

### *Supporting Information*

#### **I<sub>2</sub>-promoted formal [3+1+1+1] cyclization to construct 5-cyano-1*H*-pyrazolo[3,4-*b*]pyridine using malononitrile as a C1 synthon**

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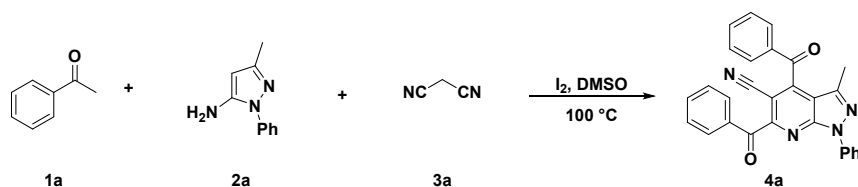
[kailuzheng@163.com](mailto:kailuzheng@163.com)

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## 1. General

All the materials and solvents were commercially available and used without further purification. TLC analysis was performed using pre-coated glass plates. Column chromatography was performed using silica gel (200–300 mesh).  $^1\text{H}$  spectra were recorded in  $\text{CDCl}_3$  and  $\text{DMSO}-d_6$  on 400 MHz NMR spectrometers and resonances ( $\delta$ ) are given in parts per million relative to tetramethylsilane. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz) and integration.  $^{13}\text{C}$  spectra were recorded in  $\text{CDCl}_3$  and  $\text{DMSO}-d_6$  on 100 MHz NMR spectrometers and resonances ( $\delta$ ) are given in ppm.  $^{19}\text{F}$  spectra were recorded in  $\text{CDCl}_3$  and  $\text{DMSO}-d_6$  on 376 MHz NMR using TMS as internal standard. HRMS were obtained on an Agilent LC1290-TOF 6224 equipped with an electrospray source. The X-ray crystal-structure determinations of **5a** was obtained on a Bruker SMART APEX CCD system.

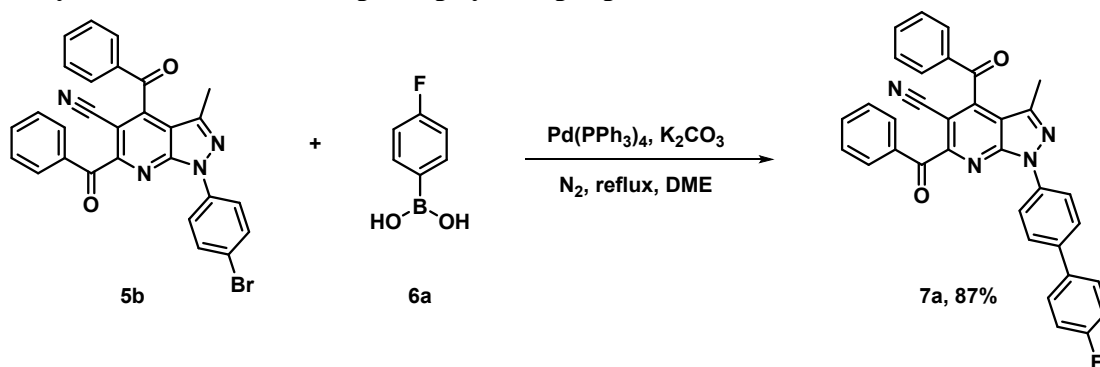
## 2. General procedure for the synthesis of 4 and 5 (4a as example)



The reactions did not require the protection of inert gases. In a 35 mL sealed tube were added acetophenone (**1a**) (120.0 mg, 1.0 mmol), iodine (254.0 mg, 1.0 mmol) and dimethyl sulfoxide (4 mL) and the resulting mixture was stirred at  $100\text{ }^\circ\text{C}$  (heating block), the reaction tube was removed after about 1 hour. Then additional **2a** (87.0 mg, 0.5 mmol) and **3a** (33.0 mg, 0.5 mmol) were added at room temperature, followed by reaction at  $100\text{ }^\circ\text{C}$  for 4 hours until substrate conversion was almost complete by TLC analysis. The reaction mixture was quenched with saturated  $\text{Na}_2\text{S}_2\text{O}_3$  solution (50 mL) and  $\text{NaCl}$  solution (150 mL), then the mixture was extracted with  $\text{EtOAc}$  (150 mL  $\times$  2), the organic layers were separated and combined, dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/ $\text{EtOAc}$  = 8:1) to afford the product **4a** (172.4 mg, 78% yield).

10.0 mmol scale (**4a**): The reactions did not require the protection of inert gases. In a 100 mL round flask were added acetophenone (**1a**) (1.20 g, 10.0 mmol), iodine (2.54 g, 10 mmol) and dimethyl sulfoxide (50 mL) and the resulting mixture was stirred in oil bath heating at  $100\text{ }^\circ\text{C}$ , the round flask was removed after about 1 hour. Then additional **2a** (865 mg, 5.0 mmol) and **3a** (330 mg, 5.0 mmol) were added at room temperature, followed by reaction at  $100\text{ }^\circ\text{C}$  for 4 hours until substrate conversion was almost complete by TLC analysis. The reaction mixture was quenched with saturated  $\text{Na}_2\text{S}_2\text{O}_3$  solution (200 mL) and  $\text{NaCl}$  solution (400 mL), then the mixture was extracted with  $\text{EtOAc}$  (400 mL  $\times$  2), the organic layers were separated and combined, dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/ $\text{EtOAc}$  = 8:1) to afford the product **4a** (1.44 g, 65% yield).

### 3. Synthesis methods and photophysical properties of AIE molecules



A mixture of **5b** (104.0 mg, 0.2 mmol), **6a** (42.0 mg, 0.3 mmol),  $\text{Pd(PPh}_3)_4$  (12.0 mg, 0.01 mmol),  $\text{K}_2\text{CO}_3$  (83.0 mg, 0.6 mmol) and DME (5 mL), and the reaction mixture was refluxed overnight under a nitrogen atmosphere. After the mixture was cooled to room temperature, water (300 mL) and EtOAc (200 mL  $\times$  2) were added. The organic layer was separated and washed with brine, dried over anhydrous  $\text{Na}_2\text{SO}_4$  and evaporated to dryness under reduced pressure. The crude product was purified by column chromatography on silica gel using petroleum ether/EtOAc (V/V, 8:1) as eluent to afford **7a** as yellow solid (93.3 mg, 87% yield)

#### Emission spectrum of AIE

The test solution of AIE molecule is diluted with stock solution ( $2.0 \times 10^{-4}$  mol/L), and the solution of equal concentration ( $10^{-5}$  mol/L) with different water content is prepared by  $\text{H}_2\text{O/THF}$  mixed solvent system. The excitation wavelength of the fluorescence test is 365 nm ultraviolet light, and the AIE solution is tested with a quartz cuvette.



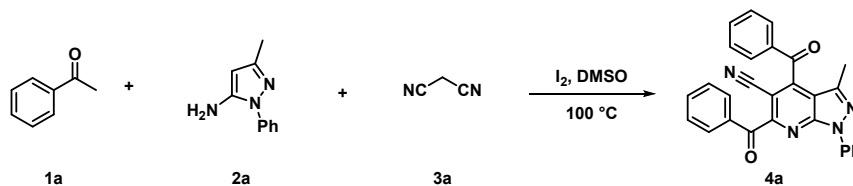
**Figure S1.** Photographs of **4p** in different THF/water mixtures (*fw*) taken under 365 nm excitation.



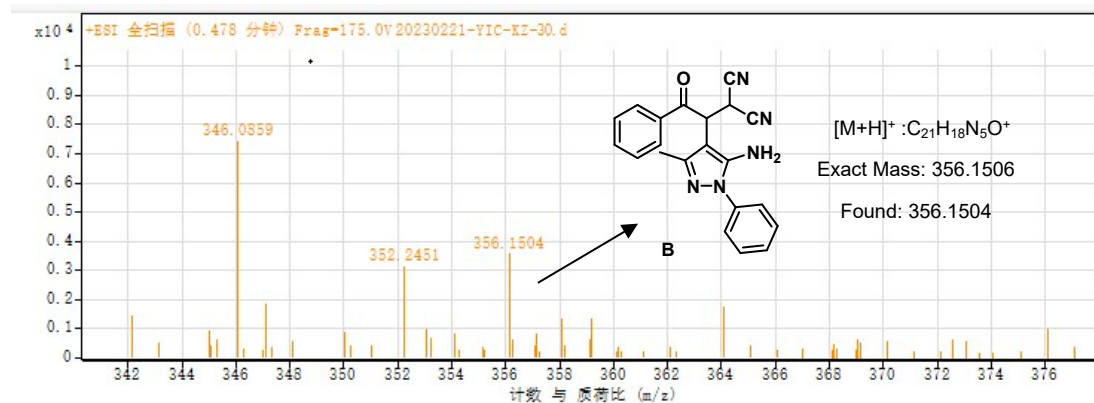
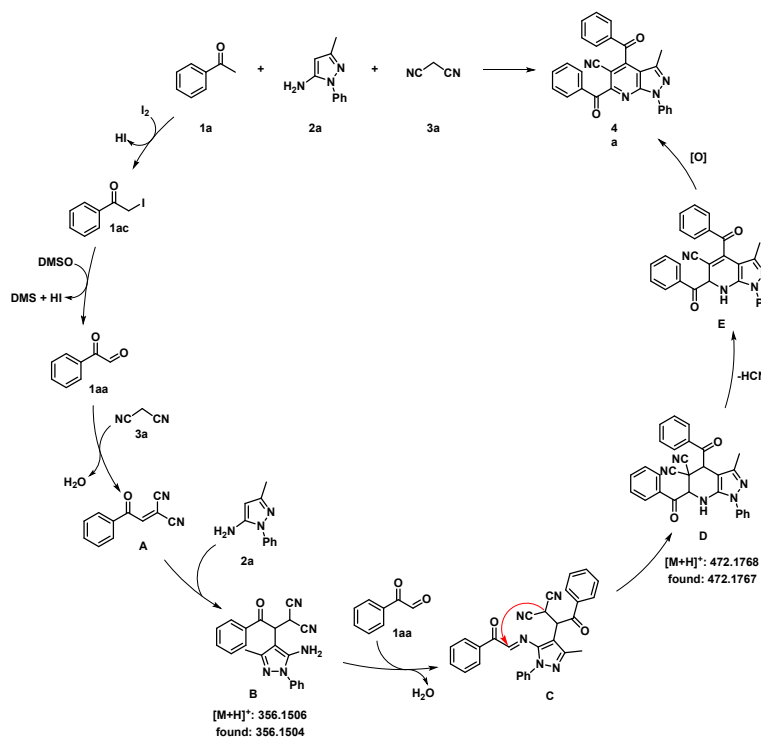
**Figure S2.** Photographs of **7a** in different THF/water mixtures (*fw*) taken under 365 nm excitation.

