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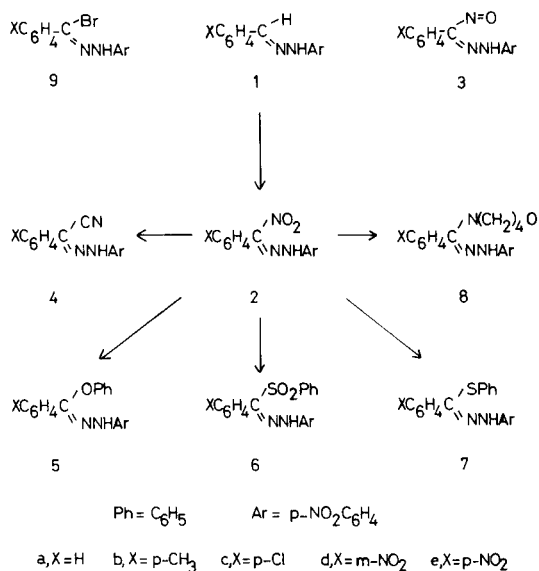
Direct nitration of substituted benzaldehyde *p*-nitrophenylhydrazones **1** gave α -nitroarylidene-*p*-nitrophenylhydrazines **2**. Reactions of **2** with nucleophiles result in displacement of the nitrite. Treatment of **2** with potassium thiocyanate gave 5-imino-1,3,4- Δ^2 -thiadiazolines **10**. Reactions of **2** with carbanions of active methylene compounds yielded the pyrazole derivatives **15-20**. 1,3-Dipolar cycloadditions of **2** onto acrylonitrile and benzalacetophenone afforded the expected cycloadducts **21** and **22**, respectively.

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Introduction.

Among the various electrophilic substitution reactions to which aldehyde arylhydrazones **1** have been subjected (1), the least studied is the direct nitration to give α -nitrohydrazones **2** (Scheme 1). Furthermore, although this latter class of compounds has been known for a long time (2-3), very little is known about their chemical reactivity (4-5) in contrast to the numerous reports on the related α -nitrosohydrazones **3**. Here we wish to report the results of direct nitration of a series of substituted benzaldehyde *p*-nitrophenylhydrazones **1a-e** and the utility of these products in the synthesis of some heterocyclic systems (Schemes 1 and 2).

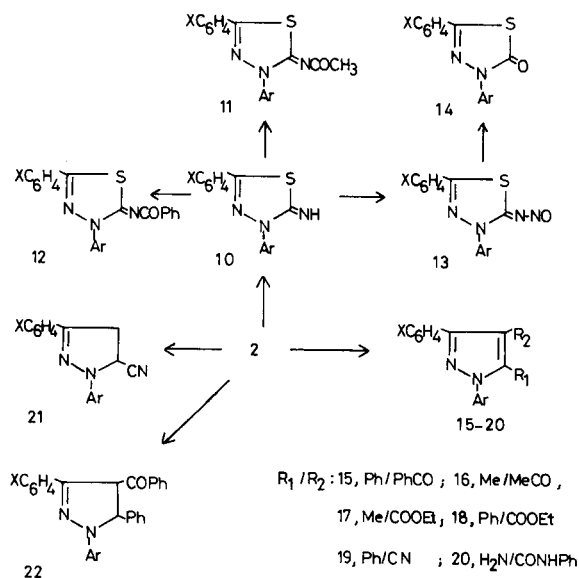
SCHEME 1



Results and Discussion.

Treatment of **1** with a mixture of sulfuric acid and nitric acid in ether at room temperature yielded the corresponding α -nitrohydrazones **2** in excellent yield (80-90%). The

SCHEME 2



structures of the latter products were established on the basis of their elemental and spectral analyses. Also, the results of their chemical investigation described below support the assigned structures **2**. The α -nitrohydrazones prepared are generally orange-red in color exhibiting intense absorption maximum ($\log \epsilon > 4$) in the region 380-400 nm. The pmr spectra of **2a-e** in deuteriochloroform showed NH proton signals in the regions δ 12.0-12.5 and 8.1-8.6 ppm, which integrated together in each case to a value of one proton, indicating that each compound exists as a mixture of both the *Z*- and *E*-isomers (4).

