Organocatalytic (5 + 1) benzannulation of Morita−Baylis−Hillman carbonates: synthesis of multisubstituted 4-benzylidene pyrazolones

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Electronic Supplementary Information (ESI)

for

New Journal of Chemistry

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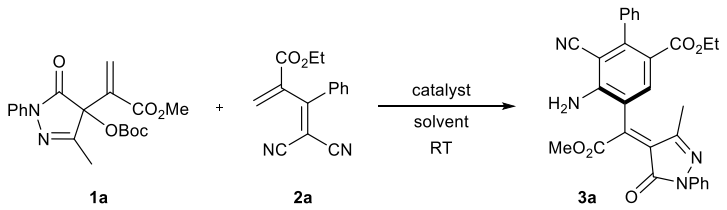
1. General Information

Nuclear magnetic resonance (NMR) spectra were recorded in $CDCl_3$ on Bruker 600, 700 MHz, or JEOL 600 NMR instrument (at 600 or 700 MHz for ^1H, at 660 MHz for ^{19}F, and at 150, or 175 MHz for ^{13}C). The ^1H NMR chemical shifts are reported in ppm with the internal $CDCl_3$ signal at 7.26 ppm (DMSO-d_6 signal at 2.50 ppm) as standard. The ^{13}C NMR chemical shifts were given using $CDCl_3$ or DMSO-d_6 as the internal standard ($CDCl_3$: δ = 77.00 ppm; DMSO-d_6: δ = 39.50 ppm). High-resolution mass spectra (HRMS) were obtained using Agilent P/N G1969-90010 or Waters/Acquity UPLC-Synapt G2HDMS. High-resolution mass spectra were reported for the molecular ion $[M+H]^+$ or $[M+Na]^+$. Melting points were recorded on BUCHI Melting Point M-565 instrument. Conduct anhydrous and anaerobic tests in the MB-Unilab Pro SP (1250/780) glove box. X-ray diffraction experiment was carried out on an Agilent Gemini and the data obtained were deposited at the Cambridge Crystallographic Data Centre. UV-Vis absorption spectra of BNCDs were measured by a TU-1901 spectrophotometer (Persee, China), the fluorescence spectra were recorded by a F97Pro fluorescence spectrophotometer (Lengguang Technology, China). Measure the oxidation reducibility of **3a** with IKA Electra Syn 2.0. UV detection was performed at 254 nm. Column chromatography was performed on silica gel (200-300 mesh) using an eluent of ethyl acetate and petroleum ether. TLC was performed on glass-backed silica plates; products were visualized using UV light. All reagents and solvents were obtained from commercial sources and used without further purification.

2. Optimization of the model reaction

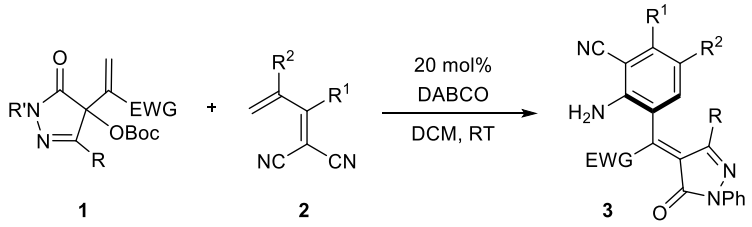


entry[a]	catalyst	solvent	(**1a**/**2a**/cat.)	T(℃)	*t* (h)	Yield [%]
1	PPh_3	DCM	1/1/0.2	RT	24	N.R.
2	DMAP	DCM	1/1/0.2	RT	24	28
3	DABCO	DCM	1/1/0.2	RT	72	67
4	Et_3N	DCM	1/1/0.2	RT	24	N.R.
5	DABCO	H_2O	1/1/0.2	RT	24	N.R.
6	DABCO	toluene	1/1/0.2	RT	72	42
7	DABCO	$CHCl_3$	1/1/0.2	RT	72	26
8	DABCO	THF	1/1/0.2	RT	72	38
9	DABCO	EA	1/1/0.2	RT	72	trace

10	DABCO	DCE	1/1/0.2	RT	72	50
11	DABCO	DCM	1.2/1/0.2	RT	72	33
12	DABCO	DCM	1/1.2/0.2	RT	72	45
13	DABCO	DCM	1/1/0.5	RT	72	29
14	DABCO	DCM	1/1/0.2	40	24	49

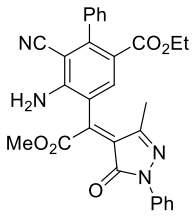
[a] Unless noted otherwise, reactions were performed using **1a** (0.10 mmol), **2a** (0.10 mmol), catalyst (0.02 mmol) in solvent (1.0 mL) at RT. Isolated yield.

3. General procedures for the (5 + 1) benzannulation



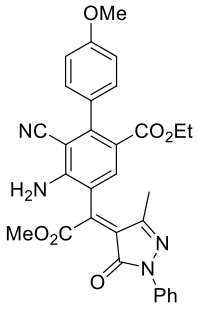
1 **2** **3**

A mixture of pyrazolone-derived MBH carbonate **1** (0.1 mmol), 2-allylidenemalononitrile **2** (0.1 mmol), and DABCO (20 mol%) in DCM (1.0 mL) was stirred at RT for 72 h (monitored by TLC). The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (ethyl acetate/petroleum ether = 1/5) to give product **3**.



3a

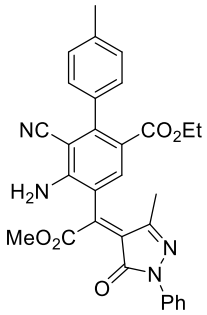
Ethyl (Z)-5-amino-6-cyano-4-(2-methoxy-1-(3-methyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxoethyl)-[1,1'-biphenyl]-2-carboxylate (3a). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3a**: 34.0 mg as a yellow solid, 67% yield; m.p. 82.6 – 83.5 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.88 (d, *J* = 7.7 Hz, 2H), 7.50 – 7.44 (m, 3H), 7.41 (t, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 4.2 Hz, 2H), 7.22 (t, *J* = 7.0 Hz, 1H), 5.52 (s, 2H), 4.02 (q, *J* = 7.0 Hz, 2H), 4.01 (s, 3H), 1.92 (s, 3H), 0.95 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 166.6, 165.3, 160.7, 150.3, 149.7, 147.5, 142.5, 137.6, 137.4, 136.2, 130.0, 129.0, 128.8, 128.2, 128.1, 125.6, 120.4, 118.8, 115.3, 115.2, 99.8, 61.2, 53.9, 16.4, 13.6 ; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{29}H_{25}N_4O_5$ 509.1825; Found 509.1825.



3b

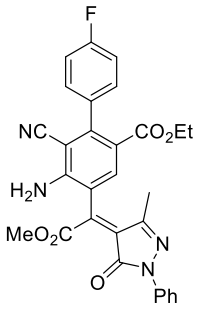
Ethyl (Z)-5-amino-6-cyano-4'-methoxy-4-(2-methoxy-1-(3-methyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxoethyl)-[1,1'-biphenyl]-2-carboxylate (3b). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3b**: 44.0 mg as a yellow solid, 82% yield; m.p. 166.0 – 167.2 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 – 7.85 (m, 3H), 7.41(t, *J* = 7.8 Hz, 2H), 7.25 – 7.19 (m, 3H), 6.99 (d, *J* = 9.0 Hz, 2H), 5.50 (s, 2H), 4.06 (q, *J* = 7.2 Hz, 2H), 4.01 (s, 3H), 3.86 (s, 3H), 1.92 (s, 3H), 1.03 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.7, 165.6, 160.8, 160.2, 150.2, 149.7, 147.6, 142.7, 137.5, 136.2, 130.0, 129.7, 129.1, 125.6, 120.8, 118.8, 115.6, 115.0,

113.8, 100.1, 61.3, 55.4, 54.0, 16.5, 13.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{30}H_{27}N_4O_6$ 539.1931; Found 539.1930.



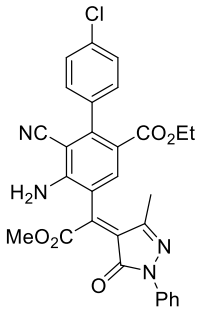
3c

Ethyl (Z)-5-amino-6-cyano-4-(2-methoxy-1-(3-methyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxoethyl)-4'-methyl-[1,1'-biphenyl]-2-carboxylate (3c). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3c**: 25.9 mg as a yellow solid, 50% yield; m.p. 145.3 – 146.5 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.87 (dd, *J* = 8.4, 0.6 Hz, 2H), 7.44 – 7.39 (m, 2H), 7.27 (d, *J* = 7.2 Hz, 2H), 7.23 – 7.17 (m, 3H), 5.51 (s, 2H), 4.05 (q, *J* = 7.2 Hz, 2H), 4.01 (s, 3H), 2.42 (s, 3H), 1.92 (s, 3H), 1.00 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.7, 165.5, 160.8, 150.6, 149.7, 147.6, 142.7, 138.8, 137.5, 136.2, 134.6, 130.0, 129.1, 128.1, 125.6, 120.6, 118.8, 115.5, 115.1, 100.0, 61.3, 54.0, 21.5, 16.4, 13.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{30}H_{27}N_4O_5$ 523.1981; Found 523.1981.



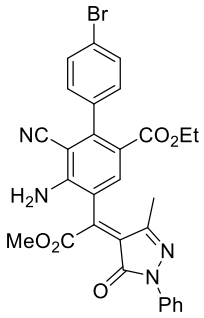
3d

Ethyl (Z)-5-amino-6-cyano-4'-fluoro-4-(2-methoxy-1-(3-methyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxoethyl)-[1,1'-biphenyl]-2-carboxylate(3d). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3d**: 47.0 mg as a yellow solid, 89% yield; m.p. 120.9 – 122.0 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.87 (d, *J* = 7.2 Hz, 2H), 7.43 – 7.40 (m, 2H), 7.28 (dd, *J* = 8.4, 5.4 Hz, 2H), 7.22 (tt, *J* = 7.8, 1.2 Hz, 1H), 7.17 (t, *J* = 8.4 Hz, 2H), 5.54 (s, 2H), 4.06 (q, *J* = 7.2 Hz, 2H), 4.01 (s, 3H), 1.91 (s, 3H), 1.02 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.5, 164.0, 162.8 (d, J_{FC}= 247.2 Hz), 161.2, 159.6, 148.7, 148.2, 146.3, 141.2, 136.3, 135.3, 132.5 (d, J_{FC}= 3.5 Hz), 132.4, 129.04 (d, J_{FC}= 9.0 Hz), 128.98, 128.0, 124.5, 119.2, 117.7, 114.5 (d, J_{FC}= 21.9 Hz), 114.4, 114.3, 114.1, 98.9, 60.3, 52.9, 15.4, 12.7; ^{19}F NMR (660 MHz, $CDCl_3$) δ -112.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{29}H_{24}FN_4O_5$ 527.1731; Found 527.1731.



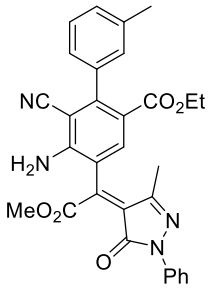
3e

Ethyl (Z)-5-amino-4'-chloro-6-cyano-4-(2-methoxy-1-(3-methyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxoethyl)-[1,1'-biphenyl]-2-carboxylate (3e). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3e**: 37.2 mg as a yellow solid, 69% yield; m.p. 112.9 – 113.7 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.90 – 7.84 (m, 2H), 7.46 – 7.40 (m, 4H), 7.25 – 7.20 (m, 3H), 5.55 (s, 2H), 4.06 (q, *J* = 7.2 Hz, 2H), 4.01 (s, 3H), 1.91 (s, 3H), 1.03 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.6, 165.0, 160.7, 149.8, 149.1, 147.4, 142.3, 137.4, 136.4, 136.1, 135.1, 130.1, 129.6, 129.1, 128.7, 125.7, 120.2, 118.8, 115.7, 115.2, 99.8, 61.4, 54.0, 16.5, 13.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{29}H_{24}ClN_4O_5$ 543.1435; Found 543.1438.



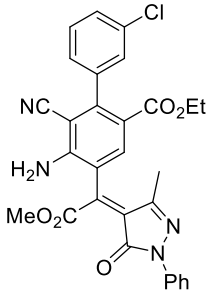
3f

Ethyl (Z)-5-amino-4'-bromo-6-cyano-4-(2-methoxy-1-(3-methyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxoethyl)-[1,1'-biphenyl]-2-carboxylate (3f). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3f**: 28.4 mg as a yellow solid, 49% yield; m.p. 144.2 – 145.8 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.87 (d, *J* = 9.0 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.41 (t, *J* = 7.8 Hz, 2H), 7.22 (td, *J* = 7.2, 1.2 Hz, 1H), 7.17 (d, *J* = 8.4 Hz, 2H), 5.56 (s, 2H), 4.06 (q, *J* = 7.2 Hz, 2H), 4.01 (s, 3H), 1.91 (s, 3H), 1.03 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.6, 165.0, 160.7, 149.9, 149.1, 147.4, 142.3, 137.4, 136.6, 136.4, 131.6, 130.1, 129.9, 129.1, 125.7, 123.3, 120.1, 118.8, 115.7, 115.2, 99.7, 61.5, 54.0, 16.5, 13.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{29}H_{24}{}^{79}BrN_4O_5$ 587.0930; Found 587.0926; Calcd for $C_{29}H_{24}{}^{81}BrN_4O_5$ 589.0910; Found 589.0908.



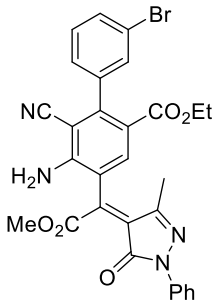
3g

Ethyl (Z)-5-amino-6-cyano-4-(2-methoxy-1-(3-methyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxoethyl)-3'-methyl-[1,1'-biphenyl]-2-carboxylate (3g). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3g**: 29.5 mg as a yellow solid, 57% yield; m.p. 110.5 – 112.1 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.87 (dq, *J* = 7.2, 0.6 Hz, 2H), 7.43 – 7.39 (m, 2H), 7.35 (t, *J* = 7.8 Hz, 1H), 7.27 (s, 1H), 7.22 (tt, *J* = 7.2, 1.2 Hz, 1H), 7.11 – 7.05 (m, 2H), 5.50 (s, 2H), 4.02 (q, *J* = 7.2 Hz, 2H), 4.01 (s, 3H), 2.41 (s, 3H), 1.92 (s, 3H), 0.96 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.7, 165.5, 150.5, 149.7, 147.6, 142.6, 137.9, 137.6, 137.5, 136.2, 130.0, 129.7, 129.1, 128.8, 128.2, 125.6, 125.3, 120.6, 118.9, 115.4, 115.2, 99.9, 61.2, 54.0, 21.5, 16.4, 13.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{30}H_{27}N_4O_5$ 523.1981; Found 523.1984.



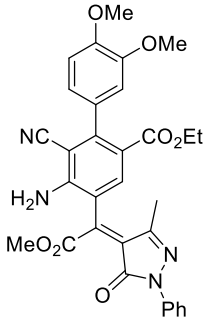
3h

Ethyl (Z)-5-amino-3'-chloro-6-cyano-4-(2-methoxy-1-(3-methyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxoethyl)-[1,1'-biphenyl]-2-carboxylate (3h). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3h**: 36.4 mg as a yellow solid, 67% yield; m.p. 114.9 – 115.3 ℃; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.91 – 7.74 (m, 2H), 7.47 – 7.39 (m, 4H), 7.29 (t, *J* = 2.1 Hz, 1H), 7.25 – 7.18 (m, 2H), 5.55 (s, 2H), 4.12 – 4.00 (m, 5H), 1.91 (s, 3H), 1.00 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 165.5, 163.8, 159.6, 148.7, 147.5, 146.3, 141.1, 138.3, 136.3, 135.4, 133.2, 129.0, 128.6, 128.0, 127.9, 127.3, 125.3, 124.6, 119.0, 117.7, 114.7, 113.9, 98.7, 60.3, 52.9, 15.4, 12.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{29}H_{24}ClN_4O_5$ 543.1435; Found 543.1435.



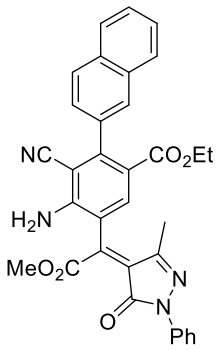
3i

Ethyl (Z)-5-amino-3'-bromo-6-cyano-4-(2-methoxy-1-(3-methyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxoethyl)-[1,1'-biphenyl]-2-carboxylate (3i). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3i**: 39.0 mg as a yellow solid, 66% yield; m.p. 59.3 – 60.1 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.87 (d, *J* = 7.8 Hz, 2H), 7.62 – 7.58 (m, 1H), 7.44 – 7.39 (m, 3H), 7.35 (t, *J* = 7.8 Hz, 1H), 7.26 – 7.20 (m, 2H), 5.57 (s, 2H), 4.12 – 4.00 (m, 5H), 1.91 (s, 3H), 1.00 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.5, 164.8, 160.6, 149.8, 148.4, 147.4, 142.1, 139.6, 137.3, 136.4, 131.8, 131.2, 130.1, 129.8, 129.0, 126.8, 125.6, 122.2, 120.0, 118.8, 115.7, 115.0, 99.6, 61.4, 53.9, 16.4, 13.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{29}H_{24}{}^{79}BrN_4O_5$ 587.0930; Found 587.0927; Calcd for $C_{29}H_{24}{}^{81}BrN_4O_5$ 589.0910; Found 589.0915.



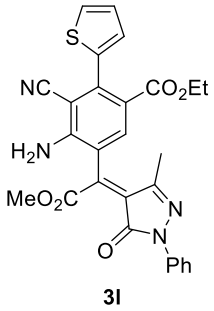
3j

Ethyl (Z)-5-amino-6-cyano-3',4'-dimethoxy-4-(2-methoxy-1-(3-methyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxoethyl)-[1,1'-biphenyl]-2-carboxylate (3j). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3j**: 36.8 mg as a yellow solid, 65% yield; m.p. 151.0 – 152.4 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 – 7.83 (m, 3H), 7.43 – 7.38 (m, 2H), 7.22 (tt, *J* = 7.2, 1.2 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 6.89 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.81 (d, *J* = 1.8 Hz, 1H), 5.49 (s, 2H), 4.07 (q, *J* = 7.2 Hz, 2H), 4.01 (s, 3H), 3.94 (s, 3H), 3.89 (s, 3H), 1.94 (s, 3H), 1.03 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.7, 165.7, 160.8, 149.9, 149.7, 148.8, 147.6, 142.6, 137.5, 136.1, 130.0, 129.9, 129.1, 125.6, 121.1, 120.9, 118.8, 115.6, 115.1, 111.8, 110.9, 100.0, 61.3, 56.1, 56.0, 53.9, 16.5, 13.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{31}H_{29}N_4O_7$ 569.2036; Found 569.2039.



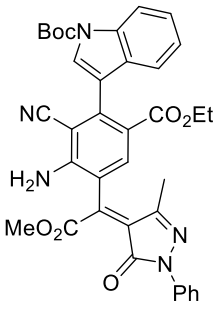
3k

Ethyl (Z)-4-amino-3-cyano-5-(2-methoxy-1-(3-methyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxoethyl)-2-(naphthalen-2-yl)benzoate (3k). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3k**: 35.5 mg as a yellow solid, 64% yield; m.p. 130.3 – 132.0 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.93 (d, *J* = 8.4 Hz, 1H), 7.92 – 7.86 (m, 4H), 7.79 (s, 1H), 7.56 – 7.52 (m, 2H), 7.44 – 7.38 (m, 3H), 7.23 (tt, *J* = 7.2, 1.2 Hz, 1H), 5.56 (s, 2H), 4.03 (s, 3H), 3.97 (q, *J* = 7.8 Hz, 2H), 1.96 (s, 3H), 0.81 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.7, 165.4, 160.8, 150.3, 149.8, 147.6, 142.6, 137.5, 136.3, 135.1, 133.3, 133.0, 130.1, 129.1, 128.4, 128.0, 127.5, 126.9, 126.7, 126.1, 125.6, 120.6, 118.9, 115.42, 115.40, 100.1, 61.3, 54.0, 16.5, 13.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{33}H_{27}N_4O_5$ 559.1981; Found 559.1982.



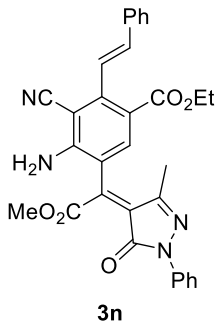
3l

Ethyl (Z)-4-amino-3-cyano-5-(2-methoxy-1-(3-methyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxoethyl)-2-(thiophen-2-yl)benzoate (3l). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3l**: 28.8 mg as a yellow solid, 56% yield; m.p. 125.3 – 126.7 ℃; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.87 (t, *J* = 4.2 Hz, 3H), 7.51 (dd, *J* = 4.9, 2.1 Hz, 1H), 7.44 – 7.39 (m, 2H), 7.22 (tt, *J* = 7.0, 1.4 Hz, 1H), 7.17 – 7.11 (m, 2H), 5.51 (s, 2H), 4.11 (q, *J* = 7.0 Hz, 2H), 4.00 (s, 3H), 1.92 (s, 3H), 1.07 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.4, 164.2, 159.6, 148.6, 146.4, 141.3, 141.1, 136.3, 136.0, 134.8, 129.0, 127.9, 127.3, 126.6, 126.1, 124.5, 120.8, 117.7, 114.9, 114.0, 99.7, 60.4, 52.9, 15.4, 12.7; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{27}H_{23}N_4O_5SNa$ 537.1209; Found 537.1219.



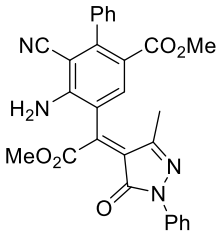
3m

Tert-butyl (Z)-3-(3-amino-2-cyano-6-(ethoxycarbonyl)-4-(2-methoxy-1-(3-methyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxoethyl)phenyl)-1H-indole-1-carboxylate (3m). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3m**: 42.0 mg as a yellow solid, 65% yield; m.p. 138.6 – 139.2 ℃; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.98 (d, *J* = 9.8 Hz, 1H), 7.88 (dd, *J* = 7.7, 3.5 Hz, 2H), 7.83 – 7.67 (m, 1H), 7.42 (t, *J* = 7.7 Hz, 2H), 7.35 (dt, *J* = 8.4, 2.8 Hz, 1H), 7.25 – 7.13 (m, 3H), 5.55 (d, *J* = 7.7 Hz, 2H), 4.03 (d, *J* = 16.8 Hz, 3H), 3.99 – 3.86 (m, 2H), 2.01 – 1.88 (m, 3H), 1.70 (s, 9H), 0.79 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-D_6) δ 166.8, 161.4, 151.9, 149.6, 149.0, 140.1, 138.1, 135.0, 131.0, 130.3, 129.6, 125.4, 125.2, 123.6, 118.6, 118.4, 116.5, 115.4, 84.9, 60.9, 53.7, 28.2, 15.7, 15.5, 13.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{36}H_{34}N_5O_7$ 648.2458; Found 648.2458.



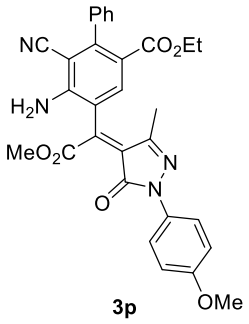
3n

Ethyl 4-amino-3-cyano-5-((Z)-2-methoxy-1-(3-methyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxoethyl)-2-((E)-styryl)benzoate (3n). . The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/10) to give the product **3n**: 31.0 mg as a yellow solid, 58% yield; m.p. 140.6 – 141.2 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.89 – 7.85 (m, 2H), 7.74 (d, *J* = 16.2 Hz, 1H), 7.61 – 7.57 (m, 2H), 7.43 – 7.39 (m, 4H), 7.34 (d, *J* = 7.8 Hz, 1H), 7.24 – 7.20 (m, 1H), 7.15 (d, *J* = 16.8 Hz, 1H), 5.57 (s, 2H), 4.33 (q, *J* = 7.2 Hz, 2H), 4.01 (s, 3H), 1.89 (s, 3H), 1.35 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.6, 164.9, 160.7, 150.6, 147.5, 147.2, 142.7, 137.4, 137.0, 136.6, 136.1, 129.8, 129.0, 128.94, 128.91, 128.8, 127.2, 125.5, 124.6, 118.7, 118.6, 116.2, 114.5, 97.2, 61.4, 53.9, 16.4, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{31}H_{27}N_4O_5$ 535.1981; Found 535.1976.



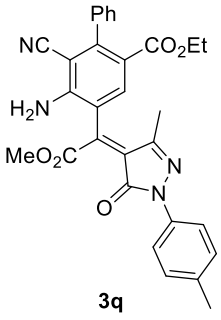
3o

Methyl (Z)-5-amino-6-cyano-4-(2-methoxy-1-(3-methyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxoethyl)-[1,1'-biphenyl]-2-carboxylate (3o). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3o**: 42.9 mg as a yellow solid, 87% yield; m.p. 171.9 – 173.1 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.87 (d, *J* = 8.4 Hz, 2H), 7.49 – 7.46 (m, 3H), 7.42 (t, *J* = 7.8 Hz, 2H), 7.30 (dd, *J* = 7.2, 3.6 Hz, 2H), 7.22 (t, *J* = 7.2Hz, 1H), 5.54 (s, 2H), 4.02 (s, 3H), 3.60 (s, 3H), 1.92 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.6, 164.4, 159.6, 149.6, 148.7, 146.4, 141.4, 136.31, 136.28, 135.2, 128.9, 128.0, 127.9, 127.2, 127.00, 126.95, 124.5, 118.7, 117.7, 114.2, 114.1, 99.0, 52.9, 51.1, 15.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{28}H_{23}N_4O_5$ 495.1668; Found 495.1664.



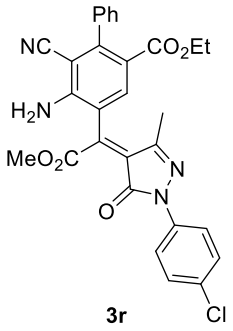
3p

Ethyl (Z)-5-amino-6-cyano-4-(2-methoxy-1-(1-(4-methoxyphenyl)-3-methyl-5-oxo-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxoethyl)-[1,1'-biphenyl]-2-carboxylate (3p). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3p**: 32.1 mg as a yellow solid, 60% yield; m.p. 75.5 – 76.4 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.75 (d, *J* = 9.0 Hz, 2H), 7.49 – 7.43 (m, 3H), 7.29 (dd, *J* = 6.0, 2.4 Hz, 2H), 6.93 (d, *J* = 9.0 Hz, 2H), 5.52 (s, 2H), 4.05 – 3.97 (m, 5H), 3.82 (s, 3H), 1.90 (s, 3H), 0.94 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.7, 165.4, 160.3, 157.4, 150.2, 149.7, 147.2, 142.3, 137.6, 136.2, 130.7, 130.0, 128.8, 128.2, 128.1, 120.7, 120.4, 115.31, 115.29, 114.1, 99.8, 61.2, 55.5, 53.9, 16.3, 13.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{30}H_{27}N_4O_6$ 539.1931; Found 539.1932.



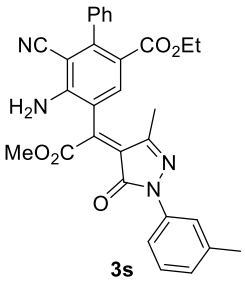
3q

Ethyl (Z)-5-amino-6-cyano-4-(2-methoxy-1-(3-methyl-5-oxo-1-(p-tolyl)-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxoethyl)-[1,1'-biphenyl]-2-carboxylate (3q). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3q**: 24.5 mg as a yellow solid, 47% yield; m.p. 80.1 – 81.8 ℃; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.74 (d, *J* = 8.4 Hz, 2H), 7.53 – 7.39 (m, 4H), 7.30 (dd, *J* = 6.3, 2.8 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 5.51 (s, 2H), 4.05 – 3.99 (m, 5H), 2.36 (s, 3H), 1.91 (s, 3H), 0.95 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (150MHz, $CDCl_3$) δ 166.7, 165.4, 160.6, 150.3, 149.7, 147.4, 142.3, 137.7, 136.3, 135.4, 135.1, 130.1, 129.6, 128.9, 128.3, 128.2, 120.5, 118.9, 115.4, 99.9, 61.3, 53.9, 21.1, 16.4, 13.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{30}H_{27}N_4O_5$ 523.1981; Found 523.1982.



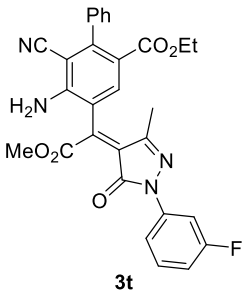
3r

Ethyl (Z)-5-amino-4-(1-(1-(4-chlorophenyl)-3-methyl-5-oxo-1,5-dihydro-4H-pyrazol-4-ylidene)-2-methoxy-2-oxoethyl)-6-cyano-[1,1'-biphenyl]-2-carboxylate (3r). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3r**: 28.2 mg as a yellow solid, 52% yield; m.p. 79.0 – 80.5 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.89 – 7.84 (m, 2H), 7.48 – 7.45 (m, 3H), 7.40 – 7.35 (m, 2H), 7.32 – 7.27 (m, 2H), 5.52 (s, 2H), 4.01 (q, *J* = 7.2 Hz, 2H), 4.00 (s, 3H), 1.92 (s, 3H), 0.94 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.6, 165.4, 160.7, 150.4, 149.7, 147.9, 143.0, 137.7, 136.3, 136.1, 130.7, 129.8, 129.1, 128.9, 128.3, 128.2, 120.6, 119.8, 115.3, 115.2, 100.0, 61.3, 54.0, 16.5, 13.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{29}H_{24}ClN_4O_5$ 543.1435; Found 543.1435.



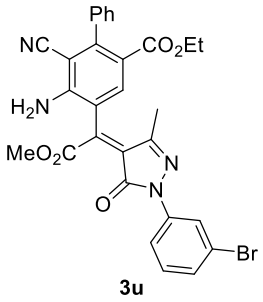
3s

Ethyl (Z)-5-amino-6-cyano-4-(2-methoxy-1-(3-methyl-5-oxo-1-(m-tolyl)-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxoethyl)-[1,1'-biphenyl]-2-carboxylate (3s). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3s**: 24.0 mg as a yellow solid, 46% yield; m.p. 78.8 – 79.4 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.70 (d, *J* = 1.8 Hz, 2H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.48 – 7.44 (m, 3H), 7.34 – 7.27 (m, 4H), 7.04 (d, *J* = 7.2 Hz, 1H), 5.52 (s, 2H), 4.02 (q, *J* = 7.2 Hz, 2H), 4.01 (s, 3H), 2.39 (s, 3H), 1.92 (s, 3H), 0.95 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.7, 165.4, 160.7, 150.3, 149.7, 147.5, 142.5, 139.0, 137.7, 137.4, 136.3, 130.1, 128.91, 128.89, 128.3, 128.2, 126.5, 120.5, 119.4, 116.1, 115.4, 99.9, 61.3, 54.0, 21.7, 16.4, 13.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{30}H_{27}N_4O_5$ 523.1981; Found 523.1982.



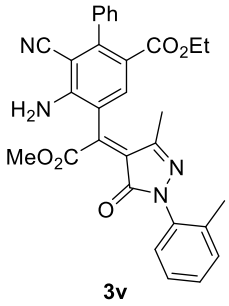
3t

Ethyl (Z)-5-amino-6-cyano-4-(1-(1-(3-fluorophenyl)-3-methyl-5-oxo-1,5-dihydro-4H-pyrazol-4-ylidene)-2-methoxy-2-oxoethyl)-[1,1'-biphenyl]-2-carboxylate (3t). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3t**: 23.1 mg as a yellow solid, 44% yield; m.p. 79.2 – 80.7 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.74 – 7.71 (m, 1H), 7.69 (dt, *J* = 10.8, 2.4 Hz, 1H), 7.48 – 7.45 (m, 3H), 7.39 – 7.34 (m, 1H), 7.32 – 7.28 (m, 2H), 6.91 (td, *J* =8.4, 2.4 Hz, 1H), 5.52 (s, 2H), 4.02 (q, *J* = 6.6 Hz, 2H), 4.01 (s, 3H), 1.93 (s, 3H), 0.94 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.5, 165.4, 163.8, 162.2 (d, J_{FC}= 243.8 Hz), 160.8, 150.4, 149.7, 148.0, 143.1, 138.9, 138.8 (d, J_{FC}= 11.0 Hz), 137.7, 136.2, 130.4, 130.3 (d, J_{FC}= 9.2 Hz), 129.8, 128.9, 128.3, 128.2, 120.6, 115.3, 115.2, 113.87, 113.85 (d, J_{FC}= 3.0 Hz), 112.3, 112.1 (d, J_{FC}= 10.1 Hz), 106.1, 105.9 (d, J_{FC}= 26.9 Hz), 100.0, 61.3, 54.0, 16.5, 13.7; ^{19}F NMR (660 MHz, $CDCl_3$) δ -111.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{29}H_{24}FN_4O_5$ 527.1731; Found 527.1731.



