Dehydrogenative [2+2+2] cycloaddition of cyano-yne-allene substrates: convenient access to 2,6-naphthyridine scaffolds

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General Considerations

Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. All reactions requiring anhydrous conditions were conducted in oven-dried glassware under a dry nitrogen atmosphere. THF was degassed and dried under nitrogen by passing it through solvent purification columns (MBraun, SPS-800). Anhydrous chlorobenzene was purchased from Aldrich. Solvents were removed under reduced pressure with a rotary evaporator. When necessary, reaction mixtures were chromatographed on silica gel (230-400 mesh) using a gradient solvent system as the eluent. *N*-4-tosylbuta-2,3-dien-1-amine **S1**[1] and *N*-(2-cyanoethyl)-(4-methylphenyl)sulfonamide **S4**[2] were prepared as previously described by our group. Diethyl 2-(2-cyanoethyl)malonate **S5**,[3] 2-(4-hydroxybut-2-ynyloxy)acetonitrile **S9**,[4] 4-(prop-2-yn-1-yloxy)but-2-yn-1-ol **S10**,[5] diethyl 2-(buta-2,3-dien-1-yl)malonate **S13**,[6] *N*-tosyl-2-aminobenzonitrile **S14**,[7] *N*-but-3-ynyl-4-methylbenzenesulfonamide **S16**[8] and *N*-(but-3-yn-1-yl)-*N*-(4-hydroxybut-2-yn-1-yl)-4-methylbenzenesulfonamide **S17**[9] were prepared following the method previously described in the literature and their identity was confirmed by spectral data.

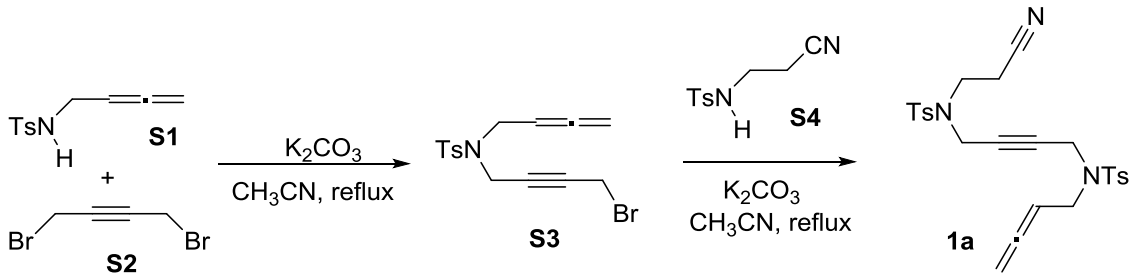
IR spectra were recorded with an FT-IR using a single reflection ATR system as a sampling accessory. ^{1}H NMR (^{13}C NMR) were recorded at 300 MHz (75 MHz) and 400 MHz (100 MHz) using Me_4Si as the internal standard. Chemical shifts are given in δ units. Characterization of compounds **2** were performed using typical gradient-

enhanced 2D experiments, such as COSY, NOESY, HSQC, and HMBC, recorded under routine conditions. Electrospray mass spectrometry analyses were recorded on an Esquire 6000 ion trap mass spectrometer (Bruker) equipped with an electrospray ion source, operated in the positive ESI(+) ion mode.

Microwave-heated reactions were performed in septum-containing, screw-capped sealed vials in an Ethos SEL Lab station (Milestone Inc.), a multimode microwave with a dual magnetron (1600 W). During the experiments, the time, temperature, and power were measured with the "EasyControl" software package. The temperature was monitored and controlled throughout the reaction by an ATC-400FO automatic fibre optic temperature control system. The wattage was automatically adjusted to maintain the appropriate temperature for the desired period of time.

Synthesis and characterization of 1a-1h, 3 and cyanodiyne S18

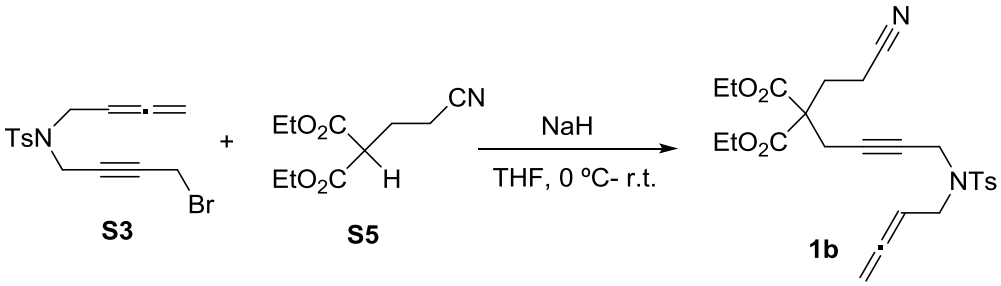
Synthesis of 1a



In a 50 mL two-necked round bottom flask, a mixture of *N*-4-tosylbuta-2,3-dien-1-amine **S1** (1.0 g, 4.48 mmol), 1,4-dibromo-2-butyne **S2** (3.05 g, 14.39 mmol) and potassium carbonate (2.51 g, 18.16 mmol) in acetonitrile (50 mL) was heated at reflux. The mixture was stirred for 6h until completion (TLC monitoring). The salts were filtered off and the solvent was removed under reduced pressure. The reaction crude was purified by column chromatography using a mixture of hexane:ethyl acetate (80:20) as the eluent to give compound **S3** (0.97 g, 61% yield) as a yellow oil. **MW:** 354.26 g/mol; **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 2.43 (s, 3H), 3.64 (t, $^5J_{H,H}$ = 2.0 Hz, 2H), 3.83 (dt, $^3J_{H,H}$ = 7.0 Hz, $^5J_{H,H}$ = 2.4 Hz, 2H), 4.19 (t, $^5J_{H,H}$ = 2.0 Hz, 2H), 4.79 (dt, $^4J_{H,H}$ = 7.0 Hz, $^5J_{H,H}$ = 2.4 Hz, 2H), 5.04 (quint. $J_{H,H}$ = 7.0 Hz, 1H), 7.33 (d, $^3J_{H,H}$ = 8.4 Hz, 2H), 7.72 (d, $^3J_{H,H}$ = 8.4 Hz, 2H); **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 13.7, 21.6, 36.3, 45.9, 76.6, 79.6, 80.5, 85.4, 127.6, 129.6, 135.8, 143.7, 209.8; **ESI-MS (m/z):** 376-378 $[M + Na]^+$; **IR (ATR) ν (cm^{-1}):** 1344, 1210, 1156, 1091; **AE:** calcd. for $[C_{15}H_{16}BrNO_2S{\cdot}0.5H_2O]$: C, 49.60; H, 4.72; N, 3.86. Found: C, 49.80; H, 4.61; N, 3.77.

In a 50 mL two-necked round bottom flask, a mixture of *N*-(2-cyanoethyl)-4-methylbenzenesulfonamide **S4** (0.50 g, 2.25 mmol), *N*-(4-bromobut-2-yn-1-yl)-*N*-(buta-2,3-dien-1-yl)-4-methylbenzenesulfonamide **S3** (0.80 g, 2.25 mmol) and potassium carbonate (1.55 g, 11.25 mmol) in acetonitrile (50 mL) was heated at reflux. The mixture was stirred for 6h until completion (TLC monitoring). The salts were filtered off and the solvent was removed under reduced pressure. The reaction crude was purified by column chromatography using a mixture of hexane:ethyl acetate (80:20) as the eluent to give compound **1a** (0.95 g, 85% yield) as a colourless solid. **MW:** 497.63 g/mol; **m.p.:** 115-117ºC; **^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm):** 2.44 (s, 3H), 2.45 (s, 3H), 2.63 (t, $^3J_{H,H}$ = 6.9 Hz, 2H), 3.29 (t, $^3J_{H,H}$ = 6.9 Hz, 2H), 3.69 (dt, $^3J_{H,H}$ = 7.2 Hz, $^5J_{H,H}$ = 2.4 Hz, 2H), 3.96 (t, $^5J_{H,H}$ = 1.8 Hz, 2H), 3.99 (t, $^5J_{H,H}$ = 1.8 Hz, 2H), 4.74 (dt, $^4J_{H,H}$ = 6.6 Hz, $^5J_{H,H}$ = 2.4 Hz, 2H), 4.91 (dq, $J_{H,H}$ = 7.2 Hz, $J_{H,H}$ = 6.6 Hz, 1H), 7.31 (d, $^3J_{H,H}$ = 8.2 Hz, 2H), 7.33 (d, $^3J_{H,H}$ = 8.2 Hz, 2H), 7.67 (d, $^3J_{H,H}$ = 8.2 Hz, 4H); **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 18.3, 21.5, 21.6, 35.8, 38.2, 42.9, 45.7, 77.8, 79.4, 85.3, 117.3, 127.5, 127.6, 129.6, 129.9, 135.0, 136.1, 143.9, 144.5, 209.7; **ESI-MS (m/z):** 498.1 $[M + H]^+$; **IR (ATR) ν (cm^{-1}):** 1338, 1158, 1003; **AE:** calcd. for $[C_{25}H_{27}N_3O_4S_2]$: C, 60.34; H, 5.47; N, 8.44. Found: C, 59.93; H, 4.99; N, 8.63.

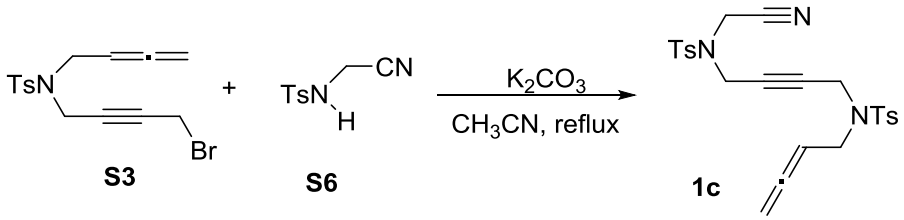
Synthesis of 1b



In 50mL 2-neck round bottom flask, a mixture of diethyl 2-(2-cyanoethyl)malonate **S5** (0.20 g, 0.96 mmol) in anhydrous THF (5 mL) was added to a solution of NaH (60% in mineral oil, 0.04 g, 1.73 mmol) in 10 mL of anhydrous THF at 0ºC and stirred for 1h. A solution of bromo derivative **S3** (0.41 g, 1.15 mmol) in anhydrous THF (5 mL) was added at 0ºC and the resulting mixture was stirred overnight at room temperature. The reaction mixture was poured onto ice-water (10 mL) and extracted with ether (3×5 mL). The combined organic layer was dried over Na_2SO_4 and concentrated in vacuum conditions. The reaction crude was purified by column chromatography using a mixture of hexane:ethyl acetate (80:20) as the eluent to give the product **1b** (0.38 g, 81% yield) as a yellow oil. **MW:** 486.58 g/mol; **^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm):** 1.25 (t, $^3J_{H,H}$ = 7.2 Hz, 6H), 2.15-2.23 (m, 2H), 2.27- 2.35 (m, 2H), 2.45 (s, 3H), 2.63 (t, $^5J_{H,H}$ = 2.4 Hz,

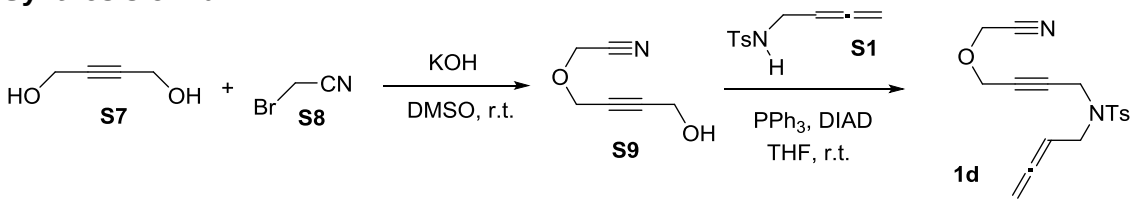
2H), 3.83 (dt, $^{3}J_{H,H}$ = 7.0 Hz, $^{3}J_{H,H}$ = 2.5 Hz, 2H), 4.10 (t, $^{5}J_{H,H}$ = 2.4 Hz, 2H), 4.19 (q, $^{3}J_{H,H}$ = 7.2 Hz, 4H), 4.80 (dt, $^{4}J_{H,H}$ = 7.0 Hz J^{5} = 2.5 Hz, 2H), 4.90 (quint., $J_{H,H}$ = 7.0 Hz, 1H), 7.32 (d, $^{3}J_{H,H}$ = 8.4 Hz, 2H), 7.67 (d, $^{3}J_{H,H}$ = 8.4 Hz, 2H); **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 12.8, 13.9, 21.6, 23.6, 28.4, 36.0, 45.6, 55.4, 62.2, 76.5, 79.1, 85.3, 118.7, 127.6, 129.6, 129.7, 136.3, 143.6, 168.9, 209.7; **ESI-MS (m/z):** 487.1 $[M + H]^{+}$; **IR (ATR) ν (cm^{-1}):** 2921, 1729, 1347, 1191, 1158; **AE:** calcd. for $[C_{25}H_{30}N_2O_6S]$: C, 61.71; H, 6.21; N, 5.76. Found: C, 61.31; H, 6.16; N, 5.65.

Synthesis of 1c



In a 50 mL two-necked round bottom flask, a mixture of N-(cyanomethyl)-(4-methylphenyl)sulfonamide **S6** (0.10 g, 0.48 mmol), bromo derivative **S3** (0.17 g, 0.48 mmol) and potassium carbonate (0.33 g, 2.39 mmol) in acetonitrile (30 mL) was heated at reflux. The mixture was stirred for 4h until completion (TLC monitoring). The salts were filtered off and the solvent was removed under reduced pressure. The reaction crude was purified by column chromatography using a mixture of hexane:ethyl acetate (80:20) as the eluent to give compound **1c** (0.18 g, 78% yield) as a yellow oil. **MW:** 483.60 g/mol; **^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm):** 2.44 (s, 3H), 2.45 (s, 3H), 3.76 (dt, $^{3}J_{H,H}$ = 7.0 Hz, $^{5}J_{H,H}$ = 2.5 Hz, 2H), 3.90 (t, $^{5}J_{H,H}$ = 1.8 Hz, 2H), 4.05 (t, $^{5}J_{H,H}$ = 1.8 Hz, 2H), 4.09 (s, 2H), 4.77 (dt, $^{4}J_{H,H}$ = 7.0 Hz, $^{5}J_{H,H}$ = 2.5 Hz, 2H), 4.97 (q, $J_{H,H}$ = 7.0 Hz, 1H), 7.30-7.40 (m, 4H), 7.65-7.78 (m, 4H); **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 21.5, 21.7, 34.7, 35.9, 37.4, 42.9, 76.5, 80.46, 80.5, 85.3, 85.3, 113.2, 127.6, 129.7, 130.1, 133.7, 135.9, 144.0, 145.2, 209.8; **ESI-MS (m/z):** 506.1 $[M + Na]^{+}$; **IR (ATR) ν (cm^{-1}):** 1596, 1342, 1157, 1091; **AE:** calcd. for $[C_{24}H_{25}N_3O_4S_2.1.5H_2O]$: C, 56.45; H, 5.53; N, 8.23. Found: C, 56.86; H, 5.00; N, 7.97.

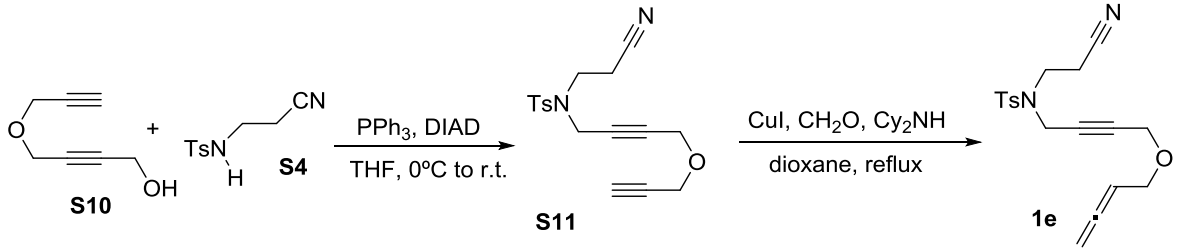
Synthesis of 1d



In a 100 mL two-necked round bottom flask, a mixture of potassium hydroxide (4.02 g, 71.64 mmol) and 2-butyne-1,4-diol **S7** (6.20 g, 72.02 mmol) in DMSO (60 mL) was stirred at room temperature. 2-Bromoacetonitrile **S8** (1.0 mL, 14.33 mmol) was then added dropwise and the resulting mixture was stirred for 2h (TLC monitoring). Water (20 mL) was added and the mixture was extracted with dichloromethane (3x40 mL). The aqueous phase was then acidified with aqueous HCl 3N (10 mL) and further extracted with dichloromethane (3x40 mL). The combined organic phases were washed with H_2O (3x30 mL), dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography using a mixture of hexane:ethyl acetate (60:40) as the eluent to give compound **S9** (0.86 g, 47% yield) as a colourless oil. **MW:** 125.13 g/mol; **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 2.41 (t, $^3J_{H,H}$ = 5.4 Hz, 1H), 4.31-4.35 (m, 2H), 4.37 (t, $^5J_{H,H}$ = 1.8 Hz, 2H), 4.38 (s, 2H).

In a 50 mL two-necked round bottom flask, a mixture of 2-(4-hydroxybut-2-ynyloxy)acetonitrile **S9** (0.20 g, 1.60 mmol), *N*-tosylbuta-2,3-dien-1-amine **S1** (0.36 g, 1.60 mmol) and triphenylphosphine (1.05 g, 4.00 mmol) in anhydrous and degassed tetrahydrofuran (30 mL) was stirred and cooled to 0ºC in an ice-water bath. Diisopropyl azodicarboxylate (0.8 mL, 4.06 mmol) was added dropwise to this solution and the resulting mixture was stirred at room temperature for 20h (TLC monitoring). The solvent was removed under reduced pressure and the reaction crude was purified by column chromatography using a mixture of hexane:ethyl acetate (90:10) as the eluent to afford product **1d** (0.38 g, 72% yield) as a yellow oil. **MW:** 330.40 g/mol; **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 2.44 (s, 3H), 3.86 (dt, $^3J_{H,H}$ = 7.2 Hz, $^5J_{H,H}$ = 2.5 Hz , 2H), 4.08 (t, $^5J_{H,H}$ = 1.8 Hz, 2H), 4.14 (s, 2H), 4.20 (t, $^5J_{H,H}$ = 1.8 Hz, 2H), 4.80 (dt, $^4J_{H,H}$ = 6.8 Hz, $^5J_{H,H}$ = 2.5 Hz, 2H), 5.05 (dq, $^3J_{H,H}$ = 7.2 Hz, $^4J_{H,H}$ = 6.8 Hz, 1H), 7.34 (d, $^3J_{H,H}$ = 8.4 Hz, 2H), 7.73 (d, $^3J_{H,H}$ = 8.4 Hz, 2H); **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** 21.7, 36.0, 46.0, 53.8, 57.9, 76.6, 78.7, 81.8, 85.4, 115.2, 127.7, 129.6, 136.0, 143.9, 209.8; **GS-MS (m/z):** 330.1 $[M]^+$; **IR (ATR) ν (cm^{-1}):** 1343, 1158, 1088; **HRMS** calcd. for $[C_{17}H_{18}N_2O_3S + Na]^+$: 353.0930. Found: 353.0938.

Synthesis of 1e

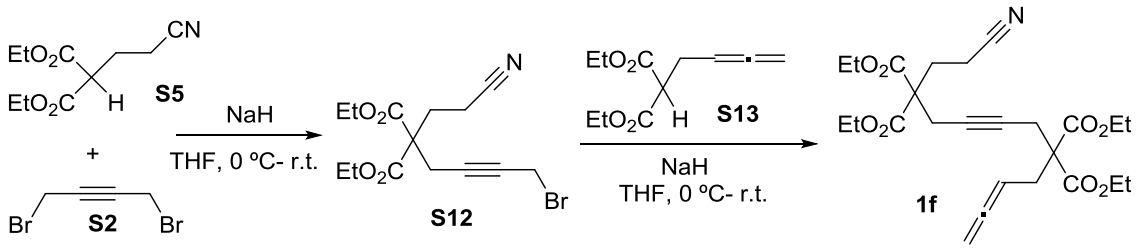


In a 50 mL two-necked round bottom flask, a mixture 4-(prop-2-yn-1-yloxy)but-2-yn-1-ol **S10** (0.30 g, 2.42 mmol), *N*-(2-cyanoethyl)-4-methylbenzenesulfonamide **S4** (0.54 g, 2.41 mmol) and triphenylphosphine (1.58 g, 6.05 mmol) in anhydrous and degassed tetrahydrofuran (30 mL) was stirred and cooled to 0ºC in an ice-water bath. Diisopropyl azodicarboxylate (1.20 mL, 6.02 mmol) was added dropwise to this solution and the resulting mixture was stirred at room temperature for 20h (TLC monitoring). The solvent was removed under reduced pressure and the reaction crude was purified by column chromatography using a mixture of hexane:ethyl acetate (90:10) as the eluent to afford compound **S11** (0.44 g, 55% yield) as a yellow oil. **MW:** 330.40 g/mol; **^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm):** 2.44 (s, 3H), 2.46 (t, $^4J_{H,H}$ = 2.4 Hz, 1H), 2.74 (t, $^3J_{H,H}$ = 7.2 Hz, 2H), 3.47 (t, $^3J_{H,H}$ = 7.2 Hz, 2H), 4.04 (d, $^4J_{H,H}$ = 2.4 Hz, 2H), 4.06 (t, $^5J_{H,H}$ = 2.0 Hz, 2H), 4.23 (t, $^5J_{H,H}$ = 2.0 Hz, 2H), 7.34 (d, $^3J_{H,H}$ = 8.4 Hz, 2H), 7.73 (d, $^3J_{H,H}$ = 8.4 Hz, 2H); **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 18.4, 21.6, 38.4, 43.1, 56.4, 56.5, 75.3, 78.6, 79.3, 81.4, 117.4, 127.7, 129.8, 135.0, 144.5; **ESI-MS (m/z):** 353.1 $[M + H]^+$; **IR (ATR) ν (cm^{-1}):** 1344, 1158, 1077; **HRMS** calcd. for $[C_{17}H_{18}N_2O_3S + Na]^+$: 353.0947. Found: 353.0930.

In a 50mL two-necked round bottom flask, a mixture of **S11** (0.17g, 0.51 mmols), formaldehyde (0.03 g, 1.29 mmol) and copper(I) iodide (0.05 g, 0.26 mmol) in dioxane (20 mL) was heated to reflux. Dicyclohexylamine (0.2 mL, 1.00 mmol) was then added dropwise to the reaction mixture and was stirred for 4h until completion (TLC monitoring). The salts were filtered off and the solvent was removed under reduced pressure. The reaction crude was purified by column chromatography using a mixture of hexane:ethyl acetate (90:10) as the eluent to afford derivative **1e** (0.09 g, 51% yield) as a yellow oil. **MW:** 344.43 g/mol; **^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm):** 2.44 (s, 3H), 2.74 (t, $^3J_{H,H}$ = 7.5 Hz, 2H), 3.47 (t, $^3J_{H,H}$ = 7.5 Hz, 2H), 3.90 (dt, $^3J_{H,H}$ = 7.0 Hz, $^5J_{H,H}$ = 2.5 Hz, 2H), 3.98 (t, $^5J_{H,H}$ = 2.1 Hz, 2H), 4.23 (t, $^5J_{H,H}$ = 2.1 Hz, 2H), 4.82 (dt, $^4J_{H,H}$ = 7.0 Hz, $^5J_{H,H}$ = 2.5 Hz, 2H), 5.15 (quint., $J_{H,H}$ = 7.0 Hz, 1H), 7.33 (d, $^3J_{H,H}$ = 8.4 Hz), 7.73 (d, $^3J_{H,H}$ = 8.4 Hz); **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 18.4, 21.9, 38.4, 43.1, 56.7, 67.4, 76.0, 78.7, 82.2, 86.8, 117.3, 127.7, 129.8, 135.0, 144.3, 209.5; **GC-MS (m/z):** 344.3

[M]$^{+}$; **IR (ATR) ν (cm^{-1}):** 2916, 1347, 1159, 1101; **AE:** calcd. for [$C_{18}H_{20}N_2O_3S.1.5H_2O$] : C, 61.17; H, 5.99; N, 7.93. Found: C, 61.47; H, 6.25; N, 7.70.

Synthesis of 1f

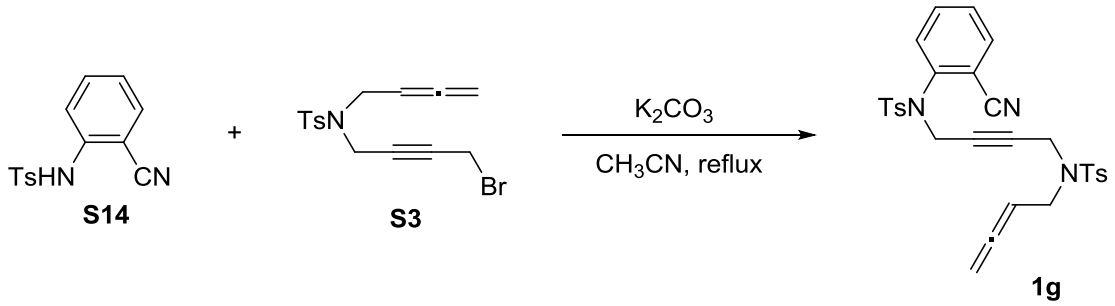


In a 50mL 2-neck round bottom flask, a mixture of diethyl 2-(2-cyanoethyl)malonate **S5** (0.50 g, 2.34 mmol) in anhydrous THF (5 mL) was added to a solution of NaH (60% in mineral oil, 0.13 g, 5.62 mmol) in 10 mL of anhydrous THF at 0ºC and stirred for 1h. A solution of 1,4-dibromo-2-butyne **S2** (1.98 g, 9.38 mmol) in anhydrous THF (5m L) was added at 0ºC and the resulting mixture was stirred overnight at room temperature. The reaction mixture was poured onto ice-water (10 mL) and extracted with ether (3×5 mL). The combined organic layer was dried over Na_2SO_4 and concentrated in vacuum conditions. The reaction crude was purified by column chromatography using a mixture of hexane:ethyl acetate (80:20) as the eluent to give the product **S12** (0.63 g, 78% yield) as a yellow oil. **MW:** 344.20 g/mol; **^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm):** 1.30 (t, $^{3}J_{H,H}$ = 7.2 Hz, 6H), 2.39-2.52 (m, 4H), 2.91 (d, $^{5}J_{H,H}$ = 2.4 Hz, 2H), 3.88 (d, $^{5}J_{H,H}$ = 2.4 Hz, 2H), 4.26 (q, $^{3}J_{H,H}$ = 7.2 Hz, 4H); **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 13.0, 14.0, 14.1, 14.3, 24.0 28.7, 55.7, 62.3, 79.2, 81.0, 118.8, 169.0; **IR (ATR) ν (cm^{-1}):** 2917, 1728, 1203; **HRMS** calcd. for [$C_{14}H_{18}NO_4Br$ + Na]$^{+}$: 366.0311. Found: 366.0309.

In a 50mL 2-neck round bottom flask, a mixture of diethyl 2-(4-bromobut-2-yn-1-yl)-2-(2-cyanoethyl)malonate **S12** (0.51 g, 1.48 mmol) in anhydrous THF (5 mL) was added to a solution of NaH (60% in mineral oil, 0.06 g, 2.50 mmol) in 10 mL of anhydrous THF at 0ºC and stirred for 1h. A solution of diethyl 2-(buta-2,3-dien-1-yl)malonate **S13** (0.24 g, 1.21 mmol) in anhydrous THF (5mL) was added at 0ºC and the resulting mixture was stirred overnight at room temperature. The reaction mixture was poured onto ice-water (10 mL) and extracted with ether (3×5 mL). The combined organic layer was dried over Na_2SO_4 and concentrated in vacuum conditions. The reaction crude was purified by column chromatography using a mixture of hexane:ethyl acetate (90:10) as the eluent to give the product **1f** (0.50 g, 86% yield) as a yellow oil. **MW:** 475.54 g/mol; **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 1.23-1.28 (m, 12H), 2.35-2.46 (m,

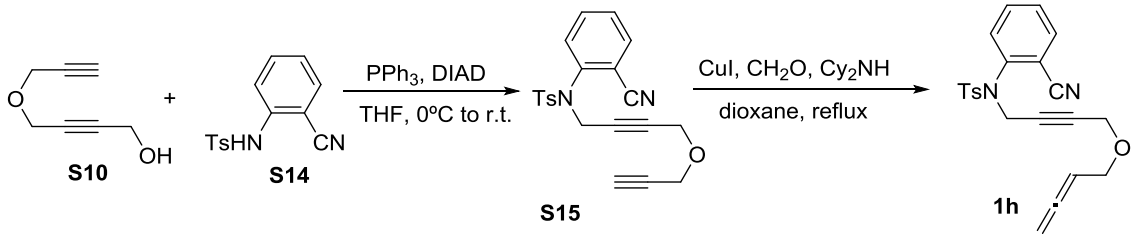
4H), 2.70 (dt, $^{3}J_{H,H}$ = 8.0 Hz, $^{5}J_{H,H}$ = 2.5 Hz, 2H), 2.77-2.80 (m, 4H), 4.20-4.26 (m, 8H), 4.69 (dt, $^{4}J_{H,H}$ = 6.6 Hz, $^{5}J_{H,H}$ = 2.5 Hz, 2H), 4.91 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** 14.0, 14.1, 22.7, 23.6, 28.4, 31.5, 55.8, 57.0, 61.6, 62.1, 74.8, 78.8, 83.8, 118.9, 169.1, 169.6, 210.2; **IR (ATR) ν (cm^{-1}):** 2923, 1726, 1443, 1280, 1185; **HRMS** calcd. for $[C_{25}H_{33}NO_8 + Na]^+$: 498.2098. Found: 498.2115.

Synthesis of 1g



In a 50 mL two-necked round bottom flask, a mixture of *N*-tosyl-2-aminobenzonitrile **S14** (0.05 g, 0.23 mmol), bromo derivative **S3** (0.08 g, 0.23 mmol) and potassium carbonate (0.16 g, 1.13 mmol) in acetonitrile (30 mL) was heated at reflux. The mixture was stirred for 5h until completion (TLC monitoring). The salts were filtered off and the solvent was removed under reduced pressure. The reaction crude was purified by column chromatography using a mixture of hexane:ethyl acetate (90:10) as the eluent to give compound **1g** (0.08 g, 70% yield) as a colourless solid. **MW:** 545.67 g/mol; **m.p.:** 120-122ºC; **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 2.43 (s, 3H), 2.44 (s, 3H), 3.61 (dt, $^{3}J_{H,H}$ = 7.0 Hz, $^{5}J_{H,H}$ = 2.5 Hz, 2H), 3.99 (t, $^{5}J_{H,H}$ = 1.9 Hz, 2H), 4.26 (t, $^{5}J_{H,H}$ = 1.9 Hz, 2H), 4.73 (dt, $^{4}J_{H,H}$ = 6.6 Hz, $^{5}J_{H,H}$ = 2.5 Hz, 2H), 4.91 (q, $J_{H,H}$ = 6.6 Hz, 1H), 7.27-7.31 (m, 5H), 7.45 (dt, $^{3}J_{H,H}$ = 7.8 Hz, $^{4}J_{H,H}$ = 1.5 Hz, 1H), 7.55 (dd, $^{3}J_{H,H}$ = 7.8 Hz, $^{4}J_{H,H}$ = 1.5 Hz, 1H), 7.57-7.66 (m, 5H); **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 21.6, 21.7, 35.0, 36.0, 40.7, 45.6, 78.6, 79.3, 85.3, 114.8, 115.9, 127.6, 128.2, 129.5, 129.8, 131.5, 134.9, 136.0, 140.8, 143.8, 144.7, 209.6; **ESI-MS (m/z):** 546.1 $[M + H]^+$, 568.2 $[M + Na]^+$; **IR (ATR) ν (cm^{-1}):** 2920, 2236, 1347, 1159, 1088; **AE:** calcd. for $[C_{29}H_{27}N_3O_4S_2]$: C, 63.83; H, 4.99; N, 7.70. Found: C, 64.04; H, 5.26; N, 7.21.

Synthesis of 1h

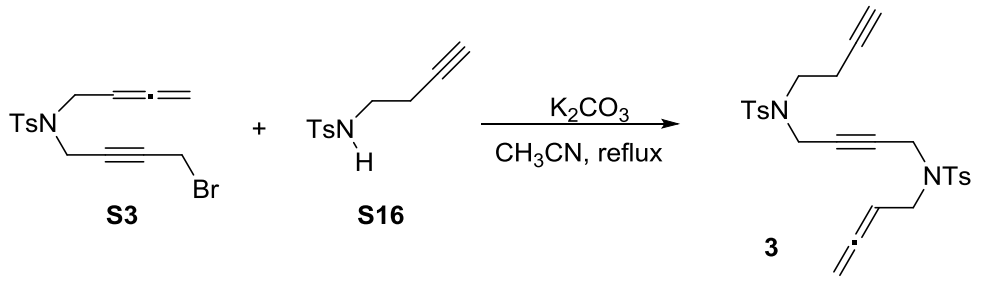


In a 100 mL two-necked round bottom flask, a mixture of 4-(prop-2-yn-1-yloxy)but-2-yn-1-ol **S10** (0.40 g, 3.23 mmol), *N*-(2-cyanophenyl)-4-methylbenzenesulfonamide **S14** (0.76 g, 3.23 mmol) and triphenylphosphine (2.12 g, 8.06 mmol) in anhydrous and degassed tetrahydrofuran (40 mL) was stirred and cooled to 0ºC in an ice-water bath. Diisopropyl azodicarboxylate (1.60 mL, 8.06 mmol) was added dropwise to this solution and the resulting mixture was stirred at room temperature for 2h (TLC monitoring). The solvent was removed under reduced pressure and the reaction crude was purified by column chromatography using a mixture of hexane:dichloromethane (70:30) as the eluent to afford compound **S15** (1.04 g, 85% yield) as a yellow oil. **MW:** 378.45 g/mol; **^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm):** 2.42 (t, $^{4}J_{H,H}$ = 2.4 Hz, 1H), 2.44 (s, 3H), 4.03 (d, $^{4}J_{H,H}$ = 2.4 Hz, 2H), 4.12 (t, $^{5}J_{H,H}$ = 1.9 Hz, 2H), 4.51 (t, $^{5}J_{H,H}$ = 1.9 Hz, 2H), 7.31 (d, $^{3}J_{H,H}$ = 8.3 Hz, 2H), 7.42-7.49 (m, 2H), 7.60 (dt, $^{3}J_{H,H}$ = 7.8 Hz, $^{4}J_{H,H}$ = 1.5 Hz, 1H), 7.68-7.70 (m, 3H); **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** 21.7, 41.2, 56.2, 56.4, 75.1, 78.7, 80.3, 81.6, 115.2, 116.1, 128.2, 129.2, 129.8, 131.3, 133.3, 133.9, 135.2, 141.2, 144.6; **IR (ATR) ν (cm^{-1}):** 3276, 2231, 1348, 1159, 1083; **HRMS** calcd. for $[C_{21}H_{18}N_2O_3S + Na]^+$: 401.0930. Found: 401.0947.

In a 50mL two-necked round bottom flask, a mixture of **S15** (0.53 g, 1.40 mmol), formaldehyde (0.10 g, 2.80 mmol) and copper(I) iodide (0.15 g, 0.70 mmol) in dioxane (20 mL) was heated to reflux. Dicyclohexylamine (0.5 mL, 2.52 mmol) was then added dropwise to the reaction mixture and stirred for 5h until completion (TLC monitoring). The salts were filtered off and the solvent was removed under reduced pressure. The reaction crude was purified by column chromatography using a mixture of hexane: dichloromethane (70:30) as the eluent to afford derivative **1h** (0.37 g, 68% yield) as a yellow oil. **MW:** 392.47 g/mol; **^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm):** 2.44 (s, 3H), 3.87 (dt, $^{3}J_{H,H}$ = 6.8 Hz, $^{5}J_{H,H}$ = 2.4 Hz, 2H), 4.03 (t, $^{3}J_{H,H}$ = 2.0 Hz, 2H), 4.51 (t, $^{5}J_{H,H}$ = 2.0 Hz, 2H), 4.78 (dt, $^{4}J_{H,H}$ = 6.8 Hz, $^{5}J_{H,H}$ = 2.4 Hz, 2H), 5.15 (quint., $J_{H,H}$ = 7.0 Hz, 1H), 7.31 (d, $^{3}J_{H,H}$ = 8.3 Hz, 2H), 7.39 (dd, $^{3}J_{H,H}$ = 8.1 Hz, $^{4}J_{H,H}$ = 1.0 Hz, 1H), 7.47 (dt, $^{3}J_{H,H}$ = 7.8 Hz, $^{4}J_{H,H}$ = 1.3 Hz, 1H), 7.59 (dt, $^{3}J_{H,H}$ = 7.8 Hz, $^{4}J_{H,H}$ = 1.5 Hz, 1H), 7.66-7.70 (m, 3H); **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** 21.6, 41.2, 56.7, 67.1, 75.8, 79.5, 82.3, 86.9, 115.2, 116.0, 128.2, 129.1, 129.7, 131.1, 133.2, 133.8, 135.1, 141.1, 144.5, 209.4; **IR (ATR) ν**

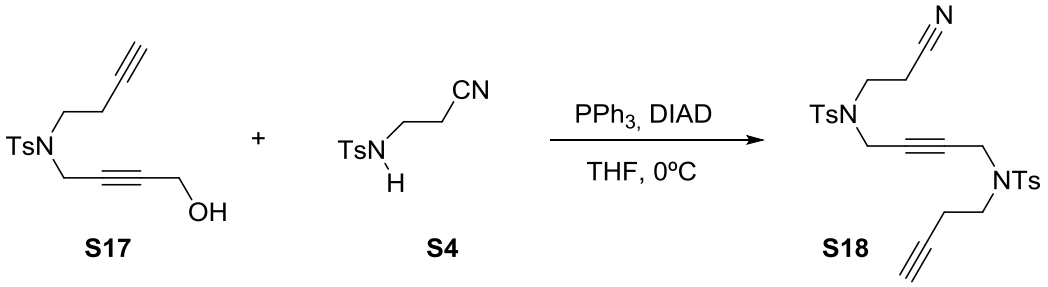
(cm^{-1}): 2918, 2231, 1349, 1155, 1074; **HRMS** calcd. for $[C_{22}H_{20}N_2O_3S + Na]^+$: 415.1087. Found: 415.1095.

Synthesis of 3



In a 50 mL two-necked round bottom flask, a mixture of bromo derivative **S3** (0.10 g, 0.27 mmol), *N*-but-3-ynyl-4-methylbenzenesulfonamide **S16** (0.06 g, 0.28 mmol) and potassium carbonate (0.19 g, 1.37 mmol) in acetonitrile (30 mL) was heated at reflux. The mixture was stirred for 3h until completion (TLC monitoring). The salts were filtered off and the solvent was removed under reduced pressure. The reaction crude was purified by column chromatography using a mixture of hexane:ethyl acetate (80:20) as the eluent to give compound **3** (0.13 g, 93% yield) as a colourless solid. **MW:** 496.64 g/mol; **m.p.:** 86-88ºC; **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 2.01 (t, $^4J_{H,H}$ = 2.7 Hz, 1H), 2.40 (dt, $^4J_{H,H}$ = 2.7 Hz, $^3J_{H,H}$ = 7.2 Hz, 2H), 2.40 (s, 3H), 2.44 (s, 3H), 3.17 (t, $^3J_{H,H}$ = 7.2 Hz, 2H), 3.66 (dt, $^3J_{H,H}$ = 7.0 Hz, $^5J_{H,H}$ = 2.5 Hz, 2H), 3.94-3.98 (m 4H), 4.74 (dt, $^4J_{H,H}$ = 7.0 Hz, $^5J_{H,H}$ = 2.5 Hz, 2H), 4.91 (quint., $J_{H,H}$ = 7.0 Hz, 1H), 7.28-7.32 (m, 4H), 7.62-7.67 (m, 4H); **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 18.9, 21.6, 35.9, 37.3, 45.3, 45.6, 70.5, 78.4, 78.5, 80.6, 85.2, 127.5, 127.6, 129.6, 129.7, 135.8, 136.0, 143.8, 143.9, 209.6; **ESI-MS (m/z):** 497.1 $[M + H]^+$; **IR (ATR) ν (cm^{-1}):** 1327, 1156, 1090; **AE:** calcd. for $[C_{26}H_{28}N_2O_4S_2.1.5H_2O]$: C, 59.63; H, 5.97; N, 5.35. Found: C, 60.03; H, 5.41; N, 5.38.

Synthesis of cyanodiyne S18

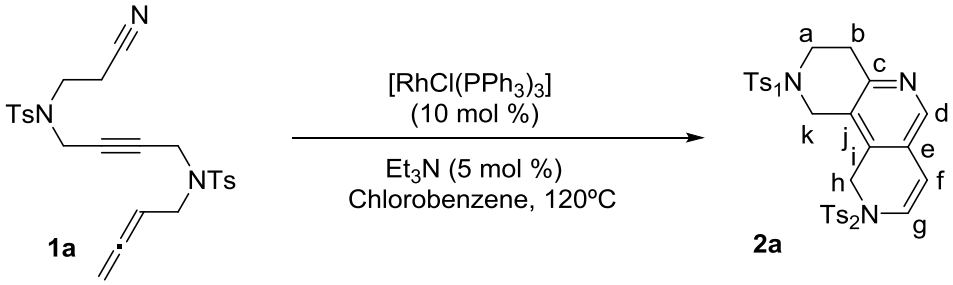


S17 **S4** **S18**

In a 50 mL two-necked round bottom flask, a mixture of N-(but-3-yn-1-yl)-N-(4-hydroxybut-2-yn-1-yl)-4-methylbenzenesulfonamide **S17** (0.40 g, 1.37 mmols), N-(2-cyanoethyl)-4-methylbenzenesulfonamide **S4** (0.31 g, 1.37 mmols) and triphenylphosphine (0.90 g, 3.43 mmols) in anhydrous and degassed tetrahydrofuran (30 mL) was stirred and cooled to 0ºC in an ice-water bath. Diisopropyl azodicarboxylate (0.7 mL, 3.45 mmols) was added dropwise to this solution and the resulting mixture was stirred at room temperature for 12h (TLC monitoring). The solvent was removed under reduced pressure and the reaction crude was purified by column chromatography using a mixture of hexane:ethyl acetate (90:10) as the eluent to afford cyanodiyne **S18** (0.54 g, 79% yield) as a yellow oil. MW: 497.63 g/mol; **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 2.03 (t, $^{4}J_{H,H}$ = 2.6 Hz, 1H), 2.40 (dt, $^{3}J_{H,H}$ = 7.0 Hz, $^{4}J_{H,H}$ = 2.6 Hz, 2H), 2.47 (s, 3H), 2.48 (s, 3H), 2.65 (t, $^{3}J_{H,H}$ = 7.0 Hz, 2H), 3.20 (t, $^{3}J_{H,H}$ = 7.2 Hz, 2H), 3.30 (t, $^{3}J_{H,H}$ = 7.2 Hz, 2H), 4.03 (s, 4H), 7.35 (m, 4H), 7.69 (d, $^{3}J_{H,H}$ = 8.2 Hz, 4H). **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 18.5, 19.0, 21.5, 21.6, 37.4, 38.4, 43.0, 45.5, 70.6, 78.0, 79.5, 80.6, 117.3, 127.50, 127.7, 129.6, 129.8, 135.0, 135.8, 144.0, 144.5.

