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57. Reactions with the Arylhydrazones of α-Cyanoketones: The Structure of 2-Arylhydrazono-3-ketimino-nitriles

by **Mohamed Hilmy Elnagdi, Mohamed Mohamed Mohamed Sallam, Hussein Mahmoud Fahmy, Saad Abdel-Motteleb Ibrahim** and **Mohamed Ajmal Mohamed Elias**

Chemistry Department, Faculty of Science, Cairo University, Giza, A.R. Egypt

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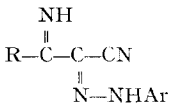
Summary. Analysis of the IR., UV., and polarographic data of a variety of 2-arylhydrazono-3-ketimino-nitriles indicated that these derivatives exist mainly in the intramolecularly chelated hydrazone structure **1**.

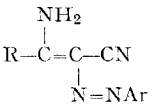
Compounds **1** reacted with hydrazine hydrate to yield the corresponding 5-amino-4-arylazopyrazoles (**3**).

Compound **3a** reacted with acetylacetone, ethyl acetoacetate, and diethyl malonate to yield the pyrazolo[1,5-*a*]pyrimidine derivatives **4**, **5**, and **7** respectively. Compound **3a** also reacted with benzoylisothiocyanate to yield the pyrazolyl thiourea derivative **8**.

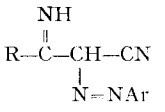
The structure and chemical behaviour of the 2-arylhydrazone derivatives of 1,2,3-triones and of 2,3-diketoesters have received much attention [1] [2]. In our previous work the structure and chemical behaviour of 2-arylhydrazono-3-ketonitriles have been established [3–5]. In continuation to this work it seemed worthwhile to investigate the structure and chemical behaviour of 2-arylhydrazono-3-ketimino-nitriles. These compounds may have any of the possible tautomeric structures A–D. In the present investigation a variety of 2-arylhydrazono-3-ketimino-nitriles (**1a–1g**) were prepared following previously reported procedures [3] [6], and the structure of these products was established *via* analysis of their IR., UV., and polarographic data. Also the behaviour of compounds **1** towards the action of hydrazine was investigated. The IR. spectra of compounds **1a–1g** revealed the presence of a conjugated cyano band at 2195 cm^{-1}. This highly shifted cyano absorption excludes the contribution of azo structures C and D for these compounds as it would require the presence of other cyano absorption at higher frequency. The spectra of compounds **1a–1g** also revealed absorption at 1630 cm^{-1}, 3280 cm^{-1}, and 3410 cm^{-1}. These absorptions, however, can be interpreted either for NH_2 (vibrational and deformational modes) or for C=NH, azomethine NH, and hydrazone NH. Thus they cannot be used for the discrimination between structures A and B. For the aim of establishing the structure of compounds **1** their electronic absorption spectra were measured. The UV. spectra of monoarylhydrazones differ from those of monoarylazo



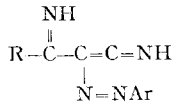
A



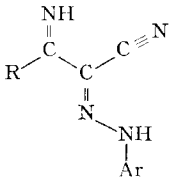
B



C



D



1

1	R	Ar
a	CH_3	C_6H_5
b	CH_3	2–$CH_3C_6H_4$
c	CH_3	3–$CH_3C_6H_4$
d	C_6H_5	C_6H_5
e	C_6H_5	2–$CH_3C_6H_4$
f	C_6H_5	3–$CH_3C_6H_4$
g	C_6H_5	4–$CH_3C_6H_4$

compounds [1] [7]: The former exhibit a strong maximum at λ = 320–390 nm, while the latter derivatives give a strong K band at λ = 280–290 nm. The UV. spectra (Table 1) of **1a–1g** were typical for arylhydrazones, thus establishing the hydrazone structure A for these compounds.

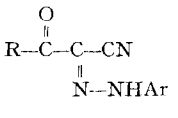
In order to gain further insight into the structure of compounds **1a–1g** at different pH values, polarograms of **1a**, taken as an example, were run and inspected. Thus, polarograms of 10^{-4}M of **1a** in 40% by volume ethanolic *Britton-Robinson* buffer solutions covering the pH range from 2 to 9 showed two waves (A) and (B) in $E_{1/2}$ limit 0.525 to 1.35; 1.46 to 1.6 V *vs* SCE respectively. The less negative wave (A) is well defined and predominent through the whole pH range studied, while the more negative wave (B) obscured by the hydrogen evolution at pH 4.8. The half-wave potential of wave (A) shifted to more negative values with increasing pH ($\Delta E_{1/2}/\Delta$pH = 63 mV/pH). By comparison of these data with the data previously obtained for **2a** [9] and **2d** [5] under similar conditions, the wave heights of (A) and (B) indicated 4 and 2 electron processes respectively. In general, the behaviour of **1a** differs from that reported for arylazo derivatives [9] but is closely related to that of 2-methylglyoxal-1-phenylhydrazone and ethyl 2-phenylhydrazono-3-keto-butyrate

