Supporting Information for

Cross-Dehydrogenative Coupling Reaction using Copper Oxide Impregnated on Magnetite in Deep Eutectic Solvents

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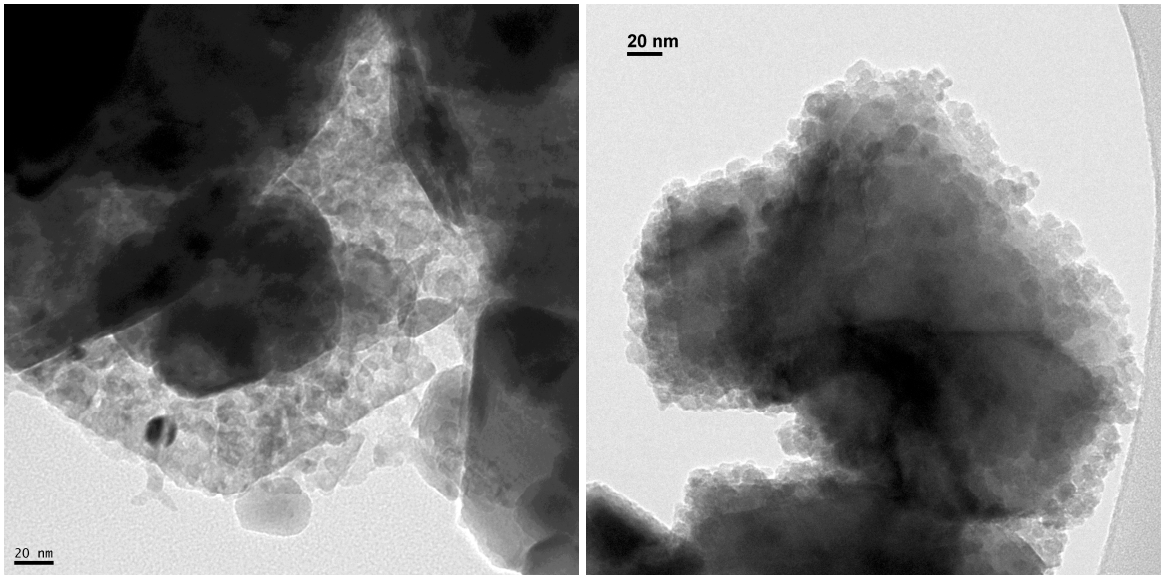
Table of Contents

I. TEM images of catalyst



A **B**

Image 1. TEM images of CuO-Fe_3O_4 catalyst before (A) and after (B) carrying out the reaction

II. Auger Electron Spectroscopy

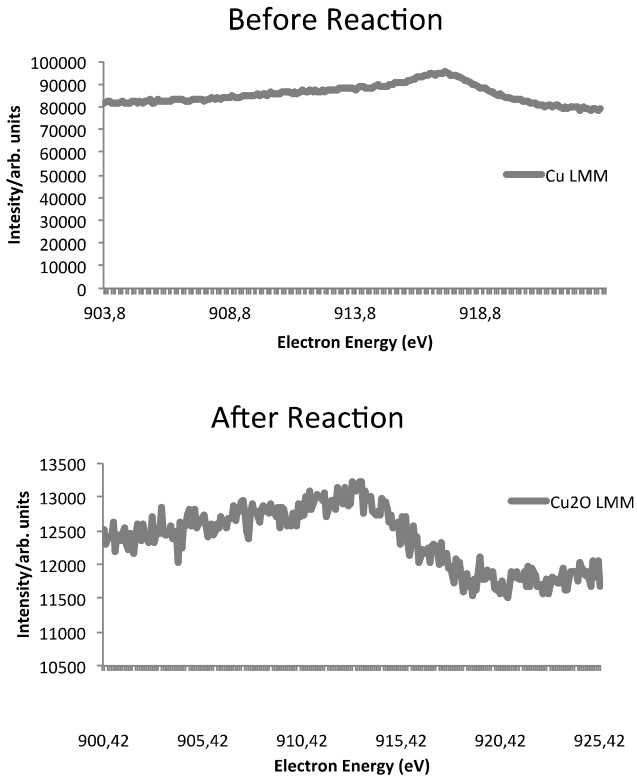


Image 2. Auger Electron Spectroscopy (AES) studies for catalyst before and after reaction was carried out.

III. Characterization data

2-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline (1a):[1] White solid; m.p. = 69-71 ºC (ethanol); t_r= 15.3; R_f= 0.6 (hexane/ethyl acetate: 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.2-7.1 (m, 4H, ArH), 6.9-7.0 (m, 4H, ArH), 4.33 (s, 2H, $ArCH_2N$), 3.48 (t, *J* = 5.9 Hz, 2H, CH_2CH_2N), 2.98 (t, *J* = 5.9 Hz, 2H, CH_2CH_2N). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.7 (d, *J* = 238.0 Hz), 147.4 (d, *J* = 1.5 Hz), 134.5, 134.3, 128.6, 126.5, 126.4, 126.0, 117.1 (d, *J* = 7.5 Hz, 2C), 115.5 (d, *J* = 22.0 Hz, 2C), 51.9, 47.8, 29.0. IR (ATR): ν 1505, 1205 cm^{-1}. MS (EI) *m/z* (%): 228 (M^++1, 14), 227 (M^+, 95), 226 (100), 104 (72), 103 (15), 95 (12), 78 (12).

2-phenyl-1,2,3,4-tetrahydroisoquinoline (1b):[2] Pale yellow solid; m.p. = 45-47 ºC (ethanol); t_r = 15.4; R_f = 0.8 (hexane/ethyl acetate : 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.3-7.25 (m, 2H, ArH), 7.2-7.1 (m, 4H, ArH), 6.96 (d, *J* = 8.0 Hz, 2H, ArH), 6.82 (t, *J* = 7.3 Hz, 1H, ArH), 4.39 (s, 2H, $ArCH_2N$), 3.53 (t, *J* = 5.8 Hz, 2H, CH_2CH_2N), 2.96 (t, *J* = 5.8 Hz, 2H, CH_2CH_2N). ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.5, 134.8, 134.4, 130.2 (2C), 129.2, 126.5, 126.3, 126.0, 118.6, 115.1 (2C), 50.7, 46.5, 29.1. IR (ATR): ν 3058, 3023, 1598, 1500, 1386 cm^{-1}. MS (EI) *m/z* (%): 210 (M^++1, 10), 209 (M^+, 82), 208 (M^+-1, 100), 104 (56), 78 (10), 77 (17).

2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (1c):[3] Pale orange solid; m.p. 92-94 ºC (ethanol); t_r = 18.56; R_f = 0.5 (hexane/ethyl acetate : 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.2-7.1 (m, 4H, ArH), 7.0-6.95 (m, 2H, ArH), 6.9-6.8 (m, 2H, ArH), 4.29 (s, 2H, $ArCH_2N$), 3.77 (s, 3H, OCH_3), 3.44 (t, *J* = 5.8 Hz, 2H, CH_2CH_2N), 2.98 (t, *J* = 5.8 Hz, 2H, CH_2CH_2N). ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.6, 145.5, 134.7 (2C), 128.8, 126.6, 126.4, 126.0, 118.1 (2C), 114.7 (2C), 55.8, 52.8, 48.6, 29.2. IR (ATR): ν 2808, 1509, 1239, 1036 cm^{-1}. MS (EI) *m/z* (%): 240 (M^++1, 16), 239 (M^+, 100), 238 (M^+-1, 93), 224 (22), 135 (27), 120 (20), 104 (24).

2-tosyl-1,2,3,4-tetrahydroisoquinoline (1d):[4] Pale yellow solid; m.p. 132-134 ºC (ethanol); t_r = 15.63; R_f = 0.4 (hexane/ethyl acetate : 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.75-7.7 (m, 2H, ArH), 7.4-7.3 (m, 2H, ArH), 7.14 (dd, *J* = 5.6, 3.5 Hz, 2H, ArH), 7.1-7.0 (m, 2H, ArH), 4.24 (s, 2H, $ArCH_2N$), 3.35 (t, *J* = 5.9 Hz, 2H, CH_2CH_2N), 2.93 (t, *J* = 5.9 Hz, 2H, CH_2CH_2N), 2.42 (s, 3H, Ar-CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.8, 133.3, 133.1, 131.7, 129.8 (2C), 129.0, 128.9, 127.8 (2C), 126.8, 126.4, 47.6, 43.8, 28.9, 21.6. IR (ATR): ν 3064, 1489, 1338, 1163 cm^{-1}. MS (EI) *m/z* (%): 287 (M^+, 5), 286 (M^+-1, 14), 132 (100), 131 (29), 130 (32), 105 (26), 104 (53), 103 (15), 91 (29), 77 (16).

2-(4-fluorophenyl)-1-(phenylethynyl)-1,2,3,4-tetrahydroisoquinoline (3a). Brown oil; t_r = 21.03; R_f = 0.6 (hexane/ethyl acetate : 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.4-7.35 (m, 1H, ArH), 7.3-7.2 (m, 8H, ArH), 7.1-7.05 (m, 2H, ArH), 7.05-7.0 (m, 2H, ArH), 5.54 (s, 1H, ArCHN), 3.65-3.6 (m, 2H, CH_2CH_2N), 3.2-3.1 (m, 1H, $CHCH_2N$), 2.96 (dt, *J* = 16.3, 3.6 Hz, 1H, $CHCH_2N$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.4 (d, *J* = 239.3 Hz), 146.4, 135.1, 134.0, 131.7 (2*C*), 129.0, 128.1 (3*C*), 127.4, 127.2, 126.2, 122.8, 119.4 (d, *J* = 7.7 Hz, 2C), 115,5 (d, *J* = 22.2 Hz, 2C), 88.1, 85.3, 53.7, 44.0, 29.0. IR (ATR): ν 3056, 3026, 1506, 1489 cm^{-1}. MS (EI) *m/z* (%): 328

(M^++1, 9), 327 (M^+, 50), 326 (M^+-1, 100), 222 (10), 207 (14), 204 (27), 203 (33), 202 (36), 102 (22). HRMS calcd. (%) for $C_{23}H_{18}FN$: 327.1423; found: 327.1412.

2-phenyl-1-(phenylethynyl)-1,2,3,4-tetrahydroisoquinoline (3b):[2] Yellow oil; t_r = 21.37; R_f = 0.6 (hexane/ethyl acetate : 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.4-7.35 (m, 1H, ArH), 7.35-7.25 (m, 4H, ArH), 7.25-7.2 (m, 6H, ArH), 7.12 (dd, *J* = 8.7, 0.9 Hz, 2H, ArH), 6.88 (dd, *J* = 7.7, 6.8 Hz, 1H, ArH), 5.64 (s, 1H, ArCHN), 3.8-3.9 (m, 1H, CH_2CH*H*N), 3.67 (ddd, *J* = 12.4, 10.2, 4.0 Hz, 1H, CH_2C*H*HN), 3.14 (ddd, *J* = 16.1, 10.2, 6.1 Hz, 1H, CH*H*CH_2N), 2.97 (dt, *J* = 16.1, 4.0 Hz, 1H, C*H*HCH_2N). ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.5, 135.4, 134.4, 131.7 (2C), 129.1 (2C), 128.9, 128.0 (2C), 128.0, 127.4, 127.2, 126.2, 123.0, 119.6, 116.7 (2C), 88.6, 84.7, 52.3, 43.4, 28.9. IR (ATR): ν 3059, 3024, 1596, 1501, 1490 cm^{-1}. MS (EI) *m/z* (%): 310 (M^+ + 1, 13), 309 (M^+, 63), 308 (100), 204 (27), 203 (21), 202 (27), 77 (8).

2-(4-methoxyphenyl)-1-(phenylethynyl)-1,2,3,4-tetrahydroisoquinoline (3c):[5] Brown oil; t_r = 25.14; R_f = 0.5 (hexane/ethyl acetate : 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35 (dd, *J* = 5.0, 3.9 Hz, 1H, ArH), 7.15-7.35 (m, 8H, ArH), 7.05-7.15 (m, 2H, ArH), 6.95-6.85 (m, 2H, ArH), 5.51 (s, 1H, ArCHN), 3.78 (s, 3H, OCH_3), 3.45-3.70 (m, 2H, CH_2C*H*$_2$N), 3.15 (ddd, *J* = 16.4, 6.2, 3.4 Hz, 1H, CH*H*CH_2N), 2.93 (dt, *J* = 16.4, 3.4 Hz, 1H, C*H*HCH_2N). ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.3, 144.1, 135.4, 134.0, 131.7 (2C), 129.0, 128.0 (2C), 127.9, 127.5, 127.1, 126.1, 123.1, 120.2 (2C), 114.4 (2C), 88.4, 85.5, 54.6, 54.4, 44.2, 29.0. IR (ATR): ν 1509, 1242, 1035 cm^{-1}. MS (EI) *m/z* (%): 339 (M^+, 82), 338 (M^+-1, 100), 291 (29), 283 (35), 281 (51), 218 (28), 208 (47), 207 (95), 204 (31), 203 (33), 202 (31), 133 (28), 115 (28), 102 (40), 92 (31), 78 (33), 61 (36).

