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Studies on Indenopyridine Derivatives and Related Compounds. I. Syntheses and Stereochemistries of 1-Substituted 1,2,3,4,4a,9a-Hexahydro-4-hydroxy-9*H*-indeno[2,1-*b*]pyridines and Related Compounds

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Reduction of the vinylogous lactam (V or VI), either chemically or catalytically, afforded the epimeric mixture of amino alcohols accompanied the dehydration products, and these stereostructure were assigned as B/C-*cis* stable form of 1-substituted 1,2,3,4,4a, 9a-hexahydro-4-hydroxy-9*H*-indeno[2,1-*b*]pyridines. Oxidation reaction of these amino alcohols were attempted.

In 1967, Horii and his co-workers[2] synthesized N,N-diethyl-4-methyl-2,3,4,4a,5,6-hexahydrobenzo[*f*]quinoline-2-carboxamide (II) as LSD_{25} (I) analog lacking only a pyrrole ring searching for compounds with potent activity related to lysergic acid.

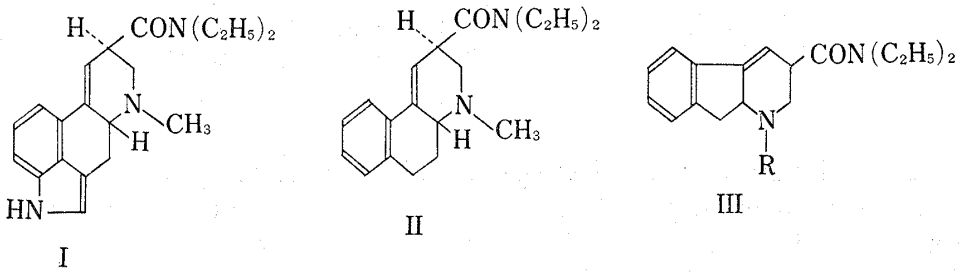

Chart 1

Inspection of Dreiding model on these two compounds (I and II) clearly shows that the conformational structure of I is rather flat and has some rigidity with respect to four rings, whereas that of II has some flexibility and the different shape from I due to the lack of pyrrole ring. However, once the B-ring of II is replaced to five menbered ring such as III, III resembles LSD_{25} very closely in conformational structure and would be expected pharmacological activity.[3] The present paper is confined the syntheses and the elucidation of stereochemistries of title compounds, objecting the synthesis of III.

The reaction of cycloalkanone and amino carboxylic acid esters in the presence of *p*-toluenesulfonic acid or, more effectively, trifluoroacetic acid[4] is well known. Horii, *et al.*,[5] reported that the reaction of methyl 2-methyl-3-methylaminopropionate with 2-tetralone in the presence of *p*-toluenesulfonic acid in ethylene glycol gave the mixture of rearranged 2,4-dimethyl-1,2,5,6-tetrahydrobenzo[*f*]quinolin-3(4*H*)-one (IV) as main product and a small amount of normally cyclized 2,4-dimethyl-3,4,5,6-tetrahydrobenzo[*f*]quinolin-1(2*H*)-one.

Heating of 2-indanone with ethyl 3-benzyl- or 3-methylaminopropionates in the presence of trifluoroacetic acid in toluene for 2 hr afforded 1-benzyl- or 1-methyl-1,2,3,4-tetrahydro-9*H*-indeno[2,1-*b*]pyridin-4-ones (V and VI) in yield of 85% and 93%. These structual assignment

1) Location: *2-10-62, Kawai, Matsubara, Osaka.*
2) Z. Horii, T. Kurihara, S. Yamamoto, and I. Ninomiya, *Chem. Pharm. Bull.* (Tokyo), **15**, 1641 (1967).
3) J. Augstein, A.L. Ham, and P.R. Leeming, *J. Med. Chem.*, **15**, 466 (1972).
4) W. Sovotka, W.N. Beverung, G.G. Munoz, J.C. Sircar, and A.I. Meyers, *J. Org. Chem.*, **30**, 3667 (1965).
5) Z. Horii, C. Iwata, I. Ninomiya, N. Imamura, M. Ito, and Y. Yamura, *Chem. Pharm. Bull.* (Tokyo), **12**, 1405 (1964).