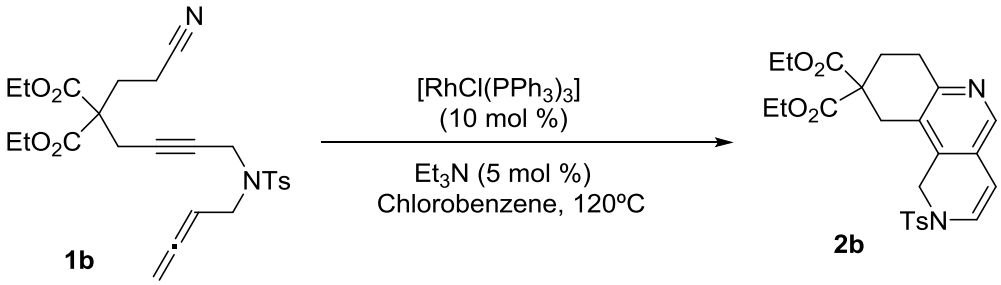
General procedure for Rh(I)-catalyzed [2+2+2] cycloaddition reactions and characterization data of 2a-2h, 4 and S19

Compound 2a



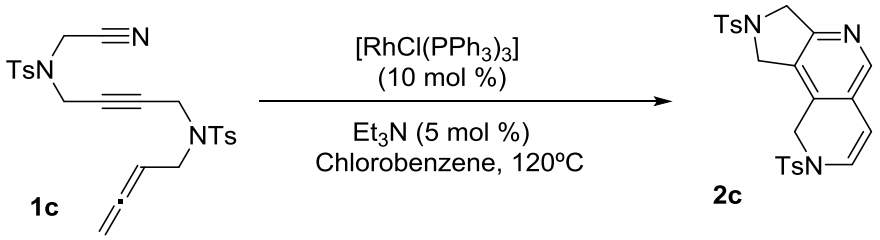
A degassed solution of chlorotris(triphenylphosphine)rhodium(I) (9.3 mg, 0.010 mmol), cyano-yne-allene derivative **1a** (50 mg, 0.100 mmol) and triethylamine (0.51 mg, 0.005 mmol) in chlorobenzene (2 mL) was heated in a sealed 10 mL septum-containing, screw-capped vial for 10 min. at 120ºC under microwave irradiation (TLC monitoring). Upon completion, the solvent was evaporated under reduced pressure and the residue was purified by column chromatography using a mixture of hexane:ethyl acetate (40:60) as the eluent to give compound **2a** (33 mg, 66% yield) as a colourless solid. **MW:** 495.61 g/mol; **^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm):** 2.43 (s, 3H, Ts_2), 2.47 (s, 3H, Ts_1), 3.01 (t, $^{3}J_{H,H}$ = 5.8 Hz, 2Hb), 3.39 (t, $^{3}J_{H,H}$ = 5.8 Hz, 2Ha), 4.11 (s, 2Hk), 4.50 (s, 2Hh), 5.79 (d, $^{3}J_{H,H}$ = 8.0 Hz, 1Hf), 6.83 (d, $^{3}J_{H,H}$ = 8.0 Hz, 1Hg), 7.33 (d, $^{3}J_{H,H}$ = 8.3 Hz, 2HTs_2), 7.39 (d, $^{3}J_{H,H}$ = 8.0 Hz, 2HTs_1), 7.73 (d, $^{3}J_{H,H}$ = 8.3 Hz, 2HTs_2), 7.76 (d, $^{3}J_{H,H}$ = 8.0 Hz, 2HTs_1), 8.00 (s, 1Hd); **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 21.5 (CH_3-Ts), 21.6 (CH_3-Ts), 32.1 (Cb), 42.6 (Ch), 43.2 (Ca), 44.0 (Ck), 105.7 (Cf), 122.9 (Cj), 124.0 (Ce), 127.1 (Ts), 127.5 (Cg), 127.7 (Ts), 130.0 (Ts), 130.1 (Ts), 132.6 (Ci), 133.0 (Ts), 133.9 (Ts), 143.4 (Cd), 144.2 (Ts), 144.8 (Ts), 152.5 (Cc); **ESI-MS (m/z):** 496.1 $[M + H]^+$; **IR (ATR) ν (cm^{-1}):** 2918, 1436, 1338, 1158; **HRMS** calcd. for $[C_{25}H_{25}N_3O_4S_2 + Na]^+$: 518.1179. Found: 518.1183.

Compound 2b



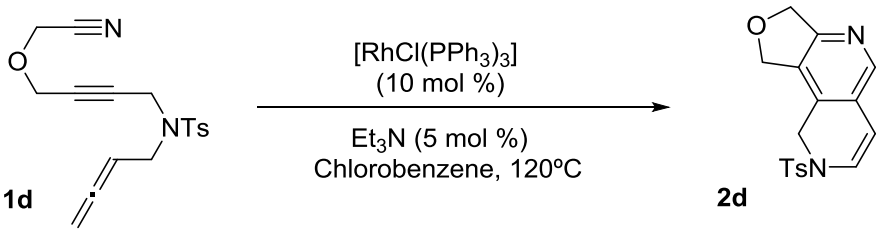
Compound **2b** was obtained following the general procedure described for **2a**. Reaction time: 40 min. Yellow oil (25 mg, 51% yield). **MW:** 484.61 g/mol; **^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm):** 1.27 (t, $^3J_{H,H}$ = 7.2 Hz, 6H), 2.36 (t, $^3J_{H,H}$ = 6.8 Hz, 2H), 2.41 (s, 3H), 2.89 (t, $^3J_{H,H}$ = 6.8 Hz, 2H), 3.04 (s, 2H), 4.15-4.28 (m, 4H), 4.64 (s, 2H), 5.77 (d, $^3J_{H,H}$ = 7.8 Hz, 1H), 6.80 (d, $^3J_{H,H}$ = 7.8 Hz, 1H), 7.32 (d, $^3J_{H,H}$ = 8.4 Hz, 4H), 7.70 (d, $^3J_{H,H}$ = 8.4 Hz, 4H), 7.97 (s, 1H); **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):**14.0, 14.1, 21.6, 34.0, 38.7, 43.3, 53.0, 61.9, 106.1, 120.2, 127.0, 127.2, 129.7, 130.0, 134.1, 142.1, 144.5, 154.1, 162.2, 170.7; **ESI-MS (m/z):** 485.1 $[M + H]^+$; **IR (ATR) ν (cm^{-1}):** 2922, 1725, 1161; **HRMS** calcd. for $[C_{25}H_{28}N_2O_6S + H]^+$: 485.1741. Found: 485.1747.

Compound 2c



Compound **2c** was obtained following the general procedure described for **2a**. Reaction time: 10 min. Yellow oil (28 mg, 57% yield). **MW:** 481.59 g/mol; **^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm):** 2.43 (s, 3H), 2.44 (s, 3H), 4.46 (s, 2H), 4.50 (s, 2H), 4.54 (s, 2H), 5.78 (d, $^3J_{H,H}$ = 7.8 Hz, 1H), 6.84 (d, $^3J_{H,H}$ = 7.8 Hz, 1H), 7.31-7.39 (m, 4H), 7.69 (d, $^3J_{H,H}$ = 8.4 Hz, 2H), 7.79 (d, $^3J_{H,H}$ = 8.1 Hz, 2H), 8.01 (s, 1H); **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 21.5, 43.5, 50.4, 53.6, 105.1, 125.2, 125.9, 127.2, 127.6, 128.0, 130.0, 130.1, 130.8, 133.2, 133.7, 144.2, 144.8, 144.9, 156.1. **ESI-MS (m/z):** 482.1 $[M + H]^+$; **IR (ATR) ν (cm^{-1}):** 2920, 1342, 1161; **HRMS** calcd. for $[C_{24}H_{23}N_3O_4S_2 + Na]^+$: 482.1203. Found: 482.1220.

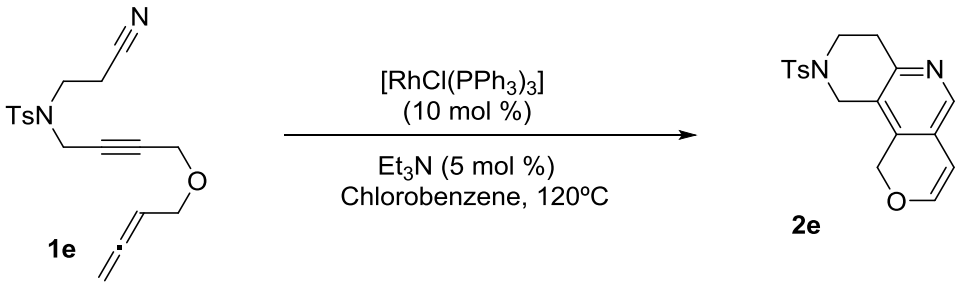
Compound 2d



Compound **2d** was obtained following the general procedure described for **2a**. Reaction time: 40 min. Colourless solid (19 mg, 38% yield). **MW:** 328.38 g/mol; **m.p.:** 234-236ºC; **^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm):** 2.42 (s, 3H), 4.50 (s, 2H), 4.98 (s, 2H), 5.05 (s, 2H), 5.85 (d, $^3J_{H,H}$ = 7.8 Hz, 1H), 6.84 (d, $^3J_{H,H}$ = 7.8 Hz, 1H), 7.33 (d, $^3J_{H,H}$ = 8.1 Hz, 2H), 7.70 (d, $^3J_{H,H}$ = 8.1 Hz, 2H), 8.06 (br s, 1H); **^{13}C NMR (75 MHz, $CDCl_3$) δ**

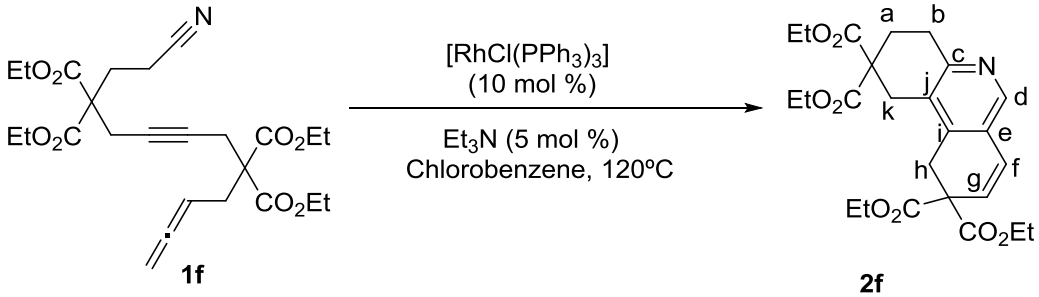
(ppm): 21.6, 43.8, 70.5, 72.8, 105.7, 124.6, 127.1, 127.6, 128.2, 129.8, 130.1, 133.9, 144.7, 144.8, 160.0; **ESI-MS (m/z):** 329.1 $[M + H]^+$; **IR (ATR) ν (cm^{-1}):** 2921, 1346, 1160; **AE:** calcd. for $[C_{17}H_{16}N_2O_3S]$: C, 62.18; H, 4.91; N,8.53. Found: C, 61.64; H, 4.92; N, 7.97.

Compound 2e



Compound **2e** was obtained following the general procedure described for **2a**. Reaction time: 20 min. Yellow oil (20 mg, 40% yield). **MW:** 342.41 g/mol; **^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm):** 2.44 (s, 3H), 3.04 (t, $^3J_{H,H}$ = 6.0 Hz, 2H), 3.42 (t, $^3J_{H,H}$ = 6.0 Hz, 2H), 4.11 (s, 2H), 5.00 (s, 2H), 5.75 (d, $^3J_{H,H}$ = 5.7 Hz, 1H), 6.83 (d, $^3J_{H,H}$ = 5.7 Hz, 1H), 7.36 (dd, $^3J_{H,H}$ = 8.1 Hz, 2H), 7.73 (d, $^3J_{H,H}$ = 8.1 Hz, 2H), 8.02 (s, 1H); **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 21.6, 32.2, 43.4, 43.9, 63.1, 101.5, 121.7, 123.7 127.7, 129.9, 132.7, 132.9, 142.1, 144.1, 146.8, 151.9; **ESI-MS (m/z):** 343.1 $[M + H]^+$; **IR (ATR) ν (cm^{-1}):** 2921, 1331, 1155; **HRMS** calcd. for $[C_{18}H_{18}N_2O_3S + H]^+$: 343.1111. Found: 343.1106.

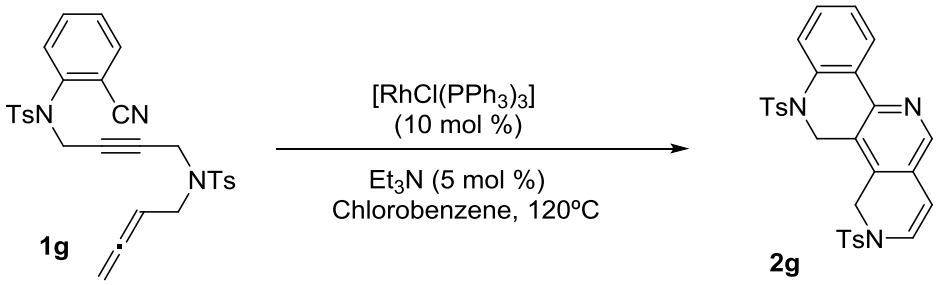
Compound 2f



Compound **2f** was obtained following the general procedure described for **2a**. Reaction time: 25 min. Yellow oil (24 mg, 49% yield). **MW:** 473.52 g/mol; **^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm):** 1.23-1.27 (m, 12H, CH_3CH_2O), 2.40 (t, $^3J_{H,H}$ = 6.8 Hz, 2Hb), 2.93 (t, $^3J_{H,H}$ = 6.8 Hz, 2Ha), 3.25 (s, 2Hk), 3.35 (s, 2Hh), 4.16-4.25 (m, 8H, CH_3CH_2O), 6.21 (d, $^3J_{H,H}$ = 9.4 Hz, 1Hg), 6.60 (d, $^3J_{H,H}$ = 9.4 Hz, 1Hf), 8.10 (s, 1Hd); **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 13.9, 14.0, 14.1, 14.2, 27.3 (Cb), 29.3 (Ca), 29.5 (Ch), 30.9 (Ck), 53.3, 54.5, 61.7, 62.1, 124.9, 125.1 (Cg), 126.4, 126.1 (Cf), 139.4, 144.8 (Cd), 155.0,

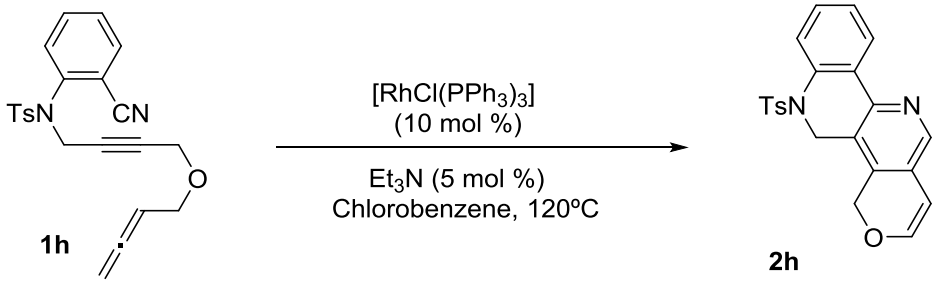
169.8 (C=O), 171.0 (C=O); **IR (ATR) ν (cm^{-1}):** 2917, 1726, 1187; **HRMS** calcd. for $[C_{25}H_{31}NO_8 + H]^+$: 474.2122 Found: 474.2123.

Compound 2g



Compound **2g** was obtained following the general procedure described for **2a**. Reaction time: 20 min. Yellow oil (27 mg, 54% yield). **MW:** 543.66 g/mol; **^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm):** 2.12 (s, 3H), 2.40 (s, 3H), 4.57 (s, 2H), 4.74 (s, 2H), 5.71 (d, $^3J_{H,H}$ = 7.8 Hz, 1H), 6.69 (d, $^3J_{H,H}$ = 7.8 Hz, 2H), 6.89-6.92 (m,3H), 7.36-7.46 (m, 4H), 7.46 (dt, $^3J_{H,H}$ = 1.5 Hz, , $^4J_{H,H}$ = 7.5 Hz, 1H), 7.74 (dd, $^3J_{H,H}$ = 1.3 Hz, , $^4J_{H,H}$ = 8.0 Hz, 1H), 7.83 (d, $^3J_{H,H}$ = 8.2 Hz, 2H), 7.88 (s, 1H), 8.04 (dd, $^3J_{H,H}$ = 1.5 Hz, $^4J_{H,H}$ = 7.5 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** 21.3, 21.6, 42.7, 44.7, 104.8, 122.0, 125.0, 125.2, 126.7, 127.3, 127.6, 127.7, 128.9, 130.1, 130.3, 134.1, 134.7, 136.9, 143.5, 143.8, 144.9, 146.8, 148.4; **IR (ATR) ν (cm^{-1}):** 2920, 1343, 1154, 1087; **HRMS** calcd. for $[C_{29}H_{25}N_3O_4S_2 + H]^+$: 544.1359. Found: 544.1371.

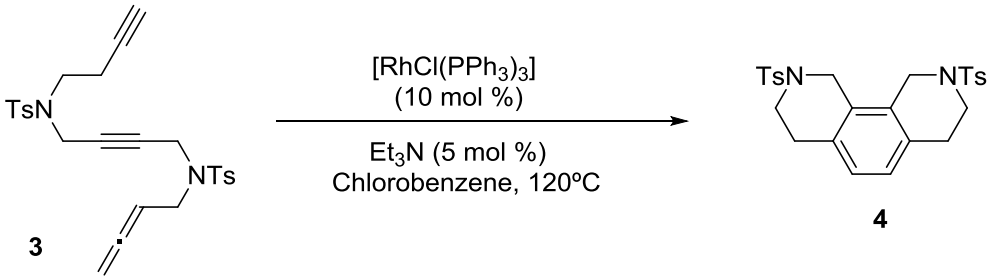
Compound 2h



Compound **2h** was obtained following the general procedure described for **2a**. Reaction time: 20 min. Yellow oil (26 mg, 52% yield). **MW:** 390.46 g/mol; **^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm):** 2.16 (s, 3H), 4.77 (s, 2H), 5.10 (s, 2H), 5.74 (d, $^3J_{H,H}$ = 5.6 Hz, 1H), 6.64 (d, $^3J_{H,H}$ = 5.6 Hz, 1H), 6.82 (d, $^3J_{H,H}$ = 8.7 Hz, 2H), 6.84 (d, $^3J_{H,H}$ = 8.7 Hz, 2H), 7.40 (dt, $^3J_{H,H}$ = 7.7 Hz, $^4J_{H,H}$ = 1.3 Hz, 1H), 7.46 (dt, $^3J_{H,H}$ = 8.0 Hz, $^4J_{H,H}$ = 1.7 Hz, 1H), 7.76 (dd, $^3J_{H,H}$ = 8.0 Hz, $^4J_{H,H}$ = 1.3 Hz 1H), 7.90 (s, 1H), 8.07 (dd, $^3J_{H,H}$ = 7.7 Hz,

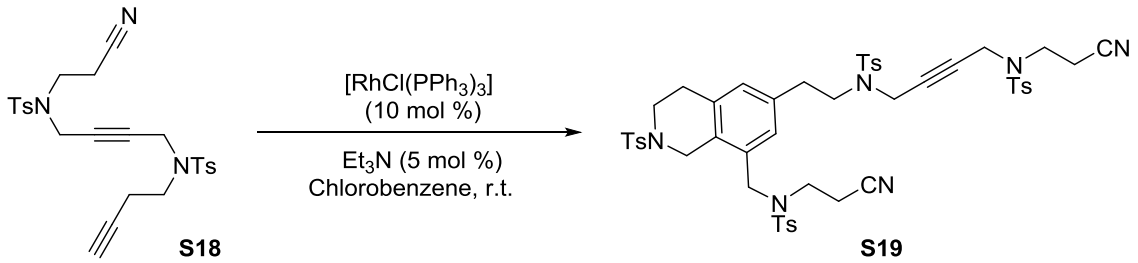
$^{4}J_{H,H}$ = 1.7 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** 21.3, 44.7, 63.4, 101.7, 120.9, 124.8, 124.9, 126.7, 127.6, 127.7, 128.9, 129.1, 129.7, 129.8, 131.3, 134.7, 136.8, 142.1, 143.8, 147.3; **IR (ATR) ν (cm^{-1}):** 2919, 1338, 1158, 1069; **HRMS** calcd. for $[C_{22}H_{18}N_2O_3S + H]^+$: 391.1111. Found: 391.1106.

Rh(I)-catalyzed [2+2+2] cycloaddition reaction of yne-yne-allene derivative 4



Compound **4** was obtained following the general procedure described for **2a**. Reaction time: 30 min. Colourless solid (45 mg, 90% yield). **MW:** 496.64 g/mol; **m.p.:** 255-257ºC; **^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm):** 2.43 (s, 6H, Ts), 2.88 (t, $^{3}J_{H,H}$ = 6.0 Hz, 4H), 3.31 (t, $^{3}J_{H,H}$ = 6.0 Hz, 4H), 4.04 (s, 4H), 6.90 (s, 2H), 7.38 (d, $^{3}J_{H,H}$ = 8.1 Hz, 4H), 7.75 (d, $^{3}J_{H,H}$ = 8.1 Hz, 4H); **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 21.6, 29.1, 43.1, 44.5, 127.3, 127.7, 128.2, 129.9, 131.3, 133.2, 143.9. **ESI-MS (m/z):** 497.1 $[M + H]^+$; **IR (ATR) ν (cm^{-1}):** 2920, 1336, 1158; **HRMS** calcd. for $[C_{26}H_{28}N_2O_4S + Na]^+$: 519.1383. Found: 519.1409.

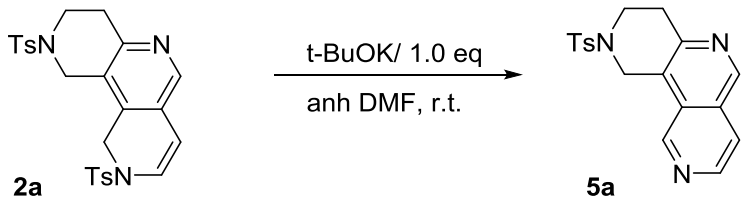
Rh(I)-catalyzed [2+2+2] cycloaddition reaction of cyano-yne-yne derivative S18



A degassed solution of chlorotris(triphenylphosphine)rhodium(I) (9.3 mg, 0.010 mmol), cyanodiyne derivative **S18** (50 mg, 0.100 mmol) and triethylamine (0.51 mg, 0.005 mmol) in chlorobenzene (2 mL) was mixed in a sealed 10 mL septum-containing, screw-capped vial. Reaction mixture immediately change color from red to brown solution. TLC monitoring showed no starting material in the reaction crude. The solvent

was evaporated under reduced pressure and ^{1}H NMR analysis of the crude showed not desired product but only homodimerization product **S19**.

NTs deprotection by dehydrosulfonylation/aromatization



In a 10 mL two-neck round bottom flask, a solution of **2a** (20 mg, 0.04 mmols) in anhydrous DMF (1 mL) was added to a mixture of potassium *tert*-butoxide (5 mg, 0.04 mmols) in anhydrous DMF (1 mL) at 0ºC. The reaction was stirred for 10 min until completion (TLC monitoring). Ethyl acetate (2mL) was then added to the reaction mixture and the resulting organic phase was washed with water (3×2 mL). The organic layer was dried over Na_2SO_4 and the solvent was removed under reduced pressure. The reaction crude was purified by column chromatography using a mixture of hexane:ethyl acetate (20:80) as the eluent to afford 2,6-naftiridine **5a** (9.9 mg, 74% yield) as a yellow oil. **MW:** 339.41 g/mol; **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 2.43 (s, 3H), 3.28 (t, $^{3}J_{H,H}$ = 5.6 Hz, 2H), 3.57 (t, $^{3}J_{H,H}$ = 5.6 Hz, 2H), 4.78 (s, 2H), 7.36 (d, $^{3}J_{H,H}$ = 8.0 Hz, 2H), 7.74 (d, $^{3}J_{H,H}$ = 5.6 Hz, 1H), 7.80 (d, $^{3}J_{H,H}$ = 8.0 Hz, 2H), 8.74 (d, $^{3}J_{H,H}$ = 5.6 Hz, 1H), 9.16 (s, 1H), 9.33 (s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** 21.6, 32.1, 43.5, 44.0, 119.7, 120.0, 127.2, 127.8, 130.0, 133.1, 144.2, 144.7, 146.6, 148.6, 150.9. **ESI-MS (m/z):** 340.1 $[M + H]^+$, **HRMS** calcd. for $[C_{18}H_{17}N_3O_2S + Na]^+$: 362.0925. Found: 362.0934.

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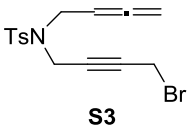
[9] Yuan, W.; Wei, Y.; Shi, M. *ChemistryOpen* **2013**, *2*, 63-68.

Spectra of all new compounds synthesized

Spectra of intermediates S3, S9, S11, S12, and S15.



S3

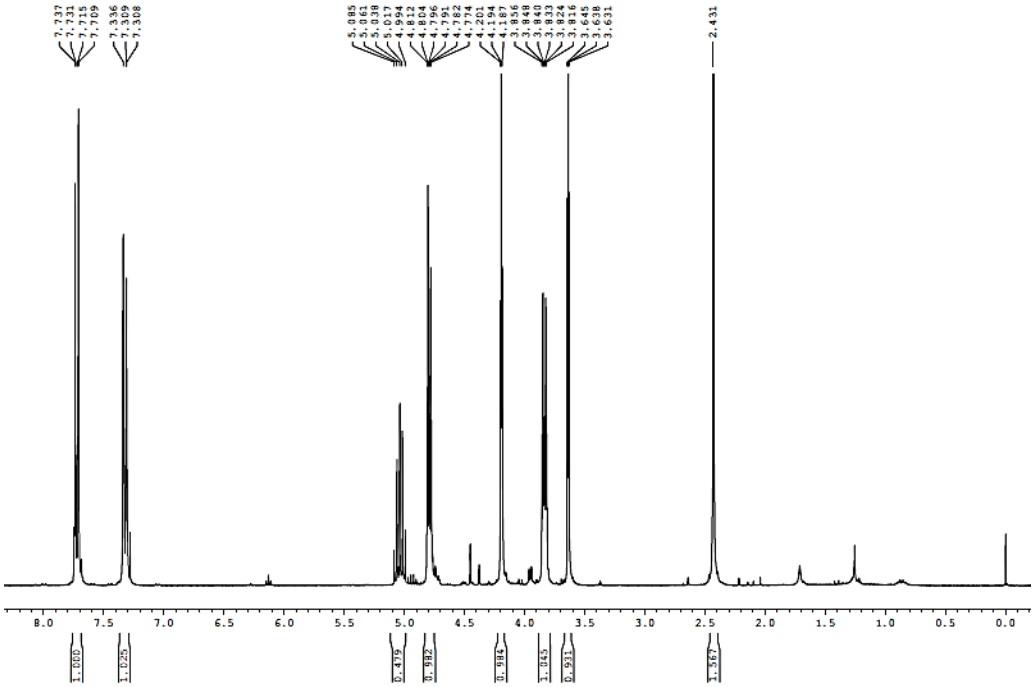
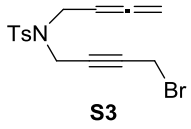


Figure S1: ^{1}H NMR spectrum (400 MHz) of **S3** in $CDCl_3$.



S3

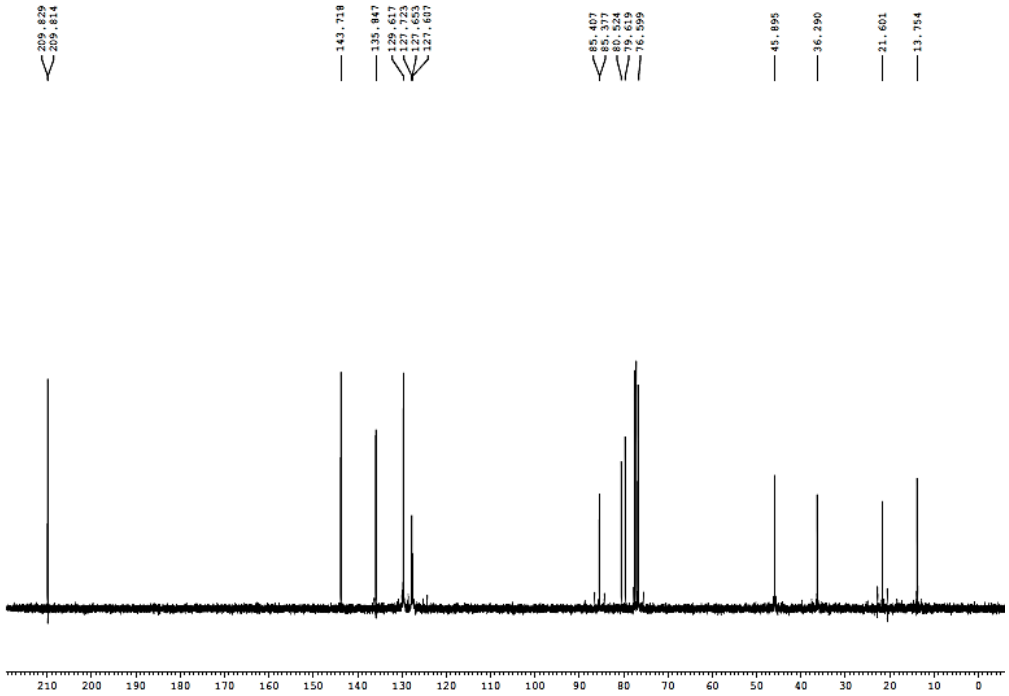
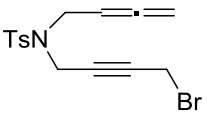


Figure S2: ^{1}H-decoupled ^{13}C NMR spectrum (75 MHz) of **S3** in $CDCl_3$.



S3

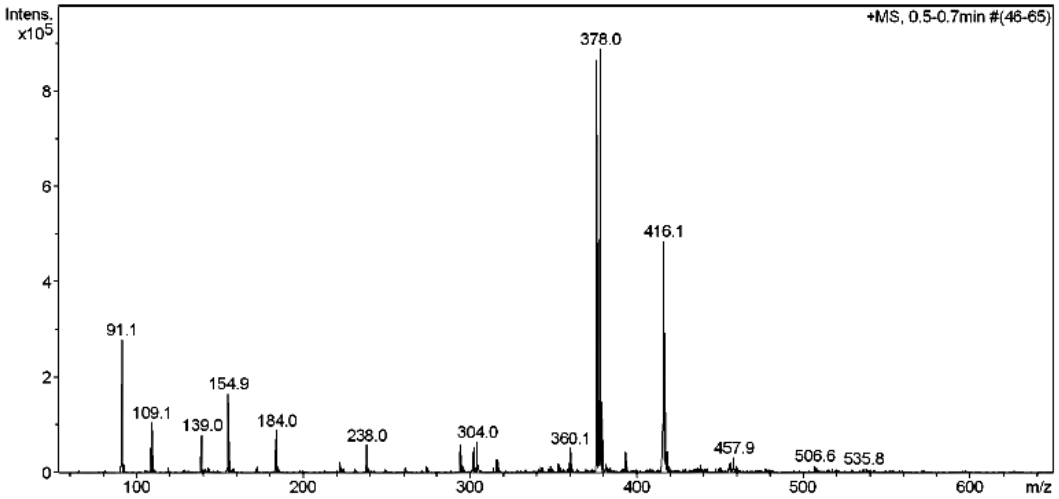
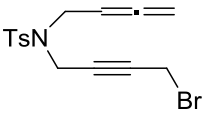


Figure S3: ESI-MS spectrum of **S3.**



S3

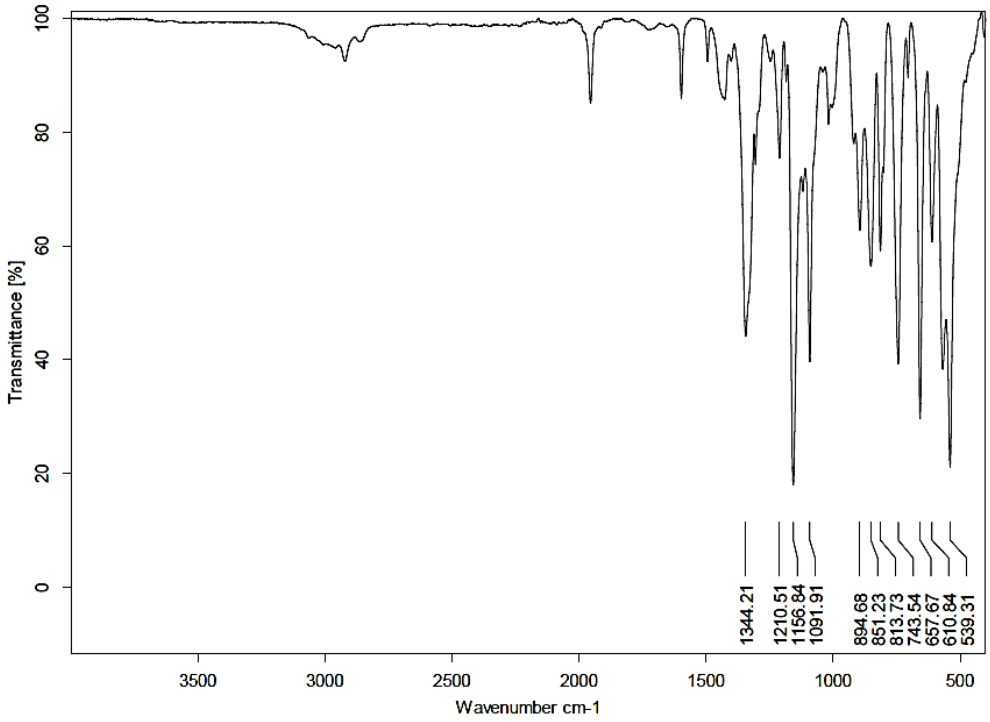
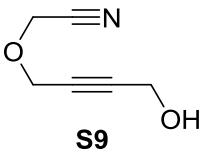


Figure S4: IR (ATR) spectrum of **S3.**



S9

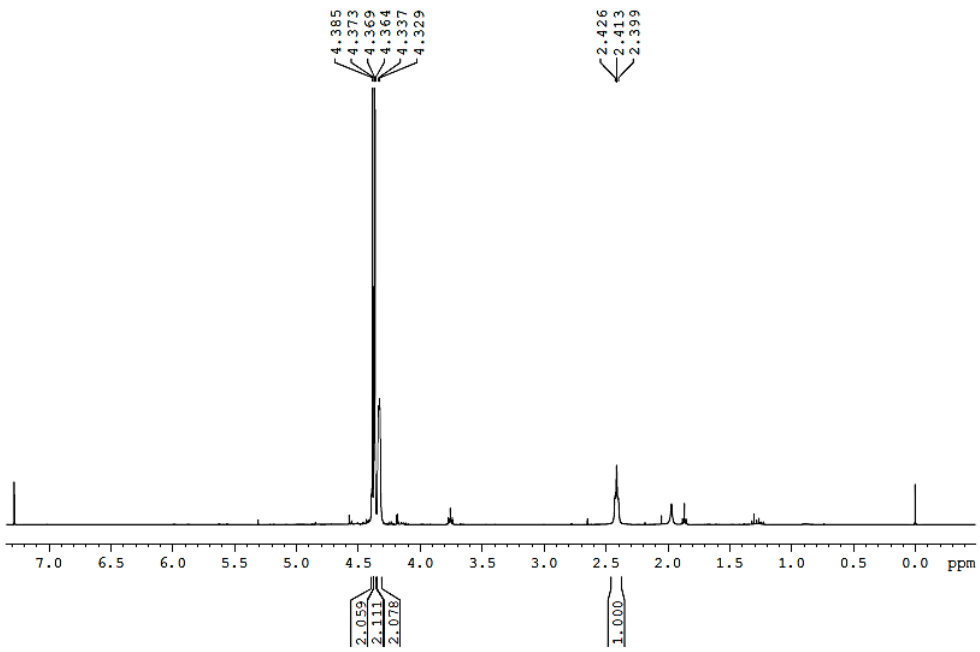
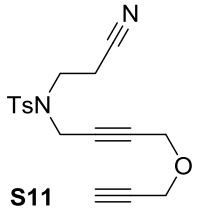


Figure S5: ^{1}H NMR spectrum (400 MHz) of **S9** in $CDCl_3$.



S11

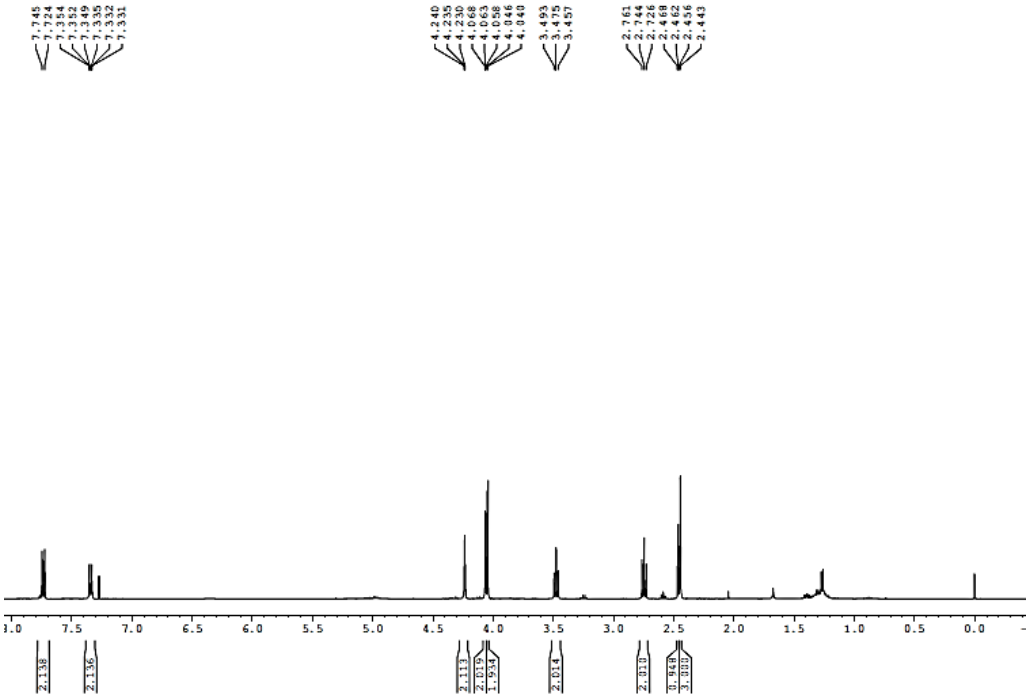


Figure S6: ^{1}H NMR spectrum (400 MHz) of **S11** in $CDCl_3$.

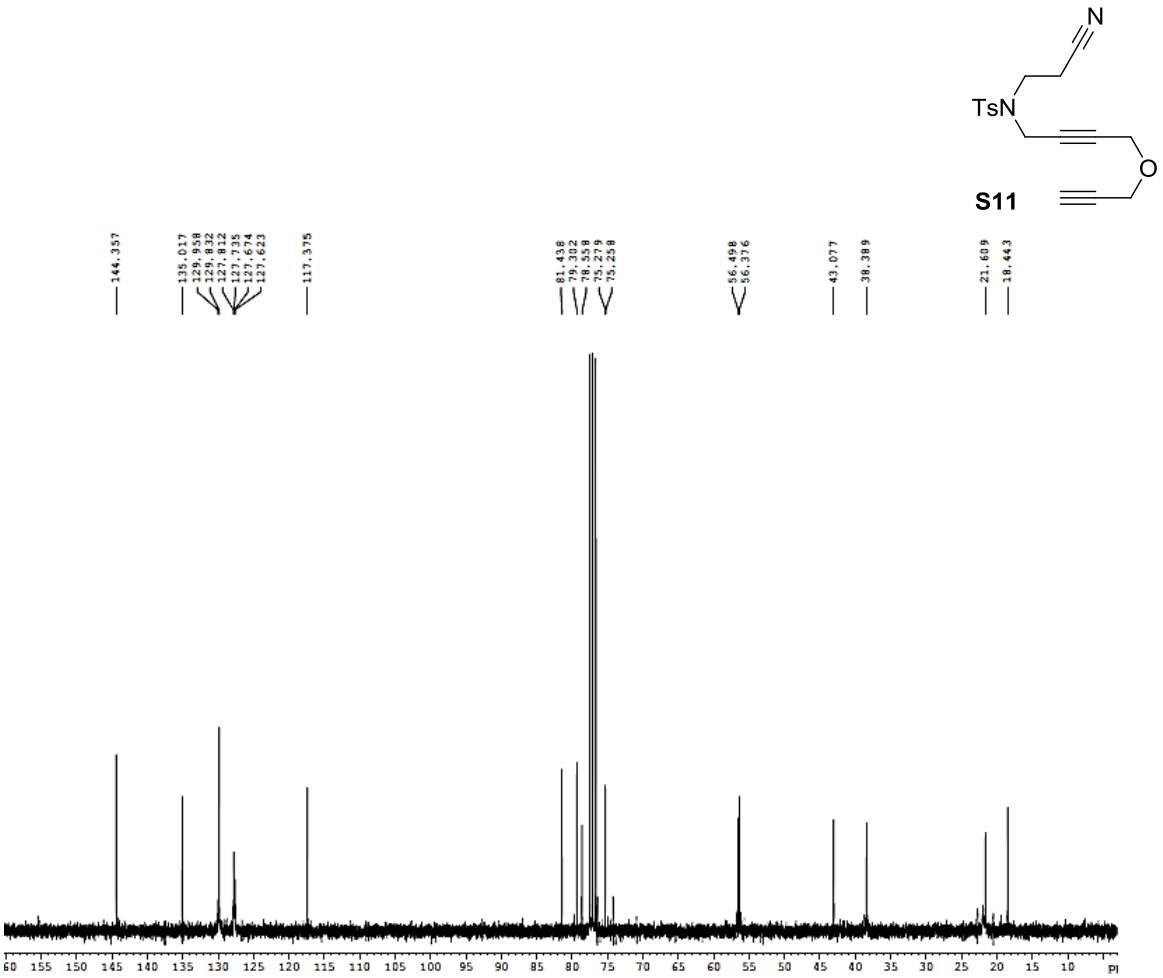


Figure S7: ^{1}H-decoupled ^{13}C NMR spectrum (75 MHz) of **S11** in $CDCl_3$.

