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DIMERIC PIPERIDINE ALKALOIDS FROM AZIMA TETRACANTHA LAM.:

AZIMINE, AZCARPINE AND CARPAINE

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Two new piperidine alkaloids were isolated from the leaves of *Azima tetracantha* Lam. (Salvadoraceae). The major alkaloid azimine I m.p. 112.0 - 113.0°C; λ_{max}^{MeOH} 207 mμ (ε = 905); $\nu_{max}^{CHCl_3}$ 1720 cm^{-1} (lactone); $[\alpha]_D^{20^0} = 0^0$ (c 0.8 in EtOH) analysed for the empirical formula $C_{24}H_{42}N_2O_4$ in agreement with the mass spectrum. A hydrochloride, m.p. 284.0 - 287.0°C was prepared, and the bis-N-methyl derivative, m.p. 92 - 93°C established the presence of two secondary amine groups. From the spectrometric information it was evident that a very close relationship exists between azimine and carpaine. It was concluded that azimine is a 22-membered analogue of carpaine recently proved to have structure II (1-4).

The mass spectrum* of azimine (Fig. I) differed from that of carpaine (3) (Fig. III) in so far that the fragments (a) and (b), proposed to possess two piperidine rings, were shifted to a lower mass value by 56 and 28 mass units, respectively, whereas the fragments (c) and (d), containing only one piperidine ring, moved down on the m/e scale by 28 units. Scheme A shows the possible routes for the formation of the more abundant peaks. The mass spectrum was compatible with the structure I suggested for azimine.

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* Mass spectra were determined on an AEI MS-9 spectrometer, with direct insertion technique.

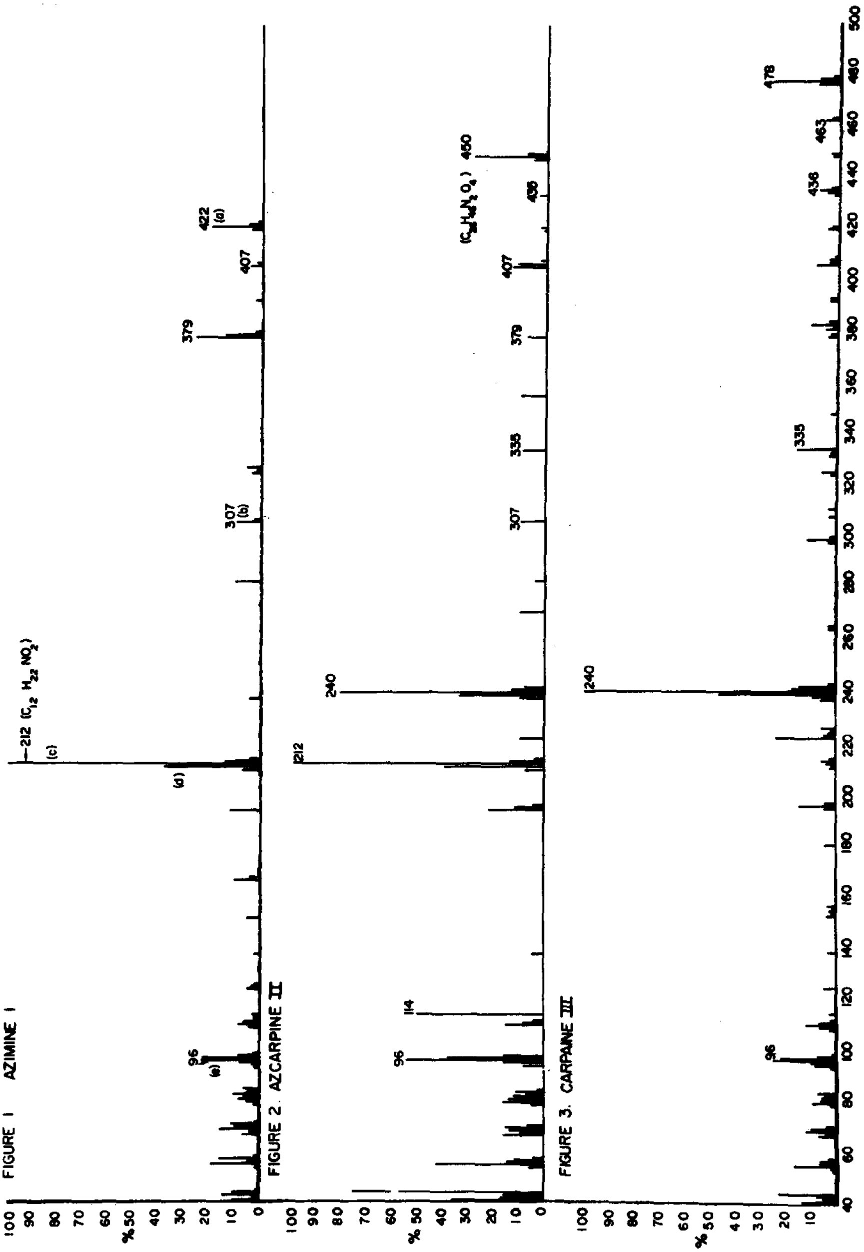
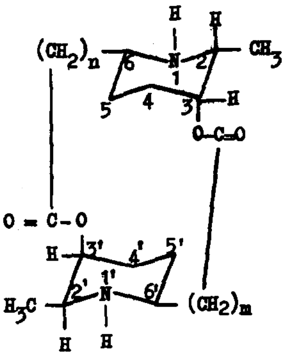


