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The Structures of Securinol B and C

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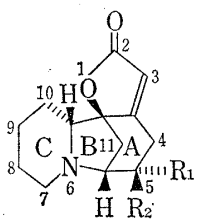
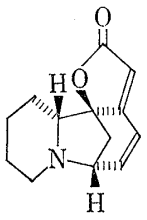
The structures of securinol B and C were determined as Ib and III by conversion of them into viroallosecurinine (II) and allosecurinine (IV), respectively, and from spectral evidences.

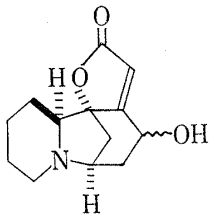
In the previous paper[2] we have reported the isolation of securinol A, B and C from the leaves of *Securinega suffruticosa* Rehd., and assigned the structure of securinol A as 4,5-dihydroviroallosecurinin-5α-ol (Ia). It has also been suggested, on the basis of spectral evidences, that securinol B may be a stereoisomer of Ia. The present paper describes new evidences which establish the structure of securinol B and the tentative structure of securinol C.[3]



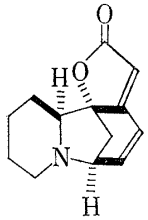
Ia : R_1 = OH, R_2 = H
Ib : R_1 = H, R_2 = OH
Ic : R_1 = H, R_2 = OSO_2CH_3



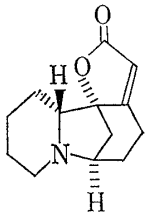
II



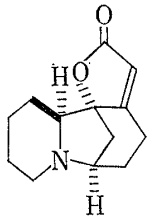
III



IV



V



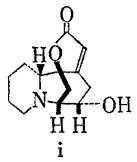
VI

Chart 2

Securinol B (Ib) was treated with methanesulfonyl chloride in pyridine to give the mesylate (Ic), mp 176—177°, mol. wt. 313 (mass spectrum), which on refluxing in collidine gave viroallosecurinine (II).[4] The nuclear magnetic resonance (NMR) spectrum of securinol

1) Location: *Toneyama, Toyonaka, Osaka.*

2) Z. Horii, M. Ikeda, Y. Tamura, S. Saito, K. Kotera, and T. Iwamoto, *Chem. Pharm. Bull.* (Tokyo), **13**, 1307 (1965). In the previous paper, securinol A was represented as formula (i), but, in the present paper, the configuration of 4,5-dihydrosecurinine skeleton is represented by the projection on the azabiclo[3,2,1]-octane system of A B ring as shown in Ia—c or IV or V. The C_{11}-proton which is axial to the cyclohexane ring was designated as *endo* proton, and the one equatorial as *exo* proton, as shown in IA or IB or IIIA.



i

Chart 1

3) Securinol C was also isolated from the roots of *Securinega suffruticosa* Rehd. var. *amamiensis* Furusawa.

4) S. Saito, T. Iwamoto, T. Tanaka, C. Matsumura, N. Sugimoto, Z. Horii, and Y. Tamura, *Chem. Ind.* (London), **1964**, 1263.

B exhibits a one-proton triplet at 4.34 τ ($J \simeq 1.5$ cps) due to the olefinic proton at C_3 coupled with two allylic protons at C_4, suggesting that the hydroxyl group in securinol B is located at C_5. The results, together with the previously reported spectral data, lead to the conclusion that securinol B is an epimer of securinol A (Ia) at C_5 and thus represented as 4,5-dihydroviroallosecurinin-5β-ol (Ib).

