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167. Zen-ichi Horii, Masazumi Ikeda, Yasumitsu Tamura,*1 Seiichi Saito, Keishi Kotera, and Tsutomu Iwamoto*2 : Isolation of Securinol A, B, and C from *Securinega suffruticosa* REHD. and the Structures of Securinol A and B.

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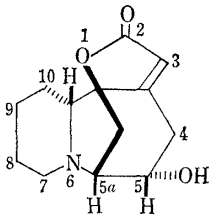
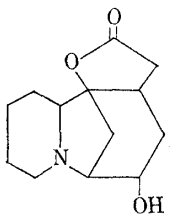
Several alkaloids have been hitherto isolated from *Securinega suffruticosa* REHD.[1~4] We have now found three new alkaloids, designated securinol A, B and C from the same plant and investigated the structures of securinol A and B.

It has been reported[5] that the extraction of the leaves with ethylene dichloride, followed by the recrystallization of the alkaloid fraction from petroleum benzin, furnished the major alkaloid, securinine. Gas-liquid chromatography (GLC) of the recrystallization mother-liquor exhibited three peaks corresponding to those of securinine, allosecurinine and dihydrosecurinine, and, when it was trimethylsilylated[6] prior to GLC, an additional new peak, which would predict the presence of alkaloids with hydroxyl function. Column chromatography of the whole mother-liquor on alumina gave allosecurinine, securinine, dihydrosecurinine and finally a mixture of the hydroxy-alkaloids. The last fraction was further separated by column chromatography and purification through picrate into securinol A, B and C. The structures of the former two alkaloids were investigated.



I



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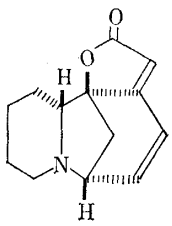

IV

Securinol A (I), m.p. 135~136°, $[\alpha]_D^{17}$ +58.2°, has molecular formula $C_{13}H_{17}O_3N$, mol. wt. 235 (mass spec.*3). The base formed a picrate monohydrate, m.p. 186~187° (decomp.). The spectral and chemical evidences indicated the presence of the α,β-unsaturated γ-lactone ring with one hydrogen in α-position : peaks at 1792 (sh.), 1754 and 1650 cm^{-1} in the infrared spectrum (Fig. 1); a maximum at 214 mμ (log ε 4.15) in the ultraviolet spectrum; a signal of one olefinic proton at 4.28 τ in the nuclear magnetic resonance spectrum*4 (Fig. 2); catalytic hydrogenation of I over platinum oxide

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*3 Mass spectra were measured with a Hitachi RMU-6D mass spectrometer, the ionizing energy having set at 80V and the ionizing current at 80 μA.
*4 NMR spectra were measured with a Varian A-60 and JNM A-60 spectrometer (Japan Electron Optics Laboratory Co., Ltd.) at 60 Mc. in $CDCl_3$.

1) V. I. Murav'eva, A. I. Ban'kovskii : Doklady Akad. Nauk S. S. S. R., **110**, 998 (1956).
2) I. Satoda, M. Murayama, J. Tsuji, E. Yoshii : Tetrahedron Letters, **1962**, 1199.
3) S. Saito, N. Shigematsu, Z. Horii : Yakugaku Zasshi, **83**, 800 (1963).
4) V. I. Murav'eva, A. D. Kozovkov : J. Gen. Chem. U. S. S. R., **33**, 685 (1963).
5) Z. Horii, T. Tanaka, Y. Tamura, S. Saito, C. Matsumura, N. Sugimoto : Yakugaku Zasshi, **83**, 602 (1963).
6) M. Makita, W. W. Wells : Anal. Biochem., **5**, 523 (1963).

in acetic acid, consumed one molar equivalent hydrogen to afford a dihydro derivative (II), characterized as a hydrochloride monohydrate, m.p. 241~242°, IR ν_{max}^{KBr} cm^{-1} : 1773 (saturated γ-lactone).

