Friedländer Condensation of 5-Aminopyrazole-4-carbaldehydes with Reactive α-Methylene Ketones: Synthesis of Pyrazolo[3,4-*b*]pyridines

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A series of 1,3,6-trisubstituted and 1,3,5,6-tetrasubstituted pyrazolo[3,4-*b*]pyridines **5** has been synthesized by *Friedländer condensation* of 5-aminopyrazole-4-carbaldehydes **3** with α-methylene ketones such as acetone (**4a**) or acetophenones **4b-f** with potassium hydroxide as basic catalyst. Condensation of 5-aminopyrazole-4-carbaldehydes **3** and unsymmetric dialkylketones **6** yielded mixtures of isomeric pyrazolo[3,4-*b*]pyridine derivatives **7** and **8**. Condensation of 5-aminopyrazole-4-carbaldehydes **3** with CH-acidic acylacetonitriles **9** and acylacetates **11** with piperidine as basic catalyst yielded pyrazolo[3,4-*b*]pyridine-5-carbonitriles **10** and pyrazolo[3,4-*b*]pyridine-5-carboxylates **12**; with diethyl malonate **13** as CH-acidic component, pyrazolo[3,4-*b*]pyridin-6-ones **14** were obtained.

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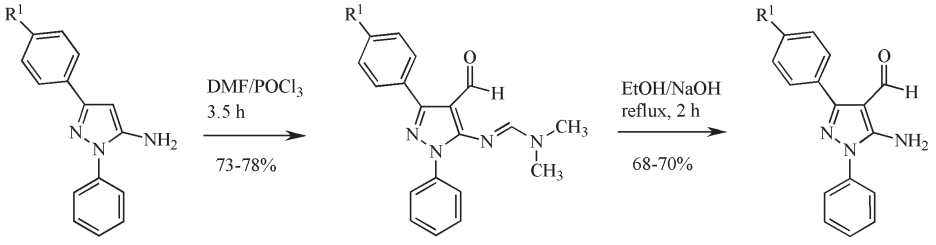
Pyrazolo[3,4-*b*]pyridines as aza-analogues of indazoles [1] are attractive targets in organic synthesis due to their significant biological activities, such as hypoglycemic [2], psychotropic [3], cytotoxic [4] or antiviral [5] activity, and in coronary [6] or neurodegenerative diseases [7]. *o*-Aminoaldehydes are the key intermediates for the synthesis of various biologically active heterocycles *e.g.* [8,9] using the *Friedländer* reaction with ketones in a 4+2 cyclocondensation [10], which prompted us to investigate the reaction pathway of 5-aminopyrazole-4-carbaldehydes with α-methylene ketones to new 1,3,6-trisubstituted and 1,3,5,6-tetrasubstituted pyrazolo[3,4-*b*]pyridines, especially to 1,3,6-triarylpyrazolo[3,4-*b*]pyridines. A literature survey shows a few reports on the synthesis of pyrazolo[3,4-*b*]pyridines using the *Friedländer* condensation [11], however with substitution patterns different to ours.

The required starting materials for the intended *Friedländer* condensation, 5-aminopyrazole-4-carbaldehydes **3**, were synthesized by cyclocondensation of *p*-substituted aroylacetonitriles, a class of compounds which was studied recently by us for other cyclization reactions [12]. *p*-Substituted aroylacetonitriles cyclize as 1,3-dicarbonyl synthons with arylhydrazines already on heating without catalysts according to known methods [13] and furnished in good to excellent yields 5-aminopyrazoles **1**, which afforded on Vilsmeier-Haack formylation with excess dimethylformamide and phosphoryl chloride 4-formyl-pyrazolyl-dimethylimidoformamides **2**. Thermal analysis of formamides **2** by differential scanning calorimetry (DSC) revealed that they are thermally stable compounds which showed thermal decomposition only above 350 °C. Hydrolysis of formamides **2** with refluxing ethanolic sodium hydroxide yielded the required 5-aminopyrazole-4-carbaldehydes **3** in good yield.

Scheme 1



1 **2** **3**

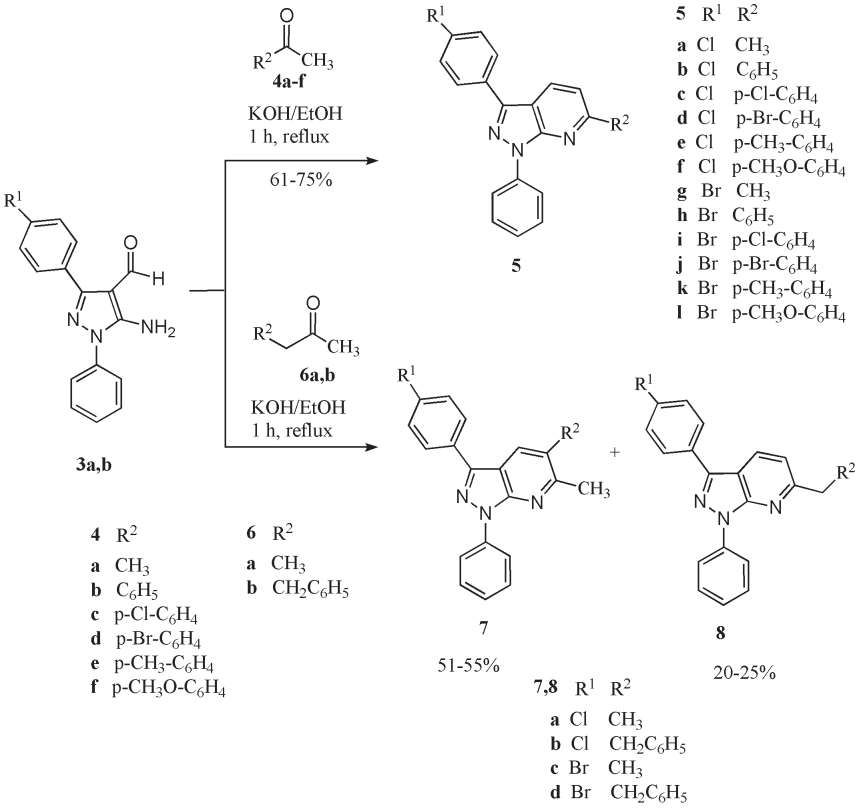
1-3 R^1
a Cl
b Br
c CH_3

The *Friedländer* condensation of *o*-aminoaldehydes such as 5-aminopyrazole-4-carbaldehydes **3** with ketones is described to take place either with strong bases or acids as catalysts; in special cases the ring closure can be observed without a catalyst at higher temperatures (*e.g.* under microwave irradiation) [10]. We obtained the best results when a mixture of the appropriate 5-aminopyrazole-4-carbaldehyde **3** and the corresponding ketone **4** or **6** were brought to reaction in refluxing ethanolic potassium hydroxide solution. With acetone (**4a**) or acetophenones **4b-f**, this reaction sequence afforded 6-alkyl-3-aryl and 3,6-diaryl-1-phenylpyrazolo[3,4-*b*]pyridines **5a-l** in good yields.

