Electronic Supplementary Material (ESI) for ChemComm.

Metal-free enaminone C-N bond cyanation for stereoselective synthesis of (*E*)- and (*Z*)-β-cyano enones

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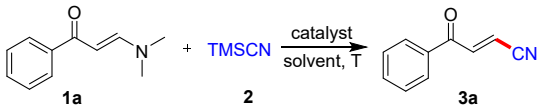
Contents

Table S1 Condition optimization on the synthesis of *E*-cyano enone[a]



1a 2 3a

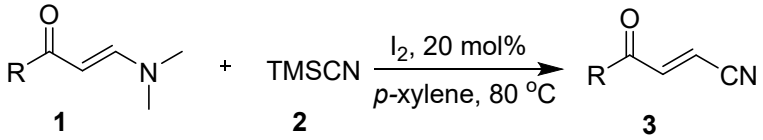
entry	catalyst	solvent	T (°C)	yield (%)[b]
1	I_2	MeCN	80	25
2	I_2	toluene	80	45
3	I_2	*p*-xylene	80	70
4	I_2	THF	80	48
5	I_2	DMF	80	41
6	KI	*p*-xylene	80	21
7	KIO_3	*p*-xylene	80	31
8	TBAI	*p*-xylene	80	38
9	*p*-TSA	*p*-xylene	80	56
10[c]	I_2	*p*-xylene	80	50
11[d]	I_2	*p*-xylene	80	80
12[d,e]	I_2	*p*-xylene	80	73
13[d,f]	I_2	*p*-xylene	80	78
14[d,g]	I_2	*p*-xylene	80	92
15[d,g,h]	I_2	*p*-xylene	90	85
16[d,g,i]	I_2	*p*-xylene	70	67

[a]General conditions: **1a** (0.2 mmol) , **2a** (0.4 mmol) , catalyst (0.04 mmol), solvent (2.0 mL), stirred at 80 °C for 17 h in sealed tube. [b]Yield of isolated product based on **1a**. [c]With **2** (0.2 mmol). [d]With **2** (0.6 mmol). [e]With 0.03 mmol I_2. [f]With 0.05 mmol I_2. [g]Stirred for 24 h. [h]Reaction at 90 °C. [i]Reaction at 70 °C.

General experimental information

The enaminones were synthesized following literature process.[1] Other chemicals and solvents used in the experiments were obtained from commercial sources and used directly without further treatment. The ^1H and ^{13}C NMR spectra were recorded in 400 MHz apparatus in $CDCl_3$. The frequencies for ^1H NMR and ^{13}C NMR test were 400 MHz and 100 MHz, respectively. The chemical shifts were reported in ppm with TMS as internal standard. Melting points were tested in X-4A instrument without correcting temperature and the HRMS data for all new products were obtained under ESI model with TOF analyzer.

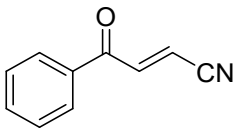
General procedure for the synthesis of cyano enones 3



In a 15 mL sealed tube were charged with enaminone **1** (0.2 mmol), TMSCN (0.6 mmol), I_2 (0.04 mmol), and *p*-xylene (2 mL). The tube was then sealed with Teflon cap and stirred at 80 °C for 24 hours with oil bath heating. Upon completion (TLC), the vessel was allowed to cool down to room temerpature. Then 5 mL water and 5 mL ethyl acetate were added to the tube. The heterogeneous mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic phase was dried over anhydrous Na_2SO_4. After filteration, the acquired solution was collected and the solvent was removed at reduced pressure. The residue obtained therein was subjected to flash silica gel column chromatography to provide pure products with the elution of mixed petroleum ether/ethyl acetate (v/v = 20:1 or 15:1).

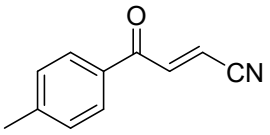
Procedure for the synthesis of 3a at 3 mmol-scale reaction

In a 75 mL sealed tube were charged with enaminone **1a** (3 mmol), TMSCN **2** (9 mmol), I_2 (0.6 mmol), and *p*-xylene (20 mL). The tube was then sealed with Teflon cap and stirred at 80 °C for 24 hours with oil bath heating. Upon completion (TLC), the vessel was allowed to cool down to room temperature. Saturated brine (15 mL) was then added, and the resulting mixture was extracted with ethyl acetate (3 × 15 mL). The organic phases were combined and washed with small amount of water for three times. After drying with anhydrous Na_2SO_4, the solid was filtered and the solvent in the acquired solution was removed under reduced pressure. The resulting residue was subjected to flash silica gel column chromatography to provide pure products **3** with the elution of mixed petroleum ether/ethyl acetate (v/v = 15:1).

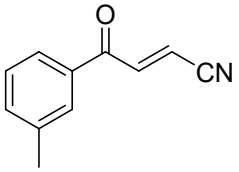


(*E*)-4-Oxo-4-phenylbut-2-enenitrile (**3a**).[2] Eluent: V_{PET}/V_{EA} = 20:1; white solid (28.9 mg, 92% yield); mp 77-78 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (dd, *J* = 8.4, 1.2 Hz,

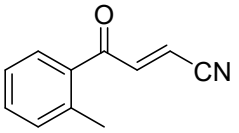
2 H), 7.74 (d, *J* = 16.0 Hz, 1 H), 7.62 -7.58 (m, 1 H), 7.49-7.45 (m, 2 H), 6.50 (d, *J* = 16.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 186.5, 141.7, 135.6, 134.6, 129.2, 128.9, 116.4, 112.0.



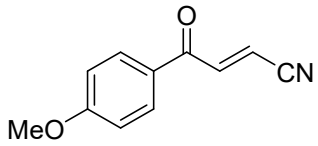
(*E*)-4-Oxo-4-(p-tolyl)but-2-enenitrile (**3b**). Eluent: V_{PET}/V_{EA} = 20:1; yellow solid (28.7 mg, 84% yield); mp 68-69 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, *J* = 8.2 Hz, 2 H), 7.79 (d, *J* = 16.0 Hz, 1 H), 7.34 (d, *J* = 8.0 Hz, 2 H), 6.55 (d, *J* = 16.0 Hz, 1 H), 2.45 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.9, 145.8, 141.9, 133.1, 129.9, 129.0, 116.5, 111.5, 21.8; ESI-HRMS Calcd for $C_{11}H_9NONa$ $[M + Na]^+$ 194.0576, found 194.0577.



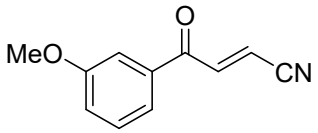
(*E*)-4-Oxo-4-(m-tolyl)but-2-enenitrile (**3c**). Eluent: V_{PET}/V_{EA} = 20:1; yellow solid (28.1 mg, 82% yield); mp 58-59 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.31 (dd, *J* = 16.0, 1.6 Hz, 1 H), 7.91 (t, 2 H), 7.55 (d, *J* = 7.6 Hz, 1 H), 7.48 (t, *J* = 7.6 Hz, 1 H), 6.72 (dd, *J* = 16.0, 1.6 Hz, 1 H), 2.41 (s, 3 H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 187.7, 143.7, 139.1, 135.9, 135.6, 129.9, 129.5, 126.8, 117.8, 111.9, 21.2; ESI-HRMS Calcd for $C_{11}H_9NONa$ $[M + Na]^+$ 194.0576, found 194.0577.



(*E*)-4-Oxo-4-(o-tolyl)but-2-enenitrile (**3d**). Eluent: V_{PET}/V_{EA} = 20:1; yellow solid (25.7 mg, 75% yield); mp 65-66 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59-7.52 (m, 2 H), 7.49-7.44 (m, 1 H), 7.32 (t, *J* = 7.6 Hz, 2 H), 6.41 (d, *J* = 16.2 Hz, 1 H), 2.51 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.1, 144.9, 139.4, 135.5, 132.7, 132.3, 129.3, 126.0, 116.2, 111.7, 21.0; ESI-HRMS Calcd for $C_{11}H_9NONa$ $[M + Na]^+$ 194.0576, found 194.0577.



(*E*)-4-(4-Methoxyphenyl)-4-oxobut-2-enenitrile (**3e**). Eluent: V_{PET}/V_{EA} = 10:1; yellow solid (31.8 mg, 85% yield); mp 103-104 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, *J* = 8.8 Hz, 2 H), 7.80 (d, *J* = 16.0 Hz, 1 H), 7.00 (d, *J* = 8.8 Hz, 2 H), 6.55 (d, *J* = 16.0 Hz, 1 H), 3.91 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.5, 164.8, 141.9, 131.4, 128.6, 116.6, 114.5, 111.1, 55.7; ESI-HRMS Calcd for $C_{11}H_9NO_2Na$ $[M + Na]^+$ 210.0525, found 210.0526.



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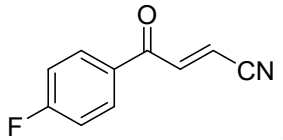
(*E*)-4-(3-Methoxyphenyl)-4-oxobut-2-enenitrile (**3f**). Eluent: V_{PET}/V_{EA} = 10:1; yellow solid (29.5 mg, 79% yield); mp 85-86 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.38 (d, *J* = 16.0 Hz, 1 H), 7.75 (d, *J* = 7.8 Hz, 1 H), 7.62 (t, 1H), 7.55 (t, *J* = 8.0 Hz, 1 H), 7.36-7.33 (m, 1 H), 6.78 (d, *J* = 16.0 Hz, 1 H), 3.90 (s, 3 H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 187.4, 160.1, 143.5, 137.2, 130.7, 122.1, 121.3, 117.8, 113.6, 112.1, 55.9; ESI-HRMS Calcd for $C_{11}H_9NO_2Na$ $[M + Na]^+$ 210.0525, found 210.0526.



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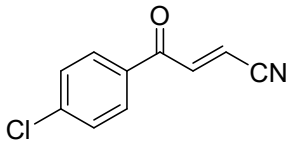
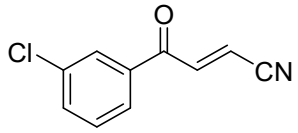
(*E*)-4-(4-Fluorophenyl)-4-oxobut-2-enenitrile (**3g**). Eluent: V_{PET}/V_{EA} = 25:1; yellow solid (26.6 mg, 76% yield); mp 88-89 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.38 (d, *J* = 16.0 Hz, 1 H), 8.27-8.24 (m, 2 H), 7.48 (t, *J* = 8.8 Hz, 2 H), 6.79 (d, *J* = 16.0 Hz, 1 H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 186.2, 167.5 (d, $^1J_{C\text{-}F}$ = 252.6 Hz), 143.4, 132.7, 132.6, 117.7, 116.8 (d, $^2J_{C\text{-}F}$ = 21.9 Hz), 112.1; ^{19}F NMR (376 MHz, DMSO-d_6): δ -103.62; ESI-HRMS Calcd for $C_{10}H_6FNONa$ $[M + Na]^+$ 198.0326, found 198.0326.

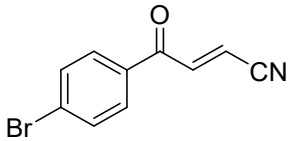


(*E*)-4-(4-Chlorophenyl)-4-oxobut-2-enenitrile (**3h**). Eluent: V_{PET}/V_{EA} = 20:1; yellow

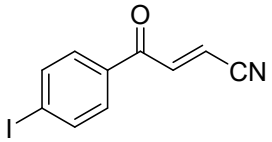
solid (27.9 mg, 73% yield); mp 138-139 °C;^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, *J* = 8.6 Hz, 2 H), 7.76 (d, *J* = 16.0 Hz, 1 H), 7.51 (d, *J* = 8.6 Hz, 2 H), 6.58 (d, *J* = 16.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.3, 141.3, 141.1, 133.9, 130.2, 129.6, 116.2, 112.4; ESI-HRMS Calcd for $C_{10}H_6ClNONa$ $[M + Na]^+$ 214.0030, found 214.0031.



(*E*)-4-(3-Chlorophenyl)-4-oxobut-2-enenitrile (**3i**). Eluent: V_{PET}/V_{EA} = 20:1; yellow solid (27.1 mg, 71% yield); mp 75-76 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (t, *J* = 2.0 Hz, 1 H), 7.84 (d, *J* = 7.8 Hz, 1 H), 7.75 (d, *J* = 16.0 Hz, 1 H), 7.64 (d, *J* = 8.0 Hz, 1 H), 7.50 (t, *J* = 8.0 Hz, 1 H), 6.60 (d, *J* = 16.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.3, 140.9, 137.1, 135.7, 134.4, 130.5, 128.9, 126.9, 116.1, 112.8; ESI-HRMS Calcd for $C_{10}H_6ClNONa$ $[M + Na]^+$ 214.0030, found 214.0031.

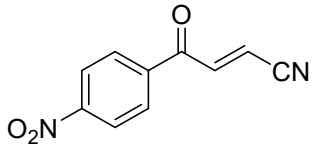


(*E*)-4-(4-Bromophenyl)-4-oxobut-2-enenitrile (**3j**). Eluent: V_{PET}/V_{EA} = 25:1; yellow solid (29.1 mg, 62% yield); mp 82-83 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.46 (d, *J* = 16.0 Hz, 1 H), 8.21 (d, *J* = 8.6 Hz, 2 H), 7.99 (d, *J* = 8.6 Hz, 2 H), 6.92 (d, *J* = 16.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.5, 141.0, 134.3, 132.6, 130.2, 130.1, 116.2, 112.5; ESI-HRMS Calcd for $C_{10}H_6BrNONa$ $[M + Na]^+$ 257.9525, found 257.9526.

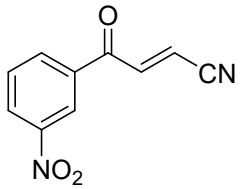


(*E*)-4-(4-Iodophenyl)-4-oxobut-2-enenitrile (**3k**). Eluent: V_{PET}/V_{EA} = 20:1; yellow solid (30.6 mg, 54% yield); mp 128-129 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.45 (d, *J* = 16.0 Hz, 1 H), 8.17 (d, *J* = 8.6 Hz, 2 H), 8.03 (d, *J* = 8.6 Hz, 2 H), 6.91 (d, *J* = 16.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.8, 141.0, 138.6, 134.8, 130.0, 116.2,

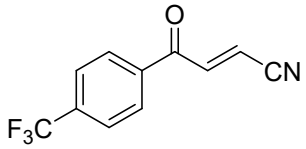
112.5, 103.1; ESI-HRMS Calcd for $C_{10}H_6INONa$ $[M + Na]^+$ 305.9386, found 305.9387.



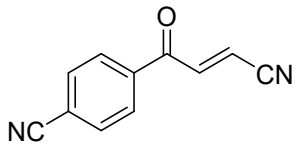
(*E*)-4-(4-Nitrophenyl)-4-oxobut-2-enenitrile (**3l**). Eluent: V_{PET}/V_{EA} = 15:1; yellow solid (16.6 mg, 41% yield); mp 106-107 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 8.39 (d, J = 9.0 Hz, 2 H), 8.34 (d, J = 7.4 Hz, 2 H), 8.31 (s, 1 H), 6.80 (d, J = 16.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.3, 151.0, 140.4, 139.9, 129.9, 124.3, 115.8, 113.7; ESI-HRMS Calcd for $C_{10}H_7N_2O_3$ $[M + H]^+$ 203.0451, found 203.0449.



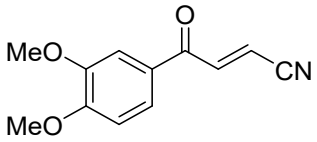
(*E*)-4-(3-Nitrophenyl)-4-oxobut-2-enenitrile (**3m**). Eluent: V_{PET}/V_{EA} = 15:1; yellow solid (14.1 mg, 35% yield); mp 95-96 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 8.78-8.76 (m, 1 H), 8.54-8.49 (m, 2 H), 8.41 (d, J = 16.0 Hz, 1 H), 7.87 (t, J = 8.0 Hz, 1 H), 6.80 (d, J = 16.0 Hz, 1 H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 186.3, 148.6, 142.9, 137.1, 135.5, 131.3, 128.8, 123.8, 117.6, 112.9; ESI-HRMS Calcd for $C_{10}H_7N_2O_3$ $[M + H]^+$ 203.0451, found 203.0449.



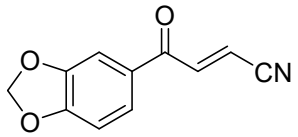
(*E*)-4-Oxo-4-(4-(trifluoromethyl)phenyl)but-2-enenitrile (**3n**). Eluent: V_{PET}/V_{EA} = 10:1; yellow solid (24.7 mg, 55% yield); mp 97-98 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, J = 8.2 Hz, 2 H), 7.83-7.78 (m, 3 H), 6.62 (d, J = 16.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.7, 140.8, 138.2, 135.8 (d, $^2J_{C\text{-}F}$ = 32.9 Hz), 129.2, 126.3 (dd, $^4J_{C\text{-}F}$ = 7.5 Hz, 3.8 Hz), 124.7 (d, $^1J_{C\text{-}F}$ = 271.3 Hz), 116.0, 113.1; ^{19}F NMR (376 MHz, $CDCl_3$): δ -63.33; ESI-HRMS Calcd for $C_{11}H_7F_3NO$ $[M + H]^+$ 226.0474, found 226.0476.



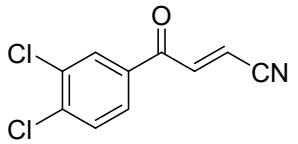
(*E*)-4-(3-Cyanoacryloyl)benzonitrile (**3o**). Eluent: V_{PET}/V_{EA} = 25:1; yellow solid (18.6 mg, 51% yield); mp 108-109 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.29 (d, J = 16.0 Hz, 1 H), 8.22 (d, J = 8.6 Hz, 2 H), 8.05 (d, J = 8.6 Hz, 2 H), 6.76 (d, J = 16.0 Hz, 1 H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 187.2, 143.1, 139.0, 133.5, 130.0, 118.4, 117.6, 116.5, 112.8; ESI-HRMS Calcd for $C_{11}H_7N_2O$ $[M + H]^+$ 183.0553, found 183.0572.



(*E*)-4-(3,4-Dimethoxyphenyl)-4-oxobut-2-enenitrile (**3p**). Eluent: V_{PET}/V_{EA} = 8:1; yellow solid (33.9 mg, 78% yield); mp 102-103 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.44 (d, J = 16.0 Hz, 1 H), 7.91-7.88 (m, 1 H), 7.61 (s, 1 H), 7.18 (d, J = 8.6 Hz, 1 H), 6.74 (d, J = 16.0 Hz, 1 H), 3.92 (d, J = 14.8 Hz, 6 H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 185.5, 154.8, 149.5, 143.6, 128.8, 125.0, 118.0, 111.6, 111.3, 111.2, 56.4, 56.1; ESI-HRMS Calcd for $C_{12}H_{11}NO_3Na$ $[M + Na]^+$ 240.0631, found 240.0632.

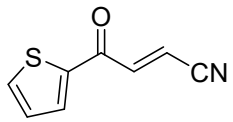


(*E*)-4-(Benzo[d][1,3]dioxol-5-yl)-4-oxobut-2-enenitrile (**3q**). Eluent: V_{PET}/V_{EA} = 15:1; yellow solid (24.1 mg, 60% yield); mp 114-115 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.28 (d, J = 16.0 Hz, 1 H), 7.81-7.78 (m, 1 H), 7.54 (s, 1 H), 7.09 (d, J = 8.2 Hz, 1 H), 6.67 (d, J = 16.0 Hz, 1 H), 6.17 (s, 2 H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 185.2, 153.2, 148.8, 143.5, 130.6, 127.0, 117.8, 111.5, 108.9, 108.3, 102.9; ESI-HRMS Calcd for $C_{11}H_7NO_3Na$ $[M + Na]^+$ 224.0318, found 224.0319.

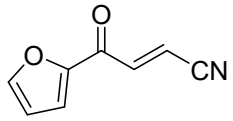


(*E*)-4-(3,4-Dichlorophenyl)-4-oxobut-2-enenitrile (**3r**). Eluent: V_{PET}/V_{EA} = 15:1;

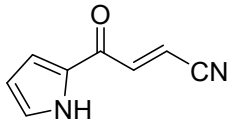
yellow solid (27.4 mg, 61% yield); mp 104-105 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.48-8.44 (m, 2 H), 8.17 (dd, J = 8.4, 2.0 Hz, 1 H), 7.99 (d, J = 8.4 Hz, 1 H), 6.89 (d, J = 16.0 Hz, 1 H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 185.8, 142.9, 137.7, 136.0, 132.7, 131.8, 131.4, 129.3, 117.6, 112.7; ESI-HRMS Calcd for $C_{10}H_5Cl_2NONa$ $[M + Na]^+$ 247.9640, found 247.9641.



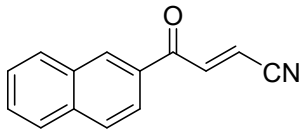
(*E*)-4-Oxo-4-(thiophen-2-yl)but-2-enenitrile (**3s**).[3] Eluent: V_{PET}/V_{EA} = 20:1; yellow solid (21.8 mg, 67% yield); mp 109-110 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.45 (d, J = 3.4 Hz, 1 H), 8.40 (d, J = 16.0 Hz, 1 H), 8.35 (d, J = 5.0 Hz, 1 H), 7.50-7.48 (m, 1 H), 6.88 (d, J = 16.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.3, 143.1, 141.6, 136.8, 133.9, 128.9, 116.3, 111.4.



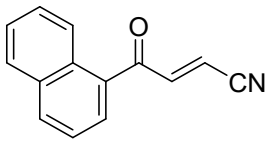
(*E*)-4-(Furan-2-yl)-4-oxobut-2-enenitrile (**3t**).[3] Eluent: V_{PET}/V_{EA} = 12:1; yellow solid (17.9 mg, 61% yield); mp 163-164 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.11 (s, 1 H), 8.00 (d, J = 16.0 Hz, 1 H), 7.85 (d, J = 3.6 Hz, 1 H), 6.78 (dd, J = 3.6, 1.4 Hz, 1 H), 6.68 (d, J = 16.0 Hz, 1 H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 174.0, 151.9, 150.9, 143.2, 123.3, 117.7, 113.8, 111.3.



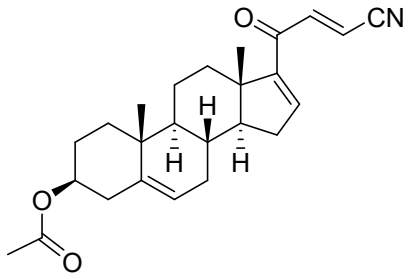
(*E*)-4-Oxo-4-(1H-pyrrol-2-yl)but-2-enenitrile (**3u**). Eluent: V_{PET}/V_{EA} = 15:1; yellow solid (14.9 mg, 51% yield); mp 98-99 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.23 (s, 1 H), 8.07 (d, J = 16.0 Hz, 1 H), 7.35 (d, J = 40.0 Hz, 2 H), 6.63 (d, J = 16.0 Hz, 1 H), 6.32-6.29 (m, 1 H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 174.5, 144.6, 132.1, 129.7, 120.8, 118.0, 111.6, 109.3; ESI-HRMS Calcd for $C_8H_7N_2O$ $[M + H]^+$ 147.0553, found 147.0552.



(*E*)-4-(Naphthalen-2-yl)-4-oxobut-2-enenitrile (**3v**). Eluent: V_{PET}/V_{EA} = 10:1; yellow solid (23.2 mg, 56% yield); mp 102-103 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.96 (s, 1 H), 8.53 (d, *J* = 16.2 Hz, 1 H), 8.19 (d, *J* = 8.0 Hz, 1 H), 8.11-8.06 (m, 3 H), 7.79-7.70 (m, 2 H), 6.84 (d, *J* = 16.0 Hz, 1 H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 187.3, 143.6, 136.0, 133.2, 132.6, 132.6, 130.3, 129.9, 129.4, 128.3, 127.8, 124.1, 117.9, 111.9; ESI-HRMS Calcd for $C_{14}H_{10}NO$ $[M + H]^+$ 208.0757, found 208.0763.



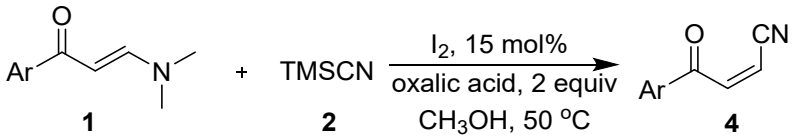
(*E*)-4-(Naphthalen-1-yl)-4-oxobut-2-enenitrile (**3w**). Eluent: V_{PET}/V_{EA} = 12:1; yellow solid (27.3 mg, 66% yield); mp 75-76 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.61 (d, *J* = 8.6 Hz, 1 H), 8.25 (d, *J* = 8.2 Hz, 1 H), 8.20 (d, *J* = 7.2 Hz, 1 H), 8.15 (d, 1 H), 8.07 (d, *J* = 7.8 Hz, 1 H), 7.70-7.64 (m, 3 H), 6.74 (d, *J* = 16.2 Hz, 1 H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 190.7, 146.6, 134.8, 133.9, 133.0, 131.5, 130.3, 129.3, 128.9, 127.3, 125.6, 125.3, 117.7, 112.2; ESI-HRMS Calcd for $C_{14}H_{10}NO$ $[M + H]^+$ 208.0757, found 208.0767.



(3S,8R,9S,10R,13S,14S)-17-((*E*)-3-Cyanoacryloyl)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15-dodecahydro-1H-cyclopenta[a]phenanthren-3-yl acetate (**3x**). Eluent: V_{PET}/V_{EA} = 10:1; yellow solid (19.7 mg, 25% yield); mp 201-202 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, *J* = 16.0 Hz, 1H), 6.92 (s, 1 H), 6.35 (d, *J* = 16.0 Hz, 1 H), 5.39 (d, *J* = 4.2 Hz, 1 H), 4.65-4.56 (m, 1 H), 2.42-2.30 (m, 5 H), 2.17-2.10 (m, 1 H), 2.03 (s, 3 H), 1.87 (d, *J* = 10.6 Hz, 2 H), 1.72-1.58 (m, 6 H), 1.50-1.44

(m, 1 H), 1.41-1.35 (m, 1 H), 1.25 (q, 1 H), 1.17 (t, 2 H), 1.07 (s, 2 H), 0.96 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.6, 170.5, 155.0, 148.4, 142.7, 140.3, 121.8, 116.6, 109.5, 73.8, 56.1, 50.3, 46.6, 38.1, 36.9, 36.8, 34.3, 33.0, 31.5, 30.1, 27.7, 21.4, 20.6, 19.2, 15.6; ESI-HRMS Calcd for $C_{25}H_{31}NO_3Na$ $[M + Na]^+$ 416.2196, found 416.2197.

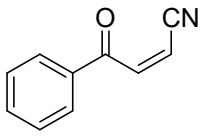
General procedure for the synthesis of cyano enones 4



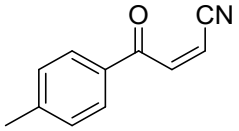
In a 15 mL sealed tube were charged with enaminone **1** (0.2 mmol), TMSCN **2** (0.6 mmol), I_2 (0.03 mmol), $C_2H_2O_4{\cdot}2H_2O$ (0.4 mmol) and CH_3OH (2 mL). The tube was then sealed with Teflon cap and the mixture was stirred at 50 °C for 24 h. Upon completion (TLC), the vessel was allowed to cool down to room temperature. The resultant mixture was diluted with ethyl acetate. The solution was directly transferred into a round bottom flask for subsequent rotary evaporation. After removing the solvent at reduced temperature, the resulting residue was subjected to flash silica gel column chromatography to provide pure products with the elution of mixed petroleum ether/ethyl acetate (v/v = 5:1).

Procedure for the synthesis of 4a at 3 mmol-scale reaction

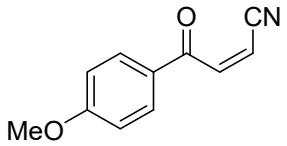
Enaminone **1a** (3 mmol), TMSCN **2** (9 mmol), I_2 (0.45 mmol) and $C_2H_2O_4{\cdot}2H_2O$ (6 mmol) were dissolved in CH_3OH (20 mL) in a 75 mL sealed tube. The tube was then sealed with Teflon cap and the mixture was stirred at 50 °C for 24 h. Upon completion (TLC), the vessel was allowed to cool down to room temperature. The resultant mixture was diluted with ethyl acetate. The resulting solution was directly transferred into a round bottom flask for subsequent rotary evaporation. After removing the solvent at reduced temperature, the resulting residue was subjected to flash silica gel column chromatography to provide pure product **4a** with the elution of mixed petroleum ether/ethyl acetate (v/v = 5:1).



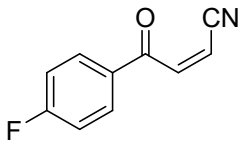
(*Z*)-4-Oxo-4-phenylbut-2-enenitrile (**4a**).[2] Eluent: V_{PET}/V_{EA} = 3:1; white solid (20.1 mg, 64% yield); mp 72-73 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, *J* = 7.8 Hz, 2 H), 7.60 (d, *J* = 7.4 Hz, 1 H), 7.56 (d, *J* = 11.6 Hz, 1 H), 7.47 (t, *J* = 7.6 Hz, 2 H), 5.93 (d, *J* = 11.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 186.7, 141.8, 135.7, 134.5, 129.1, 128.8, 115.2, 108.9.



(*Z*)-4-Oxo-4-(p-tolyl)but-2-enenitrile (**4b**). Eluent: V_{PET}/V_{EA} = 4:1; yellow solid (19.8 mg, 58% yield); mp 95-96 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 8.2 Hz, 2 H), 7.60 (d, *J* = 11.6 Hz, 1 H), 7.33 (d, *J* = 8.0 Hz, 1 H), 5.96 (d, *J* = 11.6 Hz, 1 H), 2.45 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 186.3, 145.7, 142.1, 133.2, 129.8, 129.0, 115.3, 108.5, 21.9; ESI-HRMS Calcd for $C_{11}H_9NONa$ $[M + Na]^+$ 194.0576, found 194.0577.

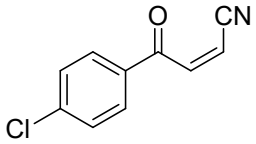


(*Z*)-4-(4-Methoxyphenyl)-4-oxobut-2-enenitrile (**4c**). Eluent: V_{PET}/V_{EA} = 3:1; yellow solid (19.8 mg, 53% yield); mp 72-73 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.05 (d, 2 H), 7.12 (d, *J* = 8.8 Hz, 2 H), 6.43 (d, *J* = 11.6 Hz, 1 H), 3.88 (s, 3 H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 186.2, 164.7, 143.9, 131.9, 128.9, 116.8, 114.9, 108.9, 56.2; ESI-HRMS Calcd for $C_{11}H_9NO_2Na$ $[M + Na]^+$ 210.0525, found 210.0526.

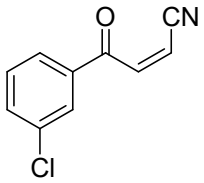


(*Z*)-4-(4-Fluorophenyl)-4-oxobut-2-enenitrile (**4d**)**.** Eluent: V_{PET}/V_{EA} = 4:1; yellow solid (15.4 mg, 44% yield); mp 74-75 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05-8.00 (m, 2 H), 7.58 (d, *J* = 11.6 Hz, 1 H), 7.21 (t, *J* = 8.6 Hz, 2 H), 6.01 (d, *J* = 11.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.3, 167.8 (d, $^1J_{C\text{-}F}$ = 256.1 Hz), 141.5, 131.7 (d, $^3J_{C\text{-}F}$

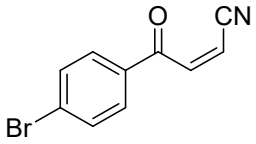
= 9.7 Hz), 116.5 (d, $^{2}J_{C\text{-}F}$ = 22.1 Hz), 115.1, 109.2; ^{19}F NMR (376 MHz, $CDCl_3$): δ -102.03; ESI-HRMS Calcd for $C_{10}H_6FNONa$ $[M + Na]^+$ 198.0326, found 198.0326.



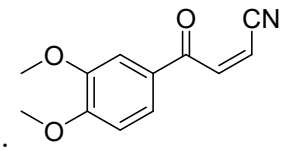
(*Z*)-4-(4-Chlorophenyl)-4-oxobut-2-enenitrile (**4e**). Eluent: V_{PET}/V_{EA} = 3:1; yellow solid (15.7 mg, 41% yield); mp 112-113 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, *J* = 8.6 Hz, 2 H), 7.57 (d, *J* = 11.6 Hz, 1 H), 7.51 (d, *J* = 8.6 Hz, 2 H), 6.01 (d, *J* = 11.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.6, 141.2, 134.0, 130.2, 129.8, 129.5, 115.1, 109.4; ESI-HRMS Calcd for $C_{10}H_6ClNONa$ $[M + Na]^+$ 214.0030, found 214.0031.



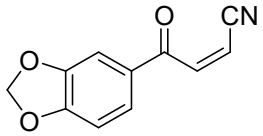
(*Z*)-4-(3-Chlorophenyl)-4-oxobut-2-enenitrile (**4f**). Eluent: V_{PET}/V_{EA} = 3:1; yellow solid (14.5 mg, 38% yield); mp 102-103 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (s, 1 H), 7.85 (d, *J* = 7.8 Hz, 1 H), 7.67-7.59 (m, 2 H), 7.56 (d, *J* = 11.6 Hz, 1 H), 7.49 (t, *J* = 7.8 Hz, 1 H), 6.03 (d, *J* = 11.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.6, 141.0, 137.2, 135.5, 134.4, 130.4, 128.8, 126.8, 115.0, 109.7; ESI-HRMS Calcd for $C_{10}H_6ClNONa$ $[M + Na]^+$ 214.0030, found 214.0031.



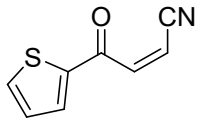
(*Z*)-4-(4-Bromophenyl)-4-oxobut-2-enenitrile (**4g**)**.** Eluent: V_{PET}/V_{EA} = 4:1; yellow solid (15.5 mg, 33% yield); mp 98-99 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, *J* = 8.4 Hz, 2 H), 7.69 (d, *J* = 8.4 Hz, 2 H), 7.54 (d, *J* = 11.6 Hz, 1 H), 6.01 (d, *J* = 11.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.8, 141.1, 134.4, 132.5, 130.2, 130.0, 115.1, 109.5; ESI-HRMS Calcd for $C_{10}H_6BrNONa$ $[M + Na]^+$ 257.9525, found 257.9526.