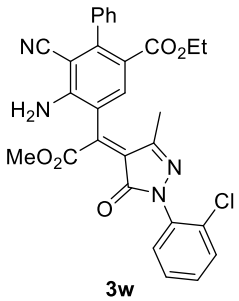
3u

Ethyl (Z)-5-amino-4-(1-(1-(3-bromophenyl)-3-methyl-5-oxo-1,5-dihydro-4H-pyrazol-4-ylidene)-2-methoxy-2-oxoethyl)-6-cyano-[1,1'-biphenyl]-2-carboxylate (3u). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3u**: 25.2 mg as a yellow solid, 43% yield; m.p. 74.8 – 75.9 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10 (t, *J* = 1.8 Hz, 1H), 7.91 (s, 1H), 7.88 – 7.86 (m, 1H), 7.47 – 7.43 (m, 3H), 7.33 – 7.30 (m, 1H), 7.29 – 7.27 (m, 2H), 7.25 (s, 1H), 5.50 (s, 2H), 4.02 (q, *J* = 7.2 Hz, 2H), 4.00 (s, 3H), 1.91 (s, 3H), 0.93 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150MHz, $CDCl_3$) δ 166.5, 165.4, 160.8, 150.4, 149.7, 148.1, 143.2, 138.6, 137.6, 136.2, 130.4, 129.7, 128.9, 128.4, 128.3, 128.2, 122.8, 121.4, 120.6, 116.9, 115.3, 115.1, 100.0, 61.3, 54.0, 16.5, 13.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{29}H_{24}{}^{79}BrN_4O_5$ 587.0930; Found 587.0925; $C_{29}H_{24}{}^{81}BrN_4O_5$ 589.0910; Found 589.0908.



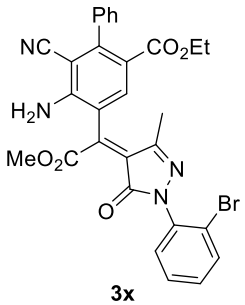
3v

Ethyl (Z)-5-amino-6-cyano-4-(2-methoxy-1-(3-methyl-5-oxo-1-(o-tolyl)-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxoethyl)-[1,1'-biphenyl]-2-carboxylate. (3v). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3v**: 25.0 mg as a yellow solid, 48% yield; m.p. 88.5 – 89.3 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.42 – 7.37 (m, 3H), 7.26 – 7.18 (m, 6H), 5.50 (s, 2H), 3.95 (q, *J* = 7.2 Hz, 2H), 3.89 (s, 3H), 2.25 (s, 3H), 1.82 (s, 3H), 0.87 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.6, 165.4, 161.3, 150.2, 149.7, 147.1, 142.5, 137.7, 136.3, 135.1, 131.3, 129.2, 128.82, 128.76, 128.2, 128.1, 126.6, 126.4, 120.4, 115.3, 99.8, 61.2, 53.9, 18.6, 16.4, 13.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{30}H_{27}N_4O_5$ 523.1981; Found 523.1980.



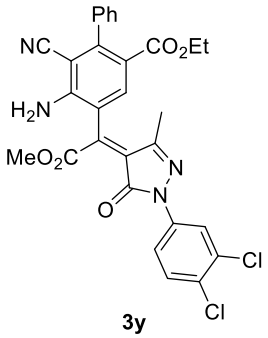
3w

Ethyl (Z)-5-amino-4-(1-(1-(2-chlorophenyl)-3-methyl-5-oxo-1,5-dihydro-4H-pyrazol-4-ylidene)-2-methoxy-2-oxoethyl)-6-cyano-[1,1'-biphenyl]-2-carboxylate. (3w). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3w**: 27.1 mg as a yellow solid, 50% yield; m.p. 79.2 – 80.8 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.54 – 7.50 (m, 1H), 7.48 – 7.44 (m, 4H), 7.38 – 7.34 (m, 2H), 7.32 – 7.28 (m, 2H), 5.57 (s, 2H), 4.03 (q, *J* = 7.2f Hz, 2H), 3.97 (s, 3H), 1.91 (s, 3H), 0.95 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.6, 165.5, 161.4, 150.4, 149.8, 147.6, 143.1, 137.7, 136.4, 134.0, 131.8, 130.8, 130.2, 128.9, 128.8, 128.3, 128.2, 127.7, 120.5, 115.4, 115.3, 99.9, 61.3, 54.0, 16.5, 13.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{29}H_{24}ClN_4O_5$ 543.1435; Found 543.1432.



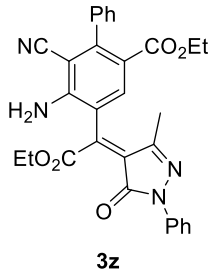
3x

Ethyl (Z)-5-amino-4-(1-(1-(2-bromophenyl)-3-methyl-5-oxo-1,5-dihydro-4H-pyrazol-4-ylidene)-2-methoxy-2-oxoethyl)-6-cyano-[1,1'-biphenyl]-2-carboxylate (3x). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3x**: 40.0 mg as a yellow solid, 67% yield; m.p. 80.6 – 81.3 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.50 – 7.45 (m, 4H), 7.37 – 7.33 (m, 1H), 7.32 – 7.28 (m, 2H), 7.25 – 7.20 (m, 2H), 5.56 (s, 2H), 4.03 (q, *J* = 7.2 Hz, 2H), 3.98 (s, 3H), 1.91 (s, 3H), 0.96 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.5, 165.4, 161.2, 157.5, 155.8, 150.4, 149.7, 148.0, 143.1, 137.7, 136.3, 129.82, 129.77, 128.9, 128.8, 128.3, 128.2, 127.0, 124.63, 124.61, 124.2, 124.1 120.5, 117.1, 117.0, 115.4, 115.2, 99.9, 61.3, 54.0, 16.5, 13.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{29}H_{24}{}^{79}BrN_4O_5$ 587.0930; Found 587.0928; Calcd for $C_{29}H_{24}{}^{81}BrN_4O_5$ 589.0910; Found 589.0910.



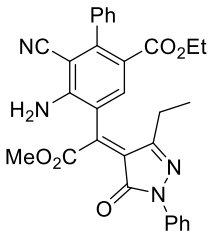
3y

Ethyl (Z)-5-amino-6-cyano-4-(1-(1-(3,4-dichlorophenyl)-3-methyl-5-oxo-1,5-dihydro-4H-pyrazol-4-ylidene)-2-methoxy-2-oxoethyl)-[1,1'-biphenyl]-2-carboxylate (3y). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3y**: 23.9 mg as a yellow solid, 41% yield; m.p. 85.2 – 86.4 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10 (d, *J* = 2.4 Hz, 1H), 7.91 (s, 1H), 7.83 (dd, *J* = 9.0, 3.0 Hz, 1H), 7.48 – 7.44 (m, 4H), 7.32 – 7.28 (m, 2H), 5.52 (s, 2H), 4.02 (q, *J* = 7.2 Hz, 2H), 4.02 (s, 3H), 1.93 (s, 3H), 0.94 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.4, 165.4, 160.8, 150.5, 149.6, 148.3, 143.6, 137.6, 136.8, 136.3, 133.0, 130.7, 129.5, 129.0, 128.8, 128.3, 128.2, 120.6, 120.0, 117.5, 115.3, 115.0, 100.1, 61.3, 54.1, 16.5, 13.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{29}H_{23}{}^{35}Cl_2N_4O_5$ 577.1046; Found 577.1046; Calcd for $C_{29}H_{23}{}^{37}Cl_2N_4O_5$ 579.1016; Found 579.1019.



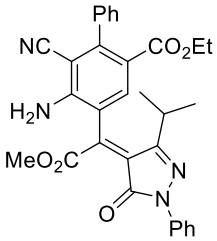
3z

Ethyl (Z)-5-amino-6-cyano-4-(2-ethoxy-1-(3-methyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxoethyl)-[1,1'-biphenyl]-2-carboxylate (3z). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3z**: 26.2 mg as a yellow solid, 50% yield; m.p. 72.5 – 73.1 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.88 (dd, *J* = 7.8, 1.8 Hz, 2H), 7.48 – 7.45 (m, 3H), 7.43 – 7.40 (m, 2H), 7.33 – 7.28 (m, 2H), 7.21 (t, *J* = 7.2 Hz, 1H), 5.55 (s, 2H), 4.56 – 4.42 (m, 2H), 4.02 (q, *J* = 7.2 Hz, 2H), 4.02 (s, 3H), 1.42 (t, *J* = 7.2 Hz, 3H), 0.95 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.3, 165.5, 160.8, 150.3, 149.8, 147.6, 142.9, 137.7, 137.5, 136.3, 129.8, 129.1, 128.9, 128.3, 128.2, 125.6, 120.4, 118.9, 115.5, 115.4, 99.9, 63.6, 61.3, 16.5, 14.0, 13.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{30}H_{27}N_4O_5$ 523.1981; Found 523.1981.



3aa

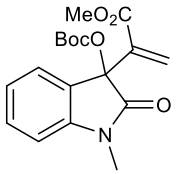
Ethyl (Z)-5-amino-6-cyano-4-(1-(3-ethyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)-2-methoxy-2-oxoethyl)-[1,1'-biphenyl]-2-carboxylate. (3aa) The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/10) to give the product **3aa**: 39.4 mg as a yellow solid, 75% yield; m.p. 75.8 – 76.4 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.92 – 7.84 (m, 2H), 7.49 – 7.45 (m, 3H), 7.45 – 7.39 (m, 2H), 7.33 – 7.28 (m, 2H), 7.24 – 7.18 (m, 1H), 5.52 (s, 2H), 4.03 (t, *J* = 7.2 Hz, 2H), 4.01 (s, 3H), 2.24 (dq, *J* = 16.8, 7.2 Hz, 1H), 2.13 (dq, *J* = 17.4, 7.8 Hz, 1H), 1.12 (t, *J* = 7.2 Hz, 3H), 0.95 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.8, 164.4, 160.0, 150.8, 149.3, 148.7, 141.2, 136.7, 136.6, 135.1, 128.7, 128.0, 127.9, 127.3, 127.2, 124.6, 119.4, 117.8, 114.5, 114.4, 98.9, 60.3, 53.0, 22.5, 12.7, 9.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{30}H_{27}N_4O_5$ 537.2138; Found 537.2133.



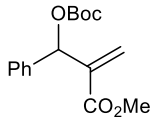
3ab

Ethyl (Z)-5-amino-6-cyano-4-(1-(3-isopropyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)-2-methoxy-2-oxoethyl)-[1,1'-biphenyl]-2-carboxylate (3ab). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/10) to give the product **3ab**: 41.1 mg as a yellow solid, 77% yield; m.p. 72.0 – 73.1 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.90 (d, *J* = 8.4 Hz, 2H), 7.49 – 7.45 (m, 3H), 7.42 (t, *J* = 7.8 Hz, 2H), 7.31 (dd, *J* = 7.2, 3.6 Hz, 2H), 7.22 (t, *J* = 7.2 Hz, 1H), 5.58 (s, 2H), 4.03 (td, *J* = 7.2, 4.2 Hz, 2H), 4.00 (s, 3H), 2.41 (hept, *J* = 7.2 Hz, 1H), 1.19 (d, *J* = 6.6 Hz, 3H), 1.03 (d, *J* = 6.6 Hz, 3H), 0.96 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.5, 162.8, 158.6, 153.0, 147.9, 147.3, 139.7, 135.2, 135.1, 133.7, 126.5, 126.44, 126.37, 125.8, 125.7, 123.0, 117.7, 116.3, 113.0, 112.9, 97.4, 58.7, 51.4, 26.2, 18.3, 17.6, 11.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{31}H_{29}N_4O_5$ 537.2138; Found 537.2136.

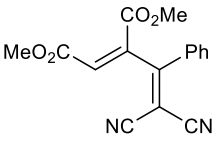
Attempts of other substrates



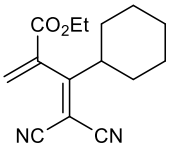
messy



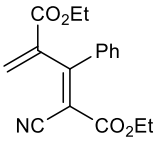
N.R.



N.R.

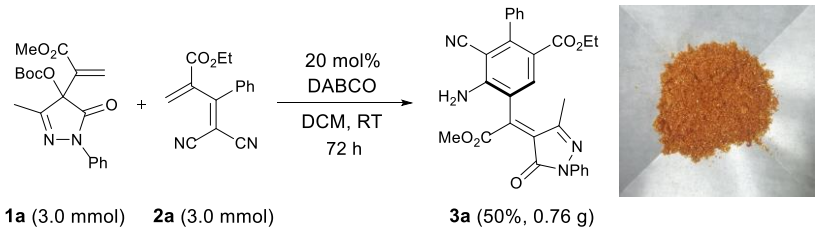


N.R.



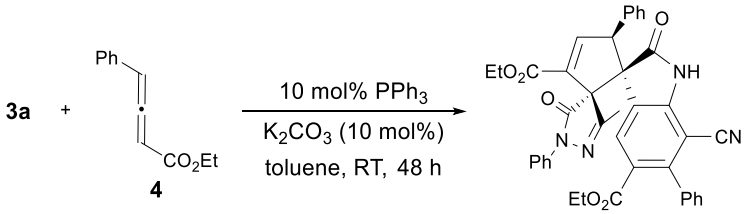
N.R.

4. Procedure for the scale-up synthesis of 3a



A mixture of **1a** (3.0 mmol), **2a** (3.0 mmol), DABCO (20 mol%) and DCM (10.0 mL) was stirred at RT for 72 h (monitored by TLC). The reaction mixture was concentrated, and the residue was purified by flash chromatography on silica gel to give product **3a**. (762.0 mg, 50% yield)

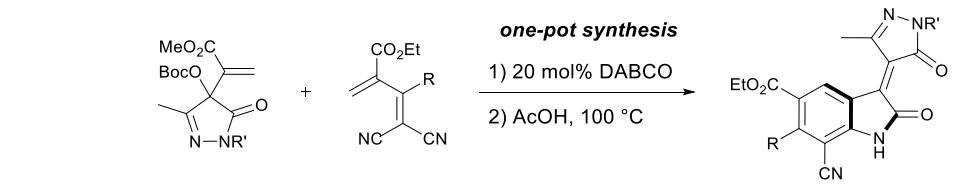
5. Synthesis of Compounds 5

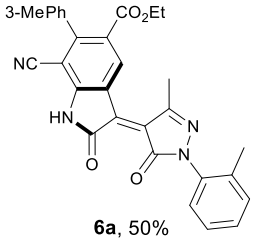


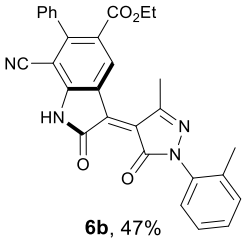
A solution of **3a** (0.10 mmol), **4** (0.12 mmol), PPh_3 (10 mol%) and K_2CO_3 (10 mol%) in toluene (1 mL) was stirred at RT for 48h. After the reaction completed (monitored by TLC), The resulting residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc = 15:1 to 10:1) to afford product **5**.

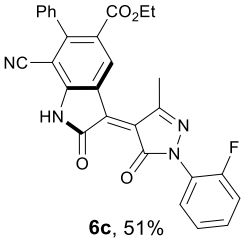
Diethyl 7-cyano-3''-methyl-2,5''-dioxo-1'',5',6-triphenyl-1'',5''-dihydrodispiro[indoline-3,2'-cyclopentane-1',4''-pyrazol]-3'-ene-3',5-dicarboxylate (5). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/12) to give the product **5**: 45.5 mg as a white solid, 68% yield; m.p. 150.3 – 151.6 ℃; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.53 (s, 1H), 7.90 – 7.72 (m, 3H), 7.65 (d, *J* = 2.1 Hz, 1H), 7.46 – 7.39 (m, 3H), 7.37 (dd, *J* = 7.0, 1.4 Hz, 2H), 7.30 – 7.27 (m, 1H), 7.23 (t, *J* = 7.7 Hz, 3H), 7.19 (tt, *J* = 7.7, 1.4 Hz, 1H), 6.97 (dt, *J* = 5.6, 0.7 Hz, 2H), 5.45 (d, *J* = 2.1 Hz, 1H), 4.26 (dq, *J* = 11.2, 7.0 Hz, 1H), 4.20 (dq, *J* = 11.2, 7.0 Hz, 1H), 4.02 (qq, *J* = 18.9, 7.0 Hz, 2H), 2.17 (s, 3H), 1.29 (t, *J* = 7.0 Hz, 3H), 0.98 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 172.8, 170.6, 165.6, 162.1, 157.8, 150.1, 147.6, 147.4, 137.2, 136.7, 134.4, 133.9, 130.8, 129.0, 128.8, 128.7, 128.6, 128.5, 128.32, 128.30, 126.7, 125.8, 124.3, 119.4, 114.0, 96.0, 70.6, 66.1, 61.6, 61.5, 56.1, 17.3, 14.0, 13.6; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{40}H_{32}N_4O_6Na$ 687.2220; Found 687.2219.

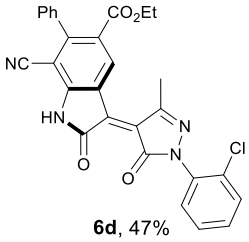
6. Synthesis of Compounds 6



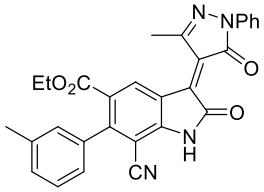

6a, 50%


6b, 47%

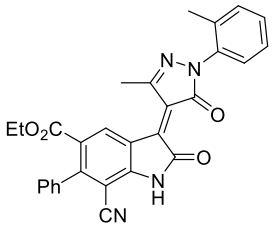

6c, 51%


6d, 47%

A mixture of **1** (0.2 mmol), **2** (0.3 mmol), and DABCO (20 mol%) in DCM (2.0 mL) was stirred at RT for 72 h (monitored by TLC). Then, the solvent was removed by rotary evaporator under reduced pressure without any other treatment. Acetic acid (1.0 mL) was directly added to the residue and reacted at 100℃ for 30 min. The reaction complex was extracted with ethyl acetate (3× 10 mL). The organic extracts were combined, dried over Na_2SO_4, filtered and concentrated in vacuo. Then, the residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1) to give product **6.**

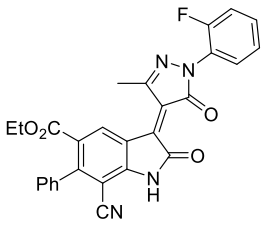

6a

Ethyl (Z)-7-cyano-3-(3-methyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxo-6-(m-tolyl)indoline-5-carboxylate (6a). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/8) to give the product **6a**: 49.0 mg as a red solid, 50% yield; m.p. 110.5 – 111.7 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.04 (s, 1H), 7.94 (dd, *J* = 9.0, 1.8 Hz, 2H), 7.48 – 7.41 (m, 2H), 7.37 (t, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 7.8 Hz, 2H), 7.25 – 7.22 (m, 1H), 7.19 – 7.11 (m, 2H), 4.09 (q, *J* = 7.2 Hz, 2H), 2.67 (s, 3H), 2.42 (s, 3H), 0.99 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.3, 164.9, 162.4, 149.8, 148.6, 147.0, 137.2, 135.55, 135.52, 133.7, 131.5, 129.2, 127.9, 127.5, 127.4, 126.4, 124.6, 124.1, 119.6, 118.1, 112.9, 94.9, 60.5, 20.4, 19.0, 12.5. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{29}H_{23}N_4O_4$ 491.1719; Found 491.1721.



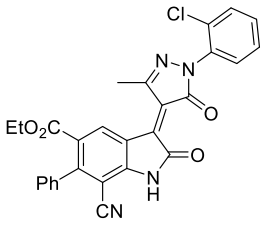
6b

Ethyl (Z)-7-cyano-3-(3-methyl-5-oxo-1-(o-tolyl)-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxo-6-phenylindoline-5-carboxylate (6b). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/8) to give the product **6b**: 45.8 mg as a red solid, 47% yield; m.p. 117.3 – 118.6 ℃; ^{1}H NMR (700 MHz, $CDCl_3$) δ 10.02 (s, 1H), 8.48 (s, 1H), 7.48 (dd, *J* = 5.6, 2.1 Hz, 3H), 7.38 – 7.27 (m, 6H), 4.02 (q, *J* = 7.0 Hz, 2H), 2.65 (s, 3H), 2.32 (s, 3H), 0.94 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 166.2, 166.1, 164.3, 150.5, 149.5, 147.9, 136.7, 136.5, 135.4, 135.3, 134.9, 131.8, 131.3, 129.5, 128.9, 128.5, 128.1, 127.6, 126.7, 126.6, 120.9, 114.0, 95.9, 61.6, 20.0, 18.5, 13.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{29}H_{23}N_4O_4$ 491.1719; Found 491.1720.



6c

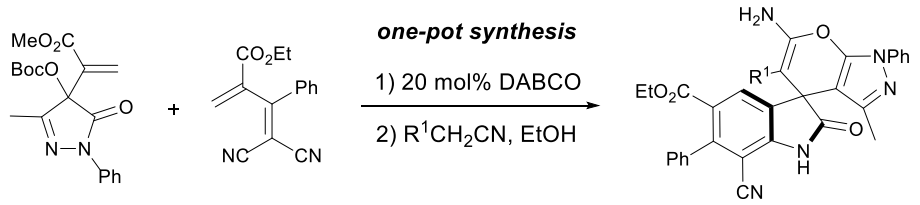
Ethyl (Z)-7-cyano-3-(1-(2-fluorophenyl)-3-methyl-5-oxo-1,5-dihydro-4H-pyrazol-4-ylidene)-2-oxo-6-phenylindoline-5-carboxylate (6c). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/8) to give the product **6c**: 50.5 mg as a red solid, 51% yield; m.p. 125.7 – 126.3 ℃; ^{1}H NMR (700 MHz, $CDCl_3$) δ 9.99 (s, 1H), 8.51 (s, 1H), 7.58 – 7.44 (m, 4H), 7.42 – 7.30 (m, 3H), 7.26 – 7.22 (m, 2H), 4.03 (q, *J* = 7.0 Hz, 2H), 2.66 (s, 3H), 0.94 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (175 MHz, $CDCl_3$) δ 166.2, 166.1, 164.1, 157.5 (d, J_{FC}= 252.0 Hz), 156.0, 150.7, 149.6, 148.7, 136.7, 136.5, 135.2, 131.4, 129.90 (d, J_{FC}= 7.9 Hz), 129.86, 129.5, 128.5, 128.1, 127.6, 127.2, 124.6 (d, J_{FC}= 3.5 Hz), 124.5, 124.3 (d, J_{FC}= 11.7 Hz), 124.2, 120.8, 117.0 (d, J_{FC}= 19.4 Hz), 116.9, 113.9, 96.0, 61.6, 20.1, 13.6; ^{19}F NMR (660 MHz, $CDCl_3$) δ -118.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{28}H_{20}FN_4O_4$ 495.1469; Found 495.1464.



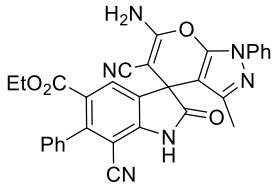
6d

Ethyl (Z)-3-(1-(2-chlorophenyl)-3-methyl-5-oxo-1,5-dihydro-4H-pyrazol-4-ylidene)-7-cyano-2-oxo-6-phenylindoline-5-carboxylate (6d). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/8) to give the product **6d**: 48.2 mg as a red solid, 47% yield; m.p. 135.0 – 136.9 ℃; ^{1}H NMR (700 MHz, $CDCl_3$) δ 9.98 (s, 1H), 8.84 (s, 1H), 7.57 – 7.50 (m, 1H), 7.50 – 7.43 (m, 4H), 7.41 – 7.36 (m, 2H), 7.36 – 7.29 (m, 2H), 4.02 (q, *J* = 7.0 Hz, 2H), 2.66 (s, 3H), 0.93 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (175 MHz, $CDCl_3$) δ 166.4, 166.3, 164.3, 150.7, 149.7, 148.5, 136.7, 136.5, 135.3, 134.1, 132.1, 131.3, 130.6, 130.2, 129.5, 128.9, 128.5, 128.1, 127.64, 127.60, 120.8, 113.9, 96.0, 61.6, 20.1, 13.6. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{28}H_{20}ClN_4O_4$ 511.1173; Found 511.1172.

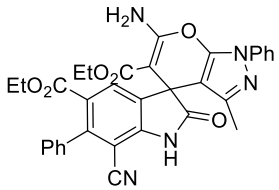
7. Synthesis of Compounds 7



A mixture of **1a** (0.1 mmol), **2a** (0.1 mmol), DABCO (20 mol%) and DCM (1.0 mL) was stirred at RT for72 h (monitored by TLC). Then, the solvent was removed by rotary evaporator under reduced pressure without any other treatment. Adding R^1CH_2CN (0.1 mmol) and ethanol (1.0 mL) to the residue and stirring at 80℃ for 3 h (monitored by TLC). The residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1) to give product **7.**

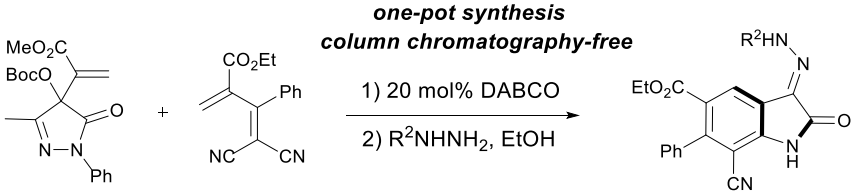

7a

Ethyl 6'-amino-5',7-dicyano-3'-methyl-2-oxo-1',6-diphenyl-1'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-5-carboxylate (7a). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/3) to give the product **7a**: 29.0 mg as a white solid, 54% yield; m.p. 127.8 – 128.2 ℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.70 (s, 1H), 7.51 (s, 1H), 7.39 – 7.33 (m, 4H), 7.09 (dd, *J* = 9.0, 7.8 Hz, 2H), 7.06 – 7.02 (m, 3H), 6.96 – 6.91 (m, 3H), 3.44 (q, *J* = 7.2 Hz, 2H), 1.24 (s, 3H), 0.36 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 178.6, 166.5, 161.8, 148.3, 146.6, 145.7, 144.1, 137.7, 137.6, 132.9, 130.4, 129.9, 129.1, 128.6, 127.3, 127.0, 120.9, 118.3, 114.8, 95.4, 95.2, 61.4, 55.0, 48.2, 13.8, 12.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{31}H_{23}N_6O_4$ 543.1781; Found 543.1783.

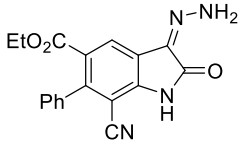

7b

Diethyl 6'-amino-7-cyano-3'-methyl-2-oxo-1',6-diphenyl-1'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-5,5'-dicarboxylate (7b). The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/3) to give the product **7b**: 28.8 mg as a white solid, 49% yield; m.p. 135.3 – 136.4 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.76 (s, 1H), 7.68 – 7.62 (m, 2H), 7.47 (tt, *J* = 6.0, 3.0 Hz, 5H), 7.37 – 7.28 (m, 3H), 4.04 – 3.92 (m, 4H), 1.85 (s, 3H), 0.96 (t, *J* = 7.2 Hz, 3H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 176.8, 165.9, 164.6, 159.5, 145.5, 144.2, 142.8, 142.2, 135.6, 135.3, 133.3, 127.55, 127.46, 126.9, 126.6, 126.5, 125.3, 124.6, 119.7, 112.6, 94.2, 93.1, 59.6, 58.6, 46.4, 11.6, 11.6, 10.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{33}H_{27}N_5O_6$ 590.2040; Found 590.2038.

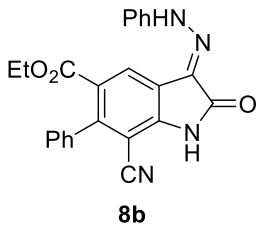
8. Synthesis of Compounds 8



A mixture of **1a** (0.1 mmol), **2a** (0.1 mmol), DABCO (20 mol%) and DCM (1.0 mL) was stirred at RT for72 h (monitored by TLC). Then, the solvent was removed. Adding R^2NHNH_2 (0.1 mmol) and ethanol (1.0 mL) to the reaction and stirring in an 80℃ oil bath for about 1 hours (monitored by TLC). After the reaction material disappears, the solids generated in the reaction solution are filtered and washed with a small amount of ethanol to obtain yellow solids.


8a

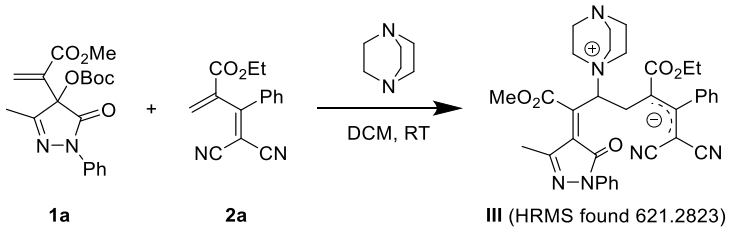
Ethyl (Z)-7-cyano-3-hydrazineylidene-2-oxo-6-phenylindoline-5-carboxylate (8a). The reaction liquid is filtered to obtain the product **8a**: 24.5 mg as a yellow solid, 73% yield; m.p. 175.3 – 176.6 ℃; ^{1}H NMR (700 MHz, DMSO-d_6) δ 11.92 (s, 1H), 10.77 (d, *J* = 14.7 Hz, 1H), 10.31 (d, *J* = 14.7 Hz, 1H), 7.93 (s, 1H), 7.44 (dd, *J* = 6.3, 2.8 Hz, 3H), 7.29 (dd, *J* = 7.7, 3.5 Hz, 2H), 3.92 (q, *J* = 7.7 Hz, 2H), 0.85 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (175 MHz, DMSO-d_6) δ 166.2, 163.0, 143.2, 138.0, 128.7, 128.2, 128.1, 128.0, 124.6, 123.2, 122.7, 121.2, 114.6, 94.9, 60.7, 13.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{18}H_{15}N_4O_3$ 335.1144; Found 335.1145.


8b

Ethyl (E)-7-cyano-2-oxo-6-phenyl-3-(2-phenylhydrazineylidene)indoline-5-carboxylate (8b). The reaction liquid is filtered to obtain the product **8b**: 32.0 mg as a yellow solid, 78% yield; m.p. 182.5 – 183.9 ℃; ^{1}H NMR (700 MHz, DMSO-d_6) δ 12.78 (s, 1H), 12.25 (s, 1H), 8.15 (s, 1H), 7.60 – 7.56 (m, 2H), 7.47 (dd, *J* = 5.6, 2.1 Hz, 3H), 7.44 – 7.40 (m, 2H), 7.35 – 7.30 (m, 2H), 7.17 – 7.11 (m, 1H), 3.96 (q, *J* = 7.7 Hz, 2H),, 0.88 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (175 MHz, DMSO-d_6) δ 166.2, 163.3, 144.7, 144.1, 142.1, 137.7, 129.6, 128.7, 128.3, 128.1, 125.3, 124.8, 124.1, 122.5, 121.7, 115.1, 114.4, 95.4, 60.8, 13.4; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{24}H_{18}N_4O_3Na$ 433.1277; Found 433.1278.

9. Mechanistic studies

9.1 Reaction intermediates



1a **2a** **III** (HRMS found 621.2823)

A mixture of 1a (0.1 mmol), 2a (0.1 mmol), DABCO (100 mol%), and DCM (1.0 mL) was stirred at RT for 5 minutes, then tested the reaction mixture with HRMS.