When instead of the symmetric acetone (**4a**) or monoalkylketones (**4b-f**) unsymmetric dialkyl ketones such as 2-butanone (**6a**) or 4-phenyl-2-butanone (**6b**) were used as condensation partner, a mixture of the two expected isomers **7** and **8** was obtained in a 2:1 ratio; the 5-substituted isomer **7** was formed by attack of the carbaldehyde moiety at the ethyl- or benzyl-CH_2 group of the ketone **6**, whereas condensation on the alpha-methyl group of **6** formed the 5-unsubstituted isomer **8**. The mixture of the isomers **7** and **8** was separated by column chromatography using toluene/hexane as the eluent. Structural assignment of **7a** and **8a** could easily be performed by ^{1}H nmr, because **7a** shows two methyl singlets at 2.42 and 2.64 ppm, together with the singlet of 4-H at 7.98 ppm, whereas **8a** shows the ethyl signal at 1.44 and 2.98 ppm, together with two doublets at 7.14 and 8.21 ppm assigned to the *ortho* coupled protons 4-H and 5-H of the pyridine ring. All other signals of aromatic protons are nearly identical. Mass spectral analysis of **7a** and **8a** showed in both cases the same mass of 333 (M) and 335 m/z (M+2,^{37}Cl isotope), however with other fragmentation patterns: the dimethyl derivative **7a** showed as the main fragmentation 297 m/z without chloro pattern, which indicates a cleavage of HCl, whereas **8a** shows as the first fragmentation 318 m/z, a cleavage of CH_3, together with the fragment 297 m/z as observed at **7a**. Similarly, the structures of bromo derivatives **7b** and **8b** could be assigned. Compound **7b** shows the methyl singlet at 2.66 and the benzyl-CH_2 singlet at 4.20 ppm; the 4-H signal appeared at 8.07 ppm. The isomer **8b** shows two CH_2-multiplets at 3.22-3.27 and 3.32-3.38 ppm, and H-4 and H-5 doublets at 7.11 and 8.23 ppm. The mass spectra of the two isomer bromo derivatives **7c** and **8c** revealed again the identical masses, 377 (M) and 379 m/z (M+2, ^{81}Br isotope).

As mentioned above, the *Friedländer* condensation can be catalyzed by various agents [10]. When we extended

Scheme 2



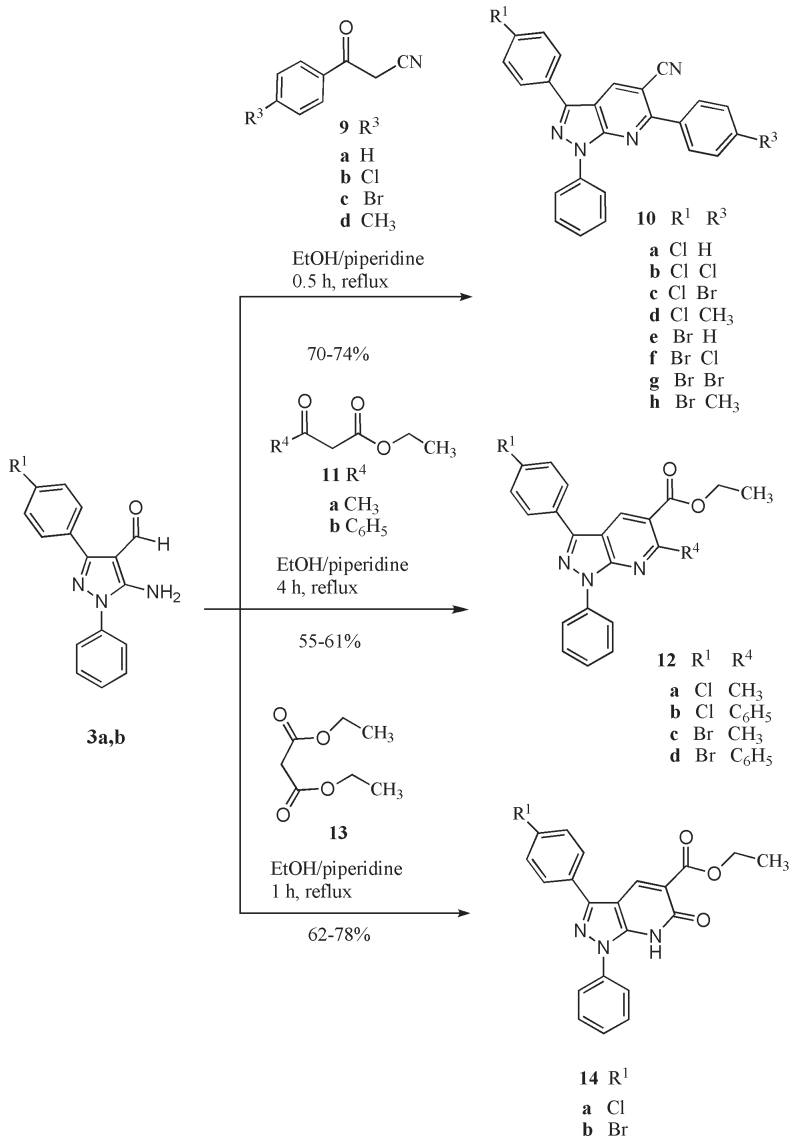
our synthetic investigations to CH-acidic compounds such as benzoylacetonitriles **9**, β-ketoesters **11** or diethyl malonate **13** as keto-component, we found that already piperidine as base was sufficiently strong to catalyze the condensation reaction, which allowed also the preparation of sensitive substituents such as ester groups without decomposition. This method provided a versatile method for the synthesis of various substituted pyrazolo[3,4-*b*]pyridines and pyrazolo[3,4-*b*]pyridones with reactive groups in position 5, ready for further reactions. The cyclocondensation of 5-aminopyrazole-4-carbaldehydes **3** with benzoylacetonitriles **9** yielded in ethanolic piperidine pyrazolo[3,4-*b*]pyridine-5-carbonitriles **10** and β-ketoesters **11** gave pyrazolo[3,4-*b*]pyridine-5-carboxylates **12**, both structures easily confirmed by nitrile and ester signals. Diethyl malonate (**13**) afforded under these conditions 5-carbethoxypyrazolo[3,4-*b*]pyridin-6-ones **14**. The mass spectra and nmr data confirmed the structures of **14**, although the ester carbonyl stretch in the IR could not be observed either in KBr disks or nujol suspension, probably because of hydrogen bonding in the solid state.

The thermal behavior of two pyrazolo[3,4-*b*]pyridine-5-carbonitriles **10** were investigated by differential scanning calorimetry (DSC) and show above 350 °C reaction peaks, a reaction temperature too high for synthetic use.

EXPERIMENTAL

Melting points were determined on a Gallenkamp Melting Point Apparatus, Mod. MFB-595 in open capillary tubes.

Scheme 3



Calorimetric data were obtained on a Rheometric Scientific DSC-Plus instrument with the differential scanning calorimetry software Orchestrator V6.2.2. The differential scanning calorimetry (DSC) plots were recorded between 25 - 500 °C, with a heating rate of 2-10 °C/min, and 1.5-3 mg compound in sealed aluminium crucibles (11 bar). The ^{1}H nmr spectra were recorded on a Varian XL-300 spectrometer (300 MHz), a Bruker AMX 360 instrument (360 MHz) or a Bruker Avance DRX 500 instrument (500 MHz). The ^{13}C nmr-spectra were recorded on a Bruker AM 360 instrument (90 MHz). Chemical shifts are reported in ppm from internal tetramethylsilane standard and are given in δ-units. The solvent for NMR spectra was deuteriochloroform unless otherwise stated. Evaluation of ^{1}H nmr spectra was performed using the software Mestrec 4. Infrared spectra were taken on a Shimadzu IR-408, a Shimadzu FTIR, or on a Galaxy Series FTIR 7000 instrument in potassium bromide pellets unless otherwise stated. Elemental analyses were performed on a Hosli CH-Analyser or on a Fisons elemental analyzer Mod. EA 1108, and are within ±0.4 of the theoretical percentages. Mass spectra were taken on a HP 1100 LC/MSD mass spectral instrument (positive or negative APCI: 50-200 eV, nitrogen). All reactions were monitored by thin layer chromatography, carried out on 0.2 mm silica gel 60 F-254 (Merck) plates using uv light (254 and 366 nm) for detection. Column chromatography was carried out on silica gel (SD Fine Chemicals, 60-80 mesh). Common reagent-grade chemicals are either commercially available and were used without further purification or prepared by standard literature procedures.