Table 1. *IR. and UV. absorption of 2-Arylhydrazono-3-keliminonitriles* **1a–1g**

1	IR. (cm^{-1})			UV. (Ethanol)
	>NH	–C≡N	–C≡N	λ_{max} nm (log ε)
a	3410; 3280	2193	1640	355 (4.15); 236 (1.58)
b	3405; 3290	2200	1645	350 (4.31); 240 (1.58)
c	3410; 3280	2198	1638	350 (4.34); 238 (1.68)
d	3420; 3280	2200	1620	370 (4.34); 240 (3.39)
e	3415; 3275	2200	1625	375 (4.36); 235 (3.32)
f	3420; 3280	2195	1615	373 (4.46); 235 (3.42)
g	3425; 3285	2200	1610	370 (4.44); 240 (3.45)

[10], and also to that of **2a** and **2d** ($\Delta E_{1/2}/\Delta$ pH = 67 mV/pH for the first and 65 mV/pH for the latter three compounds). The hydrazone structure is well established for all represented compounds. The detailed description of electrode processes as well as the mechanism of electroreduction of **1a–1d** is included in another communication [8].

The cyano absorption of **1a–1c** is 20 cm^{-1} lower than the cyano absorption measured by us for the corresponding 2-arylhydrazono-3-keto-butyronitriles (**2a–2c**) (*cf.* Table 2). Also, the cyano absorption of **1d–1g** is by around the same value lower than the cyano absorption reported for 2-arylhydrazono-3-keto-3-phenyl-propionitriles **2d–2g** [4]. IR. bands for a cyano group at exactly the same frequency were observed for **1a–1d** in dilute chloroform solution, thus excluding intermolecular chelation as a reason for cyano shifts in compounds **1a–1g**. Moreover, involvement of cyano lone electron pair in intermolecular chelation would be expected to cause shifts of cyano absorption in opposite direction [11]. *Baldwin* has reported cyano absorption for β-amido-α,β-unsaturated nitriles in the range of 2160–2200 cm^{-1} [12]. This author considered the abnormally large frequency shifts to be due to the existence of these compounds in an amino tautomeric form which permits a number of charge separate resonance forms to be written.