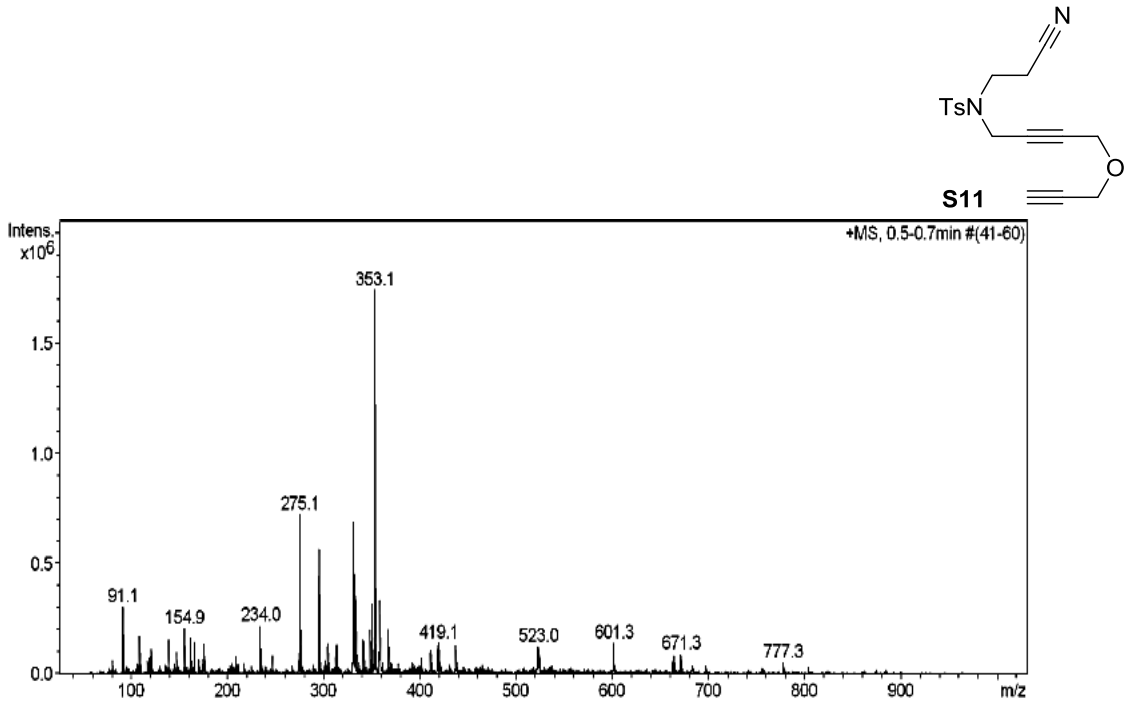
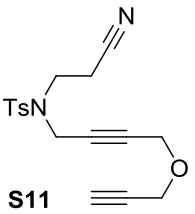


Figure S8: ESI-MS spectrum of **S11.**



S11

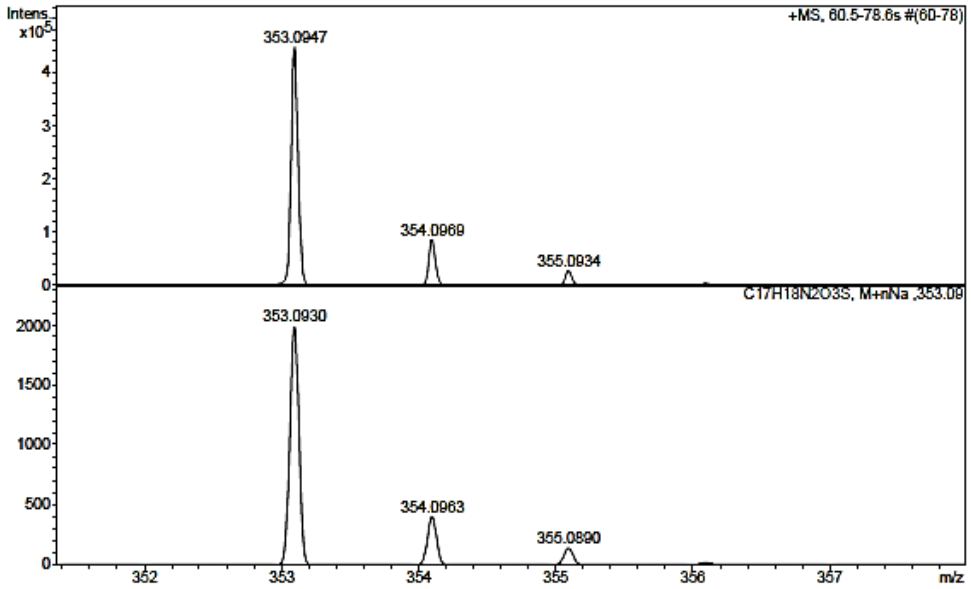
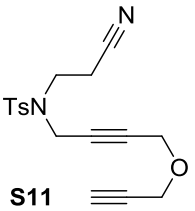


Figure S9: ESI-HRMS spectrum of **S11.**



S11

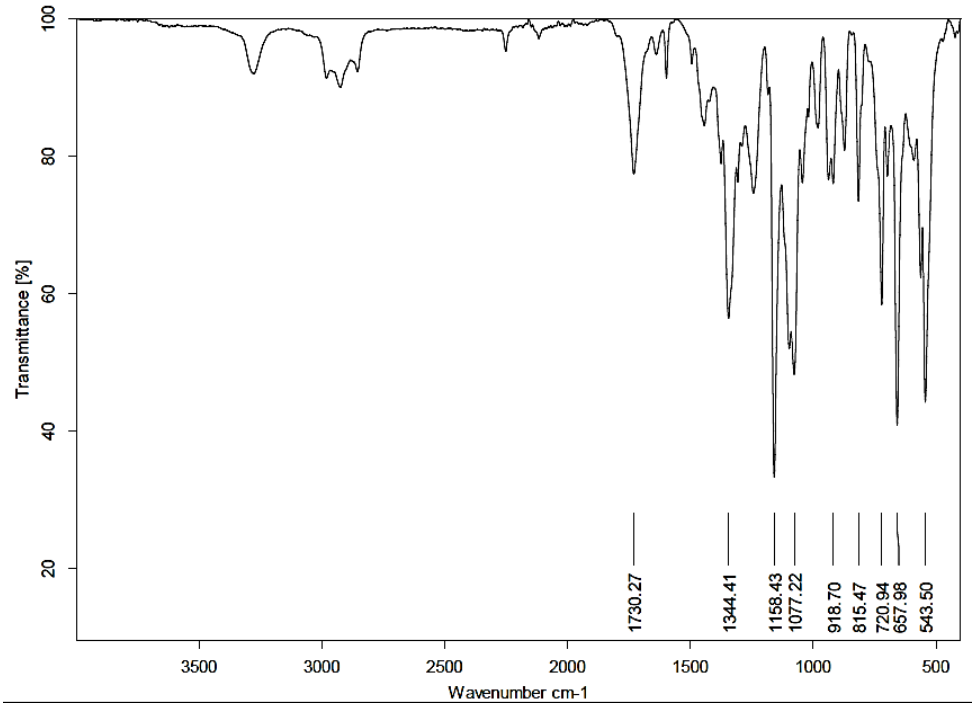
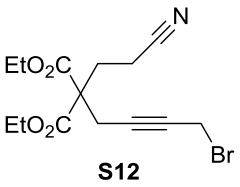


Figure S10: IR (ATR) spectrum of **S11.**



S12

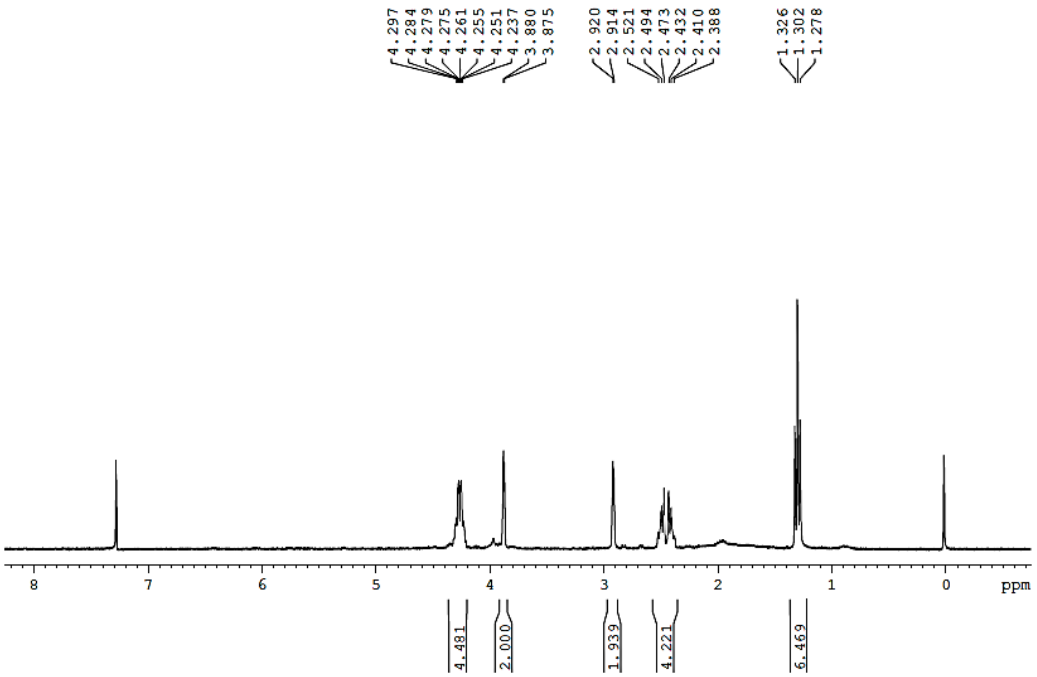
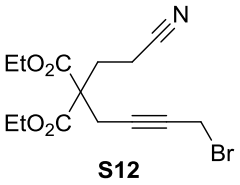


Figure S11: ^{1}H NMR spectrum (300 MHz) of **S12** in $CDCl_3$.



S12

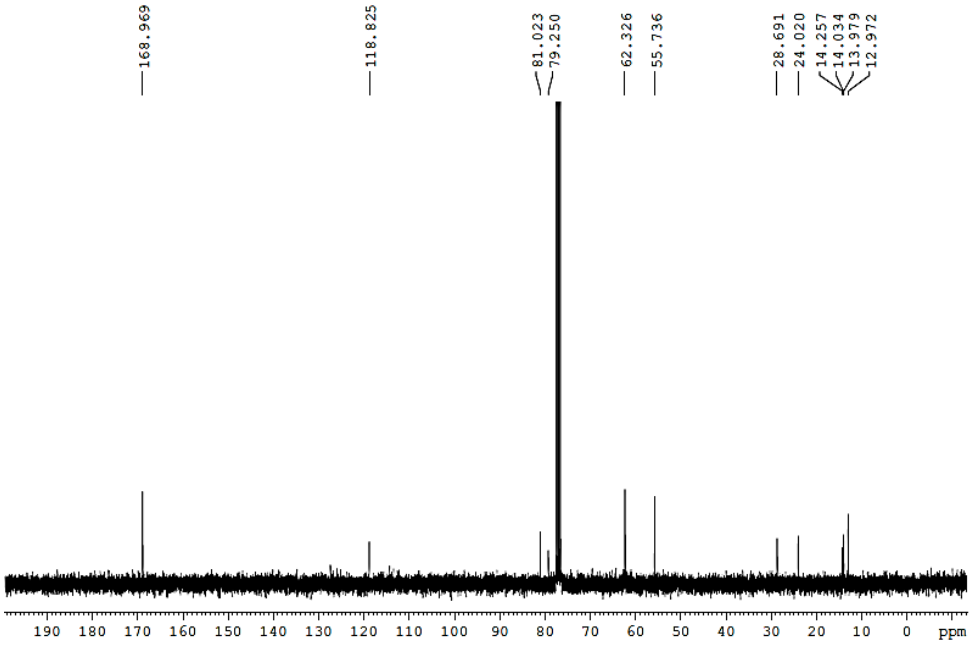
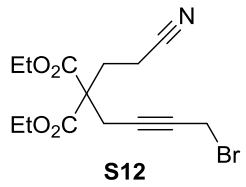


Figure S12: ^{1}H-decoupled ^{13}C NMR spectrum (75 MHz) of **S12** in $CDCl_3$.



S12

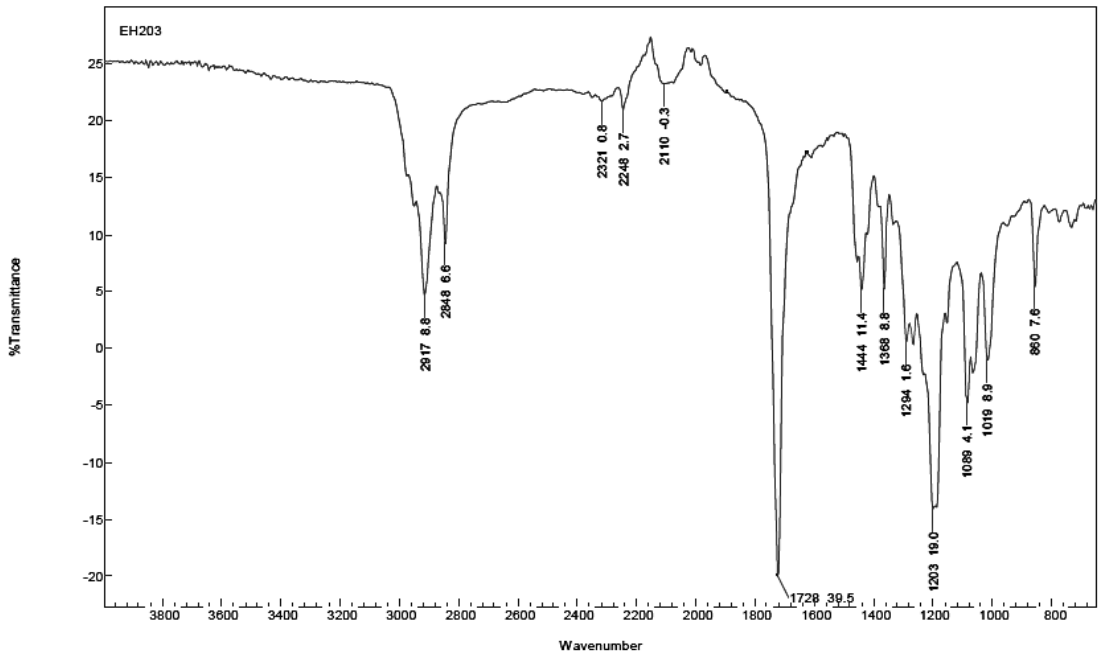
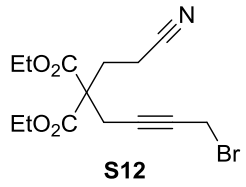


Figure S13: IR (ATR) spectrum of **S12.**



S12

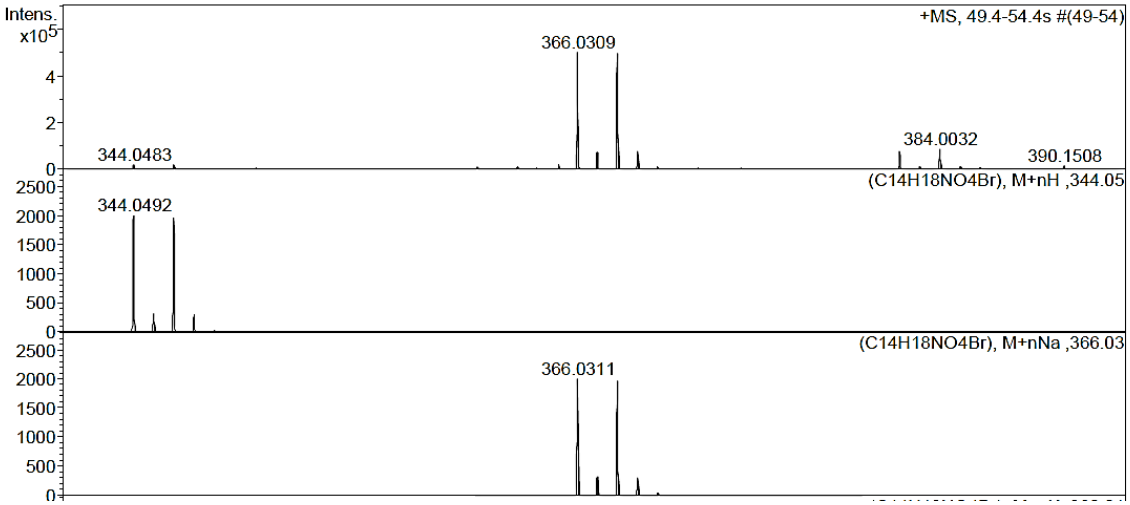
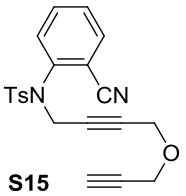


Figure S14: ESI-HRMS spectrum of **S12.**



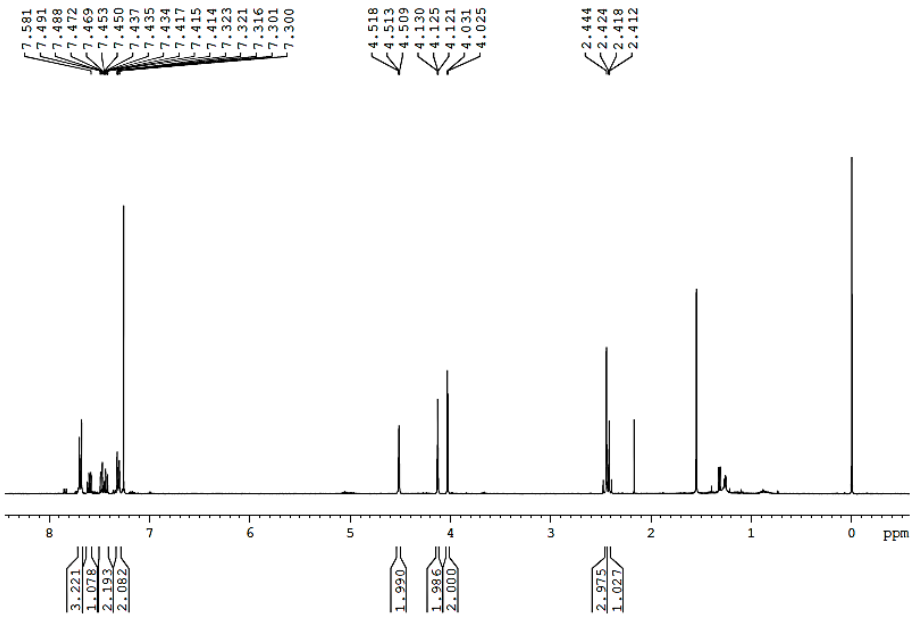
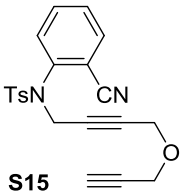


Figure S15: ^{1}H NMR spectrum (400 MHz) of **S15** in $CDCl_3$.



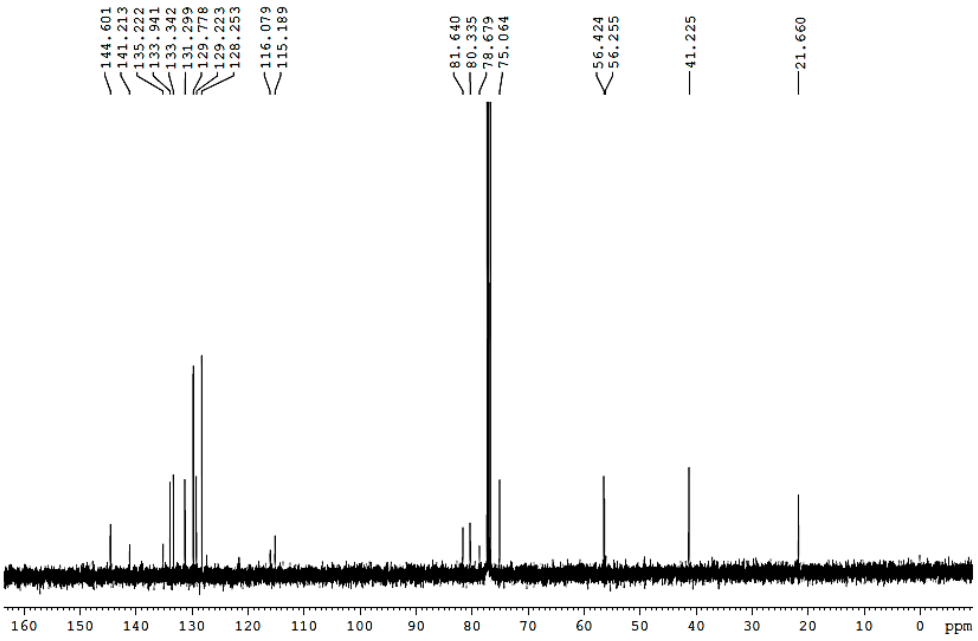
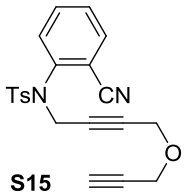


Figure S16: ^{1}H-decoupled ^{13}C NMR spectrum (100 MHz) of **S15** in $CDCl_3$.



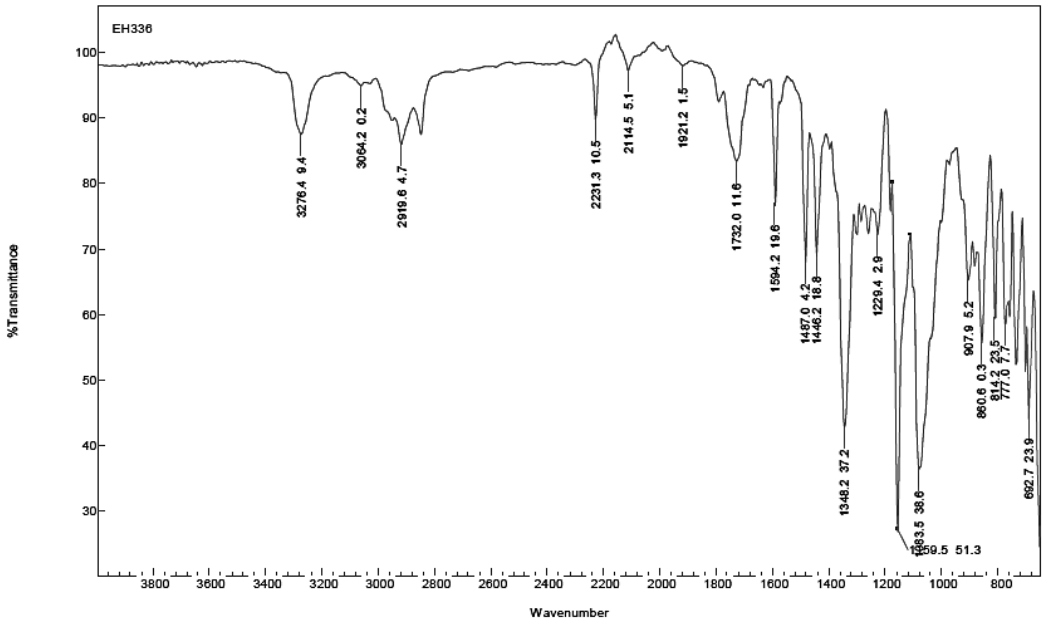
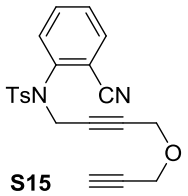


Figure S17: IR (ATR) spectrum of **S15.**



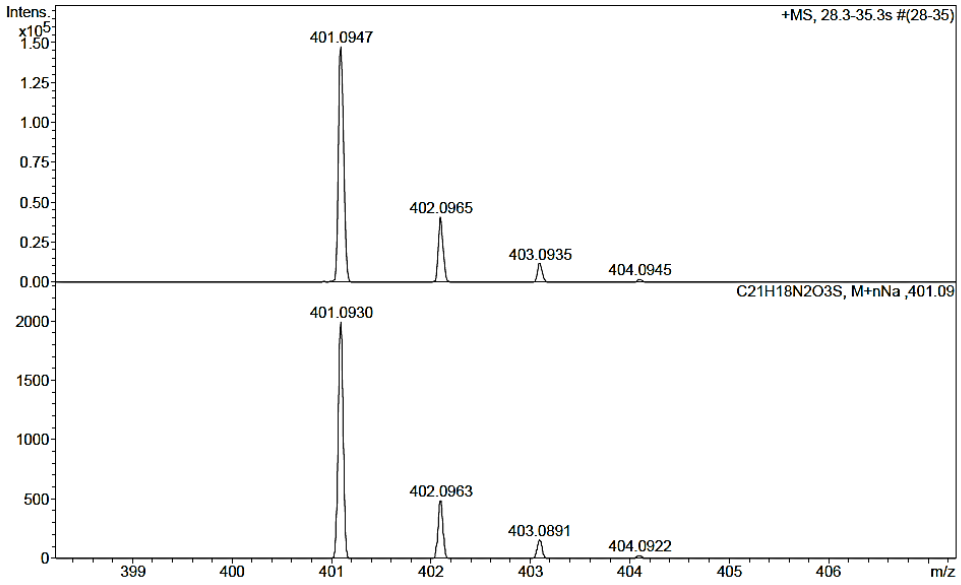
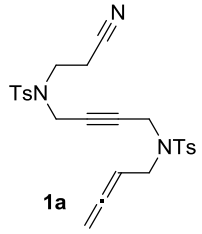


Figure S18: ESI-HRMS spectrum of **S15.**

Spectra of cyano-yne-allene substrates 1: 1a, 1b, 1c, 1d, 1e, 1f, 1g, and 1h.



1a

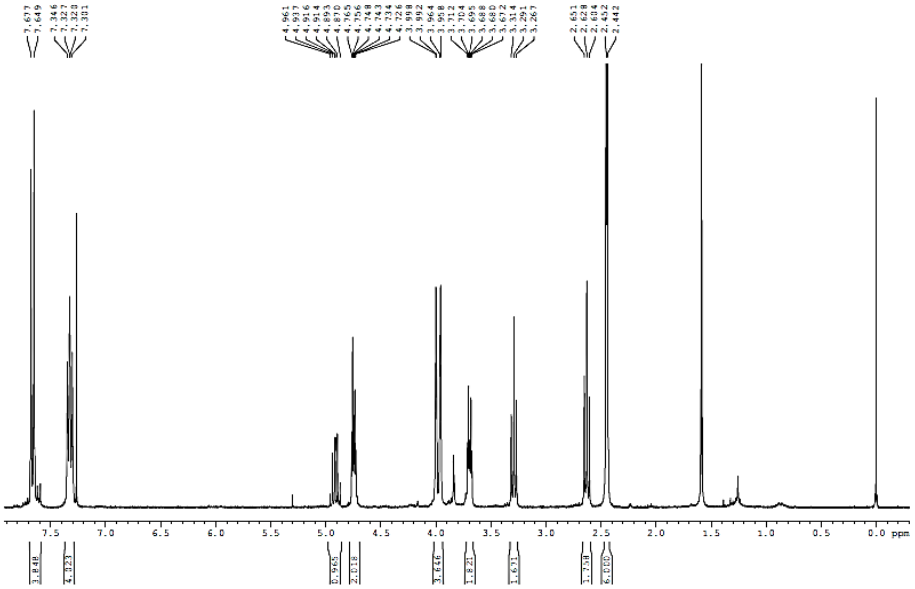
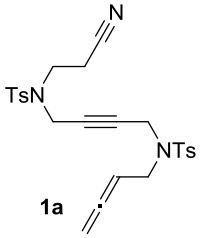


Figure S19: ^{1}H NMR spectrum (300 MHz) of **1a** in $CDCl_3$.



1a

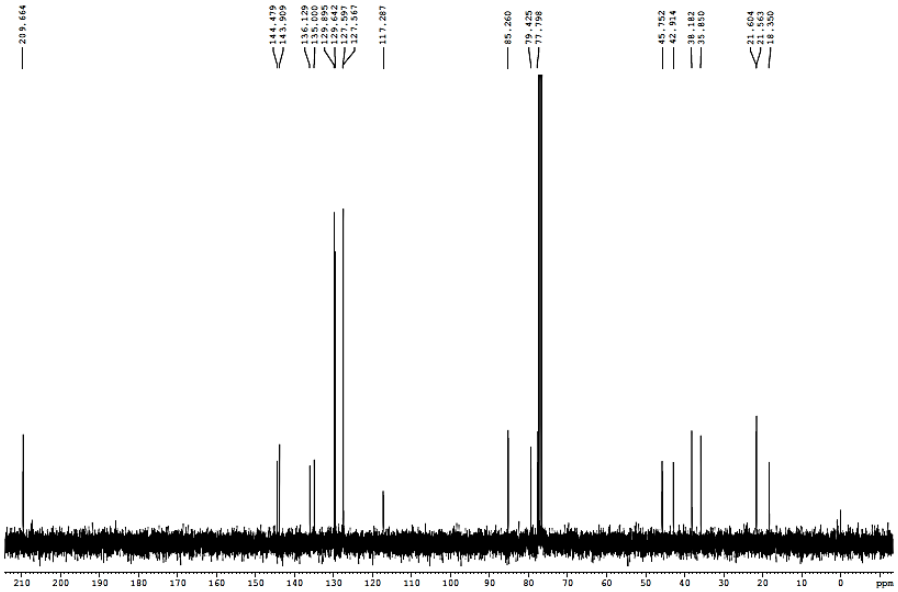


Figure S20: ^{1}H-decoupled ^{13}C NMR spectrum (75 MHz) of **1a** in $CDCl_3$.

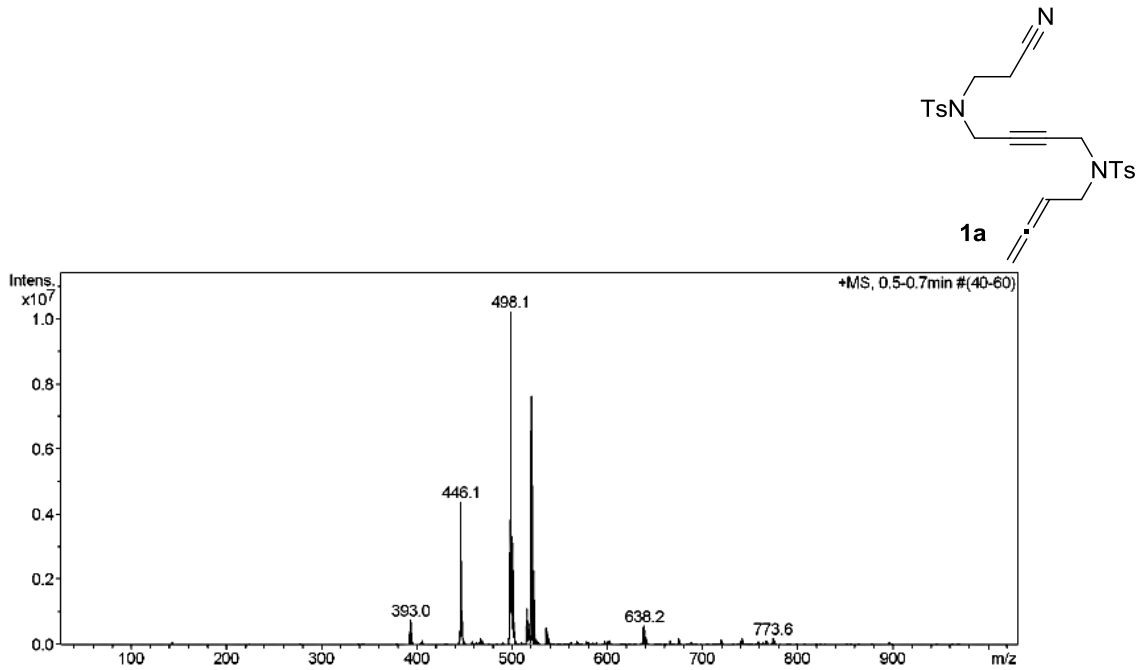


Figure S21: ESI-MS spectrum of **1a.**

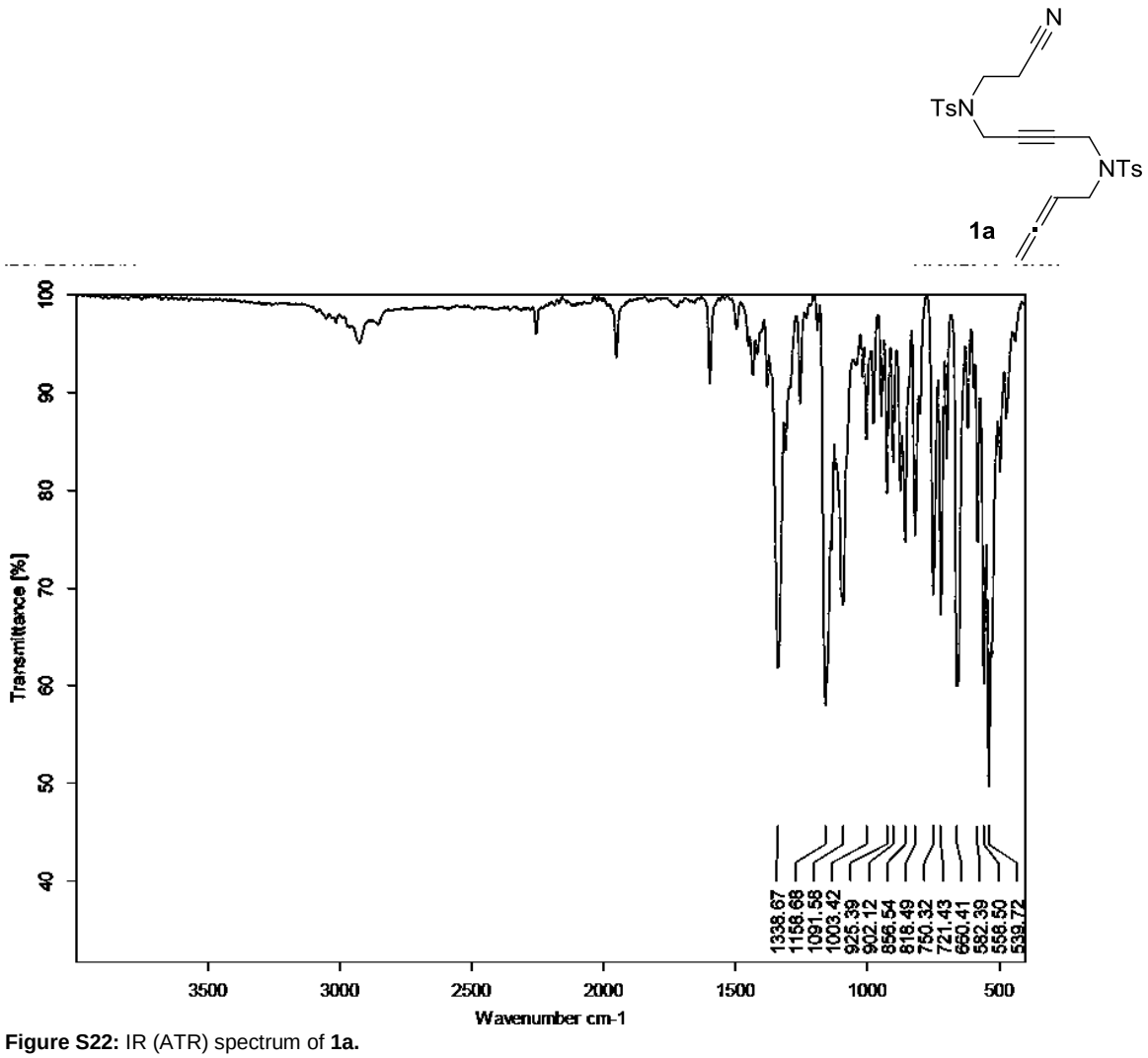


Figure S22: IR (ATR) spectrum of **1a.**

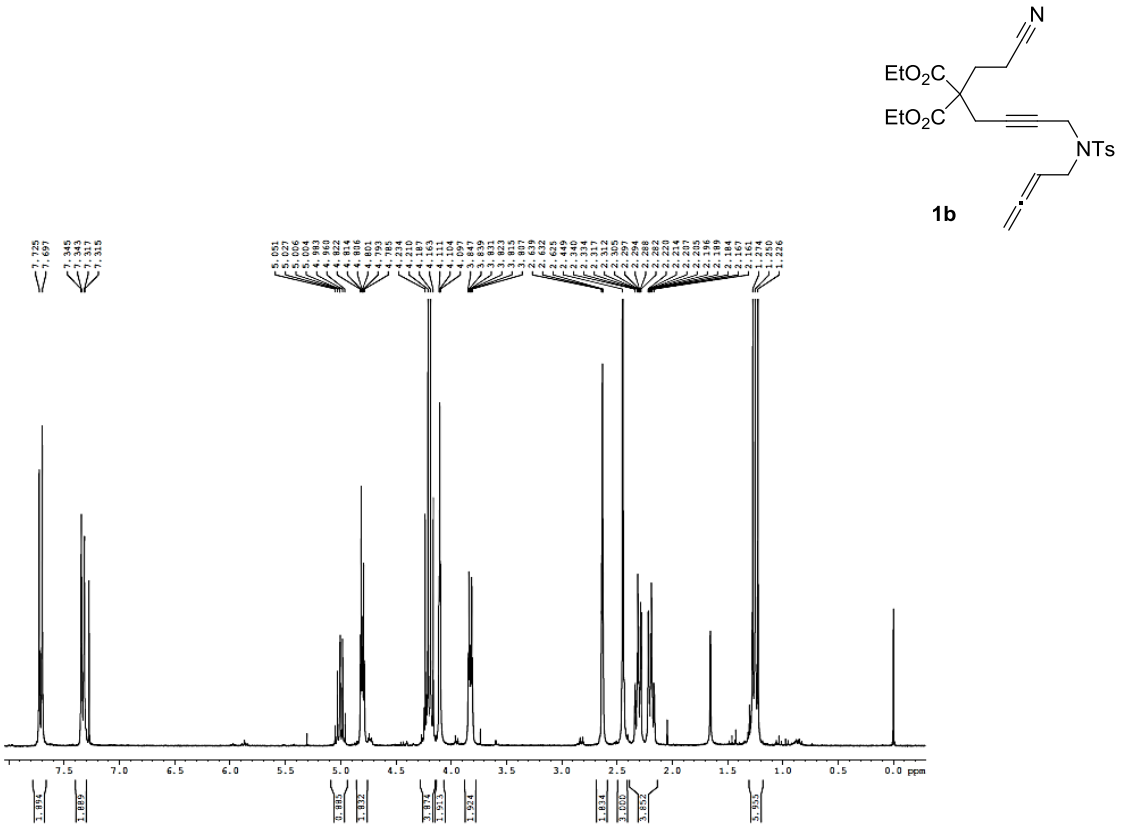


Figure S23: ^{1}H NMR spectrum (300 MHz) of **1b** in $CDCl_3$.

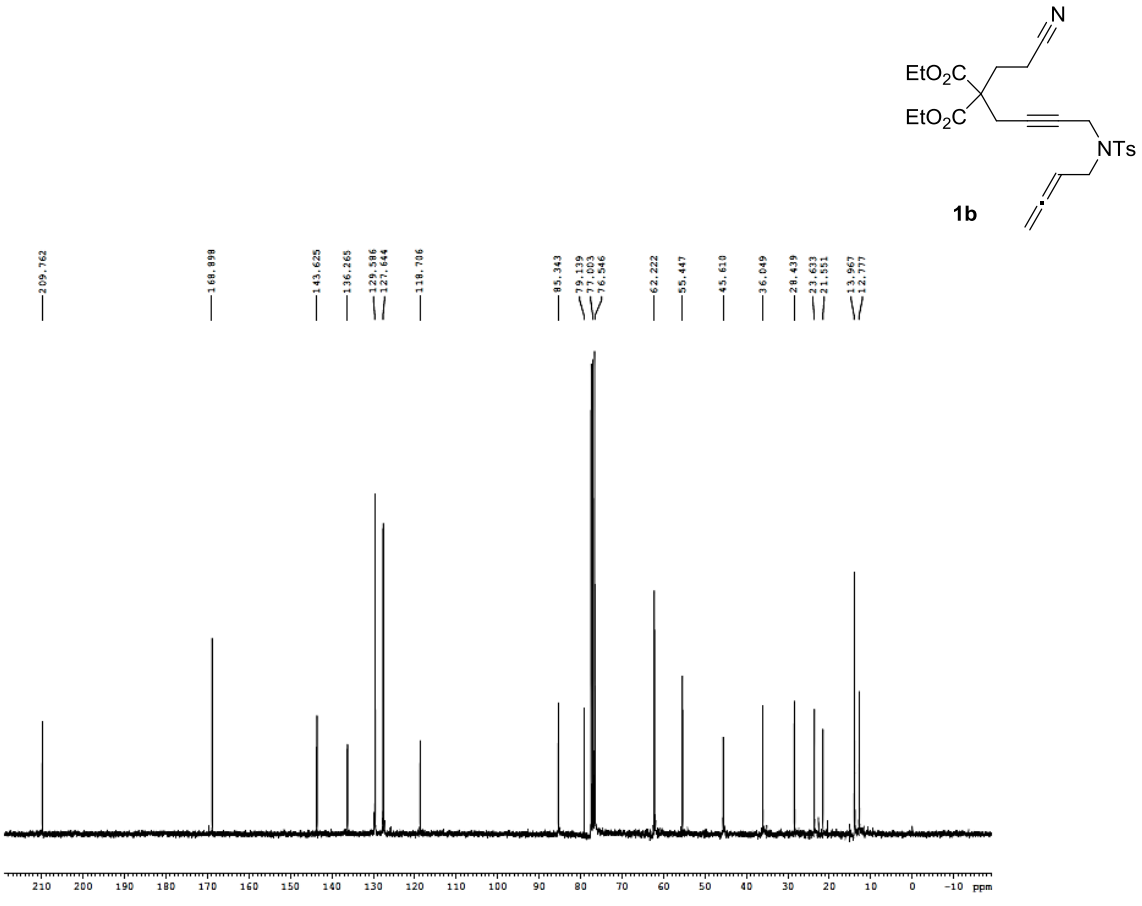


Figure S24: ^{1}H-decoupled ^{13}C NMR spectrum (75 MHz) of **1b** in $CDCl_3$.

