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SYNTHESIS OF ANALOGUES OF HUNTERIA AND ASPIDOSPERMA ALKALOIDS FROM A COMMON INTERMEDIATE

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We have described recently[1] a simple total synthesis of eburnamine and 3-methylaspidospermidine from a common intermediate. An extension of these syntheses is now described.

Alkylation of the pyrrolidine enamine of 1,2,5,6-tetrahydrobenzaldehyde (I) with methyl acrylate gave 1-(2'-methoxycarbonyl ethyl)-1,2,5,6-tetrahydrobenzaldehyde (II) b.p. 106-109°/0.8 mm. This with tryptamine readily gave the pentacyclic lactam (III) (70%) m.p. 264° [$\nu_{max.}$ 3280 (NH), 1640 (C=C) and 1618 (C=O) cm^{-1}; $\lambda_{max.}$ 224, 275, 282 and 291 mμ, $\epsilon_{max.}$ 50,660, 11,020, 11,250 and 9220] which was converted into analogues of Hunteria and Aspidosperma alkaloids.

Treatment of (III) with osmium tetroxide gave the diol (IV) m.p. 230° [$\nu_{max.}$ 3340 (unresolved OH and NH) and 1618 (C=O) cm^{-1}] which with periodate gave 21-formyl-eburnamine-N(b)-lactam (Va) characterised as its 2,4-dinitrophenylhydrazone (Vb) m.p. 160°.

Reduction of (Va) with sodium borohydride gave 21-hydroxymethyl-eburnamine N(b) lactam (Vc) m.p. 225-226° [$\nu_{max.}$ 3240 (OH) and 1620 (C=O) cm^{-1}. $\lambda_{max.}$ 226, 275, 281 and 290 mμ, $\epsilon_{max.}$ 33,980, 7870, 8020 and 6060]. Reduction of (Vc) with lithium aluminium hydride gave 21-hydroxymethyl-eburnamine (Vd) characterised as its methiodide m.p. 275°.

On the other hand, treatment of (III) with boron trifluoride etherate[1] gave the isomeric hexacyclic indolenine lactam (VI) isolated from methanol as the stable methanol adduct (VIIa) m.p. 234-235° (decomp.) [$\nu_{max.}$ 3270 (NH), 1630 (C=O) and 1610 cm^{-1} (aromatic); $\lambda_{max.}$ 248 and 300 mμ, $\epsilon_{max.}$ 5760 and 3470]. Catalytic hydrogenation of (VIIa) over platinum in 30% acetic acid (hydrogen uptake 1 mole) gave the saturated lactam (VIIb) m.p. 213-214° [$\nu_{max.}$ 3290 (NH), 1630 (C=O) and 1610 cm^{-1} (aromatic); $\lambda_{max.}$ 248 and 303 mμ, $\epsilon_{max.}$ 6980 and 3000].

Lithium aluminium hydride reduction of (VIIb) gave (VIIc) whose mass spectrum confirmed the proposed hexacyclic structure. The major features of the mass spectrum were:- m/e 294 (molecular ion, 24%), 165 (17%), 164 (100% - base peak), 144 (8%) and 130 (6.5%). The normal aspidospermine ionisation and fragmentation[2] has taken place but the elimination of an olefinic fragment from the 3,4-position is prevented by the additional ring,

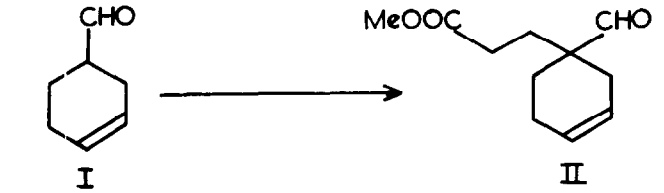
resulting in a base peak at m/e 164 (see diagram). The fragments at m/e 144 and 130 are the expected indole ions.[2]

Acetylation of (VIIc) gave the 1-acetyl compound (VIId), characterised as its perchlorate, m.p. 269-270° (decomp.) $\nu_{max.}$ 3100 ($\overset{+}{N}H$), 1655 (C=O) and 1595 cm^{-1} (aromatic); $\lambda_{max.}$ 253, 282 and 290 mμ, $\epsilon_{max.}$ 15,800, 4170 and 3560. The stereochemistry of the apparently homogeneous products (VIIb, c, d) is under investigation.

