A Simple Preparation of 5-Amino-3-cyano-2,4-diarylfurans and their Use in the Synthesis of 3-Amino-5-cyanophthalic Anhydrides[1]

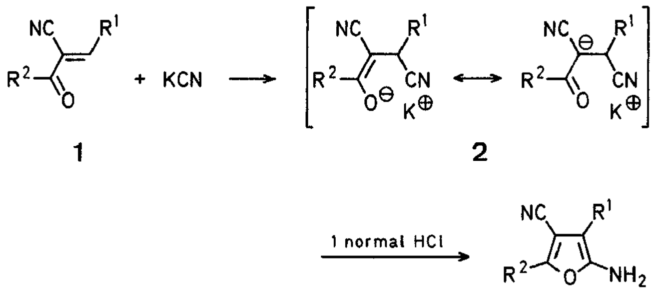
Vicente J. Aran, José L. Soto*

Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad Complutense de Madrid, Madrid 3, Spain

Simple 2-aminofurans are unstable; their stability is greatly improved by introducing electron-withdrawing groups in the ring[2]. In the past years several synthesis of these systems were described. One general method uses the reaction of suitably substituted α-halocarbonyl compounds with the sodium salts of malononitrile, an alkyl cyanoacetate[3-7], or cyanoacetone[8]. In these instances, the reaction proceeds probably through a not isolated carbanion at position three of an intermediate 4-oxobutanenitrile. In the absence of the stabilization provided at this position by a group suitable for conjugation, such as a benzoyl or an acetyl group, the cyclization does not succeed[6]. Another approach to the synthesis of 2-aminofurans is based on the Knoevenagel condensation of malononitrile and benzoins[9,10,11].

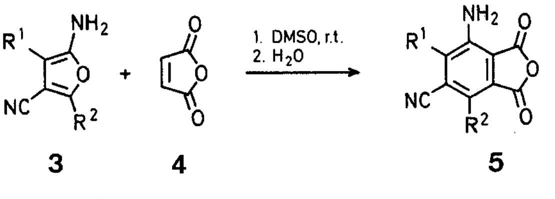
We now report a simple preparation of furan-3-carbonitriles **3** by addition of potassium cyanide to 3-aryl-2-arylmethylene-3-oxopropanenitriles **1**[12-15] followed by acidification (Scheme A).

The initially formed adducts **2** were not isolated; the furan-3-carbonitriles **3** were obtained in excellent yields and purity. Their structure was established on spectral evidence. All compounds show a strong blue fluorescence in solution (Table 1). A related base-catalyzed addition of malononitrile or an alkyl cyanoacetate to arylpropanenitriles **1** to yield 4H-pyrans has been reported[12,13,16].



Scheme A

The structure of the furan-3-carbonitriles **3** was further confirmed by a Diels-Alder reaction with maleic anhydride **(4)**. The behaviour of furans as dienes in this reaction is of general character[17]. However in this instance, the initial adducts formed were unstable. They lost water spontaneously and afforded the persubstituted phthalic anhydrides **5** (Scheme **B**, Table 2). Few examples of this further transformation are known[9,18].



Scheme **B**

3-Aryl-2-arylmethylene-3-oxopropanenitriles 1; General Procedure:

A mixture of the 3-aryl-3-oxopropanenitrile[19] (50 mmol) and an aromatic aldehyde (50 mmol) is slightly warmed in ethanol (40 ml) until solution is complete. The solution is cooled at room temperature and five drops of piperidine are added. Products **1** crystallize in a few minutes. They are collected, washed with ethanol, dried, and used without further purification. Yields and melting points of recrystallized samples are in agreement with the reported values (Refs.[12-15]). The following two compounds were previously unknown.

2-Benzylidene-3-(4-dimethylaminophenyl)-3-oxopropanenitrile **(1g)**; yield: 94%; m.p. 151–153 °C (from ethanol).

$C_{18}H_{16}N_2O$	calc.	C 78.23	H 5.84	N 10.14
(276.3)	found	78.42	5.66	10.27

3-(4-Methoxybenzylidene)-3-(4-methoxyphenyl)-3-oxopropanenitrile **(1j)**; yield: 97%; m.p. 137–138 °C (from ethanol).

