Supporting Information for

Synthesis of Nitrogen-Tethered 1,6-Enynes through CuI/TFA Catalysis

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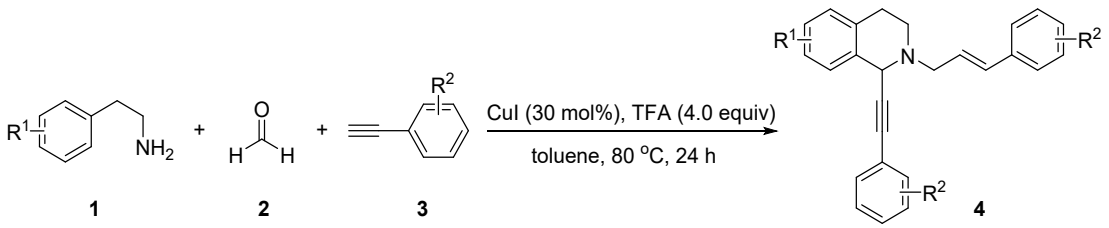
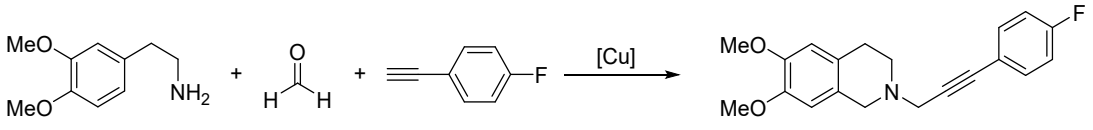
General Information

All commercially available reagents were used without purification unless otherwise noted. All reactions performed under air atmospheric pressure condition. Column chromatography was performed using silica gel (100-200 mesh). Visualization of the compounds was accomplished with UV light (254 nm) and iodine. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ operating at 400 MHz and 100 MHz, respectively. Proton chemical shifts are reported relative to the residual proton signals of the deuterated solvent $CDCl_3$ (7.29 ppm) or TMS. Carbon chemical shifts were internally referenced to the deuterated solvent signals in $CDCl_3$ (77.10 ppm). Chemical shifts are reported in δ (parts per million) values. Coupling constants *J* are reported in Hz. Proton coupling patterns were described as singlet (s), doublet (d), triplet (t), quartet (q), and multiple (m). High-resolution mass spectra were recorded on a liquid chromatograph mass spectrometer (LCMS-IT-TOF).

Experiment and Characterization Data

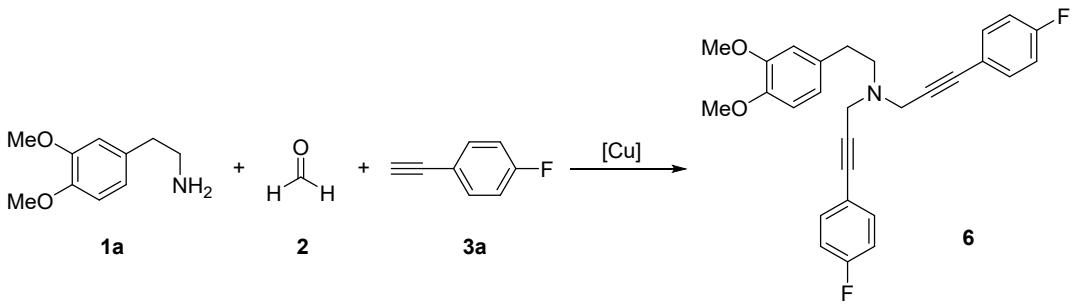


General Procedure for Synthesis of Compounds 4: In the air atmosphere, a 10 mL reaction tube was charged with the corresponding amine **1** (0.5 mmol), 37 w/w% solution **2** (1.5 mmol), alkyne **3** (1.0 mmol), CuI (30 mol%), TFA (4.0 equiv) and toluene (2.0 mL), then sealed. Subsequently, the reaction mixture was stirred at 80 °C for 24 h. Afterwards, the reaction mixture was quenched with saturated Na_2CO_3 (5.0 mL), then H_2O (5.0 mL) was added to the mixture and extracted with CH_2Cl_2 (10 mL × 3). Combined organic phase was washed with brine and dried over Na_2SO_4, and then filtered, the solvent was removed in a rotary evaporator. The residue was purified by flash chromatography (25−50% ethyl acetate in petroleum ether) to afford the desired products **4a**−**4z**.



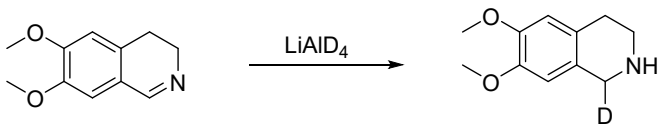
1a **2** **3a** **5a**

Synthesis of Compounds 5a[1]: In the air atmosphere, a 10 mL reaction tube was charged with the 2-(3,4-dimethoxyphenyl)ethan-1-amine **1a** (905 mg, 5 mmol), 37 w/w% formaldehyde solution **2** (891 mg, 11 mmol), 1-ethynyl-4-fluorobenzene **3a** (720 mg, 6 mmol), CuCl (30 mol%, 148 mg), TFA (570 mg, 1.0 equiv) and toluene (5.0 mL), then sealed. Subsequently, the reaction mixture was stirred at 80 °C for 24 h. Afterwards, the reaction system was directly purified by running silica gel flash column chromatography (25−50% ethyl acetate in petroleum ether) to afford the desired products **5a** (1.12 g, 70% yield).



1a **2** **3a** **6**

Synthesis of Compounds 6[1]**:** In the air atmosphere, a 10 mL reaction tube was charged with the 2-(3,4-dimethoxyphenyl)ethan-1-amine **1a** (905 mgn 5 mmol), 37 w/w% formaldehyde solution **2** (891 mg, 11 mmol), 1-ethynyl-4-fluorobenzene (1.2g, 10 mmol), CuI (20mol%, 190 mg), and toluene (5.0 mL), then sealed. Subsequently, the reaction mixture was stirred at 80 °C for 12 h. Afterwards, the reaction system was directly purified by running silica gel flash column chromatography (25−50% ethyl acetate in petroleum ether) to afford the desired products **6** (1.78 g, 80% yield).

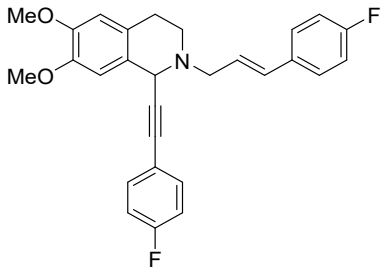


7p

Synthesis of Compounds 7p[2]**:** 50 mL dry THF were added to 7 mmol $LiAlD_4$ (336 mg) followed by addition of 6,7-dimethoxy-3,4-dihydroisoquinoline (0.764 mL, 4

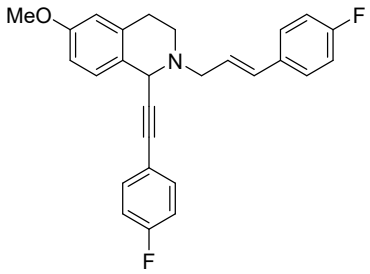
mmol) under nitrogen atmosphere. The mixture was refluxed for 40 h, cooled to 0 °C, and a 30% NaOH solution (100 mL) was added slowly. The aqueous phase was separated and extracted with THF (200 mL). The combined organic phase was dried using Na_2SO_4 and concentrated under reduced pressure to **7p** as yellow oil.

(E)-2-(3-(4-fluorophenyl)allyl)-1-((4-fluorophenyl)ethynyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline



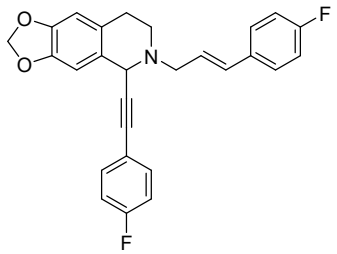
Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4a** (144.6 mg, 65% yield) as yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.46–7.38 (m, 4H), 7.02 (d, *J* = 8.7 Hz, 4H), 6.81 (s, 1H), 6.65 (d, *J* = 4.0 Hz, 2H), 6.36–6.27 (m, 1H), 4.87 (s, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.57 (d, *J* = 6.8 Hz, 2H), 3.14–2.88 (m, 3H), 2.78 (d, *J* = 14.4 Hz, 1H). **^{13}C NMR** (100 MHz, Chloroform-d) δ 163.6 (d, $J_{(C-F)}$ = 9.5 Hz), 161.1 (d, $J_{(C-F)}$ = 7.0 Hz), 148.3, 147.5, 133.6 (d, $J_{(C-F)}$ = 8.2 Hz), 133.2 (d, $J_{(C-F)}$ = 3.3 Hz), 132.1, 127.9 (d, $J_{(C-F)}$ = 8.0 Hz), 127.1, 126.5 (d, $J_{(C-F)}$= 2.4 Hz), 126.0, 119.3 (d, $J_{(C-F)}$ = 3.6 Hz), 115.6 (d, $J_{(C-F)}$= 1.8 Hz), 115.4 (d, $J_{(C-F)}$ = 1.5 Hz), 111.4, 110.5, 87.1 (d, $J_{(C-F)}$ = 1.5 Hz), 85.7, 57.7, 56.0, 55.9, 54.2, 45.9, 28.5. **^{19}F NMR** (376 MHz, Chloroform-d) δ -111.18 (s, 1F), -114.45 (s, 1F). **HRMS** m/z (ESI^+): Calculated for $C_{28}H_{26}F_2NO_2$ ($[M+H]^+$): 446.1926, found 452.1935.

(E)-2-(3-(4-fluorophenyl)allyl)-1-((4-fluorophenyl)ethynyl)-6-methoxy-1,2,3,4-tetrahydroisoquinoline



Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4b** (118.2 mg, 57% yield) as yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.47–7.38 (m, 4H), 7.25 (d, *J* = 8.5 Hz, 1H), 7.08–6.99 (m, 4H), 6.81–6.79 (m, 1H), 6.71–6.65 (m, 2H), 6.36–6.29 (m, 1H), 4.90 (s, 1H), 3.81 (s, 3H), 3.66–3.52 (m, 2H), 3.14–3.00 (m, 2H), 2.95–2.80 (m, 2H). **^{13}C NMR** (100 MHz, Chloroform-d) δ 163.6 (d, $J_{(C-F)}$ = 7.0 Hz), 161.1 (d, $J_{(C-F)}$ = 4.7 Hz), 158.6, 135.1, 133.6 (d, $J_{(C-F)}$ = 8.2 Hz), 133.2 (d, $J_{(C-F)}$ = 3.3 Hz), 132.1, 128.8, 127.9 (d, $J_{(C-F)}$ = 8.0 Hz), 127.6, 126.4 (d, $J_{(C-F)}$ = 2.2 Hz), 119.3 (d, $J_{(C-F)}$ = 3.7 Hz), 115.6 (d, $J_{(C-F)}$ = 2.3 Hz), 115.4 (d, $J_{(C-F)}$ = 2.8 Hz), 113.4, 112.5, 87.2 (d, $J_{(C-F)}$ = 1.5 Hz), 85.6, 57.7, 55.2, 54.2, 45.7, 29.1. **^{19}F NMR** (376 MHz, Chloroform-d) δ -111.21 (s, 1F), -114.48 (s, 1F). **HRMS** m/z (ESI^{+}): Calculated for $C_{27}H_{24}F_2NO([M+H]^{+})$: 416.1820, found 416.1826.

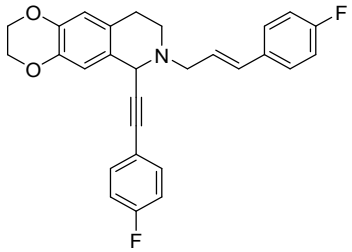
(E)-6-(3-(4-fluorophenyl)allyl)-5-((4-fluorophenyl)ethynyl)-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-g]isoquinoline



Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4c** (128.7 mg, 60% yield) as yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.46–7.42 (m, 2H), 7.41–7.37 (m, 2H), 7.06–6.99 (m, 4H), 6.77 (s, 1H), 6.65 (d, *J* = 15.8 Hz, 1H), 6.61 (s, 1H), 6.33–6.26 (m, 1H), 5.96–5.91 (m, 2H), 4.82 (s, 1H), 3.60–3.49 (m, 2H), 3.09–3.02 (m, 1H), 3.01–2.94 (m, 1H), 2.92–2.86 (m, 1H), 2.79–2.72 (m, 1H). **^{13}C NMR** (100 MHz, Chloroform-d) δ 163.6 (d, $J_{(C-F)}$ = 10.3

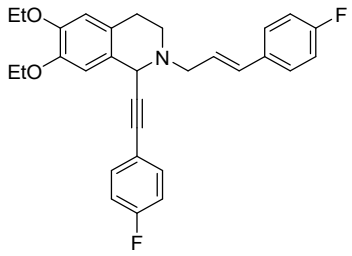
Hz), 161.2 (d, $J_{(C-F)}$ = 7.8 Hz), 146.9, 146.0, 133.6 (d, $J_{(C-F)}$ = 8.4 Hz), 133.1 (d, $J_{(C-F)}$ = 3.3 Hz), 132.3, 127.9 (d, $J_{(C-F)}$ = 8.0 Hz), 127.1, 126.1, 119.1 (d, $J_{(C-F)}$ = 3.4 Hz), 115.5 (d, $J_{(C-F)}$ = 21.9 Hz), 108.5, 107.5, 100.9, 86.7, 85.8, 57.6, 54.5, 45.7, 28.8. **^{19}F NMR** (376 MHz, Chloroform-d) δ -111.17 (s, 1F), -114.46 (s,1 F). **HRMS** m/z (ESI^+): Calculated for $C_{27}H_{21}F_2NO_2Na$ ($[M+Na]^+$):452.1433, found 452.1439.

(E)-7-(3-(4-fluorophenyl)allyl)-6-((4-fluorophenyl)ethynyl)-2,3,6,7,8,9-hexahydro-[1,4]dioxino[2,3-g]isoquinoline



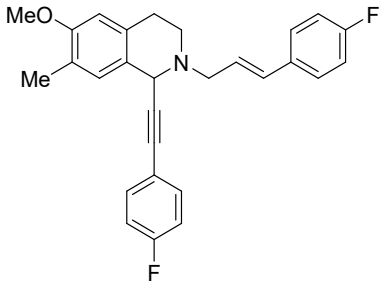
Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4d** (155.0 mg, 70% yield) as yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.39–7.29 (m, 4H), 6.95 (q, *J* = 9.0 Hz, 4H), 6.75 (s, 1H), 6.56 (d, *J* = 12.9 Hz, 2H), 6.26–6.17 (m, 1H), 4.74 (s, 1H), 4.18 (s, 4H), 3.54–3.38 (m, 2H) 3.01–2.96 (m, 1H), 2.92–2.83 (m, 1H), 2.79 (d, *J* = 13.9 Hz, 1H), 2.68 (d, *J* = 16.5 Hz, 1H). **^{13}C NMR** (100 MHz, Chloroform-d) δ 163.6 (d, $J_{(C-F)}$ = 8.2 Hz), 161.1 (d, $J_{(C-F)}$ = 5.7 Hz), 142.8, 141.9, 133.6 (d, $J_{(C-F)}$ = 8.2 Hz), 133.2 (d, $J_{(C-F)}$ = 3.3 Hz), 132.1, 128.1, 127.9 (d, $J_{(C-F)}$ = 8.0 Hz), 126.8, 126.3, 119.2 (d, $J_{(C-F)}$ = 3.5 Hz), 116.8, 115.9, 115.6 (d, $J_{(C-F)}$ = 2.9 Hz), 115.4 (d, $J_{(C-F)}$ = 3.3 Hz), 87.0, 85.6, 64.4, 64.4, 57.6, 54.1, 45.8, 28.1. **^{19}F NMR** (376 MHz, Chloroform-d) δ -111.33 (s, 1F), -114.56 (s, 1F). **HRMS** m/z (ESI^+): Calculated for $C_{28}H_{24}F_2NO_2$ ($[M+H]^+$): 444.1770, found 444.1771.

(E)-6,7-diethoxy-2-(3-(4-fluorophenyl)allyl)-1-((4-fluorophenyl)ethynyl)-1,2,3,4-tetrahydroisoquinoline



Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4e** (125.3 mg, 53% yield) as yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.45–7.38 (m, 4H), 7.03 (q, *J* = 8.6 Hz, 4H), 6.82 (s, 1H), 6.67 (d, *J* = 14.8 Hz, 2H), 6.37–6.27 (m, 1H), 4.87 (s, 1H), 4.13–4.03 (m, 4H), 3.59–3.55 (m, 2H), 3.13–3.06 (m, 1H), 3.05–2.96 (m, 1H), 2.93 (d, *J* = 13.3 Hz, 1H), 2.77 (d, *J* = 14.0 Hz, 1H), 1.48–1.45 (m, 3H), 1.45–1.42 (m, 3H). **^{13}C NMR** (100 MHz, Chloroform-d) δ 163.6 (d, $J_{(C-F)}$ = 8.4 Hz), 161.1 (d, $J_{(C-F)}$ = 6.1 Hz), 148.2, 147.1, 133.6 (d, $J_{(C-F)}$ = 8.3 Hz), 133.1 (d, $J_{(C-F)}$ = 3.2 Hz), 132.3, 127.9 (d, $J_{(C-F)}$ = 8.0 Hz), 127.0, 126.2 (d, $J_{(C-F)}$ = 2.3 Hz), 126.0, 119.2 (d, $J_{(C-F)}$ = 3.4 Hz), 115.5 (d, $J_{(C-F)}$ = 22.3 Hz), 113.6, 112.8, 87.0, 85.7, 64.7, 64.5, 57.6, 54.1, 45.8, 28.3, 14.9, 14.8. **^{19}F NMR** (376 MHz, Chloroform-d) δ -111.30 (s, 1F), -114.53 (s, 1F). **HRMS** m/z (ESI^+): Calculated for $C_{30}H_{30}F_2NO_2$ ($[M+H]^+$): 474.2239, found 474.2241.

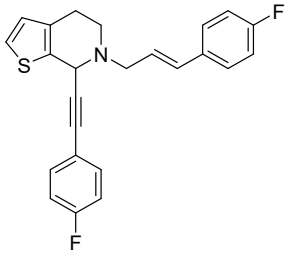
(E)-2-(3-(4-fluorophenyl)allyl)-1-((4-fluorophenyl)ethynyl)-6-methoxy-7-methyl-1,2,3,4-tetrahydroisoquinoline



Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4f** (111.5 mg, 52% yield) as yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.47–7.39 (m, 4H), 7.10–6.99 (m, 5H), 6.71–6.59 (m, 2H), 6.37–6.28 (m, 1H), 4.87 (s, 1H), 3.84 (s, 3H), 3.57 (d, *J* = 6.8 Hz, 2H), 3.14–3.07 (m, 1H), 3.06–3.01 (m, 1H), 2.95–2.89 (m, 1H), 2.88–2.78 (m, 1H), 2.23 (s, 3H). **^{13}C NMR** (100 MHz, Chloroform-d) δ 163.6 (d, $J_{(C-F)}$ = 5.4 Hz), 161.1 (d, $J_{(C-F)}$= 3.1 Hz), 156.9,

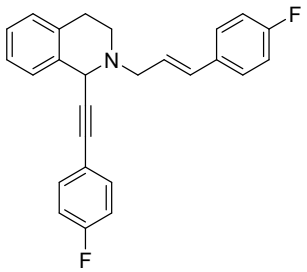
133.6 (d, $J_{(C-F)}$ = 8.3 Hz), 133.3 (d, $J_{(C-F)}$ = 3.4 Hz), 132.1 (d, $J_{(C-F)}$ = 18.0 Hz), 129.7, 127.9 (d, $J_{(C-F)}$ = 8.0 Hz), 126.8, 126.6 (d, $J_{(C-F)}$ = 2.2 Hz), 124.7, 119.4 (d, $J_{(C-F)}$ = 3.4 Hz), 115.6 (d, $J_{(C-F)}$ = 4.0 Hz), 115.4 (d, $J_{(C-F)}$ = 4.4 Hz), 109.9, 87.4, 85.4, 57.7, 55.3, 54.0, 45.8, 29.0, 15.9. **^{19}F NMR** (376 MHz, Chloroform-d) δ -111.47 (s, 1F), -114.63 (s, 1F). **HRMS** m/z (ESI$^+$): Calculated for $C_{28}H_{26}F_2NO$ ([M+H]$^+$): 430.1977, found 430.1983.

(E)-6-(3-(4-fluorophenyl)allyl)-7-((4-fluorophenyl)ethynyl)-4,5,6,7-tetrahydrothieno[2,3-c]pyridine



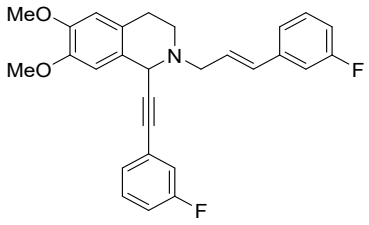
Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4g** (78.2 mg, 40% yield) as light yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.49–7.43 (m, 2H), 7.42–7.35 (m, 2H), 7.20 (d, *J* = 5.1 Hz, 1H), 7.09–6.98 (m, 4H), 6.81 (d, *J* = 5.1 Hz, 1H), 6.65 (d, *J* = 15.8 Hz, 1H), 6.36–6.24 (m, 1H), 4.99 (s, 1H), 3.69–3.62 (m, 1H), 3.57–3.49 (m, 1H), 3.20–3.10 (m, 1H), 2.95–2.70 (m, 3H). **^{13}C NMR** (100 MHz, Chloroform-d) δ 163.7 (d, $J_{(C-F)}$ = 18.4 Hz), 161.2 (d, $J_{(C-F)}$ = 15.8 Hz), 134.0 (d, $J_{(C-F)}$ = 11.4 Hz), 133.7 (d, $J_{(C-F)}$ = 8.3 Hz), 133.1 (d, $J_{(C-F)}$ = 3.1 Hz), 132.3, 127.9 (d, $J_{(C-F)}$ = 8.0 Hz), 126.8, 126.3 (d, $J_{(C-F)}$ = 2.3 Hz), 123.8, 119.0 (d, $J_{(C-F)}$ = 3.5 Hz), 115.6 (d, $J_{(C-F)}$ = 1.6 Hz), 115.4, 86.4, 85.6, 57.2, 51.7, 46.2, 25.7. **^{19}F NMR** (376 MHz, Chloroform-d) δ -110.94 (s, 1F), -114.42 (s, 1F)**. HRMS** m/z (ESI$^+$): Calculated for $C_{24}H_{20}F_2NS$([M+H]$^+$): 392.1279, found 392.1286.

(E)-2-(3-(4-fluorophenyl)allyl)-1-((4-fluorophenyl)ethynyl)-1,2,3,4-tetrahydroisoquinoline



Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4h** (100 mg, 52% yield) as light yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.47–7.38 (m, 4H), 7.35–7.31 (m, 1H), 7.25–7.20 (m, 2H), 7.19–7.16 (m, 1H), 7.10–6.98 (m, 4H), 6.68 (d, *J* = 15.9 Hz, 1H), 6.37–6.26 (m, 1H), 4.95 (s, 1H), 3.58 (d, *J* = 8.2 Hz, 2H), 3.19–3.04 (m, 2H), 2.98–2.82 (m, 2H). **^{13}C NMR** (100 MHz, Chloroform-d) δ 163.6 (d, $J_{(C-F)}$ = 9.0 Hz), 161.2 (d, $J_{(C-F)}$ = 6.6 Hz), 135.1, 133.8, 133.7, 133.6, 133.2 (d, $J_{(C-F)}$ = 3.3 Hz), 132.2, 129.0, 127.9 (d, $J_{(C-F)}$ = 7.9 Hz), 127.8, 127.1, 126.3 (d, $J_{(C-F)}$ = 2.4 Hz), 126.0, 119.2 (d, $J_{(C-F)}$ = 3.6 Hz), 115.6 (d, $J_{(C-F)}$ = 1.2 Hz), 115.4 (d, $J_{(C-F)}$ = 1.7 Hz), 86.9, 85.9, 57.6, 54.6, 45.6, 28.7. **^{19}F NMR** (376 MHz, Chloroform-d) δ -111.21 (s, 1F), -114.48 (s, 1F). **HRMS** m/z (ESI^+): Calculated for $C_{26}H_{22}F_2N([M+H]^+)$: 386.1715, found 386.1715.

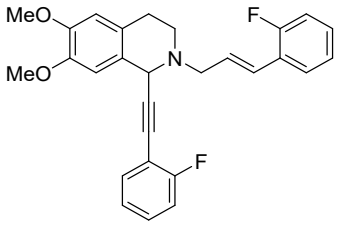
(E)-2-(3-(3-fluorophenyl)allyl)-1-((3-fluorophenyl)ethynyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline



Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4k** (140.1 mg, 63% yield) as yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.34–7.27 (m, 2H), 7.26–7.20 (m, 2H), 7.18–7.12 (m, 2H), 7.07–6.93 (m, 2H), 6.79 (s, 1H), 6.71–6.63 (m, 2H), 6.45–6.37 (m, 1H), 4.87 (s, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.58 (d, *J* = 6.9 Hz, 2H), 3.14–2.87 (m, 3H), 2.78 (d, *J* = 16.3 Hz, 1H). **^{13}C NMR** (100 MHz, Chloroform-d)δ 164.0 (d, $J_{(C-F)}$ = 79.9 Hz), 161.5 (d, $J_{(C-F)}$ = 81.0 Hz), 148.4, 147.5, 139.3 (d, $J_{(C-F)}$ = 7.7 Hz), 132.3 (d, $J_{(C-F)}$ = 2.5 Hz), 130.1 (d,

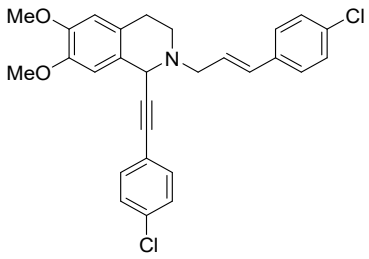
$J_{(C-F)}$ = 8.4 Hz), 129.9 (d, $J_{(C-F)}$ = 8.7 Hz), 128.1, 127.7 (d, $J_{(C-F)}$= 3.0 Hz), 126.7, 125.9, 124.9 (d, $J_{(C-F)}$ = 9.5 Hz), 122.3 (d, $J_{(C-F)}$ = 2.7 Hz), 118.6 (d, $J_{(C-F)}$ = 22.7 Hz), 115.5 (d, $J_{(C-F)}$ = 21.1 Hz), 114.4 (d, $J_{(C-F)}$ = 21.3 Hz), 112.9 (d, $J_{(C-F)}$ = 21.7 Hz), 111.4, 110.4, 88.3, 85.7 (d, $J_{(C-F)}$ = 3.4 Hz), 57.6, 56.0, 55.9, 54.1, 45.9, 28.4. **^{19}F NMR** (376 MHz, Chloroform-d) δ -113.01 (s, 1F), -113.41 (s, 1F). **HRMS** m/z (ESI^+): Calculated for $C_{28}H_{26}F_2NO_2$ ($[M+H]^+$): 446.1926, found 446.1931.

(E)-2-(3-(2-fluorophenyl)allyl)-1-((2-fluorophenyl)ethynyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline



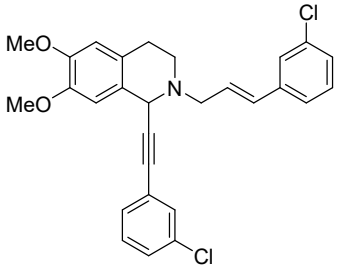
Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4l** (142.4 mg, 64% yield) as yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.57–7.51 (m, 1H), 7.45 (t, *J* = 8.2 Hz, 1H), 7.34–7.19 (m, 2H), 7.16–7.03 (m, 4H), 6.92 (d, *J* = 16.0 Hz, 1H), 6.85 (s, 1H), 6.64 (s, 1H), 6.56–6.44 (m, 1H), 4.93 (s, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.63 (d, *J* = 7.0 Hz, 2H), 3.18–2.87 (m, 3H), 2.79 (d, *J* = 16.5 Hz, 1H). **^{13}C NMR** (100 MHz, Chloroform-d) δ 162.9 (d, $J_{(C-F)}$ = 251.1 Hz), 160.2 (d, $J_{(C-F)}$ = 249.3 Hz), 148.3, 147.5, 133.5, 129.8 (d, $J_{(C-F)}$ = 7.8 Hz), 129.1 (d, $J_{(C-F)}$ = 4.6 Hz), 128.8 (d, $J_{(C-F)}$ = 8.3 Hz), 127.5 (d, $J_{(C-F)}$ = 3.8 Hz), 126.7, 125.9 (d, $J_{(C-F)}$ = 7.6 Hz), 124.8 (d, $J_{(C-F)}$ = 12.1 Hz), 124.1 (d, $J_{(C-F)}$ = 3.6 Hz), 123.8 (d, $J_{(C-F)}$ = 3.7 Hz), 115.9, 115.6 (d, $J_{(C-F)}$ = 10.3 Hz), 115.3, 111.7 (d, $J_{(C-F)}$ = 15.8 Hz), 111.4, 110.5, 92.7 (d, $J_{(C-F)}$ = 3.6 Hz), 80.1, 58.0, 56.0, 55.9, 54.3, 46.0, 28.5. **^{19}F NMR** (376 MHz, Chloroform-d) δ -109.79 (s, 1F), -118.07 (s, 1F). **HRMS** m/z (ESI^+): Calculated for $C_{28}H_{26}F_2NO_2$($[M+H]^+$): 446.1926, found 446.1933.

(E)-2-(3-(4-chlorophenyl)allyl)-1-((4-chlorophenyl)ethynyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline



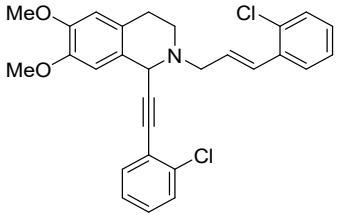
Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4m** (119.5 mg, 50% yield) as yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.40–7.34 (m, 4H), 7.33–7.28 (m, 4H), 6.78 (s, 1H), 6.65 (d, *J* = 12.5 Hz, 2H), 6.41–6.32 (m, 1H), 4.85 (s, 1H), 3.88 (s, 6H), 3.55 (d, *J* = 6.8 Hz, 2H), 3.11–2.87 (m, 3H), 2.82–2.73 (m, 1H). **^{13}C NMR** (100 MHz, Chloroform-d) δ 148.4, 147.5, 135.4, 134.2, 133.2, 133.0, 132.2, 128.8, 128.6, 127.6, 127.3, 126.7, 125.9, 121.6, 111.4, 110.4, 88.3, 85.7, 57.6, 56.0, 55.9, 54.1, 45.9, 28.4. **HRMS** m/z (ESI$^+$): Calculated for $C_{28}H_{26}Cl_2NO_2$([M+H]$^+$): 478.1335, found 478.1336.

(E)-2-(3-(3-chlorophenyl)allyl)-1-((3-chlorophenyl)ethynyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline



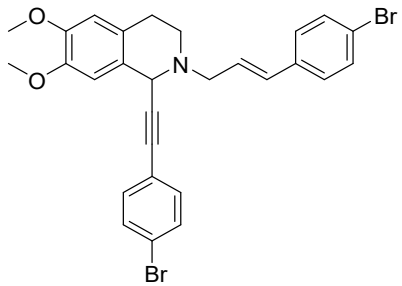
Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4n** (104.9 mg, 44% yield) as light yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.44 (d, *J* = 9.8 Hz, 2H), 7.31 (d, *J* = 10.9 Hz, 3H), 7.26 (d, *J* = 7.8 Hz, 3H), 6.78 (s, 1H), 6.69–6.61 (m, 2H), 6.46–6.36 (m, 1H), 4.85 (s, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.57 (d, *J* = 8.1 Hz, 2H), 3.12–2.88 (m, 3H), 2.78 (d, *J* = 13.0 Hz, 1H). **^{13}C NMR** (100 MHz, Chloroform-d) δ 148.4, 147.5, 138.8, 134.6, 134.1, 132.0, 131.7, 129.9, 129.8, 129.5, 128.4, 128.2, 127.5, 126.7, 126.4, 125.9, 124.8, 124.6, 111.4, 110.4, 88.6, 85.5, 57.6, 56.0, 55.9, 54.1, 45.9, 28.4. **HRMS** m/z (ESI$^+$): Calculated for $C_{28}H_{26}Cl_2NO_2$ ([M+H]$^+$): 478.1335, found 478.1336.

(E)-2-(3-(2-chlorophenyl)allyl)-1-((2-chlorophenyl)ethynyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline



Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4o** (140.4 mg, 59% yield) as yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.63–7.61 (m, 1H), 7.50–7.48 (m, 1H), 7.42–7.37 (m, 2H), 7.27–7.21 (m, 3H), 7.21–7.13 (m, 2H), 6.86 (s, 1H), 6.64 (s, 1H), 6.44–6.37 (m, 1H), 4.96 (s, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.73–3.66 (m, 2H), 3.22–3.12 (m, 1H), 3.07–3.01 (m, 1H), 2.99–2.92 (m, 1H), 2.84–2.75 (m, 1H). **^{13}C NMR** (100MHz, Chloroform-d) δ 148.3, 147.5, 136.0, 135.1, 133.4, 133.0, 129.7, 129.6, 129.5, 129.2, 129.1, 128.5, 126.9, 126.9, 126.7, 126.4, 126.0, 123.1, 111.4, 110.5, 92.8, 83.7, 57.7, 56.0, 55.9, 54.4, 46.0, 28.5. **HRMS** m/z (ESI^{+}): Calculated for $C_{28}H_{26}Cl_2NO_2$ ([M+H]$^{+}$): 478.1335, found 478.1336.

