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Synthetic Studies on the Lycopodium Alkaloids. II.[1] A Synthesis of a Key Intermediate, 2,3,5,6,7,8-Hexahydro-7β-methyl-3-oxo-1H-5,8a-propenoquinoline, for the Lycopodium Alkaloids

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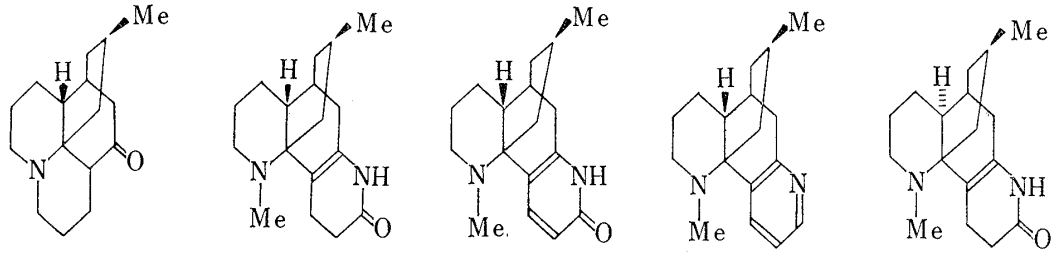
The introduction of an amino function on the bridgehead position of the bicyclo(3,3,1)nonane ring system has been smoothly achieved by the modified Curtius reaction on some bridgehead carboxylic acids. This method has been applied on 3β-methyl-9-oxobicyclo(3,3,1)non-6-ene-1-carboxylic acid (XIV) to afford the unsaturated aminoketone (XVI) as its hydrobromide *via* the carbamate. XVI was transformed into the tricyclic lactam (XVIII), *via* the pyruvamide (XVII) followed by cyclization. XVIII was then reduced *via* its lactim-ether followed by oxidation to afford 2,3,5,6,7,8-hexahydro-7β-methyl-3-oxo-1H-5,8a-propenoquinoline (XXI) in good yield, which would provide useful intermediate for syntheses of the lycopodium alkaloids.

Previously,[1] the authors have reported some basic studies on the bicyclo(3,3,1)nonane ring system in connection with the synthetic study of the lycopodium alkaloids.[3] The present paper describes the preparation of 2,3,5,6,7,8-hexahydro-7β-methyl-3-oxo-1H-5,8a-propenoquinoline (XXI), capable of serving as the important intermediate for total syntheses of the lycopodium alkaloids which have been attracted by many groups of organic chemists.[4]

During the course of elucidation of structures of these alkaloids, interconversions[5] of these alkaloids, *i.e.*, lycopodine from α-obscurine and lycodine from α-obscurine *via* β-obscurine, have been already achieved and this might afford a great advantage for the syntheses of these alkaloids.



lycopodine α—obscurine β—obscurine lycodine sauroxine

Chart 1

There exists the common structural moiety of 5,8a-propenoperhydroquinoline, in lycopodine,[6] α-obscurine,[5] sauroxine[7] and other alkaloids. Therefore, we have intended

1) Part I: Z. Horii, T. Imanishi, S. Kim, and I. Ninomiya, *Chem. Pharm. Bull.* (Tokyo), **16**, 1918 (1968).
2) Location: *Toneyama, Toyonaka, Osaka.*
3) K. Wiesner, *Fortschr. Chem. Org. Naturstoffe*, **20**, 271 (1962).
4) *a*) K. Wiesner and L. Poon, *Tetrahedron Letters*, **1967**, 4937 and previous communications; *b*) W.A. Ayer, W.R. Wowman, A. Cooke, and A.C. Soper, *ibid.*, **1966**, 2021; *c*) E. Colvin, J. Martin, W. Parker, and R.A. Raphael, *Chem. Commun.*, **1966**, 596.
5) W.A. Ayer, A.J. Berezowsky, and G.G. Iverach, *Tetrahedron*, **18**, 567 (1962).
6) D.B. Harrison and W.A. McLean, *Chem. Ind.* (London), **1960**, 261.
7) W.A. Ayer and T.E. Habgood, *Tetrahedron*, **21**, 2169 (1965).

to synthesizing these alkaloids by the route *via* the 5,8*a*-propanoperhydroquinoline derivative. So far, this approach has been attempted only as the pilot experiment by Raphael and his coworkers.[4c]

As a preliminary study, the method for introducing a nitrogen function into the bridgehead position was investigated, employing 9-oxobicyclo(3,3,1)nonane-1-carboxylic acid derivatives (I), (II) and (III), which were prepared according to the method by Cope and his coworkers.[8] The saturated keto–amide (I) was converted by the Hofmann rearrangement[9] to the saturated carbamate (IV), which was identified as 2,4-dinitrophenylhydrazone. And then the unsaturated keto–acid (II) was also treated by the modified Curtius reaction,[10] *via* the mixed anhydride with ethyl chloroformate, the acid azide and the isocyanate, to convert into the corresponding carbamate (V) in 64% yield. But, conversion of the unsaturated amide (III) into the carbamate (V) by oxidative rearrangement with lead tetraacetate[11] was attempted without success.

Then, in order to introduce an oxygen function into C-3 or C-4 position, the unsaturated carbamate (V) was treated with perbenzoic acid to give the 3,4-epoxide (VI) in 86% yield, which, however, failed to lead to the diketo–ester (VIIa) or (VIIb). The Wittig reaction[12] of the unsaturated keto–carbamate (IV) with 2-(carboxyethyl)triphenylphosphonium chloride[13] in the presence of sodium hydride in dimethyl sulfoxide to introduce an alkyl side chain was likewise fruitless.

