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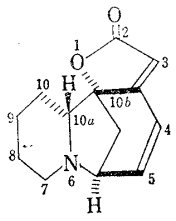
103. Seiichi Saito, Tadasu Tanaka, Keishi Kotera, Hideo Nakai, Norio Sugimoto,*1 Zen-ichi Horii, Masazumi Ikeda, and Yasumitsu Tamura*2 : Structures of Norsecurinine and Dihydronorsecurinine.*3

(*Osaka Research Laboratory, Tanabe Seiyaku Co., Ltd.*1 *and Faculty of Pharmaceutical Sciences, Osaka University*2)

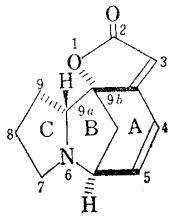
In 1963, Iketubosin and Mathieson[1] first isolated an alkaloid of the molecular formula $C_{12}H_{13}O_2N$ from *Securinega virosa* BAILL. and showed that it is a lower homologue of securinine[2] (I) and, thus, represented by the planar structure (II). This structure led to the name norsecurinine for the alkaloid.

Later, we obtained two alkaloids from *Securinega virosa* PAX. *et* HOFFM. grown in Formosa and showed that one of them is identical with norsecurinine, and the other is its dihydro derivative (III), designated as dihydronorsecurinine.[3,4]

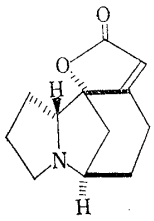
Subsequent chemical degradation on norsecurinine provided a support to the planar structure (II) and further chemical and optical rotatory dispersion (ORD) studies established the absolute stereochemistry (IIa).[4,5] The structure of dihydronorsecurinine, consequently, was established as IIIa.



I



IIa



IIIa

In the present paper we wish to give a detailed account of the experiments on the isolation of norsecurinine and dihydronorsecurinine and on the establishments of their structures (IIa) and (IIIa).

Extraction and Purification

Dried and powdered root barks of *S. virosa* were extracted with ethylene dichloride according to the method reported for the extraction of securinine.[6] The crude extract thus obtained was chromatographed on alumina column using ether as eluent. From the first fraction was obtained dihydronorsecurinine (III) $C_{12}H_{15}O_2N$, m.p. 135~136°, in 0.006% yield.

The second fraction gave norsecurinine (II), which, when freed from the solvent, polymerized to give a white resinous material. In order to prevent the polymerization

*1 962, Kashima-cho, Higashiyodogawa-ku, Osaka (斉藤清一, 田中 雅, 小寺啓司, 仲井英雄, 杉本典夫).
*2 Toneyama, Toyonaka, Osaka-fu (堀井善一, 池田正澄, 田村恭光).
*3 This paper was reported at the 8th Symposium on the Chemistry of Natural Products, Japan (Nagoya, October 21st, 1964).

1) G.O. Iketubosin, D.W. Mathieson : J. Pharm. and Pharmacol., **15**, 810 (1963).
2) *a*) S. Saito, K. Kotera, N. Sugimoto, Z. Horii, Y. Tamura : Chem. & Ind. (London), **1962**, 1652; S. Saito, K. Kotera, N. Shigematsu, A. Ide, N. Sugimoto, Z. Horii, M. Hanaoka, Y. Yamawaki, Y. Tamura : Tetrahedron, **19**, 2085 (1963). *b*) Z. Horii, M. Ikeda, Y. Yamawaki, Y. Tamura, S. Saito, K. Kotera : This Bulletin, **11**, 817 (1963); *Idem* : Tetrahedron, **19**, 2101 (1963).
3) S. Saito, T. Iwamoto T. Tanaka, C. Matsumura, N. Sugimoto, Z. Horii, Y. Tamura : Chem. & Ind. (London), **1964**, 1268.
4) S. Saito, T. Tanaka, K. Kotera, H. Nakai, N. Sugimoto, Z. Horii, M. Ikeda, Y. Tamura : This Bulletin, **12**, 1520 (1964).
5) *Idem* : *Ibid.*, **13**, 614 (1965).
6) S. Saito, T. Tanaka, T. Iwamoto, C. Matsumura, N. Sugimoto, Z. Horii, M. Makita, M. Ikeda, Y. Tamura : Yakugaku Zasshi, **84**, 1126 (1964).

norsecurinine was purified as a stable hydrochloride, which was prepared by adding ethanolic hydrogen chloride to the etherial eluate. Recrystallization of the precipitates from ethanol gave a 1.6% yield of the hydrochloride of II as colorless needles, m.p. 215~216° (decomp.). Pure free base liberated from hydrochloride was rather stable, but gradually polymerized on standing at room temperature causing a separation of a glassy mass. The physical constants for norsecurinine and its derivatives are summerized and compared with those reported by Iketubosin and Mathieson in Table I.

Table I. Some Physical Constants and Spectral Data on Norsecurinine and its Derivatives

	Norsecurinine $C_{12}H_{13}O_2N$	
	Iketubosin and Mathieson's	Ours
Habitat	Nigelia	Formosa
Species	*Securinega virosa* Baill	*Securinega virosa* Pax. et Hoffm.
Yield (%)	0.0037[a]	1.6
m.p. (°C)	81~82	oil[b]
$[\alpha]_D^{20}$	−19.5° (c=0.2, EtOH)	−272° (c=6.9, EtOH)
UV λ_{max}^{EtOH} mμ (ε) :	255.5 (22000), 256.5 (22000)[c]	
IR $\nu_{max}^{CCl_4}$ cm^{-1} :	1802, 1770, 1640	
NMR (60 Mc.p.s. in $CDCl_3$)	4.3 τ singlet (1H), ABX, AB 3~3.6 τ sextet (2H), X 6.37 τ triplet (1H)	
H_2SO_4 salt m.p. (°C)	224~225	——
HCl salt m.p. (°C)	——	223~225 (decomp.)
HCl salt $[\alpha]_D^{20}$	——	−309° (c=1.24, EtOH)
Methiodide m.p. (°C)	194~195 (yellow)	231~232 (colorless)
Picrate m.p. (°C)	232~233 (decomp.)	258~260 (decomp.)

a) Calculated for the hydrochloride.
b) It was crystallized from diisopropyl ether in colorless plates, m.p. 36~37° solvated with the solvent.
c) A shoulder band was observed at 308 mμ in hexane (ε 389), or in dioxane (ε 395) in addition to 255 mμ.

