Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Organocatalytic asymmetric synthesis of tetrahydrocarbazoles *via* inverse-electron-demand Diels-Alder reaction of 2,3-indole-dienes with enals

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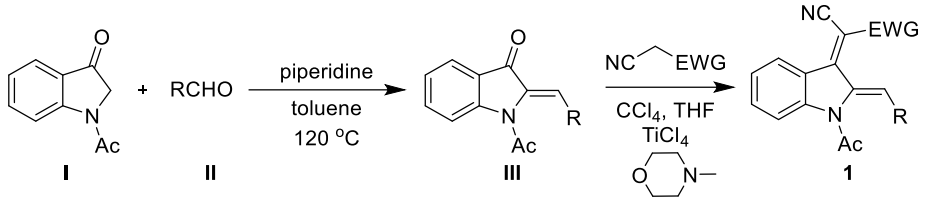
1. General information

^{1}H NMR spectra were recorded on a Bruker DPX 400 MHz spectrometer in $CDCl_3$. Chemical shifts were reported in ppm with the internal TMS signal at 0.0 ppm as a standard. The spectrums' multiplicities are interpreted as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, brs = broad singlet, coupling constant(s) *J* are reported in Hz and relative integrations are reported. ^{13}C NMR (100 MHz) spectrums were recorded on a Bruker DPX 400 MHz spectrometer in $CDCl_3$ and are proton decoupled. Chemical shifts are reported in ppm with the internal chloroform signal at 77.00 ppm as a standard. Diastereomeric ratios were determined from crude ^{1}H NMR spectroscopy interpretation or by analysis of HPLC traces. Enantiomer ratios were determined by analysis of HPLC traces, obtained by using chiralpak IF, IA, AD-H with *n*-hexane and *i*-propanol as solvents. (Chiralpak IF, IA and AD-H columns were purchased from Daicel Chemical Industries, LTD.) Mass spectrums were recorded on TOF mass Finigann MAT8401 spectrometer. Solvents were dried and distilled following usual protocols.

2. General procedure for the synthesis of indole-diene derivatives

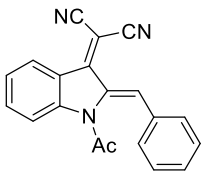


General procedure: To a solution of the 1-acetylindolin-3-one **I** (1.75 g, 10.0 mmol, 1.0 equiv) in toluene (30 mL), were added aldehyde **II** (12.0 mmol, 1.2 equiv) and piperdine (0.1 mL). The reaction mixture was stirred at 120 °C for 12 h. Solvents were evaporated under reduced pressure. The residue was directed purified by column chromatography on silica gel (petroleum ether/EtOAc = 80/1 to 20/1) to afford crude compound **III**.[1]

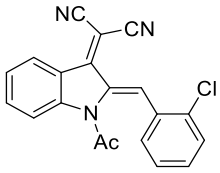
Under a nitrogen atmosphere, $TiCl_4$ (6.0 mmol, 2.0 equiv) was dissolved in CCl_4 (8 mL) and stirred at 0 °C for approximately 0.5 h. Then THF (10 mL) was added dropwise and the mixture was stirred at 0 °C for 0.5 h. Next, the solution of **III** (3.0 mmol, 1.0 equiv) and malononitrile (methyl 2-cyanoacetate) (3.6 mmol, 1.2 equiv) in THF was added dropwise and the mixture was stirred at 0 °C for 0.5 h. Finally, the solution of 4-methylmorpholine (9.0 mmol, 3.0 equiv) was added dropwise and the reaction mixture was stirred at room temperature. Once the starting material was consumed (monitored by TLC), the mixture was extracted with ethyl acetate (3 x 25 mL). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by recrystallization (ethanol) to afford the product **1**.

Reference:

[1] Buzas, A.; Merour, J. Y. *Synthesis* **1989**, *6*, 458-461.

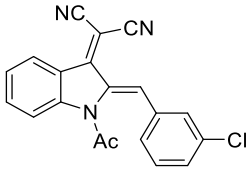


(*Z*)-2-(1-acetyl-2-benzylideneindolin-3-ylidene)malononitrile (1a) Red solid (0.73 g, 78% yield). Mp: 192-194 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 8.1 Hz, 1H), 8.25 (d, *J* = 8.3 Hz, 1H), 8.14 (s, 1H), 7.74-7.66 (m, 1H), 7.58 (d, *J* = 7.4 Hz, 2H), 7.51-7.42 (m, 3H), 7.38-7.32 (m, 1H), 1.93 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 145.8, 136.5, 136.4, 133.8, 130.7, 130.0 (2C), 130.0 (2C), 129.6, 127.1, 125.4, 125.4, 123.3, 117.1, 114.5, 114.0, 67.7, 25.0. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{20}H_{14}N_3O^+$: 312.1131, found: 312.1124.



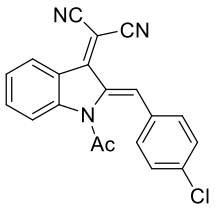
(*Z*)-2-(1-acetyl-2-(2-chlorobenzylidene)indolin-3-ylidene)malononitrile (1b)

Red solid (0.72 g, 70% yield). Mp: 201-203 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 8.1 Hz, 1H), 8.23 (d, *J* = 8.4 Hz, 1H), 8.23 (s, 1H) 7.73-7.66 (m, 1H), 7.56 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.52 (dd, *J* = 7.4, 1.8 Hz, 1H), 7.42-7.31 (m, 3H), 1.85 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 157.6, 145.7, 137.6, 136.7, 135.5, 132.8, 131.3, 130.6, 129.7, 127.6, 125.5, 125.4, 123.3, 123.0, 116.9, 114.0, 113.8, 69.1, 24.5. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{20}H_{13}{}^{35}ClN_3O^+$: 346.0742, found: 346.0741.



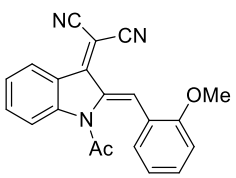
(*Z*)-2-(1-acetyl-2-(3-chlorobenzylidene)indolin-3-ylidene)malononitrile (1c)

Red solid (0.67 g, 65% yield). Mp: 151-153 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 8.0 Hz, 1H), 8.21 (d, *J* = 8.3 Hz, 1H), 8.04 (s, 1H), 7.74-7.67 (m, 1H), 7.54 (s, 1H), 7.47 (dd, *J* = 6.2, 2.3 Hz, 1H), 7.42-7.39 (m, 2H), 7.36 (t, *J* = 7.8 Hz, 1H), 1.98 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 157.8, 145.8, 137.3, 136.7, 135.7, 135.5, 130.8, 130.5, 129.8, 127.6, 125.6, 125.4, 124.9, 123.2, 117.1, 114.2, 113.7, 68.6, 25.0. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{20}H_{13}{}^{35}ClN_3O^+$: 346.0742, found: 346.0744.



(*Z*)-2-(1-acetyl-2-(4-chlorobenzylidene)indolin-3-ylidene)malononitrile (1d)

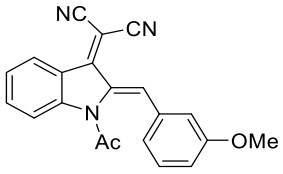
Red solid (0.77 g, 74% yield). Mp: 190-191 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 7.9 Hz, 1H), 8.21 (d, *J* = 8.3 Hz, 1H), 8.07 (s, 1H), 7.70 (t, *J* = 8.3 Hz, 1H), 7.52 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 8.6 Hz, 2H), 7.35 (t, *J* = 8.1 Hz, 1H), 1.98 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 157.9, 145.8, 136.8, 136.8, 136.6, 132.2, 131.2 (2C), 130.0 (2C), 125.6, 125.5, 125.4, 123.3, 117.1, 114.4, 113.9, 68.2, 25.0. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{20}H_{13}{}^{35}ClN_3O^+$: 346.0742, found: 346.0747.



(*Z*)-2-(1-acetyl-2-(2-methoxybenzylidene)indolin-3-ylidene)malononitrile (1e)

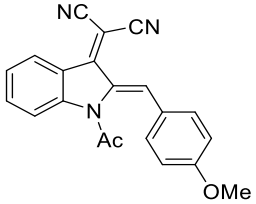
Red solid (0.61 g, 60% yield). Mp: 207-208 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 8.1 Hz, 1H), 8.41 (s, 1H), 8.26 (d, *J* = 8.4 Hz, 1H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.50 (d, *J* = 7.8 Hz, 1H), 7.47– 7.37 (m, 1H), 7.33 (t, *J* =

7.7 Hz, 1H), 7.01 (t, *J* = 8.4 Hz, 2H), 3.95 (s, 3H), 1.92 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 158.4, 157.9, 145.8, 136.3, 136.0, 132.6, 129.6, 125.3, 125.2, 123.4, 123.3, 122.9, 121.3, 116.9, 114.6, 114.5, 111.6, 67.1, 56.0, 24.9. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{21}H_{16}N_3O_2^+$: 342.1237, found: 342.1236.



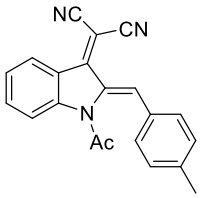
(*Z*)-2-(1-acetyl-2-(3-methoxybenzylidene)indolin-3-ylidene)malononitrile (1f)

Red solid (0.62 g, 61% yield). Mp: 149-151 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 8.1 Hz, 1H), 8.24 (d, *J* = 8.3 Hz, 1H), 8.10 (s, 1H), 7.68 (t, *J* = 8.3 Hz, 1H), 7.36 (dt, *J* = 15.3, 7.7 Hz, 2H), 7.16 (d, *J* = 7.7 Hz, 1H), 7.06 (s, 1H), 6.97 (dd, *J* = 8.2, 2.3 Hz, 1H), 3.83 (s, 3H), 1.94 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 160.3, 158.0, 145.9, 136.7, 136.6, 135.0, 130.7, 127.0, 125.4, 125.4, 123.2, 122.5, 117.0, 117.0, 114.5, 114.5, 114.1, 67.8, 55.4, 25.1. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{21}H_{16}N_3O_2^+$: 342.1237, found: 342.1240.



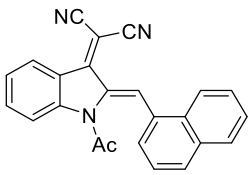
(*Z*)-2-(1-acetyl-2-(4-methoxybenzylidene)indolin-3-ylidene)malononitrile (1g)

Red solid (0.72 g, 71% yield). Mp: 197-199 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 8.1 Hz, 1H), 8.24 (d, *J* = 8.3 Hz, 1H), 8.13 (s, 1H), 7.68 (t, *J* = 7.8 Hz, 1H), 7.57 (d, *J* = 8.8 Hz, 2H), 7.34 (t, *J* = 7.7 Hz, 1H), 6.99 (d, *J* = 8.8 Hz, 2H), 3.88 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 161.7, 158.0, 145.8, 136.2, 134.6, 132.5 (2C), 127.8, 126.0, 125.3, 125.3, 123.7, 117.1, 115.2 (2C), 115.0, 114.4, 66.0, 55.5, 25.2. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{21}H_{16}N_3O_2^+$: 342.1237, found: 342.1232.



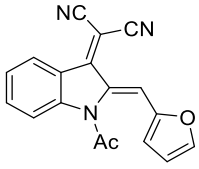
(*Z*)-2-(1-acetyl-2-(4-methylbenzylidene)indolin-3-ylidene)malononitrile (1h)

Red solid (0.72 g, 74% yield). Mp: 156-158 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.1 Hz, 1H), 8.17 (d, *J* = 8.3 Hz, 1H), 8.04 (s, 1H), 7.60 (t, *J* = 8.4 Hz, 1H), 7.40 (d, *J* = 8.1 Hz, 2H), 7.26 (t, *J* = 8.1 Hz, 1H), 7.20 (d, *J* = 8.2 Hz, 2H), 2.34 (s, 3H), 1.89 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 158.1, 145.8, 141.7, 136.3, 135.7, 130.9, 130.4 (2C), 130.2 (2C), 127.6, 125.3, 125.3, 123.4, 117.1, 114.7, 114.2, 67.0, 25.1, 21.7. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{21}H_{16}N_3O^+$: 326.1288, found: 326.1290.



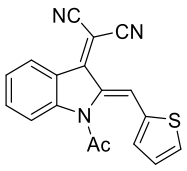
(*Z*)-2-(1-acetyl-2-(naphthalen-1-ylmethylene)indolin-3-ylidene)malononitrile (1i)

Red solid (0.73 g, 68% yield). Mp: 173-175 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 1H), 8.55 (d, *J* = 8.1 Hz, 1H), 8.29 (d, *J* = 8.3 Hz, 1H), 8.12 (d, *J* = 8.3 Hz, 1H), 7.99–7.92 (m, 2H), 7.70 (q, *J* = 6.6 Hz, 3H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.53 (t, *J* = 7.7 Hz, 1H), 7.36 (t, *J* = 7.7 Hz, 1H), 1.68 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 158.4, 145.9, 137.6, 136.7, 133.9, 131.5, 131.3, 131.0, 129.1, 128.3, 127.6, 127.2, 125.6, 125.4, 125.4, 124.7, 123.8, 123.1, 117.0, 115.0, 114.0, 68.0, 24.9. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{24}H_{16}N_3O^+$: 362.1288, found: 362.1287.



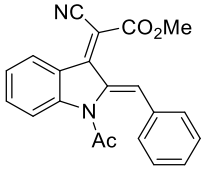
(*Z*)-2-(1-acetyl-2-(furan-2-ylmethylene)indolin-3-ylidene)malononitrile (1j)

Red solid (0.52 g, 58% yield). Mp: 175-177 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, *J* = 8.1 Hz, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 7.94 (s, 1H), 7.70 (s, 1H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.30 (t, *J* = 7.7 Hz, 1H), 6.97 (d, *J* = 3.4 Hz, 1H), 6.67-6.61 (m, 1H), 2.18 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 157.3, 148.6, 147.5, 145.8, 136.2, 133.1, 125.1, 125.0, 123.0, 121.4, 116.4, 115.0, 114.4, 113.9, 113.4, 65.8, 24.4. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{18}H_{12}N_3O_2^+$: 302.0924, found: 302.0926.



(*Z*)-2-(1-acetyl-2-(thiophen-2-ylmethylene)indolin-3-ylidene)malononitrile (1k)

Red solid (0.47 g, 50% yield). Mp: 170-172 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 8.1 Hz, 1H), 8.32 (s, 1H), 8.20 (d, *J* = 8.3 Hz, 1H), 7.68 (t, *J* = 7.6 Hz, 2H), 7.52 (d, *J* = 3.2 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.20-7.15 (m, 1H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 157.8, 151.0, 145.9, 136.1, 135.2, 133.4, 129.0, 128.6, 125.6, 125.2, 123.9, 121.7, 117.5, 114.8, 114.2, 66.3, 25.1. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{18}H_{12}N_3OS^+$: 318.0696, found: 318.0697.

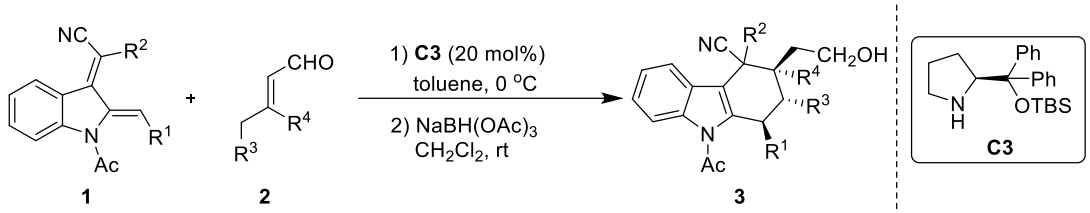


Methyl 2-((*Z*)-1-acetyl-2-((*Z*)-benzylidene)indolin-3-ylidene)-2-cyanoacetate (1l)

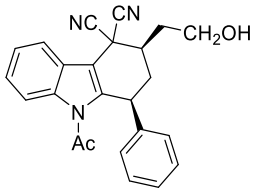
Red solid (0.62 g, 60% yield). Mp: 185-187 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, *J* = 8.1 Hz, 1H), 8.26 (d, *J* = 8.3 Hz, 1H), 8.02 (s, 1H), 7.58 (dd, *J* = 18.8, 7.7 Hz, 3H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.38 (d, *J* = 7.3 Hz, 1H), 7.27-7.20 (m, 1H), 3.97 (s, 3H), 1.94 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6,

163.0, 157.5, 145.6, 138.3, 135.1, 134.1, 129.9, 129.6 (2C), 129.4 (2C), 128.7, 126.0, 124.8, 124.0, 118.0, 117.0, 92.4, 53.2, 24.7. HRMS (ESI-TOF) calcd [$M+H^+$] for $C_{21}H_{17}N_2O_3^+$: 345.1234, found: 345.1236.

3. General procedure for the asymmetric synthesis of tetrahydrocarbazoles

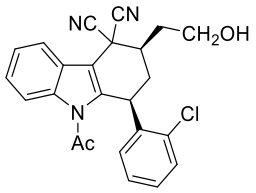


General procedure: Enal **2** (0.15 mmol, 1.5 equiv) was added to a solution of catalyst **C3** (0.02 mmol, 0.2 equiv) and indole-diene **1** (0.10 mmol, 1.0 equiv) in toluene (1.0 mL) at 0 °C. The reaction mixture was stirred at 0 °C until indole-diene **1** was consumed (indicated by TLC). Solvents were evaporated under reduced pressure. The residue was directed purified by column chromatography on silica gel (petroleum ether/EtOAc = 10/1 to 4/1) to afford crude aldehyde compound. The IEDDA product was dissolved in dichloromethane, then $NaBH(OAc)_3$ (0.2 mmol, 2.0 equiv.) was added. After the reaction was completed (indicated by TLC), the solvent was evaporated and the residue was purified by column chromatography on silica gel (petroleum ether/EtOAc=8/1 to 2/1) to afford product **3**.



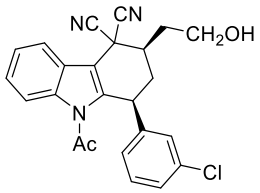
(*1S,3R*)-9-acetyl-3-(2-hydroxyethyl)-1-phenyl-1,2,3,9-tetrahydro-4H-carbazole-4,4-dicarbonitrile (3aa)

White solid (31.9 mg, 83% yield). Mp: 116-117 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01-7.93 (m, 1H), 7.76-7.71 (m, 1H), 7.48-7.39 (m, 2H), 7.30-7.17 (m, 3H), 6.97 (d, *J* = 6.5 Hz, 2H), 4.68 (dd, *J* = 10.8, 6.5 Hz, 1H), 3.99 (dt, *J* = 10.6, 5.2 Hz, 1H), 3.87 (ddd, *J* = 11.1, 8.9, 4.4 Hz, 1H), 2.94-2.83 (m, 1H), 2.62 (ddd, *J* = 14.5, 6.7, 2.3 Hz, 1H), 2.37 (s, 3H), 2.35-2.28 (m, 1H), 1.91 (ddt, *J* = 14.5, 9.8, 4.7 Hz, 1H), 1.71 (ddd, *J* = 14.4, 12.8, 11.0 Hz, 1H), 1.26 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 142.9, 140.1, 135.7, 128.9 (2C), 127.1, 127.1 (2C), 125.7, 125.0, 123.9, 118.7, 114.6, 113.9, 113.3, 111.4, 59.2, 42.3, 39.8, 36.9, 36.7, 34.6, 26.6. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{24}H_{22}N_3O_2$+: 384.1707, found: 384.1708. 96% ee; determined by HPLC (Chiralpak IA, hexane/*i*-PrOH = 90/10, 1.0 mL/min, 254 nm) t_R = 12.49 min (minor), 28.43 min (major). $[\alpha]_D^{22}$ = +56.3 (c = 0.1, CH_2Cl_2).



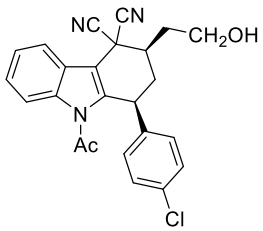
(*1S,3R*)-9-acetyl-1-(2-chlorophenyl)-3-(2-hydroxyethyl)-1,2,3,9-tetrahydro-4H-carbazole-4,4-dicarbonitrile (3ba)

White solid (32.7 mg, 78% yield). Mp: 108-110 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03-7.94 (m, 1H), 7.82-7.76 (m, 1H), 7.51-7.38 (m, 3H), 7.17 (t, *J* = 7.7 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.53 (d, *J* = 7.6 Hz, 1H), 5.21 (dd, *J* = 10.4, 6.5 Hz, 1H), 4.01 (dt, *J* = 10.6, 5.1 Hz, 1H), 3.90 (td, *J* = 11.4, 10.1, 4.5 Hz, 1H), 2.94-2.84 (m, 1H), 2.76 (dd, *J* = 14.3, 6.1 Hz, 1H), 2.41 (s, 3H), 2.33 (dq, *J* = 13.3, 4.7, 4.1 Hz, 1H), 1.92 (ddt, *J* = 14.3, 9.6, 4.5 Hz, 1H), 1.66 (s, 1H), 1.62-1.50 (td, *J* = 13.7, 10.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 140.7, 139.1, 135.8, 133.3, 129.8, 128.4, 127.7, 126.4, 125.9, 125.1, 124.1, 118.8, 114.5, 114.4, 113.2, 112.2, 59.2, 39.7, 39.1, 36.6, 34.7, 34.1, 26.5. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{24}H_{21}{}^{35}ClN_3O_2^+$: 418.1317, found: 418.1323. 97% ee; determined by HPLC (Chiralpak IA, hexane/*i*-PrOH = 90/10, 1.0 mL/min, 254 nm) t_R = 14.29 min (minor), 19.04 min (major). $[\alpha]_D^{22}$ = +62.5 (c = 0.1, CH_2Cl_2).



(*1S,3R*)-9-acetyl-1-(3-chlorophenyl)-3-(2-hydroxyethyl)-1,2,3,9-tetrahydro-4H-carbazole-4,4-dicarbonitrile (3ca)

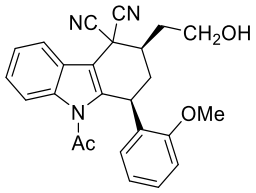
White solid (34.7 mg, 83% yield). Mp: 110-112 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 6.2, 2.5 Hz, 1H), 7.71 (dd, *J* = 6.1, 2.7 Hz, 1H), 7.54 -7.41 (m, 2H), 7.20 (d, *J* = 4.7 Hz, 2H), 7.02 (d, *J* = 10.3 Hz, 1H), 6.83 (s, 1H), 4.70 (dd, *J* = 10.7, 6.5 Hz, 1H), 4.00 (dt, *J* = 10.5, 5.1 Hz, 1H), 3.88 (td, *J* = 11.1, 9.9, 4.2 Hz, 1H), 2.92-2.81 (m, 1H), 2.61 (ddd, *J* = 14.3, 6.5, 2.1 Hz, 1H), 2.46 (s, 3H), 2.39-2.28 (m, 1H), 1.92 (ddd, *J* = 14.3, 9.6, 4.6 Hz, 1H), 1.75-1.63 (m, 1H), 1.60 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 145.1, 139.6, 135.6, 134.5, 130.1, 127.3, 127.3,125.8, 125.2, 124.0, 118.9, 114.4, 114.4, 113.9, 113.2, 111.8, 59.2, 42.2, 39.8, 36.6, 36.6, 34.5, 26.7. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{24}H_{21}{}^{35}ClN_3O_2^+$: 418.1317, found: 418.1321. 96% ee; determined by HPLC (Chiralpak IA, hexane/*i*-PrOH = 90/10, 1.0 mL/min, 254 nm) t_R = 12.45 min (minor), 24.99 min (major). $[\alpha]_D^{22}$ = +68.7 (c = 0.1, CH_2Cl_2).



(*1S,3R*)-9-acetyl-1-(4-chlorophenyl)-3-(2-hydroxyethyl)-1,2,3,9-tetrahydro-4H-carbazole-4,4-dicarbonitrile (3da)

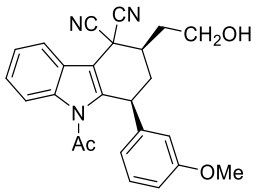
White solid (33.9 mg, 81% yield). Mp: 105-107 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02-7.95 (m, 1H), 7.74-7.66 (m, 1H), 7.50-7.42 (m, 2H), 7.24 (d, *J* = 8.3 Hz, 2H), 6.92 (d, *J* = 7.4 Hz, 2H),

4.71 (dd, *J* = 10.5, 6.6 Hz, 1H), 4.00 (dt, *J* = 10.3, 5.0 Hz, 1H), 3.93 – 3.84 (m, 1H), 2.86 (t, *J* = 11.3 Hz, 1H), 2.60 (dd, *J* = 14.3, 6.4 Hz, 1H), 2.45 (s, 3H), 2.39-2.29 (m, 1H), 1.91 (ddt, *J* = 13.9, 9.0, 4.3 Hz, 1H), 1.75-1.61 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 141.6, 134.0, 135.6, 132.7, 129.0 (2C), 128.5 (2C), 125.8, 125.1, 124.0, 118.9, 114.4, 113.9, 113.2, 111.7, 59.2, 41.8, 39.8, 36.7, 36.6, 34.5, 26.7. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{24}H_{21}{}^{35}ClN_3O_2^+$: 418.1317, found: 418.1316. 96% ee; determined by HPLC (Chiralpak IA, hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm) t_R = 6.50 min (minor), 12.37 min (major). $[\alpha]_D^{22}$ = +127.3 (c = 0.1, CH_2Cl_2).



(*1S,3R*)-9-acetyl-3-(2-hydroxyethyl)-1-(2-methoxyphenyl)-1,2,3,9-tetrahydro-4H-carbazole-4,4-dicarbonitrile (3ea)

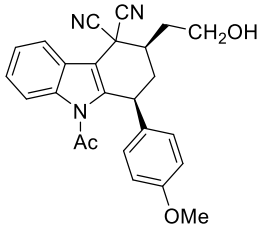
White solid (31.9 mg, 77% yield). Mp: 104-106 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00-7.84 (m, 2H), 7.49-7.35 (m, 2H), 7.21 (t, *J* = 7.8 Hz, 1H), 6.98-6.73 (m, 2H), 6.47 (t, *J* = 7.1 Hz, 1H), 5.18-5.07 (m, 1H), 4.07-3.98 (m, 1H), 3.95 (s, 3H), 3.92-3.84 (m, 1H), 2.94-2.83 (m, 1H), 2.68 (dd, *J* = 14.5, 4.1 Hz, 1H), 2.32 (m, 4H), 1.92 (ddt, *J* = 14.3, 9.5, 4.6 Hz, 1H), 1.58 (d, *J* = 10.7 Hz, 1H), 1.25 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 156.1, 139.7, 136.1, 131.3, 128.4, 126.3, 125.7, 125.0, 123.9, 121.4, 118.4, 114.8, 114.6, 113.3, 111.6, 110.7, 59.3, 55.7, 39.7, 36.7, 34.9, 34.9, 34.8, 26.2. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{25}H_{24}N_3O_3^+$: 414.1812, found: 414.1810. 96% ee; determined by HPLC (Chiralpak IF, hexane/*i*-PrOH = 90/10, 1.0 mL/min, 254 nm) t_R = 16.14 min (minor), 37.16 min (major). $[\alpha]_D^{22}$ = +81.6 (c = 0.1, CH_2Cl_2).



(*1S,3R*)-9-acetyl-3-(2-hydroxyethyl)-1-(3-methoxyphenyl)-1,2,3,9-tetrahydro-4H-carbazole-4,4-dicarbonitrile (3fa)

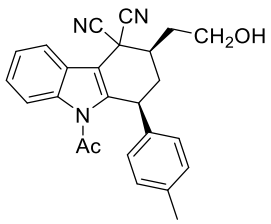
White solid (29.4 mg, 71% yield). Mp: 98-100 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99-7.92 (m, 1H), 7.80-7.73 (m, 1H), 7.44 (dt, *J* = 7.2, 2.3 Hz, 2H), 7.18 (t, *J* = 8.0 Hz, 1H), 6.75 (dd, *J* = 8.1, 2.3 Hz, 1H), 6.53 (s, 2H), 4.65 (dd, *J* = 10.7, 6.5 Hz, 1H), 4.00 (dt, *J* = 10.7, 5.2 Hz, 1H), 3.87 (ddd, *J* = 11.1, 8.9, 4.3 Hz, 1H), 3.74 (s, 3H), 2.92-2.82 (m, 1H), 2.66-2.59 (m, 1H), 2.42 (s, 3H), 2.37-2.28 (m, 1H), 1.91 (ddt, *J* = 14.5, 9.7, 4.7 Hz, 1H), 1.78-1.66 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 159.9, 144.6, 139.8, 135.7, 130.0, 130.0, 125.7, 125.7, 125.0, 123.8, 118.7, 114.6, 114.0, 113.2, 111.9, 111.4, 59.2, 55.2, 42.3, 39.8, 36.8, 36.7, 34.6, 26.7. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{25}H_{24}N_3O_3^+$: 414.1812, found: 414.1815. 96%

ee; determined by HPLC (Chiralpak IA, hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm) t_R = 18.53 min (minor), 33.30 min (major). $[\alpha]_D^{22}$ = +92.6. (c = 0.1, CH_2Cl_2).



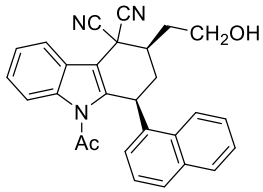
(*1S,3R*)-9-acetyl-3-(2-hydroxyethyl)-1-(4-methoxyphenyl)-1,2,3,9-tetrahydro-4H-carbazole-4,4-dicarbonitrile (3ga)

White solid (32.7 mg, 79% yield). Mp: 101-103 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99-7.91 (m, 1H), 7.78-7.71 (m, 1H), 7.48-7.39 (m, 2H), 6.88 (d, *J* = 7.8 Hz, 2H), 6.79 (d, *J* = 8.4 Hz, 2H), 4.61 (dd, *J* = 10.5, 6.6 Hz, 1H), 3.99 (dt, *J* = 10.4, 5.0 Hz, 1H), 3.91-3.83 (m, 1H), 3.76 (s, 3H), 2.86 (t, *J* = 11.3 Hz, 1H), 2.64-2.55 (m, 1H), 2.38 (s, 3H), 2.37-2.27 (m, 1H), 1.91 (ddt, *J* = 14.3, 9.6, 4.4 Hz, 1H), 1.77-1.64 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 158.5, 140.5, 135.8, 134.9, 128.3 (2C), 125.7, 125.0, 123.9, 118.7, 114.7, 114.3 (2C), 114.0, 113.3, 111.2, 59.7, 55.3, 41.5, 39.8, 37.2, 36.8, 34.6, 26.7. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{25}H_{24}N_3O_3^+$: 414.1812, found: 414.1809. 96% ee; determined by HPLC (Chiralpak IA, hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm) t_R = 7.36 min (minor), 14.02 min (major). $[\alpha]_D^{22}$ = +78.3 (c = 0.1, CH_2Cl_2).



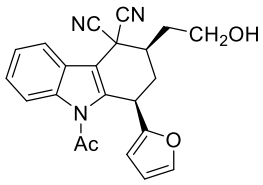
(*1S,3R*)-9-acetyl-3-(2-hydroxyethyl)-1-(p-tolyl)-1,2,3,9-tetrahydro-4H-carbazole-4,4-dicarbonitrile (3ha)

White solid (31.9 mg, 83% yield). Mp: 108-110 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99-7.93 (m, 1H), 7.79-7.74 (m, 1H), 7.44 (q, *J* = 4.8, 3.7 Hz, 2H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.85 (d, *J* = 7.1 Hz, 2H), 4.63 (dd, *J* = 10.7, 6.5 Hz, 1H), 4.00 (dt, *J* = 10.7, 5.2 Hz, 1H), 3.87 (ddd, *J* = 11.1, 8.9, 4.4 Hz, 1H), 2.92-2.81 (m, 1H), 2.63-2.55 (m, 1H), 2.39 (s, 3H), 2.36-2.32 (m, 1H), 2.30 (s, 3H), 1.90 (ddt, *J* = 14.6, 9.8, 4.7 Hz, 1H), 1.77-1.62 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 140.2, 139.9, 136.8, 135.8, 129.6 (2C), 127.0 (2C), 125.7, 125.0, 123.8, 118.6, 114.6, 114.0, 113.3, 111.3, 59.2, 41.9, 39.7, 37.1, 36.7, 34.6, 26.7, 21.0. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{25}H_{24}N_3O_2^+$: 398.1863, found: 398.1866. 92% ee; determined by HPLC (Chiralpak IA, hexane/*i*-PrOH = 90/10, 1.0 mL/min, 254 nm) t_R = 10.35 min (minor), 20.72 min (major). $[\alpha]_D^{22}$ = +57.3 (c = 0.1, CH_2Cl_2).



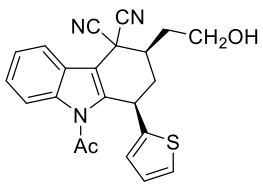
(*1S,3R*)-9-acetyl-3-(2-hydroxyethyl)-1-(naphthalen-1-yl)-1,2,3,9-tetrahydro-4H-carbazole-4,4-dicarbonitrile (3ia)

White solid (34.7 mg, 80% yield). Mp: 130-132 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.5 Hz, 1H), 8.01 (dd, *J* = 5.9, 3.0 Hz, 1H), 7.90 (d, *J* = 8.2 Hz, 1H), 7.80 (dd, *J* = 6.3, 2.8 Hz, 1H), 7.72 (d, *J* = 8.2 Hz, 1H), 7.67-7.61 (m, 1H), 7.56 (d, *J* = 7.7 Hz, 1H), 7.47 (td, *J* = 6.8, 6.1, 4.2 Hz, 2H), 7.27 (t, *J* = 7.7 Hz, 1H), 6.66 (d, *J* = 7.2 Hz, 1H), 5.59 (dd, *J* = 10.6, 6.4 Hz, 1H), 3.98 (dt, *J* = 10.7, 5.1 Hz, 1H), 3.84 (ddd, *J* = 11.1, 8.9, 4.3 Hz, 1H), 3.04-2.95 (m, 1H), 2.85 (ddd, *J* = 14.6, 6.5, 2.2 Hz, 1H), 2.38-2.30 (m, 1H), 2.27 (s, 3H), 1.87 (ddt, *J* = 14.5, 8.7, 4.7 Hz, 2H), 1.73 (ddd, *J* = 14.4, 12.8, 10.9 Hz, 1H), 1.58 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 140.2, 140.0, 135.8, 133.8, 130.8, 129.2, 127.7, 126.9, 126.1, 125.8, 125.7, 125.2, 124.0, 122.6, 122.0, 118.7, 114.7, 114.3, 113.3, 112.0, 59.2, 39.8, 37.5, 36.7, 35.6, 34.6, 26.5. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{28}H_{24}N_3O_2^+$: 434.1863, found: 434.1864. 92% ee; determined by HPLC (Chiralpak IA, hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm) t_R = 13.96 min (minor), 29.22 min (major). $[\alpha]_D^{22}$ = +102.1 (c = 0.1, CH_2Cl_2).



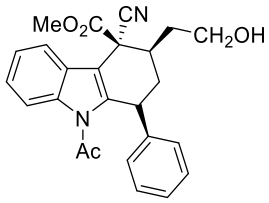
(*1R,3R*)-9-acetyl-1-(furan-2-yl)-3-(2-hydroxyethyl)-1,2,3,9-tetrahydro-4H-carbazole-4,4-dicarbonitrile (3ja)

White solid (28.1 mg, 75% yield). Mp: 117-118 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97-7.92 (m, 1H), 7.81-7.76 (m, 1H), 7.48-7.39 (m, 2H), 7.28 (s, 1H), 6.31-6.26 (m, 1H), 5.95 (d, *J* = 3.2 Hz, 1H), 4.86 (dd, *J* = 10.5, 6.4 Hz, 1H), 4.01 (dt, *J* = 10.7, 5.2 Hz, 1H), 3.89 (td, *J* = 11.0, 9.9, 4.3 Hz, 1H), 2.91-2.79 (m, 1H), 2.75-2.64 (m, 1H), 2.50 (s, 3H), 2.40-2.28 (m, 1H), 2.00-1.92 (m, 1H), 1.92-1.82 (m, 1H), 1.58 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 154.6, 141.4, 137.3, 135.9, 125.9, 125.0, 123.9, 118.8, 114.5, 114.0, 113.0, 110.9, 110.6, 105.9, 59.3, 39.5, 36.5, 35.8, 34.4, 33.5, 26.5. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{22}H_{20}N_3O_3^+$: 374.1499, found: 374.1498. 93% ee; determined by HPLC (Chiralpak IF, hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm) t_R = 9.86 min (minor), 14.12 min (major). $[\alpha]_D^{22}$ = -147.3 (c = 0.1, CH_2Cl_2).



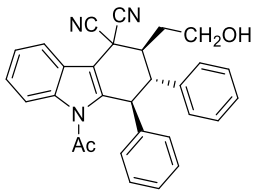
(*1R,3R*)-9-acetyl-3-(2-hydroxyethyl)-1-(thiophen-2-yl)-1,2,3,9-tetrahydro-4H-carbazole-4,4-dicarbonitrile (3ka)

White solid (27.8 mg, 71% yield). Mp: 113-115 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01-7.93 (m, 1H), 7.79-7.73 (m, 1H), 7.45 (dd, *J* = 5.9, 3.4 Hz, 2H), 7.18-7.12 (m, 1H), 6.88 (dd, *J* = 5.0, 3.6 Hz, 1H), 6.69 (d, *J* = 3.0 Hz, 1H), 5.02 (dd, *J* = 10.6, 6.5 Hz, 1H), 4.02 (dt, *J* = 10.6, 5.2 Hz, 1H), 3.89 (ddd, *J* = 11.1, 8.9, 4.3 Hz, 1H), 2.92-2.82 (m, 1H), 2.72 (ddd, *J* = 14.6, 6.6, 2.1 Hz, 1H), 2.50 (s, 3H), 2.40-2.28 (m, 1H), 1.99-1.90 (m, 1H), 1.90-1.80 (m, 1H), 1.61 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 145.6, 139.4, 135.8, 126.8, 125.9, 124.9, 124.8, 124.0, 123.9, 118.9, 114.5, 113.9, 113.0, 111.0, 59.3, 39.8, 37.6, 37.3, 36.6, 34.5, 26.6. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{22}H_{20}N_3O_2S^+$: 390.1271, found: 390.1274. 95% ee; determined by HPLC (Chiralpak IF, hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm) t_R = 9.24 min (minor), 16.44 min (major). $[\alpha]_D^{22}$ = -192.8 (c = 0.1, CH_2Cl_2).



Methyl (1*R*,3*R*,4*R*)-9-acetyl-4-cyano-3-(2-hydroxyethyl)-1-phenyl-2,3,4,9-tetrahydro-1H-carbazole-4-carboxylate (3la)

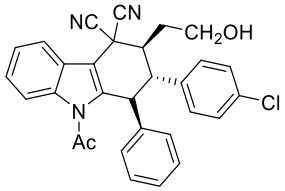
White solid (28.3 mg, 68% yield). Mp: 99-101 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82-7.77 (m, 1H), 7.76-7.70 (m, 1H), 7.38-7.30 (m, 2H), 7.28-7.17 (m, 3H), 7.05 (d, *J* = 6.9 Hz, 2H), 4.64 (dd, *J* = 10.5, 6.9 Hz, 1H), 3.97-3.90 (m, 1H), 3.85 (s, 3H), 3.84-3.78 (m, 1H), 2.83 (ddt, *J* = 13.2, 10.2, 3.0 Hz, 1H), 2.40 (ddd, *J* = 14.3, 6.9, 2.9 Hz, 1H), 2.36 (s, 3H), 2.27-2.17 (m, 1H), 2.13-2.05 (m, 1H), 1.66 (s, 1H), 1.52 (ddt, *J* = 13.9, 10.4, 5.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 167.3, 144.1, 140.0, 135.9, 128.6 (2C), 127.4 (2C), 126.7, 126.1, 125.1, 123.4, 118.8, 118.8, 114.4, 113.9, 60.0, 53.7, 47.9, 42.2, 39.8, 35.5, 34.2, 26.6. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{25}H_{25}N_2O_4^+$: 417.1809, found: 417.1816. 95% ee; determined by HPLC (Chiralpak IA, hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm) t_R = 10.95 min (minor), 28.32 min (major). $[\alpha]_D^{22}$ = -373.3 (c = 0.1, CH_2Cl_2).