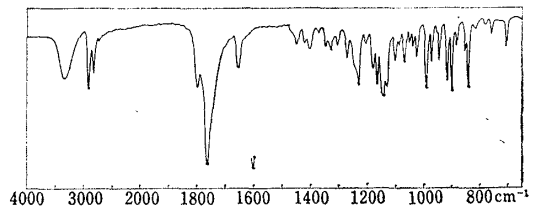


Fig. 1. Infrared Spectrum of Securinol A in Potassium Bromide

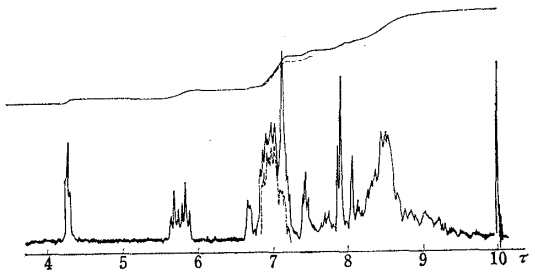


Fig. 2. Nuclear Magnetic Resonance Spectrum of Securinol A (---- signals obtained by treatment with D_2O)

The presence of the secondary hydroxyl group in I was indicated from the following data : the infrared spectrum in a highly diluted carbon tetrachloride solution showed a non-bonded OH band at 3625 cm^{-1}; the nuclear magnetic resonance spectrum showed a hydroxyl proton signal at 7.14 τ (disappeared on treatment with deuterium oxide[7]) and a signal of one proton attached to the carbon bearing the hydroxyl group at 5.75 τ; formation of a mono 3,5-dinitrobenzoate (III), m.p. 198~199°, $[\alpha]_D^{17}$ +55.3°, by treating with 3,5-dinitrobenzoyl chloride in pyridine at room temperature.

Treatment of I with methanesulfonyl chloride in pyridine gave yellow crystals, m.p. 134~135°, $[\alpha]_D$ +1200°, which were identified with viroallosecurinine[8] (IV) by mixed melting point determination and by comparison of Rf values in thin-layer chromatography (TLC), retention times of GLC and infrared spectra.

These results clearly demonstrate that securinol A is 4,5-dihydroviroallosecurinine, possessing a hydroxyl group at C_4 or C_5.

The nuclear magnetic resonance spectra of I and III gave further informations about the position and the configuration of the hydroxyl group. A signal corresponding to a hydrogen attached to the carbon bearing the hydroxyl or the 3,5-dinitrobenzoyloxyl group appeared as a doublet of triplets centered at 5.75 τ and 4.39 τ, respectively. This splitting pattern suggests the presence of >CH-CH(OR)-CH_2- group in securinol A, and thus the location of the hydroxyl group at C_5. Further, analysis by the first order approximation indicates that $J_{4.5} \simeq J_{5.5a} \simeq 3$ c.p.s and $J_{4'.5} = 8$ c.p.s. This suggests that the hydroxyl group is equatorial.[9] Another support regarding to the configuration of the hydroxyl group was obtained by an application of the benzoate rule[10] to I and III. The difference in molecular rotation between I and III was +100°. The result predicts that the absolute configuration at C_5 is *S*-form (hence equatorial), which is in accordance with the above conclusion.

On the basis of these evidences the structure of securinol A should be assigned to I.

Structure (I) is interpreted well by the mass spectrum of securinol A (Fig. 3), which showed characteristic peaks at m/e 235 (M^+), 191, 163, 140, 134, 110, 106, 84, 55 and

7) H. M. Fales, A. V. Robertson : Tetrahedron Letters, **1962**, 111.
8) S. Saito, T. Tanaka, T. Iwamoto, C. Matsumura, N. Sugimoto, Z. Horii, M. Makita, M. Ikeda, Y. Tamura : Yakugaku Zasshi, **84**, 1126 (1964).
9) H. Conroy : "Advances in Organic Chemistry," Vol. II, 311 (1960), Interscience Publishers, Inc., N. Y.
10) J. H. Brewster : Tetrahedron, **13**, 106 (1961).

