# Synthesis of 5-Cyanopyrazolo[3,4-*b*]pyridines in the Reaction of 5-Amino-3-methyl-1-phenylpyrazole with Arylidene Derivatives of Malonodinitrile and Ethyl Cyanoacetate



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This paper describes the synthesis of a new series of 6-amino-4-aryl-5-cyanopyrazolo[3,4-*b*]pyridines **4** and 4-aryl-5-cyano-6*H*-pyrazolo[3,4-*b*]pyridin-6-ones **5** from the reaction of 5-amino-3-methyl-1-phenylpyrazole **1** with arylidene derivatives of malonodinitrile **2** and ethyl cyanoacetate **3**. The structure of the final compounds was determined on the basis of nmr measurements, especially by $^1$H,$^1$H-, $^1$H, $^{13}$C-COSY, DEPT and X-ray diffraction.

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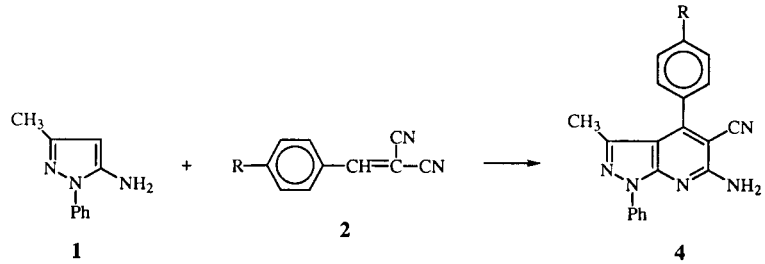
Synthesis and study of the pyrazolo[3,4-*b*]pyridines have been of interest for their potential biological and pharmacological activities properties [1-5].

We have previously reported that the reaction of 5-aminopyrazoles with chalcones [6,7], β-dimethylamino-propiophenones [8], benzylidene [9] and methoxymethylene [10] derivatives of Meldrum's acid has been presented as an efficient method of synthesis of pyrazolo-[3,4-*b*]pyridines. It has been our interest to examine this method and its application to synthesis of new pyrazolo[3,4-*b*]pyridine derivatives from benzylidenemalonodinitrile and ethyl benzylidenecyanoacetate as α,β-unsaturated component.

In this work we studied the reaction of 5-amino-3-methyl-1-phenylpyrazole **1** with benzylidene derivatives of malonodinitrile **2** and ethyl cyanoacetate **3**. A solution of equimolar amounts of amine **1** and **2** was heated to reflux for 1-1.5 hours, the reaction mixture was cooled and precipitate formed was filtrated, to give 6-amino-4-aryl-5-cyanopyrazolo[3,4-*b*]pyridines **4** (Scheme 1).

Scheme 1




**1** **2** **4**

| | 4a | 4b | 4c | 4d |
|---|---|---|---|---|
| **R** | H | $CH_3O$ | Cl | $NO_2$ |

The formation of **4** was confirmed by their spectroscopy analysis. Thus, the ir spectra of compounds **4** measured in potassium bromide pellets show one band of the elongation vibrations of the C=N group at 2212-2221 $cm^{-1}$ and two bands for $NH_2$ groups at 3329-3484 $cm^{-1}$.

In the $^1$H-nmr spectra of compounds **4** measured in dimethyl-$d_6$ sulfoxide (Table 1) were observed the signal of $CH_3$ group at 1.85-1.90 ppm, the aromatic proton signals at 7.50-8.53 ppm and the signal of 6-$NH_2$ group at 6.36-6.75 ppm.

Table 1

$^1$H-NMR Data of Compounds **4** and **5**
(δ values, Tetramethylsilane as the Internal Standard, in Dimethyl-$d_6$ Sulfoxide, 300 MHz)

| Compound | $CH_3$ s | 6-$NH_2$ s | 7-NH s | 1-Ph | 4-Ar |
|---|---|---|---|---|---|
| **4a** | 1.90 | 6.63 | --- | 7.47-7.58 | 7.50-8.17 |
| **4b** | 1.85 | 6.57 | --- | 7.48-7.57 | 7.55-8.20 |
| **4c** | 1.85 | 6.36 | --- | 7.50-7.70 | 7.60-8.22 |
| **4d** | 1.90 | 6.75 | --- | 7.51-8.30 | 7.90-8.53 |
| **5a** | 1.80 | --- | 12.01 | 7.30-7.52 | 7.42-8.12 |
| **5b** | 1.85 | --- | 12.05 | 7.40-7.53 | 7.45-7.60 |
| **5c** | 1.90 | --- | 12.09 | 7.45-7.55 | 7.52-7.65 |
| **5d** | 1.90 | --- | 12.12 | 7.50-8.02 | 7.80-8.42 |

