One-Step Synthesis of 4-Cyano-3,3-diaryl-5-methyl-2-oxo-2,3-dihydropyrroles through the Benzilic Acid Rearrangement

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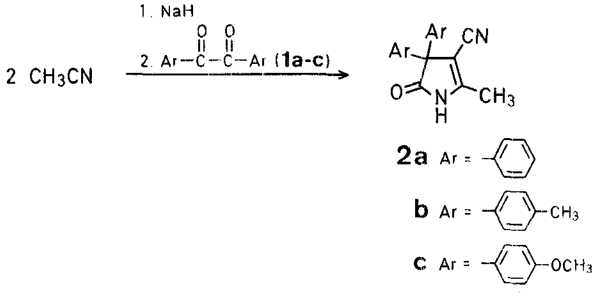
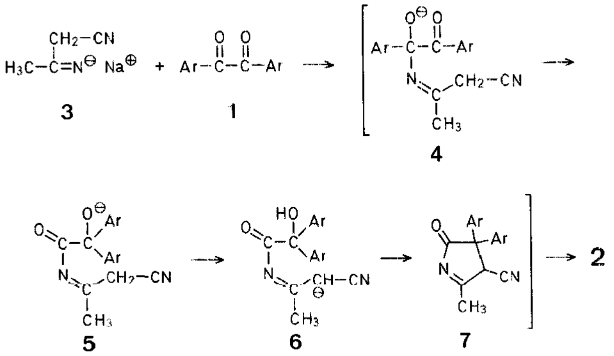
In the course of our studies on phase transfer-catalyzed reactions and their use for the synthesis of heterocycles, we have found that sodio-3-iminobutanenitrile (3), derived from acetonitrile on treatment with sodium hydride, is a useful reagent for the synthesis of 2-oxo-dihydropyrroles. We report here the convenient, one-step synthesis of 4-cyano-3,3-diaryl-5-methyl-2-oxo-2,3-dihydropyrroles 2 by the reaction of benzils 1 with acetonitrile in the presence of sodium hydride through the benzilic acid rearrangement. Although a number of investigations[1] have been made concerning the preparation of 2-oxo-2,3-dihydropyrroles, syntheses starting from these compounds have not yet been reported.



Structural elucidation of 2 was accomplished on the basis of spectral data and microanalysis. In the I.R. spectrum of 2a, the absorption at $\nu = \sim 1720$ cm^{-1} could be assigned to the carbonyl group of the unsaturated five membered lactam ring. In agreement with this observation, the ^{13}C-N.M.R. spectrum showed signals at $\delta = 177.7$ ppm (C=O), 127.5 and 92.5 (C=C), 116.0 (C≡N), 63.2 (>C<), 13.6 ppm (CH$_3$) as well as the typical peaks of two symmetrical phenyl groups. The ^{1}H-N.M.R. spectrum confirmed this structure by signals at $\delta = 2.26$ (s, 3H, CH$_3$), 7.28 (m, 10H$_{arom}$), and 9.30 ppm (br s, 1H, NH).

Although we have not undertaken a detailed investigation of the reaction mechanism, a possible pathway accounting for the formation of 2 is shown below. In this reaction, sodio-3-iminobutanenitrile[2] (3) was generated from acetonitrile by treatment with sodium hydride and reacted with an excess of benzil 1a-c. The intermediate 4 was cyclized into corresponding unsaturated pyrrolidinone derivative 2 via rearrangement of a phenyl group to the neighbouring carbonyl carbon atom.



The best known reaction of benzils with a nucleophile is that with hydroxide ion in which rearrangement occurs giving the conjugated base of benzilic acid[3]. However, phenoxide ion[4] failed to react with benzils in alcohol or benzene solution: presumably owing to the insufficient basicity on the part of the nucleophile. Furthermore, it was recently reported that condensation of benzils with 3-amino-2,4-dicyanocrotonic ester and the dimer of ethyl cyanoacetate gave 2-(cyanoethoxycarbonylmethylene)-4,5-diaryl-5-hydroxy-2,5-dihydropyrrole[5].

