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Synthetic Studies on the Lycopodium Alkaloids. III.[1] Synthesis of a Key Intermediate, Ethyl Octahydro-4aβ-hydroxy-7β-methyl-10-oxo-1*H*-5,8*a*-propanoquinoline-1-carbamate, for the Lycopodium Alkaloids

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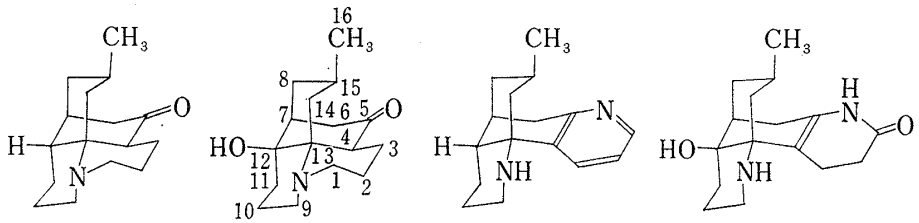
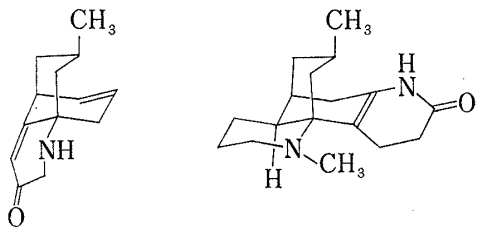
A tricyclic key intermediate (II) for the lycopodine and the lycodine type of alkaloids was synthesized from 9-oxobicyclo(3,3,1)nonene system (IV) by a series of reactions shown in Chart 2. Dehydration of II with strong acid resulted in the rearrangement of carbon skeleton into an enamino-ketone (III). The stereochemistry of stereoselective C_9-alkylation in IV with sulfonium ylid was also discussed.

In recent years the efforts which have been devoted to the synthetic approach to the Lycopodium alkaloids[3] have culminated in the total synthesis of lycopodine by Stork, *et al.*[4] or Ayer, *et al.*,[5] and of annotinine by Wiesner, *et al.*[6] The authors have also been investigating the synthetic pathway to two representatives of Lycopodium alkaloids, the lycopodine and the lycodine type of alkaloids, *via* the same tricyclic intermediate, and reported the synthesis of the tricyclic amino-ketone (I) in the previous paper.[1] The present paper describes the synthesis of ethyl octahydro-4aβ-hydroxy-7β-methyl-10-oxo-1*H*-5,8*a*-propanoquinoline-1-carbamate (II), a key intermediate for the lycopodium alkaloids, and its novel rearrangement



lycopodine lycodoline lycodine hydroxy-des-N-methyl-α-obscurine



I sauroxine

Chart 1

1) Part II: Z. Horii, S. Kim, T. Imanishi, and I. Ninomiya, *Chem. Pharm. Bull.* (Tokyo), **16**, 2107 (1968).
2) Location: 6-5 *Toneyama, Toyonaka, Osaka.*
3) K. Wiesner, *Fortsch. Chem. Org. Naturstoffe*, **20**, 271 (1962); D.B. MacLean, "The Alkaloids," Vol. X, Academic Press Inc., New York, 1968, p. 305.
4) G. Stork, R.A. Kretchmer, and R.H. Schlessinger, *J. Am. Chem. Soc.*, **90**, 1647 (1968).
5) W.A. Ayer, W.R. Bowman, T.C. Joseph, and P. Smith, *J. Am. Chem. Soc.*, **90**, 1648 (1968).
6) K. Wiesner and L. Poon, *Tetrahedron Letters*, **1967**, 4937.

to the enamino-ketone (III) analogous to the pathway postulated in the biogenesis of the serratinine series of alkaloids.[7]

Although the tricyclic amino-ketone (I) had been synthesized by extending the side chain on the amino group in the keto-carbamate (IV),[1] another construction of tricyclic ring system was undertaken by extension of three-carbon unit on the keto group in IV. Since one-step introduction[1] of the side chain on the keto group by Wittig reaction[8] had been fruitless presumably due to less reactivity of the keto group, two-step procedure, in which a highly reactive sulfonium ylid was used as a nucleophile, was designed.

