Molecular Rearrangements Yielding Δ^2-Pyrazolin-5-ones: Halohydrin Rearrangement

By M. J. NYE* and W. P. TANG

(*Department of Chemistry, University of Guelph, Guelph, Ontario, Canada*)

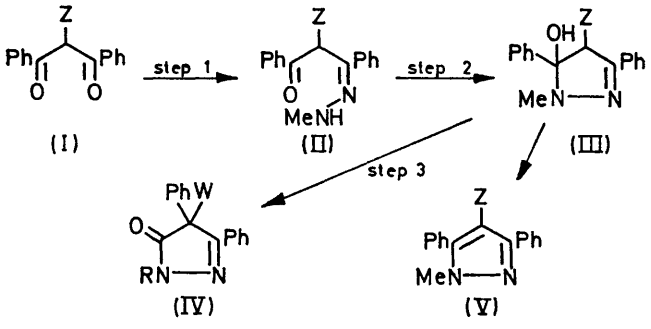
Summary 1-Methyl-3,4-diphenyl-Δ^2-pyrazolin-5-one may be prepared by treatment of 2-bromo-1,3-diphenylpropanedione with methylhydrazine, a reaction involving reorganization of the carbon skeleton, probably proceeding *via* a halohydrin rearrangement.

TREATMENT of 2-bromo-1,3-diphenylpropanedione (Ia) with methylhydrazine in ethanol at room temperature gives 1-methyl-3,4-diphenyl-Δ^2-pyrazolin-5-one (IVb) (56%) m.p. 216—219°, identical (i.r. spectra and mixed m.p.) with a sample made by the well established[1] route to Δ^2-pyrazolin-5-ones from β-oxocarboxylic acid derivatives. α-Phenyl-α-benzoylacetamide was heated with methylhydrazine dihydrochloride in refluxing ethanol for 4 h to yield (IVb) (50%). Further evidence for the structure (IVb) was its oxidation to (IVc) by H_2O_2 (44% yield). The conditions of the reaction were similar to those used by Jucker and Lindenmann[2] for a similar conversion of another substituted Δ^2-pyrazolin-5-one. The identity of (IVc) made by this route was established by mixed m.p. and by a comparison of its i.r. spectrum with that of (IVc) prepared by a base-catalysed acyloin rearrangement of

5-hydroxy-3 5-diphenyl-Δ^2-pyrazolin-4-one [3] Additional evidence in favour of the proposed structures is the observation that (IVb) may be converted into (IVc) simply by heating at 225 °C in the presence of air Aerial oxidation of Δ^2-pyrazolin-5-ones in this way is well documented [4]

This new route to Δ^2-pyrazolin-5-ones may be of synthetic importance since in many cases it would be more convenient than the standard route *via* the β-oxocarboxylic acid derivative A case in point is the one reported herein Benzyl cyanide was condensed with ethyl benzoate to give α-phenylbenzoylacetonitrile which was hydrolysed to α-phenylbenzoylacetamide, and thence converted into (IVb) Only two steps from the available dibenzoylmethane are required in the new synthesis, namely bromination to give (Ia), and then treatment with methylhydrazine dihydrochloride

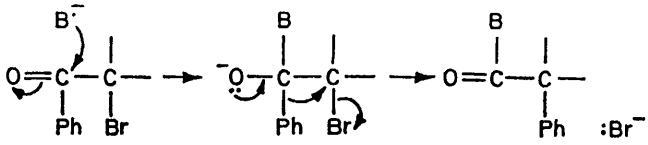
The reaction may proceed *via* (IIa) and (IIIa) (Scheme 1)



SCHEME 1

	Z	W	R
a,	Br	—	—
b,	—	H	Me
c,	—	OH	Me
d,	OH	—	—
e,	OAc	—	—
f,	—	H	H
g,	—	H	Ph

Steps 1 and 2 are standard ketone reactions and step 3 is a base-catalysed halohydrin rearrangement If steps 2 and 3 are considered together this is an example of a Favorski reaction proceeding *via* the semibenzilic mechanism[5] (Scheme 2) Alternative routes may also occur simultaneously in competition, but that involving (IIIa) was favoured since certain stable analogues have been isolated [6] Further evidence for the intermediacy of (IIIa) arises from



SCHEME 2

the possibility at this stage that OH may be the leaving group rather than Z, in particular when Z = OAc, a much poorer leaving group than Br Thus treatment of (Ie) with methylhydrazine gives the unrearranged product (Vd) (92%) †

(IVb) may also be obtained by treatment of 2,2-dibromo-1,3-diphenylpropanedione with a fourfold excess of methylhydrazine in ethanol Although this reaction must involve an extra reduction step compared with the conversion of (Ia) into (IVb), both reactions give yields of *ca* 55%

(IVf) and (IVg) were synthesized by the standard treatment of α-phenylbenzoylacetamide with hydrazine dihydrochloride and phenylhydrazine hydrochloride, respectively, and their m p s were identical with literature values [7,8] (IVb) had m p (double) 216—219° and 235—237° compared with that (272—274°) reported by Grunanger and Finzi [7] These workers prepared the compound by methylation of 5-ethoxy-3,4-diphenylpyrazole followed by hydrolytic removal of the ethyl group We suggest that methylation had in fact occurred at N-2, and that their product is 2-methyl-3,4-diphenyl-Δ^3-pyrazolin-5-one rather than (IVb)

It is of interest that the spectra of (IVb) in the solid state or in 95% EtOH or $CHCl_3$ solutions show that the substance does not exist as the formula structure, but instead as either the NH form (1-methyl-3,4-diphenyl-Δ^3-pyrazolin-5-one) or the OH form (5-hydroxy-1-methyl-3,4-diphenylpyrazole), in accord with other observations on this ring system,[9] ν_{max} (Nujol) (< 2000 cm^{-1}) 1601 cm^{-1} [*ca* 1700 cm^{-1} expected for (IVc)], δ ($CDCl_3$) 6 35 (s, 3H, NMe) and 7 2—7·4 (m, 10H, Ar*H*) p p m (the OH or NH signal was present on deuterium-exchange in Me_2SO solvent containing a little ^2H_2O), λ_{max} (95% EtOH) 240sh (ϵ 14,700), 265sh (11,200), and 300sh (300) nm [long wavelength band expected for (IVc) absent]

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† At what stage the acetoxy-group becomes hydrolysed to hydroxy has not been established. (Ve) may be isolated as the main product if the solvent is acetic acid

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