



Supporting Information

for

Electrocatalytic C(sp³)–H/C(sp)–H cross-coupling in continuous flow through TEMPO/copper relay catalysis

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General procedure, characterization data for electrolysis products and NMR spectra

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1. General information

1,1,1,3,3,3-Hexafluoro-2-propanol (HFIP) and 2,2,2-trifluoroethanol (TFE) were purchased from aladdin. Anhydrous acetonitrile was obtained by distillation from CaH₂/benzophenone. Flash column chromatography was performed with silica gel (100–200, 200–300 mesh). NMR spectra were recorded on Bruker AV-400 and Bruker AV-500 instruments. Data were reported as chemical shifts in ppm relative to CDCl₃ (7.26 ppm) for ¹H and CDCl₃ (77.2 ppm) for ¹³C. The abbreviations used for explaining the multiplicities were as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad.

2. General procedure for the flow electrolysis

The electrolysis was conducted using a flow electrolytic cell equipped with a Pt anode and a Pt cathode with a surface area of 10 cm² and an interelectrode distance of 250 μm. The solution of tetrahydroisoquinoline (0.03 M, 1.0 equiv), alkyne (0.45 M, 1.5 equiv), Cu(OTf)₂ (0.003 M, 10 mol %), TEMPO (0.006 M, 20 mol %), *n*-Bu₄NPF₆ (0.006 M, 0.2 equiv), and TFE (0.105 M, 3.5 equiv) in dry MeCN was stirred for 120 min at room temperature under air. The reaction solution was pumped *via* a micro syringe pump at a flow rate of 0.2 mL min⁻¹ through the flow electrolytic cell operated at a constant current of 30 mA. Once the electrolysis was stable, the outlet solution was collected for 35 min (7 mL). The solution was concentrated under reduced pressure on a rotary evaporator. The residue was chromatographed through silica gel eluting with ethyl acetate/hexanes to give the desired product.

3. Procedure for scale up

The solution of substrate 2-phenyl-1,2,3,4-tetrahydroisoquinoline (**1a**, 0.98 g, 4.68 mmol), 1-(*tert*-butyl)-4-ethynylbenzene (**22**, 1.11 g, 7.02 mmol), Cu(OTf)₂ (169.4 mg, 0.47 mmol), TEMPO (146.1 mg, 0.94 mmol), *n*-Bu₄NPF₆ (362.2 mg, 0.94 mmol), and TFE (1.2 mL) in dry

MeCN (156 mL) was stirred for 240 min at room temperature under air. The reaction solution was pumped *via* a micro syringe pump at a flow rate of 0.2 mL min⁻¹ through the flow electrolytic cell operated at a constant current of 30 mA. The combined organic solution was concentrated under reduced pressure on a rotary evaporator. The residue was chromatographed through silica gel eluting with ethyl acetate/hexanes to give **14** in 61% yield (1.05 g).

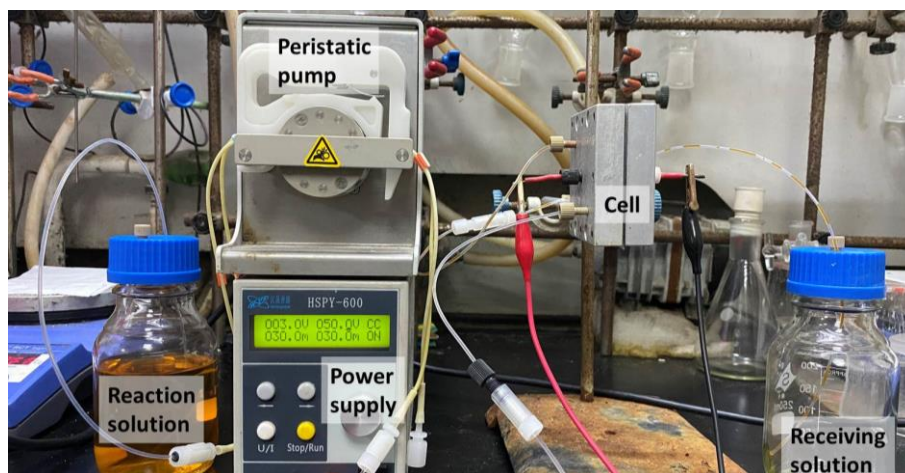
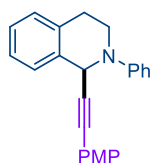


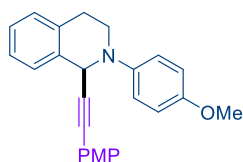
Figure S1. Reaction setup for scale up.

4. Characterization data for the electrolysis products

Note: all the products are known in the literature.

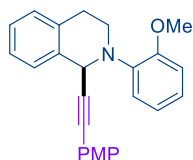


1-((4-Methoxyphenyl)ethynyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline¹ (3). Colorless oil, 61.2 mg, 86% yield. ¹H NMR (500 MHz, CDCl₃) δ 7.39 – 7.35 (m, 1H), 7.35 – 7.28 (m, 2H), 7.25 – 7.17 (m, 5H), 7.12 (d, *J* = 8.1 Hz, 2H), 6.88 (t, *J* = 7.3 Hz, 1H), 6.79 – 6.69 (m, 2H), 5.63 (s, 1H), 3.79 – 3.72 (m, 4H), 3.68 (ddd, *J* = 12.3, 10.2, 4.2 Hz, 1H), 3.14 (ddd, *J* = 16.2, 10.2, 6.0 Hz, 1H), 2.98 (dt, *J* = 16.1, 3.8 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 159.6, 149.8, 135.9, 134.6, 133.3, 129.3, 129.1, 127.6, 127.3, 126.4, 119.7, 116.9, 115.4, 113.9, 87.3, 84.8, 55.4, 52.5, 43.6, 29.1.



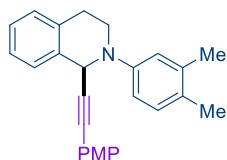
2-(4-Methoxyphenyl)-1-((4-methoxyphenyl)ethynyl)-1,2,3,4-tetrahydroisoquinoline¹ (4).

Colorless oil, 63.2 mg, 81% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.40 – 7.32 (m, 1H), 7.23 (q, *J* = 7.3, 6.0 Hz, 5H), 7.13 (d, *J* = 8.7 Hz, 2H), 6.96 – 6.84 (m, 2H), 6.76 (d, *J* = 8.3 Hz, 2H), 5.51 (s, 1H), 3.80 (s, 3H), 3.77 (s, 3H), 3.65 (td, *J* = 11.4, 4.1 Hz, 1H), 3.61 – 3.51 (m, 1H), 3.16 (ddd, *J* = 16.8, 10.7, 6.2 Hz, 1H), 2.94 (dt, *J* = 16.4, 3.4 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 159.5, 154.4, 144.4, 135.9, 134.2, 133.3, 129.2, 127.7, 127.2, 126.3, 120.3, 115.4, 114.6, 113.9, 87.2, 85.5, 55.8, 55.4, 54.6, 44.4, 29.2.



2-(2-Methoxyphenyl)-1-((4-methoxyphenyl)ethynyl)-1,2,3,4-tetrahydroisoquinoline¹ (5).

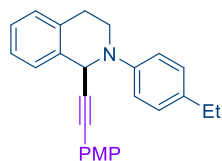
Colorless oil, 53.2 mg, 69% yield. ¹H NMR (500 MHz, CDCl₃) δ 7.37 – 7.32 (m, 1H), 7.25 – 7.21 (m, 3H), 7.21 – 7.16 (m, 3H), 7.09 (td, *J* = 7.7, 1.6 Hz, 1H), 7.00 (td, *J* = 7.6, 1.5 Hz, 1H), 6.93 (dd, *J* = 8.1, 1.4 Hz, 1H), 6.77 – 6.72 (m, 2H), 5.76 (s, 1H), 3.89 (s, 3H), 3.76 (s, 3H), 3.71 (td, *J* = 11.7, 4.2 Hz, 1H), 3.46 (ddt, *J* = 11.9, 6.4, 1.5 Hz, 1H), 3.26 (ddd, *J* = 17.3, 11.5, 6.4 Hz, 1H), 2.92 (ddd, *J* = 16.4, 4.2, 1.7 Hz, 1H). ¹³C NMR (126 MHz, CDCl₃) δ 159.4, 152.9, 140.0, 136.1, 133.9, 133.2, 129.3, 127.8, 127.0, 126.0, 123.7, 121.5, 120.9, 115.6, 113.8, 111.3, 87.5, 85.5, 55.7, 55.4, 53.1, 44.2, 29.4.



2-(3,4-Dimethylphenyl)-1-((4-methoxyphenyl)ethynyl)-1,2,3,4-tetrahydroisoquinoline¹ (6).

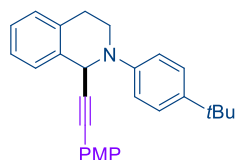
Yellow oil, 42.3 mg, 55% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.40 – 7.34 (m, 1H), 7.27 – 7.17 (m, 5H), 7.08 (d, *J* = 8.2 Hz, 1H), 6.96 (d, *J* = 2.6 Hz, 1H), 6.90 (dd, *J* = 8.2, 2.7 Hz, 1H), 6.79 – 6.73 (m, 2H), 5.59 (s, 1H), 3.77 (s, 3H), 3.74 – 3.61 (m, 2H), 3.15 (ddd, *J* = 16.5, 9.8, 6.9 Hz, 1H), 2.95 (dt, *J* = 16.2, 3.6 Hz, 1H), 2.29 (s, 3H), 2.22 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ

159.5, 148.1, 137.2, 136.0, 134.5, 133.3, 130.3, 129.1, 128.2, 127.6, 127.2, 126.3, 119.3, 115.5, 115.0, 113.9, 87.5, 85.1, 55.4, 53.1, 43.9, 29.2, 20.4, 19.0.



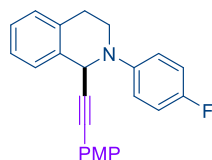
2-(4-Ethylphenyl)-1-((4-methoxyphenyl)ethynyl)-1,2,3,4-tetrahydroisoquinoline¹ (7).

Yellow oil, 55.2 mg, 72% yield. ¹H NMR (500 MHz, CDCl₃) δ 7.41 – 7.35 (m, 1H), 7.28 – 7.15 (m, 7H), 7.09 (d, *J* = 8.5 Hz, 2H), 6.79 – 6.73 (m, 2H), 5.61 (s, 1H), 3.77 (s, 3H), 3.73 – 3.64 (m, 2H), 3.16 (ddd, *J* = 16.5, 10.0, 6.6 Hz, 1H), 2.97 (dt, *J* = 16.1, 3.7 Hz, 1H), 2.63 (q, *J* = 7.6 Hz, 2H), 1.25 (t, *J* = 7.6 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 159.5, 147.9, 135.9, 135.8, 134.5, 133.3, 129.1, 128.6, 127.6, 127.2, 126.3, 117.5, 115.4, 113.9, 87.4, 85.0, 55.4, 53.0, 43.9, 29.1, 28.2, 16.0.



2-(4-(tert-Butyl)phenyl)-1-((4-methoxyphenyl)ethynyl)-1,2,3,4-tetrahydroisoquinoline¹ (8).

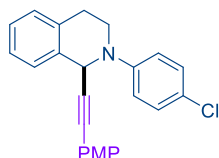
Colorless oil, 55.3 mg, 67% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.38 – 7.31 (m, 3H), 7.25 – 7.14 (m, 5H), 7.10 – 7.03 (m, 2H), 6.78 – 6.71 (m, 2H), 5.59 (s, 1H), 3.76 (s, 3H), 3.68 (tdd, *J* = 12.3, 8.2, 3.7 Hz, 2H), 3.13 (ddd, *J* = 16.2, 10.1, 6.2 Hz, 1H), 2.95 (dt, *J* = 16.1, 3.7 Hz, 1H), 1.31 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 159.5, 147.4, 142.5, 136.0, 134.6, 133.4, 129.1, 127.6, 127.3, 126.4, 126.1, 116.7, 115.5, 113.9, 87.5, 84.9, 55.5, 52.7, 43.8, 34.2, 31.7, 29.2.



2-(4-Fluorophenyl)-1-((4-methoxyphenyl)ethynyl)-1,2,3,4-tetrahydroisoquinoline¹ (9).

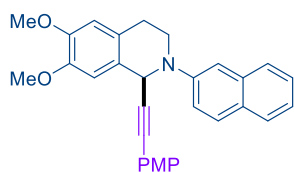
Yellow oil, 50.0 mg, 67% yield. ¹H NMR (500 MHz, CDCl₃) δ 7.36 (dt, *J* = 7.4, 3.7 Hz, 1H), 7.27 – 7.18 (m, 5H), 7.12 – 7.07 (m, 2H), 7.03 (t, *J* = 8.7 Hz, 2H), 6.79 – 6.74 (m, 2H), 5.54 (s, 1H), 3.76 (s, 3H), 3.63 (dddd, *J* = 21.1, 15.2, 11.3, 6.5 Hz, 2H), 3.15 (ddd, *J* = 16.5, 10.5, 6.2

Hz, 1H), 2.96 (dt, $J = 16.2, 3.6$ Hz, 1H). ^{13}C NMR (126 MHz, CDCl_3) δ 159.5, 157.5 (d, $J = 239.0$ Hz), 146.6, 146.6, 135.5, 134.1, 133.2, 128.3 (d, $J = 190.3$ Hz), 126.8 (d, $J = 121.2$ Hz), 119.4 (d, $J = 7.7$ Hz), 115.7, 115.5, 115.1, 113.8, 86.8, 85.3, 55.3, 53.8, 44.1, 29.1. ^{19}F NMR (471 MHz, CDCl_3) δ -124.1.



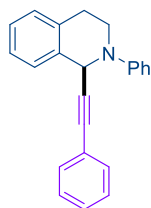
2-(4-Chlorophenyl)-1-((4-methoxyphenyl)ethynyl)-1,2,3,4-tetrahydroisoquinoline¹ (10).

Yellow oil, 59.1 mg, 75% yield. ^1H NMR (500 MHz, CDCl_3) δ 7.35 (dd, $J = 5.4, 3.6$ Hz, 1H), 7.24 (dd, $J = 5.2, 1.9$ Hz, 4H), 7.22 (d, $J = 2.7$ Hz, 2H), 7.20 – 7.16 (m, 1H), 7.05 – 7.00 (m, 2H), 6.78 – 6.72 (m, 2H), 5.56 (s, 1H), 3.75 (s, 3H), 3.71 – 3.59 (m, 2H), 3.12 (ddd, $J = 16.1, 9.8, 6.3$ Hz, 1H), 2.97 (dt, $J = 16.0, 3.9$ Hz, 1H). ^{13}C NMR (126 MHz, CDCl_3) δ 159.6, 148.3, 135.4, 134.2, 133.3, 129.1, 129.0, 127.5, 127.4, 126.5, 124.5, 118.0, 115.0, 113.9, 86.7, 84.9, 55.4, 52.4, 43.7, 29.0.



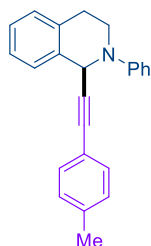
6,7-Dimethoxy-1-((4-methoxyphenyl)ethynyl)-2-(naphthalen-2-yl)-1,2,3,4-

tetrahydroisoquinoline¹ (11). White solid, 60.9 mg, 64% yield. ^1H NMR (500 MHz, CDCl_3) δ 7.78 (d, $J = 8.8$ Hz, 1H), 7.73 (dd, $J = 8.2, 3.4$ Hz, 2H), 7.41 (ddd, $J = 8.3, 4.9, 2.2$ Hz, 3H), 7.32 – 7.27 (m, 1H), 7.25 – 7.20 (m, 2H), 6.91 (s, 1H), 6.76 – 6.70 (m, 2H), 6.68 (s, 1H), 5.70 (s, 1H), 3.95 – 3.86 (m, 7H), 3.79 – 3.70 (m, 4H), 3.13 (ddd, $J = 16.6, 11.0, 6.0$ Hz, 1H), 2.89 (dt, $J = 15.8, 3.3$ Hz, 1H). ^{13}C NMR (126 MHz, CDCl_3) δ 159.6, 148.5, 147.9, 147.6, 134.9, 133.4, 128.9, 128.7, 127.6, 127.6, 127.0, 126.5, 126.4, 123.5, 119.7, 115.3, 113.9, 111.8, 111.7, 110.5, 87.3, 85.1, 56.3, 56.2, 55.4, 52.4, 43.8, 28.7.

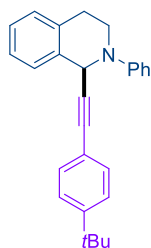


2-Phenyl-1-(phenylethynyl)-1,2,3,4-tetrahydroisoquinoline² (12). Colorless oil, 45.4 mg, 70%

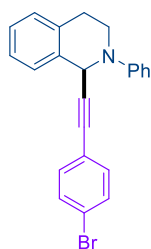
yield. ^1H NMR (500 MHz, CDCl_3) δ 7.38 – 7.34 (m, 1H), 7.33 – 7.25 (m, 4H), 7.20 (tdd, J = 11.3, 5.6, 3.5 Hz, 6H), 7.11 (d, J = 8.1 Hz, 2H), 6.88 (t, J = 7.3 Hz, 1H), 5.63 (s, 1H), 3.74 (ddd, J = 12.7, 6.1, 3.5 Hz, 1H), 3.66 (ddd, J = 12.4, 10.3, 4.2 Hz, 1H), 3.13 (ddd, J = 16.3, 10.3, 6.0 Hz, 1H), 2.96 (dt, J = 16.0, 3.8 Hz, 1H). ^{13}C NMR (126 MHz, CDCl_3) δ 149.8, 135.6, 134.6, 131.9, 129.3, 129.1, 128.3, 128.2, 127.6, 127.4, 126.5, 123.2, 119.8, 116.9, 88.8, 85.0, 52.5, 43.6, 29.1.



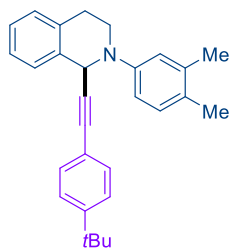
2-Phenyl-1-(p-tolylethynyl)-1,2,3,4-tetrahydroisoquinoline² (13). Colorless oil, 54.9 mg, 81% yield. ^1H NMR (500 MHz, CDCl_3) δ 7.34 – 7.29 (m, 1H), 7.29 – 7.23 (m, 2H), 7.20 – 7.16 (m, 2H), 7.16 – 7.11 (m, 3H), 7.09 – 7.04 (m, 2H), 6.96 (d, J = 7.9 Hz, 2H), 6.83 (tt, J = 7.3, 1.1 Hz, 1H), 5.58 (s, 1H), 3.72 – 3.66 (m, 1H), 3.62 (ddd, J = 12.3, 10.2, 4.2 Hz, 1H), 3.08 (ddd, J = 16.1, 10.2, 6.0 Hz, 1H), 2.92 (dt, J = 16.1, 3.8 Hz, 1H), 2.23 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 149.8, 138.2, 135.8, 134.6, 131.8, 129.3, 129.1, 129.0, 127.6, 127.3, 126.4, 120.1, 119.7, 116.9, 88.0, 85.1, 52.5, 43.6, 29.1, 21.6.



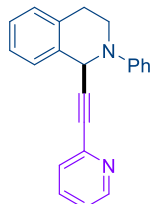
1-((4-(tert-Butyl)phenyl)ethynyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline² (14). Yellow oil, 60.1 mg, 78% yield. ^1H NMR (400 MHz, CDCl_3) δ 7.43 (dd, J = 5.3, 3.6 Hz, 1H), 7.40 – 7.34 (m, 2H), 7.28 (d, J = 10.4 Hz, 6H), 7.27 – 7.22 (m, 1H), 7.21 – 7.16 (m, 2H), 6.94 (tt, J = 7.2, 1.1 Hz, 1H), 5.70 (s, 1H), 3.80 (dddd, J = 12.5, 6.2, 3.5, 1.0 Hz, 1H), 3.73 (ddd, J = 12.3, 10.1, 4.2 Hz, 1H), 3.19 (ddd, J = 16.1, 10.1, 6.1 Hz, 1H), 3.03 (dt, J = 16.1, 3.8 Hz, 1H), 1.32 (s, 9H). ^{13}C NMR (101 MHz, CDCl_3) δ 151.4, 149.8, 135.7, 134.5, 131.6, 129.3, 129.1, 127.6, 127.3, 126.4, 125.2, 120.2, 119.8, 116.9, 88.1, 85.0, 52.6, 43.6, 34.9, 31.3, 29.1.