The facts that both specimens showed quite the same nuclear magnetic resonance (NMR) spectra*4 in the whole ranges and had very similar maximum values in the infrared (IR) and ultraviolet (UV) absorption spectra (Fig. 1) suggest both compounds essentially identical. However, there were observed significant differences in specific rotation and melting point on the free base and derivatives, *e.g.*, the picrate and the methiodide. The lower specific rotation of Iketubosin and Mathieson's specimen may be ascribable to contamination*5 of its enantiomer to norsecurinine as has been oberved in the previous investigation on *Securinega suffruticosa* Rehd. var. *amamiensis* Furusawa.[6]

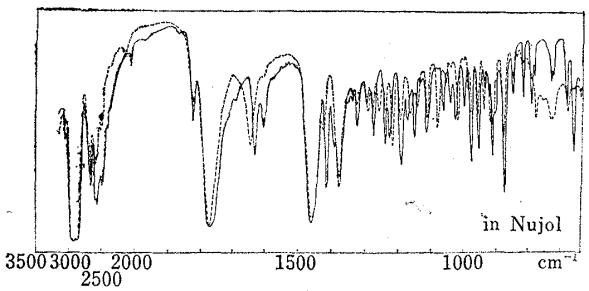


Fig. 1. Infrared Spectra of Norsecurinine (IIa)·hydrochloride and Dihydronorsecurinine (IIIa)·hydrochloride.

——— IIa HCl salt
– – – – – IIIa HCl salt

*4 NMR spectra were measured by JNM A-60 spectrometer (Japan Electron Optical Laboratory Co., Ltd.) opperated at 60Mc.
*5 Degradation product (XIX) derived from norsecurinine of our isolation showed an almost identical ORD curve with that derived from securinine (See Experimental).

Planar Structure

Iketubosin and Mathieson have proposed the planar structure (II) for norsecurinine on the basis of IR, UV, NMR, and mass spectral evidences without any definite chemical evidences. The following degradation and synthesis provided chemical supports to structure (II) as shown in Chart 1.

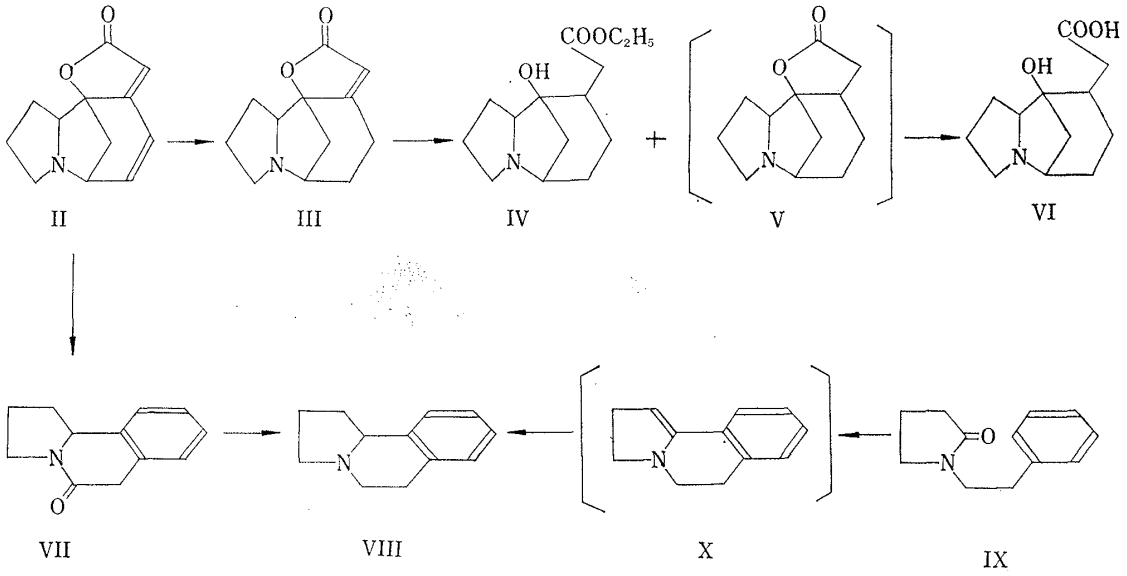


Chart 1.

Reduction of norsecurinine (II) with sodium borohydride afforded a quantitative yield of 4,5-dihydronorsecurinin (III), whose structure was supported by its IR and UV spectra. The IR spectrum of III showed bands at 1820, 1750 (α,β-unsaturated γ-lactone), 1640 cm^{-1} (-C=C-) and the UV spectrum showed a maximum at 214 mμ (ε 14400) due to α,β-unsaturated γ-lactone.

This reduction attitude of II toward sodium borohydride supports structure II in the light of similar attitudes of securinine and allosecurinine.[7] Identification of the synthetic III with the natural dihydronorsecurinine establishes the structure of the latter compound.

Catalytic hydrogenation of III over platinum oxide in ethanol gave a crystalline product (IV) and an oily product. The structure of IV was proved from its NMR spectrum [5.8 τ (2H), quartet due to $-\overset{O}{\overset{\|}{C}}-O-CH_2-CH_3$] and its IR spectrum [3300 (OH) and 1740 cm^{-1} (ester C=O)].

The oily product was supposed to be tetrahydronorsecurinine (V) contaminated with a small amount of IV from the thin-layer chromatography and the IR spectrum. The thin-layer chromatogram showed two spots, one of which has the same Rf-value as that of IV, and the IR spectrum exibited a band at 1790 cm^{-1} (saturated γ-lactone) in addition to that of IV. Column chromatography of the oily product on alumina caused lactone ring opening to give an oxyamino acid (VI) [IR spectrum; 3200 (OH), 2700, 2570 ($-\overset{+}{N}-H$) and 1560 cm^{-1} (COO^-)]. The easy ring opening observed on the reduction products (IV) and (V) might suggest that *trans* lactone rather than *cis* one is formed on the reduction of III.[8]

7) I. Satoda, M. Murayama, J. Tsuji, E. Yoshii: Tetrahedron Letters, **1962**, 1199.
8) Cf. Z. Horii, M. Hanaoka, M. Ikeda, Y. Yamawaki, Y. Tamura, S. Saito, N. Shigematsu, K. Kotera: This Bulletin, **13**, 27 (1965).

Other important chemical evidences for structure II were obtained from the following degradation and synthesis. Reduction of II with zinc-dust and sulfuric acid brought about reductive cleavage of C_{5a}-N bond and ring opening of lactone, followed by aromatization and lactamization, to afford an oily 1,2,3,10*b*-tetrahydropyrrolo[2,1-*a*]-isoquinolin-5(6*H*)-one (VII), which was immediately reduced with lithium aluminum hydride to give an oily base 1,2,3,5,6,10*b*-hexahydropyrrolo[2,1-*a*]isoquinoline (VIII), characterized as the picrate. The following synthesis proved the structure of VIII. Cyclization of 1-phenethyl-2-pyrrolidinone[9] (IX) with phosphorus pentoxide in boiling tetralin gave an unstable red oil (X) which was reduced with sodium borohydride to give racemic VIII, characterized as the picrate. This racemic VIII showed an identical IR spectrum in carbon tetrachloride with that of the natural VIII derived from norsecurinine. (Fig. 2).