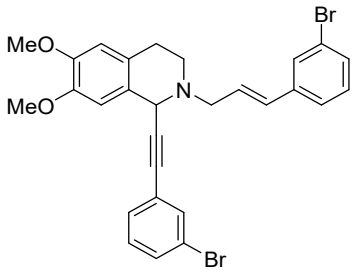
(E)-2-(3-(4-bromophenyl)allyl)-1-((4-bromophenyl)ethynyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline



Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4p** (163.8 mg, 58% yield) as yellow oil. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.48–7.44 (m, 4H), 7.31 (d, *J* = 7.8 Hz, 4H), 6.78 (s, 1H), 6.64 (t, *J* = 7.9 Hz, 2H), 6.43–6.34 (m, 1H), 4.85 (s, 1H), 3.88 (s, 6H), 3.55 (d, *J* = 6.8 Hz, 2H), 3.12–2.88 (m, 3H), 2.77 (d, *J* = 14.1 Hz, 1H). **^{13}C NMR** (100 MHz, Chloroform-d) δ 148.4, 147.5, 135.9, 133.2, 132.2, 131.7, 131.5, 127.9, 127.5, 126.7, 125.9, 122.3,

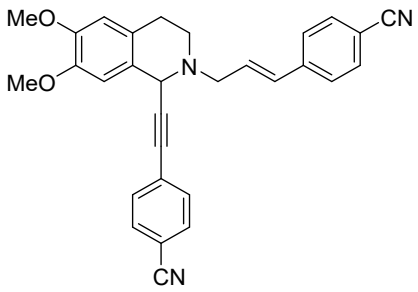
122.1, 121.4, 111.4, 110.4, 88.5, 85.8, 57.6, 56.0, 55.9, 54.2, 45.9, 28.4. **HRMS** m/z (ESI$^+$): Calculated for $C_{28}H_{26}Br_2NO_2$ ([M+H]$^+$): 566.0325, found 566.0325.

(E)-2-(3-(3-bromophenyl)allyl)-1-((3-bromophenyl)ethynyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline



Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4q** (157.9 mg, 56% yield) as yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.59 (d, *J* = 7.3 Hz, 2H), 7.46 (d, *J* = 7.4 Hz, 1H), 7.42–7.33 (m, 3H), 7.26–7.17 (m, 2H), 6.77 (s, 1H), 6.67–6.60 (m, 2H), 6.45–6.35 (m, 1H), 4.85 (s, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.56 (d, *J* = 6.5 Hz, 2H), 3.11–2.88 (m, 3H), 2.77 (d, *J* = 14.8 Hz, 1H). **^{13}C NMR** (100 MHz, Chloroform-d) δ 148.4, 147.5, 139.1, 134.5, 131.9, 131.3, 130.4, 130.3, 130.1, 129.7, 129.4, 128.3, 126.6, 125.9, 125.1, 125.0, 122.8, 122.1, 111.4, 110.4, 88.7, 85.4, 57.6, 56.0, 55.9, 54.1, 45.9, 28.4. **HRMS** m/z (ESI$^+$): Calculated for $C_{28}H_{26}Br_2NO_2$ ([M+H]$^+$): 566.0325, found 566.0325.

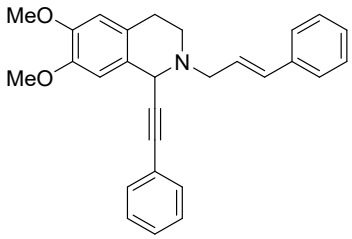
(E)-4-((2-(3-(4-cyanophenyl)allyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl)ethynyl)benzonitrile



Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4r** (84.9mg, 37 w/w% yield) as yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.62 (t, *J* = 6.8 Hz, 4H), 7.56–7.47 (m, 4H), 6.76 (s, 1H), 6.71 (d, *J* = 15.9 Hz, 1H), 6.65 (s, 1H), 6.58–6.46 (m, 1H), 4.87 (s, 1H), 3.88 (s, 6H), 3.59 (d,

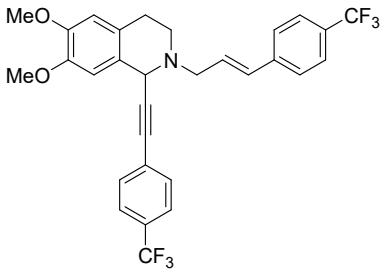
J=6.5 Hz, 2H), 3.12–2.90 (m, 3H), 2.80 (s, 1H). **^{13}C NMR** (100 MHz, Chloroform-d) δ 148.6, 147.6, 141.3, 132.5, 132.3, 132.0, 131.6, 130.8, 127.9, 126.9, 126.0, 125.9, 118.9, 118.4, 111.6, 111.5, 110.9, 110.3, 92.0, 85.5, 57.5, 56.1, 55.9, 54.3, 46.0, 28.3. **HRMS** m/z (ESI$^+$): Calculated for $C_{30}H_{26}N_3O_2$([M+H]$^+$): 460.2020, found 460.2020.

2-cinnamyl-6,7-dimethoxy-1-(phenylethynyl)-1,2,3,4-tetrahydroisoquinoline



Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4s** (77.7 mg, 38% yield) as light yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.50–7.44 (m, 4H), 7.40–7.32 (m, 5H), 7.28 (t, *J* = 7.3 Hz, 1H), 6.82 (s, 1H), 6.73 (d, *J* = 15.9 Hz, 1H), 6.64 (s, 1H), 6.46–6.37 (m, 1H), 4.89 (s, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.60 (d, *J* = 5.6 Hz, 2H), 3.18–2.86 (m, 3H), 2.82–2.74 (m, 1H). **^{13}C NMR** (100 MHz, Chloroform-d) δ 148.3, 147.5, 137.0, 133.4, 131.8, 128.6, 128.3, 128.1, 127.6, 127.2, 126.7, 126.4, 126.0, 123.2, 111.4, 110.5, 87.4, 86.8, 57.8, 56.0, 55.9, 54.2, 45.9, 28.5. **HRMS** m/z (ESI$^+$): Calculated for $C_{28}H_{28}NO_2$([M+H]$^+$): 410.2115, found 410.2112.

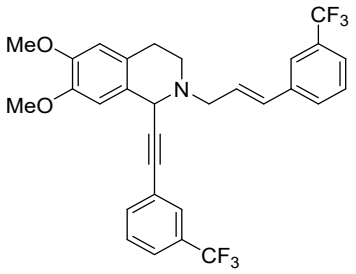
(E)-6,7-dimethoxy-2-(3-(4-(trifluoromethyl)phenyl)allyl)-1-((4-(trifluoromethyl)phenyl)ethynyl)-1,2,3,4-tetrahydroisoquinoline



Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4t** (109.0 mg, 40% yield) as yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.63–7.52 (m, 8H), 6.80 (s, 1H), 6.75 (d, *J* = 15.9 Hz, 1H), 6.66 (s, 1H), 6.51 (d, *J* = 15.9 Hz, 1H), 4.90 (s, 1H), 3.89 (s, 6H), 3.61 (d, *J* = 7.1 Hz, 2H),

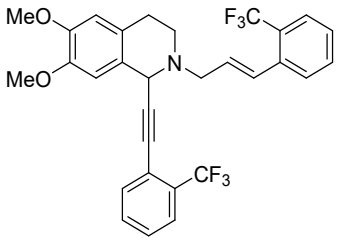
3.15–2.91 (m, 3H), 2.80 (d, *J*=16.2 Hz, 1H). **^{13}C NMR** (100 MHz, Chloroform-d) δ 148.5, 147.6, 140.3, 132.2, 132.0, 130.1 (q, $J_{(C-F)}$ = 3.7 Hz), 129.2 (q, $J_{(C-F)}$ = 19.0 Hz), 128.2, 128.0, 126.8, 126.6, 126.2, 125.8, 125.6 (q, $J_{(C-F)}$ = 4.0 Hz), 125.2 (q, $J_{(C-F)}$ = 3.7 Hz), 111.4, 110.4, 89.7, 85.7, 57.5, 56.0, 55.7, 54.1, 45.9, 28.2. **^{19}F NMR** (376 MHz, Chloroform-d) δ -62.52 (s, 3F), -62.82 (s, 3F). **HRMS** m/z (ESI$^+$): Calculated for $C_{30}H_{26}F_6NO_2$ ([M+H]$^+$): 546.1862, found 546.1862.

(E)-6,7-dimethoxy-2-(3-(3-(trifluoromethyl)phenyl)allyl)-1-((3-(trifluoromethyl)phenyl)ethynyl)-1,2,3,4-tetrahydroisoquinoline



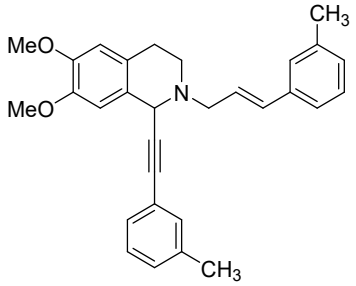
Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4u** (133.5 mg, 49% yield) as yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.71 (s, 1H), 7.68 (s, 1H), 7.66–7.55 (m, 3H), 7.51 (s, 1H), 7.47 (d, *J* = 10.3 Hz, 2H), 6.79 (s, 1H), 6.75 (d, *J* = 15.8 Hz, 1H), 6.66 (s, 1H), 6.55–6.43 (m, 1H), 4.91 (s, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.62 (d, *J* = 6.7 Hz, 2H), 3.20–2.91 (m, 3H), 2.80 (d, *J* = 16.5 Hz, 1H). **^{13}C NMR** (100 MHz, Chloroform-d)δ 148.5, 147.6, 137.6, 134.9, 132.1, 131.0 (q, $J_{(C-F)}$ = 32.4, 14.0 Hz), 129.5, 129.1, 128.8, 128.6 (q, $J_{(C-F)}$ = 3.9 Hz), 126.4, 125.8, 124.2 (q, $J_{(C-F)}$ = 3.9 Hz), 124.0, 123.2 (q, $J_{(C-F)}$ = 4.0 Hz), 122.7, 111.4, 110.3, 88.8, 85.5, 57.5, 56.0, 55.9, 54.1, 45.9, 28.3. **^{19}F NMR** (376 MHz, Chloroform-d) δ -62.82 (s, 3F), -62.95 (s, 3F). **HRMS** m/z (ESI$^+$): Calculated for $C_{30}H_{26}F_6NO_2$ ([M+H]$^+$): 546.1862, found 546.1862.

(E)-6,7-dimethoxy-2-(3-(2-(trifluoromethyl)phenyl)allyl)-1-((2-(trifluoromethyl)phenyl)ethynyl)-1,2,3,4-tetrahydroisoquinoline



Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4v** (144.1 mg, 53% yield) as yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.70 (d, *J* = 7.9 Hz, 1H), 7.66 (d, *J* = 7.8 Hz, 2H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.54–7.46 (m, 2H), 7.41–7.34 (m, 2H), 7.12 (d, *J* = 16.0 Hz, 1H), 6.83 (s, 1H), 6.65 (s, 1H), 6.43–6.31 (m, 1H), 4.93 (s, 1H), 3.89 (s, 6H), 3.65 (d, *J* = 6.6 Hz, 2H), 3.15–3.08 (m, 1H), 3.06–2.97 (m, 1H), 2.93 (d, *J* = 10.8 Hz, 1H), 2.79 (d, *J* = 16.5 Hz, 1H). **^{13}C NMR** (100 MHz, Chloroform-d) δ 148.3, 147.5, 136.3 (q, $J_{(C-F)}$= 1.9 Hz), 134.1, 131.9, 131.2 (q, $J_{(C-F)}$ = 15.5 Hz), 129.3, 129.2, 127.8, 127.5, 127.2, 126.6, 126.0, 125.7 (q, $J_{(C-F)}$ = 5.3 Hz), 125.0, 123.0, 122.3, 121.4 (q, $J_{(C-F)}$ = 2.4 Hz), 111.4, 110.4, 93.6, 82.9, 57.5, 55.9, 55.9, 54.5, 45.9, 28.5. **^{19}F NMR** (376 MHz, Chloroform-d) δ -59.52 (s, 3F), -62.08 (s, 3F). **HRMS** m/z (ESI^+): Calculated for $C_{30}H_{26}F_6NO_2$ ($[M+H]^+$): 546.1862, found 546.1862.

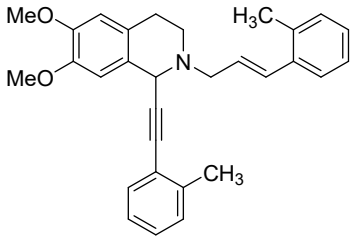
(E)-6,7-dimethoxy-2-(3-(m-tolyl)allyl)-1-(m-tolylethynyl)-1,2,3,4-tetrahydroisoquinoline



Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4w** (72.1 mg, 33% yield) as light yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.30 (s, 3H), 7.28–7.24 (m, 2H), 7.22 (d, *J* = 7.5 Hz, 1H), 7.15 (d, *J* = 7.6 Hz, 1H), 7.10 (d, *J* = 5.8 Hz, 1H), 6.81 (s, 1H), 6.74–6.63 (m, 2H), 6.45–6.36 (m, 1H), 4.89 (s, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.59 (d, *J* = 6.1 Hz, 2H), 3.17–2.88 (m, 3H), 2.79 (d, *J* = 11.2 Hz, 1H), 2.37 (d, *J* = 10.5 Hz, 6H). **^{13}C NMR** (100 MHz,

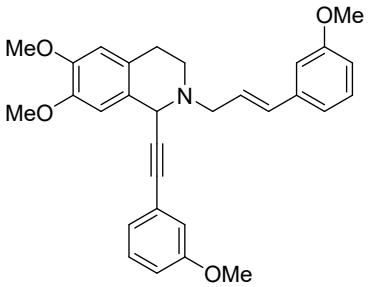
Chloroform-d) δ 148.2, 147.4, 138.2, 137.9, 137.0, 133.5, 132.4, 129.0, 128.9, 128.5, 128.4, 128.2, 127.3, 127.2, 126.5, 125.9, 123.6, 123.1, 111.4, 110.5, 87.0, 86.9, 57.8, 56.0, 55.9, 54.1, 45.9, 28.5, 21.4, 21.2. **HRMS** m/z (ESI^+): Calculated for $C_{30}H_{32}NO_2$ ($[M+H]^+$): 438.2428, found 438.2425.

(E)-6,7-dimethoxy-2-(3-(o-tolyl)allyl)-1-(o-tolylethynyl)-1,2,3,4-tetrahydroisoquinoline



Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4x** (104.6 mg, 48% yield) as yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.57–7.54 (m, 1H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.23–7.12 (m, 6H), 6.95 (d, *J* = 15.7 Hz, 1H), 6.83 (s, 1H), 6.65 (s, 1H), 6.35–6.27 (m, 1H), 4.95 (s, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.64 (d, *J* = 6.8 Hz, 2H), 3.16–3.09 (m, 1H), 3.08–2.99 (m, 1H), 2.95–2.92 (m, 1H), 2.80 (d, *J* = 16.6 Hz, 1H), 2.46 (s, 3H), 2.40 (s, 3H). **^{13}C NMR** (100 MHz, Chloroform-d) δ 148.2, 147.4, 140.0, 136.1, 135.3, 132.0, 131.2, 130.3, 129.4, 128.1, 127.9, 127.5, 126.2, 125.9, 125.7, 125.5, 123.1, 111.4, 110.4, 91.4, 85.8, 58.1, 56.0, 55.9, 54.3, 45.9, 28.6, 21.1, 19.9. **HRMS** m/z (ESI^+): Calculated for $C_{30}H_{32}NO_2$ ($[M+H]^+$): 438.2428, found 438.2425.

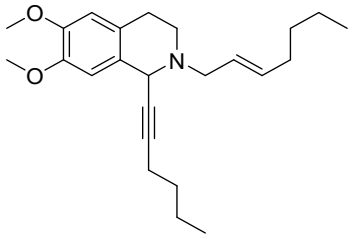
(E)-6,7-dimethoxy-2-(3-(3-methoxyphenyl)allyl)-1-((3-methoxyphenyl)ethynyl)-1,2,3,4-tetrahydroisoquinoline



Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4y** (131.3 mg, 56% yield) as yellow oil. **^{1}H NMR** (400 MHz,

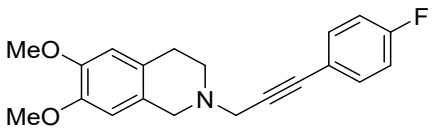
Chloroform-d) δ 7.32–7.25 (m, 1H), 7.24 (s, 1H), 7.12–7.03 (m, 2H), 7.01 (s, 2H), 6.93–6.86 (m, 1H), 6.83 (d, *J* = 13.9 Hz, 2H), 6.70 (d, *J* = 15.8 Hz, 1H), 6.65 (s, 1H), 6.47–6.35 (m, 1H), 4.89 (s, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.84 (s, 3H), 3.82 (s, 3H), 3.59 (d, *J* = 7.0 Hz, 2H), 3.17–2.88 (m, 3H), 2.79 (d, *J* = 16.5 Hz, 1H). **^{13}C NMR** (100MHz, Chloroform-d) δ 159.9, 159.3, 148.3, 147.5, 138.5, 133.3, 129.6, 129.3, 127.1, 127.0, 126.0, 124.4, 124.2, 119.2, 116.8, 114.6, 113.4, 111.6, 111.4, 110.5, 87.2, 86.6, 57.7, 56.0, 55.9, 55.3, 55.2, 54.2, 45.9, 28.5. **HRMS** m/z (ESI$^+$): Calculated for $C_{30}H_{32}NO_4$ ([M+H]$^+$): 470.2326, found 470.2332.

(E)-2-(hept-2-en-1-yl)-1-(hex-1-yn-1-yl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline



Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **4z** (72.1 mg, 39% yield) as yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 6.75 (s, 1H), 6.57 (s, 1H), 5.79–5.67 (m, 1H), 5.61–5.50 (m, 1H), 4.54 (s, 1H), 3.87 (s, 3H), 3.85 (s, 3H), 3.35–3.18 (m, 2H), 2.97–2.84 (m, 2H), 2.78–2.66 (m, 2H), 2.27–2.19 (m, 2H), 2.09 (q, *J* = 6.7 Hz, 2H), 1.54–1.30 (m, 8H), 0.97–0.87 (m, 6H). **^{13}C NMR** (100 MHz, Chloroform-d) δ 148.06, 147.35, 134.83, 128.26, 126.40, 125.89, 111.43, 110.66, 86.64, 77.92, 57.32, 55.95, 55.84, 53.75, 45.42, 32.04, 31.43, 31.04, 28.39, 22.18, 21.92, 18.49, 13.86, 13.51. **HRMS** m/z (ESI+): Calculated for $C_{24}H_{36}NO_2$ ([M+H]$^+$): 370.2741, found 370.2744.

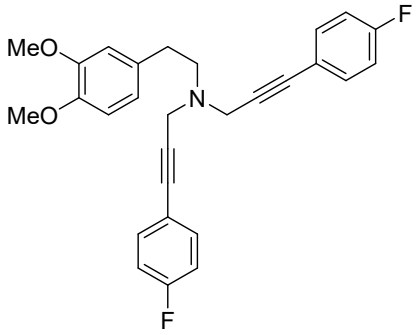
2-(3-(4-fluorophenyl)prop-2-yn-1-yl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline



Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **5a** (1.13 g, 70% yield) as yellow oil. **^{1}H NMR** (400 MHz,

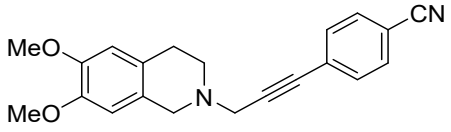
Chloroform-d) δ 7.44–7.40 (m, 2H), 6.99 (t, *J* = 8.7 Hz, 2H), 6.61 (s, 1H), 6.56 (s, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 3.76 (s, 2H), 3.70 (s, 2H), 2.89 (s, 4H). **^{13}C NMR (**100 MHz, Chloroform-d) δ 162.4 (d, *J* = 249.1 Hz), 147.7, 147.4, 133. 6 (d, *J* = 8.3 Hz), 126.4, 125.8, 119.2 (d, *J* = 3.4 Hz), 115.6, 115.4, 111.5, 109.6, 84.3 (d, *J* = 8.7 Hz), 55.9, 55.9, 54.2, 50.0, 47.5, 28.8. **^{19}F NMR** (376 MHz, Chloroform-d) δ -111.25 (s, 1F). **HRMS** m/z (ESI+): Calculated for $C_{20}H_{21}FNO_2$ ([M+H]$^+$): 326.1551, found 326.1542.

N-(3,4-dimethoxyphenethyl)-3-(4-fluorophenyl)-N-(3-(4-fluorophenyl)prop-2-yn-1-yl)prop-2-yn-1-amine



Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **6** (1.78g, 80% yield) as yellow oil. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.48–7.38 (m, 4H), 7.01 (t, *J* = 8.7 Hz, 4H), 6.81 (d, *J* = 5.6 Hz, 3H), 3.87 (s, 3H), 3.85 (s, 3H), 3.78 (s, 4H), 2.98–2.94 (m, 2H), 2.88–2.84 (m, 2H). **^{13}C NMR** (100 MHz, Chloroform-d) δ 162.4 (d, *J* = 249.3 Hz), 149.0, 147.6, 133.6 (d, *J* = 8.3 Hz), 132.6, 120.6, 119.2 (d, *J* = 3.5 Hz), 115.6, 115.4, 112.2, 111.5, 84.3 (d, *J* = 1.5 Hz), 84.2, 56.0, 55.8, 55.1, 43.4, 33.9. **^{19}F NMR** (376 MHz, Chloroform-d) δ -111.08 (s, 2F). **HRMS** m/z (ESI+): Calculated for $C_{28}H_{26}F_2NO_2$ ([M+H]$^+$): 446.1926, found 446.1925.

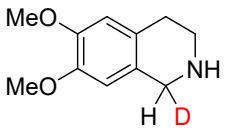
4-(3-(6,7-dimethoxy-3,4-dihydroisoquinolin-2(1H)-yl)prop-1-yn-1-yl)benzonitrile



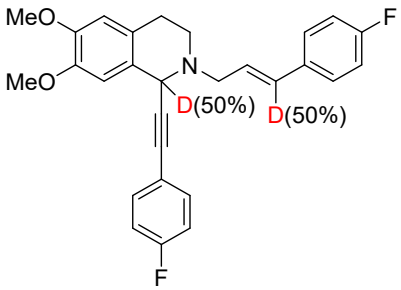
Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum

ether) afforded **5p** (83 mg, 50% yield) as yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.59 (d, *J* = 8.4 Hz, 2H), 7.52 (d, *J* = 8.4 Hz, 2H), 6.62 (s, 1H), 6.56 (s, 1H), 3.85 (d, *J*= 4.5 Hz, 6H), 3.76 (d, *J* = 9.0 Hz, 4H), 2.90 (s, 4H). **^{13}C NMR** (100MHz, Chloroform-d) δ 147.7, 147.4, 132.2, 132.0, 128.0, 126.2, 125.6, 118.4, 111.6, 109.6, 89.5, 84.0, 56.0, 55.9, 54.2, 50.1, 47.5, 28.8. **HRMS** m/z (ESI$^+$): Calculated for $C_{21}H_{21}N_2O_2$ ([M+H]$^+$): 333.1598, found 333.1588.

6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline



50 mL dry THF were added to 8 mmol $LiAlD_4$ (0.336 mg) followed by addition of 6,7-dimethoxy-3,4-dihydroisoquinoline (4 mmol, 0.764 mL) under nitrogen atmosphere. The mixture was refluxed for 40 h, cooled to 0 °C, 30% NaOH (100 mL) was added slowly to the reaction. The aq. phase was separated and extracted with THF (200 mL). The combined org. phase was dried (Na_2SO_4) and concentrated under reduced pressure to (yield 60-70% in two steps) as yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 6.57 (s, 1H), 6.49 (s, 1H), 3.90 (s, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.10 (t, *J* = 6.0 Hz, 2H), 2.70 (t, *J* = 5.9 Hz, 2H), 2.67 (s, 1H). **^{13}C NMR** (100 MHz, Chloroform-d) δ 147.6, 147.4, 126.5, 126.3, 112.1, 109.3, 55.9, 43.5, 29.6, 28.23

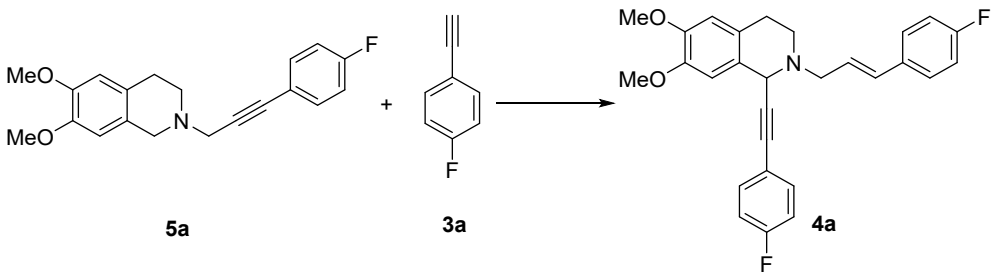


Purified by silica gel column chromatography (25−50% ethyl acetate in petroleum ether) afforded **9** (64.2 mg, 58% yield) as yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.47–7.36 (m, 4H), 7.03 (q, *J* = 8.6 Hz, 4H), 6.79 (d, *J* = 2.1 Hz, 1H), 6.66 (d, *J* = 19.0 Hz, 1.5H), 6.37 – 6.25 (m, 1H), 4.85 (s, 1H), 3.88 (s, 6H), 3.56 (d, *J* = 7.0 Hz, 2H), 3.13 – 2.96 (m, 2H), 2.95 – 2.87 (m, 1H), 2.77 (d, *J* = 15.1 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.6 (d, *J* = 9.1 Hz), 161.1 (d, *J* = 6.9 Hz), 148.4, 147.5, 133.6, 133.6, 132.2, 127.9 (d, *J* = 2.2 Hz), 127.8 (d, *J* = 2.2 Hz), 126.3 (d, *J* = 2.4 Hz), 126.2, 125.9, 119.2 (d, *J* = 3.6 Hz), 115.6, 115.4, 111.5, 110.6 (d, *J* = 2.7 Hz), 87.0 (d, *J* = 5.1 Hz), 85.7 (d, *J* = 2.9 Hz), 57.6, 56.0, 55.9, 54.1, 45.8, 28.4. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -111.18(s,1F), -114.45(s,1F).

Control Experiments

Scheme 2a



5a **3a** **4a**

Standard Conditions:

In the air atmosphere, a 10 mL reaction tube was charged with the propargylamine **5a** (81 mg, 0.25 mmol), 1-ethynyl-4-fluorobenzene **3a** (30 mg, 0.25 mmol), CuI (30 mol%, 14 mg), TFA (114 mg, 4.0 equiv) and toluene (2.0 mL), then sealed. Subsequently, the reaction mixture was stirred at 80 °C for 24 h. The desired product **4a** not detected.

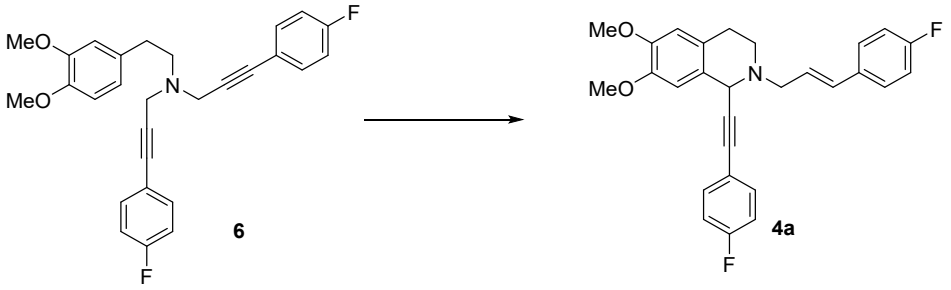
Conditions A:

In the air atmosphere, a 10 mL reaction tube was charged with the propargylamine **5a** (81 mg, 0.25 mmol), 1-ethynyl-4-fluorobenzene **3a** (30 mg, 0.25 mmol), TFA (114 mg, 4.0 equiv) and toluene (2.0 mL), then sealed. Subsequently, the reaction mixture was stirred at 80 °C for 24 h. The desired product **4a** not detected.

Conditions B:

In the air atmosphere, a 10 mL reaction tube was charged with the propargylamine **5a** (81 mg, 0.25 mmol), 1-ethynyl-4-fluorobenzene **3a** (30 mg, 0.25 mmol), CuI (30 mol%, 14 mg) and toluene (2.0 mL), then sealed. Subsequently, the reaction mixture was stirred at 80 °C for 24 h. The residue was purified by flash chromatography (25−50% ethyl acetate in petroleum ether) to afford the desired products **4a** in 25% yield.

Scheme 2b



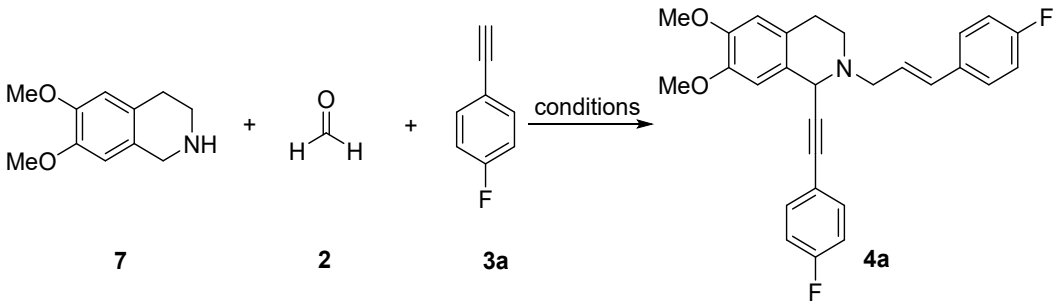
Standard Conditions:

In the air atmosphere, a 10 mL reaction tube was charged with the propargylamine **6** (111.25 mg, 0.25 mmol), CuI (30 mol%, 14 mg), TFA (114 mg, 4.0 equiv), and toluene (2.0 mL), then sealed. Subsequently, the reaction mixture was stirred at 80 °C for 24 h. The desired product **4a** not detected.

Conditions A:

In the air atmosphere, a 10 mL reaction tube was charged with the propargylamine **6** (111.25 mg, 0.25 mmol), CuI (30 mol%, 14 mg) and toluene (2.0 mL), then sealed. Subsequently, the reaction mixture was stirred at 80 °C for 24 h. The desired product **4a** not detected.

Scheme 2c



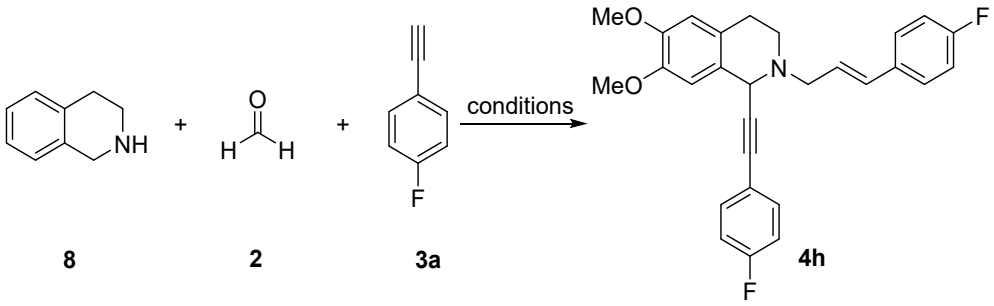
Standard Conditions:

In the air atmosphere, a 10 mL reaction tube was charged with the amine **7** (48 mg, 0.25 mmol), 37 w/w% formaldehyde solution **2** (49 mg, 0.6 mmol), 1-ethynyl-4-fluorobenzene **3a** (72 mg, 0.6 mmol), CuI (30 mol%, 14 mg), TFA (114 mg, 4.0 equiv) and toluene (2.0 mL), then sealed. Subsequently, the reaction mixture was stirred at 80 °C for 24 h. The residue was purified by flash chromatography (25−50% ethyl acetate in petroleum ether) to afford the desired products **4a** in 71%.

Conditions A:

In the air atmosphere, a 10 mL reaction tube was charged with the amine **7** (48 mg, 0.25 mmol), 37 w/w% formaldehyde solution **2** (49 mg, 0.6 mmol), 1-ethynyl-4-fluorobenzene **3a** (120 mg, 0.6 mmol), CuI (30 mol%,1 4 mg) and toluene (2.0 mL), then sealed. Subsequently, the reaction mixture was stirred at 80 °C for 24 h. The residue was purified by flash chromatography (25−50% ethyl acetate in petroleum ether) to afford the desired products **4a** in 20%.