## 4. Mechanistic studies

### The mechanism of HRMS

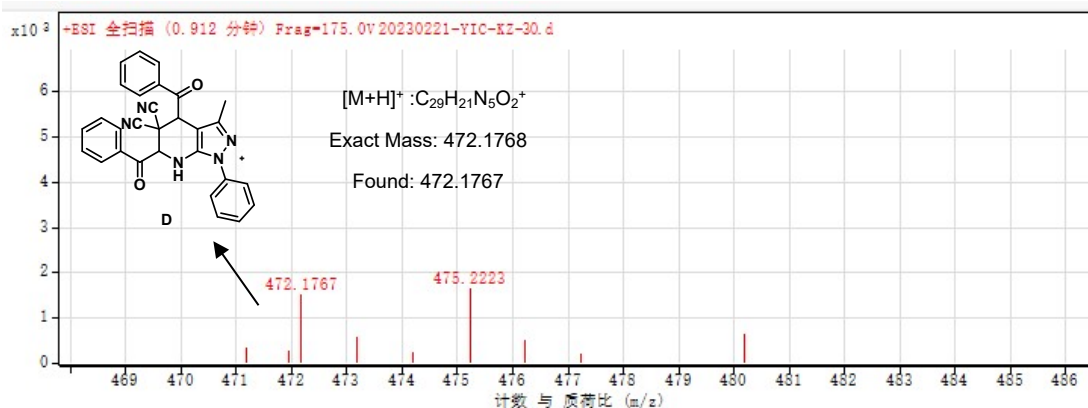


The reactions did not require the protection of inert gases. In a 35 mL sealed tube were added acetophenone (**1a**) (120.0 mg, 1.0 mmol), iodine (254.0 mg, 1.0 mmol) and dimethyl sulfoxide (4 mL) and the resulting mixture was stirred at 100 °C (heating block), the reaction tube was removed after about 1 hour. Then additional **2a** (133.0 mg, 1.0 mmol) and **3a** (270.0 mg, 1.5 mmol) were added at room temperature, followed by reaction at 100 °C for 1 hours, then wait for the reaction to cool to room temperature. Take 0.5 mL of reaction solution and dilute it with 4 mL of EtOAc. Then 1.5 mL of the extraction solution was added into the test bottle, the samples were immediately monitored by Agilent LC1290-TOF 6224 high resolution mass spectrometers.



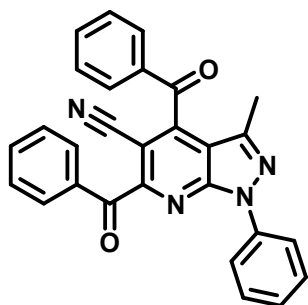
**Figure S3.** The compound **B** from the reaction mixture was detected by HRMS

**D**

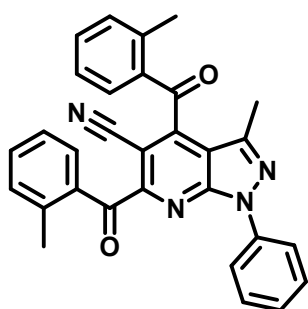


**Figure S4.** The compound **D** from the reaction mixture was detected by HRMS

## 5. Characterization data for compounds

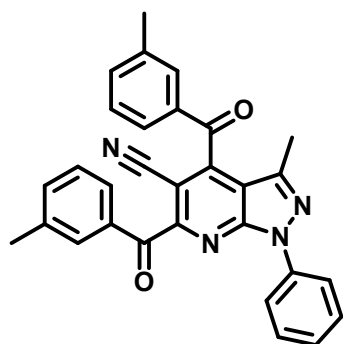


**4,6-dibenzoyl-3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4a):** Yield 78%; 172.4 mg; yellow solid; mp 150-152 °C;  $R_f$  0.16 (EtOAc/petroleum ether = 1:8);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.13 (dd,  $J = 28.8, 8.0$  Hz, 4H), 7.91 (d,  $J = 7.6$  Hz, 2H), 7.79–7.62 (m, 2H), 7.55 (dd,  $J = 15.2, 7.6$  Hz, 4H), 7.43 (s, 2H), 7.30 (s, 1H), 2.33 (s, 3H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  191.2, 190.1, 155.8, 149.2, 148.2, 143.3, 138.0, 135.6, 134.7, 134.4, 134.2, 131.1, 130.0, 129.4, 129.1, 128.4, 126.9, 120.9, 114.1, 113.4, 98.7, 13.7. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{28}\text{H}_{18}\text{N}_4\text{O}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  465.1322, found 465.1322.

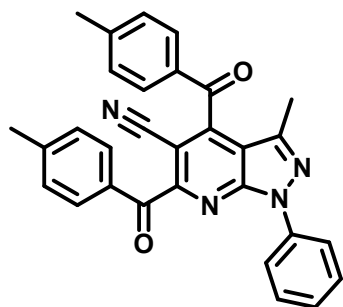


**3-methyl-4,6-bis(2-methylbenzoyl)-1-phenyl-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4b):** Yield 75%; 176.3 mg; yellow solid; mp 142-144 °C;  $R_f$  0.18 (EtOAc/petroleum ether = 1:8);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.09 (d,  $J = 8.0$  Hz, 2H),

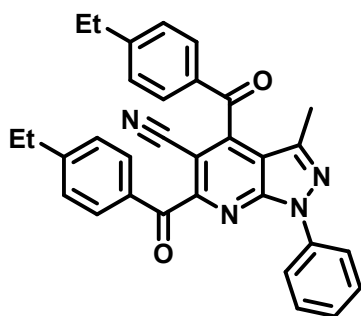
7.55 (t,  $J = 8.8$  Hz, 2H), 7.52–7.41 (m, 2H), 7.41–7.32 (m, 4H), 7.31–7.21 (m, 3H), 2.84 (s, 3H), 2.56 (s, 3H), 2.35 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  193.2, 192.8, 156.1, 150.5, 148.5, 143.3, 141.9, 140.0, 138.1, 134.8, 134.4, 133.6, 133.2, 133.0, 132.3, 131.8, 131.7, 129.1, 126.8, 126.2, 125.1, 120.7, 114.1, 113.4, 98.3, 22.1, 21.2, 13.7. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{30}\text{H}_{22}\text{N}_4\text{O}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  493.1635, found 493.1637.



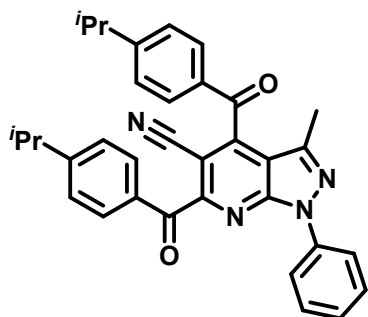
**3-methyl-4,6-bis(3-methylbenzoyl)-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carbonitrile (4c):** Yield 77%; 181.0 mg; yellowish brown solid; mp 143-145 °C;  $R_f$  0.18 (EtOAc/petroleum ether = 1:8);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.19 (d,  $J = 8.0$  Hz, 2H), 7.95 (s, 1H), 7.86 (d,  $J = 8.0$  Hz, 1H), 7.76 (s, 1H), 7.64 (d,  $J = 7.6$  Hz, 1H), 7.51 (d,  $J = 10.4$  Hz, 2H), 7.49–7.36 (m, 4H), 7.30 (t,  $J = 7.6$  Hz, 1H), 2.43 (s, 6H), 2.34 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  191.4, 190.3, 156.1, 149.4, 148.3, 143.3, 139.5, 138.4, 138.1, 136.6, 135.0, 134.8, 134.5, 131.4, 130.1, 129.2, 129.1, 128.5, 128.3, 127.7, 126.9, 120.9, 114.1, 113.4, 98.7, 21.3, 13.8. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{30}\text{H}_{22}\text{N}_4\text{O}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  493.1635, found 493.1636.



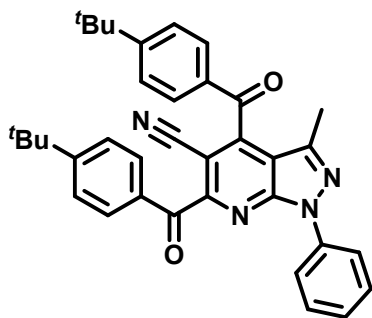
**3-methyl-4,6-bis(4-methylbenzoyl)-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carbonitrile (4d):** Yield 81%; 190.4 mg; yellow solid; mp 142-144 °C;  $R_f$  0.17 (EtOAc/petroleum ether = 1:8);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.19 (d,  $J = 8.0$  Hz, 2H), 7.99 (d,  $J = 8.0$  Hz, 2H), 7.80 (d,  $J = 8.0$  Hz, 2H), 7.46 (t,  $J = 8.0$  Hz, 2H), 7.34 (dd,  $J = 13.2, 8.0$  Hz, 5H), 2.47 (s, 6H), 2.34 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  190.8, 189.9, 156.6, 149.4, 148.4, 147.2, 145.5, 143.4, 138.2, 132.4, 132.0, 131.2, 130.3, 130.2, 129.3, 129.2, 126.9, 121.0, 114.2, 113.4, 98.7, 22.0, 21.9, 13.8. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{30}\text{H}_{22}\text{N}_4\text{O}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  493.1635, found 493.1638.



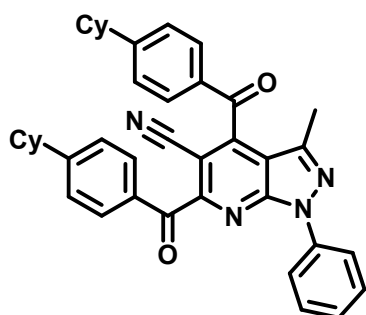
**4,6-bis(4-ethylbenzoyl)-3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4e):** Yield 80%; 199.3 mg; yellow solid; mp 146-148 °C;  $R_f$  0.19 (EtOAc/petroleum ether = 1:8);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.19 (d,  $J = 8.0$  Hz, 2H), 8.02 (d,  $J = 8.0$  Hz, 2H), 7.83 (d,  $J = 8.0$  Hz, 2H), 7.43 (d,  $J = 8.4$  Hz, 2H), 7.41–7.22 (m, 5H), 2.76 (s, 2H), 2.74 (s, 2H), 2.34 (s, 3H), 1.30 (d,  $J = 6.8$  Hz, 3H), 1.26 (d,  $J = 7.2$  Hz, 3H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  190.8, 189.9, 156.5, 153.1, 151.6, 149.4, 148.3, 143.3, 138.1, 132.5, 132.1, 131.3, 130.3, 129.1, 128.9, 128.0, 126.8, 120.9, 114.1, 113.3, 98.6, 29.1, 29.0, 15.0, 14.8, 13.7. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{32}\text{H}_{26}\text{N}_4\text{O}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  521.1948, found 521.1951.



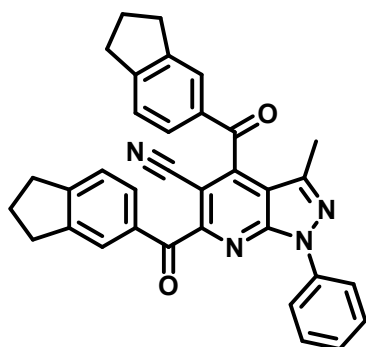
**4,6-bis(4-isopropylbenzoyl)-3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4f):** Yield 74%; 194.7 mg; light yellow solid; mp 193-195 °C;  $R_f$  0.18 (EtOAc/petroleum ether = 1:8);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.19 (d,  $J = 8.0$  Hz, 2H), 8.03 (d,  $J = 8.0$  Hz, 2H), 7.84 (d,  $J = 8.0$  Hz, 2H), 7.40 (dd,  $J = 13.2, 5.6$  Hz, 6H), 7.28 (d,  $J = 7.6$  Hz, 1H), 3.00 (dq,  $J = 13.6, 6.8$  Hz, 2H), 2.34 (s, 3H), 1.28 (t,  $J = 7.6$  Hz, 12H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  190.7, 189.8, 157.5, 156.4, 156.0, 149.3, 148.3, 143.3, 138.1, 132.6, 132.2, 131.3, 130.3, 129.0, 127.5, 126.7, 126.6, 120.8, 114.1, 113.3, 98.5, 34.4, 34.3, 23.5, 23.3, 13.7. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{34}\text{H}_{30}\text{N}_4\text{O}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  549.2261, found 549.2264.



