# Palladium(II)-Catalyzed Directed *anti*-Hydrochlorination of Unactivated Alkynes with HCl

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## SUPPORTING INFORMATION

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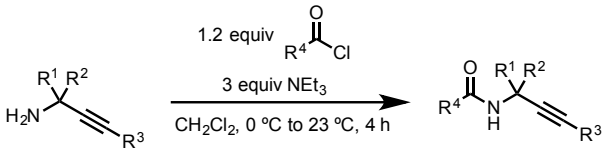
## GENERAL INFORMATION

Unless otherwise noted, all materials were used as received from commercial sources without further purification. All amines, acid chlorides, and solvents were purchased from Aldrich, Alfa Aesar, Oakwood, and Combi-Blocks. Teflon-coated magnetic stir bars were soaked in concentrated nitric acid for at least 1 h, washed repeatedly with deionized water then acetone, and dried in an oven prior to use. In air- or moisture-sensitive reactions, anhydrous solvents from a Grubbs-type solvent purification system were used. $^{1}H$ and $^{13}C$ spectra were recorded with Bruker AV-400, DRX-500 and AV-600 instruments. Spectra were internally referenced to $SiMe_4$ or solvent signals. The following abbreviations (or combinations thereof) were used to explain multiplicities: b = broad, s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septet, and m = multiplet. High-resolution mass spectra (HRMS) for new compounds were recorded on an Agilent LC/MSD TOF mass spectrometer.

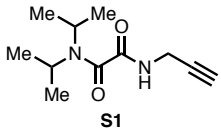
## EXPERIMENTAL PROCEDURES

*Syntheses of Terminal Alkynes with Various Directing Groups:*



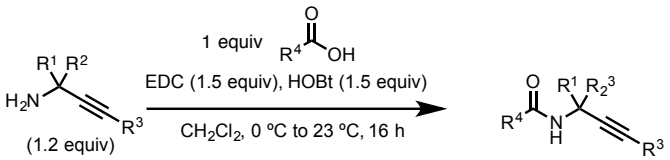

***Scheme S1:*** General depiction of condensation of propargyl amines with acid chloride.

**General Procedure for Amide Synthesis from Acid Chlorides:** To a 250-mL round-bottom flask equipped with a Teflon-coated magnetic stir bar were added the acid chloride (10.0 mmol) and anhydrous dichloromethane (50 mL). After the solution was stirred for 15 minutes at 0 °C in an ice bath, the propargyl amine (12.0 mmol) was added dropwise, followed by dropwise addition of triethylamine (30.0 mmol). The reaction was allowed to warm to room temperature and stir for 4 h. Upon completion, the reaction mixture was quenched with aqueous $NaHCO_3$ and extracted with DCM (3 × 15 mL). The organic extract was then dried with $Na_2SO_4$, filtered, and concentrated *in vacuo*. The crude amide product was purified by silica gel column chromatography.


S1

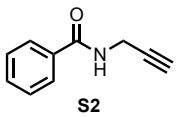
***N*,*N*-di(propan-2-yl)-*N*-(prop-2-yn-1-yl)ethanediamide (S1)**: [Di(propan-2-yl)amino](oxo)acetyl chloride was synthesized according to a literature procedure.[1] To a solution of oxalyl chloride (1.01 mL, 12.0 mmol, 1.5 equiv) in anhydrous DCM (16 mL, 0.5 M) at 0 °C was added a solution of diisopropylamine (1.12 mL, 8.0 mmol, 1.0 equiv) in DCM (8 mL, 1.0 M) in a dropwise fashion,

and the resulting mixture was stirred for 5 min. Triethylamine (1.17 mL, 8.4 mmol, 1.05 equiv) was added dropwise, and the reaction was allowed to warm to room temperature while stirring for 6 h. The solvent and excess oxalyl chloride were evaporated *in vacuo*, and the resulting mixture was re-dissolved in DCM and evaporated again. This was repeated twice. The title compound was prepared according to the general amide coupling procedure with acid chlorides using crude [di(propan-2-yl)amino](oxo)acetyl chloride (8 mmol, 1.25 equiv) from the preceding step. Purification by silica gel flash column chromatography using 50% EtOAc/hexanes as the eluent afforded the title compound as a white solid (1.03 g, 77% yield over two steps). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.12 (s, 1H), 4.81 (p, *J* = 6.7 Hz, 1H), 4.07 (dd, *J* = 5.6, 2.5 Hz, 2H), 3.53 (p, *J* = 6.8 Hz, 1H), 2.25 (dd, *J* = 3.2, 2.1 Hz, 1H), 1.42 (d, *J* = 6.8 Hz, 6H), 1.23 (d, *J* = 6.7 Hz, 6H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 162.7, 162.0, 78.7, 72.2, 49.7, 46.9, 29.3, 21.0, 20.1.

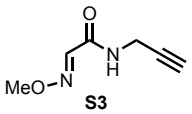



***Scheme S2:*** General depiction of condensation of propargyl amines with carboxylic acids.

**General Procedure for Amide Synthesis from Carboxylic Acids:** To carboxylic acid (1.0 equiv) in anhydrous DCM (0.24 M) at 0 °C was added EDC (1.5 equiv), and HOBt (1.5 equiv). The mixture was stirred for 10 min, before addition of the propargylamine (1.5 equiv). The reaction mixture was stirred at room temperature for 16 h, after which it was diluted with DCM. The organic phase was washed with $H_2O$ and brine, dried over $MgSO_4$ and concentrated *in vacuo*. Crude products were purified by silica gel flash column chromatography.

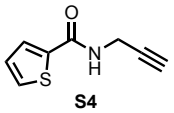

S2

***N*-(prop-2-yn-1-yl)benzamide (S2):** The title compound was prepared from benzoic acid (244 mg, 2.0 mmol) and propargyl amine (0.15 mL, 2.4 mmol) according to the general amide coupling procedure for carboxylic acids. Purification by silica gel flash column chromatography with 40% EtOAc/hexanes as the eluent afforded the title compound as a yellow oil (275.2 mg, 86% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.80–7.78 (m, 2H), 7.54–7.50 (m, 1H), 7.46–7.42 (m, 2H), 6.46 (s, 1H), 4.26 (q, *J* = 2.4 Hz, 2H), 2.29 (s, 1H) **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 167.4, 134.0, 132.1, 128.9, 127.3, 79.4, 72.2, 30.1.


S3

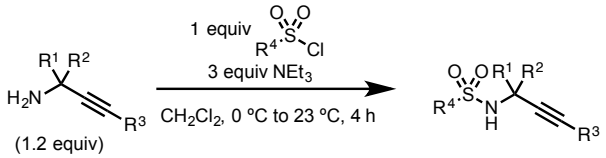
**2-(methoxyimino)-*N*-(prop-2-yn-1-yl)acetamide (S3):** (Methoxyimino) acetic acid was prepared according to literature procedure.[2] The title compound was prepared from (methoxyimino)acetic acid (206 mg, 2.0 mmol) and propargyl amine (0.15 mL, 2.4 mmol) according to the general amide coupling procedure for carboxylic acids. Purification by silica gel flash column chromatography with a gradient

solvent system (20% EtOAc/hexanes → 40% EtOAc/hexanes) as the eluent afforded the title compound as a white solid (241 mg, 86% yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.40 (s, 1H), 6.68 (bs, 1H), 4.12–4.13 (m, 2H), 3.98 (s, 3 H), 2.25–2.27 (m, 1H); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 161.4, 142.4, 79.1, 72.0, 63.3, 29.0.



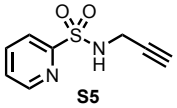
S4

***N*-(prop-2-yn-1-yl)thiophene-2-carboxamide (S4):** The title compound was prepared from thiophene-2-carboxylic acid (256 mg, 2.0 mmol) and propargyl amine (0.15 mL, 2.4 mmol) according to the general amide coupling procedure for carboxylic acids. Purification by silica gel flash column chromatography with a gradient solvent system (30% EtOAc/hexanes → 50% EtOAc/hexanes) as the eluent afforded the title compound as a white solid (267 mg, 81% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.57–7.47 (m, 2H), 7.11–7.06 (m, 1H), 6.22 (s, 1H), 4.24 (dd, $J$ = 5.3, 2.6 Hz, 2H), 2.29 (t, $J$ = 2.6 Hz, 1H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 161.91, 147.02, 138.36, 130.78, 128.97, 128.08, 79.68, 72.40, 30.09; **HRMS** (ESI-TOF) Calcd for $C_6H_9N_2O_2^+$ $[M+H]^+$ 141.0659, found 141.0659.




***Scheme S3:*** General depiction of condensation of propargyl amines with sulfonyl chlorides.

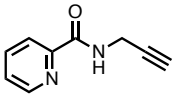
**General Procedure for Sulfonamide Synthesis:** To a 250-mL round-bottom flask equipped with a Teflon-coated magnetic stir bar were added the sulfonyl chloride (10.0 mmol) and anhydrous dichloromethane (50 mL). After the solution was stirred for 15 minutes at 0 °C in an ice bath, the propargyl amine (12.0 mmol) was added dropwise, followed by dropwise addition of triethylamine (30.0 mmol). The reaction was allowed to warm to room temperature and stir for 4 h. Upon completion, the reaction mixture was quenched with aqueous $NaHCO_3$ and extracted with DCM (3 × 15 mL). The combined organic extracts were then dried with $Na_2SO_4$, filtered, and concentrated *in vacuo*. The crude sulfonamide product was purified by silica gel flash column chromatography.



S5

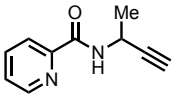
***N*-(prop-2-yn-1-yl)pyridine-2-sulfonamide (S5):** Pyridine-2-sulfonyl chloride was prepared according to a literature procedure.[3] The title compound was prepared from pyridine-2-sulfonyl chloride (177 mg, 1 mmol) and propargylamine (0.08 mL, 1.2 mmol) according to the general procedure for sulfonamide synthesis. Purification using silica gel flash column chromatography with 1:1 EtOAc:hexanes as the eluent gave the product as a white solid (157 mg, 80% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.73 (ddd, $J$ = 4.7, 1.8, 0.9 Hz, 1H), 8.03 (dt, $J$ = 7.8, 1.1 Hz, 1H), 7.92 (td, $J$ = 7.7, 1.7 Hz, 1H), 7.51 (ddd, $J$ = 7.7, 4.7, 1.2 Hz, 1H), 5.71 (s, 1H), 3.96 (dd, $J$ = 6.2, 2.6 Hz, 2H), 2.02 (t, $J$ = 2.5 Hz,

1H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 157.60, 150.42, 138.43, 127.25, 122.75, 78.37, 73.19, 33.68; **HRMS** (ESI-TOF) Calcd for $C_8H_9N_2O_2S^+$ $[M+H]^+$ 197.0379, found 197.0379.



21e

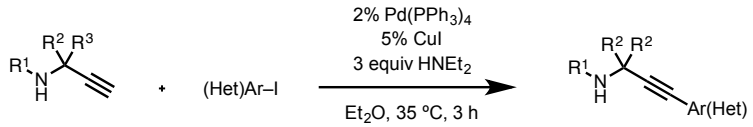
***N*-(prop-2-yn-1-yl)picolinamide (21e):** The title compound was prepared from picolinic acid (1.23 g, 10.0 mmol) and propargyl amine (0.94 mL, 15 mmol) according to the general amide coupling procedure for carboxylic acids. Purification by silica flash column chromatography with 40% EtOAc/Hexane as the eluent afforded the title compound as a white solid (1.38 g, 86% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.57 (d, *J* = 4.7 Hz, 1H), 8.20 (d, *J* = 7.9 Hz, 4H), 7.86 (td, *J* = 7.7, 1.7 Hz, 4H), 7.44 (ddd, *J* = 7.5, 4.7, 1.2 Hz, 4H), 4.28 (dd, *J* = 5.6, 2.6 Hz, 8H), 2.27 (dd, *J* = 2.8, 2.3 Hz, 4H); **$^{13}$C NMR** (125 MHz $CDCl_3$) δ 165.45, 150.81, 141.07, 121.15, 79.02, 72.52, 30.11; **HRMS** (ESI-TOF) Calcd for $C_9H_9N_2O^+$ $[M+H]^+$ 161.0709, found 161.0707.



21f

***N*-(but-3-yn-2-yl)picolinamide (21f):** The title compound was prepared from picolinic acid (1.23 g, 1.0 mmol) and 1-methyl-prop-2-ynylamine hydrochloride (106 mg mL, 1.0 mmol) according to the general amide coupling procedure for carboxylic acids. Purification by silica flash column chromatography with 40% EtOAc/Hexane as the eluent afforded the title compound as a white solid (153 mg, 86% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.56 (d, *J* = 4.8 Hz, 1H), 8.24 (s, 1H), 8.19 (d, *J* = 7.8 Hz, 1H), 7.88 – 7.82 (m, 1H), 7.46 – 7.40 (m, 1H), 5.02 (dqd, *J* = 8.3, 6.9, 2.3 Hz, 1H), 2.32 (d, *J* = 2.3 Hz, 1H), 1.55 (d, *J* = 6.9 Hz, 3H).; **$^{13}$C NMR** (125 MHz $CDCl_3$) δ 163.60, 149.87, 148.50, 137.73, 126.73, 122.72, 84.44, 70.85, 37.25, 22.65; **HRMS** (ESI-TOF) Calcd for $C_{10}H_{11}N_2O^+$ $[M+H]^+$ 175.0866, found 175.0866.

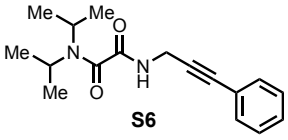
## *General Procedure for Sonogashira Coupling of Terminal Alkynes:*




***Scheme S4:*** General depiction of Sonogashira coupling.

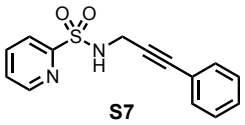
**General Procedure for Sonogashira Coupling:** To a flame-dried 25-mL round-bottom flask equipped with a Teflon-coated magnetic stir bar were added $Pd(PPh_3)_4$ (2 mol %), CuI (5 mol %), the corresponding terminal alkyne (1 mmol), and anhydrous diethyl ether (3 mL). After the addition of the solvent, the solution was stirred for 10 min at room temperature followed by the addition of appropriate aryl iodide (1.1–1.3 equiv). Diethylamine (3 equiv) was added dropwise and the reaction was allowed to stir at 35 °C for 3 hours. Upon completion, the reaction mixture

was poured carefully into a separatory funnel containing brine and extracted with $Et_2O$ (3 × 10 mL). The combined organic extracts were then dried with $Na_2SO_4$, filtered, and concentrated *in vacuo*. The crude amide product was purified by silica gel column chromatography.