α -Nitrohydrazones are readily attacked by nucleophilic reagents. Thus, treatment of **2** with potassium cyanide, sodium phenolate, sodium benzenesulfinate, sodium thiophenolate and morpholine in ethanol gave the substitution products **4-8**, respectively (Scheme 1). The identity of the product in each case was established on the basis of elemental analysis, spectral data and by alternate syn-

Table 1
Reaction Products of **2** with Nucleophiles (a)

Compound No.	M.p., °C (lit. m.p.)	Molecular Formula	Anal. Calcd./ (Found)		
			C, %	H, %	S, %
4a	205	C ₁₄ H ₁₀ N ₄ O ₂	63.2 (63.3)	3.80 (3.80)	
4b	213	C ₁₅ H ₁₂ N ₄ O ₂	64.30 (64.17)	4.30 (4.25)	
4c	256	C ₁₄ H ₉ ClN ₄ O ₂	55.90 (55.8)	3.01 (3.20)	
4d	249	C ₁₄ H ₉ N ₅ O ₄	54.02 (54.20)	2.91 (3.0)	
4e	298	C ₁₄ H ₉ N ₅ O ₄	54.02 (54.05)	2.91 (2.9)	
5a	170 (170-171) (6)				
6a	178	C ₁₅ H ₁₅ N ₃ O ₄ S			8.4 (8.4)
6b	201	C ₂₀ H ₁₇ N ₃ O ₄ S			8.2 (8.2)
6c	222	C ₁₅ H ₁₄ ClN ₃ O ₄ S			7.7 (7.5)
6d	200	C ₁₅ H ₁₄ N ₄ O ₆ S			7.5 (7.2)
6e	222	C ₁₅ H ₁₄ N ₄ O ₆ S			7.5 (7.3)
7a	118 (118-119) (6)				
8a	157 (174-175) (7)				

(a) Ir (potassium bromide) spectra of **4a-e** showed in each case a nitrile absorption band near 2250 cm⁻¹, whereas those of **6a-e** exhibited two bands at 1344 and 1160 cm⁻¹ assignable to the sulfone group.

Table 2
2,4-Diaryl-5-imino-Δ²-1,3,4-thiadiazolines (**10**) and their *N*-Acyl Derivatives (**11-12**)

Compound No.	M.p., °C	Molecular Formula	Anal. Calcd./ (Found)			
			C, %	H, %	N, %	S, %
10a	186	C ₁₄ H ₁₀ N ₄ O ₂ S	56.36 (56.01)	3.37 (3.22)	18.79 (18.50)	10.75 (10.60)
10c	228	C ₁₄ H ₉ ClN ₄ O ₂ S	50.36 (50.20)	2.71 (2.51)	16.78 (16.82)	9.60 (9.52)
10d	235	C ₁₄ H ₉ N ₅ O ₄ S	48.98 (48.61)	2.64 (2.71)	20.40 (20.31)	9.34 (8.90)
10e	260	C ₁₄ H ₉ N ₅ O ₄ S	48.98 (48.88)	2.64 (2.55)	20.40 (20.21)	9.34 (9.21)
11a	200	C ₁₆ H ₁₂ N ₄ O ₃ S	56.46 (56.00)	3.54 (3.52)	16.47 (16.31)	9.42 (9.20)
11c	237	C ₁₆ H ₁₁ ClN ₄ O ₃ S	51.27 (50.99)	2.96 (2.86)	14.95 (14.63)	8.55 (8.22)
11d	230	C ₁₆ H ₁₁ N ₅ O ₅ S	49.87 (49.35)	2.88 (2.81)	18.18 (18.22)	8.32 (8.20)
11e	270	C ₁₆ H ₁₁ N ₅ O ₅ S	49.87 (49.40)	2.88 (2.71)	18.18 (18.00)	8.32 (8.11)
12a	208	C ₂₁ H ₁₄ N ₄ O ₃ S	62.67 (62.61)	3.51 (3.20)	13.93 (13.80)	7.96 (7.72)
12c	252	C ₂₁ H ₁₃ ClN ₄ O ₃ S	57.73 (57.29)	2.93 (2.72)	12.54 (12.83)	7.34 (7.17)
12d	270	C ₂₁ H ₁₃ N ₅ O ₅ S	56.37 (56.10)	2.92 (2.71)	15.61 (15.71)	7.10 (6.96)
12e	270	C ₂₁ H ₁₃ N ₅ O ₅ S	56.37 (56.66)	2.92 (2.61)	15.61 (15.40)	7.10 (7.32)

