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Structure of Serratinidine and Fawcettidine. A New Type of Lycopodium Alkaloid[1,2]

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Structures of two Lycopodium alkaloids, serratinidine (I) from *Lycopodium serratum* Thunb. *var. serratum f. serratum* and fawcettidine (XIX) from *Lycopodium fawcettii* Lyloyd *et* Underwood, were examined.

In the previous papers,[4,5] the authors suggested the biogenesis of serratinine and in connection of this, the skeletal structure ((B) in Chart 1) for serratinidine was selected as a working hypothesis. The validity of this assumption was shown by chemical correlation of serratinine ((C), R=OH, in Chart 1) of established structure with serratinidine through the route shown in Chart 2.

On the other hand, fawcettidine was first isolated by Burnell[6] from a Jamaican Lycopodium plant but since then there has been no report on the structure. From physical and spectral properties of this alkaloid appeared in the literature,[6] the authors postulated the same skeletal structure for fawcettidine as that of serratinidine. Then, this assumption was proved by chemical conversion of serratinine into fawcettidine along the schemes shown in Chart 5. The present study reveals a new structural type of Lycopodium alkaloid.

In previous papers[4,5] we reported the isolation and structure elucidation of three new alkaloids, serratinine and serratine and serratanidine from *Lycopodium serratum* Thunb. *var. serratum f. serratum.* Serratinidine is another minor alkaloid isolated from the same plant. On the other hand, fawcettidine was first isolated by Burnell[6] from a Jamaican Lycopodium plant, *Lycopodium fawcettii* Lyloyd *et* Underwood, and characterization of this alkaloid has been already presented but there has been no report on the structure of this alkaloid.

In preliminary communications,[2] we reported the structure elucidation of serratinidine and fawcettidine by chemical correlation with serratinine of established structure. These studies demonstrated that serratinidine and fawcettidine are related in the skeletal structure of a new type of Lycopodium alkaloid. In a present paper, we wish to describe a full detail of structure elucidation of serratinidine (I) and fawcettidine (XIX).

Serratinidine was obtained as colorless needles, mp 232—234°, $[\alpha]_D^{10}$ +224.2° (c=1.08, EtOH) and the molecular formula, $C_{18}H_{28}O_2N_2$ was fixed on the basis of analytical and mass

1) Studies on the Constituents of Domestic Lycopodium Genus Plants, Part X: Part IX, Y. Inubushi, T. Harayama, M. Akatsu, H. Ishii, and Y. Nakahara, *Chem. Pharm. Bull.* (Tokyo), **16**, 2463 (1968).
2) The preliminary reports on this work appeared in *Tetrahedron Letters*, **1966**, 3967 and *ibid.*, **1966**, 6215.
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4) Y. Inubushi, H. Ishii, B. Yasui, M. Hashimoto and T. Harayama, *Tetrahedron Letters*, **1966**, 1537, 1551; *idem, Chem. Pharm. Bull.* (Tokyo), **16**, 82, 92, 101 (1968).
5) Y. Inubushi, T. Harayama, M. Akatsu, H. Ishii and Y. Nakahara, *Chem. Pharm. Bull.* (Tokyo), **16**, 2463 (1968).
6) R.H. Burnell, *J. Chem. Soc.*, **1959**, 3091; R.H. Burnell, C.G. Chin, B.S. Mootoo and D.R. Tayler, *Can. J. Chem.*, **41**, 3091 (1963).

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spectral data (M^+ 304). The infrared (IR) spectrum[7] showed the presence of the NH and/or OH, amide and olefinic function by absorption bands at 3310, 1659 and 3110 cm^{-1}, respectively. The amide II band was also observed at 1563 cm^{-1}. In the nuclear magnetic resonance (NMR) spectrum,[7] the following signals were observed; 4.72 τ (1H, m, half-band width 4.0 cps, vinyl proton); 5.67 τ (1H, m, >CH–NHAc), 6.31 τ (1H, m, >CH–OH); 8.00 τ (3H, s, $-NHCOCH_3$) and 8.89 τ (3H, d, J=7.5 cps, $>CH-CH_3$).

Acetylation of serratinidine afforded acetylserratinidine (II), mp 105—108°, $[\alpha]_D^{16}$ +177.0° (c=1.19, EtOH), which showed the presence of an acetoxyl group by absorption bands at 1729 and 1235 cm^{-1} in the IR spectrum and by the signals at 4.99 τ (1H, q, J=5.0 cps, J=8.0 cps, >CH–OAc), 7.89 τ (3H, s, $OCOCH_3$) in the NMR spectrum.

These data led us to a conclusion that serratinidine must be a tetracyclic alkaloid having the rational formula, $C_{10}H_{16}$ (>N–), (>CH–NHAc), (>CH–OH), ($>CH-CH_3$), (>C=CH–).