The method described above was applicable to arylidene derivatives of ethyl cyanoacetate for the synthesis of pyrazolo[3,4-*b*]pyridines. Reactions of **1** with arylidene derivatives of ethyl cyanoacetate **3** in ethanol gave exclusively 4-aryl-5-cyano-1-phenyl-6*H*-pyrazolo[3,4-*b*]-pyridin-6-ones **5** in good yields (Scheme 2).

The formation of **5** was confirmed by their spectroscopy analysis. Thus, the ir spectra of compounds **5** measured in potassium bromide pellets show bands of the elongation vibrations of the C=O group at 1623-1642 $cm^{-1}$, C=N group at 2206-2222 $cm^{-1}$ and NH group at 3251-3435 $cm^{-1}$.

In the $^1$H-nmr spectra of compounds **5** measured in dimethyl-$d_6$ sulfoxide (Table 1) besides the signal of the $CH_3$ group at 1.80-1.90 ppm and the aromatic proton signals at 7.42-8.42 ppm, there were observed one singlet at δ = 12.01-12.12 ppm corresponding to the NH group at position 7 of pyrazolopyridine ring.

The final elucidation of structure of compounds **4** and **5** was carried out by analysis of the $^{13}$C-nmr spectra (Table 2).

The formation of **4** and **5** in these reactions is assumed to proceed *via* a sequence similar to that discussed in [8, 10-13]. These reactions must occur by 1,4-addition of the amine **1** at the 5 position to α,β-unsaturated systems of **2** or **3** followed by cyclization and air oxidation (Scheme 3).

An unambiguous structure proof of compound **4** was achieved by an examination of the crystal structure of **4a**. Figure 1 shows an X-ray crystal structure of compound **4a**.

Scheme 2

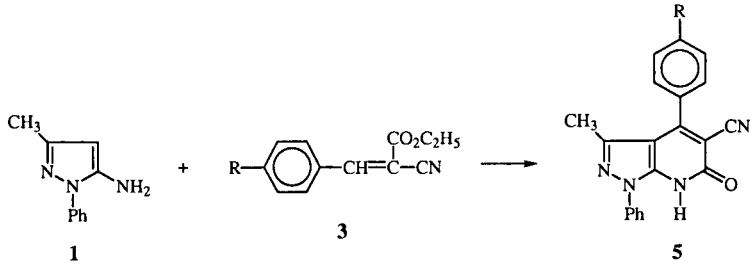
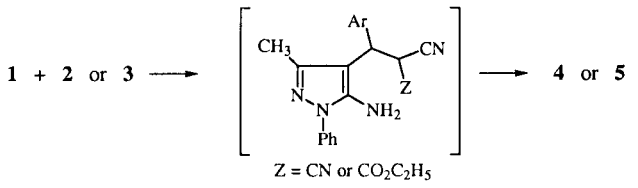



Table 2

$^{13}$C-NMR Data of Compounds **4** and **5**
(δ values, Tetramethylsilane as the Internal Standard, in Dimethyl-$d_6$ Sulfoxide, 300 MHz)