Scheme 2d

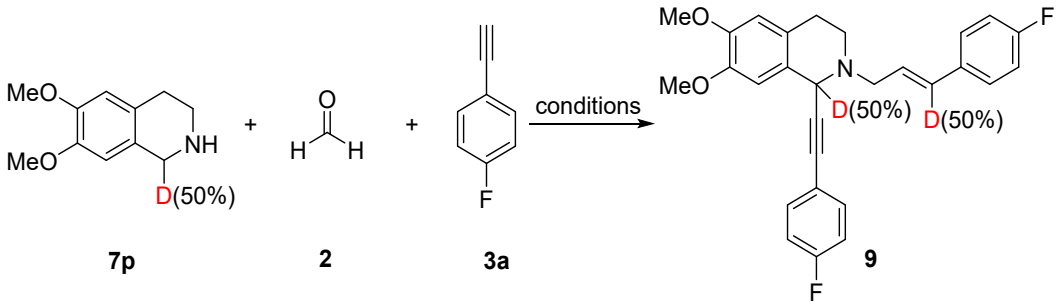


8 **2** **3a** **4h**

Standard Conditions:

In the air atmosphere, a 10 mL reaction tube was charged with the amine **8** (33 mg, 0.25 mmol), 37 w/w% formaldehyde solution **2** (49 mg, 0.6 mmol), 1-ethynyl-4-fluorobenzene **3a** (72 mg, 0.6 mmol), CuI (30 mol%, 14 mg), TFA (114 mg, 4.0 equiv) and toluene (2.0 mL), then sealed. Subsequently, the reaction mixture was stirred at 80 °C for 24 h. The residue was purified by flash chromatography (25−50% ethyl acetate in petroleum ether) to afford the desired products **4h** in 52%.

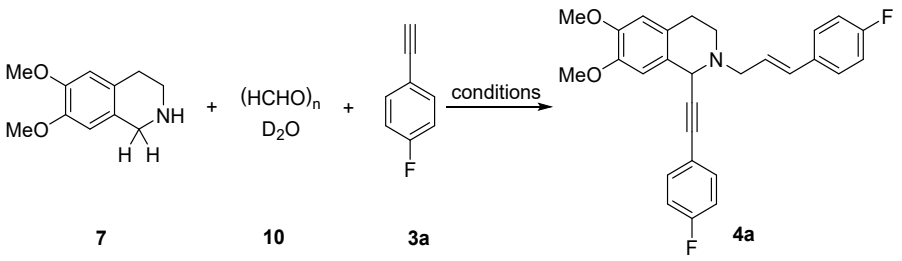
Scheme 2e



7p **2** **3a** **9**

In the air atmosphere, a 10 mL reaction tube was charged with the amine **7p** (48 mg, 0.25 mmol), 37 w/w% formaldehyde solution **2** (49 mg, 0.6 mmol), 1-ethynyl-4-fluorobenzene **3a** (72 mg, 0.6 mmol), CuI (30 mol%, 14 mg), TFA (114 mg, 4.0 equiv) and toluene (2.0 mL), then sealed. Subsequently, the reaction mixture was stirred at 80 °C for 24 h. The residue was purified by flash chromatography (25−50% ethyl acetate in petroleum ether) to afford the desired products **9** in 58%.

Scheme 2f



In the air atmosphere, a 10 mL reaction tube was charged with the amine **7** (48 mg, 0.25 mmol), paraformaldehyde solution in D_2O **10** (0.5 mL, 0.6 mmol), 1-ethynyl-4-fluorobenzene **3a** (72 mg, 0.6 mmol), CuI (30 mol%, 14 mg), TFA (114 mg, 4.0 equiv1) and toluene (2.0 mL), then sealed. Subsequently, the reaction mixture was stirred at 80 °C for 24 h. The residue was purified by flash chromatography (25−50% ethyl acetate in petroleum ether) to afford the desired products **4a** in 50%.

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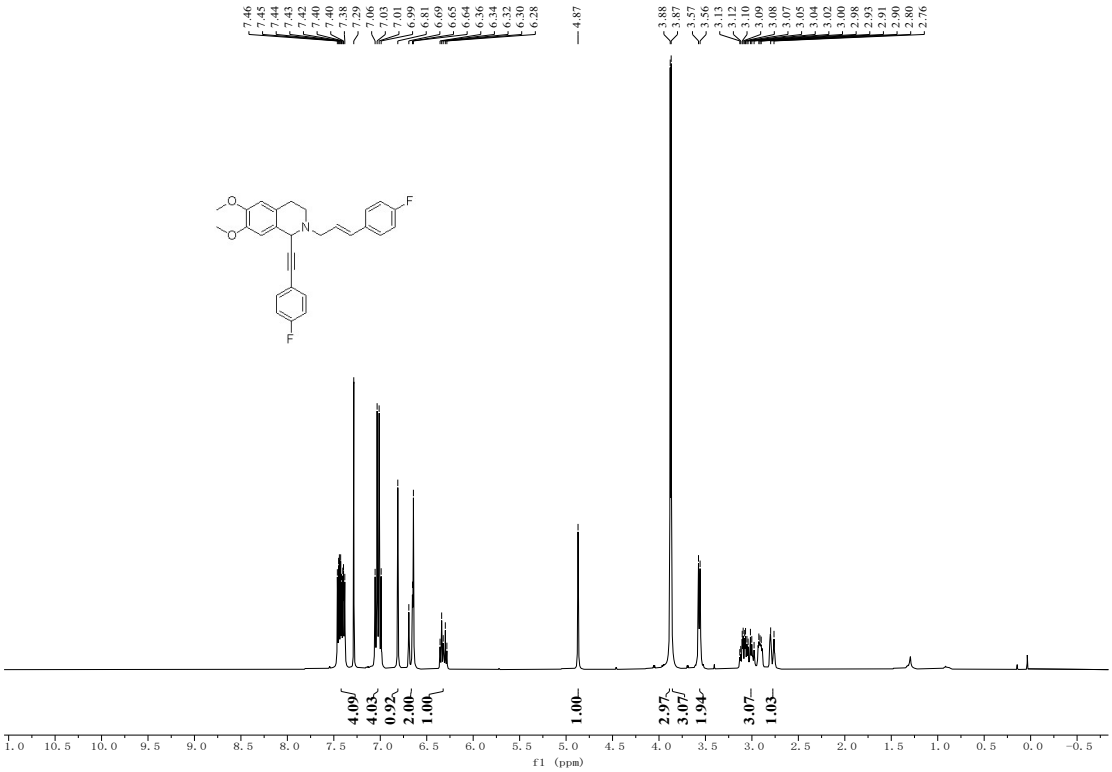
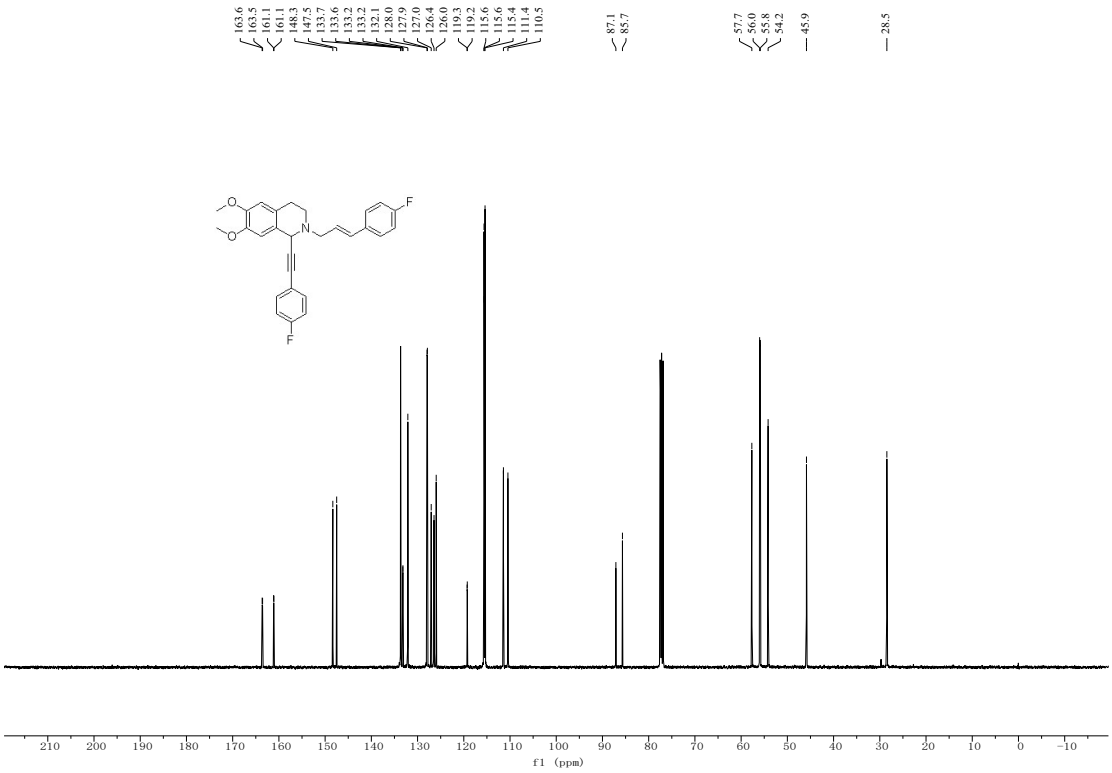
(1) Zhang, Y. Z.; Huang, L. L.; Li, X. Y.; Wang, L.; Feng, H. D. Chemo- and Diastereoselective Synthesis of *N*-Propargyl Oxazolidines through a Copper-Catalyzed Domino A^3 Reaction. *J. Org. Chem*., **2019**, *84*, 5046−5055.

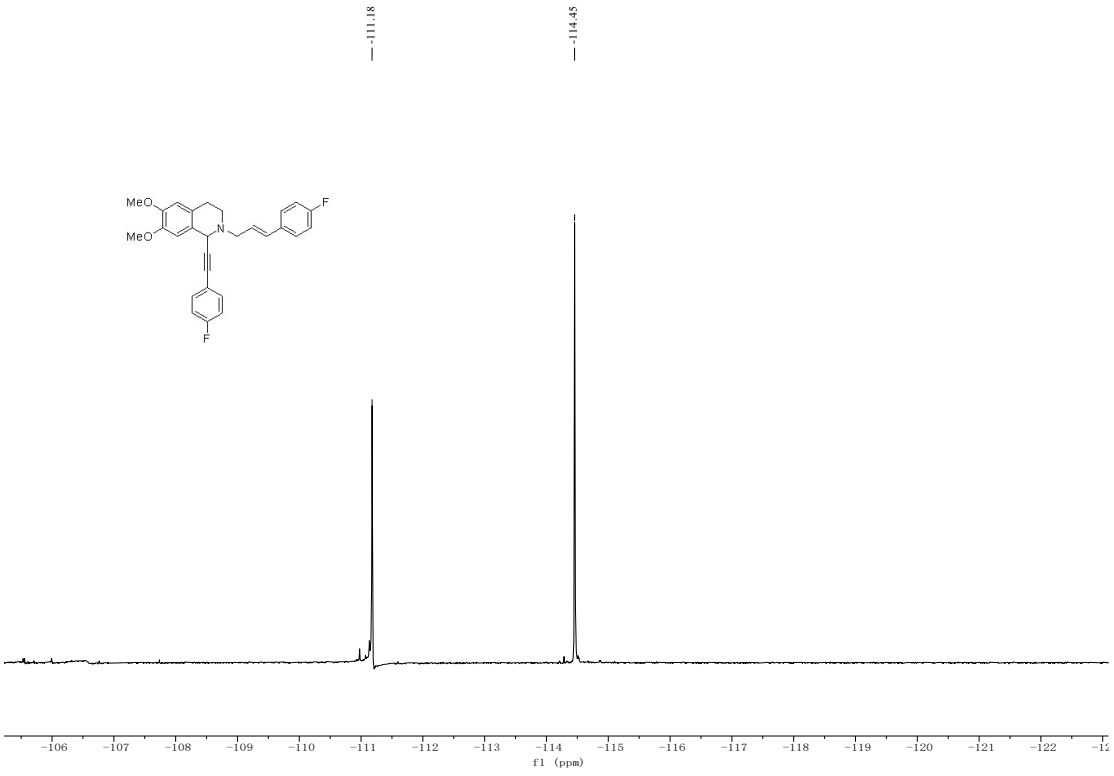
(2) Daniel, R.; Waldemar, S.; Anne, G.; Yu, Z.; Shoubhik, D. CO_2-Catalyzed Efficient Dehydrogenation of Amines with Detailed Mechanistic and Kinetic Studies. *ACS Catal.*, **2018**, *8*, 11679–11687.

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

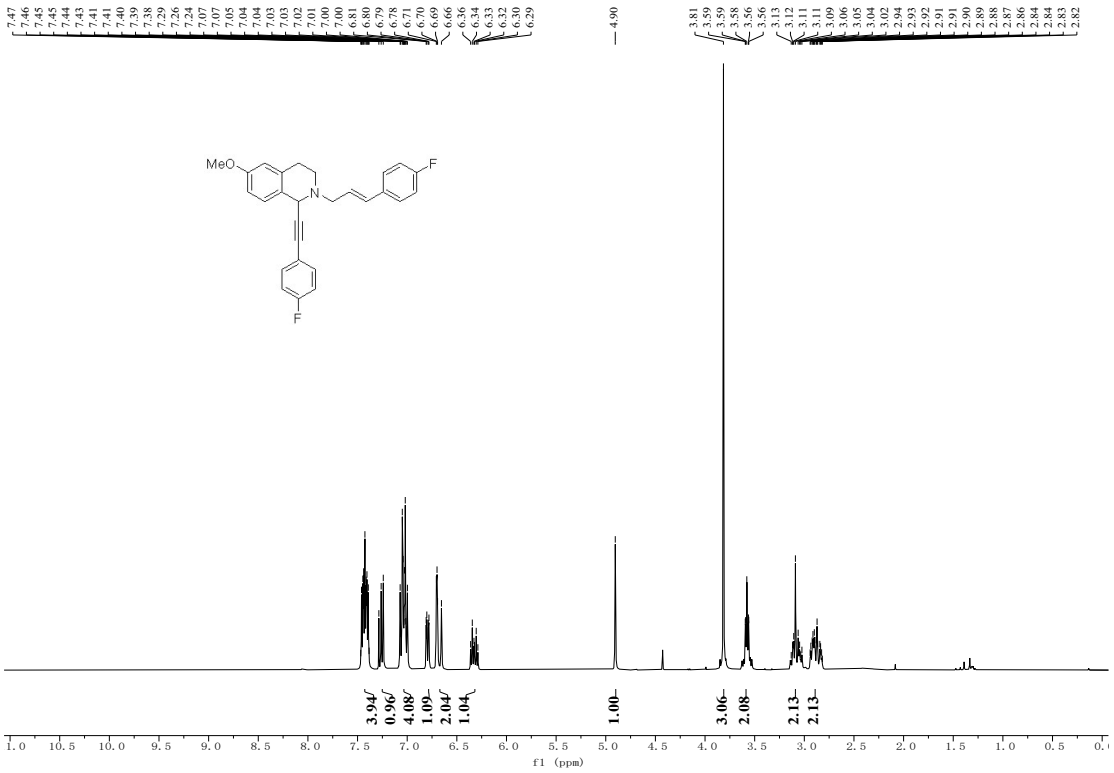
(E)-2-(3-(4-fluorophenyl)allyl)-1-((4-fluorophenyl)ethynyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline **(4a)**

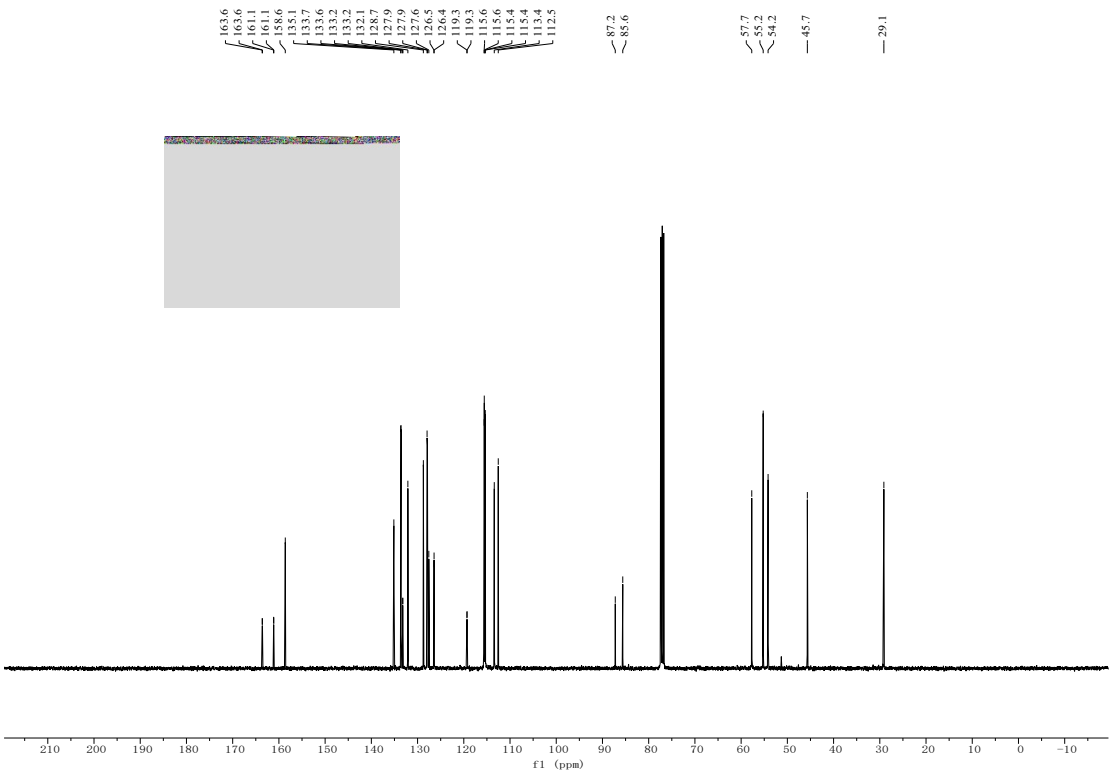




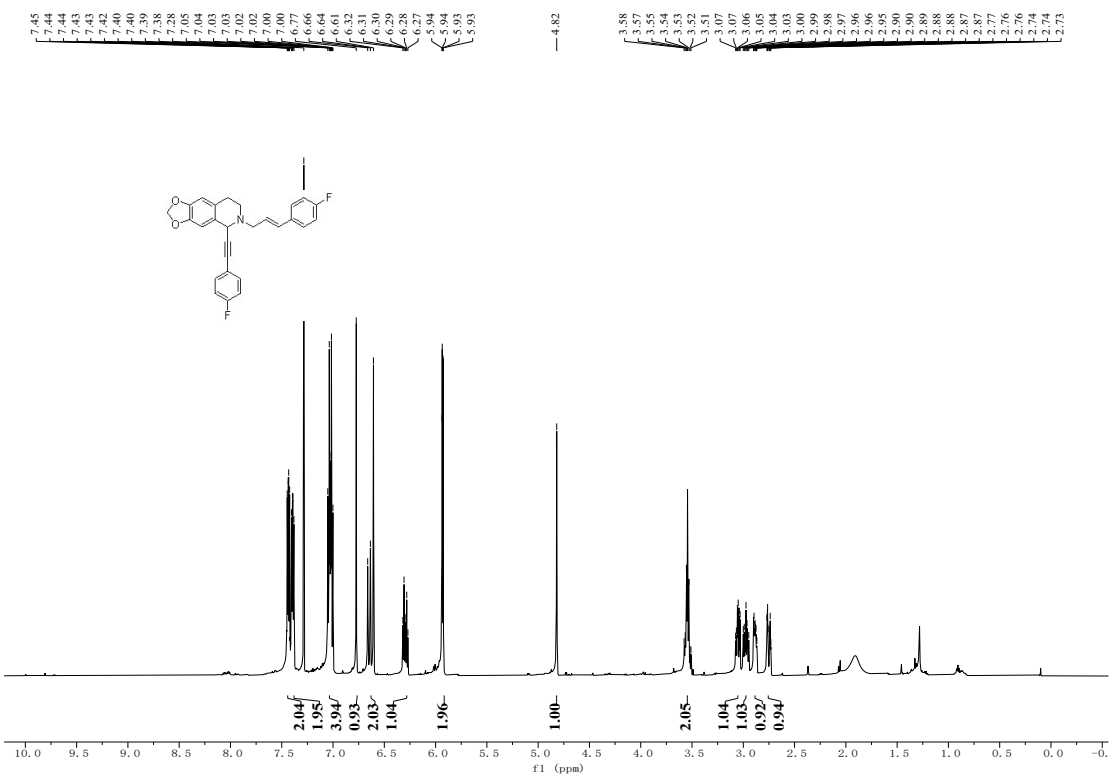


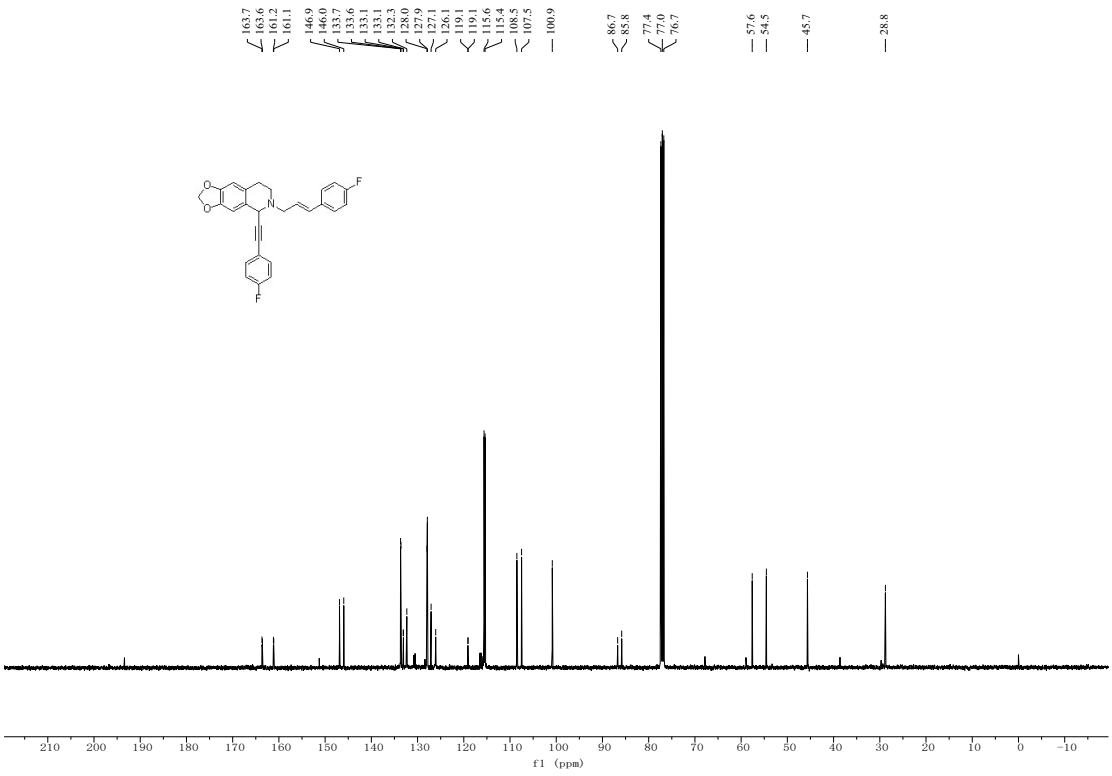
(E)-2-(3-(4-fluorophenyl)allyl)-1-((4-fluorophenyl)ethynyl)-6-methoxy-1,2,3,4-tetrahydroisoquinoline **(4b)**

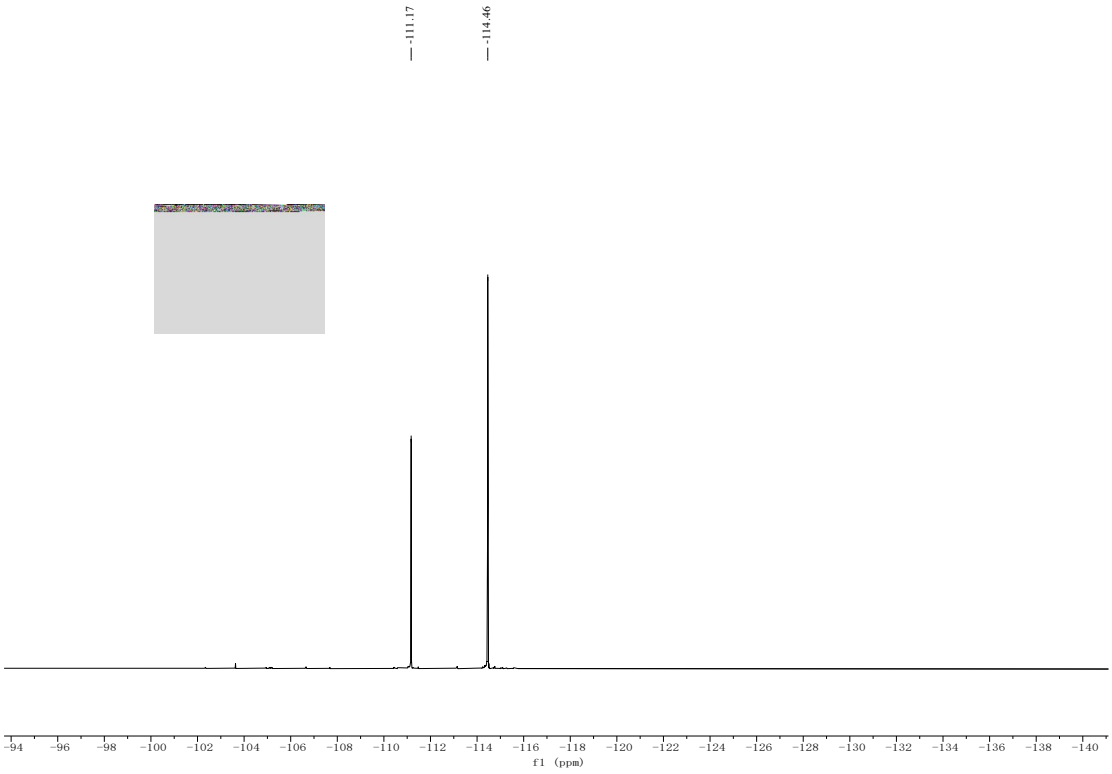




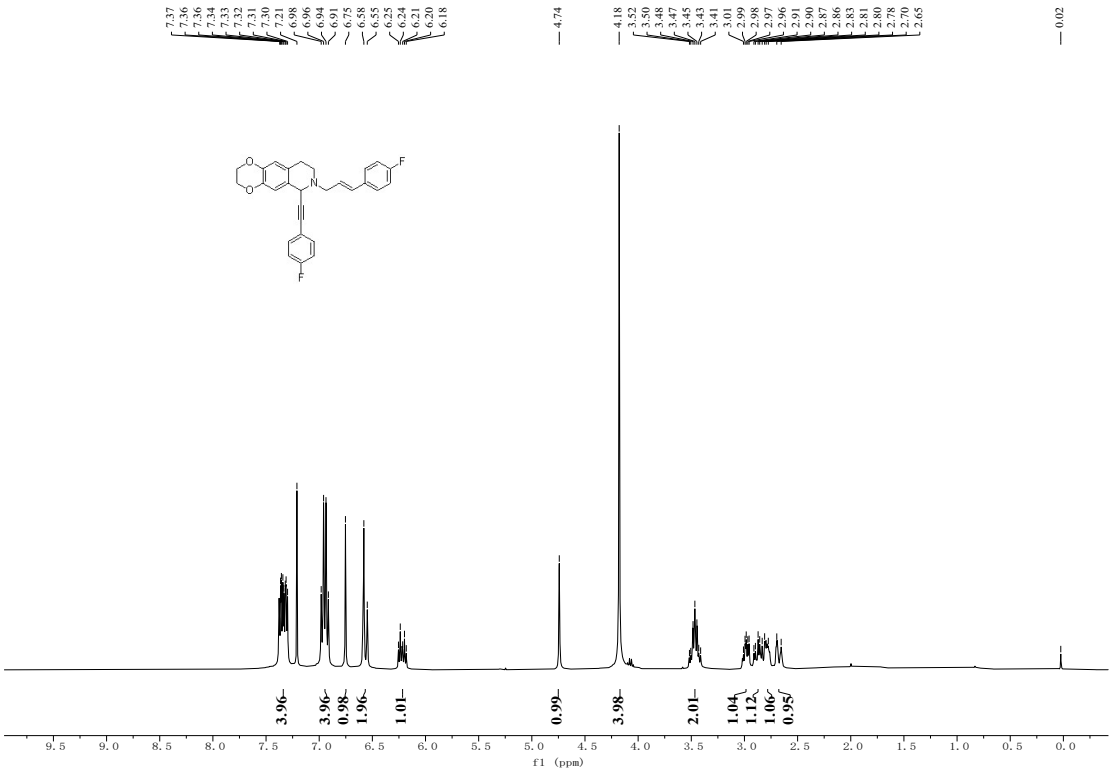
***(E)-6-(3-(4-fluorophenyl)allyl)-5-((4-fluorophenyl)ethynyl)-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-g]isoquinoline* (4c)**

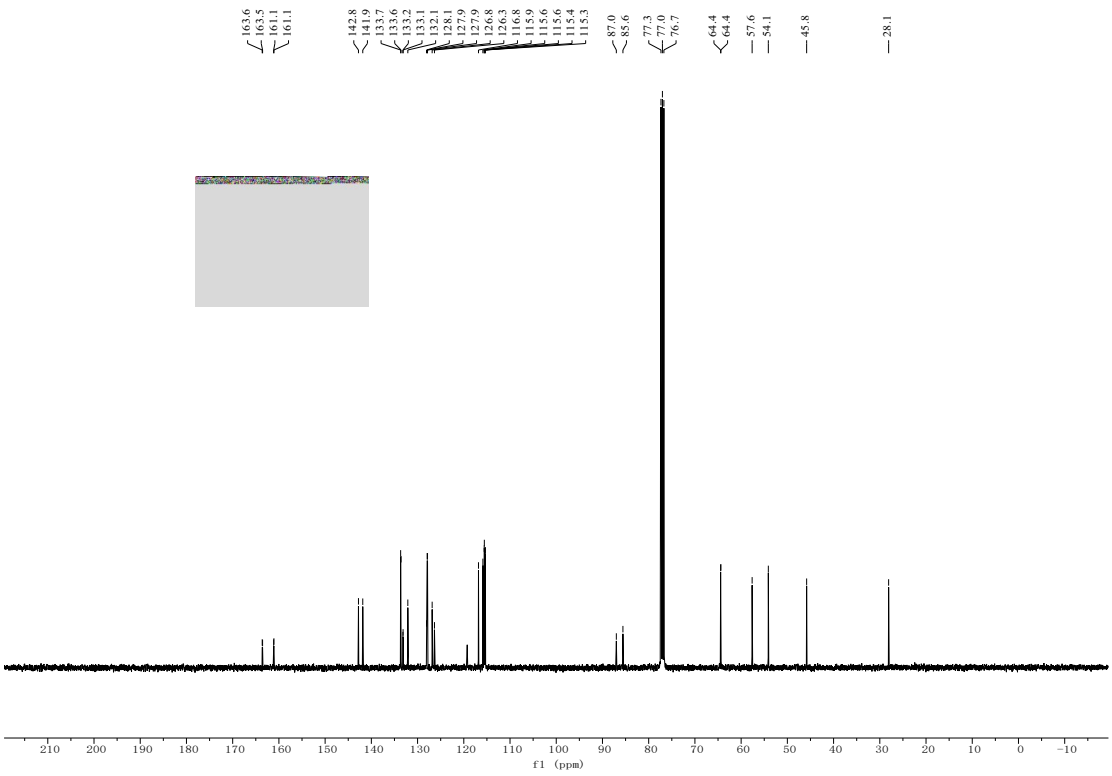

7.45 7.44 7.44 7.43 7.43 7.42 7.40 7.40 7.39 7.38 7.28 7.05 7.04 7.03 7.02 7.02 7.00 7.00 6.77 6.66 6.64 6.61 6.32 6.31 6.30 6.29 6.28 6.27 5.94 5.94 5.93 5.93
4.82
3.58 3.57 3.55 3.54 3.53 3.52 3.51 3.07 3.07 3.06 3.05 3.04 3.03 3.00 2.99 2.98 2.97 2.96 2.96 2.95 2.90 2.90 2.89 2.88 2.88 2.87 2.87 2.77 2.76 2.76 2.74 2.74 2.73
O
O
N
F
F
2.04 1.95 3.94 0.93 2.03 1.04 1.96 1.00 2.05 1.04 1.03 0.92 0.94
f1 (ppm)