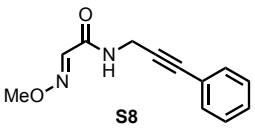
**S6**

***N*'-(3-phenylprop-2-yn-1-yl)-*N*,*N*-dipropan-2-ylurea (S6)**: The title compound was prepared from *N*,*N*-di(propan-2-yl)-N-(prop-2-yn-1-yl)ethanediamide (**S1**) (421 mg, 2 mmol) and iodobenzene (0.22 mL, 2 mmol) according to the general Sonogashira coupling procedure. Purification by silica gel flash column chromatography using 20% EtOAc/Hex as the eluent afforded the title compound as an off-white solid (502 mg, 88% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.44–7.38 (m, 2H), 7.34–7.27 (m, 3H), 7.22 (bs, 1H), 4.81 (hept, *J* = 6.7 Hz, 1H), 4.29 (d, *J* = 5.4 Hz, 2H), 3.53 (hept, *J* = 6.9 Hz, 1H), 1.43 (d, *J* = 6.8 Hz, 6H), 1.24 (d, *J* = 6.7 Hz, 6H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 162.7, 162.3, 131.9, 128.6, 128.4, 122.6, 83.9, 49.7, 46.9, 30.1, 21.0, 20.2; **HRMS** (ESI-TOF) Calcd for $C_{17}H_{23}N_2O_2^+$ $[M+H]^+$ 287.1754, found 287.1754



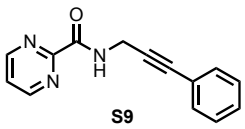
**S7**

***N*-(3-phenylprop-2-yn-1-yl)pyridine-2-sulfonamide (S7)**: The title compound was prepared from **S5** (196 mg, 1 mmol) and iodobenzene (0.22 mL, 1.5 mmol) according to the general Sonogashira coupling procedure. Purification by silica gel flash column chromatography using 50% EtOAc/hexane as the eluent afforded the title compound as a white solid (239 mg, 88% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.69 (ddt, *J* = 4.9, 1.7, 0.8 Hz, 1H), 8.05 (d, *J* = 8.3 Hz, 1H), 7.85 (td, *J* = 7.9, 1.2 Hz, 1H), 7.39 (dd, *J* = 7.6, 4.7 Hz, 1H), 7.32–7.20 (m, 3H), 7.15 (d, *J* = 7.2 Hz, 2H), 5.48 (t, *J* = 6.2 Hz, 1H), 4.19 (d, *J* = 6.2 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 157.84, 150.47, 138.34, 131.96, 128.98, 128.58, 127.11, 122.68, 122.39, 85.22, 83.54, 34.65; **HRMS** (ESI-TOF) Calcd for $C_{13}H_{12}N_3O_2S^+$ $[M+H]^+$ 274.0645, found 274.0645.

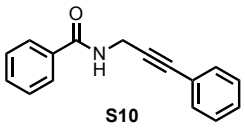


**S8**

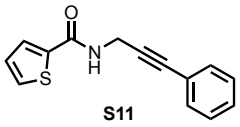
**(*E*)-2-(methoxyimino)-*N*-(3-phenylprop-2-yn-1-yl)acetamide (S8)**: The title compound was prepared from **S3** (154 mg, 1 mmol) and iodobenzene (0.13 mL, 1.2 mmol) according to the general Sonogashira coupling procedure. Purification by silica gel flash column chromatography using 70% EtOAc/hexanes as the eluent afforded the title compound as a yellow solid (186 mg, 86% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.45–7.41 (m, 3H), 7.33–7.31 (m, 2H), 4.36 (d, *J* = 5.5 Hz, 2H), 3.99 (s, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 161.65, 142.84, 132.18, 128.95, 128.73, 128.73, 84.55, 84.02, 63.57, 30.12, 0.40; **HRMS** (ESI-TOF) Calcd for $C_{12}H_{13}N_2O_2^+$ $[M+H]^+$ 217.0972, found 217.0972.



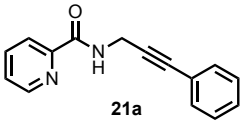
***N*-(3-phenylprop-2-yn-1-yl)pyrimidine-2-carboxamide (S9)**: The title compound was prepared from pyrimidine-2-carboxylic acid (124 mg, 1 mmol) and 3-phenylprop-2-yn-1amine hydrochloride (200.4 mg, 1.2 mmol) according to the general amide coupling procedure from carboxylic acids. Purification by silica gel flash column chromatography using 100% EtOAc as the eluent afforded the title compound as an off-white solid (177.8 mg, 75% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.91 (s, 2H), 8.23 (s, 1H), 7.49–7.40 (m, 3H), 7.35–7.28 (m, 3H), 4.56 (d, *J* = 5.4 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 157.88, 132.71, 132.19, 128.91, 128.71, 122.89, 101.51, 84.65, 84.16, 30.92; **HRMS** (ESI-TOF) Calcd for $C_{14}H_{12}N_3O^+$ $[M+H]^+$ 238.0975, found 238.0975.



***N*-(3-phenylprop-2-yn-1-yl)thiophene-2-carboxamide (S10)**: The title compound was prepared from **S2** (159 mg, 1 mmol) and iodobenzene (0.17 mL, 1.5 mmol) according to the general Sonogashira coupling procedure. Purification by silica gel flash column chromatography using 50% EtOAc/hexane as the eluent afforded the title compound as a white solid (188 mg, 80% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.84-7.81 (m, 2H), 7.52-7.42 (m, 5H), 7.35-7.27 (m, 3H), 6.46 (bs, 1H), 4.49 (d, *J* = 5,1, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ167.1, 133.9, 131.7, 128.6, 128.5, 128.3, 127.0, 122.5, 84.7, 83.7, 30.6.



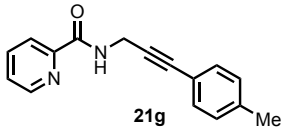
***N*-(3-phenylprop-2-yn-1-yl)thiophene-2-carboxamide (S11)**: The title compound was prepared from **S4** (165 mg, 1 mmol) and iodobenzene (0.17 mL, 1.5 mmol) according to the general Sonogashira coupling procedure. Purification by silica gel flash column chromatography using 50% EtOAc/hexane as the eluent afforded the title compound as a white solid (200 mg, 83% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 3.7, 1.1 Hz, 1H), 7.50 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.44 (dd, *J* = 7.5, 2.1 Hz, 2H), 7.35–7.27 (m, 3H), 7.09 (dd, *J* = 5.0, 3.8 Hz, 1H), 6.25 (s, 1H), 4.47 (d, *J* = 5.2 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 161.85, 138.59, 132.17, 130.68, 128.93, 128.87, 128.72, 128.06, 122.83, 84.89, 84.18, 77.16, 30.93; **HRMS** (ESI-TOF) Calcd for $C_{14}H_{12}NOS^+$ $[M+H]^+$ 242.0634, found 242.0634.



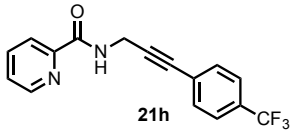
***N*-(3-phenylprop-2-yn-1-yl)picolinamide (21a):** The title compound was prepared from *N*-(prop-2-yn-1-yl)picolinamide (**21e**) (160 mg, 1 mmol) and iodobenzene (0.13 mL, 1.13 mmol) according to the general Sonogashira coupling procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a white-yellow solid (234 mg, 99% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.58 (d, *J* = 5.5 Hz, 1H), 8.26 (s, 1H), 8.22 (d, *J* = 7.8 Hz, 1H), 7.86 (td, *J* = 7.8, 1.7 Hz, 1H), 7.45 (dd, *J* = 6.8, 2.9 Hz, 3H), 7.30 (dd, *J* = 5.5, 1.6 Hz, 3H), 4.51 (d, *J* = 5.5 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.37, 149.93, 148.58, 137.77, 132.18, 128.79,

128.67, 126.77, 123.05, 122.78, 85.10, 83.80, 77.66, 77.41, 77.16, 30.41, 0.40; **HRMS** (ESI-TOF) Calcd for $C_{15}H_{13}N_2O^+$ $[M+H]^+$ 237.1022, found 237.1024.

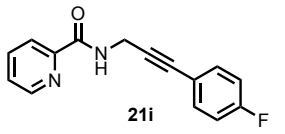
## *Synthesis of 3-Aryl Propargyl Picolinamide Substrates*




***N*-(3-(*p*-tolyl)prop-2-yn-1-yl)picolinamide (21g):** The title compound was prepared from *N*-(prop-2-yn-1-yl)picolinamide (**21e**) (160 mg, 1 mmol) and iodotoluene (283 mg, 1.3 mmol) according to the general Sonogashira coupling procedure. Purification using silica gel flash column chromatography with 33% EtOAc:hexanes as the eluent gave the product as a yellow oil (210 mg, 84% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.25 (s, 1H), 8.22 (d, $J$ = 7.8 Hz, 1H), 7.86 (t, $J$ = 7.4 Hz, 1H), 7.48–7.40 (m, 1H), 7.34 (d, $J$ = 8.0 Hz, 2H), 7.11 (d, $J$ = 7.9 Hz, 2H), 4.50 (d, $J$ = 5.4 Hz, 2H), 2.34 (s, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.05, 149.62, 148.25, 138.57, 137.42, 131.74, 129.11, 126.42, 122.43, 119.64, 84.07, 83.59, 77.16, 30.13, 21.54; **HRMS** (ESI-TOF) Calcd for $C_{16}H_{15}N_2O^+$ $[M+H]^+$ 251.1179, found 251.1176.

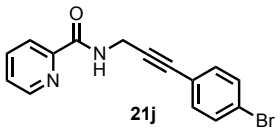



***N*-(3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-yl)picolinamide (21h):** The title compound was prepared from *N*-(prop-2-yn-1-yl)picolinamide (**21e**) (160 mg, 1 mmol) and 1-iodo-4-(trifluoromethyl)benzene (354 mg, 1.3 mmol) according to the general Sonogashira coupling procedure. Purification using silica gel flash column chromatography with 33% EtOAc:hexanes as the eluent gave the product as a brown solid (225 mg, 74% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.58 (d, $J$ = 4.2 Hz, 1H), 8.22 (d, $J$ = 7.8 Hz, 1H), 7.87 (td, $J$ = 7.7, 1.6 Hz, 1H), 7.58–7.51 (m, 4H), 7.48–7.43 (m, 1H), 4.52 (d, $J$ = 5.7 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) $^{13}$C NMR (150 MHz, $CDCl_3$) δ 164.04, 149.39, 148.20, 137.44, 132.03, 130.03 (q, $J_{C-F}$ = 22.4 Hz), 126.57, 126.48, 125.22 (q, $J_{C-F}$ = 3.6 Hz), 124.76, (q, $J_{C-F}$ = 180.7 Hz) 121.16, 87.39, 81.99, 29.85; **HRMS** (ESI-TOF) Calcd for $C_{16}H_{12}F_3N_2O^+$ $[M+H]^+$ 305.0896, found 305.0895.

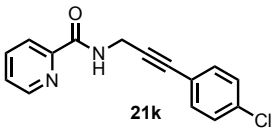



***N*-(3-(4-fluorophenyl)prop-2-yn-1-yl)picolinamide (21i):** The title compound was prepared from *N*-(prop-2-yn-1-yl)picolinamide (**21e**) (160 mg, 1 mmol) and 1-fluoro-4-iodobenzene (289 mg, 1.3 mmol) according to the general Sonogashira coupling procedure. Purification using silica gel flash column chromatography with 33% EtOAc:hexanes as the eluent gave the product as a yellow solid (224 mg, 88% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.58 (d, $J$ = 4.7 Hz, 1H), 8.26 (s, 1H), 8.22 (d, $J$ = 7.8 Hz, 1H), 7.86 (td, $J$ = 7.9, 1.4 Hz, 1H), 7.48–7.38 (m, 3H), 6.99 (t, $J$ = 8.7 Hz, 2H), 4.49 (d, $J$ = 5.6 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 163.99, 162.54 (d, $J$ = 249.5 Hz), 149.48, 148.18, 137.40, 133.69 (d, $J$ = 8.4 Hz), 126.41, 122.39, 115.56 (d, $J$ = 22.1 Hz),

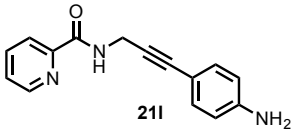
84.46, 82.29, 29.91; **HRMS** (ESI-TOF) Calcd for $C_{15}H_{12}FN_2O^+$ $[M+H]^+$ 255.0928, found 255.0925.



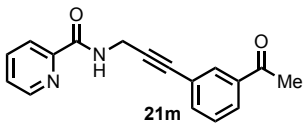

***N*-(3-(4-bromophenyl)prop-2-yn-1-yl)picolinamide (21j):** The title compound was prepared from *N*-(prop-2-yn-1-yl)picolinamide (**21e**) (160 mg, 1 mmol) and 1-bromo-4-iodobenzene (367 mg, 1.3 mmol) according to the general Sonogashira coupling procedure. Purification using silica gel flash column chromatography with 50% EtOAc:hexanes as the eluent gave the product as a white solid (286 mg, 91% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.58 (d, *J* = 4.7 Hz, 1H), 8.26 (s, 1H), 8.22 (d, *J* = 7.8 Hz, 1H), 7.86 (td, *J* = 7.8, 1.6 Hz, 1H), 7.47–7.41 (m, 3H), 7.30 (d, *J* = 8.4 Hz, 2H), 4.49 (d, *J* = 5.6 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.40, 149.86, 148.58, 137.81, 133.62, 131.95, 126.83, 123.06, 122.81, 122.02, 86.38, 82.70, 30.33; **HRMS** (ESI-TOF) Calcd for $C_{15}H_{12}BrN_2O^+$ $[M+H]^+$ 315.0128, found 315.0128.




***N*-(3-(4-chlorophenyl)prop-2-yn-1-yl)picolinamide (21k):** The title compound was prepared from *N*-(prop-2-yn-1-yl)picolinamide (**21e**) (160 mg, 1 mmol) 1-chloro-4-iodobenzene (309 mg, 1.3 mmol) according to the general Sonogashira coupling procedure. Purification using silica gel flash column chromatography with 33% EtOAc:hexanes as the eluent gave the product as a yellow-brown solid (267 mg, 98% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.58 (d, *J* = 4.7 Hz, 1H), 8.27 (s, 1H), 8.22 (d, *J* = 7.8 Hz, 1H), 7.86 (td, *J* = 7.7, 1.7 Hz, 1H), 7.45 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.37 (d, *J* = 8.6 Hz, 2H), 7.27 (d, *J* = 8.7 Hz, 2H), 4.50 (d, *J* = 5.6 Hz, 2H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 164.13, 149.60, 148.32, 137.53, 134.58, 133.15, 128.75, 126.55, 122.54, 121.29, 85.93, 82.37, 77.16, 30.05; **HRMS** (ESI-TOF) Calcd for $C_{15}H_{12}ClN_2O_2^+$ $[M+H]^+$ 271.0633, found 271.0633.

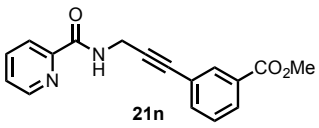



***N*-(3-(4-aminophenyl)prop-2-yn-1-yl)picolinamide (21l):** The title compound was prepared from *N*-(prop-2-yn-1-yl)picolinamide (**21e**) (160 mg, 1 mmol) and 4-iodoaniline (285 mg, 1.3 mmol) according to the general Sonogashira coupling procedure. Purification using silica gel flash column chromatography with 50% EtOAc:hexanes as the eluent gave the product as a white solid (176 mg, 70% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.57 (d, *J* = 4.6 Hz, 1H), 8.23 (s, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 7.85 (td, *J* = 7.8, 1.6 Hz, 1H), 7.43 (dd, *J* = 6.7, 4.9 Hz, 1H), 7.24 (d, *J* = 8.5 Hz, 2H), 6.58 (d, *J* = 8.5 Hz, 2H), 4.48 (d, *J* = 5.4 Hz, 2H), 3.80 (s, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.30, 150.00, 148.54, 147.11, 137.71, 133.51, 126.68, 122.71, 115.03, 112.35, 84.36, 82.69, 77.16, 30.57; **HRMS** (ESI-TOF) Calcd for $C_{15}H_{14}N_3O^+$ $[M+H]^+$ 252.1131, found 252.1127.