| Compound | | **4a** | **4b** | **4c** | **4d** | **5a** | **5b** | **5c** | **5d** |
|---|---|---|---|---|---|---|---|---|---|
| $CH_3$ | | 14.0 | 14.5 | 14.7 | 15.1 | 14.5 | 14.5 | 14.3 | 15.1 |
| C-3 | | 143.6 | 143.7 | 144.0 | 144.8 | 142.5 | 142.6 | 161.0 | 153.7 |
| C-3a | | 108.0 | 108.1 | 108.0 | 109.6 | 110.0 | 109.5 | 162.2 | 163.5 |
| C-4 | | 138.8 | 139.0 | 139.2 | 142.2 | 141.3 | 141.5 | 95.0 | 94.5 |
| C-5 | | 159.1 | 159.2 | 159.5 | 160.4 | 90.1 | 90.0 | 37.0 | 38.7 |
| C-6 | | 88.0 | 88.0 | 88.1 | 89.3 | 1563 | 156.3 | 156.0 | 157.5 |
| C-7a | | 152.4 | 152.3 | 152.0 | 152.4 | 135.0 | 135.2 | 151.4 | 137.2 |
| -CN | | 116.3 | 116.3 | 116.5 | 116.9 | 122.2 | 122.1 | 122.3 | 122.7 |
| Ar | Ci | 134.0 | 134.5 | 134.9 | 140.5 | 134.7 | 134.5 | 133.0 | 132.7 |
| | | 151.0 | 151.0 | 151.9 | 150.0 | 139.5 | 139.3 | 138.5 | 140.3 |
| | $C_{o,m}$ | 120.4 | 120.5 | 120.8 | 121.7 | 125.1 | 125.0 | 124.9 | 124.2 |
| | | 128.3 | 128.6 | 128.9 | 124.7 | 125.1 | 125.1 | 125.0 | 124.5 |
| | | 128.4 | 128.8 | 129.3 | 130.0 | 128.1 | 128.0 | 128.7 | 130.3 |
| | | 128.9 | 129.0 | 131.0 | 131.6 | 130.4 | 130.5 | 130.2 | 132.6 |
| | $C_p$ | 125.4 | 125.8 | 126.0 | 126.7 | 128.0 | 128.0 | 127.5 | 127.3 |
| | | 129.5 | 130.2 | 133.3 | 151.2 | 133.0 | 132.5 | 132.0 | 149.0 |

Scheme 3




The most important geometric features of this new compound **4a** are listed in Tables 3-8.

Table 3

Crystal Data and Structure Refinement for 6-Amino-5-cyano-3-methyl-1,4-diphenylpyrazolo[3,4-*b*]pyridine

| | |
|---|---|
| Empirical formula | $C_{20}H_{15}N_5$ |
| Formula weight | 325.35 |
| Temperature | 293(2) K |
| Wavelength | 0.71073 A |
| Crystal system | Monoclinic |
| Space group | P21/c |
| Unit cell dimensions | a = 11.654(3) Å α = 90° |
| | b = 11.729(5) Å β = 110.4790(3)° |
| | c = 13.098(4) Å γ = 90° |
| Volume | 1677.2(10) Å$^3$ |
| Z | 4 |
| Density (calculated) | 1.186 Mg/m$^3$ |
| Absorption coefficient | 0.073 mm$^{-1}$ |
| F(000) | 628 |
| Crystal size | 0.16 x 0.12 x 0.08 mm |
| Theta range for data collection | 2.40 to 25.32° |
| Index ranges | -14<=h<=13, 0<=k<=14, 0<=l<=15 |
| Reflections collected | 3186 |
| Independent reflections | 3047 [R(int) = 0.0667] |
| Refinement method | Full-matrix least-squares on F$^2$ |
| Data/restraints/parameters | 3047/0/233 |
| Goodness-of-fit on F$^2$ | 1.124 |
| Final R indices [I>2sigma(I)] | R1 = 0.0527, wR2 = 0.1123 |
| R indices (all data) | R1 = 0.1934, wR2 = 0.1848 |
| Extinction coefficient | 0.0021(8) |
| Largest diff. peak and hole | 0.212 and -0.176 e. Å$^{-3}$ |

Table 4

Fractional Coordinates (Å x 10$^4$) of Non-hydrogen Atoms and Isotropic Temperature Factors with Estimated in Parentheses

| | x | y | z | U(eq) |
|---|---|---|---|---|
| N(1) | 699(3) | 8968(3) | 7697(3) | 55(1) |
| N(2) | 462(3) | 9902(3) | 6995(3) | 62(1) |
| C(3) | 741(4) | 10820(4) | 7612(3) | 56(1) |
| C(3A) | 1162(4) | 10516(3) | 8745(3) | 50(1) |
| C(7A) | 1092(4) | 9319(4) | 8756(3) | 49(1) |
| C(4) | 1539(4) | 11087(3) | 9744(3) | 50(1) |
| C(5) | 1770(4) | 10396(3) | 10658(3) | 50(1) |
| C(6) | 1645(4) | 9184(3) | 10574(3) | 50(1) |
| N(7) | 1320(3) | 8633(3) | 9624(3) | 50(1) |
| N(3) | 2632(5) | 11212(3) | 12603(3) | 89(1) |
| N(4) | 1852(4) | 8538(3) | 11480(3) | 62(1) |
| C(8) | 453(4) | 7853(4) | 7233(3) | 54(1) |
| C(9) | -315(4) | 7739(4) | 6163(3) | 62(1) |
| C(10) | -540(4) | 6667(4) | 5701(4) | 69(1) |
| C(11) | -31(5) | 5710(5) | 6290(4) | 80(2) |

