Synthesis and Cycloaddition of 3-Phenyl-Δ^2-pyrroline-4,5-dione, a New Dienophile

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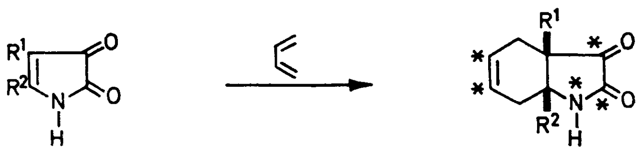
Summary 3-Phenyl-Δ^2-pyrroline-4,5-dione has been synthesized; it is a useful dienophile and yields an angularly substituted *cis*-fused tetrahydro-indole.

CYCLOADDITIONS of butadienes to pyrroles yielding hydroindoles, although potentially useful reactions, in most cases give disappointing results. We considered that Δ^2-pyrroline-4,5-diones (**1**) would be suitable dienophiles for this purpose, though little is known about them.[1] With appropriate substituents R^1 and R^2, the product (**2**) is a potential intermediate in the synthesis of various natural alkaloids possessing the hydroindole partial structure, particularly those of Amaryllidaceae (*e.g.* crinine), Aizoaceae (mesembrine), Menispermaceae (hasubanonine), and Erythrina (erythraline) species, since substitution at the positions marked with an asterisk is relatively easy. Here we report the synthesis and cycloaddition of 3-phenyl-Δ^2-pyrroline-4,5-dione (**5**).



(1) (2)

The pyruvate (**3**)[2] was converted (Raney Ni; H_2, 1 mol. equiv.) into the gummy imine (**4**) which cyclized to the white crystalline ethoxy-derivative (**6a**)†, m.p. 144—149° (30—40%) when heated in ethanol. (**6a**) was also obtained from (**4**) in lower yield by the action of EtO^-. Spectroscopic evidence (i.r., u.v., and n.m.r.), colouration (green) with ferric chloride, and the following reactions confirmed its structure. Crystallization from methanol converted (**6a**) into (**6b**), m.p. 187—194°. Methylation of (**6a**)

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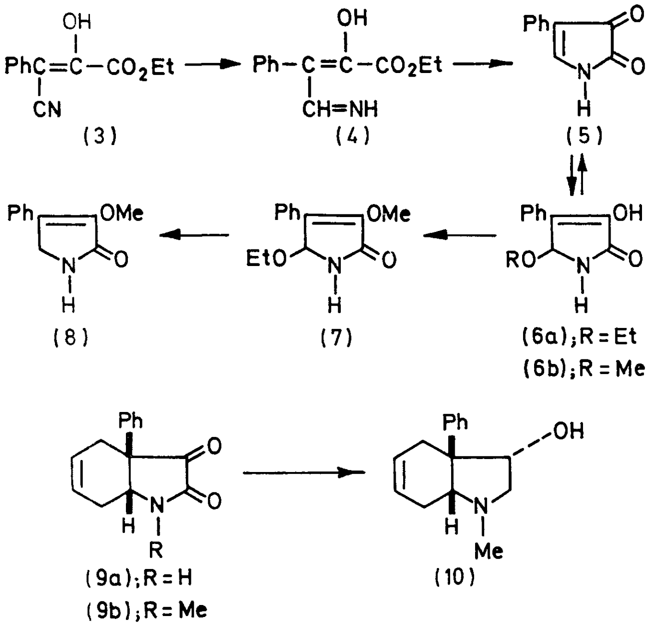
† Satisfactory C, H, and N analyses were obtained for all crystalline compounds.



(MeI,EtONa–EtOH) yielded the methyl ether (**7**), m.p. 108—110°, which on reduction with $LiAlH_4$ afforded (**8**), m.p. 199—201°, (i.r. 1692 cm^{-1}).

Heating of (**6a**) in Me_2SO caused its conversion into the pyrrolinedione (**5**); the solution turned red (λ_{max} 450 nm; ϵ 560) [*cf.* original absorptions at 295 (ϵ 14,500) (EtOH) and 330 nm (ϵ 14,500) (EtOH–EtONa)]. The change is reversible and the colour slowly diminished on cooling. Similar, but more rapid reversible changes were observed when (**6a**) was heated in toluene with acid (p-Me-$C_6H_4 \cdot SO_3H$) or with base (Et_3N).

Thus heating of (**6a**) with butadiene in Me_2SO (or in $HCONMe_2$) at 150° furnished the expected oxoindole (**9a**), m.p. 158—159° (60—70%), which was also obtained directly from (**4**) by similar treatment (15—20%) suggesting that the cyclization (**4**) → (**5**) occurs thermally. The structure of (**9a**) was confirmed by its i.r. (1725 and 1770 cm^{-1}) and n.m.r. spectra [δ 7·35 (5H, s, Ar), 6·01 (2H, m, $CH{=}CH$), 4·58 (1H, t, J 4 Hz, $CO \cdot NH \cdot CH \cdot CH_2$), and 9·49 (1H, br, NH)], and also by its methylation with Me_2SO_4 and KOH to the *N*-methyl derivative (**9b**) (oil; 100%). Reduction of (**9b**) with $LiAlH_4$ quantitatively yielded the indole (**10**)‡ (picrate, m.p. 215—216°).

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‡ The stereochemistry of the hydroxy-group in (**10**) is discussed in the following communication.

[1] *Cf.* O. Mumm and G. Munchmeyer, *Ber.*, 1910, **43**, 3345; O. Mumm and H. Hornhardt, *ibid.*, 1937, **70**, 1930; L. Horwitz, *J. Amer. Chem. Soc.*, 1953, **75**, 4060.

[2] Erlenmeyer, jun., *Annalen*, 1892, **271**, 173.