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An efficient cascade synthesis of substituted 6,9-dihydro-1*H*-pyrazolo[3,4-*f*]quinoline-8-carbonitriles

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Abstract: The synthesis of pyrazolo[3,4-*f*]quinoline-8-carbonitriles **4a–h** and **6a–k** involves the reaction of an aromatic aldehyde, 1*H*-indazol-6-amine and 3-(1*H*-indol-3-yl)-3-oxopropanenitrile or 3-oxo-3-arylpropanenitrile in ethanol under mild conditions.

Keywords: catalyst-free; multi-component domino reactions; pyrazoloquinoline.

Introduction

Multi-component domino reactions (MDRs), as the effective approach to improve synthetic efficiency, have been successfully applied to the synthesis of various heterocycles. These reactions can involve high levels of diversity giving rise to complex structures by simultaneous formation of three or more bonds from simple substrates [1–3]. Such transformations can avoid tedious steps of protection and deprotection of functional groups and isolation of intermediates, thereby dramatically reducing production of waste. Recently, various MDRs have efficiently been used for the construction of heterocyclic compounds with biological activities [4–6].

The indole moiety has been found in various biologically active compounds [7, 8]. Many indole alkaloids are recognized as one of the rapidly growing groups of marine invertebrate metabolites for their broad spectrum of biological properties [9, 10], such as anticancer, antitumour [11], anti-inflammatry, hypoglycemic, analgesic and antipyretic activities. On the other hand, pyrazole-fused quinolines are also useful heterocycles that possess various bioactivities including antimalarial [12], analgesic [13], antipsychotic [14] and antimicrobial properties [15]. Many procedures have been reported to synthesize such compounds in the past few years [16–18].

In continuation of our interest in the synthesis of new heterocyclic compounds by one-pot multicomponent reactions [19–21], herein we report an efficient synthetic approach to substituted pyrazolo[3,4-*f*]quinolines **4a–h** and **6a–k** (Schemes 1 and 2). The synthesis was conducted by reacting an aromatic aldehyde, 1*H*-indazol-6-amine and 3-(1*H*-indol-3-yl)-3-oxopropanenitrile or 3-oxo-3-phenylpropanenitrile in ethanol in the absence of any metal catalyst.

Results and discussion

Our initial investigations focused on the three-component reaction of 1*H*-indazol-6-amine (**1**), benzaldehyde (**2a**) and 3-(1*H*-indol-3-yl)-3-oxopropanenitrile (**3**) as a simple model for optimization of the reaction conditions (Scheme 1).

In the absence of any catalyst, the reaction conducted under reflux conditions furnished product **4a** in the yield of 88%. Different bases, including NaOH, $NaHCO_3$, piperidine and Et_3N, were used in an attempt to promote the reaction. However, under these conditions the yield of **4a** was not improved. Other solvents, including methanol, tetrahydrofuran, acetonitrile and dioxane, were also tested but ethanol proved to be superior. Furthermore, the analytically pure product precipitated from the ethanolic solution upon cooling the mixture.

With the optimized reaction conditions in hand, commercially available aromatic aldehydes **2** bearing either electron-withdrawing or electron-donating functional groups such as chloro, bromo, nitro and alkyl, were all found to be suitable for the reaction with 1*H*-indazol-6-amine (**1**) and 3-(1*H*-indol-3-yl)-3-oxopropanenitrile (**3**) to obtain pyrazolo[3,4-*f*]quinoline derivatives. It was noted that aromatic aldehydes with an electron-donating group always require more time to react. The reaction of 3-oxo-3-phenylpropanenitrile (**5**) with aromatic aldehydes **2** and 1*H*-indazol-6-amine also furnished the expected

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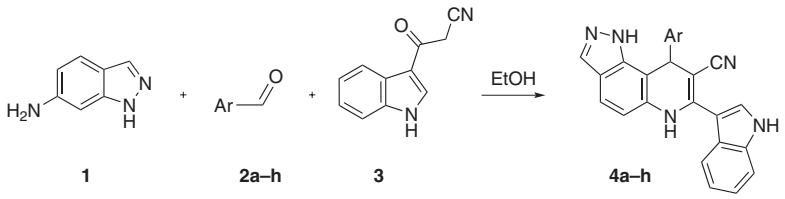
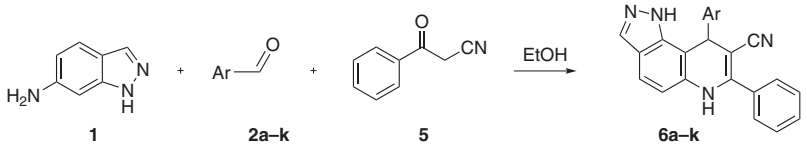