3-(4-Substituted aryl)-1-phenyl-1*H*-pyrazol-5-amines **1a-c**.

These compounds were synthesized from *p*-chloro-, *p*-bromo- or *p*-methyl-benzoylacetonitrile [12] and phenylhydrazine in excellent yields by refluxing in ethanol for 4-6 h according to ref. [13].

N'-[3-(4-Chlorophenyl)-4-formyl-1-phenyl-1*H*-pyrazol-5-yl]-*N*,*N*-dimethylimidoformamide (**2a**).

To a solution of 3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazol-5-amine (**1a**) (26.9 g, 0.1 mol) in dimethylformamide (37 mL, 0.5 mol), phosphoryl chloride (46 mL, 0.3 mol) was added in small portions at 10-15 °C with stirring. Then the reaction mixture was stirred at 65-70 °C for 3.5 hours and poured into ice/water (900 mL). The precipitated product was filtered by suction, and washed with water. The yield was 27.5 g (78%) colorless prisms, mp 133-134 °C (ethanol); calorimetric data for the thermolysis: mp at 136.1 °C onset, 137.7 °C maximum, ΔH = 107 J/g, decomposition at 346.5 °C onset, 347.9 °C maximum, ΔH = –61 J/g, decomposition at 448.7 °C onset, 448.9 °C maximum, ΔH = –451 J/g; ir: 1655 s, 1615 m cm^{-1}; ^{1}H nmr: δ 2.86 (s, CH_3), 2.97 (s, CH_3), 7.32-7.62 (m, 5 PhH), 7.63-7.65 (m, 4 ArH), 8.48 (s, N=CH), 9.52 (s, CH=O).

Anal. Calcd. for $C_{19}H_{17}ClN_4O$: C, 64.68; H, 4.86; N, 15.88. Found: C, 64.80; H, 4.76; N, 15.98.

N'-[3-(4-Bromophenyl)-4-formyl-1-phenyl-1*H*-pyrazol-5-yl]-*N*,*N*-dimethylimidoformamide (**2b**).

This compound was obtained from 3-(4-bromophenyl)-1-phenyl-1*H*-pyrazol-5-amine (**1b**) (3.14 g, 0.1 mol) using the procedure described for **2a**; the yield was 30.1 g (76%), colorless prisms, mp 138-139 °C (ethanol); calorimetric data for the thermolysis: mp at 142.3 °C onset, 144.2 °C maximum, ΔH = 85 J/g, decomposition at 374.3 °C onset, 394.8 °C maximum, ΔH = –139 J/g; ir: 1650 s, 1600 m cm^{-1}; ^{1}H nmr: δ 3.05 (s, CH_3), 3.16 (s, CH_3), 7.26-7.44 (m, 3 ArH), 7.60-7.87 (m, 6 ArH), 8.63 (s, N=CH), 9.67 (s, CH=O).

Anal. Calcd. for $C_{19}H_{17}BrN_4O$: C, 57.44; H, 4.31; N, 14.10. Found: C, 57.40; H, 4.06; N, 13.92.

N'-[4-Formyl-3-(4-methylphenyl)-1-phenyl-1*H*-pyrazol-5-yl]-*N*,*N*-dimethylimidoformamide (**2c**).

This compound was obtained from 3-(4-methylphenyl)-1-phenyl-1*H*-pyrazol-5-amine (**1c**) (24.9 g, 0.1 mol) using the procedure described for **2a**; the yield was 24.0 g (72%), colorless prisms, mp 127-128 °C (ethanol); ir: 1655 s, 1620 m cm^{-1}; ^{1}H nmr: δ 2.41 (s, Ar-CH_3), 3.04 (s, N-CH_3), 3.15 (s, N-CH_3), 7.26-7.42 (m, 5 PhH), 7.57-7.89 (m, 4 ArH), 8.71 (s, N=CH), 9.70 (s, CH=O).

Anal. Calcd. for $C_{20}H_{20}N_4O$: C, 72.27; H, 6.06; N, 16.86. Found: C, 72.16; H, 6.19; N, 16.94.

5-Amino-3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde (**3a**).

A solution of pyrazolylimidoformamide **2a** (35.2 g, 0.1 mol) in ethanol (275 mL) and aqueous sodium hydroxide solution (27.5 mL, 40%) was heated under reflux for 2 hours. It was then poured into water (800 mL) and the precipitated solid was filtered by suction, washed with water and dried. The yield was 20.5 g (69%), pale yellow prisms, mp 137-138 °C (ethanol); ir: 3450 m, 3345 m, 1642 s cm^{-1}; ^{1}H nmr: δ 6.00 (s, NH_2, exchangeable with D_2O), 7.37-7.68 (m, 9 ArH), 9.85 (s, CH=O).

Anal. Calcd. for $C_{16}H_{12}ClN_3O$: C, 64.54; H, 4.06; N, 14.11. Found: C, 64.23; H, 3.96; N, 14.24.

5-Amino-3-(4-bromophenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde (**3b**).

This compound was obtained from pyrazolylimidoformamide **2b** (39.7 g, 0.1 mol) using the procedure described for **3a**; the yield was 23.9 g (70%), pale yellow prisms, mp 142-143 °C (ethanol); ir: 3350 m, 3450 m, 1645 s cm^{-1}; ^{1}H nmr: δ 6.01 (s, NH_2, exchangeable with D_2O), 7.44-7.60 (m, 9 ArH), 9.83 (s, CH=O).

Anal. Calcd. for $C_{16}H_{12}BrN_3O$: C, 56.16; H, 3.53; N, 12.28. Found: C, 56.05; H, 3.63; N, 12.08.

5-Amino-3-(4-methylphenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde (**3c**).

This compound was obtained from pyrazolylimidoformamide **2c** (33.2 g, 0.1 mol) using the procedure described for **3a**; the yield was 18.8 g (68%), pale yellow prisms, mp 130-131 °C (ethanol); ir: 3350 m, 3455 m, 1645 s cm^{-1}; ^{1}H nmr: δ 2.41 (s, CH_3), 5.98 (s, NH_2, exchangeable with D_2O), 7.28-7.61 (m, 9 ArH), 9.85 (s, CH=O).

Anal. Calcd. for $C_{17}H_{15}N_3O$: C, 73.63; H, 5.45; N, 15.15. Found: C, 73.36; H, 5.68; N, 15.32.

3-(4-Chlorophenyl)-6-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (**5a**).

A mixture of pyrazolecarbaldehyde **3a** (0.59 g, 2 mmol), acetone (**4a**) (0.12 g, 2 mmol) and ethanolic potassium hydroxide solution (10 mL, 2%) was heated under reflux for one hour. The mixture was then cooled to room temperature and the obtained solid was collected by suction filtration and washed with ethanol. The yield was 0.39 g (61%), colorless prisms, mp 140-141° (ethyl acetate); ir: 2350 w, 1600 m cm^{-1}; ^{1}H nmr: δ 2.75 (s, CH_3),

7.13 (d, J = 8.4 Hz, 5-H), 7.28-7.55 (m, 5 PhH), 7.96 (d, J = 8.4 Hz, 2 ArH), 8.20 (d, J = 8.4 Hz, 4-H), 8.36 (d, J = 8.4 Hz, 2 ArH).