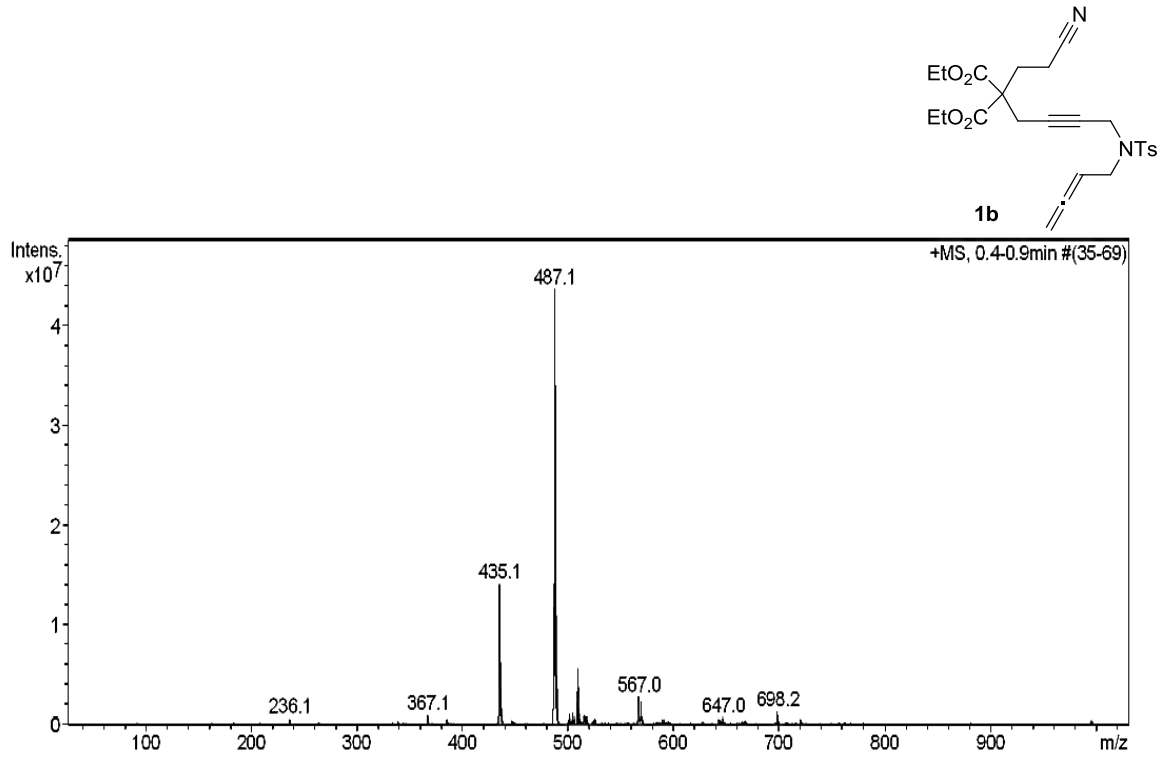


Figure S25: ESI-MS spectrum of **1b.**

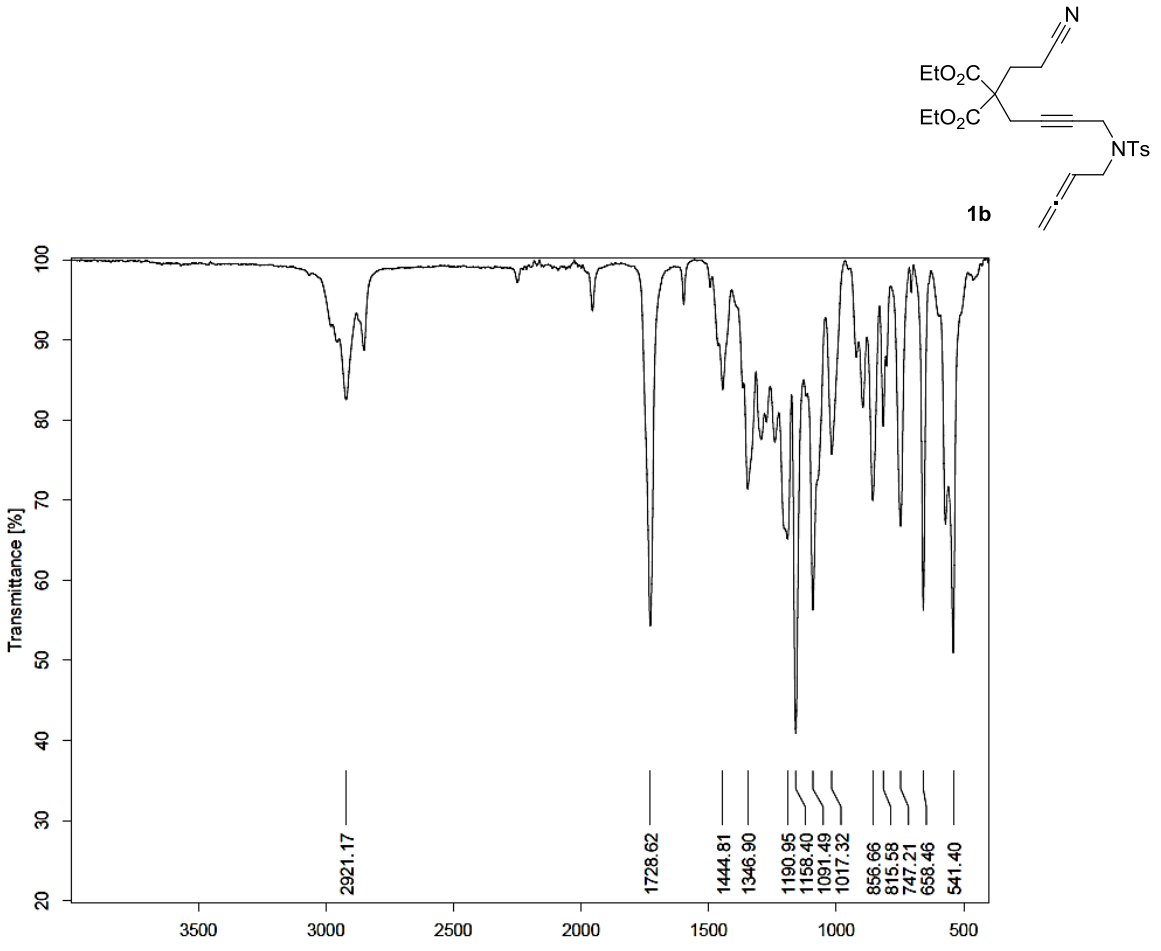
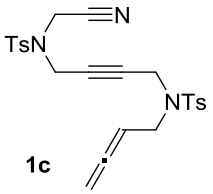


Figure S26: IR (ATR) spectrum of **1b.**



1c

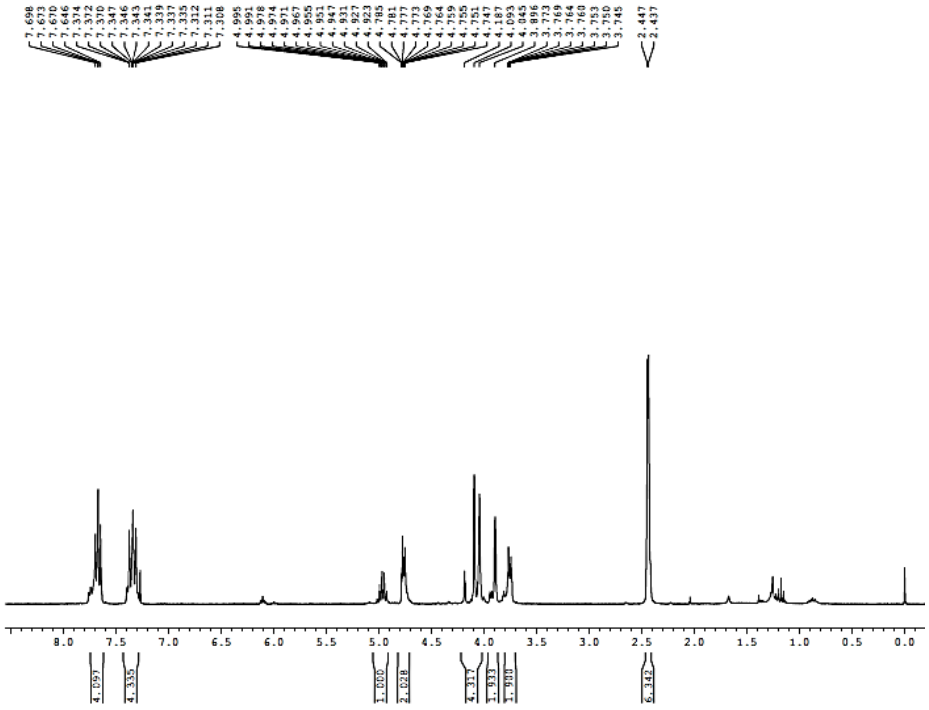
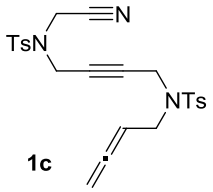


Figure S27: ^{1}H NMR spectrum (300 MHz) of **1c** in $CDCl_3$.



1c

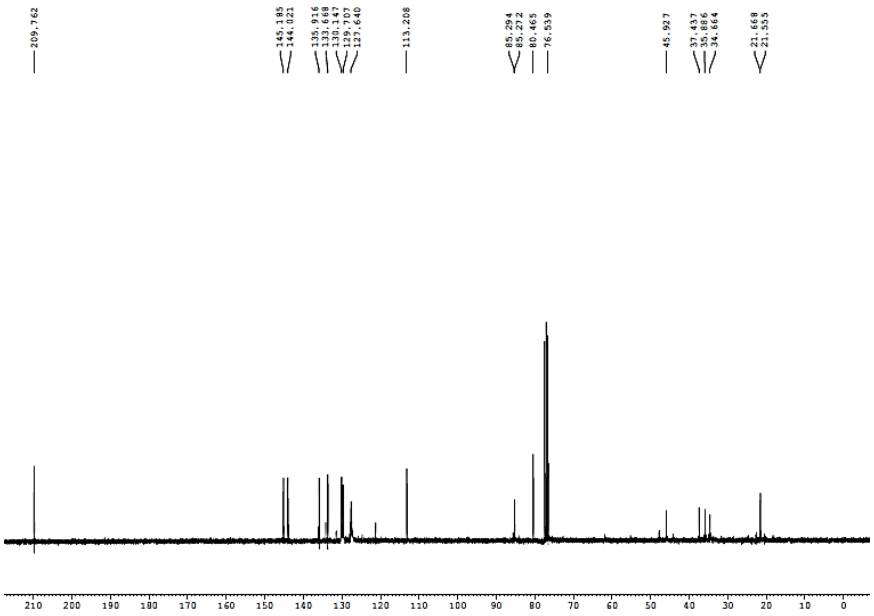
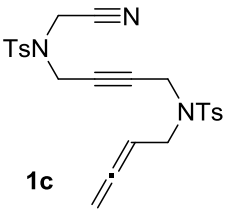


Figure S28: ^{1}H-decoupled ^{13}C NMR spectrum (75 MHz) of **1c** in $CDCl_3$.



1c

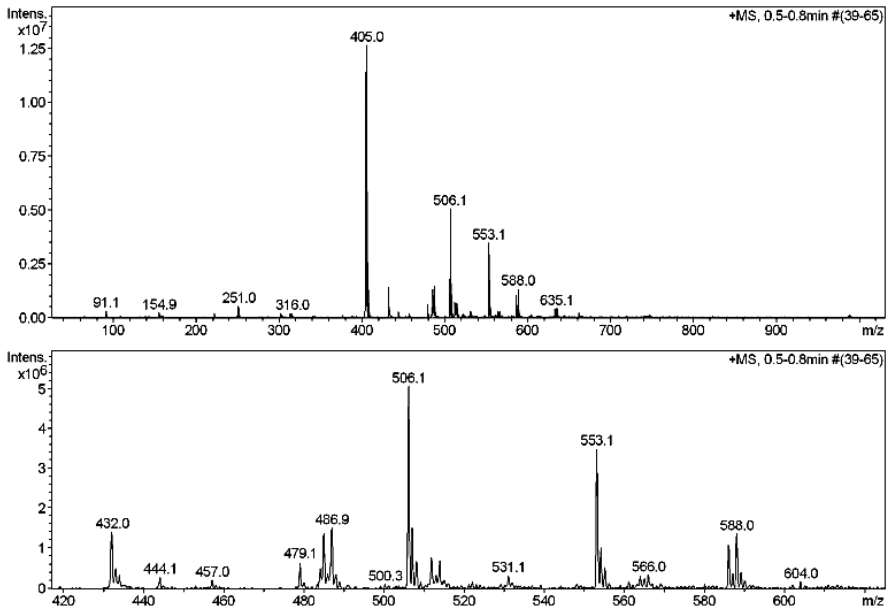
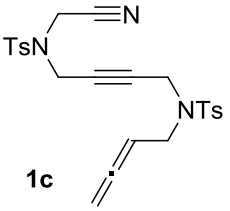


Figure S29: ESI-MS spectrum of **1c.**



1c

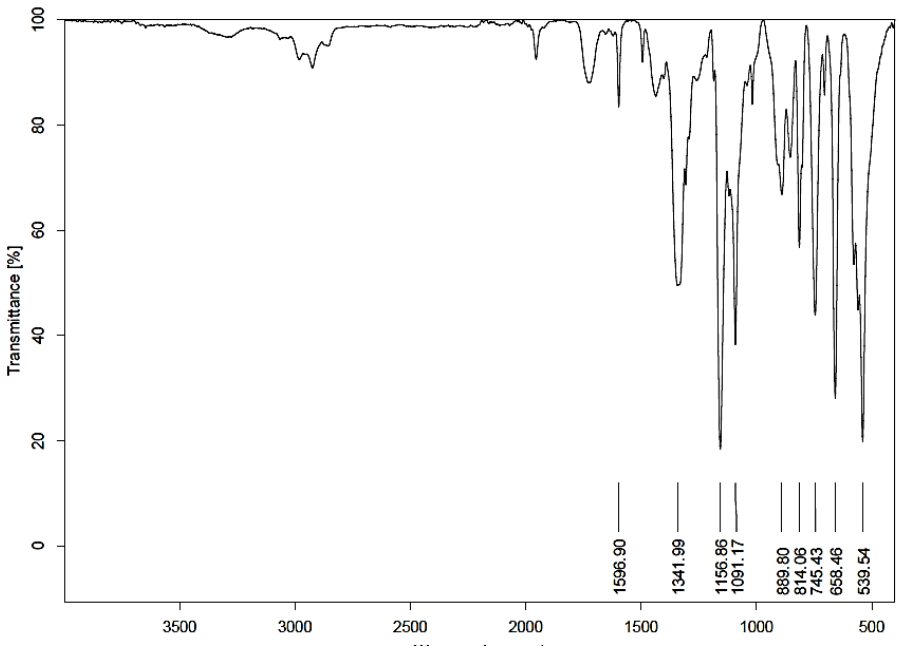
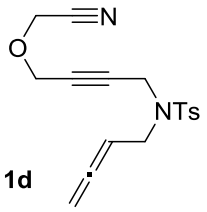


Figure S30: IR (ATR) spectrum of **1c.**



1d

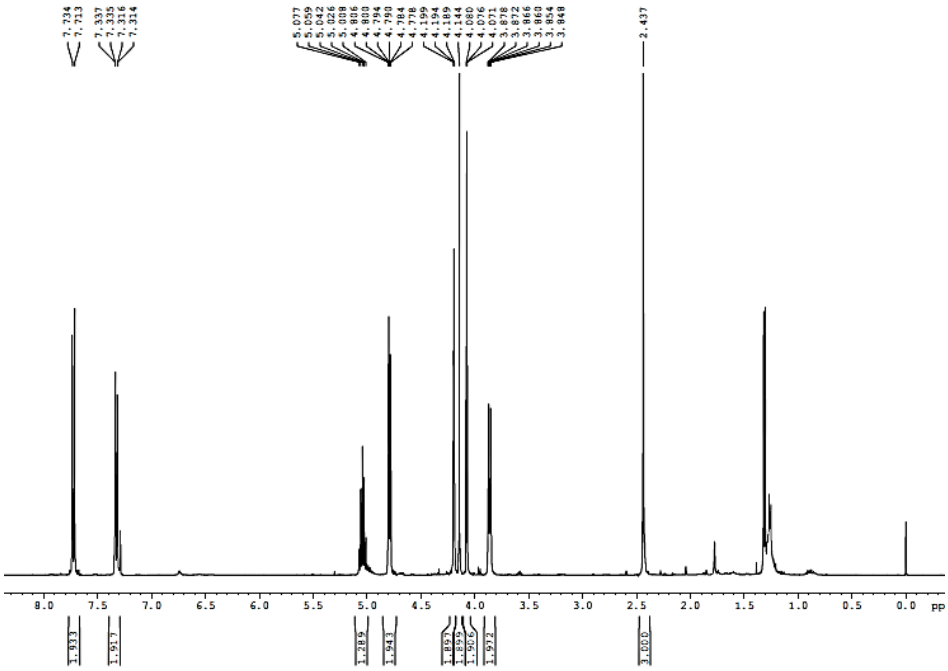
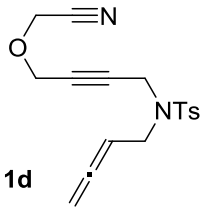


Figure S31: ^{1}H NMR spectrum (400 MHz) of **1d** in $CDCl_3$.



1d

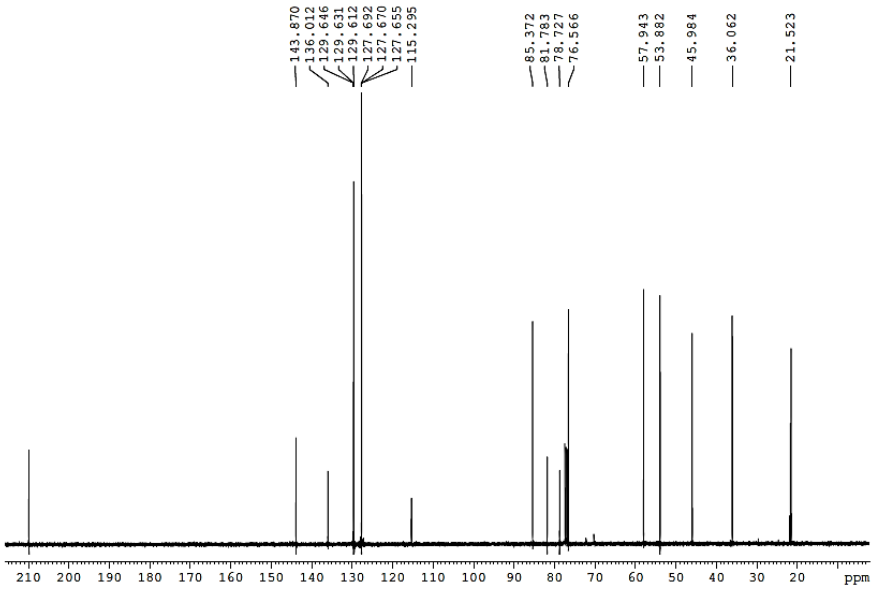
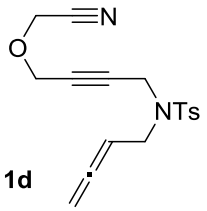


Figure S32: ^{1}H-decoupled ^{13}C NMR spectrum (100 MHz) of **1d** in $CDCl_3$.



1d

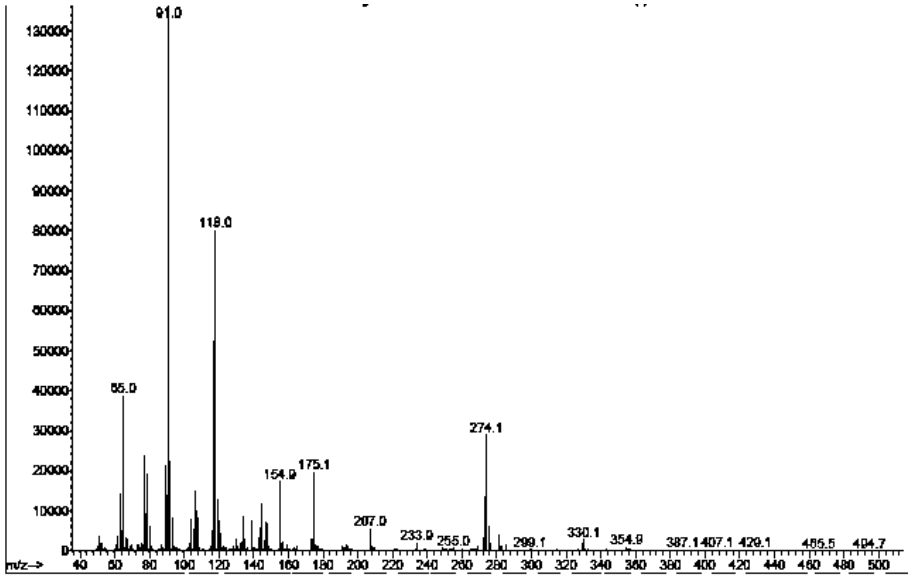
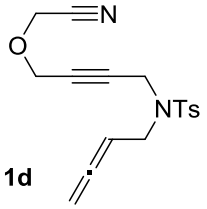


Figure S33: GC-MS spectrum of **1d.**



1d

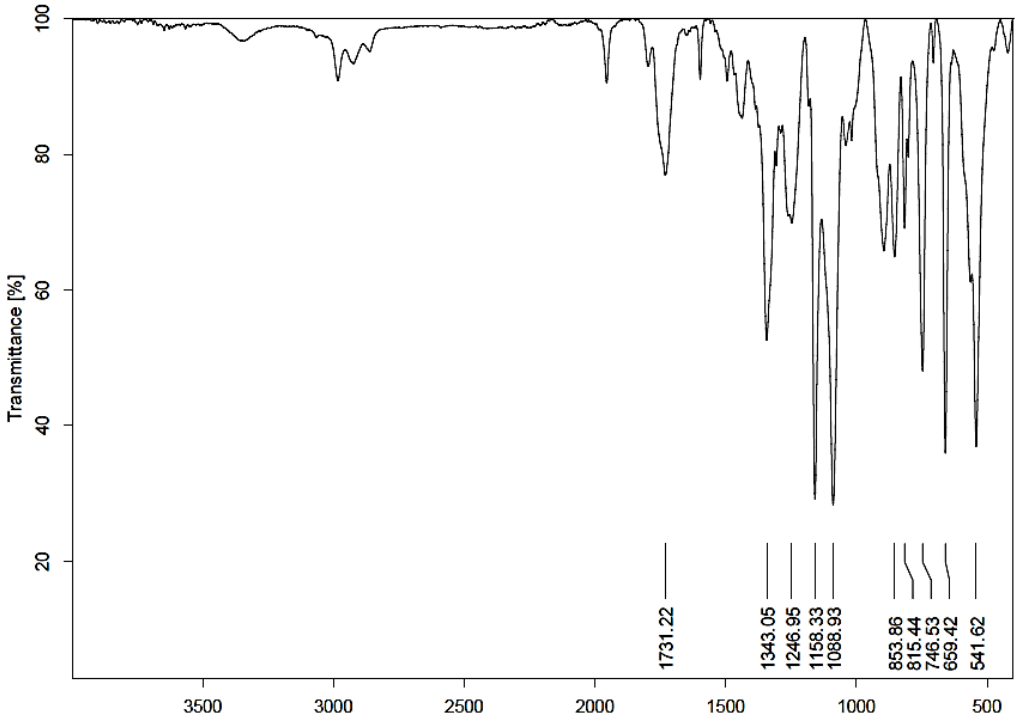
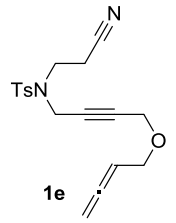


Figure S34: IR (ATR) spectrum of **1d**



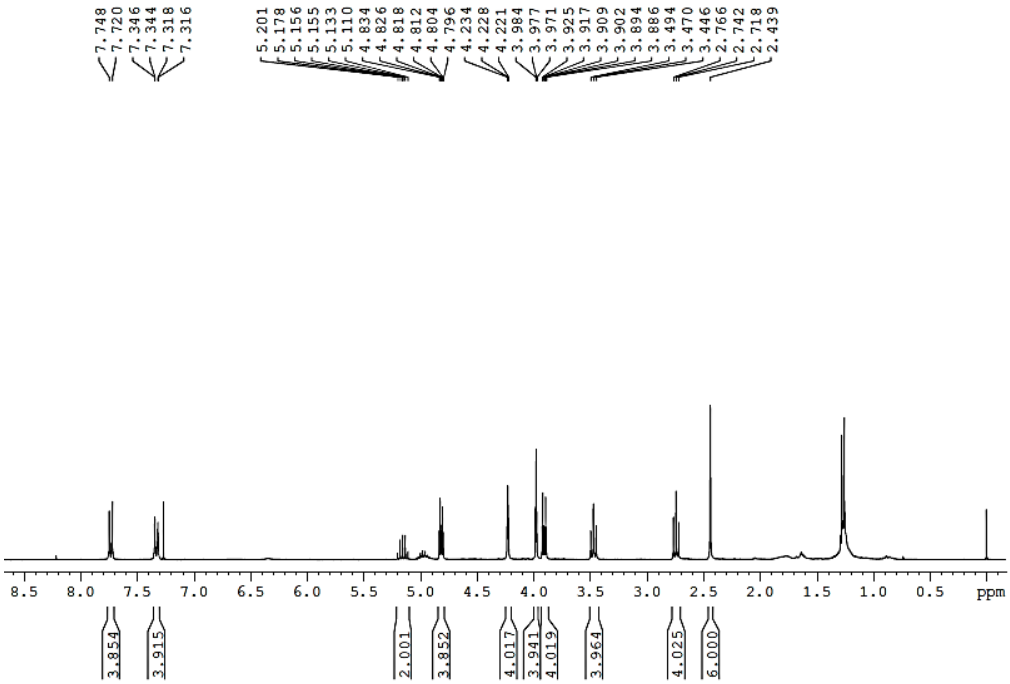
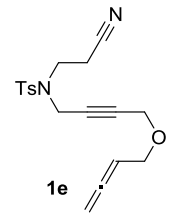


Figure S35: ^{1}H NMR spectrum (300 MHz) of **1e** in $CDCl_3$.



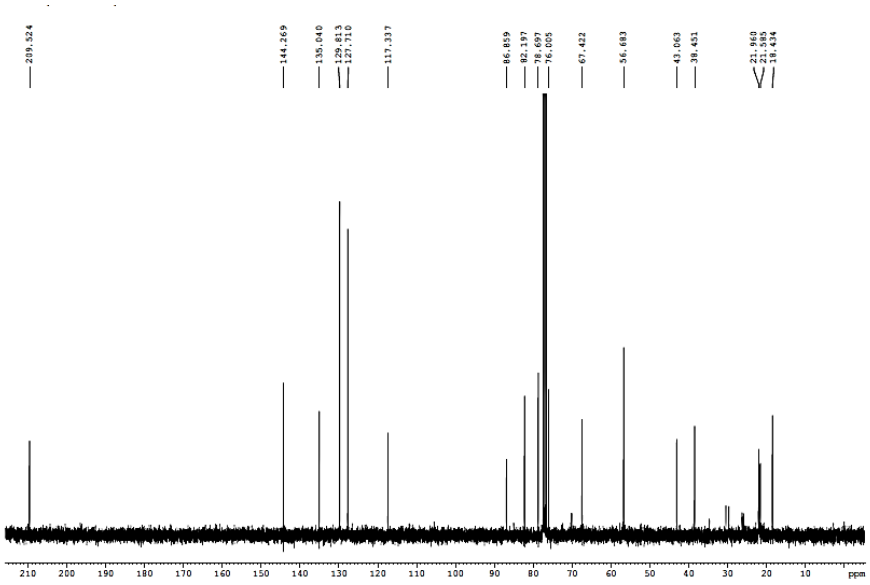
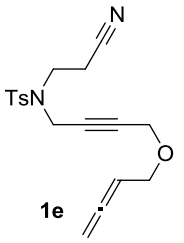


Figure S36: ^{1}H-decoupled ^{13}C NMR spectrum (75 MHz) of **1e** in $CDCl_3$.



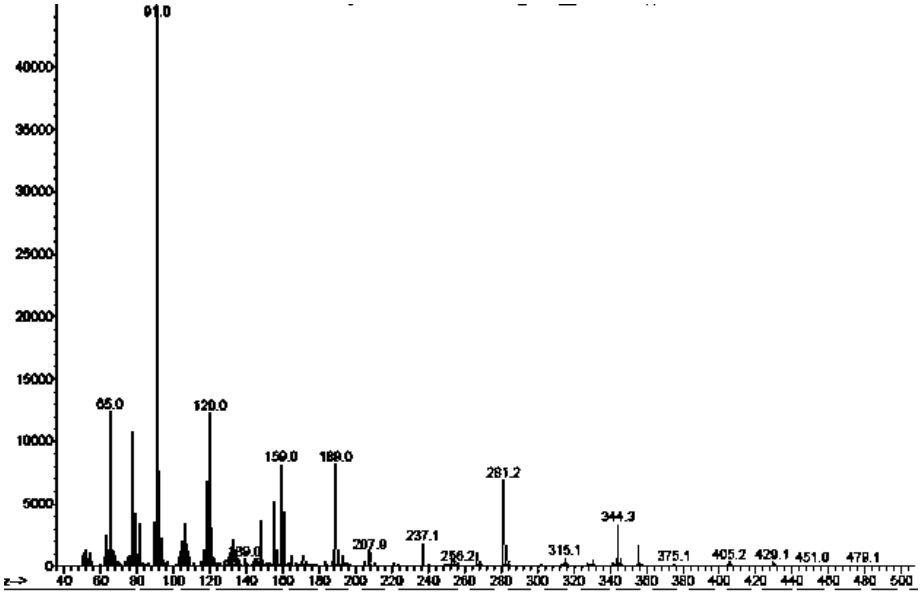
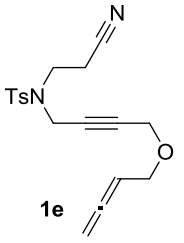


Figure S37: GC-MS spectrum of **1e.**



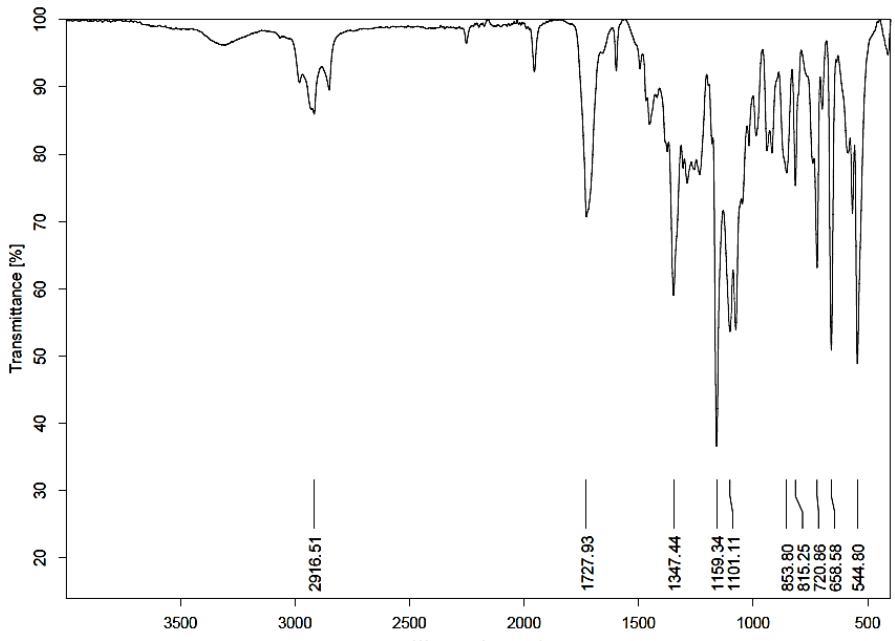


Figure S38: IR (ATR) spectrum of **1e.**

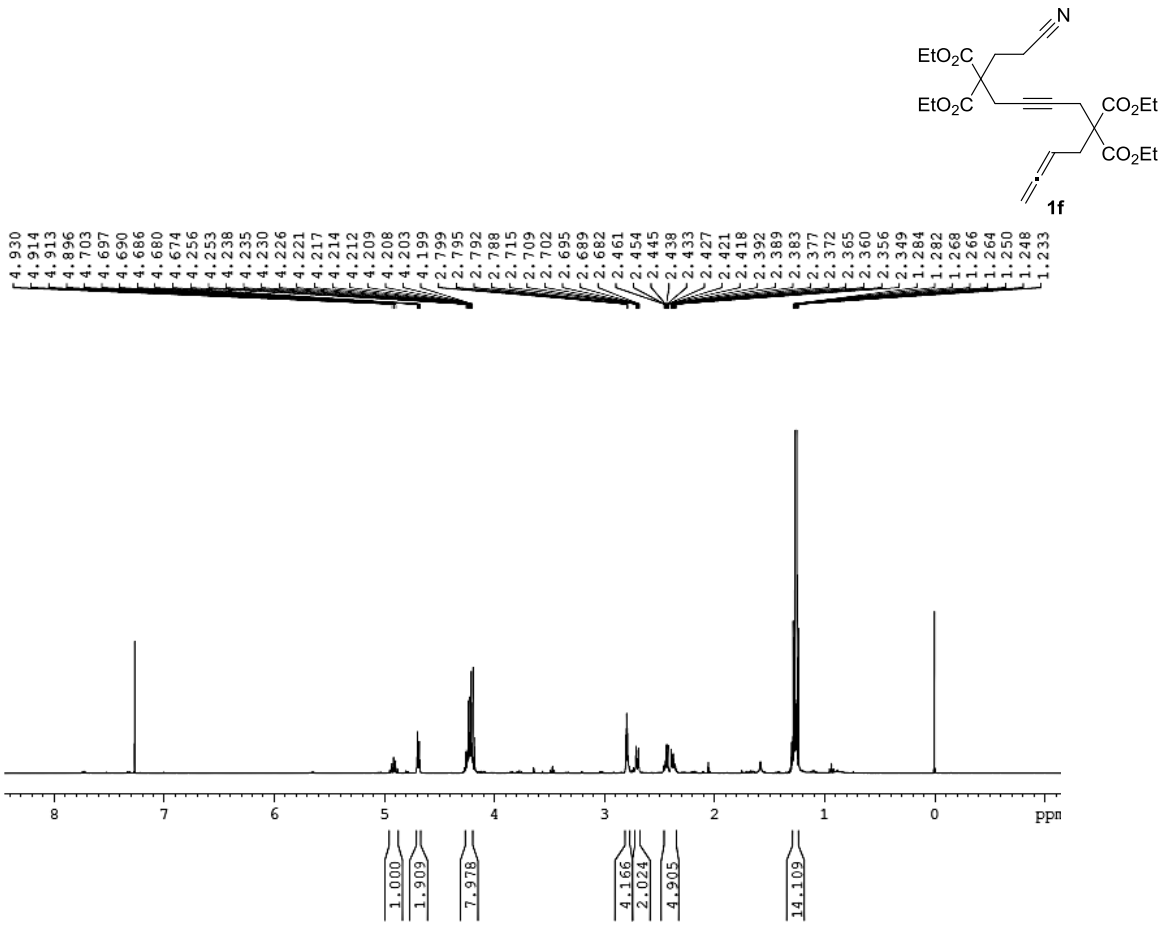


Figure S39: ^{1}H NMR spectrum (400 MHz) of **1f** in $CDCl_3$.

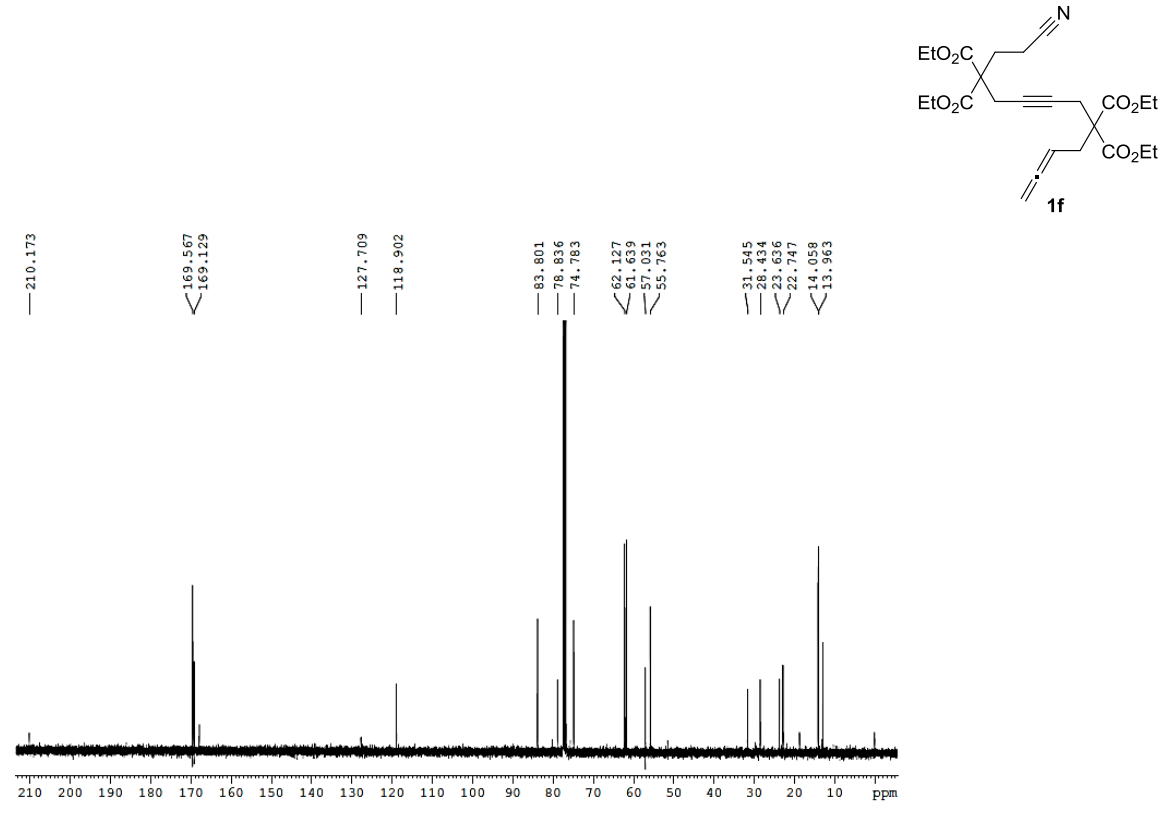
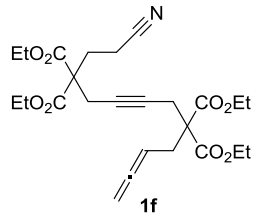


Figure S40: ^{1}H-decoupled ^{13}C NMR spectrum (100 MHz) of **1f** in $CDCl_3$.



1f

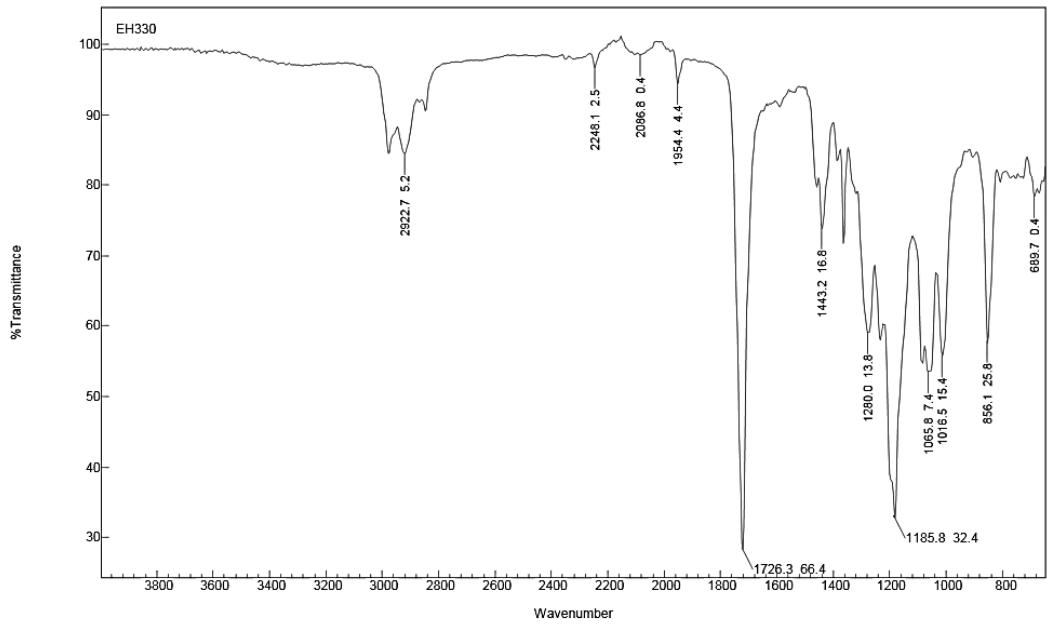
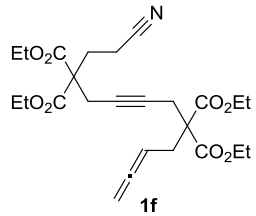


Figure S41: IR (ATR) spectrum of **1f.**



1f

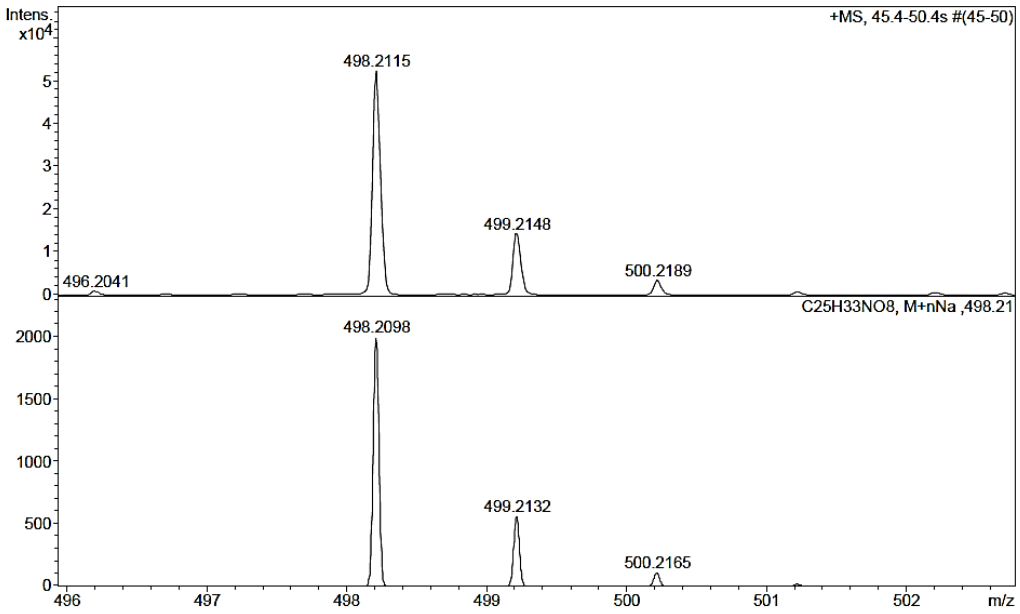
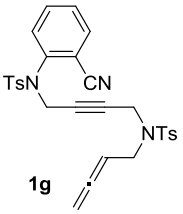


Figure S41: ESI-HRMS spectrum of **1f.**



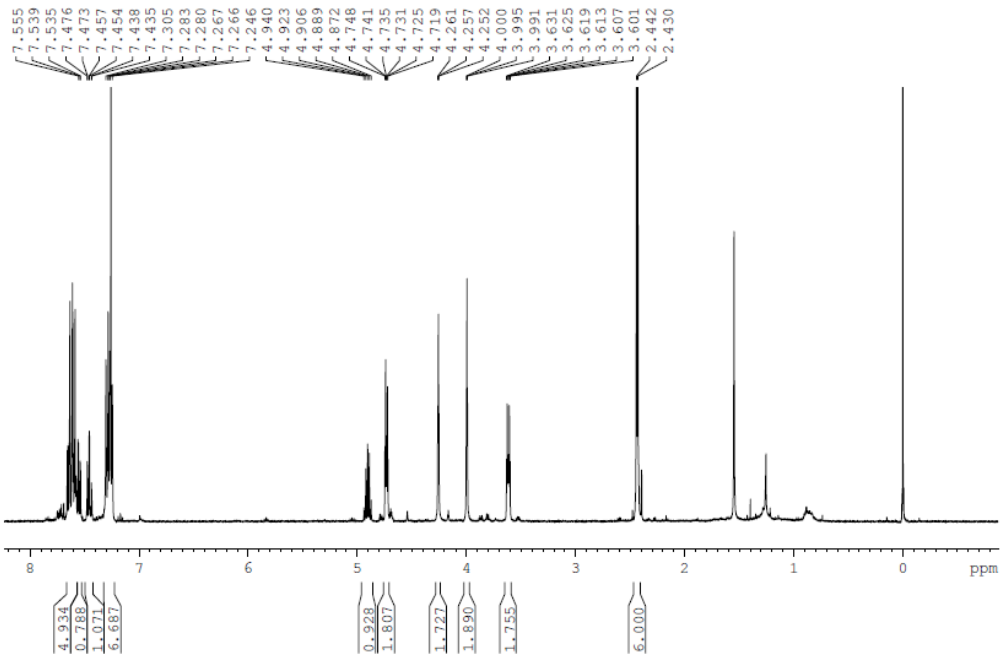
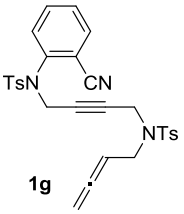


Figure S43: ^{1}H NMR spectrum (400 MHz) of **1g** in $CDCl_3$.



