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CARPAINE AND PSEUDOCARPAINE

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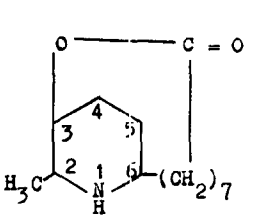
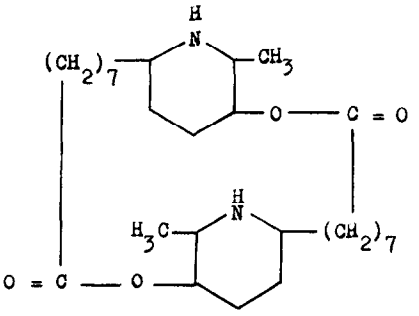
The alkaloid, carpaine (1), from Carica papaya L., was shown by degradation to have the gross structure I (2,3). This has been recently revised to the dimeric structure II by Spiteller and Spiteller on the basis of mass spectrometric studies (4). The minor alkaloid of Carica papaya, pseudocarpaine, was assigned the gross structure I (5), the two alkaloids being considered to be epimeric at the hydroxylic carbon atom, C-3. We would like to place on record some of our recent observations on these alkaloids.

The mass spectrum of pseudocarpaine (Fig.1) with the molecular ion peak at 478, clearly shows that it is also dimeric. Further the fragmentation pattern observed for pseudocarpaine was identical with that of carpaine (Fig.2) but for a minor difference in the relative intensities of the ions at m/e 241 and 242. The two alkaloids must therefore have the same gross structure II.



I



II

Acid hydrolysis of carpaine resulted in a single compound, carpamic acid. Likewise lithium aluminium hydride reduction yielded only carpamodiol (6,4). Carpaine is therefore composed of two identical halves. The 60 Mc NMR spectrum* of carpaine, besides providing confirmatory evidence for the above conclusion, afforded insight into its stereochemistry. The two C-methyl groups at C-2 were seen as one doublet at δ 1.02 (J = 7 cps) and the protons at C-2 as a broadened quartet at δ 2.83 (J = 7 cps), showing a further small coupling of 1-2 cps with the protons at C-3. The signals from the last protons appeared as an unresolved singlet at δ 4.75, with a width at half height of 5-6 cps. The stereochemistry of the C-2 and C-6 side chains in carpamic acid, and hence in carpaine, was established chemically to be cis (7). Models indicate that the dimeric carpaine molecule is flexible and that the two piperidine rings can assume the chair forms without restraint. The C-2 and

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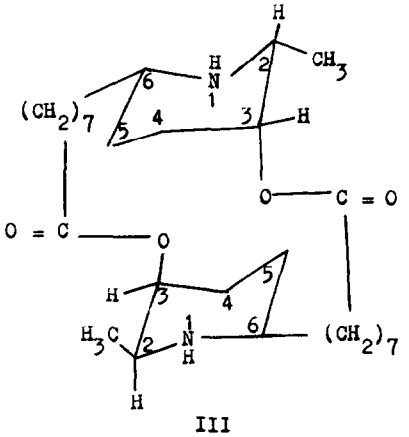
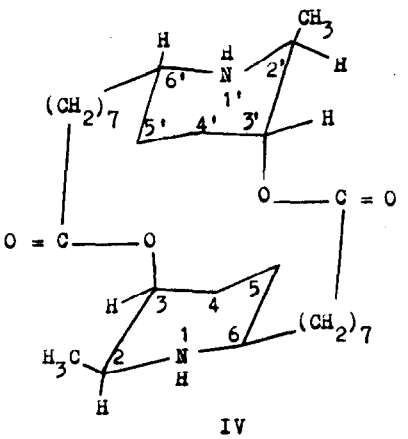
* All NMR spectra were determined in $CDCl_3$.