References

1. J. E. D. Barton and J. Harley-Mason, Chem. Commun., 1965 (14), 298.

2. K. Biemann, M. Spiteller-Friedmann and G. Spitteler, J. Amer. Chem. Soc., 1963, 85, 631.



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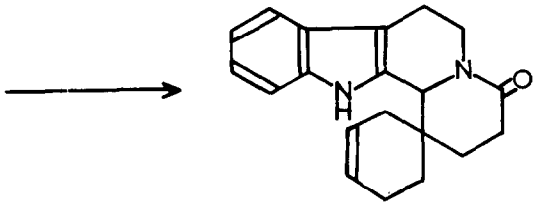

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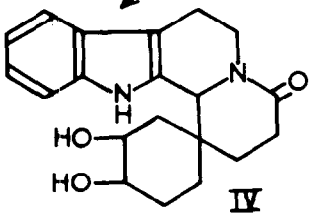

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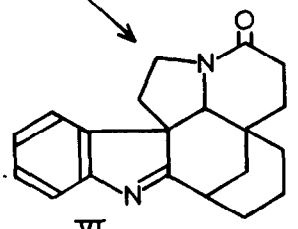
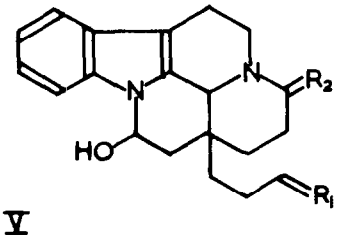


VI



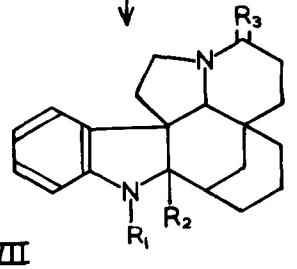
V

(a) $R_1 = O$, $R_2 = O$

(b) $R_1 = N.NH\,C_6H_3(NO_2)_2$, $R_2 = O$

(c) $R_1 = H, OH$, $R_2 = O$

(d) $R_1 = H, OH$, $R_2 = 2H$



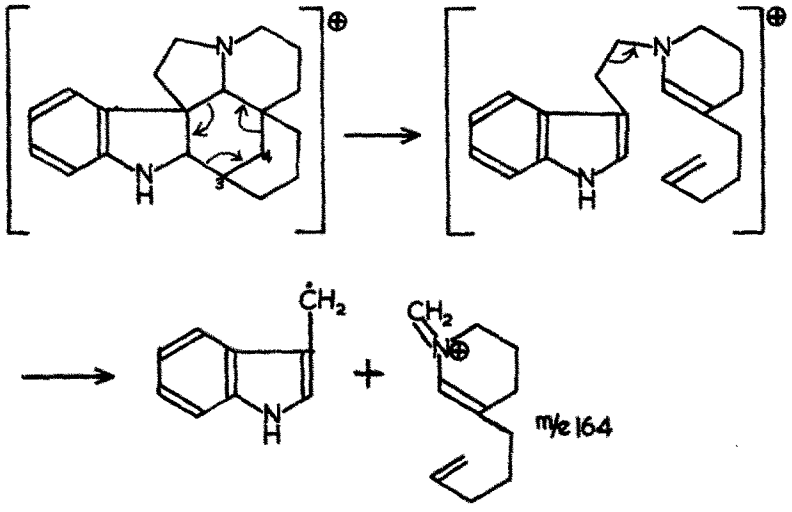
VII

(a) $R_1 = H$, $R_2 = OMe$, $R_3 = O$

(b) $R_1 = R_2 = H$, $R_3 = O$

(c) $R_1 = R_2 = H$, $R_3 = 2H$

(d) $R_1 = COCH_3$, $R_2 = H$, $R_3 = 2H$


N
H
3
N
H
N
H
CH2
CH2
N⊕
m/e 164