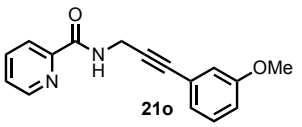
21m

***N*-(3-(3-acetylphenyl)prop-2-yn-1-yl)picolinamide (21m):** The title compound was prepared from *N*-(prop-2-yn-1-yl)picolinamide (**21e**) (160 mg, 1 mmol) and 1-(3-iodophenyl)ethan-1-one (320 mg, 1.3 mmol) according to the general Sonogashira coupling procedure. Purification using silica gel flash column chromatography with 33% EtOAc:hexanes as the eluent gave the product as a yellow solid (267 mg, 96% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.58 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 8.29 (s, 1H), 8.21 (dq, *J* = 7.8, 1.0 Hz, 1H), 8.01 (d, *J* = 1.9 Hz, 1H), 7.91–7.83 (m, 2H), 7.61 (dq, *J* = 7.8, 1.1 Hz, 1H), 7.47–7.42 (m, 1H), 7.42–7.37 (m, 1H), 4.52 (d, *J* = 5.6 Hz, 2H), 2.58 (d, *J* = 0.9 Hz, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 197.67, 164.43, 149.84, 148.60, 137.81, 137.54, 136.40, 132.21, 129.05, 128.35, 126.84, 123.69, 122.80, 86.35, 82.70, 30.27, 27.03; **HRMS** (ESI-TOF) Calcd for $C_{17}H_{15}N_2O_2^+$ $[M+H]^+$ 279.1128, found 267.1128.



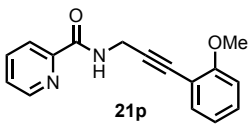
21n

**methyl 3-(3-(picolinamido)prop-1-yn-1-yl)benzoate (21n):** The title compound was prepared from *N*-(prop-2-yn-1-yl)picolinamide (**21e**) (160 mg, 1 mmol) and methyl-3-iodobenzoate (524 mg, 1.3 mmol) according to the general Sonogashira coupling procedure. Purification using silica gel flash column chromatography with 33% EtOAc:hexanes as the eluent gave the product as a yellow-white solid (247 mg, 84% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.58 (d, *J* = 4.6 Hz, 1H), 8.28 (s, 1H), 8.22 (d, *J* = 7.9 Hz, 1H), 8.12 (s, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.89–7.84 (m, 1H), 7.61 (d, *J* = 7.7 Hz, 1H), 7.45 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.38 (t, *J* = 7.8 Hz, 1H), 4.51 (d, *J* = 5.6 Hz, 2H), 3.91 (s, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 166.73, 164.42, 149.86, 148.60, 137.80, 136.28, 133.34, 130.80, 129.79, 128.83, 126.82, 123.51, 122.80, 86.16, 82.74, 52.66, 30.30; **HRMS** (ESI-TOF) Calcd for $C_{17}H_{15}N_2O_3^+$ $[M+H]^+$ 295.1077, found 295.1076.



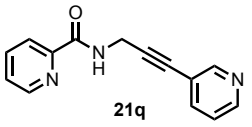
21o

***N*-(3-(3-methoxyphenyl)prop-2-yn-1-yl)picolinamide (21o):** The title compound was prepared from *N*-(prop-2-yn-1-yl)picolinamide (**21e**) (160 mg, 1 mmol) and 1-iodo-3-methoxybenzene (0.11 mL, 1.3 mmol) according to the general Sonogashira coupling procedure. Purification using silica gel flash column chromatography with 50% EtOAc:hexanes as the eluent gave the product as a dark brown solid (210 mg, 79% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.57 (dt, *J* = 4.8, 1.3 Hz, 1H), 8.26 (s, 1H), 8.21 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.86 (td, *J* = 7.7, 1.7 Hz, 1H), 7.44 (ddd, *J* = 7.7, 4.8, 1.2 Hz, 1H), 7.20 (t, *J* = 7.9 Hz, 1H), 7.04 (dt, *J* = 7.5, 1.2 Hz, 1H), 6.97 (dd, *J* = 2.7, 1.4 Hz, 1H), 6.87 (ddd, *J* = 8.4, 2.7, 1.0 Hz, 1H), 4.50 (d, *J* = 5.5 Hz, 2H), 3.79 (s, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.37, 159.66, 149.90, 148.57, 137.76, 129.73, 126.77, 124.69, 124.01, 122.77, 116.95, 115.49, 84.93, 83.68, 77.16, 55.66, 30.36; **HRMS** (ESI-TOF) Calcd for $C_{16}H_{15}N_2O_2^+$ $[M+H]^+$ 267.1128, found 267.1127.



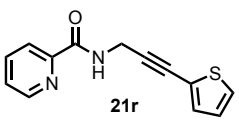
21p

***N*-(3-(2-methoxyphenyl)prop-2-yn-1-yl)picolinamide (21p):** The title compound was prepared from *N*-(prop-2-yn-1-yl)picolinamide (**21e**) (160 mg, 1 mmol) and 1-iodo-3-methoxybenzene (304 mg, 1.3 mmol) according to the general Sonogashira coupling procedure. Purification using silica gel flash column chromatography with 33% EtOAc:hexanes as the eluent gave the product as a brown solid (245 mg, 92% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.57 (d, *J* = 4.7 Hz, 1H), 8.27 (s, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 7.85 (td, *J* = 7.7, 1.7 Hz, 1H), 7.43 (td, *J* = 7.7, 1.4 Hz, 2H), 7.32–7.27 (m, 1H), 6.92–6.84 (m, 2H), 4.57 (d, *J* = 5.5 Hz, 2H), 3.88 (s, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 160.51, 149.99, 148.55, 137.72, 134.37, 130.29, 126.70, 122.75, 120.84, 112.15, 110.99, 89.08, 80.15, 56.17, 30.76; **HRMS** (ESI-TOF) Calcd for $C_{16}H_{15}N_2O_2^+$ $[M+H]^+$ 267.1128, found 267.1126.



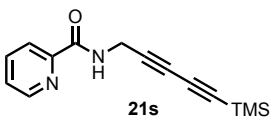
21q

***N*-(3-(pyridin-3-yl)prop-2-yn-1-yl)picolinamide (21q):** The title compound was prepared from *N*-(prop-2-yn-1-yl)picolinamide (**21e**) (160 mg, 1.0 mmol) and 3-bromopyridine (0.13 mL, 1.3 mmol) according to the general Sonogashira coupling procedure. Purification using silica gel flash column chromatography with 33% EtOAc:hexanes as the eluent gave the product as a white solid (114 mg, 51% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.58 (d, *J* = 4.7 Hz, 1H), 8.53 (d, *J* = 3.9 Hz, 1H), 8.30 (s, 1H), 8.22 (d, *J* = 7.8 Hz, 1H), 7.86 (td, *J* = 7.7, 1.4 Hz, 1H), 7.72 (d, *J* = 7.9 Hz, 1H), 7.45 (dd, *J* = 7.9, 5.2 Hz, 1H), 7.23 (dd, *J* = 7.8, 4.8 Hz, 1H), 4.52 (d, *J* = 5.7 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.18, 152.60, 149.53, 148.89, 148.34, 138.85, 137.56, 126.60, 123.09, 122.56, 119.97, 88.48, 80.17, 77.16, 29.99; **HRMS** (ESI-TOF) Calcd for $C_{14}H_{12}N_3O^+$ $[M+H]^+$ 238.0975, found 238.0975.



21r

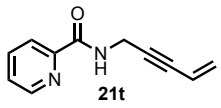
***N*-(3-(thiophen-2-yl)prop-2-yn-1-yl)picolinamide (21r):** The title compound was prepared from *N*-(prop-2-yn-1-yl)picolinamide (**21e**) (160 mg, 1 mmol) and 2-iodothiophene (0.1 mL, 1.3 mmol) according to the general Sonogashira coupling procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a brown solid (211 mg, 87% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.57 (d, *J* = 6.2 Hz, 1H), 8.26 (s, 1H), 8.21 (d, *J* = 8.7 Hz, 1H), 7.86 (t, *J* = 8.2 Hz, 1H), 7.48–7.40 (m, 1H), 7.22 (dd, *J* = 13.4, 4.4 Hz, 2H), 6.98–6.92 (m, 1H), 4.52 (d, *J* = 5.6 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.12, 149.61, 148.33, 137.53, 132.48, 127.33, 127.04, 126.55, 122.74, 122.54, 88.84, 77.16, 30.28; **HRMS** (ESI-TOF) Calcd for $C_{13}H_{11}N_2OS^+$ $[M+H]^+$ 243.0586, found 243.0586.



21s

***N*-(5-(trimethylsilyl)penta-2,4-diyn-1-yl)picolinamide (21s):** The title compound was prepared from *N*-(prop-2-yn-1-yl)picolinamide (**21e**) (160 mg, 1 mmol) and (iodoethynyl)trimethylsilane (291 mg, 1.3 mmol)

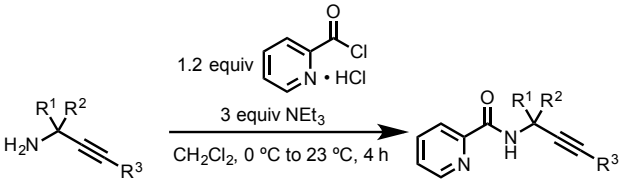
according to the general Sonogashira coupling procedure. Purification using silica gel flash column chromatography with 50% EtOAc:hexanes as the eluent gave the product as a brown solid (200 mg, 78% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.64 (d, $J$ = 4.7 Hz, 1H), 8.26 (d, $J$ = 7.8 Hz, 2H), 7.93 (td, $J$ = 7.7, 1.7 Hz, 1H), 7.53 (dd, $J$ = 7.3, 4.5 Hz, 1H), 4.44 (d, $J$ = 5.6 Hz, 2H), 0.27 (s, 8H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.10, 149.38, 148.34, 137.54, 126.63, 122.53, 87.56, 86.54, 77.16, 73.81, 68.54, 29.90, -0.33; **HRMS** (ESI-TOF) Calcd for $C_{14}H_{17}N_2OSi^+$ $[M+H]^+$ 257.1104, found 257.1104.



**21t**

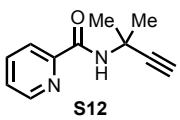
***N*-(pent-4-en-2-yn-1-yl)picolinamide (21t):** The title compound was prepared from *N*-(prop-2-yn-1-yl)picolinamide (**21e**) (160 mg, 1 mmol) and vinyl bromide solution (1.0 M in THF, 0.75 mL, 12 mmol) according to a slightly modified version of the general Sonogashira coupling procedure in which DMF was used as solvent in place of diethyl ether. Purification using silica gel flash column chromatography with 33% EtOAc:hexanes as the eluent gave the product as a yellow oil (26.1 mg, 96% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.56 (d, $J$ = 4.6 Hz, 1H), 8.26–8.17 (m, 2H), 7.85 (t, $J$ = 7.7 Hz, 1H), 7.47–7.41 (m, 1H), 5.79 (ddt, $J$ = 17.5, 11.1, 2.0 Hz, 1H), 5.65 (dd, $J$ = 17.6, 2.1 Hz, 1H), 5.48 (dd, $J$ = 11.1, 2.1 Hz, 1H), 4.40 (d, $J$ = 5.6 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.36, 149.85, 148.55, 137.73, 127.86, 122.71, 117.06, 85.81, 82.39, 30.23; **HRMS** (ESI-TOF) Calcd for $C_{11}H_{11}N_2O^+$ $[M+H]^+$ 187.0866, found 187.0864.

## *Syntheses of 3-Alkyl and Branched Propargyl Picolinamide Substrates:*



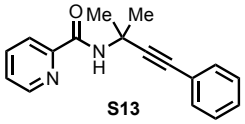

***Scheme S5:*** General depiction of condensation of alkynyl amine with picolinoyl chloride hydrochloride.

**General Procedure for Amide Coupling:** To an appropriately sized round-bottom flask equipped with a Teflon-coated magnetic stir bar were added the amine (1 equiv) (which was either commercially available or prepared using the sequence outlined in Scheme S6 and used crude), picolinoyl chloride hydrochloride (1.2 equiv) and dichloromethane (1.2 M). The reaction mixture was cooled to 0 °C, and triethylamine was added dropwise. The reaction mixture was allowed to warm to room temperature and stir overnight. The following morning, the reaction mixture was poured carefully into a separatory funnel containing brine (20 mL) and extracted with DCM (3 × 15 mL), dried with $Na_2SO_4$, and concentrated *in vacuo*. The crude amide product was purified by silica gel column chromatography.



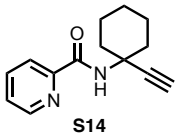
S12

***N*-(2-methylbut-3-yn-2-yl)picolinamide (S12):** The title compound was prepared from picolinoyl chloride hydrochloride (2.0 g, 10.0 mmol) 2-methylbut-3-yn-2-amine (1.30 mL, 12 mmol) according to the general amide coupling procedure for acid chlorides. Purification using silica gel chromatography with 50% EtOAc:hexanes as the eluent gave the product as an off-white powder (1.61 g, 85% yield). The product was carried on without characterization.



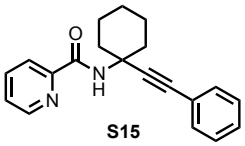
S13

***N*-(2-methyl-4-phenylbut-3-yn-2-yl)picolinamide (S13):** The title compound was prepared from *N*-(2-methylbut-3-yn-2-yl)picolinamide (**S12**) (188 mg, 1 mmol) and iodobenzene (0.11 mL, 10 mmol) according to the general Sonogashira procedure. Purification using silica gel flash column chromatography with 33% EtOAc:hexanes as the eluent gave the product as an orange solid (253 mg, 96% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.54 (d, $J$ = 4.0 Hz, 1H), 8.30 (s, 1H), 8.21 (d, $J$ = 7.8 Hz, 1H), 7.84 (td, $J$ = 7.7, 1.1 Hz, 1H), 7.49–7.39 (m, 3H), 7.32–7.26 (m, 3H), 1.88 (s, 6H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 163.02, 150.25, 147.74, 137.23, 131.74, 128.01, 127.96, 125.98, 122.87, 121.85, 92.54, 81.14, 77.16, 48.17, 28.95; **HRMS** (ESI-TOF) Calcd for $C_{17}H_{17}N_2O^+$ $[M+H]^+$ 265.1335, found 267.1333.



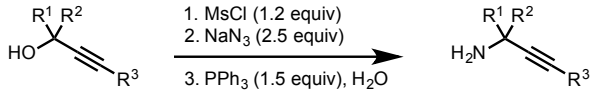
S14

***N*-(1-ethynylcyclohexyl)picolinamide (S14):** The title compound was prepared from picolinoyl chloride hydrochloride (2.0 g, 11.24 mmol) 1-ethynylcyclohexan-1-amine (1.51 mL, 11.24 mmol) according to the general amide coupling procedure for acid chlorides. Purification using silica gel chromatography with 50% EtOAc:hexanes as the eluent gave the product as a white powder (1.64 g, 64% yield). The product was carried on without characterization.



S15

***N*-(1-(phenylethynyl)cyclohexyl)picolinamide (S15):** The title compound was prepared from *N*-(1-ethynylcyclohexyl)picolinamide (**S14**) (228 g, 1 mmol) and iodobenzene (0.11 mL, 9.13 mmol) according to the general Sonogashira procedure. Purification using silica gel flash column chromatography with 60% EtOAc:hexanes as the eluent gave the product as a brown solid (298 mg, 98% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.54 (d, $J$ = 4.7 Hz, 1H), 8.26 (s, 1H), 8.22 (d, $J$ = 7.8 Hz, 1H), 7.84 (td, $J$ = 7.6, 1.4 Hz, 1H), 7.46 (dd, $J$ = 6.6, 3.0 Hz, 2H), 7.44–7.39 (m, 1H), 7.30–7.26 (m, 3H), 2.31 (d, $J$ = 13.0 Hz, 2H), 2.18–2.09 (m, 2H), 1.80 (dd, $J$ = 10.5, 3.5 Hz, 2H), 1.75–1.67 (m, 2H), 1.68–1.61 (m, 1H), 1.43–1.31 (m, 1H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 163.06, 150.64, 147.97, 137.47, 132.03, 128.23, 128.08, 126.17, 123.42, 122.16, 77.16, 52.46, 37.13, 25.53, 22.98; **HRMS** (ESI-TOF) Calcd for $C_{20}H_{21}N_2O^+$ $[M+H]^+$ 305.1648, found 305.1648.