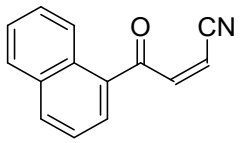
(*Z*)-4-(3,4-Dimethoxyphenyl)-4-oxobut-2-enenitrile (**4h**)**.** Eluent: V_{PET}/V_{EA} = 3:1; yellow solid (22.1 mg, 51% yield); mp 115-116 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61-7.53 (m, 3 H), 6.92 (d, *J* = 8.4 Hz, 1 H), 5.94 (d, *J* = 11.6 Hz, 1 H), 3.98 (s, 3 H), 3.95 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.1, 154.7, 149.7, 141.9, 129.0, 124.0, 115.5, 110.5, 110.1, 108.2, 56.2, 56.1; ESI-HRMS Calcd for $C_{12}H_{11}NO_3Na$ $[M + Na]^+$ 240.0631, found 240.0632.



(*Z*)-4-(Benzo[d][1,3]dioxol-5-yl)-4-oxobut-2-enenitrile (**4i**). Eluent: V_{PET}/V_{EA} = 3:1; yellow solid (22.1 mg, 55% yield); mp 104-105 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.30 (d, *J* = 11.6 Hz, 1 H), 7.81 (dd, *J* = 8.2, 1.6 Hz, 1 H), 7.57 (d, *J* = 1.6 Hz, 1 H), 7.11 (d, *J* = 8.2 Hz, 1 H), 6.68 (d, *J* = 11.6 Hz, 1 H), 6.19 (s, 2 H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 185.3, 153.3, 148.8, 143.6, 130.6, 127.0, 117.9, 111.6, 108.9, 108.3, 102.9; ESI-HRMS Calcd for $C_{11}H_7NO_3Na$ $[M + Na]^+$ 224.0318, found 224.0319.

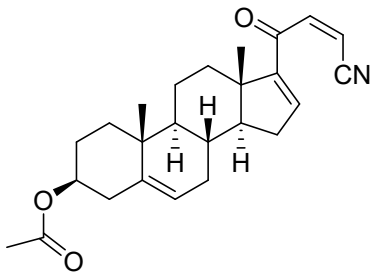


(*Z*)-4-Oxo-4-(thiophen-2-yl)but-2-enenitrile (**4j**).[3] Eluent: V_{PET}/V_{EA} = 2.5:1; yellow solid (10.4mg, 32% yield); mp 124-125 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.20 (d, 2 H), 7.99 (d, *J* = 11.6 Hz, 1 H), 7.33 (t, *J* = 4.2 Hz, 1 H), 6.49 (d, *J* = 11.4 Hz, 1 H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 179.8, 143.7, 142.4, 138.4, 136.0, 134.0, 129.8, 116.6, 109.5.



(*Z*)-4-(Naphthalen-1-yl)-4-oxobut-2-enenitrile (**4k**). Eluent: V_{PET}/V_{EA} = 3:1; yellow solid (18.2 mg, 44% yield); mp 84-85 °C;^{1}H NMR (400 MHz, DMSO-d_6): δ 8.72 (d, 1

H), 8.27 (d, J = 8.2 Hz, 1 H), 8.17 (d, 1 H), 8.08 (d, J = 8.0 Hz, 1 H), 7.96 (d, J = 11.6 Hz, 1 H), 7.73-7.66 (m, 4 H), 6.54 (d, J = 11.6 Hz, 1 H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 190.9, 146.6, 134.9, 134.0, 133.1, 131.5, 130.2, 129.3, 129.1, 127.3, 125.6, 125.3, 116.6, 109.0; ESI-HRMS Calcd for $C_{14}H_{10}NO$ $[M + H]^+$ 208.0757, found 208.0759.



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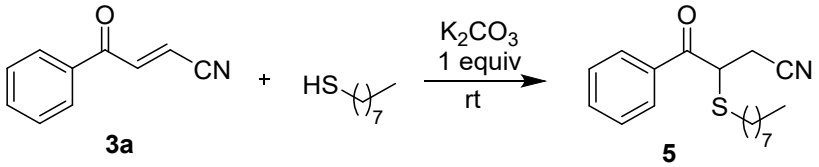
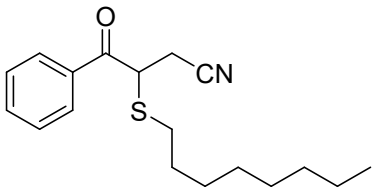
(3S,8R,9S,10R,13S,14S)-17-((*Z*)-3-Cyanoacryloyl)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15-dodecahydro-1H-cyclopenta[a]phenanthren-3-yl acetate (**4l**). Eluent: V_{PET}/V_{EA} = 3:1; yellow solid (11.8 mg, 15% yield); mp 129-130 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.76 (d, J = 11.6 Hz, 1 H), 5.39 (d, J = 4.0 Hz, 1 H), 4.64-4.57 (m, 1 H), 4.14 (t, J = 6.8 Hz, 1 H), 3.06-3.02 (m, 1 H), 2.34 (s, 5 H), 2.04 (s, 4 H), 1.87 (d, J = 10.8 Hz, 2 H), 1.71-1.56 (m, 6 H), 1.44 (t, J = 8.4 Hz, 1 H), 1.38-1.32 (m, 1 H), 1.14 (d, 1 H), 1.06 (s, 3 H), 0.93 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.9, 170.5, 154.6, 145.1, 144.9, 140.3, 121.9, 116.3, 73.8, 56.2, 53.7 (d, J = 4.2 Hz), 50.3 (d, J = 4.0 Hz), 46.5, 42.1 (d, J = 2.6 Hz), 41.0, 40.8, 38.1, 36.9, 36.8, 34.5, 34.4, 32.5, 31.5, 30.1, 27.7, 21.4, 20.6, 19.2, 15.8 (d, J = 4.0 Hz); ESI-HRMS Calcd for $C_{25}H_{31}NO_3Na$ $[M + Na]^+$ 416.2196, found 416.2197.

Procedure for the synthesis of compound 5



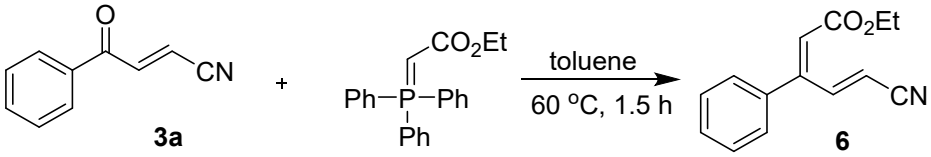
In a 15 mL reaction tube was equipped with cyano enone **3a** (0.1 mmol), octanethiol (0.1 mmol), K_2CO_3 (0.1 mmol) and CH_2Cl_2 (2 mL). The mixture was then stirred at room temperature for 4 h. Upon completion (TLC), the reaction mixture was diluted with ethyl acetate, and transferred into a round bottom flask. After removing the solvent atreduced temperature, the resulting mixture was purified by silica gel column

chromatography with the election of mixed petroleum ether and ethyl acetate (v: v=15:1).

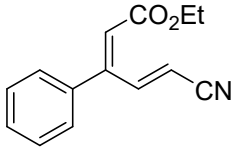


3-(Octylthio)-4-oxo-4-phenylbutanenitrile (**5**). Eluent: V_{PET}/V_{EA} = 15:1; colorless oil (23.3 mg, 77% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 8.0 Hz, 2 H), 7.62 (t, *J* = 7.2 Hz, 1 H), 7.50 (t, *J* = 7.8 Hz, 2 H), 4.22 (t, 1 H), 3.60 (dd, *J* = 17.8, 7.8 Hz, 1 H), 3.45 (dd, *J* = 17.8, 6.2 Hz, 1 H), 2.88-2.76 (m, 2 H), 1.73-1.64 (m, 2 H), 1.45-1.39 (m, 2 H), 1.29 (s, 8 H), 0.88 (t, *J* = 6.5 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.9, 135.6, 134.1, 128.9, 128.2, 119.1, 41.6, 32.4, 31.8, 29.1, 29.1, 28.9, 28.8, 27.4, 22.6, 14.1; ESI-HRMS Calcd for $C_{18}H_{26}NOS$ $[M + H]^+$ 304.1730, found 304.1743.

Procedure for the synthesis of compound 6



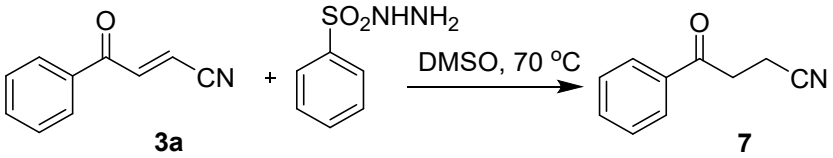
In a 15 mL reaction tube was equipped with cyano enone **3a** (0.2 mmol), phosphorus ylide (0.4 mmol) and toluene (2 ml). The tube was then sealed with Teflon cap and stirred at 60 °C for 1.5 hours with oil bath heating. Upon completion (TLC), the reaction mixture diluted with ethyl acetate, and transferred into a round bottom flask. After adding petroleum ether and filtering to remove the triphenylphosphonium oxide solid, the solvent was then removed at reduced temperature. The resulting residue was purified by silica gel column chromatography with the election of mixed petroleum ether and ethyl acetate (v: v=10:1).



Ethyl (*2E*,*4E*)-5-cyano-3-phenylpenta-2,4-dienoate (**6**). Eluent: V_{PET}/V_{EA} = 10:1; colourless oil (21.8 mg, 48% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (t, 2 H), 7.20 (t, 2 H), 7.04 (dd, *J* = 6.2, 2.6 Hz, 2 H), 6.14 (s, 1 H), 5.14 (d, *J* = 16.2 Hz, 1 H), 3.94

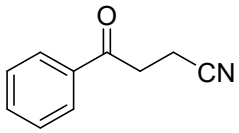
(q, J = 7.0 Hz, 2 H), 0.99 (t, J = 7.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.6, 152.0, 150.2, 133.9, 128.7, 128.4, 128.3, 126.9, 117.1, 105.3, 60.7, 13.8; ESI-HRMS Calcd for $C_{14}H_{14}NO_2$ $[M + H]^+$ 228.1019, found 228.1016.

Procedure for the synthesis of compound 7



3a **7**

In a 10 mL reaction tube was charged with cyano enone **3a** (0.2 mmol), benzenesulfonyl hydrazine (0.3 mmol), and DMSO (2 mL). The mixture was then stirred at 70 °C for 5 h. Upon completion (TLC), 5 mL water and 5 mL ethyl acetate were added to the tube. The heterogeneous mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic phase was dried over anhydrous Na_2SO_4. After filtrations, the acquired solution was collected and the solvent was removed at reduced pressure. The residue obtained therein was subjected to flash silica gel column chromatography to provide pure products with the elution of mixed petroleum ether/ethyl acetate (v/v = 7:1)



4-Oxo-4-phenylbutanenitrile (**7**). Eluent: V_{PET}/V_{EA} = 7:1; colourless oil (20.4 mg, 64% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 7.6 Hz, 2 H), 7.62 (t, J = 7.4 Hz, 1 H), 7.50 (t, J = 7.6 Hz, 2 H), 3.38 (t, J = 7.2 Hz, 2 H), 2.78 (t, J = 7.2 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.3, 135.6, 133.9, 128.9, 128.0, 119.2, 34.3, 11.8; ESI-HRMS Calcd for $C_{10}H_{10}NO$ $[M + H]^+$ 160.0757, found 160.0755.

References

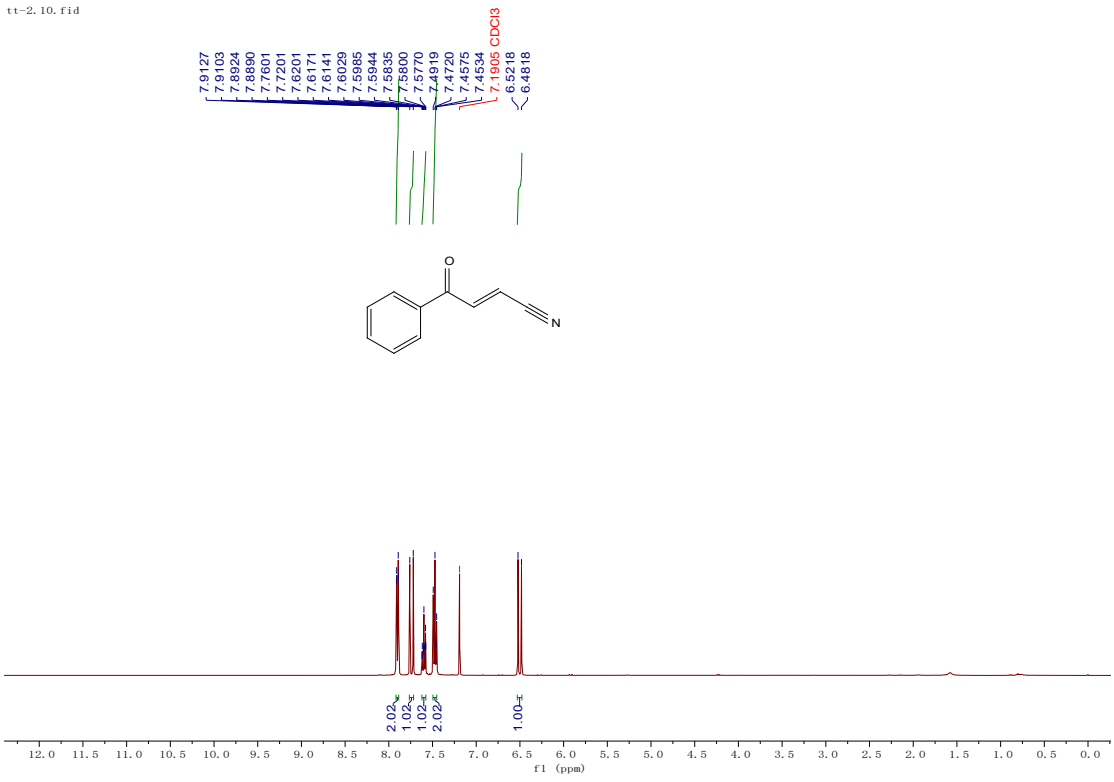
1. (a) F. M. A. A. EL-Taweel and M. H. Elnagdi, *J. Heterocyclic Chem.,* 2001, **38**, 981. (b) Y. Gao, Y. Liu and J.-P. Wan, *J. Org. Chem*., 2019, **84**, 2243.

2. T. Houssam, G. Régis and R. Gérard, *Eur. J. Org. Chem*. 2010, **30**, 5884.

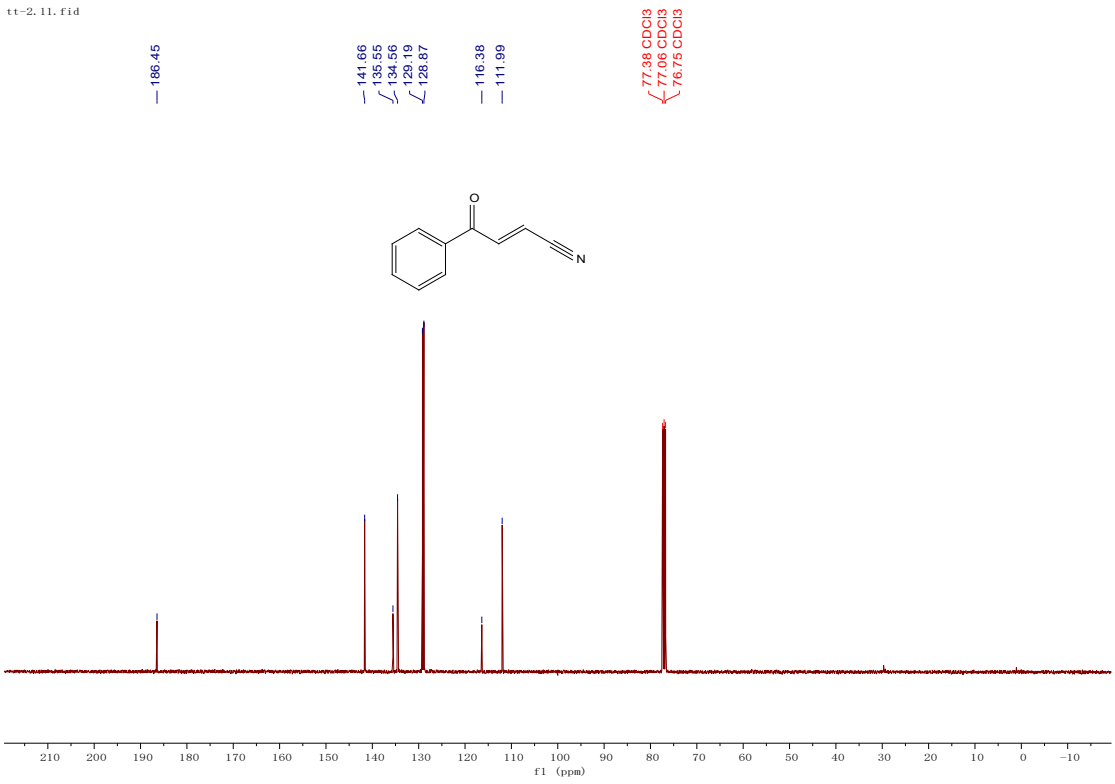
3. T. David, D.-H. Samuel, C. Lucia and G.-T. Fernando, *Chem. Eur. J.* 2019, **25**, 15046.

4. M.-T. Sean and R. Tomislav, *J. Am. Chem. Soc.* 2021, **143**, 2729.

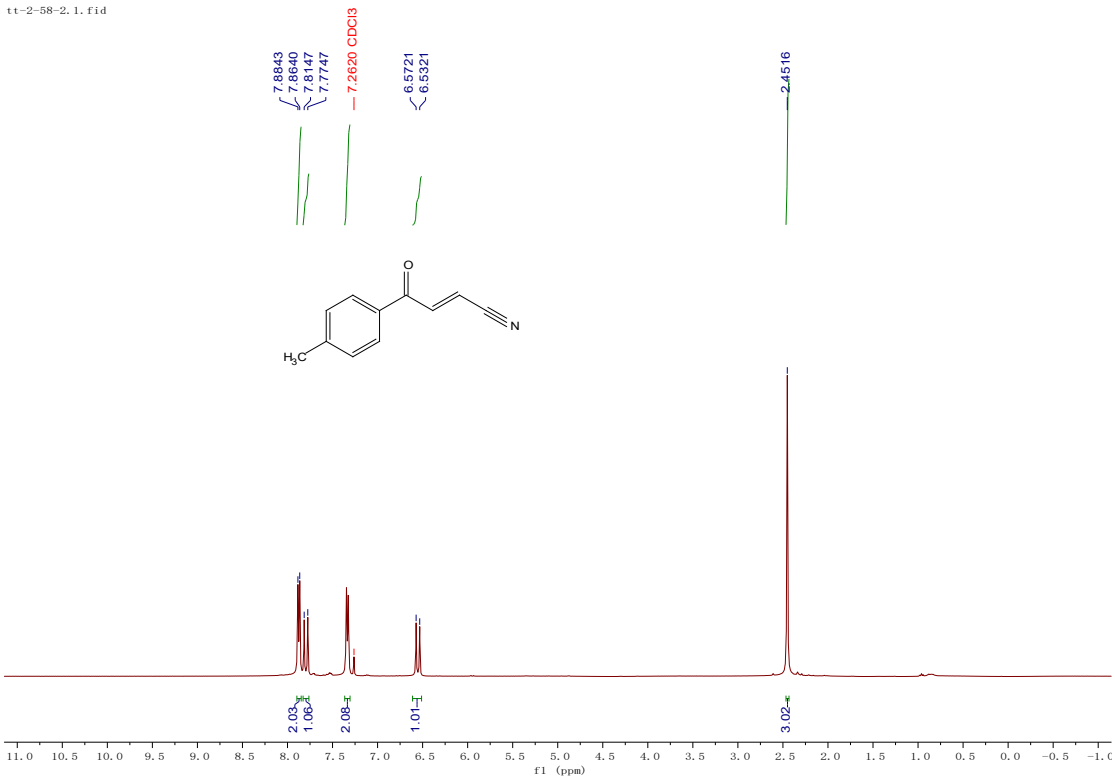
The ^{1}H and ^{13}C NMR spectra



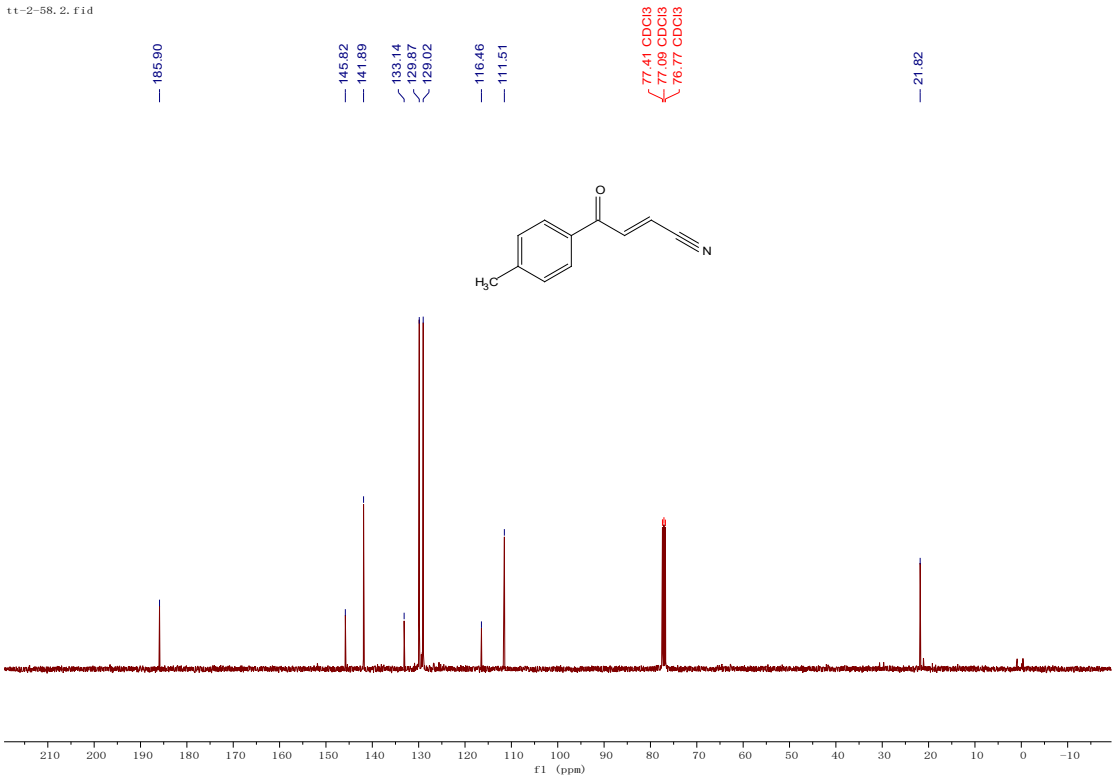
^{1}H NMR spectrum of 3a (400 MHz, $CDCl_3$)



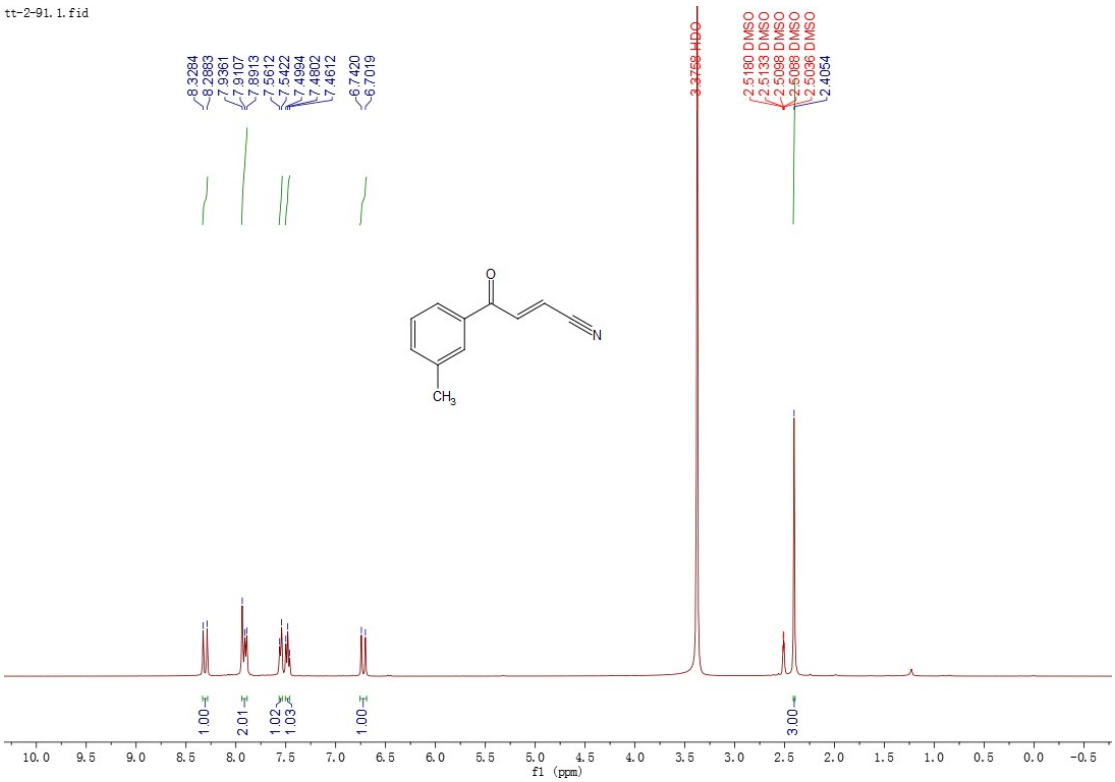
^{13}C NMR spectrum of 3a (100 MHz, $CDCl_3$)



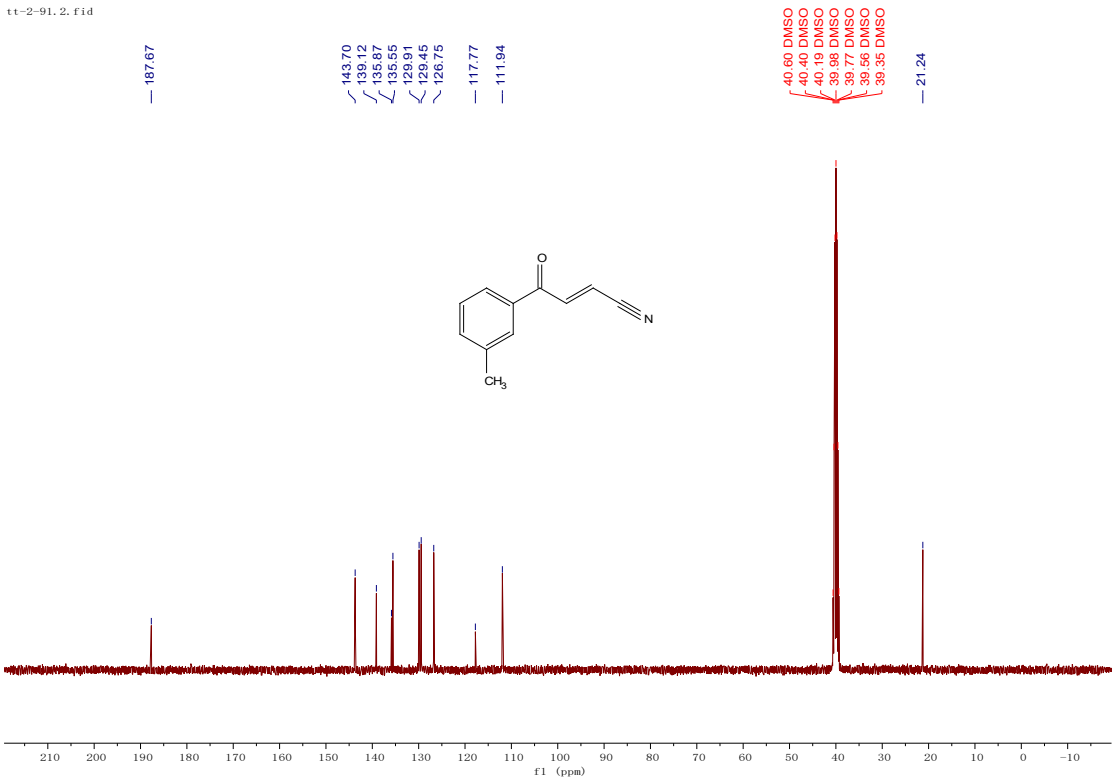
^{1}H NMR spectrum of 3b (400 MHz, $CDCl_3$)



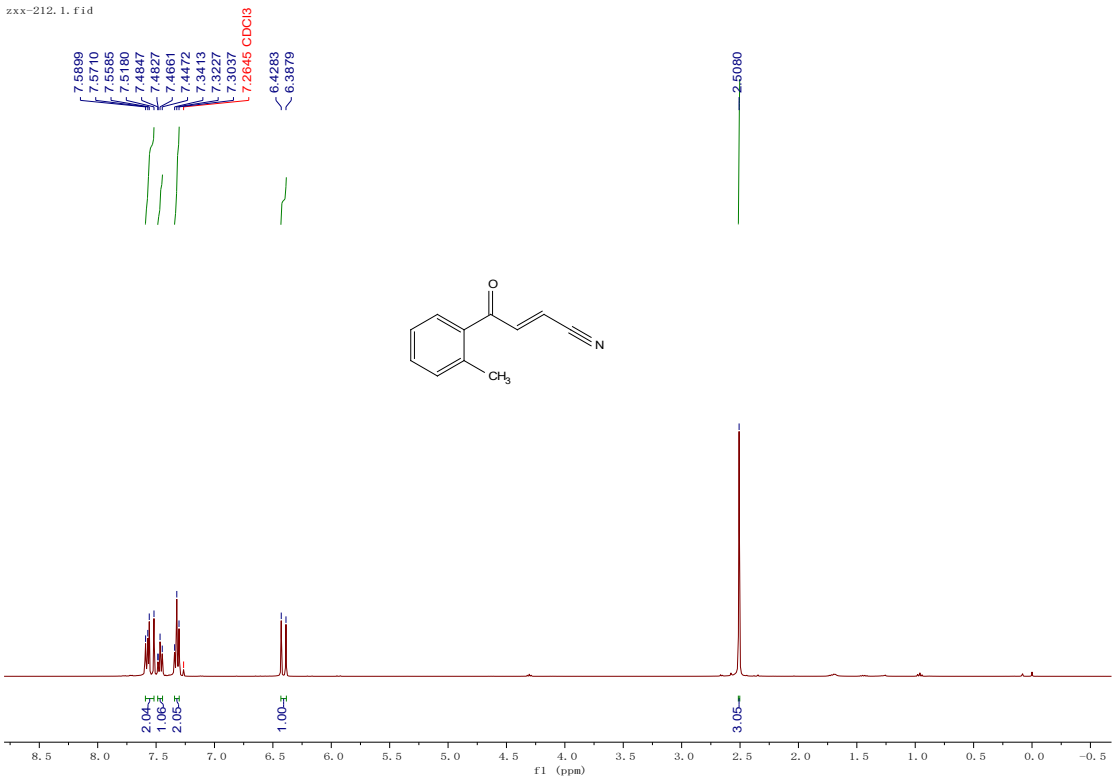
^{13}C NMR spectrum of 3b (100 MHz, $CDCl_3$)



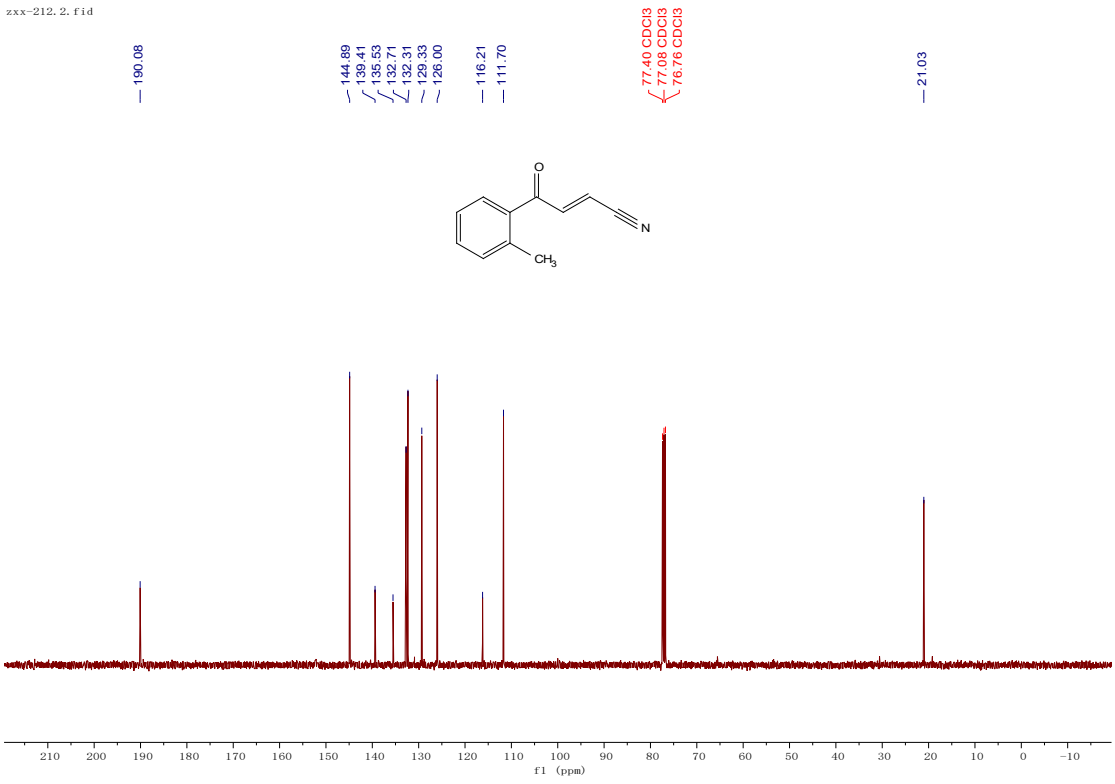
^{1}H NMR spectrum of 3c (400 MHz, DMSO-d_6)