1-((4-Bromophenyl)ethynyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline³ (15). Colorless oil, 58.0 mg, 71% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.40 – 7.28 (m, 5H), 7.23 (ddd, *J* = 10.6, 6.4, 3.6 Hz, 3H), 7.18 – 7.07 (m, 4H), 6.90 (tt, *J* = 7.2, 1.1 Hz, 1H), 5.63 (s, 1H), 3.76 (dddd, *J* = 12.3, 6.0, 3.5, 1.1 Hz, 1H), 3.65 (ddd, *J* = 12.3, 10.2, 4.2 Hz, 1H), 3.15 (ddd, *J* = 16.2, 10.2, 5.9 Hz, 1H), 2.98 (dt, *J* = 16.1, 3.9 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 149.7, 135.3, 134.6, 133.4, 131.5, 129.4, 129.2, 127.6, 127.5, 126.5, 122.4, 122.1, 120.0, 116.9, 90.0, 83.9, 52.6, 43.6, 29.1.

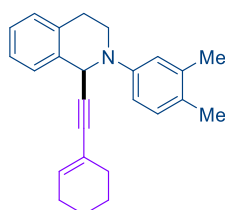


1-((4-(tert-Butyl)phenyl)ethynyl)-2-(3,4-dimethylphenyl)-1,2,3,4-tetrahydroisoquinoline¹ (16). Yellow oil, 56.4 mg, 68% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.42 – 7.36 (m, 1H), 7.31 – 7.18 (m, 7H), 7.10 (d, *J* = 8.2 Hz, 1H), 6.99 (d, *J* = 2.6 Hz, 1H), 6.93 (dd, *J* = 8.2, 2.7 Hz, 1H), 5.62 (s, 1H), 3.76 – 3.63 (m, 2H), 3.17 (ddd, *J* = 16.5, 9.8, 6.8 Hz, 1H), 2.97 (dt, *J* = 16.2, 3.6 Hz, 1H), 2.31 (s, 3H), 2.24 (s, 3H), 1.30 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 151.3, 148.1, 137.2, 135.9, 134.5, 131.6, 130.3, 129.1, 128.3, 127.6, 127.2, 126.3, 125.2, 120.3, 119.3, 115.1, 88.3, 85.4, 53.2, 43.9, 34.9, 31.3, 29.2, 20.4, 19.0.



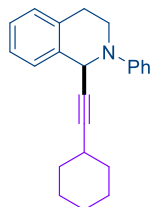
2-Phenyl-1-(pyridin-2-ylethynyl)-1,2,3,4-tetrahydroisoquinoline⁴ (17). Colorless oil, 46.6 mg, 72% yield. ¹H NMR (400 MHz, CDCl₃) δ 8.54 – 8.46 (m, 1H), 7.54 (td, *J* = 7.8, 1.8 Hz, 1H), 7.42 – 7.38 (m, 1H), 7.36 – 7.29 (m, 2H), 7.29 – 7.26 (m, 1H), 7.21 (dtd, *J* = 9.4, 5.6, 3.7

Hz, 3H), 7.14 (dd, $J = 7.9, 5.3$ Hz, 3H), 6.89 (t, $J = 7.3$ Hz, 1H), 5.69 (s, 1H), 3.79 (ddd, $J = 12.5, 6.0, 3.6$ Hz, 1H), 3.72 (ddd, $J = 12.4, 10.0, 4.2$ Hz, 1H), 3.16 (ddd, $J = 16.1, 10.0, 6.1$ Hz, 1H), 3.00 (dt, $J = 16.1, 3.9$ Hz, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 150.0, 149.5, 143.3, 136.1, 134.8, 134.7, 129.4, 129.1, 127.7, 127.6, 127.5, 126.6, 122.8, 119.8, 116.6, 88.9, 84.4, 52.2, 43.7, 29.0.

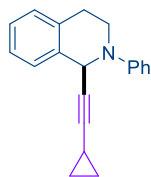


1-(Cyclohex-1-en-1-ylethynyl)-2-(3,4-dimethylphenyl)-1,2,3,4-tetrahydroisoquinoline¹

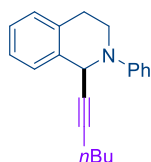
(18). Colorless oil, 54.1 mg, 76% yield. ^1H NMR (400 MHz, CDCl_3) δ 7.32 (dd, $J = 5.5, 3.6$ Hz, 1H), 7.25 – 7.15 (m, 3H), 7.08 (d, $J = 8.2$ Hz, 1H), 6.93 (d, $J = 2.6$ Hz, 1H), 6.87 (dd, $J = 8.2, 2.7$ Hz, 1H), 6.05 – 5.92 (m, 1H), 5.50 (s, 1H), 3.72 – 3.56 (m, 2H), 3.13 (ddd, $J = 16.5, 10.3, 6.4$ Hz, 1H), 2.93 (dt, $J = 16.1, 3.6$ Hz, 1H), 2.29 (s, 3H), 2.23 (s, 3H), 2.03 (p, $J = 4.2, 3.4$ Hz, 4H), 1.64 – 1.49 (m, 4H). ^{13}C NMR (101 MHz, CDCl_3) δ 148.1, 137.1, 136.3, 134.5, 134.4, 130.2, 129.1, 128.0, 127.6, 127.1, 126.2, 120.7, 119.2, 114.9, 87.1, 86.0, 52.9, 43.8, 29.5, 29.1, 25.7, 22.4, 21.7, 20.4, 19.0.



1-(Cyclohexylethynyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline² (19). Yellow oil, 41.5 mg, 63% yield. ^1H NMR (500 MHz, CDCl_3) δ 7.31 (ddd, $J = 8.9, 6.1, 3.3$ Hz, 3H), 7.24 – 7.15 (m, 3H), 7.09 (d, $J = 8.1$ Hz, 2H), 6.88 (t, $J = 7.3$ Hz, 1H), 5.45 (s, 1H), 3.71 (ddd, $J = 12.4, 5.9, 3.4$ Hz, 1H), 3.59 (ddd, $J = 12.3, 10.5, 4.2$ Hz, 1H), 3.11 (ddd, $J = 16.3, 10.5, 5.9$ Hz, 1H), 2.94 (dt, $J = 16.0, 3.8$ Hz, 1H), 2.39 – 2.26 (m, 1H), 1.65 (ddd, $J = 11.6, 7.3, 3.5$ Hz, 2H), 1.57 (dtt, $J = 13.5, 6.9, 3.4$ Hz, 2H), 1.38 – 1.17 (m, 6H). ^{13}C NMR (126 MHz, CDCl_3) δ 149.9, 136.5, 134.3, 129.1, 128.9, 127.5, 127.0, 126.2, 119.5, 116.9, 89.5, 79.3, 52.1, 43.3, 32.8, 32.7, 29.1, 29.1, 26.1, 24.7.

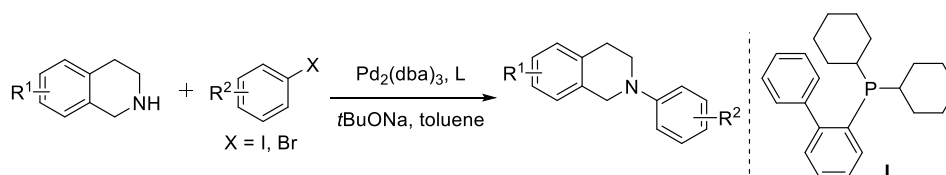


1-(Cyclopropylethynyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline² (20). Colorless oil, 32.9 mg, 57% yield. ¹H NMR (500 MHz, CDCl₃) δ 7.31 (dt, *J* = 9.1, 6.3 Hz, 3H), 7.21 (dt, *J* = 7.3, 3.8 Hz, 2H), 7.19 – 7.15 (m, 1H), 7.06 (d, *J* = 8.0 Hz, 2H), 6.90 – 6.85 (m, 1H), 5.40 (s, 1H), 3.70 (ddt, *J* = 10.5, 3.9, 2.3 Hz, 1H), 3.60 (ddd, *J* = 12.3, 10.4, 4.2 Hz, 1H), 3.10 (ddd, *J* = 16.2, 10.4, 5.9 Hz, 1H), 2.94 (dt, *J* = 16.1, 3.9 Hz, 1H), 1.16 (dddd, *J* = 13.2, 8.2, 4.9, 1.6 Hz, 1H), 0.67 (dt, *J* = 8.2, 3.1 Hz, 2H), 0.55 (dt, *J* = 4.7, 3.1 Hz, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 149.8, 136.3, 134.4, 129.2, 129.0, 127.5, 127.2, 126.3, 119.5, 116.7, 88.5, 74.5, 51.9, 43.4, 29.0, 8.5, -0.2.



1-(Hex-1-yn-1-yl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline² (21). Yellow oil, 24.1 mg, 40% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.31 (td, *J* = 7.2, 3.2 Hz, 3H), 7.20 (ddd, *J* = 13.2, 7.8, 3.8 Hz, 3H), 7.12 – 7.04 (m, 2H), 6.88 (t, *J* = 7.3 Hz, 1H), 5.43 (s, 1H), 3.71 (ddd, *J* = 12.4, 6.0, 3.6 Hz, 1H), 3.60 (ddd, *J* = 12.2, 10.3, 4.2 Hz, 1H), 3.11 (ddd, *J* = 16.2, 10.3, 6.0 Hz, 1H), 2.94 (dt, *J* = 16.1, 3.9 Hz, 1H), 2.11 (td, *J* = 7.0, 2.0 Hz, 2H), 1.43 – 1.34 (m, 2H), 1.33 – 1.23 (m, 2H), 0.84 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 149.9, 136.4, 134.4, 129.2, 129.0, 127.5, 127.1, 126.3, 119.5, 116.8, 85.4, 79.3, 52.0, 43.4, 31.0, 29.1, 22.0, 18.7, 13.7.

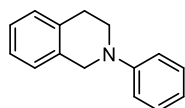
5. Synthesis and characterization for the 2-aryl-1,2,3,4-tetrahydroisoquinolines



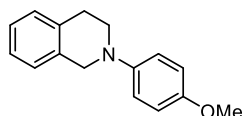
Scheme S1. General reaction for synthesizing of 2-aryl-1,2,3,4-tetrahydroisoquinolines.

General Procedure: The substrates were prepared by following a modified reported procedure.⁵ A mixture of Pd₂(dba)₃ (3 mol %), ligand (2-(dicyclohexylphosphino)biphenyl) (8 mol %) and 15 mL of dry toluene were placed in an oven-dried tube. The tube was sealed and the solution was degassed with bubbling argon for 1 h. Aryl halide (1.0 equiv), 1,2,3,4-tetrahydroisoquinolines (1.2 equiv), and *t*-BuONa (1.4 equiv) were added sequentially. Then the reaction mixture was heated at 100 °C for 12 h. The reaction mixture was cooled to room temperature, quenched by adding water, and extracted with ethyl acetate. The organic layer was dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel using hexanes/ethyl acetate as the eluent to afford the desired products.

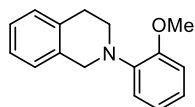
Note: all the substrates are known in the literature.



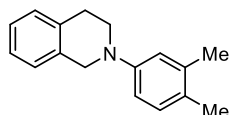
2-Phenyl-1,2,3,4-tetrahydroisoquinoline¹ (1a) was synthesized following **General Procedure** from 1,2,3,4-tetrahydroisoquinoline and iodobenzene. Colorless oil, 60% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.29 (m, 2H), 7.26 – 7.14 (m, 4H), 7.08 – 6.96 (m, 2H), 6.87 (tt, *J* = 7.3, 1.1 Hz, 1H), 4.45 (s, 2H), 3.60 (t, *J* = 5.9 Hz, 2H), 3.02 (t, *J* = 5.8 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 150.8, 135.1, 134.7, 129.4, 128.7, 126.7, 126.5, 126.2, 118.9, 115.3, 51.0, 46.7, 29.3.



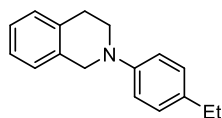
2-(4-Methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline¹ (1b) was synthesized following **General Procedure** from 1,2,3,4-tetrahydroisoquinoline and 1-iodo-4-methoxybenzene. White solid, 41% yield. ¹H NMR (500 MHz, CDCl₃) δ 7.20 – 7.10 (m, 4H), 7.01 – 6.95 (m, 2H), 6.90 – 6.84 (m, 2H), 4.30 (s, 2H), 3.78 (s, 3H), 3.45 (t, *J* = 5.9 Hz, 2H), 2.99 (t, *J* = 5.9 Hz, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 153.7, 145.6, 134.8, 134.8, 128.9, 126.7, 126.5, 126.1, 118.2, 114.8, 55.9, 52.9, 48.7, 29.3.



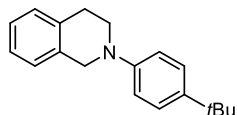
2-(2-Methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline¹ (1c) was synthesized following **General Procedure** from 1,2,3,4-tetrahydroisoquinoline and 1-iodo-2-methoxybenzene. Yellow oil, 33% yield. ¹H NMR (500 MHz, CDCl₃) δ 7.19 – 7.12 (m, 3H), 7.12 – 7.08 (m, 1H), 7.02 (dd, *J* = 8.0, 6.7 Hz, 2H), 6.96 – 6.87 (m, 2H), 4.30 (s, 2H), 3.90 (s, 3H), 3.42 (t, *J* = 5.8 Hz, 2H), 2.99 (t, *J* = 5.8 Hz, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 152.8, 141.4, 135.4, 134.8, 129.1, 126.6, 126.3, 125.9, 123.2, 121.1, 119.2, 111.5, 55.7, 53.3, 49.2, 29.1.



2-(3,4-Dimethylphenyl)-1,2,3,4-tetrahydroisoquinoline¹ (1d) was synthesized following **General Procedure** from 1,2,3,4-tetrahydroisoquinoline and 4-bromo-1,2-dimethylbenzene. White solid, 67% yield. ¹H NMR (500 MHz, CDCl₃) δ 7.18 (tdd, *J* = 9.3, 6.1, 3.5 Hz, 4H), 7.06 (d, *J* = 8.2 Hz, 1H), 6.84 (d, *J* = 2.6 Hz, 1H), 6.78 (dd, *J* = 8.2, 2.7 Hz, 1H), 4.37 (s, 2H), 3.52 (t, *J* = 5.8 Hz, 2H), 3.00 (t, *J* = 5.8 Hz, 2H), 2.28 (s, 3H), 2.21 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 149.3, 137.4, 135.0, 134.9, 130.4, 128.8, 127.4, 126.7, 126.4, 126.1, 117.7, 113.5, 51.8, 47.5, 29.4, 20.5, 18.9.

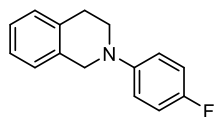


2-(4-Ethylphenyl)-1,2,3,4-tetrahydroisoquinoline¹ (1e) was synthesized following **General Procedure** from 1,2,3,4-tetrahydroisoquinoline and 1-ethyl-4-iodobenzene. White solid, 79% yield. ¹H NMR (500 MHz, CDCl₃) δ 7.23 – 7.09 (m, 6H), 6.98 – 6.92 (m, 2H), 4.38 (s, 2H), 3.53 (t, *J* = 5.8 Hz, 2H), 3.00 (t, *J* = 5.8 Hz, 2H), 2.60 (q, *J* = 7.6 Hz, 2H), 1.23 (t, *J* = 7.6 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 149.0, 135.1, 135.0, 134.8, 128.8, 128.7, 126.7, 126.5, 126.1, 116.0, 51.6, 47.4, 29.4, 28.1, 16.0.

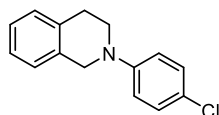


2-(4-(*tert*-Butyl)phenyl)-1,2,3,4-tetrahydroisoquinoline¹ (1f) was synthesized following **General Procedure** from 1,2,3,4-tetrahydroisoquinoline and 1-(*tert*-butyl)-4-iodobenzene. Light yellow solid, 74% yield. ¹H NMR (500 MHz, CDCl₃) δ 7.34 – 7.29 (m, 2H), 7.17 (qq, *J* = 6.3, 3.5, 2.8 Hz, 4H), 6.98 – 6.92 (m, 2H), 4.39 (s, 2H), 3.54 (t, *J* = 5.8 Hz, 2H), 2.99 (t, *J* = 5.8 Hz, 2H), 1.31 (s,

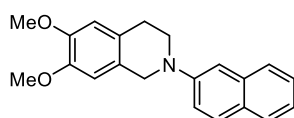
9H). ^{13}C NMR (126 MHz, CDCl_3) δ 148.6, 141.8, 135.1, 134.8, 128.8, 126.7, 126.5, 126.2, 126.2, 115.3, 51.4, 47.0, 34.1, 31.7, 29.4.



2-(4-Fluorophenyl)-1,2,3,4-tetrahydroisoquinoline¹ (1g) was synthesized following **General Procedure** from 1,2,3,4-tetrahydroisoquinoline and 1-fluoro-4-iodobenzene. White solid, 74% yield. ^1H NMR (500 MHz, CDCl_3) δ 7.18 (ddt, $J = 17.2, 11.9, 4.7$ Hz, 4H), 7.00 (t, $J = 8.7$ Hz, 2H), 6.97 – 6.91 (m, 2H), 4.34 (s, 2H), 3.50 (t, $J = 5.9$ Hz, 2H), 3.00 (t, $J = 5.9$ Hz, 2H). ^{13}C NMR (126 MHz, CDCl_3) δ 157.0 (d, $J = 237.9$ Hz), 147.6 (d, $J = 2.1$ Hz), 134.6 (d, $J = 31.2$ Hz), 127.8 (d, $J = 267.7$ Hz), 126.6, 126.2, 117.4, 117.3, 115.9, 115.7, 52.1, 48.0, 29.2. ^{19}F NMR (471 MHz, CDCl_3) δ -125.6.



2-(4-Chlorophenyl)-1,2,3,4-tetrahydroisoquinoline¹ (1h) was synthesized following **General Procedure** from 1,2,3,4-tetrahydroisoquinoline and 1-chloro-4-iodobenzene. White solid, 56% yield. ^1H NMR (400 MHz, CDCl_3) δ 7.25 – 7.11 (m, 6H), 6.92 – 6.85 (m, 2H), 4.38 (s, 2H), 3.54 (t, $J = 5.9$ Hz, 2H), 2.98 (t, $J = 5.8$ Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 149.3, 134.9, 134.3, 129.2, 128.7, 126.7, 126.7, 126.4, 123.5, 116.3, 50.9, 46.7, 29.2.



6,7-Dimethoxy-2-(naphthalen-2-yl)-1,2,3,4-tetrahydroisoquinoline¹ (1i) was synthesized following **General Procedure** from 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline and 2-bromonaphthalene. White solid, 44% yield. ^1H NMR (500 MHz, CDCl_3) δ 7.75 (d, $J = 9.0$ Hz, 1H), 7.70 (dd, $J = 14.4, 8.1$ Hz, 2H), 7.39 (ddd, $J = 8.1, 6.8, 1.3$ Hz, 1H), 7.35 (dd, $J = 9.0, 2.5$ Hz, 1H), 7.29 – 7.24 (m, 2H), 7.17 (d, $J = 2.4$ Hz, 1H), 6.69 (d, $J = 22.9$ Hz, 2H), 4.44 (s, 2H), 3.90 (s, 3H), 3.88 (s, 3H), 3.66 (t, $J = 5.8$ Hz, 2H), 2.96 (t, $J = 5.8$ Hz, 2H). ^{13}C NMR (126 MHz, CDCl_3) δ 148.7, 147.9, 147.8, 135.0, 129.0, 128.3, 127.7, 126.8, 126.8, 126.5, 126.4, 123.2, 119.1, 111.7, 109.7, 109.7, 56.2, 56.2, 51.1, 47.6, 28.9.

6. Reference

- (1) Gao, P.-S.; Weng, X.-J.; Wang, Z.-H.; Zheng, C.; Sun, B.; Chen, Z.-H.; You, S.-L.; Mei, T.-S., *Angew. Chem. Int. Ed.* **2020**, 59, 15254-15259.
- (2) Rueping, M.; Koenigs, R. M.; Poscharny, K.; Fabry, D. C.; Leonori, D.; Vila, C., *Chem. Eur. J.* **2012**, 18, 5170-5174.
- (3) Li, Z. P.; Li, C. J., *Org. Lett.* **2004**, 6, 4997-4999.
- (4) Su, W.; Yu, J.; Li, Z.; Jiang, Z., *J. Org. Chem.* **2011**, 76, 9144-9150.
- (5) Mudithanapelli, C.; Dhorma, L. P.; Kim, M.-h., *Org. Lett.* **2019**, 21, 3098-3102.

