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BREVICARINE FROM BREVICOLLINE

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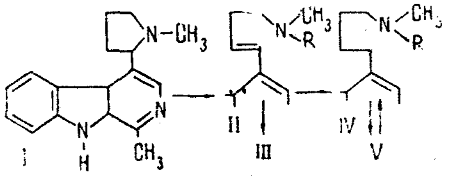
The alkaloids brevicolline and brevicarine, which have been isolated previously from Carex brevicollis DC [1,2] are β-carboline derivatives. The structures of these substances are similar and therefore not only is their biogenetic relationship possible but also chemical conversions of one into the other. It is known that the pyrrolidine ring—in nicotine, for example—opens under the action of benzoyl chloride [3]. We have performed the benzoylation of brevicolline (I). It was found that in contrast to the case of nicotine, the opening of the pyrrolidine ring is accompanied by the simultaneous splitting off of hydrogen chloride and the formation of the amide II. The further conversion of this intermediate into brevicarine is possible by two routes: first alkaline hydrolysis and then hydrogenation of the double bond, or hydrogenation and subsequent hydrolysis. These conversions are represented by the scheme



II,IV R=COC$_6$H$_5$ III,V R=H

The final product (V) was identical in all respects with brevicarine. However, it has not been possible to effect the transition from brevicarine to brevicolline similarly by methods described in the literature.

Experimental

The melting points were determined on a Kofler block and are uncorrected.

4-[4-(Benzoylmethylamino)but-3-enyl]-1-methyl-β-carboline (II). A mixture of brevicolline (5 g) and 10 ml of freshly-distilled benzoyl chloride was boiled for 30 min. After the cooling of the reaction mixture, 200 ml of 5% HCl was added and, after 15 minutes' boiling, the aqueous layer was decanted through a filter. This operation was repeated five times, when the excess of benzoyl chloride had been hydrolyzed completely and the reaction product had been exhaustively extracted. The combined filtrates were left in the refrigerator for crystallization. The precipitate, consisting of a mixture of benzoic acid and the salt of the benzoyl derivative, was filtered off, washed with water, suspended in 250 ml of water, and treated with a 25% solution of caustic soda (until the reaction of the solution was alkaline). The precipitate was filtered off and dried. After three crystallizations from benzene, 2.5 g (40%) of a substance with mp 208–209° C was obtained.

Found, %: C 77.56; H 6.64; N 11.29. Calculated for $C_{24}H_{25}OH_3$, %: C 77.60; H 6.78; N 11.31.

1-Methyl-4-(4-methylaminobut-3-enyl)-β-carboline (III). A solution of 1.5 g of II in 10 ml of 5% KOH in methanol was boiled in the water bath for 3 hr. The cooled reaction mixture was diluted with 50 ml of water and the precipitate that formed was filtered off and washed with water. After two crystallizations from benzene, the yield of product was 1 g (90%), mp 150–151° C.

Found, %: C 76.83; H 7.06; N 15.81. Calculated for $C_{17}H_{19}N_3$, %: C 76.94; H 7.21; N 15.83.

4-[4-(Benzoylmethylamino)butyl]-1-methyl-β-carboline (IV). At room temperature, 1 g of II in 15 ml of methanol was hydrogenated in the presence of 100 mg of PtO_2. The calculated amount of hydrogen was absorbed in 3 hr. The solution was filtered from the catalyst and evaporated to dryness. The residue was crystallized twice from benzene. Yield quantitative, mp 187° C.

Found, %: C 77.56; H 6.64; N 11.29. Calculated for $C_{24}H_{25}OH_3$, %: C 77.60; H 6.78; N 11.31.

Brevicarine. A) Substance III (0.5 g) was hydrogenated over PtO_2 under the conditions described above. After two crystallizations from acetone, mp 61° C. A mixture with the natural material melted without depression.

B) A solution of 1 g of IV in 10 ml of 5% methanolic KOH was boiled in the water bath for 3 hr. The cooled solution was diluted with 50 ml of water and the precipitate was filtered off and washed with water. Mp 61° C (from acetone). A mixture with natural brevicarine melted without depression.

Benzoylbrevicarine. A mixture of 1 g of natural brevicarine, 10 ml of benzene, 2 ml of pyridine, and 5 ml of 10% NaOH solution was heated in the water bath for 1 hr. The benzene layer was separated off, washed with water, dried with sodium sulfate, filtered, and evaporated to dryness. The residue was dissolved in 10 ml of 5% HCl and the benzoyl derivative was precipitated with a solution of sodium carbonate at pH 8. Then it was filtered off and the dried product was recrystallized. Mp 187° C (from benzene). A mixture with the benzoyl derivative IV gave no depression of the melting point.

Conclusions

The brevicarine obtained by the cleavage of the pyrrolidine ring of brevicolline is identical with the natural alkaloid, which is an additional proof of its structure.

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