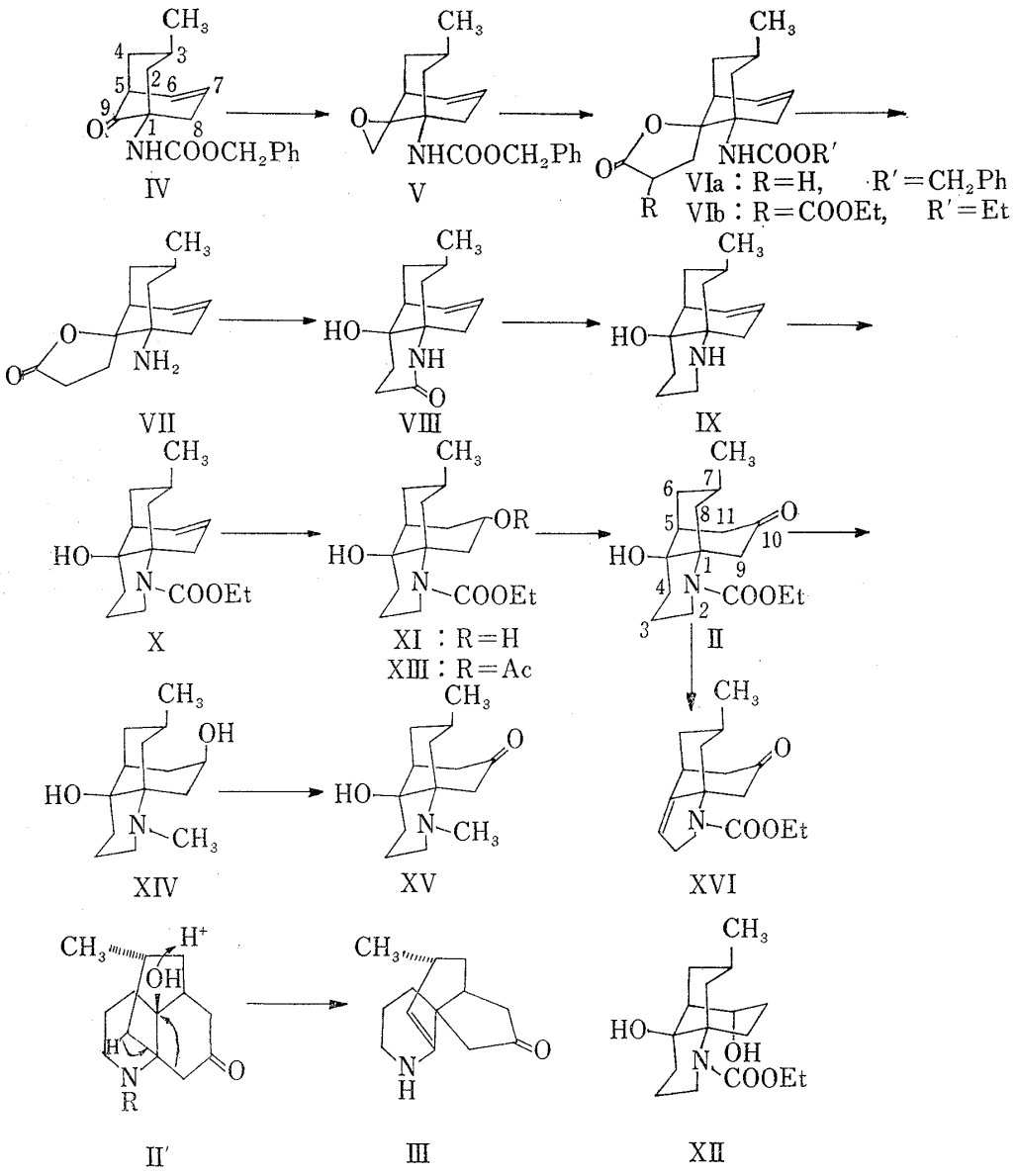


Chart 2

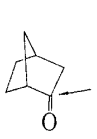
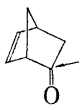
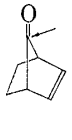
On treatment of IV with five molar excess of dimethyl sulfonium methylide in dimethylsulfoxide (DMSO) and tetrahydrofuran, an oxirane (V) was obtained in 66% yield. When the reaction was carried out with equimolar quantity or two and a half molar excess of the ylid, a large amount of the starting material was recovered unchanged. No methylene trans-

7) Y. Inubushi, H. Ishii, B. Yasui, and T. Harayama, *Tetrahedron Letters*, **1966**, 1551; Y. Inubushi, H. Ishii, and T. Harayama, *ibid.*, **1967**, 1069.
8) H.S. Corey, Jr., J.R.D. McCormick, and W.E. Swensen, *J. Am. Chem. Soc.*, **86**, 1884 (1964).

fer reaction occurred with dimethyloxosulfonium methylide in DMSO.[9] On the stereochemistry of the oxirane ring in V, it would be most probable to assume that the carbon-carbon bond lies in the α-side, as illustrated in Chart 2, with attacking of the ylid from the under side of II.

