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RING OPENING IN THE PYRAZOLE SERIES

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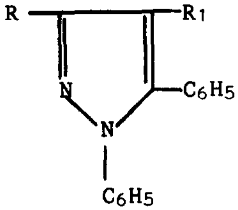
In a previous communication(1) we reported the ring cleavage of 3-carboxy- and 3-unsubstituted-1-phenyl-pyrazoles bearing in position 4 an electronattracting group. We then anticipated that the pyrazole ring opening could occur, by the attack of the proper nucleophile, also in the case of analogous substrates having in position 3 a group capable of originating the incipient carbanion (A).

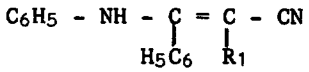
We now wish to report the ring opening of the following substrates: 3-benzoyl-1,5-diphenyl-4-tosyl-pyrazole (I), 3,4-dibenzoyl-1,5-diphenyl-pyrazole (II) and phenyl-3-(1,5-diphenyl)-pyrazolyl-carbinol (III).



(I) : R = COC_6H_5; R_1 = $SO_2C_6H_4CH_3$(p).
(II) : R = R_1 = COC_6H_5.
(III) : R = $CHOHC_6H_5$; R_1 = COC_6H_5.
(IV) : R = H; R_1 = COC_6H_5.
(V) : R = COC_6H_5; R_1 = H .
(VI) : R = COC_6H_5; R_1 = C_6H_5.
(VII) : R = $CHOHC_6H_5$; R_1 = C_6H_5.

Pyrazoles (I,m.p.223°) and (II,m.p.172-3°), not yet described in the literature, have been synthetized in 80-82% yield by condensing α-chloro-β-phenylglyoxal-α-phenylhydrazone with sodium salt respectively of ω-tosyl-acetophenone and dibenzoylmethane. The borohydride reduction of (I) gave the unknown carbinol (III,m.p.190-2°).

The reaction of pyrazole (I) with two moles of $NaNH_2$ in boiling xylene (3 hrs.) afforded the known 2-anilino-2-phenyl-1-tosyl-acrylonitrile (VIII, m.p.190-1°)(1) and benzamide, isolated in 67 and 52% yields respectively, no starting material being recovered.



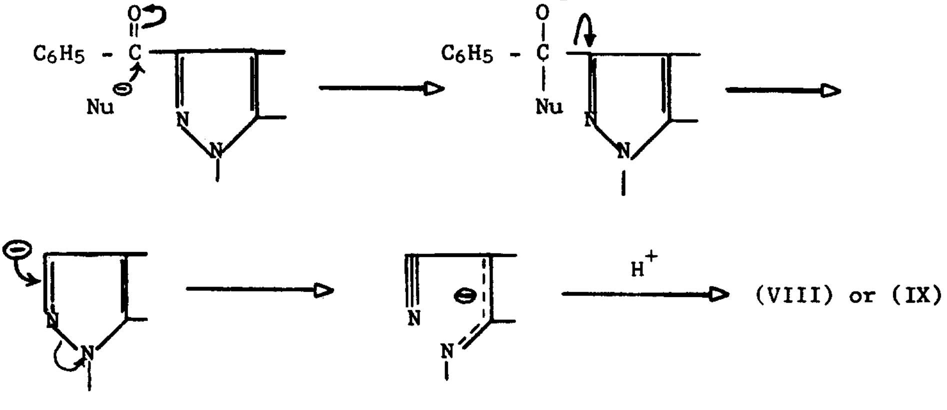
$$C_6H_5-NH-\underset{H_5C_6}{C}=\underset{R_1}{C}-CN$$

(VIII) : $R_1 = SO_2C_6H_4CH_3(p)$. (IX) : $R_1 = COC_6H_5$.

Pyrazole (II) upon treatment with $NaNH_2$ (2 moles) in boiling toluene (2 hrs.) gave 2-anilino-1-benzoyl-2-phenyl-acrylonitrile (IX,m.p.162-3°,lit.(2) 165°) and benzamide, isolated respectively in 50 and 75% yields(*), 35% of the starting material being recovered unchanged. Pyrazole (II) underwent the ring opening also by the action of a milder base such as potassium tert-butoxide: in fact by prolonged heating (65 hrs.) with two moles of the above base in tert-butyl alcohol, (II) gave 7%(*) of the acrylonitrile (IX), 17%(*) of 4-benzoyl-1,5-diphenyl-pyrazole (IV,m.p.144°, lit.(3) 144-5°), 24% of the starting material being recovered unaffected.