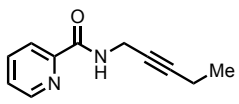



***Scheme S6:*** General depiction of alkynyl amine synthesis.

**General Procedure for Synthesis of Mesylates:**[4] To an oven-dried, 100-mL round-bottom flask equipped with a Teflon-coated magnetic stir bar and under a nitrogen atmosphere were added the appropriate alkynyl alcohol (5.0 mmol, 1 equiv), triethylamine (15 mmol, 3 equiv), and anhydrous diethyl ether (8 mL). The reaction mixture was cooled to 0 °C, and methanesulfonyl chloride (6 mmol, 1.2 equiv) was added dropwise. The reaction was allowed to warm to room temperature for 3 h. After this time, the reaction mixture was poured carefully into a separatory funnel containing brine (10 mL) and extracted with $Et_2O$ (3 × 15 mL). The combined organic extracts were dried with $Na_2SO_4$, filtered, and concentrated *in vacuo*. The crude mesylate product was carried on to the next step without purification (quantitative yield).

**General Procedure for Azide Displacement:**[4] To an oven-dried 50-mL round-bottom flask containing a Teflon-coated magnetic stir bar and under a nitrogen atmosphere, were added the crude mesylate from the previous step, anhydrous DMF (0.5 M), and $NaN_3$ (2.5 equiv). The reaction was heated to 70 °C and allowed to stir for 3 h. After this time, the reaction mixture was allowed to cool to room temperature, poured carefully into a separatory funnel containing brine (10 mL), and extracted with $Et_2O$ (3 × 15 mL). The combined organic extracts were dried with $Na_2SO_4$, filtered, and concentrated *in vacuo*. The crude azide product was stored under nitrogen and carried on to the next step without further purification.

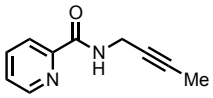
**General Procedure for Staudinger Reduction:**[4] To an appropriately sized round-bottom flask equipped with a Teflon-coated magnetic stir bar were added the crude azide from the previous step and anhydrous diethyl ether (0.5 M). The reaction mixture was cooled to 0 °C, and the vessel was charged with $PPh_3$ (1.5 equiv) and left to stir at 0 °C. After 3 h, $H_2O$ (2 equiv) was added, and the reaction mixture was allowed to warm to room temperature and stir overnight. The following morning, the reaction mixture was poured carefully into a separatory funnel containing 10% HCl (20 mL) and extracted with $Et_2O$ (3 × 15 mL). The organic extracts were discarded. The aqueous layer was treated with 6 N NaOH solution until it reached a pH of 10. The crude amine was extracted with diethyl ether (5 × 15 mL), dried with $Na_2SO_4$, and concentrated *in vacuo*. The crude amine product was carried on to the next step without further purification.



**21b**

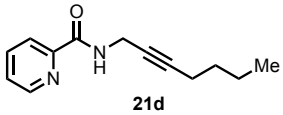
***N*-(pent-2-yn-1-yl)picolinamide (21b):** The title compound was prepared from pent-2-yn-1-amine (83 mg, 1 mmol) and picolinoyl chloride

hydrochloride (170 mg, 1.2 mmol) according to the general amide coupling procedure from acid chlorides. Pent-2-yn-1-amine was prepared from pent-2-yn-1-ol following the amine synthesis procedure. Purification using silica gel flash column chromatography with 33% EtOAc:hexanes as the eluent gave the product as a yellow solid (115 mg, 61% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.56 (ddd, *J* = 4.7, 1.8, 0.9 Hz, 1H), 8.19 (dt, *J* = 7.8, 1.1 Hz, 1H), 8.12 (s, 1H), 7.84 (td, *J* = 7.7, 1.7 Hz, 1H), 7.43 (ddd, *J* = 7.6, 4.8, 1.3 Hz, 1H), 4.27–4.20 (m, 2H), 2.20 (qt, *J* = 7.5, 2.2 Hz, 2H), 1.13 (t, *J* = 7.5 Hz, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.30, 150.01, 148.53, 137.72, 126.66, 122.72, 85.73, 77.16, 75.04, 30.06, 14.17, 12.78; **HRMS** (ESI-TOF) Calcd for $C_{11}H_{13}N_2O^+$ $[M+H]^+$ 189.1022, found 189.1022.



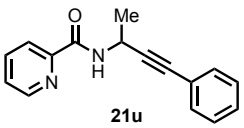
21c

***N*-(but-2-yn-1-yl)picolinamide (21c):** The title compound was prepared from but-2-yn-1-amine (69 mg, 1 mmol) and picolinoyl chloride hydrochloride (170 mg, 1.2 mmol) according to the general amide coupling procedure from acid chlorides. But-2-yn-1-amine was prepared from but-2-yn-1-ol following the amine synthesis procedure. Purification using silica gel flash column chromatography with 33% EtOAc:hexanes as the eluent gave the product as a yellow solid (108 mg, 62%). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.55 (d, *J* = 5.3 Hz, 1H), 8.18 (d, *J* = 7.8 Hz, 1H), 8.12 (s, 1H), 7.83 (td, *J* = 7.7, 1.6 Hz, 1H), 7.42 (dd, *J* = 7.7, 5.3 Hz, 1H), 4.20 (dq, *J* = 5.0, 2.3 Hz, 2H), 1.81 (t, *J* = 2.4 Hz, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.04, 149.73, 148.25, 137.43, 126.38, 122.42, 79.53, 77.16, 74.65, 29.74, 3.65; **HRMS** (ESI-TOF) Calcd for $C_{10}H_{11}N_2O^+$ $[M+H]^+$ 175.0866, found 175.0862.



21d

***N*-(hept-2-yn-1-yl)picolinamide (21d):** The title compound was prepared from hept-2-yn-1-amine (111 mg, 1 mmol) and picolinoyl chloride hydrochloride (170 mg, 1.2 mmol) according to the general amide coupling procedure from acid chlorides. Hept-2-yn-1-amine was prepared from hept-2-yn-1-ol following the amine synthesis procedure. Purification using silica gel flash column chromatography with 33% EtOAc:hexanes as the eluent gave the product as a yellow oil (128 mg, 59% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.49 (d, *J* = 4.0 Hz, 1H), 8.12 (d, *J* = 7.8 Hz, 2H), 7.77 (td, *J* = 7.7, 1.7 Hz, 1H), 7.36 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 4.23–4.14 (m, 2H), 2.12 (tt, *J* = 7.1, 2.2 Hz, 2H), 1.42 (p, *J* = 7.0 Hz, 2H), 1.33 (dq, *J* = 14.0, 6.9 Hz, 2H), 0.83 (t, *J* = 7.3 Hz, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.28, 150.04, 148.53, 137.72, 126.65, 122.71, 84.47, 75.61, 31.10, 30.09, 22.36, 18.80, 13.99; **HRMS** (ESI-TOF) Calcd for $C_{13}H_{17}N_2O^+$ $[M+H]^+$ 217.1335, found 217.1333.

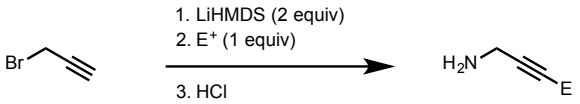


21u

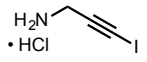
***N*-(4-phenylbut-3-yn-2-yl)picolinamide (21u):** The title compound was prepared from 4-phenylbut-3-yn-2-amine (145 mg, 1 mmol) and picolinoyl chloride hydrochloride (170 mg, 1.2 mmol) according to the general amide coupling procedure from acid chlorides. 4-Phenylbut-3-yn-2-amine was

prepared from 4-phenylbut-3-yn-2-ol following the amine synthesis procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a yellow solid (54 mg, 30% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.58 (d, *J* = 4.7 Hz, 1H), 8.28 (d, *J* = 4.9 Hz, 1H), 8.22 (d, *J* = 7.8 Hz, 1H), 7.86 (td, *J* = 7.7, 1.6 Hz, 1H), 7.49–7.39 (m, 3H), 7.30 (dd, *J* = 5.0, 1.9 Hz, 3H), 5.29–5.21 (m, 1H), 1.63 (d, *J* = 6.9 Hz, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 163.04, 149.57, 148.01, 137.25, 131.67, 128.12, 126.19, 122.61, 122.30, 99.49, 89.24, 82.23, 77.16, 37.54, 22.55; **HRMS** (ESI-TOF) Calcd for $C_{16}H_{15}N_2O^+$ $[M+H]^+$ 251.1179, found 251.1180.

## *Synthesis of 3-Heteroatom-Substituted Propargyl Picolinamide Substrates:*

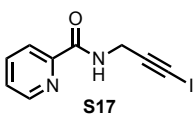



***Scheme S7:*** General depiction of synthetic route to heteroatom-substituted alkynyl amines.



**S16**

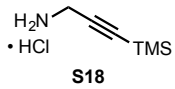
**3-iodoprop-2-yn-1-amine hydrochloride (S16):** The title compound was prepared according to a literature procedure.[5] Hexamethyldisilazane (4.17 mL, 20 mmol) was added to dry diethyl ether (10 mL) at 0 °C followed by dropwise addition of *n*-BuLi solution (2.5 M in hexanes, 8 mL, 20 mmol). The mixture was allowed to reach room temperature and stirred for 1 h. The reaction flask was covered in aluminum foil and cooled to –78 °C. Propargyl bromide (1.1 mL, 10 mmol, 80 wt.% in toluene) was added dropwise, and the reaction was allowed to reach room temperature and stir for 2 h. $I_2$ (2.54 g, 10 mmol) was added at –78 °C, and the reaction mixture was stirred at room temperature overnight. The reaction mixture was quenched with saturated $Na_2S_2O_3$ solution, and the organic phase was dried over $MgSO_4$, filtered, and concentrated to a brown solid, *N*,*N*-bis(TMS)-3-iodo-prop-2-yn-1-amine. Lastly, the *N*,*N*-bis(TMS) group was deprotected. To dry methanol (8 mL) at 0 °C, acetyl chloride (2.5 mL, 35 mmol) was added slowly, and the resulting mixture was stirred for 30 min at room temperature. The crude brown solid was dissolved in dichloromethane (4 mL) and added dropwise at 0 °C, resulting in the immediate formation of the title compound as a pale brown precipitate (869 mg, 40% yield). This compound was used in the next step without additional purification.



**S17**

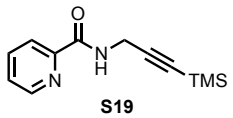
***N*-(3-iodoprop-2-yn-1-yl)picolinamide (S17):** The title compound was prepared from 3-iodopropargyl-amine hydrochloride (220 mg, 1.01 mmol) (**S18**) (327 mg, 2 mmol) and picolinoyl chloride hydrochloride (140 mg, 0.79 mmol) according to the general amide coupling procedure from acid chlorides.

Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a white solid (50 mg, 18% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.64 (dt, *J* = 4.7, 1.4 Hz, 1H), 8.27 (br d, 1H), 8.14 (br, 1H), 7.94 (m, 1H), 7.52 (ddp, *J* = 8.1, 4.7, 1.6 Hz, 1H), 4.51 (dd, *J* = 5.6, 1.9 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.33, 148.58, 137.79, 126.85, 100.00, 89.96, 77.68, 77.63, 77.43, 77.17, 31.39, 0.40; **HRMS** (ESI-TOF) Calcd for $C_9H_8IN_2O^+$ $[M+H]^+$ 286.9676, found 286.9676.



**S18**

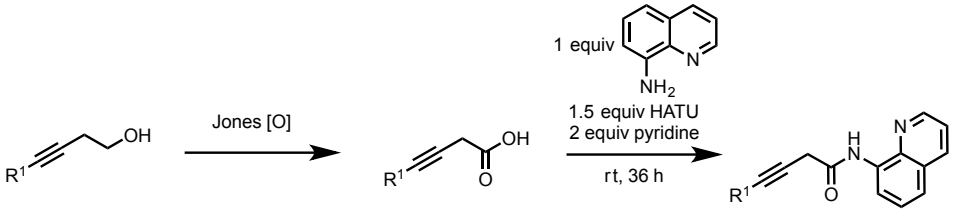
**3-(trimethylsilyl)prop-2-yn-1-amine hydrochloride (S18):** The title compound was prepared according adapted from a literature procedure.[5] Hexamethyldisilazane (4.17 mL, 20 mmol) was added to dry diethyl ether (10 mL) at 0 °C followed by dropwise addition of *n*-BuLi solution (2.5 M in hexanes, 8 mL, 20 mmol). The mixture was allowed to reach room temperature and stirred for 1 h. The reaction flask was covered in aluminum foil and cooled to –78 °C. Propargyl bromide (1.1 mL, 10 mmol, 80 wt.% in toluene) was added dropwise, and the reaction was allowed to reach room temperature and stir for 2 h. TMSCl (1.27 mL, 10 mmol) was added at –78 °C, and the reaction mixture was stirred at room temperature overnight. The reaction mixture was quenched with saturated $Na_2S_2O_3$ solution, and the organic phase was dried over $MgSO_4$, filtered and concentrated to a brown solid, *N*,*N*-bis(TMS)-3-(TMS)prop-2-yn-1-amine. Lastly, the *N*,*N*-bis(TMS) group was deprotected. To dry methanol (8 mL) at 0 °C; acetyl chloride (2.5 mL, 35 mmol) was added slowly, and the resulting mixture was stirred for 30 min at room temperature. The crude brown solid was dissolved in dichloromethane (4 mL) and added dropwise at 0 °C, resulting in the immediate formation of the title compound as a pale brown precipitate (986 mg, 60%). This compound was used in the next step without additional purification.



**S19**

***N*-(3-(trimethylsilyl)prop-2-yn-1-yl)picolinamide (S19):** The title compound was prepared from 3-trimethylsilylpropargyl-amine hydrochloride (**S16**) (327 mg, 2 mmol) and picolinoyl chloride hydrochloride (274 mg, 1.54 mmol) according to the general amide coupling procedure from acid chlorides. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as an off-white solid (44 mg, 16%). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.66 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.27 (dt, *J* = 7.9, 1.1 Hz, 1H), 8.22 (s, 1H), 7.93 (td, *J* = 7.7, 1.7 Hz, 1H), 7.52 (ddd, *J* = 7.7, 4.8, 1.3 Hz, 1H), 4.38 (d, *J* = 5.5 Hz, 2H), 0.26 (d, *J* = 0.5 Hz, 9H), 0.08 (d, *J* = 0.5 Hz, 1H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.23, 149.92, 137.75, 126.73, 101.44, 88.80, 77.67, 77.62, 77.41, 77.16, 30.58, 0.40; **HRMS** (ESI-TOF) Calcd for $C_{17}H_{17}N_2OSi^+$ $[M+H]^+$ 233.1105, found 233.1105.

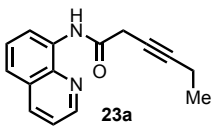
*Synthesis of 3-Butynoic Acids with 8-Aminoquinoline Auxiliary:*




***Scheme S8:*** General depiction of synthetic route to alkynyl acetic acid AQ substrates.

**General Procedure for Synthesis of Carboxylic Acids from Homopropargyl Alcohols:**[6] To a 50-mL Erlenmeyer flask equipped with a Teflon-coated magnetic stir bar were added chromium(VI) oxide (2.73 g, 2.7 M) and distilled water (4 mL). The reagent mixture was cooled to 0 °C, and concentrated sulfuric acid (2.3 mL) was added dropwise, thereby forming Jones reagent. The solution of Jones reagent was then diluted to 10 mL with distilled water. To a 100-mL round-bottom flask equipped with a Teflon-coated magnetic stir bar were added the corresponding homopropargyl alcohol and acetone (30 mL). The reaction mixture was then cooled to 0 °C. Jones reagent was added slowly into the reaction mixture over a 30-min period. The reaction was maintained at 0 °C for an additional 2 h. After this time, the reaction mixture was quenched with EtOH (20 mL) while cooling. The reaction mixture was poured carefully into a separatory funnel containing water (30 mL) and extracted with DCM (2 × 30 mL). The combined organic extracts were dried with $Na_2SO_4$, filtered, and concentrated *in vacuo*. The crude carboxylic acid product was then carried on to the next step without further purification.