1 **2a–h** **3** **4a–h**

a: Ar = Ph
b: Ar = 4-ClC_6H_4
c: Ar = 4-$NO_2C_6H_4$
4d: Ar = 4-MeC_6H_4
4e: Ar = 4-$OMeC_6H_4$
4f: Ar = 3-ClC_6H_4
4g: Ar = 3-BrC_6H_4
4h: Ar = 3,4-$Cl_2C_6H_3$

Scheme 1



1 **2a–k** **5** **6a–k**

6a: Ar = Ph
6b: Ar = 4-ClC_6H_4
6c: Ar = 4-$NO_2C_6H_4$
6d: Ar = 4-MeC_6H_4
6e: Ar = 4-$OMeC_6H_4$
6f: Ar = 3-ClC_6H_4
6g: Ar = 3-BrC_6H_4
6h: Ar = 2-ClC_6H_4
6i: Ar = 2-$OMeC_6H_4$
6j: Ar = 3,4-$Cl_2C_6H_3$
6k: Ar = 2-furanyl

Scheme 2

pyrazolo[3,4-*f*]quinoline-8-carbonitriles **6a–k** in high yields (Scheme 2). All products were characterized by ^{1}H NMR, ^{13}C NMR, IR and HRMS spectral data.

A plausible reaction mechanism for this reaction is illustrated in Scheme 3 using 3-oxo-3-arylpropanenitrile (**5**) as the substrate. The initial Knoevenagel condensation between **2** and **5** generates an intermediate product **A**. Then another intermediate product **B** is generated in the Michael addition reaction of 1*H*-indazol-6-amine (**1**) to **A**. Compound **B** undergoes tautomerization to **C**, the intramolecular cyclization-dehydration of which generates the final intermediate product **D** which is the direct precursor to the observed pyrazolo[3,4-*f*]quinoline **6**.

Conclusion

A highly efficient method for the synthesis of 6,9-dihydro-1*H*-pyrazolo[3,4-*f*]quinoline-8-carbonitrile derivatives was developed. This procedure has several attractive characteristics such as ready availability of starting materials, mild reaction conditions, high yields and operational simplicity.

Experimental

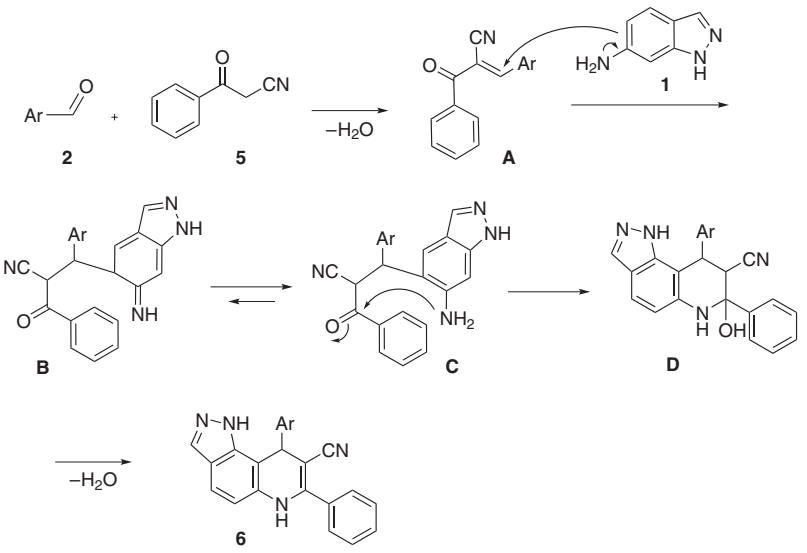
Melting points were determined in open capillaries and are uncorrected. IR spectra were taken on a Fourier-transform infrared (FT-IR)-Tensor 27 spectrometer in KBr pellets. ^{1}H NMR spectra (400 MHz) and ^{13}C NMR spectra (100 MHz) were measured on a Bruker DPX spectrometer in DMSO-d_6. ^{1}H NMR and ^{13}C NMR spectra for all compounds **4a–h**, **6a–k** are shown in supplementary material. The exact mass measurements were carried out using a Bruker micro-TOF-Q-MS analyzer.

