

Synthesis of Several New Pyridazines and 3,5-Diarylanilines

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(Received April 11, 1989)

Synopsis. Several new pyridazines and 3,5-diarylanilines were obtained from (1-arylethylidene)malononitriles **1b–e** as starting compounds.

In recent years great emphasis has been placed on the utilities of organic cyano compounds in organic synthesis.^{1,2)} In previous work³⁾ we could show that the methyl function in (1-phenylethylidene) malononitrile (**1a**) is extremely reactive toward electrophilic reagents. This extra reactivity could be utilized to the synthesis of a variety of polyfunctionally substituted cyclic aromatic compounds. The reactivity of this methyl function was however decreased by replacing the phenyl substituent (in **1**) by a 2-furyl or 2-thienyl substituent.⁴⁾ In order to shed further light on the effect of substituent in this position on the reactivity of methyl function, a variety of **1** were prepared and their reactivity toward electrophilic reagents was investigated. It has been found that the product of coupling **1** with benzenediazonium chloride depends on applied reaction conditions. Thus, **1b–d** couple with benzenediazonium chloride in EtOH/NaOAc to yield the corresponding coupling products **2a–c**. These were readily cyclized into the 3(2*H*)-pyridazinones **3a–c** on reflux in aqueous acetic acid. Compounds **3a–c** are assumed to be formed via intermediacy of the imines **4a–c**. Attempted isolation of the imines **4a–c** were unsuccessful.

However, long contact of **1e** with benzenediazonium chloride afforded the bis-coupling product **5**. The behavior of **1e** is thus similar to the reported formation of bis-coupling products by reaction of **1a** with benzenediazonium and *p*-toluenediazonium chlorides under these conditions.³⁾ Attempted cyclization of **5** in refluxing acetic acid in the presence of acetic anhydride afforded the acetyl derivative **6**. This is assumed to be formed via exchange of one of

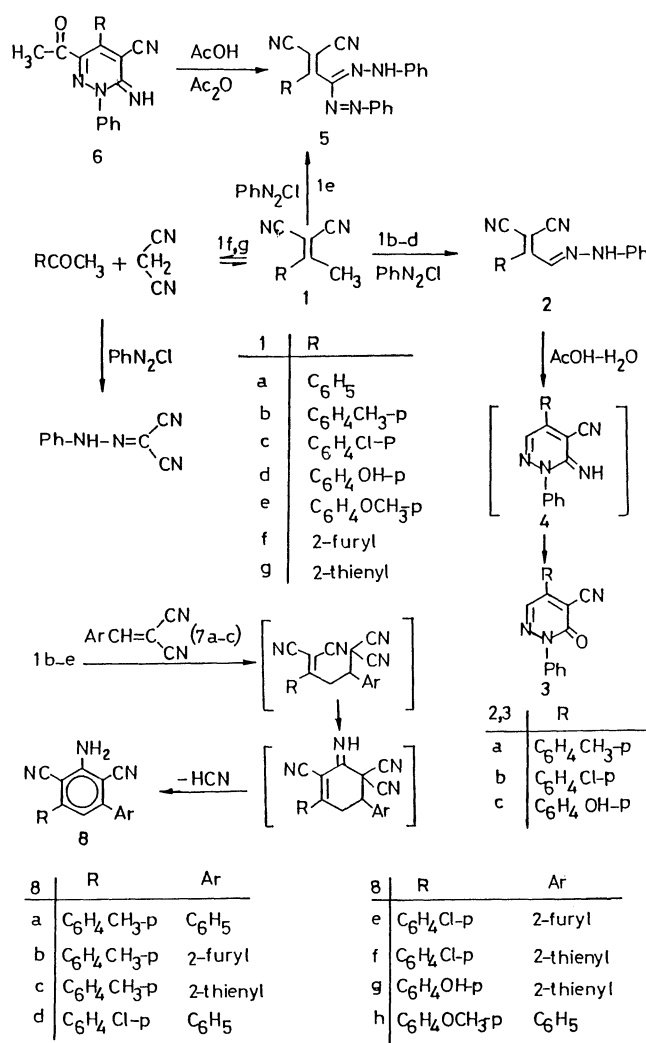


Chart 1.