Methyl (*1S,2S,3S*)-9-acetyl-4-cyano-3-(2-hydroxyethyl)-1,2-diphenyl-2,3,4,9-tetrahydro-1H-carbazole-4-carboxylate (3ab)

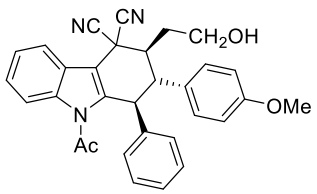
White solid (30.1 mg, 61% yield). Mp: 116-118 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06–8.00 (m, 1H), 7.66 (dd, *J* = 6.6, 1.9 Hz, 1H), 7.50–7.41 (m, 2H), 7.29 (s, 3H), 7.05 (dt, *J* = 14.0, 6.8 Hz, 5H), 6.51 (d, *J* = 6.9 Hz, 2H), 4.84 (d, *J* = 9.8

Hz, 1H), 3.57 (dt, *J* = 11.7, 6.4 Hz, 1H), 3.21 (dq, *J* = 11.5, 5.0 Hz, 2H), 2.94 (dd, *J* = 11.9, 9.9 Hz, 1H), 2.34 (s, 3H), 2.02 (dq, *J* = 12.4, 6.2 Hz, 1H), 1.90–1.81 (m, 1H), 1.58 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 140.9, 140.3, 138.6, 135.8, 128.8, 128.8 (2C), 128.0 (2C), 128.0 (2C), 127.9 (2C), 126.8, 125.7, 124.9, 123.9, 119.1, 114.9, 113.7, 113.6, 110.8, 59.8, 54.9, 50.0, 42.2, 37.4, 35.1, 26.5. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{30}H_{26}N_3O_2$+: 460.2020, found: 460.2024. 95% ee; determined by HPLC (Chiralpak IF, hexane/*i*-PrOH = 90/10, 1.0 mL/min, 254 nm) t_R = 22.02 min (major), 27.60 min (minor). $[\alpha]_D^{22}$ = +167.1 (c = 0.1, CH_2Cl_2).



Methyl (1*S*,2*S*,3*S*)-9-acetyl-2-(4-chlorophenyl)-4-cyano-3-(2-hydroxyethyl)-1-phenyl-2,3,4,9-tetrahydro-1H-carbazole-4-carboxylate (3ac)

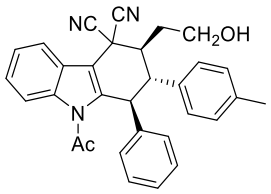
White solid (38.0 mg, 72% yield). Mp: 127-128 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 6.2, 2.3 Hz, 1H), 7.64 (dd, *J* = 6.5, 2.2 Hz, 1H), 7.52–7.42 (m, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.15–6.94 (m, 5H), 6.51 (d, *J* = 6.8 Hz, 2H), 4.77 (d, *J* = 9.8 Hz, 1H), 3.65 (dt, *J* = 12.0, 6.3 Hz, 1H), 3.32–3.23 (m, 1H), 3.20 (dt, *J* = 11.4, 5.4 Hz, 1H), 2.93 (dd, *J* = 11.9, 10.0 Hz, 1H), 2.34 (s, 3H), 2.06–1.96 (m, 1H), 1.82 (dq, *J* = 15.0, 6.0 Hz, 1H), 1.64 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 140.6, 140.1, 137.2, 135.7, 133.7, 130.5 (2C), 130.4 (2C), 129.0 (2C), 128.1 (2C), 127.0, 125.7, 124.9, 123.9, 119.1, 114.8, 113.6, 113.5, 110.8, 59.6, 54.3, 50.0, 41.9, 37.3, 34.9, 26.5. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{30}H_{25}{}^{35}ClN_3O_2^+$: 494.1630, found: 494.1630. 96% ee; determined by HPLC (Chiralpak IA, hexane/*i*-PrOH = 90/10, 1.0 mL/min, 254 nm) t_R = 22.34 min (major), 30.41 min (minor). $[\alpha]_D^{22}$ = +192.5 (c = 0.1, CH_2Cl_2).



Methyl (1*S*,2*S*,3*S*)-9-acetyl-4-cyano-3-(2-hydroxyethyl)-2-(4-methoxyphenyl)-1-phenyl-2,3,4,9-tetrahydro-1H-carbazole-4-carboxylate (3ad)

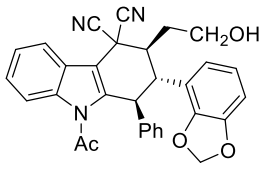
White solid (30.4 mg, 58% yield). Mp: 121-123 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 6.3, 2.6 Hz, 1H), 7.67 (dd, *J* = 6.6, 2.3 Hz, 1H), 7.51-7.40 (m, 2H), 7.12-6.93 (m, 5H), 6.83 (d, *J* = 8.0 Hz, 2H), 6.55-6.47 (m, 2H), 4.79 (d, *J* = 9.8 Hz, 1H), 3.81 (s, 3H), 3.56 (dt, *J* = 12.0, 6.2 Hz, 1H), 3.22 (dt, *J* = 11.1, 6.7 Hz, 1H), 3.14 (dt, *J* = 10.9, 5.4 Hz, 1H), 2.88 (dd, *J* = 12.0, 9.8 Hz, 1H), 2.34 (s, 3H), 2.00 (ddd, *J* = 11.9, 7.3, 3.9 Hz, 1H), 1.86 (dq, *J* = 15.0, 6.1 Hz, 1H), 1.59 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 159.0, 141.1, 140.4, 135.7,

130.4, 128.0 (2C), 126.8 (2C), 125.7 (2C), 124.9, 123.8, 119.0, 114.9, 114.1 (2C), 114.0, 113.7 (2C), 113.7, 110.8, 59.9, 55.2, 54.1, 50.0, 42.4, 37.5, 35.2, 26.5. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{31}H_{28}N_3O_3^+$: 490.2125, found: 490.2128. 98% ee; determined by HPLC (Chiralpak IA, hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm) t_R = 16.74 min (major), 20.11 min (minor). $[\alpha]_D^{22}$ = +114.9 (c = 0.1, CH_2Cl_2).



Methyl (1*S*,2*S*,3*S*)-9-acetyl-4-cyano-3-(2-hydroxyethyl)-1-phenyl-2-(p-tolyl)-2,3,4,9-tetrahydro-1H-carbazole-4-carboxylate (3ae)

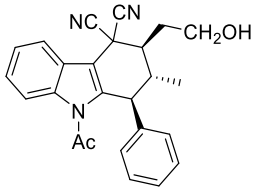
White solid (30.9 mg, 61% yield). Mp: 115-117 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05-8.00 (m, 1H), 7.67 (dd, *J* = 6.5, 2.3 Hz, 1H), 7.49-7.40 (m, 2H), 7.13-6.90 (m, 7H), 6.52 (d, *J* = 6.7 Hz, 2H), 4.82 (d, *J* = 9.8 Hz, 1H), 3.55 (dt, *J* = 12.2, 6.2 Hz, 1H), 3.18 (ddt, *J* = 22.8, 10.9, 4.9 Hz, 2H), 2.90 (dd, *J* = 12.0, 9.8 Hz, 1H), 2.34 (s, 3H), 2.34 (s, 3H), 2.04-1.96 (m, 1H), 1.85 (dq, *J* = 15.0, 6.1 Hz, 1H), 1.59 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 141.1, 140.4, 137.6, 135.8, 135.4, 129.5 (3C), 127.9 (3C), 126.8 (2C), 125.6 (2C), 124.9, 123.8, 119.0, 114.9, 113.7, 113.6, 110.8, 59.9, 54.4, 49.9, 42.3, 37.5, 35.1, 26.5, 21.1. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{31}H_{28}N_3O_2$+: 474.2176, found: 474.2170. 97% ee; determined by HPLC (Chiralpak IA, hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm) t_R = 8.30 min (major), 11.08 min (minor). $[\alpha]_D^{22}$ = +126.1 (c = 0.1, CH_2Cl_2).



Methyl (1*S*,2*S*,3*S*)-9-acetyl-2-(benzo[d][1,3]dioxol-4-yl)-4-cyano-3-(2-hydroxyethyl)-1-phenyl-2,3,4,9-tetrahydro-1H-carbazole-4-carboxylate (3af)

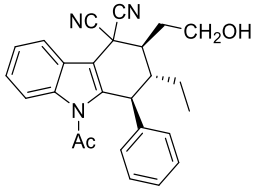
White solid (36.0 mg, 67% yield). Mp: 133-135 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 6.3, 2.4 Hz, 1H), 7.65 (dd, *J* = 6.6, 2.2 Hz, 1H), 7.49–7.41 (m, 2H), 7.08 (q, *J* = 6.0 Hz, 3H), 6.74–6.35 (m, 5H), 5.99 (d, *J* = 4.0 Hz, 2H), 4.77 (d, *J* = 9.8 Hz, 1H), 3.64 (dt, *J* = 11.7, 6.1 Hz, 1H), 3.40–3.29 (m, 1H), 3.10 (dt, *J* = 11.3, 5.4 Hz, 1H), 2.86 (dd, *J* = 11.9, 9.9 Hz, 1H), 2.34 (s, 3H), 2.06–1.97 (m, 1H), 1.95–1.85 (m, 1H), 1.57 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 148.0, 147.1, 141.0, 140.3, 135.7, 132.2, 128.2, 128.2, 128.0 (2C), 127.1, 126.9 (2C), 125.7, 124.9, 123.8, 119.0, 114.9, 113.7, 113.6, 110.7, 108.4, 101.3, 59.9, 54.6, 50.0, 42.4, 37.3, 35.0, 26.5. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{31}H_{26}N_3O_4^+$: 504.1918, found: 504.1921. 95% ee; determined by HPLC (Chiralpak IF, hexane/*i*-PrOH = 90/10, 1.0 mL/min, 254 nm) t_R = 13.47 min (major), 16.50 min (minor). $[\alpha]_D^{22}$ = +251.7 (c = 0.1,

CH_2Cl_2).



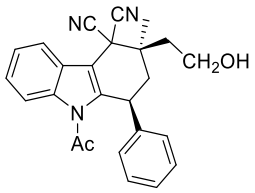
Methyl (1*S*,2*S*,3*S*)-9-acetyl-4-cyano-3-(2-hydroxyethyl)-2-methyl-1-phenyl-2,3,4,9-tetrahydro-1H-carbazole-4-carboxylate (3ag)

White solid (22.0 mg, 51% yield). Mp: 106-108 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99–7.94 (m, 1H), 7.61–7.56 (m, 1H), 7.46–7.37 (m, 2H), 7.23 (t, *J* = 8.3 Hz, 3H), 6.96 (d, *J* = 6.3 Hz, 2H), 4.23 (d, *J* = 9.4 Hz, 1H), 4.08 (dt, *J* = 11.8, 6.1 Hz, 1H), 3.90 (dt, *J* = 11.0, 7.0 Hz, 1H), 2.65–2.58 (m, 1H), 2.31 (s, 3H), 2.24–2.17 (m, 2H), 2.02 (ddd, *J* = 11.4, 5.7, 2.5 Hz, 1H), 1.68 (s, 1H), 1.19 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 141.4, 140.8, 135.6, 129.2, 128.2 (2C), 127.1 (2C), 125.5, 124.9, 123.7, 119.0, 115.0, 113.8, 113.4, 110.7, 60.7, 49.6, 43.5, 41.6, 37.4, 34.5, 26.4, 16.1. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{25}H_{24}N_3O_2^+$: 398.1863, found: 398.1868. 96% ee; determined by HPLC (Chiralpak IF, hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm) t_R = 16.05 min (minor), 17.70 min (major). $[\alpha]_D^{22}$ = +16.7 (c = 0.1, CH_2Cl_2).



Methyl (1*S*,2*S*,3*S*)-9-acetyl-4-cyano-2-ethyl-3-(2-hydroxyethyl)-1-phenyl-2,3,4,9-tetrahydro-1H-carbazole-4-carboxylate (3ah)

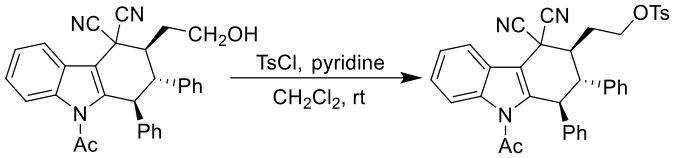
White solid (22.3 mg, 50% yield). Mp: 110-112 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94–7.87 (m, 1H), 7.57–7.47 (m, 1H), 7.41–7.31 (m, 2H), 7.15 (dd, *J* = 9.9, 7.1 Hz, 3H), 6.89 (d, *J* = 6.7 Hz, 2H), 4.52 (d, *J* = 9.2 Hz, 1H), 4.04 (dt, *J* = 11.7, 6.4 Hz, 1H), 3.88 (dt, *J* = 11.6, 6.3 Hz, 1H), 2.75 (dt, *J* = 11.5, 5.9 Hz, 1H), 2.27 (s, 3H), 2.17 (dq, *J* = 18.7, 6.5, 5.3 Hz, 1H), 2.07–1.95 (m, 2H), 1.65 (s, 1H), 1.57 (ddt, *J* = 11.5, 7.8, 4.1 Hz, 2H), 1.01 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 141.9, 140.9, 135.7, 128.8 (2C), 128.3 (2C), 127.1, 125.4, 125.0, 123.7, 119.1, 115.3, 113.8, 113.5, 110.1, 59.8, 45.5, 43.9, 40.3, 36.5, 33.9, 26.5, 20.0, 8.2. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{26}H_{26}N_3O_2^+$: 412.2020, found: 412.2015. 98% ee; determined by HPLC (Chiralpak IF, hexane/*i*-PrOH = 90/10, 1.0 mL/min, 254 nm) t_R = 17.53 min (minor), 19.96 min (major). $[\alpha]_D^{22}$ = +17.0 (c = 0.1, CH_2Cl_2).



Methyl (*1S,3R*)-9-acetyl-4-cyano-3-(2-hydroxyethyl)-3-methyl-1-phenyl-2,3,4,9-tetrahydro-1H-carbazole-4-carboxylate (3ai)

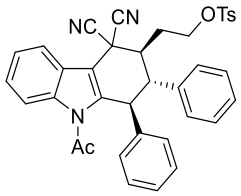
White solid (30.6 mg, 71% yield). Mp: 107-109 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 6.3, 2.7 Hz, 1H), 7.71 (dq, *J* = 8.1, 4.0, 3.6 Hz, 1H), 7.49-7.40 (m, 2H), 7.25 (dt, *J* = 15.3, 6.8 Hz, 3H), 6.97 (d, *J* = 5.6 Hz, 2H), 4.60 (dd, *J* = 10.8, 6.5 Hz, 1H), 3.97 (ddt, *J* = 17.5, 10.9, 5.2 Hz, 2H), 2.51 (dd, *J* = 14.6, 6.5 Hz, 1H), 2.41 (s, 3H), 2.24-2.08 (m, 2H), 1.93 (dd, *J* = 14.6, 10.9 Hz, 1H), 1.61 (s, 1H), 1.52 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 142.8, 139.0, 135.7, 128.8 (2C), 127.4 (2C), 127.0, 125.6, 125.5, 123.8, 118.9, 114.1, 113.8, 113.6, 110.1, 58.5, 43.0, 41.8, 41.5, 41.2, 39.5, 26.6, 18.4. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{25}H_{24}N_3O_2^+$: 398.1863, found: 398.1865. 43% ee; determined by HPLC (Chiralpak IF, hexane/*i*-PrOH = 90/10, 1.0 mL/min, 254 nm) t_R = 17.02 min (minor), 20.91 min (major). $[\alpha]_D^{22}$ = +132.3 (c = 0.1, CH_2Cl_2).

4. General procedure for the synthesis of 4ab



3ab **4ab**

General procedure: To a solution of **3ab** (23.0 mg, 0.05 mmol) in dichloromethane (1.0 mL) was added TsCl (15.3 mg, 0.08 mmol) and pyridine (0.1 mL) at 0 °C. The reaction mixture was stirred for 12 h at room temperature. Once the starting material was consumed (monitored by TLC), the residue was directed purified by column chromatography on silica gel (petroleum ether/EtOAc = 8/1 to 2/1) to afford compound **4ab**.



2-((*1S,2S,3S*)-9-acetyl-4,4-dicyano-1,2-diphenyl-2,3,4,9-tetrahydro-1H-carbazol-3-yl)ethyl 4-methylbenzenesulfonate (4ab)

White solid (27.6 mg, 90% yield). Mp: 122-124 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03–7.96 (m, 1H), 7.69 (d, *J* = 8.3 Hz, 2H), 7.67–7.64 (m, 1H), 7.46 (q, *J* = 5.3, 3.7 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.28 (s, 4H), 7.04 (dt, *J* = 14.0, 6.9 Hz, 4H), 6.49 (d, *J* = 7.0 Hz, 2H), 4.85 (d, *J* = 9.7 Hz, 1H), 3.70 (dt, *J* = 10.5, 6.1 Hz, 1H), 3.44 (ddd, *J* = 10.2, 8.0, 6.1 Hz, 1H), 3.05 (ddd, *J* = 10.2, 6.6, 3.5 Hz, 1H), 2.91 (dd, *J* = 11.9, 9.8 Hz, 1H), 2.43 (s, 3H), 2.34 (s, 3H), 2.19 (dtd, *J* = 14.7, 7.4, 3.4 Hz, 1H), 1.92 (dq, *J* = 15.0, 5.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 144.9, 140.7, 140.2, 137.8, 135.7, 132.7, 129.8 (3C), 129.0 (2C), 128.3 (2C), 128.0 (2C), 128.0 (3C), 126.9 (2C), 125.8, 124.8, 123.9, 119.0, 114.0, 113.7, 113.4, 110.4, 67.2, 54.7, 49.8, 42.3, 37.6, 31.8, 26.5, 21.6. HRMS (ESI-TOF) calcd [M+H$^+$] for $C_{37}H_{32}N_3O_4S^+$: 614.2108, found: 614.2110. 95% ee; HPLC (Chiralpak AD-H, n-hexane/i-propanol = 80/20, 1.0 mL/min, 254 nm) t_R= 16.48 min (major), 20.63 min (minor). $[\alpha]_D^{22}$ = +130.3 (c = 0.1, CH_2Cl_2).

5. The absolute configuration determination of (*1S, 2S, 3S*)-4ab

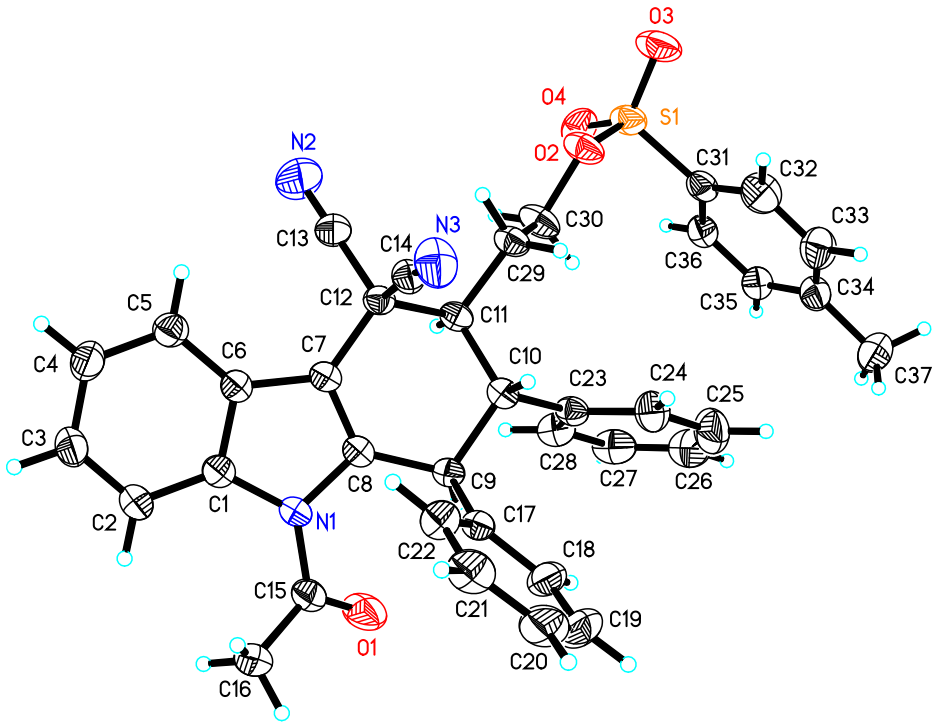


Fig S1. X-ray structure of (*1S,2S,3S*)-**4ab**.Ellipsoids are drawn at the 30%probability level.

Crystal data and structure refinement for CCDC 1854800

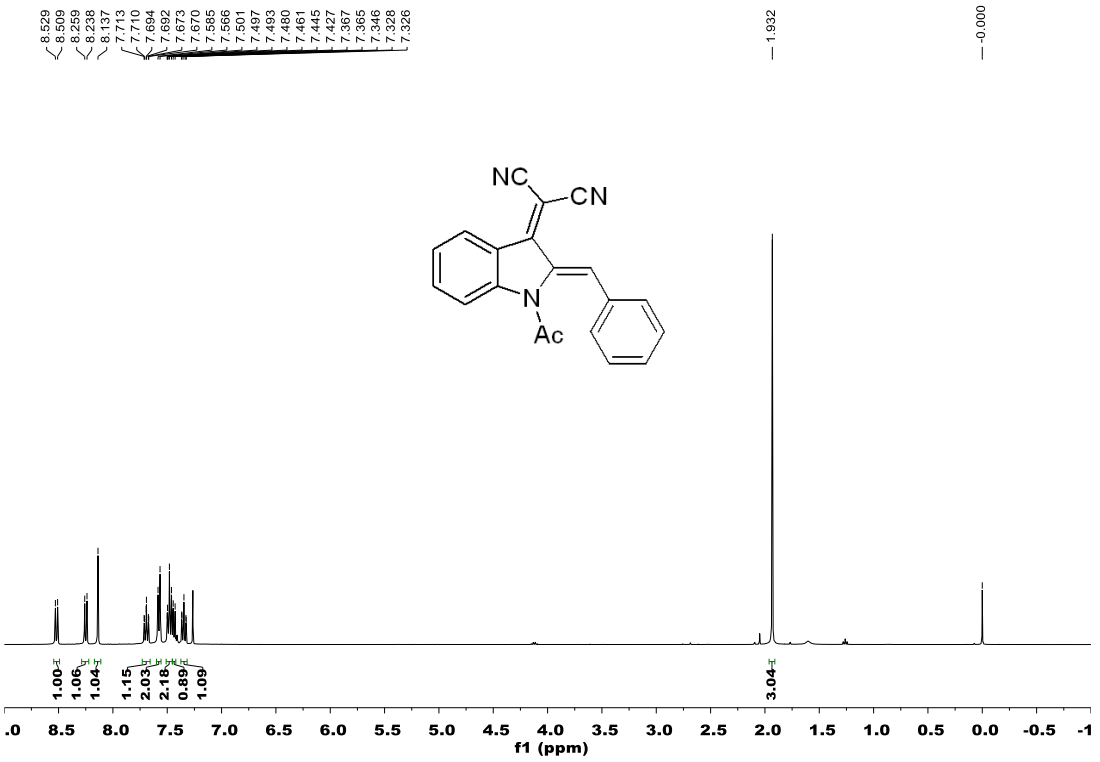
(CCDC 1854800 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html.)

Identification code	mo_d8v18344_0m	
Empirical formula	$C_{37}H_{31}N_3O_4S$	
Formula weight	613.71	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 13.6363(6) Å	α = 90 °.
	b = 8.5322(3) Å	β = 116.2050(10) °.
	c = 15.2209(8) Å	γ = 90 °.
Volume	1588.90(12) $Å^3$	
Z	2	
Density (calculated)	1.283 Mg/m^3	

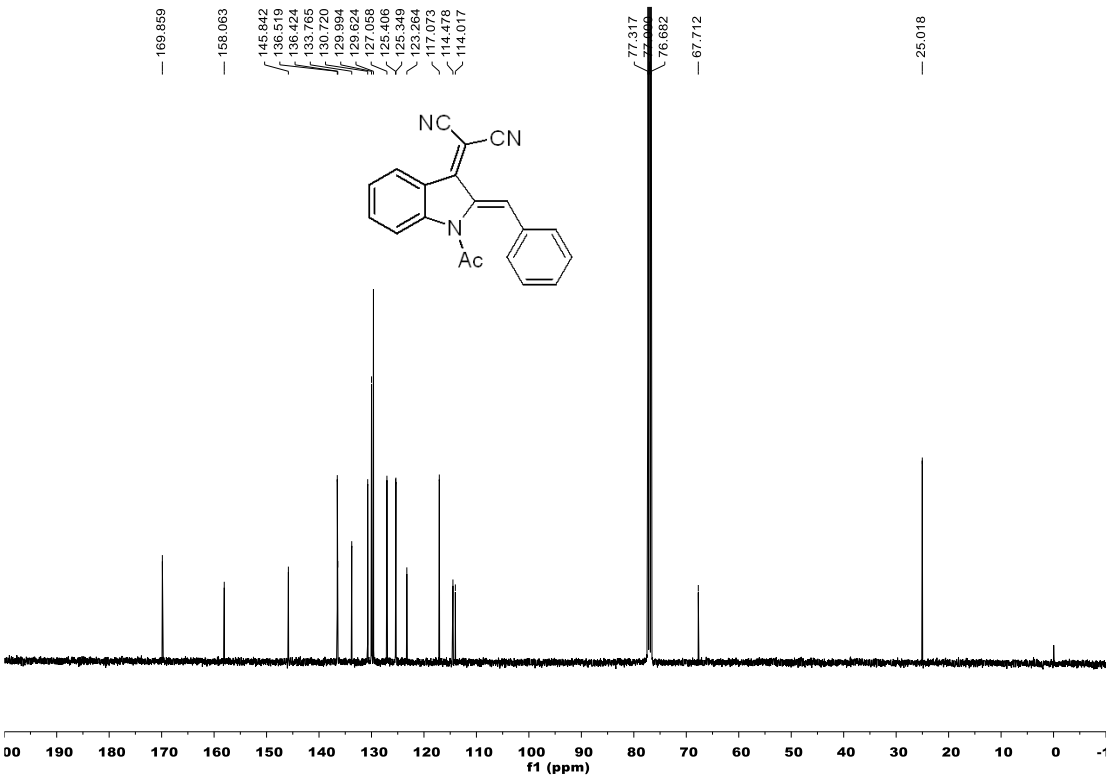
Absorption coefficient	0.147 mm^{-1}
F(000)	644
Crystal size	0.200 x 0.170 x 0.130 mm^3
Theta range for data collection	2.681 to 25.999 °.
Index ranges	-16<=h<=16, -10<=k<=10, -18<=l<=18
Reflections collected	23737
Independent reflections	6224 [R(int) = 0.0457]
Completeness to theta = 25.242 °	99.4 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.7065
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6224 / 4 / 409
Goodness-of-fit on F^2	1.063
Final R indices [I>2sigma(I)]	R1 = 0.0388, wR2 = 0.0783
R indices (all data)	R1 = 0.0513, wR2 = 0.0857
Absolute structure parameter	-0.03(4)
Extinction coefficient	0.028(3)
Largest diff. peak and hole	0.127 and -0.173 e.$Å^{-3}$