2

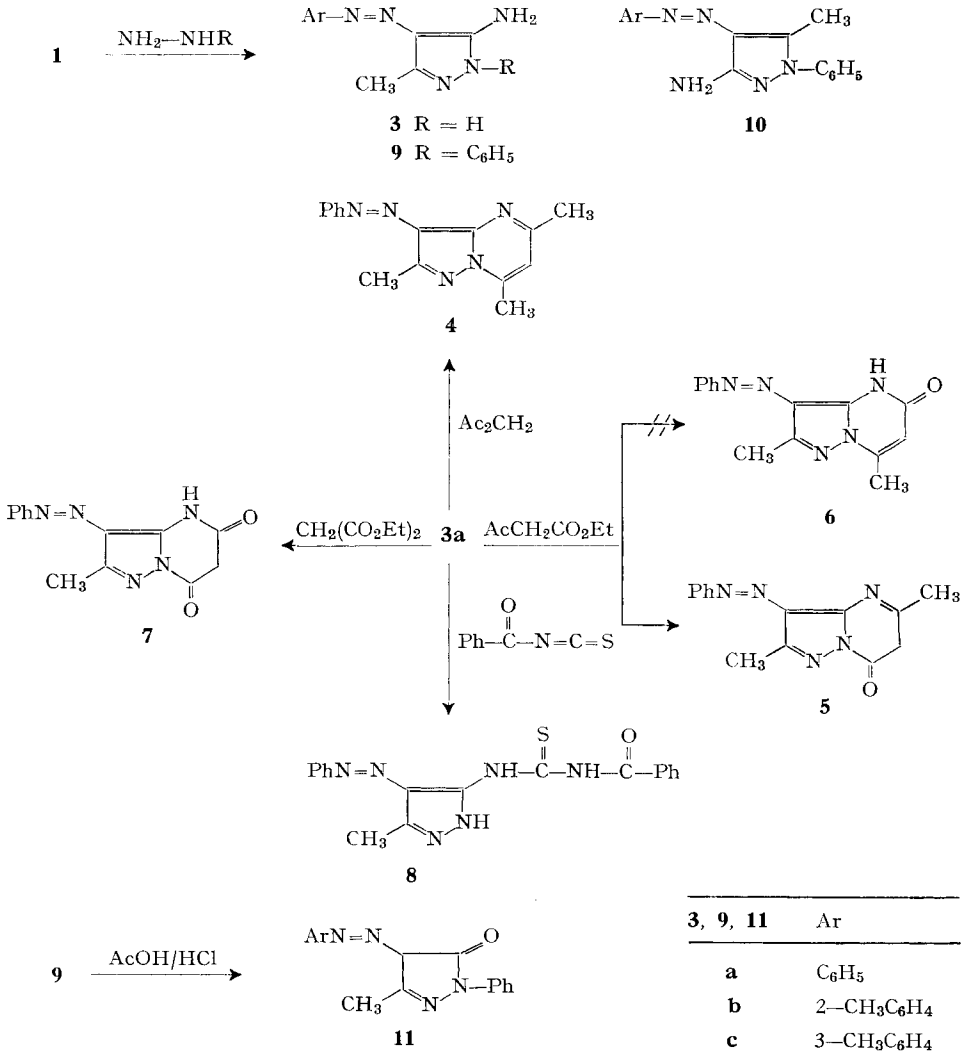
Table 2. *Compounds* **2a–2g**

2	R	Ar	IR. (cm^{-1}) –C≡N
a	CH_3	C_6H_5	2215
b	CH_3	2–$CH_3C_6H_4$	2215
c	CH_3	3–$CH_3C_6H_4$	2215
d	C_6H_5	C_6H_5	2217
e	C_6H_5	2–$CH_3C_6H_4$	2215
f	C_6H_5	3–$CH_3C_6H_4$	2215
g	C_6H_5	4–$CH_3C_6H_4$	2210

The ketimino structure for **1a–1g**, however, does not permit contribution of similar charge separated resonance forms which can lead to similar cyano frequency shifts. The low frequency of the cyano bands in **1a–1g** as compared with the cyano bands of other α,β-unsaturated nitriles may be attributed to the existence of intramolecular hydrogen bonding between the cyano group and either hydrazone or azomethine NH. As steric reasons do not permit this bond to be formed with the lone electron pair of the cyano nitrogen atom, one can assume bonding with the cyano π-electron. Since the cyano bands in **2a–2g** appeared at normal positions expected for α,β-unsaturated nitriles, bonding was considered, most likely, to occur between azomethine NH and CN group. Hydrogen bonding with cyano π-electrons has been previously suggested to account for the presence of intramolecular hydrogen bonds in *o*-cyanophenols [13–15], *o*-cyanoanils [14] and certain cyanohydrins [15].

In continuation to previous interest in the synthesis of 5-aminopyrazoles [16] as intermediates for the preparation of pyrazolo[1,5-*a*]pyrimidines, the reaction of

1a–1c with hydrazines was investigated as a possible route for the synthesis of 5-amino-4-arylazo-pyrazoles. Thus, when **1a–1c** were treated with hydrazine hydrate in refluxing ethanol solution, 5-amino-4-arylazo-3-methyl-pyrazoles **3a–3c** (or possible tautomers) were formed. The pyrazole structure for these derivatives was admitted as probable, considering the absence of CN and C=O absorptions in the IR. of **3a–3c**, the stability towards the action of acetic acid[1]), and the ready reaction of **3a** with acetylacetone yielding 2,5,7-trimethyl-3-phenylazo-pyrazolo-[1,5-*a*]pyrimidine (**4**). This behaviour is typical for 1-unsubstituted 5-aminopyrazoles [18]. Compounds **3a** also reacted with ethyl acetoacetate to yield a product for which



3, 9, 11	Ar
a	C_6H_5
b	2—$CH_3C_6H_4$
c	3—$CH_3C_6H_4$

[1]) *Cf.* the ready cyclisation of 3-arylhydrazono-nitriles into the corresponding aminopyrazoles under similar conditions [17].

structure **5** or possible isomeric **6** seemed probable. Structure **5** was preferred on the basis of analogy to the well established behaviour of 5-aminopyrazoles toward β-ketoesters [19]. The IR. spectrum of this reaction product provides further evidence for the proposed structure. Thus, its IR. spectrum shows pyrimidine ring CO absorption at 1705 cm^{-1}, almost identical with that reported for the pyrimidine ring absorption of 4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrimidines. If this compound from **3a** and ethyl acetoacetate is the isomeric **6**, it should present a downward shift of the frequency of the CO group due to conjugation of the CO with the >C=C<.

