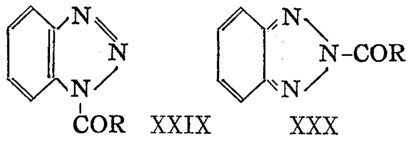
XXIX XXX

Chart 3.

Benzotriazole Derivatives

Acylation of benzotriazole (VI) should give an unsymmetric compound (XXIX) and a symmetric one (XXX). In the symmetric model compound, the aromatic protons exhibited the pattern of A_2B_2 system (Fig. 1, A, B), while in the unsymmetric compounds the pattern of this system disappeared (Fig. 1, C, D).

Since the nuclear magnetic resonance spectra of N-aryloxyacylbenzotriazoles synthesized showed no A_2B_2 system, these compounds should be assigned to 1-aryloxyacylbenzotriazoles (XXIX).

The authors wish to express their deep gratitude to Dr. T. Harukawa of these laboratories for his encouragement and to Takeda Chemical Industries, Ltd. for permission to publish this report. Thanks are also due to Miss F. Kasahara for the NMR spectra measurement.

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Structure and Stereochemistry of Norsecurinine and Dihydronorsecurinine

Two alkaloids have now been isolated from the roots of *Securinega virosa* PAX. et HOFFM. grown in Formosa. The first base has a molecular formula $C_{12}H_{13}O_2N$ [the hydrochloride, m.p. 225° (decomp.), IR ν_{max}^{Nujol} cm^{-1} : 1821, 1770, 1635, UV : λ_{max}^{EtOH} 254 mμ (ε (17,600), $[\alpha]_D^{20}$ −309° (c=1.24, EtOH) (*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 methiodide, 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, 4.16); the picrate, m.p. 258~260° (decomp.) (*Anal.* Calcd. for $C_{18}H_{16}O_8N_5$: C, 50.00; H, 3.73; N, 12.96. Found: C, 50.27; H, 3.47; N, 12.92)]. The free base [$[\alpha]_D^{23}$ -272° (c=6.9, EtOH), IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1802, 1770, 1640, UV : λ_{max}^{EtOH} 256.5 mμ (ε 22,000), obtained as an oil from the hydrochloride] showed the same nuclear magnetic resonance, infrared and ultraviolet spectra as those reported by Iketubosin and Mathieson[1] for norsecurinine [m.p. 81~82°, $[\alpha]_D^{20}$ −19.5° (c=0.2, EtOH), IR $\nu_{max}^{CCl_4}$ cm^{-1} : 1802, 1770, 1640, UV : λ_{max}^{EtOH} 255.5 mμ (ε 22,000); the methiodide, m.p. 194~195°; the picrate, m.p. 232~233°]. This proves both alkaloids to be identical. However, there is a considerable discrepancy in the physical constants between the specimens obtained by both groups. The lower specific optical rotation shown by the Iketubosin and Mathieson's specimen may be ascribable to contamination of its enantiomer as has been observed in case of *Securinega suffruticosa* REHD. var. *amamiensis* FURUSAWA.[2]

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[1] G. O. Iketubosin, D. W. Mathieson : J. Pharm. and Pharmacol., 15, 810 (1963).

[2] S. Saito, T. Tanaka, T. Iwamoto, C. Matsumura, N. Sugimoto, Z. Horii, M. Makita, M. Ikeda, Y. Tamura : Yakugaku Zasshi, 84, 1126 (1964).

Iketubosin, *et al.* have proposed a planar structure, I, for norsecurinine on the basis of infrared, ultraviolet, nuclear magnetic resonance and mass spectral evidences. However, no chemical evidence has been provided. The following degradation and synthesis provide a chemical support to structure (I).

