One-step Synthesis of an Androcymbine-like Compound

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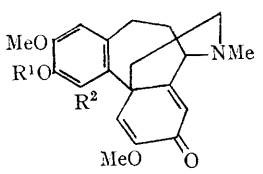
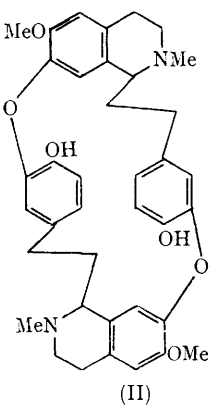
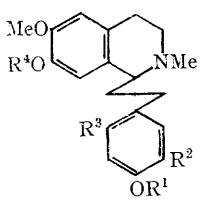
ANDROCYMBINE, an alkoloid co-existed with melanthioidine (II) and colchicine in *Androcymbium melanthioides* var. stricta[1], was assigned to the structure (I) by chemical and spectroscopic



(I) R^1=H, R^2=OMe
(III) R^1=Me, R^2=H



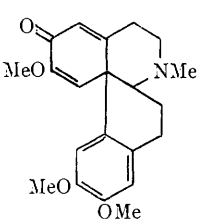
(II)



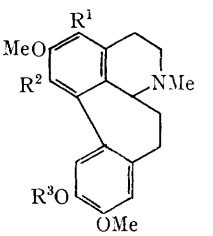
(IV) R^1=R^4=Me, R^2=OMe, R^3=NH_2
(V) R^1=Me, R^2=OMe, R^3=NH_2, R^4=CH_2Ph

methods by Battersby.[2] As this alkaloid is biogenetically derived from 1-phenethylisoquinoline,[3] several efforts to synthesise this alkaloid by phenolic oxidation were made, without success.[4,5] We report a synthesis of the androcymbine skeleton (III) by a modified Pschorr cyclisation.

Aminoisoquinoline (IV), synthesised by the standard method,[6] was diazotised with 10% sodium nitrite in 5% sulphuric acid at 0° and the resulting diazonium salt was decomposed and



(VI)



(VII) R^1=OH, R^2=H, R^3=Me
(VIII) R^1=OMe, R^2=H, R^3=Me
(IX) R^1=H, R^2=OMe, R^3=Me
(X) R^1=R^3=H, R^2=OH

coupled at 70°.[7] The careful work up involving silica gel chromatography using chloroform–methanol (99 : 1) as an eluent gave the cyclohexadienone (III) in 1·5% yield. Mass spectrometry (M^+: m/e 355) confirmed the molecular formula of $C_{21}H_{25}NO_4$: ν_{max} ($CHCl_3$) 1667, 1640, and 1615 $cm.^{-1}$, λ_{max} (MeOH) 280 and 240 mμ, consistent with a cross-conjugated cyclohexadienone system. N.m.r. spectrum ($CDCl_3$) showed the methyl resonance at τ 7·65 (s, NMe), 6·38 (s, olefinic OMe), 6·19 and 6·12 (two s, aromatic OMe), olefinic protons at 3·10 s and 3·69 s, and aromatic protons at 3·93 s and 3·53 s (similar to Battersby's n.m.r. data[2]).

These spectral data correspond to one of the two dienones (III) or (VI); (VI) is ruled out by the following reactions. The second aminoisoquinoline (XI) gave the same dienone (III) on diazotization; if the correct structure of dienone were (VI), the diazotization products of the aminoisoquinolines [(IV) and (X)] should be different. Acid-catalysed rearrangement[8] of the dienone gave the homoaporphine (VII), ν_{max} 3500 cm.$^{-1}$ ($CHCl_3$), λ_{max} 288 and 263 mμ (MeOH), whose Gibbs test was negative. The methylation of homoaporphine (VII) gave the second homoaporphine (VIII), λ_{max} 282 and 263 mμ (MeOH) M^+: m/e 369, different from the third homoaporphine (IX), which was prepared from dihydroxyhomoaporphine (X).[9] If the structure of the dienone were (VI), the rearrangement of the dienone, followed by methylation, should give the third homoaporphine (IX).

(*Received, June 4th*, 1968; *Com.* 725.)

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