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SYNTHESIS OF 1-(1-AROYL-2-ARYLVINYL)-2-DICYANOMETHYLEN-1,2-DIHYDROPYRIDINES FROM 2-CHLOROPYRIDINIUM SALTS AND UNSATURATED NITRILES

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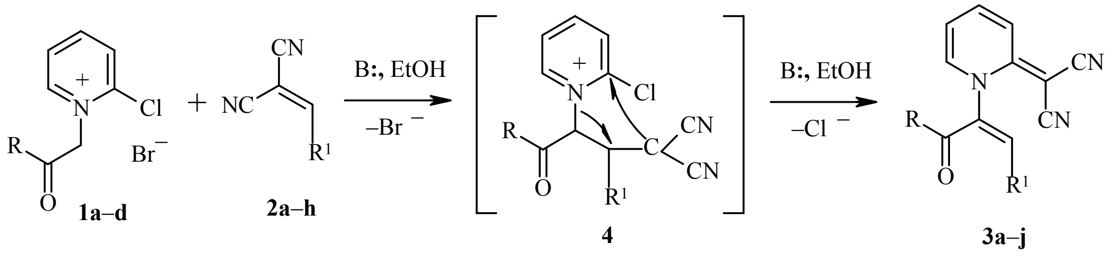
1-(1-Aroyl-2-arylvinyl)-2-dicyanomethylene-1,2-dihydropyridines are formed from 1-(aroylmethyl)-2-chloropyridinium bromides and arylmethylenemalonitriles in ethanol at room temperature in the presence of a twofold excess of triethylamine. The products are converted into 2-amino-3-aroyl-1-cyanoindolizines on boiling in acetic acid.

Keywords: 1-(aroylmethyl)-2-chloropyridinium bromides, reactions with arylmethyleneindolonitriles, 1-(1-aroyl-2-arylvinyl)-2-dicyanomethylene-1,2-dihydropyridines.

In a continuation of investigations, which are aimed at simple methods for the synthesis of 2-dicyanomethylenepyridines [1, 2], it was found that 1-(aroylmethyl)-2-chloropyridinium bromides **1a-d** reacted with arylmethylenemalononitriles **2a-h** in the presence of a twofold excess of a tertiary base to give 1-(1-aroyl-2-arylvinyl)-2-dicyanomethylene-1,2-dihydropyridines **3a-j** [3] (Table 1). The reactions occur under mild conditions, probably via intermediate **4**. The structures of compounds **3a-j** have been confirmed by IR and ^{1}H NMR spectroscopy (Table 2).



1a–d **2a–h** **4** **3a–j**

1 a R = C_6H_5, **b** R = 4-BrC_6H_4, **c** R = 4-ClC_6H_4, **d** 2-thienyl; **2 a** R^1 = 4-$CH_3OC_6H_4$, **b** R^1 = 3-FC_6H_4, **c** R^1 = 4-FC_6H_4, **d** R^1 = 3,4-$(CH_3O)_2C_6H_3$, **e** R^1 = 2,4-$(C_2H_5O)_2C_6H_3$, **f** R^1 = 2-ClC_6H_4, **g** R^1 = 2-furyl, **h** R^1 = C_6H_5; **3 a** R = C_6H_5, R^1 = 4-$CH_3OC_6H_4$, **b** R = C_6H_5, R^1 = 3-FC_6H_4, **c** R = C_6H_5, R^1 = 4-FC_6H_4, **d** R = C_6H_5, R^1 = 3,4-$(CH_3O)_2C_6H_3$, **e** R = C_6H_5, R^1 = 2,4-$(C_2H_5O)_2C_6H_3$, **f** R = C_6H_5, R^1 = 2-ClC_6H_4, **g** R = 4-BrC_6H_4, R^1 = 4-FC_6H_4, **h** R = 4-BrC_6H_4, R^1 = 2-furyl, **i** R = 4-ClC_6H_4, R^1 = 2-furyl, **j** R = 2-thienyl, R^1 = C_6H_5; B = Et_3N

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TABLE 1. Characteristics of Compounds **3a-j**

