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# SYNTHESIS OF ARYL(OR BENZYL)-(Z)-*N*-[2-AMINO-1,2-DICYANOVINYL]FORMAMIDINES

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## ABSTRACT

Starting from readily available ethyl(Z)-N-(2-amino-1,2-dicyanovinyl)formimidate (1), the *N*-aryl (or benzyl)-N'(-(2-amino-1,2-dicyanovinyl)formamidines (2) can be prepared in good yields by reaction with aromatic amines at room temperature in the presence of a catalytic amount of aniline hydrochloride.

Amidines are an important class of compounds which have proved to be intermediates in a number of biological processes.<sup>[1–3]</sup> The chemistry and preparation of amidines have been reviewed by Shriner and Neumann.<sup>[4]</sup> Synthesis and characterization of several alkyl, aryl amidine and also the amidrazone have been reported previously.<sup>[5–7]</sup> We decided that we could

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prepared various aryl and benzyl amidines of type (2a-2d) by reaction of imidate (1) with aromatic amines.

In order to synthesis the required amidines (2a-2d), the following method, which involves treatment of imidate (1) with the appropriate aryl or benzyl amine, was used Sch. 1. Ethyl(Z)-*N*-(2-amino-1,2-dicyanovinyl)-formimidate (1) was prepared according to a previously reported procedure by treatment of equimolar quantities of triethylorthoformate and diamino-maleonitrile in refluxing dioxane.<sup>[6,8–9]</sup>

Having obtained the imidate (1) in good yield (94%) it was then treated with aryl or benzylamine in a 1:1 molar ratio in ethanol in the presence of a catalytic amount of aniline hydrochloride. The reaction mixture was stirred under an inert atmosphere at room temperature with the exclusion of light. A homogeneous solution was obtained and within 10 min a white solid precipitated out. The product was filtered off after 3–4 h. It was washed with diethyl ether and was found be pure by TLC, <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy.



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The elemental analysis results of amidine (2) were satisfactory. The mass spectrum showed a peak at m/z 260, 286, 272 and 242 for 2a, 2b, 2c and 2d, respectively. Initial fragmentation, involve loss of the amidine segment  $(M-C_5H_4N_5)^+$ . The <sup>1</sup>H NMR spectra of compound 2a and 2b in  $[{}^{2}H_{6}]$ dimethyl sulfoxide ( $[{}^{2}H_{6}]$ DMSO) had some interesting features. The two benzylic protons (H<sub>6</sub>) appeared as a doublet at  $\delta$  4.58 and  $\delta$ 4.68 ppm respectively, caused by a coupling to the NH proton which appeared as a broad doublet at  $\delta$  8.08–8.16 ppm. The HC=N proton was also a doublet (J<sub>H,NH</sub> 6.0–6.5 Hz), at  $\delta$  7.62–7.78 ppm and showed a small additional coupling (<1 Hz) to the benzylic protons. The fact that the HC=N and the benzylic protons are coupled to NH was also confirmed by D<sub>2</sub>O exchange, after which the two doublets (HC=N & CH<sub>2</sub>) appeared as sharp singlets. The <sup>13</sup>C NMR spectrum show two peaks of relatively low intensity at  $\delta$  118.8–120.1 and  $\delta$  119.9–121.4 ppm due to the two cyano groups and a peak due to HC=N at  $\delta$  149.0–154.5 ppm in the amidine molecule. The infrared spectrum of amidine (2a-2d) showed two strong absorption in the region 2195–2230 cm<sup>-1</sup> characteristic of CN stretching vibrations, together with an NH and a C=N stretching vibration at 3480-3120 and 1655-1640 cm<sup>-1</sup> respectively.



#### **EXPERIMENTAL**

The <sup>1</sup>H NMR spectra were recorded on Hitachi-Perkin-Elmer R24B (60 MHz) or Bruker XL 300 (300 MHz) instruments (with *J*-values given in Hz), <sup>13</sup>C NMR spectra (with DEPT 135) either on a Bruker WP80 or

MA.

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XL300 instrument, and IR spectra on a Shimadzu IR-435 spectrophotometer. Mass spectra were recorded on a Kratos Concept instrument. The melting points were measured on an Electrothermal digital melting point apparatus and are uncorrected.

General procedure for the preparation of the *N*-aryl-*N*'-[2-amino-1,2-dicyanovinyl]formamidines (2a-2d): The aromatic amine (1.01 g, 6.07 mmol) was added to a suspension of 1 (1.00 g, 6.09 mmol) in dry ethanol or ethyl acetate, which contained aniline hydrochloride (0.02). The mixture was stirred at room temperature until TLC (9:1 chloroform/ethanol eluant) showed that all the formimidate had disappeared (usually 3–4h) and the amidine was isolated by filtration. The most cases the product was pale green to white. The precipitate was washed with dry diethyl ether and was dried under vacuum to give the analytically pure products (2a–2d).

