A NOVEL HETEROCYCLIC REARRANGEMENT : CONVERSION OF BENZOYL PYRAZOLINES INTO PHENYLPYRIDAZINONES

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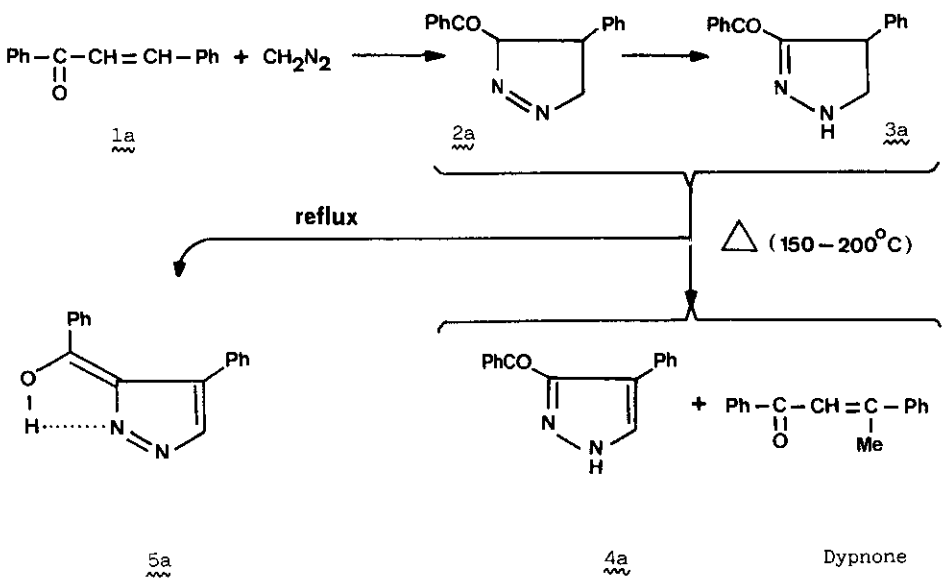
Abstract - Diarylpyridazinones could be obtained, in a two-step procedure, from chalcones and diazomethane. The second step involves the rearrangement of a benzoylpyrazoline and proceeds with low yields. The structures have been established by mass and ion-kinetic energy spectrometry.

Recently the results despicted in Scheme 1 were described by some of us (C.B.R., P.N.V.R.)[1].



1a 2a 3a 5a 4a Dypnone

Scheme 1

Both the Δ^1- 2a and the Δ^2-pyrazoline 3a, on pyrolysis yield the 3(5)-benzoyl-4-phenylpyrazole 4a and dypnone. However, when 2a or 3a was refluxed in benzene or dioxan an isomer of the pyrazole was obtained for which the structure 5a was proposed[1]. The rather unusual structure of 5a, a non-aromatic pyrazolenine, and the fact that in general prototropic tautomers display identical spectra in solution[2] whereas 4a and 5a afford different nmr spectra in DMSO-d_6, prompted us to reinvestigate the structure of the "abnormal" pyrazole 5a.

After several unsuccesful attempts to obtain monocrystals suitable for a X-ray determination, it was decided to use mass spectrometry to identify the structure of 5a, since nmr (both ^{1}H and ^{13}C) does not give much information due to the presence of two different phenyl rings. Some acylazoles dimerise, by addition of the NH of one molecule to the carbonyl group of another[3]. To exclude a dimer the molecular weight of the "anormal" isomer was determined using a chemical ionisation source: ions $[MH]^+$ at 249 and $[M+NH_4]^+$ at 266 were observed, in agreement with the monomeric formula $C_{16}H_{12}N_2O$ for 5a.

The mass spectra and the ion-kinetic energy spectra (CID-MIKE) of both isomers were recorded (Figure 1).