2-(4-fluorophenyl)-1-((4-methoxyphenyl)ethynyl)-1,2,3,4-tetrahydroisoquinoline (3f). Pale yellow oil; t_r = 26.42; R_f = 0.4 (hexane/ethyl acetate : 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35-7.30 (m, 1H, ArH), 7.25-7.20 (m, 3H, ArH), 7.15-7.20 (m, 2H, ArH), 7.10-7.05 (m, 2H, ArH), 7.05-7.0 (m, 2H, ArH), 6.75-6.70 (m, 2H, ArH), 5.52 (s, 1H, ArCHN), 3.75 (s, 3H, OCH_3), 3.65-3.55 (m, 2H, CH_2C*H*$_2$N), 3.2-3.1 (m, 1H, CH*H*CH_2N), 2.94 (dt, *J* = 16.2, 3.6 Hz, C*H*HCH_2N). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.4, 157.4 (d, *J* = 238.8 Hz), 146.4, 135.4, 133.9, 133.1 (2C), 128.9, 127.4, 127.2, 126.2, 115.4 (d, *J* = 22.1 Hz, 2C), 114.9, 113.7 (2C), 86.6, 85.2, 55.2, 53.7, 44.0, 28.9. IR (ATR): ν 3050, 1604, 1506 cm^{-1}. MS (EI) *m/z* (%): 357 (M^+, 82), 356 (M^+-1, 100), 283 (10), 208 (11), 207 (54), 191 (19), 190 (10), 189 (29), 133 (15), 73 (12), 65 (10). HRMS calcd. (%) for $C_{24}H_{20}FNO$: 357.1529; found: 357.1517.

1-((4-bromophenyl)ethynyl)-2-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline (3g): Brown oil; t_r = 26.5; R_f = 0.6 (hexane/ethyl acetate : 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.4-7.3 (m, 3H, ArH), 7.25-7.15 (m, 3H, ArH), 7.15-6.95 (m, 6H, ArH), 5.52 (s, 1H, ArCHN), 3.60 (dd, *J* = 8.6, 3.7 Hz, 2H, CH_2C*H*$_2$N), 3.13 (dt, *J* = 16.3, 8.6 Hz, 1H, CH*H*CH_2N), 2.95 (dt, *J* = 16.3, 3.7 Hz, 1H, C*H*HCH_2N). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.6 (d, *J* = 239.3 Hz), 146.6, 135.0, 134.1, 133.2, 131.5, 129.2, 127.5 (2C), 126.4, 122.4, 121.9, 119.5 (d, *J* = 7.7 Hz, 2C), 115.7 (d, *J* = 22.2 Hz, 2C), 49.5, 84.4, 53.9, 44.2, 29.1. IR (ATR): ν 3058, 3025, 1657, 1507 cm^{-1}. MS (EI) *m/z* (%): 408 (M^++2, 11), 407 (M^++1, 54), 406 (M^+, 100), 404 (M^+-2, 94), 284 (26), 282 (27), 350 (15), 226 (10), 224 (25), 207 (10), 203 (23), 202 (83), 201 (16), 200 (12), 122 (15), 95 (17). HRMS calcd. (%) for ($C_{23}H_{17}BrFN$ - H): 404.0450; found: 404.0437.

2-(4-fluorophenyl)-1-((4-(trifluoromethyl)phenyl)ethynyl)-1,2,3,4-tetrahydroisoquinoline (3h). Orange oil, t_r = 20.23; R_f = 0.5 (hexane/ethyl acetate : 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.5-7.45 (m, 2H, ArH), 7.4-7.3 (m, 3H, ArH), 7.25-7.20 (m, 3H, ArH), 7.15-6.95 (m, 4H, ArH), 5.56 (s, 1H, ArCHN), 3.61 (dd, *J* = 8.5, 3.6 Hz, 2H, CH_2CH_2N), 3.2-3.1 (m, 1H, $CH\mathit{H}CH_2N$), 2.96 (dt, *J* = 16.2, 3.6 Hz, 1H, $C\mathit{H}HCH_2N$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.5 (d, *J* = 239.5), 146.2, 134.6, 134.0, 131.9 (2*C*), 129.8 (q, J = 32.6 Hz), 129.0, 127.4 (2*C*), 126.6, 126.3, 125.0 (q, J = 3.6 Hz, 2C), 123.8 (q, *J* = 271.1 Hz), 119.4 (d, *J* = 7.7 Hz, 2C), 115.6 (d, *J* = 22.1 Hz, 2C), 90.8, 84.0, 53.8, 44.0, 28.9. IR (ATR): ν 3065, 1614, 1507 cm^{-1}. MS (EI) *m/z* (%): 396 (M^++1, 12), 395 (M^+, 64), 394 (M^+-1, 100), 272 (46), 203 (10), 202 (31), 95 (12). HRMS calcd. (%) for $C_{24}H_{17}F_4N$: 395.1297; found: 395.1287.

1-((3-chlorophenyl)ethynyl)-2-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline (3i): Yellow oil; t_r = 23.6; R_f = 0.7 (hexane/ethyl acetate : 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35-7.3 (m, 1H, ArH), 7.3-7.2 (m, 5H, ArH), 7.15-7.1 (m, 2H, ArH), 7.10-6.95 (m, 4H, ArH), 5.52 (s, 1H, ArCHN), 3.60 (dd, *J* = 8.3, 3.6 Hz, 2H, $CH_2C\mathit{H}_2N$), 3.2-3.05 (m, 1H, $CH\mathit{H}CH_2N$), 2.95 (dt, *J* = 16.2, 3.4 Hz, 1H, $C\mathit{H}HCH_2N$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.7 (d, *J* = 239.3 Hz), 146.4, 134.9, 134.1 (2C), 131.7, 130.0, 129.5, 129.2, 128.5, 127.5 (2C), 126.5, 124.7, 119.5 (d, *J* = 7.6 Hz, 2C), 115.7 (d, *J* = 22.2 Hz, 2C), 89.6, 84.1, 53.8, 44.2, 29.1. IR (ATR): ν 3061, 2924, 2832, 1591, 1507 cm^{-1}. MS (EI) *m/z* (%): 362 (M^++1, 42), 361 (M^+, 67), 360 (M^+-1, 100), 238 (35), 208 (13), 207 (56), 203 (21), 202 (52), 136 (13). HRMS calcd. (%) for ($C_{23}H_{17}ClFN$ - H): 360.0955; found: 360.0966.

1-((2-bromophenyl)ethynyl)-2-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline (3j): Brown oil; t_r = 25.4; R_f = 0.4 (hexane/ethyl acetate : 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.48 (dd, *J* = 7.9, 1.3 Hz, 1H, ArH), 7.4-7.35 (m, 1H, ArH), 7.29 (dd, *J* = 7.6, 1.8 Hz, 1H, ArH), 7.25-7.15 (m, 3H, ArH), 7.15-6.95 (m, 6H, ArH), 5.59 (s, 1H, ArCHN), 3.75-3.55 (m, 3H, $CH_2C\mathit{H}_2N$), 3.15 (m, 1H, $CH\mathit{H}CH_2N$), 2.97 (dt, *J* = 16.3, 3.7 Hz, 1H, $C\mathit{H}HCH_2N$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.6 (d, *J* = 239.1 Hz), 146.4, 134.9, 134.2, 133.5, 132.4, 129.4, 129.1, 127.7, 127.5, 126.9, 126.4, 125.7, 125.1, 119.6 (d, *J* = 7.6 Hz, 2C), 115.7 (d, *J* = 22.1 Hz, 2C), 93.1, 84.1, 53.9, 44.3, 29.2. IR (ATR): ν 3063, 2920, 1507, 1468 cm^{-1}. MS (EI) *m/z* (%): 407 (M^++1, 5), 406 (M^+, 12), 405 (M^+-1, 5), 404 (M^+-2, 12), 281 (20), 209 (36), 207 (100), 202 (11). HRMS calcd. (%) for ($C_{23}H_{17}BrFN$ - H): 404.0450; found: 404.0451.

1-(cyclohex-1-en-1-ylethynyl)-2-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline (3k). Brown oil; t_r = 20.99; R_f = 0.6 (hexane/ethyl acetate : 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.3-7.25 (m, 1H, ArH), 7.20-7.15 (m, 4H, ArH), 7.05-6.95 (m, 3H, ArH), 5.95-5.9 (m, 1H, C=CH), 5.42 (s, 1H, ArCHN), 3.6-3.50 (m, 2H, $CH_2C\mathit{H}_2N$), 3.15-3.05 (m, 1H, $CH\mathit{H}CH_2N$), 2.91 (dt, *J* = 16.2, 3.6 Hz, 1H, $C\mathit{H}HCH_2N$), 2.0-1.95 (m, 4H, CH-$C_4H_4\mathit{H}_4$-C=), 1.55-1.50 (m, 4H, CH-$C_4\mathit{H}_4H_4$-C=). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.3 (d, *J* = 238.7 Hz), 146.4, 135.6, 134.6, 133.8, 128.9, 127.4, 127.0, 126.1, 120.2, 119.2 (d, *J* = 7.6 Hz, 2C), 115.4 (d, *J* = 22.1 Hz, 2C), 87.1, 85.2, 53.5, 43.9, 29.2, 28.9, 25.5, 22.2, 21.4. IR (ATR): ν 3050, 3023, 2927, 2857, 1507 cm^{-1}. MS (EI) *m/z* (%): 331 (M^+, 18), 330 (M^+-1, 34), 281 (15), 208 (14), 207 (100). HRMS calcd. (%) for $C_{23}H_{22}FN$: 331.1736; found: 331.1719.

1-(cyclohexylethynyl)-2-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline (3l). Yellow oil; t_r = 19.87, R_f = 0.3 (hexane/ethyl acetate 9/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.3-7.25 (m, 1H, ArH), 7.2-7.1 (m, 3H, ArH), 7.05-6.95 (m, 4H, ArH), 5.32 (s, 1H, ArCHN), 3.52 (dd, *J* = 8.5, 3.6 Hz, 2H, CH_2CH_2N), 3.10-3.05 (m, 1H, $CHCH_2N$), 2.89 (dt, *J* = 16.2, 3.6 Hz, 1H, $CHCH_2N$), 2.3-2.25 (m, 1H, C_6H_{11}), 1.65-1.5 (m, 4H, C_6H_{11}), 1.45-1.4 (m, 1H, C_6H_{11}), 1.3-1.15 (m, 5H, C_6H_{11}). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.3 (d, *J* = 238.6 Hz), 146.6, 136.0, 133.7, 128.8, 127.3, 126.9, 126.0, 119.3 (d, *J* = 7.6 Hz, 2C), 115.3 (d, *J* = 22.1 Hz, 2C), 89.9, 78.6, 53.2, 43.8, 32.5 (2C), 29.0, 28.8 (2C), 25.8, 24.4. IR (ATR): ν 3061, 3024, 2927, 2852, 1507 cm^{-1}. MS (EI) *m/z* (%): 334 (M^++1, 11), 333 (M^+, 74), 332 (M^+-1, 100), 250 (30), 224 (12), 167 (16), 165 (13), 153 (11), 141 (13), 128 (17), 115 (12), 95 (13). HRMS calcd. (%) for $C_{23}H_{24}FN$: 333.1893; found: 333.1885.

2-(4-fluorophenyl)-1-(nona-1,8-diyn-1-yl)-1,2,3,4-tetrahydroisoquinoline (3m). Pale yellow oil; t_r = 20.50, R_f = 0.5 (hexane/ethyl acetate : 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30-7.25 (m, 1H, ArH), 7-20-7.10 (m, 3H, ArH), 7.05-6.95 (m, 4H, ArH), 5.31 (s, 1H, ArCHN), 3.60-3.50 (m, 2H, CH_2CH_2N), 3.09 (dt, *J* = 16.4, 8.3, 1H, $CHCH_2N$), 2.90 (dt, *J* = 16.4, 3.6 Hz, 1H, $CHCH_2N$), 2.15-2.00 (m, 4H, 2x C≡C-CH_2), 1.92 (t, *J* = 2.6 Hz, 1H, C≡C-H), 1.50-1.15 (m, 6H, (m, 6H, C≡C-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-C≡C). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.4 (d, *J* = 238.8 Hz), 146.6, 136.1, 133.9, 129.0, 127.5, 127.2, 126.3, 119.2 (d, *J* = 7.6 Hz, 2C), 115.5 (d, *J* = 22.1 Hz, 2C), 85.7, 84.6, 79.1, 68.4, 53.8, 43.9, 29.1, 28.3, 28.1, 27.9, 18.7, 18.4. IR (ATR): ν 3303, 2937, 2859, 1508 cm^{-1}. MS (EI) *m/z* (%): 345 (M^+, 38), 344 (M^+-1, 100), 302 (12), 276 (27), 264 (13), 262 (31), 250 (27), 226 (12), 224 (19), 207 (18), 155 (13), 153 (13), 142 (11), 141 (23), 95 (13). HRMS calcd. (%) for $C_{24}H_{24}FN$: 345.1893; found: 345.1877.