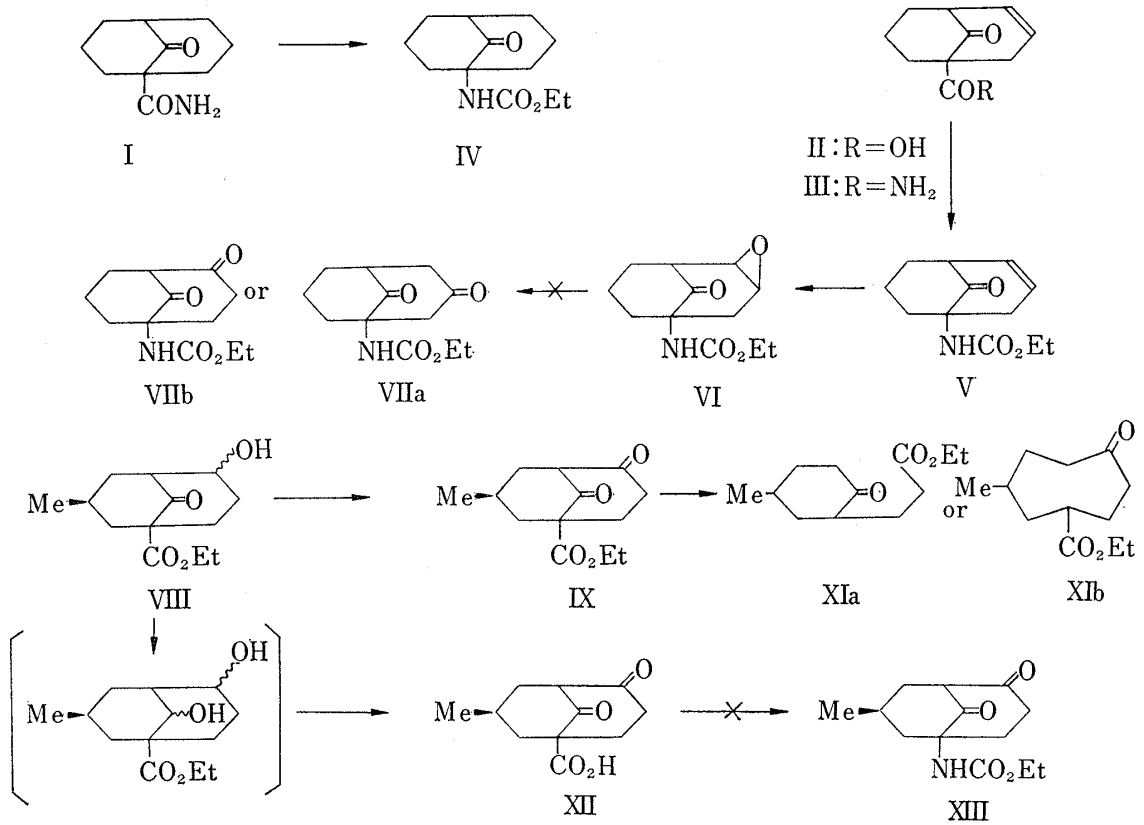


Chart 2

8) A.C. Cope and M.E. Synerholm, *J. Am. Chem. Soc.*, **72**, 5228 (1950).
9) E.S. Wallis and J.F. Lane, *Organic Reactions*, **3**, 267 (1946).
10) J. Weinstock, *J. Org. Chem.*, **26**, 3511 (1961).
11) H.E. Baumgarten and A. Staklis, *J. Am. Chem. Soc.*, **87**, 1142 (1965); B. Acott and A.L.J. Beckwith, *Chem. Commun.*, **1965**, 161; B. Acott, A.L.J. Beckwith, A. Hassanali, and J.W. Redmond, *Tetrahedron Letters*, **1965**, 4039.
12) H.S. Corey Jr., J.R.D. McCormick, and W.E. Swensen, *J. Am. Chem. Soc.*, **86**, 1884 (1964); R. Greenwald, M. Chaykovsky, and E.J. Corey, *J. Org. Chem.*, **28**, 1128 (1963).
13) D.B. Denney and L.C. Smith, *J. Org. Chem.*, **27**, 3404 (1962).

From these preliminary studies, which established the method of introducing a nitrogen function into the bridgehead position, we now have focused our effort onto the synthetic work toward the lycopodium alkaloids themselves, starting with the compound having necessary substituents.

First, we employed ethyl 5-benzyloxy-2-oxocyclohexanecarboxylate as the starting compound, which was subjected to the Michael condensation with methacrolein in order to prepare the bicyclo(3,3,1)nonane derivative with methyl and oxygen functions at the required positions. However, the reaction failed to lead to the bicyclo(3,3,1)nonane ring system.

