

Supporting Information for

Sequential hydroarylation/Prins cyclization: An efficient strategy for the synthesis of angularly fused tetrahydro-2H-pyrano[3,4-c]quinolines

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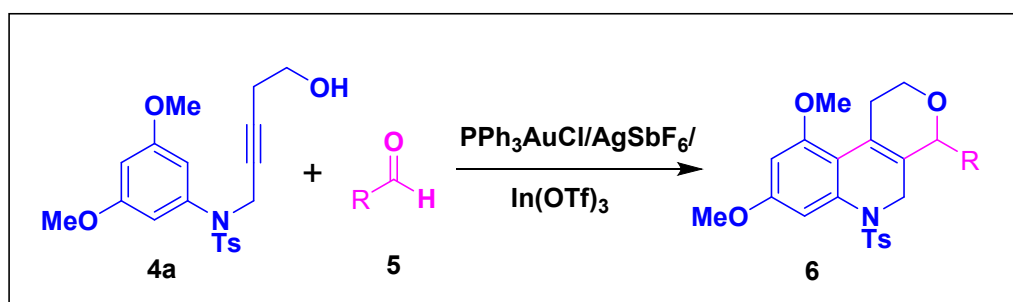
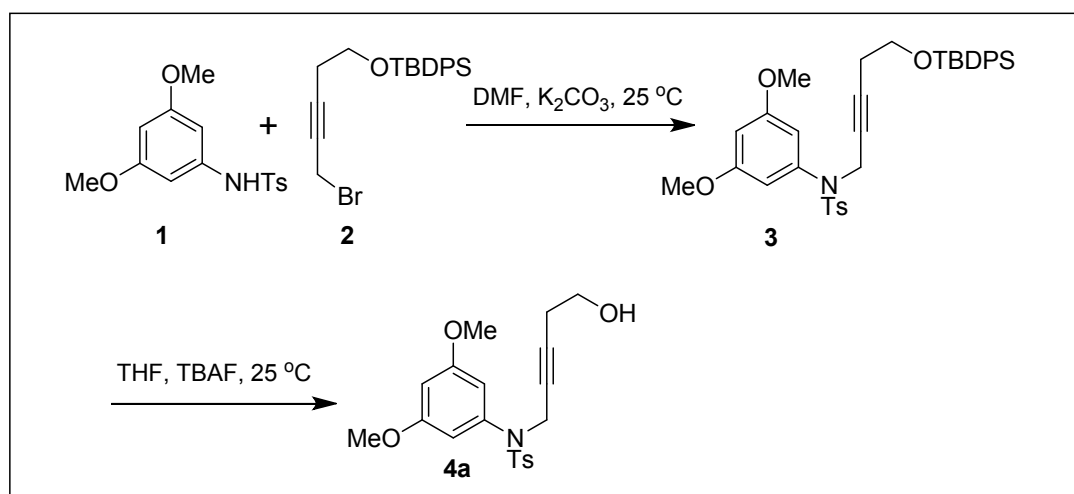


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1. Preparation of starting material



***N*-(3,5-Dimethoxyphenyl)-*N*-(5-hydroxypent-2-yn-1-yl)-4-methylbenzenesulfonamide**

(4a): To a stirred solution of *N*-(3,5-dimethoxyphenyl)-4-methylbenzenesulfonamide (1 g, 3.257 mmol) in DMF (10 mL) were added K₂CO₃ (0.99 g, 7.16 mmol) followed by ((5-bromopent-3-yn-1-yl)oxy)(tert-butyl)diphenylsilane (1.43 g, 3.58 mmol) at 0 °C. The resulting mixture was allowed to stir for 12 h at room temperature. The mixture was diluted with ethyl acetate (2x50 mL) and washed with water (3 x 20 mL). The mixture was then dried over Na₂SO₄ and concentrated in vacuo to afford the TBDPS ether **3**, which was directly used for the next step. To a solution of **3** (2.0 g, 3.257 mmol) in THF (15 ml) at 0 °C was added TBAF (0.99 g, 3.827 mmol) and the resulting mixture was allowed to stir at room temperature for 2h. After completion, as indicated by TLC, the reaction was quenched with sat. solution of NaHCO₃ and the aqueous layer was extracted with ethyl acetate. Removal of the solvent followed by purification on silica gel column chromatography (silica gel, 60-120 mesh) using ethyl acetate/*n*-hexane gradient mixture afforded the alcohol **4** in (1.0 g, 80%) yield as a pale yellow solid.

(4b): *N*-(5-Hydroxypent-2-yn-1-yl)-4-methyl-*N*-phenylbenzenesulfonamide was prepared according to the above procedure.

(4c): *N*-(3,5-Dimethoxyphenyl)-*N*-(5-hydroxypent-2-yn-1-yl)methanesulfonamide was prepared according to the above procedure.

(4d): 5-((3,5-Dimethoxyphenyl)amino)pent-3-yn-1-ol was prepared from **4a** according to the literature.¹

(4e): 5-(Benzyl(3,5-dimethoxyphenyl)amino)pent-3-yn-1-ol: Compound **3** (1 g, 1.59 mmol) was subjected to tosyl deprotection according to the literature procedure.¹ The crude compound was dissolved in dry DMF and then K₂CO₃ (2.0 eq) and benzyl bromide (1.2 eq) were added. The mixture was stirred at 80 °C for 2h. Up on completion, the mixture was diluted with ethyl acetate (2x50 mL) and washed with water (3 x 20 mL). The mixture was then dried over Na₂SO₄ and concentrated in vacuo followed by purification on silica gel column chromatography (60-120 mesh) using ethyl acetate/*n*-hexane gradient mixture gave the *N*-benzyl derivative (0.712 g, 80%) yield as a pale yellow liquid. To a solution of *N*-benzyl compound (0.712 g, 1.26 mmol) in THF (15 ml) at 0 °C was added TBAF (1.2 equiv) and the resulting mixture was allowed to stir at room temperature for 2h. After completion, as indicated by TLC, the reaction was quenched with sat. solution of NaHCO₃ and the aqueous layer was extracted with ethyl acetate. Removal of the solvent followed by purification on silica gel column chromatography (silica gel, 60-120 mesh) using ethyl acetate/*n*-hexane gradient mixture afforded the alcohol **4e** in (0.300 g, 73%) yield as a pale yellow liquid.

***N*-(3,5-Dimethoxyphenyl)-*N*-(5-hydroxypent-2-yn-1-yl)-4-methylbenzenesulfonamide**

(4a): Yield 80%, pale yellow solid, , m.p.95°C, ¹H NMR (500 MHz, CDCl₃): δ 7.61 (d, *J* = 8.2 Hz, 2H), 7.27-7.24 (m, 2H), 6.42-6.40 (m, 3H), 4.38 (t, *J* = 2.1 Hz, 2H), 3.72 (s, 6H), 3.55 (t, *J* = 6.2 Hz, 2H), 2.42 (s, 3H), 2.32-2.28 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 160.4, 143.6, 141.1, 135.5, 129.0, 127.9, 106.2, 100.1, 82.8, 76.1, 60.5, 55.2, 41.4, 22.8, 21.3. MS (ESI) *m/z* 412 [M+Na]⁺; HRMS : Exact mass calcd for C₂₀H₂₃O₅NNaS [M+Na]⁺: 412.11891. Found: 412.11879.

***N*-(5-Hydroxypent-2-yn-1-yl)-4-methyl-*N*-phenylbenzenesulfonamide(4b):**

Yield 80%, white solid, m.p. 90°C, ¹H NMR (400 MHz, CDCl₃) δ 7.53 (d, *J* = 8.3 Hz, 2H), 7.31 (m, 3 H), 7.22 (m, 4H), 4.4 (t, *J* = 2.2 Hz, 2 H), 3.52 (t, *J* = 6.2 Hz, 2H), 2.41 (s, 3H), 2.28 (t, *J* = 2.2 Hz, 2H).. ¹³C NMR (125 MHz, CDCl₃): δ 143.6, 139.4, 135.4, 129.1., 128.8, 128.0, 82.9, 80.9, 76.1, 60.6, 41.4, 22.9, 21.4.

***N*-(3,5-Dimethoxyphenyl)-*N*-(5-hydroxypent-2-yn-1-yl)methanesulfonamide (4c):**

Yield 70%, pale yellow solid, m.p. 95°C. ¹H NMR (400 MHz, CDCl₃):δ 6.76 (d, *J* = 2.1 Hz, 2H), 6.43 (t, *J* = 2.1 Hz, 1 H), 4.40 (t, *J* = 1.8 Hz, 2H), 3.80 (s, 6H), 3.74 (t, *J* = 6.2 Hz, 2H), 3.04 (s, 3H), 2.52-2.48 (m, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 160.9, 141.8, 105.4, 99.8, 83.5, 60.9, 55.4, 41.5, 41.5, 31.7, 23.0.

5-((3,5-Dimethoxyphenyl)amino)pent-3-yn-1-ol (4d):

Yield 60%, ¹H NMR (400 MHz, CDCl₃): δ 5.94 (t, *J* = 2.20 Hz, 1H), 5.86 (d, *J* = 2.07 Hz, 2H), 3.89 (t, *J* = 2.2 Hz, 2H), 3.76 (s, 6H), 3.68 (t, *J* = 6.2 Hz, 3H), 2.48-2.41 (t, *J* = 2.0 Hz, 2H). ¹³C NMR (125 MHz, CDCl₃): δ 161.54, 149.6, 92.31, 90.56, 80.3, 78.8, 60.9, 55.1, 34.0, 23.0.

5-(Benzyl(3,5-dimethoxyphenyl)amino)pent-3-yn-1-ol (4e):

Yield 65%, ¹H NMR (400 MHz, CDCl₃) δ 7.34-7.24 (m, 5H), 6.06 (d, *J* = 2.0 Hz, 2 H), 5.97 (t, *J* = 2.0 Hz, 1H), 4.53 (s, 2H), 4.0 (t, *J* = 2.0 Hz, 2H), 3.74 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ 161.5, 150.6, 128.5, 127.0., 126.9, 93.1, 89.94, 80.9, 77.5, 61.0, 55.1, 55.0, 40.4, 23.1.

2. General procedure for the domino Prins cyclization (6):

To a stirred solution of *N*-(3,5-dimethoxyphenyl)-*N*-(5-hydroxypent-2-yn-1-yl)-4-methylbenzenesulfonamide (**4a**) (1 equiv, 0.05 g) and aldehyde (**5**) (1.5 equiv) in anhydrous DCE (2 mL) was added PPh₃AuCl/AgSbF₆/In(OTf)₃ (all three catalysts 10 mol% each) at 0 °C. The resulting mixture was allowed to stir at room temperature under nitrogen atmosphere for 2h. After completion, the reaction mass was quenched with NaHCO₃ solution (5 mL) and then extracted with dichloromethane (2x5 mL). The organic phases were washed with brine solution (2x5 mL) and dried over anhydrous Na₂SO₄. Removal of the solvent followed by purification on silica gel column chromatography (60-120 mesh) using ethyl acetate/*n*-hexane gradient mixture afforded the product **6** (Table 2).

3. Characterization data of products (6a-o):

8,10-Dimethoxy-4-(4-methoxyphenyl)-6-tosyl-2,4,5,6-tetrahydro-1H-pyrano[3,4-c]quinoline (6a): Yield (53 mg) 82%, white solid, m.p. 156°C, ¹H NMR (500 MHz, CDCl₃): δ 7.40 (d, *J* = 8.3 Hz, 2H), 7.27-7.15 (m, 4H), 6.93 (d, *J* = 2.3 Hz, 1H), 6.82 (d, *J* = 8.6 Hz, 2H), 6.42 (d, *J* = 2.4 Hz, 1H), 4.53 (s, 1H), 4.00 (d, *J* = 17.3 Hz, 1H), 3.87 (s, 3H), 3.79 (s, 3H), 3.78 (s, 3H), 3.77-3.72 (m, 1H), 3.34-3.27 (m, 1H), 2.98-2.86 (m, 1H), 2.56 (td, *J* = 11.2, 2.8 Hz, 1H), 2.38 (s, 2H), 1.62-1.59 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 159.8, 159.2, 157.1, 143.5, 137.0, 136.5, 130.0, 129.5, 129.1, 126.9, 126.7, 125.9, 114.5, 113.9, 103.8, 98.3, 79.2, 63.8, 55.6, 55.3, 55.2, 45.4, 27.5. MS(ESI) *m/z* 530 [M+Na]⁺; HRMS : Exact mass calcd for C₂₈H₂₉O₅NNaS [M+Na]⁺: 530.16078. Found: 530.16164.

4-(4-Fluorophenyl)-8,10-dimethoxy-6-tosyl-2,4,5,6-tetrahydro-1H-pyrano[3,4-c]quinoline (6b): Yield (47 mg) 75%, white solid, m.p. 103°C, ¹H NMR (500 MHz, CDCl₃): δ 7.40 (d, *J* = 8.3 Hz, 2H), 7.28-7.24 (m, 2H), 7.22 (d, *J* = 7.9 Hz, 2H), 7.02-6.97 (m, 2H), 6.93 (d, *J* = 2.4 Hz, 1H), 6.42 (d, *J* = 2.4 Hz, 2H), 4.57 (s, 1H), 3.99 (d, *J* = 17.3 Hz, 1H), 3.87 (s, 3H), 3.79 (s, 3H), 3.78-3.74 (m, 1H), 3.31-3.25 (m, 1H), 2.97-2.88 (m, 1H), 2.56 (td, *J* = 11.2, 2.8 Hz, 1H), 2.38 (s, 3H), 1.64 (d, *J* = 17.3 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 159.3(¹*J*_{CF} = 247.1 Hz), 157.1, 143.6, 137.0, 136.5, 133.9, 130.1(³*J*_{CF} = 8.2 Hz), 130.0, 129.0, 126.7, 126.3 (⁴*J*_{CF} = 2.8 Hz), 115.6 (²*J*_{CF} = 21.6 Hz), 115.4, 114.3, 103.8, 98.3, 78.9, 63.8, 55.6, 55.3, 45.3, 27.5, 21.4. MS(ESI) *m/z* 496 [M+H]⁺; HRMS: Exact mass calcd for C₂₇H₂₇O₅NFS [M+H]⁺: 496.15885. Found: 496.15980.

8,10-Dimethoxy-4-(4-nitrophenyl)-6-tosyl-2,4,5,6-tetrahydro-1H-pyrano[3,4-c]quinoline (6c): Yield (47 mg) 71%, pale yellow solid, m.p. 140°C, ¹H NMR (500 MHz, CDCl₃): δ 8.18 (d, *J* = 8.8 Hz, 2H), 7.44 (d, *J* = 8.8 Hz, 2H), 7.41 (d, *J* = 8.3 Hz, 2H), 7.23 (d, *J* = 8.3 Hz, 2H), 6.93 (d, *J* = 2.4 Hz, 1H), 6.42 (d, *J* = 2.3 Hz, 1H), 4.71 (s, 1H), 4.03 (d, *J* = 17.3 Hz, 1H), 3.87 (s, 3H), 3.8 (s, 3H), 3.29-3.20 (m, 1H), 2.57 (td, *J* = 11.2, 2.8 Hz, 1H), 2.39 (s, 3H), 1.69 (d, *J* = 18.3 Hz, 1H), 1.55 (d, *J* = 18.3 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 159.6, 157.2, 148.0, 145.6, 143.7, 137.0, 136.5, 129.2, 129.2, 127.1, 126.7, 124.9, 123.8, 114.0, 103.7, 98.3, 78.7, 63.8, 55.6, 55.4, 45.1, 27.4, 21.4. MS (ESI) *m/z* 523 [M+H]⁺; HRMS: Exact mass calcd for C₂₀H₂₄O₇N₂S [M+H]⁺: 523.15455. Found: 523.15396.

4-(4-Bromophenyl)-8,10-dimethoxy-6-tosyl-2,4,5,6-tetrahydro-1H-pyrano[3,4-c]quinoline (6d): Yield (57 mg) 80%, white solid, m.p. 172°C, ¹H NMR (500 MHz, CDCl₃):

δ 7.44 (d, $J = 8.3$ Hz, 2H), 7.40 (d, $J = 8.3$ Hz, 2H), 7.22 (d, $J = 7.9$ Hz, 2H), 7.16 (d, $J = 8.5$ Hz, 2H), 6.93 (d, $J = 2.4$ Hz, 1H), 6.42 (d, $J = 2.4$ Hz, 1H), 4.54 (s, 1H), 3.99 (d, $J = 17.3$ Hz, 1H), 3.87 (s, 3H), 3.8 (s, 3H), 3.78-3.74 (m, 1H), 3.30-3.24 (m, 1H), 2.97-2.87 (m, 1H), 2.55 (td, $J = 11.2, 2.8$ Hz, 1H), 2.38 (s, 3H), 1.64 (d, $J = 17.3$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 159.4, 157.1, 143.6, 137.2, 137.1, 136.6, 130.7, 130.0, 129.2, 126.7, 126.4, 125.9, 122.6, 114.3, 103.7, 98.3, 79.0, 63.8, 55.6, 45.2, 27.5, 21.4. MS (ESI) m/z 578 $[\text{M}+\text{Na}]^+$; HRMS : Exact mass calcd for $\text{C}_{27}\text{H}_{26}\text{O}_5\text{NBrNaS}$ $[\text{M}+\text{Na}]^+$: 578.06073. Found: 578.06141.

2-(8,10-Dimethoxy-6-tosyl-2,4,5,6-tetrahydro-1H-pyrano[3,4-c]quinolin-4-

yl)benzotrile (6e): Yield (44 mg) 69%, white solid, m.p. 144°C , ^1H NMR (500 MHz, CDCl_3): δ 7.62 (d, $J = 8.3$ Hz, 2H), 7.43-7.39 (m, 4H), 7.23 (d, $J = 8.0$ Hz, 2H), 6.92 (d, $J = 2.4$ Hz, 1H), 6.42 (d, $J = 2.4$ Hz, 1H), 4.64 (s, 1H), 4.01 (d, $J = 17.3$ Hz, 1H), 3.87 (s, 3H), 3.82-3.75 (m, 4H), 3.27-3.20 (m, 1H), 2.99-2.88 (m, 1H), 2.56 (td, $J = 11.4, 2.7$ Hz, 1H), 2.39 (s, 3H), 1.67 (d, $J = 17.3$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 159.6, 157.2, 143.7, 143.6, 137.0, 136.5, 132.4, 129.2, 129.0, 127.0, 126.7, 125.0, 118.4, 114.0, 112.5, 103.7, 98.3, 79.0, 63.8, 55.6, 55.3, 45.1, 27.4, 21.4. MS (ESI) m/z 525 $[\text{M}+\text{Na}]^+$; HRMS : Exact mass calcd for $\text{C}_{28}\text{H}_{26}\text{O}_5\text{N}_2\text{NaS}$ $[\text{M}+\text{Na}]^+$: 525.14546. Found: 525.14647.