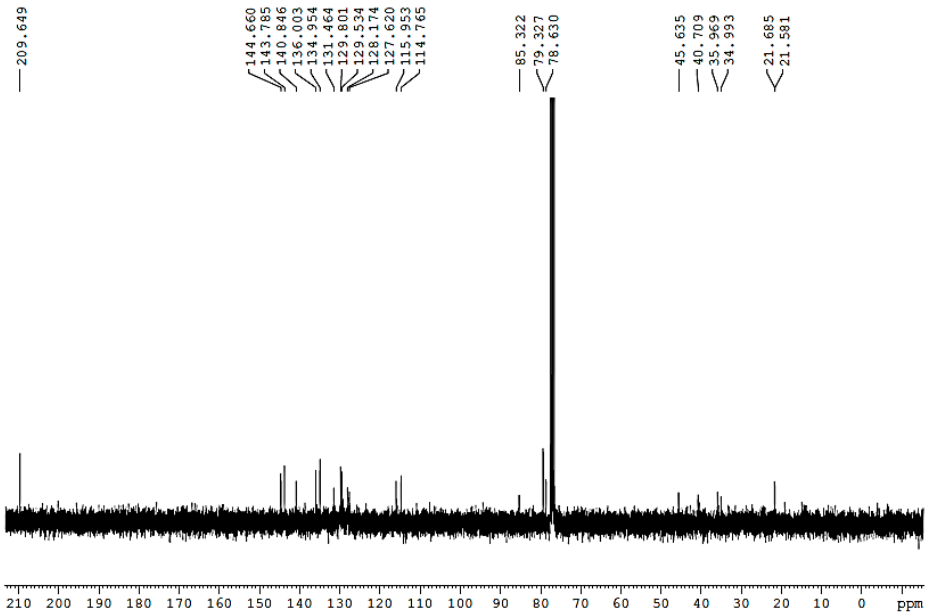


Figure S44: ^{1}H-decoupled ^{13}C NMR spectrum (75 MHz) of **1g** in $CDCl_3$.

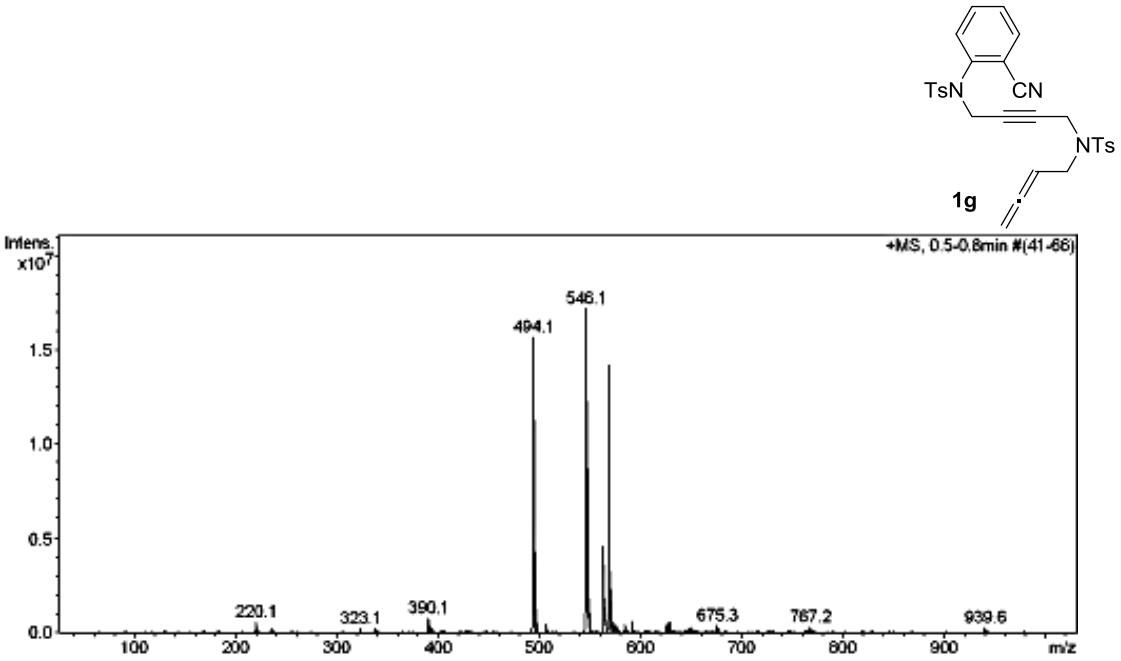


Figure S45: ESI-MS spectrum of **1g.**

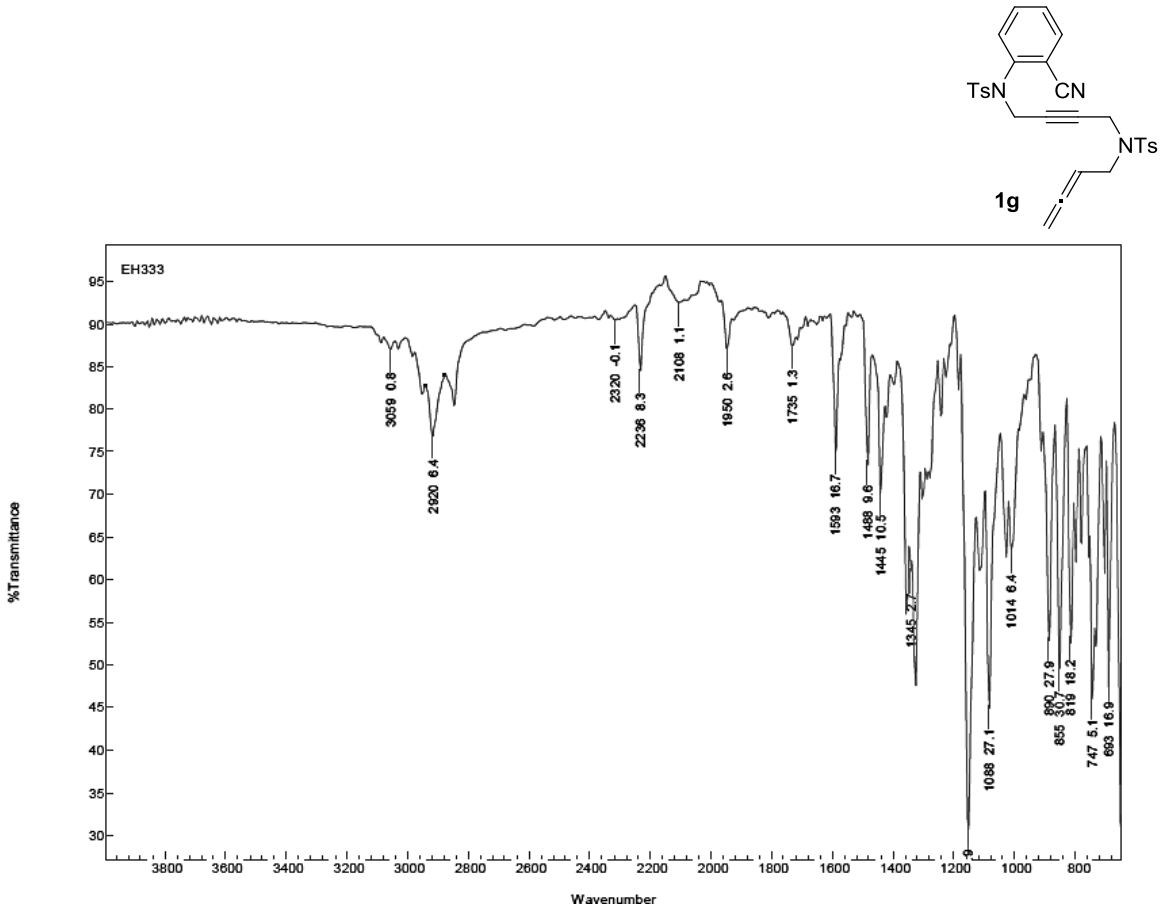
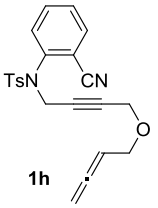


Figure S46: IR (ATR) spectrum of **1g.**



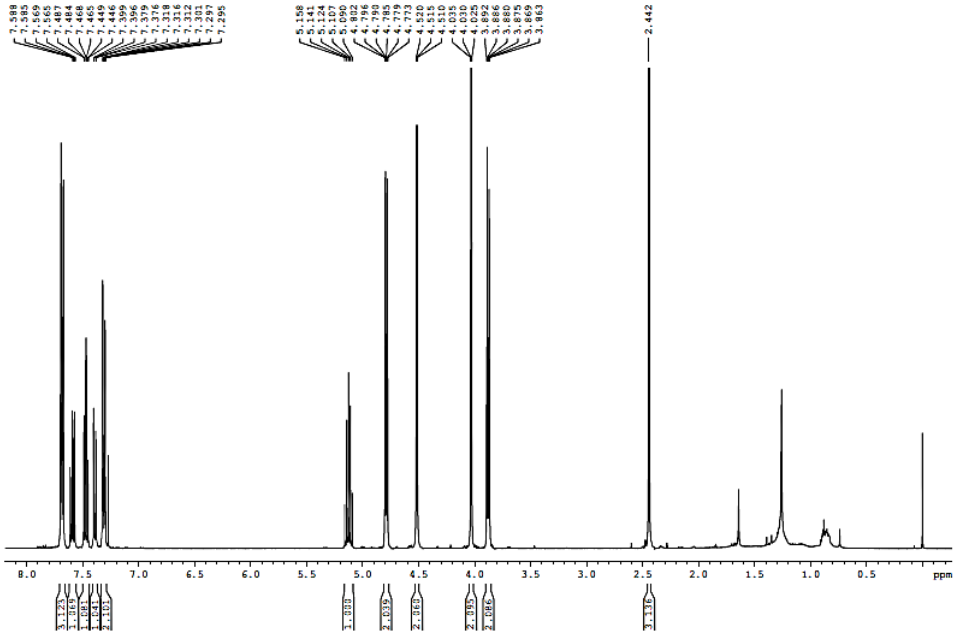
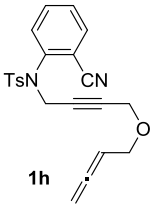


Figure S47: ^{1}H NMR spectrum (400MHz) of **1h** in $CDCl_3$.



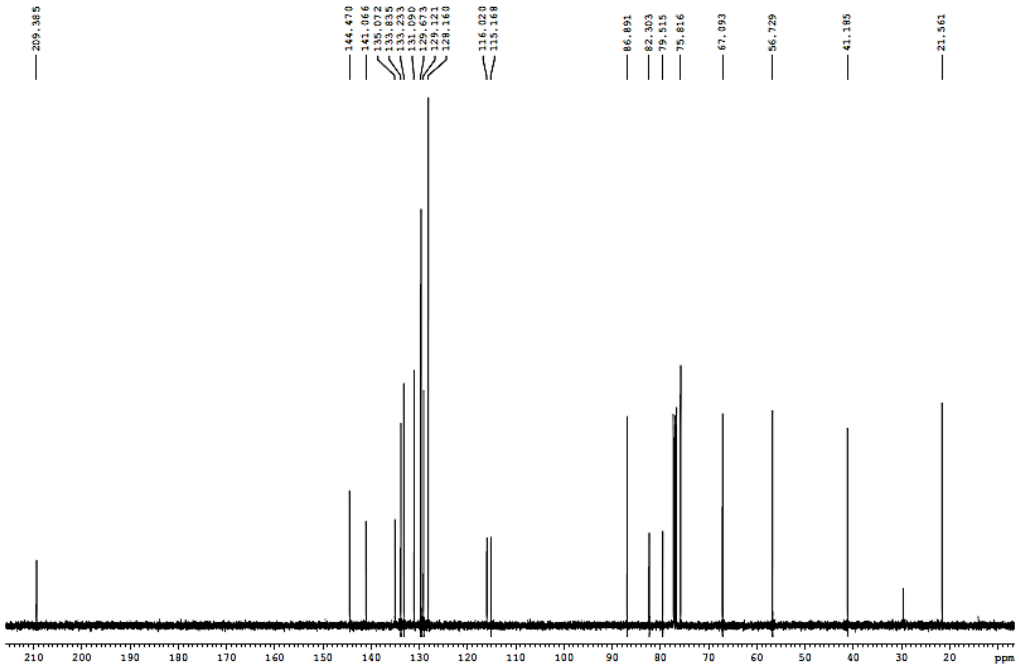


Figure S48: ^{1}H-decoupled ^{13}C NMR spectrum (100 MHz) of **1h** in $CDCl_3$.

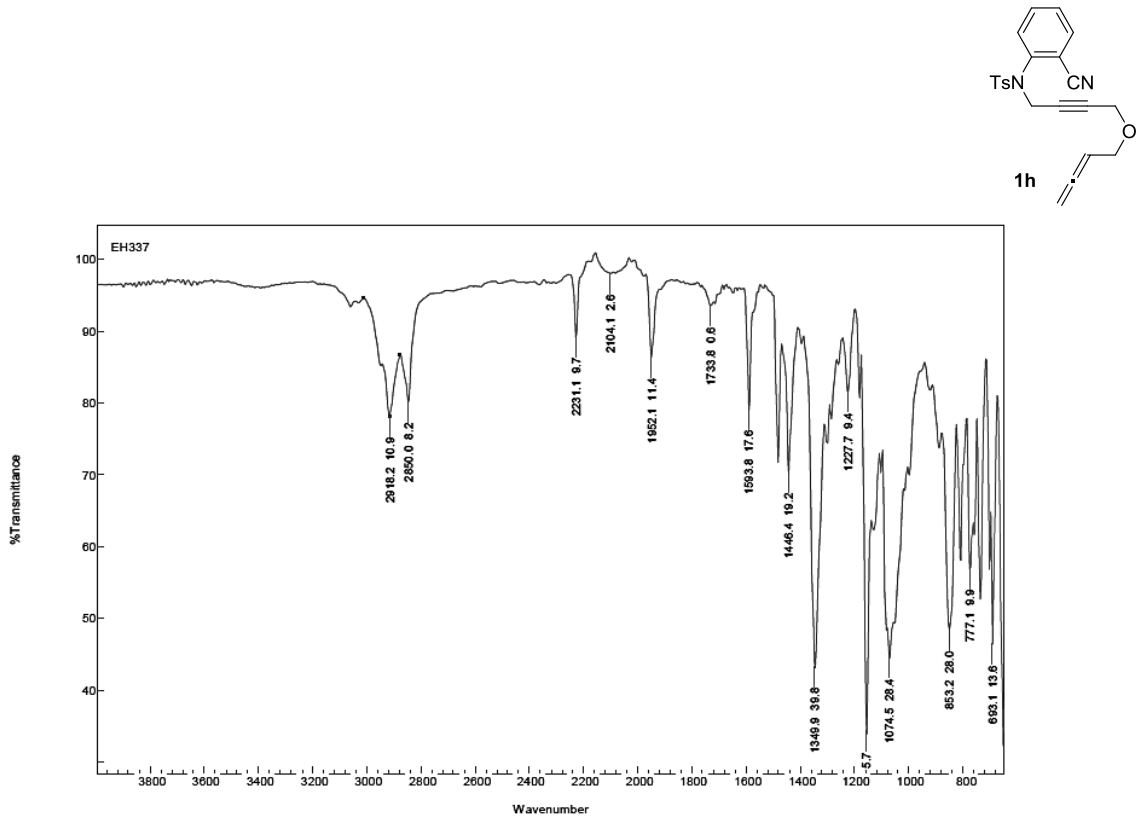


Figure S49: IR (ATR) spectrum of **1h.**

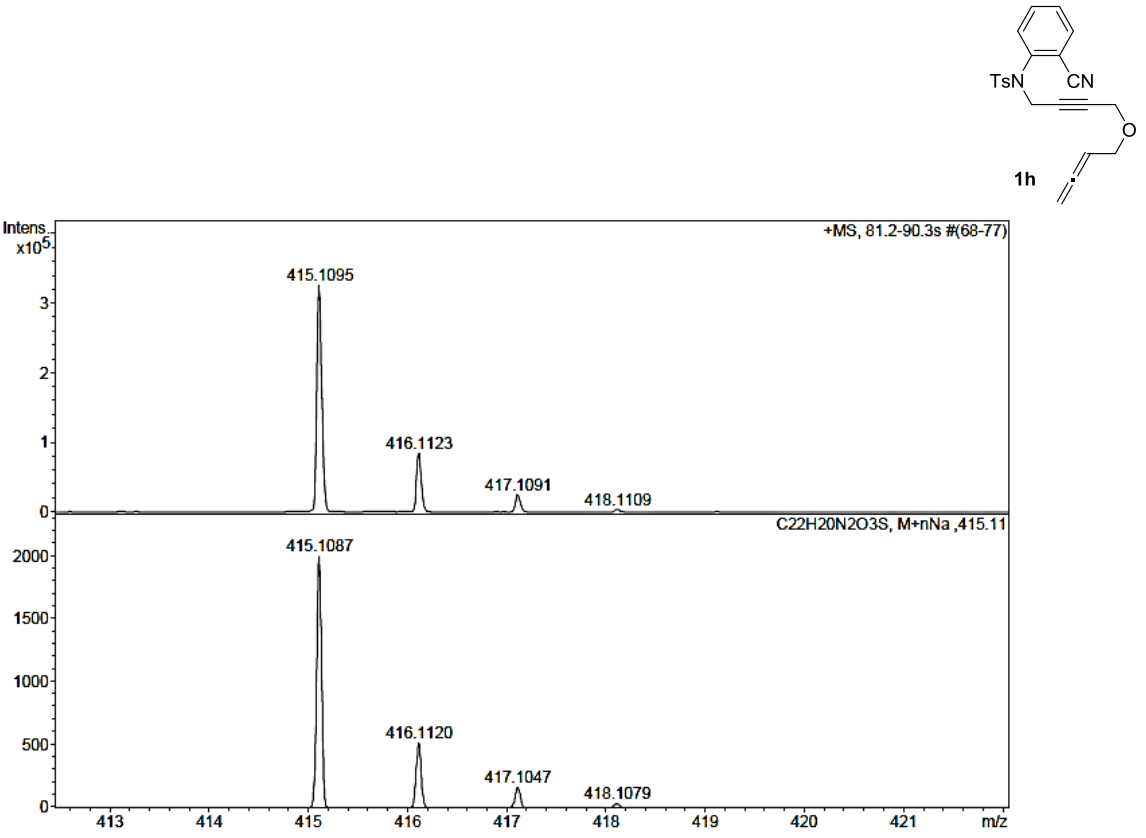
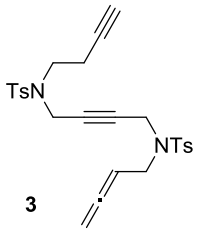


Figure S50: ESI-HRMS spectrum of **1h.**

Spectra of allene-yne-yne derivative 3



3

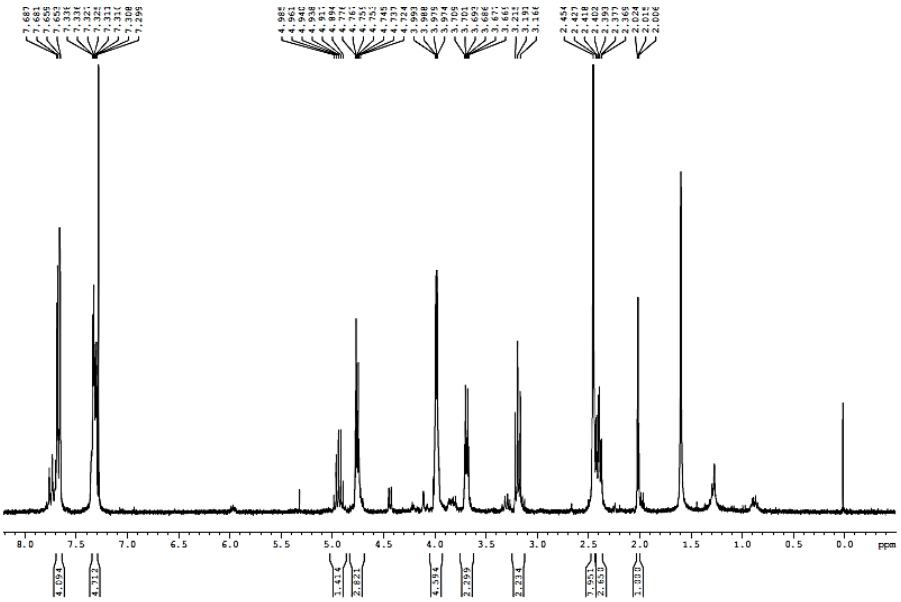
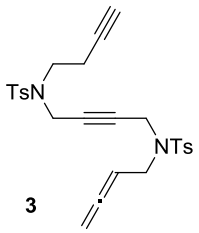


Figure S51: ^{1}H NMR spectrum (400 MHz) of **3** in $CDCl_3$.



3

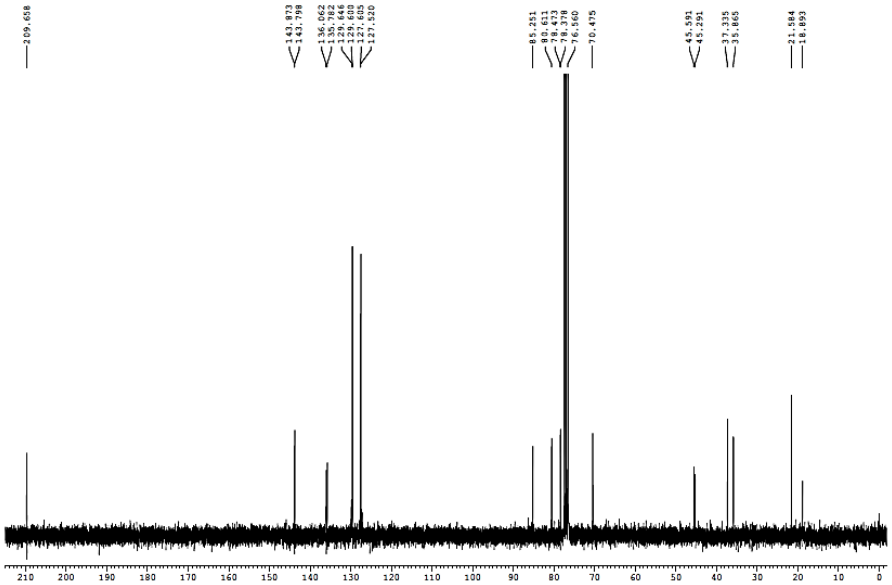


Figure S52: ^{1}H-decoupled ^{13}C NMR spectrum (75 MHz) of **3** in $CDCl_3$.

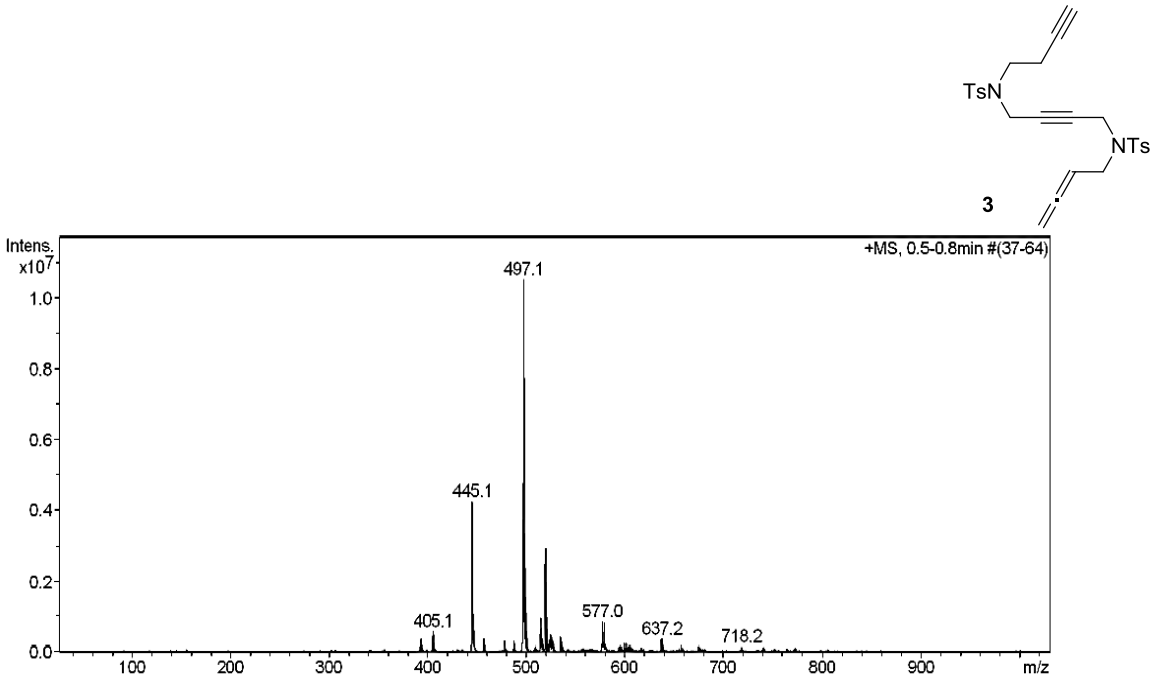


Figure S53: ESI-MS spectrum of **3.**

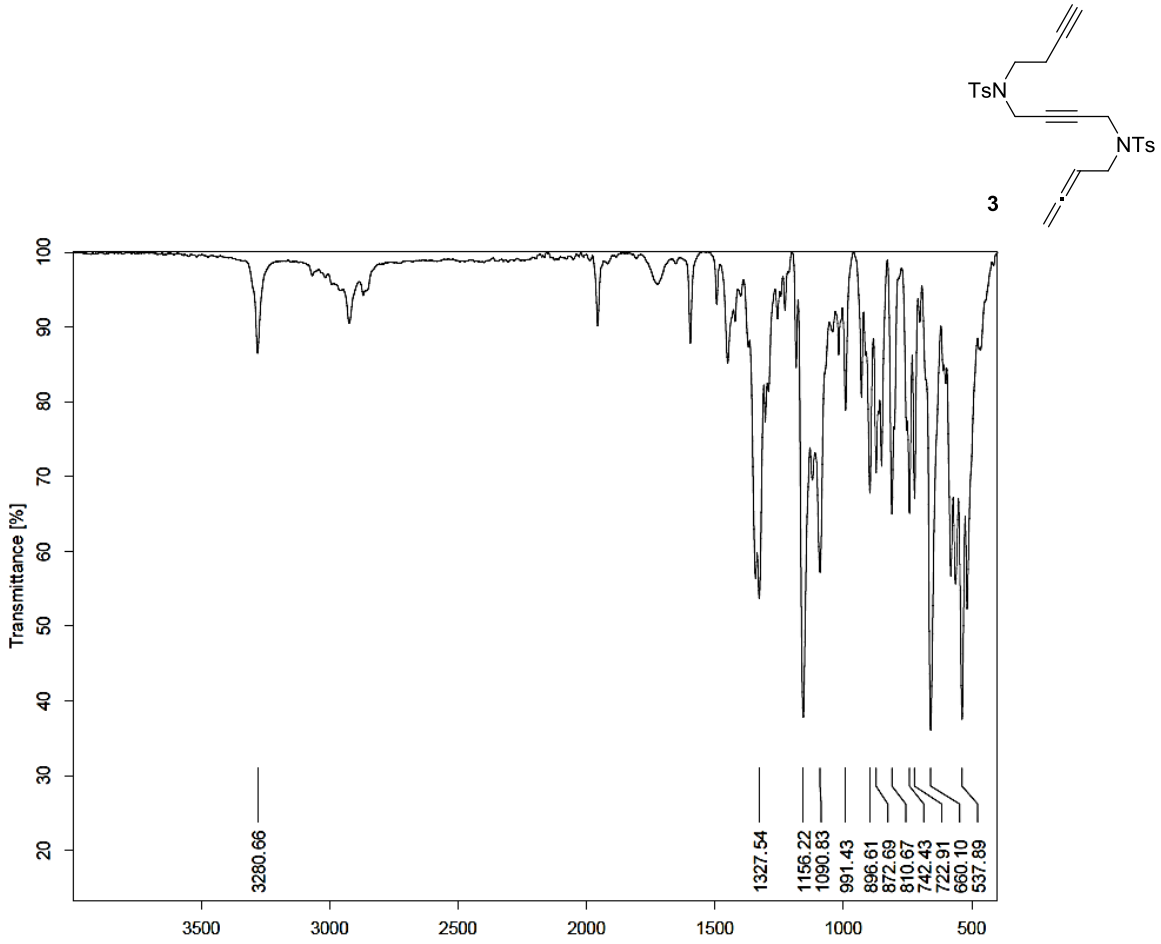
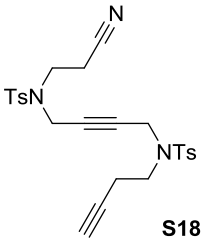


Figure S54: IR (ATR) spectrum of **3.**

Spectra of cyano-yne-yne derivative S18



S18

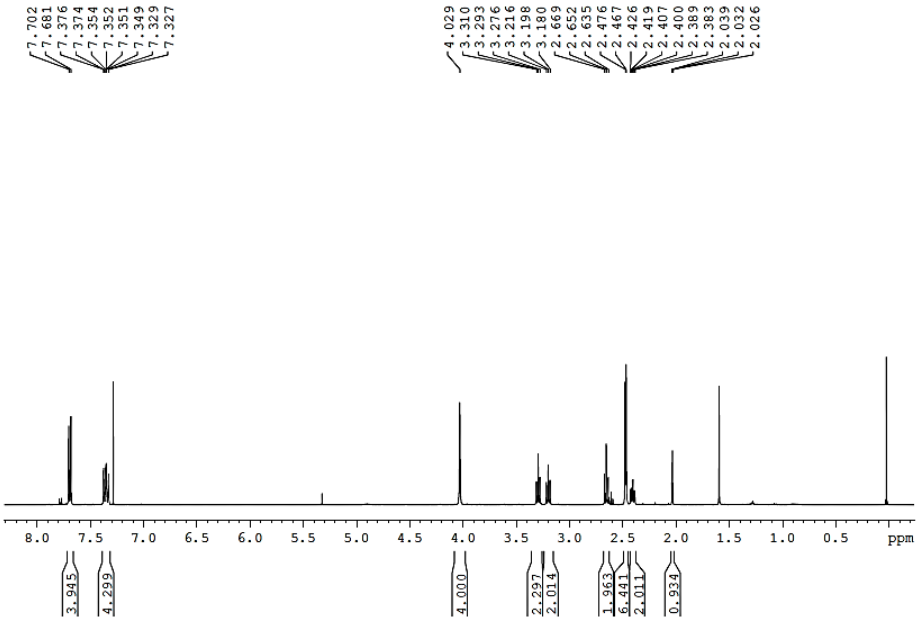
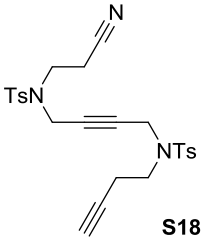


Figure S55: ^{1}H NMR spectrum (400 MHz) of **S18** in $CDCl_3$.



S18

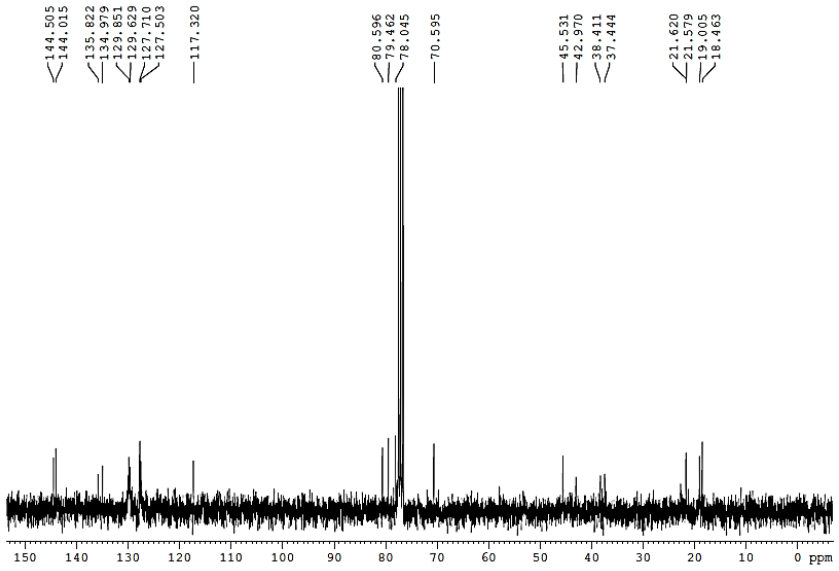
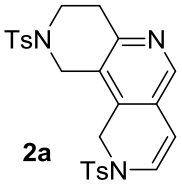


Figure S56: ^{1}H-decoupled ^{13}C NMR spectrum (100 MHz) of **S18** in $CDCl_3$.

Spectra of cycloadducts 2: 2a, 2b, 2c, 2d, 2e, 2f, 2g, 2h, 4 and S19



2a

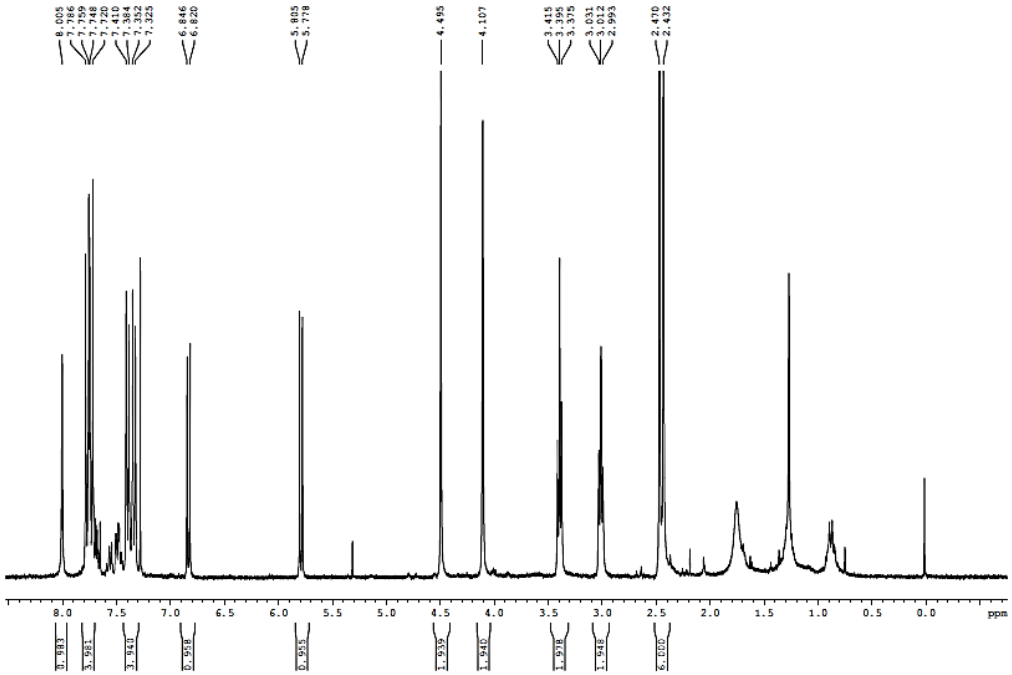
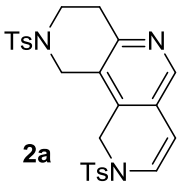


Figure S57: ^{1}H NMR spectrum (300 MHz) of **2a** in $CDCl_3$ (the sample is impurified with traces of Ph_3PO which could not be completely eliminated through column chromatography)



2a

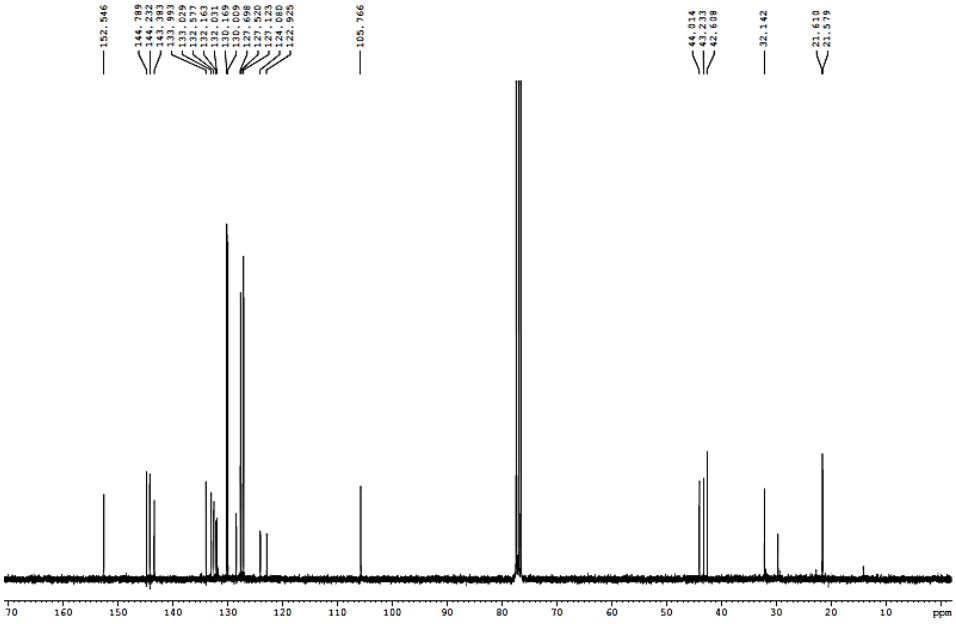


Figure S58: ^{1}H-decoupled ^{13}C NMR spectrum (75 MHz) of **2a** in $CDCl_3$.

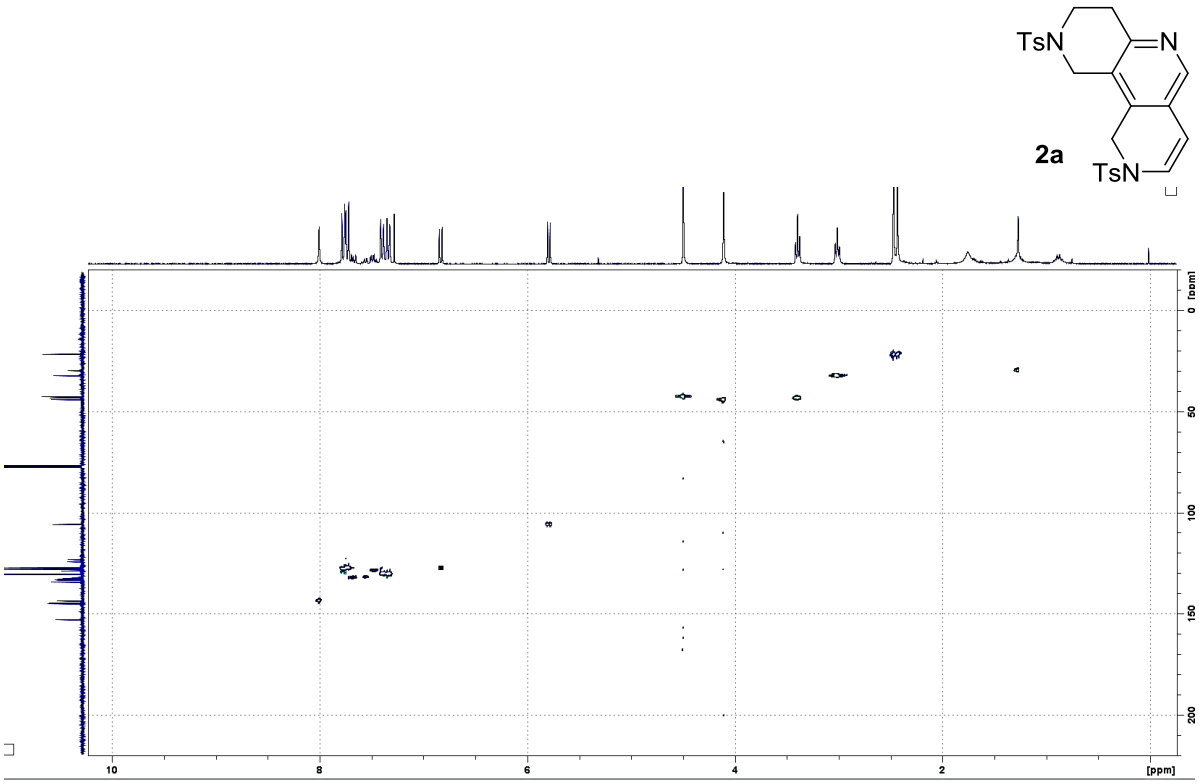


Figure S59: 2D ^{1}H-^{13}C HSQC correlation of **2a** in $CDCl_3$.