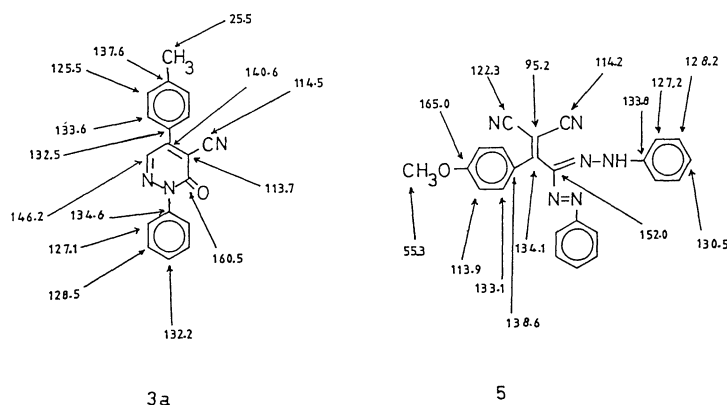


Fig. 1.

the arylazo functions in **5** by an acetyl group. Exchange of arylazo functions by protons and by acyl groups has been previously observed.³⁾ The structure assigned for compounds **3** and **5** was confirmed by ¹³CNMR.⁵⁾

Compounds **1b–e** also reacted with (arylmethylene) malononitrile derivatives **7a–c** to yield products of condensation via HCN elimination. These were formulated as **8a–h** based on analogy to the well established behavior of **1a**, **f**, and **g** toward **7**.^{3,4)}

Compounds **1b–e** failed to react with trichloroacetonitrile under conditions utilized to effect addition of the latter reagent toward **1a**.³⁾

In conclusion it can be assumed that the activity of the methyl function in **1** is not affected by substitution in the aryl moiety. Such a group which adjacent to activated double bond with two cyano groups on the β -carbon is sufficiently acidic. However, when this aryl function is replaced by a five membered heterocycle, the behavior toward arenediazonium salts changes.⁴⁾ Since **1e** has been shown to couple with benzenediazonium chloride, it can be stated that the difference in the behavior toward arenediazonium salts between **1f**, **g**, and **e** may be rationalized by assuming that both **1f** and **g** exist in equilibrium with their constituents in slightly basic media.

Experimental

All melting points are uncorrected. IR spectra were recorded (KBr) with a Pye-Unicam SP-1100 spectrophotometer. ¹H NMR were measured in DMSO on a Varian EM-390-90 MHz spectrometer using TMS as internal standard and chemical shifts are expressed as δ (ppm). Analytical data were obtained from the analytical data unit at Cairo University.

1-(Arylethylidene)malononitrile derivatives **1b–e** were synthesized following our previously reported procedure.⁴⁾

[1-(4-Tolyl)ethylidene]malononitrile (**1b**) formed colorless crystals from ethanol; mp 90 °C; yield 80%; IR: 2970 (CH₃); 2200, 2190 cm⁻¹ (CN bands). ¹H NMR: δ =1.12, 1.31 (two singlets, 6H, 2CH₃); 7.3–8.2 (m, 4H, C₆H₄).

C ₁₂ H ₁₀ N ₂	Found	C 79.12	H 5.39	N 15.36%
(182.2)	Calcd	C 79.09	H 5.53	N 15.37%

[1-(4-Chlorophenyl)ethylidene]malononitrile (**1c**) formed colorless crystals from ethanol; mp 88 °C; yield 75%; IR: 2980 (CH₃); 2200, 2190 cm⁻¹ (CN bands).

C ₁₁ H ₇ N ₂ Cl	Found	C 65.22	H 3.33	N 13.86%
(184.2)	Calcd	C 65.19	H 3.48	N 13.82%

[1-(4-Hydroxyphenyl)ethylidene]malononitrile (**1d**) formed yellow crystals from ethanol; mp 125 °C; yield 70%; IR: 2990 (CH₃); 2200, 2190 cm⁻¹ (CN bands).

C ₁₁ H ₈ N ₂ O	Found	C 71.74	H 4.31	N 15.22%
(184.2)	Calcd	C 71.72	H 4.37	N 15.21%

[1-(4-Methoxyphenyl)ethylidene]malononitrile (**1e**) formed pale yellow crystals from ethanol; mp 76 °C; yield 75%; IR: 2990 (CH₃); 2200, 2190 cm⁻¹ (CN bands).

C ₁₂ H ₁₀ N ₂ O	Found	C 72.54	H 4.92	N 14.02%
(198.2)	Calcd	C 72.70	H 5.08	N 14.13%

Coupling of Compound 1 with Benzenediazonium Chloride (General Procedure): (a) **Monocoupling Product.** An ice cold solution of 0.01 mol of benzenediazonium chloride (prepared from 0.01 mol of aniline and the appropriate amount of sodium nitrite and hydrochloric acid) was added to a solution of **1b–d** (0.01 mol) in ethanol (50 ml) containing sodium acetate (5 g). The precipitate was filtered off

and crystallised from dioxane.

