

ACTION OF GRIGNARD REAGENTS ON 3-ANILINO-4-ARYLHYDRAZONO-2-PYRAZOLIN-5-ONES

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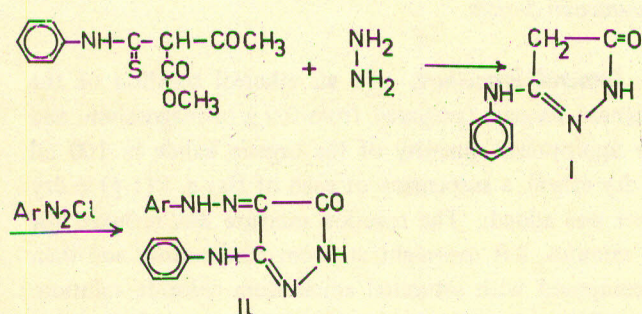
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A series of 3-anilino-4-arylhydrazono-2-pyrazolin-5-ones (IIa-e) were prepared by the coupling reaction of aryldiazonium salts with 3-anilino-2-pyrazolin-5-one (I). These pyrazolones underwent 1, 2-addition of Grignard reagents to the exocyclic C = N group followed by the loss of one molecule of hydrogen to yield 4-aryl-hydrazono-3-anilino-3-alkyl or aryl-1-pyrazolin-5-ones Va-e. The reaction sequence was confirmed by treatment of compound Ve with acetic anhydride afforded the monoacetyl VI. While similar treatment of IIb gave the diacetyl VII. The stability of the carbonyl group in II toward the action of Grignard reagents has been discussed.

In spite of the enormous literature concerning the synthesis and chemical reactions of 4-arylhydrazono derivatives of 3-alkyl-2-pyrazolin-5-ones, we have not found any reports dealing with those of 3-anilino analogues. This promoted us to synthesize the latter type and study the effect of 3-anilino group on their chemical behaviour.

The normal starting material for the synthesis of 3-anilino-4-arylhydrazono-2-pyrazolin-5-ones (IIa-f) is the parent 3-anilino-2-pyrazolin-5-one (I). This has been prepared after Worrall [1] by treating α -phenylthiocarbonyl-acetoacetate with hydrazine hydrate. Aromatic diazonium salts coupled readily with the methylene group in (I), activated with both the C = O and the C = N groups, to give the highly coloured 3-anilino-4-arylhydrazono-2-pyrazolin-5-ones (IIa-f).



- Ar = (a) C₆H₅, (b) C₆H₄CH₃-o,
(c) C₆H₄CH₃-p,
(d) C₆H₄OCH₃-o,
(e) C₆H₄OCH₃-p, (f) C₆H₄Cl-p.

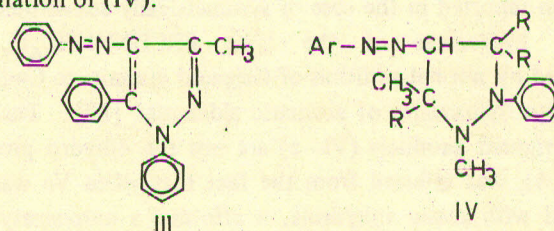
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Compounds (IIa-f) were given the hydrazono structure II rather than the azo derivatives according to the work of Yasuda [2] on the azopyrazolone dyes.

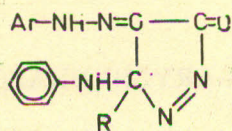
Formulation II was based on the correct analytical data and the IR spectra which showed absorption at 1670 (CO), 3400 (NH) and 1600 (CN) cm⁻¹ and revealed no (CH) absorption. Furthermore, compounds (IIa-f) did not give the characteristic phenolic colour with ferric chloride.

Organomagnesium compounds add to the carbonyl function in 4-arylhydrazono-3-methyl-1-phenyl-2-pyrazolin-5-ones yielding the 1,5-diphenyl derivatives (III) [3]. The reaction of 4-arylazoantipyridines with Grignard reagents has been shown [4] to involve three molecules of the reagent effecting hetero ring opening, followed by recyclisation, and addition to the endocyclic C = C group with the formation of (IV).



In extension of this work, the behaviour of 3-anilino-4-arylhydrazono-2-pyrazolin-5-ones towards the action of organomagnesium compounds has been investigated. Thus when IIa-c, f were treated with the appropriate Grignard reagent, followed by hydrolysis, they afforded 4-arylhydrazono-3-anilino-3-alkyl or aryl-1-pyrazolin-5-ones (Va-e).