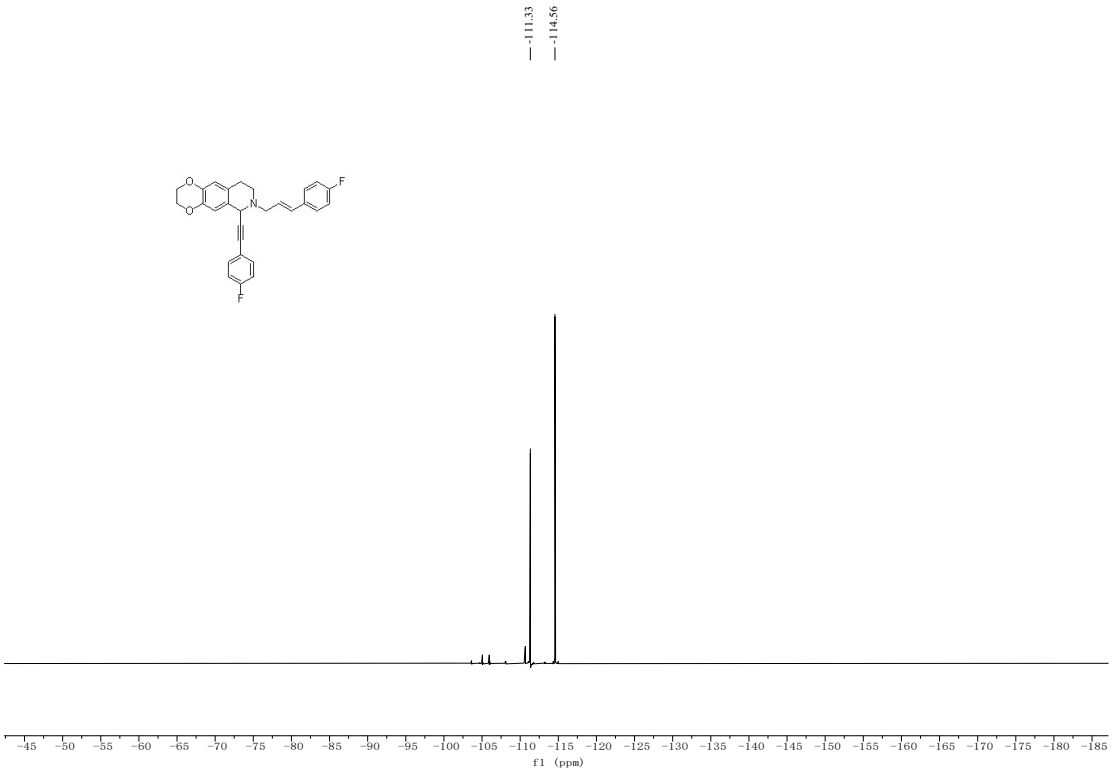

163.7 163.6 161.2 161.1 146.9 146.0 133.7 133.6 133.1 133.1 132.3 128.0 127.9 127.1 126.1 119.1 119.1 115.6 115.4 108.5 107.5 100.9 86.7 85.8 77.4 77.0 76.7 57.6 54.5 45.7 28.8
O
O
N
F
F
f1 (ppm)



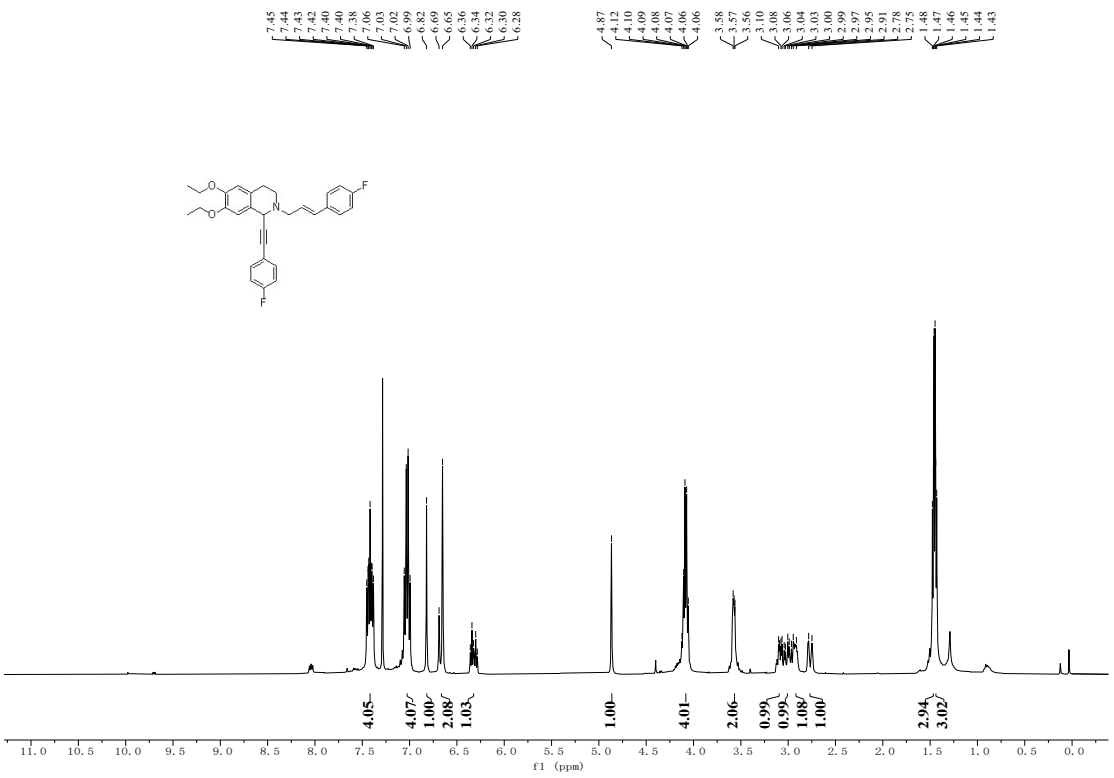
(E)-7-(3-(4-fluorophenyl)allyl)-6-((4-fluorophenyl)ethynyl)-2,3,6,7,8,9-hexahydro-[1,4]dioxino[2,3-g]isoquinoline **(4d)**

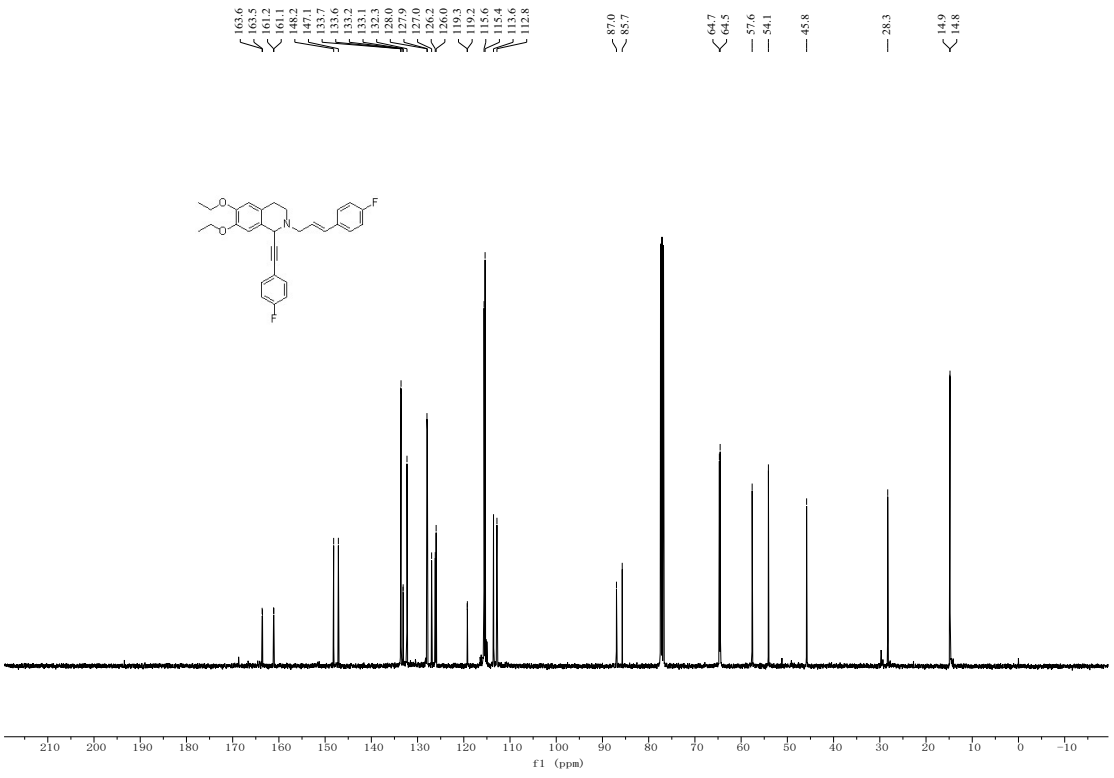


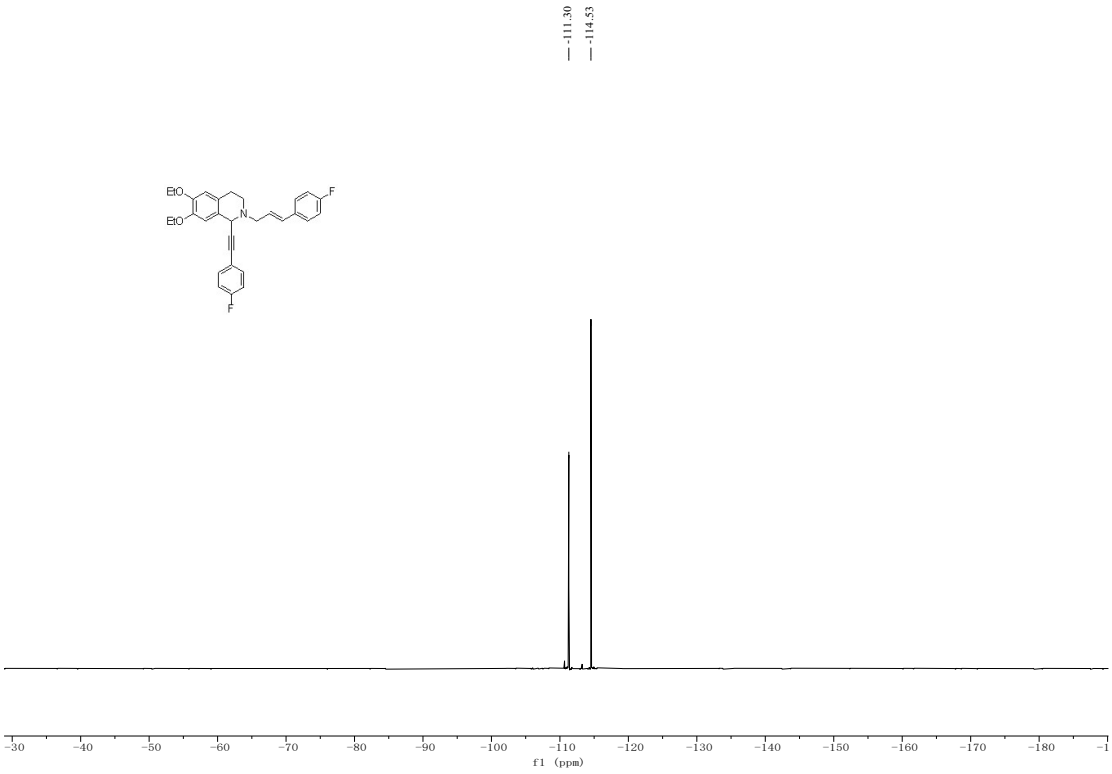




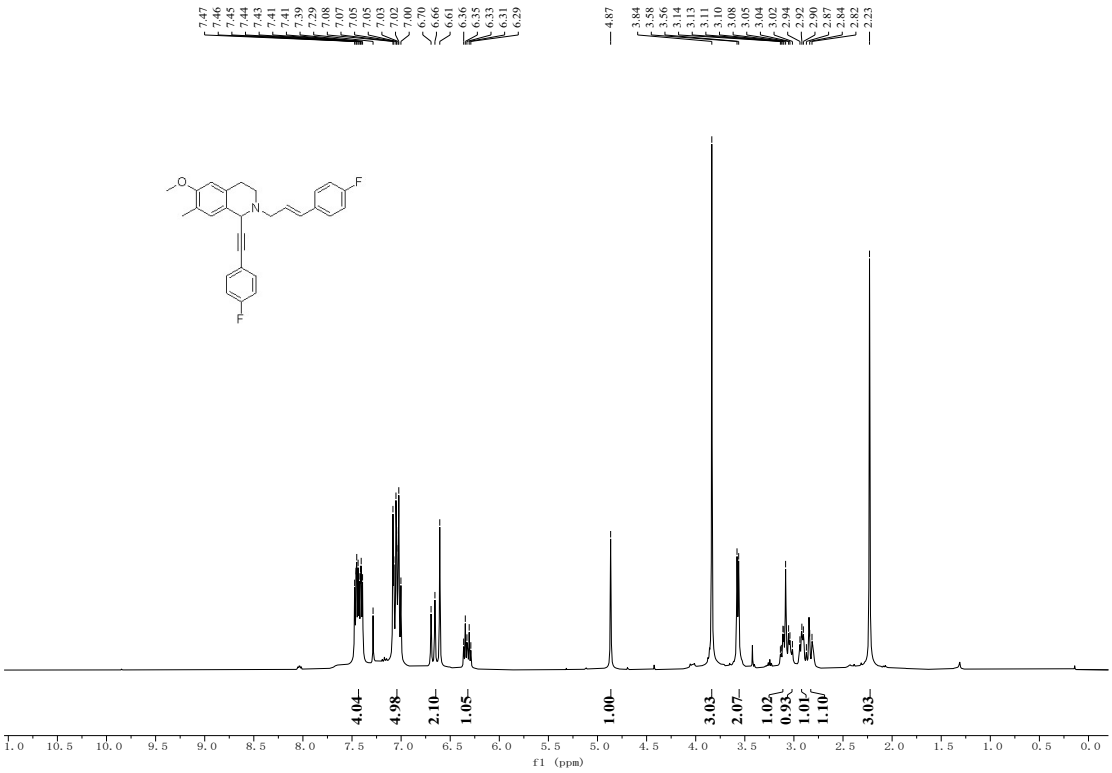
***(E)-6,7-diethoxy-2-(3-(4-fluorophenyl)allyl)-1-((4-fluorophenyl)ethynyl)-1,2,3,4-tetrahydroisoquinoline* (4e)**

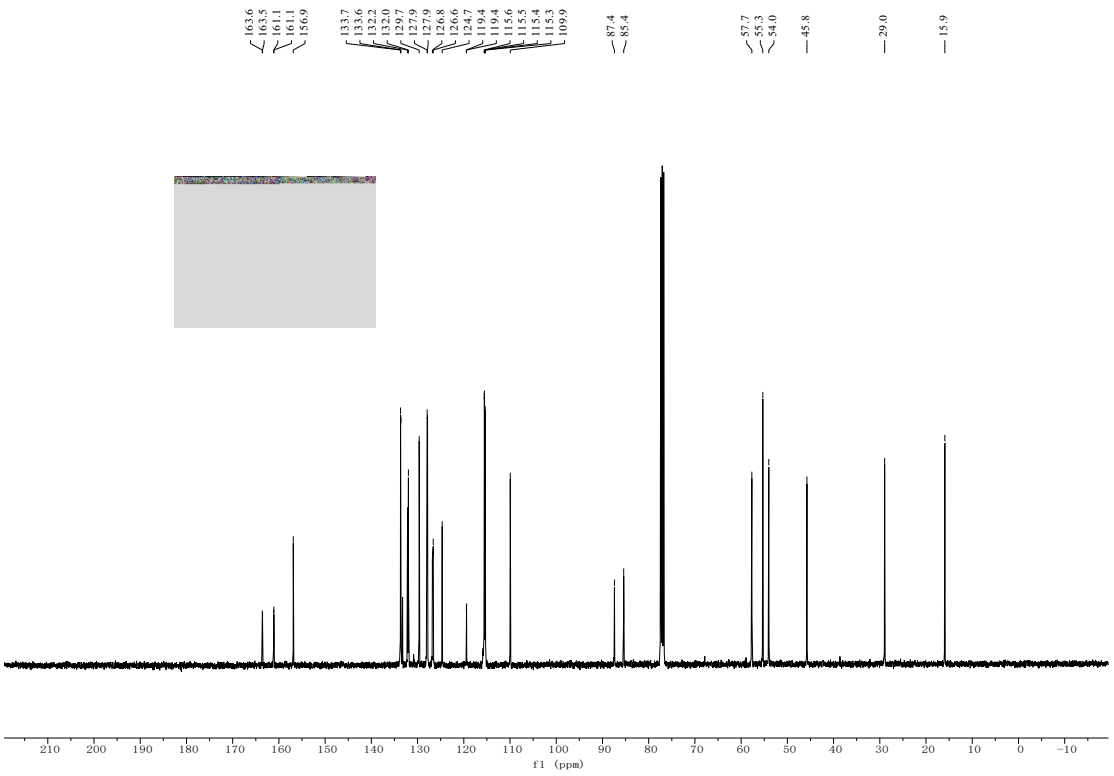

7.45
7.44
7.43
7.42
7.40
7.40
7.38
7.06
7.03
7.02
6.99
6.82
6.69
6.65
6.36
6.34
6.32
6.30
6.28
4.87
4.12
4.10
4.09
4.08
4.07
4.06
4.06
3.58
3.57
3.56
3.10
3.08
3.06
3.04
3.03
3.00
2.99
2.97
2.95
2.91
2.78
2.75
1.48
1.47
1.46
1.45
1.44
1.43
O
O
N
F
F
4.05
4.07
1.00
2.08
1.03
1.00
4.01
2.06
0.99
0.99
1.08
1.00
2.94
3.02
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

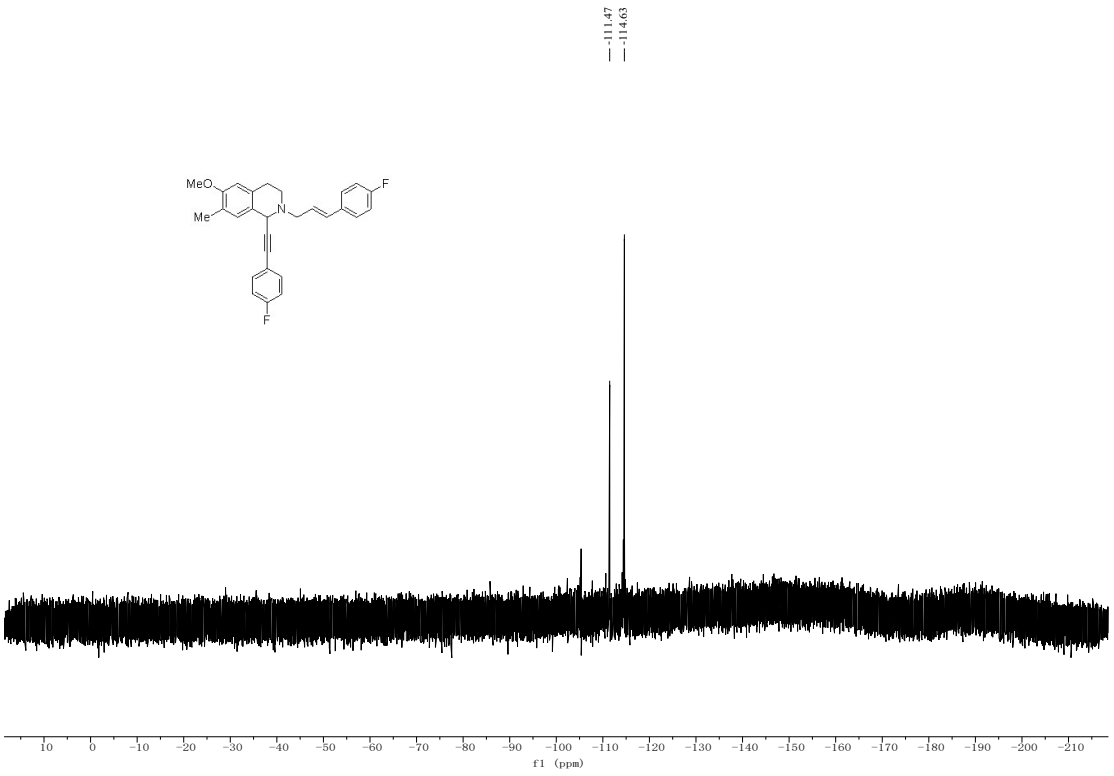

163.6
163.5
161.2
161.1
148.2
147.1
133.7
133.6
133.2
133.1
132.3
128.0
127.9
127.0
126.2
126.0
119.3
119.2
115.6
115.4
113.6
112.8
87.0
85.7
64.7
64.5
57.6
54.1
45.8
28.3
14.9
14.8
O
O
N
F
F
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)



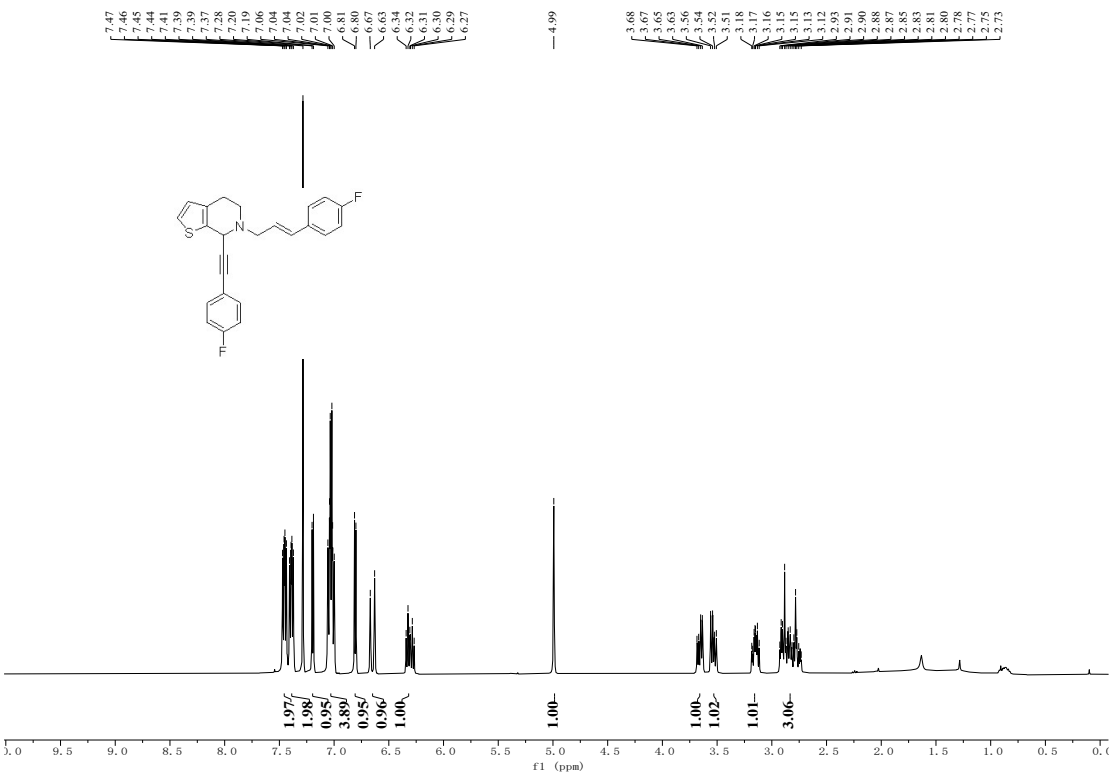
(E)-2-(3-(4-fluorophenyl)allyl)-1-((4-fluorophenyl)ethynyl)-6-methoxy-7-methyl-1,2,3,4-tetrahydroisoquinoline **(4f)**







***(E)-6-(3-(4-fluorophenyl)allyl)-7-((4-fluorophenyl)ethynyl)-4,5,6,7-tetrahydrothieno[2,3-c]pyridine* (4g)**


7.47
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7.39
7.39
7.37
7.28
7.20
7.19
7.06
7.04
7.04
7.02
7.01
7.00
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6.63
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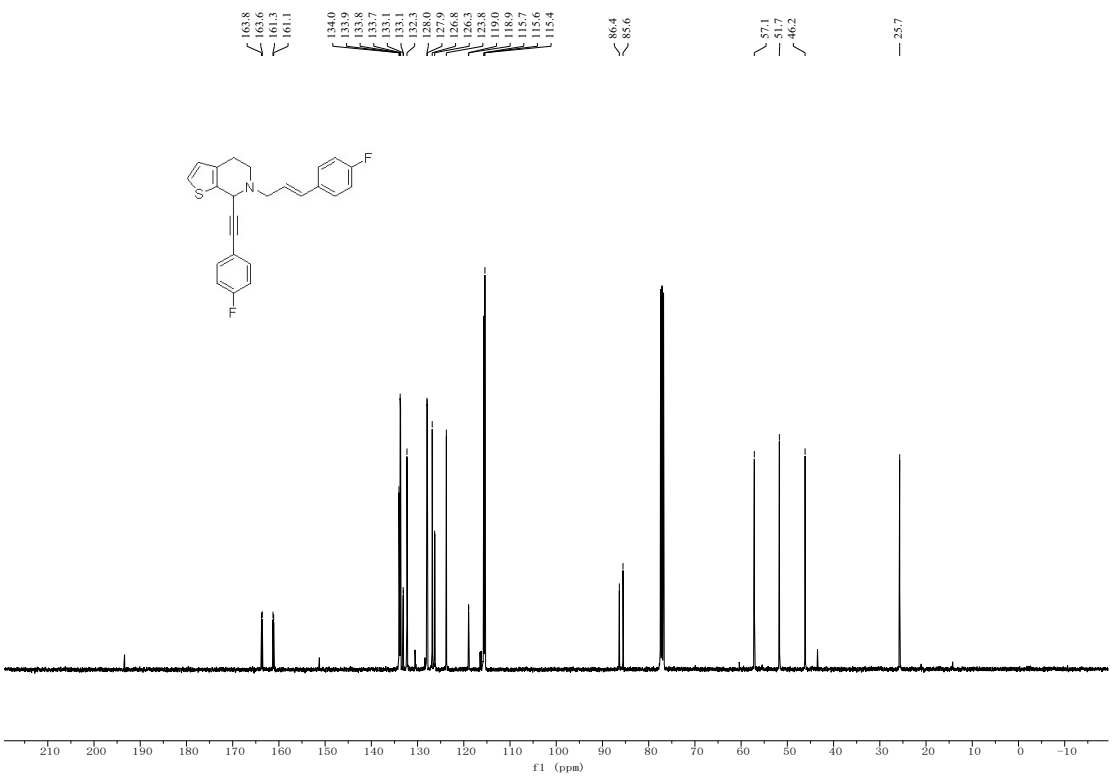
4.99
3.68
3.67
3.65
3.63
3.56
3.54
3.52
3.51
3.18
3.17
3.16
3.15
3.15
3.13
3.12
2.93
2.91
2.90
2.88
2.87
2.85
2.83
2.81
2.80
2.78
2.77
2.75
2.73
F
S
N
F
1.97
1.98
0.95
3.89
0.95
0.96
1.00
1.00
1.00
1.02
1.01
3.06
f1 (ppm)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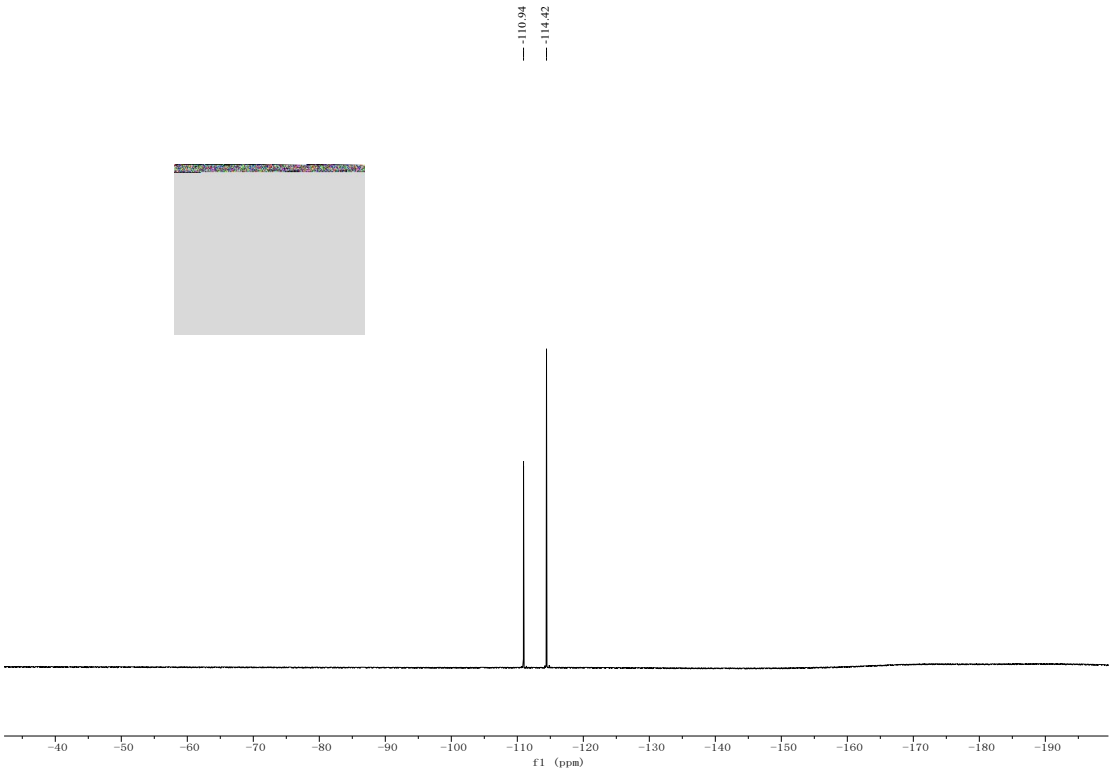
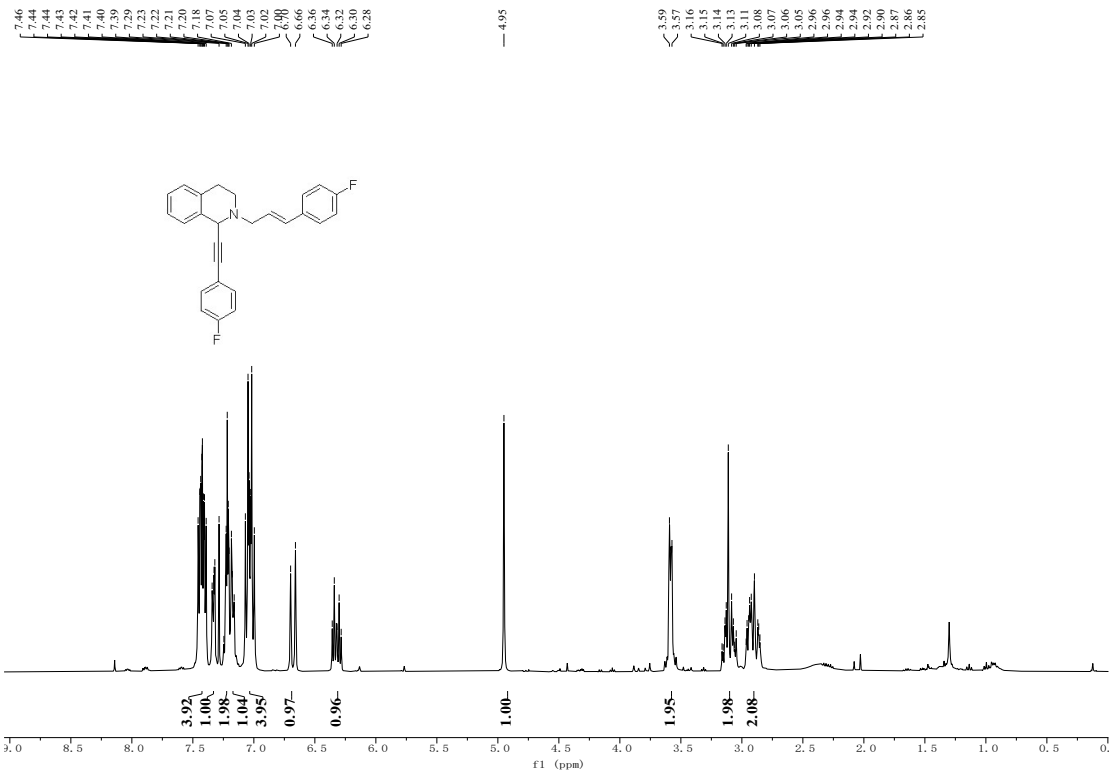
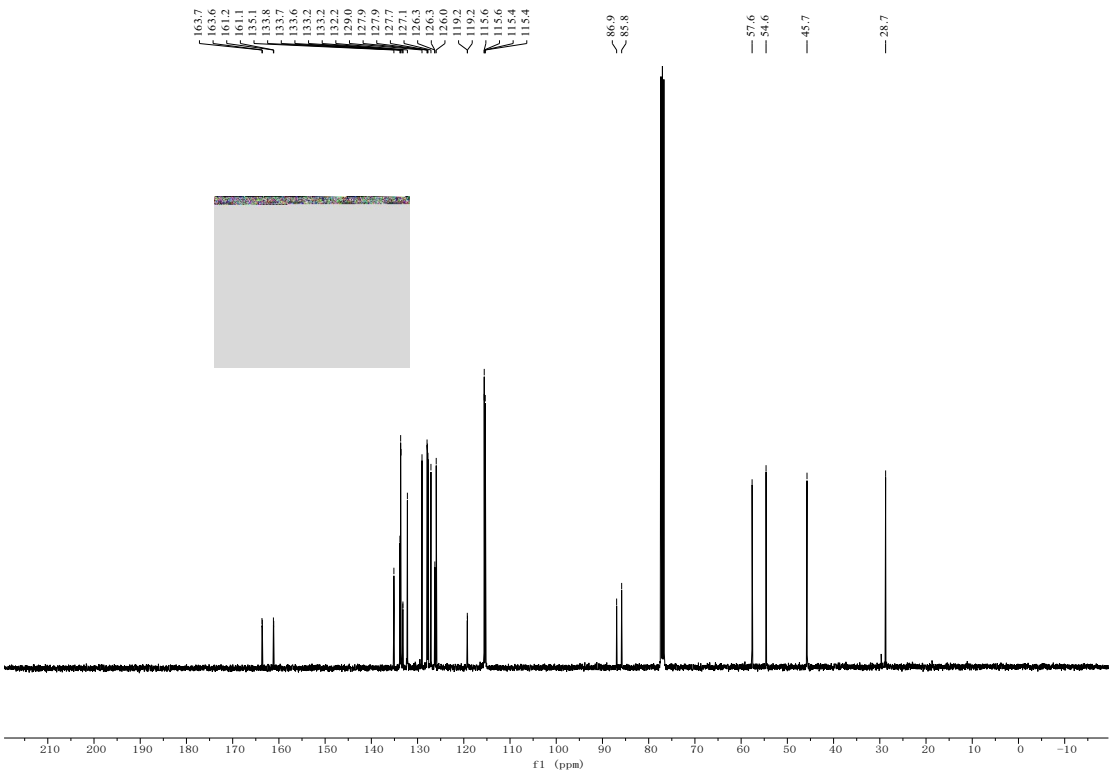
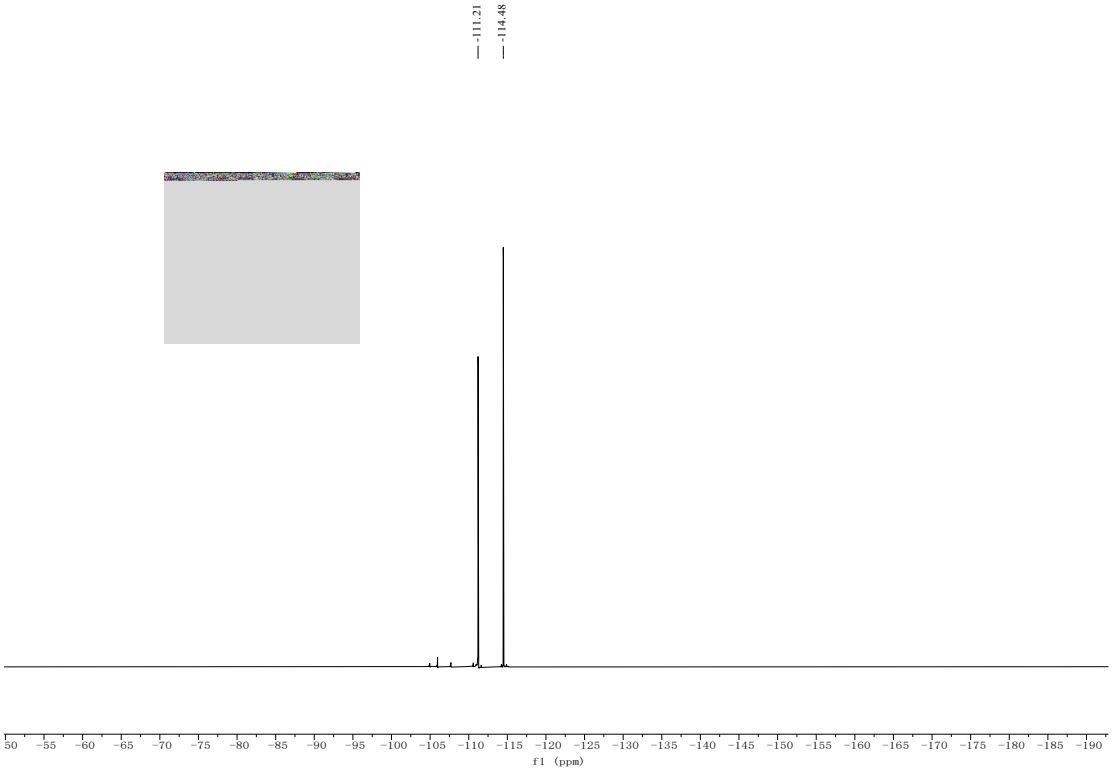
133.9
133.8
133.7
133.1
133.1
132.3
128.0
127.9
126.8
126.3
123.8
119.0
118.9
115.7
115.6
115.4
86.4
85.6
57.1
51.7
46.2
25.7
F
S
N
F
f1 (ppm)