(b) **Biscoupling Product 5.** An ice cold solution of 0.01 mol of benzenediazonium chloride was added to a solution of **1e** (0.01 mol) in ethanol (50 ml) containing sodium acetate (5 g). The reaction mixture was left for 6 hours. The solid product, so formed, was collected by filtration and crystallised from dioxane.

[2-Phenylhydrazono-1-(4-tolyl)ethylidene]malononitrile (**2a**), brown crystals; mp 186 °C; yield 78%; IR: 3340 (NH); 2200 cm⁻¹ (br., CN bands). ¹H NMR: δ =2.32 (s, 3H, CH₃); 7.4–7.8 (m, 11H, aromatic, ylidenic and NH protons).

C ₁₈ H ₁₄ N ₄	Found	C 75.58	H 4.82	N 19.57%
	Calcd	C 75.50	H 4.92	N 19.56%

[2-Phenylhydrazono-1-(4-chlorophenyl)ethylidene]malononitrile (**2b**), brown crystals; mp 204 °C; yield 70%; IR 3260 (NH); 2220, 2210 (CN bands); 1590 cm⁻¹ (C=C). ¹H NMR: δ =7.4–7.7 (m, 10H, aromatic, ylidenic and NH protons).

C ₁₇ H ₁₁ N ₄ Cl	Found	C 66.48	H 3.87	N 18.32%
(306.8)	Calcd	C 66.55	H 3.61	N 18.26%

[2-Phenylhydrazono-1-(4-hydroxyphenyl)ethylidene]malononitrile (**2c**), brown crystals; mp>250 °C; yield 60%; IR: 3240 (NH); 2220, 2210 cm⁻¹ (CN bands).

C ₁₇ H ₁₂ N ₄ O	Found	C 70.34	H 4.18	N 19.22%
(288.3)	Calcd	C 70.82	H 4.19	N 19.43%

[2-Phenylazo-2-phenylhydrazono-1-(4-methoxyphenyl)ethylidene]malononitrile **5**, brown crystals; mp 130 °C; yield 50%; IR: 3240 (NH); 2220 cm⁻¹ (br. CN bands).

C ₂₄ H ₁₈ N ₆ O	Found	C 70.84	H 4.58	N 20.49%
(406.5)	Calcd	C 70.92	H 4.46	N 20.67%

5-Aryl-3-oxo-2-phenyl-2,3-dihydropyridazine-4-carbonitriles (3a–c). A solution of either **2a–c** (0.01 mol) in aqueous acetic acid (30 ml; 70%) was refluxed for 2 h then left to cool. The solid products so formed were collected by filtration and crystallised from the proper solvent.

3-Oxo-2-phenyl-5-(4-tolyl)-2,3-dihydropyridazine-4-carbonitrile (**3a**) formed orange crystals from acetic acid-water mixture; mp 100 °C; yield 70%; IR: 2220 (CN); 1680 cm⁻¹ (C=O). ¹H NMR: δ =2.33 (s, 3H, CH₃); 7.2, 7.8 (m, 9H, aromatic protons).

C ₁₈ H ₁₃ N ₃ O	Found	C 75.19	H 4.62	N 14.53%
(287.3)	Calcd	C 75.24	H 4.56	N 14.62%

5-(4-Chlorophenyl)-3-oxo-2-phenyl-2,3-dihydropyridazine-4-carbonitrile (**3b**) formed red crystals from acetic acid-water mixture; mp 280 °C; yield 60%; IR: 2220 (CN); 1690 cm⁻¹ (C=O). ¹H NMR: δ =7.0–7.9 (m, 9H, aromatic protons).

C ₁₇ H ₁₀ N ₃ OCl	Found	C 66.23	H 3.24	N 13.48%
(307.8)	Calcd	C 66.34	H 3.27	N 13.65%

5-(4-Hydroxyphenyl)-3-oxo-2-phenyl-2,3-dihydropyridazine-4-carbonitrile (**3c**), formed yellow crystals from ethanol; mp 210 °C; yield 60%; IR 2220 (CN); 1680 cm⁻¹ (C=O).

C ₁₇ H ₁₁ N ₃ O ₂	Found	C 70.32	H 3.68	N 14.22%
(289.3)	Calcd	C 70.57	H 3.83	N 14.52%

6-Acetyl-5-(4-methoxyphenyl)-3-oxo-2-phenyl-2,3-dihydropyridazine-4-carbonitrile (**6**), formed yellow crystals from acetic acid-water mixture; mp 259 °C; yield 65%; IR: 2990 cm⁻¹ (CH₃); 2220 (CN); 1690–1670 cm⁻¹ (br. CO groups).