6. ^{1}H and ^{13}C NMR spectra

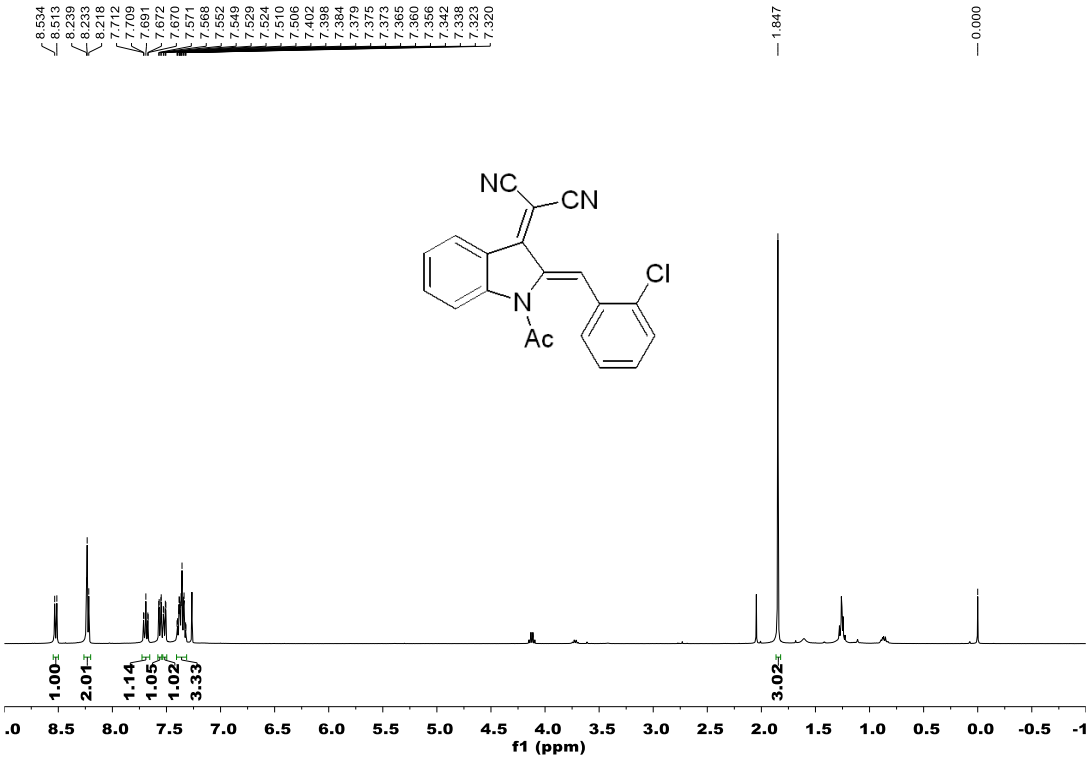
^{1}H NMR spectrum of 1a



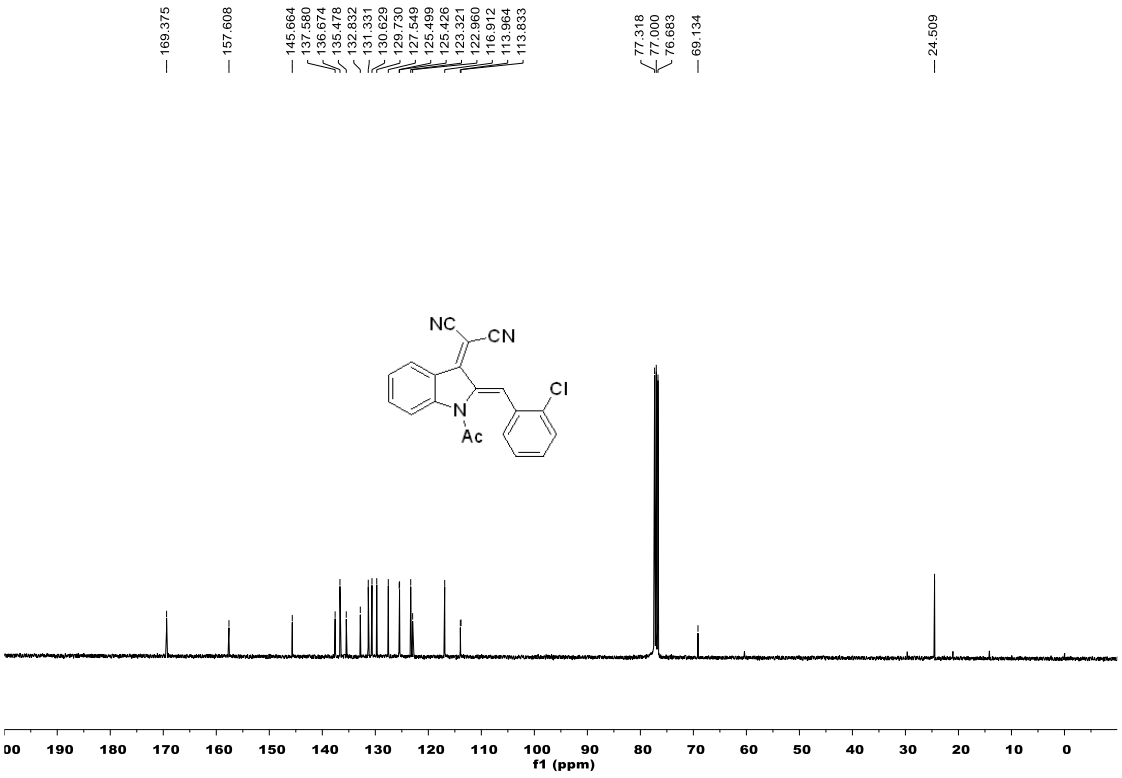
^{13}C NMR spectrum of 1a



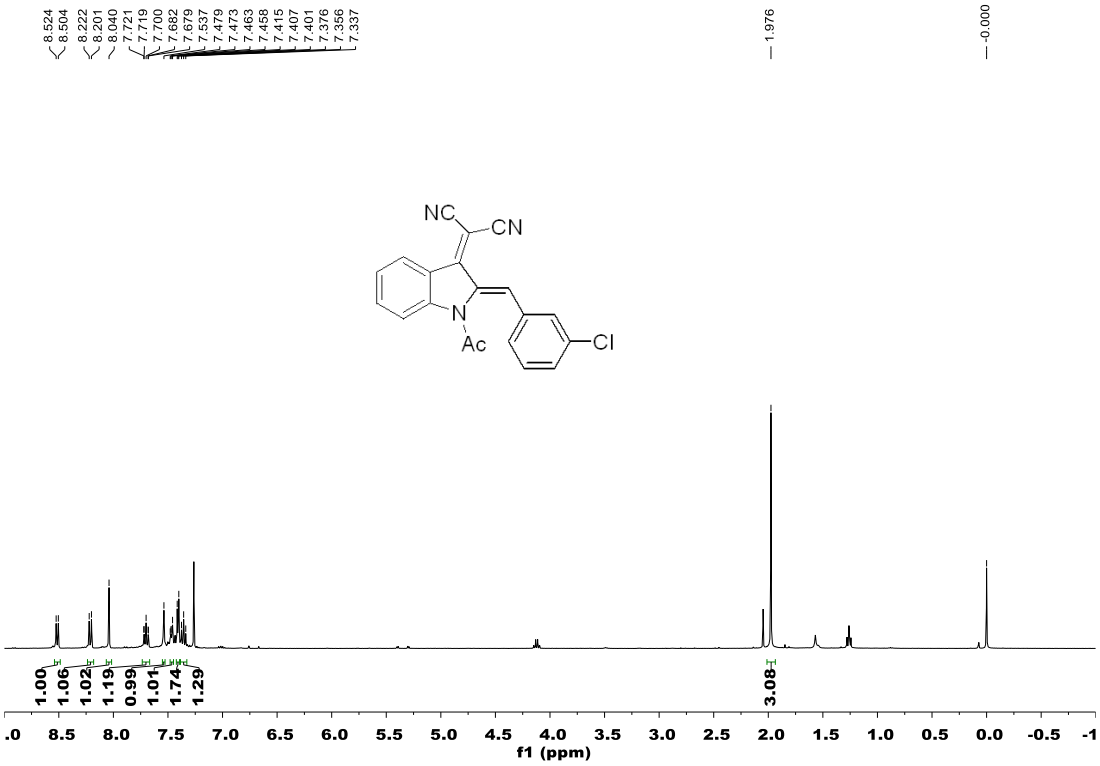
^{1}H NMR spectrum of 1b



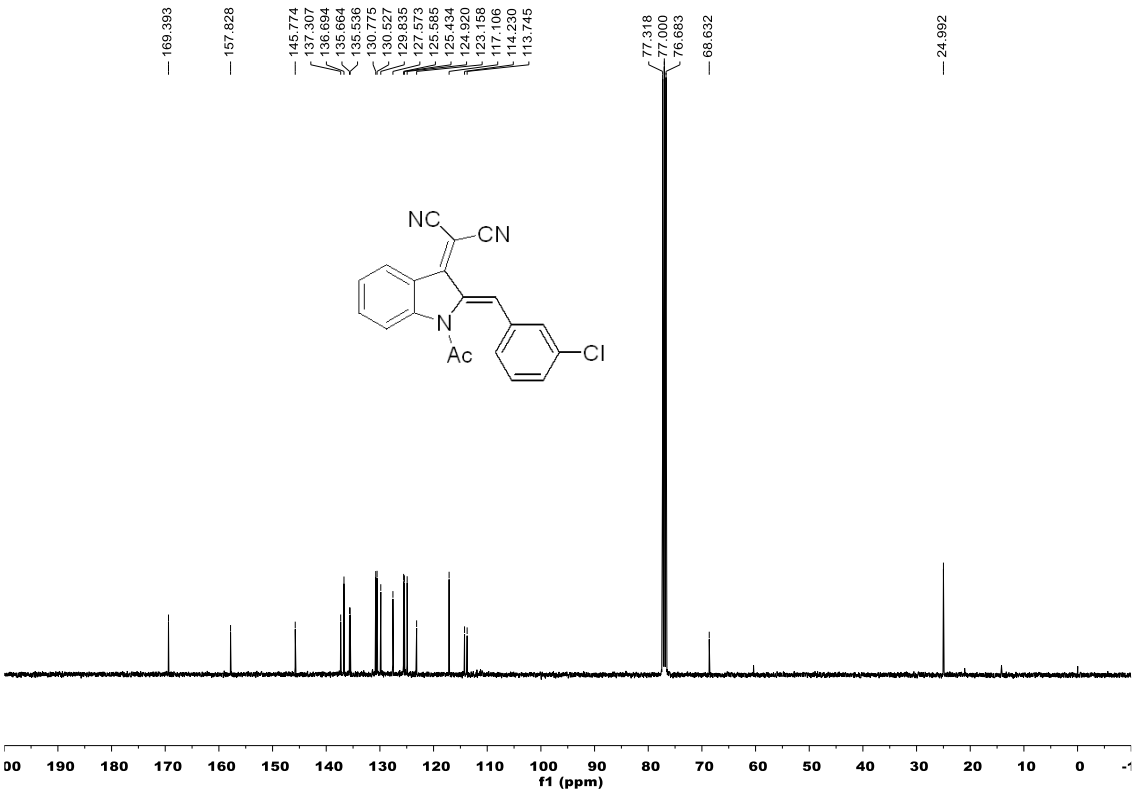
^{13}C NMR spectrum of 1b



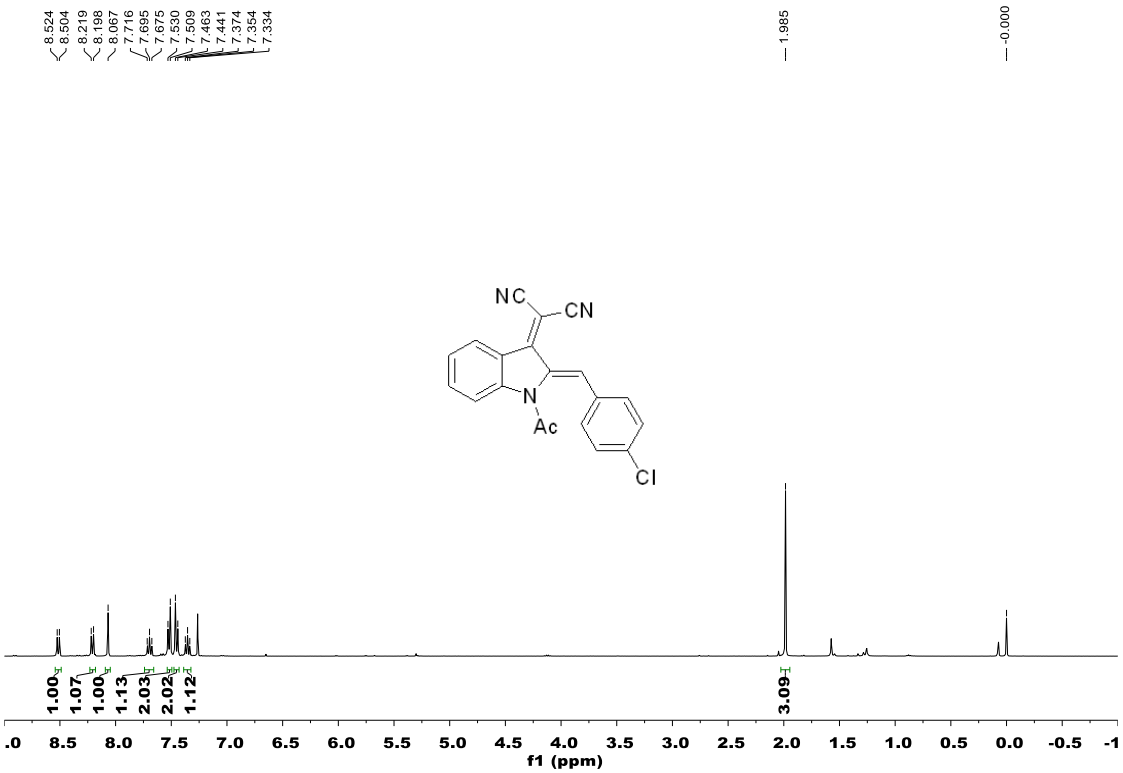
^{1}H NMR spectrum of 1c



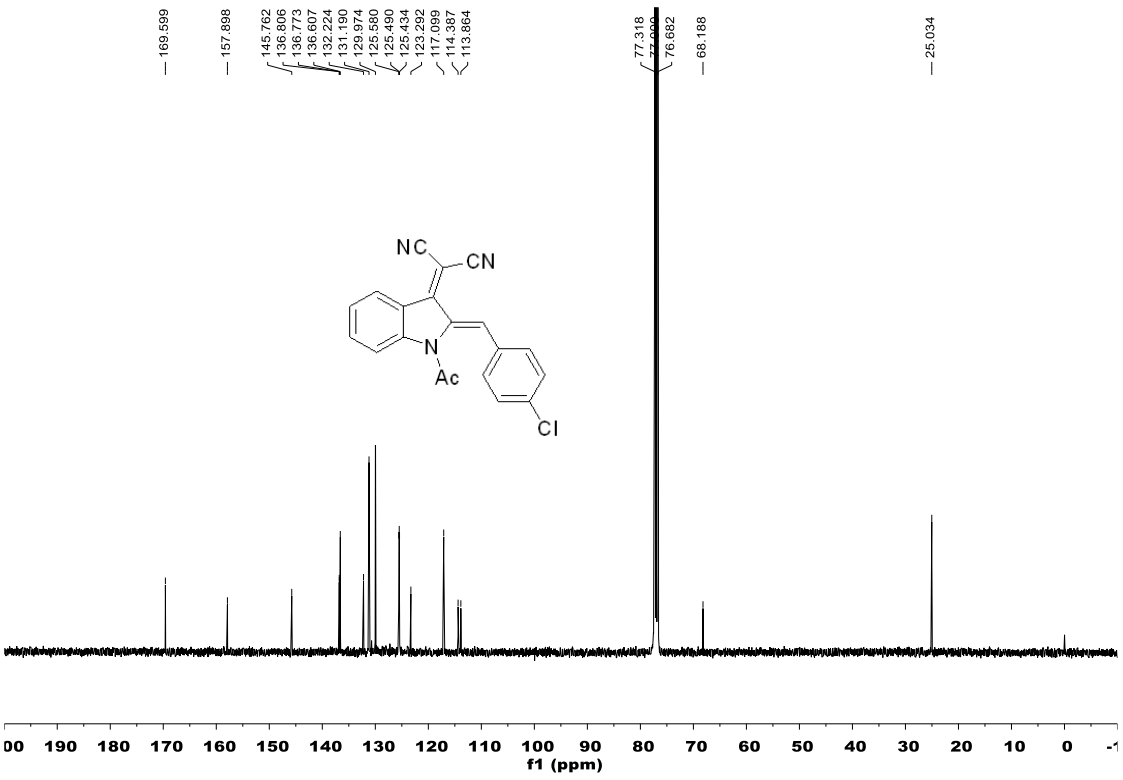
^{13}C NMR spectrum of 1c



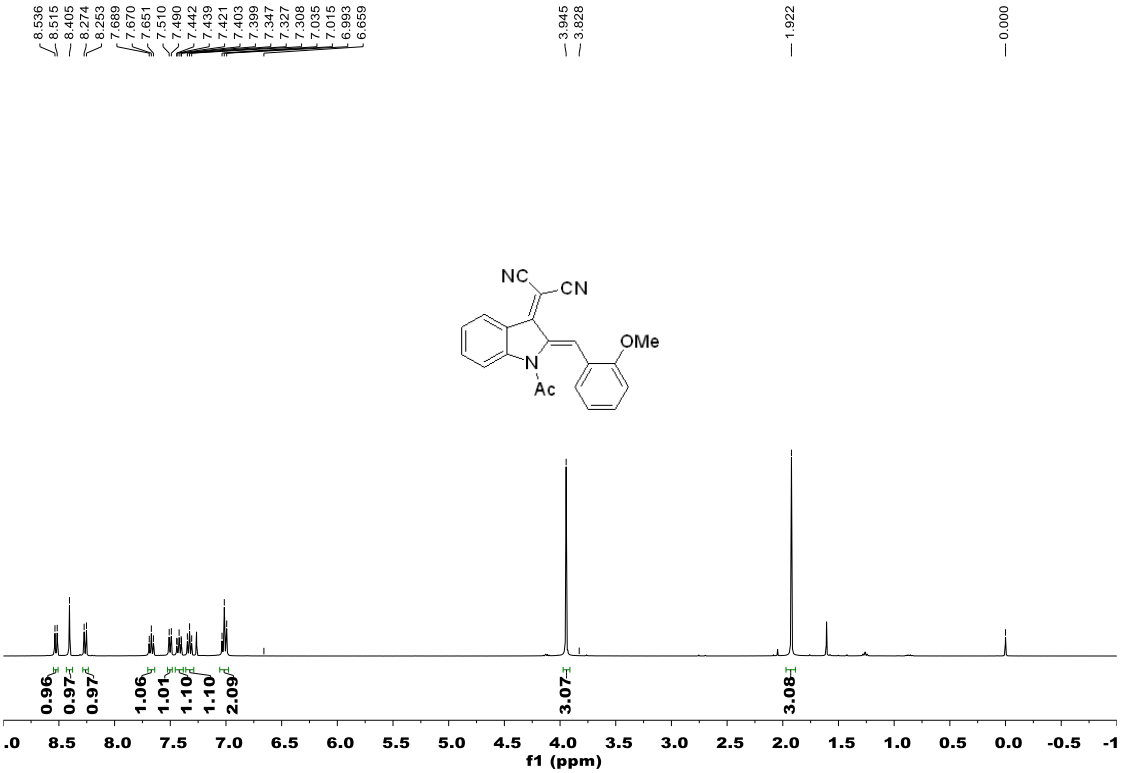
^{1}H NMR spectrum of 1d



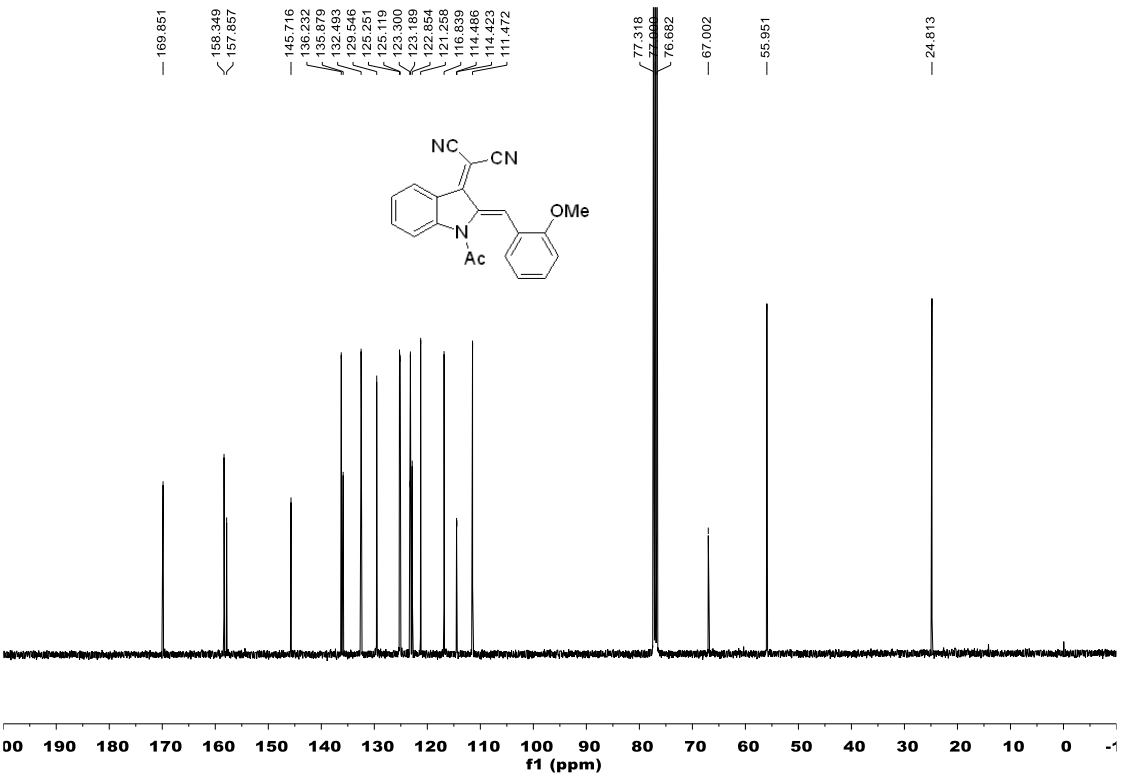
^{13}C NMR spectrum of 1d



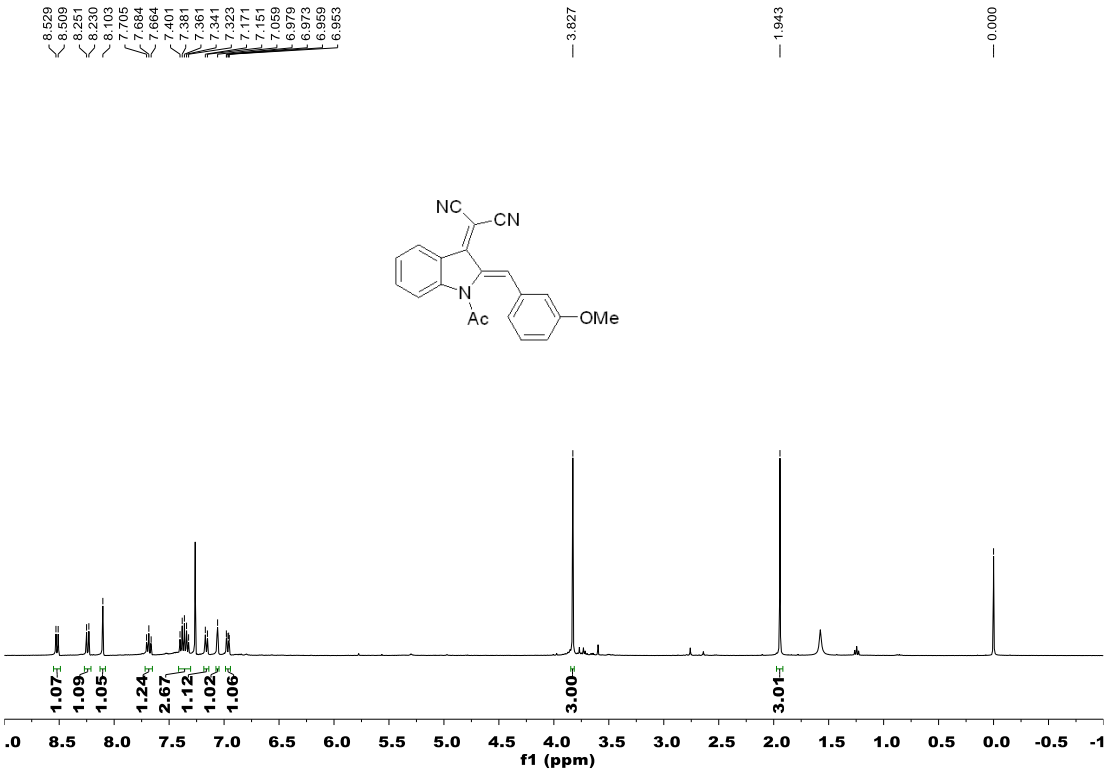
^{1}H NMR spectrum of 1e



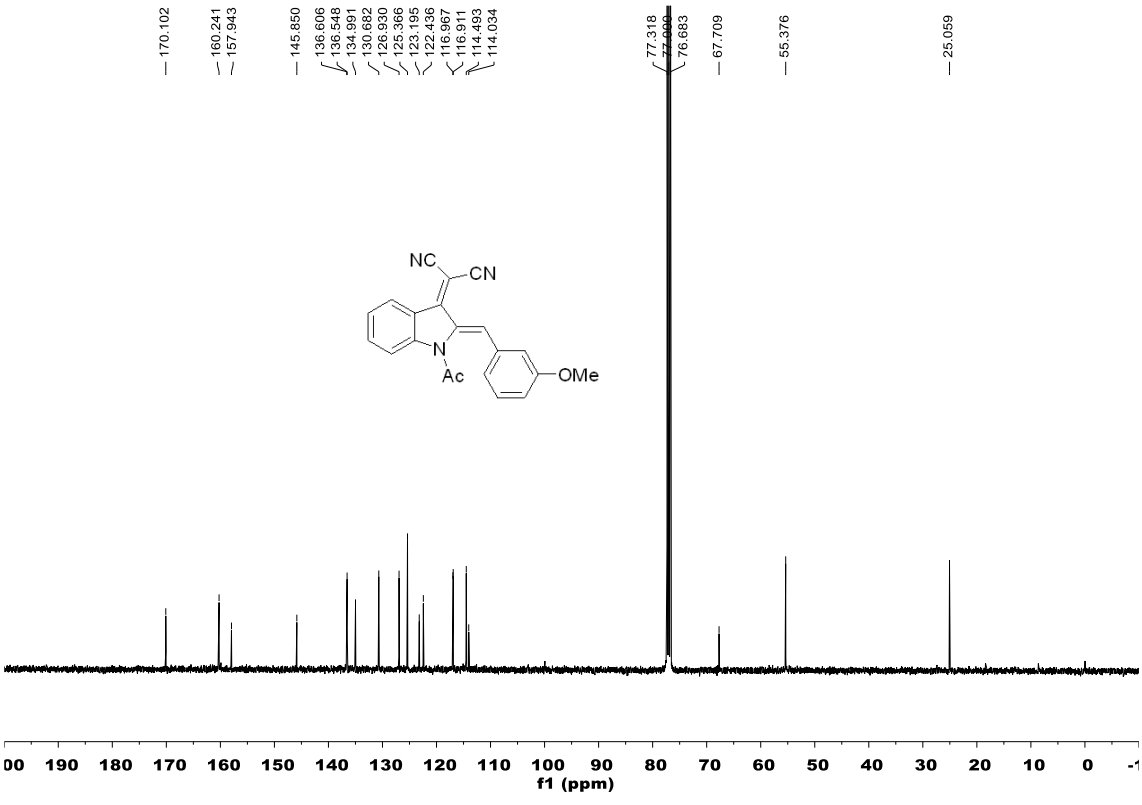
^{13}C NMR spectrum of 1e



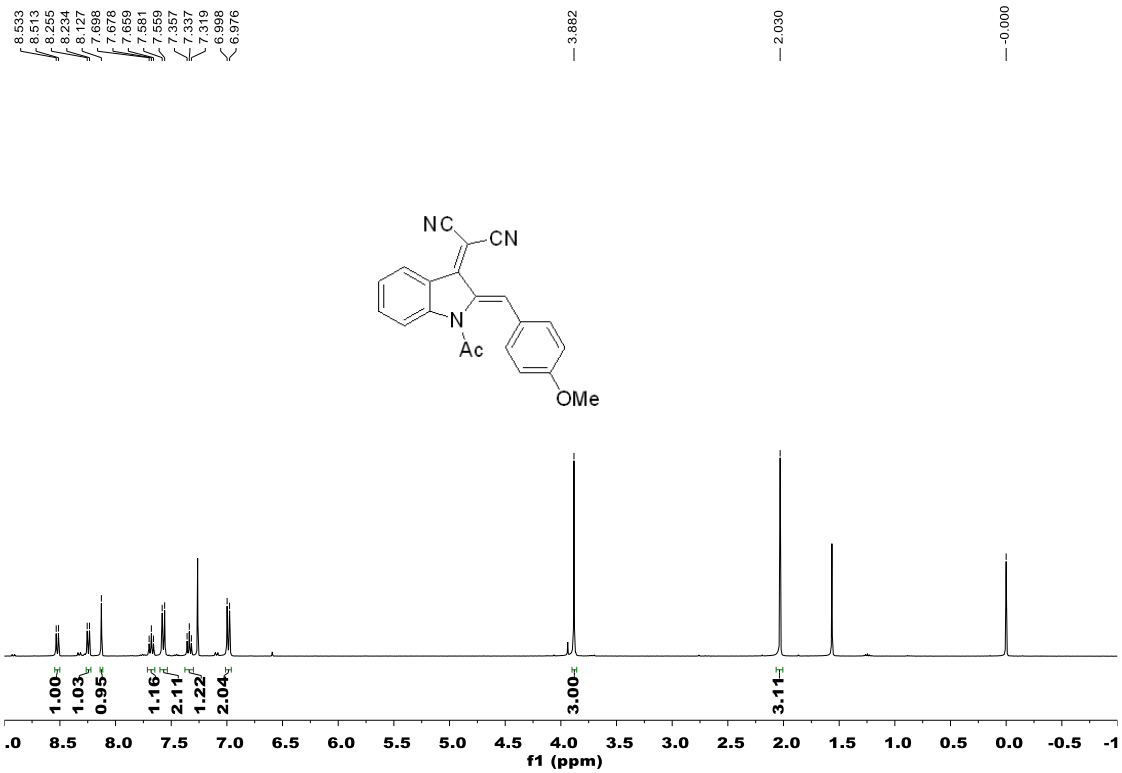
^{1}H NMR spectrum of 1f



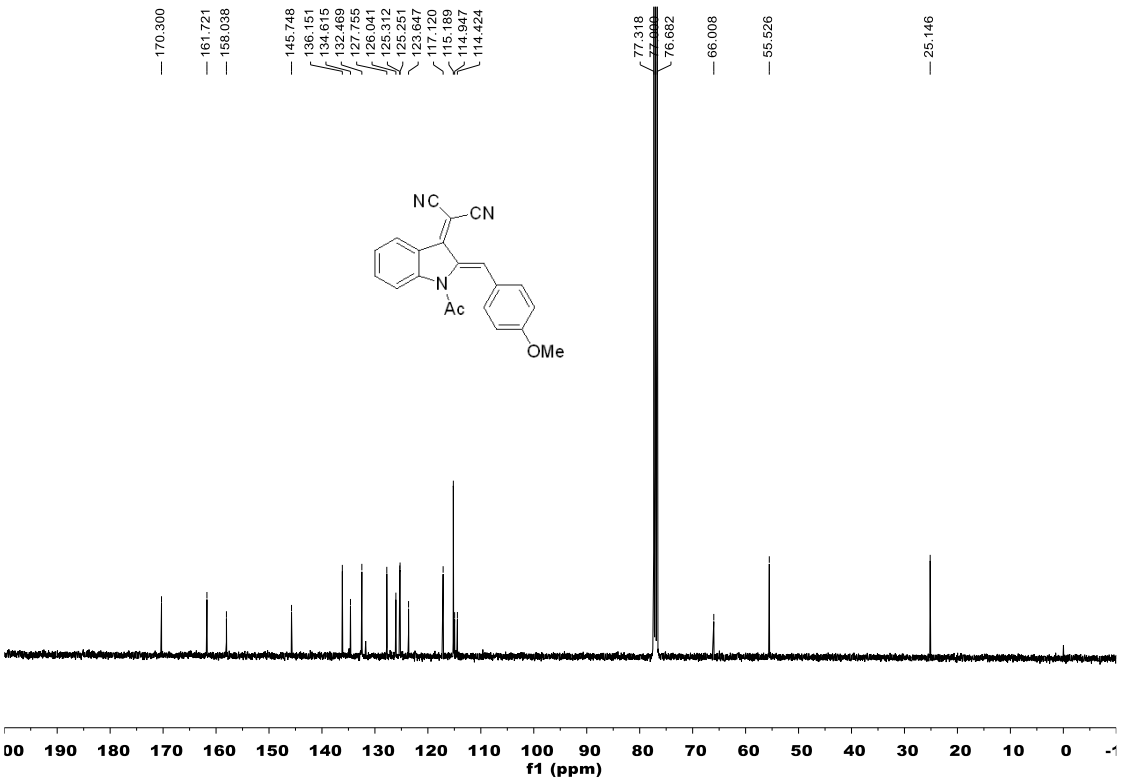
^{13}C NMR spectrum of 1f



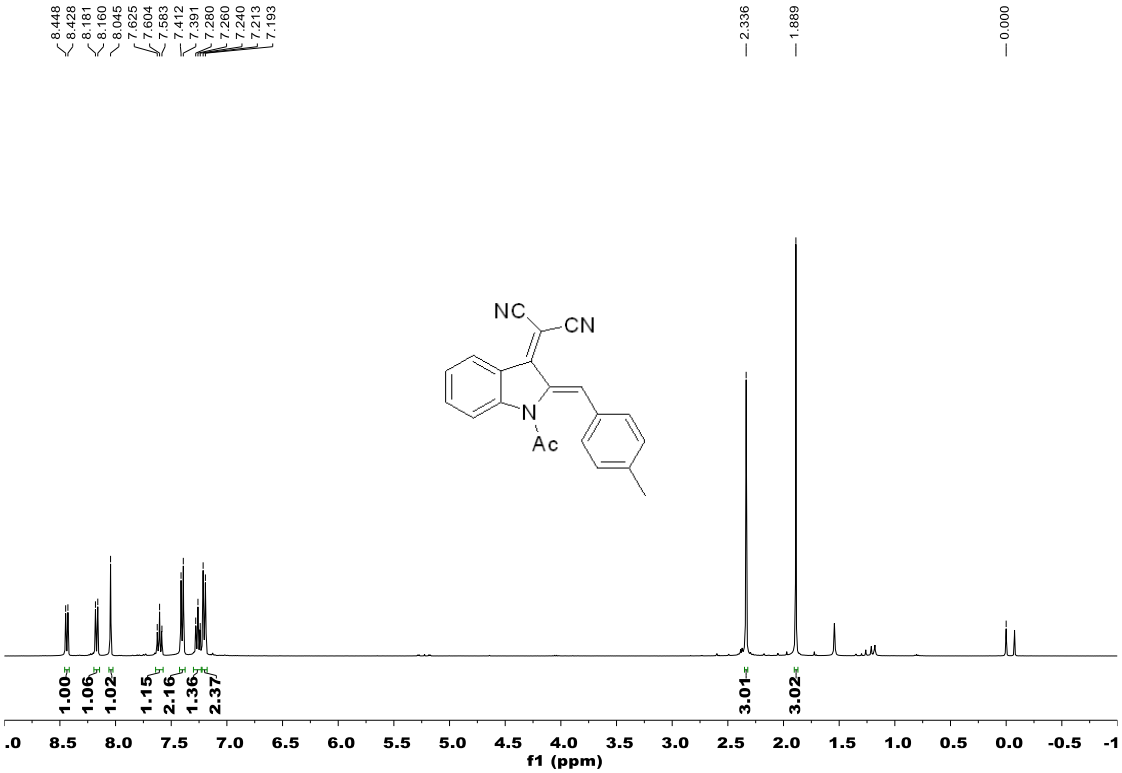
^{1}H NMR spectrum of 1g



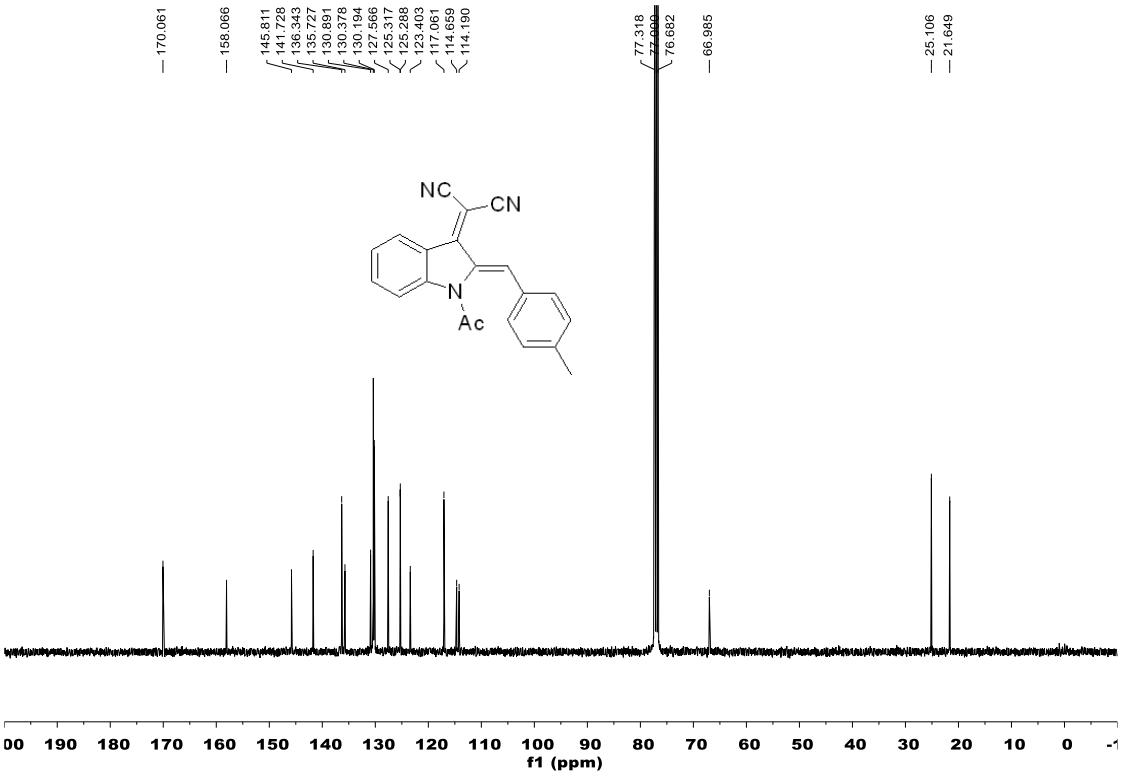
^{13}C NMR spectrum of 1g



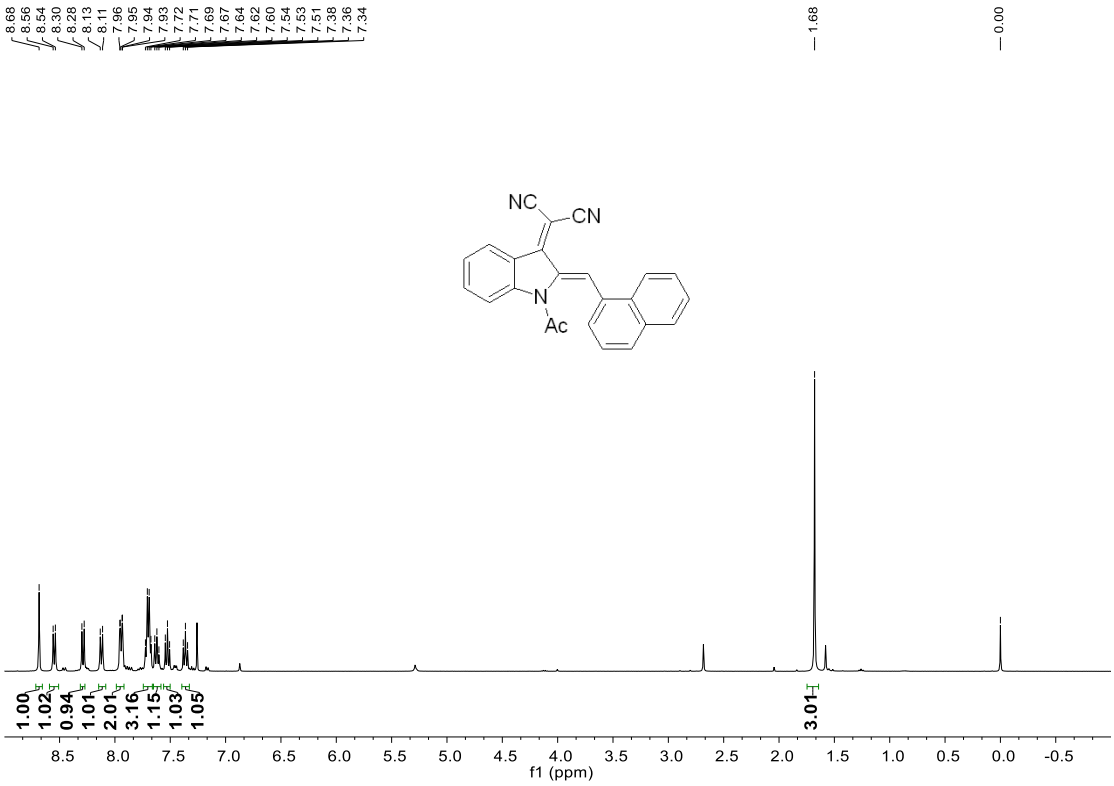
^{1}H NMR spectrum of 1h



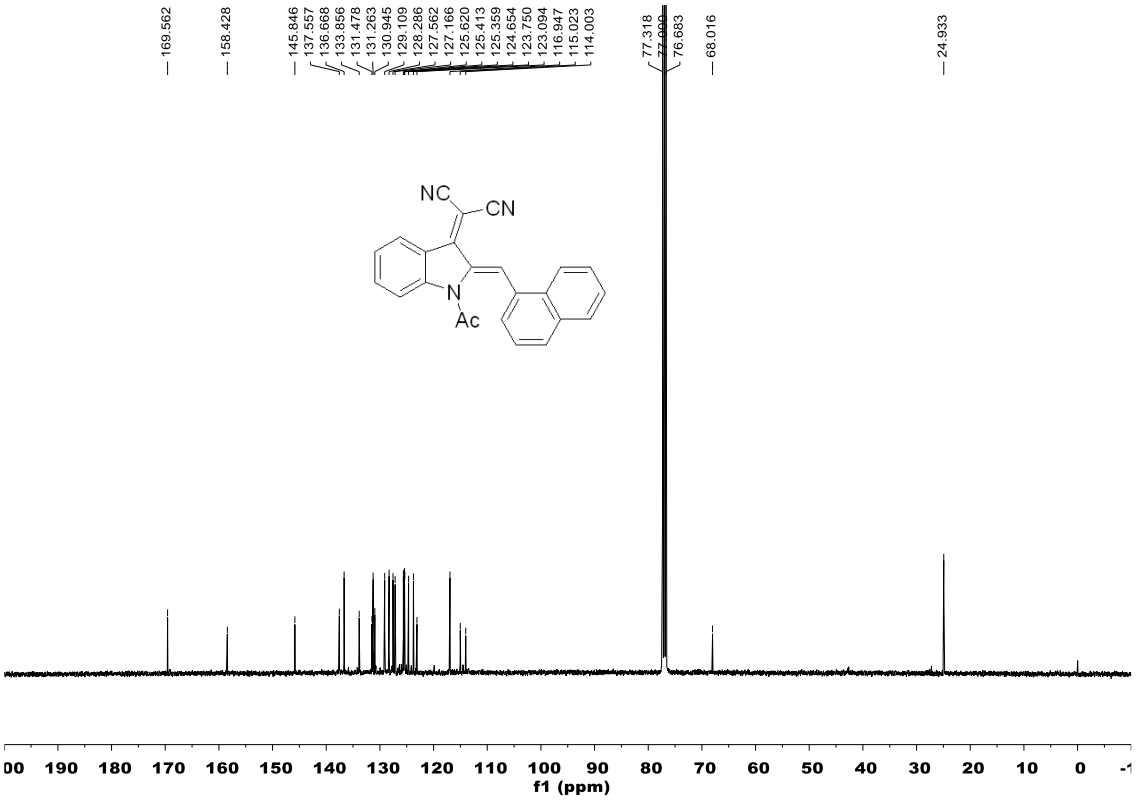
^{13}C NMR spectrum of 1h



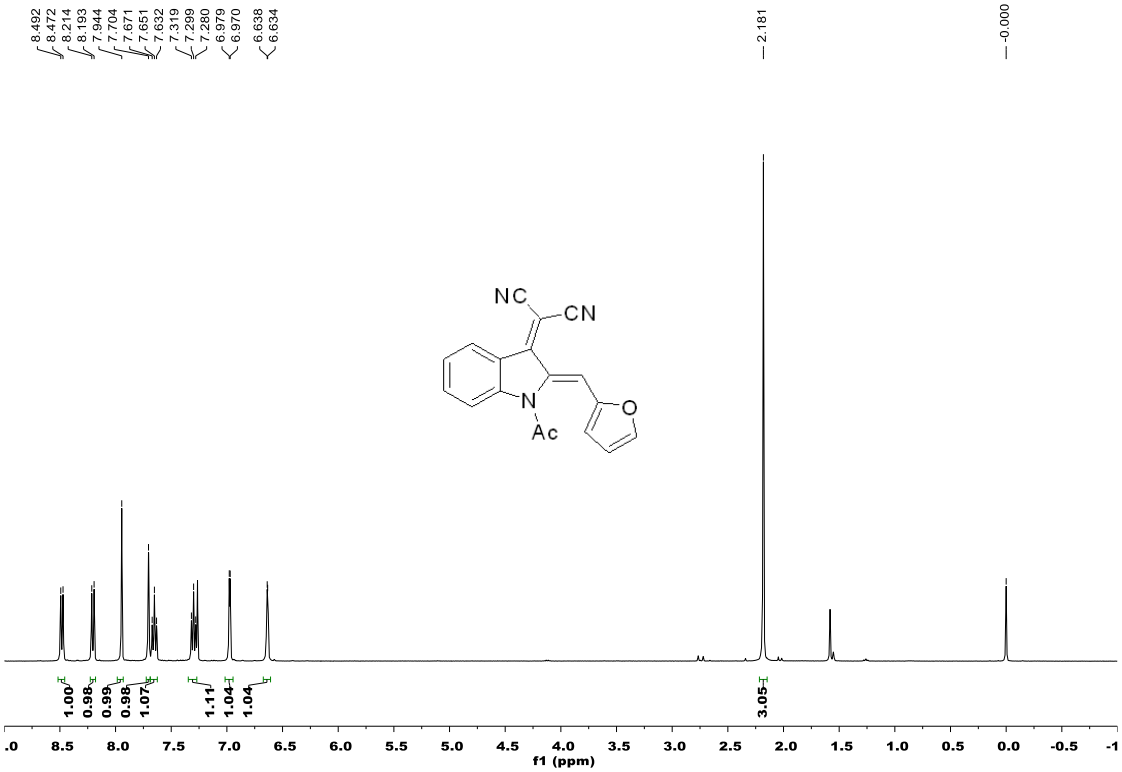
^{1}H NMR spectrum of 1i



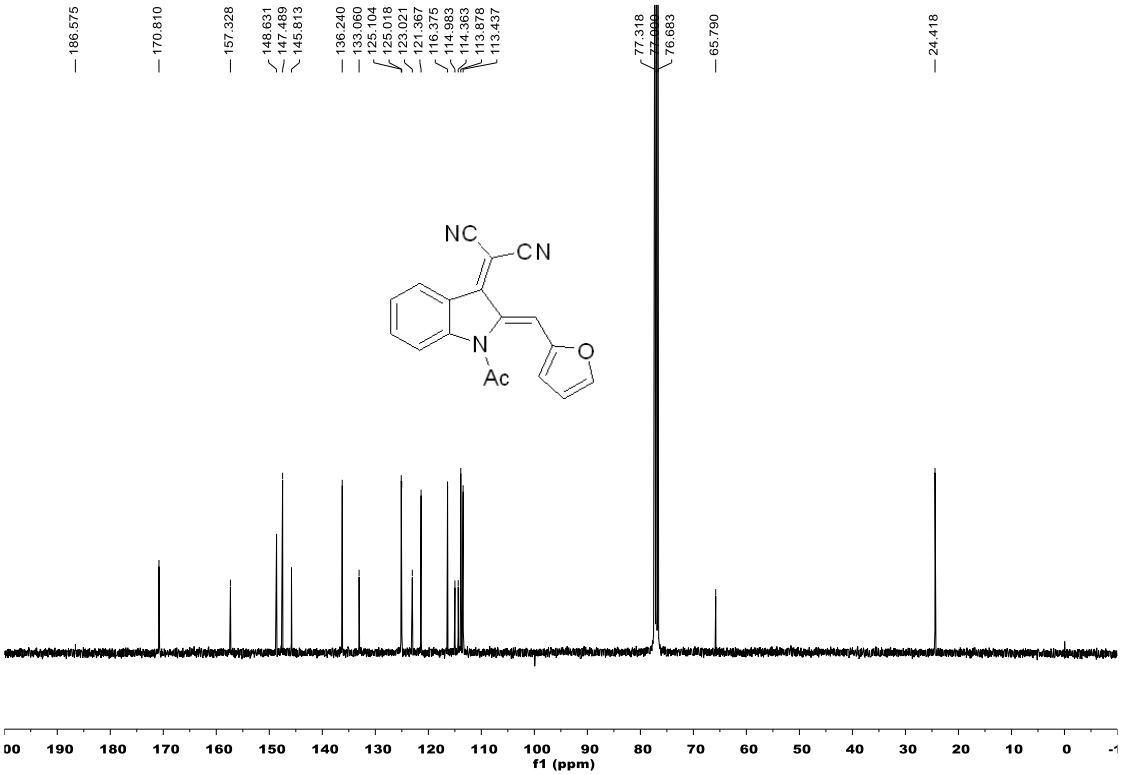