7. NMR spectra

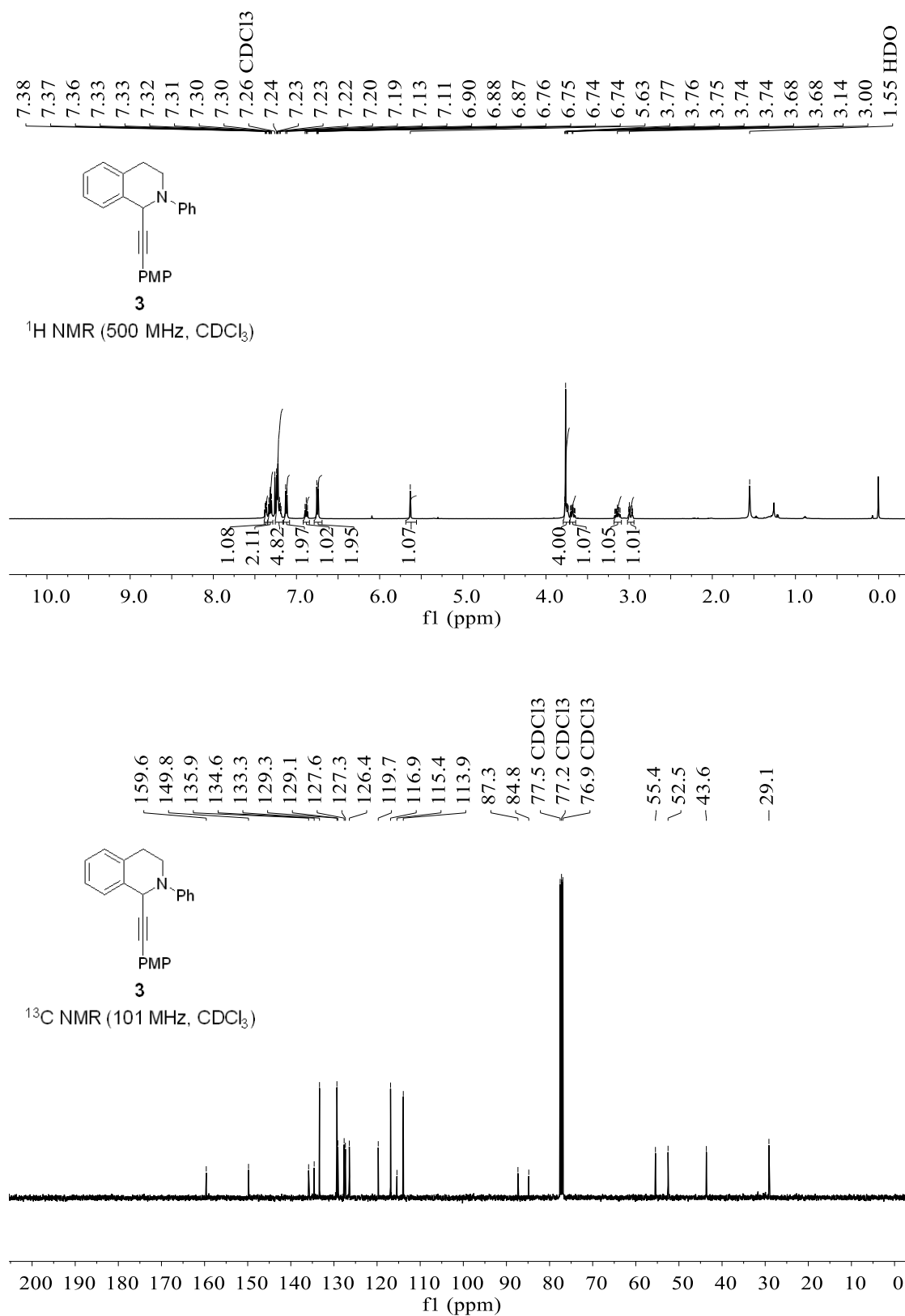


Figure S2. ¹H NMR and ¹³C NMR spectra of compound **3**.

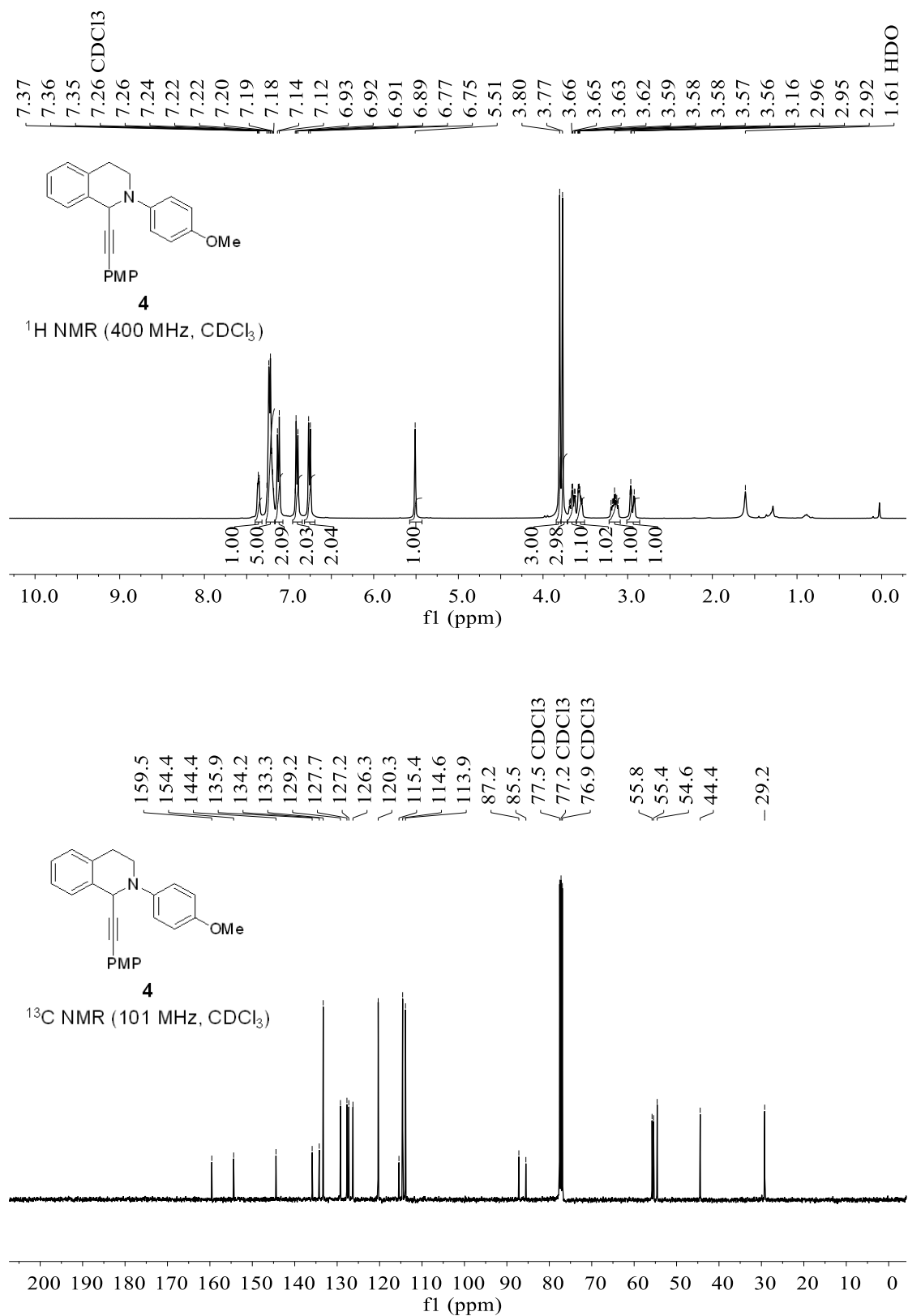


Figure S3. ¹H NMR and ¹³C NMR spectra of compound **4**.

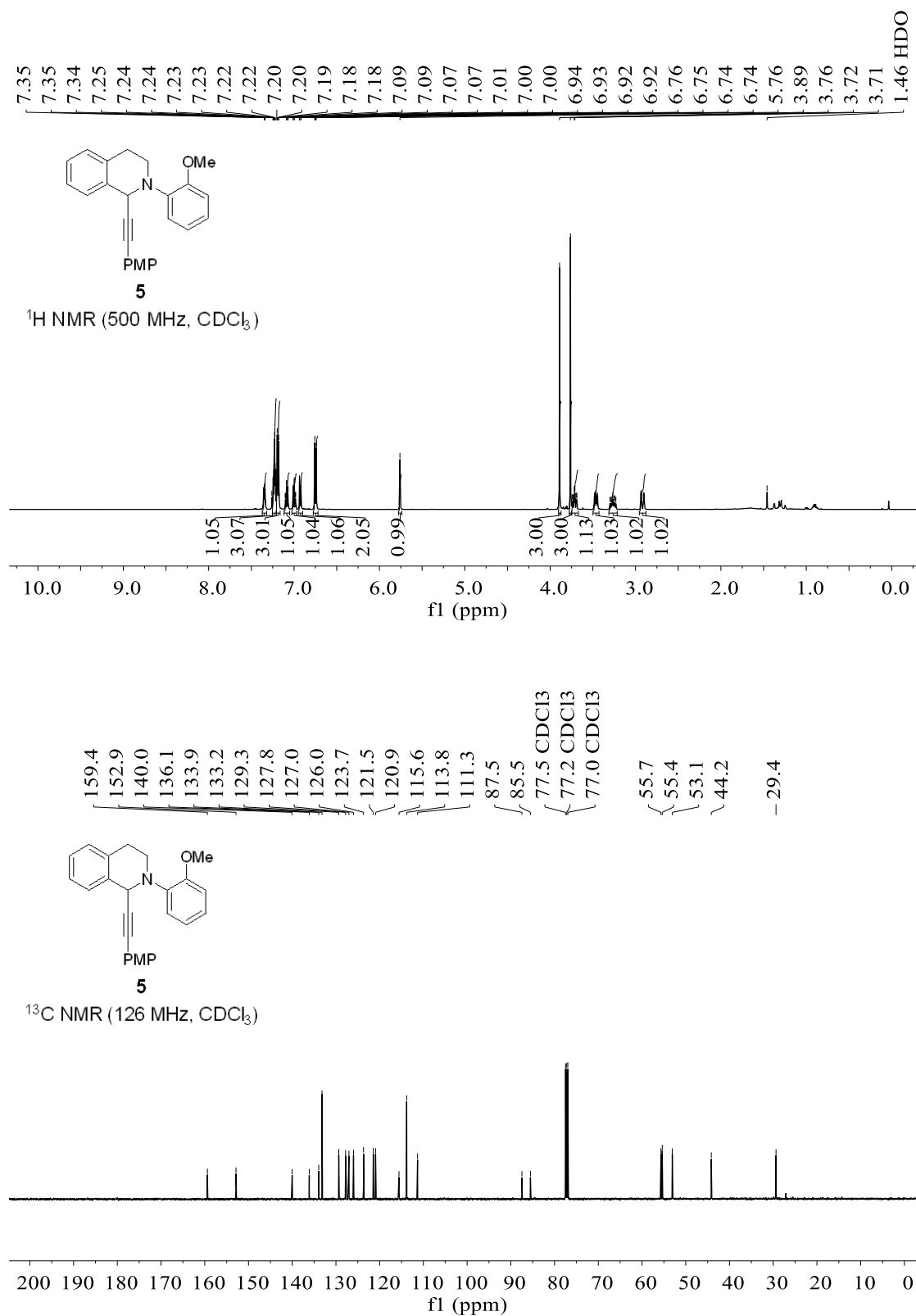


Figure S4. ¹H NMR and ¹³C NMR spectra of compound **5**.

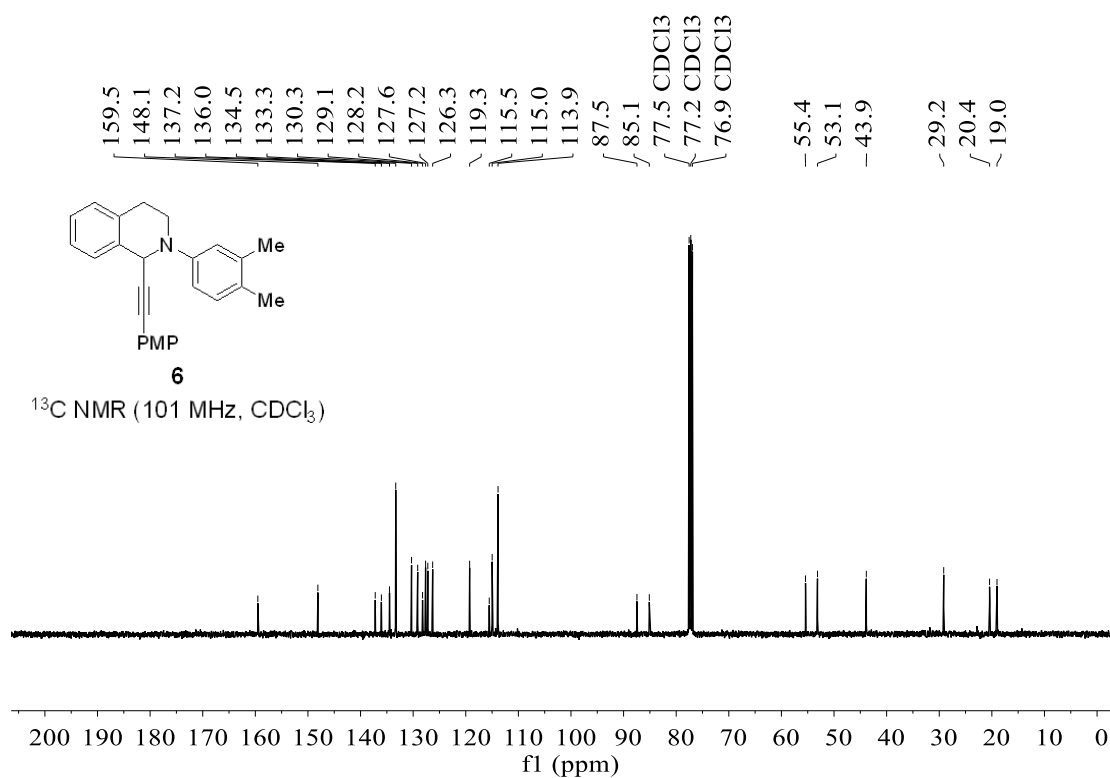
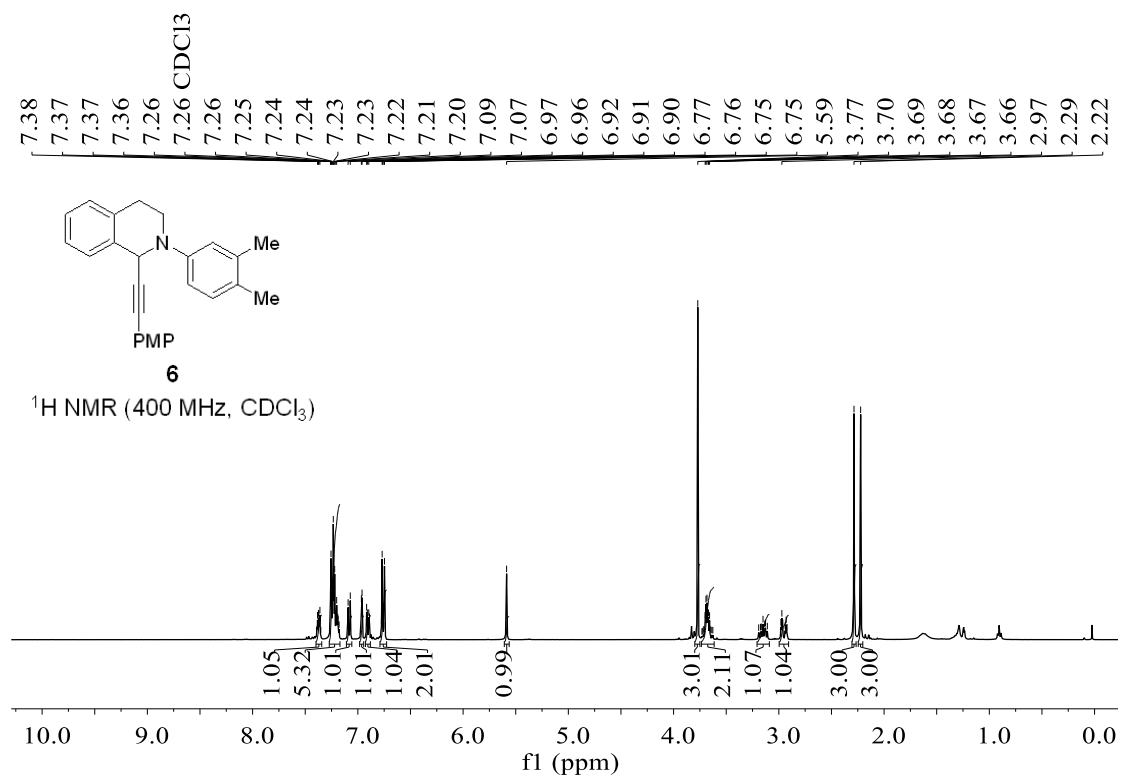


Figure S5. ¹H NMR and ¹³C NMR spectra of compound **6**.

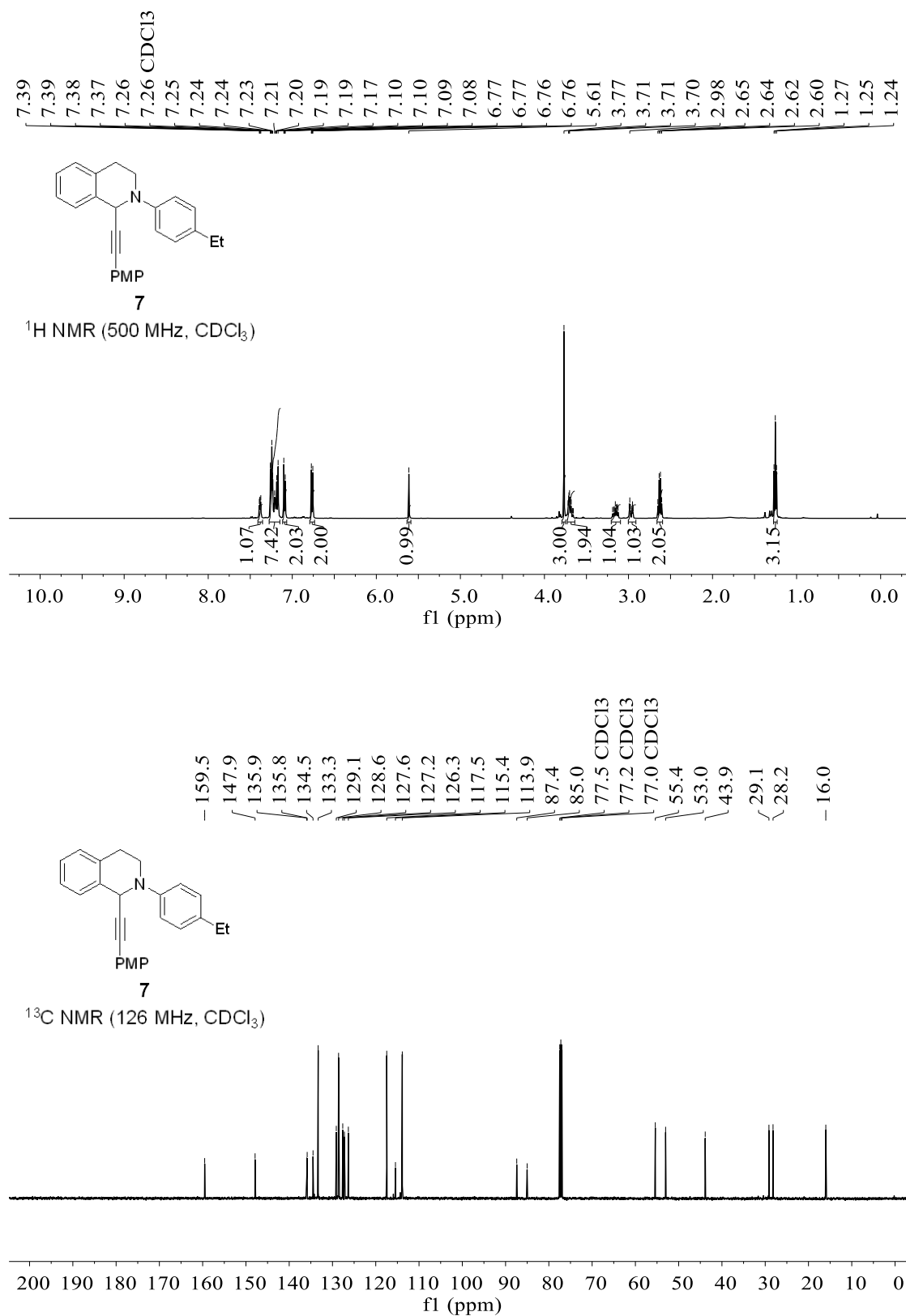


Figure S6. ¹H NMR and ¹³C NMR spectra of compound **7**.