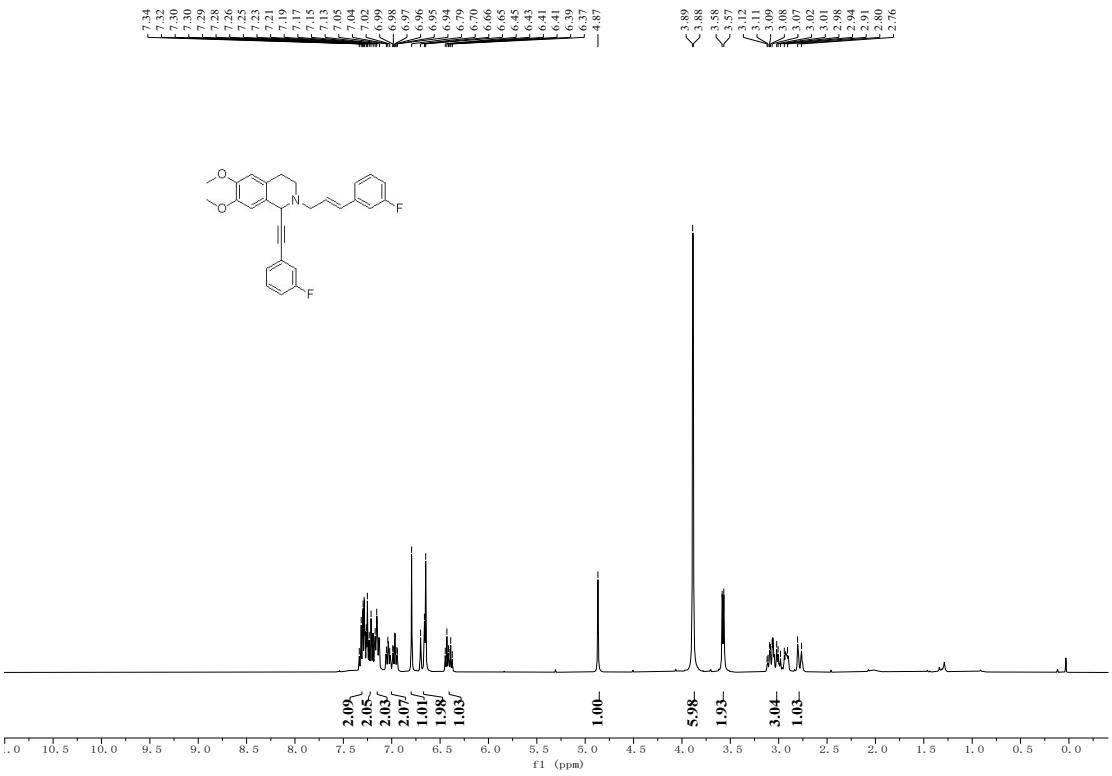
***(E)-2-(3-(4-fluorophenyl)allyl)-1-((4-fluorophenyl)ethynyl)-1,2,3,4-tetrahydroisoquinoline*(4h)**







***(E)-2-(3-(3-fluorophenyl)allyl)-1-((3-fluorophenyl)ethynyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline* (4k)**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7.25
7.23
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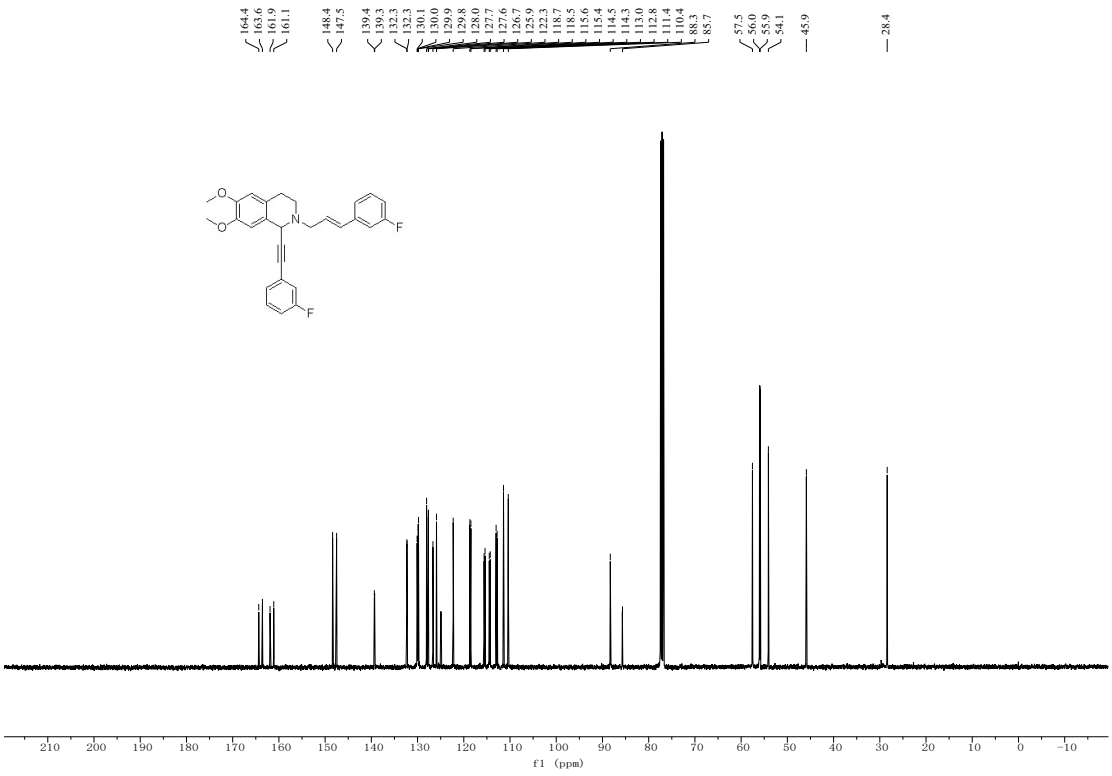
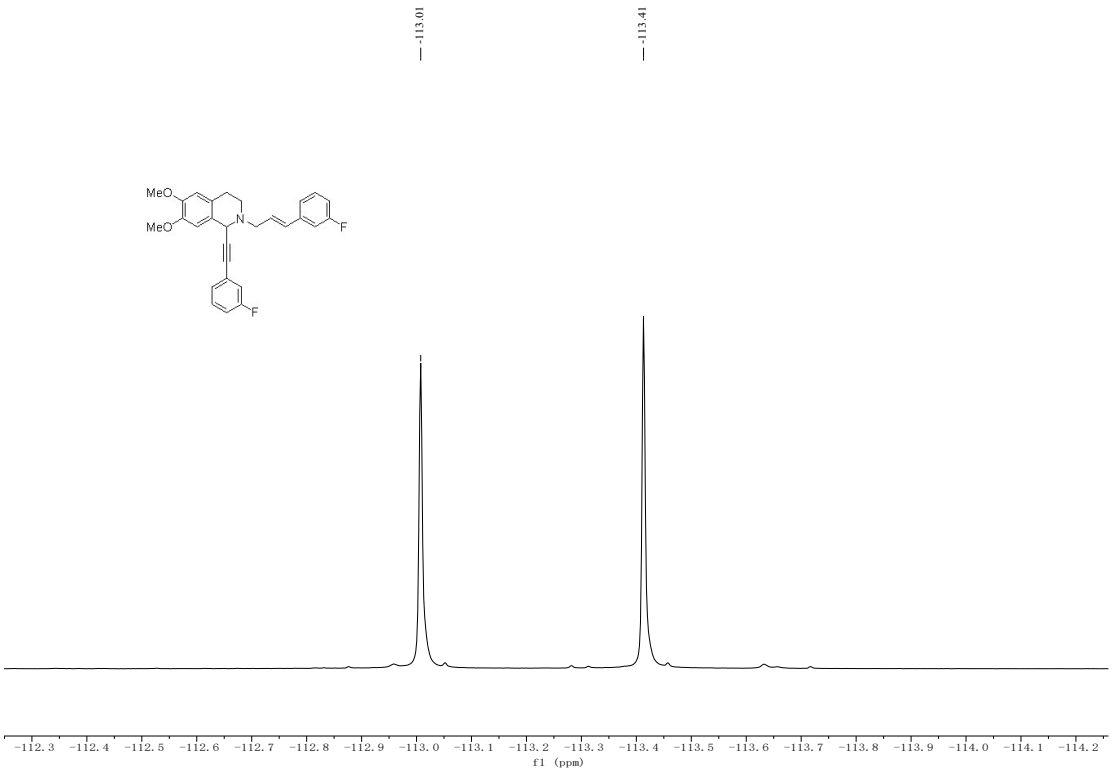
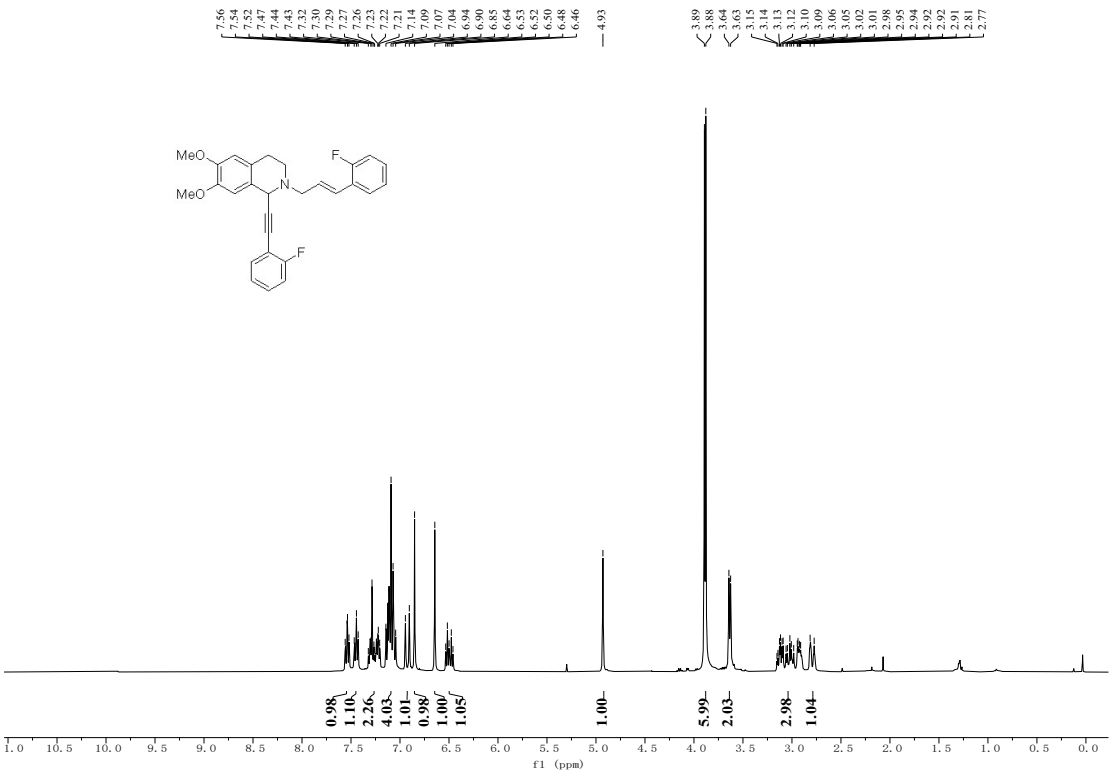
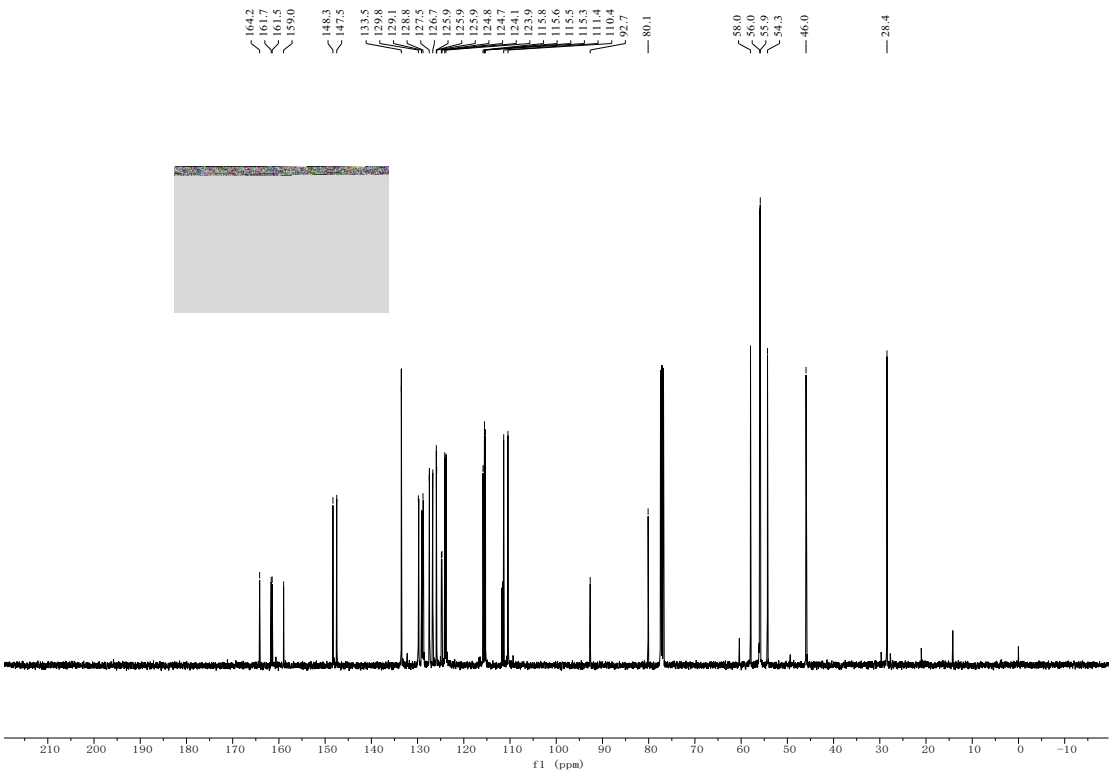
7.19
7.17
7.15
7.13
7.05
7.04
7.02
6.99
6.98
6.97
6.96
6.95
6.94
6.79
6.70
6.66
6.65
6.45
6.43
6.41
6.41
6.39
6.37
4.87
3.89
3.88
3.58
3.57
3.12
3.11
3.09
3.08
3.07
3.02
3.01
2.98
2.94
2.91
2.80
2.76
O
O
N
F
F
2.09
2.05
2.03
2.07
1.01
1.98
1.03
1.00
5.98
1.93
3.04
1.03
f1 (ppm)


164.4
163.6
161.9
161.1
148.4
147.5
139.4
139.3
132.3
132.3
130.1
130.0
129.9
129.8
128.0
127.7
127.6
126.7
125.9
122.3
118.7
118.5
115.6
115.4
114.5
114.3
113.0
112.8
111.4
110.4
88.3
85.7
57.5
56.0
55.9
54.1
45.9
28.4
O
O
N
F
F
f1 (ppm)

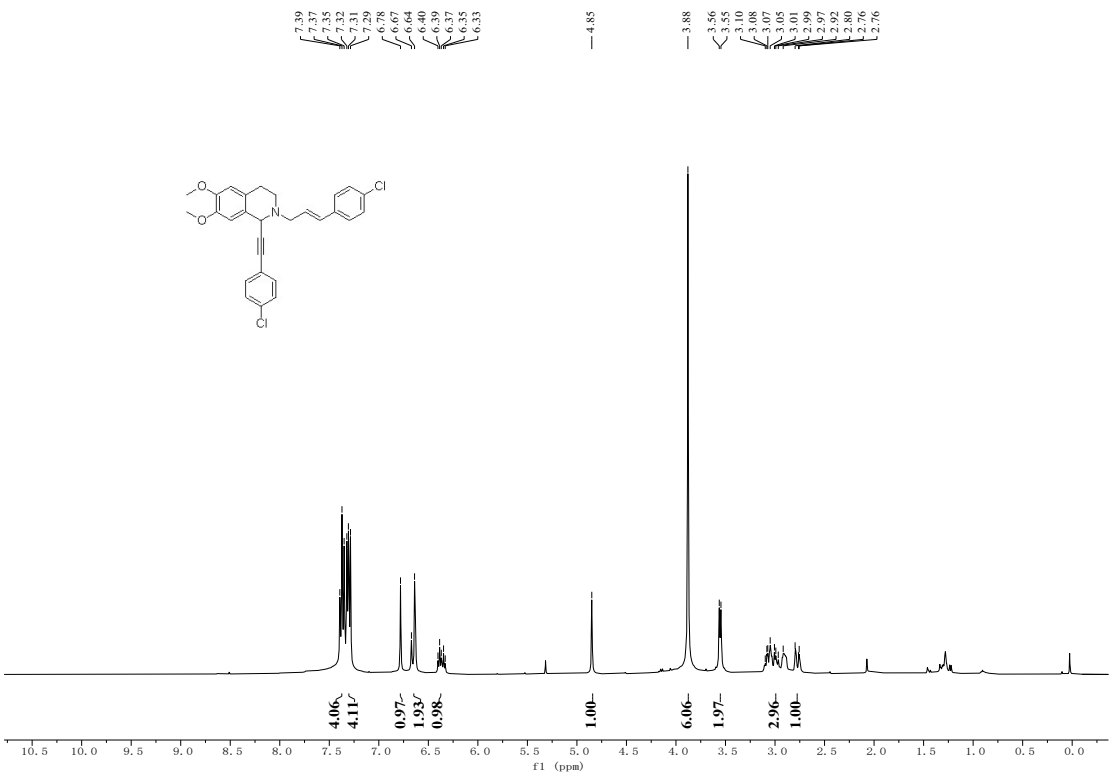


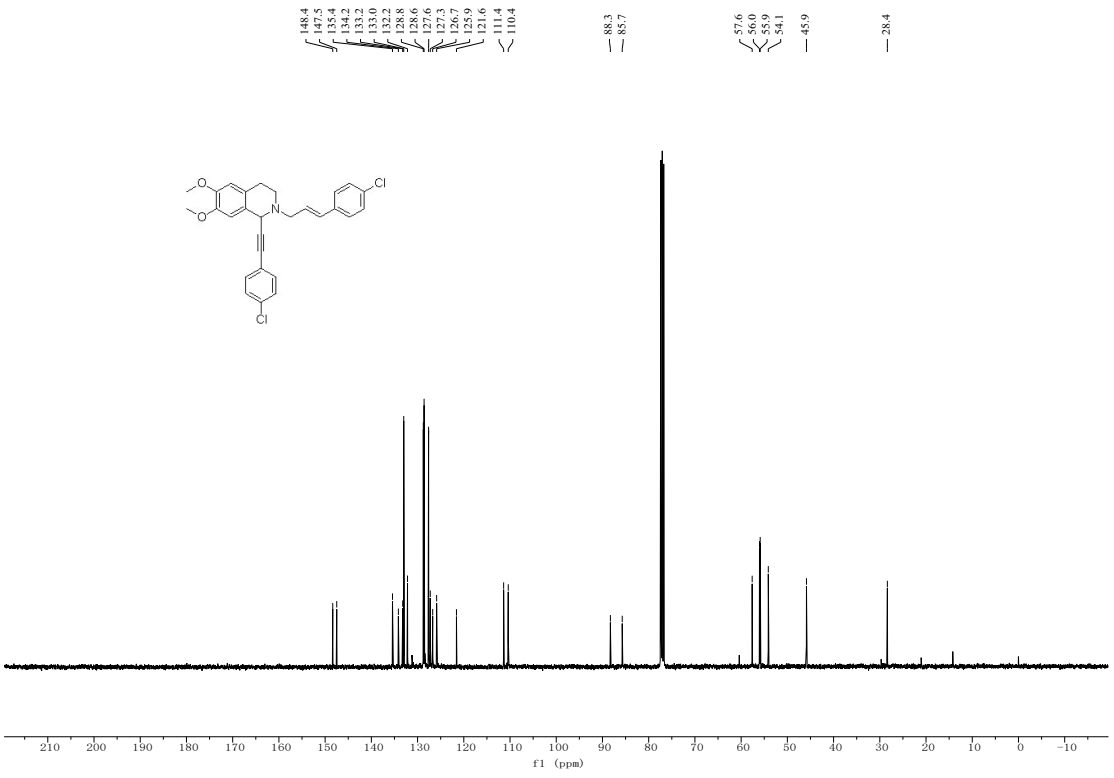
(E)-2-(3-(2-fluorophenyl)allyl)-1-((2-fluorophenyl)ethynyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline **(4l)**



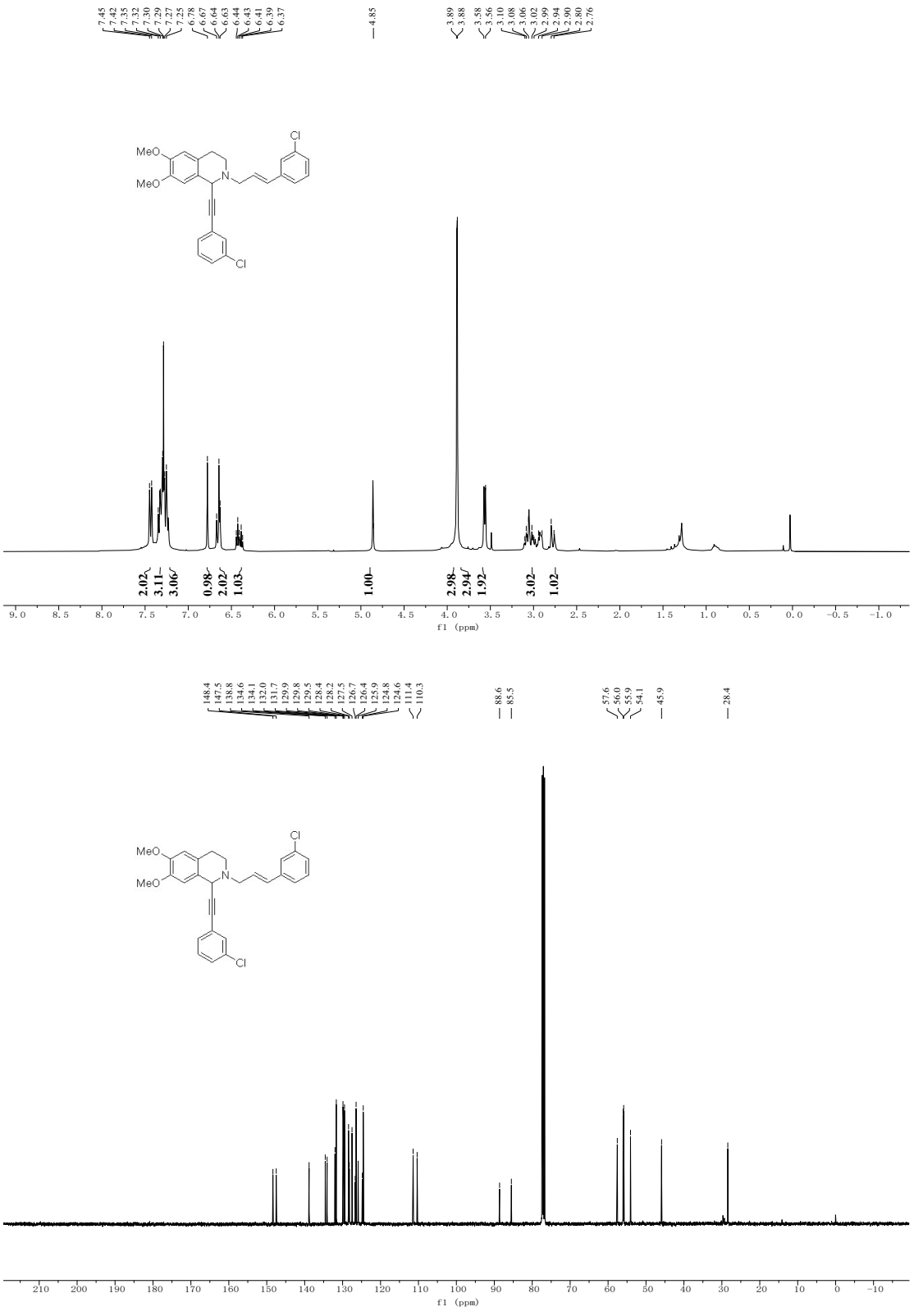


***(E)-2-(3-(4-chlorophenyl)allyl)-1-((4-chlorophenyl)ethynyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline* (4m)**

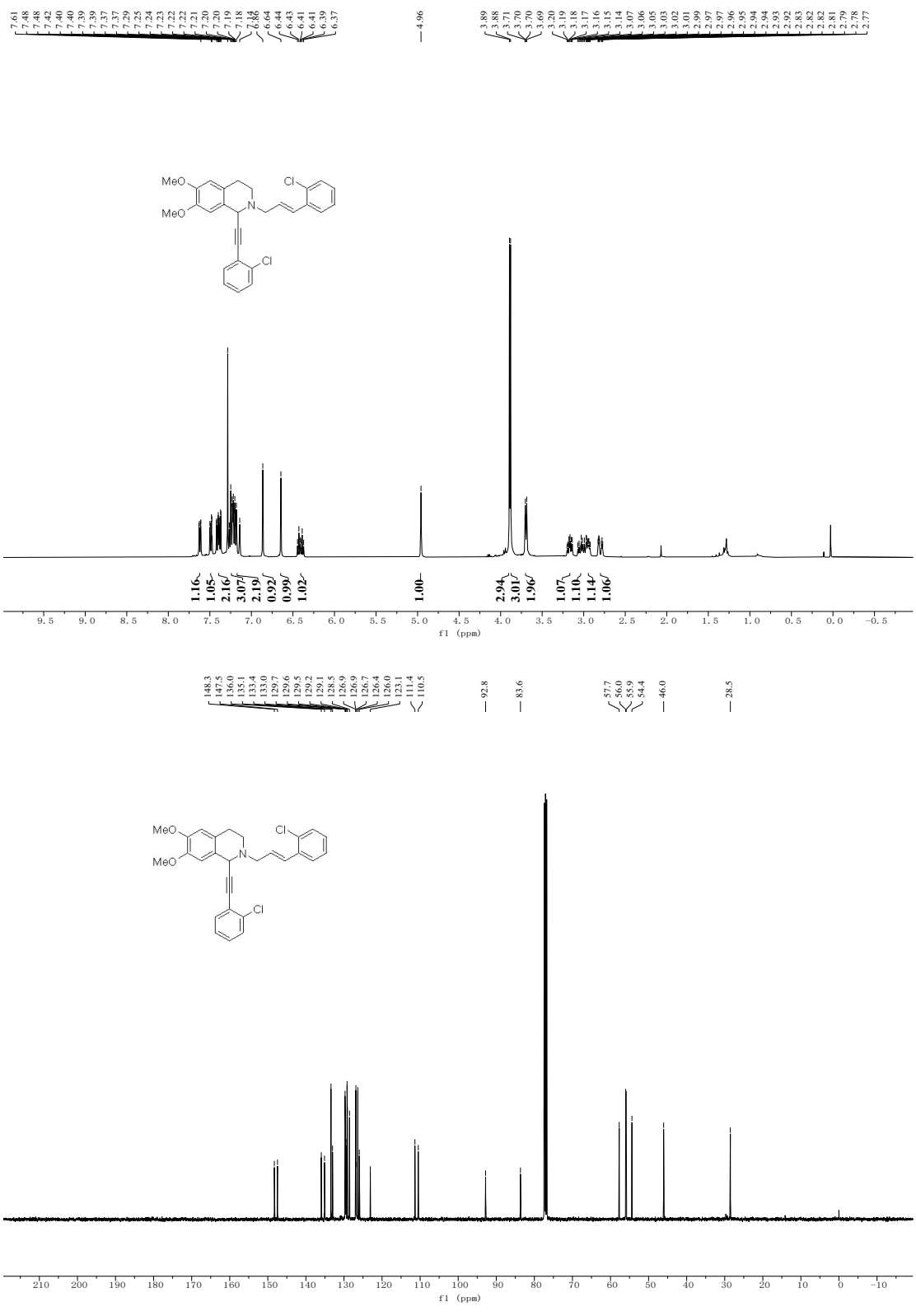




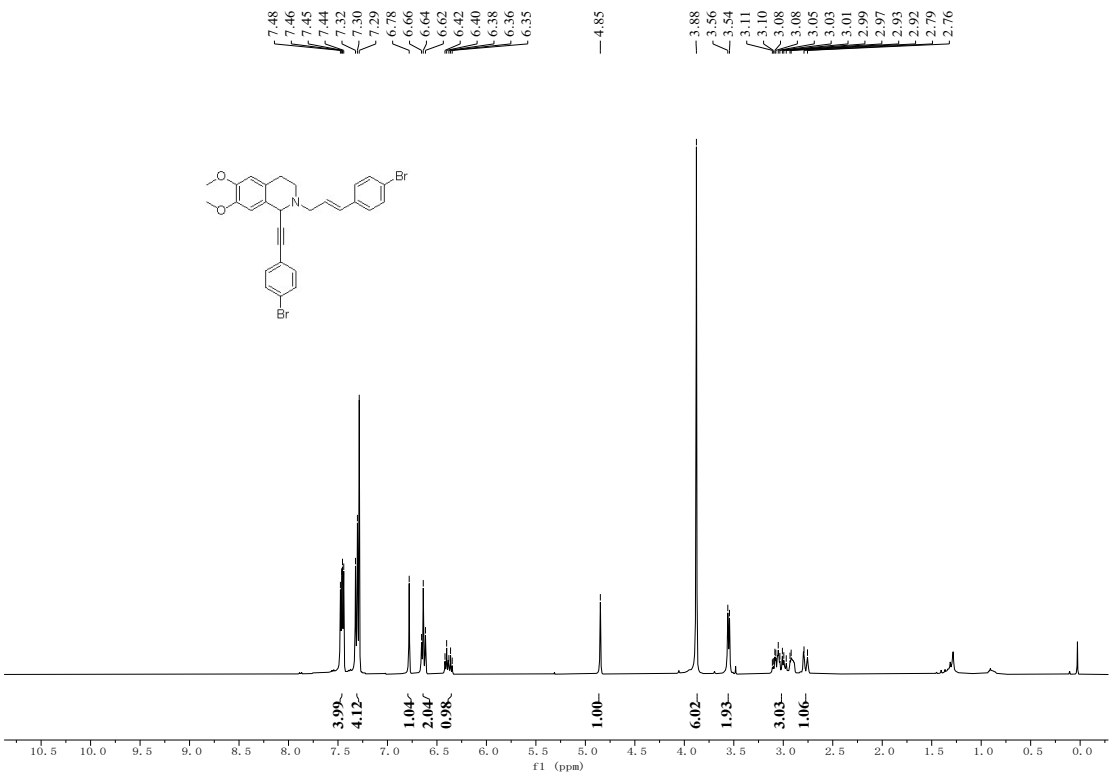
***(E)-2-(3-(3-chlorophenyl)allyl)-1-((3-chlorophenyl)ethynyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline* (4n)**