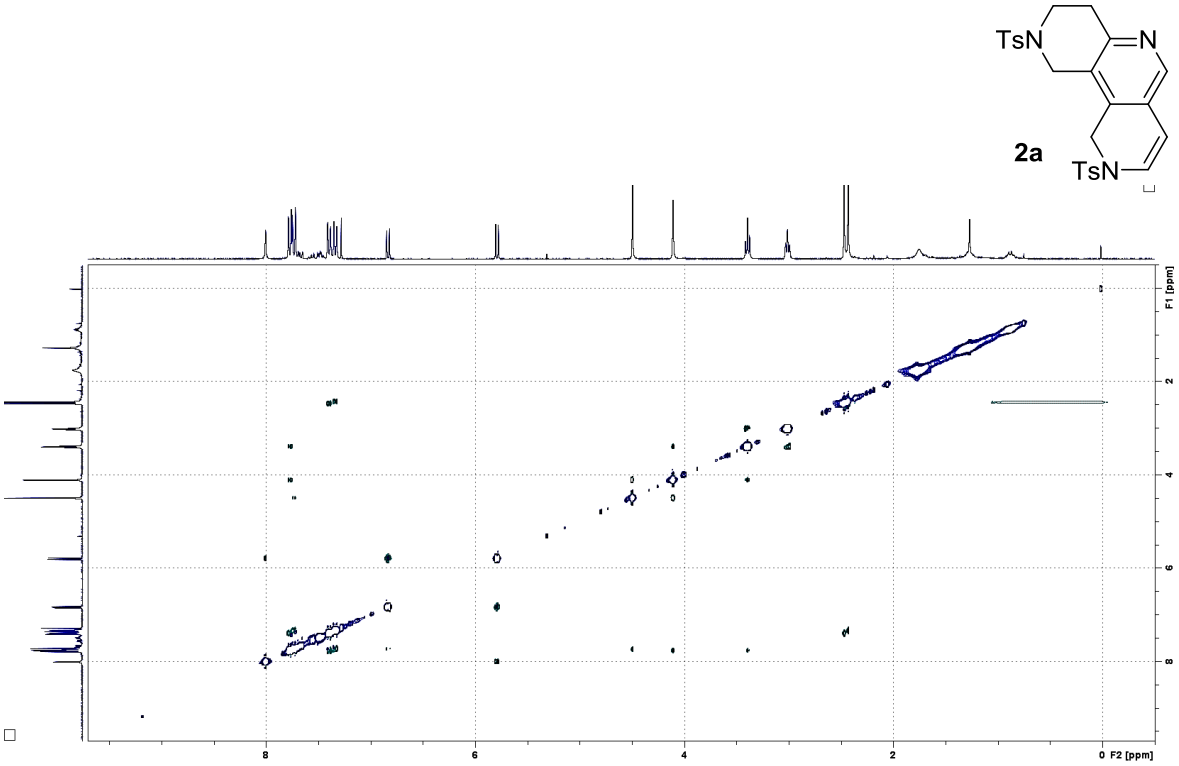


Figure S60: 2D ^{1}H-^{13}C HMBC correlation of **2a** in $CDCl_3$.

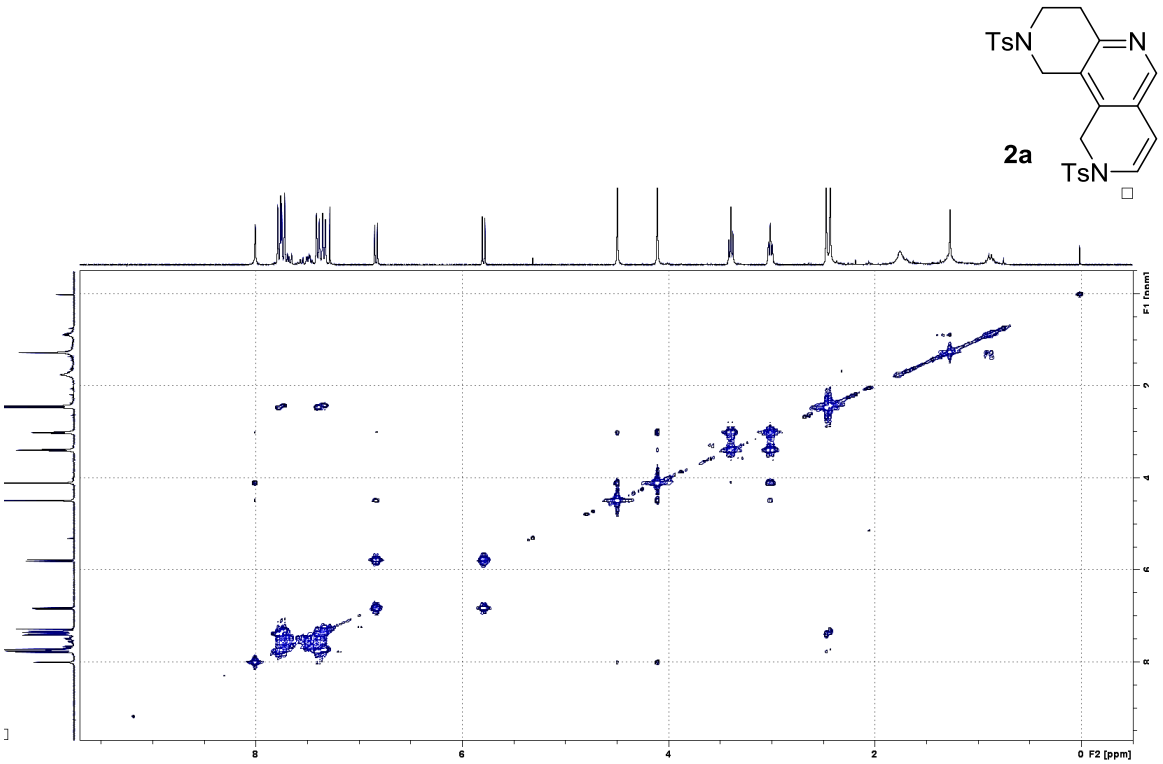


Figure S61: 2D ^{1}H-^{1}H COSY correlation spectrum of **2a** in $CDCl_3$.

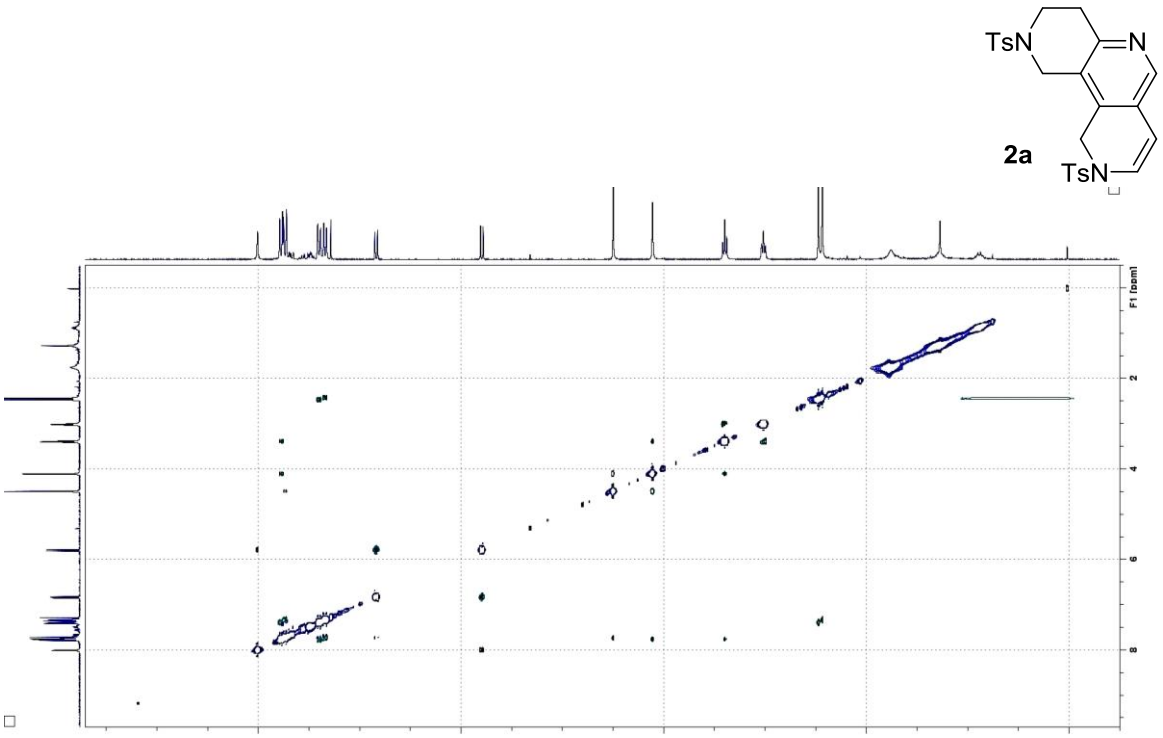
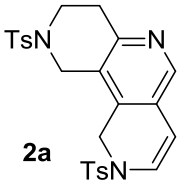


Figure S62: 2D 1H-1H NOESY correlation of **2a** in $CDCl_3$.



2a

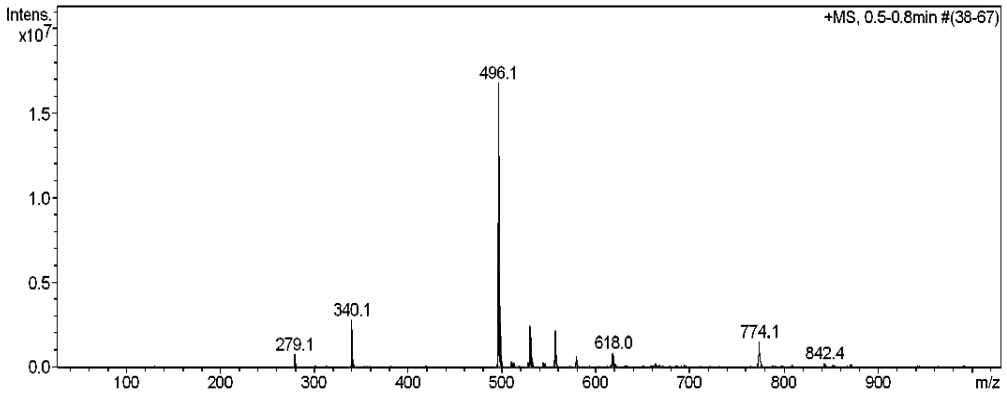
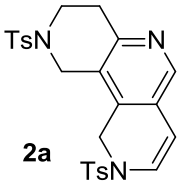


Figure S63: ESI-MS spectrum of **2a.**



2a

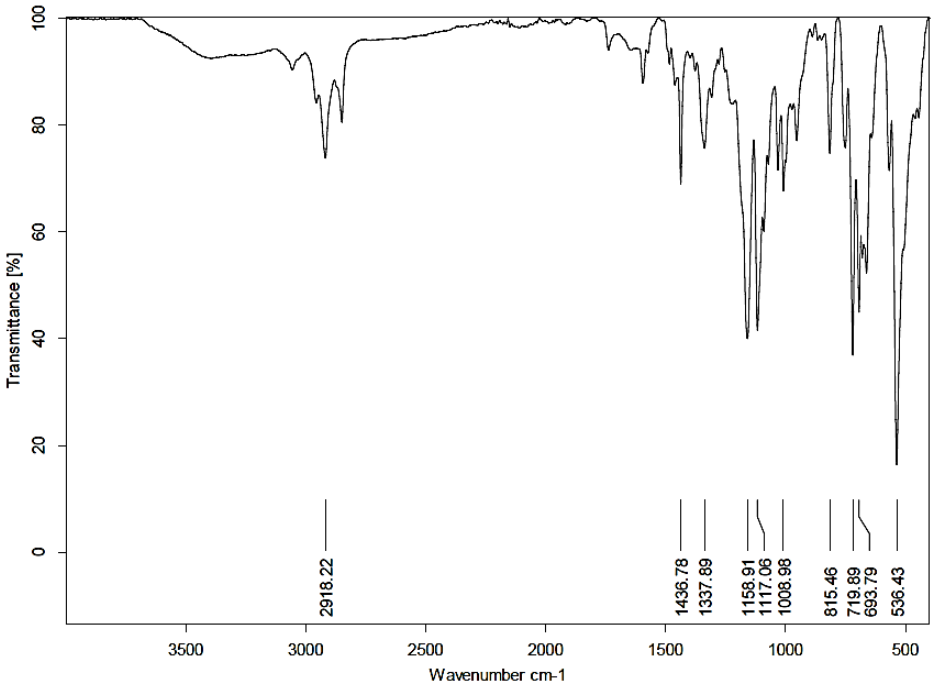
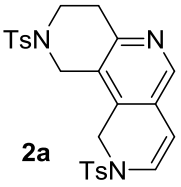


Figure S64: IR (ATR) spectrum of **2a.**



2a

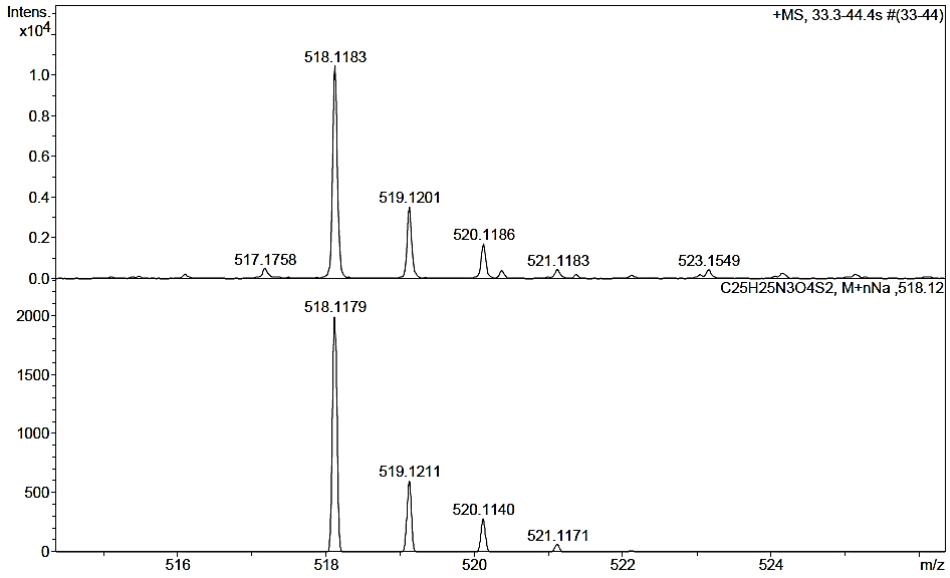
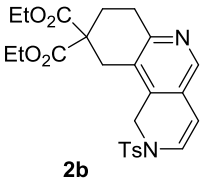


Figure S65: ESI-HRMS spectrum of **2a.**



2b

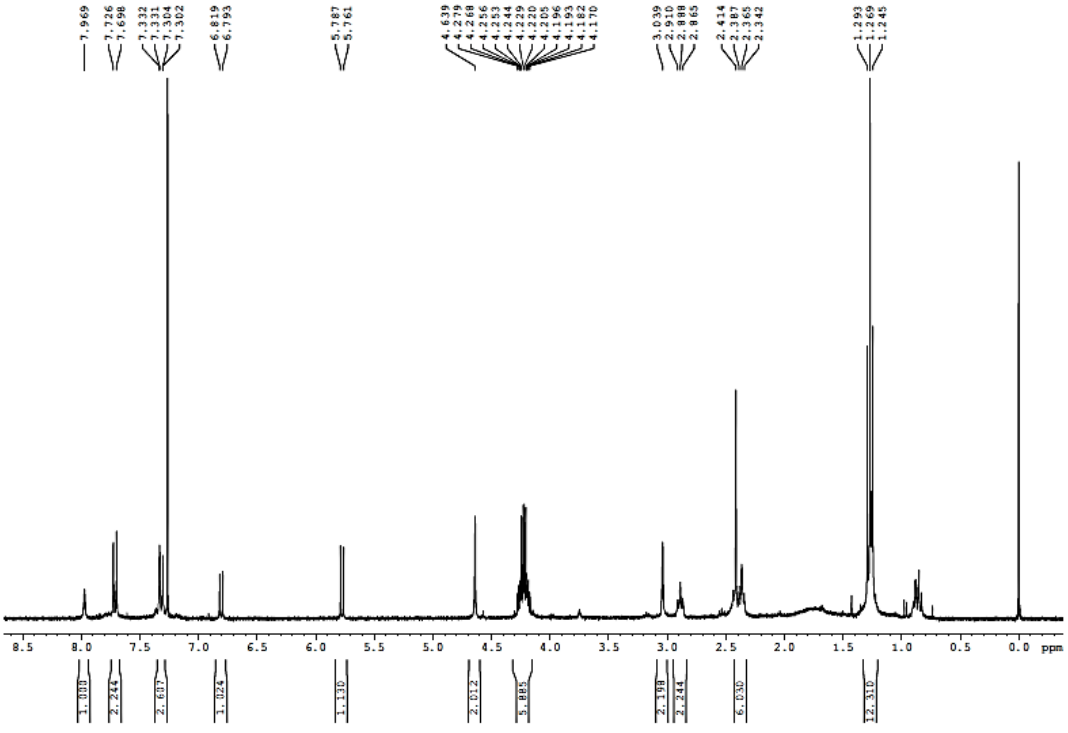


Figure S66: ^{1}H NMR spectrum (300 MHz) of **2b** in $CDCl_3$.

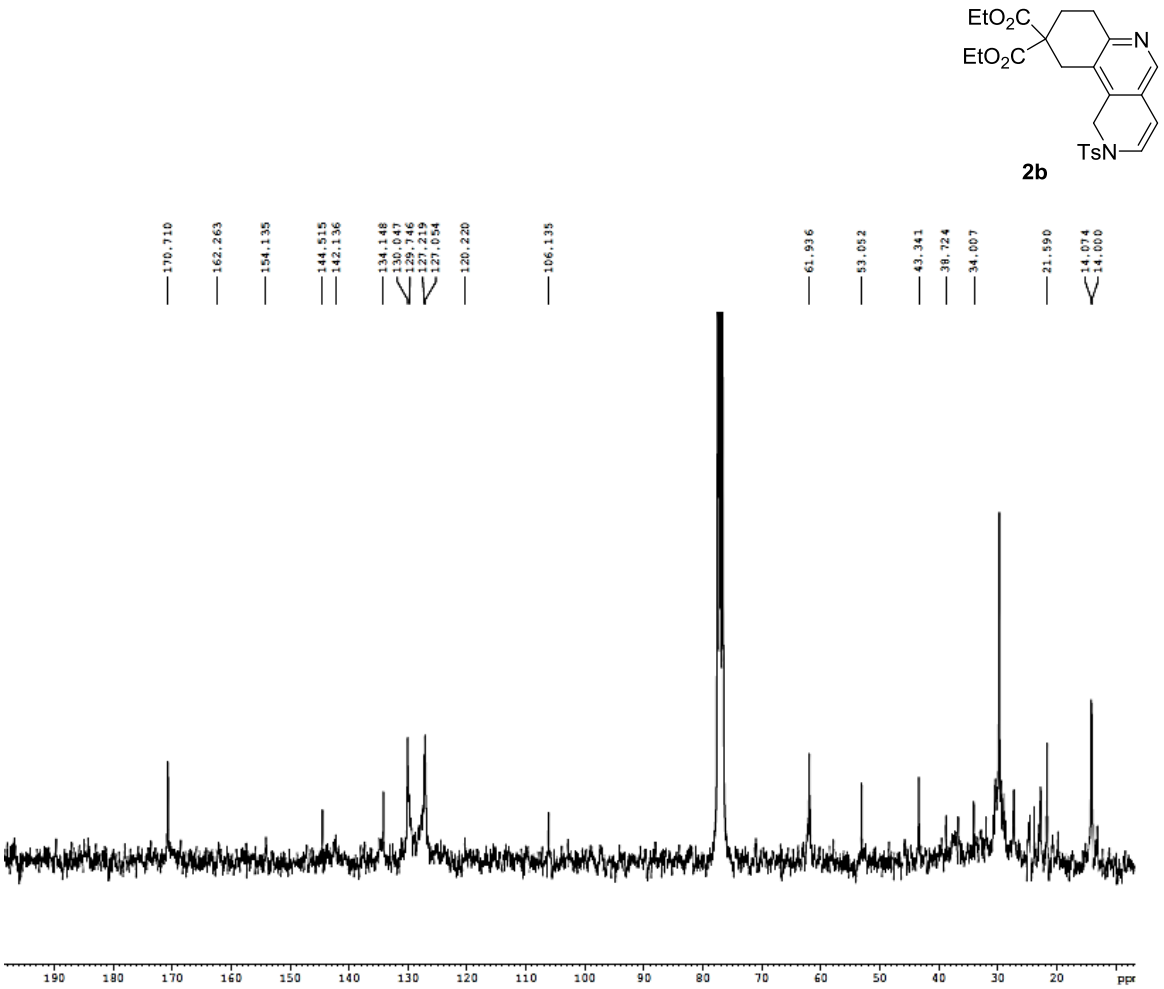


Figure S67: ^{1}H-decoupled ^{13}C NMR spectrum (75 MHz) of **2b** in $CDCl_3$.

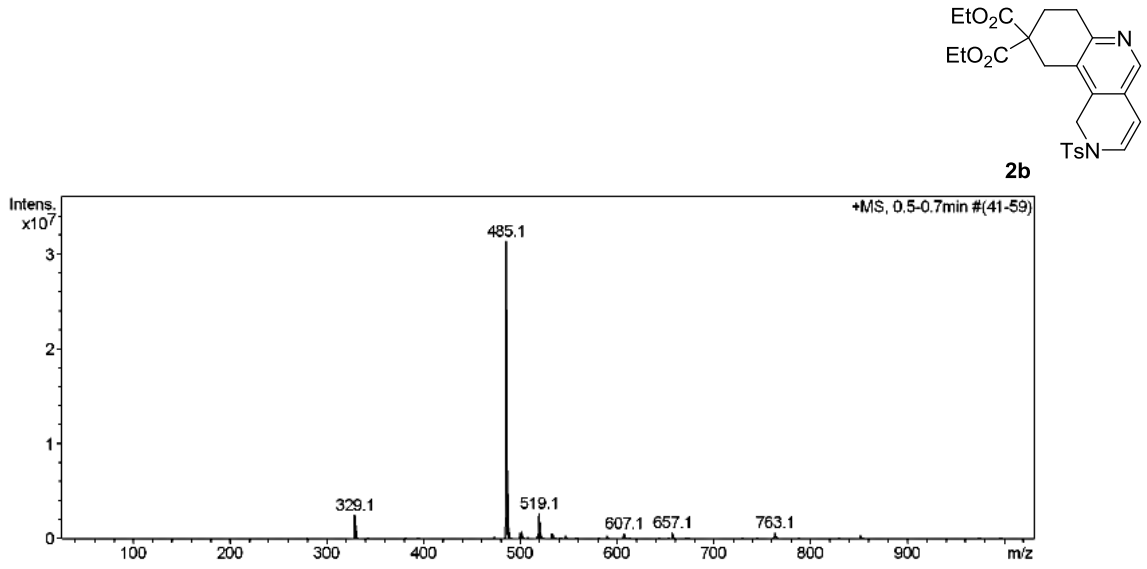
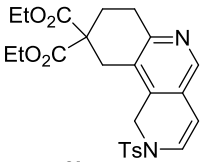


Figure S68: ESI-MS spectrum of **2b.**



2b

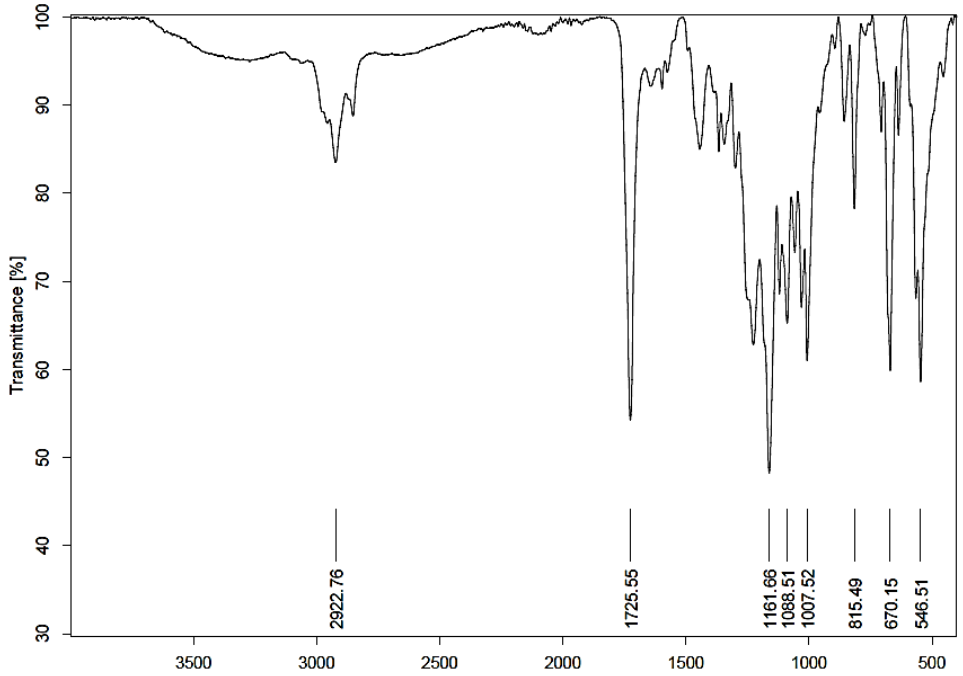
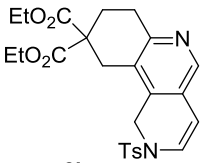


Figure S69: IR (ATR) spectrum of **2b.**



2b

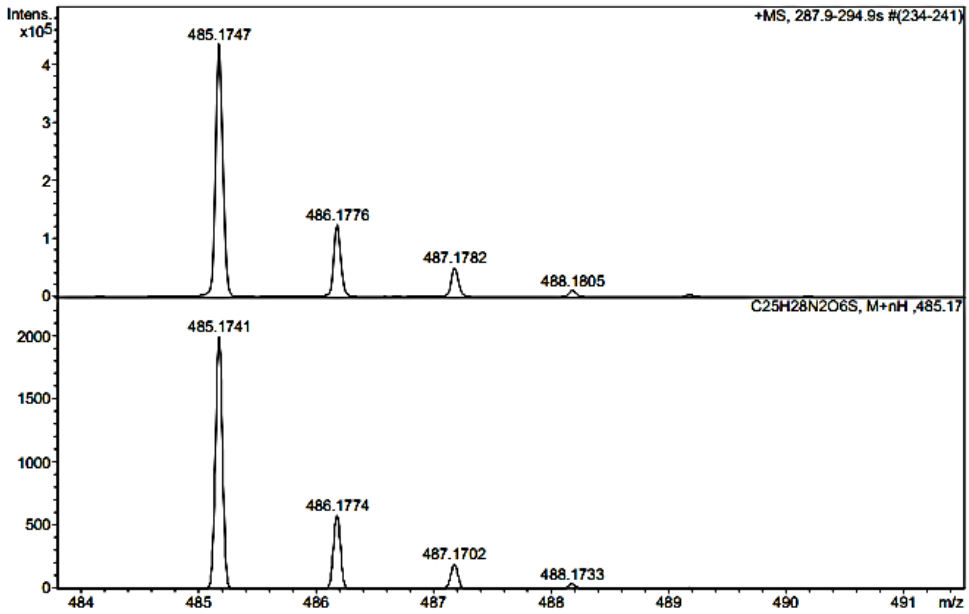
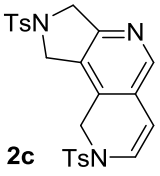


Figure S70: ESI-HRMS spectrum of **2b.**



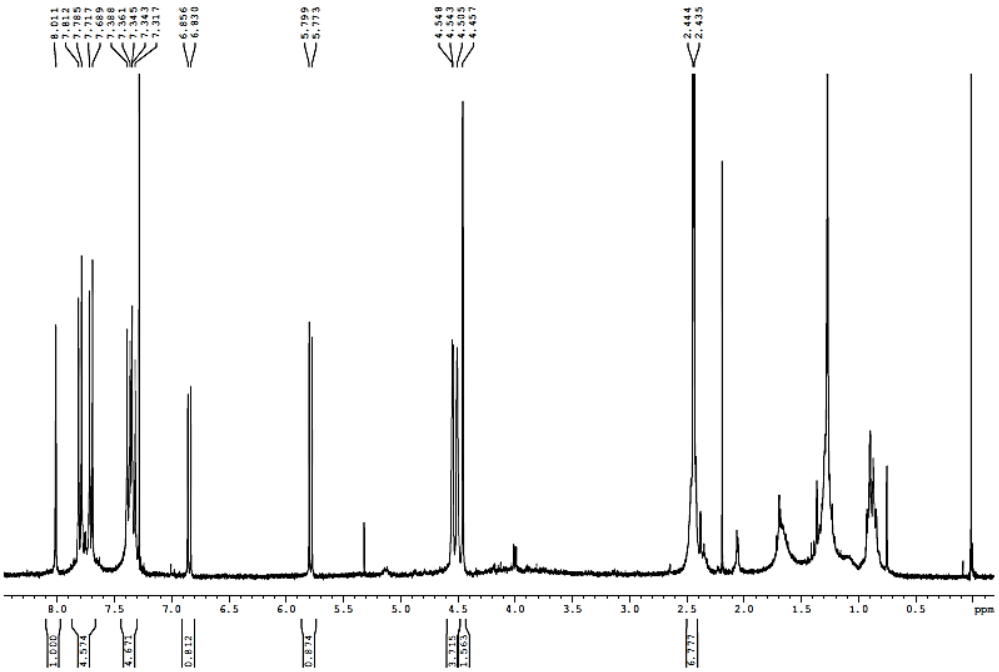
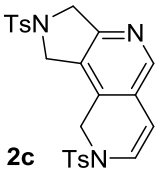


Figure S71: ^{1}H NMR spectrum (300 MHz) of **2c** in $CDCl_3$.



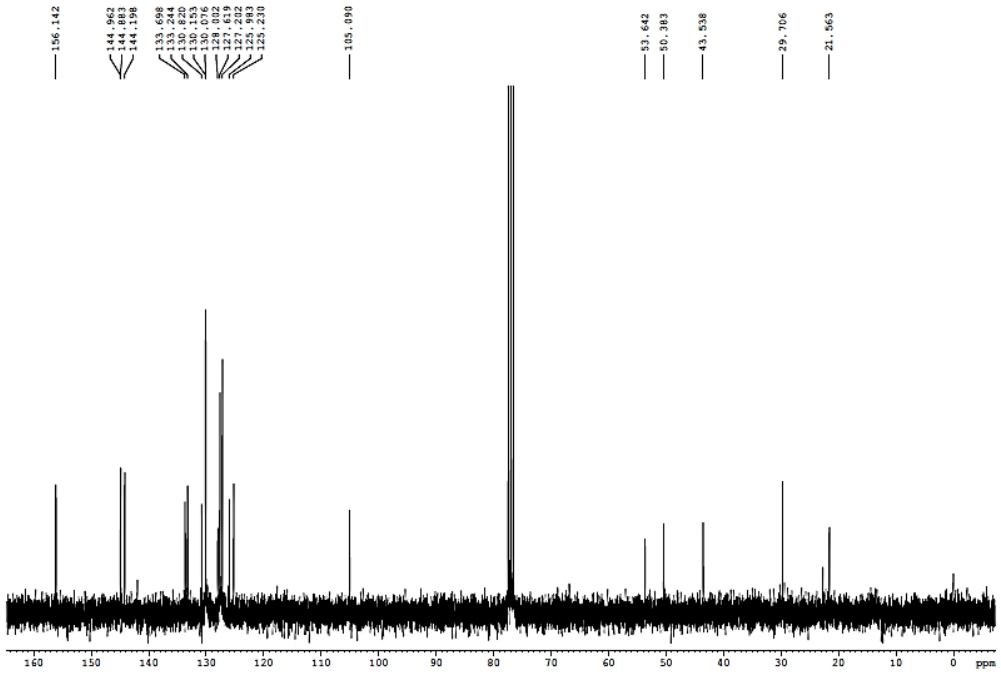


Figure S72: ^{1}H-decoupled ^{13}C NMR spectrum (75 MHz) of **2c** in $CDCl_3$.

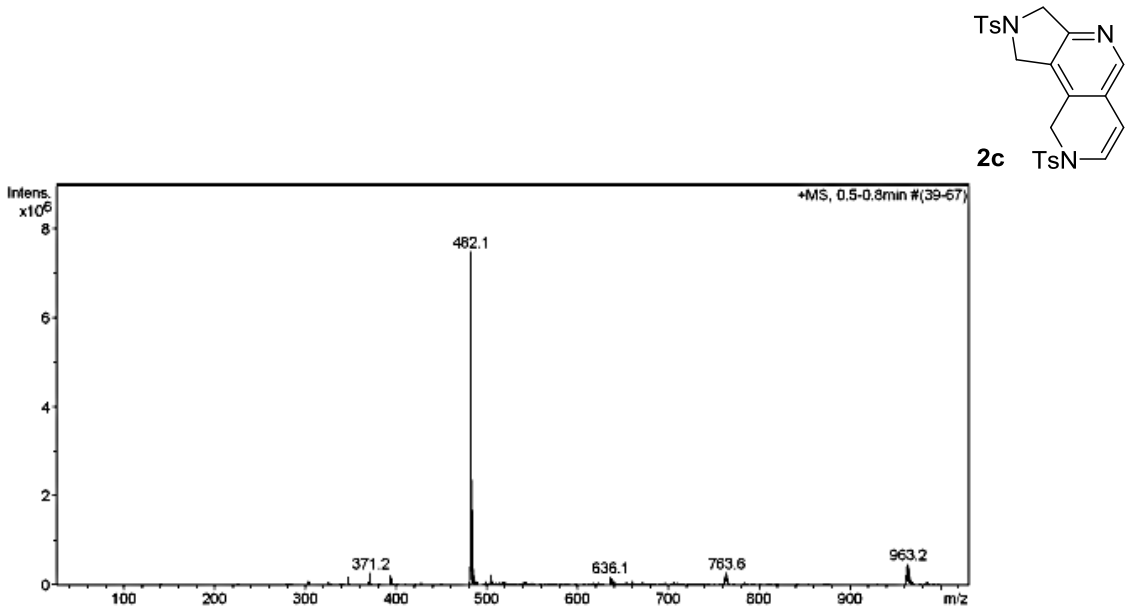


Figure S73: ESI-MS spectrum of **2c.**

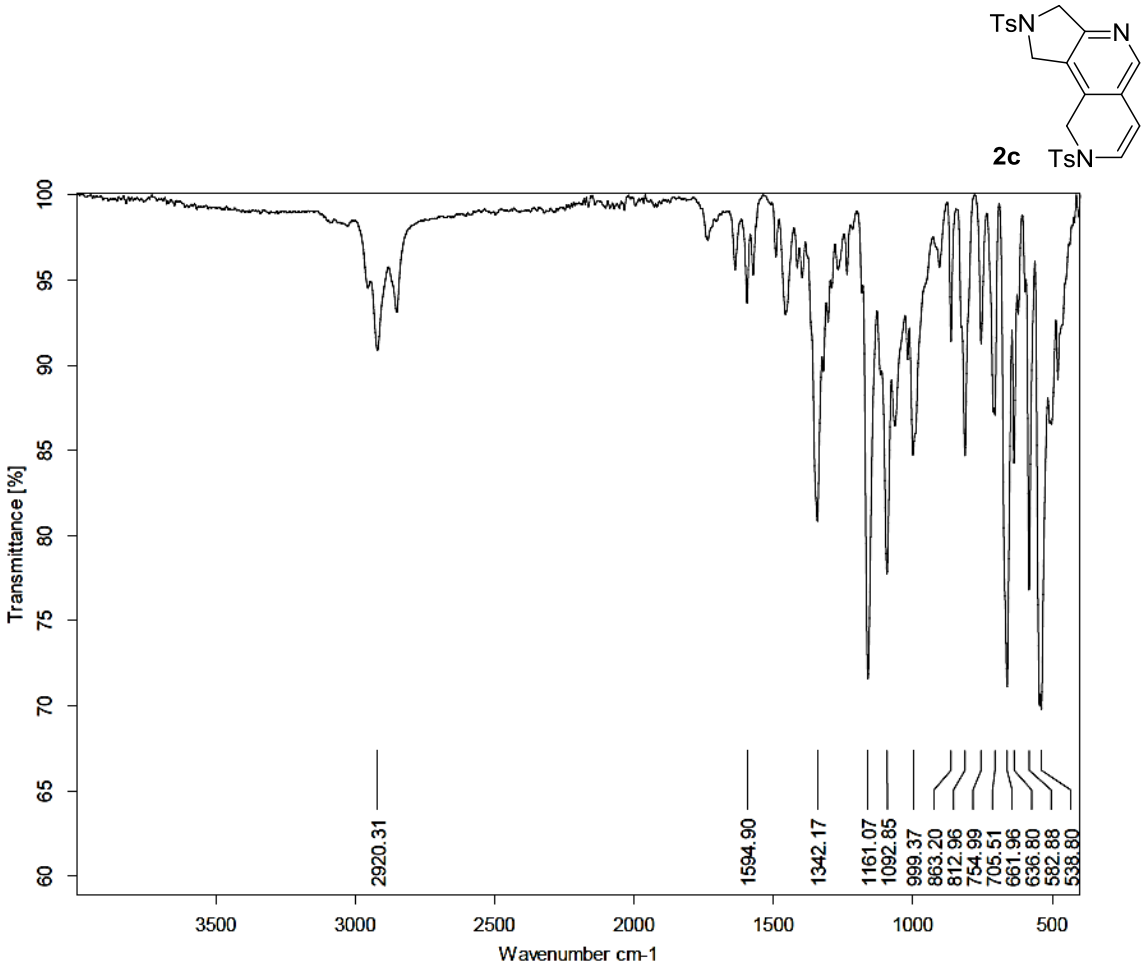
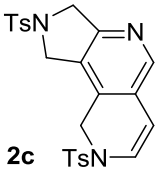


Figure S74: IR (ATR) spectrum of **2c.**



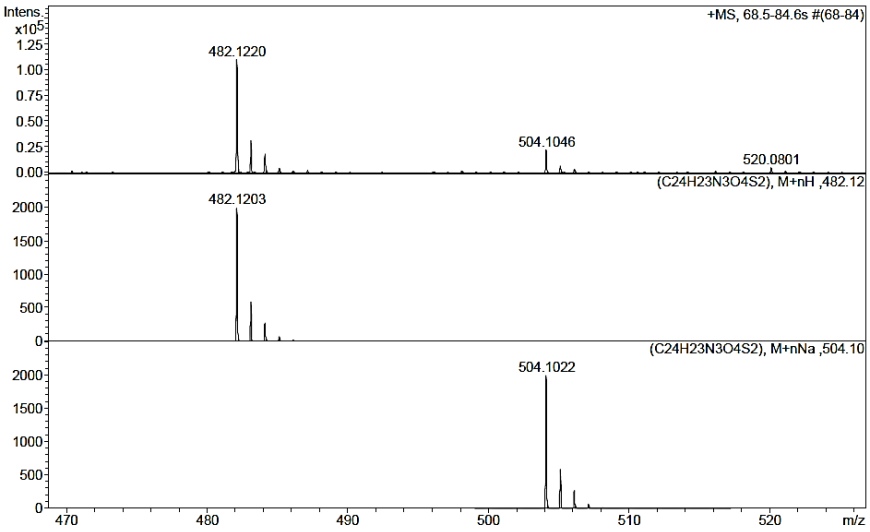
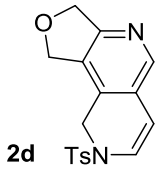


Figure S75: ESI-HRMS spectrum of **2c.**



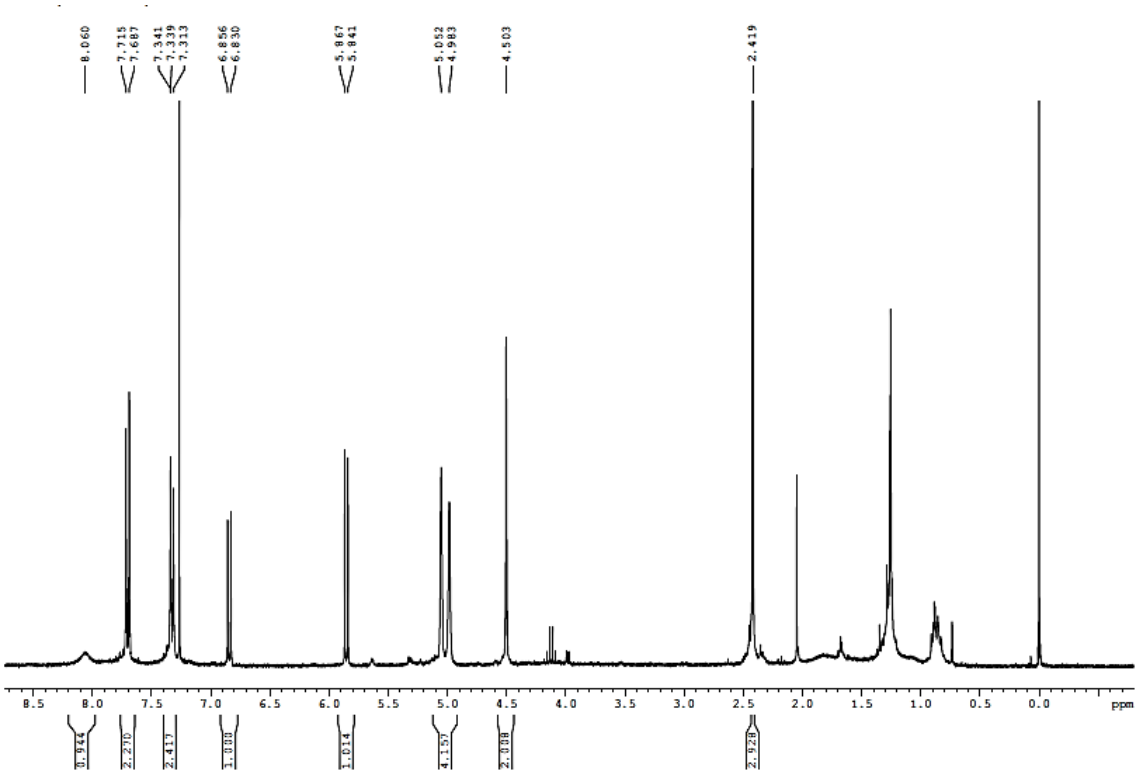


Figure S76: ^{1}H NMR spectrum (300 MHz) of **2d** in $CDCl_3$.