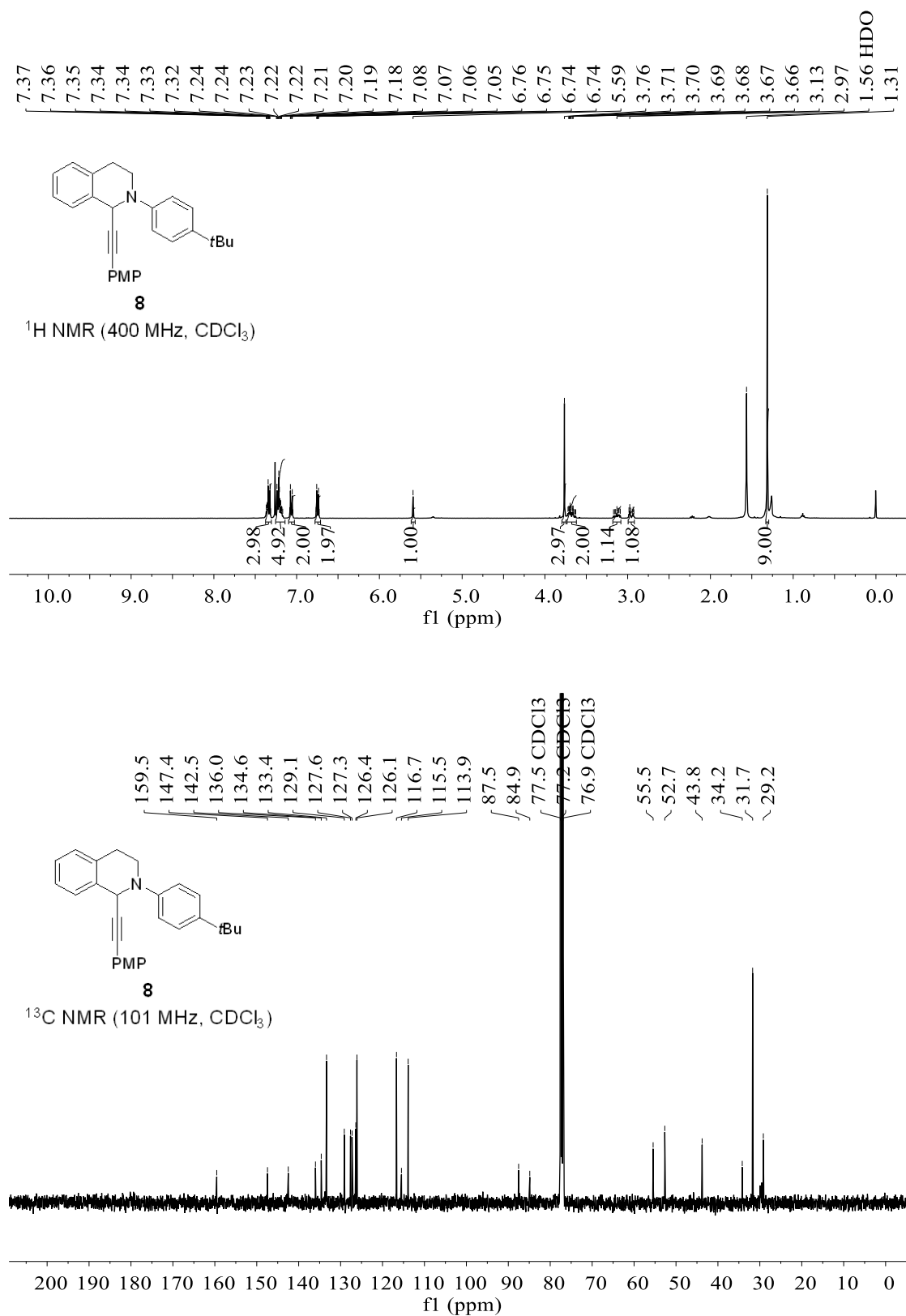
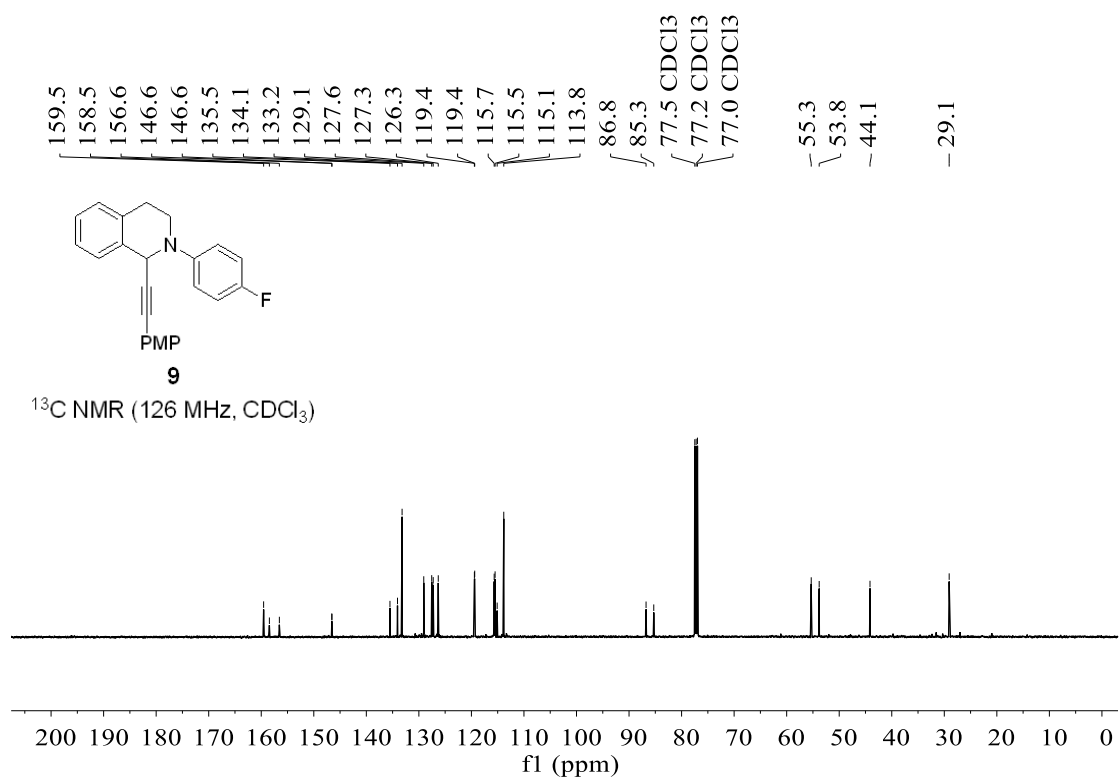
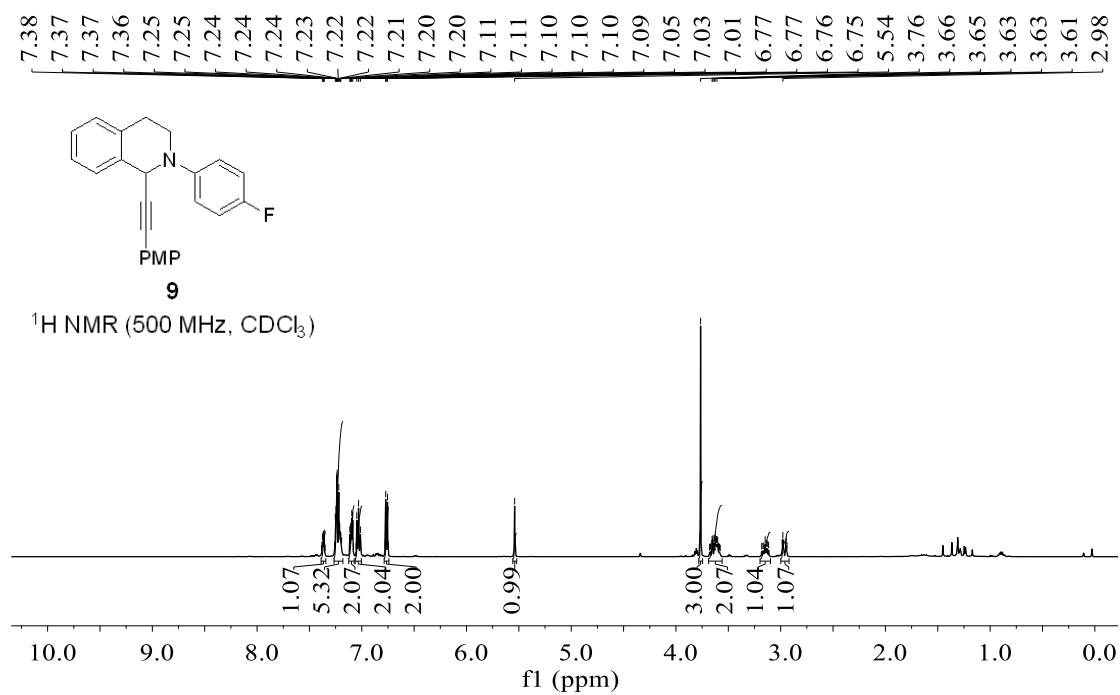


Figure S7. ¹H NMR and ¹³C NMR spectra of compound **8**.



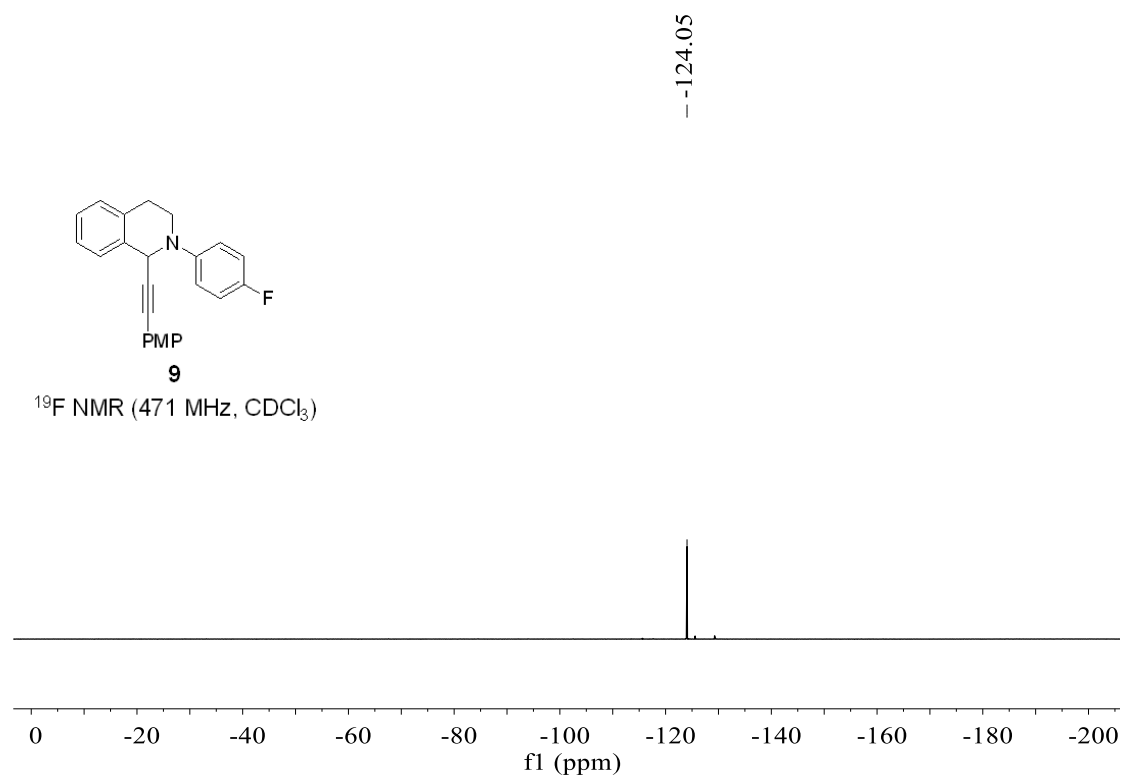


Figure S8. ¹H NMR, ¹³C NMR and ¹⁹F NMR spectra of compound **9**.

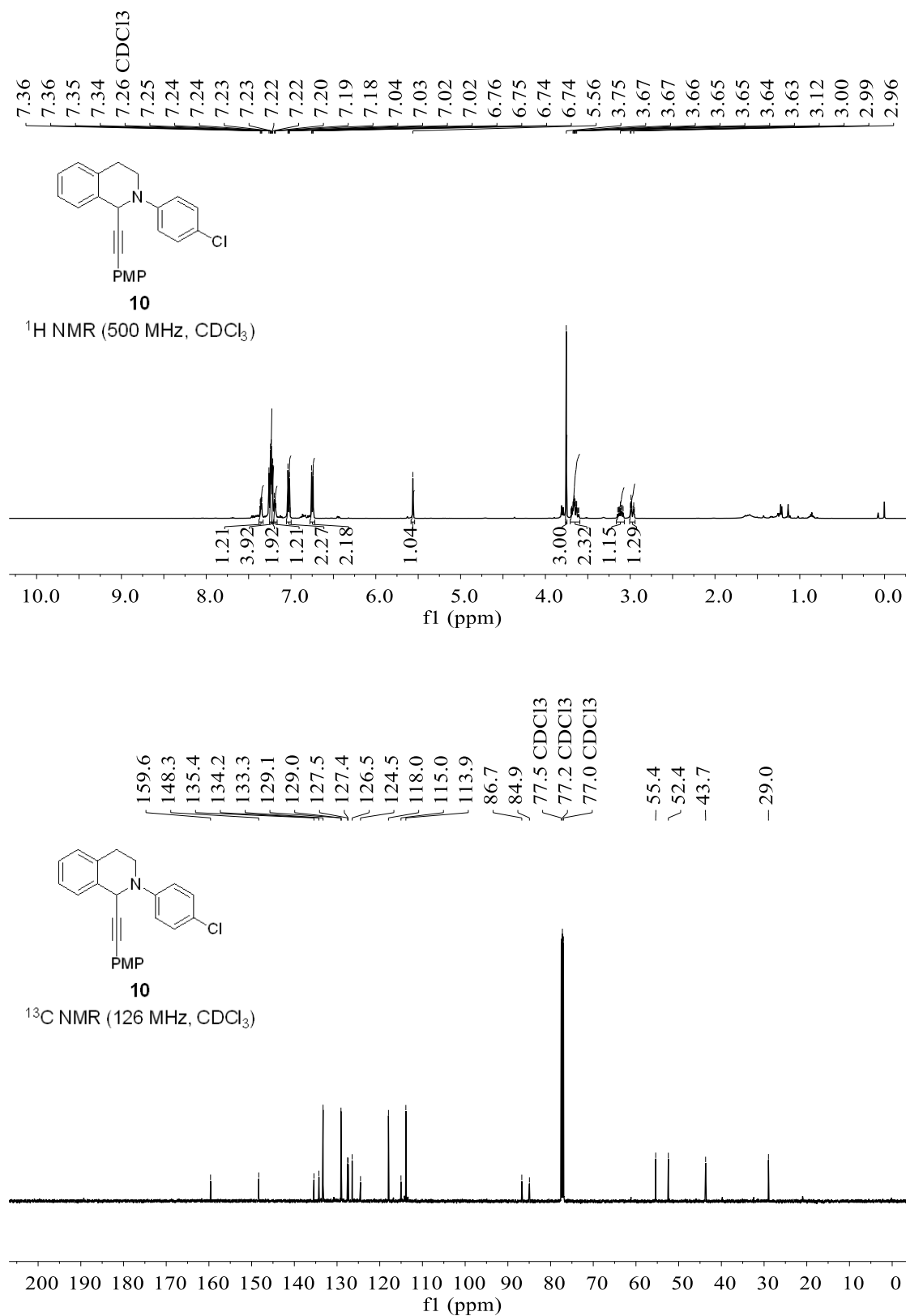


Figure S9. ¹H NMR and ¹³C NMR spectra of compound **10**.

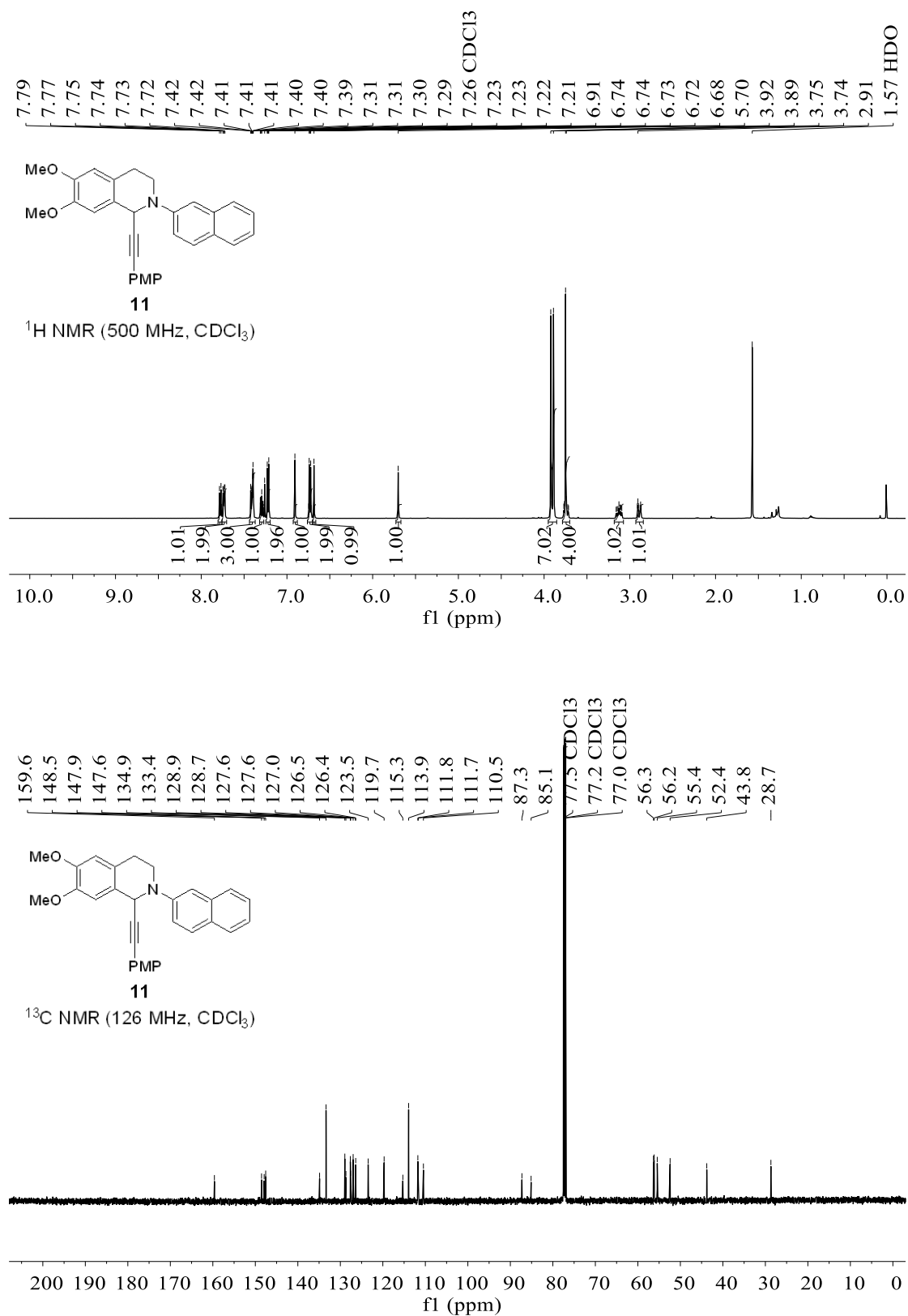


Figure S10. ¹H NMR and ¹³C NMR spectra of compound **11**.