2-(4-fluorophenyl)-1-(3-((tetrahydro-2*H*-pyran-2-yl)oxy)prop-1-yn-1-yl)-1,2,3,4-tetrahydroisoquinoline (3n): Colourless oil; t_r = 22.28; R_f = 0.4 (hexane/ethyl acetate : 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30-7.15 (m, 4H, ArH), 7.05-6.95 (m, 4H, ArH), 5.39 (s, 1H, ArCHN), 4.56 (t, *J* = 3.2 Hz, 1H, O-CH-O), 4.18 (d, *J* = 1.9 Hz, 2H, C≡C-CH_2O), 3.8-3.65 (m, 1H, CH_2CH_2O), 3.6-3.5 (m, 2H, CH_2CH_2N), 3.45-3.35 (m, 1H, CH_2CH_2O), 3.10 (ddd, *J* = 16.3, 9.7, 7.0 Hz, 1H, $CHCH_2N$), 2.90 (dt, *J* = 16.3, 3.5 Hz, 1H, $CHCH_2N$), 1.80-1.70 (m, 1H, $CHCH_2CH_2CH_2CH_2O$), 1.65-1.40 (m, 5H, $CHCH_2CH_2CH_2CH_2O$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.5 (d, *J* = 239.2 Hz), 146.5, 135.0, 134.0, 129.1, 127.5, 127.4, 126.3, 119.3 (d, *J* = 7.7 Hz, 2C), 115.6 (d, *J* = 22.1 Hz, 2C), 96.4, 84.8, 81.2, 62.1, 54.3, 53.3, 43.9, 30.3, 29.0, 25.5, 19.2. IR (ATR): ν 2923, 2849, 1230, 1021 cm^{-1}. MS (EI) *m/z* (%): 365 (M^+, 16), 364 (M^+-1), 281 (16), 280 (16), 264 (56), 263 (37), 262 (100), 250 (19), 248 (29), 235 (12), 226 (22), 224 (21), 207 (27), 141 (21), 140 (12), 139 (13), 129 (14), 128 (14), 122 (15), 115 (26), 95 (18), 85 (17), 84 (46), 83 (24), 57 (12), 56 (25), 55 (60), 54 (12). HRMS calcd. (%) for $C_{23}H_{24}FNO_2$: 365.1791; found: 365.1781.

2-(4-fluorophenyl)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (3o):[3] Yellow oil; t_r = 17.45; R_f = 0.3 (hexane/ethyl acetate : 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.3-7.05 (m, 4H, ArH), 6.95-6.85 (m, 4H, ArH), 5.42 (dd, *J* = 8.6, 5.9 Hz, 1H, ArCHN), 4.82 (dd, *J* = 12.0, 8.6 Hz, 1H, $CHNO_2$), 4.55 (dd, *J* = 12.0, 5.9 Hz, 1H, $CHNO_2$), 3.6-3.55 (m, 2H, CH_2CH_2N), 3.05-2.95 (m, 1H, $CHCH_2N$), 2.70 (dt, *J* = 16.5, 4.2 Hz, 1H, $CHCH_2N$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.1 (d, *J* = 239.1 Hz), 145.3, 135.2, 132.5, 129.4, 128.0, 126.9, 126.7, 117.8 (d, *J* = 7.6 Hz, 2C), (d, *J* = 22.2 Hz, 2C), 115.8,

78.7, 58.6, 42.7, 25.7. IR (ATR): ν 2913, 2843, 1547, 1506 cm^{-1}. MS (EI) *m/z* (%): 286 (M^+, 5), 227 (M^+, 23), 226 (100), 225 (29), 224 (68), 128 (10), 104 (13), 95 (12).

2-(4-fluorophenyl)-1-(1-methyl-1*H*-indol-3-yl)-1,2,3,4-tetrahydroisoquinoline (3p): White solid; m.p. 137-139 ºC (ethanol); t_r = 24.6; R_f = 0.5 (hexane/ethyl acetate : 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42 (dt, *J* = 8.0, 0.9 Hz, 1H, ArH), 7.25-7.1 (m, 6H, ArH), 7.0 (ddd, *J* = 8.0, 6.8, 1.3 Hz, 1G, ArH), 6.95-6.85 (m, 4H, ArH), 6.43 (s, 1H, C=CHN), 6.0 (s, 1H, ArCHN), 3.61 (s, 3H, N-CH_3), 3.60-3.40 (m, 2H, CH_2CH_2N), 3.02 (ddd, *J* = 16.1, 9.8, 5.8 Hz, 1H, $CHCH_2N$), 2.79 (d, *J* = 16.1, 4.3 Hz, $CHCH_2N$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.7 (d, *J* = 237.7 Hz), 146.9, 137.6, 137.4, 135.4, 129.0 (2C), 128.3, 127.2, 126.7, 125.9, 121.8, 120.2, 119.3, 118.6 (d, *J* =7.5 Hz, 2C), 117.5, 115.6 (d, *J* = 22.0 Hz, 2C), 109.3, 57.7, 43.4, 32.8, 26.9. IR (ATR): ν 3047, 2957, 1505 cm^{-1}; MS (EI) *m/z* (%): 355 (M^+-1, 1%), 262 (20), 186 (13), 170 (37), 169 (14), 168 (23), 142 (10), 141 (26), 115 (12), 104 (12), 94 (66), 78 (100), 77 (43), 76 (16), 66 (16), 65 (16), 52 (13), 51 (22), 50 (17). HRMS calcd. (%) for $C_{24}H_{21}FN_2$: 356.1689; found: 356.1692.

(diethyl(2-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)phosphonate (3q):[6] Pale pink oil; t_r = 17.52, R_f = 0.3 (hexane/ethyl acetate : 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40-7.30 (m, 1H, ArH), 7.25-7.10 (m, 3H, ArH), 7.0-6.85 (m, 4H, ArH), 5.06 (d, *J* = 20.2 Hz, 1H NCHP), 4.3-3.8, 3.6-3.45 (2m, 1 and 5H, respectively, CH_2CH_2N + 2xOCH_2CH_3), 3.10-2.85 (m, 2H, CH_2CH_2N), 1.24 (t, *J* = 7.07, 3H, OCH_2CH_3), 1.14 (td, *J* = 7.07, 0.28, 3H, OCH_2CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.5 (d, *J* = 237.7 Hz), 146.3 (dd, *J* = 6.4, 1.9 Hz), 136.4 (d, *J* = 5.5 Hz), 130.5, 128.9 (2C), 127.6, 126.0, 116.7 (d, *J* = 7.4 Hz, 2C), 115.6 (d, *J* = 22.1 Hz, 2C), 63.4 (d, *J* = 7.3 Hz), 62.4 (d, *J* = 7.7 Hz), 59.4 (d, *J* = 158.4 Hz), 44.38, 16.5 (d, *J* = 5.9 Hz), 26.64, 16.4 (d, *J* = 5.9 Hz). IR (ATR): ν 1508, 1234, 1018 cm^{-1}. MS (EI) *m/z* (%): 363 (M^+, 1), 227 (21), 226 (100), 224 (13).

2-(2-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)cyclohexanone (3r):[7] Yellow oil; t_r = 19.73, R_f = 0.4 (hexane/ethyl acetate : 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.25-6.75 (4m, 1, 7, 7 y 1H, respectively, ArH), 5.56 (d, *J* = 8.5 Hz, 1H, ArCHN *anti*), 5.47 (d, *J* = 5.2 Hz, 1H, ArCHN *syn*), 3.5-3.7 (2m, 2 y 2H, respectively, CH_2CH_2N), 2.8-2.9 (m, 6H, CH_2CH_2N + C*H*C=O), 2.15-2.45 (2m, 2 y 2H, respectively, CH_2-C=O), 1.25-1.9 (m, 12H, 6xCH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 212.1 (*anti*), 211.9 (*syn*), 156.3 (d, *J* = 237.5 Hz, *syn*), 155.2 (d, *J* = 235.3 Hz, *anti*), 146.2 (2C, *anti*, *syn*), 140.1 (*anti*), 135.8 (*syn*), 135.0 (*syn*), 134.5 (*anti*), 128.9 (*syn*), 128.1 (*anti*), 128.0 (*syn*), 127.3 (*anti*), 126.8 (2C, *anti*, *syn*), 126.4 (*anti*), 125.8 (*syn*), 117.1 (d, *J* = 7.3 Hz, *syn*), 115.5 (d, *J* = 22.0 Hz, *syn*), 115.4 (d, *J* = 22.0 Hz, *anti*), 113.6 (d, *J* = 7.3 Hz, *anti*), 59.4 (*anti*), 56.5 (*syn*), 55.8 (*syn*), 54.7 (*anti*), 44.1 (*anti*), 43.5 (*syn*), 43.2 (*anti*), 41.4 (*syn*), 32.8 (*anti*), 30.5 (*syn*), 28.8 (*anti*), 27.5 (*syn*), 27.4 (*anti*), 26.8 (*syn*), 25.7 (*anti*), 23.8 (*syn*). IR (ATR): ν 2938, 2862, 1703, 1507 cm^{-1}. MS (EI) *m/z* (%): 323 (M^+, 0.5%), 227 (19), 226 (100), 55 (14).

1-(2-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)but-3-en-2-one (3s). Yellow oil; t_r = 17.51, R_f = 0.4 (hexane/ethyl acetate : 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.2-7.1(m, 4H, ArH), 7.0-6.8 (m, 4H, ArH), 6.29 (dd, *J* = 17.6, 10.5 Hz, 1H, C=CH*H*), 6.10 (dd, *J* = 17.6, 1.1 Hz, 1H, C*H*=CH_2), 5.76 (dd, *J* = 10.5 Hz, 1.1 Hz, 1H, CH=C*H*H), 5.37 (t, *J* = 6.3 Hz, 1H, ArCHN), 3.45-3.65 (m, 2H, CH_2CH_2N), 3.19 (dd, *J* = 16.1, 6.3 Hz, 1H, CH*H*C=O), 3.04 (m, 1H, $CHCH_2N$), 2.94 (dd, *J* = 16.1, 6.3 Hz,

1H, C*H*HC=O), 2.80 (dt, *J* = 16.2, 4.5 Hz, 1H, C*H*HCH$_2$N). ^{13}C NMR (75 MHz, $CDCl_3$): δ 199.1, 156.5 (d, *J* = 237.3 Hz), 145.8, 138.2, 136.9, 134.3, 128.9, 128.7, 127.1, 127.0, 126.4, 116.9 (d, *J* = 7.4 Hz, 2C), 115.8 (d, *J* = 22.1 Hz, 2C), 55.9, 46.1, 42.6, 27.1. IR (ATR): ν 3052, 1676, 987, 956 cm^{-1}. MS (EI) *m/z* (%): 295 (M$^+$, 6), 227 (19), 226 (100), 225 (11), 207 (17), 55 (11). HRMS calcd. (%) for $C_{19}H_{18}FNO$: 295.1862; found: 295.1845.

(*E*)-2-(4-fluorophenyl)-1-styryl-1,2,3,4-tetrahydroisoquinoline (3t). Orange oil; t_r = 21.48, R_f = 0.6 (hexane/ethyl acetate : 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45-7.10 (m, 9H, ArH), 7.05-6.75 (m, 4H, ArH), 6.40 (d, *J* = 15.9 Hz, 1H, CH=C*H*-Ph), 6.3 (dd, *J* = 15.9, 4.7 Hz, 1H, CHC*H*=CH-Ph), 5.25 (d, *J* = 4.7 Hz 1H, ArCHN), 3.63 (ddd, *J* = 12.2, 7.3, 5.1 Hz, 1H, CH$_2$CH*H*N), 3.55-3.45 (m, 1H, CH$_2$C*H*HN), 3.10-2.85 (m, 2H, C*H*$_2$CH$_2$N). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.4 (d, *J* = 237.0 Hz), 146.5 (2C), 136.9, 136.5, 135.4, 131.0, 130.4, 128.6 (2C), 127.8, 127.6, 127.0, 126.6 (2C), 126.4, 116.6 (d, *J* = 7.4 Hz, 2C), 115.7 (d, *J* = 22.1 Hz, 2C), 62.4, 43.9, 28.4. IR (ATR): ν 3025, 2904, 2834, 1735, 1507 cm^{-1}. MS (EI) *m/z* (%): 329 (M$^+$, 52), 328 (M$^+$-1, 38), 252 (10), 238 (30), 237 (20), 226 (100), 224 (17), 128 (12), 115 (14), 95 (11), 91 (24). HRMS calcd. (%) for $C_{23}H_{20}FN$: 329.1580; found: 329.1577.