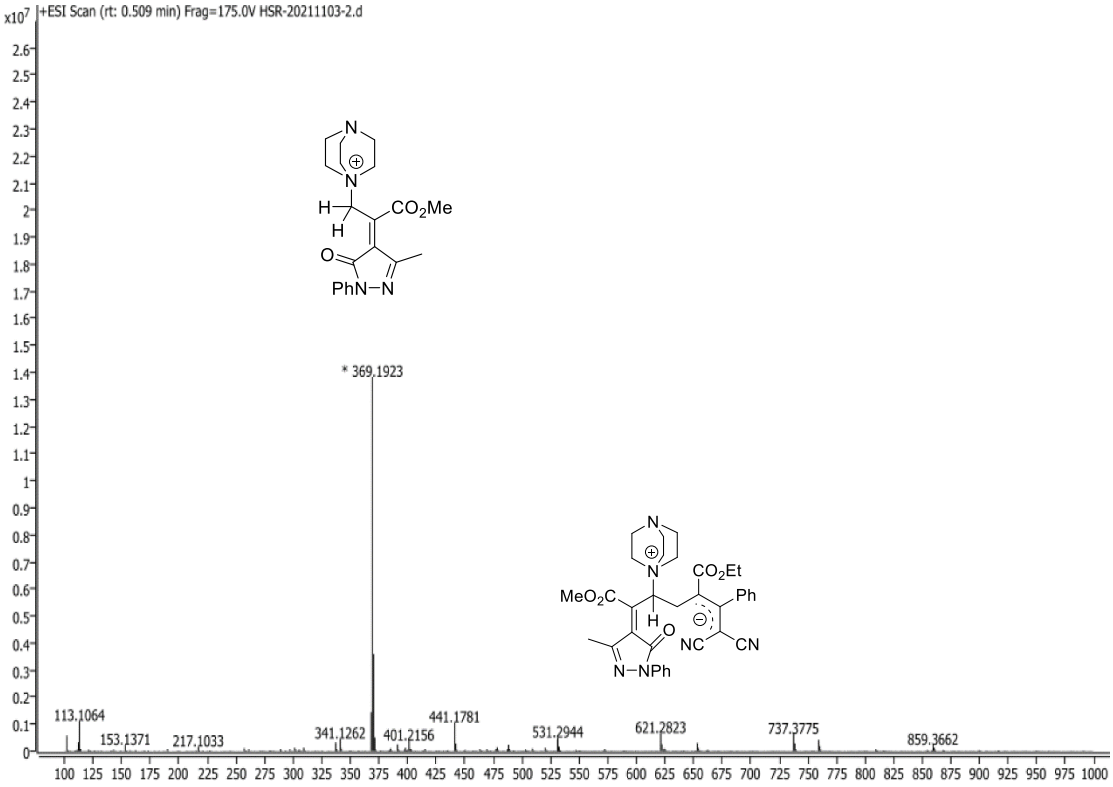


Figure S1. Reaction intermediates in HRMS

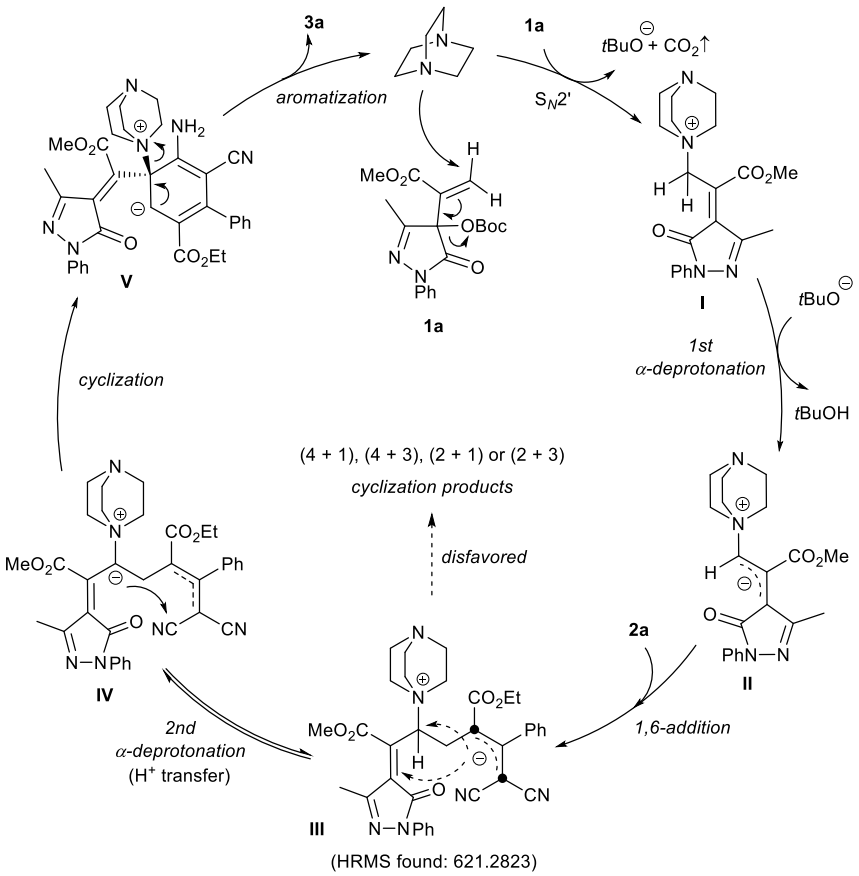
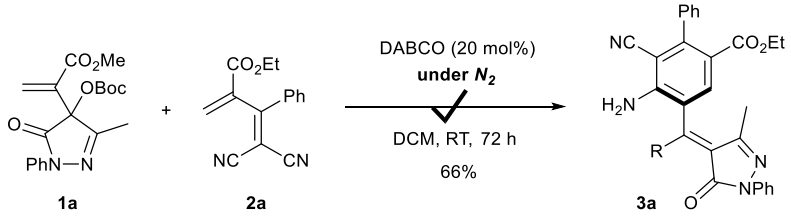


Figure S2. Proposed reaction mechanism.

9.2 Control experiment

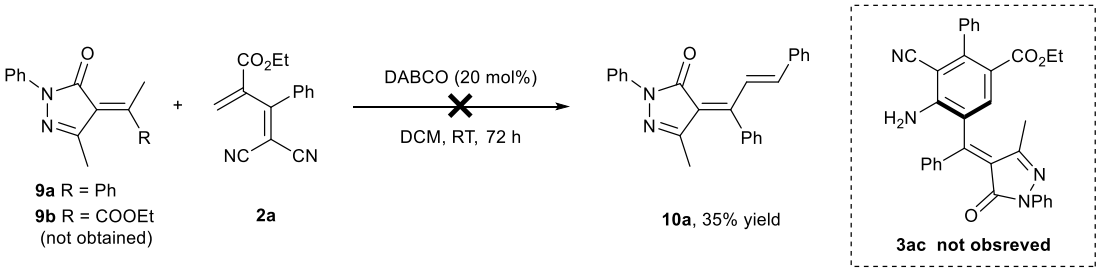
Control experiments were conducted to investigate the reaction mechanism of this unprecedented (5 + 1) benzannulation reaction of MBH carbonates. At first, we tested the reaction between α-arylidene pyrazolone **9a** and **2a**. α-arylidene pyrazolones were reported to serve as 1C bisnucleophiles in annulation reactions, but **9a** showed low reactivity. Side product **10a** was formed in the reaction. Neither (5 + 1) reaction nor other annulation reactions occurred between **9a** and **2a**, even heating the reaction at 80 °C. Additionally, we tried different methods to prepare the ester-substituted ethylidene pyrazolone **9b**, while all the attempts failed. These results further demonstrated the advantage of our Lewis base-catalyzed (5 + 1) benzannulation strategy. Next, we conducted the reaction of **1a** with **2a** in a nitrogen glove box. Monitoring under nitrogen atmosphere, we observed that **3a** was well generated, indicating that the oxygen did not affect the reaction.



In a glove box, a mixture of MBH carbonate **1a** (0.1 mmol), 2-allylidenemalononitrile **2a** (0.1 mmol), and DABCO (20 mol%) in DCM (1.0 mL) was stirred at RT for 72 h (monitored by TLC).

The reaction was monitored by TLC (in the glove box) and crude ^{1}HNMR using a schlenk NMR tube. Then, the solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel to give compound **3a** (33.5 mg, 66% yield).

9.3 Reaction of α-arylidene pyrazolone 9a with 2a



A mixture of **9a** (0.5 mmol), **2a** (0.5 mmol), DABCO (20 mol%) and DCM (10.0 mL) was stirred at RT for a specified reaction time until the reaction completed (monitored by TLC). The reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel to give product **10a** (63.0 mg, 35% yield). Neither (5 + 1) reaction nor other annulation reactions occurred between **9a** and **2a**, even heating the reaction at 80 °C.

10. Optical properties of selected compounds

General UV spectra measurements: The solutions of **3a, 3q, 3r, 3y, 3g, 3b, 3j** and **3k** were prepared by directly dissolving in DCM (c = 2×10^{-5} M) for the spectroscopic determination.

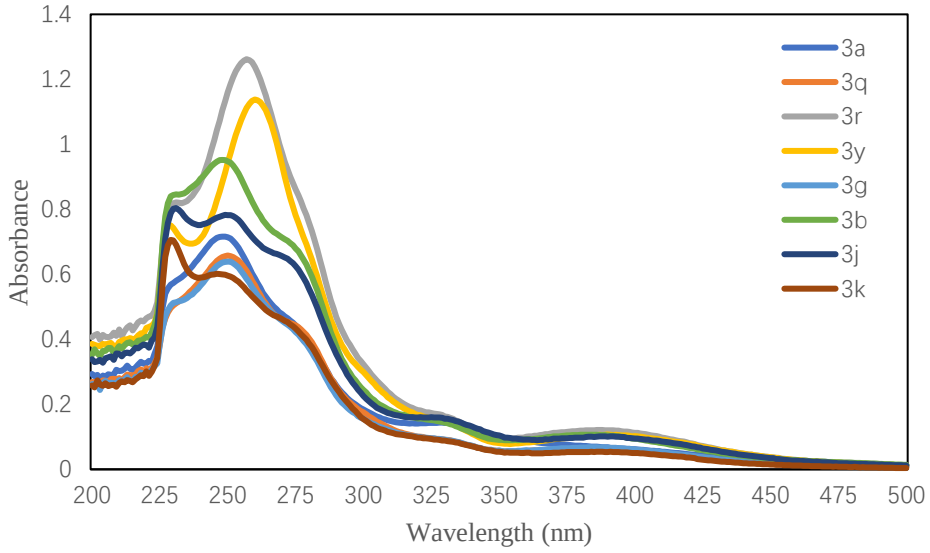


Figure S3. UV / Vis spectra of **3a, 3q, 3r, 3y, 3g, 3b, 3j** and **3k** (2×10^{-5} M in DCM).

General fluorescence spectra measurements: The powders of **3q, 3y, 3b** and **3k** were directly for the spectroscopic determination.

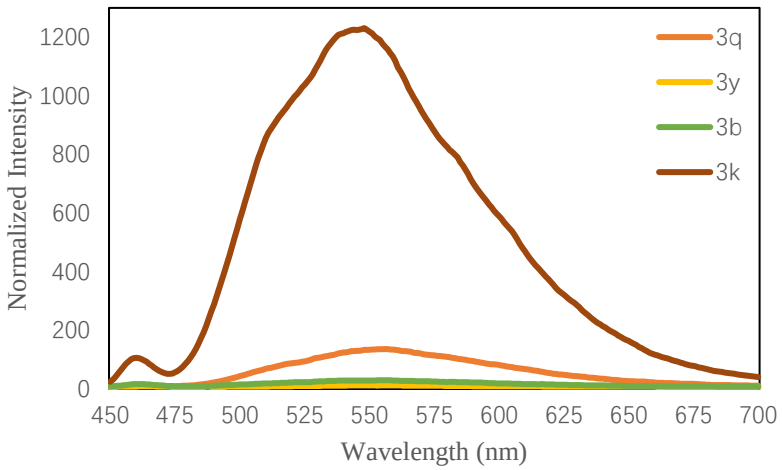
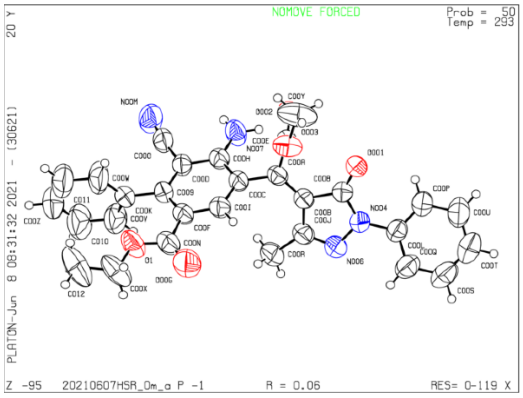
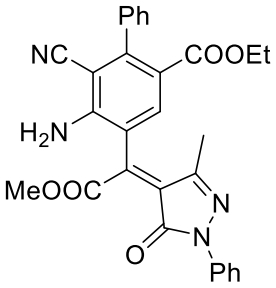


Figure S4. Fluorescence spectra of **3q, 3y, 3b** and **3k** (excitation wavelength = 450 nm, 2×10^{-5} M in DCM).

11. X-ray crystal structures of 3a and 5

To a 10 mL tube containing **3a** (30.0 mg) was added a mixture of solvent (6.0 mL, petroleum ether/ethyl acetate = 5:1). A clear solution was obtained through ultrasound treatment and was kept at room temperature and the crystals were obtained after the solvent evaporated, which were characterized by X-ray single crystal diffraction. X-ray diffraction experiment was carried out on an Agilent D8 QUEST and the data obtained were deposited at the Cambridge Crystallographic Data Centre.





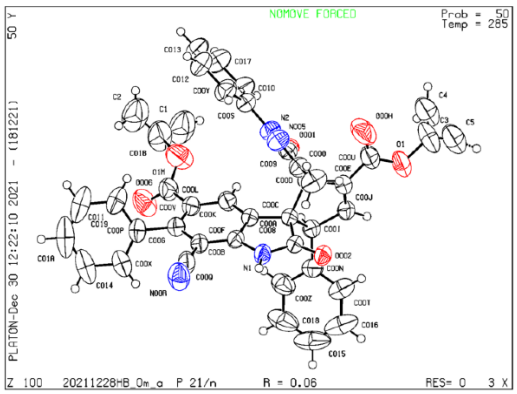
3a
CCDC 2125152

(Ellipsoid contour probability 50%)

Identification code	20210607HSR
Chemical formula	$C_{29}H_{24}N_4O_5$
Formula weight	508.52 g/mol
Temperature	293(2) K
Wavelength	1.54178 Å
Crystal system	triclinic
Space group	P -1
Unit cell dimensions	a = 9.1555(3) Å α=87.333(2)°
	b = 9.7802(3) Å β=85.052(2)°
	c = 15.0579(5) Å γ=86.919(2)°
Volume	1340.17(8) $Å^3$
Z	2
Density (calculated)	1.260 g/cm^3
Absorption coefficient	0.722 mm^{-1}
F (000)	532
Theta range for data collection	2.95 to 68.26°
Index ranges	-10<=h<=11, -11<=k<=11, -14<=l<=17
Reflections collected	24770
Independent reflections	4703 [R(int) = 0.0682]
Coverage of independent reflections	95.8%
Absorption correction	Multi-Scan
Structure solution technique	direct methods
Structure solution program	SHELXT 2014/5 (Sheldrick, 2014)

Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL-2016/6 (Sheldrick, 2016)
Function minimized	Σ w $(F_o^2 - F_c^2)^2$
Data / restraints / parameters	4703 / 0 / 335
Goodness-of-fit on F^2	1.097
Final R indices	2467 data; I>2σ(I) R1 = 0.0617, wR2 = 0.1281
	all data R1 = 0.1202, wR2 = 0.1576
Weighting scheme	$w=1/[\sigma^2(F_o^2) + (0.0457P)^2 + 0.3818P]$
	where $P= (F_o^2 + 2F_c^2)/3$
Extinction coefficient	0.0095(6)
Largest diff. peak and hole	0.248 and - 0.196 eÅ^{-3}
R.M.S. deviation from mean	0.038 eÅ^{-3}

To a 10 mL tube containing **5a** (30.0 mg) was added a mixture of solvent (6.0 mL, petroleum ether/ethyl acetate = 2:1, v/v). A clear solution was obtained through ultrasound treatment and was kept at room temperature and the crystals were obtained after the solvent evaporated, which were characterized by X-ray single crystal diffraction. X-ray diffraction experiment was carried out on an Agilent D8 QUEST and the data obtained were deposited at the Cambridge Crystallographic Data Centre.



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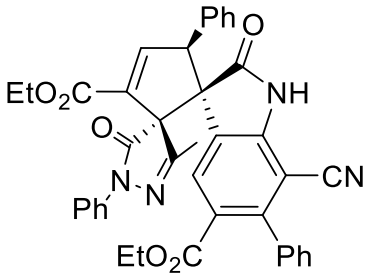


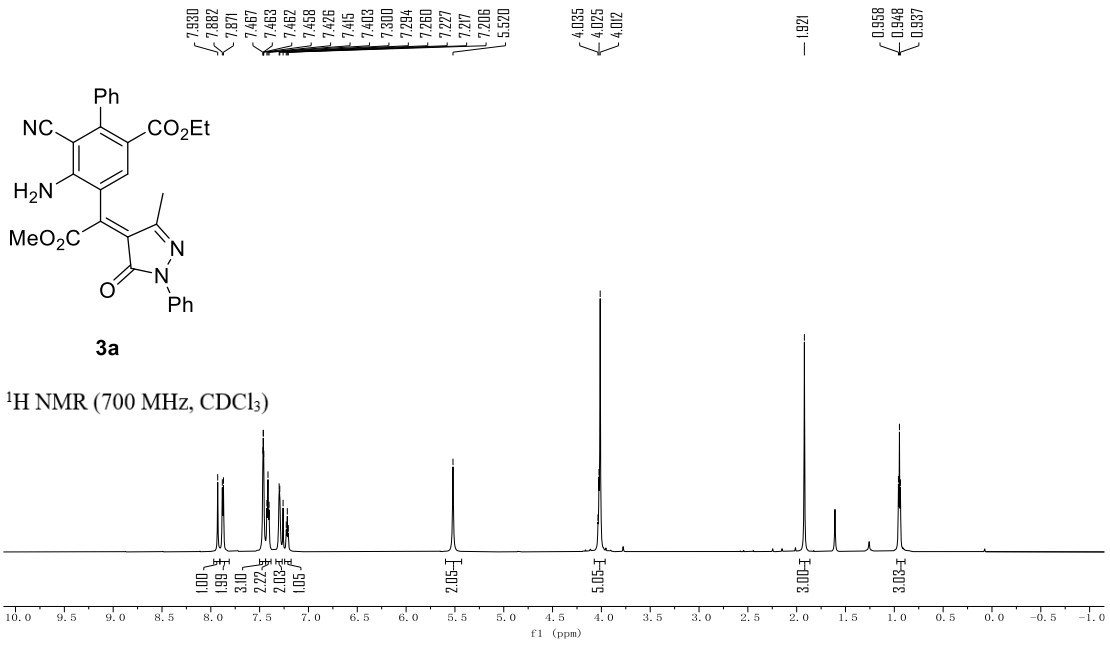
5, CCDC 2153404

(Ellipsoid contour probability 50%)

Identification code	20211228HB
Chemical formula	$C_{40}H_{32}N_4O_6$
Formula weight	664.72 g/mol
Temperature	285(2) K
Wavelength	1.54178 Å
Crystal system	monoclinic
Space group	P 1 21/n 1
Unit cell dimensions	a=12.3454(5) Å α=90°
	b=17.3923(6) Å β=95.603(2)°
	c=16.0726(6) Å γ=90°

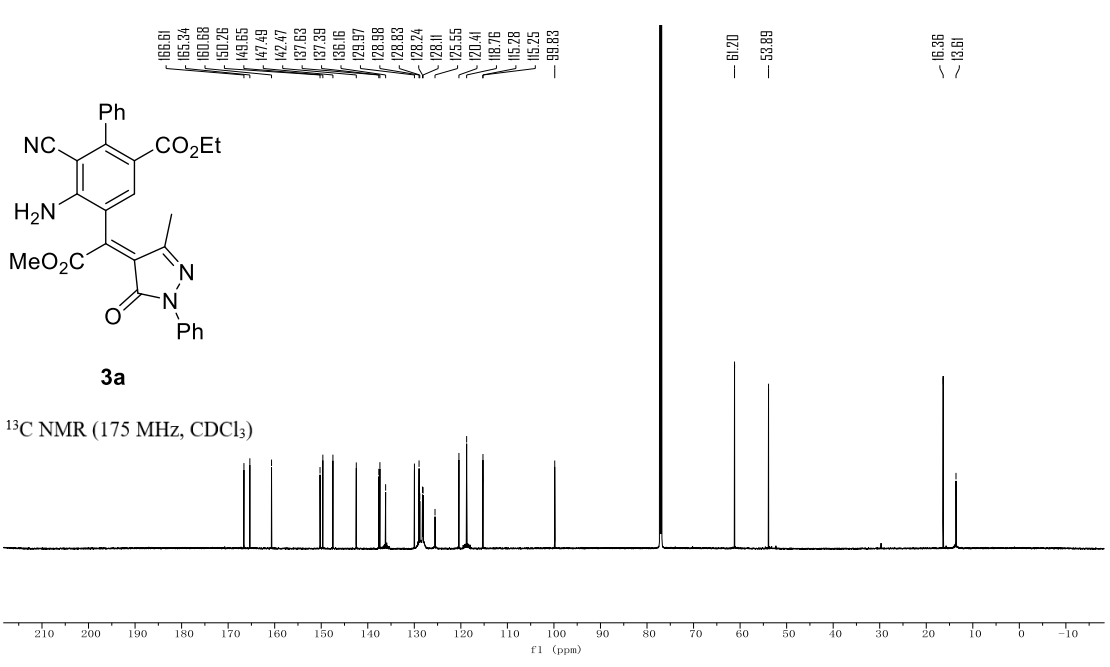
Volume	3434.5(2) $Å^3$
Z	4
Density (calculated)	1.272 g/cm^3
Absorption coefficient	0.714 mm^{-1}
F (000)	1365
Theta range for data collection	3.75 to 68.42°
Index ranges	-14<=h<=14, -20<=k<=20, -19<=l<=19
Reflections collected	36009
Independent reflections	6280 [R(int) = 0.0538]
Coverage of independent reflections	99.6%
Absorption correction	Multi-Scan
Structure solution technique	direct methods
Structure solution program	SHELXT 2014/5 (Sheldrick, 2014)
Refinement method	Full-matrix least-squares on F2
Refinement program	SHELXL-2016/6 (Sheldrick, 2016)
Function minimized	$\Sigma\ w(F_o2 - F_c2)2$
Data / restraints / parameters	6280 / 0 / 464
Goodness-of-fit on F^2	1.051
Final R indices	4556 data; $I>2\sigma(I)$ R1 = 0.0606, wR2 = 0.1719
	all data R1 = 0.0805, wR2 = 0.1959
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.1077P)^2+0.9218P]$ where $P=(F_o^2+2F_c^2)/3$
Extinction coefficient	0.0059(5)
Largest diff. peak and hole	0.399 and -0.258 $eÅ^{-3}$
R.M.S. deviation from mean	0.050 $eÅ^{-3}$

12. ^{1}H NMR and ^{13}C NMR Spectra



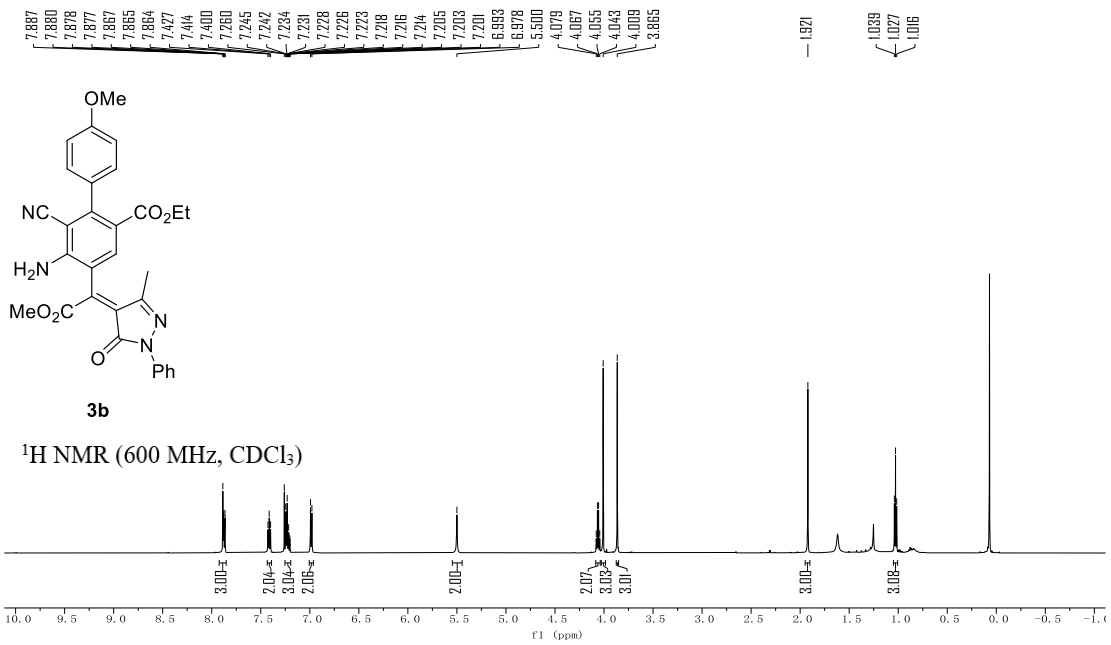
3a

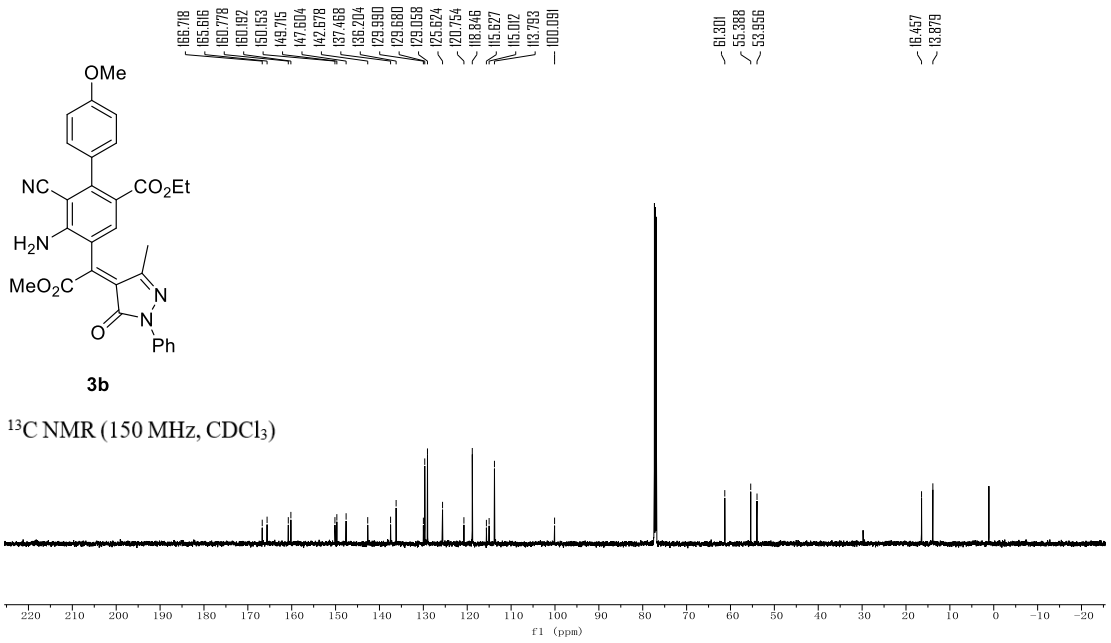
^{1}H NMR (700 MHz, $CDCl_3$)

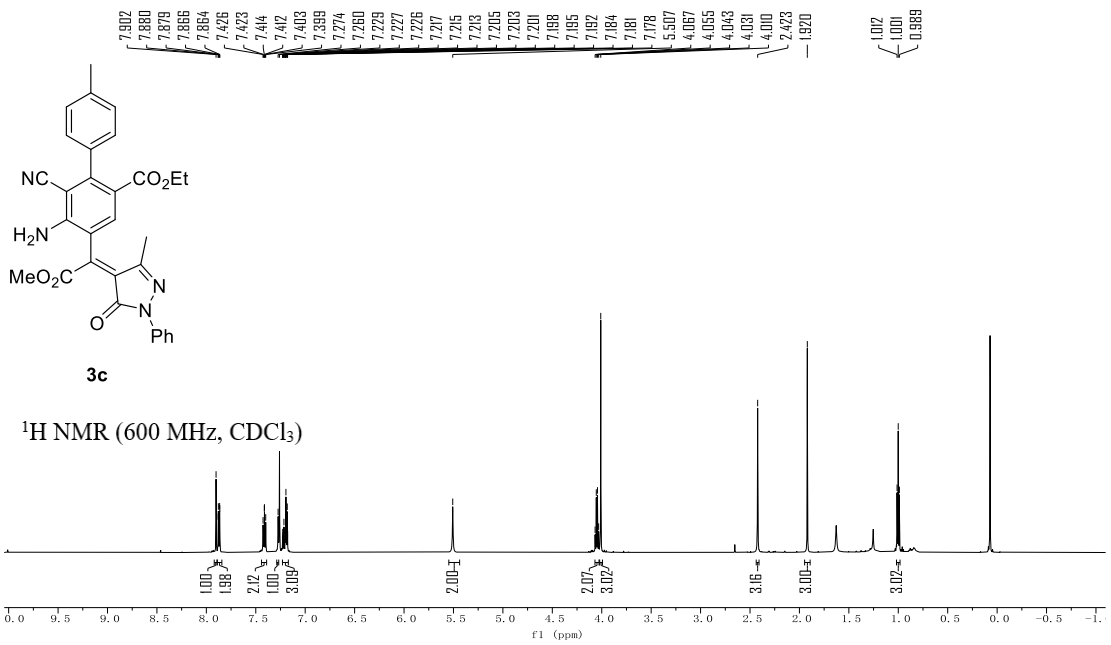


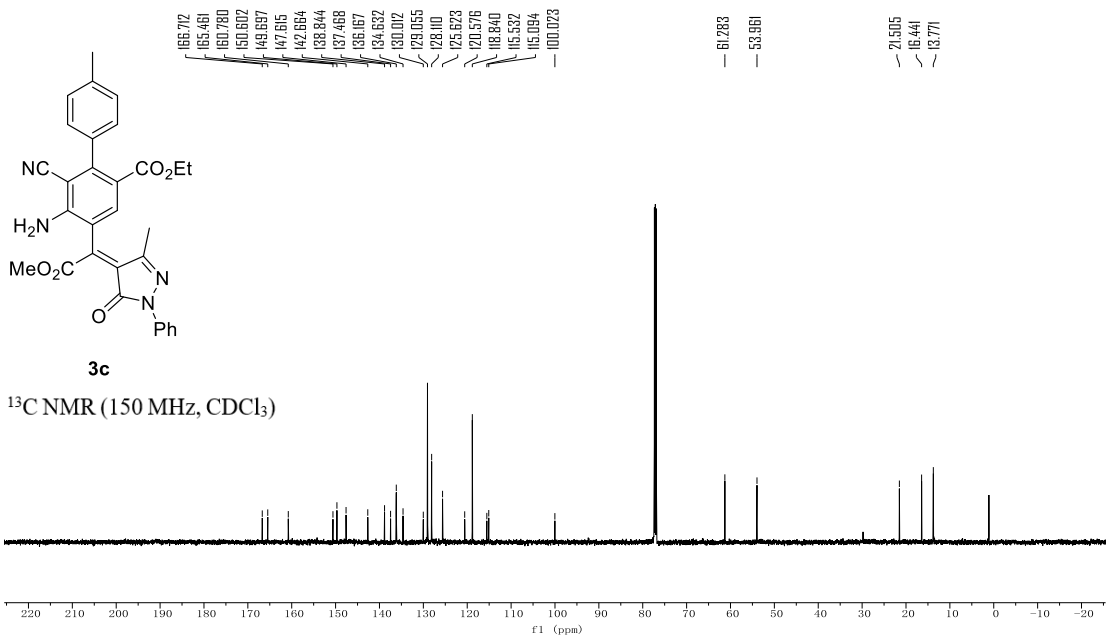
3a

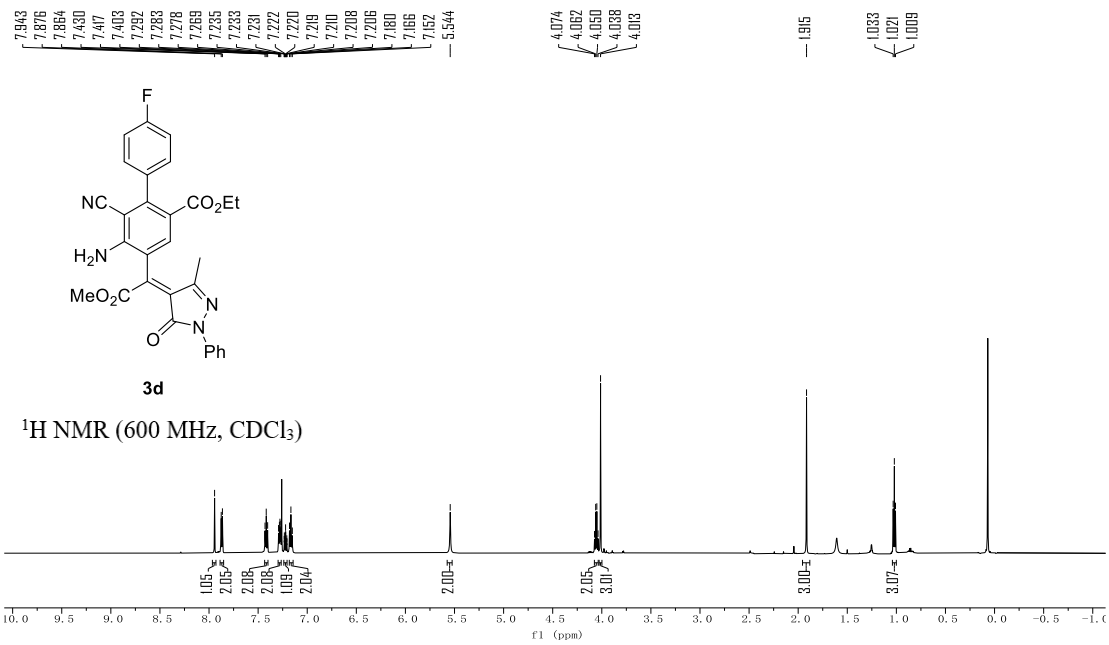
^{13}C NMR (175 MHz, $CDCl_3$)