Methyl 2-(8,10-dimethoxy-6-tosyl-2,4,5,6-tetrahydro-1H-pyrano[3,4-c]quinolin-4-yl)benzoate (6f): Yield (53 mg) 77%, red solid, m.p. 164°C , ^1H NMR (500 MHz, CDCl_3): δ 7.84 (d, $J = 7.6$ Hz, 1H), 7.53 (d, $J = 8.0$ Hz, 2H), 7.43-7.39 (m, 2H), 7.34-7.29 (m, 2H), 7.24 (d, $J = 8.0$ Hz, 1H), 6.93 (d, $J = 2.1$ Hz, 1H), 6.41 (d, $J = 2.1$ Hz, 1H), 5.73 (s, 1H), 4.30 (d, $J = 17.3$ Hz, 1H), 4.05 (s, 3H), 3.87 (s, 3H), 3.79 (s, 3H), 3.78-3.73 (m, 4H), 3.22 (d, $J = 17.3$ Hz, 1H), 3.13 (s, 1H), 3.0-2.90 (m, 1H), 2.56 (td, $J = 11.1, 2.1$ Hz, 1H), 2.38 (s, 3H), 1.46-1.39 (m, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 167.6, 159.1, 156.1, 143.3, 139.4, 137.1, 136.5, 132.0, 130.5, 129.9, 129.4, 129.1, 128.0, 127.5, 125.6, 114.5, 103.9, 98.2, 73.9, 63.9, 55.6, 55.3, 52.4, 44.8, 27.5, 21.4. MS (ESI) m/z 558 $[\text{M}+\text{Na}]^+$; HRMS : Exact mass calcd for $\text{C}_{29}\text{H}_{29}\text{O}_7\text{NNaS}$ $[\text{M}+\text{Na}]^+$: 558.15569. Found: 558.15613.

8,10-Dimethoxy-4-(p-tolyl)-6-tosyl-2,4,5,6-tetrahydro-1H-pyrano[3,4-c]quinoline (6g): Yield (50 mg) 80%, white solid, m.p. 182°C , ^1H NMR (500 MHz, CDCl_3): δ 7.41 (d, $J = 8.2$ Hz, 2H), 7.22 (d, $J = 8.0$ Hz, 2H), 7.15 (d, $J = 8.0$ Hz, 2H), 7.11 (d, $J = 8.0$ Hz, 2H), 6.93 (d, $J = 2.4$ Hz, 1H), 6.42 (d, $J = 2.4$ Hz, 1H), 4.00 (d, $J = 17.2$ Hz, 1H), 3.87 (s, 3H), 3.79 (s, 3H), 3.78-3.74 (m, 1H), 3.33-3.27 (m, 1H), 2.98-2.88 (s, 1H), 2.56 (td, $J = 11.2, 2.7$ Hz, 1H), 2.38 (s, 3H), 2.31 (s, 3H), 1.63 (d, $J = 17.2$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ

159.2, 157.1, 143.5, 138.5, 137.1, 136.6, 134.9, 129.3, 129.2, 128.3, 126.8, 126.0, 114.6, 103.8, 98.3, 79.5, 63.9, 55.6, 55.4, 45.5, 27.6, 21.4, 21.3. MS (ESI) m/z 514 $[M+Na]^+$; HRMS : Exact mass calcd for $C_{28}H_{29}O_5NNaS$ $[M+Na]^+$: 514.16586. Found: 514.16423.

4-(3-Chlorophenyl)-8,10-dimethoxy-6-tosyl-2,4,5,6-tetrahydro-1H-pyrano[3,4-

c]quinoline (6h): Yield (50 mg) 76%, pale yellow solid, m.p. 167°C, 1H NMR (500 MHz, $CDCl_3$): δ 7.41 (d, $J = 8.3$ Hz, 2H), 7.28-7.16 (m, 6H), 6.93 (d, $J = 2.4$ Hz, 1H), 6.42 (d, $J = 2.4$ Hz, 1H), 4.55 (s, 1H), 4.01 (d, $J = 17.3$ Hz, 1H), 3.87 (s, 3H), 3.81-3.74 (m, 4H), 3.34-3.27 (m, 1H), 2.99-2.87 (m, 1H), 2.54 (td, $J = 11.3, 2.8$ Hz, 1H), 2.38 (s, 3H), 1.65 (d, $J = 17.3$ Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.4, 157.1, 143.6, 140.2, 137.0, 136.5, 134.5, 129.8, 129.2, 128.8, 128.2, 126.7, 126.6, 126.5, 125.7, 114.2, 103.8, 98.3, 79.11, 63.8, 55.6, 55.3, 45.2, 27.4, 21.3. MS (ESI) m/z 534 $[M+Na]^+$; HRMS : Exact mass calcd for $C_{27}H_{26}O_5NCINaS$ $[M+Na]^+$: 534.11124. Found: 534.10967.

8,10-Dimethoxy-4-(thiophen-2-yl)-6-tosyl-2,4,5,6-tetrahydro-1H-pyrano[3,4-c]quinoline

(6i): Yield (48 mg) 78%, white solid, m.p. 170°C, 1H NMR (500 MHz, $CDCl_3$): δ 7.39 (d, $J = 8.2$ Hz, 2H), 7.27-7.25 (m, 1H), 7.21 (d, $J = 8.0$ Hz, 2H), 7.07-7.05 (m, 1H), 6.96-6.93 (m, 2H), 4.90 (s, 1H), 4.12 (d, $J = 17.2$ Hz, 1H), 3.88 (s, 3H), 3.80-3.75 (m, 4H), 3.52-3.46 (m, 1H), 2.96-2.86 (m, 1H), 2.58 (td, $J = 11.1, 2.8$ Hz, 1H), 2.37 (s, 3H), 1.62 (d, $J = 17.2$ Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.3, 157.2, 143.5, 141.4, 137.1, 136.5, 129.1, 127.0, 126.6, 126.4, 126.2, 125.7, 114.3, 103.7, 98.3, 74.2, 63.7, 55.5, 55.3, 45.3, 27.2, 21.3. MS (ESI) m/z 506 $[M+Na]^+$; HRMS: Exact mass calcd for $C_{25}H_{25}O_5NNaS_2$ $[M+Na]^+$: 506.10664. Found: 506.10740.

4-Ethyl-8,10-dimethoxy-6-tosyl-2,4,5,6-tetrahydro-1H-pyrano[3,4-c]quinoline (6j): Yield

(37 mg) 68%, white solid, m.p. 154°C, 1H NMR (500 MHz, $CDCl_3$): δ 7.33 (d, $J = 8.3$ Hz, 2H), 7.15 (d, $J = 8.0$ Hz, 2H), 6.97 (d, $J = 2.4$ Hz, 1H), 6.40 (d, $J = 2.4$ Hz, 1H), 4.29 (d, $J = 16.9$ Hz, 1H), 3.88 (s, 3H), 3.77-3.71 (m, 5H), 3.66-3.60 (m, 1H), 2.76-2.63 (m, 1H), 2.34 (s, 3H), 1.69-1.57 (m, 2H), 1.51 (d, $J = 17.2$ Hz, 1H), 1.41-1.30 (m, 1H), 0.86 (t, $J = 7.3$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.0, 156.9, 143.4, 136.8, 136.4, 129.0, 127.5, 126.7, 125.9, 114.8, 103.7, 98.3, 76.7, 63.0, 55.6, 55.3, 45.1, 27.7, 25.0, 21.3, 8.9. MS (ESI) m/z 578 $[M+Na]^+$; HRMS : Exact mass calcd for $C_{27}H_{26}O_5NBrNaS$ $[M+Na]^+$: 578.06073. Found: 578.06141.

4-Isopropyl-8,10-dimethoxy-6-tosyl-2,4,5,6-tetrahydro-1H-pyrano[3,4-c]quinoline (6k):

Yield (38 mg) 67%, white solid, m.p. 192°C, 1H NMR (500 MHz, $CDCl_3$): δ 7.33 (d, $J = 8.3$

Hz, 2H), 7.15 (d, $J = 8.0$ Hz, 2H), 6.98 (d, $J = 2.4$ Hz, 1H), 6.40 (d, $J = 2.4$ Hz, 1H), 4.32 (d, $J = 17.2$ Hz, 1H), 3.89 (s, 3H), 3.74 (s, 3H), 3.70-3.59 (m, 3H), 2.70-2.58 (m, 1H), 2.33 (s, 3H), 2.25 (td, $J = 2.6, 10.8$ Hz, 1H), 1.82-1.73 (m, 1H), 1.49 (d, $J = 17.2$ Hz, 1H), 1.03 (d, $J = 6.9$ Hz, 3H), 0.67 (d, $J = 6.9$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 159.0, 156.8, 143.4, 136.6, 136.4, 129.0, 127.3, 126.7, 126.5, 114.9, 103.7, 98.4, 80.2, 62.8, 55.6, 55.3, 45.2, 29.2, 27.7, 21.3, 19.4, 15.0. MS (ESI) m/z 466 $[\text{M}+\text{Na}]^+$; HRMS : Exact mass calcd for $\text{C}_{24}\text{H}_{29}\text{O}_5\text{NNaS}$ $[\text{M}+\text{Na}]^+$: 466.16586. Found: 466.16491.

4-(4-Ethylphenyl)-8,10-dimethoxy-6-tosyl-2,4,5,6-tetrahydro-1H-pyrano[3,4-c]quinoline (6l): Yield (52 mg) 80%, white semi solid, ^1H NMR (500 MHz, CDCl_3): δ 7.41 (d, $J = 8.3$ Hz, 2H), 7.22 (d, $J = 8.0$ Hz, 2H), 7.19-7.11 (m, 4H), 6.93 (d, $J = 2.4$ Hz, 1H), 6.42 (d, $J = 2.4$ Hz, 1H), 4.54 (s, 1H), 4.01 (d, $J = 17.2$ Hz, 1H), 3.87 (s, 3H), 3.79 (s, 3H), 3.78-3.73 (m, 1H), 3.36-3.27 (m, 1H), 2.99-2.86 (m, 1H), 2.69-2.52 (m, 3H), 2.38 (s, 3H), 1.63 (d, $J = 17.3$ Hz, 1H), 1.19 (t, $J = 7.7$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 159.1, 157.0, 144.7, 143.5, 137.0, 136.5, 135.1, 130.2, 129.1, 128.3, 128.0, 127.9, 126.8, 126.7, 125.9, 114.5, 103.8, 98.3, 79.5, 63.8, 55.5, 55.3, 45.4, 28.5, 27.5, 21.3, 15.4. MS (ESI) m/z 528 $[\text{M}+\text{Na}]^+$; HRMS : Exact mass calcd for $\text{C}_{29}\text{H}_{31}\text{O}_5\text{NNaS}$ $[\text{M}+\text{Na}]^+$: 528.18151. Found: 528.18248.

8,10-Dimethoxy-4-(naphthalen-1-yl)-6-tosyl-2,4,5,6-tetrahydro-1H-pyrano[3,4-c]quinoline (6m): Yield (55 mg) 82%, white solid, m.p. 180°C , ^1H NMR (500 MHz, CDCl_3): δ 8.2 (d, $J = 8.6$ Hz, 1H), 7.86-7.79 (m, 2H), 7.52-7.37 (m, 6H), 7.29 (d, $J = 7.9$ Hz, 2H), 6.92 (d, $J = 2.2$ Hz, 1H), 6.44 (d, $J = 2.4$ Hz, 1H), 5.35-4.96 (m, 1H), 4.02 (d, $J = 17.3$ Hz, 1H), 3.92-3.85 (m, 4H), 3.83 (s, 3H), 3.45-3.19 (m, 1H), 3.17-3.02 (m, 1H), 2.74 (td, $J = 11.1, 3.0$ Hz, 1H), 2.43 (s, 3H), 1.74 (d, $J = 17.5$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 159.2, 157.2, 143.6, 137.3, 136.6, 134.1, 133.0, 129.5, 129.2, 128.7, 126.8, 126.3, 125.6, 125.1, 114.4, 103.8, 98.4, 64.3, 55.6, 55.4, 45.3, 27.4, 21.4. MS- MS (ESI) m/z 550 $[\text{M}+\text{Na}]^+$; HRMS : Exact mass calcd for $\text{C}_{31}\text{H}_{29}\text{O}_5\text{NNaS}$ $[\text{M}+\text{Na}]^+$: 550.16586. Found: 550.16719.

4-(2-Bromophenyl)-8,10-dimethoxy-6-tosyl-2,4,5,6-tetrahydro-1H-pyrano[3,4-c]quinoline (6n): Yield (55 mg) 78%, white solid, m.p. 198°C , ^1H NMR (500 MHz, CDCl_3): δ 7.57 (d, $J = 7.7$ Hz, 1H), 7.48 (d, $J = 8.2$ Hz, 2H), 7.26 (d, $J = 8.0$ Hz, 2H), 7.22-7.20 (m, 2H), 7.16-7.12 (m, 1H), 6.94 (d, $J = 2.4$ Hz, 1H), 6.42 (d, $J = 2.4$ Hz, 1H), 5.11 (s, 1H), 4.08 (d, $J = 17.3$ Hz, 1H), 3.87 (s, 3H), 3.79 (s, 3H), 3.78-3.76 (m, 1H), 3.34-3.28 (m, 1H), 2.99-2.90 (m, 1H), 2.53 (td, $J = 11.2, 2.7$ Hz, 1H), 2.40 (s, 3H), 1.68 (d, $J = 17.2$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 159.2, 157.0, 143.6, 137.2, 136.6, 132.9, 130.0, 129.2, 127.8,

126.8, 126.3, 126.1, 124.6, 114.2, 103.9, 98.2, 77.7, 63.9, 55.5, 55.3, 44.9, 27.4, 21.4. MS (ESI) m/z 578 $[M+Na]^+$; HRMS : Exact mass calcd for $C_{27}H_{26}O_5NBrNaS$ $[M+Na]^+$: 578.06073. Found: 578.06141.

4-(3-Fluorophenyl)-8,10-dimethoxy-6-tosyl-2,4,5,6-tetrahydro-1H-pyrano[3,4-

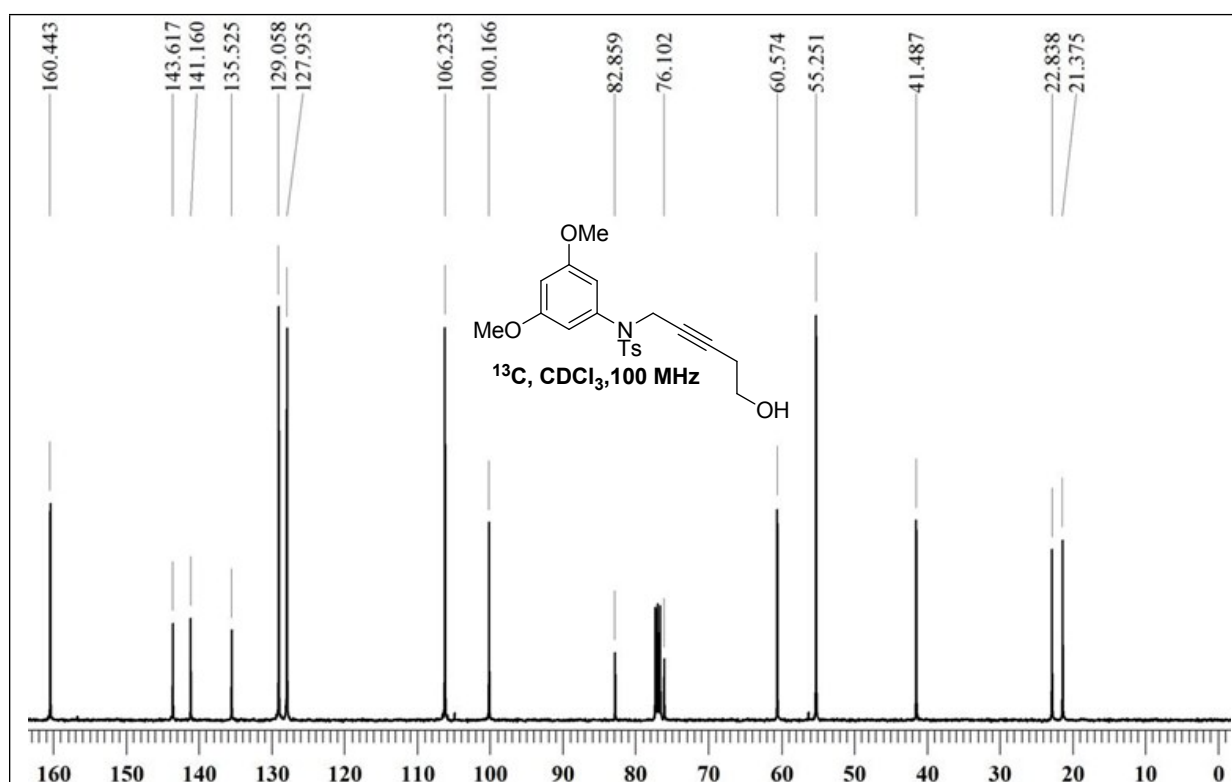
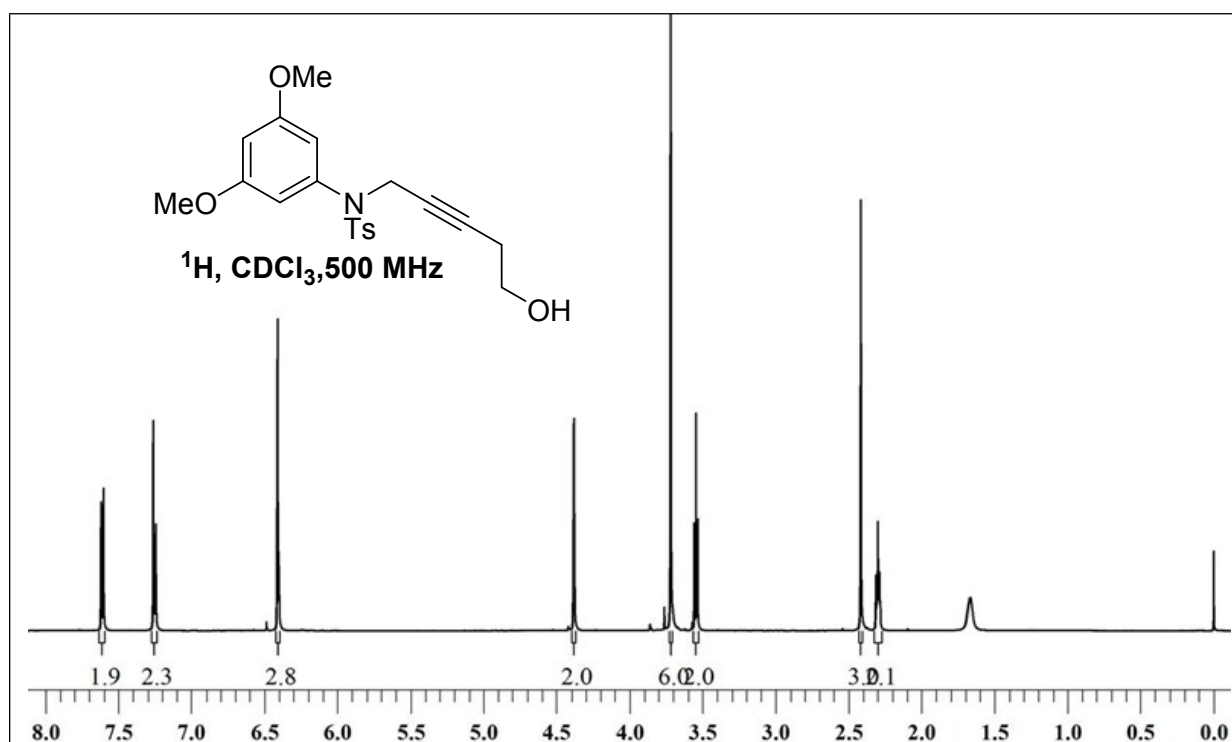
c]quinoline (6o): Yield (43 mg) 68%, white semi solid, m.p. 95°C, 1H NMR (500 MHz, $CDCl_3$): δ 7.41 (d, $J = 8.2$ Hz, 2H), 7.37-7.27 (m, 1H), 7.22 (d, $J = 8.2$ Hz, 2H), 7.09 (d, $J = 7.6$ Hz, 1H), 7.01-6.97 (m, 2H), 6.93 (d, $J = 2.4$ Hz, 1H), 6.42 (d, $J = 2.4$ Hz, 1H), 4.58 (m, 1H), 4.03 (d, $J = 17.2$ Hz, 1H), 3.87 (s, 3H), 3.79 (s, 3H), 3.78-3.75 (m, 1H), 3.33-3.27 (m, 1H), 2.98-2.88 (m, 1H), 2.55 (td, $J = 11.2, 2.7$ Hz, 1H), 2.38 (s, 3H), 1.65 (d, $J = 17.2$ Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.8($^1J_{CF} = 246.9$ Hz), 161.8, 159.3, 157.1, 143.6, 140.7($^3J_{CF} = 6.6$ Hz), 140.6, 137.0, 136.5, 130.1($^3J_{CF} = 8.1$ Hz), 130.0, 129.1, 126.7, 126.4, 125.8, 124.0($^4J_{CF} = 2.0$ Hz), 115.7($^2J_{CF} = 21.2$ Hz),, 115.5, 115.0($^2J_{CF} = 21.7$ Hz), 114.9, 114.2, 103.8, 98.3, 79.0, 63.8, 55.5, 55.3, 45.2, 27.4, 21.3. MS (ESI) m/z 496 $[M+H]^+$; HRMS : Exact mass calcd for $C_{27}H_{27}O_5NFS$ $[M+H]^+$: 496.15885. Found: 496.15980.