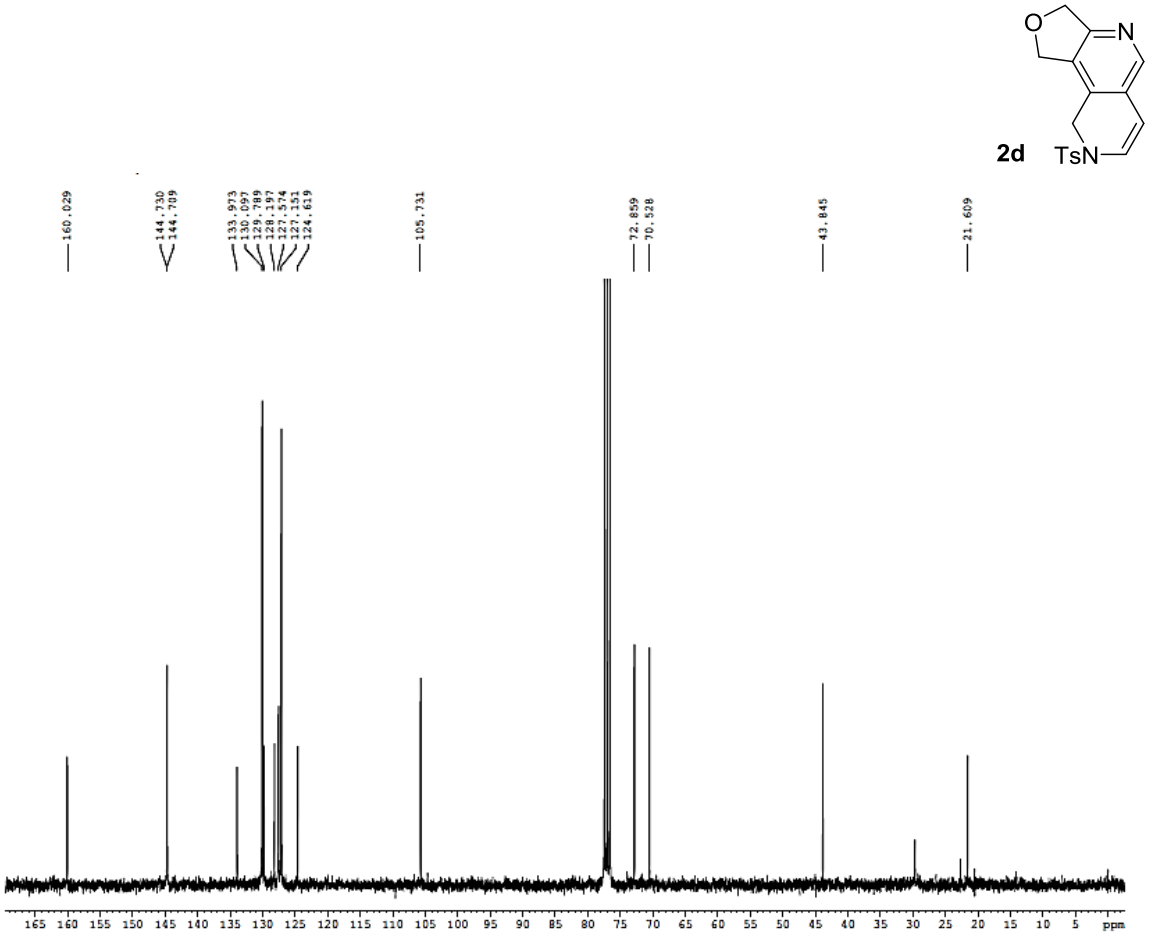


Figure S77: ^{1}H-decoupled ^{13}C NMR spectrum (75 MHz) of **2d** in $CDCl_3$.

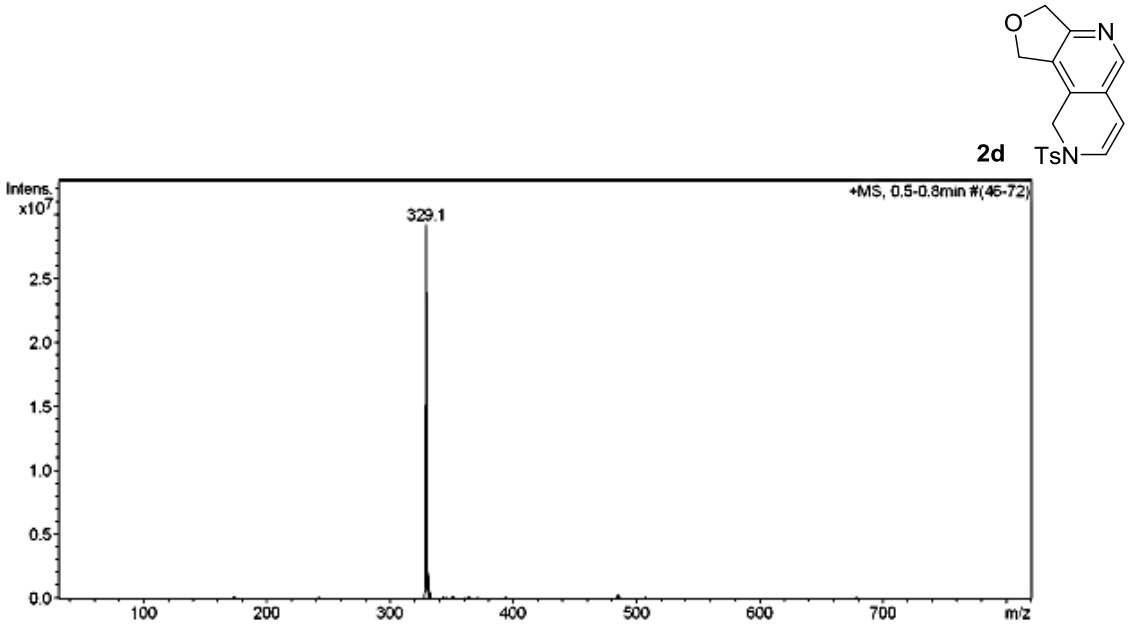


Figure S78: ESI-MS spectrum of **2d.**

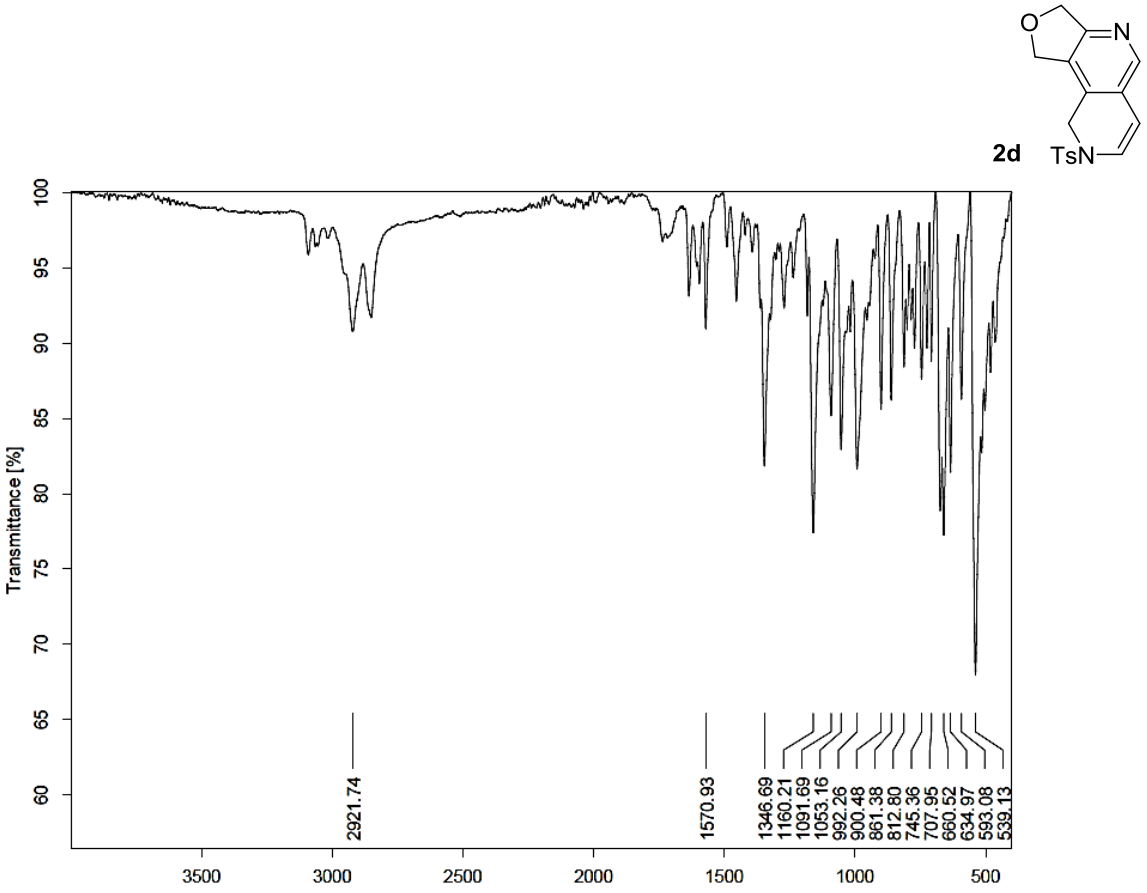


Figure S79: IR (ATR) spectrum of **2d.**

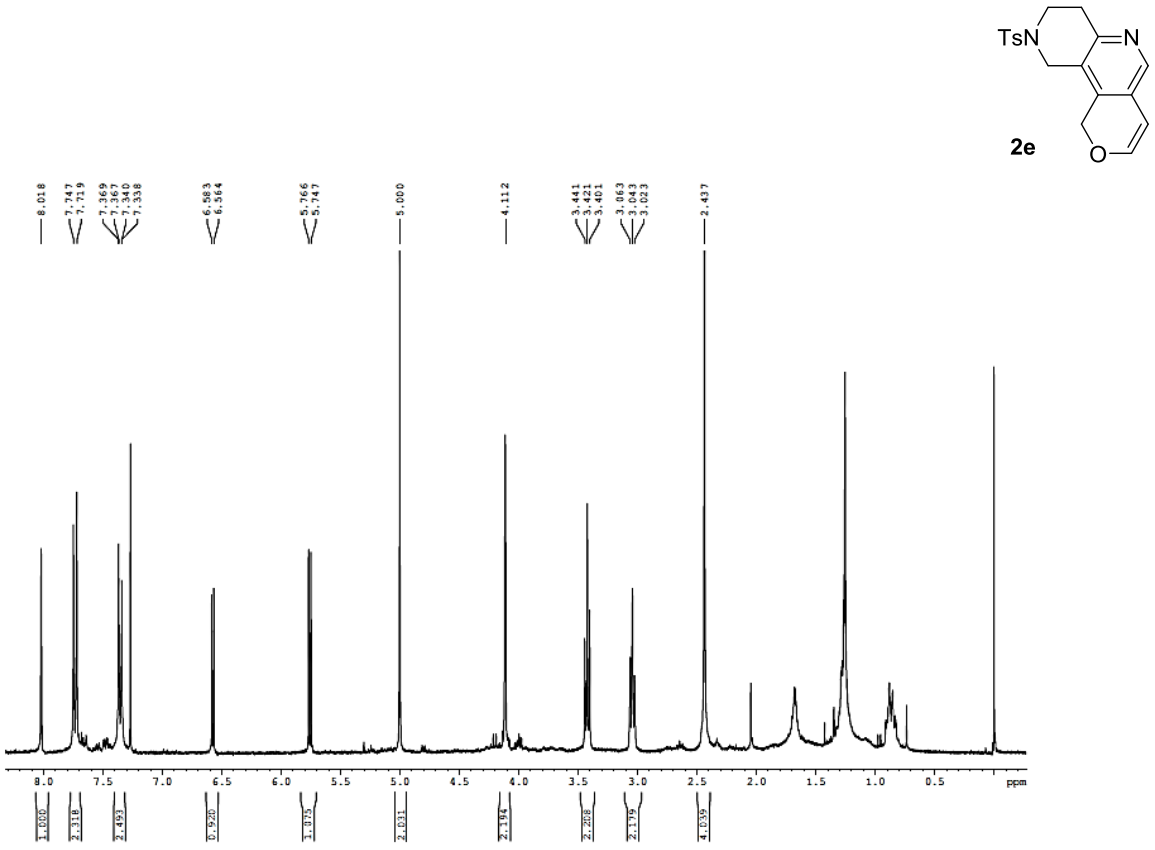


Figure S80: ^{1}H NMR spectrum (300 MHz) of **2e** in $CDCl_3$.

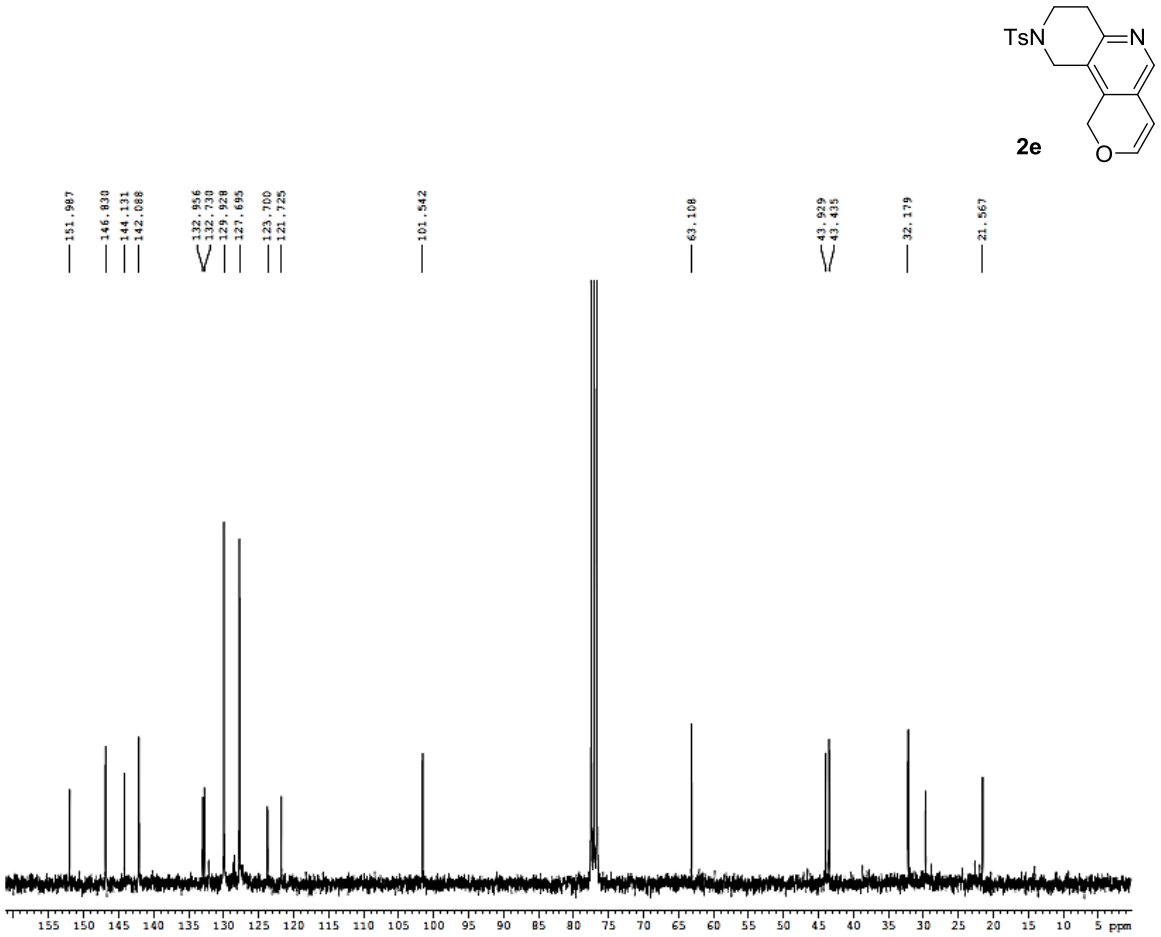


Figure S81: ^{1}H-decoupled ^{13}C NMR spectrum (75 MHz) of **2e** in $CDCl_3$.

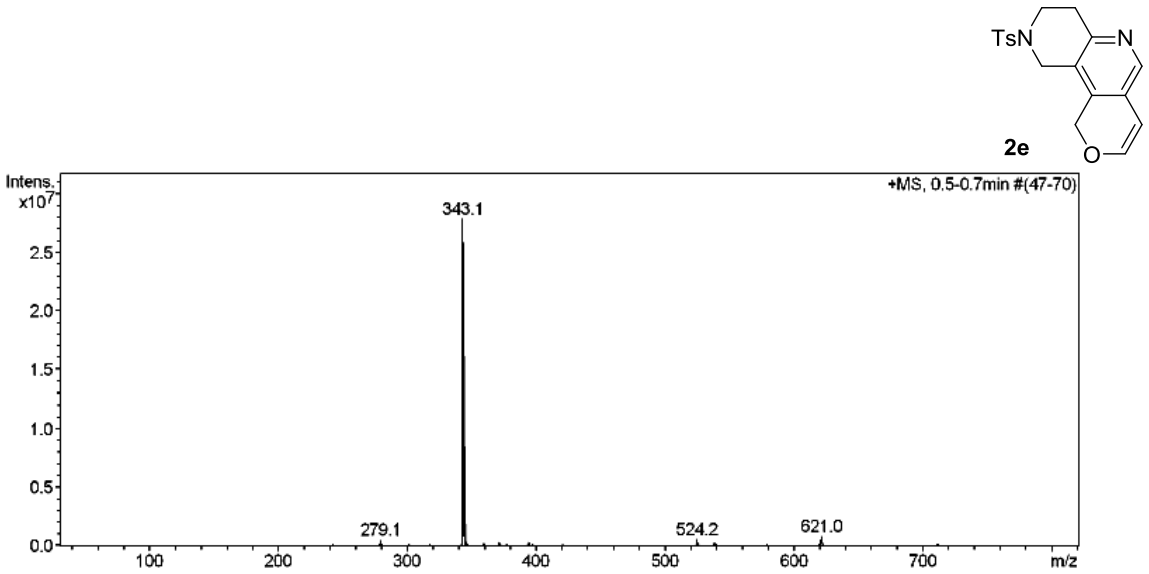


Figure S82: ESI-MS spectrum of **2e**.

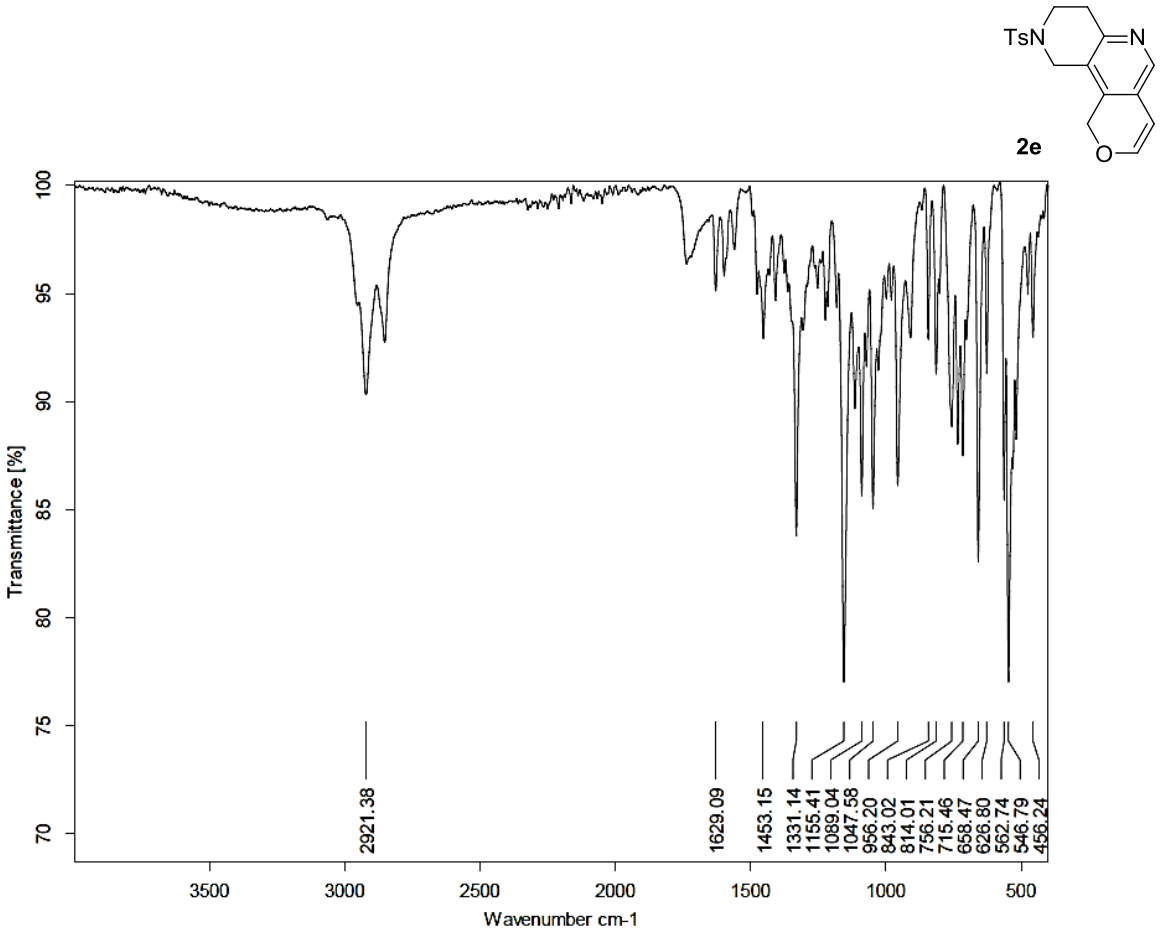


Figure S83: IR (ATR) spectrum of **2e.**

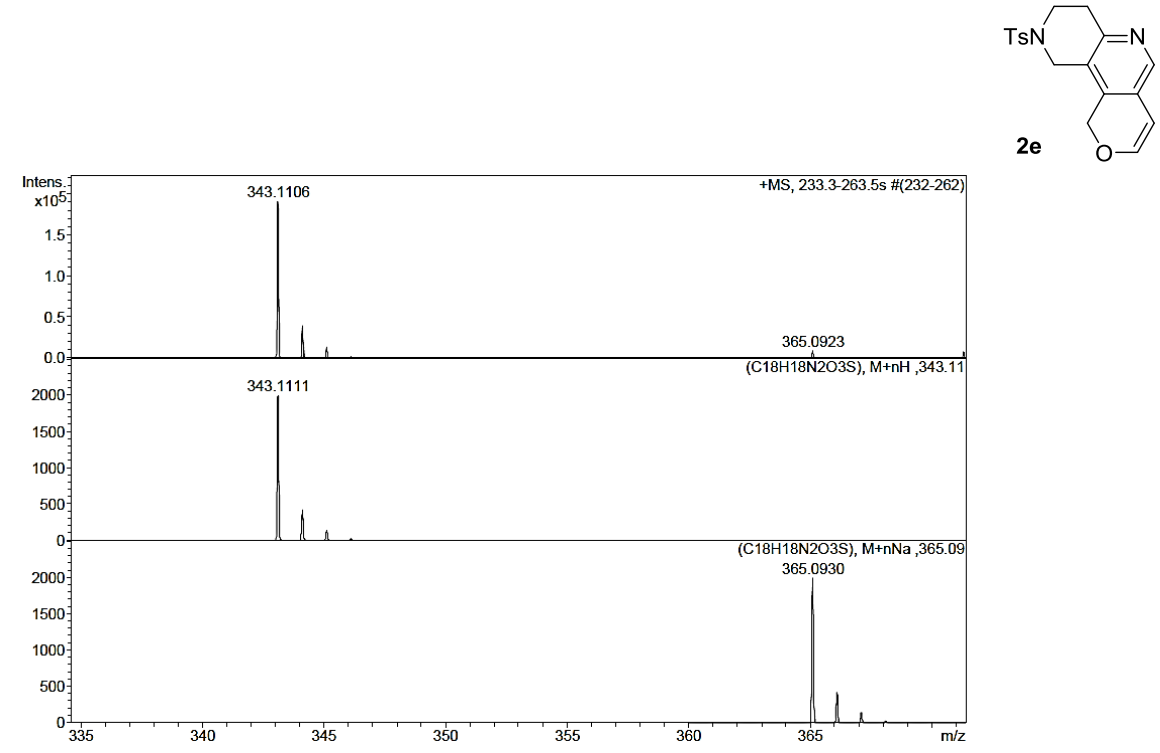


Figure S84: ESI-HRMS spectrum of **2e.**

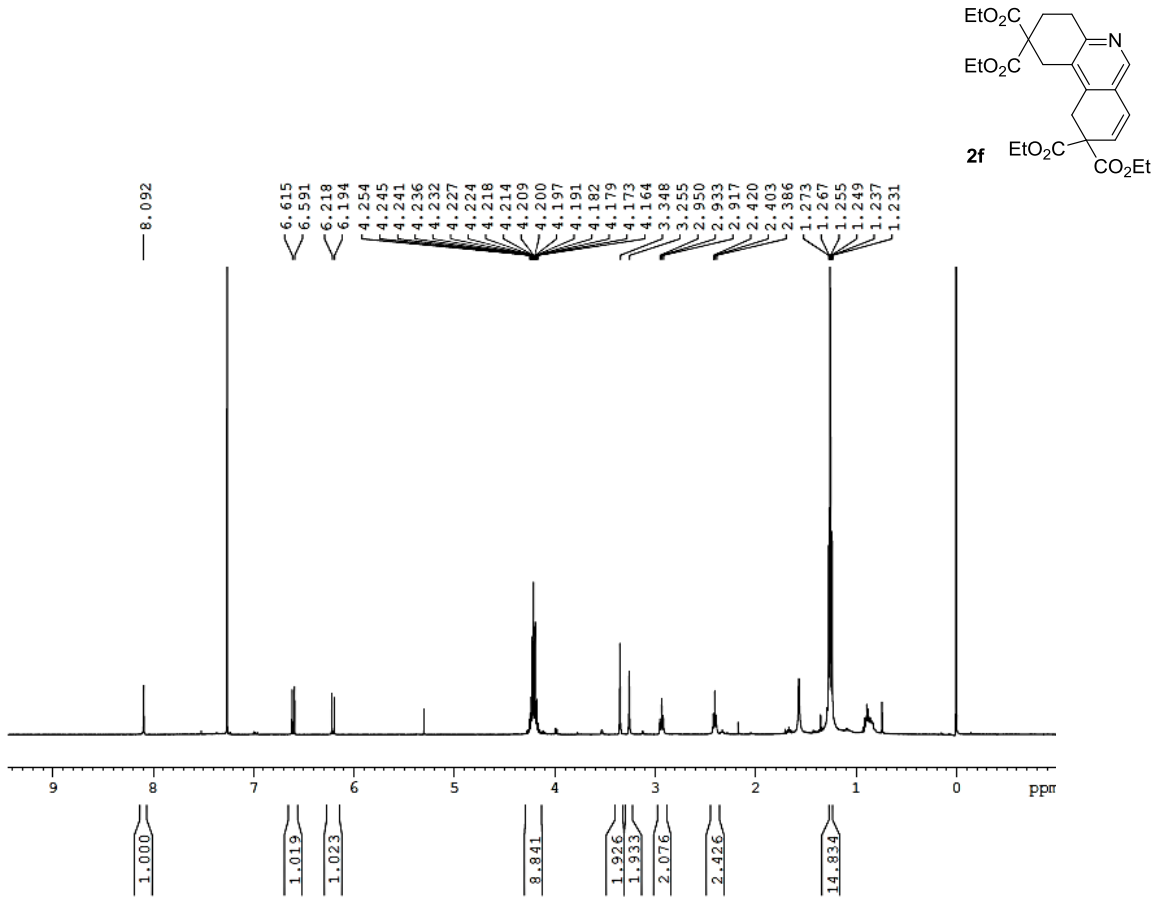


Figure S85: ^{1}H NMR spectrum (400 MHz) of **2f** in $CDCl_3$.

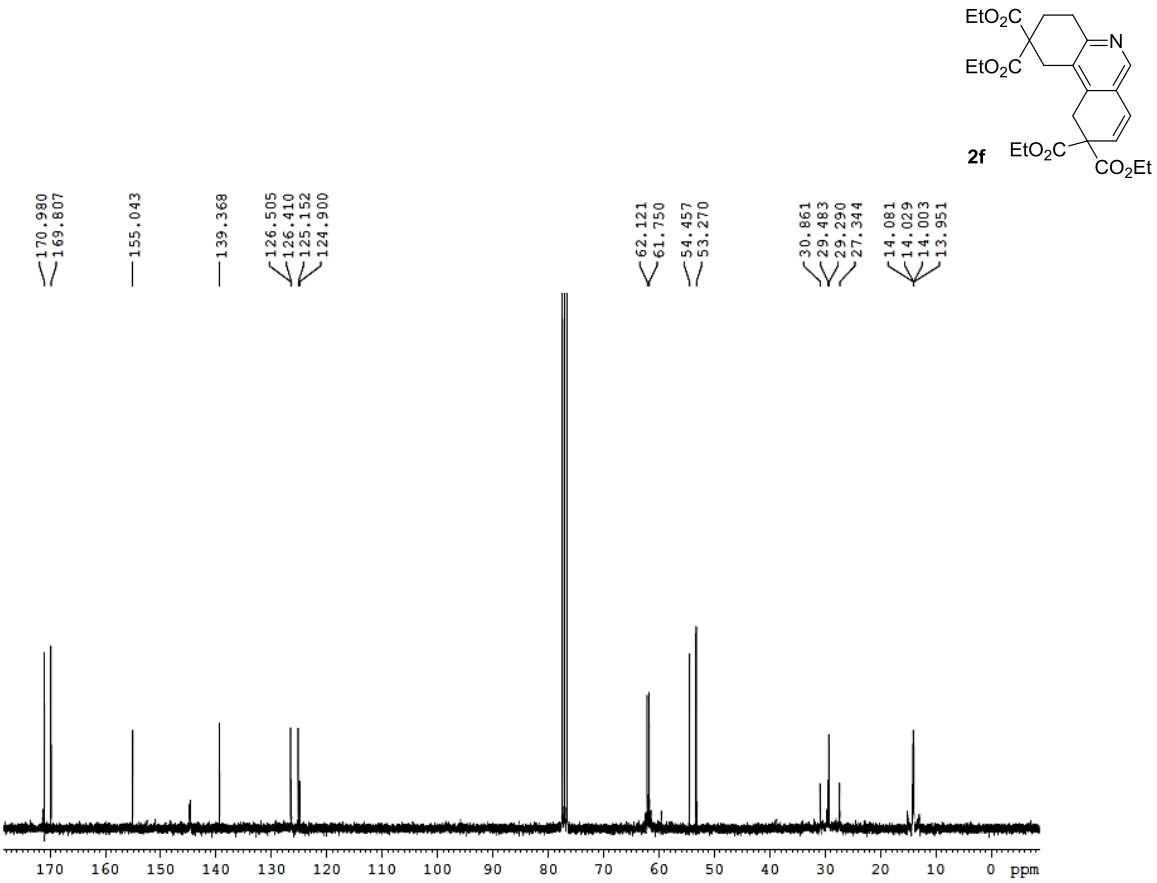


Figure S86: ^{1}H-decoupled ^{13}C NMR spectrum (75 MHz) of **2f** in $CDCl_3$.

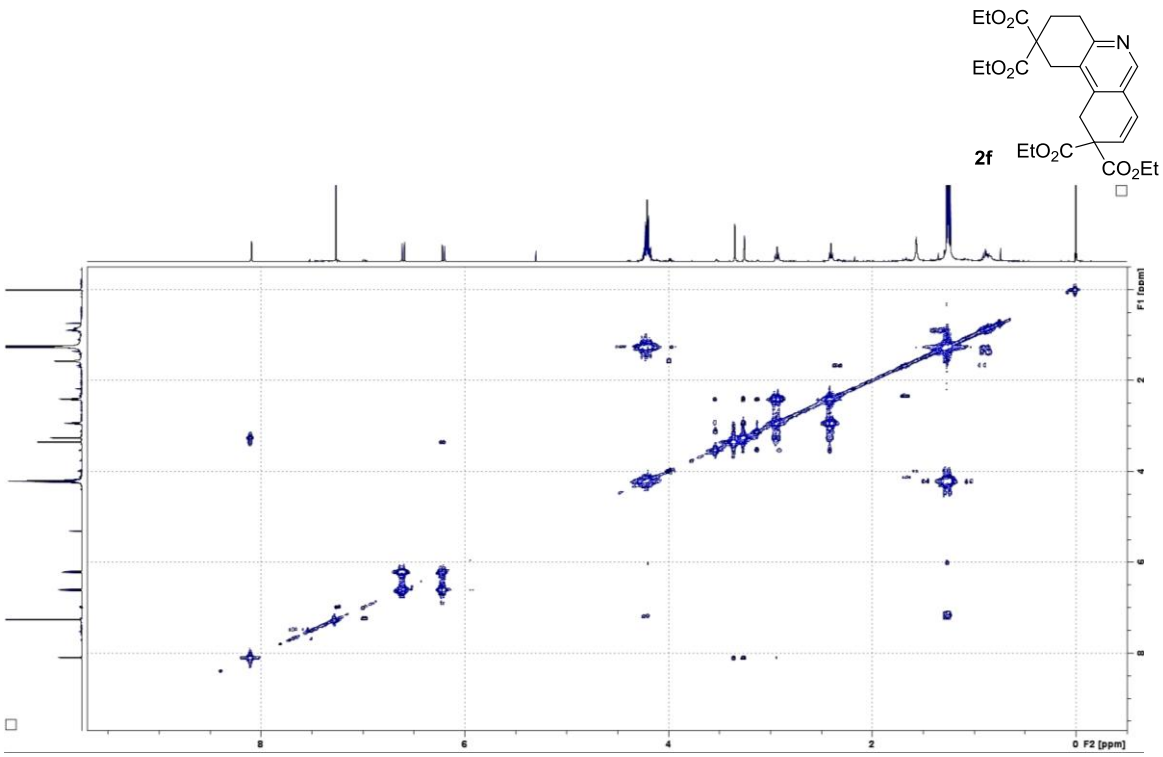


Figure S87: 2D ^{1}H-^{1}H COSY correlation spectrum of **2f** in $CDCl_3$.

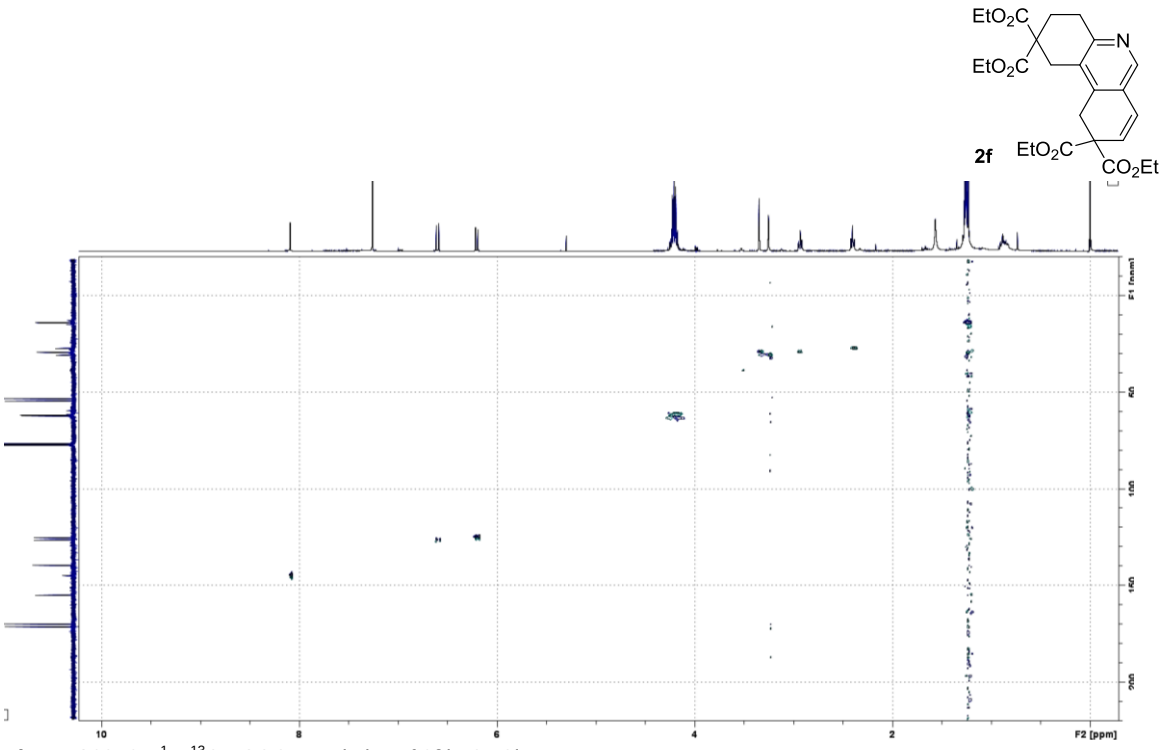
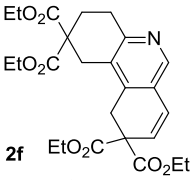


Figure S88: 2D ^{1}H-^{13}C HSQC correlation of **2f** in $CDCl_3$.



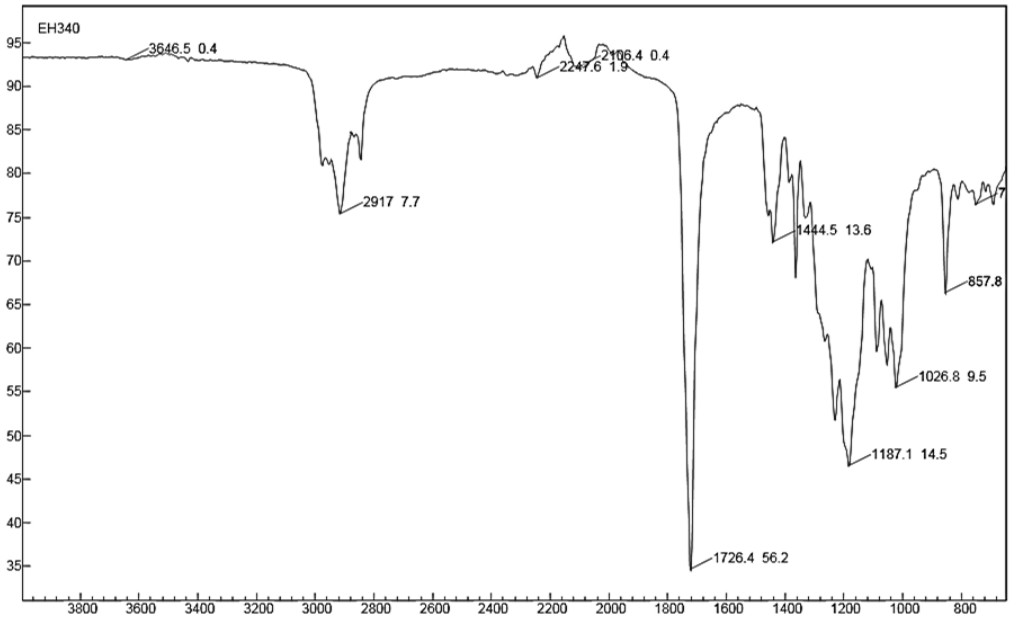
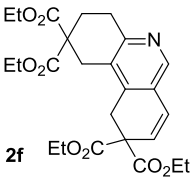


Figure S89: IR (ATR) spectrum of **2f.**



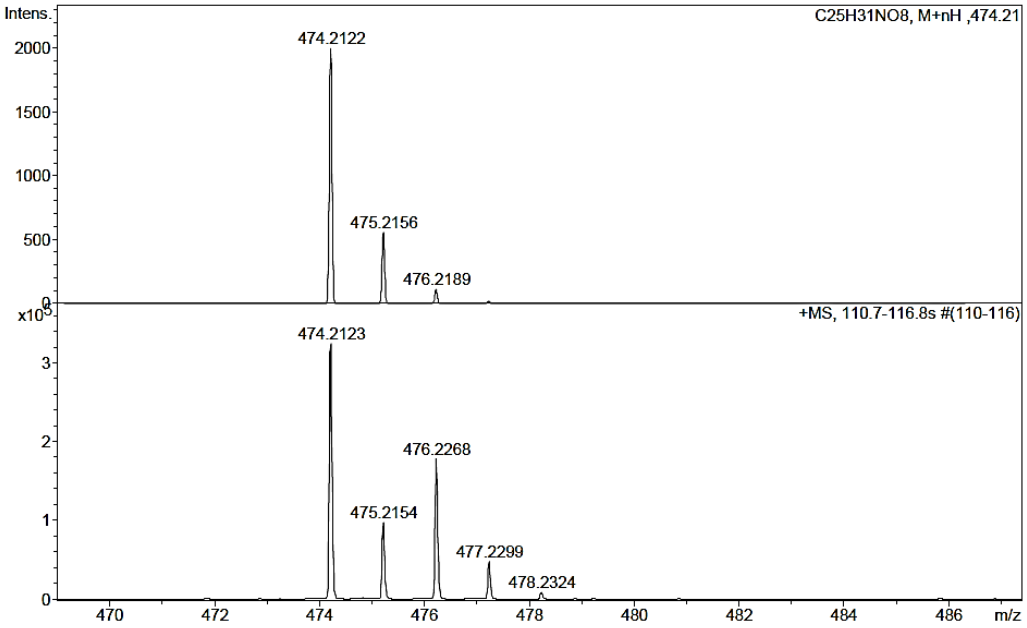
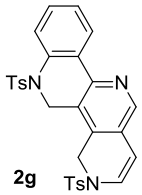


Figure S90: ESI-HRMS spectrum of **2f.**



2g

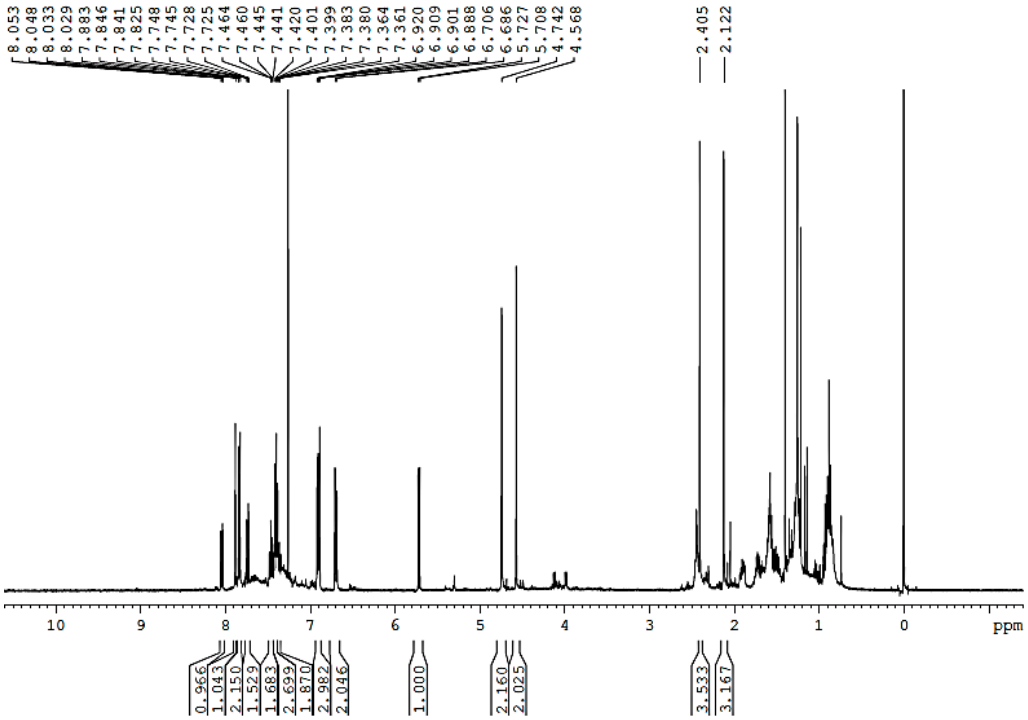
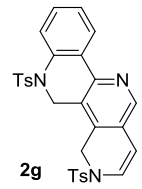


Figure S91: ^{1}H NMR spectrum (400 MHz) of **2g** in $CDCl_3$.