In turn, the Michael condensation of 4-methylcyclohexanone with acrolein, followed by acid-catalyzed cyclization proceeded smoothly to afford the epimeric keto-alcohols (VIII) in good yield, which gave the diketo-ester (IX) on oxidation and the unsaturated keto-ester (X) on dehydration and the orientation of methyl group in these products has the favorable β-equatorial, identical with that in natural products, as described in the previous paper.[1)]

Now, we have intended to prepare the diketo-acid (XII), which seemed suitable for introducing amino group on the bridgehead position and oxygen function at C-7 position. First, hydrolysis of the diketo-ester (IX) under the acidic and alkaline media were examined but spontaneous ring cleavage was taken place to give, upon the following esterification, possibly either XIa or XIb, having the infrared absorption different from that of the starting ester (IX), but the structure was not determined yet. Thus, to avoid unfavorable ring cleavage possibly due to the presence of the carbonyl groups, the keto-alcohols (VIII) were first reduced with sodium borohydride to give the dihydroxy-ester, which was hydrolyzed and then oxidized with Jones reagent[14)] to the diketo-acid (XII) in 62% yield from VIII. However, the modified Curtius reaction on XII as described in II to obtain the diketo-carbamate (XIII) was likewise unsuccessful.

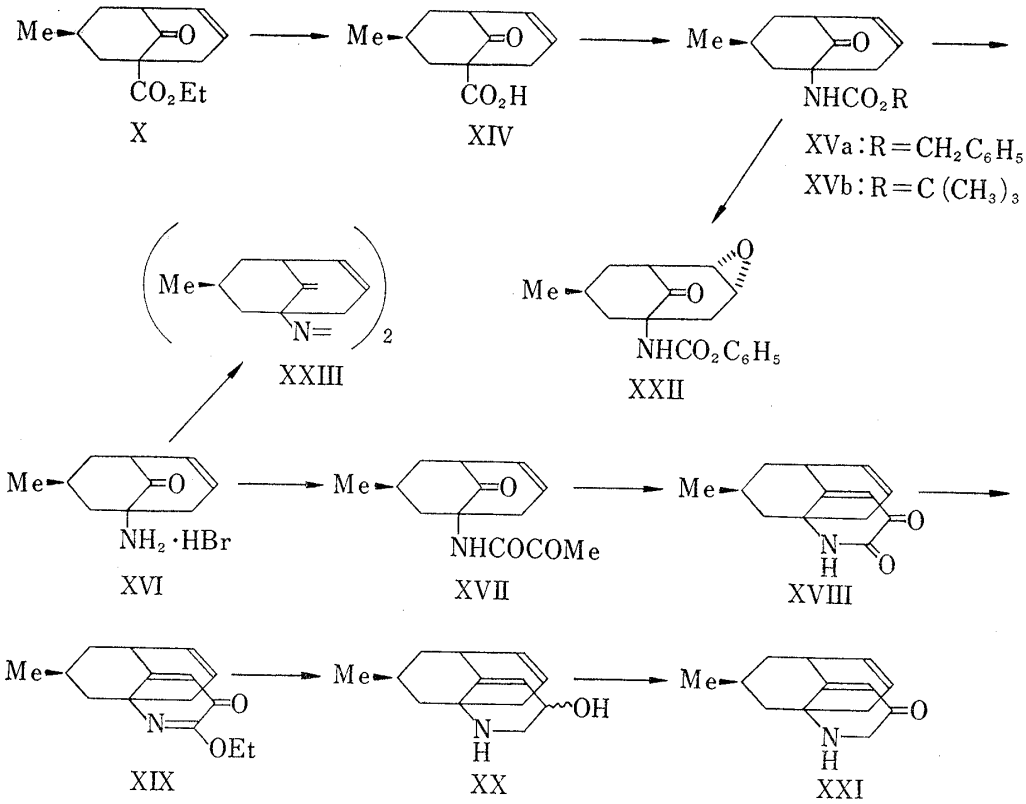


Chart 3

14) A. Bowers, T.G. Halsall, E.R.H. Jones, and A.J. Lemin, *J. Chem. Soc.*, **1953**, 2548.

Finally, we chose the unsaturated keto–ester (X) for further syntheses. 3β-Methyl-9-oxobicyclo(3,3,1)non-6-ene-1-carboxylic acid (XIV), which was obtained by mild hydrolysis in alkaline medium of X, was converted smoothly by the modified Curtius reaction into the benzyl carbamate (XVa) or *tert*–butyl carbamate (XVb), upon treatment with the respective alcohols, structures being assured by the infrared maxima at 3380—3390 and 1710—1720 cm^{-1} for NH and carbamate carbonyl groupings. Epoxidation of the unsaturated benzyl carbamate (XVa) with perbenzoic acid gave the α-epoxide (XXII) as a sole product, having the α-configuration of the epoxide ring assumed from the consideration of steric requirements. The epoxide (XXII) was likewise unaffected to various treatments for ring opening of the epoxide, as in the case of VI. Both carbamates (XVa) and (XVb) underwent hydrolytic decarboxylation with anhydrous hydrogen bromide in glacial acetic acid[15] to afford the aminoketone (XVI), isolated as its hydrobromide in order to avoid dimerization.

Direct alkylation of the amine hydrobromide (XVI) with monobromoacetone ethylene-ketal[16] in the presence of base, *i.e.*, triethylamine or potassium carbonate, failed to afford the desired monoalkylated secondary amine but *in situ* the dimeric product (XXIII) was isolated. Thus, the construction of the third ring was performed following the manner reported briefly by Raphael and his coworkers.[4c]

The oily pyruvamide (XVII), obtained from the amine hydrobromide (XVI) by acylation[17] with a mixture of pyruvic acid and phosphorous oxychloride in the presence of triethylamine, was cyclized in excellent yield by means of sodium hydride in refluxing tetrahydrofuran to give the tricyclic lactam (XVIII), which exhibited the infrared absorptions at 1681 and 1639 cm^{-1} and a singlet signal at 3.63 τ in NMR spectrum both due to the α,β-unsaturated carbonyl grouping.