Anal. Calcd. for $C_{19}H_{14}ClN_3$: C, 71.36; H, 4.41; N, 13.14. Found: C, 71.56; H, 4.77; N, 13.29.

3-(4-Chlorophenyl)-1,6-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridine (**5b**).

This compound was obtained from pyrazolecarbaldehyde **3a** (0.59 g, 2 mmol) and acetophenone (**4b**) (0.24 g, 2 mmol) using the method and work-up as described for **5a**; the yield was 0.52 g (68%) pale yellow prisms, mp 164-165 °C (ethyl acetate); ir: 2345 w, 1600 m cm^{-1}; ^1H nmr: δ 7.33-7.56 (m, 8 ArH), 7.75 (d, J = 8.4 Hz, 5-H), 8.00 (d, J = 8.4 Hz, 2 ArH), 8.19 (d, J = 7.8 Hz, 2 ArH), 8.38 (d, J = 8.4 Hz, 4-H), 8.50 (d, J = 7.8 Hz, 2 ArH).

Anal. Calcd. for $C_{24}H_{16}ClN_3$: C, 75.49; H, 4.22; N, 11.00. Found: C, 75.62; H, 4.06; N, 11.23.

3,6-Bis(4-chlorophenyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (**5c**).

This compound was obtained from pyrazolecarbaldehyde **3a** (0.59 g, 2 mmol) and 4-chloroacetophenone (**4c**) (0.31 g, 2 mmol) using the method described for **5a**; the yield was 0.63 g (75%), pale yellow prisms, mp 196-198 °C (ethyl acetate); ir: 2339 w, 1591 m, cm^{-1}; ^1H nmr: δ 7.34-7.59 (m, 7 ArH), 7.70 (d, J = 8.4 Hz, 5-H), 8.01 (d, J = 8.4 Hz, 2 ArH), 8.10 (d, J = 8.7 Hz, 2 ArH), 8.37 (d, J = 8.4 Hz, 4-H), 8.40 (d, J = 8.7 Hz, 2 ArH).

Anal. Calcd. for $C_{24}H_{15}Cl_2N_3$: C, 69.24; H, 3.63; N, 10.09. Found: C, 69.54; H, 3.40; N, 9.92.

6-(4-Bromophenyl)-3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazolo-[3,4-*b*]pyridine (**5d**).

This compound was obtained from pyrazolecarbaldehyde **3a** (0.59 g, 2 mmol) and 4-bromoacetophenone (**4d**) (0.40 g, 2 mmol) using the method described for **5a**; the yield was 0.66 g (72%), pale yellow prisms, mp 199-200 °C (ethyl acetate); ir: 2335 w, 1595 m cm^{-1}; ^1H nmr: δ 7.34-7.66 (m, 7 ArH), 7.68 (d, J = 8.7 Hz, 5-H), 8.00 (d, J = 8.1 Hz, 2 ArH), 8.02 (d, J = 8.4 Hz, 2 ArH), 8.35 (d, J = 8.7 Hz, 4-H), 8.42 (d, J = 8.4 Hz, 2 ArH).

Anal. Calcd. for $C_{24}H_{15}Br_{Cl}N_3$: C, 62.56; H, 3.28; N, 9.12. Found: C, 62.31; H, 3.14; N 9.06.

3-(4-Chlorophenyl)-6-(4-methylphenyl)-1-phenyl-1*H*-pyrazolo-[3,4-*b*]pyridine (**5e**).

This compound was obtained from pyrazolecarbaldehyde **3a** (0.59 g, 2 mmol) and 4-methylacetophenone (**4e**) (0.27 g, 2 mmol) using the method described for **5a**; the yield was 0.56 g (71%), colorless prisms, mp 192-194 °C (ethyl acetate); ir: 2338 w, 1600 m cm^{-1}; ^1H nmr: δ 2.45 (s, CH_3), 7.31-7.64 (m, 7 ArH), 7.71 (d, J = 8.4 Hz, 5-H), 7.92 (d, J = 8.7 Hz, 2 ArH), 8.05 (d, J = 6.6 Hz, 2 ArH), 8.32 (d, J = 8.4 Hz, 4-H), 8.47 (d, J = 7.5 Hz, 2 ArH).

Anal. Calcd. for $C_{25}H_{18}ClN_3$: C, 75.85; H, 4.58; N, 10.61. Found: C, 75.45; H, 4.71; N, 10.45.

3-(4-Chlorophenyl)-6-(4-methoxyphenyl)-1-phenyl-1*H*-pyrazolo-[3,4-*b*]pyridine (**5f**).

This compound was obtained from pyrazolecarbaldehyde **3a** (0.59 g, 2 mmol) and 4-methoxyacetophenone (**4f**) (0.30 g, 2 mmol) using the method described for **5a**; the yield was 0.62 g (75%), colorless prisms, mp 209-210 °C (ethyl acetate); ir: 2336 w, 1747 m, 1595 m cm^{-1}; ^1H nmr: δ 3.89 (s, OCH_3), 7.02 (d, J = 8.7 Hz, 2 ArH), 7.31-7.57 (m, 5 ArH), 7.67 (d, J = 8.4 Hz, 5-H), 7.97 (d, J = 8.7 Hz, 2 ArH), 8.15 (d, J = 8.7 Hz, 2 ArH), 8.31 (d, J = 8.4 Hz, 4-H) 8.46 (d, J = 8.7 Hz, 2 ArH).

Anal. Calcd. for $C_{25}H_{18}ClN_3O$: C, 72.90; H, 4.40; N, 10.20. Found: C, 73.11; H, 4.43; N, 10.12.

3-(4-Bromophenyl)-6-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]-pyridine (**5g**).

This compound was obtained from pyrazolecarbaldehyde **3b** (0.68 g, 2 mmol) and acetone (**4a**) (0.12 g, 2 mmol) using the method described for **5a**; the yield was 0.44 g (60%), colorless prisms, mp 144-145 °C (ethyl acetate); ir: 2335 w, 1596 m cm^{-1}; ^1H nmr: δ 2.74 (s, CH_3), 7.12 (d, J = 8.4 Hz, 5-H), 7.28-7.66 (m, 5 PhH), 7.89 (d, J = 8.4 Hz, 2 ArH), 8.19 (d, J = 8.4 Hz, 4-H), 8.36 (d, J = 7.5 Hz, 2 ArH).

Anal. Calcd. for $C_{19}H_{14}BrN_3$: C, 62.65; H, 3.87; N, 11.54. Found: C, 62.82; H, 3.65; N, 11.74.

3-(4-Bromophenyl)-1,6-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridine (**5h**).

This compound was obtained from pyrazolecarbaldehyde **3b** (0.68 g, 2 mmol) and acetophenone (**4b**) (0.24 g, 2 mmol) using the method described for **5a**; the yield was 0.57 g (66%), pale yellow prisms, mp 168-170 °C (ethyl acetate); ir: 2339 w, 1594 m, cm^{-1}; ^1H nmr: δ 7.33-7.59 (m, 6 ArH), 7.65 (d, J = 7.5 Hz, 2 ArH), 7.75 (d, J = 8.4 Hz, 5-H), 7.94 (d, J = 7.8 Hz, 2 ArH), 8.19 (d, J = 8.4 Hz, 2 ArH), 8.36 (d, J = 8.4 Hz, 4-H), 8.47 (d, J = 7.5 Hz, 2 ArH).