4-(4-fluorophenyl)-8,10-dimethoxy-6-(methylsulfonyl)-2,4,5,6-tetrahydro-1H-pyrano[3,4-c]quinoline (6r)

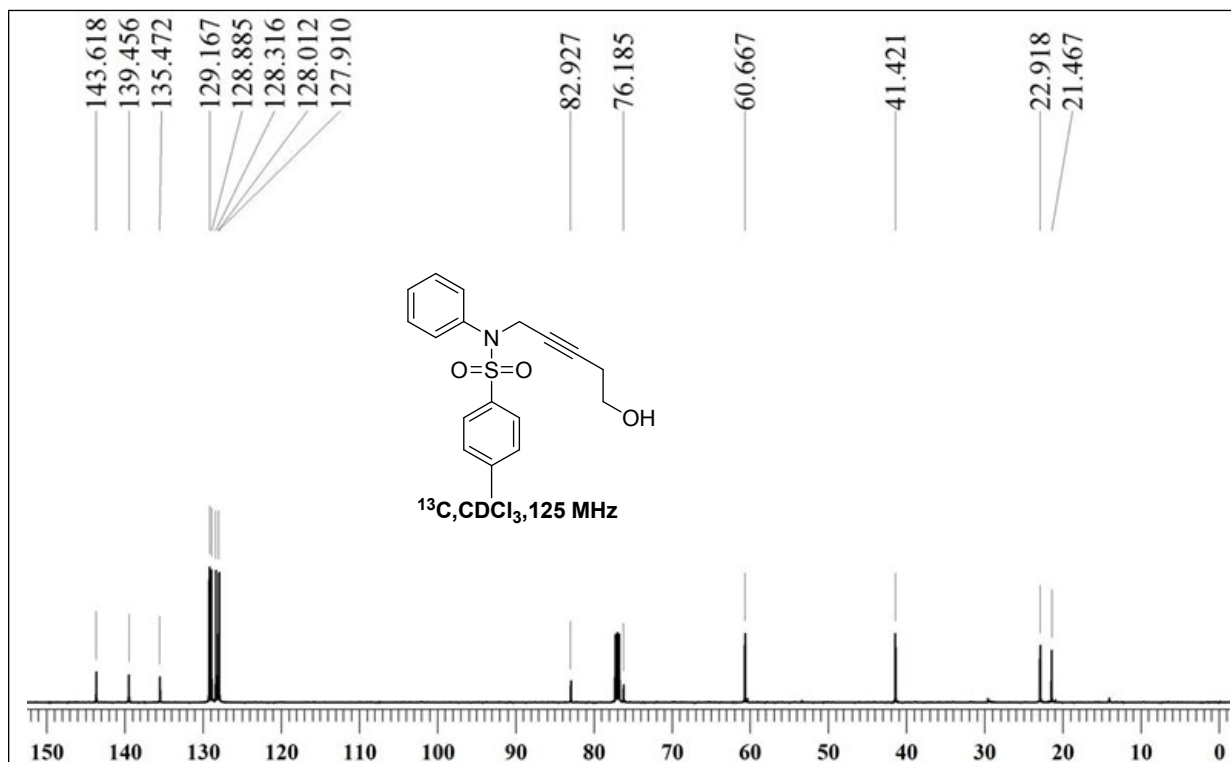
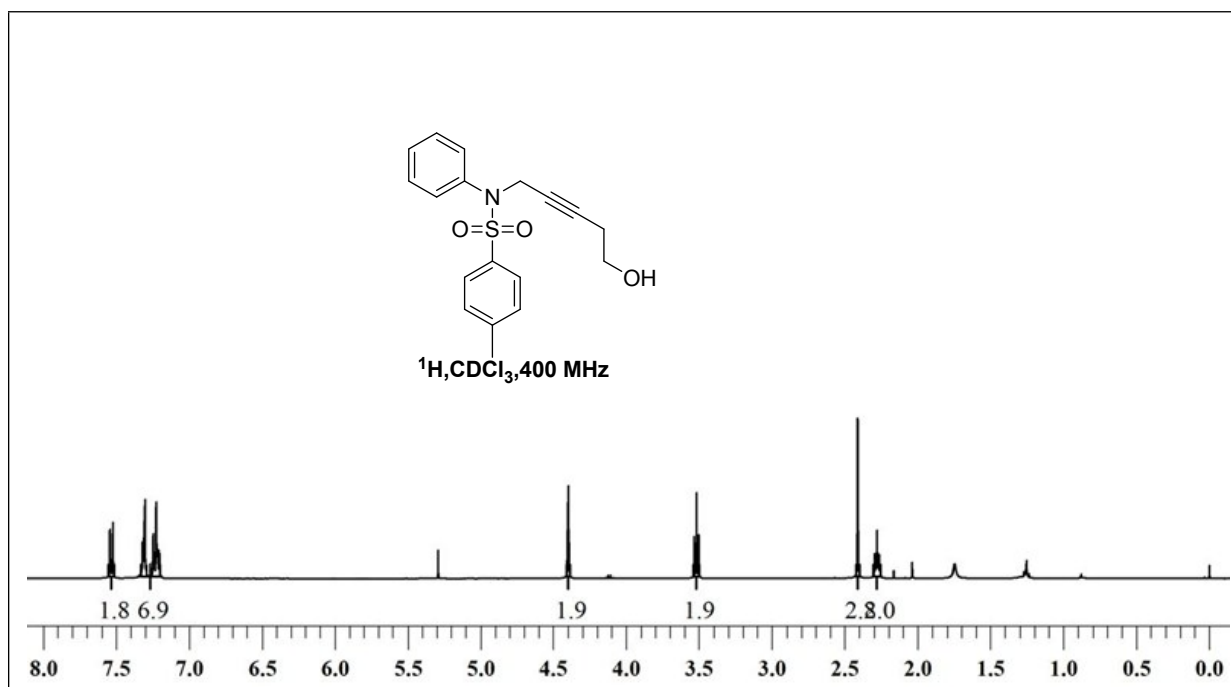
Yield (13mg) 20%, white solid, m.p. 85°C, 1H NMR (400 MHz, $CDCl_3$): δ 7.41-7.32 (m, 2H), 7.05 (d, $J = 7.9$ Hz, 2H), 6.80 (s,1H), 6.42 (s, 1H), 5.15 (s, 1H), 4.25-4.15 (m 1H), 4.07 (d, $J = 1.6$ Hz, 1H), 3.85 (s, 3H), 3.82 (s, 3H), 3.65 (t, $J = 9.51$ Hz H), 3.33 (d, $J = 17.23$ Hz H),), 2.76,(s, 3H), 2.38 (d, $J = 17.23$ Hz, 1H),1.27(s,1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.7, 157.6, 137.1, ,133.9, 130.2, 127.2, 127.0, 115.7, 115.5, 113.4, 102.9, , 98.1, 78.8, 64.8, 55.6, 55.4, 45.6,38.1, 27.9.

4. 1H & ^{13}C NMR spectra of compounds (4a-e& 6a-o and 6r):

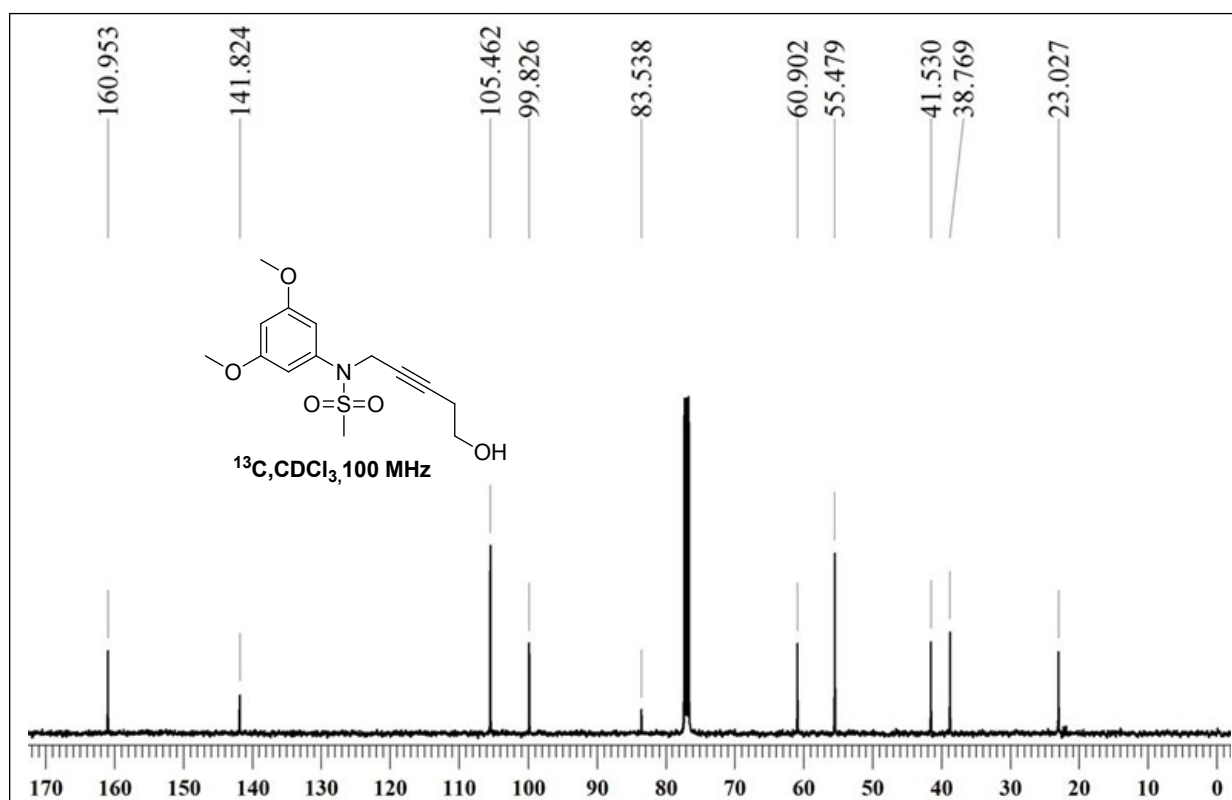
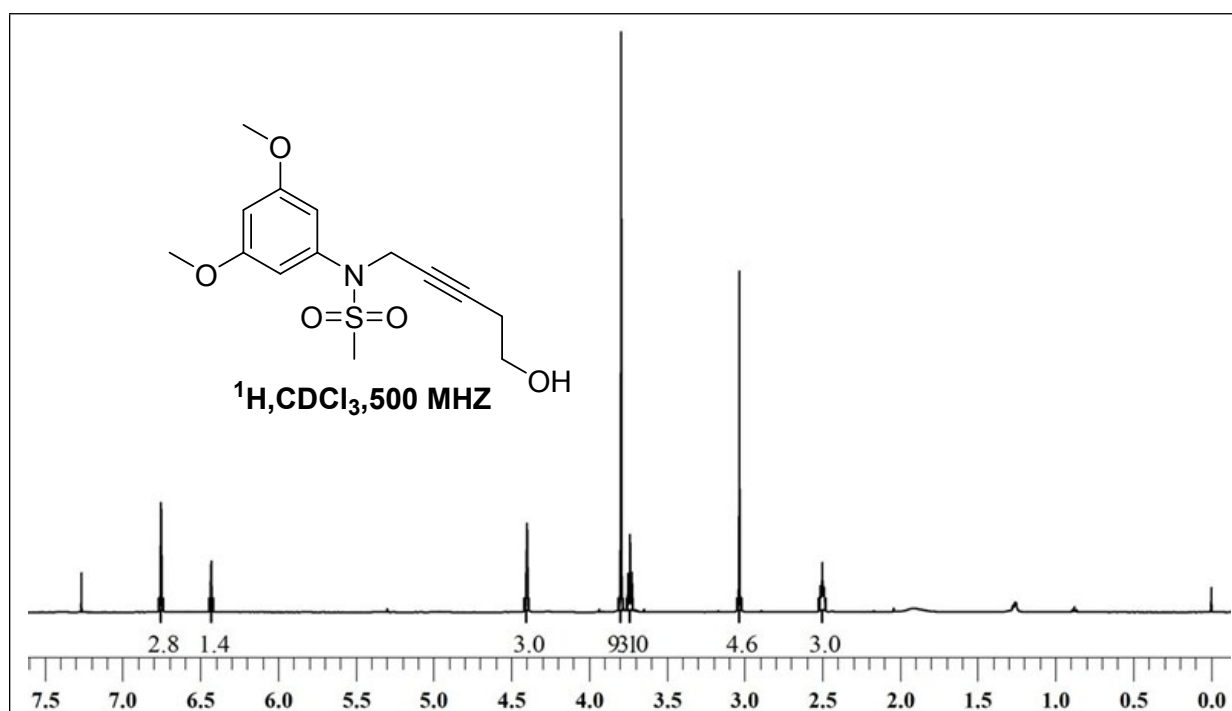
^1H and ^{13}C NMR spectra of compound 4a



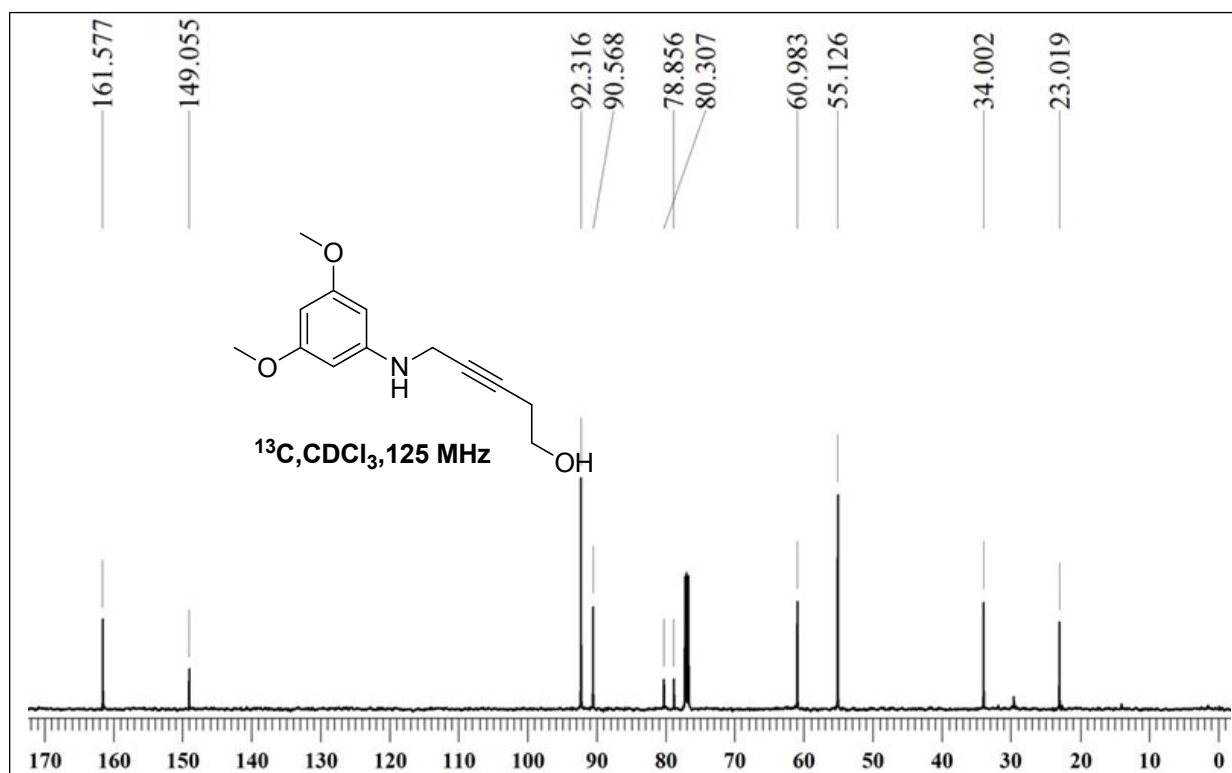
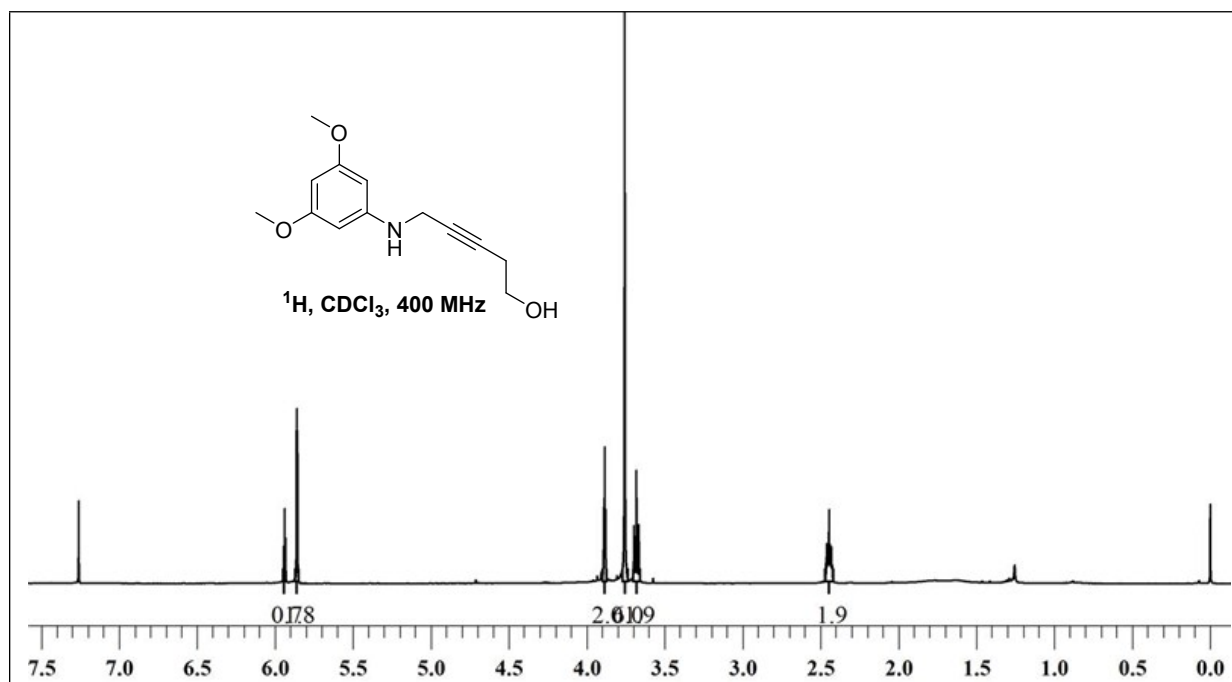
^1H and ^{13}C NMR spectra of compound 4b