Table 4 (continued)

| | x | y | z | U(eq) |
|---|---|---|---|---|
| C(12) | 725(5) | 5845(4) | 7362(4) | 87(2) |
| C(13) | 967(5) | 6914(4) | 7828(4) | 77(2) |
| C(14) | 1725(4) | 12338(3) | 9861(3) | 48(1) |
| C(15) | 1119(4) | 12994(4) | 10397(3) | 56(1) |
| C(16) | 1351(4) | 14141(4) | 10552(3) | 60(1) |
| C(17) | 2205(4) | 14651(4) | 10199(4) | 69(1) |
| C(18) | 2818(4) | 14011(4) | 9672(4) | 67(1) |
| C(19) | 2577(4) | 12860(4) | 9499(3) | 58(1) |
| C(20) | 568(4) | 11971(4) | 7099(4) | 76(2) |
| C(21) | 2234(4) | 10875(3) | 11725(4) | 61(1) |

U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Table 5

Bond Lengths [Å] and Angles [°] with Estimated Standard Deviations in Parentheses

| | |
|---|---|
| N(1)-C(7A) | 1.363(5) |
| N(1)-N(2) | 1.394(4) |
| N(1)-C(8) | 1.428(5) |
| N(2)-C(3) | 1.317(5) |
| C(3)-C(3A) | 1.436(5) |
| C(3)-C(20) | 1.490(6) |
| C(3A)-C(4) | 1.397(5) |
| C(3A)-C(7A) | 1.406(5) |
| C(7A)-N(7) | 1.341(5) |
| C(4)-C(5) | 1.391(5) |
| C(4)-C(14) | 1.484(5) |
| C(5)-C(21) | 1.426(6) |
| C(5)-C(6) | 1.429(5) |
| C(6)-N(7) | 1.334(5) |
| C(6)-N(4) | 1.356(5) |
| N(3)-C(21) | 1.150(5) |
| C(8)-C(13) | 1.361(6) |
| C(8)-C(9) | 1.381(5) |
| C(9)-C(10) | 1.380(6) |
| C(10)-C(11) | 1.373(6) |
| C(11)-C(12) | 1.381(6) |
| C(12)-C(13) | 1.379(6) |
| C(14)-C(19) | 1.384(5) |
| C(14)-C(15) | 1.389(5) |
| C(15)-C(16) | 1.373(6) |
| C(16)-C(17) | 1.373(6) |
| C(17)-C(18) | 1.376(6) |
| C(18)-C(19) | 1.381(6) |
| C(7A)-N(1)-N(2) | 110.7(3) |
| C(7A)-N(1)-C(8) | 130.9(4) |
| N(2)-N(1)-C(8) | 118.3(3) |
| C(3)-N(2)-N(1) | 106.7(3) |
| N(2)-C(3)-C(3A) | 110.7(4) |
| N(2)-C(3)-C(20) | 119.9(4) |
| C(3A)-C(3)-C(20) | 129.4(4) |
| C(4)-C(3A)-C(7A) | 118.0(4) |
| C(4)-C(3A)-C(3) | 137.0(4) |
| C(7A)-C(3A)-C(3) | 105.0(4) |
| N(7)-C(7A)-N(1) | 125.3(4) |
| N(7)-C(7A)-C(3A) | 127.7(4) |
| N(1)-C(7A)-C(3A) | 106.9(4) |
| C(5)-C(4)-C(3A) | 115.4(4) |
| C(5)-C(4)-C(14) | 120.7(4) |
| C(3A)-C(4)-C(14) | 123.9(4) |
| C(4)-C(5)-C(21) | 120.4(4) |
| C(4)-C(5)-C(6) | 122.0(4) |