thesis from the corresponding hydrazidoyl bromide **9** (6-7).

Reaction of **2** with two moles of potassium thiocyanate in ethanol gave in each case the corresponding 5-imino-thiadiazoline derivative **10**, which was also obtained by

reaction of **2** with thiourea (Scheme 2). Both elemental and spectral data of **10** were consistent with their assigned structures. The latter were also confirmed by their reactions. Thus, **10** with acetic anhydride in acetic acid and

Table 3
5-*N*-Nitrosoimino- Δ^2 -1,3,4-thiadiazolines (**13**) and - Δ^2 -1,3,4-thiadiazolin-5-ones (**14**) (a)

Compound No.	M.p., °C	Molecular Formula	Anal. Calcd./(Found)			
			C, %	H, %	N, %	S, %
13a	168	C ₁₁ H ₉ N ₃ O ₃ S	51.36 (51.10)	2.77 (2.61)	21.40 (21.01)	9.79 (9.62)
13c	170	C ₁₁ H ₉ ClN ₃ O ₃ S	46.47 (46.22)	2.22 (2.11)	19.36 (19.21)	8.86 (8.66)
13d	175	C ₁₁ H ₉ N ₆ O ₅ S	45.16 (44.91)	2.16 (1.99)	22.57 (22.22)	8.61 (8.41)
13e	200	C ₁₁ H ₉ N ₆ O ₅ S	45.16 (44.81)	2.16 (2.00)	22.57 (22.30)	8.61 (8.44)
14a	160	C ₁₁ H ₉ N ₃ O ₃ S	56.18 (55.88)	3.03 (3.00)	14.04 (14.20)	10.71 (10.61)
14c	190	C ₁₁ H ₉ ClN ₃ O ₃ S	50.37 (50.20)	2.41 (2.31)	12.59 (12.33)	9.60 (9.50)
14d	210	C ₁₁ H ₉ N ₆ O ₅ S	48.83 (48.60)	2.34 (2.30)	16.28 (15.98)	9.31 (9.11)
14e	230	C ₁₁ H ₉ N ₆ O ₅ S	48.83 (48.62)	2.34 (2.21)	16.28 (16.00)	9.31 (9.21)

(a) Electronic spectra of **13a-e** in EtOH show two absorption maxima near 480 ($n-\pi^*$, $\log \epsilon < 4$) and 350 ($\pi-\pi^*$, $\log \epsilon > 4$) nm. Ir spectra of **14a-e** revealed carbonyl bands near 1700 cm⁻¹; uv (ethanol): λ max 310 ($\log \epsilon > 4$) nm.