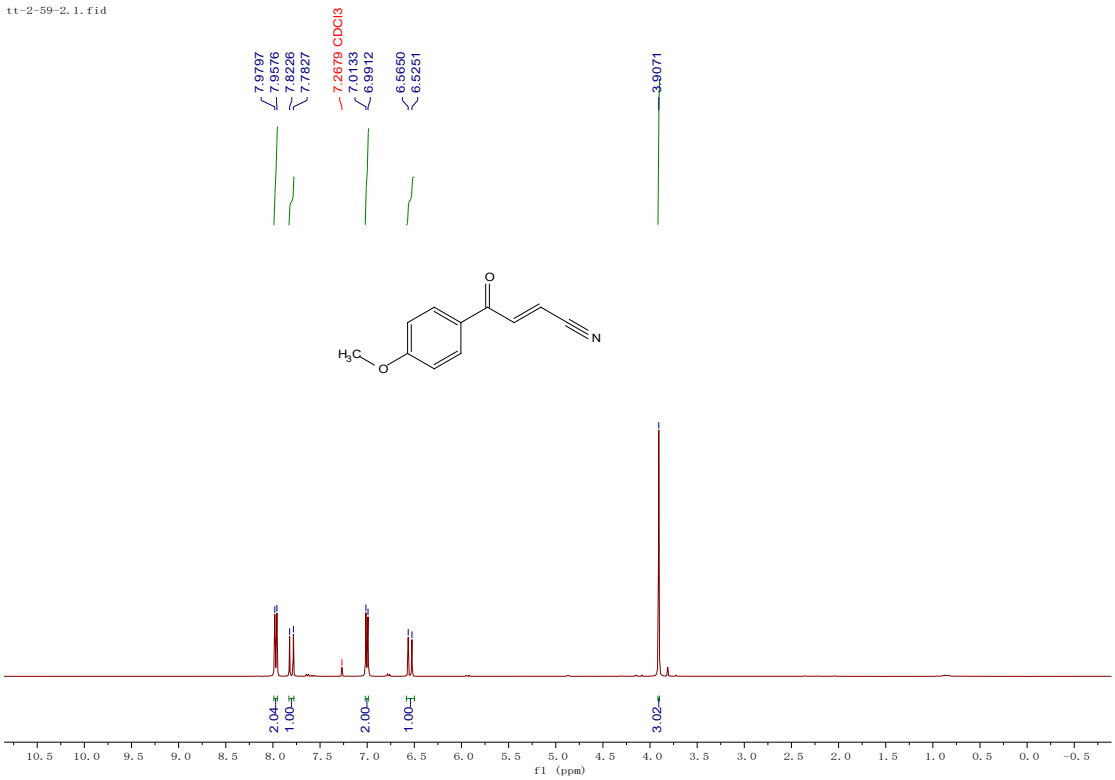
^{13}C NMR spectrum of 3c (100 MHz, DMSO-d_6)



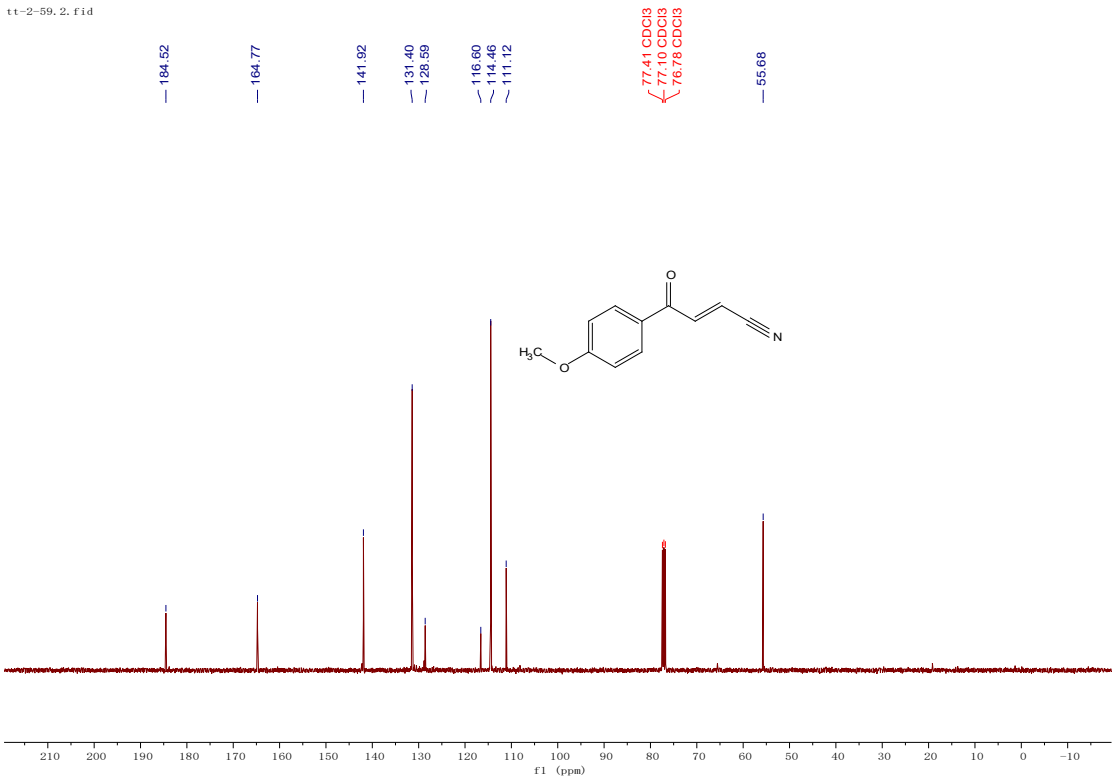
^{1}H NMR spectrum of 3d (400 MHz, $CDCl_3$)



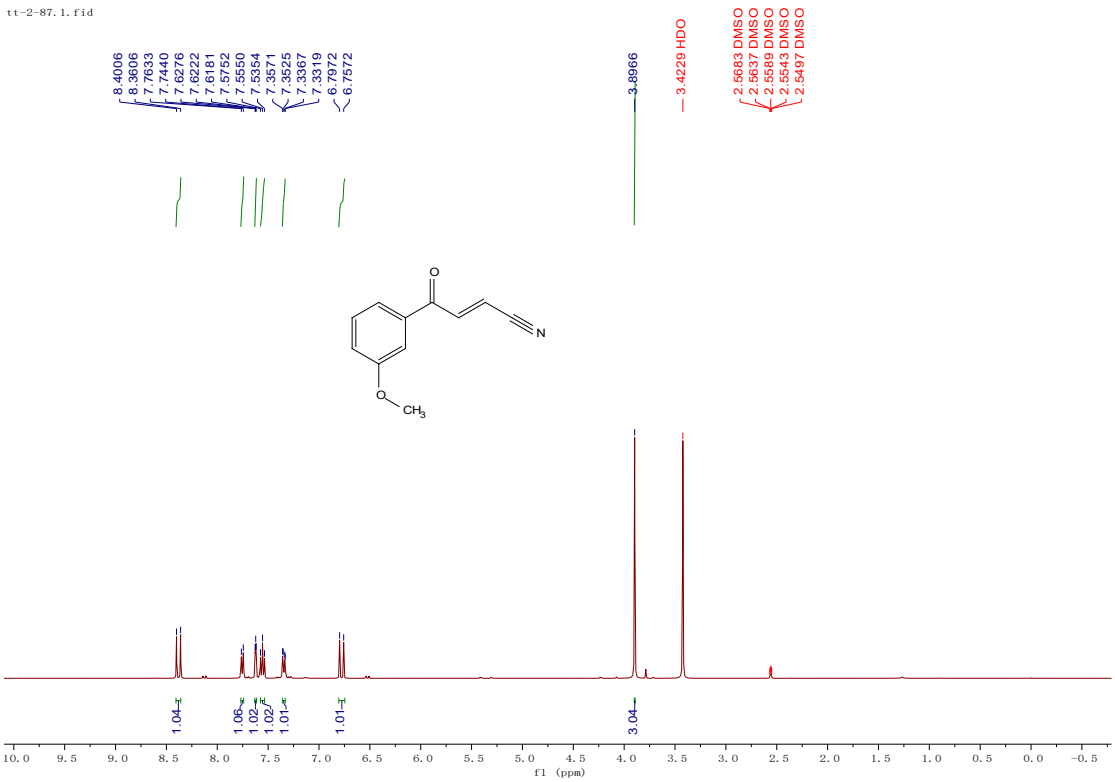
^{13}C NMR spectrum of 3d (100 MHz, $CDCl_3$)



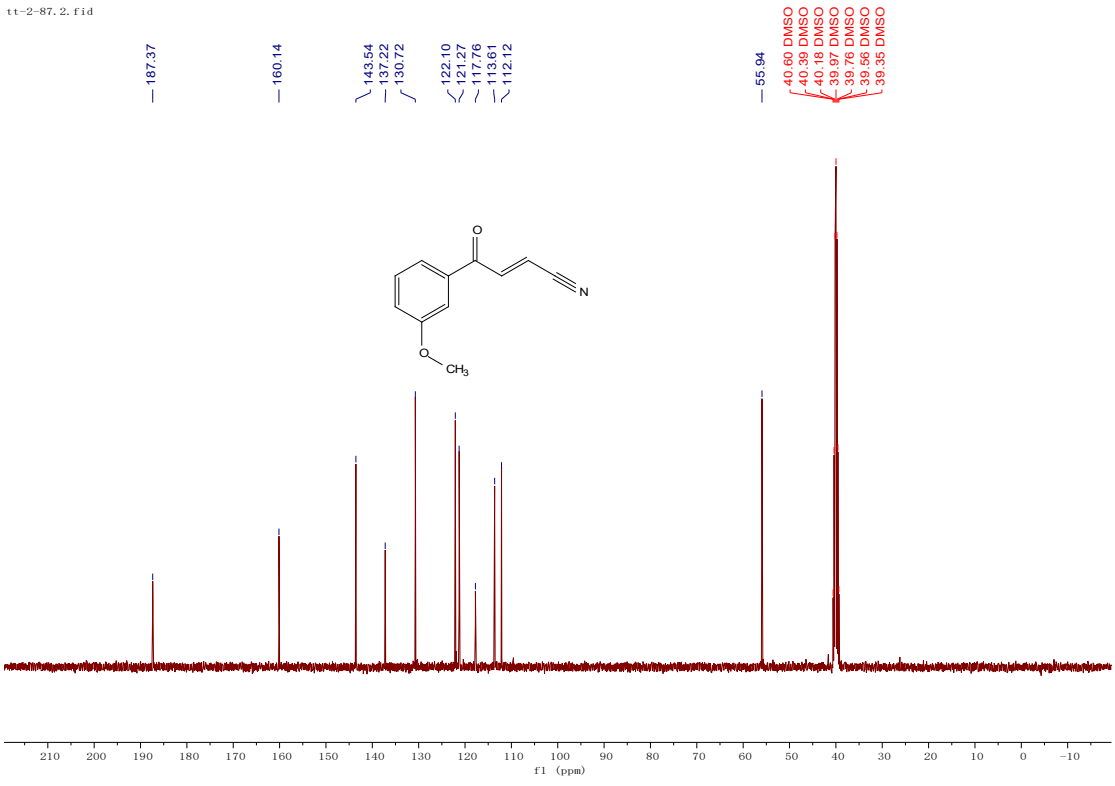
^{1}H NMR spectrum of 3e (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of 3e (100 MHz, $CDCl_3$)

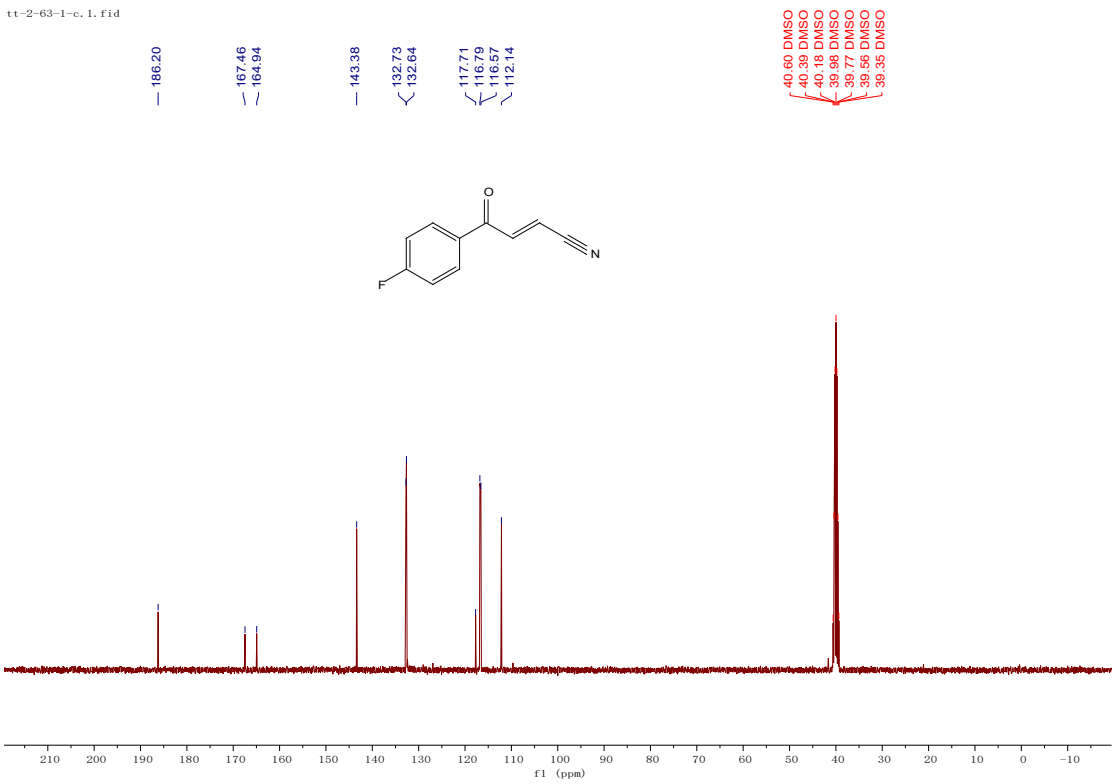


^{1}H NMR spectrum of 3f (400 MHz, DMSO-d_6)

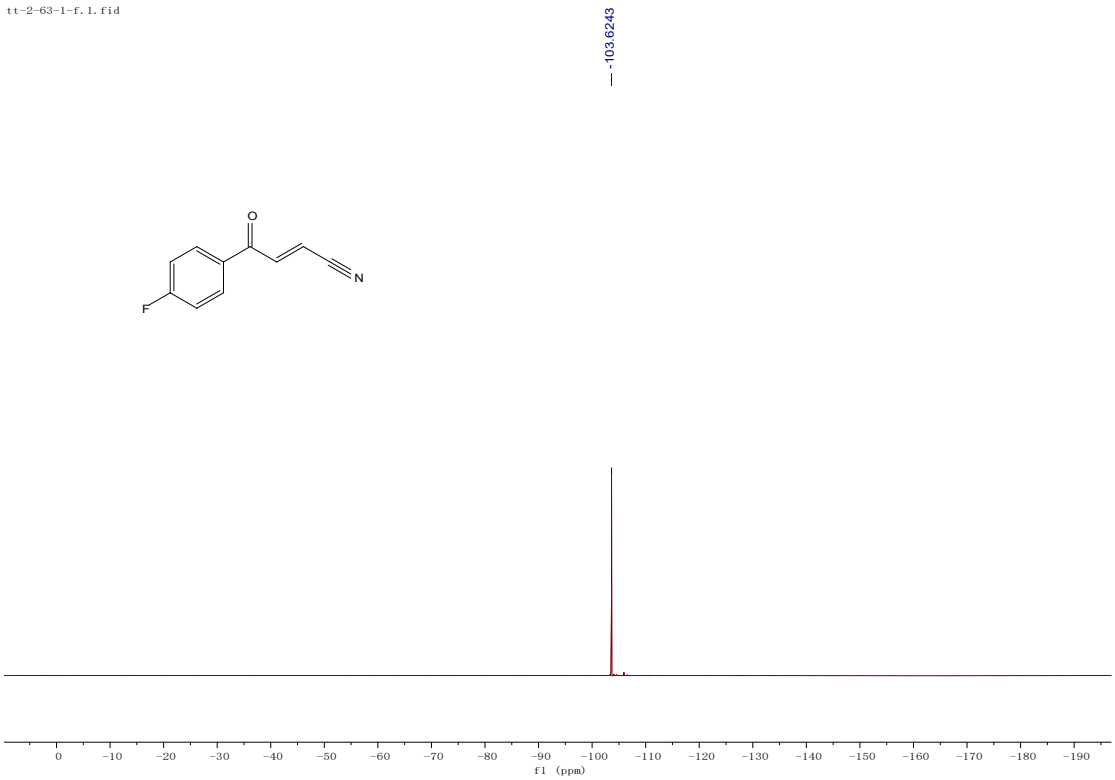


^{13}C NMR spectrum of 3f (100 MHz, DMSO-d_6)

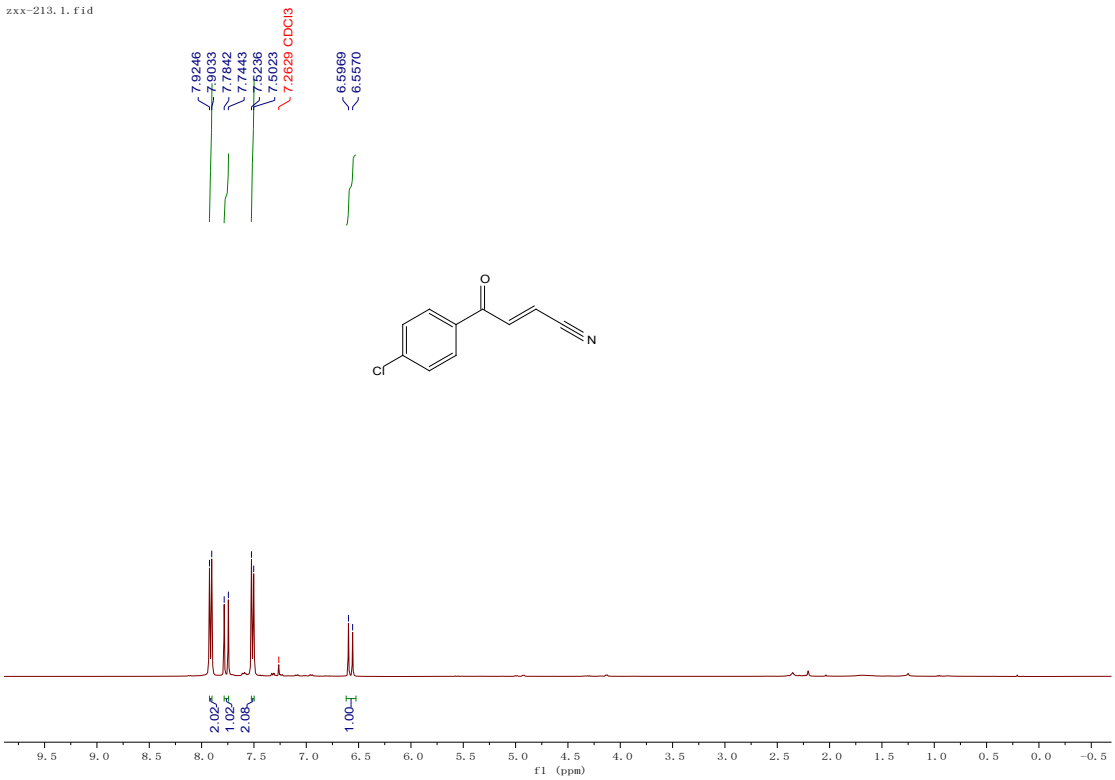
^{1}H NMR spectrum of 3g (400 MHz, DMSO-d_6)



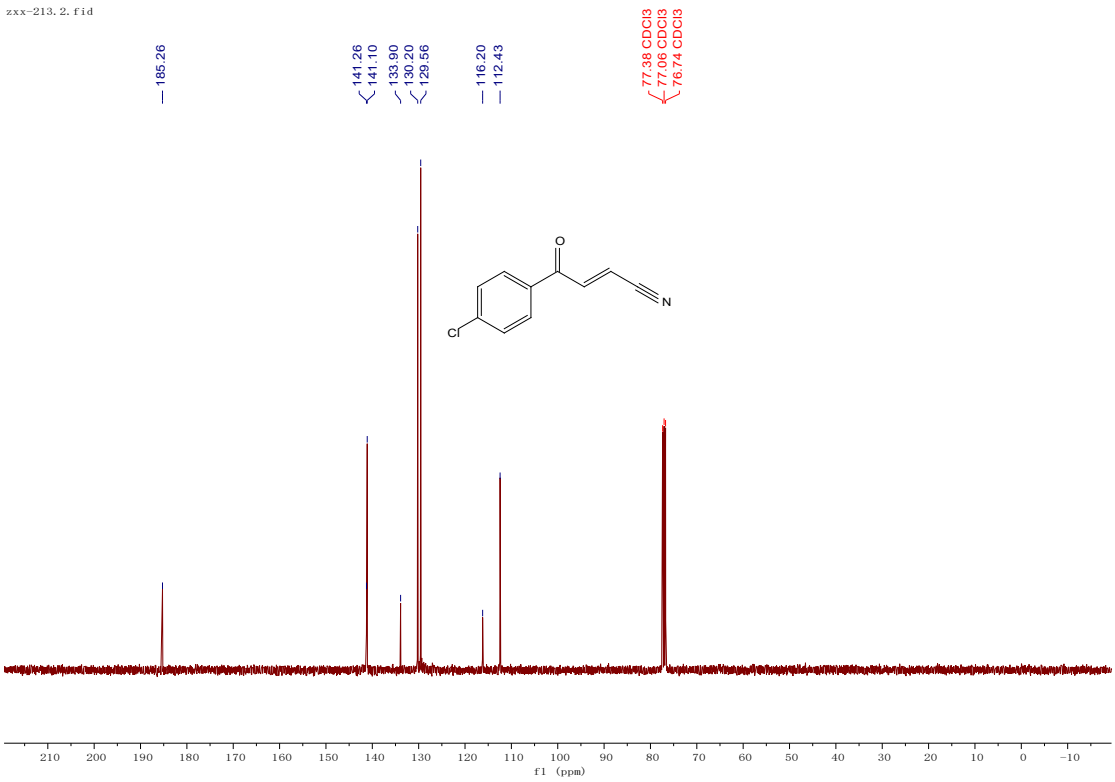
^{13}C NMR spectrum of 3g (100 MHz, DMSO-d_6)



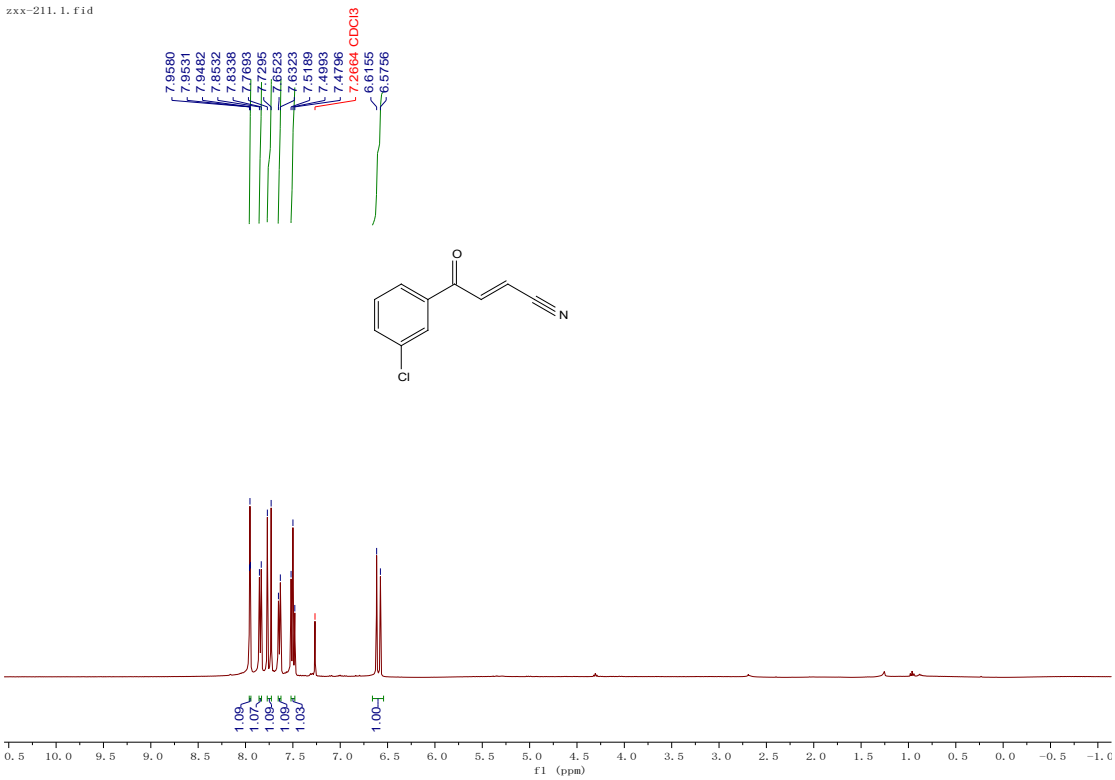
^{19}F NMR spectrum of 3g (376 MHz, DMSO-d_6)



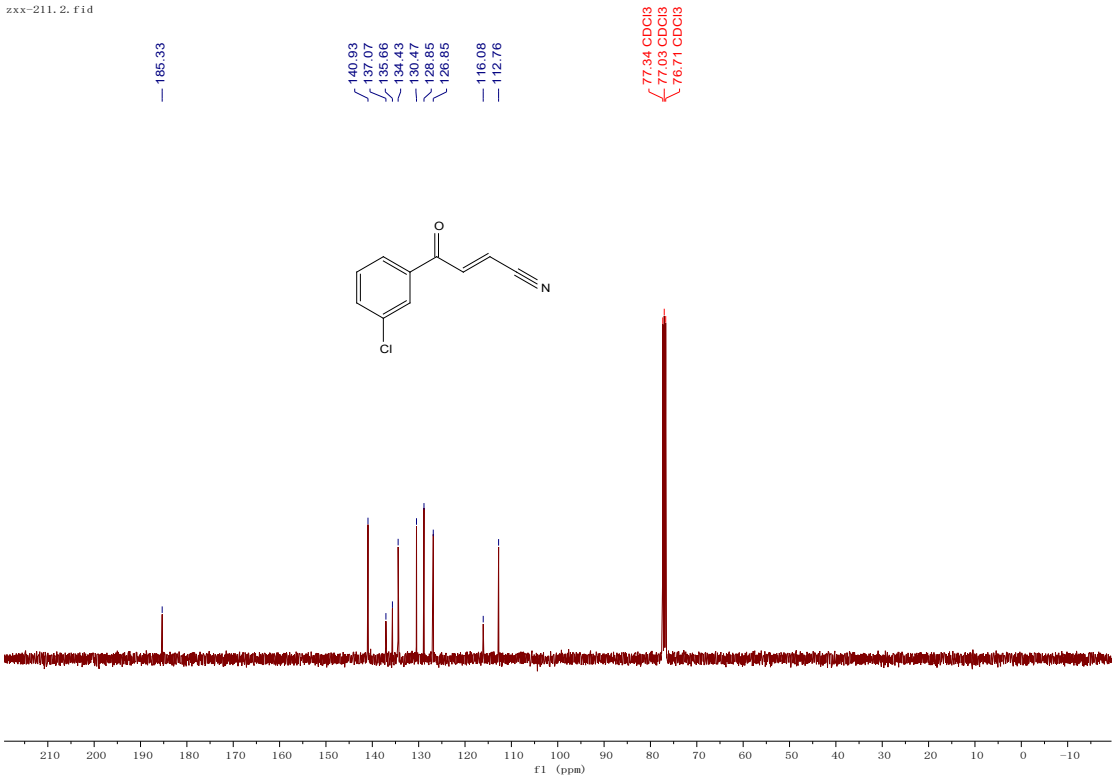
^{1}H NMR spectrum of 3h (400 MHz, $CDCl_3$)



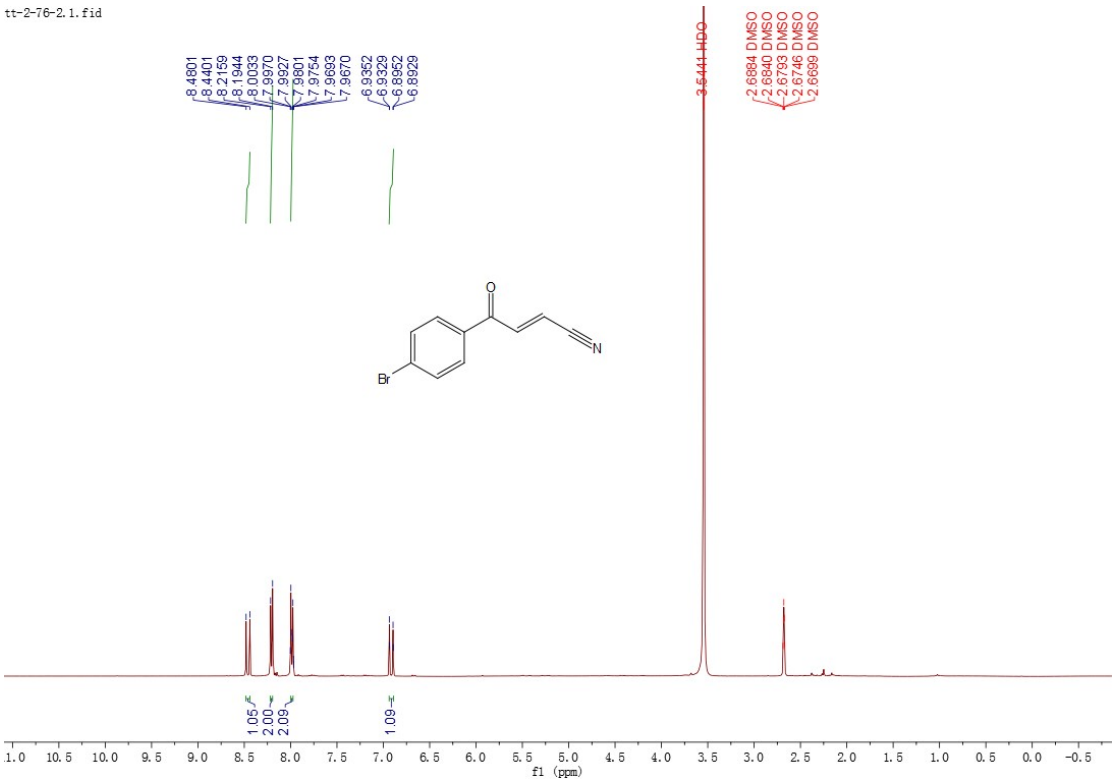
^{13}C NMR spectrum of 3h (100 MHz, $CDCl_3$)



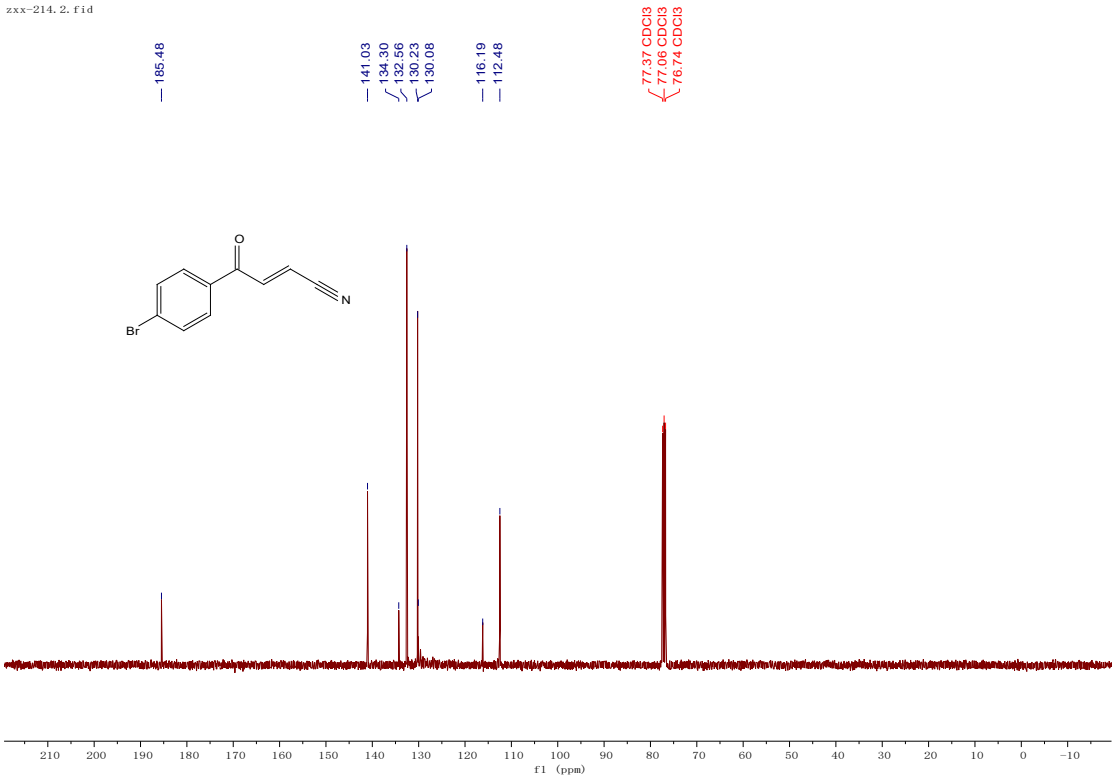
^{1}H NMR spectrum of 3i (400 MHz, $CDCl_3$)