(2-Chlorobenzyl)-(Z)-*N*-[2-amino-1,2-dicyanovinyl]formamidine (2a): M.p. 108–110°C (decomp.). Yield 92%. [Found C, 55.5; H, 3.7; N, 27.3; Cl, 13.6. Calc. for C<sub>12</sub>H<sub>10</sub>N<sub>5</sub>Cl requires C, 55.6; H, 3.8; N, 27.0; Cl, 13.5%]; *m/z* (FAB) 260 (M + 1)<sup>+</sup> 65.5%, 259 (M)<sup>+</sup> 78%, 224 (M-Cl)<sup>+</sup> 18.2%, 165 [(M-1)-C<sub>4</sub>H<sub>3</sub>N<sub>3</sub>]<sup>+</sup> 100%, 164 (M-C<sub>4</sub>H<sub>4</sub>N<sub>3</sub>]<sup>+</sup> 90.8%, 142 (12.12%), 125 (81.8%), 119 (30.3%), 109 (9.0%);  $\delta_{\rm H}$  (300 MHz, d<sub>6</sub>-DMSO, TMS Int. Ref.) 4.58 (d, 2H, <sup>3</sup>J<sub>6,NH</sub> 6.5 Hz, H6), 6.80 (s, 2H, NH<sub>2</sub>), 7.40–7.44 (complex m, 2H, H11 & H12), 7.45–7.56 (complex m, 2H, H9 & H10), 7.78 (d, 1H, <sup>3</sup>J<sub>5,NH</sub> 6.5 Hz, H5), 8.16–8.24 (br.d, 1H, <sup>3</sup>J<sub>NH,5</sub> 6.5 Hz, NH) ppm;  $\delta_{\rm C}$  (75 MHz, d<sub>6</sub>-DMSO) 45.9 (C6), 110.0 (C1), 119.1 (C2), 120.1 (C3), 121.4 (C4), 131.2 (C11), 132.9 (C12), 133.0 (C10), 133.5 (C9), 136.6 (C8), 139.7 (C7), 154.5 (C5) ppm;  $\nu_{\rm max}$  (Nujol mull) 3420 s, 3380 s, 3320 s, 3180 m (NH str.), 3000 m, 2980 m, 2950 m, 2220 s (CN str.), 2200 s (CN str.), 1655 s (C=N str.), 1580 m (NH bend), 1470 m, 1460 s, 1450 s, 1430 m, 1380 s, 1360 s, 1260 s, 1235 w, 1220 w, 1170 m, 1060 s, 1040 s, 1015 s, 980 w, 950 s, 815 s, 790 m, 760 s cm<sup>-1</sup>.

(3,4-Dimethoxybenzyl)-(Z)-*N*-[2-amino-1,2-dicyanovinyl]formamidine (2b): M.p. 124–126°C (decomp.). Yield 94%. [Found C, 59.2; H, 5.5; N, 24.3. Calc. for  $C_{14}H_{15}N_5O_2$ : C, 58.9; H, 5.3; N, 24.6%]; *m*/*z* (EI) 286 (M + 1)<sup>+</sup> 3.2%, 245 [(M + 1)-CH<sub>2</sub>N<sub>2</sub>]<sup>+</sup> 1.8%, 168 [(M + 1)-C<sub>5</sub>H<sub>2</sub>N<sub>4</sub>]<sup>+</sup> 9.8%, 151 (M-C<sub>5</sub>H<sub>4</sub>N<sub>5</sub>)<sup>+</sup> 100%;  $\delta_{\rm H}$  (300 MHz, d<sub>6</sub>-DMSO) 3.95 (s, 3H, OCH<sub>3</sub>), 3.97 (s, 3H, OCH<sub>3</sub>), 4.68 (d, 2H, <sup>3</sup>J<sub>6,NH</sub> 6 Hz, H6), 6.40 (s, 2H, NH<sub>2</sub>), 6.78–7.02 (m, 3H, H8, H9 & H12), 7.62 (d, 1H, <sup>3</sup>J<sub>5,NH</sub> 6 Hz, H<sub>5</sub>), 8.08–8.16 (br, d, 1H, <sup>3</sup>J<sub>5,NH</sub> 6 Hz, NH) ppm;  $\delta_{\rm C}$  (75 MHz, d<sub>6</sub>-DMSO) 43.9 (C6, by DEPT 135), 55.5 and 55.7 (C13 & C14), 110.4 (C1), 115.8 and 116.1 (C9, C12), 119.3 and 120.4 (C3 & C4), 121.1 (C2), 124.1 (C8), 135.2 (C7), 152.0 and 152.7 (C10 & C11), 154.4 (C5) ppm;  $\nu_{\rm max}$  (Nujol mull) 3480 s, 3380 s (NH str.), 2225 s (CN str.), 2205 s (CN str.), 1645 s (C=N str.), 1600 m (NH bend), 1520 m, 1275 s, 1250 m, 1230 w, 1170 s, 1155 w, 1040 s, 980 m, 965 w, 880 s, 850 s, 815 s, 780 s cm<sup>-1</sup>.