^{13}C NMR spectrum of 1i



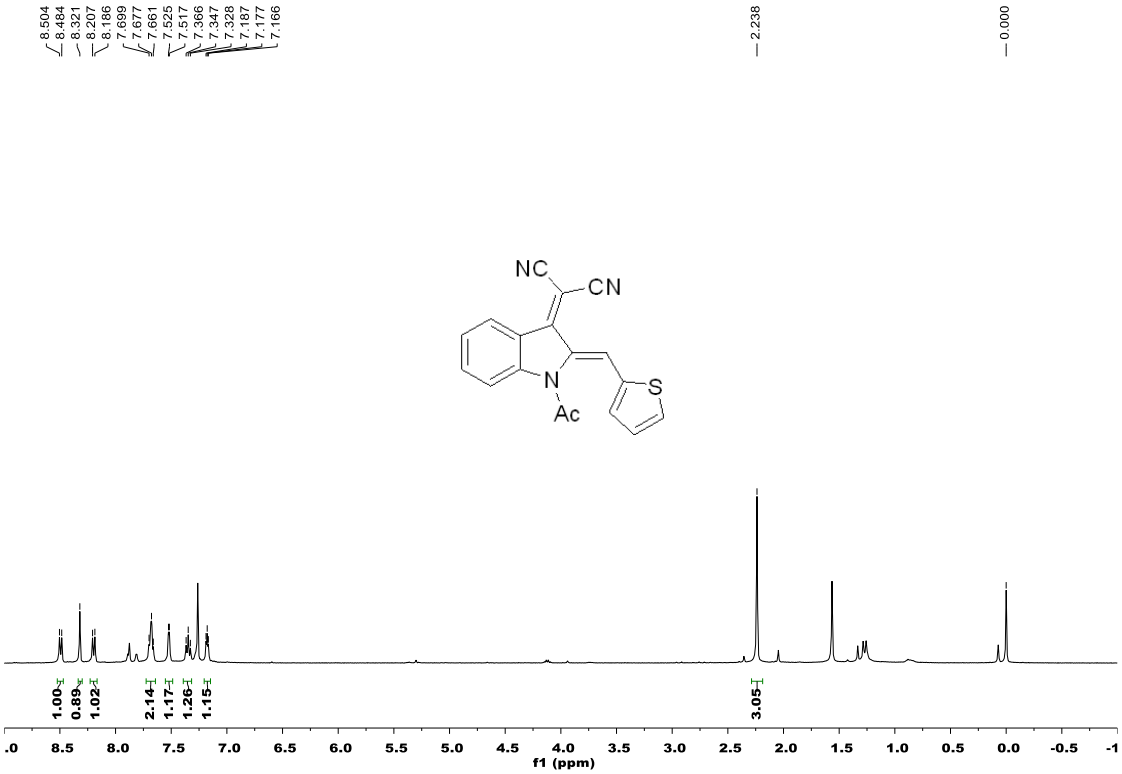
^{1}H NMR spectrum of 1j



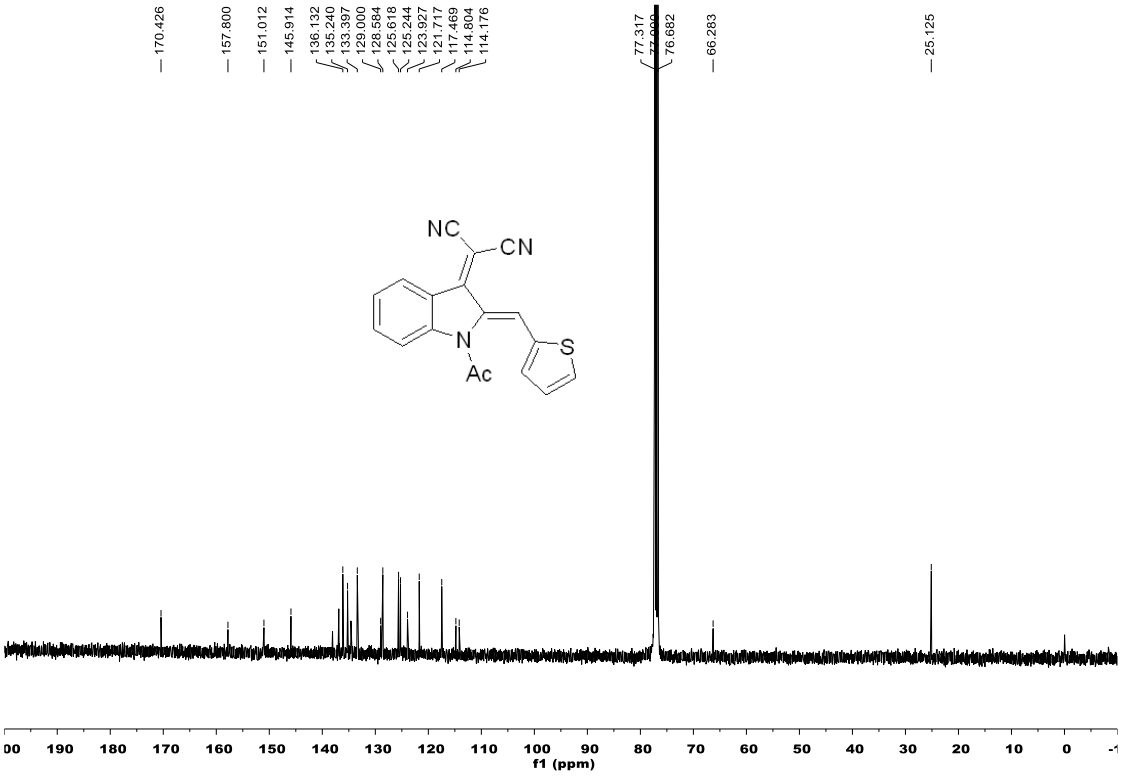
^{13}C NMR spectrum of 1j



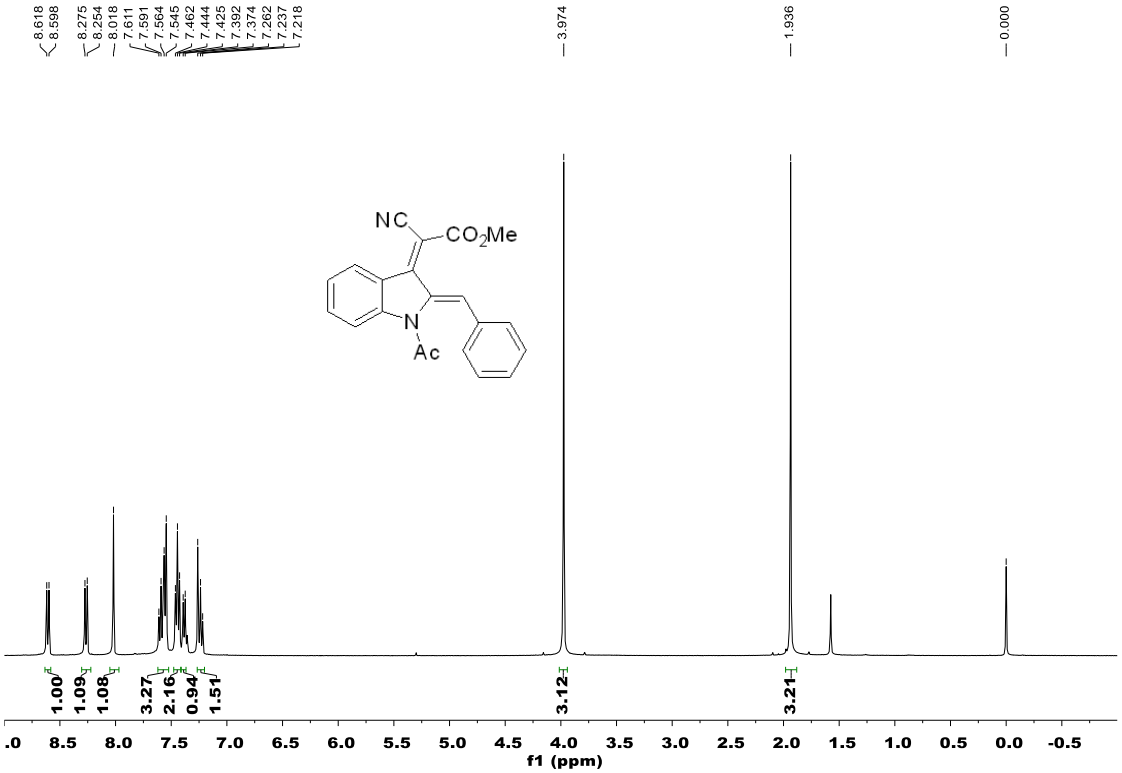
^{1}H NMR spectrum of 1k



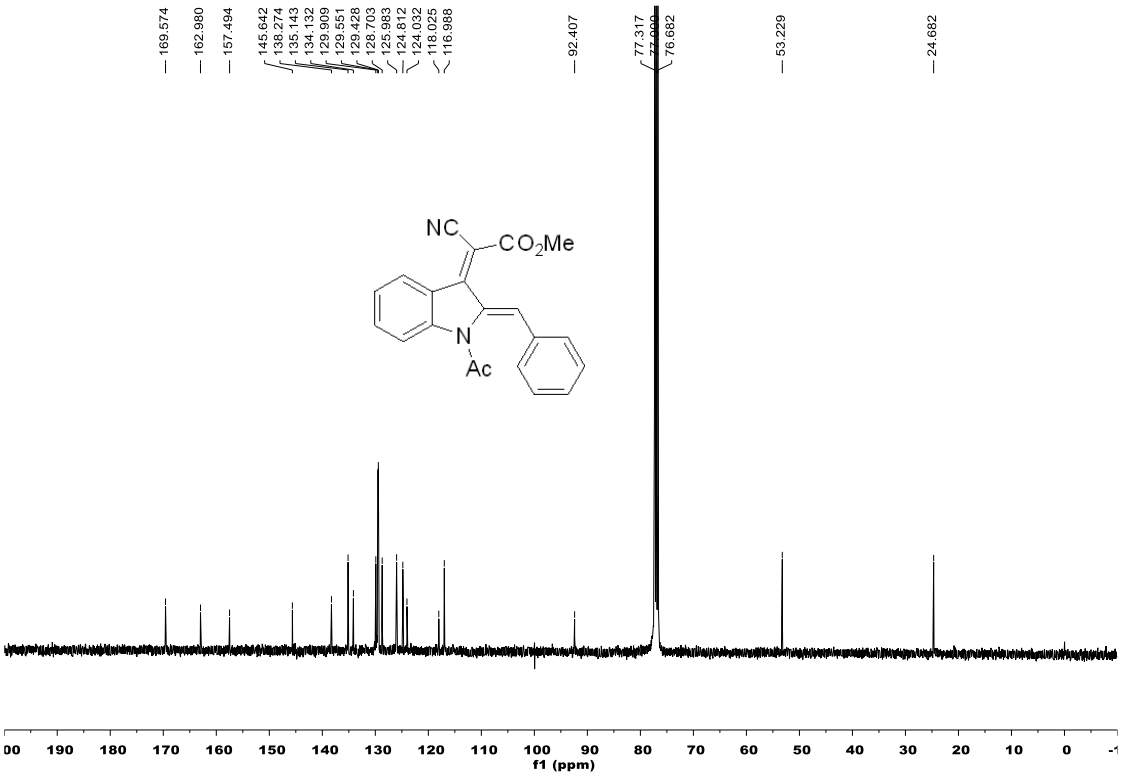
^{13}C NMR spectrum of 1k



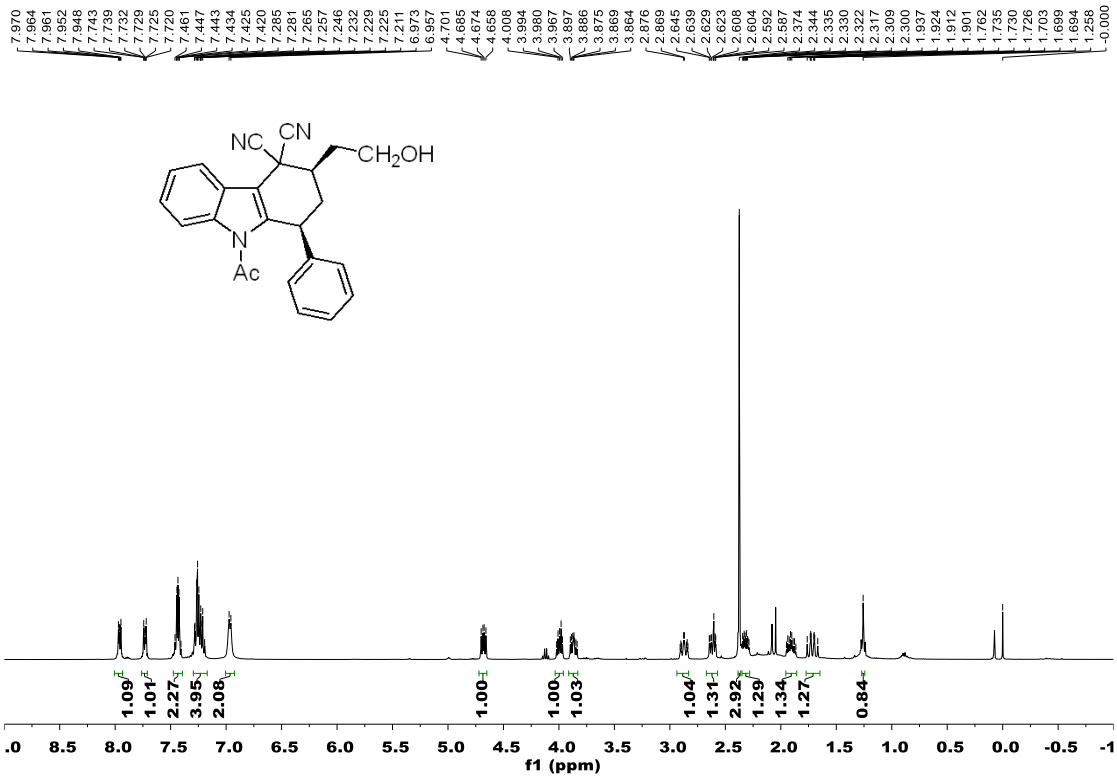
^{1}H NMR spectrum of 1l



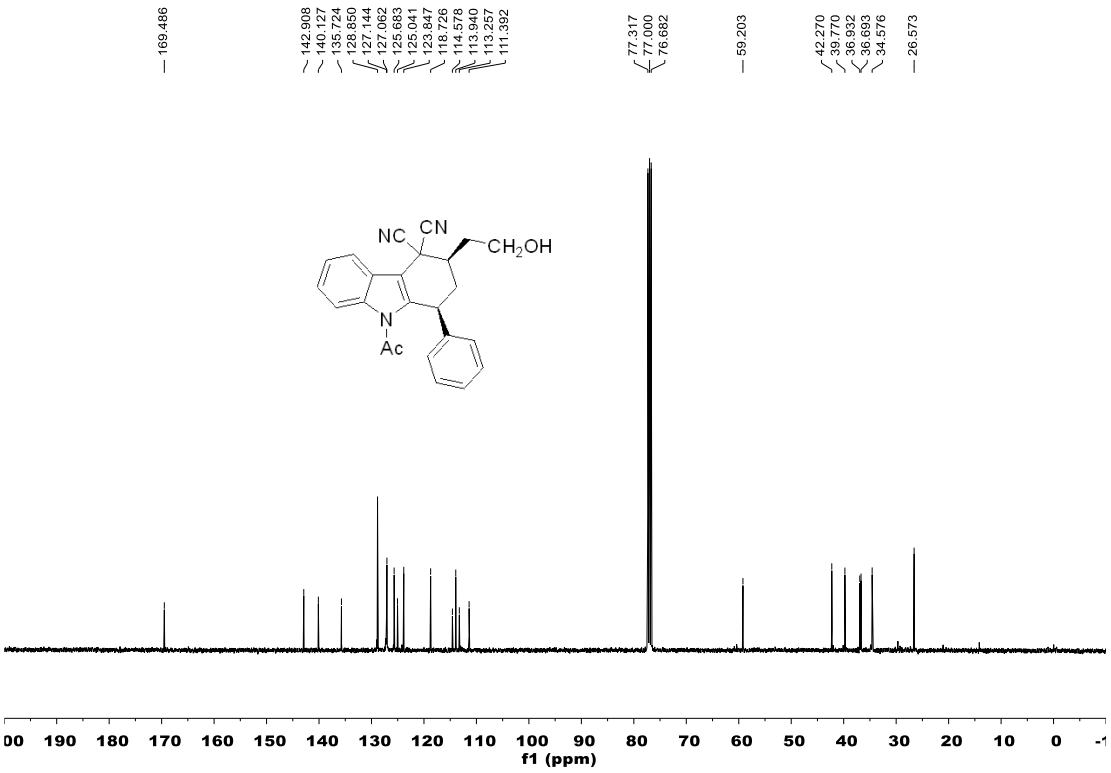
^{13}C NMR spectrum of 1l



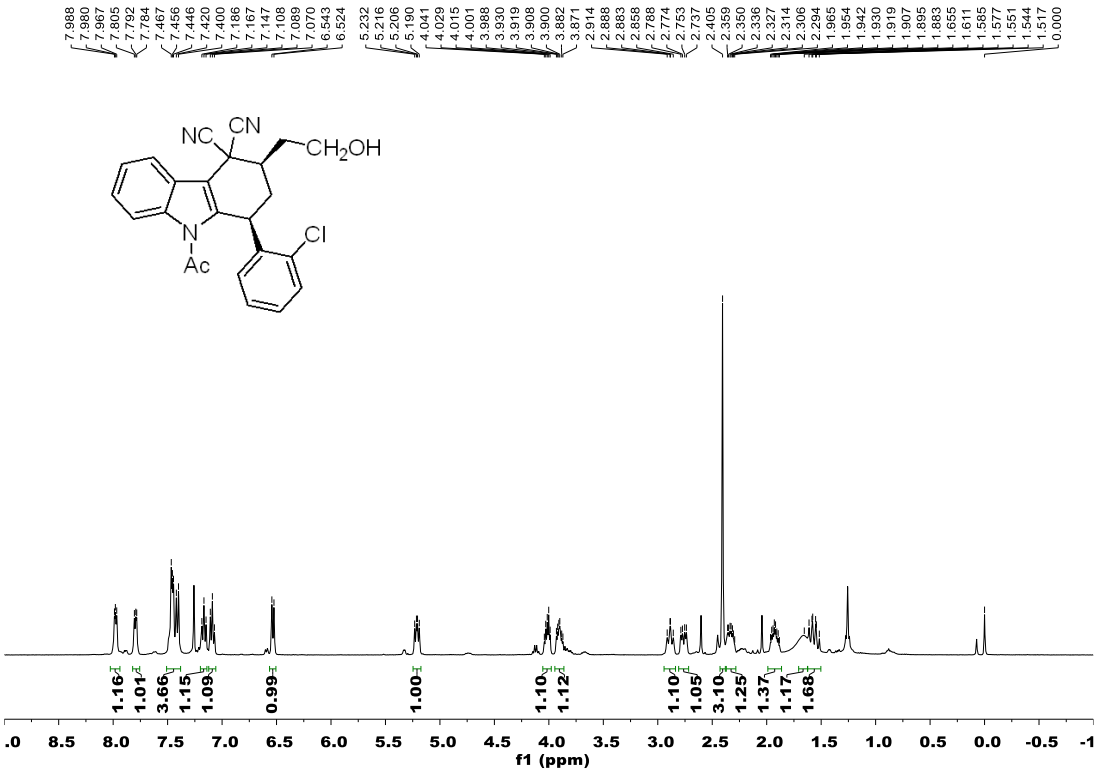
^{1}H NMR spectrum of 3aa



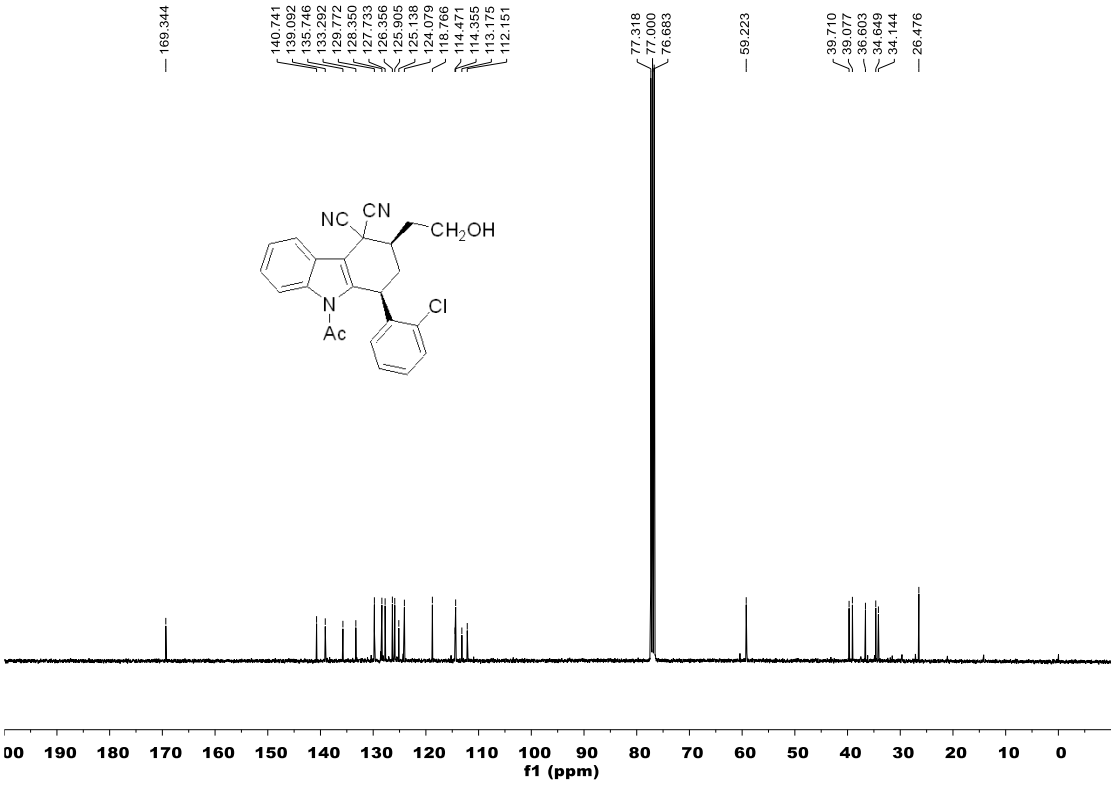
^{13}C NMR spectrum of 3aa



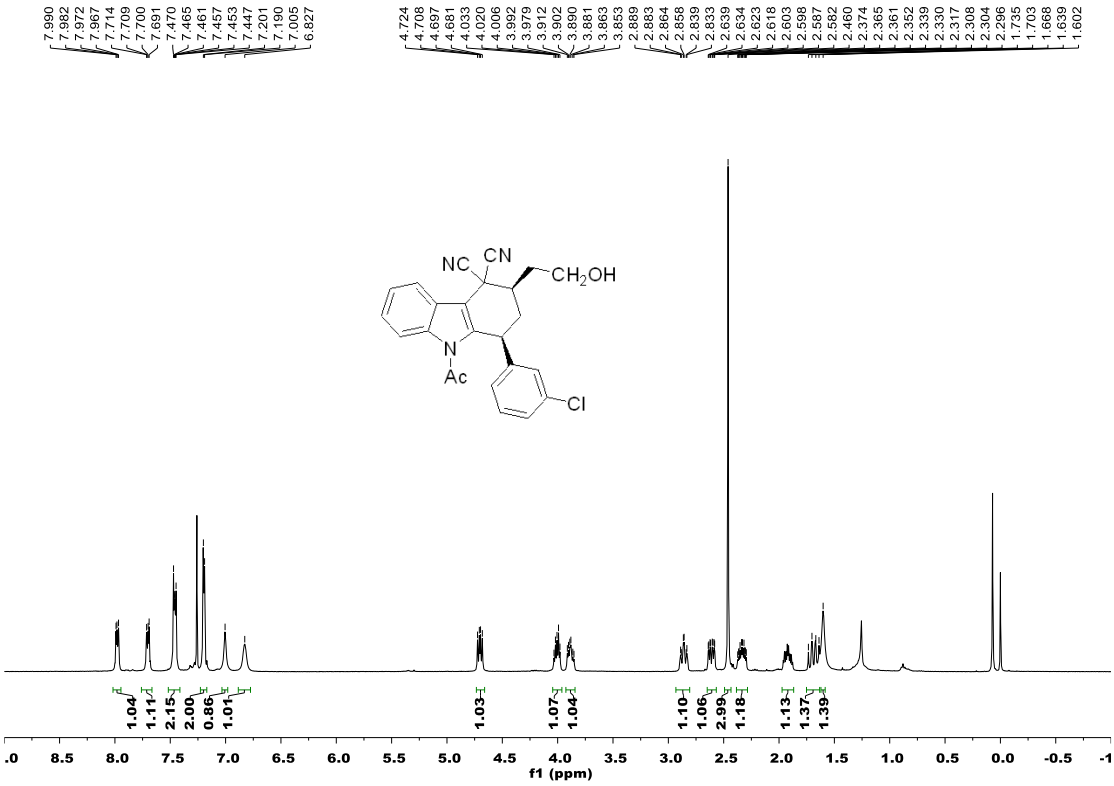
^{1}H NMR spectrum of 3ba



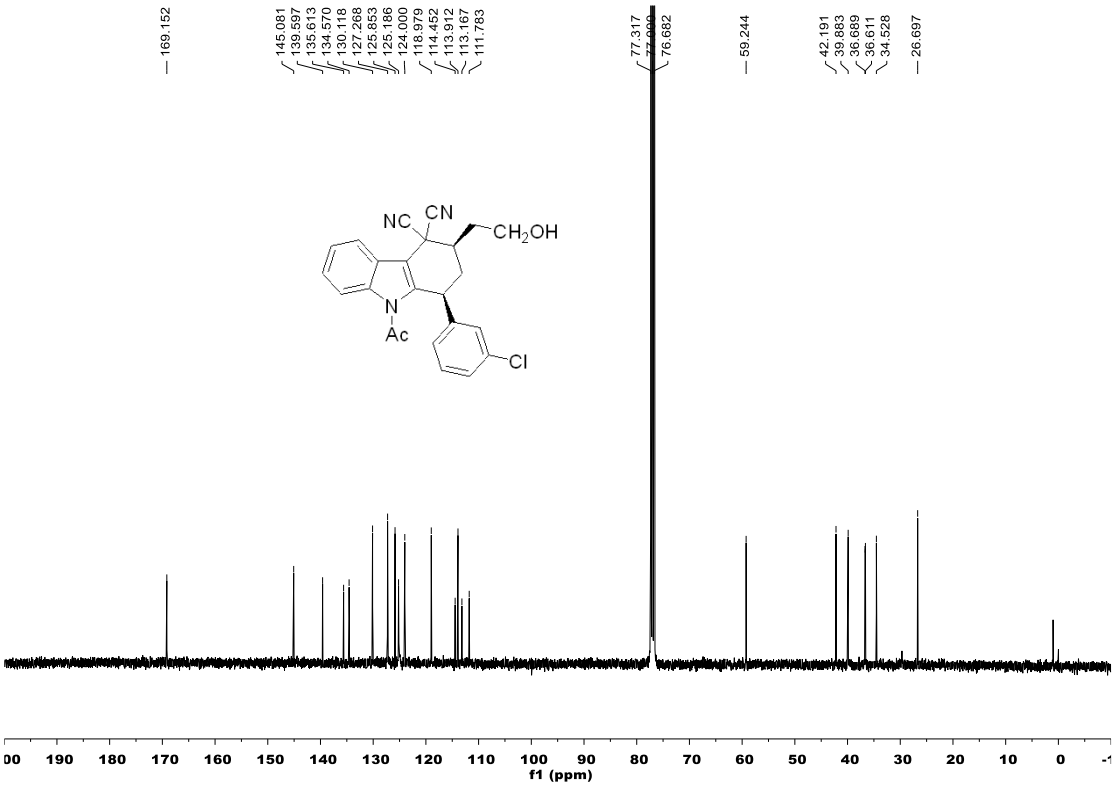
^{13}C NMR spectrum of 3ba



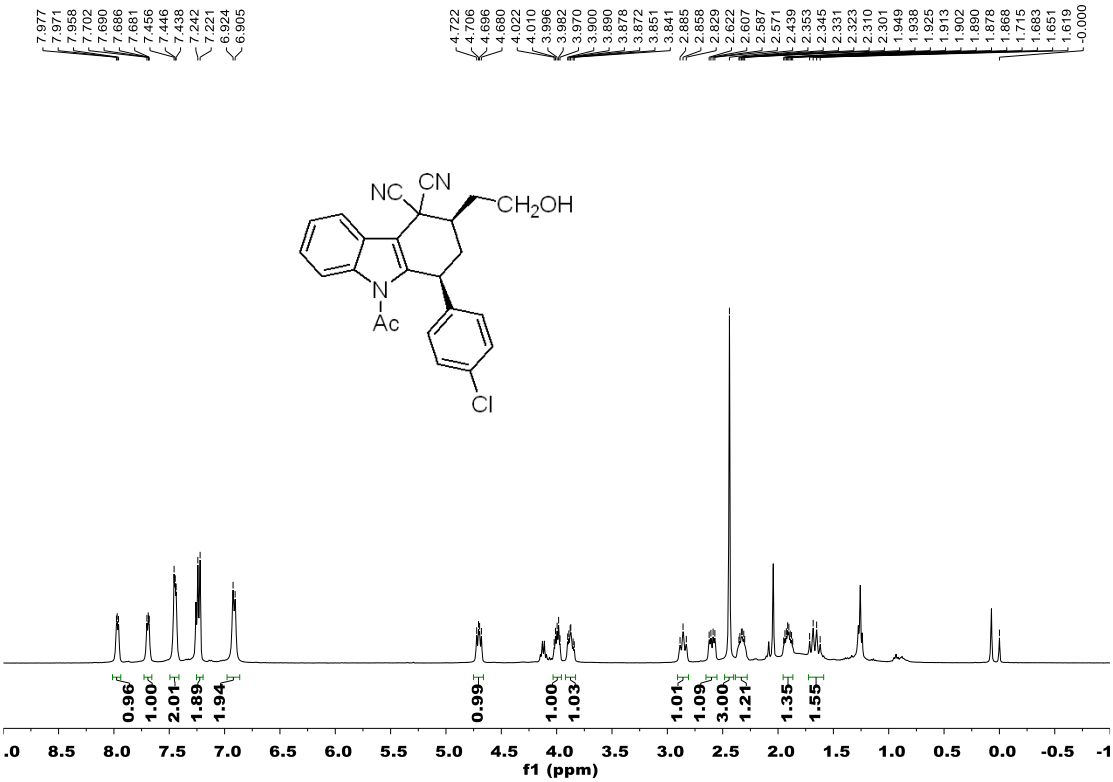
^{1}H NMR spectrum of 3ca



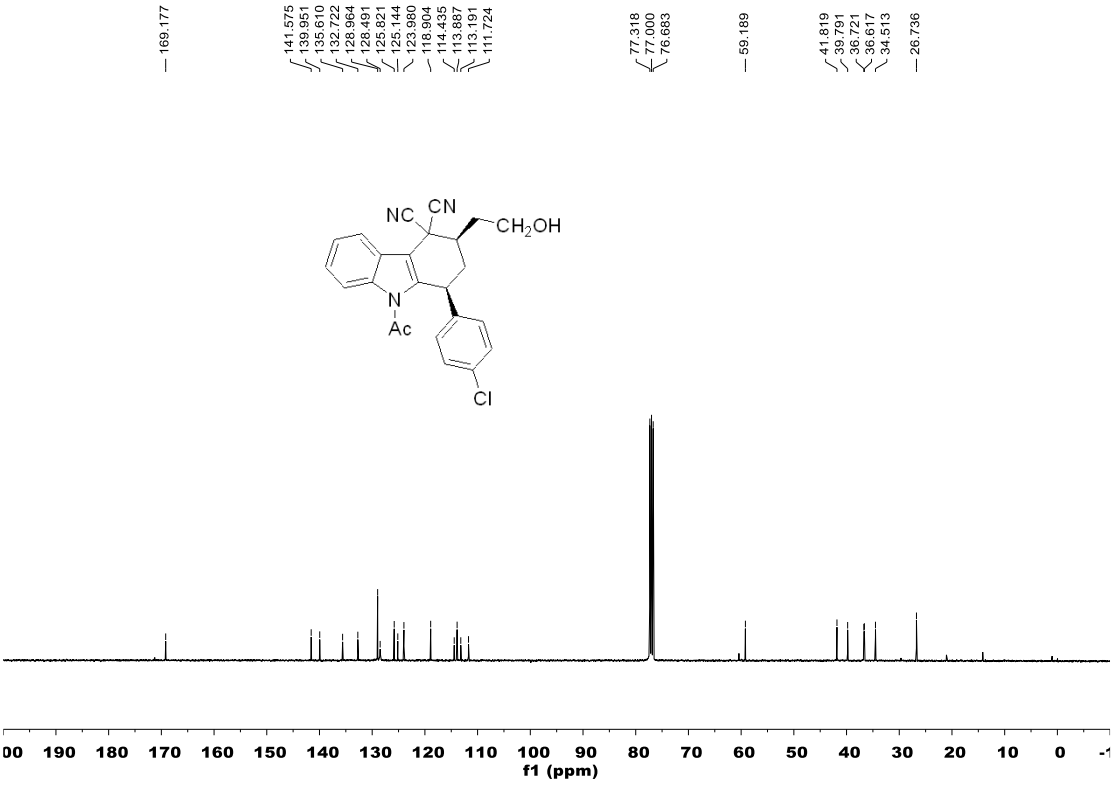
^{13}C NMR spectrum of 3ca



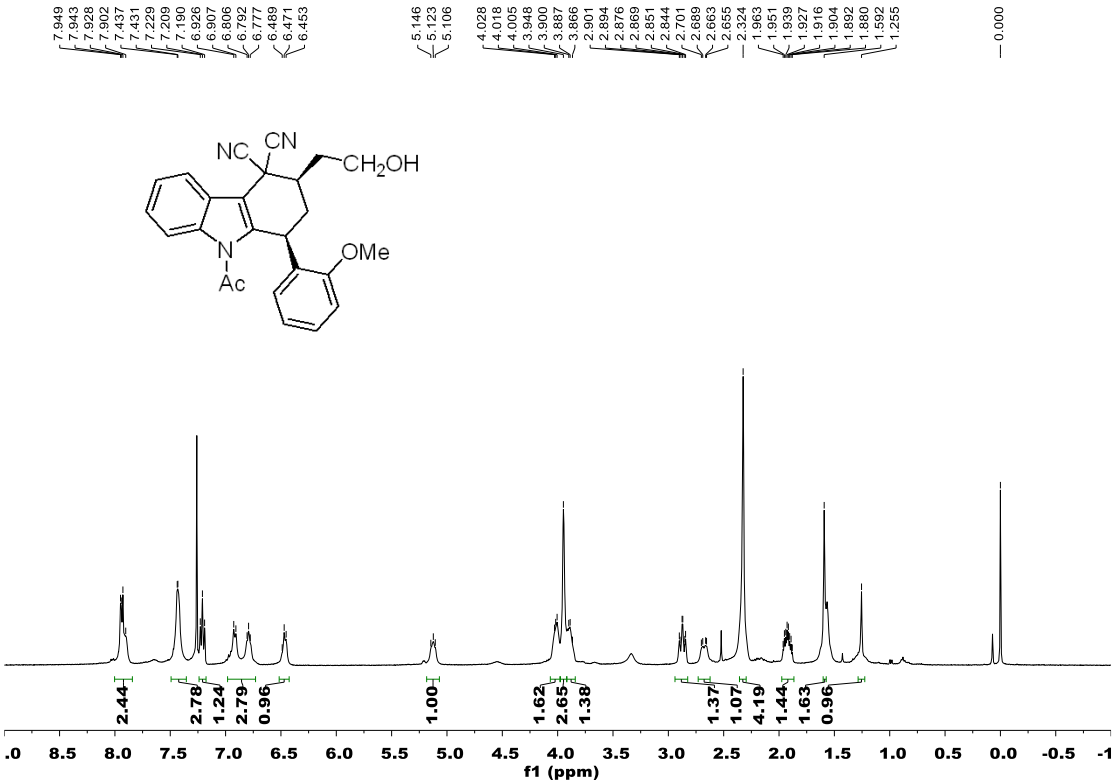
^{1}H NMR spectrum of 3da



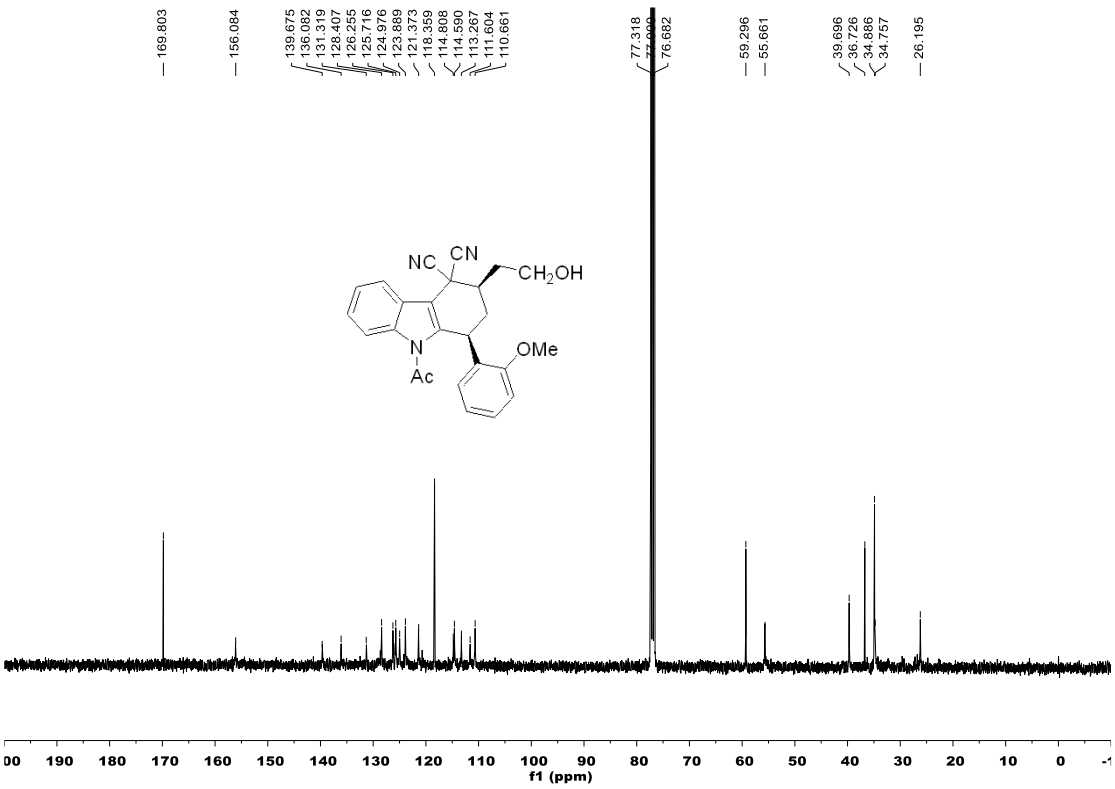
^{13}C NMR spectrum of 3da



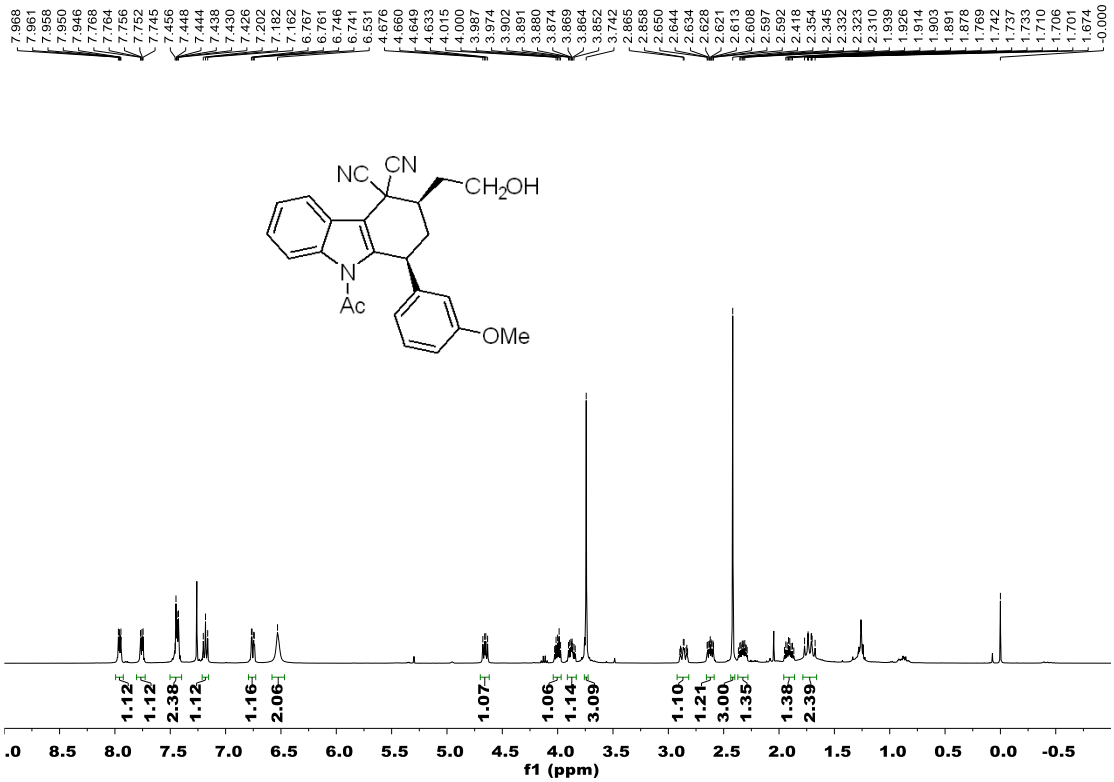
^{1}H NMR spectrum of 3ea



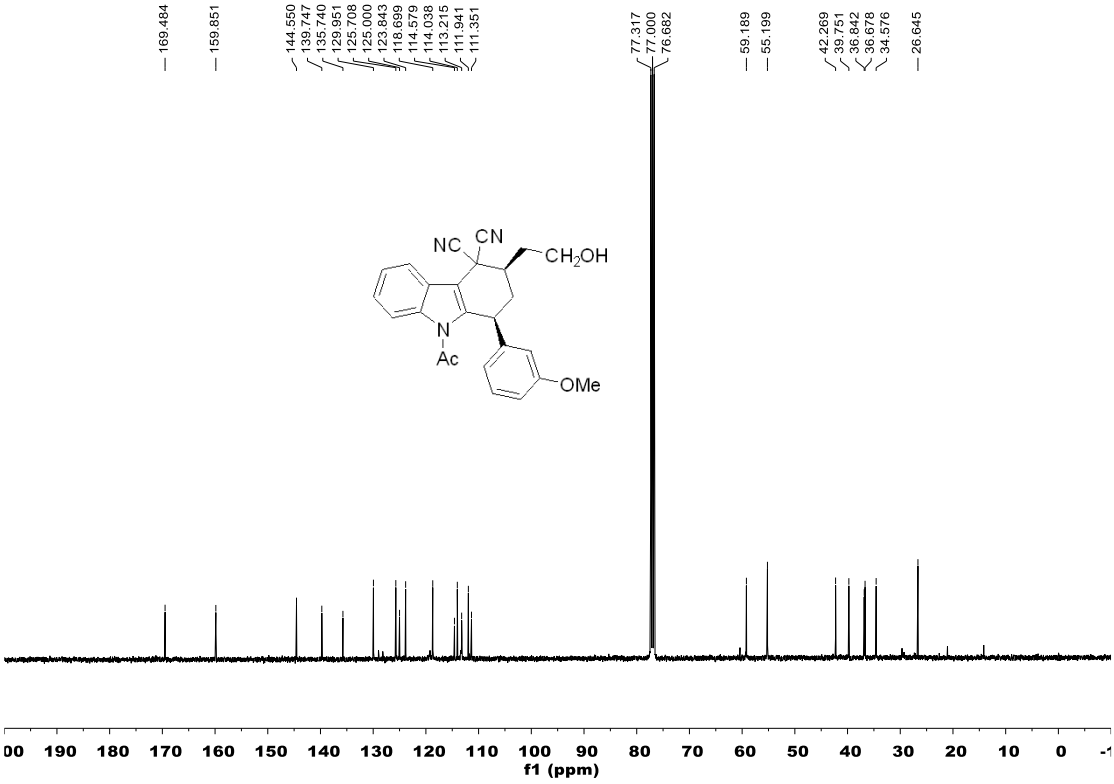
^{13}C NMR spectrum of 3ea



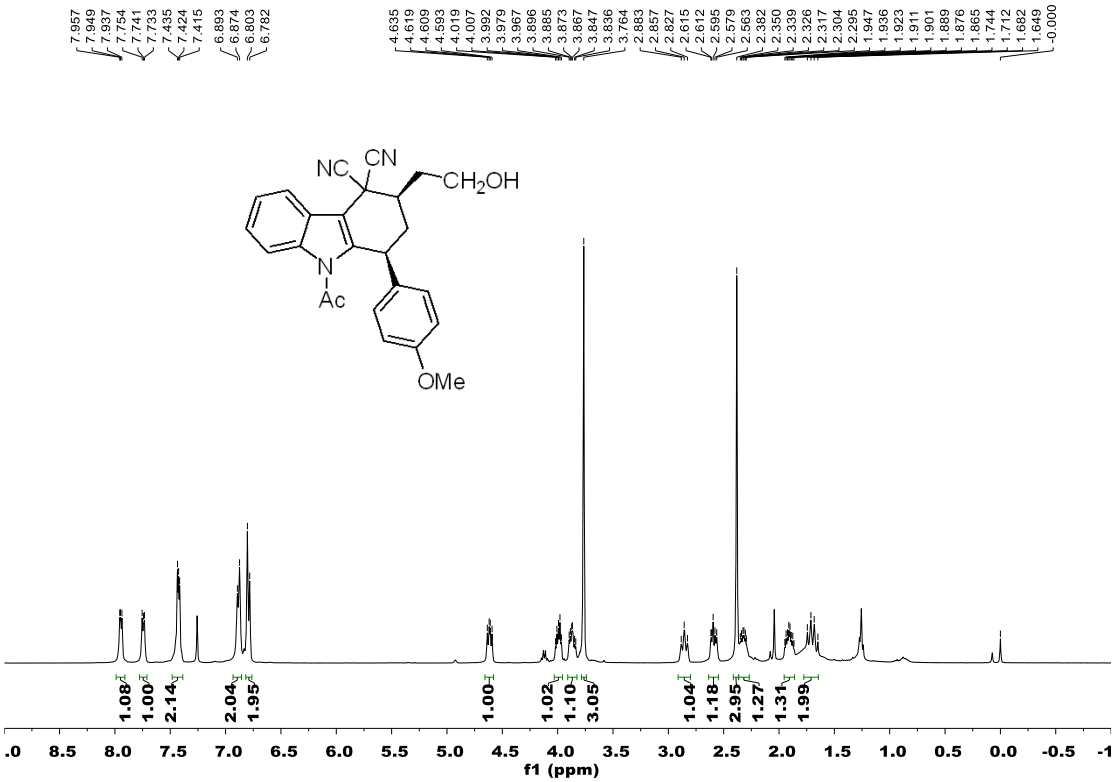
^{1}H NMR spectrum of 3fa



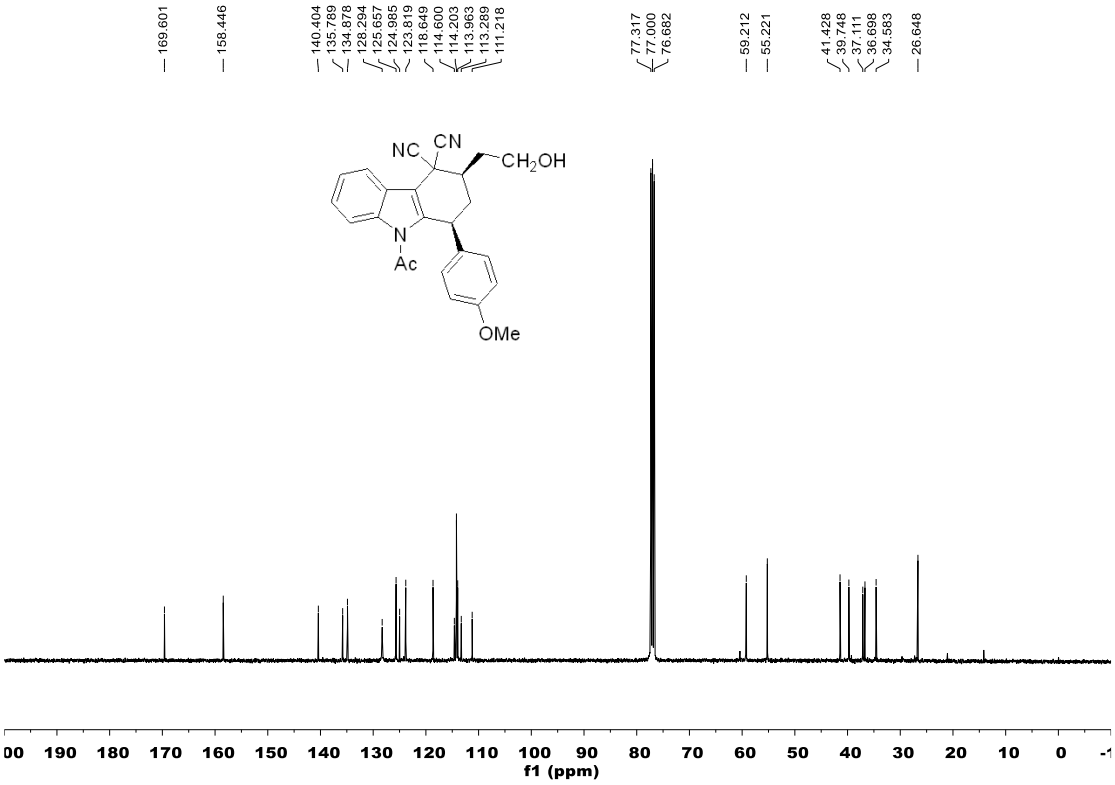
