Tetrahedron Letters No. 21, pp. 781-784, 1961. Pergamon Press Ltd. Printed in Great Britain.

THE STRUCTURE OF HELLER'S DIHYDROQUINOLINE DIMERS

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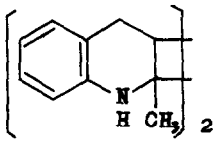
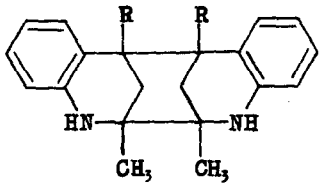
(Received 13 November 1961)

Heller[1] has reported the preparation of a number of methyldihydroquinoline dimers by the reduction of methylquinolines with zinc and acid. These dimers are weakly basic diamines which are unreactive toward most amine reagents, but are readily oxidized to the parent quinolines. Meisenheimer[2] has suggested the formulation I for dihydroquinaldine dimer. This structure, while consistent with the chemical evidence available, seems improbable on mechanistic grounds and has now been found to be incompatible with the n.m.r. spectrum of the dimer.



I



II, R = H

III, R = CH_3

[1] G. Heller and A. Sourlis, Ber. 41, 2692 (1908); G. Heller, ibid. 44, 2106 (1911); 47, 2893 (1914).

Dihydroquinaldine dimer was prepared by a modification of Heller's method with the use of zinc amalgam and hydrochloric acid; the dimer had m.p. 183.5 - 184.0° (lit.[2] 179-180°) after repeated sublimation [Calcd. for $C_{20}H_{22}N_2$: C, 82.72; H, 7.64; N, 9.65: M.W., 290. Found: C, 82.77; H, 7.60; N, 9.70: M.W., 324. (Calcd. for $C_{20}H_{20}N_2$: C, 83.29; H, 6.99; N, 9.71)]. Its infrared spectrum shows the presence of NH (2.95 u) and the absence of ethylenic double bond absorption. Its ultraviolet spectrum in neutral solution [λ_{max}^{EtOH} (ϵ) 251 (16,000), 315 (5500) mμ] resembles that of 1,2,3,4-tetrahydroquinaldine [λ_{max}^{EtOH} (ϵ) 248 (7300), 299 (2000) mμ] insofar as the positions of the bands are concerned and indicates, on the basis of the band intensities, that two such systems are present. In 0.25 M acid solution the spectrum corresponds to that of an equimolar mixture of 1,2,3,4-tetrahydroquinaldine and its hydrochloride, demonstrating the presence of the monoprotonated species. Prolonged treatment of the dimer with boiling acetic anhydride gives a mono-acetyl derivative, m.p. 178.5-182° (Calcd. for $C_{22}H_{24}N_2O$: C, 79.49; H, 7.28; N, 8.43. Found: C, 79.41; H, 7.15; N, 8.19). Potentiometric titration confirms the ultraviolet spectral evidence in that only one amino group is titratable (pK_b 10.5) under the conditions used.[3] This together with the fact that the monoacetyl derivative is a weaker base (pK_b 11.2) than the dimer itself suggests that the two amino groups are close-lying. The ready oxidation of the dimer to quinaldine[1,2] has been confirmed; with silver nitrate in aqueous acetone as oxidant quinaldine is

[2] J. Meisenheimer and E. Stotz, ibid. 58, 2330 (1925).

[3] J.S.Fritz, Anal. Chem. 25, 407 (1953).

formed in 78% yield (based on the formation of two moles from one mole of dimer), demonstrating that the two monomer units retain their skeletal integrity in the dimer.

The n.m.r. spectrum of the dimer is particularly informative. The methyl hydrogen signal (τ=8.82 p.p.m.) is unsplit, thus fixing two of the four termini of the two bonds between the monomer units as 2 and 2'. The remainder of the spectrum consists of the aromatic hydrogen multiplet (τ=2.85-3.63 p.p.m.), the NH hydrogen signal (τ=6.27 p.p.m.), and a complex doublet (τ=7.15 p.p.m.) - quartet (τ=7.93, 8.13,(8.80), 9.00] pattern assignable to two ABX groupings. Although structures of type I contain two ABX groupings, the AB hydrogen atoms are benzylic and their signals would be expected to occur at appreciably lower fields than those observed. The only structure which is consistent with this spectrum and the other data is II, in which the monomer units are joined 2,2' and 4,4'; this possesses two identical ABX groupings, but the AB hydrogen atoms are not benzylic.[4]

Support for the assignment of structure II is forthcoming from the n.m.r. spectrum of the related 2,4-dimethyldihydroquinoline dimer, m.p. 215-216° (lit.[1] m.p.176°), $\lambda_{max}^{CHCl_3}$ 2.95u [Calcd. for $C_{22}H_{26}N_2$: C, 82.97; H, 8.23; N, 8.80; M.W., 318. Found: C, 83.03; H, 8.28; N, 8.68; M.W.330 (Calcd. for $C_{22}H_{24}N_2$: C, 83.50; H, 7.64; N, 8.85)], formed by reduction of 2,4-dimethylquinoline with zinc and hydrochloric acid. This spectrum showed, in addition to the aromatic hydrogen multiplet (τ=2.74 - 3.65 p.p.m.) and NH hydrogen singlet (τ=6.18 p.p.m.), an unsplit methyl hydrogen

[4] The related structure with the monomer units joined 2,4' and 4,2' is rejected on the basis of the pK_b data.

band (τ=8.80 p.p.m.) attributable to superimposition of signals due to the 2,2',4 and 4' methyl groups, and a simple AB quartet [τ=8.05, 8.28,(8.80), 9.00 p.p.m.]. Its relationship to the n.m.r. spectrum of dihydroquinaldine dimer can readily be interpreted in terms of structure III, analogous to II, but not in terms of structures analogous either to I or to other formulations for dihydroquinaldine dimer.

Although the stereochemistry of dihydroquinaldine dimer has not been rigorously determined, we propose the provisional assignment of structure IV, rather than the other diastereoisomer of II in which the two NH groups are in the cis-relationship with respect to the cyclohexane ring. This assignment appears to be in better accord with the relatively small increase in the pK_b of the dimer which results on monoacetylation, and with the magnitude of the relative chemical shift (δ=0.85 p.p.m.) for the hydrogen atoms of each methylene group. It may be noted that the other diastereoisomer, which requires a boat or twist form of the cyclohexane ring, is subject to severe steric interactions absent in structure IV.

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