Upon treatment with the Meerwein's reagent,[18] the lactam (XVIII) was converted to the lactim–ether (XIX) quantitatively, which was then reduced with lithium aluminum hydride in refluxing tetrahydrofuran to the amino–alcohol (XX) as a sole product. Oxidation of XX with Jones reagent afforded the α,β-unsaturated keto–amine (XXI), which was characterized as its hydrochloride.

This product (XXI) would serve as the important intermediate for the syntheses of both lycopodine and suroxine types of the alkaloids. Further work with XXI toward the lycopodium alkaloids are now extensively in progress.

Experimental

Melting points and boiling points are uncorrected. NMR spectra were taken on Hitachi Perkin–Elmer H-60 type Spectrometer at 60 Mc in deuterochloroform with tetramethylsilane as an internal standard.

Ethyl 9-Oxobicyclo(3,3,1)nonane-1-carbamate (IV)——To an alcoholic solution of NaOEt prepared from Na (119 mg) and abs. EtOH (10 ml) was added the acid amide[8] (I; 448 mg) followed by a solution of Br_2 (271 mg) in EtOH (3 ml). The resulting mixture was stirred at room temperature for 10 min followed by refluxing for 15 min. After cooling, the reaction mixture was poured into ice–water (50 ml) and extracted with AcOEt (3×20 ml). The combined extracts were washed with brine, dried and evaporated to give a viscous oil (350 mg), which was chromatographed on silica gel (8 g). Elutions with CCl_4 followed by $CHCl_3$ were performed and the $CHCl_3$ elute afforded the carbamate (100 mg), homogeneous on thin–layer chromatography (TLC). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3420 (NH), 1720 (CO). 2,4-Dinitrophenylhydrazone was recrystallized from C_6H_6–petr. benzin to give orange leaflets, mp 148.5—149°. IR ν_{max}^{KBr} cm^{-1}: 3390, 3311 (NH), 1730 (CO_2Et), 1621 (C=N). *Anal.* Calcd. for $C_{18}H_{23}O_6N_5$: C, 53.33; H, 5.72; N, 17.28. Found: C, 53.36; H, 5.73; N, 17.34.

Treatments of III with Pb(OAc)$_4$——The unsaturated amide[8] (III) was treated with excessive amount of $Pb(OAc)_4$ in MeOH or in DMF at the temperature ranging from room to refluxing temperatures for 2—5 hr. However, only the starting material was recovered from any of these reactions.

15) D. Ben-Ishai, *J. Org. Chem.*, **19**, 62 (1954).
16) M. Kühn, *J. Prakt. Chem.*, **156**, 103 (1940).
17) T. Wieland and B. Heinke, *Ann.*, **599**, 70 (1956).
18) G. Hinz, P. Hofmann, E. Kroning, H. Meerwein, and E. Pfeil, *J. prakt. Chem.*, **147**, 257 (1937).

Ethyl 9-Oxobicyclo(3,3,1)non-3-ene-1-carbamate (V)——To a stirred solution of the unsaturated acid[8] (II; 2.05 g) in acetone (10 ml) containing H_2O (2 ml) was added triethylamine (1.17 g) in acetone (5 ml) dropwise while maintaining the solution below 0° with ice–salt cooling and stirring was continued for 30 min. After adding ethyl chloroformate (1.15 g) in acetone (5 ml) followed by stirring for 30 min, a solution of NaN_3 (900 mg) in H_2O (5 ml) was added to the reaction mixture above and stirred for another 1 hr. The reaction temperature was maintained below 0° through-out the reaction. The mixture was poured into ice-water and extracted with ether (3×50 ml). The combined extracts were washed with brine and dried over anhyd. $MgSO_4$. To the dried organic layer was added dry toluene (20 ml) and ether was evaporated under reduced pressure at room temperature. The resulting organic layer was heated under reflux on an oil bath for 2 hr and upon adding EtOH (10 ml), refluxing was continued for 5 hr. After removing the solvent, the residue was submitted to chromatography on silica gel (10 g). Elution with $CHCl_3$ gave a pale yellow oil (1.62 g 64.3%), bp 110—115° (0.01 mmHg). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3320 (NH), 1710 (CO). NMR τ: 3.75 (1H, broad s, –NH), 4.28 (2H, m, –CH=CH–), 5.95 (2H, q, J=7 cps, $-CH_2CH_3$), 8.76 (3H, t, J=7 cps, $-CH_2CH_3$). 2,4-Dinitrophenylhydrazone was recrystallized from EtOH to give yellow leaflets, mp 174—174.5°. IR ν_{max}^{KBr} cm^{-1}: 3367, 3279 (NH), 1718 (CO_2Et), 1613 (C=N). *Anal.* Calcd. for $C_{18}H_{21}O_6N_5$: C, 53.59; H, 5.25; N, 17.36. Found: C, 53.52; H, 5.08; N, 17.54.

