Supporting Information

N-Heterocyclic Carbene-Catalyzed Enantioselective Annulation of 2-Amino-*1H*-indoles and Bromoenals for Synthesis of Chiral 2-Aryl-2,3-dihydropyrimido[1,2-a] indol-4 (*1H*)-ones

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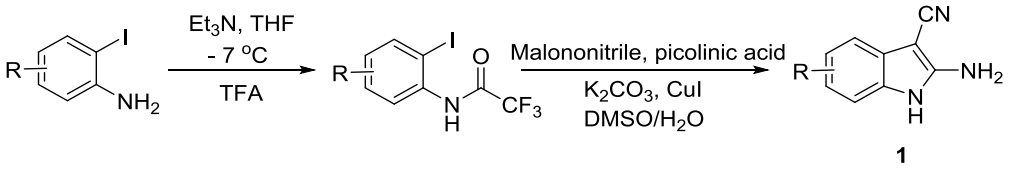
1. General Information

Unless otherwise mentioned, all commercial reagents and solvents were used directly as purchased. Flash chromatography was performed on silica gel (200 - 300 mesh) with petroleum ether/ethyl acetate as the eluent. ^{1}H, ^{13}C, and ^{19}FNMR spectra were performed on a 400 MHz NMR or 600 MHz NMR spectrometer. The ^{1}H NMR spectra of the compounds were measured at 400 MHz or 600 MHz are internally referenced to residual protic $CDCl_3$ (δ 7.26 ppm) or DMSO-d_6 (δ 3.36, 2.50 ppm). ^{13}C NMR spectra were measured at 151/101 MHz and data are reported referenced to $CDCl_3$ (δ 77.0 ppm, the middle peak) or DMSO-d_6 (δ 39.5 ppm). ^{19}F NMR spectra were measured at 565 MHz. *J* values are given in hertz (Hz).

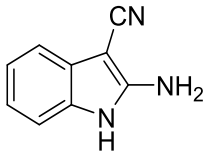
2. Preparation of Substrates

2.1 Preparation of 2-amino-1H-indole-3-carbonitrile[1]

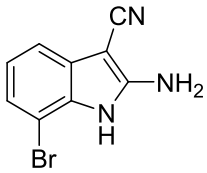


Step 1: Corresponding 2-iodoaniline derivative (1.0 mmol) was dissolved in dry THF (5 mL), Et_3N (1.2 mmol) was added and resulting solution cooled down to -7˚C. Trifluroacetic anhydride (1.2 mmol) dissolved in dry THF was added dropwise within 5 min and then the reaction was allowed to warm up to RT and was stirred overnight. After completion the reaction was diluted with water and the product extracted to EtOAc. Organic layer was washed with brine, dried over Na_2SO_4 and evaporated to obtain 2,2,2-trifluoro-N-(2-iodophenyl)acetamide as solid, Products were used for the next step without further purification.

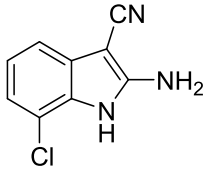
Step 2: Corresponding 2,2,2-trifluoro-N-(2-iodophenyl)acetamide derivative (1.0 equiv), malononitrile (1.2 equiv), K_2CO_3 (2.0 equiv) and L-proline (0.2 equiv) were dispersed in DMSO/H_2O (1:1, 2 mL/mmol) and stirred for 15 min at RT. Then CuI (0.1 equiv) was added and the reaction mixture stirred at 60˚C overnight. After completion the reaction mixture was filtrated and filter washed extensively with MeOH. The filtrate was concentrated and resulting liquid diluted with water and extracted with Et_2O. Organic layer was washed with brine, dried over Na_2SO_4 and evaporated to obtain 2-amino-1H-indole-3-carbonitrile as beige solid. In case of 2-amino-1H-indole-3-carbonitrile, the crude product was purified by flash chromatography (hex/EtOAc) to afford product.



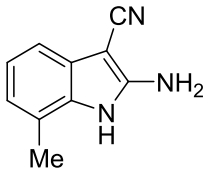
2-Amino-1H-indole-3-carbonitrile (1a).[2] (yield: 65%). Brown solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 1/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.71 (s, 1H), 7.14 (d, J = 8.0 Hz, 2H), 6.99 - 6.89 (m, 2H), 6.75 (s, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 154.3, 132.6, 128.7, 121.0, 120.1, 118.4, 115.6, 110.7, 62.1.



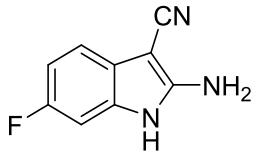
2-Amino-7-bromo-1H-indole-3-carbonitrile (1b). (yield: 54%). Brown solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 1/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.97 (s, 1H), 7.20 (d, J = 7.6 Hz, 1H), 7.14 (d, J = 7.6 Hz, 1H), 6.97 (t, J = 7.6 Hz, 1H), 6.74 (s, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 154.7, 130.7, 130.3, 122.7, 122.5, 117.5, 115.0, 102.9, 63.3. HRMS (ESI, m/z) calcd for $C_9H_6N_3BrNa$ $[M + Na]^+$: 257.9643, found: 257.9646.



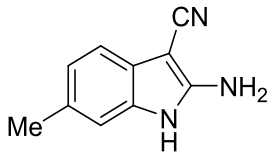
2-Amino-7-chloro-1H-indole-3-carbonitrile (1c). (yield: 60%). Brown solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 1/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.15 (s, 1H), 7.15 (dd, J = 6.4, 2.0 Hz, 1H), 7.01 (m, 2H), 6.75 (s, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 154.8, 130.5, 129.1, 122.3, 119.7, 117.5, 114.8, 114.6, 63.2. HRMS (ESI, m/z) calcd for $C_9H_7N_3Cl$ $[M + H]^+$: 192.0328, found: 192.0327.



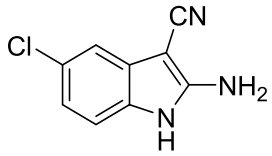
2-Amino-7-methyl-1H-indole-3-carbonitrile (1d). (yield: 66%). Brown solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 1/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.75 (s, 1H), 6.98 (d, J = 7.6 Hz, 1H), 6.88 (t, J = 7.6 Hz, 1H), 6.73 (d, J = 7.2 Hz, 1H), 6.49 (s, 2H), 2.33 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 154.2, 131.4, 128.4, 121.4, 121.2, 119.7, 118.4, 113.5, 62.6, 16.9. HRMS (ESI, m/z) calcd for $C_{10}H_9N_3Na$ $[M + Na]^+$: 194.0694, found: 194.0695.



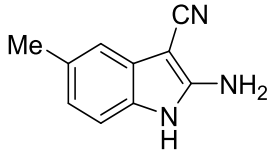
2-Amino-6-fluoro-1H-indole-3-carbonitrile (1e). (yield: 51%). Brown solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 1/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.77 (s, 1H), 7.08 (dd, J = 8.4, 5.2 Hz, 1H), 6.97 (dd, J = 9.6, 2.4 Hz, 1H), 6.83 - 6.77 (m, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 158.8, 156.1 (d, J = 356.7 Hz), 132.7 (d, J = 12.5 Hz), 125.0, 118.0, 115.9 (d, J = 9.8 Hz), 108.1 (d, J = 23.6 Hz), 98.2, 98.0, 61.6. ^{19}F NMR (565 MHz, DMSO-d_6) δ -123.8 (td, J = 10.2, 5.1 Hz). HRMS (ESI, m/z) calcd for $C_9H_6N_3FNa$ $[M + Na]^+$: 198.0443, found: 198.0440.



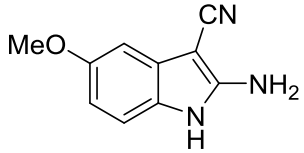
2-Amino-6-methyl-1H-indole-3-carbonitrile (1f). (yield: 47%). Brown solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 1/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.59 (s, 1H), 7.02 (d, J = 7.6 Hz, 1H), 6.95 (s, 1H), 6.79 (d, J = 8.0 Hz, 1H), 6.63 (s, 2H), 2.30 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 154.1, 132.9, 129.1, 126.2, 122.1, 118.6, 115.4, 111.0, 61.8, 21.6. HRMS (ESI, m/z) calcd for $C_{10}H_9N_3Na$ $[M + Na]^+$: 194.0694, found: 194.0698.



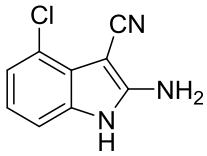
2-Amino-5-chloro-1H-indole-3-carbonitrile (1g). (yield: 42%). Brown solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 1/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.85 (s, 1H), 7.11 (d, J = 8.4 Hz, 1H), 7.08 (d, J = 2.0 Hz, 1H), 6.95 (s, 2H), 6.90 (dd, J = 8.4, 2.0 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 155.1, 131.3, 130.3, 125.6, 119.7, 117.6, 114.7, 111.9, 62.1. HRMS (ESI, m/z) calcd for $C_9H_7N_3Cl$ $[M + H]^+$: 192.0328, found: 192.0325.



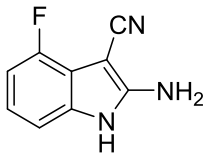
2-Amino-5-methyl-1H-indole-3-carbonitrile (1h). (yield: 62%). Brown solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 1/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.55 (s, 1H), 7.00 (d, J = 7.6 Hz, 1H), 6.93 (d, J = 1.6 Hz, 1H), 6.71 (dd, J = 8.0, 1.6 Hz, 1H), 6.65 (s, 2H), 2.30 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 154.3, 130.7, 129.7, 129.0, 121.1, 118.4, 115.8, 110.3, 61.8, 21.6. HRMS (ESI, m/z) calcd for $C_{10}H_9N_3Na$ $[M + Na]^+$: 194.0694, found: 194.0689.



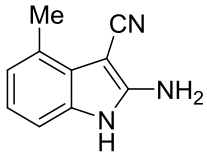
2-Amino-5-methoxy-1H-indole-3-carbonitrile (1i). (yield: 45%). Brown solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 1/1). ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.50 (s, 1H), 7.01 (d, J = 8.4 Hz, 1H), 6.67 (s, 1H), 6.67 (s, 2H), 6.50 (dd, J = 8.4, 2.4 Hz, 1H), 3.73 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 155.1, 154.6, 129.6, 127.0, 118.4, 111.2, 107.8, 99.8, 62.6, 55.7. HRMS (ESI, m/z) calcd for $C_{10}H_9N_3ONa$ $[M + Na]^+$: 210.0643, found: 210.0641.



2-Amino-4-chloro-1H-indole-3-carbonitrile (1j). (yield: 63%). Brown solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 1/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.01 (s, 1H), 7.09 (dd, J = 7.7, 1.1 Hz, 1H), 6.95 (dd, J = 7.9, 1.0 Hz, 1H), 6.93 (s, 2H), 6.88 (t, J = 7.8 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 155.6, 133.9, 125.3, 121.4, 121.2, 120.9, 118.0, 109.6, 61.8. HRMS (ESI, m/z) calcd for $C_9H_7N_3Cl$ $[M + H]^+$: 192.0328, found: 192.0325.

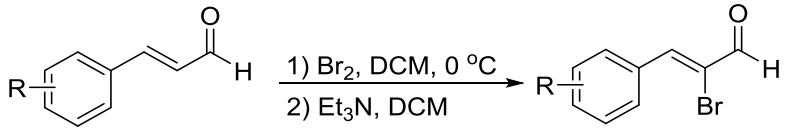


2-Amino-4-fluoro-1H-indole-3-carbonitrile (1k). (yield: 54%). Brown solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 1/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.97 (s, 1H), 6.98 (d, J = 7.6 Hz, 1H), 6.92 - 6.83 (m, 3H), 6.78 - 6.73 (m, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 154.8, 153.8 (d, J = 239.8 Hz), 135.2 (d, J = 11.0 Hz), 120.6 (d, J = 7.0 Hz), 118.1, 115.9 (d, J = 19.5 Hz), 107.3 (d, J = 2.4 Hz), 106.7 (d, J = 19.0 Hz), 59.0. HRMS (ESI, m/z) calcd for $C_9H_6N_3NaF$ $[M + Na]^+$: 198.0443, found: 198.0439.



2-Amino-4-methyl-1H-indole-3-carbonitrile (1l). (yield: 48%). Brown solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 1/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.68 (s, 1H), 6.97 (d, J = 7.6 Hz, 1H), 6.80 (t, J = 7.6 Hz, 1H), 6.70 (d, J = 7.2 Hz, 1H), 6.62 (s, 2H), 2.48 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 154.8, 132.3, 126.4, 126.1, 122.1, 120.2, 119.9, 108.6, 61.8, 18.4. HRMS (ESI, m/z) calcd for $C_{10}H_9N_3Na$ $[M + Na]^+$: 194.0694, found: 194.0693.

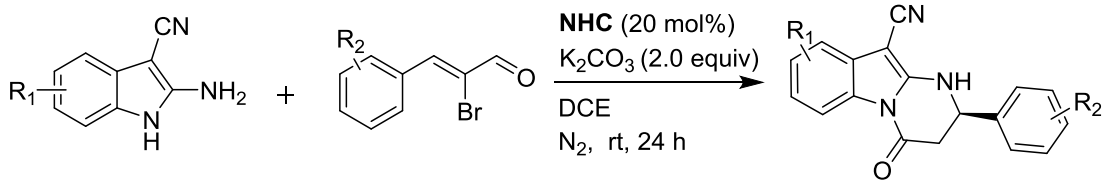
2.2 Preparation of α-bromocinnamaldehyde[3]



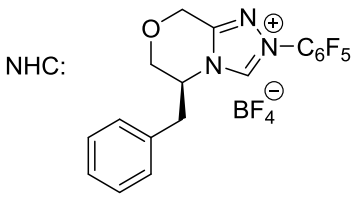
2

To a solution of cinnamaldehyde (10 mmol) in DCM (20 mL) was added Br_2 (12 mmol) at 0 °C. The reaction mixture was stirred for 15 min, followed by the addition of Et_3N (17 mmol). After stirring for an additional 15 min, the reaction mixture was diluted with DCM and washed sequentially with a 10% $NaHSO_3$ solution, H_2O, and brine. The organic layer was separated and dried over anhydrous Na_2SO_4, filtered, and concentrated to yield orange oil. Products were used for the next step without further purification.

3 General Procedure for Synthesis of Compounds 3

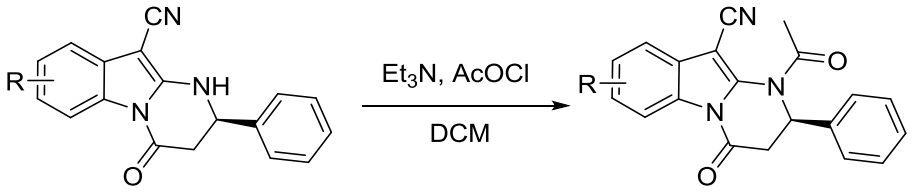


1 **2** **3**



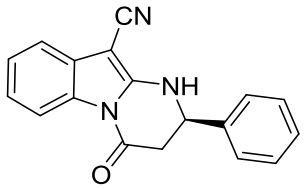
2-Amino-1H-indole-3-carbonitrile (1.0 equiv, 0.2 mmol), α-bromocinnamaldehyde (2.0 equiv, 0.4 mmol), NHC (0.2 equiv, 0.04 mmol) and K_2CO_3 (2.0 equiv, 0.4 mmol) were added to a reaction tube in DCE (2.0 mL) with N_2. The tube was stirred for 24 h at rt After completion, the crude reaction mixture was concentrated under reduced pressure and purified by flash chromatography on silica gel to give the product.

3.1 General Procedure for Synthesis of Compounds 3'

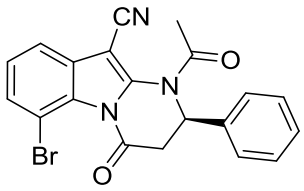


3 **3'**

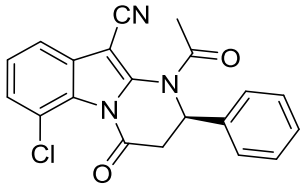
4-Oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (1.0 equiv, 0.2 mmol), Et_3N (1.2 equiv, 0.24 mmol) were added to a reaction tube in DCM (2.0 mL) at rt, then AcOCl (1.2 equiv, 0.24 mmol) were added after 30 minutes. The tube was stirred for 15-24 h at rt. After completion, the crude reaction mixture was quenched with water and extracted with ethyl acetate, then concentrated under reduced pressure and purified by flash chromatography on silica gel to give the product.



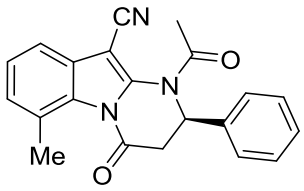
(*R*)-4-Oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3a). (yield: 72%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.20 (s, 1H), 8.05 (d, J = 8.0 Hz, 1H), 7.44 - 7.39 (m, 4H), 7.37 - 7.32 (m, 1H), 7.29 - 7.23 (m, 2H), 7.14 - 7.10 (m, 1H), 5.07 (t, J = 6.8 Hz, 1H), 3.20 - 3.18 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 166.0, 152.4, 140.6, 130.4, 129.2, 128.8, 128.6, 127.0, 125.6, 122.5, 116.4, 116.0, 115.2, 64.3, 53.8. HRMS (ESI, m/z) calcd for $C_{18}H_{13}N_3ONa$ $[M + Na]^+$: 310.0956, found: 310.0956. Enantiomeric excess: 92%, determined by HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 80:20 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{minor} = 8.24 min, t_{major} = 9.08 min; $[\alpha]_D^{24}$ = + 29.3 (c = 0.6, $CHCl_3$).



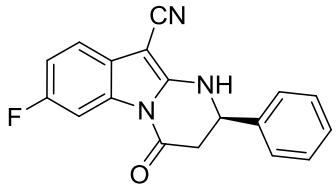
(*R*)-1-Acetyl-6-bromo-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3b'). (yield: 81%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.54 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.36 - 7.32 (m, 2H), 7.29 - 7.23 (m, 4H), 6.38 (d, *J* = 5.6 Hz, 1H), 3.59 - 3.44 (m, 2H), 2.57 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.5, 162.8, 143.0, 135.7, 132.6, 131.1, 129.7, 129.4, 128.8, 127.1, 126.1, 118.3, 112.8, 109.2, 87.3, 54.7, 38.4, 22.4. HRMS (ESI, m/z) calcd for $C_{20}H_{14}N_3O_2NaBr$ $[M + Na]^+$: 430.0167, found: 430.0171. Enantiomeric excess: 80%, determined by HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 80:20 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{major} = 30.47 min, t_{minor} = 37.94 min; $[\alpha]_D^{20}$ = + 73.7 (c = 0.3, $CHCl_3$).



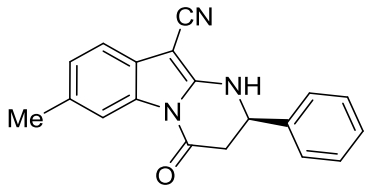
(*R*)-1-Acetyl-6-chloro-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3c'). (yield: 60%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.35 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.28 - 7.19 (m, 6H), 6.31 (d, *J* = 6.0Hz, 1H), 3.53 - 3.37 (m, 2H), 2.50 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.5, 161.8, 141.9, 134.6, 128.5, 128.4, 128.2, 128.1, 127.7, 125.8, 125.0, 121.1, 116.6, 111.8, 86.3, 53.5, 37.3, 21.4. HRMS (ESI, m/z) calcd for $C_{20}H_{14}N_3O_2NaCl$ $[M + Na]^+$: 386.0672, found: 386.0673. Enantiomeric excess: 92%, determined by HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 80:20 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{major} = 15.97 min, t_{minor} = 18.22 min; $[\alpha]_D^{27}$ = + 55.7 (c = 0.9, $CHCl_3$).



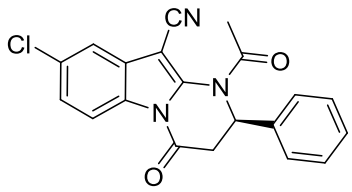
(*R*)-1-Acetyl-6-methyl-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3d'). (yield: 67%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.33 - 7.24 (m, 6H), 7.20 (dt, *J* = 7.2, 1.2 Hz, 1H), 6.40 (d, *J* = 5.4 Hz, 1H), 3.53 - 3.41 (m, 2H), 2.60 (s, 3H), 2.56 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.8, 164.4, 141.9, 135.9, 131.4, 130.4, 129.3, 128.6, 127.2, 126.1, 126.0, 116.7, 113.3, 88.2, 54.0, 38.2, 23.0, 22.4. HRMS (ESI, m/z) calcd for $C_{21}H_{17}N_3O_2Na$ $[M + Na]^+$: 366.1218, found: 366.1223. Enantiomeric excess: 82%, determined by HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 95:5 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{major} = 30.18 min, t_{minor} = 35.45 min; $[\alpha]_D^{20}$ = + 29.8 (c = 0.4, $CHCl_3$).



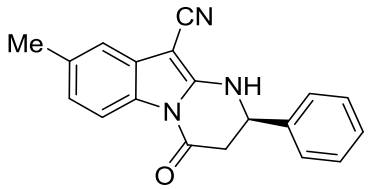
(*R*)-7-Fluoro-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3e). (yield: 60%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.25 (d, *J* = 2.4 Hz, 1H), 7.83 (dd, *J* = 10.2, 3.0 Hz, 1H), 7.43 - 7.40 (m, 4H), 7.38 -7.34 (m, 1H), 7.26 (dd, *J* = 8.4, 4.8 Hz, 1H), 7.13 (ddd, *J* = 9.6, 8.4, 2.4 Hz, 1H), 5.09 - 5.06 (m, 1H), 3.19 (dd, *J* = 7.8, 6.0 Hz, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 166.2, 159.5, 158.0, 152.9, 140.4, 130.2 (d, *J* = 12.5 Hz), 129.2, 128.6, 127.0, 125.1, 116.9 (d, *J* = 8.5 Hz), 115.8, 112.6 (d, *J* = 23.4 Hz), 103.1 (d, *J* = 29.1 Hz), 63.8, 53.8. ^{19}F NMR (565 MHz, DMSO-d_6) δ -120.4 (d, *J* = 10.2 Hz). HRMS (ESI, m/z) calcd for $C_{18}H_{12}N_3ONaF$ $[M + Na]^+$: 328.0862, found: 328.0856. Enantiomeric excess: 90%, determined by HPLC (Daicel Chiralpak OD-H, hexane/*i*-PrOH = 80:20 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{minor} = 9.31 min, t_{major} = 13.14 min; $[\alpha]_D^{25}$ = + 25.5 (c = 0.5, $CHCl_3$).



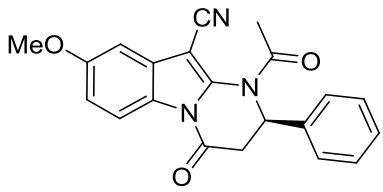
(*R*)-7-Methyl-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3f). (yield: 55%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.09 (d, *J* = 2.4 Hz, 1H), 7.91 (d, *J* = 1.2 Hz, 1H), 7.43 - 7.40 (m, 4H), 7.37 - 7.32 (m, 1H), 7.15 (d, *J* = 8.0 Hz, 1H), 7.08 (dd, *J* = 7.6, 1.2 Hz, 1H), 5.06 - 5.02 (m, 1H), 3.18 (dd, *J* = 5.6, 3.2 Hz, 2H), 2.35 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 166.0, 152.2, 140.6, 131.8, 130.7, 129.2, 128.5, 126.9, 126.4, 126.2, 116.1, 116.1, 115.7, 64.1, 53.7, 21.7. HRMS (ESI, m/z) calcd for $C_{19}H_{15}N_3ONa$ $[M + Na]^+$: 324.1113, found: 324.1108. Enantiomeric excess: 86%, determined by HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 80:20 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{minor} = 18.27 min, t_{major} = 21.87 min; $[\alpha]_D^{26}$ = + 37.1 (c = 0.5, $CHCl_3$).



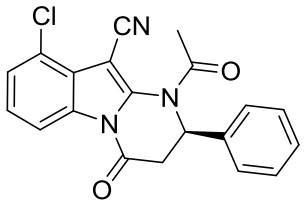
(*R*)-1-Acetyl-8-chloro-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3g'). (yield: 71%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.4 Hz, 1H), 7.48 (d, *J* = 2.0 Hz, 1H), 7.28 - 7.13 (m, 6H), 6.29 (d, *J* = 5.6 Hz, 1H), 3.48 - 3.31 (m, 2H), 2.53 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.5, 163.5, 140.4, 134.5, 130.8, 128.5, 128.2, 127.8, 126.1, 126.0, 124.7, 117.8, 116.3, 111.9, 84.4, 53.2, 36.6, 21.6. HRMS (ESI, m/z) calcd for $C_{20}H_{14}N_3O_2NaCl$ $[M + Na]^+$: 386.0672, found: 386.0671. Enantiomeric excess: >99%, determined by HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 80:20 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{major} = 10.12 min, t_{minor} = 12.83 min; $[\alpha]_D^{26}$ = + 100.4 (c = 0.5, $CHCl_3$).



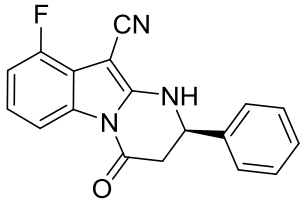
(*R*)-8-Methyl-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3h). (yield: 53%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.92 (d, *J* = 2.0 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.19 - 7.15 (m, 4H), 7.15 - 7.08 (m, 1H), 6.83 (t, *J* = 1.2 Hz, 1H), 6.68 (ddd, *J* = 8.4, 1.6, 0.4 Hz, 1H), 4.80 (td, *J* = 7.2, 2.0 Hz, 1H), 2.92 (d, *J* = 6.8 Hz, 2H), 2.11 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 165.8, 152.5, 140.6, 134.8, 129.2, 128.9, 128.6, 128.4, 127.0, 123.3, 116.6, 116.0, 114.9, 64.1, 53.8, 21.5. HRMS (ESI, m/z) calcd for $C_{19}H_{15}N_3ONa$ $[M + Na]^+$: 324.1113, found: 324.1112. Enantiomeric excess: 80%, determined by HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 80:20 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{major} = 21.90 min, t_{minor} = 23.24 min; $[\alpha]_D^{25}$ = + 109.8 (c = 0.5, $CHCl_3$).



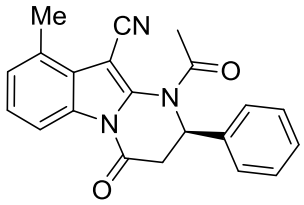
(*R*)-1-Acetyl-8-methoxy-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3i'). (yield: 55%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.8 Hz, 1H), 7.34 - 7.22 (m, 5H), 7.00 (d, *J* = 2.8 Hz, 1H), 6.96 (dd, *J* = 9.2, 2.8 Hz, 1H), 6.37 (d, *J* = 5.6 Hz, 1H), 3.84 (s, 3H), 3.52 - 3.36 (m, 2H), 2.60 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.7, 164.5, 158.1, 140.7, 135.8, 129.4, 128.7, 127.0, 125.9, 125.2, 117.2, 115.4, 113.6, 101.6, 86.2, 55.8, 54.2, 37.5, 22.5. HRMS (ESI, m/z) calcd for $C_{21}H_{17}N_3O_3Na$ $[M + Na]^+$: 382.1168, found: 382.1170. Enantiomeric excess: 93%, determined by HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 80:20 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{major} = 13.83 min, t_{minor} = 20.32 min; $[\alpha]_D^{27}$ = + 32.3 (c = 0.6, $CHCl_3$).



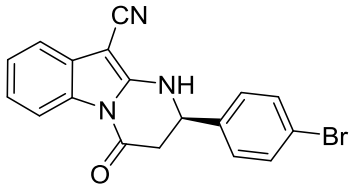
(*R*)-1-Acetyl-9-chloro-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3j'). (yield: 61%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (dd, *J* = 6.4, 3.2 Hz, 1H), 7.36 - 7.24 (m, 7H), 6.44 (d, *J* = 6.0 Hz, 1H), 3.58 - 3.38 (m, 2H), 2.63 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.7, 164.8, 142.8, 135.5, 132.0, 129.5, 128.8, 127.5, 126.5, 126.0, 125.9, 122.9, 114.7, 113.6, 85.6, 53.9, 37.6, 22.5. HRMS (ESI, m/z) calcd for $C_{20}H_{14}N_3O_2NaCl$ $[M + Na]^+$: 386.0672, found: 386.0671. Enantiomeric excess: 98%, determined by HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 80:20 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{major} = 17.98 min, t_{minor} = 24.20 min; $[\alpha]_D^{20}$ = + 68.5 (c = 0.6, $CHCl_3$).



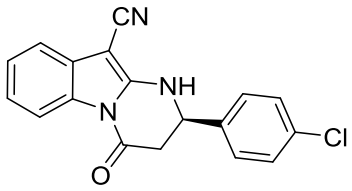
(*R*)-9-Fluoro-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3k). (yield: 65%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.34 (d, *J* = 2.4 Hz, 1H), 7.91 - 7.89 (m, 1H), 7.44 - 7.41 (m, 4H), 7.40 - 7.32 (m, 1H), 7.13 - 7.07 (m, 2H), 5.09 (td, *J* = 7.2, 2.0 Hz, 1H), 3.22 - 3.20 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 166.1, 154.3, 153.0, 152.7, 140.3, 132.4 (d, *J* = 8.5 Hz), 128.6, 128.1 (d, *J* = 341.4 Hz), 123.4 (d, *J* = 7.7 Hz), 116.3, 116.2, 115.9, 111.7, 111.6, 60.8, 53.7. ^{19}F NMR (565 MHz, DMSO-d_6) δ -127.4 (dd, *J* = 9.6, 6.2 Hz). HRMS (ESI, m/z) calcd for $C_{18}H_{12}N_3OFNa$ $[M + Na]^+$: 328.0862, found: 328.0858. Enantiomeric excess: 98%, determined by HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 95:5 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{minor} = 24.91 min, t_{major} = 30.94 min; $[\alpha]_D^{27}$ = + 120.6 (c = 0.3, $CHCl_3$)



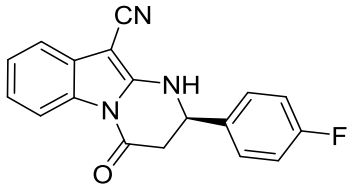
(*R*)-1-Acetyl-9-methyl-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3l'). (yield: 71%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.4 Hz, 1H), 7.34 - 7.23 (m, 6H), 7.10 (d, *J* = 7.6 Hz, 1H), 6.42 (d, *J* = 5.2 Hz, 1H), 3.55 - 3.26 (m, 2H), 2.67 (s, 3H), 2.61 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.9, 164.8, 141.6, 135.7, 131.2, 130.6, 129.4, 128.6, 127.2, 126.8, 125.9, 123.7, 115.1, 113.8, 86.0, 53.8, 37.5, 22.7, 18.3. HRMS (ESI, m/z) calcd for $C_{21}H_{17}N_3O_2Na$ $[M + Na]^+$: 366.1218, found: 366.1220. Enantiomeric excess: 88%, determined by HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 90:10 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{major} = 20.67 min, t_{minor} = 24.54 min; $[\alpha]_D^{26}$ = + 16.9 (c = 0.7, $CHCl_3$).



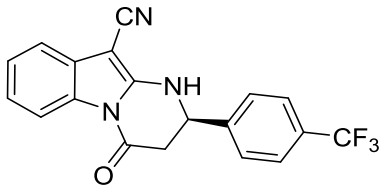
(*R*)-2-(4-Bromophenyl)-4-oxo-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3m). (yield: 58%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.17 (d, *J* = 2.4 Hz, 1H), 8.06 (d, *J* = 7.8 Hz, 1H), 7.63 - 7.61 (m, 2H), 7.41 - 7.39 (m, 2H), 7.28 - 7.24 (m, 2H), 7.14 -7.11 (m, 1H), 5.07 (td, *J* = 6.6, 1.8 Hz, 1H), 3.18 (d, *J* = 6.6 Hz, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 164.7, 151.2, 138.8, 131.0, 129.3, 128.3, 127.6, 124.5, 121.5, 120.6, 115.3, 114.9, 114.2, 63.4, 52.2. HRMS (ESI, m/z) calcd for $C_{18}H_{12}N_3ONaBr$ $[M + Na]^+$: 388.0061, found: 388.0059. Enantiomeric excess: 88%, determined by HPLC (Daicel Chiralpak OD-H, hexane/*i*-PrOH = 80:20 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{minor} = 9.50 min, t_{major} = 11.71 min; $[\alpha]_D^{26}$ = + 22.29 (c = 0.6, $CHCl_3$).



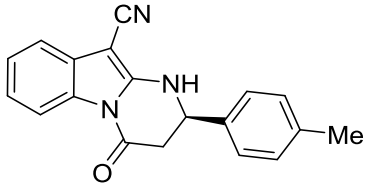
(*R*)-2-(4-Chlorophenyl)-4-oxo-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3n). (yield: 62%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.93 (d, *J* = 2.0 Hz, 1H), 7.81 (dt, *J* = 8.0, 0.8 Hz, 1H), 7.25 - 7.20 (m, 4H), 7.04 - 6.98 (m, 2H), 6.90 - 6.86 (m, 1H), 4.84 (td, *J* = 7.2, 2.0, 1H), 2.93 (d, *J* = 7.2 Hz, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 165.8, 152.3, 139.5, 133.2, 130.4, 129.2, 129.0, 128.7, 125.6, 122.6, 116.4, 116.0, 115.2, 64.5, 53.3. HRMS (ESI, m/z) calcd for $C_{18}H_{12}N_3ONaCl$ $[M + Na]^+$: 344.0567, found: 344.0562. Enantiomeric excess: 80%, determined by HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 95:5 (v/v), λ =254 nm, flow rate = 0.8 mL/min, rt): t_{minor} = 35.52 min, t_{major} = 38.64 min; $[\alpha]_D^{27}$ = + 55.7 (c = 0.3, $CHCl_3$).



(*R*)-2-(4-Fluorophenyl)-4-oxo-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3o). (yield: 70%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.18 (d, *J* = 2.4 Hz, 1H), 8.06 (d, *J* = 7.8 Hz, 1H), 7.50 - 7.47 (m, 2H), 7.28 - 7.24 (m, 4H), 7.12 (td, *J* = 7.8, 1.8 Hz, 1H), 5.10 -5.07 (m, 1H), 3.23 - 3.13 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 165.9, 163.1, 161.5, 152.3, 136.6, 130.3, 129.2 (d, *J* = 8.3 Hz), 128.7, 125.6, 122.6, 116.0, 115.9, 115.9, 115.8 (d, *J* = 176.4 Hz), 64.4, 53.2. ^{19}F NMR (565 MHz, DMSO-d_6) δ -114.2 (dt, *J* = 12.2, 6.4 Hz). HRMS (ESI, m/z) calcd for $C_{18}H_{12}N_3ONaF$ $[M + Na]^+$: 328.0862, found: 328.0862. Enantiomeric excess: 90%, determined by HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 80:20 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{minor}= 13.62 min, t_{major} = 15.20 min; $[\alpha]_D^{26}$ = + 50.1 (c = 0.6, $CHCl_3$).

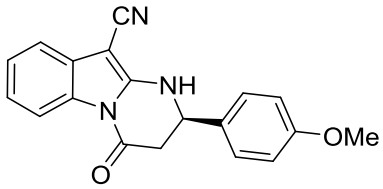


(*R*)-4-Oxo-2-(4-(trifluoromethyl)phenyl)-1,2,3,4-tetrahydropyrimido [1,2-a]indole -10-carbonitrile (3p). (yield: 68%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.29 (s, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.79 (dd, *J* = 50.8, 8.0 Hz, 4H), 7.32 (m, 2H), 7.21 -7.16 (m, 1H), 5.25 (t, *J* = 7.2 Hz, 1H), 3.28 (d, *J* = 7.2 Hz, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 165.7, 152.3, 145.2, 130.4, 129.2 (dd, *J* = 62.8, 32.0 Hz), 128.7, 128.1, 126.1 (d, *J* = 4.2 Hz), 125.6, 125.5 (dd, *J* = 545.1, 272.1 Hz),122.7, 116.4, 115.9, 115.2, 64.6, 53.5. ^{19}F NMR (565 MHz, DMSO-d_6) δ -61.0. HRMS (ESI, m/z) calcd for $C_{19}H_{12}N_3ONaF_3$ $[M + Na]^+$: 378.0830, found: 378.0825. Enantiomeric excess: 90%, determined by HPLC (Daicel Chiralpak OD-H, hexane/*i*-PrOH = 90:10 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{minor} = 12.03 min, t_{major} = 15.74 min; $[\alpha]_D^{26}$ = + 6.6 (c = 0.6, $CHCl_3$).

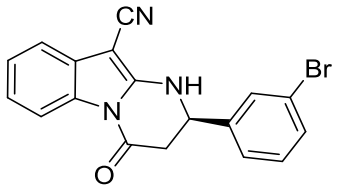


(*R*)-4-Oxo-2-(p-tolyl)-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3q). (yield: 52%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.19 (d, *J* = 2.0 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.25 (dd, *J* = 36.4, 8.0, 4H), 7.25 (dd, *J* = 6.8, 1.6 Hz, 2H), 7.13 - 7.09 (m, 1H), 5.02 (td, *J* = 7.6, 2.0 Hz, 1H), 3.15 - 3.15 (m, 2H), 2.29 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 166.1, 152.4, 137.8, 137.5, 130.4, 129.7, 128.8, 126.8, 125.5, 122.5, 116.3, 116.0, 115.2, 64.2, 53.4, 21.1. HRMS (ESI, m/z) calcd for $C_{19}H_{15}N_3ONa$ $[M + Na]^+$: 324.1113, found: 324.1107. Enantiomeric excess: 82%, determined by HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 80:20 (v/v), λ =254

nm, flow rate = 1.0 mL/min, rt): t_{minor} = 11.12 min, t_{major} = 12.60 min; $[\alpha]_D^{26}$ = + 53.1 (c = 0.6, $CHCl_3$).

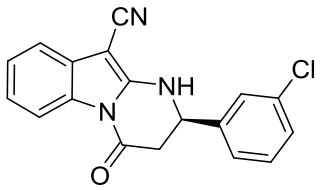


(*R*)-2-(4-Methoxyphenyl)-4-oxo-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3r). (yield: 47%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.14 (d, *J* = 2.0 Hz, 1H), 8.06 (dt, *J* = 8.0, 0.8 Hz, 1H), 7.36 - 7.32 (m, 2H), 7.28 - 7.22 (m, 2H), 7.14 - 7.10 (m, 1H), 6.99 - 6.95 (m, 2H), 5.03 - 4.99 (m, 1H), 3.75 (s, 3H), 3.18 - 3.15 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 166.2, 159.5, 152.4, 132.3, 130.3, 128.8, 128.2, 125.6, 122.5, 116.3, 116.0, 115.2, 114.5, 64.2, 55.6, 53.2. HRMS (ESI, m/z) calcd for $C_{19}H_{15}N_3O_2Na$ $[M + Na]^+$: 340.1062, found: 340.1064. Enantiomeric excess: 88%, determined by HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 80:20 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{minor} = 17.85 min, t_{major} = 19.65 min; $[\alpha]_D^{27}$ = + 77.1 (c = 0.2, $CHCl_3$).

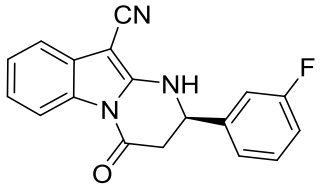


(*R*)-2-(3-Bromophenyl)-4-oxo-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3s). (yield: 65%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.17 (s, 1H), 8.07 (d, *J* = 8.4 Hz, 1H), 7.69 (t, *J* = 1.6 Hz, 1H), 7.57 (dt, *J* = 7.6, 1.6 Hz, 1H), 7.44 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.30 - 7.24 (m, 2H), 7.15 - 7.11 (m, 1H), 5.09 (dd, *J* = 10.0, 5.2 Hz, 1H), 3.25 (dd, *J* = 16.8, 9.2 Hz, 1H), 3.15 (dd, *J* = 16.8, 5.2 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 165.8, 152.3, 143.1, 131.5, 131.4, 130.3, 130.2, 128.7, 126.2, 125.6, 122.6, 122.3, 116.4, 115.9, 115.2, 64.6, 53.4. HRMS (ESI,

m/z) calcd for $C_{18}H_{12}N_3ONaBr$ $[M + Na]^+$: 388.0061, found: 388.0057. Enantiomeric excess: 80%, determined by HPLC (Daicel Chiralpak OD-H, hexane/*i*-PrOH = 80:20 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{minor} = 10.44 min, t_{major} = 15.31 min; $[\alpha]_D^{26}$ = + 9.0 (c = 0.9, $CHCl_3$).

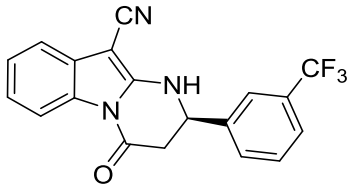


(*R*)-2-(3-Chlorophenyl)-4-oxo-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3t). (yield: 75%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.18 (s, 1H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.55 (d, *J* = 2.4 Hz, 1H), 7.48 - 7.38 (m, 3H), 7.30 - 7.24 (m, 2H), 7.15 - 7.11 (m, 1H), 5.12 - 5.08 (m, 1H), 3.25 (dd, *J* = 16.4, 8.8 Hz, 1H), 3.16 (dd, *J* = 16.6, 5.2 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 165.8, 152.3, 142.9, 133.7, 131.1, 130.3, 128.7, 128.6, 127.3, 125.8, 125.6, 122.6, 116.4, 115.9, 115.2, 64.6, 53.4. HRMS (ESI, m/z) calcd for $C_{18}H_{12}N_3ONaCl$ $[M + Na]^+$: 344.0567, found: 344.0566. Enantiomeric excess: 84%, determined by HPLC (Daicel Chiralpak IB-3, hexane/*i*-PrOH = 80:20 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{minor} = 10.73 min, t_{major} = 14.52 min; $[\alpha]_D^{26}$ = + 96.6 (c = 0.5, $CHCl_3$).

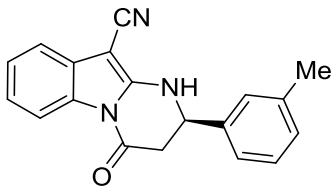


(*R*)-2-(3-Fluorophenyl)-4-oxo-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3u). (yield: 58%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.14 (d, *J* = 2.0 Hz, 1H), 7.99 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.39 (td, *J* = 8.0, 6.4 Hz, 1H), 7.26 - 7.22 (m, 1H), 7.21 - 7.18 (m, 3H), 7.13 (td, *J* = 8.4, 2.8 Hz, 1H), 7.08 -7.04 (m, 1H), 5.05 - 5.01 (m, 1H), 3.20 - 3.08 (m, 2H). ^{13}C NMR (151 MHz,) δ 165.8, 163.5, 161.9, 152.3,

143.3 (d, *J* = 7.1 Hz), 131.3 (d, *J* = 8.3 Hz), 130.3, 128.7, 125.6, 123.1 (d, *J* = 2.1 Hz), 122.6, 116.4, 115.9, 115.2, 114.8 (dd, *J* = 198.4, 20.8 Hz), 64.5, 53.4. ^{19}F NMR (565 MHz, DMSO-d_6) δ -112.5 (q, *J* = 8.0 Hz). HRMS (ESI, m/z) calcd for $C_{18}H_{13}N_3OF$[M + Na]$^+$: 306.1043, found: 306.1046. Enantiomeric excess: 84%, determined by HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 95:5 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{minor} = 23.01 min, t_{major} = 26.16 min; $[\alpha]_D^{26}$ = + 23.5 (c = 0.3, $CHCl_3$).



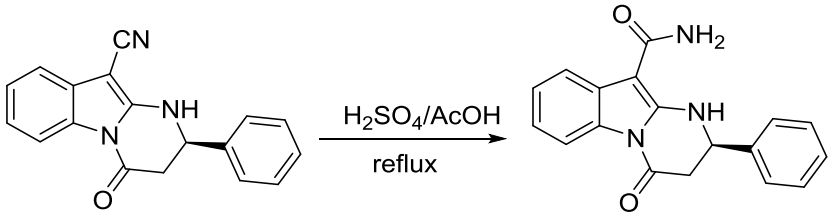
(*R*)-4-Oxo-2-(3-(trifluoromethyl)phenyl)-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3v). (yield: 65%). White solid, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 3/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.19 (s, 1H), 8.09 (d, *J* = 7.6 Hz, 1H), 7.87 (s, 1H), 7.78 - 7.74 (m, 2H), 7.67 (t, *J* = 7.6 Hz, 1H), 7.31 - 7.24 (m, 2H), 7.16 - 7.12 (m, 1H), 5.21 (ddd, *J* = 10.0, 5.2, 1.6 Hz, 1H), 3.32 (dd, *J* = 16.4, 10.0 Hz, 1H), 3.16 (dd, *J* = 16.4, 4.8 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 165.8, 152.4, 141.7, 131.4, 130.6, 130.3, 129.8 (dd, *J* = 64.0, 32.0 Hz), 128.7, 125.6, 125.5 (dd, *J* = 545.0, 273.2 Hz), 124.3 (dt, *J* = 187.4, 5.4 Hz), 122.7, 116.4, 115.9, 115.3, 64.7, 53.7. ^{19}F NMR (565 MHz, DMSO-d_6) δ -61.0. HRMS (ESI, m/z) calcd for $C_{19}H_{12}N_3ONaF_3$ [M + Na]$^+$: 378.0830, found: 378.0823. Enantiomeric excess: 86%, determined by HPLC (Daicel Chiralpak OD-3, hexane/*i*-PrOH = 90:10 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{minor} = 17.09 min, t_{major} = 19.00 min; $[\alpha]_D^{26}$ = + 67.8 (c = 0.4, $CHCl_3$).



(*R*)-4-Oxo-2-(m-tolyl)-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3w). (yield: 75%). White solid, purified by flash column chromatography (eluent:

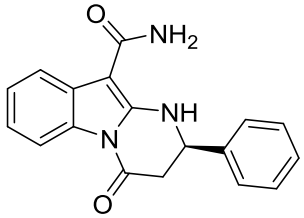
Petroleum ether/EtOAc = 3/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.18 (s, 1H), 8.06 (d, J = 8.4 Hz, 1H), 7.31 - 7.25 (m, 4H), 7.23 - 7.10 (m, 3H), 5.02 (t, J = 6.8 Hz, 1H), 3.17 (d, J = 6.8 Hz, 2H), 2.32 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 166.1, 152.4, 140.4, 138.4, 130.3, 129.2, 129.1, 128.8, 127.6, 125.6, 123.9, 122.5, 116.3, 116.0, 115.2, 64.2, 53.7, 21.5. HRMS (ESI, m/z) calcd for $C_{19}H_{15}N_3ONa$ $[M + Na]^+$: 324.1113, found: 324.1113. Enantiomeric excess: 82%, determined by HPLC (Daicel Chiralpak OD-H, hexane/*i*-PrOH = 90:10 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{minor} = 14.78 min, t_{major} = 19.33 min; $[\alpha]_D^{25}$ = + 16.1 (c = 0.6, $CHCl_3$).

3.2 The transformation of Compounds 3a to 4a



3a **4a**

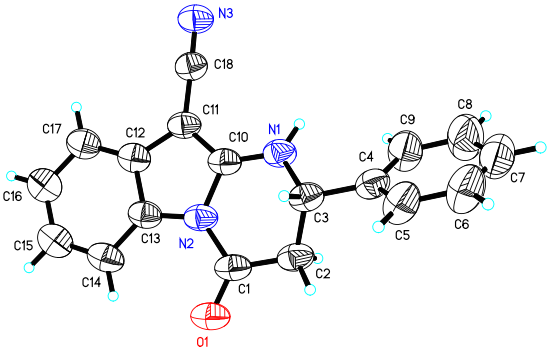
To a stirred solution of **3a** (0.2 mmol) in AcOH (2.0 mL), cooled in an ice bath, was added 50% H_2SO_4 (1.0 mL), the reaction was allowed to warm up to 120 ^{o}C. After 1 h , distilled aq. Na_2CO_3 (10 mL) was added, cooling applied and the product was collected by chromatography on silica gel.