^{13}C NMR spectrum of 3fa



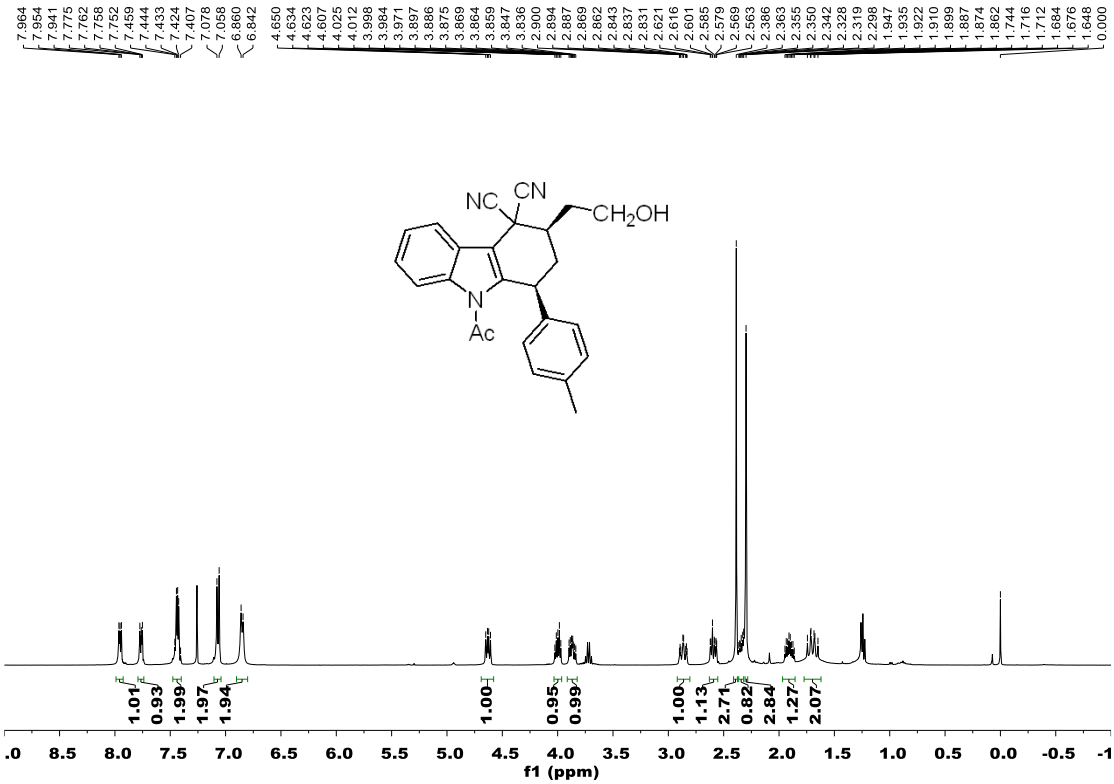
^{1}H NMR spectrum of 3ga



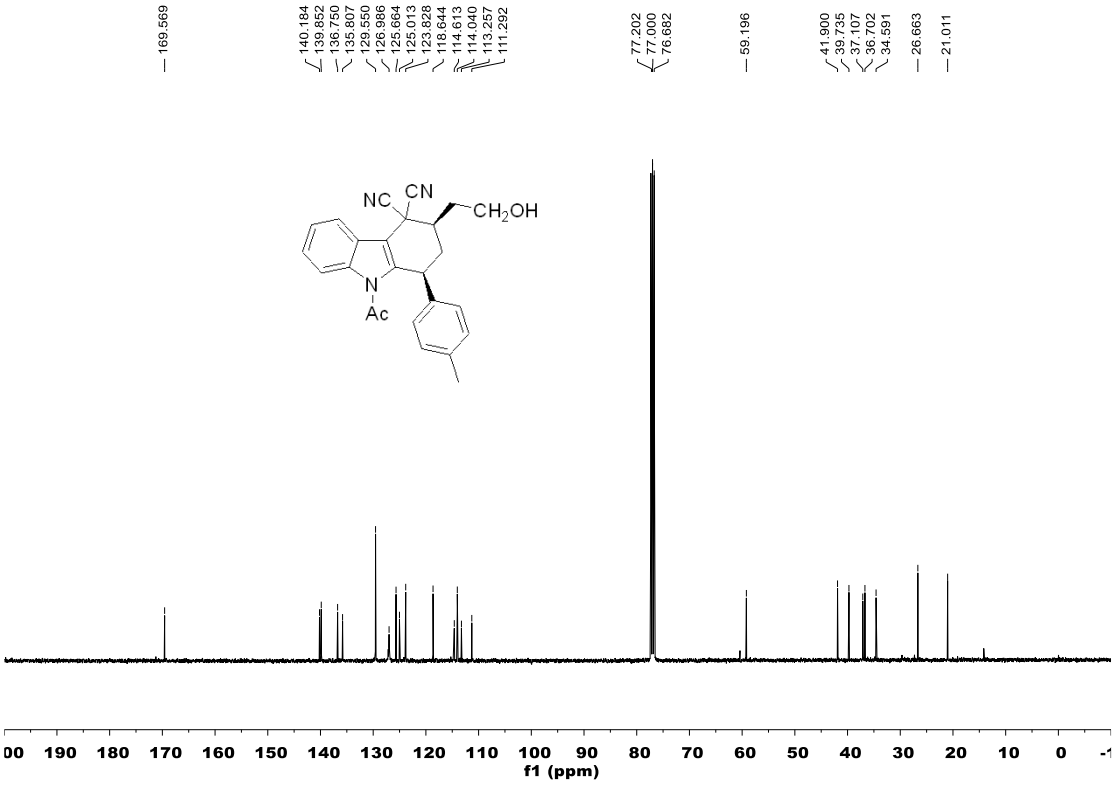
^{13}C NMR spectrum of 3ga



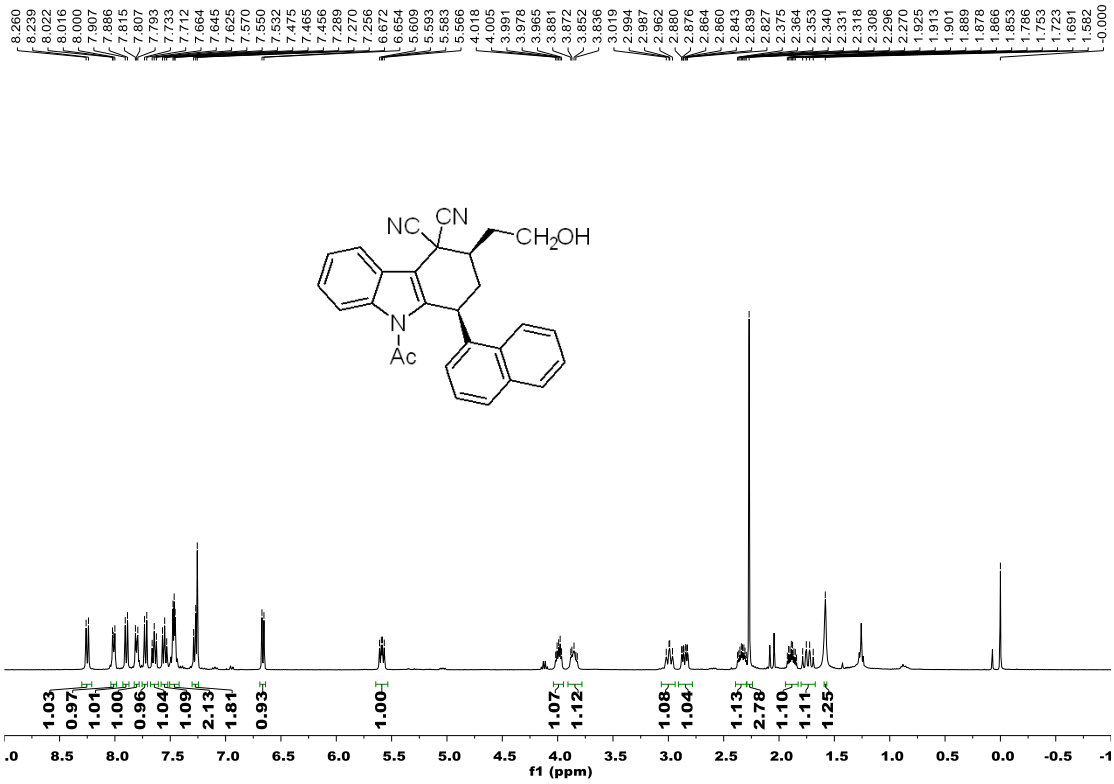
^{1}H NMR spectrum of 3ha



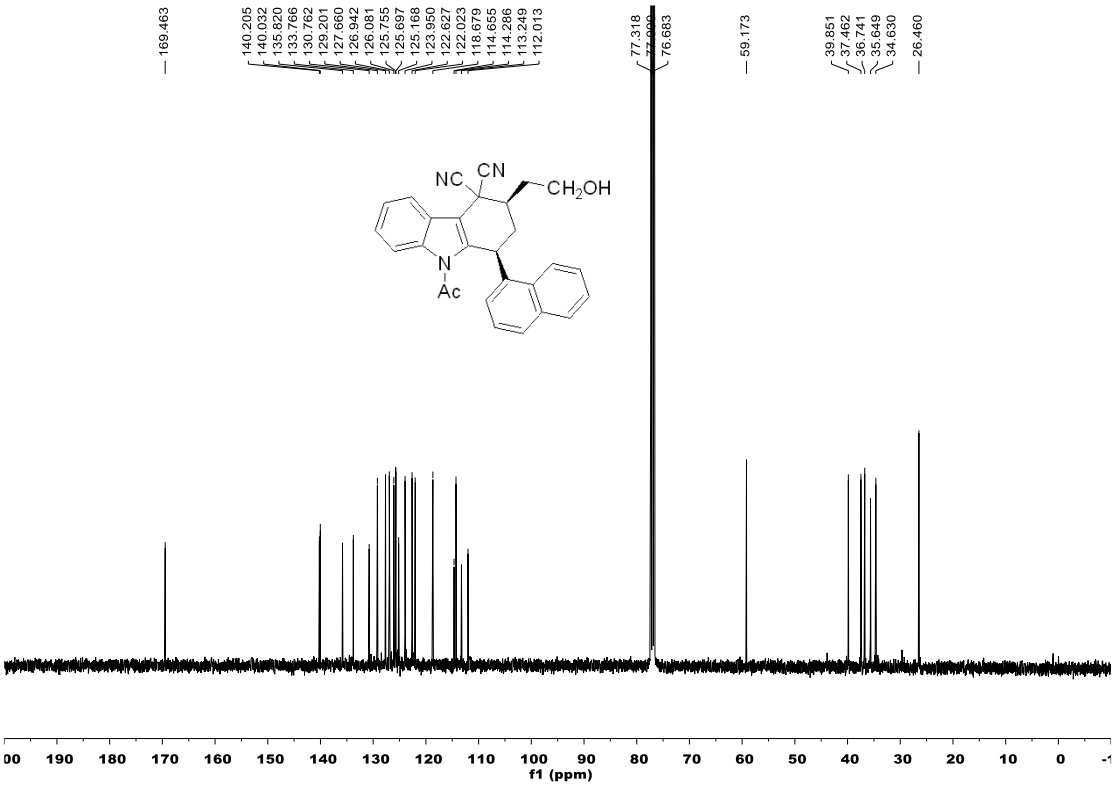
^{13}C NMR spectrum of 3ha



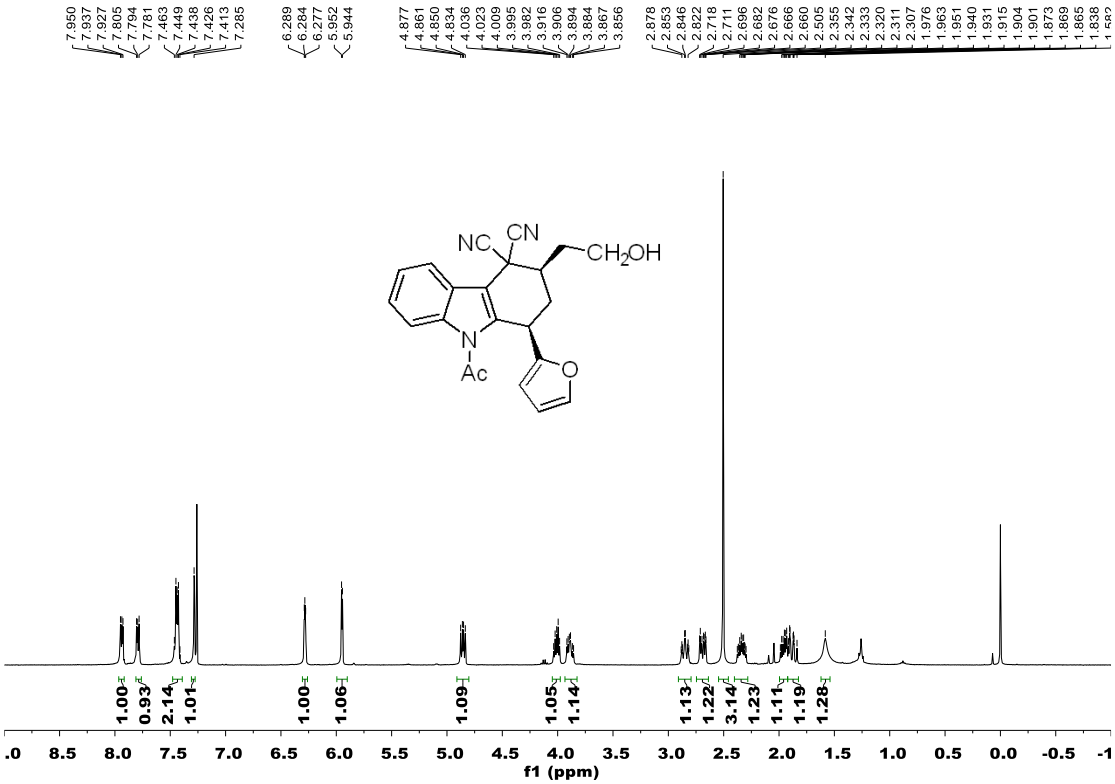
^{1}H NMR spectrum of 3ia



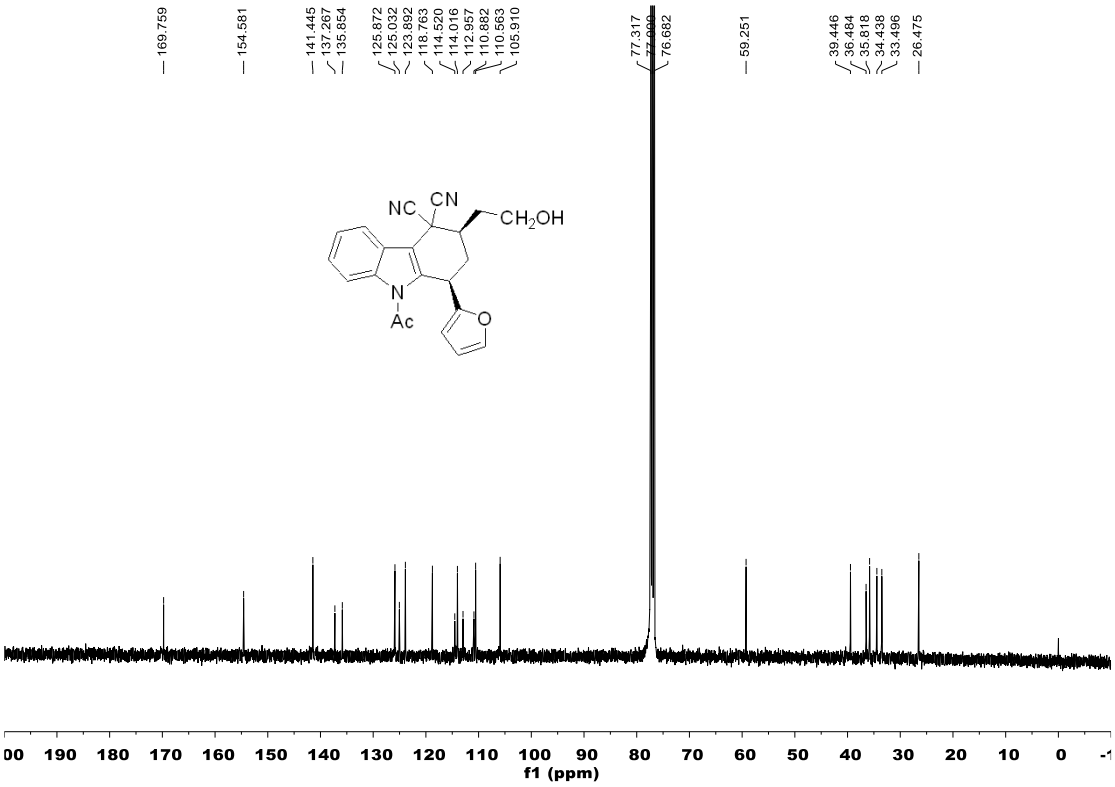
^{13}C NMR spectrum of 3ia



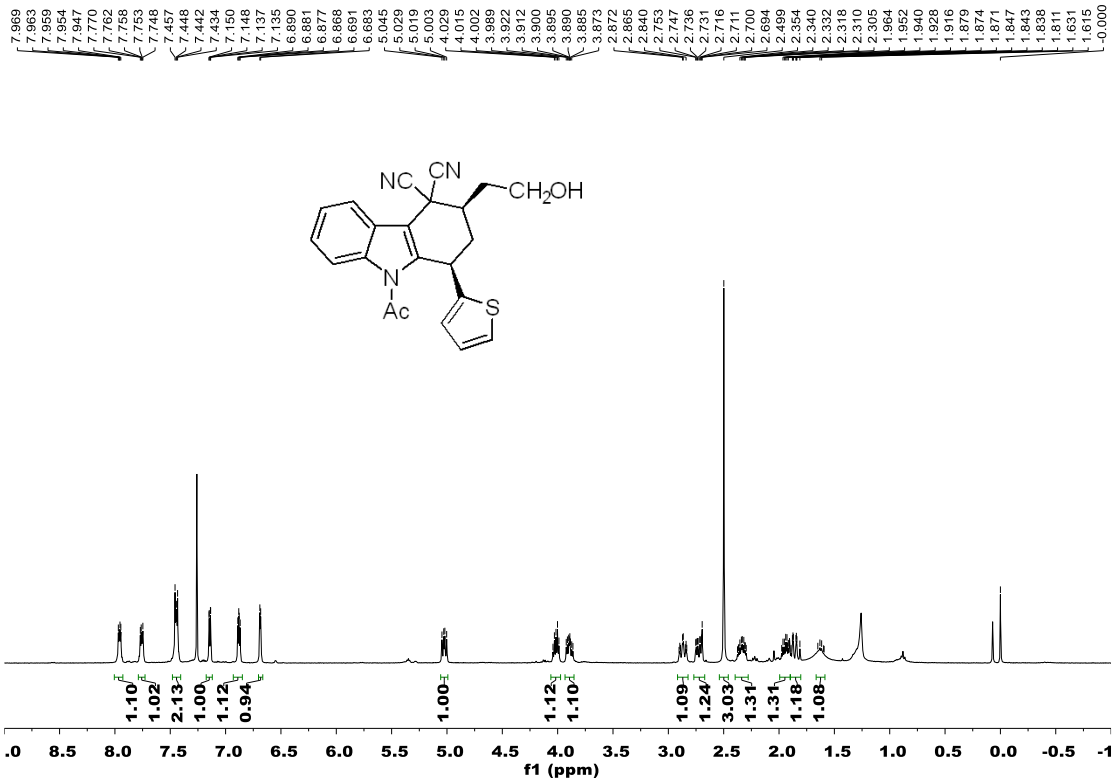
^{1}H NMR spectrum of 3ja



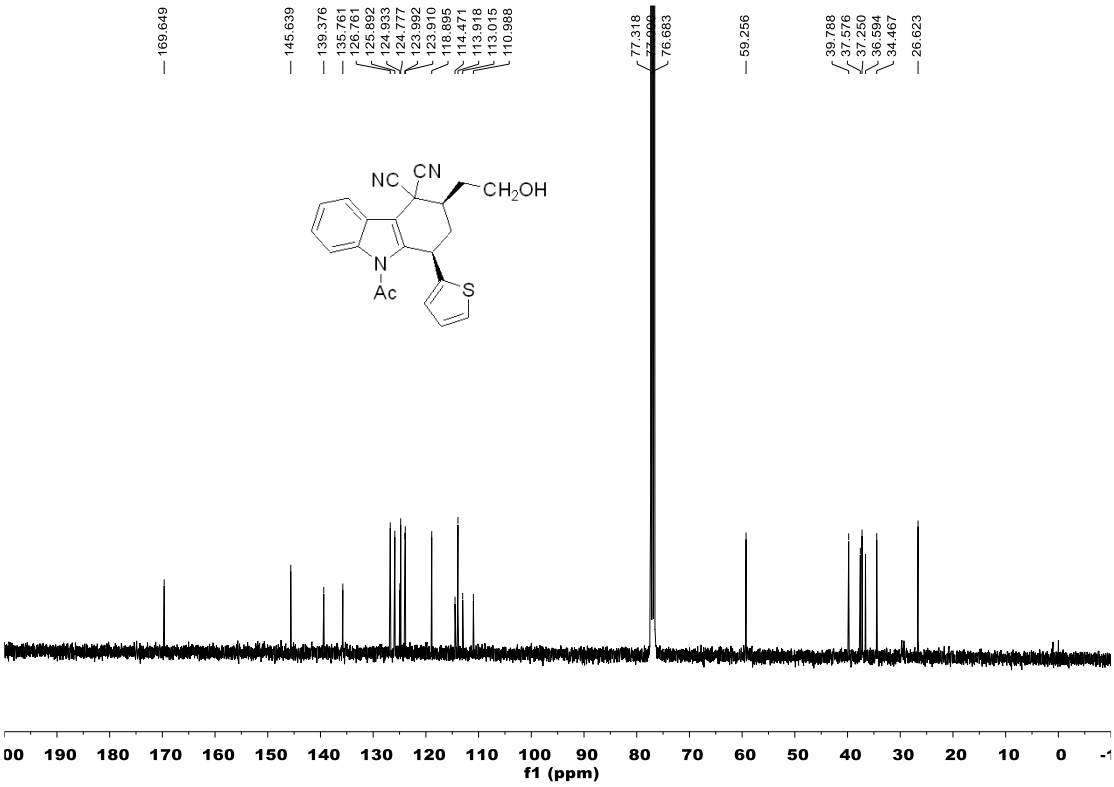
^{13}C NMR spectrum of 3ja



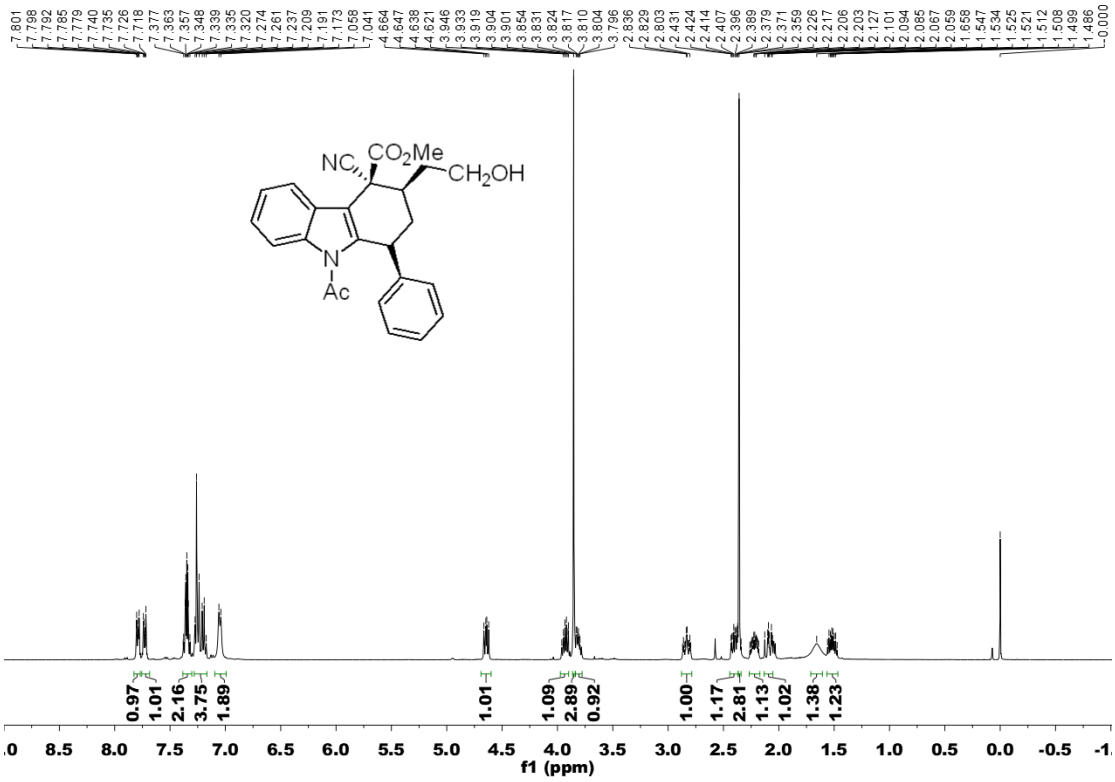
^{1}H NMR spectrum of 3ka



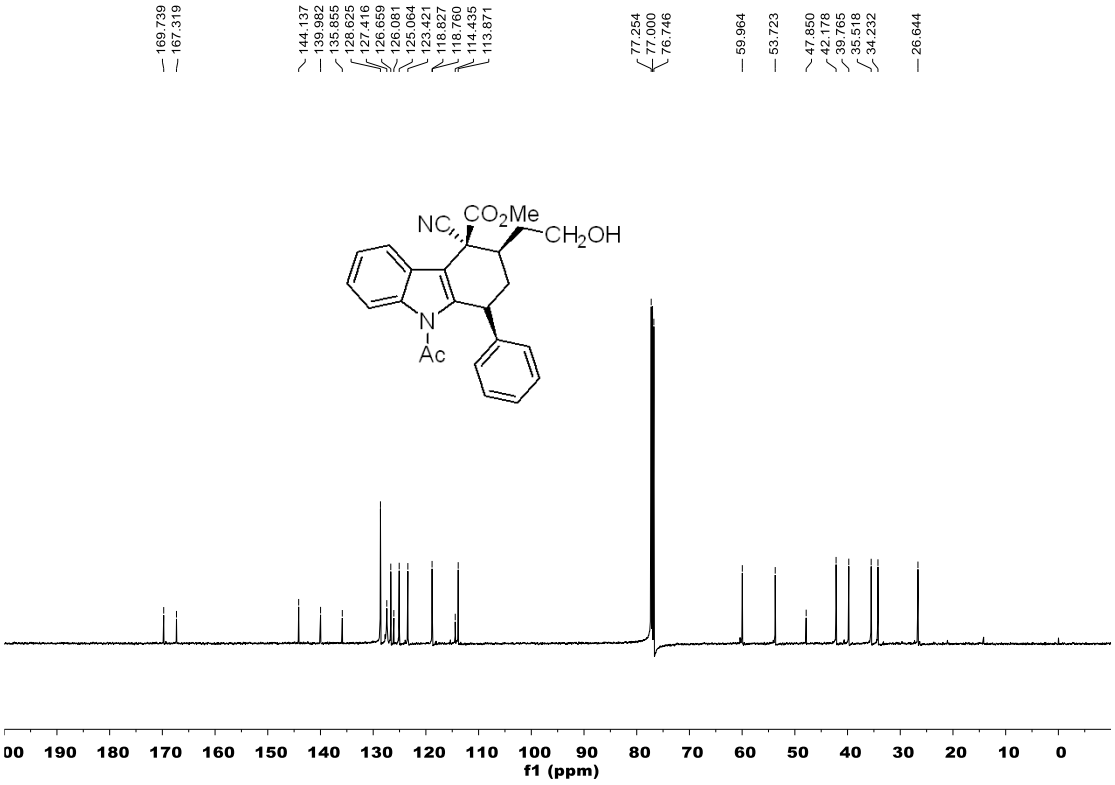
^{13}C NMR spectrum of 3ka



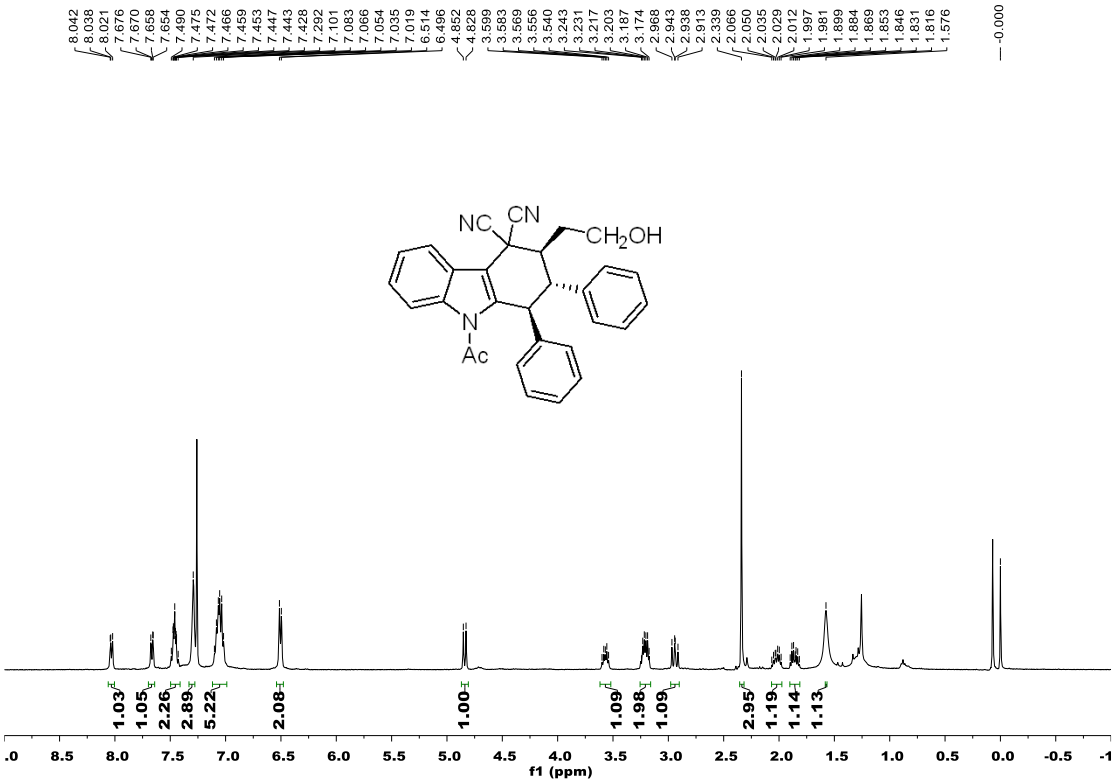
^{1}H NMR spectrum of 3la



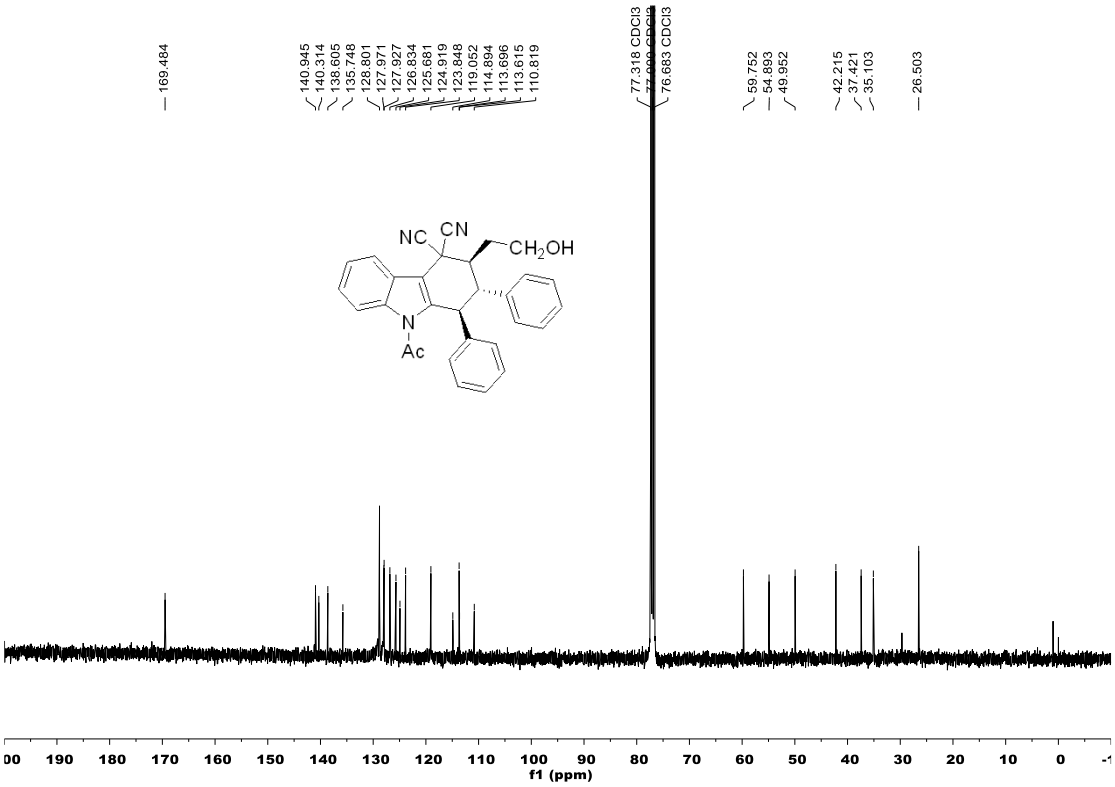
^{13}C NMR spectrum of 3la



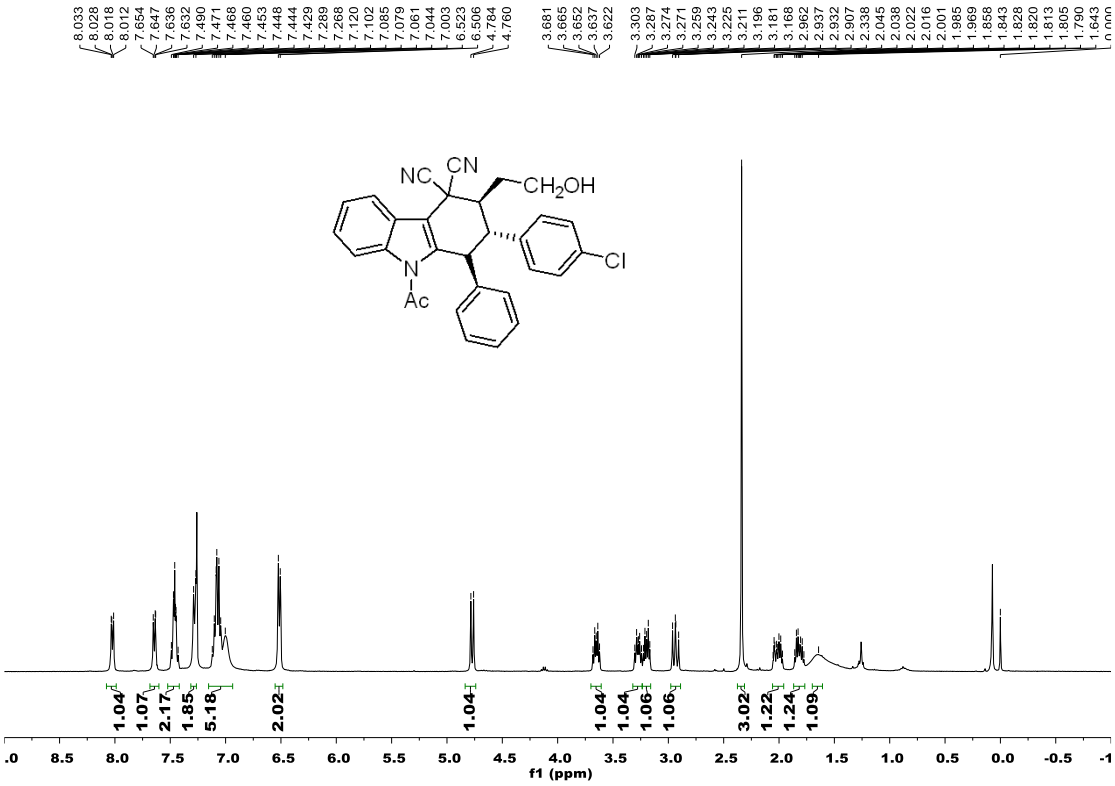
^{1}H NMR spectrum of 3ab



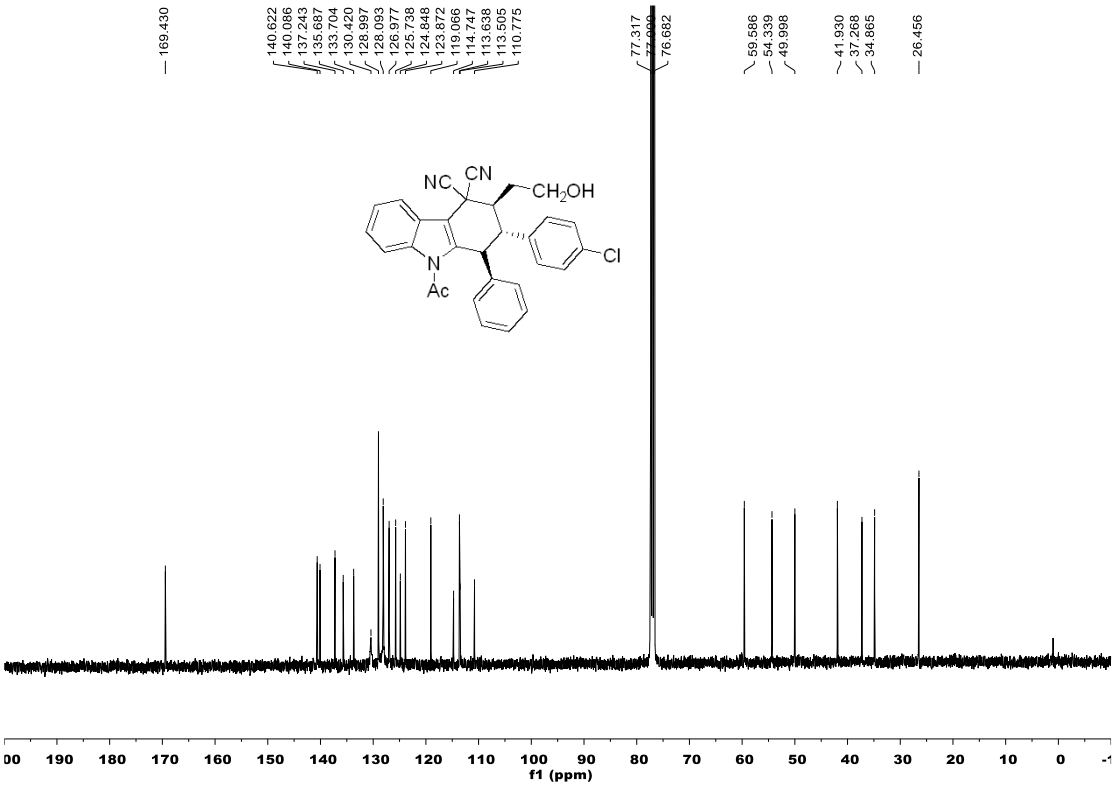
^{13}C NMR spectrum of 3ab



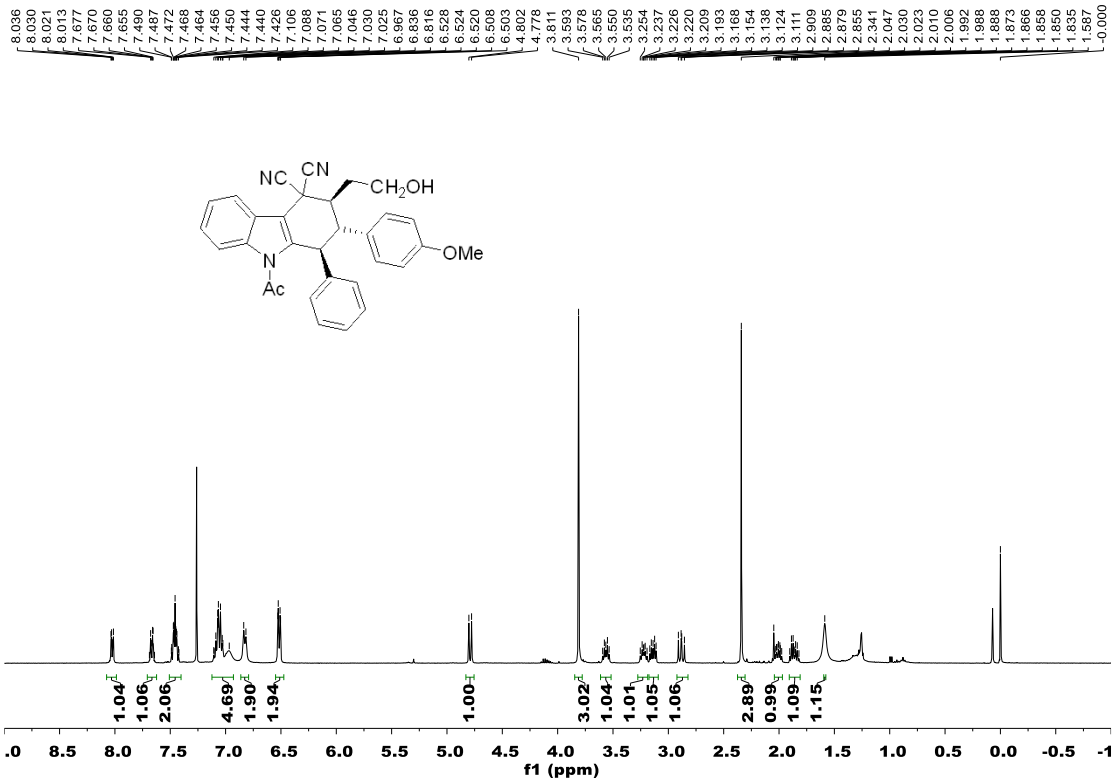
^{1}H NMR spectrum of 3ac



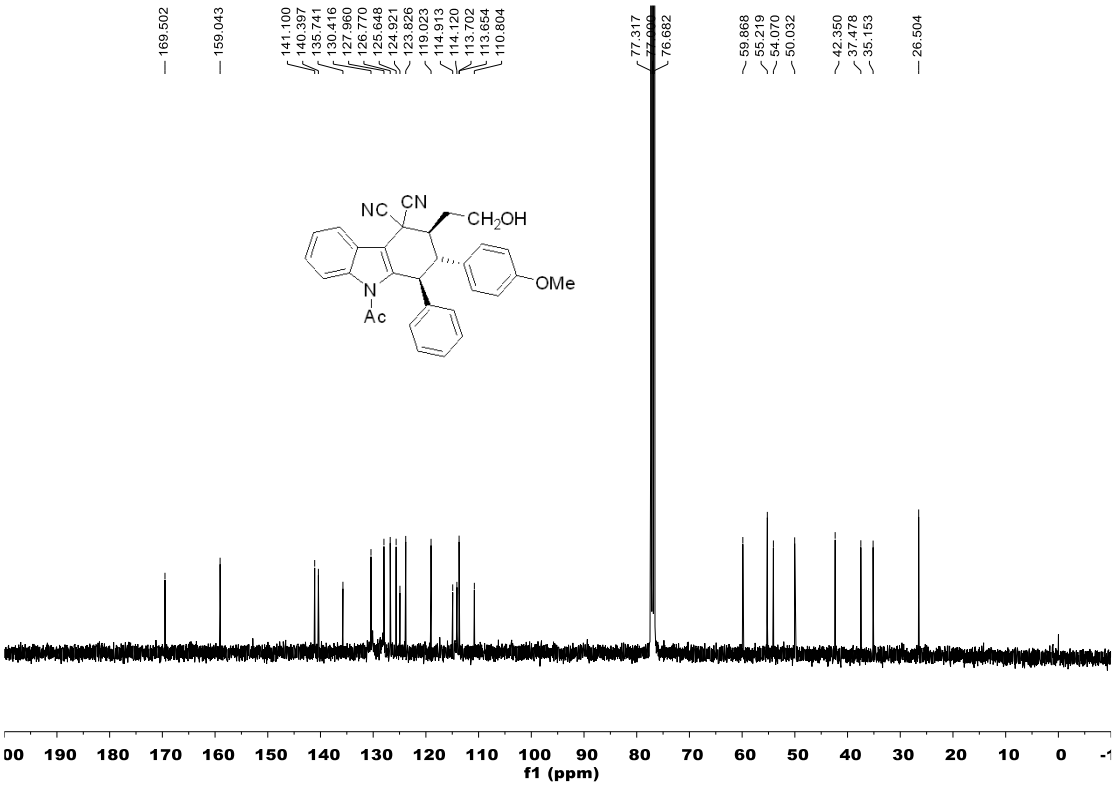
^{13}C NMR spectrum of 3ac



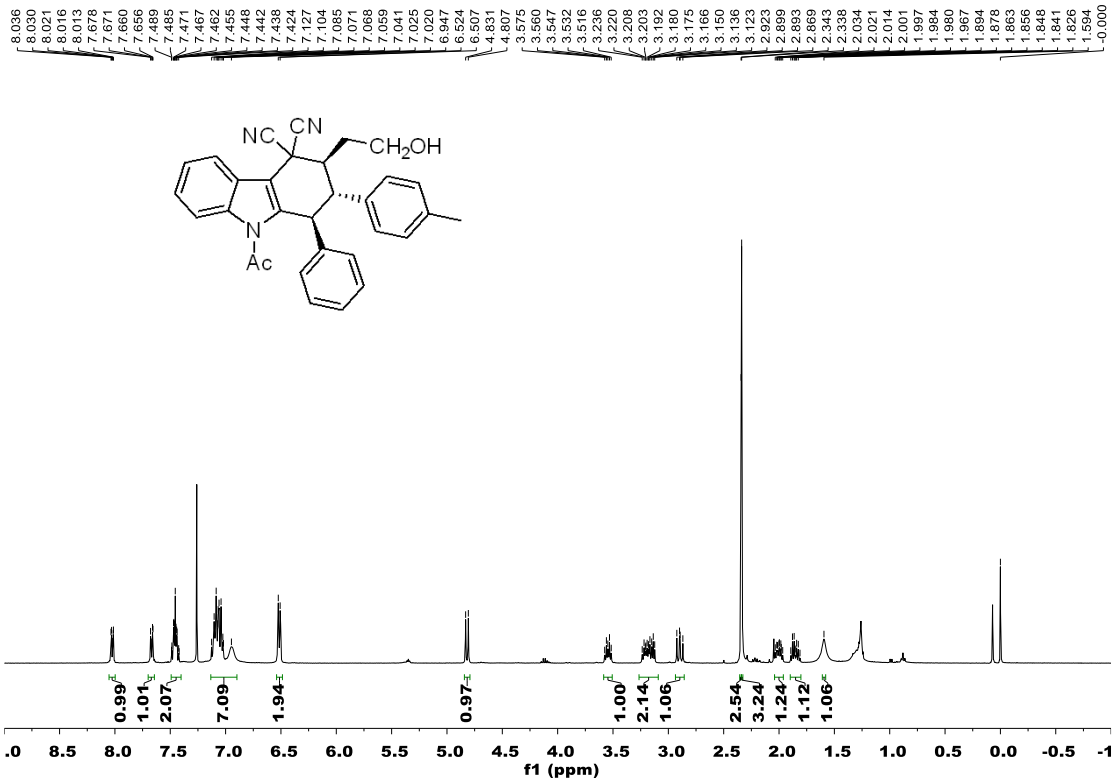
^{1}H NMR spectrum of 3ad