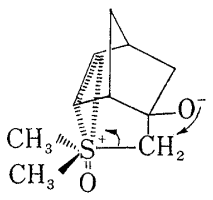
It has been known that both the sulfonium and the oxosulfonium ylid have high stereoselectivity in the methylene transfer reaction with the former more reactive than the latter. For instance, Bly and his coworkers[10] studied the kinetics and the mechanism of both ylids in the reaction. The bicyclic ketones (**a**), (**b**) and (**c**) gave the corresponding oxiranes in the ratio, shown in Table I, with attacking of the ylid from the side marked by an arrow. With

Table I. The Stereochemistry of the Methylene Transfer Reaction with the Sulfonium Ylids

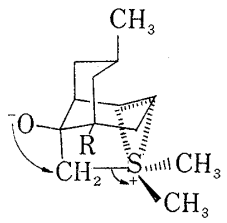
	 a	 b	 c
$Me_2\overset{O}{\overset{\|}{S}}=CH_2$	90	29	100
$Me_2S=CH_2$	95	94	100

the exception of **b** in the reaction with the oxosulfonium ylid, were obtained the oxiranes predominantly or exclusively in which the methylene bond was formed at the less hindered side marked by an arrow. From the results, they concluded that both ylids attacked the ketones predominantly from the less hindered side, and suggested, in the reaction of **b** with the oxosulfonium ylid, a participation of π-electrons of the double bond *via* the intermediate (**b'**).

In the reaction of IV with the sulfonium ylid, the sterically favorable side may be the α-side on the ring bearing double bond, where the π-electron participation would also be assumed in the transition state (IV') similar to **b'**.



b'



IV' : R=NHCOOCH$_2$Ph

Chart 3

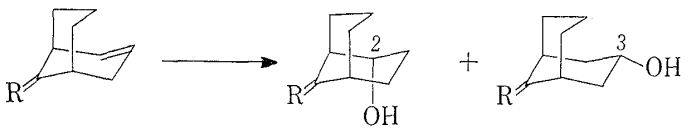
The oxirane (V) was reacted with ethyl sodiomalonate in boiling ethanol to give the lactone (VIa) in a poor yield, while the lactone-ester (VIb) was obtained, in 61% yield from V, on treatment with ethyl ethoxymagnesium malonate. The structures of VIa and VIb were assigned from their infrared (IR) and nuclear magnetic resonance (NMR) spectra; the former exhibited IR bands at 3268, 1776 and 1701 cm^{-1} due to the carbamate and the lactone group and NMR signals at 2.70 (5H, singlet) and 4.99τ (2H, singlet) due only to the benzoxyl group (absence of ethoxyl group), and the latter exhibited IR bands at 3344 (NH), 1770 (lactone) and 1718 cm^{-1} (ester and urethan) and NMR signals at 5.77 and 5.99 τ (2H, q, J=8 cps), 8.73 and 8.82 τ (each 3H, t, J=8 cps) due to two ethoxyl groups (absence of benzoxyl group). The amino-lactone (VII) was obtained by hydrolysis of VIa or VIb with concentrated hydrochloric acid in acetic acid, and was transformed smoothly into the tricyclic hydroxy-lactam (VIII) by treatment with a catalytic amount of Triton B in boiling ethanol. The lactam

9) E.J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **87**, 1353 (1965).
10) R.S. Bly and C.M. DuBose, Jr., *J. Org. Chem.*, **33**, 2188 (1968).

(VIII) exhibited the IR absorptions at 3330, 3215 and 1647 cm^{-1} due to the hydroxyl and the lactam group.

The tricyclic ring system was thus constructed, and in the next stage was conducted an introduction of hydroxyl function at the position corresponding to C_5 in the natural alkaloids. The amino-alcohol (IX) obtained by reduction of VIII with lithium alminum hydride was condensed with ethyl chloroformate in the presence of anhydrous potassium carbonate to give the carbamate (X) in 60% yield. Oxymercuration[11] of X was unsuccessful under recovery of the starting material, while a diol (XI) was obtained, in 74% yield from X, by hydroboration method.[12] On steric grounds, two isomeric diols XI and XII were expected to be produced, but it was difficult to isolate the minor isomer (XII) which was predicted on thin-layer chromatography (TLC) and gas liquid chromatography GLC. The diol (XI) was treated with acetic anhydride in pyridine to give the monoacetate (XIII).

Although the NMR signal of carbinyl proton at C_{10} in XI was difficult to be assigned due to its overlap with that of methylene protons of the carbamate group, the carbinyl proton in XIII appeared as a multiplet centered at 4.64τ with a half-band width of more than 20 cps, which indicated the proton to be axial conformation.[13] In the hydroboration reaction of the bicyclo(3,3,1)non-2-ene derivative (**d**) or (**e**), there have been reported the isolation of two isomeric alcohols, in a 3: 2 ratio with the 2-ol as the major,[14] as illustrated in Chart 4. The high yield of XI seems to be unusual and is presumed to result from the steric effect of the third ring in X.



d: R=H_2
e: R=$-O(CH_2)_2O-$

Chart 4

The diol (XI) was oxidized with Jones reagent to give the keto-carbamate (II), the title compound, which showed the IR absorptions at 3448, 1701 (shoulder) and 1681 cm^{-1} due to the hydroxyl and the carbonyl group. The N-methyl diol (XIV), obtained by reduction of II with lithium aluminum hydride, was oxidized with Jones reagent to the N-methyl ketone (XV). The NMR spectrum of XIV showed a sharp heptet centered at 5.7τ due to the carbinyl protone (J=4.2 cps, X part of A_2B_2X system) and this fact provided further support to the structure of XI. On the other hand, the keto-carbamate (II) was treated with phenylphosphonic dichloride[15] in pyridine to afford the anhydro-ketone (XVI), which exhibited a triplet signal centered at 4.23τ (J=4 cps) due to the olefinic proton.