C ₂₀ H ₁₆ N ₄ O ₂	Found	C 69.53	H 4.52	N 16.57%
(344.4)	Calcd	C 69.75	H 4.68	N 16.27%

Condensation of Compounds 1b–e with (Arylmethylene)malononitrile Derivatives 7a–c (General Procedure). A solution of compound **1b–e** (0.01 mol) and the appropriate (arylmethylene)malononitrile derivatives (0.01 mol) in ethanol (50 ml) was treated with piperidine (1.0 ml). The reaction mixture was heated under reflux for 3 h and then evaporated in vacuo. The solid product, so formed, was collected by filtration and recrystallized from the proper solvent.

Compound **8a** formed orange crystals from ethanol; mp 248 °C; yield 75%; IR: 3360, 3100 (NH₂); 2210, 2190 (CN bands); 1630 cm⁻¹ (δ NH₂). ¹H NMR: δ=2.31 (s, 3H, CH₃); 7.0–7.9 (m, 10H, aromatic protons); 8.82 (s, 2H, NH₂).

C ₂₁ H ₁₅ N ₃	Found	C 81.48	H 5.07	N 13.72%
(309.4)	Calcd	C 81.52	H 4.88	N 13.58%

Compound **8b** formed pale yellow crystals from acetone; mp 247 °C; yield 76%; IR: 3390 (NH₂); 2220 (CN bands); 1640 cm⁻¹ (δ NH₂). ¹H NMR δ=2.32 (s, 3H, CH₃); 7.2–7.9 (m, 8H, aromatic protons); 8.3 (br., s, 2H, NH₂).

C ₁₉ H ₁₃ N ₃ O	Found	C 76.47	H 4.56	N 14.22%
(299.3)	Calcd	C 76.23	H 4.37	N 14.03%

Compound **8c** formed pale yellow crystals from ethanol; mp 231 °C; yield 77%; IR: 3390 (NH₂); 2220, 2210 (CN bands); 1640 cm⁻¹ (δ NH₂).

C ₁₉ H ₁₃ N ₃ S	Found	C 72.48	H 4.37	N 13.22	S 10.32%
(315.4)	Calcd	C 72.35	H 4.15	N 13.32	S 10.16%

Compound **8d** formed colorless crystals from acetone; mp 253 °C; yield 77%; IR: 3390, 3250 (NH₂); 2220 (CN bands); 1645 cm⁻¹ (δ NH₂). ¹H NMR: δ=7.2–7.9 (m, 10H, aromatic protons); 8.2 (br. s, 2H, NH₂).

C ₂₀ H ₁₂ N ₃ Cl	Found	C 72.53	H 3.65	N 12.58%
(329.8)	Calcd	C 72.83	H 3.66	N 12.74%

Compound **8e** formed pale yellow crystals from dioxane; mp 275 °C; yield 72%; IR: 3360, 3260 (NH₂); 2210 (CN bands); 1650 cm⁻¹ (δ NH₂).

C ₁₈ H ₁₀ N ₃ OCl	Found	C 67.68	H 3.55	N 13.36%
(319.8)	Calcd	C 67.61	H 3.15	N 13.14%

Compound **8f** formed pale yellow crystals from dioxane; mp 277 °C; yield 70%; IR: 3370, 3260 (NH₂); 2220 (CN); 1650 cm⁻¹ (δ NH₂).

C ₁₈ H ₁₀ N ₃ SCl	Found	C 64.52	H 3.08	N 12.48	S 9.52%
(335.8)	Calcd	C 64.37	H 3.00	N 12.51	S 9.54%

Compound **8g** formed yellow crystals from ethanol; mp >250 °C; yield 60%; IR: 3380 (NH₂); 2220 (CN bands); 1640 cm⁻¹ (δ NH₂).

C ₁₈ H ₁₁ N ₃ OS	Found	C 68.55	H 3.43	N 13.01%
(317.4)	Calcd	C 68.12	H 3.49	N 13.24%

Compound **8h** formed orange crystals from acetone; mp 255 °C; yield 70%; IR: 3380, 3250 (NH₂); 2220, 2210 (CN bands); 1640 cm⁻¹ (δ NH₂).

C ₂₁ H ₁₅ N ₃ O	Found	C 77.57	H 4.44	N 12.82%
(325.4)	Calcd	C 77.52	H 4.64	N 12.91%

K. U. Sadek is indebted to the Alexander von Humboldt foundation for granting a fellowship.

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