picrylsulfonate, m.p. 161~162° (from H_2O. *Anal.* Calcd. for $C_{13}H_{20}O_{15}N_4S_3$: C, 27.46; H, 3.52; N, 9.86. Found : C, 27.88; H, 3.55; N, 9.89), and 2,2′-dihydroxy-N-methyldipropylamine yielded 2,2′-dimesyloxy-N-methyldipropylamine (No. 840) isolated as its picrylsulfonate, m.p. 150° (from Me_2CO-EtOH. *Anal.* Calcd. for $C_{15}H_{24}O_{15}N_4S_3$: C, 30.20; H, 4.03; N, 9.34. Found : C, 30.02; H, 4.02; N, 9.35), and 3,3′-dihydroxy-N-methyldipropylamine yielded 3,3′-dimesyloxy-N-methyldipropylamine (No. 838) isolated as its hydrochloride, m.p. 95° (from MeOH-Et_2O. *Anal.* Calcd. for $C_9H_{22}O_6NS_2Cl$: C, 31.76; H, 6.47; N, 4.12. Found : C, 31.80; H, 6.73; N, 3.99). By the reaction with methyl iodide in ether, the free base No. 838 yielded 3,3′-dimesyloxy-N-dimethyldipropylammonium salt (No. 844) isolated as picrylsulfonate, m.p. 65~75° (from Me_2CO-EtOH. *Anal.* Calcd. for $C_{16}H_{26}O_{15}N_4S_3$: C, 31.42; H, 4.42; N, 9.17. Found : C, 31.31; H, 3.93; N, 8.88).

The compounds and their biological data so far obtained are summarized in Table I. Out of these compounds, No. 838 was of particular interest as its antitumor activity on *Yoshida sarcoma* was found to be of the same order as that of methyl-bis 2-chloroethyl amine N-oxide. Further investigation is in progress and details of this work will be published in the near future.

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Partial Synthesis of Securinine

The structure (I) of securinine, a major alkaloid of *Securinega suffruticosa* REHD., has been established by the recent works (the constitution,[1] relative[2] and absolute configuration[3]). This alkaloid possesses a clinically useful strychnine-like activity, which makes us interested in its synthesis. The present report concerns with the partial synthesis of securinine from the degradation products (II) and (III),[2] involving reconstitution of the 6-azabicyclo[3.2.1]octane system.

Bromination of the hydrochloride monohydrate of II,[2] m.p. 218~220°, $[\alpha]_D^{25}$ +94.8° (c=1, EtOH), with bromine in chloroform gave a 71% yield of the hydrochloride of the

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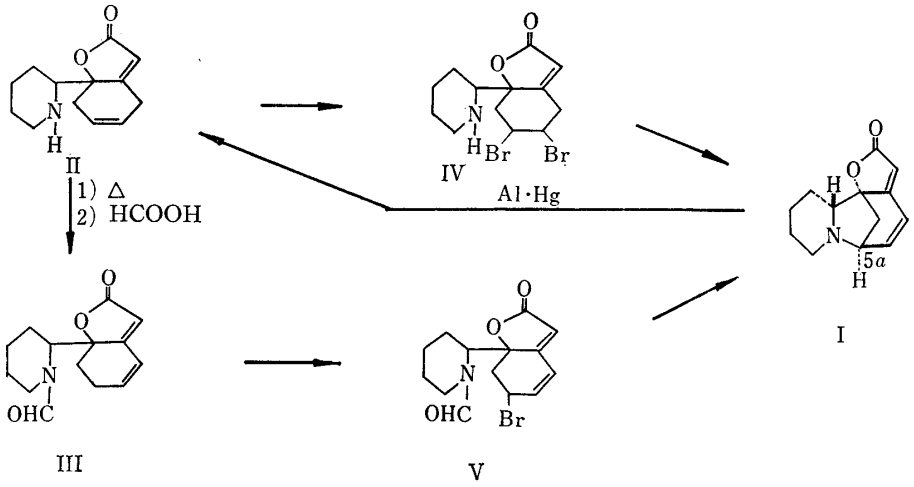

Chart 1.

dibromide (IV), m.p. 205~206°. (*Anal.* Calcd. for $C_{13}H_{18}O_2NBr_2Cl$: C, 37.57; H, 4.36; N, 3.37). Found : C, 37.36; H, 4.01; N, 3.38). Cyclization and simultaneous dehydrobromination by refluxing a wet chloroform solution of IV in the presence of potassium carbonate, followed by chromatographical purification using alumina and chloroform, gave a 14% yield of securinine, m.p. 142~143°, $[\alpha]_D^{21}$ −1052° (c=1, EtOH) in yellow needles.

The synthesis of securinine was also accomplished by an alternative route from III.[2] Bromination with N-bromosuccinimide in carbon tetrachloride converted III, m.p. 161~163°, $[\alpha]_D^{26}$ −34.9° (c=0.13, EtOH), to the bromide (V), m.p. 181~183° (decomp.) in 60% yield. (*Anal.* Calcd. for $C_{14}H_{16}O_3NBr$: C, 51.54; H, 4.94; N. 4.29. Found : C, 51.99; H, H, 5.03; N, 4.25). Hydrolysis of V with 20% hydrochloric acid at 90° and subsequent cyclization in the same manner as employed in the cyclization of IV gave a 7.5% yield of securinine, m.p. 142~143°. The synthetic securinines thus obtained by the two methods showed no depression in melting point on admixture with natural securinine, m.p. 143~144°, $[\alpha]_D^{20}$ −1042° (c=1, EtOH), and their infrared spectra were identical throughout the range.

These syntheses provide a further definite confirmation of the presence of the linkage C_{5a}–N in the structure of securinine and, furthermore, important steps in its total synthesis.

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