UDC 581.19 : 582.757.2

On the Absolute Configuration of Securinine

In a preliminary communication1) the relative configuration (I) for securinine2,3) from *Securinega suffruticosa* Rehd was established. Now we wish to report that the formula (I) (Chart 1)also expresses the absolute configuration of this alkaloid and that the favorable conformation is shown in Chart 2, that is, C_{10a}-C_{10b} and N-C_{5a} are *cis* to each other.

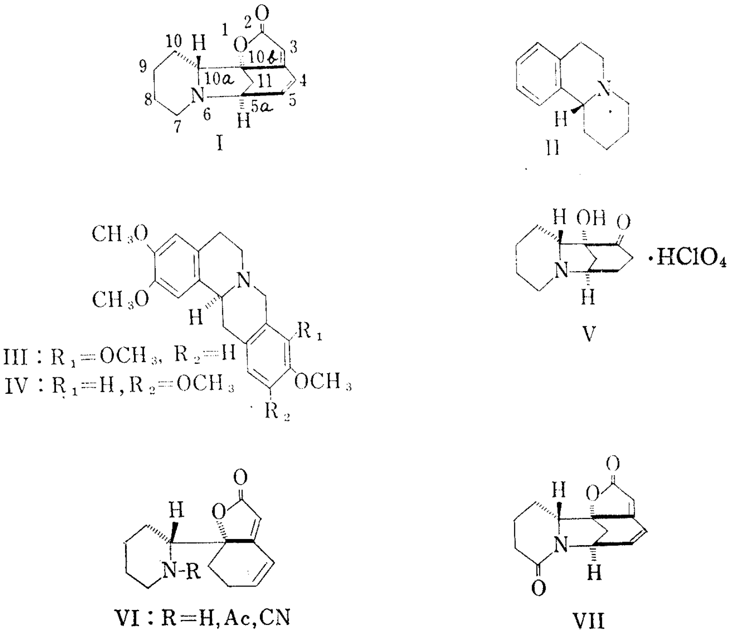

Chart 1.

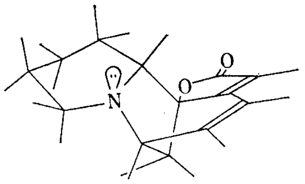

Chart 2.

Reduction of securinine with zinc-dust and sulfuric acid4) followed by the lithium aluminum hydride reduction5) gave the benzoquinolizidine (II), characterized as the hydrochloride (IIa), m.p. 256~257° (*Anal.* Calcd. for $C_{13}H_{18}NCl$: C, 69.78; H, 8.11. Found: C, 69.64; H, 8.04); the perchlorate (IIb), m.p. 160~161° (*Anal.* Calcd. for $C_{13}H_{18}NO_4Cl$: C, 54.26: H, 6.31. Found : C, 54.02; H, 6.30); the methiodide (IIc), m.p. 173~174° (*Anal.* Calcd. for $C_{14}H_{20}NI$: C, 51.07, H, 6.12. Found : C, 50.66, H, 6.11). Compounds (II) and (IIa-c) exhibited positive rotatory dispersion curves[*1,2] (Fig. 1) as were the opposite

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[*1] RD curves were measured with the Rudolph automatic recording spectroploarimeter using 1 cm. cell and methanol as solvent.

[*2] The RD curves of compounds (II) and (V) were measured by Dr. K. Kuriyama, Shionogi Research Laboratory, Shionogi & Co., Ltd. whom authors thank.

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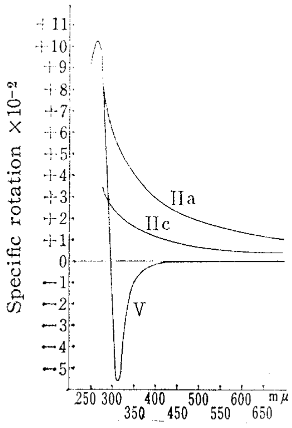
case with S-(−)tetrahydropalmatine⁽6⁾ (III) and S-(−)norcoralydine⁽7⁾ (IV). Molecular rotations, $[M]_D$, of compounds (II) and (IIb) are +415° (in pyridine) and +235° (in ethanol), respectively,[*3] whose sign and values were compared with those reported by Battersby, *et al.*[8] and Ban, *et al.*[9] on emetine derivatives, (−) canadine, (−) tetrahydroprotoberberine etc. These results suggest that securinine should have the R-configuration at C_{10a} and, consequently, the absolute configuration (I), if epimerization at C_{10a} did not occur during the course of the degradation.

The perchlorate (V), m.p. 179~181°, of the hydroxyketone, IR: $\nu_{C=O}$ 1737 cm⁻¹ (KBr), (*Anal.* Calcd. for $C_{11}H_{18}NO_6Cl$: C, 44.67; H, 6.13. Found: C, 44.67; H, 6.24), which was obtained by Satoda, *et al.*[4] exhibited a strong negative Cotton effect[*2] (Fig. 1.). Comparison with the case of (−)-homocamphor[10] and application of the octant rule[10] predict that compound (V) should have the S-configuration at C_{10b} of securinine. This result is consistent with the conclusion obtained above.



Rotatory Dispersion of IIa, IIc, V

Fig. 1.

The ultraviolet spectrum of securinine showed a minor absorption at 330 mμ (log ε 3.30), in which the strong Cotton effect in the rotatory dispersion curve of securinine would originate, and which was not influenced in intensity and wave length by altering solvent (ethanol, dioxane and hexane). On the other hand, the hydrochloride of securinine and the compounds (VI) and (VII)[*4] were all colorless and lacked the absorption at 330 mμ in the ultraviolet. This absorption as well as the yellow-coloring of securinine is supposed to have its origin in transannular interaction[11] between the nitrogen and the conjugated system. Thus, it would be preferable to assign the conformation of securinine as shown in Chart 1 or its conformer in regard to the piperidine ring, in which C_{10a}-C_{10a} and N-C_{5b} and *cis*.

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March 14, 1963

[*3] The corresponding compounds, (−) II and (−) IIb, obtained from virosecurinine show $[M]_D$ −392° and −217°, respectively.

[*4] Obtained by ozonolysis of securinine: m.p. 238~240°, UV: λ_{max}^{EtOH} 256 mμ (log ε 4.31), $[\alpha]_D$ −700° (c=0.1, EtOH) (*Anal.* Calcd. for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67. Found: C, 67.09; H, 5.57). (Unpubished experiment).

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