7.887
7.880
7.878
7.877
7.867
7.865
7.864
7.427
7.414
7.400
7.260
7.245
7.242
7.234
7.231
7.228
7.226
7.223
7.218
7.216
7.214
7.205
7.203
7.201
6.993
6.978
5.300
4.079
4.067
4.055
4.043
4.009
3.865
1.921
1.039
1.027
1.016
OMe
NC
CO2Et
H2N
MeO2C
N
O
N
Ph
3b
1H NMR (600 MHz, CDCl3)
3.00
2.04
3.04
2.06
2.00
2.07
3.03
3.01
3.00
3.08
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
f1 (ppm)


166.718
165.616
160.778
160.192
150.153
149.715
147.604
142.678
137.468
136.204
129.990
129.680
129.058
125.624
120.754
118.846
115.627
115.012
113.793
100.091
61.301
55.388
53.956
16.457
13.879
OMe
NC
CO2Et
H2N
MeO2C
N
O
N
Ph
3b
13C NMR (150 MHz, CDCl3)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20
f1 (ppm)

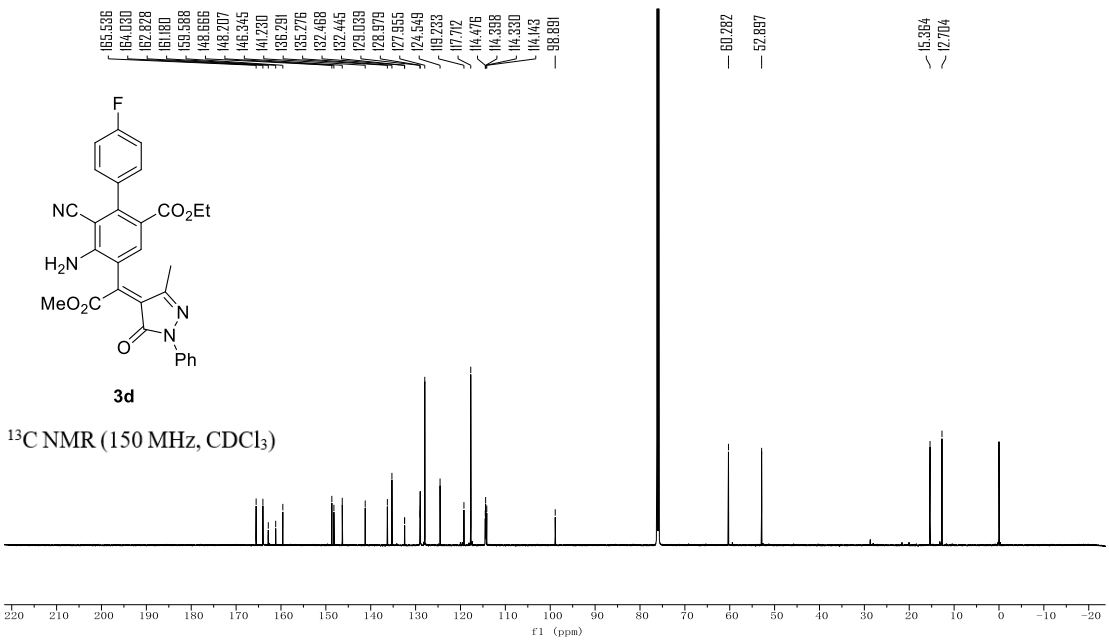

7.902
7.880
7.879
7.866
7.864
7.426
7.423
7.414
7.412
7.403
7.399
7.274
7.260
7.229
7.227
7.226
7.217
7.215
7.213
7.205
7.203
7.201
7.198
7.195
7.192
7.184
7.181
7.178
5.507
4.067
4.055
4.043
4.031
4.010
2.423
1.920
1.012
1.001
0.989
NC
CO2Et
H2N
MeO2C
N
O
N
Ph
3c
1H NMR (600 MHz, CDCl3)
1.00
1.98
2.12
1.00
3.09
2.00
2.07
3.02
3.16
3.00
3.02
f1 (ppm)


166.712
165.461
160.780
150.602
149.697
147.615
142.664
138.844
137.468
136.167
134.632
130.012
129.055
128.110
125.823
120.576
118.840
115.532
115.094
100.023
61.283
53.961
21.505
16.441
13.771
NC
CO2Et
H2N
MeO2C
N
O
N
Ph
3c
13C NMR (150 MHz, CDCl3)
f1 (ppm)



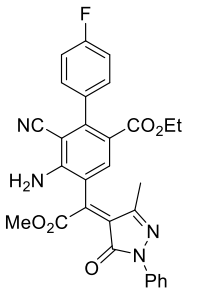
3d

^{1}H NMR (600 MHz, $CDCl_3$)



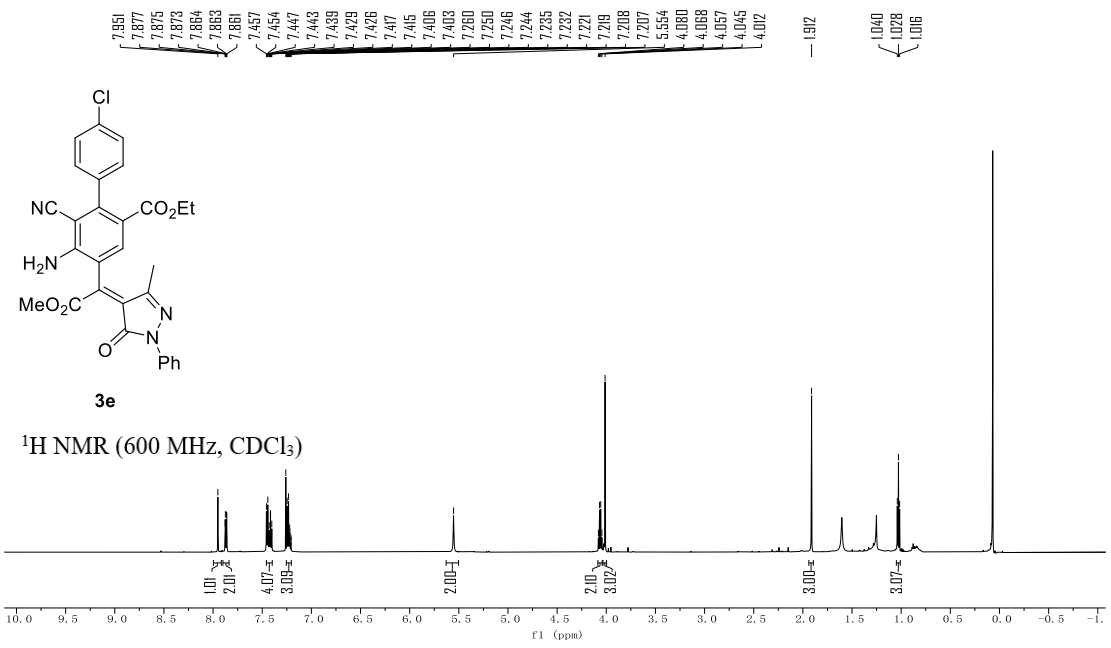
3d

^{13}C NMR (150 MHz, $CDCl_3$)



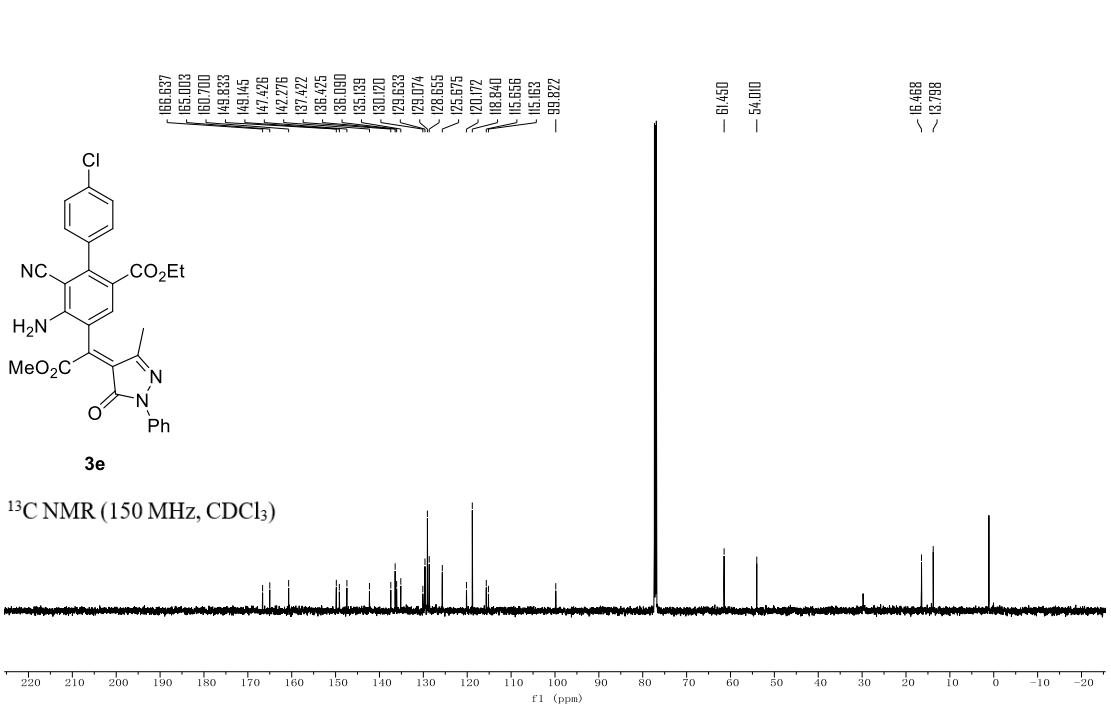
3d

^{19}F NMR (660 MHz, $CDCl_3$)



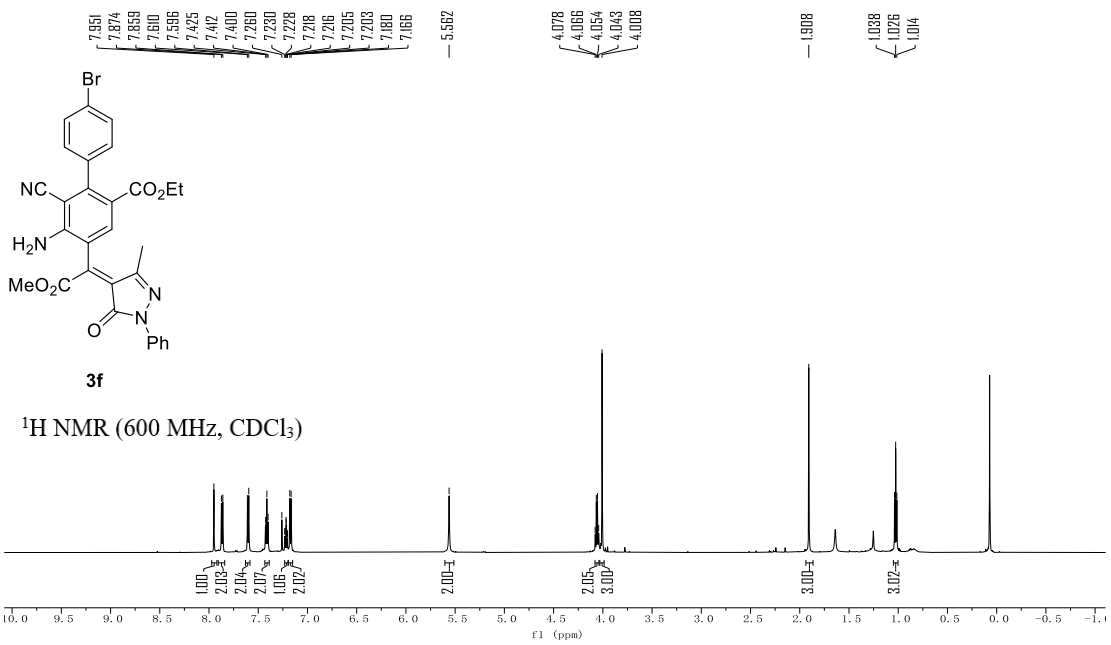
3e

^{1}H NMR (600 MHz, $CDCl_3$)



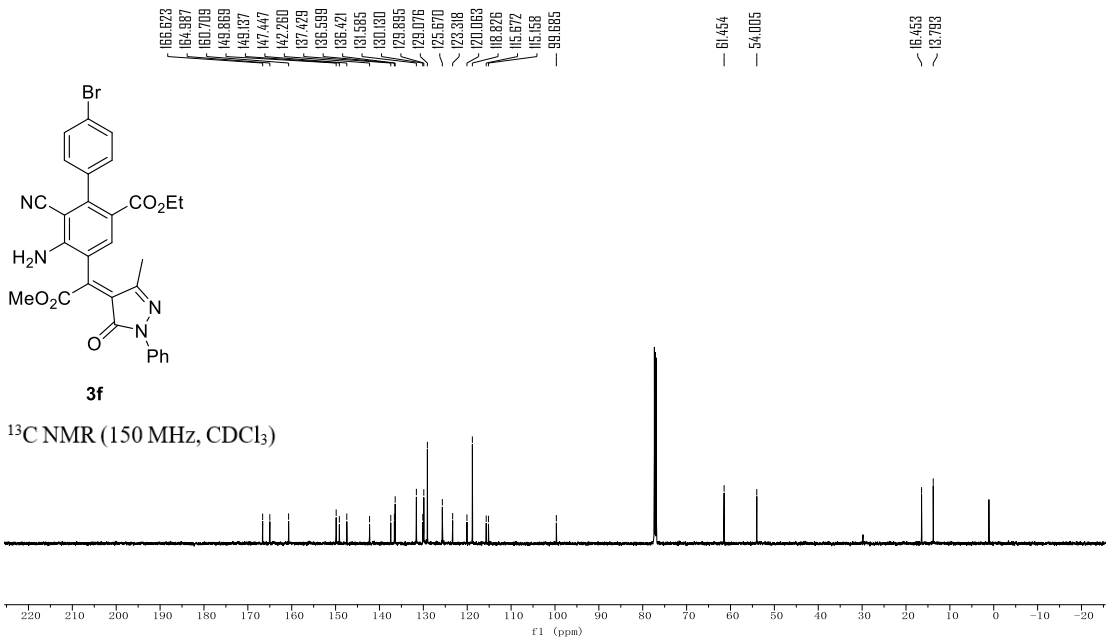
3e

^{13}C NMR (150 MHz, $CDCl_3$)



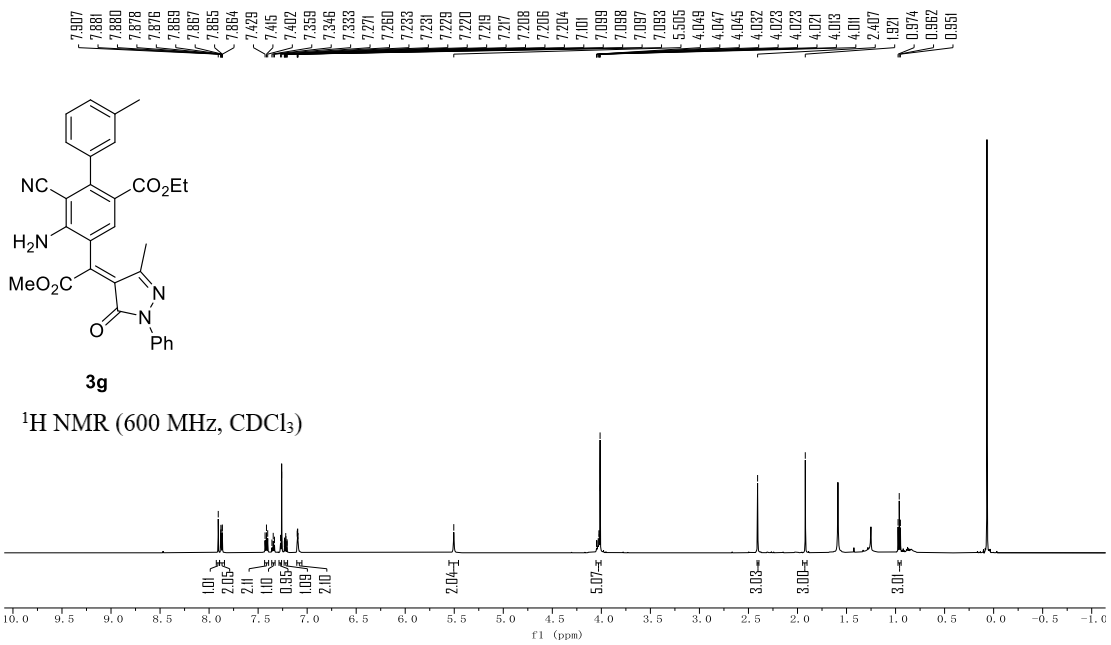
3f

^{1}H NMR (600 MHz, $CDCl_3$)



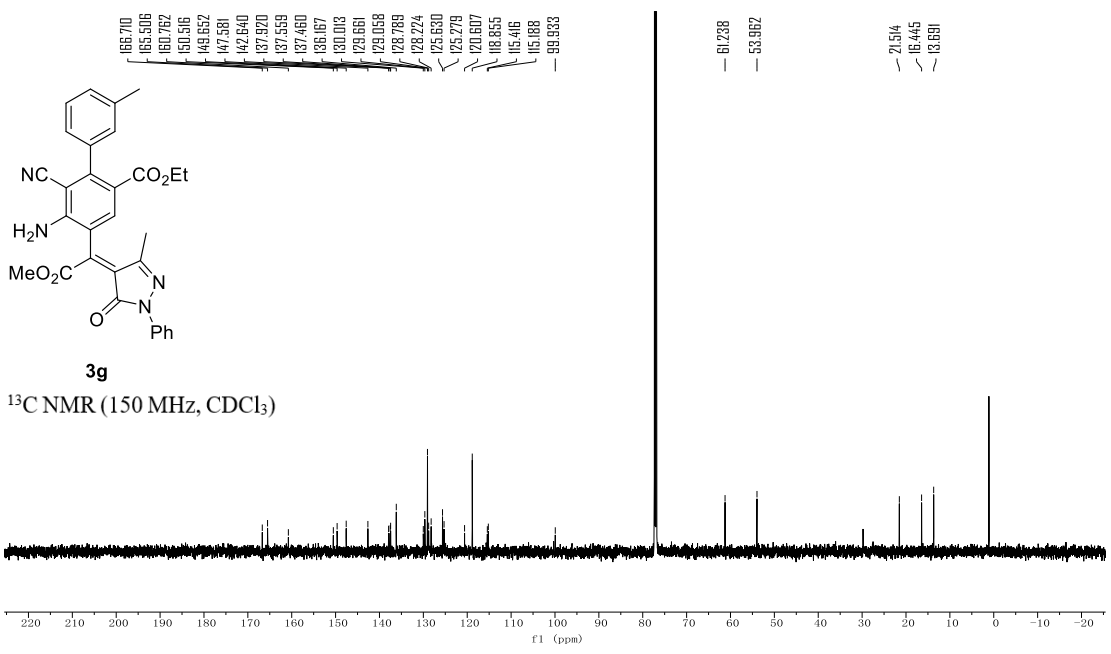
3f

^{13}C NMR (150 MHz, $CDCl_3$)



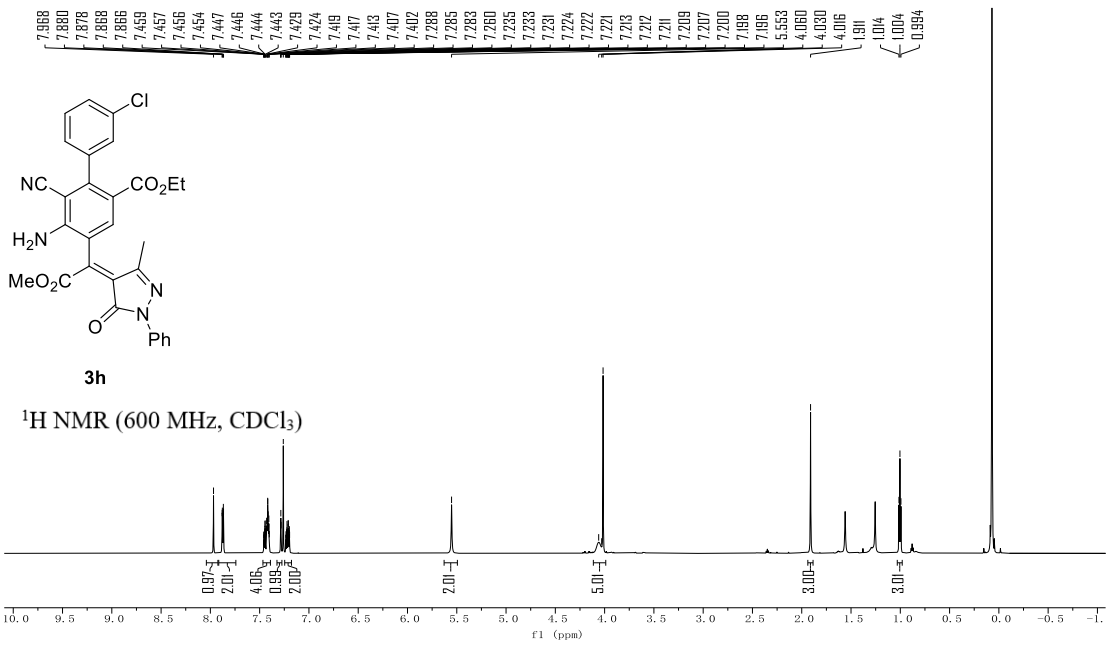
3g

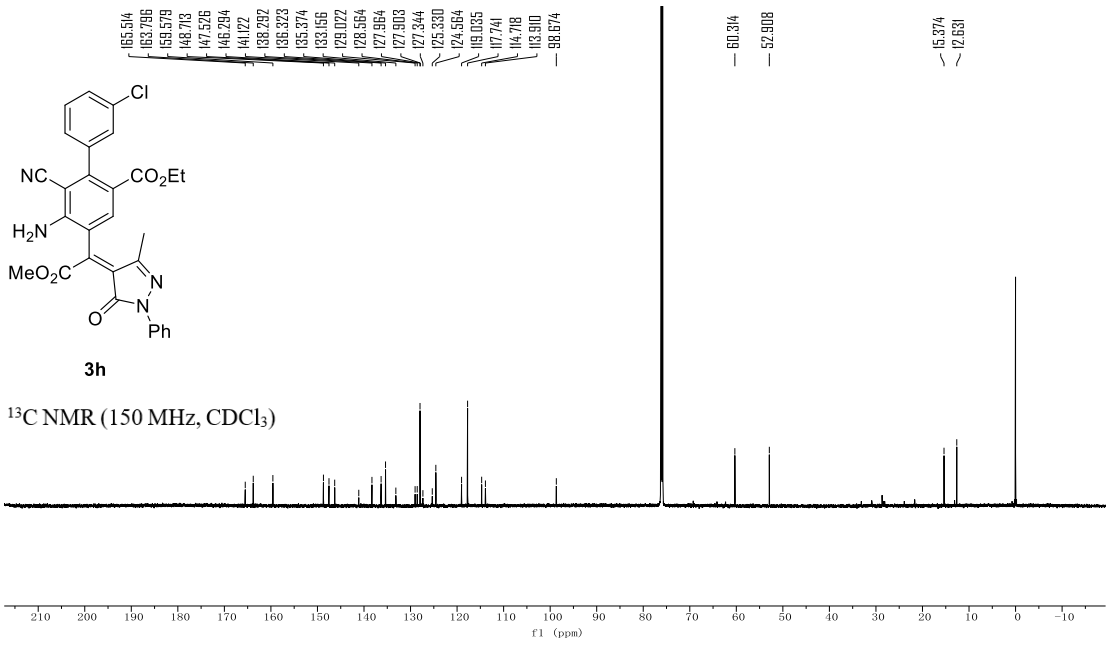
^{1}H NMR (600 MHz, $CDCl_3$)

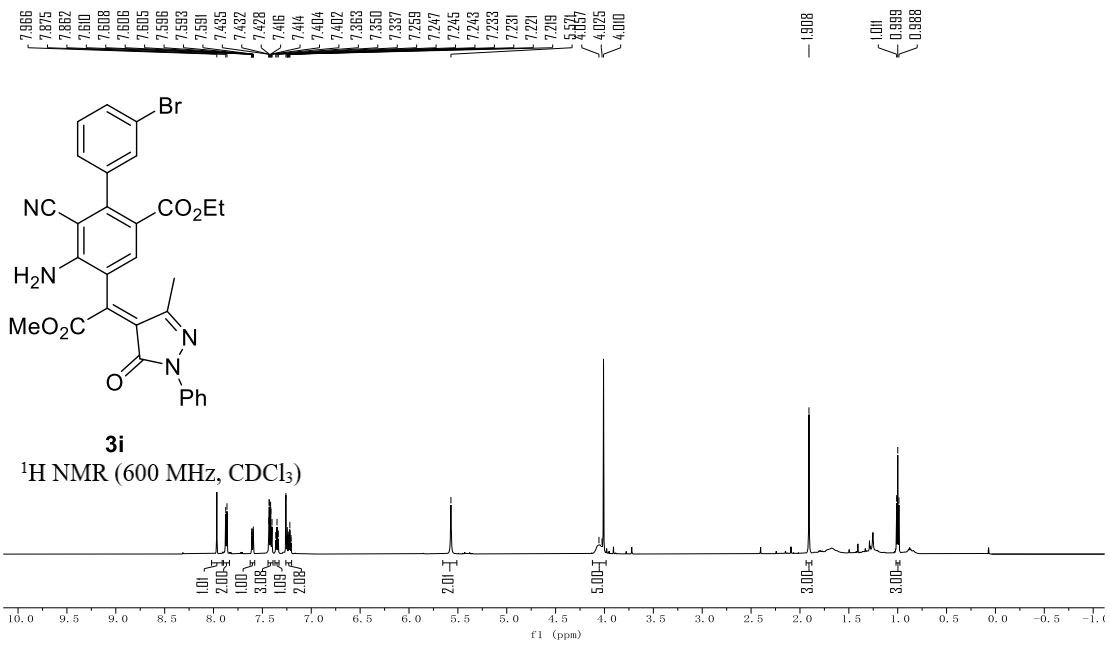


3g

^{13}C NMR (150 MHz, $CDCl_3$)

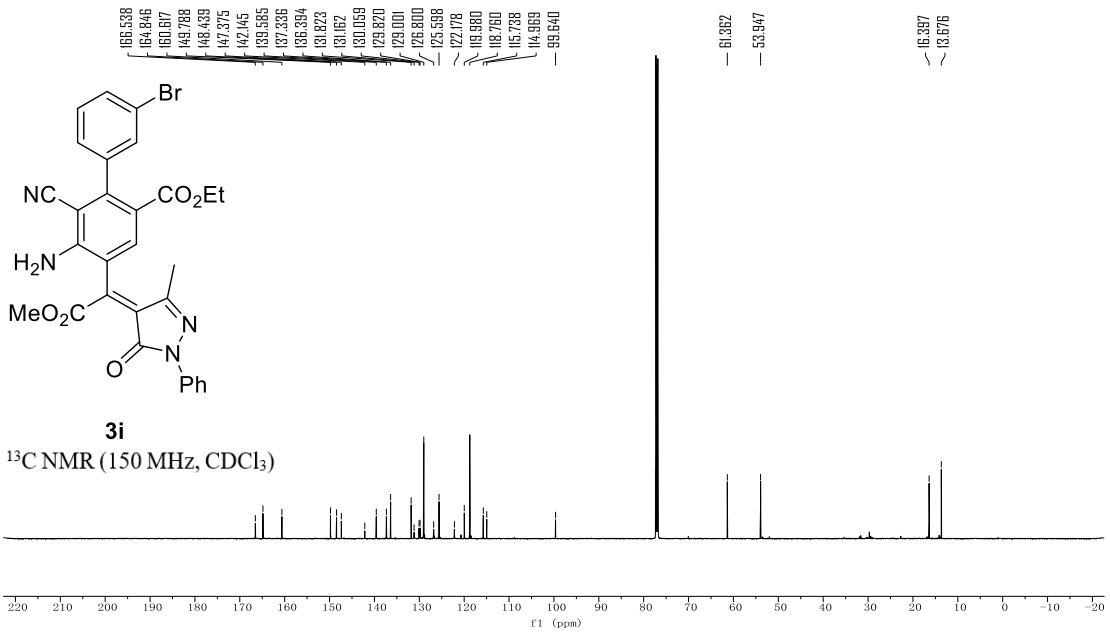

7.968
7.880
7.878
7.868
7.866
7.459
7.457
7.456
7.454
7.447
7.446
7.444
7.443
7.429
7.424
7.419
7.417
7.413
7.407
7.402
7.288
7.285
7.283
7.260
7.235
7.233
7.231
7.224
7.222
7.221
7.213
7.212
7.211
7.209
7.207
7.200
7.198
7.196
5.553
4.060
4.030
4.016
1.911
1.014
1.004
0.994
Cl
NC
CO2Et
H2N
MeO2C
N
O
N
Ph
3h
1H NMR (600 MHz, CDCl3)
0.97
2.01
4.06
0.99
2.00
2.01
5.01
3.00
3.01
f1 (ppm)


165.514
163.796
159.579
148.713
147.526
146.284
141.122
138.292
136.323
135.374
133.156
129.022
128.564
127.964
127.903
127.344
125.330
124.564
119.035
117.741
114.718
113.910
98.674
60.314
52.908
15.374
12.631
Cl
NC
CO2Et
H2N
MeO2C
N
O
N
Ph
3h
13C NMR (150 MHz, CDCl3)
f1 (ppm)