Table 4
Pyrazole Derivatives (**19** and **20**)

Compound No.	M.p., °C	Molecular Formula	Anal. Calcd./(Found)		
			C, %	H, %	N, %
19a	179	C ₂₂ H ₁₄ N ₄ O ₂	72.12 (72.00)	3.85 (3.90)	15.29 (15.35)
19b	176	C ₂₂ H ₁₆ N ₄ O ₂	72.61 (72.55)	4.24 (4.30)	14.73 (14.80)
19c	180	C ₂₂ H ₁₃ ClN ₄ O ₂	65.91 (65.81)	3.26 (3.11)	13.98 (13.62)
19e	209	C ₂₂ H ₁₃ N ₅ O ₄	64.22 (63.92)	3.18 (3.00)	17.02 (17.20)
20a	230	C ₂₂ H ₁₇ N ₅ O ₃	66.15 (66.01)	4.29 (4.20)	17.53 (17.11)
20c	228	C ₂₂ H ₁₆ ClN ₅ O ₃	60.89 (60.80)	3.71 (3.54)	16.14 (16.42)
20d	256	C ₂₂ H ₁₆ N ₆ O ₅	59.45 (59.22)	3.62 (3.50)	18.91 (18.60)

benzoyl chloride in pyridine gave the *N*-acetyl and *N*-benzoyl derivatives **11** and **12**, respectively. Nitrosation of **10** yielded the *N*-nitroso compounds **13** which decomposes upon heating in xylene to give 5-thiadiazolinones **14** (Scheme 2).

Addition of **2** to an equivalent amount of the sodium salts of dibenzoylmethane, acetylacetone, ethylacetoacetate ethylbenzoylacetate ω -cyanoacetophenone and cyanoacetanilide, in ethanol yielded the corresponding pyrazole derivatives **15-20**, respectively (Scheme 2). The products **15-18** were previously prepared by the reaction

of **9** with the appropriate active methylene compounds (**8**). The spectral properties of the new pyrazole derivatives **19** and **20** were in agreement with their assigned structures (see Experimental).

When compound **2a** were treated with acrylonitrile and sodium ethoxide in ethanol, 1-*p*-nitrophenyl-3-phenyl-5-cyano-4,5-dihydro-2-pyrazoline **21a** was produced. The infrared spectrum of **21a** showed no absorption band due to the carbonitrile group, however. The absence of nitrile absorption in the infrared spectrum supports its structure (**9**). The pmr spectrum of **21a** in deuteriochloroform

exhibits signals at δ 5.10 (t, 1H, $J = 9$ Hz, 5-CH), 3.55 (d, 2H, $J = 9$ Hz, 4-CH), 7.1-8.5 (m, 9H, ArH) ppm.

Compound **2a** reacts with benzalacetophenone in ethanol in presence of sodium ethoxide to give the cyclo-adduct **22a**. The latter product was alternatively prepared from **9a** and benzalacetophenone in benzene in presence of triethylamine. The pmr spectrum of **22a** revealed two doublets at δ 5.78 (1H, $J = 6$ Hz, 4-CH) and δ 4.7 (1H, $J = 6$ Hz, 5-CH) and a multiplet at δ 6.9-8.5 (9H, ArH) ppm. The infrared spectrum of **22a** in potassium bromide revealed two strong bands at 1700 and 1600 cm^{-1} , assignable to the benzoyl CO and C=N groups, respectively.

The foregoing results indicate that α -nitrohydrazones, like α -bromohydrazones, are eminantly suitable intermediates for the synthesis of various heterocyclic compounds.

EXPERIMENTAL

Melting points are uncorrected. Pmr spectra of the compounds in deuteriochloroform were recorded on Varian T-60A spectrometer using tetramethylsilane as internal reference. Infrared (potassium bromide) and electronic absorption (ethanol) spectra were taken on Unicam SP 1000 and SP 8000 spectrophotometers respectively.

α -Nitrohydrazones (**2a-e**). General.