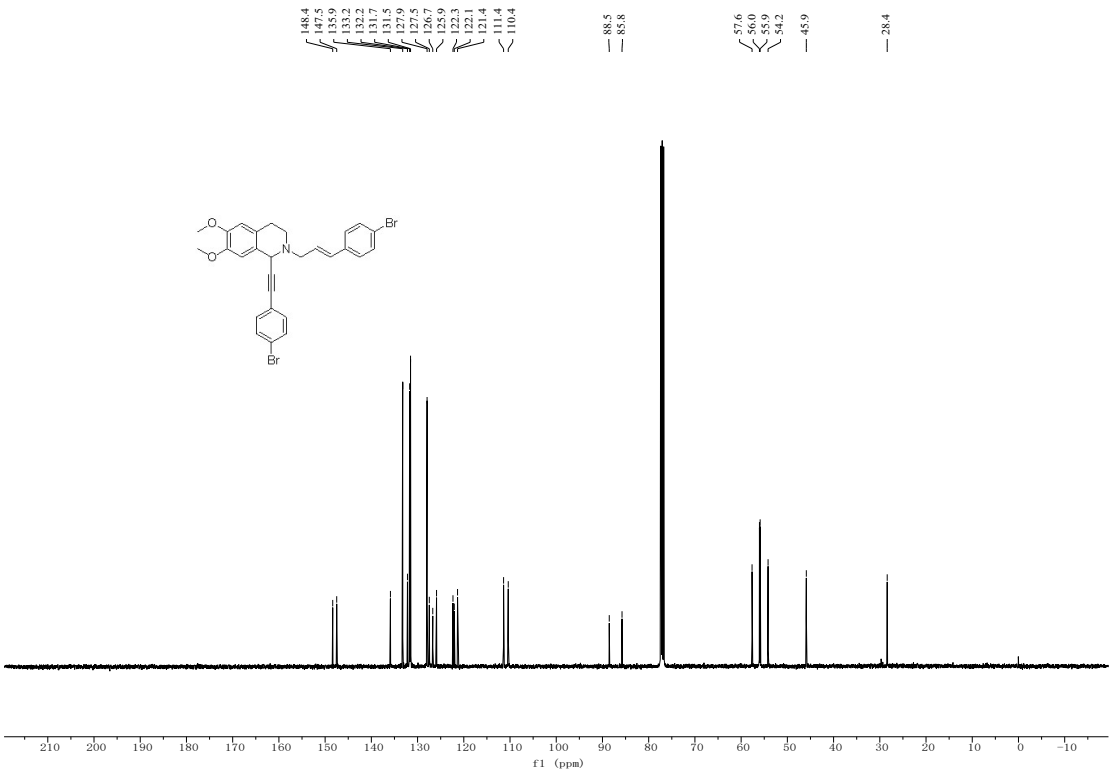


***(E)-2-(3-(2-chlorophenyl)allyl)-1-((2-chlorophenyl)ethynyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline* (4o)**

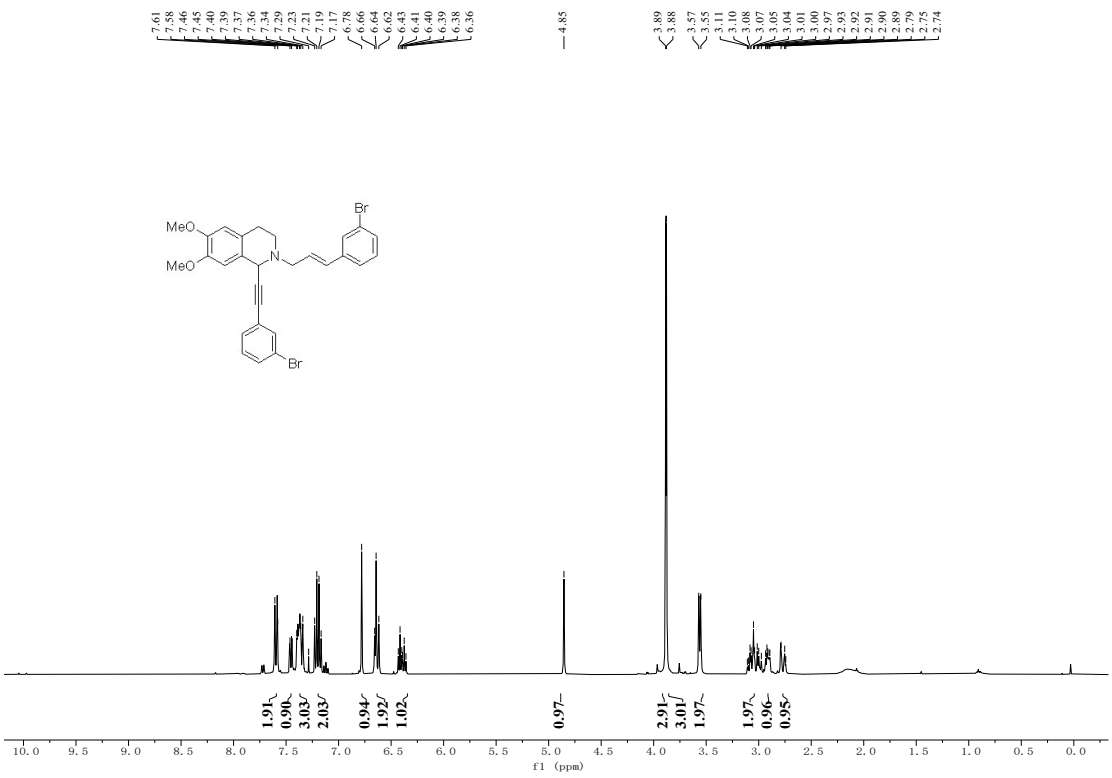


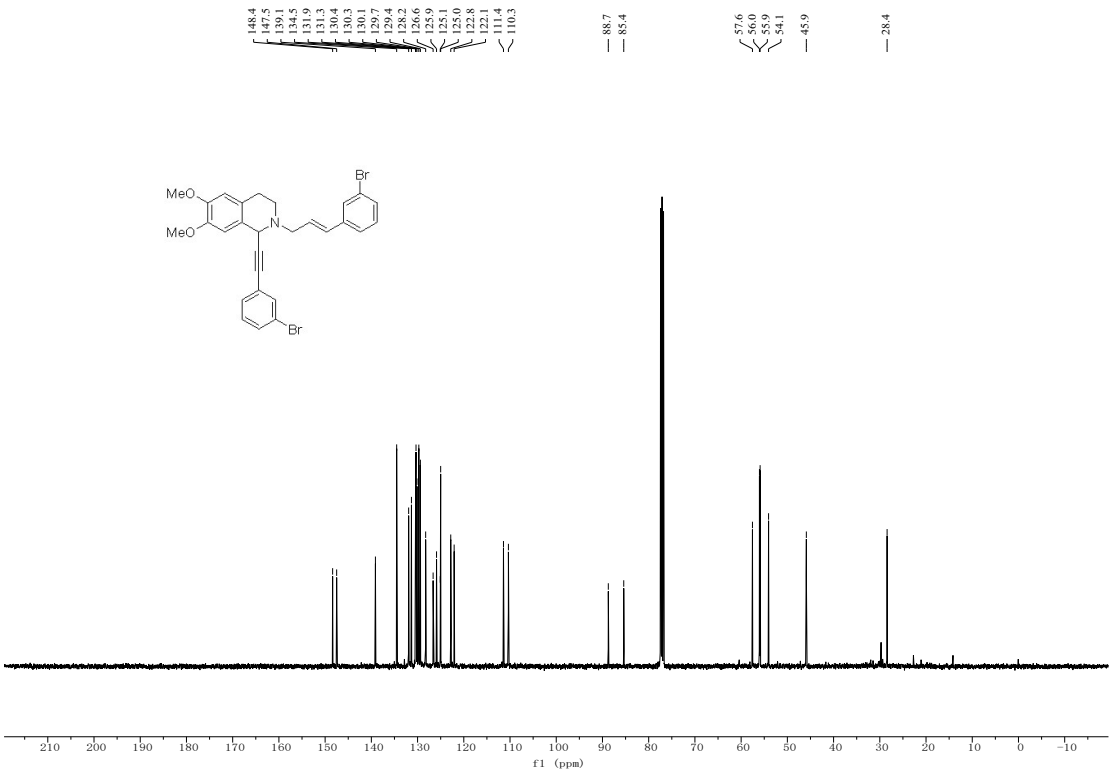
(E)-2-(3-(4-bromophenyl)allyl)-1-((4-bromophenyl)ethynyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline **(4p)**



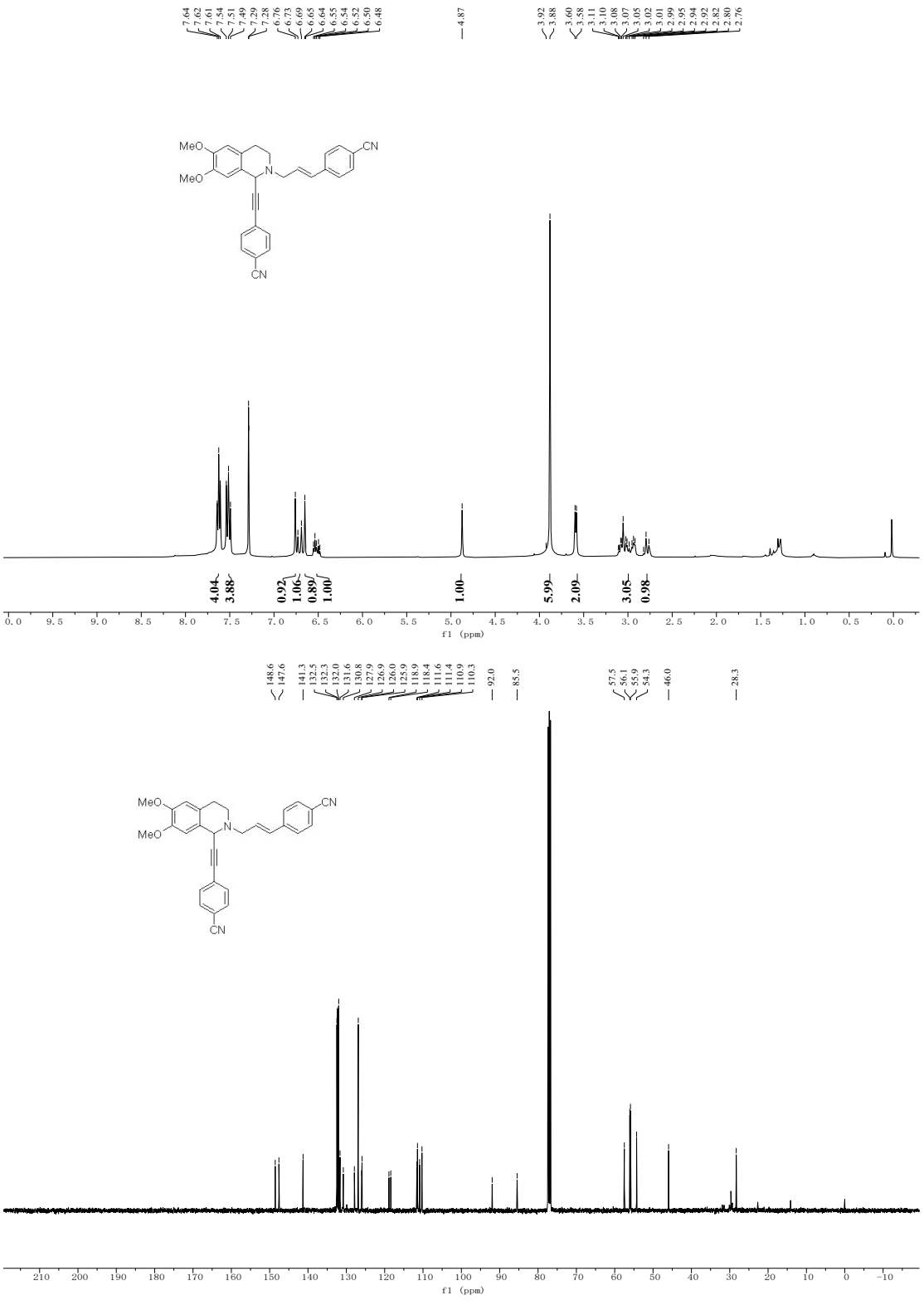


***(E)-2-(3-(3-bromophenyl)allyl)-1-((3-bromophenyl)ethynyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline* (4q)**

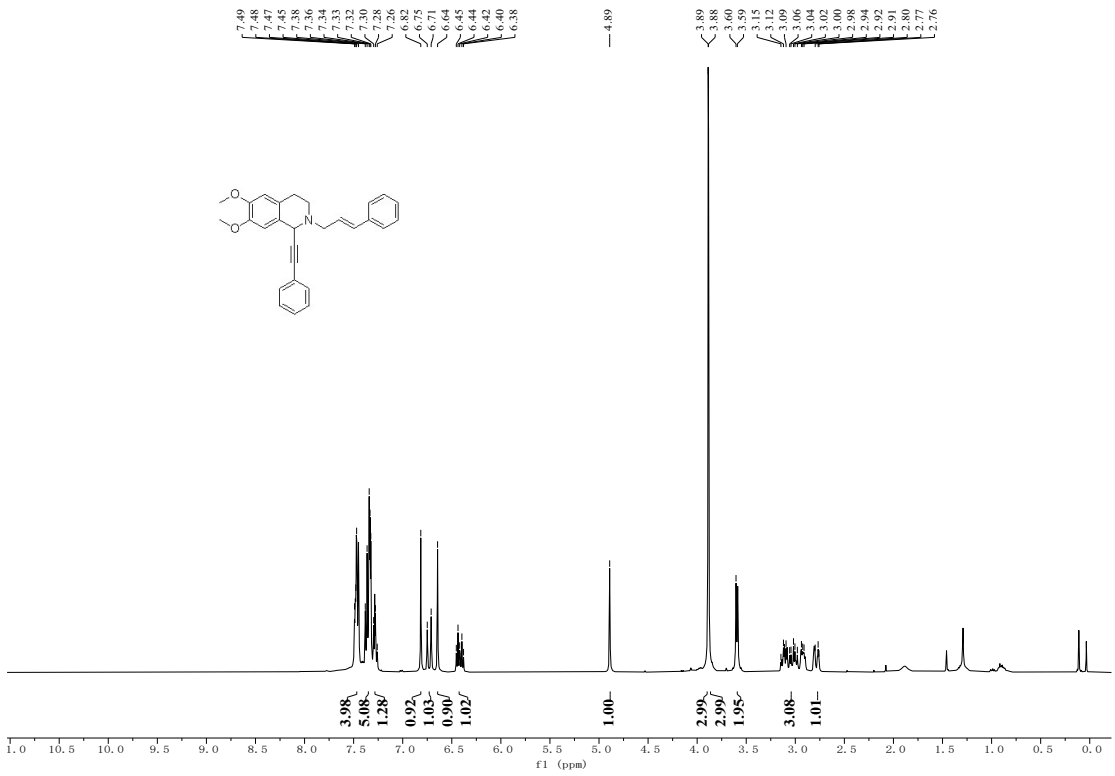




***(E)-4-((2-(3-(4-cyanophenyl)allyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl)ethynyl)benzonitrile* (4r)**



2-cinnamyl-6,7-dimethoxy-1-(phenylethynyl)-1,2,3,4-tetrahydroisoquinoline **(4s)**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7.33
7.32
7.30
7.28
7.26
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6.71
6.64
6.45
6.44
6.42
6.40
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3.89
3.88
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3.15
3.12
3.09
3.06
3.04
3.02
3.00
2.98
2.94
2.92
2.91
2.80
2.77
2.76
3.98
5.08
1.28
0.92
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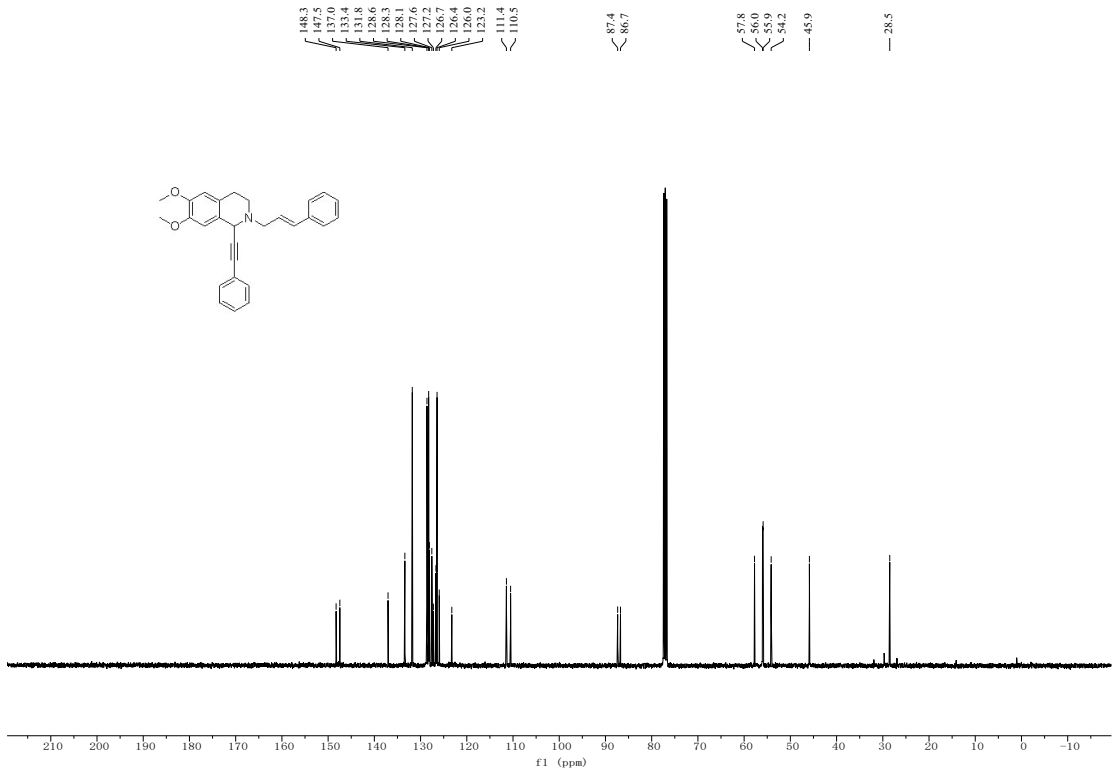
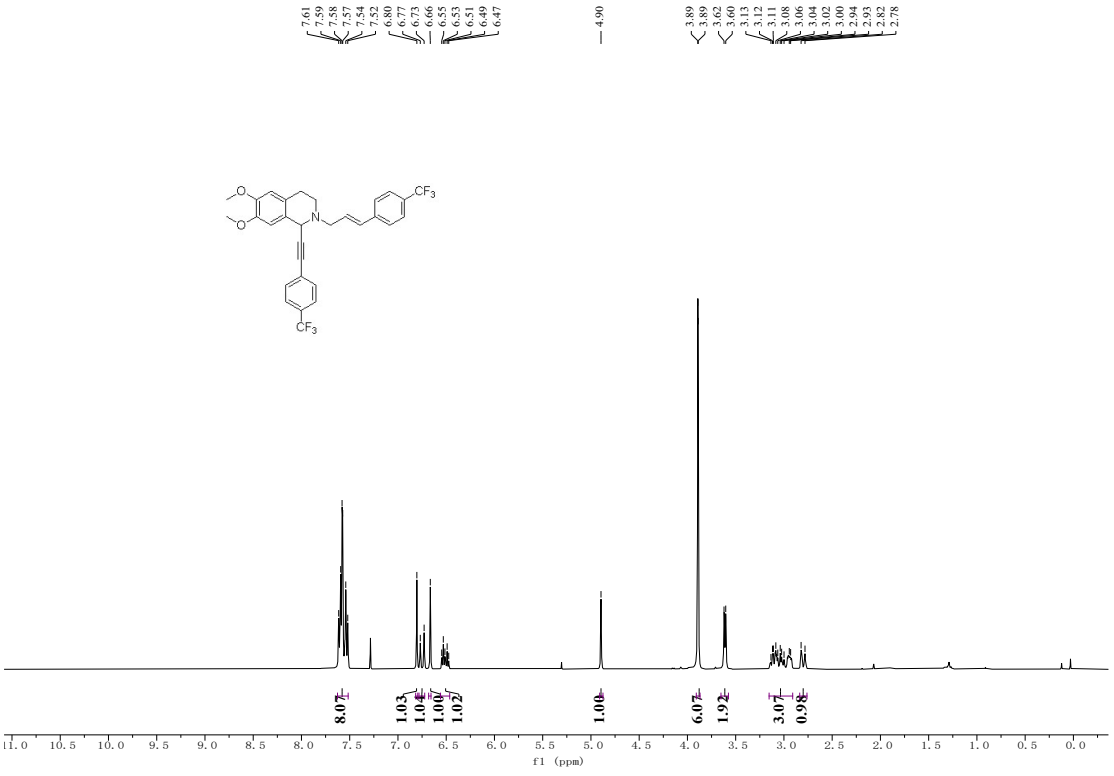
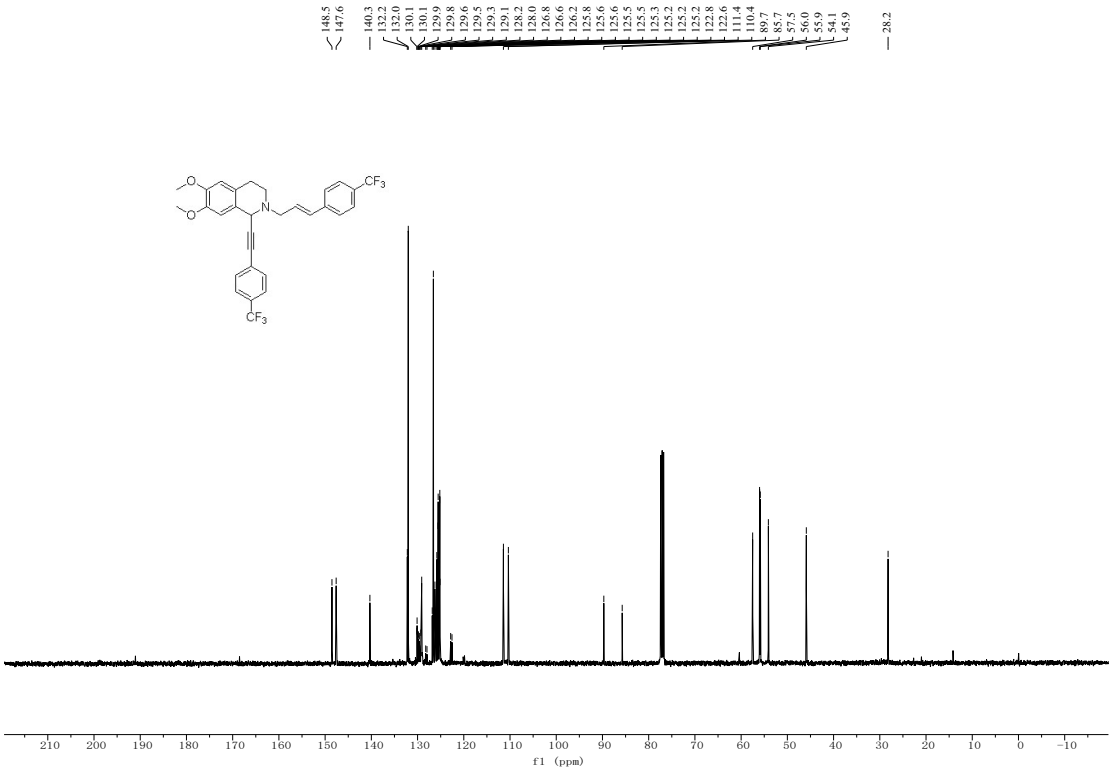
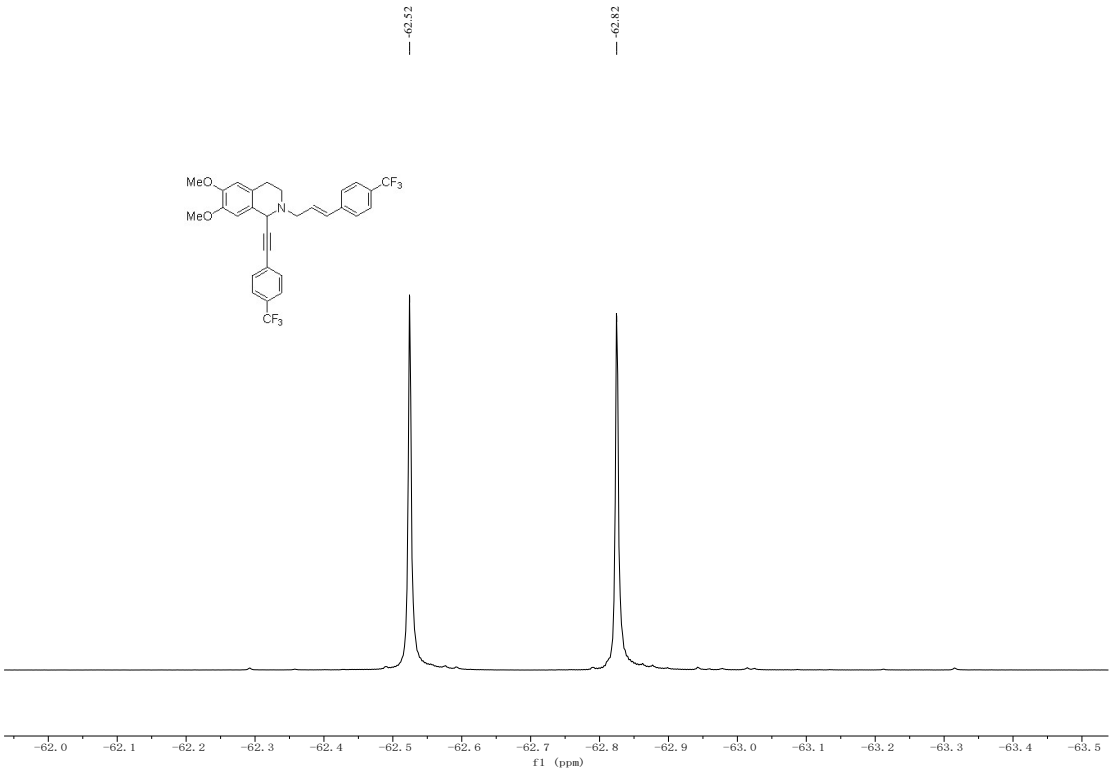
0.90
1.02
1.00
2.99
2.99
1.95
3.08
1.01
f1 (ppm)


148.3
147.5
137.0
133.4
131.8
128.6
128.3
128.1
127.6
127.2
126.7
126.4
126.0
123.2
111.4
110.5
87.4
86.7
57.8
56.0
55.9
54.2
45.9
28.5
f1 (ppm)

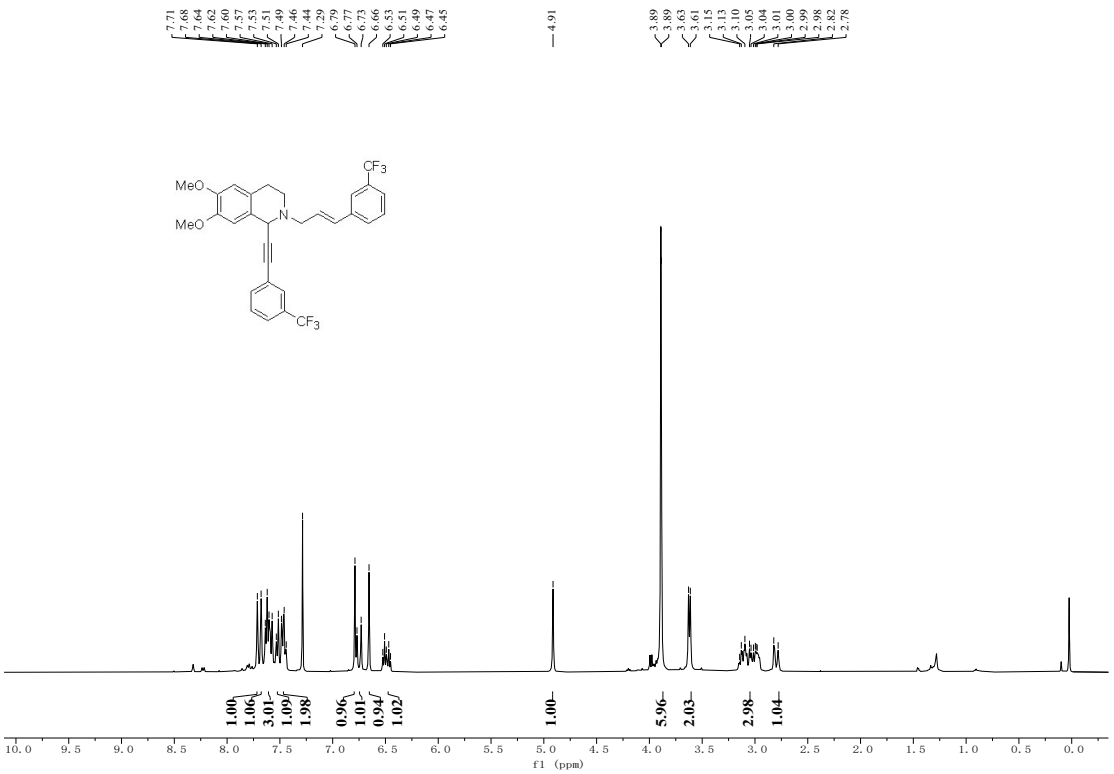
***(E)-6,7-dimethoxy-2-(3-(4-(trifluoromethyl)phenyl)allyl)-1-((4-(trifluoromethyl)phenyl)ethynyl)-1,2,3,4-tetrahydroisoquinoline* (4t)**