Anal. Calcd. for $C_{24}H_{16}BrN_3$: C, 67.62; H, 3.78; N 9.86. Found: C, 67.86; H, 3.50; N, 9.70.

3-(4-Bromophenyl)-6-(4-chlorophenyl)-1-phenyl-1*H*-pyrazolo-[3,4-*b*]pyridine (**5i**).

This compound was obtained from pyrazolecarbaldehyde **3b** (0.68 g, 2 mmol) and 4-chloroacetophenone (**4c**) (0.31 g, 2 mmol) using the method described for **5a**; the yield was 0.68 g (73%), pale yellow prisms, mp 199-201 °C (ethyl acetate); ir: 2335 w, 1591 m cm^{-1}; ^1H nmr: δ 7.30-7.64 (m, 7 ArH), 7.71 (d, J = 8.4 Hz, 5-H), 7.90 (d, J = 7.2 Hz, 2 ArH), 8.08 (d, J = 7.5 Hz, 2 ArH), 8.35 (d, J = 8.4 Hz, 4-H), 8.42 (d, J = 8.1 Hz, 2 ArH).

Anal. Calcd. for $C_{24}H_{15}BrClN_3$: C, 62.56; H, 3.28; N 9.12. Found: C, 62.62; H, 3.38; N, 9.20.

3,6-Bis(4-bromophenyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (**5j**).

This compound was obtained from pyrazolecarbaldehyde **3b** (0.68 g, 2 mmol) and 4-bromoacetophenone (**4d**) (0.40 g, 2 mmol) using the method described for **5a**; the yield 0.71 g (70%), pale yellow prisms, mp 204-205 °C (ethyl acetate); ir: 1593 m, 2336 w cm^{-1}; ^1H nmr: δ 7.34-7.68 (m, 7 ArH), 7.69 (d, J = 8.7 Hz, 5-H), 7.91 (d, J = 8.4 Hz, 2 ArH), 8.02 (d, J = 8.4 Hz, 2 ArH), 8.36 (d, J = 8.7 Hz, 4-H), 8.42 (d, J = 7.5 Hz, 2 ArH).

Anal. Calcd. for $C_{24}H_{15}Br_2N_3$: C, 57.06; H, 2.99; N 8.32. Found: C, 56.68; H, 2.99; N, 8.30.

3-(4-Bromophenyl)-6-(4-methylphenyl)-1-phenyl-1*H*-pyrazolo-[3,4-*b*]pyridine (**5k**).

This compound was obtained from pyrazolecarbaldehyde **3b** (0.68 g, 2 mmol) and 4-methylacetophenone (**4e**) (0.27 g, 2 mmol) using the method described for **5a**; the yield was 0.50 g

(70%) colorless prisms, mp 195-196 °C (ethyl acetate); ir: 2339 w, 1595 m cm^{-1}; ^1H nmr: δ 2.45 (s, CH_3) 7.32-7.65 (m, 7 ArH), 7.72 (d, J = 8.4 Hz, 5-H), 7.93 (d, J = 8.7 Hz, 2 ArH), 8.06 (d, J = 8.4 Hz, 2 ArH), 8.34 (d, J = 8.4 Hz, 4-H), 8.47 (d, J = 8.7 Hz, 2 ArH).

Anal. Calcd. for $C_{25}H_{18}BrN_3$: C, 68.19; H, 4.12; N 9.54. Found: C, 68.24; H, 4.16; N, 9.60.

3-(4-Bromophenyl)-6-(4-methoxyphenyl)-1-phenyl-1*H*-pyrazolo-[3,4-*b*]pyridine (**5l**).

This compound was obtained from pyrazolecarbaldehyde **3b** (0.68 g, 2 mmol) and 4-methoxyacetophenone (**4f**) (0.30 g, 2 mmol) using the method described for **5a**; the yield was 0.67 g (73%) colorless prisms, mp 212-214 °C (ethyl acetate); ir: 2335 w, 1745 m, 1596 m cm^{-1}; ^1H nmr: δ 3.90 (s, OCH_3), 7.03-7.51 (m, 7ArH), 7.65 (d, J = 8.7 Hz, 5-H), 7.93 (d, J = 8.7 Hz, 2 ArH), 8.13 (d, J = 9.0 Hz, 2 ArH), 8.33 (d, J = 8.7 Hz, 4-H), 8.46 (d, J = 8.1 Hz, 2 ArH).

Anal. Calcd. for $C_{25}H_{18}BrN_3O$: C, 65.80; H, 3.98; N, 9.21. Found: C, 65.52; H, 4.21; N, 9.46.

General Procedure for the Preparation of 3-(4-Halophenyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridines **7** and **8**.

A mixture of the appropriate pyrazolecarbaldehyde **3** (2 mmol), the corresponding ketone **4** (2 mmol) and ethanolic potassium hydroxide solution (10 mL, 2%) was heated under reflux for one hour. A colorless solid precipitated and was filtered by suction. It contained two compounds according to tlc analysis (R_f values: 0.95 and 0.73 in toluene). This mixture was dissolved in acetone and separated by column chromatography (18 x 300 mm, eluent toluene/hexane 5:100, eluation volume for **7**: 400-420 mL, for **8**: 240-260 mL); detection by tlc analysis (254 nm).

3-(4-Chlorophenyl)-5,6-dimethyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]-pyridine (**7a**).

This compound was obtained from pyrazolecarbaldehyde **3a** (0.59 g, 2 mmol) and 2-butanone (**6a**) (0.14 g, 2 mmol); the yield was 0.35 g (52%), colorless prisms, mp 161-162 °C (ethyl acetate); ir: 2283 w, 1595 m, 1556 m cm^{-1}; ^1H nmr: δ 2.42 (s, CH_3), 2.64 (s, CH_3), 7.22-7.51 (m, 5 PhH), 7.92 (d, J = 8.4 Hz, 2 ArH), 7.98 (s, 4-H), 8.35 (d, J = 8.4 Hz, 2 ArH); ms: *m/z* (%) 335 (40, M+2), 333 (100, M), 297 (17, M–36), 221 (20), 196 (30), 194 (5), 181 (24).

Anal. Calcd. for $C_{20}H_{16}ClN_3$: C, 71.96; H, 4.83; N, 12.59. Found: C, 71.80; H, 4.78; N, 12.76.

5-Benzyl-3-(4-chlorophenyl)-6-methyl-1-phenyl-1*H*-pyrazolo-[3,4-*b*]pyridine (**7b**).

This compound was obtained from pyrazolecarbaldehyde **3a** (0.59 g, 2 mmol) and 4-phenylbutan-2-one (**6b**) (0.30 g, 2 mmol); the yield was 0.50 g (55%), colorless prisms, mp 174-175 °C (ethyl acetate); ir: 2282 w, 1593 m, 1552 m cm^{-1}; ^1H nmr: δ 2.66 (s, CH_3), 4.20 (s, CH_2), 7.16-7.59 (m, 10 PhH), 7.97 (d, J = 8.4 Hz, 2 ArH), 8.07 (s, 4-H), 8.44 (d, J = 8.4 Hz, 2 ArH).

Anal. Calcd. for $C_{26}H_{20}ClN_3$: C, 76.18; H, 4.92; N, 10.25. Found: C, 76.38; H, 5.14; N, 10.48.

3-(4-Bromophenyl)-5,6-dimethyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]-pyridine (**7c**).