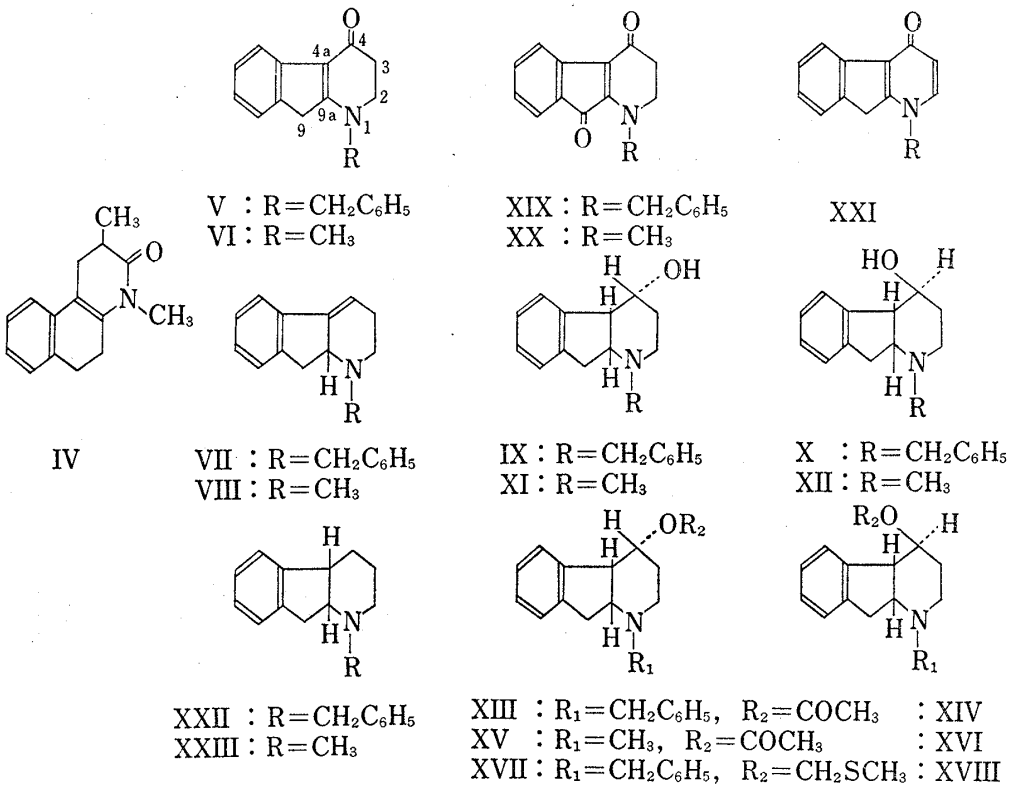

Chart 2

was mainly obtained from infrared (IR) spectra, ultra violet (UV) spectra, and $FeCl_3$ color test as shown in experimental part.[6] Reduction of V with sodium borohydride in ethanol gave a mixture of two epimeric 1-benzyl-1,2,3,4,4a,9a-hexahydro-4-hydroxy-9*H*-indeno-[2,1-*b*]pyridines (IX and X) in 48% yield, accompanied by 1-benzyl-1,2,3,9a-tetrahydro-9*H*-indeno[2,1-*b*]pyridine (VII) in 4.2% yield. Catalytic hydrogenation of V over platinum oxide in the mixture of ethanol and acetic acid (1: 1) also afforded two epimeric alcohols (IX and X) in yield of 45% and 15%, respectively. Reduction of VI with sodium borohydride in ethanol gave a mixture of two epimeric 1-methyl-1,2,3,4,4a,9a-hexahydro-4-hydroxy-9*H*-indeno[2,1-*b*]pyridines (XI and XII) in 58% yield and 1-methyl-1,2,3,9a-tetrahydro-9*H*-indeno[2,1-*b*]pyridine (VIII) in 12% yield. It is known, in general, that lithium aluminum hydride reduction of vinylogous lactam system gives the saturated ketone among products.[7] However, when VI was reduced with lithium aluminum hydride in ether at room temperature, products were XI in 47%, and VIII in 35% yield and it was failed to detect XII and saturated ketone. Dehydration of these amino alcohols (IX, X, XI, and XII) under condition of thionyl chloride in pyridine at room temperature[8] gave VII or VIII, respectively, which were identical with authentic samples.

Interestingly, these amino alcohols showed the resistance for oxidation reaction under several conditions. Chromium trioxide oxidation of IX, either in pyridine or in acetic acid as solvent, gave a dark blue crystalline substance (XIX), which showed the elemental composition of $C_{19}H_{15}O_2N$, IR band at 1718, 1624, and 1590 cm^{-1}, and UV absorption maximum at 275 and 300 mμ. The nuclear magnetic resonance (NMR) spectrum of XIX exhibited the disappearance of the signal attributable to C_9-methylene protons. Thus the structure

6) F. Bohlmann and O. Schmidt, *Ber.*, **97**, 1354 (1964).
7) J.M. Osbond, *J. Chem. Soc.*, **1961**, 4711; A.I. Meyers, G.G. Munoz, W. Sobotka, and K. Baburao, *Tetrahedron Letters*, **1965**, 225; Z. Horii, K. Morikawa, and I. Ninomiya, *Chem. Pharm. Bull.* (Tokyo), **16**, 1472 (1968).
8) S. Bernstein, R.H. Lenhart, and J.H. Williams, *J. Org. Chem.*, **19**, 41 (1954).

