HETEROCYCLES. Vol.12, No.9, 1979

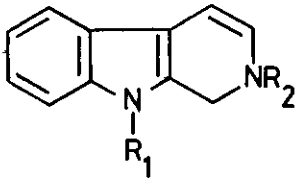
β-CARBOLINE DERIVATIVES FROM AN AMINOACETALDEHYDE DIMETHYLACETAL

Kenneth Curness and Stanley Dyke*

School of Chemistry, University of Bath, Bath BA2 7AY, England

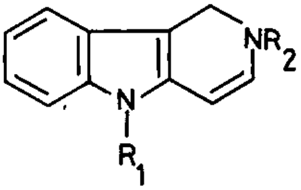
Abstract - Cyclisation of the acetal (3) with dilute HCl gave the hydroxy-β-carboline (8), and not the hydroxy-γ-carboline (4), as previously reported.

As part of a programme on the synthetic utility of cyclic enamines, we wished to prepare the dihydrocarbolines (1) and (2). From our experience with 1,2-dihydroisoquinolines[1,2] we anticipated that these β- and γ-carboline derivatives might be unstable, but would, nevertheless, exhibit useful enamine properties.



(1)

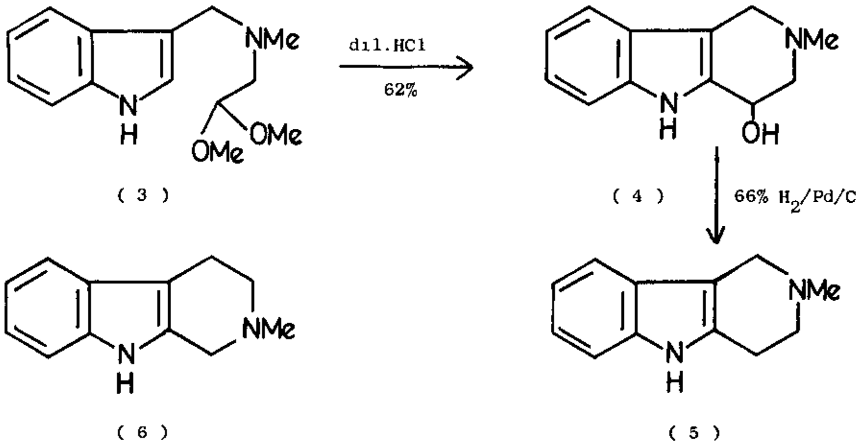
R_1,R_2 = H or alkyl



(2)

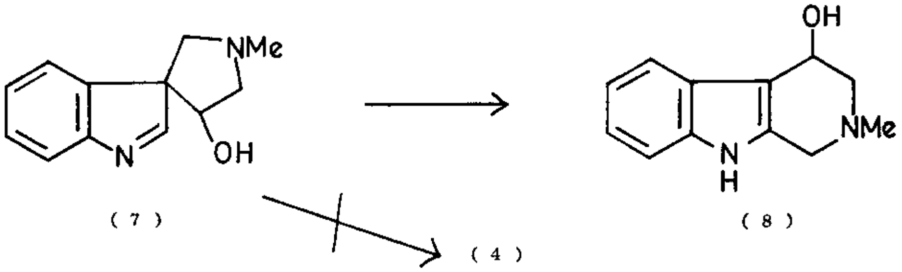
Bobbitt, et al[3] have recently described the preparation of (3), m.p. 79-80°, by the Mannich condensation between indole, formaldehyde and N.methylaminoacetaldehyde dimethylacetal, and the conversion of it with dilute HCl into the γ-carboline derivative (4), m.p. 205-206°. No spectral data were recorded for (3) or (4), but the structure of (4) depended upon the fact that hydrogenolysis of it gave the known[4] N.methyl-1,2,3,4-tetrahydro-γ-carboline (5), m.p. 172-173°, although a direct comparison with an authentic specimen was apparently not carried out.

We, too, have carried out this sequence of reactions[5] but, interestingly, with different results. Our sample of (3), m.p. 77-78° [^{1}H NMR ($CDCl_3$), δ 8.84 s [1]; 7.74 m [1]; 7.34-7.08 m [3]; 6.93 d, J = 2 Hz [1]; 4.56 t, J = 5 Hz [1]; 3.76 s [2]; 3.29 s [6]; 2.61 d, J = 5 Hz [2]; 2.32 s [3]] was treated with 6M HCl exactly as described by Bobbitt and we, too, obtained a hydroxycarboline derivative (52% yield) m.p. 202-203° [^{1}H NMR ($CDCl_3$/d_6 DMSO), δ 9.88 s [1];



7.4-7.24 m [2]; 7.08-7.0 m [3]; 4.82 t, J = 5 Hz [1]; 3.80 d, J = 5 Hz [2]; 3.5 q, J = 14 [2]; 2.48 s [3]]. However, when this compound was reduced, either catalytically or with LAH/$AlCl_3$, the tetrahydrocarboline obtained (63% yield) had m.p. 215-216^{c}, picrate m.p. 195-196°. This compound was found to be identical (mixed m.p. of the base and the picrate) with N-methyl-1,2,3,4-tetrahydro-β-carboline (6), prepared[4] by reduction of N-methyl-β-carbolinium iodide, and not with N-methyl-1,2,3,4-tetrahydro-γ-carboline (5), m.p. 170-171°, picrate m.p. 129-130°, also prepared by an independent route[6].

On one occasion when (3) was treated with dilute HCl, an intermediate was isolated, the spectral characteristics of which strongly supported the indolenine structure (7), although it could not be obtained analytically pure [^{1}H NMR ($CDCl_3$) δ 10.42 s [1]; 7.71 s [1]; 7.4-7.29 m [2]; 7.16-6.98 m [2]; 4.88 t [1]; 3.66 br s [2]; 2.86 dd, J = 12 Hz and 4 Hz [2]; 2.36 s [3]]. Such an intermediate could be anticipated[7] to rearrange to either the β- or the γ-carboline skeleta (8) or (4), respectively; in our case it was clearly the β-carboline (8) that was formed.



References

1. S.F.Dyke in Advances in Heterocyclic Chemistry, eds.A.R.Katritsky and A.J.Boulton, Academic Press, 1972, Vol.14, p 279.

2. 1,2-Dihydroisoquinolines Part XX, R.G.kinsman, A.W.C.White and S.F.Dyke, Tetrahedron, 1975, 31, 449 and previous papers in this series.

3. J.M.Bobbitt, C.L.Kulkarni, C.P.Dutta, H.Kofod and K.Ng Chiong, J.Org.Chem., 1978, 43, 3541.

4. V.Boekelheide and C.Ainsworth, J.Amer.Chem.Soc., 1950, 72, 2132.

5. We thank Professor Bobbitt for experimental details well before publication of his results.

6. N.P.Buu-Hoi, O.Roussel and P.Jacquignon, J.Chem.Soc., 1963, 708.

7. A.H.Jackson and A.E.Smith, Tetrahedron, 1968, 24, 203;
A.H.Jackson and P.Smith, ibid., 1968, 24, 2227;
R.Iyer, A.H.Jackson, P.V.R.Shannon and B.Naidoo, J.Chem.Soc.Perkin I, 1973, 878.

Received, 7th May, 1979