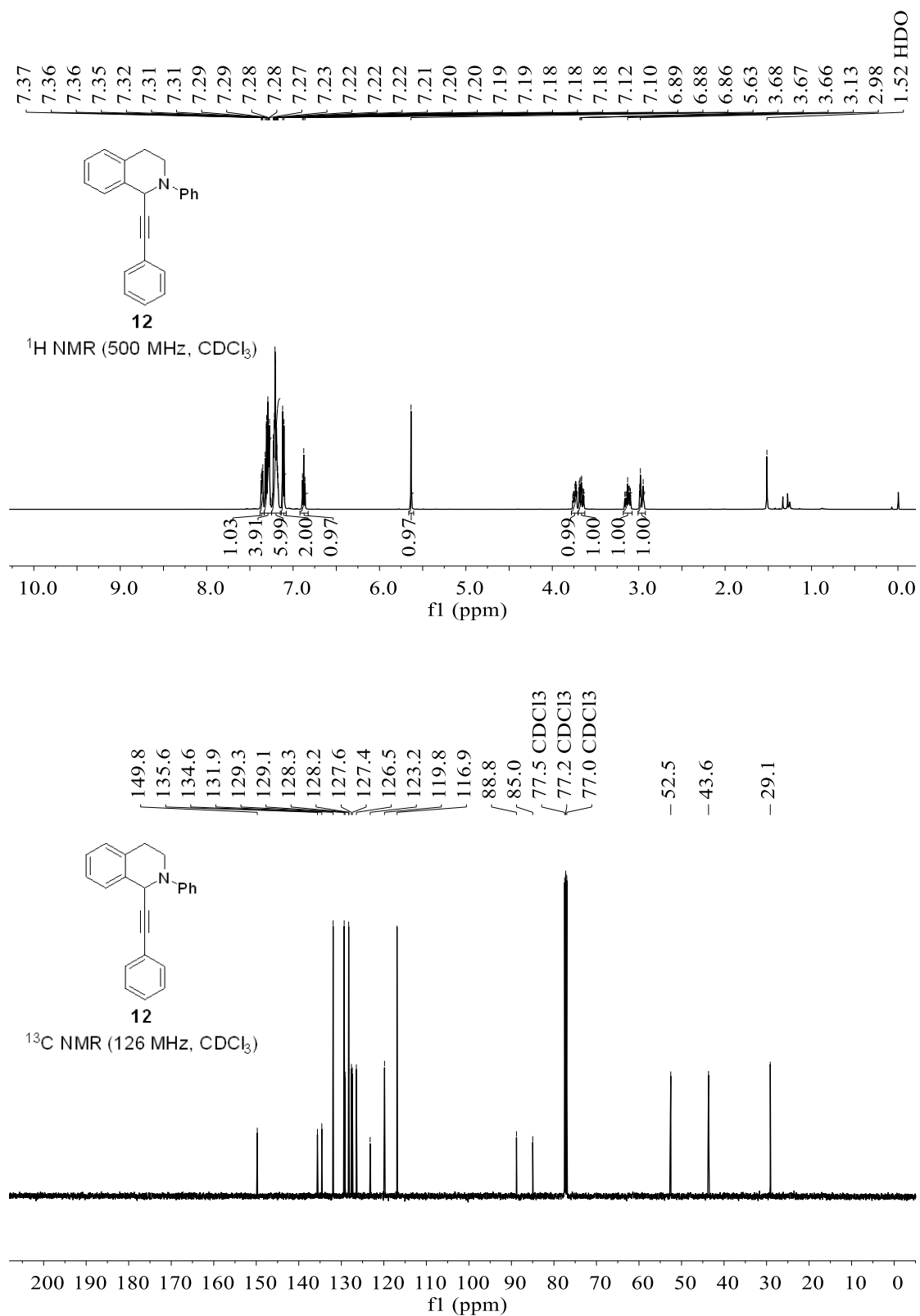
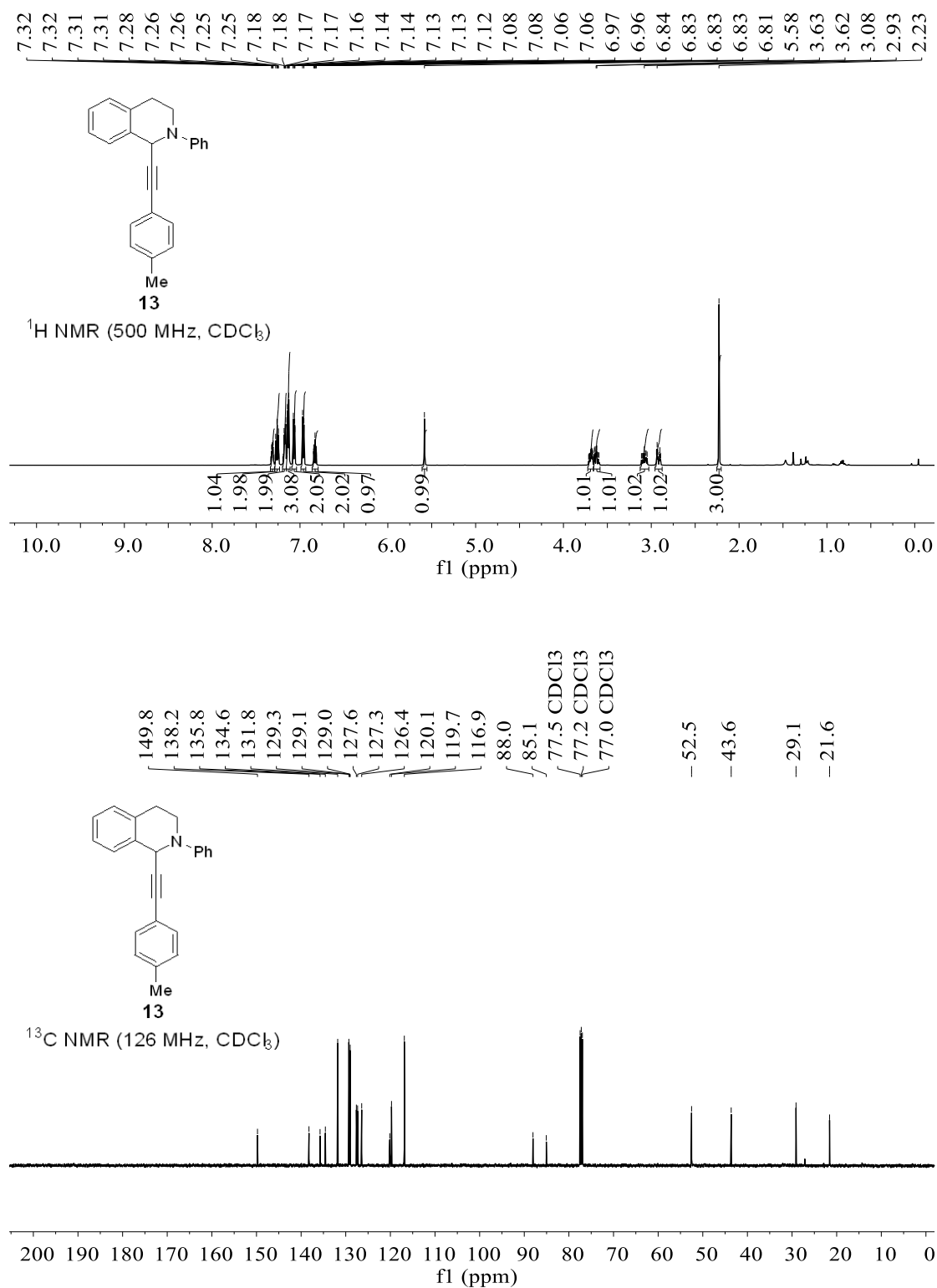


Figure S11. ¹H NMR and ¹³C NMR spectra of compound **12**.



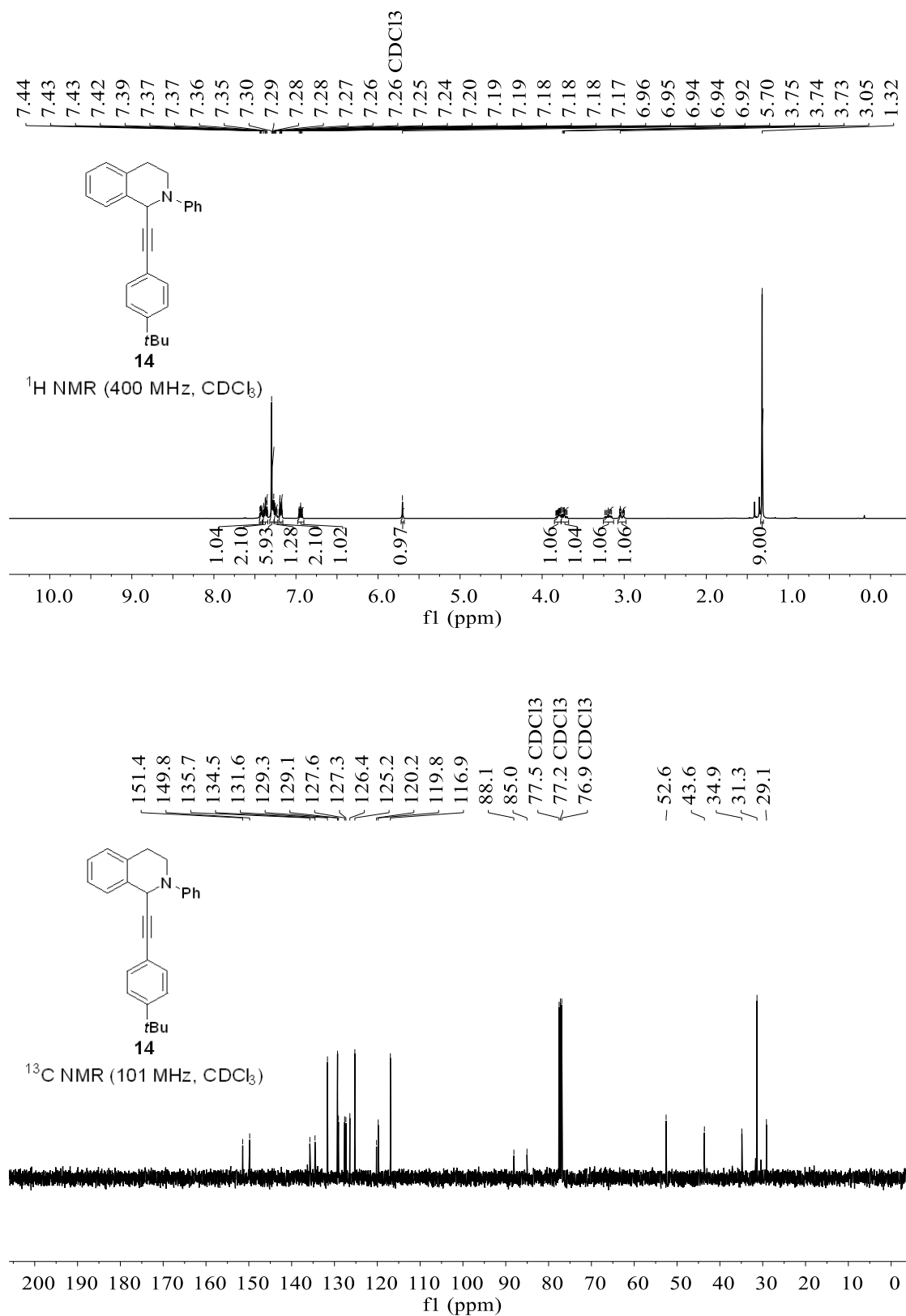


Figure S13. ¹H NMR and ¹³C NMR spectra of compound **14**.

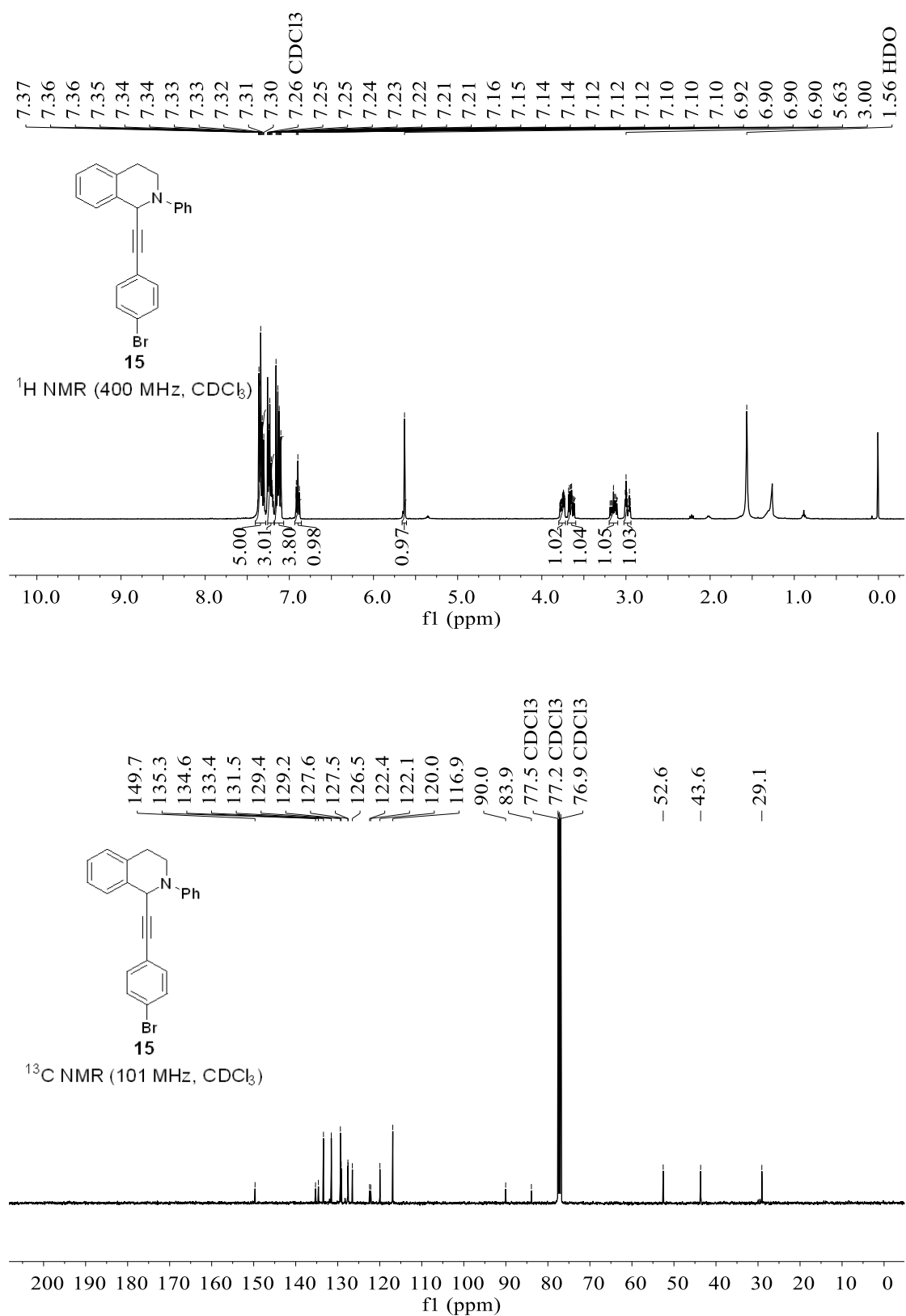


Figure S14. ¹H NMR and ¹³C NMR spectra of compound **15**.

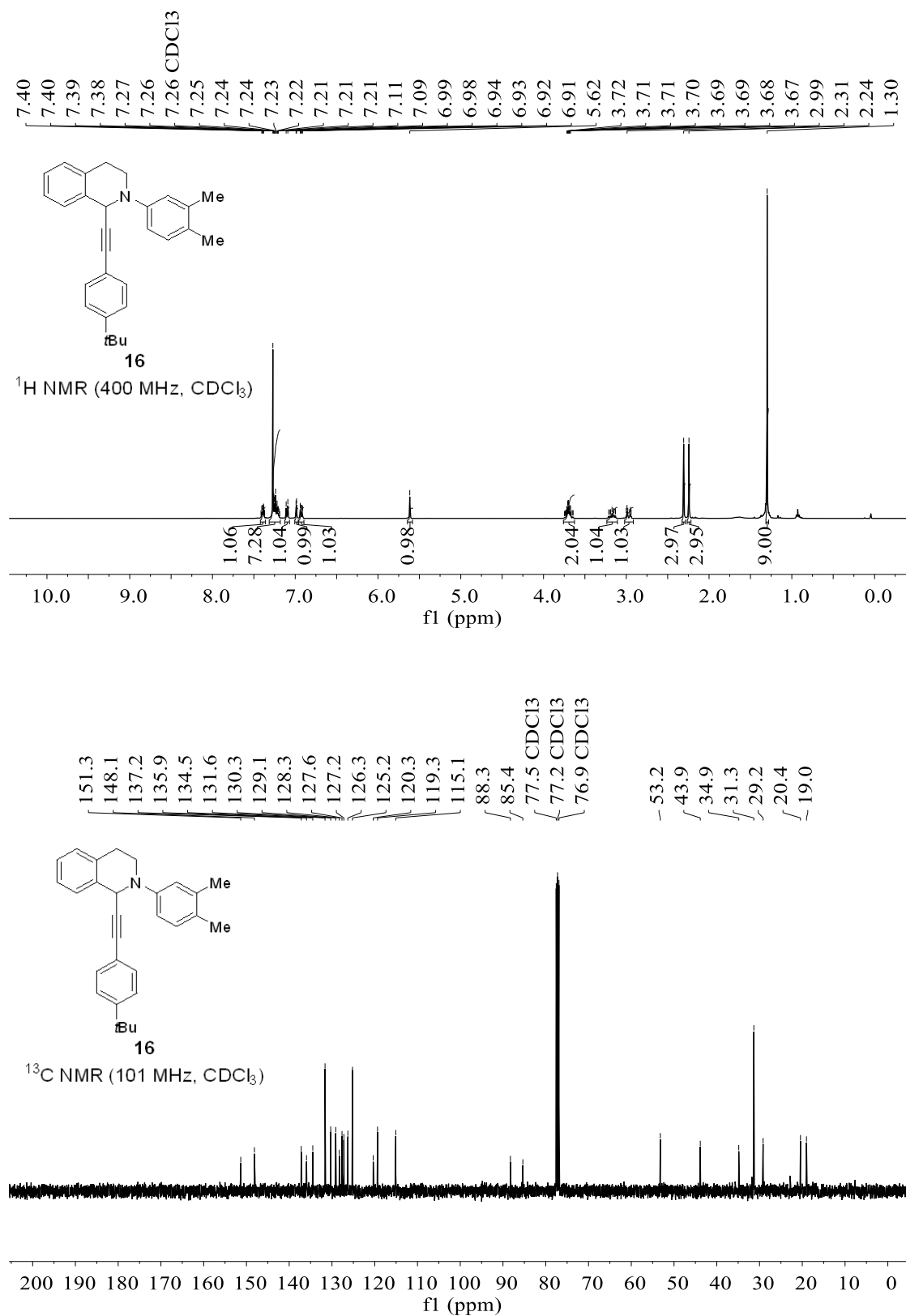


Figure S15. ¹H NMR and ¹³C NMR spectra of compound **16**.

