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Supporting Information

Picolinamides and Iodoalkynes Enable Palladium-Catalyzed *syn*-Aminoalkynylation of Di- and Trisubstituted Alkenes to Give Pyrrolidines

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Contents

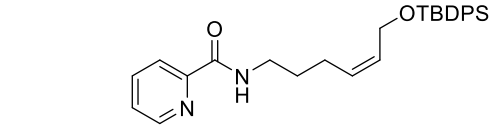
1. General Information

Unless otherwise noted, all reactions were carried out under ambient atmosphere, and all reagents were purchased from commercial suppliers (ABCR, ACROS, Sigma Aldrich, Fluka, TCI, Strem, Alfa, Combi-Blocks or Fluorochem) and used without further purification. Anhydrous solvents over molecular sieves were purchased from Acros and used as received. Analytical thin layer chromatography (TLC) was performed on Merck silica gel 60 F254 TLC glass plates and visualized with 254 nm light and potassium permanganate or ceric ammonium molybdate staining solutions followed by heating. Organic solutions were concentrated by rotary evaporation at 40 °C. Purification of reaction products was carried out by flash chromatography using Brunschwig silica 32-63, 60 Å under 0.3–0.5 bar overpressure. ^{1}H NMR spectra were recorded on a Bruker AVIII 600 MHz spectrometer with He or prodigy N_2 cryoprobes, Bruker AVIII HD 500 MHz and 400 MHz spectrometers as well as Bruker Neo 500 MHz and 400 MHz spectrometers, and are reported in ppm with the solvent resonance as the reference unless noted otherwise ($CDCl_3$ at 7.26 ppm, CD_2Cl_2 at 5.32 ppm, DMSO-d_6 at 2.50 ppm, CD_3CN at 1.94 ppm). Peaks and their apparent multiplicities (as analyzed by MestreNova) are reported as (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or unresolved, br = broad signal, coupling constant(s) in Hz, integration). ^{13}C NMR spectra were recorded with ^{1}H-decoupling on Bruker AVIII 150 MHz spectrometers with He or prodigy N_2 cryo-probes, Bruker AVIII HD 125 MHz and 100 MHz spectrometers as well as Bruker Neo 125 MHz and 100 MHz spectrometers, and are reported in ppm with the solvent resonance as the reference unless noted otherwise ($CDCl_3$ at 77.16 ppm, CD_2Cl_2 at 54.00 ppm, DMSO-d_6 at 39.52 ppm, CD_3CN at 1.32 ppm). Infrared spectra were recorded neat on a Perkin-Elmer Spectrum Two FT-IR spectrometer. The peaks are reported as absorption maxima (cm^{-1}). Optical rotations were measured on a Jasco P-2000 Polarimeter, 10 cm, 1.5 mL cell. High resolution mass spectrometric data were obtained at the mass spectrometry service operated by the Laboratory of Organic Chemistry at the ETHZ on VG-TRIBRID for electron impact ionization (EI), Varian IonSpec Spectrometer for electrospray ionization (ESI), or IonSpec Ultima Fourier Transform Mass Spectrometer for matrix-assisted laser desorption/ionization (MALDI) and are reported as (m/z). Melting point ranges were determined on a Büchi B545 Melting Point Apparatus.

2. Experimental and Characterization Data

2.1 Compounds prepared According to Literature Procedures

The following starting materials were prepared according to our previous reports:[1]



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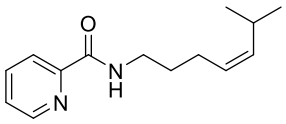

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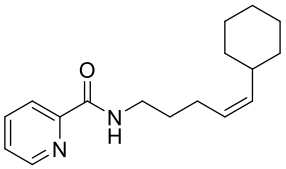

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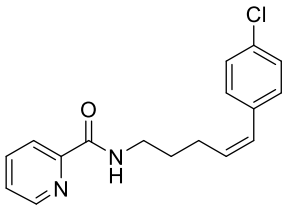

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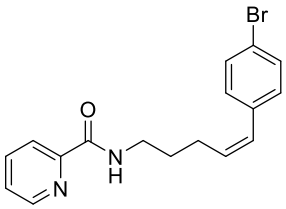

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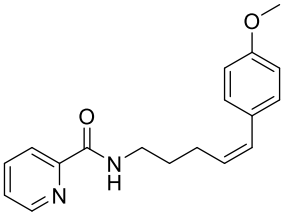

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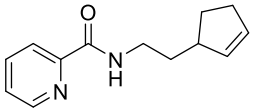

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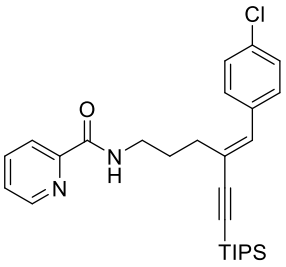

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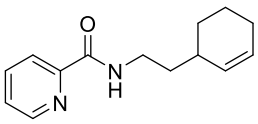
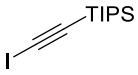


1n

The following iodoalkynes were prepared according to literature known procedures.[2,3,4]



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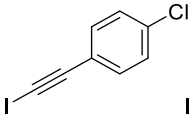

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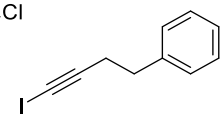

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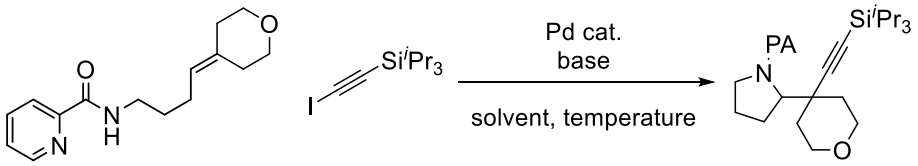
The literature references for other literature known building blocks used are given in the appropriate experimental procedures.

2.2 Reaction optimization



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

A vial (1.6 mL screw-cap vial or 7 mL microwave vial) was charged with the substrate picolinamide **1a** (0.10 mmol, 1.0 equiv), base (0.20 mmol, 2.0 equiv), Pd catalyst (0.010 mmol, 0.10 equiv) and alkyne **3** (0.12 mmol, 1.2 equiv) under ambient atmosphere. After addition of a magnetic stirring bar and the solvent (1 mL), the vial was sealed, and placed in a pre-heated heating block. The reaction was allowed to cool to room temperature, filtered through celite and concentrated under reduced pressure to give the crude alkynylated product **2a**. 1 mL $CDCl_3$ and exactly 10 µL $C_2H_2Cl_4$ were added to determine the crude yield by ^{1}H-NMR.

Standard equivalents/conditions (if not otherwise stated):

Alkyne: 1.2 equiv

Catalyst: 0.10 equiv

Base: 2.0 equiv

Concentration: 0.10 molar

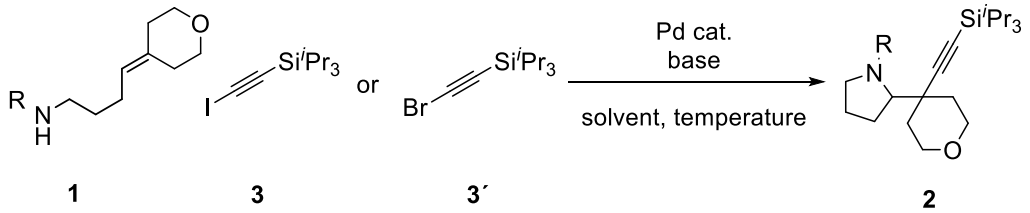
Scale: 0.10 mmol picolinamide

Table S1: Optimization conditions for the Pd-catalyzed aminoalkynylation.

Entry	Cat. (10 mol%)	Base	Solvent	Temp (°C)	Time (h)	Yield (%)*
1	$Pd(OAc)_2$	K_2CO_3	DCE	100	3	76
2	$Pd(OAc)_2$	K_2CO_3	MeCN	100	3	22
3	$Pd(OAc)_2$	K_2CO_3	Toluene	100	3	55
4	$Pd(OAc)_2$	K_2CO_3	DMSO	100	3	0
5	$Pd(OAc)_2$	Ag_2CO_3	DCE	100	3	0
6	$Pd(OAc)_2$	Ag_2CO_3	MeCN	100	3	0
7	$Pd(OAc)_2$	Ag_2CO_3	Toluene	100	3	0
8	$Pd(OAc)_2$	Ag_2CO_3	DMSO	100	3	0

9	$Pd(OAc)_2$	Na_2CO_3	DCE	100	3	19
10	$Pd(OAc)_2$	Cs_2CO_3	DCE	100	3	48
11	$Pd(OAc)_2$	NaOAc	DCE	100	3	18
12	$Pd(OAc)_2$	KO*t*Bu	DCE	100	3	48
13	$Pd(OAc)_2$	K_2CO_3	DCE	80	3	35
14	$Pd(OAc)_2$	K_2CO_3	DCE	80	24	70
15	$PdCl_2$	K_2CO_3	DCE	80	24	50
16	$Pd(dba)_2$	K_2CO_3	DCE	80	24	80
17	**$Pd(PPh_3)_2Cl_2$**	**K_2CO_3**	**DCE**	**80**	**24**	**85**
18	$Pd(dppf)Cl_2$	K_2CO_3	DCE	80	24	38

* NMR-yield



1 **3** **3´** **2**

Table S2: Optimization conditions for the Pd-catalyzed aminoalkynylation.

Entry	Pd cat.	R	Alkyne	Base	Solvent	Temp (°C)	Time (h)	Yield (%)*
1	$Pd(PPh_3)_2Cl_2$	Boc	3	K_2CO_3	DCE	80	24	0
2	**$Pd(PPh_3)_2Cl_2$**	**PA**	**3**	**K_2CO_3**	**DCE**	**80**	**24**	**85**
3	$Pd(PPh_3)_2Cl_2$	Boc	3´	K_2CO_3	DCE	80	24	0
4	$Pd(dba)_2$, DPE-PHOS	Boc	3	NaO*t*Bu	Toluene	70	3	0
5	$Pd(dba)_2$, DPE-PHOS	Boc	3’	NaO*t*Bu	Toluene	70	3	0

* NMR-yield

Complementary reactivity caused by the use of bromo or iodo alkynes: Aminoalkynylation vs C–H alkynylation of olefins

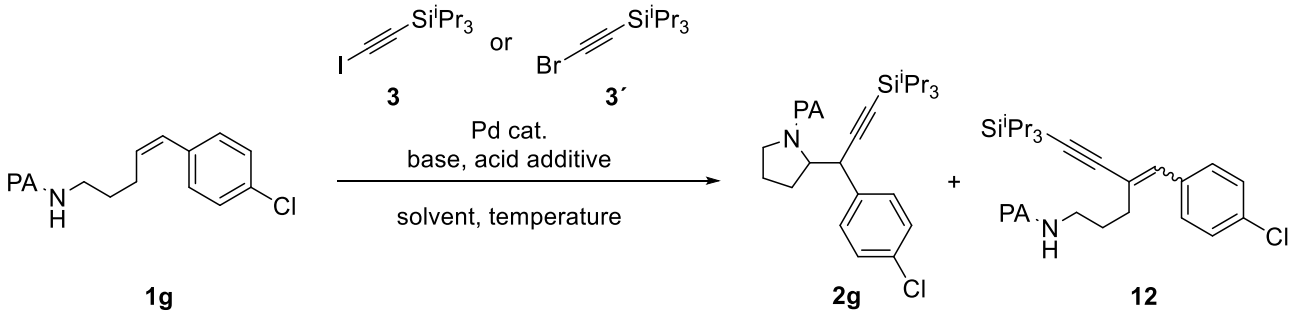


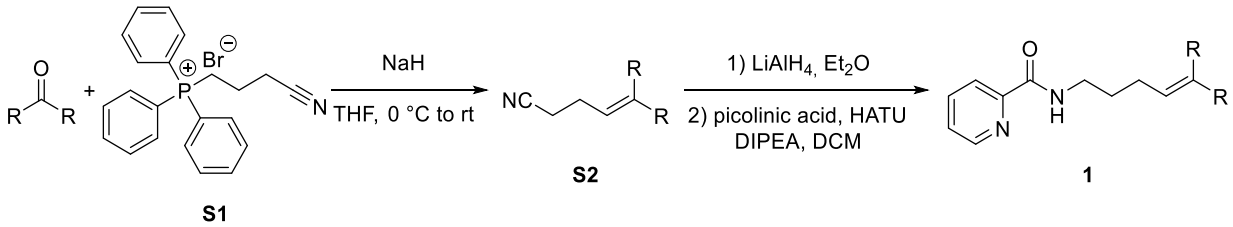
Table S3: Conditions for the Pd-catalyzed aminoalkynylation and for C–H alkynylation.

Entry	Cat. (mol%)	Alkyne	Base	Acid Additive	Solvent	Temp (°C)	Time (h)	Yield **2g** (%)	Yield **12** (%)
1	$Pd(PPh_3)_2Cl_2$ (10)	**3**	K_2CO_3	-	DCE	80	24	97[a]	0
2	$Pd(OAc)_2$ (10)	**3**	K_2CO_3	PivOH	DCE	100	3	79[b]	0
3	$Pd(OAc)_2$ (10)	**3´**	K_2CO_3	PivOH	DCE	100	6	0	86[c]

[a] isolated yield on 0.3 mmol scale; [b] isolated yield (0.1 mmol scale); [c] NMR-yield (0.1 mmol scale)

Additional reaction conditions for the C–H alkynylation of olefins can be found in our previous report.[1]

2.3 Synthesis of Starting Materials



General procedure for Wittig reactions (general procedure 1)

To a suspension of sodium hydride (60 wt% in mineral oil, 1.2 equiv) in THF (0.3 M) was added a solution of (3-cyanopropyl)triphenylphosphonium bromide **S1** (1.0 equiv) in THF at 0 °C. The reaction was stirred at 0 °C for 1 h before the aldehyde or ketone (1.1 equiv) was added in one portion. The reaction was stirred an additional 30 min at 0 °C, 20 h at room temperature, and then poured into rapidly stirred hexanes. The resulting mixture was filtered through a silica plug (washed with the indicated eluent), concentrated and purified by flash column silica gel chromatography using the indicated solvent system.

General procedure for nitrile reductions (general procedure 2)

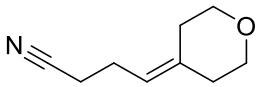
To a suspension of lithium aluminium hydride (1.5 equiv) in diethyl ether (0.3 M) under N_2 at 0 °C was slowly added a solution of nitrile **S2** (1.0 equiv, dissolved in a small volume of diethyl ether). After 15 min the reaction was allowed to warm to room temperature and stirred for an additional 90 min. The reaction was re-cooled to 0 °C, diluted with wet diethyl ether (technical grade, ca 5-10 times the reaction volume), quenched by slow addition of H_2O (1 mL per g $LiAlH_4$ used), aq. NaOH (15%, 1 mL NaOH per g $LiAlH_4$ used) and H_2O (3 mL per g $LiAlH_4$ used). The mixture was warmed to room temperature and stirred for 15 min, then sodium sulfate was added and stirred for additional 15 min. The resulting mixture was filtered through celite and concentrated under reduced pressure. The resulting crude product was used for the next step without further purification.

General procedure for HATU couplings (general procedure 3)

To a solution of amine (1.0 equiv) in DCM (0.2 M) was added 2-picolinc acid (1.1 equiv), *N,N*-diisopropylethylamine (2.0 equiv) and HATU (1.1 equiv) in this order. The reaction was stirred at room temperature for 2 h, quenched with a 1:1 mixture of

brine and sat. aq. $NaHCO_3$, extracted with DCM (2x), dried over Na_2SO_4 and concentrated. The crude residue was purified by flash column silica gel chromatography using the indicated solvent system.

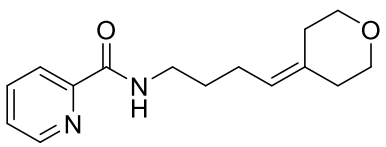
4-(Tetrahydro-4*H*-pyran-4-ylidene)butanenitrile (S2a)



In a flame-dried round-bottom flask under N_2 sodium hydride (60 wt% in mineral oil, 750 mg, 31.3 mmol,1.44 equiv) was suspended in anhydrous THF (100 mL). The reaction was cooled to 0 °C, (3-cyanopropyl)triphenylphosphonium bromide **S1** (10.7 g, 26.1 mmol, 1.20 equiv) was added in portions. The reaction was allowed to warm to room temperature and stirred for 1 h. The reaction was re-cooled to 0 °C, tetrahydro-*4H*-pyran-4-one (2.18 g, 21.7 mmol, 1.00 equiv) was added, and the reaction was allowed to warm to room temperature and stirred for 12 h. The reaction was poured into 200 mL rapidly stirred hexanes, the resulting mixture was filtered through a silica plug (washed with 7:3 Hex/EtOAc), concentrated and purified by flash column silica gel chromatography (7:3 Hex/EtOAc) to afford a pale yellow oil (2.07 g, 13.7 mmol, 63%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.24 – 5.17 (m, 1H), 3.71 – 3.65 (m, 4H), 2.41 – 2.33 (m, 4H), 2.32 – 2.20 (m, 4H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 138.6, 119.5, 118.8, 69.5, 68.8, 37.0, 29.9, 23.1, 18.1; **FT IR** (neat) 3420, 2953, 2863, 1716, 1383, 1217, 1095, 1025, 838, 760, 538 cm^{-1}; **HRMS** (ESI) *m/z* calculated for $C_9H_{14}NO$ $[M+H]^+$ 152.1070, found 152.1066; **TLC**: R_f = 0.28 (7:3 Hex/EtOAc).

***N*-(4-(Tetrahydro-4*H*-pyran-4-ylidene)butyl)picolinamide (1a)**

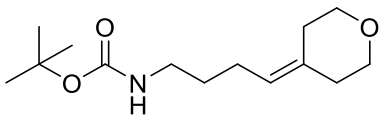


The title compound was prepared according to general procedures 2 and 3 from 4-(tetrahydro-4*H*-pyran-4-ylidene)butanenitrile **S2a** (2.50 g, 16.5 mmol). The crude

product was purified by flash column chromatography (9:1 to 1:1 Hex/EtOAc) to afford a pale yellow oil (1.99 g, 7.64 mmol, 54%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.22 (dt, *J* = 7.8, 1.1 Hz, 1H), 8.11 (s, 1H), 7.87 (td, *J* = 7.7, 1.7 Hz, 1H), 7.45 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 5.30 – 5.04 (m, 1H), 3.76 – 3.63 (m, 4H), 3.62 – 3.29 (m, 2H), 2.29 (td, *J* = 5.5, 1.3 Hz, 2H), 2.23 (ddt, *J* = 6.1, 5.1, 1.0 Hz, 2H), 2.16 (q, *J* = 7.3 Hz, 2H), 1.97 – 1.48 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 164.3, 150.1, 148.1, 137.6, 135.3, 126.2, 122.4, 122.3, 69.8, 68.9, 39.2, 37.1, 29.9, 29.9, 24.6; **FT-IR** (neat) 3381, 2955, 2856, 1671, 1590, 1569, 1526, 1465, 1434, 1230, 1099. 997, 749, 666, 620, 407 cm^{-1}; **HRMS** (ESI) *m/z* calculated for $C_{15}H_{20}N_2NaO_2$ $[M+Na]^+$ 283.1417, found 283.1414; **TLC**: R_f = 0.43 (1:1 Hex/EtOAc).

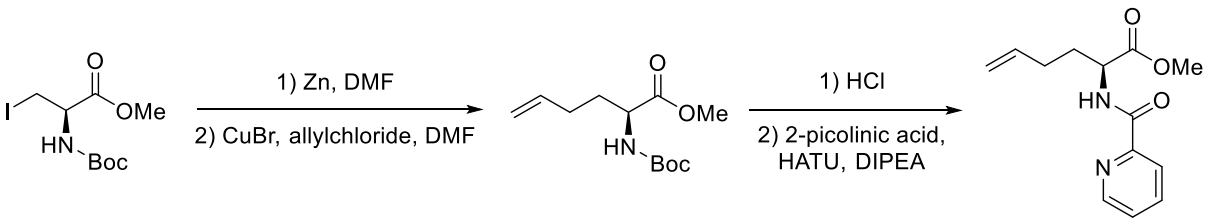
tert-Butyl (4-(tetrahydro-4*H*-pyran-4-ylidene)butyl)carbamate (1a`)



Crude amine, prepared according to general procedure 2 from 4-(tetrahydro-4*H*-pyran-4-ylidene)butanenitrile **S2a** (990 mg, 6.44 mmol, 1.00 equiv), was dissolved in THF (30 mL) and water (30 mL). $NaHCO_3$ (1.62 g, 19.3 mmol, 3.00 equiv) and Boc_2O (1.69 g, 7.73 mmol, 1.20 equiv) were added and the resulting mixture was stirred overnight. The organic layer was separated and the aqueous layer was extracted with dichloromethane (3 x 30 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by flash column chromatography (7:3 Hex/EtOAc) to afford a colorless oil (1.25 g, 4.91 mmol, 76%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.14 (tt, *J* = 7.3, 1.3 Hz, 1H), 4.57 (s, 1H), 3.62 (dt, *J* = 8.6, 5.5 Hz, 4H), 3.08 (t, *J* = 7.2 Hz, 2H), 2.22 (td, *J* = 5.6, 1.3 Hz, 2H), 2.19 – 2.12 (m, 2H), 2.01 (q, *J* = 7.4 Hz, 2H), 1.50 (p, *J* = 7.3 Hz, 2H), 1.41 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.1, 135.1, 122.4, 79.1, 69.7, 68.8, 40.3, 37.0, 30.3, 29.8, 28.5, 24.3; **FT-IR** (neat) 3345, 2931, 2846, 1691, 1520, 1364, 1249, 1165, 1099, 849, 663 cm^{-1}; **HRMS** (ESI) *m/z* calculated for $C_{14}H_{25}NNaO_3$ $[M+Na]^+$ 278.1727, found 278.1725; **TLC**: R_f = 0.50 (7:3 Hex/EtOAc).

Methyl (S)-2-(picolinamido)hex-5-enoate (1c)



Based on a literature procedure[5], a solution of methyl (*R*)-2-((*tert*-butoxycarbonyl)amino)-3-iodopropanoate (1.50 g, 4.56 mmol, 1.00 equiv) in DMF (5 mL) was added under nitrogen atmosphere dropwise to a flame dried flask containing activated zinc (1.19 g, 18.2 mmol, 4.00 equiv, zinc was activated by washing with diluted HCl, H_2O and Et_2O) at 0 °C. After 3 h of stirring at room temperature, the solids were allowed to settle to the bottom of the flask. The solution was then carefully transferred by syringe into another flame dried flask containing a suspension of copper(I) bromide (130 mg, 910 µmol, 0.200 equiv) and allyl chloride (590 mg, 7.75 mmol, 1.70 equiv) in DMF (20 mL) at –15 °C. After complete addition, the reaction mixture was allowed to warm to room temperature and stirred overnight. Then, EtOAc (10 mL) was added and stirring was continued for 15 min. The organic layer was washed with H_2O (10 mL), 1 M $Na_2S_2O_3$ (2 x 10 mL), H_2O (2 x 10 mL) and brine (2 x 10 mL) and dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography (4:1 Hex/EtOAc) to afford a colorless oil (800 mg, 3.30 mmol, 73%). The obtained characterization data were in agreement with the literature.[5]

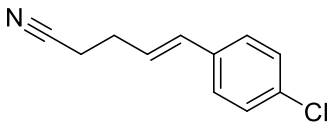
A flame dried flask was charged with a solution of boc-protected amine (400 mg, 1.64 mmol, 1.00 equiv) in dichloromethane (10 mL). A solution of hydrogen chloride (2.0 M in Et_2O, 8.20 mL, 10.0 equiv) was added dropwise at 0 °C and the resulting solution was stirred for 2 h and allowed to warm to room temperature. Then, the solution was concentrated in vacuo to afford crude amine as a colorless solid, which was used in the next step without further purification.

The crude amine (300 mg, 1.64 mmol, 1.00 equiv) was dissolved in dichloromethane (8.0 mL). 2-Picolinic acid (220 mg, 1.81 mmol, 1.10 equiv), *N*,*N*-diisopropylethylamine (920 µL, 5.43 mmol, 3.30 equiv) and then HATU (690 mg, 1.81 mmol, 1.10 equiv) were added. The resulting solution was stirred overnight at room temperature. The reaction was quenched with a 1:1 mixture of brine and sat. aq. $NaHCO_3$, extracted with

dichloromethane, dried over Na_2SO_4 and concentrated. The crude residue was purified by flash column silica (4:1 to 7:3 Hex/EtOAc) to afford a white solid (340 mg, 1.35 mmol, 82% over 2 steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 8.52 (s, 1H), 8.21 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.88 (td, *J* = 7.7, 1.7 Hz, 1H), 7.47 (ddd, *J* = 7.6, 4.8, 1.3 Hz, 1H), 5.84 (ddt, *J* = 16.9, 10.2, 6.4 Hz, 1H), 5.14 – 5.06 (m, 1H), 5.06 – 5.00 (m, 1H), 4.91 – 4.68 (m, 1H), 3.80 (s, 3H), 2.25 – 2.17 (m, 2H), 2.17 – 2.06 (m, 1H), 2.03 – 1.89 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.7, 164.2, 149.5, 148.3, 137.6, 137.0, 126.5, 122.6, 115.9, 52.5, 52.0, 32.0, 29.7; **FT-IR** (neat) 3382, 2953, 1743, 1678, 1516, 1434, 1212, 997, 916, 750, 620 cm^{-1}; **HRMS** (ESI) *m/z* calculated for $C_{13}H_{16}N_2NaO_3$ $[M+Na]^+$ 271.1053, found 271.1051; **TLC**: R_f = 0.38 (7:3 Hex/EtOAc); R_f = 0.38; $[\alpha]_D^{25}$ = +33.2 (c = 1.03 in $CHCl_3$); **Melting point**: 39.6 – 40.5 °C.

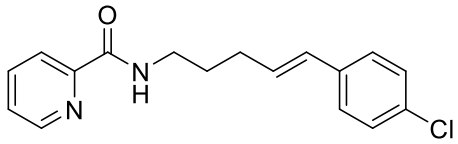
(*E*)-5-(4-Chlorophenyl)pent-4-enenitrile (S2h)



The title compound was prepared according to general procedure 1 from (3-cyanopropyl)triphenylphosphonium bromide **S1** (13.4 g, 32.5 mmol, 1.00 equiv) and 4-chlorobenzaldehyde (5.02 g, 35.8 mmol, 1.10 equiv) in 100 mL THF. After stirring for 20 h, the reaction mixture was poured into rapidly stirred hexanes (300 mL) and filtered through a silica plug (washed with Hex/EtOAc 4:1). The solution was concentrated *in vacuo* and the crude product was purified by flash column silica gel chromatography (4:1 Hex/EtOAc) to afford a colorless oil (250 mg, 1.30 mmol, 4%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (s, 4H), 6.47 (dt, *J* = 15.7, 1.4 Hz, 1H), 6.16 (dt, *J* = 15.8, 6.6 Hz, 1H), 2.60 – 2.40 (m, 4H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 134.9, 133.2, 131.7, 128.6, 127.4, 126.0, 118.9, 28.6, 17.3; **FT-IR** (neat) 3049, 2933, 2242, 1489, 1090, 971, 857, 812, 678, 513 cm^{-1}; **HRMS** (EI) *m/z* calculated for $C_{11}H_{10}NCl$ $[M]^+$ 191.0496, found 191.0495; **TLC**: R_f = 0.31 (5:1 Hex/EtOAc).

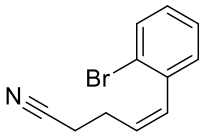
(*E*)-*N*-(5-(4-Chlorophenyl)pent-4-en-1-yl)picolinamide (1h)



The title compound was prepared according to general procedures 2 and 3 from (*E*)-5-(4-chlorophenyl)pent-4-enenitrile **S2h** (0.25 g, 1.3 mmol). The crude product was purified by flash column chromatography (Hex/EtOAc 1:1) to afford a colorless oil (0.23 g, 0.75 mmol, 57%).

^{1}H NMR (500 MHz, $CDCl_3$)) δ 8.52 (dtd, *J* = 4.8, 2.2, 1.0 Hz, 1H), 8.22 (ddt, *J* = 7.8, 1.9, 1.1 Hz, 1H), 8.15 (s, 1H), 7.92 – 7.79 (m, 1H), 7.48 – 7.39 (m, 1H), 7.26 (t, *J* = 1.7 Hz, 4H), 6.40 (ddd, *J* = 15.9, 2.7, 1.4 Hz, 1H), 6.32 – 6.15 (m, 1H), 3.72 – 3.42 (m, 2H), 2.45 – 2.23 (m, 2H), 1.85 (pd, *J* = 7.2, 2.2 Hz, 2H);**^{13}C NMR** (126 MHz, $CDCl_3$) δ 164.1, 149.8, 147.9, 137.2, 136.0, 132.3, 130.3, 129.3, 128.4, 127.1, 126.0, 122.0, 38.9, 30.4, 29.1; **HRMS** (ESI): *m/z* calc. for $C_{17}H_{18}ClN_2O^+$ $[M+H]^+$ 301.1102, found 301.1099; **TLC**: R_f = 0.20 (2:1 Hex/EtOAc).

(*Z*)-5-(2-Bromophenyl)pent-4-enenitrile (S2j)

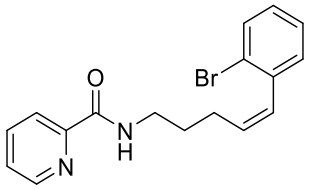


The title compound was prepared according to general procedure 1 from (3-cyanopropyl)triphenylphosphonium bromide **S1** (7.40 g, 18.0 mmol, 1.00 equiv) and 2-bromobenzaldehyde (3.66 g, 19.8 mmol, 1.10 equiv) in 60 mL THF. After stirring for 20 h, the reaction mixture was poured into rapidly stirred hexanes (80 mL) and filtered through a silica plug (washed with Hex/EtOAc 5:1). The solution was concentrated *in vacuo* and the crude product was purified by flash column silica gel chromatography (5:1 Hex/EtOAc) to afford a colorless oil (2.16 g, 9.15 mmol, 51%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.32 (td, *J* = 7.5, 1.3 Hz, 1H), 7.25 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.17 (tdd, *J* = 7.2, 1.9, 0.6 Hz, 1H), 6.65 (d, *J* = 11.3 Hz, 1H), 5.80 (dt, *J* = 11.4, 7.2 Hz, 1H), 2.58 – 2.50 (m, 2H), 2.47 – 2.40 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 136.8, 132.9, 132.0, 130.4, 129.1, 128.9, 127.3,

123.9, 119.2, 24.5, 17.4; **FT-IR** (neat) 3063, 3019, 2958, 2926, 2855, 2245, 1589, 1560, 1467, 1431, 1325, 1260, 1193, 1118 1025, 761, 739 cm^{-1}; **HRMS** (ESI): *m/z* calc. for $C_{11}H_{10}BrNNa^+$ $[M+Na]^+$ 257.9889, found 257.9892; **TLC**: R_f = 0.30 (5:1 Hex/EtOAc).

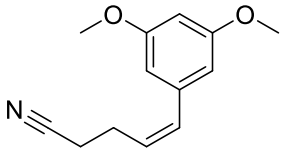
(*Z*)-*N*-(5-(2-Bromophenyl)pent-4-en-1-yl)picolinamide (1j)



The title compound was prepared according to general procedures 2 and 3 from 4-(*Z*)-5-(2-bromophenyl)pent-4-enenitrile **S2j** (2.16 g, 9.15 mmol). The crude product was purified by flash column chromatography (Hex/EtOAc 1:1) to afford an orange oil (2.30 g, 6.66 mmol, 72%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 4.7 Hz, 1H), 8.17 (d, *J* = 7.8 Hz, 1H), 8.03 (s, 1H), 7.86 – 7.78 (m, 2H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.40 (m, 1H), 7.28 – 7.18 (m, 1H), 7.08 (t, *J* = 7.6 Hz, 1H), 6.49 (d, *J* = 11.4 Hz, 1H), 5.80 (dt, *J* = 11.4, 7.5 Hz, 1H), 3.46 (dt, *J* = 7.3, 6.8 Hz, 2H), 2.28 (td, *J* = 7.4 Hz, 2H), 1.77 (p, *J* = 7.3 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.4, 150.1, 148.1, 137.5, 137.4, 132.7, 132.7, 130.6, 129.6, 128.4, 127.0, 126.1, 124.1, 122.2, 39.0, 29.6, 25.9; **FT-IR** (neat) 3384, 3056, 3012, 2982, 2862, 1731, 1674, 1590, 1569, 1524, 1465, 1433, 1372, 1348, 1043, 1025, 997, 750 cm^{-1}; **HRMS** (ESI): *m/z* calc. for $C_{17}H_{18}BrN_2O^+$ $[M+H]^+$ 345.0597, found 345.0597; **TLC**: R_f = 0.60 (1:1 Hex/EtOAc).

(*Z*)-5-(3,5-Dimethoxyphenyl)pent-4-enenitrile (S2l)

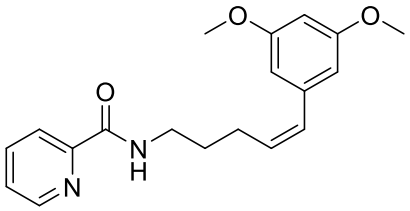


The title compound was prepared according to general procedure 1 from (3-cyanopropyl)triphenylphosphonium bromide **S1** (4.12 g, 10.0 mmol, 1.00 equiv) and 3,5-dimethoxybenzaldehyde (1.83 g, 11.0 mmol, 1.10 equiv) in 30 mL THF. After

stirring for 20 h, the reaction mixture was poured into rapidly stirred hexanes (80 mL) and filtered through a silica plug (washed with Hex/EtOAc 4:1). The solution was concentrated *in vacuo* and the crude product was purified by flash column silica gel chromatography (4:1 Hex/EtOAc) to afford a colorless oil (1.32 g, 6.08 mmol, 60%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.56 (d, *J* = 11.5 Hz, 1H), 6.38 (m, 3H), 5.65 (dt, *J* = 11.5, 7.2 Hz, 1H), 3.80 (s, 6H), 2.67 (m, *J* = 7.2, 1.8 Hz, 2H), 2.44 (t, *J* = 7.1 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 160.9, 138.6, 132.4, 128.1, 119.3, 106.9, 99.3, 55.5, 24.6, 17.7; **FT-IR** (neat) 3308, 2939, 2838, 2246, 1590, 1456, 1426, 1313, 1291, 1204, 1156, 1067, 908, 850, 729 cm^{-1}; **HRMS** (ESI): *m/z* calc. for $C_{13}H_{16}NO_2^+$ $[M+H]^+$ 218.1176, found 218.1176; **TLC**: R_f = 0.38 (4:1 Hex/EtOAc).

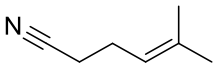
(*Z*)-*N*-(5-(3,5-Dimethoxyphenyl)pent-4-en-1-yl)picolinamide (1l)



The title compound was prepared according to general procedures 2 and 3 from (*Z*)-5-(3,5-dimethoxyphenyl)pent-4-enenitrile **S2l** (1.20 g, 5.50 mmol). The crude product was purified by flash column chromatography (Hex/EtOAc 3:2) to afford a yellow oil (1.17 g, 3.59 mmol, 65%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.17 (dt, *J* = 7.9, 1.1 Hz, 1H), 8.05 (s, 1H), 7.83 (td, *J* = 7.7, 1.7 Hz, 1H), 7.40 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 6.41 (m, 3H), 6.33 (t, *J* = 2.3 Hz, 1H), 5.68 (dt, *J* = 11.7, 7.3 Hz, 1H), 3.77 (s, 6H), 3.49 (td, *J* = 7.2, 6.2 Hz, 2H), 2.45 (qd, *J* = 7.4, 1.8 Hz, 2H), 1.79 (p, *J* = 7.3 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.4, 160.7, 150.1, 148.1, 139.5, 137.4, 132.1, 129.9, 126.2, 122.2, 106.9, 99.1, 55.4, 39.1, 29.9, 26.2; **FT-IR** (neat) 3383, 3057, 3006, 2936, 2837, 1672, 1589, 1525, 1525, 1462, 1431, 1310, 1289, 1204, 1155, 1064, 1064, 997, 929, 844 cm^{-1}; **HRMS** (ESI): *m/z* calc. for $C_{19}H_{22}N_2NaO_3^+$ $[M+Na]^+$ 349.1523, found 349.1519; **TLC**: R_f = 0.30 (3:2 Hex/EtOAc).

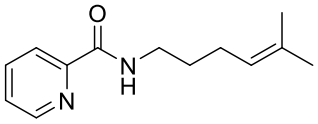
5-Methylhex-4-enenitrile (S2o)



In a flame-dried round-bottom flask under N_2 sodium hydride (60 wt% in mineral oil, 290 mg, 12.0 mmol,1.20 equiv) was suspended in anhydrous THF (46 mL). The reaction was cooled to 0 °C, (3-cyanopropyl)triphenylphosphonium bromide **S1** (4.10 g, 10.0 mmol, 1.00 equiv) was added in portions. The reaction was allowed to warm to room temperature and stirred for 1 h. The reaction was re-cooled to 0 °C, acetone (700 mg, 12.0 mmol, 1.20 equiv) was added, and the reaction was allowed to warm to room temperature and stirred for 12 h. The reaction was poured into 100 mL rapidly stirred hexanes, the resulting mixture was filtered through a silica plug (washed with 2:1 Hex/EtOAc), concentrated and purified by flash column silica gel chromatography (9.5:0.5 Hex/EtOAc) to afford a pale yellow oil (300 mg, 2.71 mmol, 27%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.13 (dq, *J* = 4.1, 2.5, 2.0 Hz, 1H), 2.42 – 2.27 (m, 4H), 1.72 (d, *J* = 1.4 Hz, 3H), 1.65 (d, *J* = 1.3 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 135.7, 120.3, 119.8, 25.8, 24.2, 17.9, 17.8; **FT-IR** (neat) 2927, 2245, 1672, 1577, 1438, 1377, 1176, 723, 542 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_7H_{12}N$ $[M+H]^+$ 110.0964, found 109.0920; **TLC**: R_f = 0.49 (9:1 Hex/EtOAc).

***N*-(5-Methylhex-4-en-1-yl)picolinamide (1o)**

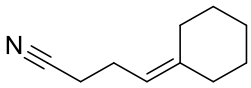


The title compound was prepared according to general procedures 2 (note that the amine intermediate is volatile, carefully concentrated reaction at 700 mbar) and 3 from 5-methylhex-4-enenitrile **S2o** (282 mg, 2.58 mmol). The crude product was purified by flash column chromatography (9:1 to 1:1 Hex/EtOAc) to afford a pale yellow oil (386 mg, 1.77 mmol, 68%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (qd, *J* = 2.8, 1.2 Hz, 1H), 8.18 (dq, *J* = 7.8, 1.3 Hz, 1H), 8.07 (s, 1H), 7.82 (tdd, *J* = 7.7, 3.2, 1.7 Hz, 1H), 7.40 (dddd, *J* = 7.6, 4.7, 3.1,

1.3 Hz, 1H), 5.14 (tdp, *J* = 7.2, 2.9, 1.4 Hz, 1H), 3.63 – 3.35 (m, 2H), 2.09 (q, *J* = 7.6, 7.2 Hz, 2H), 1.73 – 1.64 (m, 5H), 1.64 – 1.59 (m, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.3, 150.2, 148.1, 137.5, 132.5, 126.1, 123.7, 122.3, 39.3, 29.8, 25.8, 25.7, 17.8; **FT-IR** (neat) 3391, 2926, 1670, 1523, 1464, 1434, 1288, 1087, 997, 749, 819, 749, 691, 620 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{13}H_{19}N_2O$ $[M+H]^+$ 219.1492, found 219.1488; **TLC**: R_f = 0.36 (7:3 Hex/EtOAc).

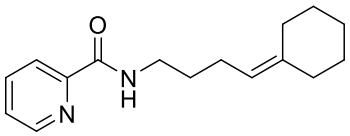
4-Cyclohexylidenebutanenitrile (S2p)



In a flame-dried round-bottom flask under N_2, (3-cyanopropyl)triphenylphosphonium bromide **S1** (3.00 g, 7.31 mmol, 1.00 equiv) was suspended in anhydrous THF (20 mL) at 0 °C. KHMDS (20 wt% in THF, 10 mL, 8.77 mmol, 1.20 equiv) was added, the reaction was stirred for 15 min, then cyclohexanone (718 mg, 7.31 mmol, 1.00 equiv) was added, the reaction was allowed to warm to rt and stirred for 20 h.The reaction was poured into 80 mL rapidly stirred hexanes, the resulting mixture was filtered through a silica plug (washed with 2:1 Hex/EtOAc). The solution was concentrated *in vacuo* to afford a colorless oil (1.00 g, 6.70 mmol, 92%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.08 (tdd, *J* = 6.0, 2.6, 1.2 Hz, 1H), 2.41 – 2.28 (m, 4H), 2.19 – 2.05 (m, 4H), 1.61 – 1.48 (m, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.8, 119.9, 116.9, 37.2, 28.9, 28.6, 28.0, 26.9, 23.3, 18.2. The analytical data are in agreement with the literature.[6]

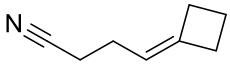
N-(4-Cyclohexylidenebutyl)picolinamide (1p)



The title compound was prepared according to general procedures 2 and 3 from 4-cyclohexylidenebutanenitrile **S2p** (1.00 g, 6.70 mmol). The crude product was purified by flash column chromatography (Hex/EtOAc 3:1) to afford a colorless oil (1.25 g, 4.82 mmol, 72%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.19 (ddd, *J* = 7.8, 0.9 Hz, 1H), 8.08 (s, 1H), 7.87 – 7.80 (m, 1H), 7.41 (ddd, *J* = 7.6, 4.8, 1.3 Hz, 1H), 5.09 (tt, *J* = 7.2, 1.2 Hz, 1H), 3.51 – 3.42 (m, 2H), 2.15 – 2.02 (m, 6H), 1.72 – 1.62 (m, 2H), 1.58 – 1.43 (m, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.3, 150.2, 148.1, 140.8, 137.4, 126.1, 122.3, 120.2, 39.2, 37.3, 30.1, 28.8, 28.7, 27.9, 27.0, 24.7; **FT-IR** (neat) 3389, 3055, 2923, 2852, 1670, 1590, 1569, 1523, 1464, 1446, 1288, 1243, 1161, 997, 819, 749, 691, 620 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{16}H_{23}N_2O$ $[M+H]^+$ 259.1805, found 259.1801; **TLC**: R_f = 0.60 (3:2 Hex/EtOAc).

4-Cyclobutylidenebutanenitrile (S2q)

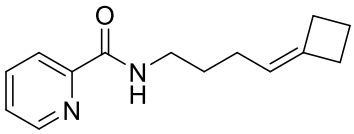


To a suspension of (3-cyanopropyl)triphenylphosphonium bromide **S1** (3.00 g, 7.30 mmol, 1.00 equiv) in THF at 0 °C was added KHMDS (20 wt% in THF, 10.4 mL, 9.14 mmol, 1.25 equiv). The suspension was stirred for 10 min, then cyclobutanone (560 mg, 8.04 mmol, 1.10 equiv) was added and the reaction was allowed to warm to rt. After stirring for 5 h, the reaction mixture was poured into rapidly stirred hexanes (80 mL) and filtered through a silica plug (washed with hexanes/EtOAc 5:1). The solution was concentrated *in vacuo* and the crude product was purified by flash column silica gel chromatography (20:1 Hex/EtOAc) to afford a colorless oil (490 mg, 4.08 mmol, 56%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.07 (tp, *J* = 7.1, 2.3 Hz, 1H), 2.75 – 2.60 (m, 4H), 2.37 – 2.30 (m, 2H), 2.28 – 2.12 (m, 2H), 2.02 – 1.88 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$)

δ 144.4, 119.8, 116.0, 31.0, 29.3, 24.2, 17.8, 17.0; **FT-IR** (neat) 2952, 2919, 2246, 1699, 1444, 1426, 1307, 841 cm^{-1}; **HRMS** (EI) *m/z* calculated for $C_8H_{11}N$ $[M]^+$ 121.0886, found 121.0886; **TLC**: R_f = 0.35 (9:1 Hex/EtOAc).

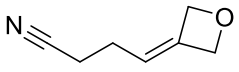
N-(4-Cyclobutylidenebutyl)picolinamide (1q)



The title compound was prepared according to general procedures 2 and 3 from 4-cyclobutylidenebutanenitrile **S2q** (420 mg, 3.47 mmol). The crude product was purified by flash column chromatography (Hex/EtOAc 4:1) to afford a colorless oil (600 mg, 2.61 mmol, 75%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (ddt, *J* = 4.8, 1.6, 0.7 Hz, 1H), 8.20 (dt, *J* = 7.9, 1.1 Hz, 1H), 8.08 (s, 1H), 7.84 (tdd, *J* = 7.7, 1.8, 0.6 Hz, 1H), 7.43 – 7.38 (m, 1H), 5.13 – 5.03 (m, 1H), 3.47 (td, *J* = 7.2, 6.1 Hz, 2H), 2.68 – 2.59 (m, 4H), 2.05 – 1.88 (m, 4H), 1.73 – 1.64 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.3, 150.3, 148.1, 141.2, 137.4, 126.1, 122.3, 119.3, 39.2, 31.0, 29.6, 29.4, 25.6, 17.2; **FT-IR** (neat) 3390, 2918, 1668, 1521, 1464, 1433, 1287, 997, 748, 620 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{14}H_{18}N_2NaO$ $[M+Na]^+$ 253.1311, found 253.1309; **TLC**: R_f = 0.46 (2:1 Hex/EtOAc).

4-(Oxetan-3-ylidene)butanenitrile (S2r)

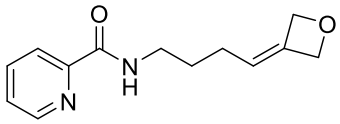


In a flame-dried round-bottom flask under N_2, (3-cyanopropyl)triphenylphosphonium bromide **S1** (3.00 g, 7.31 mmol, 1.10 equiv) was suspended in anhydrous THF (20 mL) at 0 °C. KHMDS (20 wt% in THF, 9.4 mL, 8.31 mmol, 1.25 equiv) was added, the reaction was stirred for 15 min, then 3-oxetanone (479 mg, 6.65 mmol, 1.00 equiv) was added dropwise, the reaction was allowed to warm to rt and stirred for 24 h.The reaction was poured into 80 mL rapidly stirred hexanes, the resulting mixture was filtered through a silica plug (washed with 1:1 Hex/EtOAc). The solution was

concentrated *in vacuo* (50 mbar, 40 °C) and the crude product was purified by flash column silica gel chromatography (Hex/Et_2O 1:2) to afford a faint yellow oil (630 mg, 5.10 mmol, 77%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.26 (d, *J* = 1.4 Hz, 2H), 5.22 – 5.14 (m, 3H), 2.39 (t, *J* = 6.9 Hz, 2H), 2.21 (q, *J* = 7.5 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.5, 119.1, 115.3, 79.2, 78.4, 24.4, 17.4; **FT-IR** (neat) 2930, 2860, 2245, 1447, 1426, 1293, 955, 855, 801 cm^{-1}; **HRMS** (ESI) *m/z* calculated for $C_7H_{10}NO$ $[M+H]^+$ 124.0757, found 124.0757; **TLC**: R_f = 0.35 (Et_2O).

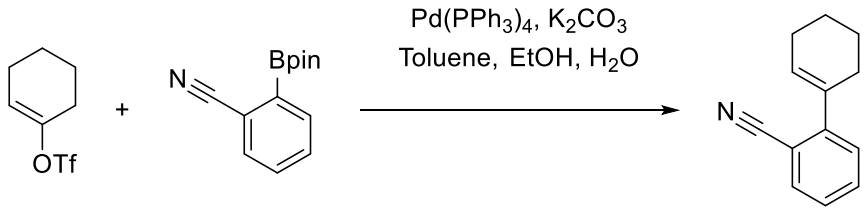
N-(4-(Oxetan-3-ylidene)butyl)picolinamide (1r)



The title compound was prepared according to general procedures 2 and 3 from 4-(oxetan-3-ylidene)butanenitrile **S2r** (360 mg, 2.92 mmol). The crude product was purified by flash column chromatography (4:6 to 3:7 Hex/EtOAc) to afford a pale yellow oil (340 mg, 1.48 mmol, 51%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 8.19 (dt, *J* = 7.9, 1.1 Hz, 1H), 8.10 (s, 1H), 7.84 (td, *J* = 7.7, 1.7 Hz, 1H), 7.42 (ddd, *J* = 7.6, 4.8, 1.3 Hz, 1H), 5.23 (dt, *J* = 4.0, 1.5 Hz, 2H), 5.17 (tq, *J* = 3.9, 2.3, 1.8 Hz, 3H), 3.48 (td, *J* = 7.1, 6.2 Hz, 2H), 2.07 – 1.84 (m, 2H), 1.82 – 1.64 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.5, 150.0, 148.2, 137.5, 135.0, 126.3, 122.4, 118.7, 79.6, 78.9, 39.0, 29.1, 25.9; **FT-IR** (neat) 3333, 2931, 1663, 1524, 1434, 1288, 1244, 1164, 997, 954, 749, 690, 620 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{13}H_{16}N_2NaO_2$ $[M+Na]^+$ 255.1104, found 255.1101; **TLC**: R_f = 0.23 (1:1 Hex/EtOAc).

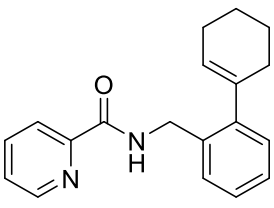
2',3',4',5'-Tetrahydro-[1,1'-biphenyl]-2-carbonitrile (S2s)



Based on a literature procedure[7], cyclohexenyl trifluoromethanesulfonate (300 mg, 1.26 mmol, 1.00 equiv) was dissolved in degassed Toluene/EtOH/H_2O (20 mL) under argon atmosphere. Potassium carbonate (720 mg, 5.21 mmol, 4.00 equiv), $Pd(PPh_3)_4$ (151 mg, 130 µmol, 0.100 equiv) and 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (448 mg, 1.95 mmol, 1.50 equiv) were added and the resulting mixture was stirred at 100 °C for 17 h. The reaction was quenched by the addition of water and the aqueous layer was extracted with DCM (3x). The combined organic layers were washed with brine, dried over magnesium sulfate, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography (Hex to Hex:EtOAc 30:1) to afford a brown oil (213 mg, 1.16 mmol, 89% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.61 (m, 1H), 7.50 (td, *J* = 7.6, 1.4 Hz, 1H), 7.29 (m, 2H), 5.98 (m, 1H), 2.38 (m, 2H), 2.24 (m, 2H), 1.85 – 1.77 (m, 2H), 1.74 – 1.67 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.4, 135.6, 133.4, 132.4, 130.1, 128.2, 126.7, 119.0, 110.6, 29.0, 25.6, 22.8, 21.7; **TLC**: R_f = 0.58 (5:1 Hex/EtOAc). The analytical data are in agreement with the literature.

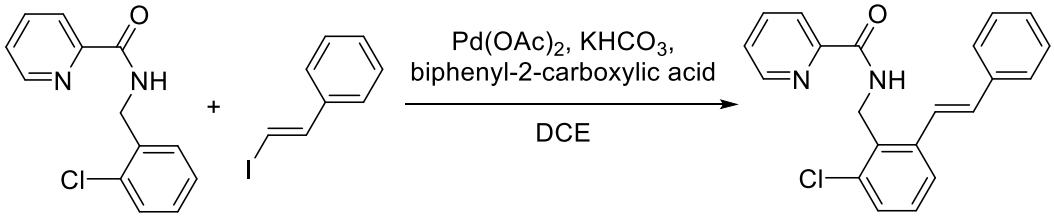
***N*-((2',3',4',5'-Tetrahydro-[1,1'-biphenyl]-2-yl)methyl)picolinamide (1s)**



The title compound was prepared according to general procedures 2 and 3 from 2',3',4',5'-tetrahydro-[1,1'-biphenyl]-2-carbonitrile **S2s** (2.13 g, 11.2 mmol). The crude product was purified by flash column chromatography (3:2 Hex/EtOAc) to afford an orange oil (2.56 g, 8.76 mmol, 76%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (ddd, *J* = 4.7, 1.8, 1.0 Hz, 1H), 8.29 (s, 1H), 8.23 (dt, *J* = 7.7, 1.7 Hz, 1H), 7.90 – 7.81 (m, 1H), 7.45 – 7.36 (m, 2H), 7.23 (m, 2H), 7.15 – 7.11 (m, 1H), 5.65 (tt, *J* = 3.7, 1.8 Hz, 1H), 4.67 (d, *J* = 5.8 Hz, 2H), 2.24 (m, 2H), 2.16 (m, 2H), 1.75 (m, 2H), 1.71 – 1.63 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.1, 150.1, 148.2, 144.7, 137.8, 137.4, 135.1, 128.9, 127.5, 127.0, 127.0, 126.2, 122.4, 41.6, 30.9, 25.5, 23.2, 22.1; **FT-IR** (neat) 3391, 3057, 3022, 2928, 2857, 2834, 1676, 1590, 1569, 1519, 1465, 1434, 1355, 1289, 1240, 1087, 999, 920, 753 cm^{-1}; **HRMS** (ESI): *m/z* calc. for $C_{19}H_{21}N_2O^+$ $[M+H]^+$ 293.1648, found 293.1648; **TLC**: R_f = 0.60 (1:3 Hex/EtOAc).

(*E*)-*N*-(2-Chloro-6-styrylbenzyl)picolinamide (18)

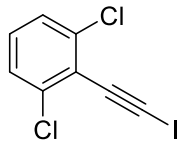


Based on a literature procedure[8] a mixture of *N*-(2-chlorobenzyl)picolinamide (148 mg, 600 µmol, 1.00 equiv), (*E*)-(2-iodovinyl)benzene (276 mg, 1.20 mmol, 2.00 equiv), $KHCO_3$ (120 mg, 1.20 mmol, 2.00 equiv), biphenyl-2-carboxylic acid (24.0 mg, 120 µmol, 0.200 equiv) and $Pd(OAc)_2$ (13.5 mg, 60.0 µmol, 0.100 equiv) was suspended in DCE (3.0 mL) in a 16 mL vial. The reaction vial was sealed, placed in a pre-heated aluminum heating block at 100 °C and stirred at this temperature for 20 h. The reaction was allowed to cool to rt, diluted with DCM, filtered through celite and concentrated under reduced pressure. Purification by flash column chromatography (4:1 Hex/EtOAc) afforded an off-white solid (165 mg, 470 µmol, 79%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.37 (s, 1H), 8.23 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.86 – 7.75 (m, 2H), 7.63 – 7.53 (m, 3H), 7.44 – 7.32 (m, 4H), 7.32 – 7.18 (m, 2H), 6.99 (d, *J* = 16.1 Hz, 1H), 4.97 (d, *J* = 6.0 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$,) δ 164.0, 149.9, 148.2, 140.0, 137.4, 137.1, 135.9, 133.1, 132.9, 129.2, 128.9, 128.7, 128.1, 127.1, 126.3, 125.9, 125.1, 122.5, 38.1; **FT-IR** (neat) 3388, 3058, 3024, 1674, 1518, 1463, 1433, 1242, 974, 782, 749, 693, 621 cm^{-1}; **HRMS** (ESI) *m/z* calculated for $C_{21}H_{17}ClN_2NaO$ $[M+Na]^+$ 371.0922, found 371.0919; **TLC**: R_f = 0.27 (4:1 Hex/EtOAc); **Melting point** 117.2 – 118.1 °C .

2.4 Synthesis of Iodoalkynes

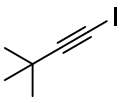
1,3-Dichloro-2-(iodoethynyl)benzene (25)



Based on a literature procedure[2,] to a stirred solution of 1,3-dichloro-2-ethynylbenzene[9] (316 mg, 1.85 mmol, 1.00 equiv) in acetone (6.5 mL), protected from light with aluminum foil, *N*-iodosuccinimide (499 mg, 2.22 mmol, 1.20 equiv) and silver nitrate (31.0 mg, 190 µmol, 0.100 equiv) were added. The mixture was stirred at room temperature for 45 min. The suspension was concentrated *in vacuo*, filtered through a plug of silica (washed with hexanes) and further concentrated *in vacuo* to afford white crystals (412 mg, 1.39 mmol, 75% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (dd, *J* = 8.1, 0.4 Hz, 2H), 7.16 (dd, *J* = 8.5, 7.7 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.4, 129.5, 127.6, 123.4, 88.3, 18.7; **FT-IR** (neat) 2995, 2173, 2036, 1874, 1700, 1759, 1553, 1431, 1383, 1246, 1194, 1103, 1062, 790, 717 cm^{-1}; **HRMS** (EI): *m/z* calc. for $C_8H_3Cl_2I^+$ $[M]^+$ 295.8651, found 295.8649; **TLC**: R_f = 0.90 (Hex).

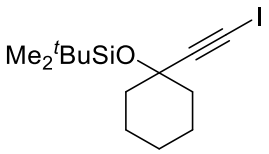
Iodo-3,3-dimethylbutyne (26)



Based on a literature procedure[2], to a stirred solution of 3,3-dimethylbut-1-yne (618 mg, 7.50 mmol, 1.00 equiv) in acetone (22 mL) protected from light with an aluminum foil, *N*-Iodosuccinimide (2.03 g, 9.00 mmol, 1.20 equiv) and silver nitrate (128 mg, 750 µmol, 0.100 equiv) were added. The mixture was stirred at room temperature for 2 h. The suspension was concentrated *in vacuo*, filtered through a plug of silica (washed with hexanes) and concentrated *in vacuo* to afford an off-white liquid (1.32 g, 6.30 mmol, 84% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 103.0, 34.1, 29.8, –8.1; **TLC**: R_f = 0.80 (Hex). The analytical data are in agreement with the literature.[10]

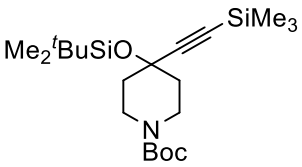
Tert-butyl((1-(iodoethynyl)cyclohexyl)oxy)dimethylsilane (28)



Based on a literature procedure[2], to a stirred solution of *tert*-butyl-(1-ethynylcyclohexyl)oxy-dimethylsilane, prepared according to a literature procedure,[11] (2.72 g, 11.4 mmol, 1.00 equiv) in acetone (35 mL) protected from light with an aluminum foil, *N*-Iodosuccinimide (3.10 g, 13.8 mmol, 1.20 equiv) and silver nitrate (199 mg, 1.17 mmol, 0.100 equiv) were added. The mixture was stirred at room temperature for 45 min. The suspension was concentrated *in vacuo*, filtered through a plug of silica (washed with hexanes) and concentrated *in vacuo* to yield a white powder (4.01 g, 11.0 mmol, 97% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.82 – 1.61 (m, 4H), 1.60 – 1.44 (m, 4H), 1.31 (s, 2H), 0.88 (s, 9H), 0.15 (s, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 99.4, 71.1, 41.2, 26.0, 25.4, 22.9, 18.4, 0.6, –2.9; **FT-IR** (neat) 2933, 2856, 2200, 1471, 1253, 1102, 836, 776 cm^{-1}; **HRMS** (ESI): *m/z* calc. for $C_{14}H_{26}IOSi^+$ $[M+H]^+$ 365.0792, found 365.0797; **Melting Point:** 41.2 – 43.0 °C; **TLC**: R_f = 0.85 (Hex).

tert-Butyl-4-((*tert*-butyldimethylsilyl)oxy)-4-((trimethylsilyl)ethynyl)piperidine-1-carboxylate (29)

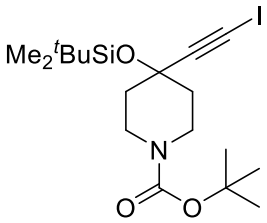


Based on a literature procedure[12], trimethylsilylacetylene (3.30 mL, 25.1 mmol, 2.30 equiv) was dissolved in anhydrous THF (23 mL) under argon atmosphere. *n*-BuLi (1.6 M in hexanes, 8.20 mL, 13.1 mmol, 1.20 equiv) was added slowly at –78 °C. The solution was stirred for 30 min at –78 °C and then, a solution of *tert*-butyl 4-oxopiperidinecarboxylate (2.17 g, 10.9 mmol, 1.00 equiv) in THF (8 mL) was added. The reaction mixture was stirred for 3 h at room temperature. The reaction was quenched by the addition of sat. aqueous solution of NH_4Cl, poured into water (30 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic layers were washed with brine (30 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was used directly without further purifcation in the next step.

The crude product was dissolved in DMF (11 mL). Imidazole (2.22 g, 32.7 mmol, 3.00 equiv) and *tert*-butyl-chloro-dimethylsilane (3.29 g, 21.8 mmol, 2.00 equiv) were added to the solution. The reaction was stirred overnight and then diluted with EtOAc (300 mL) and washed with a 1:1 mixture of sat. NH_4Cl and H_2O (300 mL) and a 1:1 mixture of sat. brine and H_2O (200 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography (Hex to Hex:EtOAc 9:1) to afford a viscous yellow oil (2.65 g, 6.44 mmol, 59% yield over 2 steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.47 (m, 4H), 1.77 (m, 2H), 1.67 (m, 2H), 1.45 (s, 9H), 0.87 (s, 9H), 0.18 (s, 6H), 0.16 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.8, 108.9, 90.1, 79.5, 67.5, 60.5, 40.2, 28.6, 25.9, 25.8, 21.2, 18.3, 14.3, -0.1, -2.8.; **TLC**: R_f = 0.90 (2:1 Hex/EtOAc). The analytical data are in agreement with the literature.[13]

tert-Butyl-4-((*tert*-butyldimethylsilyl)oxy)-4-(iodoethynyl)piperidine-1-carboxylate (30)



Based on a literature procedure[2], **29** (1.30 g, 3.16 mmol, 1.00 equiv), *N*-iodosuccinimide (788 mg, 3.55 mmol, 1.10 equiv), AgF (54.9 mg, 320 µmol,

0.100 equiv) were added mixed with acetone (32 mL). The suspension was allowed to stir for 30 min. The mixture was filtered through a pad of celite and the filtrate was diluted with ether, washed with water and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography (9:1 Hex:EtOAc) to afford a yellow solid (1.24 g, 2.65 mmol, 84% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.55 – 3.38 (m, 4H), 1.86 – 1.63 (m, 4H), 1.45 (s, 9H), 0.87 (s, 9H), 0.16 (s, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.9, 97.7, 79.7, 69.0, 40.7, 40.3, 28.6, 26.0, 18.4, 2.7, -2.9; **FT-IR** (neat) 2956, 2929, 2857, 2251,2174, 1676, 1425, 1245, 1100, 866 cm^{-1}; **HRMS (ESI)**: *m/z* calc. for $C_{18}H_{32}INNaO_3Si^+$ $[M+Na]^+$ 488.1088, found 488.1078; **Melting point:** 96.3 – 98.1 C; **TLC**: R_f = 0.70 (9:1 Hex/EtOAc).

2.5 Palladium catalyzed aminoalkynylation of olefins

General procedure 4 (using $Pd(OAc)_2$)

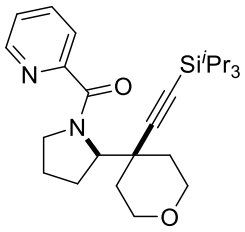
A 7 mL microwave vial was charged with picolinamide **1** (0.30 mmol, 1.0 equiv), iodoalkyne (0.36 mmol, 1.2 equiv), K_2CO_3 (83 mg, 0.60, 2.0 equiv) and $Pd(OAc)_2$ (6.7 mg, 0.030 mmol, 10 mol%) under ambient atmosphere. After addition of 1,2-dichloroethane (3.0 mL), the vial was sealed, placed in a pre-heated heating block and the reaction mixture was stirred for 24 h at 80 °C. The reaction mixture was allowed to cool to room temperature and filtered. The filtrate was concentrated *in vacuo*. The crude pyrrolidines were purified by flash chromatography using the indicated solvent system.

General procedure 5 (using $Pd(PPh_3)_2Cl_2$)

A 7 mL microwave vial was charged with picolinamide **1** (0.30 mmol, 1.0 equiv), iodoalkyne (0.36 mmol, 1.2 equiv), K_2CO_3 (83 mg, 0.60 mmol, 2.0 equiv) and $Pd(PPh_3)_2Cl_2$ (21. mg, 0.030 mmol, 10 mol%) under ambient atmosphere. After addition of 1,2-dichloroethane (3.0 mL), the vial was sealed, placed in a pre-heated heating block and the reaction mixture was stirred for 24 h at 80 °C. The reaction mixture was allowed to cool to room temperature and filtered. The filtrate was concentrated *in vacuo*. The crude pyrrolidines were purified by flash chromatography using the indicated solvent system.

Note: The synthesized pyrrolidines typically exist as a mixture of amide-bond rotamers and thus show two sets of signals in their ^1H and ^{13}C NMR spectra. The approximate ratio of rotamers was determined via ^1H NMR. If possible, ^1H peaks were assigned to the major or minor rotamer. To verify that the obtained products are in fact a mixture of rotamers and not a mixture of diastereomers we recorded NOESY spectra for several representative examples.

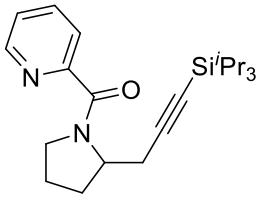
Pyridin-2-yl(2-(4-((triisopropylsilyl)ethynyl)tetrahydro-2H-pyran-4-yl)pyrrolidin-1-yl)methanone (2a)



The title compound was prepared according to general procedure 5 from *N*-(4-(tetrahydro-4*H*-pyran-4-ylidene)butyl)picolinamide **1a** (78 mg, 0.30 mmol, 1.0 equiv) and (iodoethynyl)triisopropylsilane **3** (110 mg, 0.36 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (6:4 to 1:1 Hex/EtOAc) to afford a brownish oil (123 mg, 0.28 mmol, 93%). Ratio of rotamers major:minor = 10:1.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (ddd, *J* = 4.8, 1.7, 1.0 Hz, 1H, major), 8.51 (d, *J* = 4.8 Hz, 1H, minor), 7.93 – 7.60 (m, 2H, major + minor), 7.33 (ddd, *J* = 7.2, 4.8, 1.6 Hz, 1H, major), 5.14 (t, *J* = 4.9 Hz, 1H, minor), 4.57 (dd, *J* = 8.5, 5.1 Hz, 1H, major), 4.28 – 4.11 (m, 1H, minor), 4.02 – 3.72 (m, 5H), 3.62 (ddd, *J* = 11.3, 8.1, 3.0 Hz, 1H), 2.33 – 2.14 (m, 1H), 2.14 – 1.94 (m, 3H), 1.84 – 1.53 (m, 4H), 1.10 (m, 21H, major + minor); **^{13}C NMR** (100 MHz, $CDCl_3$) 169.6, 167.3, 155.3, 154,8, 148.6, 147.6, 137.2, 136.7, 110.7, 109.8, 87.4, 86.3, 65.8, 65.1, 64.6, 64.5, 64.2, 64.0, 51.1, 47.5, 43.0, 41.6, 36.0, 35.9, 35.6, 35.0, 31.4, 27.4, 26.3, 25.5, 22.7, 18.81, 18.80, 11.7, 11.4, 11.2; **FT-IR** (neat) 2943, 2863, 2158, 1638, 1401, 1244, 1030, 995, 883, 747, 677 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{26}H_{41}N_2O_2Si$ $[M+H]^+$ 441.2932, found 441.2927; **TLC**: R_f = 0.40 (1:1 Hex/EtOAc).

Pyridin-2-yl(2-(3-(triisopropylsilyl)prop-2-yn-1-yl)pyrrolidin-1-yl)methanone (2b)

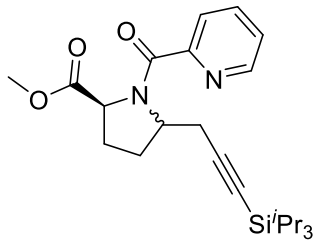


The title compound was prepared according to general procedure 4 from *N*-(pent-4-en-1-yl)picolinamide **1b** (prepared according to a literature known procedure[14]) (57 mg, 0.30 mmol, 1.0 equiv) and (iodoethynyl)triisopropylsilane **3** (110 mg, 0.36 mmol,

1.2 equiv). The crude product was purified by flash column chromatography (7:3 to 6:4 Hex/EtOAc) to afford a brownish oil (92 mg, 0.25 mmol, 82%). Ratio of rotamers major:minor = 2.5:1.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (dt, *J* = 4.7, 1.4 Hz, 1H, major), 7.85 (dt, *J* = 7.9, 1.2 Hz, 1H, minor), 7.82 – 7.71 (m, 2H), 7.37 – 7.28 (m, 1H), 4.79 (ddt, *J* = 9.9, 6.8, 3.1 Hz, 1H, minor), 4.39 (tdd, *J* = 8.4, 5.4, 3.4 Hz, 1H, major), 3.80 (tt, *J* = 13.3, 7.5 Hz, 1H,), 3.74 – 3.65 (m, 1H,), 2.90 (m, 1H, major), 2.69 (m, 1H, major), 2.55 (m, 1H, minor), 2.28 – 1.74 (m, 5H), 1.09 – 1.03 (s, 21H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.8, 166.3, 154.7, 154.3, 148.1, 148.0, 137.0, 136.8, 124.9, 124.7, 124.4, 123.9, 105.7, 105.4, 82.6, 82.2, 57.9, 57.3, 50.2, 47.5, 31.0, 29.6, 26.3, 25.0, 24.1, 21.6, 18.7, 18.7, 11.4, 11.3; **FT-IR** (neat) 2941, 2864, 2170, 1629, 1566, 1442, 1405, 1163, 995, 882, 746, 676, 619 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{22}H_{35}N_2OSi$ $[M+H]^+$ 371.2513, found 371.2518; **TLC**: R_f = 0.25 (7:3 Hex/EtOAc).

Methyl 1-picolinoyl-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)pyrrolidine-2-carboxylate (2c)

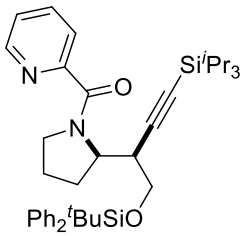


The title compound was prepared according to general procedure 4 from methyl (*R*)-2-(picolinamido)hex-5-enoate **1c** (75 mg, 0.30 mmol, 1.0 equiv) and (iodoethynyl)-triisopropylsilane **3** (110 mg, 0.36 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (7:3 Hex/EtOAc) to afford a yellow oil (92 mg, 0.22 mmol, 72%). Ratio of diasteromers = 1.4:1 and ratio of rotamers 2.6:1 (for the major diastereomer) and 2.2:1 (for the minor diastereomer), determined by integration of the OCH_3-signals in the ^{1}H NMR spectrum.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 – 8.52 (m, 1H, minor rotamers), 8.49 – 8.35 (m, 1H, major rotamers), 8.01 (ddd, *J* = 7.9, 2.9, 1.8 Hz, 1H, major rotamers), 7.95 (d, *J* = 7.9 Hz, 1H, minor rotamers), 7.78 (qdd, *J* = 7.8, 3.2, 1.6 Hz, 2H, major + minor

rotamers), 7.37 (ddd, *J* = 6.9, 5.1, 3.9 Hz, 1H, minor rotamers), 7.34 – 7.28 (m, 1H, major rotamers), 5.40 (dd, *J* = 9.2, 1.4 Hz, 1H, major diastereomer, major rotamer), 5.19 (ddt, *J* = 9.3, 6.0, 2.3 Hz, 1H), 5.08 – 4.98 (m, 1H), 4.96 (dd, *J* = 8.1, 4.1 Hz, 1H), 4.72 (dd, *J* = 9.0, 2.0 Hz, 1H), 4.69 (d, *J* = 8.4 Hz, 1H), 4.64 (ddd, *J* = 9.2, 6.4, 3.1 Hz, 1H), 4.53 (m, 1H), 3.76 (s, 3H, minor diastereomer, minor rotamer), 3.75 (s, 3H, major diastereomer, minor rotamer), 3.70 (s, 3H, minor diastereomer, major rotamer), 3.53 (s, 3H, major diastereomer, major rotamer), 3.35 (dd, *J* = 16.5, 4.0 Hz, 1H), 2.93 (dd, *J* = 16.7, 3.4 Hz, 1H), 2.74 – 1.95 (m, 6H), 1.14 – 0.96 (m, 21H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.7, 173.4, 173.1, 172.6, 166.1, 166.0, 165.9, 153.2, 153.0, 152.8, 152.7, 148.1, 148.0, 147.3, 147.1, 137.03, 136.99, 137.0, 125.4, 125.3, 125.3, 125.1, 124.94, 124.91, 124.8, 105.99, 105.95, 105.8, 105.4, 82.7, 82.4, 82.1, 81.8, 63.1, 62.5, 61.2, 61.1, 59.6, 59.3, 58.7, 52.4, 52.3, 52.2, 52.1, 30.2, 29.9, 29.8, 29.7, 28.6, 26.74, 26.68, 26.5, 26.2, 25.9, 24.2, 23.9, 18.71, 18.67, 11.4, 11.33, 11.26; **FT-IR** (neat) 2942, 2864, 2170, 1746, 1637, 1586, 1568, 1441, 1395, 1204, 1172, 996, 882, 746, 675, 621 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{24}H_{37}N_2O_3Si$ $[M+H]^+$ 429.2568, found 429.2565; **TLC**: R_f = 0.36 (7:3 Hex/EtOAc); $[\alpha]_D^{25}$ = –38.5 (c = 0.98 in $CHCl_3$).

(2-(1-((*Tert*-butyldiphenylsilyl)oxy)-4-(triisopropylsilyl)but-3-yn-2-yl)pyrrolidin-1-yl)(pyridin-2-yl)methanone (2d)

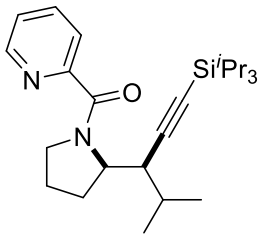


The title compound was prepared according to general procedure from 4-(*Z*)-*N*-(6-((*tert*-butyldiphenylsilyl)oxy)hex-4-en-1-yl)picolinamide **1d** (138 mg, 0.30 mmol, 1.0 equiv) and (iodoethynyl)triisopropylsilane **3** (110 mg, 0.36 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (7:3 Hex/EtOAc) to afford a yellow oil (171 mg, 0.27 mmol, 89%). Ratio of rotamers major:minor = 2.8:1.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (dt, *J* = 4.8, 1.4 Hz, 1H, major), 8.38 (dt, *J* = 4.8, 1.4 Hz, 1H, minor), 7.80 – 7.69 (m, 7H), 7.56 (ddt, *J* = 18.4, 6.7, 1.5 Hz, 2H), 7.48 –

7.33 (m, 8H), 7.30 (ddt, *J* = 6.8, 4.8, 2.2 Hz, 1H), 7.25 – 7.20 (m, 1H, minor), 5.03 – 4.86 (m, 1H, minor), 4.53 (td, *J* = 7.4, 4.0 Hz, 1H, major), 4.03 (dt, *J* = 7.7, 4.2 Hz, 1H, minor), 3.98 (ddd, *J* = 7.3, 5.8, 4.0 Hz, 1H, major), 3.85 (dd, *J* = 9.9, 5.9 Hz, 1H), 3.82 – 3.70 (m, 3H), 3.66 (dt, *J* = 12.0, 7.6 Hz, 1H, minor), 3.59 – 3.45 (m, 1H), 2.78 (ddd, *J* = 7.8, 5.9, 4.1 Hz, 1H, minor), 2.29 – 2.12 (m, 2H), 2.12 – 1.96 (m, 2H), 1.89 (dtd, *J* = 11.6, 7.4, 3.7 Hz, 1H, minor (assignment uncertain)), 1.74 (dtt, *J* = 11.9, 9.3, 7.7 Hz, 1H (assignment uncertain)), 1.09 (s, 9H, major), 1.07 – 1.03 (m, 21H), 1.00 (s, 1H, minor); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 166.8, 166.4, 154.92, 154.86, 148.3, 148.1, 137.1, 136.5, 135.8, 135.8, 135.64, 135.57, 133.6, 133.5, 133.3, 133.2, 129.9, 129.81, 129.77, 129.7, 129.6, 127.8, 127.7, 124.6, 124.5, 124.2, 123.6, 107.0, 105.8, 84.9, 83.7, 64.8, 58.5, 58.2, 50.4, 47.9, 40.7, 37.8, 28.4, 27.0, 26.93, 26.88, 26.85, 26.8, 26.7, 25.6, 22.9, 19.4, 19.3, 18.8, 18.7, 11.6, 11.5, 11.40, 11.36, 11.3, 11.2; **FT-IR** (neat) 2941, 2863, 2169, 1632, 1472, 1444, 1427, 1408, 1112, 743, 702, 676, 498 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{39}H_{55}N_2O_2Si_2$ $[M+H]^+$ 639.3797, found 639.3789; **TLC**: R_f = 0.25 (7:3 Hex/EtOAc).