In connection with the biogenesis of serratinine series of alkaloids in which lycodoline is postulated to be a precursor,[7] the keto-carbamate (II) was subjected to hydrolysis using concentrated hydrochloric acid or 48% hydrobromic acid in acetic acid. An enamino-ketone (III) was obtained, in a good yield, as a result of the novel rearrangement analogous to the biogenetic scheme, as shown in II'. The structure of III was assigned on the bases of its IR and NMR spectra and the elemental analysis of its perchlorate. The free base showed the strong absorptions at 1735 cm^{-1} due to the five membered ring ketone and at 1630 cm^{-1} due to the enamine double bond without any absorption at hydroxyl region in IR spectrum and a somewhat broad singlet signal at 6.22τ due to one olefinic proton in the enamine system.

The compounds II, XV, and XVI would serve the important intermediates for the syntheses of both the lycopodine and the lycodine types in the Lycopodium alkaloids. In addi-

11) H.C. Brown and P. Geoghegan, Jr., *J. Am. Chem. Soc.*, **89**, 1152 (1967).
12) G. Zweifel and H.C. Brown, *Organic Reactions*, 13, 1 (1963).
13) N.S. Bacca and D.H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Fransisco, 1964, p. 77 and 135.
14) M.R. Vegar and R.J. Wells, *Tetrahedron Letters*, **1969**, 2565.
15) W.A. Ayer and G.G. Iverach, *Can. J. Chem.*, **42**, 2514 (1964).

tion, the novel rearrangement of II to III would suggest possibility of the total syntheses of the serratinine series of alkaloids *via* this route.

Experimental[16]

Reaction of Benzyl 3β-Methyl-9-oxobicyclo(3,3,1)non-6-ene-1-carbamate (IV) with Dimethyloxosulfonium Methylide——To a stirred solution of dimethyloxosulfonium methylide in DMSO, prepared from NaH (192 mg of a 50% suspension in mineral oil), trimethyloxosulfonium iodide (880 mg) and dry DMSO (10 ml),[9] was added dropwise a solution of the keto-carbamate[1] (IV: 600 mg) in dry DMSO (5 ml), followed by stirring at room temperature for 2 hr. After cooling, the mixture was poured into ice–water (100 ml) and extracted with AcOEt (30 ml×3). The extract was washed with H_2O, dried, and evaporated to give an oily residue (550 mg) which showed many spots on TLC. The crude product showed IR bands at 3550, 3350 and 1670 cm^{-1}, and it was difficult to isolate any single compound.

Benzyl 9-(β-Epoxymethylene)-3β-methylbicyclo(3,3,1)non-6-ene-1-carbamate (V)——A suspension of NaH (360 mg of a 50% suspension in mineral oil) and dry DMSO (10 ml) was heated with stirring under N_2 at 70° for 45 min. After cooling, the resulting mixture was diluted with dry THF (10 ml) to prevent from freezing, and then cooled below −5° in an ice–salt bath, followed by rapid addition of a solution of trimethylsulfonium iodide (3.05 g) in dry DMSO (30 ml) below 0°.[9] The mixture was stirred for 10 min before adding a solution of the keto-carbamate (IV: 900 mg) in dry THF (5 ml). Stirring was continued at ice–salt temperature for 1 hr, and then for 1 hr at room temperature. The mixture was poured into ice–water (200 ml) and extracted with ether (50 ml×3). The extract was washed with H_2O thoroughly, dried, and evaporated to give an oily residue (850 mg), which was chromatographed on silica gel. Elution with CCl_4–$CHCl_3$ (1:1) afforded a viscous oil (620 mg: 66%), which was distilled to give an analytical sample as a pale yellow oil, bp 165—170° (0.04 mmHg). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3390 (NH), 1730 (NHCO). NMR τ: 3.70 (5H, s, C_6H_5), 5.00 (2H, s, $-C\underline{H}_2C_6H_5$), 5.14 (1H, broad s, NH), 6.97, 7.42 (each 1H, d, J=4.5 cps, $O-C\underline{H}_2-C$), 9.08 (3H, d, J=6 cps, $>CHC\underline{H}_3$). *Anal.* Calcd. for $C_{19}H_{23}O_3N$: C, 72.82; H, 7.40; N, 4.47. Found: C, 72.96; H, 7.32; N, 4.56.