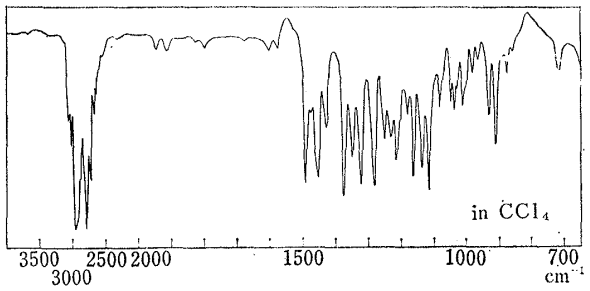


Fig. 2. Infrared Spectrum of 1,2,3,5,6,10*b*-Hexahydropyrrolo[2,1-*a*]isoquinoline (VIII)

These chemical evidences demonstrate obviously the presence of pyrrolizidine

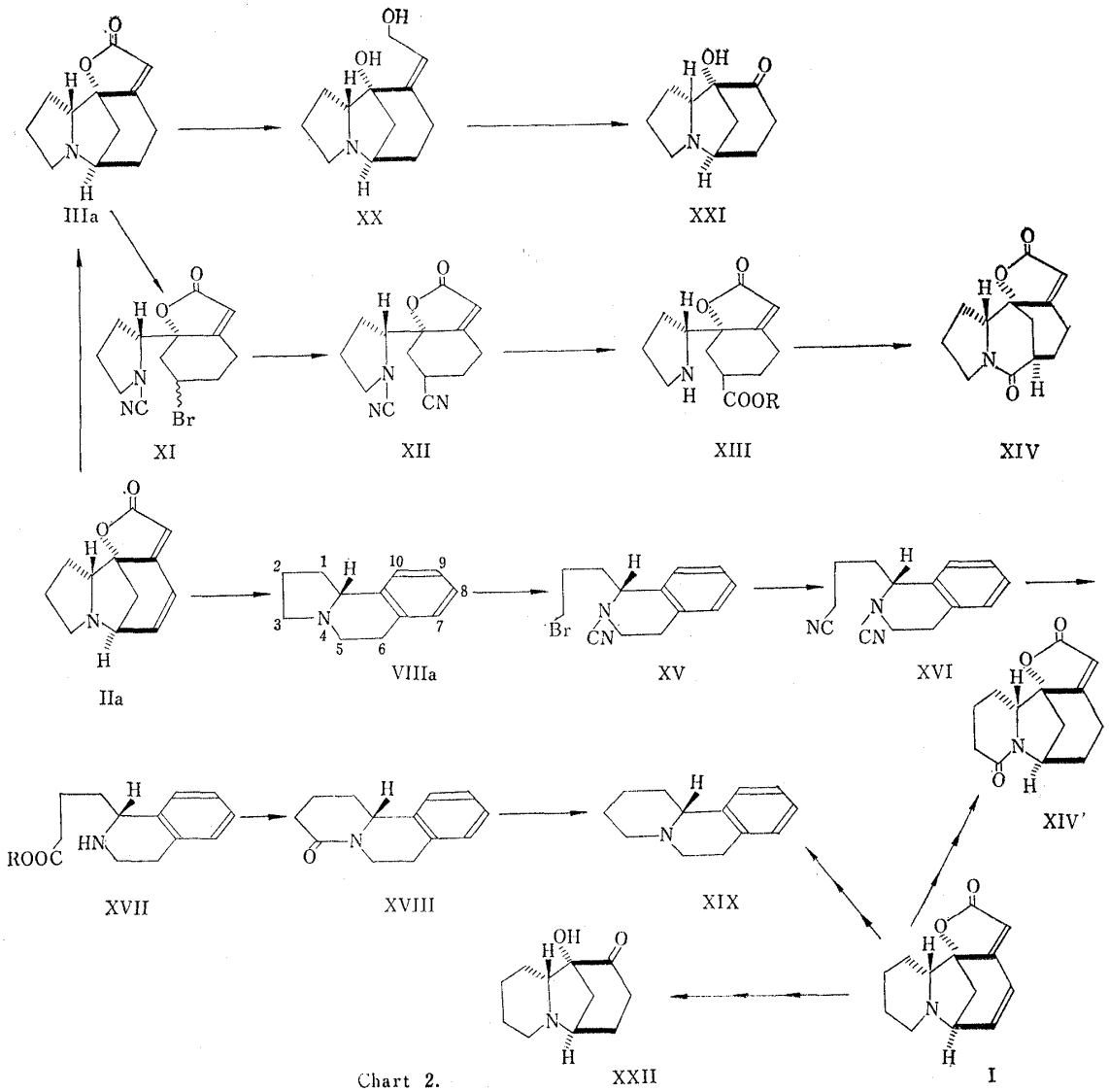


Chart 2.

9) V. Boekelheide, J. C. Godfrey : J. Am. Chem. Soc., **75**, 3679 (1953).

moiety in norsecurinine, and support structure II.

Stereochemistries

The first effort for elucidation of stereochemistry of norsecurinine was made on expansion of its C-ring leading to a derivative (cf. XIV′) of securinine or its stereoisomeric alkaloids, since stereochemistries of all these alkaloids have been estab-lished.[2b,3,6,10~12]

Von Braun reaction of 4,5-dihydronorsecurinine (III), however, caused undesirable cleavage at B-ring to give a bromocyanide (XI) in 85% yield. The structure of XI was supposed from the NMR spectrum, which showed a multiplet signal centered at 5.9 τ (1*H*) due to a proton of the C-Br carbon. As a matter of course, the lactam (XIV) derived from the bromocyanide (XI) was not identical with lactam (XIV′) obtained from securinine by means of ozone oxidation followed by catalytic hydrogenation.

On the other hand, pyrroloisoquinoline (VIIIa) obtained from norsecurinine was found to be cleaved at C_3–N linkage on von Braun degradation and to be derived to a benzoquinolizidine (XIX) by the scheme as shown in Chart 2.

Reaction of VIIIa with cyanogen bromide gave an oily bromocyanide (XV) which was converted to a dicyanide (XVI) in good yield by warming with sodium cyanide in dimethylsulfoxide. Hydrolysis of crude XVI with mineral acid, followed by esterification, gave an aminoester (XVII, R=C_2H_5) which was readily cyclized on distillation *in vacuo*. The resultant lactam (XVIII) was reduced with lithium aluminum hydride giving a benzoquinolizidine (XIX), characterized as the hydrochloride and the perchlorate. The beozoquinolizidine (XIX) was identical with the authentic sample of *R*-(+)-1,3,4,6,7,11*b*-hexahydro-2*H*-benzo[*a*]quinolizine prepared from securinine, by comparison of IR spectra and ORD curves of the free bases as well as by mixed melting point test of the perchlorates.[2b]

Therefore, it is concluded that C_{9a} of norsecurinine possesses the same absolute configuration, namely, *R*-form as that at C_{10a} of securinine.