Table 5 (continued)

| | |
|---|---|
| C(7A)-C(3A)-C(3) | 105.0(4) |
| N(7)-C(7A)-N(1) | 125.3(4) |
| N(7)-C(7A)-C(3A) | 127.7(4) |
| N(1)-C(7A)-C(3A) | 106.9(4) |
| C(5)-C(4)-C(3A) | 115.4(4) |
| C(5)-C(4)-C(14) | 120.7(4) |
| C(3A)-C(4)-C(14) | 123.9(4) |
| C(4)-C(5)-C(21) | 120.4(4) |
| C(4)-C(5)-C(6) | 122.0(4) |
| C(21)-C(5)-C(6) | 117.4(4) |
| N(7)-C(6)-N(4) | 116.8(4) |
| N(7)-C(6)-C(5) | 122.8(4) |
| N(4)-C(6)-C(5) | 120.5(4) |
| C(6)-N(7)-C(7A) | 114.1(3) |
| C(13)-C(8)-C(9) | 120.1(4) |
| C(13)-C(8)-N(1) | 121.0(4) |
| C(9)-C(8)-N(1) | 118.9(4) |
| C(10)-C(9)-C(8) | 119.3(4) |
| C(11)-C(10)-C(9) | 121.3(4) |
| C(10)-C(11)-C(12) | 118.3(5) |
| C(13)-C(12)-C(11) | 120.8(5) |
| C(8)-C(13)-C(12) | 120.1(4) |
| C(19)-C(14)-C(15) | 118.8(4) |
| C(19)-C(14)-C(4) | 119.9(4) |
| C(15)-C(14)-C(4) | 121.2(4) |
| C(16)-C(15)-C(14) | 120.5(4) |
| C(17)-C(16)-C(15) | 120.4(4) |
| C(16)-C(17)-C(18) | 119.8(4) |
| C(17)-C(18)-C(19) | 120.2(4) |
| C(18)-C(19)-C(14) | 120.3(4) |
| N(3)-C(21)-C(5) | 176.8(5) |

Symmetry transformations used to generate equivalent atoms.

Table 6

Torsion Angles (°)

| | |
|---|---|
| C7A-N1-N2-C3 | 1.9(4) |
| C8-N1-N2-C3 | 179.0(4) |
| N1-N2-C3-C3A | -0.5(5) |
| N1-N2-C3-C20 | -179.0(4) |
| N2-C3-C3A-C4 | -177.7(5) |
| C20-C3-C3A-C4 | 0.6(9) |
| N2-C3-C3A-C7A | -0.9(5) |
| C20-C3-C3A-C7A | 177.3(4) |
| N2-N1-C7A-N7 | 175.5(4) |
| C8-N1-C7A-N7 | -1.1(7) |
| N2-N1-C7A-C3A | -2.4(5) |
| C8-N1-C7A-C3A | -179.1(4) |
| C4-C3A-C7A-N7 | 1.6(7) |
| C3-C3A-C7A-N7 | -175.9(4) |
| C4-C3A-C7A-N1 | 179.5(3) |
| C3-C3A-C7A-N1 | 2.0(5) |
| C7A-C3A-C4-C5 | -2.0(6) |
| C3-C3A-C4-C5 | 174.5(5) |
| C7A-C3A-C4-C14 | 176.2(4) |
| C3-C3A-C4-C14 | -7.3(8) |
| C3A-C4-C5-C21 | 176.1(4) |
| C14-C4-C5-C21 | -2.2(6) |
| C3A-C4-C5-C6 | 0.7(6) |
| C14-C4-C5-C6 | -177.6(4) |
| C4-C5-C6-N7 | 1.2(7) |
| C21-C5-C6-N7 | -174.2(4) |
| C4-C5-C6-N4 | -178.6(4) |
| C21-C5-C6-N4 | 6.0(7) |

Table 6 (continued)

| | |
|---|---|
| N4-C6-N7-C7A | 178.1(4) |
| C5-C6-N7-C7A | -1.7(6) |
| N1-C7A-N7-C6 | -177.2(4) |
| C3A-C7A-N7-C6 | 0.3(6) |
| C7A-N1-C8-C13 | -22.3(7) |
| N2-N1-C8-C13 | 161.3(4) |
| C7A-N1-C8-C9 | 158.0(4) |
| N2-N1-C8-C9 | -18.4(5) |
| C13-C8-C9-C10 | -1.0(7) |
| N1-C8-C9-C10 | 178.8(4) |
| C8-C9-C10-C11 | 1.1(7) |
| C9-C10-C11-C12 | -0.5(8) |
| C10-C11-C12-C13 | -0.3(8) |
| C9-C8-C13-C12 | 0.2(7) |
| N1-C8-C13-C12 | -179.5(5) |
| C11-C12-C13-C8 | 0.4(8) |
| C5-C4-C14-C19 | 118.1(5) |
| C3A-C4-C14-C19 | -60.0(6) |
| C5-C4-C14-C15 | -57.5(6) |
| C3A-C4-C14-C15 | 124.4(5) |
| C19-C14-C15-C16 | 0.7(6) |
| C4-C14-C15-C16 | 176.4(4) |
| C14-C15-C16-C17 | -1.3(6) |
| C15-C16-C17-C18 | 0.9(7) |
| C16-C17-C18-C19 | 0.0(7) |
| C17-C18-C19-C14 | -0.5(6) |
| C15-C14-C19-C18 | 0.2(6) |
| C4-C14-C19-C18 | -175.5(4) |
| C4-C5-C21-N3 | -152.3(99) |
| C6-C5-C21-N3 | 23.2(103) |

