# SYNTHESIS OF CORGOINE

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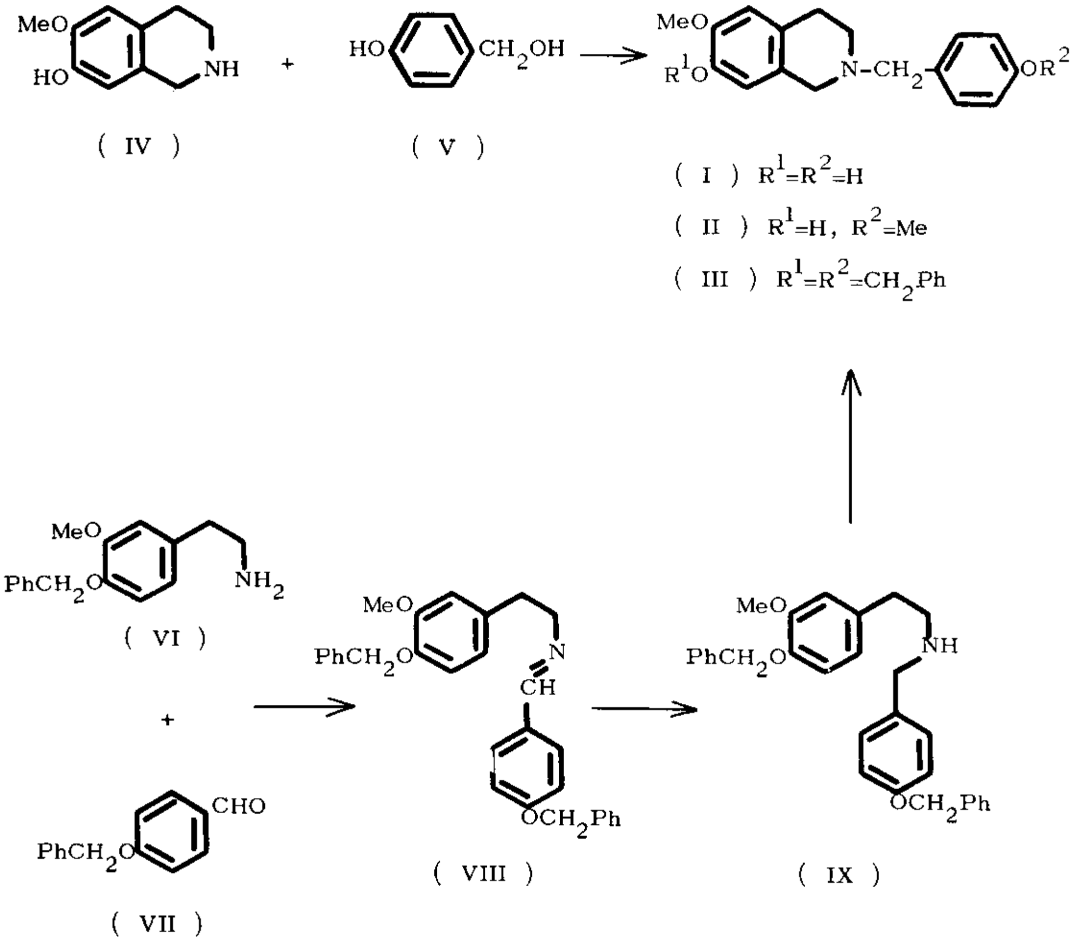
Corgoine (I) was synthesized by two different methods, which proved the suggested structure to be correct. The biogenesis of the 2-benzylisoquinoline alkaloids is also discussed.

Corgoine, $C_{17}H_{19}NO_3$, has recently been isolated from Corydalis gortschakovii,[1] and has been shown to have structure (I) by nmr spectral comparison with the known alkaloid, sendaverine (II).[2]

We now wish to report the synthesis of corgoine (I) by two different methods, which proves the suggested structure (I) to be correct.

A mixture of 1,2,3,4-tetrahydro-7-hydroxy-6-methoxyisoquinoline (IV) (0.5 m mole) and p-hydroxybenzyl alcohol (V) was heated at 150 - 160° under a current of nitrogen to give corgoine (I), mp 190 - 191°, in 44 % yield after purification by thick layer chromatography. The synthetic product was identical with the natural corgoine by direct comparisons of the spectroscopic data: $\delta$ ($CF_3CO_2H$) 6.74 (1H, s, 8 - H), 6.82 (1H, s, 5 - H), 7.09 (2H, d, J 8 Hz, 3' - H and 5' - H), and 7.42 ppm (2H, d, J 8 Ha, 2' - H and 6' - H); ir ($CHCl_3$) $\nu$ : 3550 $cm^{-1}$ (OH); uv (MeOH) $\lambda$ : 227, 284 nm.