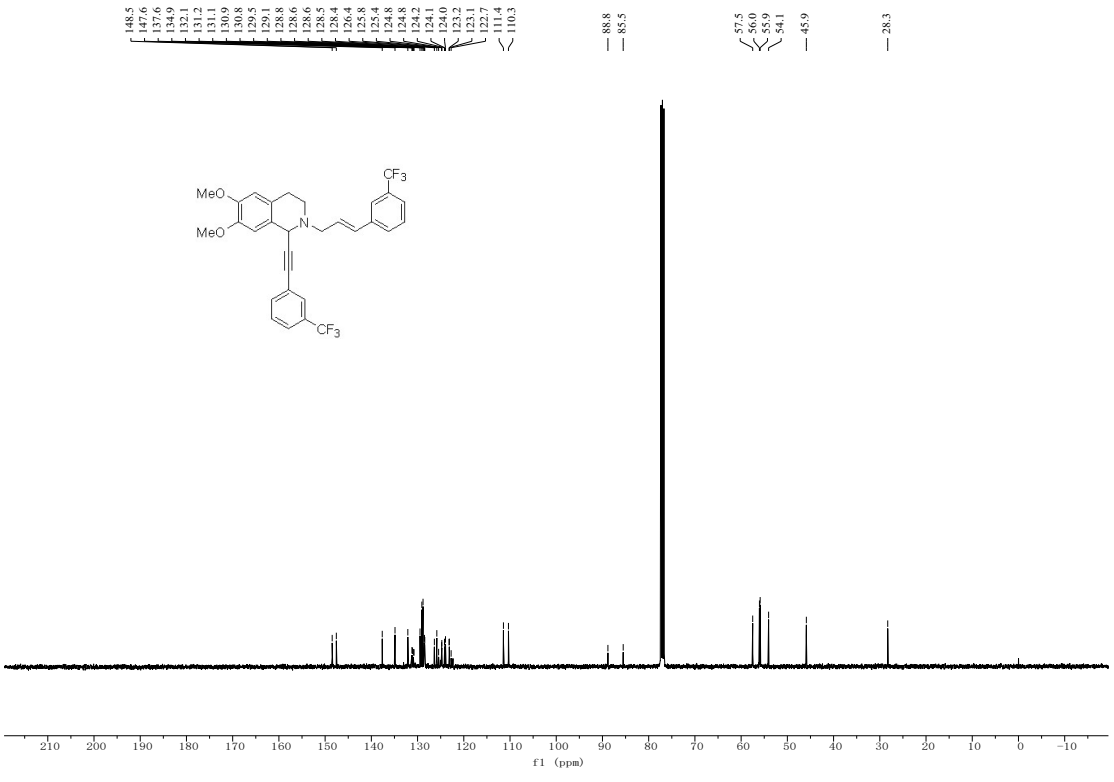


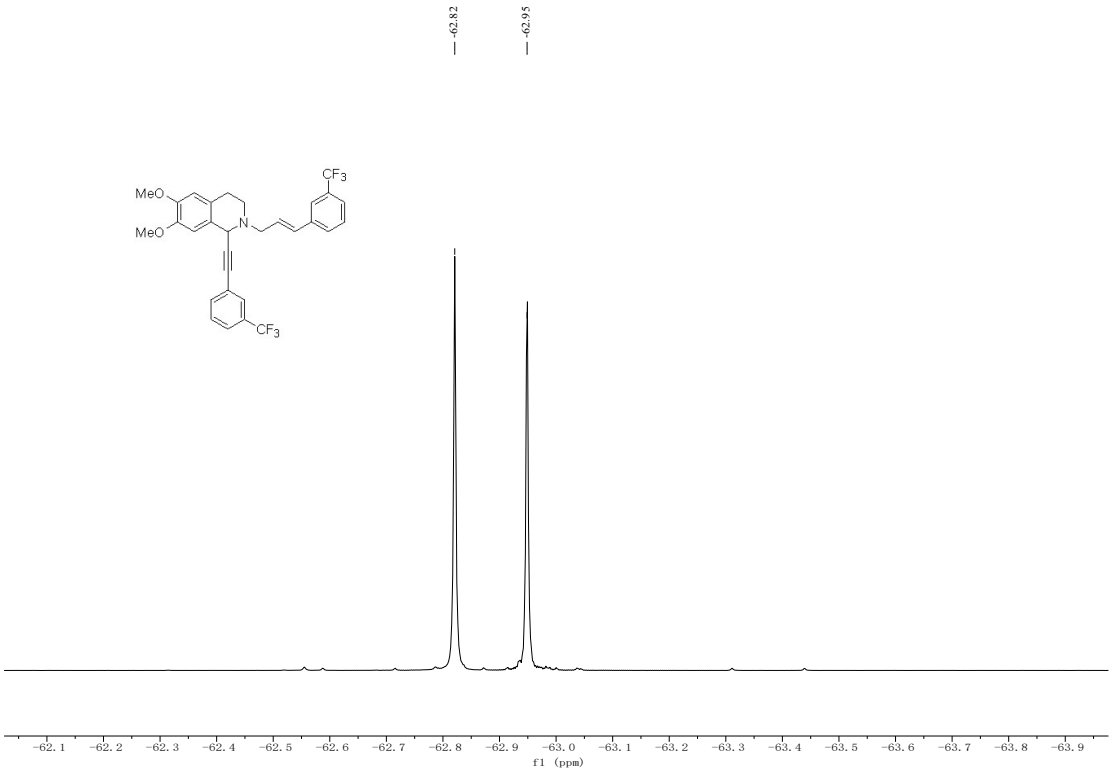




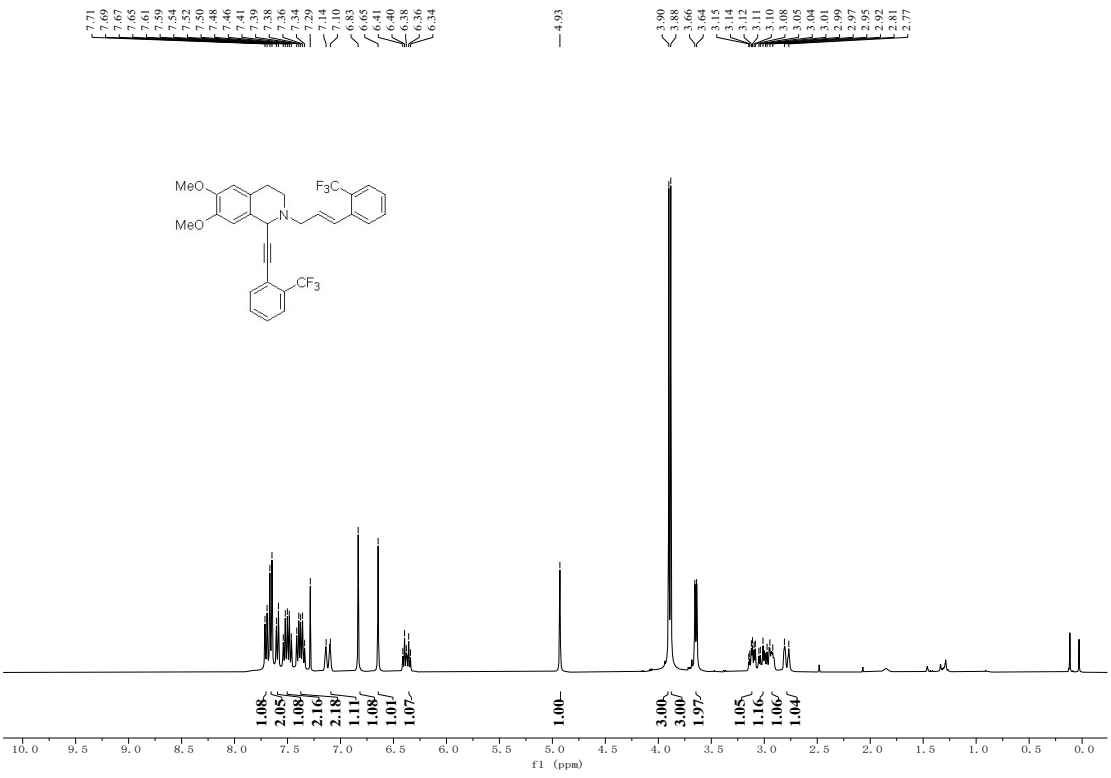
(E)-6,7-dimethoxy-2-(3-(3-(trifluoromethyl)phenyl)allyl)-1-((3-(trifluoromethyl)phenyl)ethynyl)-1,2,3,4-tetrahydroisoquinoline **(4u)**

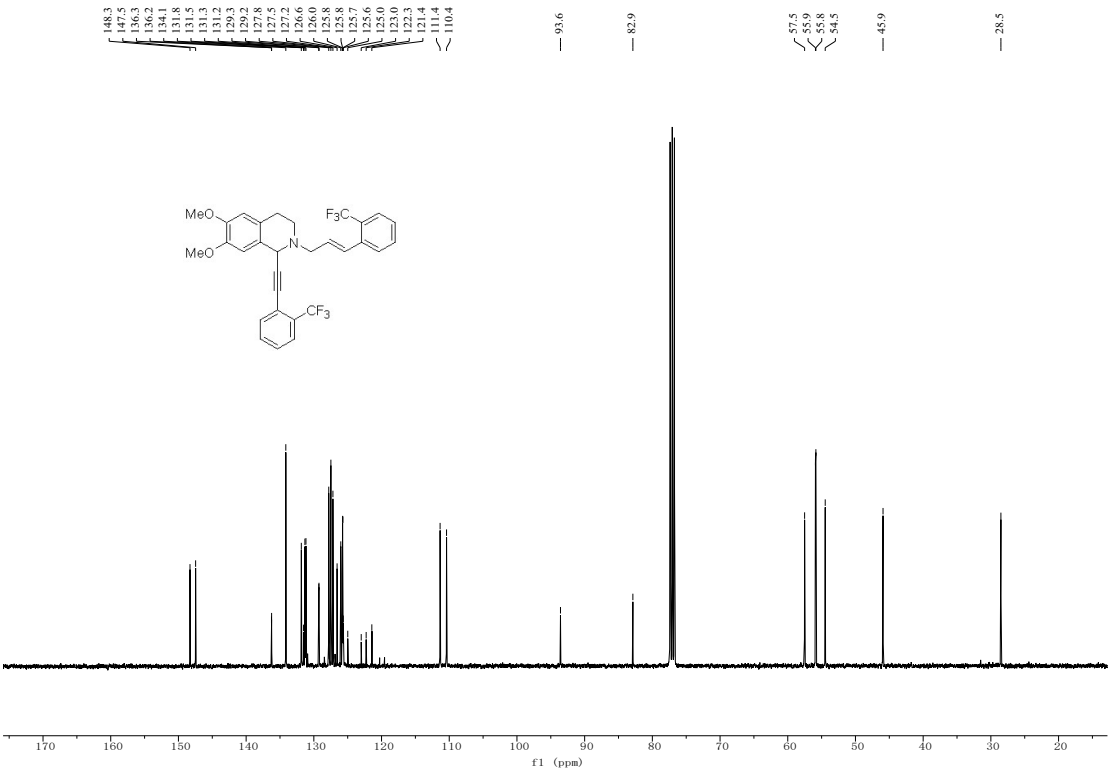

7.71
7.68
7.64
7.62
7.60
7.57
7.53
7.51
7.49
7.46
7.44
7.29
6.79
6.77
6.73
6.66
6.53
6.51
6.49
6.47
6.45
4.91
3.89
3.89
3.63
3.61
3.15
3.13
3.10
3.05
3.04
3.01
3.00
2.99
2.98
2.82
2.78
MeO
MeO
N
CF3
CF3
1.00
1.06
3.01
1.09
1.98
0.96
1.01
0.94
1.02
1.00
5.96
2.03
2.98
1.04
f1 (ppm)

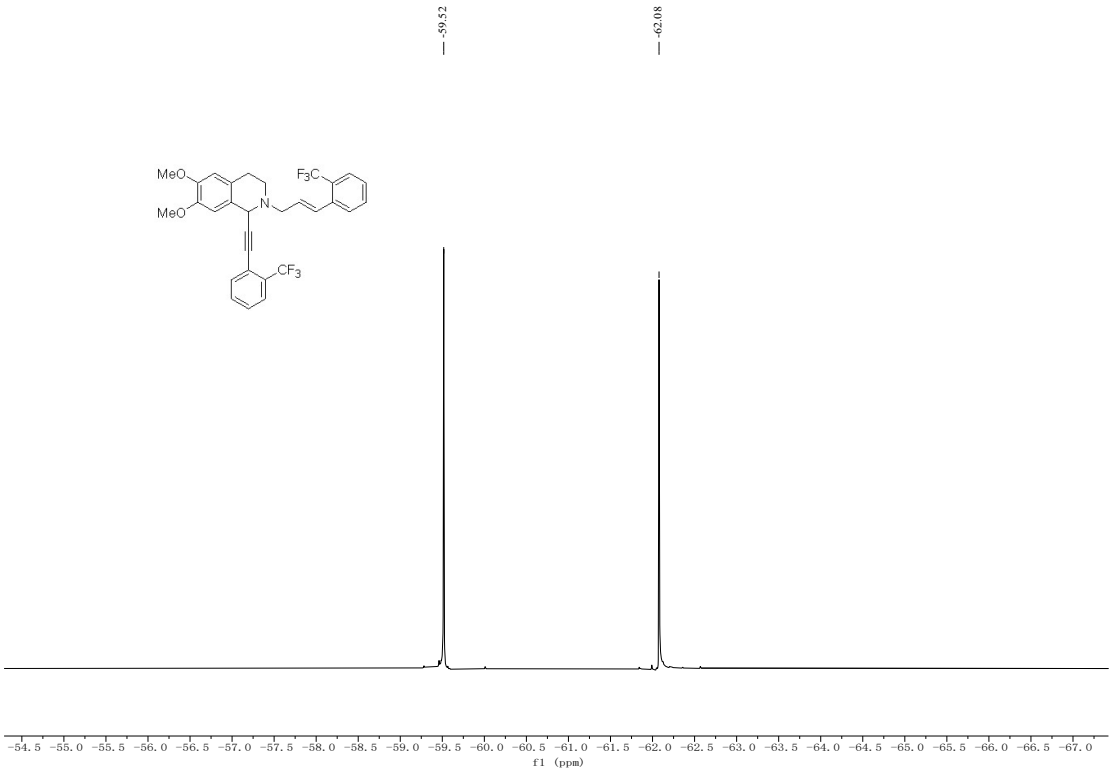

148.5
147.6
137.6
134.9
132.1
131.2
131.1
130.9
130.8
129.5
129.1
128.8
128.6
128.6
128.5
128.4
126.4
125.8
125.4
124.8
124.8
124.2
124.1
124.0
123.2
123.1
122.7
111.4
110.3
88.8
85.5
57.5
56.0
55.9
54.1
45.9
28.3
MeO
MeO
N
CF3
CF3
f1 (ppm)



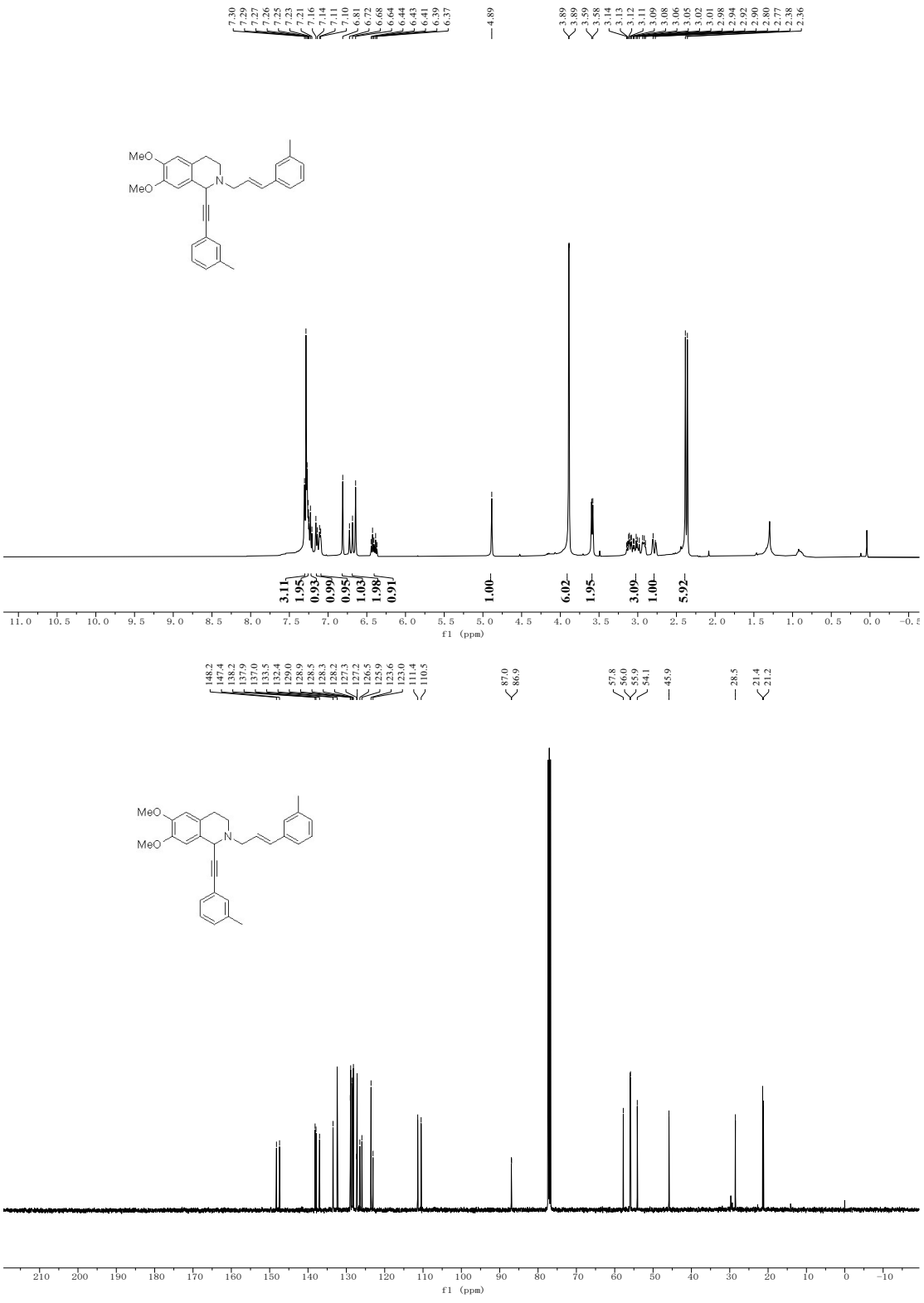
(E)-6,7-dimethoxy-2-(3-(2-(trifluoromethyl)phenyl)allyl)-1-((2-(trifluoromethyl)phenyl)ethynyl)-1,2,3,4-tetrahydroisoquinoline **(4v)**


7.71
7.69
7.67
7.65
7.61
7.59
7.54
7.52
7.50
7.48
7.46
7.41
7.39
7.38
7.36
7.34
7.29
7.14
7.10
6.83
6.65
6.41
6.40
6.38
6.36
6.34
4.93
3.90
3.88
3.66
3.64
3.15
3.14
3.12
3.11
3.10
3.08
3.05
3.04
3.01
2.99
2.97
2.95
2.92
2.81
2.77
MeO
MeO
F3C
CF3
1.08
2.05
1.08
2.16
2.18
1.11
1.08
1.01
1.07
1.00
3.00
3.00
1.97
1.05
1.16
1.06
1.04
f1 (ppm)

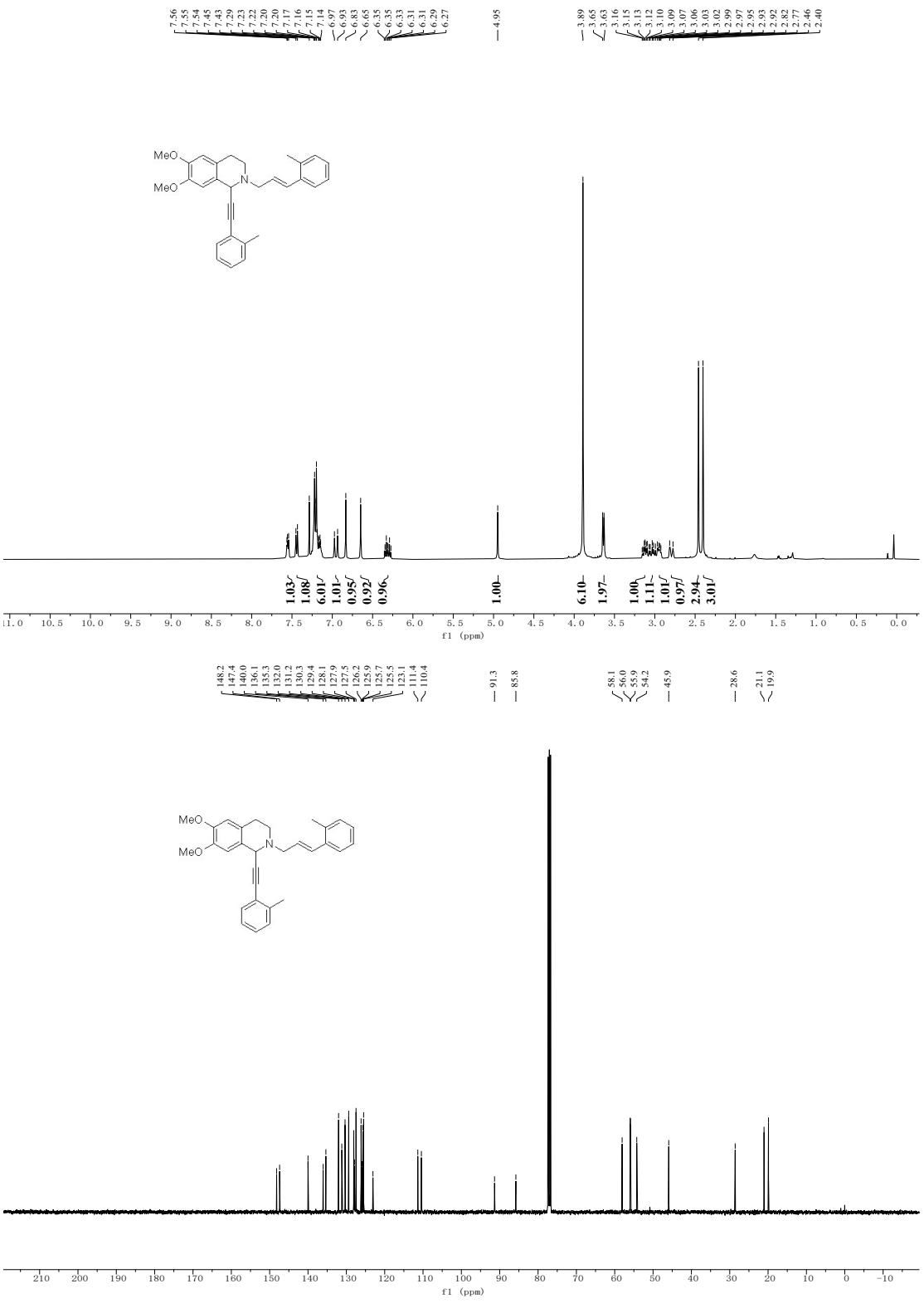

148.3
147.5
136.3
136.2
134.1
131.8
131.5
131.3
131.2
129.3
129.2
127.8
127.5
127.2
126.6
126.0
125.8
125.8
125.7
125.6
125.0
123.0
122.3
121.4
111.4
110.4
93.6
82.9
57.5
55.9
55.8
54.5
45.9
28.5
MeO
MeO
F3C
CF3
f1 (ppm)



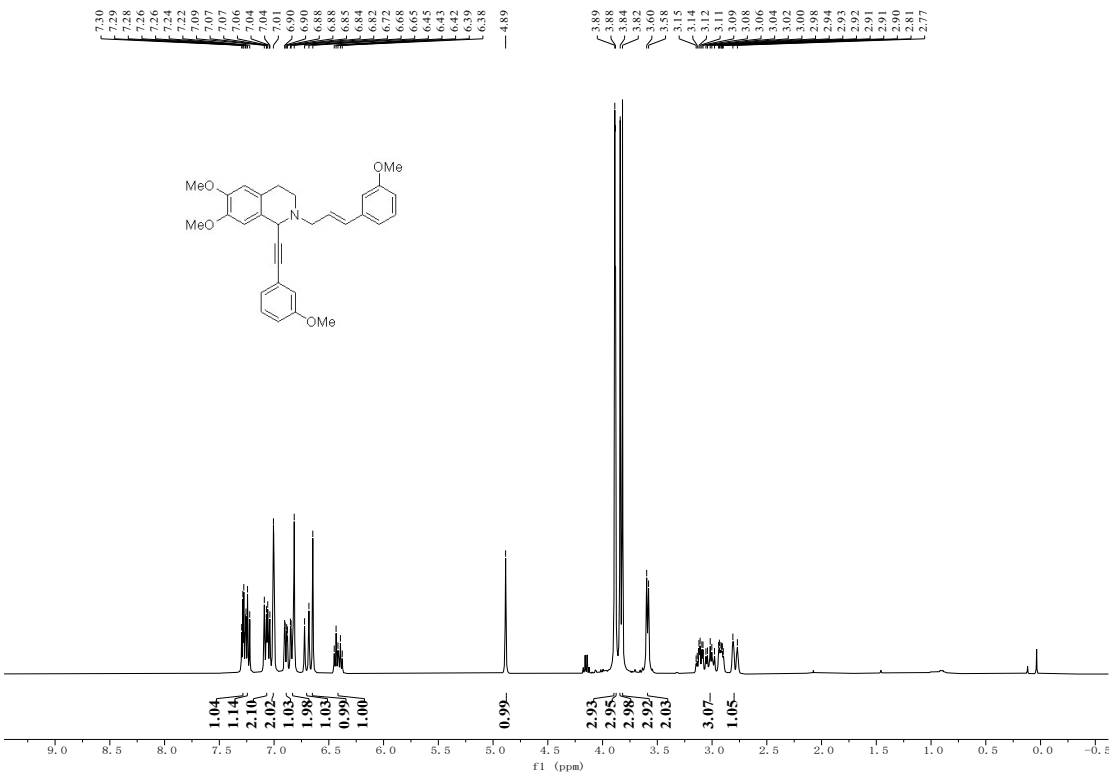
(E)-6,7-dimethoxy-2-(3-(m-tolyl)allyl)-1-(m-tolylethynyl)-1,2,3,4-tetrahydroisoquinoline **(4w)**

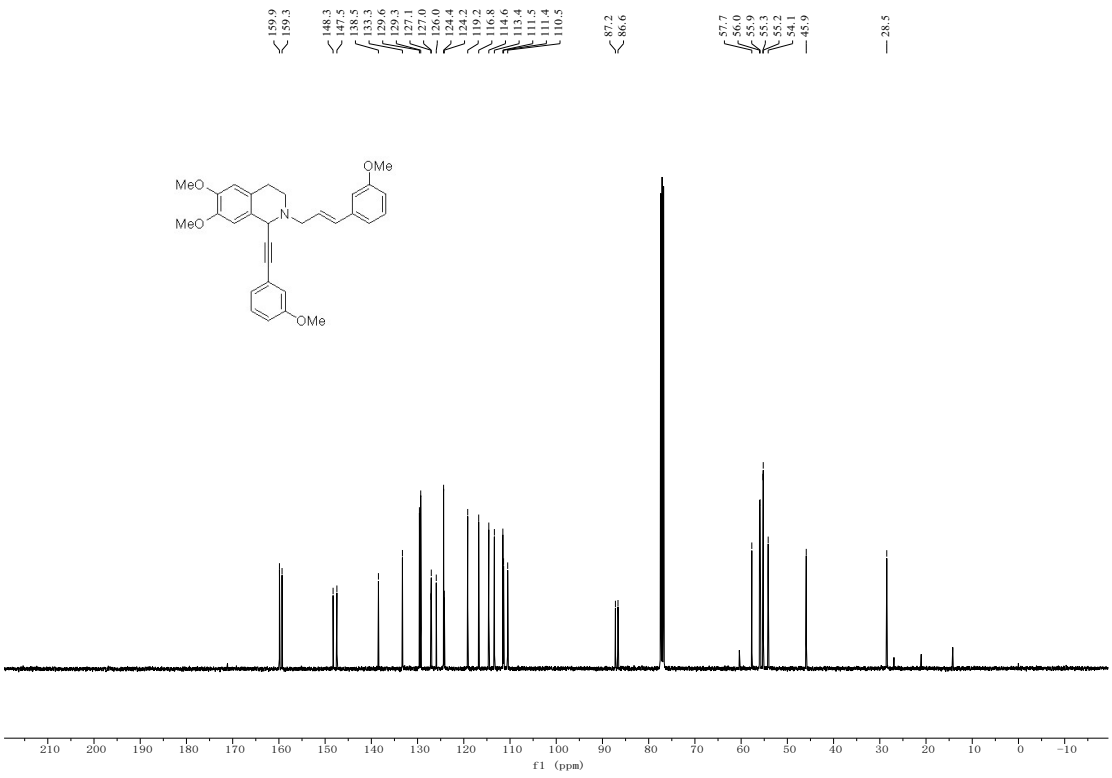


***(E)-6,7-dimethoxy-2-(3-(o-tolyl)allyl)-1-(o-tolylethynyl)-1,2,3,4-tetrahydroisoquinoline* (4x)**

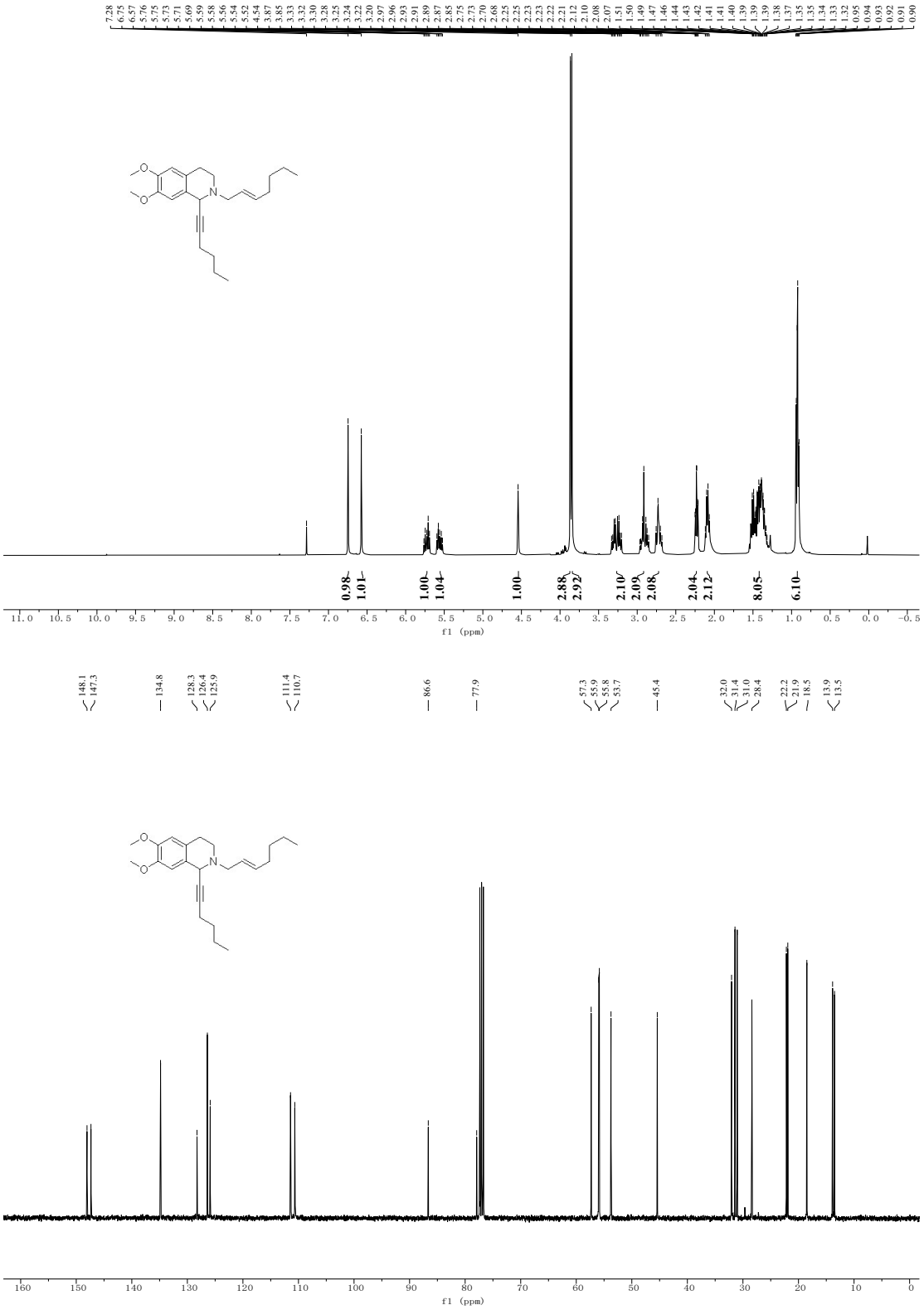


(E)-6,7-dimethoxy-2-(3-(3-methoxyphenyl)allyl)-1-((3-methoxyphenyl)ethynyl)-1,2,3,4-tetrahydroisoquinoline **(4y)**

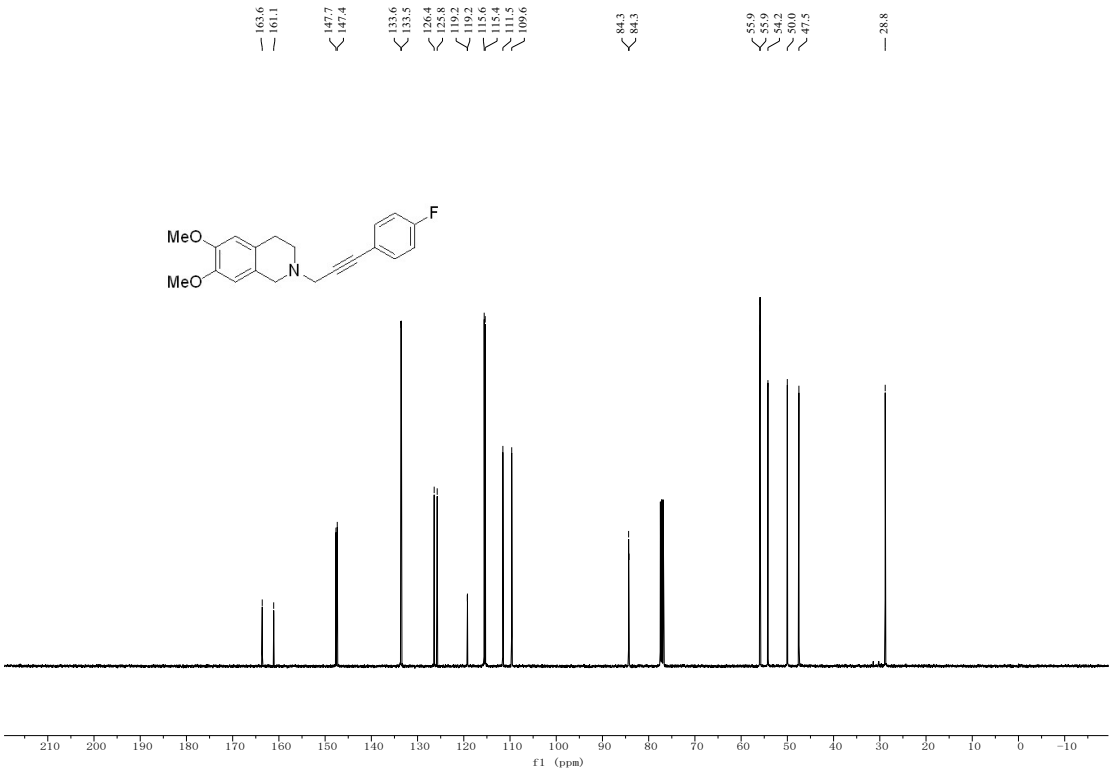

MeO
MeO
OMe
OMe
1.04
1.14
2.10
2.02
1.03
1.98
1.03
0.99
1.00
0.99
2.93
2.95
2.98
2.92
2.03
3.07
1.05
f1 (ppm)