(2-(4-Methyl-1-(triisopropylsilyl)pent-1-yn-3-yl)pyrrolidin-1-yl)(pyridin-2-yl)methanone (2e)

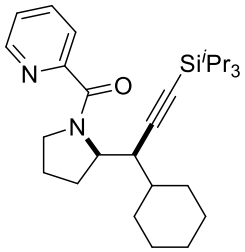


The title compound was prepared according to general procedure 4 from (*Z*)-*N*-(6-methylhept-4-en-1-yl)picolinamide **1e** (70 mg, 0.30 mmol, 1.0 equiv) and (iodoethynyl)triisopropylsilane **3** (110 mg, 0.36 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (1:3 Hex/EtOAc) to afford a brown oil (119 mg, 0.29 mmol, 96%). Ratio of rotamers major:minor = 3:1.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (m, 1H, major), 8.54 (m, 1H, minor), 7.80 (m, 1H), 7.77 – 7.73 (m, 1H), 7.36 – 7.32 (m, 1H, minor), 7.30 (m, 1H, major), 4.85 (m, 1H, minor), 4.45 (m, 1H, major), 4.00 (m, 1H, minor), 3.80 (m, 1H, major), 3.74 (m, 1H, major), 3.66 – 3.58 (m, 1H, minor), 3.24 (dd, *J* = 7.6, 4.7 Hz, 1H), 2.21 (m, 1H, major),

2.13 (m, 2H, minor), 2.07 (m, 1H, minor), 2.03 (m, 2H, major), 1.89 (m, 1H, minor), 1.82 – 1.76 (m, 1H, major), 1.74 (m, 1H, major), 1.47 (m, 1H, minor), 1.11 (d, *J* = 6.7 Hz, 3H, major), 1.07 (m, 18H), 1.02 (m, 6H), 0.73 (dd, *J* = 6.6, 4.9 Hz, 3H, min); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.9, 166.3, 155.0, 154.9, 148.3, 147.9, 137.3, 136.6, 124.8, 124.6, 124.5, 123.8, 108.7, 107.5, 84.9, 83.9, 59.2, 50.2, 47.5, 45.6, 42.9, 30.4, 30.2, 29.8, 28.7, 26.9, 25.5, 22.9, 21.3, 21.0, 20.7, 20.4, 18.8, 18.8, 11.5, 11.4; **FT-IR** (neat) 2932, 2855, 1631, 1566, 1443, 1409, 1096, 836 cm^{-1}; **HRMS** (ESI): *m/z* calc. for $C_{25}H_{40}N_2NaOSi^+$ $[M+Na]^+$ 435.2802, found 435.2802; **TLC**: R_f = 0.24 (3:1 Hex/EtOAc).

(2-(1-Cyclohexyl-3-(triisopropylsilyl)prop-2-yn-1-yl)pyrrolidin-1-yl)(pyridin-2-yl)methanone) (2f)

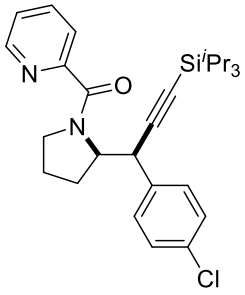


The title compound was prepared according to general procedure 5 from (*Z*)-*N*-(5-cyclohexylpent-4-en-1-yl)picolinamide **1f** (82 mg, 0.30 mmol, 1.0 equiv) and (iodoethynyl)triisopropylsilane **3** (110 mg, 0.36 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (7:3 Hex/EtOAc) to afford a yellow oil (130 mg, 0.29 mmol, 95%). Ratio of rotamers major:minor = ca 3:1.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (dt, *J* = 4.8, 1.5 Hz, 1H, major), 8.53 – 8.51 (m, 1H, minor), 7.83 – 7.66 (m, 3H), 7.32 (ddd, *J* = 5.8, 4.8, 3.0 Hz, 1H, minor), 7.29 – 7.26 (m, 1H, major), 4.86 (dt, *J* = 7.0, 4.9 Hz, 1H, minor), 4.44 (td, *J* = 7.2, 4.3 Hz, 1H, major), 4.01 – 3.93 (m, 1H, minor), 3.83 – 3.68 (m, 2H), 3.60 (dt, *J* = 12.1, 7.6 Hz, 1H, minor), 3.31 (dd, *J* = 7.9, 4.3 Hz, 1H), 2.26 – 2.16 (m, 1H), 2.11 (td, *J* = 7.7, 4.3 Hz, 1H), 2.07 – 1.94 (m, 3H), 1.87 (dqd, *J* = 10.8, 7.5, 6.9, 3.5 Hz, 1H, minor), 1.79 (dq, *J* = 11.4, 2.4 Hz, 1H), 1.71 (dddd, *J* = 17.5, 12.0, 5.6, 2.6 Hz, 3H), 1.65 – 1.55 (m, 1H), 1.55 – 1.38 (m, 2H), 1.29 – 1.10 (m, 6H), 1.06 – 1.02 (m, 21H), 0.87 – 0.70 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.7, 166.3, 155.0, 154.8, 148.2, 147.9, 137.2, 136.5, 124.7, 124.6, 124.5, 124.4, 123.7, 108.8, 107.6, 84.9, 83.7, 58.7, 58.6, 50.3, 47.4, 44.4, 41.6,

39.6, 39.2, 31.3, 31.3, 30.9, 30.4, 28.9, 26.8, 26.5, 26.3, 26.3, 26.2, 26.2, 26.0, 25.5, 22.7, 18.7, 18.7, 18.7, 11.4, 11.4; **FT-IR** (neat) 2923, 2850, 1672, 1590, 1569, 1526, 1434, 1288, 997, 749, 693, 621 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{28}H_{45}N_2OSi$ $[M+H]^+$ 453.3296, found 453.3293; **TLC**: R_f = 0.36 (7:3 Hex/EtOAc 7:3).

(2-(1-(4-Chlorophenyl)-3-(triisopropylsilyl)prop-2-yn-1-yl)pyrrolidin-1-yl)(pyridin-2-yl)methanone (2g)

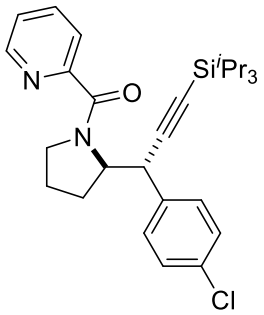


The title compound was prepared according to general procedure 5 from (*Z*)-*N*-(5-(4-chlorophenyl)pent-4-en-1-yl)picolinamide **1g** (90 mg, 0.30 mmol, 1.0 equiv) and (iodoethynyl)triisopropylsilane **3** (110 mg, 0.36 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (7:3 Hex/EtOAc) to afford a pale yellow oil (140 mg, 0.29 mmol, 97%). Ratio of rotamers major:minor = 2.5:1. A graphical comparison for the NMR-spectra of **2g** and **2h** is given in section 4 (NMR Data).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (ddd, *J* = 4.8, 1.8, 1.0 Hz, 1H, major), 8.57 – 8.53 (m, 1H, minor), 7.84 (dt, *J* = 7.8, 1.2 Hz, 1H, major), 7.78 (td, *J* = 7.7, 1.8 Hz, 1H, major), 7.74 (td, *J* = 7.7, 1.8 Hz, 1H, minor), 7.57 (dt, *J* = 7.9, 1.1 Hz, 1H, minor), 7.54 – 7.50 (m, 2H, assignment uncertain), 7.35 – 7.30 (m, 4H, assignment uncertain), 7.18 – 7.08 (m, 2H, minor), 7.08 – 7.02 (m, 2H, minor), 5.24 – 5.17 (m, 1H, minor), 5.08 (d, *J* = 4.2 Hz, 1H, major), 4.43 (td, *J* = 7.7, 7.2, 4.1 Hz, 1H, major), 3.99 (ddd, *J* = 12.3, 8.5, 5.8 Hz, 1H, minor), 3.96 – 3.83 (m, 2H), 3.76 (ddd, *J* = 12.1, 8.1, 5.6 Hz, 1H, minor), 2.29 – 1.87 (m, 3H), i1.79 – 1.64 (m, 2H), 1.10 (s, 21H, major), 1.08 (s, 21H, minor); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.1, 166.2, 154.5, 154.4, 148.3, 147.4, 137.4, 137.1, 136.8, 136.7, 133.0, 132.8, 129.6, 129.4, 128.7, 128.5, 125.0, 124.9, 124.8, 123.9, 106.1, 106.0, 86.6, 86.1, 63.4, 63.1, 51.1, 47.8, 42.8, 40.0, 29.2, 26.1, 25.3, 22.0, 18.8, 11.5, 11.4; **FT-IR** (neat) 2941, 2864, 2167, 1625, 1566, 1489, 1442, 1406,

1164, 1090, 1015, 996, 882, 745, 674, 620 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{28}H_{38}ClN_2OSi$ $[M+H]^+$ 481.2436, found 481.2435; **TLC**: R_f = 0.27 (7:3 Hex/EtOAc).

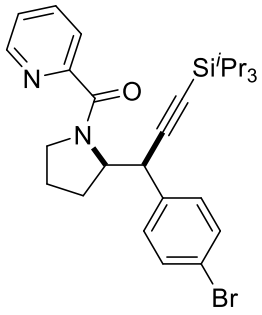
(2-(1-(4-Chlorophenyl)-3-(triisopropylsilyl)prop-2-yn-1-yl)pyrrolidin-1-yl)(pyridin-2-yl)methanone (2h)



The title compound was prepared according to general procedure 5 from (*Z*)-*N*-(5-(4-chlorophenyl)pent-4-en-1-yl)picolinamide **1h** (138 mg, 0.30 mmol, 1.0 equiv) and (iodoethynyl)triisopropylsilane **3** (110 mg, 0.36 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (7:3 Hex/EtOAc) to afford a yellow oil (82 mg, 0.17 mmol, 57%). Ratio of rotamers major:minor = 3.4:1. A graphical comparison for the NMR-spectra of **2g** and **2h** is given in section 4 (NMR Data).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (dt, *J* = 4.8, 1.4 Hz, 1H, major + minor), 7.88 (dt, *J* = 7.9, 1.2 Hz, 1H, minor), 7.85 – 7.77 (m, 2H, major+ 1H minor), 7.46 – 7.17 (m, 5H, major+minor), 5.33 (dt, *J* = 7.3, 3.7 Hz, 1H, minor), 4.94 (d, *J* = 4.4 Hz, 1H, major), 4.78 (ddd, *J* = 8.4, 5.9, 4.4 Hz, 1H, major), 4.31 (d, *J* = 4.0 Hz, 1H, minor), 3.71 (dt, *J* = 12.5, 8.3 Hz, 1H, minor), 3.48 (ddd, *J* = 11.3, 7.6, 5.1 Hz, 1H, major), 3.22 (ddd, *J* = 12.9, 9.2, 4.1 Hz, 1H, minor), 3.06 (dt, *J* = 11.3, 7.5 Hz, 1H, major), 2.20 – 1.89 (m, 2H), 1.65 – 1.46 (m, 1H), 1.13 (s, 21H, major), 1.09 (s, 21H, minor); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.4, 166.5, 154.6, 154.1, 148.4, 147.9, 137.2, 136.8, 135.9, 135.6, 133.4, 133.2, 130.9, 130.2, 128.6, 128.3, 125.1, 124.9, 124.7, 123.8, 107.1, 107.0, 85.8, 85.5, 63.0, 62.3, 50.5, 48.3, 43.0, 38.1, 28.3, 25.8, 24.6, 21.6, 18.8, 11.4; **FT-IR** (neat) 2941, 2864, 2171, 1628, 1566, 1489, 1442, 1407, 1091, 1044, 1015, 882, 832, 732, 677, 619 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{28}H_{38}ClN_2OSi$ $[M+H]^+$ 481.2436, found 481.2432; **TLC**: R_f = 0.42 (6:4 Hex/EtOAc).

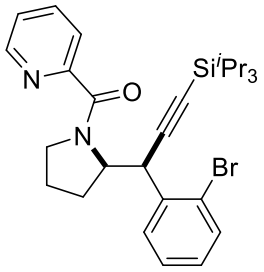
(2-(1-(4-Bromophenyl)-3-(triisopropylsilyl)prop-2-yn-1-yl)pyrrolidin-1-yl)(pyridin-2-yl)methanone (2i)



The title compound was prepared according to general procedure 5 from (*Z*)-*N*-(5-(4-bromophenyl)pent-4-en-1-yl)picolinamide **1i** (104 mg, 0.30 mmol, 1.0 equiv) and (iodoethynyl)triisopropylsilane **3** (110 mg, 0.36 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (7:3 Hex/EtOAc) to afford a brownish oil (114 mg, 0.22 mmol, 72%). Ratio of rotamers major:minor = 3:1.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 – 8.49 (m, 1H), 7.78 (t, *J* = 7.5 Hz, 1H, major), 7.73 (td, *J* = 7.7, 1.8 Hz, 1H, minor), 7.55 (dt, *J* = 7.9, 1.1 Hz, 1H, minor), 7.50 – 7.43 (m, 4H, major), 7.39 – 7.29 (m, 1H, major), 7.28 – 7.20 (m, 2H, minor), 7.03 – 6.94 (m, 2H, minor), 5.22 (td, *J* = 7.0, 3.3 Hz, 1H, minor), 5.07 (d, *J* = 4.1 Hz, 1H, major), 4.42 (dt, *J* = 7.9, 3.8 Hz, 1H, minor), 3.98 (ddd, *J* = 12.3, 8.5, 5.8 Hz, 1H, minor), 3.95 – 3.81 (m, 2H), 3.75 (ddd, *J* = 12.3, 8.4, 5.7 Hz, 1H, minor), 2.27 – 2.01 (m, 3H), 2.01 – 1.84 (m, 1H), 1.80 – 1.58 (m, 2H), 1.09 (d, *J* = 2.2 Hz, 21H, major), 1.07 (d, *J* = 1.8 Hz, 21H, minor); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.0, 166.2, 154.3, 148.2, 147.3, 137.9, 137.3, 137.1, 136.6, 131.6, 131.4, 129.9, 129.7, 124.9, 124.9, 123.8, 121.1, 120.9, 106.0, 105.9, 86.5, 86.1, 63.3, 63.0, 51.0, 47.8, 42.9, 40.0, 29.2, 26.1, 25.3, 21.9, 18.8, 18.8, 18.8, 18.7, 11.4, 11.4; **FT-IR** (neat) 2941, 2863, 2167, 1625, 1566, 1442, 1404, 1011, 996, 882, 725, 673, 619 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{28}H_{38}BrN_2OSi$ $[M+H]^+$ 525.1931, found 525.1932; **TLC**: R_f = 0.33 (7:3 Hex/EtOAc).

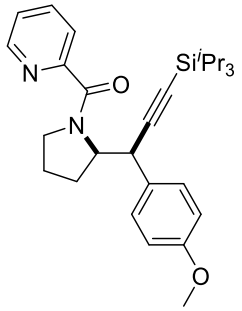
(2-(1-(2-Bromophenyl)-3-(triisopropylsilyl)prop-2-yn-1-yl)pyrrolidin-1-yl)(pyridin-2-yl)methanone (2j)



The title compound was prepared according to general procedure 5 from (*Z*)-*N*-(5-(2-bromophenyl)pent-4-en-1-yl)picolinamide **1j** (1.00 g, 2.90 mmol, 1.00 equiv) and (iodoethynyl)triisopropylsilane **3** (1.07 g, 3.48 mmol, 1.20 equiv). The crude product was purified by flash column chromatography (3:1 Hex/EtOAc) to afford an orange solid (1.33 g, 2.60 mmol, 85%). Ratio of rotamers major:minor = 2.4:1.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (dt, *J* = 4.8, 1.3 Hz, 1H, major), 8.46 (dt, *J* = 4.9, 1.4 Hz, 1H, minor), 7.87 (dt, *J* = 7.9, 1.2 Hz, 1H, major), 7.82 (dd, *J* = 7.8, 1.7 Hz, 1H, major), 7.75 (td, *J* = 7.7, 1.8 Hz, 1H, major), 7.56 (dd, *J* = 7.9, 1.3 Hz, 1H, major), 7.37 (dd, *J* = 8.0, 1.4 Hz, 1H, minor), 7.33-7.29 (m, 2H, major), 7.23 (m, 2H, minor), 7.12 (td, *J* = 7.6, 1.7 Hz, 1H, major), 6.91 (td, *J* = 7.6, 1.8 Hz, 1H, minor), 6.84 (td, *J* = 7.5, 1.4 Hz, 1H, minor), 5.50 (d, *J* = 5.2 Hz, 1H, major), 5.37 (ddd, *J* = 8.7, 7.1, 2.7 Hz, 1H, minor), 4.68 (td, *J* = 7.3, 5.1 Hz, 1H, major), 4.17 (d, *J* = 8.4 Hz, 1H, minor), 4.00 – 3.79 (m, 2H), 2.37 – 2.27 (m, 1H, minor), 2.23 – 2.17 (m, 1H, minor), 2.13 (m, 1H, major), 2.10 – 2.05 (m, 1H, minor), 2.04-1.96 (m, 1H, major), 1.73 – 1.58 (m, 2H, major), 1.11 – 1.04 (m, 21H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.1, 166.7, 154.7, 154.7, 148.1, 147.7, 138.1, 137.6, 137.0, 136.5, 133.1, 132.6, 131.1, 131.0, 128.8, 128.7, 127.4, 127.3, 124.7, 124.3, 124.1, 124.0, 124.0, 106.8, 106.6, 85.8, 85.4, 61.2, 60.2, 51.2, 48.1, 42.7, 40.4, 30.4, 26.9, 25.3, 21.8, 18.8, 18.8, 11.5, 11.4; **FT-IR** (neat) 3061, 2941, 2863, 2724, 2240, 2167, 2033, 2011, 1920, 1759, 1631, 1586, 1567, 1466, 1441, 1407, 1286, 1244, 1162, 1022, 996, 920, 882, 813, 745, 728 cm^{-1}; **HRMS** (ESI): *m/z* calc. for $C_{28}H_{37}BrN_2NaOSi^+$ $[M+Na]^+$ 547.1751, found 547.1751; **Melting Point:** 107.9 – 109.8 °C; **TLC**: R_f = 0.18 (1:1 Hex/EtOAc).

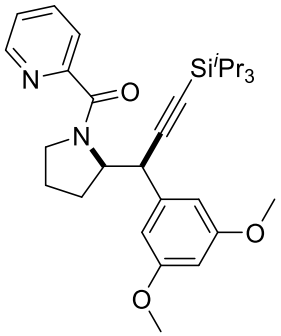
(2-(1-(4-Methoxyphenyl)-3-(triisopropylsilyl)prop-2-yn-1-yl)pyrrolidin-1-yl)(pyridin-2-yl)methanone (2k)



The title compound was prepared according to general procedure 5 from (*Z*)-*N*-(5-(4-methoxyphenyl)pent-4-en-1-yl)picolinamide **1k** (89 mg, 0.30, 1.0 equiv) and (iodoethynyl)triisopropylsilane **3** (110 mg, 0.36 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (6:4 Hex/EtOAc) to afford a yellow oil (110 mg, 0.23 mmol, 77%). Ratio of rotamers major:minor = 2:1.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 – 8.54 (m, 1H, major + minor), 7.86 (dt, *J* = 7.9, 1.2 Hz, 1H, major), 7.79 (td, *J* = 7.7, 1.7 Hz, 1H, major), 7.73 (td, *J* = 7.7, 1.8 Hz, 1H, minor), 7.62 (dt, *J* = 7.9, 1.2 Hz, 1H, minor), 7.55 – 7.47 (m, 2H), 7.34 (ddd, *J* = 7.6, 4.8, 1.3 Hz, 1H, major + minor), 7.04 (d, *J* = 8.6 Hz, 2H, minor), 6.98 – 6.88 (m, 2H), 6.75 – 6.67 (m, 2H, minor), 5.19 – 5.12 (m, 1H, minor), 5.09 (d, *J* = 4.2 Hz, 1H, major), 4.46 (td, *J* = 7.4, 4.2 Hz, 1H, major), 4.08 – 3.76 (m, 2H), 3.82 (s, 3H, major), 3.78 (s, 3H, minor), 2.32 – 2.12 (m, 2H, major), 2.11 – 2.02 (m, 2H, minor), 2.02 – 1.87 (m, 2H, minor), 1.80 – 1.62 (m, 2H, major), 1.19 – 1.06 (m, 21H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.9, 166.3, 158.7, 158.6, 154.64, 154.56, 148.2, 147.4, 137.1, 136.6, 130.9, 130.1, 129.2, 121.0, 124.8, 124.68, 124.66, 123.8, 113.9, 113.8, 107.1, 106.7, 85.8, 85.2, 63.6, 63.3, 55.4, 55.3, 51.0, 47.9, 42.5, 39.6, 28.9, 26.1, 25.3, 22.1, 18.8, 11.5, 11.4; **FT-IR** (neat) 2941, 2863, 2165, 1625, 1509, 1407, 1245, 1175, 1035, 838, 746, 675, 620 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{29}H_{41}N_2O_2Si$ $[M+H]^+$ 477.2932, found 477.2932; **TLC**: R_f = 0.33 (6:4 Hex/EtOAc).

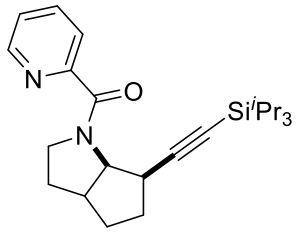
2-(1-(3,5-Dimethoxyphenyl)-3-(triisopropylsilyl)prop-2-yn-1-yl)pyrrolidin-1-yl)(pyridin-2-yl)methanone (2l)



The title compound was prepared according to general procedure 5 from (*Z*)-*N*-(5-(3,5-dimethoxyphenyl)pent-4-en-1-yl)picolinamide **1l** (1.00 g, 3.06 mmol, 1.00 equiv) and (iodoethynyl)triisopropylsilane **3** (1.13 g, 3.68 mmol, 1.20 equiv). The crude product was purified by flash column chromatography (3:2 Hex/EtOAc) to afford a brown oil (1.33 g, 2.60 mmol, 85%). Ratio of rotamers major:minor = 2:1.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (ddd, *J* = 4.7, 1.7, 0.9 Hz, 1H, minor), 8.58 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H, major), 7.84 (dt, *J* = 7.8, 1.2 Hz, 1H, major), 7.78 (td, *J* = 7.7, 1.8 Hz, 1H, major), 7.74 (td, *J* = 7.7, 1.8 Hz, 1H, minor), 7.64 (dt, *J* = 7.9, 1.1 Hz, 1H, minor), 7.33 (ddd, *J* = 7.5, 4.8, 1.3 Hz, 1H), 6.77 (d, *J* = 2.3 Hz, 2H, major), 6.36 (t, *J* = 2.3 Hz, 1H, major), 6.32 (d, *J* = 2.3 Hz, 2H, minor), 6.25 (t, *J* = 2.3 Hz, 1H, minor), 5.15 – 5.11 (m, 1H, minor), 5.10 (d, *J* = 4.3 Hz, 1H, major), 4.48 (td, *J* = 7.5, 4.2 Hz, 1H, major), 4.03 – 3.97 (m, 1H, minor), 3.95 – 3.85 (m, 1H, major), 3.83 (d, *J* = 6.1 Hz, 1H, minor), 3.80 (s, 6H, major), 3.77 – 3.74 (m, 1H, minor), 3.70 (s, 6H, minor), 2.24 – 2.21 (m, 2H, minor), 2.16 – 2.10 (m, 1H), 2.04 (s, 2H, major), 1.98 – 1.92 (m, 1H, major), 1.78 – 1.71 (m, 1H, minor), 1.70 – 1.61 (m, 1H), 1.10 (m, 21H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.9, 166.2, 160.8, 160.6, 154.55, 154.53, 148.1, 147.3, 141.1, 140.4, 137.1, 136.5, 124.6, 123.7, 106.5, 106.2, 105.9, 105.8, 99.8, 99.6, 86.1, 85.5, 63.3, 63.0, 55.4, 55.2, 51.0, 47.8, 43.5, 40.5, 28.9, 26.2, 25.2, 22.1, 18.7, 11.4; **FT-IR** (neat) 3057, 2941, 2890, 2863, 2242, 2165, 1625, 1607, 1595, 1566, 1561, 1461, 1443, 1407, 1349, 1287, 1203, 1154, 1062, 995, 882 cm^{-1}; **HRMS** (ESI): *m/z* calc. for $C_{30}H_{43}N_2O_3Si^+$ $[M+H]^+$ 507.3037, found 507.3037; **TLC**: R_f = 0.56 (1:3 Hex/EtOAc).

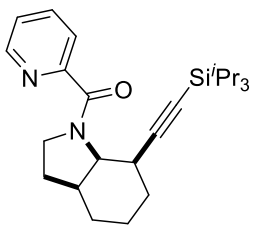
Pyridin-2-yl(6-((triisopropylsilyl)ethynyl)hexahydrocyclopenta[b]pyrrol-1(2H)-yl)methanone (2m)



The title compound was prepared according to general procedure 5 from *N*-(2-(cyclopent-2-en-1-yl)ethyl)picolinamide **1m** (65 mg, 0.30 mmol, 1.0 equiv) and (iodoethynyl)triisopropylsilane **3** (110 mg, 0.36 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (7:3 Hex/EtOAc) to afford a brownish solid (53 mg, 0.13 mmol, 44%). Ratio of rotamers major:minor = 1:1.

^{1}H NMR (500 MHz, $CDCl_3$, integrals reported as observed) δ 8.52 (dd, *J* = 4.8, 2.2 Hz, 2H), 7.87 (dd, *J* = 7.9, 5.1 Hz, 2H), 7.73 (tdd, *J* = 7.8, 4.4, 1.7 Hz, 2H), 7.29 (ddd, *J* = 7.6, 4.8, 1.3 Hz, 2H), 5.01 (t, *J* = 8.4 Hz, 1H), 4.62 (dd, *J* = 9.2, 7.4 Hz, 1H), 4.22 (ddd, *J* = 11.6, 7.8, 6.0 Hz, 1H), 3.97 (ddd, *J* = 12.3, 8.1, 6.3 Hz, 1H), 3.83 (dq, *J* = 12.3, 7.2 Hz, 2H), 3.54 (td, *J* = 7.2, 2.4 Hz, 1H), 2.88 – 2.76 (m, 1H), 2.76 – 2.64 (m, 2H), 2.10 – 1.97 (m, 3H), 1.97 – 1.65 (m, 10H), 1.01 (s, 21H), 0.93 (s, 21H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.0, 165.7, 154.9, 154.6, 147.69, 147.66, 136.7, 136.5, 124.8, 124.6, 124.6, 124.4, 109.3, 108.8, 84.3, 83.0, 66.2, 66.0, 50.4, 48.4, 44.6, 41.3, 37.5, 36.4, 34.9, 34.4, 32.33, 30.25, 30.3, 29.2, 18.71, 18.69, 18.67, 11.41, 11.36; **FT-IR** (neat) 2995, 2159, 2031, 1770, 1759, 1457, 1382, 1246, 1056 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{24}H_{37}N_2OSi$ $[M+H]^+$ 397.2670, found 397.2668; **TLC**: R_f = 0.43 (7:3 Hex/EtOAc); **Melting point**: 81.9 – 82.5 °C.

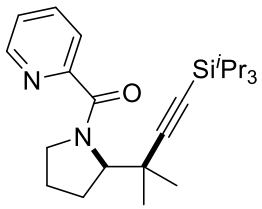
Pyridin-2-yl(7-((triisopropylsilyl)ethynyl)octahydro-1H-indol-1-yl)methanone (2n)



The title compound was prepared according to general procedure 4 from *N*-(2-(cyclohex-2-en-1-yl)ethyl)picolinamide **1n** (69 mg, 0.30 mmol, 1.0 equiv) and (iodoethynyl)triisopropylsilane **3** (110 mg, 0.36 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (7:3 to 6:4 Hex/EtOAc) to afford a brownish solid (100 mg, 0.24 mmol, 81%). Ratio of rotamers major:minor = 1.4:1.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 – 8.49 (m, 1H), 7.84 – 7.68 (m, 2H), 7.34 – 7.24 (m, 1H), 4.53 (t, *J* = 6.7 Hz, 1H, minor), 4.23 (t, *J* = 7.0 Hz, 1H, major), 4.06 – 3.98 (m, 1H. minor), 3.91 (td, *J* = 10.8, 7.3 Hz, 1H, major), 3.87 – 3.76 (m, 1H), 3.65 (ddd, *J* = 12.4, 9.9, 7.8 Hz, 1H, minor), 2.82 (dt, *J* = 7.1, 3.5 Hz, 1H, minor), 2.67 – 2.27 (m, 2H), 1.97 – 1.56 (m, 5H), 1.51 – 1.18 (m, 2H), 1.04 (m, 21H, minor), 0.99 – 0.91 (m, 21H, major); **^{13}C NMR** (101 MHz, $CDCl_3$): 166.2, 166.1, 155.0, 154.9, 147.9, 147.8, 136.9, 136.6, 124.6, 124.4, 124.2, 124.0, 111.3, 110.5, 82.2, 81.4, 59.1, 59.1, 49.4, 47.7, 38.5, 36.2, 31.7, 29.7, 29.4, 29.2, 29.2, 26.5, 26.2, 26.1, 18.7, 18.7, 18.7, 16.3, 16.0, 11.5, 11.4.; **FT-IR** (neat) 2938, 2863, 2157, 1628, 1586, 1565, 1442, 1407, 1365, 1246, 1118, 995, 882, 746, 677, 658, 620 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{25}H_{39}N_2OSi$ $[M+H]^+$ 411.2826, found 411.2822; **TLC**: R_f = 0.20 (7:3 Hex/EtOAc); **Melting point**: 90.7 – 91.7 °C.

(2-(2-Methyl-4-(triisopropylsilyl)but-3-yn-2-yl)pyrrolidin-1-yl)(pyridin-2-yl)methanone (2o)

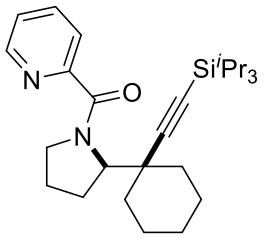


The title compound was prepared according to general procedure 4 from *N*-(5-methylhex-4-en-1-yl)picolinamide **1o** (66 mg, 0.30 mmol, 1.0 equiv) and (iodoethynyl)triisopropylsilane **3** (110 mg, 0.36 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (7:3 to 6:4 Hex/EtOAc) to afford a brownish oil (98 mg, 0.25 mmol, 82%). Ratio of rotamers major:minor = 7:1.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58 (t, *J* = 4.7 Hz, 1H, major), 8.50 (d, *J* = 4.8 Hz, 1H, minor), 7.79 – 7.64 (m, 2H), 7.29 (dt, *J* = 8.7, 4.5 Hz, 1H), 5.07 (q, *J* = 3.7, 2.6 Hz, 1H,

minor), 4.53 (dt, *J* = 8.3, 3.9 Hz, 1H, major), 4.14 (td, *J* = 9.3, 4.8 Hz, 1H, minor), 3.84 (tdd, *J* = 9.8, 7.2, 2.9 Hz, 1H, major), 3.69 (ddt, *J* = 11.9, 9.0, 4.1 Hz, 1H, minor), 3.56 (tt, *J* = 8.2, 3.4 Hz, 1H, major), 2.33 – 2.13 (m, 1H, major), 2.04 (m, 2H), 1.79 (d, *J* = 3.2 Hz, 1H, minor), 1.68 (m, 1H), 1.35 (d, *J* = 3.1 Hz, 3H), 1.29 (d, *J* = 3.4 Hz, 3H), 1.10 – 0.98 (m, 21H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 169.0, 167.0, 155.2, 154.7, 148.5, 148.3, 147.1, 136.73, 136.66, 136.3, 125.0, 124.3, 123.9, 123.4, 122.7, 114.6, 114.0, 81.7, 81.0, 64.8, 63.3, 50.3, 46.9, 40.5, 38.9, 37.8, 28.7, 28.3, 28.2, 27.1, 26.9, 26.7, 26.4, 25.9, 25.1, 23.0, 22.2, 19.8, 18.4, 18.4, 11.1, 11.0; **FT-IR** (neat) 2941, 2864, 2158, 1637, 1566, 1439, 1398, 1149, 995, 882, 746, 676, 618 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{24}H_{39}N_2OSi$ $[M+H]^+$ 399.2826, found 399.2818; **TLC**: R_f = 0.29 (7:3 Hex/EtOAc).

Pyridin-2-yl(2-(1-((triisopropylsilyl)ethynyl)cyclohexyl)pyrrolidin-1-yl)methanone (2p)

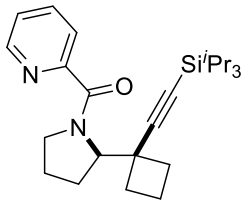


The title compound was prepared according to general procedure 5 from *N*-(4-cyclohexylidenebutyl)picolinamide **1p** (78 mg, 0.30 mmol, 1.0 equiv) and (iodoethynyl)triisopropylsilane **3** (110 mg, 0.36 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (7:3 to 6:4 Hex/EtOAc) to afford a brownish oil (98 mg, 0.22, 74%). Ratio of rotamers > 10:1

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (dt, *J* = 4.8, 1.4 Hz, 1H), 7.80 – 7.36 (m, 2H), 7.31 (ddd, *J* = 7.5, 4.8, 1.5 Hz, 1H), 4.51 (dd, *J* = 8.5, 4.8 Hz, 1H), 3.86 (ddd, *J* = 11.4, 9.6, 7.1 Hz, 1H), 3.57 (ddd, *J* = 11.2, 8.2, 2.7 Hz, 1H), 2.24 (m, 1H), 2.03 (m, 2H), 1.88 (dt, *J* = 12.2, 2.0 Hz, 1H), 1.79 (td, *J* = 6.7, 6.3, 3.3 Hz, 1H), 1.74 – 1.55 (m, 7H), 1.45 – 1.23 (m, 2H), 1.17 – 1.07 (m, 21H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.4, 155.2, 148.7, 136.6, 124.6, 123.8, 112.6, 84.8, 64.3, 50.9, 45.0, 36.1, 35.2, 26.6, 26.0, 25.5, 23.1, 22.8, 18.8, 11.5; **FT-IR** (neat) 2929, 2863, 2153, 1638, 1441, 1401, 994, 883,

677 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{27}H_{43}N_2OSi$ $[M+H]^+$ 439.3139, found 439.3137; **TLC**: R_f = 0.26 (7:3 Hex/EtOAc).

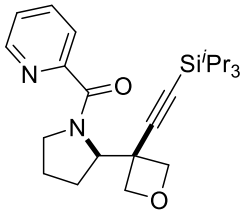
Pyridin-2-yl(2-(1-((triisopropylsilyl)ethynyl)cyclobutyl)pyrrolidin-1-yl)methanone (2q)



The title compound was prepared according to general procedure 5 from *N*-(4-cyclobutylidenebutyl)picolinamide **1q** (69 mg, 0.30 mmol, 1.0 equiv) and (iodoethynyl)triisopropylsilane **3** (110 mg, 0.36 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (7:3 to 6:4 Hex/EtOAc) to afford a brownish oil (73 mg, 0.18 mmol, 59%). Ratio of rotamers major:minor = 4:1.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (dt, *J* = 4.8, 1.4 Hz, 1H, major), 8.55 – 8.51 (m, 1H, minor), 7.77 – 7.70 (m, 2H, major + minor), 7.33 – 7.27 (m, 1H, major + minor), 5.08 (dt, *J* = 5.2, 2.8 Hz, 1H, minor), 4.60 (dd, *J* = 8.0, 5.4 Hz, 1H, major), 3.96 (ddd, *J* = 11.7, 8.5, 5.6 Hz, 1H, minor), 3.92 – 3.83 (m, 1H, major), 3.82 – 3.72 (m, 1H, minor), 3.63 (ddd, *J* = 11.4, 7.7, 3.8 Hz, 1H, major), 2.71 – 2.60 (m, 1H, major), 2.26 – 1.95 (m, 5H), 1.94 – 1.79 (m, 3H), 1.74 – 1.60 (m, 1H), 1.06 (m, 21H, major + minor); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 168.3, 166.9, 155.4, 155.0, 148.3, 148.2, 147.6, 137.0, 136.4, 124.9, 124.7, 124.4, 123.6, 114.1, 113.2, 82.8, 82.0, 77.1, 63.9, 63.6, 61.2, 50.8, 50.4, 48.1, 44.6, 44.5, 38.2, 35.0, 34.0, 33.6, 33.5, 29.7, 28.9, 27.3, 26.7, 26.3, 25.6, 25.3, 24.9, 22.2, 19.8, 18.7, 17.2, 16.8, 11.3, 11.3, 2.62, 2.55; **FT-IR** (neat) 2941, 2863, 2156, 1633, 1566, 1440, 1403, 1242, 1148, 995, 882, 746, 675 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{25}H_{39}N_2OSi$ $[M+H]^+$ 411.2826, found 411.2823; **TLC**: R_f = 0.47 (6:4 Hex/EtOAc).

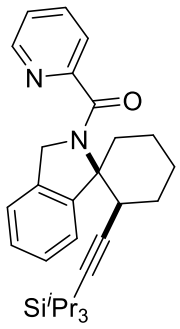
Pyridin-2-yl(2-(3-((triisopropylsilyl)ethynyl)oxetan-3-yl)pyrrolidin-1-yl)methanone (2r)



The title compound was prepared according to general procedure 5 from *N*-(4-(oxetan-3-ylidene)butyl)picolinamide **1r** (70 mg, 0.30 mmol, 1.0 equiv) and (iodoethynyl)-triisopropylsilane **3** (110 mg, 0.36 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (3:7 to 1:4 Hex/EtOAc) to afford a brownish solid (80 mg, 0.19 mmol, 65%). Only one rotamer was observed.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (dt, *J* = 4.8, 1.4 Hz, 1H), 7.78 – 7.71 (m, 2H), 7.30 (td, *J* = 5.2, 3.5 Hz, 1H), 5.33 (d, *J* = 6.2 Hz, 1H), 4.78 – 4.62 (m, 4H), 3.96 – 3.72 (m, 2H), 2.19 (qd, *J* = 7.3, 2.3 Hz, 1H), 2.09 – 1.91 (m, 1H), 1.73 (dddd, *J* = 15.0, 9.7, 6.2, 2.6 Hz, 2H), 1.04 (t, *J* = 2.7 Hz, 21H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.6, 154.4, 148.1, 136.5, 124.7, 123.8, 108.7, 85.2, 83.4, 79.4, 63.2, 51.1, 45.1, 27.9, 24.8, 18.7, 18.6, 11.2; **FT-IR** (neat) 2944, 2179, 2005, 1770, 1628, 1445, 1382, 1246, 1056, 675 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{24}H_{37}N_2O_2Si$ $[M+H]^+$ 413.2619, found 413.2619; **TLC**: R_f = 0.23 (7:3 Hex/EtOAc); **Melting point**: 71.0 – 71.6 °C.

Pyridin-2-yl(2-((triisopropylsilyl)ethynyl)spiro[cyclohexane-1,1'-isoindolin]-2'-yl)methanone (2s)

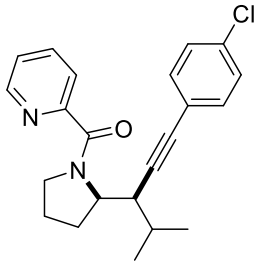


The title compound was prepared according to general procedure 4 from *N*-((2',3',4',5'-tetrahydro-[1,1'-biphenyl]-2-yl)methyl)picolinamide **1s** (88 mg, 0.30 mmol, 1.00 equiv) and (iodoethynyl)triisopropylsilane **3** (110 mg, 0.36 mmol, 1.2 equiv). The crude

product was purified by flash column chromatography (8:2 to 7:3 Hex/EtOAc) to afford a yellow oil (104 mg, 0.22 mmol, 73%). Only one rotamer was observed.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.62 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H), 7.79 (td, *J* = 7.7, 1.8 Hz, 1H), 7.68 (dt, *J* = 7.8, 1.2 Hz, 1H), 7.38 – 7.28 (m, 2H), 7.28 – 7.20 (m, 2H), 7.06 (dt, *J* = 7.5, 1.0 Hz, 1H), 5.19 (d, *J* = 14.5 Hz, 1H), 4.79 (dd, *J* = 14.5, 1.1 Hz, 1H), 3.02 (dd, *J* = 12.6, 4.5 Hz, 1H), 2.89 (qd, *J* = 12.6, 4.0 Hz, 1H), 2.66 (dddd, *J* = 17.1, 12.6, 8.6, 4.6 Hz, 1H), 2.56 (dddd, *J* = 15.0, 4.6, 3.0, 1.3 Hz, 1H), 2.12 – 2.00 (m, 2H), 1.99 – 1.90 (m, 1H), 1.68 (dt, *J* = 12.7, 4.5 Hz, 1H), 1.51 (m, 1H), 0.89 (d, *J* = 2.7 Hz, 21H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 168.2, 157.1, 148.2, 146.7, 136.8, 135.8, 127.7, 127.6, 124.1, 123.1, 122.2, 121.5, 109.3, 81.2, 73.6, 56.9, 44.4, 38.9, 29.9, 25.0, 22.5, 18.7, 18.6, 11.3; **FT-IR** (neat) 2863, 2939, 2172, 1652, 1567, 1460, 1437, 1392, 1096, 995, 907, 882, 729, 669, 617 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{30}H_{41}N_2OSi$ $[M+H]^+$ 473.2983, found 473.2982; **TLC**: R_f = 0.46 (7:3 Hex/EtOAc).

(2-(1-(4-Chlorophenyl)-4-methylpent-1-yn-3-yl)pyrrolidin-1-yl)(pyridin-2-yl)methanone (4)

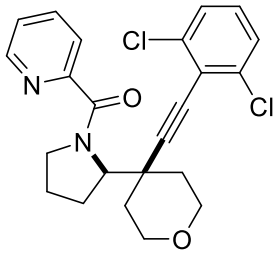


The title compound was prepared according to general procedure 4 from (*Z*)-*N*-(6-methylhept-4-en-1-yl)picolinamide **1e** (70 mg, 0.30 mmol, 1.0 equiv) and 1-chloro-4-(iodoethynyl)benzene **24** (95 mg, 0.36 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (3:2 Hex/EtOAc) to afford a brown oil (57 mg, 0.16 mmol, 52%). Ratio of rotamers major:minor = 3:1.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (ddd, *J* = 4.8, 1.7, 1.0 Hz, 1H, major), 8.55 (ddd, *J* = 4.8, 1.7, 1.0 Hz, 1H, minor), 7.86 – 7.78 (m, 1H), 7.75 (td, *J* = 7.6, 1.7 Hz, 1H), 7.37 – 7.33 (m, 2H, major), 7.31 (ddd, *J* = 7.5, 4.8, 1.4 Hz, 1H), 7.29 – 7.26 (m, 1H, minor), 7.26 – 7.21 (m, 2H), 5.01 (m, 1H, minor), 4.53 (td, *J* = 7.3, 4.5 Hz, 1H, major), 4.06 – 3.99 (m, 1H, minor), 3.83 (m, 1H, major), 3.75 (m, 1H, major), 3.70 –

3.61 (m, 1H, minor), 3.41 (dd, *J* = 8.2, 4.6 Hz, 1H, major), 2.23 (dd, *J* = 8.3, 4.5 Hz, 1H, minor), 2.20 – 2.11 (m, 2H, major), 2.10 – 2.06 (m, 2H, minor), 1.99 (m, 1H), 1.94 – 1.88 (m, 1H, minor), 1.84 (m, 1H, major), 1.78 – 1.69 (m, 1H, major), 1.57 (m, 1H, minor), 1.14 (d, *J* = 6.6 Hz, 3H, major), 1.10 (d, *J* = 6.6 Hz, 3H, major), 0.81 (d, *J* = 6.6 Hz, 3H, minor), 0.77 (d, *J*= 6.6 Hz, 3H, minor); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.8, 166.3, 154.8, 154.7, 148.2, 147.9, 137.2, 136.7, 133.8, 133.5, 133.0, 132.8, 128.6, 128.6, 124.9, 124.7, 124.5, 124.0, 122.7, 122.1, 91.4, 90.4, 83.2, 82.8, 59.2, 59.1, 50.3, 47.8, 45.3, 42.4, 30.3, 30.1, 28.5, 26.8, 25.5, 23.0, 21.12, 21.08, 20.8; **FT-IR** (neat) 3056, 2964, 2873, 2227, 1628, 1586, 1472, 1489, 1444, 1411, 1358, 1162, 1090, 1014, 829, 747 cm^{-1}; **HRMS** (ESI): *m/z* calc. for $C_{22}H_{24}ClN_2O^+$ $[M+H]^+$ 367.1572, found 367.1572; **TLC**: R_f = 0.45 (1:1 Hex/EtOAc).

(2-(4-((2,6-Dichlorophenyl)ethynyl)tetrahydro-2*H*-pyran-4-yl)pyrrolidin-1-yl)(pyridin-2-yl)methanone (5)

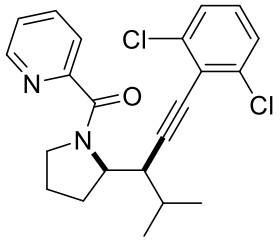


The title compound was prepared according to general procedure 4 from *N*-(4-(tetrahydro-4*H*-pyran-4-ylidene)butyl)picolinamide **1a** (78 mg, 0.30 mmol, 1.0 equiv) and 1,3-dichloro-2-(iodoethynyl)benzene **25** (107 mg, 0.36 mmol, 1.20 equiv). The crude product was purified by flash column chromatography (3:2 Hex/EtOAc) to afford a brown oil (78 mg, 0.18 mmol, 61%). Ratio of rotamers major:minor = 10:1.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (ddd, *J* = 4.8, 1.7, 1.1 Hz, 1H, major), 8.52 (m, 1H, minor), 7.81 (m, 1H, minor), 7.80 – 7.70 (m, 2H), 7.34 – 7.28 (m, 3H), 7.15 (m, 1H), 5.32 (dd, *J* = 7.7, 2.6 Hz, 1H, minor), 4.69 (dd, *J* = 8.7, 5.4 Hz, 1H, major), 4.20 (ddd, *J* = 13.2, 9.2, 4.4 Hz, 1H, minor), 4.03 – 3.86 (m, 5H, major), 3.84 – 3.72 (m, 5H, minor), 3.67 (ddd, *J* = 11.2, 8.1, 2.7 Hz, 1H, major), 2.34 (m, 2H), 2.23 – 2.12 (m, 2H), 2.10 – 2.00 (m, 1H, major), 1.98 (m, 1H, minor), 1.94 (m, 1H, minor), 1.91 – 1.82 (m, 2H), 1.77 (m, 1H, major), 1.74 – 1.64 (m, 2H, minor), 1.57 – 1.53 (m, 1H, minor), 1.46

(m, 1H, minor); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.8, 167.3, 155.3, 154.7, 148.6, 147.6, 137.5, 137.2, 136.7, 136.5, 129.0, 128.9, 127.7, 127.6, 125.4, 124.9, 124.8, 124.0, 123.4, 123.0, 103.2, 102.3, 80.8, 80.5, 65.5, 65.0, 64.6, 64.4, 64.2, 63.9, 51.1, 47.6, 43.4, 42.1, 35.8, 35.5, 35.4, 34.8, 27.6, 26.5, 25.7, 22.8; **FT-IR** (neat) 3064, 2957, 2861, 2772, 2240, 1631, 1585, 1567, 1553, 1468, 1430, 1438, 1400, 1322, 1245, 1194, 1145, 908, 778, 720 cm^{-1}; **HRMS** (ESI): *m/z* calc. for $C_{23}H_{23}Cl_2N_2O_2^+$ $[M+H]^+$ 429.1131, found 429.1131; **TLC**: R_f = 0.32 (1:1 Hex/EtOAc).

(2-(1-(2,6-Dichlorophenyl)-4-methylpent-1-yn-3-yl)pyrrolidin-1-yl)(pyridin-2-yl)methanone (6)

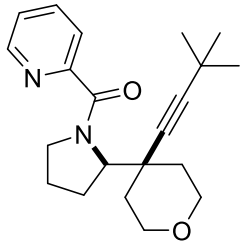


The title compound was prepared according to general procedure 4 from (*Z*)-*N*-(6-methylhept-4-en-1-yl)picolinamide **1e** (70 mg, 0.30 mmol, 1.0 equiv) and 1,3-dichloro-2-(iodoethynyl)benzene **25** (107 mg, 0.36 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (3:2 Hex/EtOAc) to afford a brown oil (111 mg, 0.28 mmol, 92%). Ratio of rotamers major:minor = 3:1.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (ddd, *J* = 4.8, 1.7, 1.0 Hz, 1H, major), 8.57 (ddd, *J* = 4.8, 1.7, 1.0 Hz, 1H, minor), 7.87 – 7.79 (m, 2H, major), 7.76 (td, *J* = 7.6, 1.7 Hz, 2H, minor), 7.36 (ddd, *J* = 7.1, 4.8, 1.7 Hz, 1H, minor), 7.33 – 7.30 (m, 1H, major), 7.29 (dd, *J* = 8.1, 1.5 Hz, 2H), 7.11 (m, 1H), 5.01 (dt, *J* = 7.5, 5.0 Hz, 1H, minor), 4.56 (td, *J* = 7.4, 4.5 Hz, 1H, major), 4.04 (ddd, *J* = 12.7, 8.3, 4.2 Hz, 1H, minor), 3.94 – 3.86 (m, 1H, major), 3.80 (ddd, *J* = 11.4, 7.8, 3.4 Hz, 1H, major), 3.72 (dt, *J* = 12.0, 7.7 Hz, 1H, minor), 3.57 (dd, *J* = 7.5, 4.5 Hz, 2H, minor), 2.34 (m, 2H, major), 2.24 – 2.05 (m, 2H), 1.99 – 1.90 (m, 1H, major), 1.81 – 1.72 (m, 1H), 1.68 – 1.62 (m, 1H, minor), 1.22 (d, *J* = 6.7 Hz, 3H, major), 1.16 (d, *J* = 6.7 Hz, 3H, major), 0.84 (d, *J* = 6.7 Hz, 3H, minor), 0.82 (d, *J* = 6.7 Hz, 3H, minor); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.1, 166.3, 155.0, 154.8, 148.3, 148.0, 137.48, 137.46, 137.3, 136.7,

128.6, 128.4, 127.6, 127.5, 124.9, 124.7, 124.0, 124.0, 123.6, 102.1, 100.7, 79.0, 78.5, 59.3, 59.2, 50.2, 47.6, 45.7, 43.1, 30.6, 30.3, 29.0, 27.2, 25.6, 23.0, 21.1, 20.8, 20.6; **FT-IR** (neat) 3063, 2963, 2873, 2228, 2038, 1770, 1759, 1626, 1585, 1444, 1410, 1248, 1194, 1152, 926, 857, 787 cm^{-1}; **HRMS** (ESI): *m/z* calc. for $C_{22}H_{23}Cl_2N_2O^+$ $[M+H]^+$ 401.1182, found 401.1182; **TLC**: R_f = 0.42 (1:1 Hex/EtOAc 1:1).

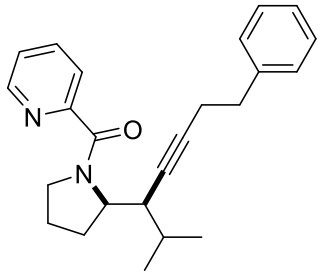
(2-(4-(3,3-Dimethylbut-1-yn-1-yl)tetrahydro-2H-pyran-4-yl)pyrrolidin-1-yl)(pyridin-2-yl)methanone (7)



The title compound was prepared according to general procedure 4 from *N*-(4-(tetrahydro-4*H*-pyran-4-ylidene)butyl)picolinamide **1a** (78 mg, 0.30 mmol, 1.0 equiv) and *tert*-butyliodoacetylene **26** (94 mg, 0.45 mmol, 1.5 equiv). The crude product was purified by flash column chromatography (1:1 Hex/EtOAc) to afford a brown oil (71 mg, 0.21 mmol, 70%). Ratio of rotamers major:minor = 6:1.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (ddd, *J* = 4.8, 1.7, 1.0 Hz, 1H, major), 8.54 (dt, *J* = 4.8, 1.4 Hz, 1H, minor), 7.80 (ddd, *J* = 7.9, 7.5, 1.7 Hz, 1H), 7.74 (ddd, *J* = 7.8, 1.4, 1.0 Hz, 1H), 7.35 (ddd, *J* = 7.5, 4.8, 1.4 Hz, 1H), 5.04 (dd, *J*= 6.7, 3.4 Hz, 1H, minor), 4.56 (dd, *J* = 8.4, 4.2 Hz, 1H, major), 4.24 – 4.17 (m, 1H, minor), 3.94 – 3.89 (m, 1H), 3.88 – 3.83 (m, 2H), 3.82 – 3.69 (m, 2H, major), 3.63 (m, 1H), 3.59 – 3.55 (m, 2H, minor), 2.31 (m, 1H, minor), 2.25 – 2.21 (m, 1H, minor), 2.20 – 2.13 (m, 1H), 2.13 – 2.06 (m, 1H, major), 2.05 – 2.01 (m, 1H), 2.01 – 1.97 (m, 1H, major), 1.81 – 1.72 (m, 1H), 1.71 – 1.65 (m, 2H), 1.56 (dd, *J* = 12.9, 2.4 Hz, 1H), 1.36 (m, 1H, minor), 1.27 (s, 9H, major), 0.93 – 0.83 (m, 9H, minor), 0.63 (m, 1H, minor); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.1, 154.8, 148.3, 147.4, 136.9, 136.5, 125.1, 124.6, 124.5, 123.7, 94.2, 80.0, 66.0, 64.9, 64.4, 64.3, 64.1, 64.0, 50.5, 47.2, 35.9, 35.6, 35.5, 35.4, 31.2, 30.9, 26.8, 25.6, 25.1, 22.4, 20.9; **FT-IR** (neat) 2966, 2860, 2242, 1633, 1587, 1567, 1407, 1362, 1245, 1148, 1029, 909, 731 cm^{-1}; **HRMS** (ESI): *m/z* calc. for $C_{21}H_{29}N_2O_2^+$ $[M+H]^+$ 341.2224, found 341.2224; **TLC**: R_f = 0.18 (1:1 Hex/EtOAc).

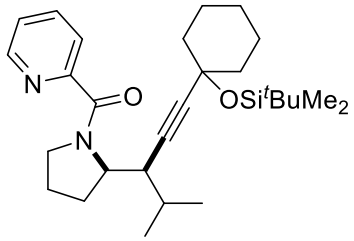
(2-(2-Methyl-7-phenylhept-4-yn-3-yl)pyrrolidin-1-yl)(pyridin-2-yl)methanone (8)



The title compound was prepared according to general procedure 4 from (*Z*)-*N*-(6-methylhept-4-en-1-yl)picolinamide **1e** (70 mg, 0.30 mg, 1.0 equiv) and (4-iodobut-3-yn-1-yl)benzene **27** (92 mg, 0.36 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (3:2 Hex/EtOAc) to afford a brown oil (41 mg, 0.11 mmol, 38%). Ratio of rotamers major:minor = 2:1.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (dt, *J* = 4.8, 1.5 Hz, 1H, major), 8.52 (dt, *J* = 4.8, 1.5 Hz, 1H, minor), 7.83 – 7.70 (m, 2H), 7.35 – 7.15 (m, 6H), 4.84 (m, 1H, minor), 4.41 (m, 1H, major), 3.96 (ddd, *J* = 12.3, 8.3, 4.2 Hz, 1H, minor), 3.70 – 3.60 (m, 2H, major), 3.53 – 3.45 (m, 1H, minor), 3.08 (ddt, *J* = 7.7, 4.6, 2.3 Hz, 1H, major), 2.83 (t, *J* = 7.4 Hz, 2H, major), 2.82 – 2.75 (m, 2H, minor), 2.54 – 2.49 (m, 2H, major), 2.49 – 2.41 (m, 2H, minor), 2.08 – 2.00 (m, 2H), 1.99 – 1.76 (m, 2H), 1.74 – 1.60 (m, 1H, major), 1.38 (m, 1H, minor), 1.03 (d, *J* = 6.7 Hz, 3H, major), 1.01 (d, *J* = 6.7 Hz, 3H, major), 0.66 (d, *J* = 4.8 Hz, 3H, minor), 0.65 (d, *J*= 4.8 Hz, 3H, minor); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.8, 166.4, 155.0, 154.9, 148.2, 147.9, 141.1, 140.9, 137.2, 136.7, 128.5, 128.4, 126.2, 124.7, 124.6, 124.4, 123.9, 83.3, 82.8, 80.4, 79.6, 59.2, 59.0, 50.0, 47.6, 44.5, 41.8, 35.6, 35.4, 30.3, 30.0, 28.2, 26.7, 25.4, 23.0, 21.2, 21.0, 20.9, 20.8, 20.74, 20.69; **FT-IR** (neat) 3061, 3027, 2959, 2871, 1626, 1586, 1566, 1524, 1489, 1472, 1443, 1410, 1289, 1237, 1150, 1089, 996, 829, 747 cm^{-1}; **HRMS** (ESI): *m/z* calc. for $C_{24}H_{29}N_2O^+$ $[M+H]^+$ 361.2274, found 361.2274; **TLC**: R_f = 0.42 (1:1 Hex/EtOAc).

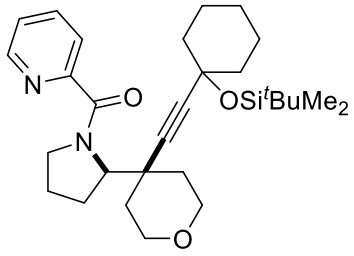
(2-(1-(1-(*Tert*-butyldimethylsilyloxy)cyclohexyl)-4-methylpentyn-3-yl)pyrrolidinyl)(pyridin-2-yl)methanone (9)



The title compound was prepared according to general procedure 4 from (*Z*)-*N*-(6-methylhept-4-en-1-yl)picolinamide **1e** (70 mg, 0.30 mmol, 1.0 equiv) and *tert*-butyl(1-(iodoethynyl)cyclohexyloxy)dimethylsilane **28** (131 mg, 0.36 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (1:3 Hex/EtOAc) to afford a brown oil (129 mg, 0.28 mmol, 92%). Ratio of rotamers major:minor = 3:1.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (m, *J* = 4.8, 1.7, 1.0 Hz, 1H, major), 8.55 (ddd, *J* = 4.8, 1.7, 1.0 Hz, 1H, minor), 7.84 – 7.78 (m, 1H), 7.78 – 7.73 (m, 1H), 7.35 (ddd, *J* = 7.3, 4.8, 1.5 Hz, 1H, minor), 7.31 (ddd, *J* = 7.3, 4.8, 1.5 Hz, 1H, major), 4.96 – 4.89 (m, 1H, minor), 4.47 (m, 1H, major), 4.02 (ddd, *J* = 12.2, 8.3, 3.9 Hz, 1H, minor), 3.83 – 3.74 (m, 2H, major), 3.58 (m, 2H, minor), 3.20 (dd, *J* = 7.7, 4.8 Hz, 1H, major), 2.19 – 2.12 (m, 1H), 2.11 (m, 2H, minor), 2.07 – 1.98 (m, 2H), 1.95 (dd, *J* = 7.9, 4.8 Hz, 1H, minor), 1.92 – 1.86 (m, 1H, minor), 1.82 – 1.70 (m, 3H), 1.66 – 1.55 (m, 6H), 1.54 – 1.45 (m, 2H, minor), 1.44 – 1.22 (m, 3H), 1.08 (dd, *J* = 21.0, 6.6 Hz, 6H, major), 0.85 (d, *J* = 6.5 Hz, 9H), 0.71 (dd, *J* = 15.2, 6.6 Hz, 6H, minor), 0.11 (dd, *J* = 14.4, 3.3 Hz, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.9, 166.3, 154.8, 148.2, 147.9, 137.2, 136.6, 124.8, 124.6, 124.6, 124.0, 88.3, 84.5, 69.7, 59.2, 58.9, 50.2, 47.6, 44.7, 41.9, 41.8, 41.6, 41.6, 41.4, 30.2, 29.9, 28.7, 27.0, 26.0, 25.6, 25.5, 23.1, 23.0, 21.3, 21.0, 20.9, 20.8, 18.3, -2.59, -2.64; **FT-IR** (neat) 2932, 2855, 1632, 1566, 1443, 1409, 1359, 1251, 1096, 837 cm^{-1}; **HRMS** (ESI): *m/z* calc. for $C_{28}H_{44}N_2NaO_2Si^+$ $[M+Na]^+$ 491.3064, found 491.3064; **TLC**: R_f = 0.24 (3:1 Hex/EtOAc).

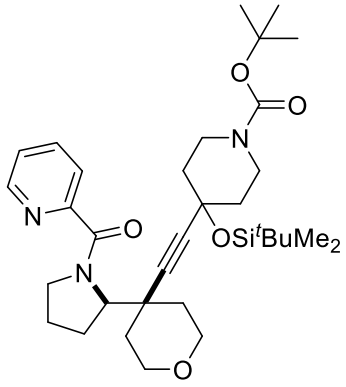
(2-(4-((1-((*tert*-Butyldimethylsilyl)oxy)cyclohexyl)ethynyl)tetrahydro-2H-pyran-4-yl)pyrrolidin-1-yl)(pyridin-2-yl)methanone (10)



The title compound was prepared according to general procedure 4 from *N*-(4-(tetrahydro-4*H*-pyran-4-ylidene)butyl)picolinamide **1a** (78 mg, 0.30 mmol, 1.0 equiv) and *tert*-butyl((1-(iodoethynyl)cyclohexyl)oxy)dimethylsilane **28** (131 mg, 0.36 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (1:3 Hex/EtOAc) to afford a brown oil (119 mg, 0.24 mmol, 80%). Ratio of rotamers major:minor = 9:1.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (ddd, *J* = 4.8, 1.7, 1.0 Hz, 1H, major), 8.51 (dt, *J* = 4.8, 1.4 Hz, 1H, minor), 7.79 (m, 2H, minor), 7.77 – 7.72 (m, 2H, major), 7.33 (ddd, *J* = 7.0, 4.8, 1.7 Hz, 1H), 5.19 (d, *J* = 7.9 Hz, 1H, minor), 4.59 (dd, *J* = 8.5, 5.0 Hz, 1H, major), 4.22 – 4.15 (m, 1H, minor), 3.92 – 3.83 (m, 2H), 3.83 – 3.71 (m, 2H), 3.70 – 3.57 (m, 1H, major), 2.30 – 2.19 (m, 1H, minor), 2.18 – 2.06 (m, 2H), 2.06 – 1.95 (m, 2H, major), 1.84 (m, 2H), 1.79 – 1.60 (m, 6H), 1.59 – 1.50 (m, 3H), 1.49 – 1.42 (m, 2H), 1.35 – 1.27 (m, 2H), 0.88 (s, 9H), 0.18 (d, *J* = 10.5 Hz, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.7, 154.8, 148.5, 136.7, 124.8, 124.0, 90.0, 86.3, 69.9, 65.1, 64.6, 64.0, 60.5, 51.2, 42.0, 41.7, 41.6, 35.7, 35.2, 26.4, 25.9, 25.5, 23.3, 23.2, 18.3, 14.3, 1.2, -2.4; **FT-IR** (neat) 2931, 2854, 2225, 1638, 1586, 1567, 1400, 1246, 1101 cm^{-1}; **HRMS** (ESI): *m/z* calc. for $C_{29}H_{44}N_2NaO_3Si^+$ $[M+Na]^+$ 519.3013, found 519.3005; **TLC**: R_f = 0.31 (1:3 Hex/EtOAc 1:3).

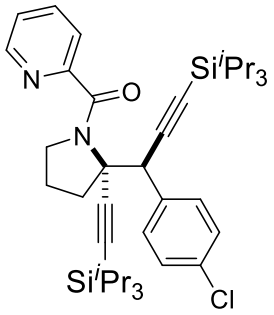
***Tert*-butyl-4-((*tert*-butyldimethylsilyl)oxy)-4-((4-(1-picolinoylpyrrolidin-2-yl)tetrahydro-2H-pyran-4-yl)ethynyl)piperidine-1-carboxylate (11)**



The title compound was prepared according to general procedure 4 from *N*-(4-(tetrahydro-4*H*-pyran-4-ylidene)butyl)picolinamide **1a** (78 mg, 0.30 mmol, 1.0 equiv) and *tert*-butyl-4-((*tert*-butyldimethylsilyl)oxy)-4-(iodoethynyl)piperidine-carboxylate **30** (209 mg, 0.45 mmol, 1.5 equiv). The crude product was purified by flash column chromatography (1:1 to 1:3 Hex/EtOAc) to afford a brown oil (109 mg, 0.18 mmol, 61%). Ratio of rotamers major:minor = 13:1.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (d, *J* = 4.7 Hz, 1H, major), 8.49 (d, *J* = 4.8 Hz, 1H, min), 7.76 (m, 1H), 7.74 (m, 1H), 7.32 (ddd, *J* = 6.1, 4.8, 2.7 Hz, 1H), 5.25 (d, *J* = 8.1 Hz, 1H, minor), 4.58 (dd, *J* = 7.5, 6.3 Hz, 1H, major), 3.92 – 3.79 (m, 2H), 3.82 – 3.78 (m, 1H), 3.76 - 3.69 (m, 1H), 3.68 – 3.62 (m, 2H), 3.62 – 3.57 (m, 2H), 3.52 – 3.44 (m, 1H), 3.38 (m, 1H), 2.11 – 2.04 (m, 2H), 2.03 – 2.01 (m, 1H), 2.01 – 1.92 (m, 1H), 1.86 (d, *J* = 9.3 Hz, 2H), 1.79 – 1.73 (m, 2H), 1.72 – 1.65 (m, 2H), 1.65 – 1.58 (m, 2H), 1.45 (s, 9H), 0.87 (s, 9H), 0.19 (d, *J* = 11.3 Hz, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.8, 167.3, 155.2, 154.7, 154.5, 148.4, 147.6, 137.3, 136.7, 125.4, 124.9, 124.0, 88.9, 88.3, 87.5, 86.6, 79.7, 79.6, 67.8, 67.6, 65.3, 65.1, 64.6, 64.5, 64.3, 63.9, 51.4, 47.9, 42.1, 40.7, 40.2, 35.3, 29.8, 28.6, 27.6, 26.4, 25.8, 25.5, 22.7, 18.2, -2.6; **FT-IR** (neat) 2955; 2928; 2855; 1695; 1640; 1567; 1464; 1401; 1278; 1244, 1148, 1103, 837 cm^{-1}; **HRMS (ESI)**: *m/z* calc. for $C_{33}H_{51}N_3NaO_5Si^+$ $[M+Na]^+$ 620.3490, found 620.3480; **TLC**: R_f = 0.48 (1:3 Hex/EtOAc).

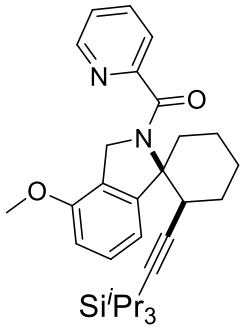
2-1-(4-Chlorophenyl)-3-(triisopropylsilyl)prop-2-yn-1-yl)-2-((triisopropylsilyl)ethynyl)pyrrolidin-1-yl)(pyridin-2-yl)methanone (13)



The title compound was prepared according to general procedure 4 from (*E*)-*N*-(4-(4-chlorobenzylidene)-6-(triisopropylsilyl)hex-5-yn-1-yl)picolinamide **12** (48 mg, 0.10 mmol, 1.0 equiv) and (iodoethynyl)triisopropylsilane **3** (37.0 mg, 0.12 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (9.5:0.5 to 9:1 Hex/EtOAc) to afford a yellow oil (42 mg, 0.072 mmol, 72%). Only one rotamer was observed.

^{1}H NMR (500 MHz, Chloroform-d) δ 8.53 (dt, *J* = 4.8, 1.4 Hz, 1H), 7.83 (dt, *J* = 7.8, 1.2 Hz, 1H), 7.75 (td, *J* = 7.7, 1.8 Hz, 1H), 7.66 – 7.57 (m, 2H), 7.30 (ddd, *J* = 7.5, 4.8, 1.3 Hz, 1H), 7.28 – 7.24 (m, 2H), 5.62 (s, 1H), 4.02 (ddt, *J* = 10.6, 7.6, 1.5 Hz, 1H), 3.91 (td, *J* = 11.2, 6.2 Hz, 1H), 2.58 (td, *J* = 12.3, 6.5 Hz, 1H), 2.03 – 1.87 (m, 2H), 1.74 (ddt, *J* = 12.1, 6.1, 1.6 Hz, 1H), 1.06 – 0.98 (m, 42H); **^{13}C NMR** (126 MHz, CDCl3) δ 165.8, 155.1, 147.7, 136.5, 136.2, 133.2, 131.5, 127.9, 124.6, 124.1, 107.9, 105.6, 86.1, 85.5, 66.1, 52.1, 43.5, 36.9, 24.3, 18.76, 18.74, 18.71, 11.44, 11.36; **FT-IR** (neat) 2941, 2864, 2172, 1640, 1567, 1438, 1393, 1091, 996, 882, 830, 745, 676, 614 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{39}H_{58}ClN_2OSi_2$ $[M+H]^+$ 661.3771, found 661.3772; **TLC**: R_f = 0.33 (9.5:0.5 Hex/EtOAc).

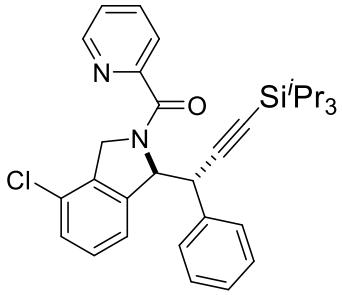
(4'-Methoxy-2-((triisopropylsilyl)ethynyl)spiro[cyclohexane-1,1'-isoindolin]-2'-yl)(pyridin-2-yl)methanone (16)



The title compound was prepared according to general procedure 4 from *N*-((3-methoxy-2',3',4',5'-tetrahydro-[1,1'-biphenyl]-2-yl)methyl)picolinamide **15** (prepared according to a literature known procedure[8]) (65 mg, 0.20 mmol, 1.0 equiv) and (iodoethynyl)triisopropylsilane **3** (74 mg, 0.24 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (8:2 to 7:3 Hex/EtOAc) to afford a yellow oil (50 mg, 0.10 mmol, 50%). Only one rotamer was observed.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H), 7.75 (td, *J* = 7.7, 1.8 Hz, 1H), 7.62 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.30 (ddd, *J* = 7.6, 4.9, 1.2 Hz, 1H), 7.28 – 7.24 (m, 1H), 6.82 (d, *J* = 7.6 Hz, 1H), 6.67 (dd, *J* = 8.1, 0.7 Hz, 1H), 5.04 (dd, *J* = 14.8, 0.8 Hz, 1H), 4.64 (dd, *J* = 14.7, 0.8 Hz, 1H), 3.73 (s, 3H), 2.97 (dd, *J* = 12.7, 4.6 Hz, 1H), 2.83 (qd, *J* = 12.8, 4.0 Hz, 1H), 2.63 (qt, *J* = 12.8, 4.6 Hz, 1H), 2.52 (dddd, *J* = 15.0, 4.6, 2.9, 1.3 Hz, 1H), 2.12 – 1.94 (m, 2H), 1.96 – 1.85 (m, 1H), 1.71 – 1.58 (m, 1H), 1.47 (qt, *J* = 12.9, 4.4 Hz, 1H), 0.96 – 0.73 (m, 21H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 168.4, 157.1, 153.8, 148.4, 148.4, 136.8, 129.2, 124.1, 124.0, 122.8, 114.3, 109.3, 108.6, 81.0, 74.1, 55.2, 54.9, 44.4, 38.6, 29.7, 25.1, 22.5, 18.62, 18.56, 11.3; **FT-IR** (neat) 2939, 2863, 2166, 1656, 1605, 1437, 1392, 1264, 1074, 883, 771, 730, 666, 616 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{31}H_{43}N_2O_2Si$ $[M+H]^+$ 503.3088, found 503.3089; **TLC**: R_f = 0.40 (7:3 Hex/EtOAc).

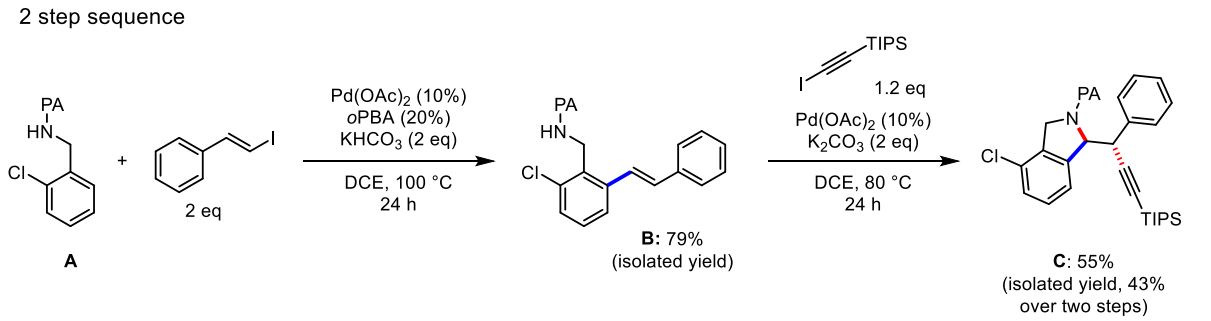
(4-Chloro-1-(1-phenyl-3-(triisopropylsilyl)prop-2-yn-1-yl)isoindolin-2-yl)(pyridin-2-yl)methanone (19)



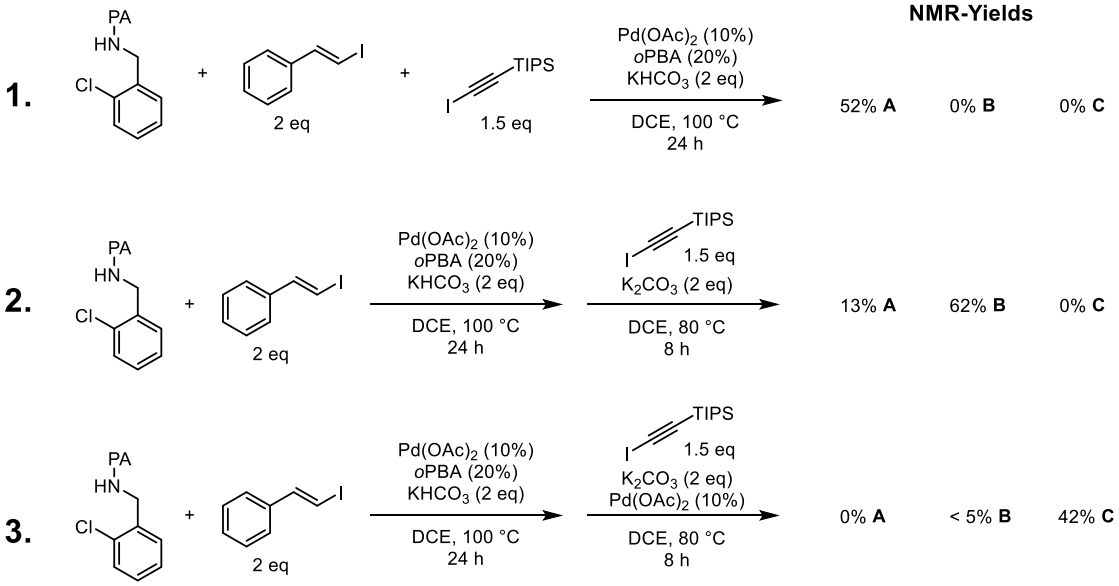
The title compound was prepared according to general procedure 4 from (*E*)-*N*-(2-chloro-6-styrylbenzyl)picolinamide **18** (101 mg, 0.30 mmol, 1.0 equiv) and (iodoethynyl)triisopropylsilane **3** (110 mg, 0.36 mmol, 1.2 equiv). The crude product was purified by flash column chromatography (8:2 Hex/EtOAc) to afford a yellow oil (88 mg, 0.17 mmol, 55%). Ratio of rotamers major:minor = 2.3:1.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H, minor), 8.67 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H, major), 8.02 (dt, *J* = 7.9, 1.1 Hz, 1H, minor), 7.97 (dt, *J* = 7.9, 1.1 Hz, 1H, major), 7.93 – 7.89 (m, 1H), 7.89 – 7.84 (m, 1H), 7.73 – 7.69 (m, 1H, minor), 7.45 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H, minor), 7.42 (ddd, *J* = 7.6, 4.8, 1.3 Hz, 1H, major), 7.28 – 6.99 (m, 10H, major + minor), 6.94 – 6.85 (m, 1H, major), 6.69 (dd, *J* = 4.0, 1.5 Hz, 1H, minor), 6.19 – 6.02 (m, 1H, major), 5.03 (d, *J* = 4.3 Hz, 1H, major), 4.89 (d, J = 16.7 Hz, 1H, minor), 4.68 (d, *J* = 15.9 Hz, 1H, major), 4.55 (d, *J* = 3.9 Hz, 1H, minor), 4.08 (dd, *J* = 15.9, 1.8 Hz, 1H, major), 3.87 (dd, *J* = 16.6, 1.6 Hz, 1H, minor), 1.17 (m, 21H, major), 1.12 (m, 21H, minor); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.6, 165.9, 153.6, 153.3, 148.4, 148.1, 140.4, 138.5, 137.4, 137.2, 137.0, 136.2, 135.9, 135.7, 129.3, 129.0, 128.6, 128.42, 128.41, 128.1, 128.0, 127.9, 127.7, 127.5, 127.4, 125.5, 125.3, 125.2, 124.3, 123.1, 122.4, 106.9, 106.5, 86.1, 68.7, 68.2, 54.4, 53.2, 45.3, 40.9, 18.85, 18.84, 18.79, 11.55, 11.48; **FT-IR** (neat) 2942, 2864, 2169, 1637, 1583, 1441, 1402, 1155, 1050, 996, 882, 730, 688 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{32}H_{38}ClN_2OSi$ $[M+H]^+$ 529.2436, found 529.2435; **TLC**: R_f = 0.47 (7.5:2.5 Hex/EtOAc).