The conformation of Ib or Ic, in which ring A has a boat conformation and the C_{5a}-hydrogen is axial, is substantiated by the results of NMR measurements. Recently, Audier and Parello[5] have reported that the $C_{5\beta}$-proton in dihydrosecurinine (V) or dihydroallosecurinine (VI), which lies equatorially as shown in IIIA (Fig. 1), exhibits a long range coupling of about 2 cps with the C_{11exo}-equatorial proton satisfying the "M" rule.[6] The proton attached to the carbon bearing the mesyloxyl group in Ic appeared as an octet of coupling constants: J=9.5, 5 and 2 cps. The smallest coupling constant (2 cps) might be ascribed to a long range coupling between the C_{5a}-equatorial proton and the C_{11exo}-equatorial proton in a chair conformation of ring A (IA). In such a conformation, however, the large coupling constant (9.5 cps) involved in the octet can not be rationalized since it must be ascribed to diaxial proton system. Inspection of a model of Ic suggests that the conformation shown in IB(R=OSO_2CH_3), where the mesyloxyl group is equatorial in ring A of near-boar form, would be favorable owing to the removal of an interaction between the $C_{5\beta}$-mesyloxyl group and the C_{11endo}-hydrogen. In this conformation, the observed coupling constants can be reasonably explained as $J_{5\alpha,4\beta}$=9.5 cps, $J_{5\alpha,4\alpha}$=5 cps, $J_{5\alpha,5a\beta}$=2 cps. In the NMR spectrum of Ib, the signal near 6.20 τ appeared as a broad multiplet (half-band width: >15 cps). Hence the proton attached to the carbon bearing the hydroxyl group may be in axial orientation as in IB (R=OH).

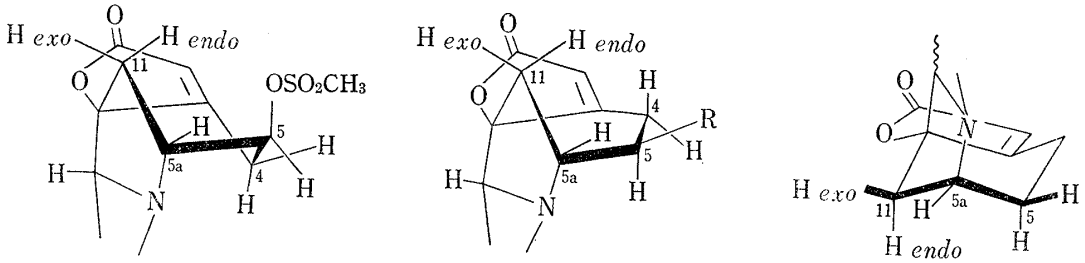


Fig. 1

Securinol C (III), $C_{13}H_{17}O_3N$, mp 114—115°, $[\alpha]_D$ −81.9°, exhibits an ultraviolet (UV) maximum at 214 mμ (log ε=4.15), infrated (IR) bands (Fig. 2) at 3422, 1823 (sh.), 1725, 1645 cm^{-1} and NMR signals at 4.27 τ (1H), 5.55 τ (1H), 7.52 τ (1H, disappeared on treatment with deuterium oxide), suggesting the presence of a hydroxyl group and an α,β-unsaturated γ-lactone ring.

Treatment of III with methanesulfonyl chloride in pyridine gave allosecurinine (IV).[7]

These data suggest that securinol C is 4,5-dihydroallosecurinine with a hydroxyl group at C_4 or C_5. However, the latter posibility is excluded from the fact that a pair of isomers, Ia and Ib, bearing the hydroxyl group at C_5 has been isolated, and that neither of these 4,5-dihydroviroallosecurinine derivatives[8] have been shown to be the enantiomer of securinol C.

The mass (Fig. 3) and NMR spectra of III gave additional supports. In the mass spectrum of III, the base peak a at *m/e* 84, which is also observed as the most abundant peak

5) H.E. Audier and J. Parello, *Bull. Soc. Chim. France*, **1968**, 1552.
6) *a*) N.S. Bhacca and D.H. Williams, "Applications of NMR Spectroscopy, in Organic Chemistry," Holden-Day, Inc., San Francisco, 1964, pp. 115—121; *b*) M.J.T. Robinson, *Tetrahedron Letters*, **1965**, 1685.
7) I. Satoda, M. Murayama, J. Tsuji, and E. Yoshii, *Tetrahedron Letters*, **1962**, 1199.
8) Viroallosecurinine is an enantiomer of allosecurinine.