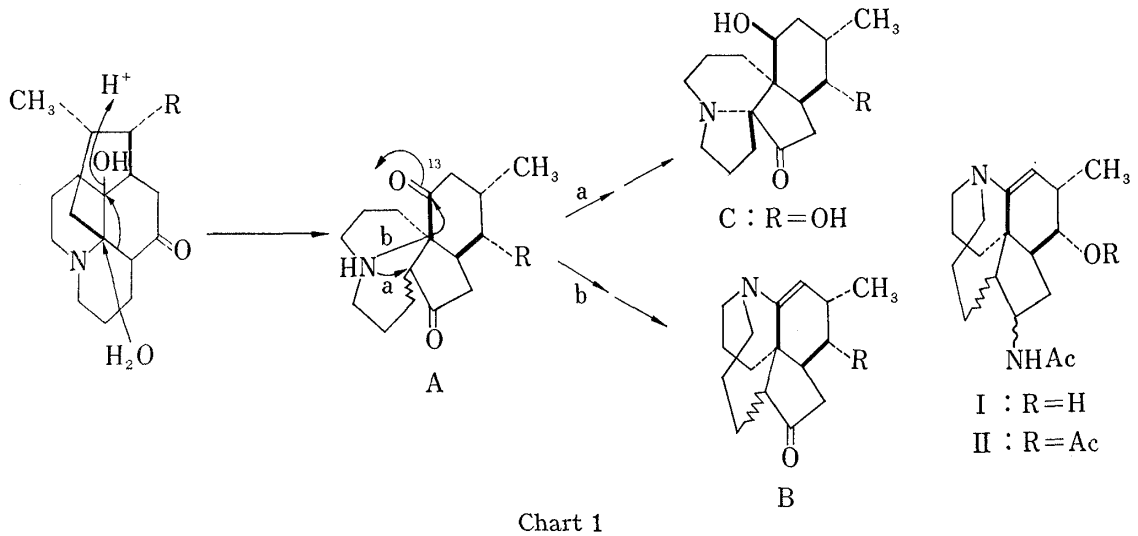

Chart 1

In the nuclear magnetic double resonance of the compound (II), irradiation on the signal due to a proton geminal to a methyl group at 7.5 τ resulted in changes of two doublet signals at 4.52 τ and 8.97 τ attributable to an olefinic proton and a secondary methyl group, respectively, into two singlets. This finding suggests the presence of $^{(N\ or\ C)}_{(C)}>C=CH-CH(CH_3)-$ system in the serratinidine molecule. In connection with the structure of serratinine,[4,5] we have suggested the biogenesis of serratinine in which the plausible intermediate ((A) in Chart 1, route a) would lie between the lycodoline type precursor and serratinine ((C), R=OH). In these schemes, it is considered feasible that a lone pair on the nitrogen atom of the intermediate would attack the carbonyl carbon atom at C_{13} (route b) to result in the compound (B). Much attention is denoted to the structure of this postulated compound (B), for this comprises the same partial structure as that of serratinidine. For establishing the structure of serratinidine, an attempt was then made to correlate serratinine ((C), R=OH) of established structure with serratinidine by chemical transformation along the route b, although there was no definite knowledge on the position of an acetamide group in the latter.

Reduction of 8-acetyl-13-dehydroserratinine (III) with Zn–acetic acid gave two kinds of basic products, anhydroacetylaposerratinine (IV), and acetylaposerratinine (V). The IR spectrum of the compound (V) showed a hydroxyl band at 3450 cm^{-1} and a carbonyl band at 1725 cm^{-1} but the six membered ring carbonyl band at 1701 cm^{-1} which had been observed in the compound (III), disappeared. From the reaction mechanism, the presence of the

7) Unless otherwise noted, all IR spectra were measured on Nujol mull and all NMR spectra were obtained in $CDCl_3$ solution with tetramethylsilane as internal standard on a Varian A-60 recording Spectrometer.

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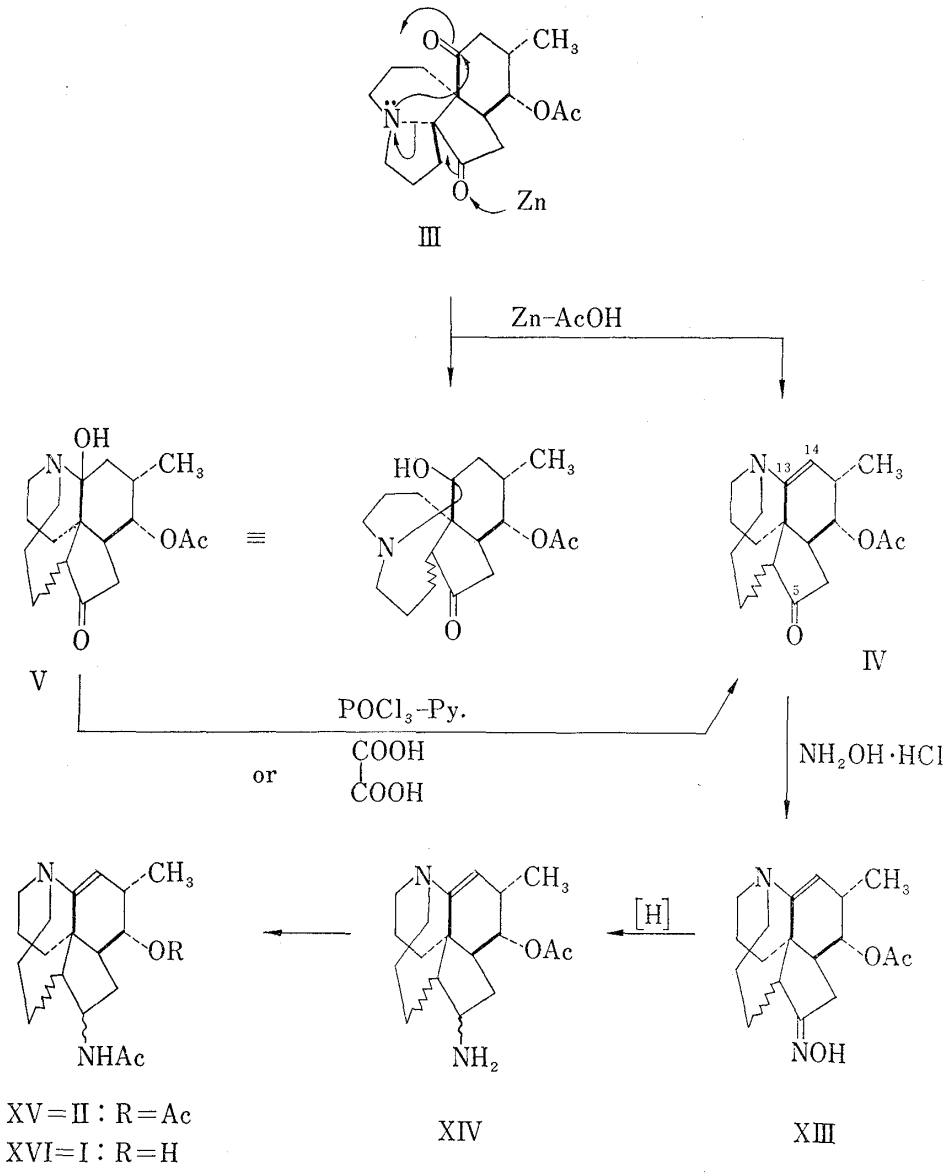

Chart 2

α-carbinol amine function is presumed in the compound (V) and this was ascertained by the following experiments.