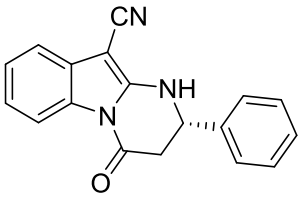


(*R*)-4-Oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carboxamide (4a). (yield: 51%). White solid, purified by flash column chromatography (eluent: Petroleum DCM/MeOH = 20/1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.48 (s, 1H), 8.11 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 7.6 Hz, 1H), 7.44 - 7.32 (m, 5H), 7.21 (td, J = 7.6, 1.2 Hz, 1H), 7.07 (t, J = 8.0 Hz, 1H), 6.99 (s, 2H), 5.12 (t, J = 6.8 Hz, 1H), 3.28 - 3.16 (m,

2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 168.0, 166.2, 151.2, 141.2, 131.0, 129.3, 128.6, 127.4, 126.7, 125.0, 121.5, 117.8, 114.8, 88.4, 53.4. HRMS (ESI, m/z) calcd for $C_{18}H_{16}N_3O_2$ $[M + H]^+$: 306.1206, found: 306.1208. Enantiomeric excess: 84%, determined by HPLC (Daicel Chiralpak IC-3, hexane/*i*-PrOH = 50:50 (v/v), λ =254 nm, flow rate = 1.0 mL/min, rt): t_{minor} = 20.23 min, t_{major} = 14.65 min; $[\alpha]_D^{26}$ = + 76.6 (c = 0.4, $CHCl_3$).

4. X-ray crystal structure of (-)3a





(-)3a

Table 1. Crystal data and structure refinement for d8v23073.

Identification code	d8v23073	
Empirical formula	C18 H13 N3 O	
Formula weight	287.31	
Temperature	293(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 5.4603(2) Å	α= 90°.
	b = 20.5881(9) Å	β= 93.864(2)°.
	c = 12.9406(6) Å	γ = 90°.
Volume	1451.44(11) $Å^3$	
Z	4	
Density (calculated)	1.315 Mg/m^3	
Absorption coefficient	0.675 mm^{-1}	
F(000)	600	
Crystal size	0.140 x 0.120 x 0.060 mm^3	
Theta range for data collection	4.041 to 67.985°.	
Index ranges	-6<=h<=6, -24<=k<=24, -15<=l<=15	
Reflections collected	19539	
Independent reflections	5271 [R(int) = 0.0789]	
Completeness to theta = 67.679°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7533 and 0.5264	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5271 / 25 / 386	
Goodness-of-fit on F^2	1.053	
Final R indices [I>2sigma(I)]	R1 = 0.0644, wR2 = 0.1718	
R indices (all data)	R1 = 0.0812, wR2 = 0.1932	
Absolute structure parameter	0.0(3)	
Extinction coefficient	0.037(6)	
Largest diff. peak and hole	0.234 and -0.206 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3)
for d8v23073. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	2818(7)	2922(2)	4510(4)	92(1)
N(1)	8661(9)	4093(2)	4194(4)	73(1)
N(2)	5974(7)	3527(2)	5233(4)	71(1)
N(3)	12314(10)	4939(3)	6561(5)	90(2)
C(1)	4572(9)	3275(2)	4383(5)	75(2)
C(2)	5352(10)	3486(3)	3354(5)	82(2)
C(3)	8079(10)	3626(2)	3366(4)	72(1)
C(4)	8905(11)	3851(3)	2343(5)	78(2)
C(5)	9498(16)	3407(4)	1625(6)	107(2)
C(6)	10380(20)	3588(6)	686(6)	133(3)
C(7)	10670(20)	4214(6)	448(7)	141(4)
C(8)	10120(30)	4666(5)	1188(8)	159(5)
C(9)	9212(19)	4487(3)	2113(6)	117(3)
C(10)	7926(8)	3956(2)	5136(5)	67(1)
C(11)	8764(9)	4157(2)	6113(4)	70(1)
C(12)	7281(9)	3841(3)	6854(5)	73(1)
C(13)	5541(9)	3460(2)	6290(5)	74(1)
C(14)	3809(11)	3094(3)	6767(7)	88(2)
C(15)	3855(13)	3121(4)	7845(7)	98(2)
C(16)	5595(13)	3492(4)	8408(6)	97(2)
C(17)	7323(12)	3855(3)	7908(6)	86(2)
C(18)	10732(10)	4582(3)	6345(5)	72(1)
O(2)	12357(8)	7077(2)	5991(4)	96(1)
N(4)	6585(8)	5903(2)	6393(4)	71(1)
N(5)	9317(7)	6430(2)	5318(4)	70(1)
N(6)	2913(10)	4998(3)	4108(5)	92(2)
C(19)	10548(10)	6761(3)	6117(5)	77(2)
C(20)	9330(12)	6725(3)	7101(5)	89(2)
C(21)	8095(11)	6087(3)	7313(5)	77(1)
C(22)	6597(9)	6117(2)	8260(3)	80(1)
C(23)	5542(13)	6690(2)	8585(5)	144(3)
C(24)	4196(14)	6691(3)	9459(5)	151(3)

C(25)	3905(14)	6119(4)	10008(5)	151(3)
C(26)	4961(17)	5546(3)	9684(6)	167(3)
C(27)	6307(14)	5545(2)	8809(5)	160(3)
C(28)	7299(9)	6023(2)	5450(4)	67(1)
C(29)	6346(9)	5827(2)	4485(4)	66(1)
C(30)	7758(10)	6137(2)	3706(5)	70(1)
C(31)	9616(10)	6498(2)	4239(5)	71(1)
C(32)	11329(11)	6852(3)	3724(6)	85(2)
C(33)	11081(13)	6843(3)	2662(6)	95(2)
C(34)	9219(13)	6498(3)	2119(6)	96(2)
C(35)	7553(12)	6140(3)	2633(5)	85(2)
C(36)	4426(10)	5383(3)	4279(5)	72(1)

Table 3. Bond lengths [Å] and angles [°] for d8v23073.

O(1)-C(1)	1.222(7)
N(1)-C(10)	1.339(8)
N(1)-C(3)	1.458(7)
N(1)-H(1)	0.8600
N(2)-C(1)	1.397(7)
N(2)-C(10)	1.396(6)
N(2)-C(13)	1.410(8)
N(3)-C(18)	1.154(7)
C(1)-C(2)	1.490(9)
C(2)-C(3)	1.516(8)
C(2)-H(2A)	0.9700
C(2)-H(2B)	0.9700
C(3)-C(4)	1.501(9)
C(3)-H(3)	0.9800
C(4)-C(9)	1.356(9)
C(4)-C(5)	1.358(9)
C(5)-C(6)	1.388(13)
C(5)-H(5)	0.9300
C(6)-C(7)	1.336(14)
C(6)-H(6)	0.9300
C(7)-C(8)	1.383(15)
C(7)-H(7)	0.9300
C(8)-C(9)	1.376(13)
C(8)-H(8)	0.9300
C(9)-H(9)	0.9300
C(10)-C(11)	1.379(8)
C(11)-C(18)	1.401(8)
C(11)-C(12)	1.450(8)
C(12)-C(17)	1.363(9)
C(12)-C(13)	1.399(8)
C(13)-C(14)	1.386(8)
C(14)-C(15)	1.395(11)
C(14)-H(14)	0.9300
C(15)-C(16)	1.387(11)
C(15)-H(15)	0.9300
C(16)-C(17)	1.397(10)

C(16)-H(16)	0.9300
C(17)-H(17)	0.9300
O(2)-C(19)	1.203(7)
N(4)-C(28)	1.329(7)
N(4)-C(21)	1.452(7)
N(4)-H(4)	0.8600
N(5)-C(19)	1.375(7)
N(5)-C(28)	1.405(6)
N(5)-C(31)	1.424(7)
N(6)-C(36)	1.155(7)
C(19)-C(20)	1.478(9)
C(20)-C(21)	1.511(8)
C(20)-H(20A)	0.9700
C(20)-H(20B)	0.9700
C(21)-C(22)	1.520(7)
C(21)-H(21)	0.9800
C(22)-C(23)	1.3900
C(22)-C(27)	1.3900
C(23)-C(24)	1.3900
C(23)-H(23)	0.9300
C(24)-C(25)	1.3900
C(24)-H(24)	0.9300
C(25)-C(26)	1.3900
C(25)-H(25)	0.9300
C(26)-C(27)	1.3900
C(26)-H(26)	0.9300
C(27)-H(27)	0.9300
C(28)-C(29)	1.381(8)
C(29)-C(36)	1.403(7)
C(29)-C(30)	1.457(8)
C(30)-C(35)	1.385(9)
C(30)-C(31)	1.401(8)
C(31)-C(32)	1.390(8)
C(32)-C(33)	1.372(10)
C(32)-H(32)	0.9300
C(33)-C(34)	1.392(10)
C(33)-H(33)	0.9300
C(34)-C(35)	1.376(9)

C(34)-H(34)	0.9300
C(35)-H(35)	0.9300

C(10)-N(1)-C(3)	117.8(4)
C(10)-N(1)-H(1)	121.1
C(3)-N(1)-H(1)	121.1
C(1)-N(2)-C(10)	123.0(5)
C(1)-N(2)-C(13)	127.5(5)
C(10)-N(2)-C(13)	109.1(4)
O(1)-C(1)-N(2)	120.5(6)
O(1)-C(1)-C(2)	124.5(5)
N(2)-C(1)-C(2)	115.0(5)
C(1)-C(2)-C(3)	112.7(5)
C(1)-C(2)-H(2A)	109.1
C(3)-C(2)-H(2A)	109.1
C(1)-C(2)-H(2B)	109.1
C(3)-C(2)-H(2B)	109.1
H(2A)-C(2)-H(2B)	107.8
N(1)-C(3)-C(4)	112.4(4)
N(1)-C(3)-C(2)	107.4(5)
C(4)-C(3)-C(2)	113.7(5)
N(1)-C(3)-H(3)	107.7
C(4)-C(3)-H(3)	107.7
C(2)-C(3)-H(3)	107.7
C(9)-C(4)-C(5)	117.5(7)
C(9)-C(4)-C(3)	122.7(6)
C(5)-C(4)-C(3)	119.7(6)
C(4)-C(5)-C(6)	122.0(8)
C(4)-C(5)-H(5)	119.0
C(6)-C(5)-H(5)	119.0
C(7)-C(6)-C(5)	121.0(9)
C(7)-C(6)-H(6)	119.5
C(5)-C(6)-H(6)	119.5
C(6)-C(7)-C(8)	117.0(9)
C(6)-C(7)-H(7)	121.5
C(8)-C(7)-H(7)	121.5
C(9)-C(8)-C(7)	122.0(9)
C(9)-C(8)-H(8)	119.0

C(7)-C(8)-H(8)	119.0
C(4)-C(9)-C(8)	120.4(8)
C(4)-C(9)-H(9)	119.8
C(8)-C(9)-H(9)	119.8
N(1)-C(10)-C(11)	132.1(5)
N(1)-C(10)-N(2)	119.5(5)
C(11)-C(10)-N(2)	108.5(5)
C(10)-C(11)-C(18)	125.9(5)
C(10)-C(11)-C(12)	107.8(5)
C(18)-C(11)-C(12)	126.3(5)
C(17)-C(12)-C(13)	119.9(5)
C(17)-C(12)-C(11)	132.8(5)
C(13)-C(12)-C(11)	107.3(5)
C(14)-C(13)-C(12)	122.2(6)
C(14)-C(13)-N(2)	130.4(6)
C(12)-C(13)-N(2)	107.4(5)
C(13)-C(14)-C(15)	117.2(6)
C(13)-C(14)-H(14)	121.4
C(15)-C(14)-H(14)	121.4
C(16)-C(15)-C(14)	120.9(7)
C(16)-C(15)-H(15)	119.6
C(14)-C(15)-H(15)	119.6
C(15)-C(16)-C(17)	120.7(7)
C(15)-C(16)-H(16)	119.6
C(17)-C(16)-H(16)	119.6
C(12)-C(17)-C(16)	119.1(6)
C(12)-C(17)-H(17)	120.5
C(16)-C(17)-H(17)	120.5
N(3)-C(18)-C(11)	177.9(7)
C(28)-N(4)-C(21)	121.3(5)
C(28)-N(4)-H(4)	119.4
C(21)-N(4)-H(4)	119.4
C(19)-N(5)-C(28)	123.5(5)
C(19)-N(5)-C(31)	127.3(5)
C(28)-N(5)-C(31)	108.7(4)
O(2)-C(19)-N(5)	122.0(6)
O(2)-C(19)-C(20)	124.4(6)
N(5)-C(19)-C(20)	113.5(5)

C(19)-C(20)-C(21)	115.5(5)
C(19)-C(20)-H(20A)	108.4
C(21)-C(20)-H(20A)	108.4
C(19)-C(20)-H(20B)	108.4
C(21)-C(20)-H(20B)	108.4
H(20A)-C(20)-H(20B)	107.5
N(4)-C(21)-C(20)	108.3(5)
N(4)-C(21)-C(22)	111.4(5)
C(20)-C(21)-C(22)	112.4(5)
N(4)-C(21)-H(21)	108.2
C(20)-C(21)-H(21)	108.2
C(22)-C(21)-H(21)	108.2
C(23)-C(22)-C(27)	120.0
C(23)-C(22)-C(21)	122.4(4)
C(27)-C(22)-C(21)	117.6(4)
C(24)-C(23)-C(22)	120.0
C(24)-C(23)-H(23)	120.0
C(22)-C(23)-H(23)	120.0
C(23)-C(24)-C(25)	120.0
C(23)-C(24)-H(24)	120.0
C(25)-C(24)-H(24)	120.0
C(26)-C(25)-C(24)	120.0
C(26)-C(25)-H(25)	120.0
C(24)-C(25)-H(25)	120.0
C(25)-C(26)-C(27)	120.0
C(25)-C(26)-H(26)	120.0
C(27)-C(26)-H(26)	120.0
C(26)-C(27)-C(22)	120.0
C(26)-C(27)-H(27)	120.0
C(22)-C(27)-H(27)	120.0
N(4)-C(28)-C(29)	131.4(5)
N(4)-C(28)-N(5)	120.2(5)
C(29)-C(28)-N(5)	108.4(5)
C(28)-C(29)-C(36)	126.4(5)
C(28)-C(29)-C(30)	108.3(5)
C(36)-C(29)-C(30)	125.3(5)
C(35)-C(30)-C(31)	119.9(5)
C(35)-C(30)-C(29)	133.2(5)

C(31)-C(30)-C(29)	106.9(5)
C(32)-C(31)-C(30)	122.0(6)
C(32)-C(31)-N(5)	130.3(5)
C(30)-C(31)-N(5)	107.7(4)
C(33)-C(32)-C(31)	116.7(6)
C(33)-C(32)-H(32)	121.7
C(31)-C(32)-H(32)	121.7
C(32)-C(33)-C(34)	122.2(6)
C(32)-C(33)-H(33)	118.9
C(34)-C(33)-H(33)	118.9
C(35)-C(34)-C(33)	120.9(7)
C(35)-C(34)-H(34)	119.6
C(33)-C(34)-H(34)	119.6
C(34)-C(35)-C(30)	118.4(7)
C(34)-C(35)-H(35)	120.8
C(30)-C(35)-H(35)	120.8
N(6)-C(36)-C(29)	177.3(6)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for d8v23073. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	61(2)	82(3)	129(4)	-12(2)	-12(2)	-11(2)
N(1)	76(3)	57(2)	84(3)	-6(2)	-8(2)	-8(2)
N(2)	58(2)	59(2)	95(3)	-8(2)	-7(2)	-5(2)
N(3)	82(3)	78(3)	109(4)	-18(3)	-1(3)	-17(3)
C(1)	53(2)	56(3)	114(5)	-13(3)	-12(3)	2(2)
C(2)	74(3)	67(3)	100(4)	-9(3)	-26(3)	-2(3)
C(3)	69(3)	53(2)	91(4)	-8(2)	-13(2)	2(2)
C(4)	82(3)	66(3)	84(4)	-5(3)	-14(3)	-5(3)
C(5)	141(6)	89(4)	89(5)	-10(4)	-15(4)	21(4)
C(6)	186(9)	133(7)	78(5)	-13(5)	-5(5)	28(7)
C(7)	193(10)	144(8)	84(5)	-5(5)	-2(6)	-30(7)
C(8)	268(14)	107(6)	100(6)	12(5)	1(7)	-41(8)
C(9)	187(9)	64(4)	96(5)	1(3)	-8(5)	-10(4)
C(10)	55(2)	48(2)	96(4)	-7(2)	-7(2)	3(2)
C(11)	61(3)	58(3)	91(4)	-12(2)	-4(2)	-2(2)
C(12)	64(3)	57(3)	99(4)	-10(3)	3(3)	4(2)
C(13)	62(3)	57(3)	104(4)	-7(3)	5(3)	1(2)
C(14)	64(3)	63(3)	139(6)	-4(3)	13(3)	-3(3)
C(15)	89(4)	90(4)	118(6)	2(4)	21(4)	0(3)
C(16)	95(4)	92(4)	106(5)	-11(4)	18(4)	-3(4)
C(17)	88(4)	74(3)	96(5)	-13(3)	7(3)	-2(3)
C(18)	70(3)	61(3)	86(4)	-11(2)	-3(2)	-1(2)
O(2)	78(2)	74(2)	135(4)	-14(2)	3(2)	-19(2)
N(4)	73(3)	61(2)	79(3)	-6(2)	0(2)	-15(2)
N(5)	67(2)	47(2)	96(3)	-4(2)	4(2)	-7(2)
N(6)	88(3)	85(3)	103(4)	-10(3)	-1(3)	-20(3)
C(19)	71(3)	51(3)	108(4)	-11(3)	-2(3)	-5(2)
C(20)	95(4)	75(4)	96(4)	-19(3)	3(3)	-16(3)
C(21)	76(3)	64(3)	89(4)	-10(3)	-5(3)	-1(2)
C(22)	83(3)	80(3)	75(3)	-8(3)	-3(3)	-3(3)
C(23)	187(7)	125(6)	124(6)	13(5)	46(5)	55(5)
C(24)	187(6)	142(5)	130(5)	2(4)	47(5)	44(5)
C(25)	184(6)	145(5)	130(5)	8(5)	55(5)	20(5)

C(26)	213(7)	133(5)	163(6)	28(5)	76(5)	10(5)
C(27)	216(8)	102(5)	171(7)	26(5)	92(6)	6(6)
C(28)	68(3)	43(2)	88(4)	-5(2)	5(2)	-6(2)
C(29)	62(3)	52(2)	86(4)	-4(2)	4(2)	-8(2)
C(30)	68(3)	54(2)	88(4)	-2(3)	11(2)	2(2)
C(31)	71(3)	46(2)	96(4)	-4(2)	11(3)	3(2)
C(32)	77(3)	61(3)	119(5)	0(3)	20(3)	-5(3)
C(33)	100(5)	80(4)	108(5)	0(4)	33(4)	-5(4)
C(34)	104(5)	84(4)	103(5)	5(4)	30(4)	7(4)
C(35)	87(4)	72(3)	97(4)	-3(3)	12(3)	2(3)
C(36)	69(3)	61(3)	88(4)	-7(2)	3(3)	-6(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for d8v23073.

	x	y	z	U(eq)
H(1)	9451	4444	4081	88
H(2A)	4448	3874	3138	98
H(2B)	4940	3148	2849	98
H(3)	8954	3222	3549	86
H(5)	9310	2968	1768	129
H(6)	10764	3270	215	160
H(7)	11223	4339	-186	169
H(8)	10372	5104	1056	191
H(9)	8806	4805	2583	140
H(14)	2666	2841	6384	106
H(15)	2702	2888	8191	118
H(16)	5611	3499	9127	116
H(17)	8487	4103	8289	103
H(4)	5201	5713	6459	85
H(20A)	8108	7067	7102	107
H(20B)	10545	6813	7666	107
H(21)	9373	5756	7437	92
H(23)	5736	7073	8217	172
H(24)	3489	7074	9677	181
H(25)	3005	6119	10593	181
H(26)	4767	5163	10051	200
H(27)	7013	5162	8592	191
H(32)	12582	7082	4081	102
H(33)	12193	7075	2293	114
H(34)	9099	6509	1399	115
H(35)	6320	5906	2269	102

Table 6. Torsion angles [°] for d8v23073.

C(10)-N(2)-C(1)-O(1)	-177.0(5)
C(13)-N(2)-C(1)-O(1)	-4.5(8)
C(10)-N(2)-C(1)-C(2)	1.5(7)
C(13)-N(2)-C(1)-C(2)	173.9(5)
O(1)-C(1)-C(2)-C(3)	-152.0(5)
N(2)-C(1)-C(2)-C(3)	29.6(6)
C(10)-N(1)-C(3)-C(4)	177.4(5)
C(10)-N(1)-C(3)-C(2)	51.6(6)
C(1)-C(2)-C(3)-N(1)	-53.9(6)
C(1)-C(2)-C(3)-C(4)	-178.9(5)
N(1)-C(3)-C(4)-C(9)	-24.9(9)
C(2)-C(3)-C(4)-C(9)	97.4(8)
N(1)-C(3)-C(4)-C(5)	151.7(6)
C(2)-C(3)-C(4)-C(5)	-86.0(7)
C(9)-C(4)-C(5)-C(6)	-0.3(11)
C(3)-C(4)-C(5)-C(6)	-177.1(7)
C(4)-C(5)-C(6)-C(7)	-0.1(15)
C(5)-C(6)-C(7)-C(8)	1.5(18)
C(6)-C(7)-C(8)-C(9)	-2.6(19)
C(5)-C(4)-C(9)-C(8)	-0.8(13)
C(3)-C(4)-C(9)-C(8)	175.9(9)
C(7)-C(8)-C(9)-C(4)	2.3(18)
C(3)-N(1)-C(10)-C(11)	156.4(5)
C(3)-N(1)-C(10)-N(2)	-22.7(7)
C(1)-N(2)-C(10)-N(1)	-6.3(7)
C(13)-N(2)-C(10)-N(1)	180.0(4)
C(1)-N(2)-C(10)-C(11)	174.4(4)
C(13)-N(2)-C(10)-C(11)	0.7(5)
N(1)-C(10)-C(11)-C(18)	-0.2(9)
N(2)-C(10)-C(11)-C(18)	178.9(5)
N(1)-C(10)-C(11)-C(12)	-179.1(5)
N(2)-C(10)-C(11)-C(12)	0.1(6)
C(10)-C(11)-C(12)-C(17)	178.9(6)
C(18)-C(11)-C(12)-C(17)	0.0(10)
C(10)-C(11)-C(12)-C(13)	-0.9(6)
C(18)-C(11)-C(12)-C(13)	-179.7(5)

C(17)-C(12)-C(13)-C(14)	0.7(8)
C(11)-C(12)-C(13)-C(14)	-179.5(5)
C(17)-C(12)-C(13)-N(2)	-178.5(5)
C(11)-C(12)-C(13)-N(2)	1.3(5)
C(1)-N(2)-C(13)-C(14)	6.3(9)
C(10)-N(2)-C(13)-C(14)	179.7(5)
C(1)-N(2)-C(13)-C(12)	-174.6(5)
C(10)-N(2)-C(13)-C(12)	-1.3(5)
C(12)-C(13)-C(14)-C(15)	0.3(8)
N(2)-C(13)-C(14)-C(15)	179.2(5)
C(13)-C(14)-C(15)-C(16)	-1.1(9)
C(14)-C(15)-C(16)-C(17)	1.0(11)
C(13)-C(12)-C(17)-C(16)	-0.8(8)
C(11)-C(12)-C(17)-C(16)	179.5(6)
C(15)-C(16)-C(17)-C(12)	0.0(10)
C(28)-N(5)-C(19)-O(2)	175.6(5)
C(31)-N(5)-C(19)-O(2)	-13.0(9)
C(28)-N(5)-C(19)-C(20)	-8.6(7)
C(31)-N(5)-C(19)-C(20)	162.8(5)
O(2)-C(19)-C(20)-C(21)	-148.1(6)
N(5)-C(19)-C(20)-C(21)	36.2(8)
C(28)-N(4)-C(21)-C(20)	36.5(7)
C(28)-N(4)-C(21)-C(22)	160.6(5)
C(19)-C(20)-C(21)-N(4)	-48.7(7)
C(19)-C(20)-C(21)-C(22)	-172.2(5)
N(4)-C(21)-C(22)-C(23)	-93.6(6)
C(20)-C(21)-C(22)-C(23)	28.2(7)
N(4)-C(21)-C(22)-C(27)	86.6(6)
C(20)-C(21)-C(22)-C(27)	-151.6(5)
C(27)-C(22)-C(23)-C(24)	0.0
C(21)-C(22)-C(23)-C(24)	-179.8(5)
C(22)-C(23)-C(24)-C(25)	0.0
C(23)-C(24)-C(25)-C(26)	0.0
C(24)-C(25)-C(26)-C(27)	0.0
C(25)-C(26)-C(27)-C(22)	0.0
C(23)-C(22)-C(27)-C(26)	0.0
C(21)-C(22)-C(27)-C(26)	179.8(5)
C(21)-N(4)-C(28)-C(29)	170.9(5)

C(21)-N(4)-C(28)-N(5)	-11.3(7)
C(19)-N(5)-C(28)-N(4)	-4.7(7)
C(31)-N(5)-C(28)-N(4)	-177.4(4)
C(19)-N(5)-C(28)-C(29)	173.5(5)
C(31)-N(5)-C(28)-C(29)	0.8(5)
N(4)-C(28)-C(29)-C(36)	-6.6(9)
N(5)-C(28)-C(29)-C(36)	175.4(5)
N(4)-C(28)-C(29)-C(30)	176.1(5)
N(5)-C(28)-C(29)-C(30)	-1.8(6)
C(28)-C(29)-C(30)-C(35)	-176.7(6)
C(36)-C(29)-C(30)-C(35)	6.0(9)
C(28)-C(29)-C(30)-C(31)	2.2(6)
C(36)-C(29)-C(30)-C(31)	-175.1(5)
C(35)-C(30)-C(31)-C(32)	-1.8(8)
C(29)-C(30)-C(31)-C(32)	179.2(5)
C(35)-C(30)-C(31)-N(5)	177.3(5)
C(29)-C(30)-C(31)-N(5)	-1.7(5)
C(19)-N(5)-C(31)-C(32)	7.2(9)
C(28)-N(5)-C(31)-C(32)	179.6(5)
C(19)-N(5)-C(31)-C(30)	-171.8(5)
C(28)-N(5)-C(31)-C(30)	0.7(5)
C(30)-C(31)-C(32)-C(33)	1.5(8)
N(5)-C(31)-C(32)-C(33)	-177.3(6)
C(31)-C(32)-C(33)-C(34)	-0.2(10)
C(32)-C(33)-C(34)-C(35)	-0.9(11)
C(33)-C(34)-C(35)-C(30)	0.7(10)
C(31)-C(30)-C(35)-C(34)	0.6(8)
C(29)-C(30)-C(35)-C(34)	179.4(6)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for d8v23073 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(32)-H(32)...O(2)	0.93	2.48	2.986(9)	114.1
C(21)-H(21)...N(3)	0.98	2.63	3.484(8)	145.2
N(4)-H(4)...N(3)#1	0.86	2.25	3.081(7)	161.9
C(14)-H(14)...O(1)	0.93	2.44	2.956(10)	115.1
C(3)-H(3)...O(2)#2	0.98	2.55	3.309(7)	134.6
C(3)-H(3)...O(1)#3	0.98	2.45	3.236(7)	136.4
N(1)-H(1)...N(6)#3	0.86	2.21	2.986(7)	150.6
N(1)-H(1)...N(6)#3	0.86	2.21	2.986(7)	150.6
C(3)-H(3)...O(1)#3	0.98	2.45	3.236(7)	136.4
C(3)-H(3)...O(2)#2	0.98	2.55	3.309(7)	134.6
C(14)-H(14)...O(1)	0.93	2.44	2.956(10)	115.1
N(4)-H(4)...N(3)#1	0.86	2.25	3.081(7)	161.9
C(21)-H(21)...N(3)	0.98	2.63	3.484(8)	145.2
C(32)-H(32)...O(2)	0.93	2.48	2.986(9)	114.1

Symmetry transformations used to generate equivalent atoms:

#1 x-1,y,z #2 -x+2,y-1/2,-z+1 #3 x+1,y,z

5. References

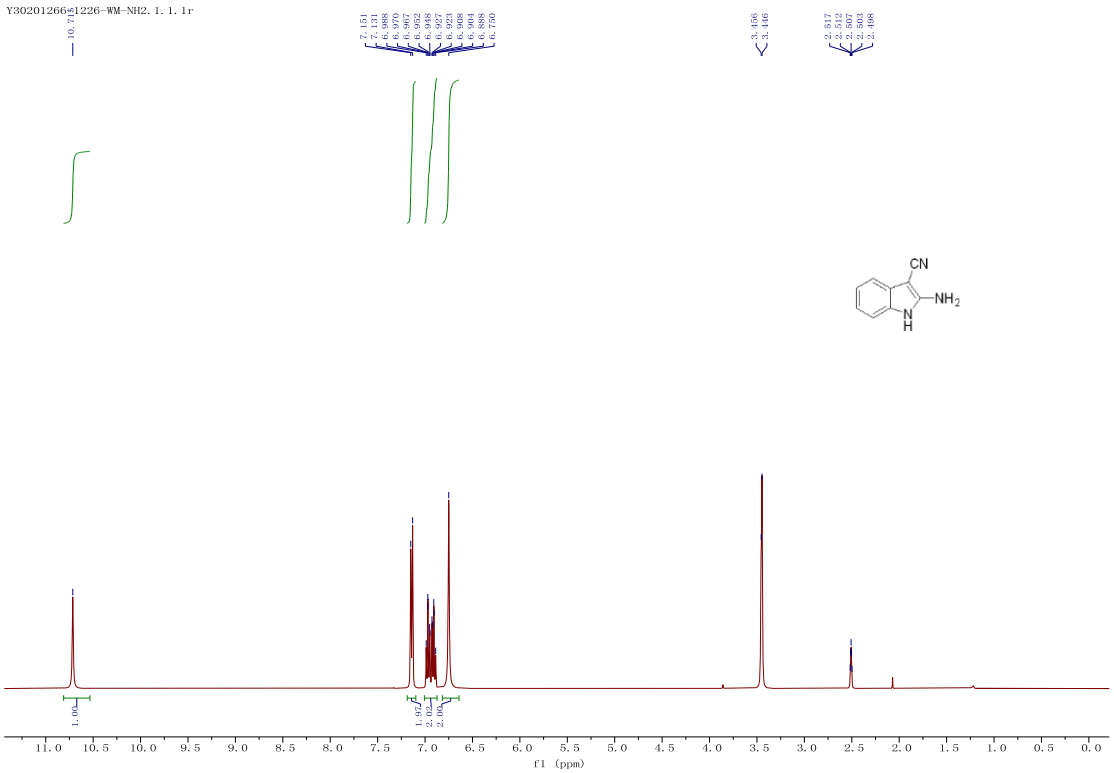
1. O. Benek., O. Soukup., M. Pasdiorova., L. Hroch., V. Sepsova., P. Jost., M. Hrabinova., D. Jun., K. Kuca., D. Zala., R. R. Ramsay., J. Marco-Contelles, and K. Musilek., *Chem. Med. Chem.*, **2016**, *11(12)*, 1264 -1269.

2. a). X.-B. Yang, H. Fu, R.-Z. Qiao, Y.-Y. Jiang, Y.-F. Zhao, *Adv. Syn & Cat*., 2010, **352**, 1033 - 1038. b). C. Willemann, R. Grünert, P. J. Bednarski, R. Troschütz. *Bioorg. Med. Chem.*, 2009, **17**, 4406 - 4419.

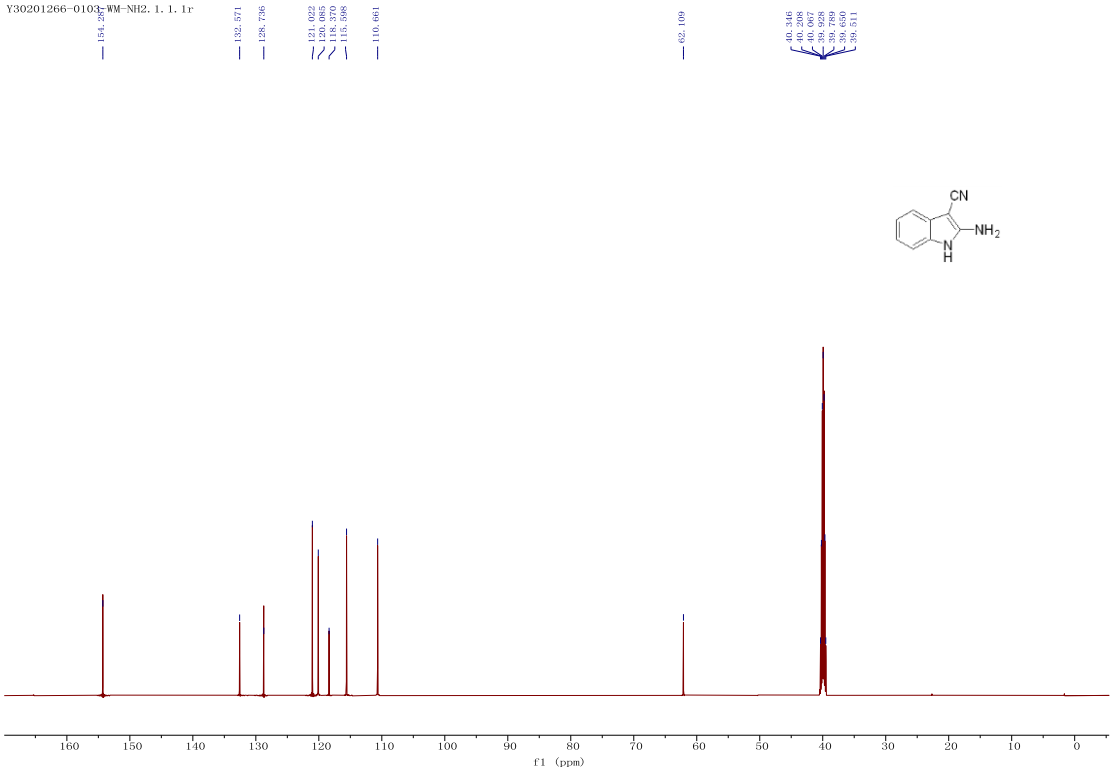
3. Y. Liu, J. Chen, Z. Zhang, J. Qin, M. Zhao and W. Zhang. *Org. Biomol. Chem.*, **2016**, *14(29)*, 7099 - 7102.

6. ^{1}H, ^{13}C and ^{19}F NMR spectra and HPLC Spectra

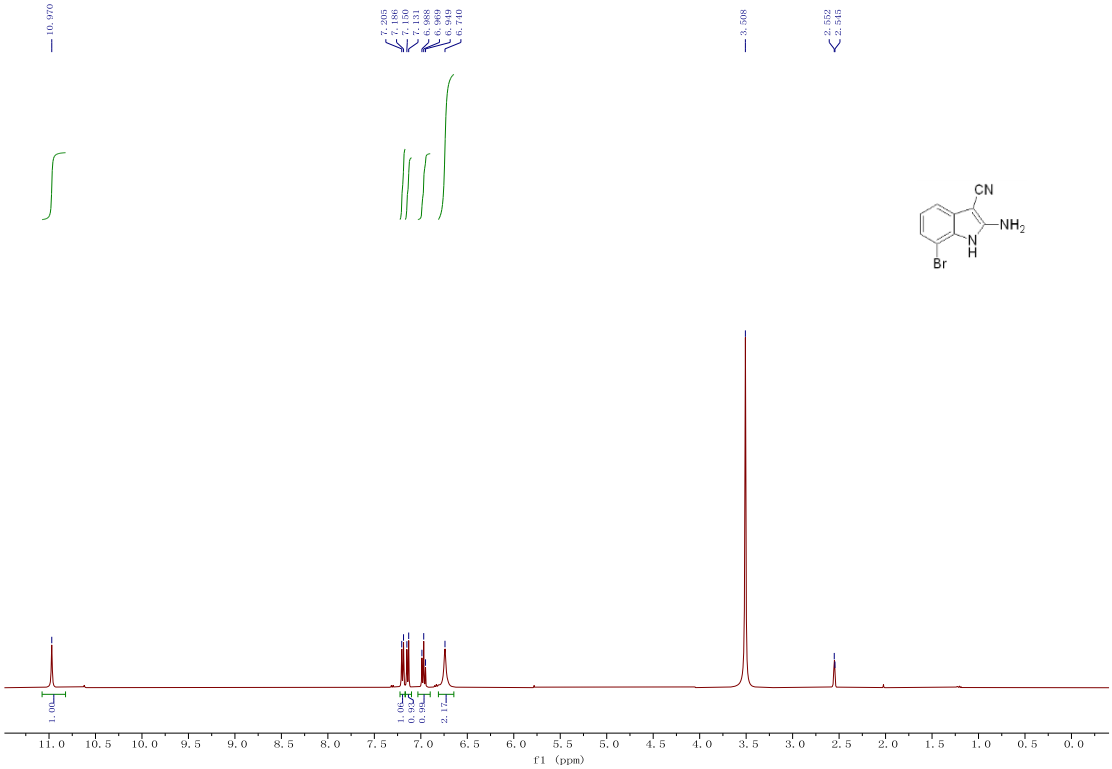
2-Amino-1H-indole-3-carbonitrile (1a). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.45, 2.50 ppm)]



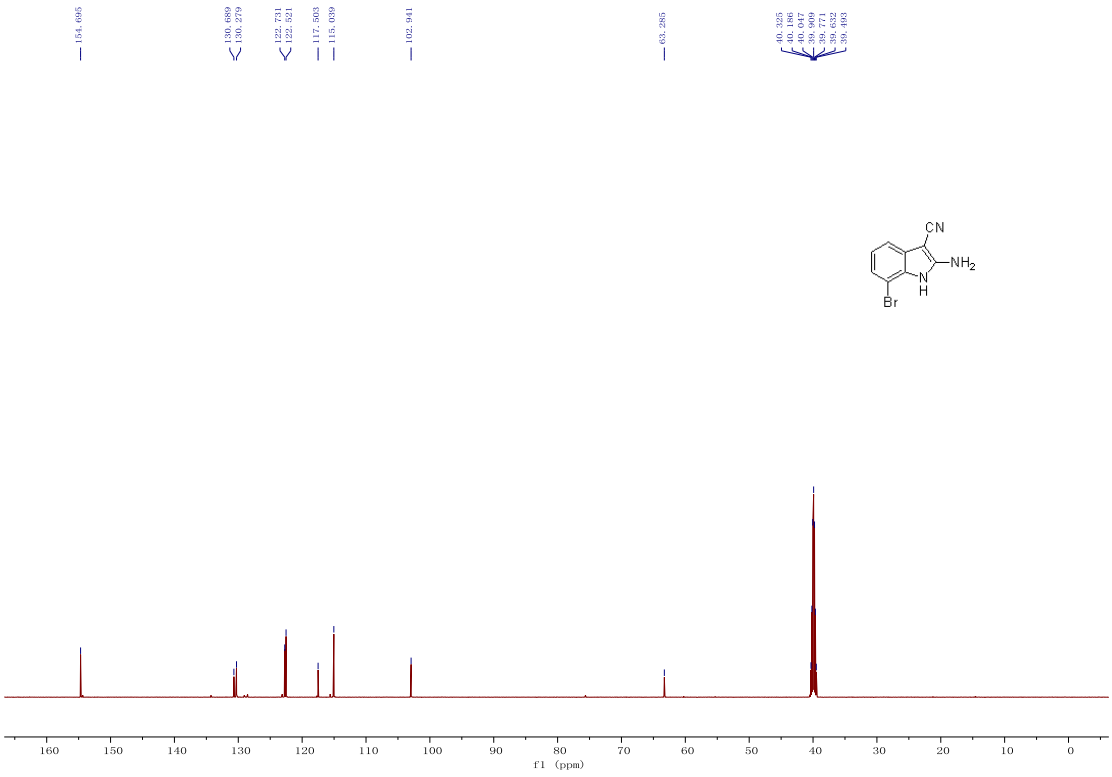
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



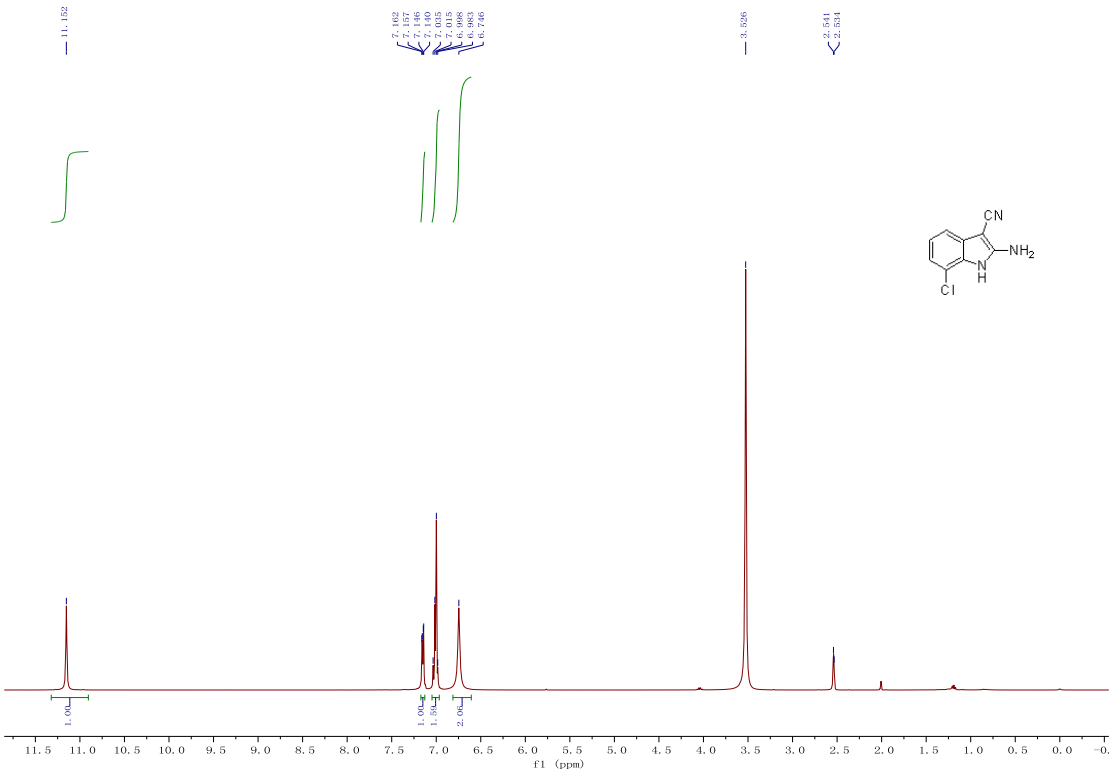
2-Amino-7-bromo-1H-indole-3-carbonitrile (1b). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.5, 2.50 ppm)]



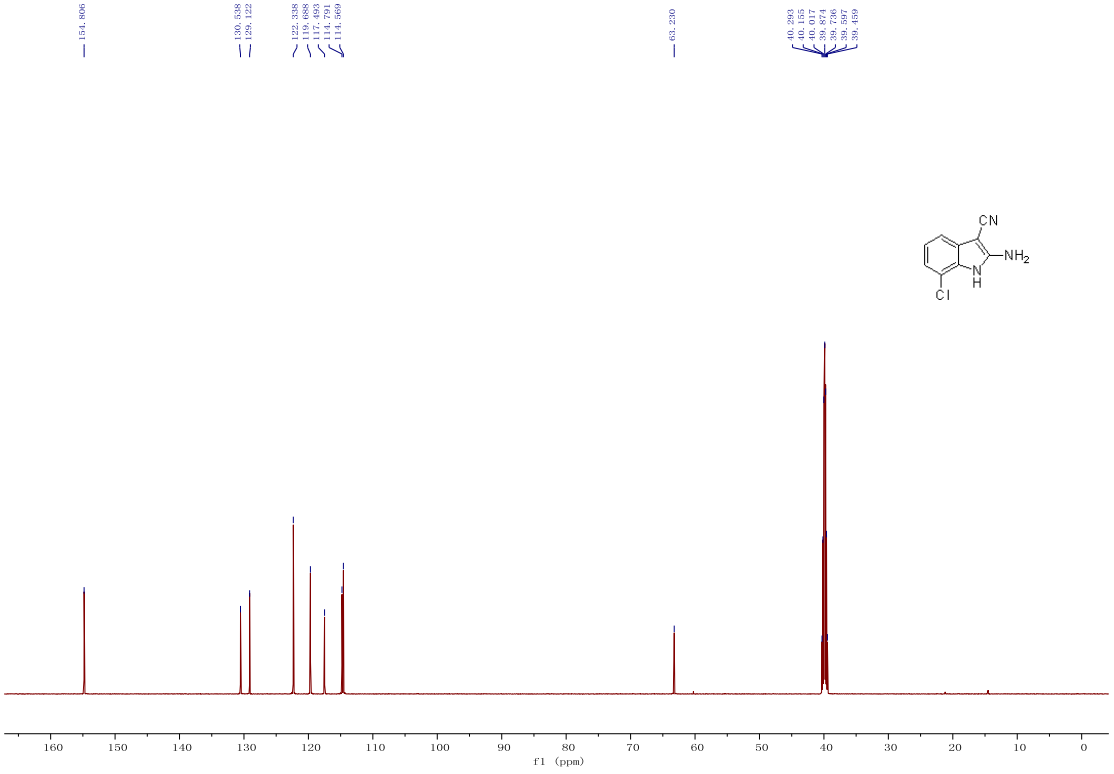
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



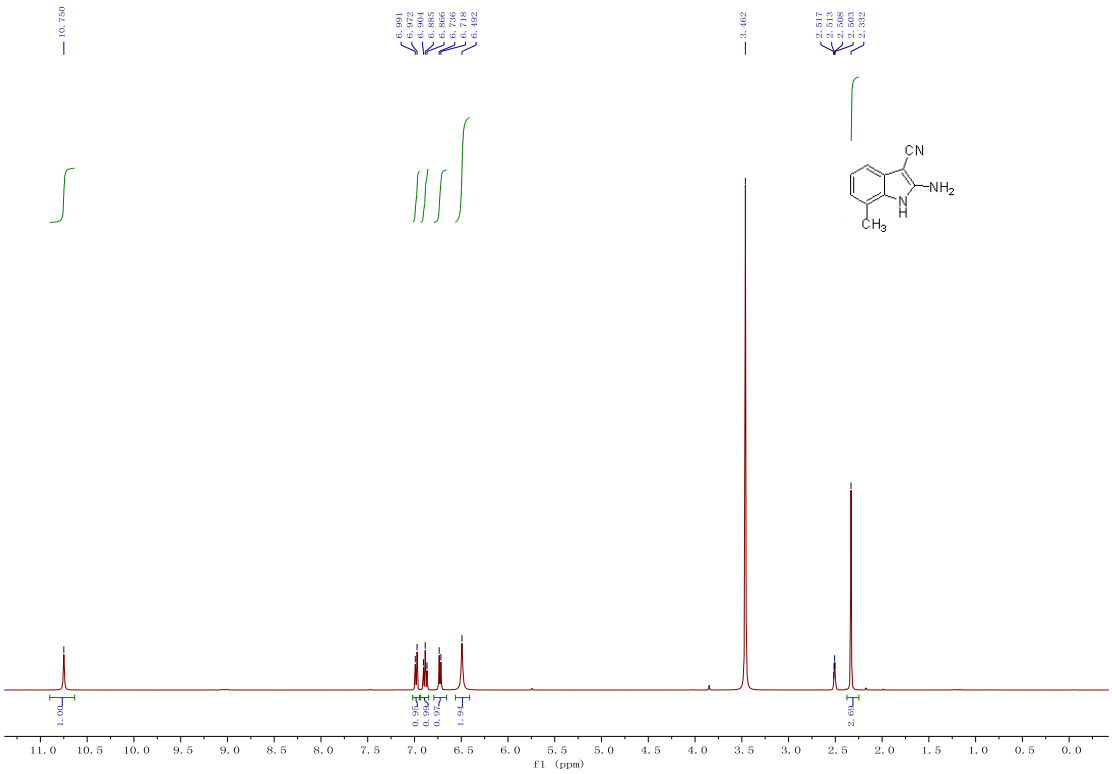
2-Amino-7-chloro-1H-indole-3-carbonitrile (1c). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