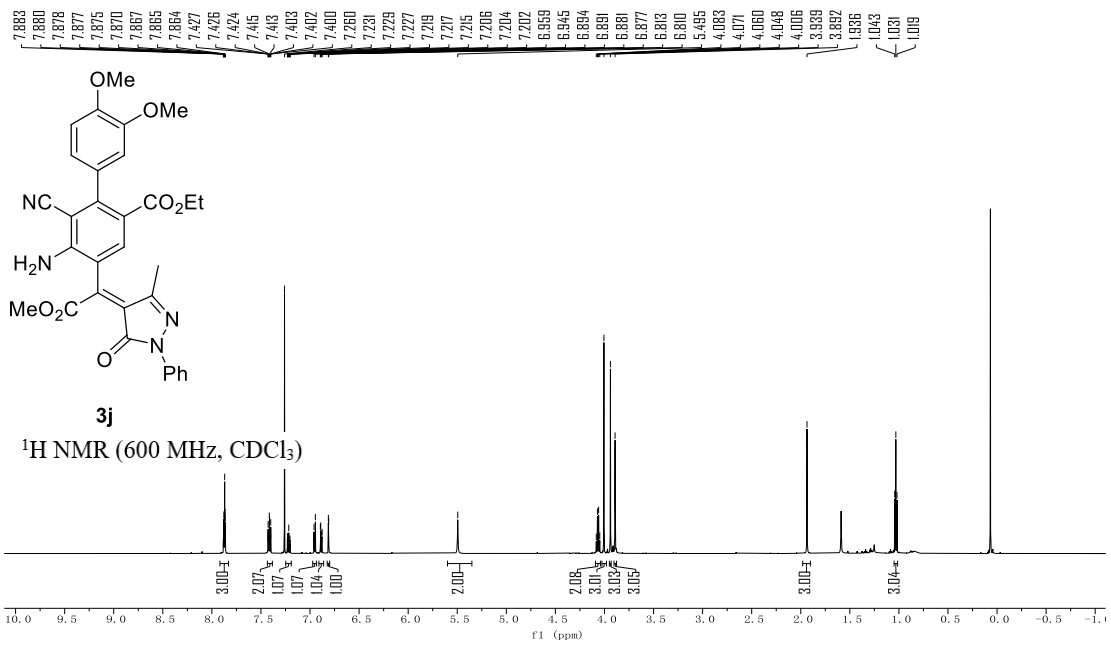
3i

^{1}H NMR (600 MHz, $CDCl_3$)



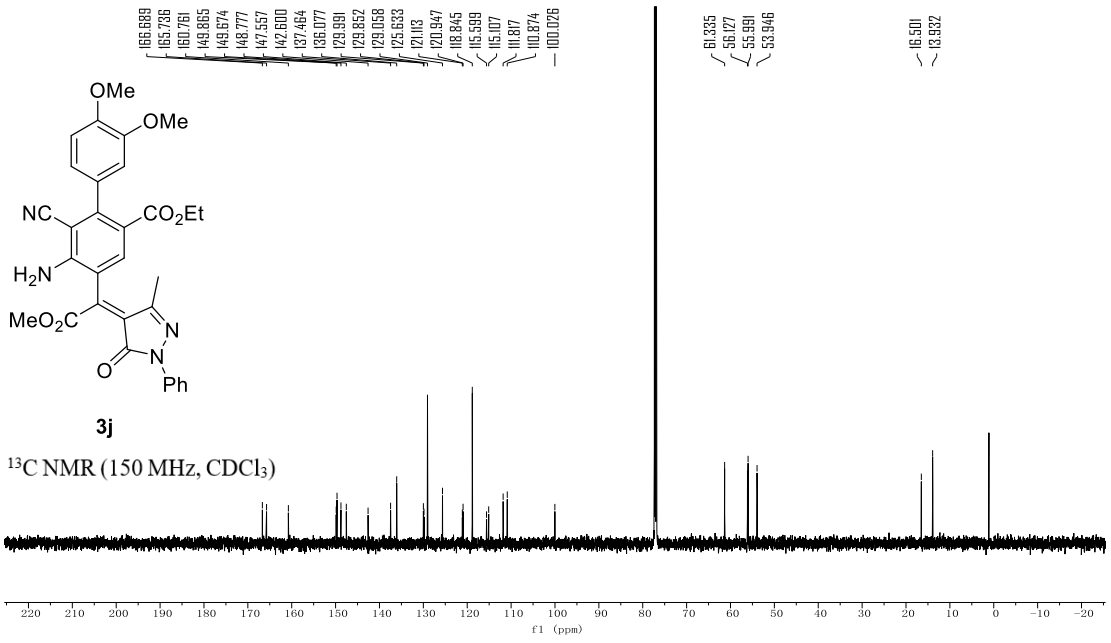
3i

^{13}C NMR (150 MHz, $CDCl_3$)



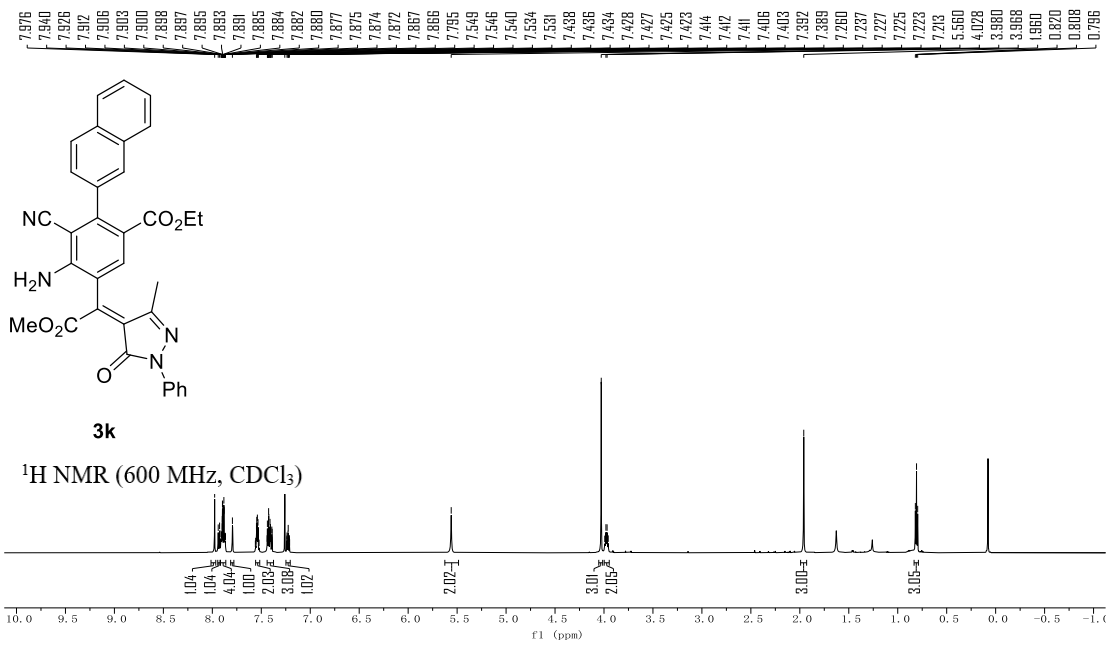
3j

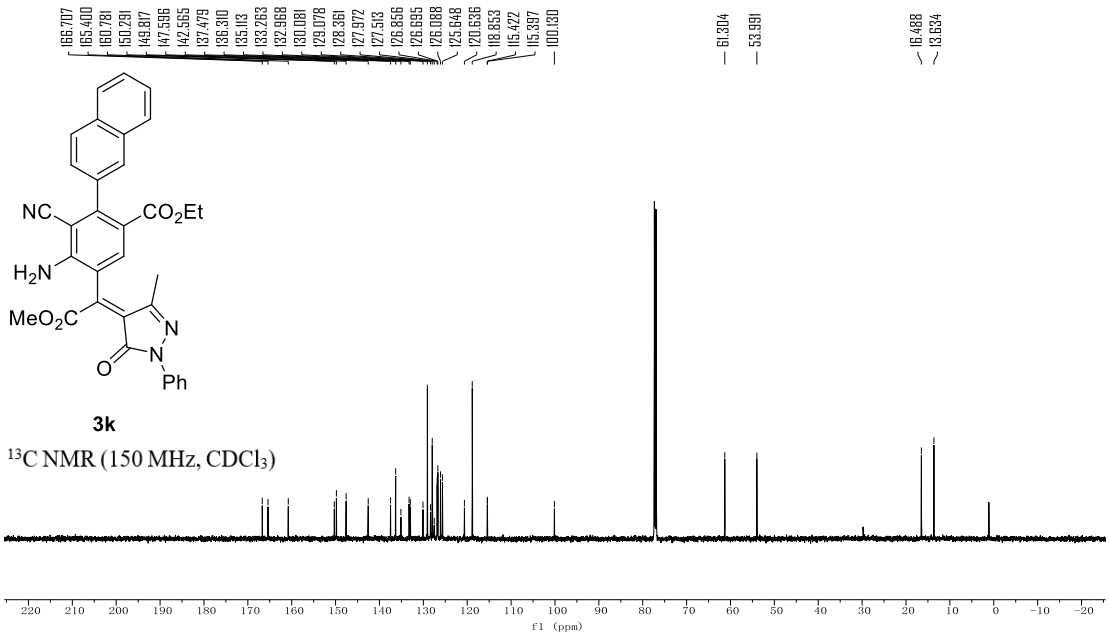
^{1}H NMR (600 MHz, $CDCl_3$)

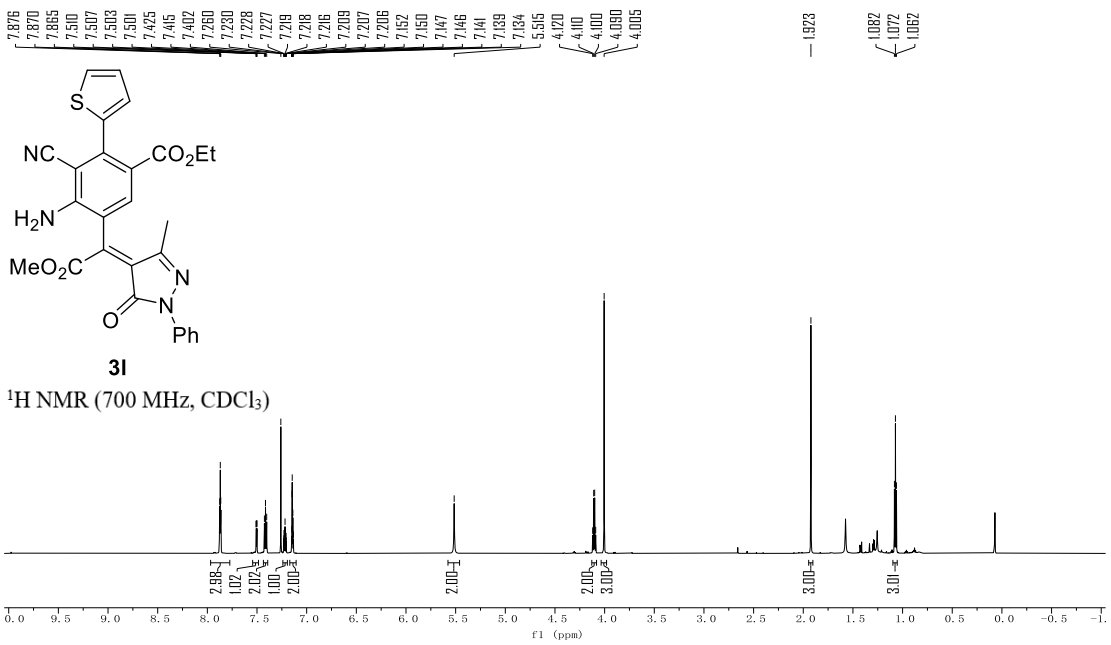


3j

^{13}C NMR (150 MHz, $CDCl_3$)

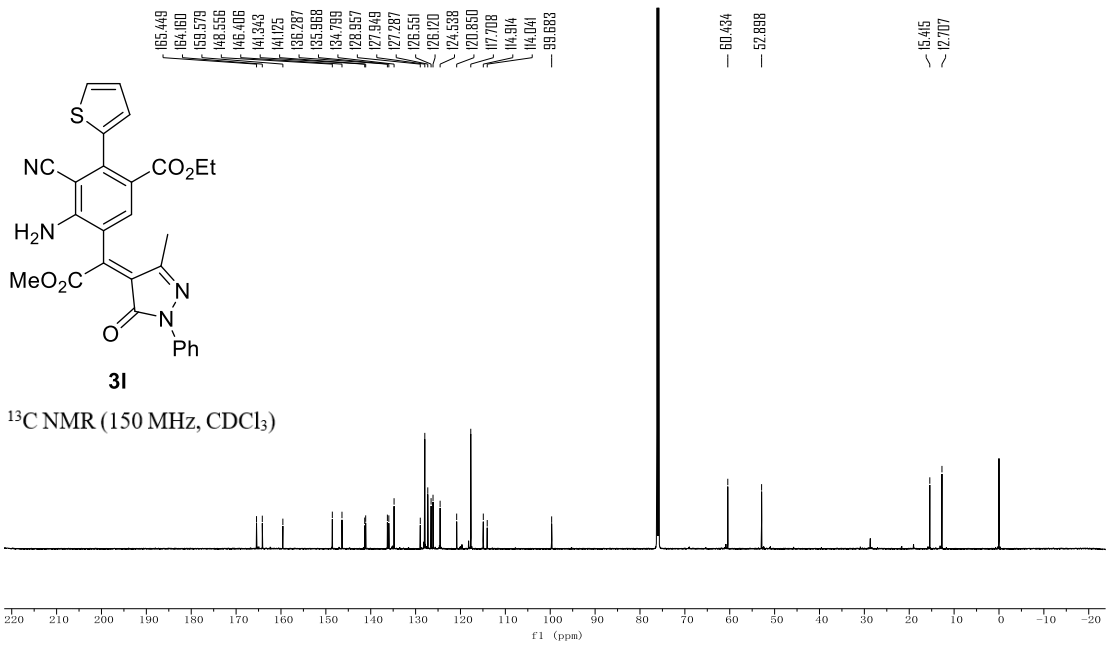

NC
CO2Et
H2N
MeO2C
N
O
N
Ph
3k
1H NMR (600 MHz, CDCl3)
f1 (ppm)


NC
CO2Et
H2N
MeO2C
N
O
N
Ph
3k
13C NMR (150 MHz, CDCl3)
f1 (ppm)



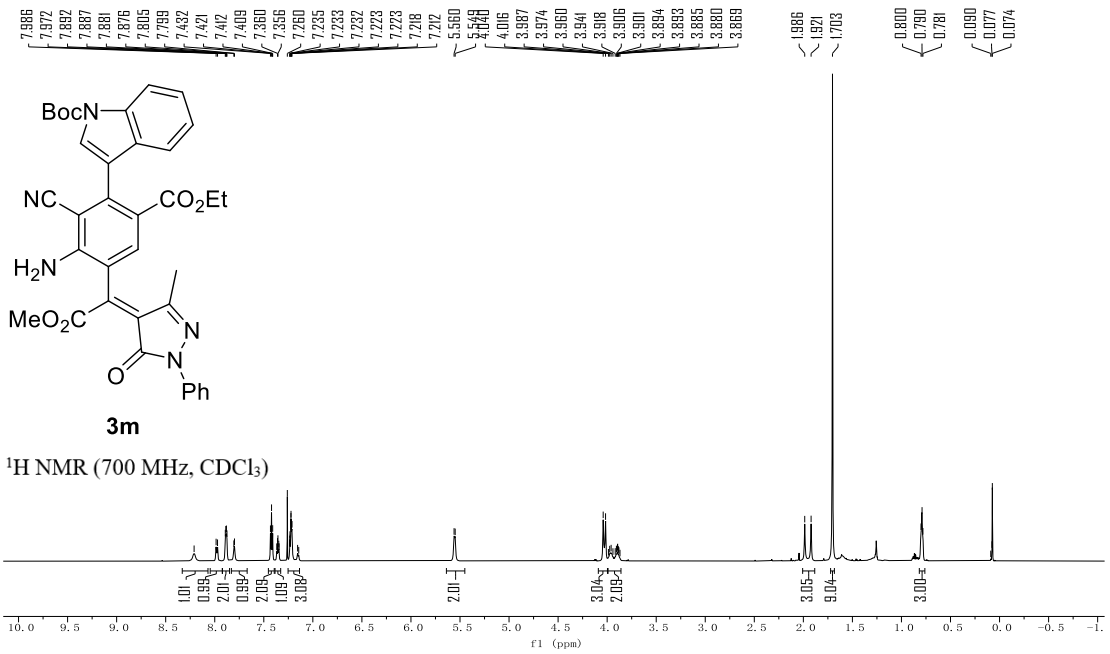
3l

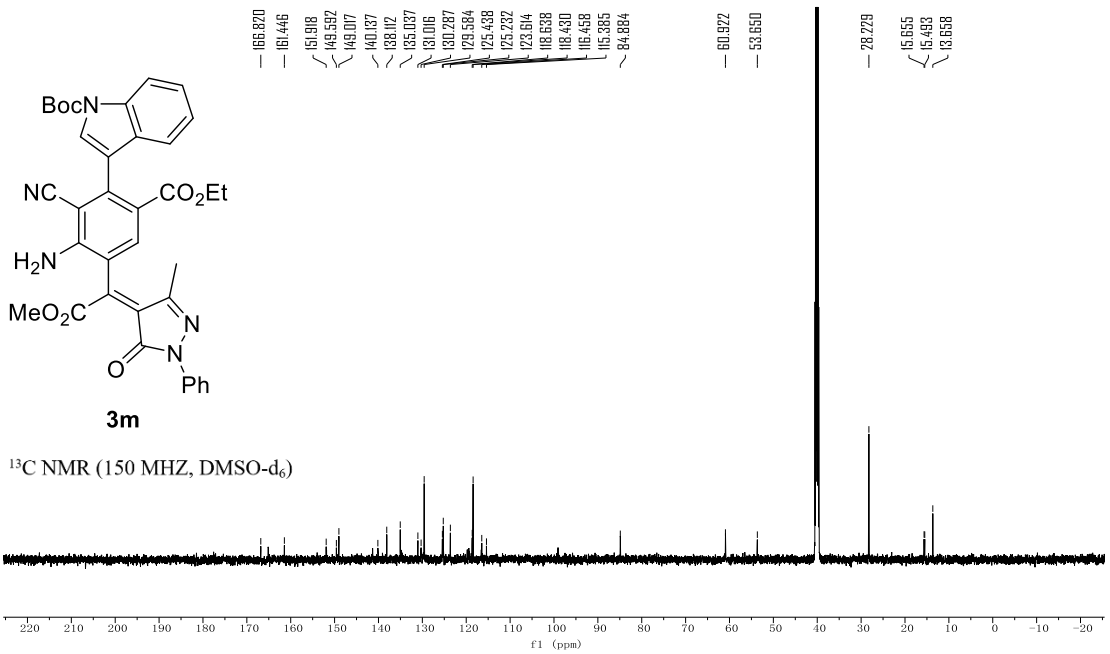
^{1}H NMR (700 MHz, $CDCl_3$)

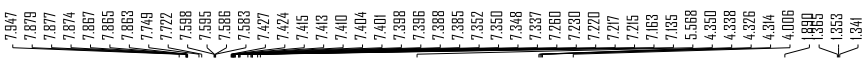


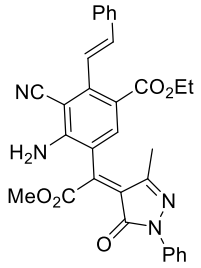
3l

^{13}C NMR (150 MHz, $CDCl_3$)


BocN
NC
CO2Et
H2N
MeO2C
N
N
O
Ph
3m
1H NMR (700 MHz, CDCl3)
f1 (ppm)

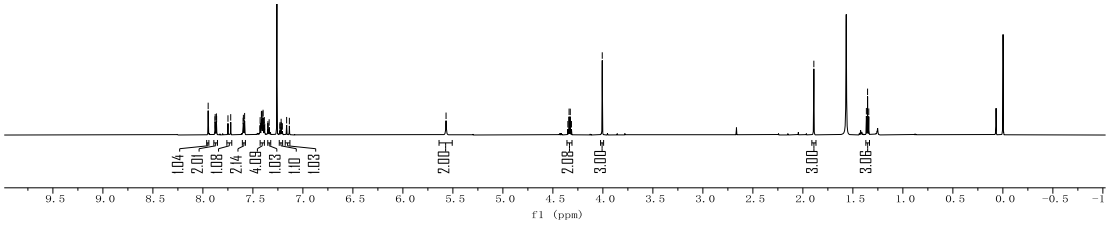

BocN
NC
CO2Et
H2N
MeO2C
N
N
O
Ph
3m
13C NMR (150 MHZ, DMSO-d6)
f1 (ppm)

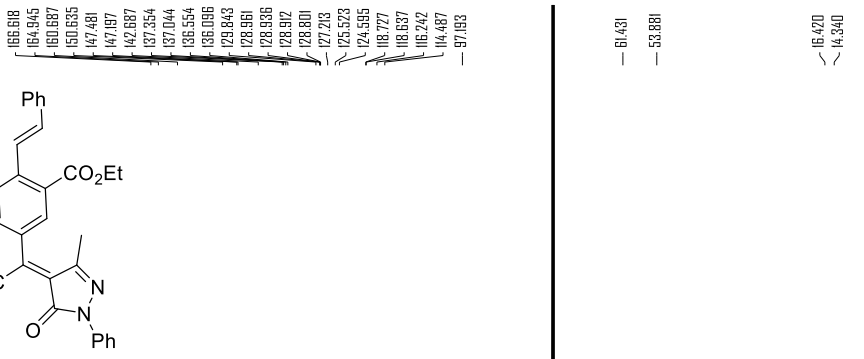




3n

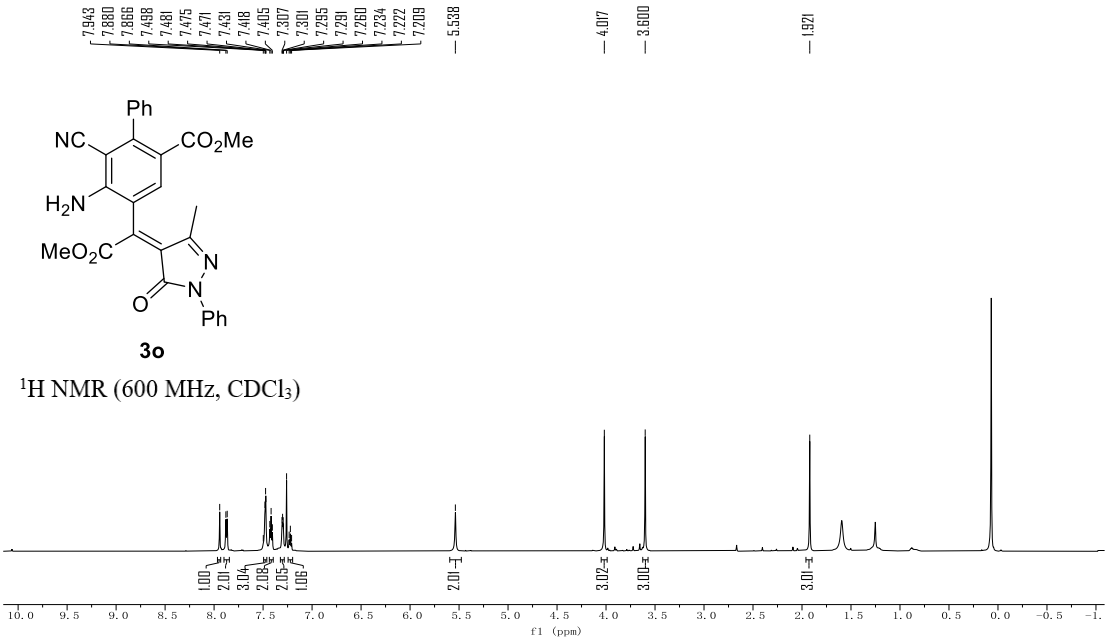
^{1}H NMR (600 MHz, $CDCl_3$)





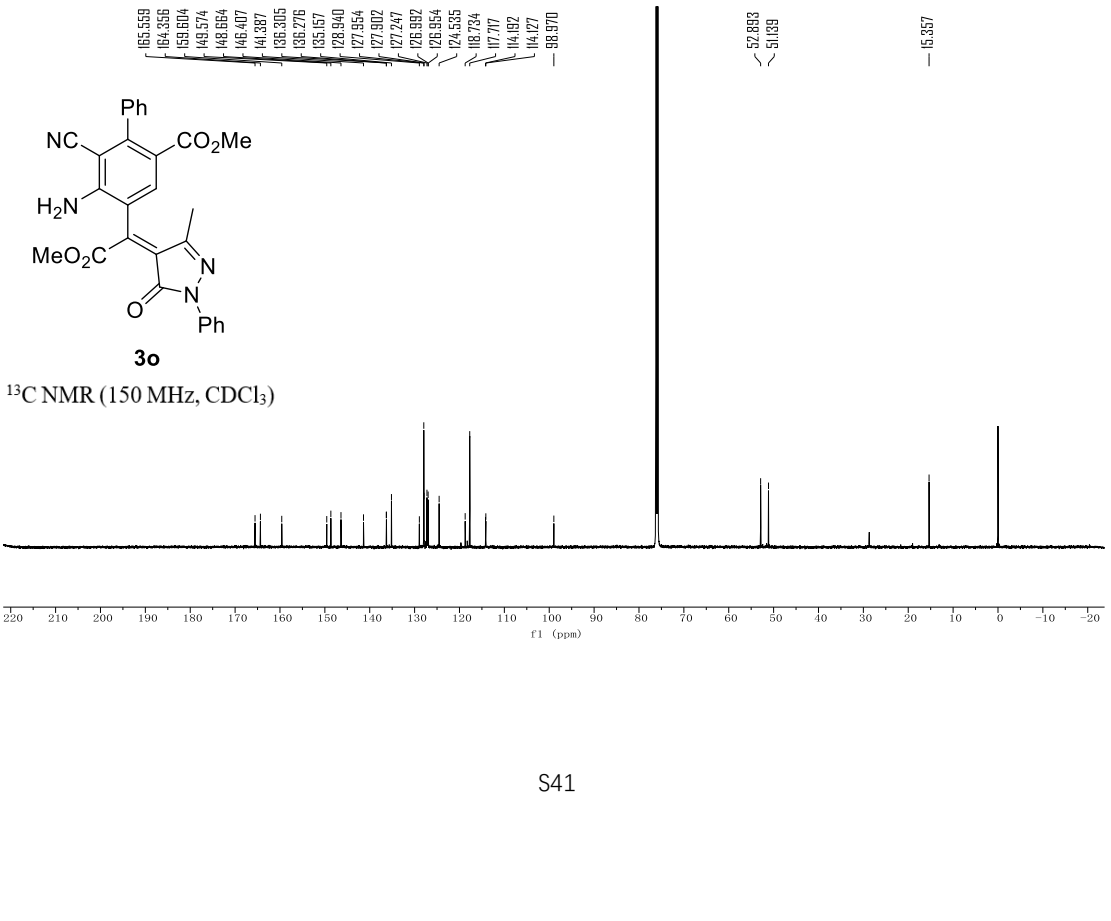
3n

^{13}C NMR (150 MHz, $CDCl_3$)



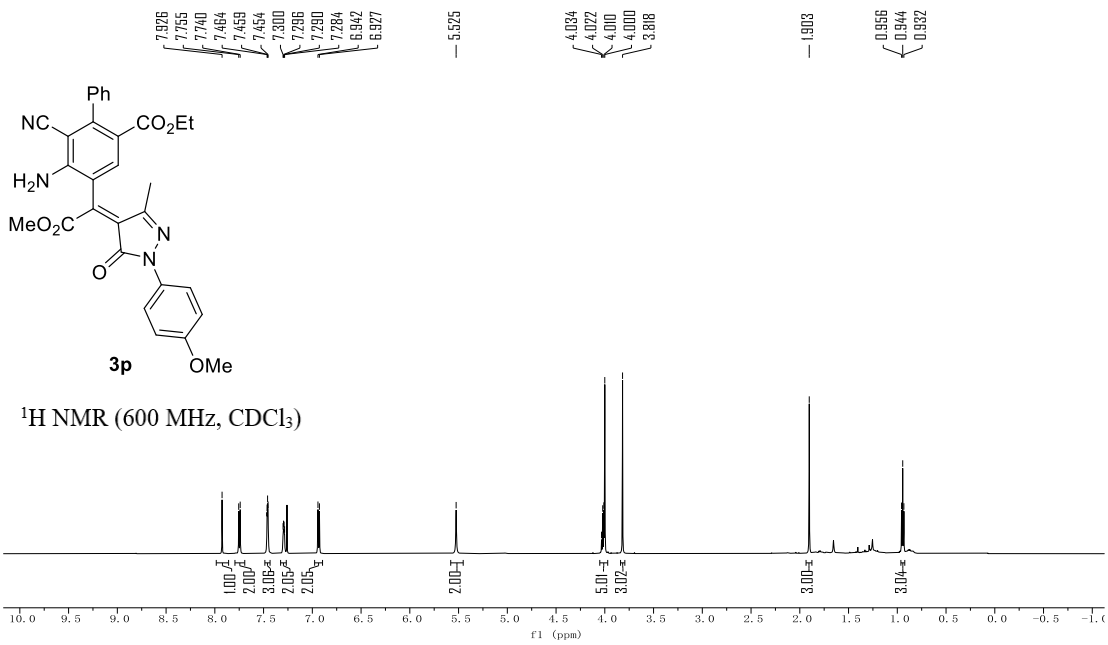
3o

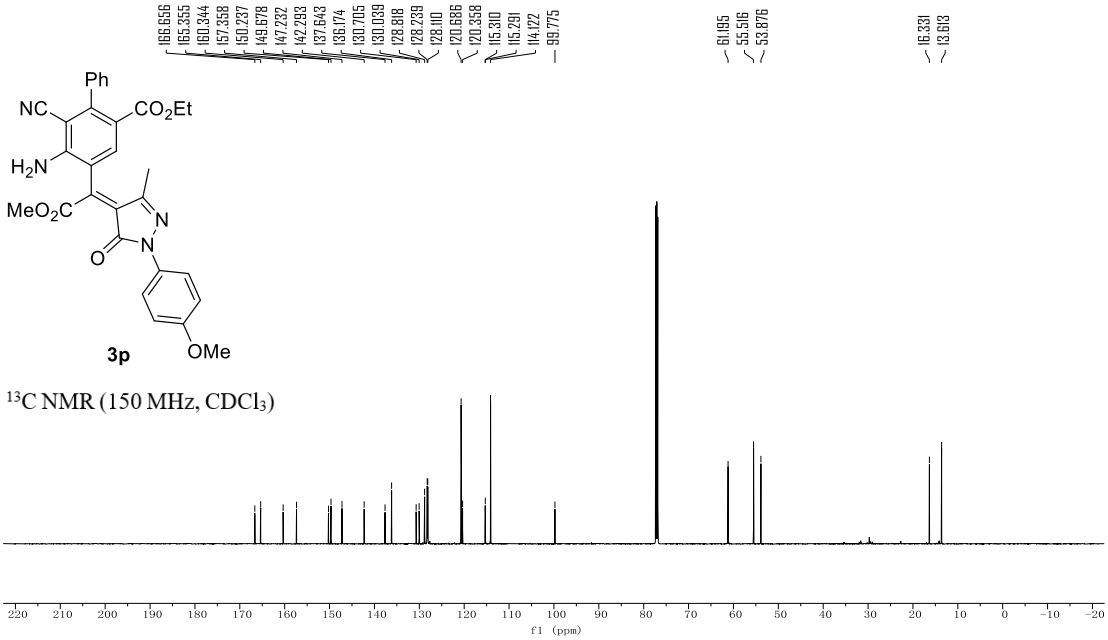
^{1}H NMR (600 MHz, $CDCl_3$)

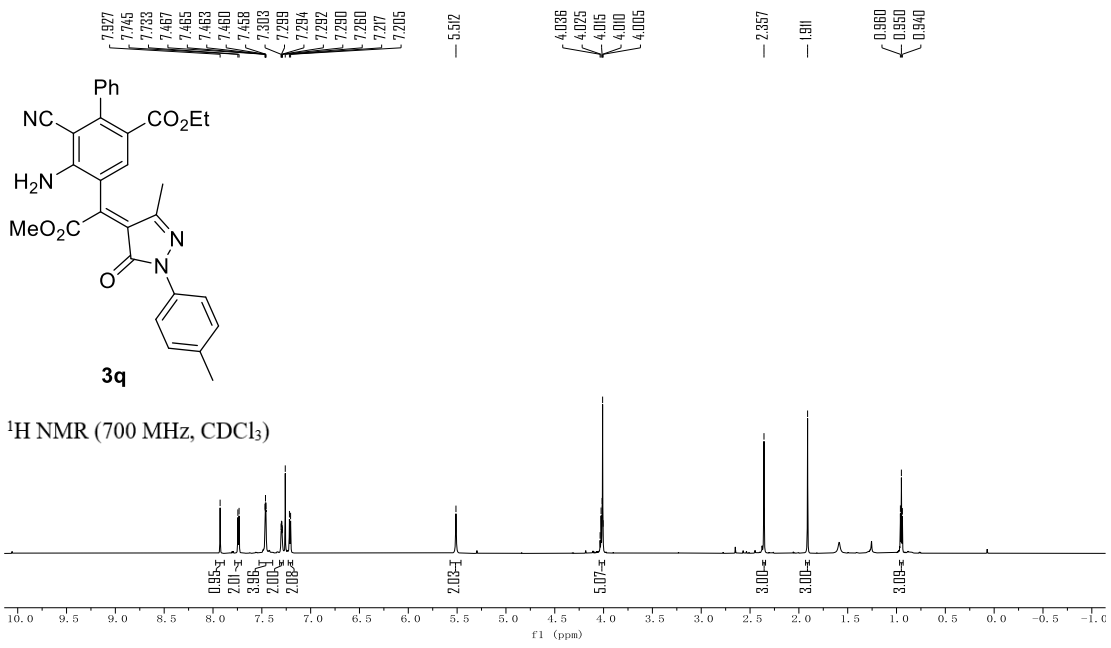


3o

^{13}C NMR (150 MHz, $CDCl_3$)