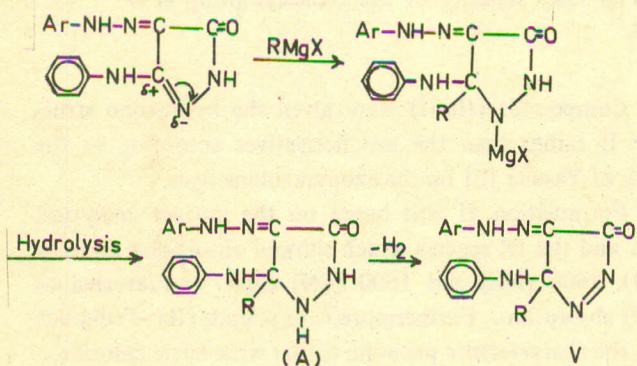
Structure (V) was assigned from the deep colour of the reaction products, the correct analytical data and the exhibition of carbonyl absorption at 1670 cm⁻¹ and NH absorption at 3420 cm⁻¹.



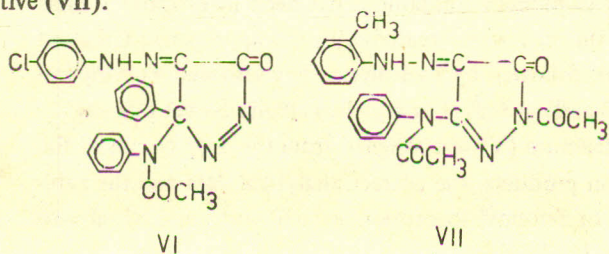
Ar= (a) C_6H_5 , R= C_2H_5 ; Ar= (b) C_6H_5 , R= $C_6H_4CH_3$ - *p*
 Ar= (c) $C_6H_4CH_3$ - *o*, R= C_6H_5 ; Ar= (d) $C_6H_4CH_3$ - *p*, R= C_2H_5
 Ar= (e) C_6H_4Cl - *p*, R= C_6H_5 .

The formation of compounds Va-e is believed to proceed via the sequence of the reaction indicated in Scheme 1.

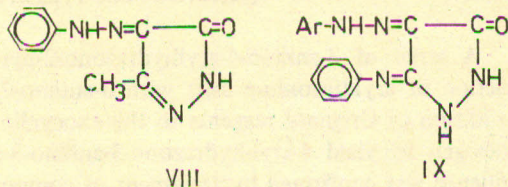
Scheme 1



The addition of the Grignard reagent to the C=N in II is analogous to the addition of the same reagent to the C=N in quinoxaline [5], in *N*-benzoylphenylhydrazone of benzaldehyde [6], in phthalazones [7] and the arylation of isoquinoline with arylmagnesium halides [8, 9]. The tetrahydro derivative A, loses hydrogen easily which probably may be attributed to autoxidation. Similar autoxidation has been reported in the case of symmetrically substituted phenyl hydrazines of the type $PR_2CHNHNHC_6H_5$, produced by normal addition of Grignard reagents to C=N of phenyl hydrazones of aromatic aldehydes [10]. That the Grignard products (Va-e) are not the dihydro products (A), was inferred from the fact that when Ve was refluxed with acetic anhydride, it afforded a monoacetyl derivative (VI), whereas the starting arylhydrazone-anilino-pyrazolones, represented by IIb, afforded a diacetyl derivative (VII).



The stability of the carbonyl group in II toward the action of Grignard reagents has been supported by the recovery of 3-methyl-4-phenylhydrazono-2-pyrazolin-5-ones (VIII) unchanged after treatment with phenylmagnesium bromide under the same experimental conditions. That the C=N group in VII did not undergo addition of Grignard reagents points to the existence of compounds II in the tautomeric form IX in which case the Grignard reagent adds to the exocyclic C=N, rather than the endocyclic one affording the same Grignard products Va-e.



EXPERIMENTAL

All m.ps. are uncorrected. IR spectra were determined by KBr-Wafer technique on a Unicam SP 1000 IR spectrophotometer.

Preparation of 3-Anilino-4-arylhya-zono-2-pyrazolin-5-ones (IIa-f)

General Procedure. To a cold solution of 11 (0.01 mole) in ethanol (40 ml), sodium acetate (0.01 mole) was added and the reaction mixture was stirred for few minutes. The appropriate freshly prepared aromatic diazonium salt (0.01 mole) was added gradually with continuous stirring. The solid product (II) that separated was filtered off and recrystallised from the appropriate organic solvent. Results are given in Table 1.