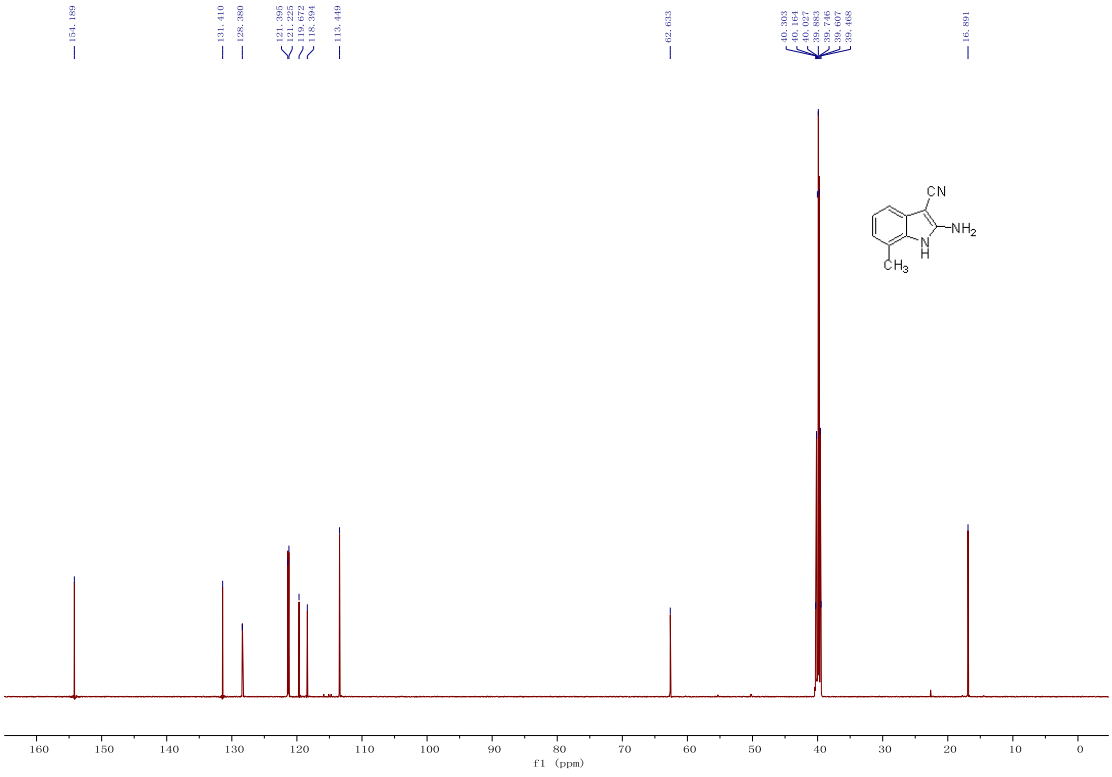
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



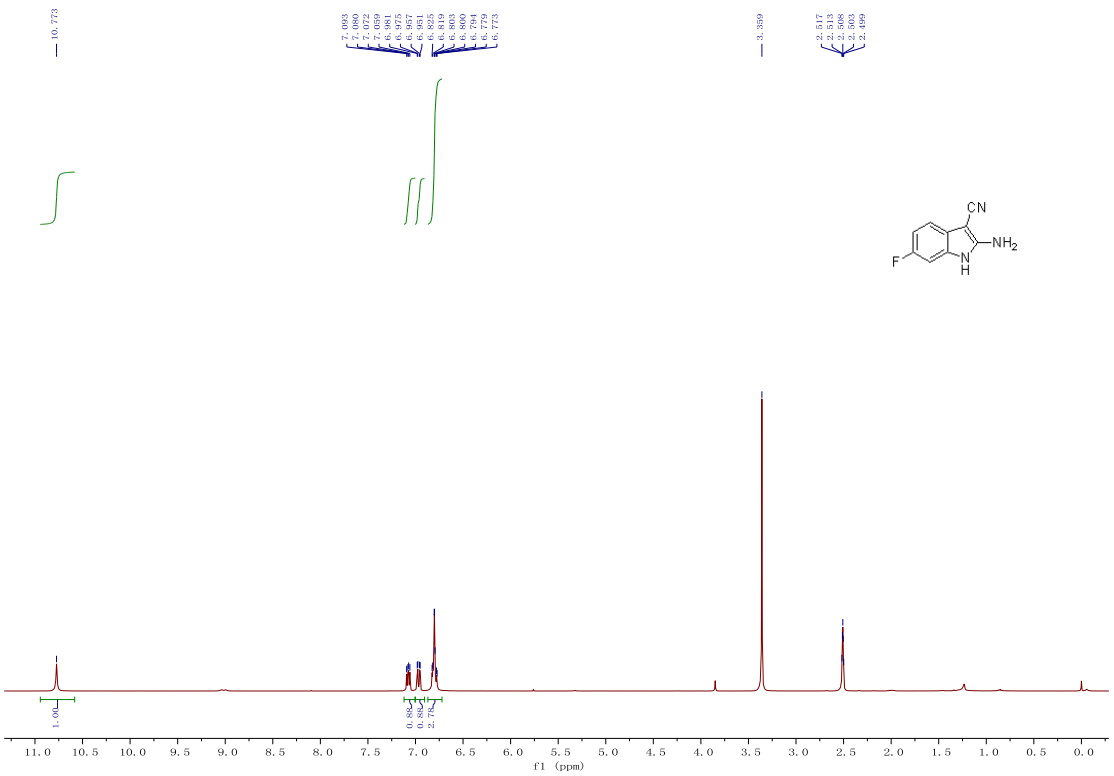
2-Amino-7-methyl-1H-indole-3-carbonitrile (1d). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



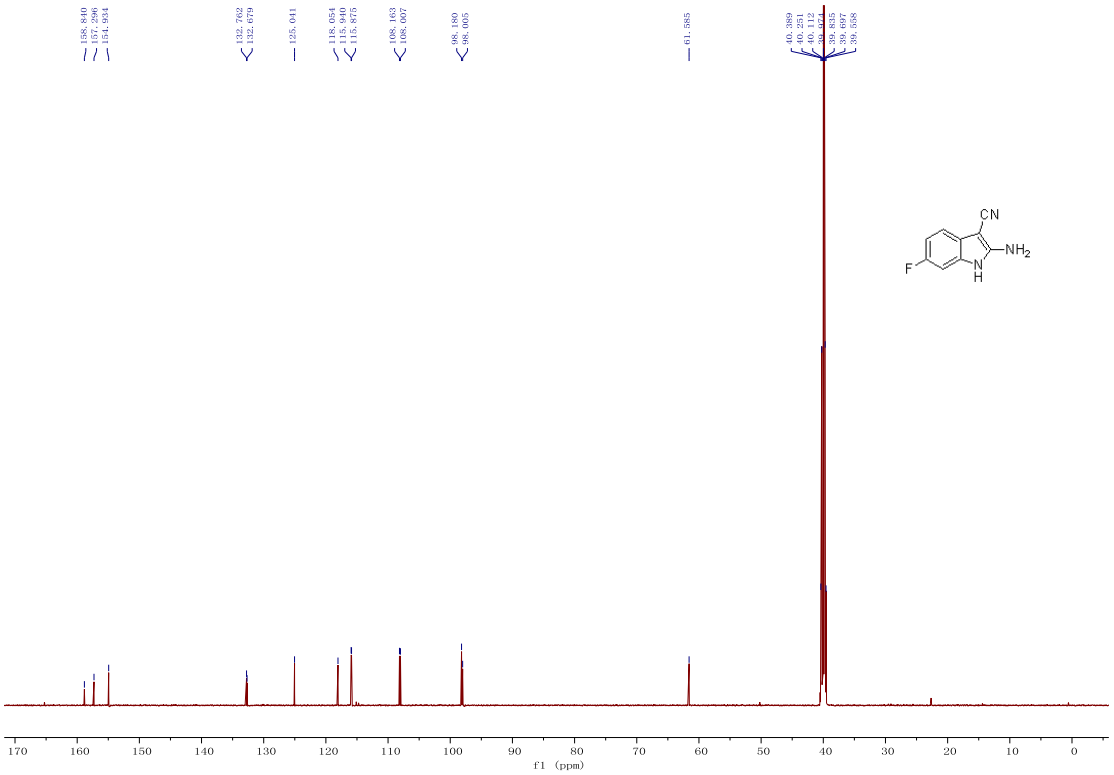
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



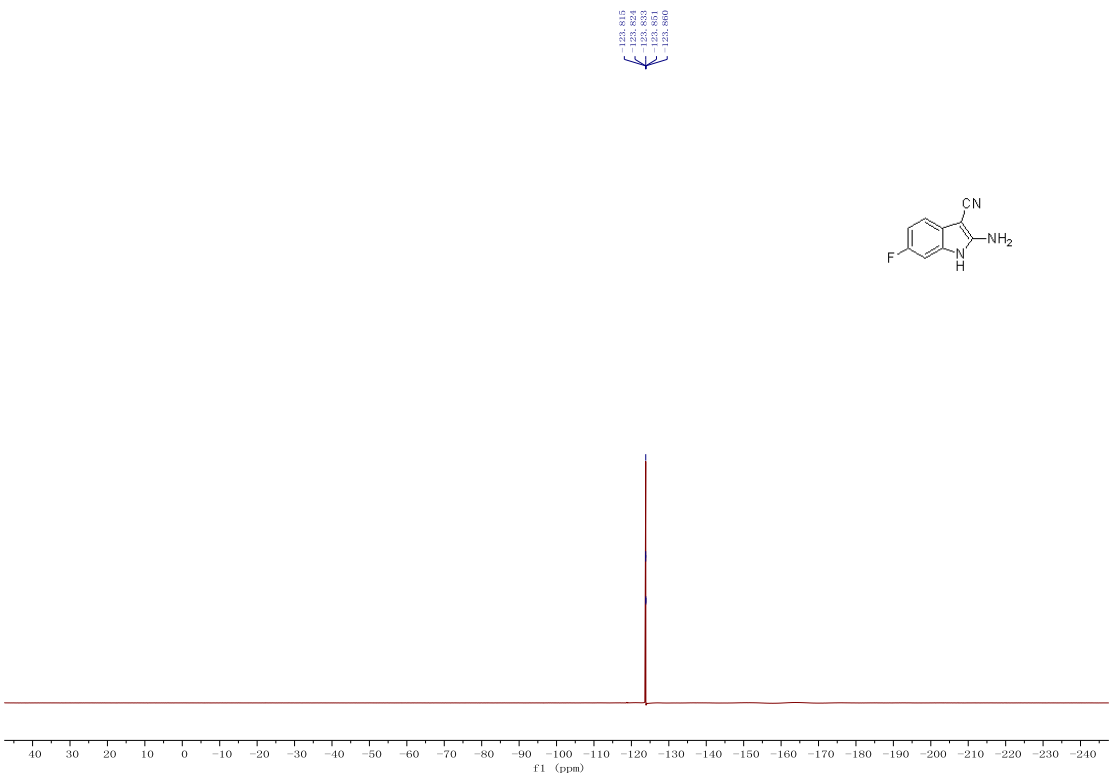
2-Amino-6-fluoro-1H-indole-3-carbonitrile (1e). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



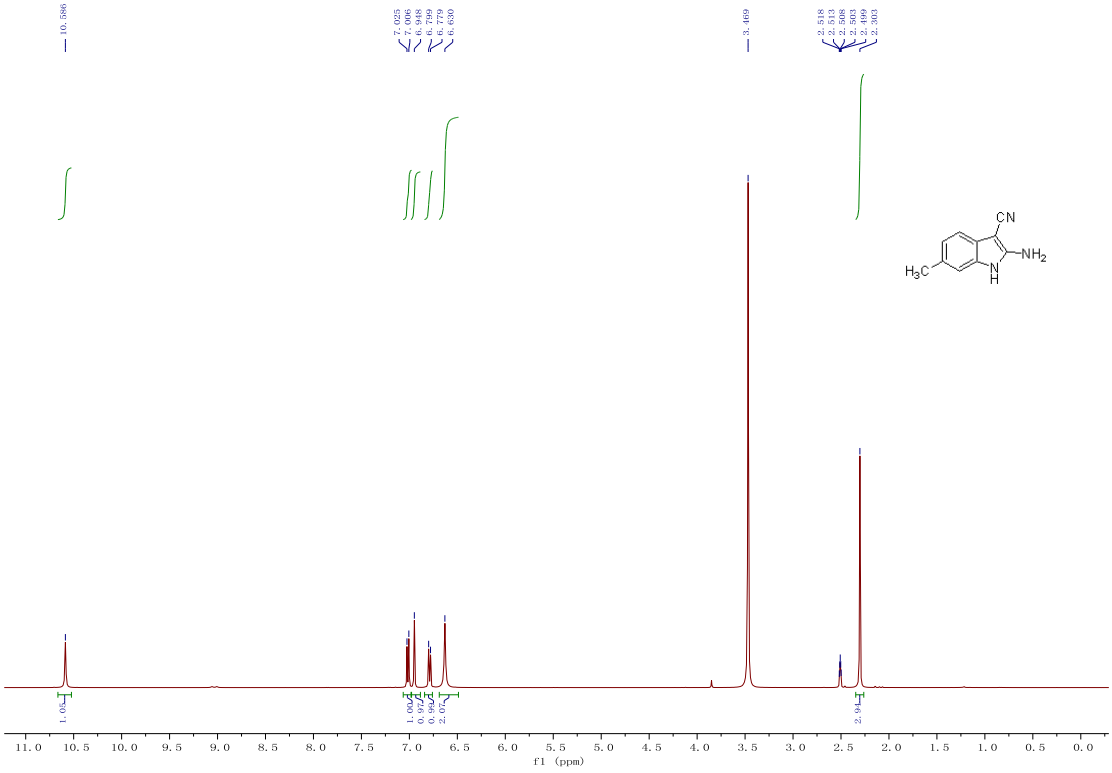
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



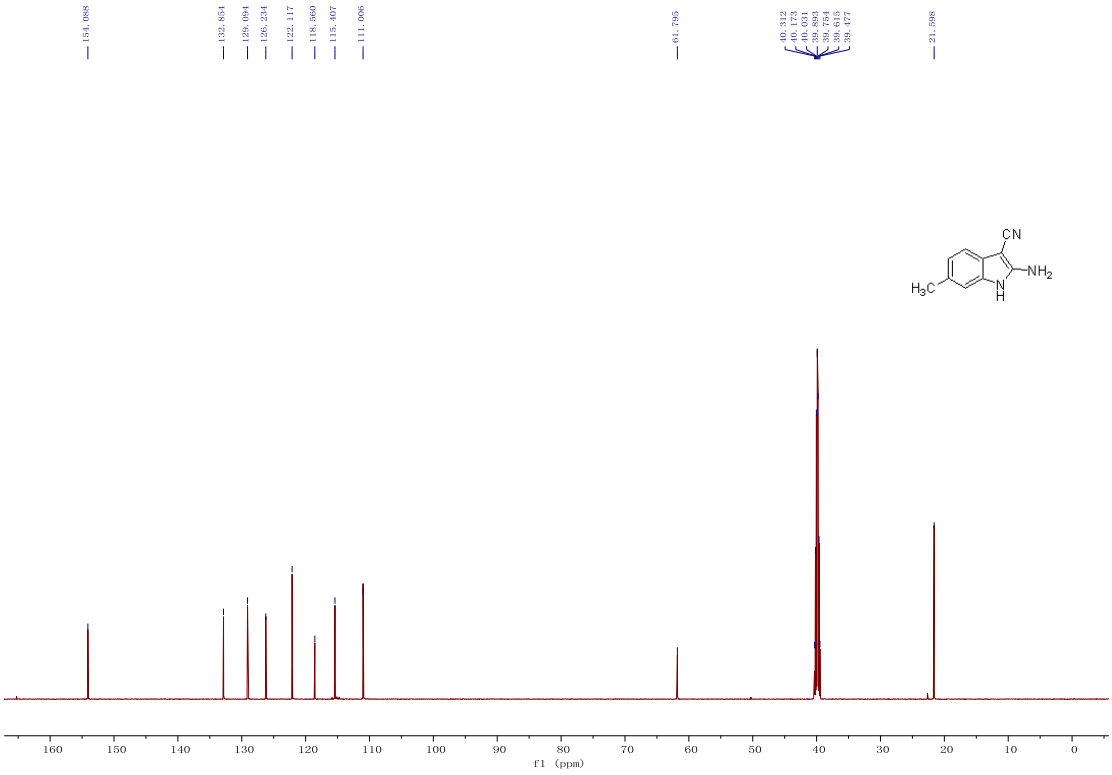
[^{19}F_NMR_565 MHz]


123.815
123.834
123.853
123.871
123.880
CN
NH2
F
N
H
40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

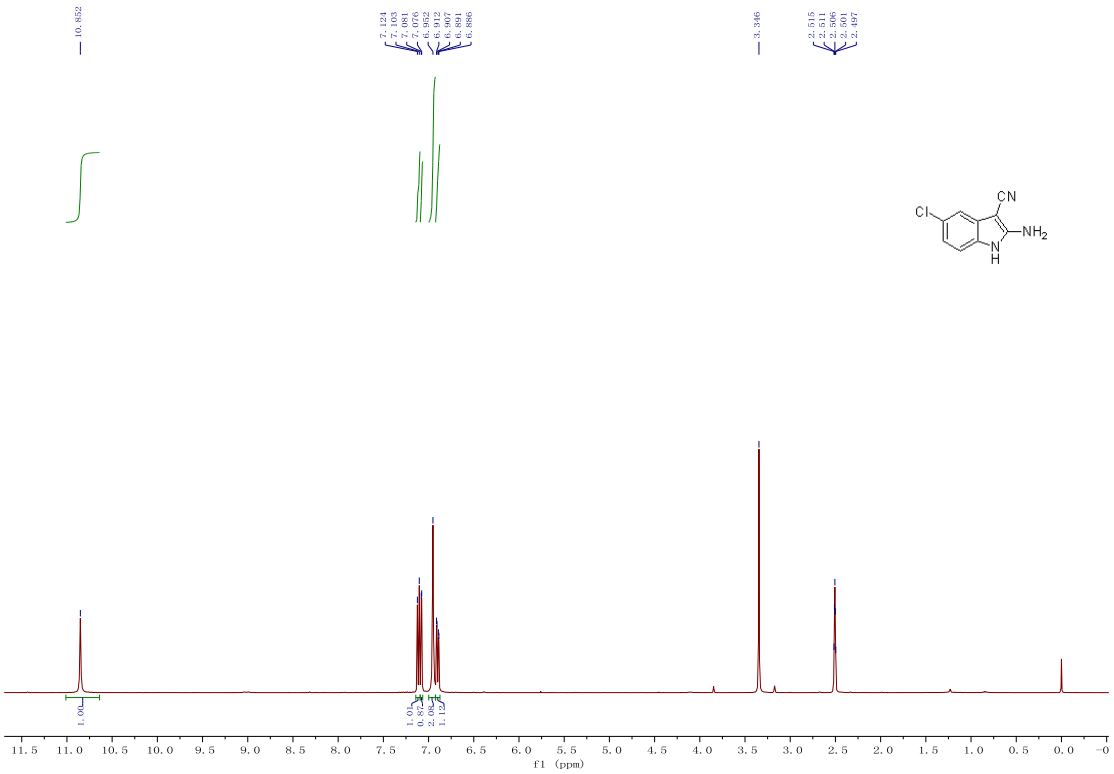
2-Amino-6-methyl-1H-indole-3-carbonitrile (1f). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



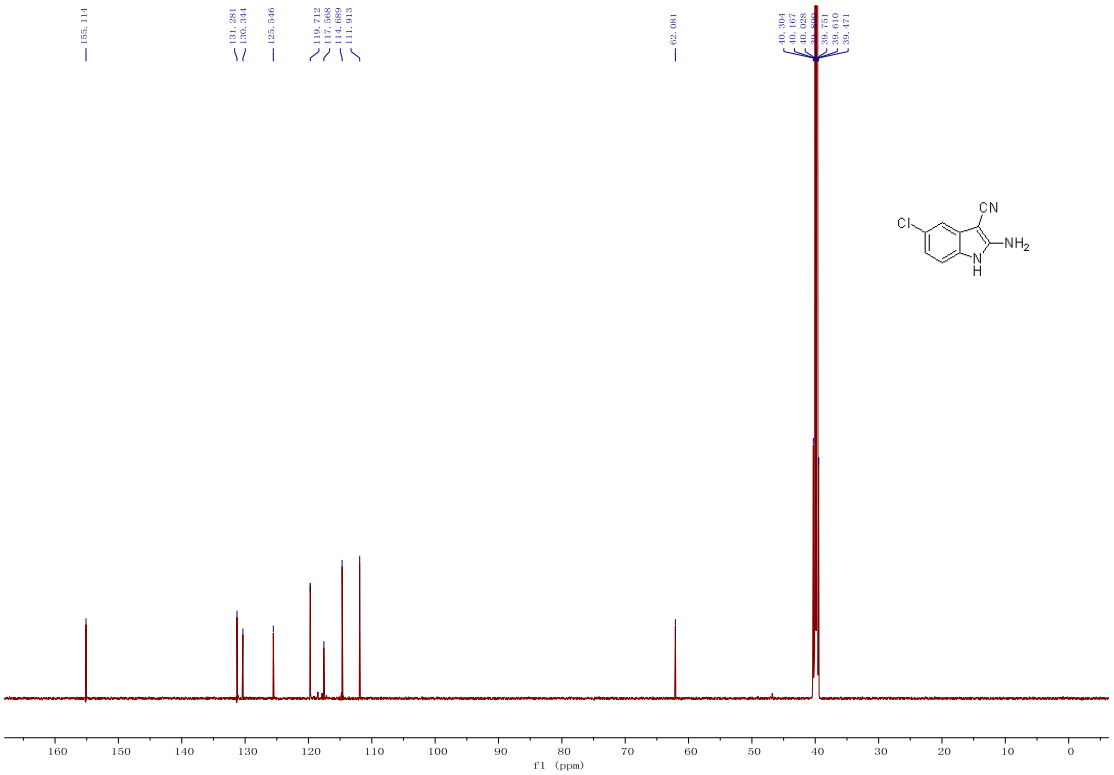
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



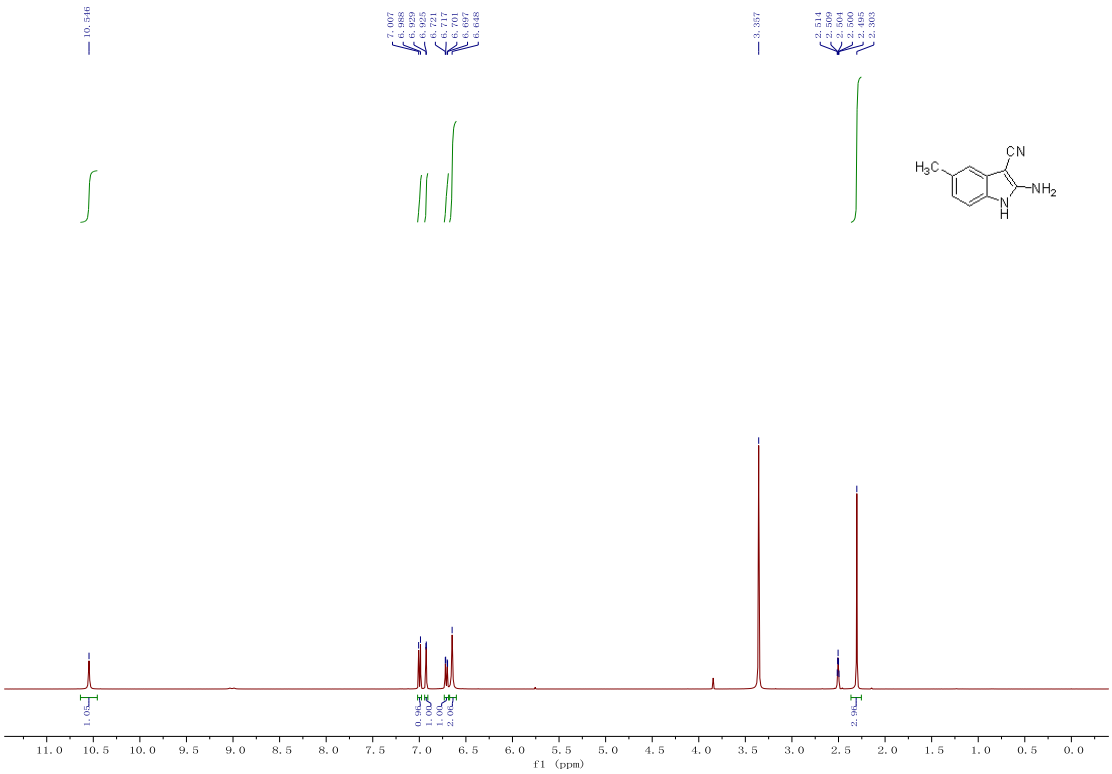
2-Amino-5-chloro-1H-indole-3-carbonitrile (1g). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



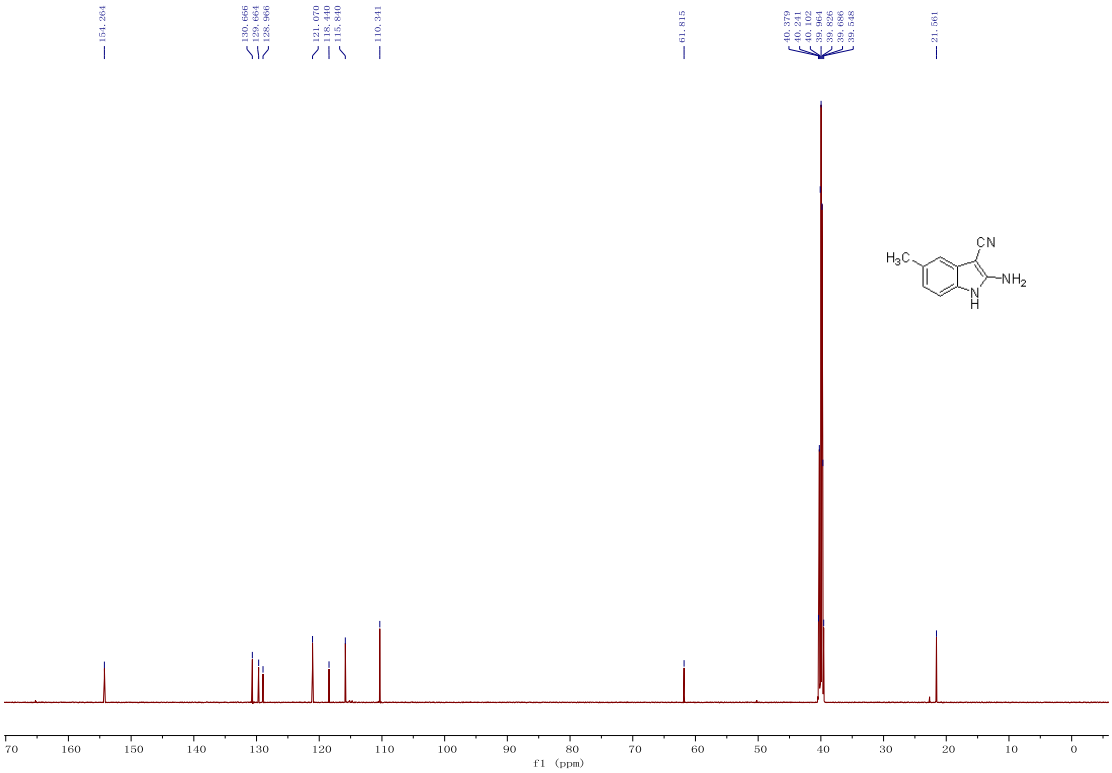
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



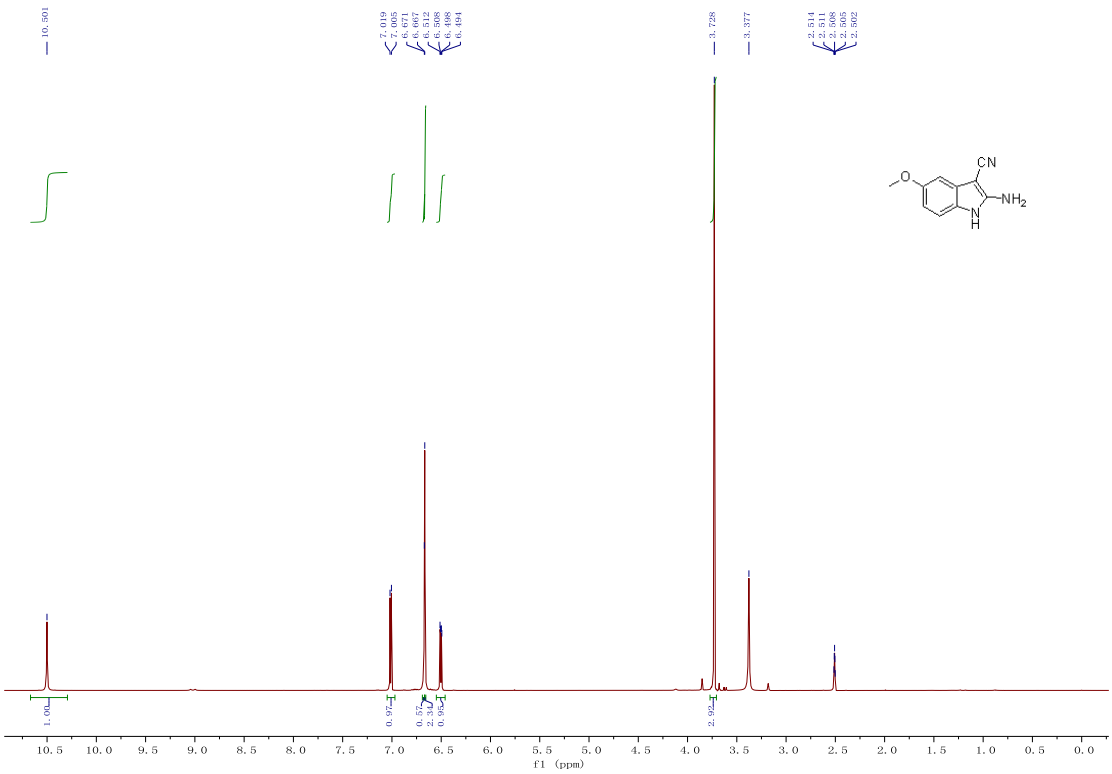
2-Amino-5-methyl-1H-indole-3-carbonitrile (1h). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



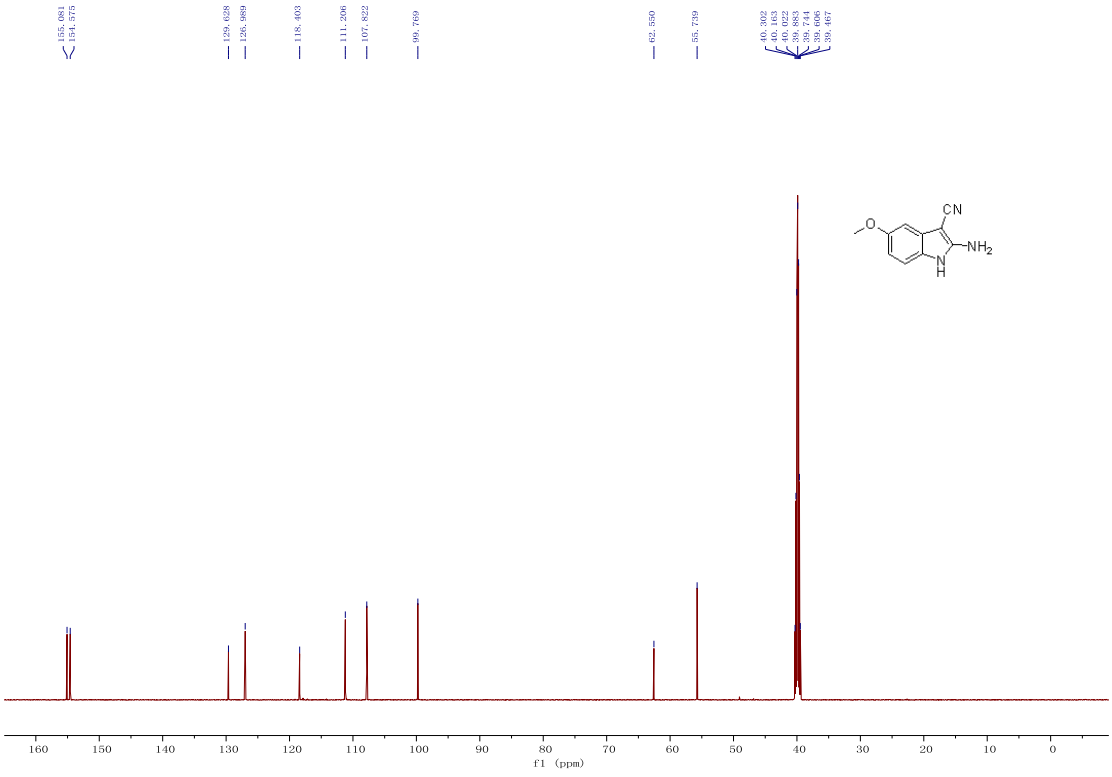
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



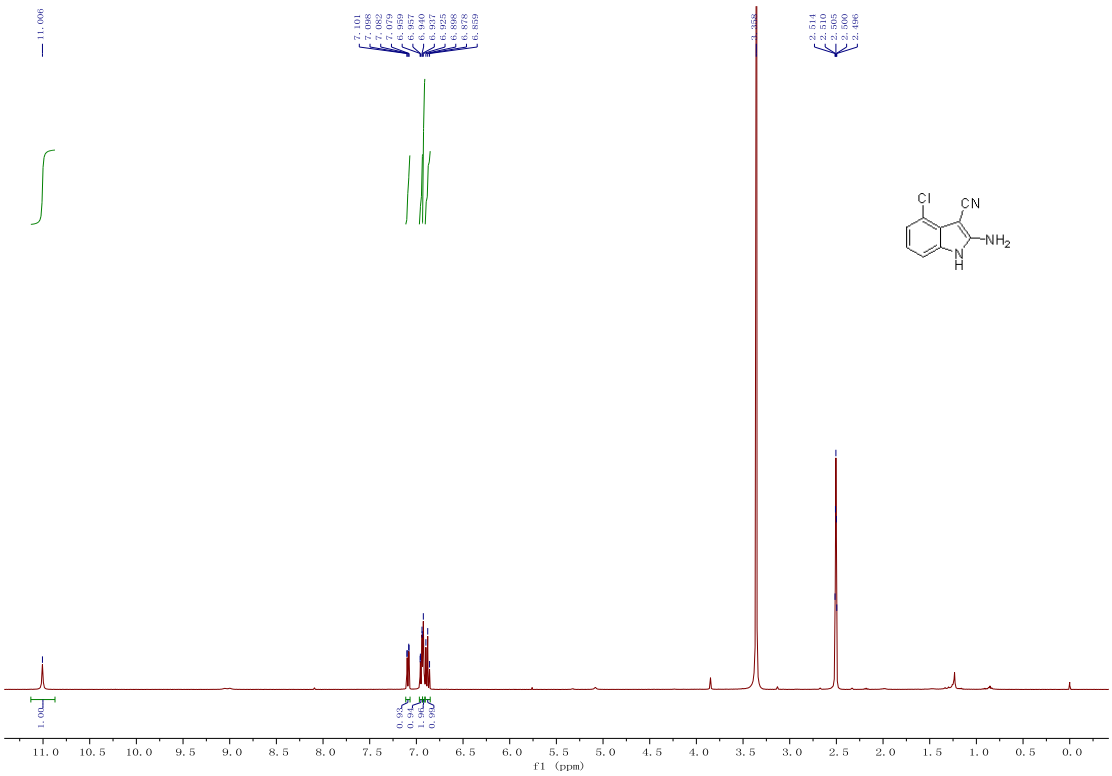
2-Amino-5-methoxy-1H-indole-3-carbonitrile (1i). [^{1}H_NMR_600 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



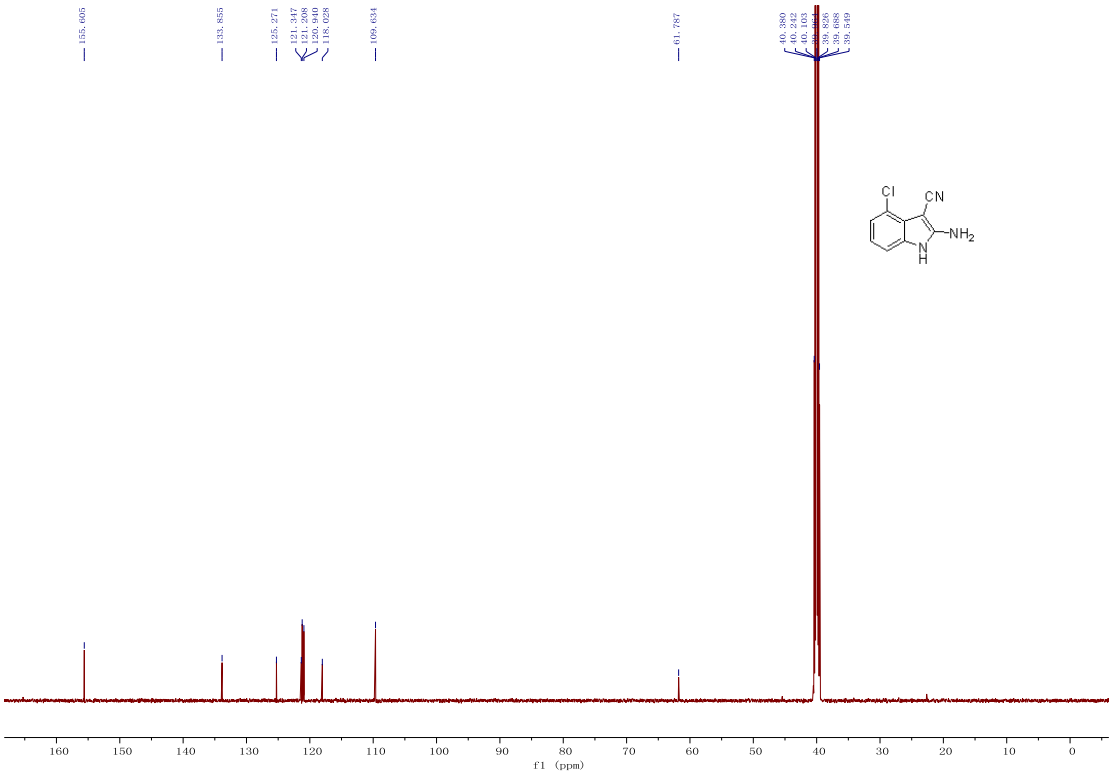
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



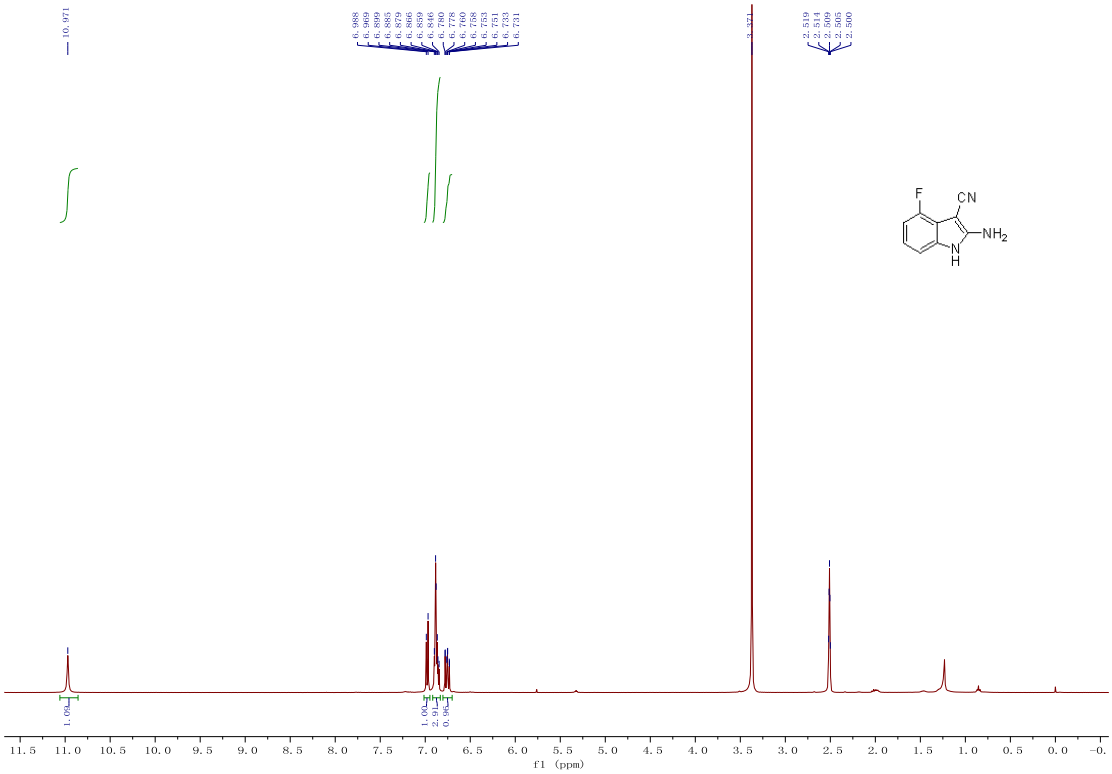
2-Amino-4-chloro-1H-indole-3-carbonitrile (1j). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



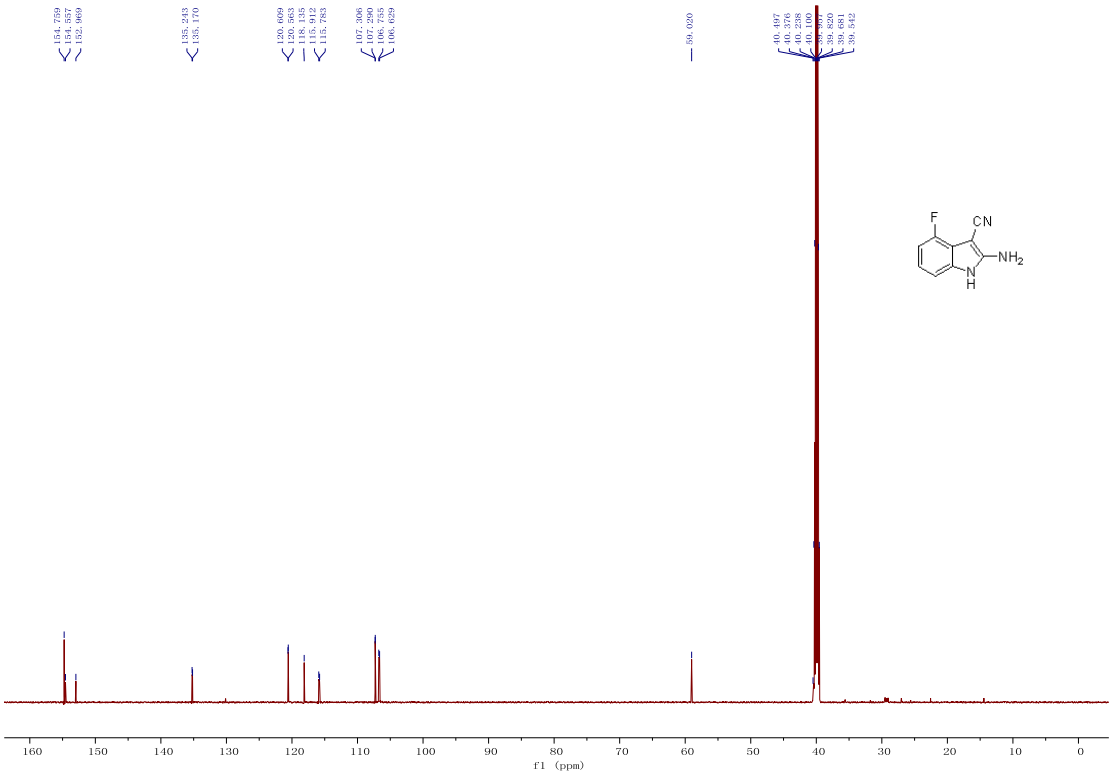
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



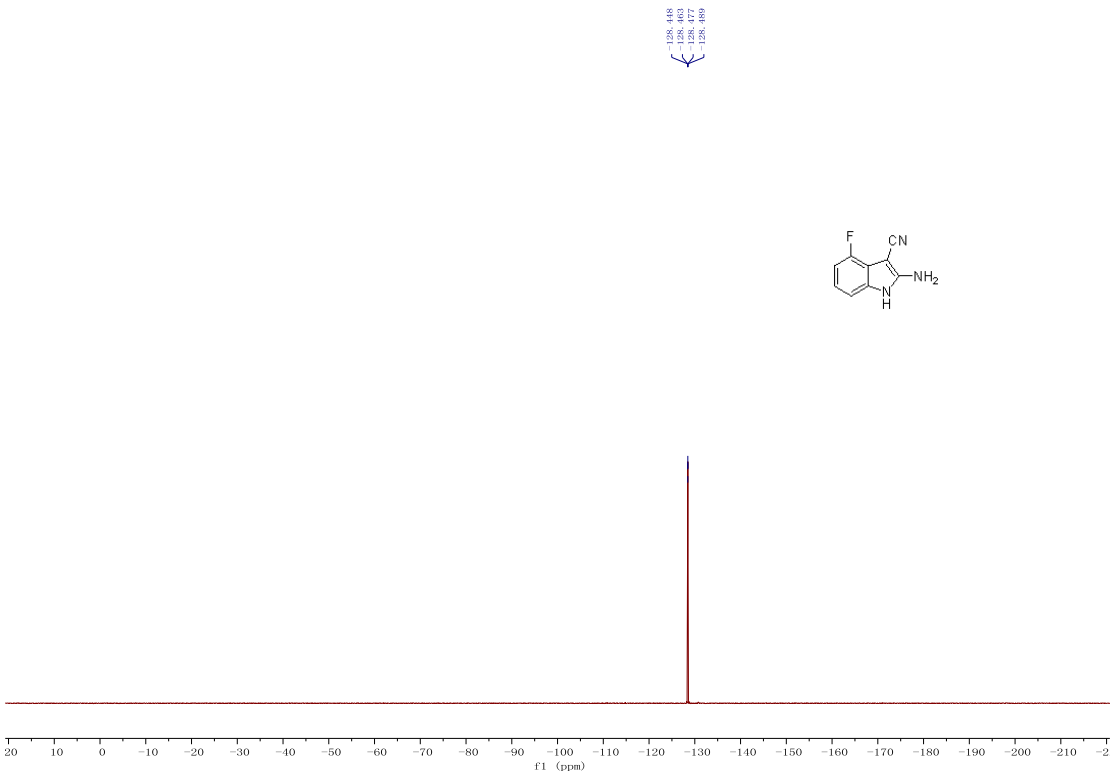
2-Amino-4-fluoro-1H-indole-3-carbonitrile (1k). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



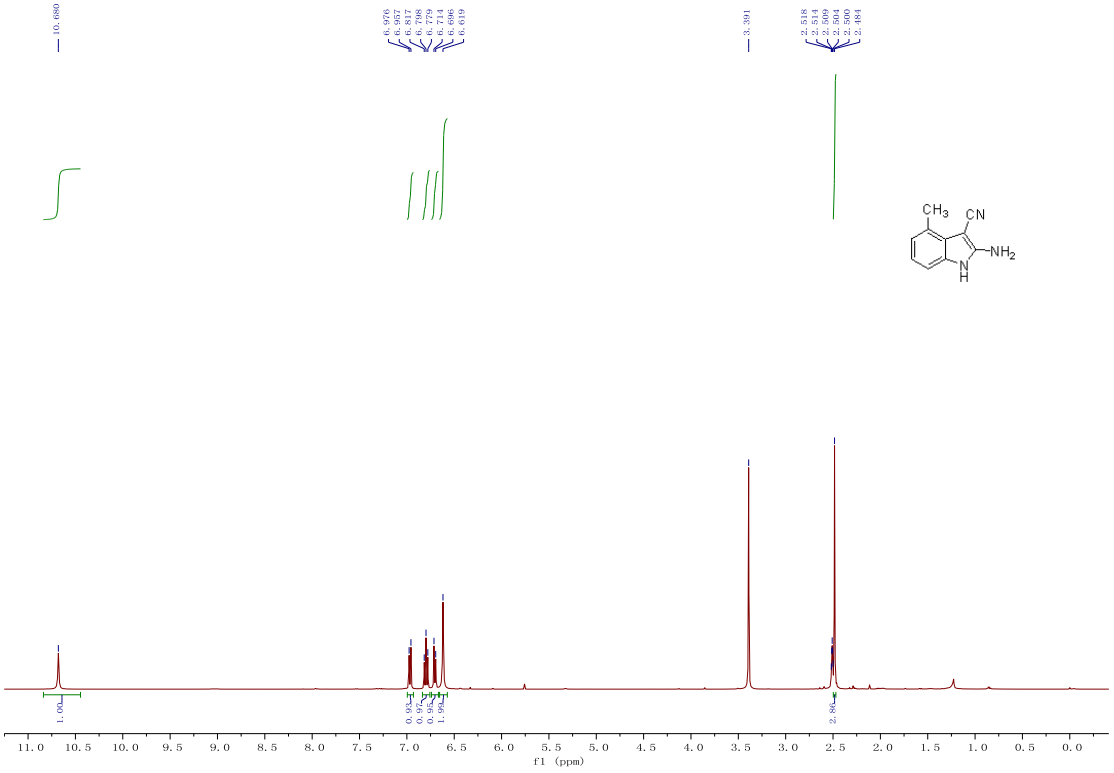
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