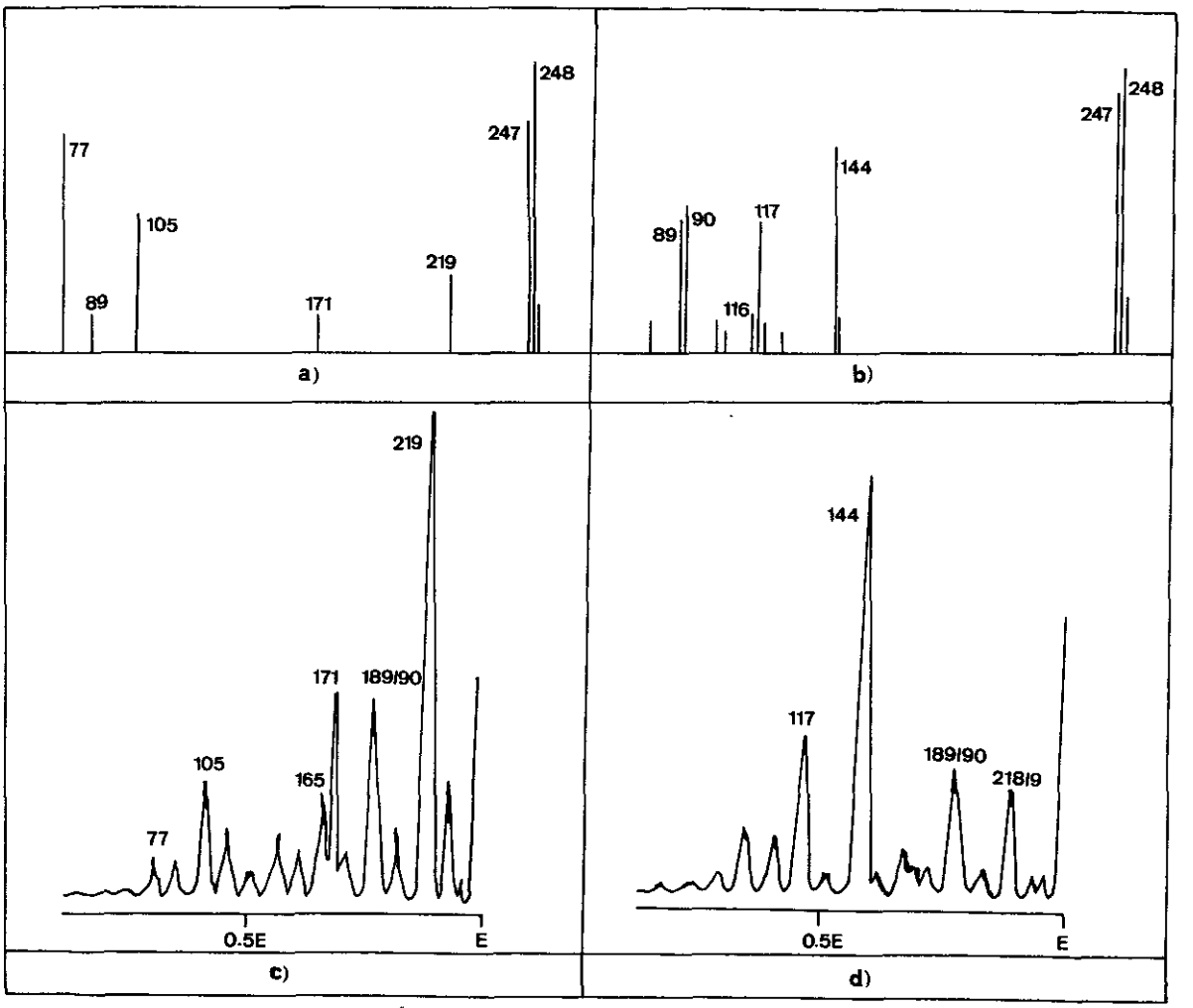
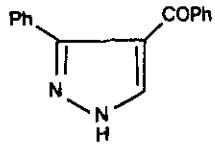


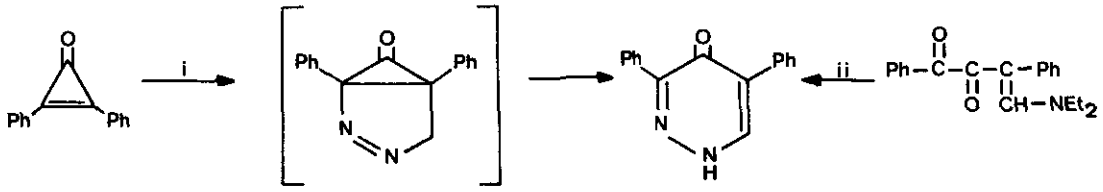
Fig. 1. a) Mass spectrum of 4a; b) Mass spectrum of 5a; c) CID-MIKE spectrum of the m/z 248 ion of 4a; d) CID-MIKE spectrum of the m/z 248 ion of 5a.

The "normal" pyrazole 4a behaves as expected : the ions m/z 105 (benzoyl cation) and m/z 77 (phenyl cation) are intense in the mass spectrum (Fig 1a). The "abnormal" compound 5a does not show the ions but instead loses H$^{\cdot}$ and subsequently PhCN ($[M-H-PhCN]^+$, m/z 144, Fig 1b). The loss of PhCN is inconsistent with the structure 5a and the absence of a benzoyl cation rules out the isomeric pyrazole structure 6a [3(5)-phenyl-4-benzoylpyrazole, whose origin from 2a or 3a would have been difficult to explain].