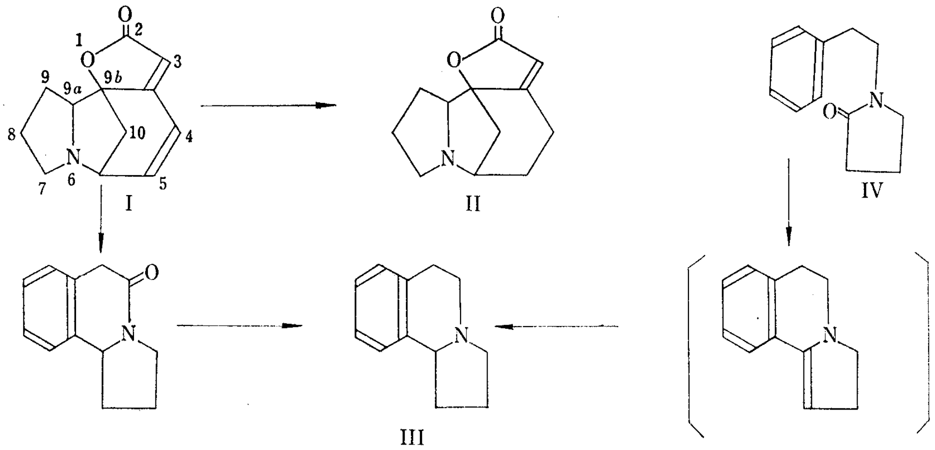

Chart 1.

Treatment of norsecurinine with zinc-dust and sulfuric acid, followed by lithium aluminum hydride reduction, gave an oily base (III), characterized as the picrate, m.p. 170~172° (decomp.). The structure of III was proved by comparison of its infrared spectrum with that of racemic III [the picrate, m.p. 170~173° (decomp.)], which was synthesized by cyclization[3] of 1-phenethyl-2-pyrrolidinone (IV) and subsequent hydrogenation as shown in Chart 1.

The second base has a molecular formula, $C_{12}H_{15}O_2N$, m.p. 135~136°, mol. wt. 205 (mass spec.[*1]), IR ν_{max}^{Nujol} cm^{-1} : 1820, 1755, 1645, UV : λ_{max}^{EtOH} 214 mμ (ε 14,440), $[\alpha]_{589}$ −13°, $[\alpha]_{300}$ −1110° (c=1.07, dioxane), which has already been reported in a previous paper.[2] The molecular formula, infrared, ultraviolet and nuclear magnetic resonance spectra suggest[4] that this base may be the 4,5-dihydro derivative (II) of norsecurinine. This assignment was confirmed definitely by sodium borohydride reduction[5] of I to II, m.p. 135~136°. This conversion also indicates that both alkaloids possess the same stereochemistry. Previously,[2] we designated this alkaloid "Virosine," but would like to change this name into "Dihydronorsecurinine" because the name "Virosine" was found to be used already for an alkaloid from *Vinca rosea* LINN.[*2, 6]

The optical rotatory dispersion (ORD) curves[*3] of norsecurinine (I) and its hydrochloride (Fig. 1) show a single strong negative Cotton effect which arises from the transoid diene chromophore conjugated with the γ-lactone [$[\alpha]_{274}$ −16,500°, $[\alpha]_{250}$ +8,300° (c=0.00241, dioxane) for the free base and $[\alpha]_{265}$ −19,000°, $[\alpha]_{235}$ +24,500° (c=0.00204, MeOH) for the hydrochloride]. The helicity rule[7] of the transoid diene, which has been successfully applied in securinine and allosecurinine,[8] predicts that an absolute configuration of norsecurinine at C_{9b} should be S-configuration. The same conclusion is obtained

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[*1] Mass spectrum was measured in Japan Electron laboratory.

[*2] The authors thank Dr. G. H. Svoboda for his kind advice.

[*3] ORD curves were measured with a Rudolph automatic recording spectropolarimeter at 20~25°.

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

4) S. Saito, K. Kotera, N. Shigematsu, A. Ide, N. Sugimoto, Z. Horii, M. Hanaoka, Y. Yamawaki, Y. Tamura : Tetrahedron, **19**, 2085 (1963).

5) cf. I. Satoda, M. Murayama, J. Tsuji, E. Yoshii : Tetrahedron Letters, **1962**, 1199.

6) G.H. Svoboda : J. Am. Pharm. Assoc., Sci. Ed., **47**, 834 (1958).

7) U. Weiss, H. Ziffer : Experientia, **19**, 108, 660 (1963).

8) Z. Horii, M. Ikeda, Y. Tamura, S, Saito, M. Suzuki, K. Kotera : This Bulletin, **12**, 1118 (1964).