Ethyl 3,4-Epoxy-9-oxobicyclo(3,3,1)nonane-1-carbamate (VI)——To a stirred solution of the unsaturated carbamate (V; 223 mg) in $CHCl_3$ (5 ml) was added a solution of perbenzoic acid (152 mg) in $CHCl_3$ (1 ml) and the resulting mixture was allowed to stand in the dark at room temperature for 3 days. After adding $CHCl_3$ (20 ml), the mixture was washed with satd. $NaHCO_3$, brine and dried. Evaporation of the solvent gave the oily residue (205 mg; 85.8%), which solidified on standing, mp 79—83°. Recrystallizatioh from petr. ether to give colorless prisms, mp 84—86°. IR ν_{max}^{KBr} cm^{-1}: 3342 (NH), 1730 (sh), 1702 (CO). NMR τ: 3.78 (1H, broad s, –NH), 5.95 (2H, q, J=7.5 cps, $-CH_2CH_3$), 8.77 (3H, t, J=7.5 cps, $-CH_2CH_3$). *Anal.* Calcd. for $C_{12}H_{17}O_4N$: C, 60.24; H, 7.16; N, 5.85. Found: C, 60.41; H, 7.09; N, 5.85.

Attempted Oxide Ring Cleavage of VI——To a stirred solution of VI (566 mg) in dry C_6H_6 (10 ml) was added BF_3·ether (0.6 ml) with ice–water cooling and stirring was continued at room temperature for 10 min. The mixture was washed with satd. $NaHCO_3$, H_2O and dried. Evaporation of the solvent gave the oily residue (492 mg), which showed many spots on TLC and was difficult to separate any single product.

Attempted Wittig Reaction of V with 2-(Carboxyethyl)triphenylphosphonium Chloride——To the mixture, prepared by adding NaH (100 mg) to dry DMSO (5 ml) followed by warming under N_2 stream at 60° for 1 hr, was added a solution of V (223 mg) and 2-(carboxyethyl)triphenylphosphonium chloride[13] (445 mg) in dry DMSO (10 ml) and stirring was continued at room temperature for 5 hr. The resulting reaction mixture was poured into ice–water (50 ml) containing dil. HCl (5 ml) and extracted with AcOEt (3×30 ml). The combined extracts were washed with brine, 5% NaOH and brine, and dried. Evaporation of the solvent gave the starting material unchanged.

Hydrolyses of Ethyl 3β-Methyl-6,9-dioxobicyclo(3,3,1)nonane-1-craboxylate (IX)——A mixture of the diketo–ester[1] (IX; 300 mg) and 5% NaOH (10 ml) containing acetone (2 ml) was stirred at room temperature for 30 hr. After washing the mixture, with ether, the aqueous layer was acidified with conc. HCl, and extracted with AcOEt. The organic extracts were washed with brine, dried and evaporated to give a crude acid, exhibiting bands at 2250—2700, and 1700 cm^{-1} in $CHCl_3$. (Hydrolysis of IX with 10% H_2SO_4 by refluxing for 6 hr gave the identical acid). Esterification of the oily crude acid with EtOH–HCl gave an ester which was different from the starting ester (XI), bp 110—115° (0.01 mmHg) (bath temp.), on TLC, IR and NMR. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1725—1710 (CO). NMR τ: 5.90 (2H, q, J=7 cps, $-CH_2CH_3$), 8.75 (3H, t, J=7 cps, $-CH_2CH_3$), 9.01 (3H, d, J=5.5 cps, >CH–CH_3). 2,4-Dinitrophenylhydrazone was recrystallized from EtOH to give orange fibers, mp 97.5—98.5°. IR ν_{max}^{KBr} cm^{-1}: 3331 (NH), 1732 (CO_2Et), 1621 (C=N). *Anal.* Calcd. for $C_{13}H_{24}O_6N_4$: C, 55.09; H, 6.17; N, 14.28. Found: C, 55.11; H, 6.07; N, 14.25.

3β-Methyl-6,9-dioxobicyclo(3,3,1)nonane-1-carboxylic Acid (XII)——To a stirred solution of the keto–alcohols[1] (VIII; 2.177 g) in EtOH (20 ml) was added $NaBH_4$ (230 mg) portionwise with ice–cooling and stirring was continued at room temperature for 3 hr and then allowed to stand overnight. Upon adding AcOH and H_2O, the solvent was evaporated under reduced pressure. The residue was extracted with AcOEt (3×20 ml) and the combined extracts were washed with H_2O, dried and concentrated to give the oily residue (2.2 g), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3350 (OH) and 1705 (CO_2Et), which was dissolved in MeOH (25 ml) containing KOH (2 g). The resulting solution was heated under reflux for 7 hr and then allowed to stand at room temperature overnight. After removing the solvent, H_2O (10 ml) was added and the mixture was extracted with ether (2×20 ml) and the aqueous layer was acidified with conc. HCl and extracted with AcOEt. (50 ml). Evaporation of the solvent gave a semi–solid (1.17 g), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3300, 2750—2300, 1700. This crude dihydroxy–acid was oxidized with Jones reagent in the usual way. Evaporation of the solvent from the dried extract gave the diketo–acid (1.17 g; 62% from VIII) as a solid. An analytical sample was recrystallized from ether–petr. ether to give colorless needles, mp 184.5—186°,(dried at 100° *in vacuo* for 24 hr). IR ν_{max}^{KBr} cm^{-1}: 2817—2439 (OH), 1724, 1693 (CO). *Anal.* Calcd. for $C_{11}H_{14}O_4$: C, 62.84; H, 6.71. Found: C, 62.80; H, 6.65.

The Modified Curtius Reaction of XII——The diketo–acid (XII; 1.81 g) was treated under the modified Curtius reaction condition as described in the preparation of V to afford a crude oil (940 mg), which was chromatographed on either silica gel or alumina, affording a semi–solid, almost homogeneous on TLC from

the latter fraction eluted by $CHCl_3$. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3320, 3200, 1755 (s), 1710 (s). This product could not be purified further by recrystallization.