6a

Searching for a compound $C_{16}H_{12}N_2O$ compatible with the mass spectral data it was found in the Chemical Abstracts the 3,5-diphenyl-4-pyridazinone 7a (Scheme 2) thrice described in the literature.



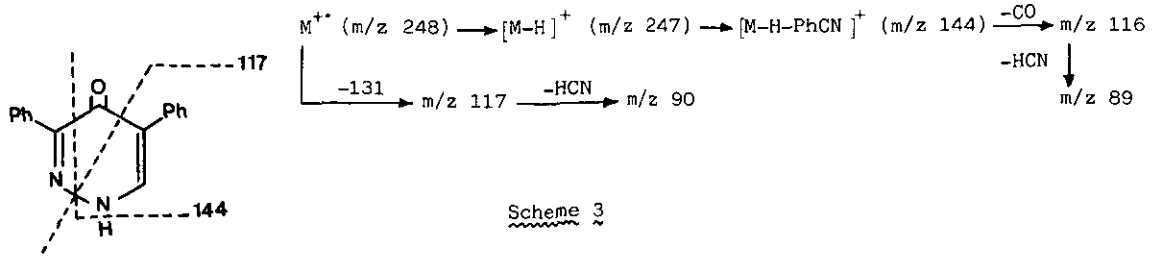
7a

i, CH_2N_2, Izzo's and Breslow's syntheses[4,5]

ii, NH_2NH_2, Abdulla's synthesis[6]

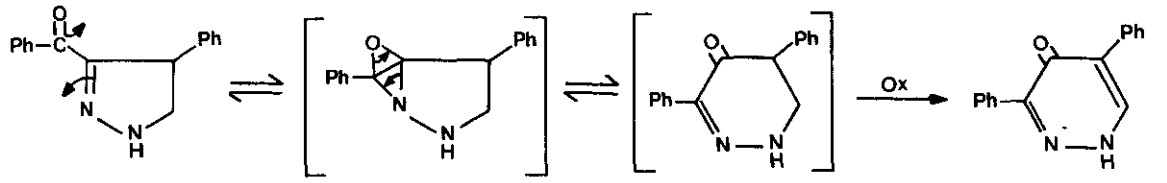
Scheme 2

The properties described for compound 7a (melting point, ir, ^{1}H nmr, uv, analysis, and molecular peak in ms) coincide with those of compound 5a. Moreover, a genuine sample of 7a was compared (ir, KBr disk; ms, CID-MIKE) with a sample of 5a[1] and both proved to be identical. A 3,5-diphenyl-4-pyridazinone structure accounts for the fragmentation pattern (Scheme 3) obtained from the CID-MIKE spectra of the principal ions of the "abnormal" compound.



Scheme 3

A survey of the authoritative van der Plas review[8] shows no comparable example of ring transformation. Since it is known that both isomers of pyrazolines, Δ^1 and Δ^2 , equilibrate thermally (even if the Δ^2-isomer is generally the most stable[9]), the rearrangement can start from 2a or from 3a. The exact mechanism is still unknown, but formally it corresponds to an isomerization followed by an oxidation, as the one represented in Scheme 4 starting from the Δ^2-pyrazoline.



3a

Scheme 4

7a

In order to verify the generality of the rearrangement, substituted chalcones 1b-1d have been converted into the corresponding Δ^1-pyrazolines, 2b-2d, which in turn rearrange under reflux into the 3,5-diaryl-4-pyridazinones 7b-7d. The carbon-13 chemical shifts are gathered in Figure 3. Since the compounds have a low solubility in DMSO-d_6, some quaternary carbons have not been observed even after 160,000 scans.