Reaction of the compound (V) with methyl iodide, followed by treatment with cold ammonia afforded a tertiary amine, N-methylacetylchanoaposerratinine (VI) which revealed newly a six membered ring ketone absorption band at 1692 cm^{-1} in the IR spectrum and the signals at 7.71 τ (3H, s, >N–C<u>H</u>$_3$ or –OCOC<u>H</u>$_3$), 7.76 τ (3H, s, –OCOC<u>H</u>$_3$ or >N–C<u>H</u>$_3$) in the NMR spectrum. This result can be accounted for by the reaction path as shown in Chart 3. Structure evidence for the compound (V) was also obtained by another series of reactions

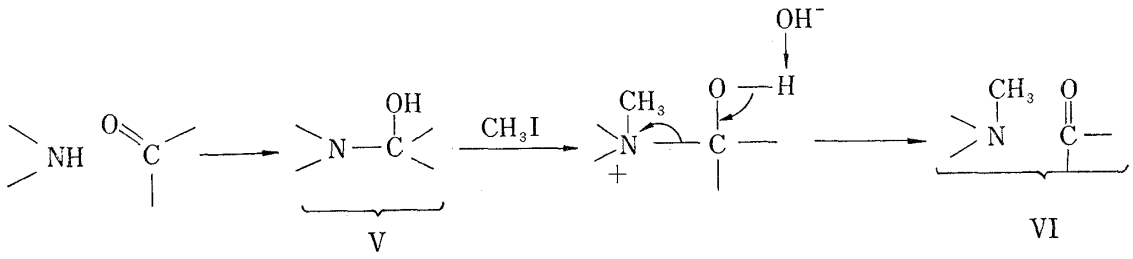

Chart 3

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(Chart 4). Thus, reduction of the compound (VI) with lithium aluminum hydride gave N-methyltriol (XI) which was identified with a sample of the reduction product of β-dihydroserratinine methyl methine (XII), derived from serratinine, with lithium aluminum hydride by comparison of IR spectrum and mixed melting point determination. Furthermore, acetylation of the compound (V) in the presence of alkali gave an oily neutral product, O,N-diacetylchanoaposerratinine (VII), which showed newly the absorption bands at 1697 (CO), 1630 cm^{-1} (>N–CO) in the IR spectrum, and reduction of the compound (VII) with lithium aluminum hydride in a sealed tube afforded a basic compound (VIII). On the other hand, reduction of serratinine with Zn–acetic anhydride afforded a neutral compound, O,O,N-triacetylchanodihydroserratinine (IX) which was reduced with lithium aluminum hydride to furnish N-ethylchanotetrahydroserratinine (VIII). This was then identified with the sample of the basic compound derived from the compound (V) as mentioned above, by comparison of IR spectrum and mixed melting point determination. The compound (VIII) was also derived from the compound (VII) by a different manner. Thus, reduction of the compound (VII) with lithium aluminum hydride in tetrahydrofuran afforded a basic monoketone (X), which showed the absorption bands at 3450 (OH) and 1703 cm^{-1} (CO) in the IR spectrum, and reduction of this monoketone with sodium borohydride gave the compound (VIII). All these experimental results made clear the presence of α-carbinol amine function in the compound (V).

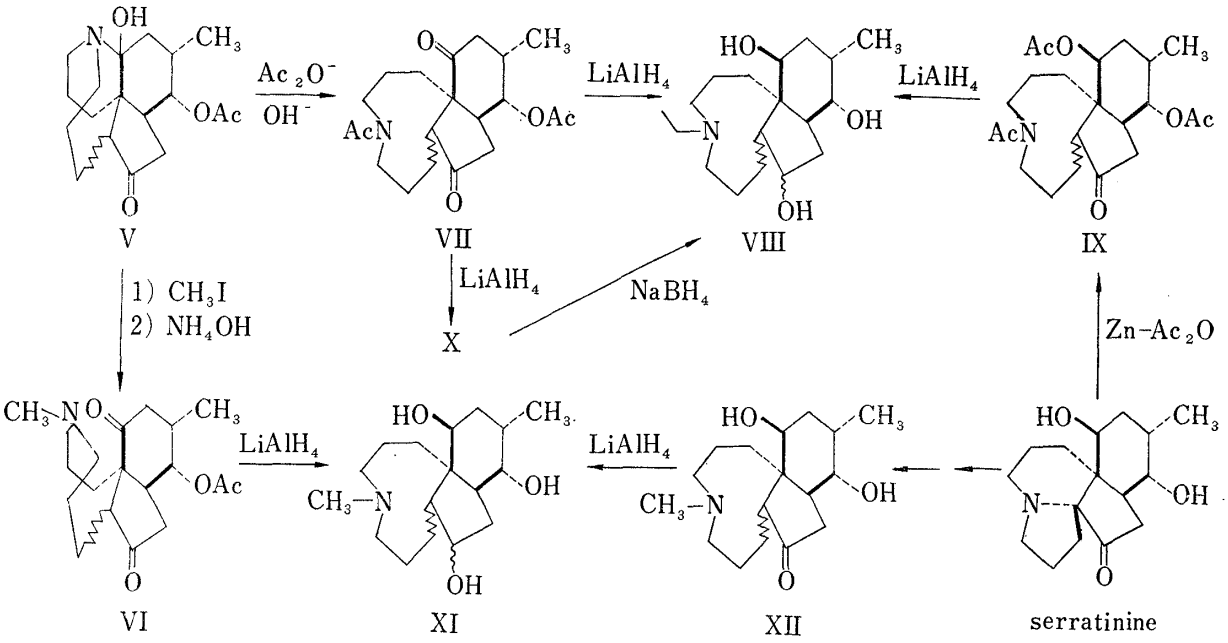

Chart 4

Treatment of the compound (V) with $POCl_3$–pyridine or with oxalic acid in acetic acid furnished the compound (IV) (see Chart 2). The presence of the ene–amine system in this compound is presumed since the α-carbinol amine function in the compound (V) has been established. The weak basicity of the compound (IV), pK_a' 6.4,[8] is consistent with the above assumption. In the IR spectrum of the compound (IV), the hydroxyl band was not observed but the band due to the newly introduced double bond was observed at 1662 cm^{-1}, and the NMR spectrum exhibited the signals at 4.39 τ (1H, d, J=6 cps, vinyl proton), 5.55 τ (1H, q, J=6.0 cps, J_2=10.0 cps, >C<u>H</u>–OAc) and 9.02 τ (3H, d, J=7 cps, >CH–C<u>H</u>$_3$). The nuclear magnetic double resonance of this compound revealed the similar feature with that of the

8) pK_a' value was measured in 1/100N H_2SO_4–50% EtOH solvent system (10 ml) by titration with 1/10N NaOH–50% EtOH solution.