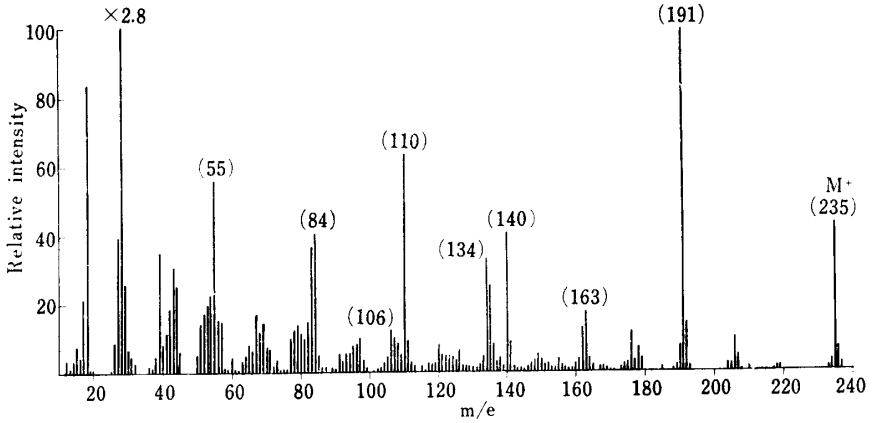


Fig. 3. Mass Spectrum of Securinol A (I)

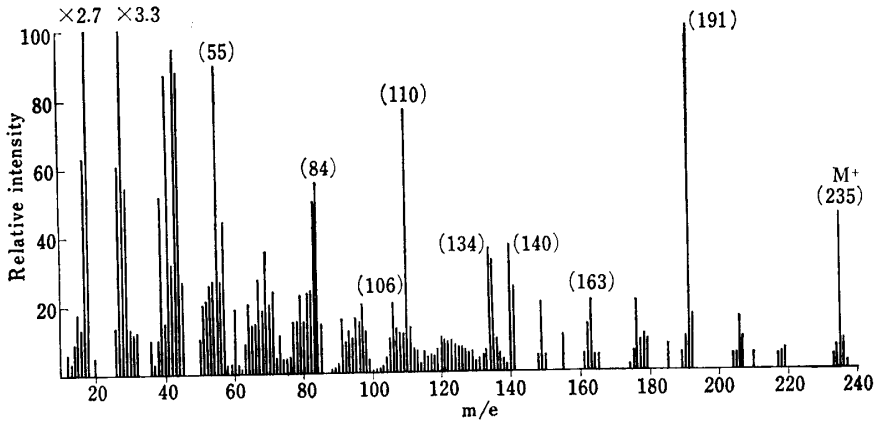
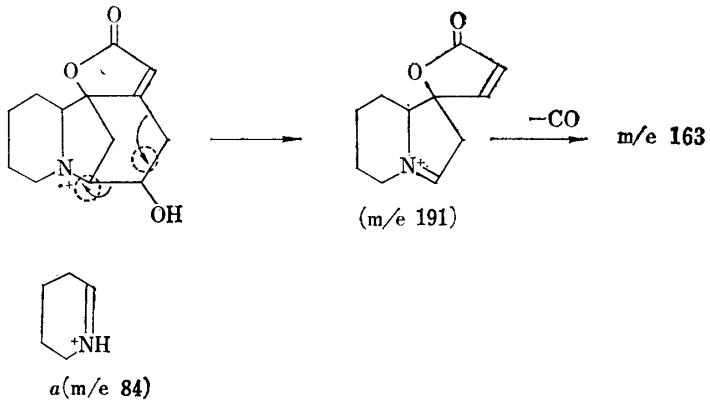