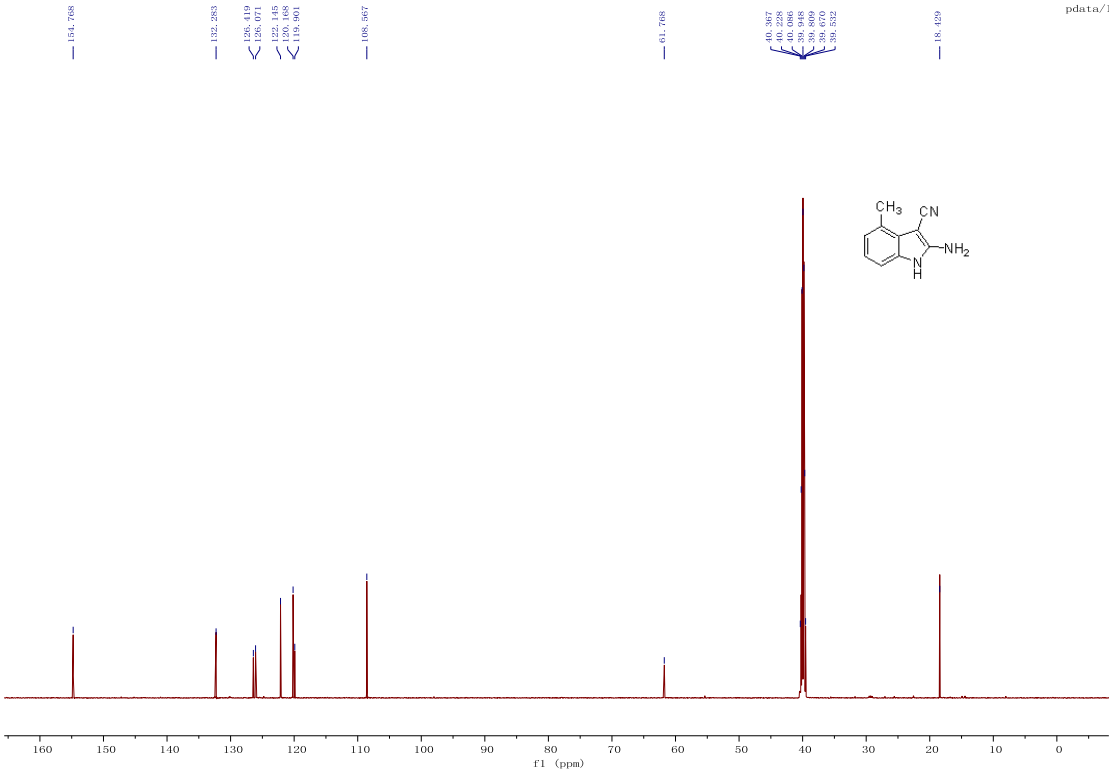
[^{19}F_NMR_565 MHz]


-128.448
-128.463
-128.477
-128.489
F
CN
NH2
N
H
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -2
f1 (ppm)

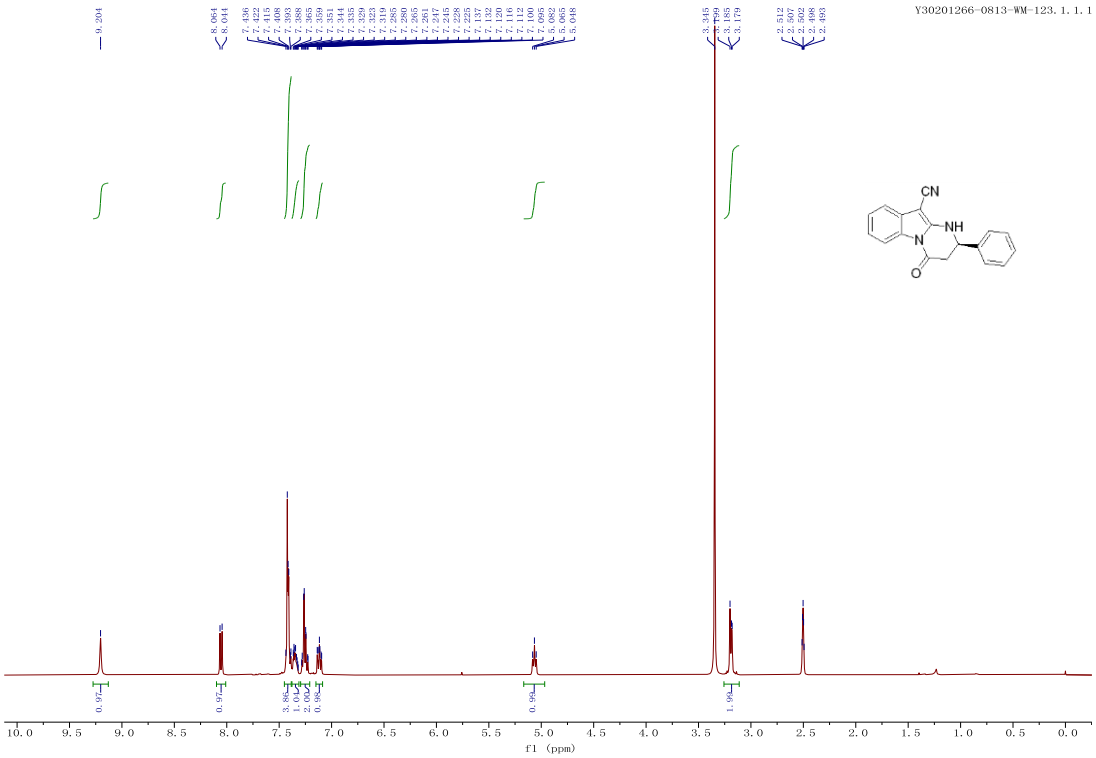
2-Amino-4-methyl-1H-indole-3-carbonitrile (1l). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



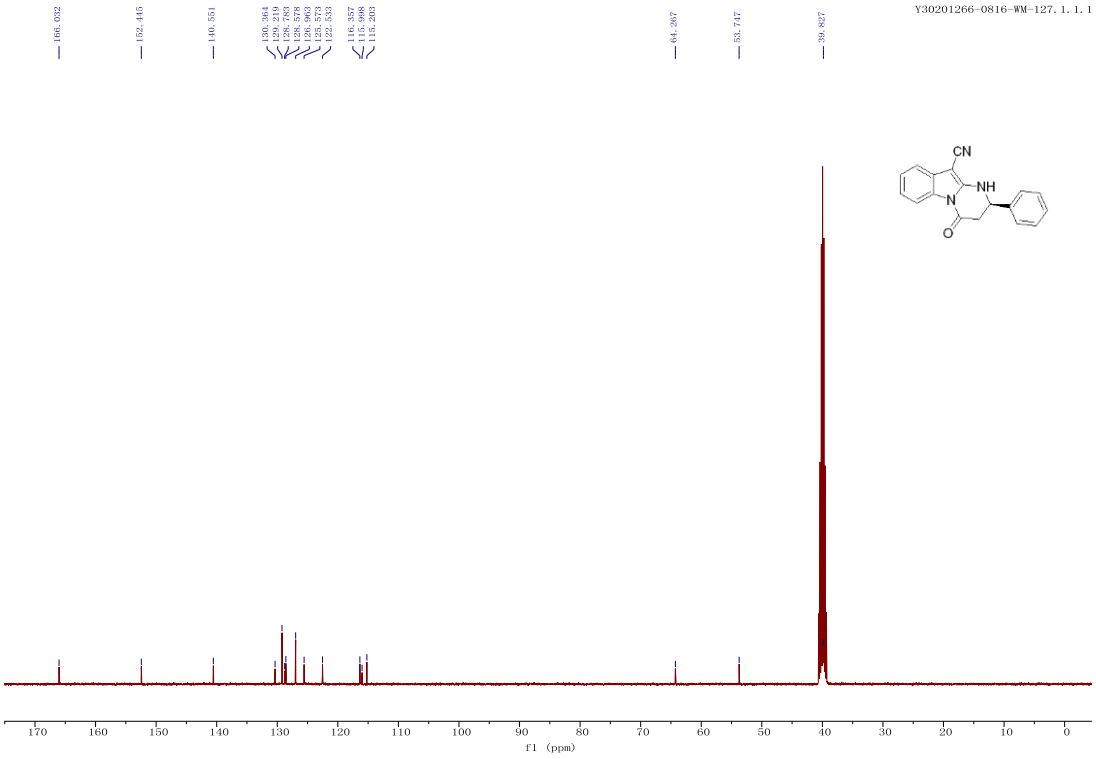
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



(*R*)-4-Oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3a). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.35, 2.50 ppm)]

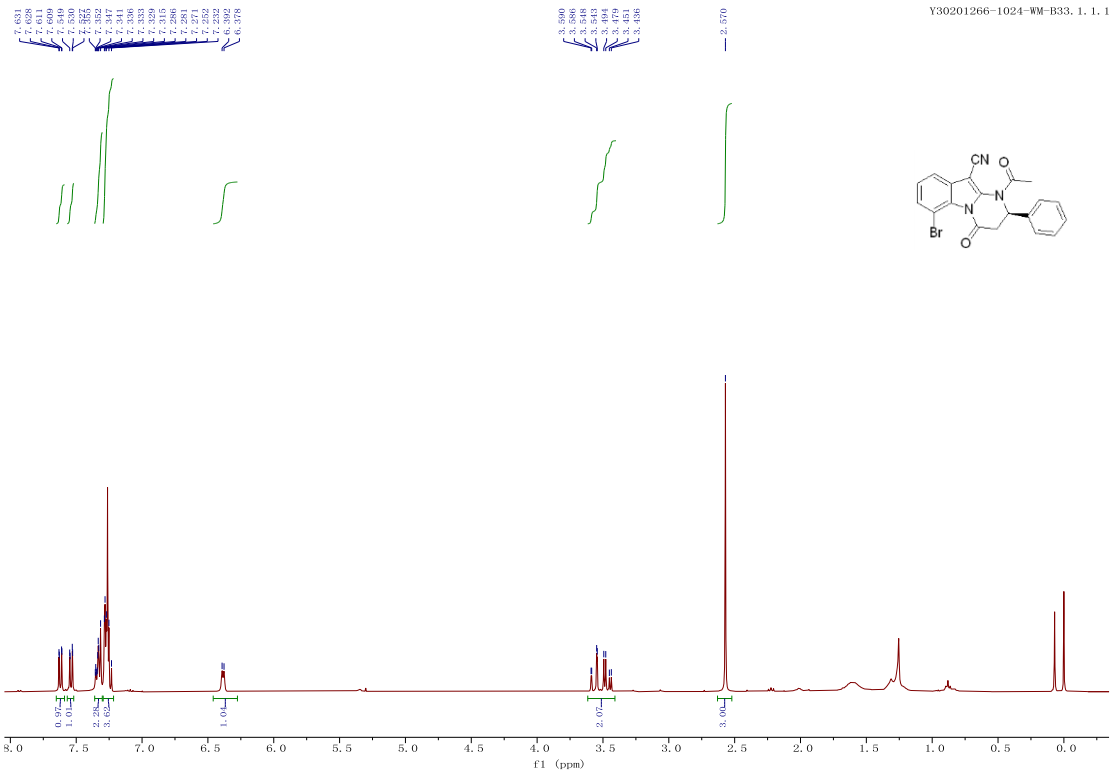


[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]

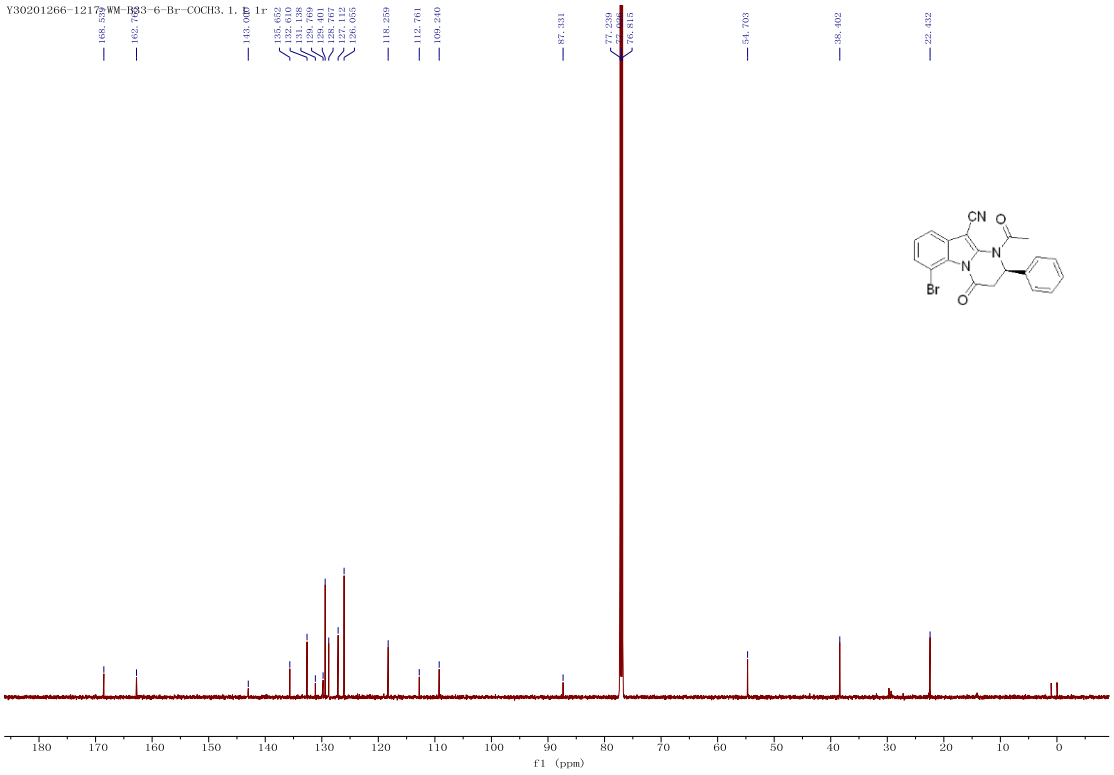


(*R*)-1-Acetyl-6-bromo-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-

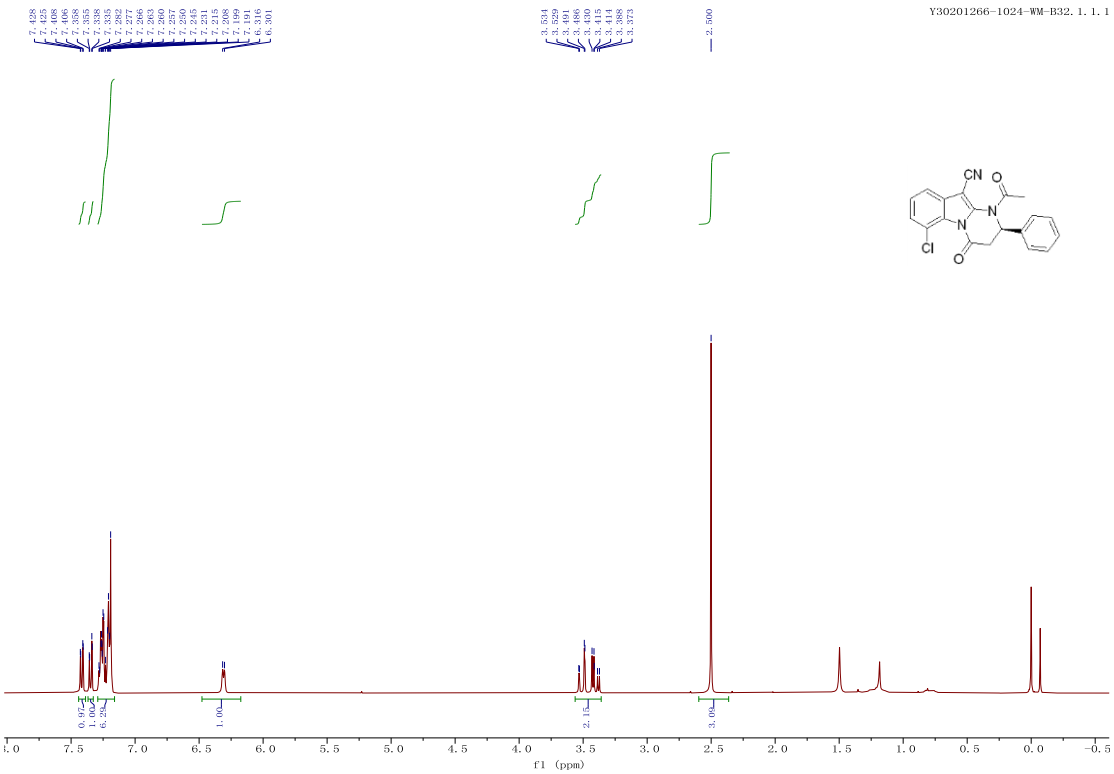
10-carbonitrile (3b'). [^{1}H_NMR_400 MHz_(CDCl$_3$: 7.26 ppm)]



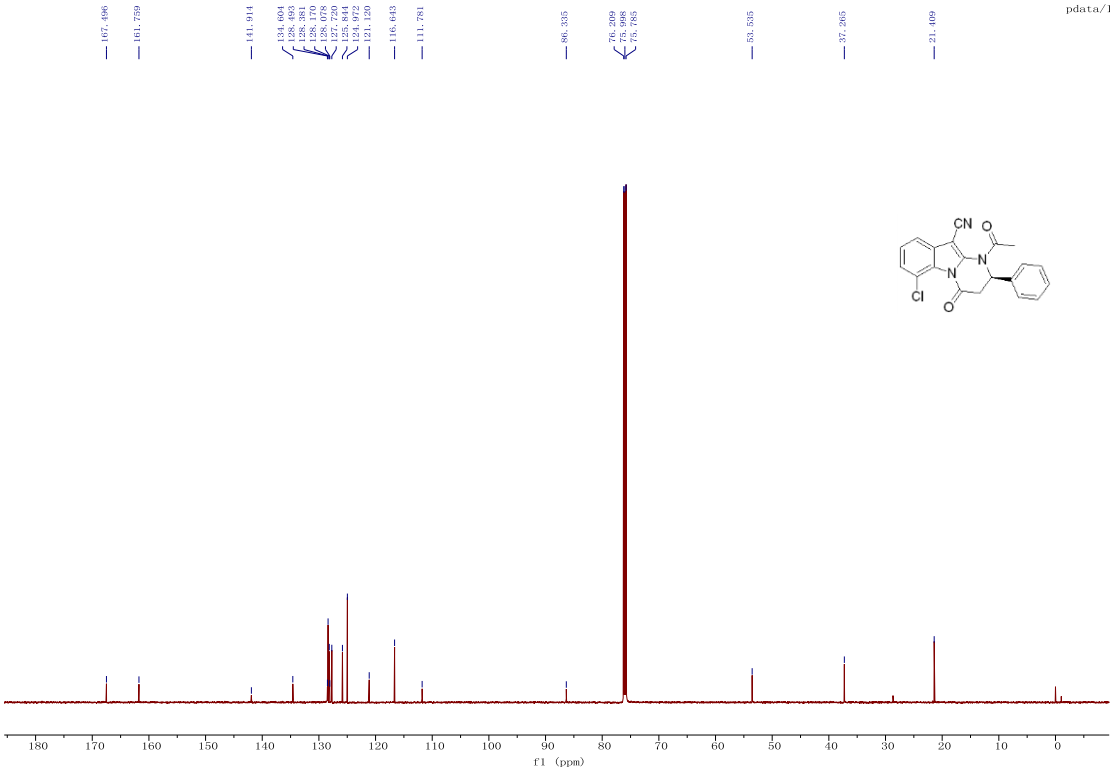
[^{13}C_NMR_151 MHz_(CDCl$_3$: 77.00 ppm)]



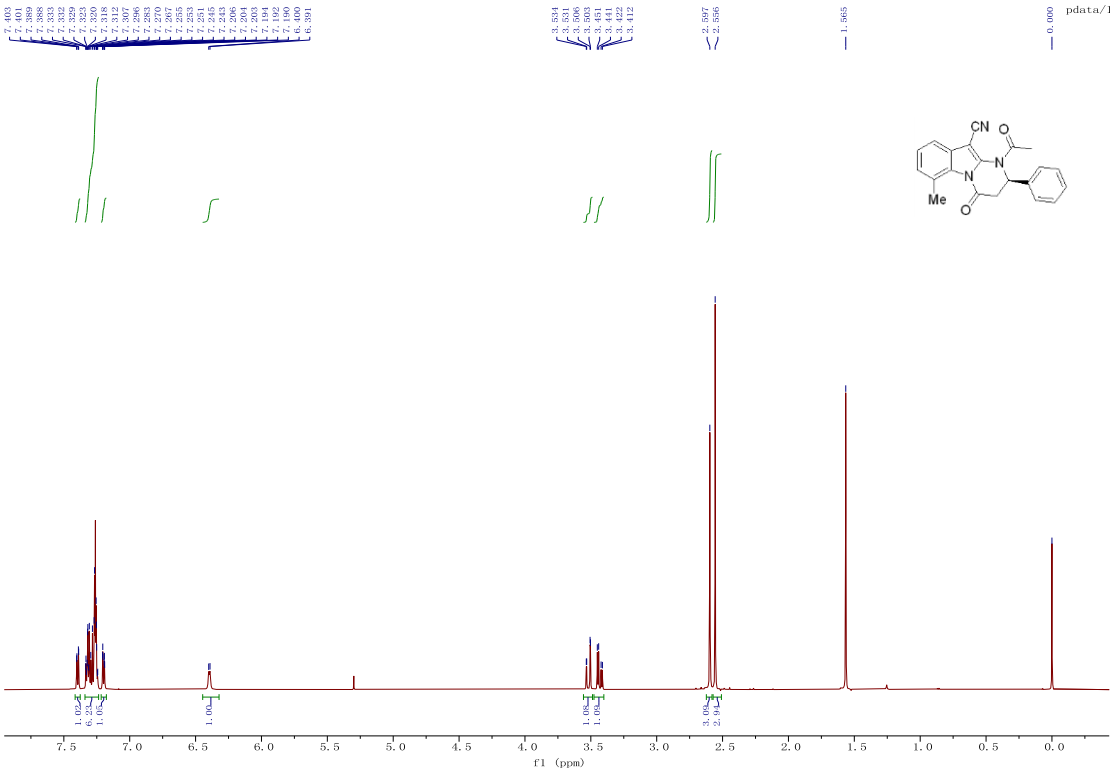
(*R*)-1-Acetyl-6-chloro-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3c'). [^{1}H_NMR_400 MHz_(CDCl$_3$: 7.26 ppm)]



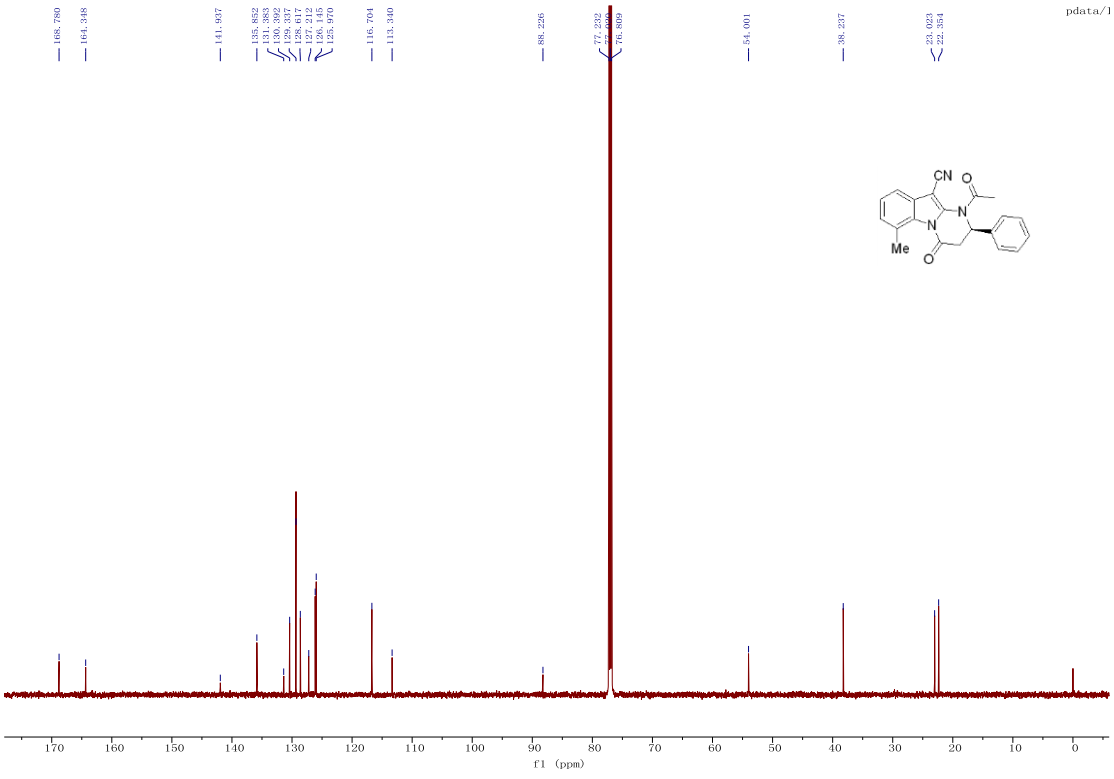
[^{13}C_NMR_151 MHz_(CDCl$_3$: 77.00 ppm)]



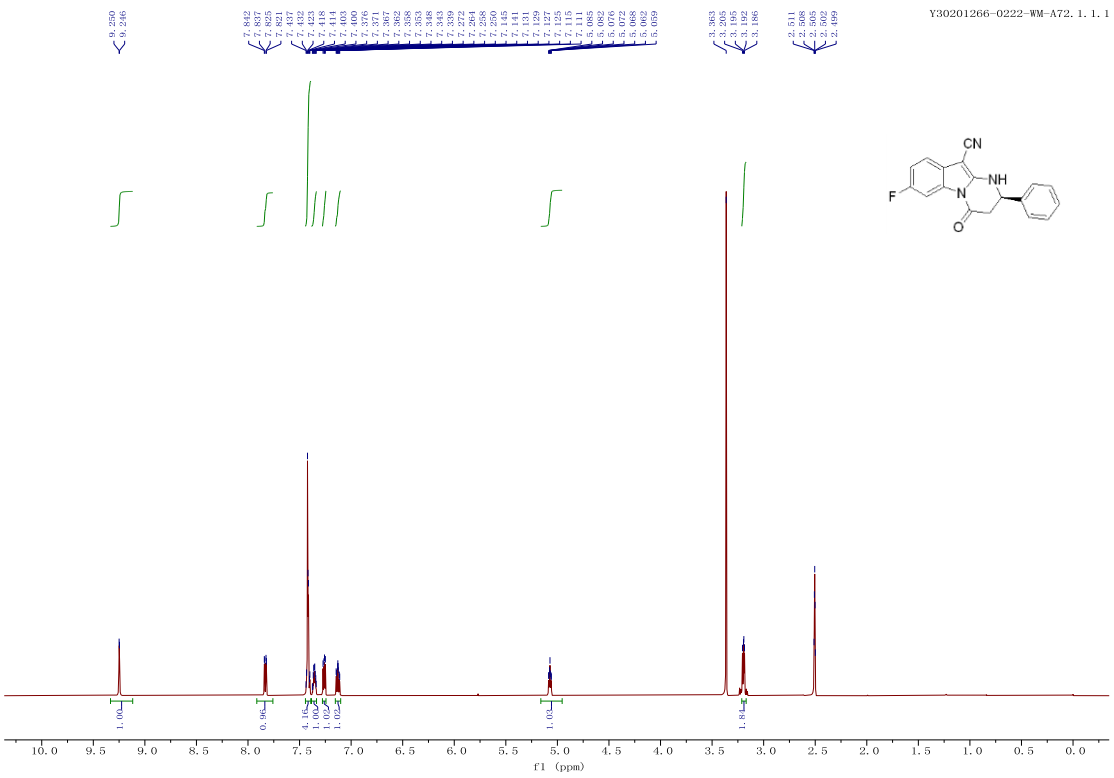
(*R*)-1-Acetyl-6-methyl-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3d'). [^{1}H_NMR_600 MHz_(CDCl$_3$: 7.26 ppm)]



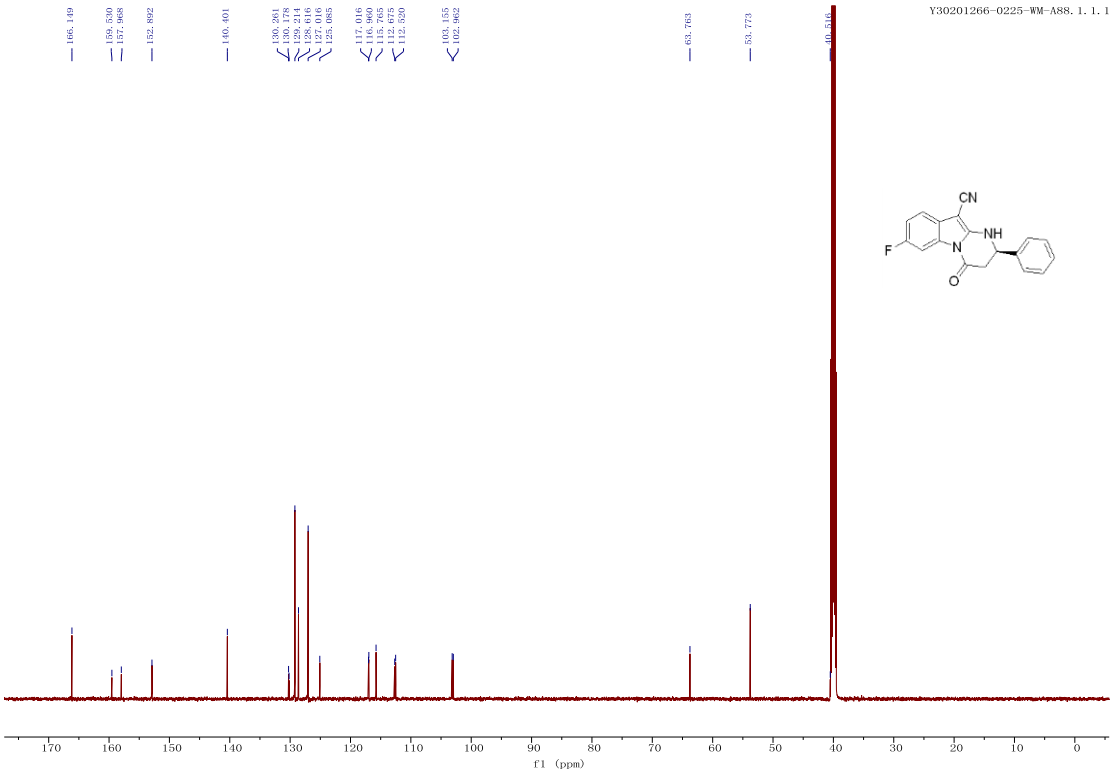
[^{13}C_NMR_151 MHz_(CDCl$_3$: 77.00 ppm)]



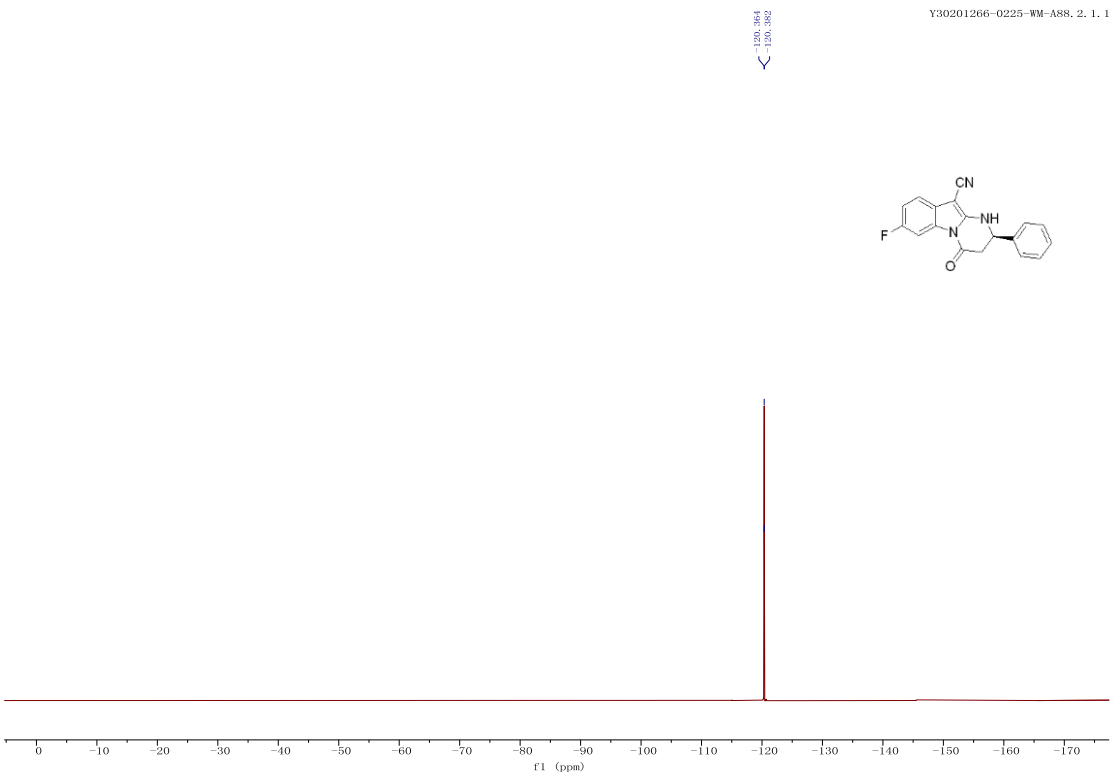
(*R*)-7-Fluoro-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3e). [^{1}H_NMR_600 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



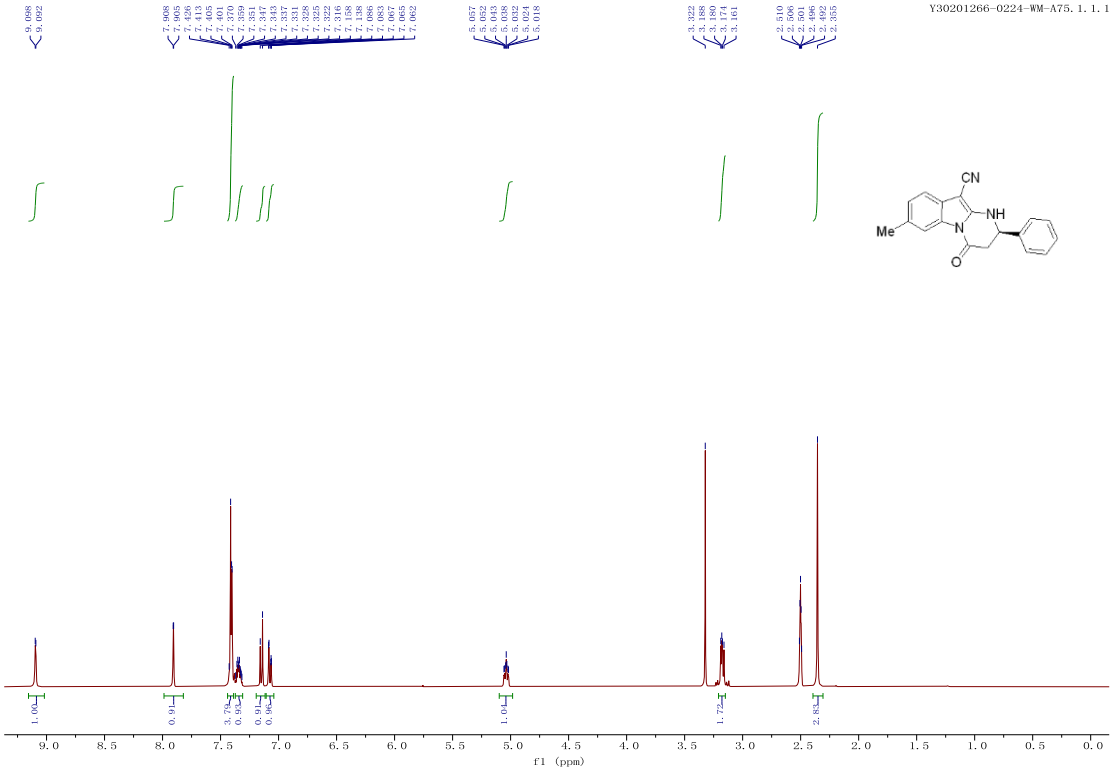
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



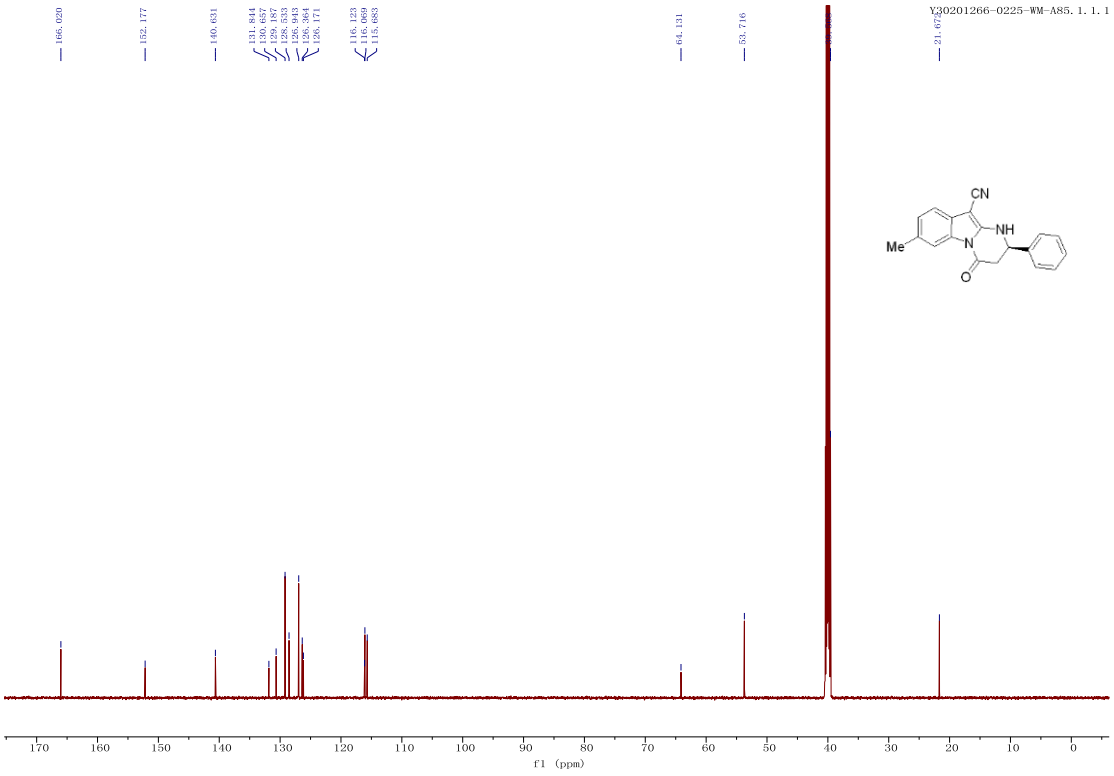
[^{19}F_NMR_565 MHz]


Y30201266-0225-WM-A88.2.1.1
-120.364
-120.382
CN
NH
F
N
O
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
f1 (ppm)

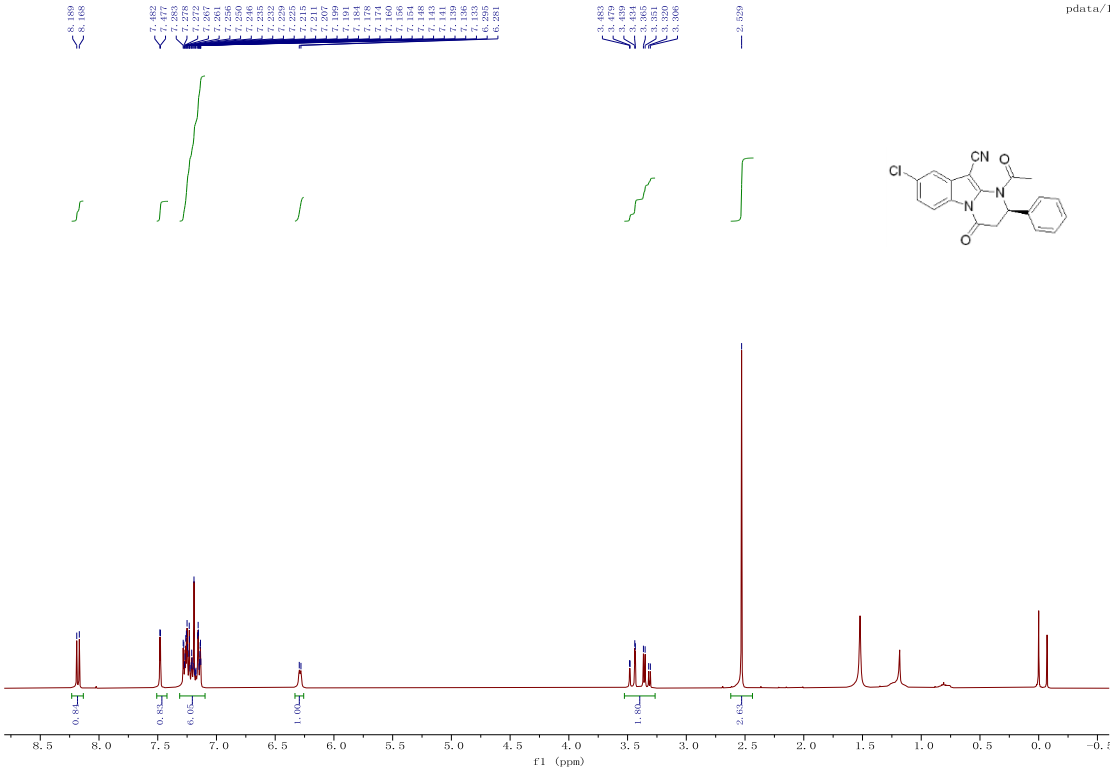
(*R*)-7-Methyl-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3f). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



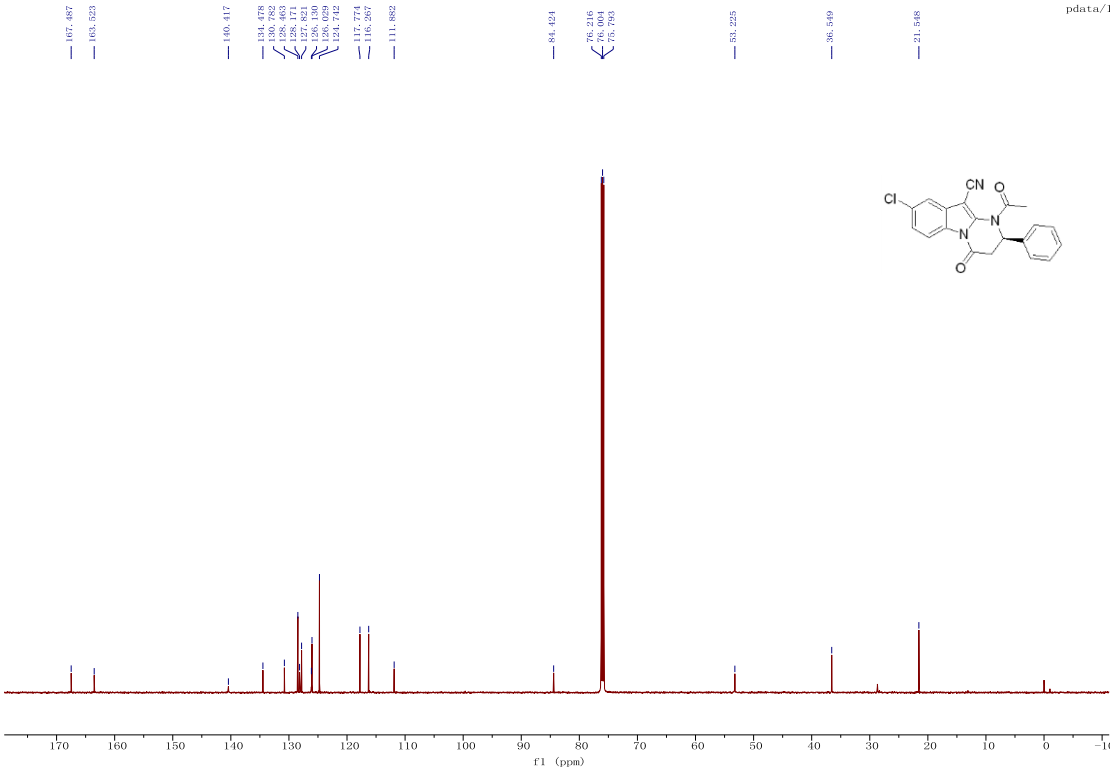
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



(*R*)-1-Acetyl-8-chloro-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3g'). [^{1}H_NMR_400 MHz_(CDCl$_3$: 7.26 ppm)]

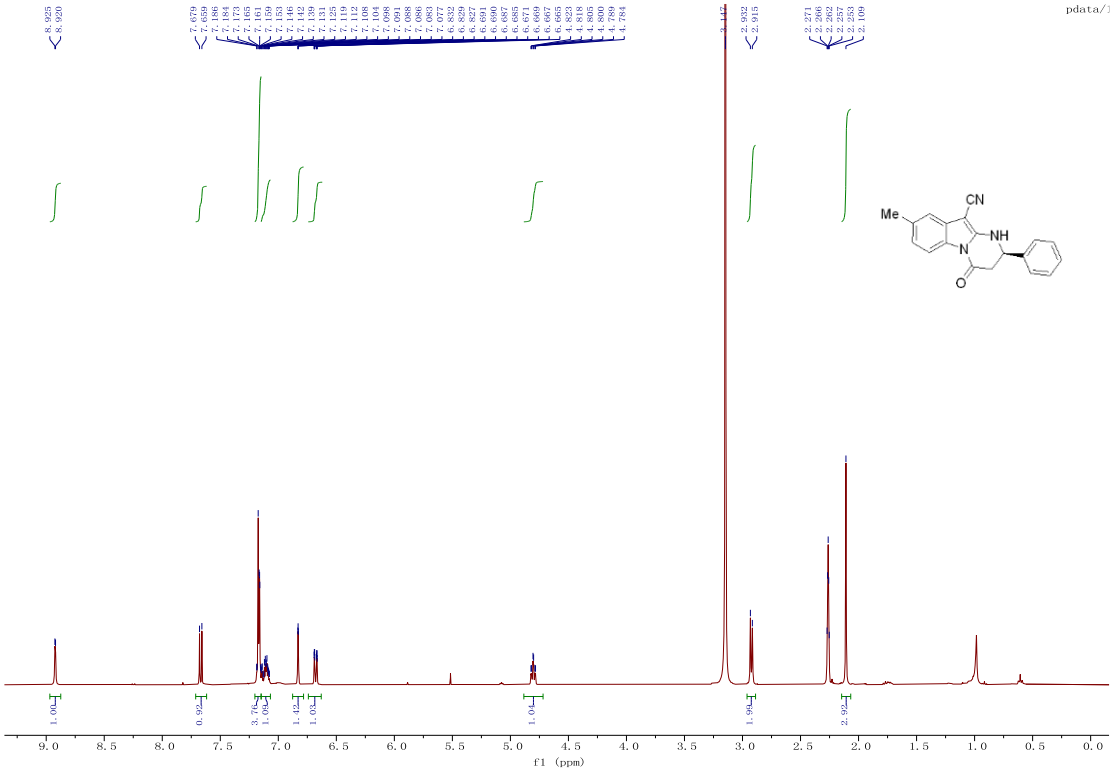


[^{13}C_NMR_151 MHz_(CDCl$_3$: 77.00 ppm)]