2-(4-fluorophenyl)-3,4-dihydroisoquinolin-1(2*H*)-one (4a). Yellow solid; m.p. 112-114 ºC (ethanol); t_r = 16.56; R_f = 0.5 (hexane/ethyl acetate : 3/2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14 (dd, *J* = 7.7, 1.2 Hz, 1H, ArH), 7.47 (td, *J* = 7.4, 1.5 Hz, 1H, ArH), 7.4-7.3 (m, 3H, ArH), 7.3-7.2 (m, 1H, ArH), 7.15-7.0 (m, 2H, ArH), 3.95 (t, *J* = 6.5 Hz, 2H, CH$_2$C*H*$_2$N), 3.14 (t, *J* = 6.5 Hz, 2H, C*H*$_2$CH$_2$N). ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.5, 160.8 (d, *J* = 245.6 Hz), 139.2, 138.3, 132.3, 130.1, 129.6, 128.8, 127.3 (d, *J* = 6.7 Hz, 2C), 127.1, 115.8 (d, *J* = 22.6, 2C), 49.7, 28.7. IR (ATR): ν 1650, 1500 cm^{-1}. MS (EI) *m/z* (%): 242 (M$^+$+1, 16), 241 (M$^+$, 91), 240 (M$^+$-1, 25), 122 (20), 119 (13), 118 (100), 95 (18), 90 (46), 89 (24). HRMS calcd. (%) for $C_{15}H_{12}FNO$: 241.0903; found: 241.0907.

IV. References

(1) J. J. Zhang, Q. Y. Meng, G. X. Wang, Q. Liu, B. Chen, K. Feng, C. H. Tung, L. Z. Wu, *Chem. Eur. J.*, 2013, **19**, 6443-6450.

(2) A. S.-K. Tsang, P. Jensen, J. M. Hook, A. S. K. Hashmi, M. H. Tood, *Pure Appl. Chem.*, 2011, **83**, 655-665.

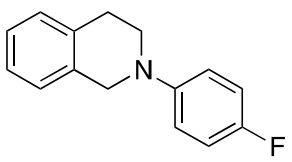
(3) M. Brzozowski, J. A. Forni, P. G. Savage, A. Polyzos, *Chem. Commun.*, 2015, **51**, 334-337.

(4) S. O'Sullivan, E. Doni, T. Tuttle, J. A. Murphy, *Angew. Chem. Int. Ed.*, 2014, **53**, 474-478.

(5) R. Hudson, S. Ishikawa, C-J. Li, A. Moores, *Synlett*, 2013, **24**, 1637-1642.

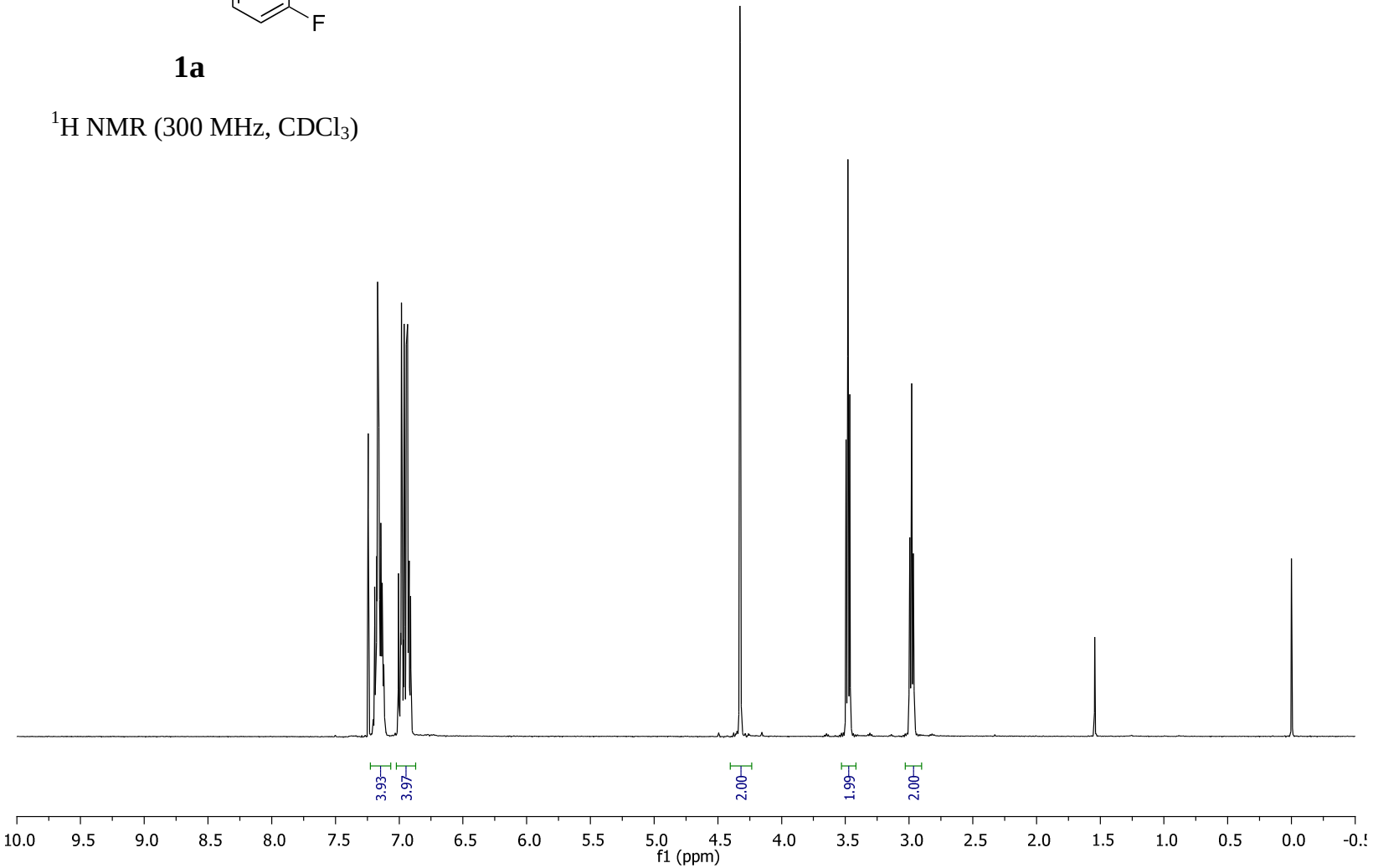
(6) M. Rueping, S. Zhu, R. M. Koenigs, *Chem. Commun.*, 2011**, 47**, 8679-8681.

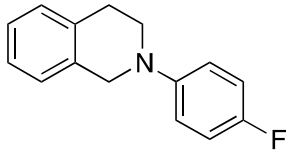
(7) G. Zhang, Y. Ma, S. Wang, W. Kong, R. Wang, *Chem. Sci.*, 2013, **4**, 2645-2651.



1a

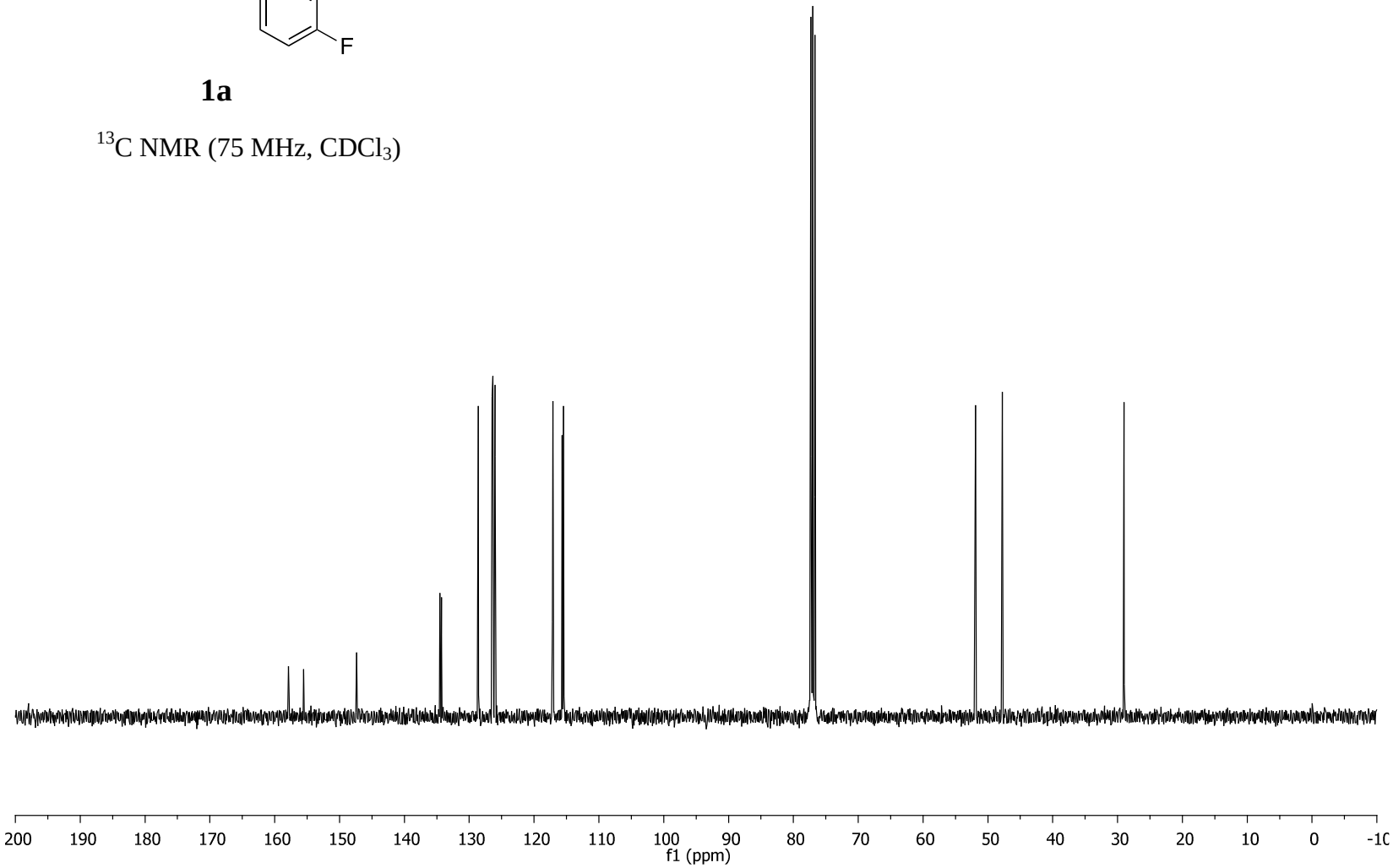
^{1}H NMR (300 MHz, $CDCl_3$)

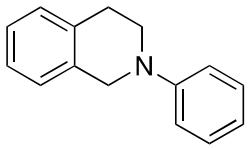




1a

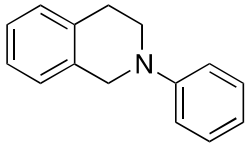
^{13}C NMR (75 MHz, $CDCl_3$)





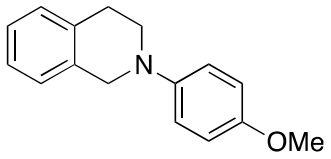
1b

^{1}H NMR (300 MHz, $CDCl_3$)



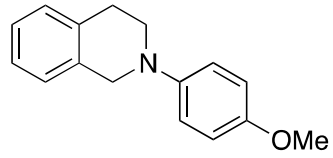
1b

^{13}C NMR (75 MHz, $CDCl_3$)