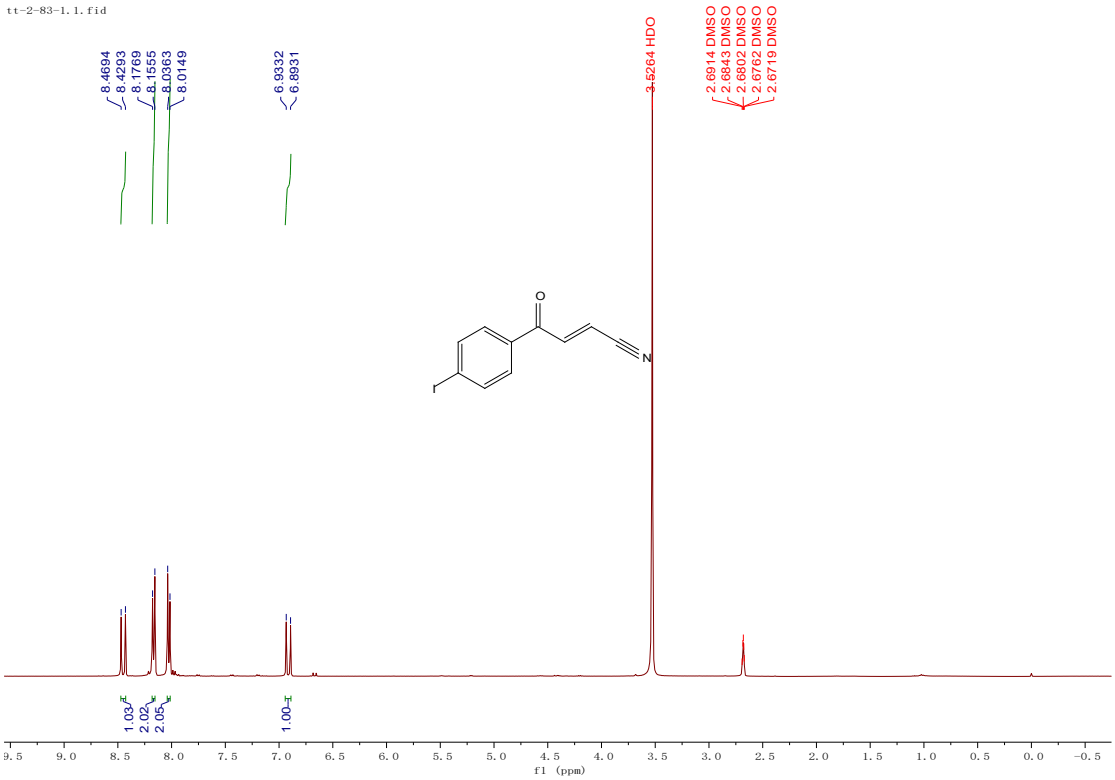
^{13}C NMR spectrum of 3i (100 MHz, $CDCl_3$)



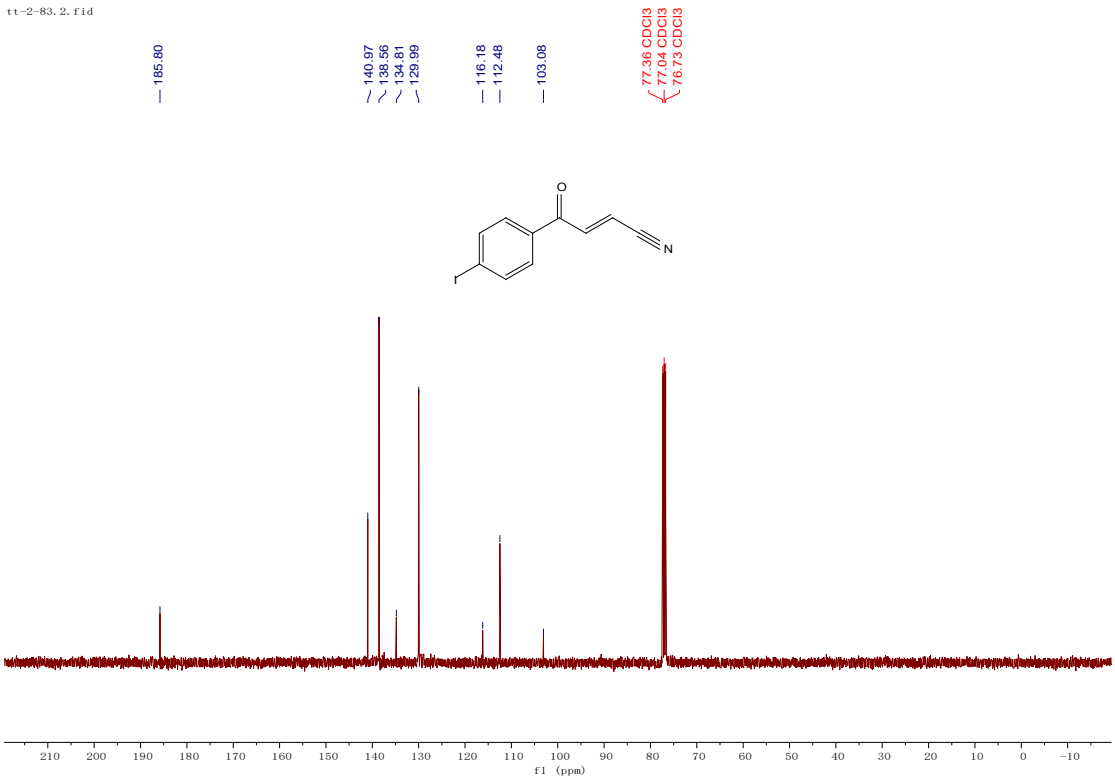
^{1}H NMR spectrum of 3j (400 MHz, DMSO-d_6)



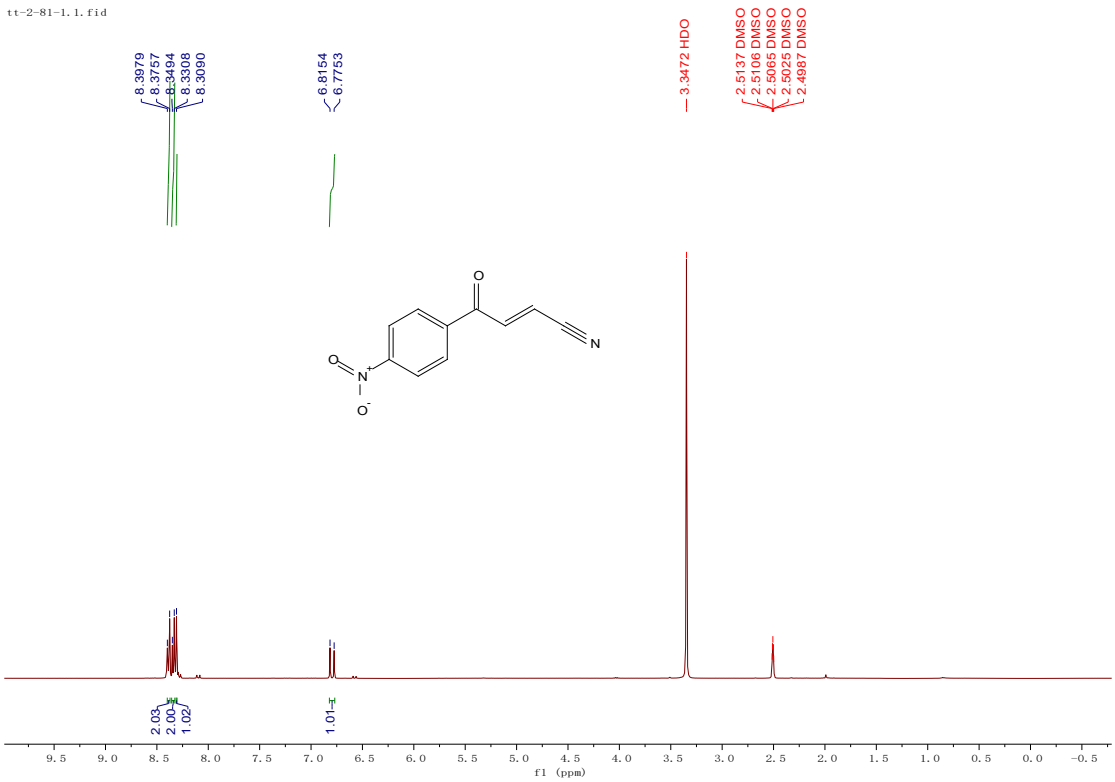
^{13}C NMR spectrum of 3j (100 MHz, $CDCl_3$)



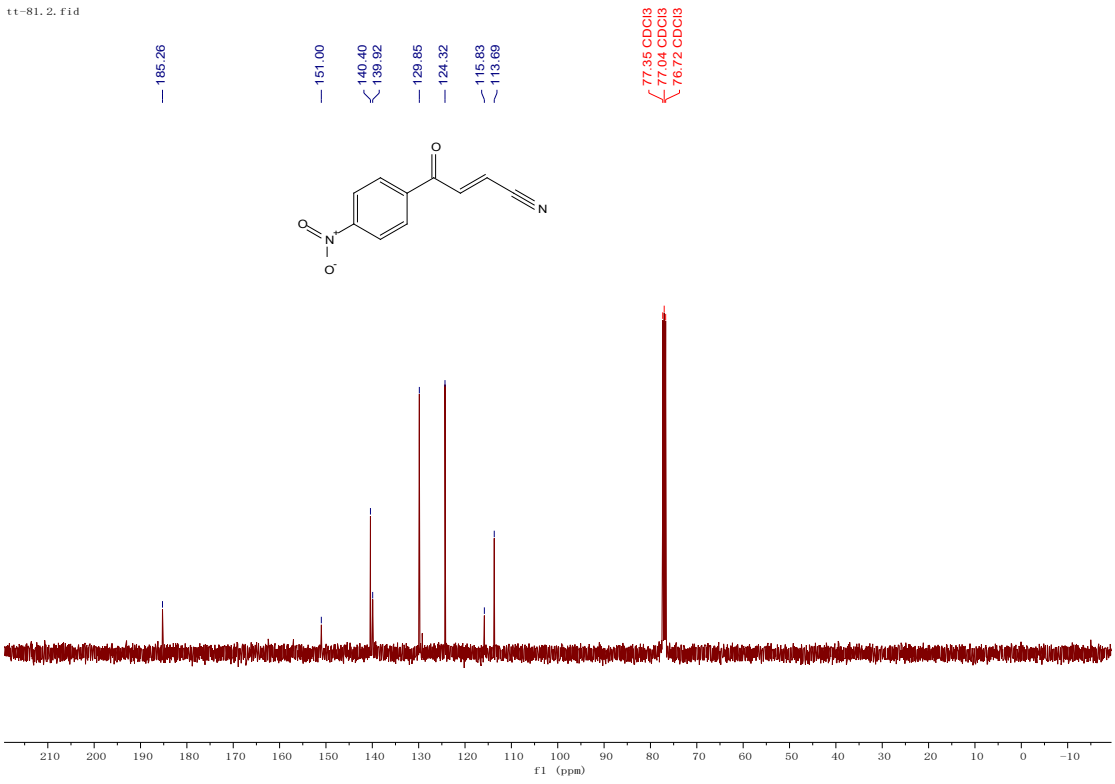
^{1}H NMR spectrum of 3k (400 MHz, DMSO-d_6)



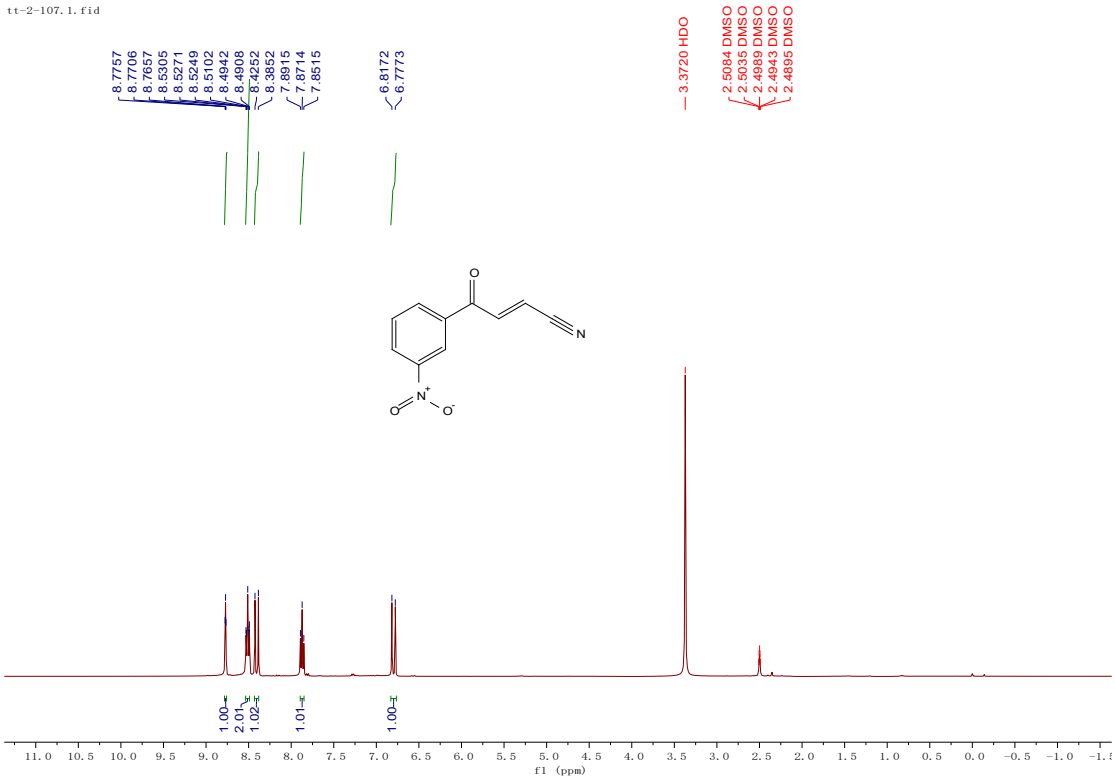
^{13}C NMR spectrum of 3k (100 MHz, $CDCl_3$)



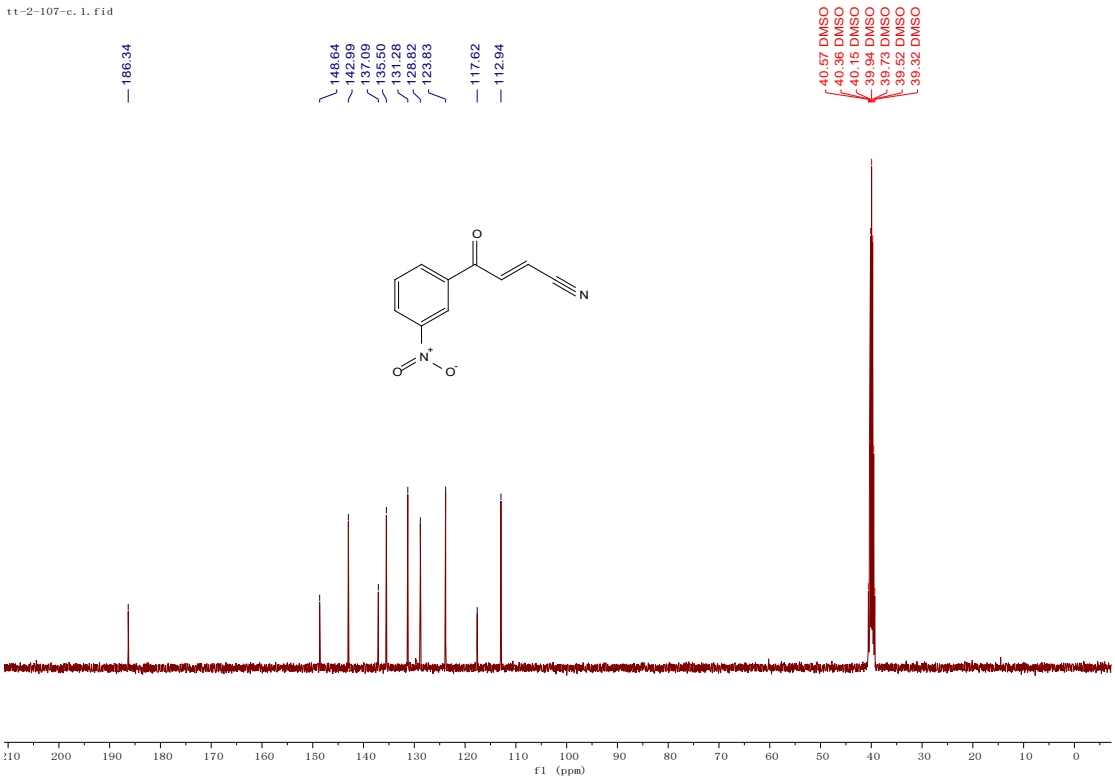
^{1}H NMR spectrum of 3l (400 MHz, DMSO-d_6)



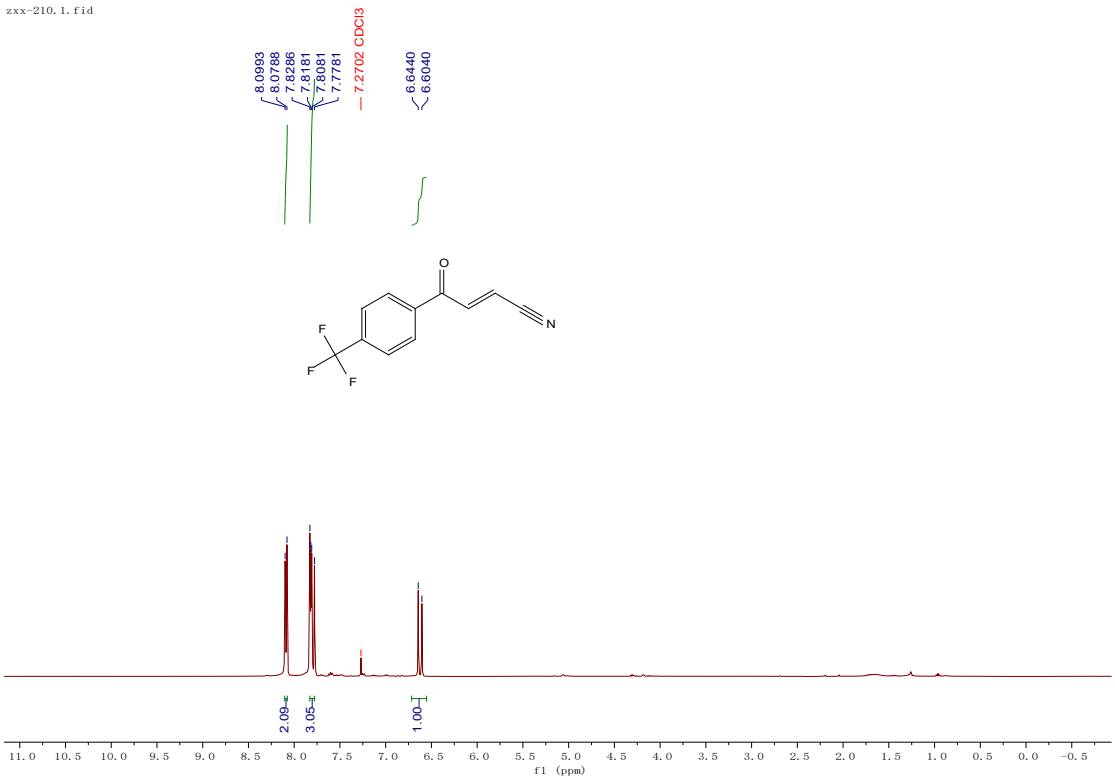
^{13}C NMR spectrum of 3l (100 MHz, $CDCl_3$)



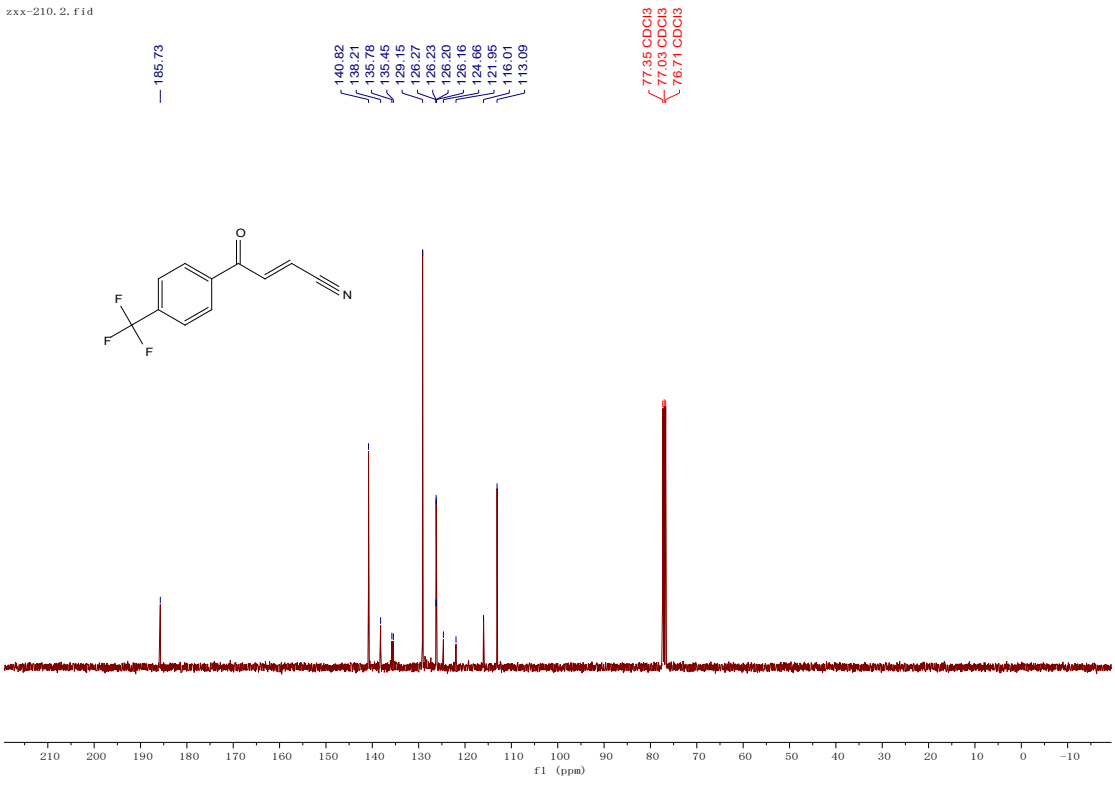
^{1}H NMR spectrum of 3m (400 MHz, DMSO-d_6)



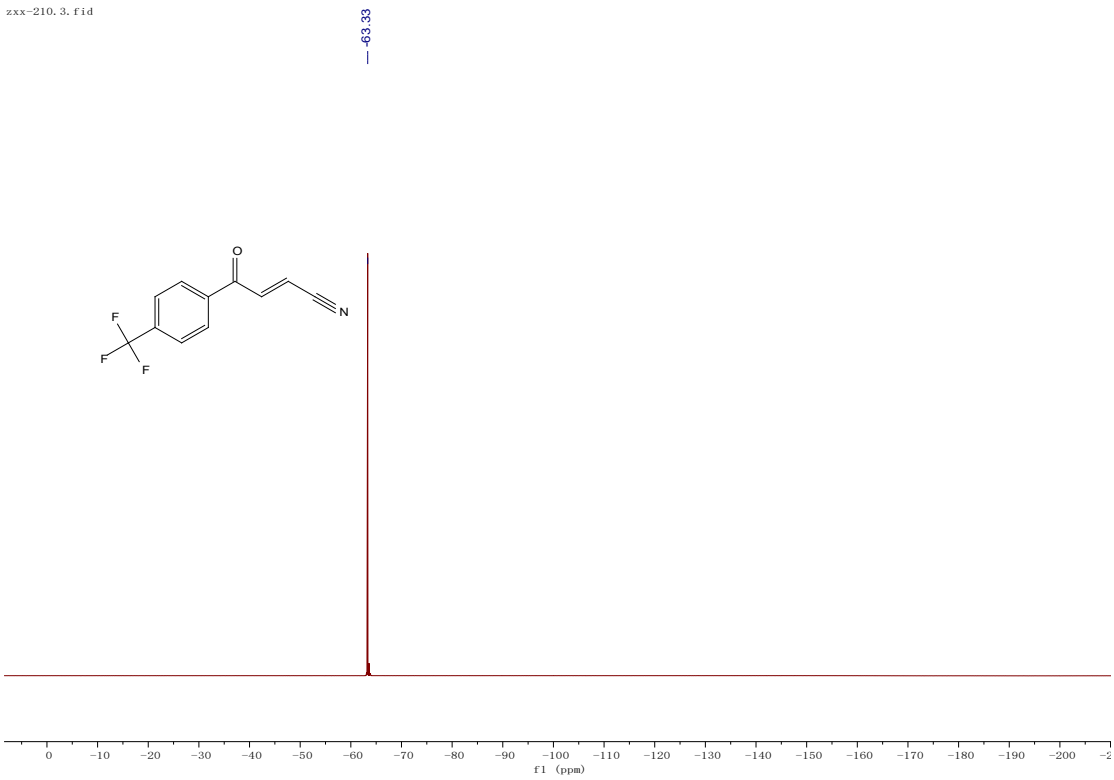
^{13}C NMR spectrum of 3m (100 MHz, DMSO-d_6)



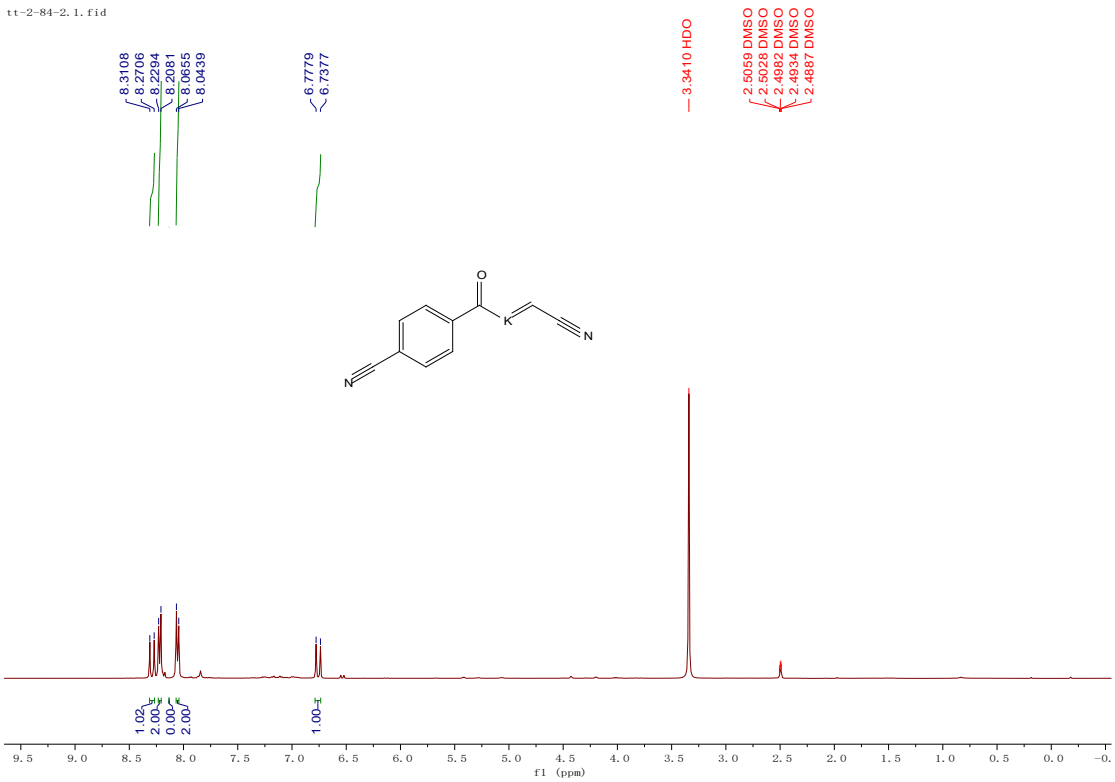
^{1}H NMR spectrum of 3n (400 MHz, $CDCl_3$)



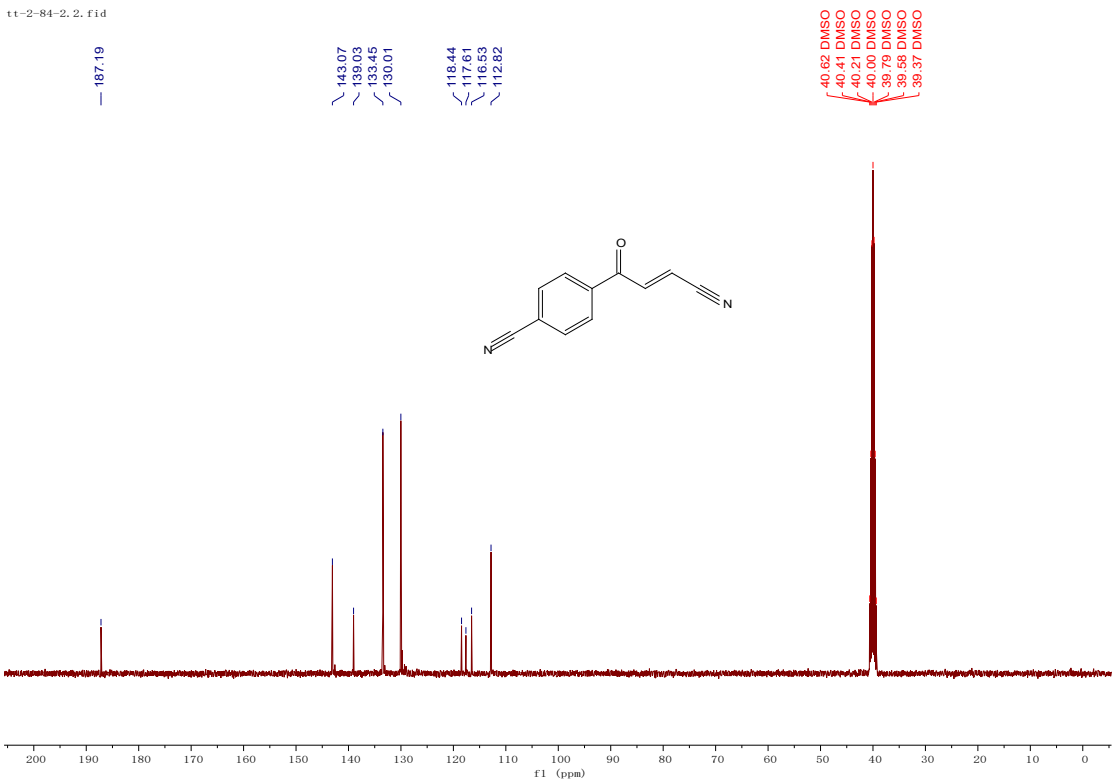
^{13}C NMR spectrum of 3n (400 MHz, $CDCl_3$)



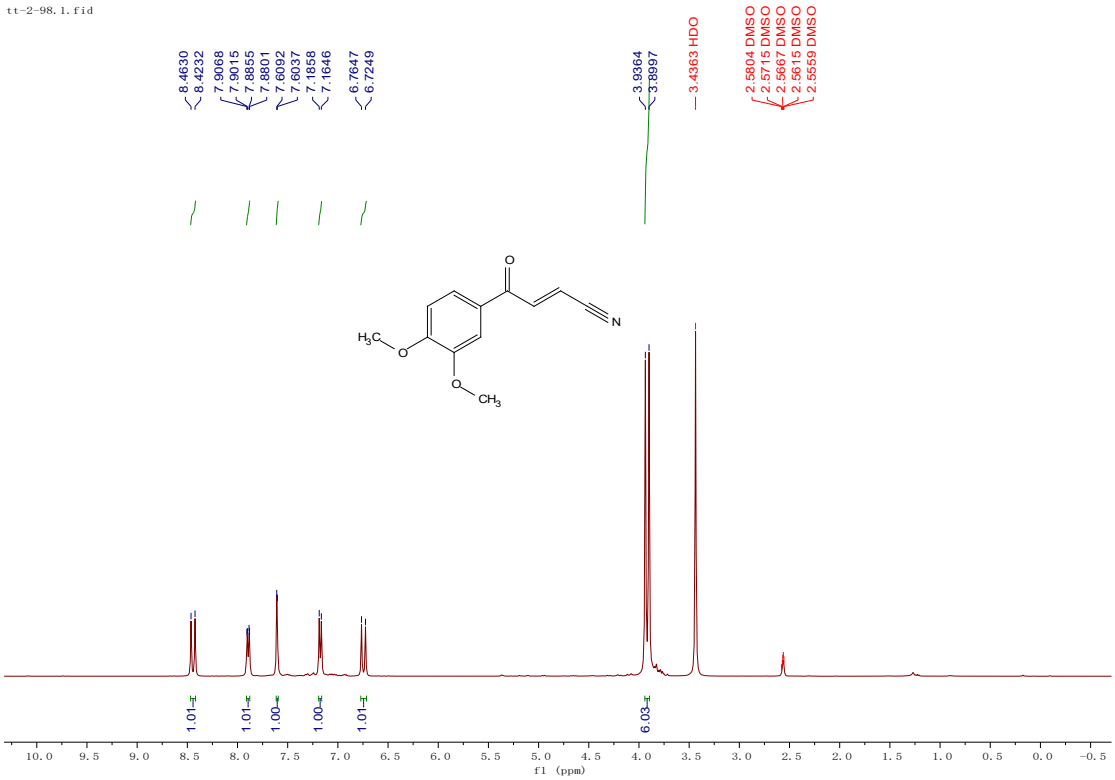
^{19}F NMR spectrum of 3n (376 MHz, $CDCl_3$)