General procedure for the synthesis of compounds 4a–4h and 6a–6k

A dry 50-mL flask was charged with 1*H*-indazol-6-amine **1** (1.0 mmol), aromatic aldehyde **2** (1.0 mmol), 3-(1*H*-indol-3-yl)-3-oxopropanenitrile **3** (1.0 mmol) or 3-oxo-3-arylpropanenitrile **5** (1.0 mmol) and EtOH (10 mL). The mixture was stirred at reflux for 3–8 h. After completion of the reaction, as indicated by thin-layer chromatography, the solid product **4** or **6** was obtained after the mixture was cooled to room temperature.

7-(1*H*-Indol-3-yl)-9-phenyl-6,9-dihydro-1*H*-pyrazolo[3,4-*f*]quinoline-8-carbonitrile (4a) White powder; yield 88%; mp >300°C; ^{1}H NMR: δ 12.87 (s, 1H, NH), 11.74 (s, 1H, NH), 9.83 (s, 1H, NH), 7.98 (s, 1H, ArH), 7.83 (d, *J* = 2.7 Hz, 1H, ArH), 7.59 (d, *J* = 8.6 Hz, 1H, ArH), 7.55–7.43 (m, 4H, ArH), 7.35–7.32 (m, 2H, ArH), 7.23–7.20 (m, 2H, ArH), 7.15–7.12 (m, 1H, ArH), 7.05 (d, *J* = 8.6 Hz, 1H, ArH), 5.29 (s, 1H, CH); ^{13}C NMR: δ 146.3, 145.6, 136.5, 135.1, 129.0, 127.8, 127.5, 127.4, 125.7, 122.9, 122.5, 120.4, 120.3, 112.6, 112.5, 108.9, 103.2, 78.1, 56.5, 41.1, 19.0; IR: 3459, 3351, 3252, 218.05, 1632, 1604, 1538, 1490, 1440, 1340, 1235, 937, 745 cm^{-1}. ESI-HR-MS. Calcd for $C_{25}H_{17}N_5$ ([M-H]$^-$): *m/z* 386.1406. Found: *m/z* 386.1396.

9-(4-Chlorophenyl)-7-(1*H*-indol-3-yl)-6,9-dihydro-1*H*-pyrazolo[3,4-*f*]quinoline-8-carbonitrile (4b) White powder; yield 80%; mp >300°C; ^{1}H NMR: δ 12.90 (s, 1H, NH), 11.77 (s, 1H, NH), 9.89 (s, 1H, NH), 8.01 (s, 1H, ArH), 7.86 (d, *J* = 2.8 Hz, 1H, ArH), 7.62



Scheme 3

(d, *J* = 8.6 Hz, 1H, ArH), 7.56–7.48 (m, 4H, ArH), 7.43 (d, *J* = 8.5 Hz, 2H, ArH), 7.24–7.21 (m, 1H, ArH), 7.17–7.14 (m, 1H, ArH), 7.08 (d, *J* = 8.6 Hz, 1H, ArH), 5.35 (s, 1H, CH); ^{13}C NMR: δ 153.8, 152.0, 145.7, 145.1, 136.5, 135.1, 132.1, 131.0, 129.3, 129.1, 127.9, 125.6, 122.7, 122.5, 121.2, 120.6, 120.4, 113.3, 112.6, 108.8, 102.7, 77.8, 40.5; IR: 3402, 3270, 2193, 1635, 1610, 1537, 1489, 1445, 1340, 1233, 932, 745 cm^{-1}. ESI-HR-MS. Calcd for $C_{25}H_{16}ClN_5$ ([M-H]$^-$): *m/z* 420.1016. Found: *m/z* 420.1015.

7-(1*H*-Indol-3-yl)-9-(4-nitrophenyl)-6,9-dihydro-1*H*-pyrazolo[3,4-*f*]quinoline-8-carbonitrile (4c) Yellow powder; yield 81%; mp > 300°C; ^{1}H NMR: δ 12.96 (s, 1H, NH), 11.79 (s, 1H, NH), 10.00 (s, 1H, NH), 8.26 (d, *J* = 8.8 Hz, 2H, ArH), 8.01 (s, 1H, ArH), 7.87 (d, *J* = 2.8 Hz, 1H, ArH), 7.72 (d, *J* = 8.8 Hz, 2H, ArH), 7.65 (d, *J* = 8.6 Hz, 1H, ArH), 7.56–7.52 (m, 2H, ArH), 7.24–7.21 (m, 1H, ArH), 7.17–7.10 (m, 2H, ArH), 5.52 (s, 1H, CH); ^{13}C NMR: δ 153.0, 147.0, 146.1, 136.5, 128.7, 128.0, 125.6, 124.5, 122.5, 122.4, 121.0, 120.5, 120.4, 112.6, 108.6, 76.9, 41.1; IR: 3409, 3226, 2199, 1637, 1605, 1540, 1493, 1447, 1341, 1233, 935, 749 cm^{-1}. ESI-HR-MS. Calcd for $C_{25}H_{16}N_6O_2$ ([M-H]$^-$): *m/z* 431.1256. Found: *m/z* 431.1257.