2g

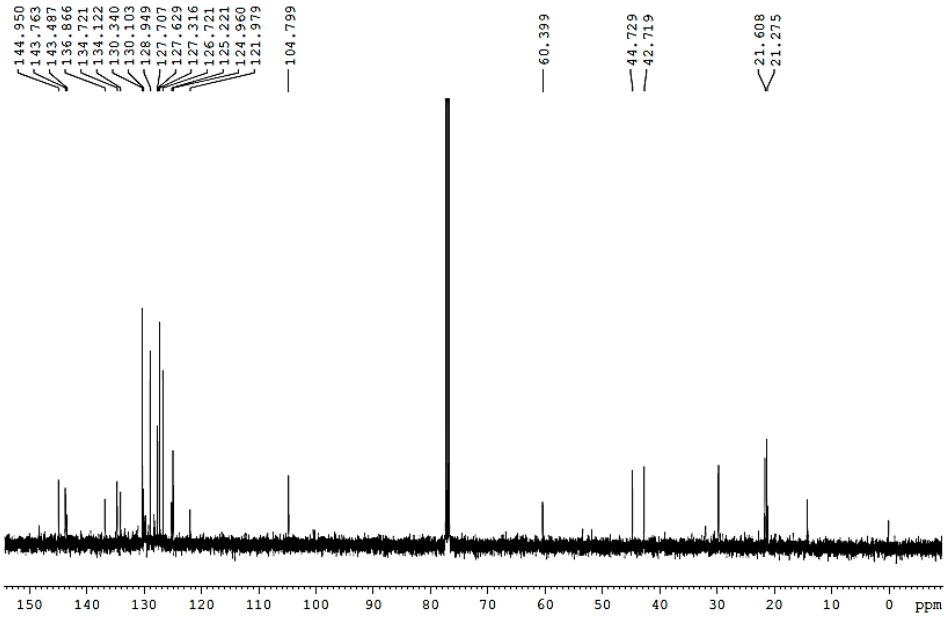


Figure S92: ^{1}H-decoupled ^{13}C NMR spectrum (100 MHz) of **2g** in $CDCl_3$.

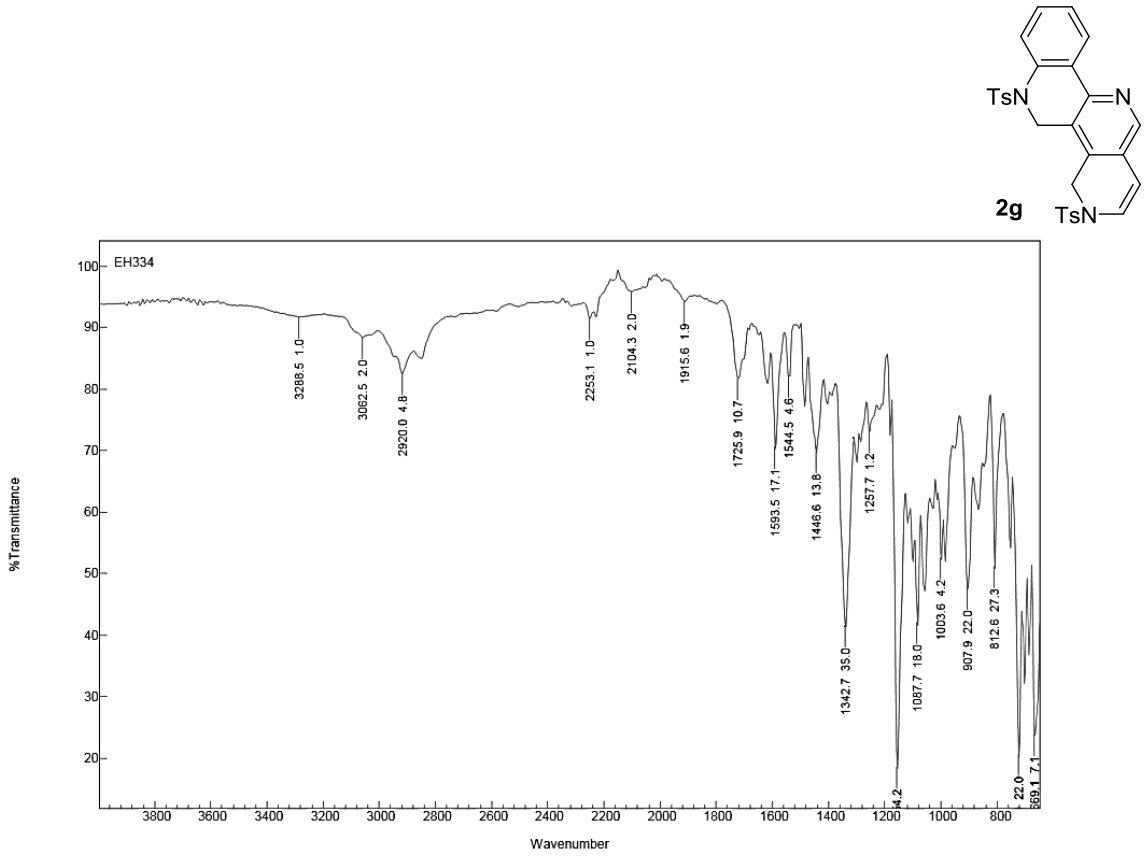


Figure S93: IR (ATR) spectrum of **2g.**

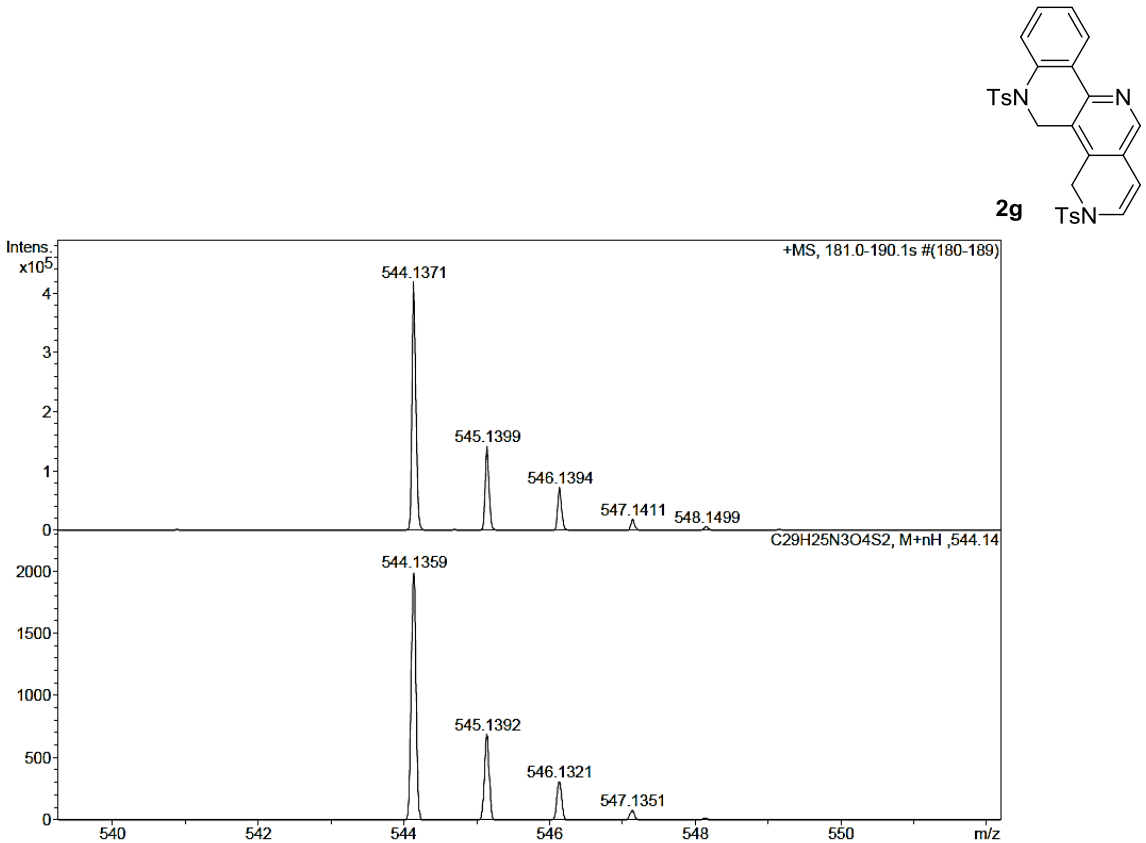
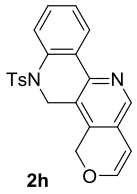


Figure S94: ESI-HRMS spectrum of **2g**.



2h

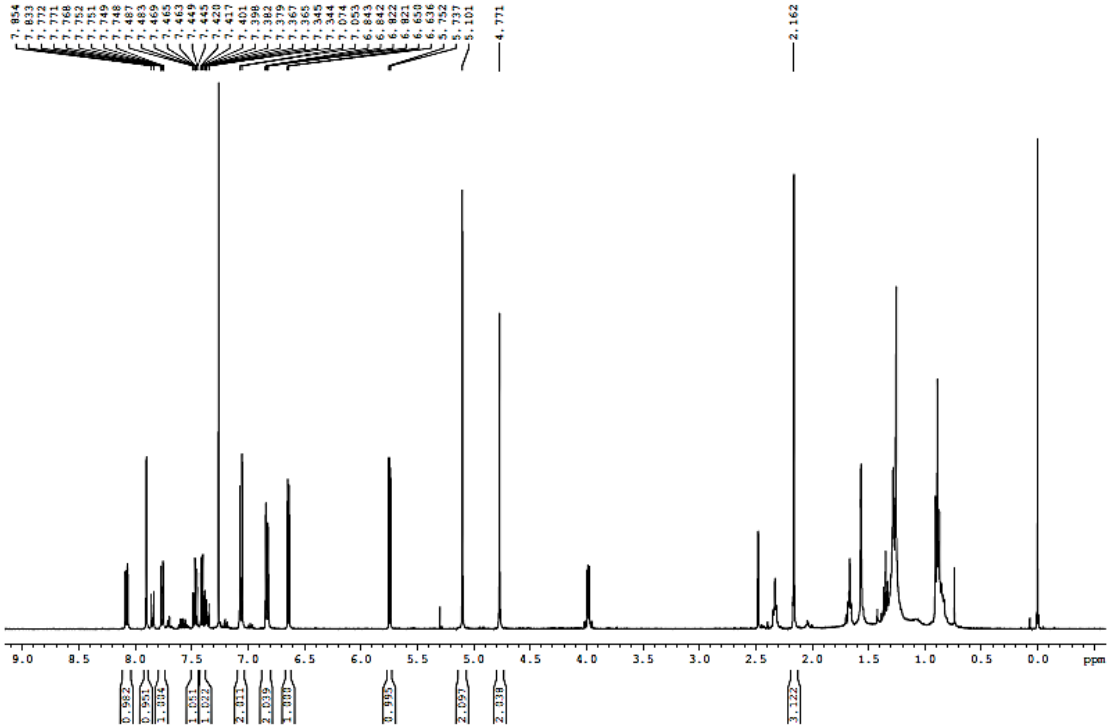
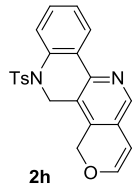


Figure S95: ^{1}H NMR spectrum (400 MHz) of **2h** in $CDCl_3$.



2h

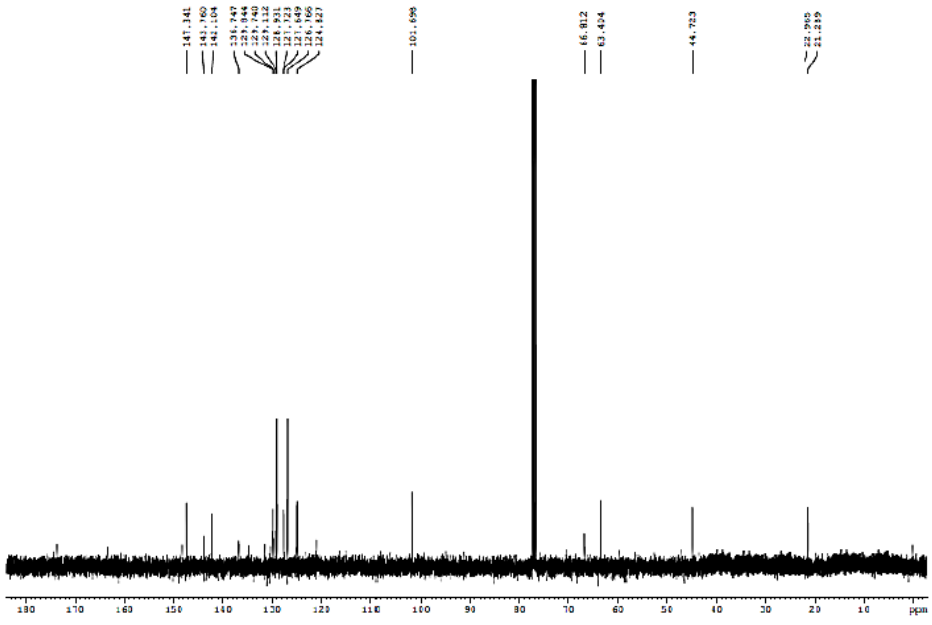
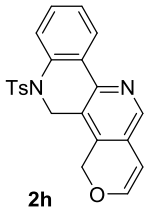


Figure S96: ^{1}H-decoupled ^{13}C NMR spectrum (100 MHz) of **2h** in $CDCl_3$.



2h

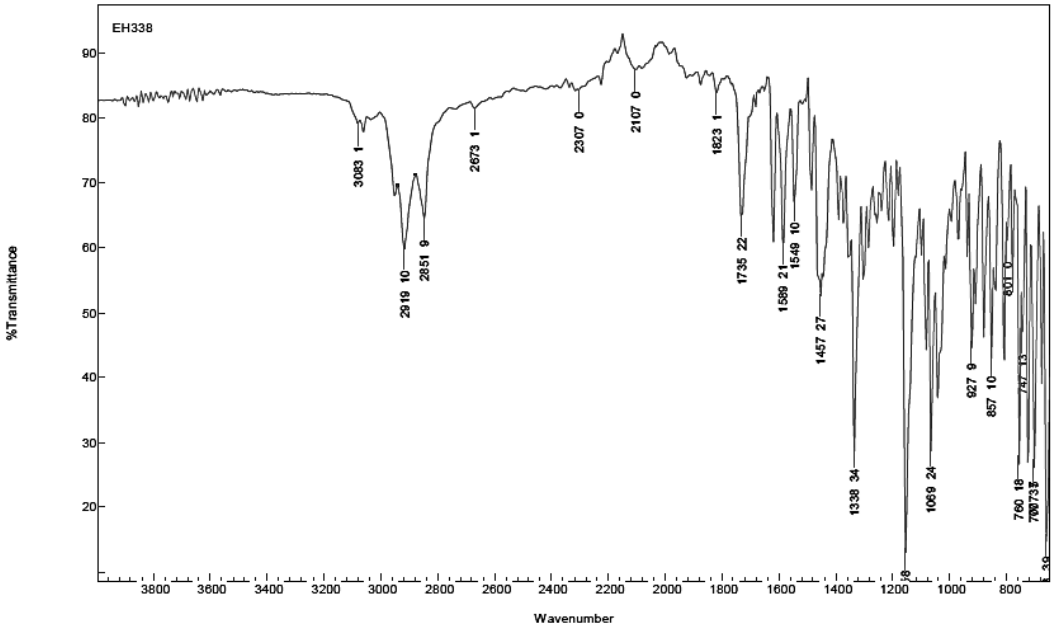
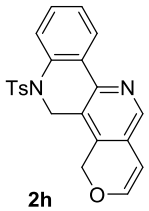


Figure S97: IR (ATR) spectrum of **2h.**



2h

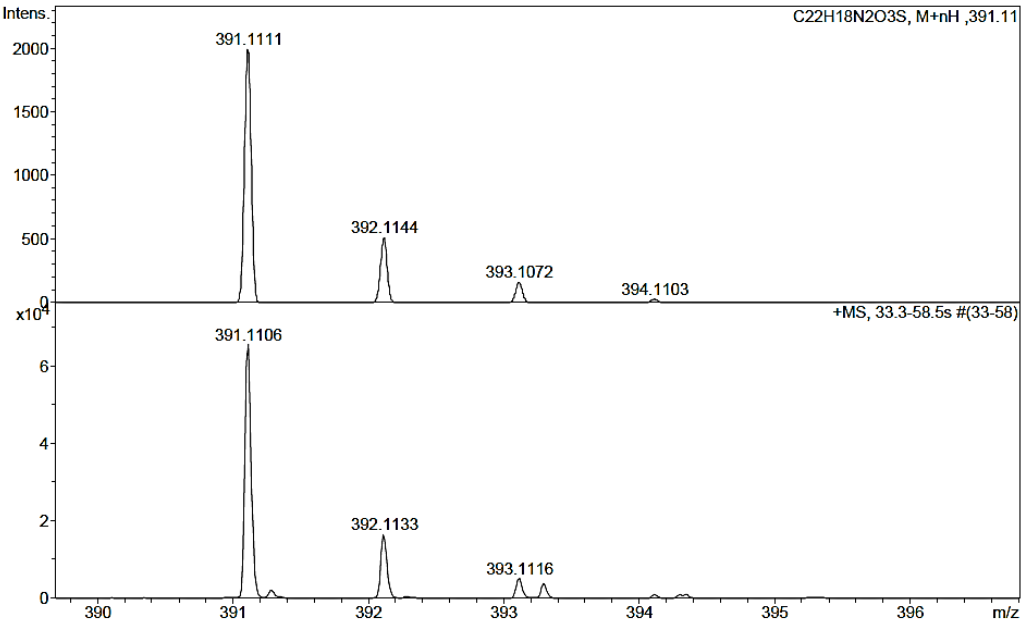


Figure S98: ESI-HRMS spectrum of **2h.**

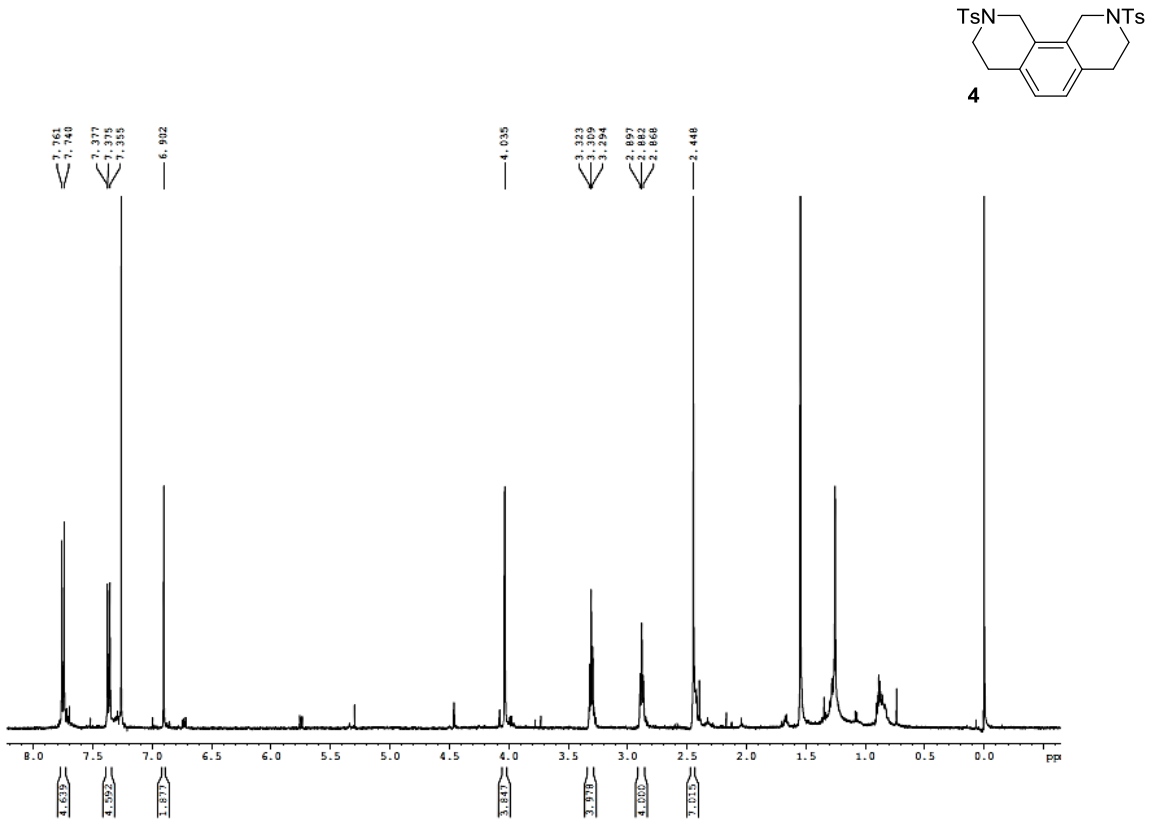


Figure S99: ^{1}H NMR spectrum (300 MHz) of **4** in $CDCl_3$.

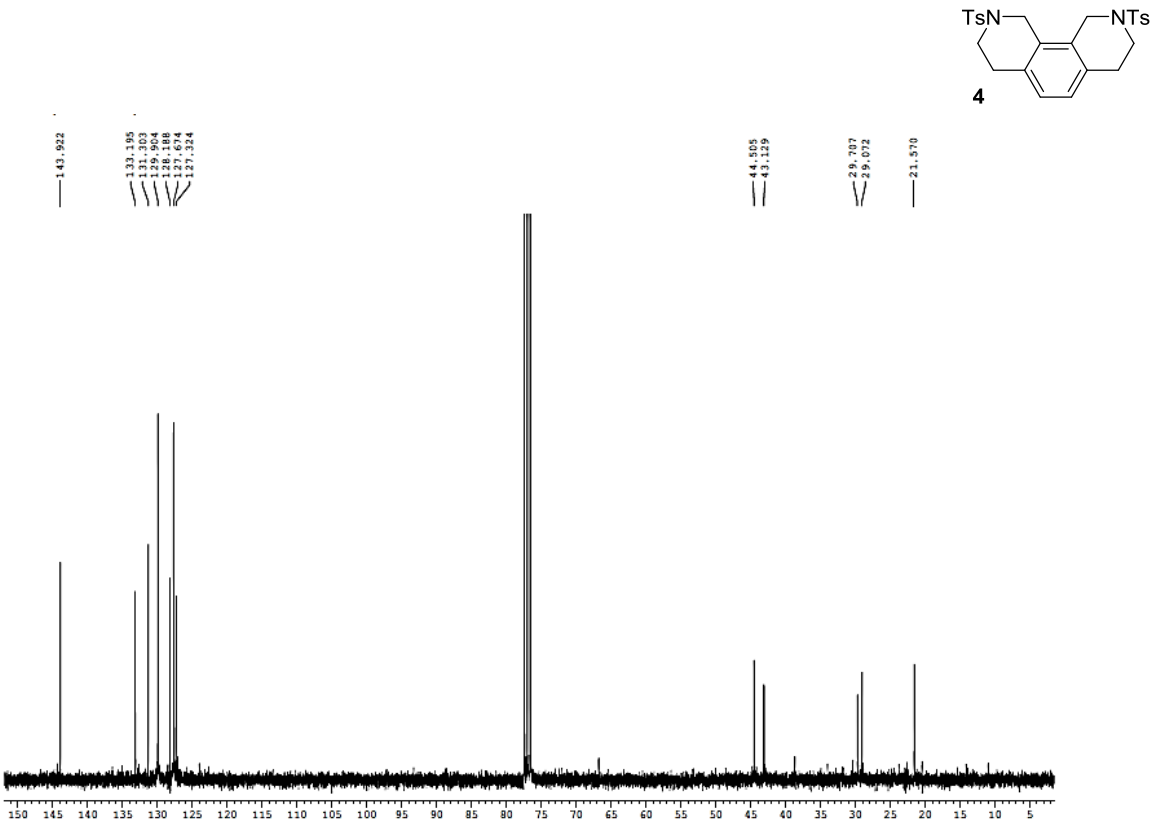
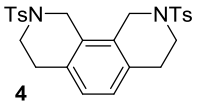


Figure S100: ^{1}H-decoupled ^{13}C NMR spectrum (75 MHz) of **4** in $CDCl_3$.



4

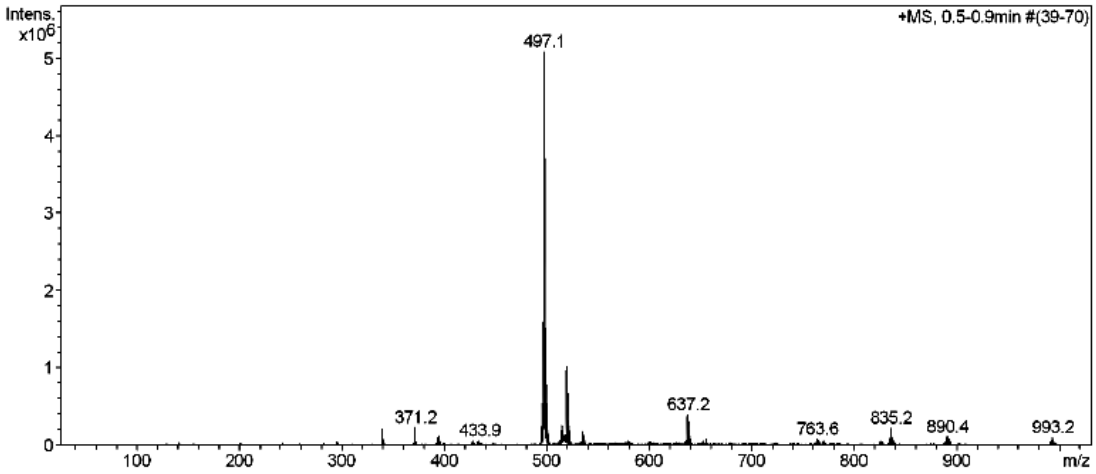
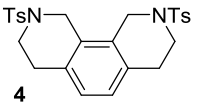


Figure S101: ESI-MS spectrum of **4.**



4

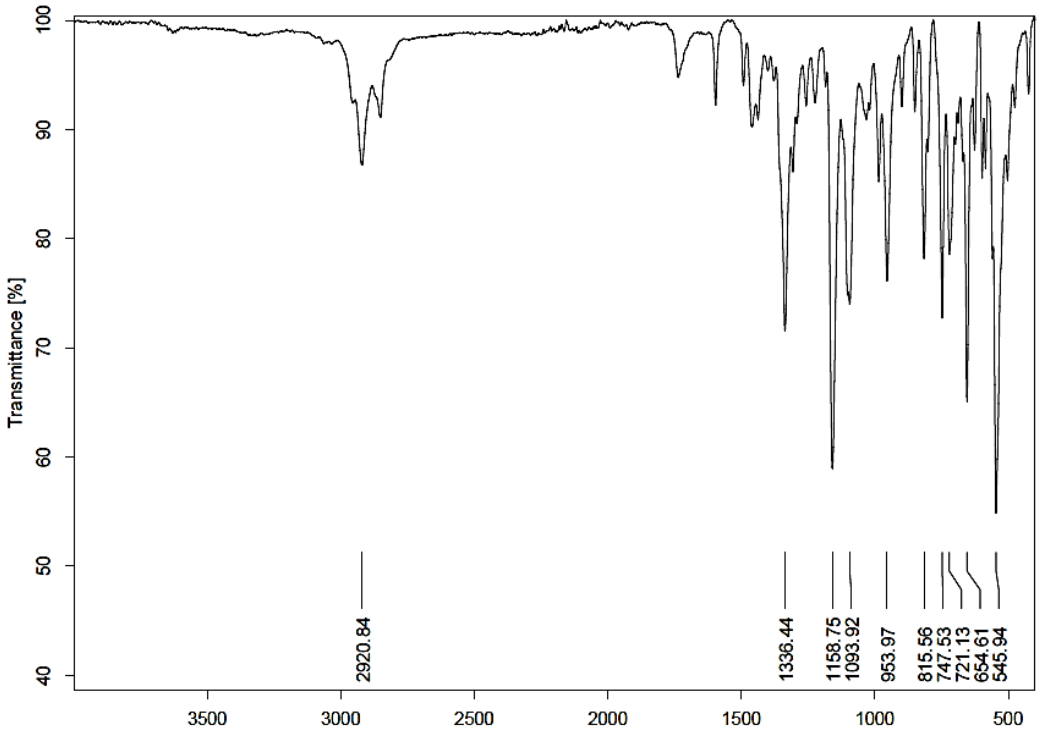
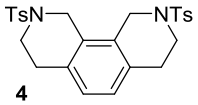


Figure S102: IR (ATR) spectrum of **4.**



4

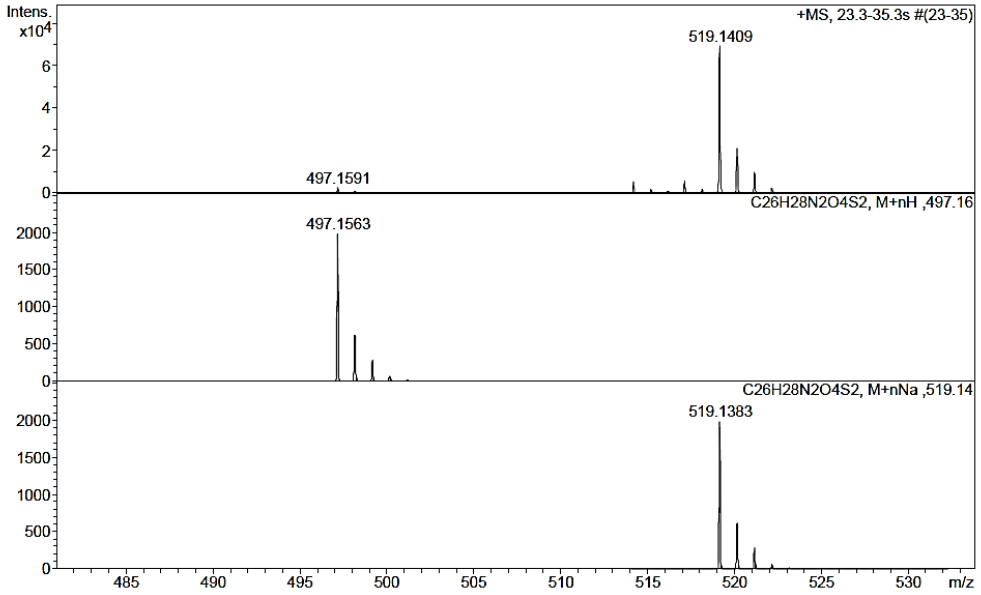
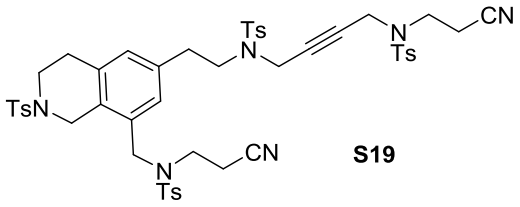


Figure S103: ESI-HRMS spectrum of **4**.



S19

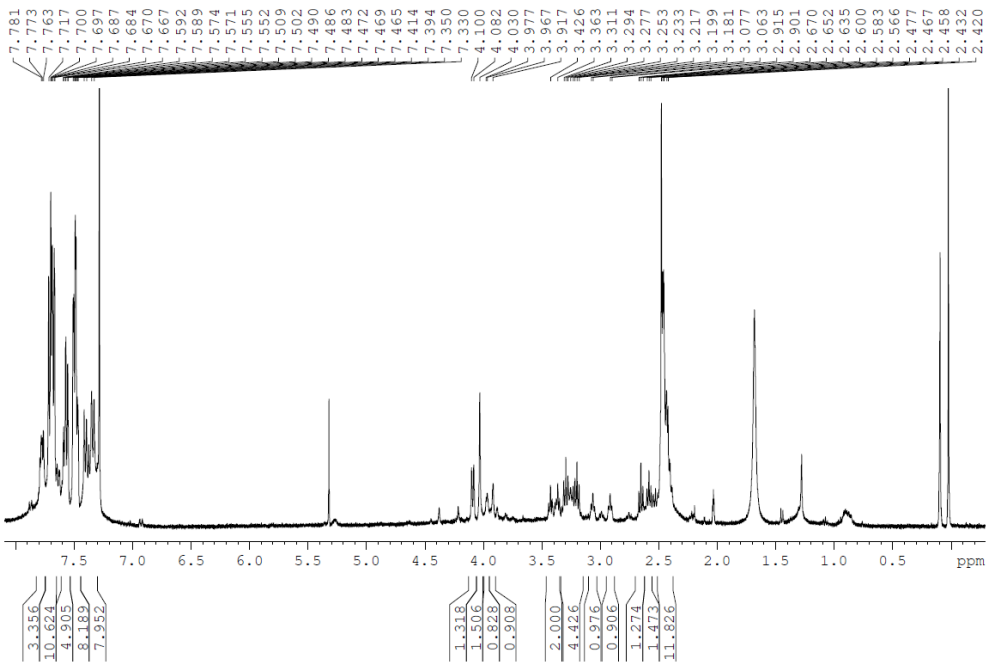
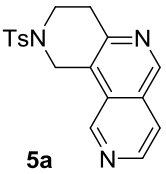


Figure S104: ^{1}H NMR spectrum (400 MHz) of **S19** in $CDCl_3$.

Spectra of 2,6-naphthyridine derivative 5a



5a

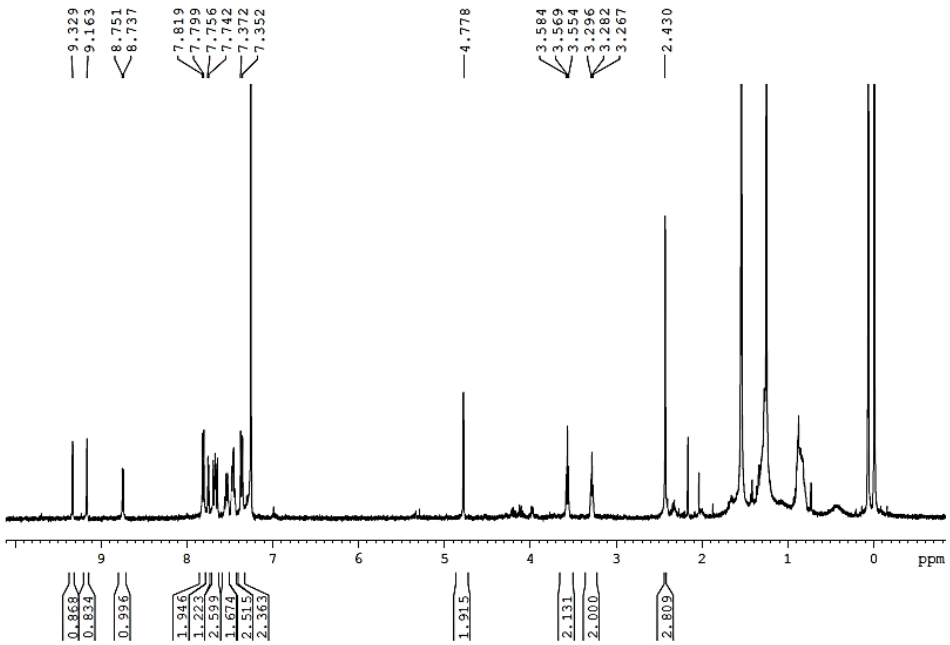
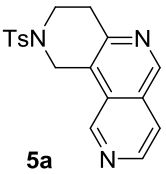


Figure S105: ^{1}H NMR spectrum (300 MHz) of **5a** in $CDCl_3$ (the sample is unpurified with Ph_3PO which was already contained in the starting material and could not be eliminated by column chromatography. This has been taken into account when calculating the yield of the reaction)



5a

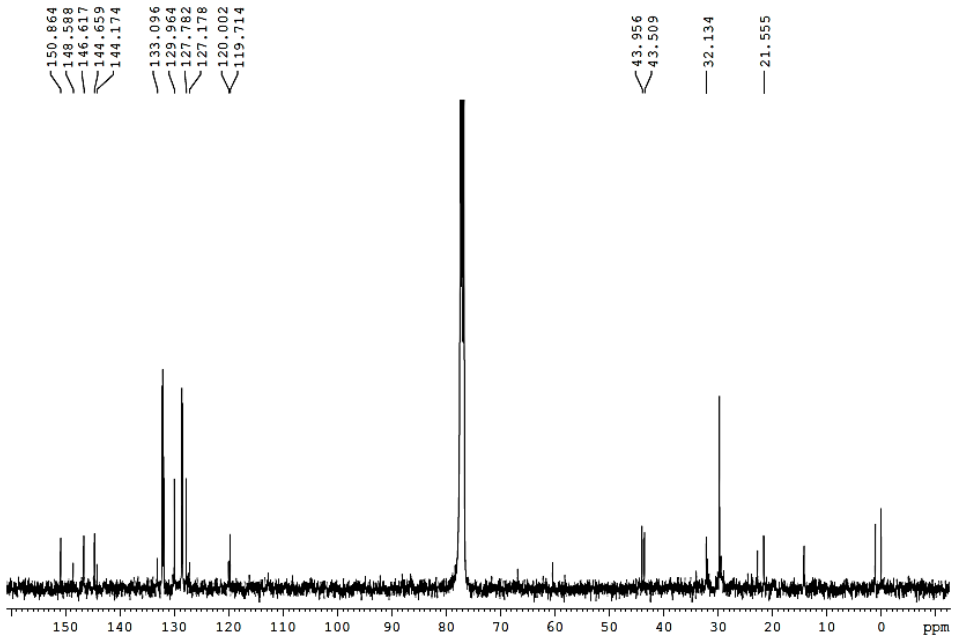
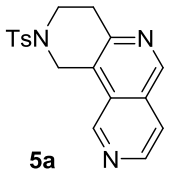


Figure 106. ^{1}H-decoupled ^{13}C NMR spectrum (75 MHz) of **5a** in $CDCl_3$.



5a

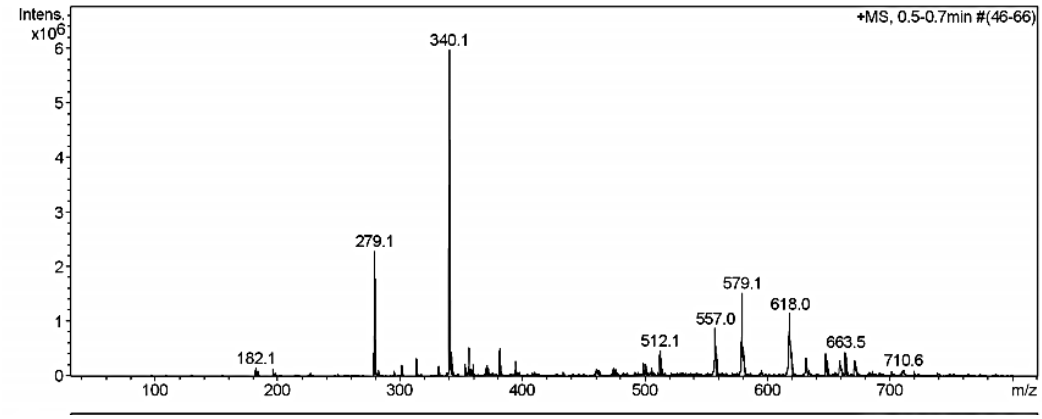
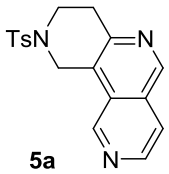


Figure S107: ESI-MS spectrum of **5a.**



5a

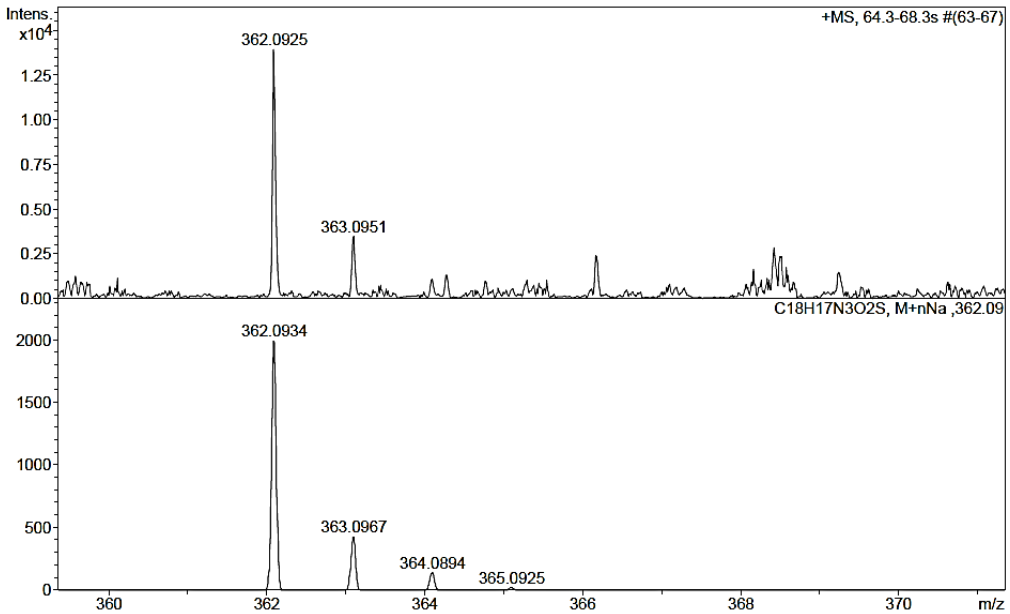


Figure S108: ESI-HRMS spectrum of **5a.**