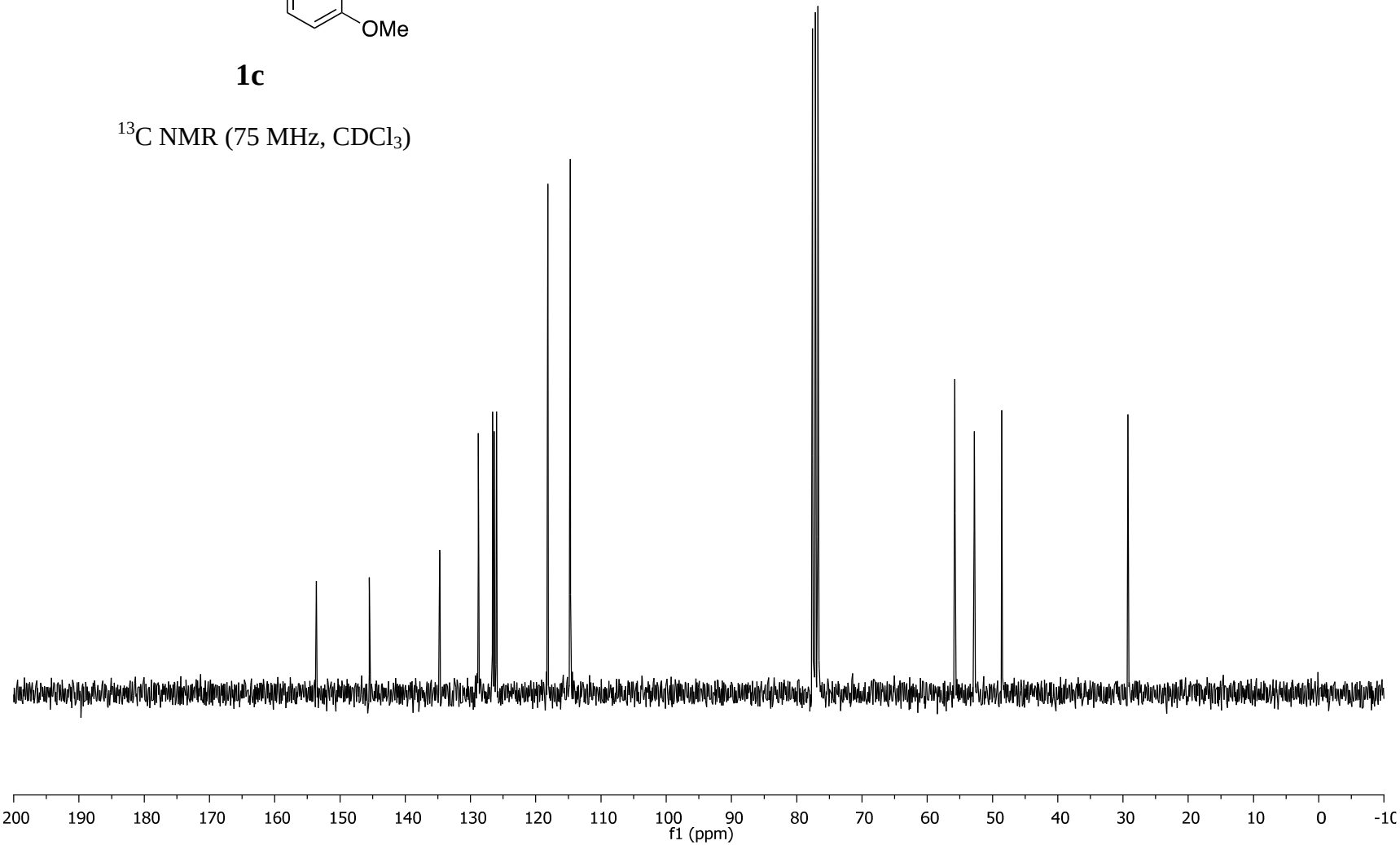
1c

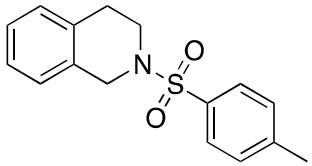
^{1}H NMR (300 MHz, $CDCl_3$)



1c

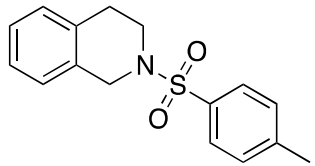
^{13}C NMR (75 MHz, $CDCl_3$)





1d

^{1}H NMR (300 MHz, $CDCl_3$)



1d

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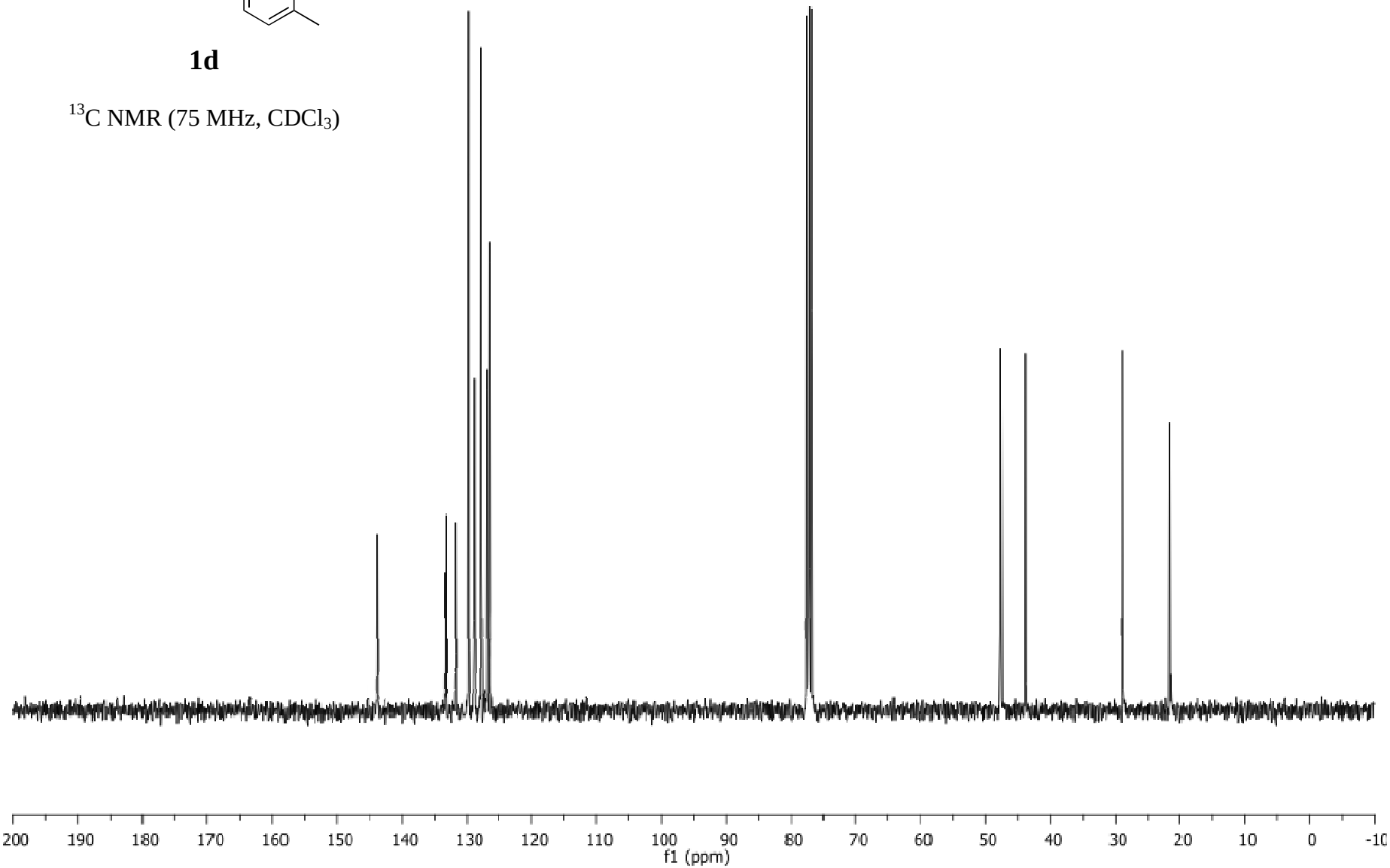
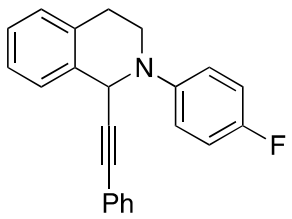
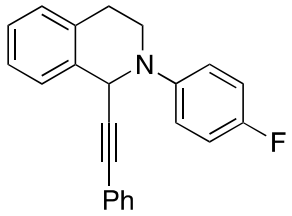




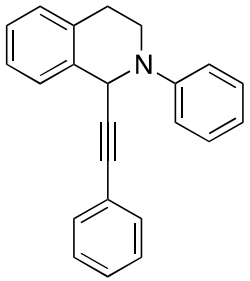
3a

^{1}H NMR (300 MHz, $CDCl_3$)



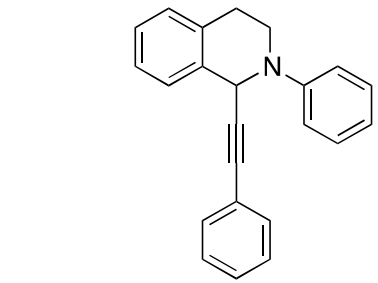
3a

^{13}C NMR (75 MHz, $CDCl_3$)



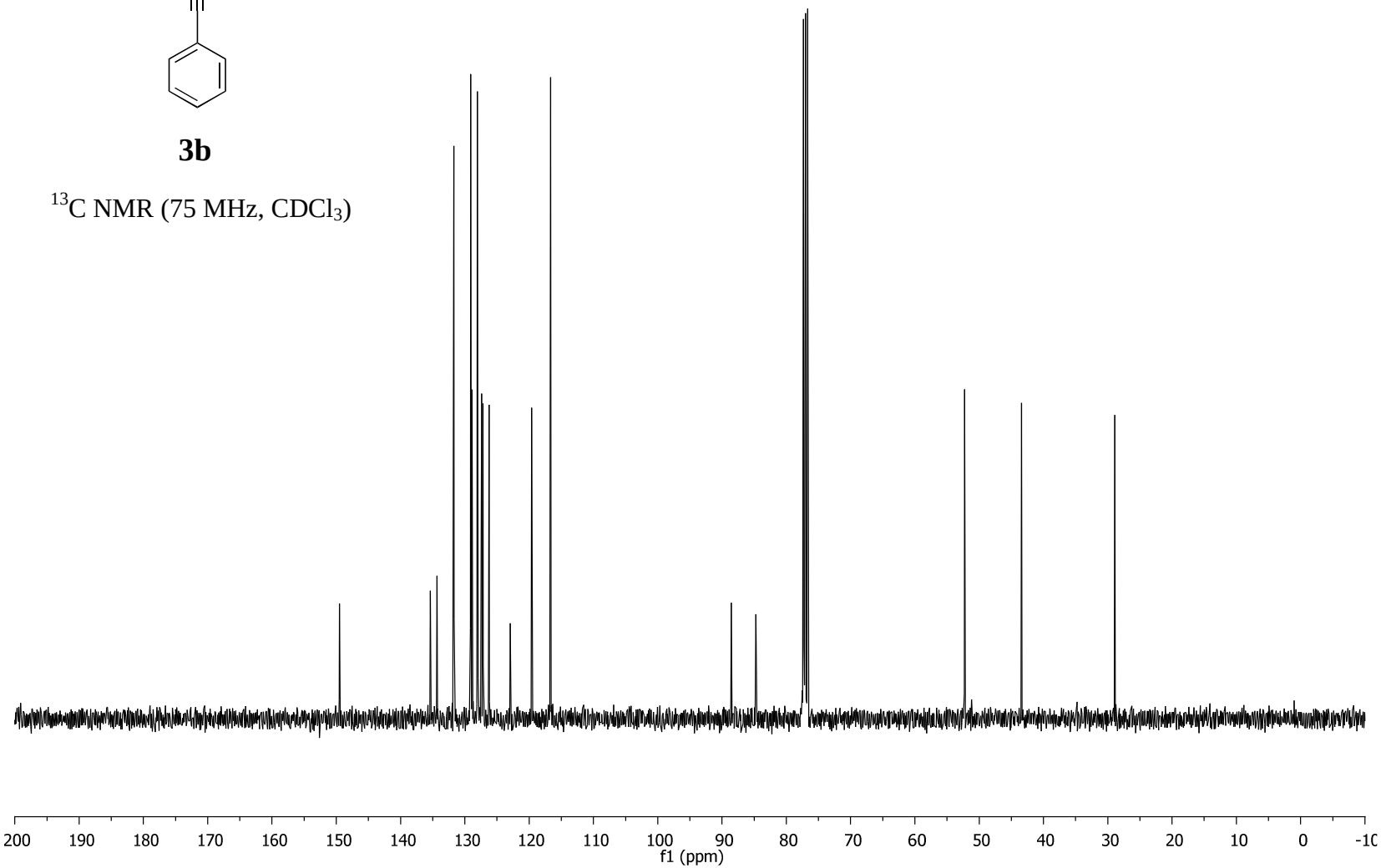
3b

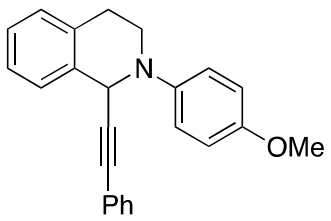
^{1}H NMR (300 MHz, $CDCl_3$)