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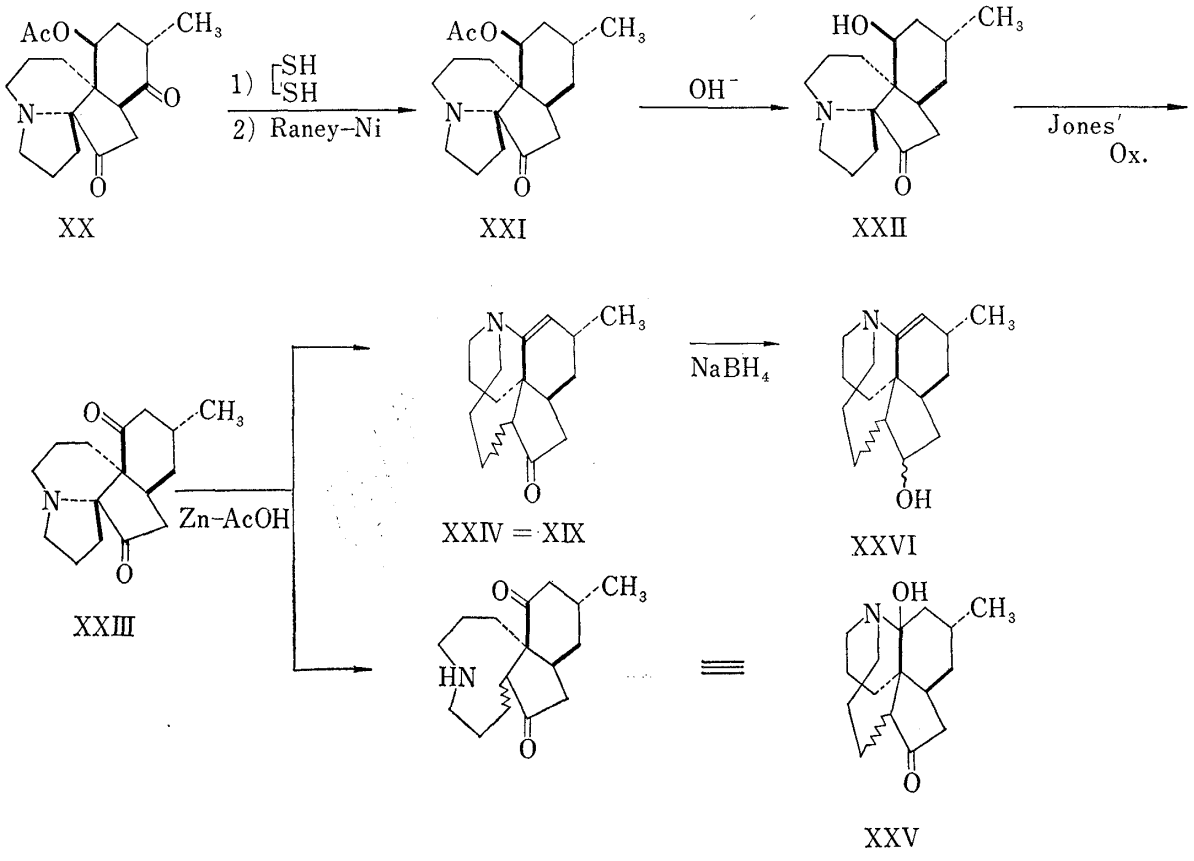
compound (II). Thus, irradiation on the signal attributable to a proton geminal to a methyl group resulted in the changes of two doublet signals due to a vinyl proton and a methyl group into two singlet signals, respectively and a signal due to a proton geminal to an acetoxyl group into a doublet. All these findings provide the evidence for the existence of the $\begin{pmatrix}C\\N\end{pmatrix}>C{=}CH{-}CH(CH_3){-}CH(OAc){-}CH<\begin{pmatrix}C\\C\end{pmatrix}$ system in the compound (IV) and consequently, anhydroacetylaposerratinine is now represented by the formula (IV).

Informations provided by the NMR spectra of acetylserratinidine (II) and anhydroacetylaposerratinine (IV), and a similarity of the spectral feature substantiate our previous suggestion that the same skeletal structure would be assigned to these two compounds.

At this stage of the study, the position of an acetylamino group in serratinidine was still obsqure but from biogenetic consideration, this group was tentatively assumed to be located at the C_5 position, and the chemical transformation of anhydroacetylaposerratinine (IV) to serratinidine was put to practice.

Treatment of the compound (IV) with hydroxyl amine hydrochloride in pyridine gave an oily anhydroacetylaposerratinine oxime (XIII) which without further purification, was reduced over Raney nickel to furnish an oily amino compound (XIV). The compound revealed two spots on thin-layer chromatography (TLC) and without further purification, was acetylated by heating with acetic anhydride, and the resulting acetates were chromatographed on alumina. The earlier eluate crystallized as colorless prisms (XV) and this compound was identical with a sample of acetylserratinidine in all respects including the specific rotation. Hydrolysis of the acetate afforded a hydroxyl compound (XVI) which was identified with a sample of natural serratinidine (I) by comparison of IR spectrum and by mixed melting point determination. Thus, serratinidine is represented by the absolute stereostructure (I). However, the configuration of the side chain at C_4 and the acetoamide group at C_5 position



XX XXI XXII XXIII XXIV = XIX XXV XXVI

Chart 5

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are still equivocal and further work is in progress. In the column chromatography of the acetylation products of the compound (XIV), the latter eluate gave an oily substance (XVII) which on alkali hydrolysis afforded a crystalline compound (XVIII). This compound is assumed to be an epimer of serratinidine with respect to the configuration of the acetoamide group.