Fig. 4. Mass Spectrum of Securinol B

metastable ion peaks at 155.2 (calcd. 155.2 for the transition m/e 235→191) and 139.0 (calcd. 139.1 for the transition m/e 191→163). Of these, the peaks at m/e 134, 106, 84 and 55 were also observed in the spectrum of securinine.[11] The peak at m/e 84 is assigned to fragment *a*[11] and, therefore, indicates the absence of the hydroxyl group in the piperidine ring of securinol A. The most important peak at m/e 191 corresponds to loss of CH_2=CHOH or CO_2 from the molecular ion as indicated by a metastable ion peak at m/e 155.2. The latter possibility, however, may be excluded from the observation that the peak (M–44) is absent in the spectra of securinine and dihydrosecurinine. The formation of this fragment may be best understandable if the hydroxyl group is situated at C_5 and the fragmentation shown in the following scheme occurs.[12,13]



The second alkaloid, securinol B, $C_{13}H_{17}O_3N$, mol. wt. 235 (mass

11) M. M. J. Parello, A. Melera, R. Goutarel: Bull. soc. chim. France, **1963**, 197, 898.
12) M. M. Janot, P. Longevialle, R. Goutarel: Bull. soc. chim. France, **1964**, 2158.
13) E. L. Blossey, H. Budzikiewicz, M. Ohashi, G. Fodor, C. Djerassi: Tetrahedron, **20**, 585 (1964).

spec.), m.p. 158~160° (decomp.), had one hydroxyl group [IR band at 3497 cm^{-1}] and an α,β-unsaturated γ-lactone [UV λ_{max}^{EtOH} 215 mμ (log ε 4.10) and IR bands at 1802 (sh.), 1733 (γ-lactone) and 1650 cm^{-1} (double bond)]. The mass spectrum of securinol B showed essentially identical pattern peaks with that of securinol A (I) as shown in Fig. 4. These data suggest that securinol B is a stereoisomer of securinol A.

Experimental*5

Isolation of Securinol A, B, and C——Powdered dry leaves of *S. suffruticosa* (108 kg.) were shaken with 10% NH_4OH (16.2 L.) in $ClCH_2CH_2Cl$ (360 L.) overnight. The extract was filtered and the leaves were washed with $ClCH_2CH_2Cl$ (70 L. × 3). The extraction was repeated three times. The combined extracts and washings were concentrated to about one-tenth and filtered. The filtrate was extracted with 10% H_2SO_4 (6 L. × 3). The acid layer was neutralized with conc. NH_4OH and reextracted with $CHCl_3$. The chloroform extract was dried ($MgSO_4$) and evaporated to dryness under reduced pressure. The residue was recrystallized from petroleum benzin to afford 167 g. of securinine. The recrystallization mother-liquor was chromatographed over alumina. Elution with ether gave a mixture of allosecurinine and securinine, and then dihydrosecurinine. Further elution with MeOH afforded a mixture of hydroxy-alkaloids, 9 g. of which was again chromatographed over alumina (200 g.). Successive elution with benzene, benzene-AcOEt (9:1) and AcOEt gave two crystalline bases and an oily base. The first eluent afforded 100 mg. of colorless needles of securinol B, m.p. 158~160° (decomp.) (from ligroin), which was shown to be homogeneous by TLC*6 (Rf = 0.36). UV λ_{max}^{EtOH} mμ (log ε) : 215 (4.10), IR ν_{max}^{KBr} cm^{-1} : 3497, 1802 (sh.), 1733, 1650. ORD, (c = 0.389, dioxane) : $[\alpha]_{589}$ +28°, $[\alpha]_{305}$ −167°, $[\alpha]_{285}$ 0°. *Anal.* Calcd. for $C_{13}H_{17}O_3N$: C, 66.36; H, 7.28; N, 5.95. Found : C, 66.85; H, 7.49; N, 5.74.