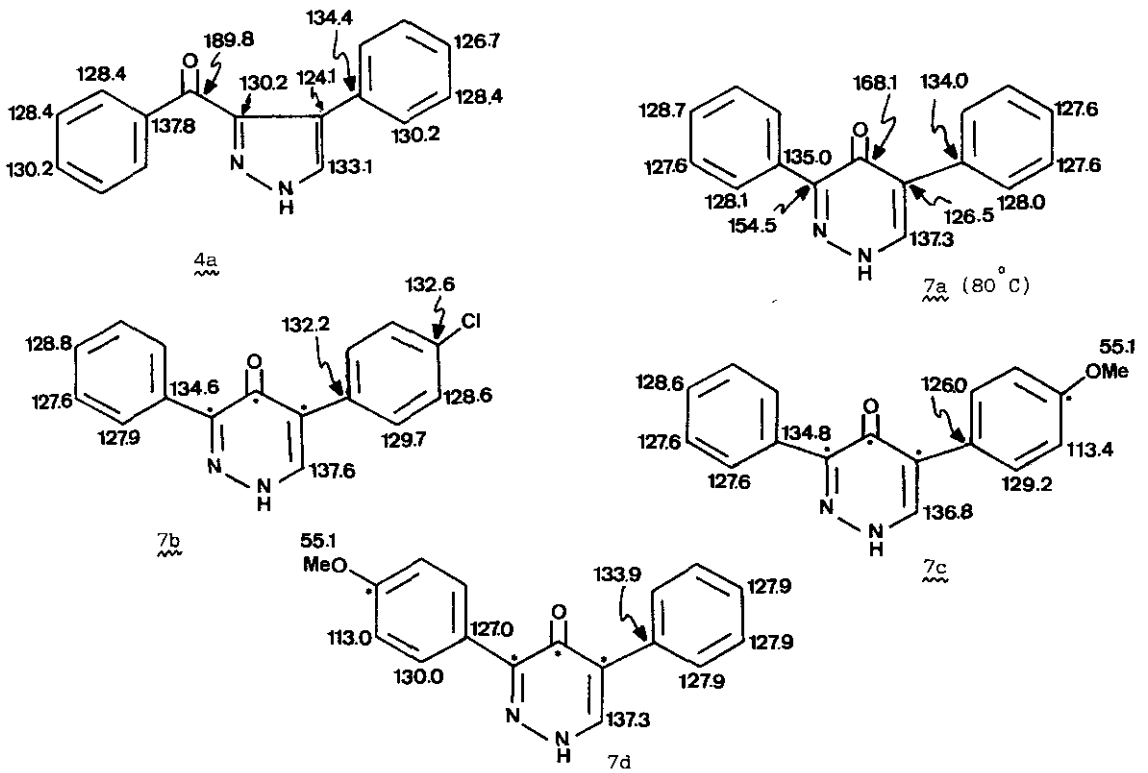


Fig. 3. ^{13}C nmr chemical shifts in DMSO-d_6; *Not observed

EXPERIMENTAL SECTION

^{13}C nmr spectra were recorded on a Bruker WP60 working at 15.08 MHz and on a Bruker WP80SY working at 20 MHz. Mass spectra were obtained from a Varian Mat 311A working at 70 eV, 1 mA, and 3 kV.

General procedure for the preparation of pyridazinones.

Method I: A solution of chalcone (5.5 g) in ether/chloroform (100 ml) was treated with diazomethane in ether and the reaction mixture kept at 0 °C. The progress of the reaction was followed by t.l.c. On completion of the reaction, the solvent was removed and the residue (6.65 g) was dissolved in chloroform. 7a remained as an insoluble solid (0.165 g) and was separated by filtration, and crystallised from hot ethanol. Yield = 3%. Even when the addition reaction was carried out at room temperature, there was no change in the yield.

Method II: Δ^1-or Δ^2-pyrazoline (2 or 3) (0.5 g) was refluxed in the solvent (10 ml) for 12 h. On cooling, the solid that separated out was filtered off. 7a (0.06 g) appeared as colourless crystals from hot ethanol. Yield = 12%.

TABLE 1. Melting points, yields, ir (KBr pellets), and ms data.

Compound	Mp(°C)	Yield (Method I)	Yield from 2 (Method II)	Yield from 3 Method II)
7a	336-339	3%	12%	12%
7b	334-338	3%	3%	3%
7c	317-320	2.5%	2.5%	2.5%
7d	335-337	2.5%	2.5%	2.5%

		ms		
Compound	ir	$M^{+\cdot}$	$[M-H]^+$	$[M-H-ArCN]^+$
7a	3200(NH),1538(CO)	248	247	144
7b	3200(NH),1535(CO)	282(284)	281(283)	144
7c	3200(NH),1530(CO)	278	277	174
7d	3195(NH),1530(CO)	278	277	144

TABLE 2. Mass spectral data for compounds 4a, 5a and 7a (abundancies relative to the base peak)

Compound	m/z: 249	248	247	219	171	145	144	124	118	117	116	105	104	102	90	89	77
4a[1]	18	100	79	28	14	0	0	0	3	10	5	54	0	0	0	16	19
5a[1]	18	100	90	0	0	10	72	9	13	47	15	0	10	17	54	46	10
7a[7]	18	99	100	0	0	9	67	11	12	40	15	0	8	16	55	47	7

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7. We are greatly indebted to Dr. Riaz F. Abdulla (Lilly Research Laboratories, Greenfield, USA) for a generous gift of 3,5-diphenyl-4-pyridazinone 7a (Lilly Serial number 089340).
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