A suspension of the appropriate arylidene *p*-nitrophenylhydrazine (4 g.) in ether (~ 50 ml.) was stirred at room temperature. The stirred mixture was treated with a nitrating mixture (16 ml., 1:1 of concentrated sulfuric and nitric acids) dropwise over a period of 20 minutes. The stirring was continued for additional 30 minutes during which the acid layer acquires a deep red color. The mixture was neutralized with sodium carbonate solution, and the other layer was collected, then the solvent was evaporated. The crude α -nitrohydrazone was collected and crystallized from ethanol or dioxane.

Compound **2a** had m.p. 141° [lit. (10) m.p. 141-142°].

Anal. Calcd. for $\text{C}_{13}\text{H}_{10}\text{N}_4\text{O}_4$: N, 19.57. Found: N, 19.60.

Compound **2b** had m.p. 136°.

Anal. Calcd. for $\text{C}_{14}\text{H}_{12}\text{N}_4\text{O}_4$: N, 18.66. Found: N, 18.59.

Compound **2c** had m.p. 156°.

Anal. Calcd. for $\text{C}_{13}\text{H}_9\text{ClN}_4\text{O}_4$: N, 17.47. Found: N, 17.81.

Compound **2d** had m.p. 136°.

Anal. Calcd. for $\text{C}_{13}\text{H}_9\text{N}_4\text{O}_4$: N, 21.14. Found: N, 21.09.

Compound **2e** had m.p. 160°.

Anal. Calcd. for $\text{C}_{13}\text{H}_9\text{N}_3\text{O}_6$: N, 21.14. Found: N, 21.16.

Reaction of **2a** with Nucleophiles. General.

Equimolecular quantities (0.005 mole each) of **2a** and the appropriate nucleophile (potassium cyanide, sodium phenoxide, sodium benzenesulfinate, sodium thiophenoxide or morpholine) in ethanol (50 ml.) were stirred for 2 hours and then left overnight at room temperature. The product was collected, washed with water and crystallized from ethanol or acetic acid. The products **4-8** obtained were identical in all respects with authentic samples prepared from **9** and the appropriate nucleophile (Table 1).

5-Imino- Δ^2 -1,3,4-thiadiazolines (**10a-e**). General.

Potassium thiocyanate (0.002 mole) in ethanol (5 ml.) was added to a warm solution of **2** (0.001 mole) in the same solvent (50 ml.). The mixture was refluxed for 15 minutes, then cooled. The crude product **10** was collected and washed with water. Crystallization from ethanol gave **10** in 70-85% yield (Table 2). The electronic spectra (ethanol) of **10a-e** exhibit two intense maxima ($\log \epsilon > 4$) near 350 and 240 nm; ir spectra (potassium bromide): ν 3340 (NH) 1610, 1635 (C=N) cm^{-1} .

When **10** was refluxed in an excess of acetic anhydride for 15 minutes and the reaction mixture was poured on ice, the crude *N*-acetyl derivatives **11** was formed. The latter was collected and crystallized from acetic acid (Table 2). The ir spectra of **11** revealed, in each case, an absorption band near 1640 (C=N-COCH₃) cm^{-1} .

The benzylation of **10** was effected by refluxing equimolecular quantities of **10** and benzoyl chloride in pyridine. The reaction mixture was cooled and poured on ice, and the product **12** separated was collected and crystallized from acetic acid (Table 2), the ir spectra of **12** showed an *N*-benzoyl carbonyl band near 1630 cm^{-1} .

Nitrosation of **10**.

A solution of **10** (0.001 mole) in acetic acid (10 ml.) was treated with sodium nitrite (0.002 mole) while stirring. The reddish product which precipitated was collected and crystallized from ethanol to give the corresponding 5-*N*-nitrosoimino derivatives **13** in almost quantitative yield (Table 3).

2,4-Diaryl- Δ^2 -1,3,4-thiadiazolin-5-ones (**14**).

The appropriate nitroso derivative **13** (0.7 g.) was refluxed in xylene (40 ml.) for 15 minutes. The solvent was removed under reduced pressure and a small amount of ethanol was added to the residue. The solid formed was collected and crystallized from ethanol. The products **14** were obtained in 80-90% yield (Table 3).