Compound **3a** did not react with diethyl malonate under the experimental conditions used to effect its reaction with acetylacetone and ethyl acetoacetate (refluxing for 10 h in acetic acid), but when it was heated for 30 h with diethyl malonate in ethanolic sodium ethoxide solution, the diketo pyrazolo[1,5-*a*]pyrimidine derivative **7** was formed.

Similar to the recently reported [20] behaviour of 5-aminopyrazoles toward acylisothiocyanate, compound **3a** readily added to benzoylisothiocyanate to yield the pyrazolylthiourea derivative **8**. The latter when refluxed with acetic acid/hydrochloric acid mixture afforded a colourless product $C_{11}H_9N_5O$. The structure of this product and the synthetic potentialities of **8** will be the subject of another communication.

Compounds **1a–1c** react with phenylhydrazine to yield products whose analytical and IR. data may be correctly interpreted for either 5-amino-4-arylazo-3-methyl-1-phenyl-pyrazoles (**9**) or the possible isomeric 3-amino-4-arylazo-5-methyl-1-phenyl-pyrazoles (**10**). The structure **9** (or possible tautomers) is confirmed by the identity of compound **9a** with an authentic specimen [21]. Moreover, long reflux of **9a–9c** with acetic acid/hydrochloric acid mixture has afforded the known 1-phenyl-3-methyl-4-arylazo-2-pyrazolin-5-one derivatives **11a–11c** [22].

Experimental Part

IR. spectra were measured in KBr on a *Perkin-Elmer* Infracord model 137 Spectrophotometer. UV. spectra were determined, in ethanol, on a *Beckman* DK-12. The polarograms were recorded with a pen recording polarograph LP60 (*Laboratorni Pristroge*, Prague). The m.p.'s are uncorrected.

2-Arylhydrazone-3-ketimino-butyronitriles (**1a–1c**). Prepared by coupling the appropriate aryldiazonium salt with 3-aminocrotononitrile following the procedure described for **1a** [6].

Compound **1a** [6]: Yellow crystals, m.p. 168° (lit. 165°).

Compound **1b**: Golden yellow crystals, m.p. 151°; yield 70%.

Compound **1c**: Brownish yellow crystals, m.p. 158°; yield 75%.

$C_{11}H_{12}N_4$ (200,24) Calc. C 65.98 H 6.04 N 27.98% Found **1b** C 66.00 H 6.23 N 27.65%
1c ,, 66.09 ,, 6.73 ,, 27.81%

2-Arylhydrazono-3-ketimino-3-phenyl-propionitriles (**1d–1g**). Prepared by the action of phenylmagnesium bromide on the appropriate arylazomalononitrile [4].

2-Arylhydrazono-3-keto-butyronitriles (**2a–2c**): Prepared by coupling acetylacetonitrile with the appropriate aryldiazonium salt after the procedure described for **2a** [6].

Compound **2a** [6]: Yellow crystals, m.p. 165° (lit. 163–164°).

Compounds **2b** and **2c**: Yellow crystals; respectively, m.p. 153°, yield 60%, and m.p. 131°, yield 65%.

$C_{11}H_{11}N_3O$ (201,23) Calc. C 65.67 H 5.51 N 20.88% Found **2b** C 56.42 H 5.31 N 20.68%
2c ,, 65.61 ,, 5.35 ,, 20.68%

5-Amino-3-methyl-4-arylazopyrazoles (**3a–3c**): To a solution of each of **1a–1c** (20.0 g) in ethanol (200 ml) hydrazine hydrate (7.0 g; 98%) was added. After refluxing for 15 h the solvent was removed *in vacuo* and the solid residue was crystallised from ethanol.

Compound **3a**: Yellow crystals; m.p. 198°, yield 80%.

$C_{10}H_{11}N_5$ (201,23) Calc. C 59.68 H 5.51 N 34.81% Found C 59.40 H 5.72 N 35.00%

Compounds **3b** and **3c**: Yellow crystals; respectively, m.p. 154°, yield 82%, and 144°, yield 80%.