7-(1*H*-Indol-3-yl)-9-(*p*-tolyl)-6,9-dihydro-1*H*-pyrazolo[3,4-*f*]quinoline-8-carbonitrile (4d) White crystals; yield 86%; mp 268–270°C; ^{1}H NMR: δ 12.83 (s, 1H, NH), 11.74 (s, 1H, NH), 9.79 (s, 1H, NH), 7.97 (s, 1H, ArH), 7.82 (d, *J* = 2.7 Hz, 1H, ArH), 7.58–7.51 (m, 3H, ArH), 7.38 (d, *J* = 8.0 Hz, 2H, ArH), 7.23–7.20 (m, 1H, ArH), 7.15–7.12 (m, 3H, ArH), 7.04 (d, *J* = 8.6 Hz, 1H, ArH), 5.24 (s, 1H, CH), 2.24 (s, 3H, CH_3); ^{13}C NMR: δ 145.4, 143.5, 136.5, 135.0, 129.6, 127.7, 127.5, 125.7, 122.9, 122.5, 120.4, 120.2, 112.6, 112.5, 109.0, 103.5, 78.3, 56.6, 40.7, 21.1, 19.0; IR: 3337, 3258, 2186, 1632, 1608, 1538, 1489, 1441, 1341, 1235, 933, 751 cm^{-1}. ESI-HR-MS. Calcd for $C_{26}H_{19}N_5$ ([M-H]$^-$): *m/z* 400.1562. Found: *m/z* 400.1559.

7-(1*H*-Indol-3-yl)-9-(4-methoxyphenyl)-6,9-dihydro-1*H*-pyrazolo[3,4-*f*]quinoline-8-carbonitrile (4e) White crystals; yield 79%; mp 270–273°C; ^{1}H NMR: δ 12.84 (s, 1H, NH), 11.73 (s, 1H, NH), 9.78 (s, 1H, NH), 7.97 (s, 1H, ArH), 7.82 (d, *J* = 2.7 Hz, 1H, ArH), 7.58–7.50 (m, 3H, ArH), 7.41 (d, *J* = 8.6 Hz, 2H, ArH), 7.23–7.19 (m, 1H, ArH), 7.17–7.12 (m, 1H, ArH), 7.03 (d, *J* = 8.6 Hz, 1H, ArH), 6.89 (d, *J* = 8.7 Hz, 2H, ArH), 5.23 (s, 1H, CH), 3.71 (s, 3H, CH_3); ^{13}C NMR: δ 158.7, 145.3, 138.6, 136.5, 134.9, 134.6, 133.3, 128.6, 127.7, 125.7, 122.9, 122.4, 120.4, 120.3, 120.1, 115.2, 114.4, 112.6, 112.5, 109.0, 103.6, 78.5, 55.5; IR: 3382, 3254, 2197, 1635, 1605, 1535, 1492, 1446, 1340, 1235, 938, 746 cm^{-1}. ESI-HR-MS. Calcd for $C_{26}H_{19}N_5O$ ([M-H]$^-$): *m/z* 416.1511. Found: *m/z* 416.1501.