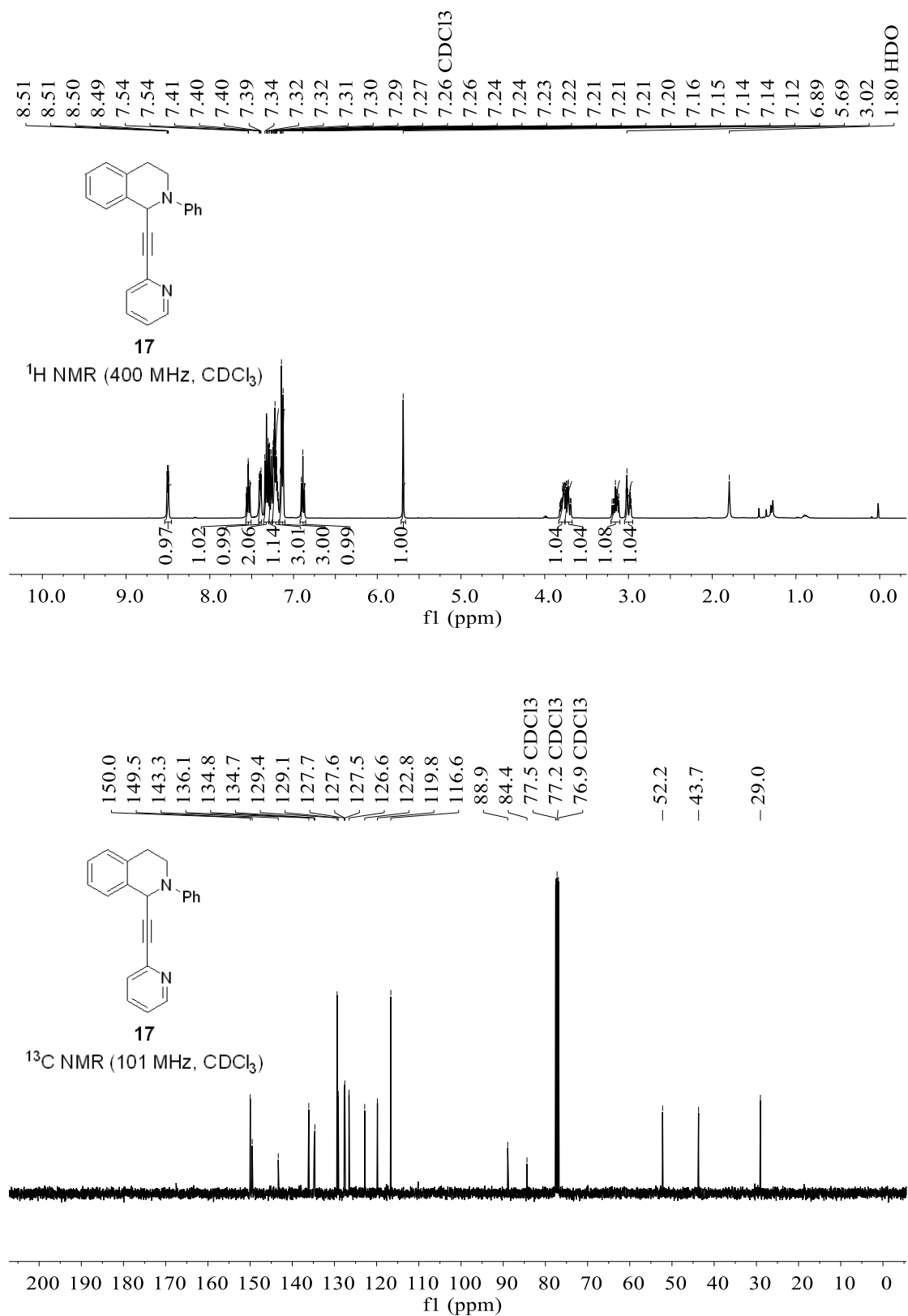


Figure S16. ¹H NMR and ¹³C NMR spectra of compound **17**.

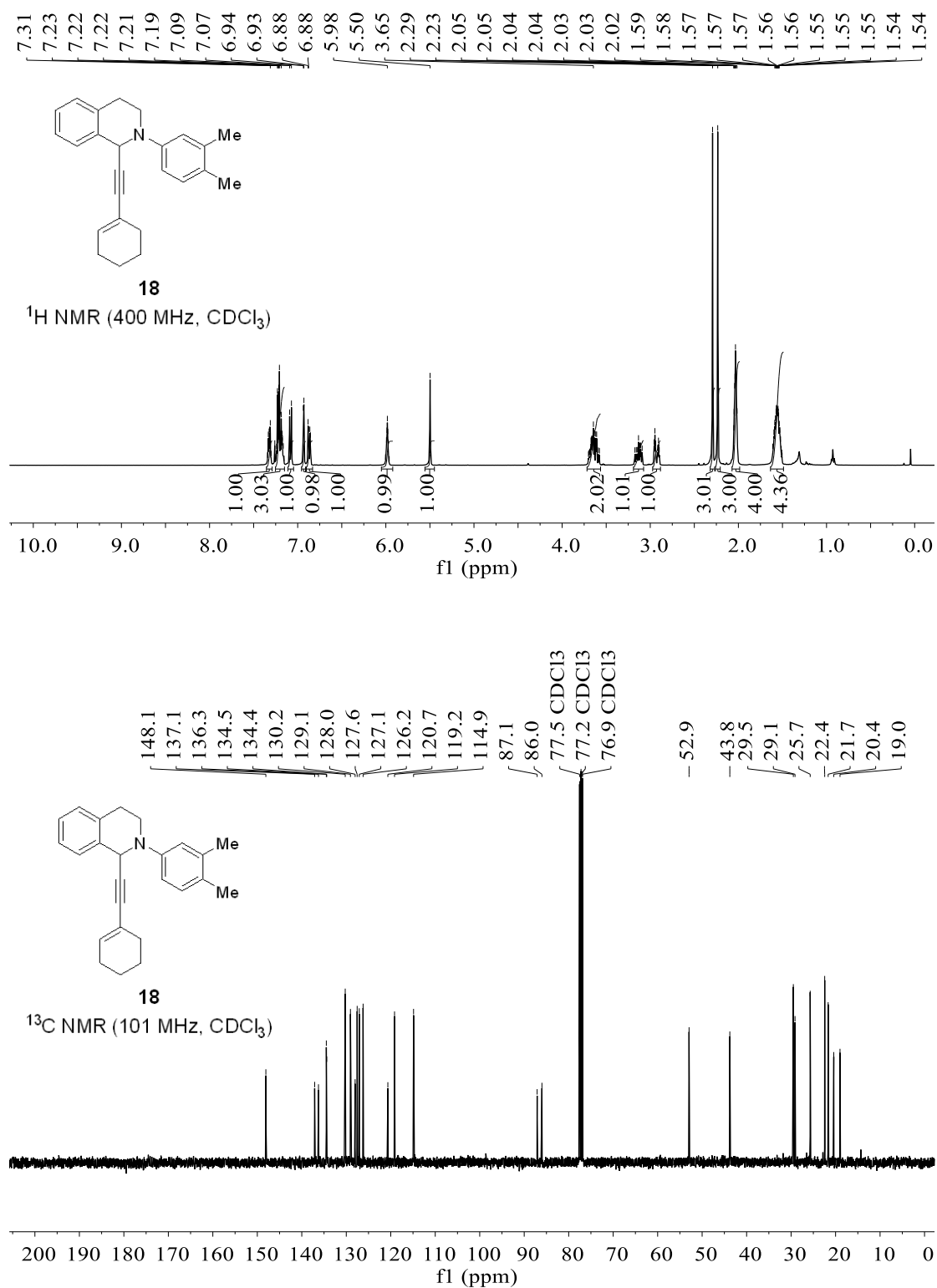


Figure S17. ¹H NMR and ¹³C NMR spectra of compound **18**.

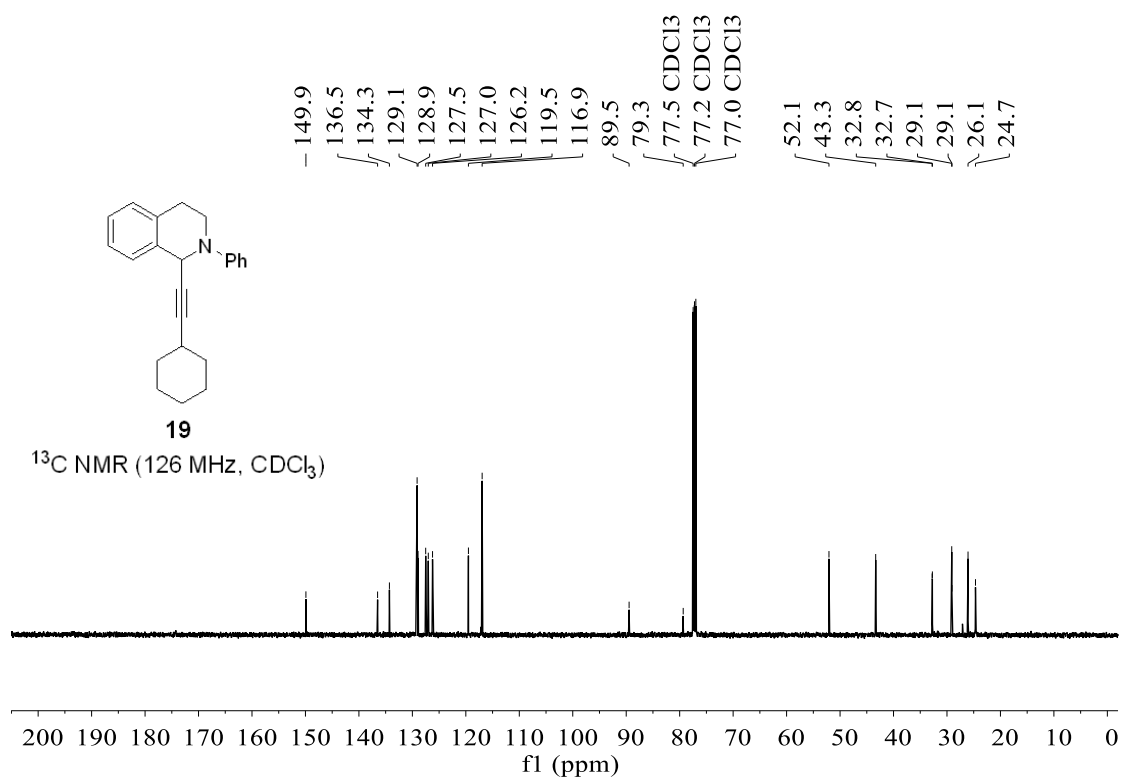
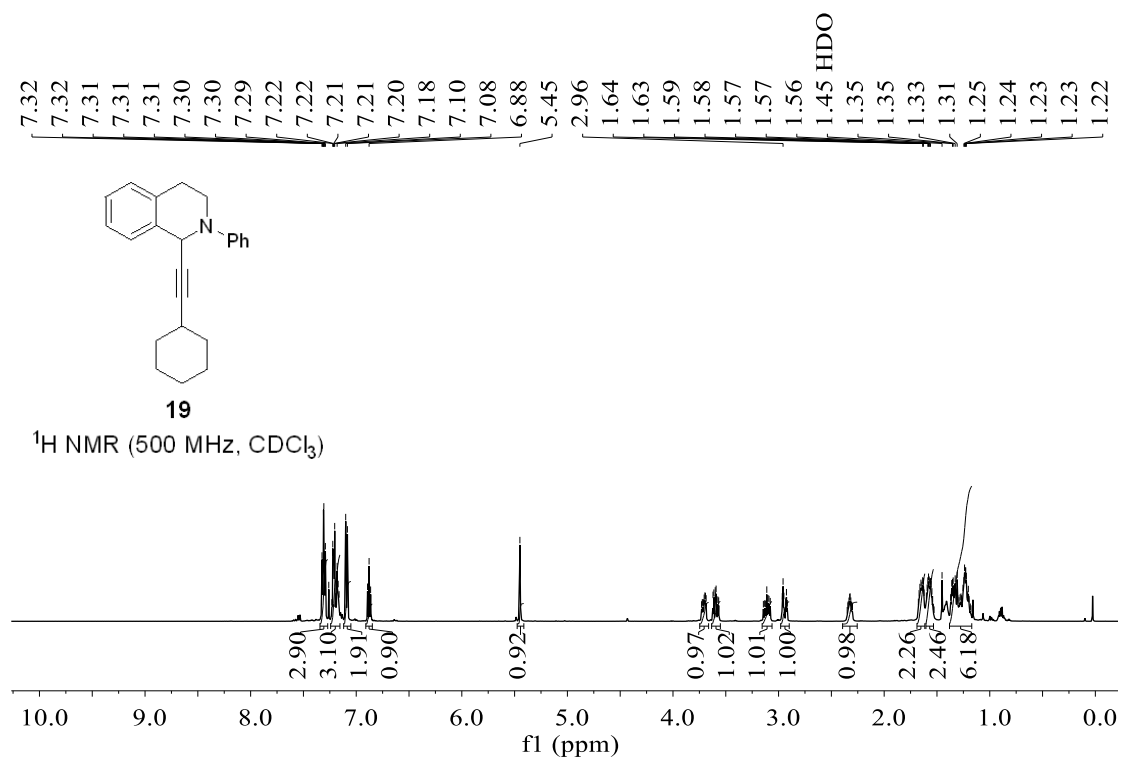


Figure S18. ¹H NMR and ¹³C NMR spectra of compound **19**.

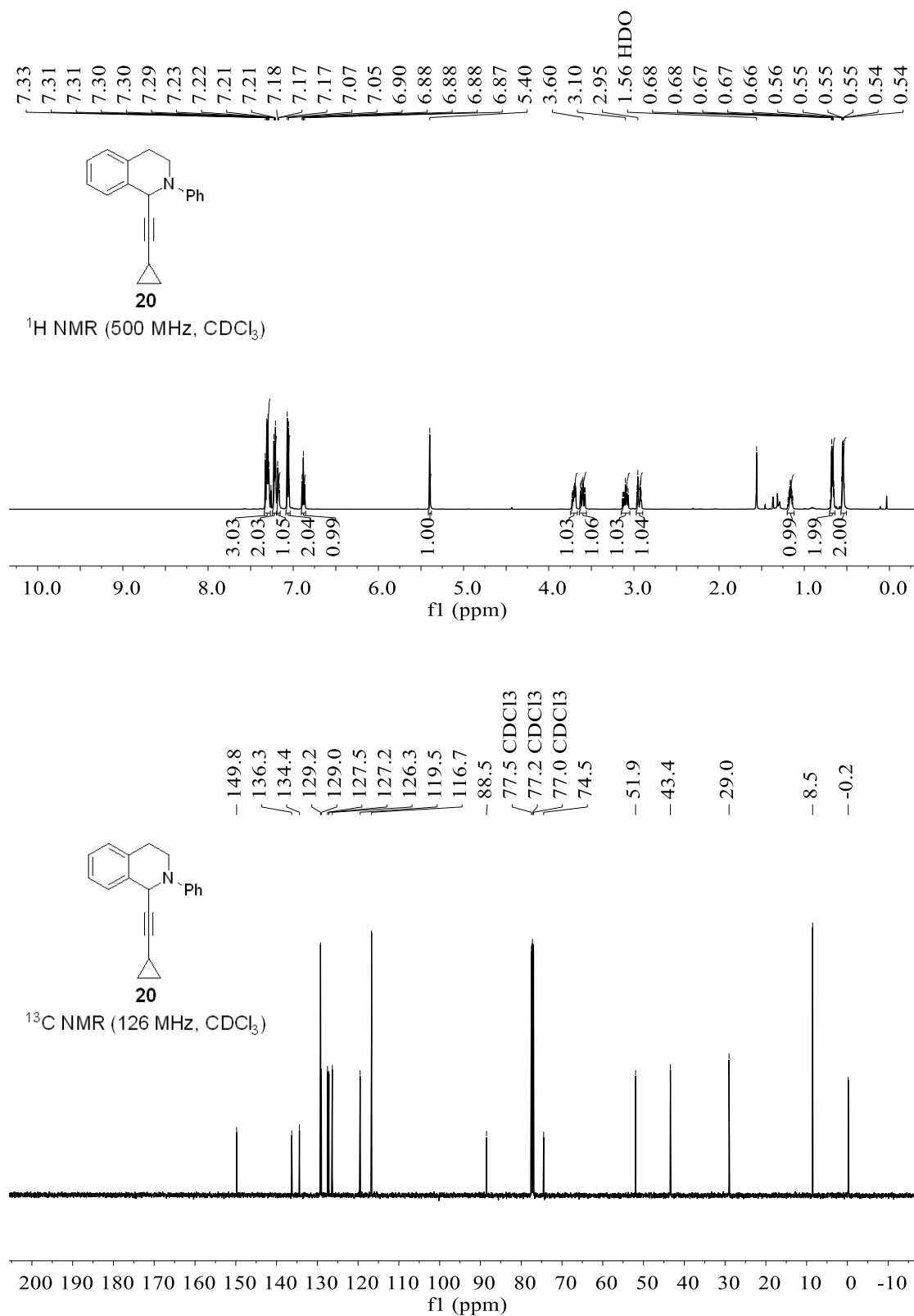
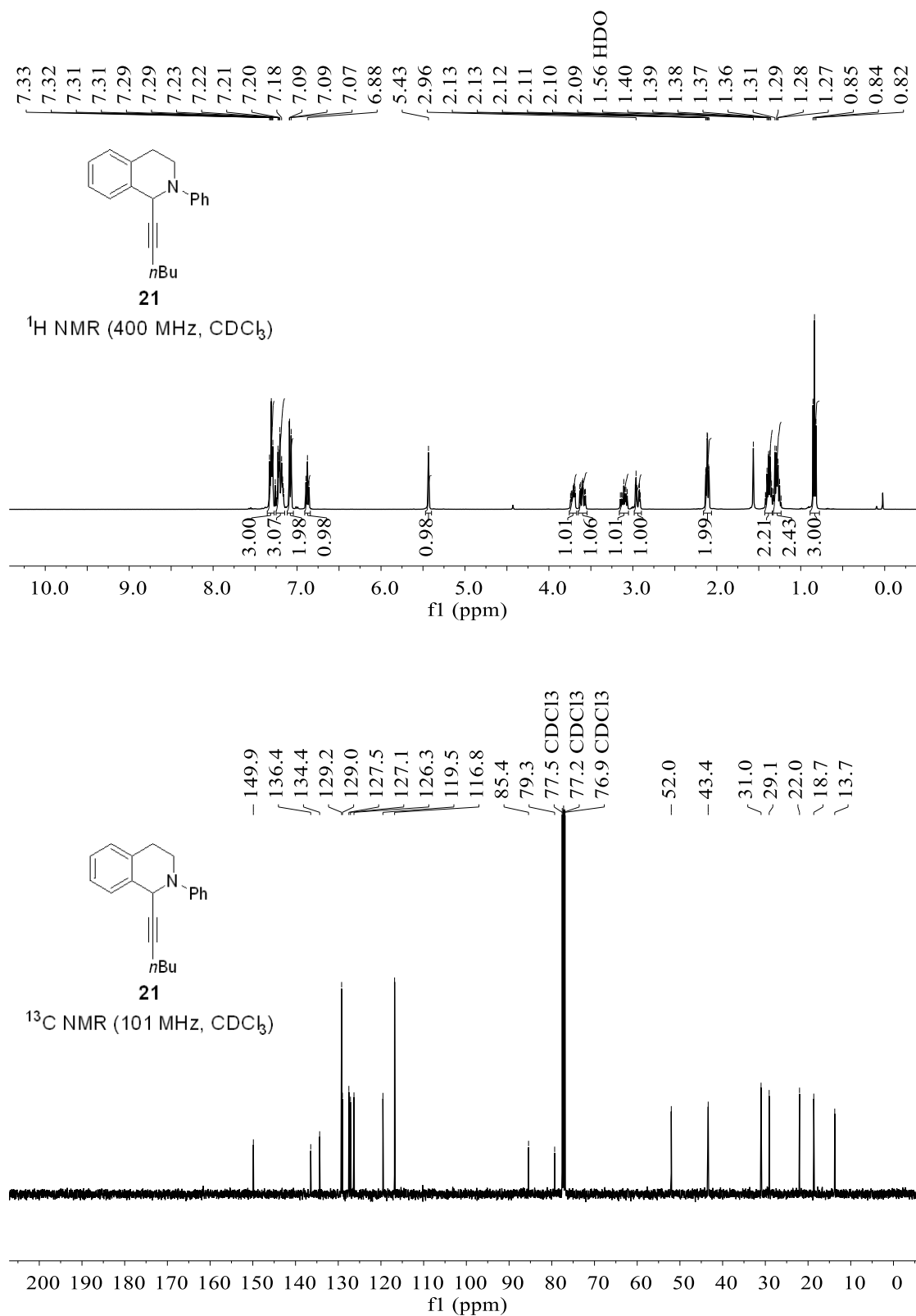


Figure S19. ¹H NMR and ¹³C NMR spectra of compound **20**.