It has been reported that fawcettidine,[6] an oily alkaloid, $C_{16}H_{23}ON$, methiodide, mp 223—225°, picrate, mp 222—223°, shows a carbonyl band at 1740 cm^{-1} in the IR spectrum and the existence of $>CH-CH_3$ and $>C=CH-$ function is shown by the NMR spectrum. In our study of serratinidine, we described that anhydroacetylaposerratinine (IV) derived from serratinine is a weak base, pK_a' 6.4. Fawcettidine, pK_a' 6.2[6] bears a marked resemblance to the compound (IV) in the basicity and in showing a five membered ring ketone absorption band in the IR spectrum. Furthermore, in view of the biogenesis of serratinidine previously suggested and the NMR feature of fawcettidine, it can be assumed that this alkaloid would have the same skeletal structure (XIX) with that of serratinidine, and the chemical transformation of serratinine into fawcettidine was then attempted for establishing the structure of the latter.

Thioketalization of 8-dehydro-13-acetylserratinine (XX) with BF_3–etherate and ethanedithiol, followed by reduction over Raney nickel gave 8-deoxy-13-acetylserratinine (XXI) which revealed the absorption bands due to an acetoxyl group at 1740, 1250 and 1236 cm^{-1} in the IR spectrum. Hydrolysis of the compound (XXI) with alkali afforded 8-deoxyserratinine (XXII) whose IR spectrum showed the absorption bands due to a hydroxy group at 3080 cm^{-1} and a five membered ring ketone group at 1735 cm^{-1}, respectively. Oxidation of the compound (XXII) with Jones reagent gave 8-deoxy-13-dehydroserratinine (XXIII) which revealed the presence of the newly resulting six membered ring ketone by an absorption band at 1693 cm^{-1} in the IR spectrum. In a similar manner as the case of the compound (III), reduction of the ketone (XXIII) with Zn–acetic acid, followed by chromatographic purification over alumina furnished two kinds of oily products; an anhydro compound (XXIV), oil, methiodide 224—226°, picrate, mp 223—225° and an alcohol (XXV), oil, methiodide, mp 253—255°. The compound (XXIV) was identified with a sample of fawcettidine picrate[9] by comparison of the IR spectrum. Reduction of the compound (XXIV) with sodium borohydride gave a dihydro compound (XXVI) whose physical properties are coincide with those of dihydrofawcettidine reported in the literature.[6] Consequently, the absolute stereostructure of fawcettidine can be now represented by the formula (XIX).

On the other hand, the IR spectrum of the alcohol (XXV) showed a single absorption band due to a five membered ring ketone at 1735 cm^{-1} in the carbonyl region together with an absorption band due to a hydroxyl group. However, the spectrum of its methiodide revealed two absorption bands at 1742 and 1687 cm^{-1} which are attributable to a five and six membered ring ketone, respectively. These physical data together with the facts that reduction of the compound (III) provided two kinds of products, (IV) and (V), suggest that this alcohol would be represented by the formula (XXV). During the course of work directed toward correlation of serratinine with fawcettimine,[10] serratinine was transformed into N-acetyl-13-dihydrofawcettimine which in turn was identified with the compound derived from fawcettimine and from this result, the structure (XXV) was allotted for fawcettimine. Therefore, this alcohol ought to be identical with fawcettimine, although the direct comparison has not been accomplished.

9) We thank Professor W.A. Ayer, University of Alberta, for kindly supplying us with an authentic IR spectrum of fawcettidine picrate.

10) Y. Inubushi, H. Ishii, T. Harayama, R.H. Burnell, W.A. Ayer and B. Altenkirk, *Tetrahedron Letters*, **1967**, 1069.

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Experimental[11]

Isolation and Characterization of Serratinidine and Preparation of Acetylserratinidine——Isolation and characterization of serratinidine were reported in an earlier paper[12] and preparation and characterization of acetylserratinidine appeared in the same paper.

Anhydroacetylaposerratinine (IV) and Acetylaposerratinine (V)——To a solution of 8-acetyl-13-dehydroserratinine ((III), 60 mg) in 3 ml of acetic adid was added 400 mg of Zn powder under stirring at 140° and stirring was continued for 6 hr at this temperature. After cooling, Zn powder was filtered off and washed with water. The filtrate was washed with ether, made alkaline with ammonia and extracted with ether. The ether extracts were combined and dried over anhyd. K_2CO_3 and evaporated to give an oily residue (60 mg). The residue in benzene was chromatographed on neutral alumina (Grade II) and the eluate with benzene crystallized. Recrystallization from ether afforded anhydroacetylaposerratinine ((IV), 23 mg), as colorless prisms, mp 153—155°, pK_a' 6.4. *Anal.* Calcd. for $C_{18}H_{25}O_3N$: C, 71.25; H, 8.31. Found: C, 71.53; H, 8.59. IR cm^{-1}: $\nu_{C=O}$ 1740, 1728; $\nu_{C=C}$ 1662; ν_{C-O} 1231. NMR τ: 4.39 (1H, d, J=6 cps, vinyl proton), 5.55 (1H, q, J_1=6 cps, J_2=10 cps, >C<u>H</u>–OAc), 7.93 (3H, s, OCOC<u>H</u>$_3$), 9.02 (3H, d, J=7 cps, >CH–C<u>H</u>$_3$). The eluate with ether crystallized and recrystallization from ether gave acetylaposerratinine ((IV), 26 mg) as colorless prisms, mp 172—175°. *Anal.* Calcd. for $C_{18}H_{27}O_4N$: C, 67.26; H, 8.47. Found: C, 66.83; H, 8.27. IR cm^{-1}: ν_{O-H} 3450; $\nu_{C=O}$ 1725; ν_{C-O} 1238 (Nujol). NMR τ: 4.98 (1H, broad s, >C<u>H</u>–OAc), 7.88 (3H, s, OCOC<u>H</u>$_3$), 9.05 (3H, d, J=6.5 cps, >CH–C<u>H</u>$_3$). The ratio of the compound (IV) to (V) depended on the reaction temperature, thus, the ratio at 110° was 1:4 and at 90° 1:9.