Carbinol (III) when treated with $NaNH_2$ (4 moles) in boiling xylene (4 hrs.) gave 94% of (VIII,m.p.191°)(1), while with potassium tert-butoxide (2 moles) in boiling tert-butyl alcohol (4 hrs.) gave 68%(*) of (VIII), 50% of the starting material being recovered unchanged.

The ring cleavage of pyrazoles (I) and (II), leading to the acrylonitriles (VIII) or (IX) respectively, can be interpreted on the basis of the following reaction mechanism:

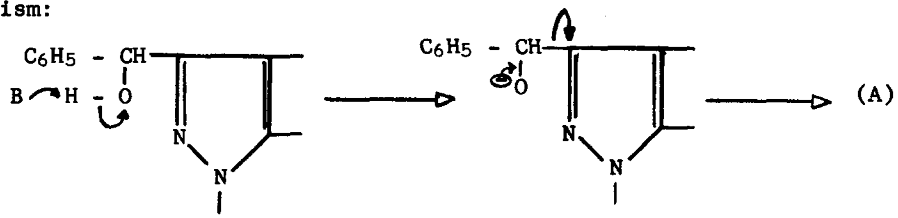


(A)

(*) The reported yields have been calculated on the basis of the reacted starting material.

The formation of pyrazole (IV) in the reaction of (II) with potassium tert-butoxide in tert-butyl alcohol can be considered a strong evidence of the occurrence of carbanion (A) as an intermediate, since (IV) can be easily formed from (A), through a proton transfer from the protic solvent.

In the case of carbinol (III) the ring cleavage could also involve the occurrence of carbanion (A), which could originate according to the following mechanism:



In the course of the present research we have studied the possibility of ring opening in the case of 3-benzoyl-1,5-diphenyl-pyrazole (V)$^{(4)}$, 3-benzoyl-1,4,5-triphenyl-pyrazole (VI)$^{(5)}$ and phenyl-3-(1,4,5-triphenyl)-pyrazolyl-carbinol (VII).

Pyrazole (V) has been prepared through an unambigous route by condensing α-chloro-β-phenylglyoxal-α-phenylhydrazone with the sodium salt of ethyl benzoyl-acetate, to give 3-benzoyl-4-carbethoxy-1,5-diphenyl-pyrazole; this however was not isolated in a pure state, but was directly hydrolysed to the corrisponding acid (m.p.192-3°) which was decarboxylated by pyrolysis at 220-30° giving (V,m.p.134°) in moderate yield.$^{(**)}$

The known pyrazole (VI) was synthetized in satisfactory yield (66%) by a different route through the reaction of α-chloro-β-phenylglyoxal-α-phenylhydrazone and 1-morpholino-1,2-diphenyl-ethylene (X,m.p.87-8°), obtained by reacting morpholine with desoxybenzoin.

The unknown pyrazole (VII,m.p.190-2°) has been obtained by sodium borohydride reduction of (VI).

Pyrazoles (V), (VI) and (VII) did not undergo the ring cleavage upon treatment either with $NaNH_2$ or potassium tert-butoxide even under more severe conditions than those employed for pyrazoles (I), (II) and (III).

(**) Literature $^{(4)}$ describes m.p.138° for the product obtained from dibenzoylacetylene and phenylhydrazine: however it is uncertain whether to this product has to be assigned the structure of 3-benzoyl-1,5-diphenyl- or 1,3-diphenyl-3-benzoyl-pyrazole.

The comparison of the results obtained with pyrazoles (I), (II), (III), (V), (VI) and (VII) clearly confirm the hypothesis that the presence of an electron-attracting group in position 4 may be one of the essential features for pyrazole ring opening.

Satisfactory analyses were obtained for all new compounds. Melting points were not corrected.

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