The Occurrence of 16,17,15,20-Tetrahydrosecodine in *Rhazya orientalis*

By R. T. BROWN, G. F. SMITH,* K. S. J. STAPLEFORD, and D. A. TAYLOR
(*Department of Chemistry, The University, Manchester* M13 9PL)

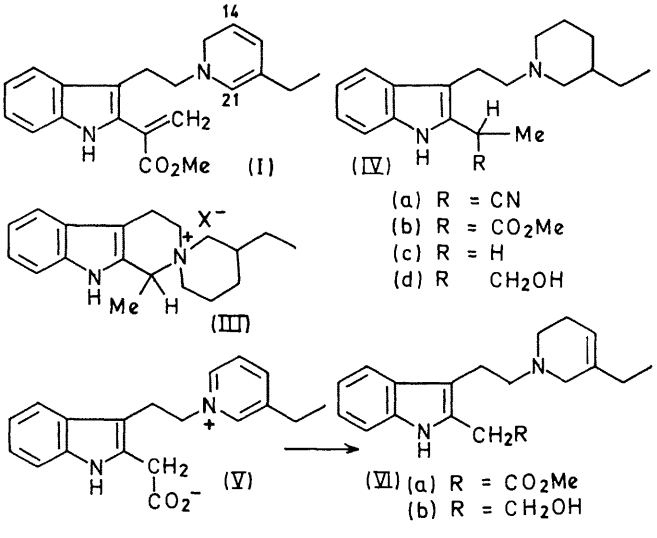
Summary Tetrahydrosecodine (IVb) has been synthesised, and shown to be present in *Rhazya orientalis* by isotopic dilution analysis.

THE hypothesis that a compound with structure (I) (14,21-dehydrosecodine) or one very closely related to it, is an intermediate in the principal indole alkaloid skeletal rearrangements is now quite widely accepted.[1] Support for this came from the isolation of (IVc) from *Tabernaemontana cumminsii* and of the secamines from *Rhazya stricta* and *R. orientalis*.[2] It was thus quite reasonable to suppose that alkaloids with the complete secodine skeleton must exist; we therefore synthesised the simplest such structure, 16,17,-15,20-tetrahydrosecodine (IVb).

1-Methyl-1,2,3,4-tetrahydro-β-carboline (II) and 1,5-diiodo-2-ethylpentane reacted to give the spiroammonium salt (III), which without isolation was treated with KCN[3] in dimethylformamide at 100° to give the nitrile (IVa), methanolysis of which yielded the desired ester (IVb) as a syrup [80% from (II)] which must be a mixture of two diastereoisomeric racemates, though this is not seen in the simple n.m.r. spectrum (all spectral and analytical data were *in accord* with structure IVb).

The related 17-*apo*-16,17-dihydrosecodine (VIa) was synthesised from the akuammicine degradation product (V)[4] by reduction with KBH_4 in MeOH followed by dry HCl at the b.p.: the product (81% yield) contained about 10% of the saturated piperidine analogue, which was cleanly separated from the main product by countercurrent distribution (Buffer pH 5·5—EtOAc). Full spectroscopic analysis established the purity of the ester (VIa).

The alkaloids of the aerial parts of one young plant of *Rhazya orientalis* were labelled by feeding with 60 μc of [2-^{14}C]tryptophan: dilution of these alkaloids with the mixture of tetrahydrosecodine racemates (IVb) and of the ester (VIa) was followed by a separation using fractional extraction and t.l.c.



The crude base (IVb) was converted into its picrolonate (m.p. 223—225° dec.), ten crystallisations of which led to a

constant radioactivity of 1925 d p m /mg (steady value from the 8th crystallisation) this corresponds to a 0 5% incorporation This high incorporation is remarkable and suggests that 16,17,15,20-tetrahydrosecodine is on a metabolic side track close to the main alkaloid biosynthetic route This fits well the notion that 14 21 dehydrosecodine (I) is the intermediate on the way to the Aspidosperma, Iboga and related rearranged alkaloids reduction being the simple reaction which in this case takes (I) out of circulation

Further work is planned to check the possibility of co-crystallisation of 16,17-dihydrosecodine picrolonate with that of (IVb)

Purification of (VIa) by t l c followed by $LiAlH_4$ reduction gave the virtually inactive alcohol (VIb), indicating the absence of (VIa) in *Rhazya orientalis*

By procedures completely analogous with those described above, bases (IVb), (VIa), and (VIb) were shown not to be present in *Amsonia tabernaemontana*

(*Received, November 14th*, 1969, *Com* 1734)

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