The absolute configuration at C_{9b} was confirmed by ORD studies. Previously we have established the following relationship between the ORD or circular dichroism (CD) curve and the absolute configuration on securinine, allosecurinine and their derivatives.[12] The sign of ORD Cotton effects as well as of CD maxima at near 250~255 mμ depends upon the skewness of the transoid diene chromophore conjugated with γ-lactone. It is speculated from Dreiding models that the direction of this skewness reflects the absolute configuration at C_{10b} of these compounds. Therefore, it is concluded that the absolute configuration at C_{10b} can be determined from the sign of ORD Cotton effect or CD maximum at near 250 mμ: when the sign is negative, C_{10b} should possess *S*-configuration.

This relationship would be applicable to norsecurinine since it contains the same rigid transoid diene system conjugated with γ-lactone. Norsecurinine and its hydrochloride showed a strong negative ORD Cotton*[6,4] effect and a negative CD maximum*[7] at 255 mμ as in the cases of securinine and allosecurinine. These results indicate that the absolute configuration at C_{9b} of norsecurinine should be *S*-form.

A further evidence was obtained from the ORD study on the α-ketol (XXI) which was derived from 4,5-dihydronorsecurinine (III) as shown in Chart 2.

Reduction of III with lithinm aluminum hydride afforded the diol (XX) which was oxidized by ozone to the α-ketol (XXI). The ORD curve of the α-ketol (XXI) showed

*6 ORD curves were measured with a Rudolph automatic recording spectropolarimeter at 20~25°.
*7 CD curve was measured with a Shimadzu CD spectrophotometer "Dichrograph."
10) S. Imado, M. Shiro, Z. Horii: Chem. & Ind. (London), **1964**, 1691.
11) T. Nakano, T. H. Yandg, S. Terao: *Ibid.*, **1963**, 1763.
12) Z. Horii, M. Ikeda, Y. Tamura, S. Saito, M. Suzuki, K. Kotera: This Bulletin, **12**, 1118 (1964).

a negative ORD Cotton effect.[4] Comparison of ORD curve of the α-ketol (XXI) with that of the α-ketol (XXII) derived from securinine,[2b] or the application of octant rule[13] to XXI led also to the conclusion that absolute configuration at C_{9b} is *S*-form.

Now, it is established that the absolute configuration at C_{9a} is *R*-form and at C_{9b} *S*-form. Accordingly, the full stereochemistry of norsecurinine are represented by structure IIa.

This structure could interpret well the stereochemistry of the following degradation products as shown in Chart 3. The degradation was carried out according to the method[2a] as have been used in the investigation of the relative configuration of securinine.

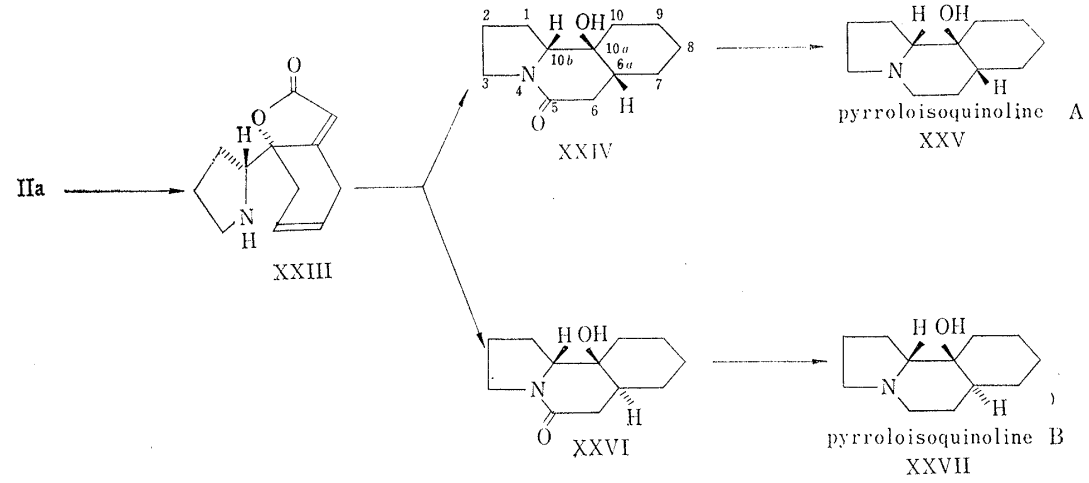


Chart 3.

Reduction of norsecurinine with aluminum amalgam in wet ether caused a fission of C_{5a}-N linkage, followed by an isomerization of one of the double bonds, to give a *sec*-amine (XXIII). The *sec*-amine (XXIII) was hydrogenated in two different manners. Catalytic hydrogenation with Raney nickel in the presence of potassium hydroxide afforded a lactam carbinol (XXIV), m.p. 168~169°, designated pyrroloisoquinoline-lactam A while reduction with platinum oxide gave another lactam carbinol (XXVI), m.p. 181~183°, designated pyrroloisoquinoline-lactam B. From consideration of the stereochemical attitudes[2a,14] of these hydrogenation in the conversion from securinine to lactam-carbinol A and B, it is assumed that both pyrroloisoquinoline-lactams is epimers at C_{6a}. Both lactam carbinols were reduced with lithium aluminum hydride. The former lactam carbinol (XXIV) gave a product (XXV) of m.p. 143~144°, designated as pyrroloisoquinoline A and the latter lactam carbinol (XXVI) gave XXVII, designated as pyrroloisoquinoline B.

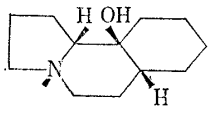
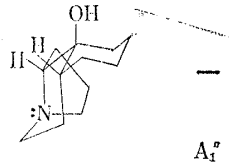
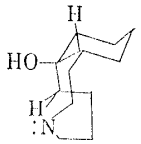
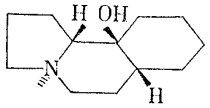
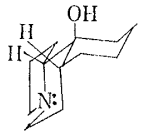
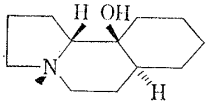
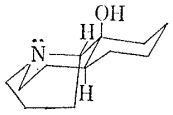
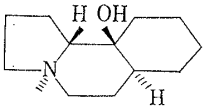
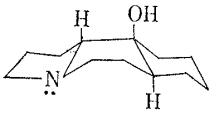
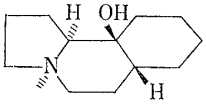
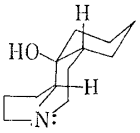
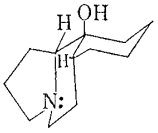
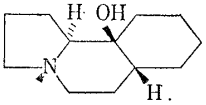
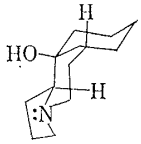
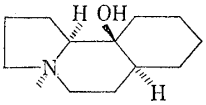
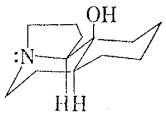
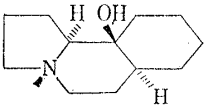
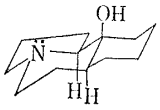
Theoretically, four diastereoisomers are possible for dodecahydropyrrolo[2,1-*a*]isoquinolin-10*a*-ol. Possibilities of Bohlmann's bands[15,16] and a band due to intramolecular hydrogen bonding between lone pair of the bridgehead nitrogen and the hydroxyl group in the IR spectra of these isomers are shown in Table II.