2.6 One-Pot C–H Activation/Aminoalkynylation Sequence



1-pot protocol



Screening procedure for 1-pot protocol

A 7 mL microwave vial was charged with picolinamide starting material (25 mg, 0.10 mmol, 1.0 equiv), iodostyrene (46 mg, 0.20 mmol, 2.0 equiv). Then, the other reagents given above the first arrow were added in the stoichiometry indicated (for reaction 1 iodoacetylene (46 mg, 0.15 mmol, 1.5 equiv) was also added at this stage). 1.0 mL of DCE and a stir-bar was added, the vial was sealed, and the reaction was stirred at 100 °C for 24 h. Reactions 2 and 3 were allowed to cool to room temperature, the reagents above the second arrow were added in the stoichiometry indicated (the iodoacetylene was added as a solution in ca 0.4 mL DCE), the vial was re-sealed, and the reaction was stirred for 8 h at 80 °C.

The reactions were allowed to cool to room temperature, concentrated, and exactly 0.10 mmol of 1,1,2,2-tetrachloroethane was added as internal standard. The reaction-mixtures were analyzed by ^{1}H-NMR spectroscopy to determine the product distributions obtained. The obtained yields are given in the scheme above.

Interpretation of the results

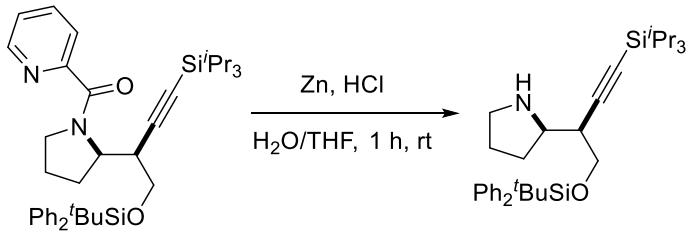
Reaction 1: Addition all reagents at the beginning and using $KHCO_3$ as base did not lead to any C–H alkenylation product. Ca 30% of a new product putatively assigned as ortho-C–H alkynylation product were formed, in addition to 52% of starting material being recovered. Presumably, the iosoacetylene is more reactive than the iodostyrene, thereby shutting the down the alkenylation reaction.

Reaction 2: Addition of iodoacetylene and K_2CO_3 after 24 h and subsequent reaction for 8 h did not afford any aminoalkynylation product. However, 62% of alkenylated intermediate **B** were recovered. This result indicates that there is no more active palladium-catalyst present after 24 h, thus no subsequent cyclization was observed.

Reaction 3: When additional palladium-catalyst was added together with the iodoacetylene and K_2CO_3 consumption of **B** and formation of **C** in 42% yield was observed. This result shows that an operationally simple and convenient one-pot C–H alkenylation/aminoalkynylation is possible. However, the yield did not improve over the 2-step sequence (43% isolated after purification).

2.7 Derivatizations

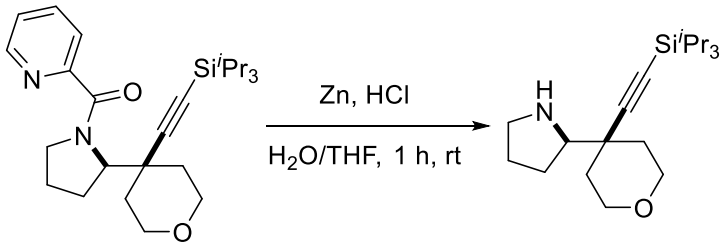
2-(1-((*Tert*-butyldiphenylsilyl)oxy)-4-(triisopropylsilyl)but-3-yn-2-yl)pyrrolidine (20)



Based on a literature procedure[15] (2-(1-((*tert*-butyldiphenylsilyl)oxy)-4-(triisopropylsilyl)but-3-yn-2-yl)pyrrolidin-1-yl)(pyridin-2-yl)methanone **2c** (15 mg, 24 µmol, 1.0 equiv) was dissolved in THF (0.5 mL). Water (0.5 mL) and 37% aq HCl (0.07 mL) were added and the reaction mixture was stirred at room temperature for 5 min. Zn dust (23 mg, 350 µmol, 15 equiv) was added in two portions and the reaction mixture was stirred at room temperature for 1 h. Upon completion, the reaction mixture was filtered through a pad of celite. 1 M NaOH (10 mL) was added to the filtrate and the aqueous phase was extracted with dichloromethane. The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography (100% DCM to 96:4 DCM/MeOH) to afford a brown oil (9.0 mg, 20 µmol, 71%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (dt, *J* = 8.0, 1.7 Hz, 4H), 7.40 (dddd, *J* = 14.1, 8.3, 6.0, 2.2 Hz, 6H), 3.83 (dd, *J* = 10.1, 5.0 Hz, 1H), 3.74 (dd, *J* = 10.1, 6.7 Hz, 1H), 3.63 – 3.48 (m, 1H), 3.07 (t, *J* = 6.0 Hz, 3H), 1.95 (q, *J* = 8.9, 6.9 Hz, 1H), 1.90 – 1.79 (m, 3H), 1.04 (m, 30H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 135.77, 135.73, 133.15, 133.07, 130.0, 127.97, 127.95 105.1, 85.5, 65.1, 59.4, 46.5, 39.8, 29.8, 28.4, 27.0, 25.2, 19.3, 18.8, 11.3; **FT-IR** (neat) 2940, 2929, 2890, 2863, 1462, 1427, 1111, 1029, 997, 938, 918, 882, 823, 701, 677, 504, 490 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{33}H_{52}NOSi_2$ $[M+H]^+$ 534.3582, found 534.3581; **TLC**: R_f = 0.23 (CH_2Cl_2/MeOH 96:4).

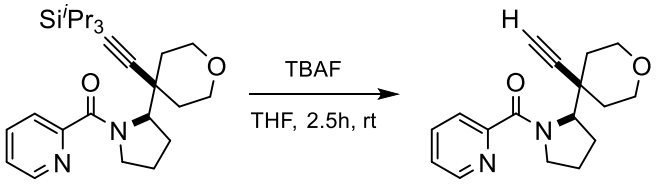
2-(4-((Triisopropylsilyl)ethynyl)tetrahydro-2H-pyran-4-yl)pyrrolidine (21)



Based on a literature procedure[15] pyridin2-yl(2-(4-((triisopropylsilyl)ethynyl)tetrahydro-2H-pyran-4-yl)pyrrolidin-1-yl)methanone **2a** (25 mg, 57 µmol, 1.0 equiv) was dissolved in THF (1.0 mL). Water (1.0 mL) and 37% aq HCl (0.13 mL) were added and the reaction mixture was stirred at room temperature for 5 min. Zn dust (56 mg, 850 µmol, 15 equiv) was added in two portions and the reaction mixture was stirred at room temperature for 1 h. Upon completion, the reaction mixture was filtered through a pad of celite. 1 M NaOH (20 mL) was added to the filtrate and the aqueous phase was extracted with dichloromethane. The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography (100% DCM to 95:5 DCM/MeOH) to afford a brown oil (15 mg, 0.040 mmol, 76%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.92 – 3.83 (m, 2H), 3.77 (tt, *J* = 12.0, 2.9 Hz, 2H), 3.18 (t, *J* = 6.4 Hz, 3H), 2.11 – 1.83 (m, 5H), 1.75 (td, *J* = 12.6, 4.5 Hz, 1H), 1.68 – 1.48 (m, 2H), 1.07 (m, 21H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 107.5, 87.9, 67.6, 64.9, 64.5, 47.0, 39.9, 36.3, 35.8, 27.4, 25.2, 18.8, 11.3; **FT-IR** (neat) 2942, 2863, 1463, 1383, 1300, 1103, 1031, 996, 882, 676 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{20}H_{38}NOSi$ $[M+H]^+$ 336.2717, found 336.2715; **TLC**: R_f = 0.20 (CH_2Cl_2/MeOH).

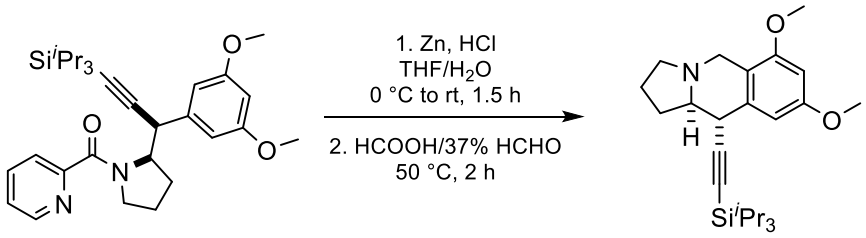
(2-(4-Ethynyltetrahydro-2H-pyran-4-yl)pyrrolidin-1-yl)(pyridin-2-yl)methanone (22)



Pyridin-2-yl(2-(4-((triisopropylsilyl)ethynyl)tetrahydro-2*H*-pyran-4-yl)pyrrolidin-1-yl)methanone **2a** (31 mg, 70 µmol, 1.00 equiv) in THF (1.2 mL) was cooled to 0 °C. TBAF (1 M solution in THF, 0.15 mL, 150 µmol, 2.1 equiv) was added dropwise and the resulting mixture stirred at room temperature for 2.5 h. The reaction mixture was diluted with water (20 mL) and the aqueous phase was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with water (20 mL) and brine (25 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography (1:4 Hex/EtOAc) to yield a viscous oil (16 mg, 60 µmol, 80%). Ratio of rotamers major:minor = 9:1.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (d, *J* = 4.8 Hz, 1H, major), 8.51 (d, *J* = 4.8 Hz, 1H, minor), 7.80 – 7.75 (m, 1H), 7.75 – 7.71 (m, 1H), 7.33 (ddd, *J* = 7.2, 4.8, 1.6 Hz, 1H), 5.17 (dd, *J* = 6.8, 2.6 Hz, 1H, minor), 4.56 (dd, *J* = 8.3, 5.0 Hz, 1H, major), 4.19 – 4.11 (m, 1H, minor), 3.90 (d, *J* = 7.1 Hz, 1H, major), 3.88 – 3.81 (m, 2H), 3.80 – 3.73 (m, 1H), 3.73 – 3.68 (m, 1H), 3.62 (m, 1H), 3.57 (m, 1H, minor), 2.28 (s, 1H, major), 2.25 – 2.23 (m, 1H, minor), 2.18 – 2.12 (m, 1H, major), 2.20 (s, 1H, minor), 2.07 (m, 2H, major), 2.02 (m, 1H, minor), 1.77 – 1.70 (m, 2H), 1.70 – 1.66 (m, 1H), 1.62 (dd, *J* = 13.1, 2.4 Hz, 2H), 1.41 – 1.38 (m, 1H, minor), 1.34 (m, *J* = 9.1, 6.6, 3.0 Hz, 1H, min); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.7, 167.4, 155.3, 154.7, 148.6, 147.6, 137.2, 136.8, 125.4, 124.9, 124.1, 86.3, 74.4, 73.8, 65.7, 64.9, 64.4, 64.3, 64.1, 51.1, 47.8, 41.7, 35.5, 35.4, 35.0, 27.3, 26.1, 25.5, 22.7; **FT-IR** (neat) 3237, 2954, 2856, 1631, 1586, 1566, 1401, 1244, 1147, 1102, 1030, 994 cm^{-1}; **HRMS** (ESI): *m/z* calc. for $C_{17}H_{21}N_2O_2^+$ $[M+H]^+$ 285.1598, found 285.1598; **TLC**: R_f = 0.28 (1:4 Hex/EtOAc).

6,8-Dimethoxy-10-((triisopropylsilyl)ethynyl)-1,2,3,5,10,10a-hexahydropyrrolo[1,2-*b*]isoquinoline (23)



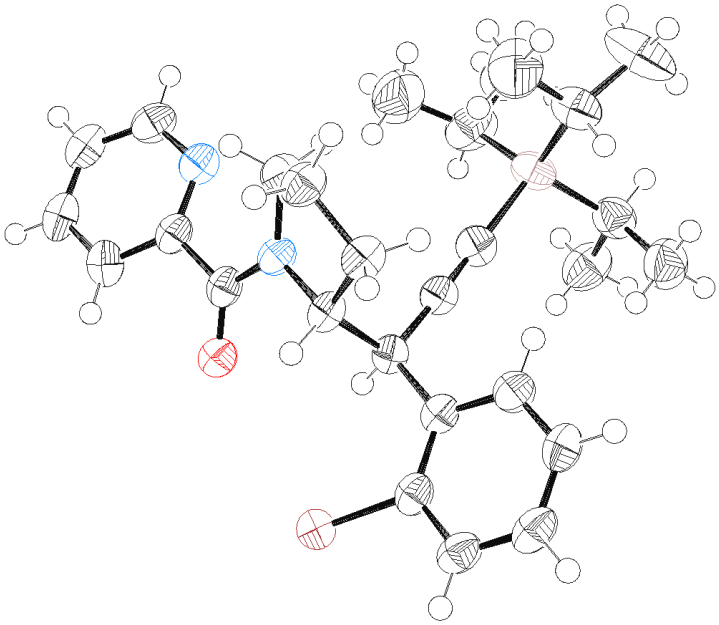
Based on a literature procedure[15] 1-(3,5-dimethoxyphenyl)-3-(triisopropylsilyl)prop-2-yn-1-yl)pyrrolidin-1-yl)(pyridin-2-yl)methanone **2k** (152 mg, 0.30 mmol, 1.0 equiv) was dissolved in THF (3 mL) and water (3 mL). 12 M HCl (0.74 mL) was added and the mixture was stirred for 5 min at 0 °C. Zinc dust (294 mg, 4.50 mmol, 15.0 equiv) was added in three portions and the mixture was stirred at room temperature. After 90 min, sand (400 mg) was added to the reaction and the mixture was filtered through a celite plug. The filtrate was mixed with 1 M NaOH (100 mL) and extracted with DCM (2 x 100 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was used in the next step without further purification.

Based on a literature procedure,[16] the crude product was dissolved in a HCOOH/37% aqueous HCHO (1:1, 2.8 mL) mixture and the reaction was stirred at 50 °C for 2 hours. The reaction mixture was allowed to cool to room temperature, K_2CO_3 was added, and the mixture was extracted with DCM (2 x 50 mL), washed with brine, dried with $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (Hex/EtOAc 4:1 to MeOH/EtOAc 1:20) to afford a yellow oil (86 mg, 0.21 mmol, 70%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (d, *J* = 2.4 Hz, 1H), 6.32 (d, *J* = 2.3 Hz, 1H), 4.18 (d, *J* = 15.2 Hz, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 3.68 (d, *J* = 10.0 Hz, 1H), 3.28 (td, *J* = 8.6, 2.3 Hz, 1H), 3.16 (dd, *J* = 15.1, 1.9 Hz, 1H), 2.42 (m, 1H), 2.36 (q, *J* = 9.0, 8.5 Hz, 1H), 2.26 (m, 1H), 1.97 – 1.88 (m, 1H), 1.83 (tt, *J* = 9.1, 2.8 Hz, 1H), 1.76 – 1.66 (m, 1H), 1.09 (d, *J* = 3.9 Hz, 21H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.1, 156.8, 136.5, 116.1, 108.3, 103.3, 97.3, 82.6, 65.2, 55.4, 55.3, 55.3, 50.5, 40.7, 30.5, 21.4, 18.8, 11.4; **FT-IR** (neat) 2942, 2865, 1770, 1610, 1463, 1382, 1315, 1241, 1202 1142,

1053, 910, 734, 677 cm^{-1}; **HRMS** (ESI): *m/z* calc. for $C_{25}H_{40}NO_2Si^+$ $[M+H]^+$ 414.2823, found 414.2823; **TLC**: R_f = 0.75 (1:3 Hex/EtOAc).

3. X-Ray Diffraction Data



ORTEP diagram of **2j**. Atomic displacement parameters at 100 K are drawn at 70% probability level. Disorder of the TIPS group has been removed for clarity.

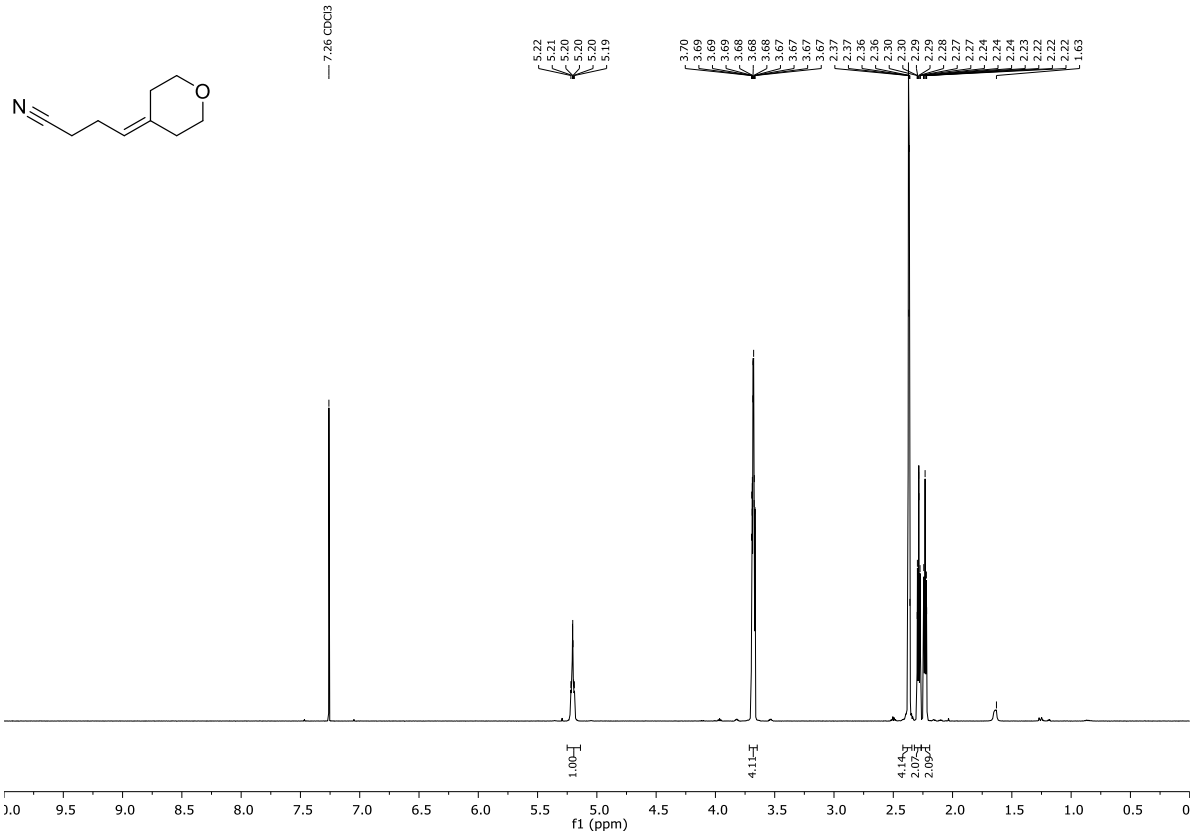
Crystal data and structure refinement for 2j.

Identification code	CCDC 2108775
Empirical formula	$C_{28}H_{37}BrN_2OSi$
Formula weight	525.59
Temperature/K	100.0(1)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	12.86950(10)
b/Å	11.98130(10)
c/Å	17.9543(2)
α/°	90
β/°	98.1430(10)
γ/°	90
Volume/Å^3	2740.52(4)
Z	4

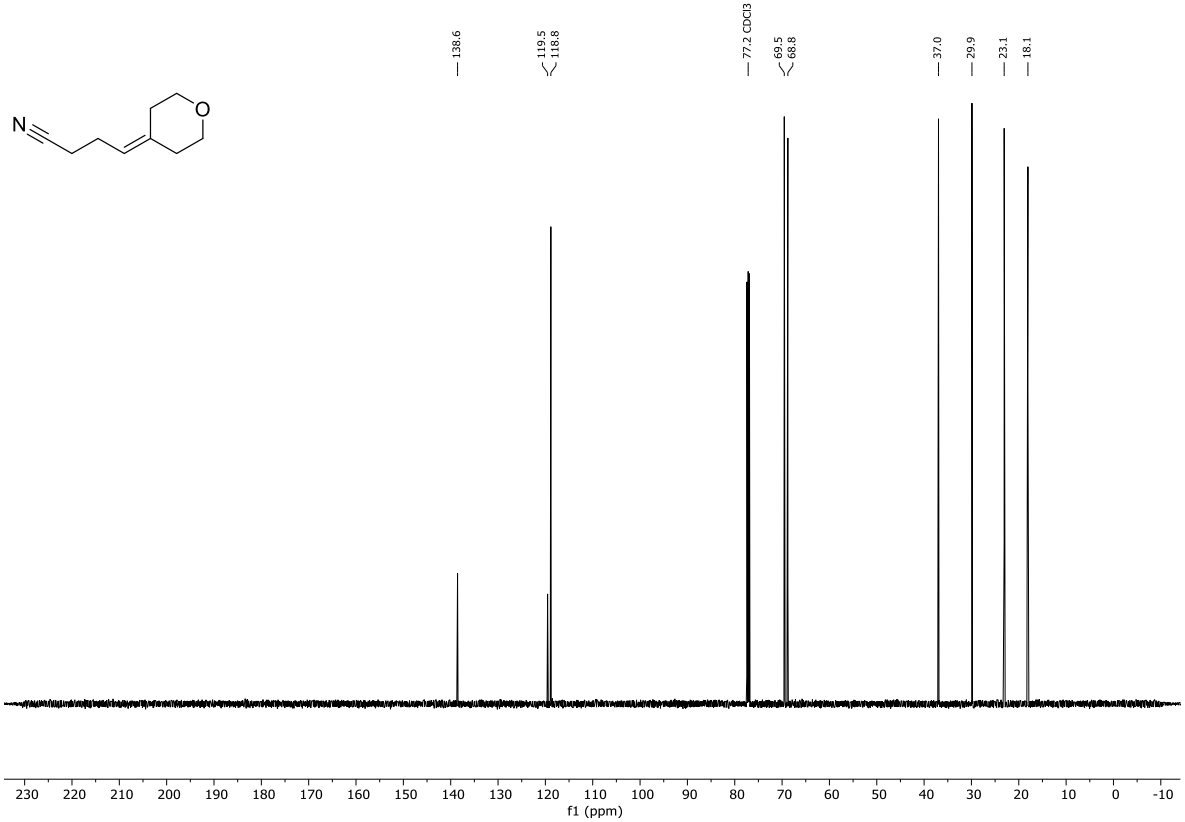
ρ_{calc}g/cm^3	1.274
μ/mm^{-1}	2.622
F(000)	1104.0
Crystal size/mm^3	0.323 × 0.284 × 0.042
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	6.938 to 160.164
Index ranges	-16 ≤ h ≤ 16, -15 ≤ k ≤ 15, -21 ≤ l ≤ 22
Reflections collected	72854
Independent reflections	5963 [R_{int} = 0.0608, R_{sigma} = 0.0237]
Data/restraints/parameters	5963/38/328
Goodness-of-fit on F^2	1.048
Final R indexes [I>=2σ (I)]	R_1 = 0.0526, wR_2 = 0.1434
Final R indexes [all data]	R_1 = 0.0547, wR_2 = 0.1449
Largest diff. peak/hole / e Å^{-3}	2.15/-0.70

4. NMR Data

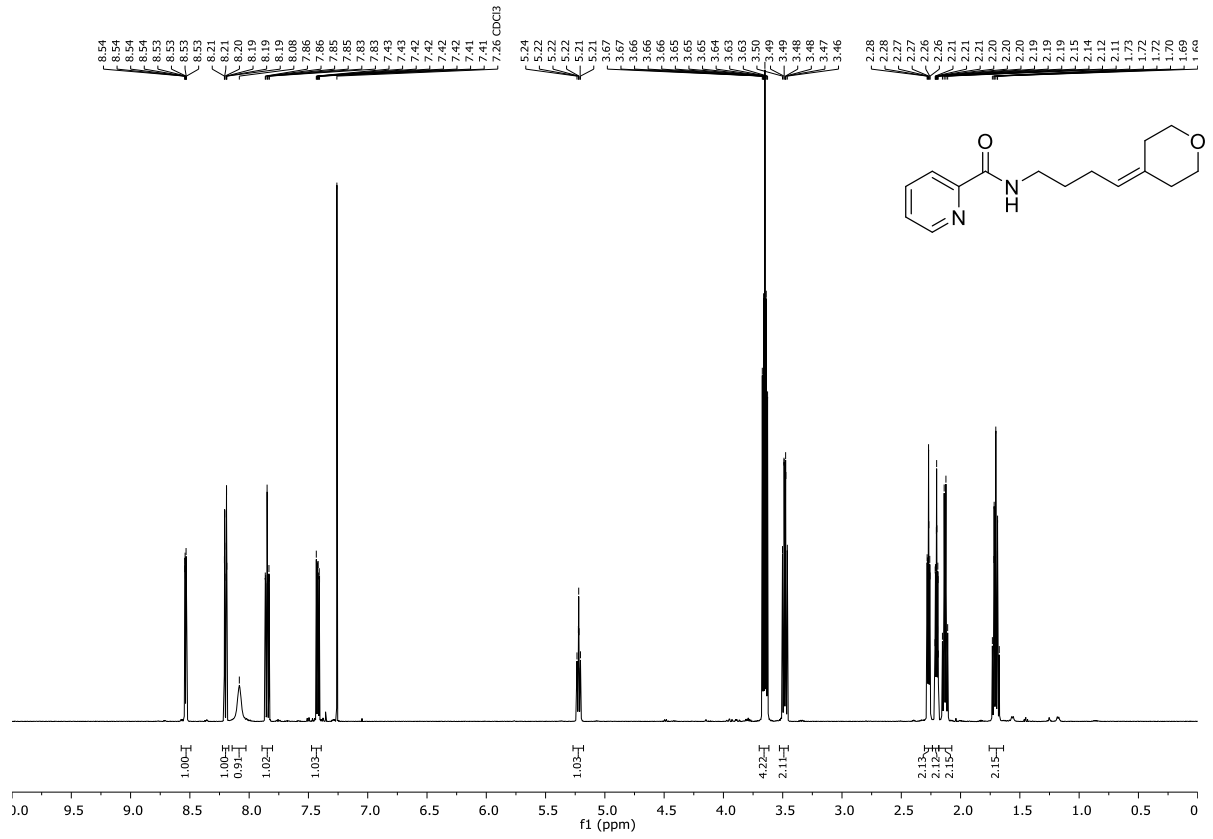
^{1}H NMR (500 MHz, $CDCl_3$) of **S2a**



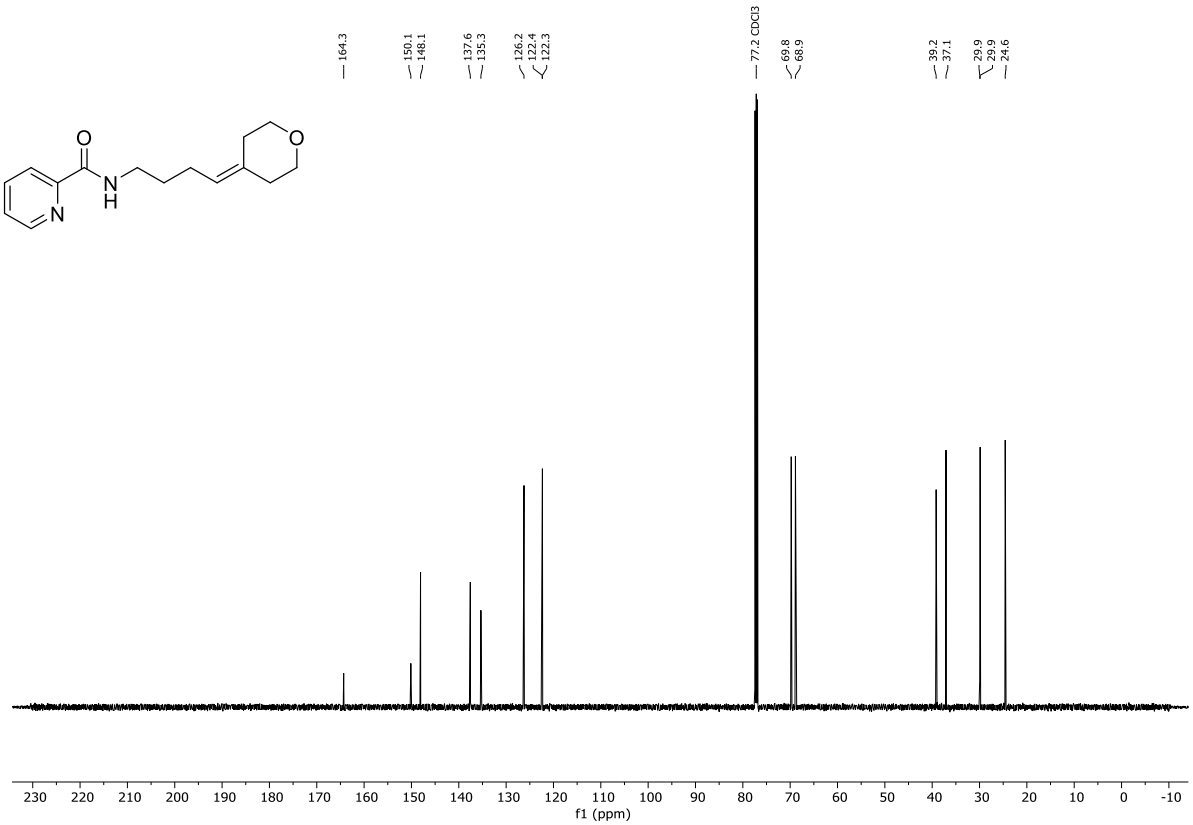
^{13}C NMR (126 MHz, $CDCl_3$) of **S2a**



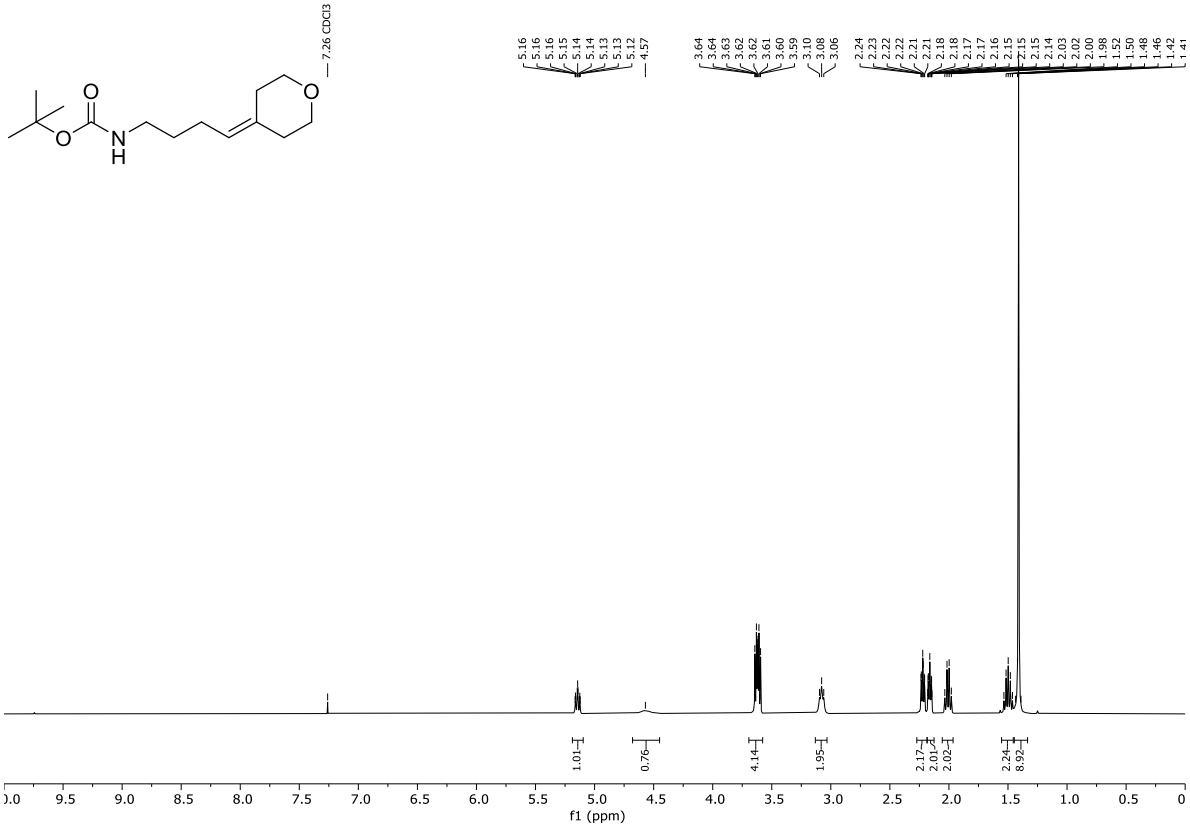
^{1}H NMR (500 MHz, $CDCl_3$) of **1a**



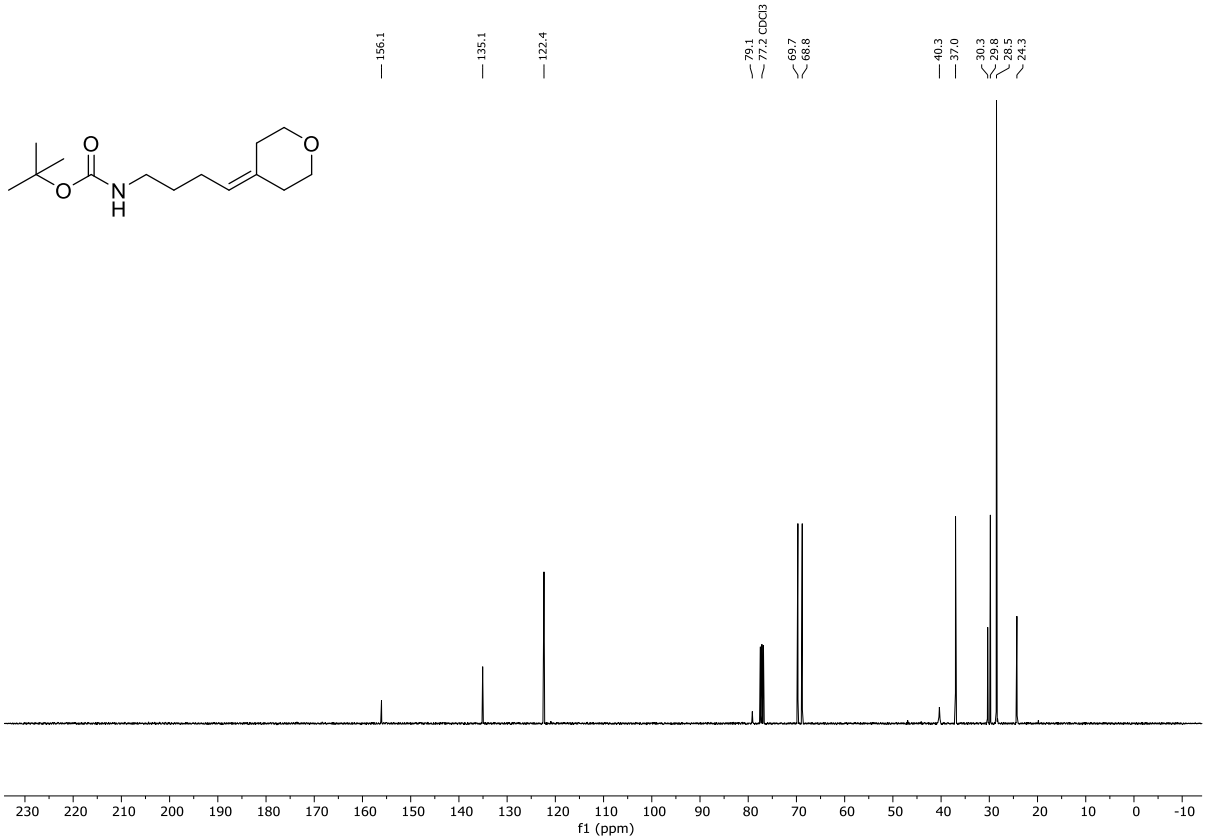
^{13}C NMR (126 MHz, $CDCl_3$) of **1a**



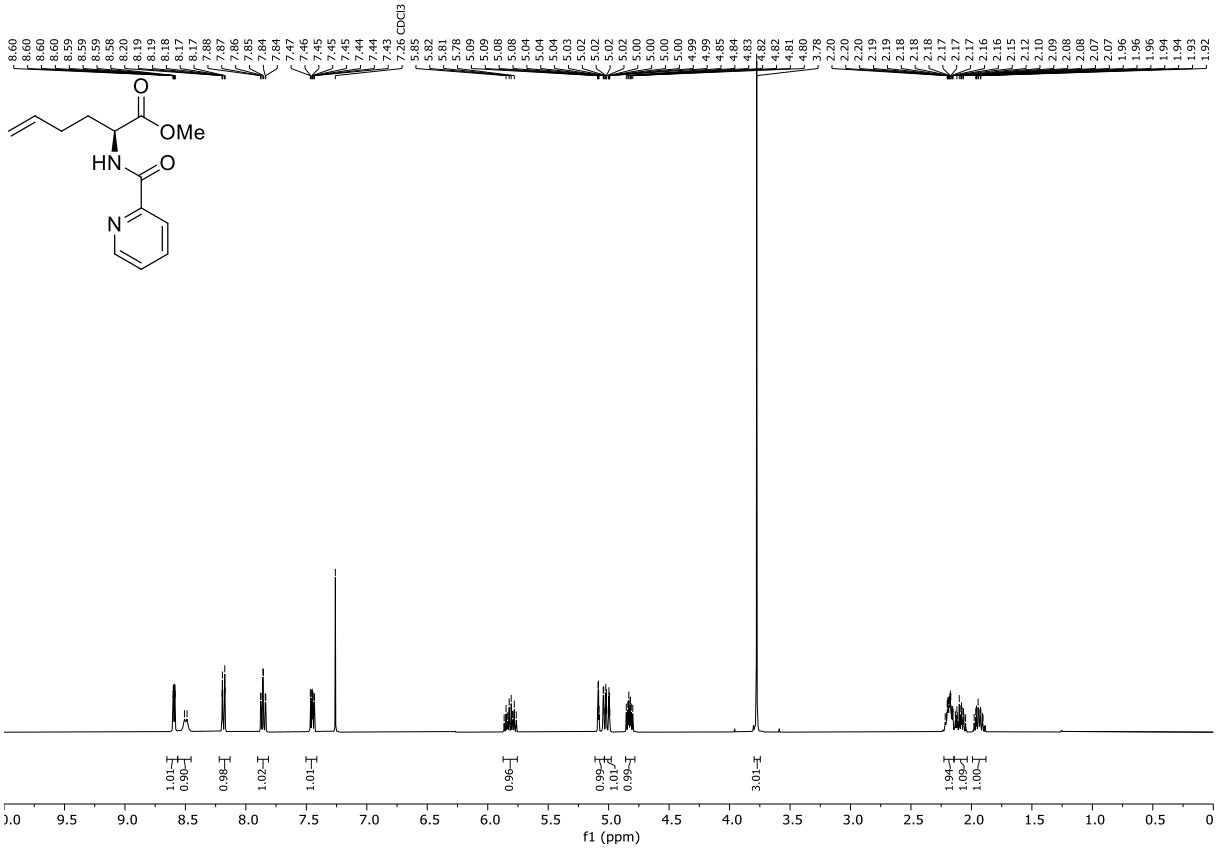
^{1}H NMR (400 MHz, $CDCl_3$) of **1a´**



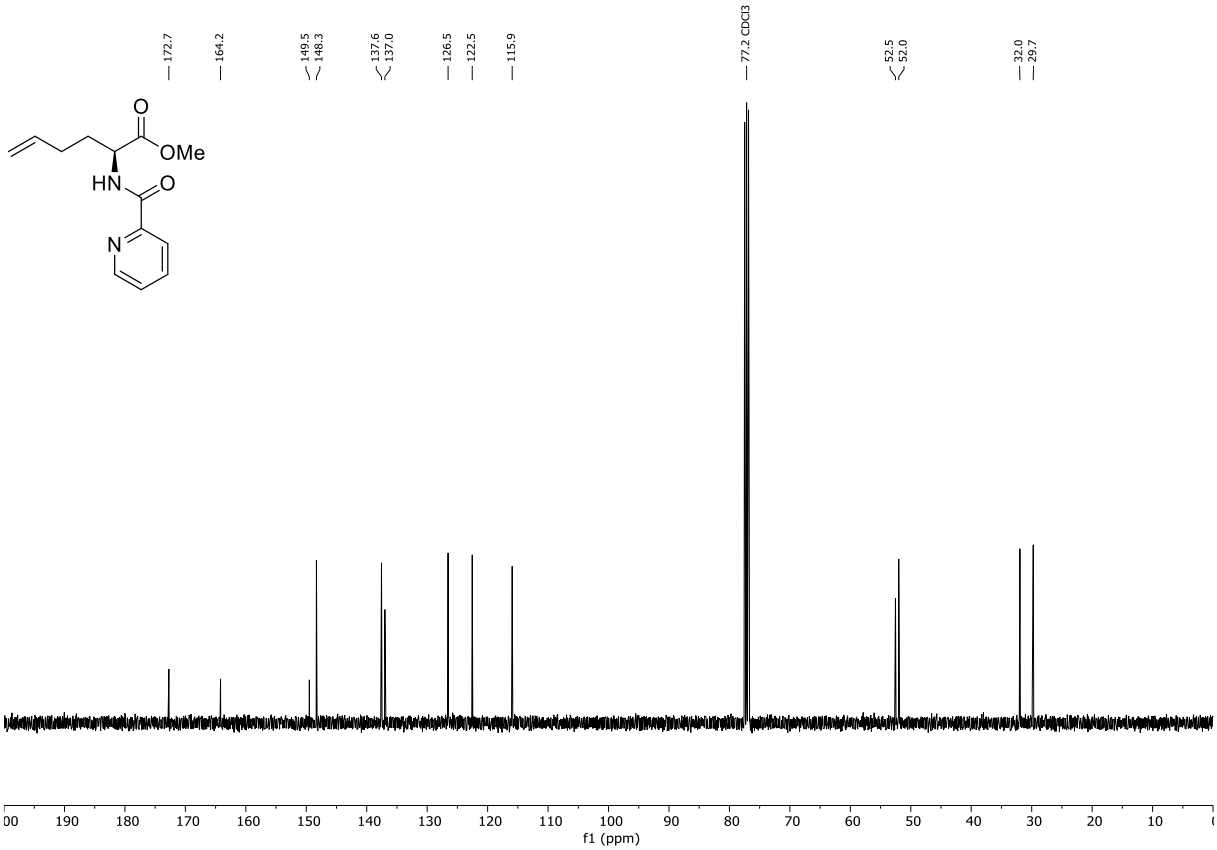
^{13}C NMR (101 MHz, $CDCl_3$) of **1a´**



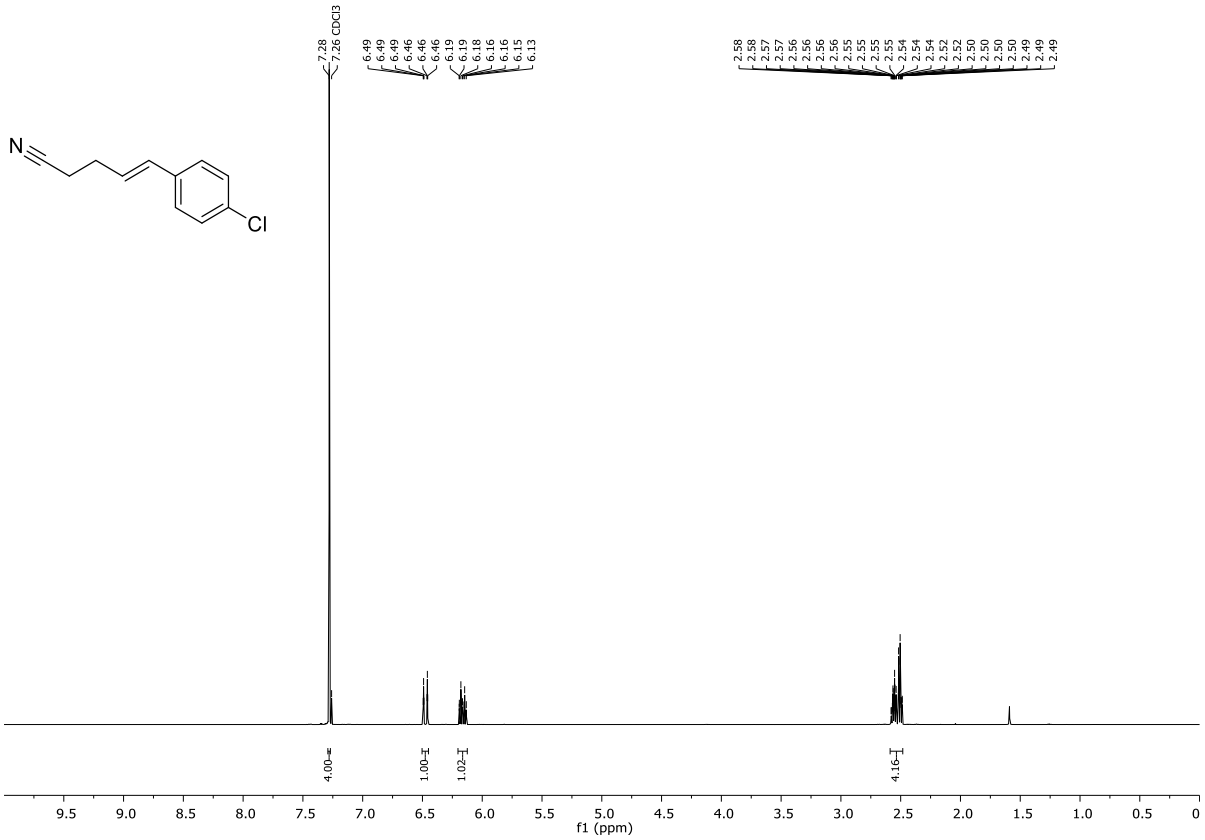
^{1}H NMR (400 MHz, $CDCl_3$) of **1c**



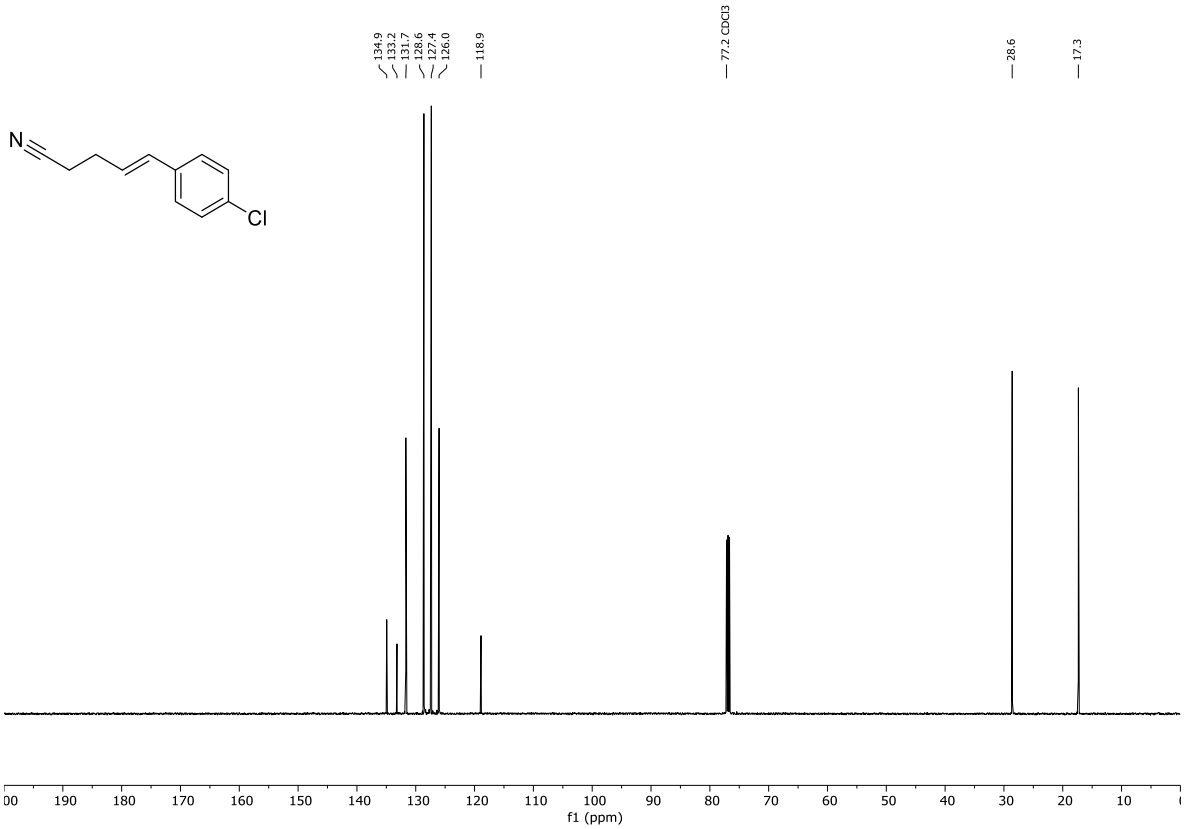
^{13}C NMR (101 MHz, $CDCl_3$) of **1c**



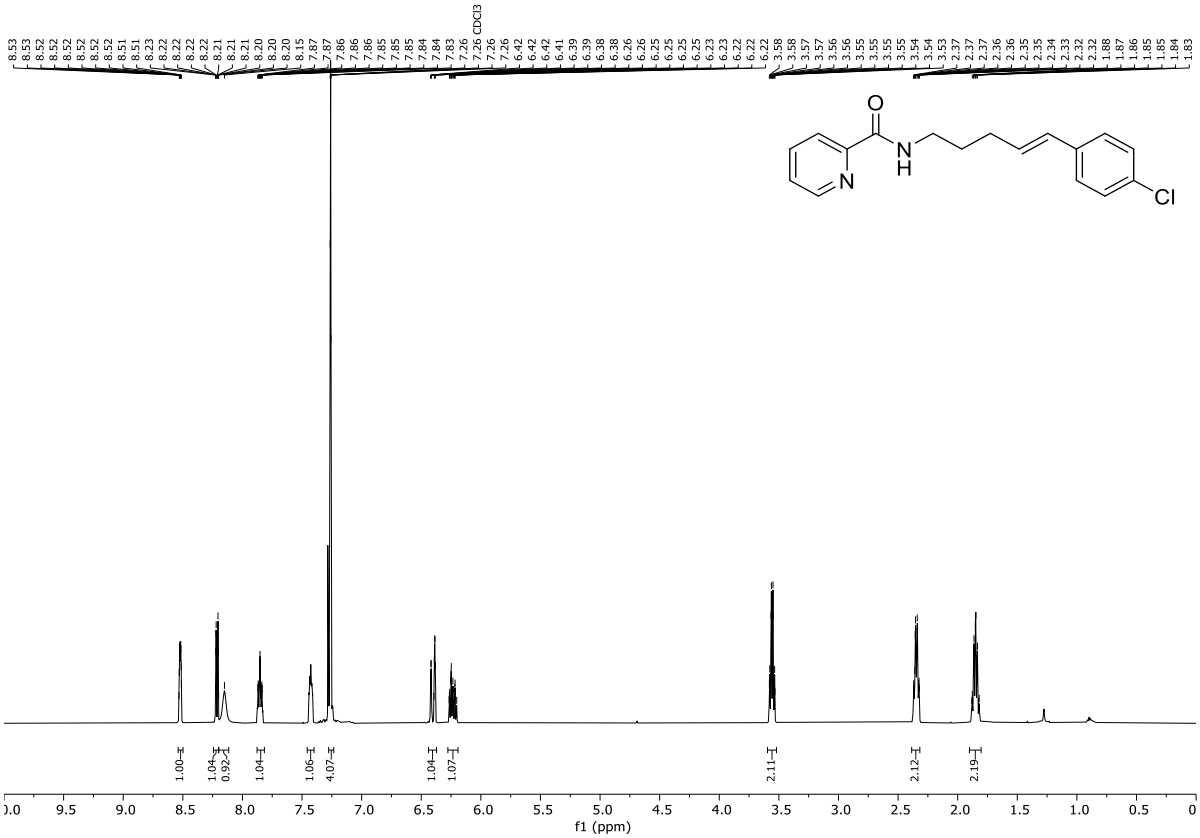
^{1}H NMR (500 MHz, $CDCl_3$) of **S2h**



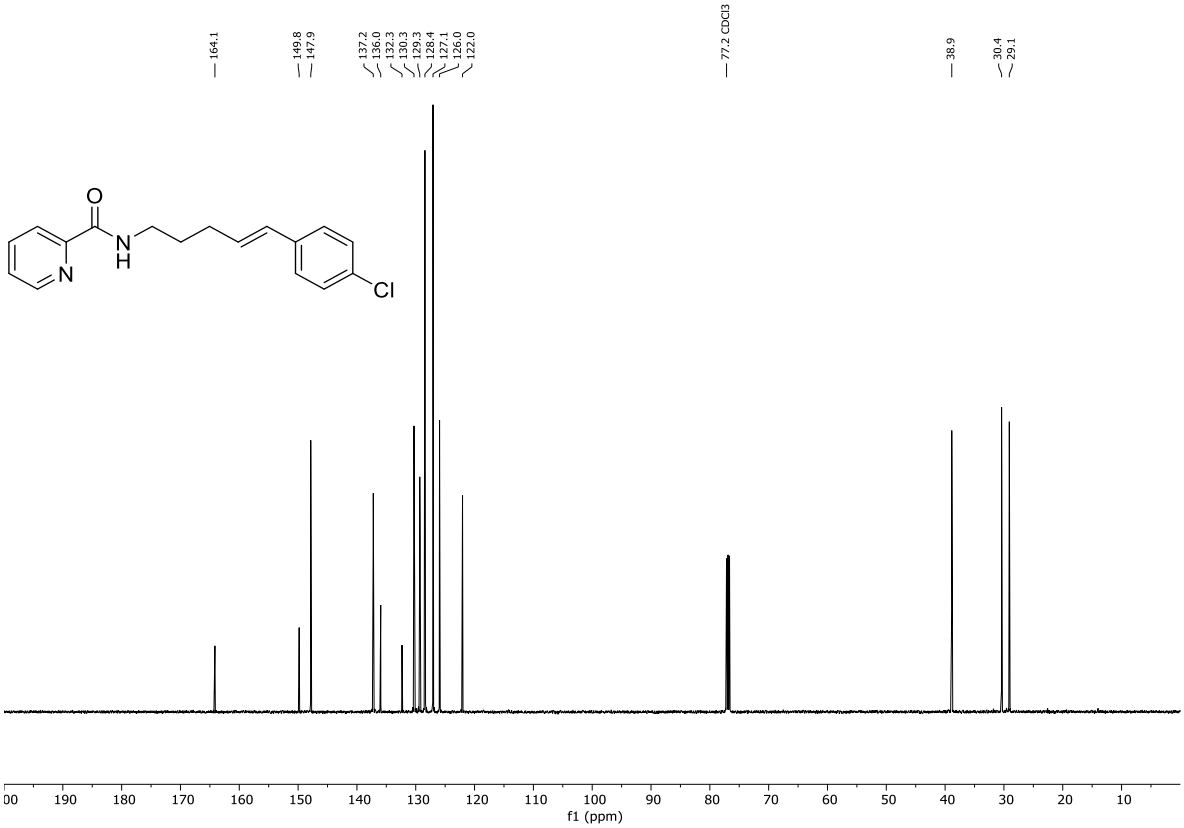
^{13}C NMR (126 MHz, $CDCl_3$) of **S2h**



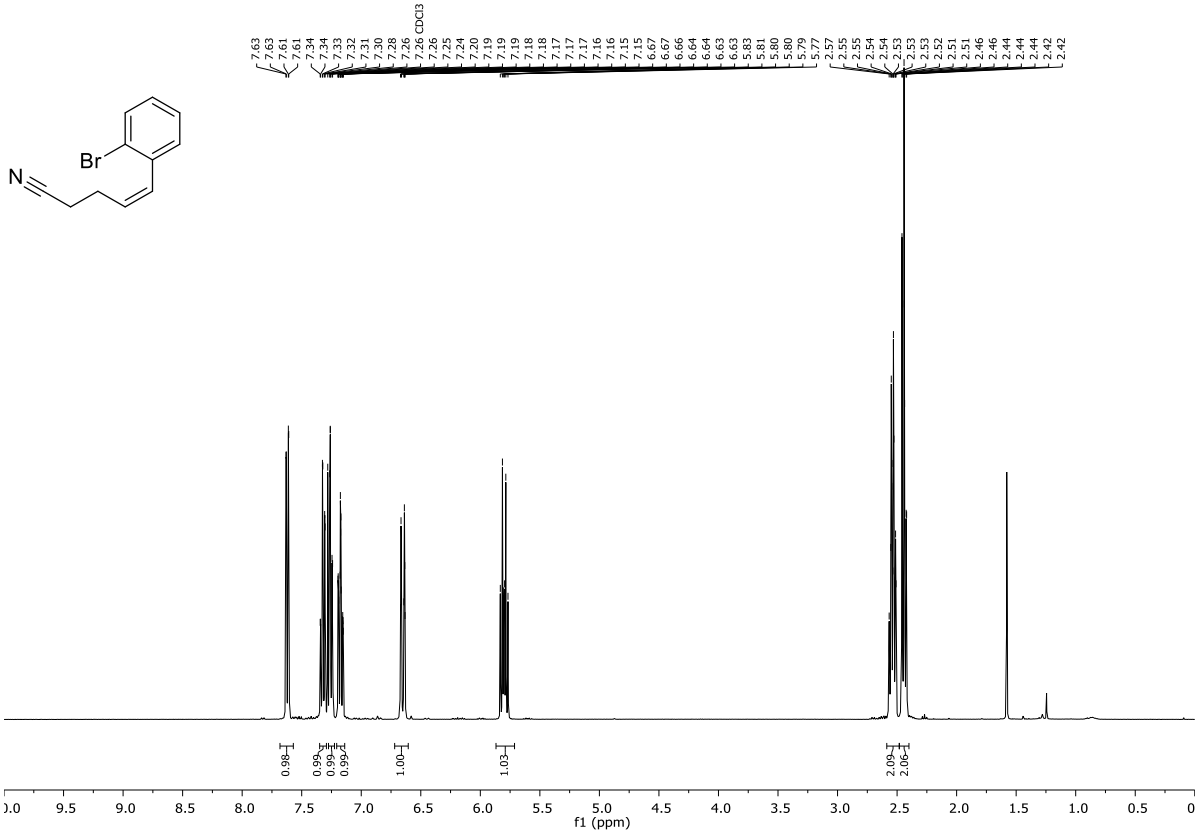
^{1}H NMR (500 MHz, $CDCl_3$) of **1h**



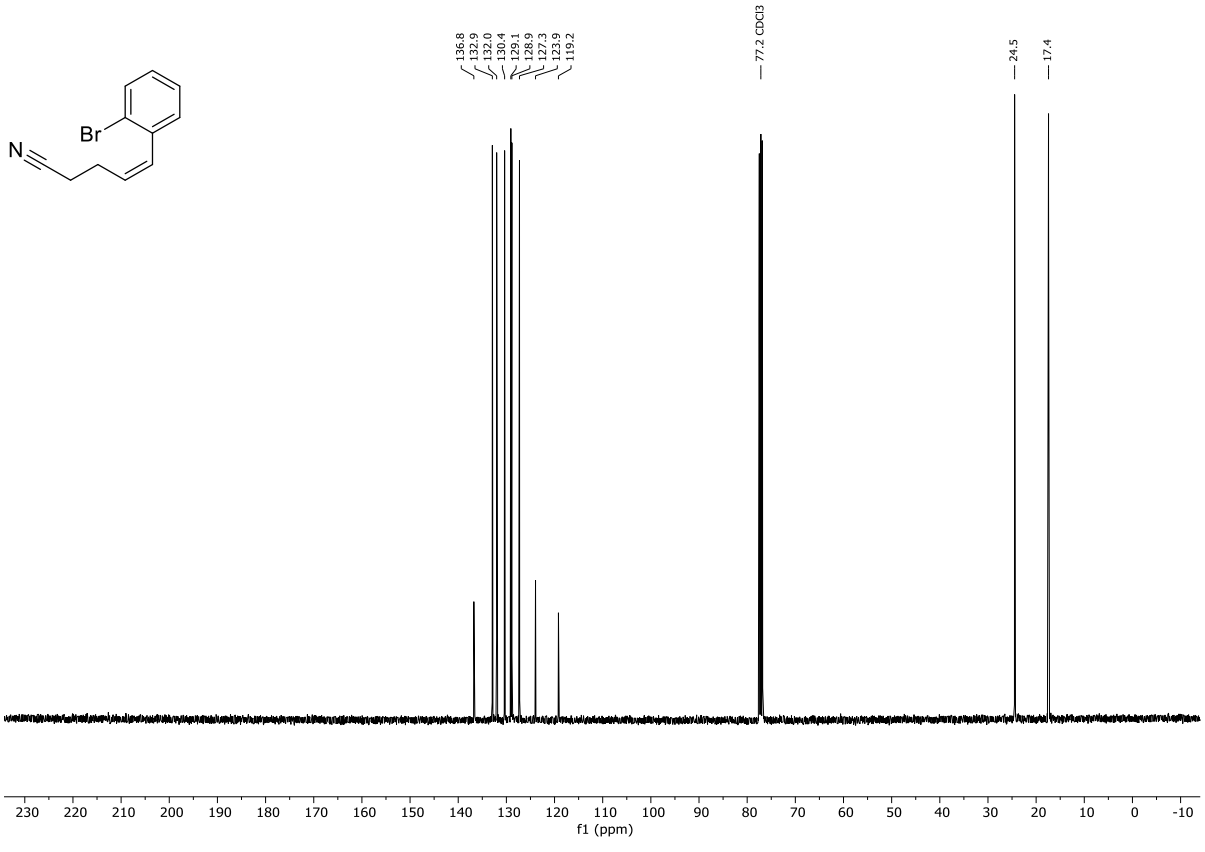
^{13}C NMR (126 MHz, $CDCl_3$) of **1h**



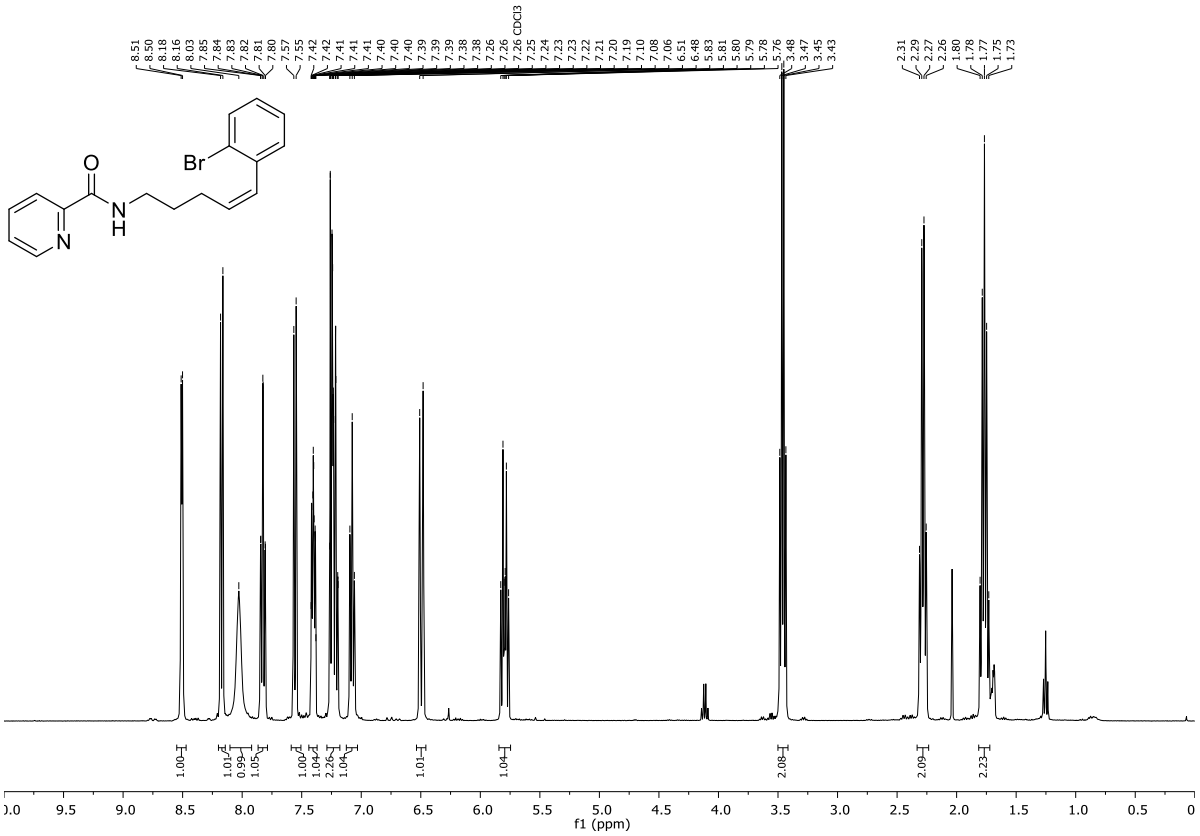
^{1}H NMR (400 MHz, $CDCl_3$) of **S2j**



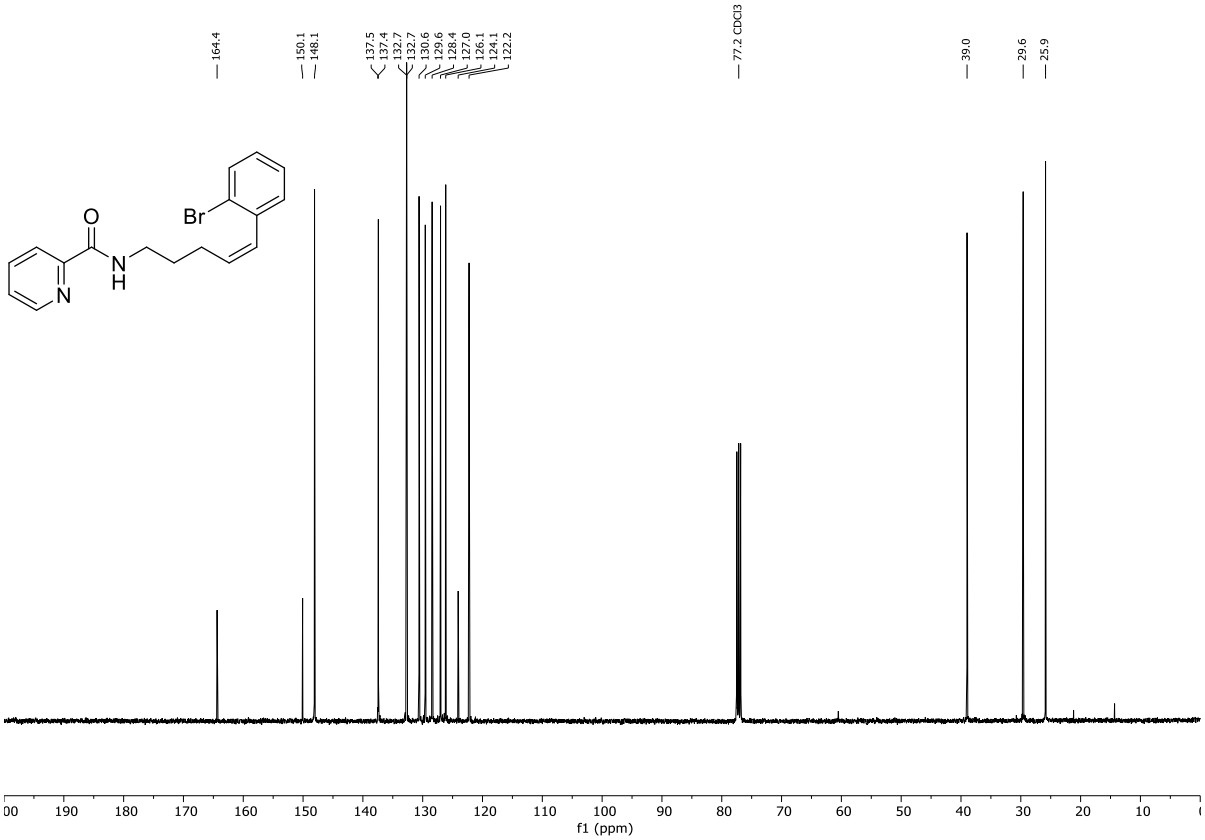
^{13}C NMR (100 MHz, $CDCl_3$) of **S2j**



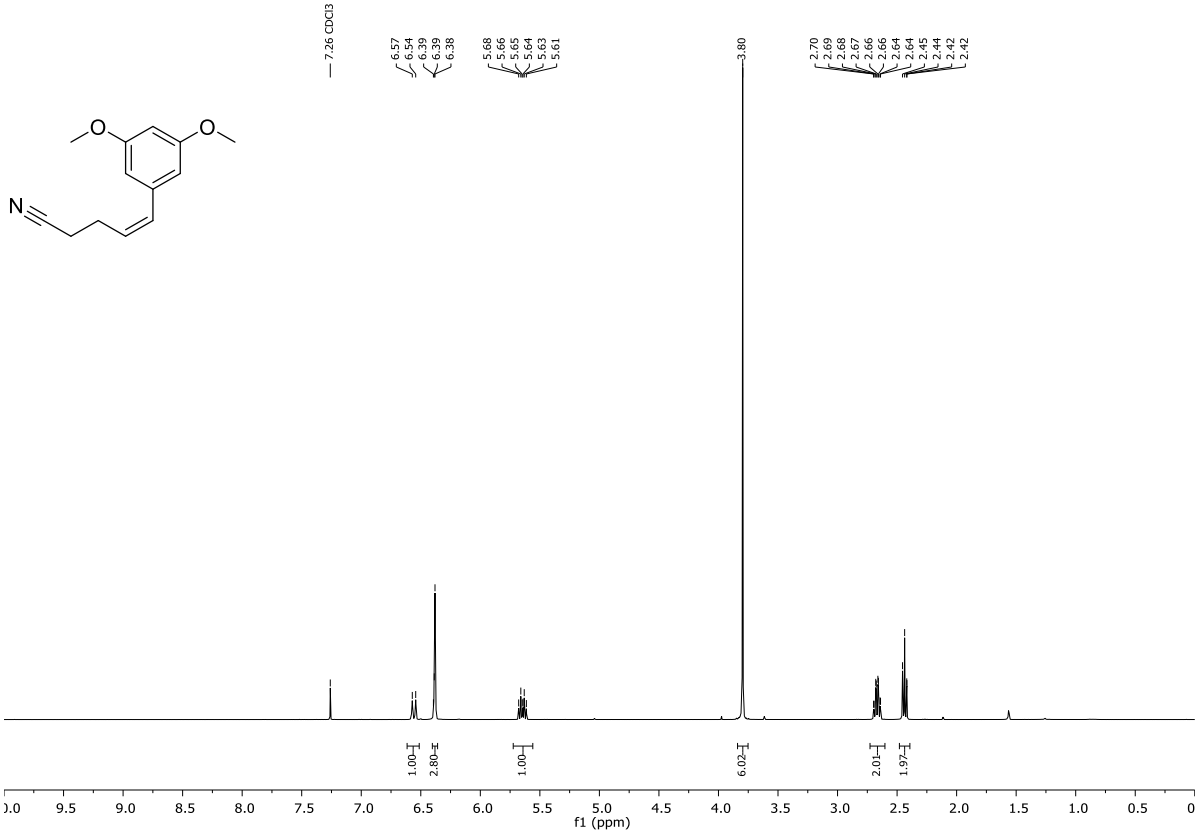
^{1}H NMR (400 MHz, $CDCl_3$) of **1j**



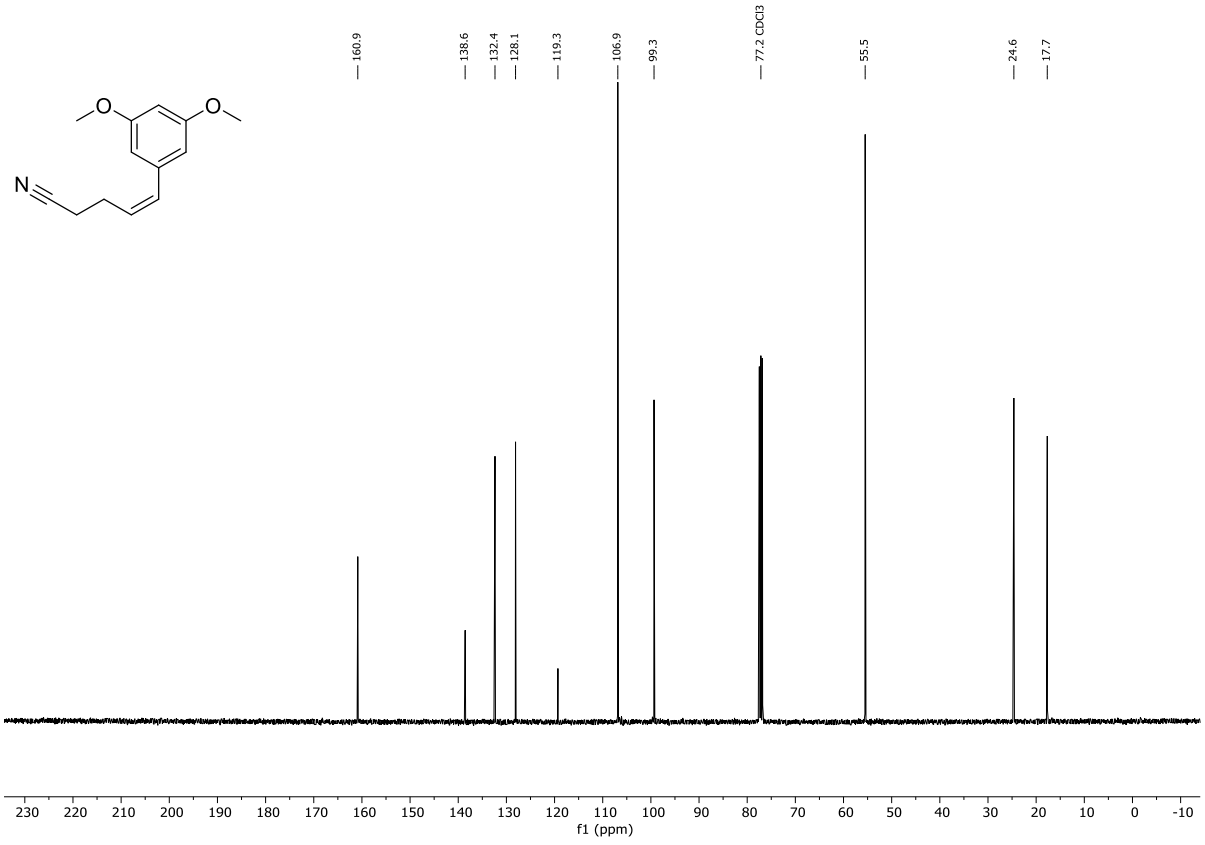
^{13}C NMR (100 MHz, $CDCl_3$) of **1j**