3b

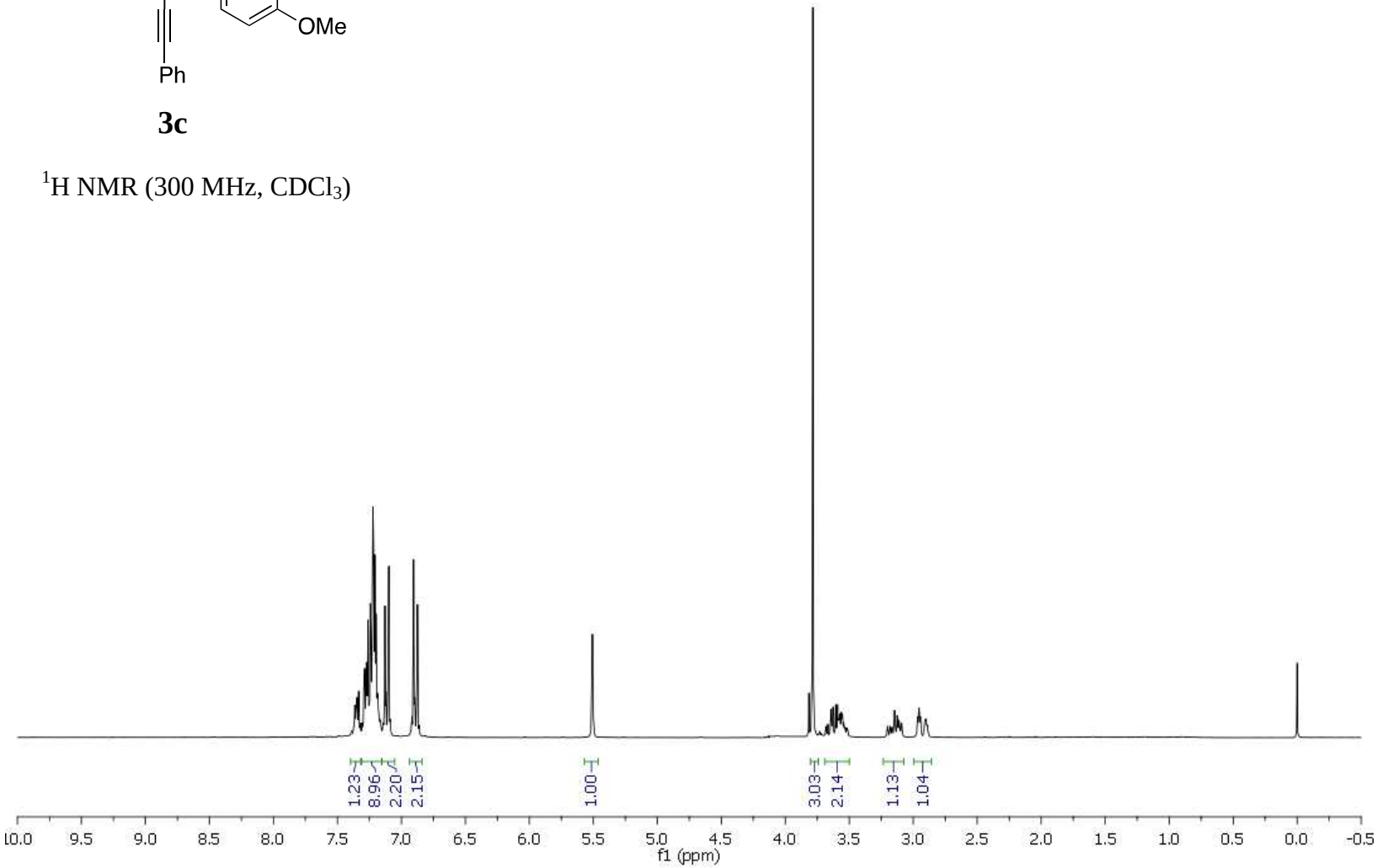
^{13}C NMR (75 MHz, $CDCl_3$)

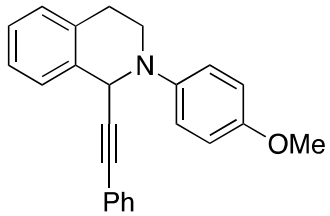




3c

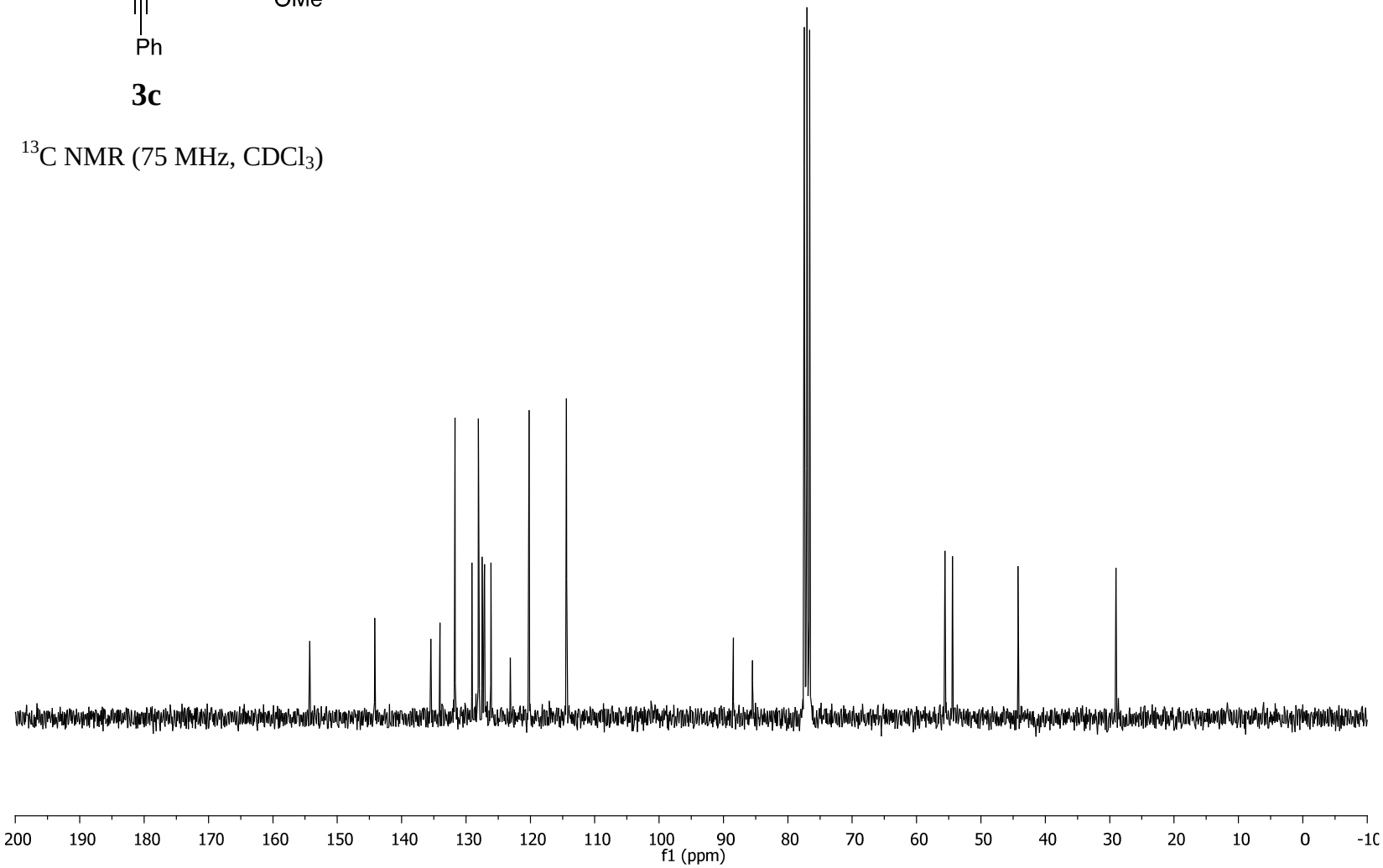
^{1}H NMR (300 MHz, $CDCl_3$)

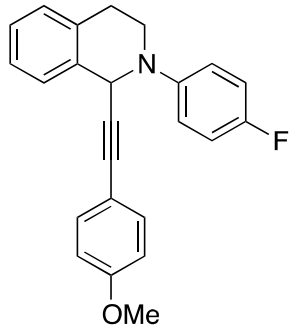




3c

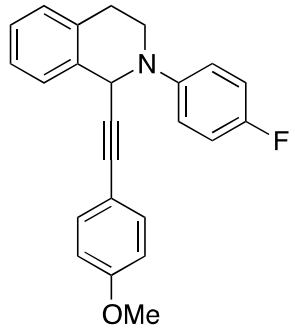
^{13}C NMR (75 MHz, $CDCl_3$)





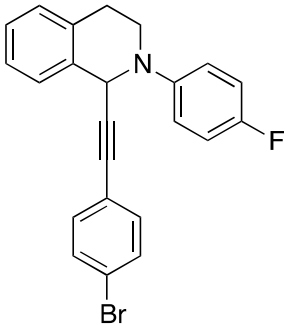
3f

^{1}H NMR (300 MHz, $CDCl_3$)



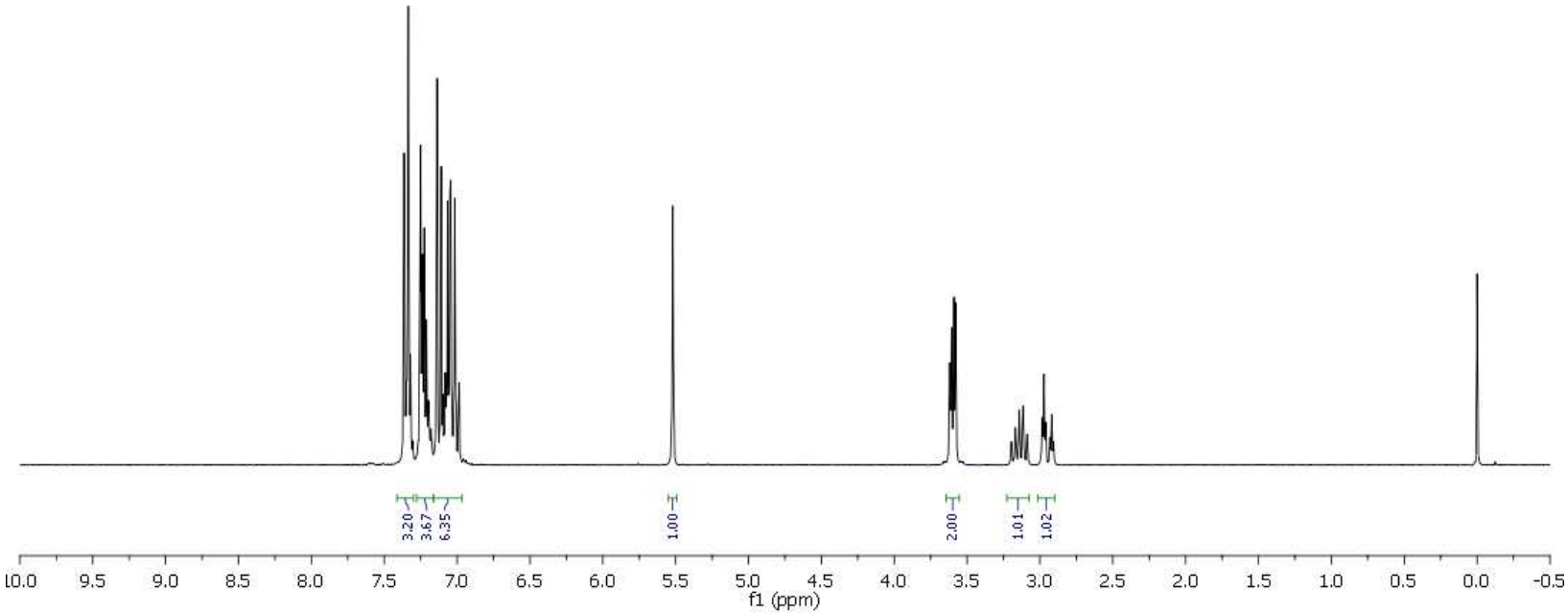
3f

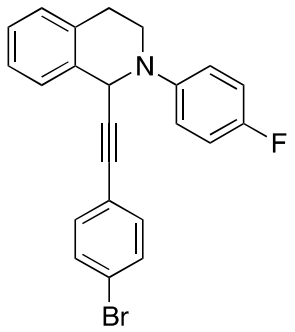
^{13}C NMR (75 MHz, $CDCl_3$)



3g

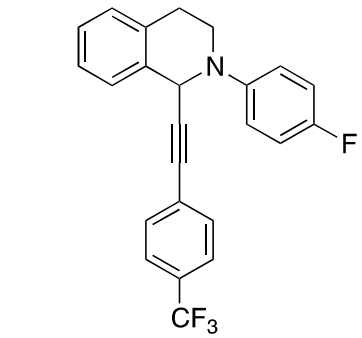
^{1}H NMR (300 MHz, $CDCl_3$)





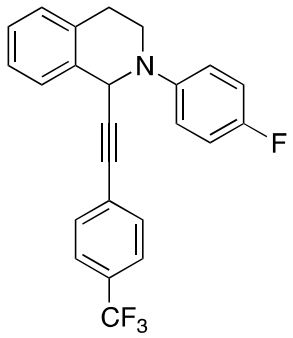
3g

^{13}C NMR (75 MHz, $CDCl_3$)



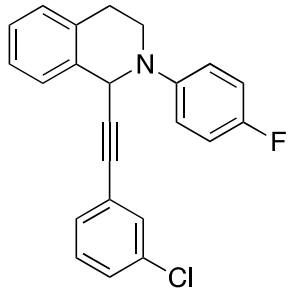
3h

^{1}H NMR (300 MHz, $CDCl_3$)