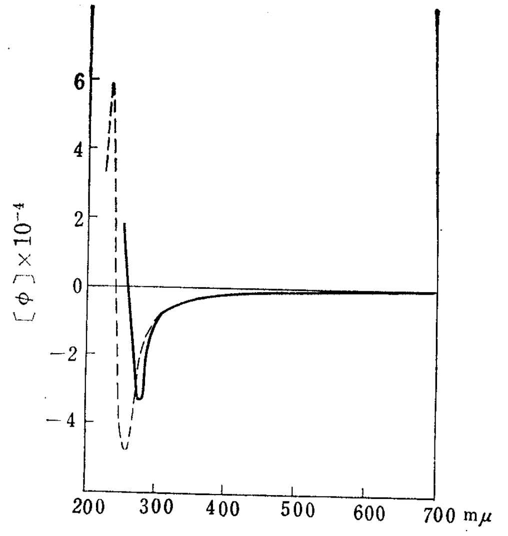

Fig. 1. Optical Rotatory Dispersion Curves of Norsecurinine (I) (——) in Dioxane and its Hydrochloride (------) in Methanol

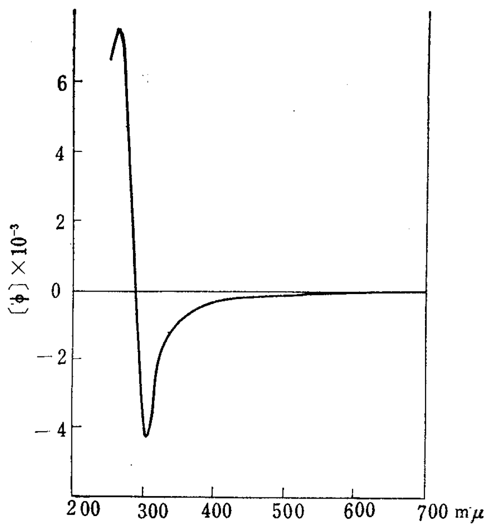

Fig. 2. Optical Rotatory Dispersion Curves of α-Ketol (V) in Methanol

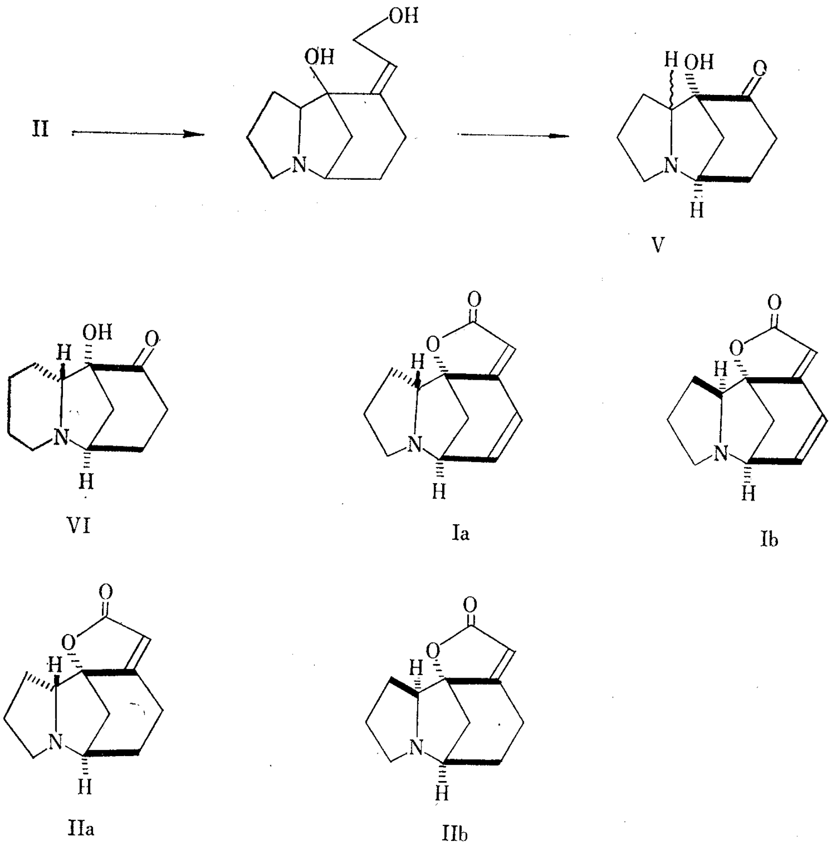

Chart 2.