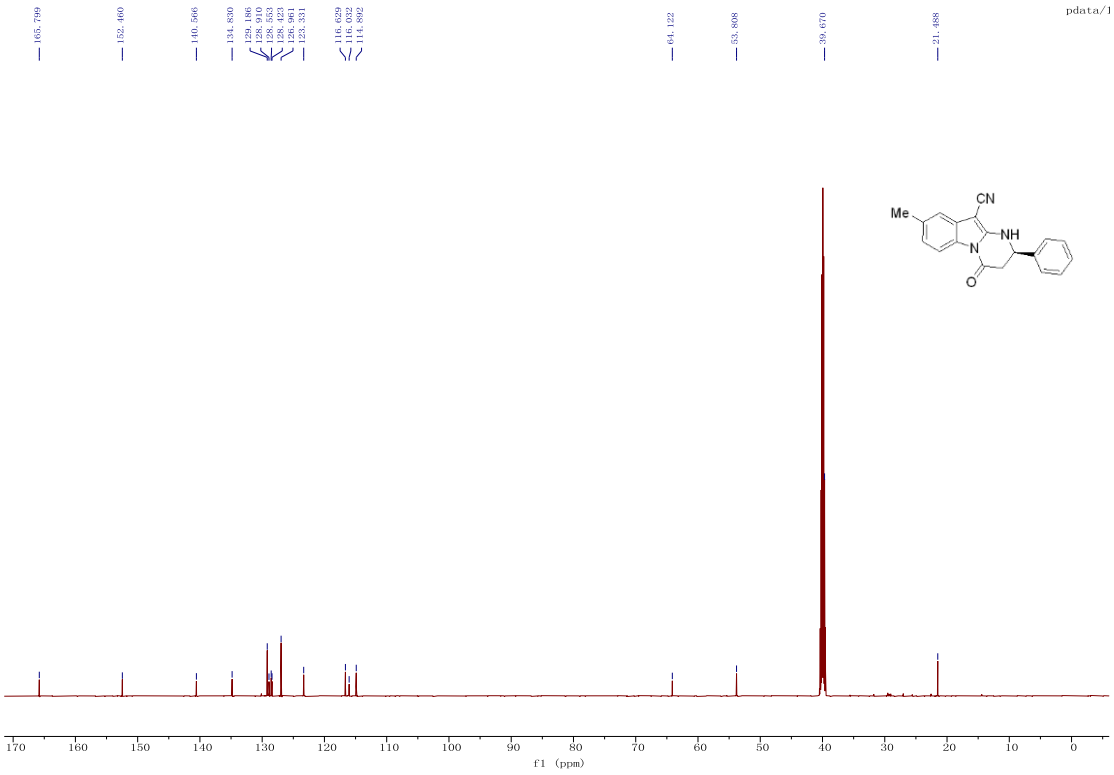


(*R*)-8-Methyl-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-

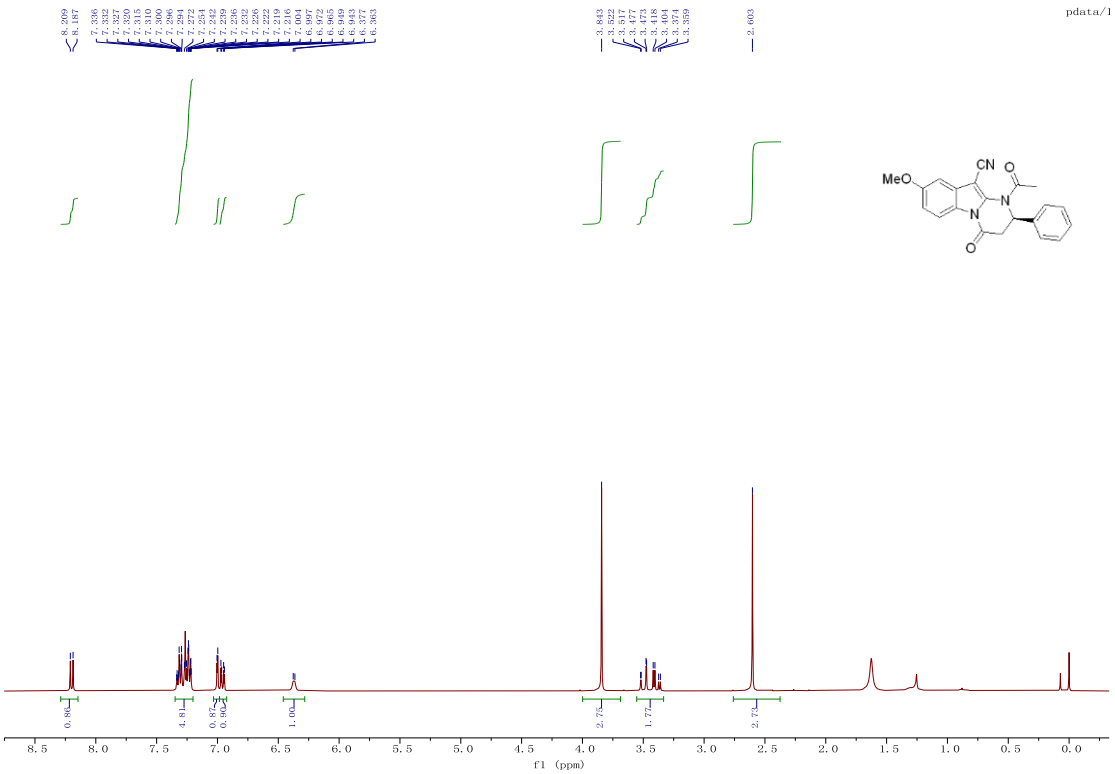
carbonitrile (3h). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



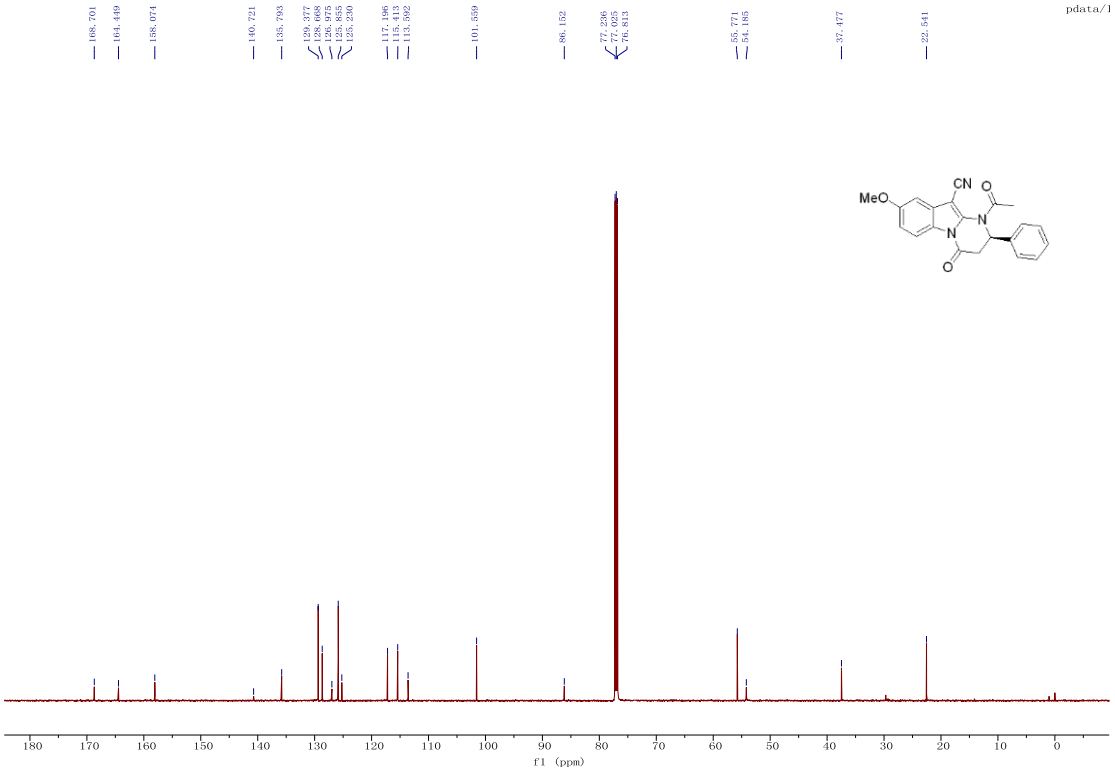
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



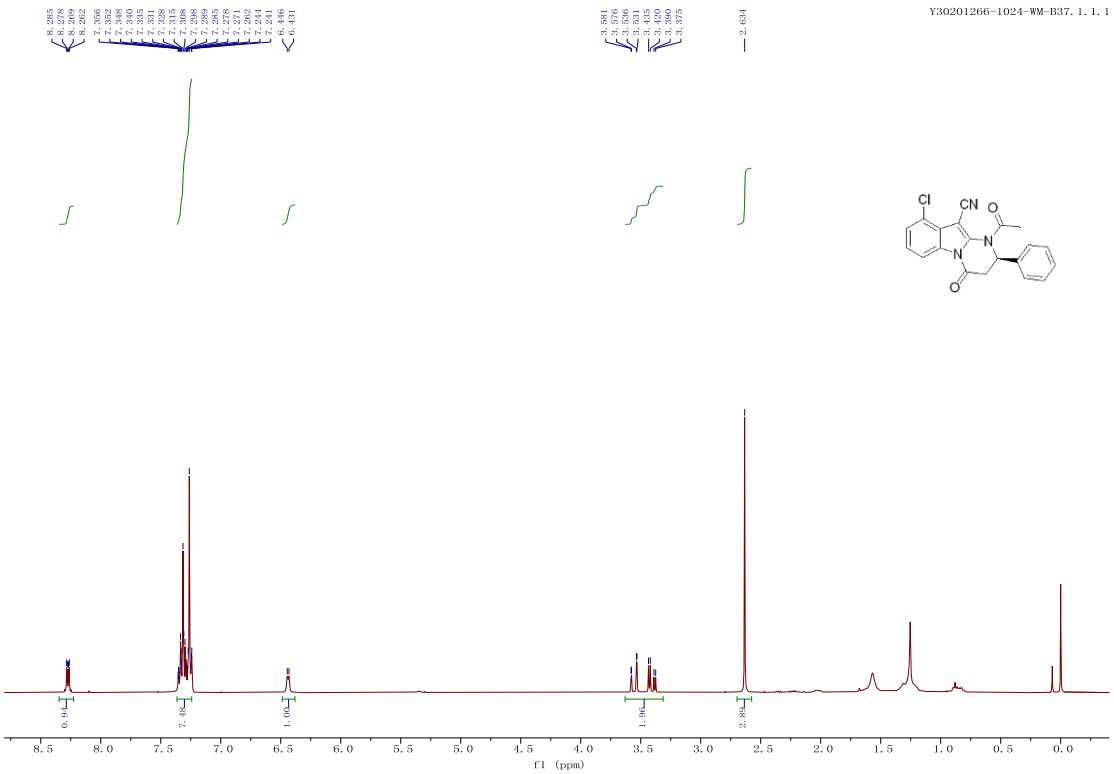
(*R*)-1-Acetyl-8-methoxy-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3i'). [^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



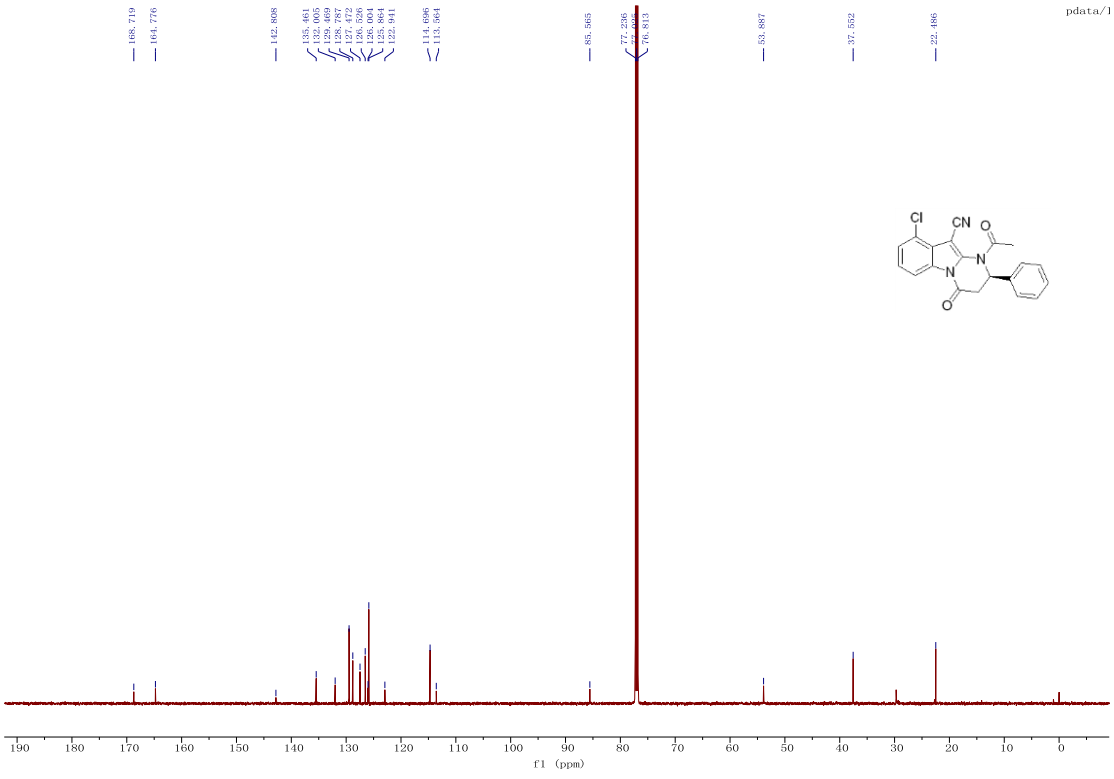
[^{13}C_NMR_151 MHz_(CDCl$_3$: 77.00 ppm)]



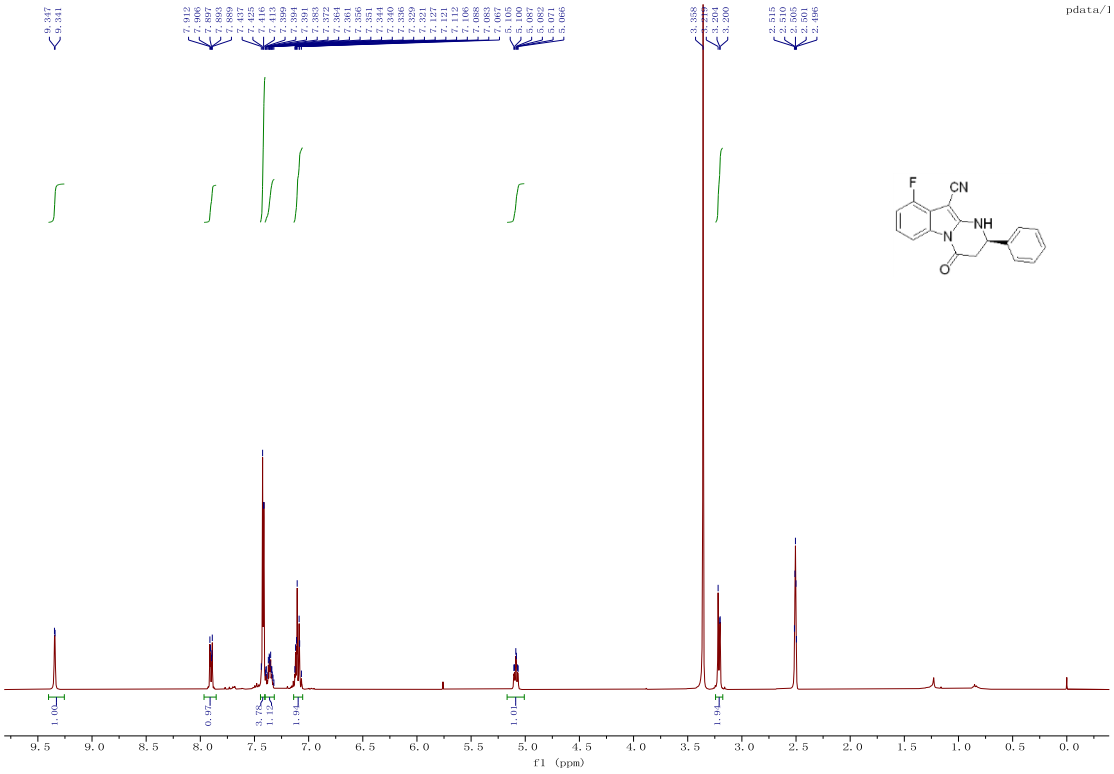
(*R*)-1-Acetyl-9-chloro-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3j'). [^{1}H_NMR_400 MHz_(CDCl$_3$: 7.26 ppm)]



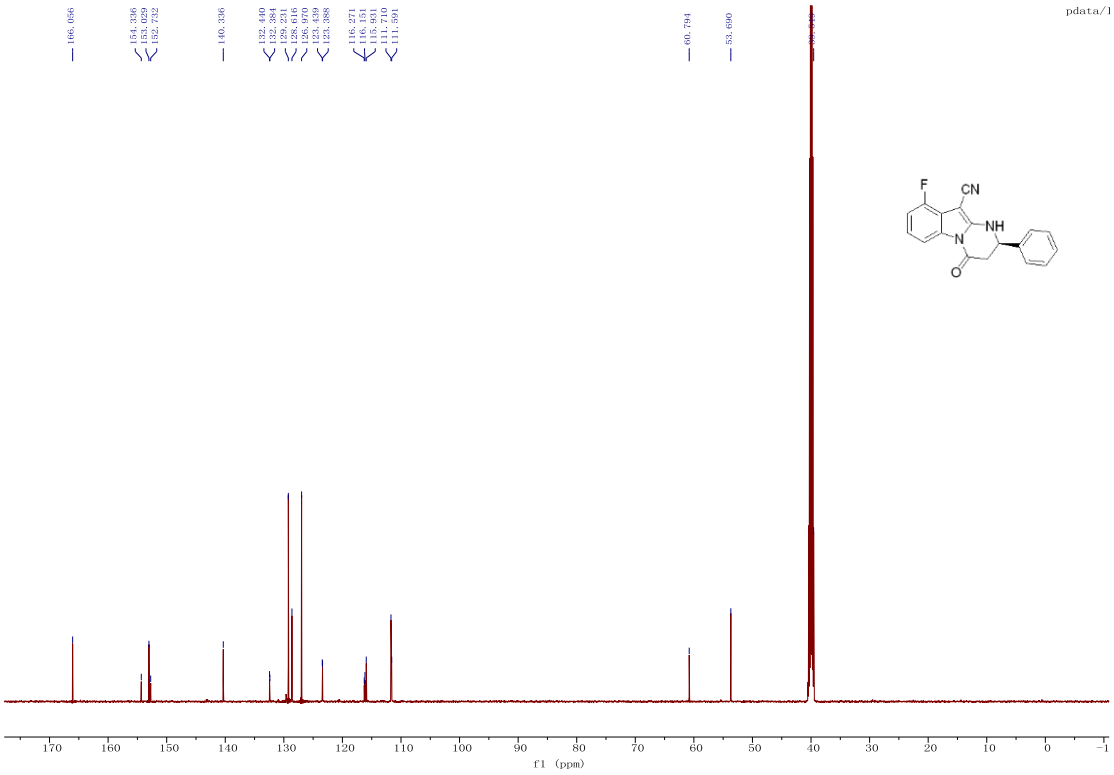
[^{13}C_NMR_151 MHz_(CDCl$_3$: 77.00 ppm)]



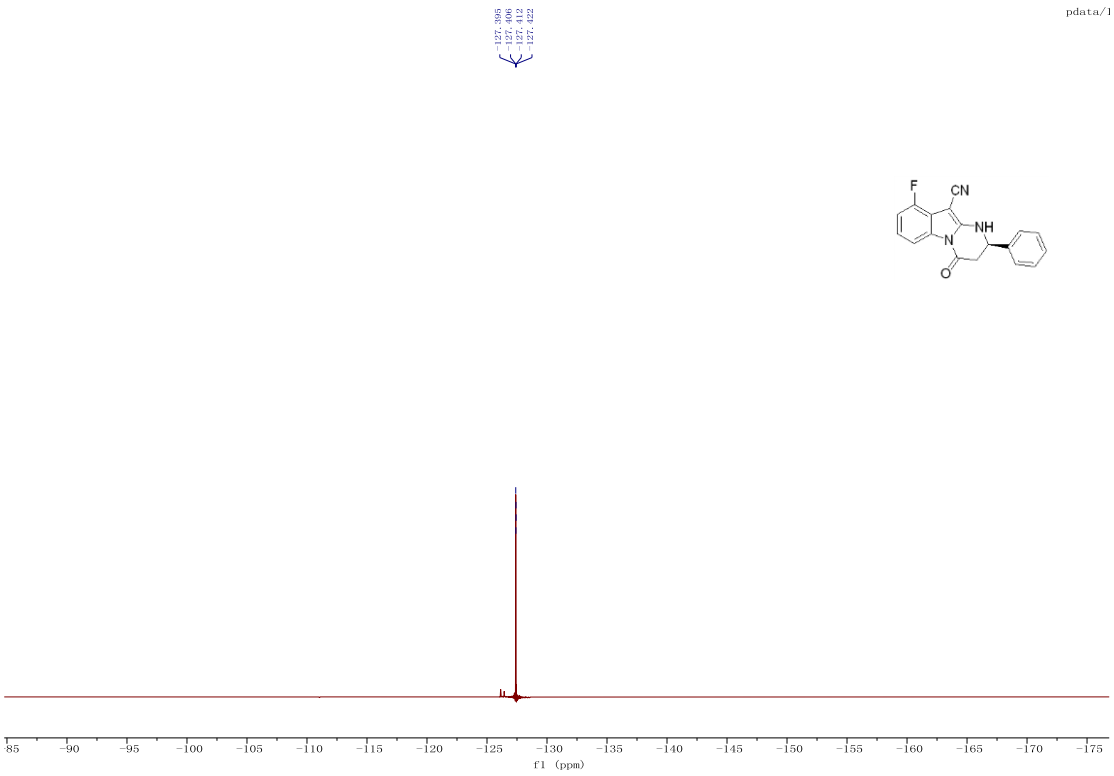
(*R*)-9-Fluoro-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3k). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



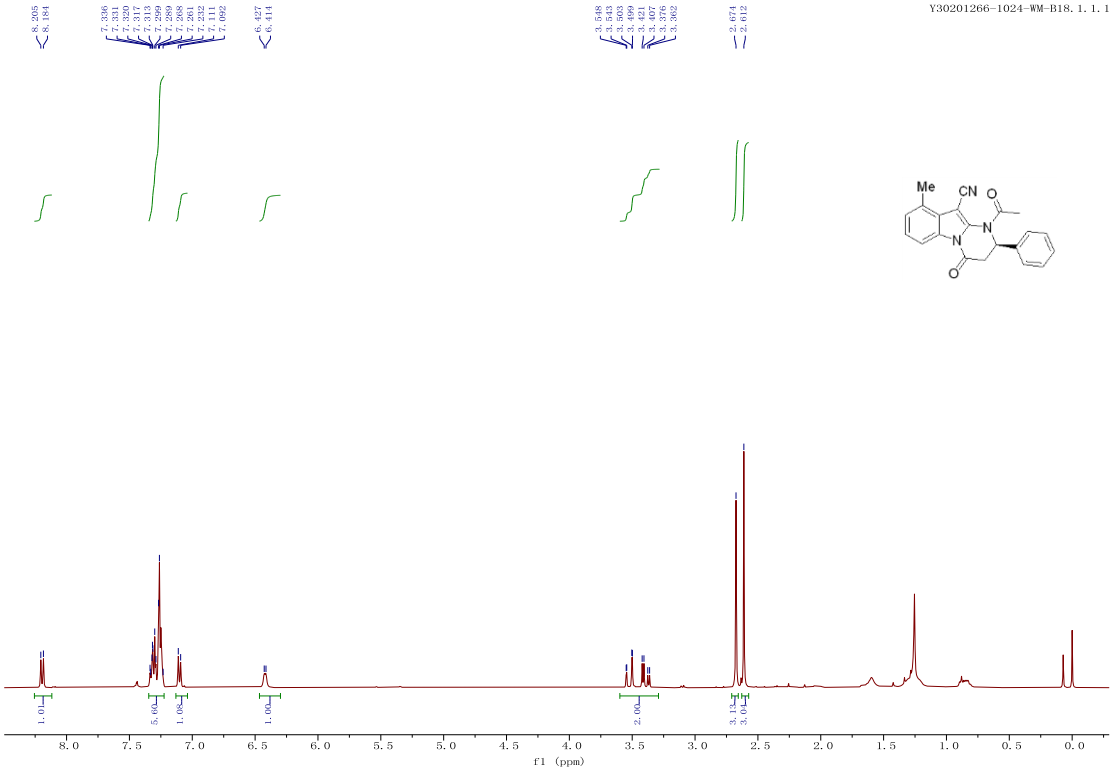
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



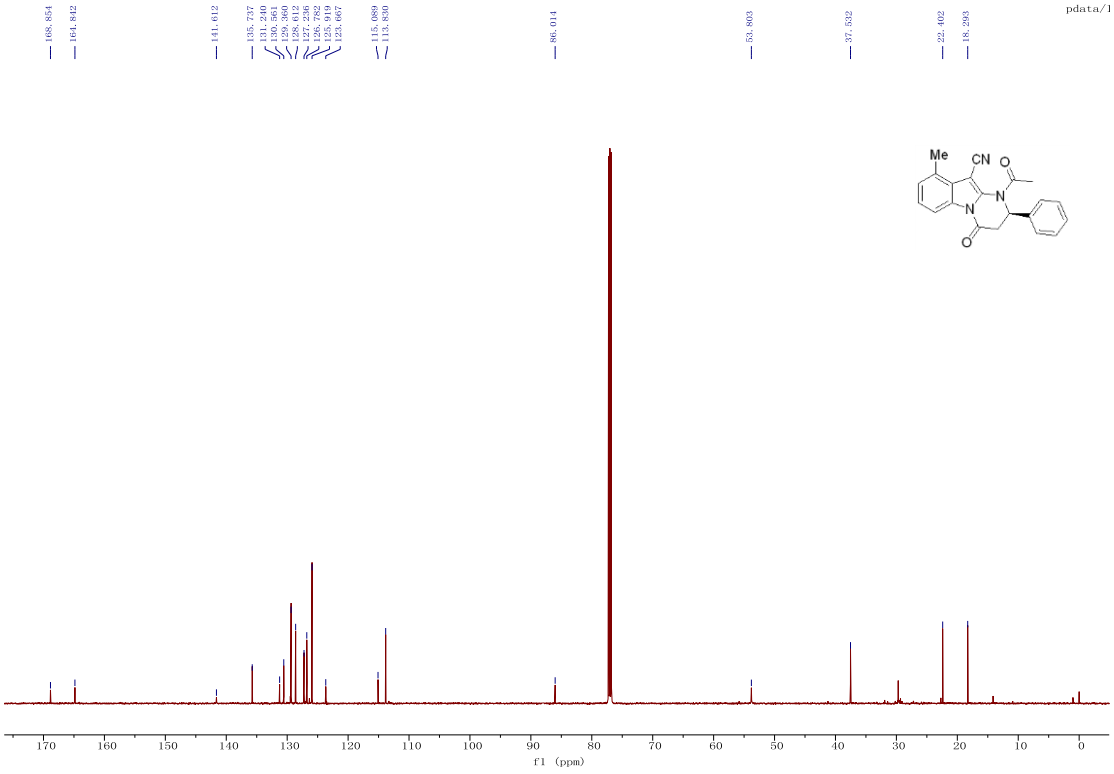
[^{19}F_NMR_565 MHz]


-127.395
-127.406
-127.412
-127.422
pdata/1
F
CN
NH
N
O
85 90 95 100 105 110 115 120 125 130 135 140 145 150 155 160 165 170 175
f1 (ppm)

(*R*)-1-Acetyl-9-methyl-4-oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3l'). [^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]

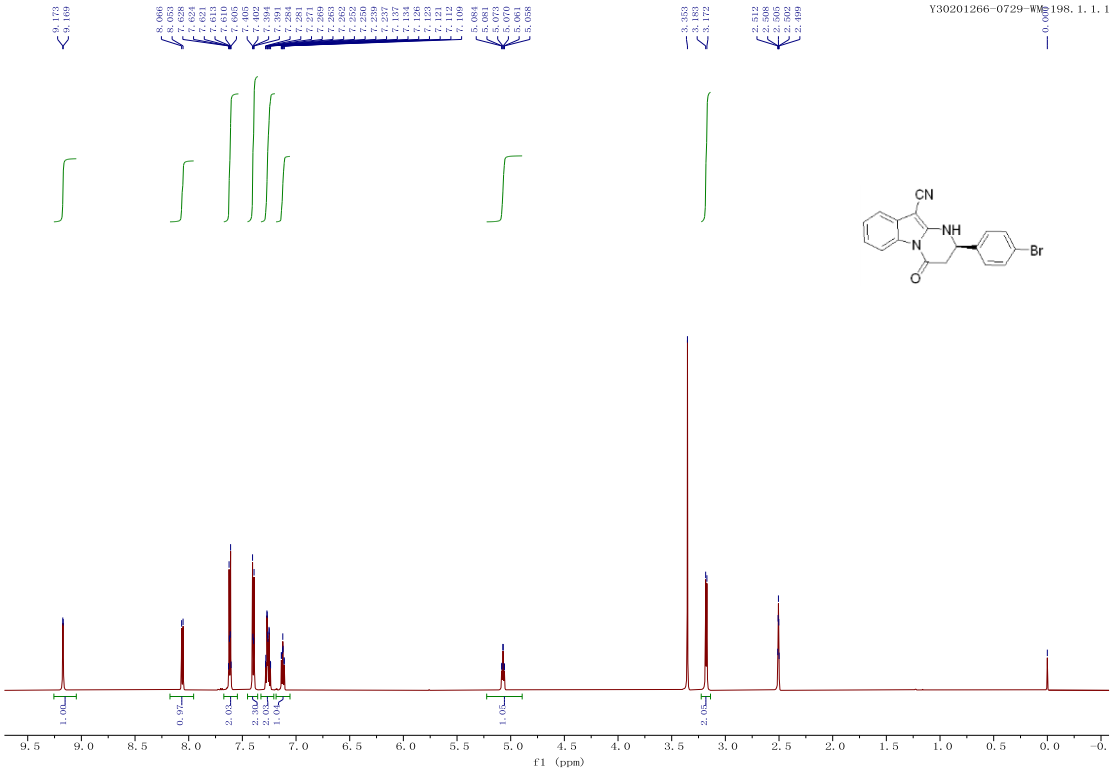


[^{13}C_NMR_151 MHz_($CDCl_3$: 77.00 ppm)]

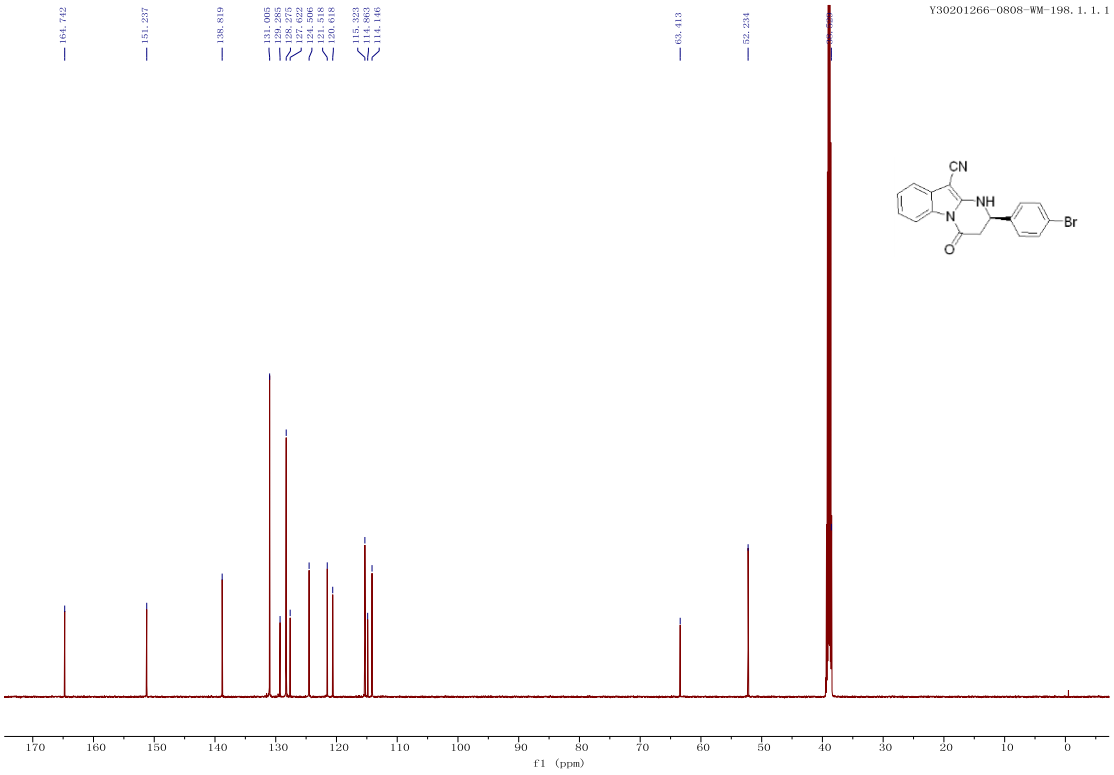


(*R*)-2-(4-Bromophenyl)-4-oxo-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-

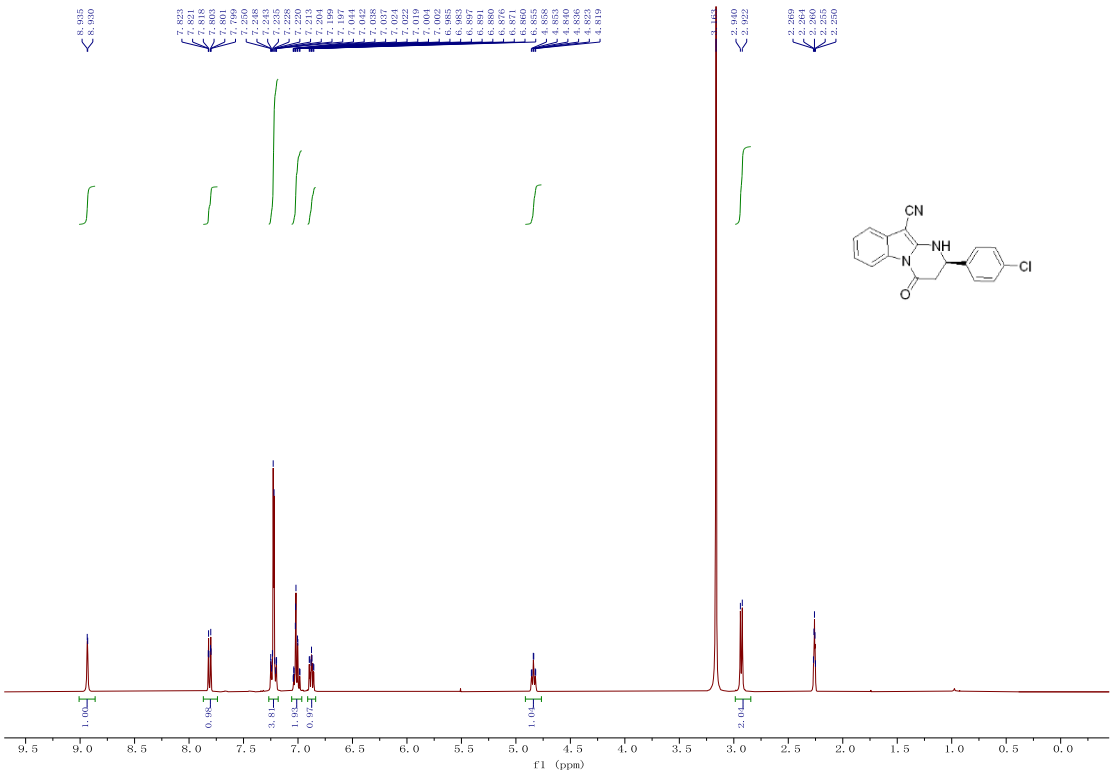
carbonitrile (3m). [^{1}H_NMR_600 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



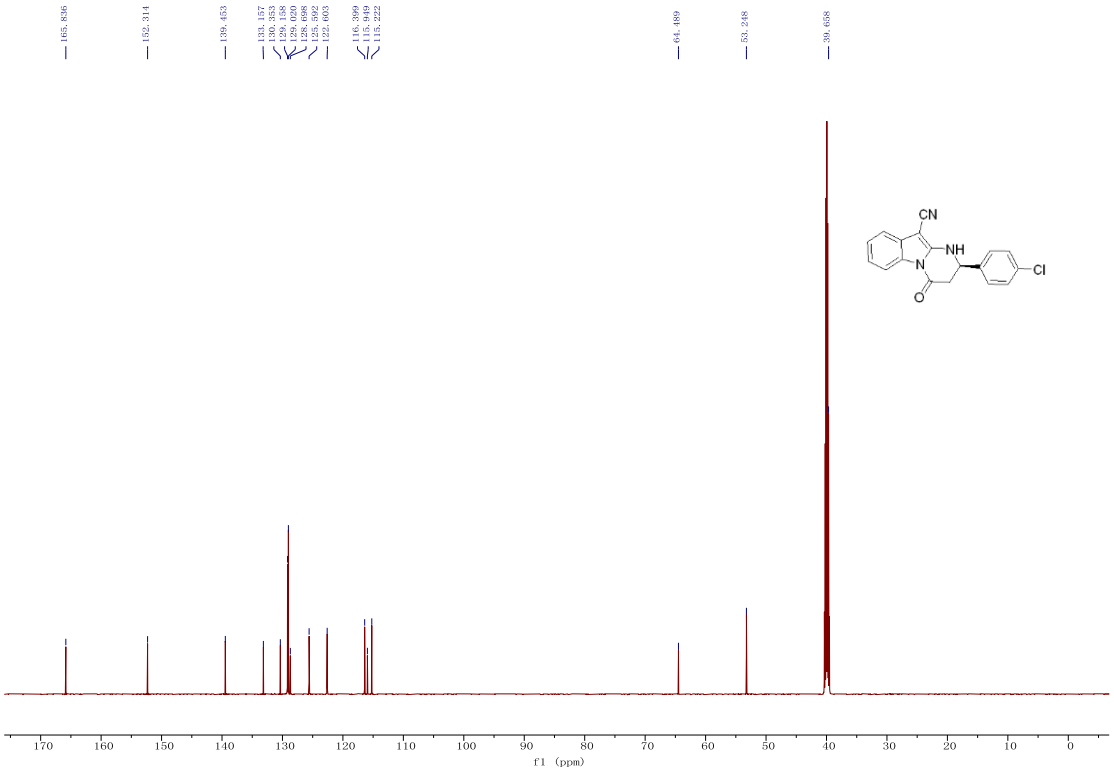
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



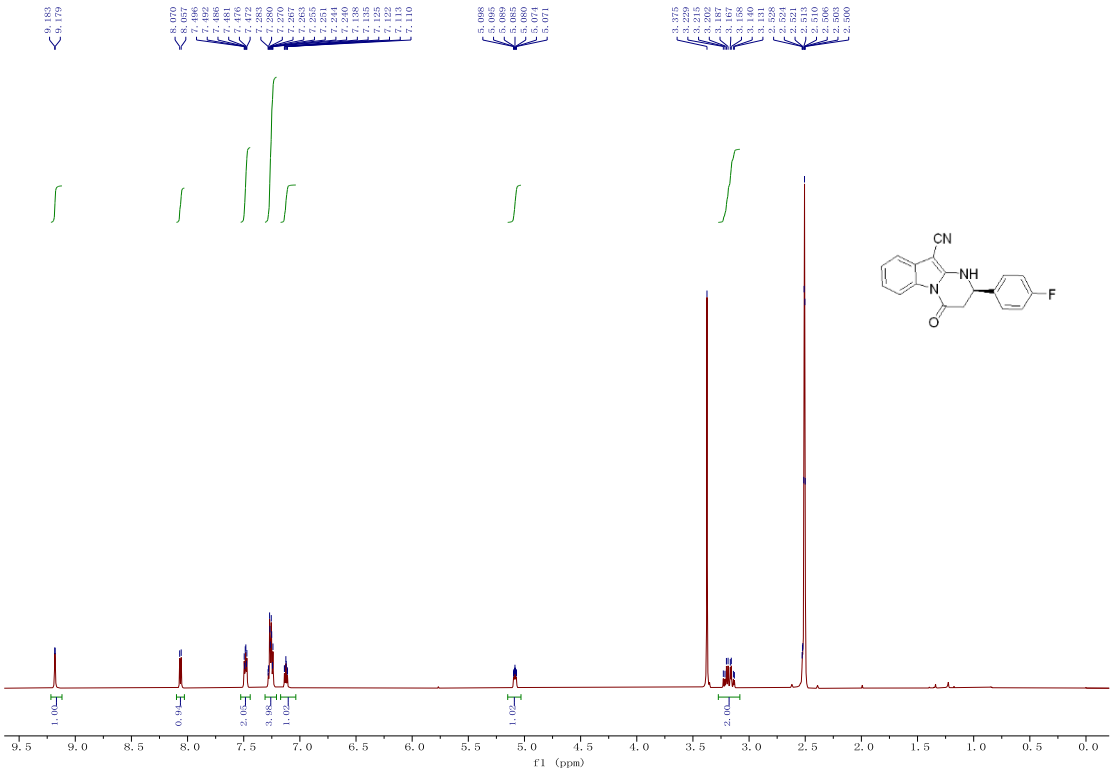
(*R*)-2-(4-Chlorophenyl)-4-oxo-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3n). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



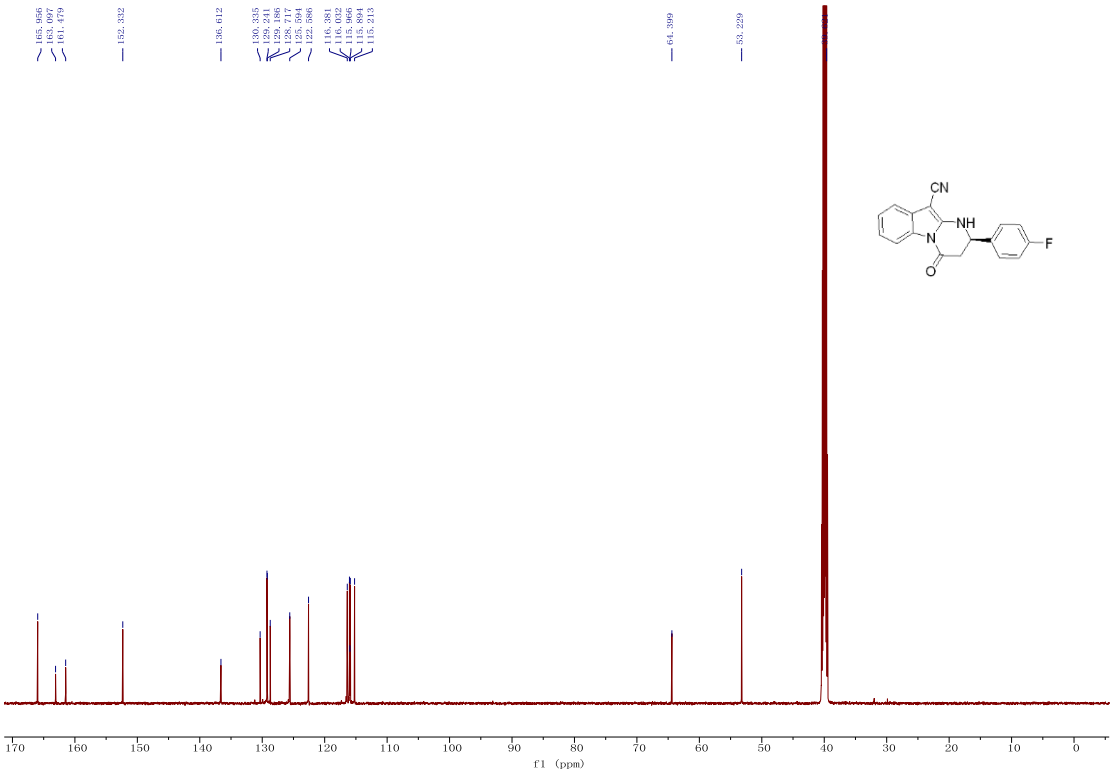
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



(*R*)-2-(4-Fluorophenyl)-4-oxo-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3o). [^{1}H_NMR_600 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]

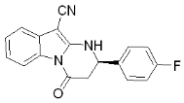


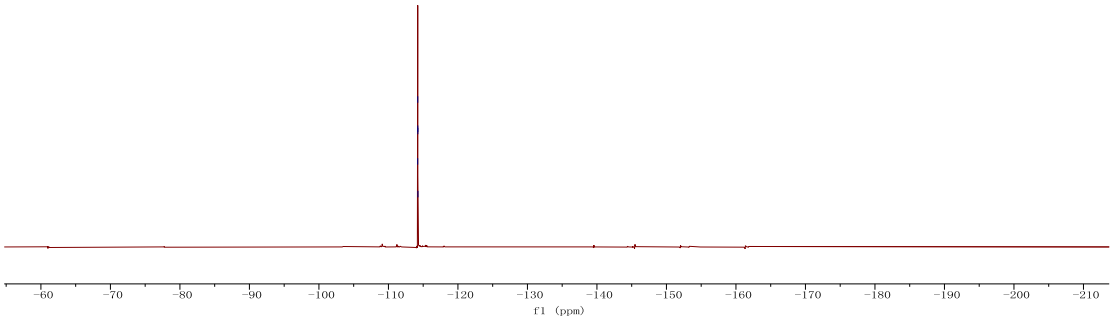
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



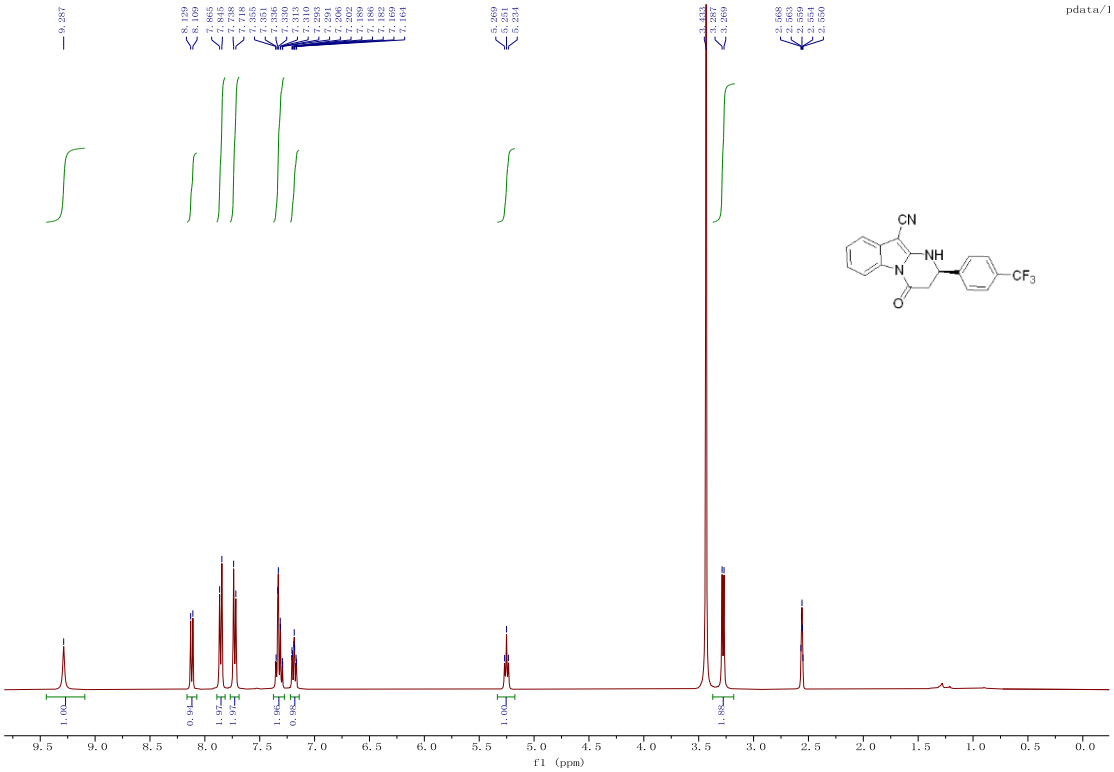
[^{19}F_NMR_565 MHz]