1-Carbobenzoxy-9β-hydroxy-3β-methylbicyclo(3,3,1)non-6-ene-9α-propionic Acid γ-Lactone (VIa)——To a stirred solution of NaOEt in abs. EtOH, prepared from Na (0.13 g) and abs. EtOH (10 ml), was added diethyl malonate (0.88 g) at room temperature, followed by stirring for 1 hr. The mixture was heated under reflux for 30 hr after adding a solution of V (1.57 g) in abs. EtOH. After cooling, the mixture was neutralized with AcOH (1 ml), concentrated under reduced pressure, diluted with H_2O, acidified with dil. HCl, and extracted with $CHCl_3$. The extract was washed with brine, satd. $NaHCO_3$ and then brine, and dried. Evaporation of the solvent gave a brown oil (1.75 g), which showed a few spots other than the starting material on TLC and was submitted to chromatography on silica gel. The starting material (1.17 g) was recovered from the fraction eluted by CCl_4 and from the forerunning fraction of CCl_4–$CHCl_3$ (3:7)-elution. The later fraction of CCl_4–$CHCl_3$ (3:7)-elution afforded 0.15 g of VIa as colorless fine needles from *n*-hexane–C_6H_6, mp 160—160.5°. IR ν_{max}^{KBr} cm^{-1}: 3268 (NH), 1776 (lactone), 1701 (carbamate), 1656 (C=C). NMR τ: 2.70 (5H, s, C_6H_5), 4.38 (2H, m, $-C\underline{H}=C\underline{H}-$), 4.99 (2H, s, $-C\underline{H}_2C_6H_5$), 5.14 (1H, broad s, NH), 9.08 (3H, d, J=6 cps, $>CHC\underline{H}_3$). *Anal.* Calcd. for $C_{21}H_{25}O_4N$: C, 70.96; H, 7.09; N, 3.94. Found: C, 71.36; H, 7.08; N, 4.27.

1-Carbethoxyamino-2′-ethoxycarbonyl-9β-hydroxy-3β-methylbicyclo(3,3,1)-non-6-ene-9α-propionic Acid γ-Lactone (VIb)——To a stirred solution of ethoxymagnesium malonate in abs. EtOH, prepared from Mg (0.14 g) and abs. EtOH (5 ml), and the mixture was heated under reflux for 35 hr. After cooling and subsequent addition of a small amount of AcOH, the solvent was removed *in vacuo* to give a syrupy residue, which was diluted with dil. HCl and extracted with $CHCl_3$. The extract was washed with brine, satd. $NaHCO_3$ and then brine, dried, and evaporated to give a brown oil (1.65 g), which was subjected to chromatography on silica gel. The fraction eluted by $CHCl_3$ gave 0.83 g (61%) of VIb as a viscous oil. An analytical sample was obtained by distillation, a colorless oil, bp 175—180° (0.04 mmHg). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3344 (NH), 1770 (lactone), 1718 (ester and carbamate), 1647 (C=C). NMR τ: 4.38 (2H, m, $-C\underline{H}=C\underline{H}-$), 5.03 (1H, broad s, NH), 5.77, 5.99 (each 2H, q, J=8 cps, $-C\underline{H}_2CH_3$), 8.73, 8.82 (each 3H, t, J=8 cps, $-CH_2C\underline{H}_3$), 9.15 (3H, d, J=5.5 cps, $>CHC\underline{H}_3$). *Anal.* Calcd. for $C_{19}H_{27}O_6N$: C, 62.45; H, 7.45; N, 3.80. Found: C, 62.25; H, 7.30; N, 3.83.

1-Amino-9β-hydroxy-3β-methylbicyclo(3,3,1)non-6-ene-9α-propionic Acid γ-Lactone (VII)——A mixture of VIb (2.25 g), conc. HCl (10 ml) and AcOH (20 ml) was heated under reflux on an oil bath for 14 hr. After cooling and subsequent saturation with anhyd. K_2CO_3, the mixture was extracted with $CHCl_3$ thoroughly, and the extract was shaken with dil. HCl. The aqueous layer was made alkaline with K_2CO_3 and extracted with $CHCl_3$. The extract was washed with brine, dried, and evaporated to give a brown oil (1.25 g), which

16) Melting points and boiling points are uncorrected. Organic extracts were dried over anhyd. $MgSO_4$. The NMR spectra were taken at 60 Mc, with tetramethylsilane as internal reference in $CDCl_3$.

was subjected to chromatography on Florisil (8 g). The fraction eluted by C_6H_6 gave VII as a yellow oil (1.08 g: 80%). NMR τ: 4.35 (2H, m, $-C\underline{H}=C\underline{H}-$), 8.76 (2H, s, $-NH_2$, disappeared with D_2O), 9.11 (3H, d, $J=6$ cps, $>CHC\underline{H}_3$). The hydrochloride was recrystallized from ether–EtOH to give colorless needles, mp 238—239° (decomp.). *Anal.* Calcd. for $C_{13}H_{20}O_2NCl$: C, 60.57; H, 7.82; N, 5.34. Found: C, 60.53; H, 7.86; N, 5.34. IR ν_{max}^{KBr} cm^{-1}: 3356 (NH), 2800—2200 (N^+H), 1776, 1757 (splitting of lactone band).