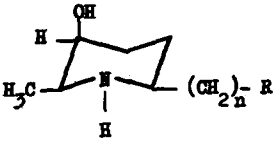
FIGURE 1 AZIMINE I

FIGURE 2. AZCARPINE II

FIGURE 3. CARPAINE III



I n = m = 5
II n = m = 7
III n = 5; m = 7



(a) n = 5
(b) n = 7
IV R = COOH
V R = COOMe
VI R = CH_2OH

Azimine on hydrolysis yielded only one acid, azimic acid IV(a) isolated as the methyl ester Va, $C_{13}H_{25}NO_3$. Reduction of azimine with $LiAlH_4$ also gave only one product azimdiol VI(a), $C_{12}H_{25}NO_2$. This information rigorously proved the symmetrical nature of the dilactone ring.

Analysis of the NMR spectrum[*] of azimine as in the case of carpaine (2) gave valuable information on the stereochemistry of this alkaloid. The two C-methyl groups on C-2 and C-2' appear as a doublet at $\tau = 8.99$ ($J = 7$ c/s), while the protons on C-2 and C-2' appear as a pair of doublets at $\tau = 8.06$ ($J = 7$ c/s), further split by a weak spin-coupling ($J = 1$-2 c/s) with the protons on C-3 and C-3'. Assuming the same cis di-equatorial relationship of the C-2 (C-2') and C-6 (C-6') side chains as in carpaine (5), an axial conformation may be assigned to the ester group on C-3 (C-3') in azimine. The direct synthetic correlation of carpaine and azimine is currently in progress.