-114.206
-114.215
-114.222
-114.231
-114.244

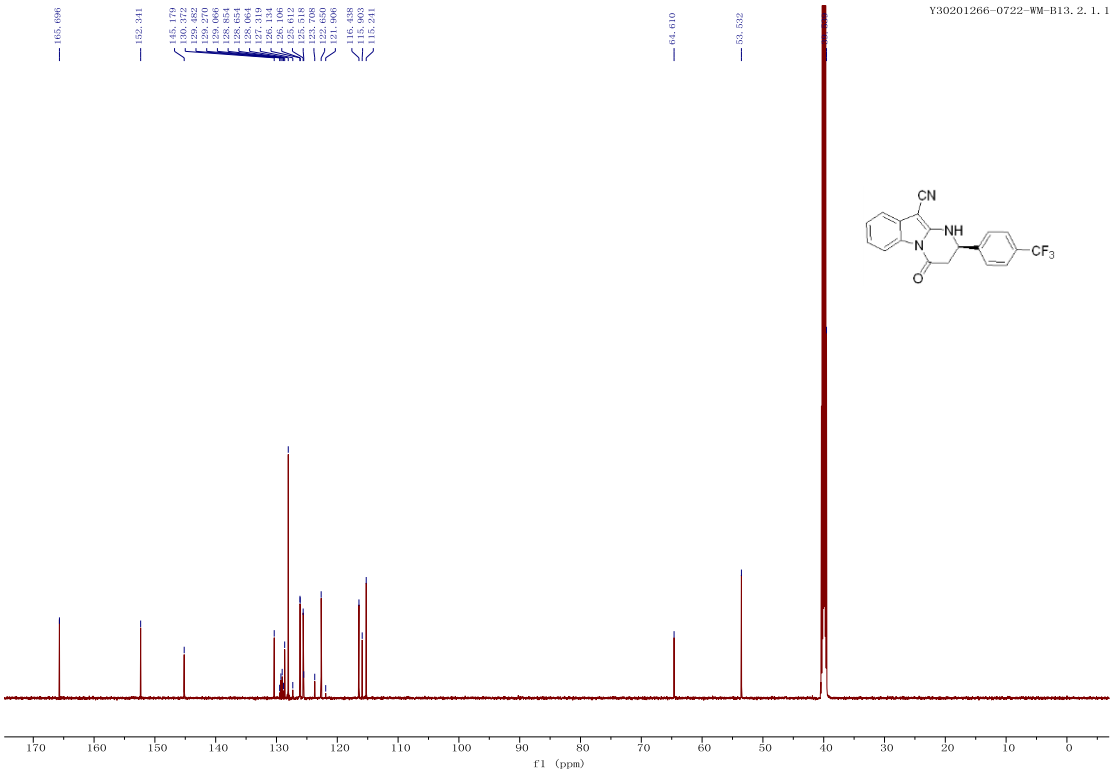

CN
NH
N
O
F


-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

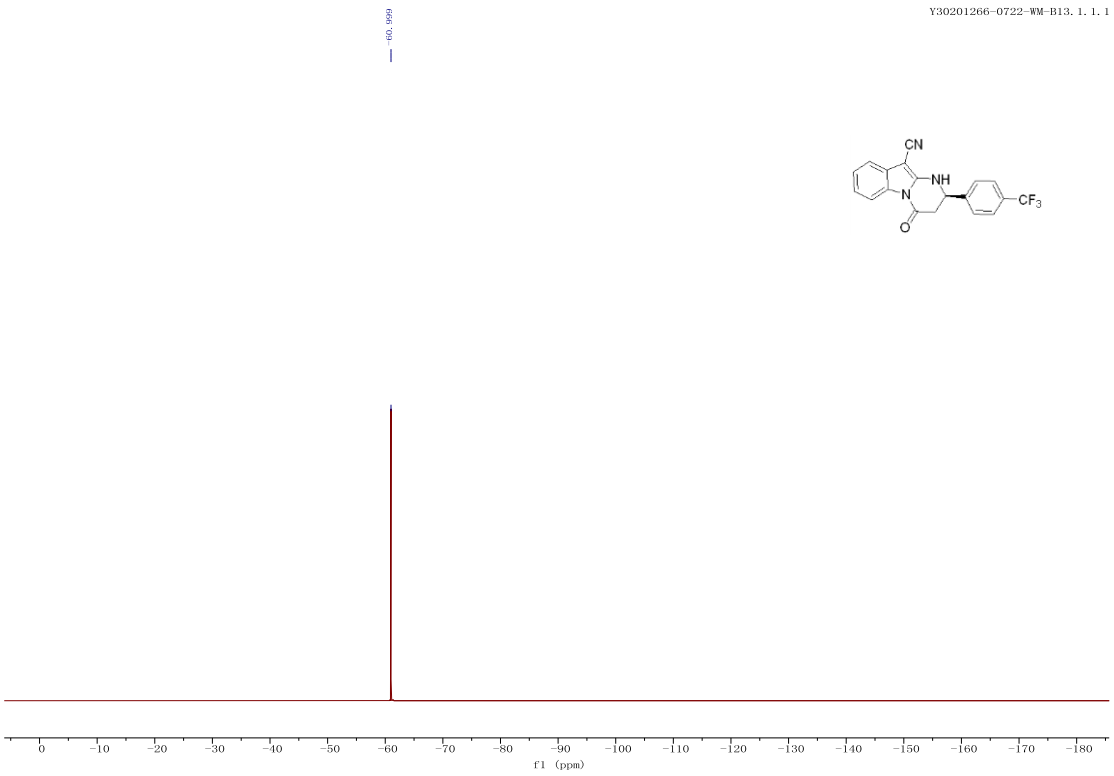
(*R*)-4-Oxo-2-(4-(trifluoromethyl)phenyl)-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3p). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



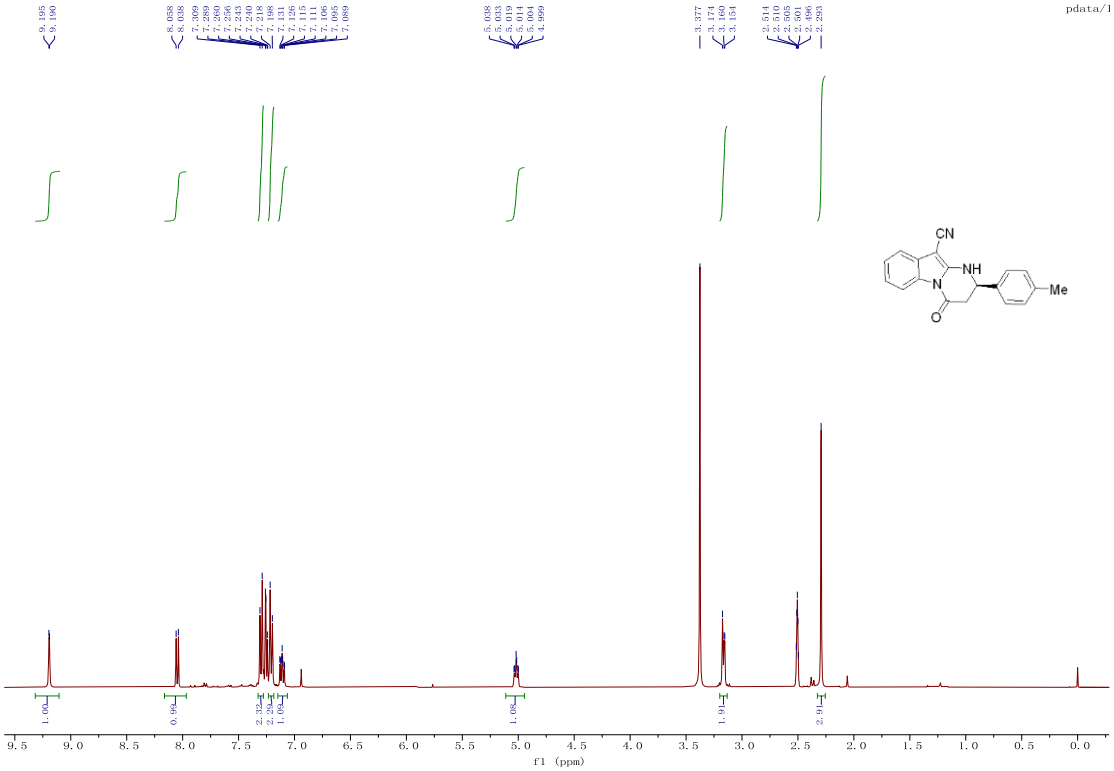
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



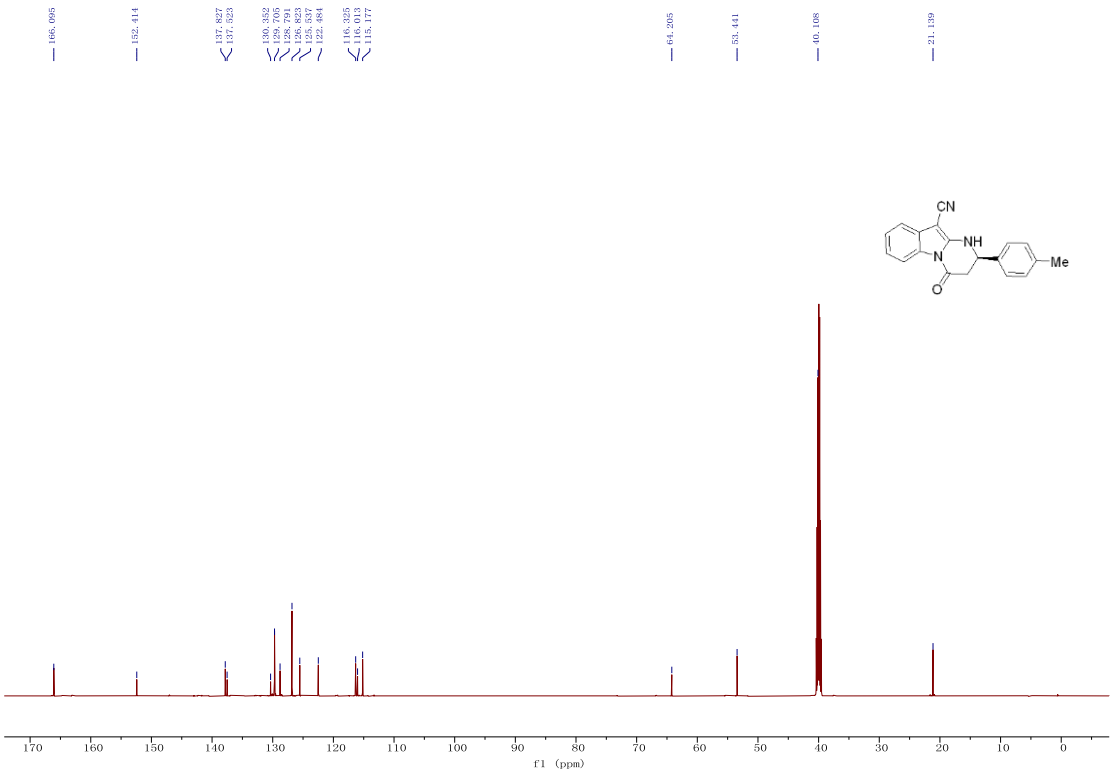
[^{19}F_NMR_565 MHz]


-60.999
CN
NH
N
O
CF3
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
f1 (ppm)

(*R*)-4-Oxo-2-(p-tolyl)-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3q). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]

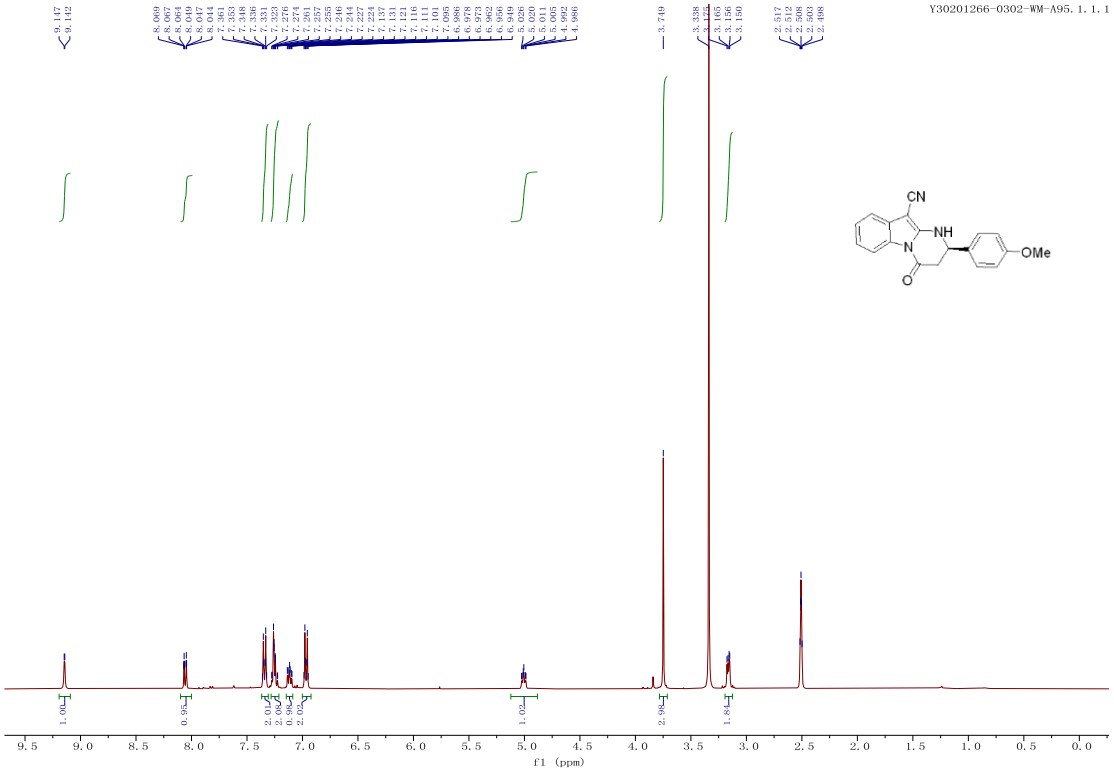


[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]

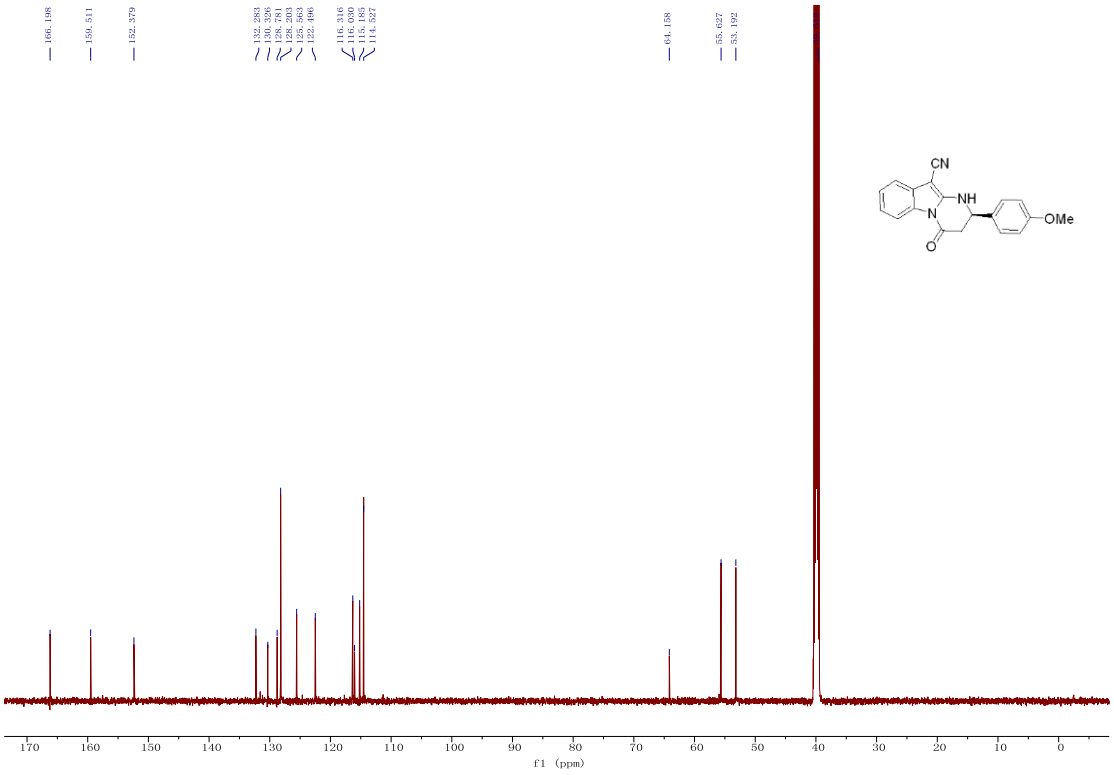


(*R*)-2-(4-Methoxyphenyl)-4-oxo-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-

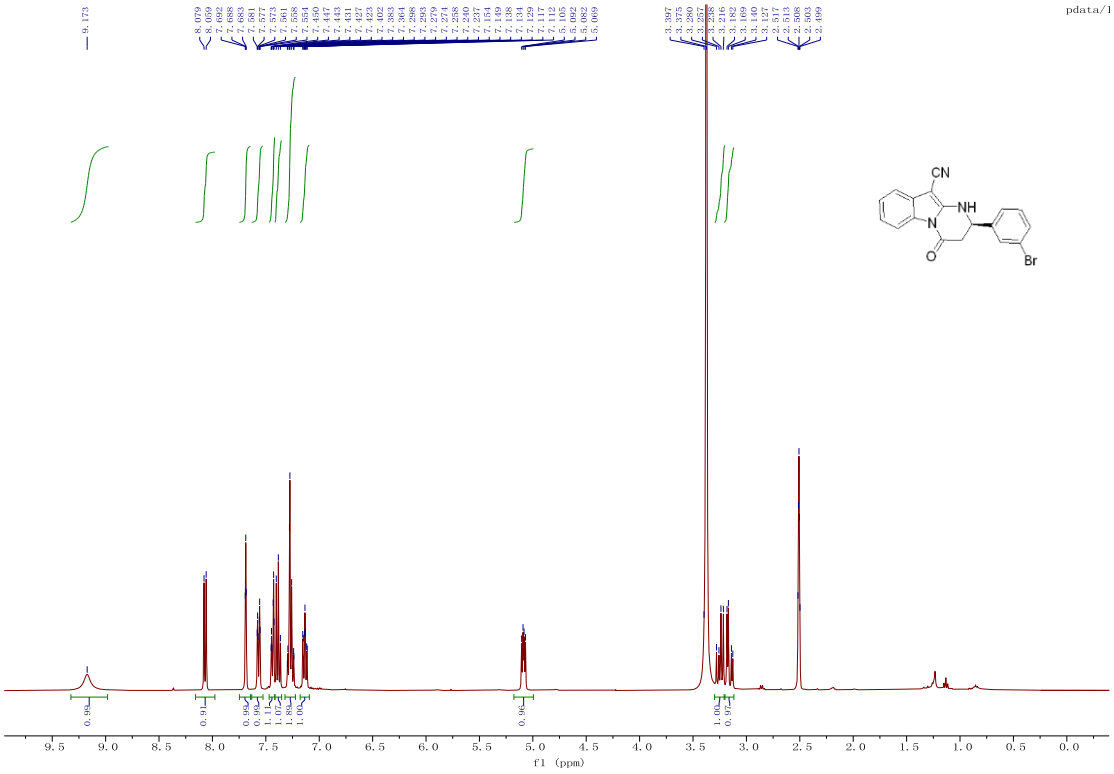
carbonitrile (3r). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



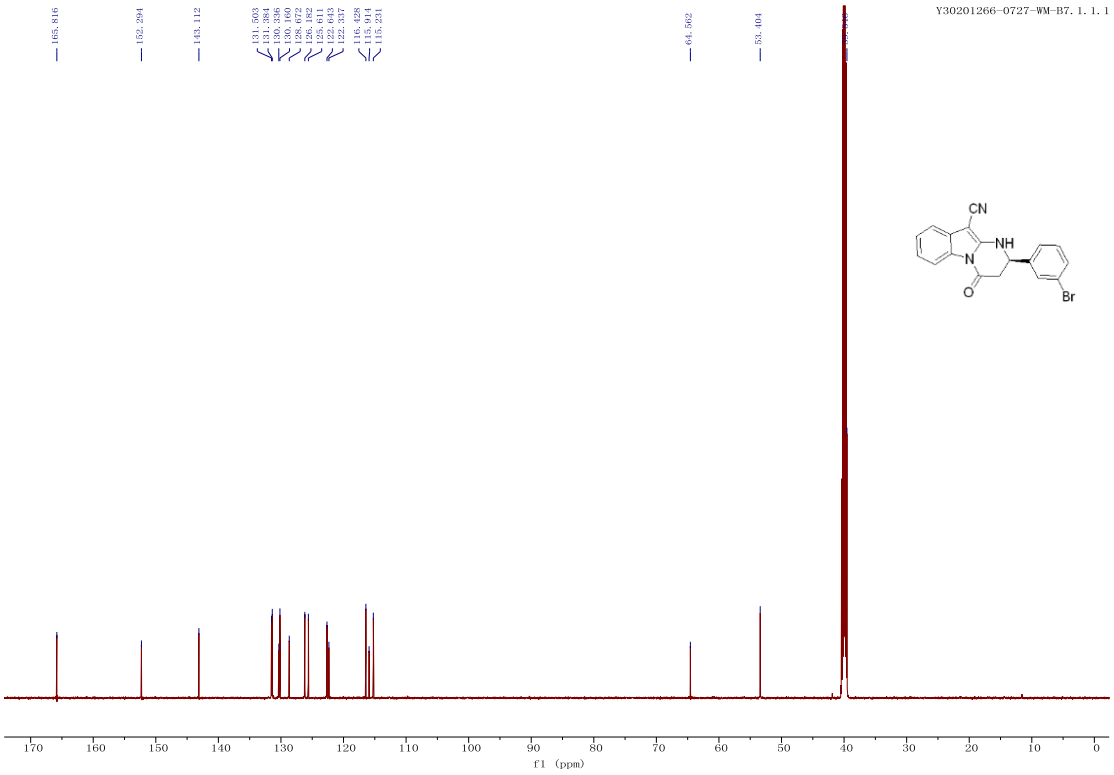
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



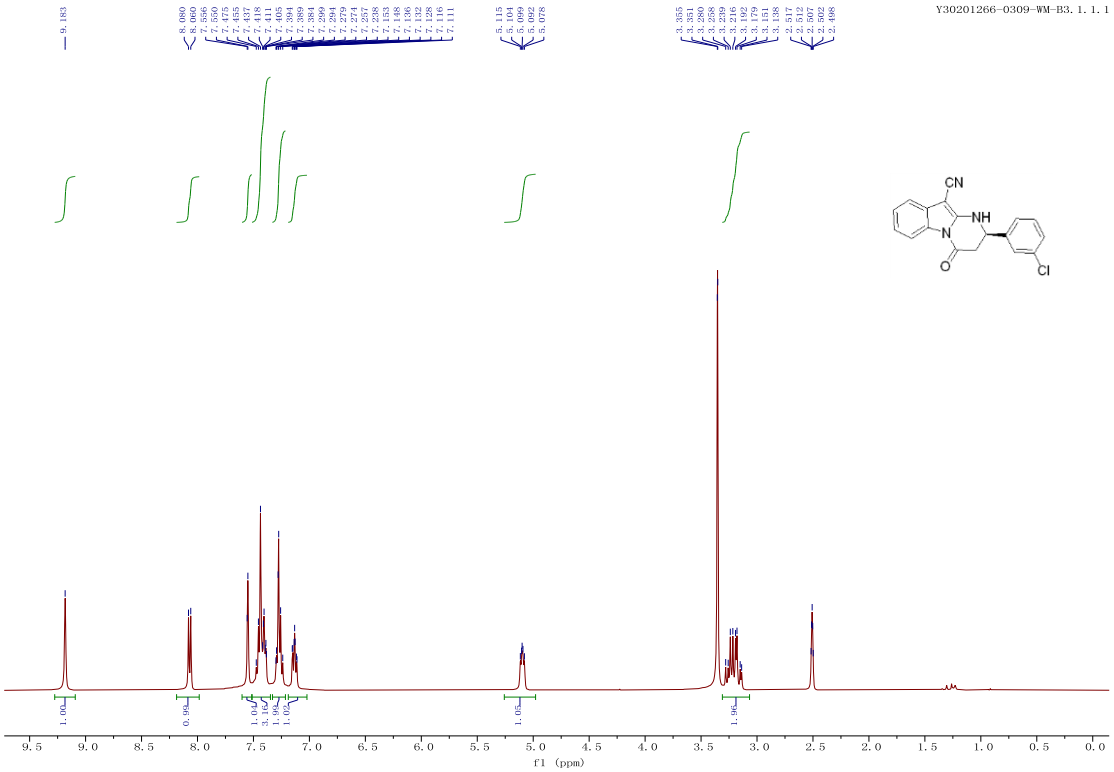
(*R*)-2-(3-Bromophenyl)-4-oxo-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3s). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



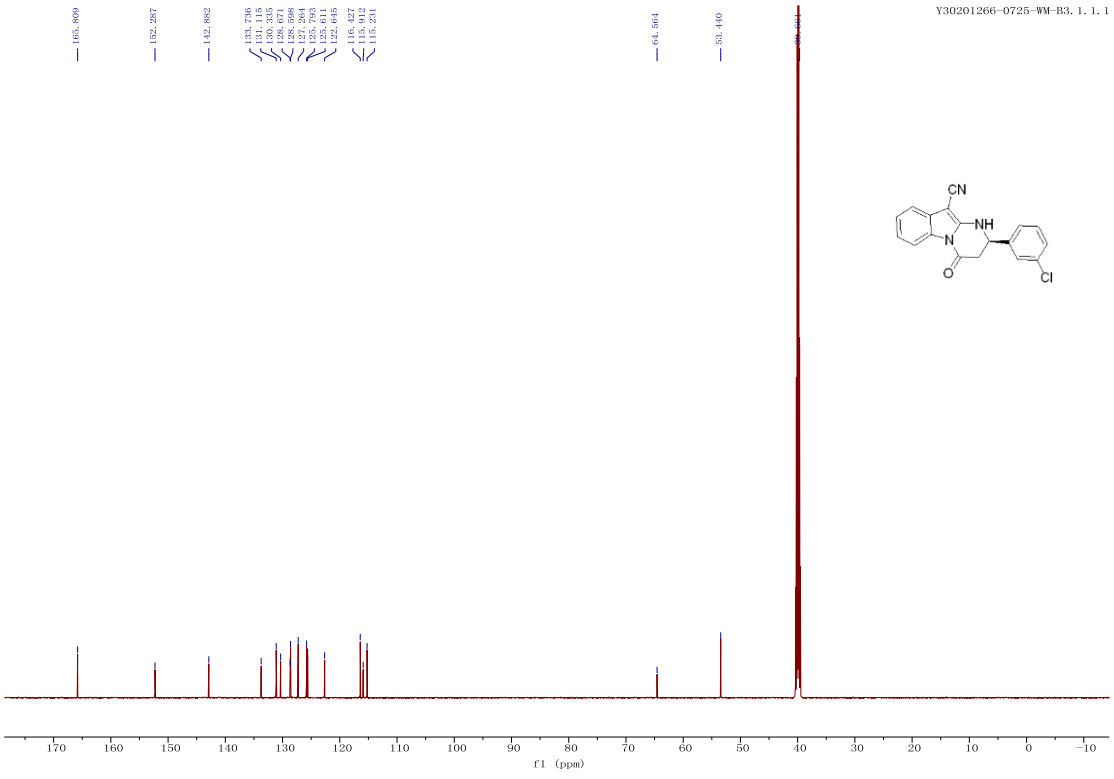
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



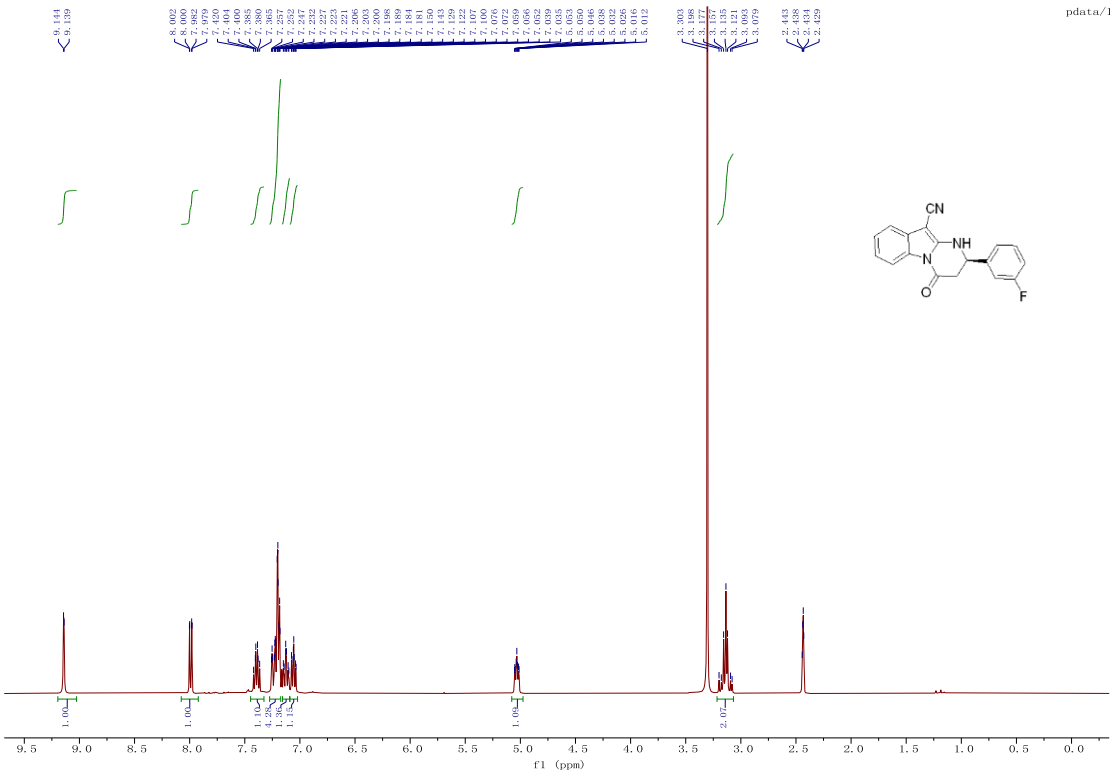
(*R*)-2-(3-Chlorophenyl)-4-oxo-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3t). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



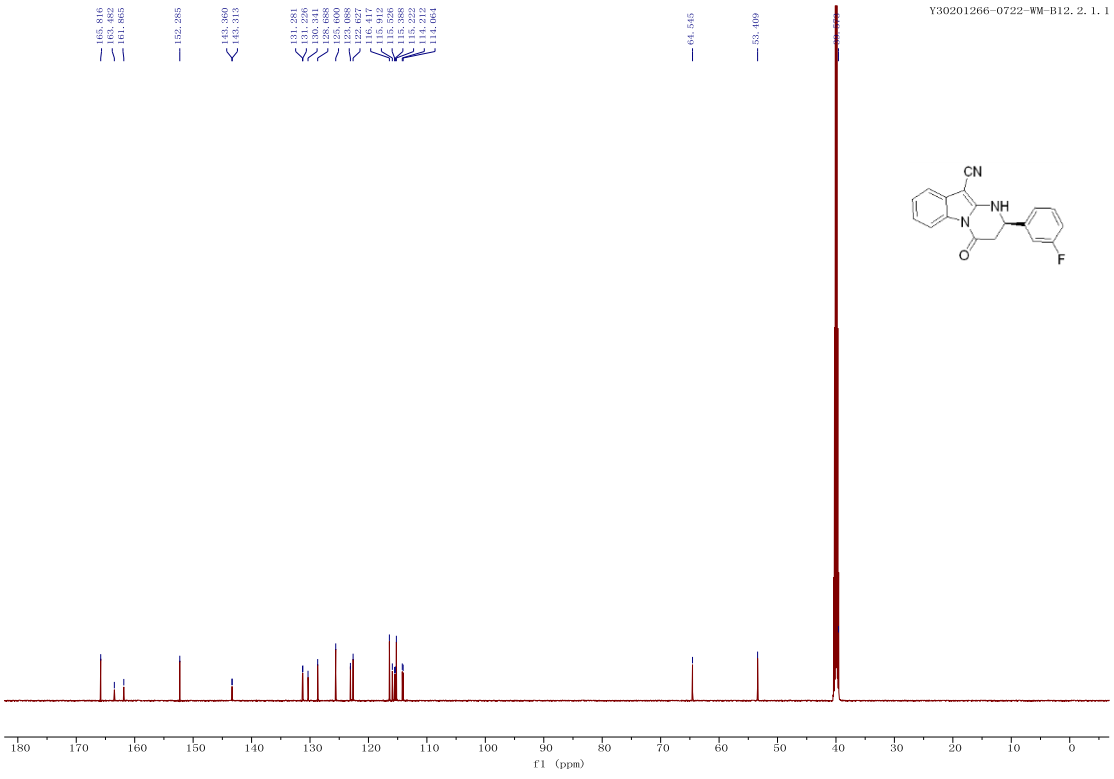
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



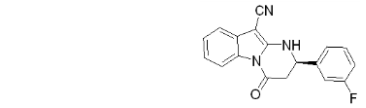
(*R*)-2-(3-Fluorophenyl)-4-oxo-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3u). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]

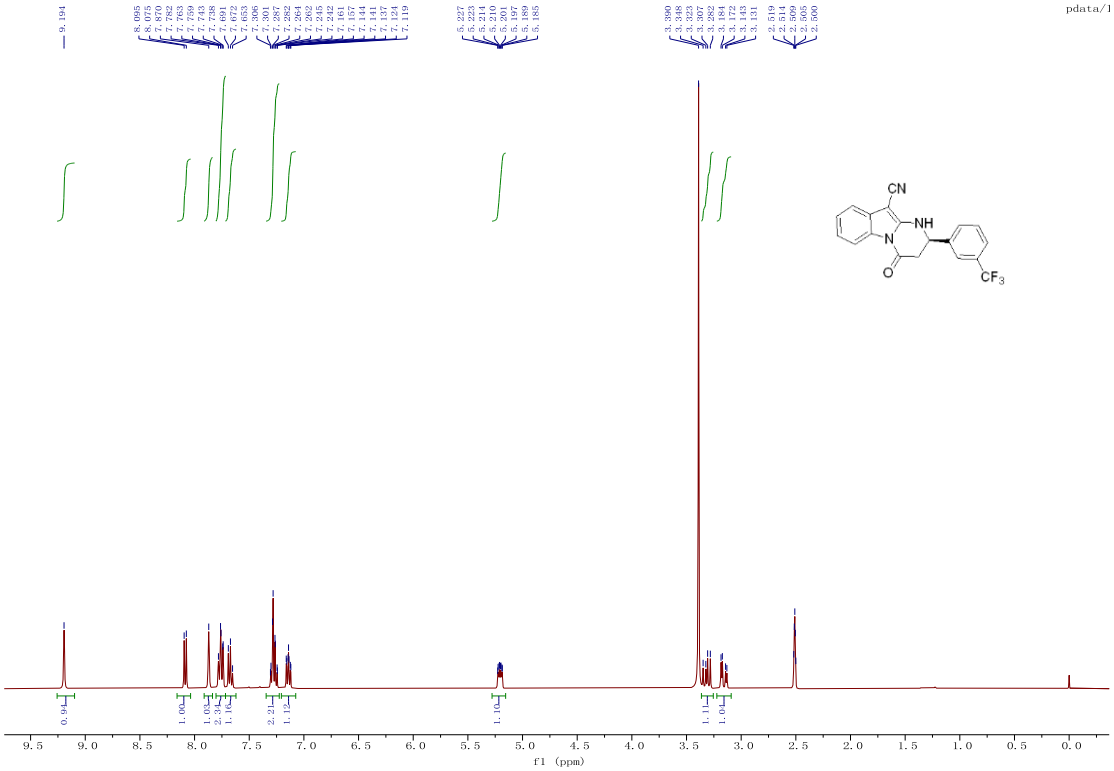


[^{19}F_NMR_565 MHz]

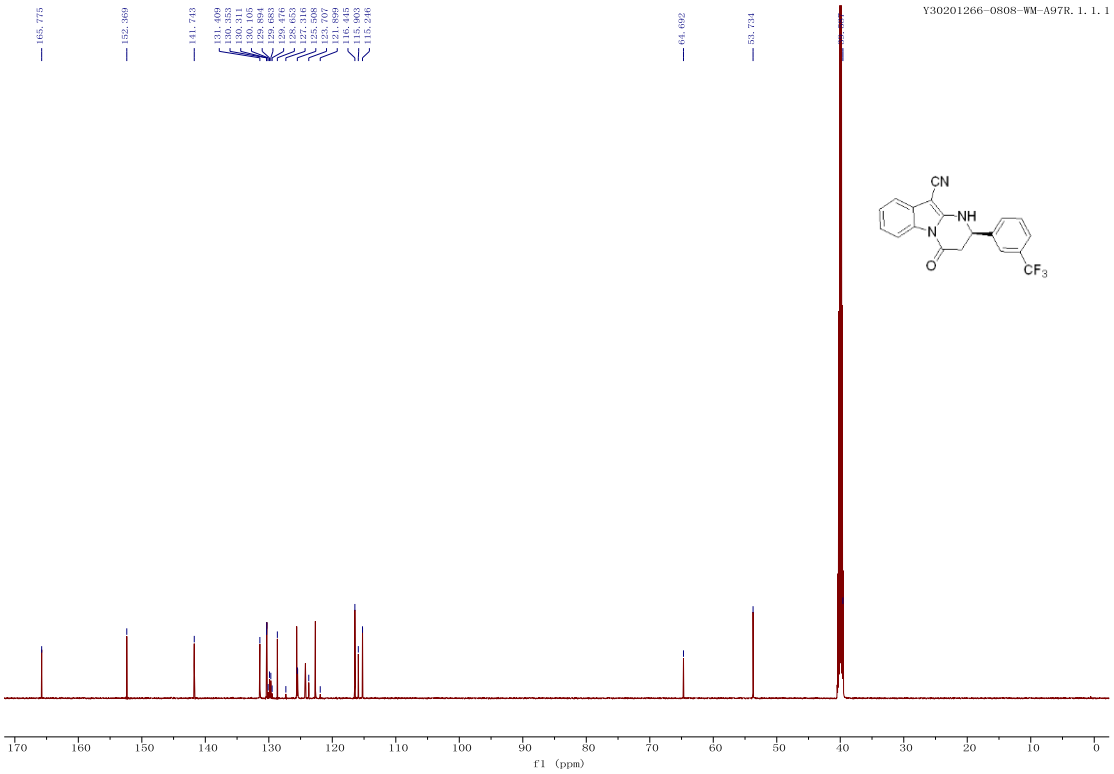

CN
NH
N
O
F

-112.493
-112.507
-112.524
-112.538
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
f1 (ppm)

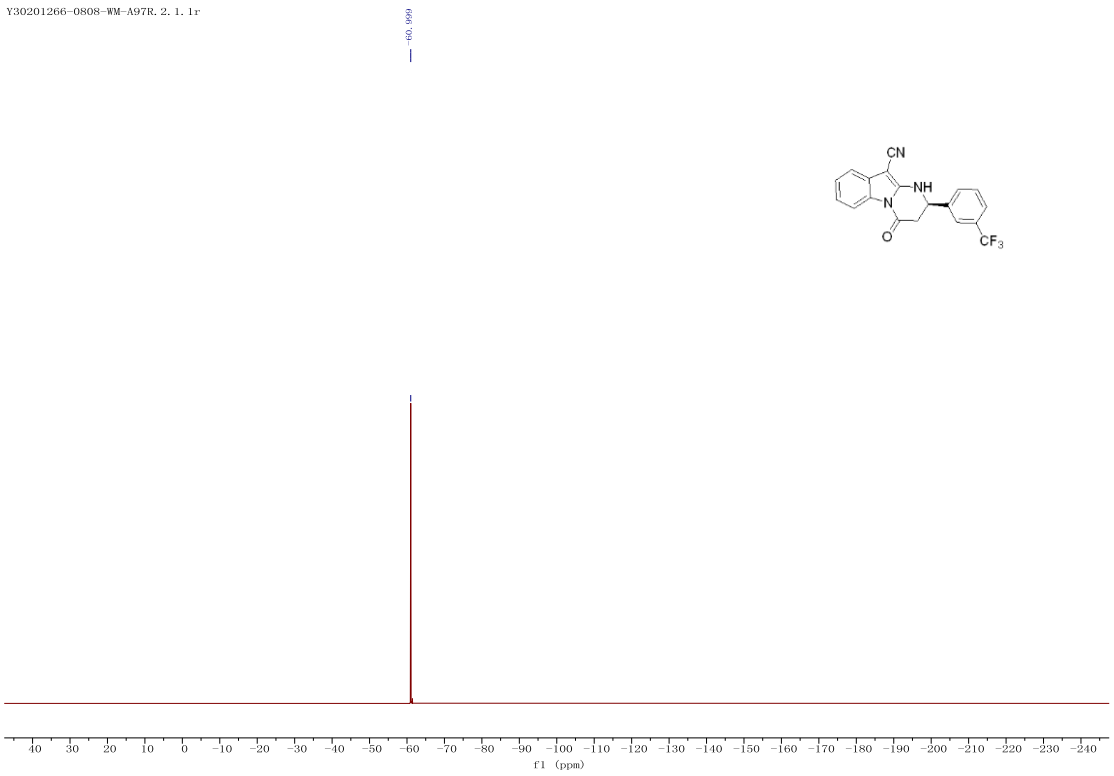
(*R*)-4-Oxo-2-(3-(trifluoromethyl)phenyl)-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3v). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



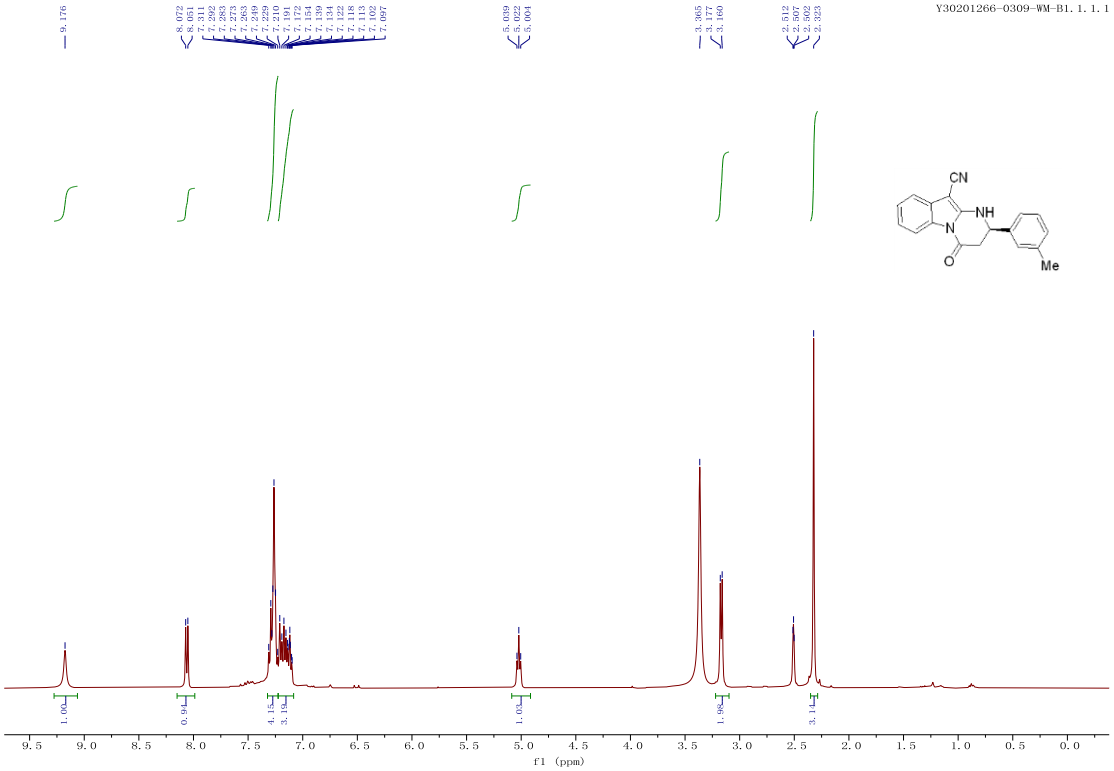
[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]



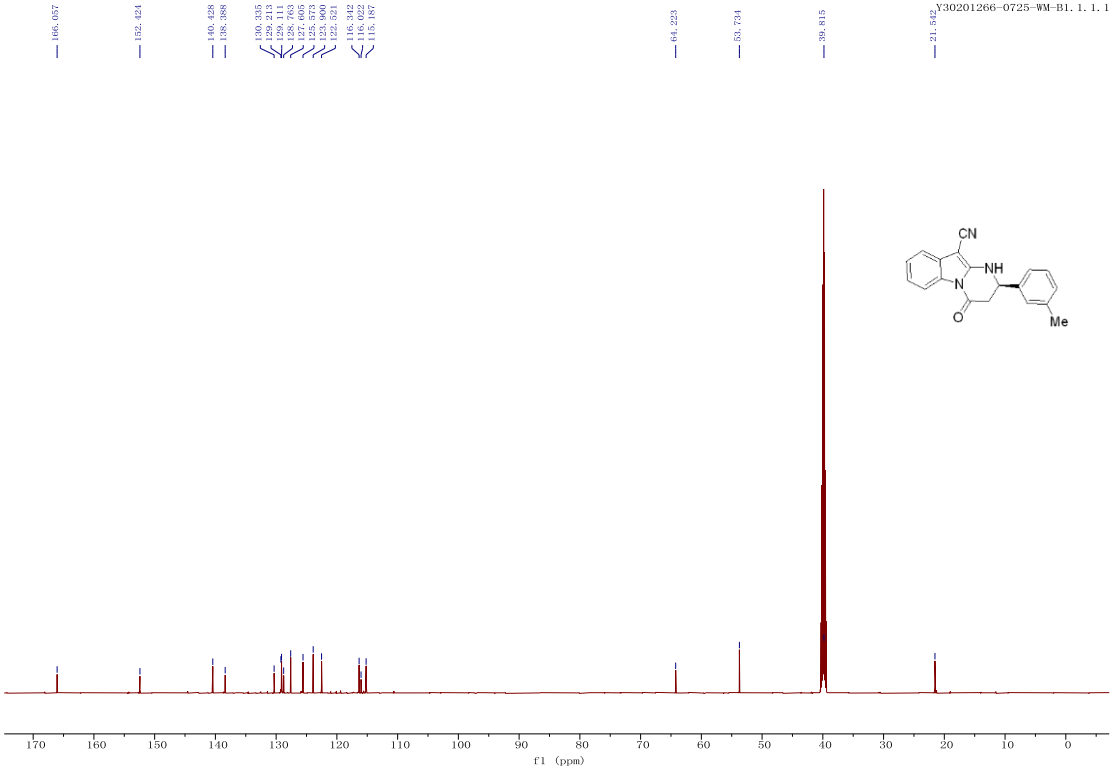
[^{19}F_NMR_565 MHz]


Y30201266-0808-WM-A97R.2.1.1r
-60.999
CN
NH
N
O
CF3
40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

(*R*)-4-Oxo-2-(m-tolyl)-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carbonitrile (3w). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]