The amino-lactone (VII) was also obtained by similar hydrolysis of VIa.

The decomposition of the amino-lactone (VII) occurred on chromatography on silica gel or alumina.

Octahydro-4aβ-hydroxy-7β-methyl-2-oxo-1*H*-5,8a-propenoquinoline (VIII)——A mixture of VII (0.1 g) and abs. EtOH (10 ml) containing a catalytic amount of Triton B was heated under reflux for 20 hr. After evaporating the solvent and subsequent addition of AcOEt (3 ml), the colorless crystals were collected and recrystallized from iso-PrOH–AcOEt to give 0.09 g of VIII as colorless leaflets, which had no sharp melting point and sublimed at 220—230°. IR ν_{max}^{KBr} cm^{-1}: 3333, 3215 (OH, NH), 1647 (lactam). *Anal.* Calcd. for $C_{13}H_{19}O_2N$: C, 70.55; H, 8.65; N, 6.23. Found: C, 70.57; H, 8.58; N, 6.25.

Octahydro-4aβ-hydroxy-7β-methyl-1*H*-5,8a-propenoquinoline (IX)——A stirred suspension of VIII (1.5 g) and $LiAlH_4$ (1 g) in dry dioxane (400 ml) was heated at 100—105° for 20 hr. After decomposing the excess reducing agent by careful addition of AcOEt and H_2O, the solvent was removed *in vacuo*, and resulting residual mass was exhaustively extracted with CH_2Cl_2. The extract was shaken with 5% HCl, and the acidic aqueous layer was made alkaline with K_2CO_3 and extracted with CH_2Cl_2. The extract was washed with brine, dried, and evaporated to give a solid (1.25 g). After trituration with $(CH_3)_2CO$ was collected colorless crystals, which were recrystallized from acetone to give 1.05 g (75%) of IX as colorless needles, mp 149—150°. IR ν_{max}^{KBr} cm^{-1}: 3367, 3155 (OH, NH), 1653 (C=C). NMR τ: 4.33 (2H, m, $-C\underline{H}=C\underline{H}-$), 8.20, 8.86 (each 1H, s, OH, NH, disappeared with D_2O), 9.11 (3H, d, $J=6$ cps, $>CHC\underline{H}_3$). *Anal.* Calcd. for $C_{13}H_{21}ON$: C, 75.31; H, 10.21; N, 6.67. Found: C, 75.13; H, 10.02; N, 6.98.

Ethyl Octahydro-4aβ-hydroxy-7β-methyl-1*H*-5,8a-propenoquinoline-1-carbamate (X)——A suspension of IX (0.68 g), $ClCO_2Et$ (2 ml) and anhyd. K_2CO_3 (1 g) in dry C_6H_6 (2 ml) was heated under reflux for 6 hr. After cooling and subsequent removal of inorganic compounds, the solvent was removed to give a residual solid. Upon trituration with *n*-hexane were obtained colorless crystals, which were recrystallized from *n*-hexane to give 0.6 g (60%) of X as colorless plates, mp 124—125°. IR ν_{max}^{KBr} cm^{-1}: 3413 (OH), 1669 (NCO_2-Et). NMR τ: 4.39 (2H, m, $>C\underline{H}=C\underline{H}-$), 5.95 (2H, q, $J=7.5$ cps, $-C\underline{H}_2CH_3$), 8.00 (1H, s, O$\underline{H}$), 8.76 (3H, t, $J=7.5$ cps, $-CH_2C\underline{H}_3$), 9.09 (3H, t, $J=5.5$ cps, $>CHC\underline{H}_3$). *Anal.* Calcd. for $C_{16}H_{25}O_3N$: C, 68.78; H, 9.02; N, 5.01. Found: C, 69.17; H, 9.00; N, 5.09.

Attempted Oxymercuration of X——To a yellow suspension of $Hg(OAc)_2$ (70 mg) in THF (4 ml) containing H_2O (1.5 ml) was added X (0.06 g), and the suspension was stirred at room temperature for 10 hr. Although disappearance of yellow coloration of the suspension is used to check the end point of the reaction, the suspension did not lose its color throughout the reaction period, and the starting material was recovered on usual working up.