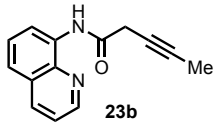
**General Procedure for Amide Coupling with 8-Aminoquinoline:**[7] To a 50-mL round-bottom flask equipped with a Teflon-coated magnetic stir bar were added the corresponding carboxylic acid (1 mmol, 1.5 equiv) and dichloromethane (20 mL). 8-Aminoquinoline (0.67 mmol, 1 equiv), pyridine (1.3 mmol, 2 equiv), and HATU (1 mmol, 1.5 equiv) were added sequentially, and the reaction mixture was stirred at ambient temperature for 36 h. (Note: It is important to use excess acid to drive the reaction to completion because the product and 8-aminoquinoline are difficult to separate by silica gel column chromatography or by other means.) The deep brown solution was diluted with EtOAc (100 mL), washed with sat. $NaHCO_3$ (2 × 100 mL) and brine (100 mL), dried over $Na_2SO_4$, filtered, and concentrated *in vacuo*. The crude amide product was purified by silica gel flash column chromatography.



**23a**

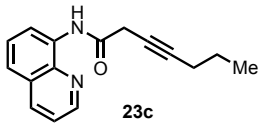
***N*-(quinolin-8-yl)hex-3-ynamide (23a):** The title compound was prepared from 3-hexynoic acid (112 mg, 1 mmol) and 8-aminoquinoline (97 mg, 0.67 mmol) according to the general amide coupling procedure with 8-aminoquinoline. 3-Hexynoic acid was prepared from hex-3-yn-1-ol

according to the general Jones oxidation procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as an yellow solid (226 mg, 95%). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.84–8.72 (m, 2H), 8.16 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.58–7.49 (m, 2H), 7.45 (dd, *J* = 8.3, 4.2 Hz, 1H), 3.45 (t, *J* = 2.4 Hz, 2H), 2.41 (q, *J* = 7.5 Hz, 2H), 1.35 (t, *J* = 7.5 Hz, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 166.61, 148.64, 139.30, 136.63, 134.66, 128.37, 127.73, 122.28, 121.99, 116.76, 89.13, 72.59, 29.79, 14.25, 13.06; **HRMS** (ESI-TOF) Calcd for $C_{15}H_{15}N_2O^+$ $[M+H]^+$ 239.1179, found 239.1179.



**23b**

***N*-(quinolin-8-yl)pent-3-ynamide (23b):** The title compound was prepared from 3-pentynoic acid (98 mg, 1 mmol) and 8-aminoquinoline (97 mg, 0.67 mmol) according to the general amide coupling procedure with 8-aminoquinoline. 3-Pentynoic acid was prepared from pent-3-yn-1-ol according to the general Jones oxidation procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as an yellow solid (181 mg, 81%). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.82 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.75 (dd, *J* = 6.6, 2.3 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.57–7.50 (m, 2H), 7.45 (dd, *J* = 8.3, 4.2 Hz, 1H), 3.43 (q, *J* = 2.5 Hz, 2H), 2.04 (t, *J* = 2.5 Hz, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 166.29, 148.55, 139.02, 136.39, 134.34, 128.11, 127.46, 122.01, 121.73, 116.49, 82.90, 77.16, 72.18, 29.53, 3.83; **HRMS** (ESI-TOF) Calcd for $C_{14}H_{13}N_2O^+$ $[M+H]^+$ 225.1022, found 225.1022.



**23c**

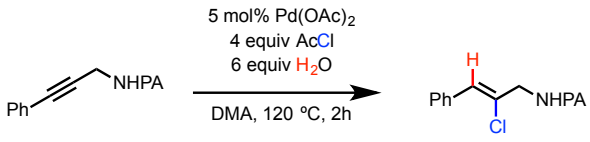
***N*-(quinolin-8-yl)hept-3-ynamide (23c):** The title compound was prepared from 3-heptynoic acid (126 mg, 1 mmol) and 8-aminoquinoline (97 mg, 0.67 mmol) according to the general amide coupling procedure with 8-aminoquinoline. 3-Heptynoic acid was prepared from hept-3-yn-1-ol according to the general Jones oxidation procedure Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a yellow solid (227 mg, 90%). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.79 (ddd, *J* = 9.1, 5.4, 2.1 Hz, 2H), 8.17 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.58–7.51 (m, 2H), 7.46 (dd, *J* = 8.3, 4.2 Hz, 1H), 3.47 (t, *J* = 2.4 Hz, 2H), 2.41–2.35 (m, 2H), 1.75 (h, *J* = 7.4 Hz, 2H), 1.11 (t, *J* = 7.4 Hz, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 166.65, 148.60, 139.31, 136.62, 134.69, 128.38, 127.73, 122.27, 121.99, 116.80, 87.65, 73.23, 29.84, 22.53, 21.39, 14.09; **HRMS** (ESI-TOF) Calcd for $C_{16}H_{17}N_2O^+$ $[M+H]^+$ 253.1335, found 253.1334.

## *Optimization of Reaction Conditions for Alkyne Hydrochlorination*

**General Procedure for Reaction Optimization:** To a 5-mL scintillation vial equipped with a Teflon-coated magnetic stir bar were added the propargyl amine substrate (0.1 mmol), chloride source (0.6 mmol), additive (0.03 mmol), and Pd(II) catalyst (0.005 mmol or 0.01 mmol). The

vial was then charged with solvent and sealed with a screw-top septum cap. [When the chloride source or additive was liquid, they were injected through the septum at this stage rather than being massed out with the solids. For example, $H_2O$ (12 µL, 0.6 mmol) was added followed by slow addition of AcCl (36 µL, 0.4 mmol)]. The reaction mixture was stirred at 120 °C for 2 h. After this time, the reaction vial was allowed cooled to room temperature, and the reaction mixture was poured into 15 mL of $H_2O$ and extracted with EtOAc (5 × 10 mL). The solvent was removed in *vacuo* to leave a brown residue, which was dissolved in $CDCl_3$. $CH_2Br_2$ (7.0 µL, 0.1 mmol) was added, and the sample was analyzed by $^1H$ NMR.

***Table S1:*** Performance of $Pd(OAc)_2$ from different suppliers and of varying purity in directed alkyne hydrochlorination under optimized reaction conditions.

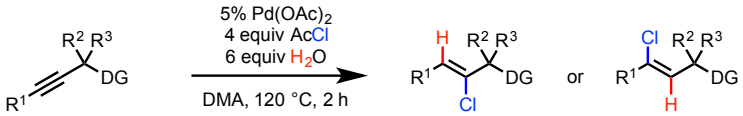



**21a** **22a**

| Entry | $Pd(OAc)_2$ | Yield **22a** (%)[a] |
|---|---|---|
| 1 | Johnson Matthey, 98% | 96 |
| 2 | Combi-Blocks, 98% | 93 |
| 3 | Ark Pharm, 98% | 94 |
| 4 | Sigma-Aldrich, 99.98% | 92 |

[a]Yield determined by $^1H$ NMR analysis of the crude reaction mixture with $CH_2Br_2$ as internal standard.

## *General Procedure for Hydrochlorination of Alkynes:*

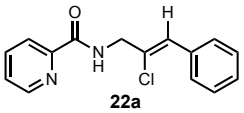



***Scheme S9:*** General depiction of alkyne hydrochlorination reaction.

**General Procedure:** To a 5-mL scintillation vial equipped with a Teflon-coated magnetic stir bar were added alkyne substrate (0.1 mmol) and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol, 5 mol %), The vial was then charged with DMA (1.0 mL) and sealed with a screw-top septum cap and. Next, $H_2O$ (12 µL, 0.6 mmol) was added followed by slow addition of AcCl (36 µL, 0.4 mmol), and the reaction mixture was stirred at 120 °C for 2 h. After this time, the reaction vial was allowed cooled to room temperature, and the reaction mixture was poured into 15 mL of $H_2O$ and extracted with EtOAc (5 × 10 mL). The solvent was removed in *vacuo* to leave a brown residue, which upon purification by silica gel column chromatography, afforded pure product.

**General Procedure for Low Catalyst Loading Experiments:** To a 5-mL scintillation vial equipped with a Teflon-coated magnetic stir bar was added alkyne substrate (0.1 mmol). A prepared stock solution of 0.005 M $Pd(OAc)_2$ in DMA was used to dispense the appropriate quantity of catalyst, and the vial was then charged with DMA to reach a total of 1.0 mL of solvent. The vial was sealed with a screw-top septum cap. Next, $H_2O$ (12 µL, 0.6 mmol) was added, followed by slow addition of AcCl (36 µL, 0.4 mmol). The reaction mixture was stirred at 120 °C. When necessary, reaction progress was monitored by taking a small aliquot, diluting with $CDCl_3$, and collecting a $^1H$ NMR spectrum at regular time intervals. After the reaction had reached completion, the reaction vessel was allowed to cool to room temperature. The reaction was worked up, and the product was purified as above.

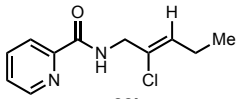

***Figure S1:*** Photographic depiction of reaction setup following the general hydrochlorination procedure. (Note: The reaction is tolerant of air and moisture.)



22a

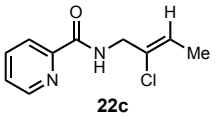
**(*Z*)-*N*-(2-chloro-3-phenylallyl)picolinamide (22a):** The title compound was prepared from **21a** (23.6 mg, 0.1 mmol or 236 mg, 1.0 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a

brown solid (26.1 mg, 96% yield and 258 mg, 95%, respectively). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 4.7 Hz, 1H), 8.49 (s, 1H), 8.23 (d, *J* = 7.8 Hz, 1H), 7.87 (td, *J* = 7.7, 1.3 Hz, 1H), 7.62 (d, *J* = 7.6 Hz, 2H), 7.46 (dd, *J* = 7.3, 4.9 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.29 (d, *J* = 7.4 Hz, 1H), 6.78 (s, 1H), 4.44 (d, *J* = 6.3 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.18, 149.38, 148.05, 137.36, 134.07, 129.75, 129.07, 128.10, 127.97, 126.33, 126.11, 122.41, 77.16, 47.33; **HRMS** (ESI-TOF) Calcd for $C_{15}H_{14}ClN_2O^+$ $[M+H]^+$ 273. 0789, found 273.0787; **X-ray** (single-crystal) Colorless needles of X-ray diffraction quality were obtained by vapor diffusion of pentane into a saturated solution of **4a** in EtOAc (CCDC 1500529).[8]



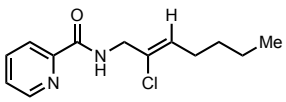
**22b**

**(*Z*)-*N*-(2-chloropent-2-en-1-yl)picolinamide (22b):** The title compound was prepared from **21b** (18.6 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a yellow oil (5 mol%: 19.5 mg, 87% yield; 25 ppm: 19.7 mg, 88% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.57 (d, *J* = 4.6 Hz, 1H), 8.34 (bs, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 7.86 (t, *J* = 8.5 Hz, 1H), 7.47–7.43 (m, 1H), 5.80 (t, *J* = 7.0 Hz, 1H), 4.26 (d, *J* = 6.2 Hz, 2H), 2.22 (p, *J* = 7.4 Hz, 2H), 1.01 (t, *J* = 7.6 Hz, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.56, 150.02, 148.56, 137.76, 130.17, 129.96, 126.71, 122.80, 46.50, 22.19, 13.28; **HRMS** (ESI-TOF) Calcd for $C_{11}H_{14}ClN_2O^+$ $[M+H]^+$ 225.0789, found 225.0789.



**22c**

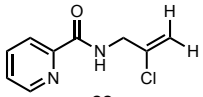
**(*Z*)-*N*-(2-chlorobut-2-en-1-yl)picolinamide (22c):** The title compound was prepared from **21c** (17.4 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 30% EtOAc:hexanes as the eluent gave the product as a yellow oil (5 mol%: 17.9 mg, 85% yield; 25 ppm: 18.3 mg, 87% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.57 (d, *J* = 4.7 Hz, 1H), 8.34 (bs, 1H), 8.20 (d, *J* = 7.8 Hz, 1H), 7.86 (d, *J* = 9.3 Hz, 1H), 7.44 (dd, *J* = 7.6, 4.8 Hz, 1H), 5.88 (q, *J* = 6.6 Hz, 1H), 4.26 (d, *J* = 6.2 Hz, 2H), 1.76 (d, *J* = 6.6, 1.2 Hz, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.61, 150.00, 148.56, 137.77, 131.46, 126.73, 123.23, 122.78, 46.52, 14.23; **HRMS** (ESI-TOF) Calcd for $C_{10}H_{12}ClN_2O^+$ $[M+H]^+$ 211.0633, found 211.0631.



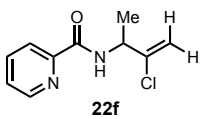
**22d**

**(*Z*)-*N*-(2-chloro-3-phenylallyl)picolinamide (22d):** The title compound was prepared from **21d** (21.6 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a colorless oil (5 mol%: 20.7 mg, 82% yield; 25 ppm: 21.4 mg, 85% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.57 (d, *J* = 4.7 Hz, 1H), 8.33 (bs, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 7.89–7.82 (m, 1H), 7.47–7.42 (m, 1H), 5.81 (t, *J* = 7.1 Hz, 1H), 4.26 (d, *J* = 7.0 Hz, 2H), 2.21 (q, *J* = 7.2 Hz, 2H), 1.44–1.28 (m, 4H), 0.90 (t, *J* = 7.1 Hz, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.56, 150.02, 148.56, 137.76, 130.38,

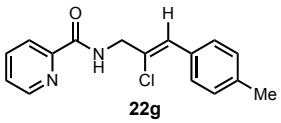
128.84, 126.71, 46.58, 30.91, 28.49, 22.71, 14.26; **HRMS** (ESI-TOF) Calcd for $C_{13}H_{18}ClN_2O^+$ $[M+H]^+$ 253.1102, found 253.1100.


22e

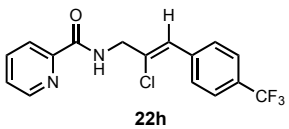
***N*-(2-chloroallyl)picolinamide (22e):** The title compound was prepared from **21e** (16.0 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a yellow solid (5 mol%: 16.3 mg, 83% yield; 25 ppm: 16.1 mg, 82% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.58 (d, *J* = 4.7 Hz, 1H), 8.39 (bs, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 7.87 (t, *J* = 8.4 Hz, 1H), 7.45 (dd, *J* = 7.1, 5.2 Hz, 1H), 5.45 (s, 1H), 5.34 (s, 1H), 4.26 (d, *J* = 6.3 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 161.18, 149.82, 148.60, 138.58, 137.82, 126.85, 122.84, 113.76, 45.84; **HRMS** (ESI-TOF) Calcd for $C_9H_{10}ClN_2O^+$ $[M+H]^+$ 197.0476, found 197.0474.