$C_{18}H_{15}NO_3$	calc.	C 73.70	H 5.15	N 4.77
(293.3)	found	73.48	5.07	4.53

5-Amino-3-cyano-2,4-diarylfurans 3; General Procedure:

To a suspension of the 3-aryl-2-arylmethylene-3-oxopropanenitrile **1** (20 mmol) in ethanol (40 ml), potassium cyanide (1.43 g, 22 mmol) in water (5 ml) is added. The reaction mixture is heated at 80 °C until solution is complete, cooled to room temperature, and poured into 1 normal hydrochloric acid (400 ml) with vigorous stirring. The furan **1** precipitates immediately as a yellow gum which solidifies after several hours. The crude product is triturated, collected, and dried. The raw material shows a single fluorescent spot (366 nm UV light) on TLC (benzene/ethyl acetate 4 : 1). The crude products **3** (yield over 90%) are recrystallized from a suitable solvent (Table 1). The reaction mixture of **3g** is carefully acidified with diluted hydrochloric acid to avoid resolution of the product.

3-Amino-5-cyano-4,6-diarylphthalic Anhydrides 5; General Procedure:

A solution of the furan-3-carbonitrile **3** (5 mmol) and maleic anhydride (**4**; 4.9 g, 50 mmol) in dimethyl sulfoxide (20 ml) is allowed to stand 24 h at room temperature and then poured into cold water (200 ml). The precipitate is collected, washed with water, dried, and recrystallized from benzene. An analytical sample is prepared by sublimation at 0.05 torr (Table 2).

Table 1. 5-Amino-3-cyano-2,4-diarylfurans **3a–j**

Product No.	R^1	R^2	Yield [%]	m.p. [°C] (solvent)	Molecular formula[a]	I.R. (KBr) ν [cm^{-1}]	^{1}H-N.M.R. (DMSO-d_6) δ [ppm]	U.V. (C_2H_5OH) λ_{max} [nm] (logε) adsorption	fluorescence
3a[b]	C_6H_5	C_6H_5	63	108–110° (C_2H_5OH)	$C_{17}H_{12}N_2O$ (260.3)	3460, 3370, 2220, 1630	—	362 (4.3)	454
3b	4-Cl—C_6H_4	C_6H_5	75	133–135° (CH_3CN)	$C_{17}H_{11}ClN_2O$ (294.7)	3450, 3360, 2230, 1630	—	362 (4.1)	452
3c	C_6H_5	4-Cl—C_6H_4	73	164–166° (CH_3CN)	$C_{17}H_{11}ClN_2O$ (294.7)	3450, 3360, 2230, 1630	—	370 (4.3)	465
3d	4-H_3CO—C_6H_4	C_6H_5	80	151–153° (CH_3CN)	$C_{18}H_{14}N_2O_2$ (290.3)	3440, 3360, 2220, 1630	—	364 (4.4)	472
3e	C_6H_5	4-H_3CO—C_6H_4	81	159–161° (C_2H_5OH)	$C_{18}H_{14}N_2O_2$ (290.3)	3460, 3340, 2220, 1630	3.73 (s, 3H); 6.20 (br s, 2H)[c]; 6.8–7.7 (m, 9H)	358 (4.3)	446
3f	2-Cl—C_6H_4	C_6H_5	54	102–104° (*n*-C_4H_9OH)	$C_{17}H_{11}ClNO_2$ (294.7)	3460, 3350, 2220, 1640	—	352 (4.2)	440
3g	C_6H_5	4-$(H_3C)_2N$—C_6H_4	70	164–166° (CH_3CN)	$C_{19}H_{17}N_3O$ (303.3)	3340, 3160, 2200, 1625	2.88 (s, 6H); 5.97 (br s, 2H)[c]; 6.5–7.5 (m, 9H)	—	—
3h	C_6H_5	4-H_3C—C_6H_4	70	126–127° (CH_3CN)	$C_{18}H_{14}N_2O$ (274.3)	3440, 3350, 2220, 1630	—	357 (4.2)	—
3i	piperonyl	C_6H_5	85	151–153° (CH_3CN)	$C_{18}H_{22}N_2O_3$ (304.3)	3420, 3330, 2240, 1630	6.05 (s, 2H); 6.35 (br s, 2H)[c]; 6.9–7.9 (m, 8H)	363 (4.2)	475
3j	4-H_3CO—C_6H_4	4-H_3CO—C_6H_4	80	151–153° (CH_3CN)	$C_{19}H_{16}N_2O_3$ (320.3)	3450, 3320, 2230, 1640	3.68 (s, 3H); 3.70 (s, 3H); 5.98 (br s, 2H)[c]; 6.8–7.6 (m, 8H)	358 (4.2)	470

[a] Satisfactory microanalyses obtained: C ±0.28, H ±0.32, N ±0.28, Cl ±0.28.

[b] M.S.: *m/e* (relative intensity) = 261 (20); 260 (M^+, 100); 231 (11); 216 (11); 105 (14); 77 (13).

[c] Exchangeable.

