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SYNTHESIS OF GIRINIMBINE AND (±) MAHANIMBINE

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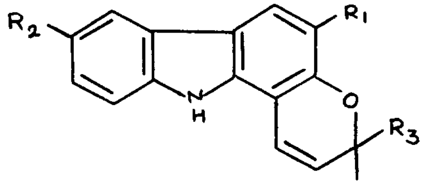
We report below the synthesis of two alkaloids, girinimbine and mahanimbine, obtained from Murraya koenigii, which possess the novel pyranocarbazole ring system. Our synthesis of girinimbine now conclusively establishes its structure.

Girinimbine

Two structures have been advocated for this alkaloid. Structure(I) was proposed by Chakraborty[1]. More recently structure(II) has been favoured[2] for the molecule, since, in the PMR spectrum it has the aromatic proton signals exactly similar to that of mahanimbine (III)[3].



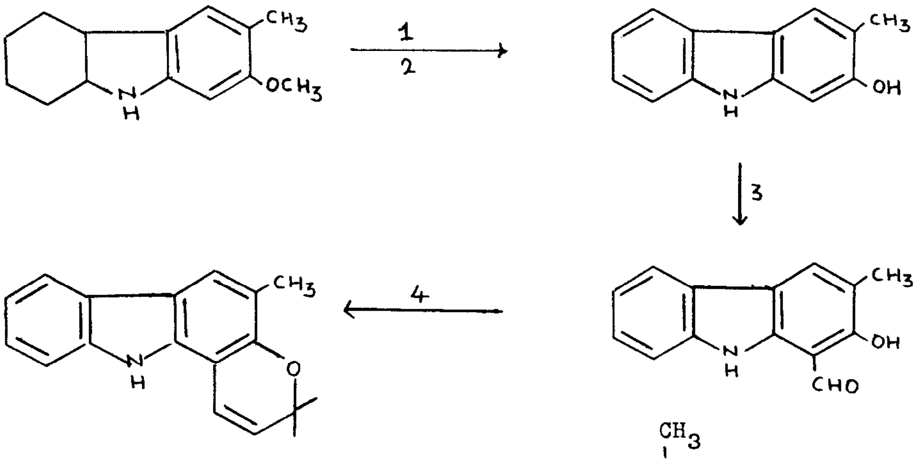
(I) $R_1 = H, R_2 = R_3 = CH_3$ (II) $R_2 = H, R_1 = R_3 = CH_3$

(III) $R_2 = H, R_1 = CH_3, R_3 = -CH_2\text{-}CH_2\text{-}CH = \underset{\substack{|\\ CH_3}}{C} - CH_3$

(IV) $R_2 = H, R_1 = CHO, R_3 = CH_3$

Girinimbine on ozonolysis is reported to yield a hydroxyaldehyde[4], $C_{14}H_{11}O_2N$, m.p. 193°. A hydroxyaldehyde having identical molecular formula and m.p. had been obtained[3] by us by the ozonolysis of mahanimbine. This suggested to us that structure (I) for girinimbine was probably incorrect and that it was better represented by structure (II). This conclusion was however at variance with another experiment in which murrayacine, another alkaloid obtained from the same plant, has been chemically correlated[5] with girinimbine. On the basis of structure (II) for girinimbine, murrayacine would have structure (IV). Dihydromurrayacine then should be identical with cycloheptaphylline whose structure (structure IV with the pyran double bond reduced) has been conclusively established by Joshi _et al_.[6] The wide difference in the m.p. of dihydromurrayacine (176°)[7] and cycloheptaphylline (250°)[6], however, appeared to preclude this possibility.

In order to resolve the conflict it appeared necessary to synthesise, by an unambiguous route, one of the structures reported for girinimbine. Since structure (II) appeared to us more probable for the molecule, we synthesised a compound corresponding to this as shown below:



1 = Pd/C, p-Cymene 2 = HBr/AcOH $3 = Ph - \overset{CH_3}{N} - CHO, POCl_3$

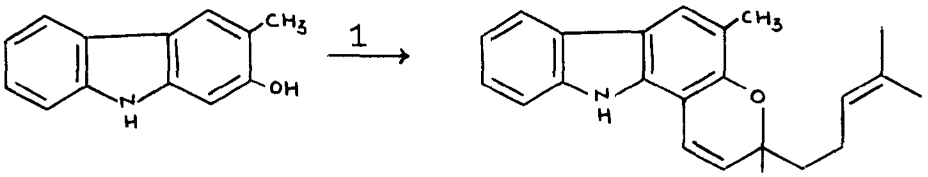
$4 = (Ph)_3 P^{\oplus} - CH_2 - \underset{CH_3}{C} = CH_2 \ Cl^{\ominus}$, NaOH

The tetrahydrocarbazole obtained[8] by the condensation of

2-hydroxy cyclohexanone and 3-methoxy 4-methyl aniline was dehydrogenated in 85 % yield to 2-methoxy 3-methyl carbazole[9]. It was then demethylated and converted to 1-formyl 2-hydroxy 3-methyl carbazole in an overall yield of 17 %. The hydroxyaldehyde was transformed into the pyran derivative, in 11 % yield, according to the procedure of Schweizer et al.[10] The compound obtained was identical in every respect with an authentic sample of girinimbine (tlc, m.p., i.r.), thus establishing structure (II) for the molecule.

Mahanimbine

Structure (III) has been derived by us for this alkaloid. This structure is now confirmed by the following synthesis:



1 = Citral/Pyridine/Ph.COOH

2-Hydroxy 3-methyl carbazole was condensed with citral (in pyridine solution by refluxing for 6 hrs.) essentially according to the procedure of Crombie[11] with the only modification that some benzoic acid (2 % by weight of the starting compound) was added as in some Knoevenagel reactions[12]. Work up gave a compound, $C_{23}H_{25}ON$, m.p. 75-76°, which was identical with racemic mahanimbine (tlc, m.p., i.r.) obtained[13] by distilling the optically active compound at 140°-175°/0.5 mm.

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