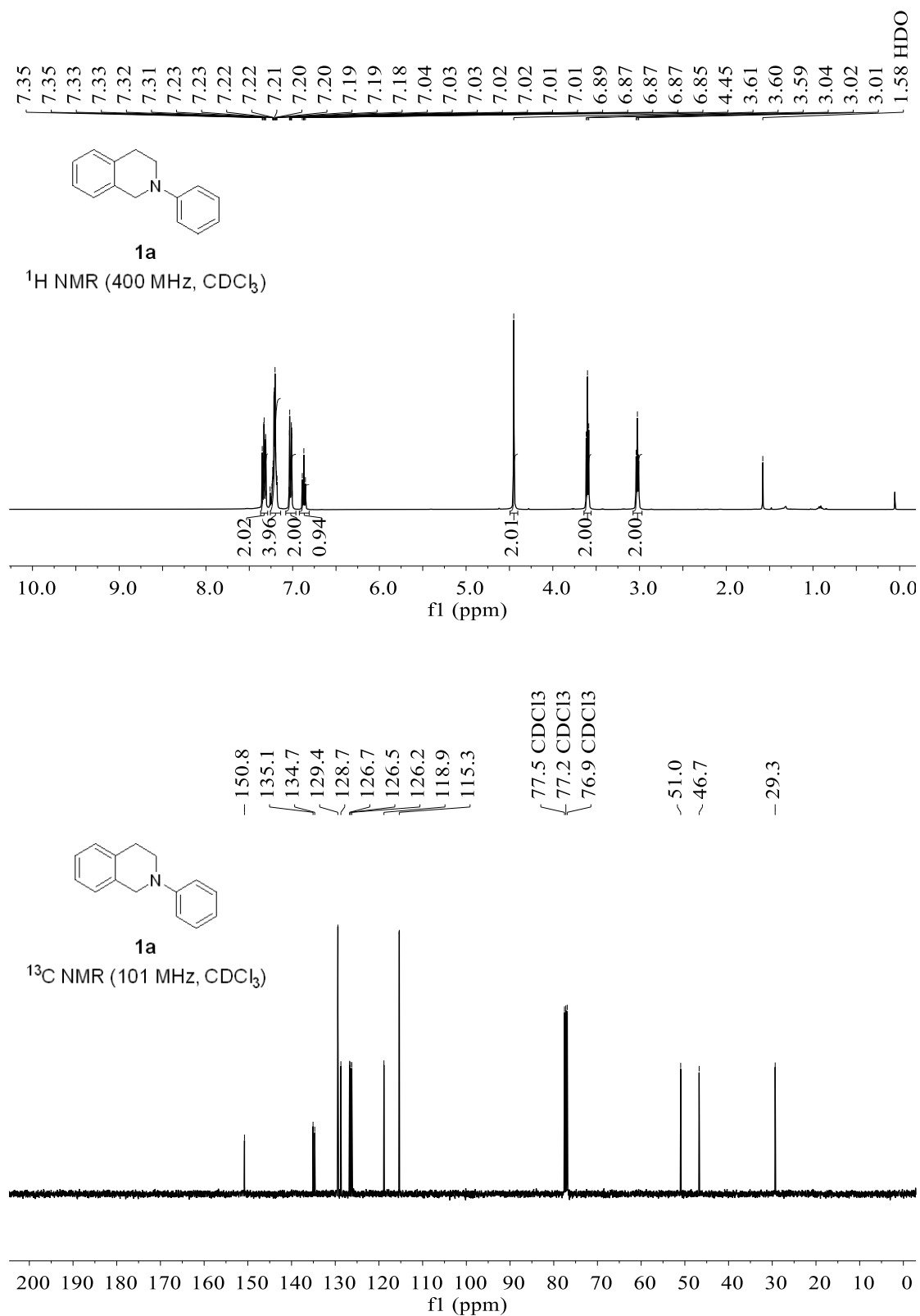


Figure S21. ¹H NMR and ¹³C NMR spectra of compound **1a**.

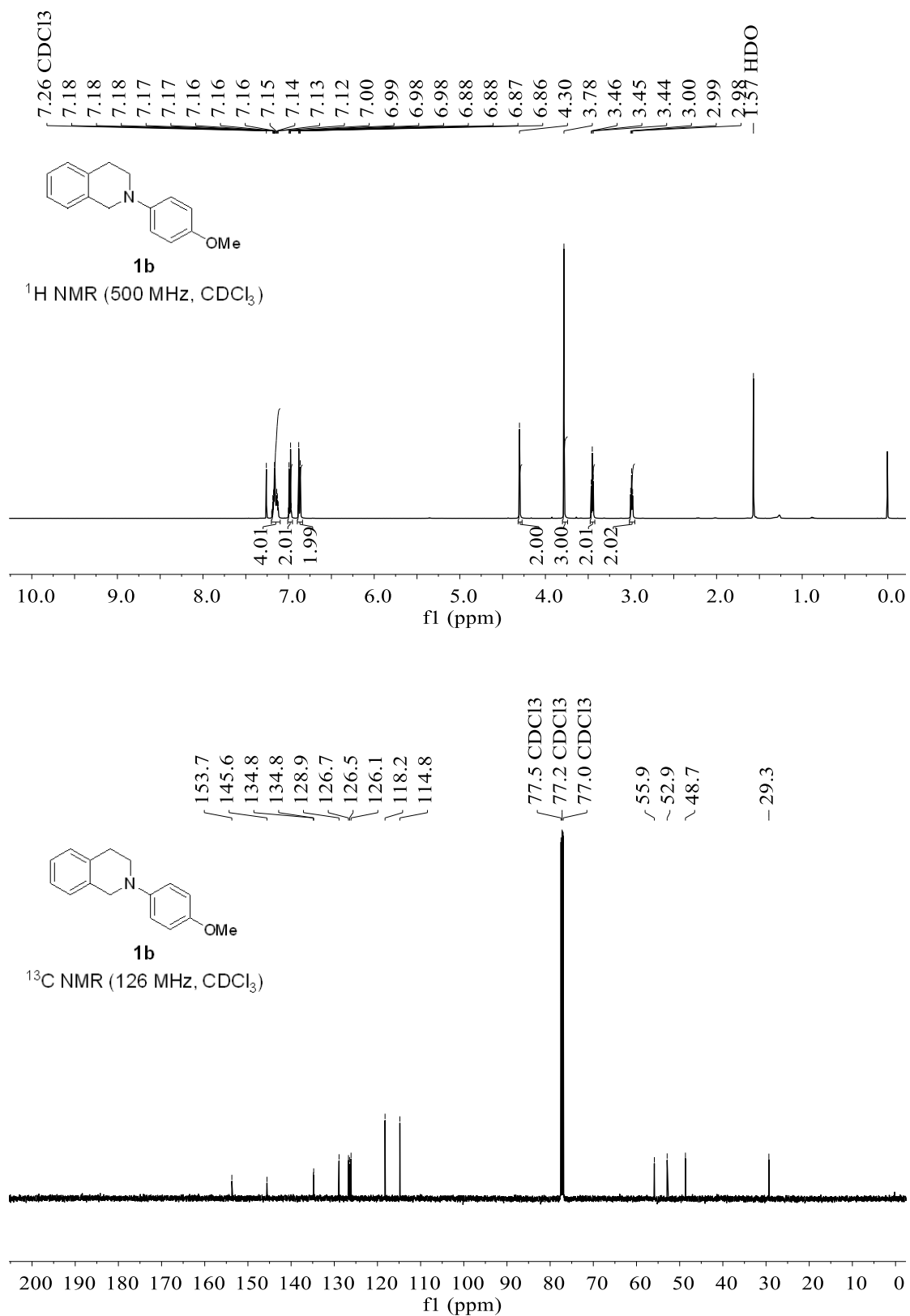


Figure S22. ¹H NMR and ¹³C NMR spectra of compound **1b**.

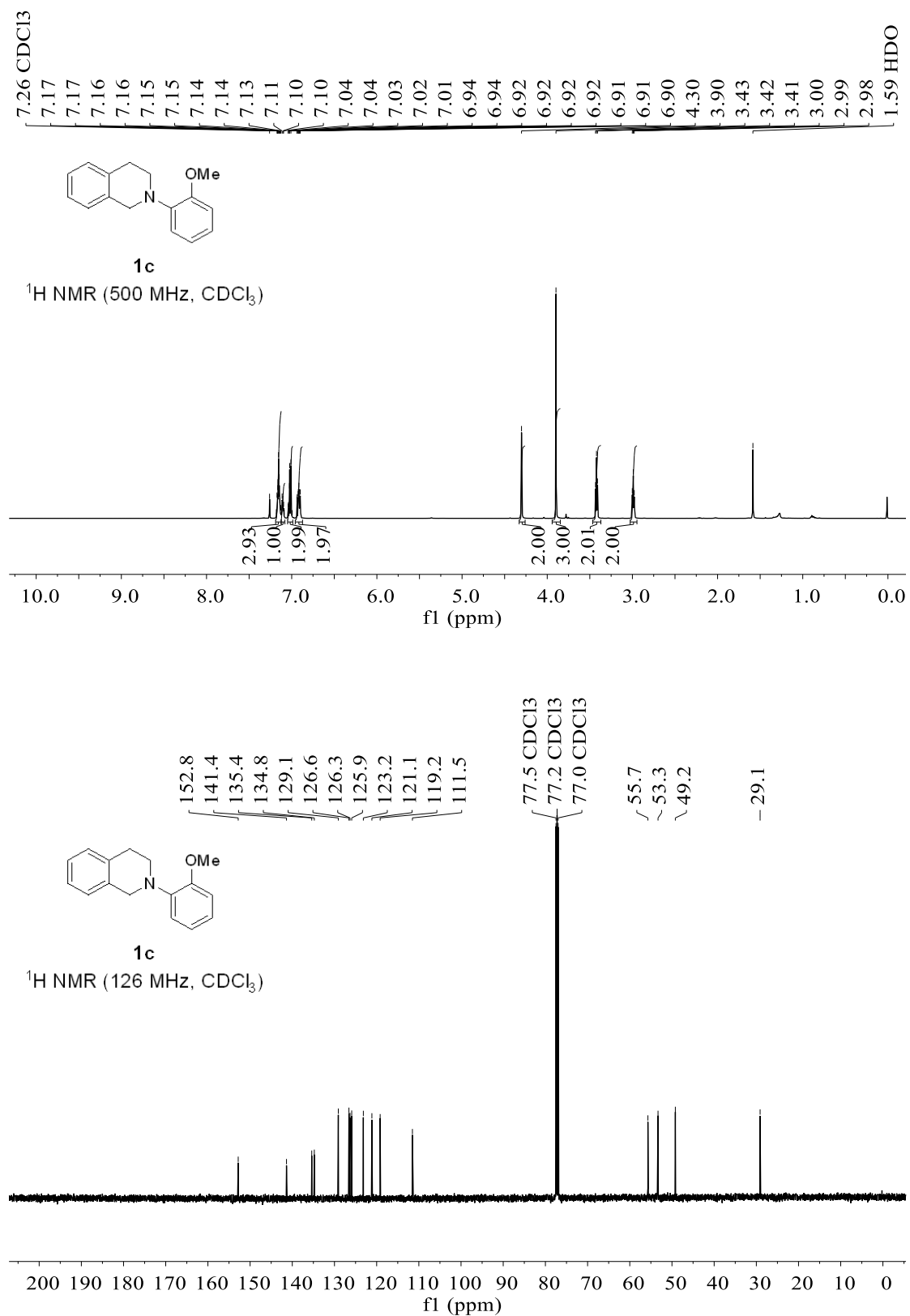


Figure S23. ¹H NMR and ¹³C NMR spectra of compound **1c**.

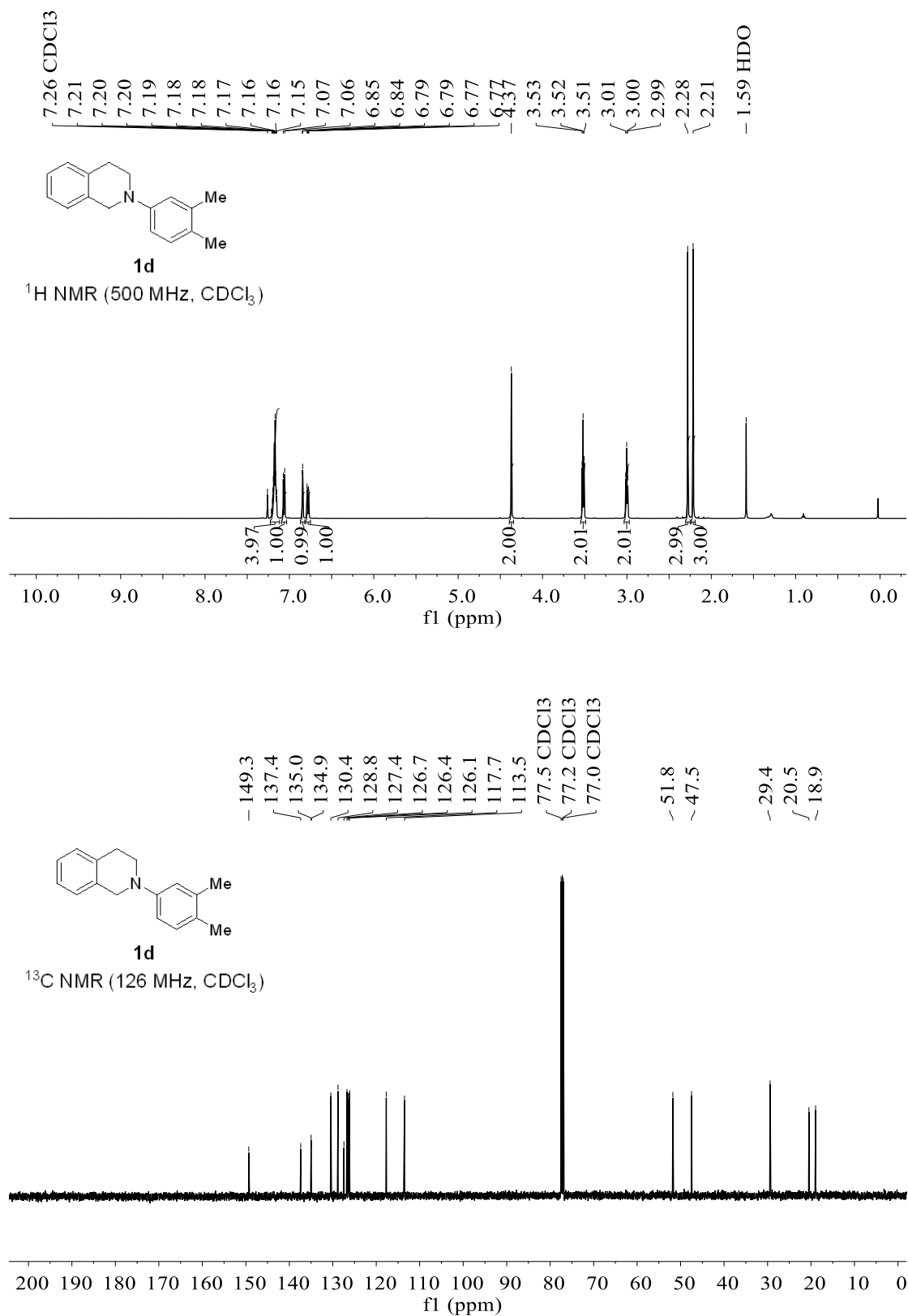


Figure S24. ¹H NMR and ¹³C NMR spectra of compound **1d**.

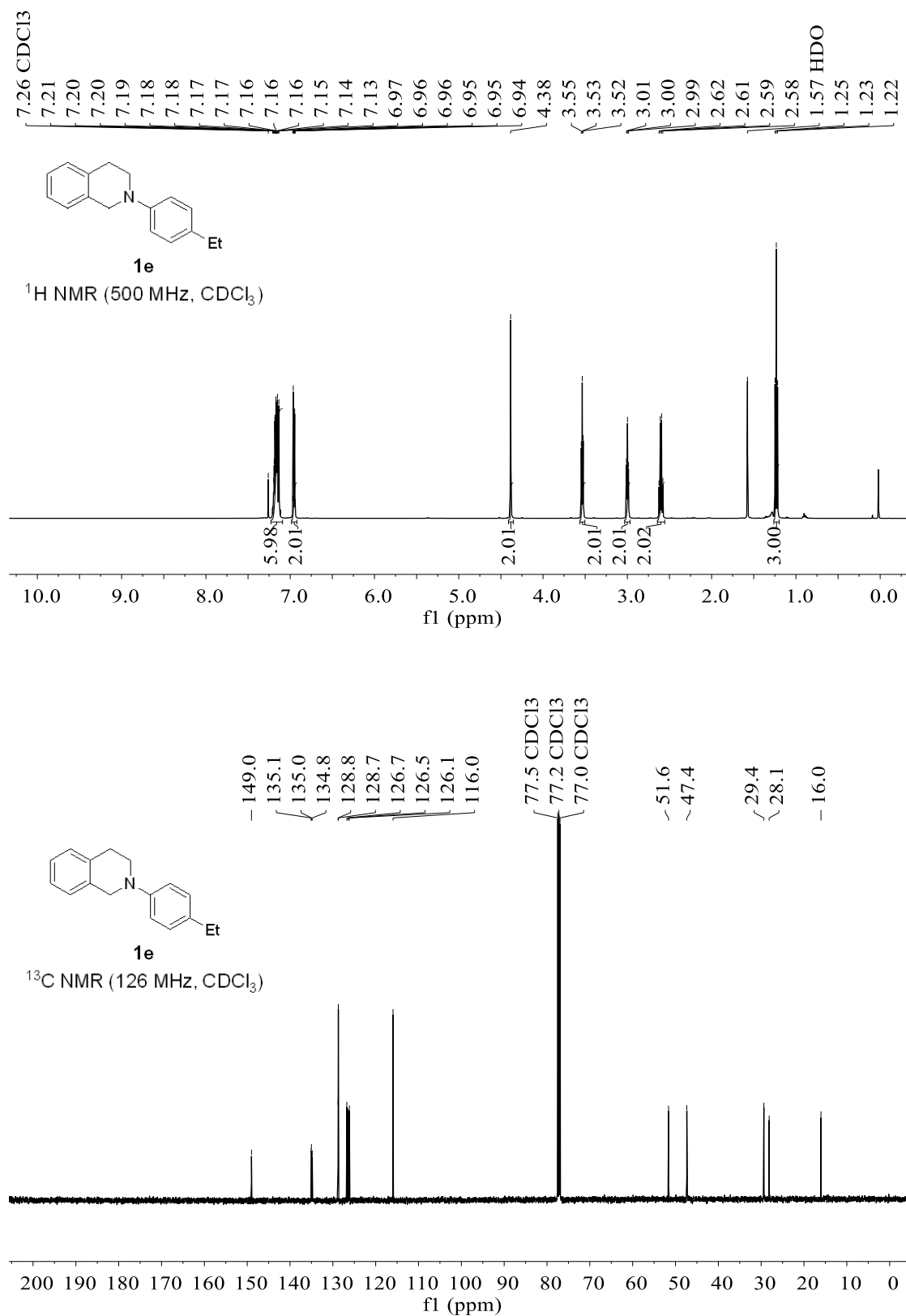


Figure S25. ¹H NMR and ¹³C NMR spectra of compound **1e**.