The second method for the synthesis of corgoine is an application of the Pictet-Spengler reaction as follows: the condensation of 4-benzyloxy-3-methoxyphenethylamine (VI) with p-benzyloxybenzaldehyde (VII), followed by sodium borohydride reduction of the resulting Schiff base (VIII), gave the corresponding secondary amine (IX). The hydrochloride of IX was subjected to the Pictet-Spengler reaction with 37 % formalin in a boiling methanol to give the tetrahydroisoquinoline (III) as colorless needles, mp 107 - 109° (lit.,[3] mp 107 - 108.5°), the hydrochloride of which gave color-



( IV )

( V )

( I ) $R^1=R^2=H$

( II ) $R^1=H$, $R^2=Me$

( III ) $R^1=R^2=CH_2Ph$

( VI )

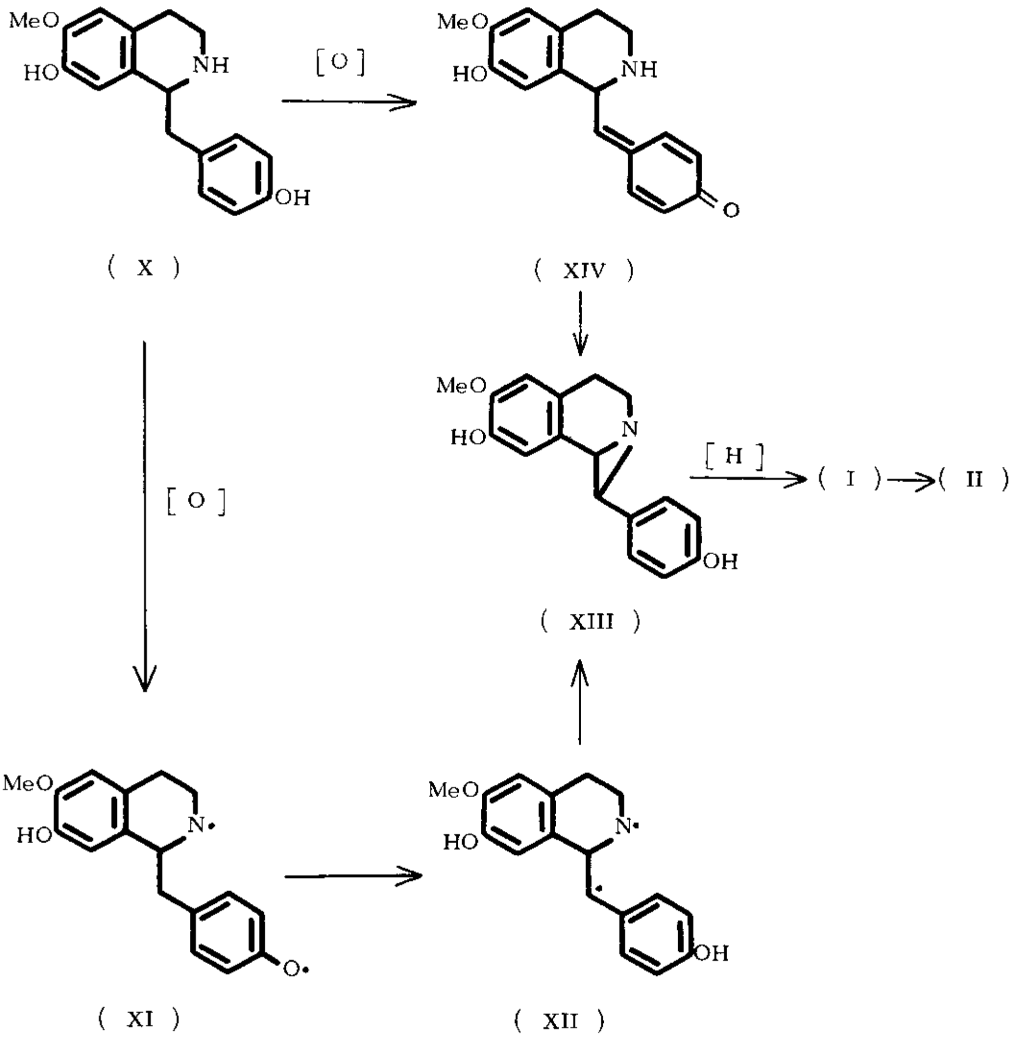
( VII )

( VIII )

( IX )

less needles, mp 175 - 179°, in 43 % yield, identical with the authentic sample.[3] Debenzylation of III[3] with ethanolic hydrochloric acid gave corgoine (I), identical with natural product.

The biogenesis of the 2-benzylisoquinoline alkaloids may possibly involve the following transformations:



Sendaverine (II) is co-existent with the protoberberine alkaloids[4] which could be biosynthesized from 1-benzylisoquinolines;[5] thus, a suitable precursor for 2-benzylisoquinolines would be coclaurine (X), which, on oxidation, would furnish the aziridine type compound (XIII) by radical pairing through the radical intermediates (XI and XII). The formation of the latter compound (XIII) would also be possible by an intramolecular Michael addition of the *p*-quinonoid intermediate (XIV). The reductive cleavage of the C–C bond of XIII by an enzyme would afford corgoine (I), which on methylation gives sendaverine (II). Inubushi[6] reported the formation of 2-benzylisoquinoline from N-norarmepavine by an enzymic oxidation, followed by sodium borohydride reduction. Determination of the exact route for the biogenesis of this type alkaloid will require critical tracer experiments.

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