This compound was obtained from pyrazolecarbaldehyde **3b** (0.68 g, 2 mmol) and 2-butanone (**6a**) (0.14 g, 2 mmol); the yield was 0.39 g (51%), colorless prisms, mp 168-170 °C (ethyl acetate); ir: 2284 w, 1596 m, 1554 m cm^{-1}; ^1H nmr: δ 2.45 (s, CH_3), 2.68 (s, CH_3), 7.28-7.62 (m, 5 PhH), 7.89 (d, J = 8.1 Hz, 2 ArH), 8.01 (s, 4-H), 8.38 (d, J = 8.1 Hz, 2 ArH); ms: *m/z* (%) 379 (100, M+2), 377 (87, M), 334 (9), 333 (42).

Anal. Calcd. for $C_{20}H_{16}BrN_3$: C, 63.50; H, 4.26; N 11.11. Found: C, 63.27; H, 4.05; N, 10.92.

5-Benzyl-3-(4-bromophenyl)-6-methyl-1-phenyl-1*H*-pyrazolo-[3,4-*b*]pyridine (**7d**).

This compound was obtained from the pyrazolecarbaldehyde **3b** (0.68 g, 2 mmol) and 4-phenylbutan-2-one (**6b**) (0.30 g, 2 mmol); the yield was 0.48 g (53%), colorless prisms, mp 183-184 °C (ethyl acetate); ir: 2284 w, 1596 m, 1555 m cm^{-1}; ^1H nmr: δ 2.66 (s, CH_3), 4.20 (s, CH_2), 7.16-7.66 (m, 10 PhH), 7.91 (d, J = 8.1 Hz, 2 ArH), 8.06 (s, 4-H) , 8.44 (d, J = 8.1 Hz, 2 ArH).

Anal. Calcd. for $C_{26}H_{20}BrN_3$: C, 68.73; H, 4.44; N 9.25. Found: C, 68.56; H, 4.52; N, 9.30.

3-(4-Chlorophenyl)-6-ethyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]-pyridine (**8a**).

This compound was obtained from pyrazolecarbaldehyde **3a** (0.59 g, 2 mmol) and 2-butanone (**6a**) (0.14 g, 2 mmol); the yield was 0.14 g (21%) colorless prisms, mp 136-138 °C (ethyl acetate); ir: 2283 w, 1595 m, 1556 m cm^{-1}; ^1H nmr: δ 1.44 (t, J = 7.2 Hz, CH_3), 2.98 (q, J = 7.2 Hz, CH_2), 7.14 (d, J = 8.4 Hz, 5-H), 7.27-7.53 (m, 5 ArH), 7.96 (d, J = 8.7 Hz, 2 ArH), 8.21 (d, J = 8.4 Hz, 4-H), 8.42 (d, J = 8.7, 1 ArH); ms: *m/z* (%) 335 (31, M+2), 333 (100, M), 318 (74, M–15), 317 (35), 297 (20, M–36), 282 (14), 181 (27).

Anal. Calcd. for $C_{20}H_{16}ClN_3$: C, 71.96; H, 4.83; N, 12.59. Found: C, 71.84; H, 4.81; N, 12.78.

3-(4-Chlorophenyl)-1-phenyl-6-(2-phenylethyl)-1*H*-pyrazolo-[3,4-*b*]pyridine (**8b**).

This compound was obtained from pyrazolecarbaldehyde **3a** (0.59 g, 2 mmol) and 4-phenylbutan-2-one (**6b**) (0.30 g, 2 mmol); the yield was 0.22 g (24%), colorless prisms, mp 148-150 °C (ethyl acetate); ir: 2285 w, 1593 m, 1553 m cm^{-1}; ^1H nmr: δ 3.22-3.27 (m, CH_2), 3.32-3.38 (m, CH_2), 7.11 (d, J = 8.4 Hz, 5-H), 7.24- 7.57 (m, 10 PhH), 8.00 (d, J = 8.7 Hz, 2 ArH), 8.23 (d, J = 8.4 Hz, 4-H), 8.42 (d, J = 8.4 Hz, 2 ArH).

Anal. Calcd. for $C_{26}H_{20}ClN_3$: C, 76.18; H, 4.92; N, 10.25. Found: C, 76.42; H, 5.20; N, 10.45.

3-(4-Bromophenyl)-6-ethyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]-pyridine (**8c**).

This compound was obtained from pyrazolecarbaldehyde **3b** (0.69 g, 2 mmol) and 2-butanone (**6a**) (0.14 g, 2 mmol); the yield was 0.15 g (20%), colorless prisms, mp 142-143 °C (ethyl acetate); ir: 2283 w, 1595 m, 1554 m cm^{-1}; ^1H nmr: δ 1.44 (t, J = 7.8 Hz, CH_3), 3.01 (q, J = 7.8 Hz, CH_2), 7.14 (d, J = 8.1 Hz, 5-H), 7.17-7.63 (m, 5 ArH), 7.90 (d, J = 8.1 Hz, 2 ArH), 8.21 (d, J = 8.1 Hz, 4-H), 8.42 (d, *J* = 8.1 Hz, 2 ArH); ms: *m/z* (%) 379 (100, M+2), 377 (85, M), 335 (5), 333 (21).

Anal. Calcd. for $C_{20}H_{16}BrN_3$: C, 63.50; H, 4.26; N 11.11. Found: C, 63.74; H, 4.21; N, 10.95.

3-(4-Bromophenyl)-1-phenyl-6-(2-phenylethyl)-1*H*-pyrazolo-[3,4-*b*]pyridine (**8d**).

This compound was obtained from pyrazolecarbaldehyde **3b** (0.68 g, 2 mmol) and 4-phenylbutan-2-one (**6b**) (0.30 g, 2 mmol);

the yield was 0.20 g (22%), colorless prisms, mp 154-155 °C (ethyl acetate); ir: 2287 w, 1594 m, 1556 m cm^{-1}; ^1H nmr: δ 3.22-3.27 (m, CH_2), 3.32-3.38 (m, CH_2), 7.11 (d, J = 8.4 Hz, 5-H), 7.20-7.66 (m, 10 PhH), 7.94 (d, J = 8.4 Hz, 2 ArH), 8.23 (d, J = 8.4 Hz, 4-H), 8.42 (d, J = 8.4 Hz, 2 ArH).

Anal. Calcd. for $C_{26}H_{20}BrN_3$: C, 68.73; H, 4.44; N 9.25. Found: C, 68.65; H, 4.58; N, 9.22.

3-(4-Chlorophenyl)-1,6-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (**10a**).

A solution of pyrazolecarbaldehyde **3a** (0.59 g, 2 mmol) and 3-oxo-3-phenylpropanenitrile (**9a**) (0.29 g, 2 mmol) in ethanol (10 mL) and piperidine (0.5 mL) was heated under reflux for 30 min. The solid obtained on cooling was filtered by suction and washed with cold ethanol (5 mL). The yield was 0.59 g (72%), colorless prisms, mp 256-257 °C (dimethylformamide); ir: 2250 s, 1594 s, 1550 m cm^{-1}; ^1H nmr (CF_3COOD): δ 7.99-8.12 (m, 5 PhH, 4 ArH), 8.19 (d, J = 7.3 Hz, 2 ArH), 8.32 (d, J = 7.4 Hz, 2 ArH), 9.72 (s, 4-H).

Anal. Calcd. for $C_{25}H_{15}ClN_4$: C, 73.80; H, 3.72; N, 13.77. Found: C, 73.62; H, 3.42; N, 13.62.

