Benzotriazole Derivatives

Acylation of benzotriazole (V) should give an unsymmetric compound (XXIX) and a symmetric one (XXX). In the symmetric model compound, the aromatic protons exhibited the pattern of A₂B₂ 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 A₂B₂ 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.

Research Laboratories,
Takeda Chemical Industries, Ltd.,
Juso-Nishino-cho, Higashiyodogawaku,
Osaka, Japan

Michihiko Ochiai (落合道を)
Toshiya Kamikado (上間敏也)

Received August 29, 1964

Structure and Stereochemistry of Norsecurine and Dihydronorsercurine

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 C₁₉H₂₁O₅N (the hydrochloride, m.p. 225° (decomp.), IR ν₃₃₂₄ cm⁻¹ : 1821, 1770, 1635, UV : λ₃₃₂₄ 254 mp (ε 17,600), [α]₂₂₂° +309° (ε=1.24, EtOH) (Anal. Calcd. for C₁₉H₂₁O₅NCl : C, 60.12; H, 5.88; N, 5.84. Found : C, 60.02; H, 5.36; N, 5.70); the methiodide, m.p. 211~212° (Anal. Calcd. for C₁₉H₂₁O₅N : 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 C₁₉H₂₁O₂N₅ : C, 50.00; H, 3.73; N, 12.96. Found : C, 50.27; H, 3.47; N, 12.92)]. The free base [α]₂₂₂° -272° (ε=6.9, EtOH), IR ν₃₃₂₄ cm⁻¹ : 1802, 1770, 1640, UV : λ₃₃₂₄ 256.5 mp (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 for norsercurine [m.p. 81~82°, [α]₂₂₂° -19.5° (ε=0.2, EtOH), IR ν₃₃₂₄ cm⁻¹ : 1802, 1770, 1640, UV : λ₃₃₂₄ 255.5 mp (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 suffrutirosa Rehm. var. amamiensis Furusawa.⁵

Iketubosin, et al. have proposed a planar structure, I, for norsecurine 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 norsecurine 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 II [the picrate, m.p. 170°-173° (decomp.), which was synthesized by cyclization3 of 1-phenethyl-2-pyrrolidinone (V) and subsequent hydrogenation as shown in Chart 1.

The second base has a molecular formula, C_{32}H_{34}O_{2}N, m.p. 135°-136°, mol. wt. 205 (mass spec.3), IR ν_{max} cm^{-1}: 1820, 1755, 1645, UV: λ_{max} cm^{-1} 214 m_{p} (ε 14,440), [α]_{208} = -13°, [α]_{208} = -1100° (c=1.07, dioxane), which has already been reported in a previous paper.5

The molecular formula, infrared, ultraviolet and nuclear magnetic resonance spectra suggest5 that this base may be the 4,5-dihydro derivative (II) of norsecurine. This assignment was confirmed definitely by sodium borohydride reduction6 of I to II, m.p. 135°-136°. This conversion also indicates that both alkaloids possess the same stereochemistry. Previously,5 we designated this alkaloid “Virosine,” but would like to change this name into “Dihyronorsecurine” because the name “Virosine” was found to be used already for an alkaloid from *Vinca rosea* LINN.6,7

The optical rotatory dispersion (ORD) curves8 of norsecurine (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 [α]_{274} = -16,500°, [α]_{208} = +8,300° (c=0.00241, dioxane) for the free base and [α]_{208} = -19,000°, [α]_{208} = +24,500° (c=0.00204, MeOH) for the hydrochloride). The helicity rule9 of the transoid diene, which has been successfully applied in securine and allosecurine,9 predicts that an absolute configuration of norsecurine at C_{9} should be S-configuration. The same conclusion is obtained

---

a1 Mass spectrum was measured in Japan Electron laboratory.

a2 The authors thank Dr. G.H. Svozoda for his kind advice.

a3 ORD curves were measured with a Rudolph automatic recording spectropolarimeter at 20°-25°.


from the ORD study on the α-ketol (V), m.p. 119–121°, [IR \( \nu_{\text{max}} \) cm\(^{-1} \): 3380 (OH), 1718 (C=O) \( \text{Anal. Calcd. for C}_{19}H_{20}O_{2}N: \) 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 \( [(\alpha)_{258} -2,400^\circ, \ (\alpha)_{258} +4,200^\circ (c=0.131, \text{MeOH})] \) (Fig. 2). Comparison of the ORD curve of V with that
of an α-ketol (VI), derived from securinine, or application of the octant rule predicts that an absolute configuration of norsecurinine at C₉₈ should be S-configuration.

Norsecurinine is, therefore, represented by either Ia or Ib and dihydronorsecurinine by either IIa or IIb. The stereochemistry at C₉₈ will be discussed in a subsequent paper.

Seiichi Saito (斎藤清一)
Tadasu Tanaka (田中 雅)
Keishi Kotera (小寺啓司)
Hideo Nakai (仲井英雄)
Norio Sugimoto (杉本典夫)
Zen-ichi Horii (齋木喜一)
Masazumi Ikeda (池田正満)
Yasunatsu Tamura (田村昌光)

Faculty of Pharmaceutical Sciences,
Osaka University,
Toyonaka,
Osaka-fu

Received September 14, 1964


On the Structure of Pergularin

The isolation of sarcostin (I), metaplexigenin (II), benzoylramanone (III), deacetylcyano-
chogenin (IV), utendin (V), pergularin (VI), and two other aglycones from Metaplexis japonica MAKINO has been reported previously. In this communication, the experimental result leading the structure of pergularin (VI) is described. Pergularin (VI), m.p. 220−224°C, C₁₃H₁₃O₅·½H₂O (Anal. Calcd.: C, 67.55; H, 8.85. Found: C, 67.65; H, 9.32); [α]D₃₂ =−33° (c=0.1, MeOH, from ORD measurement). IR νmax cm⁻¹: 3550, 3450, 1720, 1690. Although VI showed two bands in the carbonyl region of the infrared spectrum, 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 deacetylmeta-
plexigenin (IIa). Acetylation of VI with acetic anhydride-pyridine afforded a diacetate (VIII), m.p. 130−137°C, C₁₅H₁₇O₆ (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-CH₃), 8.29 (19-CH₃), 7.43 (17-COCH₃) τ in pyridine. The optical rotatory dispersion curves of pergularin (VI), and its acetate (VIII), in methanol showed negative Cotton effect.

---

9) Perugulairin (VI) is practically insoluble to CCl₄ and CHCl₃.
10) Perugulairin japonica THUMB. is the synonym of Metaplexis japonica MAKINO.
11) 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.
3) Ibid. : Ibid., in press.