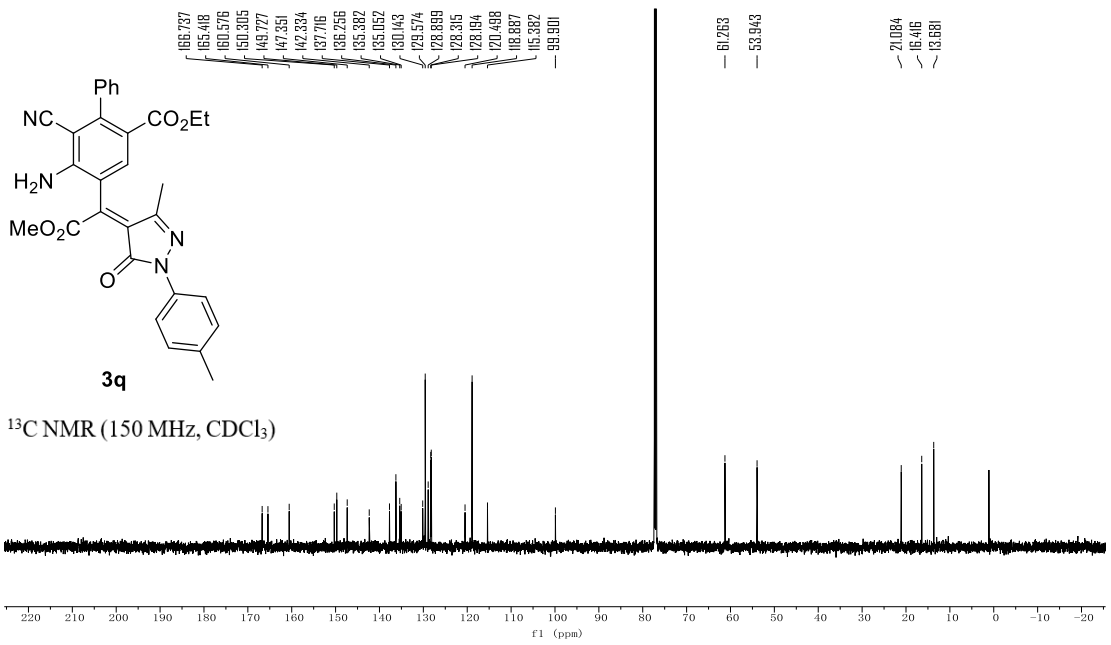

7.926
7.755
7.740
7.464
7.459
7.454
7.300
7.296
7.290
7.284
6.942
6.927
5.525
4.034
4.022
4.010
4.000
3.818
1.903
0.956
0.944
0.932
Ph
NC
CO2Et
H2N
MeO2C
N
O
N
OMe
3p
1H NMR (600 MHz, CDCl3)
1.00
2.00
3.06
2.05
2.05
2.00
5.01
3.02
3.00
3.04
f1 (ppm)


166.656
165.355
160.344
157.358
150.237
149.678
147.232
142.293
137.643
136.174
131.705
130.039
128.818
128.239
128.110
120.686
120.358
115.310
115.291
114.122
99.775
61.195
55.516
53.876
15.331
13.613
Ph
NC
CO2Et
H2N
MeO2C
N
O
N
OMe
3p
13C NMR (150 MHz, CDCl3)
f1 (ppm)



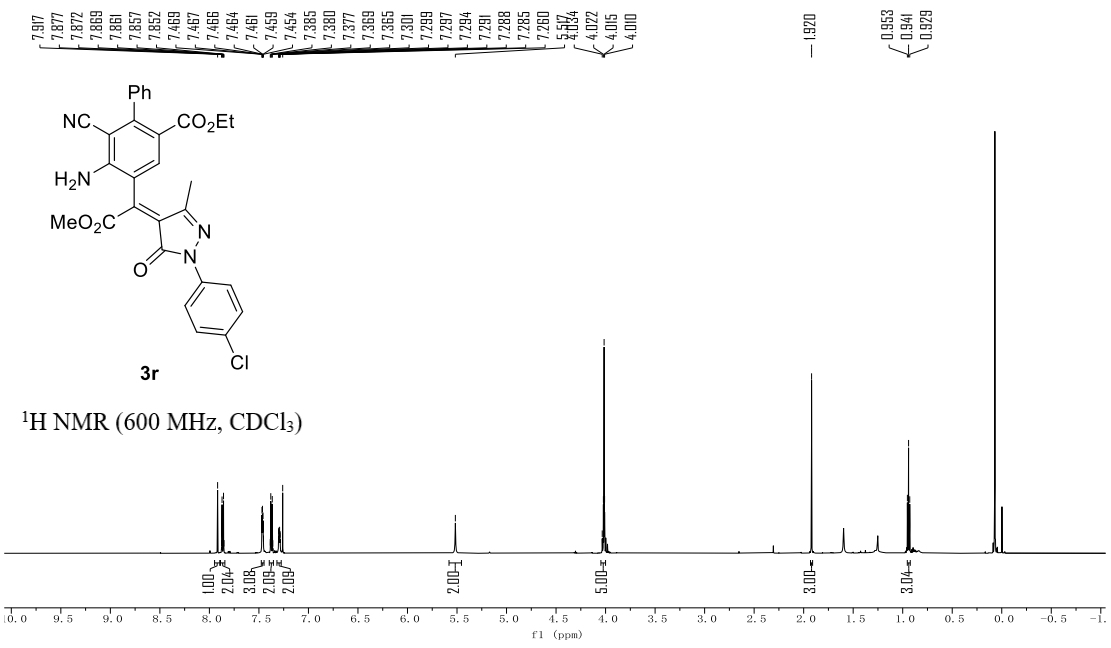
3q

^{1}H NMR (700 MHz, $CDCl_3$)

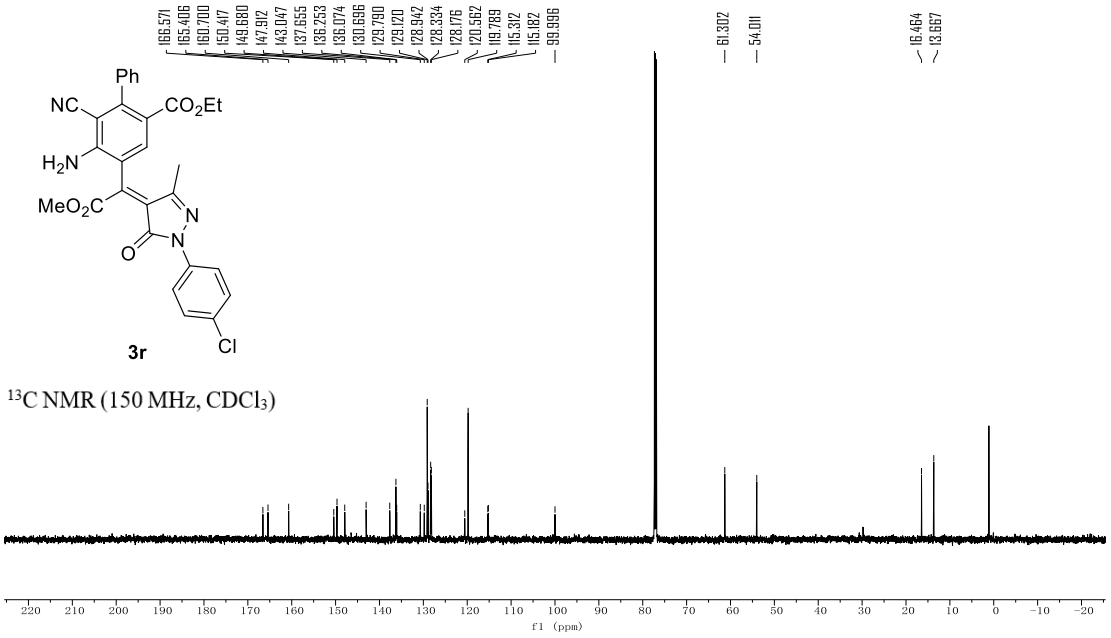


3q

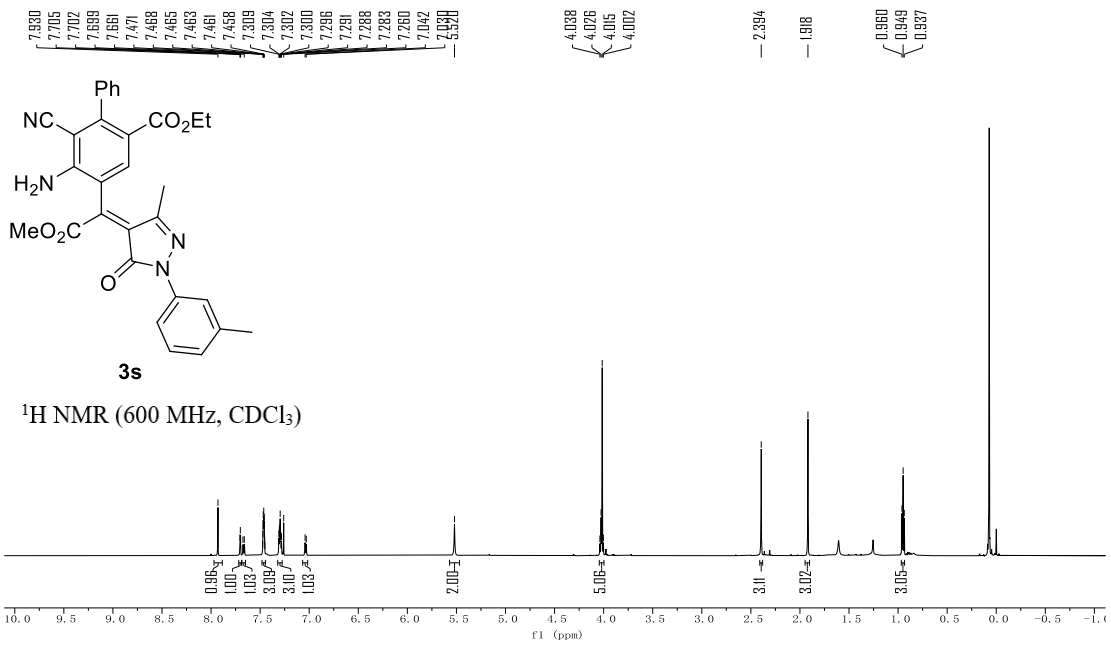
^{13}C NMR (150 MHz, $CDCl_3$)



^{1}H NMR (600 MHz, $CDCl_3$)

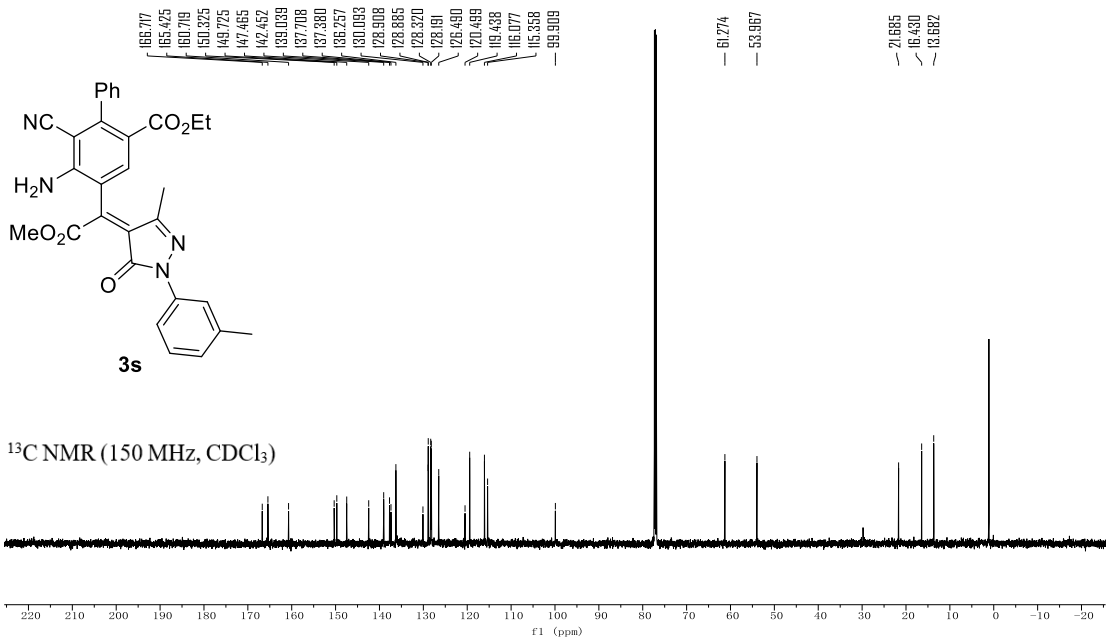


^{13}C NMR (150 MHz, $CDCl_3$)



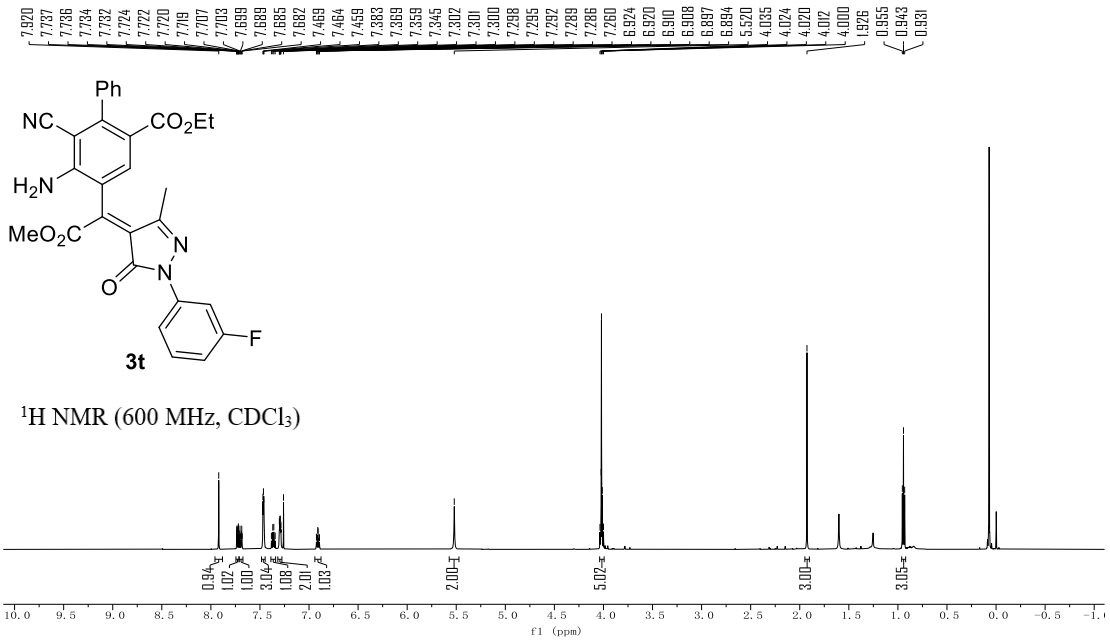
3s

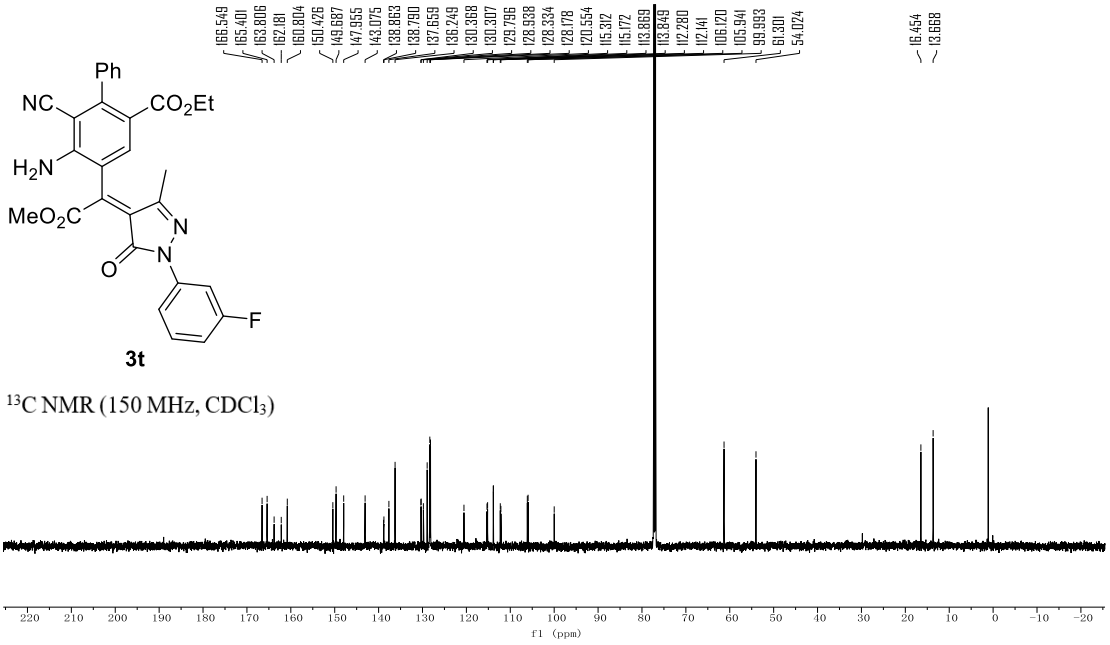
^{1}H NMR (600 MHz, $CDCl_3$)

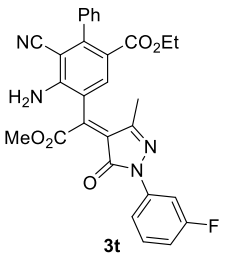


3s

^{13}C NMR (150 MHz, $CDCl_3$)

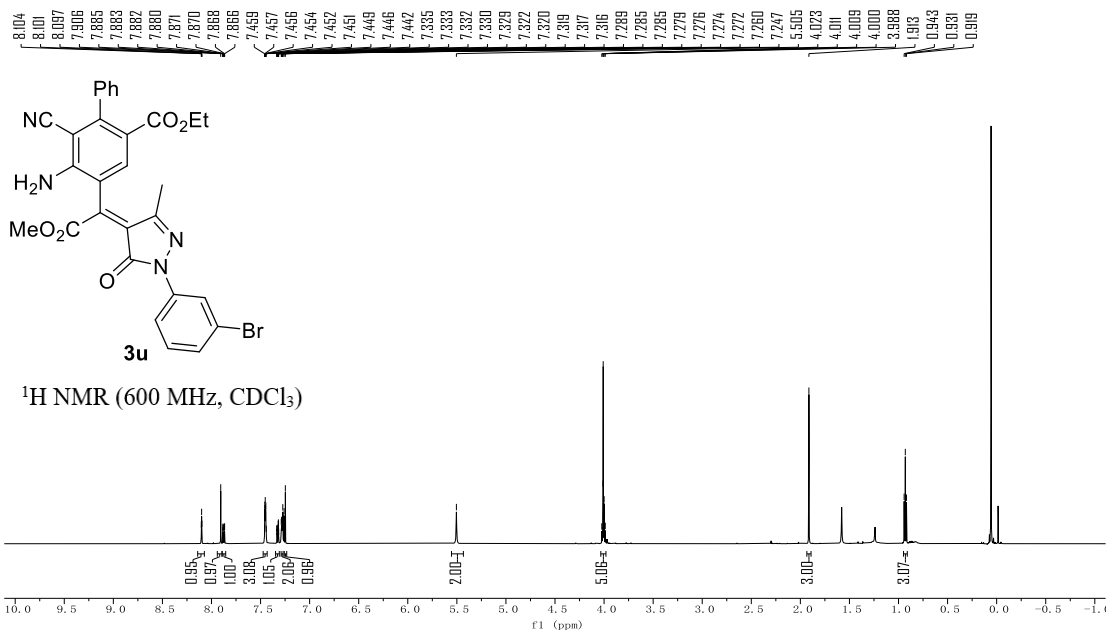

7.920
7.737
7.736
7.734
7.732
7.724
7.722
7.720
7.719
7.707
7.703
7.699
7.689
7.685
7.682
7.469
7.464
7.459
7.383
7.369
7.359
7.345
7.302
7.301
7.300
7.298
7.295
7.292
7.289
7.286
7.260
6.924
6.920
6.910
6.908
6.897
6.894
5.520
4.035
4.024
4.020
4.012
4.000
1.926
0.955
0.943
0.931
Ph
NC
CO2Et
H2N
MeO2C
N
N
O
F
3t
1H NMR (600 MHz, CDCl3)
0.94
1.02
1.00
3.04
1.08
2.01
1.03
2.00
5.02
3.00
3.05
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)

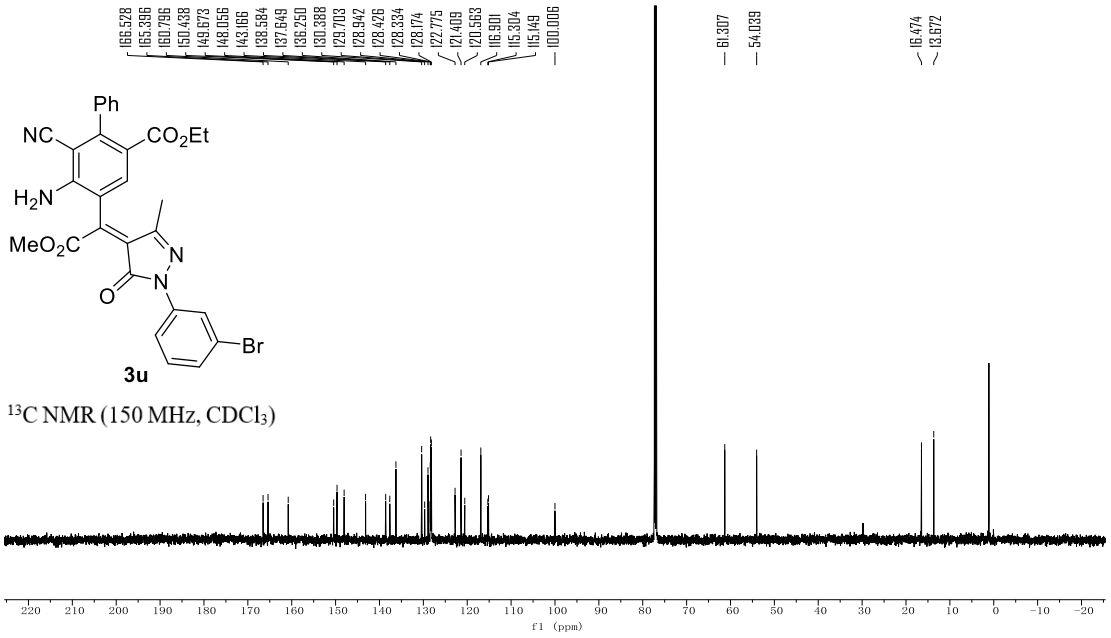

166.549
165.401
163.806
162.181
160.804
150.426
149.687
147.955
143.075
138.863
138.790
137.659
136.249
130.388
130.307
129.796
128.938
128.334
128.178
120.554
115.312
115.172
113.869
113.849
112.280
112.141
106.120
105.941
99.993
61.301
54.024
16.454
13.668
Ph
NC
CO2Et
H2N
MeO2C
N
N
O
F
3t
13C NMR (150 MHz, CDCl3)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
−20
f1 (ppm)

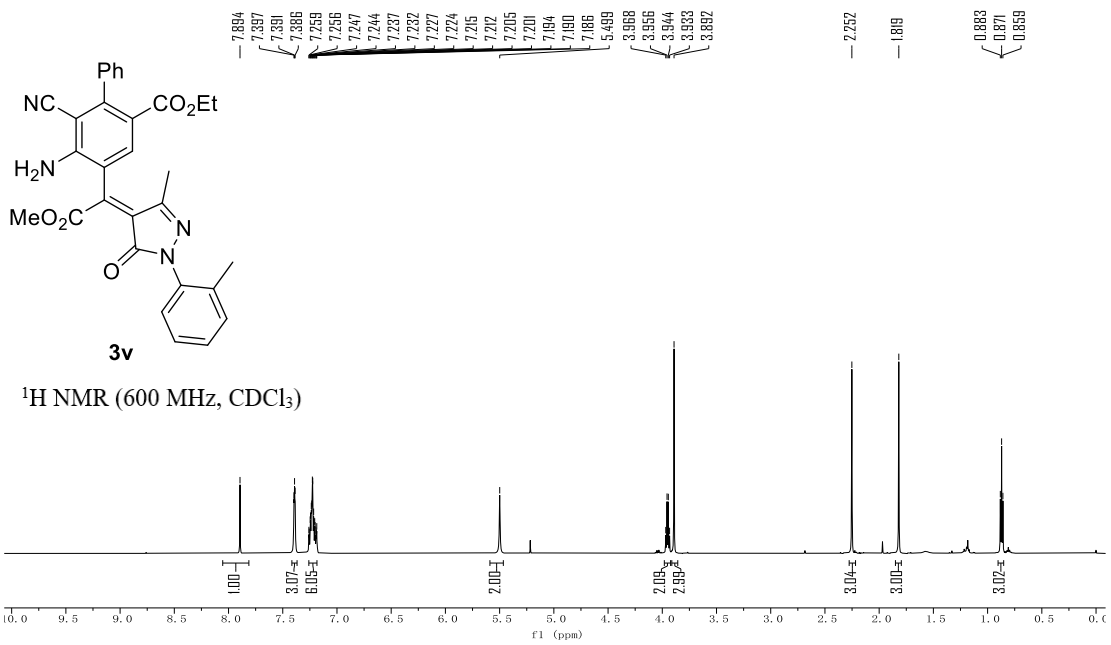


3t

^{19}F NMR (660 MHz, $CDCl_3$)

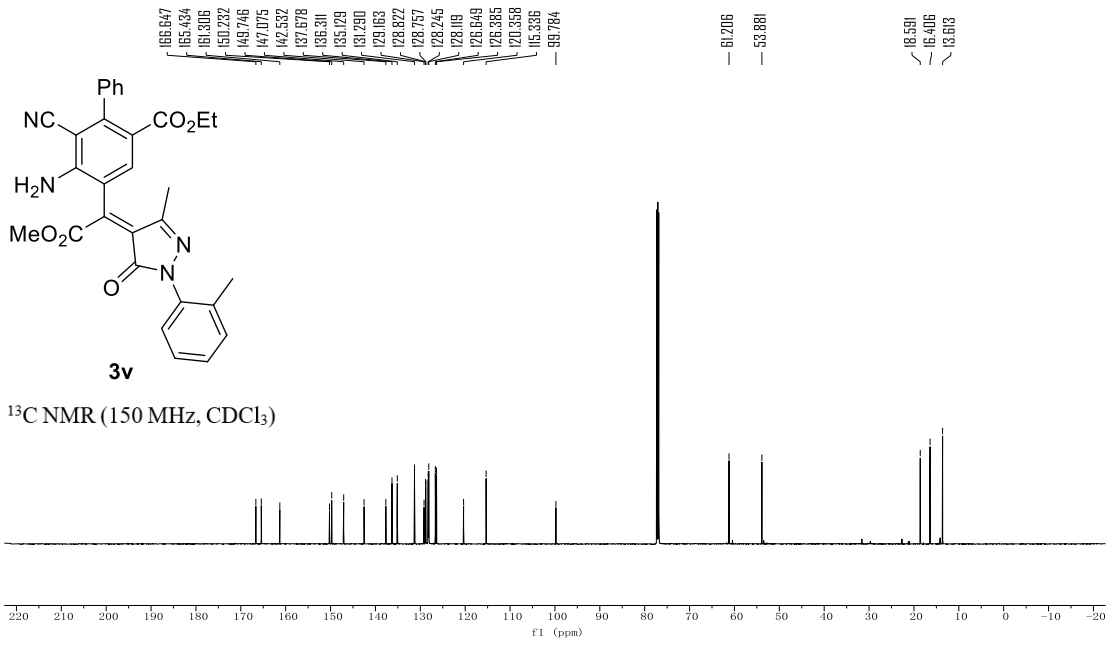

8.104
8.101
8.097
7.906
7.885
7.883
7.882
7.880
7.871
7.870
7.868
7.866
7.459
7.457
7.456
7.454
7.452
7.451
7.449
7.446
7.442
7.335
7.333
7.332
7.330
7.329
7.322
7.320
7.319
7.317
7.316
7.289
7.285
7.285
7.279
7.276
7.274
7.272
7.260
7.247
5.505
4.023
4.011
4.009
4.000
3.988
1.913
0.943
0.931
0.919
Ph
NC
CO2Et
H2N
MeO2C
N
N
O
Br
3u
1H NMR (600 MHz, CDCl3)
0.95
0.97
1.00
3.08
1.05
2.06
0.96
2.00
5.06
3.00
3.07
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
f1 (ppm)


166.528
165.386
160.796
150.438
149.673
148.056
143.166
138.584
137.649
136.250
130.388
129.703
128.942
128.426
128.334
128.174
122.775
121.409
120.563
116.901
115.304
115.149
100.000
61.307
54.039
16.474
13.672
Ph
NC
CO2Et
H2N
MeO2C
N
N
O
Br
3u
13C NMR (150 MHz, CDCl3)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20
f1 (ppm)



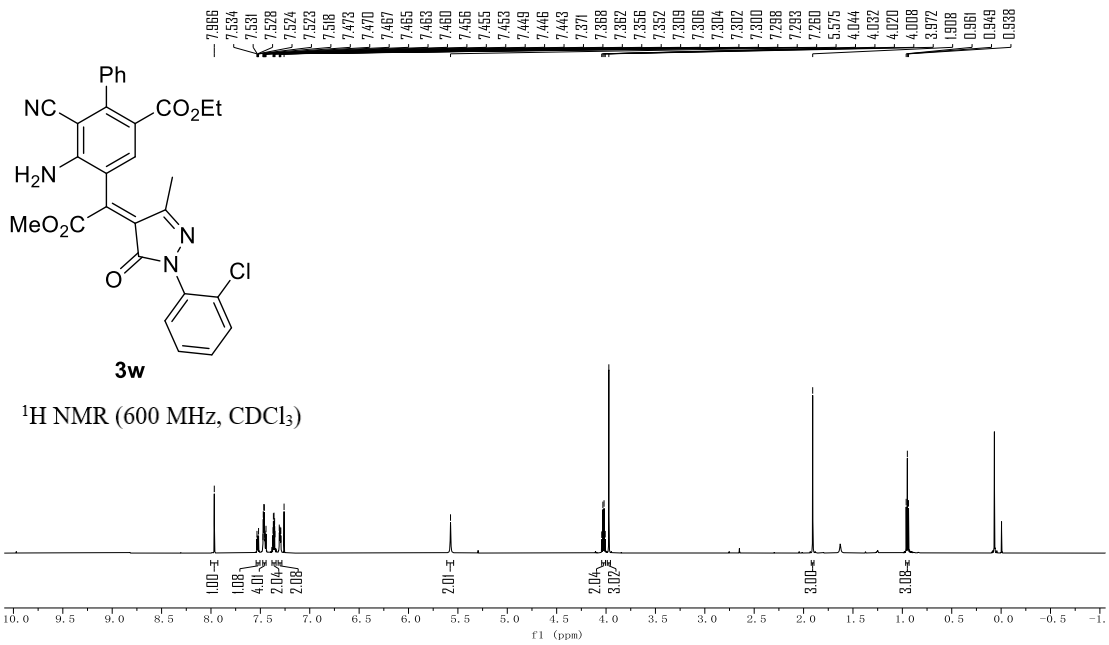
3v

^{1}H NMR (600 MHz, $CDCl_3$)



