

AN ANALOGUE OF CORYNOLINE¹

Masayuki Onda^{*}, Kumiko Yuasa, and Junko Okada
School of Pharmaceutical Sciences, Kitasato University,
Minato-ku, Tokyo 108, Japan

The analogue VIII of corynoline, which contains methoxyl groups at C-7 and C-8 instead of a methylenedioxy group, has been synthesized from the ψ -cyanide I.

Attempts to obtain corynoline and its analogues from the protopine and related alkaloids have been carried out in our laboratory and the synthesis of 10b-methylhexahydrobenzo(c)-phenanthridine derivatives has been recently carried out (1). We now wish to report the synthesis of an analogue of corynoline which contains methoxyl groups at C-7 and C-8 instead of a methylenedioxy group.

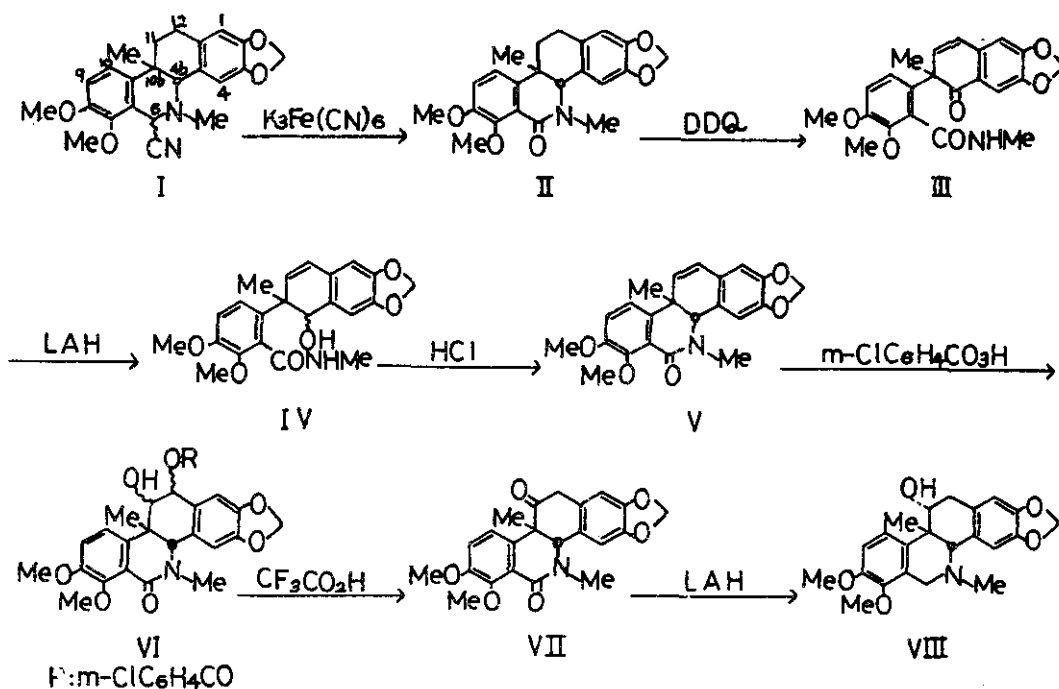
The synthesis of the ψ -cyanide I from berberine has been described in a previous paper (1). On oxidation with

1 Utilization of protopine and related alkaloids. VII.
All compounds reported gave satisfactory analyses and mass spectrometric molecular weights.

potassium ferricyanide the ψ -cyanide I gave the lactam II, $C_{22}H_{23}NO_5$, mp 262-265°, whose ir spectrum ($CHCl_3$) showed an absorption band at 1640 cm^{-1} (CON). In order to obtain the 11,12-dehydro compound, the lactam II was treated with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) to afford, unexpectedly, the keto amide III, $C_{22}H_{21}NO_6$, mp 215-217°, as the main product, whose ir spectrum (KBr) showed absorption bands at 3340 (NH), 1667 (CO) and 1648 cm^{-1} (CON), and whose nmr spectrum ($CDCl_3$) revealed signals due to the vinyl protons at δ 6.52 (d, J 10 Hz) and 6.19 (d, J 10 Hz) in addition to the four aromatic protons. These spectral data suggest that oxidative fission and dehydrogenation occurred between the 4b- and 5-positions in B ring and the 11- and 12-positions in C ring, respectively.

Compound III was reduced with lithium aluminum hydride (LAH) to give the carbinol IV, $C_{22}H_{23}NO_6$, mp 207-208°, which was converted with hydrochloric acid into the lactam V, $C_{22}H_{21}NO_5$, mp 276-278°. The ir spectrum ($CHCl_3$) of V shows an absorption band at 1640 cm^{-1} (CON). Assignment of the cis B/C ring juncture was confirmed by observance of an NOE (7 %) between the 4b-H (δ 4.87) and 10b-Me (δ 1.57) (100 MHz, CF_3CO_2D).

On treatment of V with m-chloroperbenzoic acid the diol monoester VI, $C_{29}H_{26}NO_8Cl$, mp 232.5-233.5°, was obtained via an intermediate epoxide. The positions of the hydroxyl and ester groups are on the basis of the nmr spectrum ($CDCl_3$) which shows signals due to the $\underline{C}HOH$ at δ 4.90 (d, J 4 Hz) and the $\underline{C}HOCOC_6H_4Cl(m)$ at δ 6.17 (d, J 4 Hz) and are also in accord



with mechanistic considerations. Compound VI was converted with trifluoroacetic acid into the keto lactam VII, $C_{22}H_{21}NO_6$, mp $292-297^\circ$, whose ir spectrum (KBr) showed absorption bands at 1710 (CO) and 1645 cm^{-1} (CON), while the nmr spectrum (CF_3CO_2D) revealed signals for the C-12 methylene at δ 4.52 (d, J 12 Hz) and 3.82 (d, J 12 Hz).

The LAH reduction of VII stereoselectively gave the carbinol VIII, $C_{22}H_{25}NO_5$, mp $194-196^\circ$, nmr spectrum ($CDCl_3$) δ 7.15 (d, 1H, J 8 Hz, 10-H), 6.92 (d, 1H, J 8 Hz, 9-H), 6.67 (s, 2H, 1-H and 4-H), 5.95 (s, 2H, $CH_2\text{C}(=O)$), 4.18 (d, 1H, J 16 Hz, 6-H), 3.45 (d, 1H, J 16 Hz, 6-H), 3.95 (m, 1H, 11-H), 3.90 (s, 6H, 2XOMe), 3.30 (s, 1H, 4b-H), 3.13 (d, 2H, J 3 Hz, 12-H₂), 2.25 (s, 3H, NMe), 1.15 (s, 3H, 10b-Me). The intramolecular

hydrogen bonding between the C-11 OH and the nitrogen was observed at 3190 cm^{-1} in a carbontetrachloride solution (1.5×10^{-3} mole/liter) (2).

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