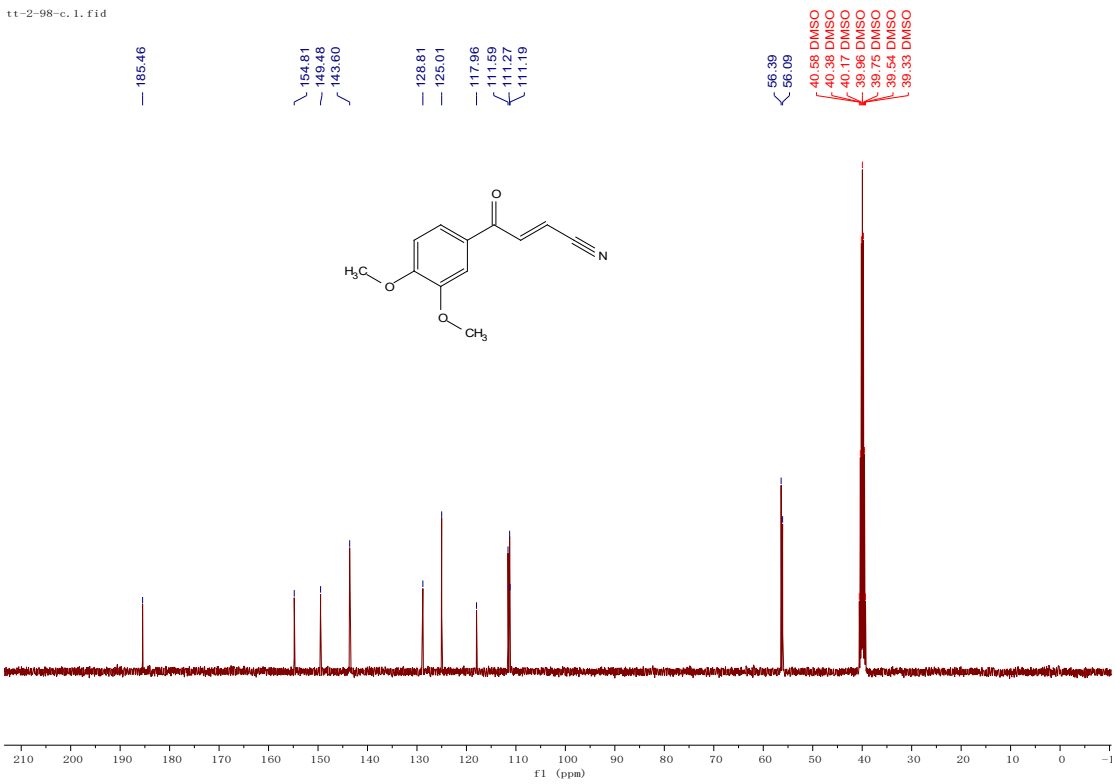
^{1}H NMR spectrum of 3o (400 MHz, DMSO-d_6)



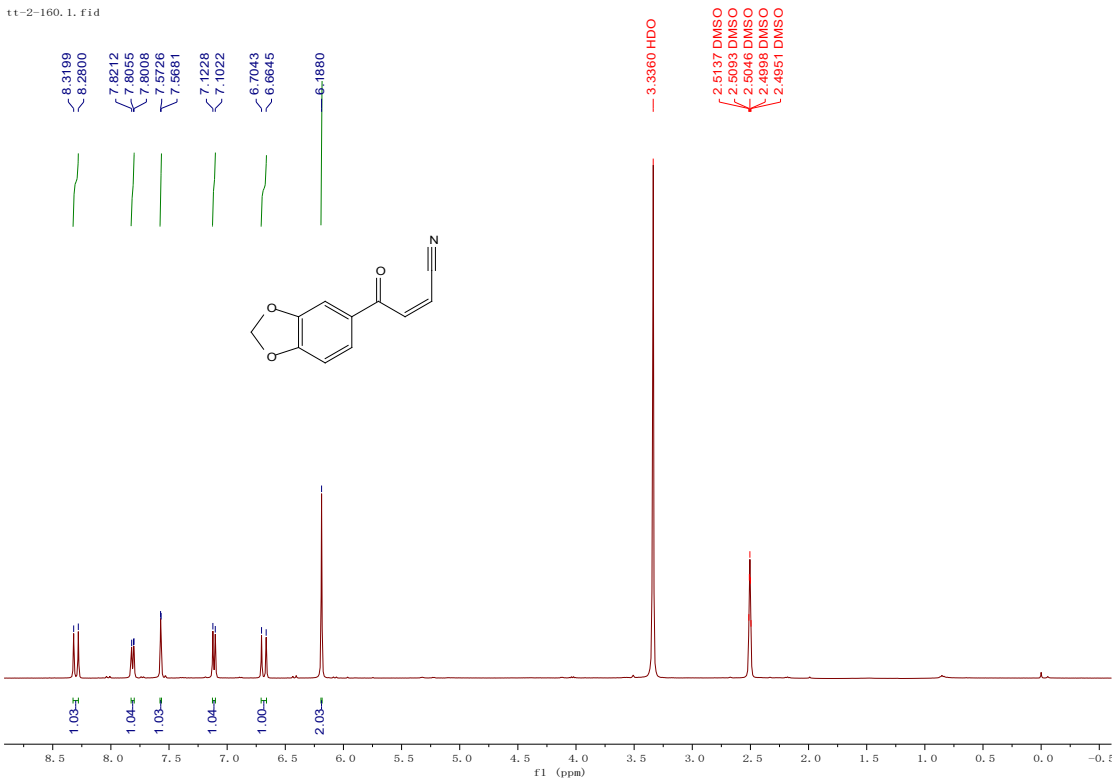
^{13}C NMR spectrum of 3o (100 MHz, DMSO-d_6)



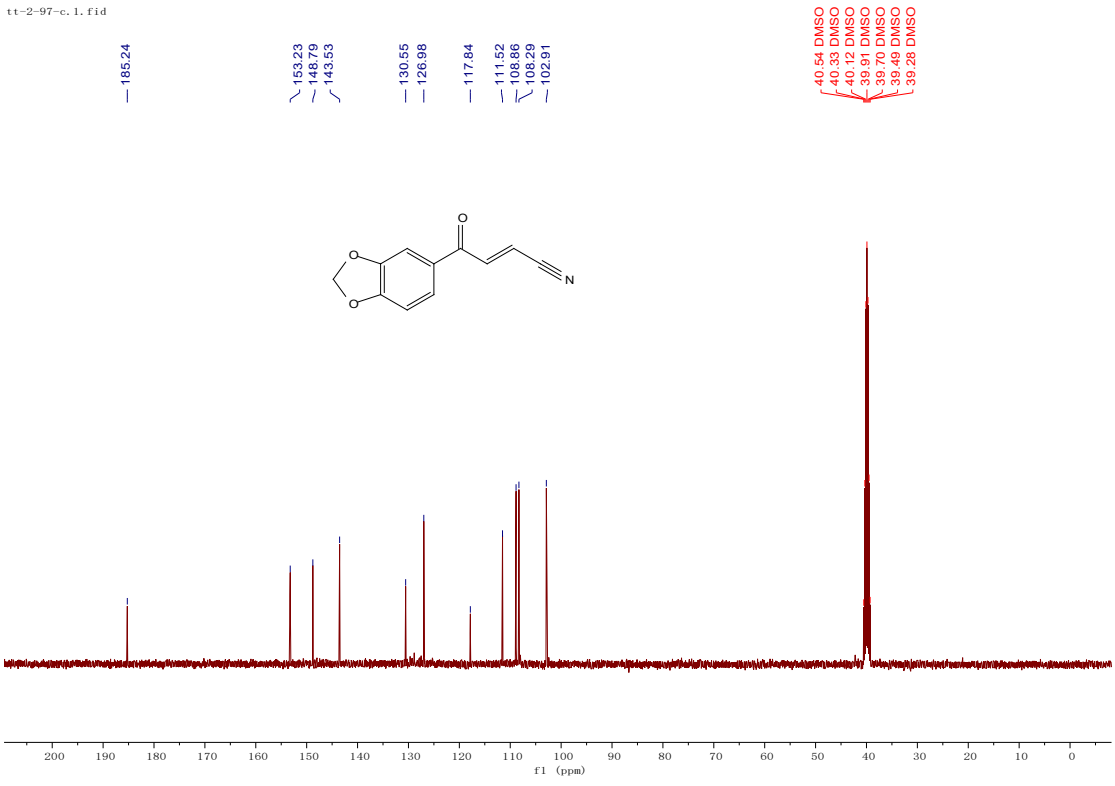
^{1}H NMR spectrum of 3p (400 MHz, DMSO-d_6)



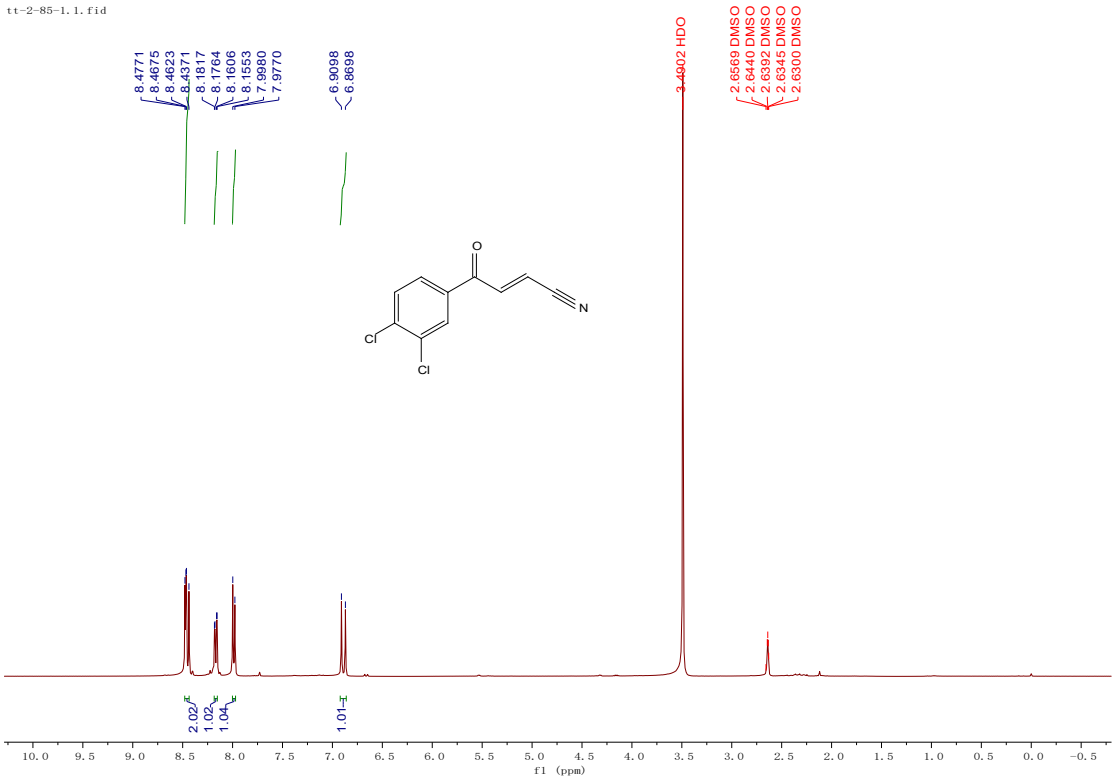
^{13}C NMR spectrum of 3p (100 MHz, DMSO-d_6)



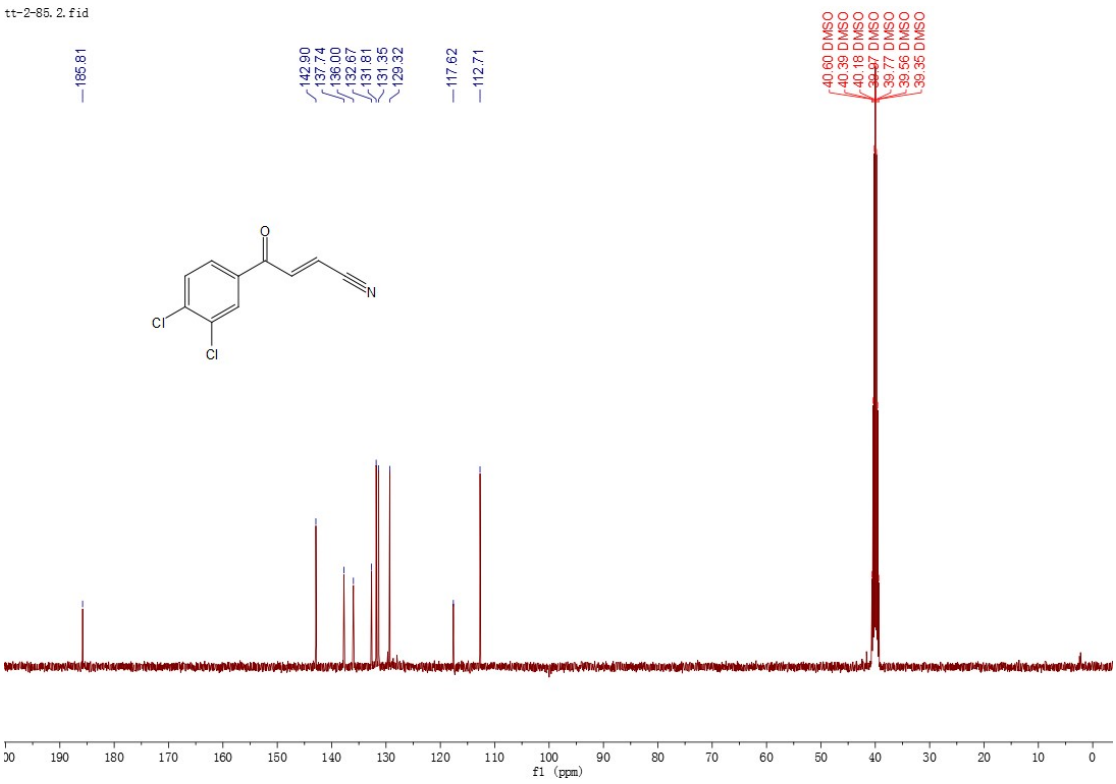
^{1}H NMR spectrum of 3q (400 MHz, DMSO-d_6)



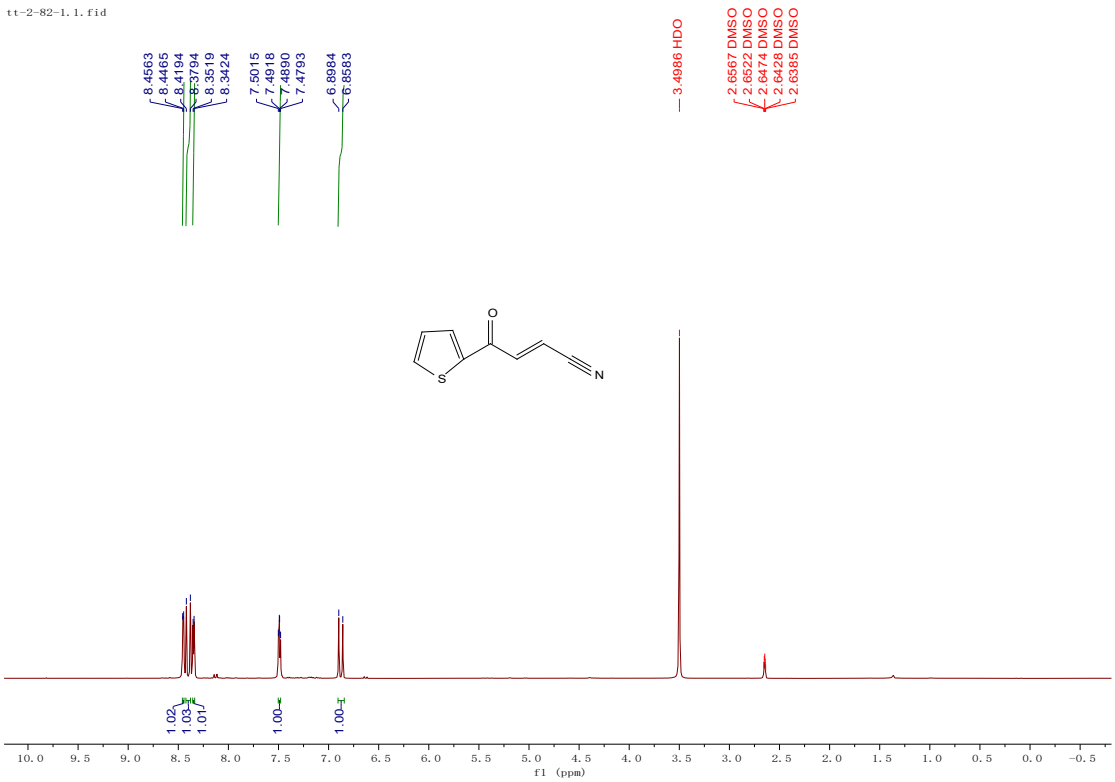
^{13}C NMR spectrum of 3q (100 MHz, DMSO-d_6)



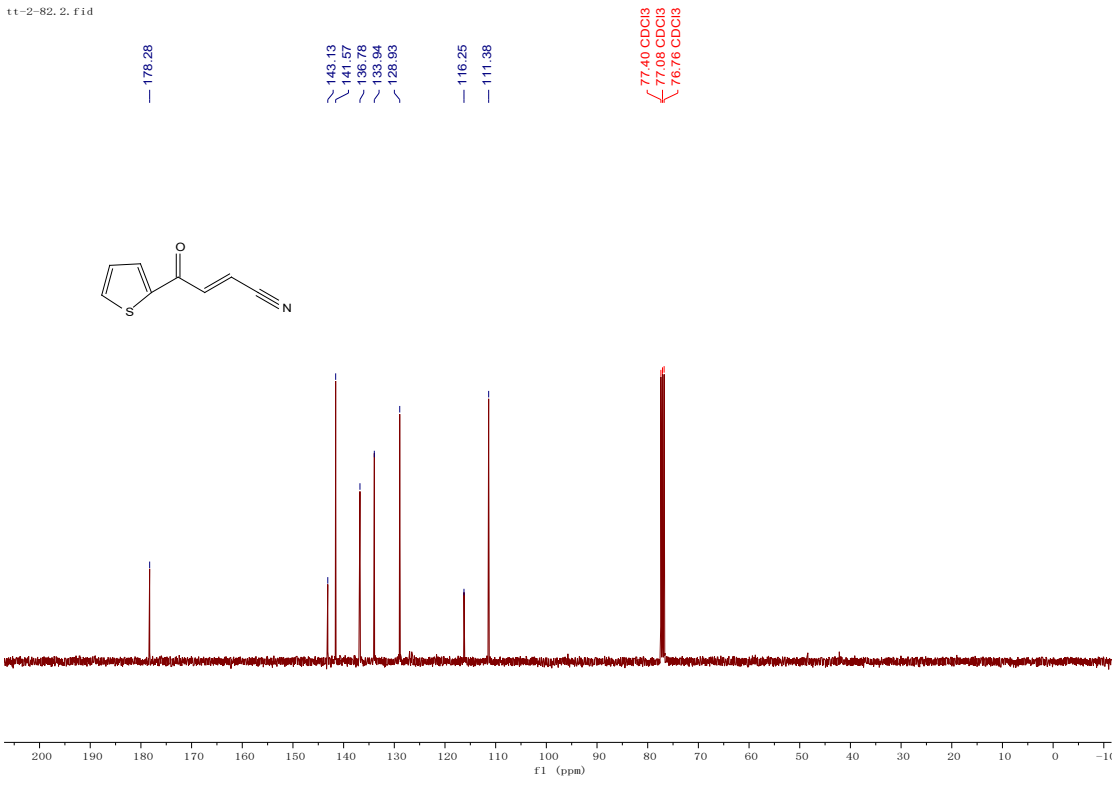
^{1}H NMR spectrum of 3r (400 MHz, DMSO-d_6)



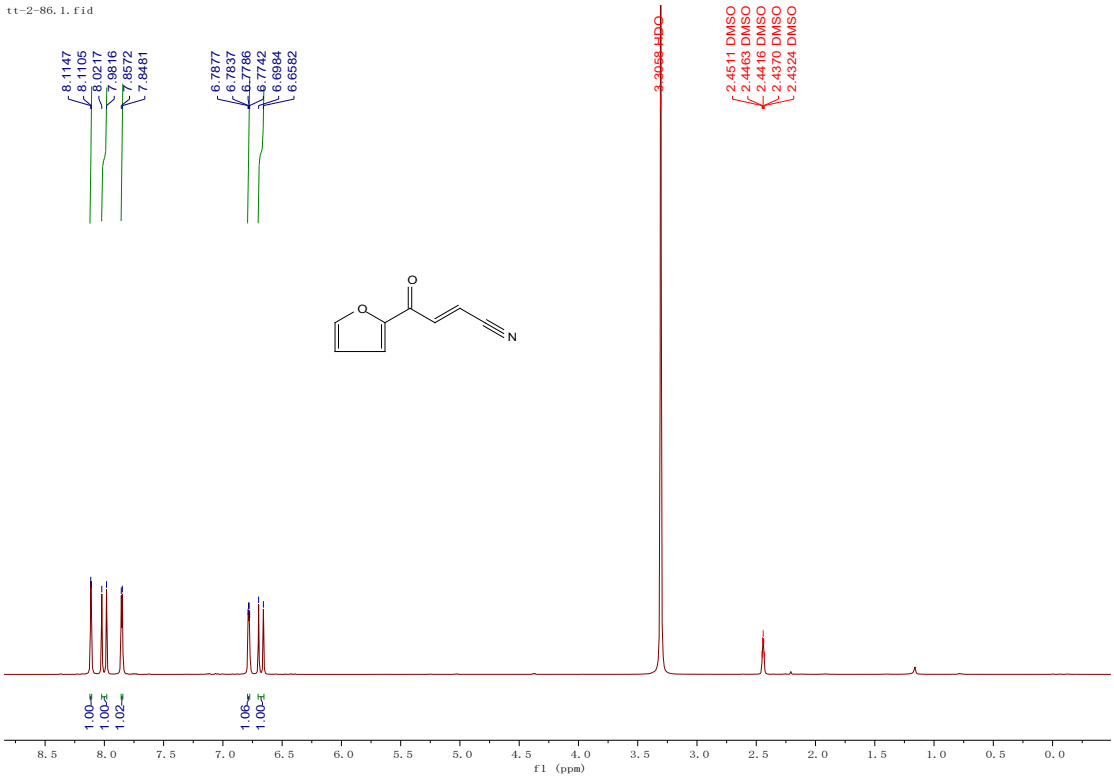
^{13}C NMR spectrum of 3r (100 MHz, DMSO-d_6)



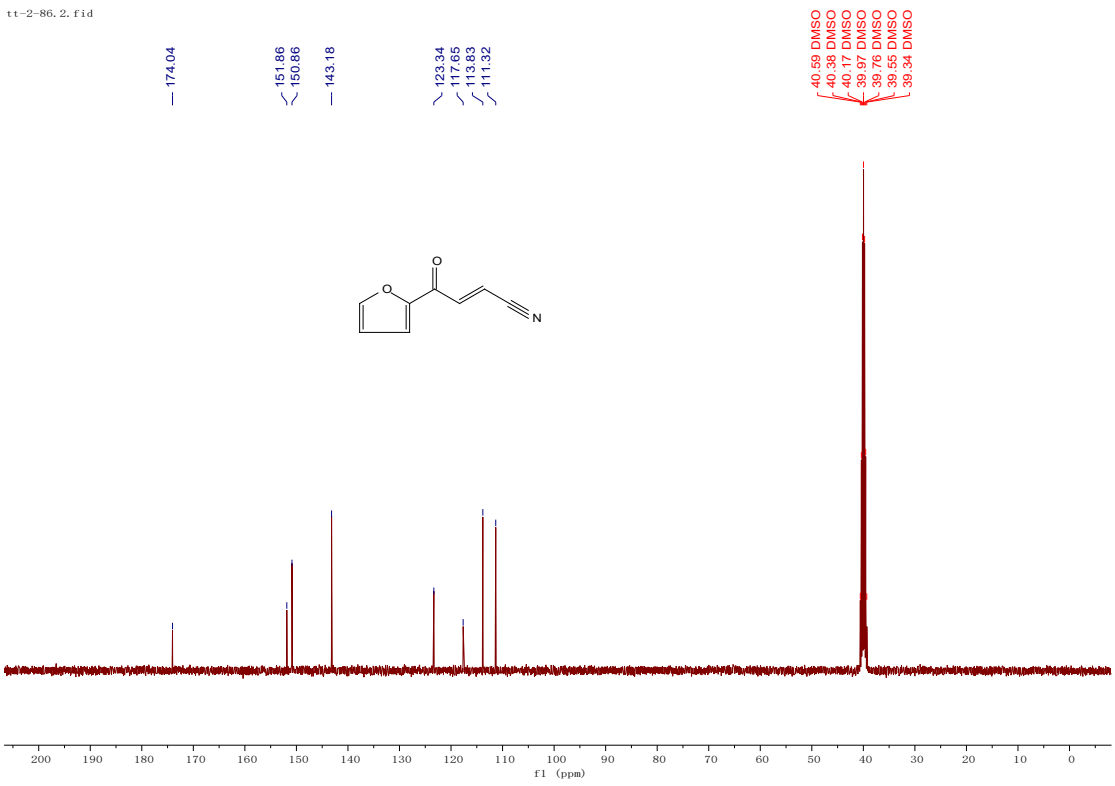
^{1}H NMR spectrum of 3s (400 MHz, DMSO-d_6)



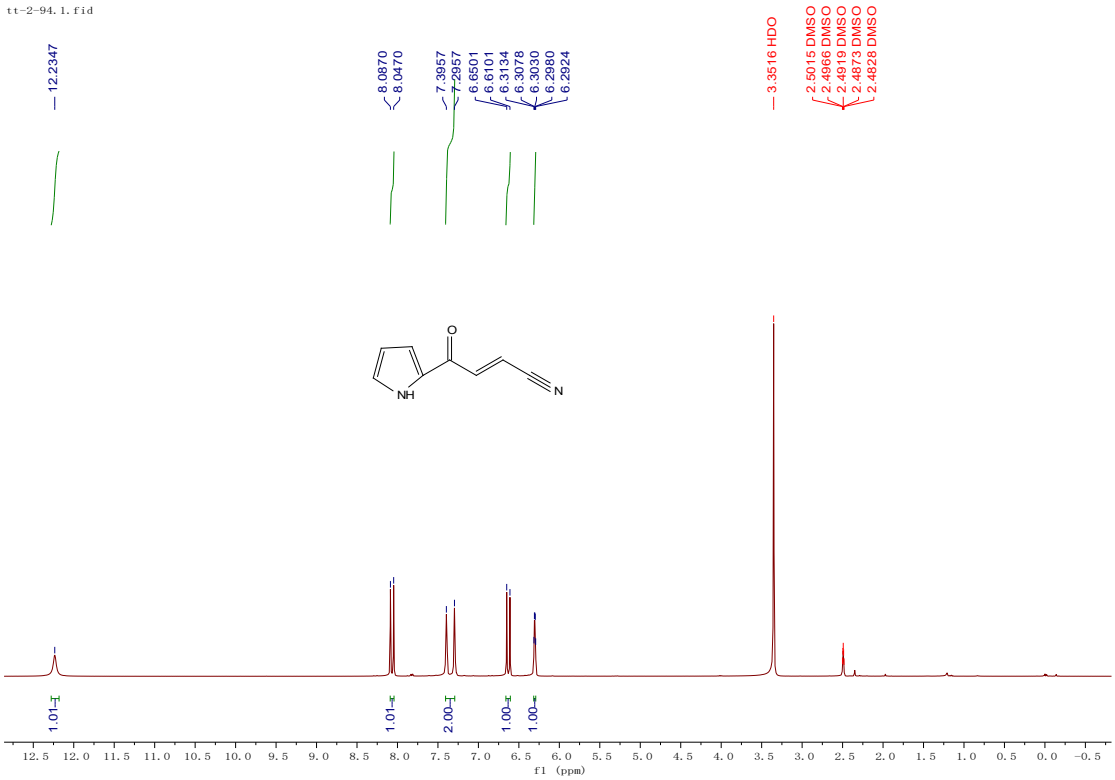
^{13}C NMR spectrum of 3s (100 MHz, $CDCl_3$)



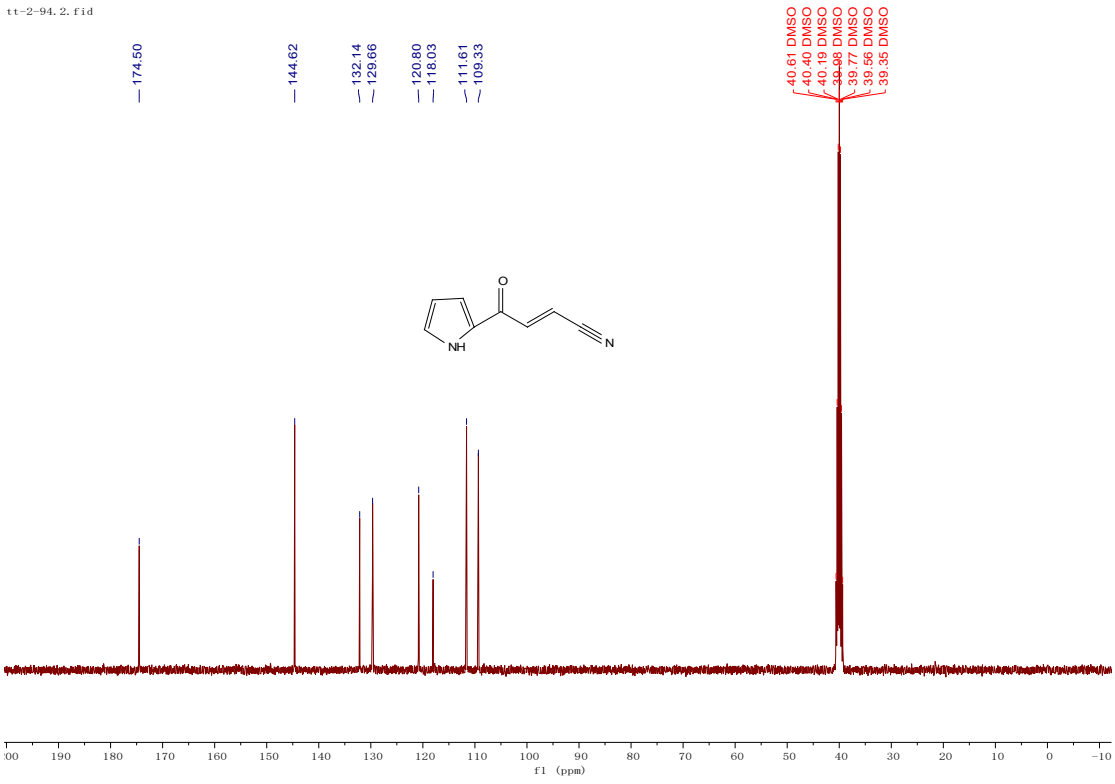
^{1}H NMR spectrum of 3t (400 MHz, DMSO-d_6)



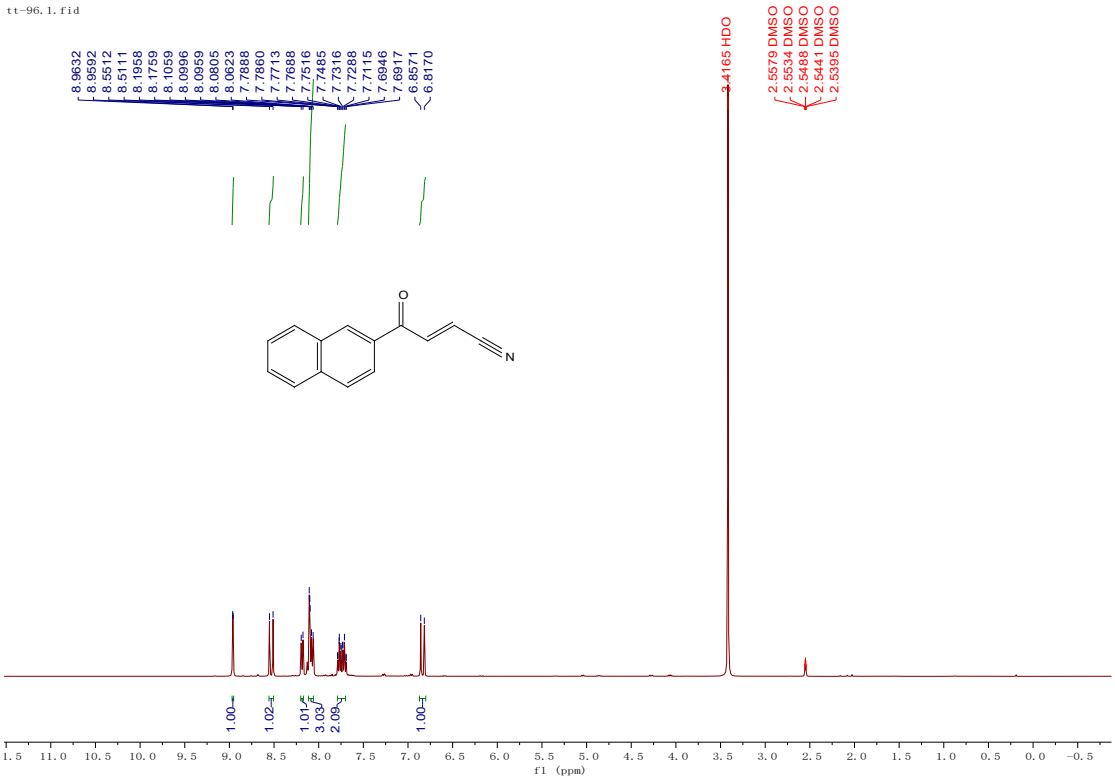
^{13}C NMR spectrum of 3t (100 MHz, DMSO-d_6)



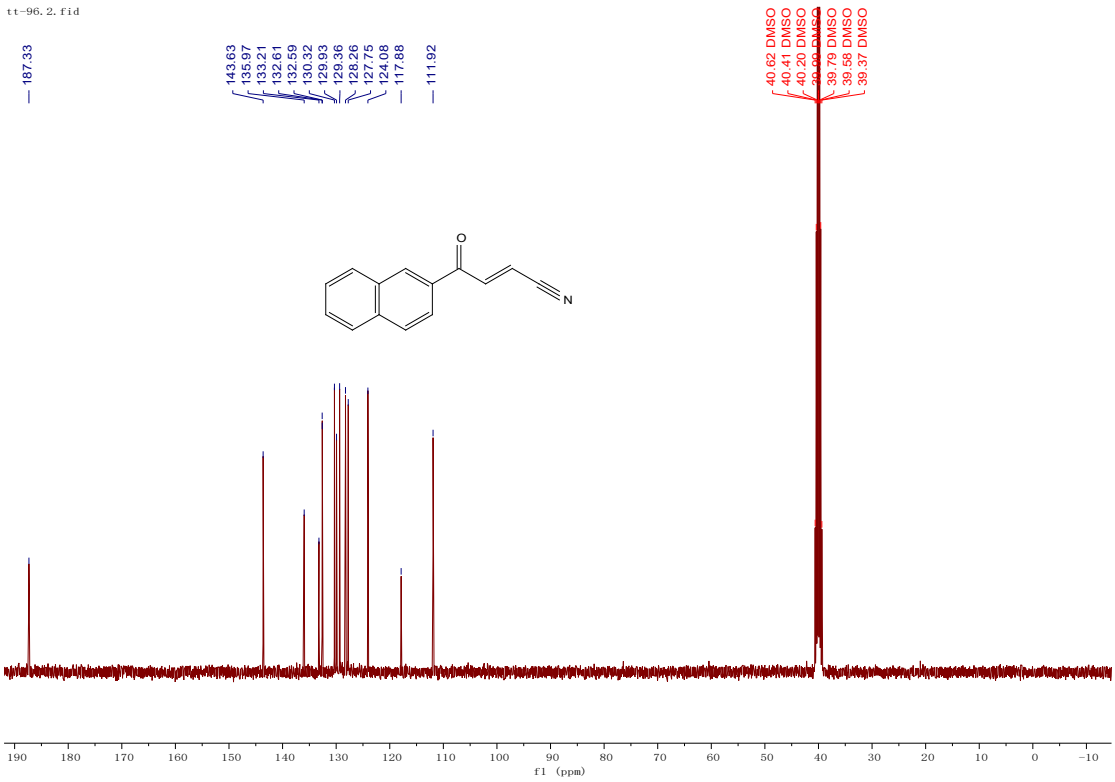
^{1}H NMR spectrum of 3u (400 MHz, DMSO-d_6)