Pyrazole Derivatives (**15-20**). General.

To an ethanolic solution of sodium ethoxide (prepared from sodium metal) (0.11 g.) and 20 ml. of absolute ethanol was added 0.005 mole of the appropriate active methylene compound after stirring for 15 minutes at room temperature the α -nitrohydrazone **2** (0.005 mole) was added and stirring was continued for 2 hours during which compound **2** dissolved and the product precipitated. The reaction mixture was left overnight at room temperature. The crude pyrazole derivative was collected washed with water, dried and finally crystallized from ethanol or acetic acid. The pyrazole derivatives **15-18** obtained were identical (m.p., mixed m.p., spectra) with authentic samples (**8**) prepared from **9** and the corresponding active methylene compound.

Compound **15** had m.p. 150-151° [lit. (8) m.p. 151°].

Compound **16** had m.p. 164° [lit. (8) m.p. 165°].

Compound **17** had m.p. 118-119° [lit. (8) m.p. 119°].

Compound **18** had m.p. 122-123° [lit. (8) m.p. 123°].

The new pyrazole derivatives **19** and **20** are listed in Table 4 together with their physical constants. Infrared spectra of **19** revealed in each case an absorption band assignable to C \equiv N group near 2200 cm^{-1} , whereas the ir spectra of **20** showed bands at 3500, 3410 (NH₂), 3300 (NH), 1655, 1550 (CONH) cm^{-1} .

1,3-Diaryl-5-cyano-4,5-dihydro-2-pyrazolines (**21**).

Compound **2a** (0.002 mole), sodium ethoxide (0.002 mole) and acrylonitrile (0.002 mole) were refluxed in ethanol (30 ml.) for 90 minutes. Cooling, filtering and crystallization from ethanol gave **21a** in 75% yield, m.p. 140°, ir: ν 1615 cm^{-1} (C=N).

Anal. Calcd. for $\text{C}_{16}\text{H}_{12}\text{N}_4\text{O}_2$: C, 65.74; H, 4.13; N, 19.17. Found: C, 65.40; H, 4.00; N, 19.32.

Compound **2b** when similarly treated gave **21b** in 70% yield, m.p. 209° (ethanol).

Anal. Calcd. for $\text{C}_{17}\text{H}_{14}\text{N}_4\text{O}_2$: C, 66.65; H, 4.60; N, 18.29. Found: C, 66.51; H, 4.66; N, 18.11.

1,3,5-Triaryl-4-benzoyl-4,5-dihydro-2-pyrazolines (**22**).

A mixture of **2a** (0.005 mole), benzalacetophenone (0.005 mole) and sodium ethoxide (0.005 mole) in ethanol (50 ml.) was refluxed for 2 hours and then cooled. The crude product was filtered and washed with water. Crystallization from acetic acid gave 1.1 g. (70%) of **22a**, m.p. 151°.

Anal. Calcd. for $\text{C}_{28}\text{H}_{21}\text{N}_3\text{O}_3$: C, 75.15; H, 4.73; N, 9.39. Found: C, 74.92; H, 4.71; N, 9.29.

Compound **22b** was similarly obtained in 75% yield from **2b** and benz-

alacetophenone following the same procedure; m.p. 219-220° (ethanol); ir: ν 1695 (PhCO), 1600 (C=N) cm^{-1} ; pmr (deuteriochloroform): δ 4.82 (d, 1H, J = 6 Hz), 5.60 (d, 1H, J = 6 Hz), 2.3 (s, 3H, CH₃, Ar), 6.8-8.00 (m, 14H, ArH).

Anal. Calcd. for C₂₉H₂₃N₃O₃: C, 75.46; H, 5.02; N, 9.10. Found: C, 75.32; H, 4.92; N, 9.01.

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