The second eluent gave 500 mg. of colorless pillars of securinol A, m.p. 135~136° (from benzene), $[\alpha]_D^{17}$ +58.2° (c = 0.14, $CHCl_3$), which was shown to be homogeneous by TLC*6 (Rf = 0.1). UV λ_{max}^{EtOH} mμ (log ε) : 214 (4.15), IR ν_{max}^{KBr} cm^{-1} : 3367, 1792 (sh.), 1754, 1650. ORD, (c = 0.500, dioxane) : $[\alpha]_{589}$ +50°, $[\alpha]_{307}$ −575°, $[\alpha]_{255}$ +840°. *Anal.* Calcd. for $C_{13}H_{17}O_3N$: C, 66.36; H, 7.28; N, 5.95. Found : C, 66.55, 65.94; H, 7.34, 7.12; N, 5.90, 5.82. The picrate was recrystallized from EtOH and dried for 2 days at 20° and 3 mm. over P_2O_5, m.p. 186~187° (decomp.). *Anal.* Calcd. for $C_{13}H_{17}O_3N \cdot C_6H_3O_7N_3 \cdot H_2O$: C, 47.30; H, 4.60; N, 11.60. Found : C, 47.36, 47.89; H, 4.45, 4.64; N, 11.40, 11.71.

The third eluent gave an oily base, which formed a picrate. Several recrystallizations of the picrate from EtOH and acetone gave 0.9 g. of the picrate of securinol C, m.p. 194° (decomp.). IR ν_{max}^{KBr} cm^{-1} : 3448, 1736, 1650. *Anal.* Calcd. for $C_{13}H_{17}O_3N \cdot C_6H_3O_7N_3$: C, 49.14; H, 4.34; N, 12.07. Found : C, 49.49; H, 4.44; N, 11.83.

Dihydrosecurinol A (II)——Securinol A (I, 250 mg.) was hydrogenated over PtO_2 (50 mg.) in glacial AcOH (15 ml.) at atmospheric pressure and room temperature. Hydrogen uptake ceased after 4 hr., absorbing 1 molar equivalent of hydrogen. The catalyst was removed and the filtrate was evaporated *in vacuo*. The residue was made alkaline with conc. aq-K_2CO_3 solution and extracted with ether. Evaporation of the dried ether extract gave a viscous oil (250 mg.). IR $\nu_{max}^{CHCl_3}$ cm^{-1} : 3450 (OH), 1780 (γ-lactone). The hydrochloride was recrystallized from iso-PrOH and dried for 2 days at 20° and 3 mm over P_2O_5, m.p. 241~242°, IR ν_{max}^{KBr} cm^{-1} : 3322 (OH), 1773 (γ-lactone). *Anal.* Calcd. for $C_{13}H_{19}O_3NCl \cdot H_2O$: C, 53.51; H, 7.60; N, 4.80. Found : C, 53.83; H, 7.42; N, 4.35.

3,5-Dinitrobenzoate (III) of Securinol A——A solution of securinol A (I, 100 mg.) and 3,5-dinitrobenzoylchloride (150 mg.) in 1 ml. of pyridine was kept overnight at room temperature. The reaction mixture was poured into H_2O (5 ml.) and the precipitated solid was collected and recrystallized from AcOEt to afford dark yellow pillars, m.p. 198~199°, $[\alpha]_D^{17}$ +55.3° (c = 0.10, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1} : 1802 (sh.), 1761 (α,β-unsaturated γ-lactone), 1721 (ester), 1650, 1629 (double bond and aromatic ring). *Anal.* Calcd. for $C_{20}H_{19}O_8N_3$: C, 55.94; H, 4.46; N, 9.79. Found : C, 55.98; H, 4.37; N, 9.57.