3,6-Bis(4-chlorophenyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (**10b**).

This compound was obtained from pyrazolecarbaldehyde **3a** (0.59 g, 2 mmol) and 3-(4-chlorophenyl)-3-oxopropanenitrile (**9b**) (0.36 g, 2 mmol) using the method described for **10a**; the yield was 0.65 g (73%), colorless prisms, mp 282-283 °C (dimethylformamide); ir: 2250 s, 1596 s, 1545 m cm^{-1}; ^1H nmr (CF_3COOD): δ 7.89 (d, J = 7.3 Hz, 2 ArH), 7.95-7.98 (m, 5 PhH), 8.04-8.11 (m, 4 ArH), 8.22 (d, J = 7.2 Hz, 2 ArH), 9.56 (s, 4-H).

Anal. Calcd. for $C_{25}H_{14}Cl_2N_4$: C, 68.04; H, 3.20; N 12.70. Found: C, 68.81; H, 3.13; N, 12.95.

6-(4-Bromophenyl)-3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazolo-[3,4-*b*]pyridine-5-carbonitrile (**10c**).

This compound was obtained from pyrazolecarbaldehyde **3a** (0.59 g, 2 mmol) and 3-(4-bromophenyl)-3-oxopropanenitrile (**9c**) (0.45 g, 2 mmol) using the method described for **10a**; the yield was 0.69 g (71%) colorless prisms, mp 290-291 °C (dimethylformamide); ir: 2250 s, 1593 s, 1545 m cm^{-1}; ^1H nmr (CF_3COOD): δ 7.99-8.11 (m, 5 PhH, 4 ArH), 8.24-8.28 (m, 4 ArH), 9.60 (s, 4-H).

Anal. Calcd. for $C_{25}H_{14}BrClN_4$: C, 61.18; H, 2.99; N, 11.53. Found: C, 61.25; H, 3.10; N, 11.74.

3-(4-Chlorophenyl)-6-(4-methylphenyl)-1-phenyl-1*H*-pyrazolo-[3,4-*b*]pyridine-5-carbonitrile (**10d**).

This compound was obtained from pyrazolecarbaldehyde **3a** (0.59 g, 2 mmol) and 3-(4-methylphenyl)-3-oxopropanenitrile (**9d**) (0.32 g, 2 mmol) using the method described for **10a**; the yield was 0.59 g (70%), mp 285-286 °C (dimethylformamide); calorimetric data for the thermolysis: mp at 286.3 °C onset, 287.5 °C maximum, ΔH = 101 J/g, mp at 412.6 °C onset, 413.9 °C maximum, ΔH = 114 J/g, decomposition at 420.1 °C onset, 424.3 °C maximum, ΔH = –140 J/g; ir: 3590-3270 m, 3062 w, 2225 m, 1595 s, 1543 w cm^{-1}; ^1H nmr (CF_3COOH): δ 2.85 (s, CH_3), 7.83 (d, J = 7.4 Hz, 2 ArH), 8.01-8.10 (m, 5 PhH, 4 ArH), 8.29 (d, J = 7.2 Hz, 2 ArH), 9.73 (s, 4-H).

Anal. Calcd. for $C_{26}H_{17}ClN_4$: C, 74.19; H, 4.07; N, 13.31. Found: C, 74.07; H, 3.86; N, 13.18.

3-(4-Bromophenyl)-1,6-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (**10e**).

This compound was obtained from pyrazolecarbaldehyde **3b** (0.68 g, 2 mmol) and 3-oxo-3-phenylpropanenitrile (**9a**) (0.29 g, 2 mmol) using the method described for **10a**; the yield was 0.63 g (70%) colorless prisms, mp 268-269 °C (dimethylformamide); ir: 2221 s, 1596 s, 1543 m cm^{-1}; ^1H nmr (CF_3COOD): δ 7.81-7.98 (m, 5 PhH, 2 ArH), 8.00 (d, J = 7.2 Hz, 2 ArH), 8.02-8.13 (m, 4 ArH), 9.61 (s, 4-H).

Anal. Calcd. for $C_{25}H_{15}BrN_4$: C, 66.53; H, 3.35; N, 12.41. Found: C, 66.60; H, 3.48; N, 12.68.

3-(4-Bromophenyl)-6-(4-chlorophenyl)-1-phenyl-1*H*-pyrazolo-[3,4-*b*]pyridine-5-carbonitrile (**10f**).

This compound was obtained from pyrazolecarbaldehyde **3b** (0.68 g, 2 mmol) and 3-(4-chlorophenyl)-3-oxopropanenitrile (**9b**) (0.36 g, 2 mmol) using the method described for **10a**; the yield was 0.67 g (69%), colorless prisms, mp 289-290 °C (dimethylformamide); ir: 2229 s, 1595 s, 1541 m cm^{-1}; ^1H nmr (CF_3COOD): δ 7.85 (d, J = 7.4 Hz, 2 ArH), 7.90-7.94 (m, 4 ArH), 7.98-8.11(m, 5 PhH, 2 ArH), 9.53 (s, 4-H).

Anal. Calcd. for $C_{25}H_{14}Br_{Cl}N_4$: C, 61.18; H, 2.99; N, 11.53. Found: C, 61.20; H, 3.17; N, 11.74.

3,6-Bis(4-bromophenyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (**10g**).

This compound was obtained from pyrazolecarbaldehyde **3b** (0.68 g, 2 mmol) and 3-(4-bromophenyl)-3-oxopropanenitrile (**9c**) (0.45 g, 2 mmol) using the method described for **10a**; the yield was 0.74 g (70%) colorless prisms, mp 300-301 °C (dimethylformamide); ir: 2225 s, 1593 s, 1541m cm^{-1}; ^1H nmr (CF_3COOD): δ 7.94-8.05 (5 PhH, 6 ArH), 8.21 (d, J = 7.2 Hz, 2 ArH), 9.54 (s, 4-H).

Anal. Calcd. For $C_{25}H_{14}Br_2N_4$: C, 56.63; H, 2.66; N, 10.57. Found: C, 56.87; H, 2.55; N, 10.56.

3-(4-Bromophenyl)-6-(4-methylphenyl)-1-phenyl-1*H*-pyrazolo-[3,4-*b*]pyridine-5-carbonitrile (**10h**).

This compound was obtained from pyrazolecarbaldehyde **3b** (0.68 g, 2 mmol) and 3-(4-methylphenyl)-3-oxopropanenitrile (**9d**) (0.32 g, 2 mmol) using the method described for **10a**; the yield was 0.65 g (70%), colorless prisms, mp 292-293 °C (dimethylformamide); calorimetric data for the thermolysis: mp at 296.7 °C onset, 298.2 °C maximum, ΔH = 90 J/g, decomposition at 372.4 °C onset, 378.4 °C maximum, ΔH = –55 J/g, mp at 418.7 °C onset, 419.2 °C maximum, ΔH = 3 J/g, decomposition at 420.5 °C onset, 424.6 °C maximum, ΔH = –228 J/g; ir: 3550-3270 s, 3064 w, 2225 m, 1605 sh, 1594s, 1542 m cm^{-1}; ^1H nmr (CF_3COOH): δ 2.86 (s, CH_3), 7.85 (d, J = 7.4 Hz, 2 ArH), 8.04-8.11 (m, 5 PhH, 2 ArH), 8.22 (d, J = 7.2 Hz, 4 ArH), 9.74 (s, 4-H).

Anal. Calcd. for $C_{26}H_{17}BrN_4$: C, 67.07; H, 3.68; N, 12.04. Found: C, 67.95; H, 3.87; N, 12.28.