9-(3-Chlorophenyl)-7-(1*H*-indol-3-yl)-6,9-dihydro-1*H*-pyrazolo-[3,4-*f*]quinoline-8-carbonitrile (4f) White powder; yield 84%; mp 295–296°C; ^{1}H NMR: δ 12.95 (s, 1H, NH), 11.79 (s, 1H, NH), 9.93 (s, 1H, NH), 8.02 (s, 1H, ArH), 7.88 (d, *J* = 2.8 Hz, 1H, ArH), 7.64 (d, *J* = 8.6 Hz, 1H, ArH), 7.55 (t, *J* = 7.8 Hz, 3H, ArH), 7.46–7.37 (m, 2H, ArH), 7.31 (d, *J* = 7.9 Hz, 1H, ArH), 7.23 (t, *J* = 7.6 Hz, 1H, ArH), 7.16 (t, *J* = 7.5 Hz, 1H, ArH), 7.09 (d, *J* = 8.6 Hz, 1H, ArH), 5.35 (s, 1H, CH); ^{13}C NMR: δ 148.5, 145.9, 136.5, 135.1, 133.6, 131.1, 127.9, 127.4, 127.2, 126.3, 125.6, 122.6, 122.5, 120.7, 120.4, 120.3, 112.7, 112.6, 108.7, 102.5, 77.5, 40.9; IR: 3418, 3234, 2209, 1634, 1610, 1536, 1490, 1449, 1350, 1233, 936, 750 cm^{-1}. ESI-HR-MS. Calcd for $C_{25}H_{16}ClN_5$ ([M-H]$^-$): *m/z* 420.1016. Found: *m/z* 420.1000.

9-(3-Bromophenyl)-7-(1*H*-indol-3-yl)-6,9-dihydro-1*H*-pyrazolo-[3,4-*f*]quinoline-8-carbonitrile (4g) White powder; yield 81%; mp >300°C; ^{1}H NMR: δ 12.95 (s, 1H, NH)), 11.78 (s, 1H, NH), 9.93 (s, 1H, NH), 8.02 (s, 1H, ArH), 7.87 (d, *J* = 2.8 Hz, 1H, ArH), 7.70 (s, 1H, ArH), 7.63 (d, *J* = 8.6 Hz, 1H, ArH), 7.56–7.53 (m, 2H, ArH), 7.48–7.43 (m, 2H, ArH), 7.34–7.31 (m, 1H, ArH), 7.24–7.21 (m, 1H, ArH), 7.17–7.14 (m, 1H, ArH), 7.08 (d, *J* = 8.6 Hz, 1H, ArH), 5.32 (s, 1H, CH); ^{13}C NMR: δ 148.5, 145.9, 136.5, 135.1, 131.5, 130.3, 130.1, 127.9, 126.7, 125.6, 122.6, 122.5, 122.4, 120.7, 120.4, 120.3, 112.7, 112.6, 108.7, 102.5, 77.6, 40.9; IR: 3406, 3237, 2209, 1634, 1610, 1536, 1491, 1449, 1350, 1234, 936, 750 cm^{-1}. ESI-HR-MS. Calcd for $C_{25}H_{16}BrN_5$ ([M-H]$^-$): *m/z* 464.0511. Found: *m/z* 464.0521.

9-(3,4-Dichlorophenyl)-7-(1*H*-indol-3-yl)-6,9-dihydro-1*H*-pyrazolo[3,4-*f*]quinoline-8-carbonitrile (4h) White powder; yield 83%; mp 295–296°C; ^{1}H NMR: δ 12.93 (s, 1H, NH), 11.79 (s, 1H, NH), 9.95 (s, 1H, NH), 8.02 (s, 1H, ArH), 7.88 (d, *J* = 2.8 Hz, 1H, ArH), 7.72 (d, *J* = 2.1 Hz, 1H, ArH), 7.64 (d, *J* = 8.3 Hz, 2H, ArH), 7.56–7.52 (m, 2H, ArH), 7.42–7.40 (m, 1H, ArH), 7.24–7.21 (m, 1H, ArH), 7.18–7.15

(m, 1H, ArH), 7.08 (d, J = 8.6 Hz, 1H, ArH), 5.35 (s, 1H, CH); ^{13}C NMR: δ 153.7, 150.4, 146.9, 145.9, 136.9, 136.5, 135.0, 131.6, 130.1, 128.0, 126.7, 125.6, 123.0, 122.7, 122.5, 120.9, 120.5, 120.3, 112.6, 108.6, 102.1, 77.2; IR: 3422, 3216, 2201, 1635, 1606, 1538, 1486, 1458, 1340, 1231, 936, 746 cm^{-1}. ESI-HR-MS. Calcd for $C_{25}H_{15}Cl_2N_5$ ([M-H]$^-$): *m/z* 454.0626. Found: *m/z* 454.0607.