**4,6-bis(4-(tert-butyl)benzoyl)-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carbonitrile (4g):** Yield 75%; 207.9 mg; yellow solid; mp 185-187 °C;  $R_f$  0.18 (EtOAc/petroleum ether = 1:8);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.20 (d,  $J = 8.0$  Hz, 2H), 8.04 (d,  $J = 8.4$  Hz, 2H), 7.84 (d,  $J = 8.0$  Hz, 2H), 7.55 (t,  $J = 8.0$  Hz, 4H), 7.44 (t,  $J = 8.0$  Hz, 2H), 7.30 (t,  $J = 7.6$  Hz, 1H), 2.35 (s, 3H), 1.38 (s, 9H), 1.36 (s, 9H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  190.8, 189.9, 159.8, 158.3, 156.5, 149.4, 148.4, 143.4, 138.2, 132.2, 131.9, 131.1, 130.1, 129.1, 126.8, 126.4, 125.5, 120.9, 114.1, 113.4, 98.6, 35.5, 35.3, 31.0, 30.9, 13.8. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{36}\text{H}_{34}\text{N}_4\text{O}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  577.2574, found 577.2575.



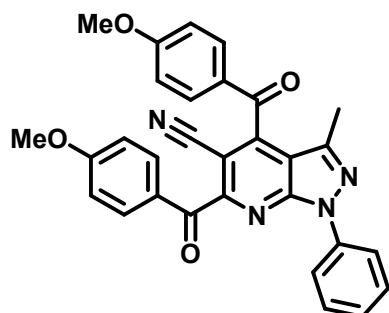
**4,6-bis(4-cyclohexylbenzoyl)-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carbonitrile (4h):** Yield 72%; 216.1 mg; light yellow solid; mp 160-162 °C;  $R_f$  0.18 (EtOAc/petroleum ether = 1:8);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.20 (d,  $J = 8.0$  Hz, 2H), 8.02 (d,  $J = 8.0$  Hz, 2H), 7.81 (d,  $J = 8.0$  Hz, 2H), 7.45 (t,  $J = 8.0$  Hz, 2H), 7.35 (dd,  $J = 18.8, 10.4$  Hz, 5H), 2.61 (t,  $J = 10.4$  Hz, 2H), 2.34 (s, 3H), 2.04–1.83 (m, 8H), 1.76 (s, 2H), 1.64–1.31 (m, 8H), 1.28 (d,  $J = 13.2$  Hz, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  190.8, 189.9, 156.7, 156.6, 155.2, 149.4, 148.4, 143.4, 138.2, 132.6, 132.3, 131.3, 130.4, 129.1, 127.9, 127.0, 126.8, 120.9, 114.1, 113.4, 98.6, 44.9, 44.8, 34.0, 33.8, 26.6, 26.5, 25.93, 25.86, 13.8. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{40}\text{H}_{38}\text{N}_4\text{O}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  629.2887, found 629.2886.



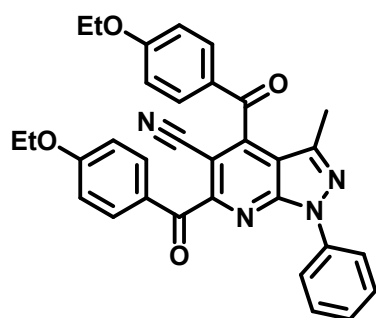
**4,6-bis(2,3-dihydro-1H-indene-5-carbonyl)-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carbonitrile (4i):** Yield 73%; 190.6 mg; yellow solid; mp 152-154 °C;  $R_f$  0.16 (EtOAc/petroleum ether = 1:8);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.20 (d,  $J = 8.0$  Hz, 2H), 7.96 (s, 1H), 7.85 (d,  $J = 8.0$  Hz, 1H), 7.78 (s, 1H), 7.65 (d,  $J = 8.0$  Hz, 1H), 7.43 (t,  $J = 8.0$  Hz, 2H), 7.35 (t,  $J = 8.8$  Hz, 2H), 7.29 (t,  $J = 7.6$  Hz, 1H), 3.12–2.88 (m, 8H), 2.35 (s, 3H), 2.19–2.07 (m, 4H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  191.0, 190.3,



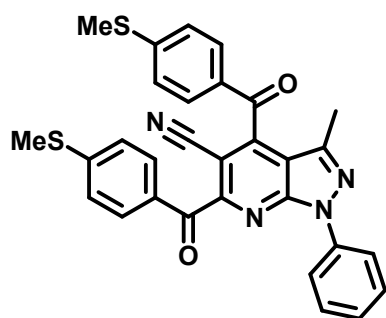
156.9, 153.6, 152.0, 149.6, 148.4, 145.8, 144.8, 143.4, 138.2, 133.3, 132.8, 129.8, 129.1, 126.8, 126.7, 125.6, 125.2, 124.3, 120.9, 114.2, 113.3, 98.5, 33.2, 33.1, 32.4, 32.3, 25.2, 25.1, 13.7. HRMS (ESI)  $m/z$  calcd for  $C_{34}H_{26}N_4O_2Na^+$  ( $M+Na$ ) $^+$  545.1948, found 545.1951.



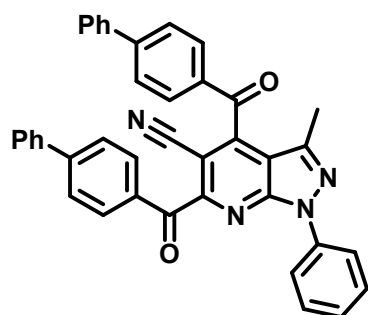
**4,6-bis(4-methoxybenzoyl)-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carbonitrile (4j):** Yield 82%; 205.9 mg; yellow solid; mp 120-122 °C;  $R_f$  0.18 (EtOAc/petroleum ether = 1:3);  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.20 (d,  $J$  = 8.0 Hz, 2H), 8.07 (d,  $J$  = 8.8 Hz, 2H), 7.88 (d,  $J$  = 8.4 Hz, 2H), 7.46 (t,  $J$  = 8.0 Hz, 2H), 7.31 (t,  $J$  = 7.6 Hz, 1H), 7.00 (dd,  $J$  = 12.0, 8.8 Hz, 4H), 3.90 (s, 6H), 2.35 (s, 3H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  189.4, 188.8, 165.5, 164.6, 156.9, 149.5, 148.4, 143.4, 138.2, 133.6, 132.7, 129.2, 127.9, 127.4, 126.8, 120.9, 114.8, 114.3, 113.9, 113.3, 98.7, 55.7, 55.6, 13.7. HRMS (ESI)  $m/z$  calcd for  $C_{30}H_{22}N_4O_4Na^+$  ( $M+Na$ ) $^+$  525.1533, found 525.1535.



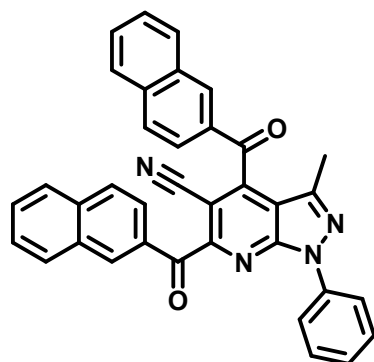
**4,6-bis(4-ethoxybenzoyl)-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carbonitrile (4k):** Yield 79%; 209.4 mg; yellow solid; mp 158-160 °C;  $R_f$  0.15 (EtOAc/petroleum ether = 1:5);  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.19 (d,  $J$  = 8.0 Hz, 2H), 8.06 (d,  $J$  = 8.4 Hz, 2H), 7.86 (d,  $J$  = 8.0 Hz, 2H), 7.45 (t,  $J$  = 8.0 Hz, 2H), 7.37-7.13 (m, 1H), 6.97 (t,  $J$  = 10.4 Hz, 4H), 4.12 (d,  $J$  = 8.0 Hz, 4H), 2.35 (s, 3H), 1.45 (s, 6H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  189.4, 188.7, 164.9, 164.0, 156.9, 149.5, 148.4, 143.4, 138.2, 133.6, 132.7, 131.4, 129.1, 127.7, 127.1, 126.8, 120.9, 115.1, 114.8, 114.3, 113.3, 98.7, 64.1, 63.9, 14.53, 14.47, 13.7. HRMS (ESI)  $m/z$  calcd for  $C_{32}H_{26}N_4O_4Na^+$  ( $M+Na$ ) $^+$  553.1846, found 553.1849.



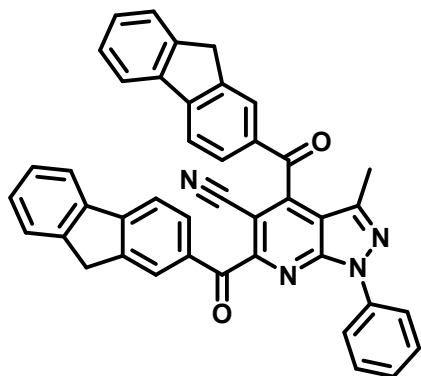
**3-methyl-4,6-bis(4-(methylthio)benzoyl)-1-phenyl-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4l):** Yield 77%; 205.6 mg; yellow solid; mp 156-158 °C;  $R_f$  0.17 (EtOAc/petroleum ether = 1:5);  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  8.07 (t,  $J$  = 7.2 Hz, 4H), 7.92 (d,  $J$  = 8.0 Hz, 2H), 7.52 (t,  $J$  = 8.0 Hz, 2H), 7.46 (t,  $J$  = 8.0 Hz, 4H), 7.36 (t,  $J$  = 7.6 Hz, 1H), 2.58 (s, 6H), 2.23 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$  190.2, 189.5, 155.9, 150.1, 148.9, 148.4, 148.0, 142.8, 137.7, 131.5, 130.5, 130.4, 130.2, 129.3, 127.1, 125.4, 124.6, 121.3, 114.7, 113.2, 97.9, 13.9, 13.8, 13.4. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{30}\text{H}_{22}\text{N}_4\text{O}_2\text{S}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  557.1076, found 557.1079.



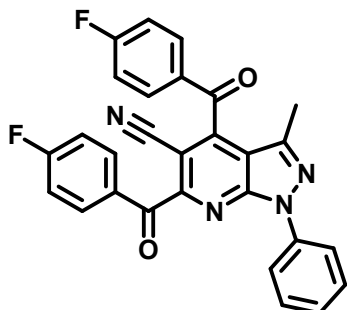
**4,6-di([1,1'-biphenyl]-4-carbonyl)-3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4m):** Yield 65%; 193.1 mg; yellow solid; mp 154-156 °C;  $R_f$  0.17 (EtOAc/petroleum ether = 1:8);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.21 (t,  $J$  = 7.2 Hz, 4H), 7.99 (d,  $J$  = 8.0 Hz, 2H), 7.77 (t,  $J$  = 8.4 Hz, 4H), 7.66 (dd,  $J$  = 12.0, 7.6 Hz, 4H), 7.56–7.38 (m, 8H), 7.33 (t,  $J$  = 7.6 Hz, 1H), 2.40 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  190.8, 189.8, 156.2, 149.4, 148.44, 148.42, 147.0, 143.5, 139.6, 139.2, 138.2, 133.4, 133.2, 131.8, 130.8, 129.3, 129.1, 129.0, 128.9, 128.6, 128.1, 127.42, 127.37, 127.2, 127.1, 121.0, 114.2, 113.5, 98.8, 13.9. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{40}\text{H}_{26}\text{N}_4\text{O}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  617.1948, found 617.1947.



