Anal.—Calcd. for $C_{12}H_{17}Br_2N$: N, 4.2; Br^-, 23.9; Br, 47.8. Found: N, 4.9; Br^-, 24.8; Br, 48.9.

1-Methyl-Δ^3-pyrroline Methobromide—A solution of 8.3 Gm. (0.1 mole) of 1-methyl-Δ^3-pyrroline in 100 ml. of methyl ethyl ketone was treated with 9.5 Gm. of methyl bromide gas. The resulting solid was filtered to yield 17.79 Gm., 100% of theory, 1-methyl-Δ^3-pyrroline methobromide, m.p. 303–304°.

Anal.—Calcd. for $C_6H_{12}BrN$: N, 7.88; Br^-, 44.9; Br, 44.9. Found: N, 8.58; Br^-, 45.37; Br, 45.40.

1-Methyl-3-bromopyrrolidine Methobromide (II)—A solution of 17.79 Gm. (0.1 mole) of 1-methyl-Δ^3-pyrroline methobromide in 67.5 Gm. of 60% HBr was reacted as described above. The excess hydrobromic acid was distilled and the residue crystallized from 2 B ethyl alcohol (90 ml.) to yield 57% of theory II, m.p. 190–191°.

Anal.—Calcd. for $C_6H_{13}Br_2N$: N, 5.4; Br^-, 30.9; Br, 61.8. Found: N, 5.3; Br^-, 32.1; Br, 62.9.

1-Ethyl-3-bromopyrrolidine Methobromide (IV)—This compound, similarly prepared from 1-ethyl-Δ^3-pyrroline methobromide, m.p. 265–266°, was extremely hygroscopic and required rapid crystallization from a mixture of methyl ethyl ketone (50 ml.) and 2 B ethyl alcohol (10 ml.), m.p. 134–135°.

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Communications

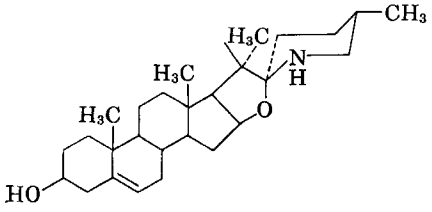
Synthesis of the *Veratrum* Alkaloid Verazine from Tomatid-5-en-3β-ol

Sir:

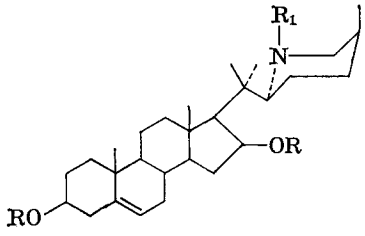
Recently, several new minor alkaloids have been isolated from *Veratrum album* subsp. *lobelianum* (Bernh.) Suessenguth (1). In a preceding communication (2) we described the structural elucidation of one of these new alkaloids, verazine, which according to chemical transformations and physical measurements possesses the structure 25*S*-22,26-epimino-cholesta-5,22(*N*)-dien-3β-ol (I). In this paper the establishment of this structure by a nine-step synthesis of compound I starting from the spirosolane alkaloid tomatid-5-en-3β-ol (II) (3) is reported.

Reduction of II with sodium borohydride in methanol afforded (22*S*:25*S*)-22,26-epimino-cholest-5-ene-3β,16β-diol (III), m.p. 165–167°, 189–191°, and $[\alpha]_D$ −69.1°[1] in 70% yield. Acetylation of III with acetic anhydride/pyridine at 20° for 14 hr. gave nearly quantitatively the amorphous *O,O,N*-triacetate (IV) with $[\alpha]_D$ −10.3°. Hydrolysis of this compound by refluxing with 5% potassium hydroxide in methanol for 2 hr. furnished (22*S*:25*S*)-22,26-acetylepimino-cholest-5-ene-3β, 16β-diol (V), m.p. 248–250°, $[\alpha]_D$ −35° (yield 81%). The *N*-acetyl-diol (V) through partial oxidation with 1 equivalent chromium trioxide in acetic acid–sodium acetate yields 80% (22*S*:25*S*)-22,26-acetylepimino-3β-hydroxy-cholest-5-en-16-one (VI), m.p. 213–215°, $[\alpha]_D$ −121.1°. Treatment of this ketone (VI) with ethanedithiol–hydrochloric acid followed by desulfurization of the obtained thioketal (VII) with Raney nickel in ethanol gave (22*S*:25*S*)-22,26-acetylepimino-cholest-5-en-3β-ol (VIII), m.p. 256–258°, and $[\alpha]_D$ −19.4° (74%).

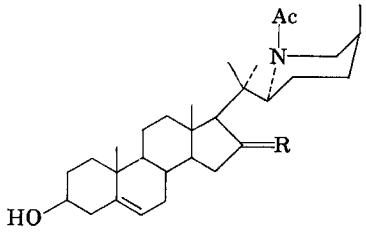
[1] Melting points are corrected. All rotations in chloroform (c = 0.5). The infrared and molecular mass spectra of all new compounds described in this communication are in agreement with the proposed structure. The authors are indebted to Dr. R. Tummler, Dresden, for the molecular mass spectra.



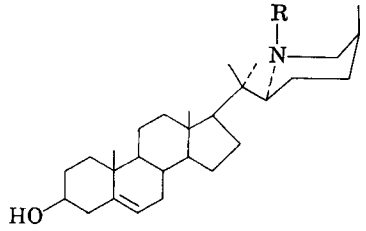
II



III, R, R_1 = H
IV, R, R_1 = Ac
V, R = H, R_1 = Ac

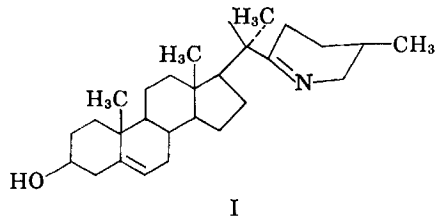


VI, R = O
VII, R = S
S



VIII, R = Ac
IX, R = H
X, R = Cl

Saponification of the amide (VIII) furnished the amine (IX) in only 11% yield even after employing the drastic Schmidt-Thome conditions [refluxing with potassium hydroxide in ethylene glycol for 8 hr. (4)]. The amine (IX) was separated from unchanged starting amide (VIII) by preparative thin-layer chromatography on Silica Gel G (development five times with chloroform) and has m.p. 167–171°, $[\alpha]_D$ −39.0°. *N*-Chlorination of IX with *N*-chloro succinimide in methylene dichloride at −5° and subsequent treatment of the unisolated *N*-chloro derivative (X) with sodium methoxide in methanol led to compound I with 24% yield, m.p. 173–176°, and $[\alpha]_D$ −83.4°, which was identical in every respect (mixed m.p., infrared spectrum, thin-layer chromatography) with authentic verazine, isolated from *V. album*. Since the starting tomatid-5-en-3β-ol (II) is already total synthetically obtainable (3,5) the above reported sequence of reactions also represents the total synthesis of verazine (I).



I

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Received April 14, 1967.
Accepted for publication June 12, 1967.
Presented to the Pharmacognosy and Natural Products Section, A.Ph.A. Academy of Pharmaceutical Sciences, Las Vegas meeting, April 1967.

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