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ALKALOIDS FROM CASSIA CARNAVAL SPEG.: CASSINE AND CARNAVALINE (1)

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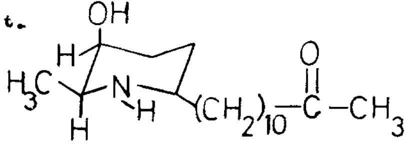
Cassine was isolated together with casselsine by Highet (3) from the leaves and twigs of Cassia excelsa Schrad. The complete structure of cassine (I) has recently been established by Rice and Coke (4), who also determined its absolute stereochemistry and by Highet and Highet (5). We have examined the basic products obtained from the leaves, bark and roots of the closely related Cassia carnaval Speg. and have isolated from the leaves four piperidine alkaloids, cassine (I) being the one present in largest amounts. We have also studied some of the physical data of cassine which showed that the previously proposed structure (3) was incorrect.

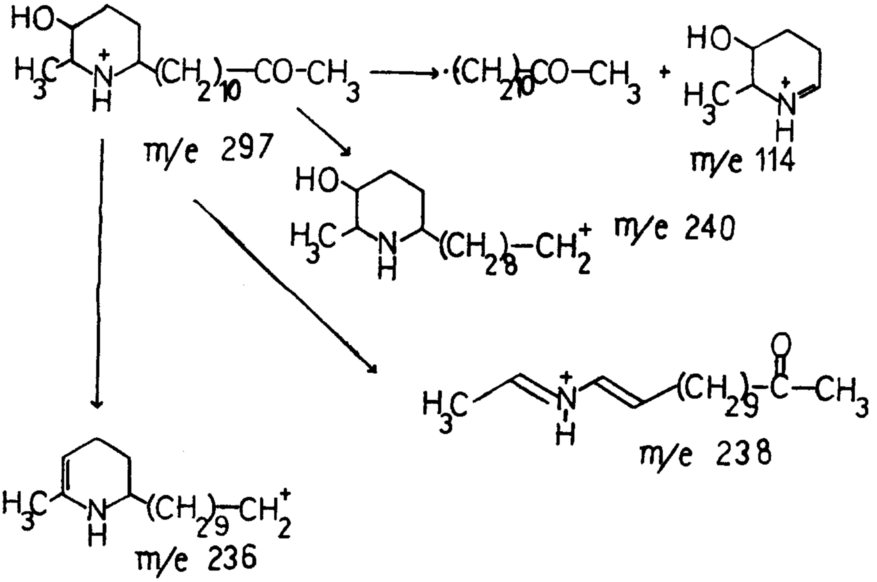


(I)

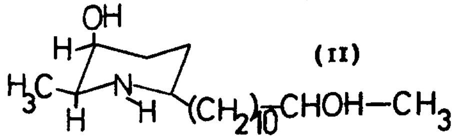
Although the u.v. spectrum of cassine hydrochloride showed a very weak maximum at 276 mμ (3) which can be attributed to the carbonyl chromophore, the o.r.d. curve for cassine was plain and negative with a fairly steep descent belowy 250 mμ in accordance with the absence of any ramification at the carbon atom α to the carbonyl group (6). It is noteworthy that cassine, in spite of having two side chains of opposite configurations, presents an o.r.d. curve similar to those published for some monosubstituted piperidine alkaloids (7). In agreement with what was pointed out for D-coniine and 2-methylpiperidine, the steep descent of the dispersion curve of cassine can be associated with an absorption band located around 200 mμ that dissapears in the hydrochloride and hence can be attributed to a transition involving the lone-pair of electrons of the nitrogen atom (7). This is in accordance with the flat o.r.d. curve of cassine hydrochloride.

The mass spectrum of cassine gave a molecular ion at m/e 297. The base peak at m/e 114 is the same as that obtained for carpaine and carpamadiol (8) and corresponds to the splitting off of the long aliphatic side chain. The formation of a relatively intense peak at m/e 240 which arises from loss of 57 mass units (•CH_2-CO-CH_3) precludes the possibility of having a ramification on the carbon atom α to the carbonyl group.

On observing the pattern formed by secondary peaks it is easy to see that these are due to the formation of ions that contain succesively one methylene group less as from m/e 240 to m/e 114. There is also a regular pattern of peaks at 2 and 4 mass units less than the above mentioned starting from the ions of mass 238 (formed by opening of the piperidine ring as described for carpamadiol (8)), and 236 which arises from loss of 61 mass units and may correspond to a process in which dehydration had occurred with simultaneous cleavage of a bond α to the carbonyl group with loss of an acetyl group. It is noteworthy that peaks of this last group are the more intense ones in a 10 e.v. spectrum.