Table 2. 3-Amino-5-cyano-4,6-diarylphthalic Anhydrides **5**

Product No.	R^1	R^2	Yield [%]	m.p. [°C]	Molecular formula[a]	I.R. (KBr) ν [cm^{-1}]	^{1}H-N.M.R. (DMSO-d_6) δ [ppm]
5a	C_6H_5	C_6H_5	45	260–261°	$C_{21}H_{12}N_2O_3$ (340.3)	3490, 3380, 2230, 1825, 1755, 1630	—
5b	4-Cl—C_6H_4	C_6H_5	60	274–275°	$C_{21}H_{11}ClN_2O_3$ (374.8)	3490, 3380, 2230, 1825, 1755, 1630	6.31 (br s, 2H)[b]; 7.2–7.6 (m, 9H)
5d	4-H_3CO—C_6H_4	C_6H_5	45	205–206°	$C_{22}H_{14}N_2O_4$ (370.4)	3490, 3370, 2240, 1830, 1760, 1620	3.73 (s, 3H); 6.16 (br s, 2H)[b]; 6.8–7.4 (m, 9H)
5f	2-Cl—C_6H_4	C_6H_5	50	184–185°	$C_{21}H_{11}ClN_2O_3$ (374.8)	3450, 3340, 2230, 1830, 1760, 1625	—
5h	C_6H_5	4-H_3C—C_6H_4	47	194–195°	$C_{22}H_{14}N_2O_3$ (354.4)	3490, 3380, 2230, 1825, 1750, 1625	2.31 (s, 3H); 6.13 (br s, 2H)[b]; 7.0–7.5 (m, 9H)
5j	4-H_3CO—C_6H_4	4-H_3CO—C_6H_4	65	246–248°	$C_{23}H_{16}N_2O_5$ (400.4)	3460, 3360, 2230, 1820, 1750, 1625	—

[a] Satisfactory microanalyses obtained: C ±0.30, H ±0.16, N ±0.30, Cl ±0.29.

[b] Exchangeable.

Received: November 4, 1981
(Revised form: January 18, 1982)

---

* Author to whom correspondence should be addressed.

[1] Part 27 of the series: Synthesis of Heterocyclic Compounds.

[2] A. P. Dunlop, F. N. Peters, *The Furans*, Reinhold, New York, 1953, p. 183.

[3] G. Westoo, *Acta Chem. Scand.* **13**, 692 (1959).

[4] F. Korte, K. Trautner, *Chem. Ber.* **95**, 307 (1962).

[5] T. I. Temnikova, R. N. Kovalevskaya, *Zh. Org. Khim.* **1**, 612 (1965); *C. A.* **63**, 2994 (1965).

[6] T. I. Temnikova, Yu. A. Sharanin, *Zh. Org. Khim.* **2**, 2018 (1966); *C. A.* **66**, 75474 (1967).

[7] T. I. Temnikova, Yu. A. Sharanin, V. S. Karavan, *Zh. Org. Khim.* **3**, 681 (1967); *C. A.* **67**, 43778 (1967).

[8] J. F. Blount, D. L. Coffen, D. A. Katonak, *J. Org. Chem.* **43**, 3821 (1978).

[9] K. Gewald, *Chem. Ber.* **99**, 1002 (1966).

[10] T. Hayashi, M. Kagawa, *Bull. Chem. Soc. Jpn.* **43**, 3290 (1970); *C. A.* **74**, 125304 (1971).

[11] J. W. Ducker, M. P. Gunter, *Aust. J. Chem.* **27**, 2229 (1974).

[12] M. Quinteiro, C. Seoane, J. L. Soto, *Tetrahedron Lett.* **1977**, 1835.

[13] M. Quinteiro, C. Seoane, J. L. Soto, *J. Heterocyclic Chem.* **15**, 57 (1978).

[14] H. Kauffmann, *Ber. Dtsch. Chem. Ges.* **50**, 515 (1917).

[15] D. A. Drapkina, V. D. Brudz, B. M. Bolotin, *Tr. Vses. Nauchno-Issled Inst. Khim. Reakt. Osobo Chist. Khim. Veshchestv* **30**, 333 (1967); *C. A.* **69**, 6727 (1968).

[16] M. Quinteiro, C. Seoane, J. L. Soto, *An. Quim.* **74**, 678 (1978).

[17] A. S. Onishchenko, *Diene Synthesis*, Israel Program for Scientific Translations, Jerusalem, 1964, p. 556–566.

[18] Ya. L. Danyushevskii, M. A. Marakatkina, Ya. L. Gol'dfarb, *Zh. Org. Khim.* **4**, 474 (1968); *C. A.* **68**, 114225 (1968).

[19] C. J. Eby, Ch. R. Hauser, *J. Am. Chem. Soc.* **79**, 723 (1957).