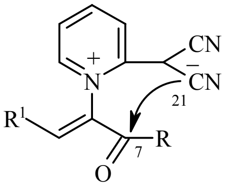
Compound	Empirical formula	Found, % Calculated, %			mp, °C (recrystallisation solvent)	Yield, %
		C	H	N		
3a	$C_{24}H_{17}N_3O_2$	76.01 75.97	4.48 4.52	11.11 11.08	146-148 (EtOH)	88
3b	$C_{23}H_{14}FN_3O$	75.22 75.19	3.87 3.84	11.41 11.44	184-186 (EtOH)	87
3c	$C_{23}H_{14}FN_3O$	75.23 75.19	3.82 3.84	11.46 11.44	126-128 (EtOH)	89
3d	$C_{25}H_{19}N_3O_3$	73.31 73.34	4.71 4.68	10.29 10.26	222-224 (EtOH)	73
3e	$C_{27}H_{23}N_3O_3$	74.09 74.12	5.31 5.30	9.64 9.60	150-152 (BuOH)	74
3f	$C_{23}H_{14}ClN_3O$	71.93 71.97	3.63 3.68	10.99 10.95	189-191 (EtOH)	59
3g	$C_{23}H_{13}BrFN_3O$	61.94 61.90	2.98 2.94	9.39 9.42	208-209 (BuOH)	64
3h	$C_{21}H_{12}BrN_3O_2$	60.35 60.31	2.93 2.89	10.08 10.05	240-242	83
3i	$C_{21}H_{12}ClN_3O_2$	67.52 67.48	3.21 3.24	11.27 11.24	261-262 (dec.)	77
3j	$C_{21}H_{13}N_3OS$	71.01 70.97	3.72 3.69	11.79 11.82	138-140 (EtOH)	82

In addition the molecular structure of 1-[1-benzoyl-2-(2-furyl)vinyl]-2-dicyanomethylene-1,2-dihydropyridine was investigated by X-ray crystallography [4].

TABLE 2. IR and ^{1}H NMR Spectroscopic Data for Compounds **3a-j**

Compound	IR spectrum, ν, cm^{-1}			^{1}H NMR spectrum, δ, ppm
	C≡N	C=O	C=C	
3a	2157, 2180	1633	1620	3.80 (3H, s, OCH_3); 6.94 (1H, s, 4-H); 7.02-8.18 (13H, m, 3-, 5-, 6-H, C_6H_4, C_6H_5,CH)
3b	2155, 2186	1653	1624	6.85-8.07 (13H, m, Py, C_6H_5, C_6H_4); 8.20 (1H, s, CH)
3c	2154, 2184	1649	1621	6.96 (1H, t, 4-H); 7.13-8.10 (13H, m, 3-, 5-, 6-H, C_6H_4, C_6H_5); 17 (1H, s, CH)
3d	2162, 2186	1652	1623	3.58 (3H, s, OCH_3); 3.81 (3H, s, OCH_3); 6.71-8.05 (12H, m, Py, C_6H_5, C_6H_3); 7.79 (1H, s, CH)
3e	2160, 2168 2185, 2195	1650	1622	1.26 (6H, t, $(CH_3)_2$); 4.08 (4H, dd, $(OCH_2)_2$); 6.64 (2H, d, C_6H_2); 6.98 (1H, t, 4-H); 7.33-7.98 (9H, m, 3-, 5-, 6-H, C_6H_1, C_6H_5); 8.25 (1H, s, CH)
3f	2152, 2180	1656	1620	6.90 (1H, t, 4-H); 6.93-8.12 (13H, m, 3-, 5-, 6-H, C_6H_4, C_6H_5, CH)
3g	2154, 2182	1654	1622	6.98 (1H, t, 4-H); 7.31-7.98 (12H, m, 3-, 5-, 6-H, C_6H_4, C_6H_4, CH)
3h	2158, 2187	1651	1624	6.74 (1H, dd, C_4H_3O); 6.92 (1H, t, 4-H); 7.17 (1H, d, C_4H_3O); 7.35 (1H, d, C_4H_3O); 7.73-7.92 (8H, m, 3-, 5-, 6-H, C_6H_4, CH)
3i	2152, 2179	1648	1620	6.72 (1H, dd, C_4H_3O); 6.94 (1H, t, 4-H); 7.15 (1H, d, C_4H_3O); 7.35 (1H, d, C_4H_3O); 7.75-8.01 (7H, m, 3-, 5-, 6-H, C_6H_4); 8.23 (1H, s, CH)
3j	2162, 2192	1656	1624	6.72-7.00 (4H, m, 4-H, C_4H_3S); 7.20-8.10 (8H, m, 5-, 6-, C_6H_5, CH); 8.20 (1H, d, 3-H)

The considerable decrease in the vibration frequencies of the cyano groups to 2152-2195 cm^{-1} in the IR spectra and the increase intensities in comparison with 2(1H)-dicyanomethylenepyrimidines (quinolines) [1, 5] indicate that the bipolar resonance form **5** contributes to the structure of compounds **3**.