Although the benzilic acid-type rearrangement does not occur here, when treated with aqueous alkali the latter product rearranged to the pyrrolidinone[5]. Therefore, it was noticed that the intermediate 4, formed by attack of nucleophile to benzil, could readily undergo a benzilic acid-type rearrangement. Furthermore, this reaction offered a simple and convenient preparation of pyrrolidinone derivatives since the starting materials are readily accessible[6]. An interesting comparison can be made between 1 and butanedione (biacetyl). Although 1 reacts readily with 2, the reaction of biacetyl gives no detectable product even after several hours. We also investigated the effect of 18-crown-6 on the above reaction. The results were usually quite similar, although slightly superior results were sometimes obtained.

4-Cyano-3,3-diphenyl-5-methyl-2-oxo-2,3-dihydropyrroles 2a; Typical Procedure:

To acetonitrile (70 ml) is added sodium hydride (0.48 g) as a 50% dispersion in oil and the mixture is stirred for 2 h at 80 °C. After all of the sodium hydride has dissolved, benzil (1a; 2.1 g, 0.01 mol) in acetonitrile (30 ml) is added dropwise, then the mixture is stirred for a further 2 h. The resulting mixture is poured into water (200 ml). The aqueous fraction is acidified with dilute hydrochloric acid (~ 10 ml), and the precipitated solid is isolated by filtration. Recrystallization of the solid from ethanol gives 2a; yield: 1.86 g (68%); m.p. 259–261 °C.

$C_{18}H_{14}N_2O$	calc.	C 78.81	H 5.14	N 10.21
(274.3)	found	78.81	5.12	10.36

M.S. (70 eV): $m/e = 274$ (M$^+$), 259 (M−CH$_3$).

I.R. (KBr): $\nu = 3240$, 2200, 1720, 1640, 1600, 1500 cm^{-1}.

^{1}H-N.M.R. (CDCl$_3$): $\delta = 2.26$ (s, 3H, CH$_3$); 7.3 (m, 10H$_{arom}$); 9.30 ppm (s, 1H, NH).

^{13}C-NMR (DMSO-d_6): $\delta = 177.7$; 156.8; 139.3; 128.7; 127.6; 127.5; 116.0; 92.5; 63.2; 13.6 ppm.

4-Cyano-3,3-bis[4-methylphenyl]-5-methyl-2-oxo-2,3-dihydropyrrole (2b) is prepared similarly; yield: 51%; m.p. 244–246 °C.

$C_{20}H_{18}N_2O$	calc.	C 79.44	H 6.00	N 9.27
(302.4)	found	79.44	6.01	9.27

M.S. (70 eV): $m/e = 302$ (M$^+$), 287 (M−CH$_3$).

I.R. (KBr): $\nu = 3240$, 2190, 1720, 1638, 1600, 1500 cm^{-1}.

^{1}H-N.M.R. (CDCl$_3$): $\delta = 2.19$ (s, 6H, CH$_3$); 2.30 (s, 3H, CH$_3$); 7.14 (s, 8H$_{arom}$); 9.14 ppm (s, 1H, NH).

^{13}C-N.M.R. (DMSO-d_6): $\delta = 178.1$; 156.2; 137.1; 136.6; 129.3; 127.6; 116.2; 92.9; 62.8; 20.5; 13.6 ppm.

4-Cyano-3,3-bis[4-methoxyphenyl]-5-methyl-2-oxo-2,3-dihydropyrrole (2c) is prepared similarly; yield: 45%; m.p. 178–180 °C.

$C_{20}H_{18}N_2O_3$	calc.	C 71.84	H 5.43	N 8.38
(334.4)	found	71.73	5.60	8.42

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M.S. (70 eV): $m/e = 334$ (M^{+}), 319 ($M - CH_3$).

I.R. (KBr): $\nu = 3240, 2190, 1720, 1640, 1600, 1500$ cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$): $\delta = 2.18$ (s, 3H, CH_3); 3.26 (s, 6H, OCH_3); 7.00 (q, 8H_{arom}); 9.40 ppm (s, 1H, NH).

^{13}C-N.M.R. (DMSO-d_6): $\delta = 178.4$; 158.75; 156.1; 131.4; 128.8; 116.3; 114.1; 93.1; 62.0; 55.1; 13.6 ppm.

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