Table 7

Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for 6-Amino-5-cyano-3-methyl-1,4-diphenylpyrazolo[3,4-*b*]pyridine

| | U11 | U22 | U33 | U23 | U13 | U12 |
|---|---|---|---|---|---|---|
| N(1) | 62(2) | 61(2) | 43(2) | 1(2) | 18(2) | 4(2) |
| N(2) | 71(3) | 62(2) | 51(2) | 4(2) | 20(2) | 6(2) |
| C(3) | 61(3) | 56(3) | 51(3) | 4(2) | 18(2) | 1(2) |
| C(3A) | 54(3) | 53(3) | 45(3) | 1(2) | 20(2) | 2(2) |
| C(7A) | 47(3) | 58(3) | 45(3) | -5(2) | 19(2) | 1(2) |
| C(4) | 49(3) | 53(2) | 50(3) | 2(2) | 20(2) | 3(2) |
| C(5) | 60(3) | 47(3) | 46(3) | -4(2) | 22(2) | 0(2) |
| C(6) | 54(3) | 51(3) | 47(3) | 3(2) | 21(2) | 2(2) |
| N(7) | 53(2) | 54(2) | 46(2) | 4(2) | 20(2) | 2(2) |
| N(3) | 149(4) | 53(3) | 53(3) | -3(2) | 22(3) | 5(3) |
| N(4) | 91(3) | 50(2) | 46(2) | 3(2) | 25(2) | 2(2) |
| C(8) | 52(3) | 60(3) | 51(3) | -7(2) | 20(2) | 1(2) |
| C(9) | 53(3) | 72(3) | 56(3) | -9(2) | 15(2) | -4(2) |
| C(IO) | 63(3) | 84(4) | 61(3) | -16(3) | 22(2) | -7(3) |
| C(I 1) | 101(4) | 71(4) | 73(4) | -22(3) | 36(3) | -9(3) |
| C(12) | 131(5) | 61(3) | 66(4) | -3(3) | 32(3) | 14(3) |
| C(13) | 104(4) | 66(3) | 56(3) | -11(3) | 21(3) | 11(3) |
| C(14) | 50(3) | 47(2) | 48(2) | 1(2) | 16(2) | -4(2) |
| C(15) | 63(3) | 51(3) | 58(3) | 0(2) | 27(2) | -1(2) |
| C(16) | 69(3) | 49(3) | 60(3) | -4(2) | 22(2) | 1(2) |
| C(17) | 76(3) | 53(3) | 71(3) | 4(2) | 17(3) | -8(3) |
| C(18) | 64(3) | 69(3) | 70(3) | 9(3) | 25(2) | -13(3) |
| C(19) | 60(3) | 61(3) | 56(3) | 1(2) | 24(2) | -4(2) |
| C(20) | 86(4) | 78(3) | 57(3) | 18(3) | 17(3) | -2(3) |
| C(21) | 91(4) | 39(3) | 53(3) | 2(2) | 26(3) | 2(2) |

The anisotropic displacement factor exponent takes the form: $-2\ pi^2\ [h^2\ a^*2\ U11 + ... + 2\ h\ k\ a^*\ b^*\ U12]$

