Biogenetic Synthesis of an Androcymbine-type Compound

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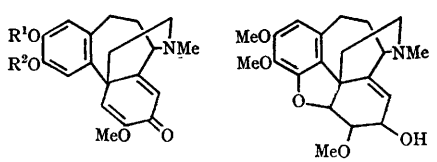
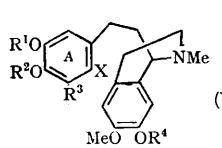
IN the biogenesis of homomorphinandienone-type alkaloids, namely androcymbine (I)[1] and kreysiginine (II),[2] phenolic oxidation[3] plays an important role. Thus, androcymbine and kreysiginine are biosynthesised by phenolic oxidation from the diphenolic base (III), or from the isomer having the positions of one methoxy- and the phenolic hydroxy-group reversed on ring A.

We report a laboratory analogy for the biogenetic route to homomorphinandienone-type compounds. Although the oxidation of diphenolic bases (IV) and (V) under a wide variety of conditions afforded polymeric products,[4] the desired coupling reaction was effected when (V) was oxidised with potassium ferricyanide in a two-phase system (5% aqueous sodium hydrogen bicarbonate–$CHCl_3$) at room temperature with stirring (2 hr., in a current of N_2). The product [0·3—0·4% after silica-gel chromatography with $CHCl_3$–MeOH (v/v, 49 : 1) as eluant] was assigned the structure (VI) on the basis of the following evidence.

The high-resolution mass spectrum (M^+ 351·1604) and microanalysis of the free base (VI), m.p. 220—221° (from $CHCl_3$–C_6H_6; methiodide, m.p. 225—226°), verified the formula $C_{20}H_{23}NO_4$



(I) R^1=Me, R^2=H, R^3=OMe (II)
(VI) R^1=R^3=H, R^2=Me
(VII) R^1=R^2=Me, R^3=H



	R^1	R^2	R^3	R^4	X
(III)	Me	H	OMe	H	H
(IV)	H	Me	OMe	H	H
(V)	H	Me	H	H	H
(VIII)	Me	Me	H	Me	NH_2

(341·1627). The i.r. [ν_{max} ($CHCl_3$) 3505, 1664, 1642, and 1620 cm.$^{-1}$], u.v. [λ_{max} (MeOH) 241 and 282 mμ log ε 4·22 and 3·85)] and mass [*m/e* 326 (M^+ — Me), 313 (M^+ — CO), 298 (M^+ — Me — CO), 284 (M^+ — C_3H_7N), 282 (M^+ — Ac), 276

(M^+ — CO — Ac), and 256 [M^+ — C_3H_7N — CO)] spectra were in accord with an α-methylated cross-conjugated cyclohexadienone structure.[5] The n.m.r. spectrum (τ in $CDCl_3$) revealed methyl resonances at τ 7·63 (NMe, s), 6·36 (OMe, s) and 6·10 (OMe, s), two olefinic protons at 3·67 (s) and 3·12 (s), and two aromatic protons at 3·93 (s) and 3·44 (s), unambiguously confirming the structure (VI).

Moreover, the product was methylated with diazomethane to give non-phenolic base, which was identical by full spectroscopic (i.r. and n.m.r.) and chromatographic comparison with the demethoxy-*O*-methylandrocymbine (VII)[6] prepared by a modified Pschorr reaction from aminoisoquinoline (VIII). Furthermore, the i.r. (KBr) spectrum of the methiodide was superimposable on that of an authentic sample,[6] m.p. 251—252°. These facts reveal that a biogenetic-type synthesis of homomorphinandienone has been accomplished. The total syntheses of androcymbine and kreysiginine by phenolic oxidation are in progress.

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