The IR spectrum*[8] of pyrroloisoquinoline A in carbon tetrachloride showed the presence of the Bohlmann's bands at 2778 and 2715 cm^{-1} and the absence of the band

*8 Measured on grating infrared spectrometer (Japan Spectroscopic Manufacturing Co., DS 402G).

13) W. Klyne : Tetrahedron, **13**, 29 (1961).
14) Z. Horii, Y. Yamawaki, M. Hanaoka, Y. Tamura, S. Saito, H. Yoshikawa : This Bulletin, **13**, 22 (1965).
15) F. Bohlmann : Chem. Ber., **91**, 2157 (1958).
16) K. Kotera : Tetrahedron, **12**, 248 (1961); Y. Sato, N. Ikegawa : J. Org. Chem., **26**, 1945 (1961); N. J. Leonard, W. K. Musker : J. Am. Chem. Soc., **82**, 5148 (1960).

Table II. Relative Configurations and Conformations of Dodecahydropyrrolo[2,1-*a*]isoquinolin-10a-ol.

		BA	IH		BA	IH
A_1	 *cis-syn-cis*	—	+	 A_1''	—	—
	 A_1'					
A_2	 *cis-syn-trans*	+	—			
						
B_1	 *trans-syn-cis*	—	+			
						
B_2	 *trans-syn-trans*	+	—			
						
C_1	 *cis-anti-cis*	—	—	 C_1''	—	—
	 C_1'					
C_2	 *cis-anti-trans*	+	+			
						
D_1	 *trans-anti-cis*	—	—			
						
D_2	 *trans-anti-trans*	+	+			
						

due to the intramolecular hydrogen bonding, whereas the spectrum of pyrroloisoquinoline B showed the absence of the former bands and the presence of the latter band at 3560 cm^{-1}. These results suggested the two possibilities on the structures of pyrroloisoquinoline A and B. One is that pyrroloisoquinoline A has structure A_2 and pyrroloisoquinoline B has structure B_1. The other is that pyrroloisoquinoline A has structure B_2 and B has A_1 existing as conformer A_1. Of these possibilities the former

would be more reasonable because *trans-syn-trans*[*9] conformer B_2 with boat-formed piperidine ring is less stable than its conformer B_1.

Therefore, it is concluded that the relative configuration between C_{10a}-O and C_{10b}-H in pyrroloisoquinoline A and B is *cis* or C_{9a}-H and C_{9b}-O in norsecurinine are *trans*. The conclusion is in agreement wlth the absolute structure (IIa). Furthermore, this successful assignment of IR spectra would provide an example showing a utility of the Bohlmann's *trans*-quinolizidine band for the stereochemical assignment of octahydroindolizine derivatives.

Structure of dihydronorsecurinine, a minor alkaloid, was assigned as 4,5-dihydronorsecurinine (III) at the beginning of this section. The absolute structure of dihydronorsecurinine is now represented by structure IIIa.

Experimental[*10]

Extraction of Norsecurinine (IIa) dihydronorsecurinine (IIIa)——Dried finely powdered root barks of *S. virosa* (2 kg.) were immersed in $Cl\cdot CH_2\cdot CH_2Cl$ (7.5 L.) containing 10% NH_4OH (400 ml.). After standing at 20~25° for 24 hr. with occational stirring the mixture was filtered by suction and the residue was then extracted by the same operation as described above for 2 more times. The whole organic layer was distilled *in vacuo* under 60° to dryness and the dark green viscous residue was dissolved in ether (300 ml.). After the removal of the undissolved impurities, the yellow solution was chromatographed on alumina (62×2.8 cm.) using ether as eluent. The eluate was separated into 100 ml. fractions and the each fraction was checked by means of thin-layer chromatography, (TLC) (acetone-ether-28% NH_4OH=5:5:1 solvent). After the elution of non basic yellow band, the fractions which showed Rf 0.39 were collected (about 200 ml.).

Evaporation of ether gave a white solid, which on repeated recrystallization from EtOAc afforded dihydronorsecurinine (IIIa) (0.12 g.) in colorless rhombs, m.p. 135~136°. ORD in dioxane (c=1.06); $[\alpha]_{589}$ −13°, $[\alpha]_{300}$ −1110°. *Anal.* Calcd. for $C_{12}H_{15}O_2N$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.11; H, 7.25; N, 6.54. The hydrochoride was crystallized from EtOH-ether in colorless needles, m.p. 228~230° (decomp.). *Anal.* Calcd. for $C_{12}H_{16}O_2NCl$: C, 60.12; H, 5.88; N, 5.84. Found: C, 60.00; H, 5.97: N, 5.75.

The methiodide was crystallized from MeOH in colorless plates, m.p. 273~274° (decomp). *Anal.* Calcd. for $C_{13}H_{18}O_2NI$: C, 44.97; H, 5.52; N, 4.03. Found: C, 44.94; H, 4.80; N, 4.24.

The following fractions which showed Rf 0.37 were collected (about 900 ml.) and to the eluate, while cooling, 20% EtOH-HCl was added. The precipitates, after standing in a refligerator for 2 hr. were collected and crystallized from EtOH to give IIa hydrohloride (34.2 g.) in colorless fine needles, m.p. 223~225° (decomp.). ORD in MeOH (c=0.00204); $[\alpha]_{265}$ −19000°, $[\alpha]_{235}$ +24500°. IR ν_{max}^{Nujol} cm^{-1}: 1822, 1770 ($\alpha\beta$-unsat. γ-lactone) 1635 (-C=C-). UV λ_{max}^{EtOH} $m\mu$ (ε): 254 (16300). *Anal.* Calcd. for $C_{12}H_{14}O_2NCl$: C, 60.12; H, 5.88; N, 5.84. Found: C, 60.02; H, 5.36; N, 5.70.

The free base IIa was obtained from the hydrochloride by neutralization with $(C_2H_5)_2NH$ and little amount of H_2O in ether suspension as an unstable water-soluble viscous liquid. ORD in dioxane (c=0.00241); $[\alpha]_{274}$ −16500°, $[\alpha]_{250}$ +8300°. CD in dioxane (c=1.42~0.028); $[\theta]_{350}$ 0, $[\theta]_{255}$ −960,000, $[\theta]_{240}$ −360,000. The picrate was crystallized from dimethyl formamide in yellow needles, m.p. 251~253° (decomp.). *Anal.* Calcd. for $C_{18}H_{16}O_9N_4$: C, 50.00; H, 3.73; N, 12.96. Found: C, 50.27; H, 3.47; N, 12.92.

The methiodide was crystallized from MeOH in colorless plates, m.p. 231~232°. *Anal.* Calcd. for $C_{13}H_{16}O_2NI$: C, 45.23; H, 4.67; N, 4.05. Found: C, 45.19; H, 4.75; N, 4.15.

