

STRUCTURE OF FAWCETTIMINE:  
CORRELATION WITH SERRATININE

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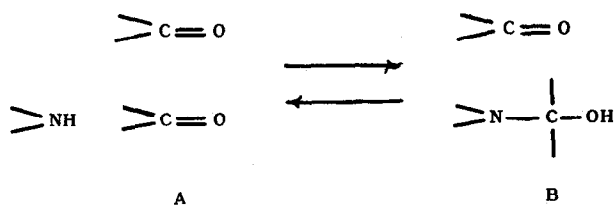
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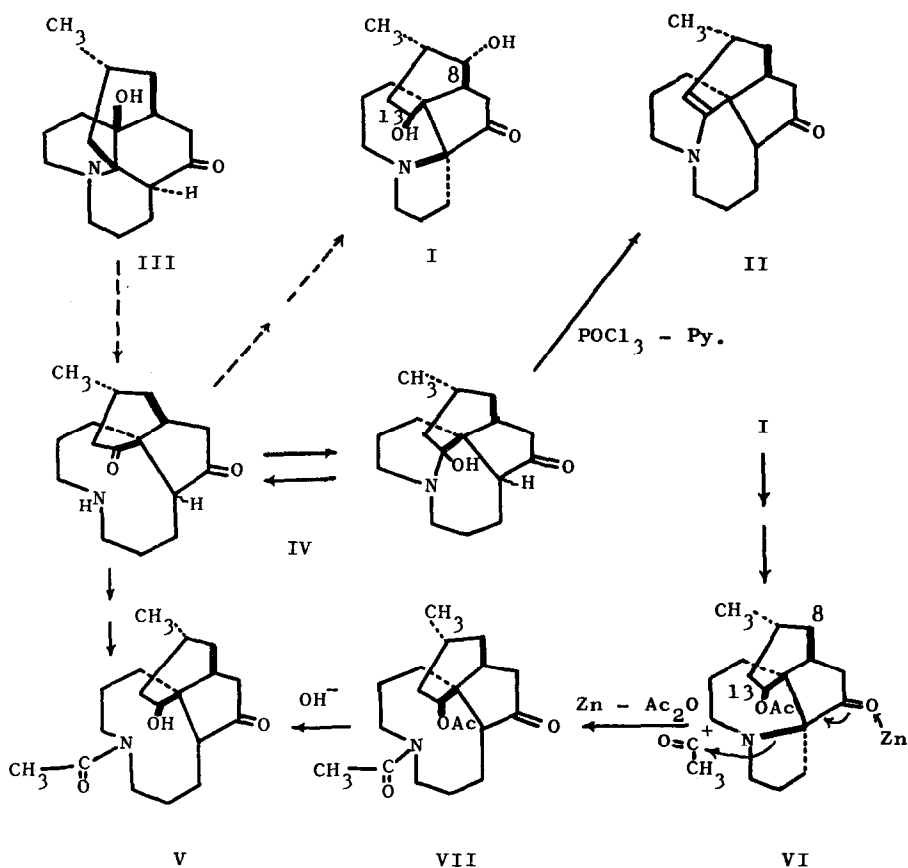
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Fawcettimine (Base A) was first isolated in 1959 from Lycopodium fawcettii Lloyd et Underwood as its crystalline perchlorate (1) and formulated as  $C_{16}H_{27}O_2N$ . The formula was later (2) revised to  $C_{16}H_{25}O_2N$ . Fawcettimine shows carbonyl absorption in the infrared ( $CCl_4$  solution) at  $1732\text{ cm}^{-1}$  as well as hydroxyl absorption at  $3300\text{ cm}^{-1}$ . Acetylation of fawcettimine (3) furnishes a neutral N-acetyl derivative  $C_{18}H_{27}O_3N$  which shows no OH or NH absorption in the infrared but which now shows carbonyl absorption at 1730, 1690 and  $1615\text{ (N-COCH}_3\text{) cm}^{-1}$ . These and other properties (2,3) of fawcettimine are easily rationalized in terms of a transannular interaction between a secondary amino group and a carbonyl group of fawcettimine as summarized in part structures A and B. In solution fawcettimine exists, at least predominantly, in form B, while the acetyl derivative is of form A. The fact that the interacting carbonyl group is a ketonic carbonyl rather than an aldehydic carbonyl is indicated by the lack of absorption for an aldehydic proton in the n.m.r. spectrum of N-acetylfawcettimine. The n.m.r. spectrum does reveal the presence of a secondary  $\beta$ -methyl group ( $\tau$  8.9, doublet).



Lack of olefinic absorption in the n.m.r. spectra of fawcettimine and N-acetylfawcettimine and their resistance to hydrogenation dictate against the presence of an olefinic linkage and suggest that N-acetylfawcettimine is tricyclic.



The fact that the absorption band due to the non-interacting carbonyl group in fawcettimine and its derivatives absorbs at  $1730 - 1740 \text{ cm}^{-1}$  suggests that it is a cyclopentanone carbonyl.

It has been suggested that serratinine (I) (4), serratinidine (5), and fawcettidine (II) (6) may be formed in the plant by rearrangement of lycodoline (III) via an intermediate of structure IV.

Since the properties of fawcettimine described above fit well into a structure such as IV, it was decided to attempt a direct correlation between serratinine (I) and fawcettimine.

Reduction of N-acetylfawcettimine with either sodium borohydride or sodium-alcohol furnishes dihydro-N-acetylfawcettimine (3) which shows hydroxyl and amide absorption as well as carbonyl absorption at  $1735 \text{ cm}^{-1}$  and thus must retain the five-membered ketone and have structure V. Compound V has now been prepared from serratinine.

During the course of work directed toward correlation of serratinine with fawcettidine (6), serratinine was transformed into 13-acetyl-8-deoxyserratinine (VI). Reduction of compound VI with  $\text{Ac}_2\text{O-Zn}$  provided O,N-di-acetylchanodihydro-8-deoxyserratinine (VII),  $\text{C}_{20}\text{H}_{31}\text{O}_4\text{N}^{*1}$ , m.p.  $181 - 183^\circ$ ;  $^{*1}$  IR,  $1733$  (ester and five-membered ketone),  $1632$  (amide)  $\text{cm}^{-1}$  which on hydrolysis gave N-acetylchanodihydro-8-deoxyserratinine,  $\text{C}_{18}\text{H}_{29}\text{O}_3\text{N}$ , m.p.  $205-207^\circ$ , IR,  $3400$  (OH),  $1735$  (five-membered ketone),  $1620$  (amide)  $\text{cm}^{-1}$ . This compound proved to be identical (IR spectrum, m.m.p., t.l.c. behavior) with compound V from fawcettimine, thus establishing that fawcettimine is indeed IV. Further confirmation of structure IV is provided by the finding that dehydration of fawcettimine with phosphorus oxychloride-pyridine affords fawcettidine (II).

The natural occurrence of an alkaloid with structure IV provides strong support for the previously proposed (4,6) biogenesis of the serratinine series of alkaloids.

#### REFERENCES

\*1 All melting points were observed on a microscopic hotstage and are

uncorrected. All compounds given by molecular formulae gave satisfactory elementary analyses.

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