Ethyl Octahydro-4aβ,10a-dihydroxy-7β-methyl-1*H*-5,8a-propanoquinoline-1-carbamate (XI)——A stirred mixture of X (0.62 g) and $NaBH_4$ (0.85 g) in dry THF (40 ml) was flushed with N_2 atmosphere, and to this was added a solution of freshly distilled BF_3-etherate (3.18 g) in dry THF (5 ml) at room temperature over a period of 40 min, followed by stirring for 1 hr. To the mixture were added dropwise H_2O (4 ml), and then 3N NaOH (8 ml) and 30% H_2O_2 (8 ml), followed by stirring at 40° for 2 hr. After adding brine (200 ml), the mixture was extracted with AcOEt (50 ml×4) and the extract was washed with brine. The dried extract was evaporated to give a residual solid (0.74 g,) which showed two main spots on TLC and the major component was sixfold of the minor in GLC analysis. After adding ether (5 ml) was collected colorless crystals, which were recrystallized from *n*-hexane–$(CH_3)_2CO$ to give 0.49 g (74%) of XI as colorless needles, mp 186—187°. IR ν_{max}^{KBr} cm^{-1}: 3367 (OH), 1656 (–NCOOEt). NMR τ: 5.97 (2H, q, $J=7.5$ cps, $-C\underline{H}_2CH_3$), 8.00 (1H, s, OH, disappeared with D_2O), 8.77 (3H, t, $J=7.5$ cps, $-CH_2C\underline{H}_3$), 9.06 (3H, d, $J=5.5$ cps, $>CHC\underline{H}_3$). *Anal.* Calcd. for $C_{16}H_{27}O_4N$: C, 64.62; H, 9.15; N, 4.71. Found: C, 64.87; H, 9.03; N, 5.16.

The isolation of the minor product was unsuccessful.

Ethyl Octahydro-10a-acetoxy-4aβ-hydroxy-7β-methyl-1*H*-5,8a-propanoquinoline-1-carbamate (XIII)——A mixture of XI (32 mg) and Ac_2O (0.5 ml) in dry pyridine (1 ml) was allowed to stand at room temperature overnight. After adding ice–water, the mixture was extracted with ether. The ethereal layer was washed with brine, satd. $NaHCO_3$, brine, dil. HCl and brine. The dried extract was evaporated to give a residue (28 mg), which was subjected to chromatography on silica gel. Elution with CH_2Cl_2 afforded colorless crystals, which were recrystallized from *n*-hexane–$(CH_3)_2CO$ to give colorless needles, mp 115—116°. IR ν_{max}^{KBr} cm^{-1}: 3390 (OH), 1727 (OCOMe), 1656 (NCO_2Et). NMR τ: 4.64 (1H, m, $W1/2>20$ cps, $>CH-OAc$), 5.99 (2H, q, $J=7$ cps, $-C\underline{H}_2CH_3$), 8.06 (1H, s, OH, disappeared with D_2O), 8.79 (3H, t, $J=7$ cps, $-CH_2C\underline{H}_3$), 9.09. (3H, d, $J=5.5$ cps, $>CHC\underline{H}_3$). *Anal.* Calcd. for $C_{18}H_{27}O_5N$: C, 64.07; H, 8.06; N, 4.15. Found: C, 63.97; H, 8.58; N, 4.05.

Ethyl Octahydro-4aβ-hydroxy-7β-methyl-10-oxo-1*H*-5,8a-propanoquinoline-1-carbamate (II)——To a stirred solution of XI (0.13 g) in purified acetone (5 ml) was added dropwise a slight excess of Jones reagent at room temperature, followed by stirring for 5 min. After decomposing the excess oxidant with MeOH, the mixture was poured into water and extracted with ether. The extract was washed with H_2O, dried,

and evaporated to give a glassy solid (0.12 g), which was subjected to chromatography on silica gel. Elution with CH_2Cl_2–CCl_4 (1:4) afforded an oily residue, which was homogeneous on TLC and solidified on standing. Recrystallization from *n*-hexane–acetone gave 0.1 g of II as colorless needles, mp 130—132°. IR ν_{max}^{KBr} cm^{-1}: 3448 (OH), 1681 (CO). NMR τ: 5.94 (2H, q, J=7 cps, $-C\underline{H}_2CH_3$), 7.74 (1H, s, OH, disappeared with D_2O), 9.08 (3H, diffused, d, >CHC$\underline{H}_3$). *Anal.* Calcd. for $C_{16}H_{25}O_4N$: C, 65.07; H, 8.53; N, 4.74. Found: C, 65.02; H, 8.36; N, 4.69.

