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A NEW SYNTHESIS OF (±)-NORCORALYDINE

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The total synthesis of (±)-norcoralydine was accomplished by the decarboxylation of 2,3,10,11-tetramethoxy-12-carboxy-5,6,13,13a-tetrahydro-8*H*-dibenzo(a,g)quinolizine (12-carboxynorcoralydine) providing a synthetic proof to the siting of the methoxyls at the 10 and 11 positions of the dibenzoquinolizine nucleus.

The alkaloid norcoralydine occurs as the (—) form in the plant *Xylopia discreta* (L. Fil.) Sprague and Hutchins. and has been isolated from it comparatively recently.[1] This is the first report of its presence in natural sources. It was known in the racemic form much earlier, having been synthesized during work on the protoberberine series of natural bases to which it belongs.[2,3]

The purpose of the present investigation was to see whether simple decarboxylation of 12-carboxynorcoralydine (II) at high temperature could be used to synthesize the comparatively unstable[2] norcoralydine (III). The scheme of work followed started with 2,3,10,11-tetramethoxy-12-carbomethoxy-5,6,13,13a-tetrahydro-8*H*-dibenzo(a,g) quinolizine (I), which was saponified to give the amino acid, 2,3,10,11-tetramethoxy-12-carboxy-5,6,13,13a - tetrahydro-8*H*-dibenzo(a,g)quinolizine (II). The latter was decarboxylated at 320°C *in vacuo* to give (±)-norcoralydine. Below 300°C the reaction does not take place to any appreciable extent.

The above sequence of reactions and the method of preparation of the starting material, 12-carbomethoxynorcoralydine, from homoveratrylamine(IV) and methyl 2-carbomethoxy-3,4-dimethoxy-6-chloromethylphenylacetate(V) and subsequent cyclization of the product (VI)[4] provides a synthetic proof as opposed to the degradative one offered earlier[2] that two of the four methoxyls in norcoralydine are in the 10 and 11 positions.

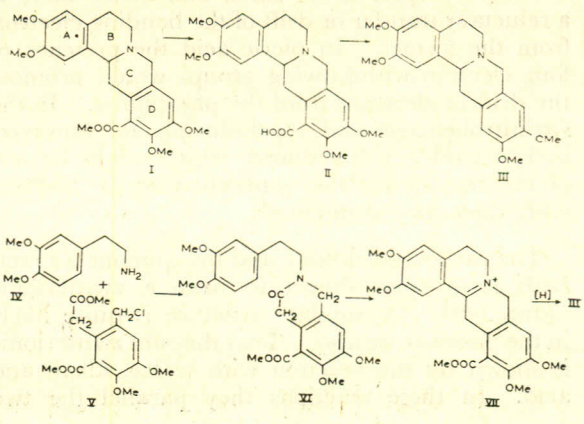
It also establishes the sequence of ring closures involving the lactam (C first and then B), novel at that time[5] claimed by one of the authors (A.M.A.) for the synthesis of the dibenzoquinolizine skeleton.[4]

Experimental

All m.ps are uncorrected and have been taken by the ordinary capillary method unless otherwise mentioned. The microanalysis has been done at the Microanalytical Section of our Laboratories. The IR spectra were measured on a Perkin-Elmer Infracord and Beckman IR-5 type instruments.

2, 3, 10, 11 - *Tetramethoxy* - 12 *-carboxy*-5,6,13,13*a-tetrahydro*-8*H-dibenzo*(*a,g*)*quinolizine* (*II*).—2,3,10, 11-Tetramethoxy - 12 - carbomethoxy - 5,6,13,13a-tetrahydro-8*H*-dibenzo(a,g)quinolizine[4] (I) (50 mg) was hydrolysed according to the method of Weisenborn,[6] in 95% ethanol (1.3 ml) and aqueous potassium hydroxide (35%; 0.9 ml). It gave a clear light yellow solution. This solution was refluxed on the water bath for 4 hr to saponify the ester, then cooled for 10 min and water (0.8 ml) added. The alcohol was then removed *in vacuo* from the reaction mixture till a slight turbidity appeared. Subsequent acidification with 33% acetic acid till pH 6 was reached (about 1 ml required) gave a white precipitate. It was filtered, washed with water and dried (46 mg; 97·5%) m.p. 217–220°C (decomp.). On recrystallization from methanol the acid (20.8 mg; 50%) was obtained, m.p. 230–232° (decomp). (Found: N, 3·75%. $C_{22}H_{25}NO_6$ requires: N, 3.51%).

The amino acid was insoluble in petroleum ether, ether, benzene, ethyl acetate and water (cold), sparingly soluble in acetone, chloroform, water (hot) and moderately soluble in methanol and ethanol.



The IR spectrum showed peaks at 1600 cm^{-1} (ionized carboxyl) and 1331 cm^{-1} among others.

2, 3, 10, 11-*tetramethoxy*-5, 16, 13, 13*a*-*tetrahydro*-8*H*-*dibenzo* (*a*,*g*)*quinolizine*, (±)-*norcoralydine* (*III*).—The above crude amino acid, m.p. 217–220°C (15 mg), was taken in a test tube with a side tube. The test tube was evacuated to 1.5 mm pressure and then heated to 320°C for 7¼ min when a greenish-yellow semisolid substance collected on the cooler sides of the tube. On crystallization from methanol this condensate (11 mg) softened at 140°C and melted at 160°C (Kofler) (lit. m.p. 159–161°C).[3]

The IR spectrum of the base agreed with that of norcoralydine in the literature.[7]

The *hydrochloride* was prepared from very dilute ethereal solution of the base by means of alcoholic hydrochloric acid, as fine needles, m.p. 233–236°C (Kofler) (lit. m.p. 234–237°C).[8] Mixed m.p. with an authentic sample of norcoralydine hydrochloride was undepressed. The IR spectra of the two were superimposable.

The *picrate* was obtained from a solution of the hydrochloride and picric acid in alcohol as yellow needles m.p. 140°C (Kofler) (lit. m.p. 140°C).[9]

The mercuric chloride derivative was prepared from an aqueous solution of the hydrochloride as a yellow precipitate m.p. 156–158°C (Kofler) (lit. m.p. 158°C).[2]

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