**4,6-di(2-naphthoyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4n):** Yield 69%; 187.1 mg; yellow solid; mp 192-194 °C;  $R_f$  0.17 (EtOAc/petroleum ether = 1:8);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.68 (s, 1H), 8.27 (s, 1H), 8.20 (dd,  $J = 12.8, 4.8$  Hz, 3H), 8.12 (d,  $J = 8.8$  Hz, 1H), 7.99 (d,  $J = 8.8$  Hz, 1H), 7.94 (d,  $J = 8.8$  Hz, 1H), 7.88 (t,  $J = 8.0$  Hz, 4H), 7.71–7.59 (m, 2H), 7.53 (q,  $J = 7.2$  Hz, 2H), 7.37 (t,  $J = 8.0$  Hz, 2H), 7.30–7.21 (m, 1H), 2.33 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  191.2, 189.9, 156.0, 149.4, 148.3, 143.4, 138.1, 136.6, 135.9, 134.4, 133.8, 132.3, 132.2, 132.1, 131.8, 130.0, 129.8, 129.7, 129.3, 129.2, 128.5, 128.0, 127.8, 127.4, 127.0, 126.9, 125.4, 123.6, 120.8, 114.3, 113.6, 99.1, 13.8. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{36}\text{H}_{22}\text{N}_4\text{O}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  565.1635, found 565.1636.

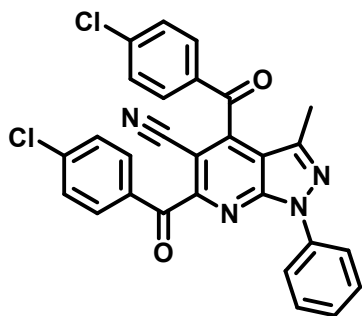


**4,6-di(9H-fluorene-2-carbonyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4o):** Yield 62%; 191.6 mg; yellow solid; mp 253-255 °C;  $R_f$  0.17 (EtOAc/petroleum ether = 1:8);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.30 (s, 1H), 8.23 (d,  $J = 8.0$  Hz, 2H), 8.13 (d,  $J = 8.0$  Hz, 2H), 7.88 (dd,  $J = 14.8, 7.2$  Hz, 5H), 7.60 (d,  $J = 6.8$  Hz, 2H), 7.51–7.36 (m, 6H), 7.29 (t,  $J = 7.6$  Hz, 1H), 3.96 (s, 4H), 2.37 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  190.9, 190.2, 156.9, 149.7, 149.2, 148.5, 147.8, 145.0, 144.8, 144.1, 143.5, 143.2, 140.2, 139.8, 138.2, 133.1, 132.8, 130.8, 130.0, 129.2, 129.0, 128.5, 127.7, 127.3, 127.2, 126.9, 126.5, 125.4, 125.3, 121.4, 121.2, 120.9, 120.5, 119.7, 114.3, 113.5, 98.9, 36.9, 13.9. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{42}\text{H}_{26}\text{N}_4\text{O}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  641.1948, found 641.1948.

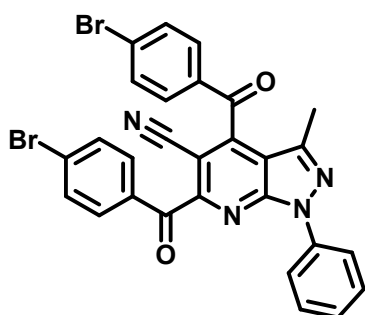


**4,6-bis(4-fluorobenzoyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4p):** Yield 76%; 181.7 mg; yellow solid; mp 198-200 °C;  $R_f$  0.20 (EtOAc/petroleum ether = 1:8);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.15 (dd,  $J = 8.8, 4.8$  Hz, 4H), 7.95 (dd,  $J = 8.4, 5.2$  Hz, 2H), 7.46 (t,  $J = 8.0$  Hz, 2H), 7.33 (t,  $J = 7.6$  Hz,

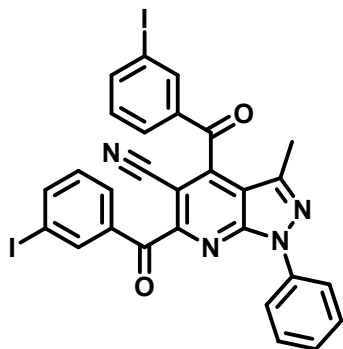
1H), 7.28–7.23 (m, 2H), 7.18 (d,  $J = 8.4$  Hz, 2H), 2.35 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  189.6, 188.4, 167.2 (d,  $J = 258.6$  Hz,  $^1J_{\text{CF}}$ ), 166.4 (d,  $J = 256.1$  Hz,  $^1J_{\text{CF}}$ ), 155.4, 148.9, 148.2, 143.2, 138.0, 134.0 (d,  $J = 9.5$  Hz,  $^3J_{\text{CF}}$ ), 133.0 (d,  $J = 9.9$  Hz,  $^3J_{\text{CF}}$ ), 131.8 (d,  $J = 9.8$  Hz,  $^3J_{\text{CF}}$ ), 131.2 (d,  $J = 2.9$  Hz,  $^4J_{\text{CF}}$ ), 130.8 (d,  $J = 2.8$  Hz,  $^4J_{\text{CF}}$ ), 129.2, 127.1, 121.0, 117.0 (d,  $J = 22.2$  Hz,  $^2J_{\text{CF}}$ ), 116.7 (d,  $J = 22.2$  Hz,  $^2J_{\text{CF}}$ ), 115.8 (d,  $J = 21.8$  Hz,  $^2J_{\text{CF}}$ ), 114.0, 113.4, 98.8, 13.8.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -99.33 (s, F), -102.27 (s, F). HRMS (ESI)  $m/z$  calcd for  $\text{C}_{28}\text{H}_{16}\text{F}_2\text{N}_4\text{O}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  501.1134, found 501.1135.



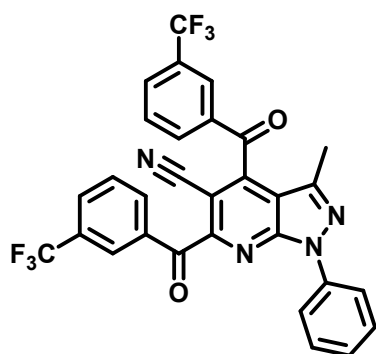
**4,6-bis(4-chlorobenzoyl)-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carbonitrile (4q):** Yield 73%; 186.2 mg; white solid; mp 218–220 °C;  $R_f$  0.31 (EtOAc/petroleum ether = 1:8);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.15 (d,  $J = 8.0$  Hz, 2H), 8.07 (d,  $J = 8.4$  Hz, 2H), 7.85 (d,  $J = 8.4$  Hz, 2H), 7.55 (d,  $J = 8.4$  Hz, 2H), 7.53–7.45 (m, 4H), 7.35 (t,  $J = 7.6$  Hz, 1H), 2.35 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  190.0, 188.8, 155.2, 148.8, 148.2, 143.3, 142.7, 141.0, 138.0, 133.0, 132.8, 132.5, 131.3, 130.0, 129.3, 128.9, 127.3, 121.0, 114.0, 113.5, 98.9, 13.8. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{28}\text{H}_{16}\text{Cl}_2\text{N}_4\text{O}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  533.0543, found 533.0554.



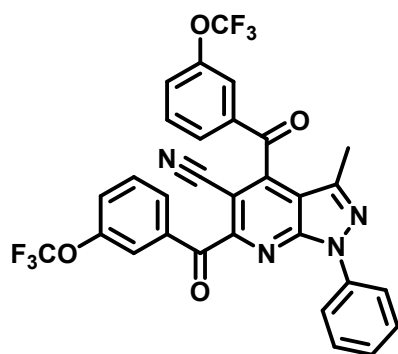
**4,6-bis(4-bromobenzoyl)-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carbonitrile (4r):** Yield 72%; 215.3 mg; yellow solid; mp 220–222 °C;  $R_f$  0.17 (EtOAc/petroleum ether = 1:8);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.14 (d,  $J = 8.0$  Hz, 2H), 7.99 (d,  $J = 8.4$  Hz, 2H), 7.74 (q,  $J = 8.4$  Hz, 4H), 7.67 (d,  $J = 8.4$  Hz, 2H), 7.48 (t,  $J = 8.0$  Hz, 2H), 7.35 (t,  $J = 7.6$  Hz, 1H), 2.35 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  190.2, 189.0, 155.1, 148.7, 148.2, 143.2, 138.0, 133.4, 133.2, 133.0, 132.6, 131.9, 131.6, 131.3, 129.9, 129.3, 127.2, 121.0, 114.0, 113.5, 98.8, 13.8. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{28}\text{H}_{16}\text{Br}_2\text{N}_4\text{O}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  622.9512, found 622.9512.



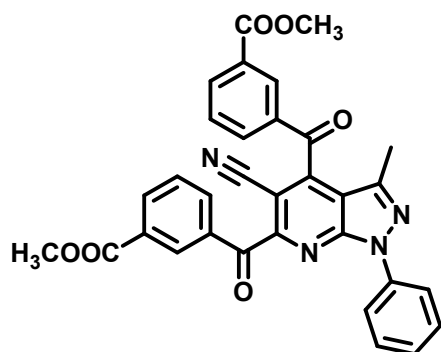
**4,6-bis(3-iodobenzoyl)-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carbonitrile (4s):** Yield 67%; 232.5 mg; yellow solid; mp 219-221 °C;  $R_f$  0.40 (EtOAc/petroleum ether = 1:5);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.55 (s, 1H), 8.31 (s, 1H), 8.14 (d,  $J = 8.0$  Hz, 2H), 8.07 (t,  $J = 7.6$  Hz, 2H), 8.01 (d,  $J = 8.0$  Hz, 1H), 7.77 (d,  $J = 8.0$  Hz, 1H), 7.52 (t,  $J = 8.0$  Hz, 2H), 7.36 (t,  $J = 7.6$  Hz, 1H), 7.33–7.26 (m, 2H), 2.36 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  189.9, 188.3, 154.3, 148.6, 148.1, 144.4, 143.2, 142.7, 140.1, 138.1, 137.9, 136.3, 131.0, 130.2, 129.5, 129.5, 127.3, 121.3, 114.0, 113.6, 99.1, 95.2, 93.8, 13.9. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{28}\text{H}_{16}\text{I}_2\text{N}_4\text{O}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  716.9255, found 716.9255.



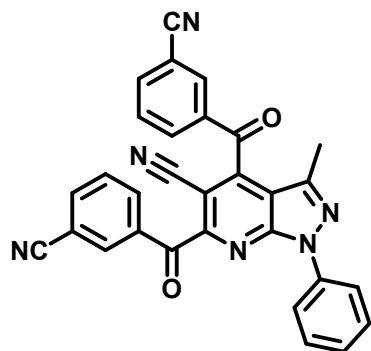
**3-methyl-1-phenyl-4,6-bis(3-(trifluoromethyl)benzoyl)-1H-pyrazolo[3,4-b]pyridine-5-carbonitrile (4t):** Yield 65%; 187.9 mg; white solid; mp 168-170 °C;  $R_f$  0.33 (EtOAc/petroleum ether = 1:5);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.51 (s, 1H), 8.36 (d,  $J = 8.0$  Hz, 1H), 8.28 (s, 1H), 8.10 (d,  $J = 8.0$  Hz, 2H), 8.01 (d,  $J = 8.0$  Hz, 2H), 7.96 (d,  $J = 8.0$  Hz, 1H), 7.72 (dd,  $J = 17.2, 8.4$  Hz, 2H), 7.47 (t,  $J = 8.0$  Hz, 2H), 7.36 (t,  $J = 7.6$  Hz, 1H), 2.37 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  190.1, 188.3, 154.0, 148.5, 148.2, 137.7, 135.2, 135.1, 134.2, 133.5, 132.4 (q,  $J = 33.3$  Hz,  $^2J_{\text{CF}}$ ), 132.1 (q,  $J = 3.3$  Hz,  $^4J_{\text{CF}}$ ), 131.0 (q,  $J = 33.0$  Hz,  $^2J_{\text{CF}}$ ), 130.4 (q,  $J = 3.4$  Hz,  $^4J_{\text{CF}}$ ), 130.3, 129.4, 129.3, 128.2 (q,  $J = 3.8$  Hz,  $^4J_{\text{CF}}$ ), 127.5, 126.2 (q,  $J = 3.5$  Hz,  $^4J_{\text{CF}}$ ), 123.6 (q,  $J = 271.2$  Hz,  $^1J_{\text{CF}}$ ), 123.2 (q,  $J = 271.2$  Hz,  $^1J_{\text{CF}}$ ), 113.9, 113.7, 99.2, 13.9.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -62.72 (s, 3F), -62.85 (s, 3F). HRMS (ESI)  $m/z$  calcd for  $\text{C}_{30}\text{H}_{16}\text{F}_6\text{N}_4\text{O}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  601.1070, found 601.1073.