Table 8

Hydrogen Coordinates (Å x $10^4$) and Isotropic Displacement Parameters (Å x $10^3$) for 6-Amino-5-cyano-3-methyl-1,4-diphenylpyrazolo-[3,4-*b*]pyridine

| | x | y | z | U(eq) |
|---|---|---|---|---|
| HN41 | 1841(35) | 7678(37) | 11405(32) | 76 |
| HN42 | 2138(39) | 8858(35) | 12100(34) | 76 |
| H(9) | -678(4) | 8377(4) | 5758(3) | 76 |
| H(10) | -1046(4) | 6591(4) | 4977(4) | 76 |
| H(11) | -191(5) | 4990(5) | 5975(4) | 76 |
| H(12) | 1075(5) | 5207(4) | 7776(4) | 76 |
| H(13) | 1482(5) | 6993(4) | 8549(4) | 76 |
| H(15) | 550(4) | 12653(4) | 10652(3) | 76 |
| H(16) | 928(4) | 14575(4) | 10899(3) | 76 |
| H(17) | 2369(4) | 15425(4) | 10315(4) | 76 |
| H(18) | 3396(4) | 14355(4) | 9431(4) | 76 |
| H(19) | 2989(4) | 12434(4) | 9137(3) | 76 |
| H(201) | 1348(4) | 12343(4) | 7281(4) | 76 |
| H(202) | 40(4) | 12417(4) | 7365(4) | 76 |
| H(203) | 205(4) | 11895(4) | 6322(4) | 76 |

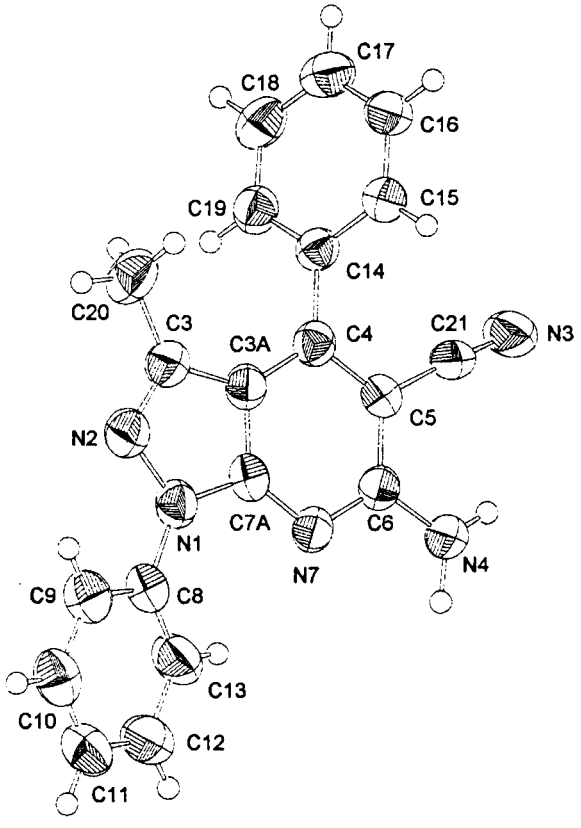



Figure 1. Molecular Structure of **4a**.

## EXPERIMENTAL

Melting points were taken on a Buchi Melting Point Apparatus and are uncorrected. The $^1$H- and $^{13}$C nmr spectra were obtained with a Bruker AMX-300 operating at 300 MHz and 75 MHz respectively, in dimethyl-$d_6$ sulfoxide as solvent and tetramethylsilane as the internal standard. Mass spectra (FAB) were performed with a Kratos MS-50 mass spectrometer using 2-hydroxyethyl disulfide as a matrix. The elemental analysis have been obtained using a LECO CHNS-900 equipment.

Synthesis of 6-Amino-4-aryl-5-cyano-1-phenylpyrazolo-[3,4-*b*]pyridines **4** and 4-Aryl-5-cyano-1-phenyl-6*H*-pyrazolo-[3,4-*b*]pyridin-6-ones **5**.

General Procedure.

A solution of 5-aminopyrazole (**1**) (1.5 mmoles) and corresponding arylidene derivative of malonodinitrile (**2**) (1.5 mmoles) or corresponding arylidene derivative of ethyl cyanoacetate (**3**) (1.5 mmoles) in 10 ml of absolute ethanol and 1 ml of triethylamine was heated to reflux for 1-1.5 hours. The reaction mixture was cooled. The cyclized products **4** or **5** were collected by filtration, washed with ethanol, dried and recrystallized from ethanol.

6-Amino-5-cyano-3-methyl-1,4-diphenylpyrazolo[3,4-*b*]pyridine **4a**.

This compound was obtained by the general procedure as white crystals, mp 208°, yield 63%; ir (potassium bromide): 2216 (CN), 3366, 3476 cm$^{-1}$ ($NH_2$); ms: FAB m/z 326 ($M^+$+1).