of XIX was assigned as 1-benzyl-1,2,3,4-tetrahydro-9*H*-indeno[2,1-*b*]pyridine-4,9-dione. Analogously chromium trioxide oxidation of XI gave 1-methyl-1,2,3,4-tetrahydro-9*H*-indeno [2,1-*b*]pyridine-4,9-dione (XX). When the vinylogous amides (V or VI) were heated with chloranil in *tert*- butyl alcohol[9] or mercuric acetate in aqueous acetic acid, which are known as dehydrogenation reaction condition to obtain the compound such as XXI, diketones (XIX or XX) were obtained in good yield. Jone's oxidation of IX gave the starting material and unidentified product. Meantime, IX, upon oxidation with dimethyl sulfoxide and acetic anhydride mixture[10] followed by the careful column chromatographical separation gave the acetate (XIII) in 15% yield and the methylthiomethyl ether (XVII), the structure of which was proven by its elemental analysis, mass spectrum, and NMR spectrum, in 55% yield. Oxidation of isomeric alcohol (X) under the same condition also gave XIV and XVIII in 20% and 48% yield. Catalytic hydrogenation of VII and VIII over platinum oxide gave 1-benzyl- and 1-methyl-1,2,3,4,4a,9a-hexahydro-9*H*-indeno[2,1-*b*]pyridines (XXII and XXIII).

Stereochemistry

Reduction of vinylogous lactam system, either chemically or catalytically, has been known to give a mixture of B/C-*cis*/and -*trans* alcohols among products.[11] The configuration of C_4-hydroxyl group of IX and X was easily assigned as follow. Products of sodium borohydride reduction of V were separated by column chromatography through alumina column employing benzene as eluent to give dehydration product (VII) of mp 77—77.5°, IX of mp 174—176° as perchlorate, and X of mp 213—215° as perchlorate in turn. Difference in their retention times in vapor phase and column chromatographies[12] might indicate that the hydroxyl group is axial in IX, while equatorial in X. On the NMR spectra of these corresponding acetates (XIII and XIV), the signal attributable to proton at C_4 of XIII appeared as multiplet with half height band width of about 10 cps at 4.65 τ, while 21 cps at 5.25 τ in XIV.[13] As

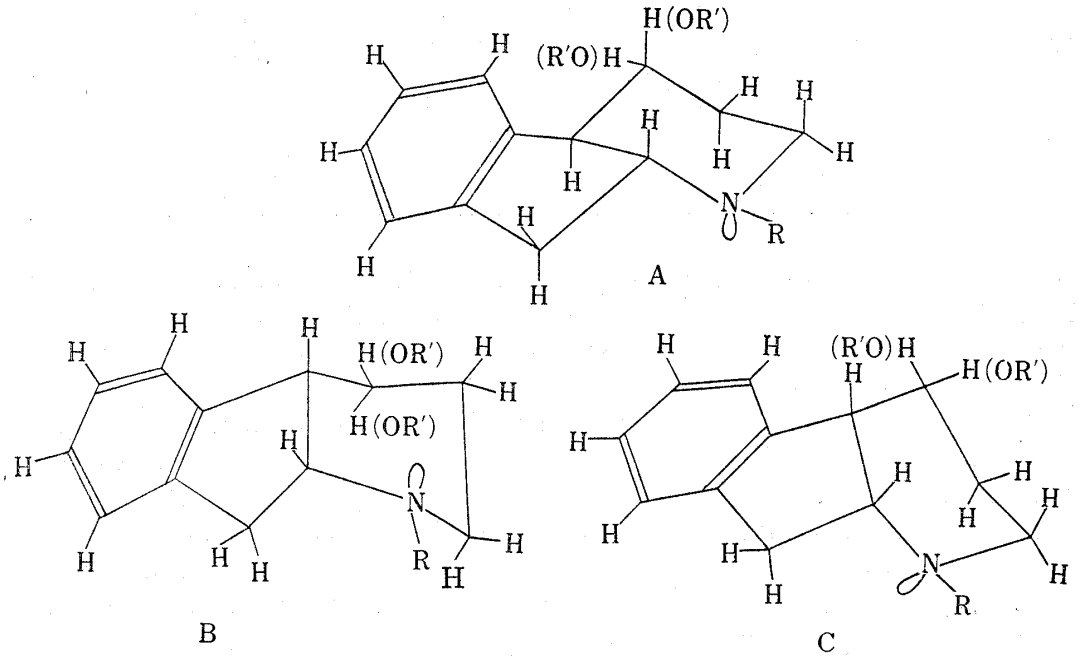

Fig. 1

9) E.J. Angello and G.D. Laubach, *J. Am. Chem. Soc.*, **82**, 4293 (1960).
10) J.D. Albright and L. Goldman, *J. Am. Chem. Soc.*, **87**, 4214 (1965).
11) N.A. Nelson, J.E. Ladbury, and R.S.P. Hsi, *J. Am. Chem. Soc.*, **80**, 6633 (1958).
12) D.H.R. Barton, *J. Chem. Soc.*, **1953**, 1027.
13) K. Tori and T. Komeno, *Tetrahedron*, **21**, 309 (1965).

a general rule that in IR spectroscopy[14] the C–OH stretching vibration for an axial hydroxyl group is at a higher wave length than that for corresponding equatorial hydroxyl group, the C-OH stretching vibration of IX and X appeared at 1015 and 1052 cm^{-1}, respectively. These facts clearly supported the above assumption. Same results were obtained in the corresponding N-methyl series.