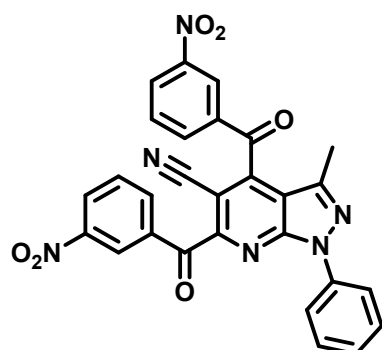
**3-methyl-1-phenyl-4,6-bis(3-(trifluoromethoxy)benzoyl)-1H-pyrazolo[3,4-b]pyridine-5-carbonitrile (4u):** Yield 66%; 201.3 mg; yellow solid; mp 162-164 °C;  $R_f$  0.32 (EtOAc/petroleum ether = 1:5);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.12 (d,  $J = 8.4$  Hz, 2H), 8.10–8.02 (m, 2H), 7.87 (s, 1H), 7.80–7.70 (m, 1H), 7.64–7.52 (m, 4H), 7.48 (t,  $J = 8.0$  Hz, 2H), 7.36 (t,  $J = 7.6$  Hz, 1H), 2.36 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  189.9, 188.3, 154.5, 150.13, 150.11, 149.21, 149.19, 148.5, 148.2, 143.2, 137.8, 136.4, 136.3, 131.2, 130.1, 129.5, 129.3, 128.7, 127.7, 127.4, 126.5, 123.5, 121.4, 121.2, 120.4 (q,  $J = 256.8$  Hz,  $^1J_{\text{CF}}$ ), 120.3 (q,  $J = 257.6$  Hz,  $^1J_{\text{CF}}$ ), 113.9, 113.6, 99.0, 13.8.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -57.86 (s, 3F), -57.87 (s, 3F). HRMS (ESI)  $m/z$  calcd for  $\text{C}_{30}\text{H}_{16}\text{F}_6\text{N}_4\text{O}_4\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  633.0968, found 633.0969.



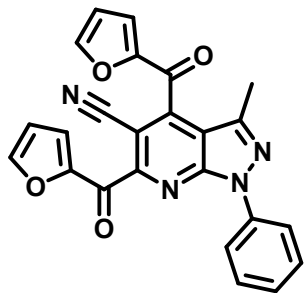
**dimethyl 3,3'-(5-cyano-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-4,6-dicarbonyl)dibenzoate (4v):** Yield 63%; 175.8 mg; yellow solid; mp 212-214 °C;  $R_f$  0.33 (EtOAc/petroleum ether = 1:1);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.87 (s, 1H), 8.52 (s, 1H), 8.40 (d,  $J = 8.0$  Hz, 1H), 8.35 (dd,  $J = 8.8, 3.2$  Hz, 2H), 8.14 (t,  $J = 6.4$  Hz, 3H), 7.86–7.60 (m, 2H), 7.43 (t,  $J = 7.6$  Hz, 2H), 7.33 (t,  $J = 7.6$  Hz, 1H), 3.94 (s, 3H), 3.92 (s, 3H), 2.35 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  190.6, 188.9, 166.0, 165.5, 154.4, 148.8, 148.2, 143.2, 137.8, 136.3, 135.04, 135.01, 134.7, 133.9, 132.6, 131.6, 130.8, 130.3, 129.8, 129.2, 128.9, 127.3, 121.4, 114.1, 113.6, 99.1, 52.6, 52.4, 13.8. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{28}\text{H}_{16}\text{N}_6\text{O}_6\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  555.1024, found 555.1024.



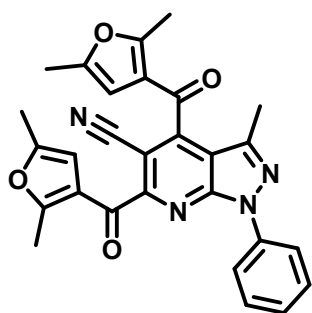
**3,3'-(5-cyano-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-4,6-dicarbonyl)dibenzonitrile (4w):** Yield 67%; 164.9 mg; yellow solid; mp 230-232 °C;  $R_f$  0.17 (EtOAc/petroleum ether = 1:3);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.54 (s, 1H), 8.37 (d,  $J = 8.0$  Hz, 1H), 8.18 (d,  $J = 8.0$  Hz, 1H), 8.13 (s, 1H), 8.06 (d,  $J = 8.0$  Hz, 2H), 8.00 (d,  $J = 8.0$  Hz, 1H), 7.95 (d,  $J = 8.0$  Hz, 1H), 7.75 (t,  $J = 8.0$  Hz, 1H), 7.69 (t,  $J = 8.0$  Hz, 1H), 7.51 (t,  $J = 8.0$  Hz, 2H), 7.38 (t,  $J = 7.6$  Hz, 1H), 2.36 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  189.4, 187.6, 153.2, 148.1, 148.0, 143.0, 138.3, 137.5, 136.6, 135.41, 135.37, 135.0, 134.9, 133.5, 133.4, 130.6, 129.5, 129.4, 127.7, 121.4, 117.6, 117.0, 114.2, 113.9, 113.6, 112.8, 99.1, 13.9. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{30}\text{H}_{16}\text{N}_6\text{O}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  515.1227, found 515.1231.



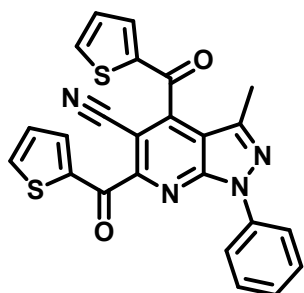
**3-methyl-4,6-bis(3-nitrobenzoyl)-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carbonitrile (4x):** Yield 58%; 154.3 mg; yellow solid; mp 194-196 °C;  $R_f$  0.21 (EtOAc/petroleum ether = 1:3);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.12 (s, 1H), 8.71 (s, 1H), 8.59 (d,  $J = 8.4$  Hz, 1H), 8.51 (dd,  $J = 15.6, 8.0$  Hz, 2H), 8.27 (d,  $J = 8.0$  Hz, 1H), 8.05 (d,  $J = 8.0$  Hz, 2H), 7.83 (t,  $J = 8.0$  Hz, 1H), 7.77 (t,  $J = 8.0$  Hz, 1H), 7.46 (t,  $J = 7.6$  Hz, 2H), 7.36 (t,  $J = 7.6$  Hz, 1H), 2.39 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  189.3, 187.3, 153.1, 148.8, 148.2, 148.0, 147.9, 143.1, 137.5, 136.5, 135.9, 135.7, 135.2, 131.0, 129.8, 129.7, 129.4, 128.2, 127.8, 126.4, 124.4, 121.8, 114.0, 113.7, 99.2, 13.9. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{28}\text{H}_{16}\text{N}_6\text{O}_6\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  555.1024, found 555.1024.



**4,6-di(furan-2-carbonyl)-3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4y):** Yield 70%; 154.7 mg; white solid; mp 187-189 °C;  $R_f$  0.17 (EtOAc/petroleum ether = 1:3);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.18 (d,  $J = 8.0$  Hz, 2H), 7.81 (d,  $J = 9.6$  Hz, 2H), 7.65 (d,  $J = 3.6$  Hz, 1H), 7.53 (t,  $J = 8.0$  Hz, 2H), 7.46–7.32 (m, 2H), 6.74 (dd,  $J = 3.6, 1.6$  Hz, 1H), 6.65 (dd,  $J = 3.6, 1.6$  Hz, 1H), 2.44 (s, 3H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  177.4, 176.4, 153.8, 151.1, 150.3, 149.8, 148.9, 148.5, 147.6, 143.4, 137.9, 129.2, 127.2, 124.5, 121.2, 113.8, 113.7, 112.9, 99.0, 13.8. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{24}\text{H}_{14}\text{N}_4\text{O}_4\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  445.0907, found 445.0908.

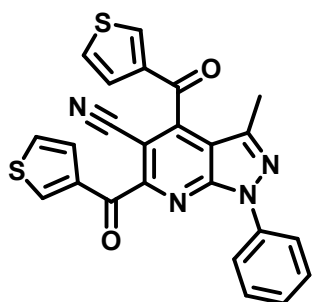


**4,6-bis(2,5-dimethylfuran-3-carbonyl)-3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4z):** Yield 66%; 157.8 mg; yellow solid; mp 157-159 °C;  $R_f$  0.40 (EtOAc/petroleum ether = 1:5);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.24 (d,  $J = 8.4$  Hz, 2H), 7.52 (t,  $J = 8.0$  Hz, 2H), 7.36 (t,  $J = 7.6$  Hz, 1H), 6.51 (s, 1H), 5.94 (s, 1H), 2.64 (s, 3H), 2.59 (s, 3H), 2.47 (s, 3H), 2.29 (s, 3H), 2.25 (s, 3H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  185.6, 185.1, 162.0, 160.7, 156.3, 151.8, 150.08, 150.06, 148.7, 143.4, 138.2, 129.2, 127.0, 121.0, 119.5, 114.4, 112.6, 107.5, 105.8, 97.4, 15.0, 14.6, 13.7, 13.11, 13.07. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{28}\text{H}_{22}\text{N}_4\text{O}_4\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  501.1533, found 501.1535.

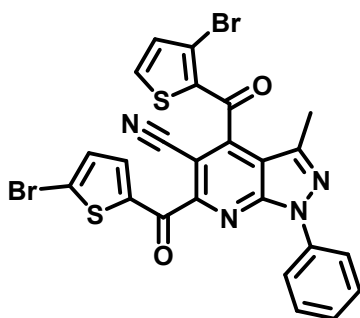




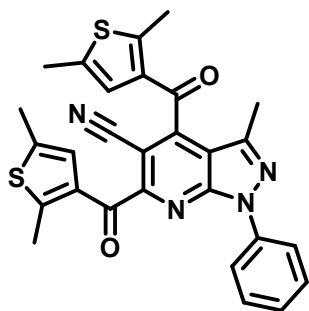
**3-methyl-1-phenyl-4,6-di(thiophene-2-carbonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4aa):** Yield 69%; 156.6 mg; yellow solid; mp 172-174 °C;  $R_f$  0.27 (EtOAc/petroleum ether = 1:3);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.19 (dd,  $J = 6.8, 4.4$  Hz, 3H), 7.96 (dd,  $J = 4.8, 1.2$  Hz, 1H), 7.81 (dd,  $J = 4.8, 1.2$  Hz, 1H), 7.50 (dd,  $J = 9.6, 6.0$  Hz, 3H), 7.36 (t,  $J = 7.6$  Hz, 1H), 7.20 (q,  $J = 4.4$  Hz, 2H), 2.40 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  182.6, 180.7, 153.9, 148.7, 148.2, 143.3, 141.6, 138.8, 138.4, 137.7, 137.43, 137.38, 137.35, 129.2, 129.1, 128.2, 127.2, 121.4, 114.1, 113.5, 98.6, 13.6. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{24}\text{H}_{14}\text{N}_4\text{O}_2\text{S}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  477.0450, found 477.0452.