4,5-Dihydronorsecurinine (IIIa)——IIa hydrochloride (1.8 g.) suspended in abs. ether (30 ml.) was neutralized by the addition of H_2O (2 ml.) and $(C_2H_5)_2NH$ (1.7 ml.). From the ether layer, after drying over anhyd. K_2CO_3, crude norsecurinine (1.2 g.) was discovered.

A solution of $NaBH_4$ (0.57 g.) in EtOH (15 ml.) was added to a solution of foregoing crude IIa in EtOH (20 ml.). After stirring for 4 hr. at 25~30°, AcOH (2.5 ml.) was added to the solution and the solvent

[*9] The prefixes *cis* and *trans* refer to the stereochemistry of the fusion of the individual terminal rings to the center rings, whereas *syn* and *anti* are used to denote the orientation of the terminal rings with respect to each other.

[*10] All melting points are uncorrected. In column chromatography, aluminum oxide standardized (E. Merck) was used. Thin-layer chromatography was on silica gel G (E. Merck). The spots were detected by spraying with the Dragendroff reagent.

was distilled *in vacuo*. The residue was suspended in ether and made free from AcOH salt by the addition of $(C_2H_5)_2NH$ (2 ml.) and a few drops of H_2O. The etherial layer was dried over anhyd. Na_2SO_4 and the solvent was removed leaving white solid which crystallized from AcOEt–Petr. ether to give IIIa (1.1 g.) in colorless rhombs, m.p. 135~136°. IIIa was fairly soluble in H_2O. This compound was identified with natural dihydronorsecurinine in the comparison of IR spectra and ORD curves.

Reduction of 4,5-Dihydronorscurinine——A solution of IIIa (0.740 g.) in abs. EtOH (15 ml.) was shaken with H_2 at room temperature and atmospheric pressure in the presence of $PtO_2 \cdot 2H_2O$ (0.10 g.). About 1.1 moles (110 ml.) of H_2 was absorbed during 2 hr. and absorption stopped. The catalyst was filtered and the solvent was distilled *in vacuo* leaving a cololess slurry from which the colorless needles were separated by filtration. It is recrystallized from AcOEt to give the hydroxy ethylester (IV) (0.475 g.) in colorless needles, m.p. 152~153°. *Anal.* Calcd. for $C_{14}H_{23}O_3N$: C, 66.37; H, 9.15; N, 5.53. Found : C, 66.29; H, 9.21; N, 5.92.

The viscous colorless filtrate, obtained from the filtration of the slurry, was dissolved in ether (10 ml.) and chromatographed on alumina column (35×1.5 cm.) using ether and then ether–MeOH (99:1) as eluent.

The first eluent gave IV (Rf 4.6 on TLC ($HN(C_2H_5)_2$–hexane=5:9)) and the latter gave a white solid which was crystallized from MeOH–ether to give the hydroxy acid (VI) (0.12 g.) in colorless sandy crystals, m.p. 290~292°. *Anal.* Calcd. for $C_{12}H_{19}O_3N$: C, 63.97; H, 8.50; N, 6.22. Found : C, 63.78; H, 8.37; N, 6.30.

1,2,3,10*b*-Tetrahydropyrrolo[2,1-*a*]isoquinolin-5(6*H*)-one (VII)——To a stirred solution of IIa (1.2 g.) in conc. H_2SO_4 (20 g.) and EtOH (15 ml.) was added Zn dust (10 g.) in 10 portions during 30 min. at 15~20°. After stirring for 20 hr. at the same temperature, inorganic material was filtered off and the mother liquor was neutralized with 28% NH_4OH. The solvent was disttilled *in vacuo* and the residue was dissolved in 20% KOH (20 ml.). The separated oil was taken up in ether and the ether layer was dried over anhyd. K_2CO_3. Evaporation of the solvent left a yellow turbid oil which had $b.p._{0.07}$ 160~170° (bath temp.). The oil was so unstable that it turned to a tan colored turibid oil on expesure to the air.

This oil formed hydrochloride by the usual way in colorless needles, m.p. 145~146° (decomp.) from EtOH–ether, but it changed into black in color during drying on P_2O_5.

***R*-(+)-1,2,3,5,6,10*b*-Hexahydropyrrolo[2,1-*a*]isoquinoline (VIII)**——To a stirred suspension of $LiAlH_4$ (0.6 a.) in anhyd. ether (300 ml.) was added dropwise a solution of VII (0.585 g.) in abs. ether (10 ml.). After stirring for 20 hr. at 20~25°, the suspension was refluxed for 5 hr. After cooling, the complex salt was decomposed by addition of H_2O (3 ml.) and the inorganic material was filtered off. The filtrate was dried over anhyd. Na_2SO_4 and the solvent was distilled leaving a yellow oil VIII (0.35 g.) which had $b.p._{0.09}$ 120~125° (bath temp.). ORD in MeOH : C=0.651 (650~310 mμ), C=0.195 (310~250 mμ); $[\alpha]_{650}$ +62°, $[\alpha]_{589}$ +77°, $[\alpha]_{400}$ +170°, $[\alpha]_{310}$ +323°, $[\alpha]_{261}$ −103, $[\alpha]_{250}$ +103°. The picrate was obtained from EtOH in yellow needles, m.p. 170~172° (decomp.). *Anal.* Calcd. for $C_{18}H_{18}O_7N_4$: C, 53.73; H, 4.51; N, 13.93. Found : C, 53.81; H, 4.49; N, 13.88.

2,3,5,6-Tetrahydropyrrolo[2,1-*a*]isoquinoline (X)——To a boiling suspension of P_2O_5 (20.0 g.) in tetralin (65 ml.) was added 1-phenethyl-2-pyrrolidinone (IX) (3 g.) and boiling was continued for 1.5 hr. An additional portion of P_2O_5 (12.5 g.) in tetralin (25 ml.) was added and the mixture was heated again for 45 min. After cooling tetralin layer was decanted from the solidified mass and the mass was decomposed by addition of ice (200 g.). The resultant solution was neutralized by 10% KOH and the separated oil was taken up in ether. The etherial solution was dried over anhyd. $MgSO_4$. Evaporation of solvent left an unstable yellow oil of X which changed to red color on exposing to the air. For the next process crude X was used directly without purification.

***rac.*-1,2,3,5,6,10*b*-Hexahydropyrrolo[2,1-*a*]isoquinoline (VIII)**——To the stirred solution of crude X (1.7 g.) in MeOH (20 ml.) was added $NaBH_4$ (0.5 g.) in MeOH (10 ml.) and the stirring continued for 4 hr. at 20~25°. The reaction mixture was decomposed by addition of AcOH (1 ml.) then the solvent was removed *in vacuo*. The residue was dissolved in 10% HCl and the solution was extracted with ether to remove any non basic substances. The H_2O layer was made alkaline with 10% NaOH and the separated oil was extracted with ether. The solvent was distilled off and the residual yellow oil was distilled to give racemic VIII (0.74 g.) in a colorless oil, $b.p._{6\sim7}$ 144~148°.

