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OF N-AMINOPYRIDINES**

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21

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# NITRILES IN HETEROCYCLIC SYNTHESIS A NEW SYNTHESIS OF N-AMINOPYRIDINES

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## ABSTRACT

A novel synthesis of N-Phenyl aminopyridone via the reaction of cyanoacetphenylhydrazide and ylidene malononitrile is reported.

In the last few years we have been interested in development of new procedures for synthesis of polyfunctionally substituted azoles and azines of potential synthetic and biological interest [1-3]. In continuation of this work we investigated the reactivity of cyanoacetphenylhydrazide I with some cinnamonitrile derivatives. Soto et al [4] have recently reported that the reaction of benzylidene cinnamonitrile 2 b with cyanoacethydrazide affords N-aminopyridine derivative, formed via Michael addition, cyclization and oxidation of the formed hydroxyridine derivative.

Now it has been found that I reacts with 2a to yield 1:1 adduct. Two structures seemed possible for this product (C.F. structures 3 and 4).

Although structure 3 seemed more logical based on analogy to previously reported behaviour of 2b and cyanoacethydrazide, [4] <sup>1</sup>HNMR spectrum of the product revealed the absence of pyridine H-3 and H-4 protons. Thus structure 3 was ruled for this product. Structure 4a could be established for the reaction product based on <sup>13</sup>CNMR which revealed only one CN signal in <sup>1</sup>HNMR and a signal at  $\delta$  138 for ylidene CH as it showed.

Similar to the behaviour of I towards 2a, compound I reacted with 2b and 2 c to yield 1:1 adducts for which structure 4b and 4c was established based on spectral data.

The behaviour of I towards 2a-c is similar to the recently reported behaviour of 2a-c towards cyanoacetamide[5] and cyanothioacetamide[6] and is in contrast to the reported behaviour of 2 b towards cyanoacetyl-drazide[4].

In contrast to the behaviour of I towards 2a-c, compound 2d-f reacted with I to yield the ylidene derivatives 5a-c. The formation of 5 from the reaction of I with 2 d-f is assumed to proceed via addition of I to the activated double bond in 2d-f and subsequent elimination of ethyl cyanoacetate. Similar proposal have recently been made to account for ylidene group exchange on treatment of 2a-f with a variety of active methylene reagents[7,8].

All compounds were obtained in good yield, thus a new simple approach for the synthesis of otherwise difficult obtainable 4 and 5 derivatives is now available.

### EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded (KBr) on a Pye Unicam SP-1000 spectrophotometer. <sup>1</sup>HNMR spectra were obtained in (C D<sub>3</sub>)<sub>2</sub>SO with a varian A-60 spectrometer with SiMe<sub>4</sub> as internal standard and chemical shifts are expressed as δ values. Micro-analytical Data Unit at Cairo University. The experimental C, H, N values agreed well with the molecular formulas given bellow. Reaction of I with 2a-F:

Reaction of I (0.01 mol) in ethanol (50 ml) was treated with 2a-F (0.01 mol) and triethylamine (0.5 ml). The reaction mixture was refluxed for 2 h and then evaporated in vacuo. The remaining solid product was collected by filtration and crystallised from the proper solvent.

Compound 4a was crystallised from acetone; m.p. 265 °c; yield 75 %. IR: 3490, 3280, 3200 (NH<sub>2</sub> and NH); 2220 (CN); 1680 (ring CO) and 1620 (C=N).

<sup>1</sup>HNMR: 3.55 (δ, 3H, OCH<sub>3</sub>); 3.8 (S, 2H, NH<sub>2</sub>); 6.8 - 7.85 (m, 11H, 2C<sub>6</sub>H<sub>5</sub> and ylidene CH); 11.0 and 12.4 two signals 2NH and NHPh). <sup>13</sup>CNMR: 186.09 C-6; 164.37 C-2; 145.38 C-aromatic; 142.76 C-8; (138.28, 130.25, 130.20, 130.02, 127.98, 127.09, 126.87) aromatic carbons; 125.49 C-5; 113.61 aromatic carbon; 113.54 C-7; 103.76 C-4; 91.78 C-3; 59.57 OCH<sub>3</sub>. C-H Coupling 100 Hz.

C<sub>20</sub>H<sub>16</sub>N<sub>5</sub>O<sub>2</sub> (358) found C, 67.30; H, 4.5; N, 19.20 calcd C, 67.31; H, 4.47; N, 19.55.

Compound 4b was crystallised from dilute DMF; m.p. 294°C yield 80 %.

IR: 3100 – 3340 (NH<sub>2</sub> and NH); 2220 (CN); 1705 (C=O) and 1640 (C=N).