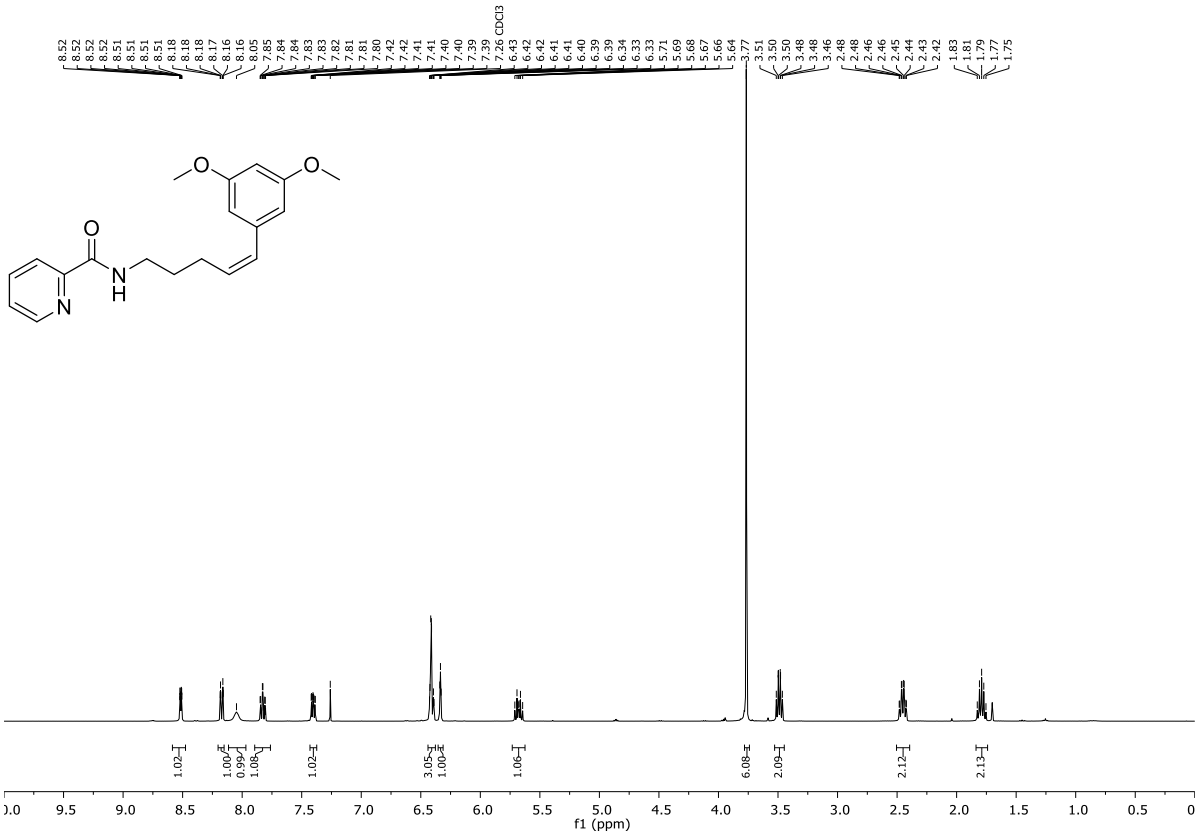
^{1}H NMR (400 MHz, $CDCl_3$) of **S2l**



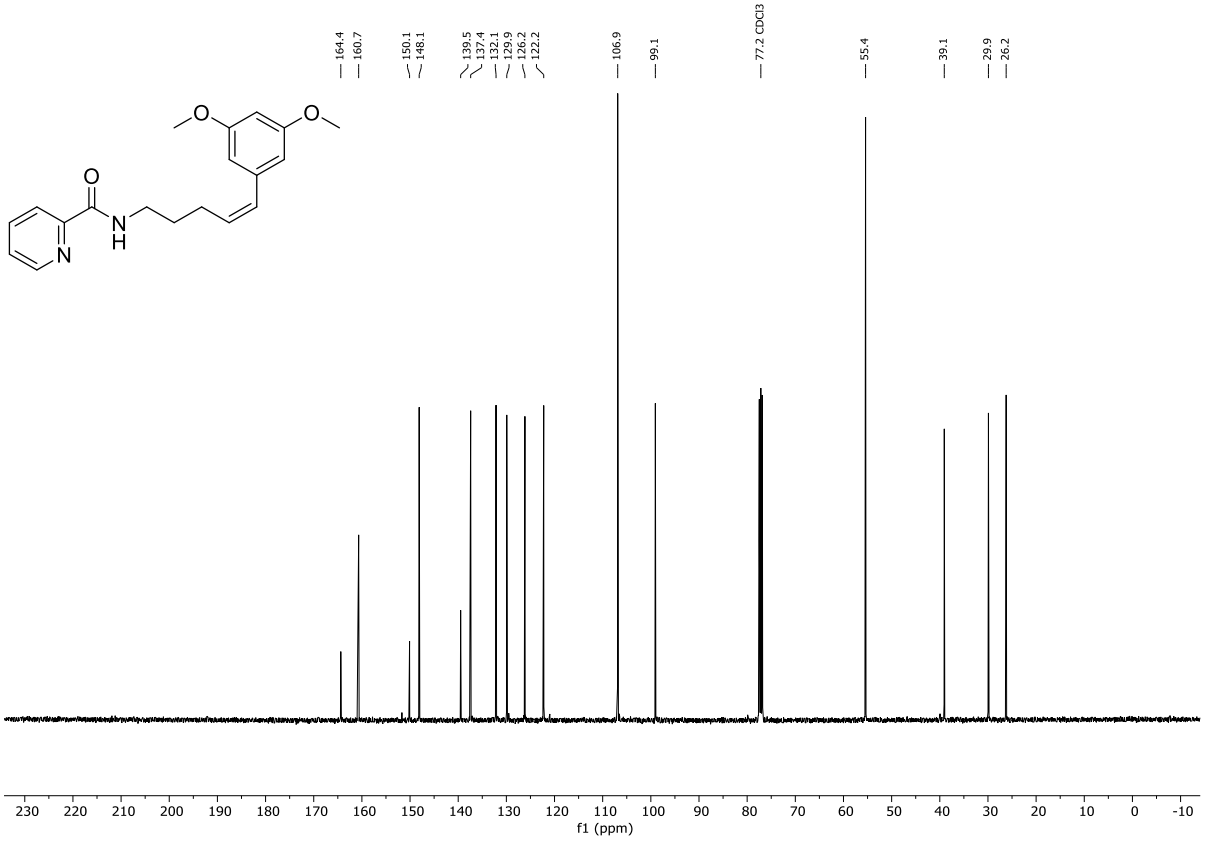
^{13}C NMR (100 MHz, $CDCl_3$) of **S2l**



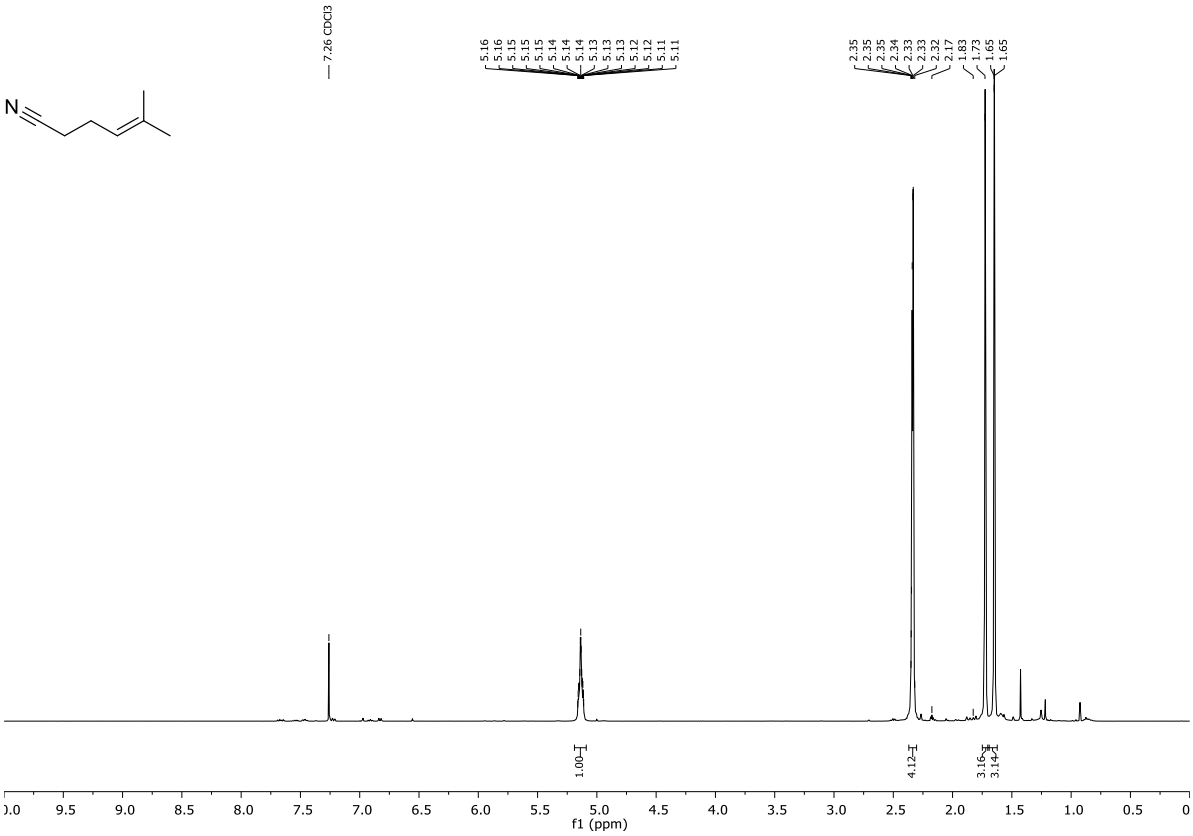
^{1}H NMR (400 MHz, $CDCl_3$) of **1l**



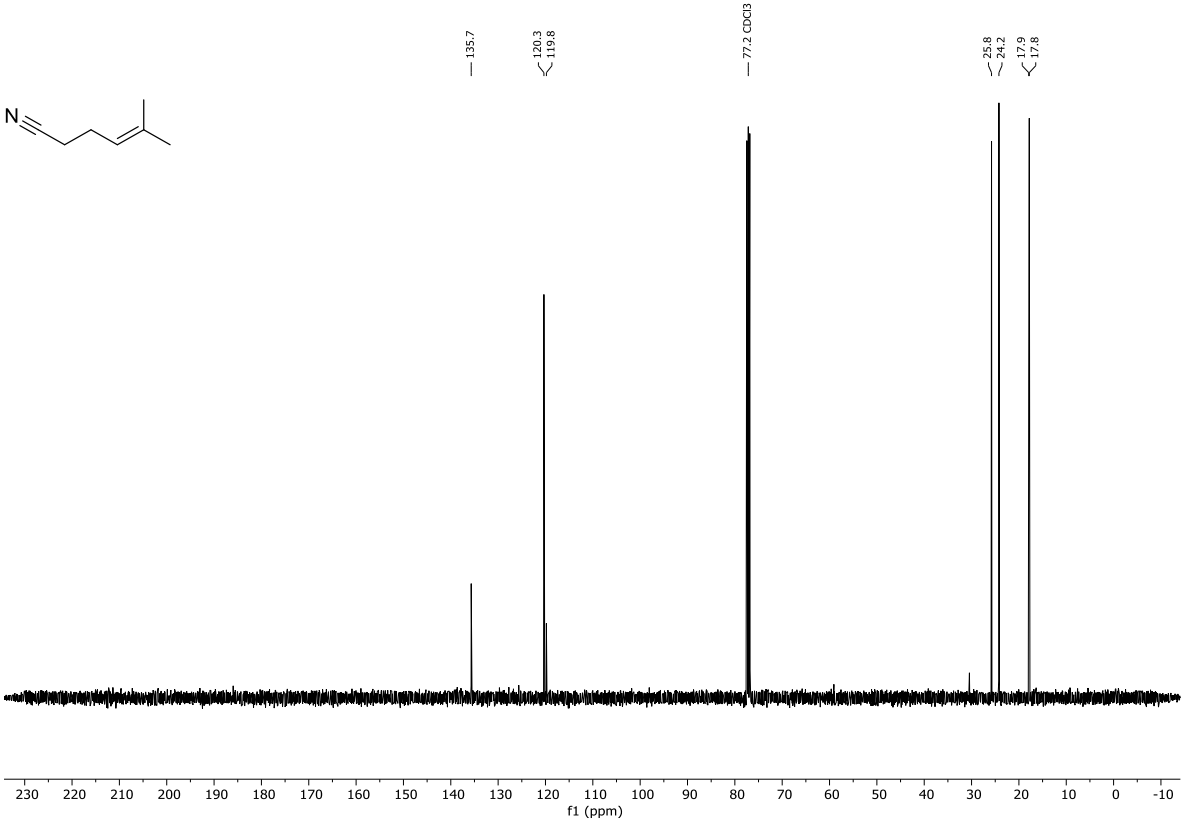
^{13}C NMR (100 MHz, $CDCl_3$) of **1l**



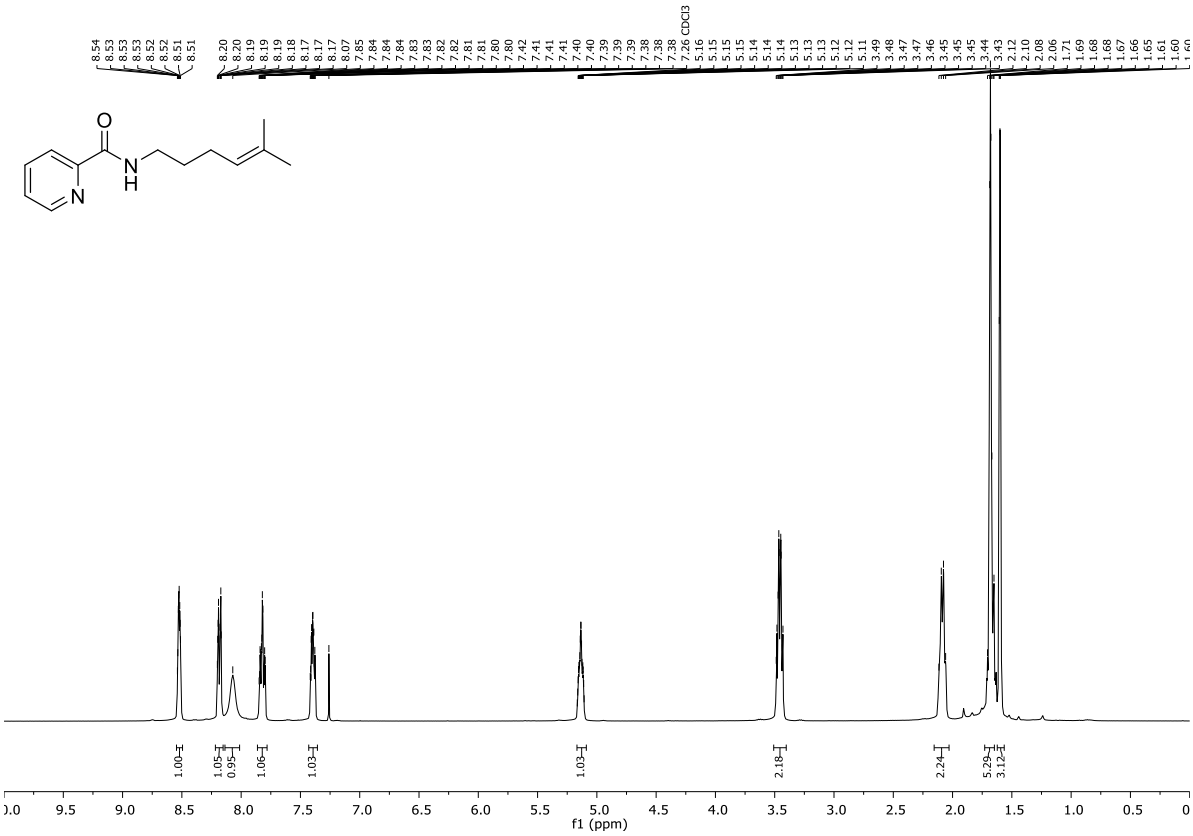
^{1}H NMR (400 MHz, $CDCl_3$) of **S2o**



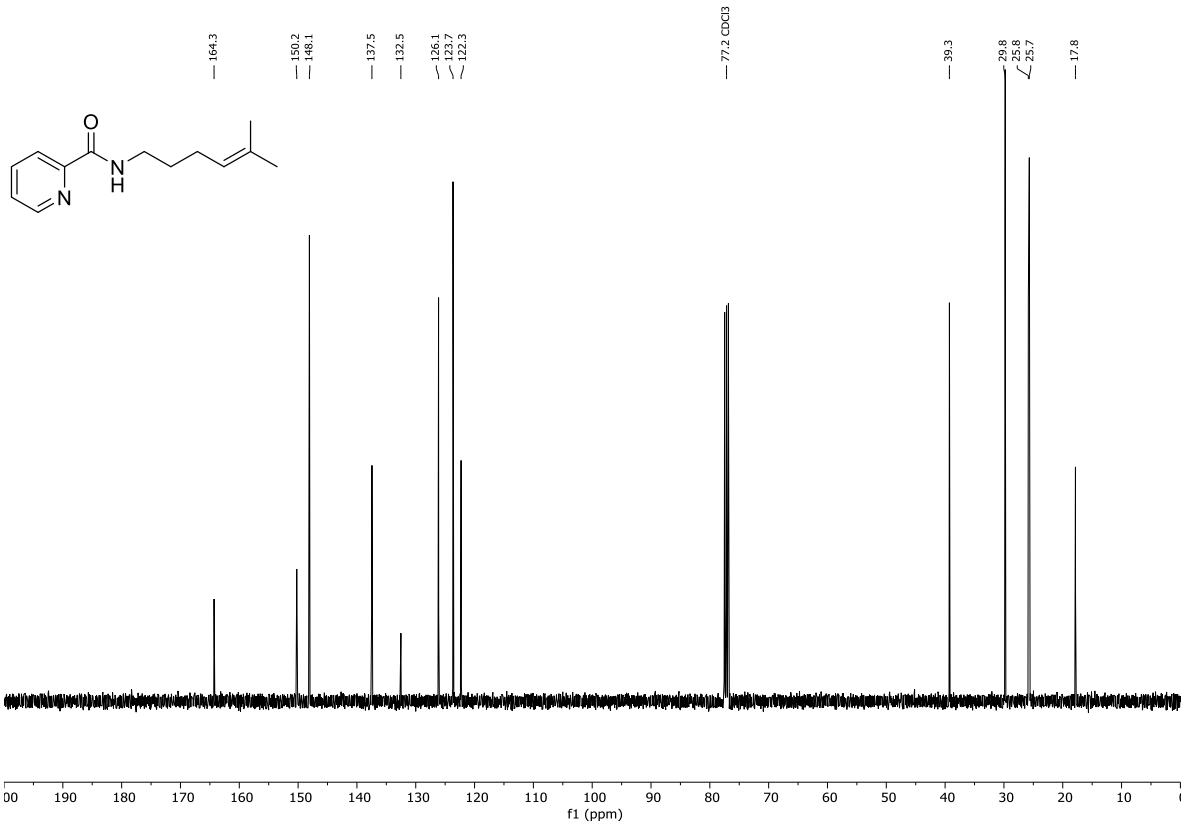
^{13}C NMR (101 MHz, $CDCl_3$) of **S2o**



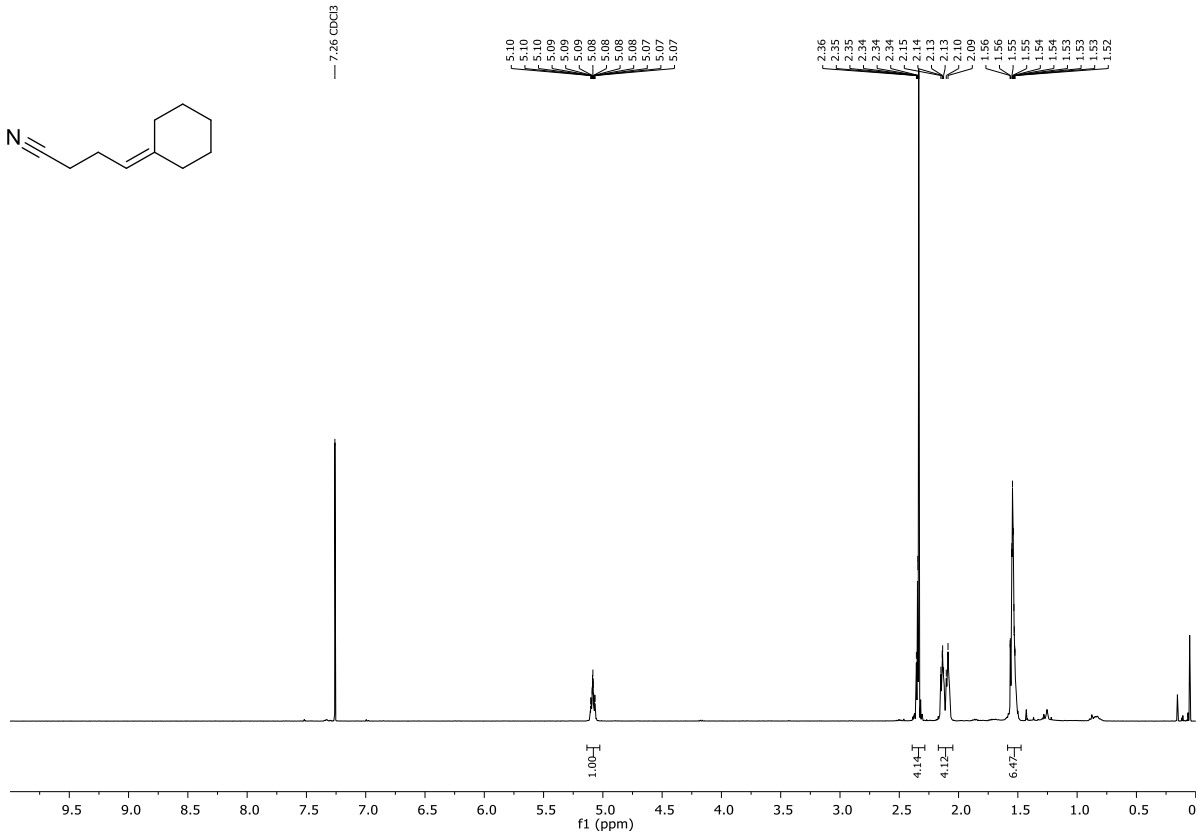
^{1}H NMR (400 MHz, $CDCl_3$) of **1o**



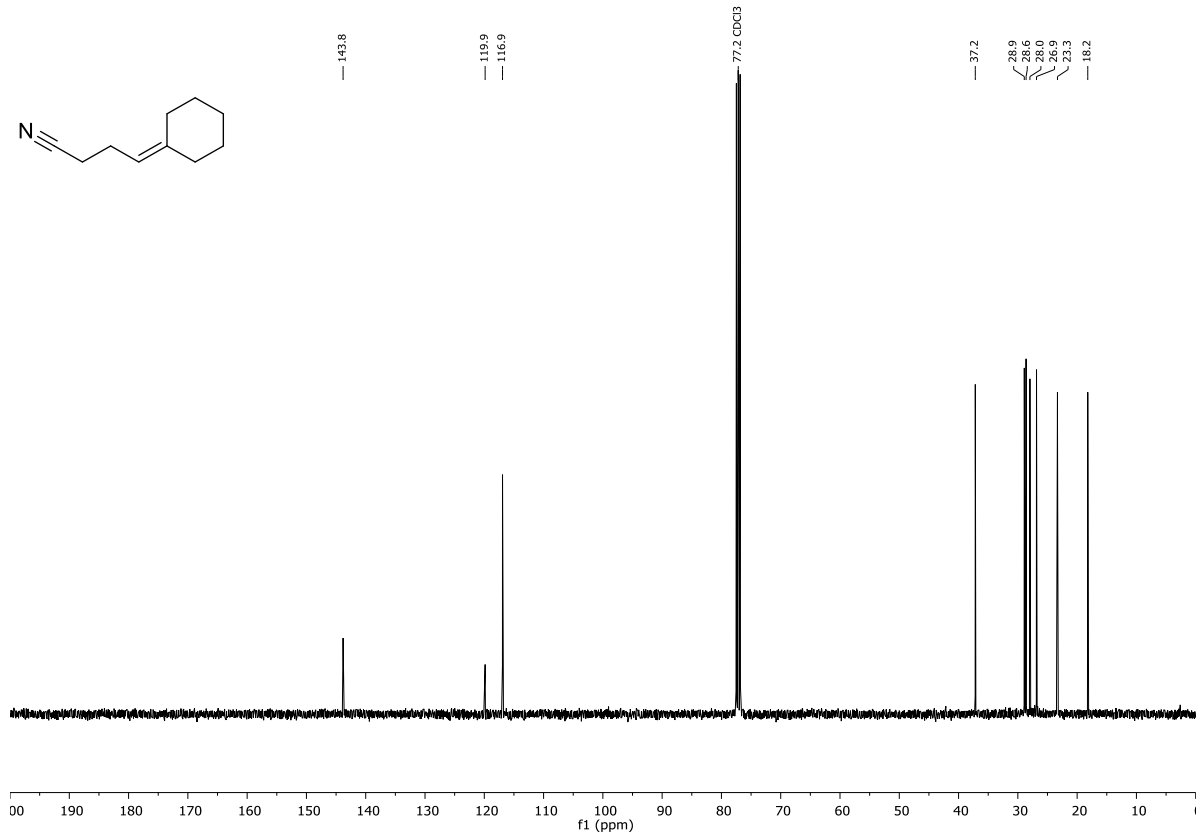
^{13}C NMR (101 MHz, $CDCl_3$) of **1o**



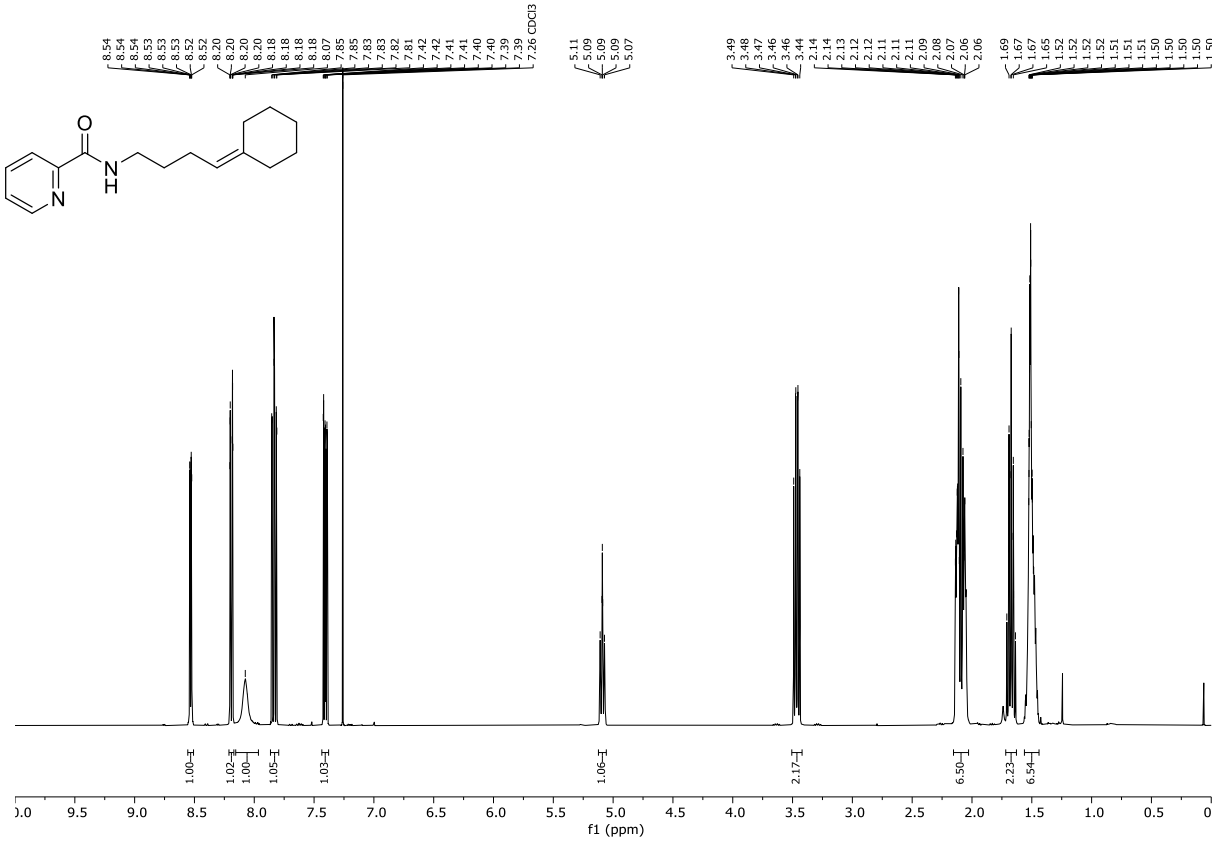
^{1}H NMR (400 MHz, $CDCl_3$) of **S2p**



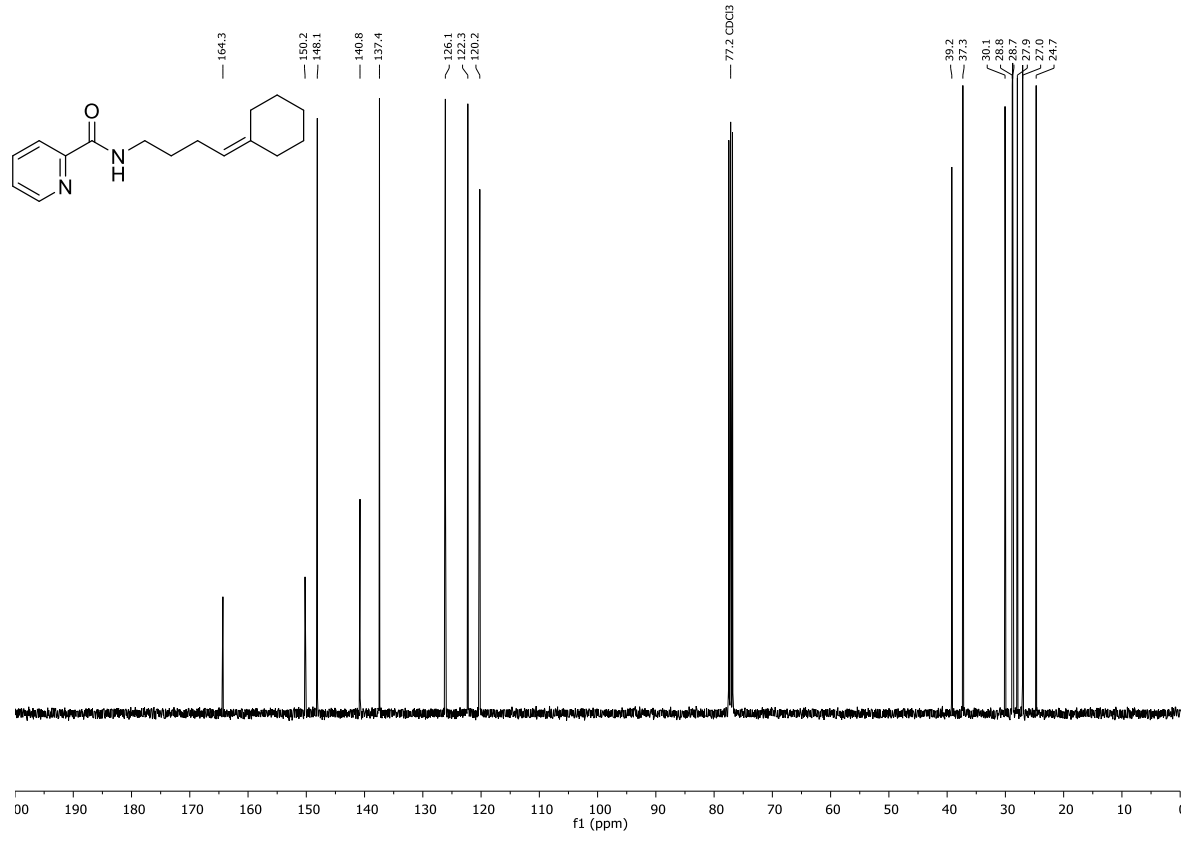
^{13}C NMR (100 MHz, $CDCl_3$) of **S2p**



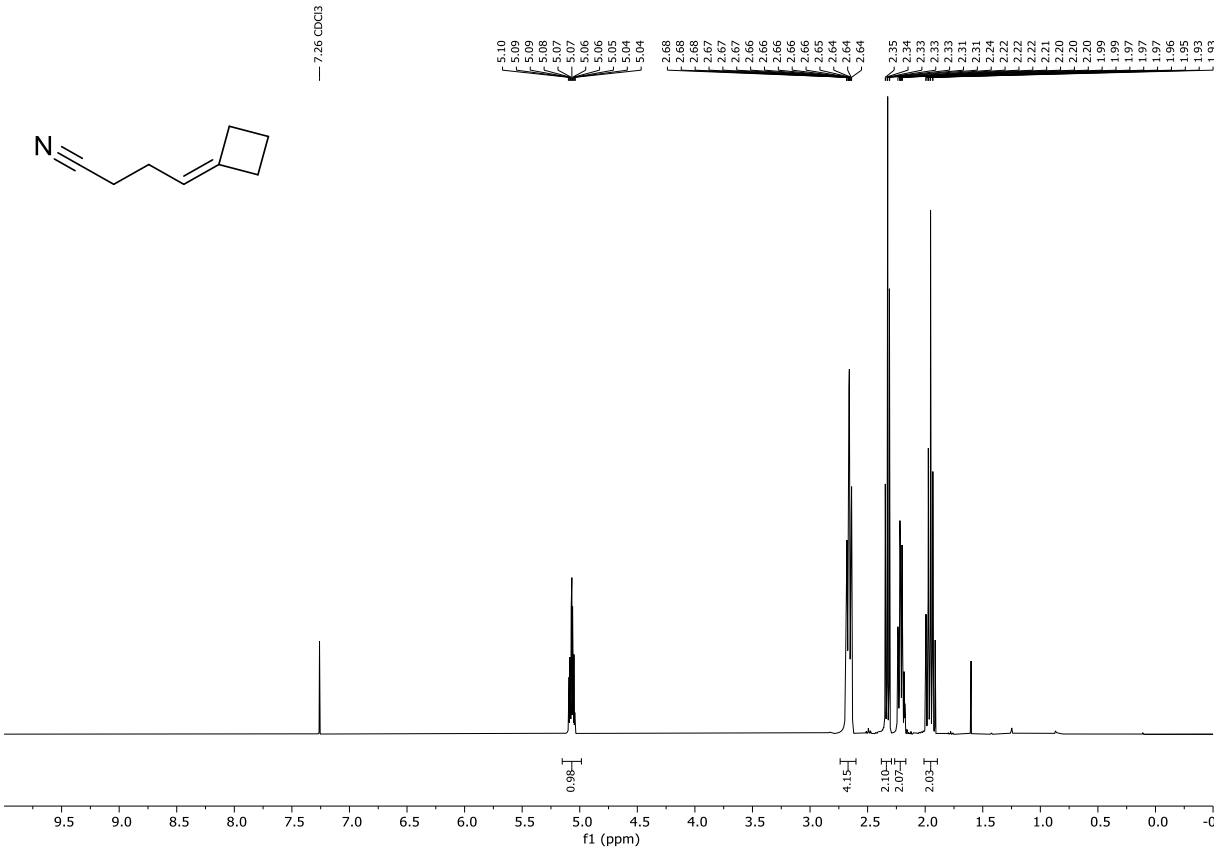
^{1}H NMR (400 MHz, $CDCl_3$) of **1p**



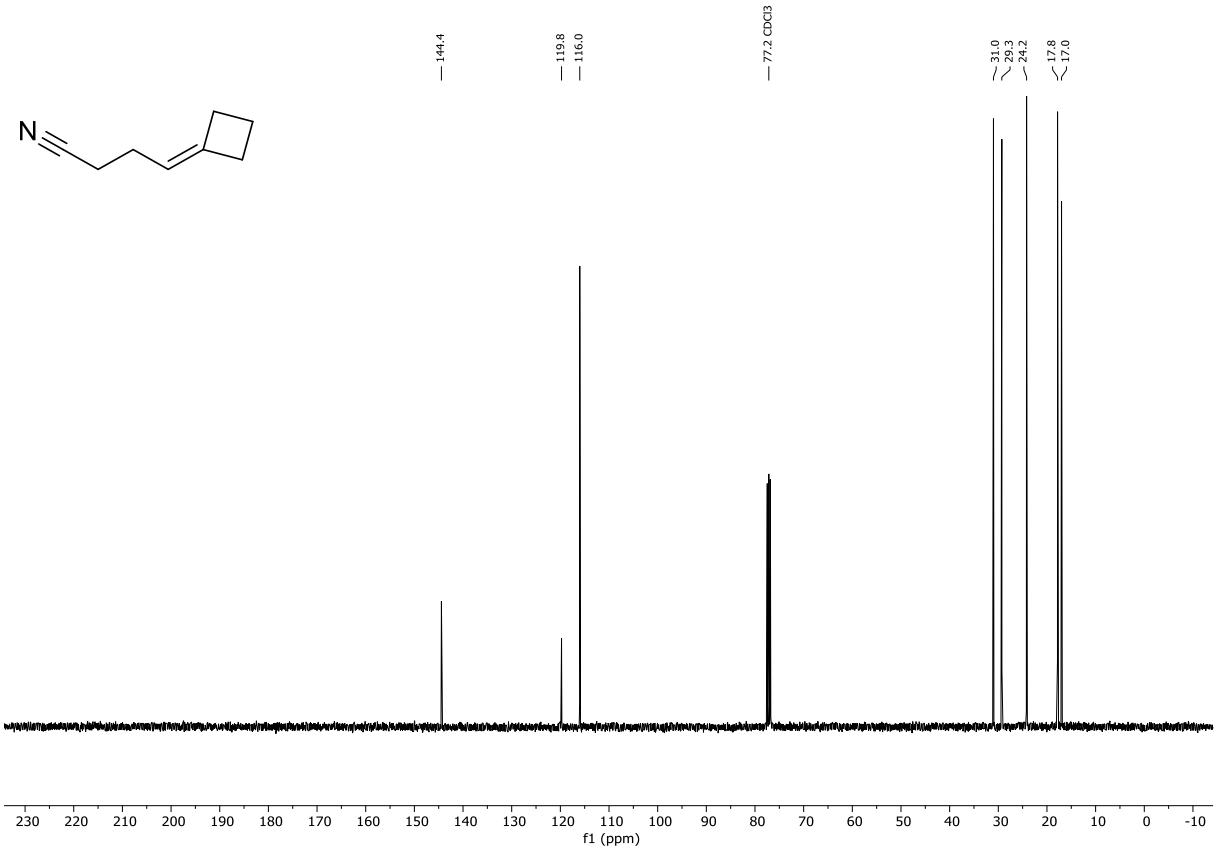
^{13}C NMR (100 MHz, $CDCl_3$) of **1p**



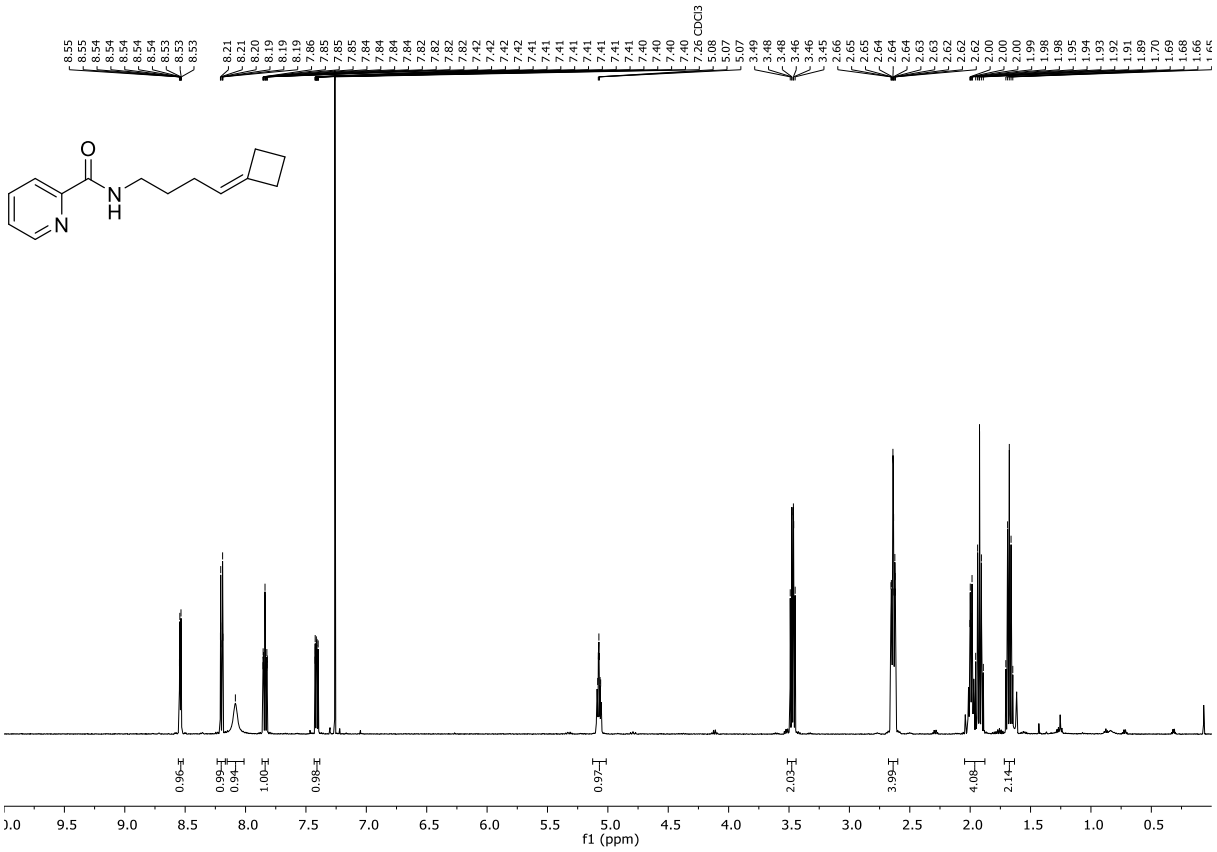
^{1}H NMR (400 MHz, $CDCl_3$) of **S2q**



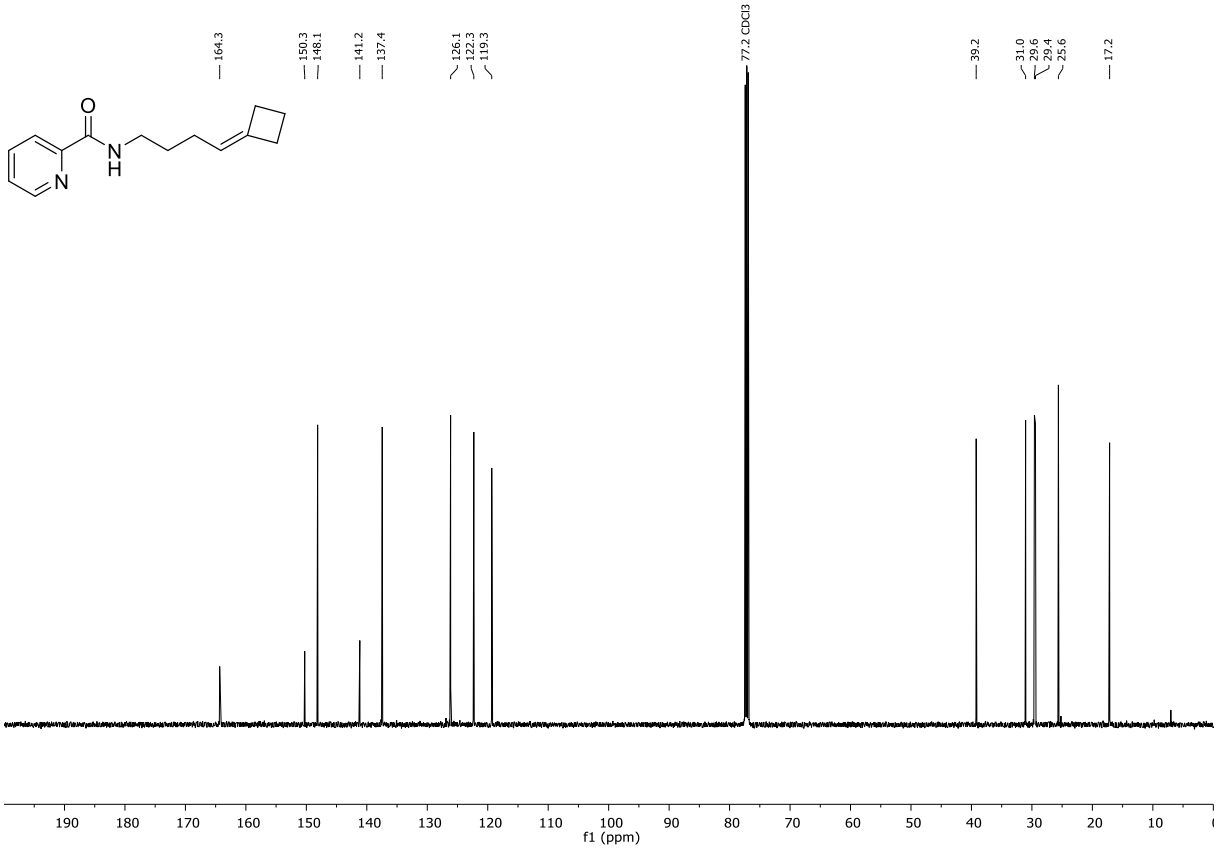
^{13}C NMR (100 MHz, $CDCl_3$) of **S2q**



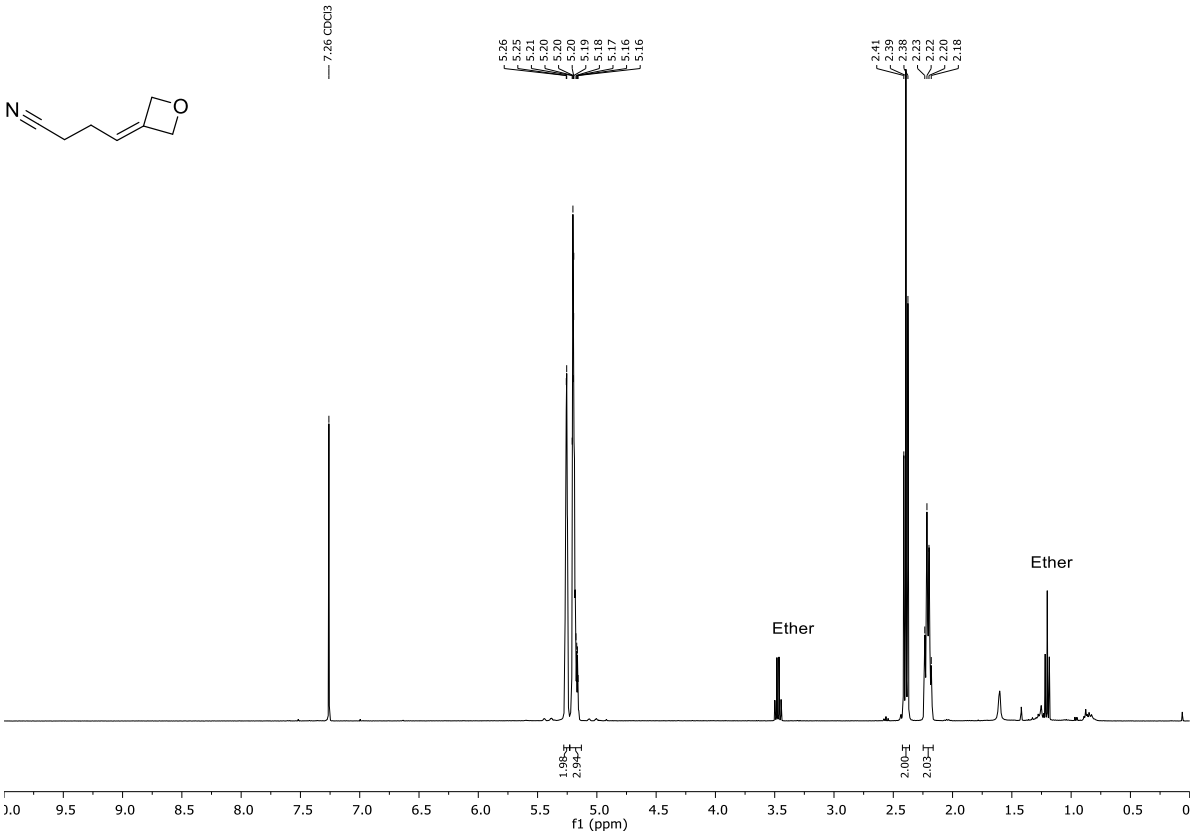
^{1}H NMR (400 MHz, $CDCl_3$) of **1q**



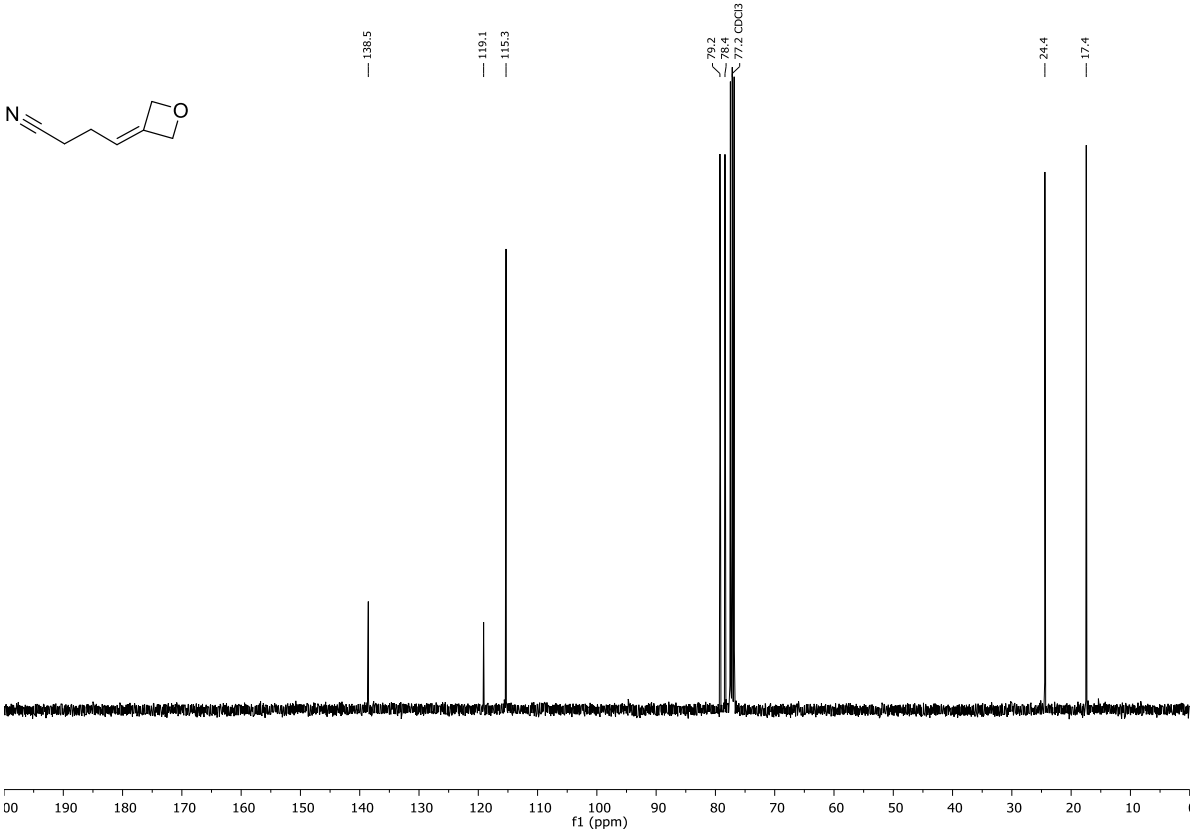
^{13}C NMR (400 MHz, $CDCl_3$) of **1q**



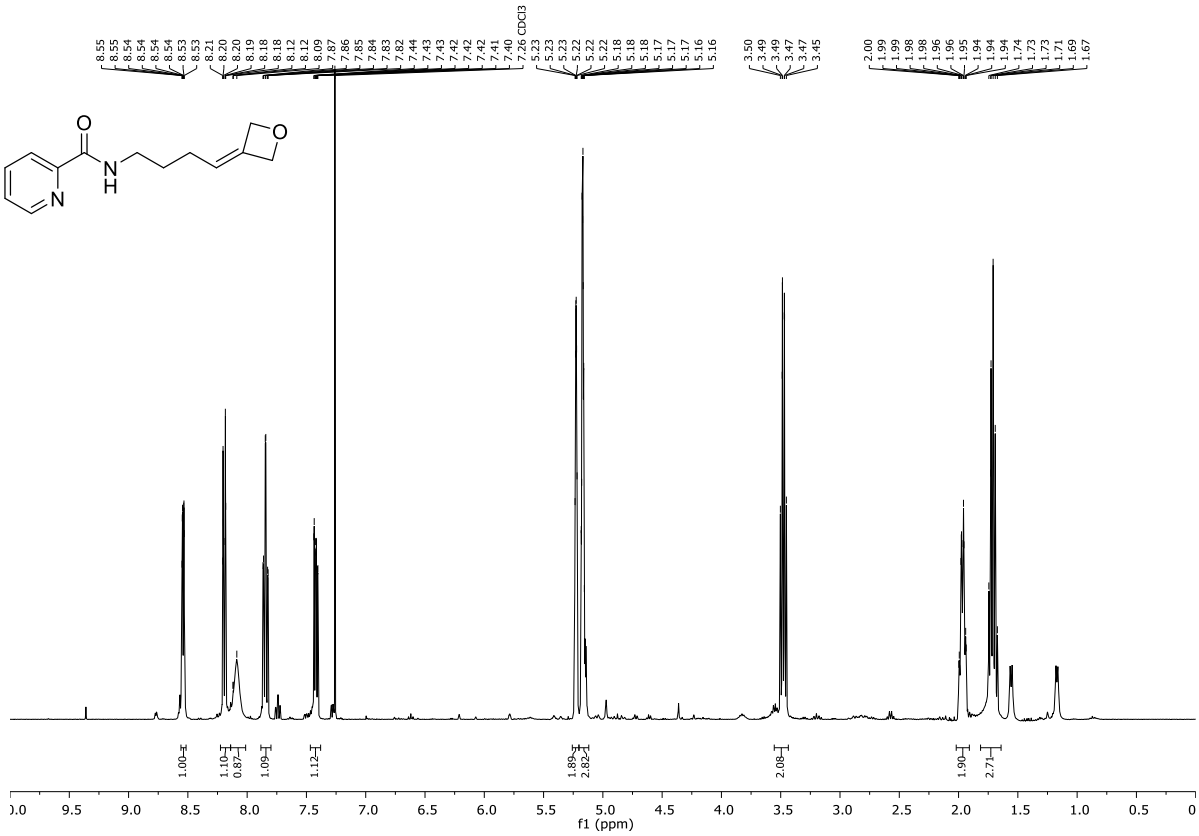
^{1}H NMR (400 MHz, $CDCl_3$) of **S2r**



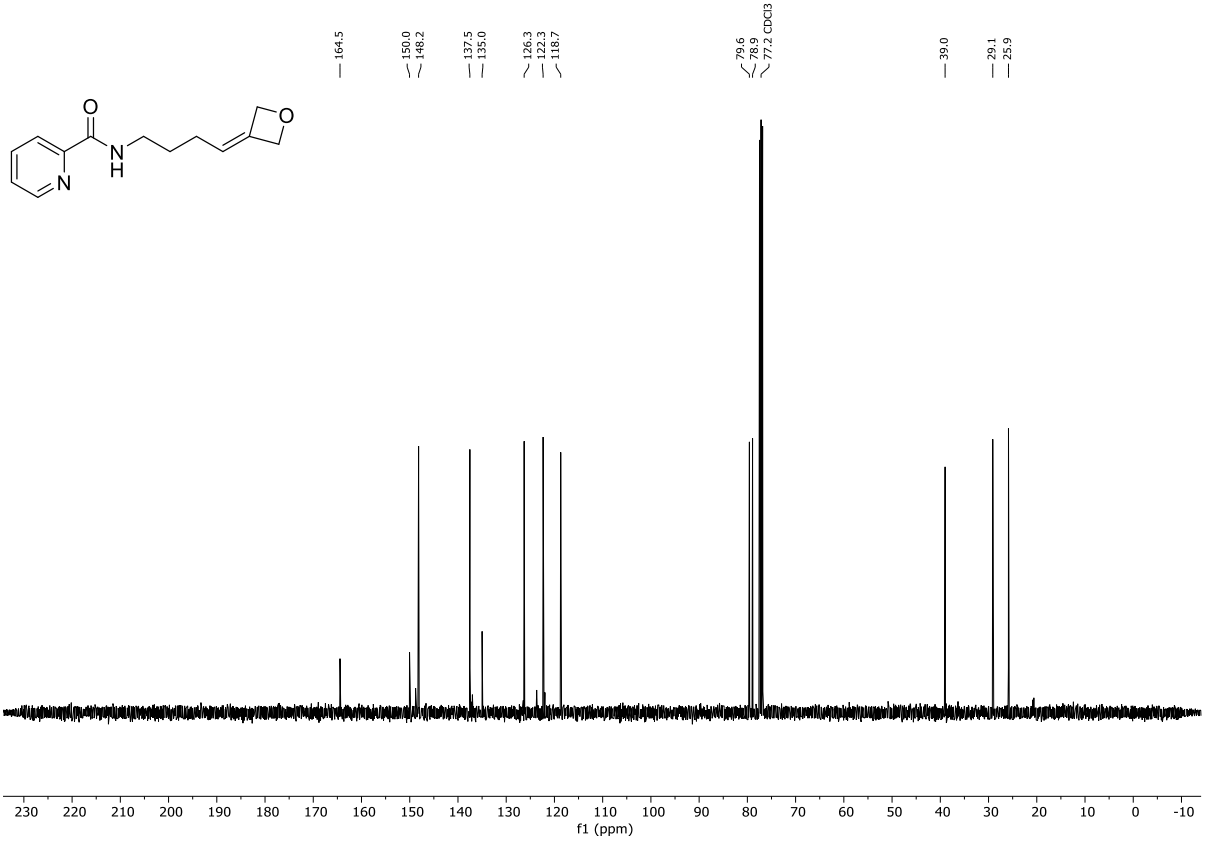
^{13}C NMR (100 MHz, $CDCl_3$) of **S2r**



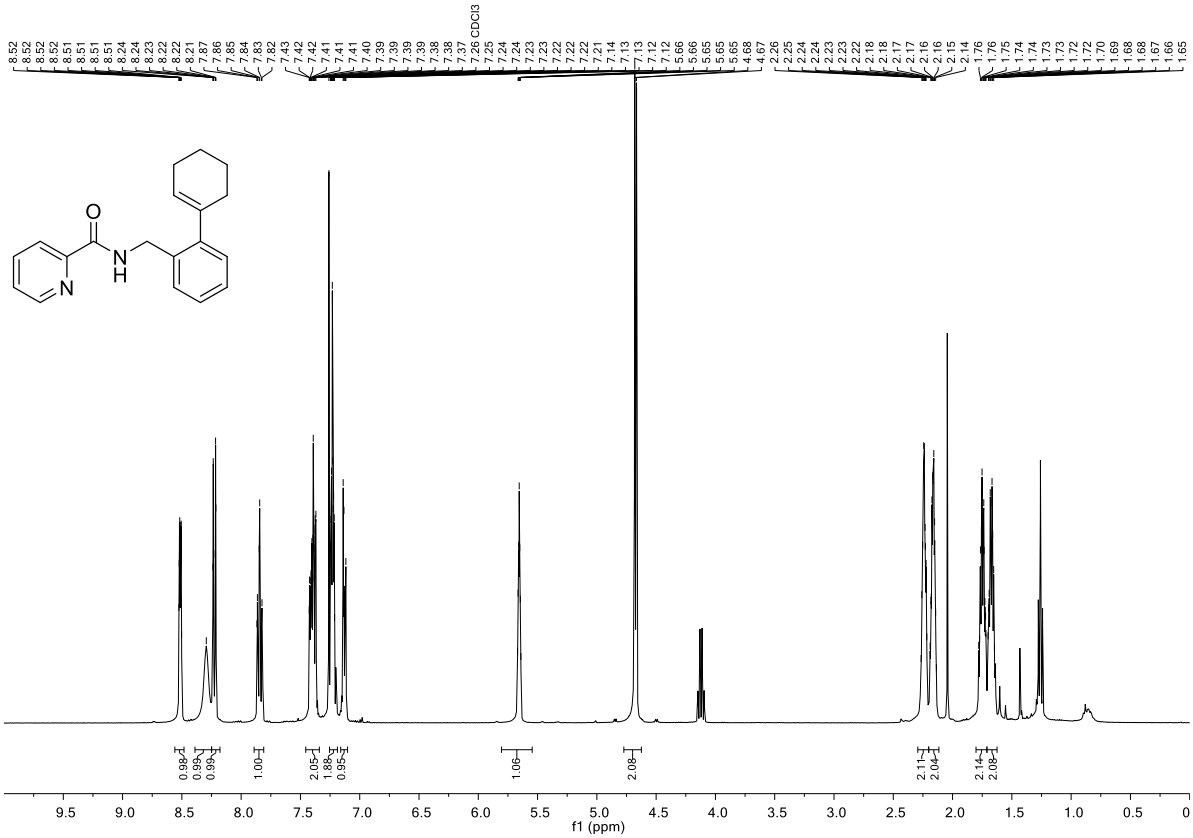
^{1}H NMR (400 MHz, $CDCl_3$) of **1r**



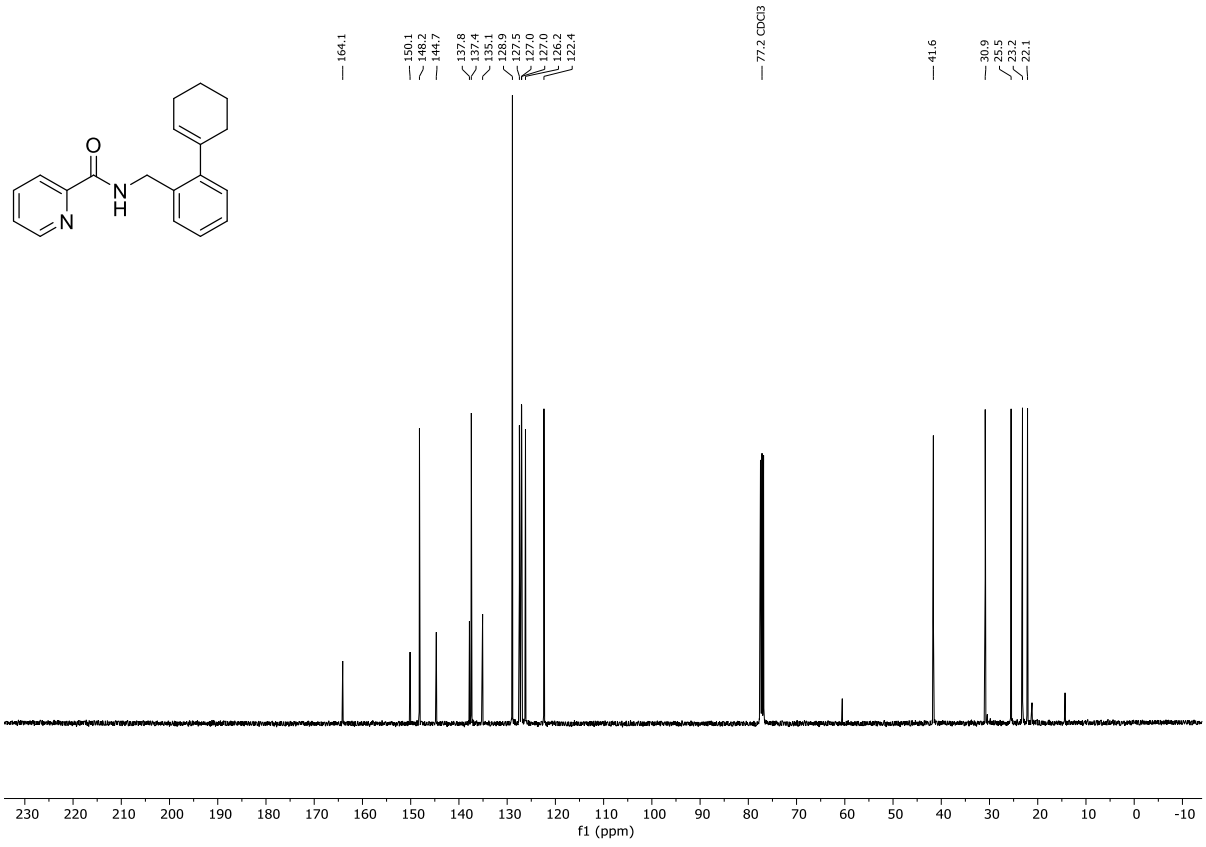
^{13}C NMR (101 MHz, $CDCl_3$) of **1r**



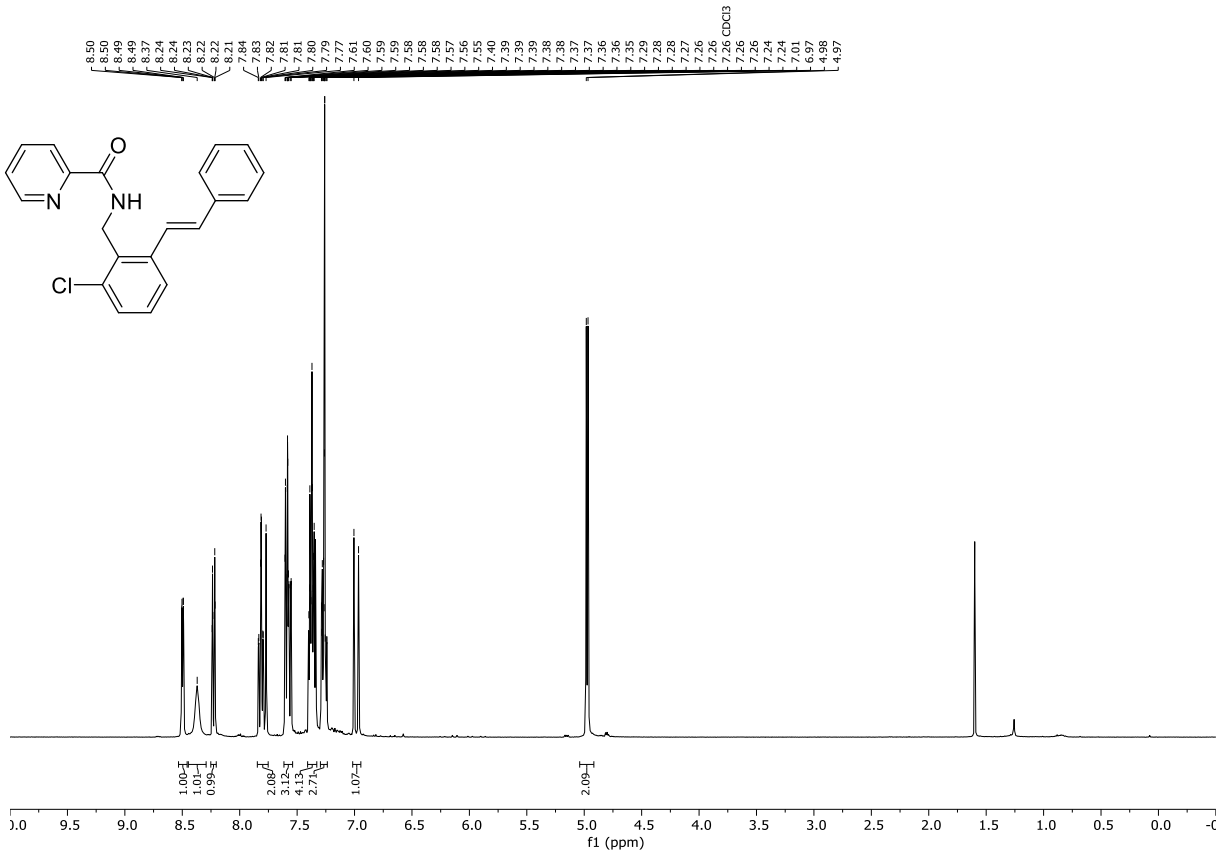
^{1}H NMR (400 MHz, $CDCl_3$) of **1s**



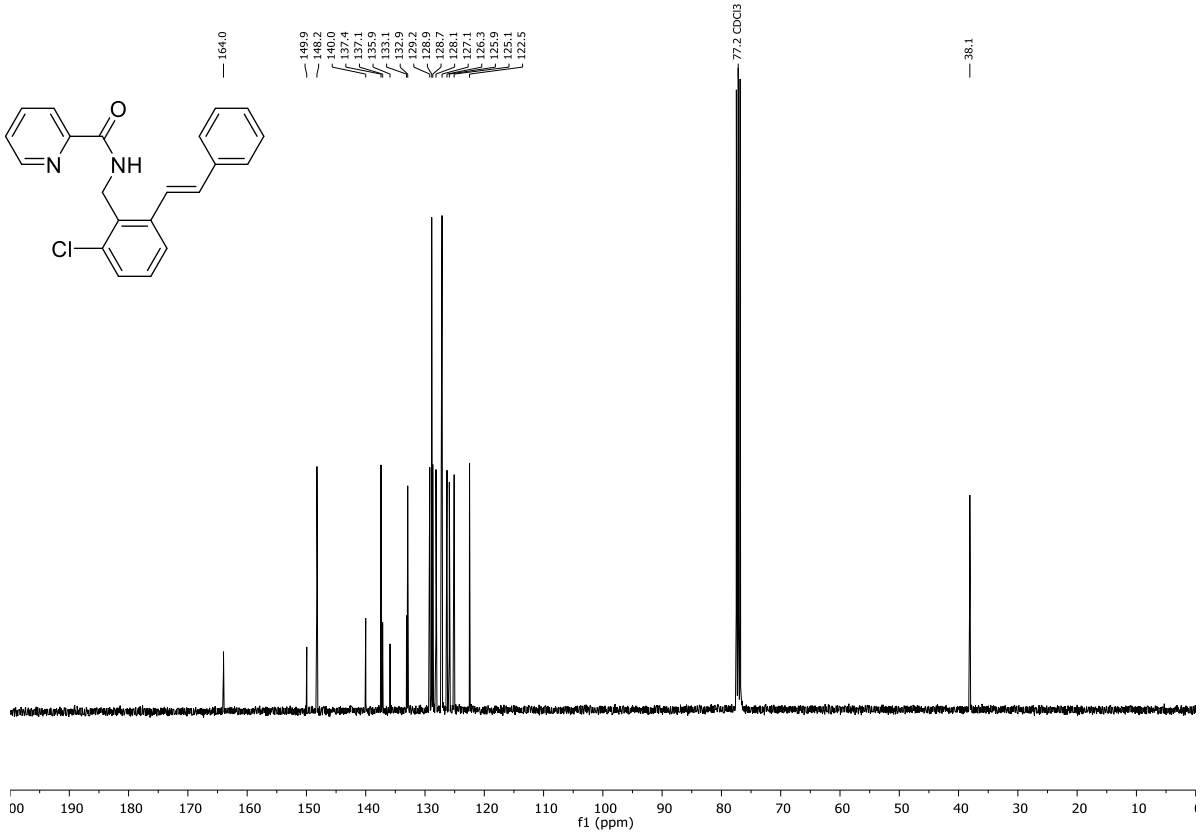
^{13}C NMR (101 MHz, $CDCl_3$) of **1s**



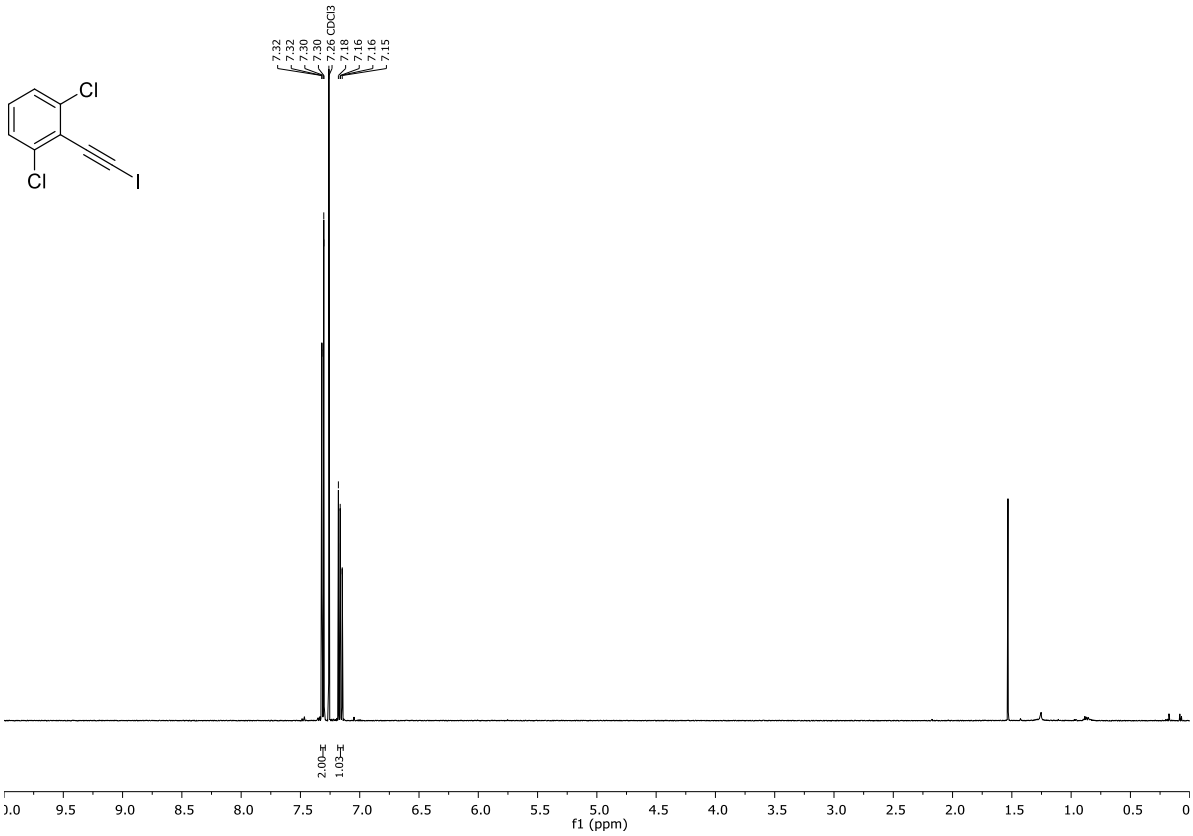
^{1}H NMR (400 MHz, $CDCl_3$) of **18**



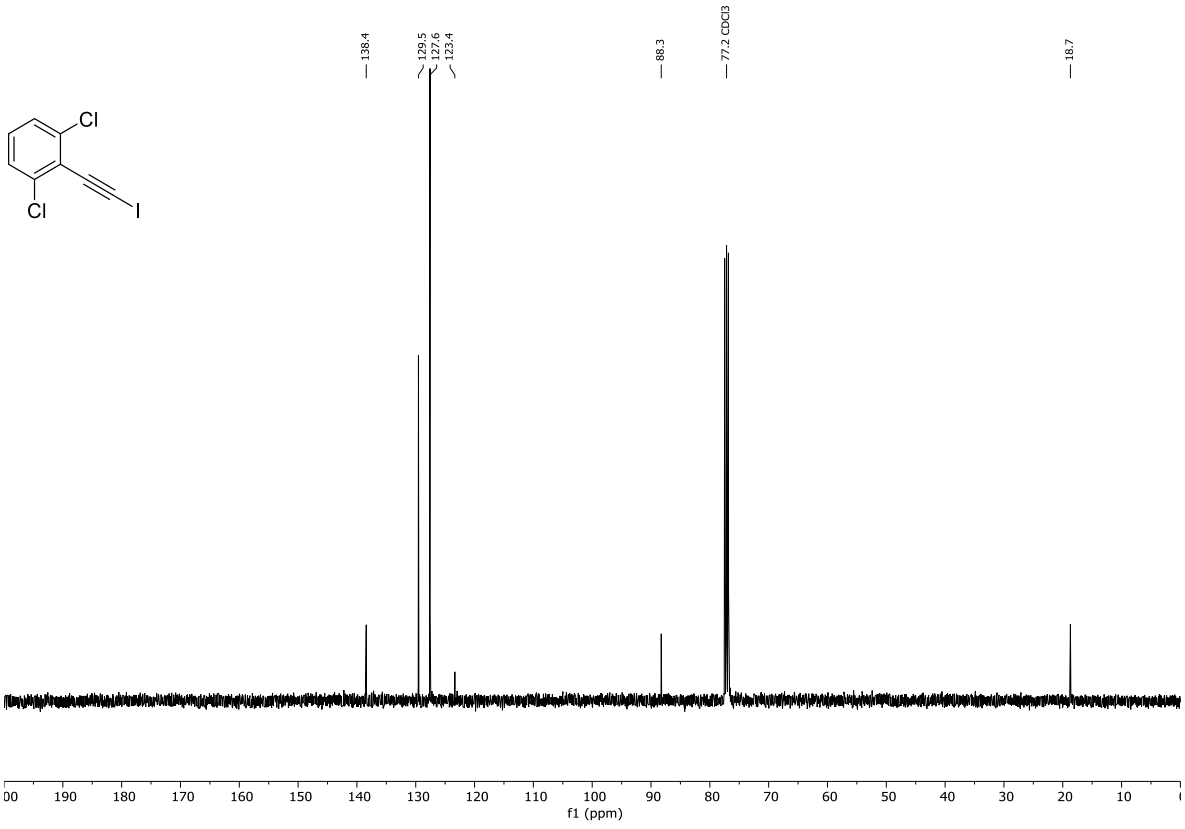
^{13}C NMR (100 MHz, $CDCl_3$) of **18**