3β-Methyl-9-oxobicyclo(3,3,1)non-6-ene-1-carboxylic Acid (XIV)——A mixture of the keto-ester[1] (X; 14.1 g), 5% NaOH (200 ml) and acetone (30 ml) was stirred at room temperature for 3 days. After washing the mixture with AcOEt (100 ml), the aqueous layer was acidified with conc. HCl. The oil thus separated was extracted with AcOEt (3×100 ml) and the combined extracts were washed with brine and dried over anhyd. $MgSO_4$. Evaporation of the solvent gave the residue which solidified on standing upon trituration with *n*-hexane (20 ml) and the crude acid was collected (10.724 g; 87.5%). An analytical specimen was obtained by recrystallization from *n*-hexane or cyclohexane to give colorless needles, mp 114—116.5°. *Anal.* Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 67.84; H, 7.21. IR ν_{max}^{KBr} cm^{-1}: 2800—2330 (OH), 1718 (sh), 1706 (CO), 1653 (C=C). NMR τ: −1.17 (1H, s, $-CO_2\underline{H}$), 4.23 (2H, m, $-C\underline{H}=C\underline{H}-$), 9.01 (3H, d, J=5.5 cps, $>CH-C\underline{H}_3$).

Benzyl 3β-Methyl-9-oxobicyclo(3,3,1)non-6-ene-1-carbamate (XVa)——To a stirred solution of the acid (XIV; 5.826 g) in acetone (40 ml) containing H_2O (3 ml) was added triethylamine (3.340 g) in acetone (10 ml) dropwise while maintaining the solution below 0° with ice–salt cooling and stirring was continued for 30 min. After adding ethyl chloroformate (3.58 g) in acetone (10 ml) dropwise over a period of 30 min, a solution of NaN_3 (2.146 g) in H_2O (5 ml) was added to the reaction mixture and stirring was continued for 1 hr. The reaction temperature was maintained below 0° through-out the reaction. The mixture was poured into ice–water (200 ml) and extracted with ether (3×60 ml). The organic layer was washed with brine and dried over anhyd. $MgSO_4$. After removing $MgSO_4$, dry toluene (50 ml) was added to the organic solution and ether was evaporated under reduced pressure at room temperature. The resulting organic layer was heated under reflux on an oil bath for 5 hr and then, after adding benzyl alcohol (10 ml), refluxing was continued for further 20 hr. After removing the solvent and benzyl alcohol *in vacuo*, the brown oily residue was chromatographed on alumina (100 g). Elution with C_6H_6 following $CHCl_3$ separated a brown oily carbamate (4.865 g; 54%) which was distilled to give a pale yellow oil, bp 160—165° (0.01 mmHg) (bath temp.). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3378 (NH), 1718 (CO), 1647 (C=C). NMR τ: 2.70 (5H, s, $-C_6\underline{H}_5$), 3.64 (1H, broad s, $-N\underline{H}$), 4.34 (2H, m, $-C\underline{H}=C\underline{H}-$), 4.97 (2H, s, $-OC\underline{H}_2C_6H_5$), 9.06 (3H, d, J=6 cps, $>CH-C\underline{H}_3$). *Anal.* Calcd. for $C_{18}H_{21}O_3N$: C, 72.21; H, 7.07; N, 4.63. Found: C, 72.07; H, 6.98; N, 4.60.

***tert*-Butyl 3β-Methyl-9-oxobicyclo(3,3,1)non-6-ene-1-carbamate (XVb)**——The crude isocyanate, obtained from the ketoacid (XIV; 5.3 g), triethylamine (3.04 g) and ethyl chloroformate (3.25 g) following the procedure described above, was dissolved in *tert.*-BuOH (30 ml) and the mixture was heated under reflux for 35 hr. Evaporation of the solvent gave the residual oil (5 g), which was submitted to chromatography on alumina (Woelm, neutral; 100 g). Elution with C_6H_6 gave a very viscous oil (3.255 g; 45%) which was distilled to give an analytical sample as a yellow oil, bp 150—160° (0.01 mmHg) (bath temp.), solidified on standing, mp 66—67.5°. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3390 (NH), 1709 (CO), 1653 (C=C). NMR τ: 3.92 (1H, broad s, $-N\underline{H}$), 4.32 (2H, m, $-C\underline{H}=C\underline{H}-$), 8.56 (9H, s, $-C(C\underline{H}_3)_3$), 9.04 (3H, d, J=6 cps, $>CH-C\underline{H}_3$). *Anal.* Calcd. for $C_{15}H_{23}O_3N$: C, 67.89; H, 8.74; N, 5.28. Found: C, 67.84; H, 8.82; N, 5.23.

