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ISOLATION OF RUBIJERVINE FROM *VERATRUM CALIFORNICUM*

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Veratrum californicum (Durand) and certain of its steroidal alkaloids containing fused furanopiperidine rings have been incriminated as causing congenital cyclopia and related cephalic malformations in lambs born to dams ingesting the plant or alkaloids on the 14th day of gestation.[1] During the course of these studies, the alkaloids veratramine, veratrosine, jervine, pseudojervine, 11-deoxojervine (cyclopamine), 3-glucosyl-11-deoxojervine (cycloposine), isorubijervine, and muldamine have been found in the plant.[2–7] All but isorubijervine have the *C*-nor-*D*-homo modified steroidal skeleton. From the point of view of the proposed biosynthesis route for veratrum alkaloids in *Veratrum grandiflorum*,[8,9] one would expect to find in *V. californicum* alkaloids of the solanidanine type with the unmodified steroid skeleton if pathways are common in the two plants because solanidanines are proposed as precursors of the *C*-nor-*D*-homo alkaloids.

We report here the isolation of rubijervine, a solanidanine alkaloid, from *V. californicum*. Rubijervine has been isolated from at least nine other members of the *Veratrum* genus[10] but had not yet been reported from *V. californicum*. The presence in *V. californicum* of rubijervine suggests that the pathway proposed for *V. grandiflorum* could operate also in *V. californicum*. That pathway is via acetate → mevalonate → cholesterol → solanidanine alkaloid (probably epirubijervine) → *C*-nor-*D*-homo alkaloids.[9]

EXPERIMENTAL

The mixed crystalline, benzene extractable alkaloid preparations obtained as previously described[11] contain largely cyclopamine, veratramine, and muldamine with traces of other alkaloids. A 9·5 g quantity of cyclopamine was recrystallized from aq. MeOH and gave a first crop (usually discarded) which on repeated recrystallization yielded 0·6 gm of rubijervine. The compound had m.p. 240–242°; $[\alpha]_D^{25}$ + 16 (C = 1·0 in EtOH); IR (KBr) ν_{max} 3430(s), 2980(s), 1460(m), 1440(w), 1390(m), 1380(m), 1320(w), 1240(w), 1210(w), 1147(w), 1064(s), 1050(m), 1012(m),

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967(m), 895(w), 824(m)cm^{-1}; NMR ($CDCl_3$) had overlapping signals centered at 0·94δ that integrated for 12 protons (C18, 19, 21, 27 methyl groups) and the expected envelope between about 1 and 2δ (methylene and methine steroid 19, 21, 27 methyl groups) and the expected envelope between about 1 and 2δ (methylene and methine steroid protons). M.P., optical rotation, IR spectrum, and NMR spectrum were essentially identical with two authentic samples of rubijervine obtained from separate suppliers.*

* S. B. Penick & Co., K and K Laboratories, Inc.