Anhydroacetylaposerratinine (IV) from Acetylaposerratinine (V)——Dehydration with $POCl_3$–Pyridine: To a solution of acetylaposerratinine ((V), 30 mg) in 2 ml of pyridine was added six drops of $POCl_3$ under cooling and allowed to stand overnight at room temperature. The reaction mixture was evaporated to dryness *in vacuo* and water was added to the residue. The aqueous solution was made alkaline with ammonia and extracted with ether. The ether extract was dried over anhyd. K_2CO_3 and evaporated. The residue in benzene was chromatographed over neutral alumina (Grade II) and the eluate with benzene gave 8 mg of the compound (IV) which was identified with the compound obtained in the preceding experiment by comparison of the IR spectrum and mixed melting point determination. From the eluate with ether was recovered 12 mg of the starting material (V).

Dehydration with Oxalic Acid in Acetic Acid: To a solution of acetylaposerratinine ((V), 20 mg) in 2 ml of acetic acid was added 200 mg of oxalic acid and the reaction mixture was heated at 150° for 3 hr. The mixture was evaporated *in vacuo* to dryness and 1% aqueous ammonia was added to the residue to be made alkaline and extracted with ether. The ether extract was dried over anhyd. K_2CO_3 and evaporated. The residue in benzene was chromatographed on neutral alumina. The eluate with benzene gave 16 mg of the compound (IV).

N-Methyl-acetylchanoaposerratinine (VI)——To a solution of acetylaposerratinine ((V), 50 mg) in 2 ml of acetone was added 0.2 ml of methyl iodide and the mixture was allowed to stand overnight at room temperature. The deposited crystals were separated by decantation and washed with ether. The quaternary base thus obtained, without further purification, was dissolved in water, washed with ether, made alkaline with cold ammonia and extracted with ether. The extract was dried over anhyd. K_2CO_3 and evaporated. Chromatography of the residue in benzene over neutral alumina (Grade II) and eluation with benzene gave 20 mg of the compound (VI). Recrystallization from the mixture of *n*-hexane and ether afforded colorless needles, mp 134—137°. *Anal.* Calcd. for $C_{19}H_{29}O_4N$: C, 68.03; H, 8.71. Found: C, 67.72; H, 8.72. IR cm^{-1}: $\nu_{C=O}$ 1742, 1692; ν_{C-O} 1230 (Nujol). NMR τ: 4.92 (1H, m, >C<u>H</u>–OAc), 7.71 (3H, s, >N–C<u>H</u>$_3$ or OCOC<u>H</u>$_3$), 7.76 (3H, s, OCOC<u>H</u>$_3$ or >N–C<u>H</u>$_3$), 8.95 (3H, d, J=7 cps, >CH–C<u>H</u>$_3$).

O,N-Diacetyldehydrochanodihydroserratinine (VII)——A solution of acetylaposerratinine ((V), 160 mg) in 5 ml of 50% aqueous tetrahydrofuran was cooled at 5° and 10 ml of 5N acetic anhydride solution in tetrahydrofuran and 10 ml of 5N sodium hydroxide solution was added at the same time during 1.5 hr period and the reaction mixture was kept at pH 8—9 throughout the experimental period. After addition of acetic anhydride and sodium hydroxide solution had completed, the reaction mixture was stirred for further 30 min at 10°, diluted with water, made acidic with hydrochloric acid and extracted with ether. The ether extract was dried over anhyd. K_2CO_3 and evaporated. The oily residue (135 mg) in benzene was chromatographed on neutral alumina (Grade II) and the eluate with benzene afforded a homogeneous oil (120 mg). IR cm^{-1}: $\nu_{C=O}$ 1735, 1697, 1630; ν_{C-O} 1230 ($CHCl_3$); $\nu_{C=O}$ 1735, 1695, 1635; $\nu_{C=O}$ 1235 (film).

N-Ethylchanotetrahydroserratinine (VIII) from the Compound (VII)——1) Reduction in a Sealed Tube: To a solution of O,N-diacetyldehydrochanodihydroserratinine ((VII), 50 mg) in 10 ml of anhydr. ether was added 100 mg of $LiAlH_4$. The reaction mixture was heated at 100° in a sealed tube for 7 hr and after cooling, the excess of $LiAlH_4$ was decomposed with wet ether. The ether layer was separated by decantation and

11) All melting points were measured on micro melting point hot stage and uncorrected.

12) Y. Inubushi, H. Ishii, B. Yasui, T. Harayama, M. Hosokawa, R. Nishino and Y. Nakahara, *Yakugaku Zasshi*, **87**, 1394 (1967).

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the residue was washed several times with ether. The ether layer and washings were combined, dried over anhyd. K_2CO_3 and evaporated. The residue crystallized and recrystallization from acetone gave the compound ((VIII), 20 mg), mp 194° which was identified with an authentic sample of N-ethylchanotetrahydroserratinine by comparison of IR spectrum and mixed melting point determination.

2) Reduction at Atmospheric Pressure: To a solution of the compound ((VII), 86 mg) in 20 ml of anhyd. tetrahydrofuran was added 100 mg of $LiAlH_4$ and the reaction mixture was heated on an oil bath at 90° for 8 hr. After cooling, the solvent was evaporated, and the ether was added to the residue and the excess of hydride was decomposed with wet ether. The ether layer was separated by decantation and the residue was washed several times with ether. The ether solution was dried over anhyd. K_2CO_3 and evaporated. The residue in benzene was chromatographed over neutral alumina, and the eluates with benzene and ether crystallized. Recrystallization from ether gave colorless prisms, the monoketone ((X), 23 mg), mp 158—161°. *Anal.* Calcd. for $C_{18}H_{31}O_3N$: C, 69.86; H, 10.10. Found: C, 69.81; H, 10.08. IR cm^{-1}: ν_{O-H} 3450; $\nu_{C=O}$ 1703. To a solution of the monoketone (X) in 5 ml of ethanol was added 30 mg of $NaBH_4$ and the mixture was refluxed on a water bath for 4 hr. The excess of $NaBH_4$ was decomposed by addition of acetic acid and the reaction mixture was diluted with water, made alkaline with ammonia and extracted with chloroform. The chloroform extract was dried over anhyd. K_2CO_3 and evaporated. The residue in benzene was chromatographed on neutral alumina (Grade II) and the eluate with benzene–ether crystallized. Recrystallization from acetone gave colorless prisms, mp 194°, the compound (VIII) which was identified with an authentic sample of N-ethylchanotetrahydroserratinine.