Dehydration of Securinol A to Viroallosecurinine (IV)——A solution of securinol A (I, 100 mg.) and methanesulfonyl chloride (0.1 ml.) in 2 ml. of pyridine was stood overnight at room temperature and then warmed on a water bath for 1 hr. The solution was diluted with H_2O and extracted with ether. The dried ether extract was evaporated. The residue was purified by chromatography over alumina (4 g.) and benzene-AcOEt (9:1) to afford 12 mg. of yellow needles, which were recrystallized from petroleum benzin, m.p. 133~134°, $[\alpha]_D$ +1200° (c = 0.01, EtOH). This sample was identified with an authentic

*5 Melting points are uncorrected. Specific optical rotations were measured with a Yanagimoto photomagnetic direct reading polarimeter model OR-20, using a 10 cm. cell. Analyses of GLC were conducted with a Shimadzu gas chromatography GC-1B equipped with a hydrogen flame ionization detector, employing SE-30 column (column temperature 175°). ORD curves were measured with a Rudolph automatic recording spectropolarimeter.

*6 TLC was carried out with $CHCl_3$ as a solvent on Aluminum oxide G (Merck Co., Ltd.).

one of viroallosecurinine,[8] m.p. 135~136°, by the mixed melting point determination and by comparison of Rf values of TLC and retention times of GLC and IR spectra.

The authors are indebted to Dr. M. Makita for GLC analysis, Dr. T. Shingu, Kyoto University, for NMR spectra measurements and Mr. H. Sato, Hitachi Ltd., for mass spectra measurements. They also thank Dr. M. Suzuki, Tanabe Seiyaku Co., Ltd., for helpful discussion.

Summary

The leaves of *Securinega suffruticosa* REHD. furnished three new alkaloids, securinol A, B and C. The structures of securinol A and B were investigated.

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168. Zen-ichi Horii, Yasuhiko Yamawaki, Yasumitsu Tamura,*1 Seiichi Saito, Hiroshi Yoshikawa, and Keishi Kotera*2 : Degradations of Allosecurinine.

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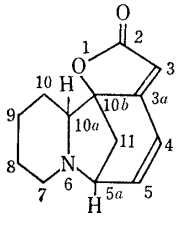
In 1962, Satoda, *et al.*[1] first isolated allosecurinine as a minor alkaloid of *Securinega suffruticosa* REHD. and showed that it is an epimer at C_{10a} of securinine[2~5,6a] (I), a major alkaloid of the same plant. At the almost same time, Parello, *et al.*[4] isolated phyllocrysine (=allosecurinine*[3,6b]) from *Rhyllanthus discoides* and reached independently to the same structural assignment as Satoda, *et al.* did. This structure was further supported by Chatterjee, *et al.*[7] Recent establishment of the absolute stereochemistry[8,9] (II) for



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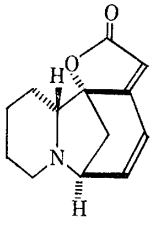

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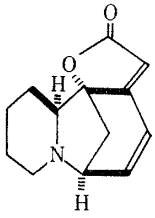

III

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*2 Higashiyodogawa-ku, Osaka (斎藤清一, 吉川 浩, 小寺啓司).
*3 Phyllocrysine was shown[10] to be identical with allosecurinine by mixed melting point determination, comparison of their infrared spectra and thin-layer chromatography.

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2) V. I. Murav'eva, A. I. Ban'kovskii : Doklady Akad. Nauk S. S. S. R., **110**, 998 (1956).
3) *a*) S. Saito, K. Kodera, N. Sugimoto, Z. Horii, Y. Tamura : Chem. & Ind. (London), **1962**, 1652. *b*) S. Saito, K. Kotera, N. Shigematsu, A. Ide, Z. Horii, Y. Tamura : Chem. & Ind. (London), **1963**, 689. *c*) S. Saito, K. Kotera, N. Shigematsu, A. Ide, N. Sugimoto, Z. Horii, M. Hanaoka, Y. Yamawaki, Y. Tamura : Tetrahedron, **19**, 2085 (1963).
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