A New Transformation during Fischer Indole Synthesis

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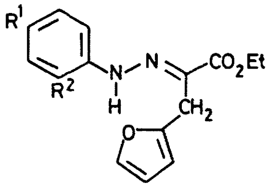
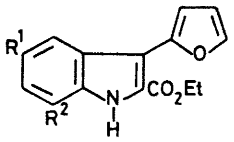
Summary A novel ring closure–opening sequence is described which allows the synthesis of pyrazole derivatives from ethyl α-(phenylhydrazono)furan-2-propionates.

During our investigations on the electrophilic substitution reactions of biheterocycles[1] 3-(2-furyl)indoles were required for nitration studies. When the sulphuric acid-catalysed cyclisation of the phenylhydrazone (**1a**) was carried out in an attempt to prepare the indole (**2a**), an unusual product was obtained in 40% yield while the desired indole (**2a**) was obtained in only 10% yield. The unusual product was assigned the pyrazole structure (**3a**) on the basis of its u.v., i.r., n.m.r., and mass spectra and satisfactory elemental analysis. This transformation was found to be a general reaction of the phenylhydrazones (**1a**—**d**). In a typical experiment a suspension of the phenylhydrazone (**1a**) (5 g) in ethanol (50 ml) containing concentrated sulphuric acid (1·5 ml) was refluxed for 2 h and was then allowed to stand overnight. The usual work-up, followed by column chromatography, gave three fractions. The first fraction yielded pale yellow crystals of (**2a**), m.p. 190—191 °C; λ_{max} (EtOH) 244 and 310 nm (log ϵ 4·02 and 3·52); ν_{max} (KBr) 3344 and 1680 cm^{-1}; δ(CDCl$_3$) 1·4 (3H, t, *J* 7 Hz, Me), 4·4 (2H, q, *J* 7 Hz, CH$_2$), 6·5 (1H, m, 4′-H), 7·0 (1H, m, 3′-H), 7·05—7·25 (3H, m, ArH), 7·45 (1H, m, 5′-H), and 8·05 br (1H, s, NH); *m/e* 289 and 291 (M^+). The second fraction yielded a sticky mass which could not be worked up. The third fraction gave the pyrazole (**3a**) as buff needles, m.p. 135—136 °C (from benzene–light petroleum); λ_{max} (EtOH) 254 nm (log ϵ 3·9); ν_{max} (KBr) 3500 and 1750 cm^{-1}; δ(CDCl$_3$) 1·35 (3H, t, *J* 7 Hz, Me), 2·95 br (1H, s, OH), 4·2—4·5 (4H, m, OCH_2Me and OCH$_2$C=), 6·05 (2H, m, CH=CH), 6·75 (1H, s, 4′-H), and 7·35 (4H, s, ArH); *m/e* and 306 and 308 (M^+).



(1)



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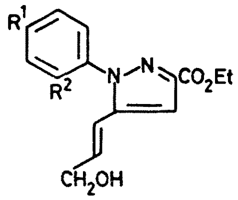

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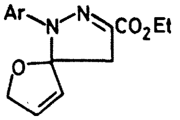

(4)

	(a)	(b)	(c)	(d)	(e)
R^1	Cl	NO$_2$	Me	H	Cl
R^2	H	H	H	H	Me
% yield of (3)	40	32	22	24	—

This transformation of phenylhydrazones (**1**) into pyrazoles (**3**) presumably occurs by protonation of the furan ring and formation and rearrangement of a spiro intermediate (**4**). However, the phenylhydrazone (**1e**) did not yield (**3e**) but yielded an isomer of (**1e**) in 48% yield.

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[1] B. S. Holla and S. Y. Ambekar, *Indian J. Chem.*, 1978, **16B**, 240.