisation is of interest since in general 3 : 4-dihydro*iso*quinolines are not easily dehydrogenated (Openshaw and Wood, *J.*, 1952, 391; Leonard and Leubner, *J. Amer. Chem. Soc.*, 1949, **71**, 3408). Further, it is noteworthy that only the tetraphenol (II; R = H) and not its tetra-acetate (II; R = Ac) is readily oxidised, suggesting that the hydroxyl groups participate in the oxidation. The mechanism indicated in the scheme is suggested, this being closely analogous to the aromatisation in the formation of dihydroxyindoles from 3 : 4-dihydroxyphenylethylamines of which the formation of (II; R = H) is, of course, itself an example. The formation of intensely coloured by-products during oxidation of (II; R = H) is undoubtedly due to the fact that the latter contains a 5 : 6-dihydroxyindole system which is readily oxidised to melanin-like products.

EXPERIMENTAL

Tetrahydropapaveroline Hydrobromide.—Tetrahydropapaverine hydriodide (Taylor, *J.*, 1952, 142) (5 g.) was refluxed for 2 hr. with hydrobromic acid (*d* 1·49; 35 c.c.). After cooling, the tetrahydropapaveroline hydrobromide, which formed colourless prisms, was collected. The product was free from iodide ion.

Oxidation of Tetrahydropapaveroline.—To a solution of the hydrobromide (1·8 g.) in water (200 c.c.), potassium ferricyanide (6 g.) and sodium hydrogen carbonate (1·6 g.) in water (200 c.c.) were added with stirring. A deep reddish-brown precipitate (probably tetrahydropapaveroline ferricyanide) was rapidly formed. The resulting suspension was quickly heated to 90° with continued stirring, most of the precipitate dissolving. The mixture was filtered hot, leaving a small amount of black residue, and a little sodium dithionite was added to the filtrate to prevent oxidation. After being kept overnight at 0°, the product which had separated as a yellow powder (0·9 g.) was recrystallised from ethyl acetate–light petroleum. 5 : 6-*Dihydro*-2 : 3 : 9 : 10-*tetrahydroxydibenzo*[b, g]*pyrrocoline* formed pale yellow prisms, m. p. 253—255° (decomp.) with preliminary darkening, soluble in ethanol and moderately soluble in ethyl acetate (Found : C, 66·6; H, 4·55; N, 5·0. $C_{16}H_{13}O_4N$ requires C, 67·0; H, 4·6; N, 4·95%). The solutions showed a violet fluorescence but soon became violet owing to oxidation. With Ehrlich's reagent an intense blue colour was given.

Acetylation (acetic anhydride–pyridine in the cold) gave the tetra-acetate which formed almost colourless prisms, m. p. 214—215° (from ethyl acetate), identical (mixed m. p.) with the material obtained from laudanosoline by Robinson and Sugasawa's (*loc. cit.*) method (Found : C, 64·0; H, 4·9. Calc. for $C_{24}H_{21}O_8N$: C, 63·85; H, 4·7%).

Further Oxidation.—A thin layer of the tetrahydroxy-compound (0·5 g.) was exposed on a watch-glass to the air for 2 days. The deep violet product thus obtained was acetylated, as above. Three recrystallisations from acetic acid–ethanol (charcoal) gave 2 : 3 : 9 : 10-*tetraacetoxydibenzo*[b, g]*pyrrocoline* (0·25 g.), yellow prisms, m. p. 269—270° (Found : C, 63·75; H, 4·3; N, 3·0. $C_{24}H_{19}O_8N$ requires C, 64·1; H, 4·25; N, 3·1%), readily soluble in acetic acid and sparingly soluble in ethanol; the solutions showed a strong bluish-green fluorescence. With Ehrlich's reagent a weak greenish colour was given.

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