Octahydro-4aβ,10β-dihydroxy-1,7β-dimethyl-1*H*-5,8a-propanoquinoline (XIV)——A suspension of II (0.24 g) and $LiAlH_4$ (0.15 g) in dry THF (20 ml) was heated under reflux for 8 hr. After cooling followed by decomposition of reducing agent with AcOEt and H_2O (2 ml), the solvent was removed to dryness. The residue was extracted with hot $CHCl_3$ repeatedly, and the extract was washed with brine, dried, and evaporated to give a syrupy residue (0.18 g), which was subjected to chromatography on Florisil. Elution with CH_2Cl_2 gave crystals which was recrystallized from *n*-hexane–acetone to afford 0.12 g of XIV as colorless crystals, mp 125—126°. IR ν_{max}^{KBr} cm^{-1}: 3378 (OH), 2809 (NCH_3). NMR τ: 5.74 (1H, a sharp heptet, J =4.2 cps, X part of A_2B_2X, >C$\underline{H}$–OH), 6.73 (1H, s, OH), 7.90 (3H, s, NCH_3), 9.08 (3H, d, J=6 cps, >CHC$\underline{H}_3$). *Anal.* Calcd. for $C_{14}H_{25}O_2N$: C, 70.25; H, 10.53; N, 5.85. Found: C, 70.71; H, 10.73; N, 5.75.

Octahydro-4aβ-hydroxy-1,7β-dimethyl-10-oxo-1*H*-5,8a-propanoquinoline (XV)——To a stirred solution of XIV (80 mg) in purified aceton (2 ml) was added dropwise Jones reagent (0.25 ml), followed by stirring at room temperature for 5 min. After decomposing the excess oxidant with MeOH and making alkaline with anhyd. K_2CO_3, the mixture was extracted with $CHCl_3$. The extract was washed with brine, dried, and evaporated to give a solid (78 mg). Recrystallization from *n*-hexane–acetone afforded colorless plates, mp 110—112°. IR ν_{max}^{KBr} cm^{-1}: 3401 (OH), 2809 (NCH_3), 1701 (CO). NMR τ: 6.62 (1H, s, OH, disappeared with D_2O), 7.90 (3H, s, NCH_3), 9.11 (3H, diffused d, >CHC$\underline{H}_3$). *Anal.* Calcd. for $C_{11}H_{23}O_2N$: C, 70.58; H, 9.77; N, 5.90. Found: C, 70.89; H, 9.76; N, 6.44.

Ethyl 2,3,5,6,7,8-Hexahydro-7β-methyl-10-oxo-1*H*-5,8a-propenoquinoline-1-carbamate (XVI)——A mixture of II (0.41 g) and phosphonic dichloride (6 ml) in dry pyridine (12 ml) was heated at 70° for 23 hr with stirring. After cooling with ice–water, H_2O (5 ml) was added dropwise, and the mixture was made alkaline with 40% NaOH solution. The mixture was extracted with $CHCl_3$ and the extract was washed with brine, dil. HCl, brine, satd. $NaHCO_3$ and brine. The dried extract was evaporated to give a brown oil (0.32 g), which exhibited IR abosptions at 3400, 1735 and 1690 cm^{-1} in $CHCl_3$ and showed a few spots on TLC. Chromatography on silica gel eluted by $CHCl_3$–CCl_4 (1:1) gave 0.14 g of XVI as a viscous oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1700 (NCOOEt, CO), 1670 (sh., C=C). NMR τ: 4.23 (1H, t, J=4 cps, >C=C$\underline{H}$–CH_2–), 5.91 (2H, q, J=8 cps $-C\underline{H}_2CH_3$), 8.75 (3H, t, J=8 cps, $-CH_2C\underline{H}_3$), 9.12 (3H, d, J=5.5 cps, >CHC$\underline{H}_3$). 2,4-Dinitrophenylhydrazone: orange yellow crystals from iso-PrOH, mp 160—161°. *Anal.* Calcd. for $C_{22}H_{27}O_6N_5$: C, 57.70; H, 5.95; N, 15.31. Found: C, 57.70; H, 5.86; N, 15.34. IR ν_{max}^{KBr} cm^{-1}: 3320 (NH), 1688 (NCOOEt), 1618 (C=N).

Any other compounds could not be isolated in pure state.

9β-Methyl-6-oxo-1,2,3,4,7,7a,8,9-octahydro-5*H*-cyclopent[*e*]quinoline (III)——A mixture of II (0.1 g) and conc. HCl (1.5 ml) (or 1.5 ml of 48% HBr) in AcOH (4.5 ml) was heated at 100—110° for 10 hr with stirring. After the solvent was removed, the cooled mixture was diluted with H_2O (3 ml), shaken with ether, made alkaline with anhyd. K_2CO_3, and extracted with $CHCl_3$. The $CHCl_3$ extract was washed with brine, dried, and evaporated to give an oil (0.07 g), which was subjected to chromatography on Florisil. Elution with C_6H_6 gave a pale yellow oil, homogeneous on TLC. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735 (CO), 1630 (N–C=C). NMR τ: 6.22 (1H, broad s, N–C=C$\underline{H}$–), 8.97 (3H, d, J=5.5 cps, >CHC$\underline{H}_3$). Perchlorate: colorless needles from iso-PrOH, mp 186—188°. *Anal.* Calcd. for $C_{13}H_{20}O_5NCl$: C, 51.06; H, 6.59; N, 4.58. Found: C, 51.09; H, 6.76; N, 4.67.