Conformational structure of these derivatives as having B/C-*cis* stable conformation was deduced from the NMR evidences. Three possible conformations, *i.e.*, B/C-*trans* form (A), B/C-*cis* stable form (B), and B/C *cis*-unstable form (C), can be considered from the examination of Dreiding model as shown in Fig. 1. The 100 MHz NMR spectrum of XV in $CDCl_3$ exhibited the C_{4a}-proton as triplet at 6.53 τ. By irradiation of C_4-proton (which appeared as a quartet at 4.71 τ), the triplet signal collapsed to a doublet with $J=6$ cps, which is in agreement with the coupling constant of B/C-*cis* ring juncture of the analogous octahydrobenzo[*f*]quinolines.[3,15] As listed in Table I, the absorption of the isomer bearing an axial substituents (–OH, $-OCOCH_3$, $-OCH_2SCH_3$) at C_4 position exhibited the N-benzylic protons as a quartet with $J=14$—15 cps, whereas that of epimer exhibited a sharp singlet.

Table I. The NMR Data given in τ Value at 60 Mc, J Value in the Parenthesis is in cps

Compounds	C_4(OH)(H)	C_4($OCOCH_3$)(H)	C_4($OCOCH_3$)(H)	>N-$CH_2C_6H_5$	>N-CH_3
IX	5.95(m)			6.30(q. 15)	
X	unidentified			6.32(s)	
XI	5.90(m)				7.66(s)
XII	unidentified				7.55(s)
XIII		4.65(m. H/W10)	8.28(s)	6.30(q. 14)	
XIV		5.25(m. H/W21)	7.96(s)	6.30(s)	
XV		4.96(m. H/W11)	8.08(s)		7.65(s)
XVI		5.00(m. H/W19)	7.91(s)		7.60(s)
XVII				6.30(q. 15)	
XVIII				6.29(s)	

This result will be explained as follow. In conformation B or C, if the substituents at C_4 are in axial configuration, these substituents and N-benzyl group are in 1,4-*cis* relationship. Hence, these substituents will cause the restriction of free rotation of N-benzyl group to break the equivalency of N-benzylic protons.

Finally the prefered conformer between B and C could be confirmed to B having a B/C-*cis* stable form by means of NMR spectra. The acetyl methyl protons resonances of XIII and XV appeared at 8.28 τ and 8.08 τ, which are in 19 cps and 11 cps higher field than corresponding isomers (XIV and XVI), respectively. In fact, Dreiding model shows that conformation B brings the axialy oriented acetoxyl group into the zone of shielding of aromatic A-ring and also benzylic phenyl ring, so accounting for the observed upfield shift. These results are in good agreement with the conformational structure of perhydroindanone or closely related hexahydro-1*H*-indeno[2,1-*c*]pyridines.[16] The structure of hexahydro derivatives (XXII and XXIII) were determined in direct comparison with alternative syntheses derived from IX and XI by tosylation followed by lithium aluminum hydride reduction.[17]

14) R.L. Clark and C.M. Mortin, *J. Am. Chem. Soc.*, **81**, 5716 (1959).
15) Z.G. Hajos, K.J. Doebel, and M.W. Goldburg, *J. Org. Chem.*, **29**, 2527 (1964).
16) A.L. Ham and P.R. Leeming, *J. Chem. Soc.* (*C*), **1969**, 523.
17) E. Shreier, *Helv. Chim. Acta*, **41**, 1984 (1958).

Experimental[18]

1-Benzyl-1,2,3,4-tetrahydro-9*H*-indeno[2,1-*b*]pyridin-4-one (V)——A mixture of 2-indanone (34.1 g) and ethyl 2-benzylaminopropionate[19] (55 g) dissolved in dry toluene (250 ml) in the presence of trifluoroacetic acid (5.5 ml) was refluxed under N_2 stream with Dean Stark water separator in order to remove water as it formed for 2 hr. After cooling, the precipitate was collected by filtration, washed with cold EtOH and recrystallized from EtOH giving a pale pink needles (62.5 g) (85%) of V, mp 158—159°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1625, 1605, 1580. UV λ_{max}^{EtOH} mμ(log ε): 278 (3.95), 359 (3.55). UV $\lambda_{max}^{EtOH+HCl}$ mμ(log ε): 256 (4.04), 358 (3.43). $FeCl_3$ color test: positive (dark green). NMR τ: 5.60 (s, 2H, N-C<u>H</u>$_2$C$_6$H$_5$). *Anal.* Calcd. for $C_{19}H_{17}ON$: C, 82.88; H, 6.22; N, 5.09. Found: C, 82.94; H, 6.24; N, 5.30.