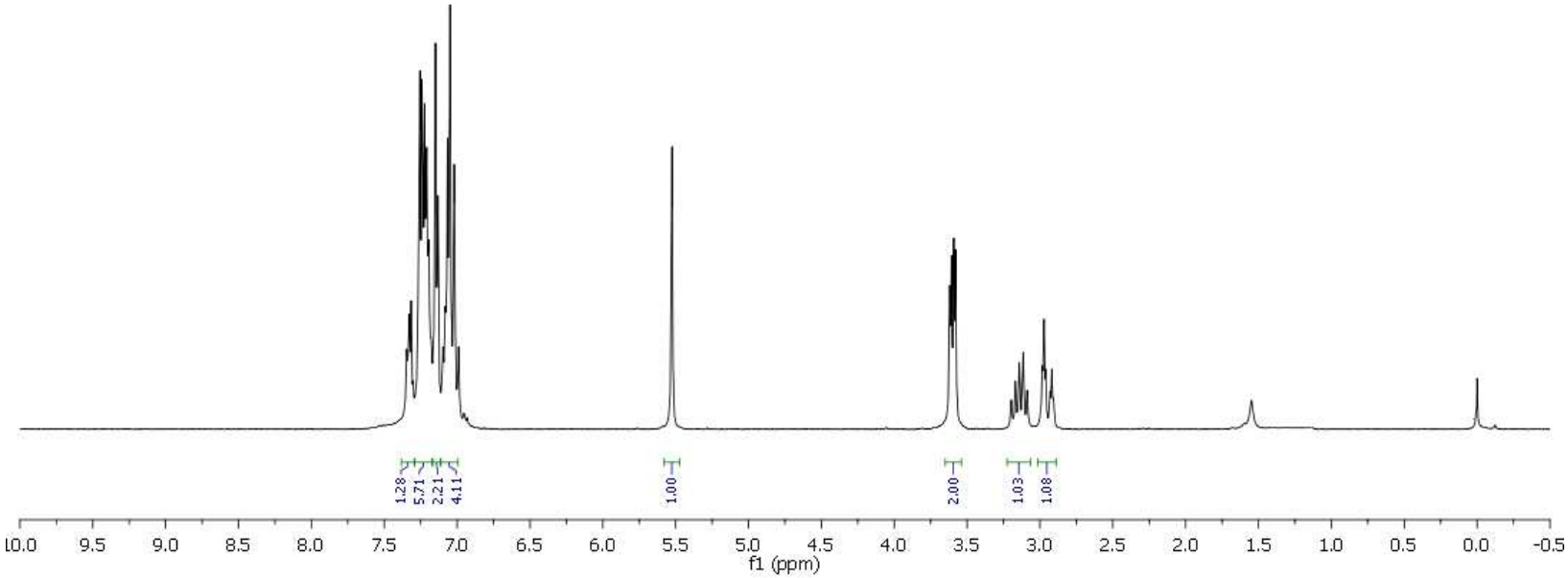
3h

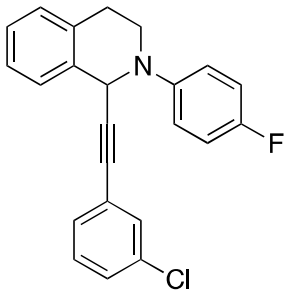
^{13}C NMR (75 MHz, $CDCl_3$)



3i

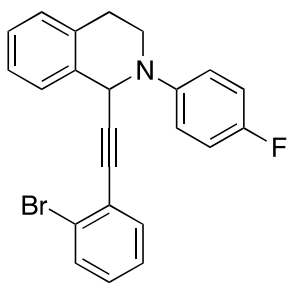
^{1}H NMR (300 MHz, $CDCl_3$)





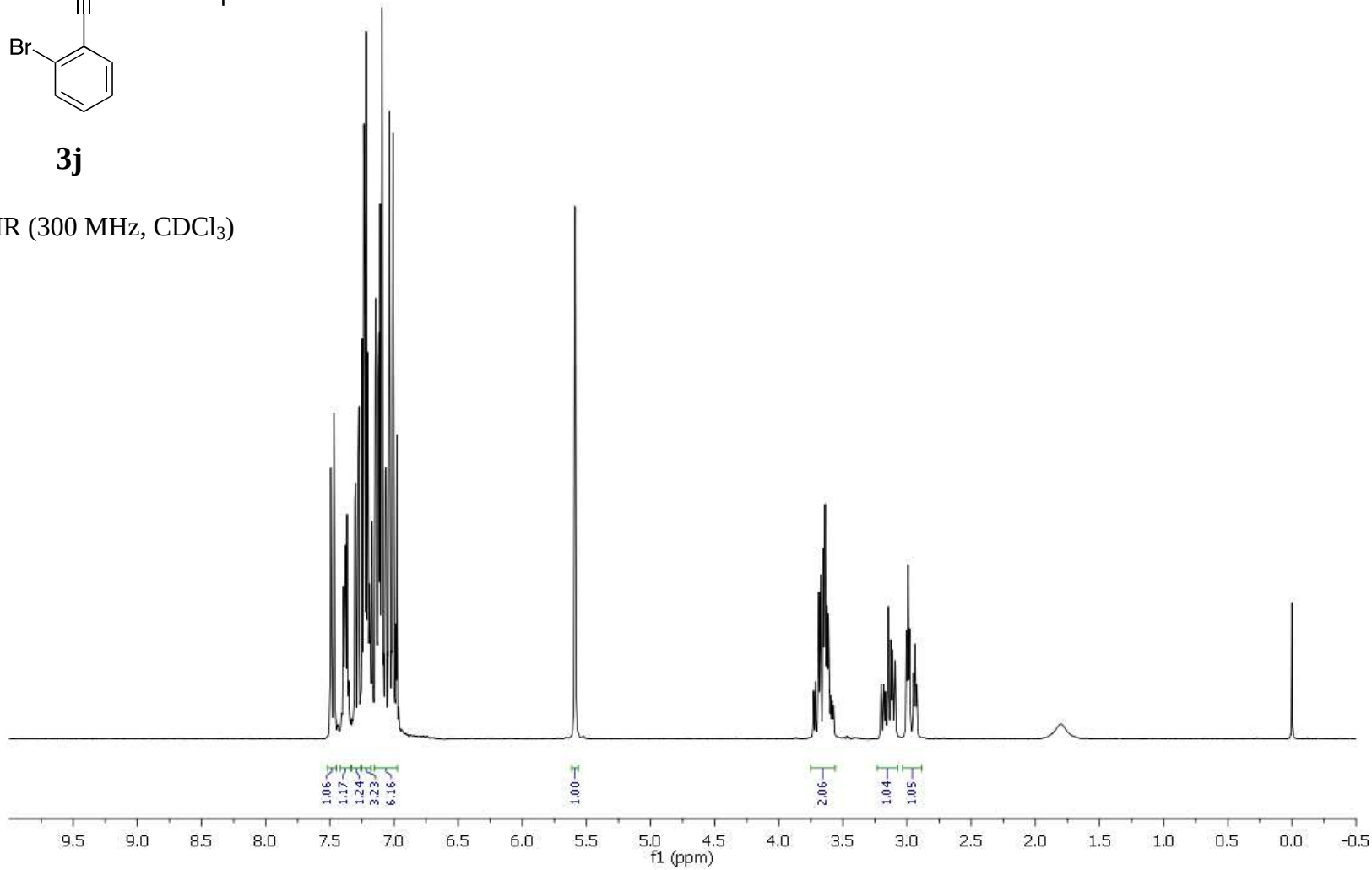
3i

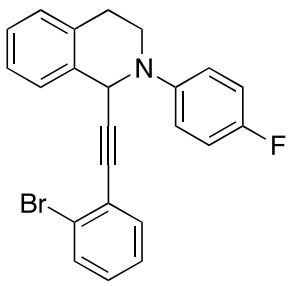
^{13}C NMR (75 MHz, $CDCl_3$)



3j

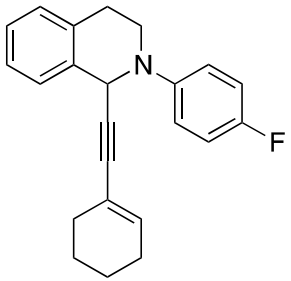
^{1}H NMR (300 MHz, $CDCl_3$)





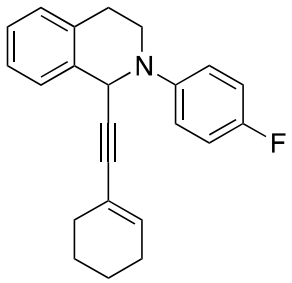
3j

^{13}C NMR (75 MHz, $CDCl_3$)



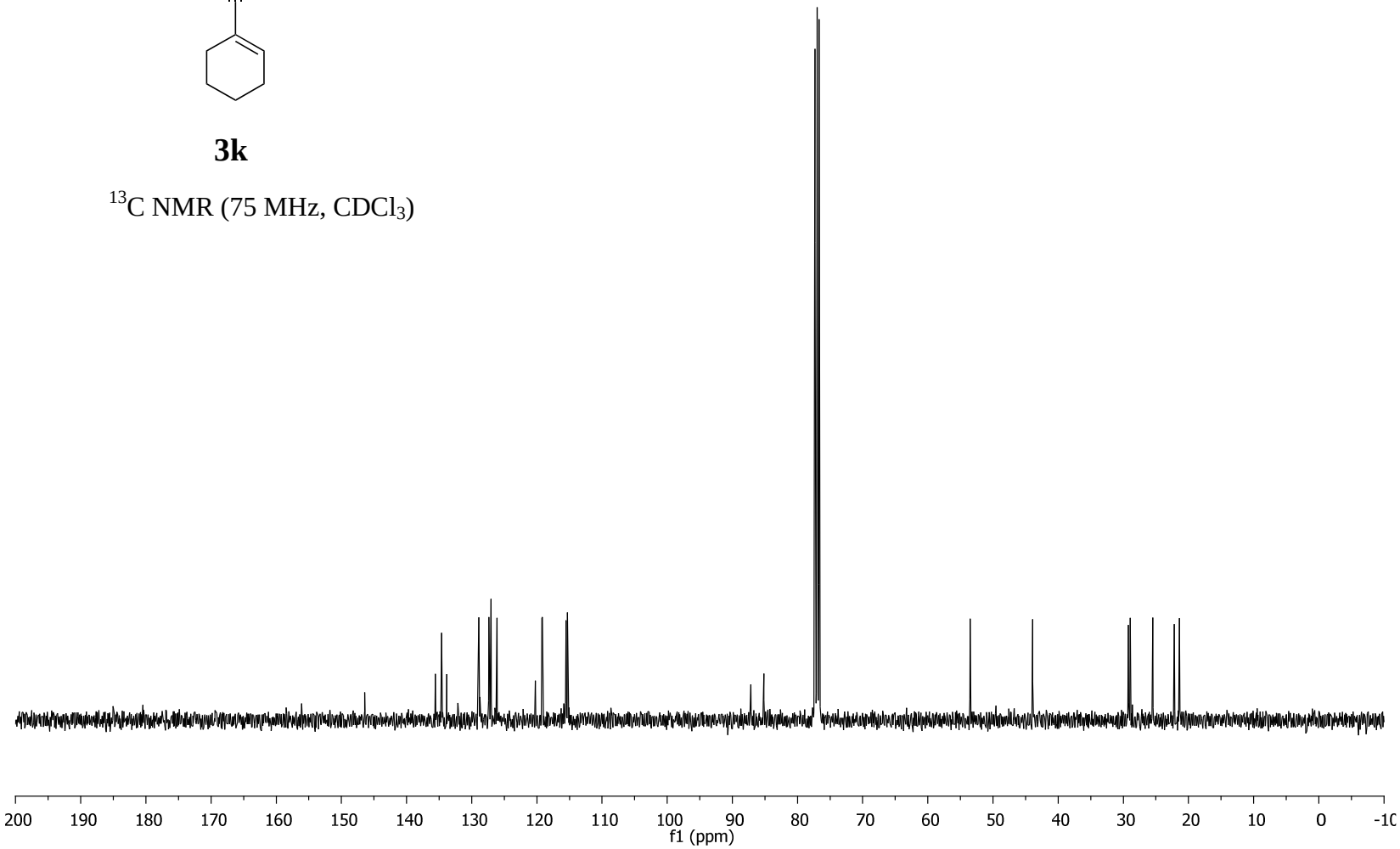
3k

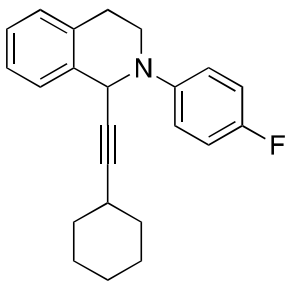
^{1}H NMR (300 MHz, $CDCl_3$)



3k

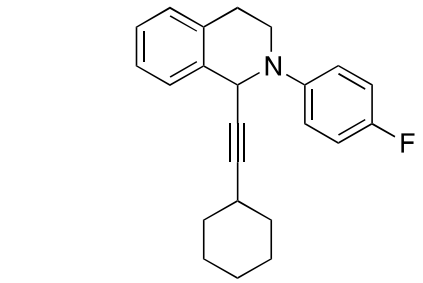
^{13}C NMR (75 MHz, $CDCl_3$)





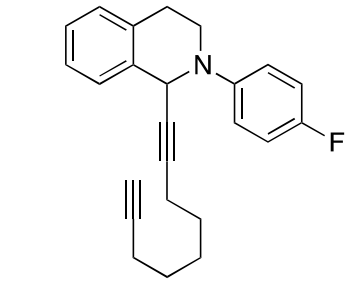
3l

^{1}H NMR (300 MHz, $CDCl_3$)