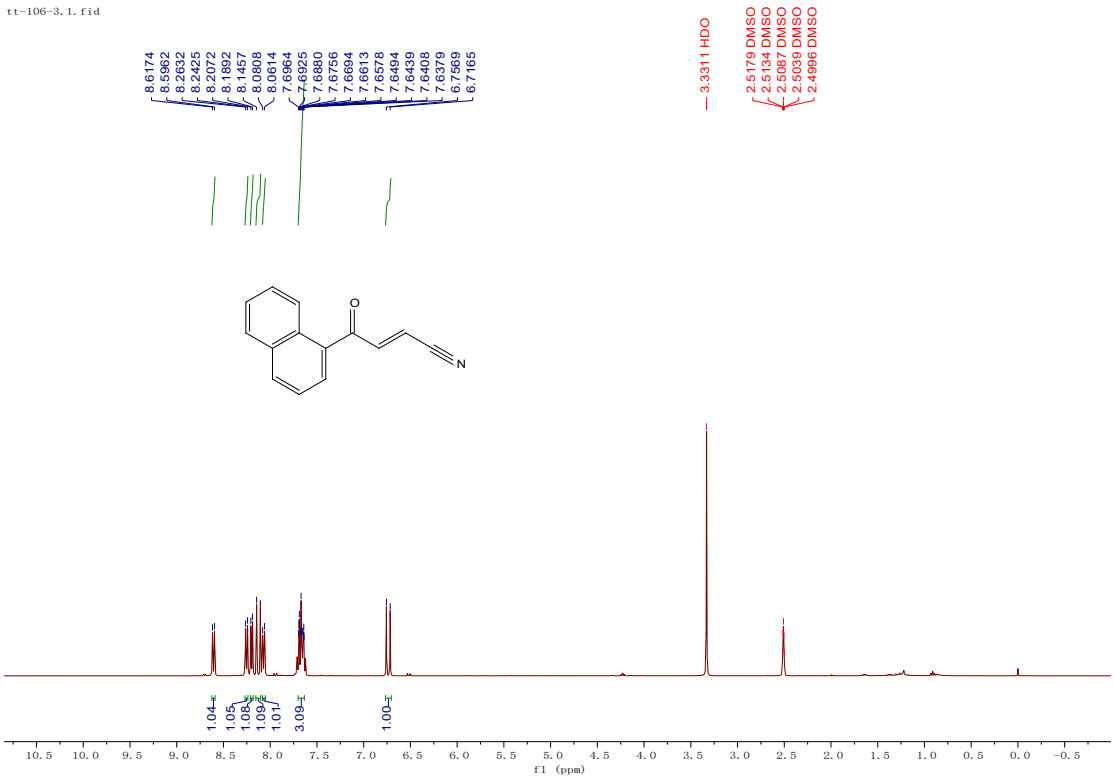
^{13}C NMR spectrum of 3u (100 MHz, DMSO-d_6)



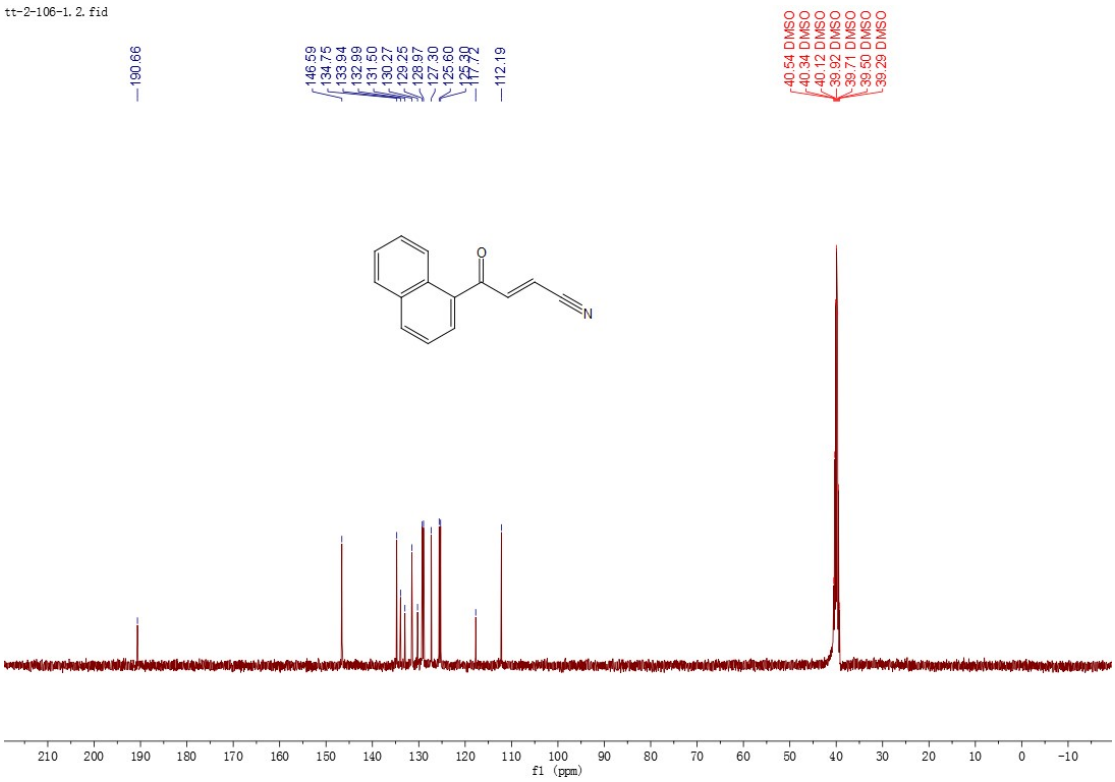
^{1}H NMR spectrum of 3v (400 MHz, DMSO-d_6)



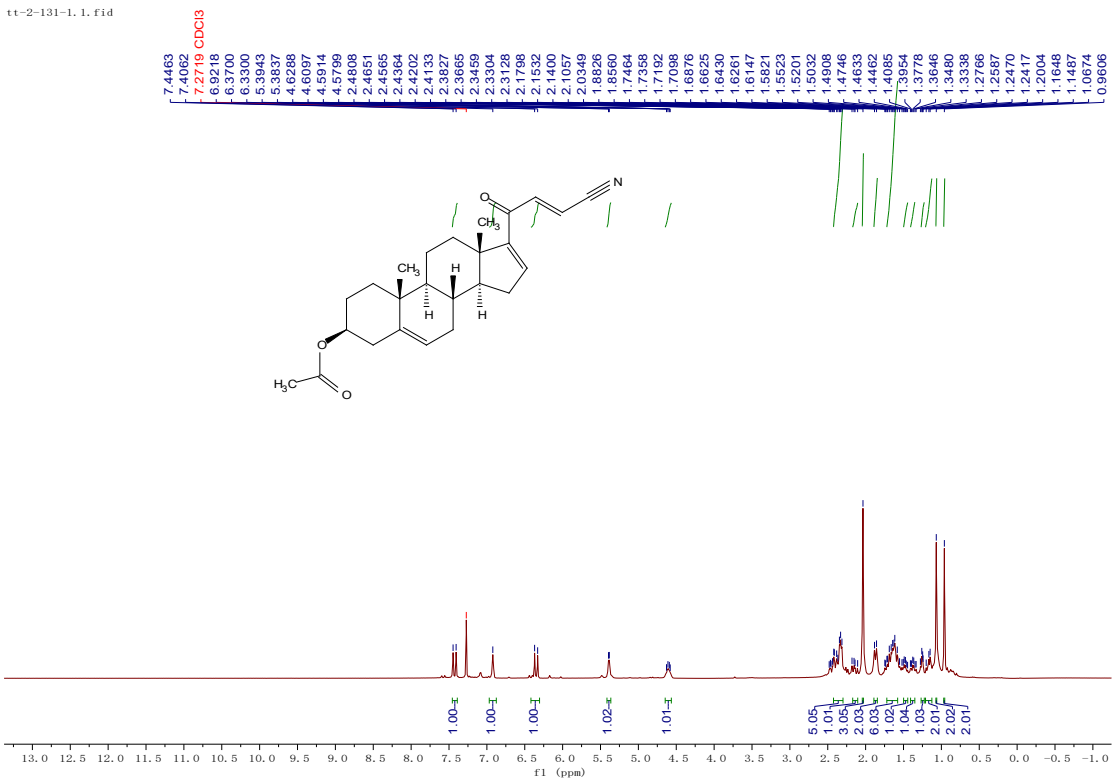
^{13}C NMR spectrum of 3v (100 MHz, DMSO-d_6)



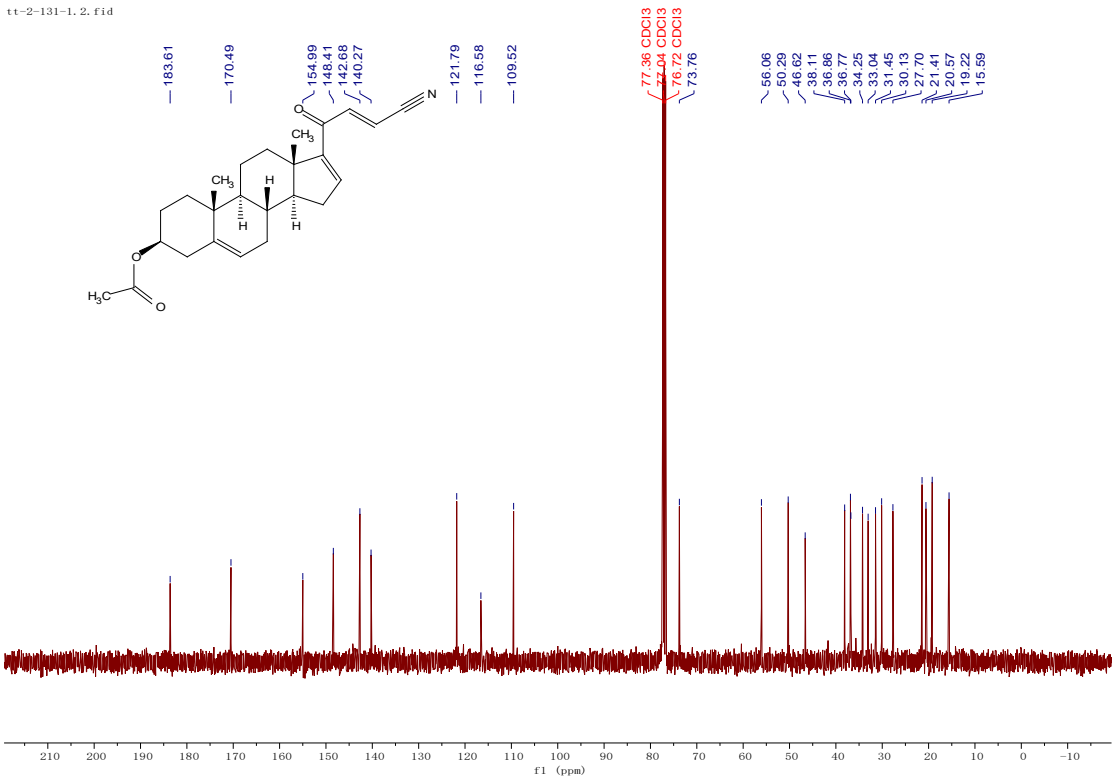
^{1}H NMR spectrum of 3w (400 MHz, DMSO-d_6)



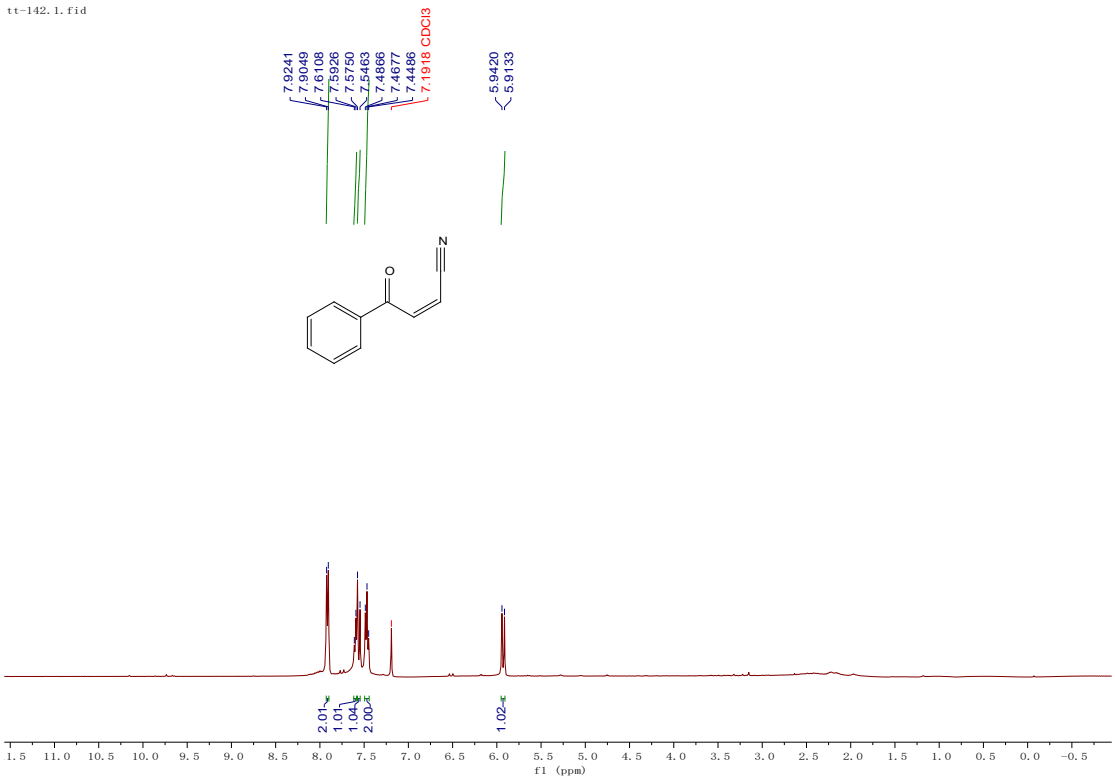
^{13}C NMR spectrum of 3w (100 MHz, DMSO-d_6)



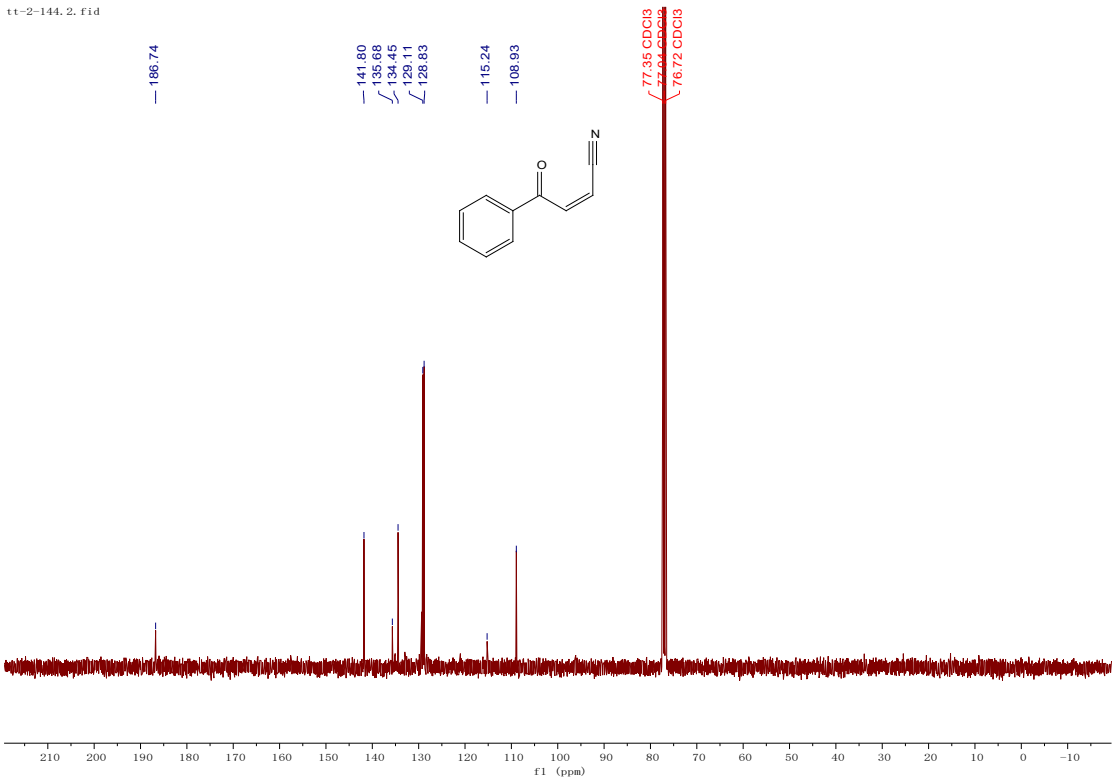
^{1}H NMR spectrum of 3x (400 MHz, $CDCl_3$)



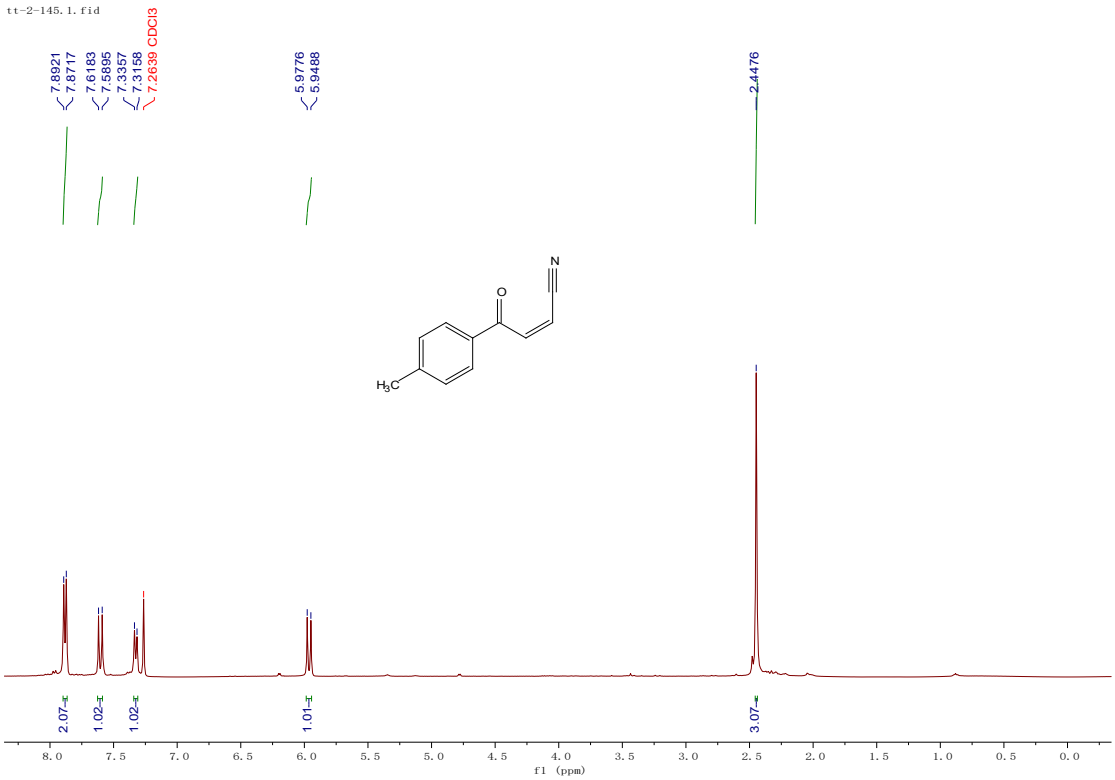
^{13}C NMR spectrum of 3x (100 MHz, $CDCl_3$)



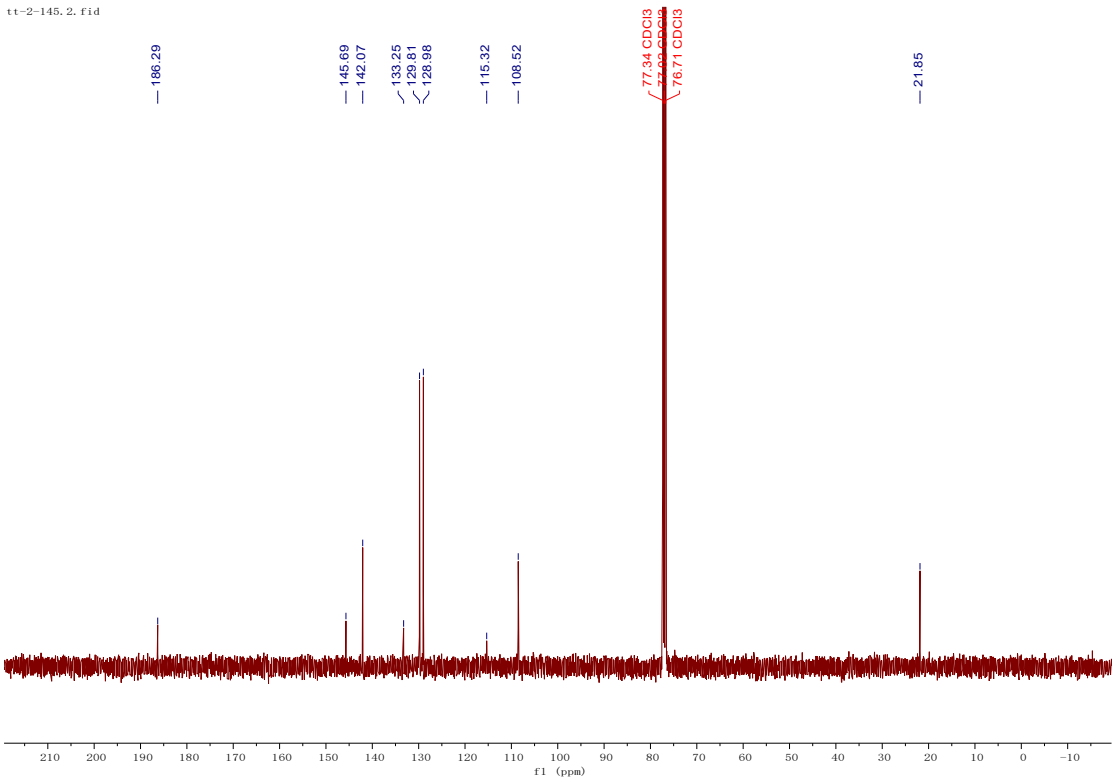
^{1}H NMR spectrum of 4a (400 MHz, $CDCl_3$)



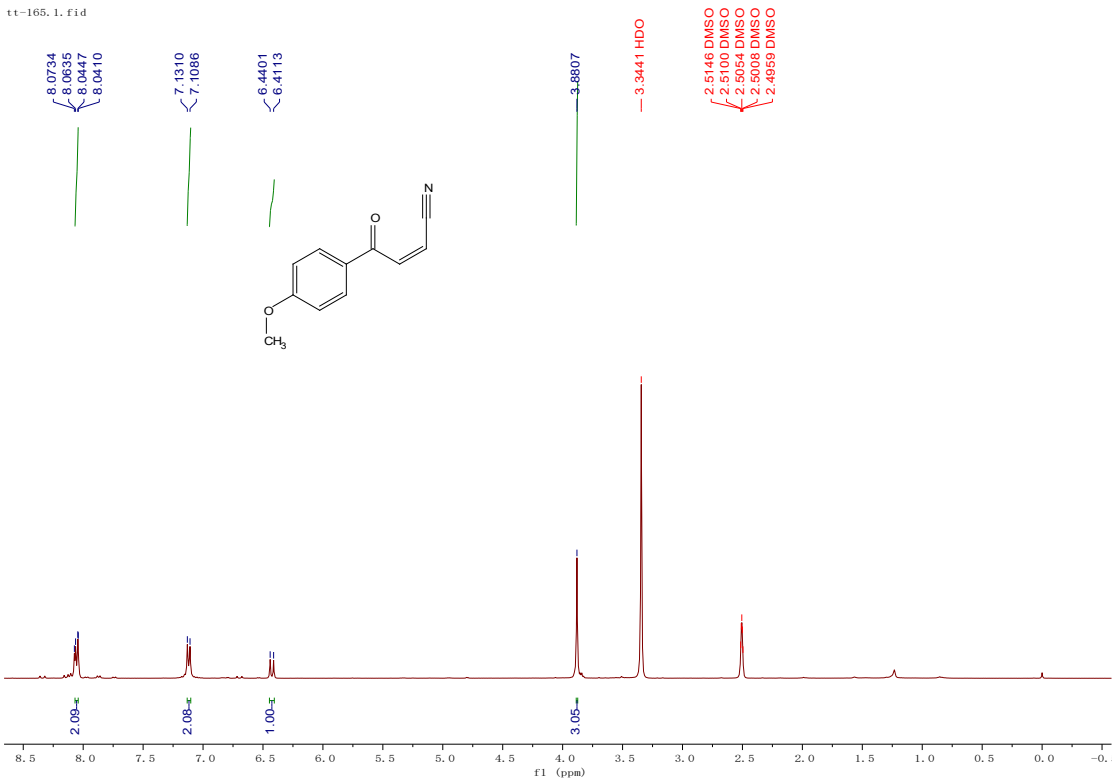
^{13}C NMR spectrum of 4a (100 MHz, $CDCl_3$)



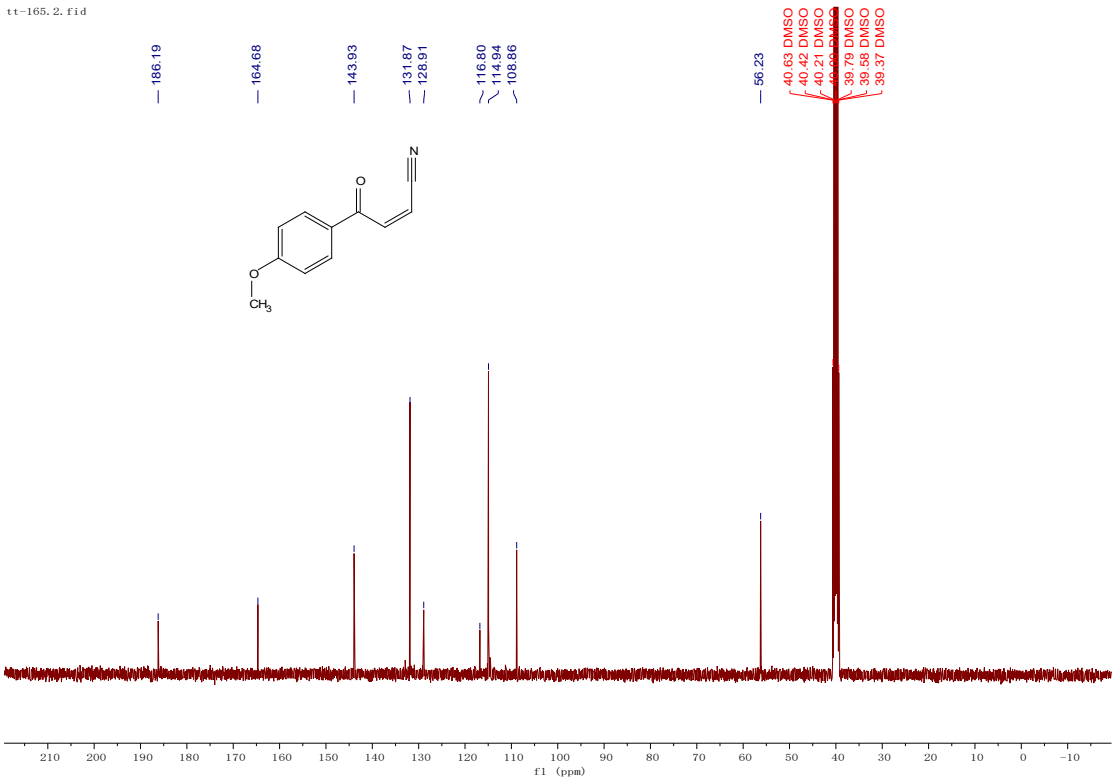
^{1}H NMR spectrum of 4b (400 MHz, $CDCl_3$)



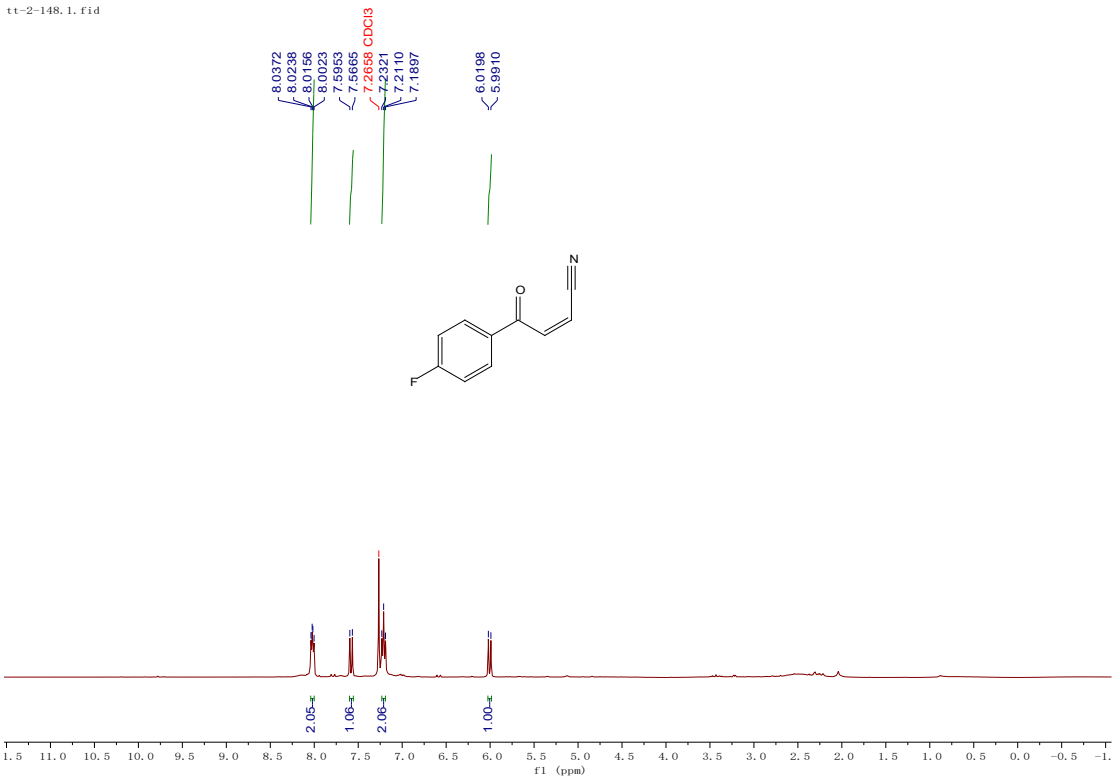
^{13}C NMR spectrum of 4b (100 MHz, $CDCl_3$)



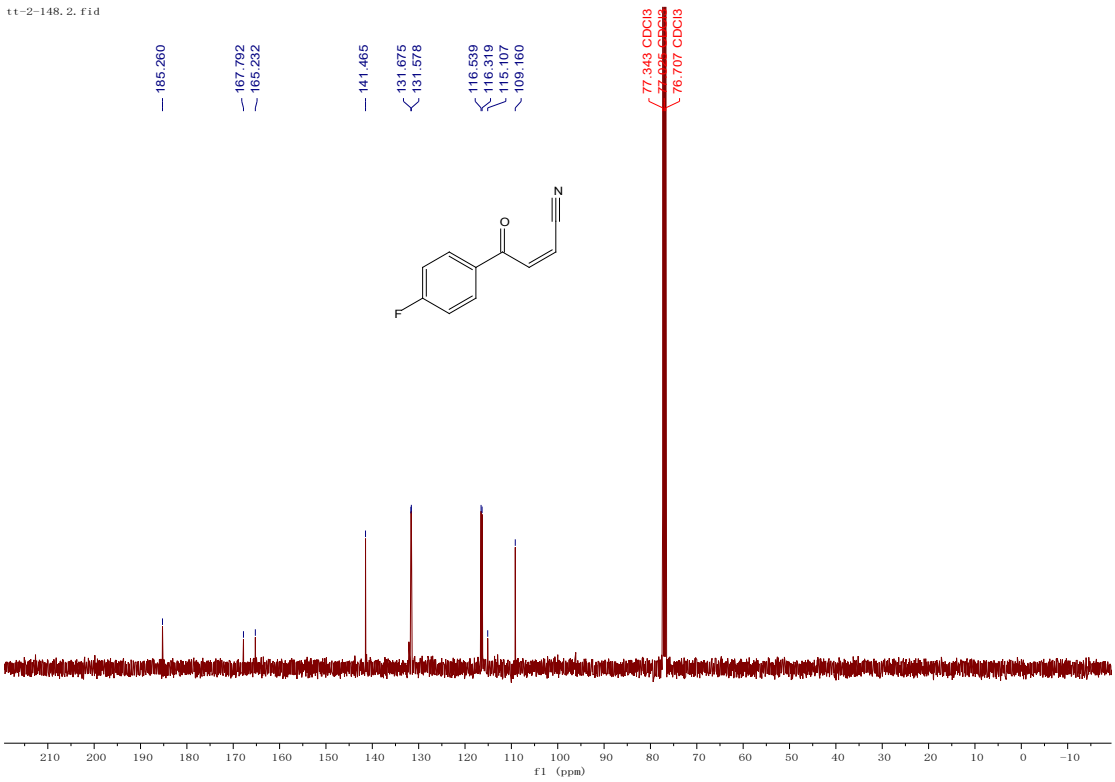
^{1}H NMR spectrum of 4c (400 MHz, DMSO-d_6)