Action of Grignard Reagents on 3-Anilino-4-arylhya-zono-2-pyrazolin-5-ones

General Procedure. To an ethereal solution of the Grignard reagent (prepared from 0.9 g of magnesium, and the appropriate quantity of the organo halide in 100 ml of dry ether), a suspension of each of IIa-c, f (1 g) in dry ether was added. The reaction mixture was refluxed for 30 minutes, left overnight at room temperature and then decomposed with saturated ammonium chloride solution. The oily residue, obtained upon evaporation of the ether layer, was triturated several times with petroleum ether (b.p.40-60°) and the resulting solid (V) was crystallised from ethenol. The results are given in Table 2.

Action of Acetic Anhydride on Ve and IIb

A suspension of Ve (0.5 g) in acetic anhydride (30

ml) was refluxed for 1 hr, cooled and poured into ice-cold water. After complete decomposition of acetic anhydride, yellow crystals separated which were collected by filtration and crystallised from ethanol.

The acetyl derivative (VI) formed deep yellow crystals, m.p. 175°, yield 63%. (Found: C 63.6, H 4.2 and N 16.3%. Calcd for $C_{23}H_{18}O_2N_5Cl$ (431.5) : C 63.96, H 4.17 N 16.22%.)

Table 1

Compound	M.p. (°C)	Colour of crystal	Yield (%)	Formula (Mol. wt)	Analysis(%)	
					Calcd	Found
IIa	220	Rosy*	60	$C_{15}H_{13}ON_5$ (279)	C 69.52	69.4
					H 4.66	4.5
					N 25.09	25.1
b	234	Deep red*	65	$C_{16}H_{15}ON_5$ (293)	C 65.53	65.1
					H 5.12	5.5
					N 23.89	23.7
c	250	Reddish brown†	60 62	$C_{16}H_{15}ON_5$ (293)	C 65.53	65.3
					H 5.12	5.3
					N 23.89	23.6
d	228	Brown†	62	$C_{16}H_{15}O_2N_5$ (309)	C 62.14	61.8
					H 4.85	5.3
					N 22.65	22.4
e	231	Deep brown†	67	$C_{16}H_{15}O_2N_5$ (309)	O 62.14	62.1
					H 4.85	5.2
					N 22.65	22.3
f	239	Red*	70	$C_{15}H_{12}ON_5Cl$ (313.5)	C 57.42	57.2
					H 3.83	3.6
					N 22.33	22.1

Crystallised from (*) toluene, (†) ethanol.

Table 2

Compound	M.p. (°C)	Colour of crystal	Yield (%)	Formula (mol.wt.)	Analysis (%)	
					Calcd	Found
IVa	170	Brown	60	$C_{17}H_{17}ON_5$ (307)	C 66.45	66.3
					H 5.54	5.4
					N 22.80	22.6
b	185	Reddish brown	60	$C_{22}H_{19}ON_5$ (369)	C 71.54	71.4
					H 5.15	4.9
					N 18.97	18.7
c	245	Brown	65	$C_{22}H_{19}ON_5$ (369)	C 71.54	71.6
					H 5.15	5.2
					N 18.97	18.8
d	244	Reddish brown	60	$C_{18}H_{19}ON_5$ (321)	C 67.29	66.9
					H 5.92	5.8
					N 21.81	21.6
e	277	Brown	50	$C_{21}H_{16}ON_5Cl$ (389.5)	C 64.70	64.63
					H 4.11	4.02
					N 17.97	17.78
					Cl 9.11	8.9

Similar treatment of IIb with acetic anhydride afforded the diacetyl derivatives VII which formed deep yellow crystals from ethanol, m.p. 155° , yield 60%. (Found: C 63.6, H 5.12 and N 18.4%. Calcd for $C_{20}H_{19}O_3N_8$ (377). C 63.66, H 5.04 and N 18.57%)

Action of Phenyl Magnesium Bromide on 3-methyl 4-phenylhydrazono-2-pyrazolin-5-one (VIII)

Compound VIII was treated with phenylmagnesium bromide as described above for compound II. After working up of the reaction mixture, the isolated substance proved to be unchanged VIII (m.p. and mixed m.p.).

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