C-6 side chains hence would both be preferentially equatorially oriented. Our earlier tentative assignment of equatorial position to the hydroxyl group at C-3 in carpamic acid and hence to the lactone bond in carpaine (7) would place the protons at C-3 in carpaine in axial conformations. As these would then each have two axial and one equatorial neighbours, a much broader signal would be expected for them than the one observed in the NMR spectrum of carpaine* (8). We would hence like to assign to the C-3 protons the equatorial position in the preferred conformation of carpaine as shown in structure III. The chemical shift of the C-3 protons in the NMR spectrum of carpaine is also



III



IV

* Dreiding models of III indicate no factor which may distort the relevant dihedral angles from their normal values in the chair forms. The sharpness of the methyl signals indicates that the ring inversion of the two piperidine chairs, if existent, is not a slow process. In a fast equilibrium, it is reasonable to assume that the chair forms depicted in structure III should be weighted much in preference to the ring inverted ones.

in agreement with this assignment (9). It may also be noted that Tichy and Sicher had reached this conclusion through infrared spectral data on methyl carpamate (10).

Pseudocarpaine has the gross structure II, and yields carpamic and pseudocarpamic acids on hydrolysis (5). Ethyl pseudocarpamate has been also dehydrogenated to ethyl carpyrinate (5). These data and our present mass spectral evidence show that pseudocarpaine is composed of two halves having the same gross structure, but differing in stereochemistry. We have sought to use NMR data to locate this difference. The 60 Mc NMR spectrum of pseudocarpaine showed the two methyl groups as two separate doublets at δ 1.02 (J = 7 cps) and δ 1.07 (J = 7 cps). The proton at C-2' was seen as a multiplet at δ 3.15 and the one at C-2 as a broad quartet at δ 2.85*. The latter corresponded to the signals from the C-2 protons in carpaine. The protons at C-3 and C-3' were seen at approximately δ 4.83 as an overlapping multiplet and a broad singlet. The signals from the C-2 and C-2' protons were better recognised in the 100 Mc NMR spectrum of pseudocarpaine, examined relative to that of carpaine (Fig.3). An octet was seen for the C-2' proton in pseudocarpaine at δ 3.16 (J_1 = 7 cps; J_2 = ca 3 cps). The smaller coupling was recognizable in the multiplet due to the C-3' proton at δ 4.83. The signal from the C-2 proton appeared as a quartet at δ 2.86*, corresponding in position to the quartet found for the C-2 protons in the spectrum of carpaine.

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* Integration shows 2 protons to be present here; we believe the second represents the proton at C-6'.

The NMR data thus provide confirmatory evidence for the build-up of pseudocarpaine from two dissimilar halves, one representing the carpamic acid moiety and the other the pseudocarpamic acid residue. The near identical chemical shifts of the protons at C-3 and C-3' in pseudocarpaine would suggest identical conformations for both, namely equatorial. The slight difference in the δ values of the two methyl groups at C-2 and C-2' and large difference in the shifts of the protons on the above carbon atoms would indicate that the difference between carpaine and pseudocarpaine lies in the stereochemistry at C-2', leading to stereostructure IV for pseudocarpaine*. Experiments are in progress to test the validity of the present conclusions and also to derive the absolute configuration of the two alkaloids.

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* It is unlikely that they also differ at C-6', as this would lead in the pseudocarpaine molecule, in the preferred conformation of the piperidine chairs, to equatorial dispositions of the C-2' and C-6' side chains and to an axial conformation for the C-3' proton. The latter would then be expected to have a different chemical shift and also show larger couplings.