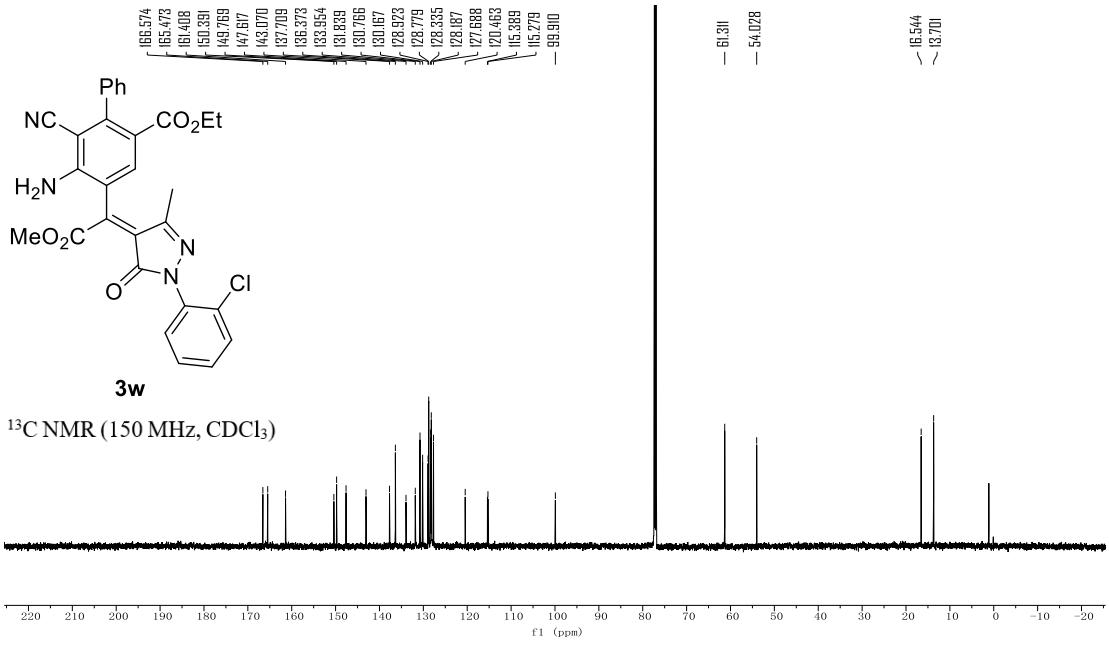
3v

^{13}C NMR (150 MHz, $CDCl_3$)



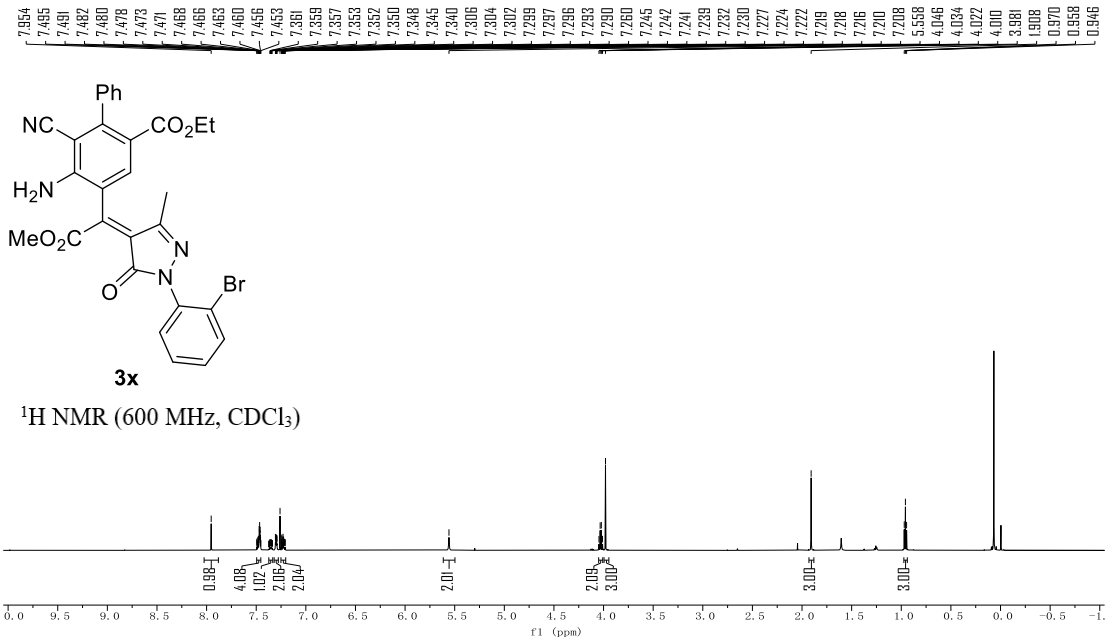
3w

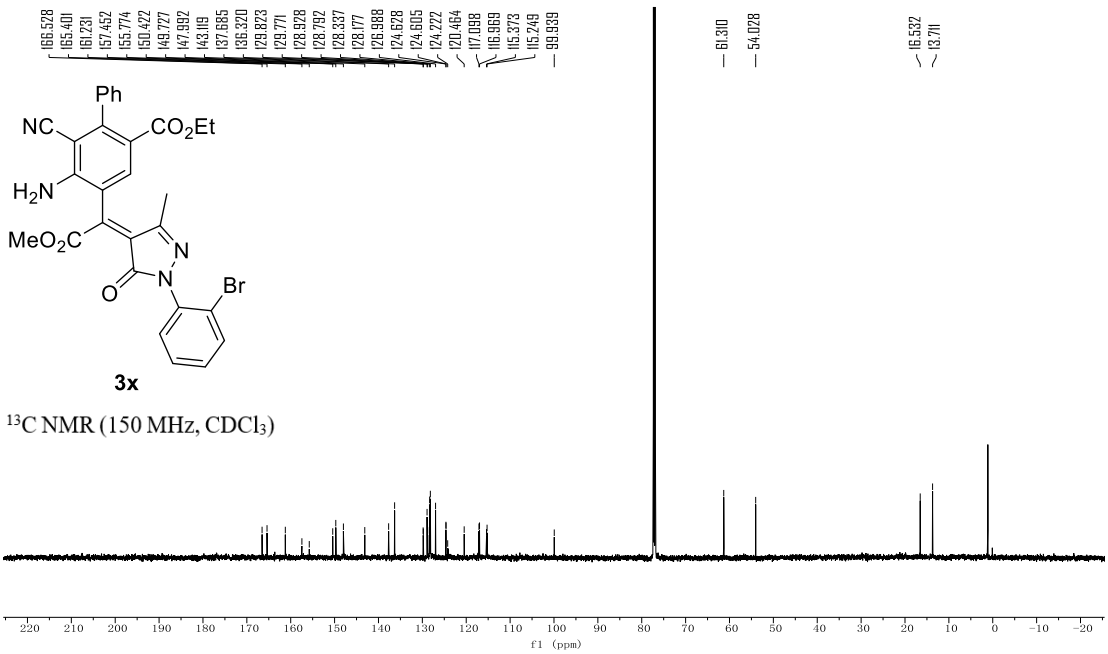
^{1}H NMR (600 MHz, $CDCl_3$)

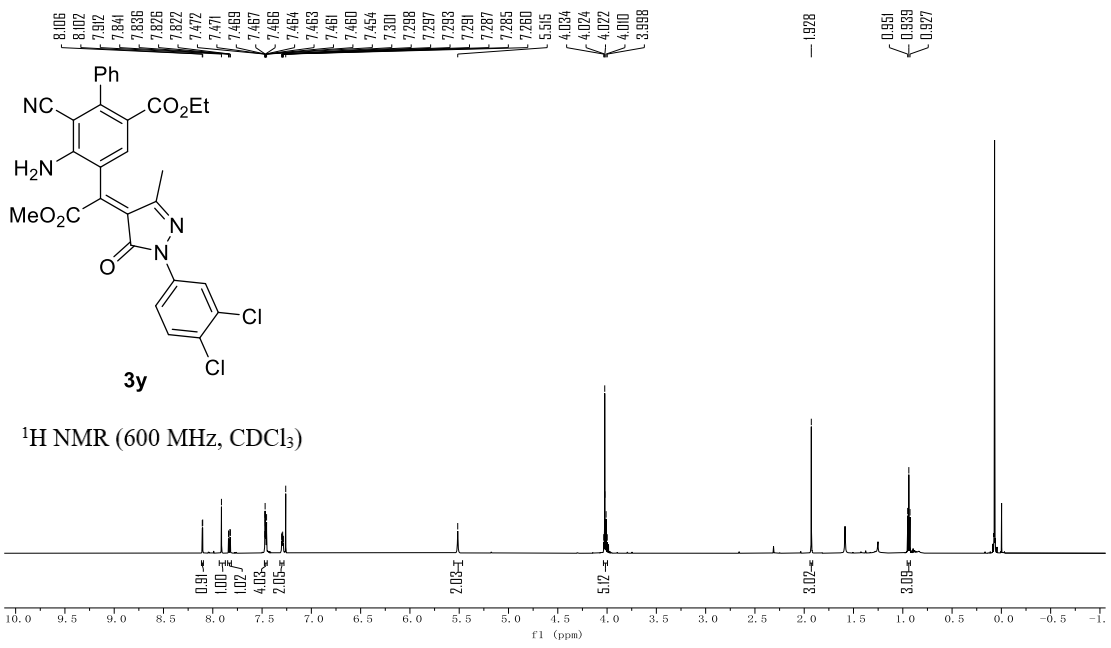


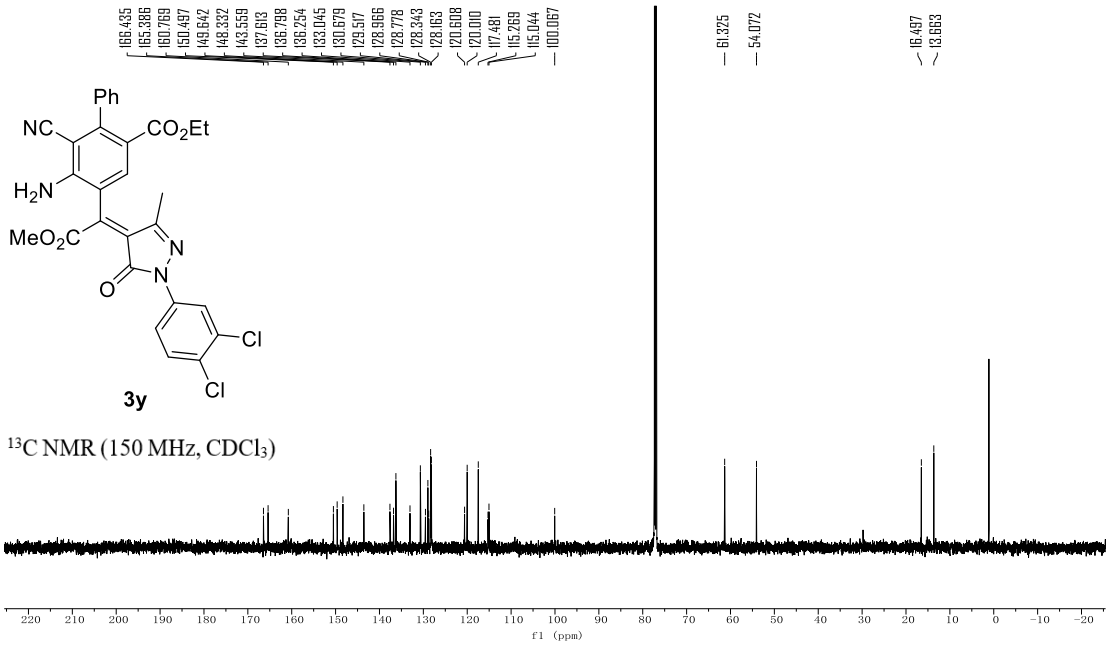
3w

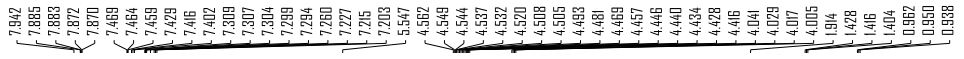
^{13}C NMR (150 MHz, $CDCl_3$)

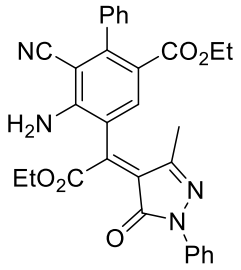

7.954
7.495
7.491
7.482
7.480
7.478
7.473
7.471
7.468
7.466
7.463
7.460
7.456
7.453
7.361
7.359
7.357
7.353
7.352
7.350
7.348
7.345
7.340
7.306
7.304
7.302
7.299
7.297
7.296
7.293
7.290
7.260
7.245
7.242
7.241
7.239
7.232
7.230
7.227
7.224
7.222
7.219
7.218
7.216
7.210
7.208
5.558
4.046
4.034
4.022
4.010
3.881
1.908
0.970
0.958
0.946
Ph
NC
CO2Et
H2N
MeO2C
N
O
N
Br
3x
1H NMR (600 MHz, CDCl3)
0.98
4.08
1.02
2.06
2.04
2.01
2.09
3.00
3.00
3.00
f1 (ppm)


166.528
165.401
161.231
157.452
155.774
150.422
149.727
147.992
143.119
137.685
136.320
129.823
129.771
128.928
128.792
128.337
128.177
126.988
124.628
124.605
124.222
120.464
117.098
116.969
115.373
115.249
99.939
61.310
54.028
16.532
13.711
Ph
NC
CO2Et
H2N
MeO2C
N
O
N
Br
3x
13C NMR (150 MHz, CDCl3)
f1 (ppm)


8.106
8.102
7.912
7.841
7.838
7.826
7.822
7.472
7.471
7.469
7.467
7.466
7.464
7.463
7.461
7.460
7.454
7.301
7.298
7.297
7.293
7.291
7.287
7.285
7.260
5.515
4.034
4.024
4.022
4.010
3.998
1.928
0.951
0.939
0.927
Ph
NC
CO2Et
H2N
MeO2C
N
N
O
Cl
Cl
3y
1H NMR (600 MHz, CDCl3)
0.91
1.00
1.02
4.03
2.05
2.03
5.12
3.02
3.09
f1 (ppm)

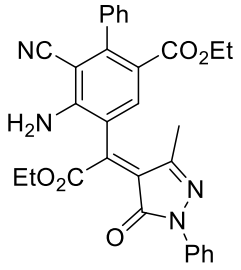

166.435
165.386
160.769
150.497
149.642
148.332
143.559
137.613
135.798
135.254
133.045
130.679
129.517
128.966
128.778
128.343
128.163
121.608
120.010
117.481
115.269
115.044
100.067
61.325
54.072
15.497
13.663
Ph
NC
CO2Et
H2N
MeO2C
N
N
O
Cl
Cl
3y
13C NMR (150 MHz, CDCl3)
f1 (ppm)





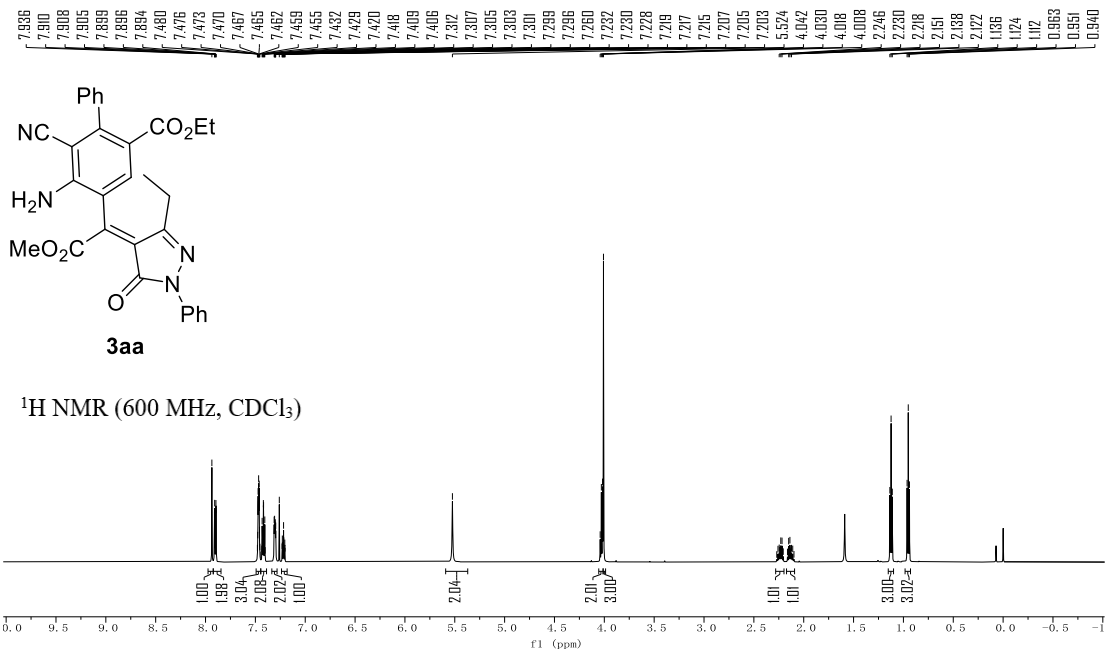
3z

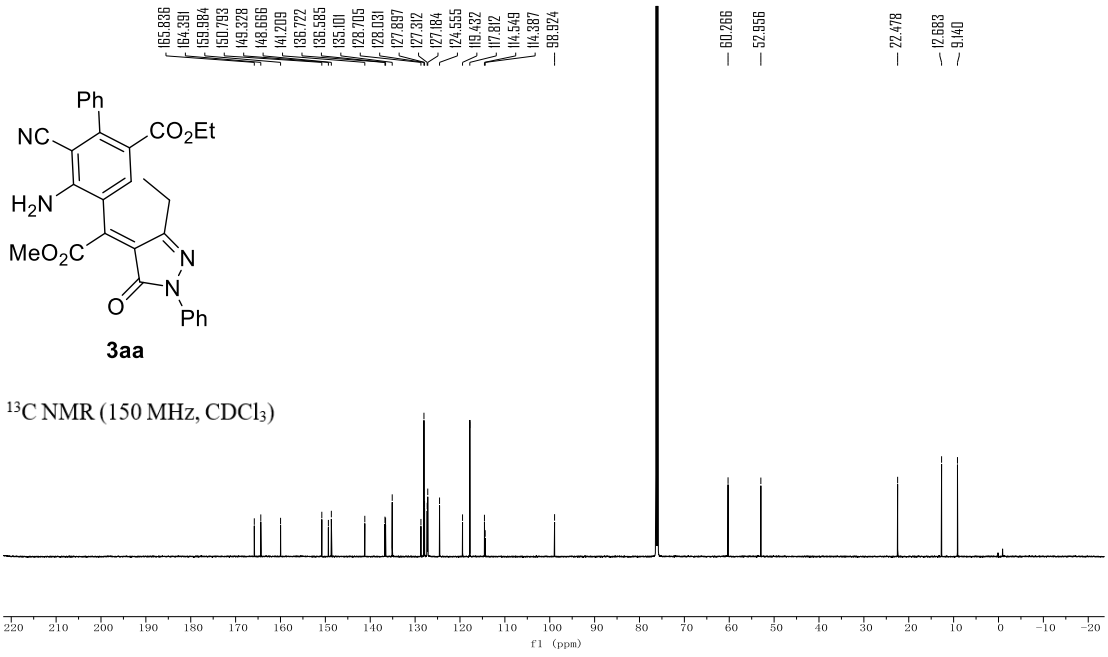
^{1}H NMR (600 MHz, $CDCl_3$)

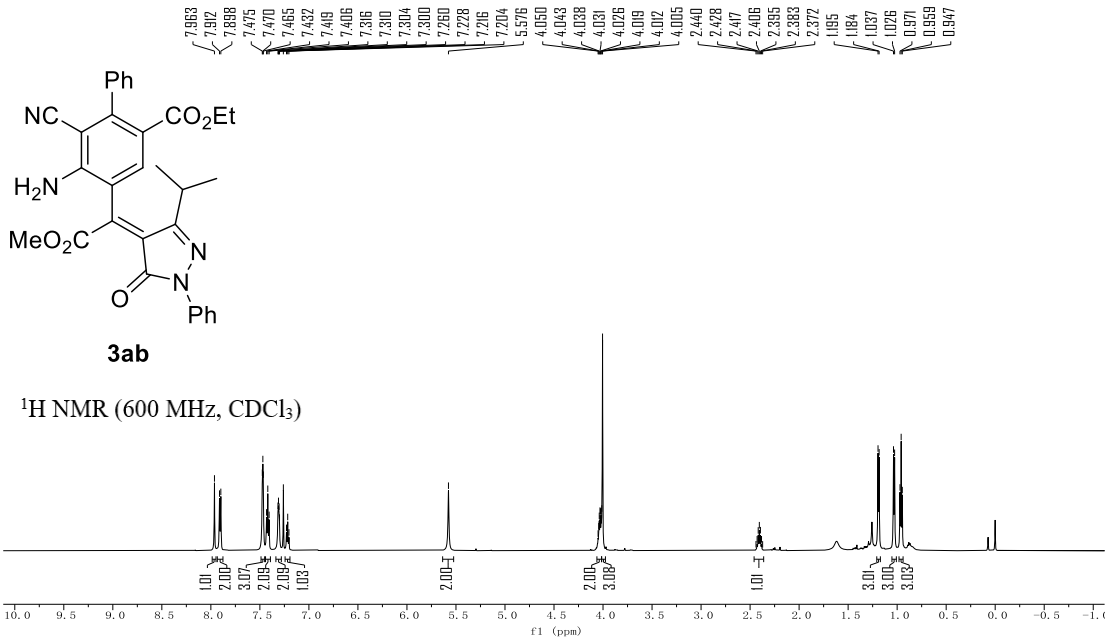


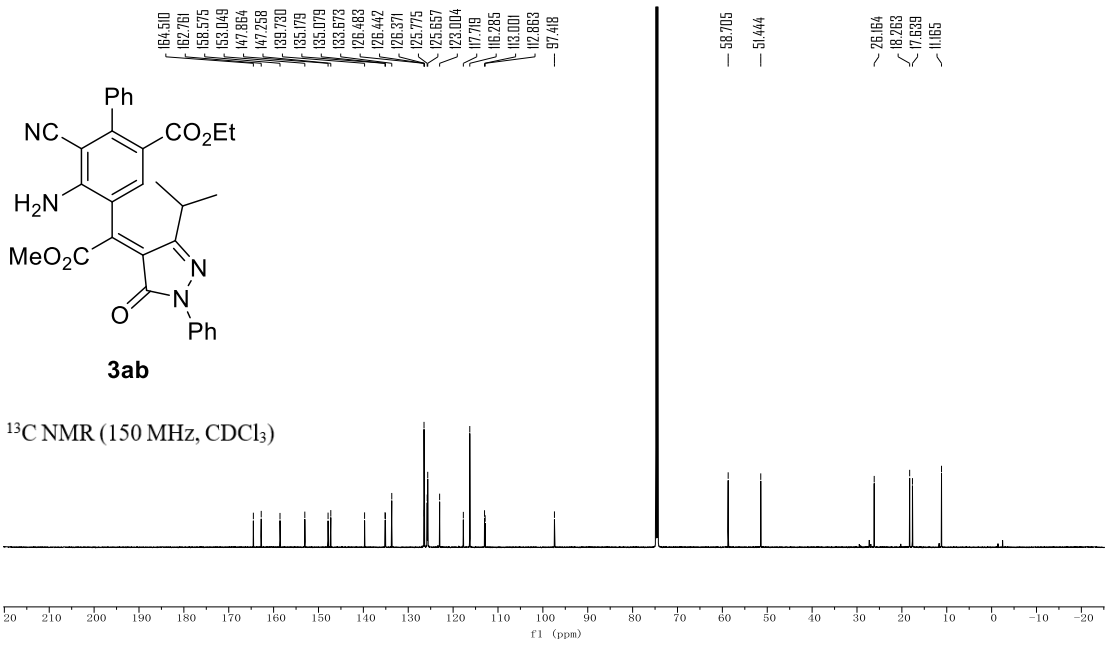
3z

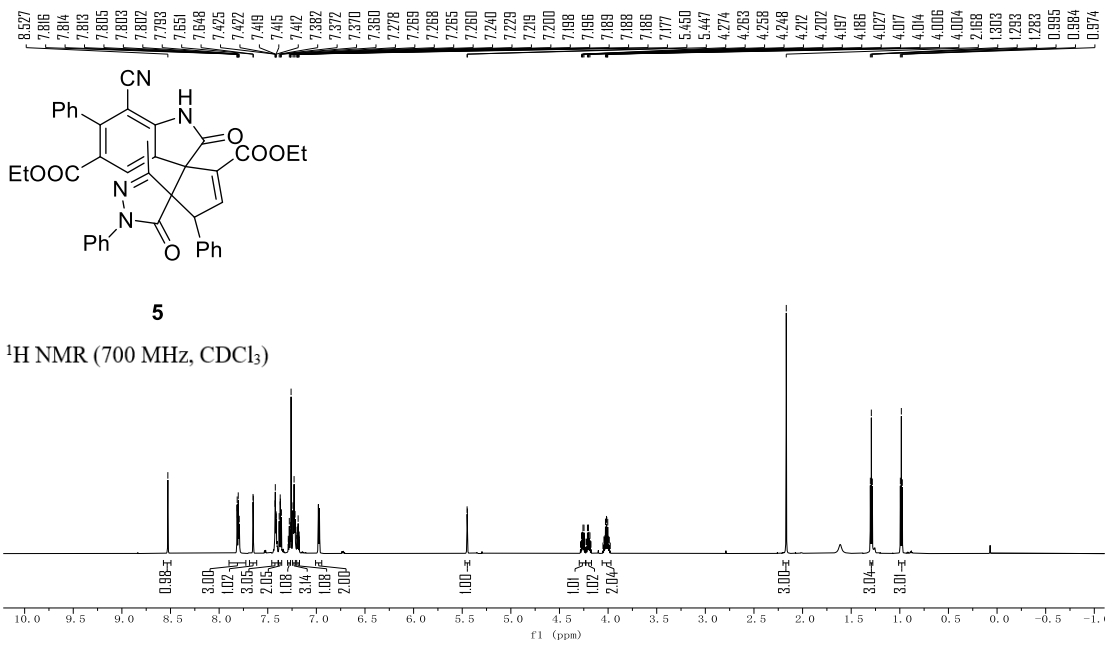
^{13}C NMR (150 MHz, $CDCl_3$)


7.936
7.910
7.908
7.905
7.899
7.896
7.894
7.480
7.476
7.473
7.470
7.467
7.465
7.462
7.459
7.455
7.432
7.429
7.420
7.418
7.409
7.406
7.312
7.307
7.305
7.303
7.301
7.299
7.296
7.260
7.232
7.230
7.228
7.219
7.217
7.215
7.207
7.205
7.203
5.524
4.042
4.030
4.018
4.008
2.246
2.230
2.218
2.151
2.138
2.122
1.136
1.124
1.112
0.963
0.951
0.940
Ph
NC
CO2Et
H2N
MeO2C
N
O
N
Ph
3aa
1H NMR (600 MHz, CDCl3)
1.00
1.98
3.04
2.08
2.02
1.00
2.04
2.01
3.00
1.01
1.01
3.00
3.02
f1 (ppm)


165.836
164.391
159.984
150.793
149.328
148.666
141.209
136.722
136.585
135.101
128.705
128.031
127.897
127.312
127.184
124.555
119.432
117.812
114.549
114.387
98.924
60.266
52.956
22.478
12.683
9.140
Ph
NC
CO2Et
H2N
MeO2C
N
O
N
Ph
3aa
13C NMR (150 MHz, CDCl3)
f1 (ppm)

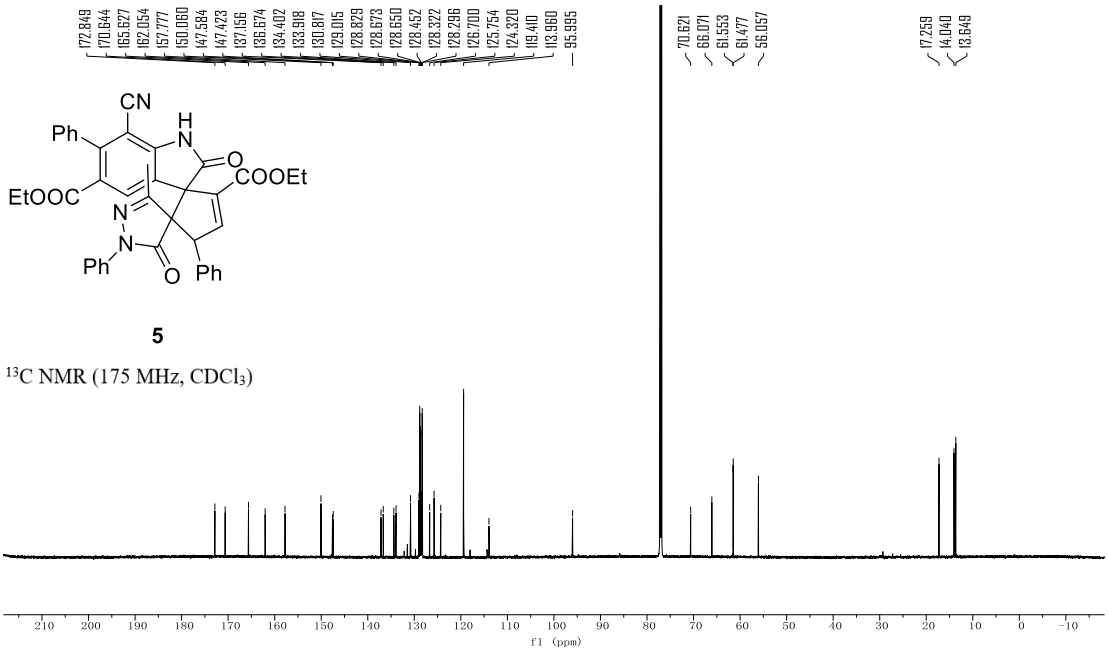

Ph
NC
CO2Et
H2N
MeO2C
N
N
O
Ph
3ab
1H NMR (600 MHz, CDCl3)
f1 (ppm)


Ph
NC
CO2Et
H2N
MeO2C
N
N
O
Ph
3ab
13C NMR (150 MHz, CDCl3)
f1 (ppm)



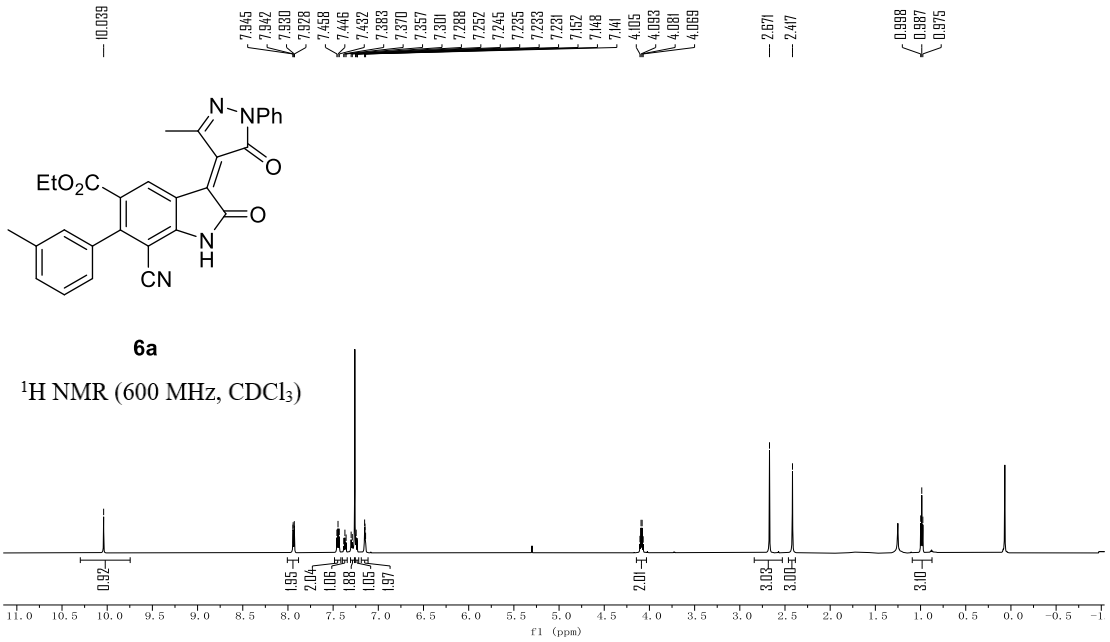
5

^{1}H NMR (700 MHz, $CDCl_3$)