from the ORD study on the α-ketol (V), m.p. 119~121°, [IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1} : 3380 (OH), 1718 (C=O) (*Anal.* Calcd. for $C_{10}H_{15}O_2N$: C, 66.27; H, 8.34. Found : C, 66.21; H, 8.86)], which was obtained by lithium aluminum hydride reduction of dihydronorsecurinine (II) followed by ozone oxidation. The ORD curve of V shows a negative Cotton effect [$[\alpha]_{305}$ −2,400°, $[\alpha]_{262}$ +4,200° (c=0.131, MeOH)] (Fig. 2). Comparison of the ORD curve of V with that of an α-ketol[9] (VI), derived from securinine, or application of the octant rule[10] predicts that an absolute configuration of norsecurinine at C_{9b} should be S-configuration.

Norsecurinine is, therefore, represented by either Ia or Ib and dihydronorsecurinine by either IIa or IIb. The stereochemistry at C_{9a} will be discussed in a subsequent paper.

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9) Z. Horii, M. Ikeda, Y. Yamawaki, Y. Tamura, S. Saito, K. Kotera : Tetrahedron, **19**, 2101 (1963).
10) W. Klyne : *Ibid.*, **13**, 29 (1961).

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UDC 547.92.02

On the Structure of Pergularin

The isolation of sarcostin (I), metaplexigenin (II), benzoylramanone (III), deacylcynanchogenin (IV), utendin (V), pergularin (VI), and two other aglycones from *Metaplexis joponica* Makino has been reported previously.[1~5] In this communication, the experimental result leading the structure of pergularin (VI) is described. Pergularin (VI), m.p. 220~234°, $C_{21}H_{32}O_5 \cdot \frac{1}{2}H_2O$ (*Anal.* Calcd. : C, 67.55; H, 8.85. Found : C, 67.65; H, 9.32). $[\alpha]^{19}_{589}$ −33° (c=0.1, MeOH, from ORD measurement). IR $\nu^{\text{Nujol}}_{\text{max}}$ cm^{-1} : 3550, 3450, 1720, 1690. Although VI showed two bands in the carbonyl region of the infrared spectrum,[*1] it gave only a monooxime (VII) which revealed no carbonyl absorption. Therefore, VI possesses only one carbonyl group. Very similar facts were reported in the case of deacylmetaplexigenin (IIa).[2,3] Acetylation of VI with acetic anhydride-pyridine afforded a diacetate (VIII), m.p. 130~137°, $C_{25}H_{36}O_7$ (*Anal.* Calcd. : C, 66.94; H, 8.09. Found : C, 66.97; H, 8.46). The nuclear magnetic resonance spectrum of pergularin (VI) showed three singlet at 8.96 (18-CH_3), 8.29 (19-CH_3), 7.43 (17-$COCH_3$) τ in pyridine.[*3] The optical rotatory dispersion curves of pergularin (VI), and its acetate (VIII), in methanol showed negative Cotton effect.

[*1] Pergularin (VI) is practically insoluble to CCl_4 and $CHCl_3$.
[*2] *Pergularia japonica* Thunb. is the synonym of *Metaplexis japonica* Makino.
[*3] In this paper, 10 p.p.m. value (from tetramethylsilane, used as internal standard) is used as τ.

1) H. Mitsuhashi, T. Nomura, Y. Shimizu, I. Takemori, E. Yamada : This Bulletin, **10**, 811 (1962). In the report, pergularin was expressed as crystal 3, and utendin as crystal 4.
2) H. Mitsuhashi, T. Nomura : *Ibid.*, **11**, 1333 (1963).
3) *Idem* : *Ibid.*, in press.
4) H. Mitsuhashi, T. Nomura, M. Hirano : Presented as a paper at the Annual Meeting of the Pharmacognostical Society of Japan, Sept. 19, 1964, Kanazawa.
5) H. Mitsuhashi, T. Nomura : Steroids, **3**, 271 (1964).