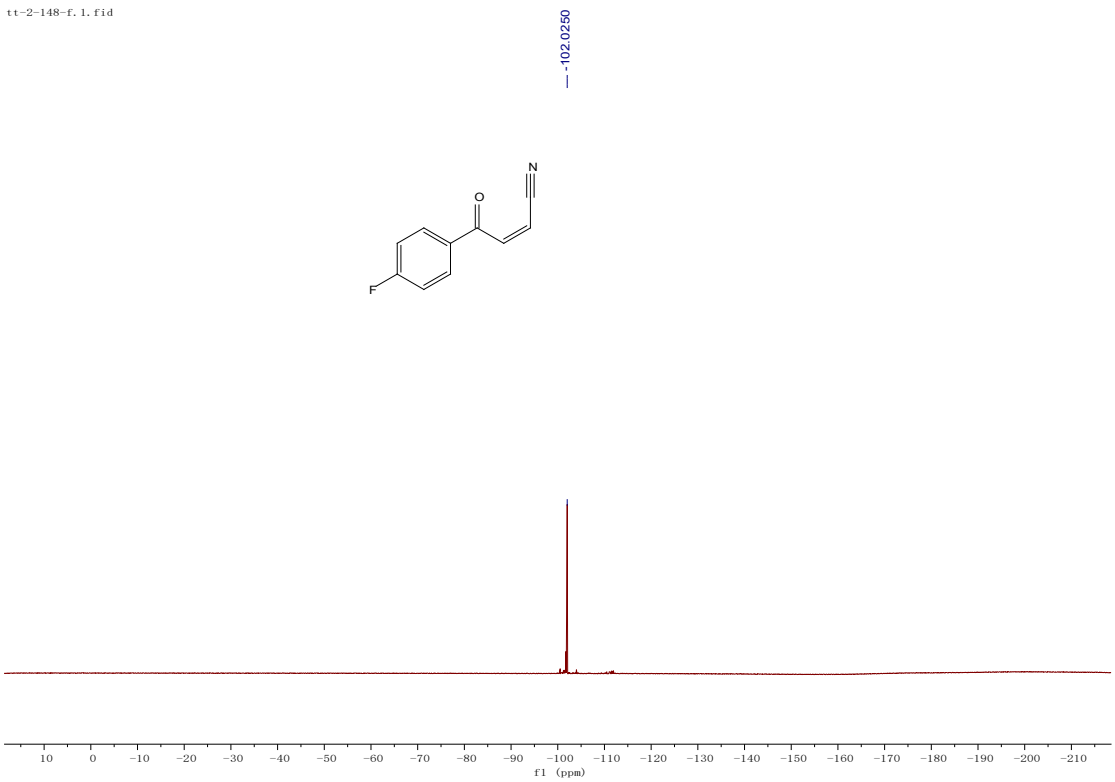
^{13}C NMR spectrum of 4c (100 MHz, DMSO-d_6)



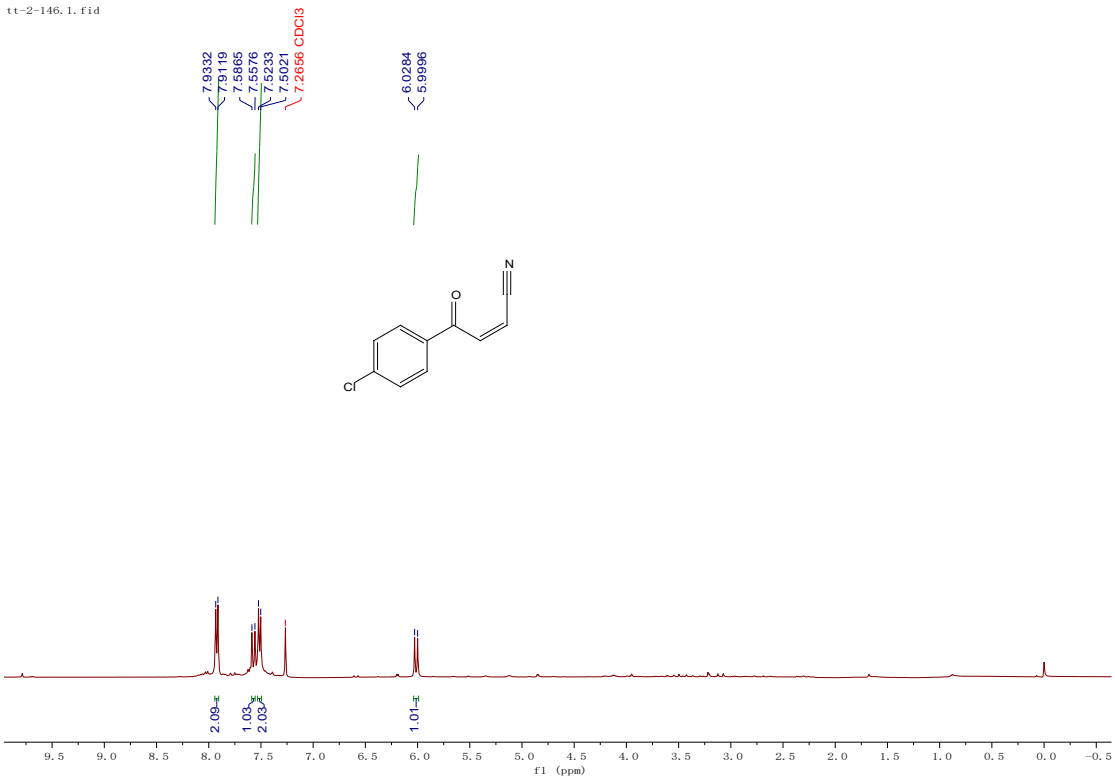
^{1}H NMR spectrum of 4d (400 MHz, $CDCl_3$)



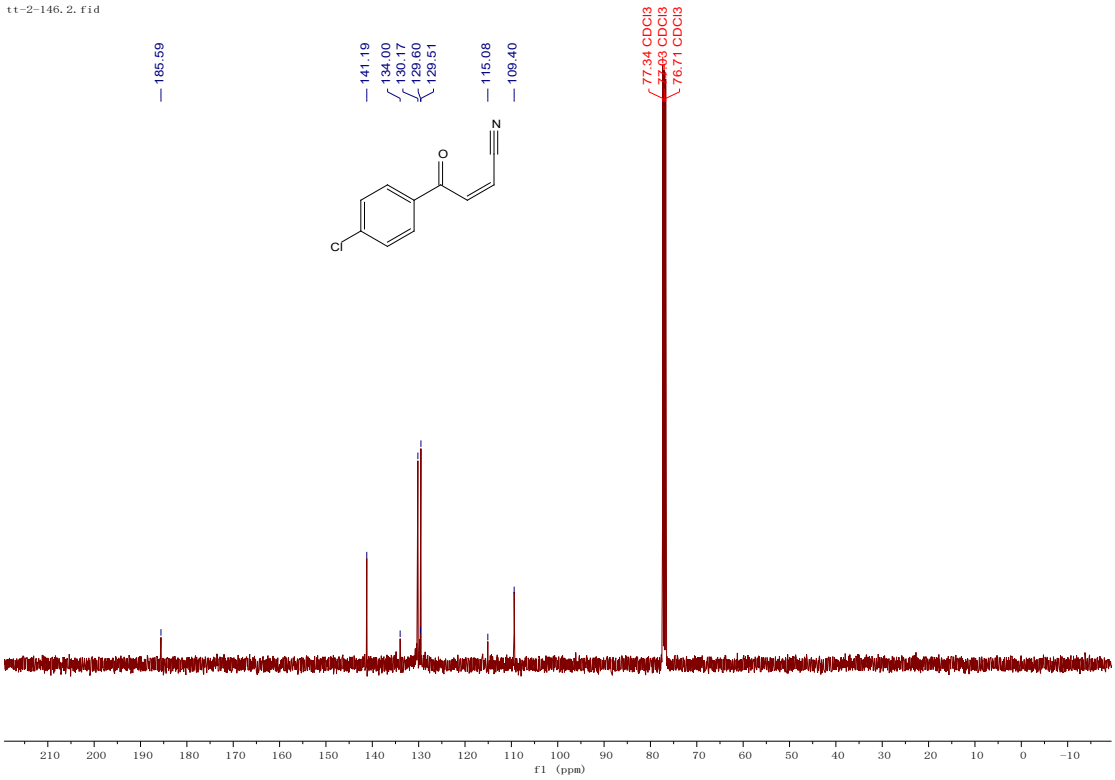
^{13}C NMR spectrum of 4d (100 MHz, $CDCl_3$)



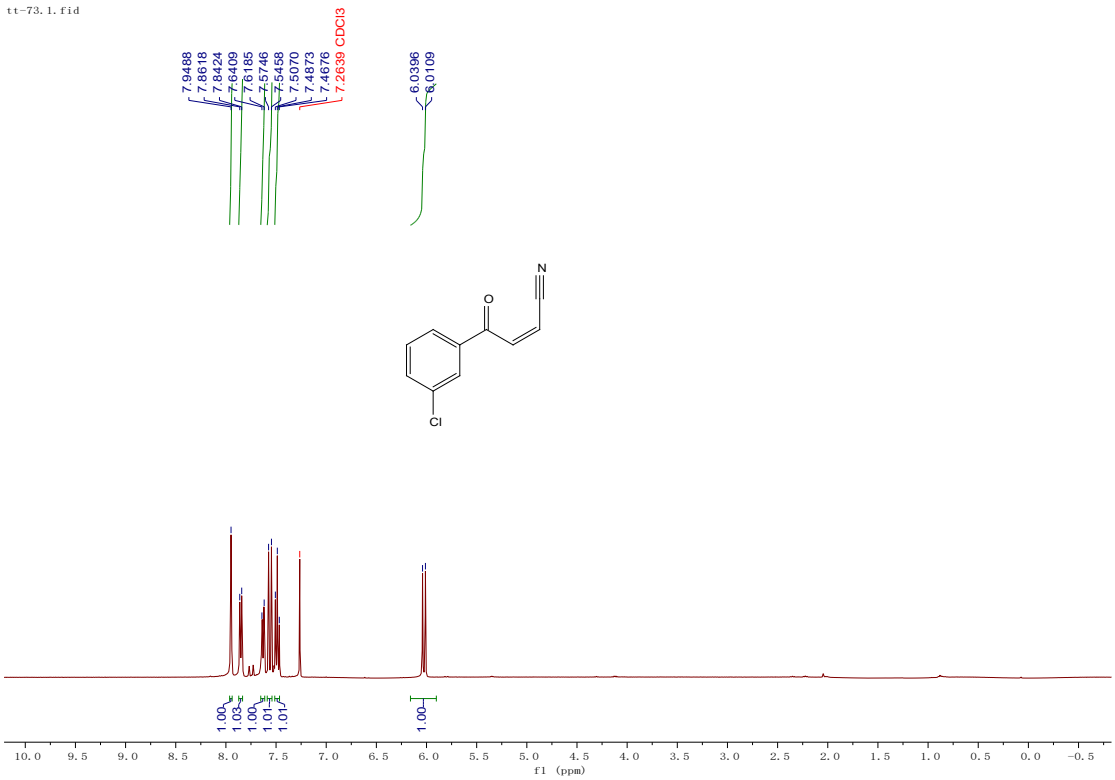
^{19}F NMR spectrum of 4d (376 MHz, $CDCl_3$)



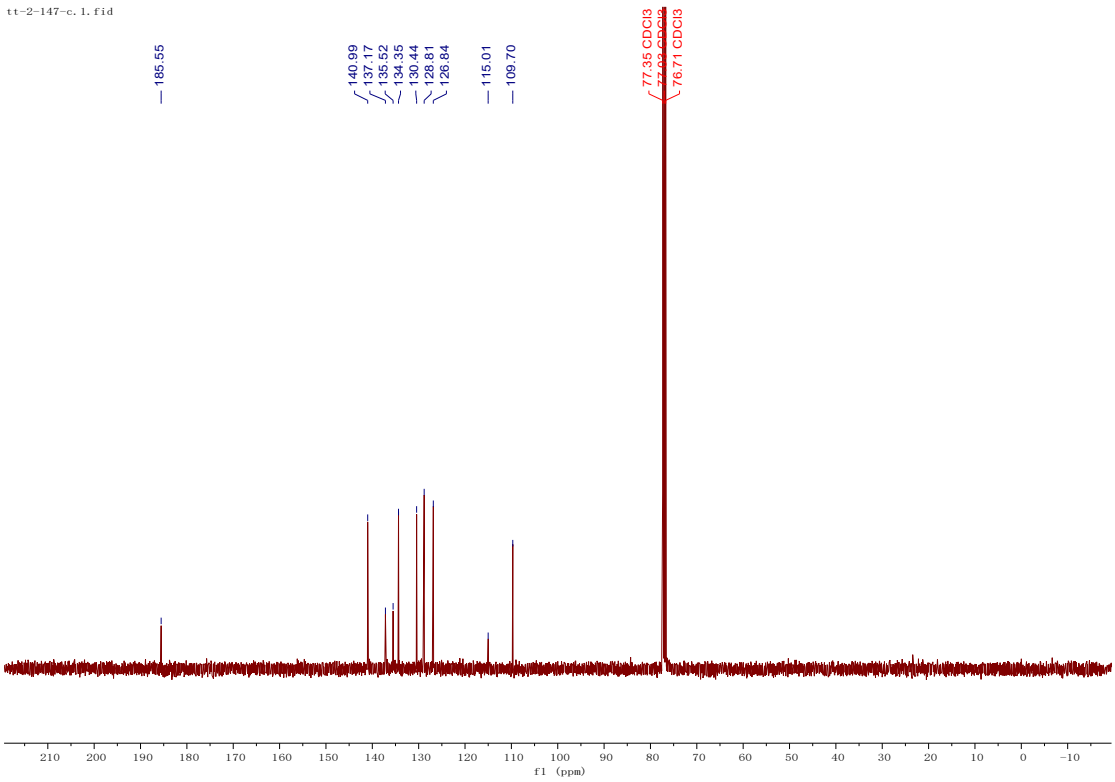
^{1}H NMR spectrum of 4e (400 MHz, $CDCl_3$)



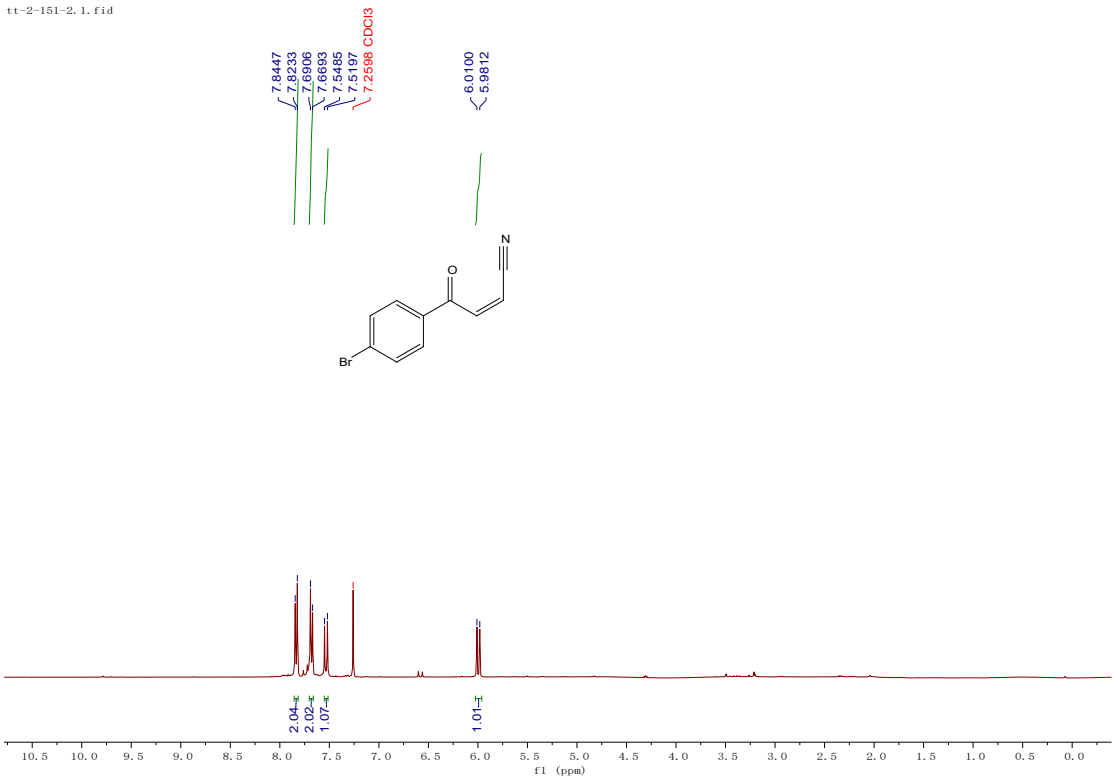
^{13}C NMR spectrum of 4e (100 MHz, $CDCl_3$)



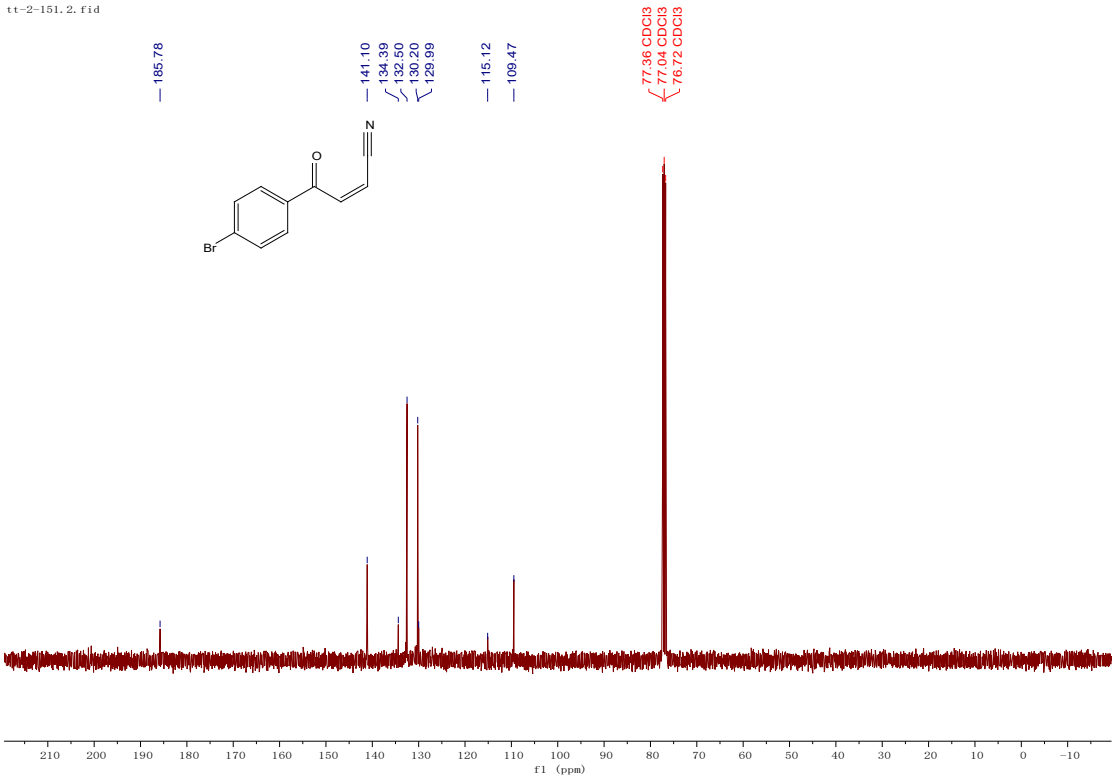
^{1}H NMR spectrum of 4f (400 MHz, $CDCl_3$)



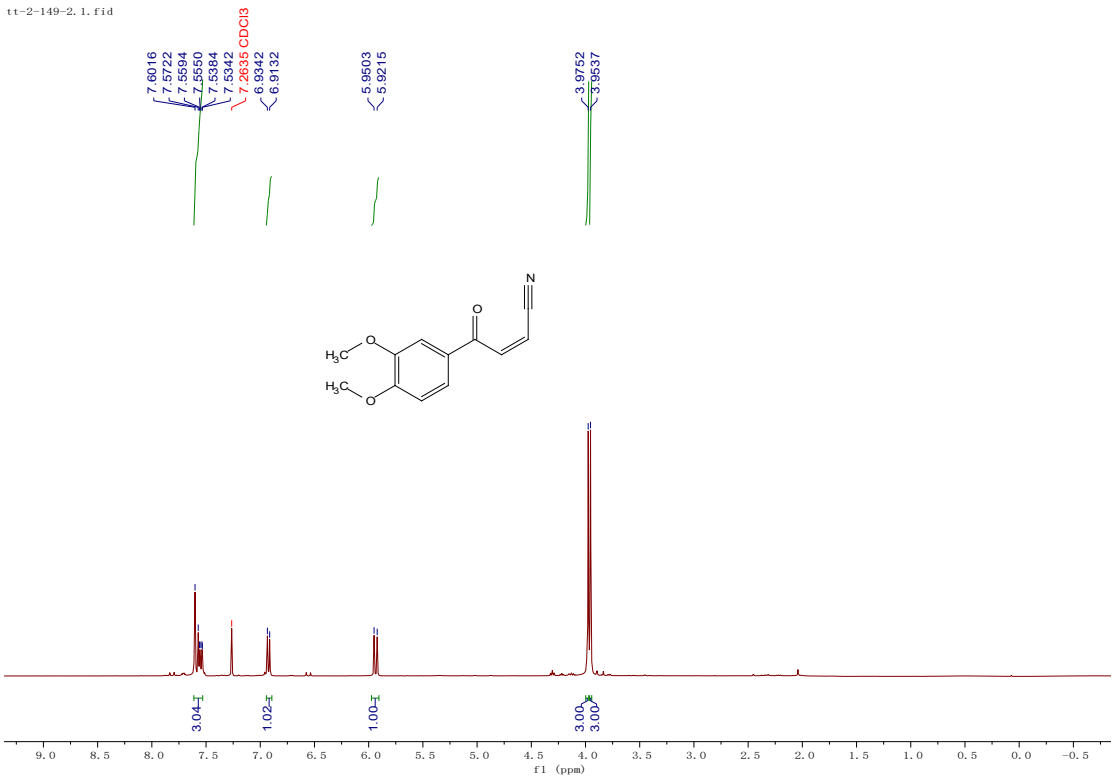
^{13}C NMR spectrum of 4f (100 MHz, $CDCl_3$)



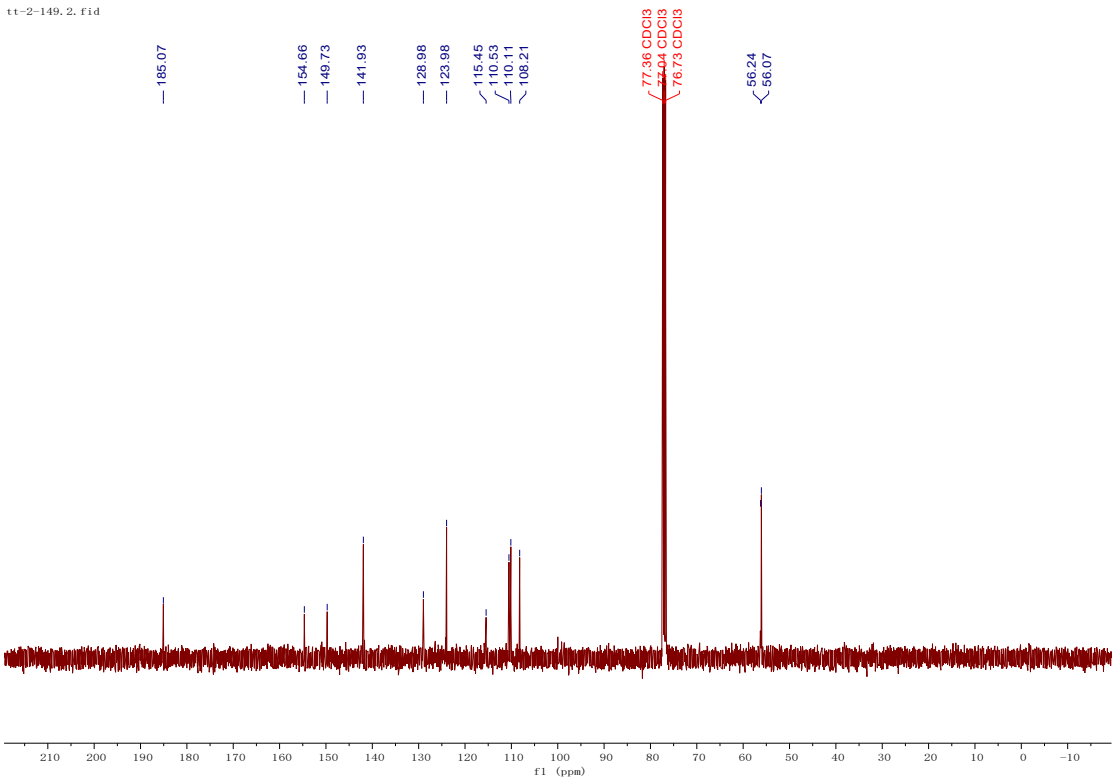
^{1}H NMR spectrum of 4g (400 MHz, $CDCl_3$)



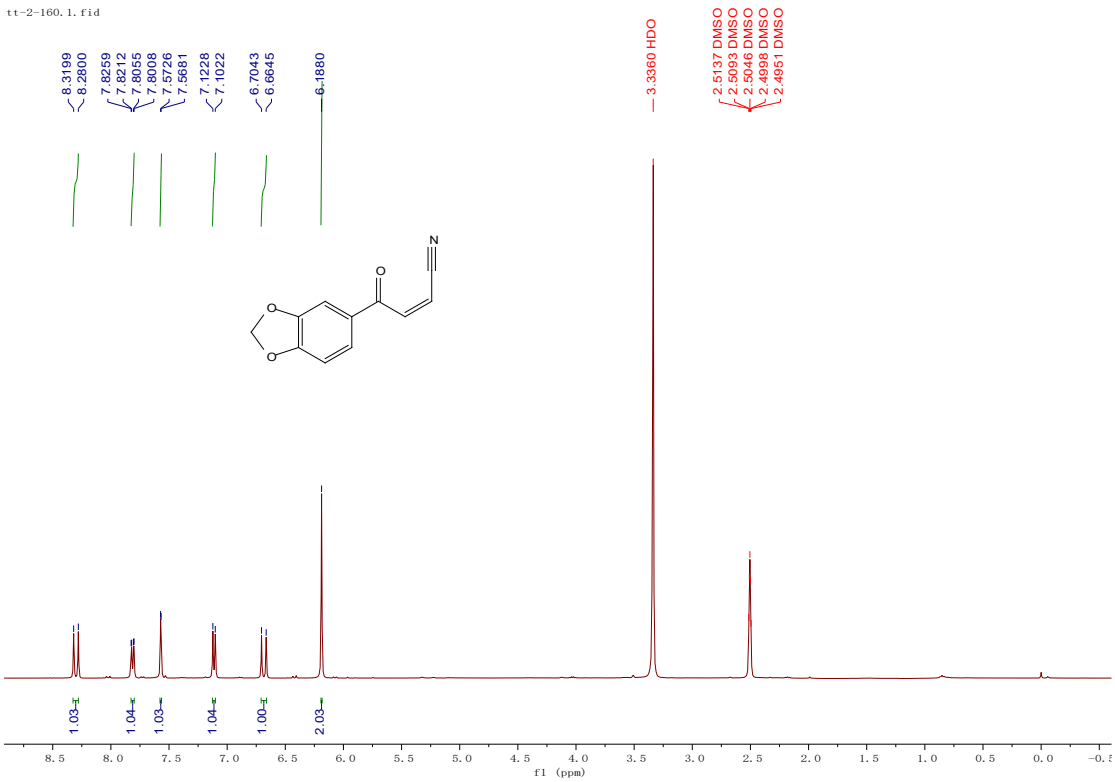
^{13}C NMR spectrum of 4g (100 MHz, $CDCl_3$)



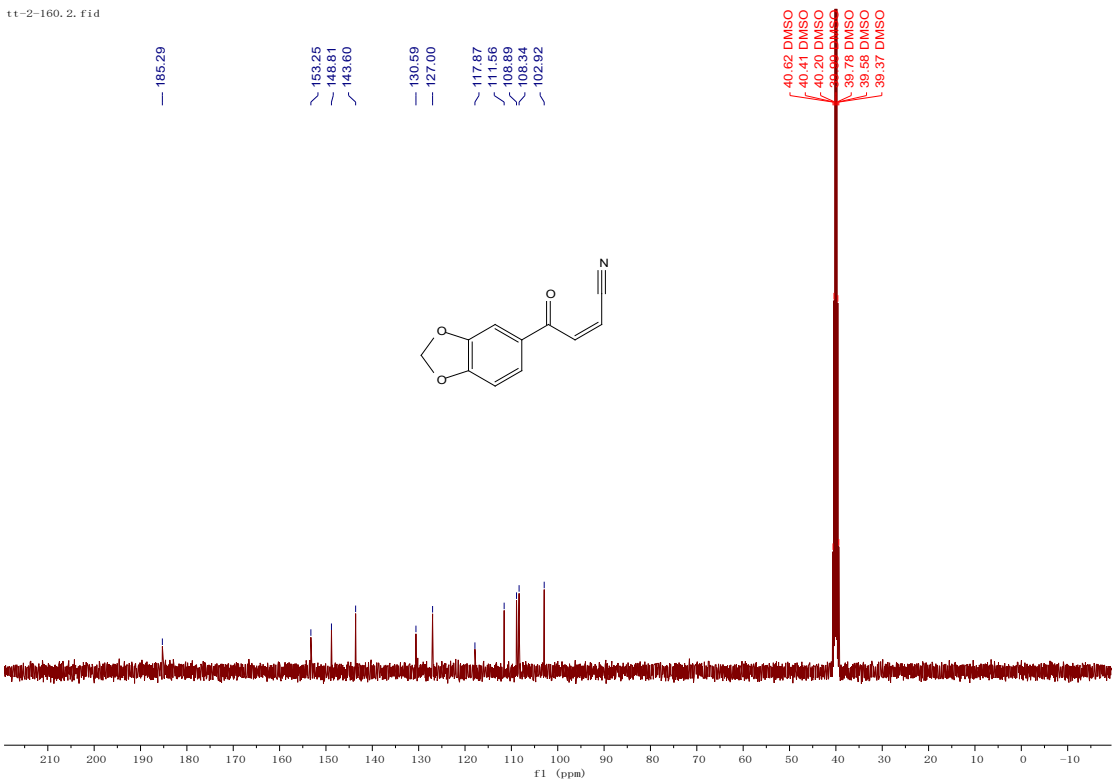
^{1}H NMR spectrum of 4h (400 MHz, $CDCl_3$)



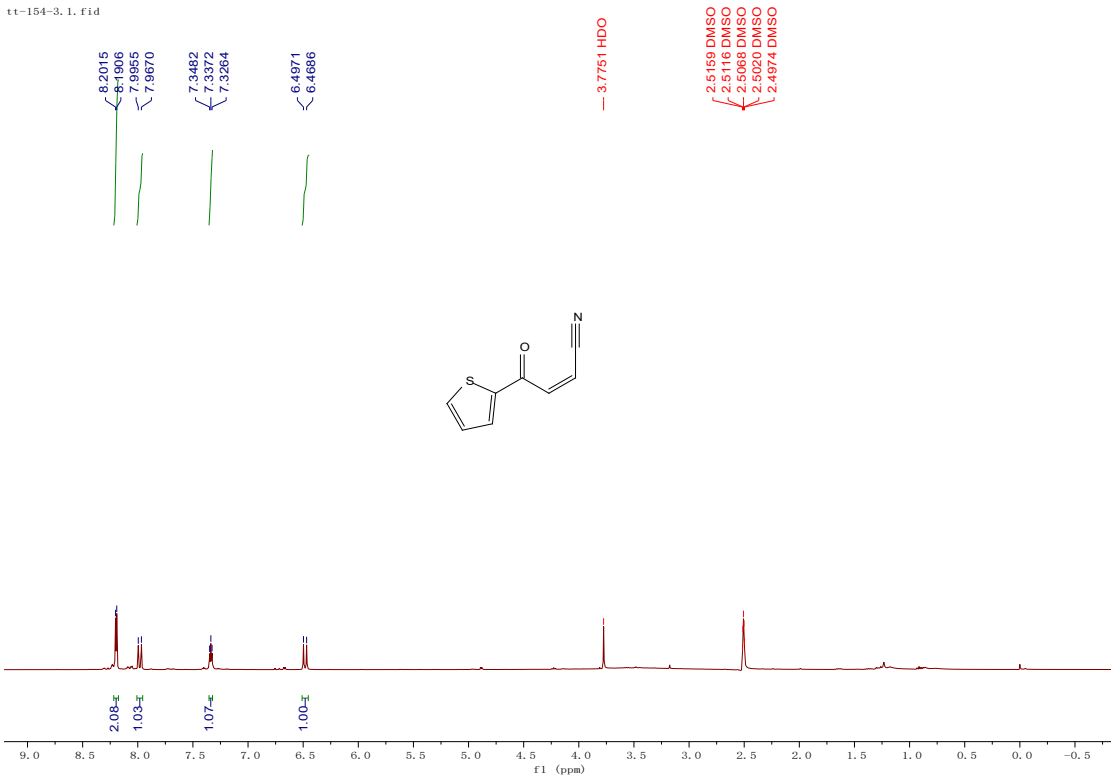
^{13}C NMR spectrum of 4h (100 MHz, $CDCl_3$)