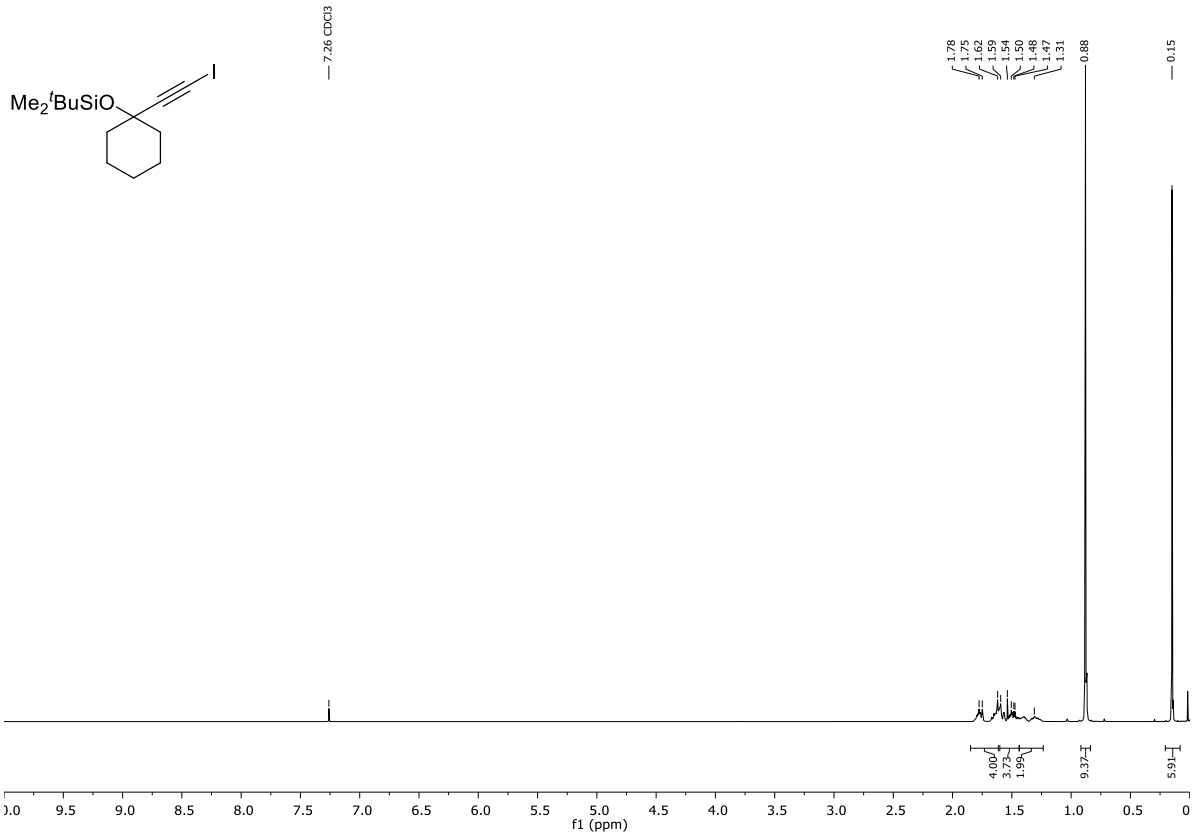
^{1}H NMR (400 MHz, $CDCl_3$) of **25**



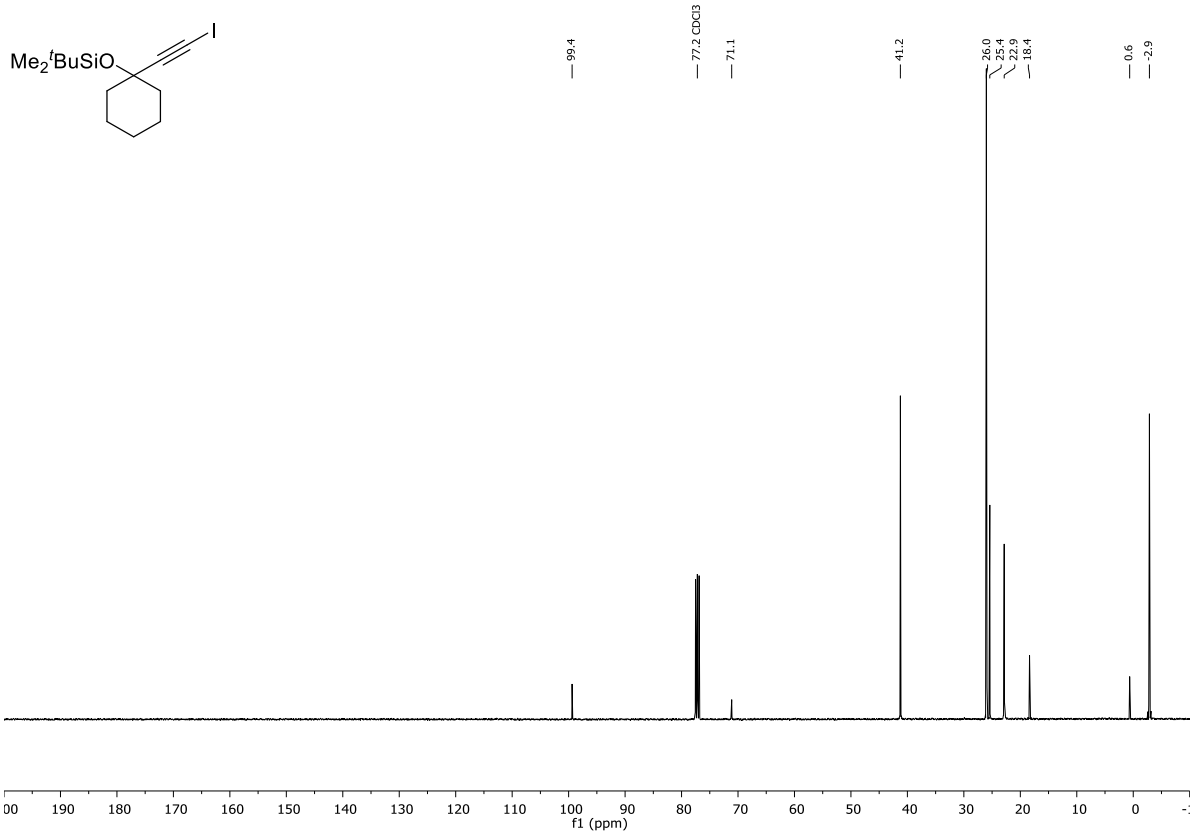
^{13}C NMR (100 MHz, $CDCl_3$) of **25**



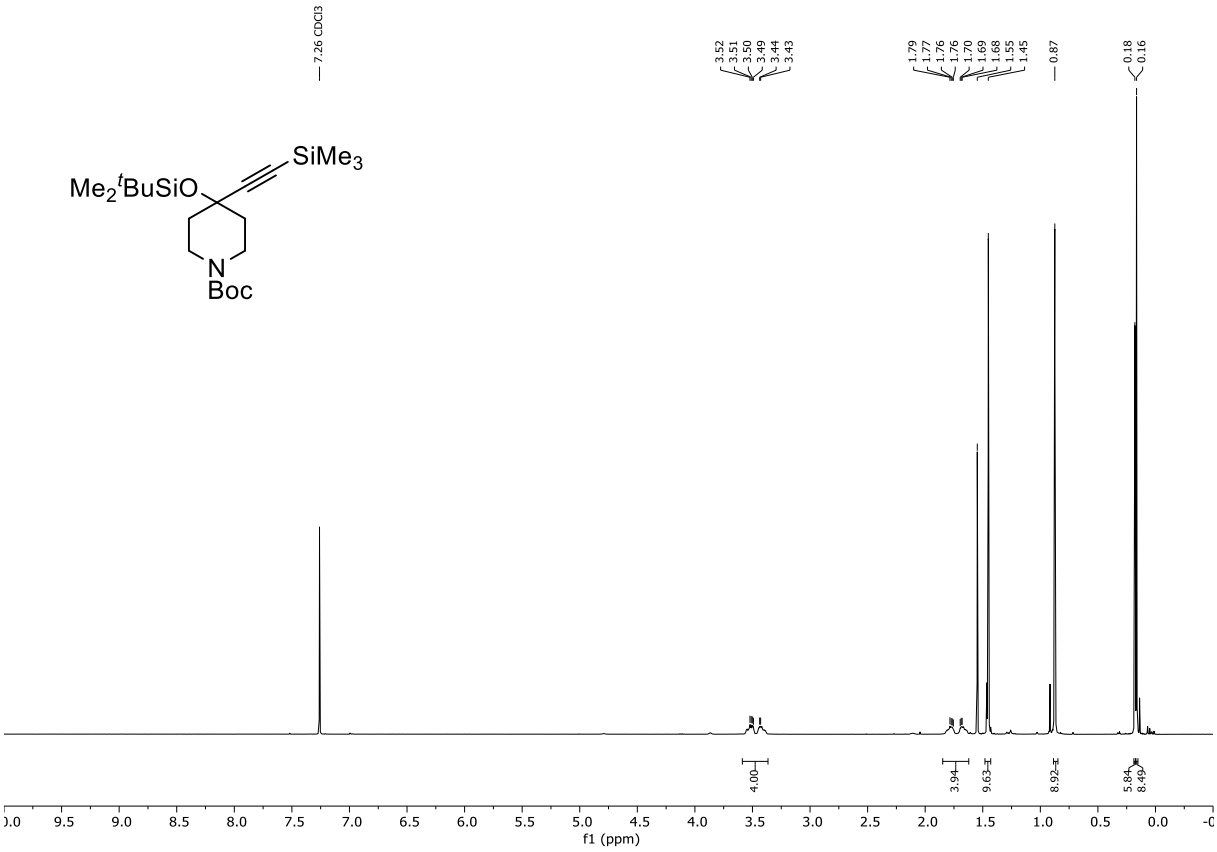
^{1}H NMR (400 MHz, $CDCl_3$) of **28**



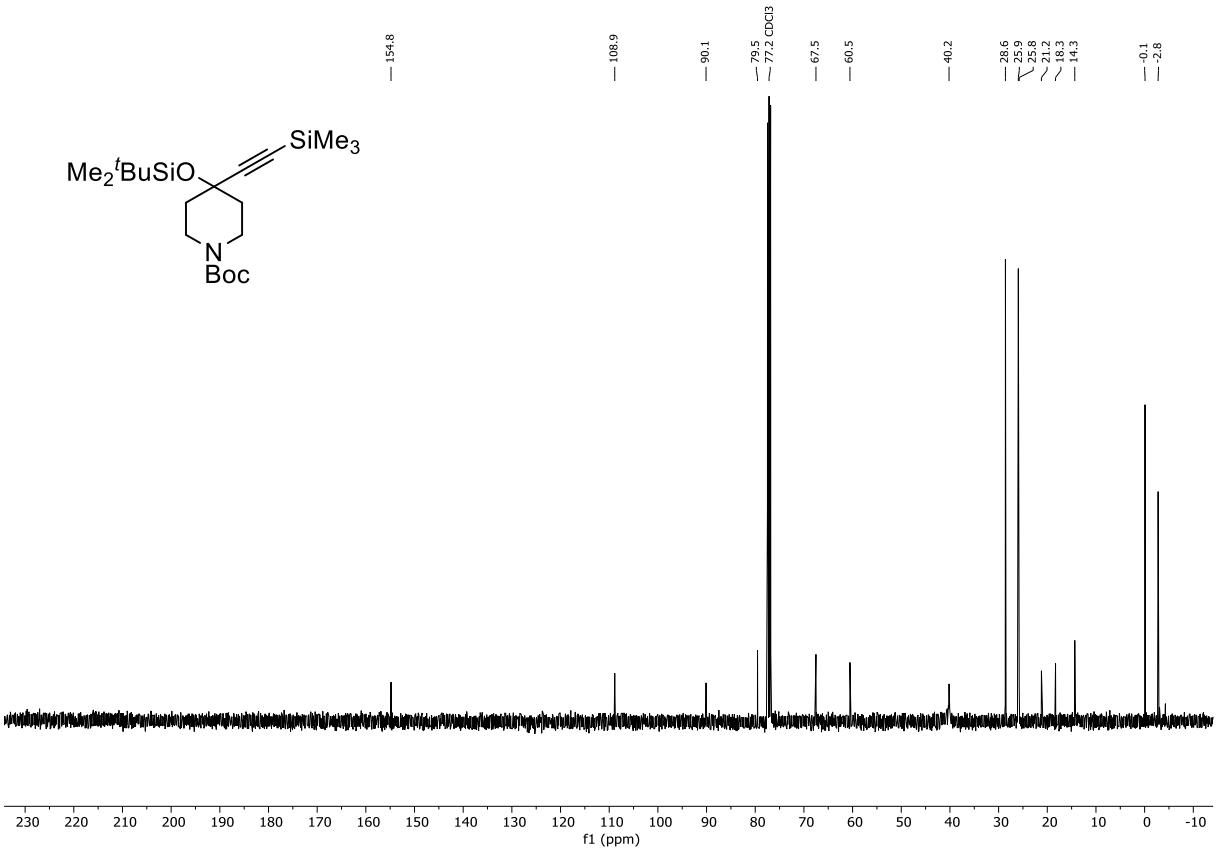
^{13}C NMR (101 MHz, $CDCl_3$) of **28**



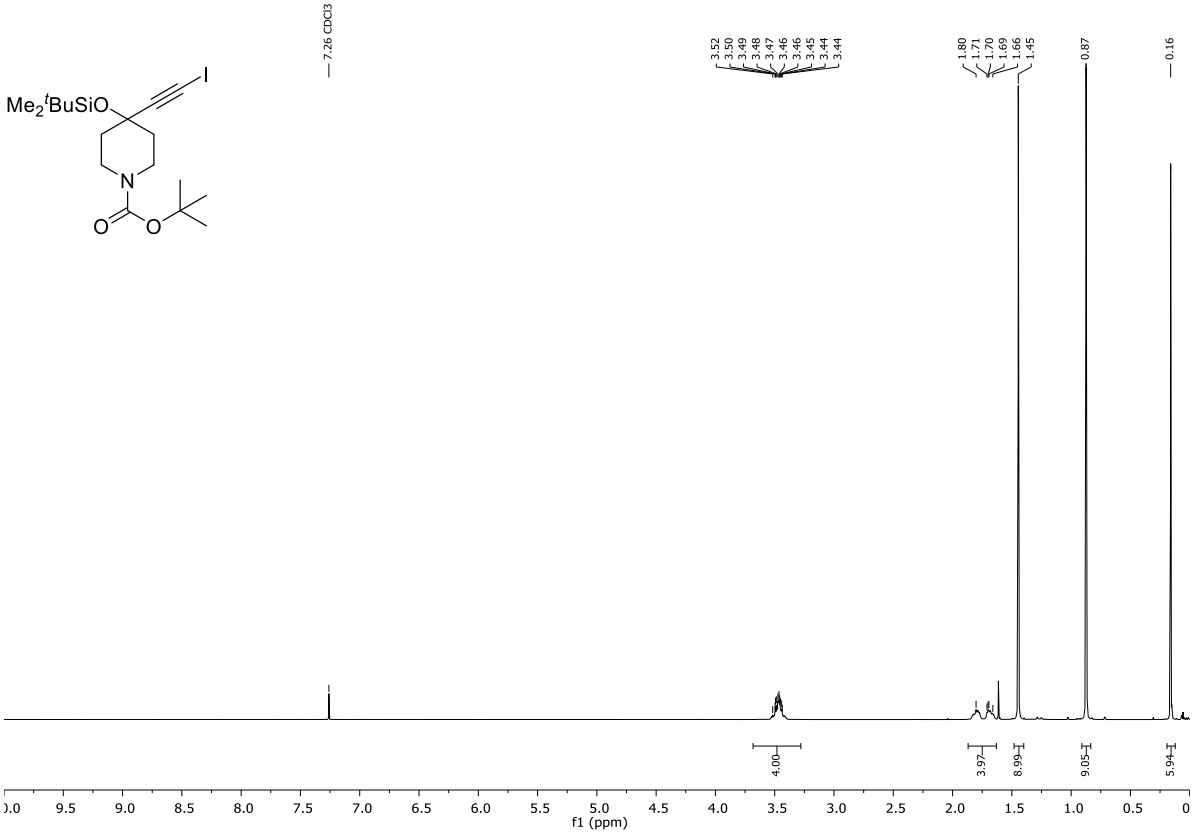
^{1}H NMR (400 MHz, $CDCl_3$**)** of **29**



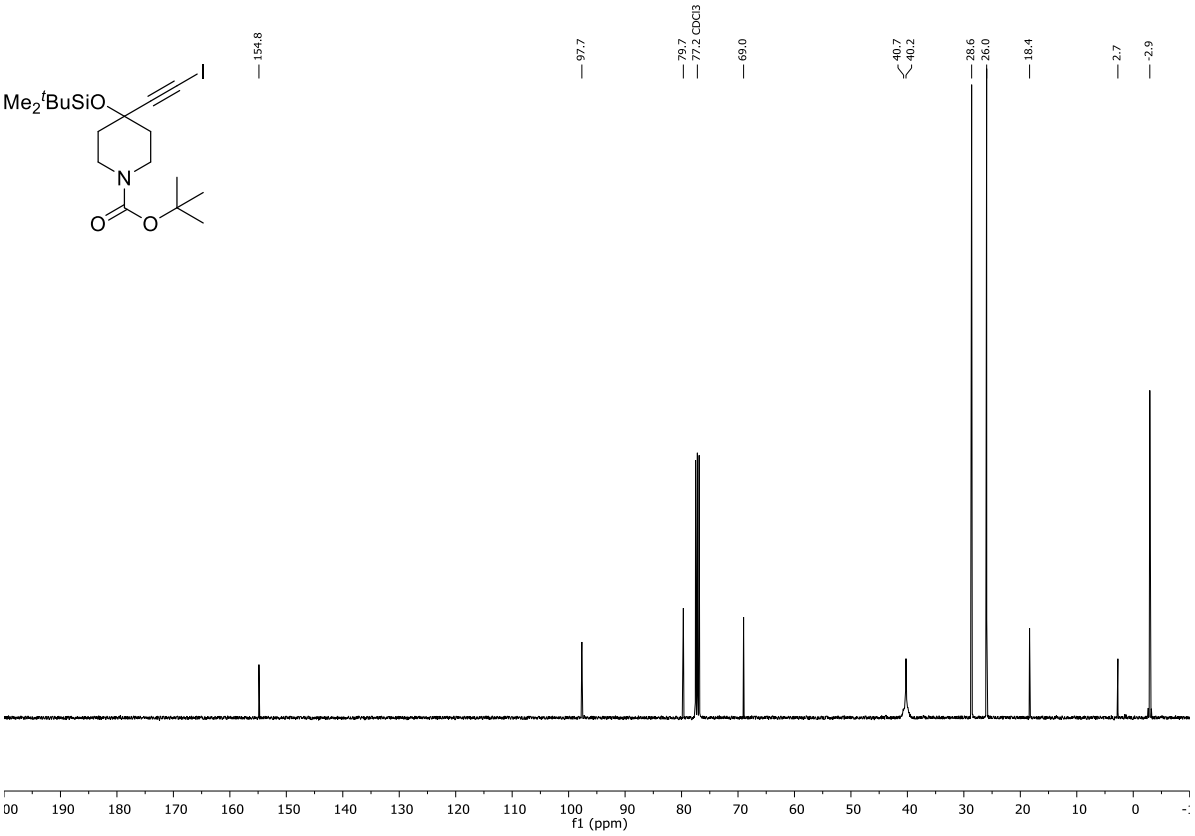
^{13}C NMR (100 MHz, $CDCl_3$**)** of **29**



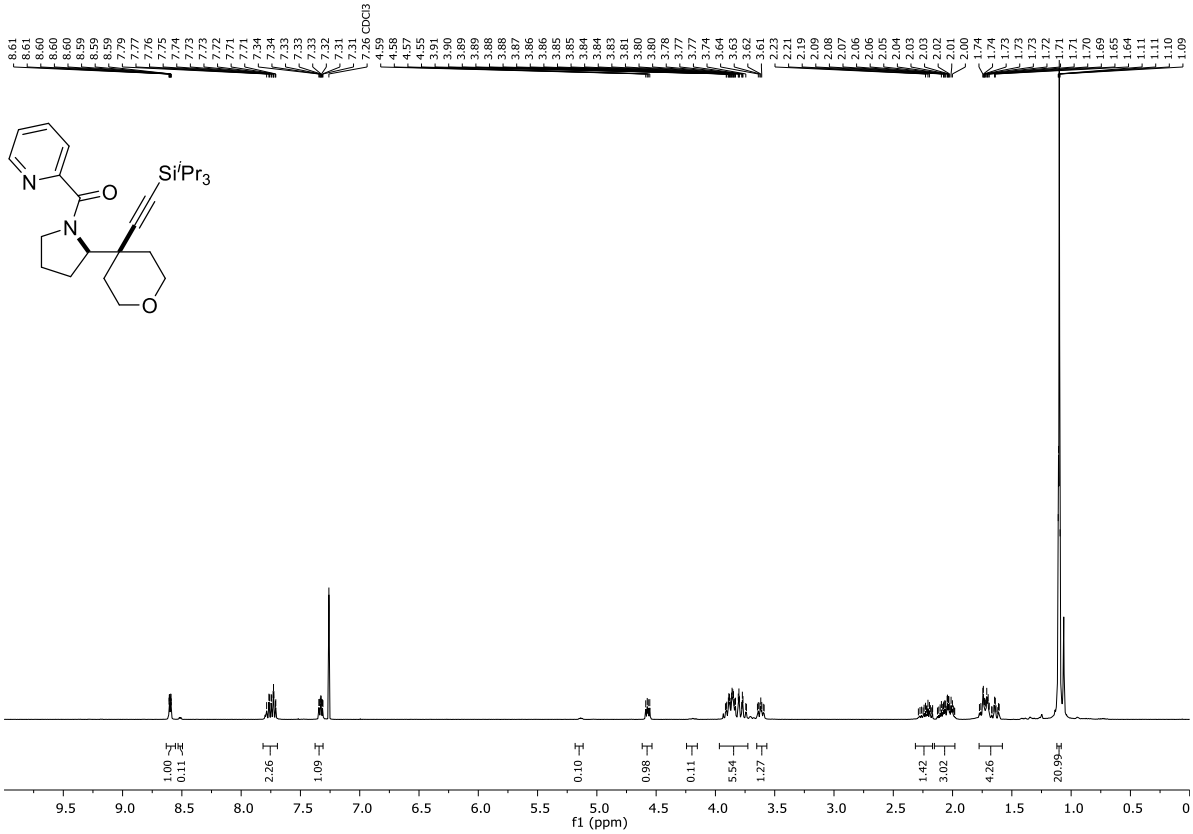
^{1}H NMR (400 MHz, $CDCl_3$) of **30**



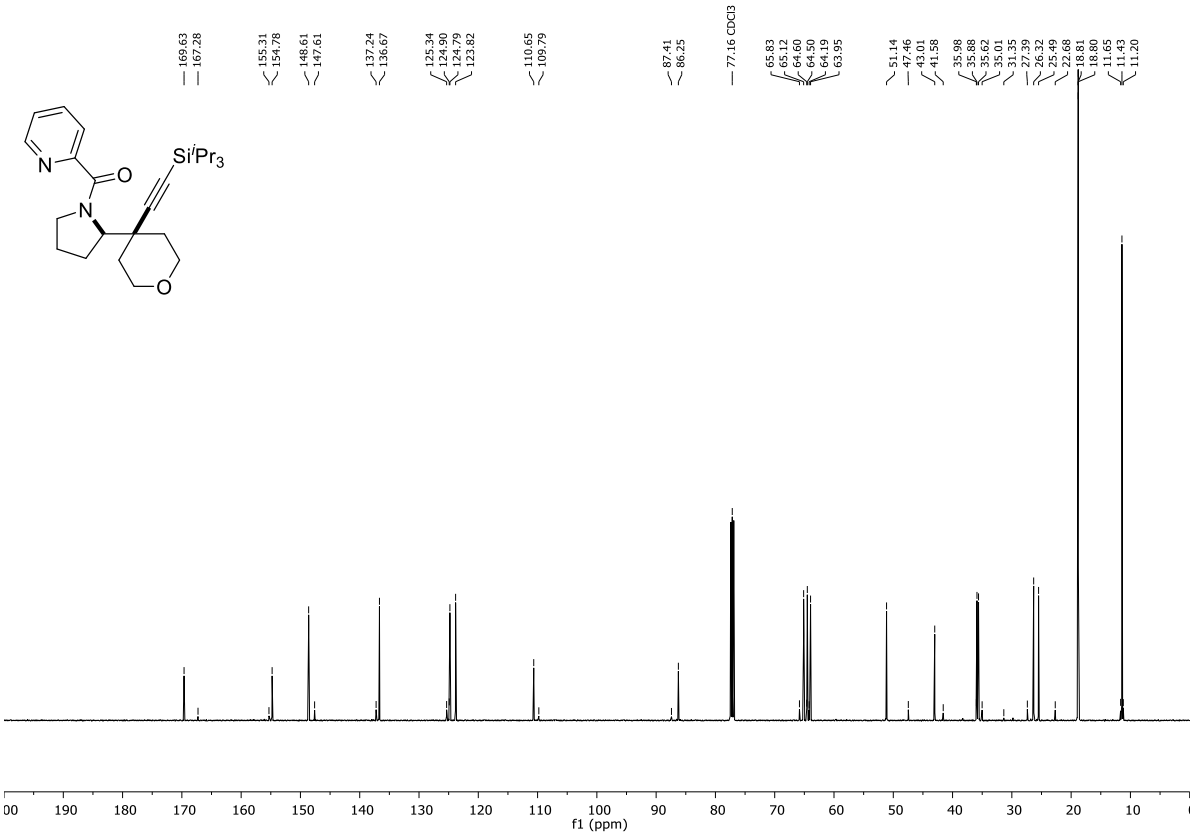
^{13}C NMR (101 MHz, $CDCl_3$) of **30**



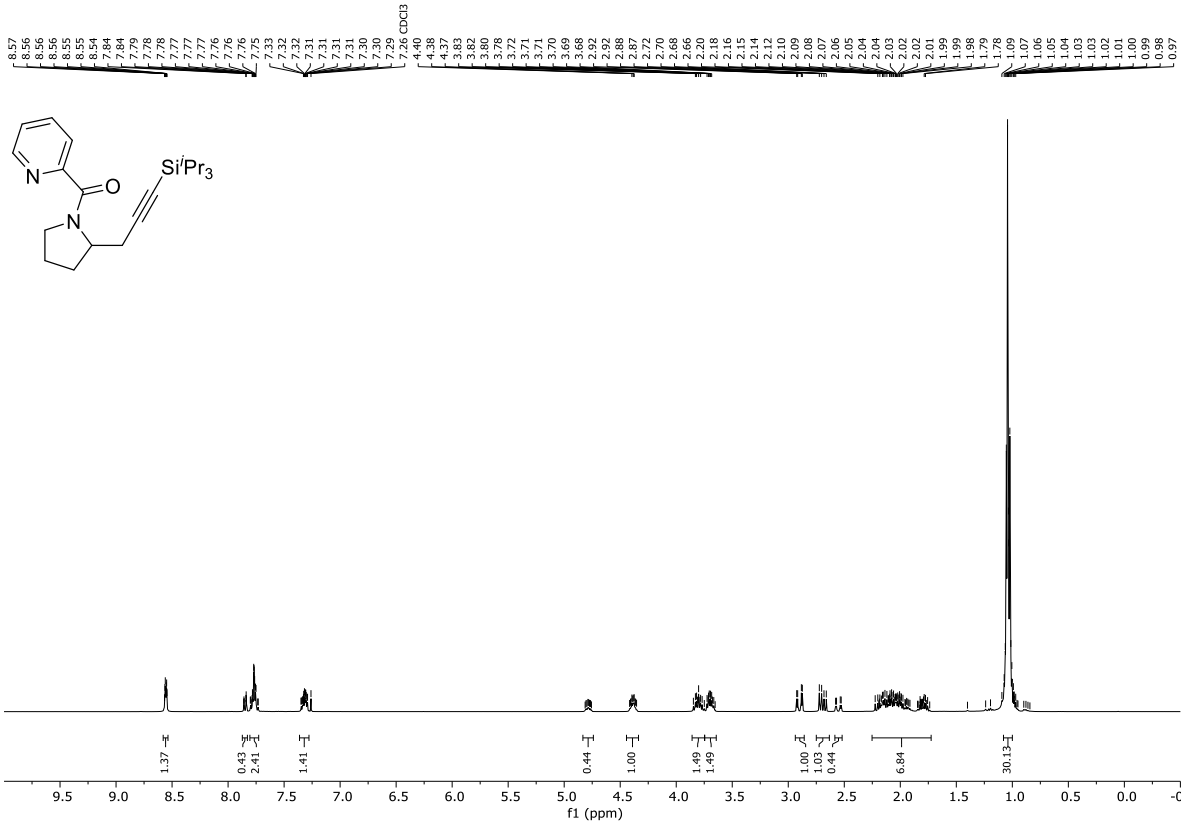
^{1}H NMR (400 MHz, $CDCl_3$) of **2a**



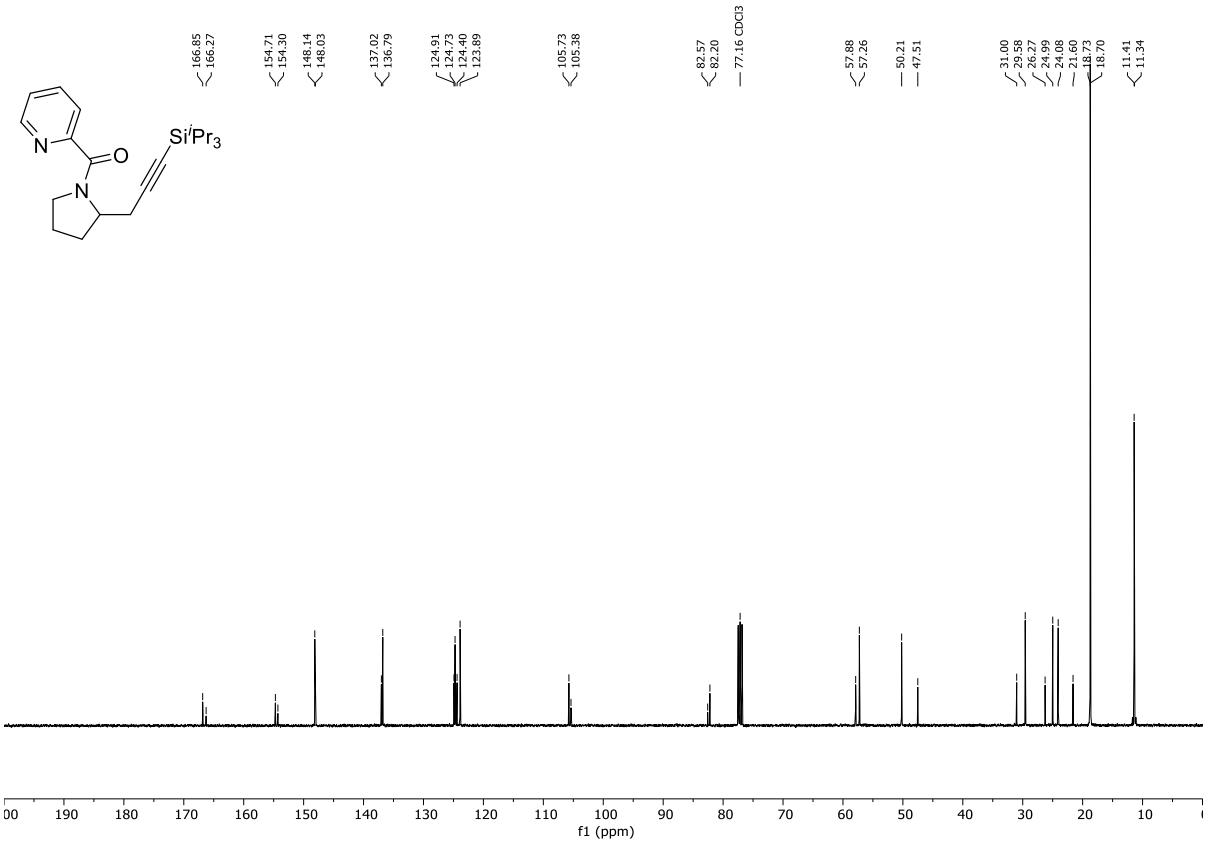
^{13}C NMR (101 MHz, $CDCl_3$) of **2a**



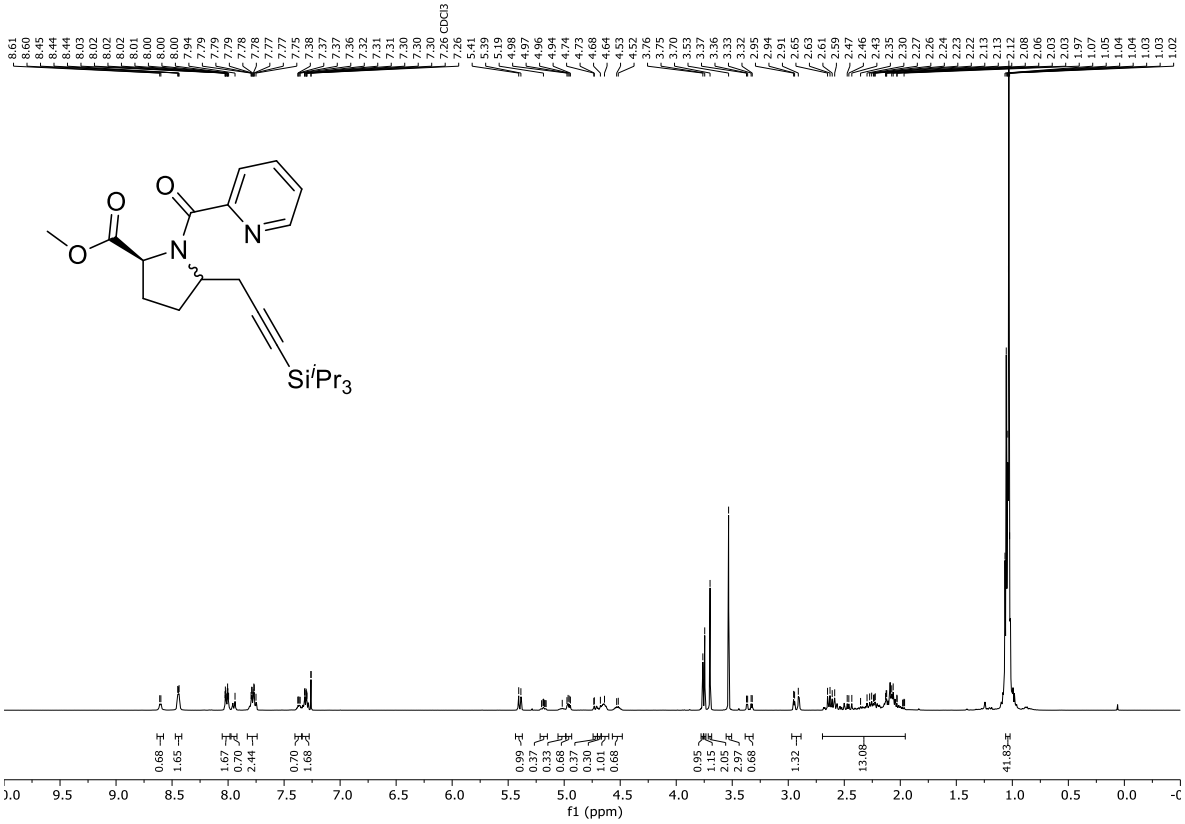
^{1}H NMR (400 MHz, $CDCl_3$) of **2b**



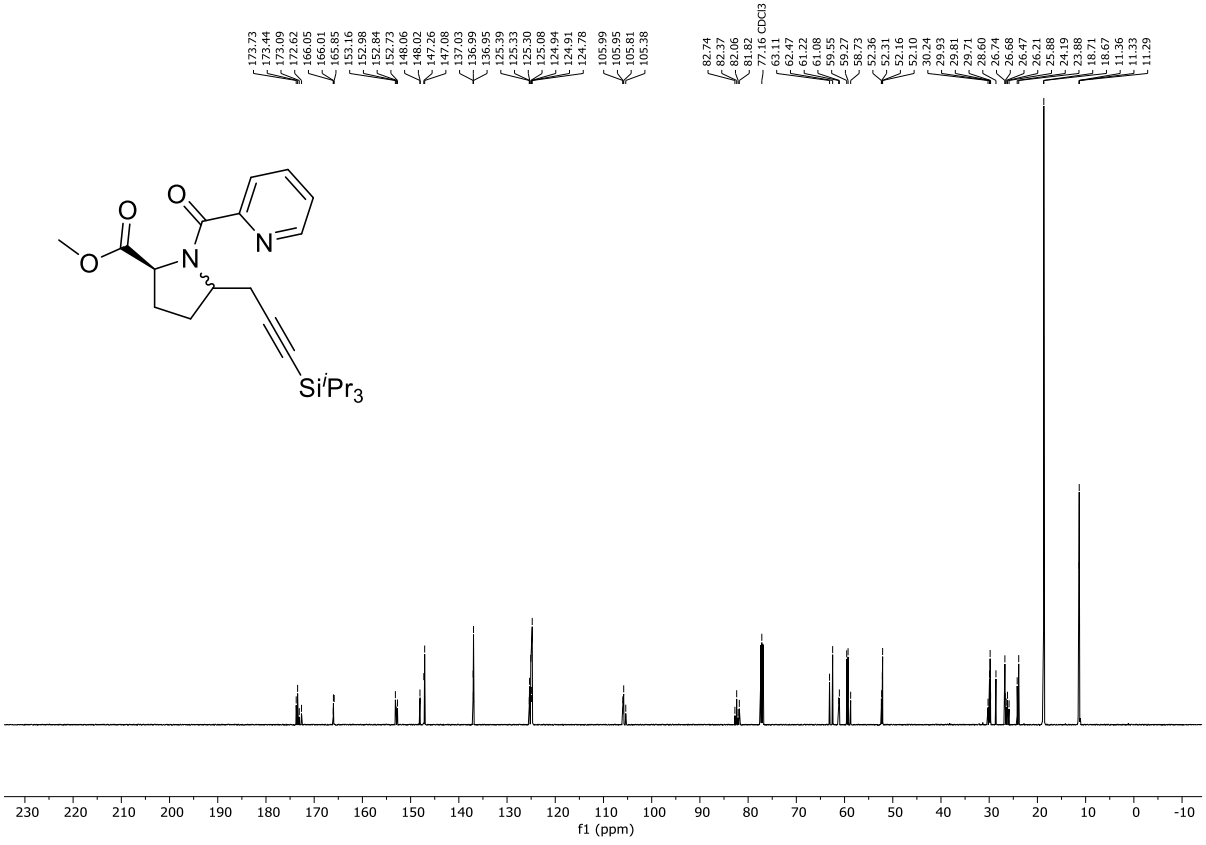
^{13}C NMR (101 MHz, $CDCl_3$) of **2b**



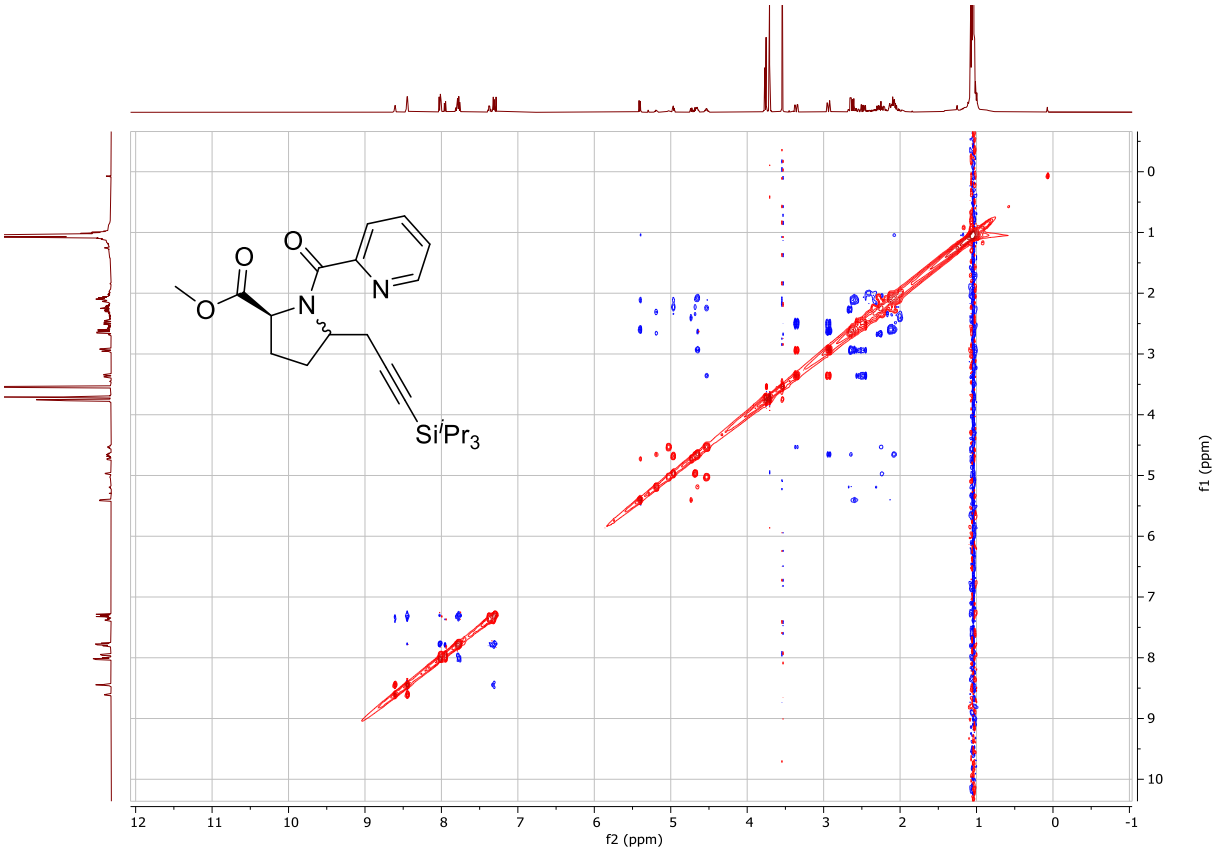
^{1}H NMR (400 MHz, $CDCl_3$) of **2c**

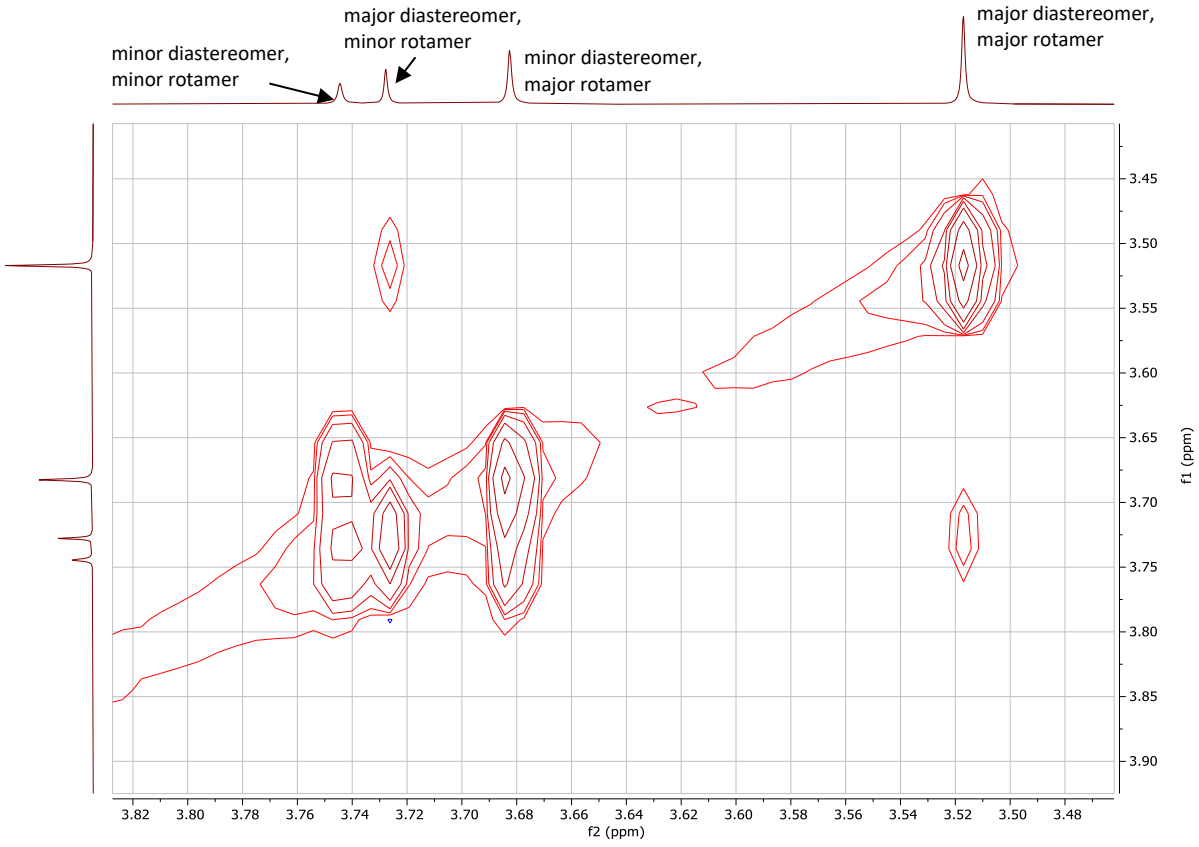


^{13}C NMR (100 MHz, $CDCl_3$) of **2c**

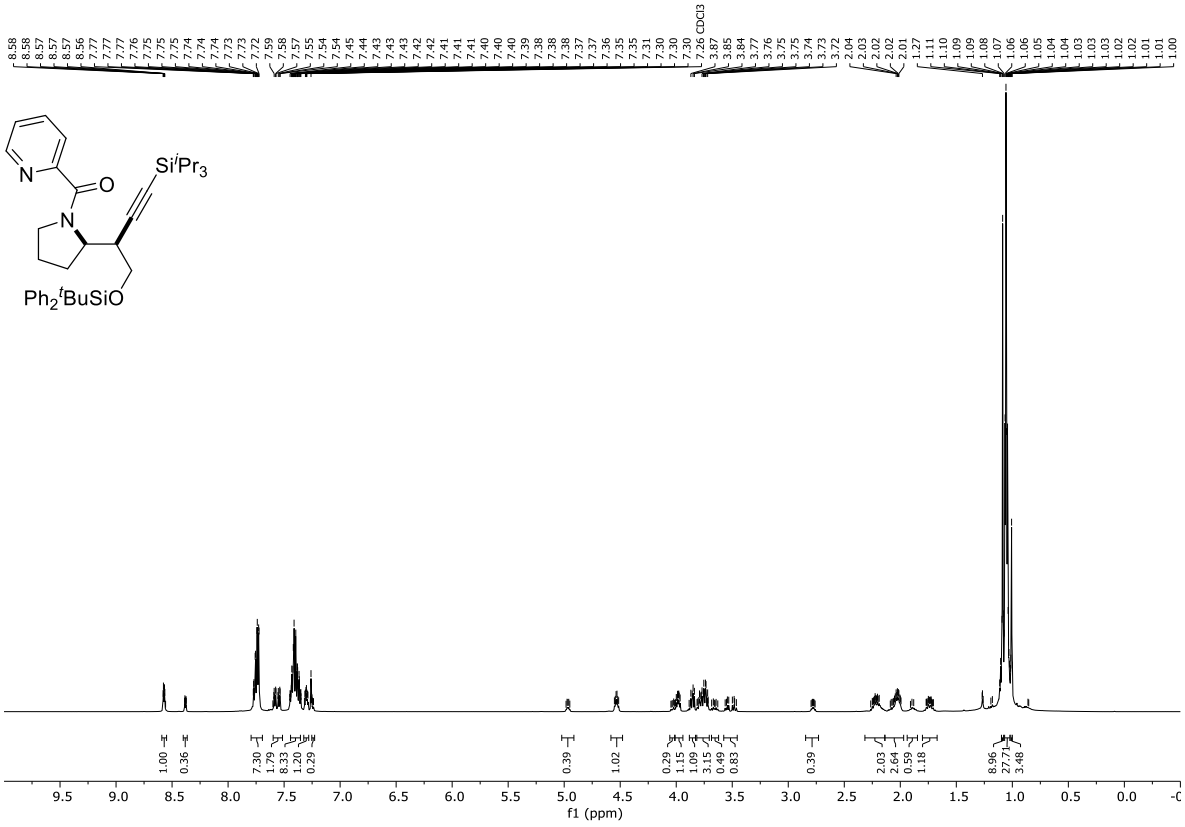


NOESY (500 MHz, $CDCl_3$, tm = 1000 ms) of **2c**

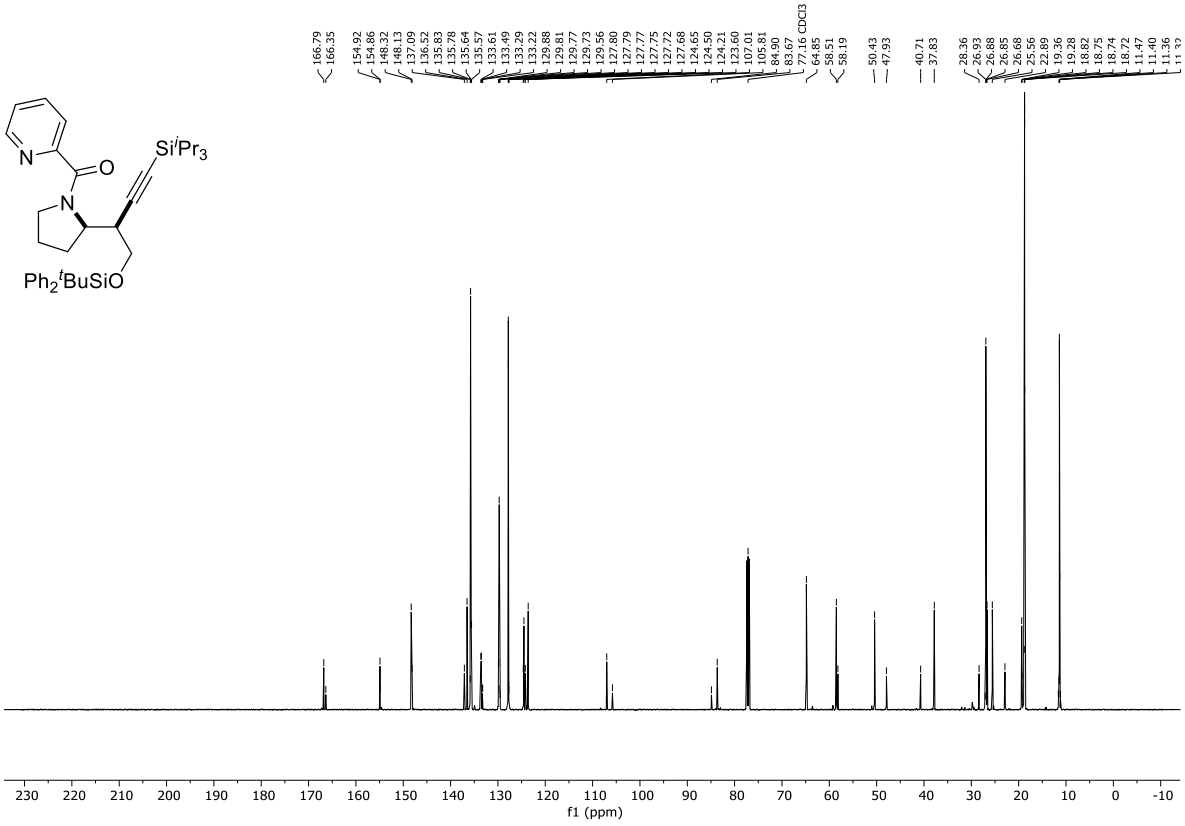




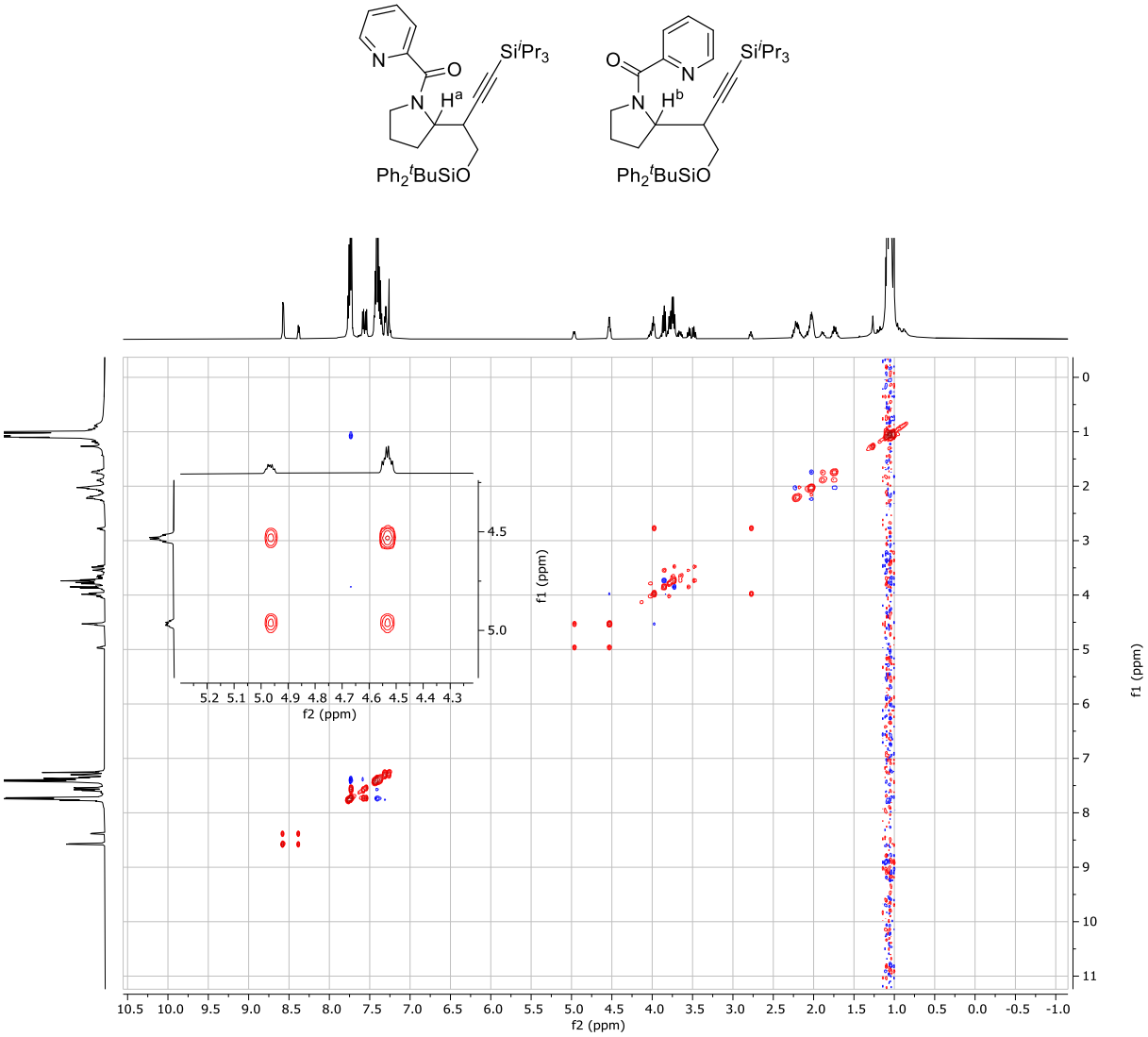
^{1}H NMR (500 MHz, $CDCl_3$) of **2d**



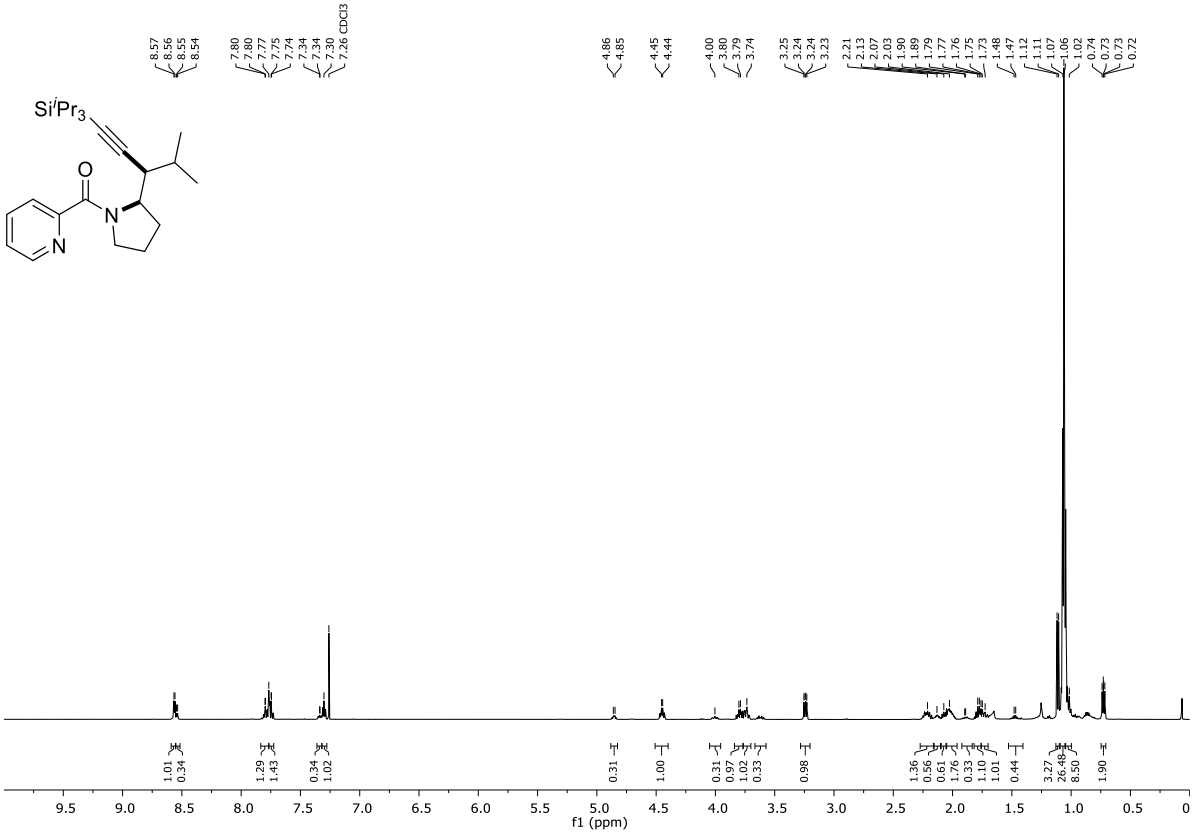
^{13}C NMR (126 MHz, $CDCl_3$) of **2d**



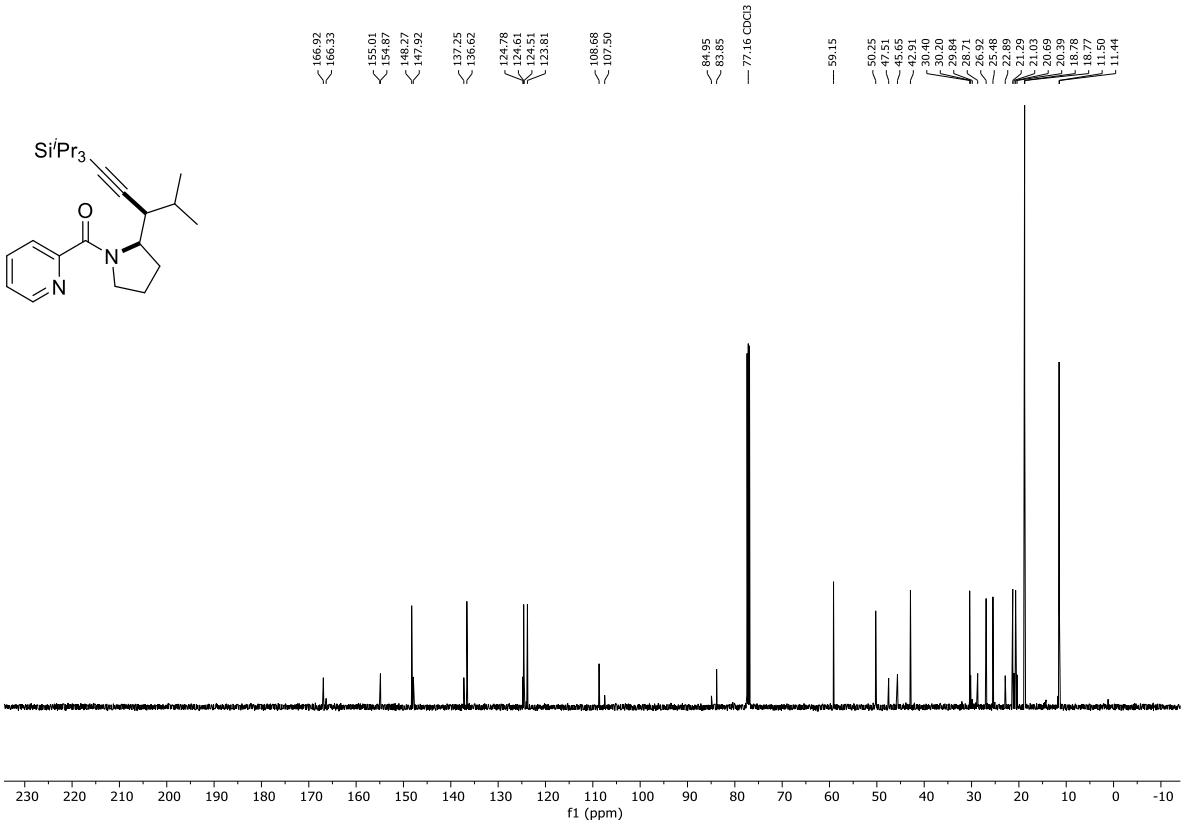
NOESY (500 MHz, $CDCl_3$, tm = 1000 ms) of **2d**



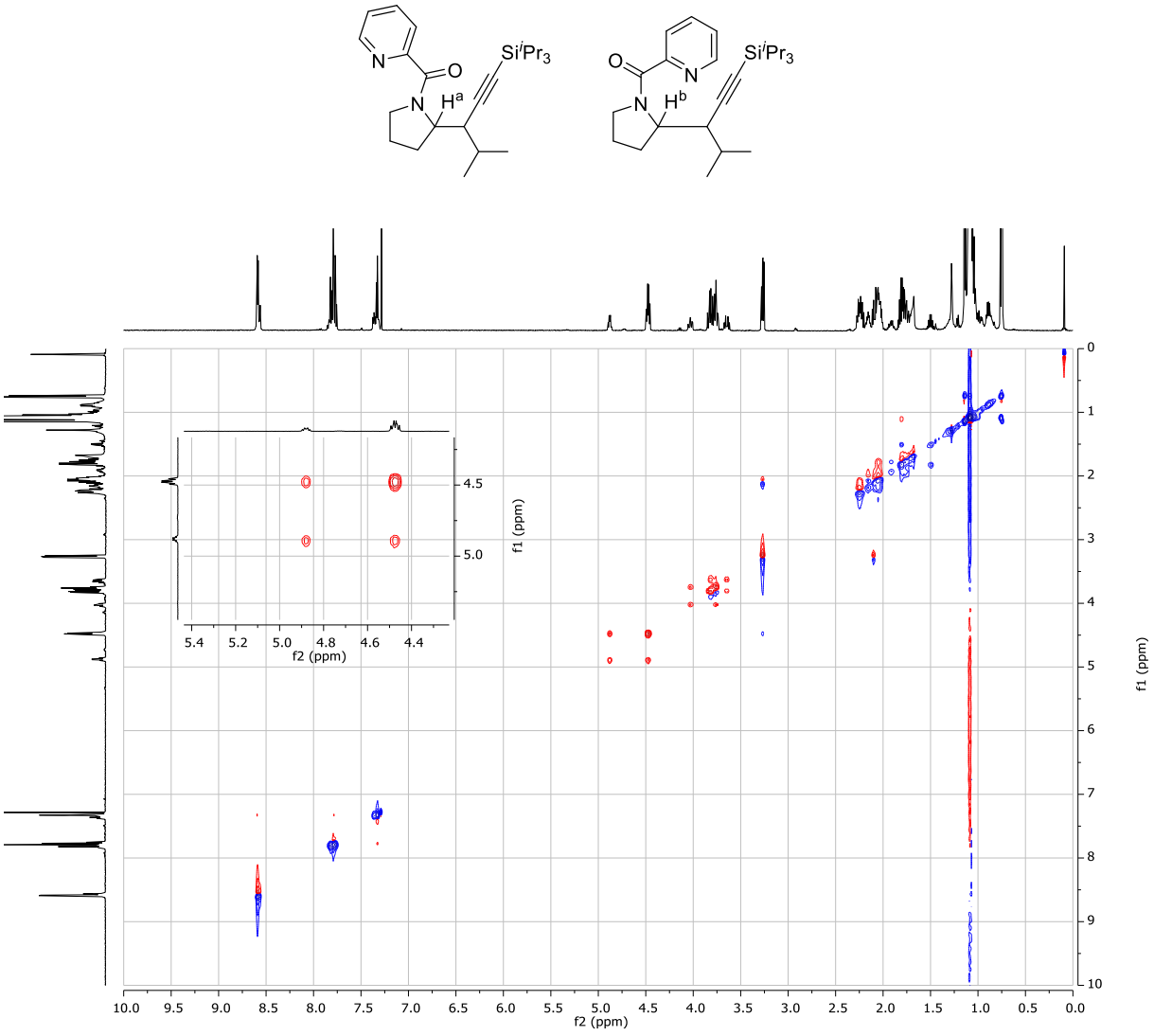
^{1}H NMR (500 MHz, $CDCl_3$) of **2e**



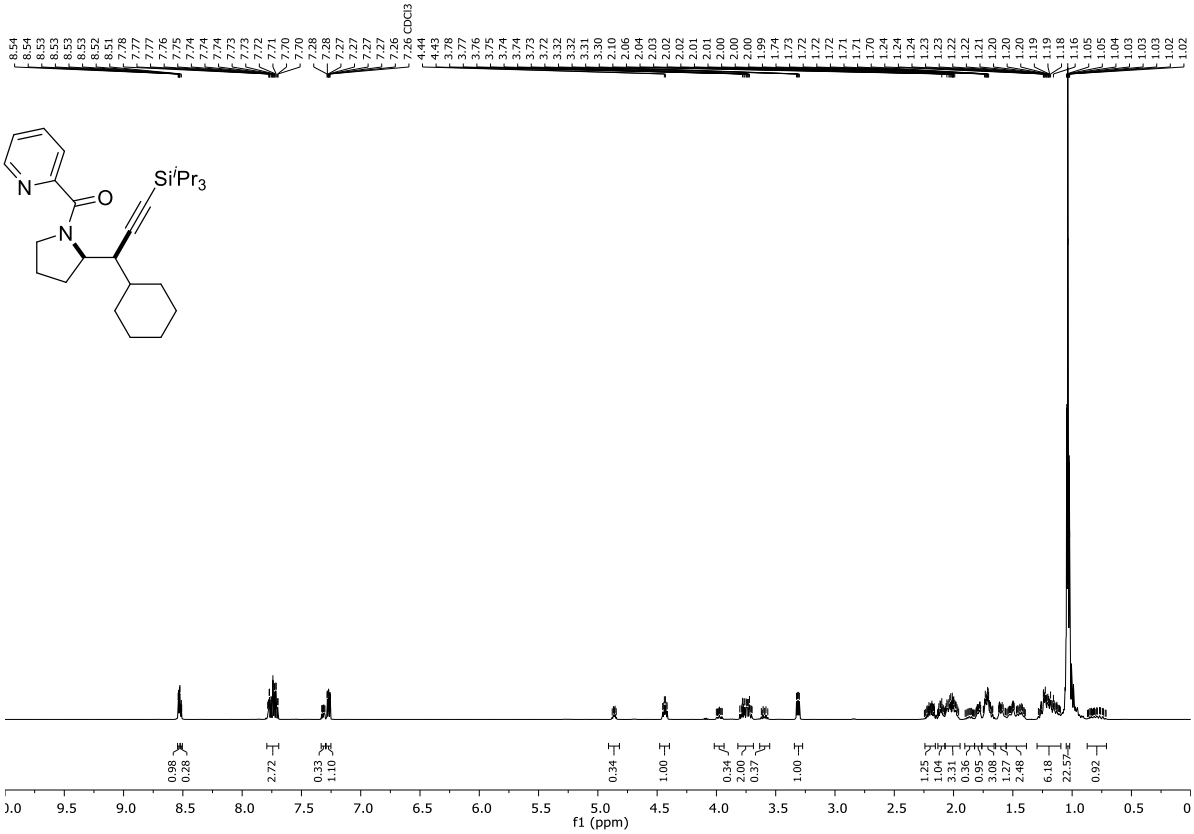
^{13}C NMR (126 MHz, $CDCl_3$) of **2e**



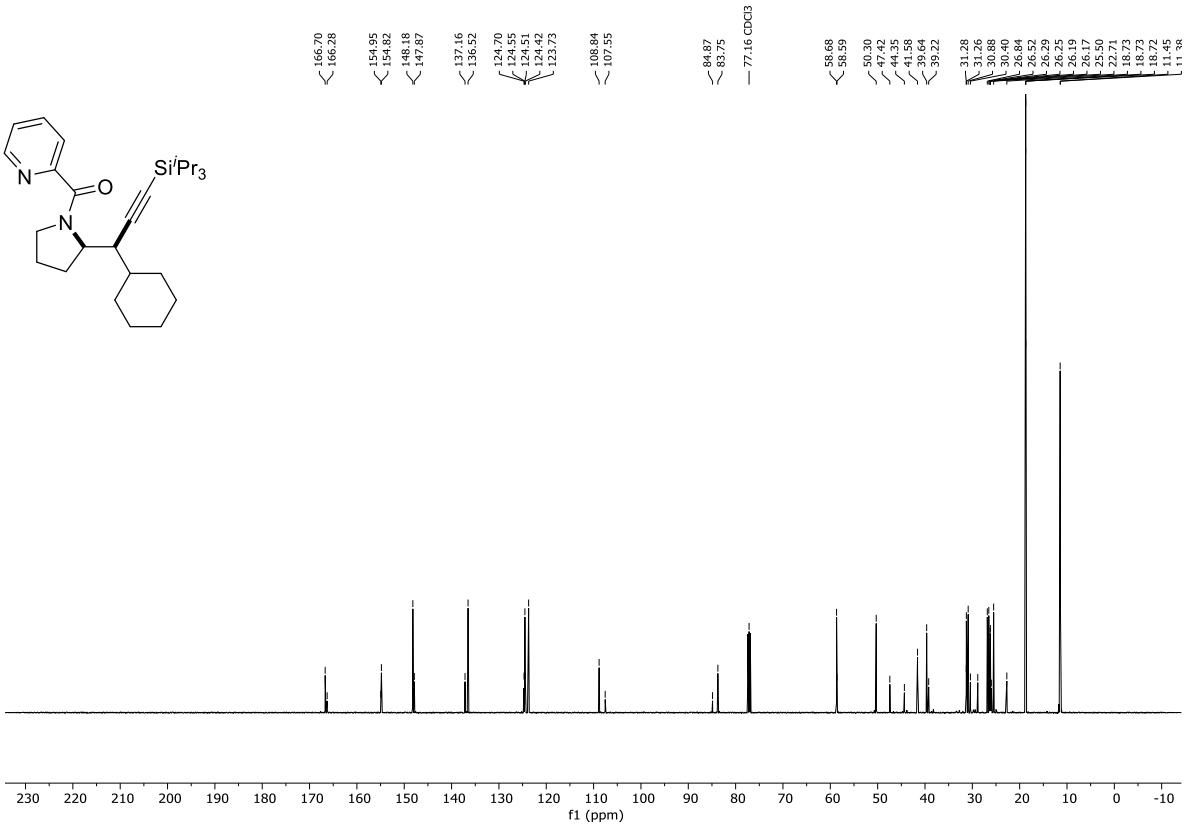
NOESY (500 MHz, $CDCl_3$, tm = 1000 ms) of **2e**



