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A RING EXPANSION REACTION OF THE 4,5-DIHYDROPYRAZOLE SYSTEM(*)

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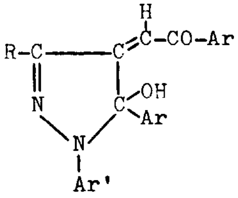
In a previous paper(1) the reaction between N-pyridinium phenacylids and nitrile imines, which affords bright red compounds, has been reported.

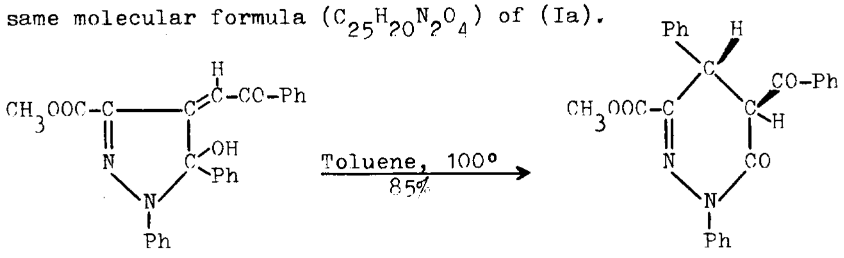
Structure (I) was assigned to these compounds on the basis of their chemical behaviour and of the X-ray crystal structure analysis.



(I)

By heating in inert solvents compounds (I) undergo a new ring expansion reaction with formation of 4,5-dihydro-3(2H)-pyridazinonic derivatives.

Compound (Ia) (m.p. 184°), obtained from methyl phenylhydrazonochloroacetate and N-phenacylpyridinium bromide, by heating in toluene solution at 100° for 6-8 hrs. afforded, in 85% yield, a colorless compound (II) (m.p. 160°) which had the same molecular formula ($C_{25}H_{20}N_2O_4$) of (Ia).



(Ia) (II)

The IR spectrum (CCl_4 solution) shows the presence of three C=O bands at 1720, 1695 and 1670 cm^{-1} respectively; the NMR spectrum (C_5D_5N solution) shows the following signals: 6.32 τ (s) 3H (CH_3OCO); 5.0 and 5.43 τ (J = 18 cps)(2) (two doublets) 2H (H_4 and H_5); 1.9 - 2.6 τ (m) 15H (aromatic protons).

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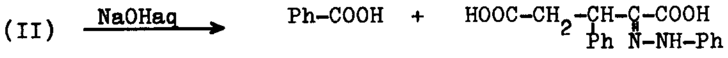
The H_4 proton is acidic for the presence of the α-carbonyl groups, and by adding deuterated water in the presence of catalytic amounts of triethylamine, the two doublets at 5.0 and 5.43 τ, collapse to a sharp singlet at 5.1 τ.

Alkaline hydrolysis of (II) gave at room temperature the corresponding acid (III) (m.p. 216°) which, after treatment with potassium ferricyanide, was converted into 2,5-diphenyl-6-carboxy-4-benzoyl-3(2H)-pyridazinone (IV) (m.p. 223°).

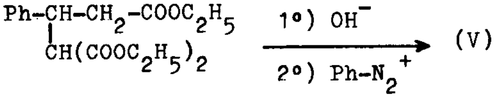
In the same conditions but by heating the mixture to reflux, compound (II) afforded, in 75% yield, benzoic acid and a dicarboxylic acid (V) (m.p. 193°) (dimethyl ester: m.p. 116°).



$$\text{(II)} \xrightarrow{\text{NaOHaq}} \text{Ph-COOH} + \text{HOOC-CH}_2\text{-}\underset{\text{Ph}}{\text{CH}}\text{-}\underset{\text{N-NH-Ph}}{\text{C}}\text{-COOH}$$

(V)

The structure of compound (V) was proved by independent synthesis from ester (VI)$^{(3)}$ which by alkaline hydrolysis, followed by reaction with benzene diazonium chloride, gave (V).

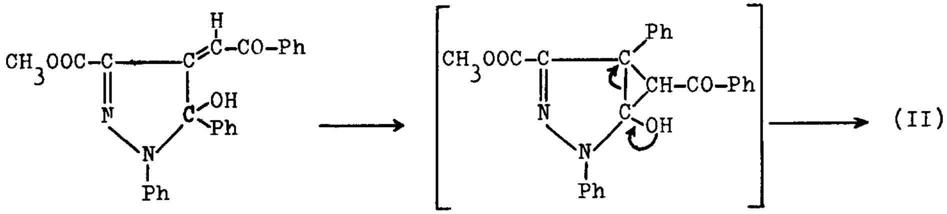


$$\underset{\text{CH(COOC}_2\text{H}_5)_2}{\text{Ph-CH}}\text{-CH}_2\text{-COOC}_2\text{H}_5 \xrightarrow[\text{2°) Ph-N}_2^{+}]{\text{1°) OH}^-} \text{(V)}$$

(VI)

Formation of (V) from (II) can be seen as a cleavage of the benzoyl group of a β-ketoamide followed by hydrolytic ring opening of the dihydropyridazinone system.

The mechanism of the ring expansion reaction (Ia)⟶(II) is under investigation; as a tentative explanation we may assume the intermediate formation of a bicyclic system (VII) as indicated in the following scheme:



(Ia) (VII)

REFERENCES AND NOTES

1) R.Fusco and P.Dalla Croce, Tetr.Lett. 3061 (1970).
2) This value of the coupling constant for H_4 and H_5 strongly suggests a trans configuration.
3) S.Ruhemann and A.V.Cunnington, J.Chem.Soc. 73 1006 (1898).