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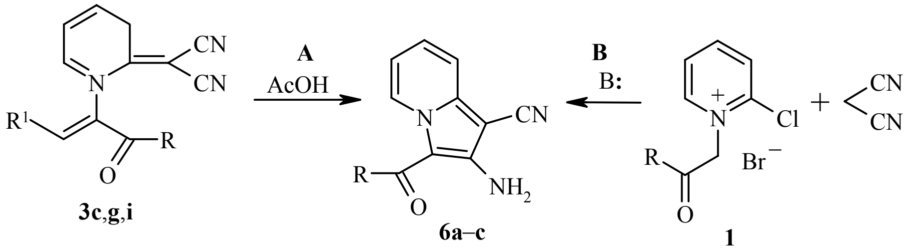
The decrease in the frequencies of the keto groups to 1633-1656 cm^{-1} [6] indicates a large amount of conjugation in the α,β-unsaturated ketone unit. In the ^{1}H NMR spectra the olefinic proton is shifted to low field at 7.67-8.03 ppm which also confirmed conjugation of the double bond and the keto group. On the whole the ^{1}H NMR spectra are not in contradictory with suggested structure **3**, however the basic part of signals were overlapped by the resonances of the aromatic protons at 6.71-8.21 ppm.

It was predicted with high probability on the basis of the X-ray crystallographic results (an enforced short nonbonding intramolecular contact C(7)···C(21) [2.797(4) Å] [4]) and spectroscopic studies (redistribution of the electron density in molecules **3**) that compounds **3** would undergo further cyclisation to the indolizines **6**. In fact when compounds **3c,g,i** were boiled for a short time in acetic acid they gave 2-amino-3-aroyl-1-cyanoindolizines **6a-c** (route **A**) (in small yields because of insufficient solubility). The ^{1}H NMR spectra and characteristics of these compounds are given in Table 3.



B = Et$_3$N

TABLE 3. Characteristics and ^{1}H NMR Spectra of Compounds **6a-c**

Compound	Empirical formula	Found, % / Calculated, % C	H	N	mp, °C (ethanol)	^{1}H NMR spectrum, δ, ppm	Yield, % A/B
6a	$C_{16}H_{11}N_3O$	73.58 73.55	4.22 4.24	16.04 16.08	161-163	5.66 (2H, br. s, NH$_2$); 6.98 (1H, m, 7-H); 7.50 (2H, dd, 5-, 6-H); 7.58 (5H, s, C$_6$H$_5$); 9.16 (1H, d, 8-H)	32/90
6b	$C_{16}H_{10}BrN_3O$	56.52 56.49	2.99 2.96	12.33 12.35	192-194	5.92 (2H, br. s, NH$_2$); 7.00 (1H, m, 7-H); 7.55 (2H, dd, 5-, 6-H); 7.68 (4H, dd, C$_6$H$_4$); 9.17 (1H, d, 8-H)	43/94
6c	$C_{16}H_{10}ClN_3O$	65.01 64.98	3.44 3.41	14.17 14.21	199-201	5.88 (2H, br. s, NH$_2$); 6.97 (1H, dt, 7-H); 7.48 (2H, dd, 5-, 6-H); 7.60 (4H, s, C$_6$H$_4$); 9.14 (1H, d, 8-H)	41/96

The indolizines **6a-c** were also obtained by direct synthesis from the pyridinium salts **1a-c** and malonodinitrile (route **B**) [7].

EXPERIMENTAL

IR spectra of nujol mulls were recorded with an IKS-29. ^{1}H NMR spectra were recorded with a Bruker WP-100 SY (100.13 MHz, internal standard TMS). Commercial DMSO-d_6 was used as solvent without further purification. Purity of the products was monitored by TLC (Silufol UV-254, 3:5 acetone–hexane).

1-(1-Aroyl-2-arylvinyl)-2-dicyanomethylene-1,2-dihydropyridines (3a-j). Triethylamine (0.7 ml, 5.0 mmol) was added with stirring to a suspension of a salt **1** (2.5 mmol) and an unsaturated nitrile **2** (2.5 mmol) in ethanol (15-20 ml). The mixture was stirred for 3 h at 20°C. The precipitate was filtered off and washed with ethanol and hexane. Where necessary it was recrystallized from a suitable solvent. Characteristics of the products are cited in Tables 1 and 2.

2-Amino-3-aroyl-1-cyanoindolizines (6a-c). A. A solution of a 1,2-dihydropyridine **3** (1.0 mmol) in acetic acid (5 ml) was boiled for 5 min and kept for 1 day at 20°C. The precipitate was filtered off and washed with ethanol and hexane.

B. Triethylamine (1.4 ml, 10.0 mmol) was added to a suspension of a salt **1** (5.0 mmol) and malononitrile (0.4 g, 6.0 mmol) in ethanol (15 ml). The mixture was stirred at 20°C for 1 h, then kept for 1 day in a refrigerator. The precipitate was filtered off, washed with ethanol and hexane, and recrystallized from ethanol. Characteristics of the compounds obtained are cited in Table 3.

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