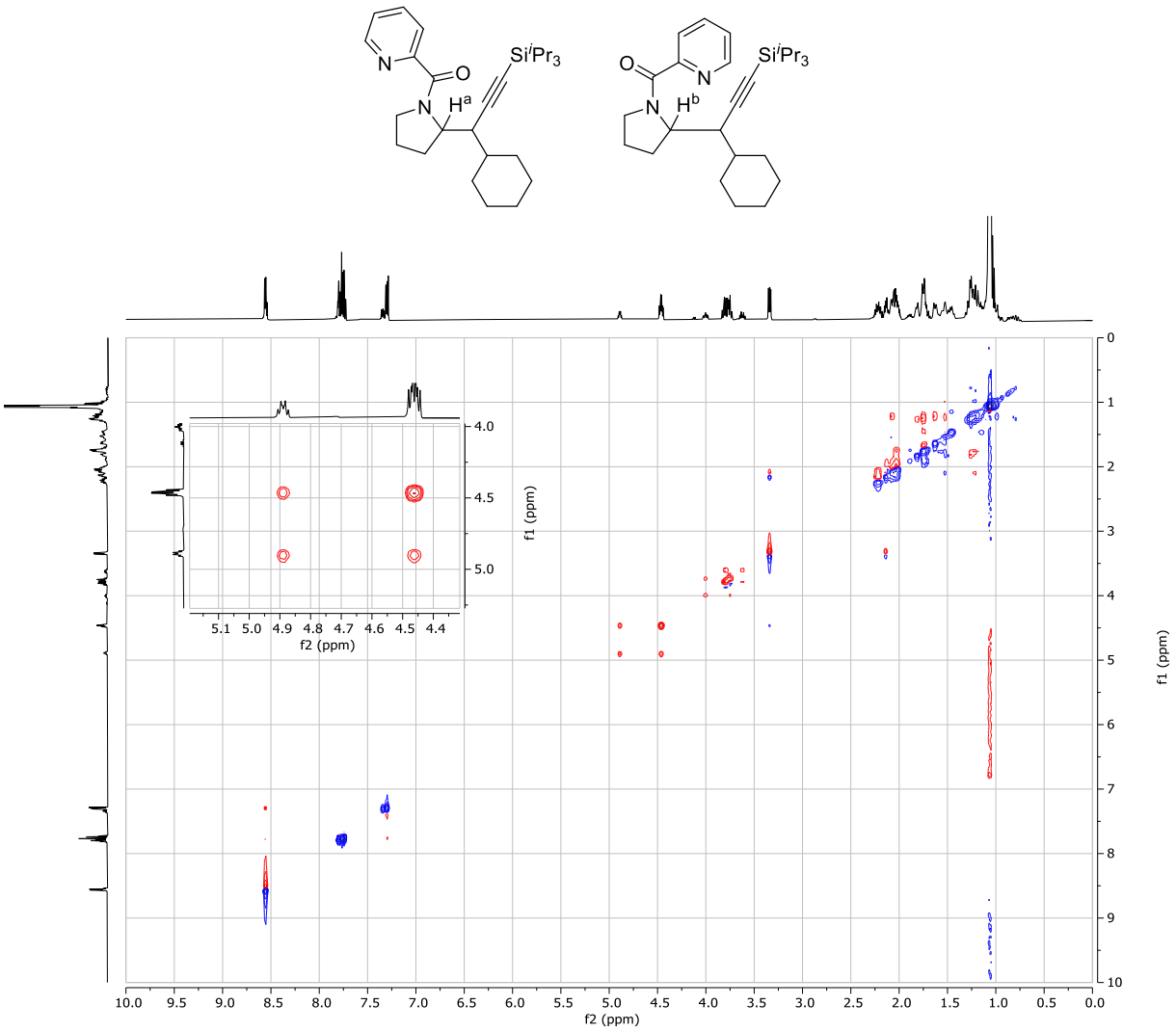
^{1}H NMR (500 MHz, $CDCl_3$) of **2f**



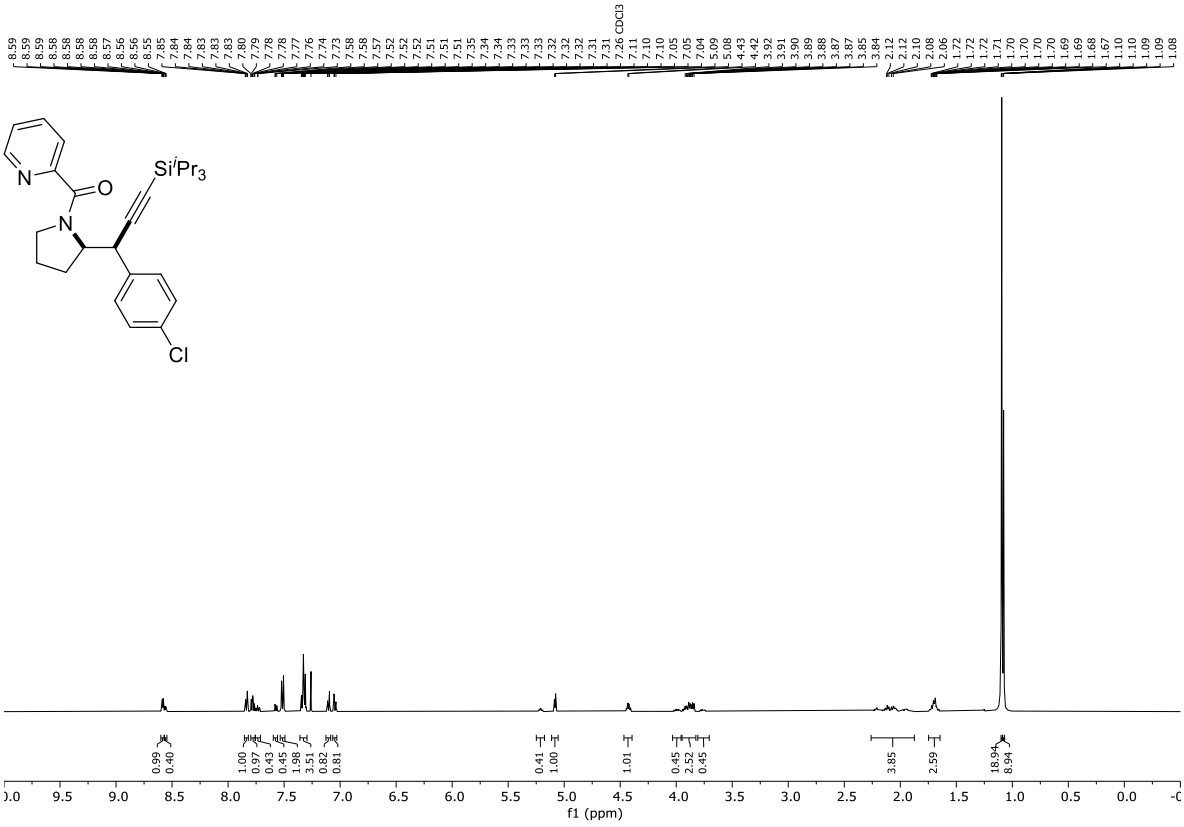
^{13}C NMR (126 MHz, $CDCl_3$) of **2f**



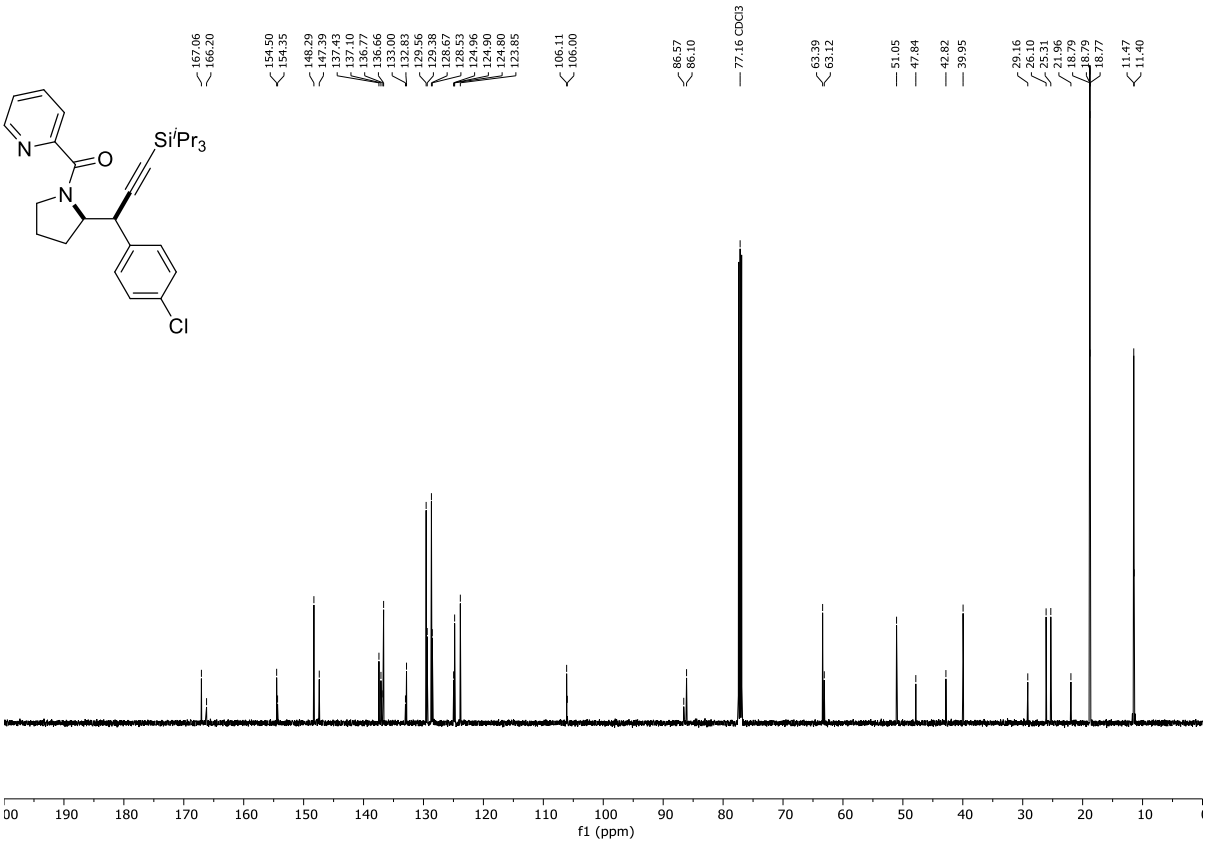
NOESY (500 MHz, $CDCl_3$, tm = 1000 ms) of **2f**



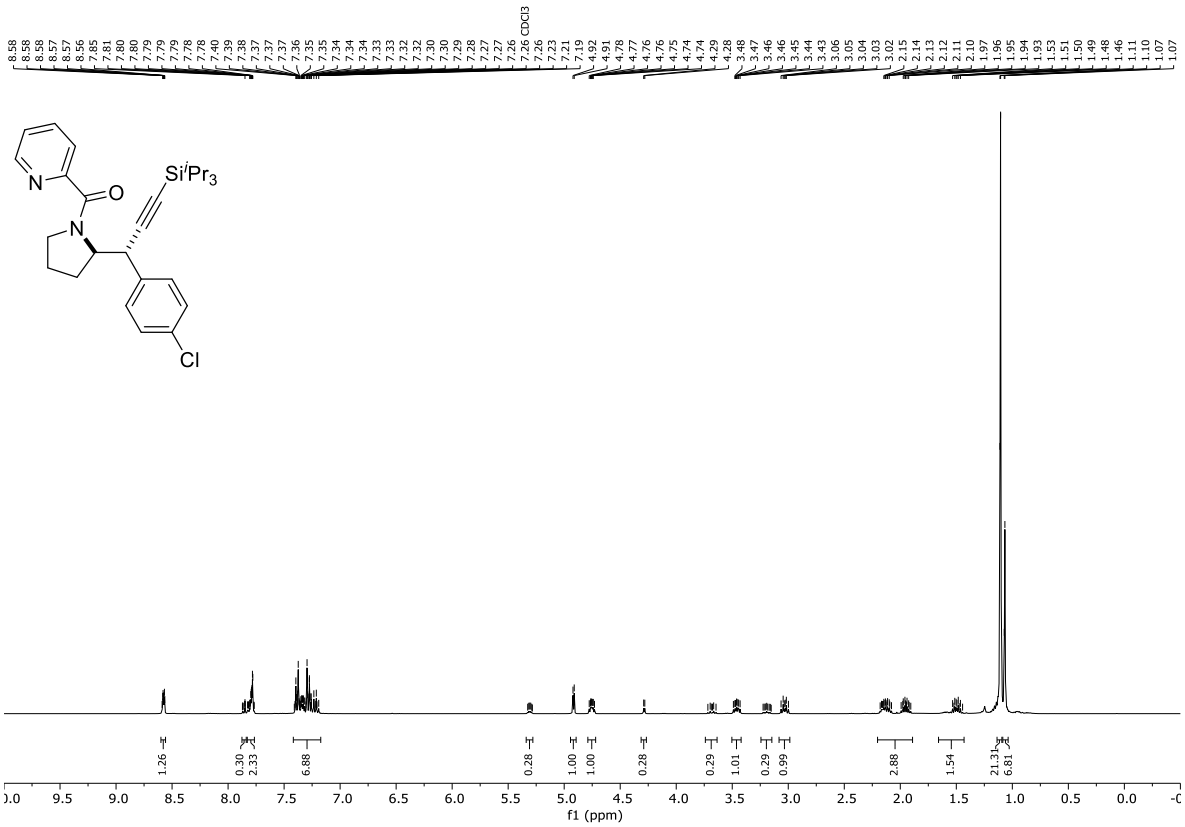
^{1}H NMR (500 MHz, $CDCl_3$) of **2g**



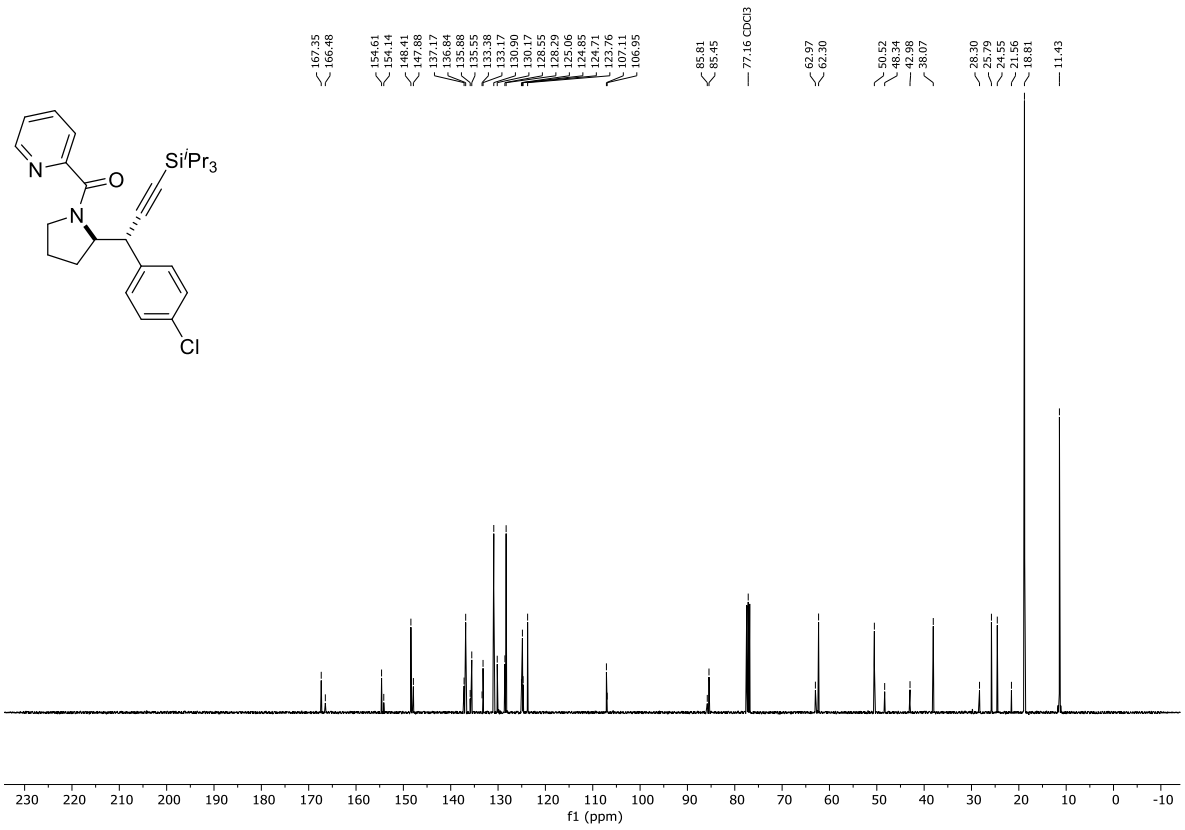
^{13}C NMR (126 MHz, $CDCl_3$) of **2g**



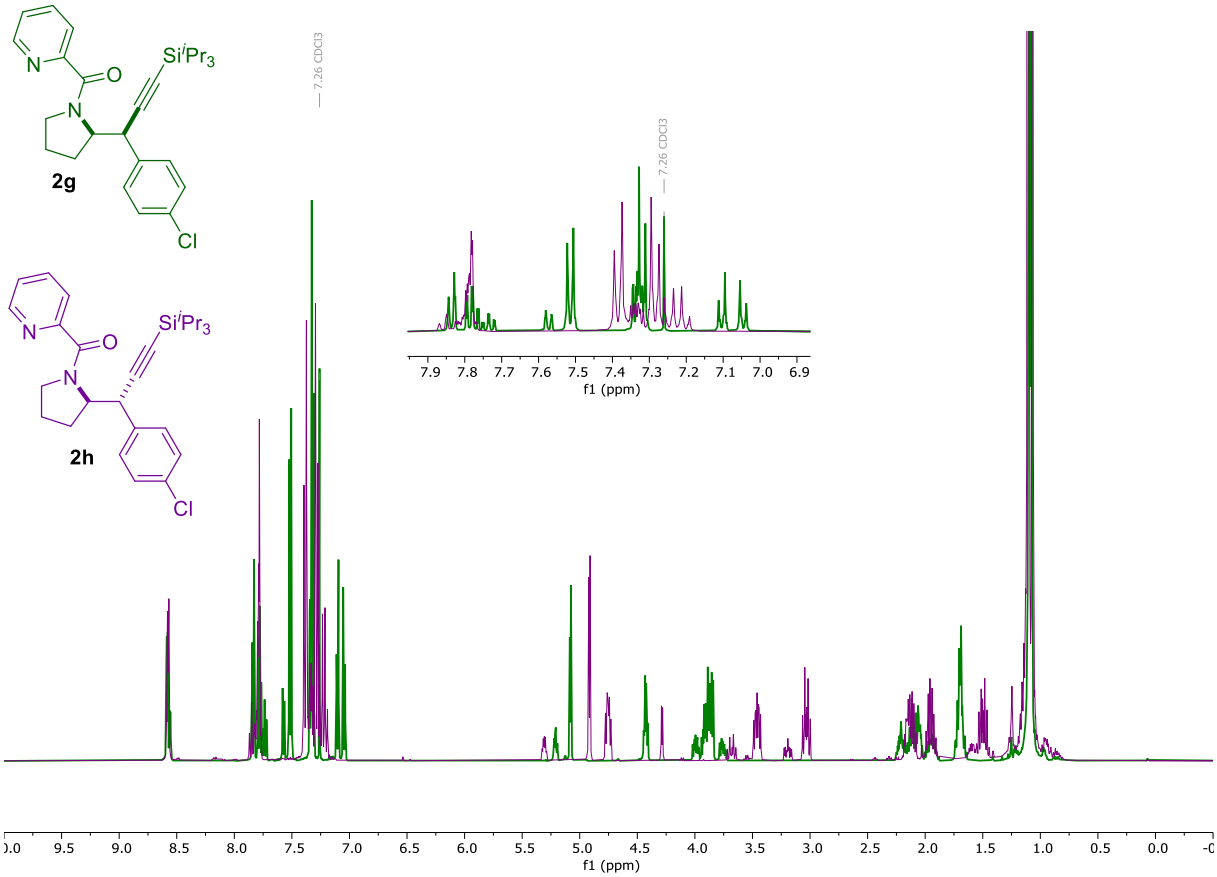
^{1}H NMR (400 MHz, $CDCl_3$) of **2h**



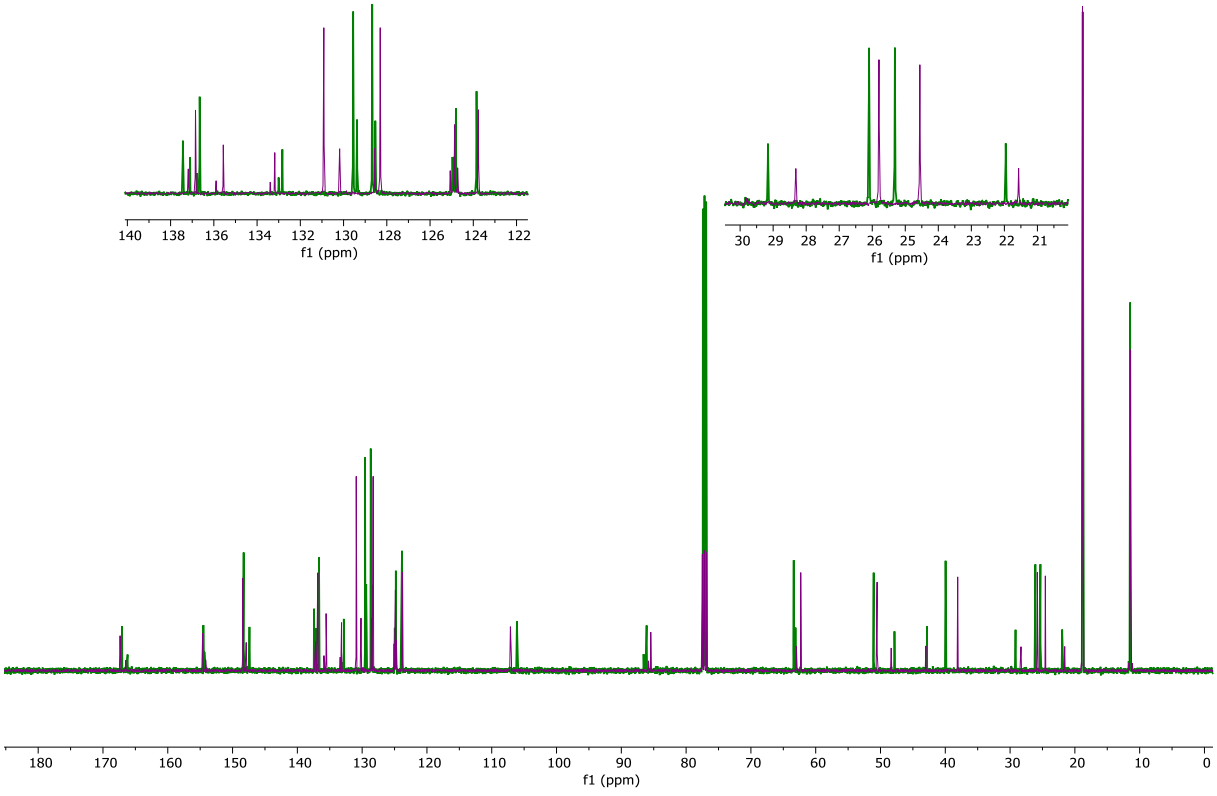
^{13}C NMR (101 MHz, $CDCl_3$) of **2h**



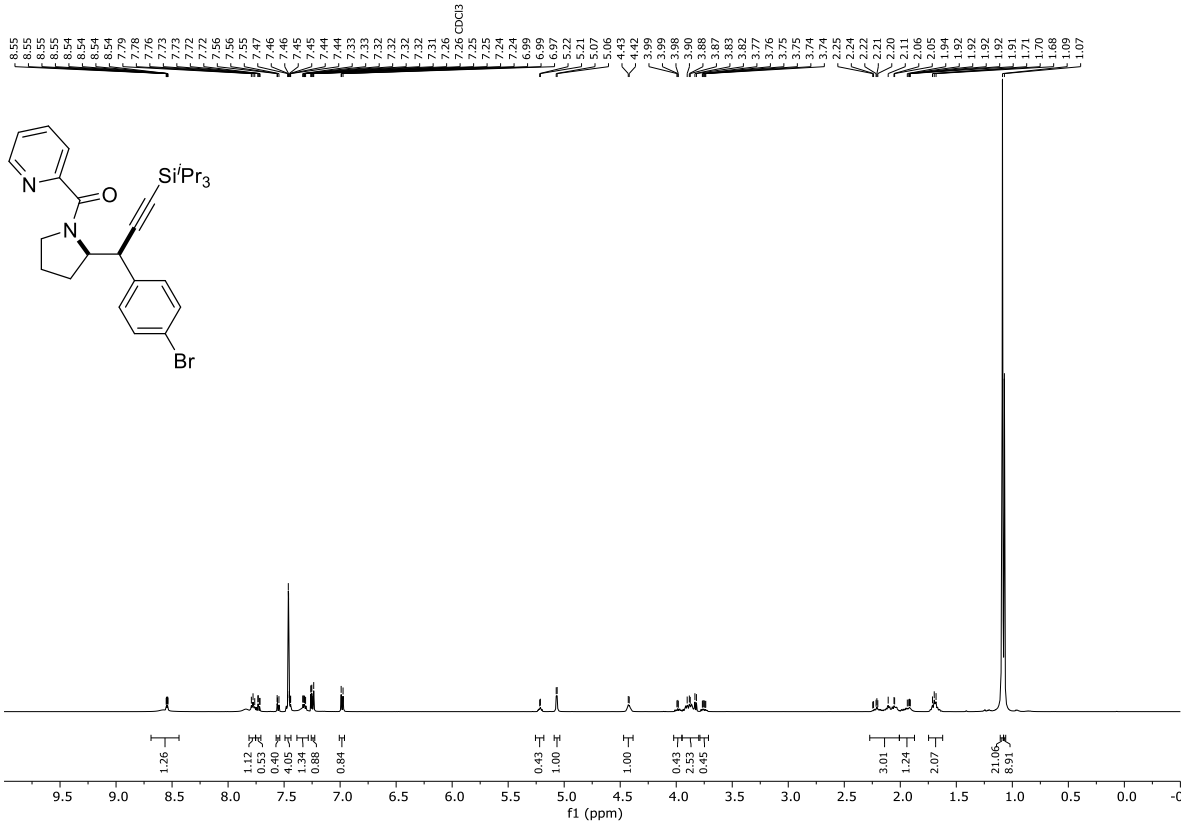
Overlay of the ^{1}H-NMR spectra of **2g** (green, 500 MHz) and **2h** (violet, 400 MHz) in $CDCl_3$



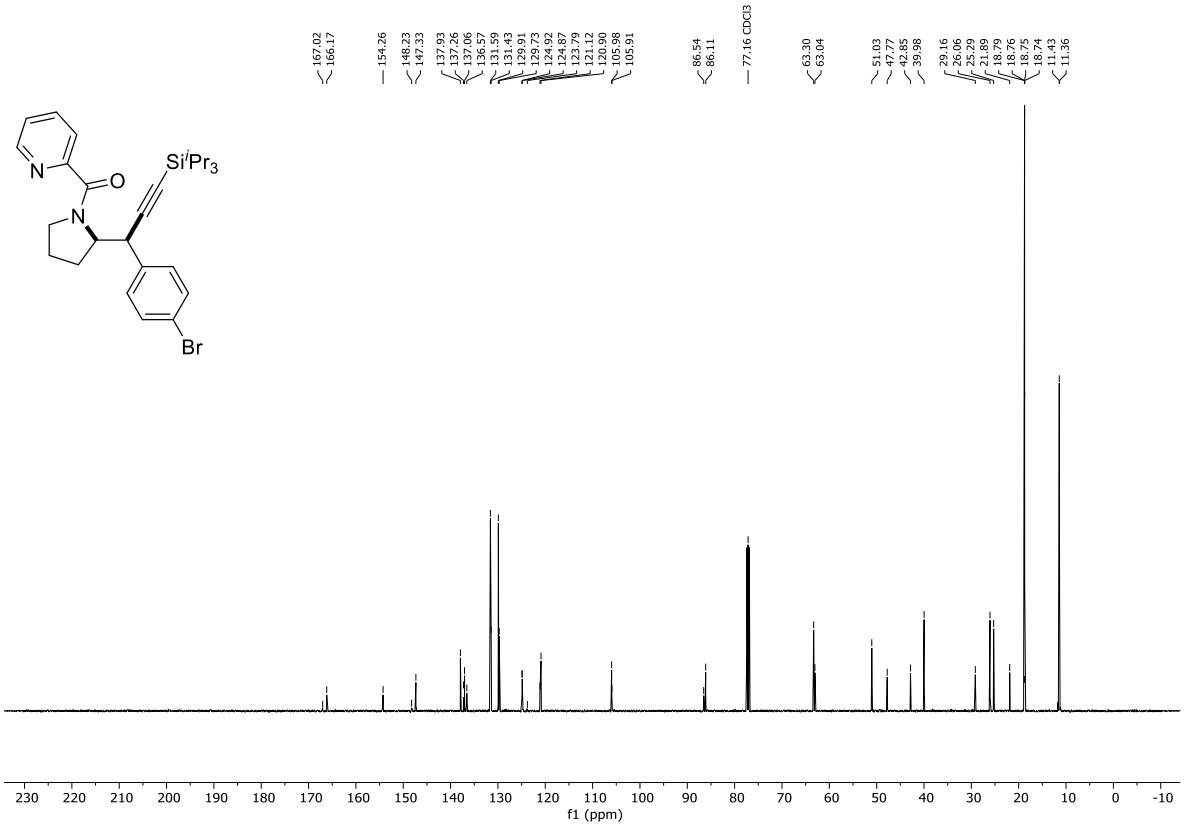
Overlay of the ^{13}C-NMR spectra of **2g** (green, 126 MHz) and **2h** (violet, 101 MHz) in $CDCl_3$



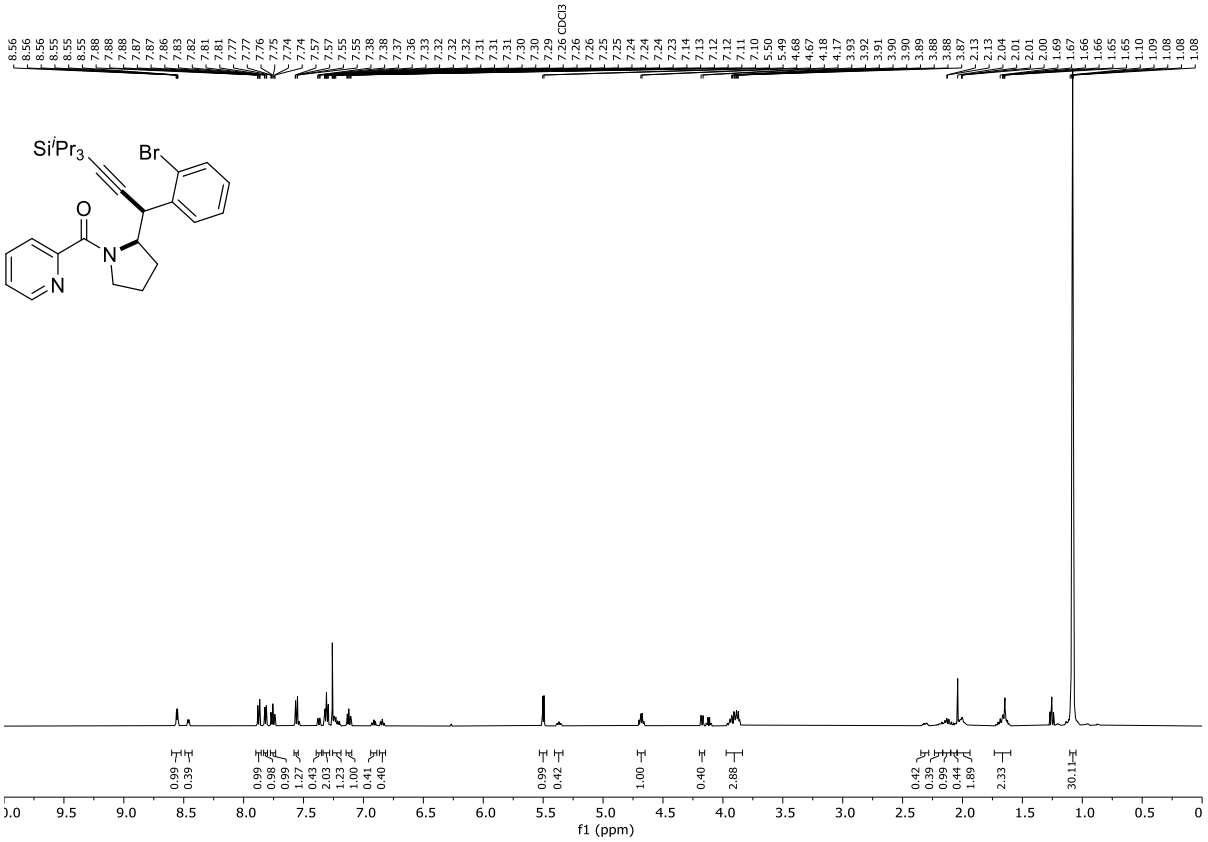
^{1}H NMR (500 MHz, $CDCl_3$) of **2i**



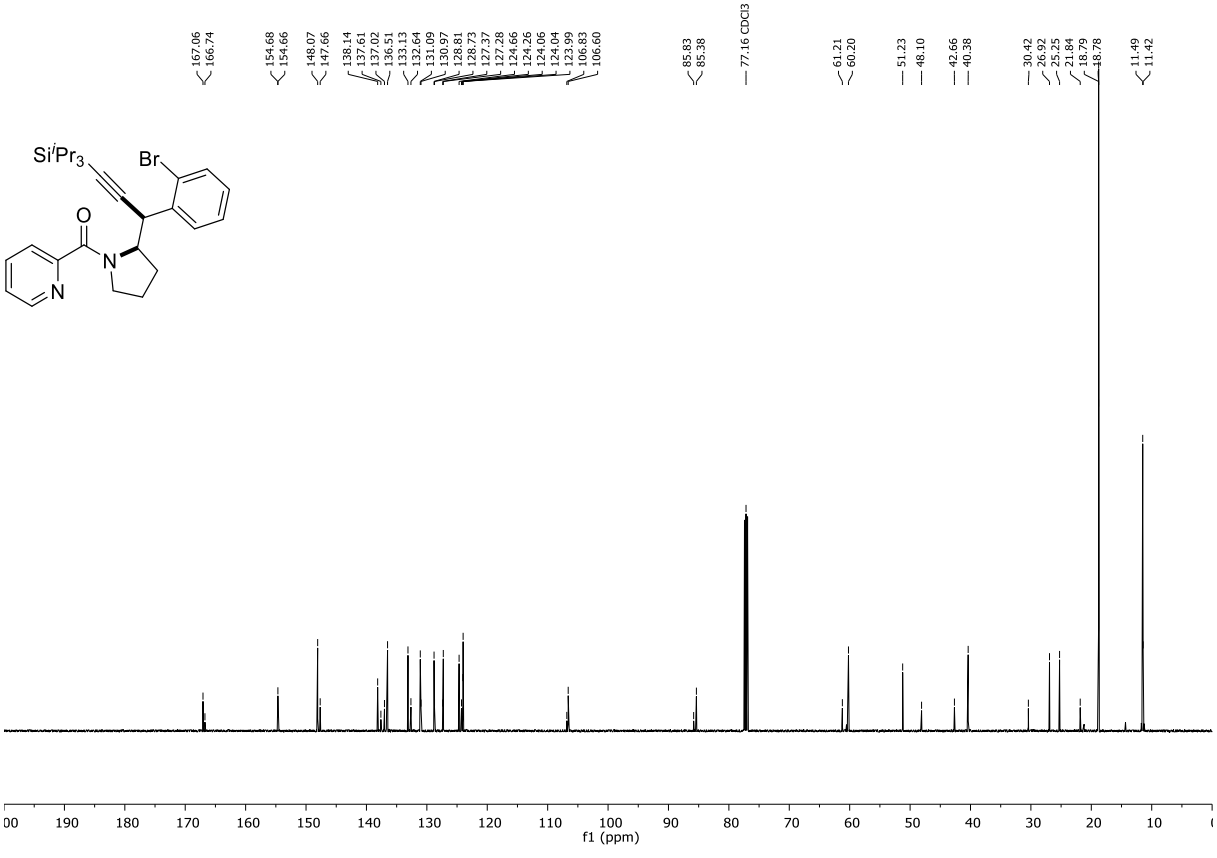
^{13}C NMR (126 MHz, $CDCl_3$) of **2i**



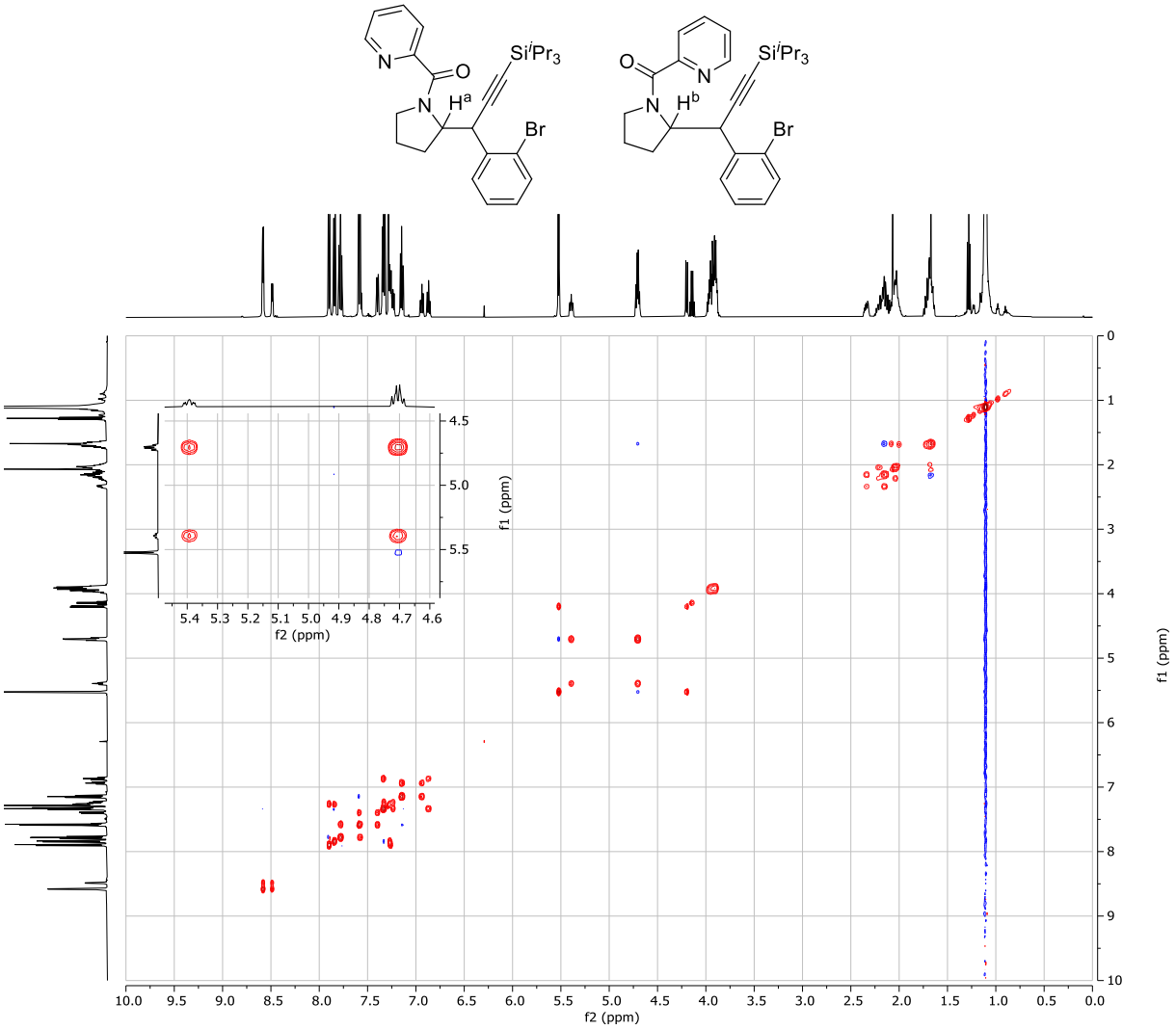
^{1}H NMR (500 MHz, $CDCl_3$) of **2j**



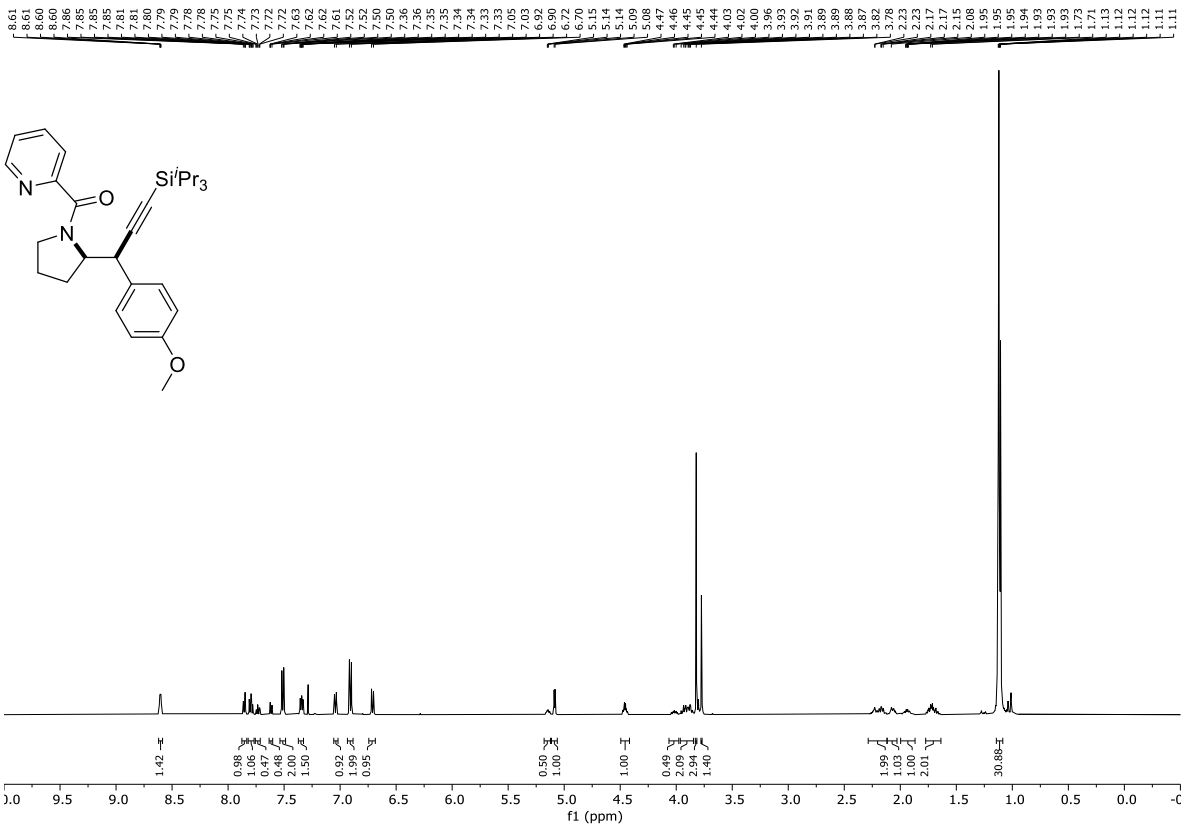
^{1}H NMR (126 MHz, $CDCl_3$) of **2j**



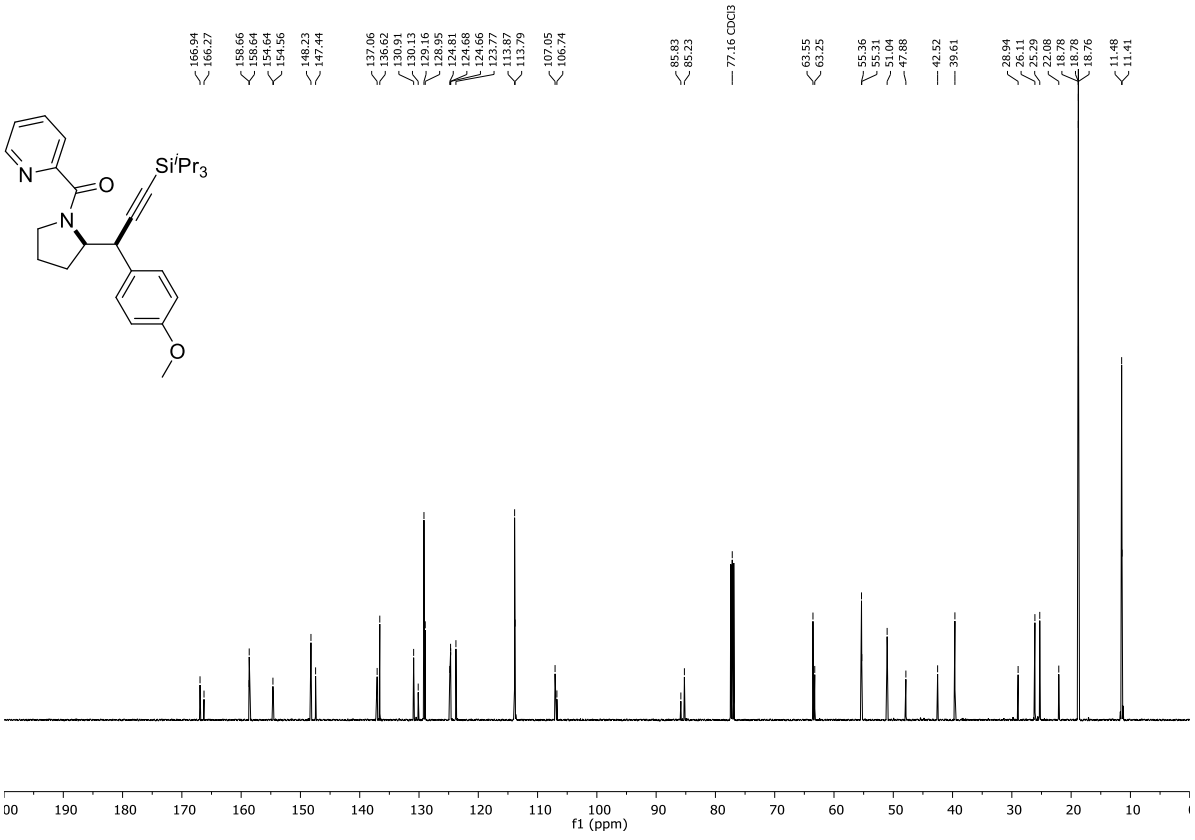
NOESY (500 MHz, $CDCl_3$, tm = 1000 ms) of **2j**



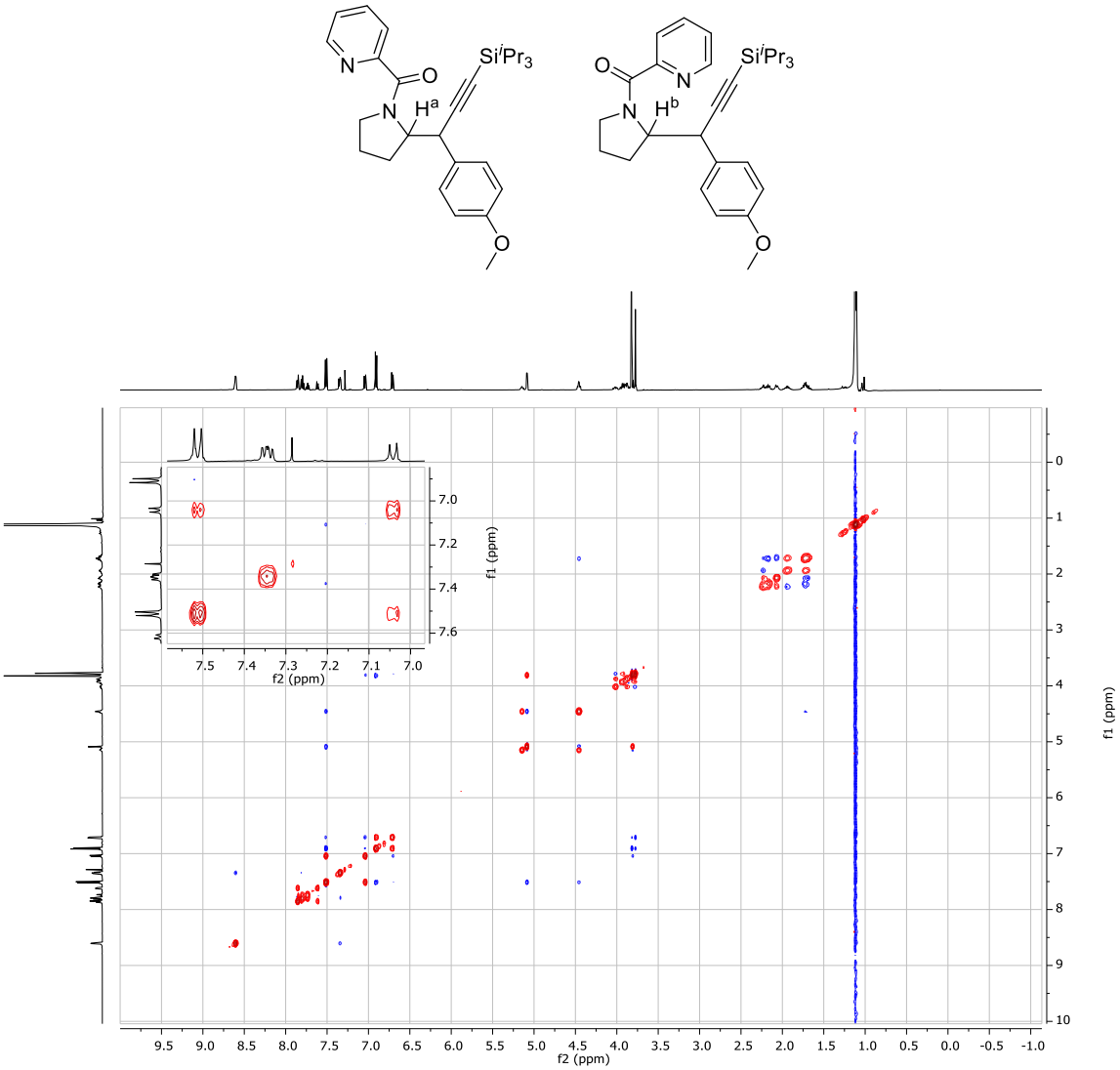
^{1}H NMR (500 MHz, $CDCl_3$) of **2k**



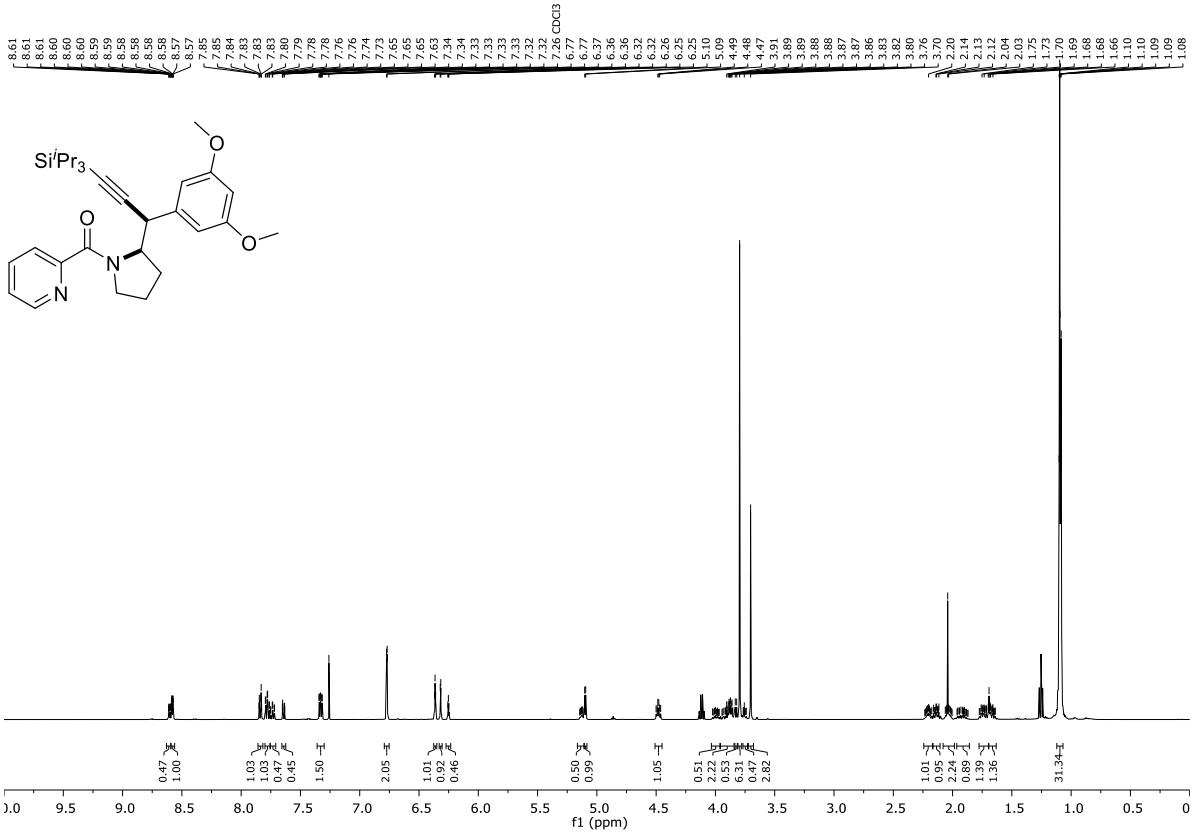
^{13}C NMR (126 MHz, $CDCl_3$) of **2k**



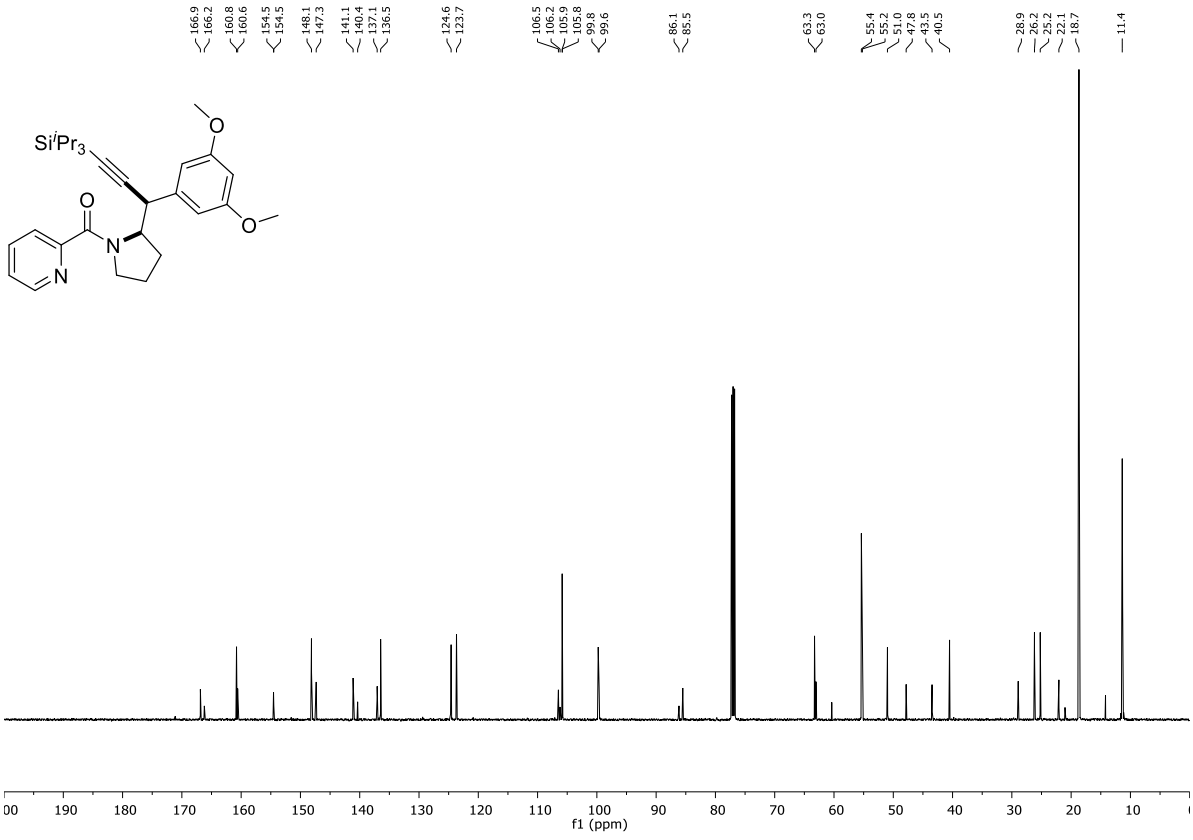
NOESY (500 MHz, $CDCl_3$, tm = 1000 ms) of **2k**



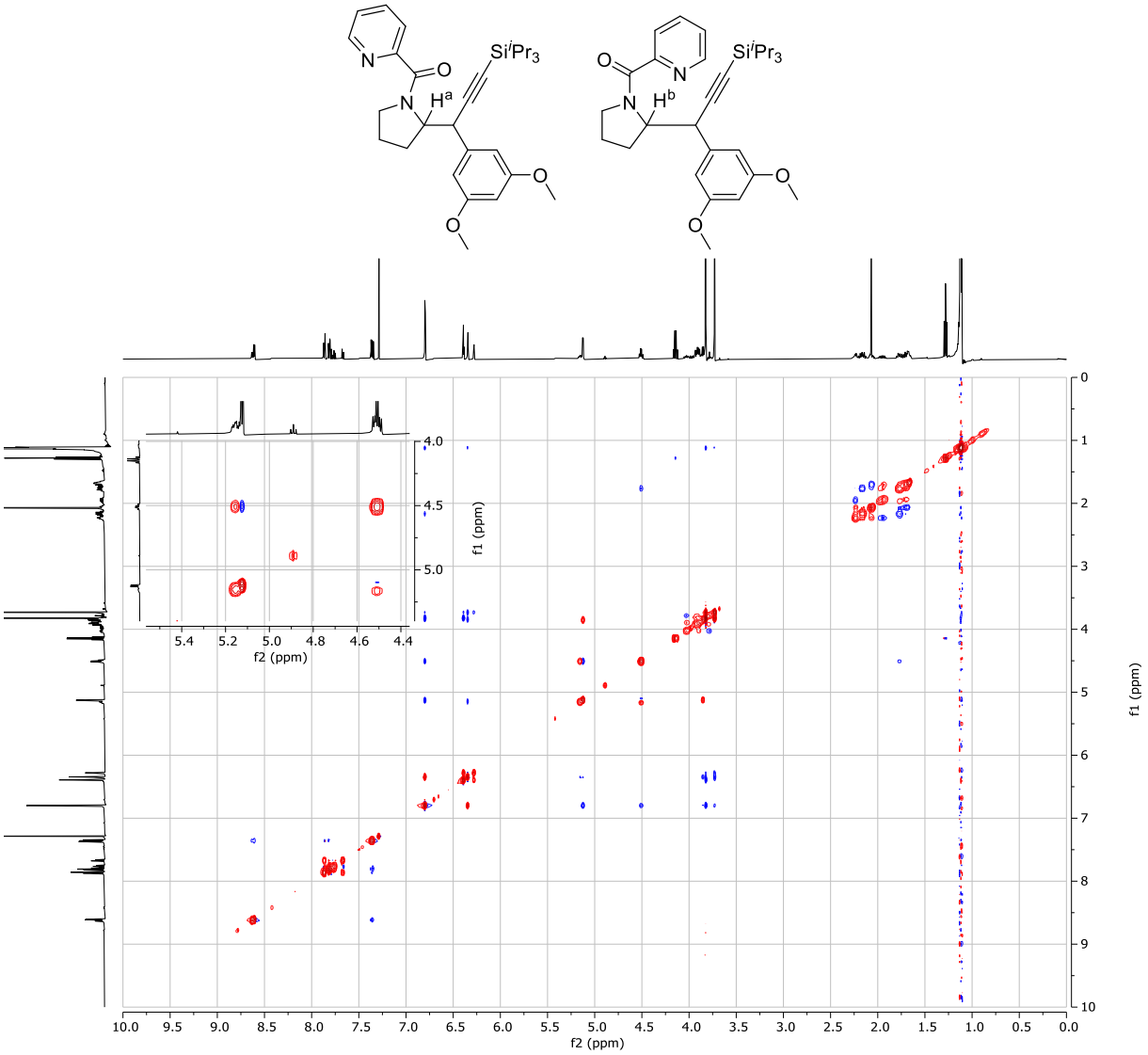
^{1}H NMR (500 MHz, $CDCl_3$) of **2l**



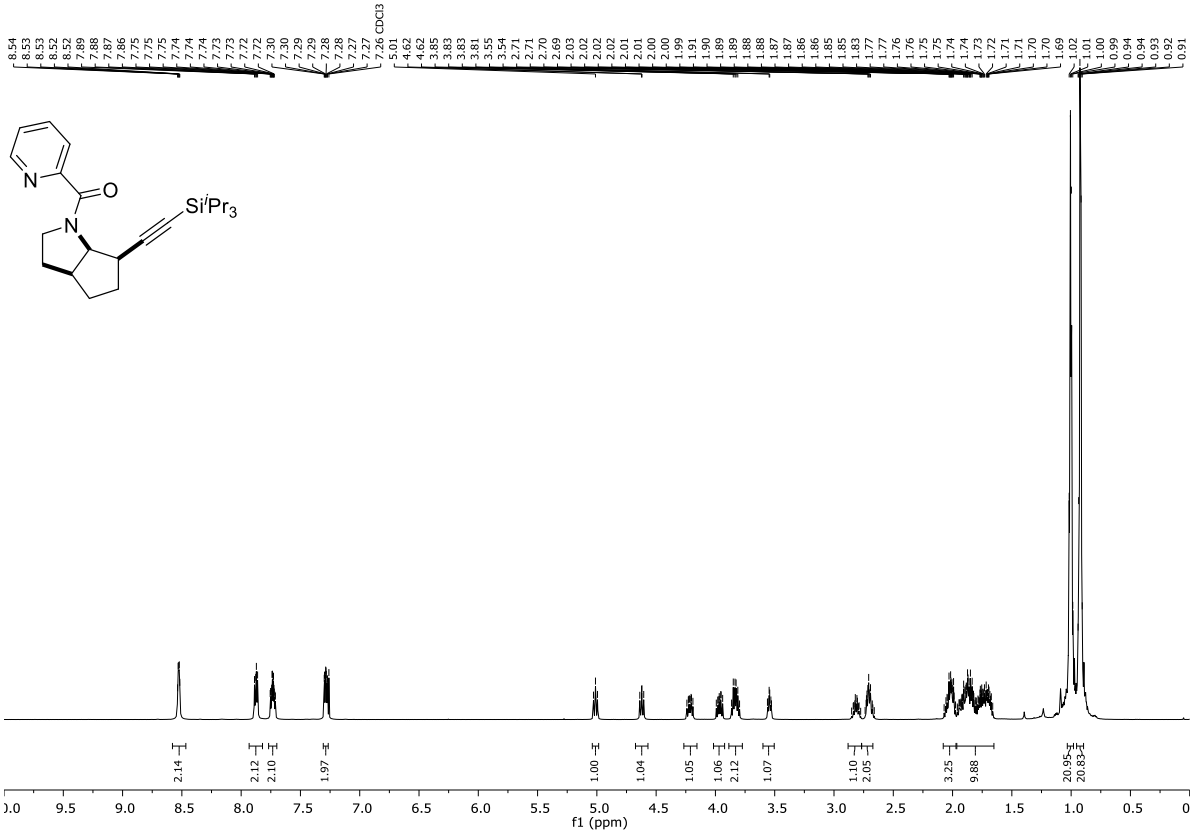
^{13}C NMR (126 MHz, $CDCl_3$) of **2l**



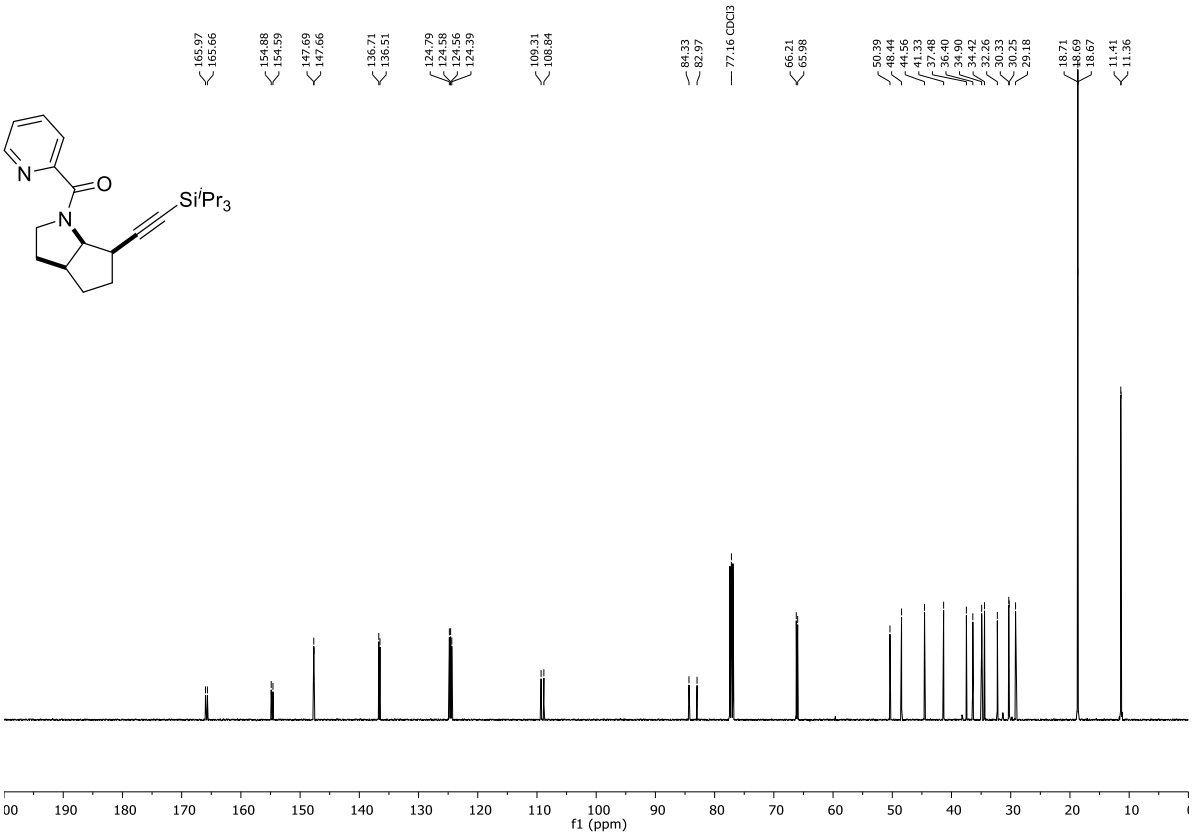
NOESY (500 MHz, $CDCl_3$, tm = 1000 ms) of **2l**



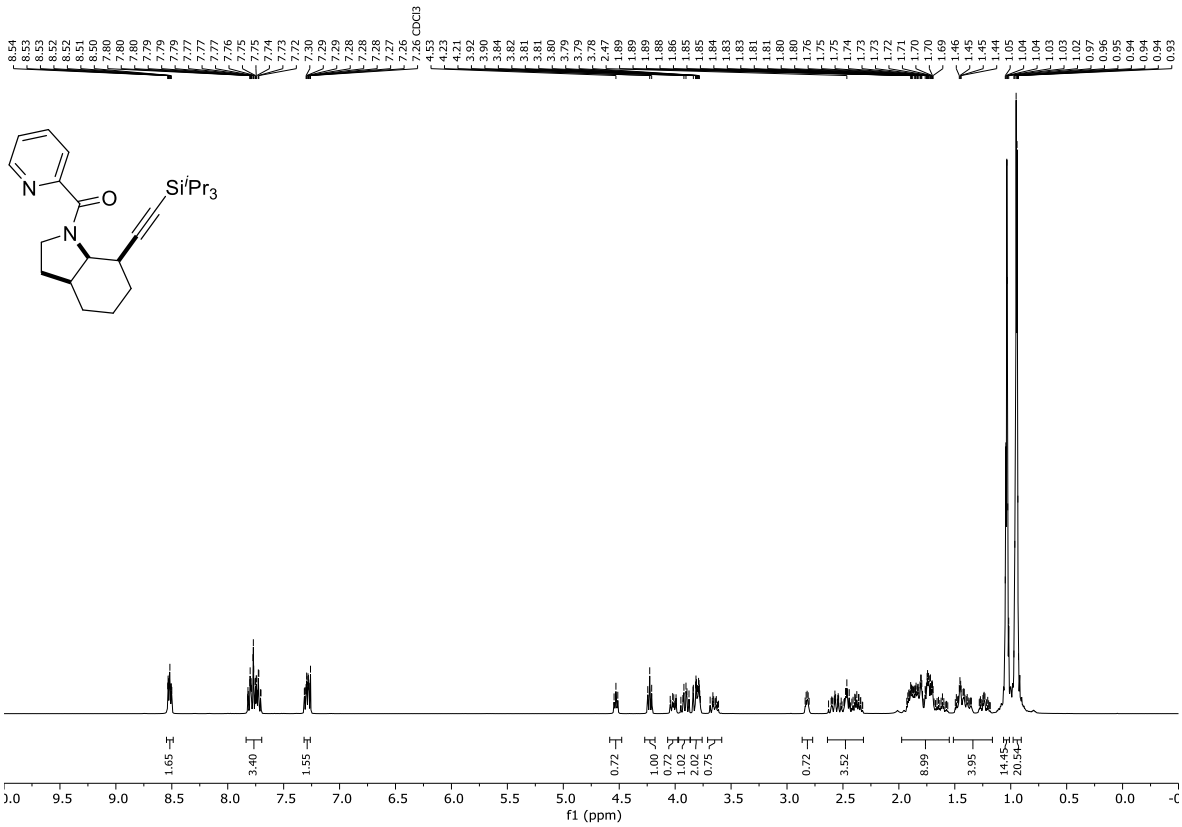
^{1}H NMR (500 MHz, $CDCl_3$) of **2m**



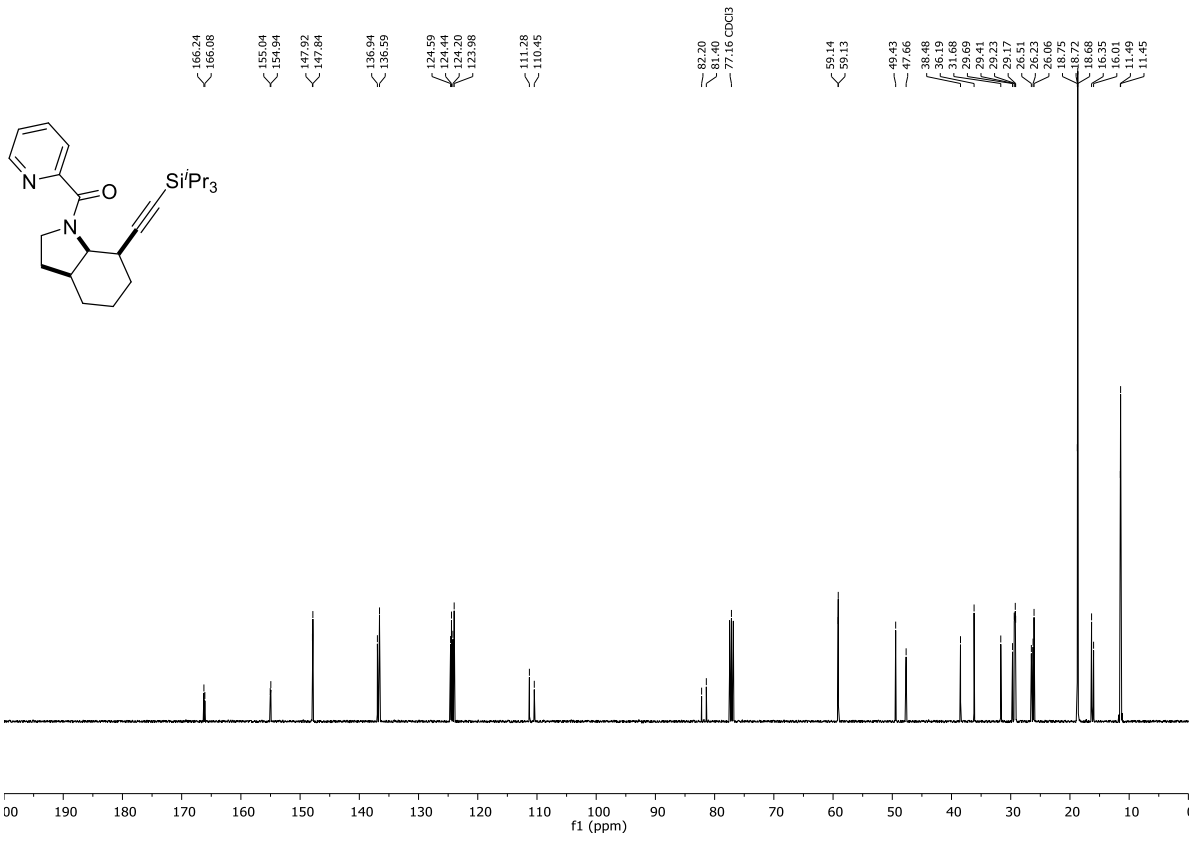
^{13}C NMR (126 MHz, $CDCl_3$) of **2m**



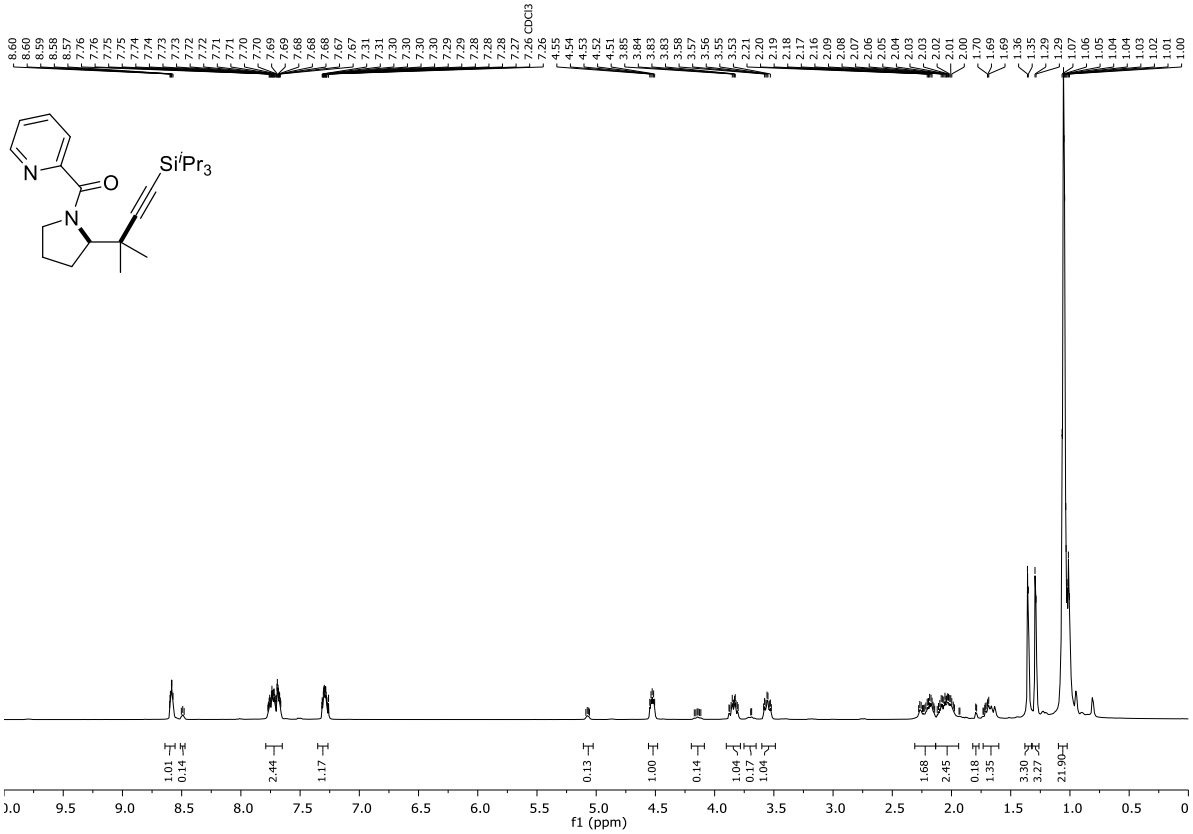
^{1}H NMR (400 MHz, $CDCl_3$) of **2n**



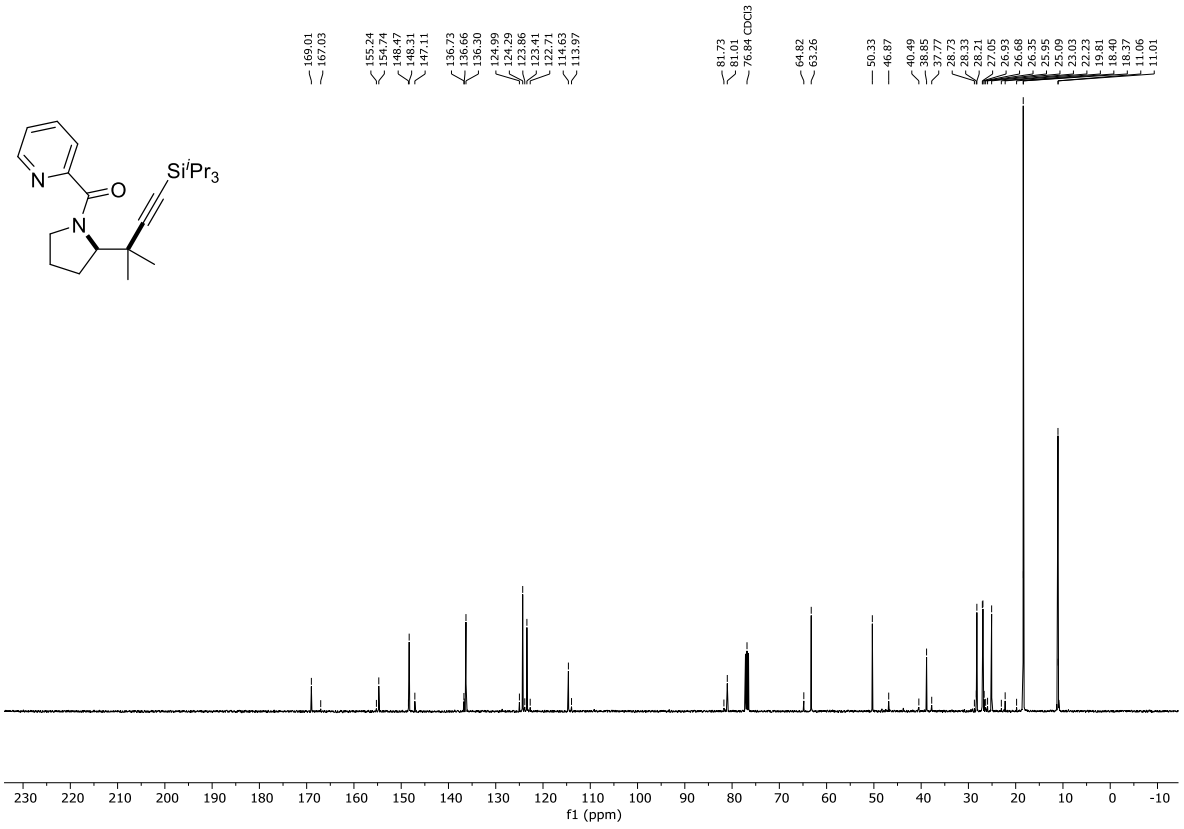
^{13}C NMR (101 MHz, $CDCl_3$) of **2n**