<sup>1</sup>HNMR: 3.85 (s, 3H, NH<sub>2</sub> and NH); 6.7–7.7 (m, 10H, 2C<sub>6</sub>H<sub>5</sub>); 8.55 (s, 1H, ylidene CH) and 9.1 (s, 1H, NHPH).

C<sub>19</sub>H<sub>15</sub>N<sub>5</sub>O (329) found C, 69.0; H, 4.20; N, 21.10 calcd C, 69.30; H, 4.55; N, 21.27.

Compound 4c was crystallised from DMF; m.p. > 300°C; yield 80 %.

IR: 3480, 3220 (NH<sub>2</sub> and NH); 2220 (CN); 1690 (C=O) and 1640 (C=N).

<sup>1</sup>HNMR: 3.6 (broad, 3H, NH and NH); 7.0–7.9 (m, 13 H, aromatic protons); 8.45 (s, 1H, ylidene CH) and 9.8 (s, H, NHPH).

C<sub>17</sub>H<sub>13</sub>N<sub>5</sub>O<sub>2</sub> (319) found C, 64.20; H, 4.10; N, 21.70 calcd C, 63.90; H, 4.07; N, 21.94.

Compound 5a was crystallised from ethanol, m.p. 224°C; yield 85 %.

<sup>1</sup>HNMR: 7.3–7.75 (m, 10 H); 8.0 (s, 1H, ylidene CH).

C<sub>16</sub>H<sub>13</sub>N<sub>3</sub>O (263) found C, 72.9; H, 4.70; N, 16.1 calcd C, 73.04; H, 4.94; N, 15.97.

Compound 5b was crystallised from ethanol m.p. > 300°C; yield 75 %.

IR: 3150 (NH); 2220 (CN); 1705 (C=O); and 1650 (C=C).

<sup>1</sup>HNMR: 4.65 (s, br, NH); 7.25–7.8 (m, 10 H); 8.2 (s, 1H, ylidene CH).

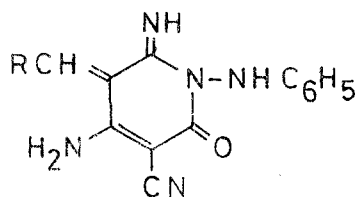
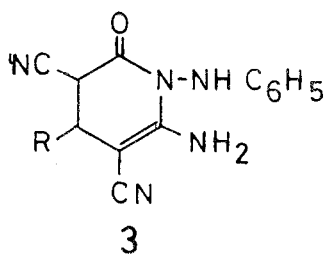
C<sub>16</sub>H<sub>12</sub>N<sub>3</sub>OCl (297) found C, 64.20; H, 4.0; Cl, 11.70 calcd C, 64.64; H, 4.04; Cl, 11.95.

Compound 5c was crystallised from ethanol m.p. 175°C; yield 80 %.

IR: 3150 (NH); 2215 (CN); 1705 (C=O).

<sup>1</sup>HNMR: 4.85 (s, br, NH); 7.35 – 8.6 (m, 11 H, aromatic and ylidene CH).

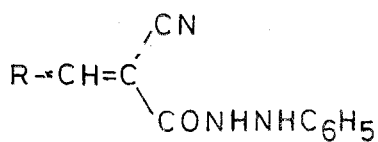
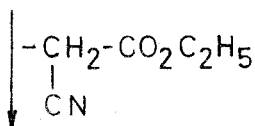
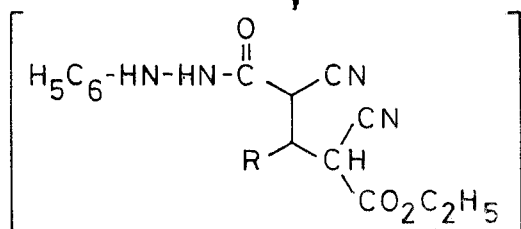
C<sub>16</sub>H<sub>12</sub>N<sub>4</sub>O<sub>3</sub> (308) found C, 62.0; H, 4.1; N, 18.3 calcd C, 62.13; H, 3.8; N, 18.18.



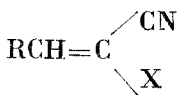
2 a - c

1

2 d - f



- 5 a, R = C<sub>6</sub>H<sub>5</sub>  
 b, R = C<sub>6</sub>H<sub>4</sub>Cl-p  
 c, R = C<sub>6</sub>H<sub>4</sub>NO<sub>2</sub>-m



1

2a, R=C<sub>6</sub>H<sub>4</sub>OCH<sub>3</sub>-P; X=CNb, R=C<sub>6</sub>H<sub>5</sub>; X=CN

c, R=Furyl; X=CN

d, R=C<sub>6</sub>H<sub>5</sub>; X=CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>e, R=C<sub>6</sub>H<sub>4</sub>Cl-P; X=CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>f, R=C<sub>6</sub>H<sub>4</sub>NO<sub>2</sub>-m; X=CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>

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