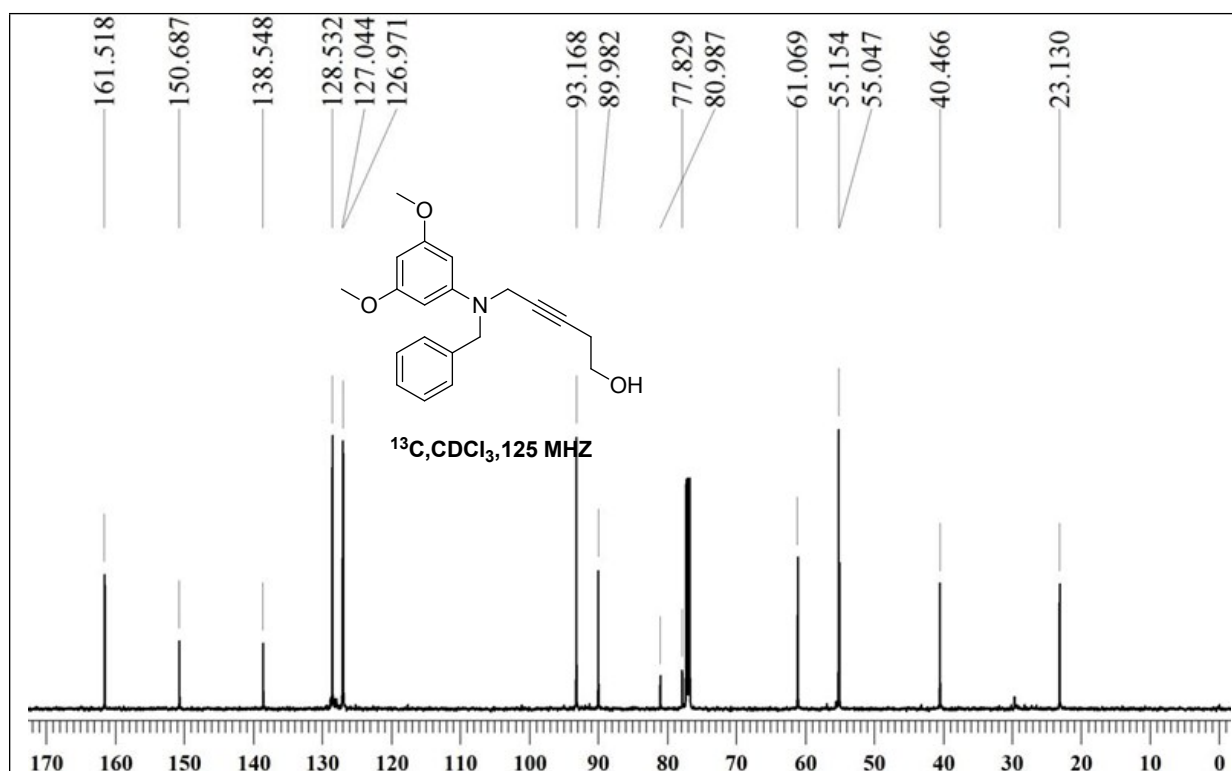
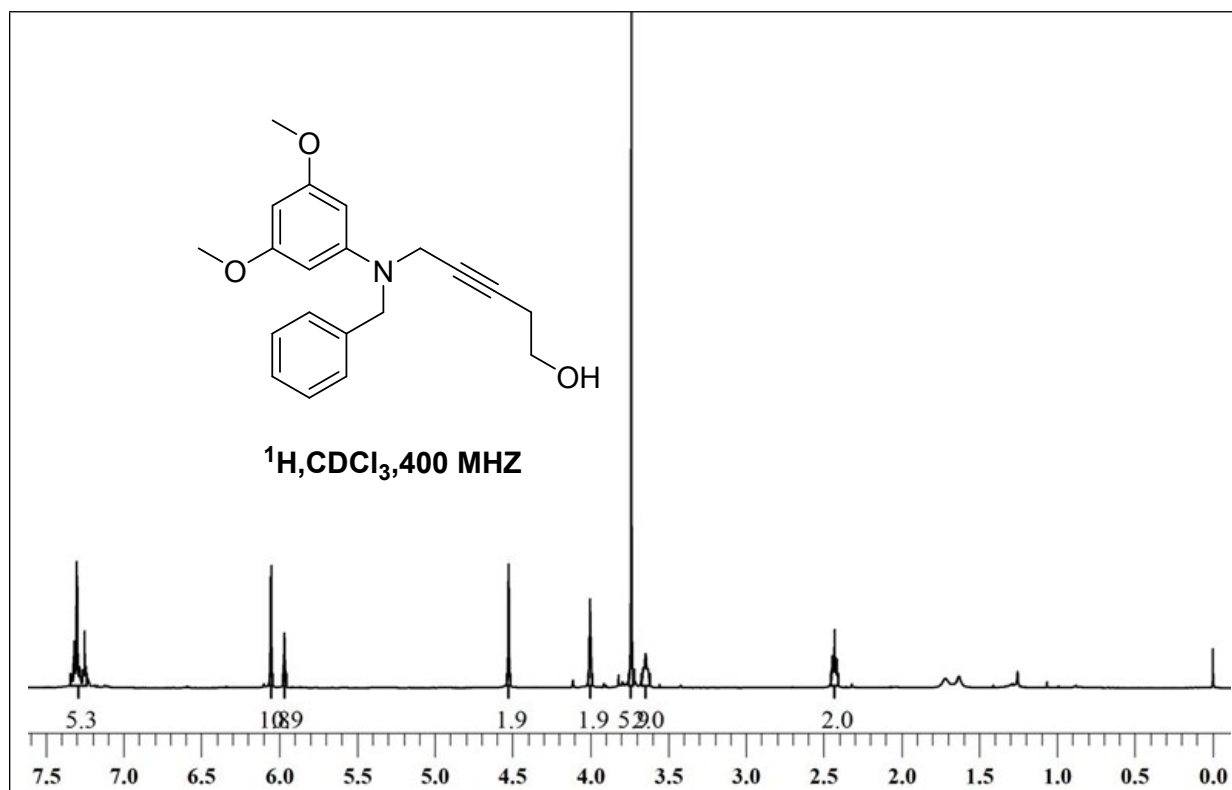
¹H and ¹³C NMR spectra of compound 4c



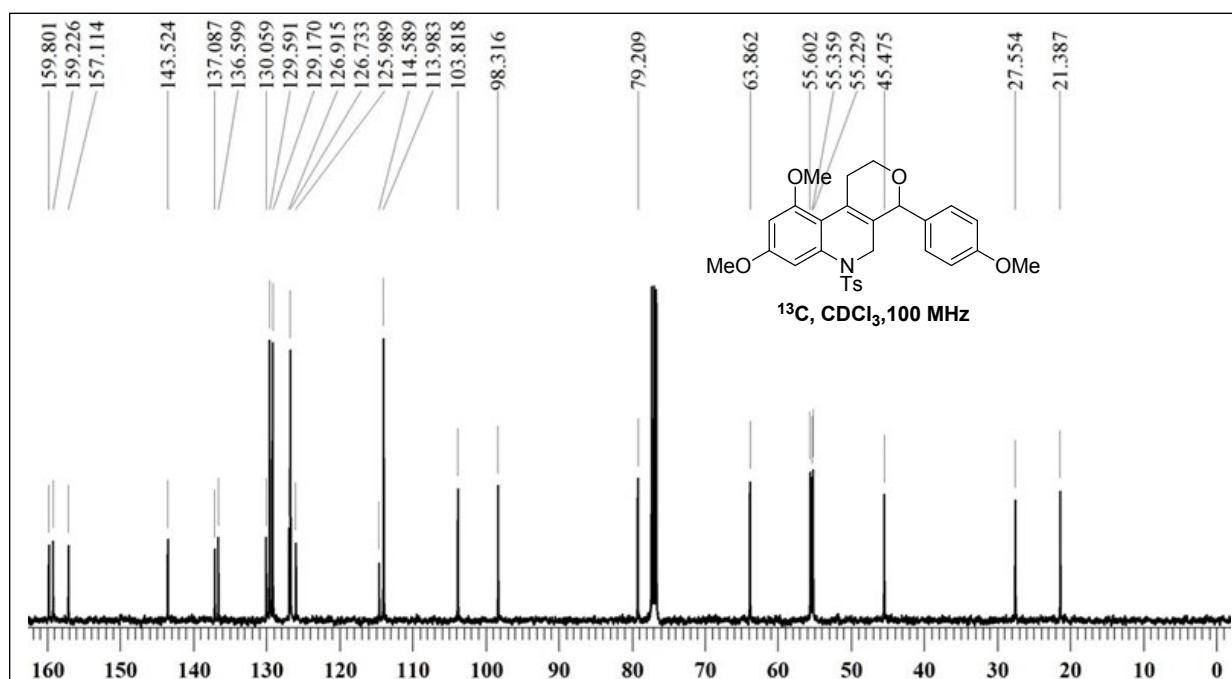
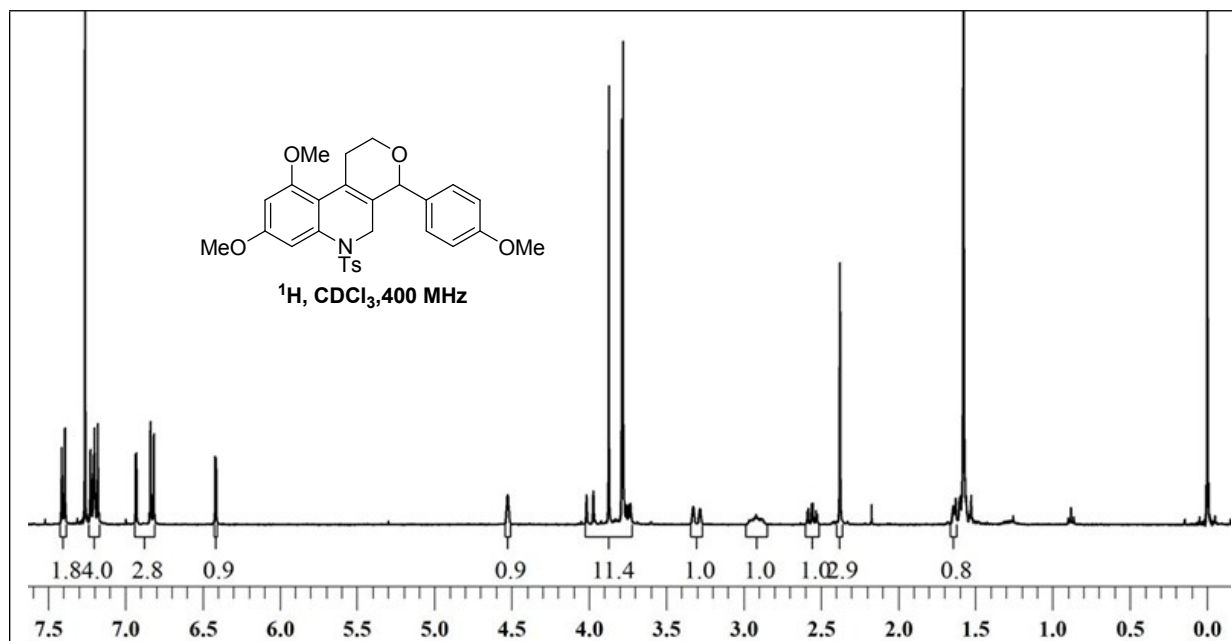
^1H and ^{13}C NMR spectra of compound 4d



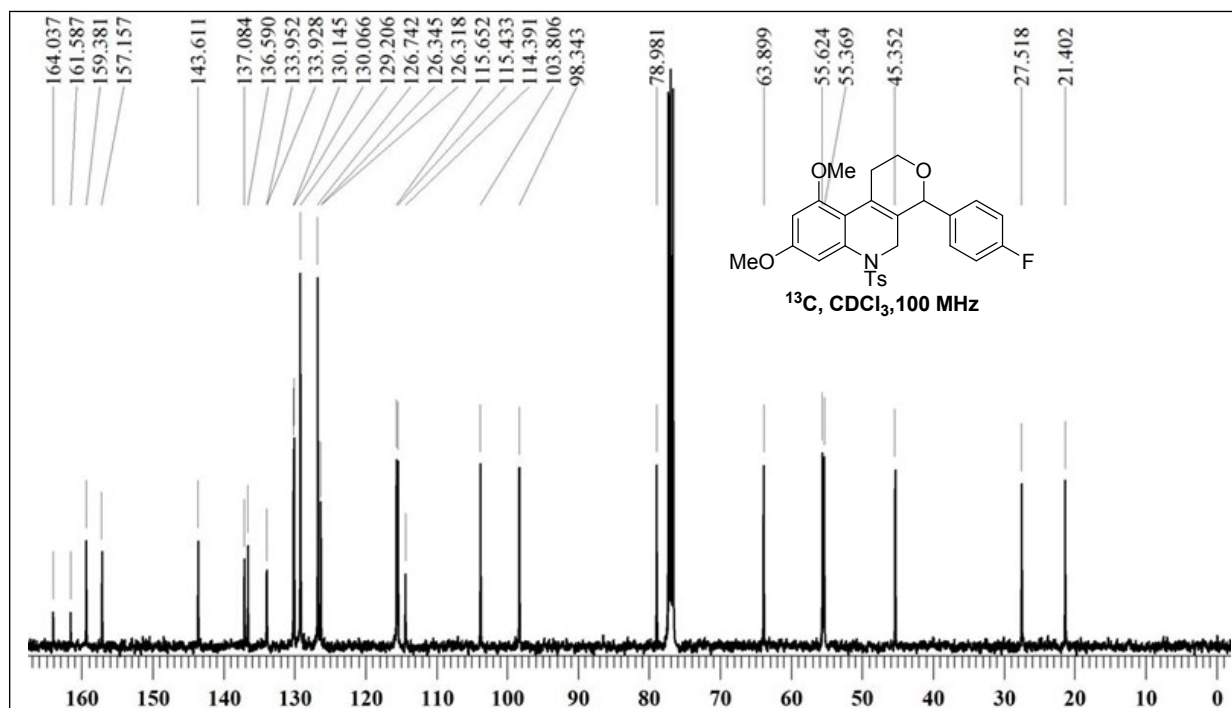
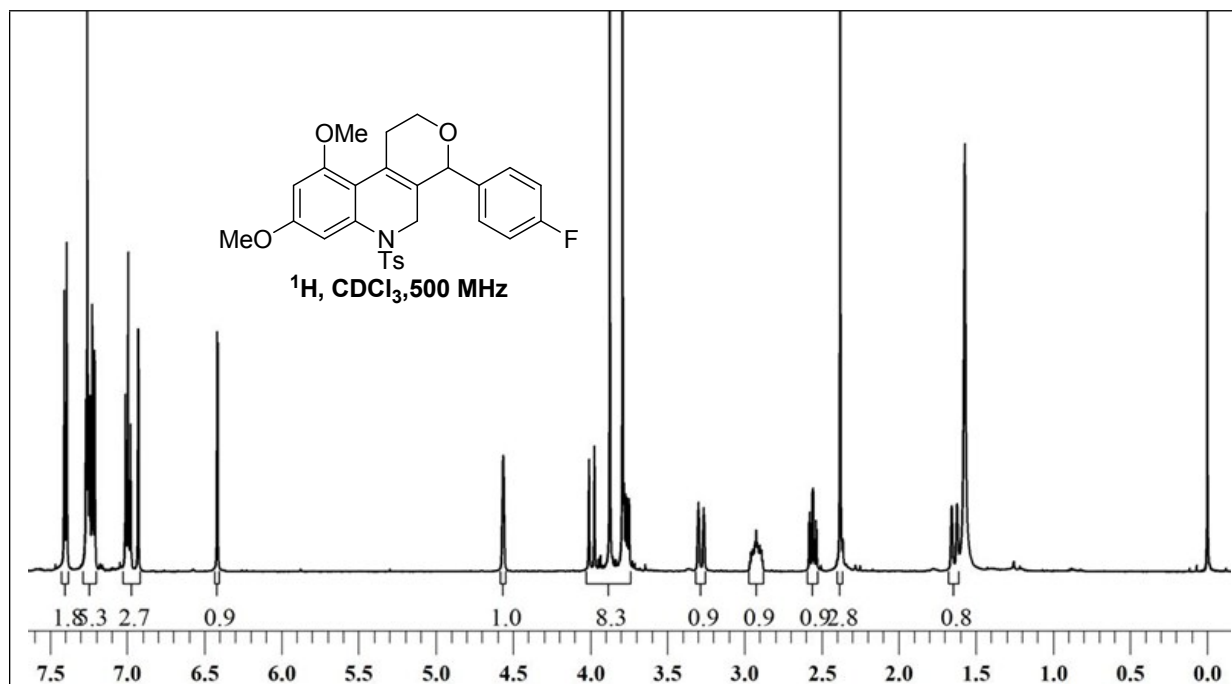
^1H and ^{13}C NMR spectra of compound 4e