7,9-Diphenyl-6,9-dihydro-1*H*-pyrazolo[3,4-*f*]quinoline-8-carbonitrile (6a) White powder; yield 84%; mp 172–184°C; ^{1}H NMR: δ 12.85 (s, 1H, NH), 9.95 (s, 1H, NH), 7.96 (s, 1H), 7.64–7.58 (m, 3H, ArH), 7.56 (m, 4H, ArH), 7.44 (d, J = 7.7 Hz, 2H, ArH), 7.32 (m, 2H, ArH), 7.20 (m, 1H, ArH), 7.01 (d, J = 8.6 Hz, 1H, ArH), 5.27 (s, 1H, CH); ^{13}C NMR: δ 150.6, 145.8, 138.5, 134.8, 134.7, 134.2, 130.8, 129.1, 129.0, 128.9, 127.6, 127.5, 121.9, 120.6, 120.5, 112.4, 102.8, 79.3, 56.5, 41.0, 19.0; IR: 3273, 2191, 1633, 1607, 1540, 1495, 1355, 1283, 945, 917, 726 cm^{-1}. ESI-HR-MS. Calcd for $C_{23}H_{16}N_4$ ([M-H]$^-$): *m/z* 347.1297. Found: *m/z* 347.1280.

9-(4-Chlorophenyl)-7-phenyl-6,9-dihydro-1*H*-pyrazolo[3,4-*f*]quinoline-8-carbonitrile (6b) White powder; yield 80%; mp 221–226°C; ^{1}H NMR: δ 12.87 (s, 1H, NH), 10.00 (s, 1H, NH), 7.98 (s, 1H, ArH), 7.59 (m, 6H, ArH), 7.42 (d, J = 10.5 Hz, 4H, ArH), 7.02 (d, J = 8.2 Hz, 1H, ArH), 5.31 (s, 1H, CH); ^{13}C NMR: δ 150.2, 144.1, 138.0, 134.3, 133.6, 131.7, 130.4, 129.0, 128.6, 128.4, 121.2, 120.3, 120.1, 111.9, 101.7, 78.5; IR: 3294, 2185, 1629, 1599, 1533, 1497, 1357, 1283, 945, 916, 781 cm^{-1}. ESI-HR-MS. Calcd for $C_{23}H_{15}ClN_4$ ([M-H]$^-$): *m/z* 381.0907. Found: *m/z* 381.0891.

9-(4-Nitrophenyl)-7-phenyl-6,9-dihydro-1*H*-pyrazolo[3,4-*f*]quinoline-8-carbonitrile (6c) Yellow powder; yield 81%; mp 246–249°C; ^{1}H NMR: δ 12.93 (s, 1H, NH), 10.11 (s, 1H, NH), 8.23 (d, J = 8.5 Hz, 2H, ArH), 7.99 (s, 1H, ArH), 7.70–7.57 (m, 8H, ArH), 7.05 (d, J = 8.6 Hz, 1H, ArH), 5.49 (s, 1H, CH); ^{13}C NMR: δ 152.3, 151.2, 147.1, 138.5, 134.9, 134.8, 133.9, 131.0, 129.1, 128.9, 128.8, 124.5, 121.5, 121.2, 120.7, 112.5, 101.4, 78.2, 40.9; IR: 3471, 3385, 3259, 2192, 1634, 1605, 1540, 1509, 1350, 1276, 947, 914, 772 cm^{-1}. ESI-HR-MS. Calcd for $C_{23}H_{15}N_5O_2$ ([M-H]$^-$): *m/z* 392.1147. Found: *m/z* 392.1136.

7-Phenyl-9-(*p*-tolyl)-6,9-dihydro-1*H*-pyrazolo[3,4-*f*]quinoline-8-carbonitrile (6d) White crystals; yield 86%; mp 232–234°C; ^{1}H NMR: δ 12.83 (s, 1H, NH), 9.92 (s, 1H, NH), 7.96 (s, 1H, ArH), 7.61–7.56 (m, 6H, ArH), 7.37 (d, J = 8.0 Hz, 2H, ArH), 7.00 (d, J = 8.5 Hz, 1H, ArH), 6.88 (d, J = 7.9 Hz, 2H, ArH), 5.22 (s, 1H, CH), 3.69 (s, 3H, CH_3); ^{13}C NMR: δ 151.1, 143.7, 139.2, 137.4, 135.4, 135.3, 135.0, 131.5, 130.3, 129.8, 129.6, 128.2, 122.6, 121.2, 121.1, 113.1, 103.7, 80.2, 57.2, 21.8; IR: 3385, 3257, 2192, 1634, 1605, 1576, 1509, 1350, 1276, 947, 914, 772 cm^{-1}. ESI-HR-MS. Calcd for $C_{24}H_{18}N_4$ ([M-H]$^-$): *m/z* 361.1453. Found: *m/z* 361.1458.