22f

***N*-(2-chloroallyl)picolinamide (22f):** The title compound was prepared from **21f** (17.3 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a white solid (5 mol%: 18.7 mg, 89% yield; 25 ppm: 17.2 mg, 82% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.57 (d, *J* = 4.6 Hz, 1H), 8.28 – 8.15 (m, 2H), 7.85 (t, *J* = 7.7 Hz, 1H), 7.44 (dd, *J* = 7.4, 5.0 Hz, 1H), 5.48 (s, 1H), 5.29 (s, 1H), 4.97 (dt, *J* = 8.6, 6.8 Hz, 1H), 1.49 (d, *J* = 6.8 Hz, 3H); **$^{13}$C NMR** δ 149.97, 148.55, 143.42, 126.73, 122.76, 113.25, 50.93, 20.06; **HRMS** (ESI-TOF) Calcd for $C_{10}H_{12}ClN_2O^+$ $[M+H]^+$ 211.0633, found 211.0633.

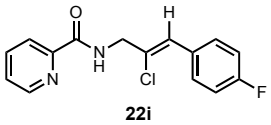

22g

**(*Z*)-*N*-(2-chloro-3-(*p*-tolyl)allyl)picolinamide (22g):** The title compound was prepared from **21g** (25.0 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a yellow oil (5 mol%: 26.8 mg, 94% yield; 25 ppm: 25.9 mg, 91% yield). **$^1$H NMR** (600 MHz, $CDCl_3$) δ 8.58 (dt, *J* = 4.8, 1.3 Hz, 1H), 8.46 (s, 1H), 8.23 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.86 (td, *J* = 7.7, 1.7 Hz, 1H), 7.52 (d, *J* = 8.1 Hz, 2H), 7.45 (ddd, *J* = 7.6, 4.8, 1.3 Hz, 1H), 7.15 (d, *J* = 8.0 Hz, 2H), 6.74 (s, 1H), 4.43 (d, *J* = 6.3, 1.0 Hz, 2H), 2.34 (s, 3H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 164.68, 149.97, 148.59, 138.46, 137.80, 131.72, 129.50, 129.36, 129.32, 126.79, 126.60, 122.86, 47.90, 21.71; **HRMS** (ESI-TOF) Calcd for $C_{16}H_{16}ClN_2O^+$ $[M+H]^+$ 287.0946, found 287.0943.


22h

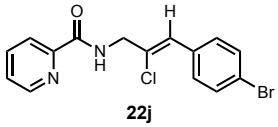
**(*Z*)-*N*-(2-chloro-3-(4-(trifluoromethyl)phenyl)allyl)picolinamide (22h):** The title compound was prepared from **21h** (30.4 mg, 0.1 mmol)

according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a colorless oil (5 mol%: 29.9 mg, 88% yield; 25 ppm: 30.2 mg, 89% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.59 (d, $J$ = 4.0 Hz, 1H), 8.52 (s, 1H), 8.23 (d, $J$ = 7.8 Hz, 1H), 7.88 (t, $J$ = 7.7 Hz, 1H), 7.70 (d, $J$ = 8.2 Hz, 2H), 7.60 (d, $J$ = 8.3 Hz, 2H), 7.47 (dd, $J$ = 7.6, 4.8 Hz, 1H), 6.81 (s, 1H), 4.45 (d, $J$ = 6.4 Hz, 2H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 164.40, 149.36, 148.24, 137.70 (q, $J_{C-F}$ = 1.4 Hz), 137.49, 132.43, 130.08, 129.86, 129.64, 129.43, 129.38, 126.71, 125.17 (q, $J_{C-F}$ = 21.7 Hz), 124.91 (q, $J_{C-F}$ = 180.7 Hz), 124.64, 123.11, 122.51, 121.31, 47.18; **HRMS** (ESI-TOF) Calcd for $C_{16}H_{13}ClF_3N_2O^+$ $[M+H]^+$ 341.0663, found 341.0662.



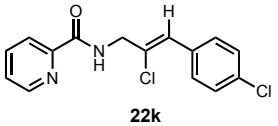
**22i**

**(*Z*)-*N*-(2-chloro-3-(4-fluorophenyl)allyl)picolinamide (22i):** The title compound was prepared from **21i** (25.4 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a colorless oil (5 mol%: 26.7 mg, 92% yield, 25 ppm: 25.2 mg, 87% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.58 (d, $J$ = 4.3 Hz, 1H), 8.23 (d, $J$ = 7.7 Hz, 1H), 7.87 (s, 1H), 7.60 (t, $J$ = 8.0 Hz, 2H), 7.46 (t, $J$ = 5.8 Hz, 1H), 7.02 (d, $J$ = 10.7 Hz, 2H), 6.74 (s, 1H), 4.42 (d, $J$ = 6.1 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.76, 162.61 (d, $J$ = 248.5 Hz), 149.87, 148.61, 139.01 (d, $J$ = 5.6 Hz), 137.85, 131.38 (d, $J$ = 8.5 Hz), 130.12, 126.87, 125.45, 122.89, 115.61 (d, $J$ = 21.3 Hz), 47.75; **HRMS** (ESI-TOF) Calcd for $C_{15}H_{13}ClFN_2O^+$ $[M+H]^+$ 291.0695, found 291.0694.



**22j**

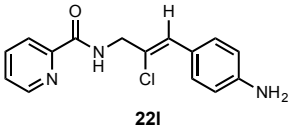
**(*Z*)-*N*-(3-(4-bromophenyl)-2-chloroallyl)picolinamide (22j):** The title compound was prepared from **21j** (31.5 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a colorless oil (5 mol%: 32.9 mg, 94% yield; 25 ppm: 32.2 mg, 92% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.58 (m, 1H), 8.22 (bs, 1H), 7.86 (d, $J$ = 7.1 Hz, 1H), 7.47 (m, 5H), 6.71 (s, 1H), 4.42 (d, $J$ = 5.7 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.75, 149.83, 148.62, 137.85, 133.48, 131.79, 131.21, 131.12, 126.89, 125.34, 122.89, 122.43, 47.72; **HRMS** (ESI-TOF) Calcd for $C_{15}H_{13}BrClN_2O^+$ $[M+H]^+$ 350.9894, found 350.9892.



**22k**

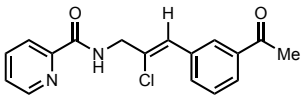
**(*Z*)-*N*-(2-chloro-3-(4-chlorophenyl)allyl)picolinamide (22k):** The title compound was prepared from **21k** (27.0 mg, 0.1 mmol or 270 mg, 1.0 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a yellow oil (28.3 mg, 93% yield and 277 mg, 91%, respectively). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.58 (d, $J$ = 4.7 Hz, 1H), 8.49 (s, 1H), 8.22 (d, $J$ = 7.8 Hz, 1H), 7.55 (d, $J$ = 8.6 Hz, 2H), 7.31 (d, $J$ = 8.5 Hz, 2H), 6.73 (s, 1H), 4.42 (d, $J$ = 6.4 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.76, 149.84, 148.62, 137.85, 134.18, 133.02, 131.06,

130.85, 128.83, 126.89, 125.31, 122.88, 47.72; **HRMS** (ESI-TOF) Calcd for $C_{15}H_{13}Cl_2N_2O^+$ $[M+H]^+$ 307.0399, found 307.0397.



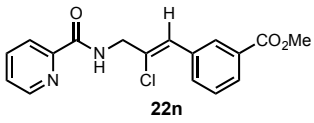
**22l**

**(*Z*)-*N*-(3-(4-aminophenyl)-2-chloroallyl)picolinamide (22l):** The title compound was prepared from **21l** (25.1 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 50% EtOAc:hexanes as the eluent gave the product as an off-white solid (5 mol%: 22.4 mg, 78% yield, 25 ppm: 20.7 mg, 72% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.23 (d, *J* = 6.4 Hz, 1H), 7.91–7.84 (m, 1H), 7.61 (d, *J* = 7.2 Hz, 2H), 7.52–7.42 (m, 3H), 7.21 (s, 1H), 6.72 (s, 1H), 4.42 (d, *J* = 6.7 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.81, 148.65, 138.24, 137.85, 130.35, 129.29, 126.88, 125.98, 122.83, 119.65, 47.90, 25.01; **HRMS** (ESI-TOF) Calcd for $C_{15}H_{15}ClN_3O^+$ $[M+H]^+$ 288.0898, found 288.0896.



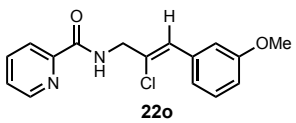
**22m**

**(*Z*)-*N*-(3-(3-acetylphenyl)-2-chloroallyl)picolinamide (22m):** The title compound was prepared from **21m** (27.8 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a white solid (5 mol%: 28.5 mg, 91% yield; 25 ppm: 28.8 mg, 92% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 5.5 Hz, 1H), 8.52 (bs, 1H), 8.23 (d, *J* = 7.8 Hz, 1H), 8.16 (s, 1H), 7.90 (s, 1H), 7.85 (dd, *J* = 20.6, 8.1 Hz, 3H), 7.50–7.43 (m, 2H), 6.83 (s, 1H), 4.46 (d, *J* = 6.4 Hz, 2H), 2.60 (s, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 198.24, 164.79, 149.80, 148.64, 137.87, 137.49, 135.08, 133.91, 131.82, 129.60, 128.93, 128.13, 126.92, 125.39, 122.89, 47.59, 27.07; **HRMS** (ESI-TOF) Calcd for $C_{17}H_{16}ClN_2O_2^+$ $[M+H]^+$ 315.0895, found 315.0893.



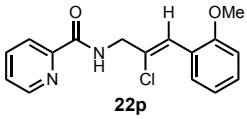
**22n**

**methyl(*Z*)-3-(2-chloro-3-(picolinamido)prop-1-en-1-yl)benzoate (22n):** The title compound was prepared from **21n** (29.4 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as an off-white solid (5 mol%: 31.0 mg, 94% yield; 25 ppm: 30 mg, 91% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 4.8 Hz, 1H), 8.50 (bs, 1H), 8.23 (d, *J* = 7.5 Hz, 2H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.91–7.81 (m, 2H), 7.49–7.40 (m, 2H), 6.81 (s, 1H), 4.44 (d, *J* = 6.3 Hz, 2H), 3.91 (s, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 167.21, 164.77, 149.82, 148.63, 137.86, 134.92, 133.71, 131.69, 130.83, 130.61, 129.45, 128.72, 126.90, 125.42, 122.89, 52.60, 47.61; **HRMS** (ESI-TOF) Calcd for $C_{17}H_{16}ClN_2O_3^+$ $[M+H]^+$ 331.0844, found 331.0843.



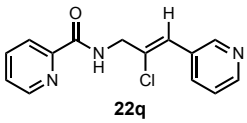
**22o**

**(*Z*)-*N*-(2-chloro-3-(3-methoxyphenyl)allyl)picolinamide (22o):** The title compound was prepared from **21o** (26.6 mg, 0.1 mmol or 266 mg, 1.0 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a yellow oil (27.4 mg, 91% yield and 274 mg, 91%, respectively). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.48 (bs, 1H), 8.23 (d, $J$ = 9.5 Hz, 1H), 7.87 (t, $J$ = 9.5 Hz, 1H), 7.18 (d, $J$ = 8.3 Hz, 1H), 6.84 (d, $J$ = 8.0 Hz, 1H), 6.76 (s, 1H), 4.44 (d, $J$ = 9.0 Hz, 2H), 3.81 (s, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.72, 159.75, 149.91, 148.61, 137.83, 135.84, 130.52, 129.57, 126.84, 126.49, 122.87, 122.26, 114.77, 114.39, 100.00, 55.66, 47.82; **HRMS** (ESI-TOF) Calcd for $C_{16}H_{16}ClN_2O_2^+$ $[M+H]^+$ 303.0895, found 303.0893.



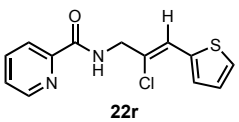
**22p**

**(*Z*)-*N*-(2-chloro-3-(2-methoxyphenyl)allyl)picolinamide (22p):** The title compound was prepared from **21p** (26.6 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a yellow oil (5 mol%: 21.4 mg, 71% yield; 25 ppm: 20.5 mg, 68% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.58 (d, $J$ = 5.4 Hz, 1H), 8.45 (bs, 1H), 8.23 (d, $J$ = 7.8 Hz, 1H), 7.90–7.81 (m, 2H), 7.28 (d, $J$ = 7.3 Hz, 1H), 7.01 (s, 1H), 6.99–6.92 (m, 1H), 6.87 (d, $J$ = 8.3 Hz, 1H), 4.47 (d, $J$ = 6.2 Hz, 2H), 3.83 (s, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 157.41, 150.05, 148.57, 137.77, 130.59, 130.25, 129.80, 126.73, 122.87, 122.20, 120.49, 110.73, 55.88, 47.92; **HRMS** (ESI-TOF) Calcd for $C_{16}H_{16}ClN_2O_2^+$ $[M+H]^+$ 303.0895, found 303.0896.



**22q**

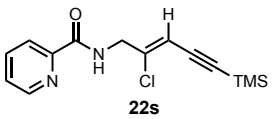
**(*Z*)-*N*-(2-chloro-3-(pyridin-3-yl)allyl)picolinamide (22q):** The title compound was prepared from **21q** (23.7 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a colorless oil (5 mol%: 22.4 mg, 82% yield; 25 ppm: 20.5 mg, 75% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.59 (d, $J$ = 4.7 Hz, 1H), 8.51 (dd, $J$ = 11.8, 5.9 Hz, 2H), 8.22 (d, $J$ = 7.8 Hz, 1H), 8.05 (d, $J$ = 8.0 Hz, 1H), 7.91–7.84 (m, 1H), 7.50–7.43 (m, 1H), 7.30–7.26 (m, 1H), 6.75 (s, 1H), 4.45 (d, $J$ = 7.2 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.82, 150.90, 149.76, 149.24, 148.64, 137.88, 136.14, 133.15, 130.68, 126.95, 123.48, 122.94, 122.90, 47.56; **HRMS** (ESI-TOF) Calcd for $C_{14}H_{13}ClN_3O^+$ $[M+H]^+$ 274.0742, found 274.0722.



**22r**

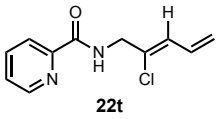
**(*Z*)-*N*-(2-chloro-3-(thiophen-2-yl)allyl)picolinamide (22r):** The title compound was prepared from **21r** (24.2 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 50% EtOAc:hexanes as the eluent gave the product as a tan solid (5 mol%: 22.8 mg, 82% yield; 25 ppm: 23.1 mg, 83% yield). **$^1$H NMR**

(500 MHz, $CDCl_3$) δ 8.58 (d, *J* = 4.8 Hz, 1H), 8.46 (bs, 1H), 8.22 (d, *J* = 7.8 Hz, 1H), 7.90–7.83 (m, 1H), 7.45 (dd, *J* = 7.0, 5.4 Hz, 1H), 7.35 (d, *J* = 5.1 Hz, 1H), 7.23 (s, 1H), 7.03 (d, *J* = 3.7 Hz, 1H), 7.02 (s, 1H), 4.44 (d, *J* = 6.3 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 161.45, 149.88, 148.60, 137.82, 137.08, 130.14, 127.89, 127.41, 126.84, 126.75, 122.86, 121.16, 47.28; **HRMS** (ESI-TOF) Calcd for $C_{13}H_{12}ClN_2OS^+$ $[M+H]^+$ 279.0353, found 279.0355.



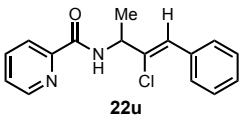
**22s**

**(*Z*)-*N*-(2-chloro-5-(trimethylsilyl)pent-2-en-4-yn-1-yl)picolinamide (22s):** The title compound was prepared from **21s** (25.6 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a white solid (5 mol%: 19.8 mg, 68% yield; 25 ppm: 20.4 mg, 70% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.56 (d, *J* = 5.5 Hz, 1H), 8.37 (bs, 1H), 8.19 (d, *J* = 7.8 Hz, 1H), 7.86 (t, *J* = 8.6 Hz, 1H), 7.49–7.43 (m, 1H), 5.95 (s, 1H), 4.32 (d, *J* = 6.4 Hz, 2H), 0.20 (s, 9H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.63, 148.60, 142.34, 137.83, 126.92, 122.85, 109.00, 103.03, 99.99, 99.44, 45.88; **HRMS** (ESI-TOF) Calcd for $C_{14}H_{18}ClN_2OSi^+$ $[M+H]^+$ 293.0871, found 293.0868.