Benzyl 6α,7α-Epoxy-3β-methyl-9-oxobicyclo(3,3,1)nonane-1-carbamate (XXII)——To a stirred solution of the unsaturated ketocarbamate (XVa; 325 mg) in $CHCl_3$ (5 ml) was added a solution of perbenzoic acid (154 mg) in $CHCl_3$ (1 ml) and the resulting mixture was allowed to stand in the dark for 4 days. Then, after adding $CHCl_3$ (30 ml), the reaction mixture was washed with satd. $NaHCO_3$, and brine and dried over anhyd. $MgSO_4$. Evaporation of the solvent afforded the oily residue (310 mg), which was chromatographed on silica gel (5 g) with a mixture of $CHCl_3$–CCl_4 (2:1) as eluent. The fore-running fraction gave the starting material (118 mg), identified from IR and TLC and the latter fraction afforded a viscous oil (180 mg), homogeneous on TLC, which solidified on standing and was recrystallized from ether–petr. ether to give the epoxide (XXII) as colorless prisms, mp 91.5—93°. IR ν_{max}^{KBr} cm^{-1}: 3390 (NH), 1709 (CO). NMR τ: 2.70 (5H, s, $-C_6\underline{H}_5$), 3.69 (1H, broad s, $-N\underline{H}$), 4.99 (2H, s, $-C\underline{H}_2C_6H_5$), 9.04 (3H, d, J=6 cps, $>CH-C\underline{H}_3$). *Anal.* Calcd. for $C_{18}H_{21}O_4N$: C, 68.55; H, 6.71; N, 4.44. Found: C, 68.44; H, 6.65; N, 4.41.

Attempted Oxide Ring Cleavage of XXII——A solution of the epoxide (XXII; 630 mg) in dry C_6H_6 (10 ml) in the presence of BF_3·ether (1 ml) was stirred at room temperature for 24 hr. The reaction mixture was washed with satd. $NaHCO_3$, and brine, dried and evaporated. The residual oil thus obtained (550 mg) showed several spots on TLC and was unable to isolate any single product.

3β-Methyl-9-oxobicyclo(3,3,1)non-6-ene-1-amine Hydrobromide (XVI)——Dry HBr gas was introduced by bubbling into a solution of the benzyl carbamate (XVa; 1.126 g) in glac. AcOH (30 ml) for 3 hr and the mixture was allowed to stand at room temperature for 2 hr. Upon adding H_2O (100 ml), the mixture was washed with C_6H_6 and the aqueous layer was concentrated completely *in vacuo* to give a solid (786 mg; 85%), mp 190—200°. Recrystallization from ether–EtOH gave an analytical sample as colorless needles, mp 198—199°. IR ν_{max}^{KBr} cm^{-1}: 3390 (NH), 2740—2469 ($-N^+$), 1739 (CO) 1637 (C=C). *Anal.* Calcd. for $C_{10}H_{16}ONBr$: C, 48.79; H, 6.71; N, 5.78. Found: C, 48.56; H, 6.62; N, 5.66.

Reaction of XVI with Bromoacetone Ethyleneketal——A mixture of the amine hydrobromide (XVI; 460 mg), bromoacetone ethyleneketal[16] (340 mg) and anhydrous K_2CO_3 (1 g) in acetone (50 ml) was heated under reflux for 8 hr. After removing the inorganic salt and evaporating the solvent, the residue was dissolved in ether and extracted with dil. HCl (3×10 ml). The acidic extracts were allowed to stand at room tem-

perature for 30 hr, followed by neutralization with Na_2CO_3, and extracted with $CHCl_3$ (3×20 ml). The organic extracts were washed with brine, dried and evaporated to give the residual semi-solid (220 mg). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720, 1667 and 1647. Chromatography on either silica gel or alumina gave a fraction showing two absorptions at 1667 and 1647 cm^{-1} in IR, which crystallized on standing to colorless crystals, sublimed at 100°/0.01 mm, mp 105.5—110.5°. The following physical properties and also analysis suggested its dimeric structure, most plausibly as 1,2,3,4,5*a*,6,7,8,9,9*a*-decahydro-3,8-dimethyl-1,4*a*:6,9*a*-dipropenophenazine (XXIII). IR ν_{max}^{KBr} cm^{-1}: 1667, 1647 (C=C, C=N). NMR τ: 4.35 (4H, m, $-CH=CH-\times2$), 9.07 (6H, d, $J=6$cps, $>CH-CH_3\times2$). *Anal.* Calcd. for $C_{20}H_{26}N_2$: C, 81.58; H, 8.90; N, 9.52. Found: C, 81.34; ,H 8.80; N, 9.45.

The reaction described above was also carried out in the presence of triethylamine in C_6H_6, resulting the isolation of the identical dimeric product (XXIII) as above.

3*β*-Methyl-9-oxobicyclo(3,3,1)non-6-ene-1-pyruvamide (XVII)——To a suspension of the amine hydrobromide (XVI; 930 mg) in dry THF (20 ml) was added dropwise triethylamine (1.146 g) and pyruvic acid (332 mg) successively while maintaining the reaction temperature below −10°. After stirring for 30 min, a solution of $POCl_3$ (578 mg) in dry THF (5 ml) was added to the mixture during 2 min and stirring was continued for another 1 hr at the same temperature. Upon adding H_2O (20 ml) and saturating with NaCl, the organic layer was separated and the aqueous layer was extracted with ether thoroughly. The combined extracts were washed with brine and dried over anhyd. $MgSO_4$. The solvent was evaporated to give a brown oil (536 mg), which was submitted to chromatography on silica gel (10 g). Elution with $CHCl_3$ afforded a yellow oil (496 mg; 70.6%), boiled at 110—115° under 0.01 mm as colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3356 (NH), 1736 (CO), 1686 (NCOCO), 1653 (sh, C=C). NMR τ: 1.62 (1H, broad, s $-NH-$), 4.30 (2H, m, $-CH=CH-$), 7.58 (3H, s, $-CO-CH_3$), 9.04 (3H, d, $J=6$ cps, $-CH-CH_3$). *Anal.* Calcd. for $C_{13}H_{17}O_3N$: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.13; H, 7.26; N, 5.84.