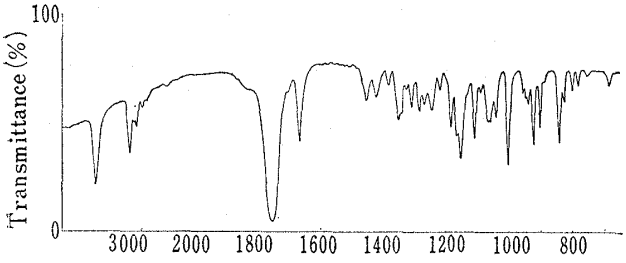


Fig. 2. Infrared Spectrum (KBr Tablet) of Securinol C

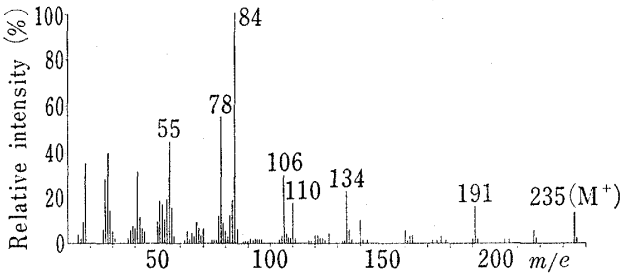


Fig. 3. Mass Spectrum of Securinol C

in the spectra of other Securinega alkaloids, is assumed to arise from the pathway analogous to the fragmentation pattern proposed in the case of securinine.[9] It has been postulated[2] that the base peak at *m/e* 191 in the mass sepctrum of securinol A corresponds to fragment ion b which is formed by α-cleavage between C_5 and C_{5a} followed by C_{3a}–C_4 bond rupture as illustrated in Chart 3.

Comparison of the mass spectrum of III with that of Ia or Ib revealed that the intensity ratio of the *m/e* 191-peak to the *m/e* 84-peak was about 2:1 in the latter, while in the former it was about 1:5, suggesting the absence of a hydroxyl group at C_5 in III. In the NMR spectrum of III, the signal at 4.27 τ due to the olefinic proton at C_3 appeared as a broad singlet, whose broadening may be caused by an allylic coupling with the proton geminal to the hydroxyl group at C_4.

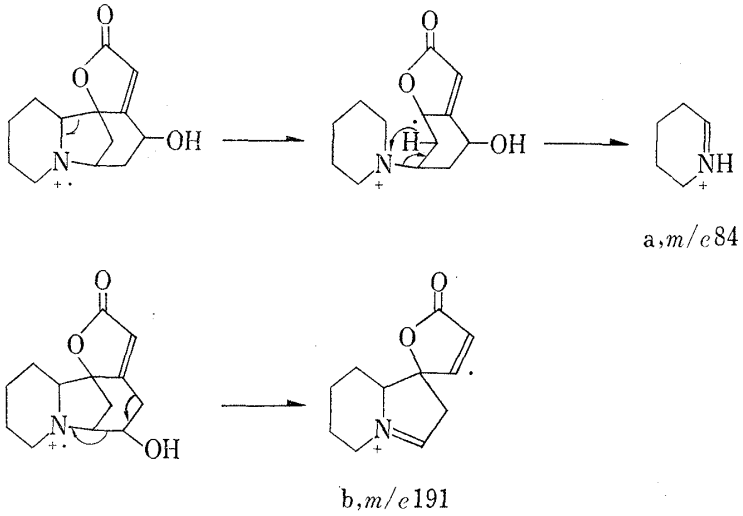


Chart 3

These complete the assigment of the structure and absolute configuration of securinol C in terms of the expression III, with the exception of the secondary hydroxyl group attached to C_4. The broad quartet (J=9.5 and 4 cps) at 5.55 τ in the NMR spectrum demonstrates that the hydroxyl group at C_4 must be equatorial, but it can be assigned to α- or β-notation, depending upon whether the ring A of sequrinol C possesses chair or boat conformation.

Experimental[10]

Securinol B (Ib)——Additional spectral data to ref. 2: $[\alpha]_D$ +120° (c=0.15, EtOH); NMR τ: 4.34 (1H, triplet, C_3-H, J=1.5 cps), 6.20 (1H, multiplet, C_5-H), 6.76 (1H, OH).