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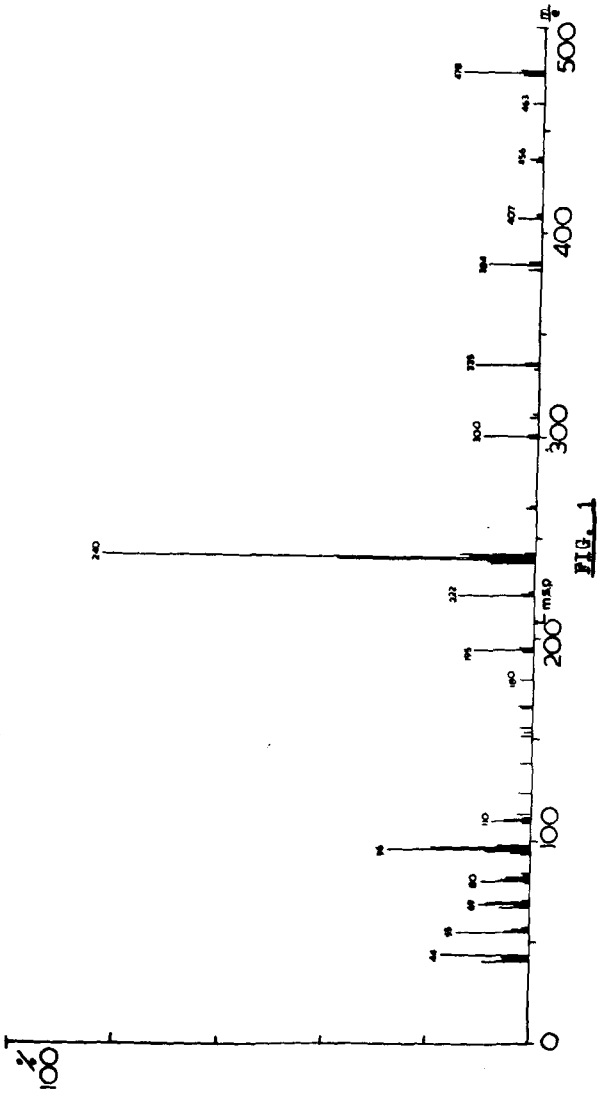