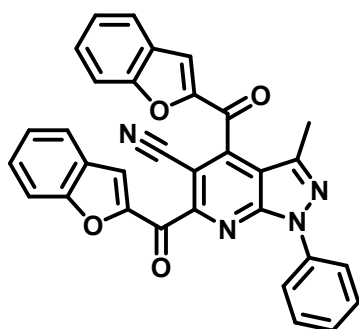
**3-methyl-1-phenyl-4,6-di(thiophene-3-carbonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4ab):** Yield 67%; 152.1 mg; yellow solid; mp 176-178 °C;  $R_f$  0.17 (EtOAc/petroleum ether = 1:5);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.50 (s, 1H), 8.17 (d,  $J = 8.0$  Hz, 2H), 7.99 (s, 1H), 7.80 (s, 1H), 7.65 (d,  $J = 17.2$  Hz, 1H), 7.48 (s, 3H), 7.37 (s, 2H), 2.37 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  184.3, 182.8, 155.2, 149.5, 148.4, 143.4, 140.3, 138.6, 137.9, 137.7, 135.7, 129.2, 128.9, 128.3, 127.1, 126.7, 126.1, 121.0, 114.2, 113.3, 98.6, 13.7. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{24}\text{H}_{14}\text{N}_4\text{O}_2\text{S}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  477.0450, found 477.0452.



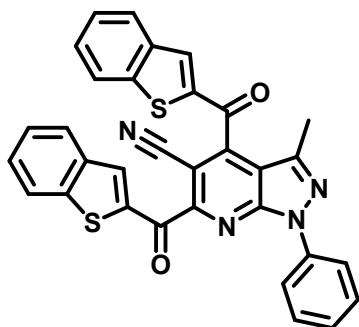
**4-(3-bromothiophene-2-carbonyl)-6-(5-bromothiophene-2-carbonyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4ac):** Yield 52%; 158.6 mg; yellow solid; mp 189-191 °C;  $R_f$  0.31 (EtOAc/petroleum ether = 1:5);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.15 (d,  $J = 8.0$  Hz, 2H), 8.02 (d,  $J = 4.4$  Hz, 1H), 7.61 (t,  $J = 8.0$  Hz, 2H), 7.47 (t,  $J = 7.6$  Hz, 1H), 7.22–7.14 (m, 3H), 2.47 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  181.4, 179.0, 152.8, 148.31, 148.27, 143.5, 142.9, 138.9, 137.7, 137.6, 137.4, 132.4, 131.1, 129.4, 128.5, 127.9, 127.1, 122.4, 114.1, 113.9, 99.0, 13.8. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{24}\text{H}_{12}\text{Br}_2\text{N}_4\text{O}_2\text{S}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  634.8640, found 634.8639.



**4,6-bis(2,5-dimethylthiophene-3-carbonyl)-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carbonitrile (4ad):** Yield 63%; 160.7 mg; yellow solid; mp 164-166 °C;  $R_f$  0.17 (EtOAc/petroleum ether = 1:10);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.23 (d,  $J = 8.0$  Hz, 2H), 7.49 (t,  $J = 8.0$  Hz, 2H), 7.34 (t,  $J = 7.6$  Hz, 1H), 7.08 (s, 1H), 6.52 (s, 1H), 2.84 (s, 3H), 2.78 (s, 3H), 2.41 (s, 6H), 2.34 (s, 3H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  185.2, 185.1, 157.2, 152.7, 152.6, 150.4, 148.6, 143.4, 138.2, 136.9, 134.8, 133.6, 132.9, 129.2, 128.1, 126.9, 126.8, 120.9, 114.3, 112.6, 97.6, 16.5, 16.3, 14.9, 13.7. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{28}\text{H}_{22}\text{N}_4\text{O}_2\text{S}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  533.1076, found 533.1079.

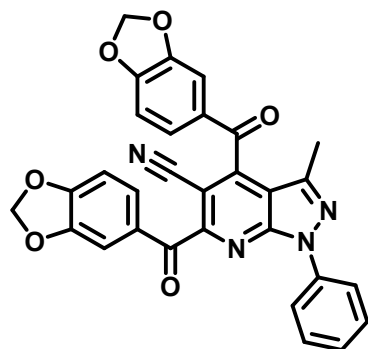


**4,6-di(benzofuran-2-carbonyl)-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carbonitrile (4ae):** Yield 60%; 156.6 mg; yellow solid; mp 206-208 °C;  $R_f$  0.17 (EtOAc/petroleum ether = 1:5);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.26 (d,  $J = 8.0$  Hz, 2H), 8.03 (s, 1H), 7.75 (t,  $J = 8.4$  Hz, 2H), 7.71–7.64 (m, 2H), 7.63–7.50 (m, 5H), 7.45–7.31 (m, 3H), 2.48 (s, 3H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  179.6, 178.3, 157.0, 156.4, 153.5, 150.6, 150.3, 148.6, 147.6, 143.5, 138.0, 130.4, 129.6, 129.3, 127.4, 127.1, 126.7, 124.8, 124.3, 124.1, 123.9, 121.3, 120.5, 114.0, 113.8, 112.9, 112.6, 99.2, 14.0. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{32}\text{H}_{18}\text{N}_4\text{O}_4\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  545.1220, found 545.1223.

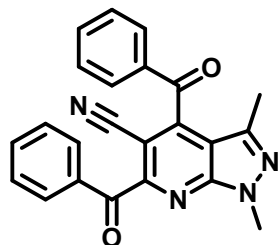


**4,6-bis(benzo[*b*]thiophene-2-carbonyl)-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carbonitrile (4af):** Yield 58%; 160.7 mg; white solid; mp 255-257 °C;

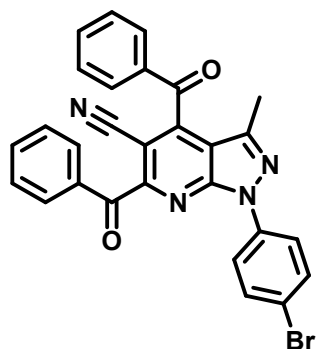
$R_f$  0.24 (EtOAc/petroleum ether = 1:5);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.54 (s, 1H), 8.27 (d,  $J = 8.0$  Hz, 2H), 8.06–7.79 (m, 4H), 7.74 (s, 1H), 7.65–7.46 (m, 4H), 7.43 (t,  $J = 6.8$  Hz, 3H), 2.46 (s, 3H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  184.4, 182.4, 153.7, 148.6, 148.4, 144.2, 143.5, 141.1, 139.2, 138.73, 138.67, 137.9, 135.39, 135.35, 129.3, 129.1, 128.3, 127.4, 126.9, 126.6, 125.7, 125.3, 123.2, 122.8, 121.6, 114.1, 113.8, 99.0, 13.8. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{32}\text{H}_{18}\text{N}_4\text{O}_2\text{S}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  577.0763, found 577.0765.



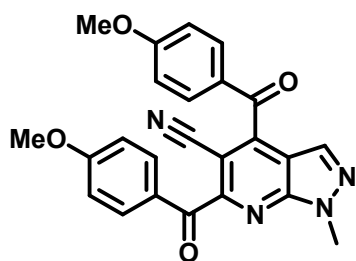
**4,6-bis(benzo[*d*][1,3]dioxole-5-carbonyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4ag):** Yield 67%; 177.6 mg; yellow solid; mp 177-179 °C;  $R_f$  0.18 (EtOAc/petroleum ether = 1:3);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.17 (d,  $J = 8.0$  Hz, 2H), 7.60 (t,  $J = 4.0$  Hz, 2H), 7.48 (dd,  $J = 18.4, 10.8$  Hz, 3H), 7.36–7.22 (m, 2H), 6.87 (dd,  $J = 8.4, 3.6$  Hz, 2H), 6.10 (d,  $J = 13.2$  Hz, 4H), 2.37 (s, 3H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  189.0, 188.4, 156.7, 154.2, 153.1, 149.2, 149.1, 148.32, 148.30, 143.4, 138.1, 129.7, 129.2, 129.0, 128.9, 128.7, 126.9, 121.0, 114.1, 113.3, 109.7, 108.6, 108.2, 107.9, 102.5, 102.2, 98.6, 13.7. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{30}\text{H}_{18}\text{N}_4\text{O}_6\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  553.1119, found 553.1120.



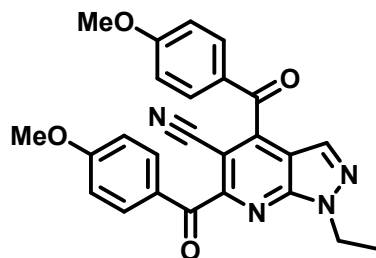
**4,6-dibenzoyl-1,3-dimethyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (5a):** Yield 76%; 144.4 mg; yellow solid; mp 147-149 °C;  $R_f$  0.20 (EtOAc/petroleum ether = 1:3);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.05 (s, 2H), 7.87 (s, 2H), 7.70 (s, 2H), 7.55 (s, 4H), 4.13 (s, 3H), 2.24 (s, 3H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  191.5, 190.7, 156.1, 149.2, 149.0, 141.9, 135.6, 134.8, 134.5, 134.3, 131.0, 130.1, 129.4, 128.6, 114.3, 111.5, 97.6, 34.2, 13.6. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{23}\text{H}_{16}\text{N}_4\text{O}_2\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  403.1166, found 403.1165.



**4,6-dibenzoyl-1-(4-bromophenyl)-3-methyl-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (5b):** Yield 68%; 176.8 mg; yellow solid; mp 181-183 °C;  $R_f$  0.17 (EtOAc/petroleum ether = 1:8);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.08 (t,  $J = 9.2$  Hz, 4H), 7.89 (d,  $J = 7.6$  Hz, 2H), 7.80–7.62 (m, 2H), 7.64–7.42 (m, 6H), 2.30 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  191.0, 190.0, 155.7, 149.2, 148.1, 143.6, 137.0, 135.7, 134.5, 134.27, 134.25, 132.1, 131.0, 130.0, 129.4, 128.4, 121.9, 120.0, 113.9, 113.6, 99.0, 13.7. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{28}\text{H}_{18}\text{BrN}_4\text{O}_2$  ( $\text{M}+\text{H}$ ) $^+$  521.0608, found 521.0607.

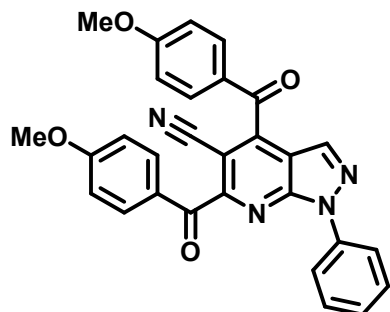


**4,6-bis(4-methoxybenzoyl)-1-methyl-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (5c):** Yield 75%; 159.8 mg; yellow solid; mp 224-226 °C;  $R_f$  0.17 (EtOAc/petroleum ether = 1:2);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.19–7.92 (m, 3H), 7.85 (d,  $J = 8.4$  Hz, 2H), 6.99 (d,  $J = 8.8$  Hz, 4H), 4.21 (s, 3H), 3.91 (s, 6H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  189.2, 189.0, 165.4, 164.7, 157.5, 148.6, 147.9, 133.5, 132.9, 132.6, 127.6, 127.4, 114.5, 114.4, 114.0, 112.9, 98.7, 55.7, 55.6, 34.6. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{24}\text{H}_{18}\text{N}_4\text{O}_4\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  449.1220, found 449.1221.

