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INTRAMOLECULAR CYCLIZATION OF 5-ARYL-3-ARYLAMINO-4-BENZOYL-1H-3-PYRROLIN-2-ONES TO PYRROLO[3,4-*b*]QUINOLINES

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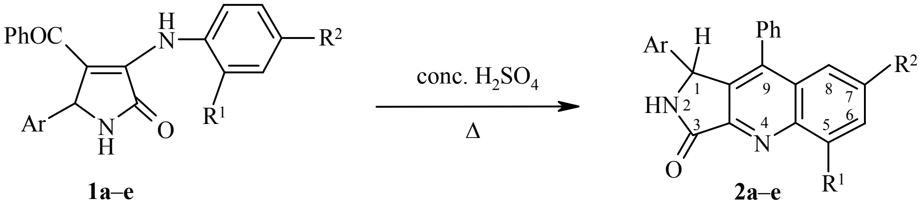
It has been shown that 5-aryl-3-arylamino-4-benzoyl-1H-3-pyrrolin-2-ones cyclize in the presence of conc. H_2SO_4 to give pyrrolo[3,4-b]quinolines.

Keywords: 5-aryl-3-arylamino-4-benzoyl-1H-3-pyrrolin-2-ones, pyrrolo[3,4-*b*]quinolines.

3-Arylamino derivatives of 4-ethoxycarbonyl-3-pyrrolin-2-ones can undergo cyclization to a condensed pyrroloquinoline system [1-4].

In this connection it was of interest to investigate the possibility of a similar cyclization for the previously prepared 5-aryl-3-arylamino-4-benzoyl-1H-3-pyrrolin-2-ones (**1a,b,d,e**) [5] and also for the novel 5-(*p*-bromophenyl)-3-(*p*-methoxyphenyl)amino-4-benzoyl-1H-3-pyrrolin-2-one (**1c**).

We have shown that compounds **1a-e** undergo an intramolecular cyclization to the 1-aryl-(5,7)-R-9-phenylpyrrolo[3,4-*b*]quinolin-3-ones (**2a-e**) when heated for a short time and then held for a prolonged period at room temperature in conc. H_2SO_4 medium.



1a–e **2a–e**

1, **2** **a–c** R^1 = H, **d**, **e** R^1 = Me; **a** R^2 = Br, **b** R^2 = Me, **c** R^2 = OMe, **d**, **e** R^2 = H;
a, **b**, **d** Ar = Ph; **c**, **e** Ar = 4-BrC_6H_4

The intramolecular cyclization observed apparently occurs by an electrophilic substitution mechanism where the sulphuric acid aids the formation of electrophilic species which protonate the carbonyl group of the benzoyl fragment.

Compounds **2a-e** are colorless, crystalline materials with a high melting point and are readily soluble in DMSO and DMF (Table 1).

Their ^1H NMR spectra show the presence of the singlet for the methine proton of the pyrrole ring at 5.75-5.80 ppm, a multiplet centered at 7.2-7.5 ppm for the aromatic protons, and also a singlet for the NH group proton of the pyrrole fragment at 9.45-9.60 ppm. The signal for the second NH group present in the ^1H NMR spectrum of the starting materials **1a-e** at 8.3-8.6 ppm is absent in the spectra of compounds **2a-e** and this supports the proposed structure (Table 2).

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TABLE 1. Characteristics of Compounds **2a-e**

Compound	Empirical formula	Found, % Calculated, %				mp, °C (solvent)	Yield, %
		C	H	N	Br		
2a	$C_{23}H_{15}BrN_2O$	66.56 66.52	3.65 3.62	6.77 6.75	19.29 19.26	300-302 (1-butanol)	61.0
2b	$C_{24}H_{18}N_2O$	82.33 82.29	5.12 5.14	8.04 8.00		282-284 (ethanol)	91.4
2c	$C_{24}H_{17}BrN_2O_2$	64.78 64.73	3.80 3.82	6.25 6.29	17.93 17.96	286-288 (ethanol)	62.5
2d	$C_{24}H_{18}N_2O$	82.24 82.29	5.17 5.14	8.03 8.00		260-262 (ethanol)	82.9
2e	$C_{24}H_{17}BrN_2O$	67.09 67.15	3.91 3.96	6.56 6.54	18.65 18.63	279-281 (2-propanol)	60.5