*Anal.* Calcd. for $C_{20}H_{15}N_5$: C, 73.85; H, 4.61; N, 21.54. Found: C, 73.74; H, 4.67; N, 21.47.

6-Amino-5-cyano-4-(4-methoxyphenyl)-3-methyl-1-phenylpyrazolo[3,4-*b*]pyridine **4b**.

This compound was obtained by the general procedure as white crystals, mp 197°, yield 65%; ir (potassium bromide): 2221 (CN), 3342, 3420 cm$^{-1}$ ($NH_2$); ms: FAB m/z 356 ($M^+$+1).

*Anal.* Calcd. for $C_{21}H_{17}N_5O$: C, 70.98; H, 4.79; N, 19.72. Found: C, 70.86; H, 4.86; N, 19.65.

6-Amino-4-(4-chorophenyl)-5-cyano-3-methyl-1-phenylpyrazolo[3,4-*b*]pyridine **4c**.

This compound was obtained by the general procedure as white crystals, mp 195°, yield 67%; ir (potassium bromide): 2212 (CN), 3329, 3454 cm$^{-1}$ ($NH_2$); ms: FAB M/z 360/362 ($M^+$+1).

*Anal.* Calcd. for $C_{20}H_{14}N_5Cl$: C, 66.76; H, 3.90; N, 19.47. Found: C, 66.88; H, 3.98; N, 19.29.

6-Amino-5-cyano-3-methyl-4-(4-nitrophenyl)-1-phenylpyrazolo[3,4-*b*]pyridines **4d**.

This compound was obtained by the general procedure as pale yellow crystals, mp 215°, yield 82%; ir (potassium bromide): 2213 (CN), 3349, 3484 cm$^{-1}$ ($NH_2$); ms: FAB m/z 371 ($M^+$+1).

*Anal.* Calcd. for $C_{20}H_{14}N_6O_2$: C, 64.87; H, 3.78; N, 22.70. Found: C, 64.80; H, 3.61; N, 22.56.

5-Cyano-3-methyl-1,4-diphenyl-7*H*-pyrazolo[3,4-*b*]pyridin-6-one **5a**.

This compound was obtained by the general procedure as white crystals, mp 183°, yield 65%; ir (potassium bromide): 1623 (C=O), 2206 (CN), 3435 cm$^{-1}$ (NH); ms: FAB m/z 327 ($M^+$+1).

*Anal.* Calcd. for $C_{20}H_{14}N_4O$: C, 70.18; H, 4.09; N, 16.37. Found: C, 70.32; H, 4.15; N, 16.25.

5-Cyano-4-(4-methoxyphenyl)-3-methyl-1-phenyl-7*H*-pyrazolo[3,4-*b*]pyridin-6-one **5b**.

This compound was obtained by the general procedure as white crystals, mp 320°, yield 60%; ir (potassium bromide): 1634 (C=O), 2222 (CN), 3431 $cm^{-1}$ (NH); ms: FAB m/z 357 ($M^+$+1).

*Anal.* Calcd. for $C_{21}H_{16}N_4O_2$: C, 70.79; H, 4.49; N, 15.73. Found: C, 70.66; H, 4.57; N, 15.82.

4-(4-Chlorophenyl)-5-cyano-3-methyl-1-phenyl-7*H*-pyrazolo[3,4-*b*]pyridin-6-one **5c**.

This compound was obtained by the general procedure as white crystals, mp 278°, yield 70%; ir (potassium bromide): 1642 (C=O), 2216 (CN), 3351 $cm^{-1}$ (NH); ms: FAB m/z 361/363 ($M^+$+1).

*Anal.* Calcd. for $C_{20}H_{13}N_4OCl$: C, 66.57; H, 3.61; N, 15.53. Found: C, 66.67; H, 3.54; N, 15.45.

5-Cyano-3-methyl-4-(4-nitrophenyl)-1-phenyl-7*H*-pyrazolo-[3,4-*b*]pyridin-6-one **5d**.

This compound was obtained by the general procedure as pale yellow crystals, mp 308°, yield 76%; ir (potassium bromide): 1633 (C=O), 2220 (CN), 3367 $cm^{-1}$ (NH); ms: FAB m/z 372 ($M^+$+1).

*Anal.* Calcd. for $C_{20}H_{13}N_5O_3$: C, 64.69; H, 3.50; N, 18.87. Found: C, 64.53; H, 3.37; N, 18.98.

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