SYNTHESIS OF YENHUSOMINE AND YENHUSOMIDINE

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Yenhusomine and yenhusomidine, previously isolated from Corydalis ochotensis Turcz. were synthesised by reduction of synthetically obtained oxo-yenhusomine with sodium borohydride in a regio- and stereo-selective manner.

A recent report[1] concerning the transformation of the phthalideisoquinoline, dehydrocordrastine, into spirobenzyl-isoquinolines, congeners of yenhusomine (I)[2] and yenhusomidine (II)[2], both of which have been isolated from Corydalis ochotensis Turcz. and have two groups in ring C has prompted us to publish our recent synthetic results on these alkaloids.

The keto group at the C_8 position of oxo-yenhusomine (III) is sterically more hindered than the C_{13}-keto group. Therefore, we expected that the methylenedioxy group in ring D would have a subtle effect on the susceptibility of the two keto groups to reduction with hydride reagents: the C_8-keto group is in the ortho-position to the methylenedioxy moiety, while the C_{13}-keto group is in the para-position.

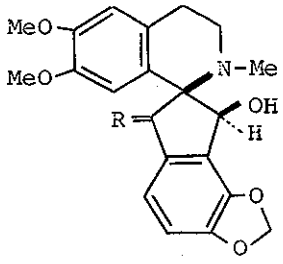
A model experiment was carried out using 4,5-dimethoxy-

ninydrin (IV) which was prepared from 4,5-dimethoxyindanone by oxidation with selenium dioxide in 65% yield in the same manner as for the preparation of 4,5-methylenedioxyninhydrin [3]. Condensation of homoveratrylamine hydrochloride with the ninhydrine (IV) in acetic acid at 50-55° overnight gave the diketo-spiroisoquinoline (V)[4] in 60% yield, m.p. 181-186°, $\nu_{max.}$ (KBr); 1706 and 1738cm^{-1}, δ ($CDCl_3$); 1.92 (NH), 3.58, 3.84, 4.02, and 4.08 (3H each, s, OMe), 6.02 (1H, s, C_1-H), 6.67 (1H, s, C_4-H), 7.43 (1H, d, J=8Hz, C_{11}-H) and 7.80 (1H, d, J=8Hz, C_{12}-H). Reduction of the spiroisoquinoline (V) (1 m mole) with sodium borohydride (1.5 m mole, added in three portions during two days) in tetrahydrofuran at 0° yielded the monoketo-spiroisoquinoline (VI) (15%) and the diol-spiroisoquinoline (VII) (53%). Although there has been no stereochemical assignment to these alcohols so far, the former showed a typical AB-type quartet at δ 7.14 and 7.64 (J=8Hz.) which can be assigned to the two aromatic protons on ring D, thus confirming the 8-ol-13-keto structure.

Condensation of the ninhydrin (VIII) with homoveratrylamine in the same way as for IV gave the diketo-spiroisoquinoline (IX) in 50% yield, m.p. 214-215° , $\nu_{max.}$ (KBr); 1706 and 1730cm^{-1}, δ ($CDCl_3$); 1.90 (NH), 3.59 and 3.83 (3H each, s, OMe), 6.03 (1H, s, C_1-H), 6.30 (2H, s, O-CH_2-O), 6.67 (1H, s, C_4-H), 7.27 (1H, d, J=8Hz, C_{11}-H), and 7.65 (1H, d, J=8Hz, C_{12}-H). Treatment of the diketo-spiroisoquinoline (IX) with formic acid and 37% aqueous formaldehyde under reflux gave the N-methyl-di-

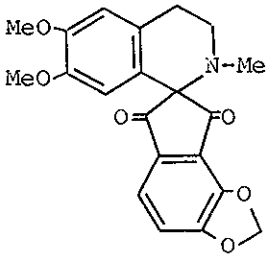
keto-spiroisoquinoline (X) and the N-formyl-spiroisoquinoline (XI) in 50 and 6% yield, respectively. The n.m.r. signals of the former were identical with those of oxo-yenhusomine[2] reported by Lu et al. The latter showed three carbonyl bands at 1740, 1710, and 1660cm^{-1} and the following signals in its n.m.r. spectrum; δ ($CDCl_3$); 3.58 and 3.83 (3H each, s, OMe), 6.18 (1H, s, C_1-H), 6.30 (2H, q, J=1Hz, O-CH_2-O), 6.73 (1H, s, C_4-H), 7.23 (1H, d, J=8Hz, C_{11}-H), 7.67 (1H, d, J=8Hz, C_{12}-H), and 8.18 (1H, s, N-CHO).

Treatment of synthetic oxo-yenhusomine (X) (1 m mole) with sodium borohydride (1.8 m mole, which was added in portions while monitoring the reaction mixture by thin layer chromatography) in tetrahydrofuran at 4° for 4 days gave yenhusomidine (II), m.p. 242-243°, and dl-yenhusomine (I), m.p. 221-223°, in 45 and 25% yield, respectively, both of which were easily separated, since the hydrochloride of yenhusomidine (II) is soluble in chloroform. The i.r. spectrum (KBr) of the former was identical with that of yenhusomidine[5] from naturel sources, since natural yenhusomidine has been isolated in racemic form (it is thought to be due to Aldol-retro-Aldol reaction of the β-hydroxyketone system in yenhusomidine). The i.r. ($CHCl_3$) and n.m.r. ($CDCl_3$) spectra of the latter were superimposable upon those of yenhusomine.

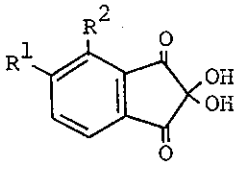


(I) R= 

(II) R=O

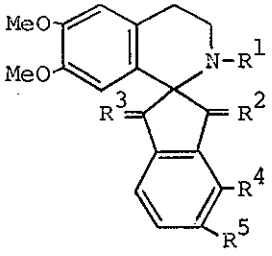


(III)



(IV) $R^1=R^2=OMe$

(VIII) $R^1,R^2=O-CH_2-O$



(V) $R^1=H$, $R^2=R^3=O$, $R^4=R^5=OMe$

(VI) $R^1=H$, $R^2=$  , $R^3=O$, $R^4=R^5=OMe$

(VII) $R^1=H$, $R^2=R^3=$, $R^4=R^5=OMe$

(IX) $R^1=H$, $R^2=R^3=O$, $R^4,R^5=O-CH_2-O$

(X) $R^1=Me$, $R^2=R^3=O$, $R^4,R^5=O-CH_2-O$

(XI) $R^1=CHO$, $R^2=R^3=O$ $R^4,R^5=O-CH_2-O$

References

1) H.L.Holland, D.B.MacLean, R.G.A.Rodrigo, and R.H.F.Manske, Tetrahedron Letters, 1975, 4323.

2) S-T.Lu, T-S.Su, T.Kametani, and M.Ihara, Heterocycles, 1975, 3, 301.

3) B.Nalliah, Q.A.Ahmed, R.H.F.Manske, and R.Rodrigo, Canad. J. Chem., 1972, 50, 1819.

4) All the new compounds cited in this report showed satisfactory elemental analysis and mass spectral data.

5) We thank Professor S-T.Lu for sending us the valuable sample of yenhusomine and the copies of the n.m.r. and i.r. spectra of yenhusomidine.

Received, 13th March, 1976