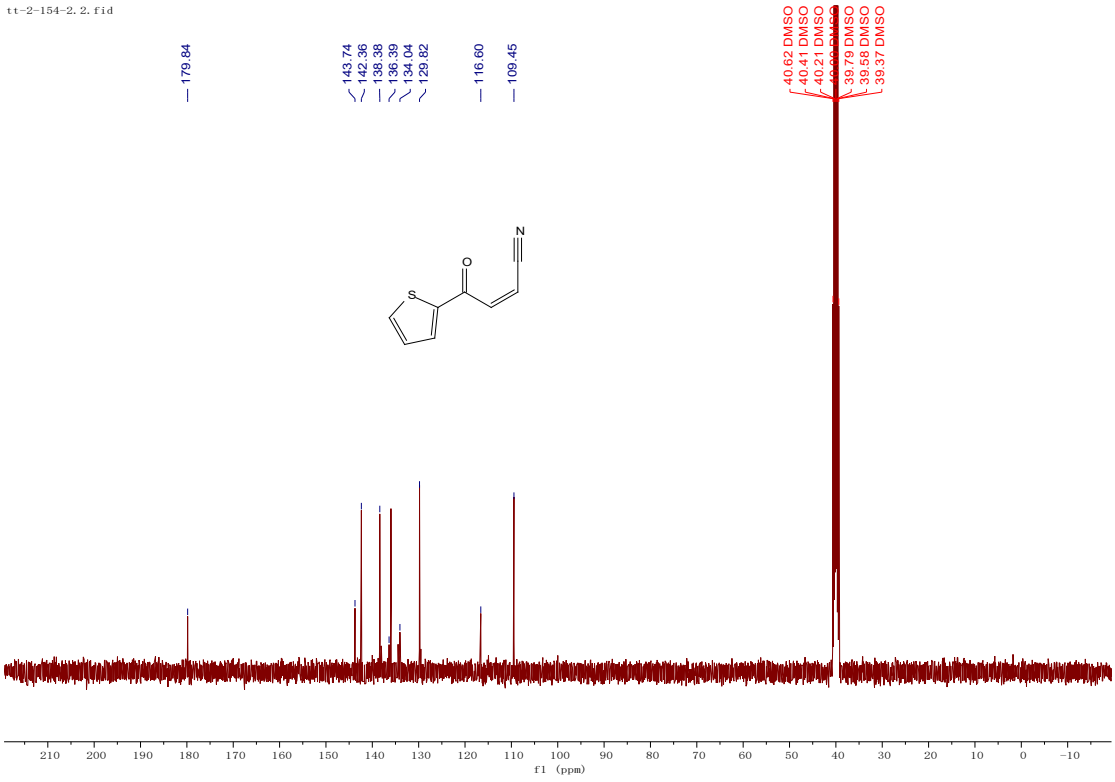
^{1}H NMR spectrum of 4i (400 MHz, DMSO-d_6)



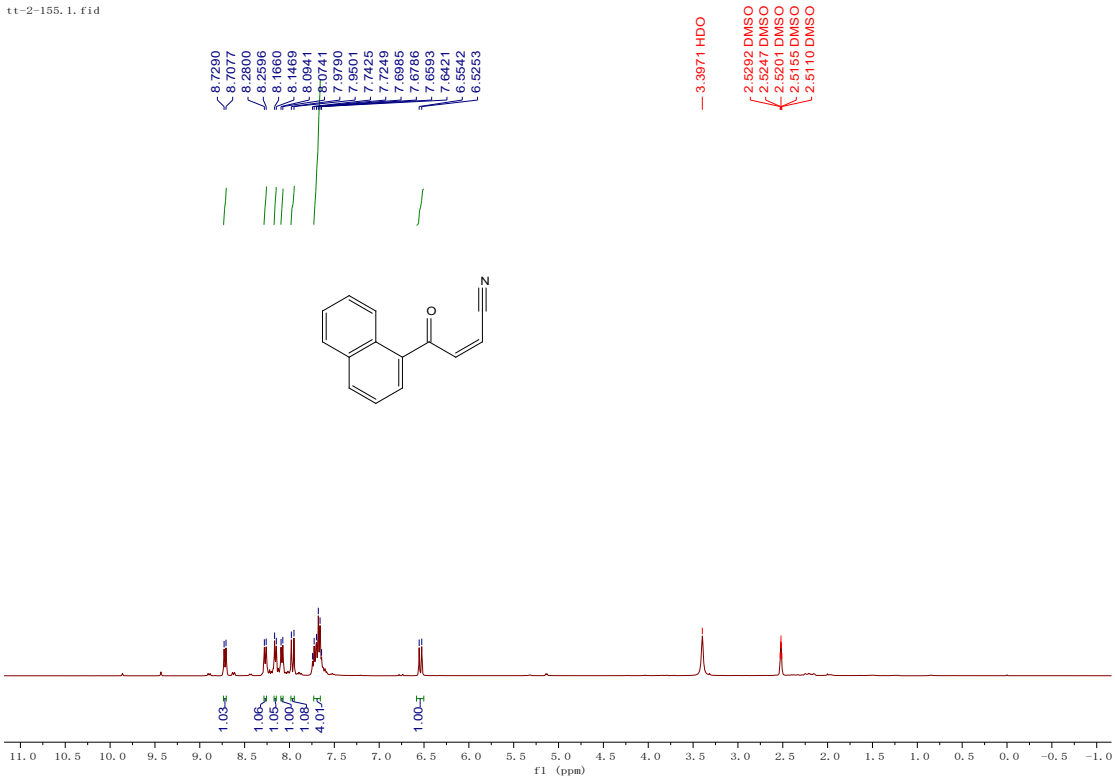
^{13}C NMR spectrum of 4i (100 MHz, DMSO-d_6)



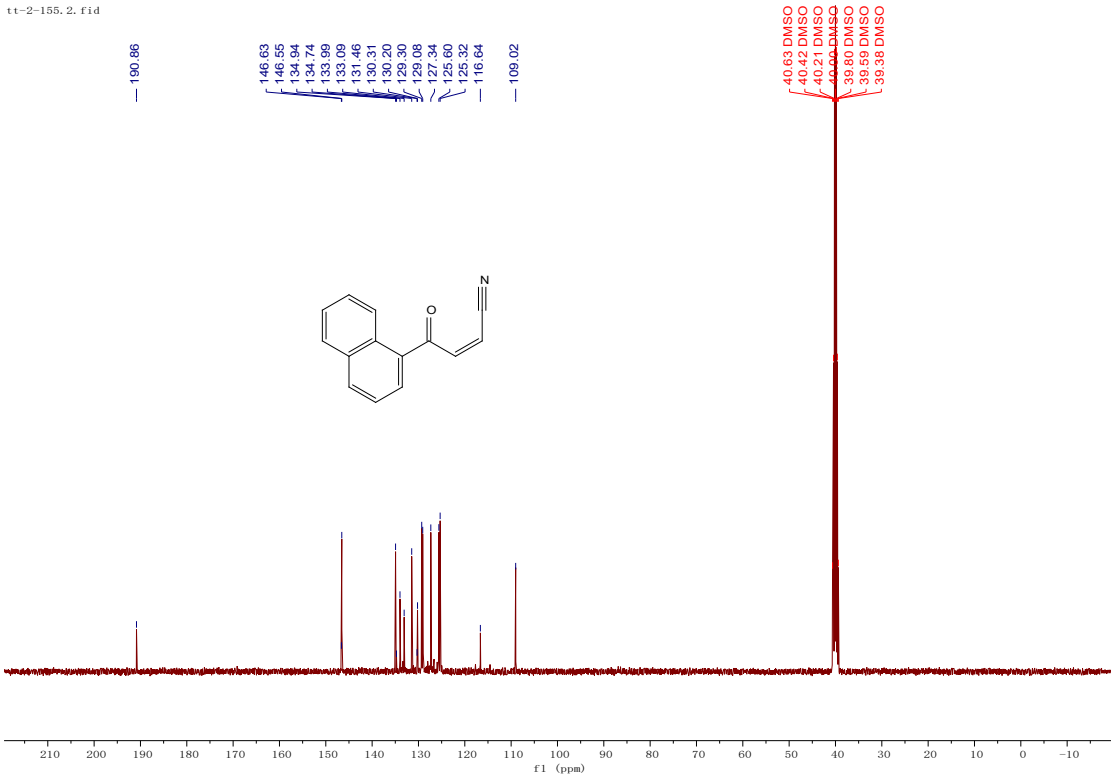
^{1}H NMR spectrum of 4j (400 MHz, DMSO-d_6)



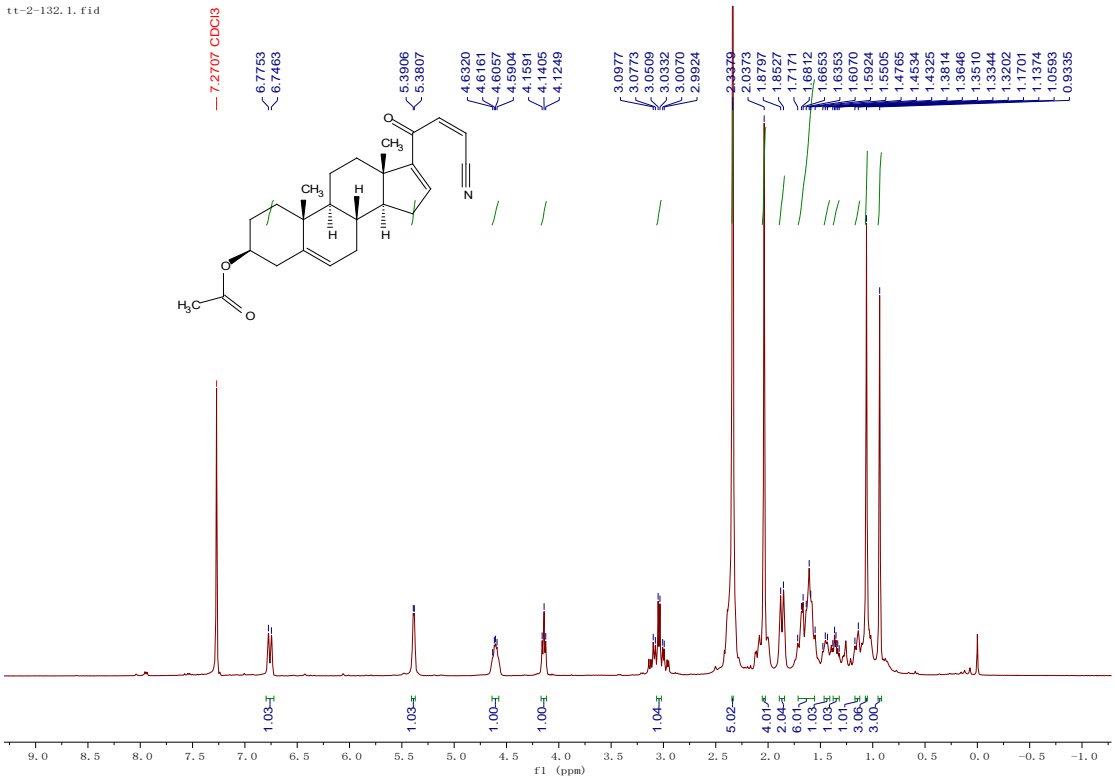
^{13}C NMR spectrum of 4j (100 MHz, DMSO-d_6)



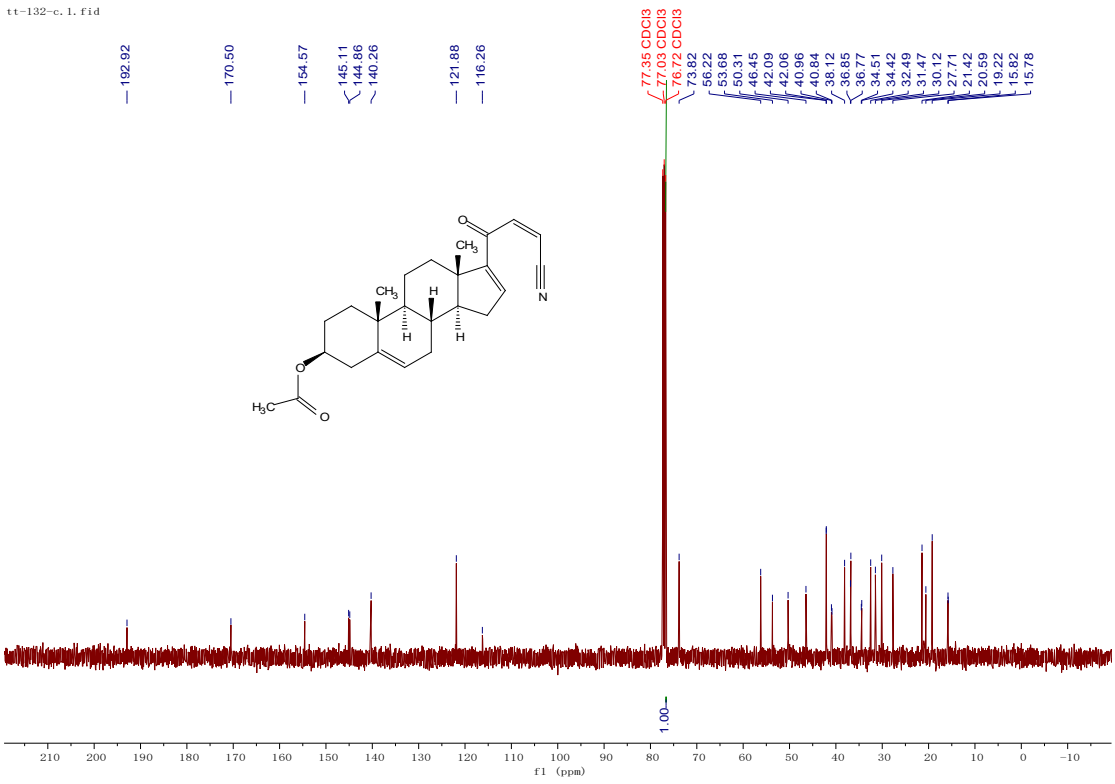
^{1}H NMR spectrum of 4k (400 MHz, DMSO-d_6)



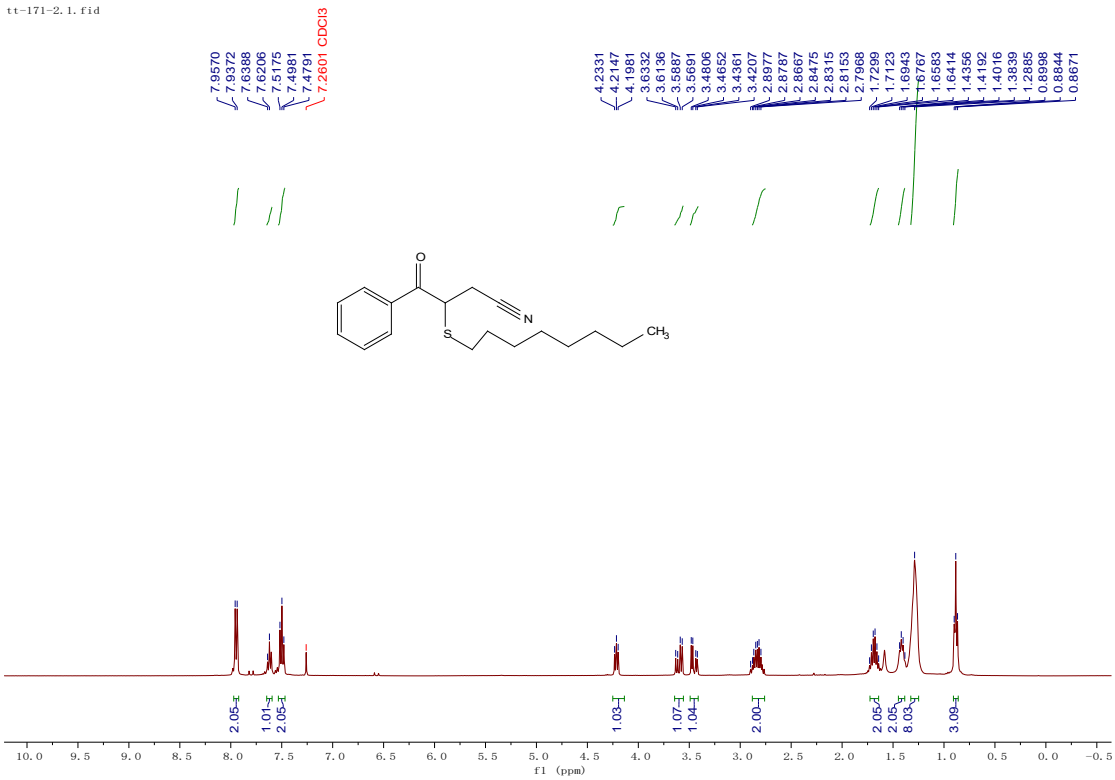
^{13}C NMR spectrum of 4k (100 MHz, DMSO-d_6)



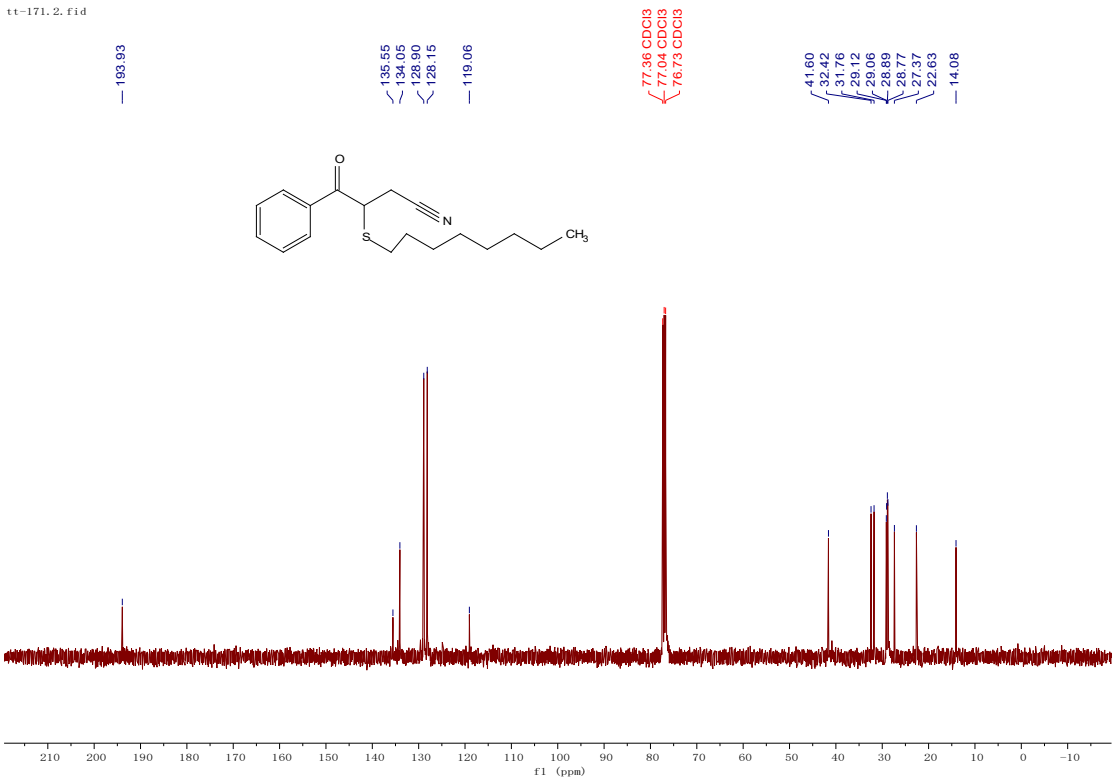
^{1}H NMR spectrum of 4l (400 MHz, $CDCl_3$)



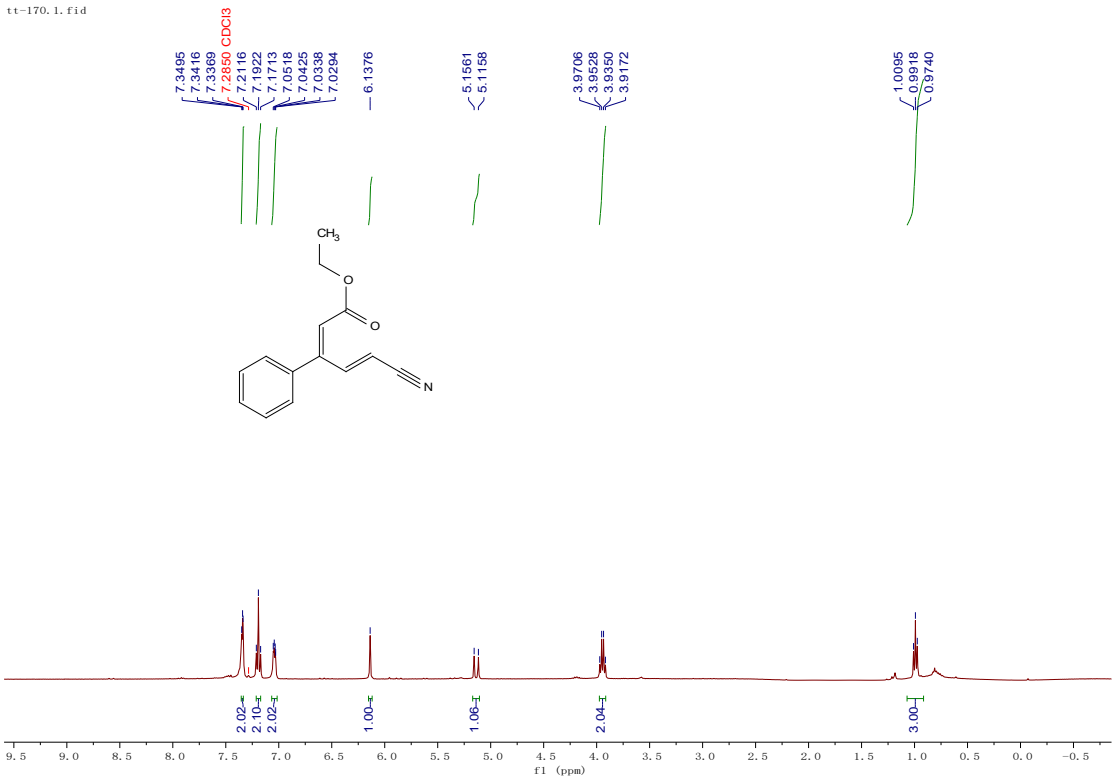
^{13}C NMR spectrum of 4l (100 MHz, $CDCl_3$)



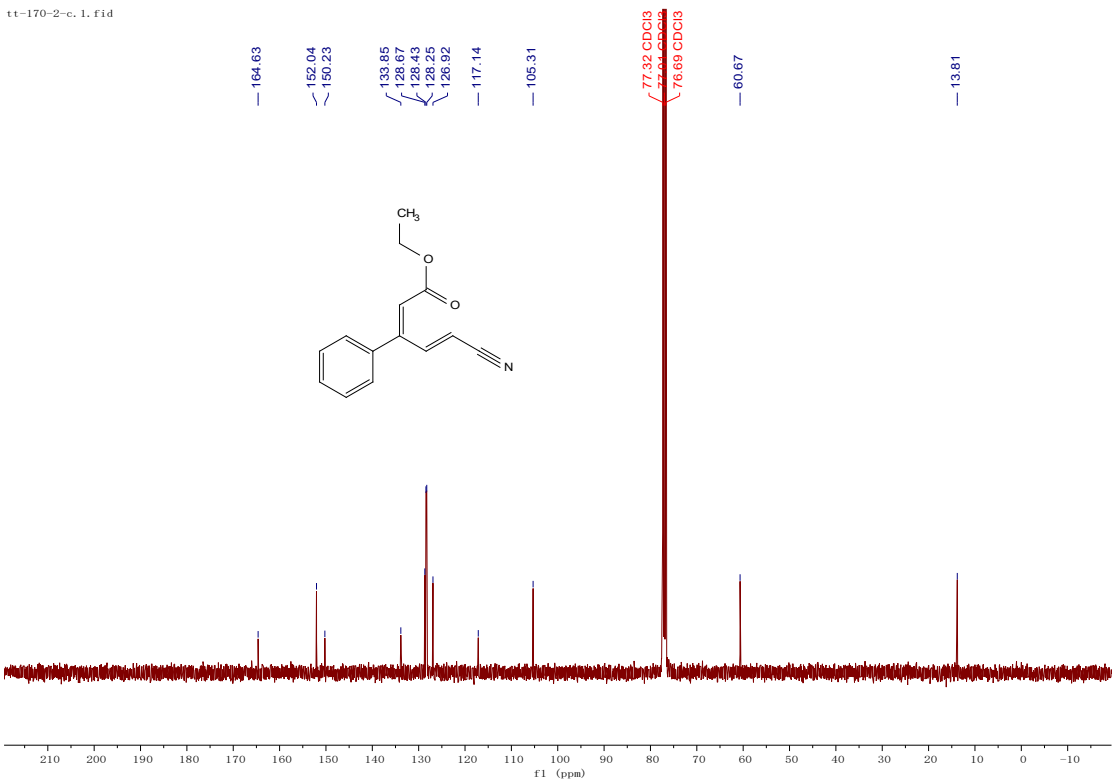
^{1}H NMR spectrum of 5 (400 MHz, $CDCl_3$)



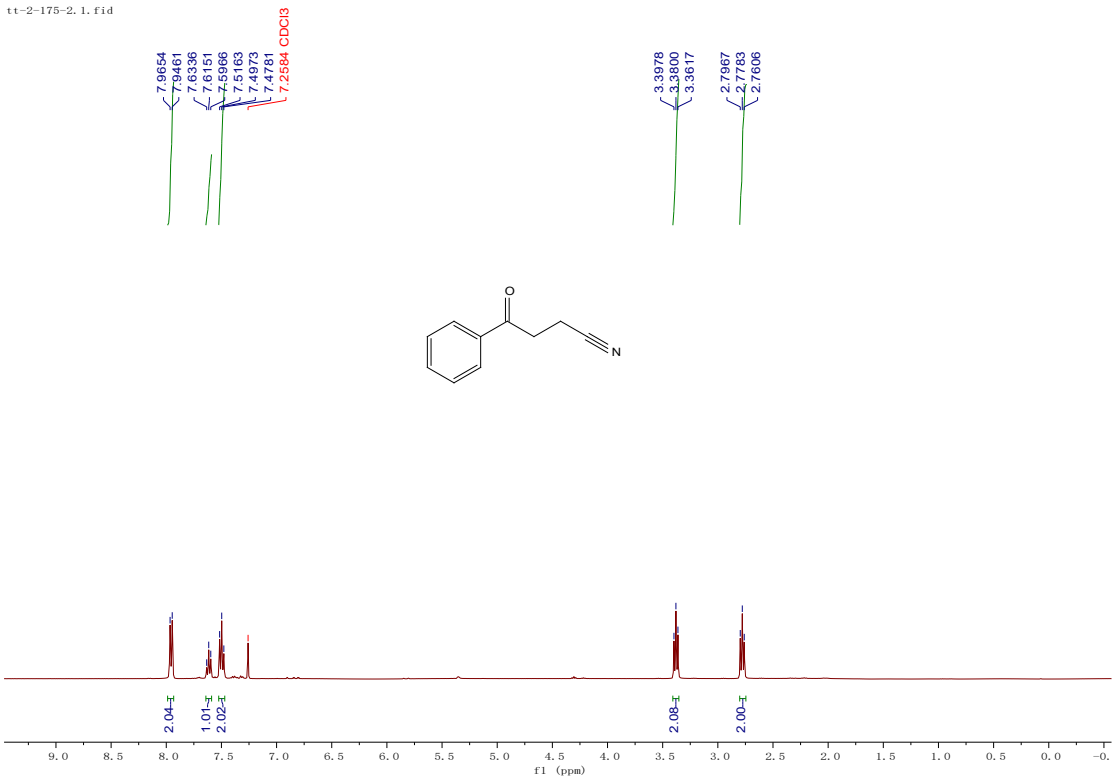
^{13}C NMR spectrum of 5 (100 MHz, $CDCl_3$)



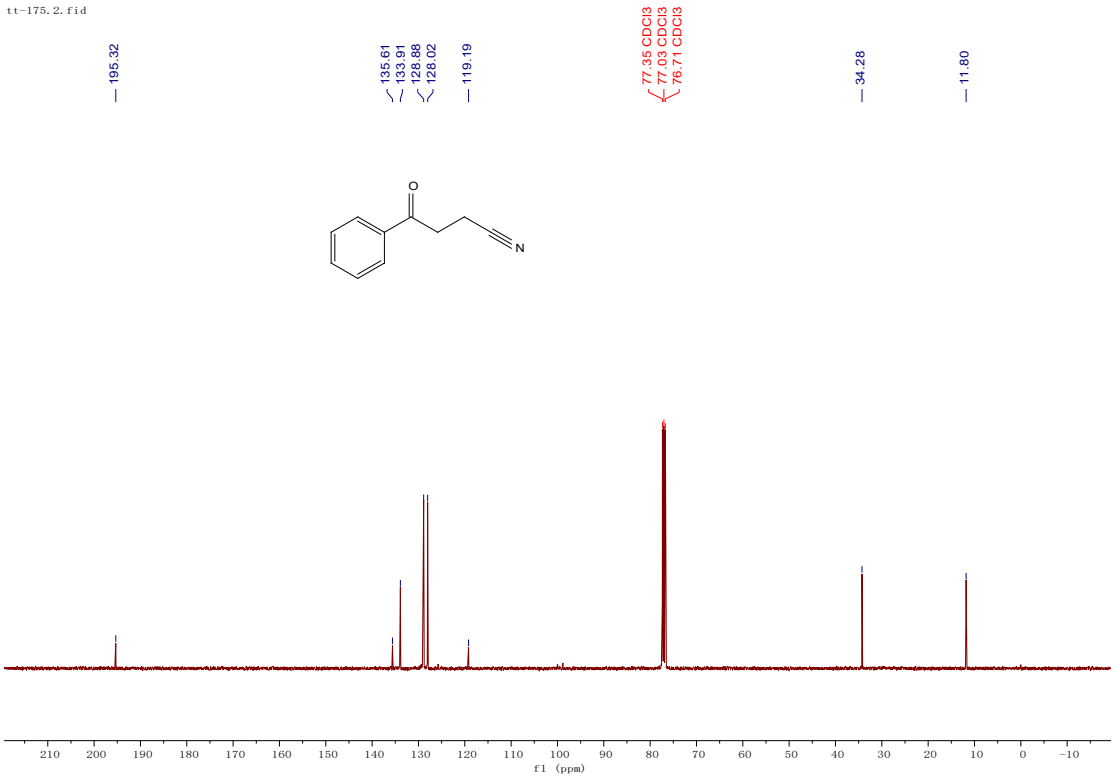
^{1}H NMR spectrum of 6 (400 MHz, $CDCl_3$)



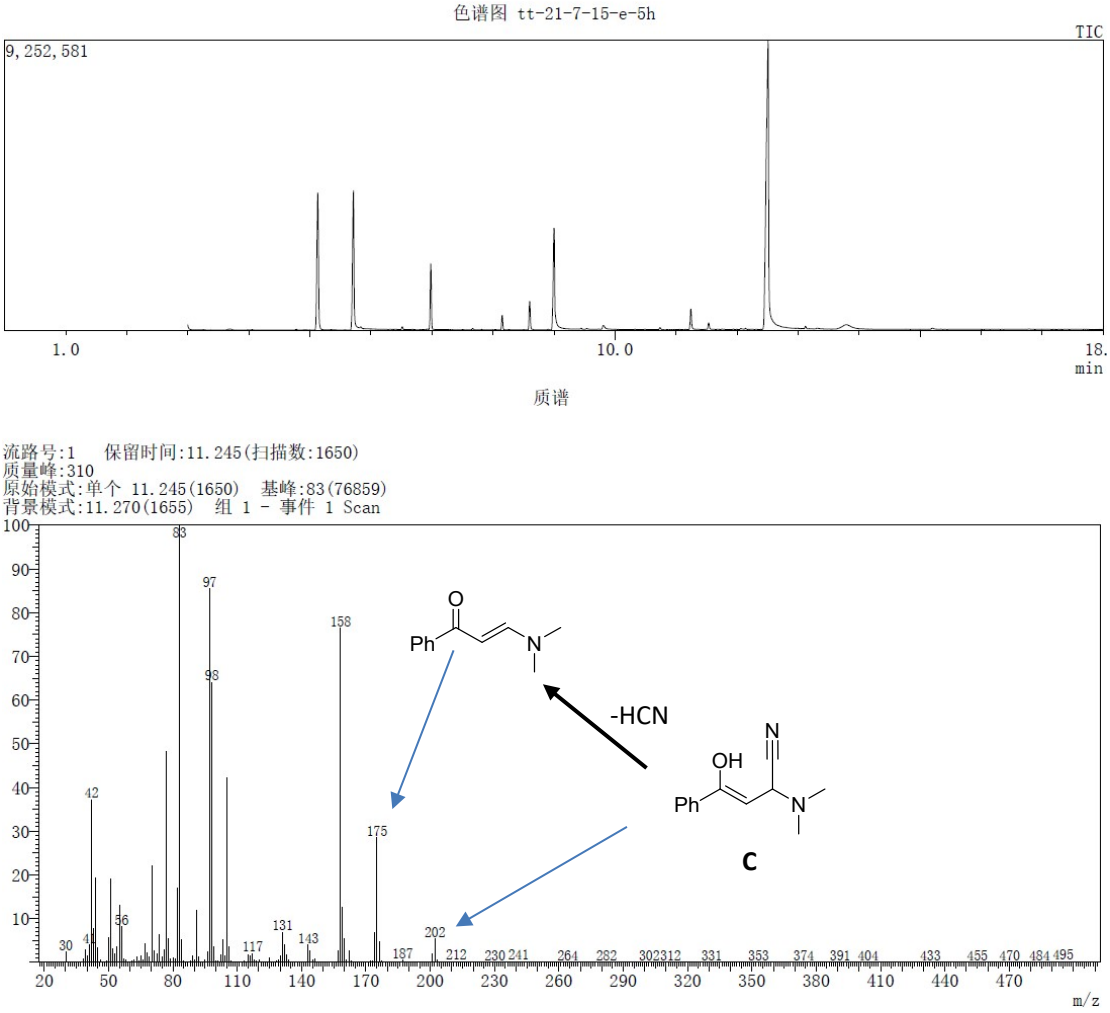
^{13}C NMR spectrum of 6 (100 MHz, $CDCl_3$)



^{1}H NMR spectrum of 7 (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of 7 (100 MHz, $CDCl_3$)



GC-MS detection on the proposed intermediate **C**