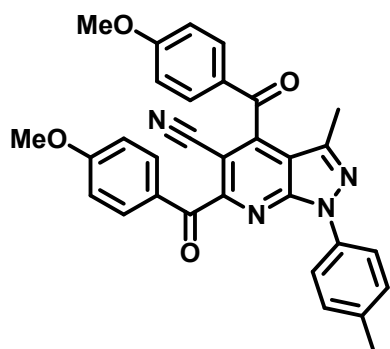


**1-ethyl-4,6-bis(4-methoxybenzoyl)-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (5d):** Yield 79%; 173.9 mg; yellow solid; mp 144-146 °C;  $R_f$  0.20 (EtOAc/petroleum ether = 1:3);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.11–7.98 (m, 2H), 7.97 (s, 1H), 7.89–7.81 (m, 2H), 7.17–6.50 (m, 4H), 4.62 (q,  $J = 7.2$  Hz, 2H), 3.90 (s, 3H), 3.89 (s, 3H), 1.56

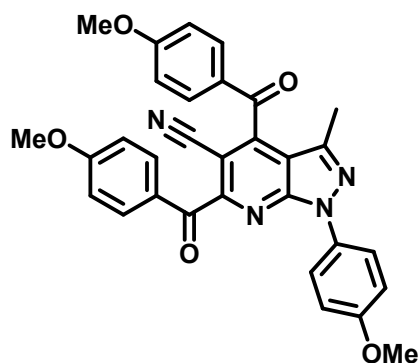
(t,  $J = 7.2$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  189.2, 189.0, 165.3, 164.6, 157.1, 147.9, 147.8, 133.4, 132.8, 132.5, 127.5, 127.3, 114.5, 114.4, 113.9, 112.9, 98.6, 55.6, 55.5, 42.9, 14.7. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{25}\text{H}_{20}\text{N}_4\text{O}_4\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  463.1377, found 463.1378.



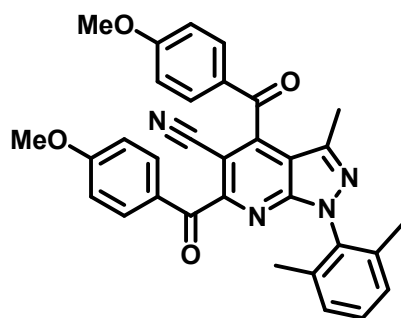
**4,6-bis(4-methoxybenzoyl)-1-phenyl-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (5e):** Yield 80%; 195.3 mg; yellow solid; mp 149-151 °C;  $R_f$  0.37 (EtOAc/petroleum ether = 1:3);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.30–8.18 (m, 2H), 8.16 (s, 1H), 8.08–8.01 (m, 2H), 7.93–7.84 (m, 2H), 7.54–7.43 (m, 2H), 7.41–7.31 (m, 1H), 7.08–6.92 (m, 4H), 3.91 (s, 6H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  188.79, 188.75, 165.5, 164.7, 157.6, 148.2, 147.8, 138.2, 134.0, 133.6, 133.0, 129.3, 127.5, 127.32, 127.28, 121.2, 114.7, 114.2, 114.0, 99.7, 55.7, 55.6. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{29}\text{H}_{20}\text{N}_4\text{O}_4\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  511.1377, found 511.1379.



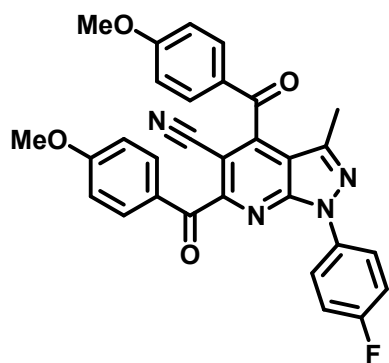
**4,6-bis(4-methoxybenzoyl)-3-methyl-1-(*p*-tolyl)-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (5f):** Yield 81%; 209.1 mg; yellow solid; mp 120-122 °C;  $R_f$  0.43 (EtOAc/petroleum ether = 1:3);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.17–8.00 (m, 4H), 7.92 (d,  $J = 8.4$  Hz, 2H), 7.31 (s, 1H), 7.29 (s, 1H), 7.04 (dd,  $J = 11.6, 8.8$  Hz, 4H), 3.944 (s, 3H), 3.937 (s, 3H), 2.42 (s, 3H), 2.39 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  189.5, 188.8, 165.5, 164.5, 156.8, 149.4, 148.2, 143.1, 136.8, 135.8, 133.6, 132.7, 129.7, 127.9, 127.4, 120.9, 114.7, 114.3, 113.9, 113.1, 98.5, 55.7, 55.6, 21.0, 13.7. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{31}\text{H}_{24}\text{N}_4\text{O}_4\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  539.1690, found 539.1691.



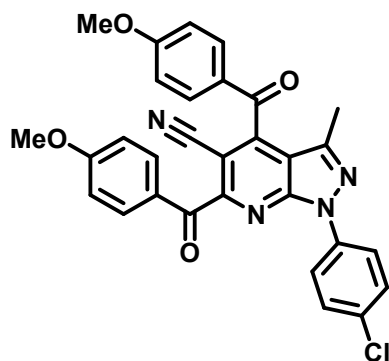
**4,6-bis(4-methoxybenzoyl)-1-(4-methoxyphenyl)-3-methyl-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (5g):** Yield 78%; 207.5 mg; yellow solid; mp 116-118 °C;  $R_f$  0.33 (EtOAc/petroleum ether = 1:3);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.04 (dd,  $J$  = 11.2, 8.8 Hz, 4H), 7.88 (d,  $J$  = 8.4 Hz, 2H), 7.01 (s, 1H), 7.00–6.92 (m, 5H), 3.88 (s, 6H), 3.81 (s, 3H), 2.33 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  189.5, 188.8, 165.4, 164.5, 158.2, 156.7, 149.4, 147.9, 142.9, 133.5, 132.6, 131.3, 127.8, 127.2, 122.5, 114.7, 114.4, 114.2, 113.8, 112.8, 98.2, 55.7, 55.5, 55.4, 13.6. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{31}\text{H}_{24}\text{N}_4\text{O}_5\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  555.1639, found 555.1641.



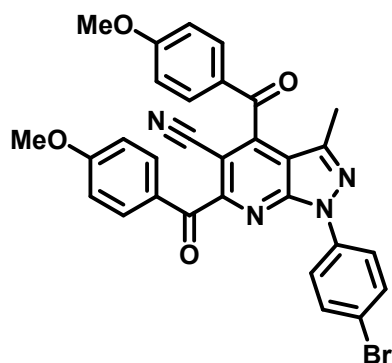
**1-(2,6-dimethylphenyl)-4,6-bis(4-methoxybenzoyl)-3-methyl-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (5h):** Yield 77%; 204.1 mg; yellow solid; mp 197-199 °C;  $R_f$  0.36 (EtOAc/petroleum ether = 1:3);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.91 (t,  $J$  = 8.4 Hz, 4H), 7.38–7.19 (m, 1H), 7.18 (d,  $J$  = 7.6 Hz, 2H), 7.04 (d,  $J$  = 8.8 Hz, 2H), 6.89 (d,  $J$  = 8.8 Hz, 2H), 3.91 (s, 3H), 3.85 (s, 3H), 2.37 (s, 3H), 1.99 (s, 6H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  189.8, 189.1, 165.5, 164.6, 157.9, 149.7, 149.4, 143.4, 136.6, 134.9, 133.3, 132.7, 129.9, 128.4, 127.8, 127.3, 114.8, 114.3, 113.8, 111.2, 98.0, 55.7, 55.5, 17.8, 13.8. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{32}\text{H}_{26}\text{N}_4\text{O}_4\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  553.1846, found 553.1848.



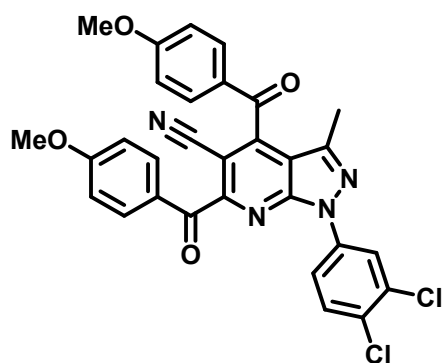
**1-(4-fluorophenyl)-4,6-bis(4-methoxybenzoyl)-3-methyl-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (5i):** Yield 80%; 208.1 mg; yellow solid; mp 159-161 °C;  $R_f$  0.43 (EtOAc/petroleum ether = 1:3);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.16 (dd,  $J = 8.8, 4.8$  Hz, 2H), 8.04 (d,  $J = 8.4$  Hz, 2H), 7.87 (d,  $J = 8.4$  Hz, 2H), 7.13 (t,  $J = 8.4$  Hz, 2H), 6.99 (dd,  $J = 14.8, 8.4$  Hz, 4H), 3.89 (s, 6H), 2.34 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  189.3, 188.6, 165.5, 164.6, 160.9 (d,  $J = 246.9$  Hz,  $^1J_{\text{CF}}$ ), 156.9, 149.5, 148.2, 143.4, 134.3 (d,  $J = 3.0$  Hz,  $^4J_{\text{CF}}$ ), 133.5, 132.6, 127.8, 127.1, 122.6 (d,  $J = 8.4$  Hz,  $^3J_{\text{CF}}$ ), 115.9 (d,  $J = 22.8$  Hz,  $^2J_{\text{CF}}$ ), 114.7, 114.2, 113.8, 113.2, 98.7, 55.7, 55.6, 13.6.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -114.66 (s, F). HRMS (ESI)  $m/z$  calcd for  $\text{C}_{30}\text{H}_{21}\text{FN}_4\text{O}_4\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  543.1439, found 543.1440.



**1-(4-chlorophenyl)-4,6-bis(4-methoxybenzoyl)-3-methyl-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (5j):** Yield 78%; 104.5 mg; yellow solid; mp 134-136 °C;  $R_f$  0.50 (EtOAc/petroleum ether = 1:3);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.19 (d,  $J = 8.8$  Hz, 2H), 8.13–7.96 (m, 2H), 7.87 (d,  $J = 8.4$  Hz, 2H), 7.51–7.33 (m, 2H), 7.09–6.78 (m, 4H), 3.91 (s, 3H), 3.89 (s, 3H), 2.34 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  189.2, 188.6, 165.5, 164.6, 157.0, 149.6, 148.3, 143.8, 136.8, 133.5, 132.7, 132.1, 129.2, 127.8, 127.2, 121.8, 114.8, 114.1, 113.9, 113.5, 98.9, 55.7, 55.6, 13.7. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{30}\text{H}_{21}\text{ClN}_4\text{O}_4\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  559.1144, found 559.1144.