TABLE 2. IR and ^{1}H NMR Spectra of Compounds **2a-e**

Compound	IR spectrum, ν, cm^{-1}		^{1}H NMR spectrum, δ, ppm			
	C=O	NH	H-4, s	Ar–H	NH, s	Other protons
2a	1714	3188	5.80	6.50 (1H, d, H); 7.05 (5H, m, C_6H_5); 7.50 (5H, m, C_6H_5); 7.65 (1H, s, H-8); 7.90 (1H, d, H-6)	9.60	
2b	1726	3216	5.75	7.20 (13H, m)	9.50	2.40 (3H, s, CH_3)
2c	1720	3208	5.75	7.65 (12H, m)	9.51	3.65 (3H, s, OCH_3)
2d	1708	3170	5.75	6.50-6.75 (3H, m, H-6,7,8); 7.05 (5H, m, C_6H_5); 7.50 (5H, m, C_6H_5)	9.45	2.90 (3H, s, CH_3)
2e	1710	3199	5.75	6.55 (3H, m, H-6,7,8); 7.30 (9H, m, C_6H_5, *n*-Br–C_6H_4)	9.50	2.90 (3H, s, CH_3)

The IR spectrum of compound **2e** shows the presence of a lactam carbonyl absorption band at 1710 and an NH group at 3199 cm^{-1}.

The mass spectrum of compound **2b** has a peak for the molecular ion at *m/z* (*I*, %) 350 (100) together with peaks for the fragment ions: 273 $[M-C_6H_5]^+$ (80), 245 $[M-C_6H_5-CO]^+$ (30), and 70 (30).

The mass spectrum of compound **2a** shows a peak for the molecular ion with *m/z* 414-416 (20) which is in agreement with the structure proposed.

EXPERIMENTAL

^{1}H NMR spectra were recorded on Bruker AM-300 (300 MHz) and NR-60 (60 MHz) spectrometers using DMSO-d_6 and HMDS internal standard (δ 0.05 ppm). IR spectra were recorded in vaseline oil on a UR-20 spectrometer. Mass spectra were taken on an MX-1320 instrument with an electron ionizing energy of 70 eV. The purity and identification of the compounds were determined by TLC on Silufol-254 plates in the system benzene–acetone–hexane (3:1:1) and revealed using iodine vapor.

5-Aryl-3-arylamino-4-benzoyl-3-hydroxy-1H-3-pyrrolin-2-ones (1a,b,d,e) were prepared as described in [5].

5-(*p*-Bromophenyl)-3-(*p*-methoxyphenyl)amino-4-benzoyl-1H-3-pyrrolin-2-one (1c) was prepared using the same method [5]. Yield 40.5%; mp 165-167°C (xylene–hexane, 2:1). IR spectrum, ν, cm^{-1}: 1724 (C=O), 3312 (NH). ^1H NMR spectrum, δ, ppm: 3.75 (3H, s, OCH_3); 5.76 (1H, s, H-5); 7.42 (13H, m, Ar); 8.29 (H, s, NH); 9.56 (1H, s, NH,). Found, %: C 62.18; H 4.03; Br 17.32; N 6.1. $C_{24}H_{19}BrN_2O_3$. Calculated, %: C 62.22; H 4.10; Br 17.26; N 6.05.

1-Aryl-(5,7)-R-9-phenylpyrrolo[3,4-*b*]quinolin-3-ones 2a-e. A solution of compound **1** (1 mmol) in conc. H_2SO_4 (5 ml) was heated for 10-15 min until the color had changed from reddish to greenish-brown. The reaction mixture was then poured into cold water (200 ml) and the precipitate was filtered off, washed on the filter with dilute sodium carbonate solution and then water, dried, and recrystallized.

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