5(10 → 9)*abeo*-Ergolines from 9-Hydroxyergolines

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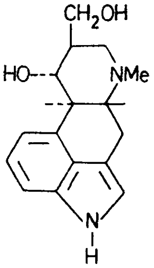
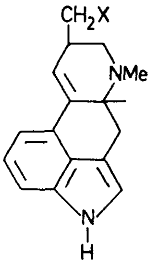
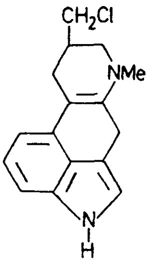
Summary Treatment of 9-hydroxyergolines with $POCl_3$-pyridine yields 5(10 → 9)*abeo*-9,10-didehydroergolines.



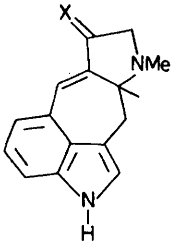
(1)



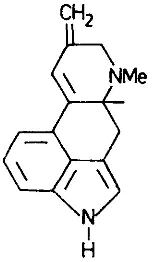
(2) X = Cl
(3) X = OH



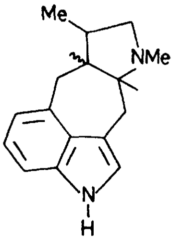
(4)



(5) X = H, CH_2Cl
(6) X = CH_2



(7)



(B); (C)

Lysergic acid (5 g) in tetrahydrofuran (200 ml) was treated overnight with diborane (0·55M; 135 ml), and 5% methanolic KOH (250 ml) was then added followed by 35% H_2O_2 (25 ml). The solution was diluted with water and extracted with ether. The extract was evaporated *in vacuo* and the residue boiled for 3 h with methanol; on dilution with water the diol (**1**) (2·8 g), m.p. 275—278 °C, separated.[1] When a sample of (**1**) (2 g) was treated at 70 °C for 2 h with $POCl_3$–HCl–pyridine (3 : 3 : 20) a compound (A), m.p. 184 °C, $[\alpha]_D^{20}$ — 148° (pyridine), resulting from the replacement of a hydroxy-group by chlorine and loss of one molecule of H_2O, was obtained. Since its u.v. spectrum showed λ_{max} 323 nm as in lysergic acid, (A) was assumed to have structure (**2**). However treatment of lysergol (**3**) with $POCl_3$–pyridine gave the known[2] chloromethylergolene derivative (**2**) which was different from (A) (m.p., optical rotation, and i.r. spectrum). The isomeric structure (**4**) could be ruled out since the u.v. spectrum was unchanged in strongly acid solution and moreover the presence in the ^{1}H n.m.r. spectrum of (A) of a singlet at δ 6·26 suggested the existence of an isolated vinylic proton.

Finally, catalytic hydrogenation and dehalogenation of (A) in methanol (Pd–C; KOH) gave two isomeric compounds {(B), m.p. 255 °C; $[\alpha]_D^{20}$ — 164° (pyridine); (C) m.p. 178 °C; $[\alpha]_D^{20}$ — 48° (pyridine)} whose ^{1}H n.m.r. spectrum showed the presence of the expected Me–CH doublet (δ 1·1 and 1·23, respectively). However neither (B) or (C) had physical constants in accord with those reported for the known 8-methylergolines[3] and therefore it must be concluded that the ergoline skeleton was no longer present in (A).

A Merwein–Wagner rearrangement involving the anti-periplanar C-9–OH and C-5–C-10 bonds followed by loss of a proton would give compound (**5**). Assignment of formula (**5**) to (A) is in accord with the ^{1}H n.m.r. spectrum: δ [$(CD_3)_2SO$] 2·26 (s, 3H, NMe), 3·96 (m, 2H, CH_2Cl), 6·26 br (s, 1H, 10-H), 6·4–7·1 (m, 4H, indole-H), and 10·5 (s, 1H, NH)], and is further substantiated by the formation of the diene (**6**) (m.p. > 300 °C) by treatment of (A) in benzene with 1,5-diazabicyclo[5.4.0]undec-5-ene at 80 °C for 6 h. Comparison of the u.v. spectra of (**6**) [λ_{max} (MeOH) 357 mn; log ϵ 3·81] and lysergene (**7**)[2] [λ_{max} (MeOH) 337 nm; log ϵ 4·11] confirms the *cisoid* diene structure of (**6**), since it is known[4] that these absorb at longer wavelength but with a lower intensity in comparison with *transoid* dienes. We therefore conclude that compound (A) has structure (**5**).

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[3] A. Stoll and A. Hofmann, in 'The Alkaloids,' ed., R. F. Manske, Vol. 8, Academic Press, New York, 1965, p. 725.
[4] A. I. Scott, 'Interpretation of the Ultraviolet Spectra of Natural Products,' Pergamon, Oxford, 1964, p. 46.