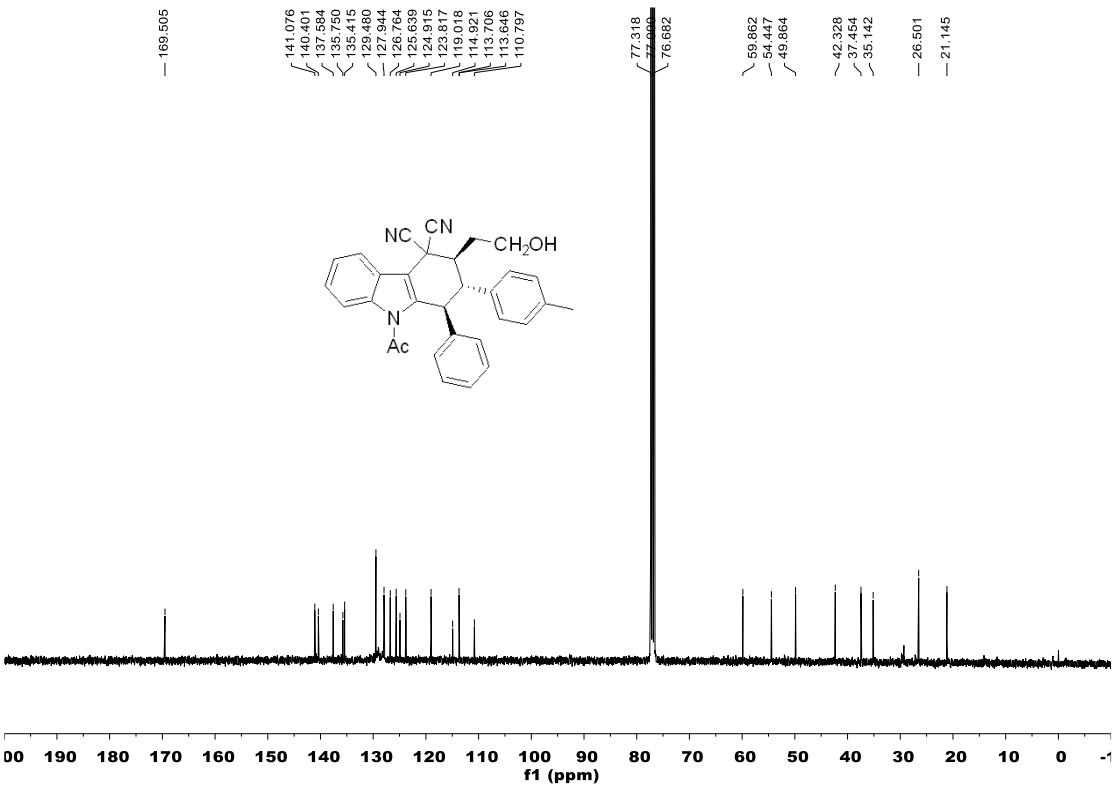
^{13}C NMR spectrum of 3ad



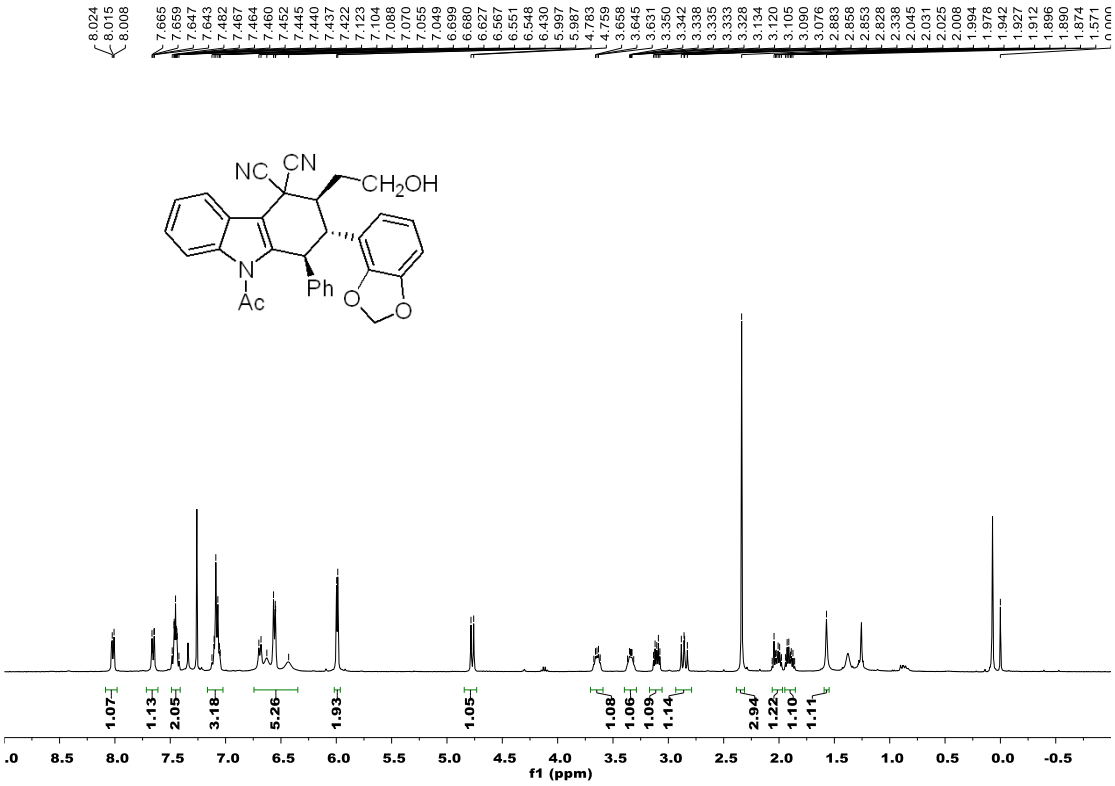
^{1}H NMR spectrum of 3ae



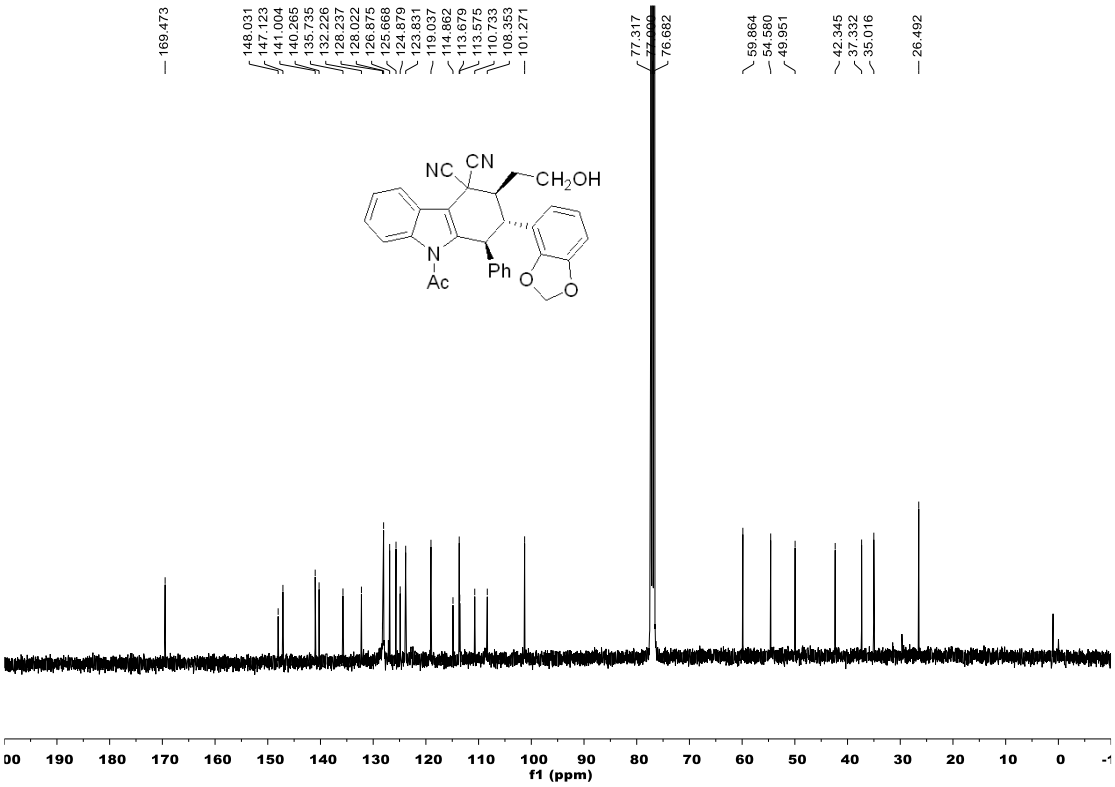
^{13}C NMR spectrum of 3ae



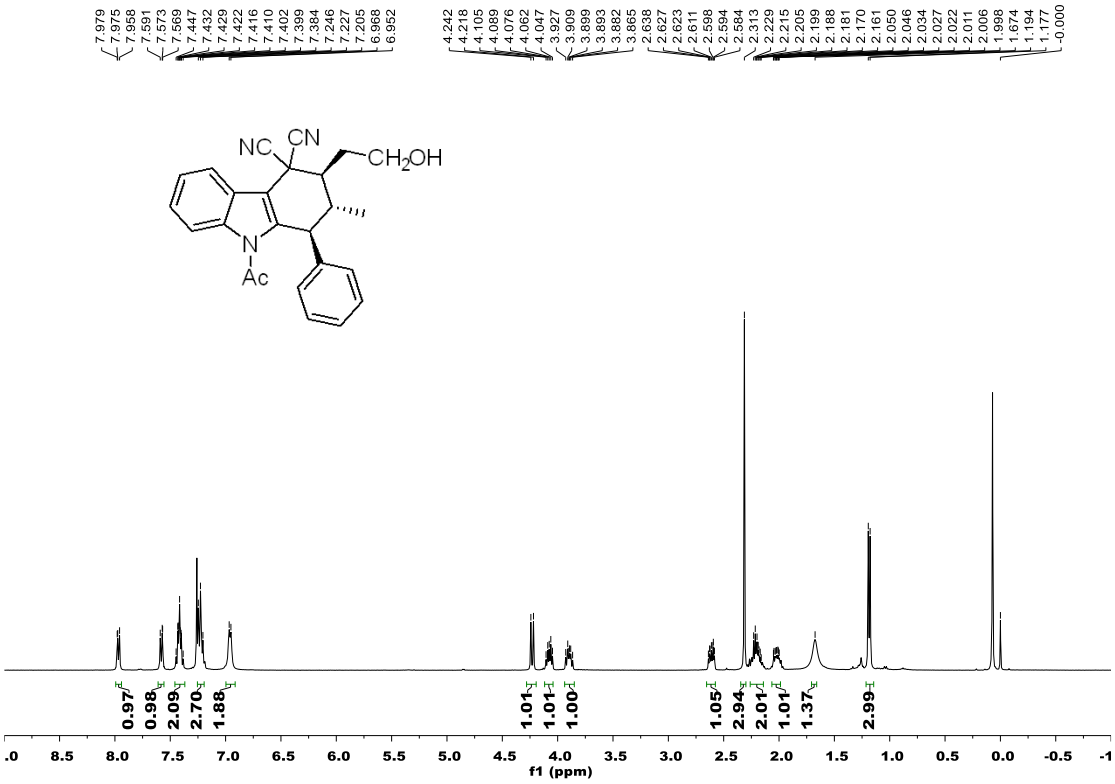
^{1}H NMR spectrum of 3af



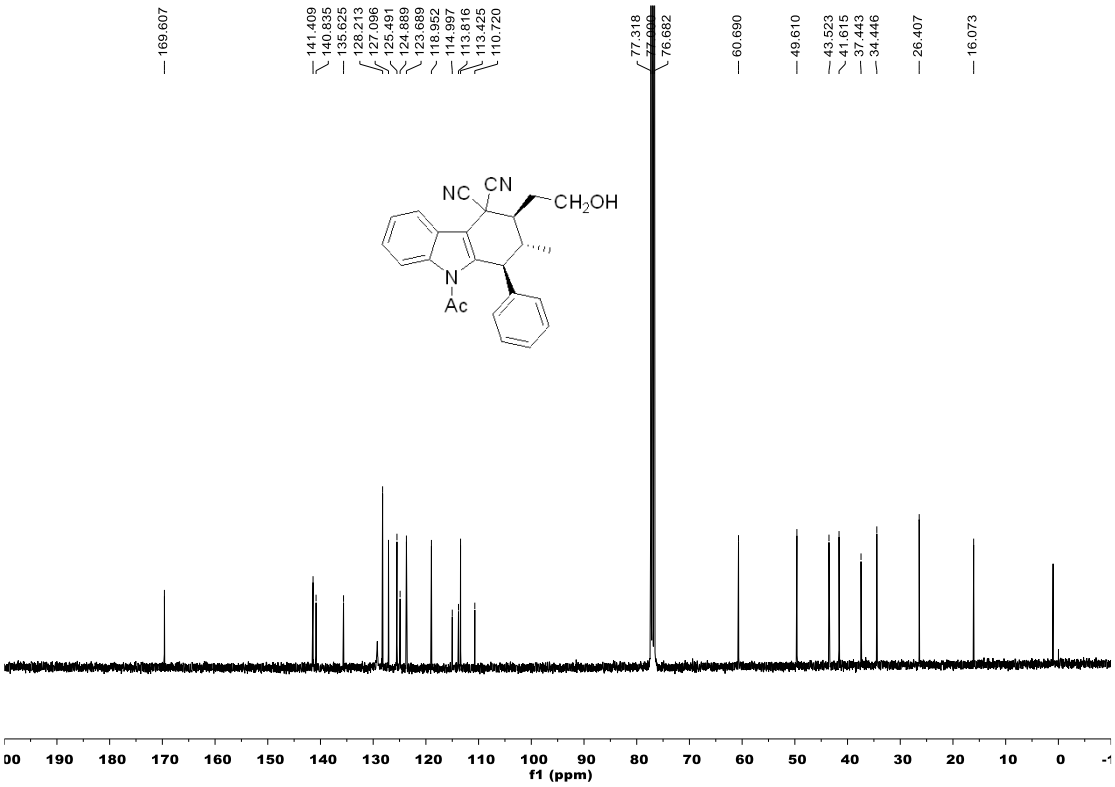
^{13}C NMR spectrum of 3af



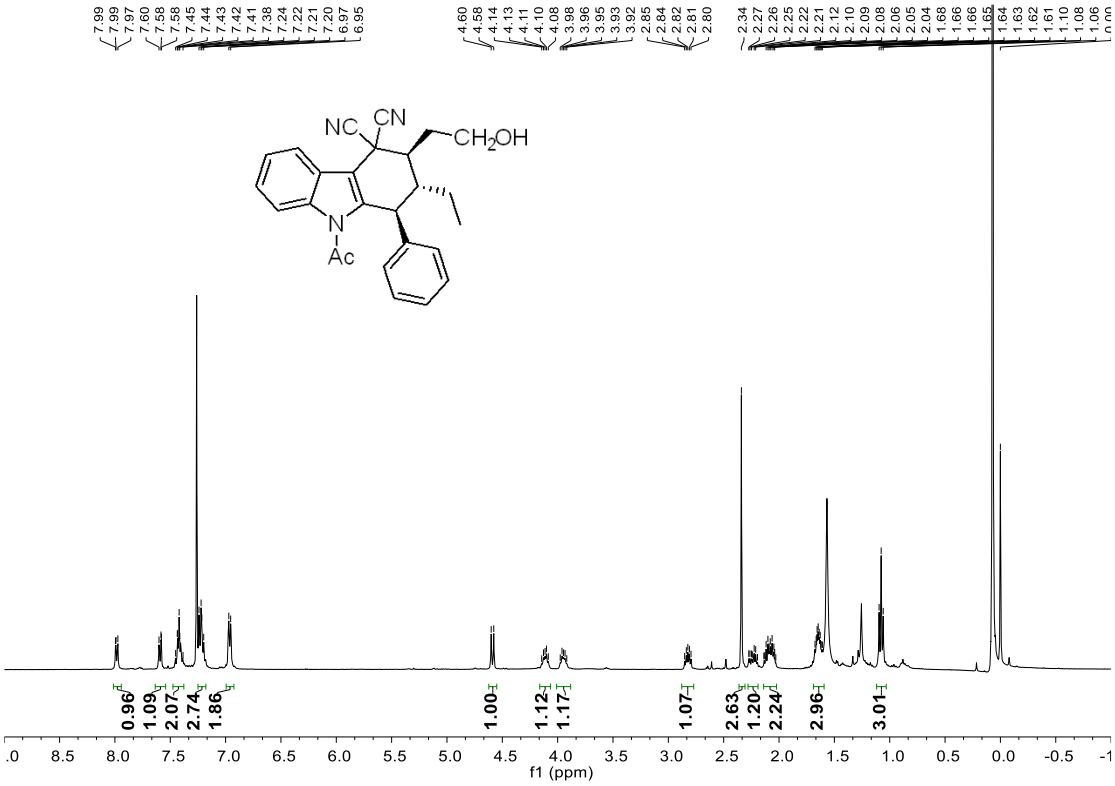
^{1}H NMR spectrum of 3ag



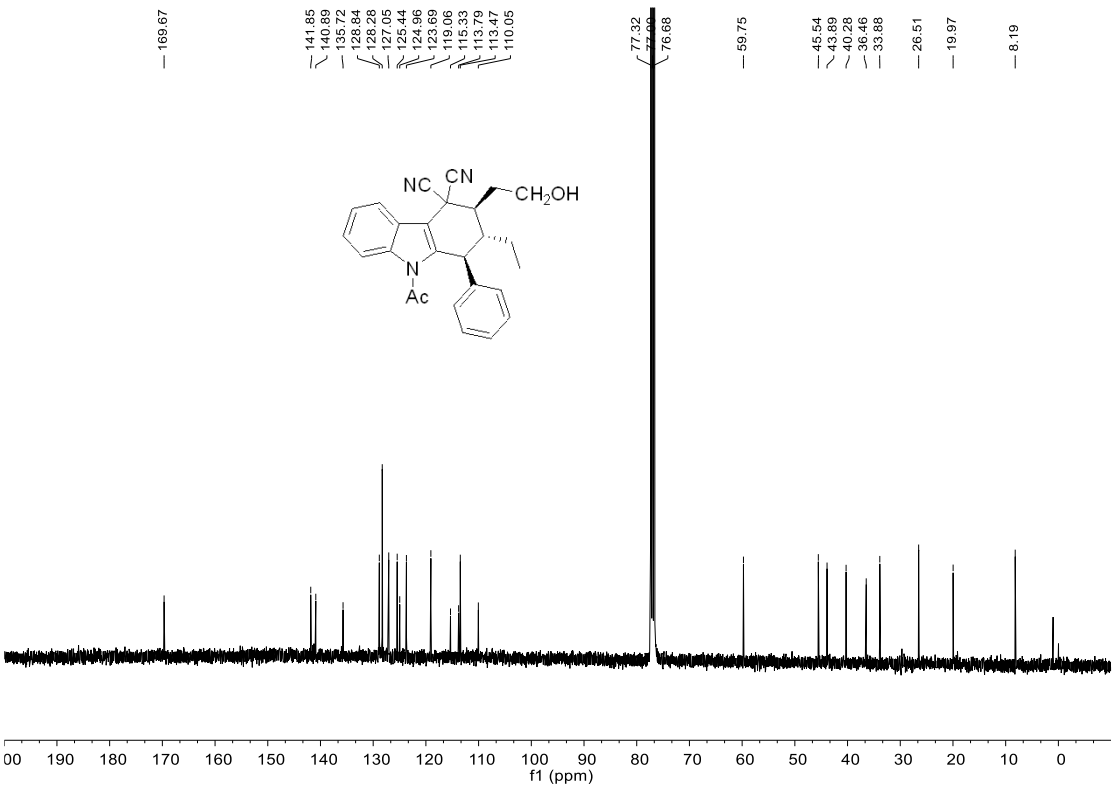
^{13}C NMR spectrum of 3ag



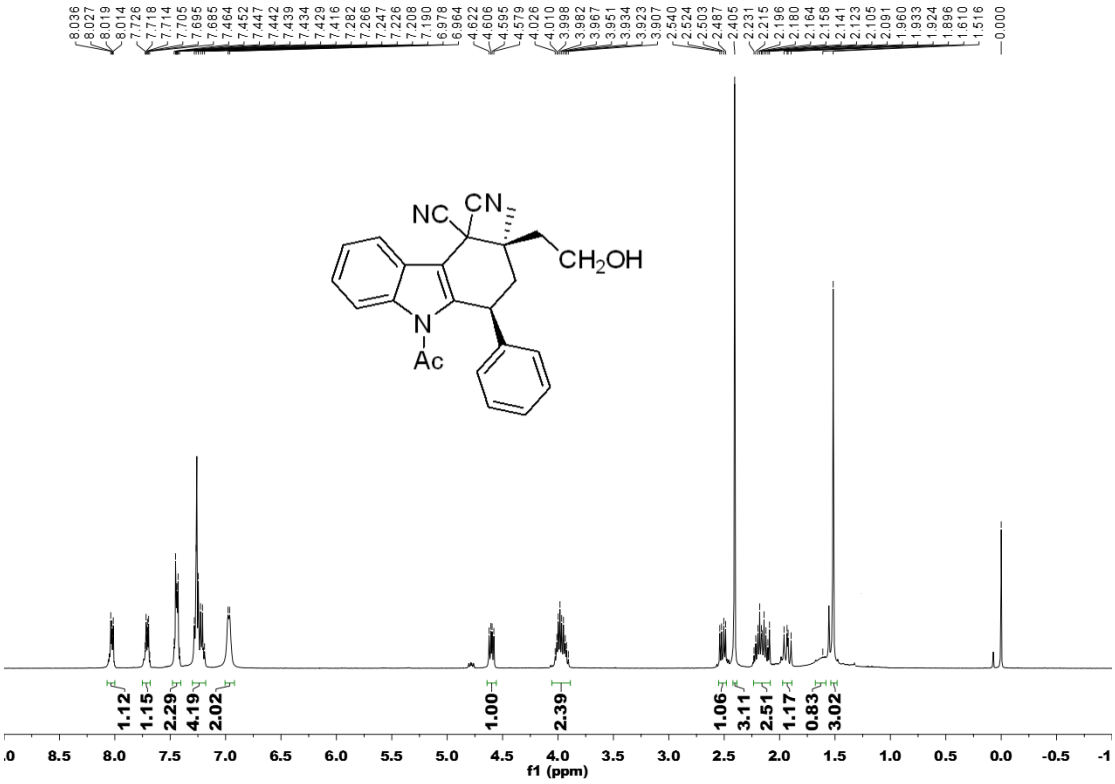
^{1}H NMR spectrum of 3ah



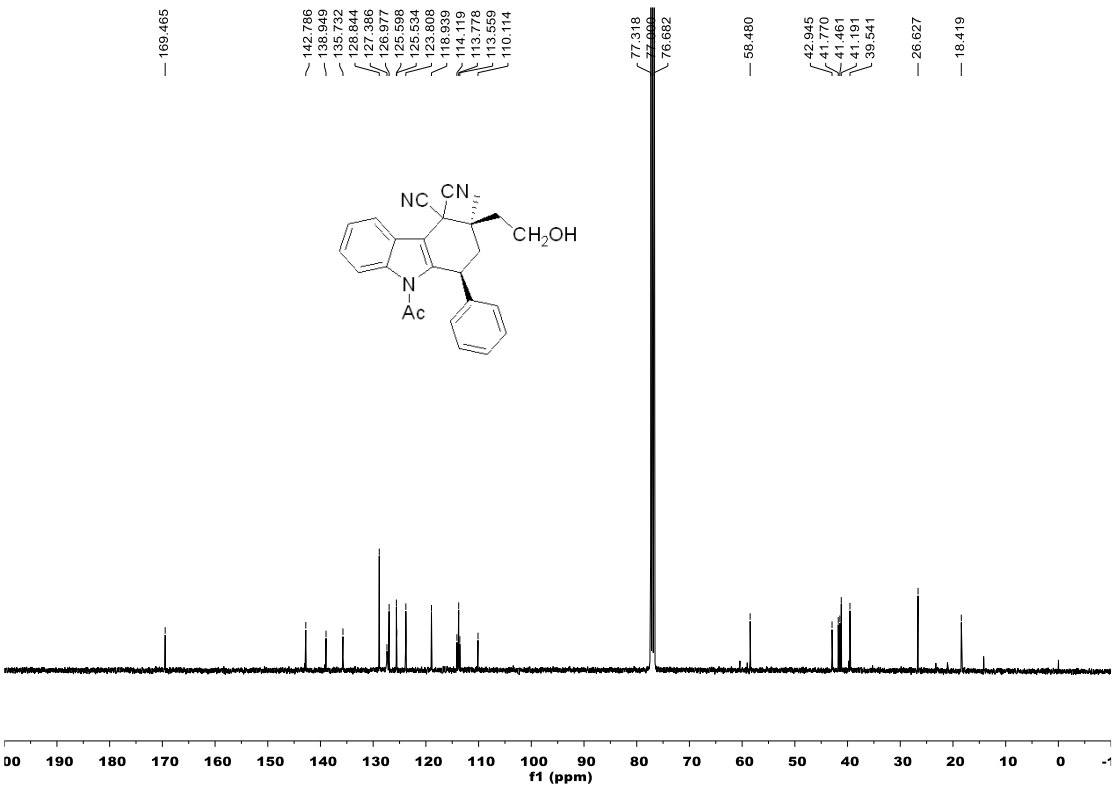
^{13}C NMR spectrum of 3ah



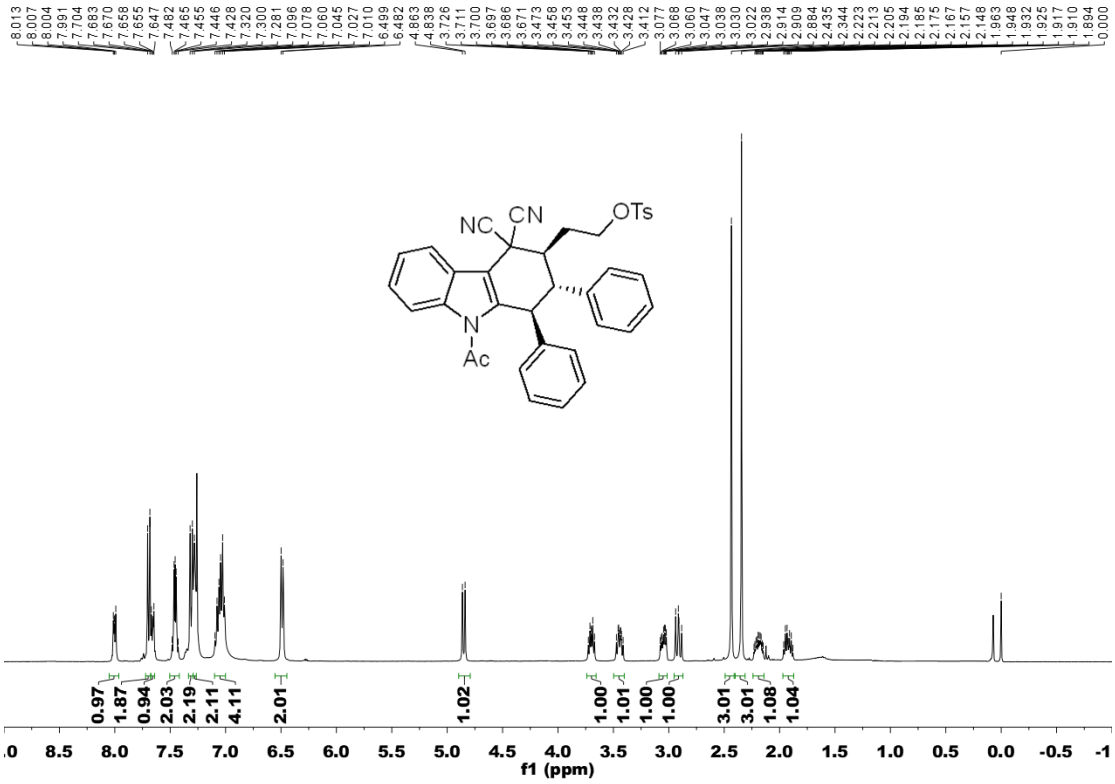
^{1}H NMR spectrum of 3ai



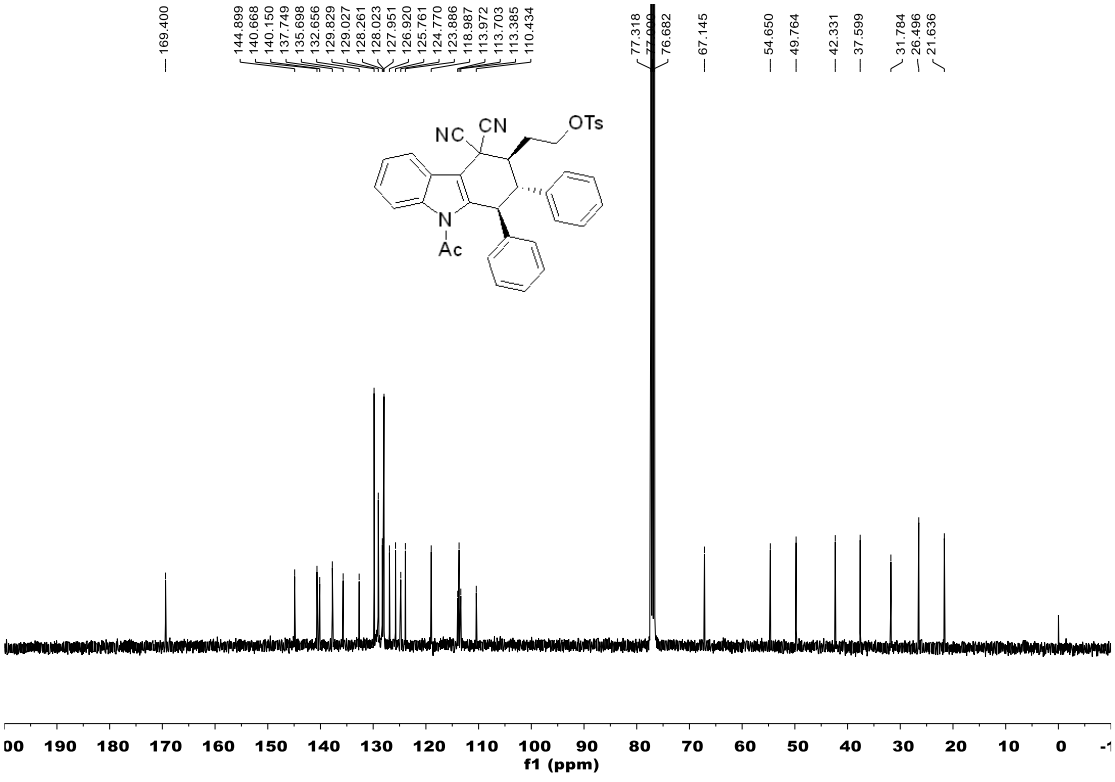
^{13}C NMR spectrum of 3ai



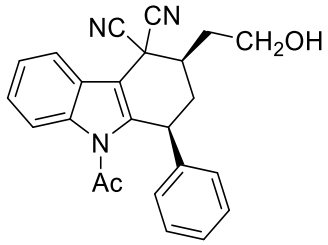
^{1}H NMR spectrum of 4ab



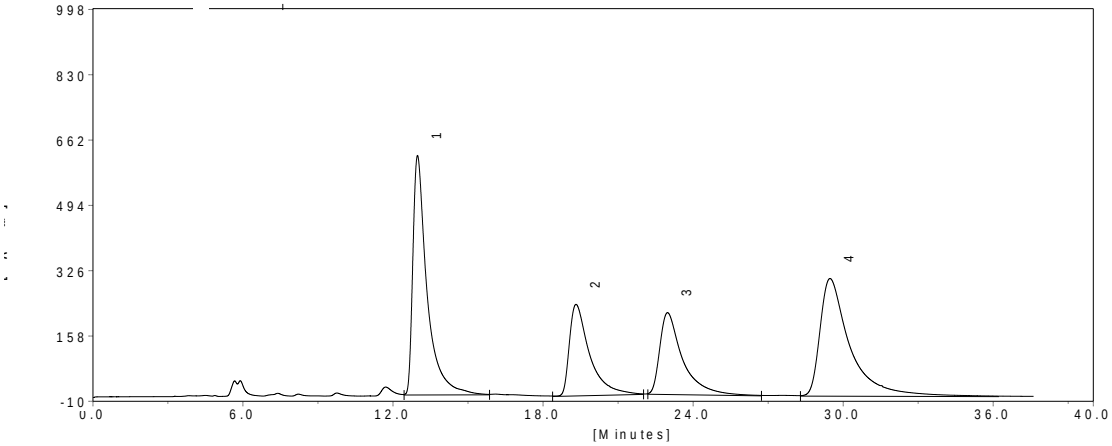
^{13}C NMR spectrum of 4ab



7. Chiral HPLC chromatograms

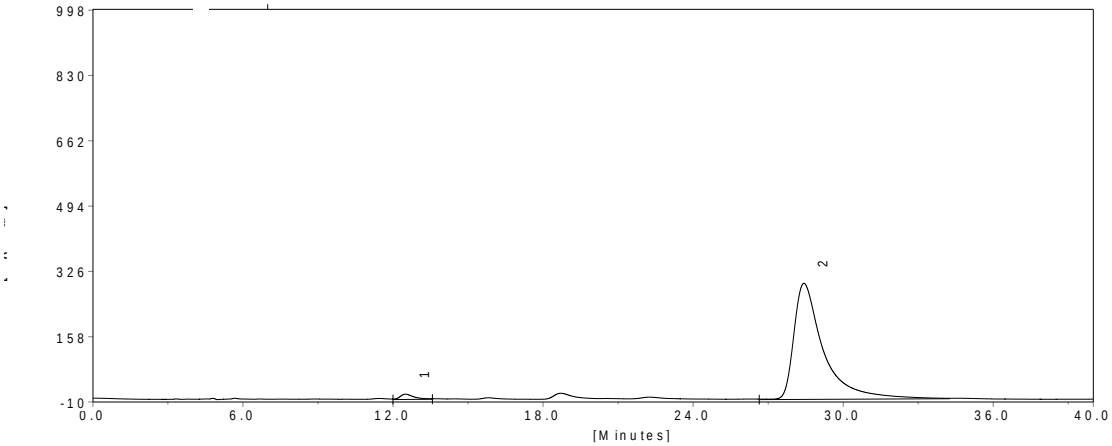


HPLC chromatogram of racemic **3aa**

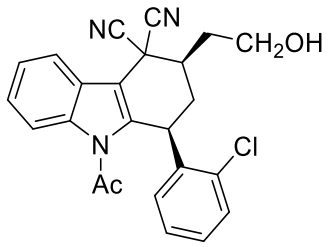


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	12.98000	615.08	24079.01	32.1464
2	19.31750	234.44	12997.36	17.3520
3	22.97583	209.54	13063.98	17.4409
4	28.77333	301.46	24763.75	33.0606