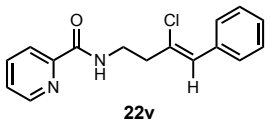
**22t**

**(*Z*)-*N*-(2-chloro-3-phenylallyl)picolinamide (22t):** The title compound was prepared from **21t** (18.6 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 30% EtOAc:hexanes as the eluent gave the product as a colorless oil (5 mol%: 12.2 mg, 55% yield; 25 ppm: 11.1 mg, 50% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.58 (d, *J* = 5.5 Hz, 1H), 8.40 (bs, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 7.87 (t, *J* = 7.7 Hz, 1H), 7.49–7.43 (m, 1H), 6.67 (dt, *J* = 17.0, 10.2 Hz, 1H), 6.39 (d, *J* = 10.8 Hz, 1H), 5.40–5.24 (m, 2H), 4.33 (d, *J* = 6.3 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.64, 148.56, 137.84, 131.81, 131.58, 127.40, 126.82, 122.87, 121.11, 46.46; **HRMS** (ESI-TOF) Calcd for $C_{11}H_{12}ClN_2O^+$ $[M+H]^+$ 223.0633, found 223.0632.



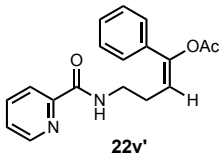
**22u**

**(*Z*)-*N*-(3-chloro-4-phenylbut-3-en-2-yl)picolinamide (22u):** The title compound was prepared from **21u** (25.0 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a colorless oil (5 mol%: 26.0 mg, 91% yield; 25 ppm: 26.8 mg, 94% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.58 (d, *J* = 5.5 Hz, 1H), 8.38 (d, *J* = 8.5 Hz, 1H), 8.20 (d, *J* = 7.8 Hz, 1H), 7.89–7.81 (m, 1H), 7.62 (d, *J* = 7.3 Hz, 2H), 7.44 (dd, *J* = 8.2, 5.4 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 2H), 7.28 (d, *J* = 7.4 Hz, 1H), 6.84 (s, 1H), 5.12 (dq, *J* = 8.7, 6.8 Hz, 1H), 1.58 (s, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 163.78, 150.05, 148.56, 137.76, 134.98, 134.66, 129.72, 128.56, 128.40, 126.71, 125.75, 122.77, 52.59, 20.39; **HRMS** (ESI-TOF) Calcd for $C_{16}H_{16}ClN_2O^+$ $[M+H]^+$ 287.0946, found 287.0943.



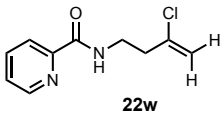
22v

**(*Z*)-*N*-(3-chloro-4-phenylbut-3-en-1-yl)picolinamide (22v):** The title compound was prepared from *N*-(4-phenylbut-3-yn-1-yl)picolinamide (**21v**)[9] (25.0 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 30% EtOAc:hexanes as the eluent gave the title compound as a white solid (5 mol%: 15.4 mg, 54% yield; 25 ppm: 15.1 mg, 53% yield) along with byproduct **5p'**. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.61 (d, *J* = 4.7 Hz, 1H), 8.34 (bs, 1H), 8.28 (d, *J* = 7.8 Hz, 1H), 7.93 (t, *J* = 8.5 Hz, 1H), 7.65 (d, *J* = 7.5 Hz, 2H), 7.50 (dd, *J* = 7.0, 4.2 Hz, 1H), 7.42 (d, *J* = 7.8 Hz, 2H), 7.35 (t, *J* = 7.3 Hz, 1H), 6.65 (s, 1H), 3.89 (q, *J* = 6.5 Hz, 2H), 2.91 (t, *J* = 6.6 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 164.90, 150.18, 148.51, 137.73, 135.18, 131.63, 129.44, 128.56, 128.13, 127.17, 126.59, 122.56, 41.50, 37.73; **HRMS** (ESI-TOF) Calcd for $C_{16}H_{16}ClN_2O^+$ $[M+H]^+$ 287.0946, found 287.0945.



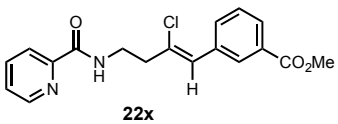
22v'

**(*Z*)-1-phenyl-4-(picolinamido)but-1-en-1-yl acetate (21v'):** The title compound was formed as a byproduct in the synthesis of **21v** (see above). Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a yellow oil (5 mol%: 15.4 mg, 42% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.54 (d, *J* = 4.5 Hz, 1H), 8.16 (d, *J* = 7.8 Hz, 1H), 8.13 (s, 1H), 7.86–7.79 (m, 1H), 7.43–7.39 (m, 1H), 7.38 (d, *J* = 8.2 Hz, 2H), 7.31 (q, *J* = 7.1, 6.7 Hz, 3H), 5.51 (t, *J* = 7.7 Hz, 1H), 3.55 (q, *J* = 6.7 Hz, 2H), 2.54 (q, *J* = 7.2 Hz, 2H), 2.13 (s, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 169.89, 164.71, 150.23, 148.64, 148.39, 137.69, 134.55, 129.00, 128.64, 126.50, 122.58, 117.02, 99.97, 77.16, 39.51, 28.00, 21.40; **HRMS** (ESI-TOF) Calcd for $C_{18}H_{19}N_2O_3^+$ $[M+H]^+$ 311.1390, found 311.1393.



22w

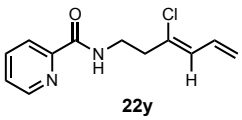
***N*-(3-chlorobut-3-en-1-yl)picolinamide (22w):** The title compound was prepared from *N*-(4-phenylbut-3-yn-1-yl)picolinamide (**21w**)[9] (17.4 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 30% EtOAc:hexanes as the eluent gave the title compound as a colorless oil (25 ppm: 17.3 mg, 81% yield). **$^1$H NMR** (600 MHz, $CDCl_3$) δ 8.54 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 2H), 8.18 (dt, *J* = 7.8, 1.1 Hz, 2H), 7.84 (td, *J* = 7.7, 1.7 Hz, 2H), 7.42 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 2H), 5.28–5.22 (m, 4H), 3.71 (q, *J* = 6.5 Hz, 4H), 2.68 (td, *J* = 6.5, 1.0 Hz, 4H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 164.42, 149.73, 148.11, 139.51, 137.34, 126.21, 122.18, 114.51, 39.13, 36.92; **HRMS** (ESI-TOF) Calcd for $C_{10}H_{12}ClN_2O^+$ $[M+H]^+$ 211.0633, found 211.0636.



22x

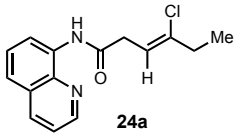
**methyl (*Z*)-3-(2-chloro-4-(picolinamido)but-1-en-1-yl)benzoate (22x):** The title compound was prepared from methyl 3-(4-(picolinamido)but-1-yn-1-yl)benzoate (**21x**)[9] (30.8 mg, 0.1

mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the title compound as a colorless oil (25 ppm: 28.3 mg, 83% yield). **$^1$H NMR** (600 MHz, $CDCl_3$) δ 8.57–8.52 (m, 1H), 8.19 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.84 (td, *J* = 7.7, 1.8 Hz, 1H), 7.42 (ddd, *J* = 7.6, 4.7, 1.2 Hz, 1H), 6.39 (dd, *J* = 16.5, 10.5 Hz, 1H), 5.84 (t, *J* = 7.2 Hz, 1H), 5.59 (d, *J* = 16.5 Hz, 1H), 5.19 (d, *J* = 10.5 Hz, 1H), 3.60 (q, *J* = 6.8 Hz, 2H), 2.69 (t, *J* = 7.1 Hz, 2H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 164.45, 148.06, 137.35, 134.61, 134.32, 127.62, 126.16, 122.20, 116.19, 38.14, 29.38; **HRMS** (ESI-TOF) Calcd for $C_{18}H_{18}ClN_2O_3^+$ $[M+H]^+$ 345.1000, found 345.1001.



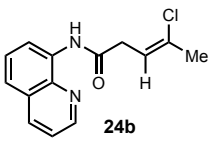
22y

**(*Z*)-*N*-(3-chlorohexa-3,5-dien-1-yl)picolinamide (22y):** The title compound was prepared from *N*-(hex-5-en-3-yn-1-yl)picolinamide (**21y**)[9] (20.0 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 20% EtOAc:hexanes as the eluent gave the title compound as an off-white solid (25 ppm: 17.1 mg, 73% yield). **$^1$H NMR** (600 MHz, $CDCl_3$) δ 8.53 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 2H), 8.28 (d, *J* = 6.5 Hz, 2H), 8.24–8.17 (m, 4H), 7.93 (dt, *J* = 7.8, 1.4 Hz, 2H), 7.84 (td, *J* = 7.7, 1.7 Hz, 2H), 7.80–7.75 (m, 2H), 7.45–7.38 (m, 4H), 6.59 (s, 2H), 3.91 (s, 6H), 3.80 (q, *J* = 6.5 Hz, 4H), 2.84 (td, *J* = 6.6, 0.9 Hz, 4H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 166.89, 164.55, 149.68, 148.15, 137.39, 135.08, 133.25, 132.62, 130.26, 130.14, 128.74, 128.26, 126.27, 125.92, 122.20, 52.20, 41.04; **HRMS** (ESI-TOF) Calcd for $C_{12}H_{14}ClN_2O^+$ $[M+H]^+$237.0789, found 237.0784.



24a

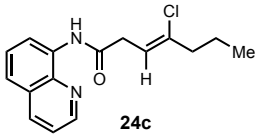
**(*Z*)-4-chloro-*N*-(quinolin-8-yl)hex-3-enamide (24a):** The title compound was prepared from **23a** (23.8 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a yellow oil (5 mol%: 21.6 mg, 79% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 10.10 (s, 1H), 8.91–8.62 (m, 2H), 8.24 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.73–7.55 (m, 2H), 7.53 (ddd, *J* = 8.3, 4.2, 0.9 Hz, 1H), 6.01 (t, *J* = 7.0, 1.1 Hz, 1H), 3.58 (dq, *J* = 7.0, 1.0 Hz, 2H), 2.58 (qt, *J* = 7.4, 1.1 Hz, 2H), 1.33 (td, *J* = 7.4, 0.9 Hz, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 168.95, 148.59, 141.55, 138.85, 136.69, 134.77, 128.32, 127.76, 122.01, 117.23, 116.86, 38.34, 33.40, 12.96; **HRMS** (ESI-TOF) Calcd for $C_{16}H_{18}ClN_2O^+$ $[M+H]^+$ 289.1102, found 275.0944.



24b

**(*Z*)-4-chloro-*N*-(quinolin-8-yl)pent-3-enamide (24b):** The title compound was prepared from **23b** (22.4 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a yellow oil (5 mol%: 21.8 mg, 84% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 9.97 (s, 1H), 8.75 (d, *J*

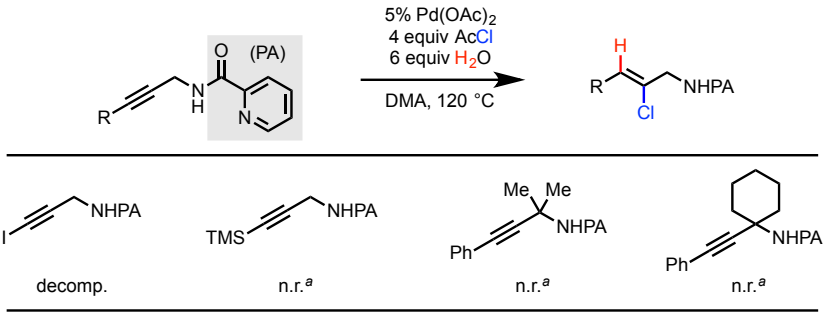
= 8.7 Hz, 2H), 8.16 (d, *J* = 9.8 Hz, 1H), 7.57–7.47 (m, 2H), 7.45 (dd, *J* = 8.2, 4.2 Hz, 1H), 5.91 (t, *J* = 7.6 Hz, 1H), 3.48 (d, *J* = 8.1 Hz, 2H), 2.24 (s, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 168.88, 148.65, 138.82, 136.71, 134.89, 134.79, 128.32, 127.77, 122.01, 118.83, 116.84, 38.50, 26.67; **HRMS** (ESI-TOF) Calcd for $C_{14}H_{14}ClN_2O^+$ $[M+H]^+$ 261.0789, found 261.0790.



**24c**

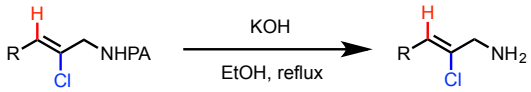
**(*Z*)-4-chloro-*N*-(quinolin-8-yl)hept-3-enamide (24c):** The title compound was prepared from **23c** (25.2 mg, 0.1 mmol) according to the general hydrochlorination procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as a yellow oil (5 mol%: 23.3 mg, 81% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 10.00 (s, 1H), 8.77 (dd, *J* = 13.4, 5.8 Hz, 2H), 8.15 (d, *J* = 8.2 Hz, 1H), 7.55–7.50 (m, 2H), 7.44 (dd, *J* = 8.3, 4.2 Hz, 1H), 5.91 (t, *J* = 7.0 Hz, 1H), 3.50 (d, *J* = 7.0 Hz, 2H), 2.48–2.41 (m, 2H), 1.74–1.64 (m, 3H), 0.98 (t, *J* = 7.4 Hz, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 168.92, 148.56, 139.80, 138.84, 136.68, 134.81, 128.31, 127.76, 122.00, 121.98, 118.32, 116.84, 41.91, 38.43, 21.06, 13.56; **HRMS** (ESI-TOF) Calcd for $C_{15}H_{16}ClN_2O^+$ $[M+H]^+$ 275.0946, found 289.1100.

***Table S2.*** Unsuccessful Examples.



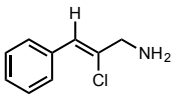

[a] n.r. = no reaction.

## *General Procedure for Removal of Picolinamide Directing Group*




***Scheme S10:*** Hydrolysis of the picolinamide directing group.

**General Picolinamide Hydrolysis Procedure:** Removal of the picolinamide directing group was carried out by adapting a literature procedure.[8] To a flame-dried 250-mL sealed vessel was added the hydrochlorination product (1 mmol), KOH (60 mmol, 60 equiv), and 30 mL of EtOH. The resulting mixture was stirred at 125 °C for 48 h. After the reaction was complete, the reaction mixture was allowed to cool to room temperature, diluted by addition of EtOAc (50 mL) and washed with $H_2O$ (2 × 20 mL). The organic layer was dried over $Na_2SO_4$ and concentrated *in vacuo* to give pure amine product.