1-Methyl-1,2,3,4-tetrahydro-9*H*-indeno[2,1-*b*]pyridin-4-one (VI)——A mixture of 2-indanone (24.6 g) and ethyl 2-methylaminopropionate[20] (25 g) in the presence of trifluoroacetic acid (2 ml) in dry toluene (150 ml) was worked up in the same manner as described for the synthesis of V giving a pale yellow needles (30.5 g) (92%) of VI, mp 187—188°, recrystallized from EtOH. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1625, 1603, 1580. UV λ_{max}^{EtOH} mμ(log ε): 277 (4.02), 358 (3.65). UV $\lambda_{max}^{EtOH+HCl}$ mμ(log ε): 259 (4.12), 357 (3.53). $FeCl_3$ color test: positive (dark green). NMR τ: 7.08 (s, 3H, N-C<u>H</u>$_3$). *Anal.* Calcd. for $C_{13}H_{13}ON$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.33; H, 6.64; N, 7.28.

Reduction of V with Sodium Borohydride——To a hot solution of V (10 g) in EtOH (200 ml) was added $NaBH_4$ (5.6 g) in small portions and the mixture was refluxed until the disappearance of V on the thin-layer chromatography (TLC) (required for 3—4 hr). After neutralization with dilute acetic acid, most of the solvent was evaporated under reduced pressure below 40°. The residue was poured into water and extracted with $CHCl_3$. The extract was washed with H_2O, dried over anhyd. $MgSO_4$ and evaporated to give a dark violet residue (6.2 g), which showed the presence of three components in the ratio of 8.9: 67.9: 23.7 by VPC. By chromatographical separation over Al_2O_3 column using benzene as eluent was obtained VII (0.4 g as crude oil) from first fraction. Repurification over neutral Al_2O_3 column chromatography eluted *n*-hexane gave pure VII, which solidified by adding a drop of petr. ether. Recrystallization from petr. ether gave colorless needles, mp 77—77.5°. UV λ_{max}^{EtOH} mμ(log ε): 253 (3.73), 289 (3.40). NMR τ: 4.05 (s, 1H, -C<u>H</u>=C). *Anal.* Calcd. for $C_{19}H_{19}N$: C, 87.31; H, 7.33; N, 5.36. Found: C, 87.25; H, 7.30; N, 5.48. From the second fraction was obtained IX (3.6 g). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610 (OH). Mass Spectrum *m/e*: 279 (M^+). The perchlorate of IX was recrystallized from EtOH–$(C_2H_5)_2O$ to colorless needles, mp 174—176°. *Anal.* Calcd. for $C_{19}H_{22}O_5NCl$: C, 60.08; H, 5.85; N, 3.69. Found: C, 60.25; H, 5.97; N, 3.78. From the third fraction was obtained X (1.1 g), IR $\nu_{max}^{CHCl_3}$: 3620 (OH), which solidified by adding a drop of ligroin. Recrystallization from ligroin gave colorless needles, mp 94—95°. Mass Spectrum *m/e*: 279 (M^+). *Anal.* Calcd. for $C_{19}H_{21}ON$: C, 81.68; H, 7.58; N, 5.01. Found: C, 81.85; H, 7.64; N, 5.30. The perchlorate of X was recrystallized from EtOH–$(C_2H_5)_2O$ to colorless needles, mp 213—214°. *Anal.* Calcd. for $C_{19}H_{22}O_5NCl$: C, 60.08; H, 5.85; N, 3.69. Found: C, 59.94; H, 5.80; N, 3.58.

Hydrogenation of V with Platinum Oxide Catalyst——A solution of V (1.0 g) in AcOH–EtOH (1: 1) mixture (30 ml) was hydrogenated over PtO_2 catalyst (0.2 g) using Skita apparatus for 10 hr. The catalyst was removed by filtration and most of the solvent was evaporated. The acidic residue was poured into H_2O, made alkaline by adding $NaHCO_3$ and extracted with $CHCl_3$. The extract was washed with H_2O, dried over anhyd. $MgSO_4$ and evaporated. The residue (0.7 g) showing the presence of three components on TLC was submitted on Al_2O_3 column chromatography using benzene as eluent giving IX (0.45 g), X (0.15 g) and the starting material, identified with the authentic samples by comparison of their IR spectra, respectively.