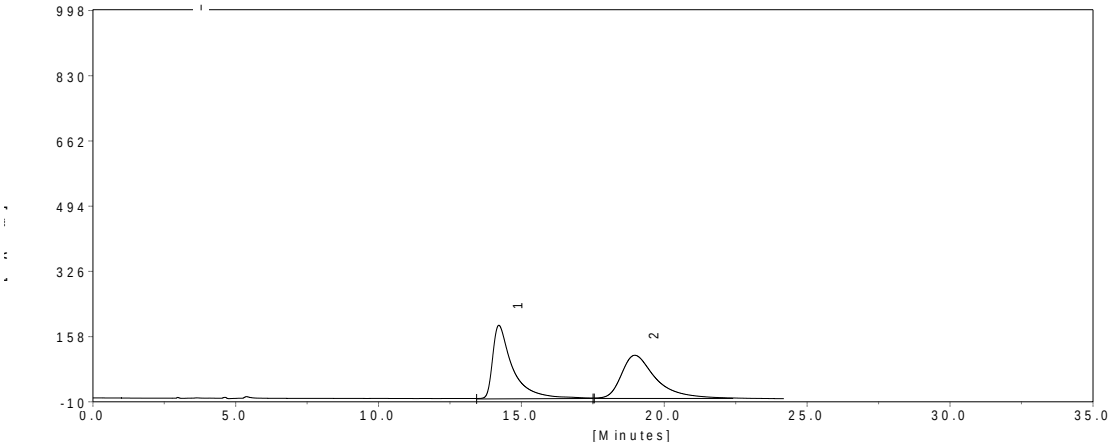
HPLC chromatogram of (1*S*,3*S*)-**3aa** (96% ee)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	12.49917	12.32	413.42	1.6880
2	28.43250	297.42	24078.16	98.3120

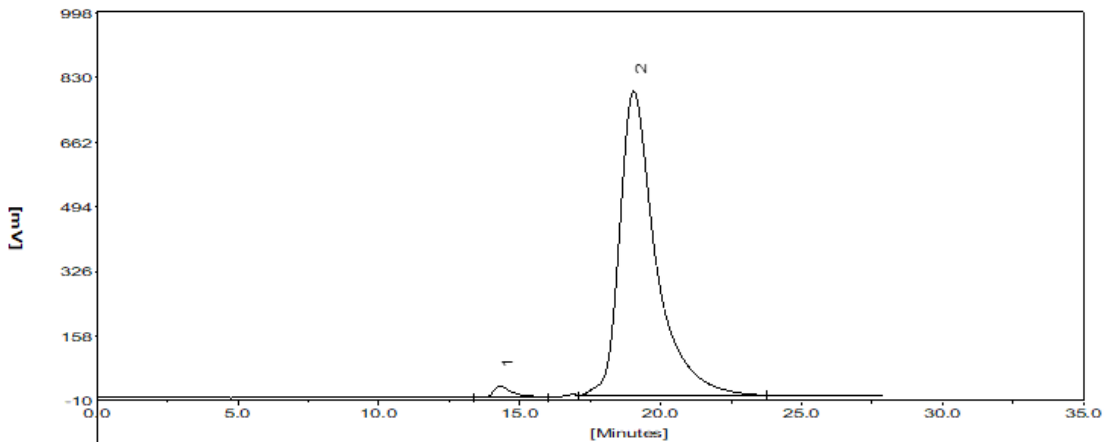


HPLC chromatogram of racemic **3ba**

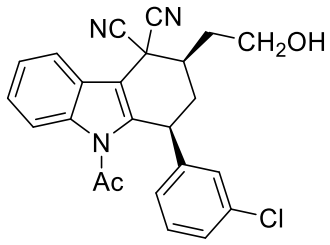


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	14.20833	188.51	8965.88	49.8873
2	18.96833	110.09	9006.41	50.1127

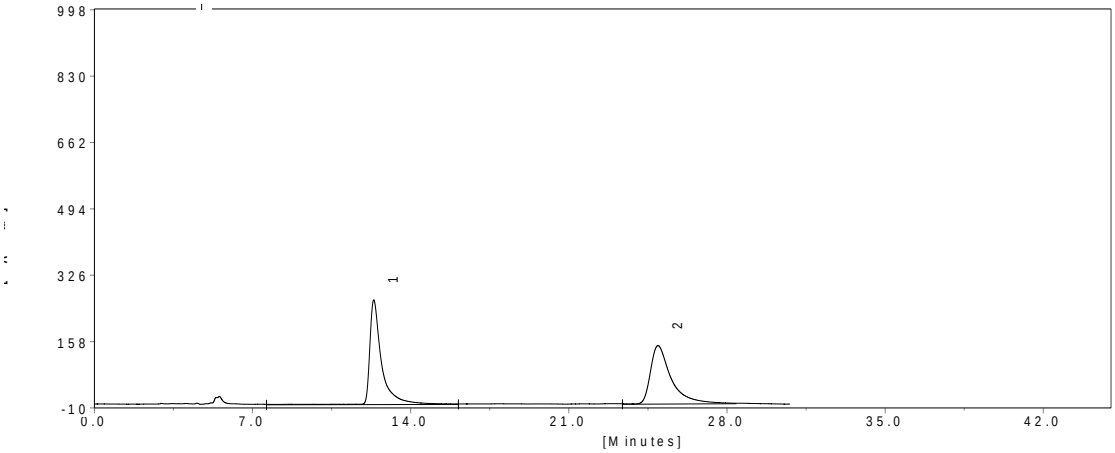
HPLC chromatogram of (1*S*,3*S*)-**3ba** (97% ee)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	14.29833	28.17	1248.66	1.7324
2	19.04500	789.44	70004.43	98.2776

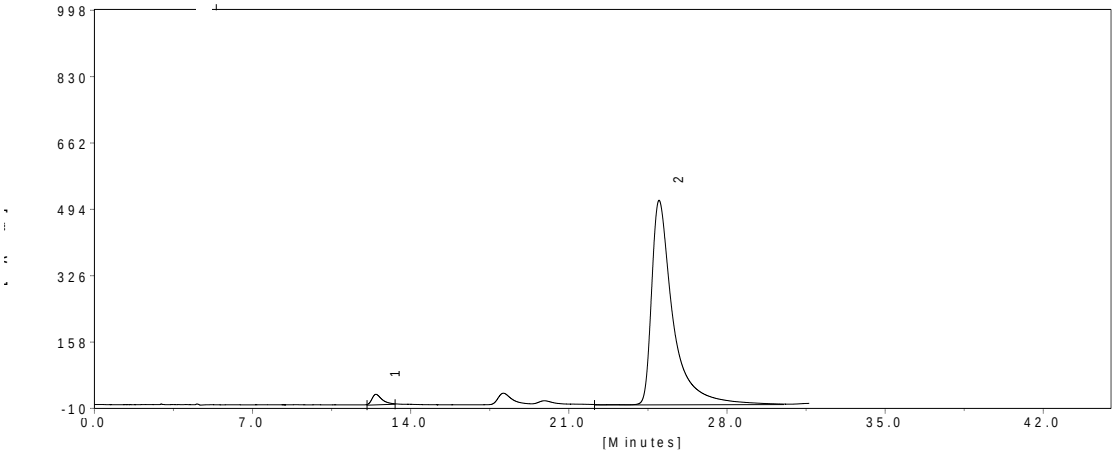


HPLC chromatogram of racemic **3ca**

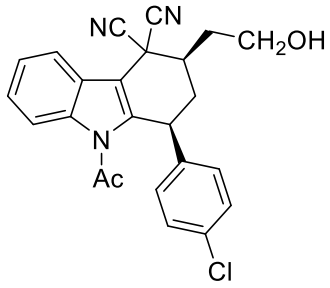


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	12.36750	264.02	9246.21	50.3280
2	24.94750	146.89	9125.68	49.6720

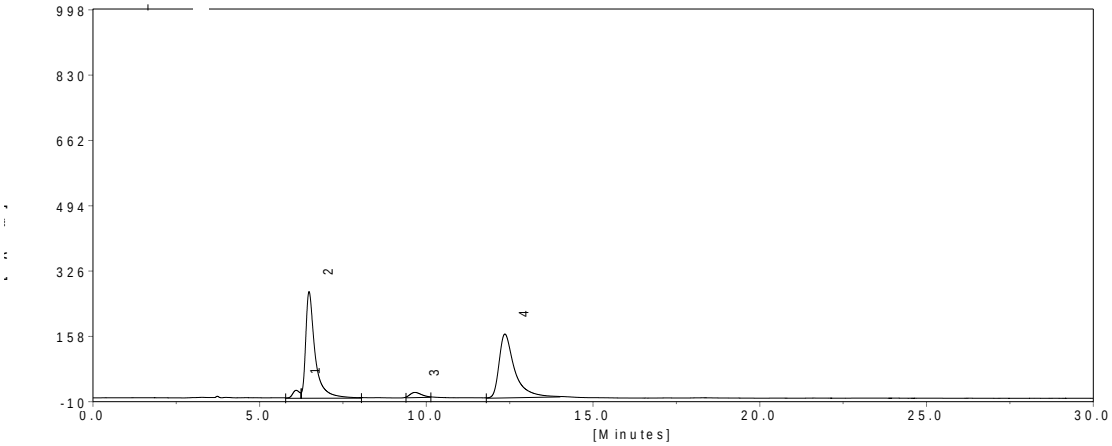
HPLC chromatogram of (1*S*,3*S*)-**3ca** (96% ee)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	12.45750	25.45	751.81	2.1902
2	24.99333	516.82	33574.04	97.8098

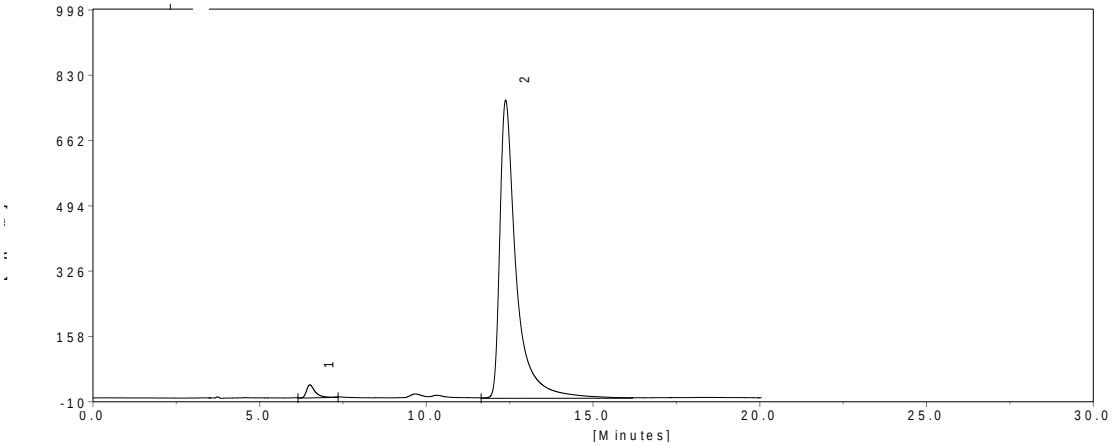


HPLC chromatogram of racemic **3da**

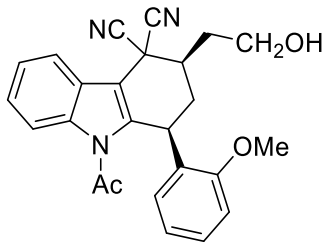


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	6.09417	19.31	262.99	2.3906
2	6.48250	273.11	5276.42	47.9623
3	9.66250	12.11	271.71	2.4698
4	12.35667	163.36	5190.06	47.1773

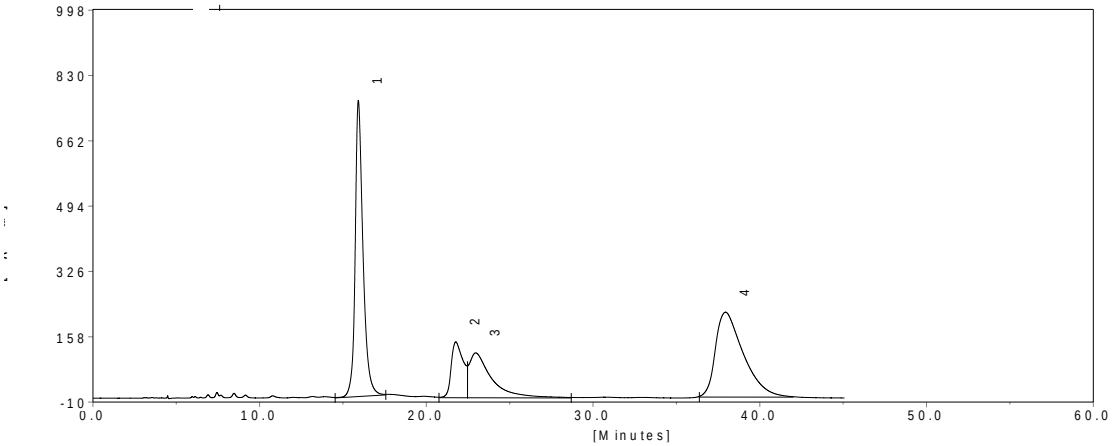
HPLC chromatogram of (1*S*,3*S*)-**3da** (96% ee)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	6.50583	32.59	546.14	2.0571
2	12.37750	766.22	26003.16	97.9429

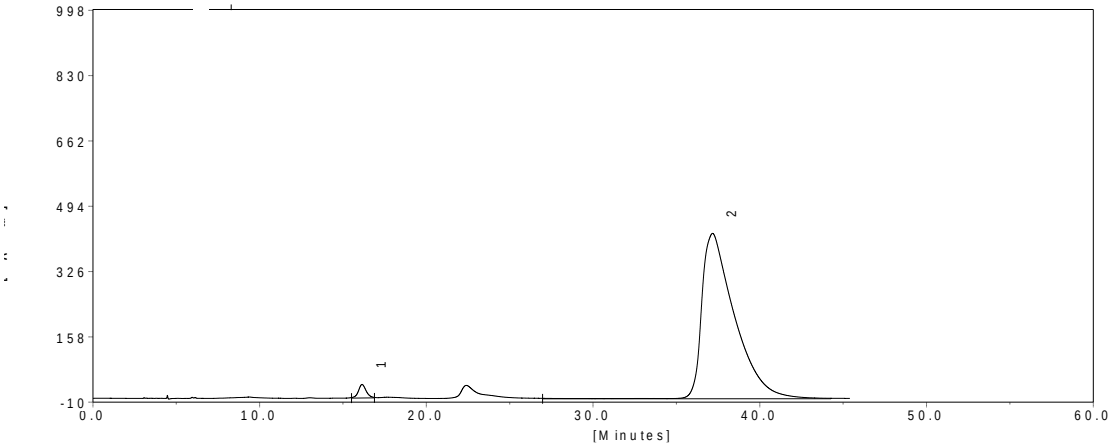


HPLC chromatogram of racemic **3ea**

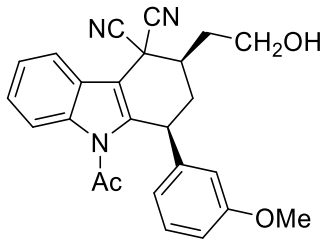


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	15.92083	760.51	24619.61	36.6972
2	21.76333	142.84	7040.78	10.4948
3	22.96500	114.34	10452.51	15.5802
4	37.95333	217.21	24975.54	37.2278

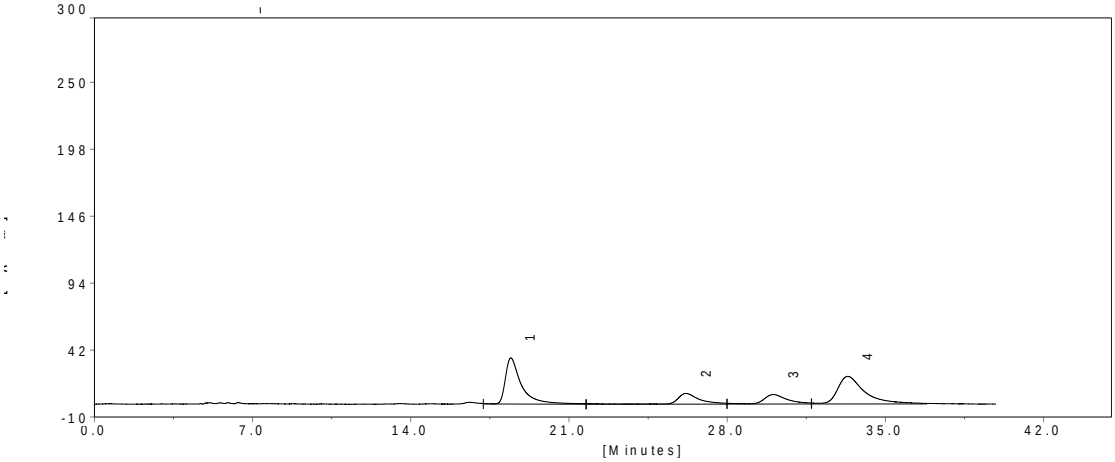
HPLC chromatogram of (1*S*,3*S*)-**3ea** (96% ee)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	16.14000	33.62	1033.22	1.7779
2	37.16750	424.32	57082.50	98.2221

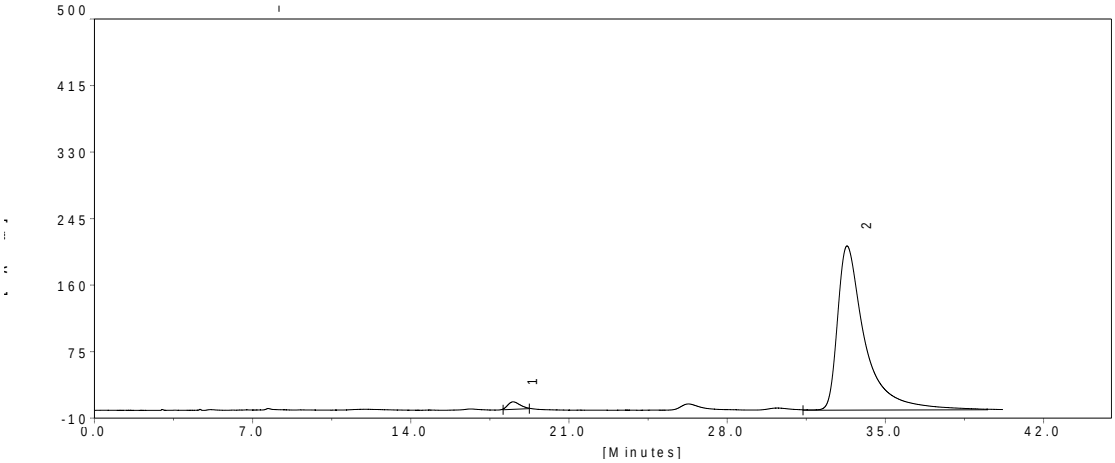


HPLC chromatogram of racemic **3fa**

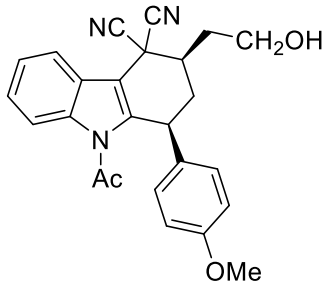


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	18.42333	35.45	1673.48	39.4370
2	26.21167	7.86	425.80	10.0343
3	30.07833	6.99	460.35	10.8485
4	33.34750	21.09	1683.79	39.6802

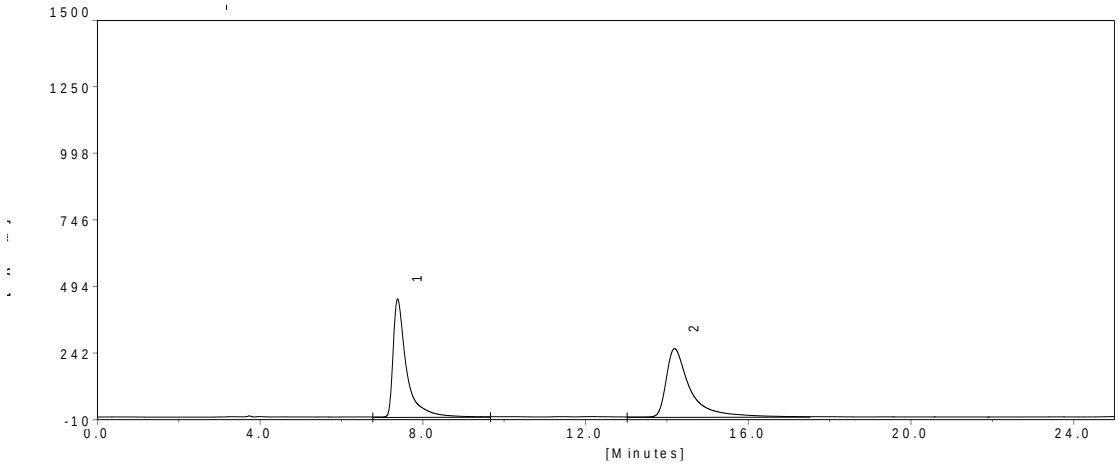
HPLC chromatogram of (1*S*,3*S*)-**3fa** (96% ee)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	18.53167	8.93	314.65	1.7779
2	33.30250	209.31	17382.93	98.2221

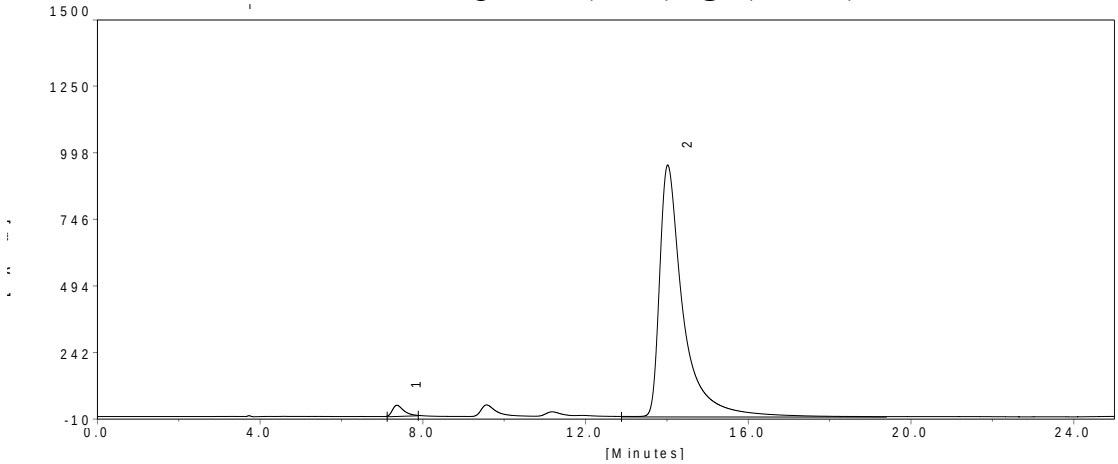


HPLC chromatogram of racemic **3ga**

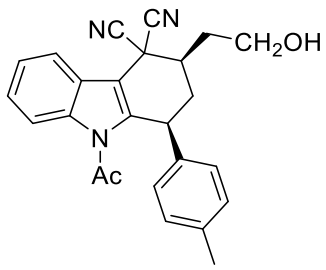


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	7.38000	446.79	10067.71	49.1655
2	14.18750	258.25	10409.48	50.8345

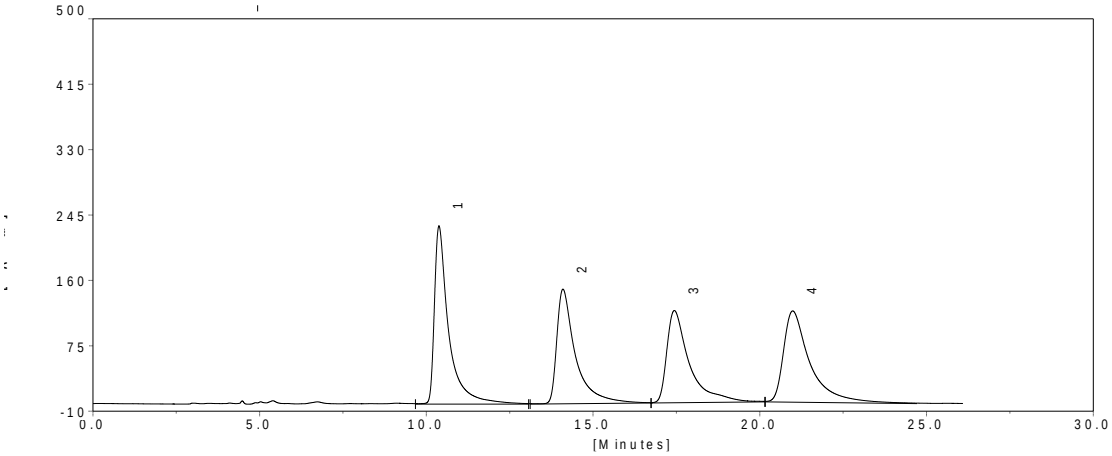
HPLC chromatogram of (1*S*,3*S*)-**3ga** (96% ee)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	7.36083	40.61	756.17	1.9605
2	14.02000	951.70	37813.97	98.0395

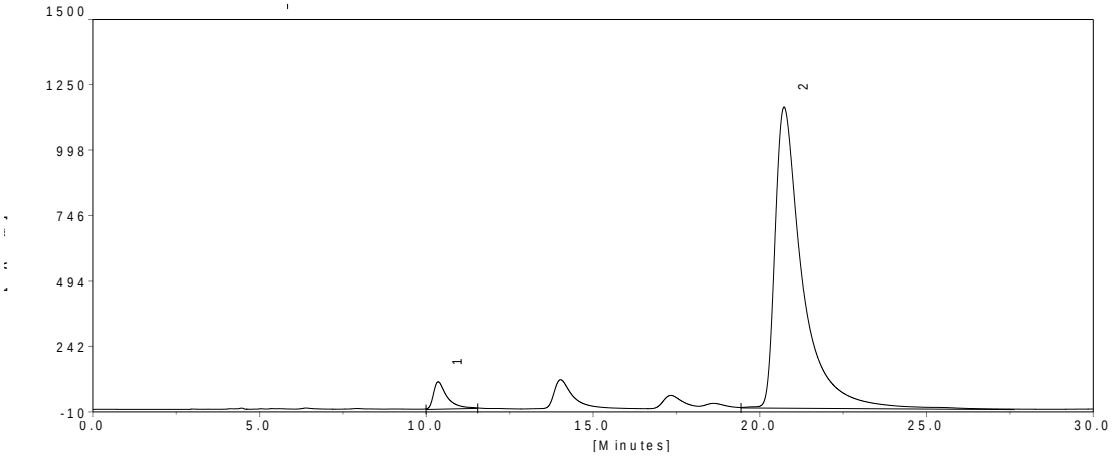


HPLC chromatogram of racemic **3ha**

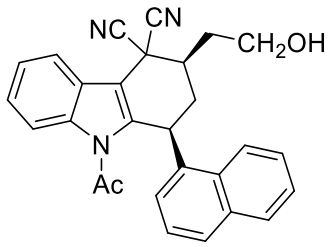


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	10.37917	230.98	6797.01	27.8627
2	14.09667	148.49	5686.78	23.3116
3	17.43917	119.26	5509.40	22.5845
4	20.98917	118.05	6401.42	26.2411

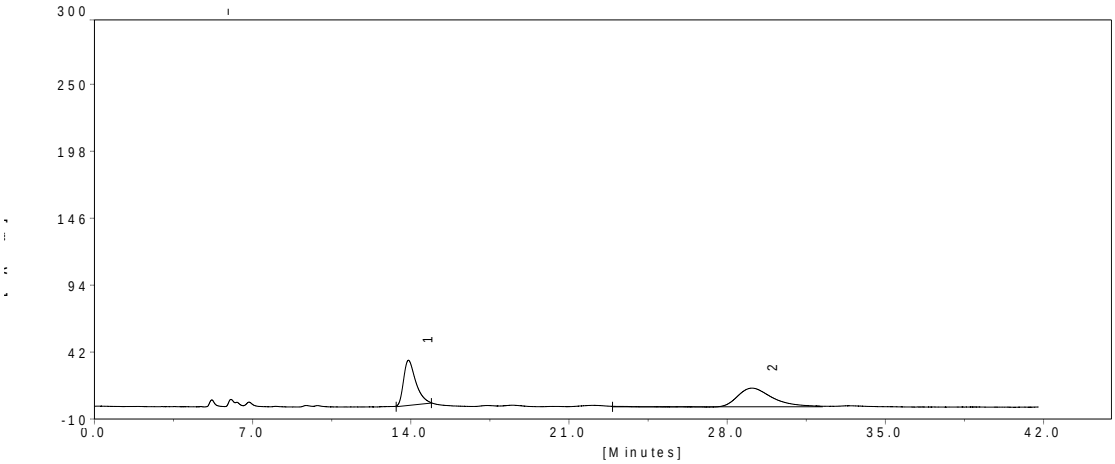
HPLC chromatogram of (1*S*,3*S*)-**3ha** (92% ee)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	10.35417	103.77	2839.50	4.1320
2	20.72833	1157.43	65881.07	95.8680

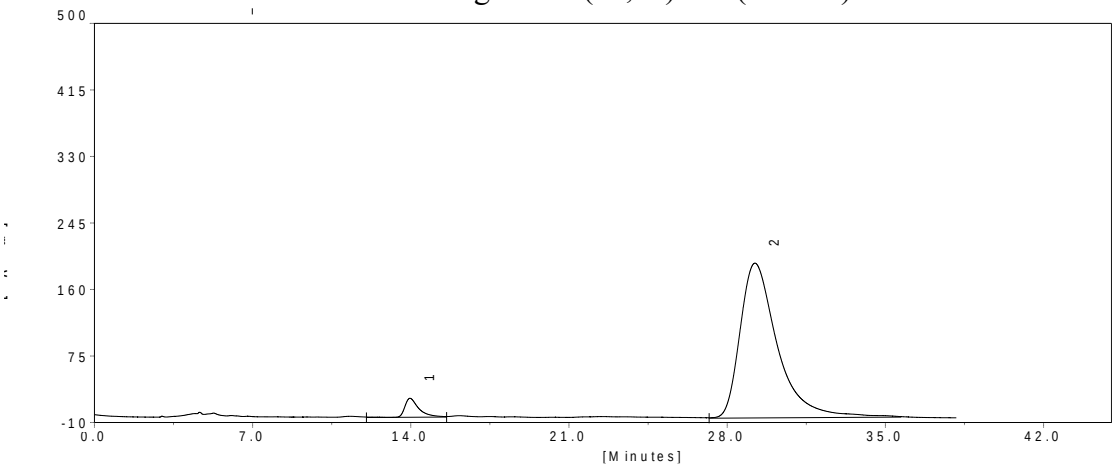


HPLC chromatogram of racemic **3ia**

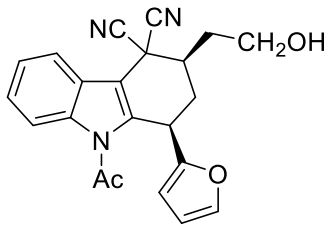


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	13.89417	34.73	1281.80	49.1228
2	29.14917	14.05	1327.58	50.8772

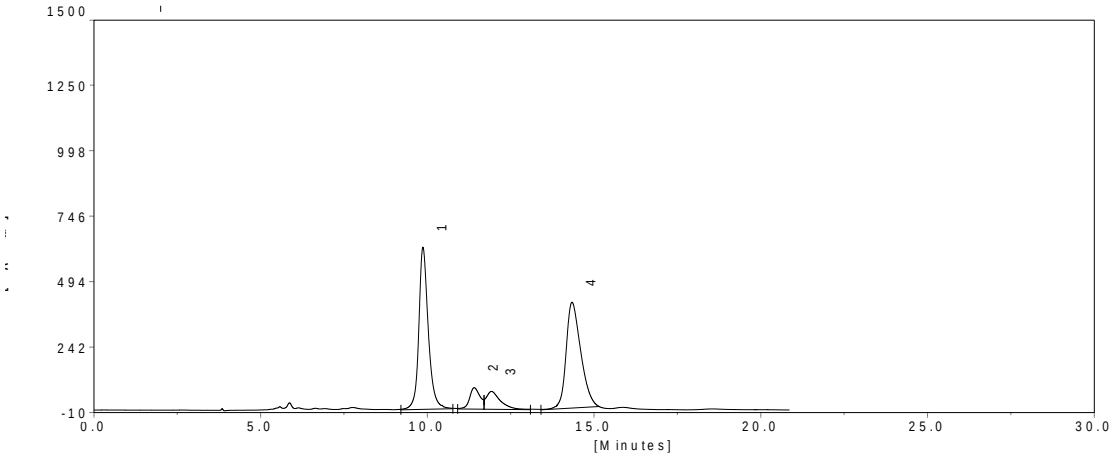
HPLC chromatogram of (1*S*,3*S*)-**3ia** (92% ee)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	13.96833	23.65	930.84	3.9819
2	29.22667	197.20	22445.65	96.0181

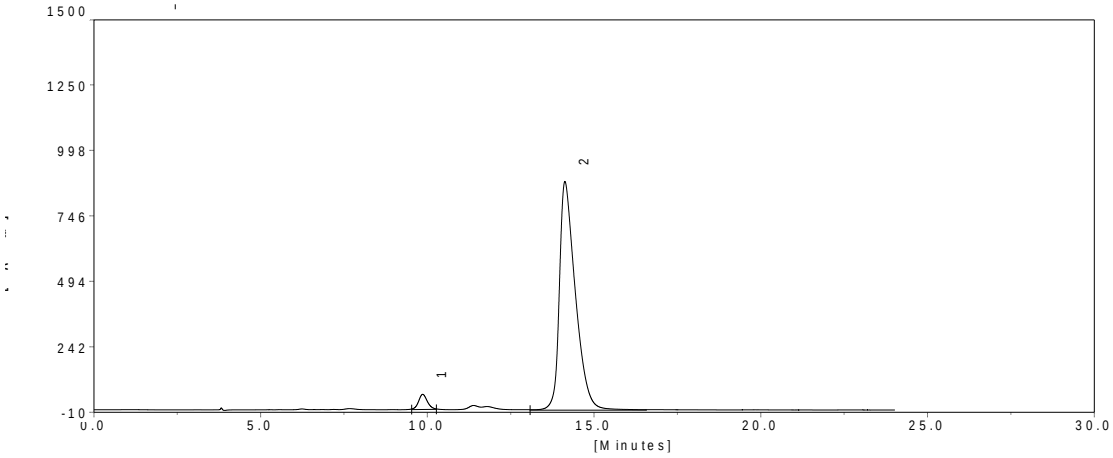


HPLC chromatogram of racemic **3ja**

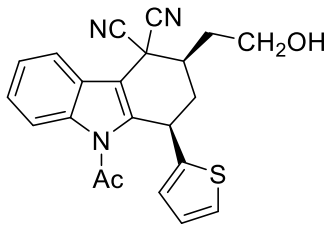


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	9.86750	622.45	12132.15	43.4176
2	11.40583	80.62	1683.18	6.0236
3	11.92417	66.92	1922.77	6.8810
4	14.33917	405.49	12204.84	43.6777

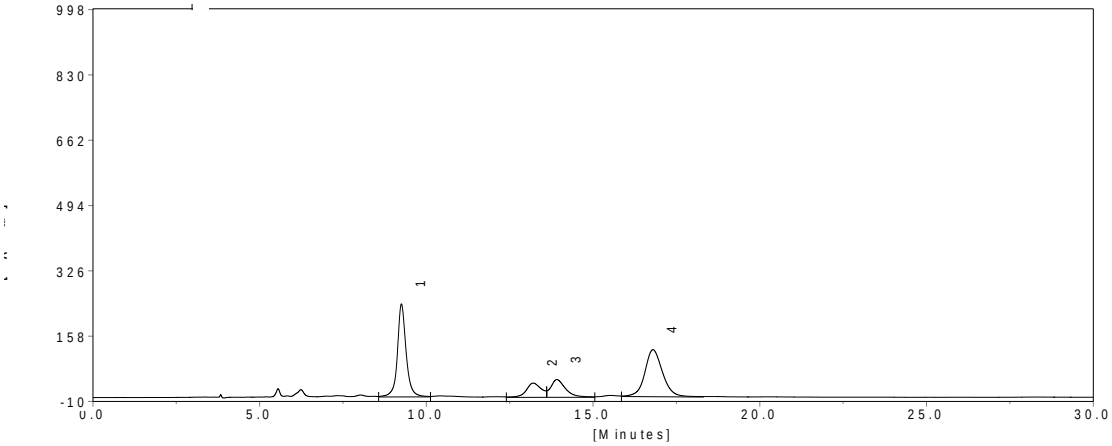
HPLC chromatogram of (1*S*,3*S*)-**3ja** (93% ee)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	9.86000	56.58	995.71	3.3121
2	14.12583	878.52	29067.03	96.6879