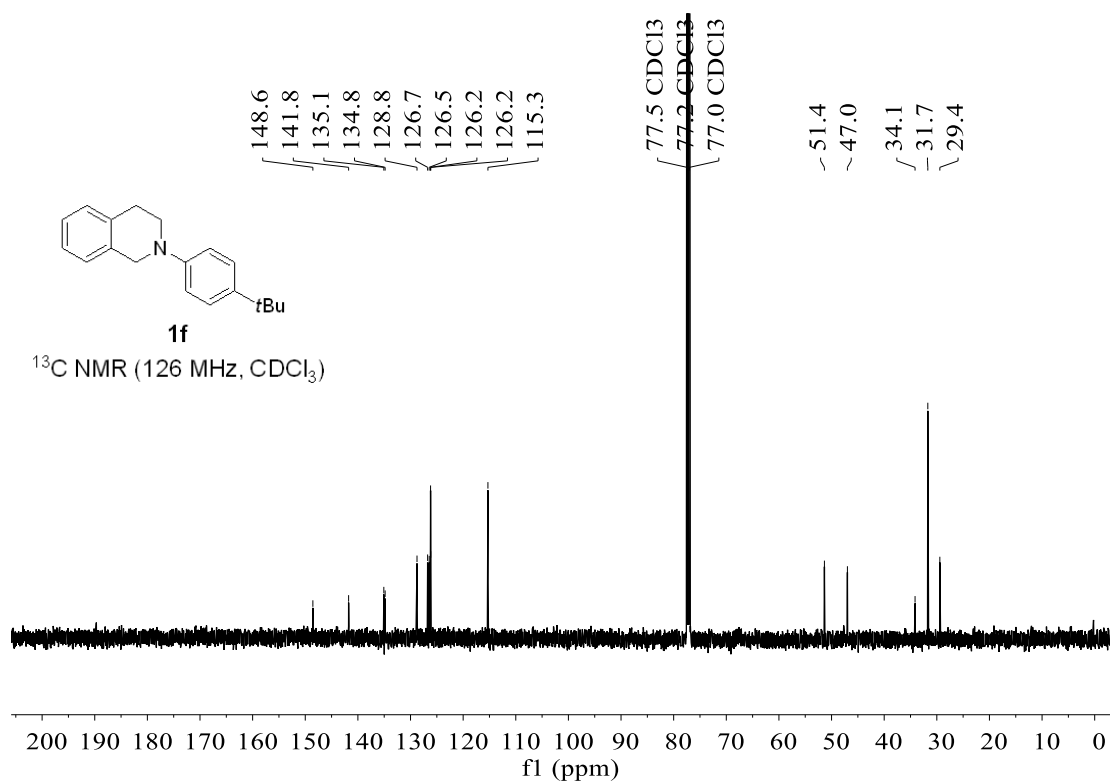
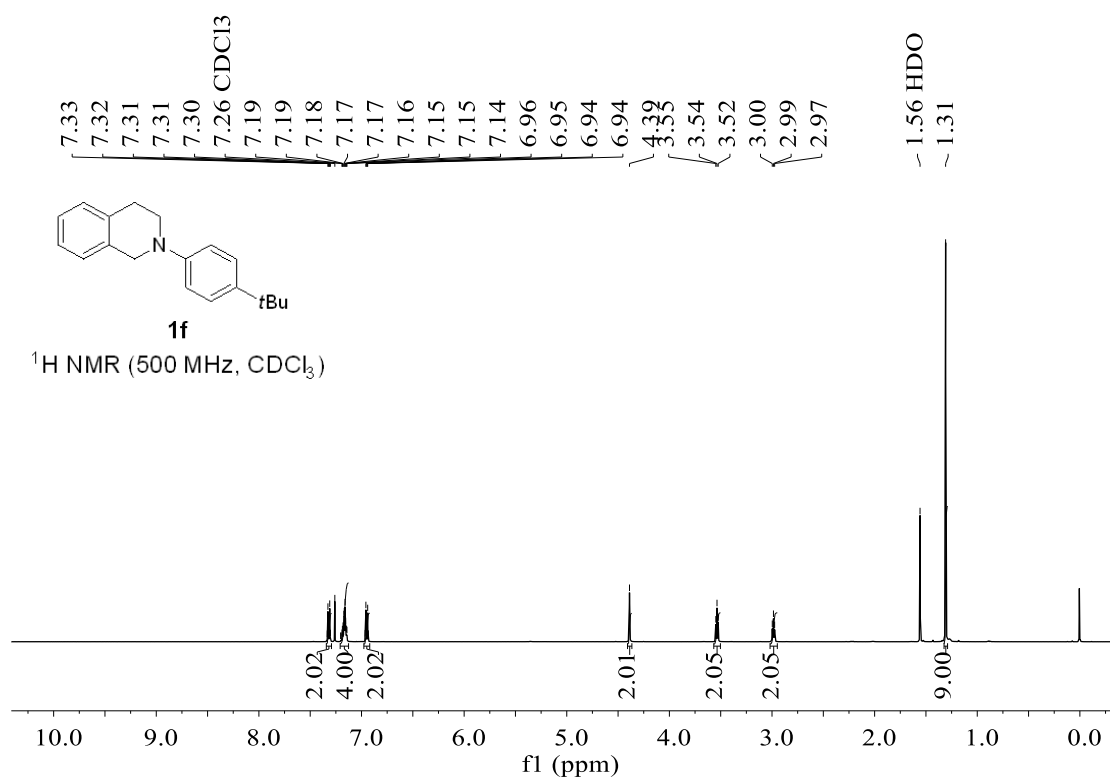
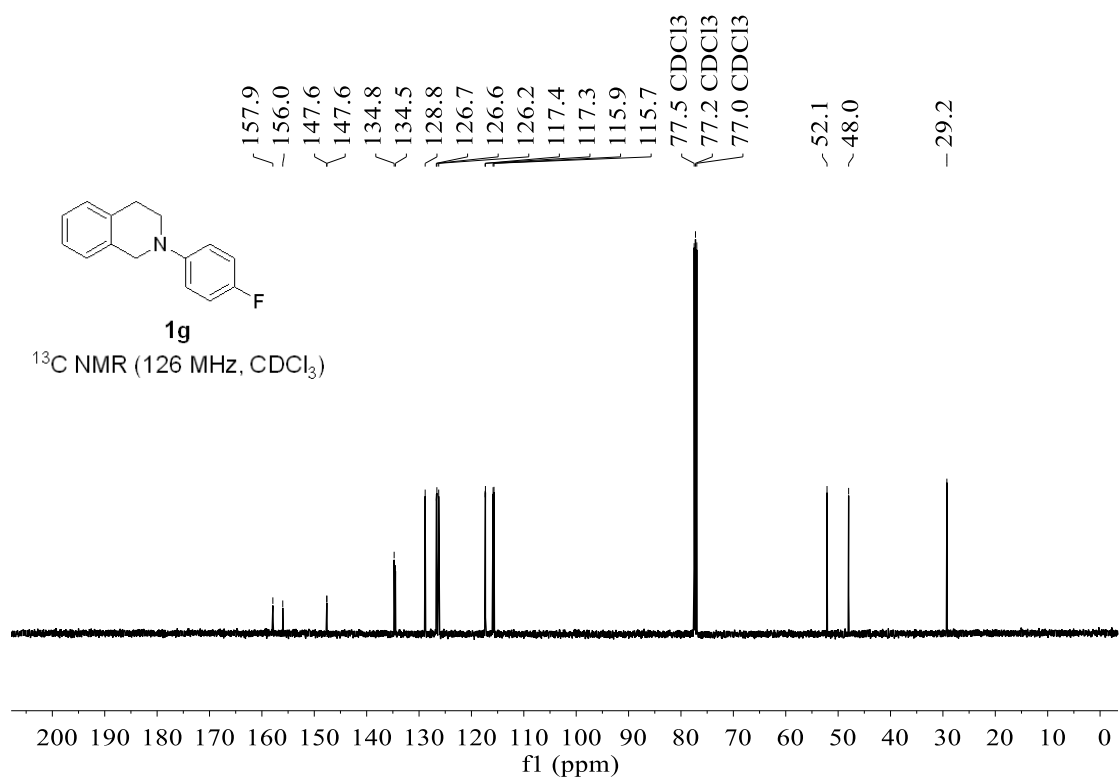
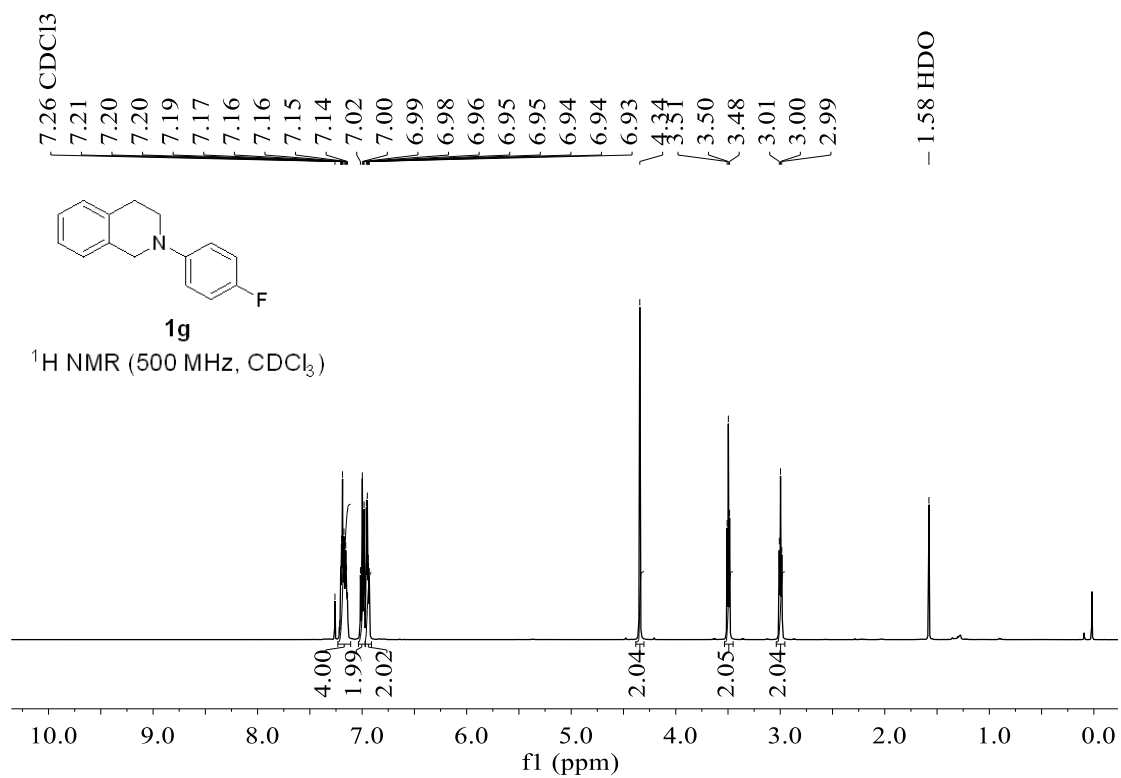


Figure S26. ¹H NMR and ¹³C NMR spectra of compound **1f**.



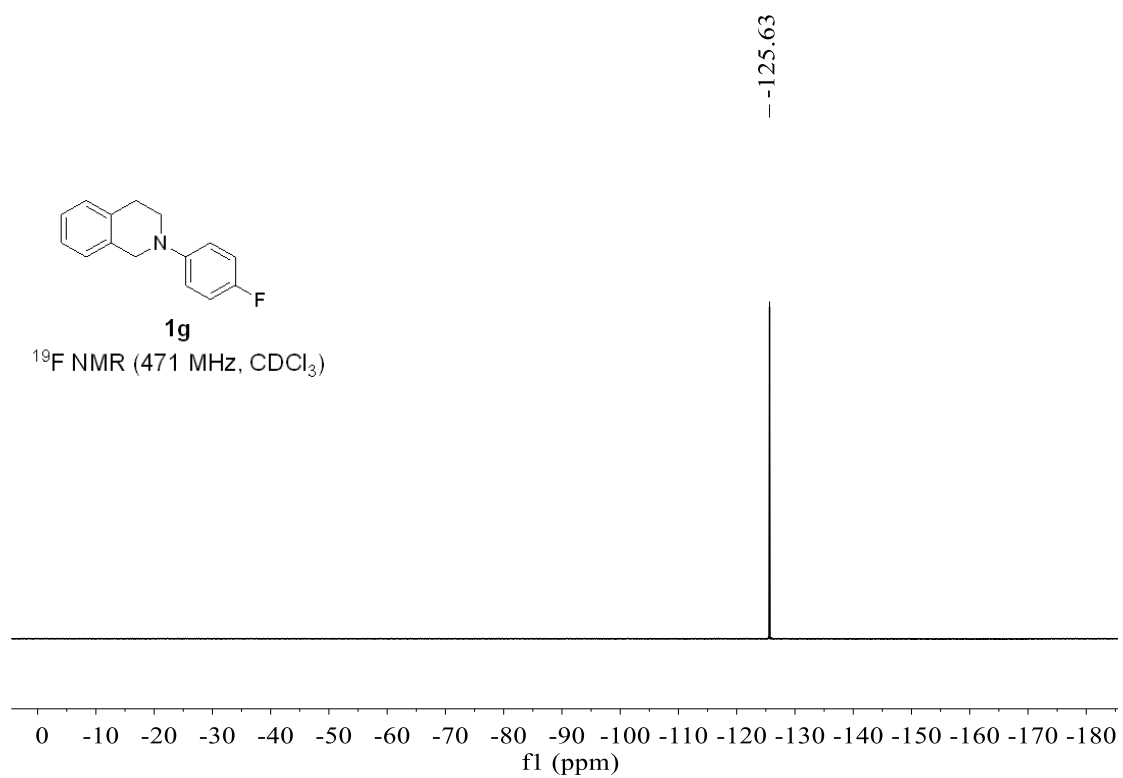


Figure S27. ¹H NMR, ¹³C NMR and ¹⁹F NMR spectra of compound **1g**.

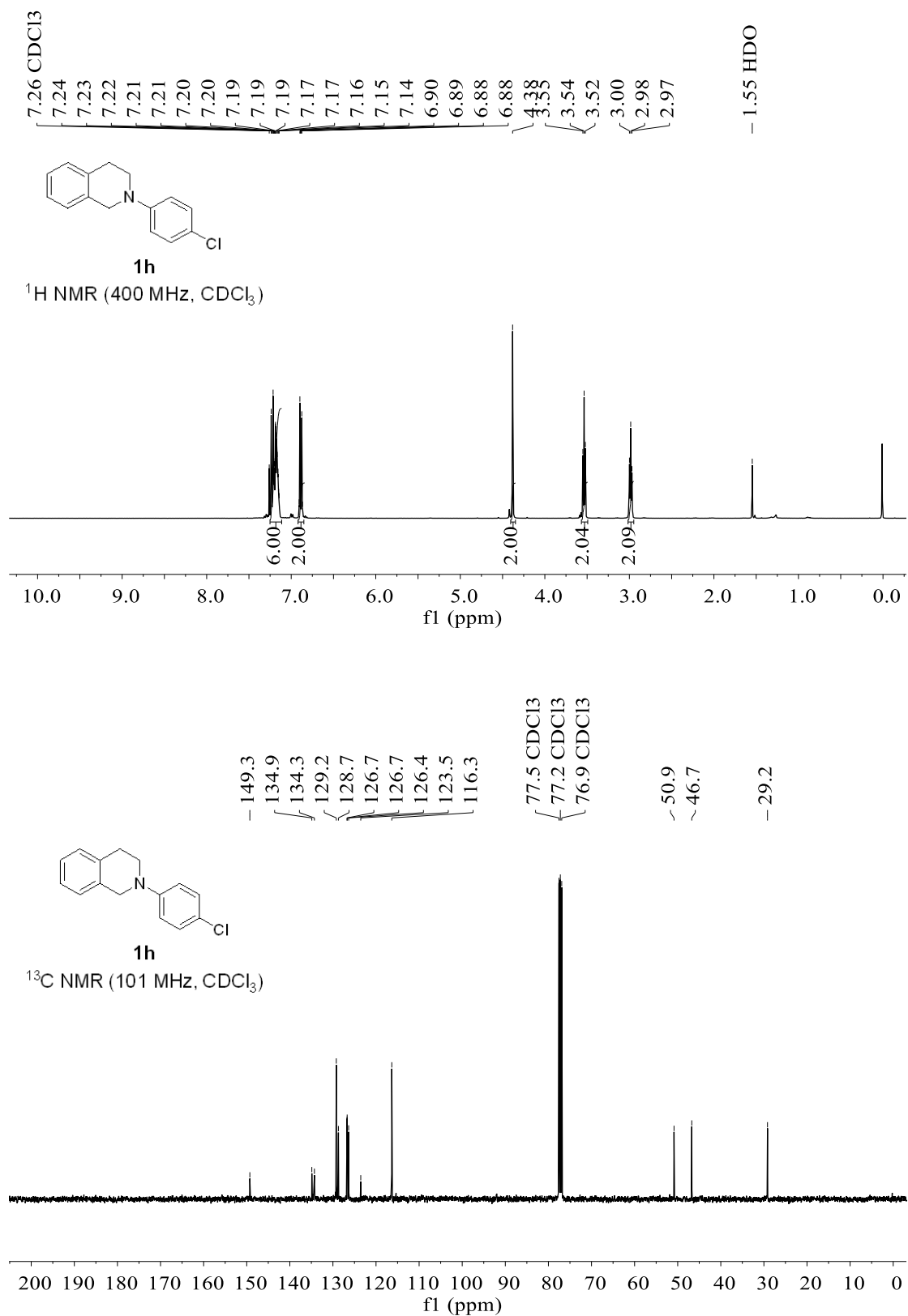


Figure S28. ¹H NMR and ¹³C NMR spectra of compound **1h**.

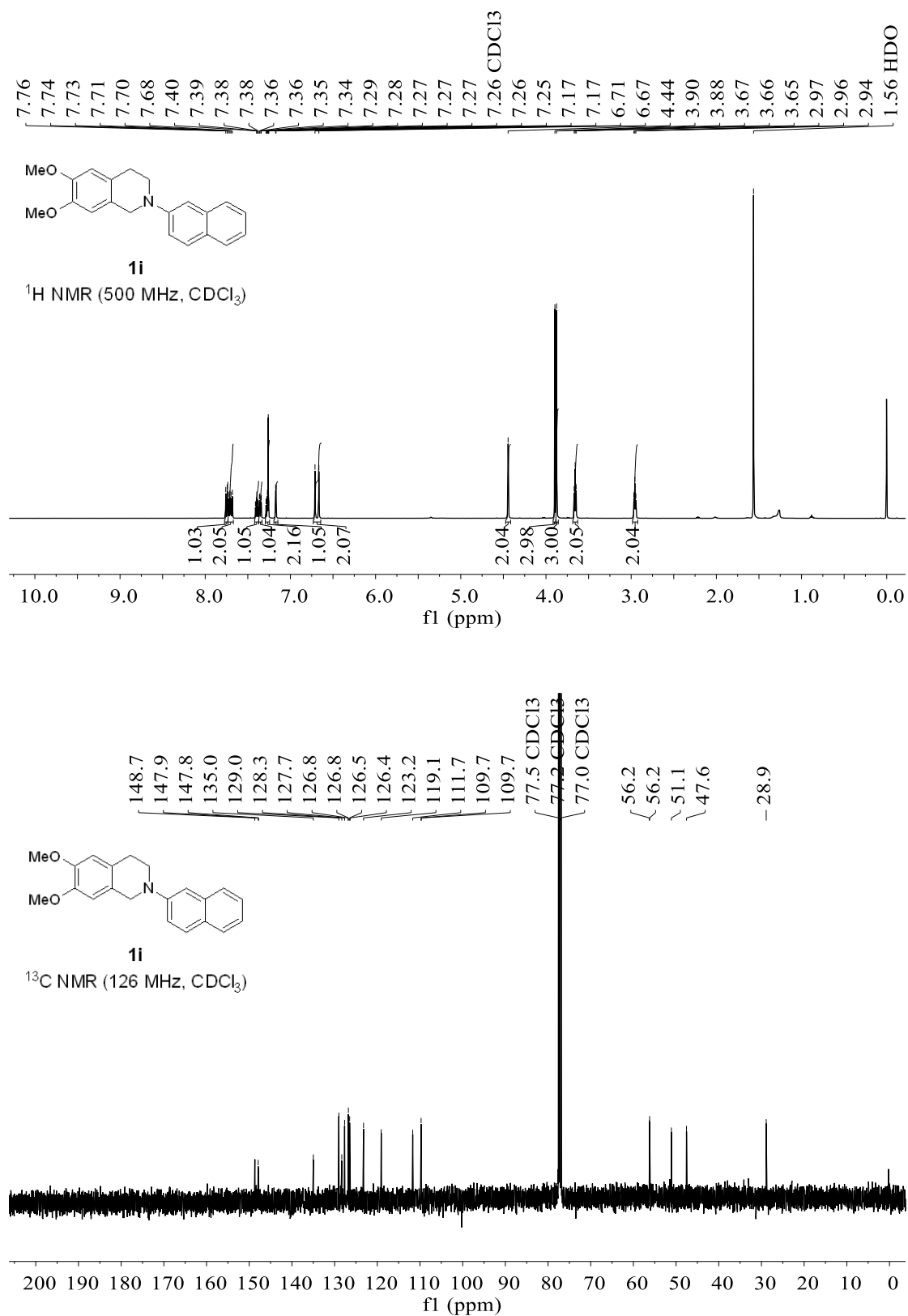


Figure S29. ¹H NMR and ¹³C NMR spectra of compound **1i**.