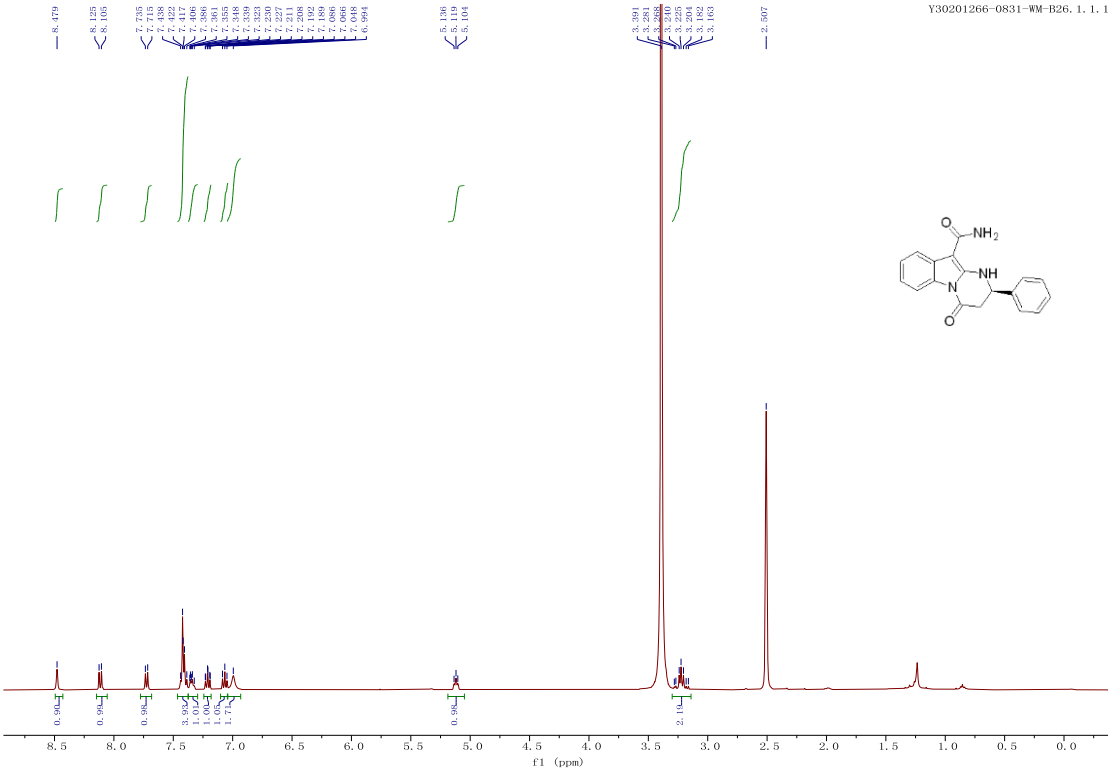


[^{13}C_NMR_151 MHz_(DMSO-d_6: 39.5 ppm)]

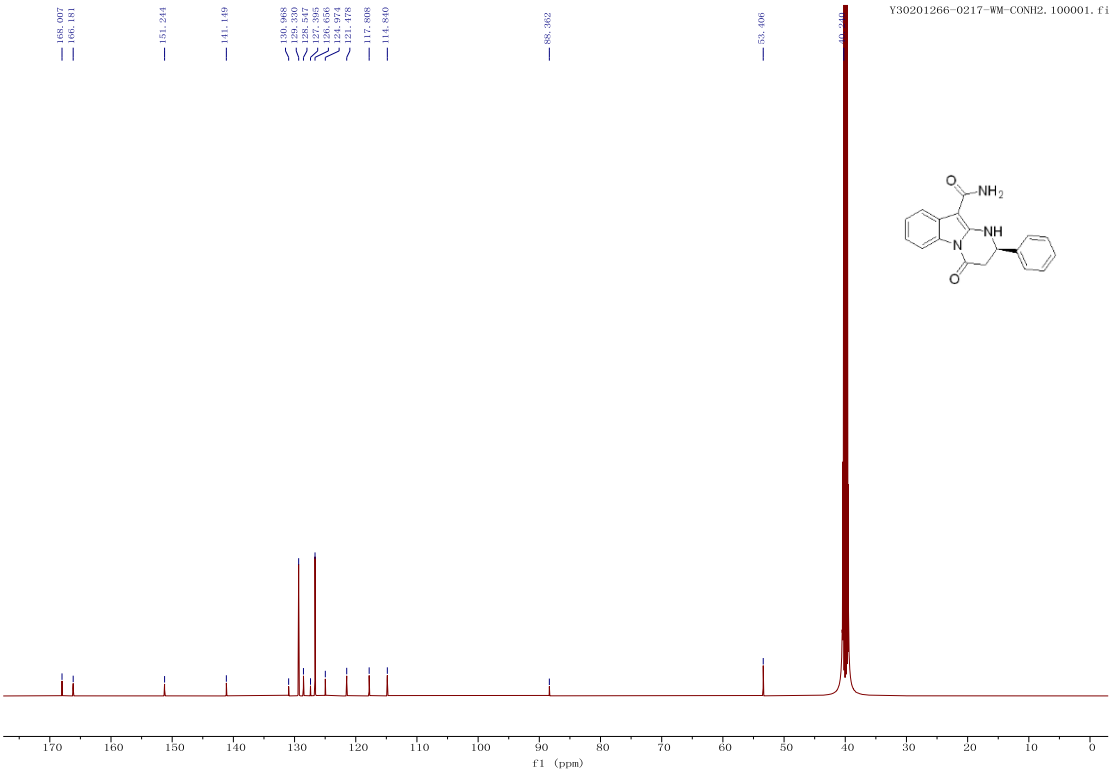


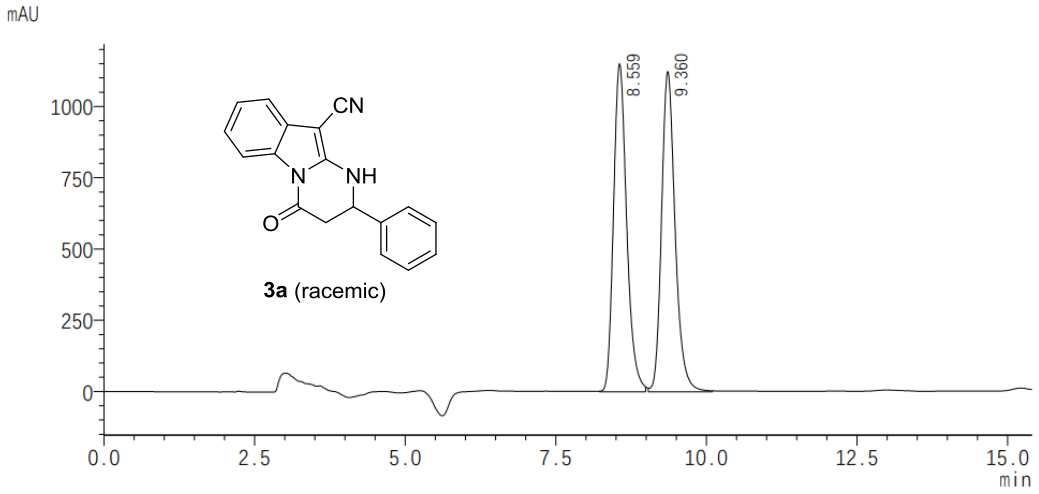
(*R*)-4-Oxo-2-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]indole-10-carboxamide

(4a). [^{1}H_NMR_400 MHz_(DMSO-d_6: 3.36, 2.50 ppm)]



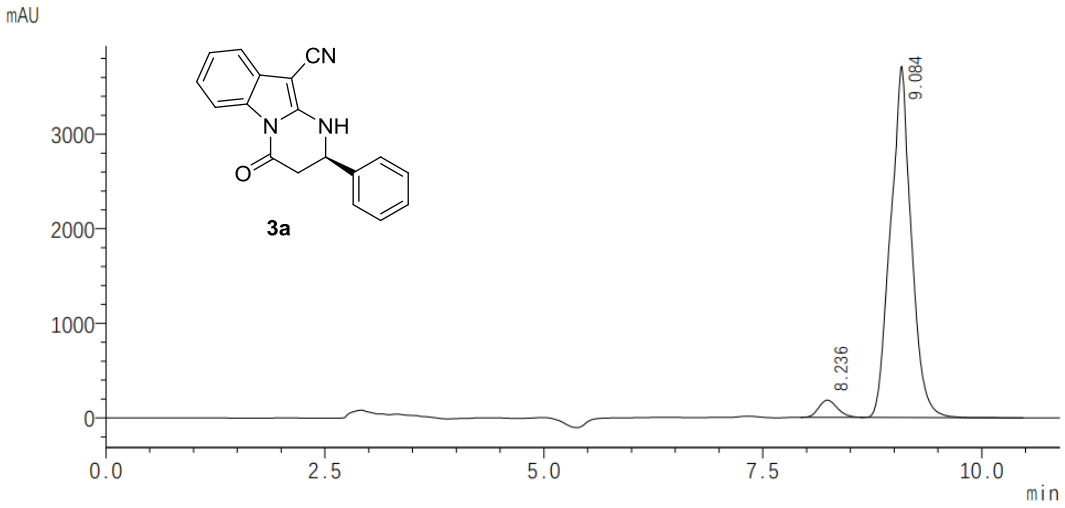
^{13}C NMR (151 MHz, DMSO-d_6) spectrum of compound **4a**





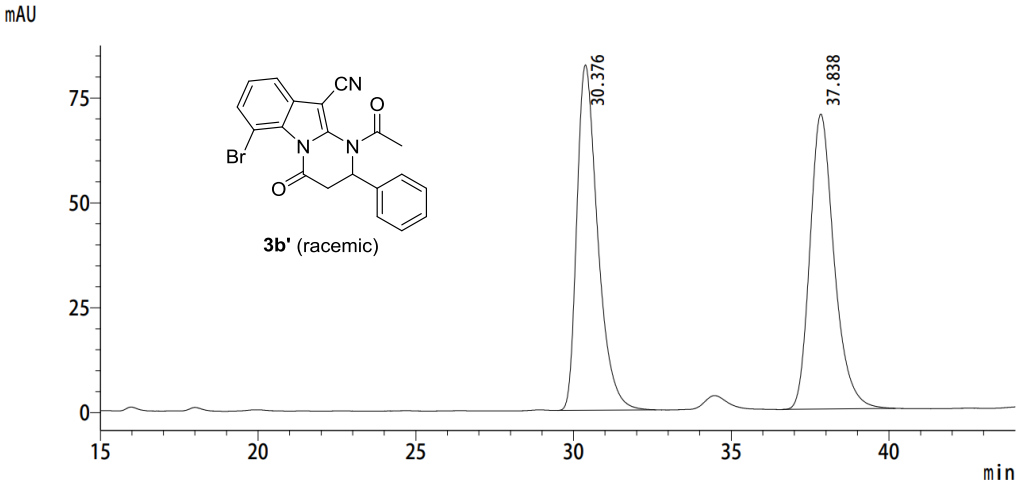
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Hight %
1	8.559	17472800	1149727	49.691	50.591
2	9.360	17689787	1122865	50.309	49.409



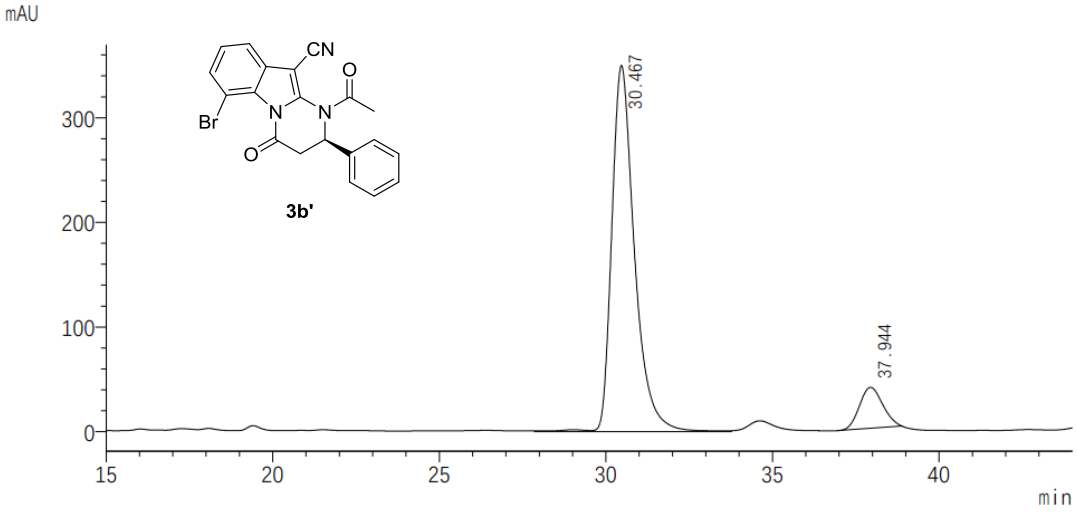
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Hight %
1	8.236	2695564	181755	4.205	4.669
2	9.084	61414595	3711178	95.795	95.331



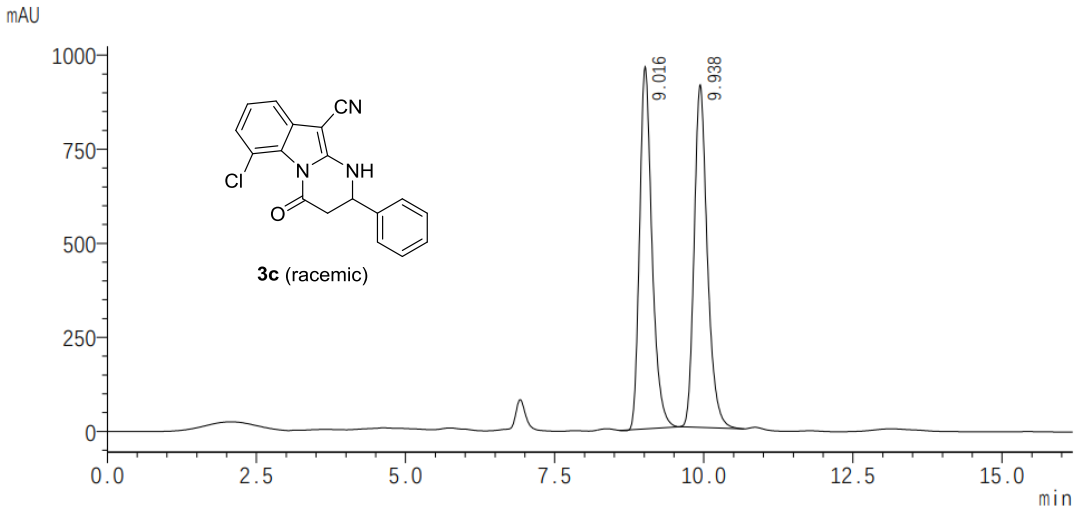
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Hight [mAU]	Area %	Hight %
1	30.376	3778053	82289	50.070	53.926
2	37.838	3767500	70308	49.930	46.074



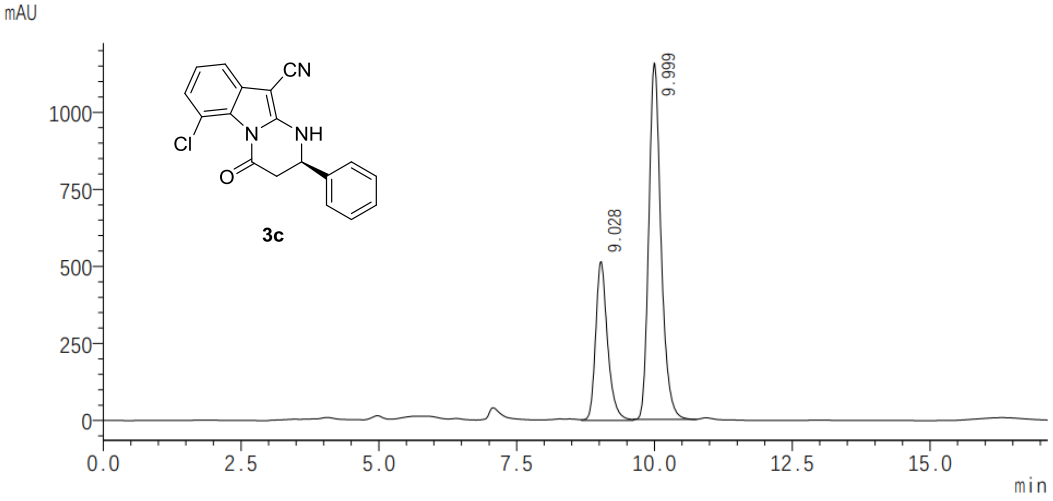
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Hight [mAU]	Area %	Hight %
1	30.467	16558116	349838	89.729	89.945
2	37.944	1895257	39110	10.271	10.055



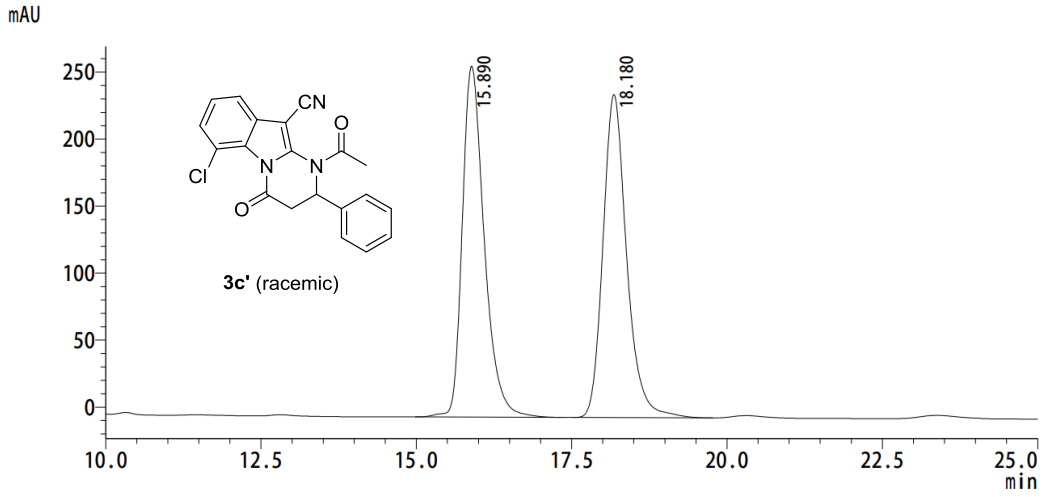
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Hight %
1	9.016	13923075	961822	49.855	51.371
2	9.938	14003852	910470	50.145	48.629



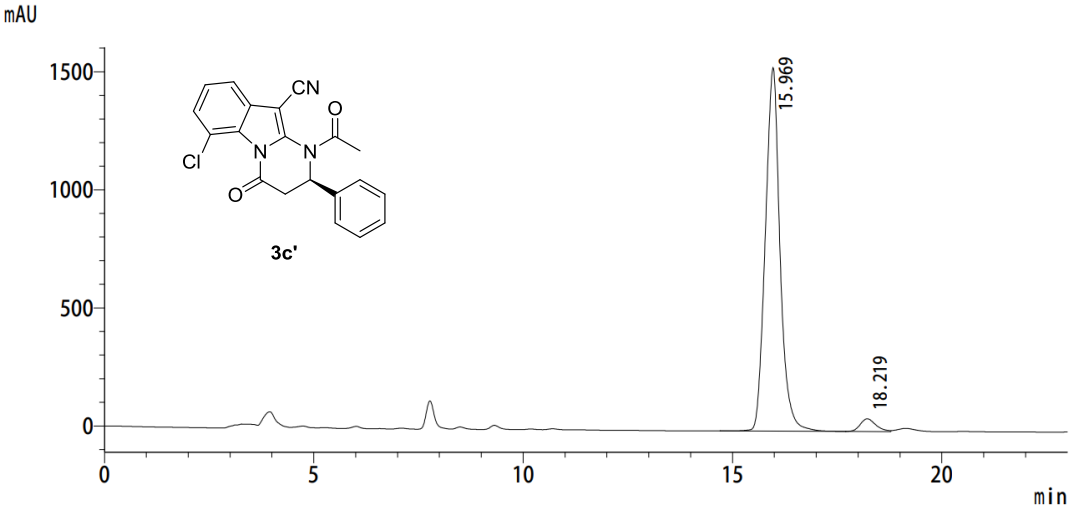
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Hight %
1	9.028	7789704	515591	30.379	30.857
2	9.999	17852313	1155331	69.621	69.143



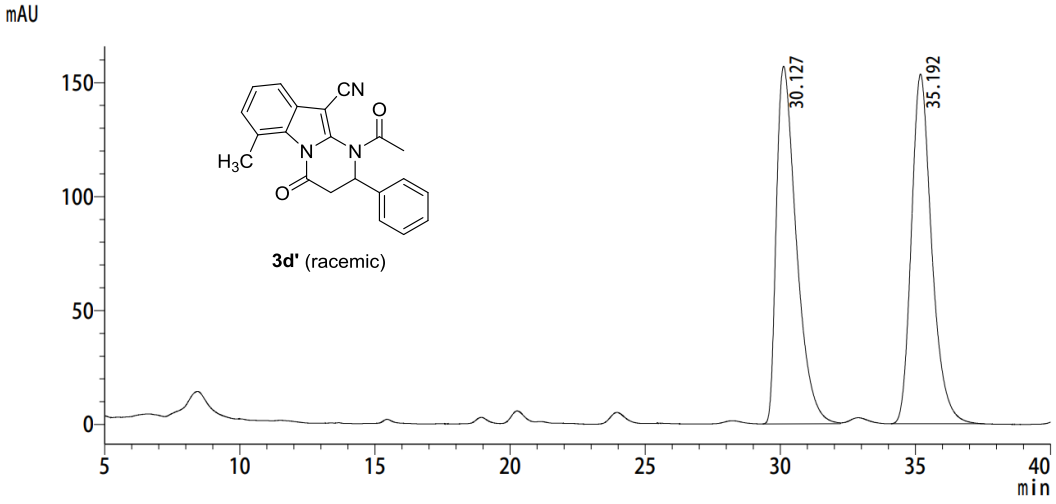
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Hight [mAU]	Area %	Hight %
1	15.890	6445577	261850	50.169	52.073
2	18.180	6402254	241005	49.831	47.927



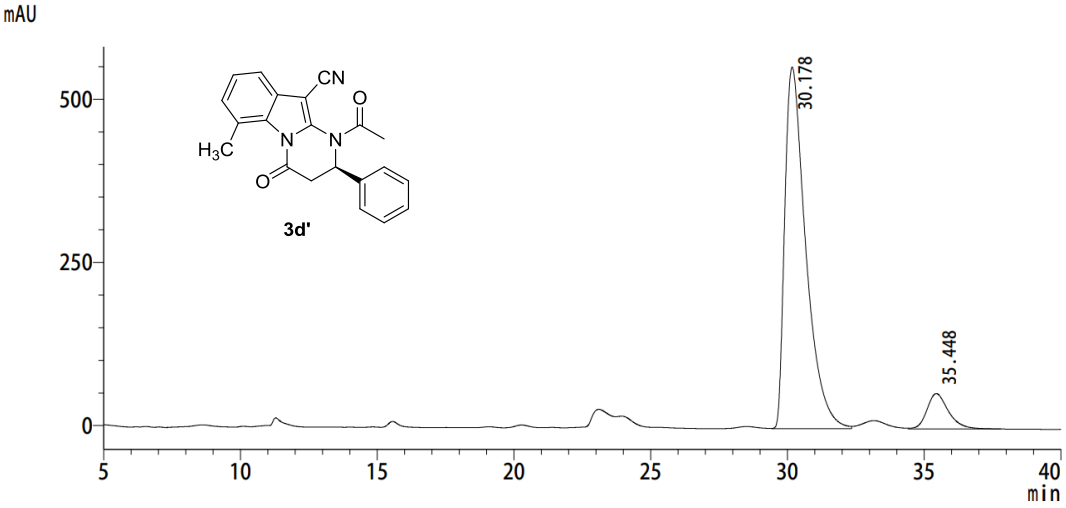
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Hight [mAU]	Area %	Hight %
1	15.969	37565870	1539364	96.441	96.637
2	18.219	1386317	53566	3.559	3.363



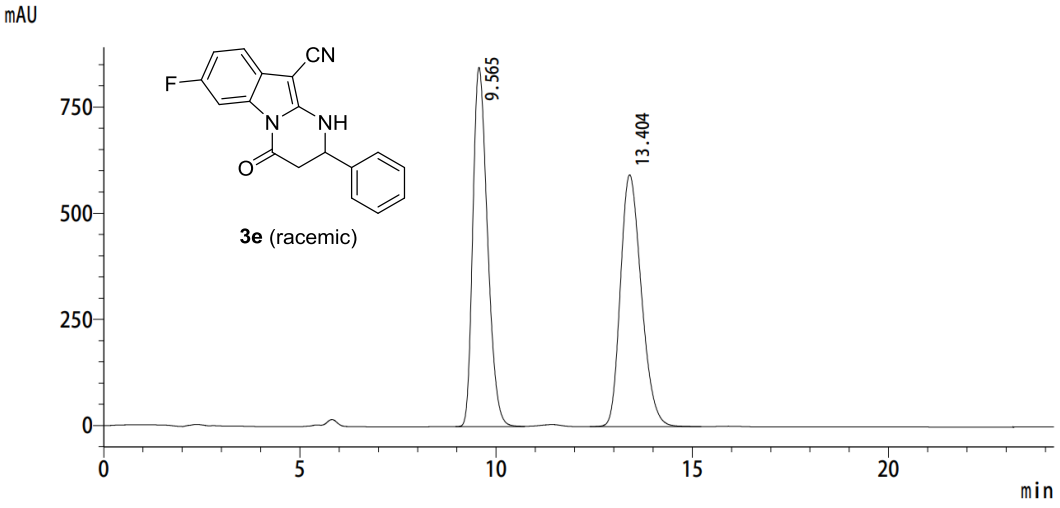
PDA Ch1 254nm

Peak #	Ret. Time [min]	Area [mAU*s]	Hight [mAU]	Area %	Hight %
1	30.127	8057517	156884	50.061	50.555
2	35.192	8037814	153440	49.939	49.445



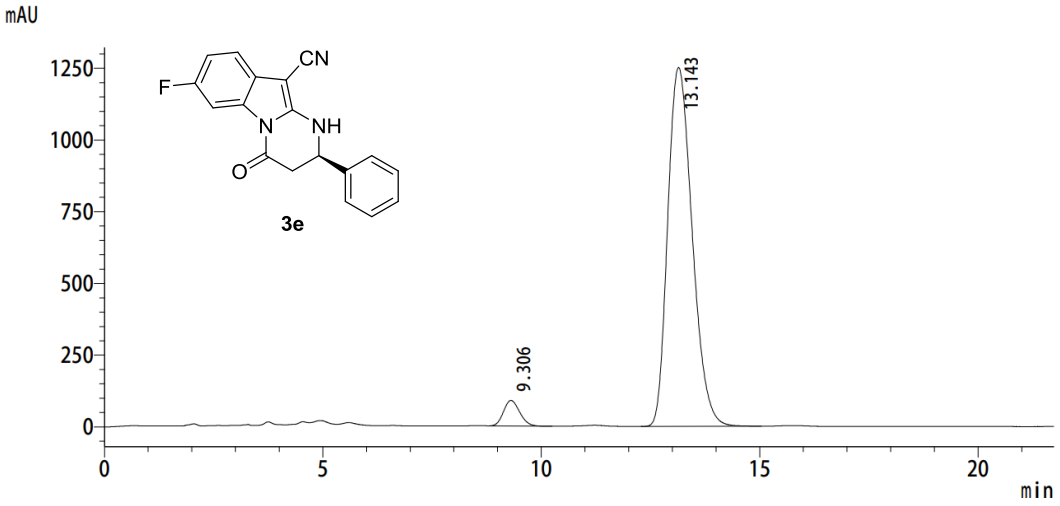
PDA Ch1 254nm

Peak #	Ret. Time [min]	Area [mAU*s]	Hight [mAU]	Area %	Hight %
1	30.178	29623830	554091	90.928	91.104
2	35.448	2955440	54105	9.072	8.896



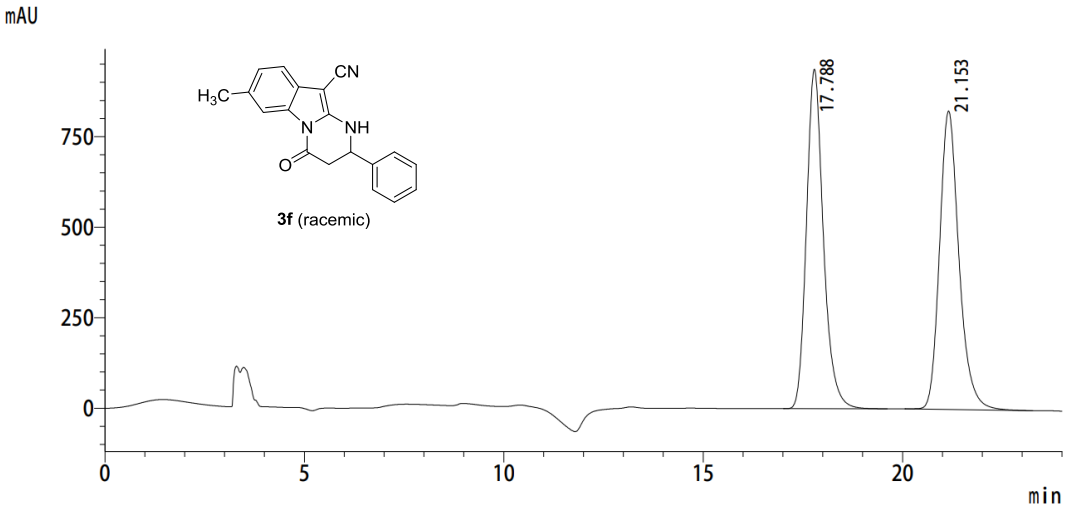
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Height %
1	9.565	21983654	846334	49.917	58.781
2	13.404	22056509	593472	50.083	41.219



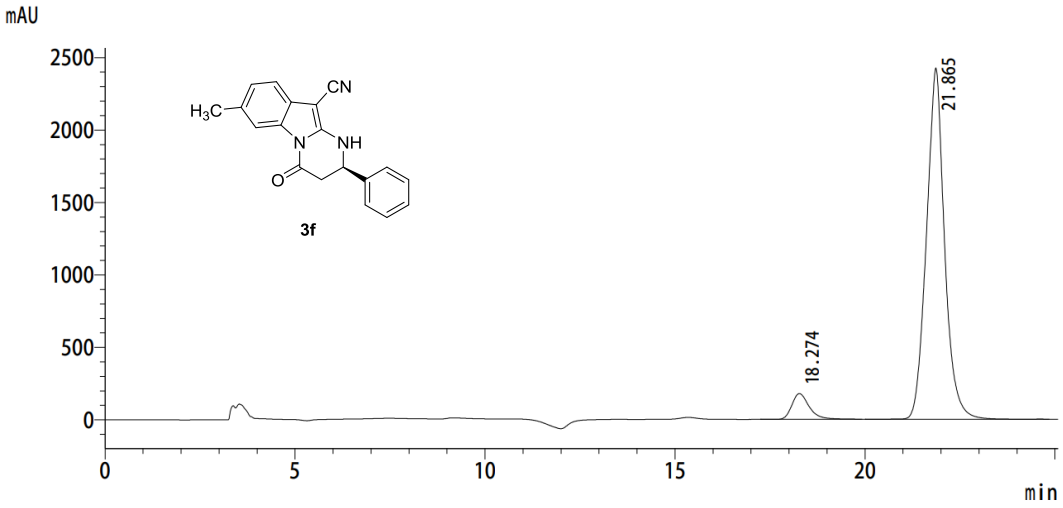
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Height %
1	9.306	2308916	89494	4.528	6.677
2	13.143	48686883	1250898	95.472	93.323



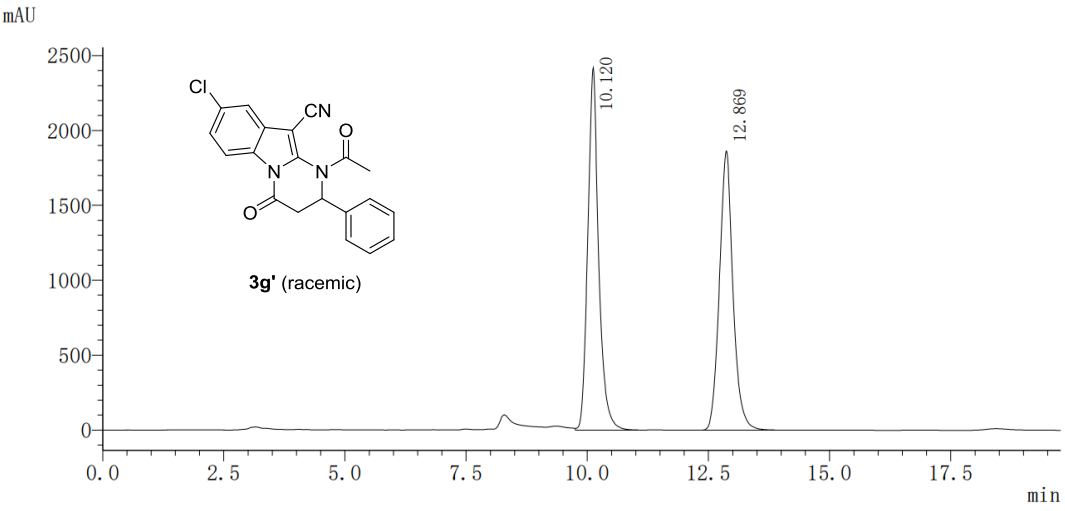
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Height %
1	17.788	27744260	937424	49.811	53.198
2	21.153	27954554	824710	50.189	46.802



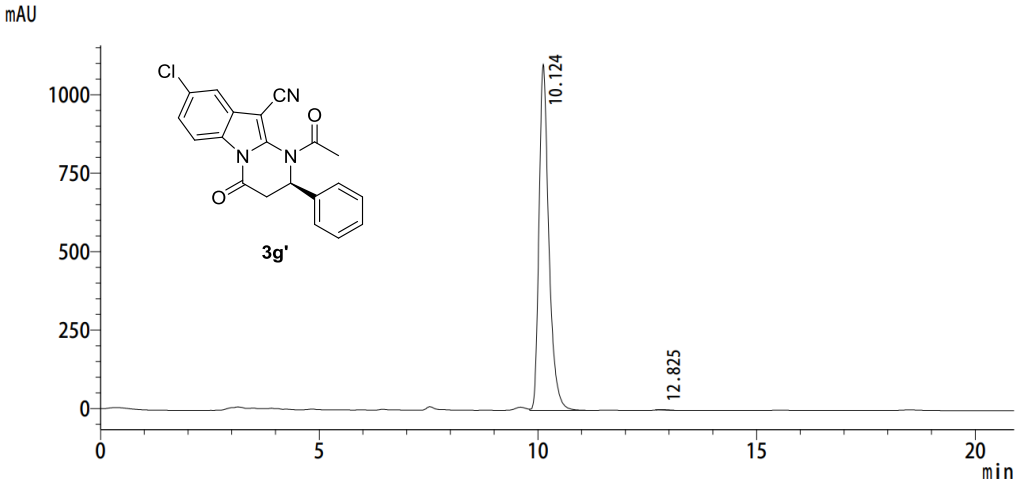
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Hight [mAU]	Area %	Hight %
1	18.274	5626591	177943	6.567	6.842
2	21.865	80049160	2422767	93.433	93.158



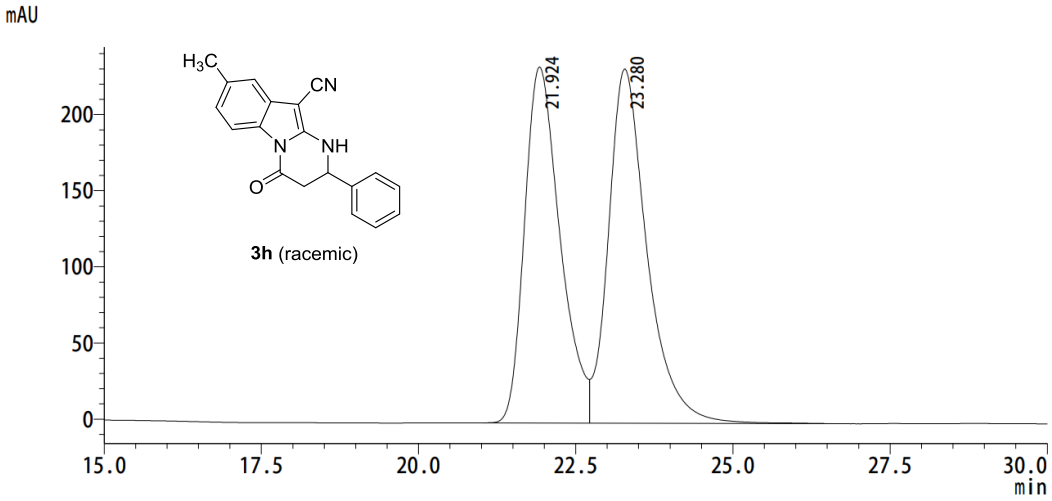
PDA Ch1 254nm

Peak #	Ret. Time [min]	Area [mAU*s]	Hight [mAU]	Area %	Hight %
1	10.120	37536444	2419430	50.854	56.499
2	12.869	36276278	1862798	49.146	43.501



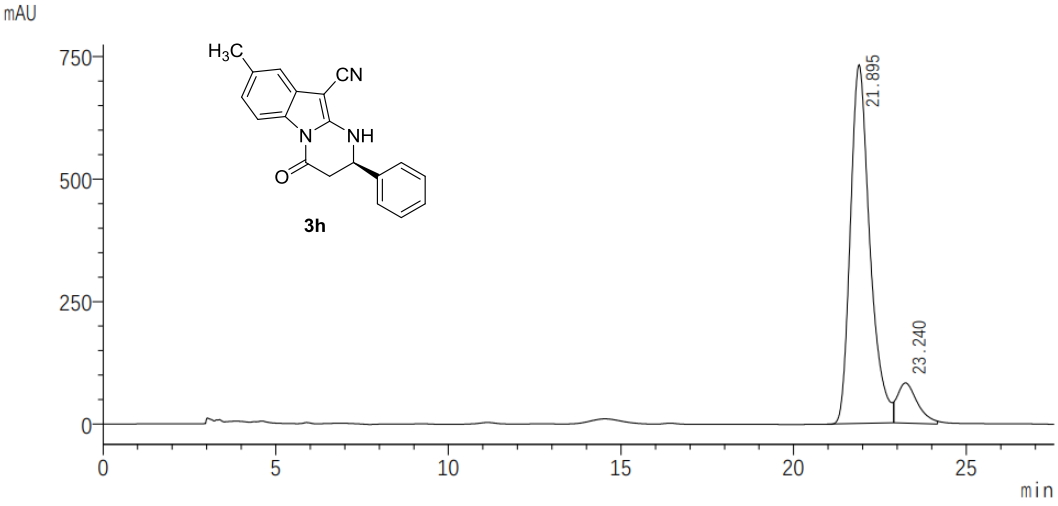
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Hight [mAU]	Area %	Hight %
1	10.124	17250470	1101452	99.869	99.855
2	12.825	22604	1600	0.131	0.145



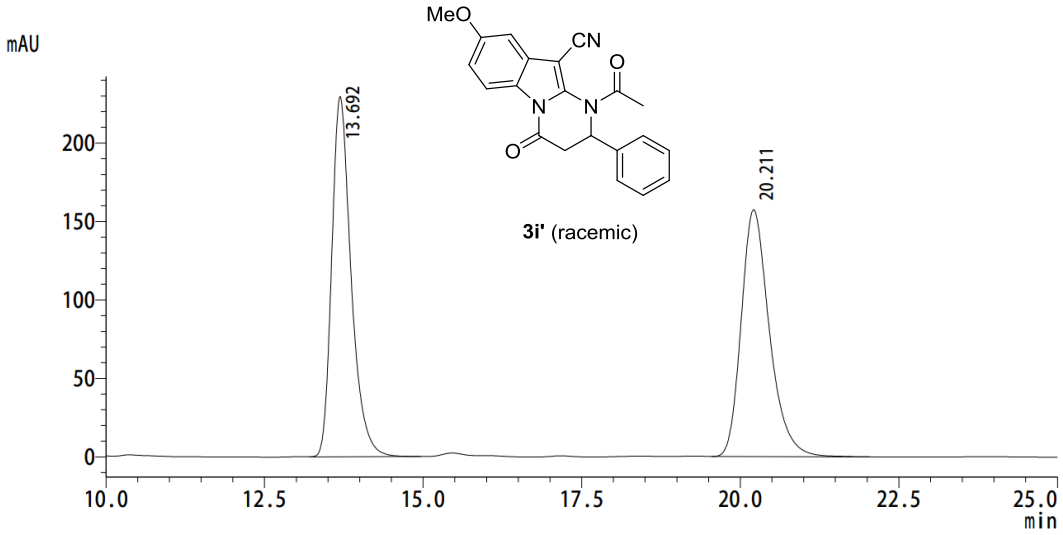
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Height %
1	21.924	9191345	233762	48.052	50.132
2	23.280	9936688	232533	51.948	49.868



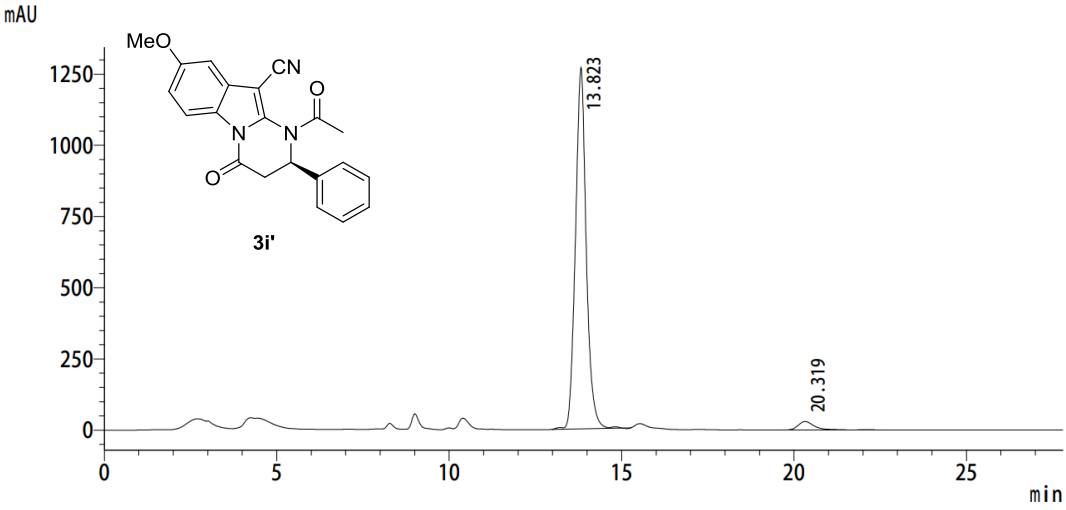
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Hight %
1	21.895	28784850	731603	89.650	89.905
2	23.240	3323122	82152	10.350	10.095



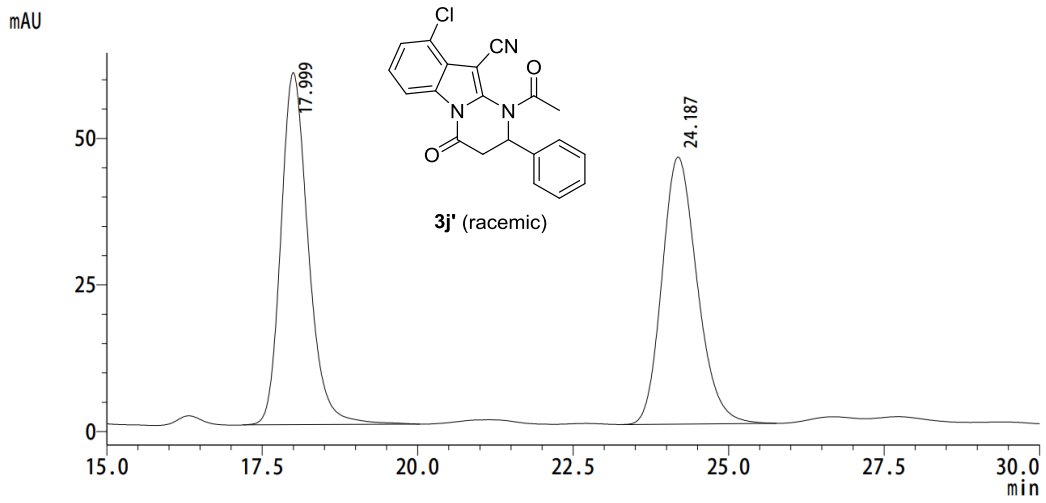
PDA Ch1 254nm

Peak #	Ret. Time [min]	Area [mAU*s]	Hight [mAU]	Area %	Hight %
1	13.692	4889912	229531	50.061	59.327
2	20.211	4877985	157358	49.939	40.673



PDA Ch1 254nm

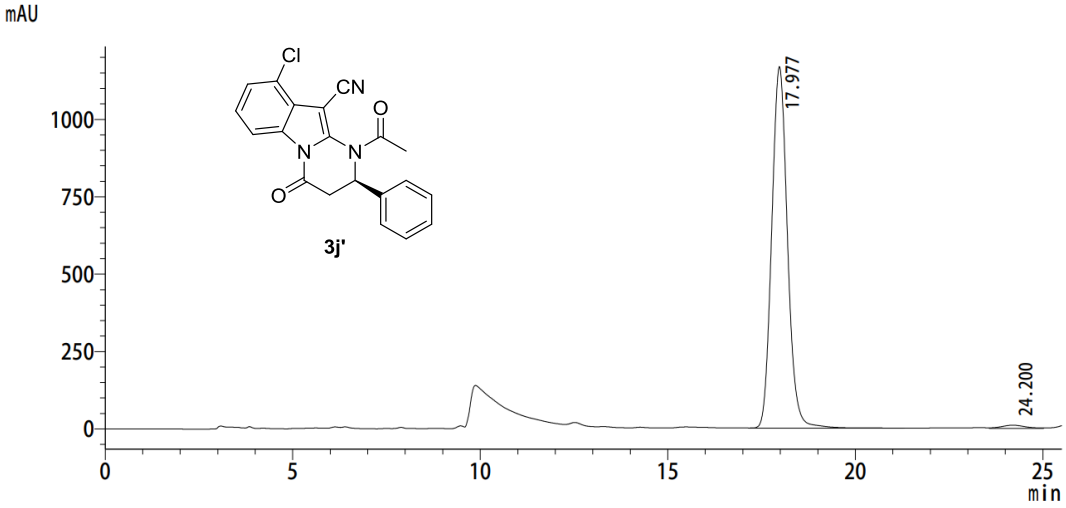
Peak#	Ret. Time [min]	Area [mAU*s]	Hight [mAU]	Area %	Hight %
1	13.823	27589754	1268924	96.500	97.718
2	20.319	1000536	29632	3.500	2.282



3j' (racemic)

PDA Ch1 254nm

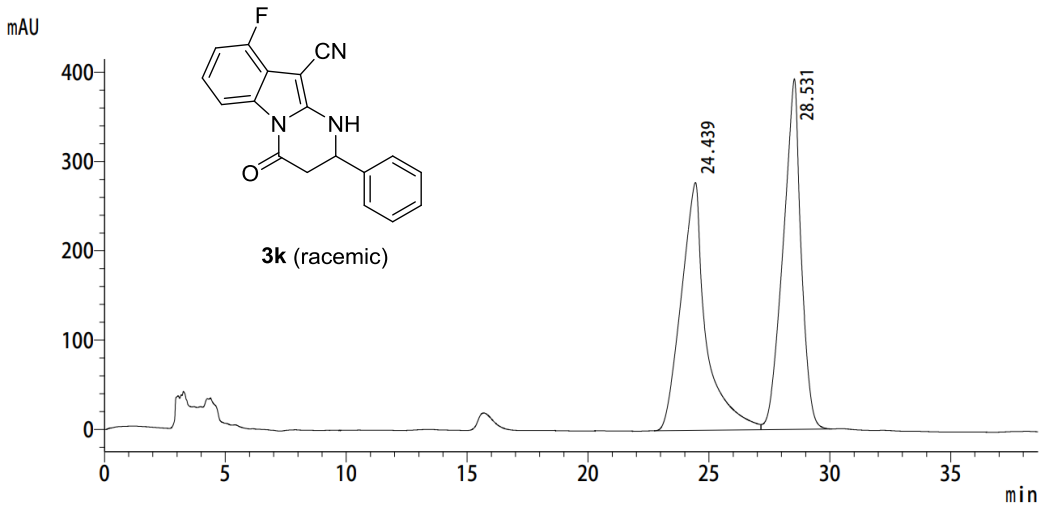
Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Hight %
1	17.999	1845865	60046	50.684	56.863
2	24.187	1796039	45552	49.316	43.137



3j'