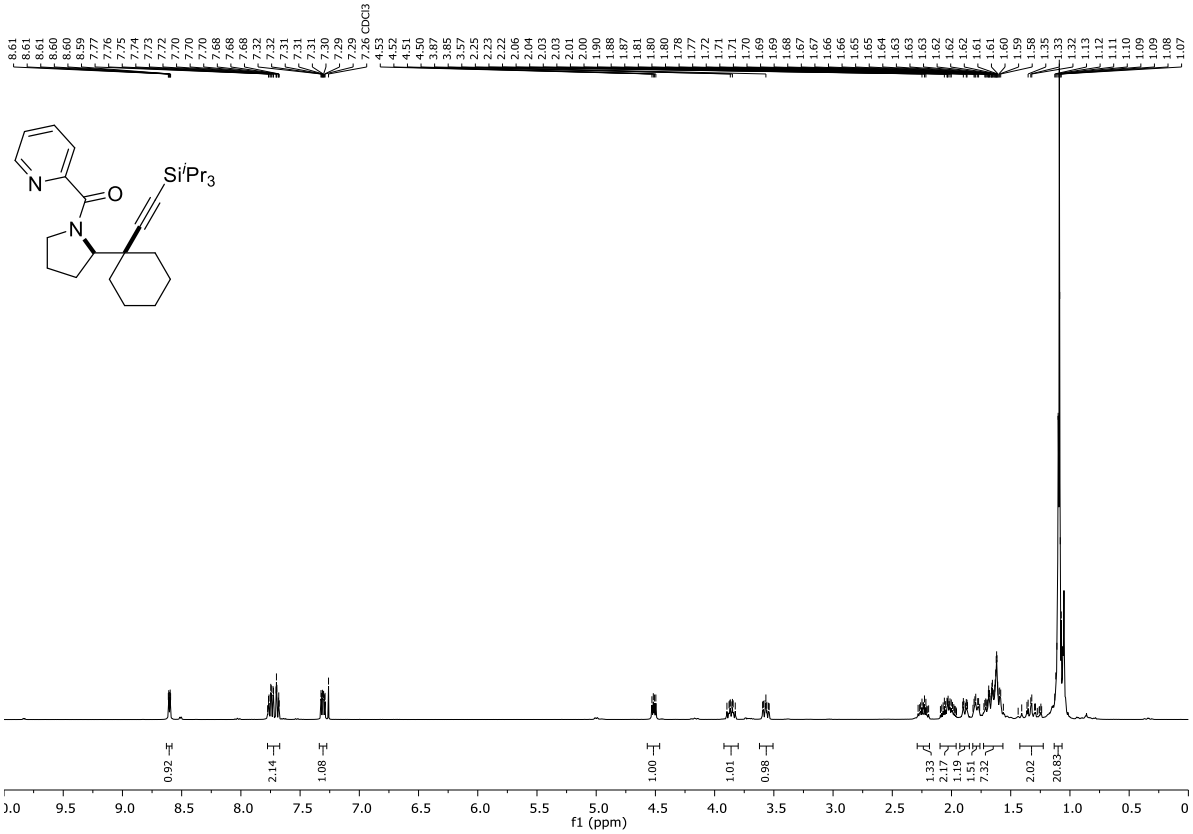
^{1}H NMR (400 MHz, $CDCl_3$) of **2o**



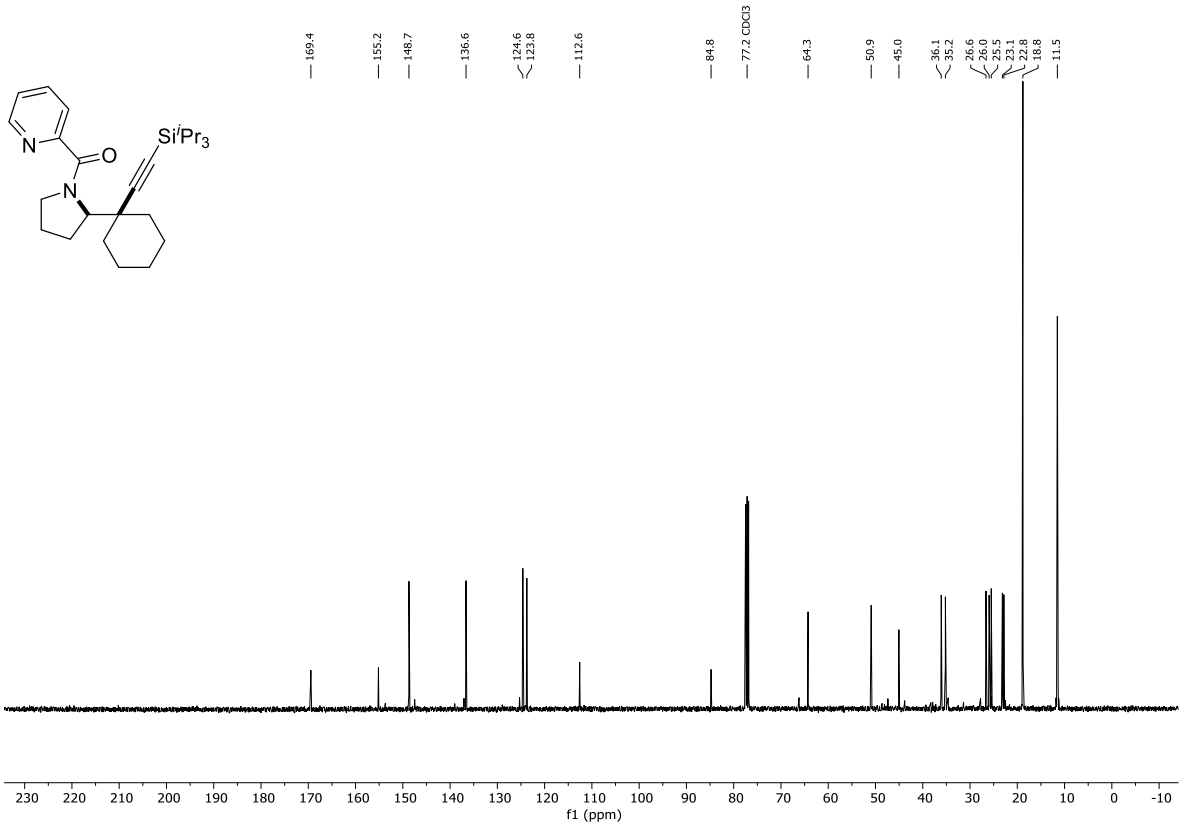
^{13}C NMR (101 MHz, $CDCl_3$) of **2o**



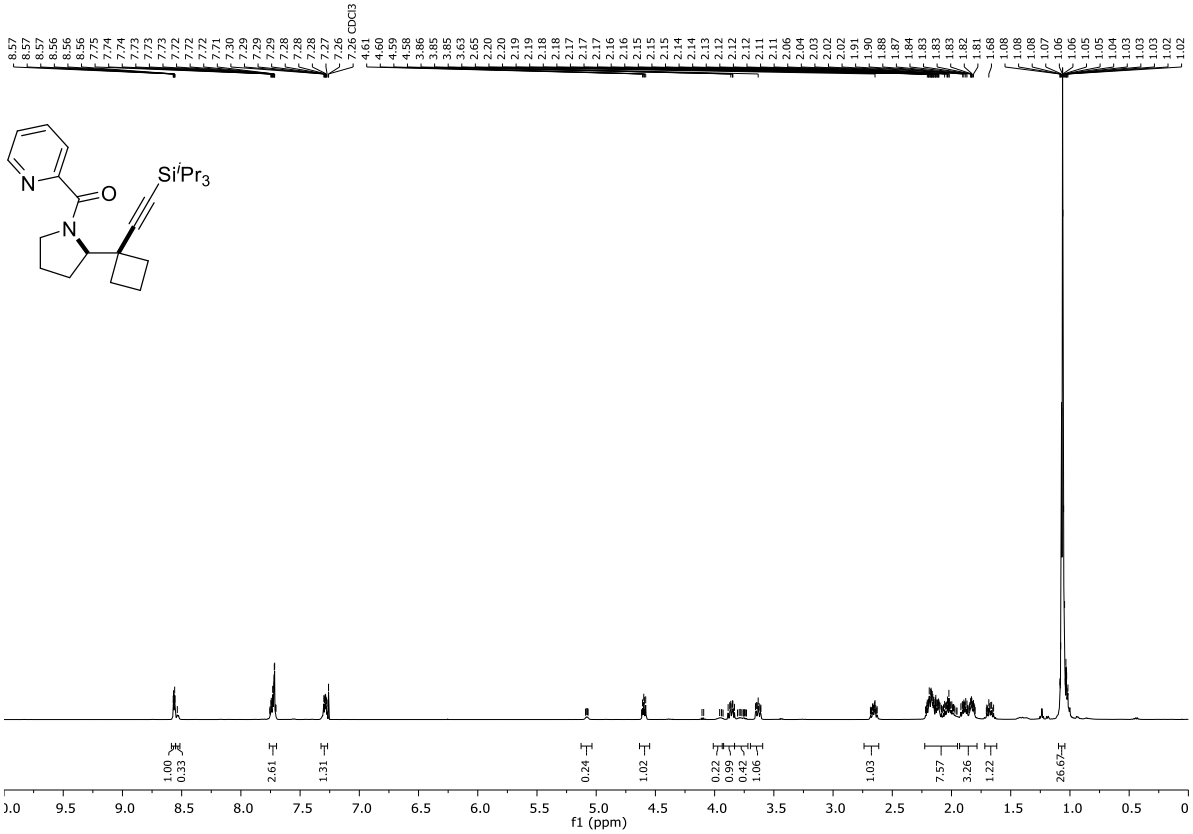
^{1}H NMR (400 MHz, $CDCl_3$) of **2p**



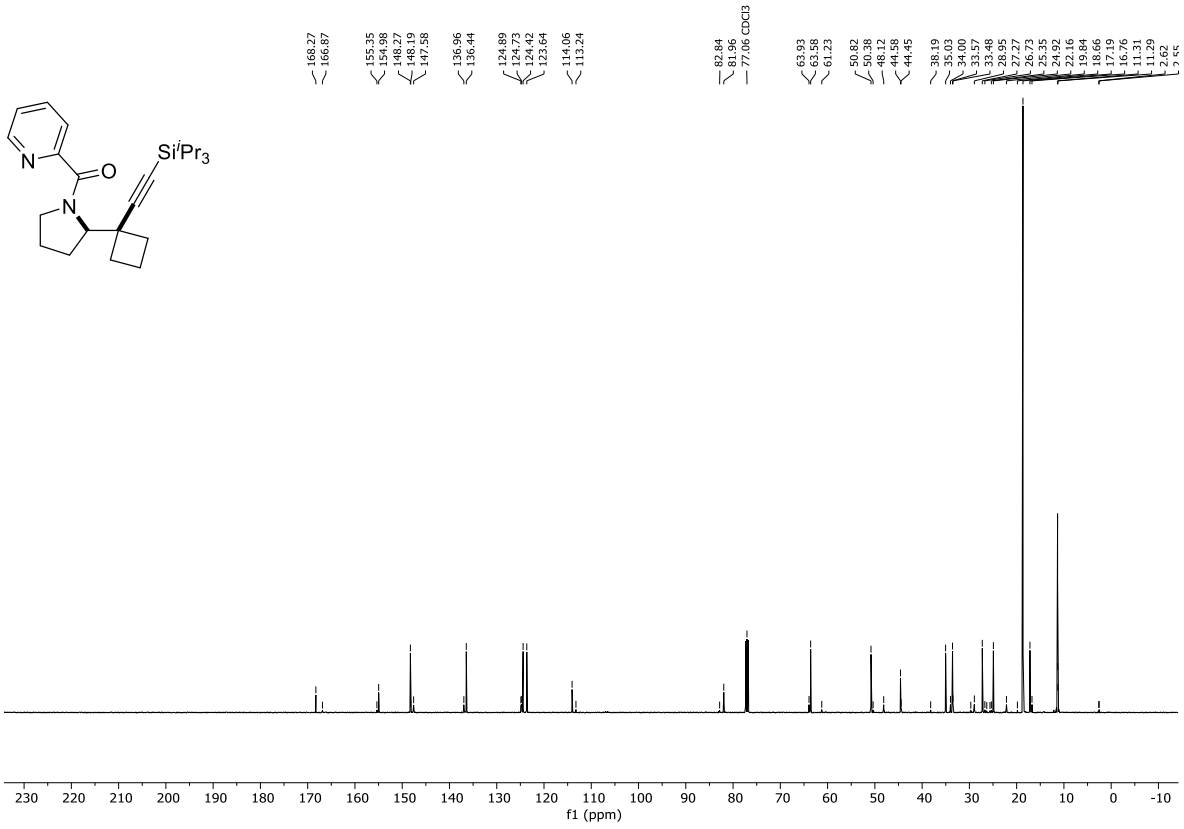
^{13}C NMR (101 MHz, $CDCl_3$) of **2p**



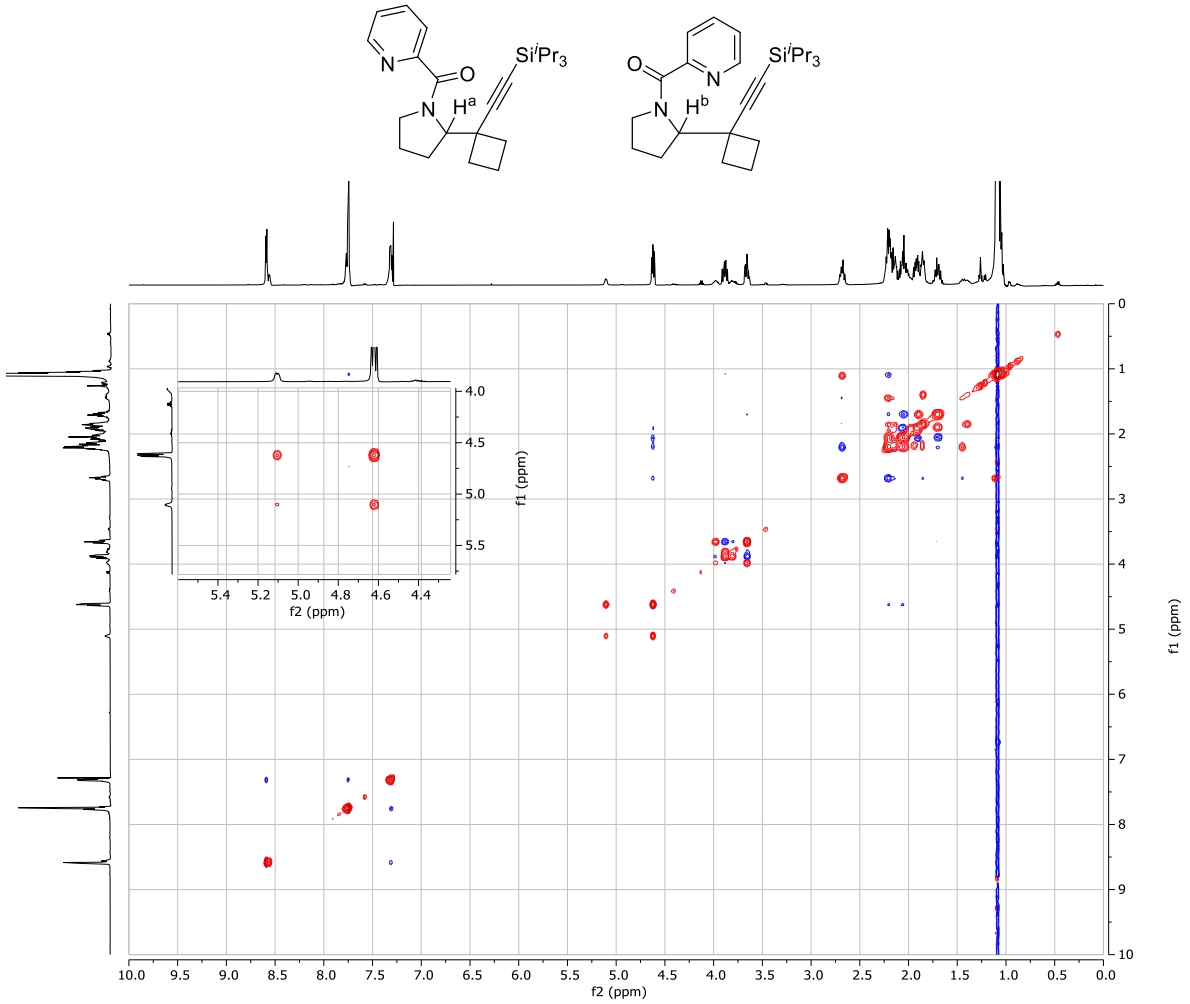
^{1}H NMR (500 MHz, $CDCl_3$) of **2q**



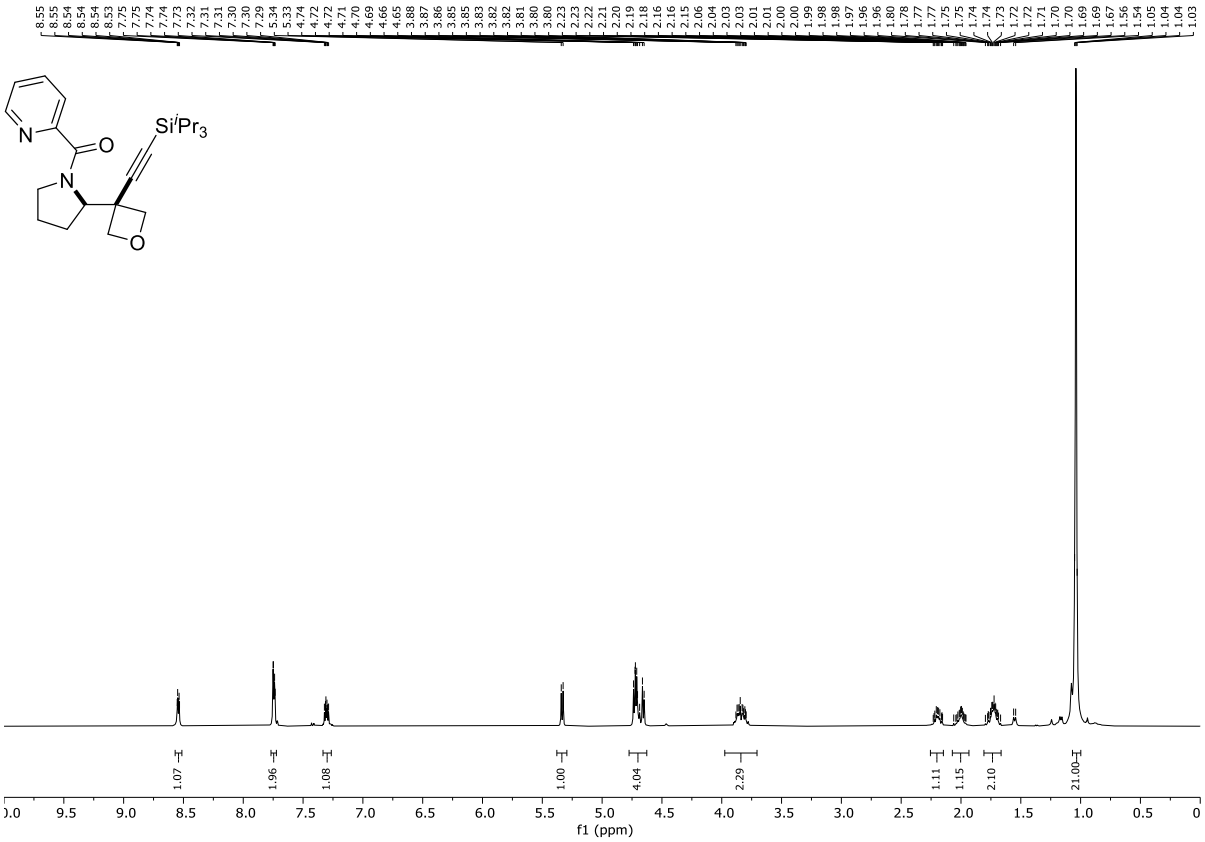
^{13}C NMR (126 MHz, $CDCl_3$) of **2q**



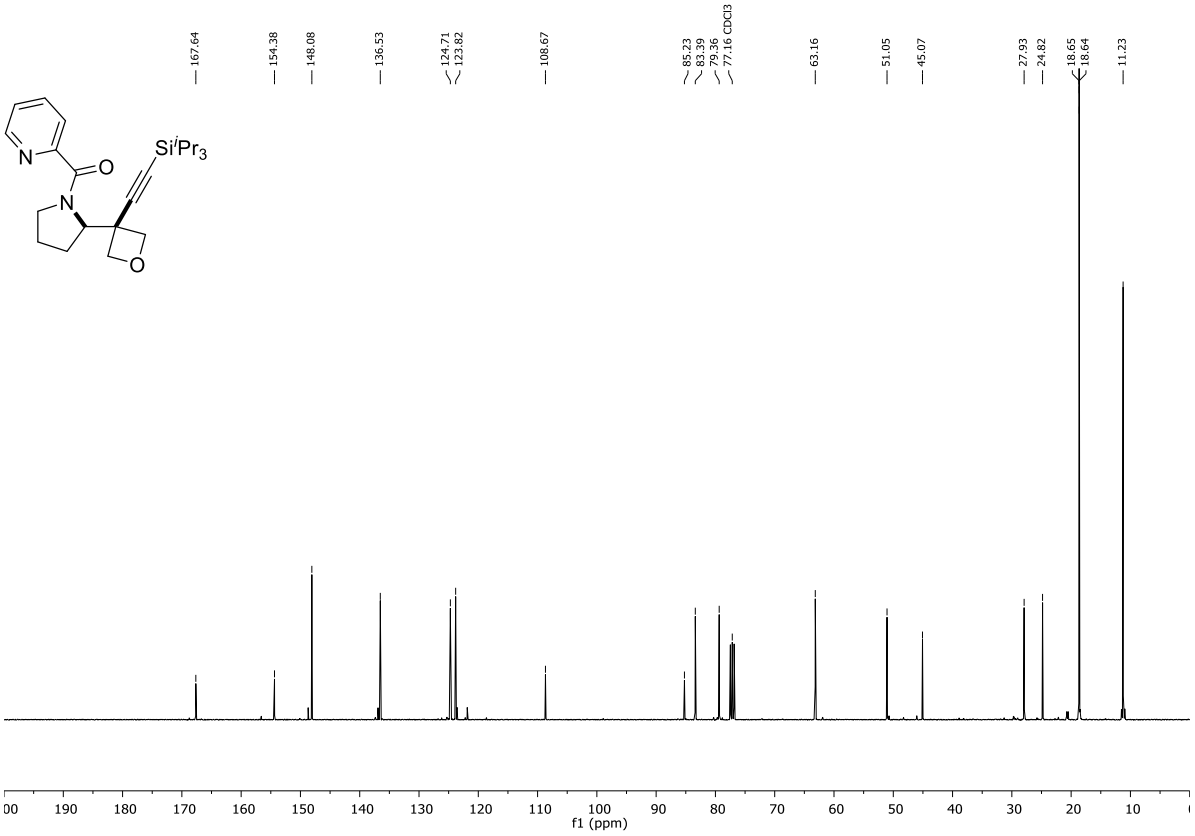
NOESY (500 MHz, $CDCl_3$, tm = 1000 ms) of **2q**



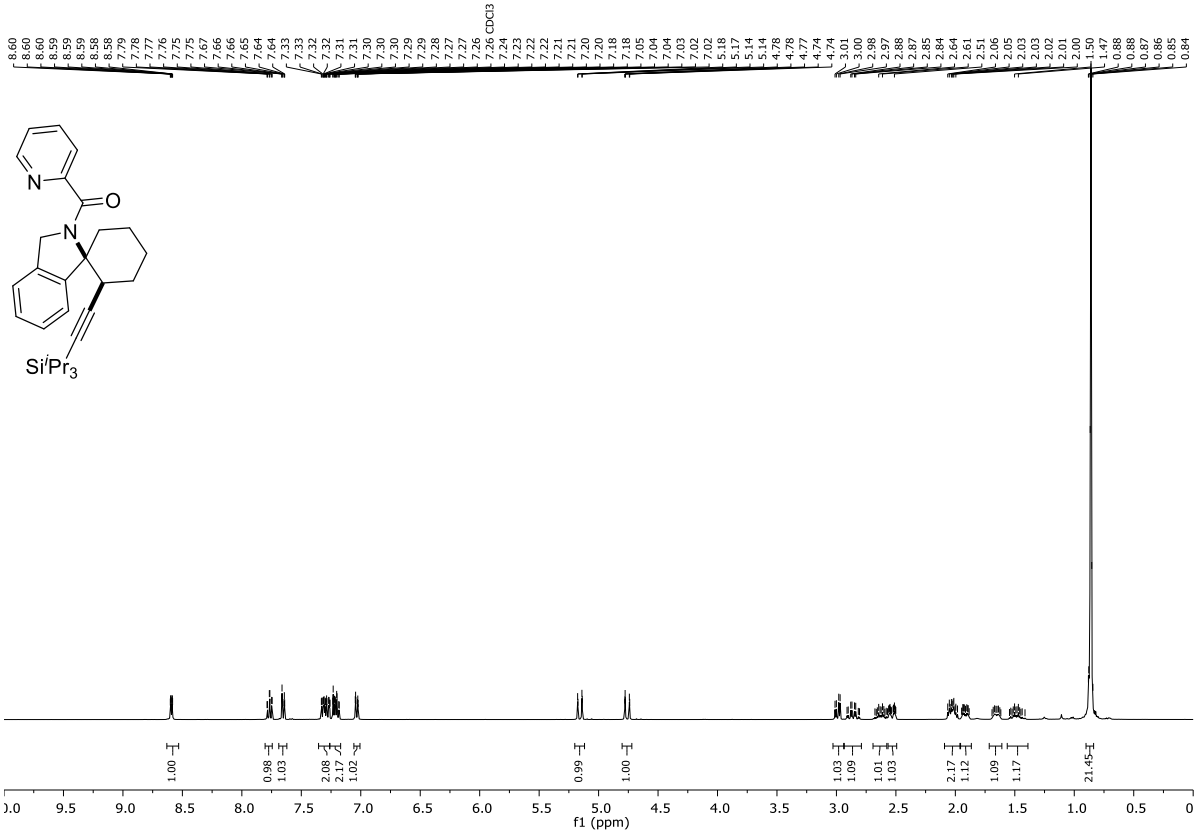
^{1}H NMR (400 MHz, $CDCl_3$) of **2r**



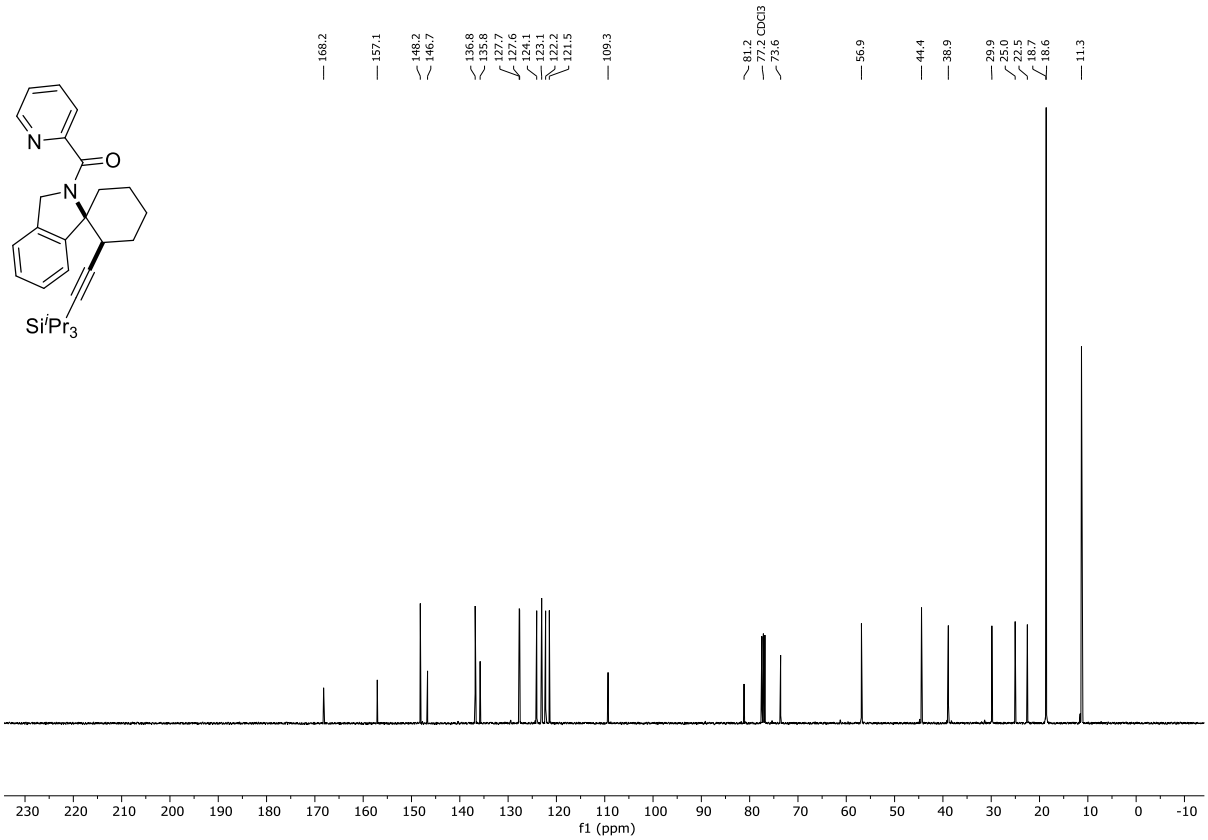
^{13}C NMR (101 MHz, $CDCl_3$) of **2r**



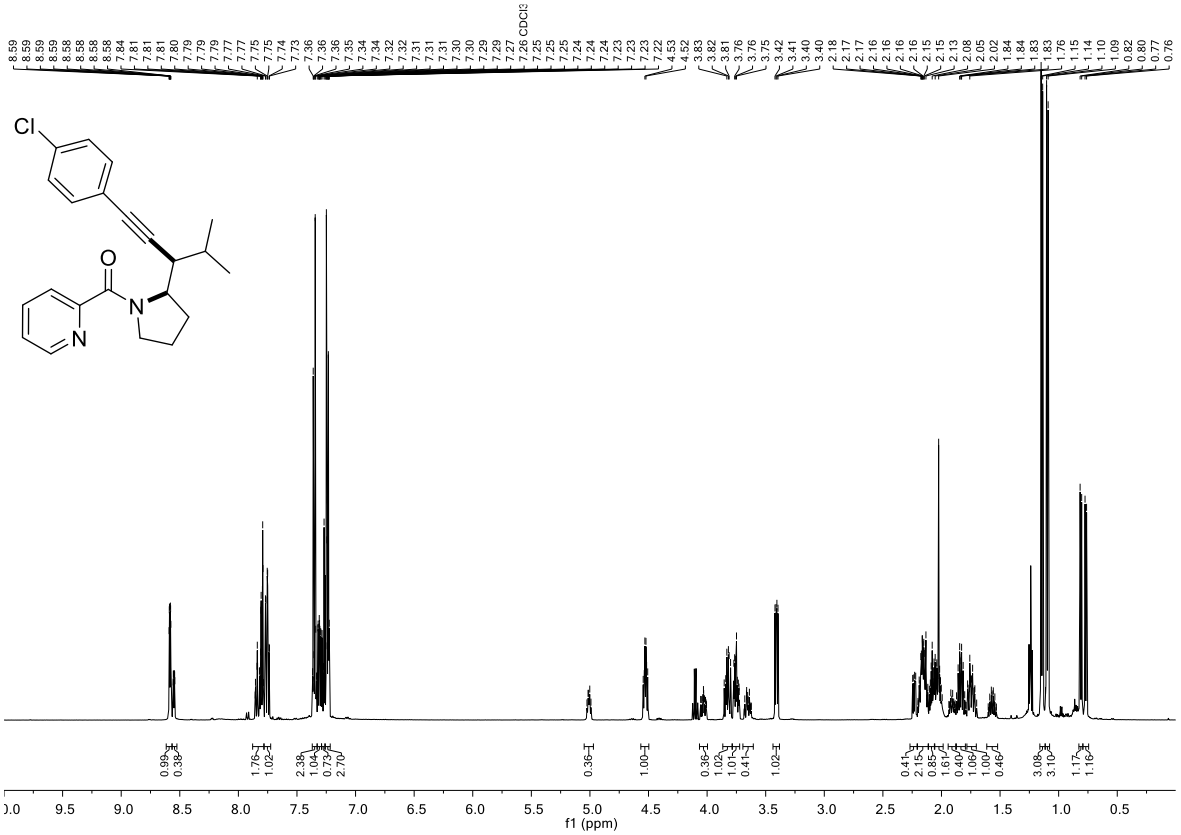
^{1}H NMR (400 MHz, $CDCl_3$) of **2s**



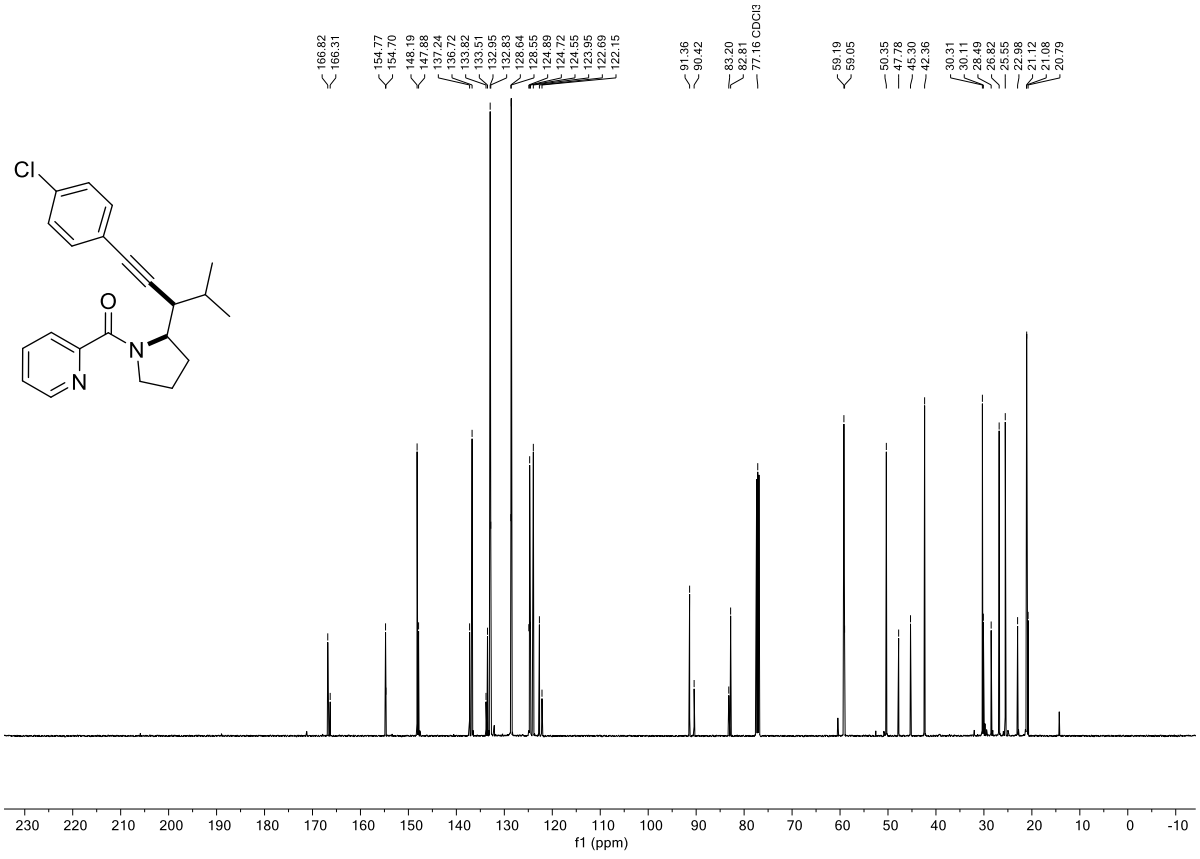
^{13}C NMR (101 MHz, $CDCl_3$) of **2s**



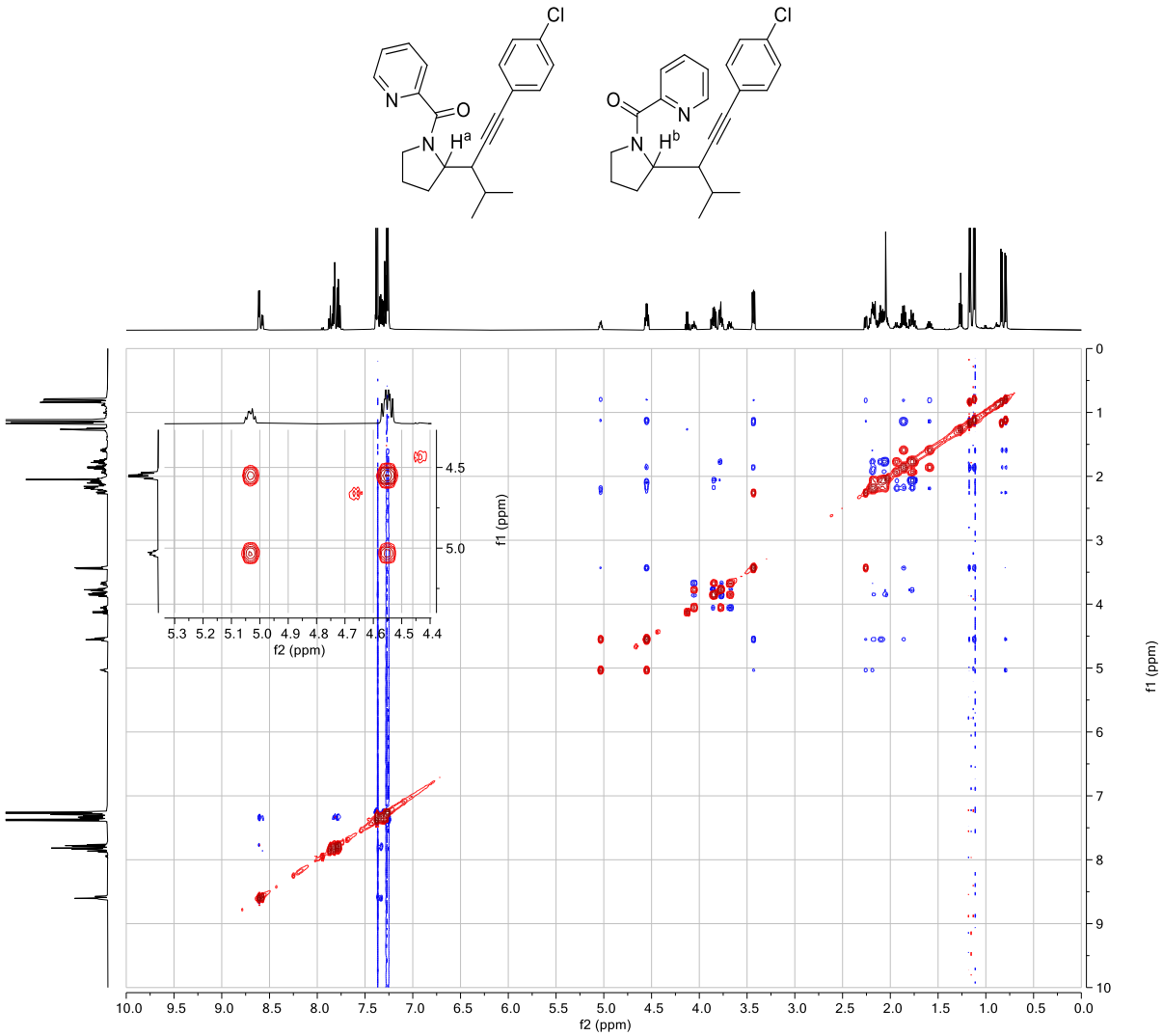
^{1}H NMR (500 MHz, $CDCl_3$) of **4**



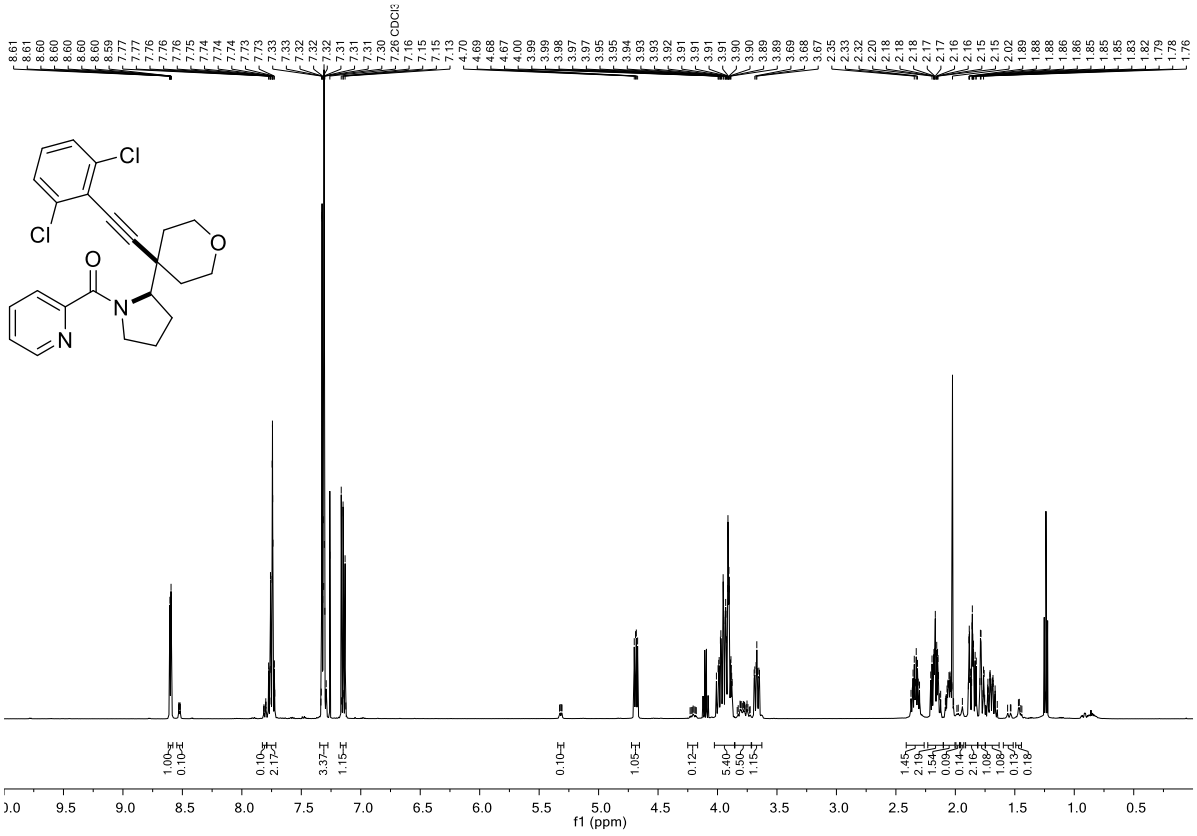
^{13}C NMR (126 MHz, $CDCl_3$) of **4**



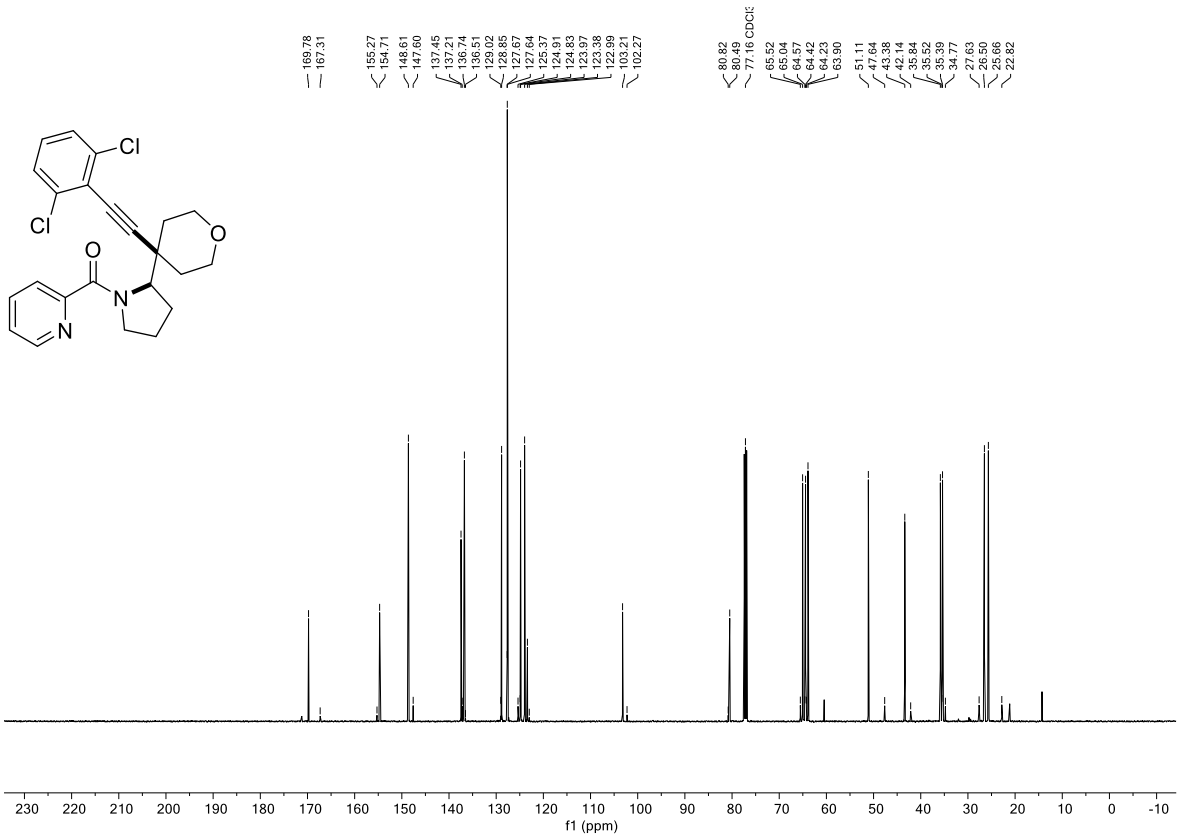
NOESY (500 MHz, $CDCl_3$, tm = 1000 ms) of **4**



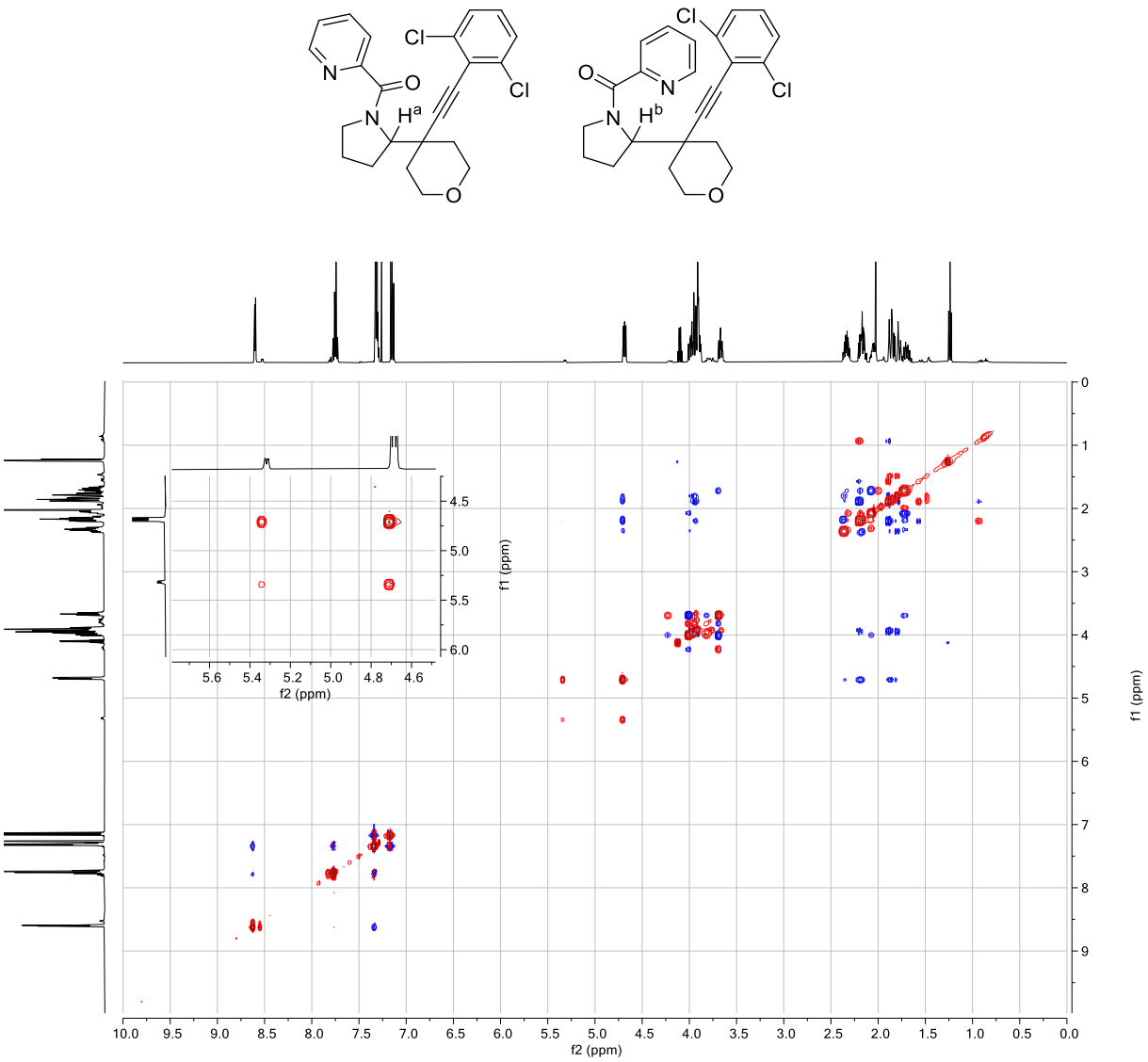
^{1}H NMR (500 MHz, $CDCl_3$) of **5**



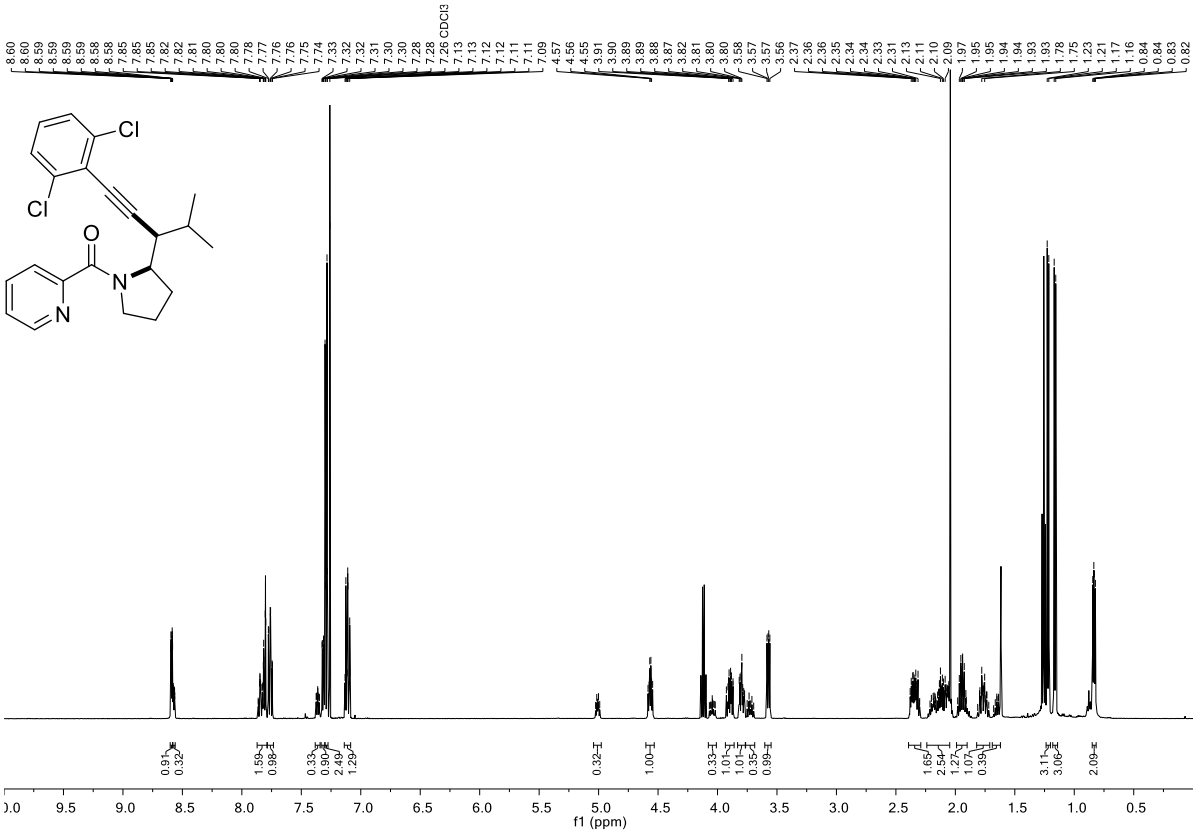
^{13}C NMR (126 MHz, $CDCl_3$) of **5**



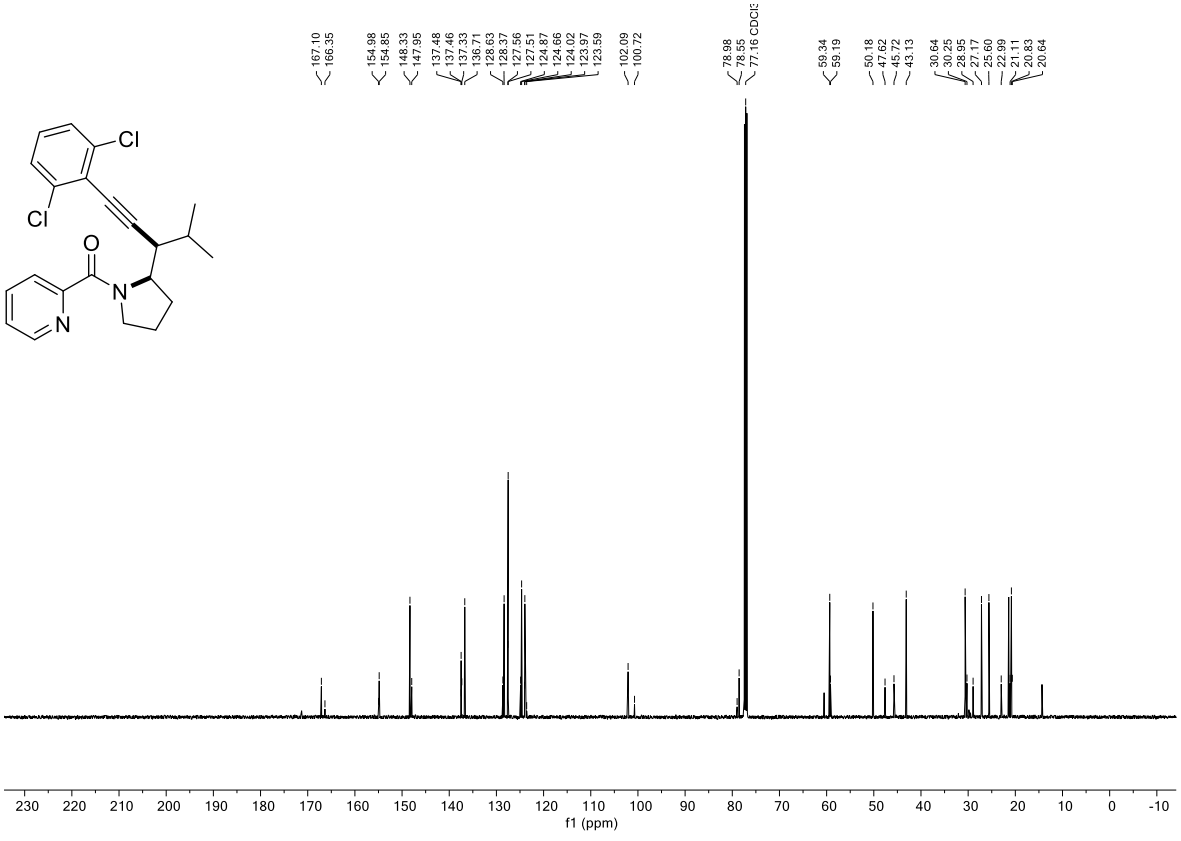
NOESY (500 MHz, $CDCl_3$, tm = 1000 ms) of **5**



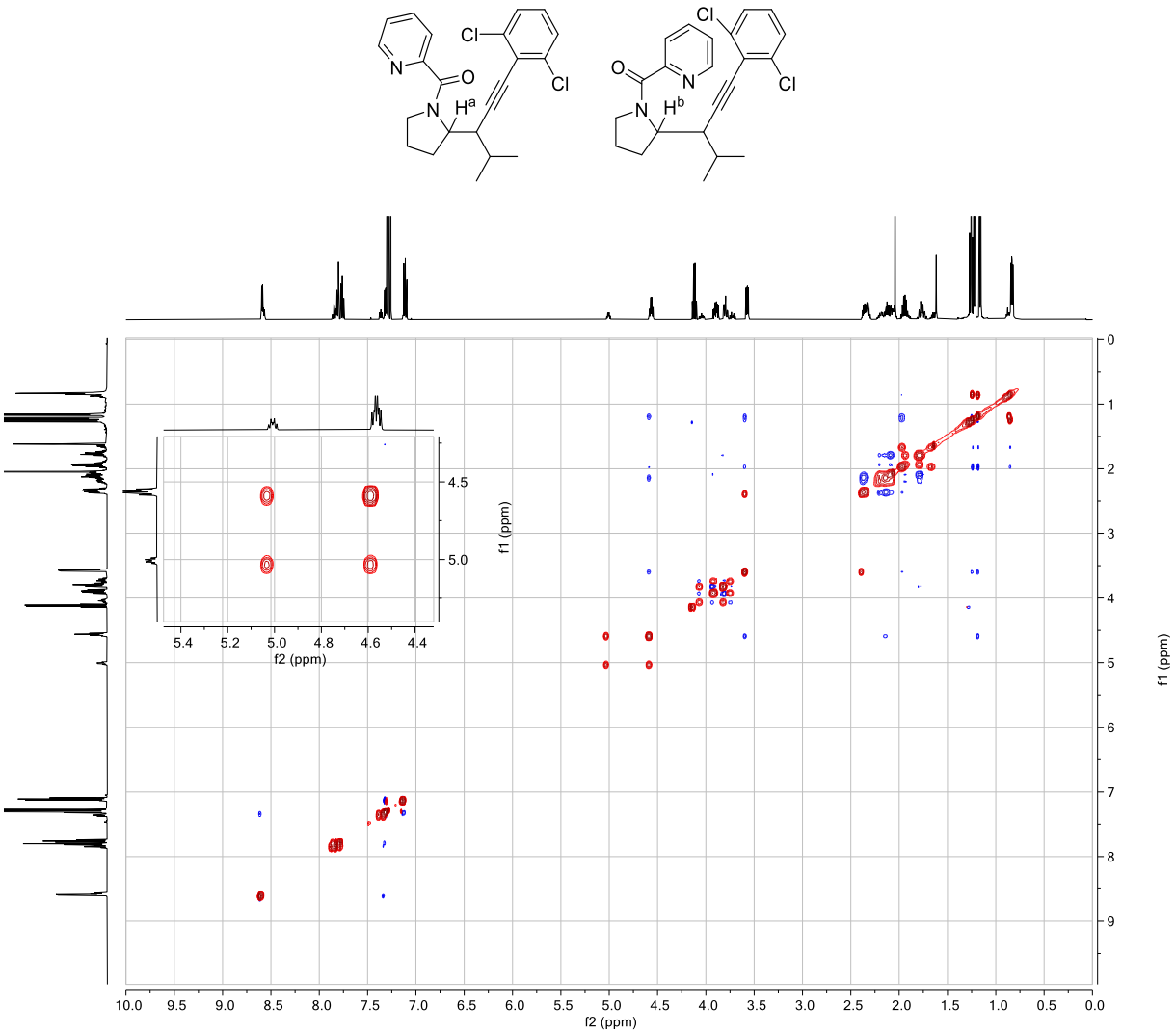
^{1}H NMR (500 MHz, $CDCl_3$) of **6**



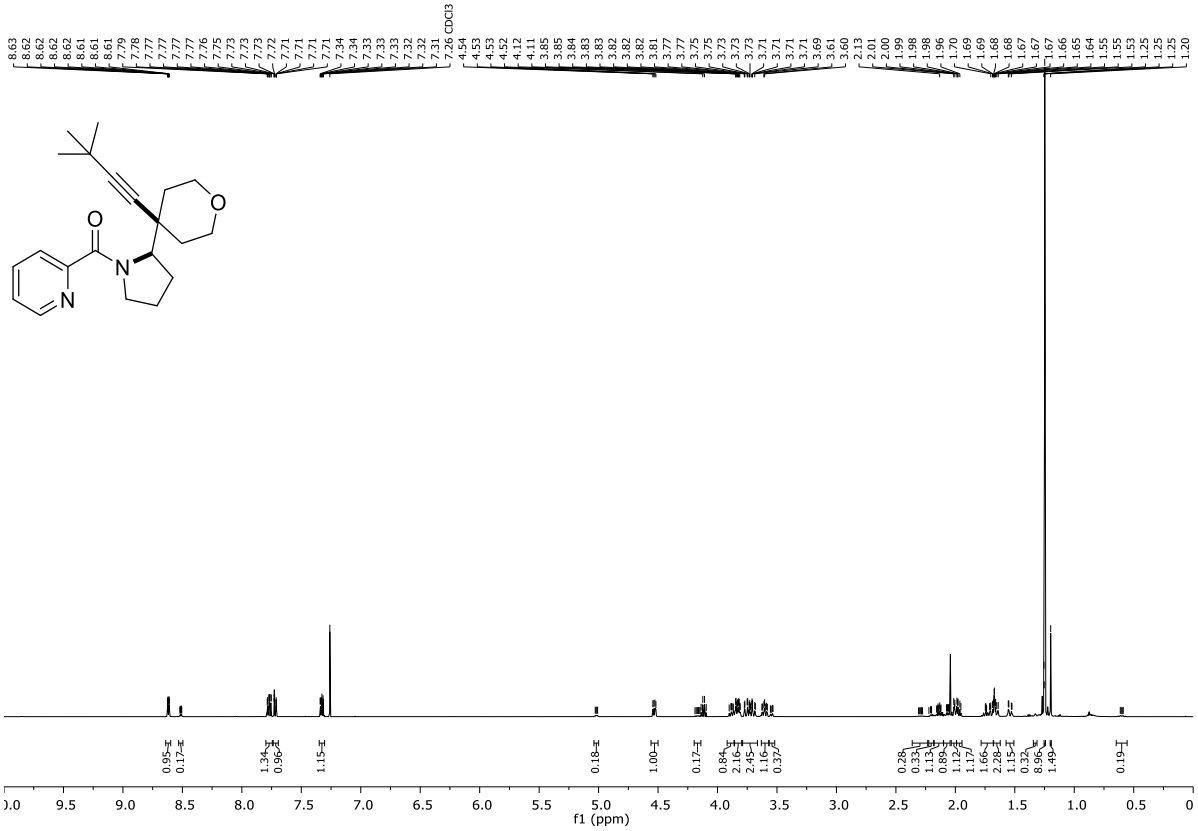
^{13}C NMR (126 MHz, $CDCl_3$) of **6**



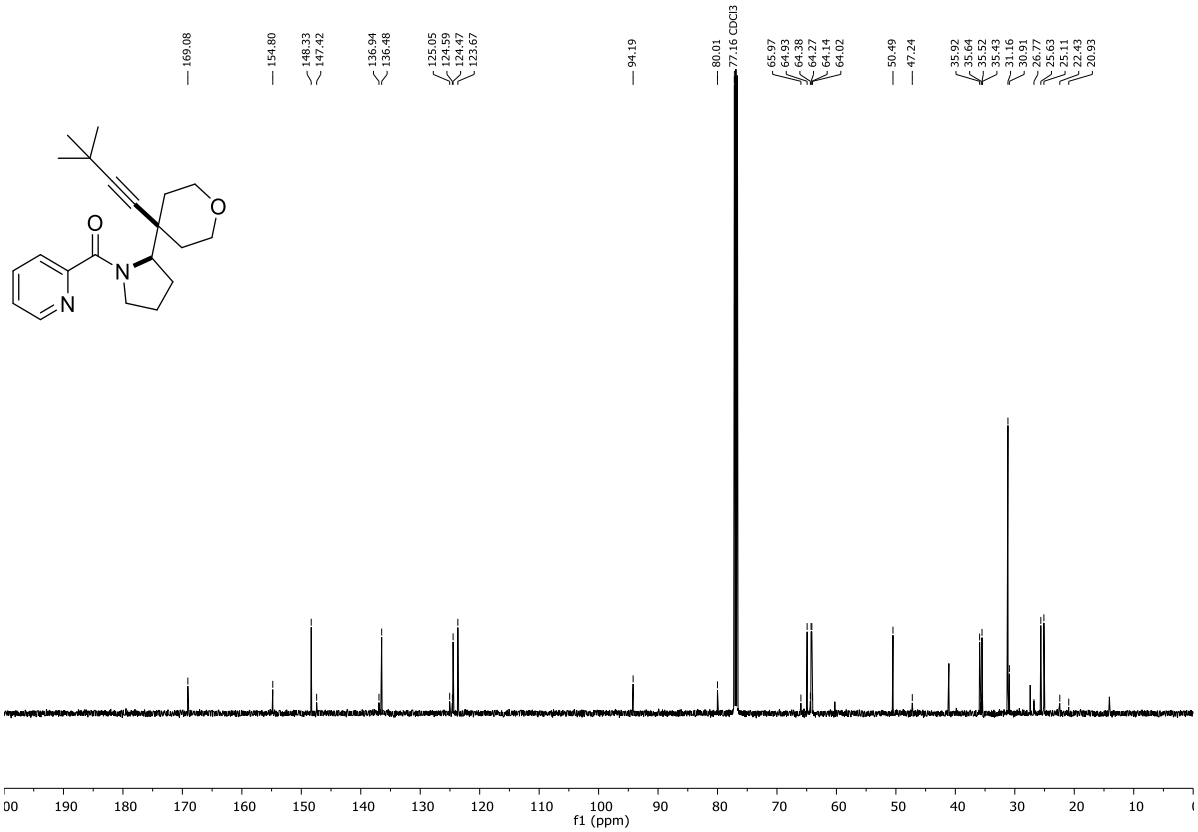
NOESY (500 MHz, $CDCl_3$, tm = 1000 ms) of **6**



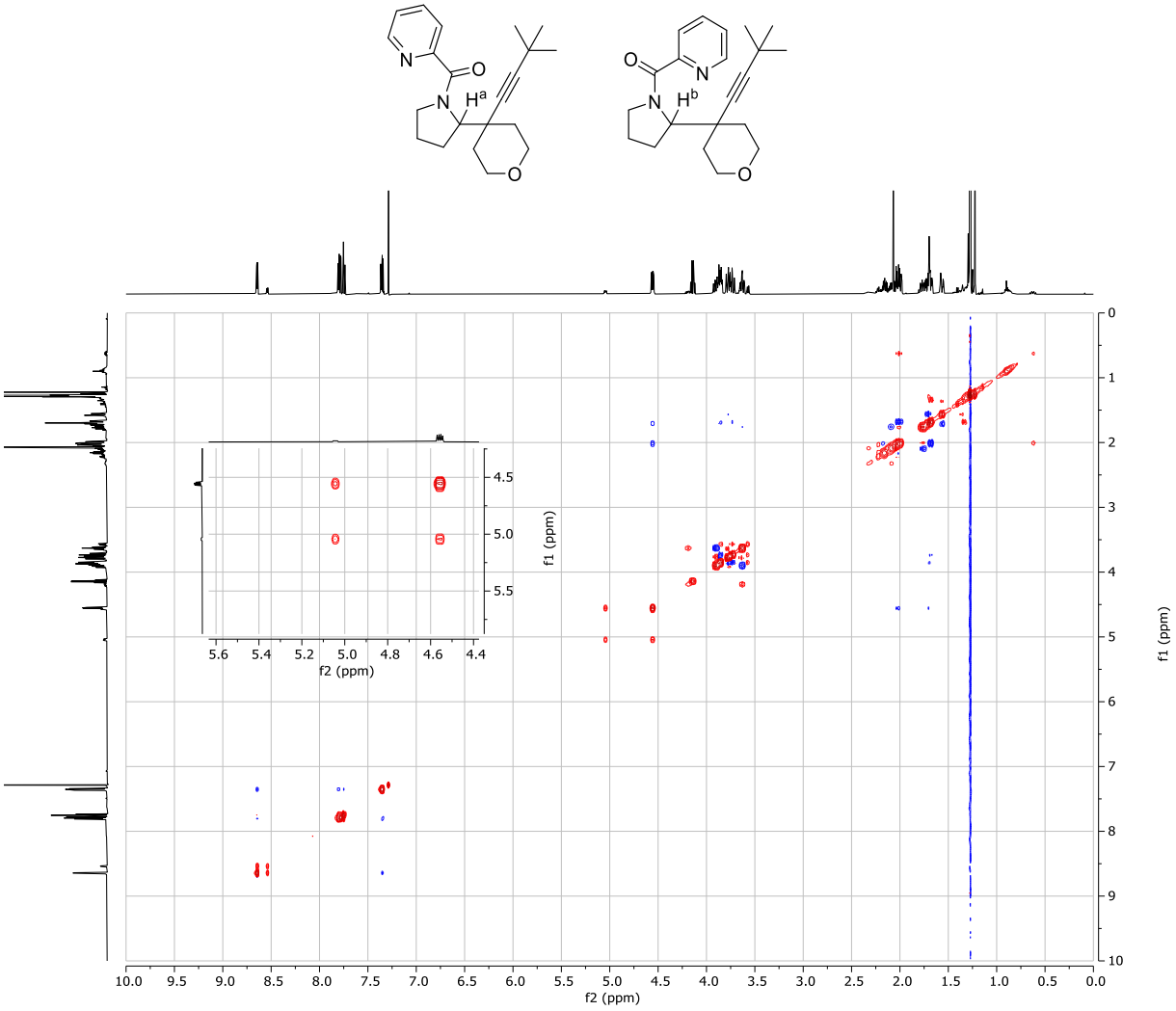
^{1}H NMR (500 MHz, $CDCl_3$) of **7**



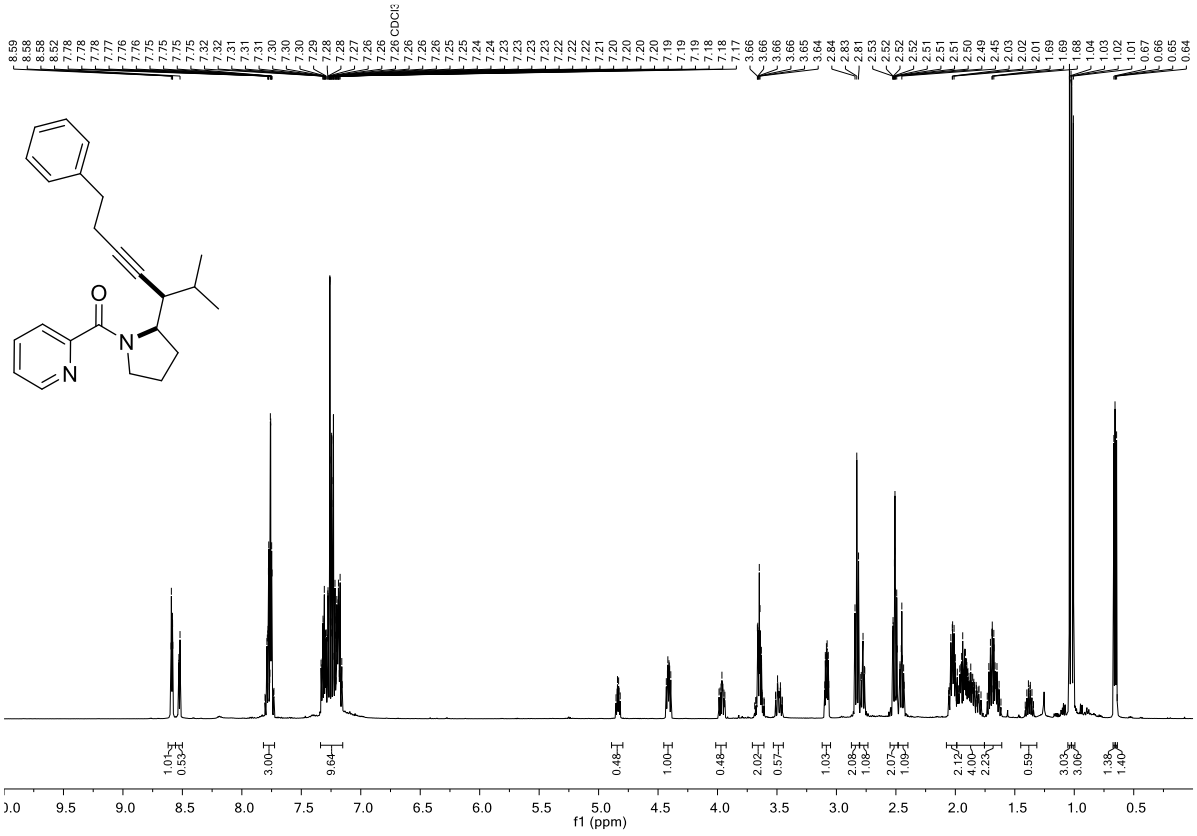
^{13}C NMR (126 MHz, $CDCl_3$) of **7**



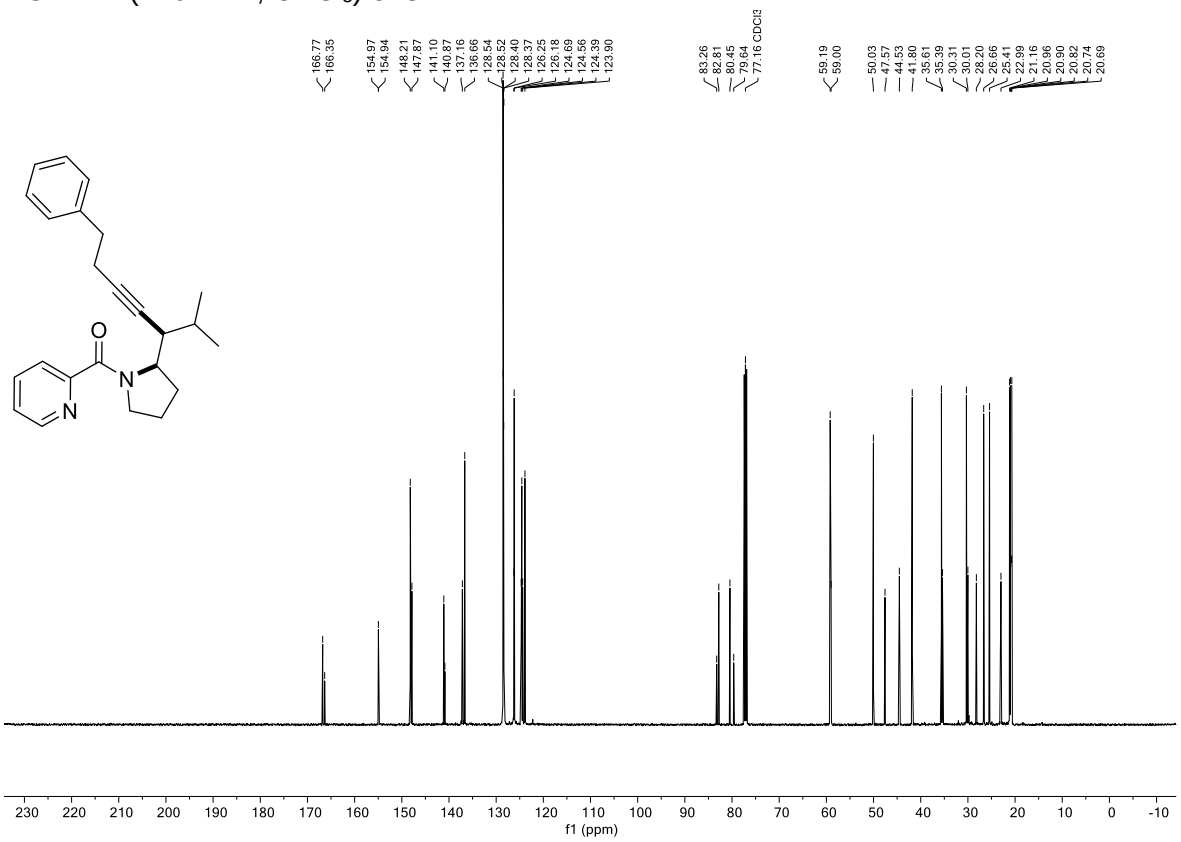
NOESY (500 MHz, $CDCl_3$, tm = 1000 ms) of **7**