9-(4-Methoxyphenyl)-7-phenyl-6,9-dihydro-1*H*-pyrazolo[3,4-*f*]quinoline-8-carbonitrile (6e) White powder; yield 79%; mp 170–174°C; ^{1}H NMR: δ 12.83 (s, 1H, NH), 9.94 (s, 1H, NH), 7.96 (s, 1H, ArH), 7.60–7.56 (m, 6H, ArH), 7.33 (d, J = 7.7 Hz, 2H, ArH), 7.12 (d, J = 7.6 Hz, 2H, ArH), 7.00 (d, J = 8.5 Hz, 1H, ArH), 5.23 (s, 1H, CH), 2.23 (s, 3H, CH_3); ^{13}C NMR: δ 158.8, 150.3, 138.5, 138.2, 134.7, 134.3, 130.8, 129.1, 128.9, 128.7, 122.0, 120.5, 120.4, 114.4, 112.4, 103.2, 79.7, 55.5; IR: 3275, 2191, 1634, 1605, 1537, 1495, 1346, 1279, 947, 914, 773 cm^{-1}; ESI-HR-MS. Calcd for $C_{24}H_{18}N_4O$ ([M-H]$^-$): *m/z* 377.1402. Found: *m/z* 377.1400.

9-(3-Chlorophenyl)-7-phenyl-6,9-dihydro-1*H*-pyrazolo[3,4-*f*]quinoline-8-carbonitrile (6f) White powder; yield 84%; mp 188–191°C; ^{1}H NMR: δ 12.91 (s, 1H, NH), 10.04 (s, 1H, NH), 8.00 (s, 1H, ArH), 7.66–7.57 (m, 7H, ArH), 7.44–7.39 (m, 2H, ArH), 7.32–7.28 (m, 1H, ArH), 7.04 (d, J = 8.6 Hz, 1H, ArH), 5.30 (s, 1H, CH);^{13}C NMR: δ 150.9, 148.2, 138.4, 134.8, 134.7, 134.0, 131.6, 131.0, 130.5, 130.1, 129.2 128.9, 126.8, 122.4, 121.7, 120.9, 120.7, 112.4, 102.0, 78.8, 40.8; IR: 3379, 3284, 2194, 1632, 1612, 1564, 1540, 1492, 1354, 1277, 945, 911, 767 cm^{-1}. ESI-HR-MS. Calcd for $C_{23}H_{15}ClN_4$ ([M-H]$^-$): *m/z* 381.0907 Found: *m/z* 381.0897.

9-(3-Bromophenyl)-7-phenyl-6,9-dihydro-1*H*-pyrazolo[3,4-f]quinoline-8-carbonitrile (6g) White powder; yield 81%; mp 252–255°C; ^{1}H NMR: δ 12.92 (s, 1H, NH), 10.05 (s, 1H, NH), 8.00 (s, 1H, ArH), 7.67–7.57 (m, 7H, ArH), 7.44–7.40 (m, 2H, ArH), 7.33–7.29 (m, 1H, ArH), 7.04 (d, J = 8.5 Hz, 1H, ArH), 5.31 (s, 1H, CH); ^{13}C NMR: δ 150.4, 147.7, 137.9, 134.3, 133.5, 131.0, 130.5, 130.0, 129.7, 128.7, 128.4, 126.3, 121.9, 121.2, 120.4, 120.2, 111.9, 101.5, 78.3, 40.3; IR: 3373, 3222, 2189, 1633, 1606, 1570, 1540, 1500, 1351, 1274, 945, 917, 797 cm^{-1}. ESI-HR-MS. Calcd for $C_{23}H_{15}BrN_4$ ([M-H]$^-$): *m/z* 425.0402. Found: *m/z* 425.0403.