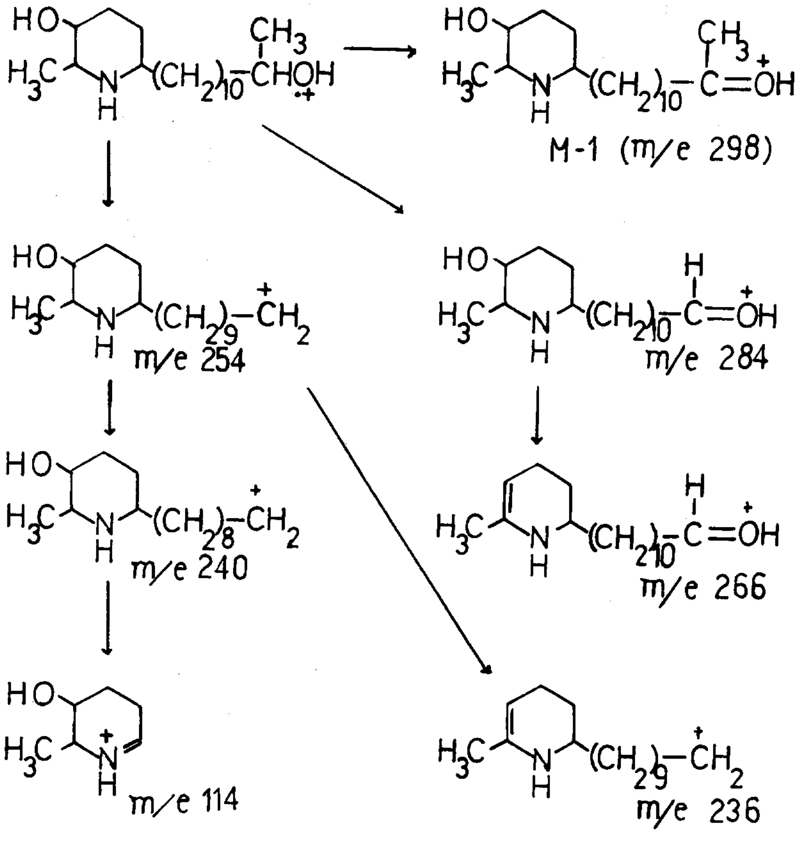
Carnavaline (m.p. 60.7-61.2) is a new piperidine alkaloid similar to cassine and was isolated from the basic extracts of C. carnaval by chromatography through a column of silica gel. Its structure (II) has been determined by mass spectroscopy, n.m.r. and i.r. spectra. It was further confirmed by borohydride reduction of cassine (I) that gave a crystalline compound which was shown to be identical to carnavaline by i.r., n.m.r. and t.l.c. in different solvent systems and by a similar identification of their oily acetates. The absolute configuration of the secondary side chain alcohol has not yet been determined.



(II)

The i.r. of carnavaline showed no carbonyl absorption and an intense and extremely broad band at 3330 cm^{-1} which on acetylation dissapears with appearance of two intense carbonyl bands at 1740 cm^{-1} and 1653 cm^{-1} and an "ester band" at 1245 cm^{-1}. The n.m.r. spectrum of carnavaline showed two methyl doublets centered at δ = 1.10 (J = 5 cps) and at δ = 1.19 (J = 5 cps). The first one corresponds to a methyl group attached to the piperidine ring as in cassine - δ = 1.10 (J = 6 cps) - and the second corresponds to a methyl group α to a secondary alcoholic group as in 2-octanol - δ = 1.15 (J = 6 cps). The intense peak corresponding to the aliphatic methylene groups appears at δ = 1.28 as in cassine. Two not clearly defined doublets are shown at approximately δ = 2.7 (J = 6 cps) and δ = 2.92 (J = 6 cps) which could be attributed to the methine protons of the piperidine nucleus. The equatorial hydrogen of the hydroxylic carbon atom in the nucleus appears as a broad singlet at δ = 3.6 (δ = 3.55 in cassine) and the hydrogen of the hydroxylic carbon of the side chain is a broad multiplet centered at δ = 3.82. On acetylation these signals are shifted to δ = 4.25 and to δ = 4.89 respectively, three peaks appear at δ = 2.02, 2.07 and 2.12 corresponding to the methyl hydrogens of the three acetyl groups and the two methyl doublets dissapear under the pattern of the intense methylene absorption.

The fragmentation pattern of the mass spectrum of carnavaline (II) is fairly similar to that of cassine (I) although the molecular ion is less abundant than the M-1 peak, which can be attributed to the elimination of the hydrogen atom α to the side chain alcoholic group to give a stable oxonium ion at m/e 298. A similar type of cleavage furnishes an oxonium ion of mass 284 by loss of a methyl group and the simultaneous dehydration of the cyclic hydroxyl group (see above similar process for cassine) leads to a peak at m/e 266. The peak at m/e 254 could be assigned to the elimination of a fragment of mass 45 (CH_3–CHOH·) and the ones of lower mass starting from peaks at m/e 240, 236 and 196 may correspond to those already described for cassine since again the base peak is that of m/e 114 (9).



References

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