

TOTAL SYNTHESIS OF 11-EPICORYNOLINE

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Treatment of the 11,12-dehydro derivatives (V and VI) of B/C-cis-benzo[c]phenanthridines with performic acid afforded all possible stereoisomers (IX, X, II, and XI) of the 11,12-dihydroxyamine, of which the 11 β -isomers (IX and X) were successfully converted into 11-epicorynoline (III).

As an extension of synthetic study on the alkaloids of corynoline group¹, we now report total synthesis of 11-epicorynoline (III), a minor alkaloid of Corydalis plants.^{2,3}

The starting 11,12-dehydrolactam (V) was prepared as described in the previous communication¹, from the photocyclised lactam (IV) upon reduction followed by dehydrogenation with 2,3-dichloro-5,6-dicyanobenzoquinone.

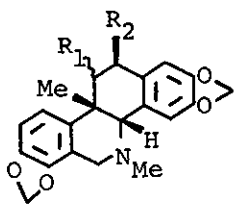
Oxidation of the 11,12-dehydrolactam (V) with performic acid followed by treatment with alkali furnished a mixture of the insoluble 11 β ,12 α -dihydroxylactam (VII) (20 %), ir (nujol) 3550, 3350 (OH), and 1645 cm⁻¹ (NCO), and the soluble 11 β ,12 β -dihydroxylactam (VIII) (40 %), ir (CHCl₃) 3600 (OH) and 1640 cm⁻¹ (NCO).

On the other hand, the oxidation of the corresponding 11,12-dehydroamine (VI) was shown to afford the homogeneous 11 α ,12 β -dihydroxyamine, 12-hydroxycorynoline (II) (91 %) as described previously.¹

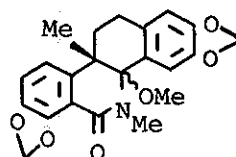
Lithium aluminium hydride reduction of the dihydroxylactams (VII and VIII) yielded the corresponding dihydroxyamines, 11 β ,12 α - (IX), nmr (CDCl₃) δ 4.36 and 4.32 (2H, ABq, J=7.5Hz, 11- and 12-H), 3.11 (1H, s, 4b-H), and 11 β ,12 β - (X), nmr (CDCl₃) δ 4.72 (1H, d, J=5Hz, 12-H), 4.44 (1H, d, J=5Hz, 11-H), and 3.48 (1H, s, 4b-H), in good yields respectively.

Hydrogenolysis of either the 11 β ,12 α -dihydroxyamine (IX) or the epimeric 11 β ,12 β -dihydroxyamine (X) with 40 % palladium on charcoal afforded 11-epicorynoline (III) in 40 % yield, which was identical with the natural alkaloid upon comparisons of their i.r. and n.m.r. spectra.³

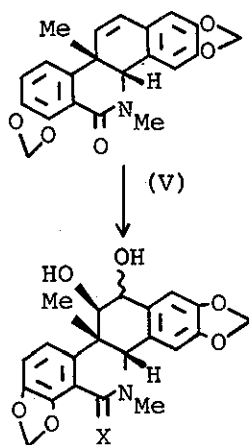
Reinvestigation of hydrogenolysis of the 11 α ,12 β -dihydroxyamine (II) revealed that the epimeric 11 α ,12 α -dihydroxyamine³ (XI), nmr (CDCl₃) δ 4.59 (1H, d, J=5Hz, 12-H), 3.90 (1H, d-d, J=5 and 2Hzs, 11-H), and 3.28 (1H, d, J=2Hz, 4b-H), was formed beside corynoline (I)¹. The ratio of epimerisation and hydrogenolysis was depending upon the reaction time; the longer the reaction time, the more corynoline was formed.



- (I) R₁ = ---OH , R₂ = H
 (II) R₁ = ---OH , R₂ = OH
 (III) R₁ = ---OH , R₂ = H

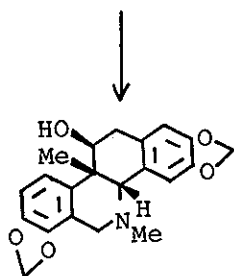


(IV)

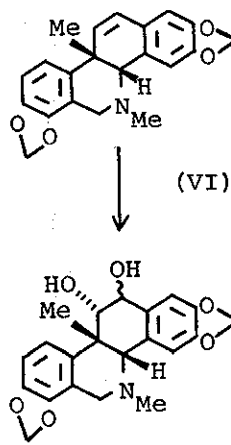


(V)

- (VII) ---OH (12 α), X=O
 (VIII) ---OH (12 β), X=O
 (IX) ---OH (12 α), X=H₂
 (X) ---OH (12 β), X=H₂

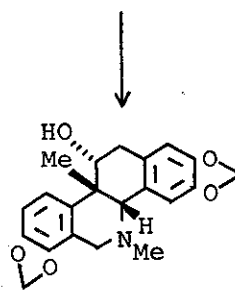


(III)



(VI)

- (II) ---OH (12 β)
 (XI) ---OH (12 α)



(I)

In addition to the spectral data, the preparation of all the possible epimers of the 11,12-dihydroxyamines (IX, X, II, and XI) facilitated to determine the stereochemistry of these compounds.

Since we have already reported total synthesis of corynoline (I) and 12-hydroxycorynoline (II), the present work completed syntheses of all the cis-alkaloids of corynoline group. Synthesis of the remaining trans-alkaloid, 14-epicorynoline², is now under progress.

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