9) *a*) J. Parello, A. Melera, and R. Goutarel, *Bull. Soc. Chim. France*, **1963**, 898; *b*) H. Budzikiwiez, C. Djerassi, and D.H. Williams, "Structure Elucidation of Natural Products by Mass spectrometry," Vol. 1, Holden-Day, Inc., San Francisco, 1964, p. 223.

10) Melting points are uncorrected. Extracts were dried over anhyd. Na_2SO_4. Column chromatographies were carried out with alumina (E. Merck's Brockmann, grade II-III, neutral) and silica gel (Mallinckrodt). The NMR spectra were measured with a Hitachi Parkin-Elmer H-60 type (60 Mc) spectrometer with tetramethylsilane as internal reference in $CDCl_3$. Mass spectra were measured with Hitachi RMU-6D mass spectrometer, the ionizing energy having set at 80 eV and the ionizing current at 80 μA. Specific optical rotations were measured with a Yanagimoto Photomagnetic Direct Reading Polarimeter Model OR-20. Analyses of GLC were conducted with a Parkin–Elmer Gas Chromatograph 800, employing SE-52 column (column temperature at 160°).

Securinol B Mesylate (Ic)——A solution of securinol B (1b, 17 mg) and methanesulfonyl chloride (one drop) in pyridine (0.5 ml) was allowed to stand at room temperature overnight. The reaction mixture was diluted with H_2O (10 ml), and extracted with ether. Evaporation of the dried ethereal extract gave a brown residue, which was purified by chromatography on silica gel (2 g) in $CHCl_3$ to afford the mesylate (Ic, 21 mg) as white crystals, mp 176—177°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1794 (sh.), 1764, 1656, 1361—1335. NMR τ: 4.28 (1H, triplet, C_3-H, $J=1.5$ cps), 5.34 (1H, octet, C_5-H, $J=9.5$, $J=5$, $J=2$ cps), 6.94 (3H, singlet, OSO_2CH_3). Mass Spectrum m/e: 313 (M^+).

Viroallosecurinine (III) from the Mesylate (Ic)——A solution of Ib (21 mg) in collidine (1 ml) was heated under reflux for 6 hr. After cooling, the reaction mixture was diluted with H_2O (10 ml), and extracted with ether. The dried ethereal extract was evaporated to give a dark brown oil, which was chromatographed on silica gel. Elution with $CHCl_3$ gave unchanged mesylate (trace). Further elution with $CHCl_3$–MeOH (99:1) gave about 3 mg of yellow needles (from C_6H_6–*n*-Hexane), mp 133—134°, $[\alpha]_D$ +1030° ($c=0.08$, EtOH). This sample was identified with authentic viroallosecurinine, by the mixed melting point determination and by comparison of *Rf* values on TLC and IR spectra.

Securinol C (III)——The picrate[2] of securinol C (0.2 g) was treated with 2% LiOH aqueous solution and extracted with $CHCl_3$. The $CHCl_3$ extract was dried and evaporated to dryness to give 50 mg of securinol C as colorless needles, mp 114—115° (from C_6H_6–petroleum benzin), $[\alpha]_D$ −81.9° ($c=0.58$, EtOH). UV λ_{max}^{EtOH} mμ (log ε): 214 (4.15). IR ν_{max}^{KBr} cm^{-1}: 3422, 1823 (sh.), 1725, 1645. NMR τ: 4.27 (1H, broad singlet, C_3-H), 5.55 (1H, broad quartet, C_4-H), 7.52 (1H, OH). *Anal.* Calcd. for $C_{13}H_{17}O_3N$: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.65; H, 7.21; N, 5.81.

Dehydration of Securinol C (II) to Allosecurinine (IV)——A solution of III (25 mg) and methanesulfonyl chloride (two drops) in pyridine (1 ml) was allowed to stand overnight at room temperature and then warmed on a steam bath for 1.5 hr. The solution was diluted with H_2O (15 ml) and extracted with ether. The dried ethereal extract was evaporated. The residue was purified by chromatography on alumina (2 g) in ether to afford allosecurinine, mp 134—135°, $[\alpha]_D$ −1000° ($c=0.12$, EtOH), which was identified with an authentic sample, by the mixed melting point determination and by comparison of *Rf* values of TLC, retention times of GLC, and IR spectra.