2,3,5,6,7,8-Hexahydro-7*β*-methyl-2,3-dioxo-1H-5,8a-propenoquinoline (XVIII)——To a stirred suspension of NaH (535 mg of 58.5% oil dispersion, washed with dry THF before use) in dry THF (50 ml) was added the pyruvamide (XVII; 1.68 g) and the mixture was heated under reflux for 5 hr. After adding a small amount of EtOH with ice-cooling, the solvent was evaporated, extracted with $CHCl_3$ and dried. Evaporation of the solvent gave a viscous oily residue (1.62 g),from which a crystalline product was collected upon trituration with *n*-hexane (20 ml). Yield was 1.371 g (85%), mp 200—205°. Recrystallization from iso-PrOH–*n*-hexane gave colorless fine needles, mp 214—216°. IR ν_{max}^{KBr} cm^{-1}: 3215 (NH), 1681 (NCOCO), 1639 (C=C). NMR τ: −0.08 (1H, broad s, $-NH-$), 3.63 (1H, s, $-C=CH-CO-$), 4.28 (2H, m, $-CH=CH-$), 9.08 (3H, d, $J=5.5$ cps, $>CH-CH_3$). *Anal.* Calcd. for $C_{13}H_{15}O_2N$: C, 71.86; H, 6.96; N, 6.45. Found: C, 71.68; H, 6.85; N, 6.42.

5,6,7,8-Tetarhydro-2-ethoxy-7*β*-methyl-3-oxo-3H-5,8a-propenoquinoline (XIX)——To a solution of the keto-lactam (XVIII; 1.086 g) in CH_2Cl_2 (20 ml) was added a solution of freshly prepared excess Meerwein reagent[18] in CH_2Cl_2 with ice-cooling and the resulting mixture was allowed to stand at room temperature overnight. The mixture was poured into ice-water and the organic layer was separated, washed with H_2O, satd. $NaHCO_3$, H_2O, dried and concentrated. The residue (1.09 g), was chromatographed on silica gel (10 g) using $CHCl_3$ as eluent to give a yellow oil (920 mg; 80%), bp 115—120° (0.01 mmHg) (bath temp.). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1667 (C=C–CO), 1631 (C=C). NMR τ: 3.76 (1H, s, $-C=CH-CO-$), 4.27 (2H, m, $-CH=CH-$), 5.81 (2H, q, $J=7$ cps, $-OCH_2CH_3$), 8.64 (3H, t, $J=7$ cps, $-OCH_2CH_3$), 9.08 (3H, d, $J=6$ cps, $>CH-CH_3$). *Anal.* Calcd. for $C_{15}H_{19}O_2N$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.27; H, 7.72; N, 5.66.

2,3,5,6,7,8-Hexahydro-3-hydroxy-7*β*-methyl-1H-5,8a-propenoquinoline (XX)——To a suspension of $LiAlH_4$ (337 mg) in dry THF (20 ml)was added a solution of the lactim-ether (XIX; 725 mg) in dry THF (10 ml) dropwise with ice-cooling and the resulting mixture was heated under reflux for 6 hr. After decomposing excess $LiAlH_4$ with AcOEt, the solvent was removed and extracted with hot $CHCl_3$ repeatedly. The combined extracts were washed with brine and dried. Evaporation of the solvent gave a solid (545 mg; 90%), which was recrystallized from AcOEt to give colorless leaflets, mp 184—185° (measured in sealed tube). IR ν_{max}^{KBr} cm^{-1}: 3279 (NH, OH), 1667, 1634 (C=C). *Anal.* Calcd. for $C_{13}H_{19}ON$: C, 76.05; H, 9.33; N, 6.82. Found: C, 75.79; H, 9.24; N, 6.82.

2,3,5,6,7,8-Hexahydro-7*β*-methyl-3-oxo-1H-5,8a-propenoquinoline (XXI)——To a stirred solution of the amino-alcohol (XX; 320 mg) in purified acetone (5 ml) containing a few drops of conc. H_2SO_4, was added one equivalent amount of Jones reagent at 0° and stirring was continued for 10 min. Upon adding H_2O (20 ml), the mixture was made alkaline with 5% NaOH and extracted with $CHCl_3$ (3×15 ml). The organic layer was washed with H_2O, and dried. Evaporation of the solvent gave a brown oil (278 mg), which was chromatographed on alumina (Woelm, neutral, 5 g). Elution with $CHCl_3$ afforded a pale yellow oil (267 mg, 84%), bp 115—120° (0.01 mmHg) (bath temp.). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3311 (NH), 1664 (–C=C–CO–), 1637 (sh, –C=C). NMR τ: 4.11 (1H, s, $-C=CH-CO-$), 4.32 (2H, m, $-CH=CH-$), 6.54 (2H, s, $-N-CH_2-CO-$), 9.07 (3H, d, $J=6$ cps, $>CH-CH_3$).

The hydrochloride, prepared in the usual way, was recrystallized from iso-PrOH–ether, to give colorless needles, mp 212—214° (decomp.). IR ν_{max}^{KBr} cm^{-1}: 2732—2364 ($-N^+$), 1685 (C=C–CO), 1639 (C=C). *Anal.* Calcd. for $C_{13}H_{18}ONCl$: C, 65.12; H, 5.75; N, 5.84. Found: C, 65.07; H, 7.53; N, 5.85.