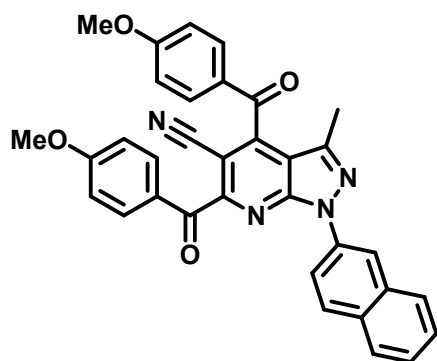


**1-(4-bromophenyl)-4,6-bis(4-methoxybenzoyl)-3-methyl-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (5k):** Yield 75%; 217.5 mg; yellow solid; mp 137-139 °C;  $R_f$  0.50 (EtOAc/petroleum ether = 1:3);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.07 (d,  $J$  = 37.6 Hz, 4H), 7.87 (s, 2H), 7.53 (s, 2H), 6.98 (s, 4H), 3.88 (s, 6H), 2.33 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  189.2, 188.5, 183.2, 165.4, 164.5, 156.8, 149.5, 148.3, 143.7, 137.2, 133.5, 132.6, 132.1, 127.7, 127.0, 121.9, 119.9, 114.7, 114.1, 113.8, 113.5, 98.9, 55.7, 55.6, 13.7. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{30}\text{H}_{21}\text{BrN}_4\text{O}_4\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  603.0638, found 603.0639.

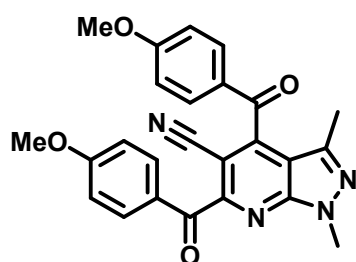


**1-(3,4-dichlorophenyl)-4,6-bis(4-methoxybenzoyl)-3-methyl-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (5l):** Yield 73%; 219.5 mg; yellow solid; mp 208-210 °C;  $R_f$  0.40 (EtOAc/petroleum ether = 1:3);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.98 (d,  $J$  = 8.8 Hz, 2H), 7.87 (d,  $J$  = 8.4 Hz, 2H), 7.56 (d,  $J$  = 2.4 Hz, 1H), 7.49 (d,  $J$  = 8.4 Hz, 1H), 7.36 (dd,  $J$  = 8.4, 2.4 Hz, 1H), 6.99 (d,  $J$  = 8.8 Hz, 2H), 6.92 (d,  $J$  = 8.8 Hz, 2H), 3.87 (s, 3H), 3.86 (s, 3H), 2.35 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  189.3, 188.7, 165.5, 164.6, 157.6, 149.8, 149.6, 144.2, 136.0, 133.5, 133.2, 132.6, 132.5, 130.3, 130.2, 128.0, 127.6, 126.9, 114.7, 114.2, 113.8, 112.1, 98.8, 55.7, 55.5, 13.7. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{30}\text{H}_{20}\text{Cl}_2\text{N}_4\text{O}_4\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  593.0754, found 593.0756.

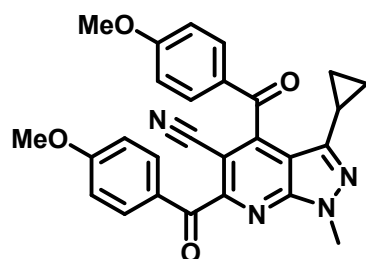




**4,6-bis(4-methoxybenzoyl)-3-methyl-1-(naphthalen-2-yl)-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (5m):** Yield 73%; 201.5 mg; yellow solid; mp 236-238 °C;  $R_f$  0.43 (EtOAc/petroleum ether = 1:3);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.70 (d,  $J = 2.4$  Hz, 1H), 8.36 (dd,  $J = 8.8, 2.4$  Hz, 1H), 8.22–8.06 (m, 2H), 8.02–7.81 (m, 4H), 7.82–7.72 (m, 1H), 7.64–7.39 (m, 2H), 7.17–6.88 (m, 4H), 3.91 (s, 3H), 3.90 (s, 3H), 2.39 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  189.4, 188.7, 165.5, 164.5, 156.6, 149.6, 148.5, 143.6, 135.7, 133.7, 133.3, 132.7, 131.8, 129.2, 128.2, 127.9, 127.7, 127.4, 126.8, 126.2, 119.6, 118.6, 114.8, 114.3, 113.9, 113.5, 99.0, 55.8, 55.6, 13.8. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{34}\text{H}_{24}\text{N}_4\text{O}_4\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  575.1689, found 575.1691.

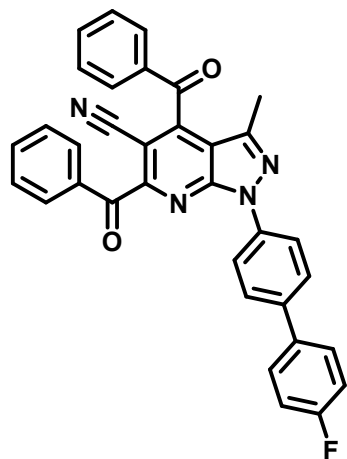


**4,6-bis(4-methoxybenzoyl)-1,3-dimethyl-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (5n):** Yield 74%; 162.9 mg; yellow solid; mp 188-190 °C;  $R_f$  0.17 (EtOAc/petroleum ether = 1:2);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.09–7.98 (m, 2H), 7.83 (d,  $J = 8.4$  Hz, 2H), 7.08–6.94 (m, 4H), 4.13 (s, 3H), 3.91 (s, 3H), 3.90 (s, 3H), 2.26 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  189.7, 189.3, 165.4, 164.6, 156.9, 149.3, 149.2, 142.0, 133.5, 132.6, 127.9, 127.4, 114.7, 114.5, 113.9, 111.4, 97.4, 55.7, 55.6, 34.1, 13.6. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{25}\text{H}_{20}\text{N}_4\text{O}_4\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  463.13768, found 463.13779.



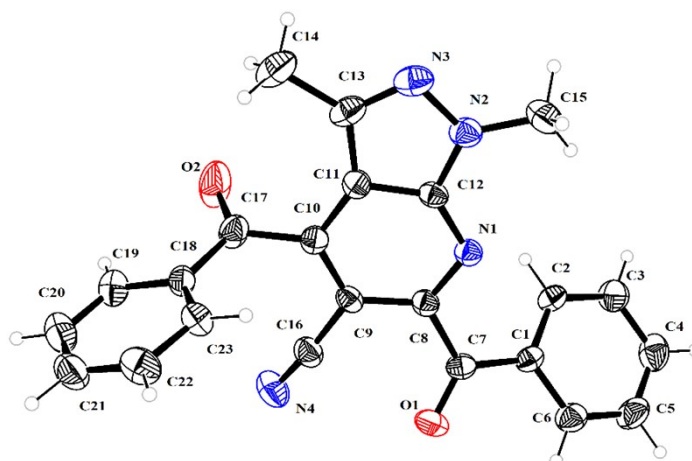
**3-cyclopropyl-4,6-bis(4-methoxybenzoyl)-1-methyl-1H-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (5o):** Yield 70%; 163.2 mg; yellow solid; mp 188-190 °C;  $R_f$  0.20

(EtOAc/petroleum ether = 1:2);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.02 (d,  $J = 8.8$  Hz, 2H), 7.84 (d,  $J = 8.4$  Hz, 2H), 6.99 (dd,  $J = 8.8, 3.2$  Hz, 4H), 4.09 (s, 3H), 3.91 (s, 3H), 3.90 (s, 3H), 1.92–1.48 (m, 1H), 0.77 (d,  $J = 59.6$  Hz, 4H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  190.1, 189.3, 165.3, 164.6, 157.0, 149.3, 149.2, 147.2, 133.5, 132.6, 128.1, 127.5, 114.6, 113.9, 111.8, 97.4, 55.7, 55.6, 34.1, 8.5, 7.6. HRMS (ESI)  $m/z$  calcd for  $\text{C}_{27}\text{H}_{22}\text{N}_4\text{O}_4\text{Na}^+$  ( $\text{M}+\text{Na}$ ) $^+$  489.1533, found 489.1535.



**4,6-dibenzoyl-1-(4'-fluoro-[1,1'-biphenyl]-4-yl)-3-methyl-1H-pyrazolo[3,4-b]pyridine-5-carbonitrile (7a):** Yield 87%; 93.3 mg; yellow solid; mp 205-207 °C;  $R_f$  0.17 (EtOAc/petroleum ether = 1:8);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.25 (d,  $J = 8.8$  Hz, 2H), 8.11 (d,  $J = 7.6$  Hz, 2H), 7.92 (d,  $J = 7.6$  Hz, 2H), 7.78–7.65 (m, 2H), 7.64–7.47 (m, 8H), 7.12 (t,  $J = 8.8$  Hz, 2H), 2.34 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  191.2, 190.2, 162.5 (d,  $J = 240.2$  Hz,  $^1J_{\text{CF}}$ ), 155.9, 149.3, 148.3, 143.5, 138.7, 137.3, 136.0 (d,  $J = 3.2$  Hz,  $^4J_{\text{CF}}$ ), 135.7, 134.7, 134.5, 134.3, 131.1, 130.1, 129.5, 128.50 (d,  $J = 8.0$  Hz,  $^3J_{\text{CF}}$ ), 128.52, 127.6, 121.1, 115.7 (d,  $J = 21.4$  Hz,  $^2J_{\text{CF}}$ ), 114.1, 113.6, 98.9, 13.8.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -114.96 (s, F) HRMS (ESI)  $m/z$  calcd for  $\text{C}_{34}\text{H}_{22}\text{FN}_4\text{O}_2^+$  ( $\text{M}+\text{H}$ ) $^+$  537.1721, found 537.1720.

## 6. Crystallographic data and molecular structure of compounds 5a



**Figure S1.** X-ray crystal structure of **5a** with 30% probability ellipsoids (ORTEP) Crystal Data for Compound **5a**: CCDC 2264899 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic.

Sample preparation: In a 10 mL glass bottle, 15 mg of pure 5a was completely dissolved in the mixed solvent of 3 mL EtOAc, 1 mL MeOH and 1 mL CHCl<sub>3</sub>; and then 2 mL of *n*-hexane was added slowly. After a week of solvent evaporation, some colorless transparent crystals were obtained. The crystals were mounted on a glass fiber for diffraction experiments. Intensity data were collected on a Bruker SMART APEX CCD diffractometer with Mo K $\alpha$  radiation (0.71073 Å) at room temperature.

Bond precision:	C-C = 0.0062 Å	Wavelength=0.71073	
Cell:	a=9.378 (4)	b=28.538 (12)	c=14.882 (6)
	alpha=90	beta=95.505 (7)	gamma=90
Temperature:	296 K		
	Calculated	Reported	
Volume	3965 (3)	3964 (3)	
Space group	P 21/c	P 1 21/c 1	
Hall group	-P 2ybc	-P 2ybc	
Moiety formula	C23 H16 N4 O2	C23 H16 N4 O2	
Sum formula	C23 H16 N4 O2	C23 H16 N4 O2	
Mr	380.40	380.40	
Dx, g cm <sup>-3</sup>	1.275	1.275	
Z	8	8	
Mu (mm <sup>-1</sup> )	0.084	0.084	
F000	1584.0	1584.0	
F000'	1584.64		
h, k, lmax	11, 35, 18	11, 35, 18	
Nref	8169	7930	
Tmin, Tmax	0.989, 0.992	0.586, 0.745	
Tmin'	0.989		
Correction method= # Reported T Limits: Tmin=0.586 Tmax=0.745			
AbsCorr = MULTI-SCAN			
Data completeness=	0.971	Theta(max)= 26.426	
R(reflections)=	0.0732( 3299)	wR2(reflections)=	
S =	0.977	0.2136( 7930)	
	Npar= 527		

## 7. $^1\text{H}$ , $^{13}\text{C}$ and $^{19}\text{F}$ NMR spectra of compounds