The picrate was crystallized from dioxane in yellow needles, m.p. 165~168°. *Anal.* Calcd. for $C_{18}H_{18}O_7N$: C, 53.74; H, 4.51; N, 13.93. Found : C, 53.88; H, 4.73; N, 13.62.

2-(1-Cyano-2-pyrrolidinyl)-2-hydroxy-4-bromo-$\Delta^{1,\alpha}$-cyclohexane-acetic Acid γ-Lactone (XI)——To a solution of IIIa (4.0 g.) in $CHCl_3$ (60 ml.) was added a solution of BrCN (2.4 g.) in $CHCl_3$ (50 ml.) and the resultant solution was refluxed for 2.5 hr. After cooling, the solution was washed with 5% $NaHCO_3$, saturated NaCl and dried over anhyd. $MgSO_4$. Evaporation of the solvent left the solid residue which was crystallized from dioxane to give (4.17 g.) in colorless leaflets, m.p. 197~198°. IR ν_{max}^{Nujol} cm^{-1} : 2230 (-N-C≡N). Br (+). *Anal.* Calcd. for $C_{13}H_{15}O_2N_2Br$: C, 50.17; H, 4.85; N, 9.00. Found : C, 50.41; H, 4.55; N, 9.20.

2-(1-Cyano-2-pyrrolidinyl)-2-hydroxy-4-cyano-$\Delta^{1,\alpha}$-cyclohexane-acetic Acid γ-Lactone (XII)——NaCN (0.3g.) was suspended in $(CH_3)_2SO$ (7 ml.). To the suspension, while stirring, finely powdered XI (1.5 bg.)

was added at once and the whole was heated at 70～85° for 1.5 hr. The reaction mixture was then poured onto the mixture of HCl and crashed ice and the separated oil was extracted with $CHCl_3$. The $CHCl_3$ layer was washed with 5% $NaHCO_3$ and saturated NaCl, and dried over anhyd. Na_2SO_4. The solvent was distilled *in vacuo* leaving a tan colored viscous oil which solidified gradually on standing in a refrigerator. Repeated recrystallization from AcOEt-Petr. ether gave XI (0.72 g.) in slightly yellow plates, m.p. 132～134°. IR ν_{max}^{Nujol} cm^{-1}: 2240 (-C-C≡N), 2200 (-N-C≡N). *Anal.* Calcd. for $C_{14}H_{15}O_2N_3$: C, 65.35; H, 5.88; N, 16.33. Found: C, 65.28; H, 5.62; N, 16.09.

6-Oxo-4,5-dihydro-B-homonorsecurinine (XIV)——A mixture of XII (0.57 g.) and 12% HCl wsa refluxed for 16 hr. and the solvent was distilled *in vacuo*. The solid residue was suspended in EtOH (16 ml.) and dry HCl gas was derived for 1 hr. while cooling in ice-bath. Then, the mixture was refluxed for 1 hr. HCl gas was again derived for one more hour, and kept overnight at room temperature. EtOH was distilled and to the residual slurry was added 10% K_2CO_3 (20 ml.). The separated oil was extracted with AcOEt and dried over anhyd. K_2CO_3. Evaporation of the solvent left a colorless liquid which was purified by distillation to give XIV (0.284 g.) in a colorless liquid, $b.p._{0.07}$ 190～210° (bath temp.). It was solidified on standing at room temperature. Crystallization from AcOEt gave m.p. 214～216° of colorless needles. IR ν_{max}^{Nujol} cm^{-1}: 1812, 1755 ($\alpha\beta$-unsatd. γ-lactone) 1635 (lactam -C=O). *Anal.* Calcd. for $C_{13}H_{15}O_3N$: C, 66.93; H, 6.48; N, 6.01. Found: C, 67.25; H, 6.19; N, 6.16.

1-(3-Bromopropyl)-2-cyano-1,2,3,4-tetrahydroisoquinoline (XV)——To a solution of VIIIa (1.43 g.) in $CHCl_3$ (7 ml.) was added BrCN (1.05 g.) dissolved in $CHCl_3$ (10 ml.). The mixture was refluxed for 2 hr. then washed with 5% $NaHCO_3$, and dried. Evaporation of the solvent left a yellow oil of XV which decomposed on being distilled *in vacuo*. The crude XV was used for the next operation without purification.

2-Cyano-1, 2, 3, 4-tetrahydro-1-isoquinolinebutyronitrile (XVI)——To a stirred suspension of NaCN (0.47 g.) in $(CH_3)_2SO$ (5 ml.) was added a solution of foregoing crude bromide XV (2.46 g.) in $(CH_3)_2SO$ (3 ml.) and the whole was heated at 90～95° for 2 hr. The resultant brown colored viscous liquid was poured into H_2O and extracted with $CHCl_3$. The $CHCl_3$ layer was washed with H_2O and dried. Removal of the solvent afforded, after distillation, XVI (1.06 g.) in a yellow oil, $b.p._{0.07}$ 220～230° (bath temp.). *Anal.* Calcd. for $C_{14}H_{15}N_3$: N, 18.65. Found: N, 18.39.

1,2,3,6,7,11*b*-Hexahydro-4*H*-benzo[*a*]quinolizin-4-one (XVIII)——A mixture of XVI (1.06 g.) in conc. HCl (15 ml.) and dioxane (5 ml.) was refluxed for 14 hr. The solvent, after treating with decolorizing carbon, was distilled off and the residue was suspended in abs. MeOH (12 ml.) and dry HCl gas was bubbled into the suspension for 2 hr. without external cooling. After standing at room temperature for 14 hr. the solvent was distilled and 10% K_2CO_3 solution was added to the residue. Separated oil was taken up in ether and dried over anhyd. K_2CO_3. Solvent was removed and the residual oil was purified by distillation to give XVIII (0.585 g.) as colorless oil, $b.p._{0.04}$ 150～160° (bath temp.).

1,3,4,6,7,11*b*-Hexahydro-2*H*-benzo[*a*]quinolizine (XIX)——To a stirred suspension of $LiAlH_4$ (0.5 g.) in abs. ether (20 ml.) was added at 20～25° a solution of XVIII (0.585 g.) in ether (5 ml.). The mixture was stirred for 5 hr. at the same temperature then refluxed for 5 hr. After cooling, the complex salt was decomposed by H_2O (3 ml.) and the inorganic salt was filtered off.

The solvent, after drying over anhyd. K_2CO_3, was removed leaving an orange oil which was distilled to give XIX (0.385 g.) in a slightly yellow oil, $b.p._{0.04}$ 110～120° (bath temp.). ORD in MeOH (c=0.735); $[\alpha]_{700}$ +88.5°, $[\alpha]_{589}$ +123.0, $[\alpha]_{400}$ +327.0°, $[\alpha]_{350}$ +476.0°, $[\alpha]_{310}$ +657.0°. The perchlorate was crystallized from MeOH-ether in colorless needles, m.p. 165～166°. *Anal.* Calcd. for $C_{13}H_{18}O_4NCl$: C, 54.26; H, 6.31; N, 4.86. Found: C, 54.14; H, 6.07; N, 5.32.