N-Methyl Triol (XI)——1) $LiAlH_4$ Reduction of β-Dihydroserratinine Methyl Methine (XII): To a solution of the compound ((XII), 18 mg) in 3 ml of anhyd. ether was added 50 mg of $LiAlH_4$ and the mixture was refluxed on a water bath for 2 hr. The excess of hydride was decomposed with wet ether and the ether layer was separated by decantation and the residue was washed several times with ether. The ether solution was dried over anhyd. K_2CO_3, and evaporated. The residue crystallized and recrystallization from the mixture of *n*-hexane and ether gave colorless prisms, mp 119—122°, the compound ((XI), 15 mg). *Anal.* Calcd. for $C_{17}H_{31}O_3N$: C, 68.64; H, 10.51. Found: C, 68.92; H, 10.49. IR cm^{-1}: ν_{O-H} 3300.

2) $LiAlH_4$ Reduction of N-Methyl Acetylchanoaposerratinine (VI): To a solution of the compound ((VI), 16 mg) in 50 ml of anhyd. ether was added 50 mg of $LiAlH_4$ and the mixture was refluxed on a water bath for 8 hr. After cooling, the reaction mixture was treated as the procedure in 1). The ether solution thus obtained was extracted with hydrochloric acid and the hydrochloric acid extract was made alkaline with ammonia and extracted with ether. The ether extracts were dried over anhyd. K_2CO_3 and evaporated. The residue crystallized and recrystallization from the mixture of *n*-hexane–ether gave colorless prisms, mp 118—121°, the compound ((XI), 11 mg) which was identified with an authentic sample by comparison of IR spectrum and mixed melting point determination.

Anhydroacetylaposerratinine Oxime (XIII)——To a solution of anhydroacetylaposerratinine ((IV), 150 mg) in 3 ml of pyridine was added a solution of 150 mg of hydroxylamine hydrochloride in 3 ml of pyridine and the mixture was allowed to stand overnight at room temperature and then, heated on a water bath for 1 hr. The solvent was evaporated *in vacuo* and the residue was diluted with water, made alkaline with ammonia and extracted with ether. The ether extract was dried over anhyd. K_2CO_3 and evaporated to leave an oily product, 150 mg. Formation of oxime was confirmed by IR spectrum of the compound obtained by hydrolysis of the product which showed no carbonyl band. It was recognized that chromatographic purification of the product caused decomposition of oxime function, so without further purification, the crude oxime was employed in the subsequent experiment.

Preparation of the Compound (XIV) by Reduction of the Oxime (XIII) with Raney Nickel——A solution of 150 mg of the oxime (XII) in 50 ml of ethanol was hydrogenated over Raney nickel under atmospheric pressure at room temperature. Hydrogen uptake ceased at absorption of 2 moles of hydrogen during 4 hr period. Then, catalyst was removed by filtration and the filtrate was evaporated to dryness. The residue was diluted with 1% aqueous ammonia and extracted with ether. The ether extract was dried over anhyd. K_2CO_3 and evaporated to leave an oily product ((XIV), 105 mg). This showed two spots on TLC and without further purification was employed in the subsequent experiment because of its instability to alumina chromatography.

Acetylserratinidine (II) and Serratinidine (I)——A solution of the compound ((XIV), 55 mg) in 3 ml of pyridine and 1 ml of acetic anhydride was allowed to stand overnight at room temperature, and then evaporated to dryness *in vacuo*. The residue was dissolved in 1% hydrochloric acid, washed with ethe, made alkaline with ammonia and extracted with ether. The ether extract was dried over anhyd. K_2CO_3 and evaporated. Distillation of the residue at 200—210°/2 mmHg gave 49 mg of an oily product which in benzene was chromatographed on neutral alumina (Grade II). Elution with the mixture of benzene and ether gave colorless prisms, mp 103—106°, 27 mg, $[\alpha]_D^{16}$ +162.5° (c=0.63, EtOH) which was identified with an authentic sample of acetylserratinidine (II) by comparison of IR spectrum and admixture melting point. A solution of 6 mg of this product in 2 ml of 5% ethanolic sodium hydroxide solution was warmed at 70° for 20 min and then concentrated *in vacuo*, diluted with water and extracted with chloroform. The chloroform extract was dried over anhydr. K_2CO_3 and evaporated to give crystals. Recrystallization

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from acetone afforded colorless needles, mp 231—234° which was identified with an authentic sample of serratinidine (I) by comparison of IR spectrum and admixture melting point.

The Base (XVIII)——Elution with ether of the above mentioned column gave 15 mg of a homogeneous oil, $[\alpha]_D^{16}$ +84.8° (c=0.96, EtOH). IR cm^{-1}: ν_{N-H} 3460; $\nu_{C=O}$ 1721, 1664; δ_{N-H} 1509; ν_{C-O} 1240 ($CHCl_3$). NMR τ: 4.46 (1H, d, J=6 cps, vinyl proton), 5.15 (1H, q, J_1=6 cps, J_2=10 cps, >C<u>H</u>–OAc), 5.88 (1H, m, >C<u>H</u>–NHAc), 7.89 (3H, s, COC<u>H</u>$_3$), 8.01 (3H, s, COC<u>H</u>$_3$), 9.05 (3H, d, J=8 cps, >CH–C<u>H</u>$_3$). The oily substance was hydrolysed by the procedure mentioned above to give the compound (XVIII). Recrystallization from acetone furnished colorless needles, mp 246—248°. *Anal.* Calcd. for $C_{18}H_{28}O_2N_2$: C, 71.01; H, 9.27. Found: C, 70.35; H, 9.26. $[\alpha]_D^{17}$ +167° (c=0.452, EtOH), IR cm^{-1}: $\nu_{O-H,N-H}$ 3420, 3310; $\nu_{C=O}$ 1650; δ_{N-H} 1551.