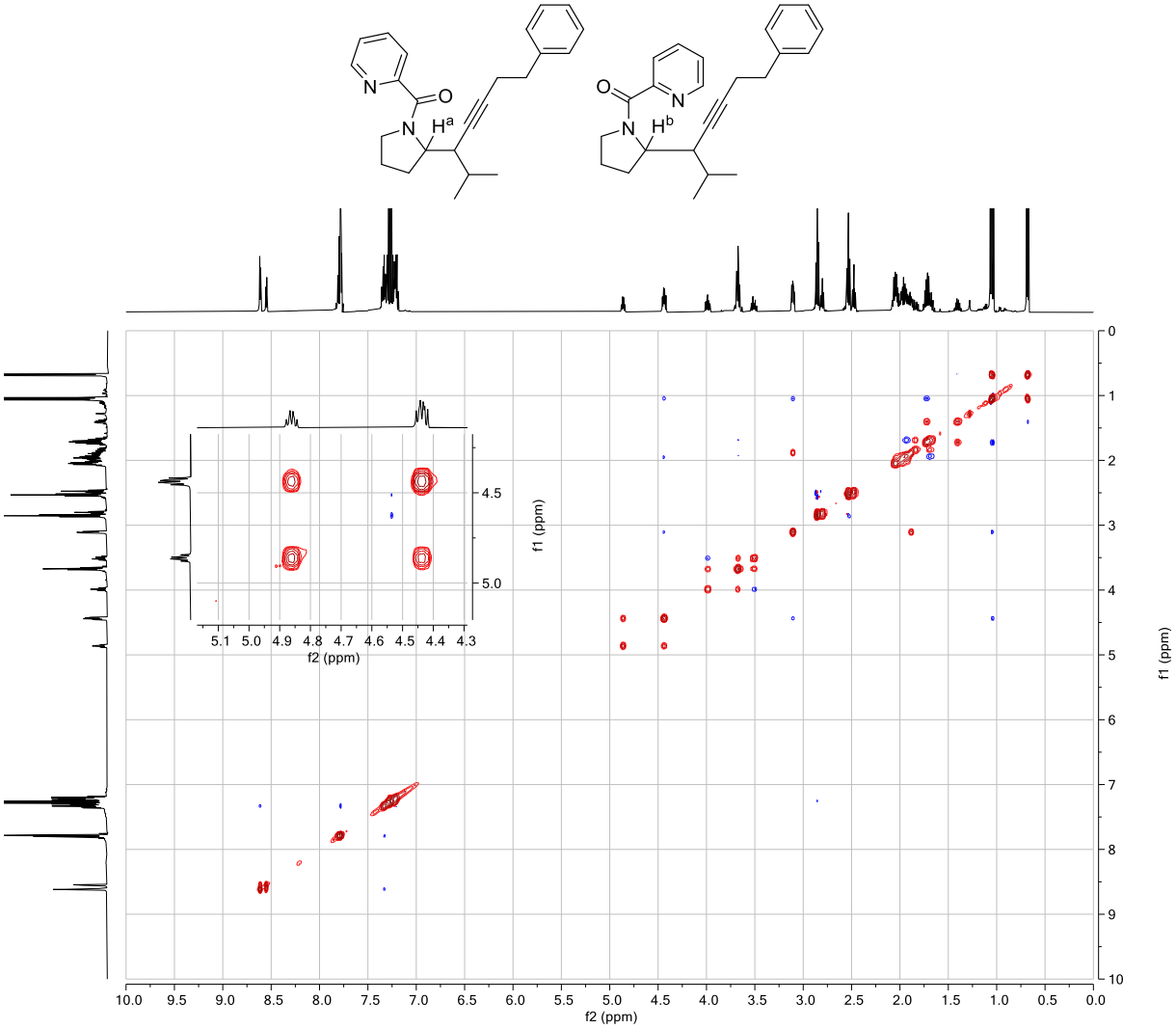
^{1}H NMR (500 MHz, $CDCl_3$) of **8**



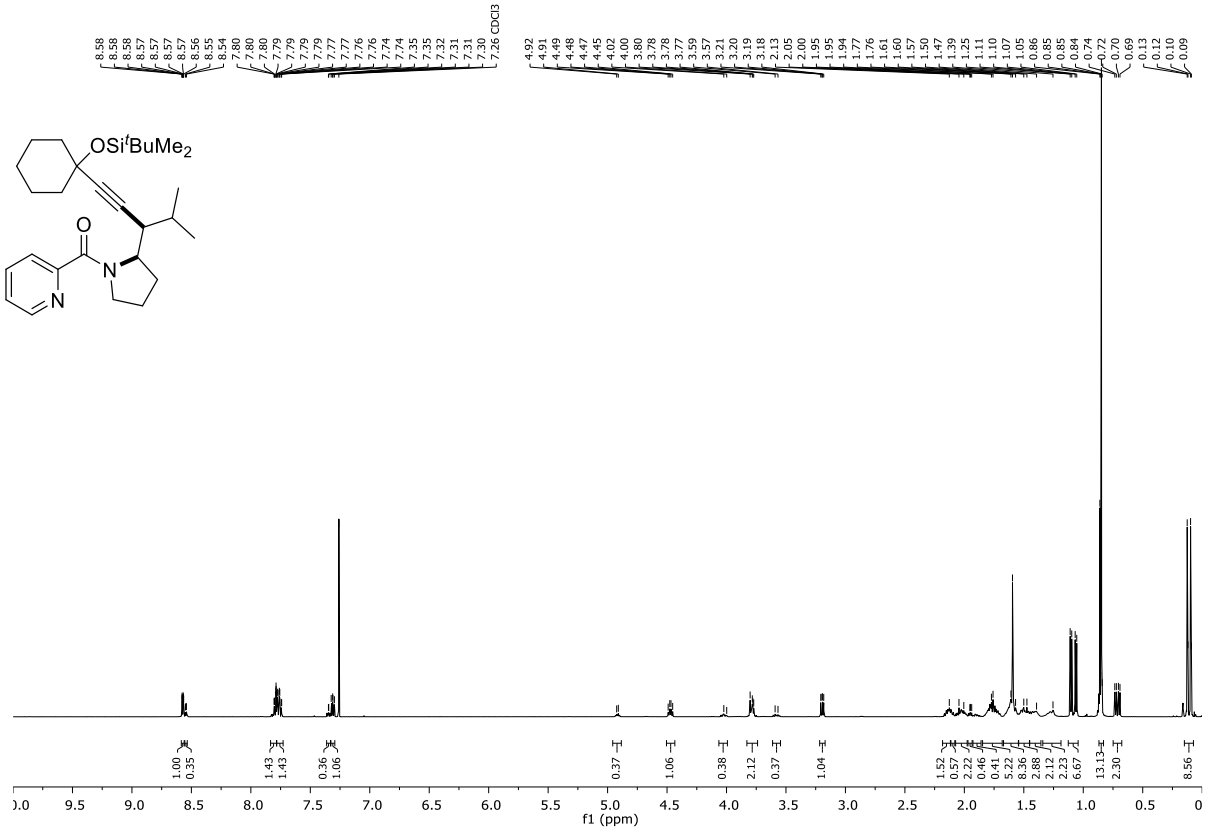
^{13}C NMR (126 MHz, $CDCl_3$) of **8**



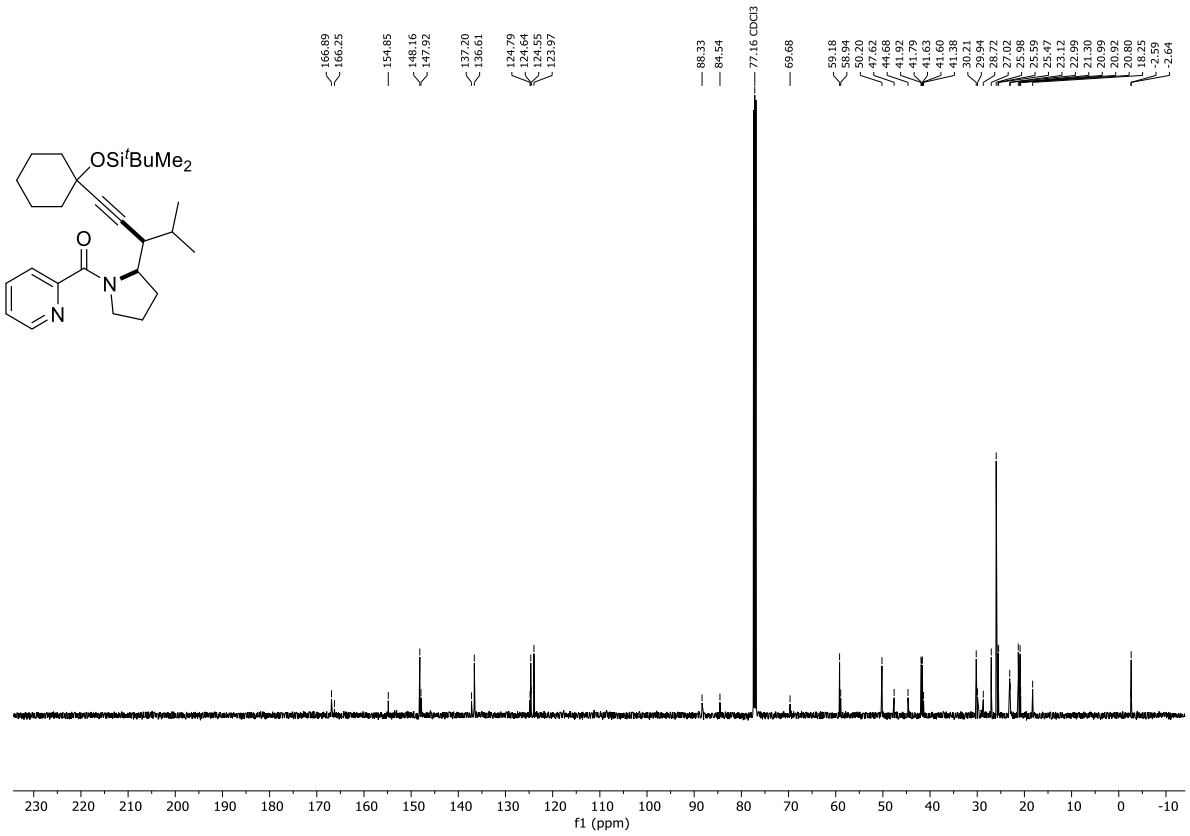
NOESY (500 MHz, $CDCl_3$, tm = 1000 ms) of **8**



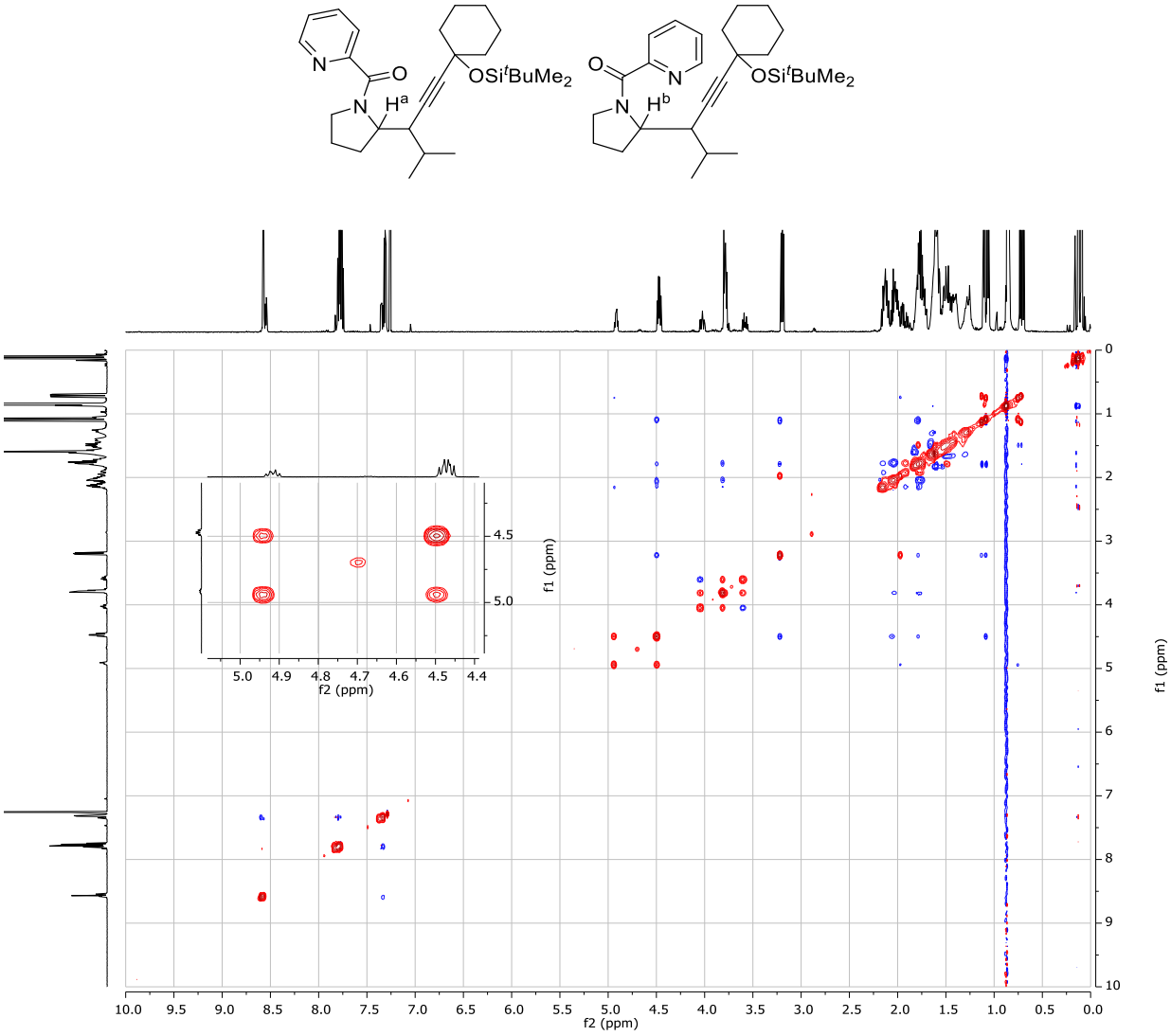
^{1}H NMR (500 MHz, $CDCl_3$) of **9**



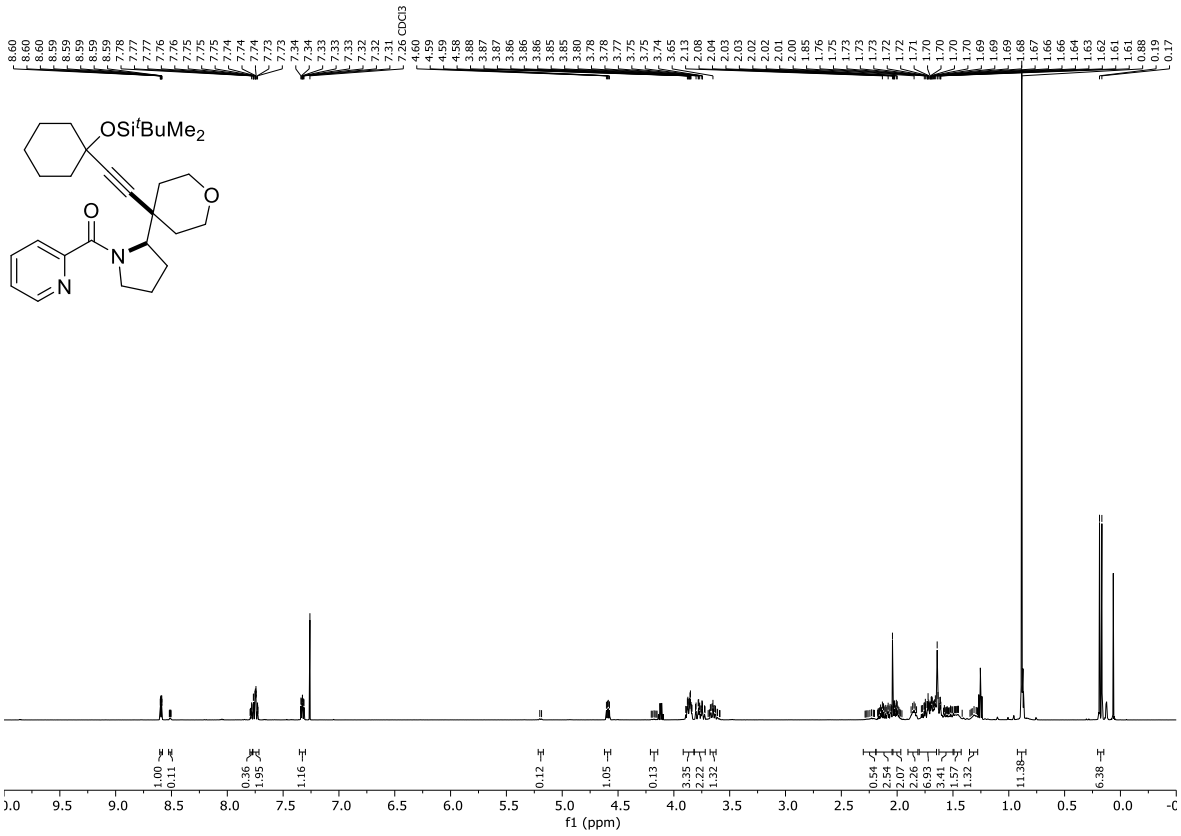
^{13}C NMR (126 MHz, $CDCl_3$) of **9**



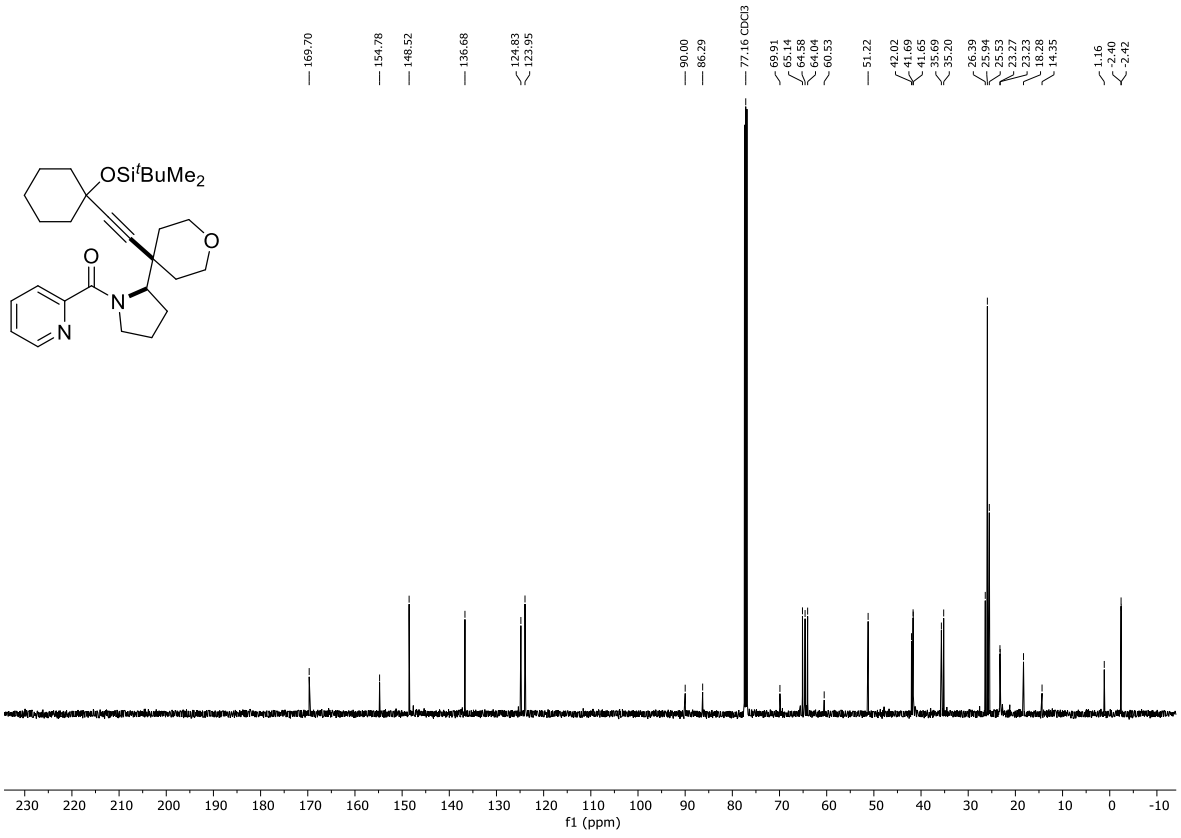
(500 MHz, $CDCl_3$, tm = 1000 ms) of **9**



^{1}H NMR (500 MHz, $CDCl_3$) of **10**

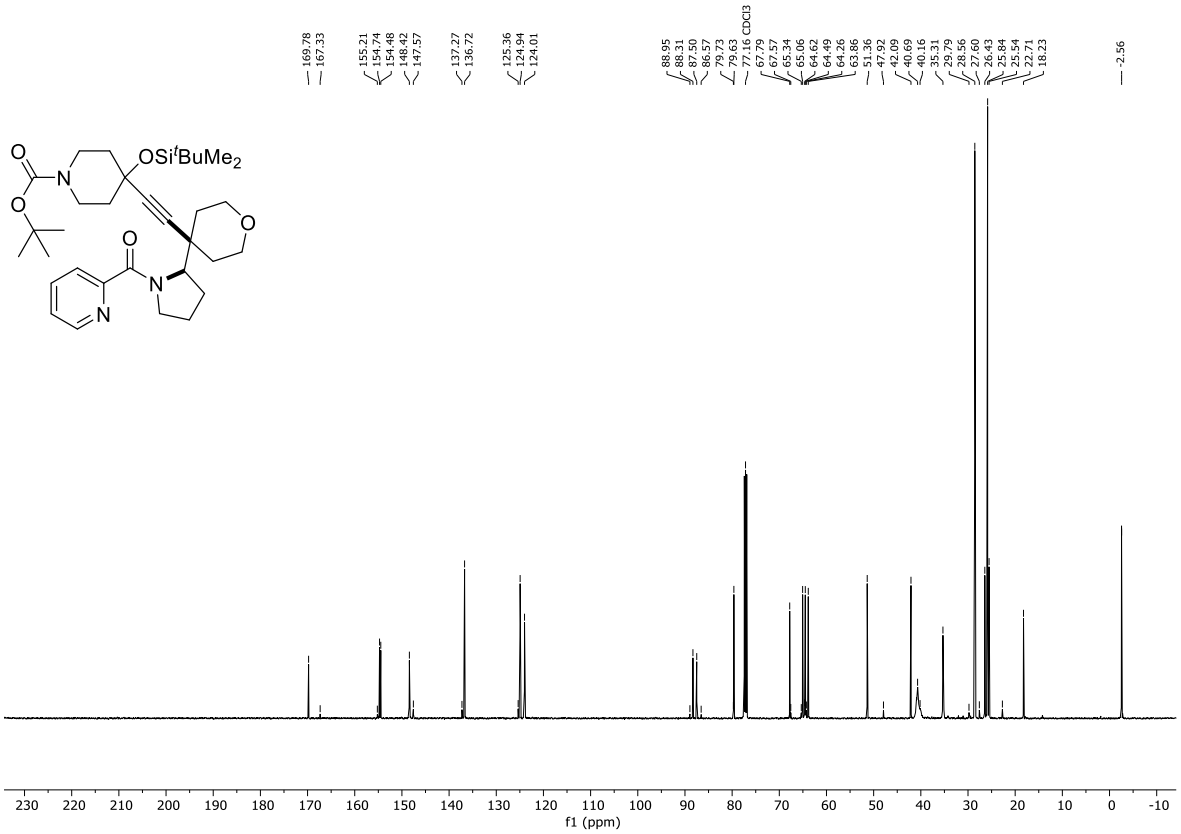


^{13}C NMR (126 MHz, $CDCl_3$) of **10**

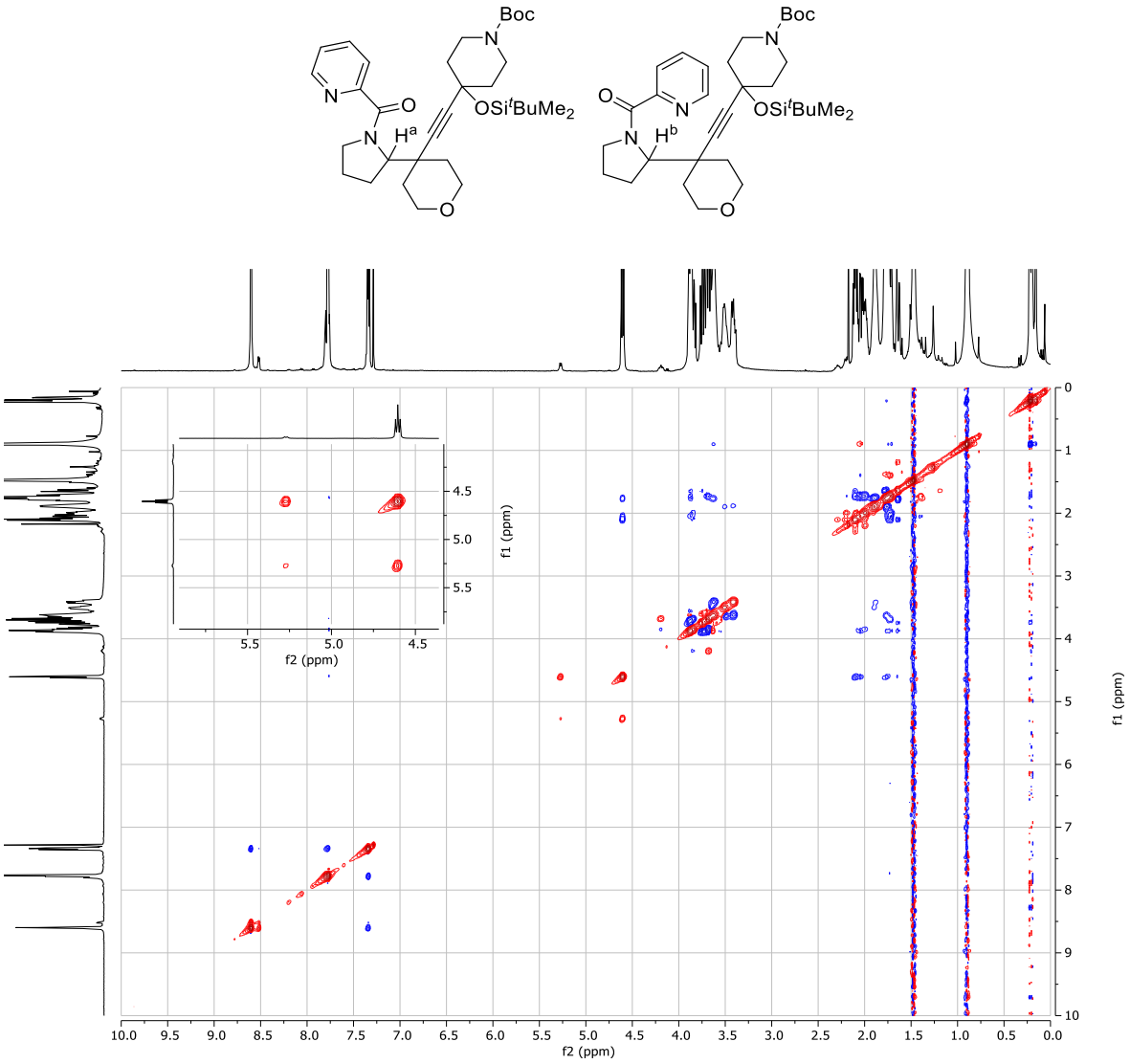


^{1}H NMR (500 MHz, $CDCl_3$) of **11**

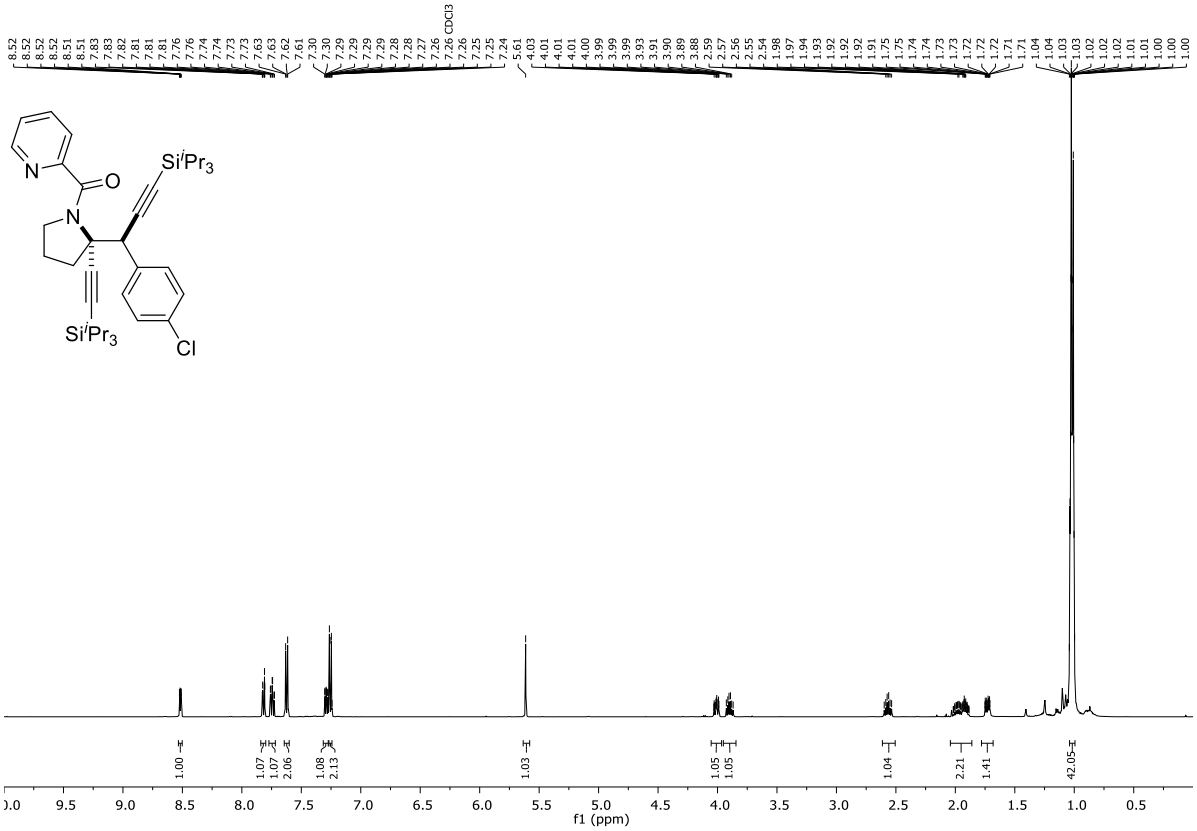
^{13}C NMR (126 MHz, $CDCl_3$) of **11**



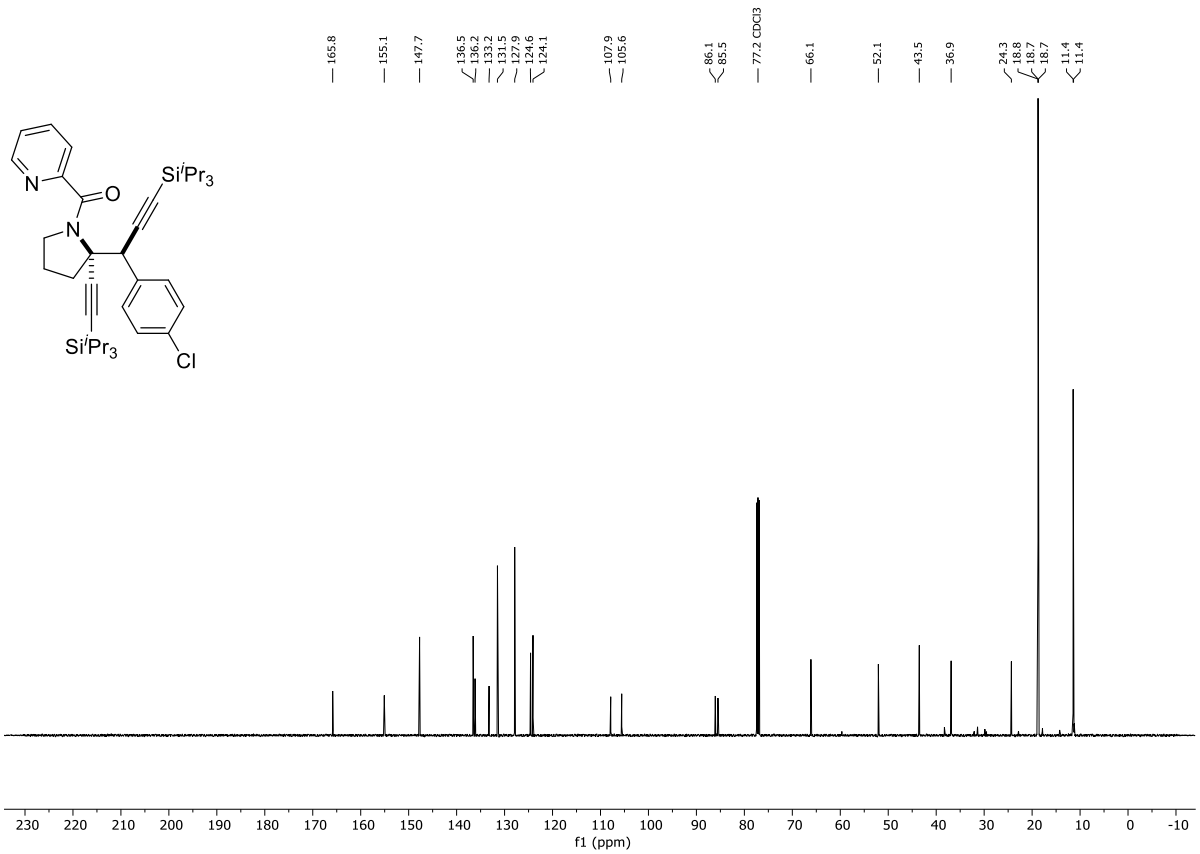
NOESY (500 MHz, $CDCl_3$, tm = 1000 ms) of **11**



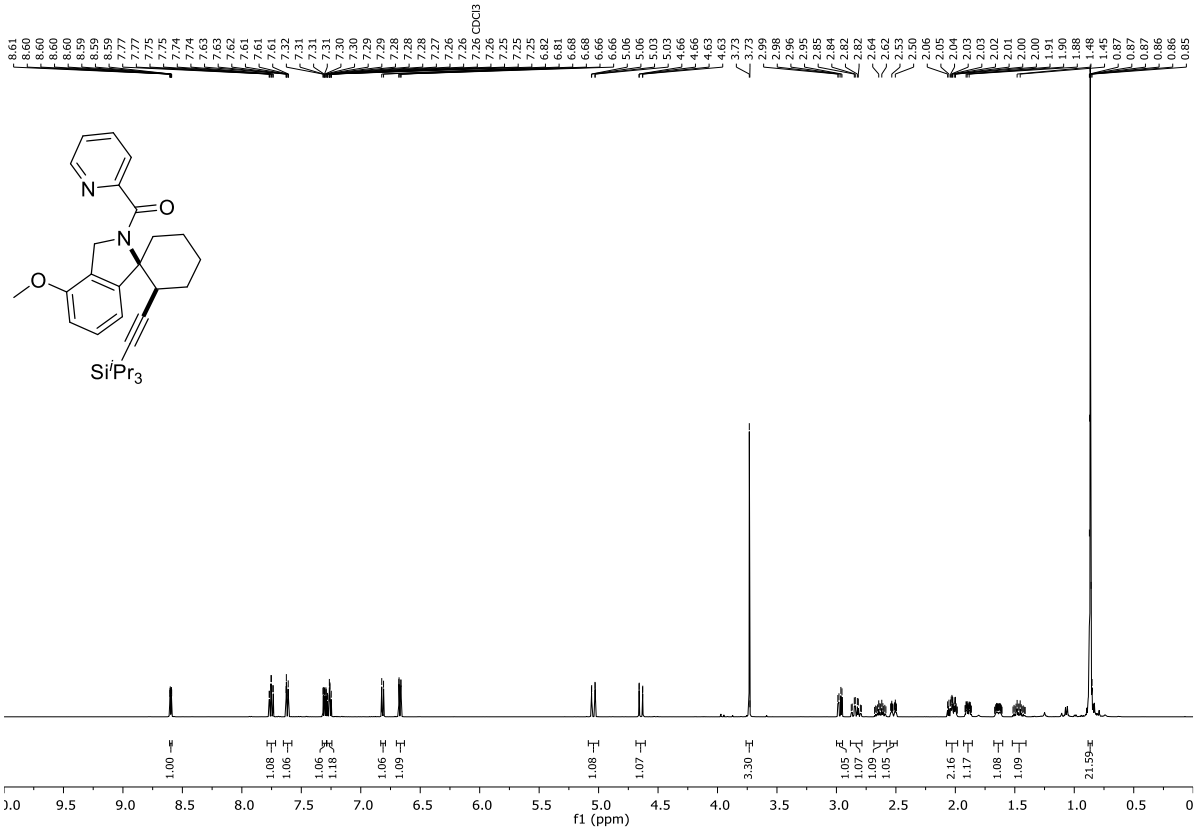
^{1}H NMR (500 MHz, $CDCl_3$) of **13**



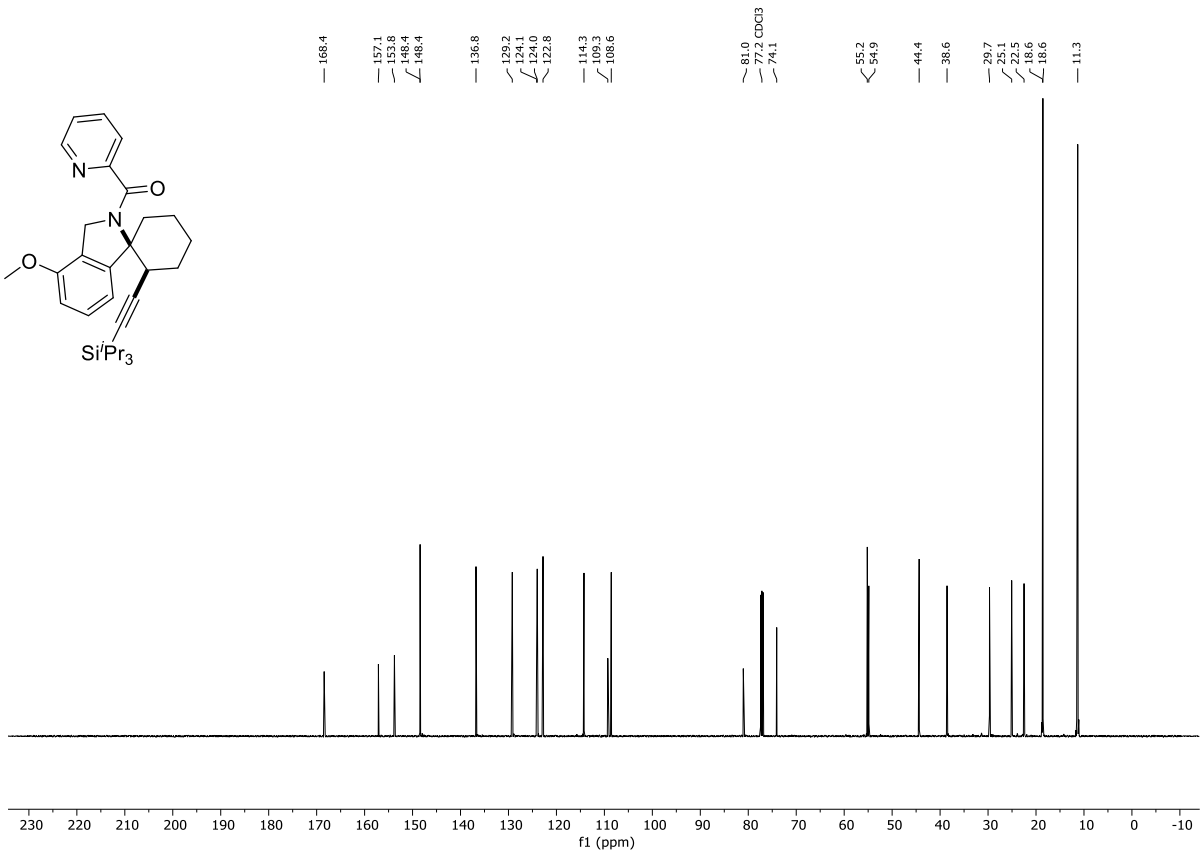
^{13}C NMR (126 MHz, $CDCl_3$) of **13**



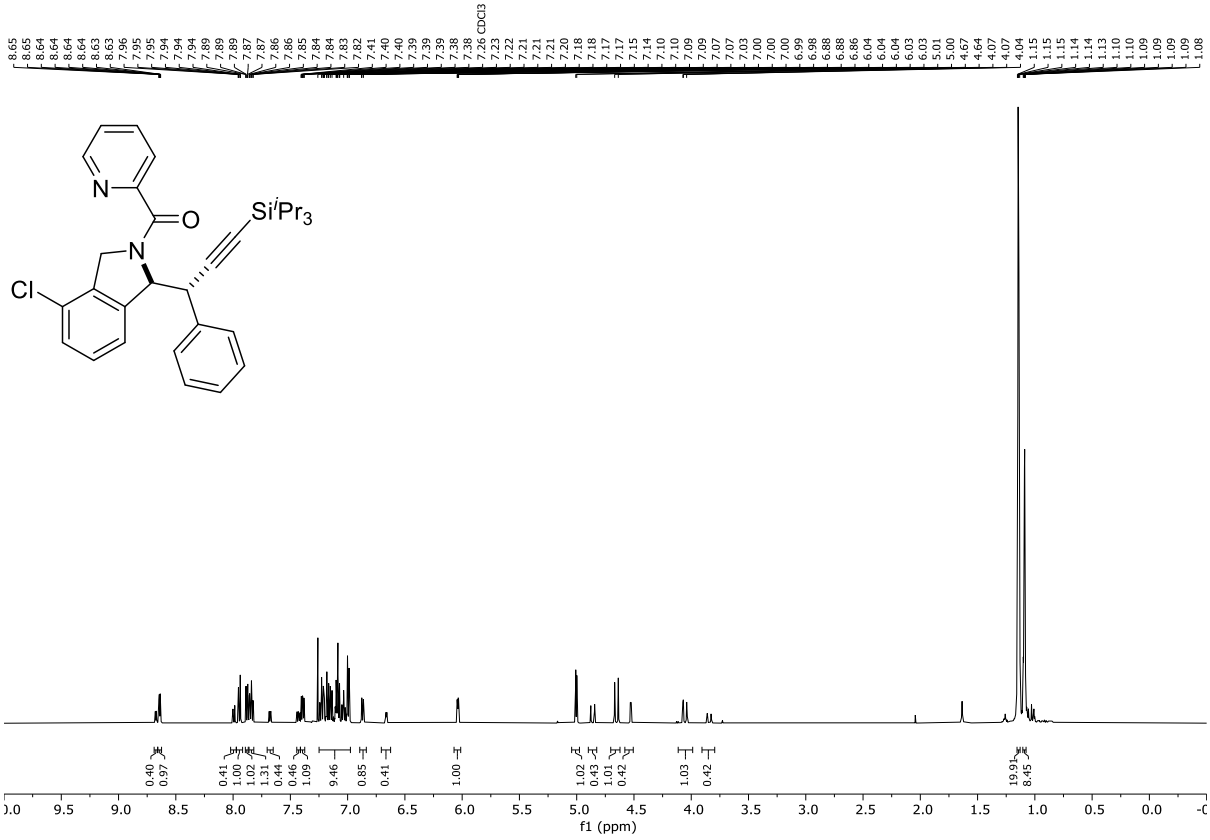
^{1}H NMR (500 MHz, $CDCl_3$) of **16**



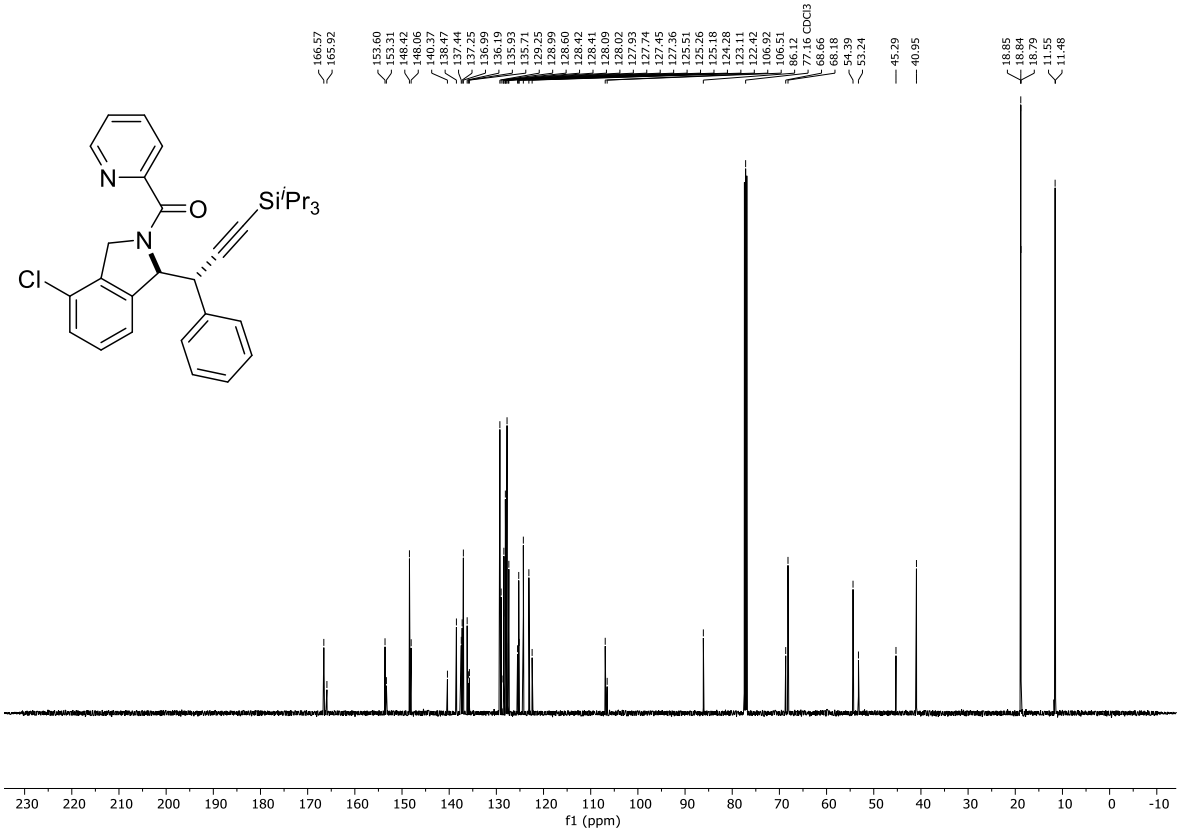
^{13}C NMR (126 MHz, $CDCl_3$) of **16**



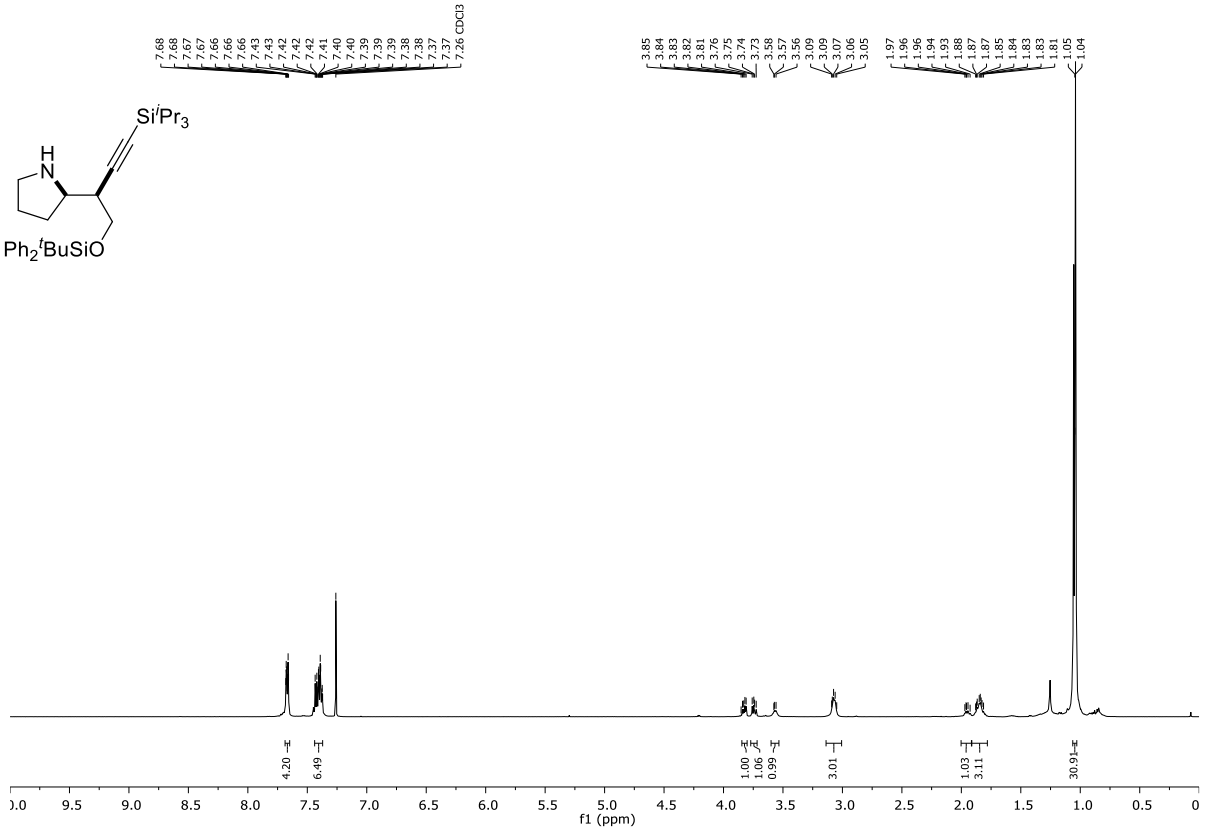
^{1}H NMR (500 MHz, $CDCl_3$) of **19**



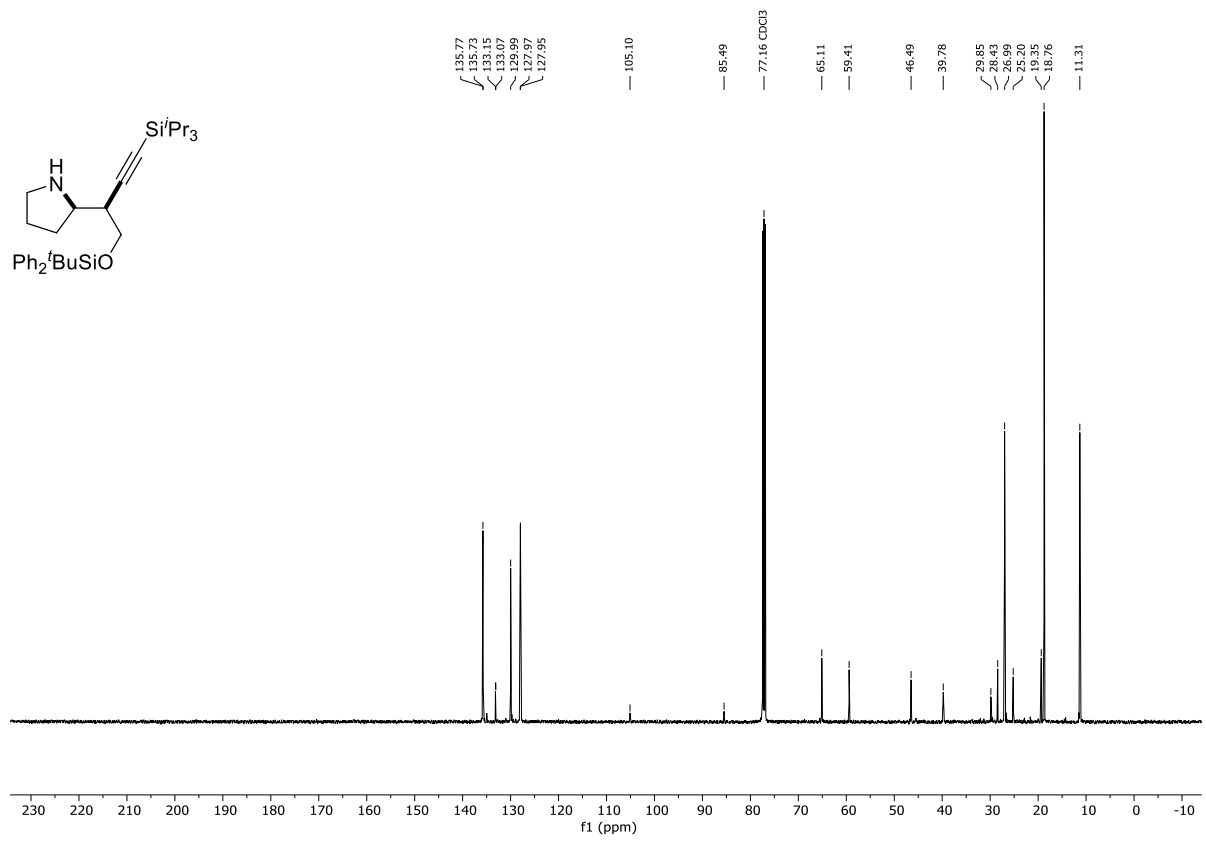
^{13}C NMR (126 MHz, $CDCl_3$) of **19**



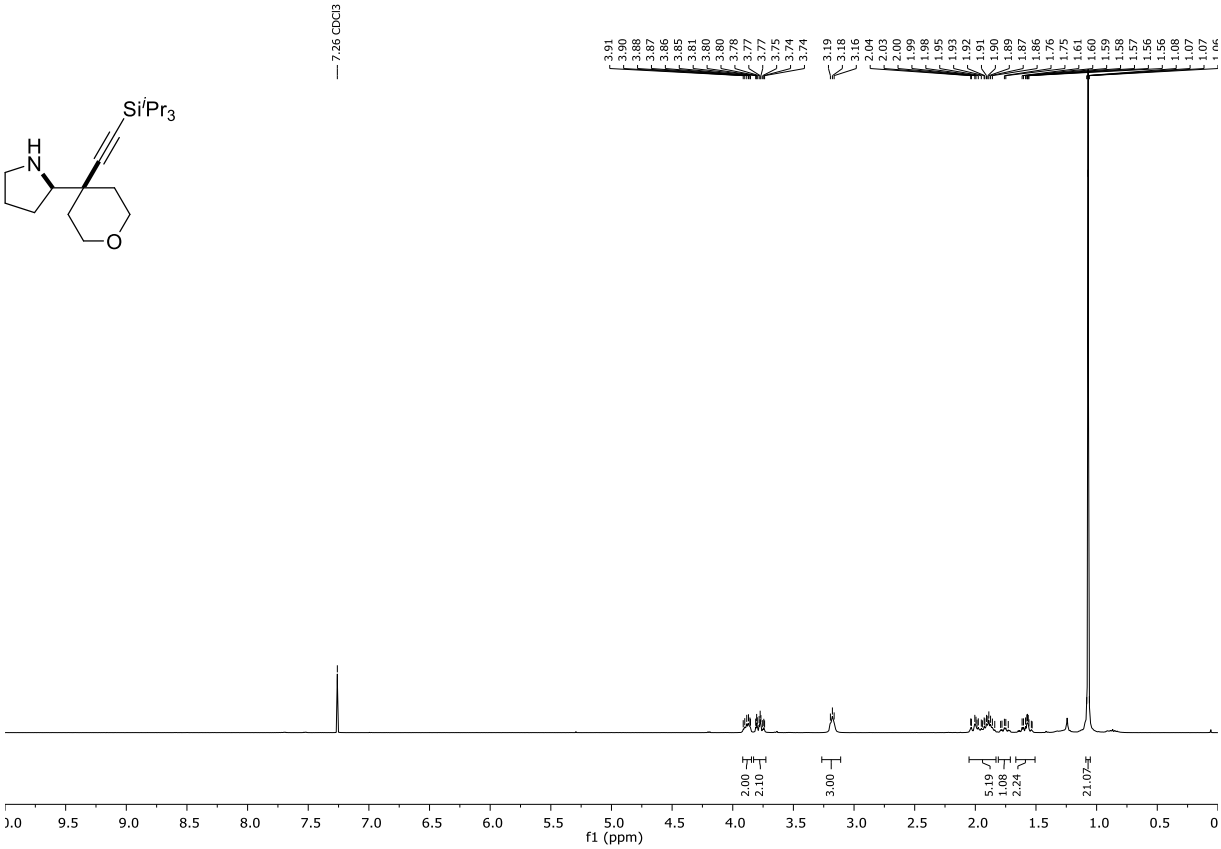
^{1}H NMR (500 MHz, $CDCl_3$) of **20**



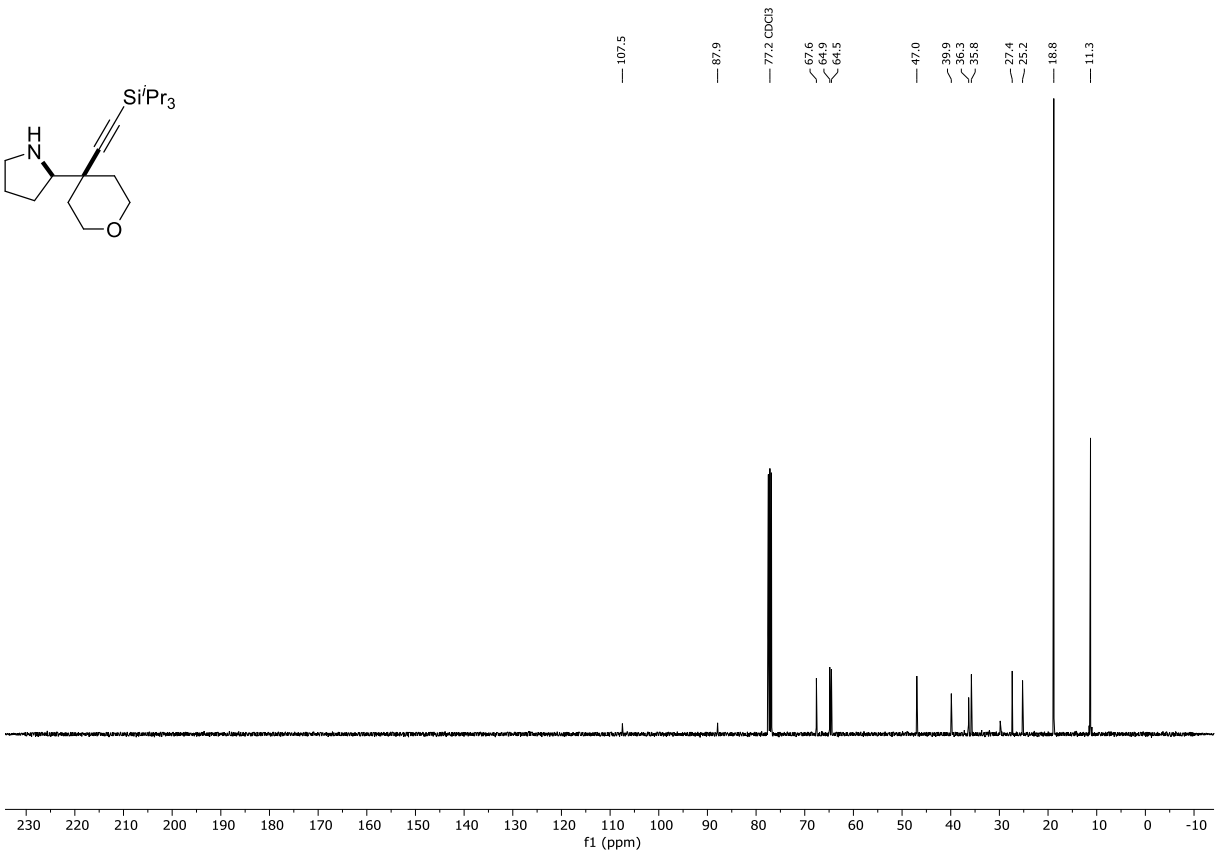
^{13}C NMR (126 MHz, $CDCl_3$) of **20**



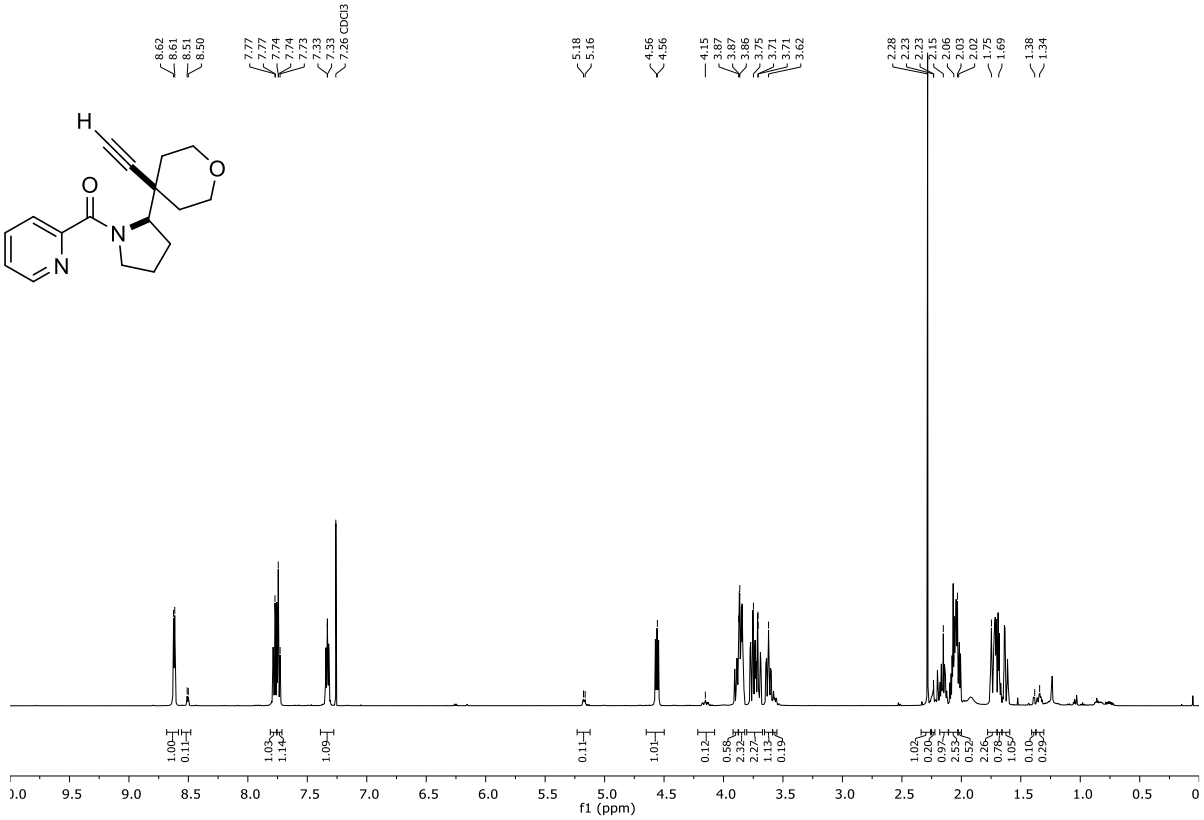
^{1}H NMR (400 MHz, $CDCl_3$) of **21**



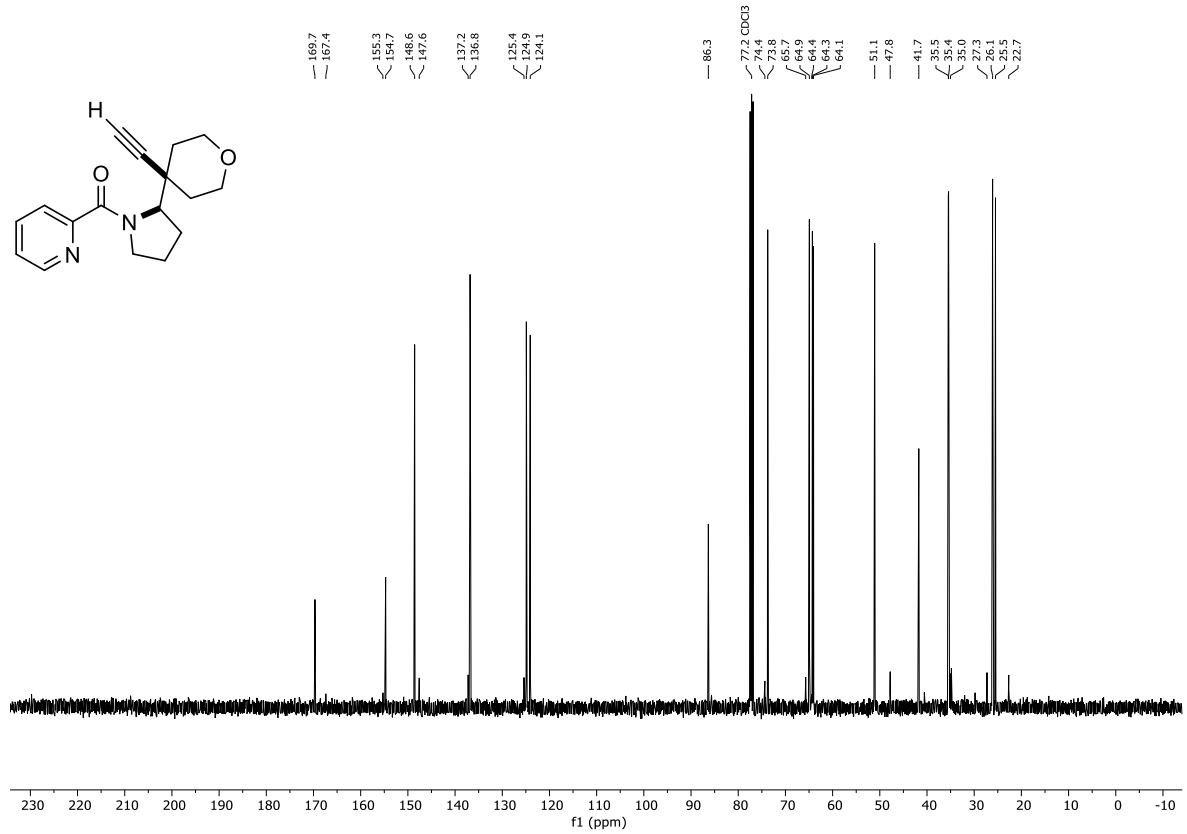
^{13}C NMR (101 MHz, $CDCl_3$) of **21**



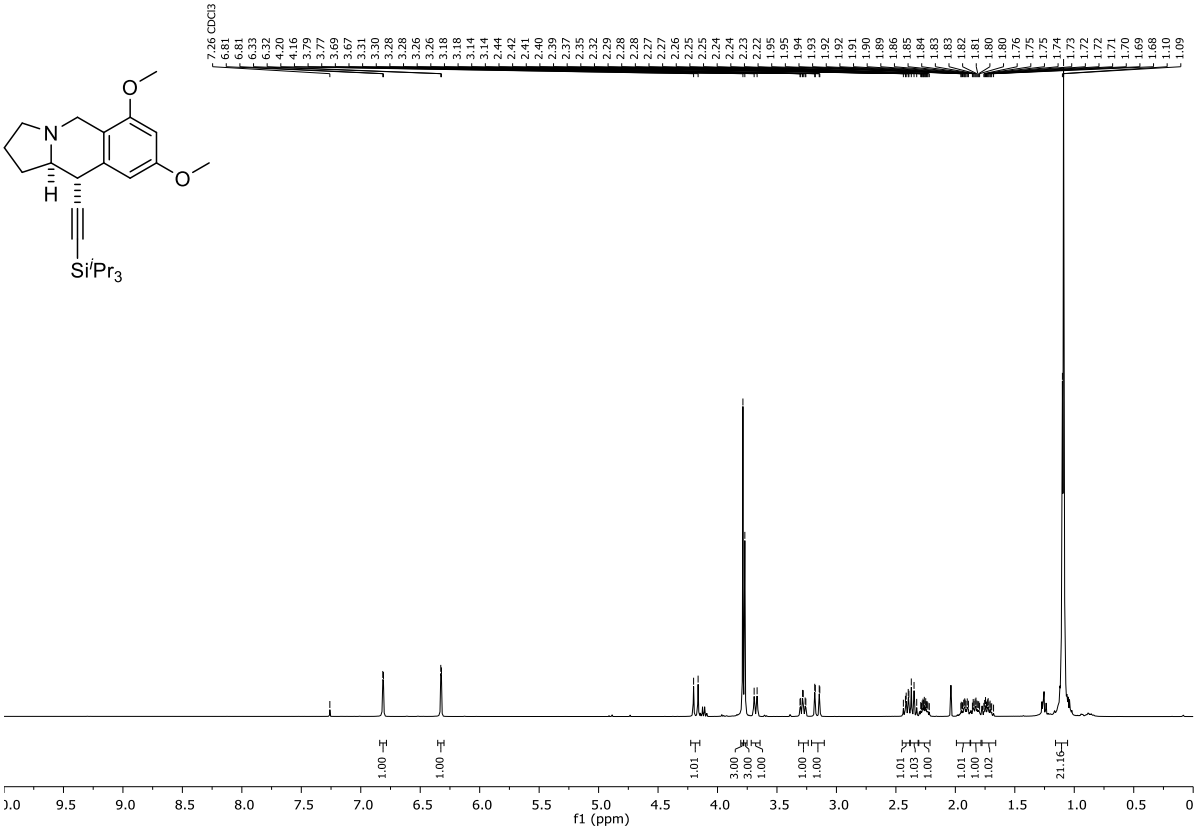
^{1}H NMR (500 MHz, $CDCl_3$) of **22**



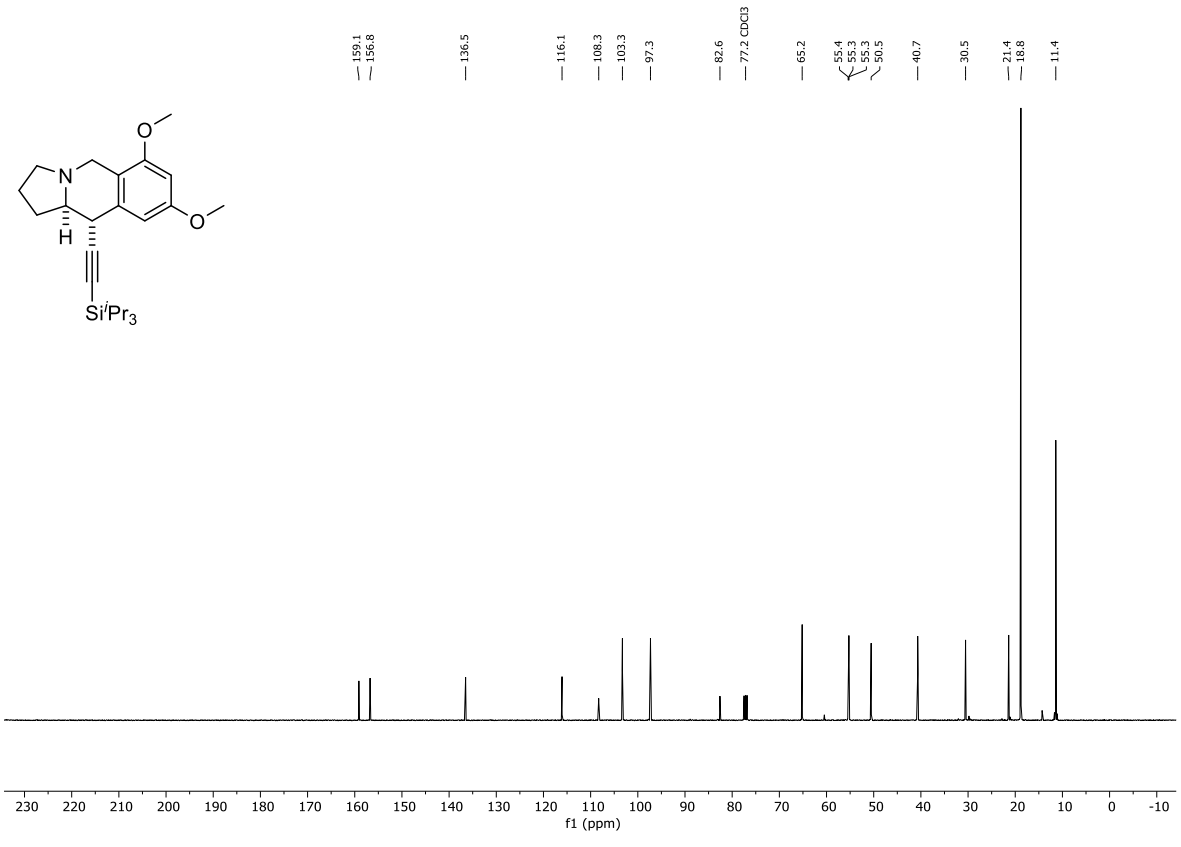
^{13}C NMR (126 MHz, $CDCl_3$) of **22**



^{1}H NMR (400 MHz, $CDCl_3$) of **23**



^{13}C NMR (100 MHz, $CDCl_3$) of **23**



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