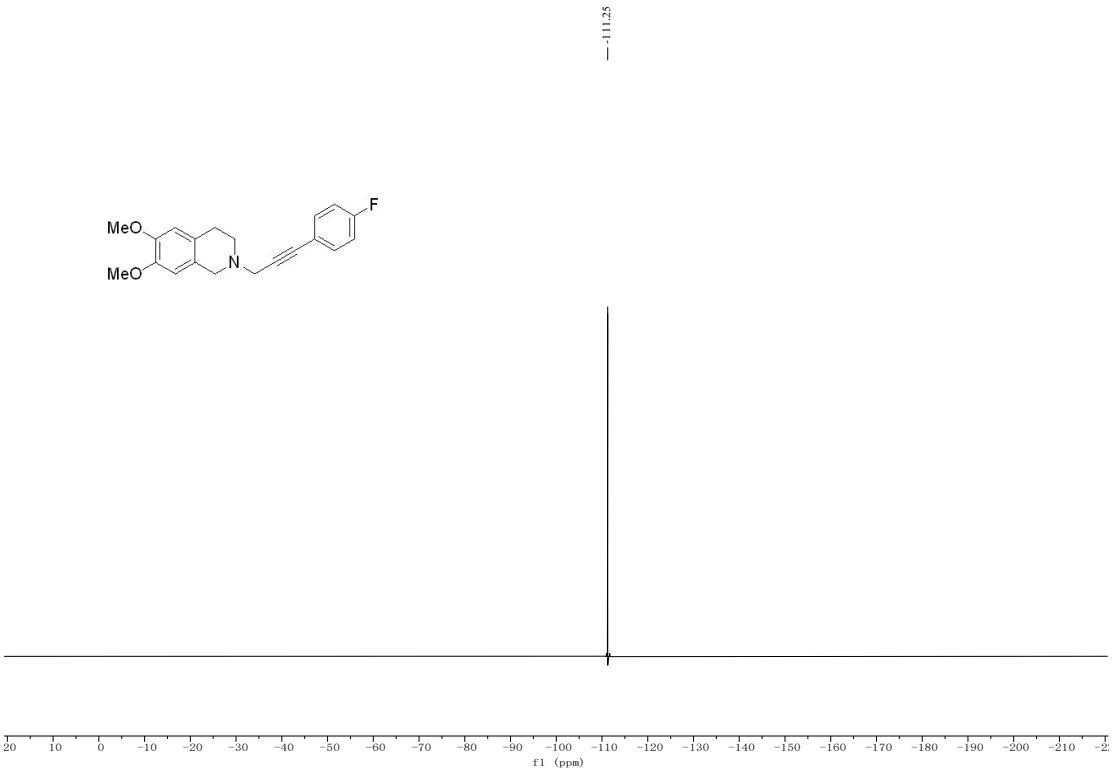

MeO
MeO
OMe
OMe
f1 (ppm)

***(E)-2-(hept-2-en-1-yl)-1-(hex-1-yn-1-yl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline*(4z)**

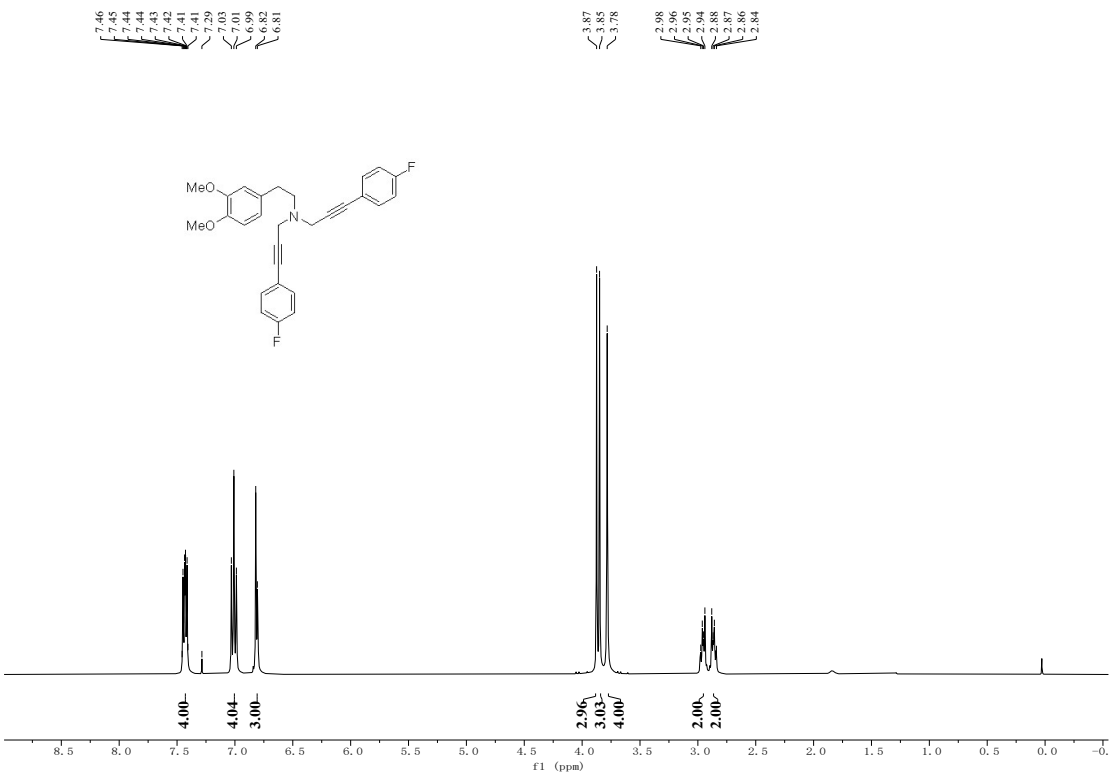


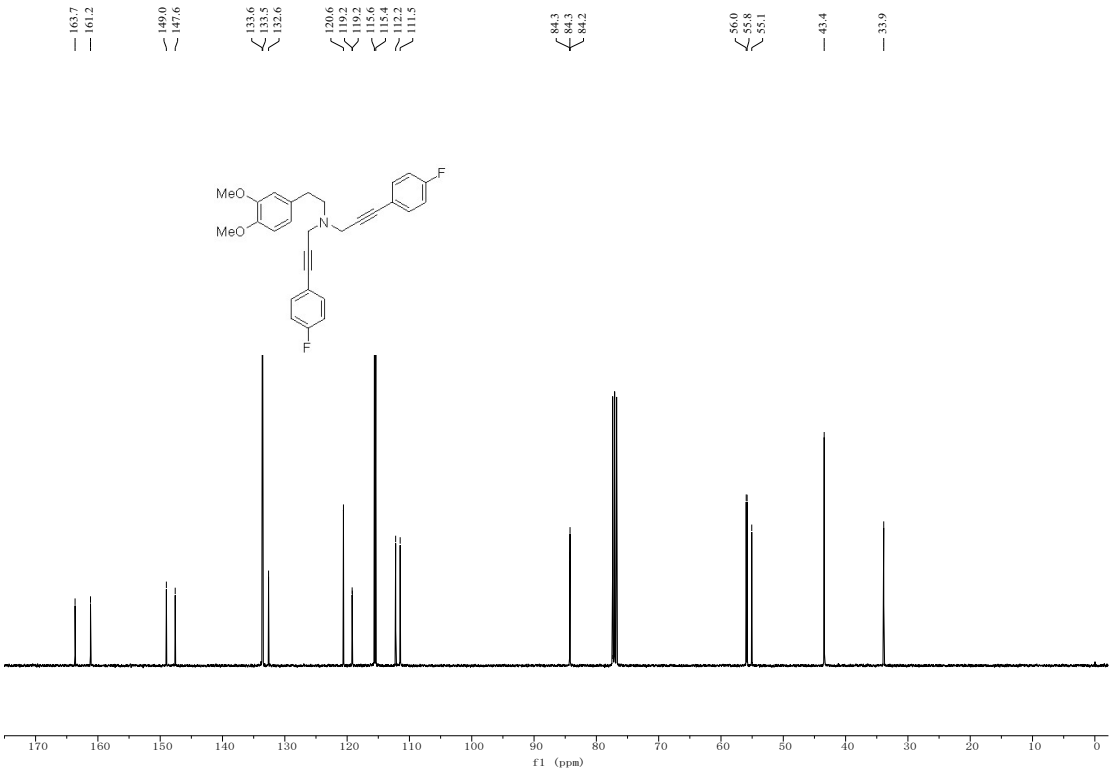
***2-(3-(4-fluorophenyl)prop-2-yn-1-yl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline*(5a)**

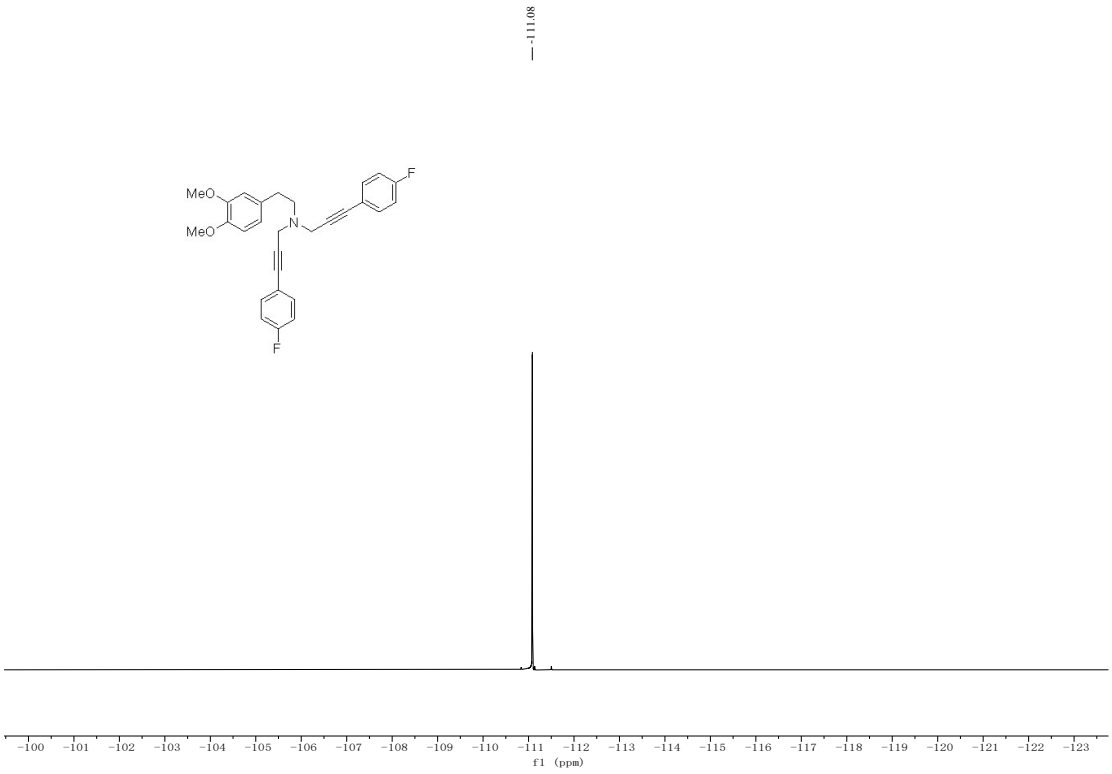




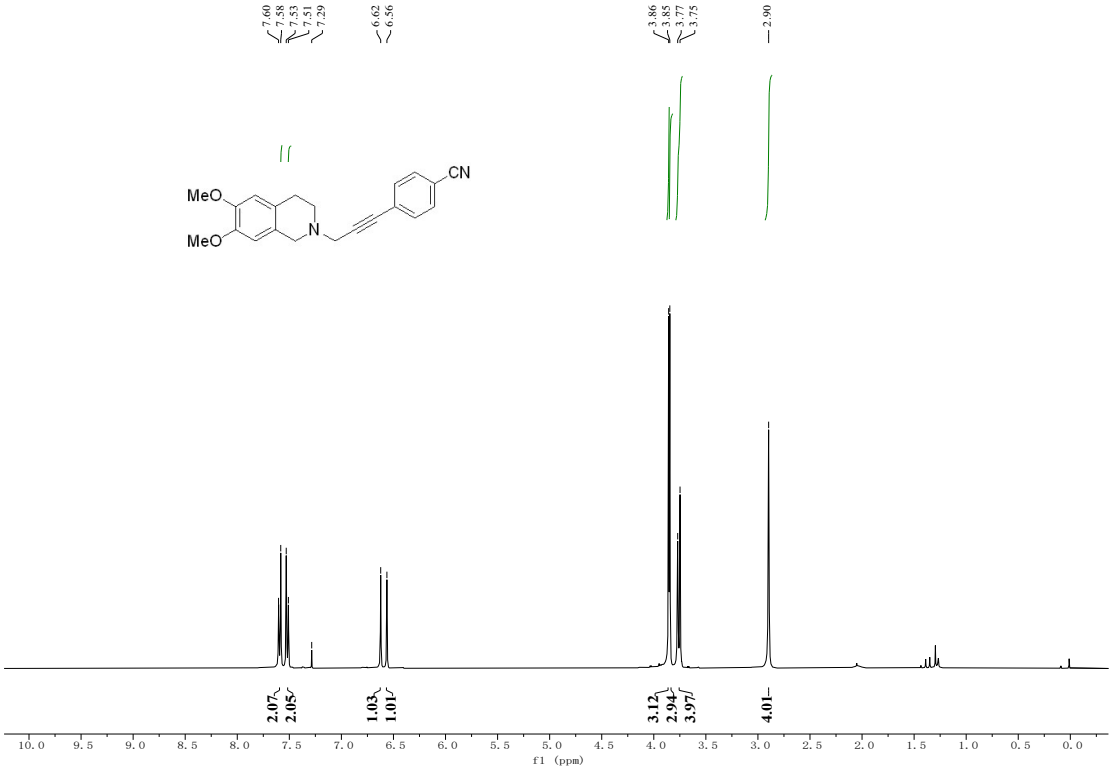
***N-(3,4-dimethoxyphenethyl)-3-(4-fluorophenyl)-N-(3-(4-fluorophenyl)prop-2-yn-1-yl)prop-2-yn-1-amine*(6)**

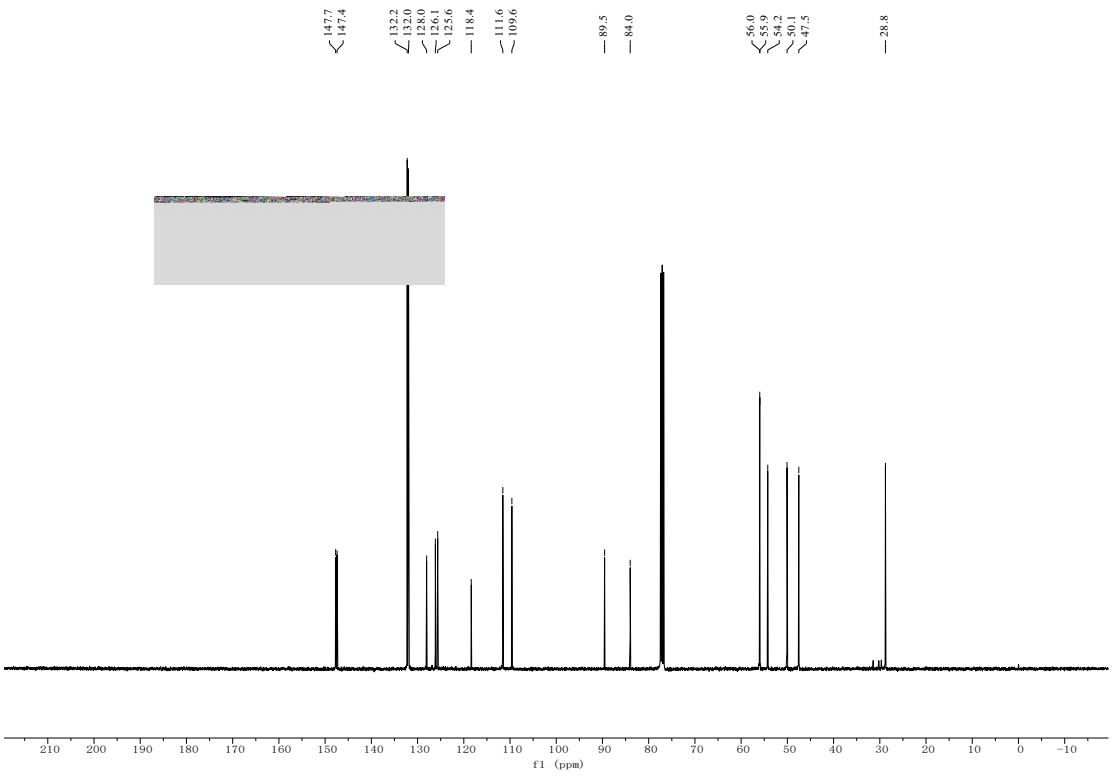

7.46
7.45
7.44
7.44
7.43
7.42
7.41
7.41
7.29
7.03
7.01
6.99
6.82
6.81
3.87
3.85
3.78
2.98
2.96
2.95
2.94
2.88
2.87
2.86
2.84
MeO
MeO
N
F
F
4.00
4.04
3.00
2.96
3.03
4.00
2.00
2.00
f1 (ppm)


163.7
161.2
149.0
147.6
133.6
133.5
132.6
120.6
119.2
119.2
115.6
115.4
112.2
111.5
84.3
84.3
84.2
56.0
55.8
55.1
43.4
33.9
MeO
MeO
N
F
F
f1 (ppm)

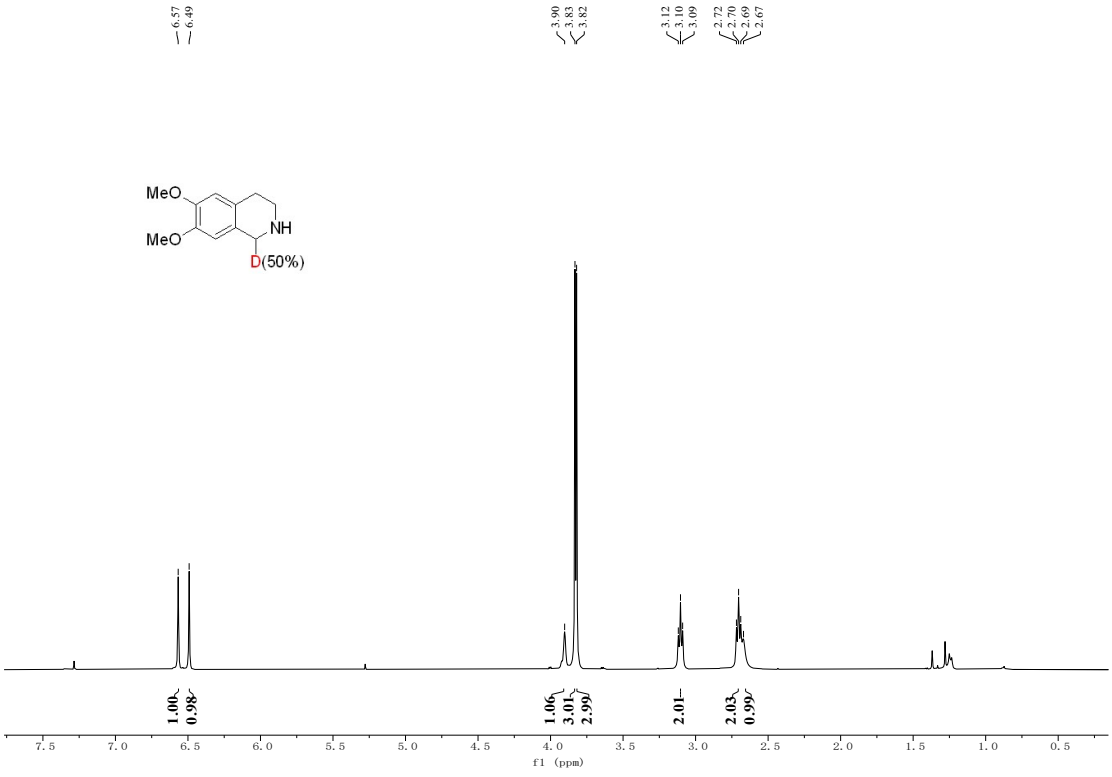


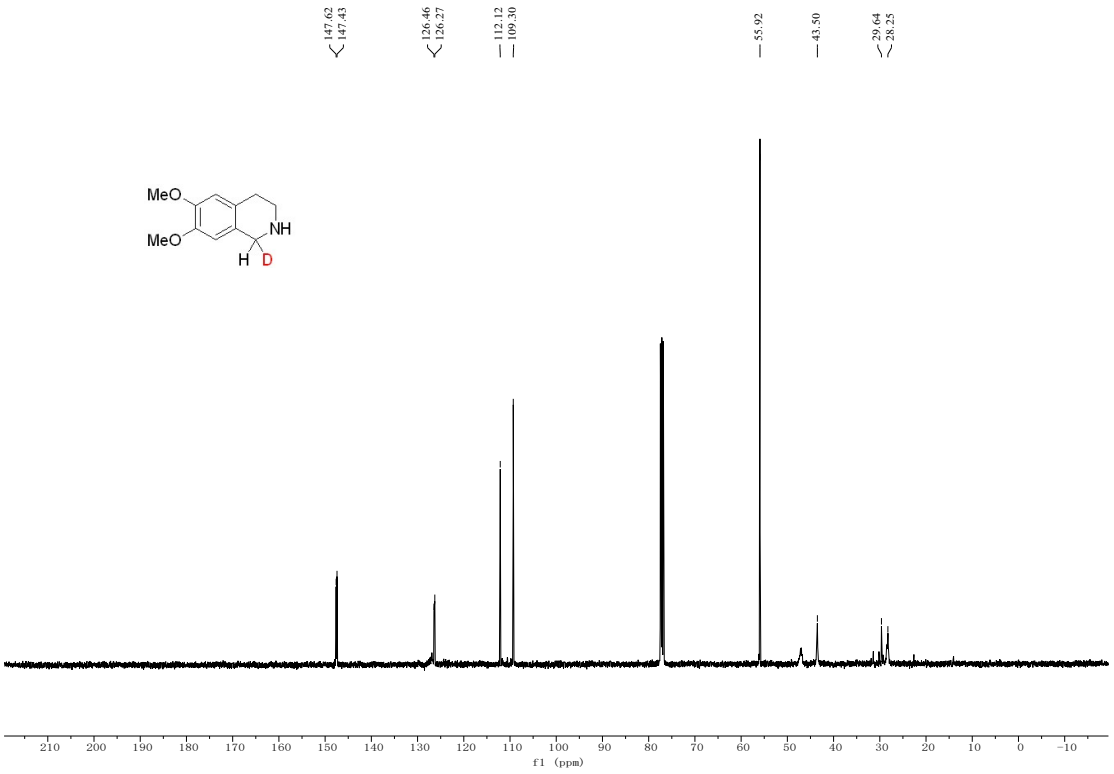
***4-(3-(6,7-dimethoxy-3,4-dihydroisoquinolin-2(1H)-yl)prop-1-yn-1-yl)benzonitrile*(5p)**

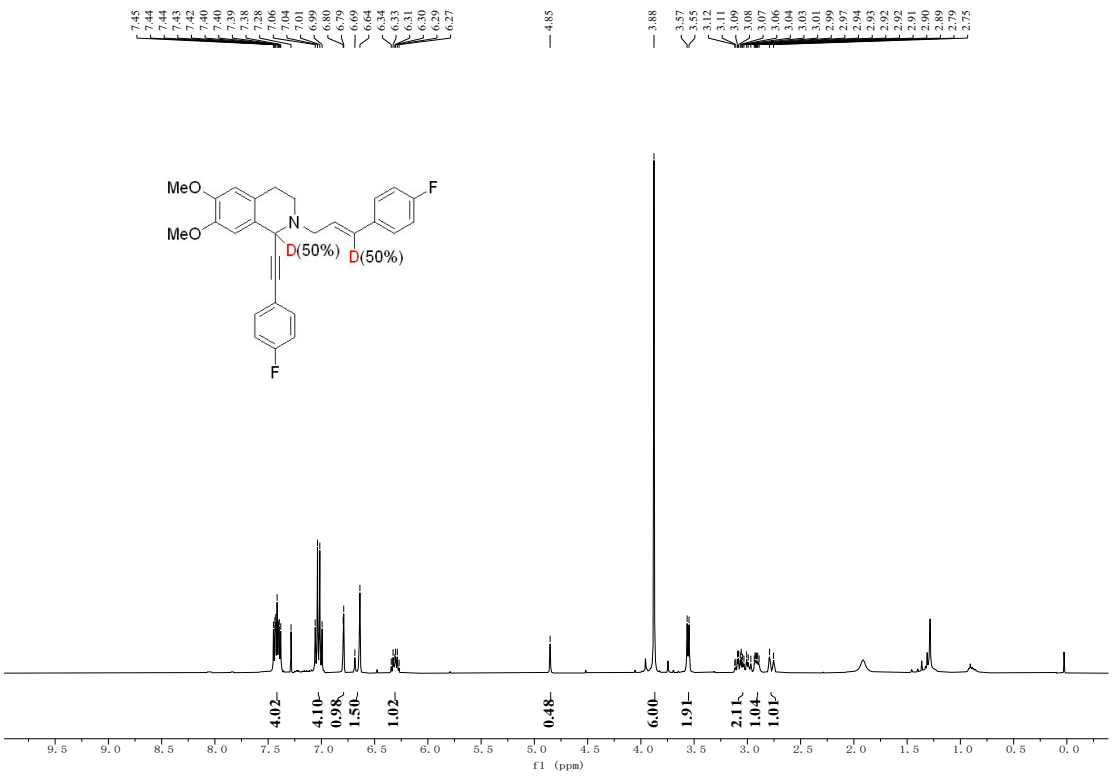


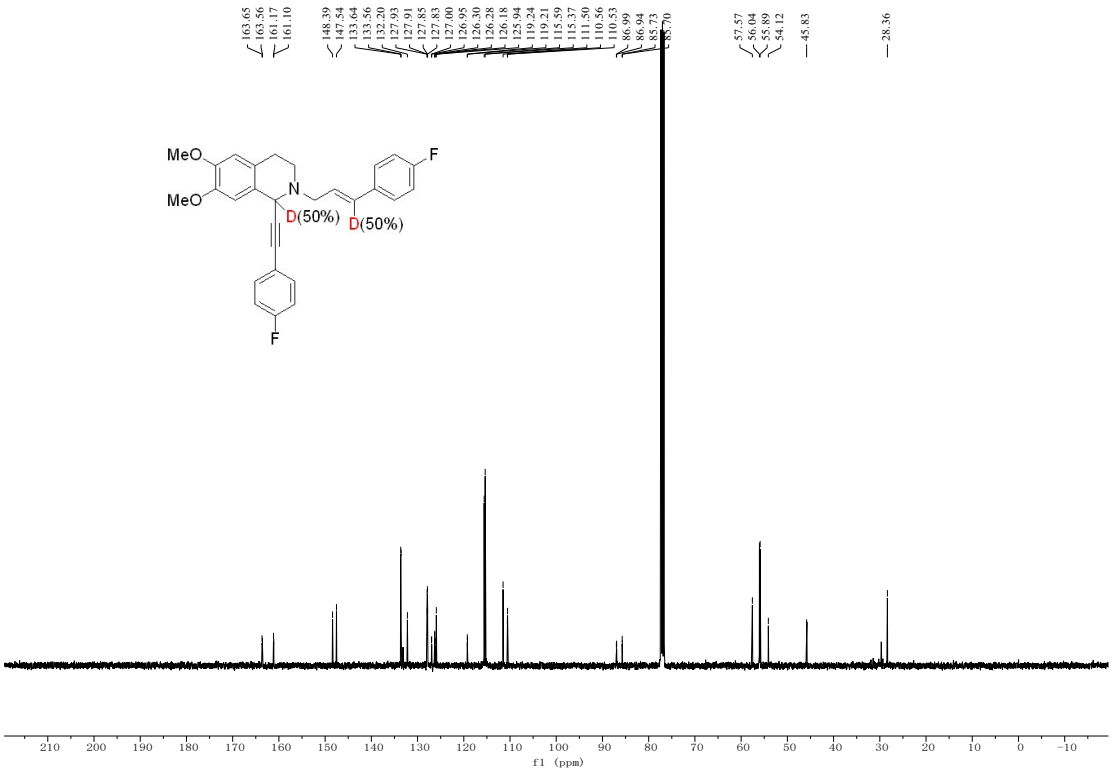


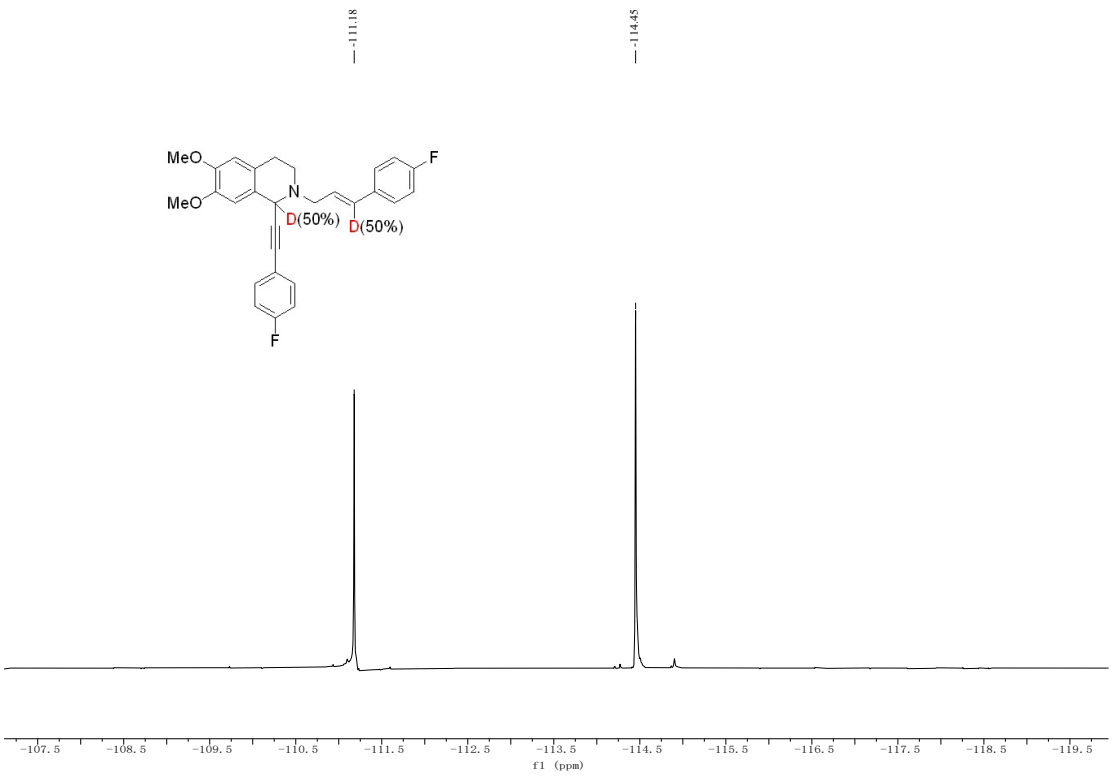
6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline(7p)




147.62
147.43
126.46
126.27
112.12
109.30
55.92
43.50
29.64
28.25
MeO
MeO
NH
H
D
f1 (ppm)


7.45
7.44
7.44
7.43
7.42
7.40
7.40
7.39
7.38
7.28
7.06
7.04
7.01
6.99
6.80
6.79
6.69
6.64
6.34
6.33
6.31
6.30
6.29
6.27
4.85
3.88
3.57
3.55
3.12
3.11
3.09
3.08
3.07
3.06
3.04
3.03
3.01
2.99
2.97
2.94
2.93
2.92
2.92
2.91
2.90
2.89
2.79
2.75
MeO
MeO
N
F
D(50%)
D(50%)
F
4.02
4.10
0.98
1.50
1.02
0.48
6.00
1.91
2.11
1.04
1.01
f1 (ppm)


163.65
163.56
161.17
161.10
148.39
147.54
133.64
133.56
132.20
127.93
127.91
127.85
127.83
127.00
126.95
126.30
126.28
126.18
125.94
119.24
119.21
115.59
115.37
111.50
110.56
110.53
86.99
86.94
85.73
57.57
56.04
55.89
54.12
45.83
28.36
MeO
MeO
N
D(50%)
D(50%)
F
F
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)


-111.18
-114.45
MeO
MeO
N
D(50%)
D(50%)
F
F
−107.5 −108.5 −109.5 −110.5 −111.5 −112.5 −113.5 −114.5 −115.5 −116.5 −117.5 −118.5 −119.5
f1 (ppm)