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(3,4-Dimethoxyphenyl)-(Z)-*N*-[2-amino-1,2-dicyanovinyl]formamidine (2c): M.p. 138–140°C (decomp.). Yield 96%. [Found C, 57.9; H,4.8; N, 25.4. Calc. for  $C_{13}H_{13}N_5O_2$ : C, 57.6; H, 4.8; N, 25.8%]; *m*/*z* (EI) 272 (M + 1)<sup>+</sup> 8.9%, 271 (M)<sup>+</sup> 47.8%, 270 (M – 1)<sup>+</sup> 11.0%, 244 [(M – 1)-CN]<sup>+</sup> 32.9%, 164 [(M-1)-C<sub>4</sub>H<sub>2</sub>N<sub>4</sub>]<sup>+</sup> 37.6%;  $\delta_{\rm H}$  (300 MHz, d<sub>6</sub>-DMSO) 3.60 (s, 6H, 2 × OCH<sub>3</sub>), 6.25 (br.s, 2H, NH<sub>2</sub>), 6.76 (d, 1H, <sup>3</sup>J<sub>8,7</sub> 8.5Hz, H8), 7.45–7.70 (br. complex m, 3H, H7, H11 & H5), 9.70 (br.s, 1H, NH) ppm;  $\delta_{\rm C}$  (75MHz, d<sub>6</sub>-DMSO) 59.4 and 59.7 (C12 &C13), 110.0 (C1), 116.0 (C7), 116.3 (C8), 116.6 (C11), 119.0 and 120.0 (C3 & C4), 122.5 (C2), 137.1 (C6), 149.0 (C5), 153.0 and 153.3 (C9 & C10) ppm;  $\nu_{\rm max}$  (Nujol mull) 3470 s, 3340 s, 3235 s (NH str.), 2230 s (CN str.), 2195 s (CN str.), 1640 m (C = N str.), 1600 m (NH bend), 1580 s, 1510 s, 1300 s, 1255 s, 1230 s, 1165 s, 1145 s, 1130 s, 1025 s, 965 w, 935 s, 830 s, 795 s, 765 s cm<sup>-1</sup>.

(4-Methoxyphenyl)-(Z)-*N*-[2-amino-1,2-dicyanovinyl]formamidine (2d): M.p. 123–124°C (decomp.). Yield 93%. [Found C, 59.7; H, 4.5; N, 28.7. Calc. for C<sub>12</sub>H<sub>11</sub>N<sub>5</sub>O C, 59.8; H, 4.6; N, 29.0%]; *m*/*z* (EI) 242 (M + 1)<sup>+</sup> 100%, 241 (M)<sup>+</sup> 2.8%, 215 (M-CN)<sup>+</sup> 40.9%, 136 [(M + 1)-C<sub>4</sub>H<sub>2</sub>N<sub>4</sub>]<sup>+</sup> 4.9%, 124 [(M +)-C<sub>5</sub>H<sub>2</sub>N<sub>4</sub>]<sup>+</sup> 44.9%, 108 [(M + 1)-C<sub>5</sub>H<sub>4</sub>N<sub>5</sub>]<sup>+</sup> 4.3%;  $\delta_{\rm H}$  (300 MHZ, d<sub>6</sub>-DMSO) 3.78 (s, 3H, OCH<sub>3</sub>), 6.40 (br.s, 2H, NH<sub>2</sub>), 6.92 (d, 2H, <sup>3</sup>*J*<sub>8,7</sub> 8 Hz, H8 & H10), 7.42–7.90 (br. complex m, 3H, H7, H11 & H5), 9.90 (br.s, 1H, NH) ppm;  $\delta_{\rm C}$  (75 MHz, d<sub>6</sub>-DMSO) 59.1 (C12), 109.0 (C1), 118.1 (C8 & C10), 118.8 and 119.9 (C3 & C4), 122.3 (C2), 124.5 (C7 & C11), 136.6 (C6), 150.9 (C5), 159.1 (C9) ppm;  $\nu_{\rm max}$  (Nujol mull) 3470 w, 3450 s, 3345 s, 3300 m, 3250 s, 3120 m (NH str.), 2215 s (CN str.), 2195 s (CN str.), 1650 m (C=N str.), 1600 m (NH bend), 1575 w, 1515 m, 1310 s, 1290 m, 1245 s, 1220 s, 1175 m, 1030 s, 960 w, 820 s, 785 s cm<sup>-1</sup>.

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