FIG. 1

Mass spectrum of pseudocarpaine

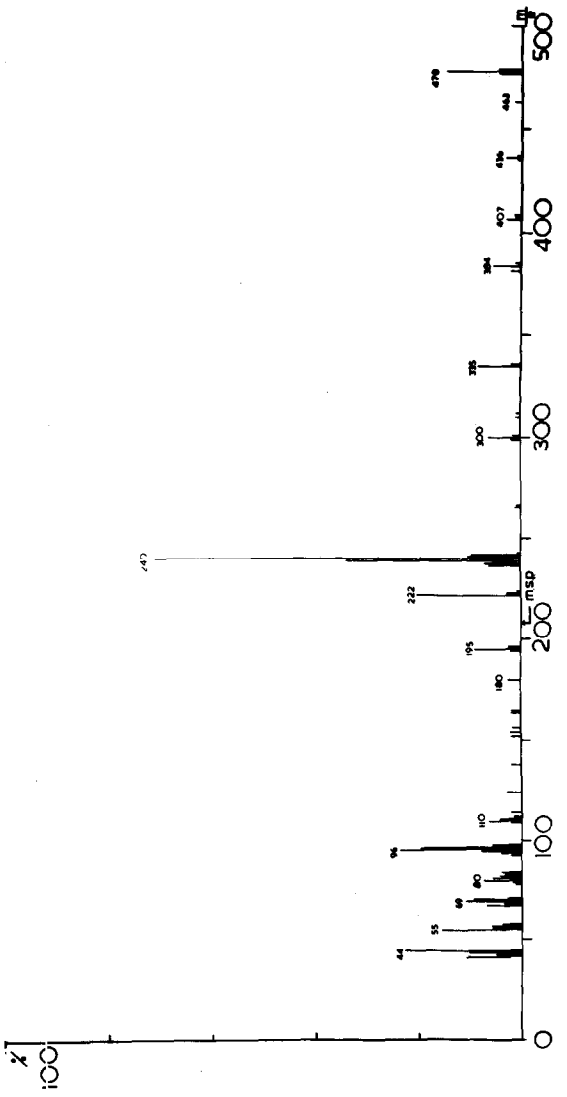

FIG. 2

Mass spectrum of carpaine

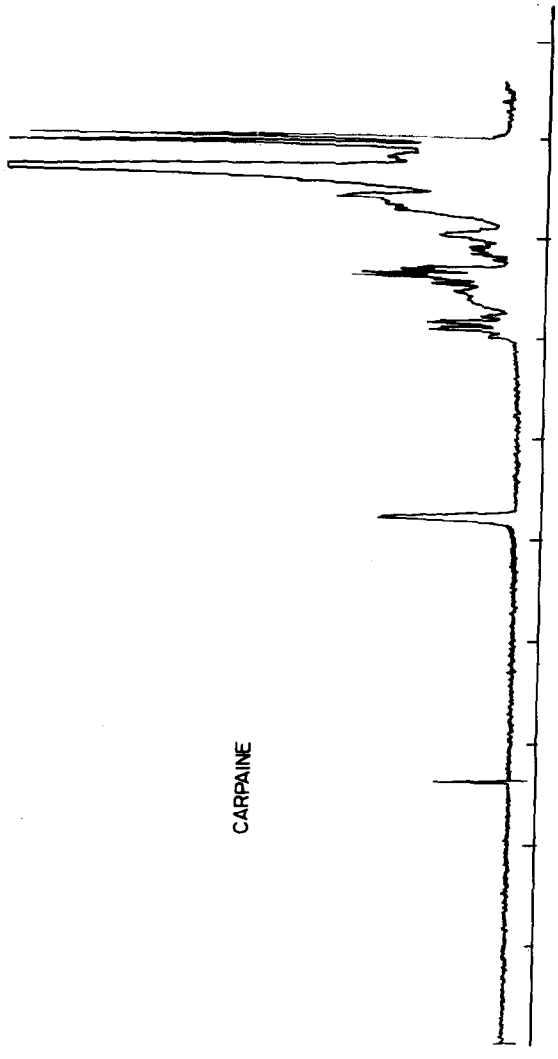

Fig. 3

100 Mc NMR spectra of carpaine and pseudocarpaine

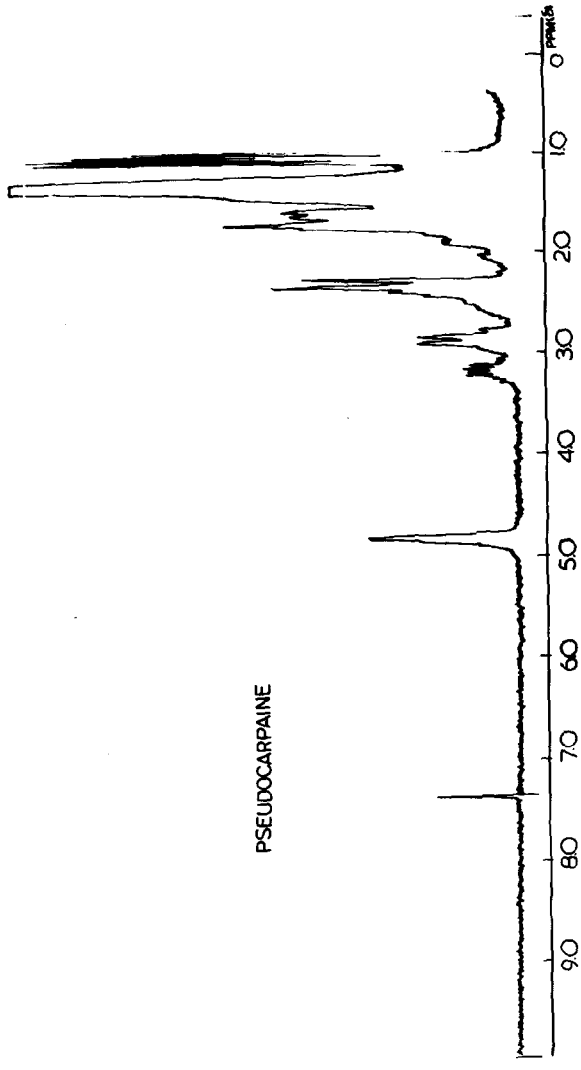

Fig. 3 continued