9-(2-Chlorophenyl)-7-(1H-indol-3-yl)-6,9-dihydro-1*H*-pyrazolo[3,4-*f*]quinoline-8-carbonitrile (6h) White powder; yield 83%; mp 261–264°C; ^{1}H NMR: δ 12.20 (s, 1H, NH), 10.05 (s, 1H, NH), 7.97 (s, 1H, ArH), 7.61–7.54 (m, 7H, ArH), 7.44–7.42 (m, 1H, ArH), 7.33–7.27 (m, 2H, ArH), 6.97 (d, J = 8.6 Hz, 1H, ArH), 5.76 (s, 1H, CH); ^{13}C NMR: δ 151.4, 140.8, 138.7, 135.9, 135.0, 134.3, 133.2, 131.9, 131.0, 130.8, 129.5, 129.1, 128.8, 127.8, 121.4, 121.0, 120.8, 112.2, 100.7, 77.2, 56.5, 40.6, 19.0; IR: 3416, 3260, 2191, 1633, 1607, 1536, 1496, 1346, 1276, 942, 914, 773 cm^{-1}. ESI-HR-MS. Calcd for $C_{23}H_{15}ClN_4$ ([M-H]$^-$): *m/z* 381.0907. Found: *m/z* 381.0902.

9-(2-Methoxyphenyl)-7-phenyl-6,9-dihydro-1*H*-pyrazolo[3,4-*f*]quinoline-8-carbonitrile (6i) White powder; yield 74%; mp 155–157°C; ^{1}H NMR: δ 7.89 (s, 1H, ArH), 7.67 (d, J = 7.6 Hz, 2H, ArH), 7.49–7.45 (m, 5H, ArH), 7.00–6.98 (s, 2H, ArH), 6.75 (s, 1H, ArH), 6.63 (d, J = 8.5 Hz, 1H, ArH), 5.83 (s, 1H, CH), 4.09 (s, 3H, CH_3); ^{13}C NMR: δ 154.4, 150.1, 139.0, 135.1, 134.1, 133.4, 133.3, 130.7, 130.4, 129.1, 128.9, 127.8, 122.9, 120.3, 120.1, 112.2, 111.7, 103.5, 77.4, 77.1, 76.8, 33.6, 18.4; IR: 3278, 3416, 2190, 1634, 1607, 1535, 1493, 1350, 1280, 945, 914, 756 cm^{-1}. ESI-HR-MS. Calcd for $C_{24}H_{18}N_4O$ ([M-H]$^-$): *m/z* 377.1402. Found: *m/z* 377.1398.

9-(3,4-Dichlorophenyl)-7-phenyl-6,9-dihydro-1*H*-pyrazolo[3,4-*f*]quinoline-8-carbonitrile (6j) White powder; yield 82%; mp 184–186°C; ^{1}H NMR: δ 12.89 (s, 1H, NH), 10.06 (s, 1H, NH), 8.00 (s, 1H, ArH), 7.70–7.57 (m, 8H, ArH), 7.35 (d, J = 8.3 Hz, 1H, ArH), 7.04 (d, J = 8.6 Hz, 1H, ArH), 5.33 (s, 1H, CH); ^{13}C NMR: δ 151.0, 146.3, 138.4, 134.9, 134.8, 134.0, 131.7, 131.5, 131.0, 130.3, 129.3, 129.2, 128.9, 128.2, 121.5, 121.1, 120.7, 112.4, 101.6, 78.5, 56.5, 19.0; IR: 3265, 3212, 2196, 1633, 1604, 1537, 1500, 1346, 1276, 944, 918, 772 cm^{-1}. ESI-HR-MS. Calcd for $C_{23}H_{14}Cl_2N_4$ ([M-H]$^-$): *m/z* 415.0517. Found: *m/z* 415.0543.

9-(4-(Furan-2-yl)phenyl)-7-phenyl-6,9-dihydro-1*H*-pyrazolo[3,4-*f*]quinoline-8-carbonitrile (6k) White powder; yield 85%; mp >300 °C; ^{1}H NMR: δ 12.94 (s, 1H, NH), 9.99 (s, 1H, NH), 7.99 (s, 1H, ArH), 7.59 (m, 7H, ArH), 6.96 (d, J = 8.6 Hz, 1H, ArH), 6.36 (s, 2H, ArH), 5.51 (s, 1H, CH); ^{13}C NMR: δ 155.9, 151.8, 143.2, 138.6, 135.0, 134.5, 134.1, 131.0, 129.2, 129.0, 121.7, 120.7, 120.5, 112.3, 110.9, 106.5, 100.0, 75.0, 34.9; IR: 3321, 2187, 1633, 1606, 1531, 1496, 1355, 1276, 945, 907, 761 cm^{-1}. ESI-HR-MS. Calcd for $C_{27}H_{18}N_4O$ ([M-H]$^-$): *m/z* 413.1402. Found: *m/z* 413.1405.

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