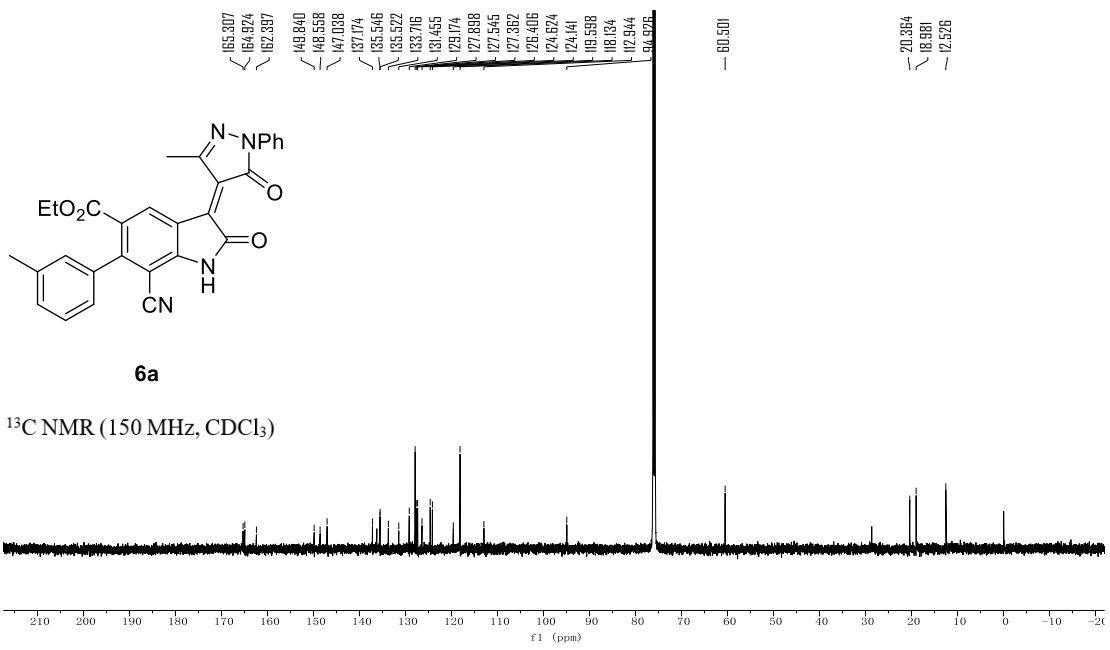
5

^{13}C NMR (175 MHz, $CDCl_3$)



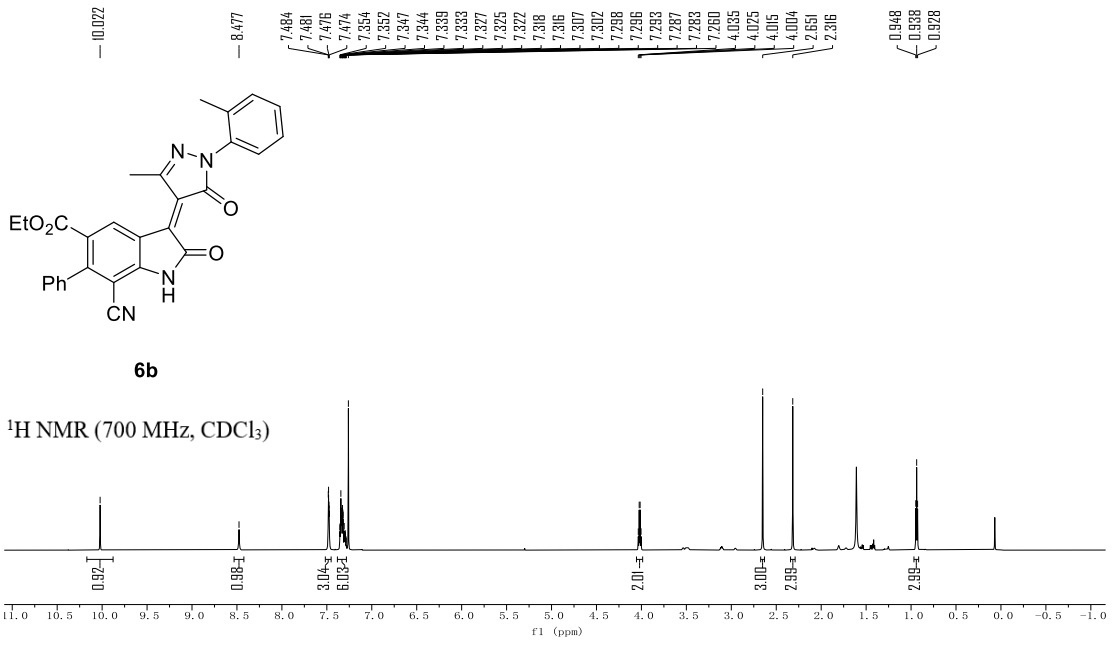
6a

^{1}H NMR (600 MHz, $CDCl_3$)



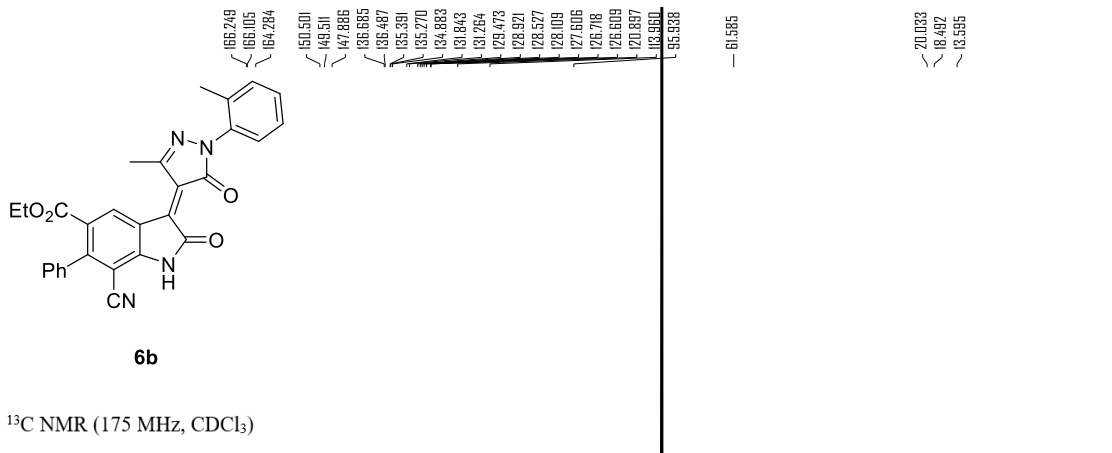
6a

^{13}C NMR (150 MHz, $CDCl_3$)



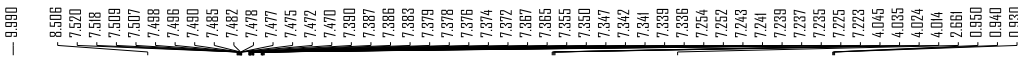
6b

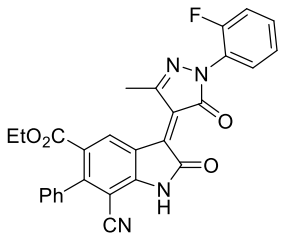
^{1}H NMR (700 MHz, $CDCl_3$)



6b

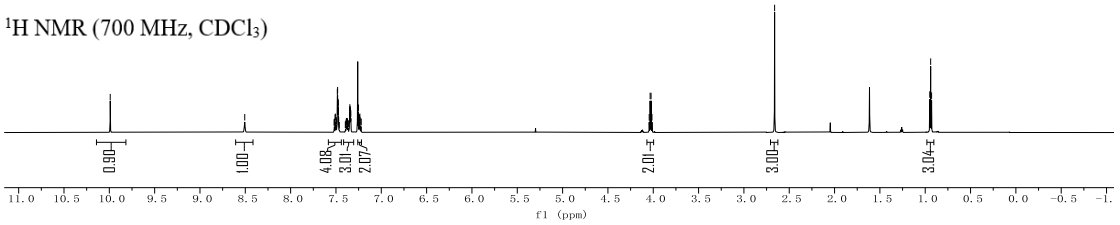
^{13}C NMR (175 MHz, $CDCl_3$)

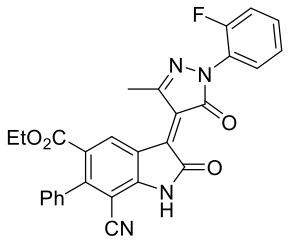




6c

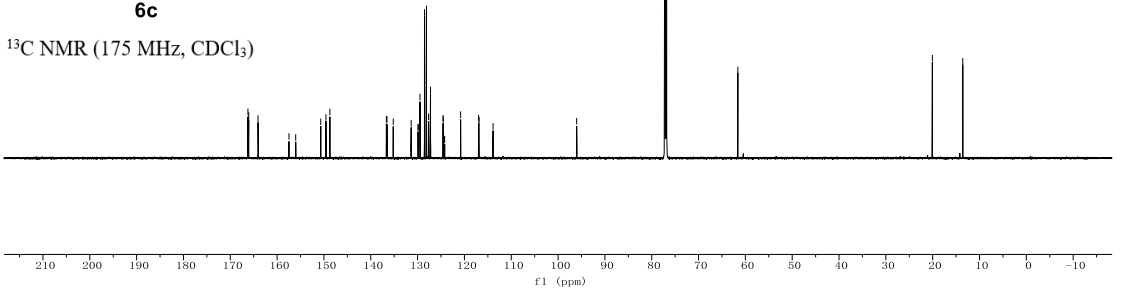
^{1}H NMR (700 MHz, $CDCl_3$)

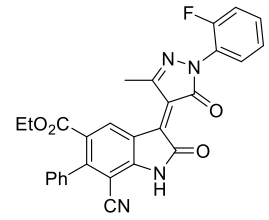




6c

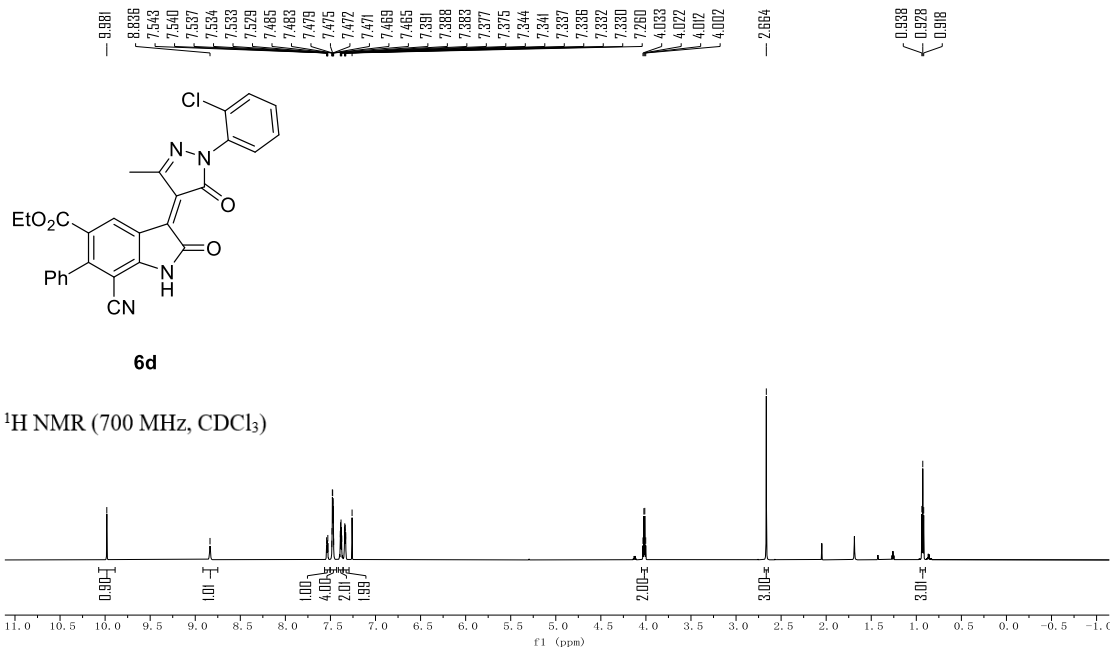
^{13}C NMR (175 MHz, $CDCl_3$)

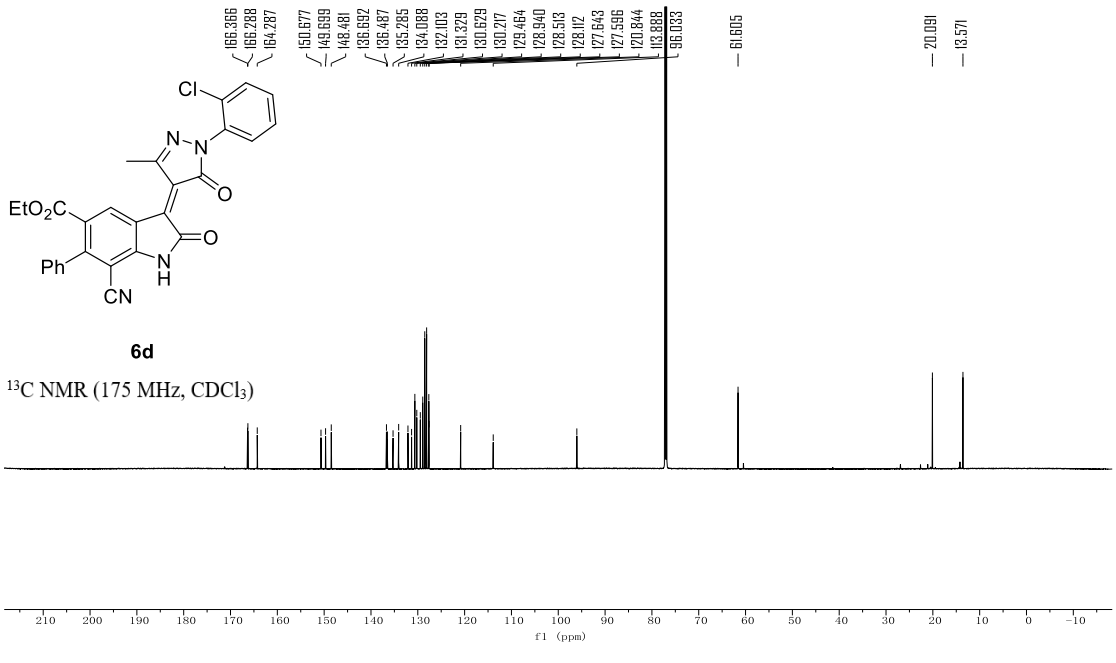


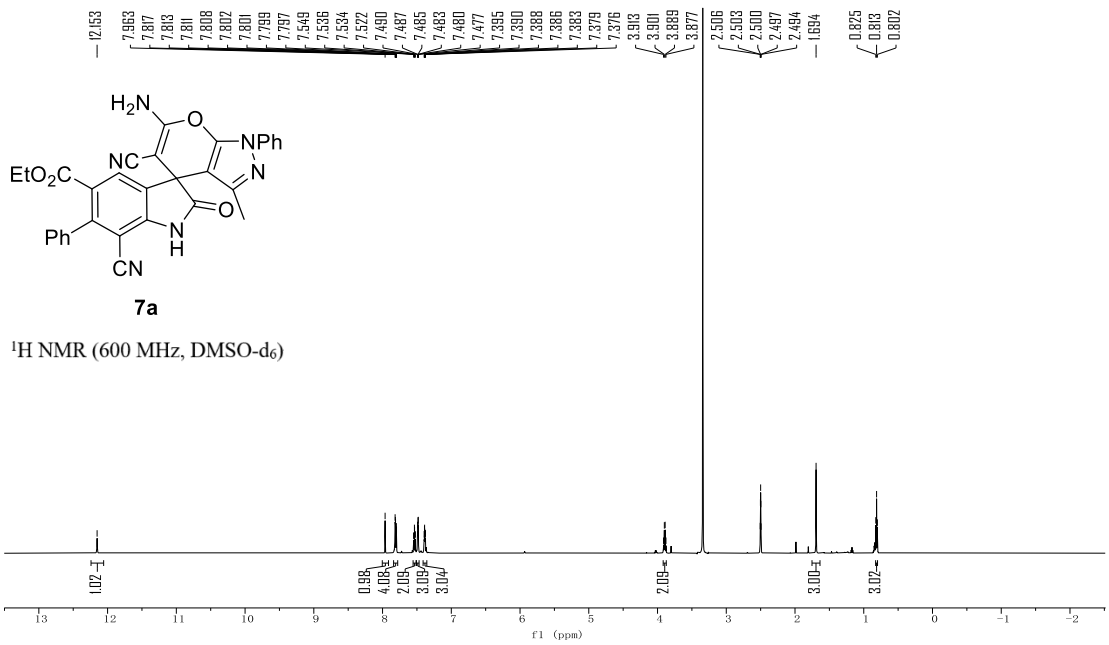


6c

^{19}F NMR (660 MHz, $CDCl_3$)

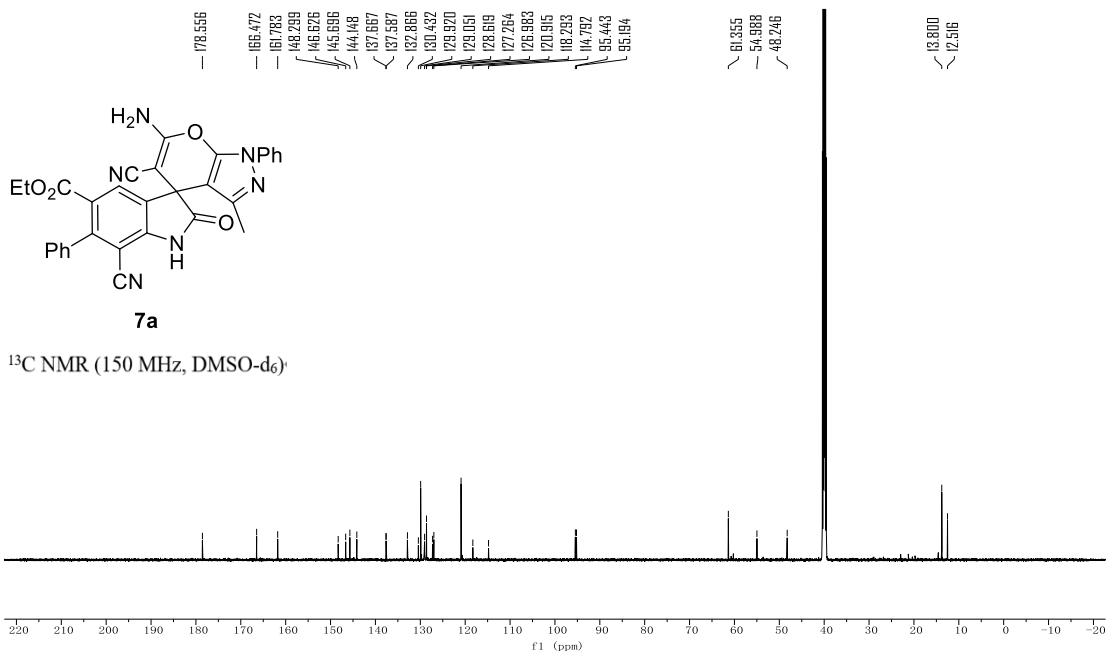

9.981
8.836
7.543
7.540
7.537
7.534
7.533
7.529
7.485
7.483
7.479
7.475
7.472
7.471
7.469
7.465
7.391
7.388
7.383
7.377
7.375
7.344
7.341
7.337
7.336
7.332
7.330
7.260
4.033
4.022
4.012
4.002
2.664
0.938
0.928
0.918
Cl
N
N
O
EtO2C
O
Ph
N
H
CN
6d
1H NMR (700 MHz, CDCl3)
0.90
1.01
1.00
4.00
2.01
1.99
2.00
3.00
3.01
f1 (ppm)


166.366
166.288
164.287
150.677
149.699
148.481
136.692
135.487
135.285
134.088
132.103
131.329
130.629
130.217
129.464
128.940
128.513
128.112
127.643
127.596
120.844
113.888
96.033
61.605
20.091
13.571
Cl
N
N
O
EtO2C
O
Ph
N
H
CN
6d
13C NMR (175 MHz, CDCl3)
f1 (ppm)



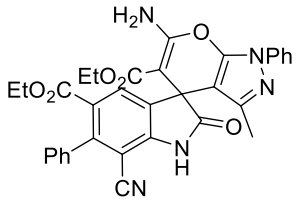
7a

^{1}H NMR (600 MHz, DMSO-d$_6$)



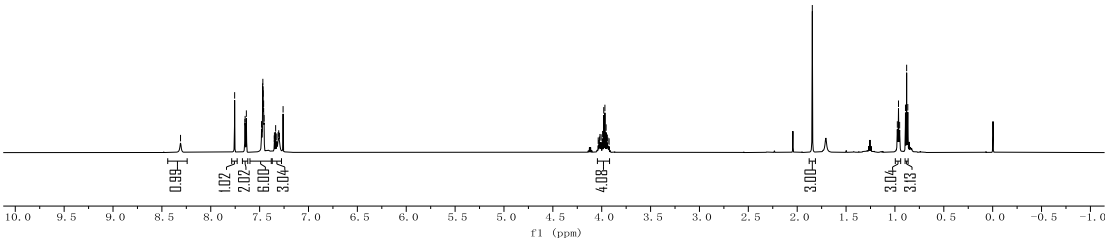
7a

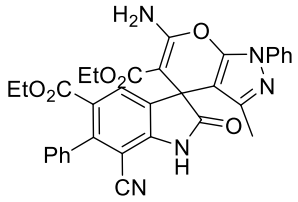
^{13}C NMR (150 MHz, DMSO-d$_6$)



7b

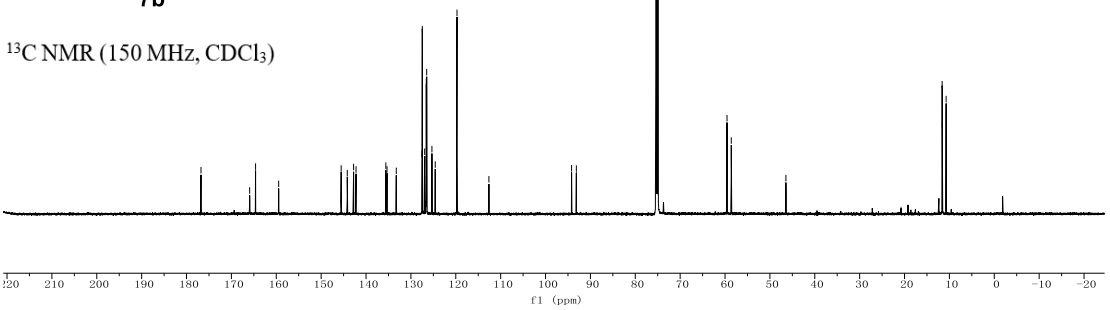
^{1}H NMR (600 MHz, $CDCl_3$)

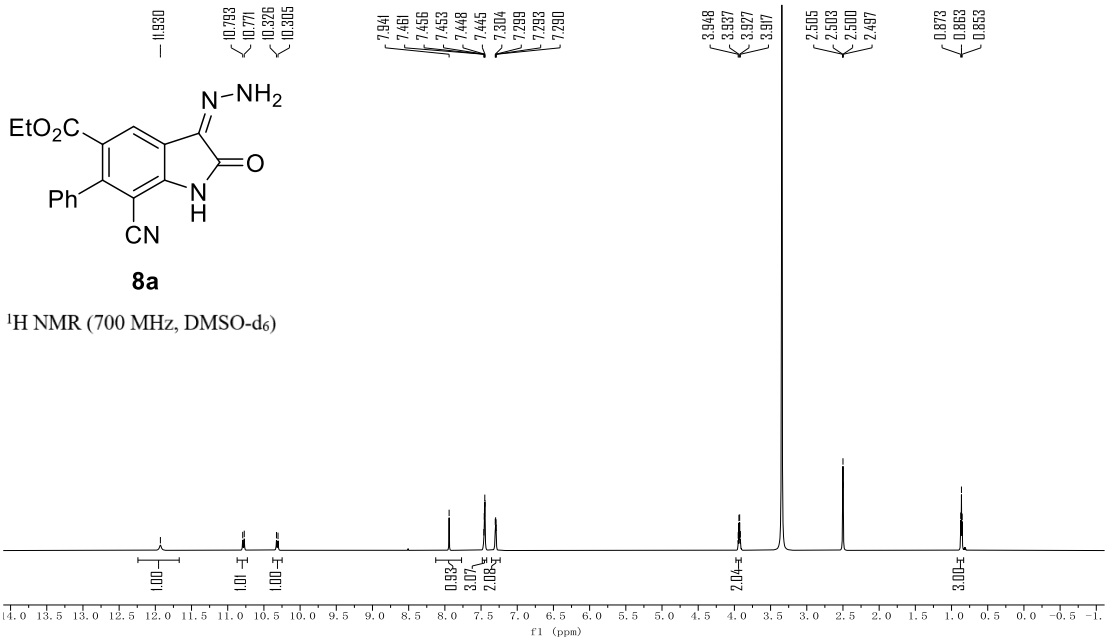




7b

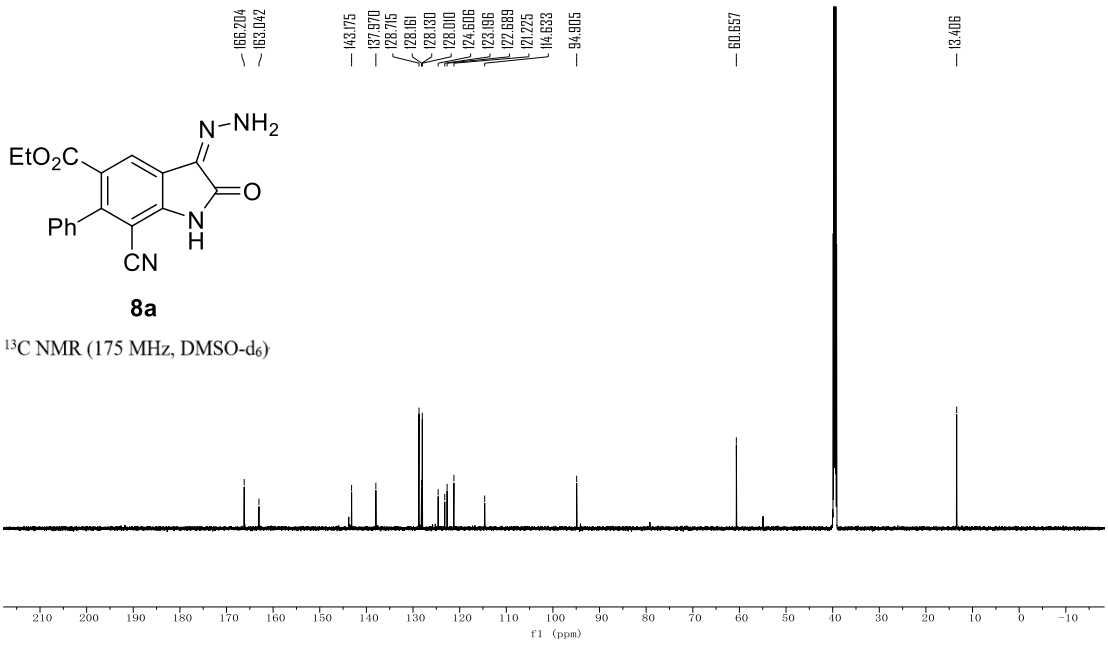
^{13}C NMR (150 MHz, $CDCl_3$)





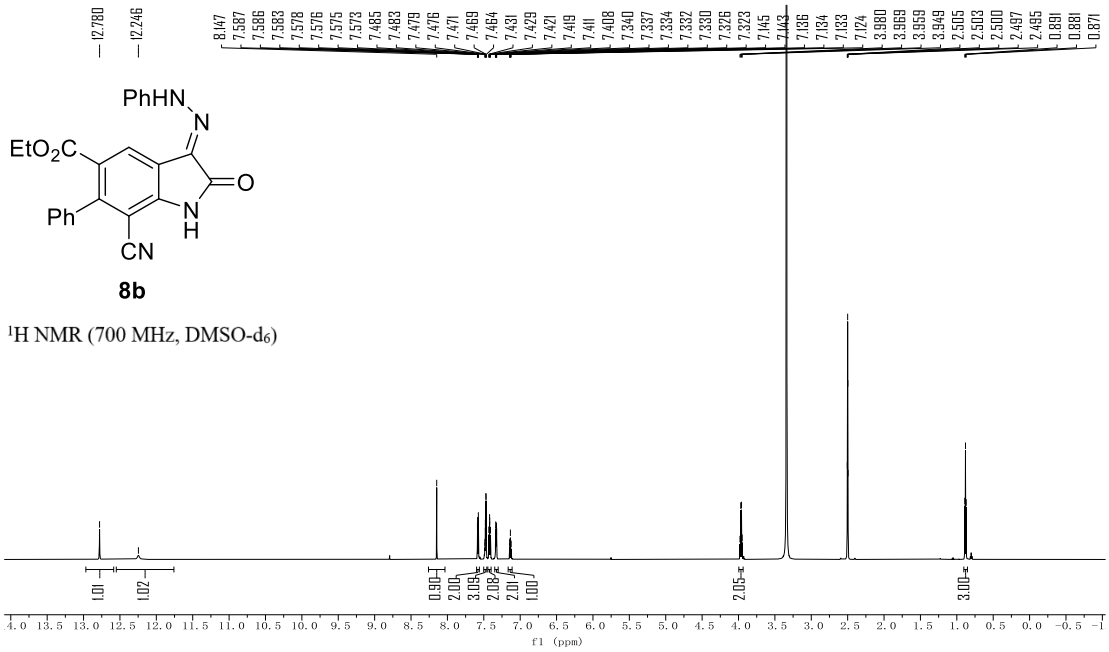
8a

^{1}H NMR (700 MHz, DMSO-d_6)



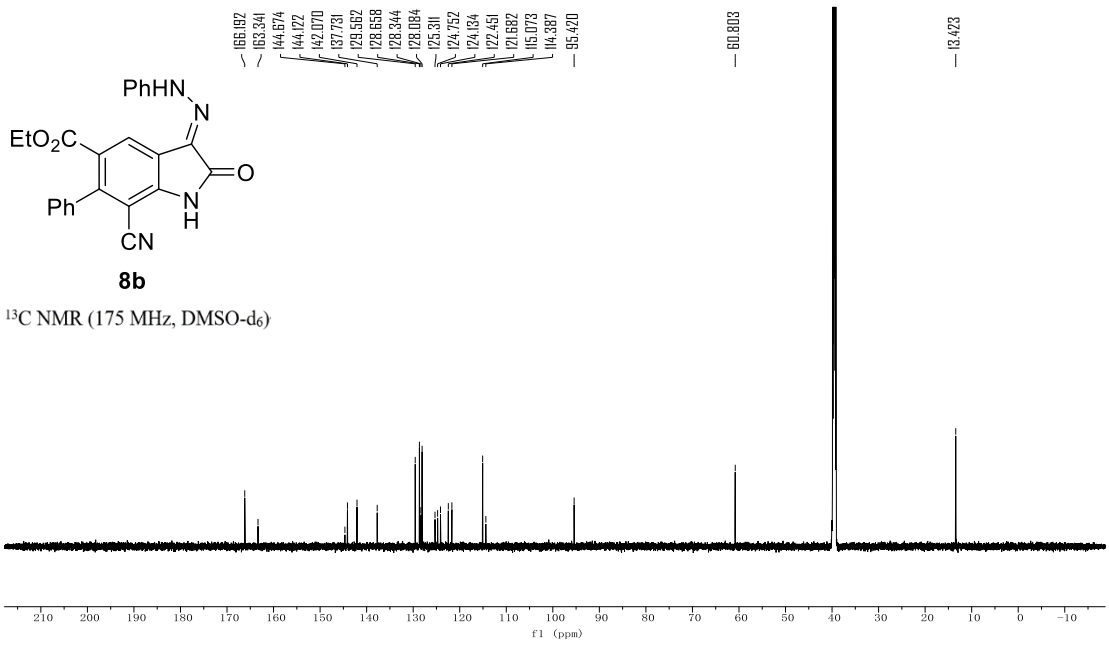
8a

^{13}C NMR (175 MHz, DMSO-d_6)



8b

^{1}H NMR (700 MHz, DMSO-d$_6$)



8b

^{13}C NMR (175 MHz, DMSO-d$_6$)