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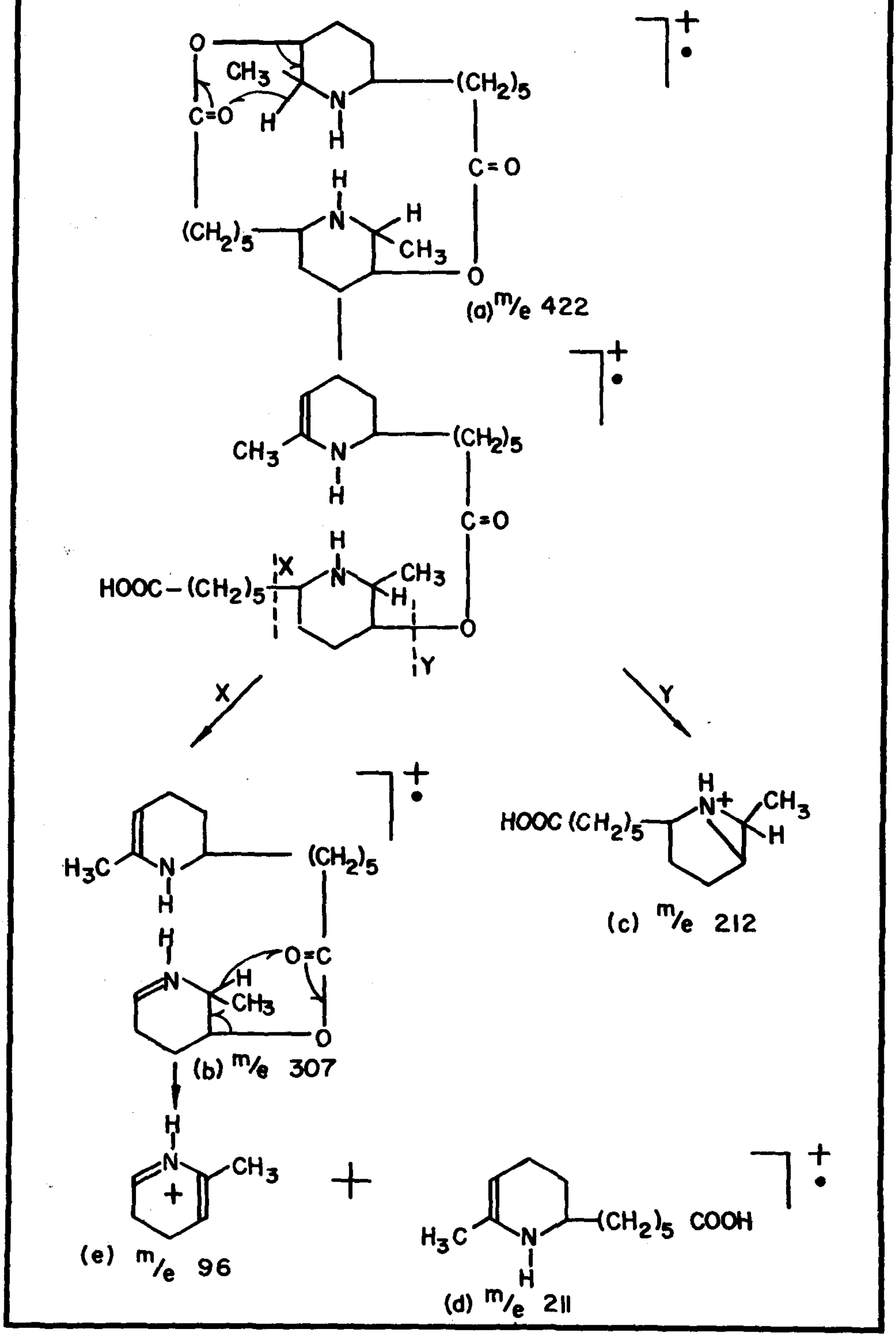
[*] NMR spectra were determined with a Varian HA-100 instrument with T.M.S. as internal standard ($\tau = 10.00$) in $CDCl_3$.

SCHEME A



A second non-crystalline alkaloid azcarpine III was isolated in much smaller quantities. The molecular formula $C_{26}H_{46}N_2O_4$ was derived by accurate mass determination. (Found M^+ 450.346; $C_{26}H_{46}N_2O_4$ requires 450.345). The mass spectrum of azcarpine was most informative (Fig. II). The molecular ion appeared at m/e 450, the rest of the spectrum being similar to that expected from a mixture of carpaine and azimine. This information strongly suggested that the alkaloid is an unsymmetrical dilactone composed of the hydroxy acids, carpamic IV(b) and azimic IV(a) acids. This was confirmed by the analysis of the hydrolysis products of III. The NMR spectrum of azcarpine differed only in minor features from that of azimine.

A third alkaloid isolated in minute quantities m.p. 117.5 - 118.5°C was shown to be identical with an authentic specimen* of carpaine II (mixed m.p., mass spectrum (Fig. III) and chromatographic behaviour).

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