Reduction of VI with Sodium Borohydride——To a hot solution of VI (10 g) in EtOH (200 ml) was added $NaBH_4$ (5.61 g) in small portions. The reaction mixture was treated as described for the reduction of V giving a dark violet residue (7.9 g), which showed the presence of three components in the ratio of 11.5: 79.5: 9 by VPC. By chromatographical separation over Al_2O_3 column using benzene as eluent was obtained VIII (1.1 g as crude crystals) from the first fraction. Repeated sublimation *in vacuo* afforded pure VIII, mp 50—51°. UV λ_{max}^{EtOH} mμ(log ε): 253 (4.09), 290 (3.29). NMR τ: 4.05 (s, 1H, -C<u>H</u>=C), 7.63 (s, 3H, N-C<u>H</u>$_3$). *Anal.* Calcd. for $C_{13}H_{15}N$: C, 84.28; H, 8.16; N, 7.56. Found: C, 84.31; H, 8.30; N, 7.64. From the second fraction was obtained XI (5.12 g), recrystallized from *n*-hexane to colorless needles, mp 147—148°. *Anal.* Calcd. for $C_{13}H_{17}ON$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.96; H, 8.45; N, 6.66. From

18) All melting points and boiling points were uncorrected. The IR and UV spectra were taken with JASCO Model IRA-1 and Hitachi Model EPS-3T spectrophotometers, respectively. The mass spectra were taken with Hitachi Mass Spectrometer RMU-7L and the NMR spectra were taken with Varian A-60 and Varian HA-100 spectrometers using tetramethylsilane as the internal standard. Vapor Phase Chromatographies (VPC) were measured on Shimazu 4-BMPF gas chromatograph, employing SE-30 column (column temperature 210—230°).

19) P.L. Sauthvick and R.T. Crouch, *J. Am. Chem. Soc.*, **75**, 3413 (1953).

20) R.W. Holley and A.D. Holley, *J. Am. Chem. Soc.*, **71**, 2126 (1949).

the third fraction was obtained XII (0.75 g). Mass Spectrum *m/e*: 203 (M^+). The perchlorate of XII was recrystallized from EtOH–$(C_2H_5)_2O$ to colorless needles, mp 78—79°. *Anal.* Calcd. for $C_{13}H_{18}O_5NCl$: C, 51.40; H, 5.97; N, 4.61. Found: C, 51.64; H, 6.07; N, 4.63.

Reduction of VI with Lithium Aluminum Hydride——To a stirred suspension of VI (1.0 g) in anhyd. $(C_2H_5)_2O$ (100 ml) was added $LiAlH_4$ (200 mg) and the mixture was stirred for 3 hr at room temperature. After adding of AcOEt (10 ml) followed by 30% KOH (20 ml) under ice cooling, the organic layer was separated and the aqueous layer was extracted with $(C_2H_5)_2O$. The combined organic layer was washed with saturated brine and dried over anhyd. $MgSO_4$. Evaporation of the solvent gave a pasty residue (0.85 g), which was chromatographed over Al_2O_3. The first fraction eluted with benzene gave VIII (0.35 g), which was identical with the authentic sample by comparison of their IR spectra. The second fraction eluted with a mixture of benzene–$CHCl_3$ (1: 1) gave XI (0.47 g), which was also identical with the authentic sample by comparison of their IR spectra.

General Procedure for Acetylation of Amino Alcohols (IX, X, XI and XII)——A solution of amino alcohols (0.5 g), pyridine (1 ml) and Ac_2O (5 ml) was stand overnight at room temperature. The mixture was poured into ice water, made alkaline by adding $NaHCO_3$ and extracted with $CHCl_3$. The extract was washed with H_2O, dried over anhyd. $MgSO_4$ and evaporated. The residue was purified by passing through Al_2O_3 column using benzene as eluent. XIII: mp 192—193° (ligroin), *Anal.* Calcd. for $C_{21}H_{23}O_2N$: C, 78.47; H, 7.21; N, 4.36. Found: C, 78.56; H, 7.40; N, 4.49. XIV: as $HClO_4$ salt, mp 227—228° (EtOH–$(C_2H_5)_2O$), *Anal.* Calcd. for $C_{21}H_{24}O_6NCl$: C, 59.78; H, 5.73; N, 3.31. Found: C, 59.85; H, 5.84; N, 3.51. XV: mp 60—61° (*n*-hexane), *Anal.* Calcd. for $C_{15}H_{19}O_2N$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.64; H, 7.96; N, 5.93. XVI: as $HClO_4$ salt, mp 137—139° (EtOH–$(C_2H_5)_2O$), *Anal.* Calcd. for $C_{15}H_{20}O_6NCl$: C, 52.16; H, 5.83; N, 4.05. Found: C, 52.33; H, 6.01; N, 4.27.

1-Benzyl-1,2,3,9a-tetrahydro-9*H*-indeno[2,1-*b*]pyridine (VII)——a) From IX: A mixture of IX (0.1 g) and $SOCl_2$ (0.5 ml) in anhyd. pyridine (2 ml) was kept at 20° for 1 hr. The reaction mixture was poured into ice water and extracted with $CHCl_3$. The extract was washed with H_2O, dried over anhyd. $MgSO_4$ and evaporated giving a dark brown oil (70 mg), which was submitted on column chromatography through Al_2O_3 using *n*-hexane as eluent to give VII (25 mg), identified with the authentic sample by comparison of their IR spectra.

b) From X: A mixture of X (0.1 g) and $SOCl_2$ (0.5 ml) in anhyd. pyridine (2 ml) was treated as described above giving VII (20 mg), identified with the authentic sample by comparison of their IR spectra.