$C_{11}H_{13}N_5$ (215,26) Calc. C 61.37 H 6.09 N 32.54% Found **3b** C 61.28 H 5.90 N 32.47%
3c ,, 61.25 ,, 5.80 ,, 32.46%

Compounds **3a–3c** showed IR. bands at 1630–1650 cm^{-1} (δ NH_2), 3410–3400 cm^{-1}, and 3300–3305 cm^{-1} (ν NH_2).

2,5,7-Trimethyl-3-phenyl-azopyrazolo[1,5-a]pyrimidine (**4**): To a solution of **3a** (4.0 g) in acetic acid (50 ml) acetylacetone (2.0 ml) was added. After refluxing for 10 h the solvent was removed *in vacuo* and the solid residue was crystallised from ethanol: Yellow crystals, m.p. 224°.

$C_{15}H_{15}N_5$ (265.32) Calc. C 67.92 H 5.70 N 26.40% Found C 67.90 H 5.52 N 26.33%

2,5-Dimethyl-3-phenylazo-7-oxo-6,7-dihydropyrazolo[1,5-a]pyrimidine (**5**): Ethyl acetoacetate (2.0 ml) was added to a solution of **3a** (4.0 g) in acetic acid (50 ml). After refluxing for 10 h the solvent was removed *in vacuo* and the residue was triturated with water. The solid formed was crystallised from acetic acid: Yellow crystals; m.p. 250°, yield 80%.

$C_{14}H_{13}N_5O$ (267.29) Calc. C 62.91 H 4.90 N 26.20% Found C 62.65 H 4.69 N 25.90%

2-Methyl-5,7-dioxo-3-phenylazo-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine (**7**). To a suspension of **3a** (4.0 g) in ethanol (30 ml) diethyl malonate (2.0 ml) and a sodium ethoxide solution prepared from Na (2.3 g) were added. The mixture was refluxed for 30 h, cooled, diluted with water, and acidified. The resulting solid was crystallised from ethanol: Yellow crystals; m.p. 222°, yield 40%. It showed IR. bands at 1700–1710 cm^{-1} (ring C=O) and 3300 cm^{-1} (>NH).

$C_{13}H_{11}N_5O_2$ (269.26) Calc. C 57.98 H 4.12 N 26.07% Found C 58.20 H 3.90 N 26.33%

N-(3-Methyl-4-phenylazopyrazol-5-yl)-N'-benzoylthiourea (**8**). To a benzoylisothiocyanate solution (prepared by adding 14.5 g of benzoyl chloride to a suspension of 7.5 g of ammonium thiocyanate in 100 ml of acetone) 0.1 mol of compound **3a** was added. After refluxing for 2 h the mixture was poured onto water. The solid that separated on standing was crystallized from ethanol: Yellow crystals; m.p. 220, yield 60%.

$C_{18}H_{16}N_6OS$ (364.42) Calc. C 59.33 H 4.43 N 23.07 S 8.78%
Found ,, 59.05 ,, 4.19 ,, 22.86 ,, 8.80%

5-Amino-4-arylazo-3-methyl-1-phenyl-pyrazoles (**9a–9c**). A mixture of each of **1a–1c** (4.0 g) and phenylhydrazine (30 ml) was heated at 120° (bath temperature) for 6 h, left to cool, and dissolved in hot diluted ethanol. Addition of 5 ml of concentrated hydrochloric acid precipitated a solid product which was crystallised from ethanol.

Compound **9a**: Yellow crystals; m.p. and mixed m.p. with an authentic specimen [21] 140°.

Compound **9b**: Brownish-yellow crystals; m.p. 151°, showed IR. bands at 3415 and 3250 cm^{-1} (NH_2 vibrations).

Compounds **9c**: Yellow crystals; m.p. 102°, showed IR. bands at 3400 and 3255 cm^{-1} (NH_2 vibrations).

$C_{17}H_{17}N_5$ (291.36) Calc. C 70.08 H 5.88 N 24.04% Found **9b** C 69.89 H 5.92 N 24.04%
9c ,, 69.90 ,, 5.71 ,, 24.00%

4-Arylazo-3-methyl-1-phenyl-2-pyrazolin-5-ones (**11a–11c**). To a solution of each of **9a–9c** (4.0 g) in acetic acid (60 ml) concentrated hydrochloric acid (15 ml; 35%) was added. After refluxing for 48 h the mixture was left to cool. The crystals that separated on standing were identified (m.p. and mixed m.p.) as **11a–11c** [18], respectively.

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