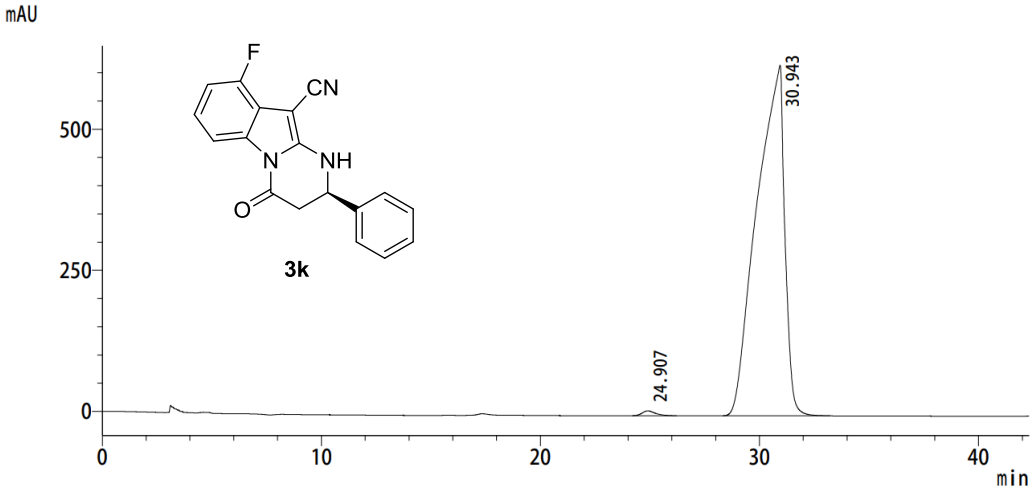
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Height %
1	17.977	34058008	1167274	98.697	99.131
2	24.200	449801	10232	1.303	0.869



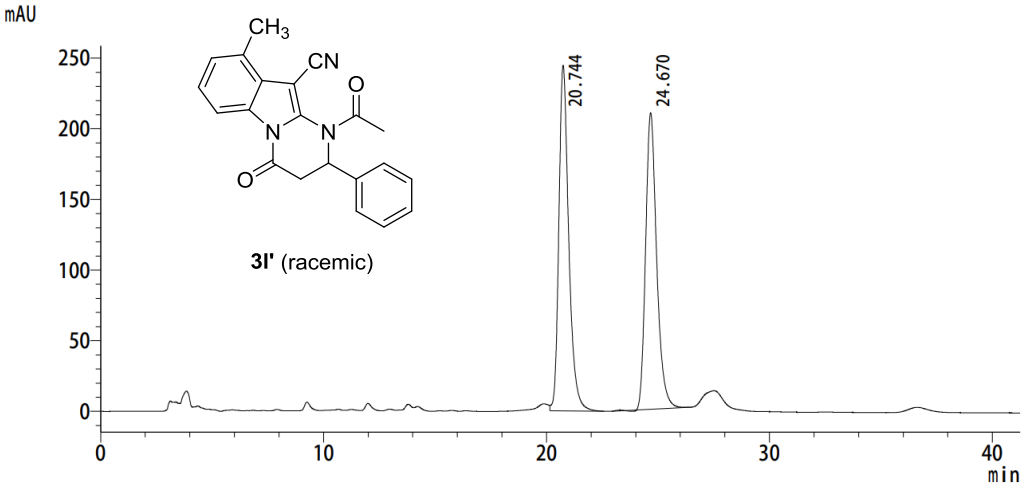
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Height %
1	24.439	19873109	277670	49.423	41.422
2	28.531	20337455	392672	50.577	58.578



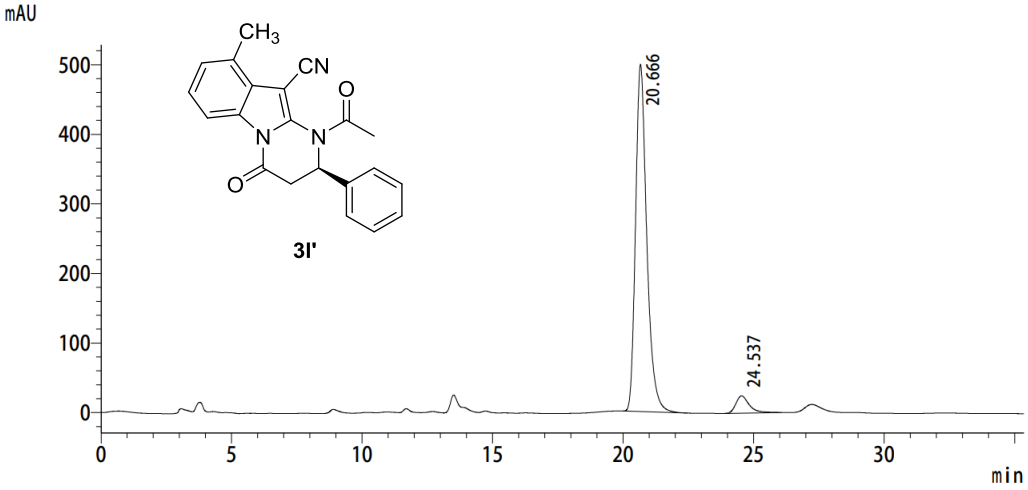
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Height %
1	24.907	363967	8600	0.661	1.366
2	30.943	54726874	620835	99.339	98.634



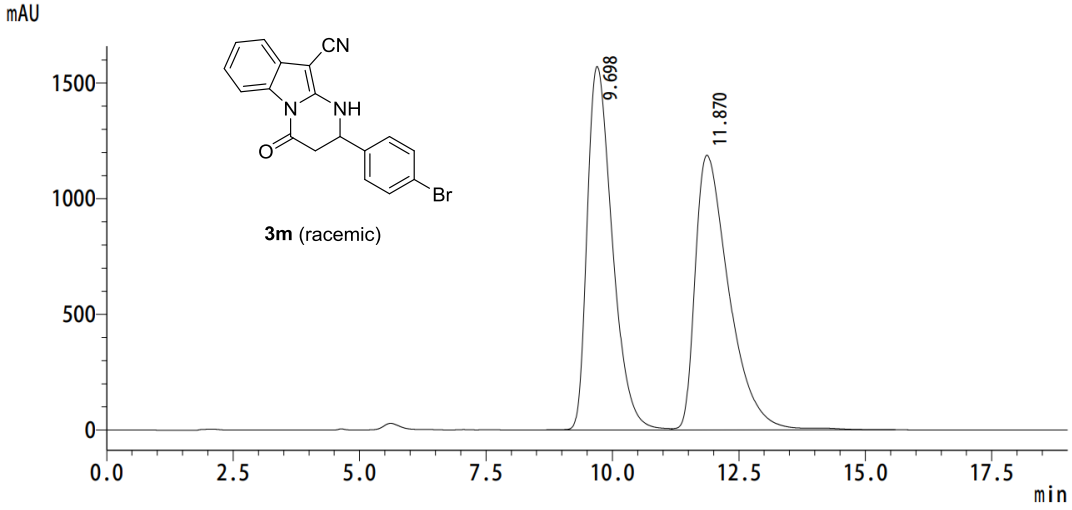
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Height %
1	20.744	7528445	244564	51.014	53.814
2	24.670	7229293	209900	48.986	46.186



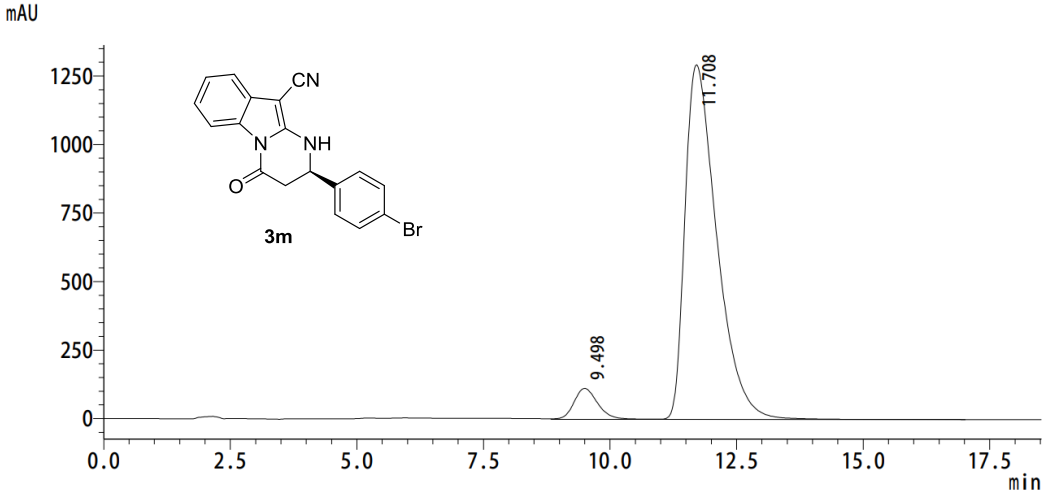
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Hight %
1	20.666	14896185	499087	94.381	95.254
2	24.537	886825	24864	5.619	4.746



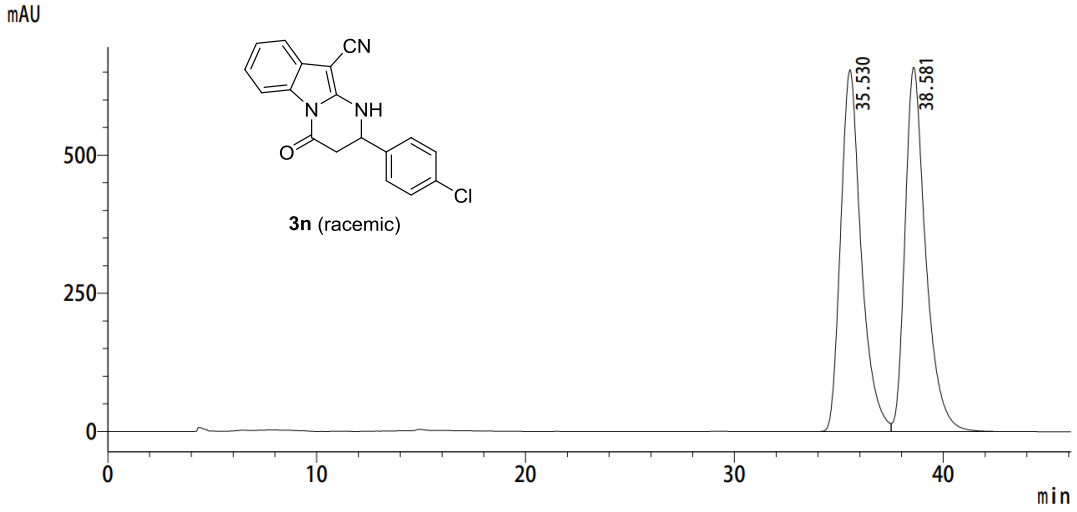
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Height %
1	9.698	54280600	1570765	49.530	56.955
2	11.870	55311736	1187133	50.470	43.045



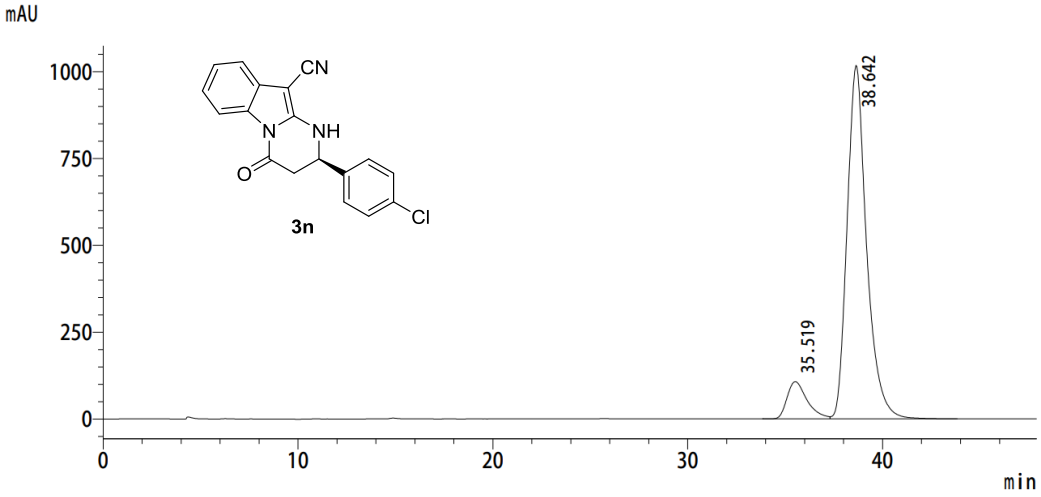
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Height %
1	9.498	3713397	112918	6.151	8.029
2	11.708	56656395	1293467	93.849	91.971



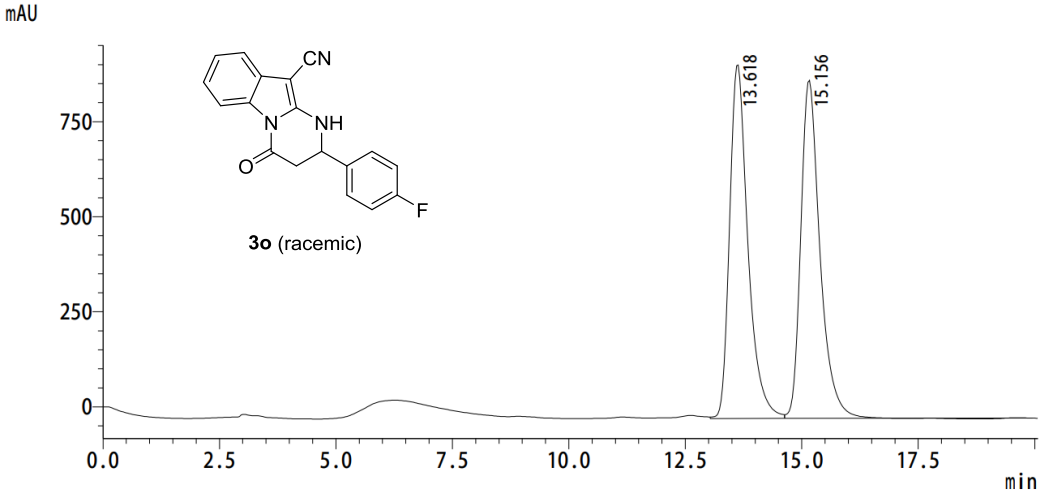
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Height %
1	35.530	44827959	654273	49.679	49.830
2	38.581	45407905	658732	50.321	50.170



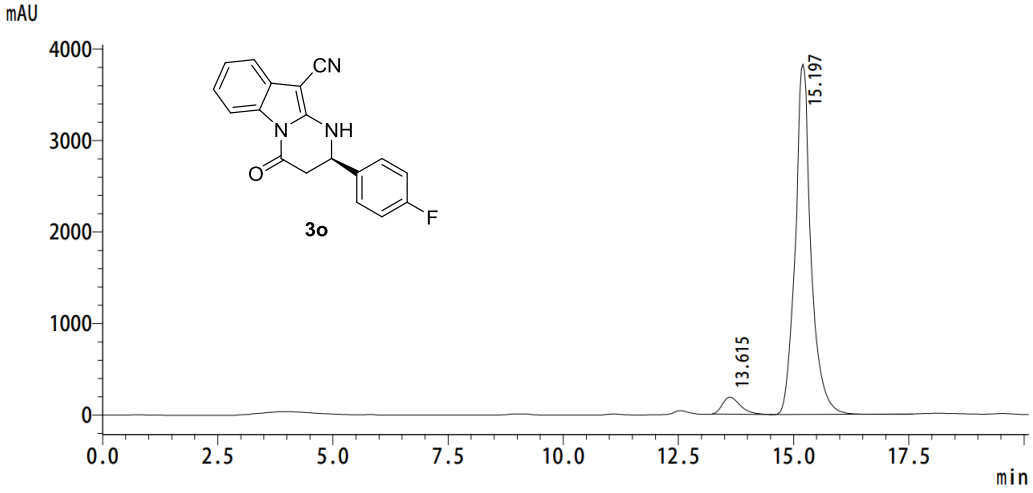
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Hight [mAU]	Area %	Hight %
1	35.519	7698932	107113	9.826	9.527
2	38.642	70651089	1017166	90.174	90.473



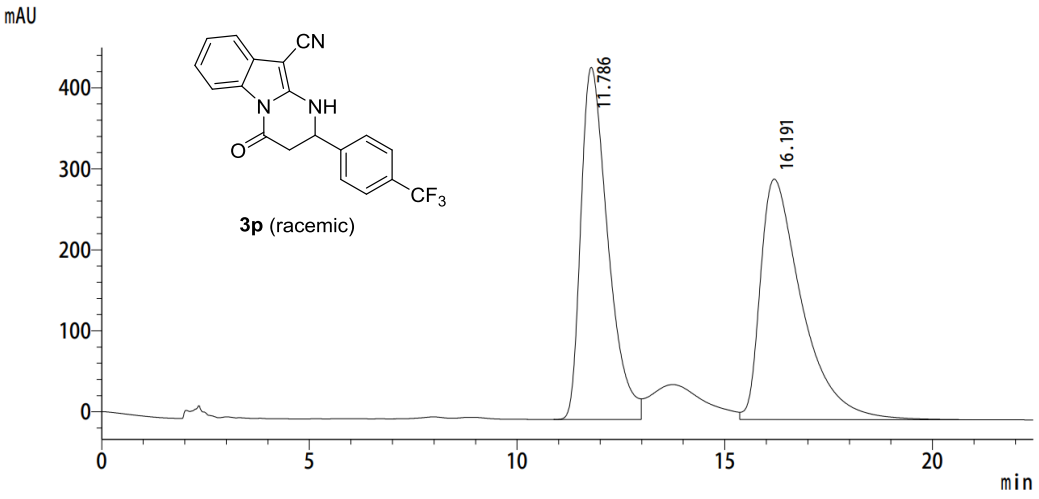
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Height %
1	13.618	25452729	929497	50.116	51.103
2	15.156	25335164	889388	49.884	48.897



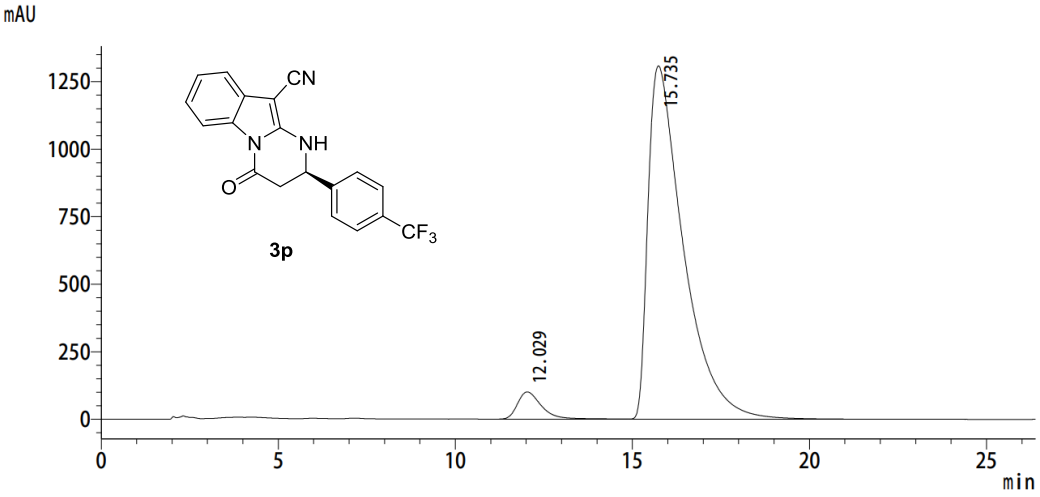
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Hight [mAU]	Area %	Hight %
1	13.615	5025183	185894	5.236	4.636
2	15.197	90940005	3823504	94.764	95.364



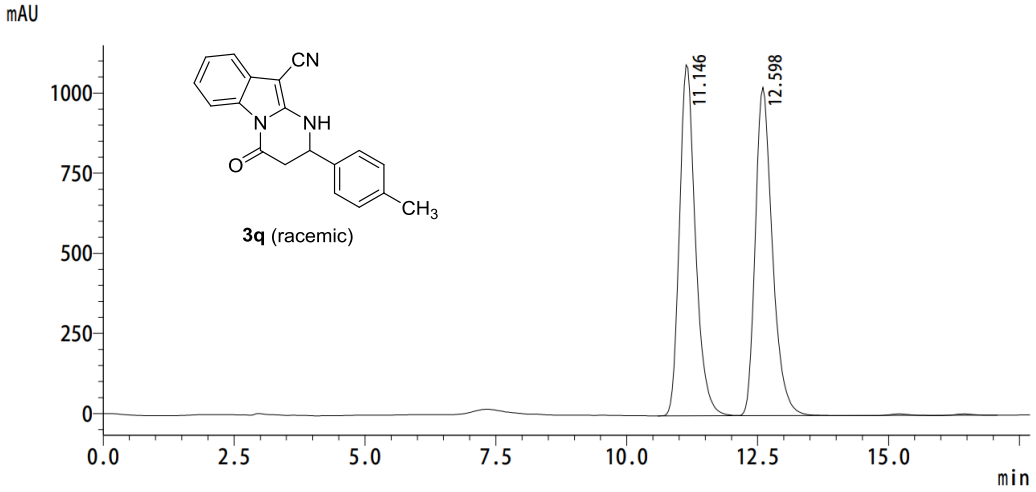
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Height %
1	11.786	19644789	434764	48.697	59.418
2	16.191	20695901	296943	51.303	40.582



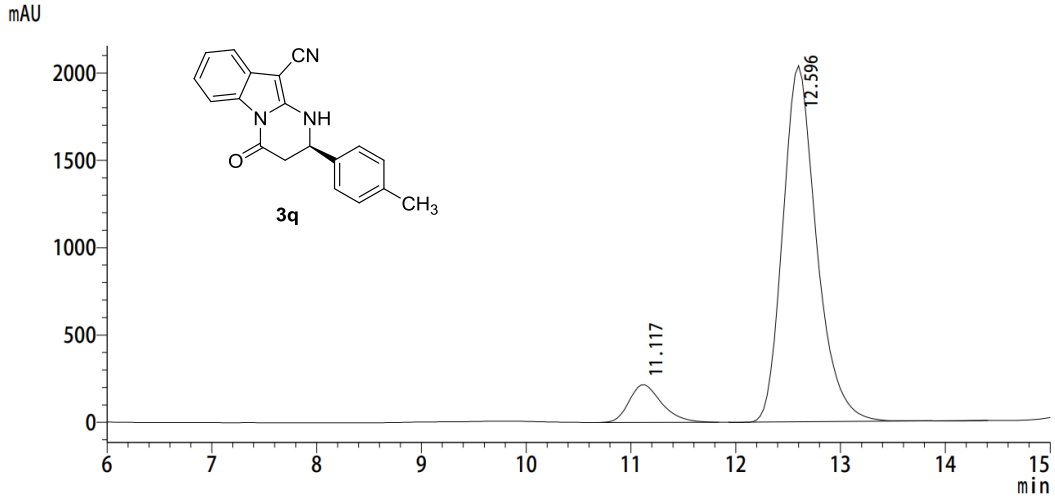
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	面积 %	Height %
1	12.029	4806375	100748	5.013	7.151
2	15.735	91064396	1308186	94.987	92.849



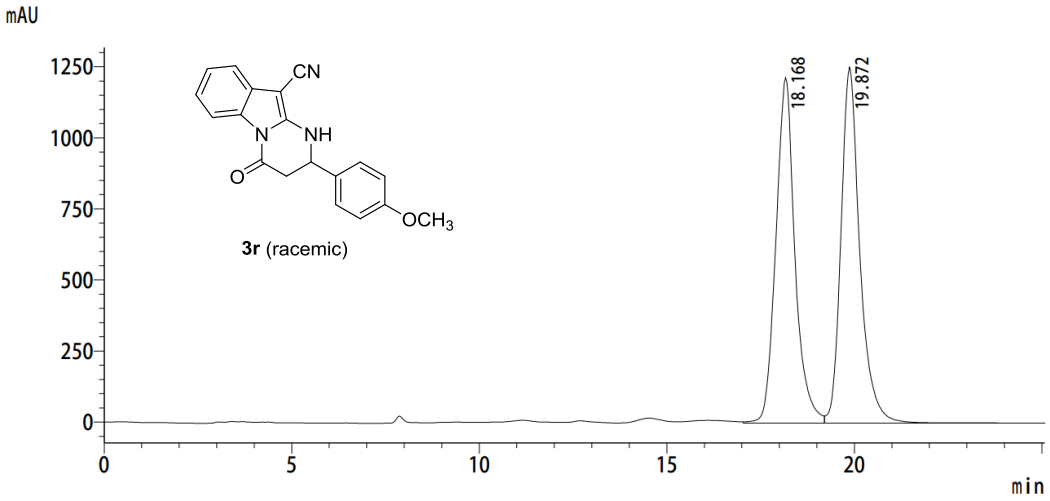
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Height %
1	11.146	23221039	1094659	49.784	51.668
2	12.598	23422741	1023968	50.216	48.332



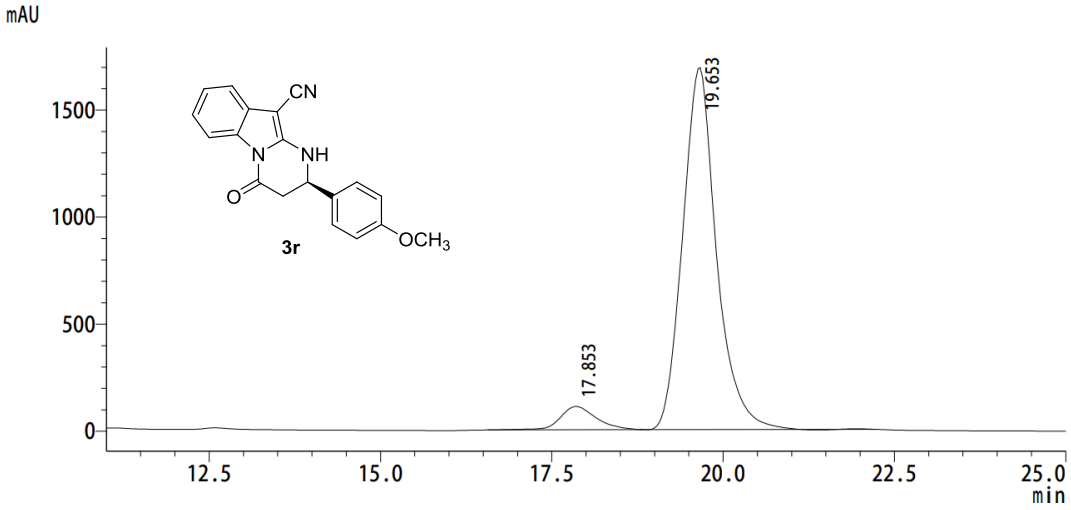
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Hight [mAU]	Area %	Hight %
1	11.117	4658563	213992	9.257	9.500
2	12.596	45666905	2038486	90.743	90.500



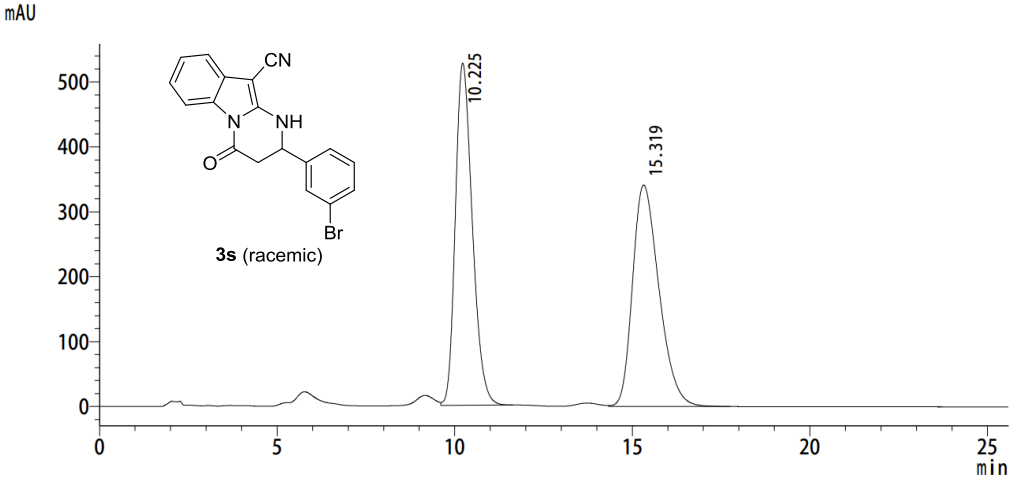
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Height %
1	18.168	43004787	1215731	49.540	49.267
2	19.872	43802876	1251902	50.460	50.733



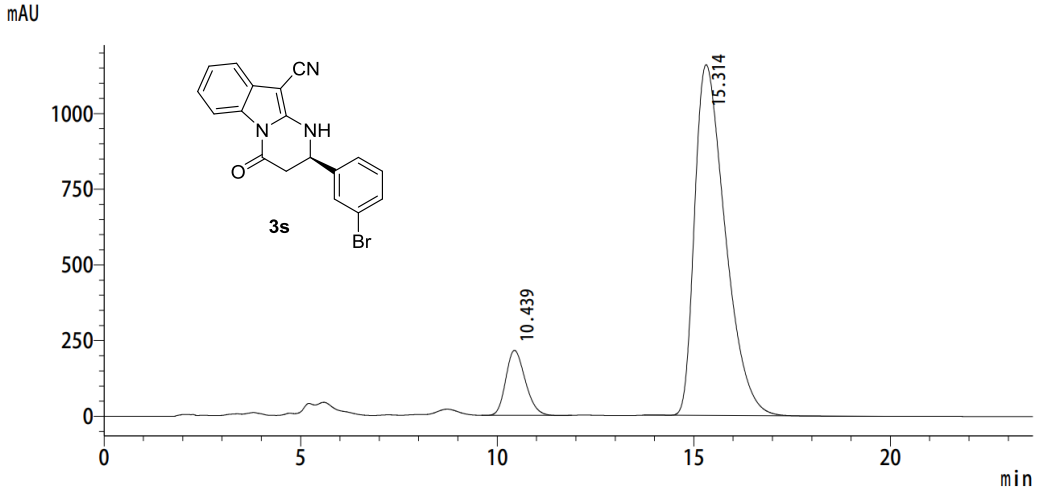
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Hight [mAU]	Area %	Hight %
1	17.853	3989371	108659	6.444	6.041
2	19.653	57915891	1689946	93.556	93.959



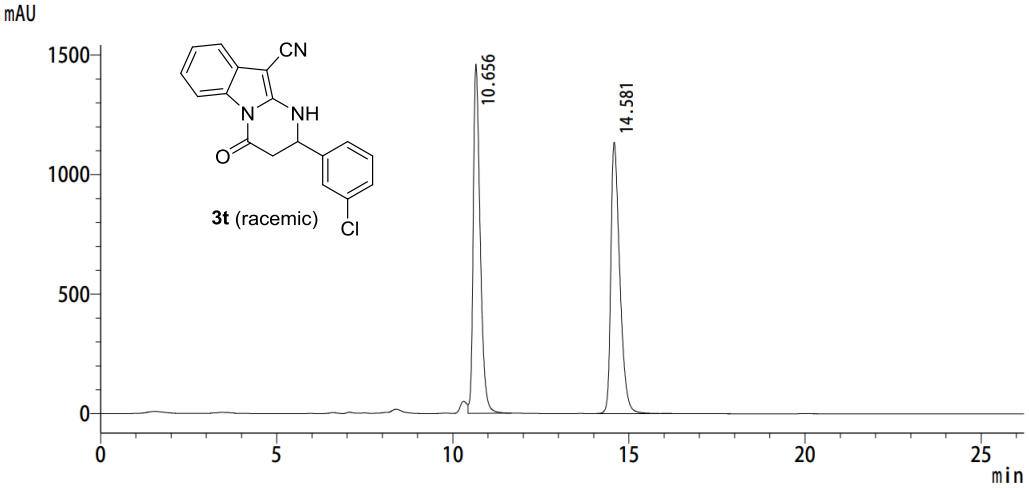
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Hight [mAU]	Area %	Hight %
1	10.225	17551233	527407	49.836	60.721
2	15.319	17666879	341164	50.164	39.279



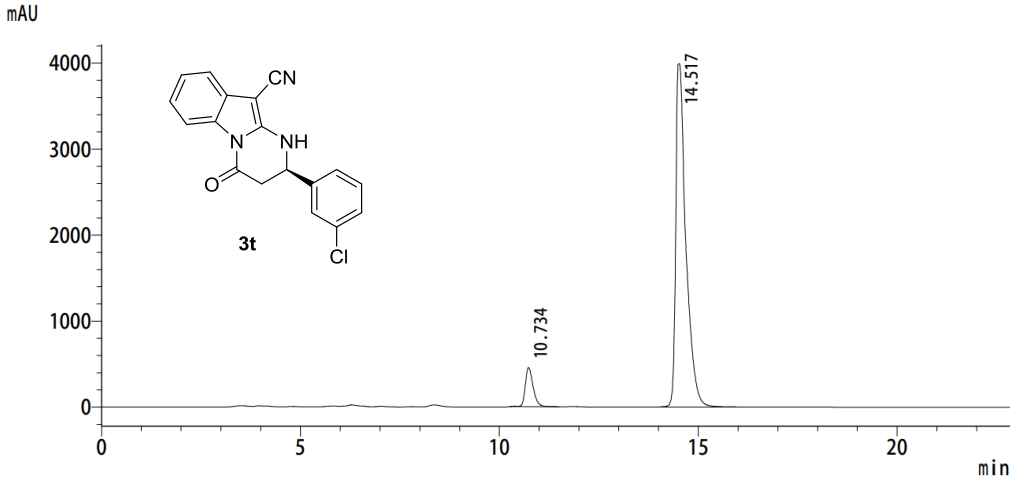
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Hight [mAU]	Area %	Hight %
1	10.439	7342590	214645	10.496	15.637
2	15.314	62614241	1158042	89.504	84.363



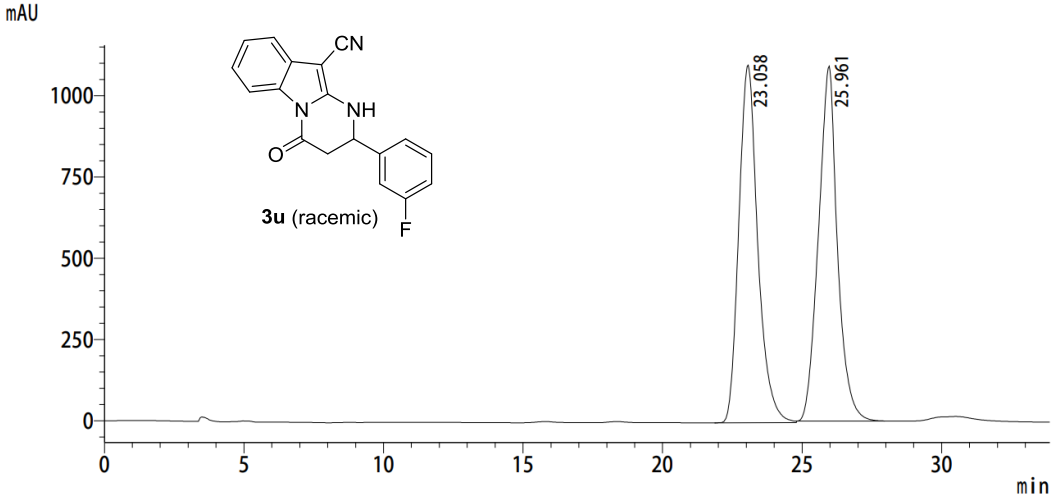
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Height %
1	10.656	20011635	1458850	49.790	56.234
2	14.581	20180534	1135380	50.210	43.766



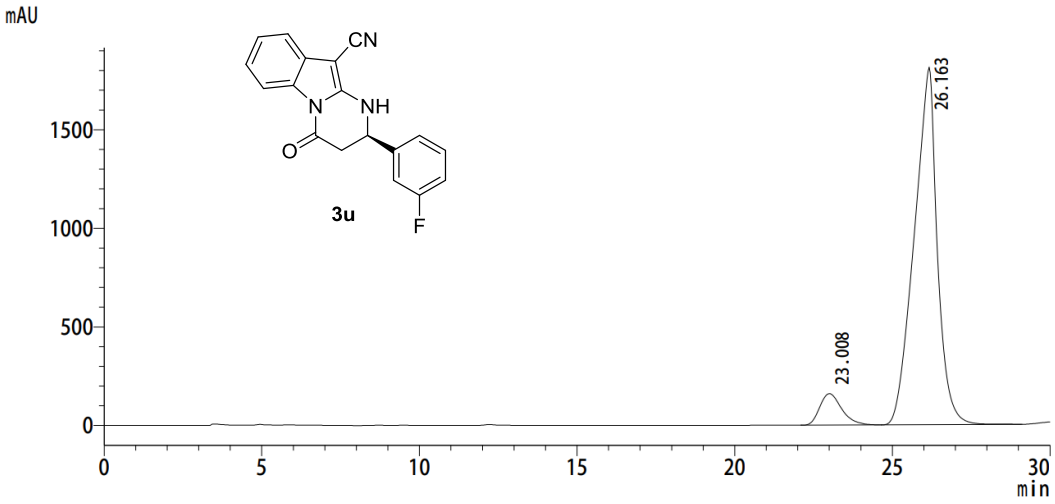
PDA Ch1 254nm

Peak#	Ret. Time	Area [mAU*s]	Hight [mAU]	Area %	Hight %
1	10.734	6246011	454968	8.125	10.229
2	14.517	70629071	3992982	91.875	89.771



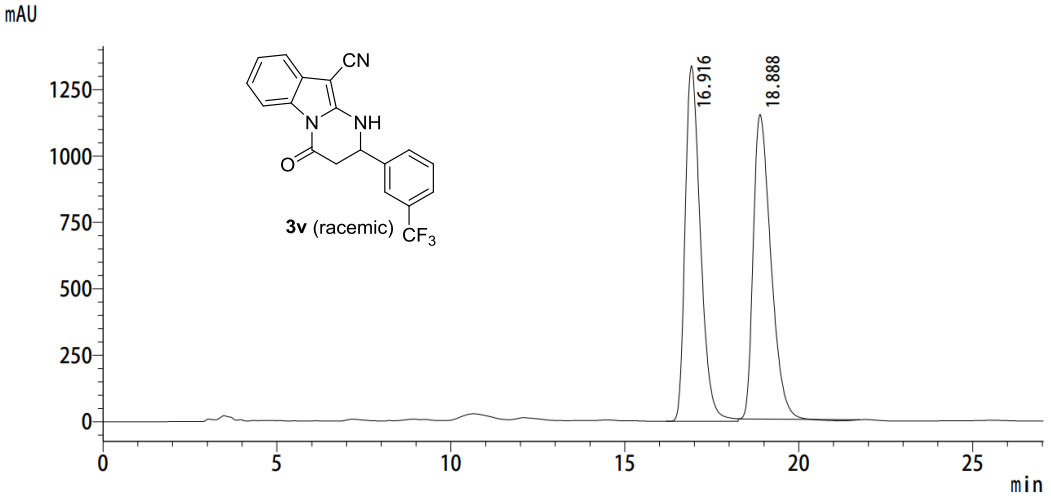
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Height %
1	23.058	52030130	1099952	50.213	50.190
2	25.961	51588910	1091645	49.787	49.810



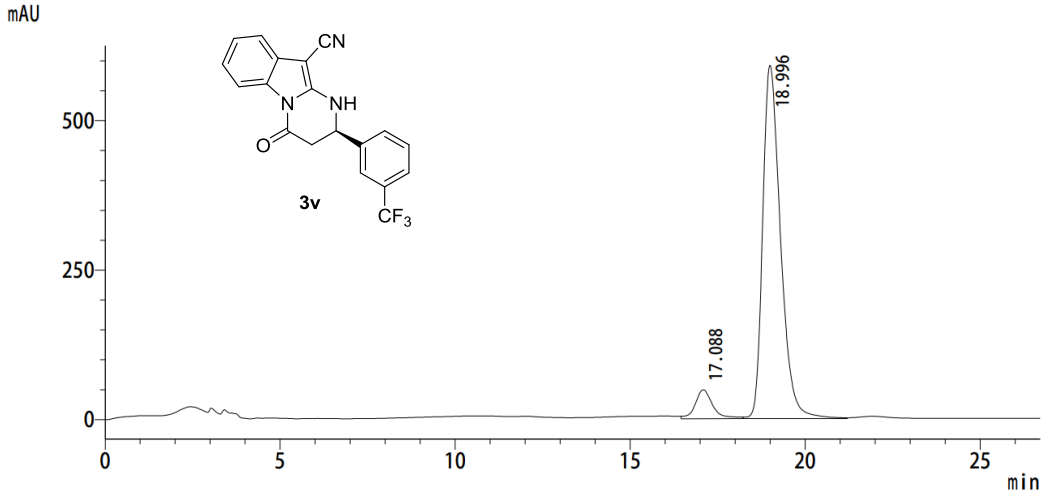
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Hight [mAU]	Area %	Hight %
1	23.008	7754280	159834	7.758	8.111
2	26.163	92198764	1810650	92.242	91.889



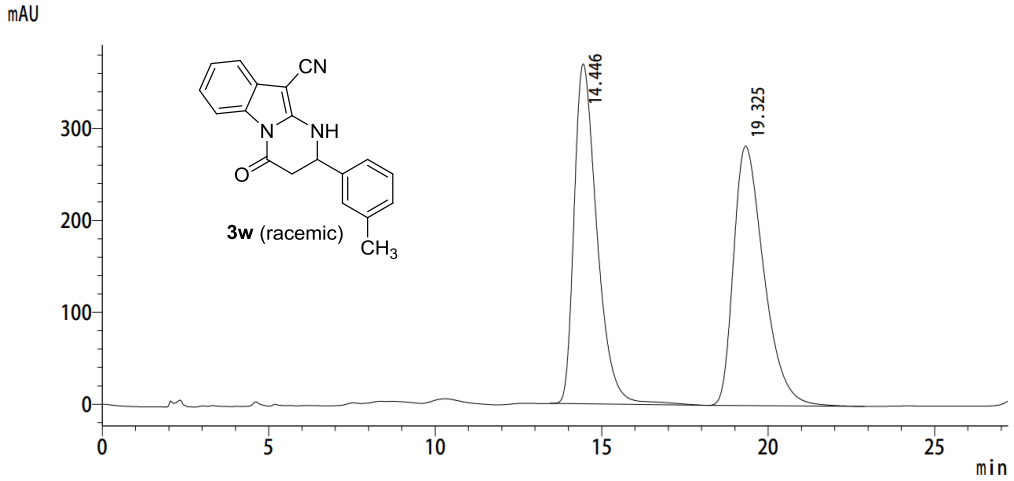
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Height %
1	16.916	40968881	1337657	50.450	53.840
2	18.888	40237342	1146847	49.550	46.160



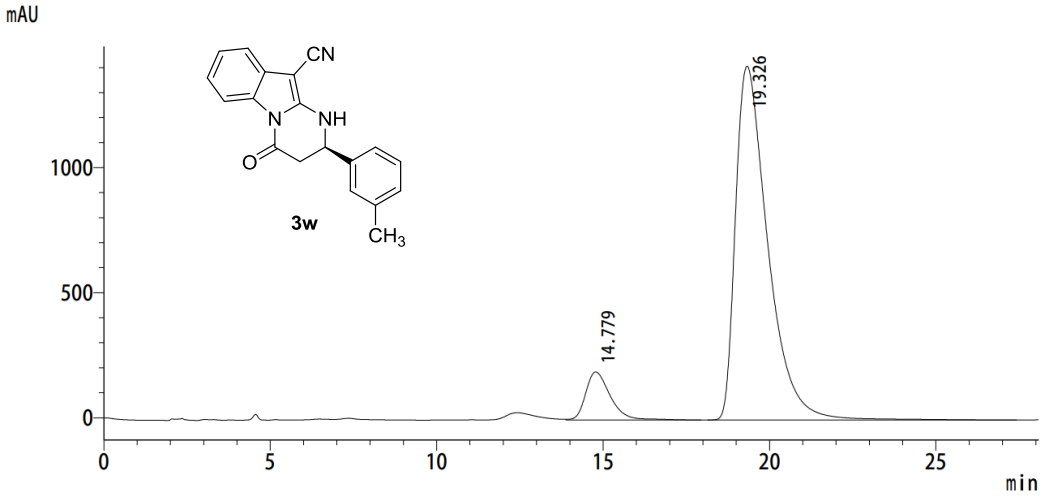
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Hight [mAU]	Area %	Hight %
1	17.088	1694542	48410	7.484	7.572
2	18.996	20948723	590951	92.516	92.428



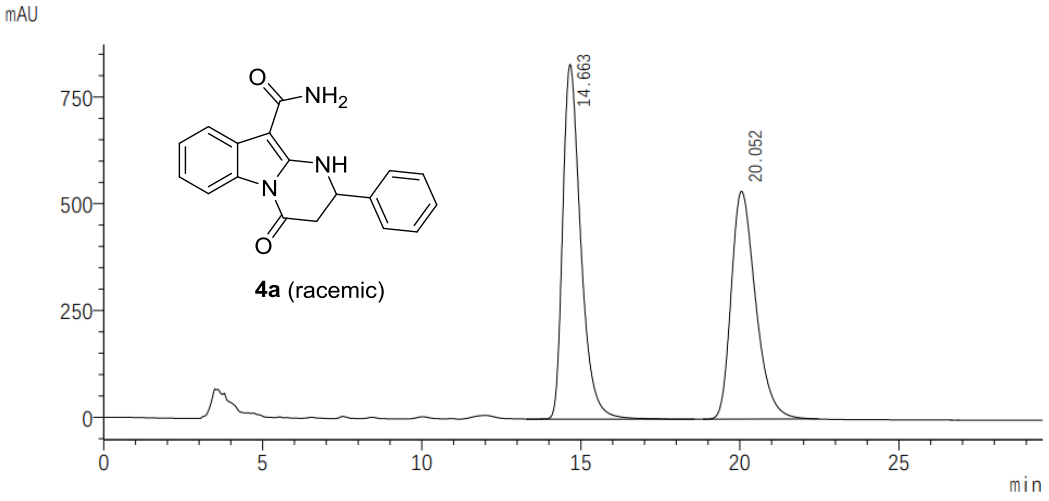
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Height %
1	14.446	17702961	369782	49.744	56.705
2	19.325	17884963	282333	50.256	43.295



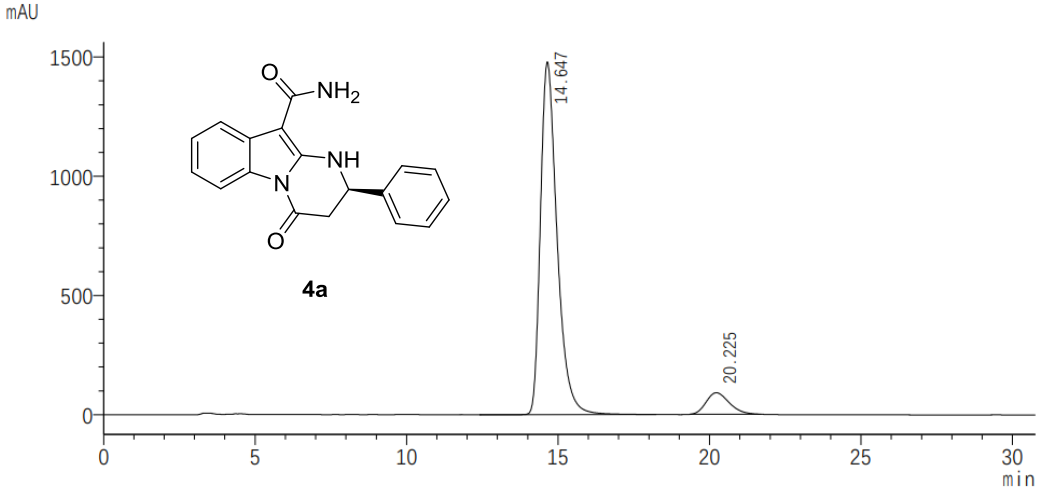
PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Hight [mAU]	Area %	Hight %
1	14.779	9829394	191966	9.324	11.951
2	19.326	95587043	1414268	90.676	88.049



PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Hight %
1	14.663	32768039	830254	53.474	60.879
2	20.052	28509975	533513	46.526	39.121



PDA Ch1 254nm

Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Area %	Hight %
1	14.647	56533798	1479151	92.166	94.236
2	20.225	4805098	90479	7.834	5.764