Oxidation of IX——a) With Chromium Trioxide in Pyridine: To a complex from CrO_3 (1.5 g) and pyridine (10 ml) was added a solution of IX (1 g) dissolved in pyridine (10 ml). The mixture was allowed to stand overnight at room temperature. After adding H_2O (100 ml), the resulting solution was extracted with $CHCl_3$. The extract was washed with H_2O, dried over anhyd. $MgSO_4$ and evaporated giving a dark blue crystal (0.9 g), which was submitted on column chromatography through Al_2O_3 using $CHCl_3$ as eluent. The first fraction afforded XIX (0.47 g) as a dark blue solid, which was recrystallized from EtOH, mp 161—162°. IR ν_{max}^{KBr} cm^{-1}: 1718, 1624, 1590. UV λ_{max}^{EtOH} $m\mu(\log\varepsilon)$: 275 (4.85), 300 (3.99). NMR τ: 4.88 (s, 2H, N–C$\underline{H}_2$C$_6$H$_5$). Mass Spectrum *m/e*: 289 (M^+). *Anal.* Calcd. for $C_{19}H_{15}O_2N$: C, 78.87; H, 5.23; N, 4.84. Found: C, 78.84; H, 5.20; N, 4.84. The second fraction gave IX (0.25 g).

b) With Chromium Trioxide in AcOH: To a solution of IX (0.5 g) in AcOH (10 ml) was added CrO_3 (1.0 g), and the resulting mixture was warmed at 70° for 5 hr. After cooling, H_2O (50 ml) followed solid Na_2CO_3 were added to make the solution alkaline. After extraction with $CHCl_3$, the extract was washed with H_2O, dried over anhyd. $MgSO_4$ and evaporated giving a dark blue solid (0.25 g), which showed the presence of XIX and IX on TLC.

c) With Dimethyl Sulfoxide in Acetic Anhydride: A mixture of IX (0.66 g) and dimethyl sulfoxide (4.8 ml) in Ac_2O (3.2 ml) was allowed to stand at room temperature for 35 hr and then poured into ice water. The resulting solution was made alkaline with $NaHCO_3$ and extracted with $(C_2H_5)_2O$. The extract was washed with H_2O several times, dried over anhyd. $MgSO_4$ and evaporated. Column chromatography of the residue through Al_2O_3 using benzene as eluent afforded the corresponding acetate (XIII) (47 mg) from the first fraction, which was identical with the authentic sample by comparison of their IR spectra. The second fraction afforded methylthiomethyl ether (XVII) (440 mg), which solidified on standing overnight. Recrystallization from petr. ether gave a colorless needles, mp 82—83°. IR ν_{max}^{KBr} cm^{-1}: 1040 (ether). Mass Spectrum *m/e*: 339 (M^+). NMR τ: 5.52 (s, 2H, –OC$\underline{H}_2$–S), 8.04 (s, 3H, –SC$\underline{H}_3$). *Anal.* Calcd. for $C_{21}H_{25}$-ONS: C, 74.30; H, 7.42; N, 4.12. Found: C, 74.51; H, 7.52; N, 4.30. The perchlorate of XVII was recrystallized from EtOH–$(C_2H_5)_2O$ to colorless needles, mp 124—125°. *Anal.* Calcd. for $C_{21}H_{26}O_5NClS$: C, 57.33; H, 5.96; N, 3.18. Found: C, 57.34; H, 5.99; N, 3.40.

Oxidation of X with Dimethyl Sulfoxide in Acetic Anhydride——A mixture of X (0.33 g) and dimethyl sulfoxide (2.4 ml) in Ac_2O (1.6 ml) was treated as described for the oxidation of IX. The residue was submitted on column chromatography through Al_2O_3 using benzene as eluent afforded the corresponding acetate (XIV) (18 mg) from the first fraction. The second fraction afforded oily methylthiomethyl ether (XVIII) (190 mg). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1040 (ether). Mass Spectrum *m/e*: 339 (M^+). NMR τ: 5.42 (s, 2H, –OC$\underline{H}_2$–S), 8.01 (s, 3H, –SC$\underline{H}_3$). The perchlorate of XVIII was recrystallized from EtOH–$(C_2H_5)_2O$ to colorless needles,

mp 162-—164°. *Anal.* Calcd. for $C_{21}H_{26}O_5NClS$: C, 57.33; H, 5.96; N, 3.18. Found: C, 57.42; H, 6.02; N, 3.35.

Oxidation of XI with Chromium Trioxide in Pyridine——To a complex from CrO_3 (1.4 g) and pyridine (10 ml) was added a solution of XI (1.0 g) dissolved in pyridine (10 ml). The resulting mixture was treated as described for the oxidation of IX to give a dark blue residue (0.85 g), which was submitted on column chromatography through Al_2O_3 using $CHCl_3$ as eluent. The first fraction afforded XX (490 mg) as a dark blue solid, which was recrystallized from EtOH, mp 166—167°. IR ν_{max}^{KBr} cm^{-1}: 1718, 1640, 1590. UV λ_{max}^{EtOH} mμ(log ε): 274 (4.11), 301 (3.65). NMR τ: 6.54 (s, 3H, N-C<u>H</u>$_3$). *Anal.* Calcd. for $C_{13}H_{11}O_2N$: C, 73.22; H, 5.02; N, 6.57. Found: C, 73.33; H, 5.61; N, 6.56. The second fraction gave the starting material (220 mg).