Ethyl 3-(4-Chlorophenyl)-6-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]-pyridine-5-carboxylate (**12a**).

A solution of pyrazolecarbaldehyde **3a** (0.60 g, 2 mmol) and ethyl 3-oxobutanoate (**11a**) (0.26 g, 2 mmol) in ethanol (10 mL) and piperidine (0.5 mL) was heated under reflux for 4 hours. The solid obtained on cooling was filtered by suction and washed with cold ethanol (5 mL). The yield was 0.31 g (61%), colorless prisms, mp 119-120 °C (ethyl acetate); ir: 1730 s, 1592 s, 1556 m cm^{-1}; ^1H

nmr: δ 1.44 (t, J = 7.2 Hz, CH_3), 3.01 (s, CH_3), 4.41 (q, J = 7.2 Hz, CH_2), 7.33-7.57 (m, 5 PhH), 7.97 (d, J = 8.4 Hz, 2 ArH), 8.36 (d, J = 8.4 Hz, 2 ArH), 8.90 (s, 4-H).

Anal. Calcd. for $C_{22}H_{18}ClN_3O_2$: C, 82.61; H, 5.67; N, 13.14. Found: C, 82.82; H, 5.56; N, 13.28.

Ethyl 3-(4-Chlorophenyl)-1,6-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate (**12b**).

This compound was obtained from pyrazolecarbaldehyde **3a** (0.60 g, 2 mmol) and ethyl 3-oxo-3-phenylpropanoate (**11b**) (0.38 g, 2 mmol) using the method described for **12a**; the yield was 0.52 g (57%), colorless prisms, mp 173-174 °C (ethyl acetate); ir: 1720 s, 1596 s, 1550 m cm^{-1}; ^1H nmr: δ 1.04 (t, J = 7.2 Hz, CH_3), 4.15 (q, J = 7.2 Hz, CH_2), 7.29-7.67 (m, 10 PhH), 8.01 (d, J = 8.4 Hz, 2 ArH), 8.40 (d, J = 7.8 Hz, 2 ArH), 8.81 (s, 4-H).

Anal. Calcd. for $C_{27}H_{20}ClN_3O_2$: C, 71.44; H, 4.44; N 9.26. Found: C, 71.63; H, 4.40; N, 9.35.

Ethyl 3-(4-Bromophenyl)-6-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]-pyridine-5-carboxylate (**12c**).

This compound was obtained from pyrazolecarbaldehyde **3b** (0.68 g, 2 mmol) and ethyl 3-oxobutanoate (**11a**) (0.26 g, 2 mmol) using the method described for **12a**; the yield was 0.53 g (60%) colorless prisms, mp 128-129 °C (ethyl acetate); ir: 1706 s, 1593 s, 1552 m cm^{-1}; ^1H nmr: δ 1.43 (t, J = 7.2 Hz, CH_3), 2.99 (s, CH_3), 4.40 (q, J = 7.2 Hz, CH_2), 7.30-7.64 (m, 5 PhH) 7.89 (d, J = 8.4 Hz, 2 ArH), 8.35 (d, J = 7.8 Hz, 2 ArH), 8.87 (s, 4-H).

Anal. Calcd. for $C_{22}H_{18}BrN_3O_2$: C, 60.56; H, 4.16; N; 9.63. Found: C, 60.56; H, 4.35; N, 9.72.

Ethyl 3-(4-Bromophenyl)-1,6-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate (**12d**).

This compound was obtained from pyrazolecarbaldehyde **3b** (0.68 g, 2 mmol) and ethyl 3-oxo-3-phenylpropanoate (**11b**) (0.38 g, 2 mmol) using the method described for **12a**; the yield was 0.55 g (55%), colorless prisms, mp 180-181 °C (ethyl acetate); ir: 1712 s, 1595 s, 1548 m cm^{-1}; ^1H nmr: δ 1.02 (t, J = 7.2 Hz, CH_3), 4.14 (q, J = 7.2 Hz, CH_2), 7.28-7.69 (m, 10 PhH), 7.94 (d, J = 8.7 Hz, 2 ArH), 8.38 (d, J = 8.1 Hz, 2 ArH), 8.79 (s, 4-H).

Anal. Calcd. for $C_{27}H_{20}BrN_3O_2$: C, 65.07; H, 4.04; N, 8.43. Found: C, 65.10; H, 4.13; N, 8.52.

Ethyl 3-(4-Chlorophenyl)-6-oxo-1-phenyl-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate (**14a**).

A solution of pyrazolecarbaldehyde **3a** (0.60 g, 2 mmol) and diethyl malonate (**13**) (0.32 g, 2 mmol) in ethanol (10 mL) and piperidine (0.5 mL) was heated under reflux for 1 hour. The solid obtained on cooling was collected by suction filtration and washed with cold ethanol (5 mL). The yield was 0.61 g (78%) colorless prisms, mp 133-134 °C (ethyl acetate); ir: 3450 w, 1674 s, 1670 sh, 1619 w, 1595 m cm^{-1}; ir (nujol): 2950-2850 s, 1673 m, 1660 m cm^{-1}; ^1H nmr: δ 1.47 (t, J = 7.2 Hz, CH_3), 4.49 (q, J = 7.2 Hz, CH_2), 7.31 (t, J = 7.1 Hz, 1 ArH), 7.47-7.53 (m, 4 ArH), 7.90 (d, J = 8.4 Hz, 2 ArH), 8.27 (d, J = 8.4 Hz, 2 ArH), 8.82 (s, 4-H), 12.06 (s, NH, exchangeable by deuterium oxide); ^{13}C nmr (DMSO-d_6): δ 14.5 (Me), 61.9 (CH_2), 109.0, 109.4, 121.5, 126.9, 129.2, 129.6, 129.7, 130.8, 134.3, 136.5, 138.8, 144.4, 150.9 (14 ArC), 163.2 (ester-C=O), 166.8 (amide-C=O); ms: *m/z* (%) 395 (24, M+2), 393 (100, M), 323 (10), 321 (38).

Anal. Calcd. for $C_{21}H_{16}ClN_3O_3$: C, 64.05; H, 4.10; N, 10.67. Found: C, 64.11; H, 4.34; N, 10.86.

Ethyl 3-(4-Bromophenyl)-6-oxo-1-phenyl-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate (**14b**).

This compound was obtained from pyrazolecarbaldehyde **3b** (0.68 g, 2 mmol) and diethyl malonate (**13**) (0.32 g, 2 mmol) using the method described for **14a**; the yield was 0.49 g (62%) colorless prisms, mp 142-143 °C (ethyl acetate); ir: 3500-3200 m, b, 1681 s, 1617m, 1596m, 1561 w cm^{-1}; ^1H nmr: δ 1.49 (t, J = 7.2 Hz, CH_3), 4.49 (q, J = 7.2 Hz, CH_2), 7.29-7.65 (m, 5 PhH), 7.84 (d, J = 8.7 Hz, 2 ArH), 8.26 (d, J = 8.1 Hz, 2 ArH), 8.83 (s, 4-H), 12.05 (s, NH, exchangeable by deuterium oxide); ms: *m/z* (%) 439 (33, M+2), 437 (36, M), 379 (88), 377 (100, M–60), 335 (31), 333 (79).

Anal. Calcd. for $C_{21}H_{16}BrN_3O_3$: C, 57.55; H, 3.68; N, 9.59. Found: C, 57.62; H, 3.60; N, 9.65.

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