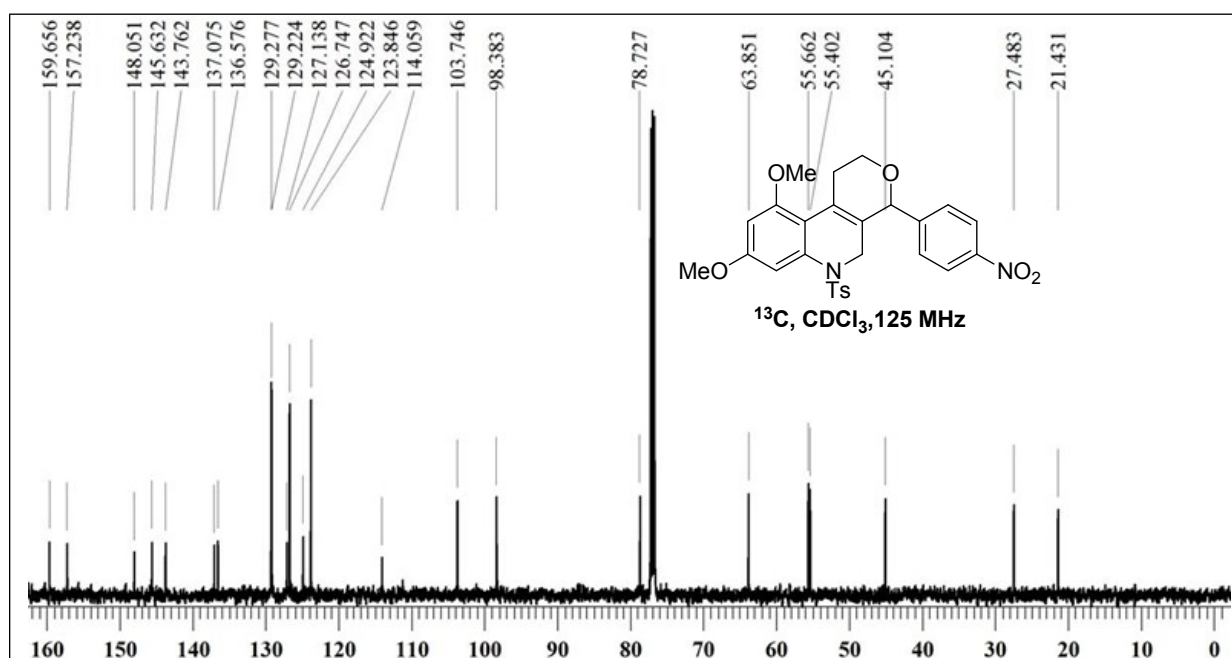
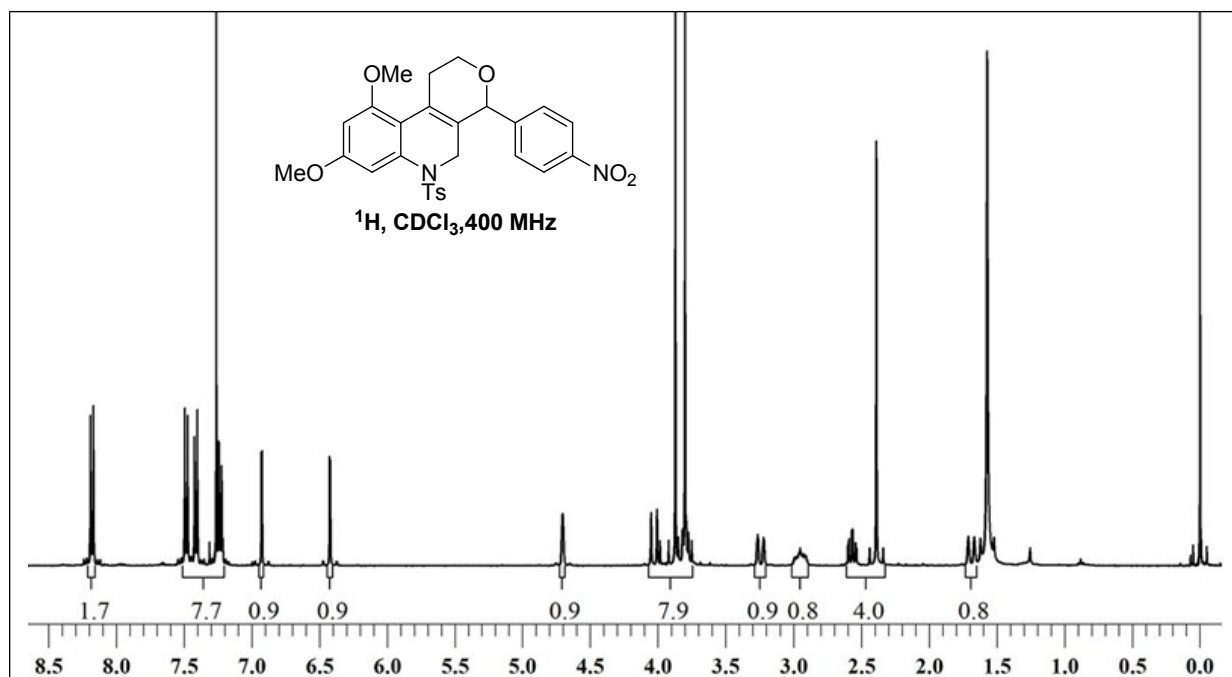
^1H and ^{13}C NMR spectra of compound 6a:



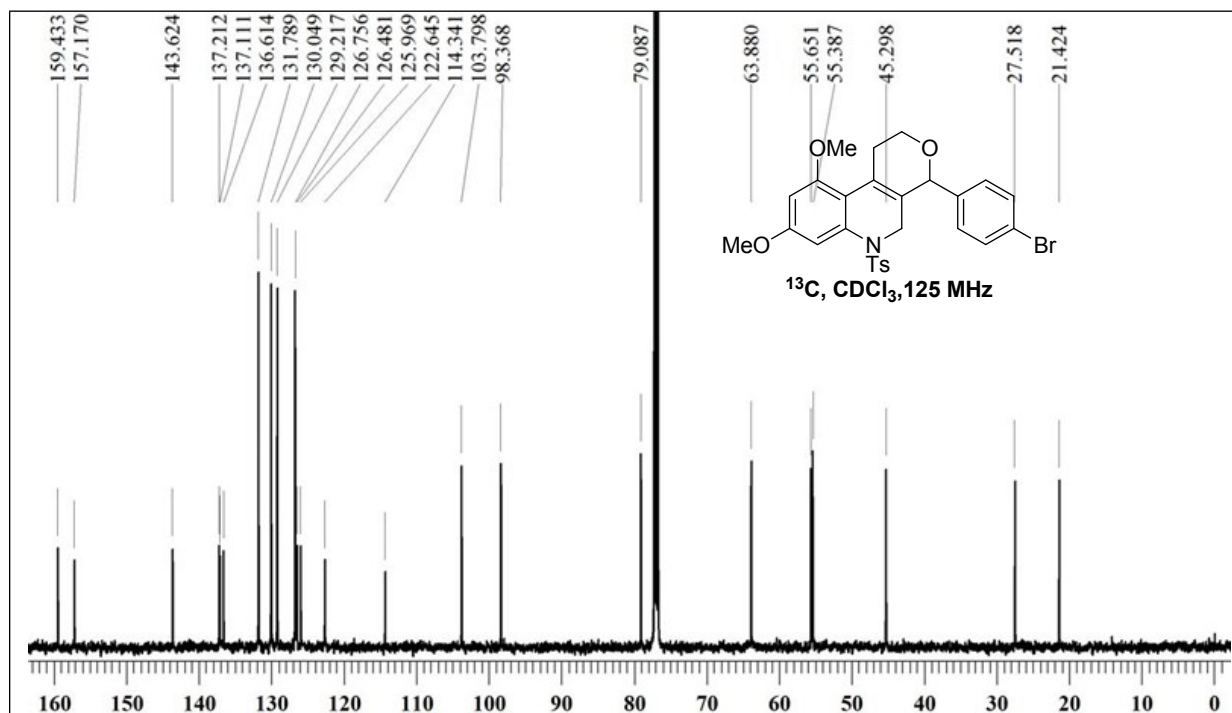
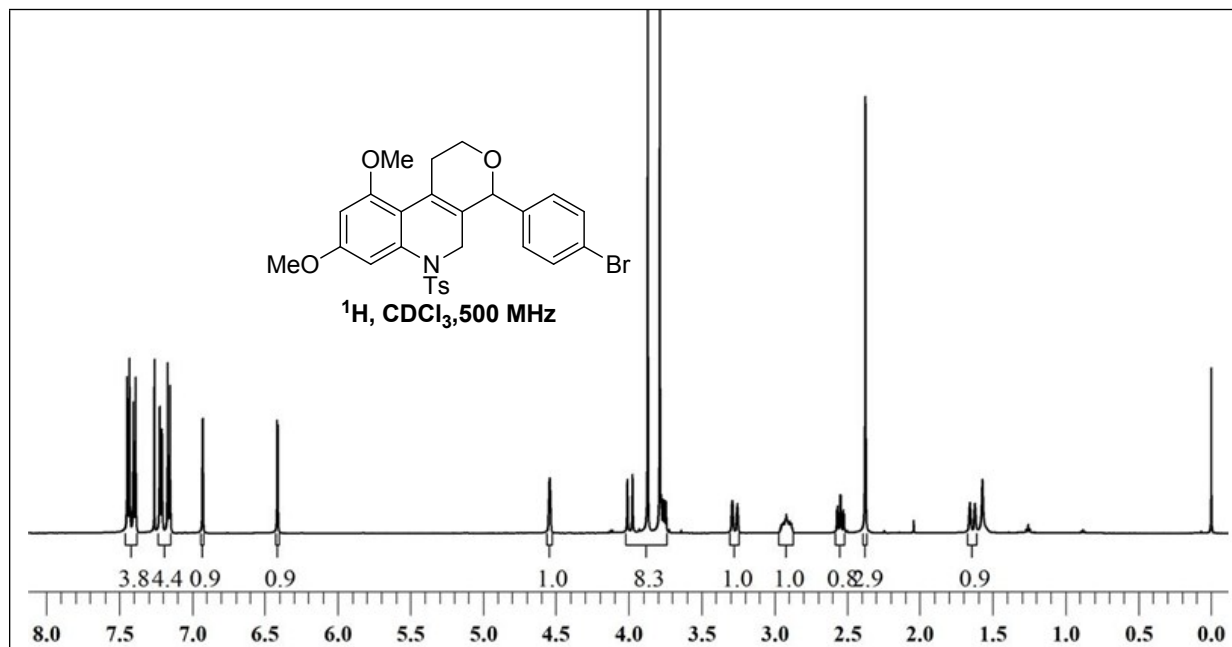
^1H and ^{13}C NMR spectra of compound 6b:



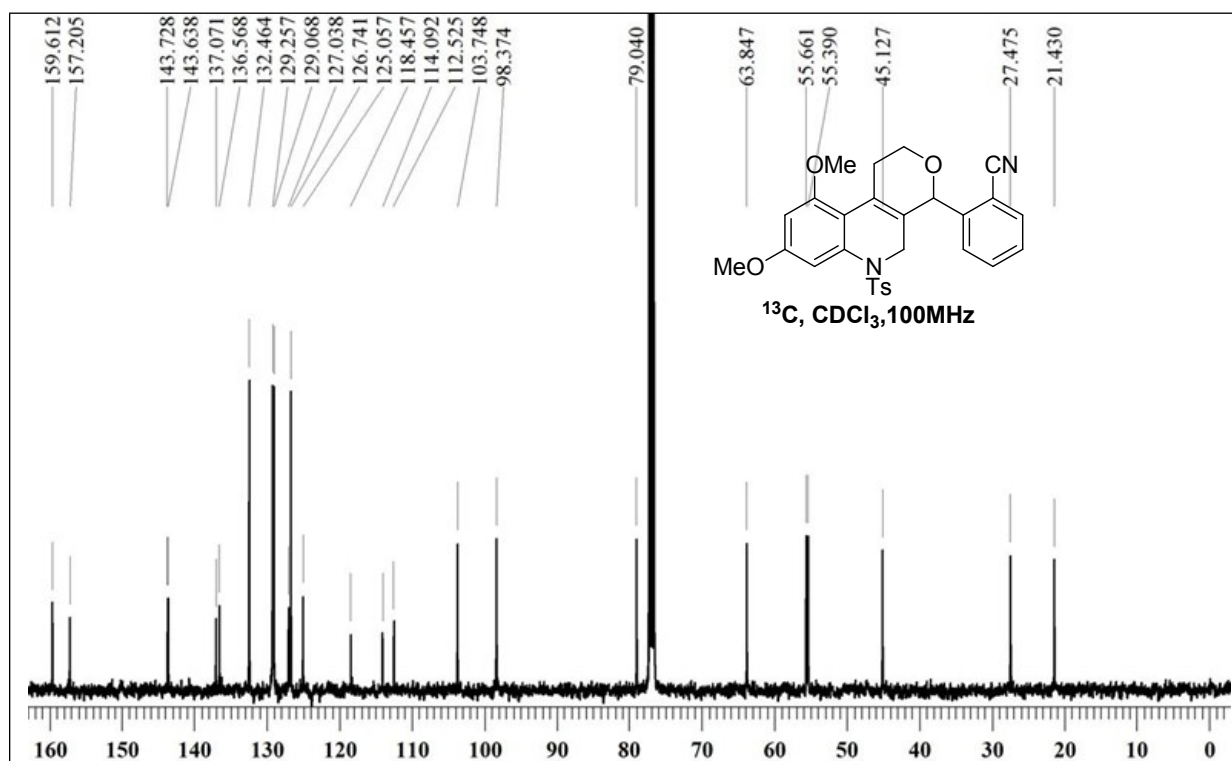
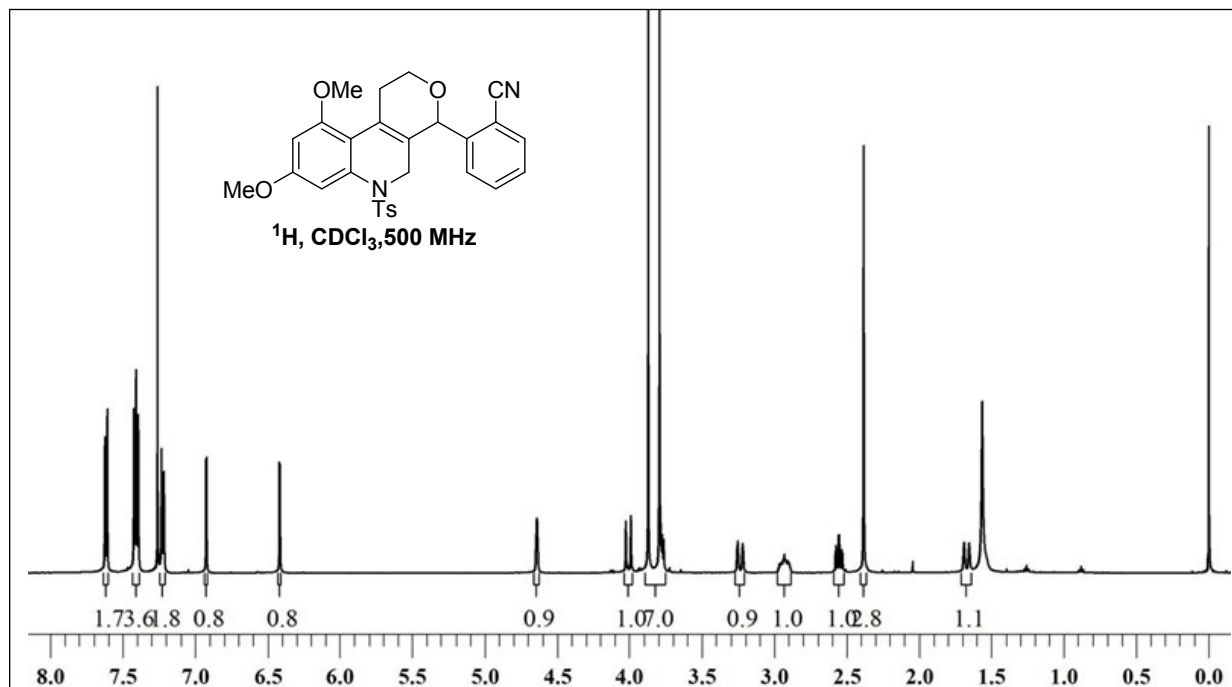
^1H and ^{13}C NMR spectra of compound 6c:



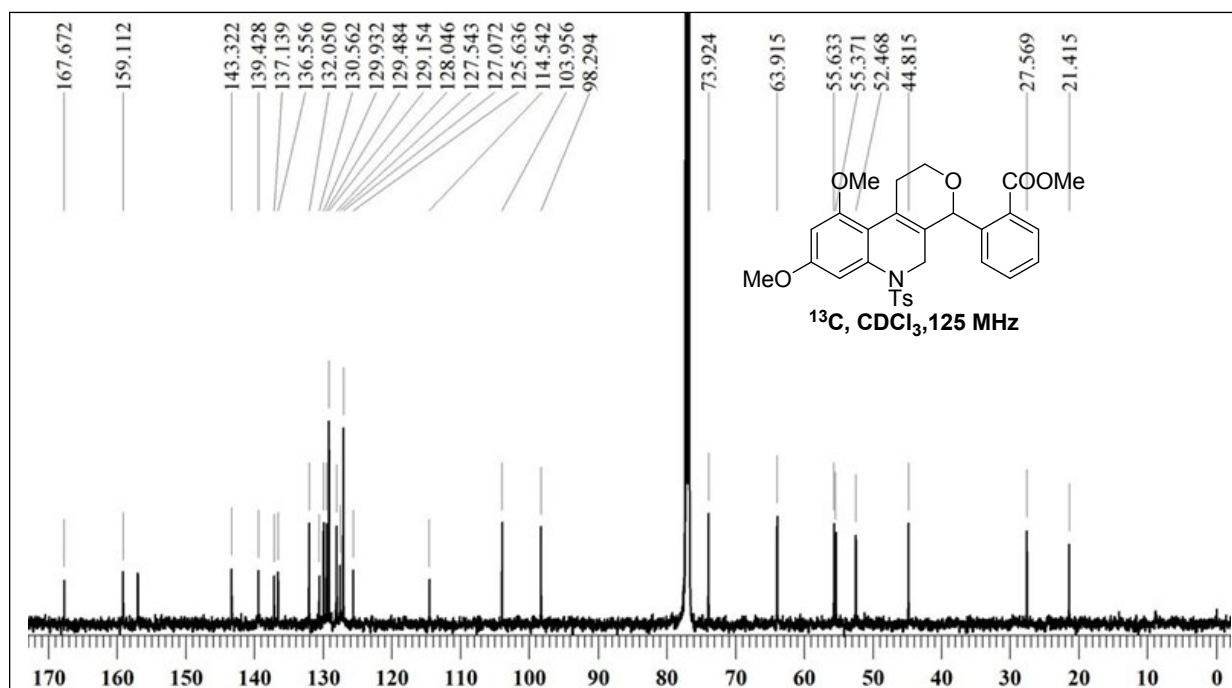
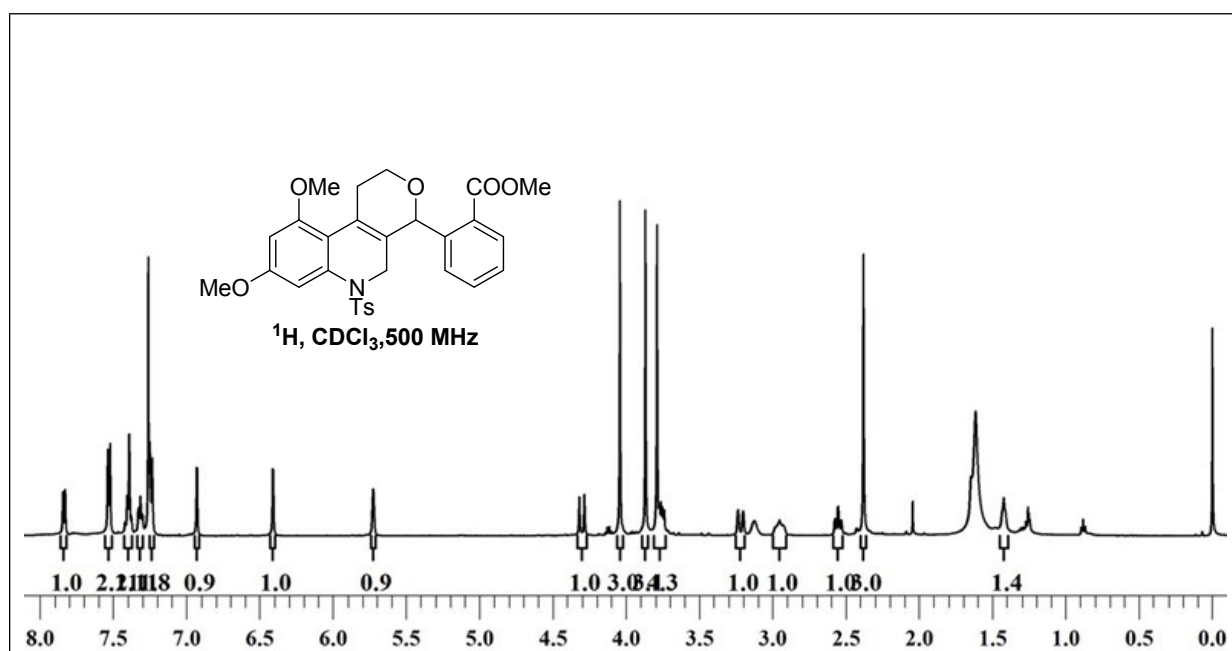
^1H and ^{13}C NMR spectra of compound 6d:



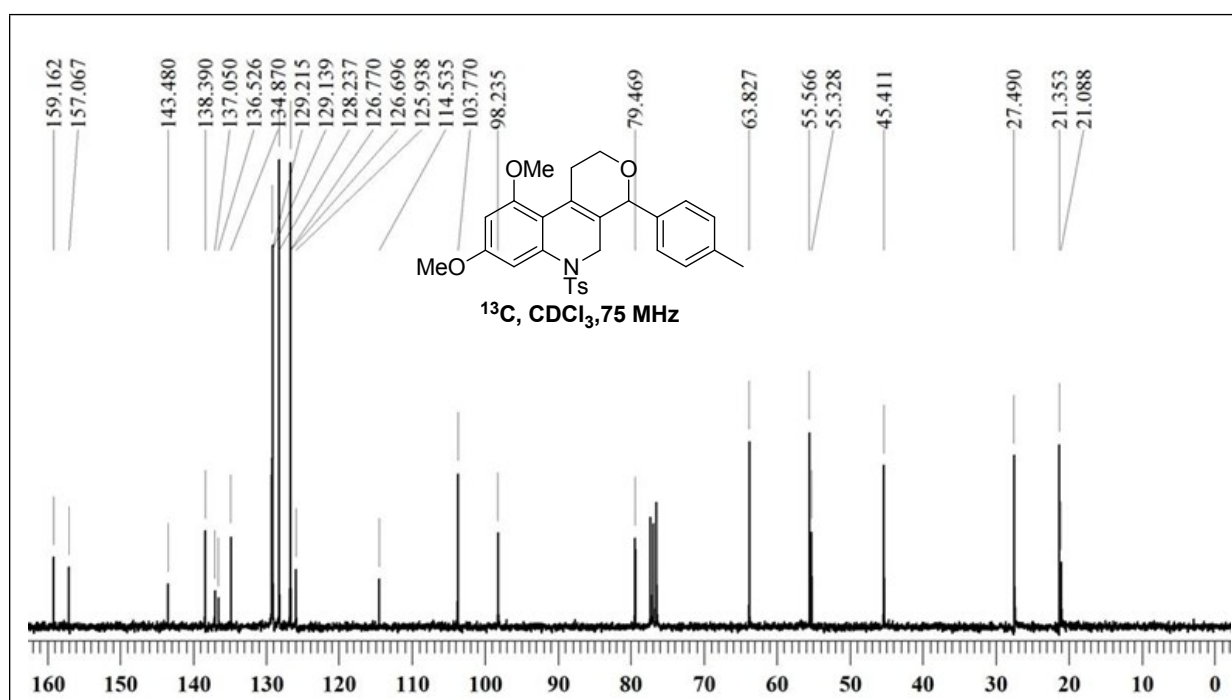
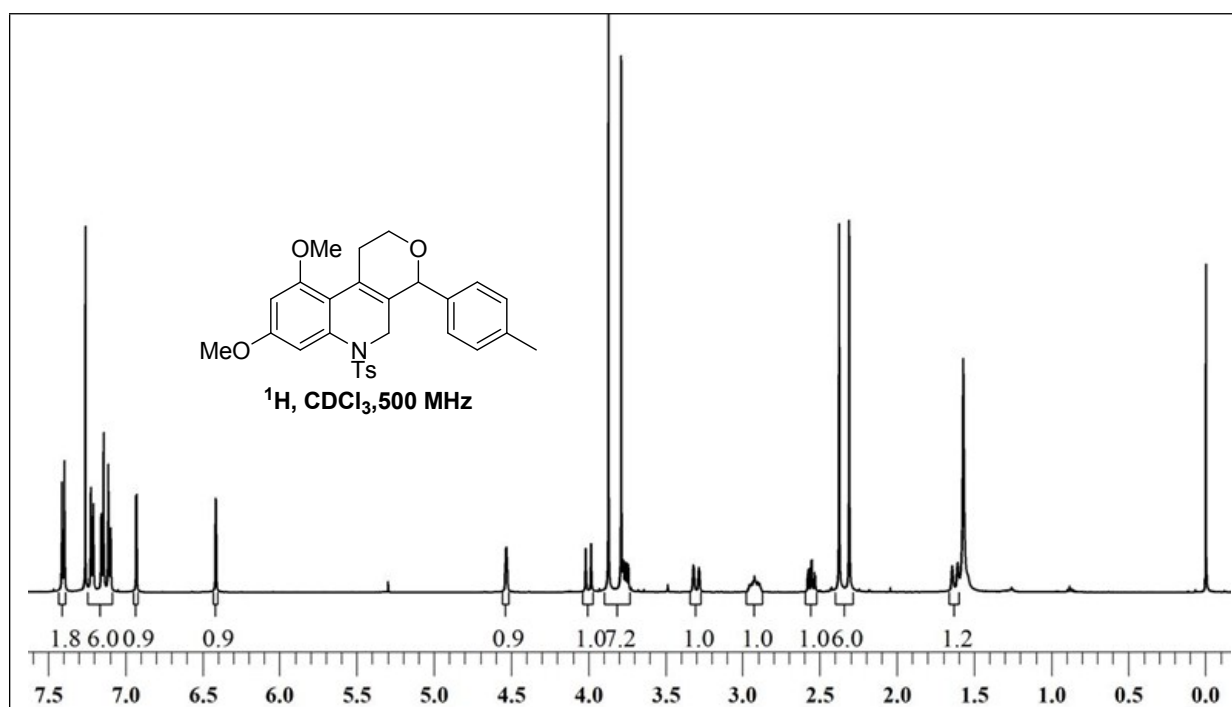
^1H and ^{13}C NMR spectra of compound 6e:



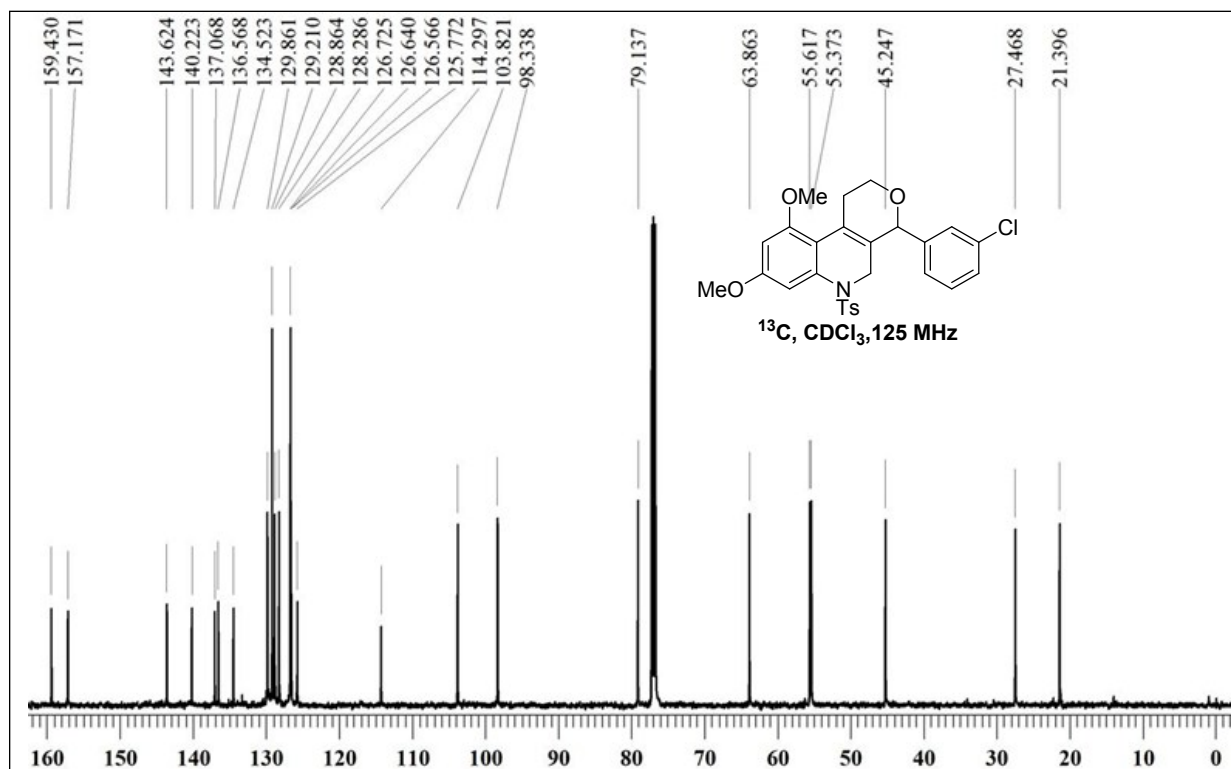
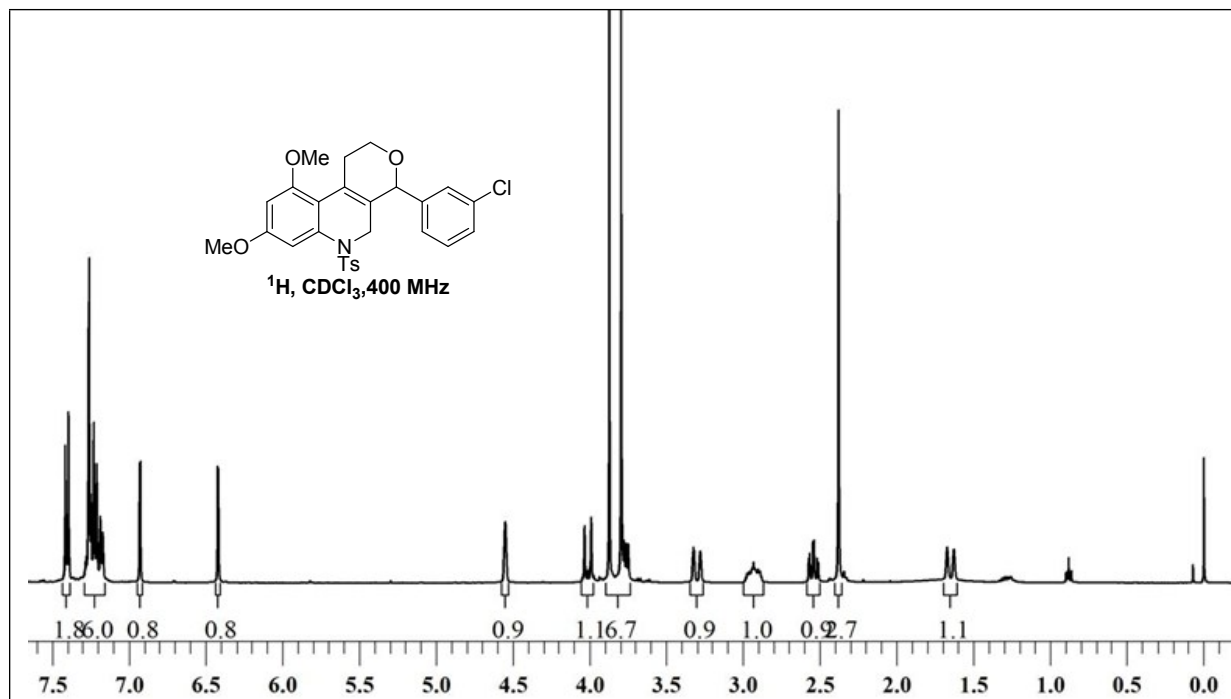
^1H and ^{13}C NMR spectra of compound 6f:



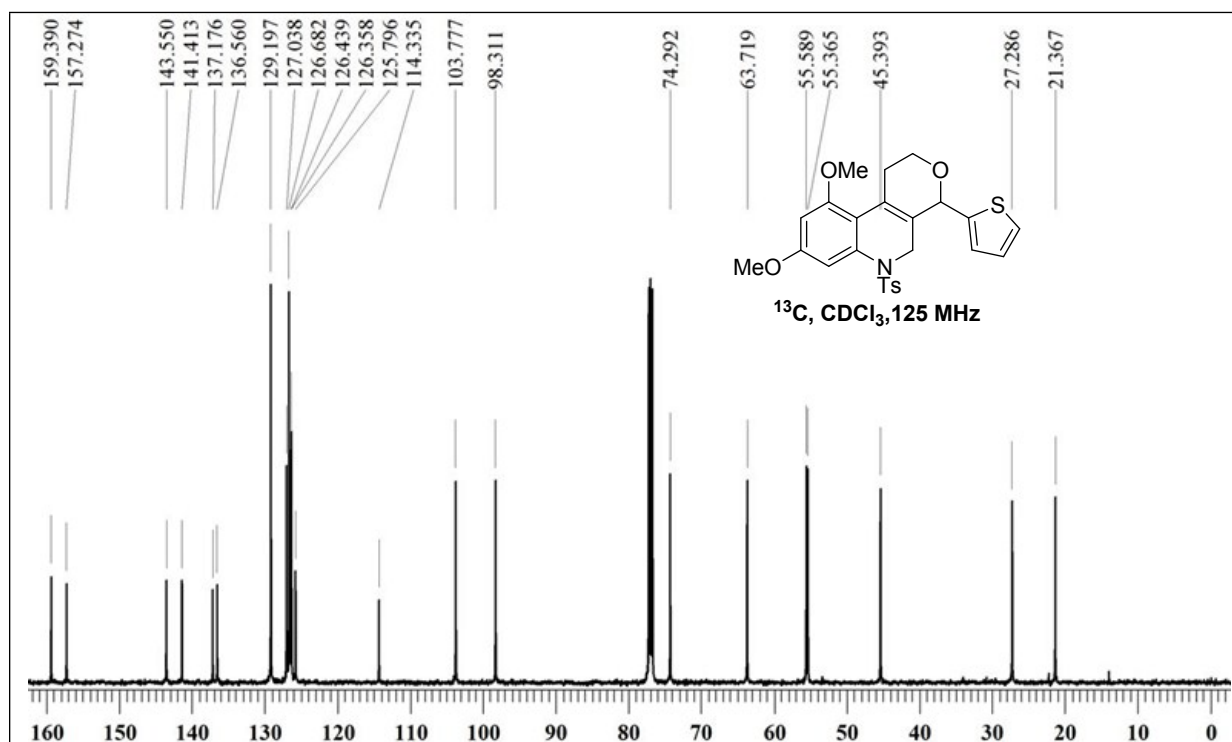
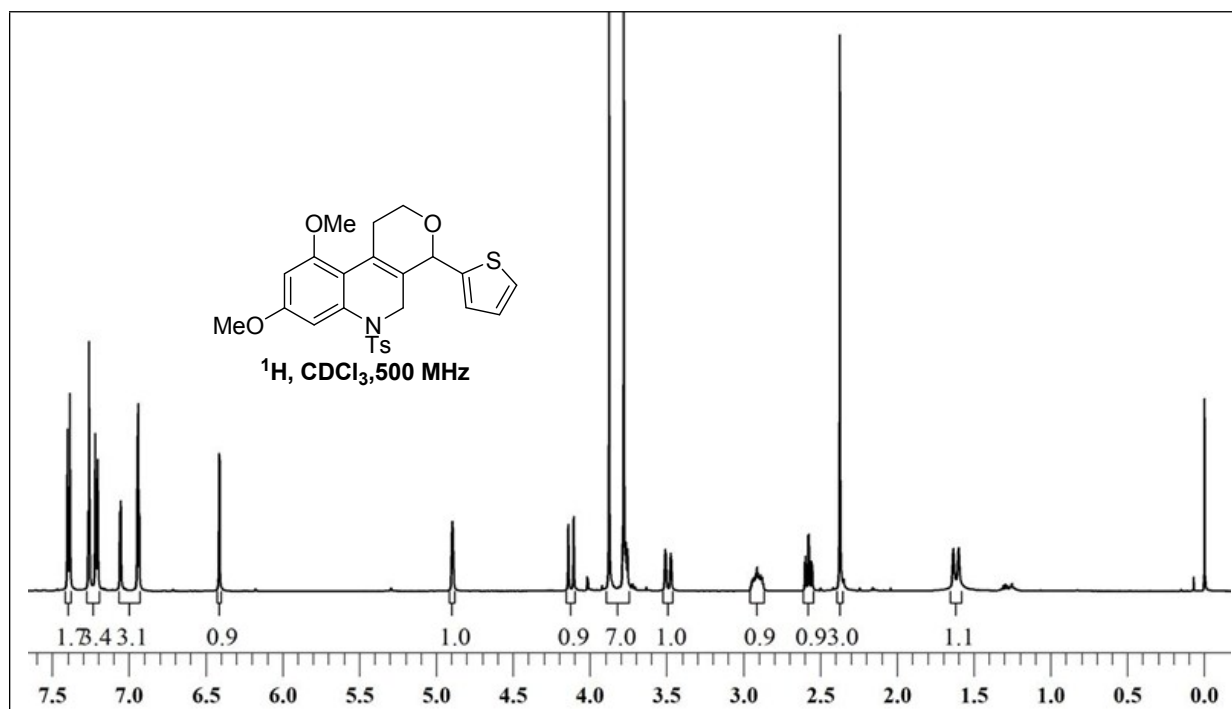
^1H and ^{13}C NMR spectra of compound 6g:



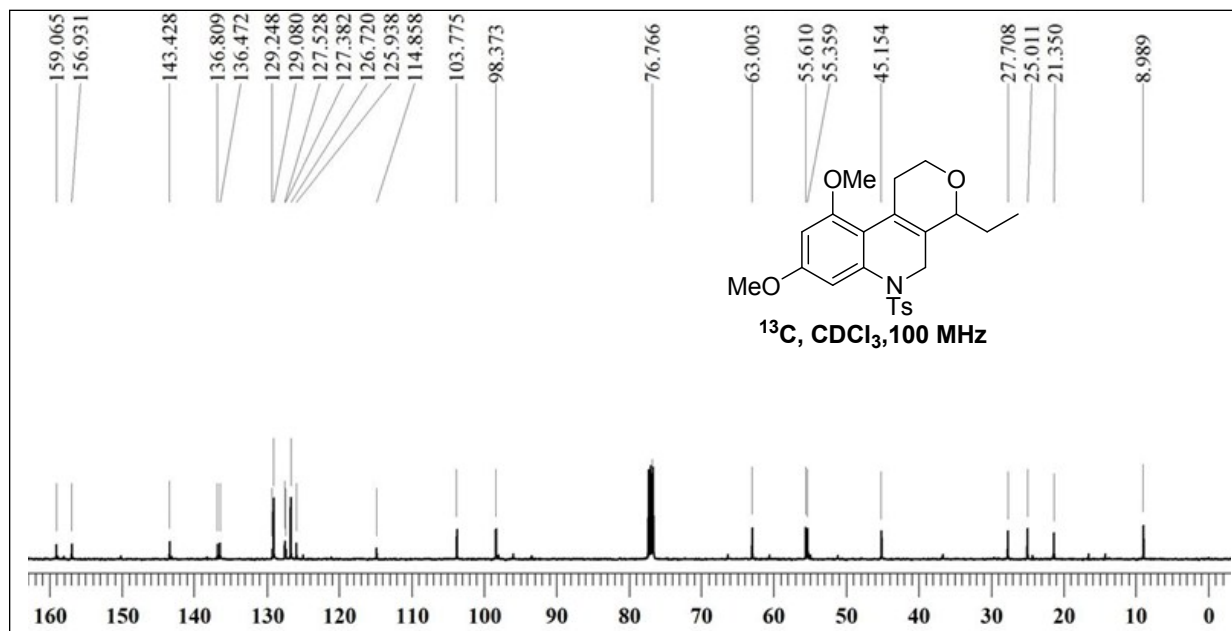
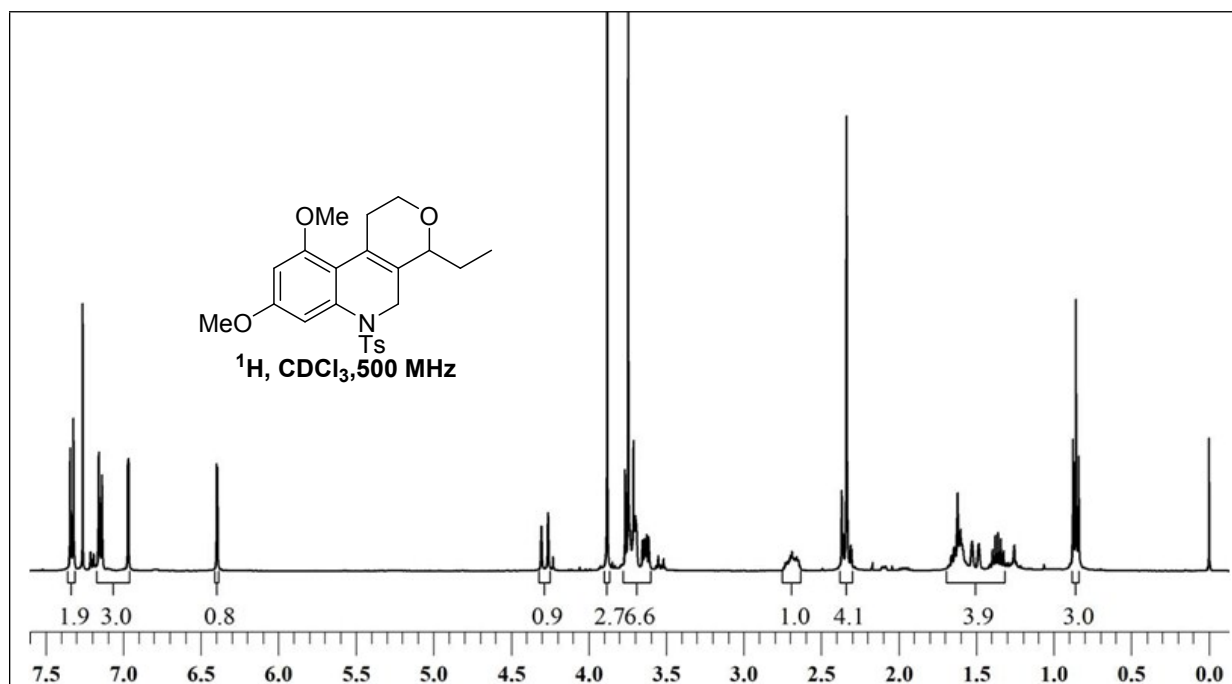
^1H and ^{13}C NMR spectra of compound 6h:



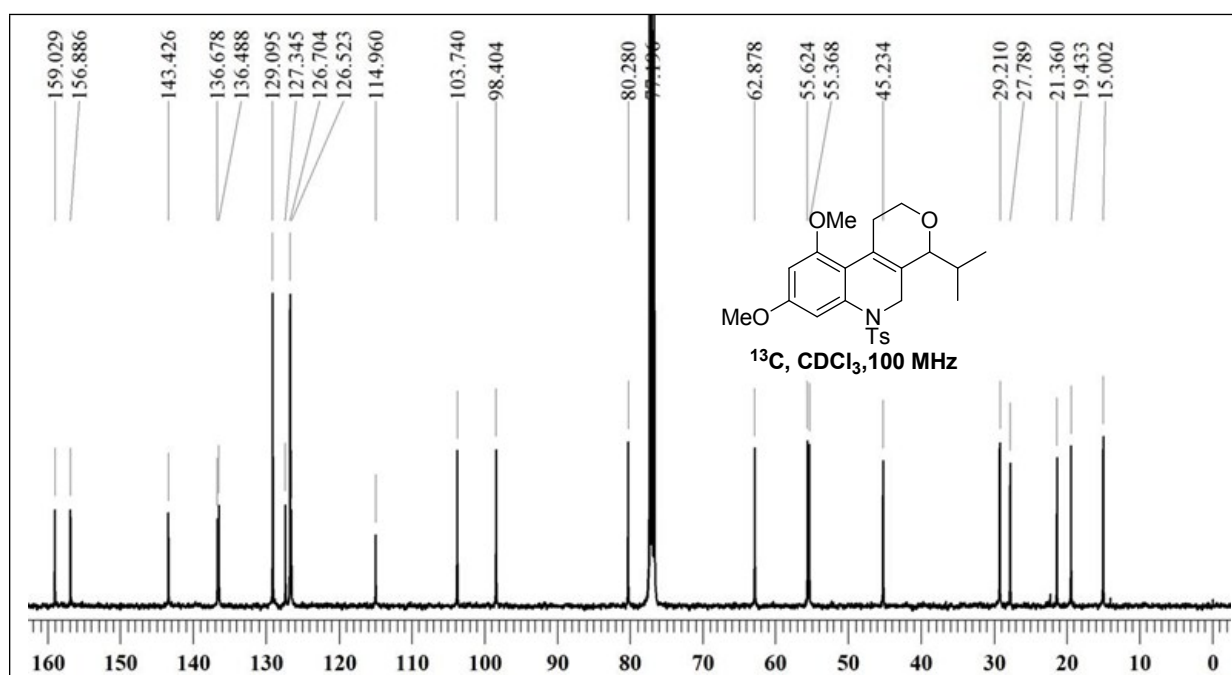
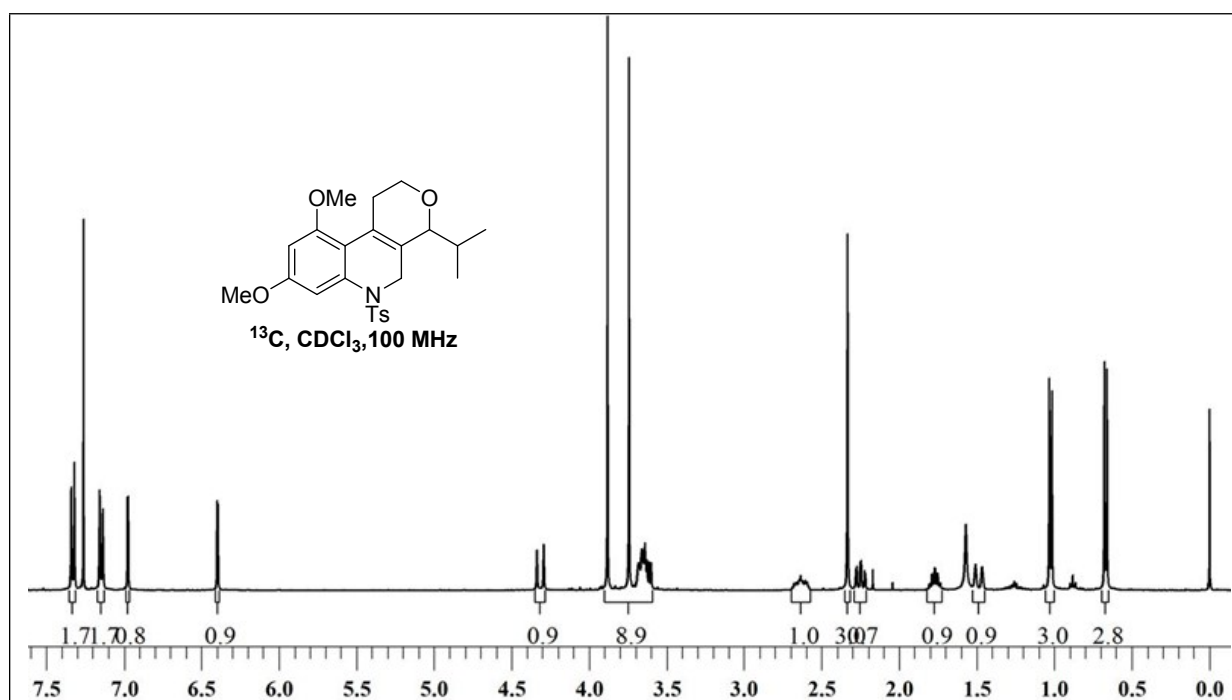
^1H and ^{13}C NMR spectra of compound 6i:



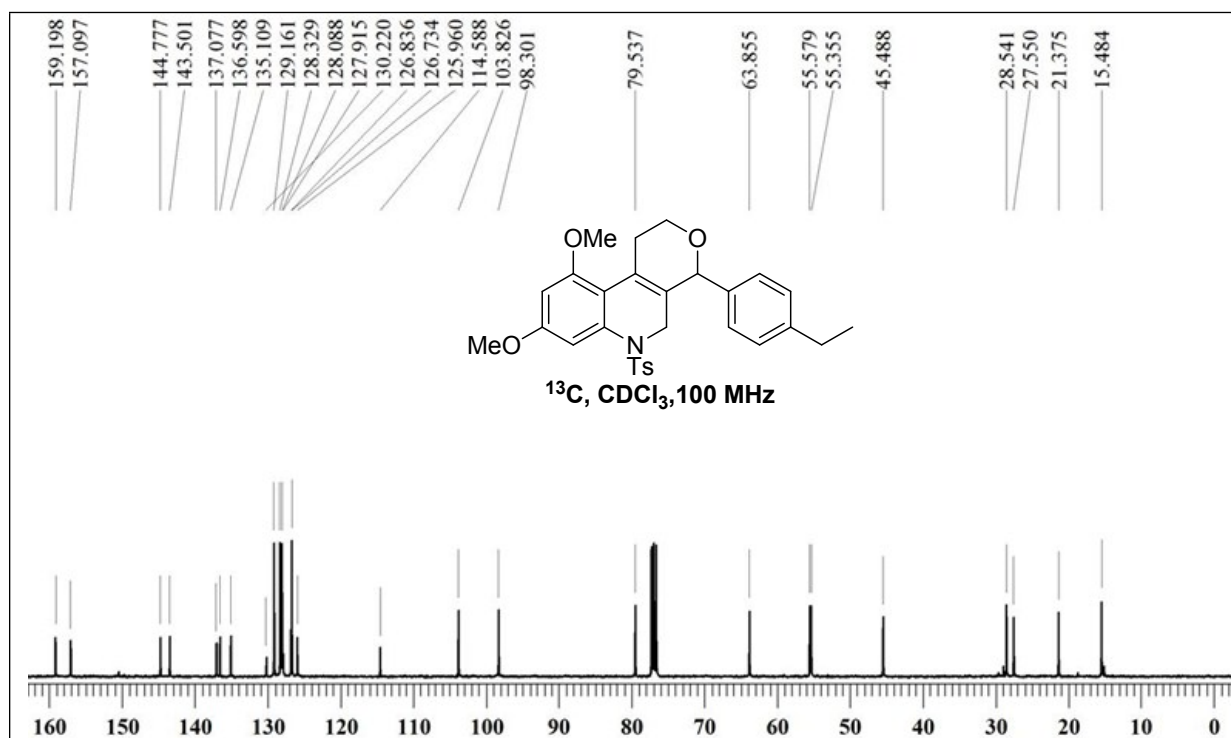
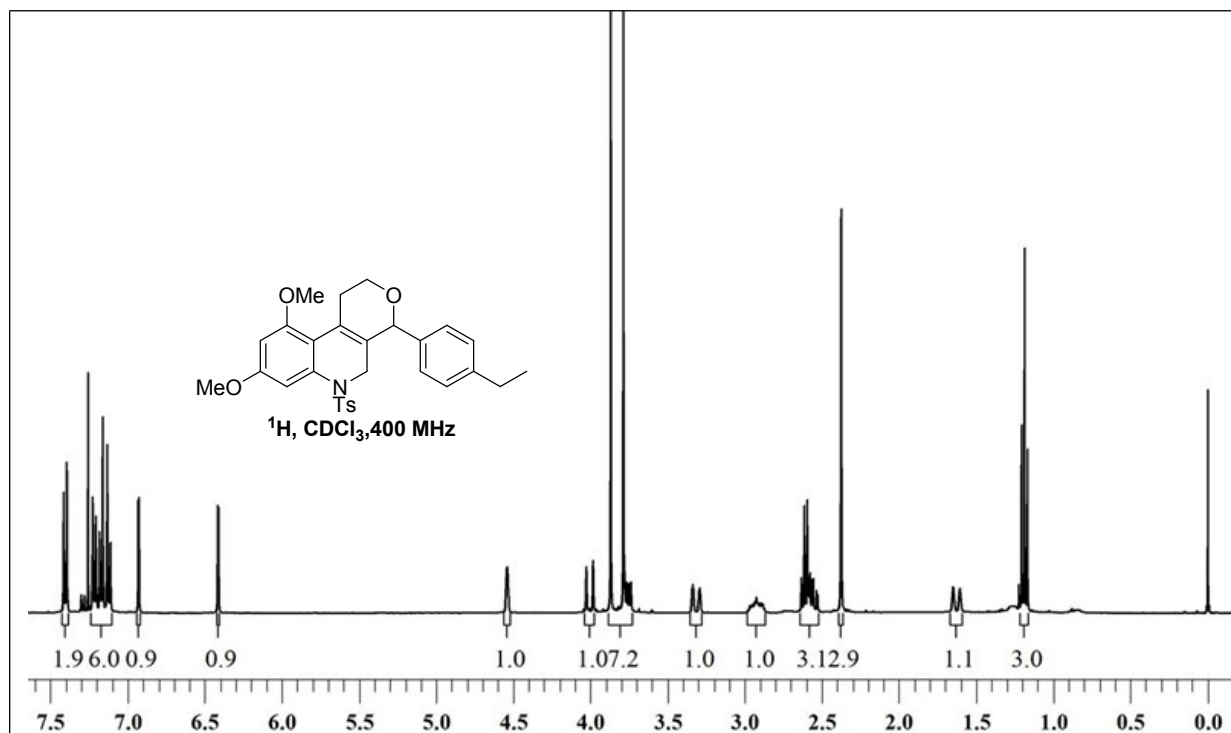
^1H and ^{13}C NMR spectra of compound 6j:



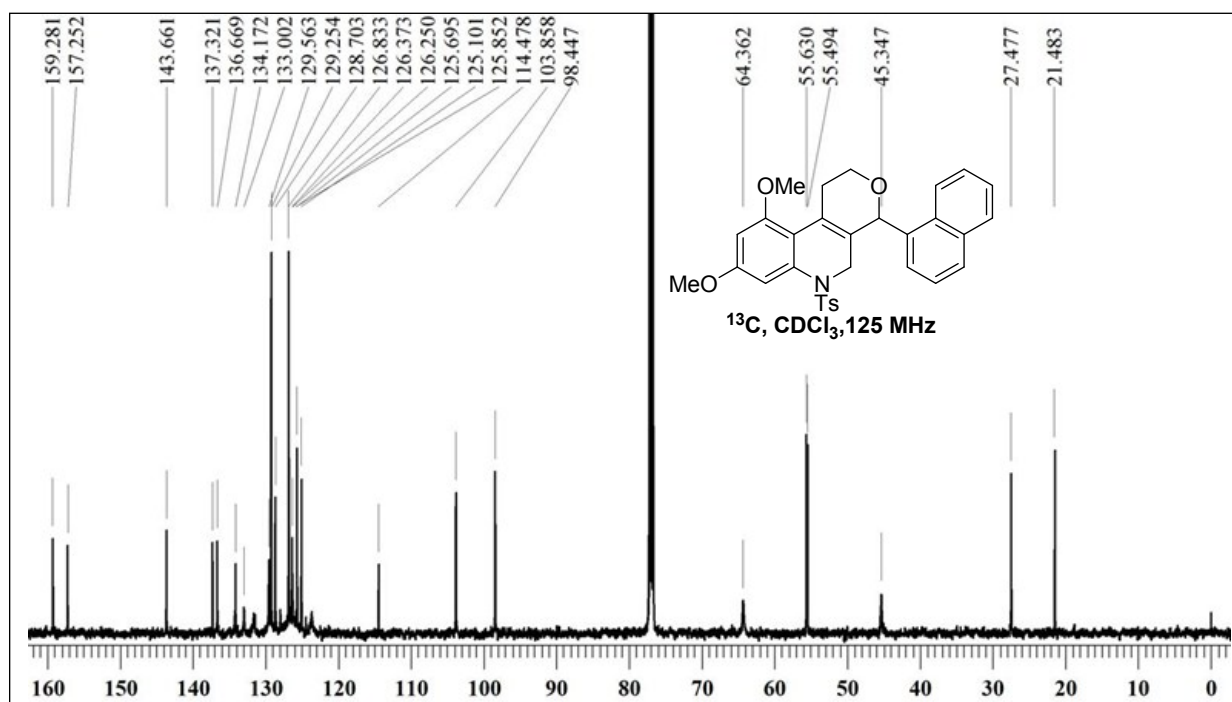
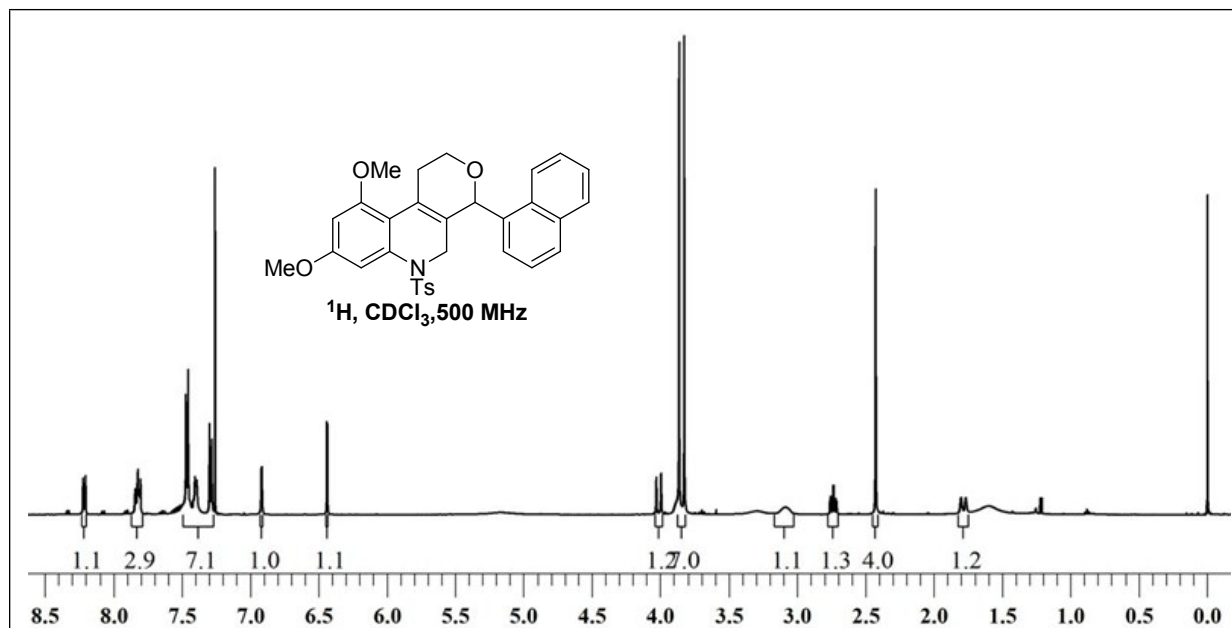
^1H and ^{13}C NMR spectra of compound 6k:



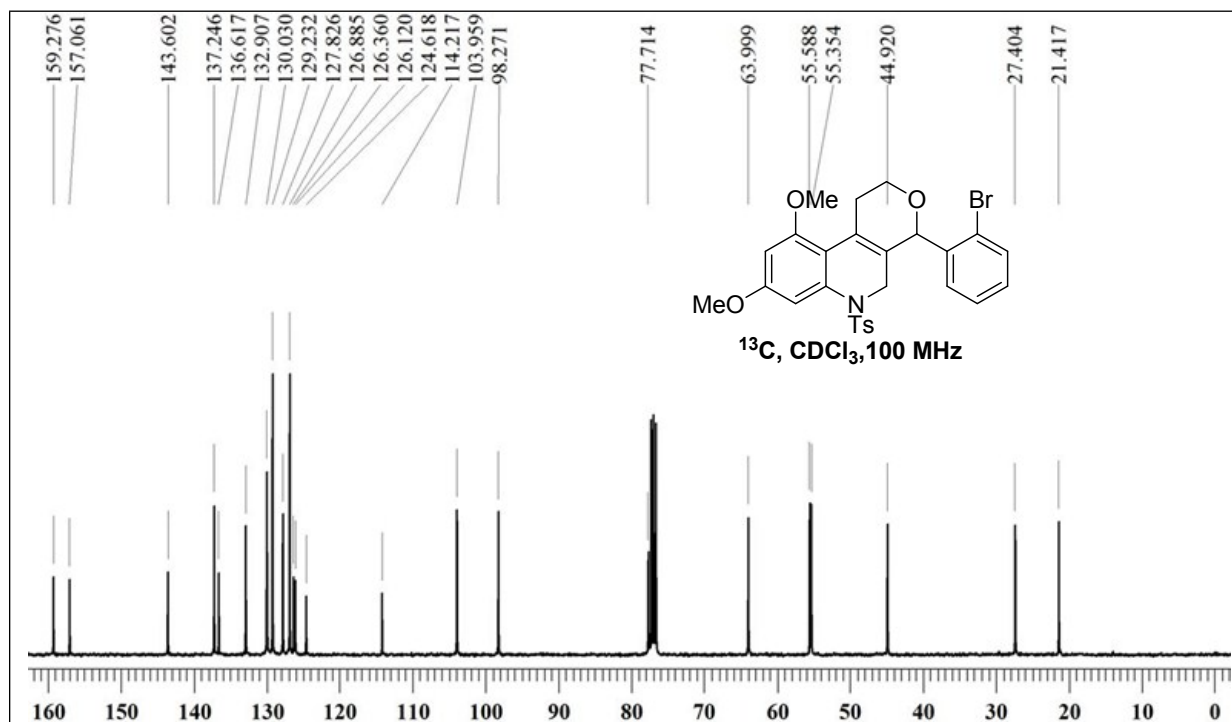
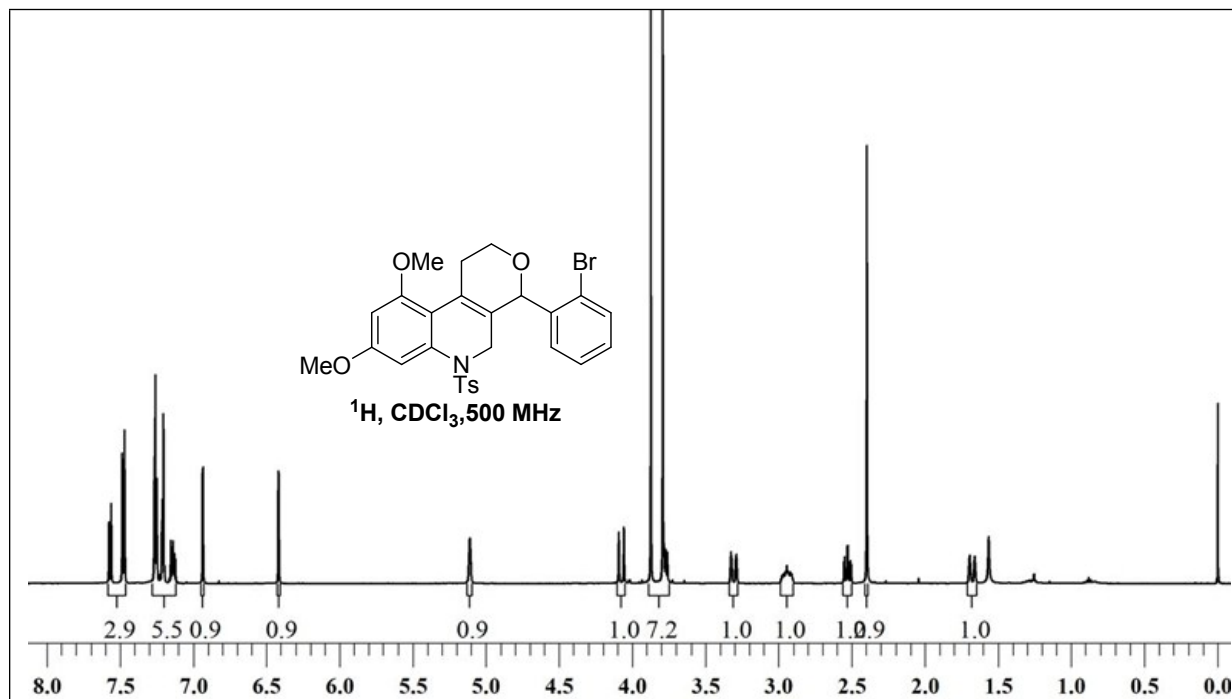
^1H and ^{13}C NMR spectra of compound 6l:



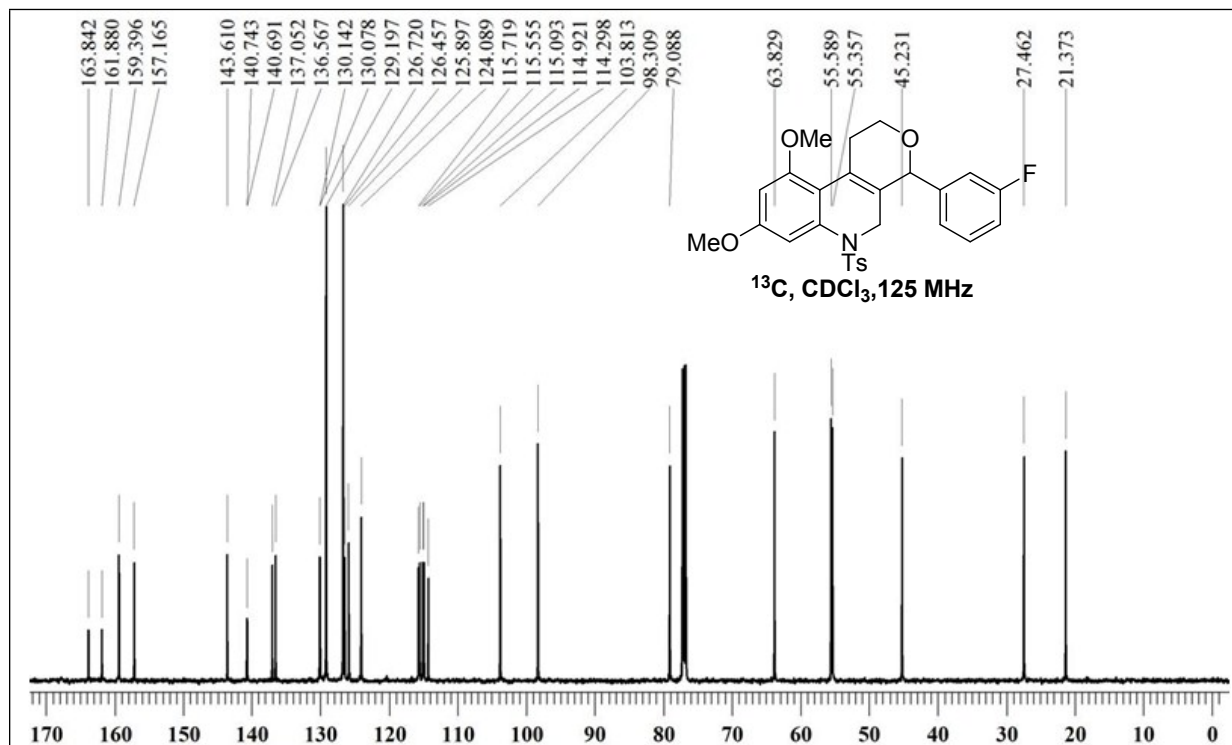
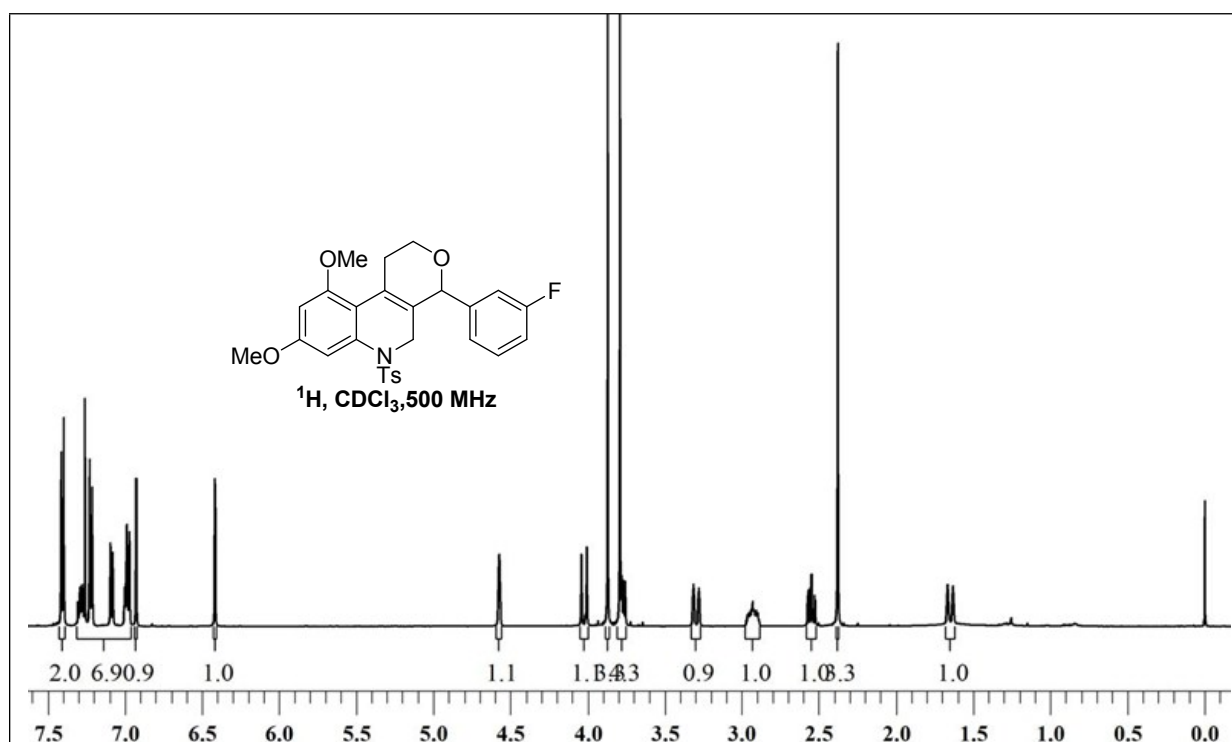
^1H and ^{13}C NMR spectra of compound 6m:



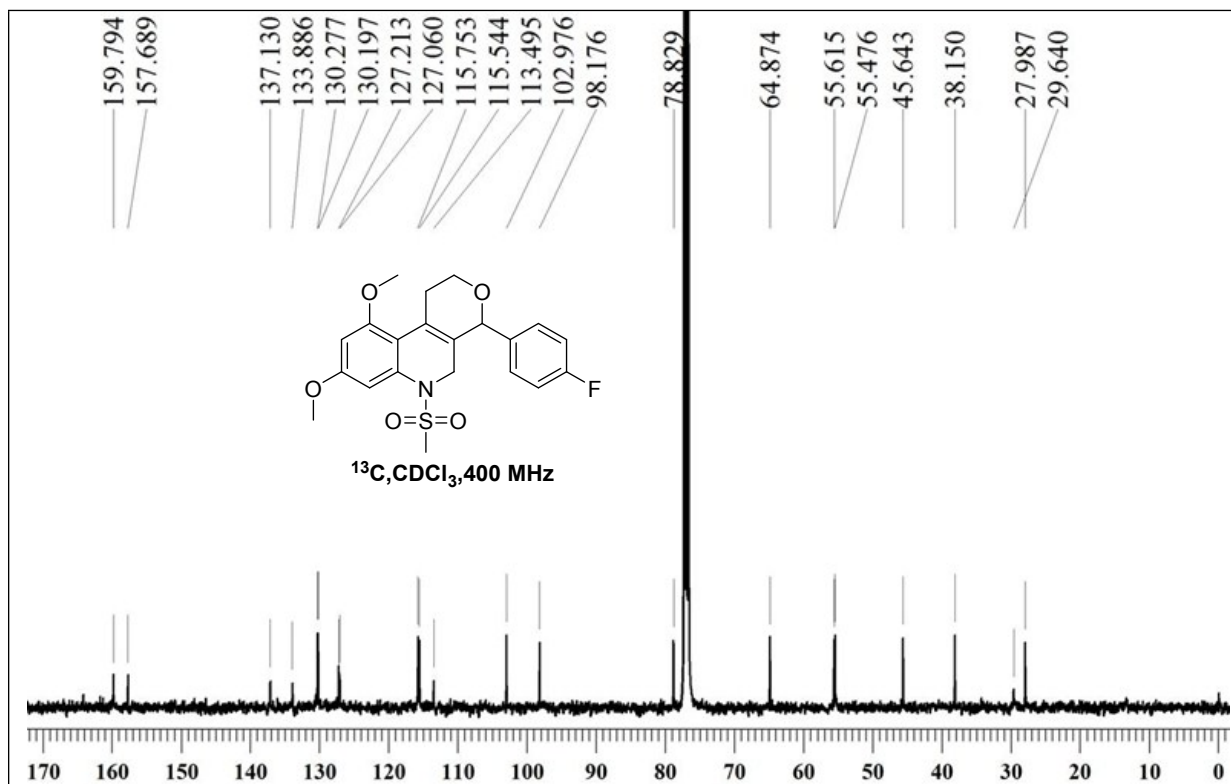
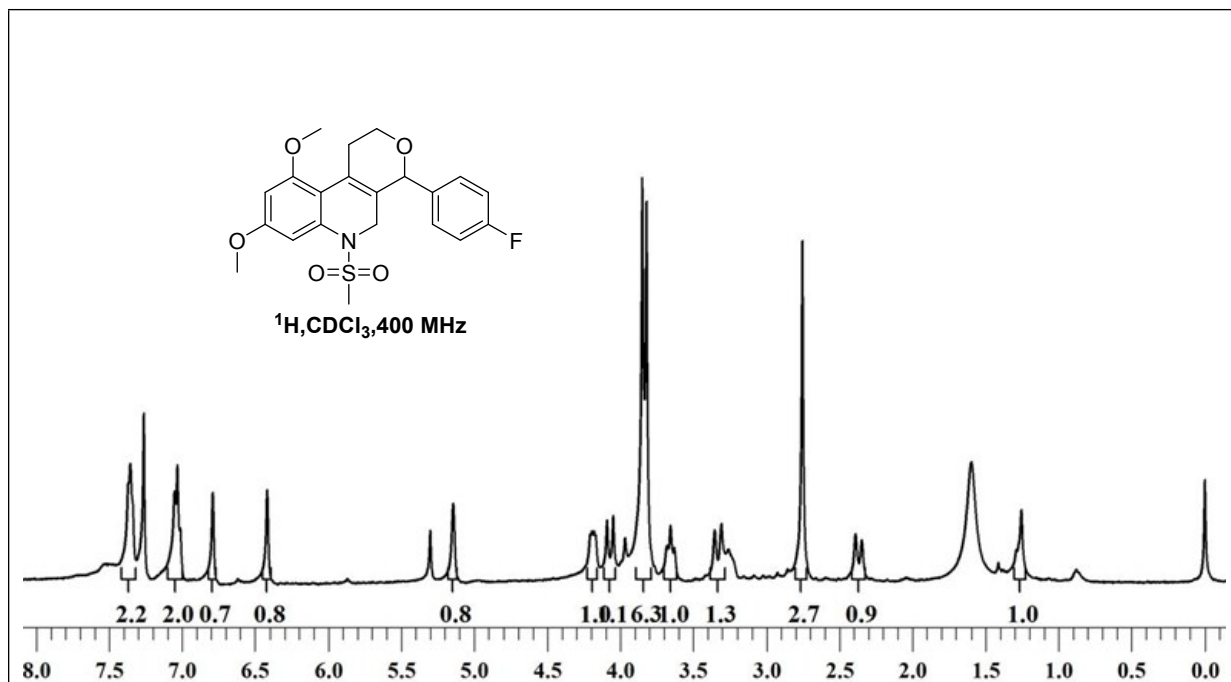
^1H and ^{13}C NMR spectra of compound 6n:



^1H and ^{13}C NMR spectra of compound 60:



^1H and ^{13}C NMR spectra of compound 6r



5. X-ray Crystallography

X-ray data for the compounds were collected at room temperature using a Bruker Smart Apex CCD diffractometer with graphite monochromated MoK α radiation ($\lambda=0.71073\text{\AA}$) with ω -scan method [1]. Preliminary lattice parameters and orientation matrices were obtained from four sets of frames.

Integration and scaling of intensity data was accomplished using SAINT program [1]. The structure was solved by direct methods using SHELXS [2] and refinement was carried out by full-matrix least-squares technique using SHELXL [2]. Anisotropic displacement parameters were included for all non-hydrogen atoms. All H atoms were positioned geometrically and treated as riding on their parent C atoms [C-H = 0.93-0.97 \AA and $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{C})$ for methyl H or $1.2U_{\text{eq}}(\text{C})$ for other H atoms]. The methyl groups were allowed to rotate but not to tip.

Crystal Data for 6j: C₂₃H₂₇NO₅S ($M=429.54$): orthorhombic, space group Pbc_a (no. 61), $a = 13.2828(14)\text{\AA}$, $b = 14.5265(15)\text{\AA}$, $c = 22.502(2)\text{\AA}$, $V = 4341.8(8)\text{\AA}^3$, $Z = 8$, $T = 294.15\text{ K}$, $\mu(\text{MoK}\alpha) = 0.183\text{ mm}^{-1}$, $D_{\text{calc}} = 1.3141\text{ g/mm}^3$, 48256 reflections measured ($4.54 \leq 2\theta \leq 56.66$), 5343 unique ($R_{\text{int}} = 0.0288$) which were used in all calculations. The final R_1 was 0.0659 ($I > 2\sigma(I)$) and wR_2 was 0.1685 (all data). CCDC 1493462 contains supplementary Crystallographic data for the structure. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk].

1. Bruker (2001). SAINT (Version 6.28a) & SMART (Version 5.625). Bruker AXS Inc., Madison, Wisconsin, USA.
2. Sheldrick G. M. (2015) *Acta Crystallogr C* 71: 3-8.

Figure 2. A view of **6j**, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are represented by circles of arbitrary radii.

1, B. V. S. Reddy, M. Durgaprasad, B. Sridhar, S. Kiran Kumar. *J. Org. Chem.*, 2014, **79**2289–2295;