The Condensation of Acetone with 2,5-Disubstituted Pyrroles

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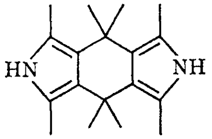
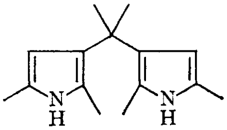
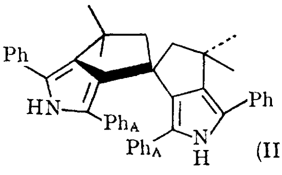
THE susceptibility of the 3-position of 2,5-disubstituted pyrroles to electrophilic attack is well known,[1] and frequently provides the basis for elaboration of functionality at the pyrrole nucleus. Acid-catalyzed condensation of acetone with 2,5-dimethylpyrrole is reported to give a product, m.p. 174°, for which the formula $C_{18}H_{26}N_2$[2,3] and structure (I)[2] have been suggested. We have found, however, that this product should be correctly formulated as $C_{15}H_{22}N_2$ on the basis of elemental analysis and molecular-weight determination (mass spectrum), and spectroscopic evidence leads to the assignment of structure (II) to this compound. Thus, the infrared spectrum indicates the presence of NH (3450 cm.$^{-1}$) and C=C (1600 cm.$^{-1}$) groupings, and a strong band at 795 cm.$^{-1}$ is attributed to a pyrrolic hydrogen atom. The n.m.r. spectrum ($CDCl_3$) shows peaks at δ 1·51 (6 H, singlet), 1·82 (6 H singlet), 2·18 (6 H singlet), 5·78 (2 H, doublet, J = 2·5 c./sec.), and 7·2 (2 H, broad), corresponding to geminal methyl groups, two (nonequivalent) pairs of pyrrolic methyl substituents, protons at the 3-position of the pyrrole ring,[4] and NH groups, respectively. Furthermore, the compound gave a strongly positive reaction with *p*-dimethylaminobenzaldehyde, indicating an unsubstituted position on the pyrrole nucleus. The formulation of this product as a derivative of 3,3′-dipyrromethane is in accord with the observation by Fischer[5] that formaldehyde condenses with 2,3,5-trisubstituted pyrroles to give products derived from one molecule of the aldehyde and two of the pyrrole.



(I)

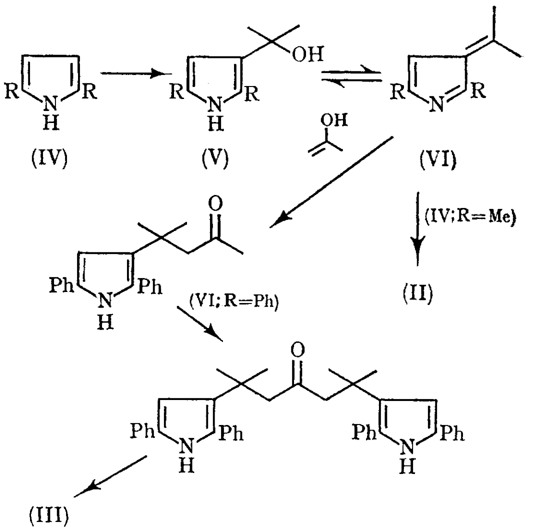


(II)



(III)

Condensation of 2,5-diphenylpyrrole with acetone takes a different course, giving a product $C_{41}H_{38}N_2$ (elemental analysis, mass spectrum), double m.p. 157° and 199—200°. The infrared spectrum shows NH absorption (3500 cm.$^{-1}$, sharp), and the ultraviolet spectrum [λ_{max} 330 mμ (ϵ 48,000)] reveals that there are two intact 2,5-diphenylpyrrole moieties. The absence of a signal in the δ 6—7 region of the n.m.r. spectrum suggests that the two pyrrole rings are fully substituted[6] and an A_2B_2 quartet (J = 13 c./sec.) at δ 2·67 and 2·90 must arise from two methylene groups with magnetically nonequivalent geminal protons. Four methyl groups appear as a pair of six-proton singlets at δ 1·31 and 1·59, and two of the four phenyl substituents give rise to a sharp ten-proton singlet at δ 7·03. The remaining two phenyl groups appear as a complex pattern at δ 7·3—7·6 and a broad singlet at δ 8·05 is assigned to two NH protons. The spectral evidence is thus in accord with structure (III), in which the spiro-system provides the chirality responsible for nonequivalence of geminal methylene protons and methyl groups. A Dreiding model of (III) suggests that steric crowding forces the "interior" phenyl groups (Ph_A) into a configuration nearly perpendicular to the attached pyrrole rings; the singlet at δ 7·03 is therefore



assigned to these aromatic protons, which are partially shielded by the unattached (but spatially proximate) pyrrole nuclei.[7]

The divergence of reaction pathway for the pyrroles (IV; R = Me, Ph) can be formalized in terms of the scheme shown below. This mechanism requires the accumulation of the azafulvene (VI; R = Ph) during the condensation of 2,5-diphenylpyrrole with acetone, and this can be verified spectroscopically. Upon quenching with water (VI) is converted rapidly into (V).

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[1] For a study of the protonation of substituted pyrroles, see: E. B. Whipple, Y. Chiang, and R. L. Hinman, *J. Amer. Chem. Soc.*, 1963, **85**, 26; and Y. Chiang and E. B. Whipple, *ibid.*, p. 2763.

[2] B. Tronow and P. Popow, *J. Russ. Phys. Chem. Soc.*, 1927, **59**, 327; *Chem. Zentr.*, 1927, **98** (4), 1696.

[3] C. F. H. Allen and D. M. Young, *Canad. J. Res.*, 1934, **10**, 771.

[4] R. J. Abraham and H. J. Bernstein, *Canad. J. Chem.*, 1959, **37**, 1056.

[5] H. Fischer and E. Fink, *Z. physiol. Chem.*, 1948, **283**, 152; H. Fischer and H. Beller, *Annalen*, 1925, **444**, 248.

[6] 2,5-Diphenylpyrrole shows a two-proton doublet ($J = 2{\cdot}5$ c./sec.) at δ 6·57.

[7] *Cf.* 1,8-Diphenylnaphthalene (H. O. House, R. W. Magin, and H. W. Thompson, *J. Org. Chem.*, 1963, **28**, 2403).