Diol (XX)——To a stirred suspension of $LiAlH_4$ (0.150 g.) in abs. ether (40 ml.) was added a mixture of IIIa (0.500 g.) in abs. ether (30 ml.) and anhyd. tetrahydrofuran (5 ml.). After stirring for 3 hr. at 20～25° the mixture was refluxed for 1 hr. The reaction mixture was decomposed by addition of H_2O (1 ml.) and the inorganic salt was filtered off. The filtrate was dried over $MgSO_4$ and the solvent removed leaving a white crystalline residue which recrystallized from MeOH-diisopropyl ether to give XX (0.41 g.) in colorless cubics, m.p. 92～93°.

The picrate was crystallized from EtOH-petr. ether in yellow needles, m.p. 194～195°. *Anal.* Calcd. for $C_{15}H_{22}O_9N_4$: C, 49.32; H, 5.06; N, 12.78. Found: C, 49.80; H, 5.04; N, 12.62.

α-Ketol (XXI)——To a solution of XX (0.40 g.) in 10% HCl (1 ml.) and H_2O (30 ml.) was bubbled at 0° ozone gas for 2 hr. Then the temperature was rised to 60° and the gas continued to pass through for additional 1 hr. After cooling, K_2CO_3 was added to make the reaction mixture alkaline and the separated oil was taken up in $CHCl_3$. The solvent, after drying over $MgSO_4$, was distilled and the residue was purified by crystallization from EtOH-acetone to give XXI (0.14 g.) in colorless plates, m.p. 120～121°. ORD in MeOH (c=0.131); $[\alpha]_{305}$ −2400°, $[\alpha]_{262}$ +4200°. IR ν_{max}^{Nujol} cm^{-1}: 3380 (-OH), 1715 (-C=O). *Anal.* Calcd. for $C_{12}H_{15}O_2N$: C, 66.27; H, 8.34. Found: C, 66.21; H, 8.86.

6-Hydroxy-6-(2-pyrrolidinyl)-3-cyclohexene-$\Delta^{1,\alpha}$-acetic Acid γ-Lactone (XXIII)——To a stirred mixture of Al-Hg (1.4 g.) and IIa (0.44 g.) in ether (10 ml.) was added H_2O (0.2 ml.) at 20～25°. After stirring for 30 min. an additional H_2O (0.2 ml.) was dropped and the stirring continued for 6 hr. The inorganic

salt was filtered and the filtrate was dried over anhyd. Na_2SO_4. The solvent was distilled to leave an unstable yellow solid which was crystallized from ether-petr. ether to give XXIII (0.32 g.) in colorless rhombs, m. p. 87~88°. UV λ_{max}^{EtOH} mμ (log ε) : 210 (3.68). The N-benzoyl derivate as prepared from crude XXIII with benzoyl chloride in pyridine by usual way. It was crystallized from EtOH-petr. ether in colorless rhombs, m.p. 159~161°. *Anal.* Calcd. for $C_{19}H_{19}O_3N$: C, 73.76; H, 6.19; N, 4.53. Found : C, 73.53; H, 6.10; N, 4.66.

Pyrroloisoquinoline Lactam A (XXIV)——XXIII (0.8 g.) was dissolved in a mixture of KOH (0.8 g.) in tetrahydrofuran (40 ml.) and H_2O (15 ml.). The solution was shaken with H_2 at room temperature and atmospheric pressure in the presence of Raney Ni (W-7) (0.6 g.). About 2 molar eqnivalents of H_2 was absorbed during 1.5 hr. and the absorption stopped. The catalyst was filtered and the filtrate was heated at 85~90° for 30 min. Then, tetrahydrofuran was distilled off at atmospheric pressure. After cooling, the solution was made acidic with 10% HCl and extracted with $CHCl_3$. From the extracts, after drying and evaporating the solvent, obtained a yellow solid residue which was crystallized from AcOEt to give XXIV (0.4 g.) in colorless needles, m.p. 168~169°. IR ν_{max}^{Nujol} cm^{-1} : 3200 (-OH), 1615 (lactam -C=O). *Anal.* Calcd. for $C_{12}H_{19}O_2N$: C, 68.86; H, 9.15; N, 6.69. Found : C, 68.67; H, 8.67; N, 6.87.

Pyrroloisoquinoline Lactam B (XXVI)——A solution of XXIII (1.0 g.) in abs. EtOH (50 ml.) was shaken with H_2 at room temperature and atmospheric pressure in the presence of $PtO_2 \cdot 2H_2O$ (0.20 g.).

Two molar equivalents of H_2 was absorbed during 3 hr. and the absorption stopped. The catalyst was filtered and the filtrate was refluxed for 3 hr. and then the solvent was distilled *in vacuo* to leave a viscous colorless oil which solidified gradually on standing at room temperature.

Crystallization from acetone afforded XXVI (0.721 g.) in colorless rhombs, m.p. 181~183°. IR ν_{max}^{Nujol} cm^{-1} : 3250 (-OH), 1605 (lactam -C=O). *Anal.* Calcd. for $C_{12}H_{19}O_2N$: C, 68.86; H, 9.15; N, 6.69. Found : C, 69.50; H. 9.01; N, 6.51.

Pyrroloisoquinoline A (XXV)——To a stirred suspension of $LiAlH_4$ (0.70 g.) in anhyd. tetrahydrofuran (20 ml.) was added a solution of XXIV (0.345 g.) in tetrahydrofuran (5 ml.) at 20~25°. The mixture was stirred for 5 hr. at the same temperature and then refluxed for 5 hr. After cooling, H_2O (2 ml.) was added and the inorganic salt was filtered. From the filtrate, after drying and evaporating the solvent, obtained a yellow soild (0.180 g.) which was crystallized from hexane in colorless needles, m.p. 143~144°. *Anal.* Calcd. for $C_{12}H_{21}ON$; C, 73.79; H, 10.84; N, 7.17. Found : C, 74.25; H, 10.43; N, 7.14.

Pyrroloisoquinoline B (XXVII)——The pyrroloisoquinoline lactam B (XXVI) was reduced with $LiAlH_4$ by the same operation as stated above to give XXII in a yellow oil, b.$p_{0.09}$ 100~105°.

The picrate was crystallized from EtOH in yellow fine needles, m.p. 252~253° (decomp.). *Anal.* Calcd. for $C_{18}H_{24}O_8N_4$: C, 50.94; H, 5.70; N, 13.20. Found : C, 51.21; H, 5.33; N, 12.81.

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Summary

Two alkaloids, norsecurinine and dihydronorsecurinine, were isolated from the root barks of *Securinega virosa* BAILL. Their planar structures and absolute stereochemistries were elucidated.

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