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 11β-isomers (IX and X) were successfully converted into 11-epicorynoline (III).

As an extension of synthetic study on the alkaloids of corynoline group[1], 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 communication[1], from the photocyclised lactam (IV) upon reduction followed by dehydrogenation with 2,3-dichloro-5,6-dicyanobenzoquinone.

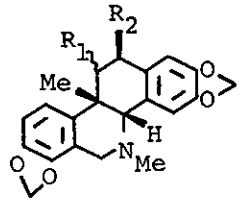
Oxidation of the 11,12-dehydrolactam (V) with performic acid followed by treatment with alkali furnished a mixture of the insoluble 11β,12α-dihydroxylactam (VII) (20 %), ir (nujol) 3550, 3350 (OH), and 1645 cm^{-1}(NCO), and the soluble 11β,12β-dihydroxylactam (VIII) (40 %), ir ($CHCl_3$) 3600 (OH) and 1640 cm^{-1}(NCO).

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

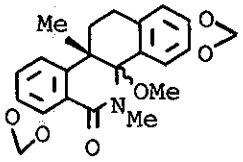
Lithium aluminium hydride reduction of the dihydroxylactams (VII and VIII) yielded the corresponding dihydroxyamines, 11β,12α-(IX), nmr ($CDCl_3$) δ 4.36 and 4.32 (2H, ABq, J=7.5Hz, 11- and 12-H), 3.11 (1H, s, 4b-H), and 11β,12β-(X), nmr ($CDCl_3$) δ 4.72 (1H, d, J=5Hz, 12-H), 4.44 (1H, d, J=5Hz, 11-H), and 3.48 (1H, s, 4b-H), in good yields respectively.

Hydrogenolysis of either the 11β,12α-dihydroxyamine (IX) or the epimeric 11β,12β-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]

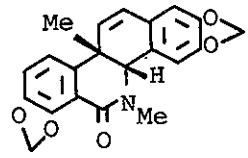
Reinvestigation of hydrogenolysis of the 11α,12β-dihydroxyamine (II) revealed that the epimeric 11α,12α-dihydroxyamine[3] (XI), nmr ($CDCl_3$) δ 4.59 (1H, d, J=5Hz, 12-H), 3.90 (1H, d-d, J=5 and 2Hzs, 11-H), and 3.28 (1H, d, J=2Hz, 4b-H), was formed beside corynoline (I)[1]. The ratio of epimerisation and hydrogenolysis was depending upon the reaction time; the longer the reaction time, the more corynoline was formed.



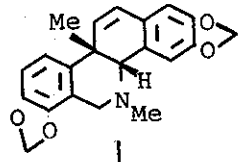
(I) R_1 = ⋯OH, R_2=H
(II) R_1 = ⋯OH, R_2=OH
(III) R_1 = ▬OH, R_2=H



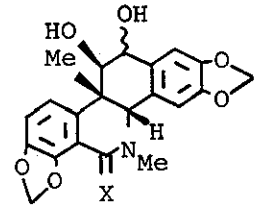
(IV)



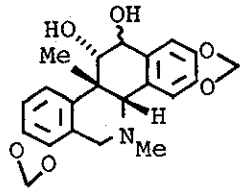
(V)



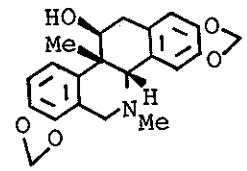
(VI)



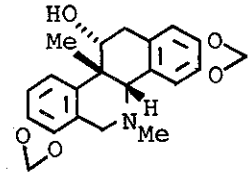
(VII) ⋯OH(12α), X=O
(VIII) ▬OH(12β), X=O
(IX) ⋯OH(12α), X=H_2
(X) ▬OH(12β), X=H_2



(II) ▬OH(12β)
(XI) ⋯OH(12α)



(III)



(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[1] 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-epicorynoline[2], is now under progress.

We thank Professor I. Nishioka and Dr. G. Nonaka of Kyushu University for i.r. and n.m.r. spectra of natural 11-epicorynoline.

REFERENCES

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3 G. Nonaka and I. Nishioka, Chem. and Pharm. Bull. (Japan), 1975, 23, 521.

Received, 21st June, 1976