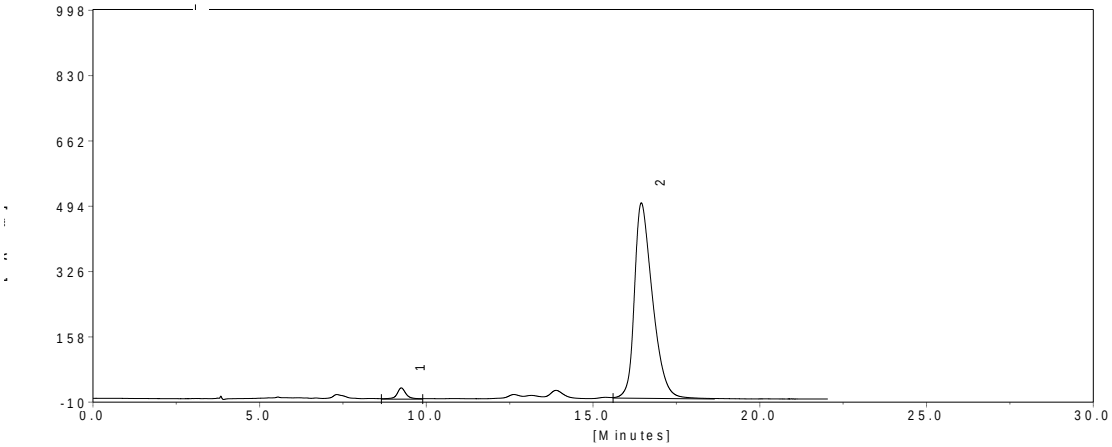


HPLC chromatogram of racemic **3ka**

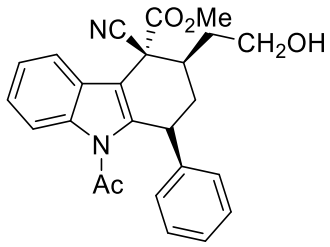


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	9.25250	238.18	4251.14	38.8231
2	13.20667	35.55	1055.28	9.6373
3	13.91417	44.56	1329.43	12.1409
4	16.79667	119.81	4314.15	39.3986

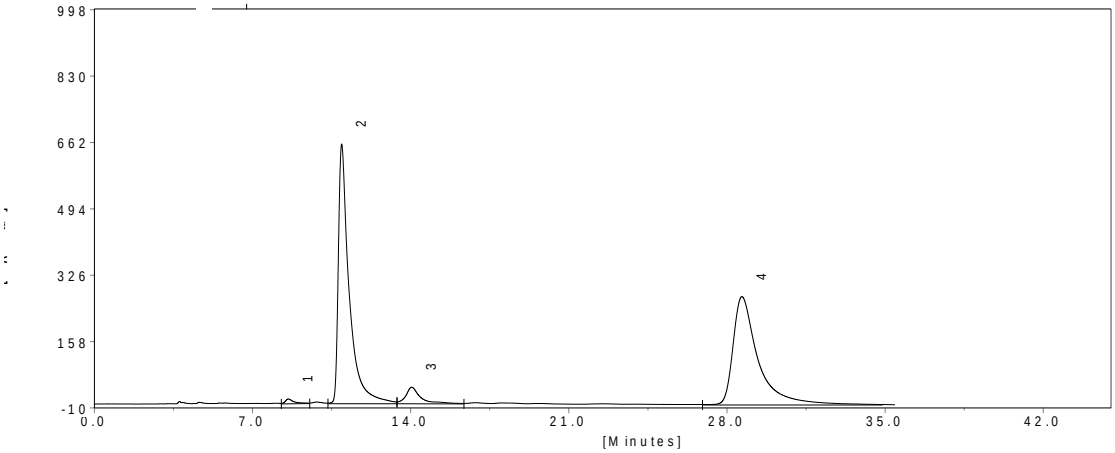
HPLC chromatogram of (1*S*,3*S*)-**3ka** (95% ee)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	9.24833	27.73	478.98	2.4943
2	16.44750	501.79	18723.89	97.5057

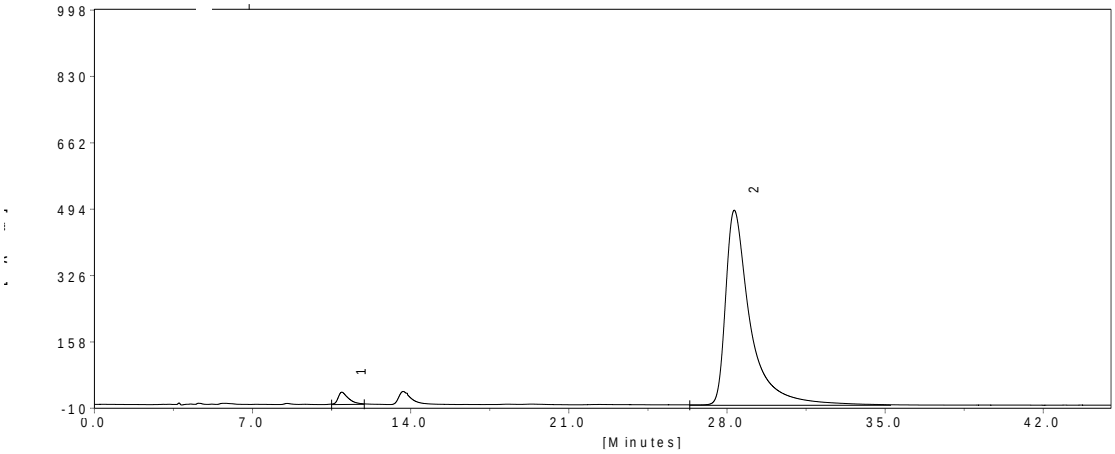


HPLC chromatogram of racemic **3la**

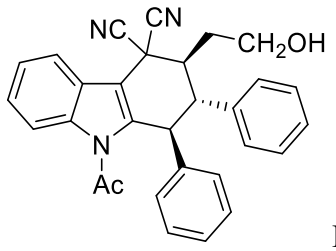


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	8.58583	11.01	248.74	0.5572
2	10.94667	656.23	21826.48	48.8964
3	14.04500	40.97	1766.73	3.9579
4	28.66167	273.24	20796.25	46.5885

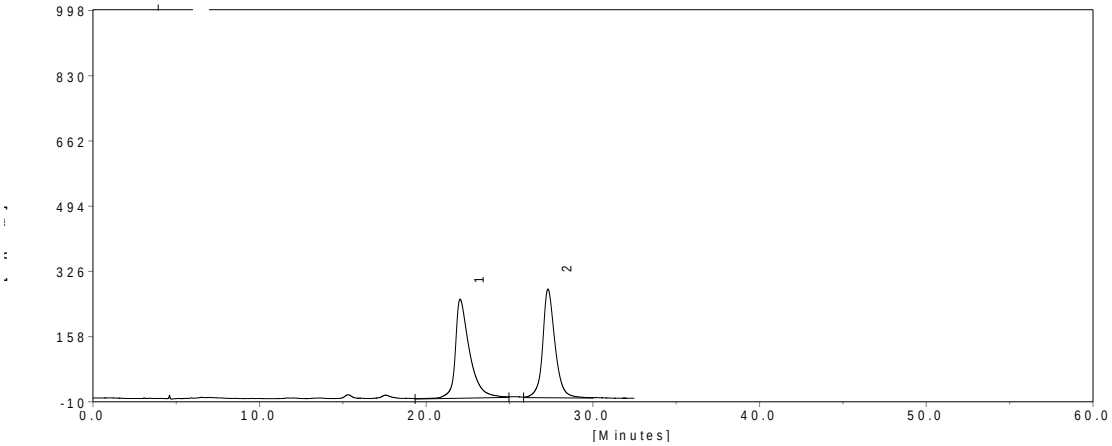
*H*PLC chromatogram of (1*R*, 3*R*, 4*R*)-**3la** (95% ee)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	10.95167	30.08	909.40	2.3888
2	28.32250	492.79	37160.13	97.6112

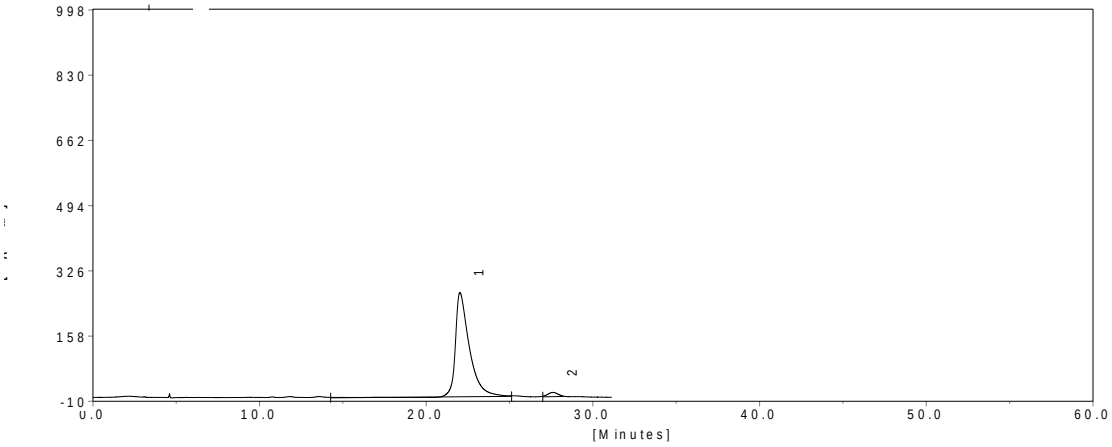


HPLC chromatogram of racemic **3ab**

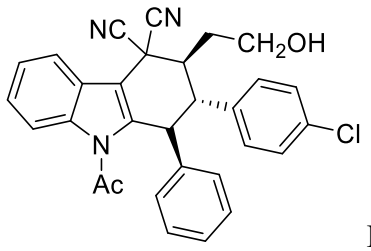


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	22.03417	251.87	14156.16	50.0716
2	27.30250	278.93	14115.67	49.9284

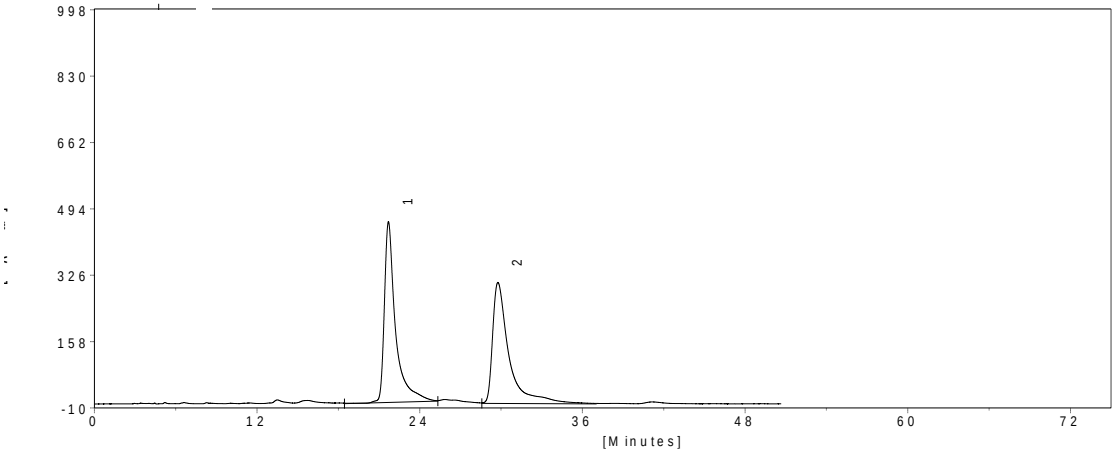
HPLC chromatogram of (1*S*, 2*S*, 3*S*)-**3ab** (95% ee)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	22.02250	267.33	14804.40	97.5679
2	27.60667	9.66	369.03	2.4321

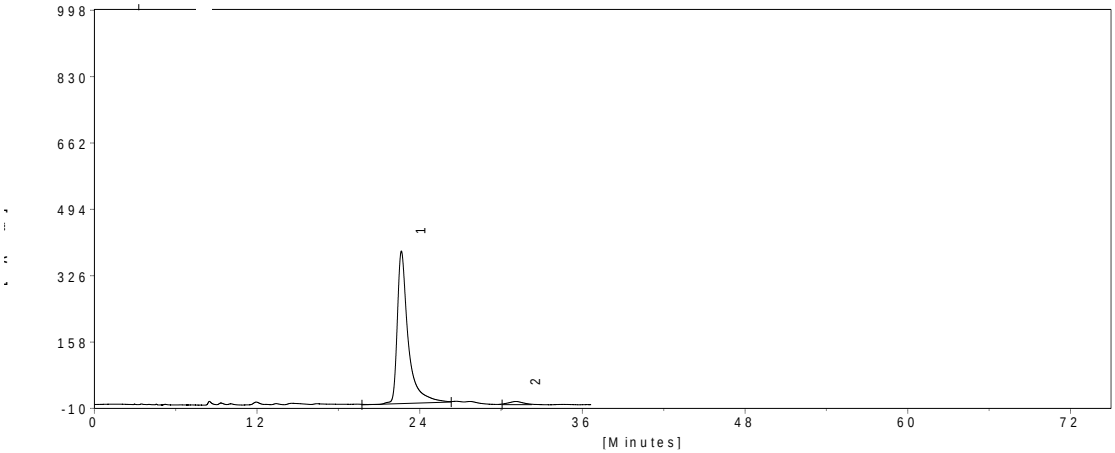


HPLC chromatogram of racemic **3ac**

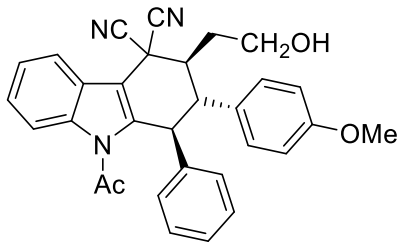


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	21.69250	456.65	25763.08	50.4820
2	29.76750	305.29	25271.16	49.5180

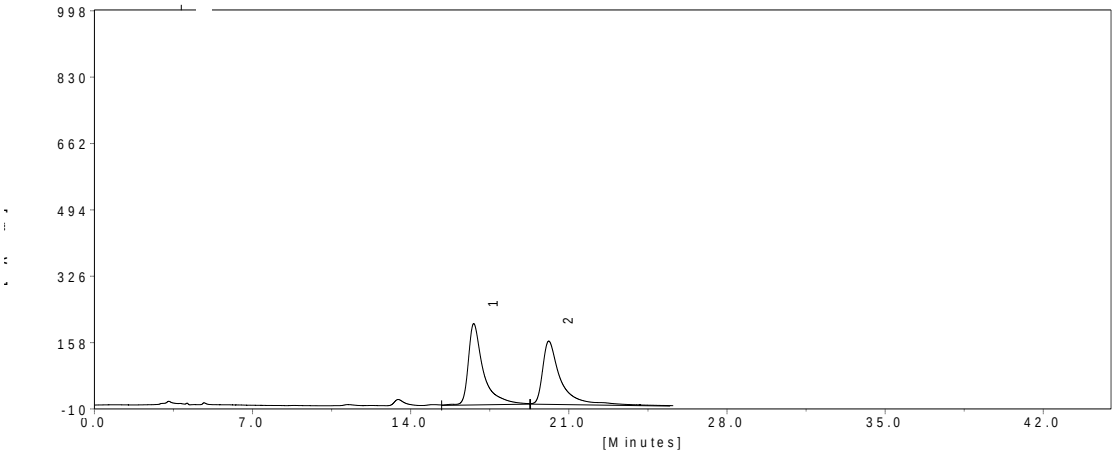
HPLC chromatogram of (1*S*, 2*S*, 3*S*)-**3ac** (96% ee)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	22.34583	385.18	21086.08	97.9642
2	30.41333	6.74	438.19	2.0358

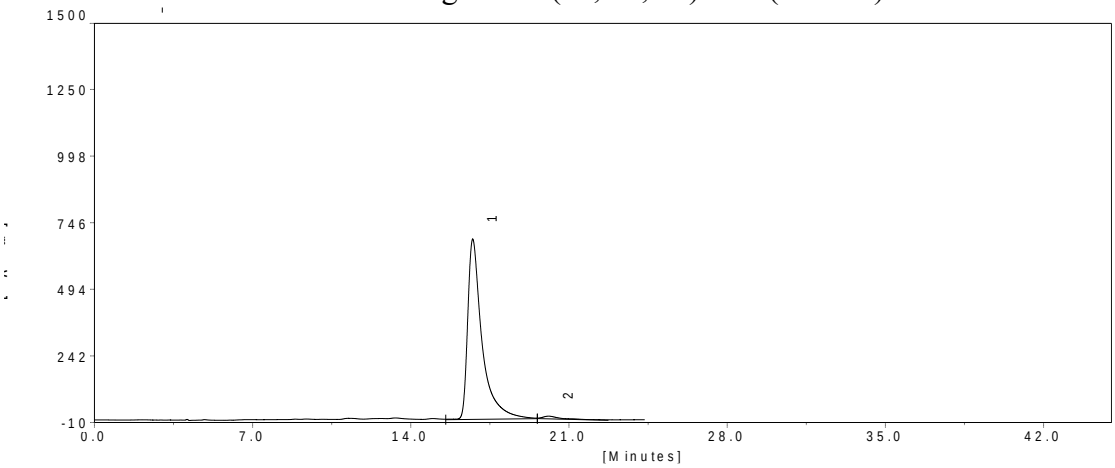


HPLC chromatogram of racemic **3ad**

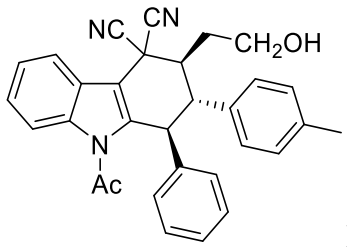


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	16.78917	204.85	8943.06	50.4967
2	20.10917	159.17	8867.43	49.5033

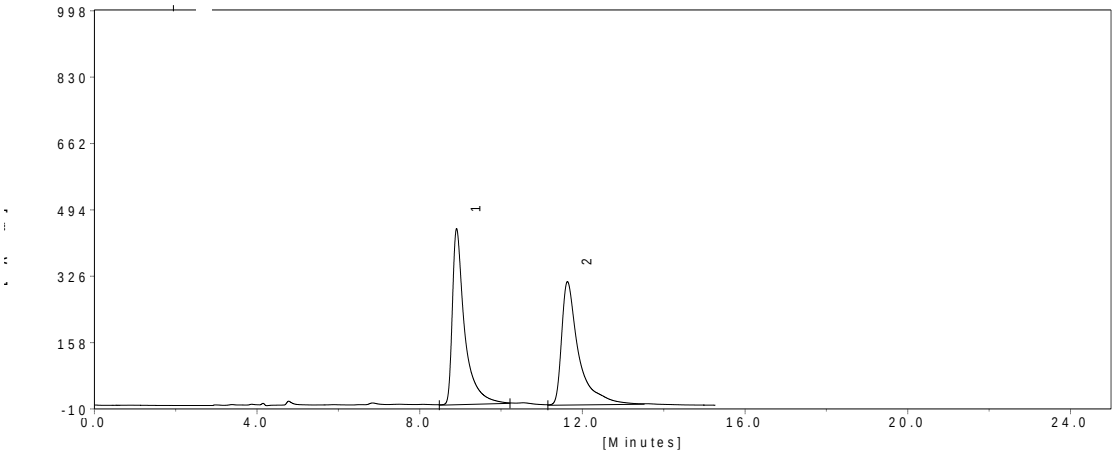
HPLC chromatogram of (1*S*, 2*S*, 3*S*)-**3ad** (98% ee)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	16.74000	680.36	29662.53	98.9757
2	20.11167	8.62	306.99	1.0243

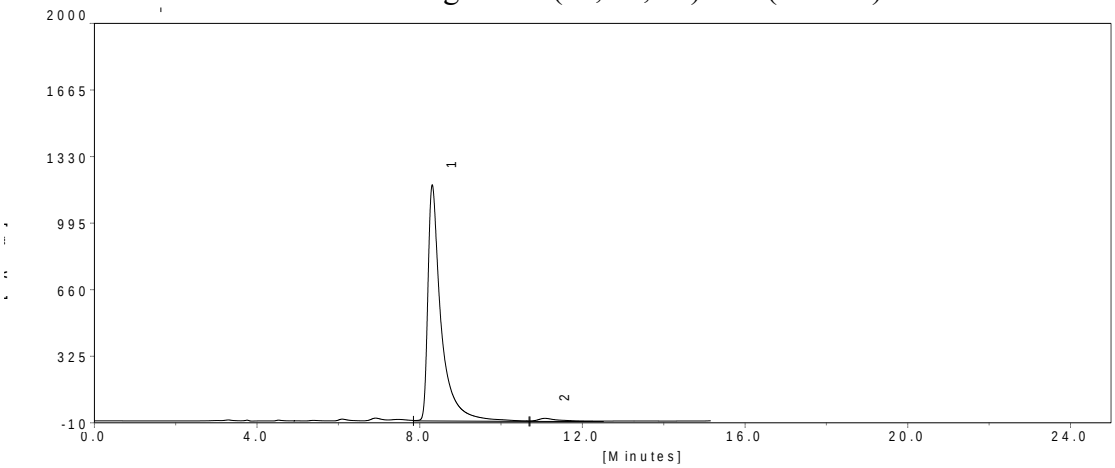


HPLC chromatogram of racemic **3ae**

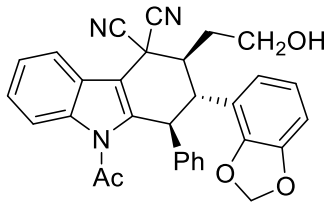


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	8.90667	444.99	9239.04	50.4831
2	11.63250	311.58	8954.11	49.5169

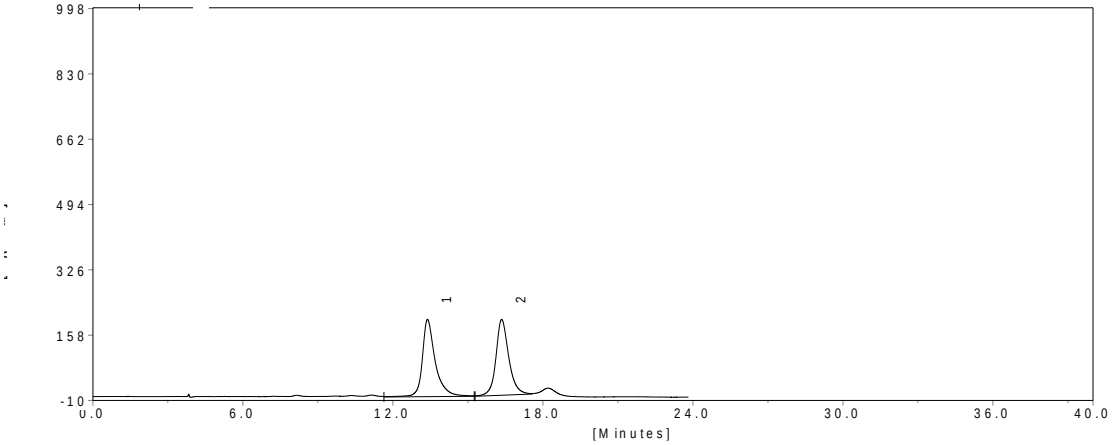
HPLC chromatogram of (1*S*, 2*S*, 3*S*)-**3ae** (97% ee)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	8.30833	1186.69	26537.01	98.6082
2	11.08167	13.10	374.56	1.3918

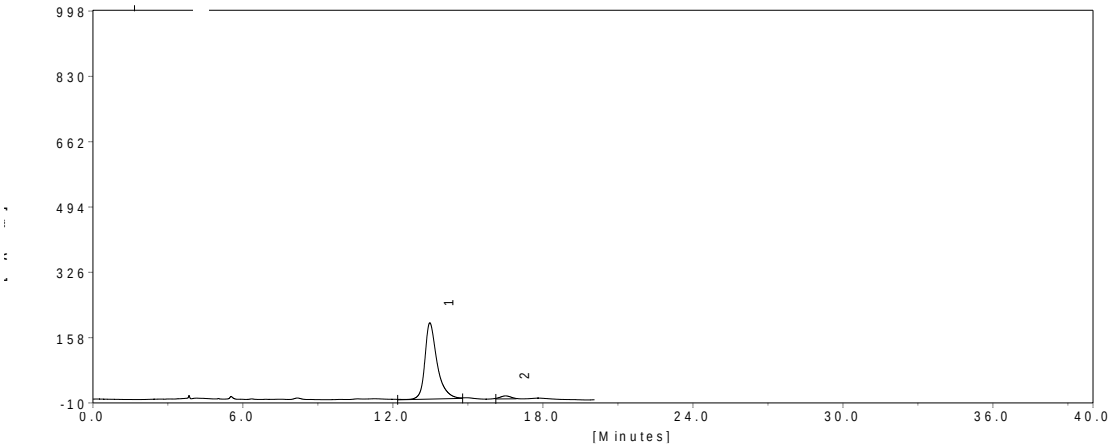


HPLC chromatogram of racemic **3af**

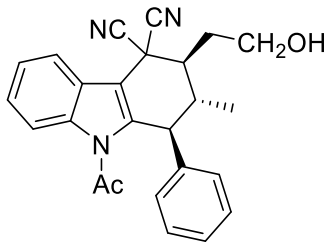


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	13.38417	197.65	6905.33	50.4730
2	16.35167	193.93	6775.90	49.5270

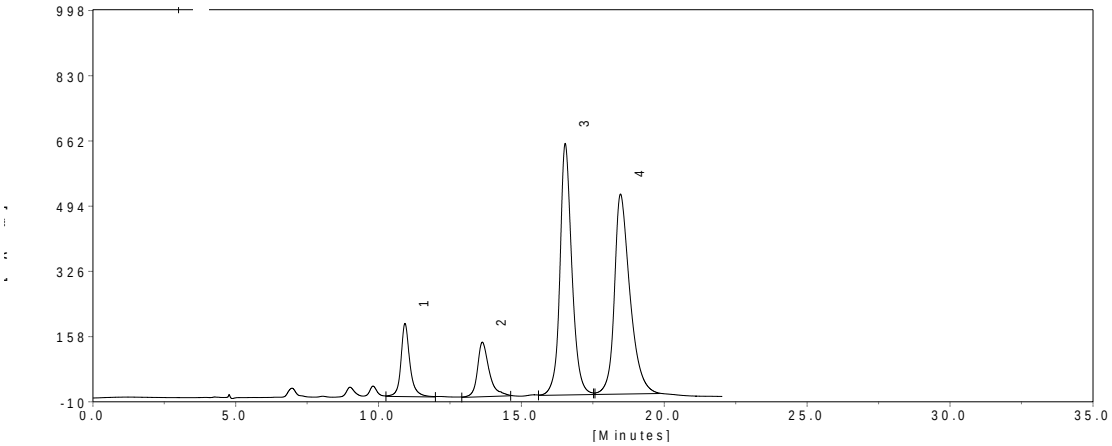
HPLC chromatogram of (1*S*, 2*S*, 3*S*)-**3af** (95% ee)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	13.47750	195.15	6452.46	97.4403
2	16.50000	6.49	169.51	2.5597

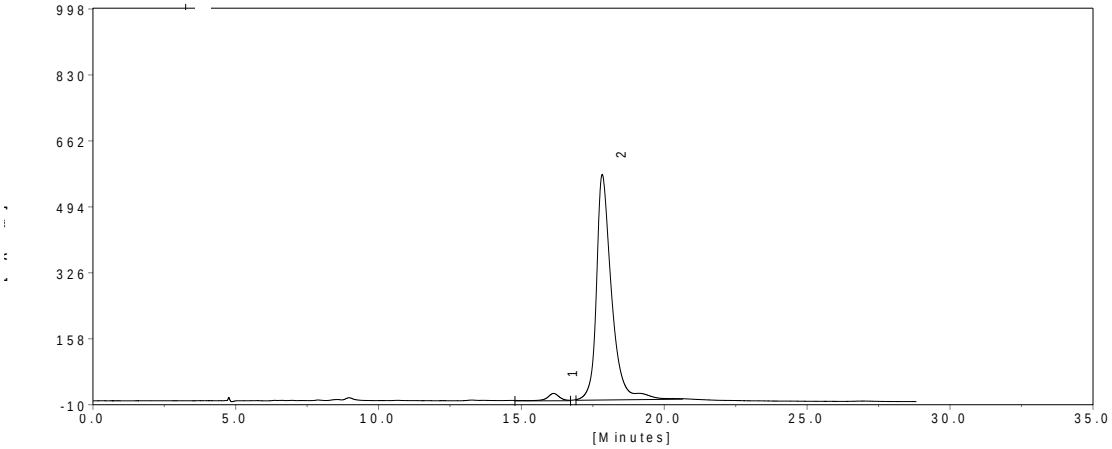


HPLC chromatogram of racemic **3ag**

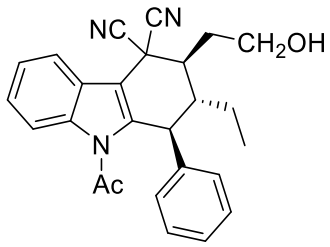


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	10.92250	187.48	3967.17	8.6651
2	13.63000	139.40	3873.29	8.4600
3	16.53083	646.97	18586.94	40.5976
4	18.46667	514.25	19355.94	42.2773

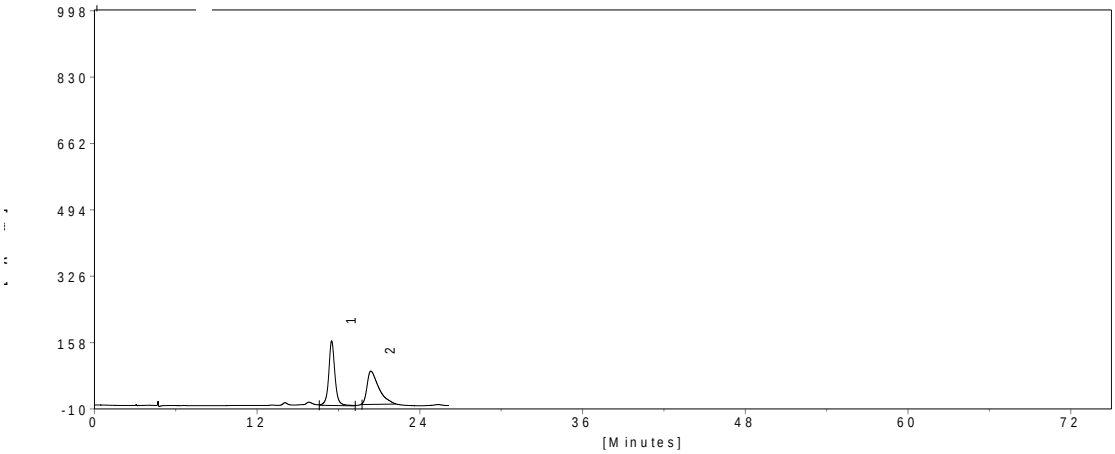
HPLC chromatogram of (1*S*, 2*S*, 3*S*)-**3ag** (95% ee)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	16.12000	17.60	439.61	2.0648
2	17.82583	573.66	20851.27	97.9352

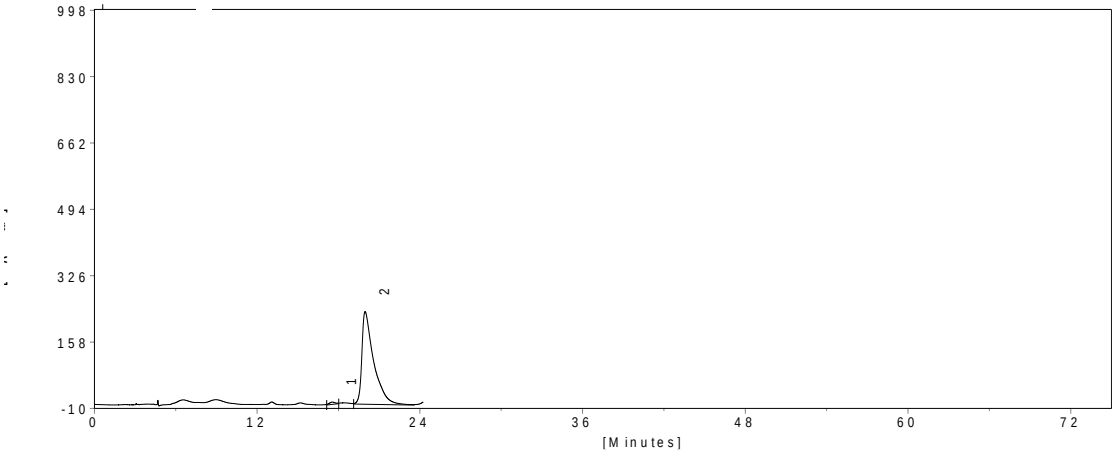


HPLC chromatogram of racemic **3ah**

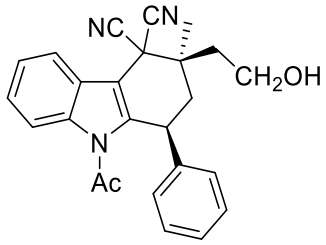


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	17.49750	162.66	4987.32	50.6757
2	19.78667	83.29	4854.32	49.3243

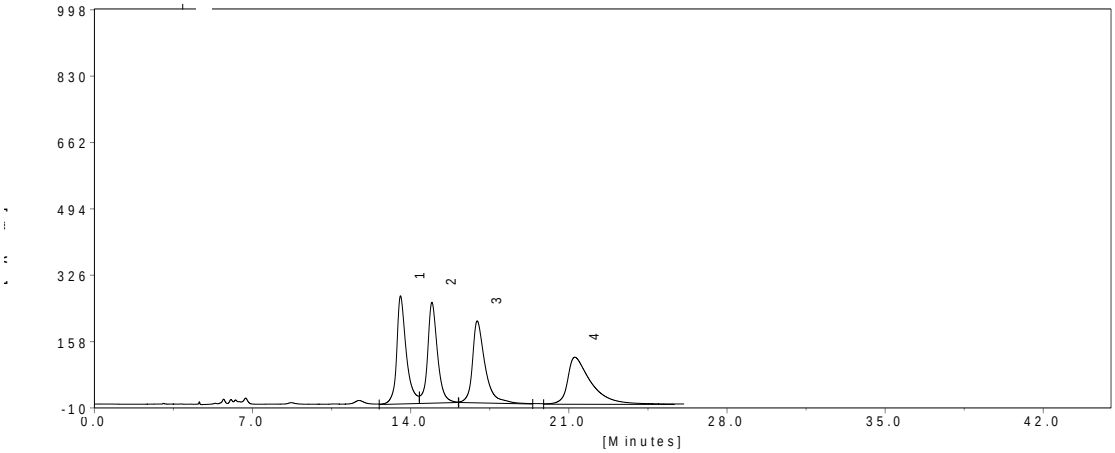
HPLC chromatogram of (1*S*, 2*S*, 3*S*)-**3ah** (98% ee)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	17.53917	4.43	110.12	0.7864
2	19.96667	233.45	13892.25	99.2136

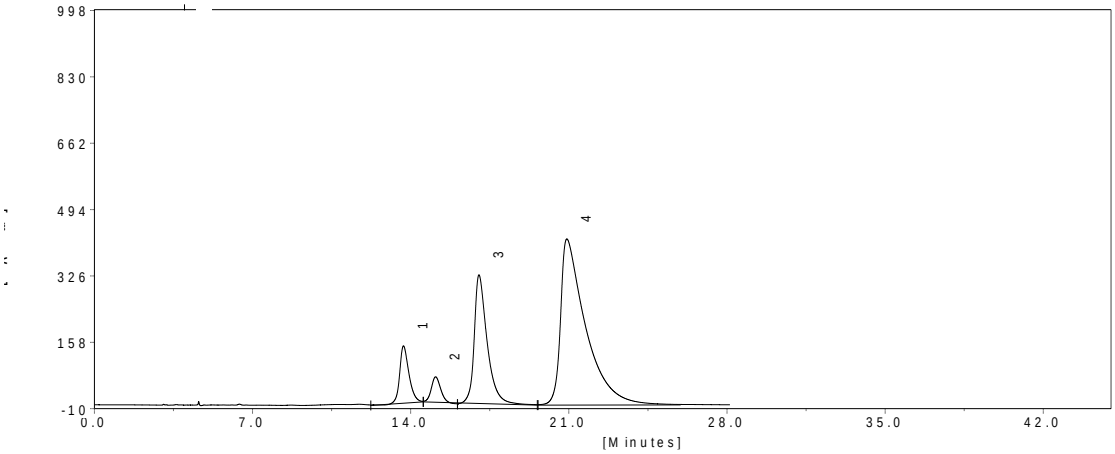


HPLC chromatogram of racemic **3ai**

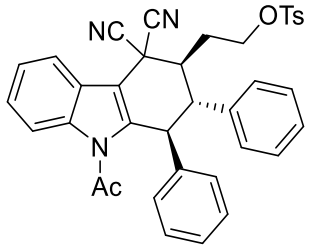


#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	13.54917	272.57	7946.47	25.0931
2	14.94000	254.21	7649.74	24.1560
3	16.94500	206.35	7799.75	24.6297
4	21.26417	117.97	8272.04	26.1212

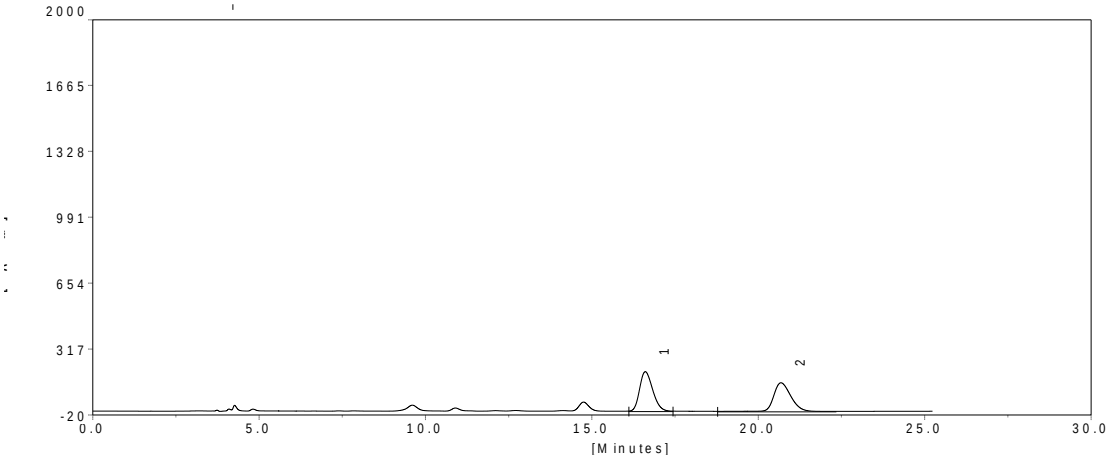
HPLC chromatogram of (1*S*, 3*S*)-**3ai** (43% ee)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	13.68083	144.00	3940.34	7.8241
2	15.10333	63.17	1682.46	3.3408
3	17.02333	324.48	12619.83	25.0586
4	20.91250	419.46	32118.66	63.7765

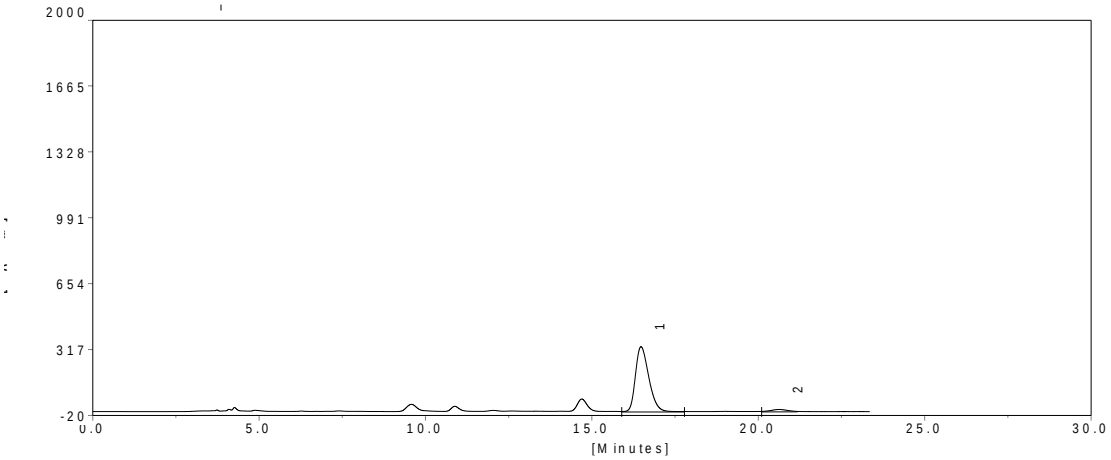


HPLC chromatogram of racemic **4ab**



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	16.60500	201.82	5376.64	50.6766
2	20.68333	146.11	5233.06	49.3234

HPLC chromatogram of (1*S*, 3*S*)-**4ab** (95% ee)



#	Ret Time(min)	Height(mV)	Area(mV.sec)	Area(%)
1	16.47667	331.56	9229.38	97.7946
2	20.62500	9.73	208.13	2.2054