13-Acetyl-8-deoxyserratinine (XXI)——To a solution of the compound ((XX), 250 mg) in 2 ml of chloroform was added 2 ml of BF_3–etherate and 1 ml of ethanedithiol and the reaction mixture was allowed to stand for 4 days at room temperature. The reaction mixture was then diluted with a large amount of water, made alkaline with ammonia and extracted with chloroform. After drying over anhyd. K_2CO_3, the extract was evaporated *in vacuo* and the residue in benzene was chromatographed on neutral alumina (Grade II). The eluate with benzene left 280 mg of an oily product. A solution of 280 mg of this thioketal in 30 ml of ethanol was refluxed with 5 g of Raney nickel (W_4) on a water bath for 8 hr. After cooling, Raney nickel was removed by filtration and washed thoroughly with ethanol. The filtrate and washings were combined and the solvent was evaporated *in vacuo* and the residue (200 mg) in benzene was chromatographed on neutral alumina (Grade II). The eluate with benzene gave 160 mg of 13-acetyl-8-deoxyserratinine (XXI) and recrystallization from *n*-hexane afforded colorless prisms, mp 190—191°. *Anal.* Calcd. for $C_{18}H_{27}O_3N$: C, 70.79; H, 8.91. Found: C, 71.00; H, 8.89. IR cm^{-1}: $\nu_{C=O}$ 1740; ν_{C-O} 1250, 1236. NMR τ: 5.32 (1H, m, >C<u>H</u>–OAc), 8.08 (3H, s, OCOC<u>H</u>$_3$), 9.10 (3H, d, J=7 cps, >CH–C<u>H</u>$_3$).

8-Deoxyserratinine (XXII)——A solution of the compound ((XXI), 400 mg) and 6 g of potassium hydroxide in 6 ml of methanol was refluxed on a water bath for 4 hr. After cooling, the reaction mixture was diluted with a large amount of water and extracted with chloroform. The extract was dried over anhyd. K_2CO_3 and evaporated to leave 350 mg of the residue which in benzene was chromatographed on neutral alumina (Grade II). The eluate with ether gave 310 mg of crystals. Recrystallization from ethyl acetate or acetone afforded fine columns, mp 223—224°, $[\alpha]_D^{17}$ −15.6° (c=1.00, EtOH). *Anal.* Calcd. for $C_{16}H_{25}O_2N$: C, 72.96; H, 9.57. Found: C, 73.02; H, 9.75. IR cm^{-1}: ν_{O-H} 3080; $\nu_{C=O}$ 1735 (Nujol).

8-Deoxy-13-dehydroserratinine (XXIII)——A solution of 8-deoxyserratinine ((XII), 310 mg) in 20 ml of acetone was oxidized with 1.5 ml of Jones reagent under stirring for 40 min. The excess of reagent was decomposed by addition of methanol and the reaction mixture was made alkaline with ammonia and extracted with ether. The ether extract was dried over anhyd. K_2CO_3 and evaporated to leave 300 mg of the residue. The residue in benzene was chromatographed on neutral alumina (Grade I). Eluates (230 mg) with benzene and ether were collected and recrystallization from *n*-hexane gave fine needles, mp 110—112°. *Anal.* Calcd. for $C_{16}H_{23}O_2N$: C, 73.53; H, 8.87. Found: C, 73.53; H, 8.74. IR cm^{-1}: $\nu_{C=O}$ 1737, 1693.

Fawcettidine (XXIV)——A solution of 230 mg of the compound (XXIII) in 30 ml of acetic acid and 700 mg of Zn powder were heated at 140° under stirring for 6 hr. After cooling, Zn powder was removed by filtration and washed with water. The filtrate and washings were combined, concentrated *in vacuo*, diluted with water, made alkaline with ammonia and extracted with chloroform. After drying over anhyd. K_2CO_3, the extract was evaporated. The residue in benzene was chromatographed on neutral alumina (Grade III) and the eluate with benzene gave 140 mg of an oily product which showed one spot on TLC. IR cm^{-1}: $\nu_{C=O}$ 1737; $\nu_{C=C}$ 1660 (film). Picrate: The picrate was obtained as usual. Recrystallization from acetone gave yellow needles, mp 223—225°. *Anall.* Calcd. for $C_{16}H_{23}ON$–$C_6H_3O_7N_3$: C, 55.69; H, 5.52. Found: C, 55.48; H, 5.77. Methiodide: The methiodide was obtained by addition of methyl iodide to a solution of the compound in acetone. Recrystallization from the mixture of methanol and acetone afforded colorless plates, mp 224—226°. IR cm^{-1}: $\nu_{C=O}$ 1737. *Anal.* Calcd. for $C_{16}H_{23}ON \cdot MeI$: C, 52.73; H, 6.77. Found: C, 52.58; H, 6.86. The picrate was identified with an authentic sample of fawcettidine picrate by IR comparison.

Alcohol (XXV)——Continued eluation of the above mentioned alumina column with chloroform gave colorless oil (20 mg) which showed one spot on TLC. IR cm^{-1}: ν_{O-H} 3580; $\nu_{C=O}$ 1735 (CCl_4). Methiodide: The methiodide was prepared as usual. Recrystallization from acetone afforded colorless plates, mp 253—255°. IR cm^{-1}: $\nu_{C=O}$ 1742, 1687. *Anal.* Calcd. for $C_{16}H_{25}O_2N \cdot CH_3I$: C, 50.37; H, 6.77. Found: C, 50.82; H, 7.13.

Dihydrofawcettidine (XXVI)——To a solution of 60 mg of fawcettidine (XXIV) in 10 ml of ethanol was added 200 mg of $NaBH_4$ and the reaction mixture was allowed to stand for 2 days. Then, the mixture was diluted with water and extracted with chloroform. The extract was dried over anhyd. K_2CO_3 and evaporated. On trituration with *n*-hexane, the residue crystallized and recrystallization from *n*-hexane gave colorless pillars (40 mg), mp 156—159°, $[\alpha]_D^{23}$ +132.8° (c=0.78, EtOH) (lit.[6] $[\alpha]_D$=+137° (c=1.0)). *Anal.* Calcd. for $C_{16}H_{25}ON$: C, 77.68; H, 10.19. Found: C, 77.75; H, 10.30. IR cm^{-1}: ν_{O-H} 3210; $\nu_{C=C}$ 1658.

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