Attempted Dehydrogenation of V——a) With Chloranil in *tert*-BuOH: To a solution of V (0.3 g) in *tert*-BuOH (40 ml) was added chloranil (0.2 g) and the resulting mixture was refluxed for 4 hr under N_2 stream. After evaporation of solvent under reduced pressure, the residue was dissolved in $CHCl_3$. The $CHCl_3$ solution was washed with 10% NaOH followed H_2O, dried over anhyd. $MgSO_4$ and evaporated giving a dark blue solid (185 mg). This was purified by passing through Al_2O_3 column using $CHCl_3$ as eluent to give a pure XIX (170 mg), which was identical with the authentic sample by comparison of their IR spectra.

b) With $Hg(OAc)_2$ in Aqueous AcOH: To a solution of V (0.2 g) dissolved in AcOH (15 ml) and H_2O (5 ml), were added $Hg(OAc)_2$ (0.27 g) and EDTA (0.25 g) and the resulting mixture was heated at 75—80° for 6 hr with stirring under N_2 stream. After cooling, the mixture was basified with Na_2CO_3, extracted with $CHCl_3$, and the organic layer was washed with H_2O and dried over anhyd. $MgSO_4$. The residue after evaporation of $CHCl_3$ was purified through Al_2O_3 column chromatography eluted with $CHCl_3$ to give XIX (145 mg), which was identical with the authentic sample prepared by the method a) by comparison of their IR spectra and the mixed melting point determination.

Attempted Dehydrogenation of VI with Chloranil in *tert*-BuOH——To a solution of VI (0.3 g) in *tert*-BuOH (40 ml) was added chloranil (0.2 g) and the resulting mixture was treated as described in the case of V to give XX (165 mg), which was identical with the authentic sample by comparison of their IR spectra and the mixed melting point determination.

1-Benzyl-1,2,3,4,4a,9a-hexahydro-9*H*-indeno[2,1-*b*]pyridine (XXII)——A solution of VII (0.25 g) in EtOH (10 ml) was hydrogenated over PtO_2 (0.1 g) under ordinary condition until one molar equivalent of H_2 was absorbed. The catalyst was filtered and the filtrate was evaporated under reduced pressure. The residue was distilled under reduced pressure to give a colorless oil (XXII) (0.21 g), bp_3 120—125° (bath temp.). NMR τ: 6.35 (q, 2H, N-C<u>H</u>$_2$C$_6$H$_5$). The perchlorate of XXII was recrystallized from EtOH-$(C_2H_5)_2O$ to colorless needles, mp 74—75°. *Anal.* Calcd. for $C_{19}H_{22}O_4NCl$: C, 62.72; H, 6.10; N, 3.85. Found: C, 62.54; H, 5.98; N, 3.63.

1-Methyl-1,2,3,4,4a,9a-hexahydro-9*H*-indeno[2,1-*b*]pyridine (XXIII)——a) From VIII: A solution of VIII (0.3 g) in EtOH (20 ml) was hydrogenated over PtO_2 (0.15 g) under ordinary condition. Evaporation of solvent after filtration of the catalyst gave oily residue, which was distilled under reduced pressure to give a colorless oil (XXIII) (0.25 g), bp_3 120—125° (bath temp.). NMR τ: 7.67 (s, 3H, N-C<u>H</u>$_3$). Mass Spectrum *m/e*: 187 (M^+).

b) From XI: To a solution of amino alcohols (XI) (0.1 g) in pyridine (10 ml) was added TsCl (1.0 g) in small pieces with stirring under ice cooling. After stirring overnight, the reaction mixture was poured into ice water, made alkaline with $NaHCO_3$ and then extracted with $CHCl_3$. The extract was washed with H_2O dried over anhyd. $MgSO_4$ and evaporated. The residue was submitted on column chromatography over Al_2O_3 using benzene as eluent to give crystalline product (0.45 g), which showed the characteristic absorption band of a tosyl group. A solution of crude tosylate in anhyd. $(C_2H_5)_2O$ (10 ml) was added dropwise to suspension of $LiAlH_4$ (0.2 g) and anhyd. $(C_2H_5)_2O$ (10 ml) under ice cooling. The mixture was refluxed for 3 hr before decomposing of excess $LiAlH_4$ by adding H_2O. The $(C_2H_5)_2O$ layer was separated and the aqueous layer was extracted with $(C_2H_5)_2O$. The combined extract was washed with brine, dried over anhyd. $MgSO_4$ and evaporated to give an oily residue, which was identical with the authentic sample prepared as above by comparison of VPC.

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