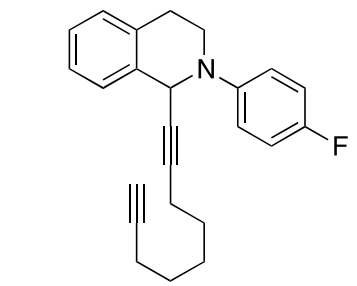
3l

^{13}C NMR (75 MHz, $CDCl_3$)



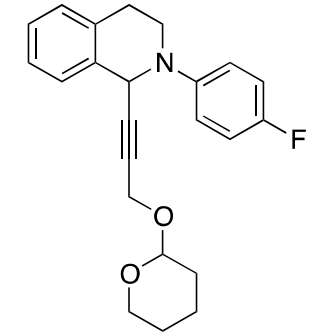
3m

^{1}H NMR (300 MHz, $CDCl_3$)



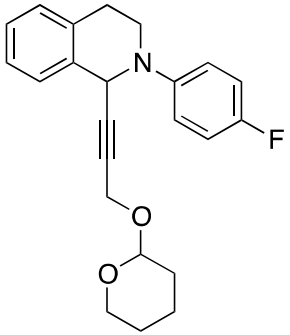
3m

^{13}C NMR (75 MHz, $CDCl_3$)



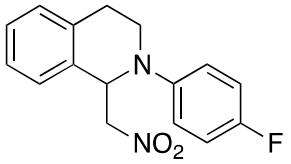
3n

^{1}H NMR (300 MHz, $CDCl_3$)



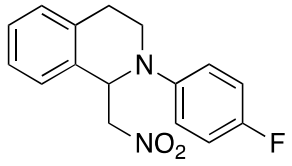
3n

^{13}C NMR (75 MHz, $CDCl_3$)



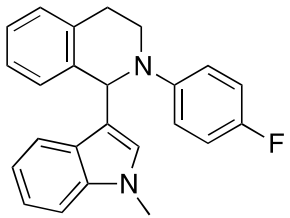
3o

^{1}H NMR (300 MHz, $CDCl_3$)



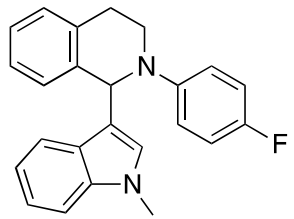
3o

^{13}C NMR (75 MHz, $CDCl_3$)



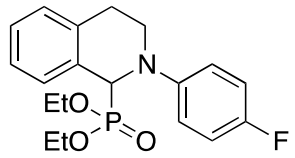
3p

^{1}H NMR (300 MHz, $CDCl_3$)



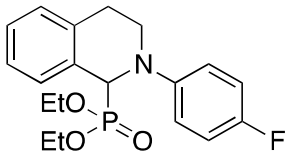
3p

^{13}C NMR (75 MHz, $CDCl_3$)



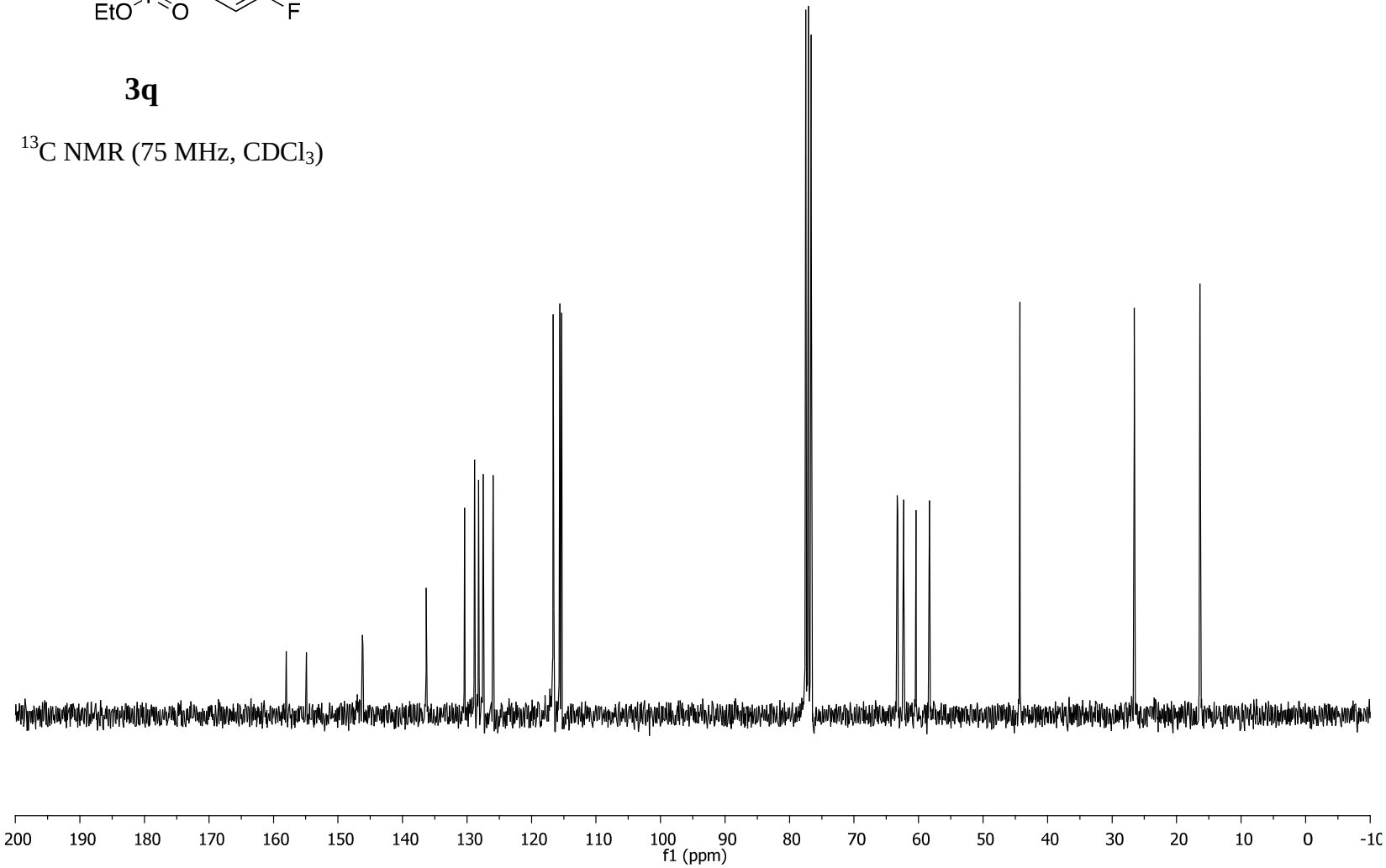
3q

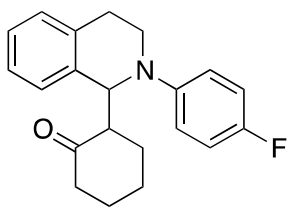
^{1}H NMR (300 MHz, $CDCl_3$)



3q

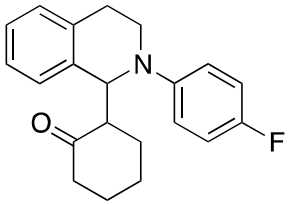
^{13}C NMR (75 MHz, $CDCl_3$)





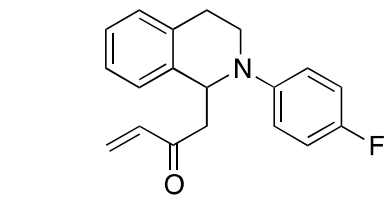
3r

^{1}H NMR (300 MHz, $CDCl_3$)



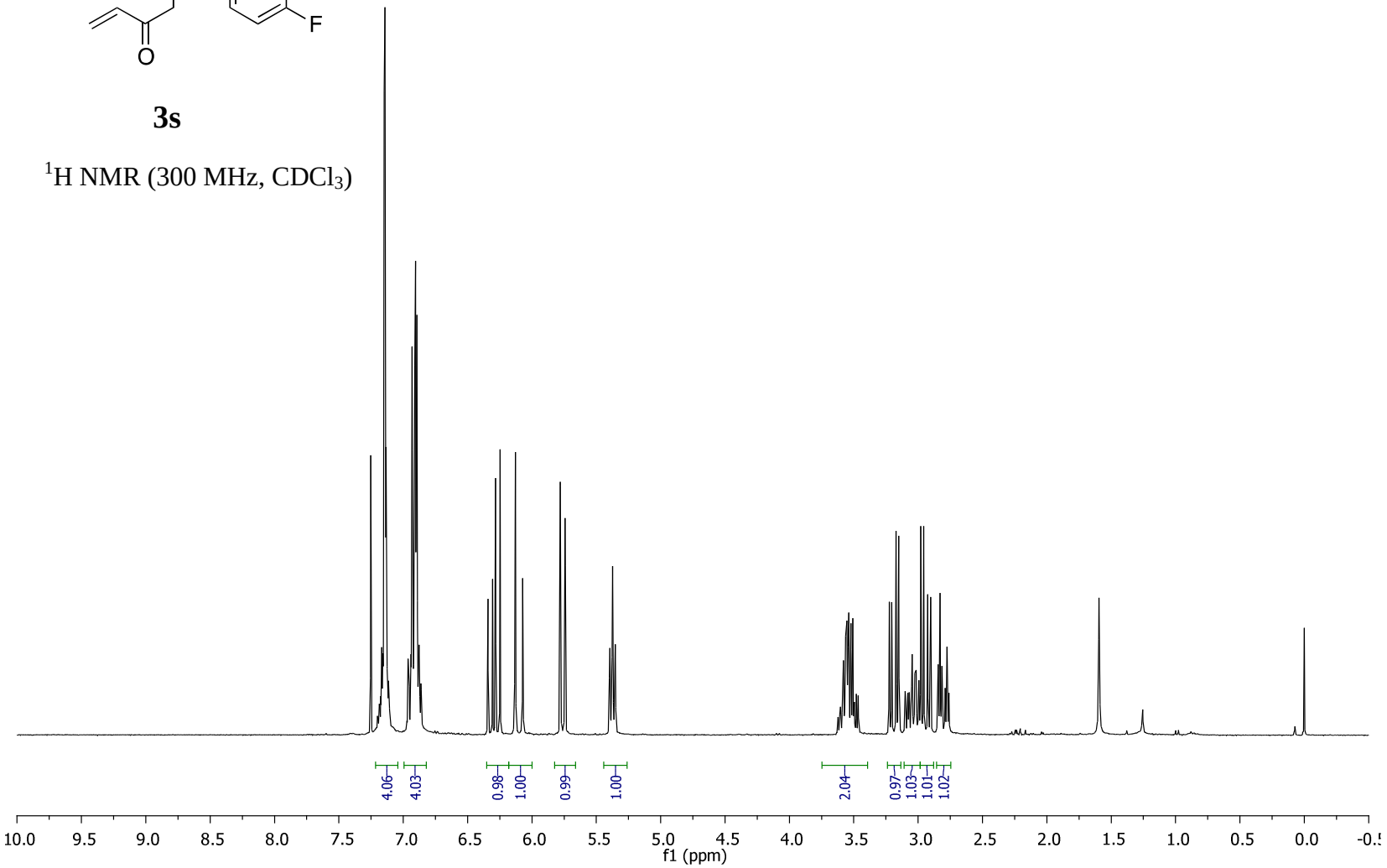
3r

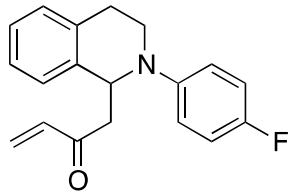
^{13}C NMR (75 MHz, $CDCl_3$)



3s

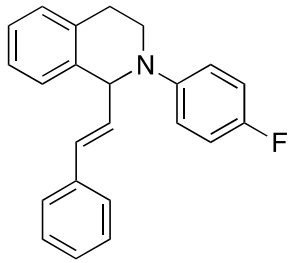
^{1}H NMR (300 MHz, $CDCl_3$)





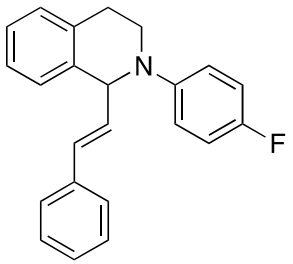
3s

^{13}C NMR (75 MHz, $CDCl_3$)



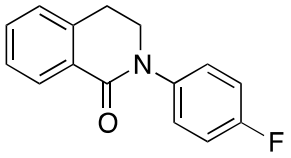
3t

^{1}H NMR (300 MHz, $CDCl_3$)



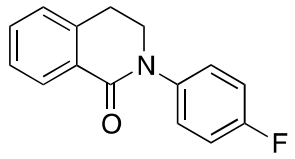
3t

^{13}C NMR (75 MHz, $CDCl_3$)



4a

^{1}H NMR (300 MHz, $CDCl_3$)



4a

^{13}C NMR (75 MHz, $CDCl_3$)