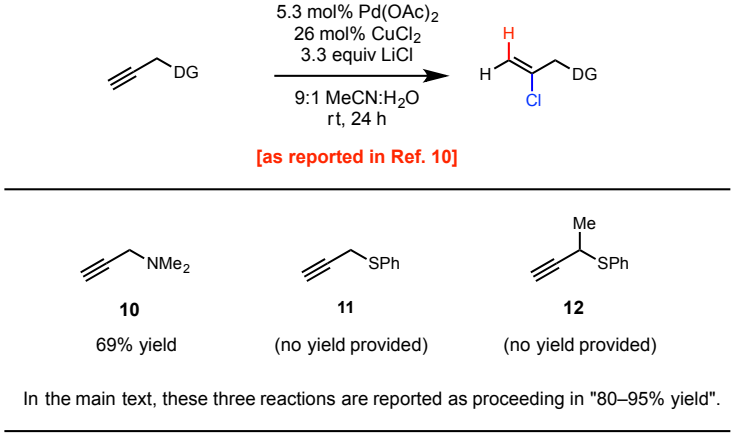


25a

**(*Z*)-2-chloro-3-phenylprop-2-en-1-amine (25a):** The title compound was prepared from (*Z*)-*N*-(2-chloro-3-phenylallyl)picolinamide (**22a**) (236 mg, 1.0 mmol) according to the general hydrolysis procedure, and the product was obtained as a yellow oil (153 mg, 92% yield). **$^{1}$H NMR** (600 MHz, $CDCl_3$) δ 7.52–7.34 (m, 5H), 6.81 (s, 1H), 4.35 (t, 2H); **$^{13}$C NMR** (150 MHz, $CDCl_3$) δ 138.5, 136.6, 132.5, 132.2, 131.9, 124.5, 47.3.

*Attempted Replication of Previously Reported Hydrochlorination Reaction:*

Dupont and coworkers previously reported an example of palladium(II)-catalyzed *anti*-hydrochlorination with three terminal propargyl amine and sulfide substrates: *N,N*-dimethyl propargyl amine (**10**), phenyl propargyl sulfide (**11**) and 1-methyl-2-propynyl phenyl sulfide (**12**).[10] In the main text of their publication, the authors write that these reaction provide "80–95% yield." In the experimental section, 69% yield is reported with *N,N*-dimethyl propargyl amine (**10**), while no yields are provided for the other two substrates.

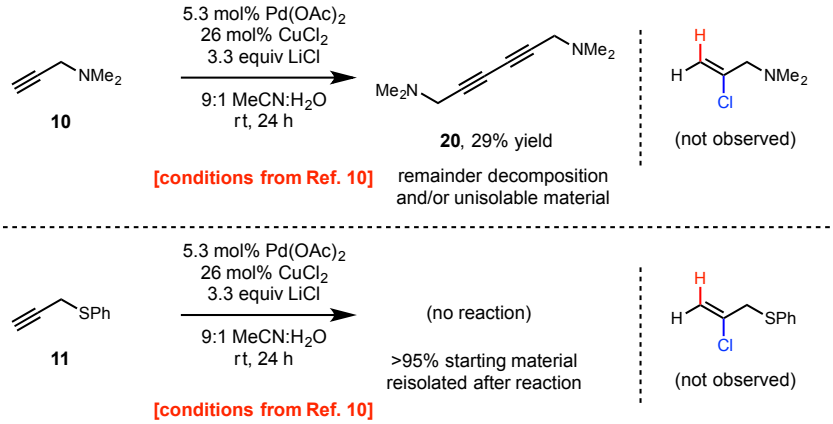



***Scheme S11.*** Terminal alkyne hydrochlorination, as reported in Ref. 10.

**Reported Procedure for Hydrochlorination of Substrates 10-12:**[10] The following method was described by Dupont and co-workers and is reproduced here verbatim for clarity:

> *N,N-Dimethyl-propargylamine (**10**) (0.25 g, 3 mmol) was added dropwise to a solution of palladium acetate (36 mg, 0.16 mmol), $CuCl_2$ (0.1 g, 0.78 mmol), and lithium chloride (0.42g, 10 mmol) in MeCN:$H_2O$ (9:1, 8.6 mL), and the reaction mixture was stirred at room temperature for 24 h. After the addition of water (15 mL), the organic phase was extracted with diethyl ether (3 × 10 mL) and dried over magnesium sulfate and the solvents were removed under reduced pressure, affording N,N-di- methyl-(2-chloroallyl)amine (13).*

In our hands, despite numerous attempts (Scheme S12, Figure S2), we have been unable to reproduce the reported results. In particular, we have found that under the reported conditions (Scheme S12) hydrochlorination is not observed. With *N,N*-dimethyl propargyl amine (**10**), we found that the substrate was consumed and that the only identifiable product in the crude reaction mixture was the corresponding Glaser homodimerization product **20**, which was formed in 29% yield. The remainder of the material appeared to succumb to decomposition and its identity could not be determined. With phenyl propargyl sulfide (**11**), no reaction was observed, and the starting material was re-isolated from the crude reaction mixture with quantitative recovery.




***Scheme S12.*** Attempts to reproduce the experiments described in Ref. 10 and the results obtained in our hands.

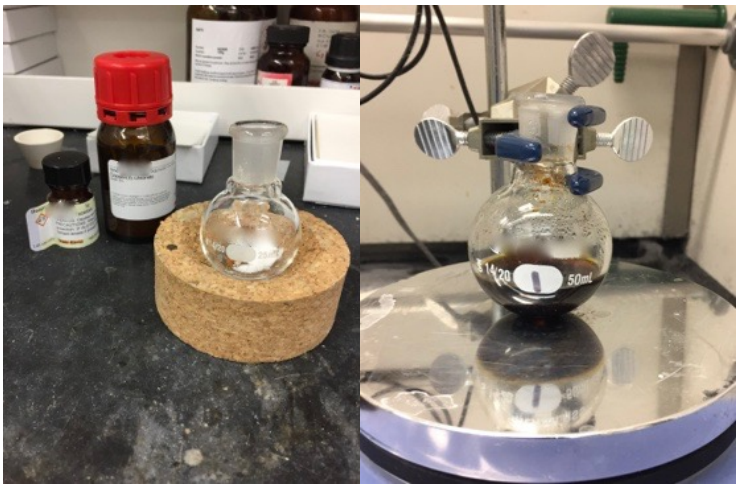
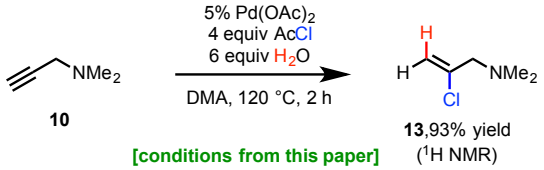


***Figure S2.*** Photographic depiction of reaction setup following the procedure according to Ref. 10. (Note: in the trials under air, the presence or absence of a cap/stopper was not found to affect reaction outcome, so experiments were generally run open to air without a cap/stopper unless otherwise specified. In addition, the propargyl amine substrate was added dropwise over a period of 1 minute, however, varying the addition time from 15 seconds to 2 minutes did not have an effect on the reaction outcome.)

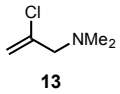

20

***N*¹,*N*¹,*N*⁶,*N*⁶-tetramethylhexa-2,4-diyne-1,6-diamine (20):** The title compound was prepared from *N,N*-dimethyl propargyl amine (249 mg, 3.0 mmol) according to Dupont's procedure.[10] After aqueous work up, extraction with diethyl ether, and careful removal of the organic solvent *in vacuo*, the analytically product was obtained as a brown oil (71.2 mg, 29% yield). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 3.35 (s, 4H), 2.31 (s, 12H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 73.42, 69.54, 48.23, 43.97; **HRMS** (ESI-TOF) Calcd for $C_{10}H_{17}N_2^+$ $[M+H]^+$ 165.1386, found 165.1366.

Subsequently, we found that when *N,N*-dimethyl propargyl amine (**10**) was submitted to the optimal conditions from the present manuscript, hydrochlorinated product **13** was formed in 93% yield ($^1$H NMR) (Scheme S13), which provided an authentic sample for comparison. Vinyl chloride **13** is extremely volatile. Hence, after extensive efforts, we were only able to obtain <2 mg of pure **13** by fractional distillation, which was nevertheless sufficient for confirming its identity by $^1$H and $^{13}$C NMR and HRMS. We note as a brief aside that while in general (and particularly with internal alkynes), the *N,N*-dimethylamino moiety is less efficient than picolinamide as a directing group, with terminal propargyl alkynes specifically, the *N,N*-dimethylamino-directed reaction is quite efficient with our optimized conditions.



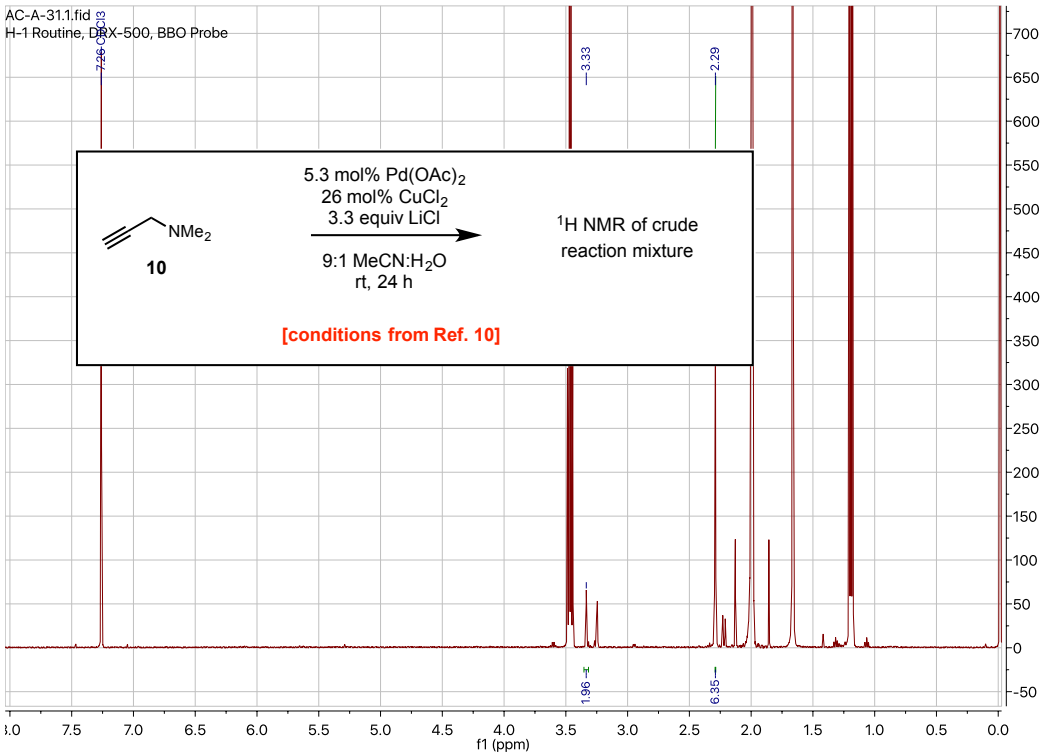

***Scheme S13.*** Hydrochlorination of *N,N*-dimethyl propargyl amine (**10**) under our optimal reaction conditions from the present paper.

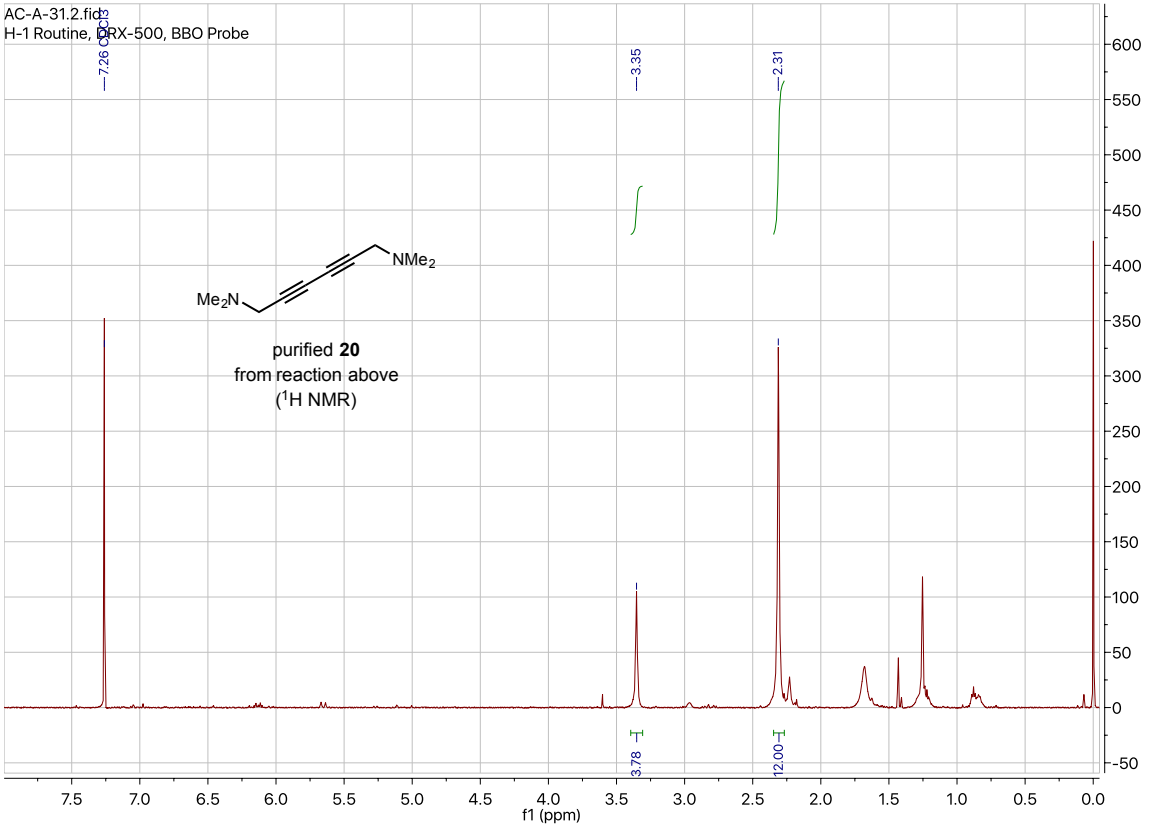



13

**2-chloro-*N,N*-dimethylprop-2-en-1-amine (13):** The title compound was prepared from *N,N*-dimethyl propargyl amine (8.3 mg, 0.1 mmol) following the general hydrochlorination procedure from the present manuscript (Scheme S9). Dibromomethane was added to the crude reaction mixture as an internal standard, and an aliquot was diluted with $CDCl_3$ and analyzed by $^1$H NMR to determine the yield (93%). In a separate experiment, this procedure was performed on 1.0-mmol scale in an attempt to isolate a pure sample of **13**. The reaction mixture was diluted with diethyl ether (15 mL) and washed with 20% NaOH (2 × 50 mL). The organic layer was directly distilled *via* fractional distillation (estimated **b.p.** = 40–60 ºC) to yield the desired product in ~95% purity as a yellow oil (<10 mg, <1% yield). (The low yield was due to the similar boiling points of the product and diethyl ether). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 5.34 (dd, $J$ = 14.8, 1.1 Hz, 1H), 3.06 (s, 1H), 2.28 (s, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 139.6, 114.66, 66.10, 44.95; **HRMS** (ESI-TOF) Calcd for $C_{10}H_{17}ClN^+$ $[M+H]^+$ 120.0575, found 120.0574.

$^1$H NMR data from several of the experiments described above are included in the ensuing pages. Notably, on page S33, we show an overlay of $^1$H NMR spectra of the following: (1) purified Glaser product **20**, (2) the crude reaction mixture using conditions from Ref. 10, and (3) the crude reaction mixture under our conditions containing **13**•HCl. To probe the possibility that the copper salts in the protocol from Ref. 10 caused major peak shifts of the product into an obfuscated region of the $^1$H NMR spectrum, we performed an additional experiment. We submitted **10** to the conditions from Ref. 10 then spiked the reaction mixture with several drops of an independently prepared solution of **13** in $Et_2O$ and collected a $^1$H NMR spectrum. Overlaying the $^1$H NMR spectra (page S38) of the spiked reaction mixture and non-spiked reaction mixture revealed that in the non-spiked reaction mixture, there are no peaks corresponding to **13** in the region where one would expect to see them. In Table S3, we compare the chemical shifts for **13** as reported in Ref. 10 to those obtained in our hands. The reported shifts are inconsistent to those found in our experiments.

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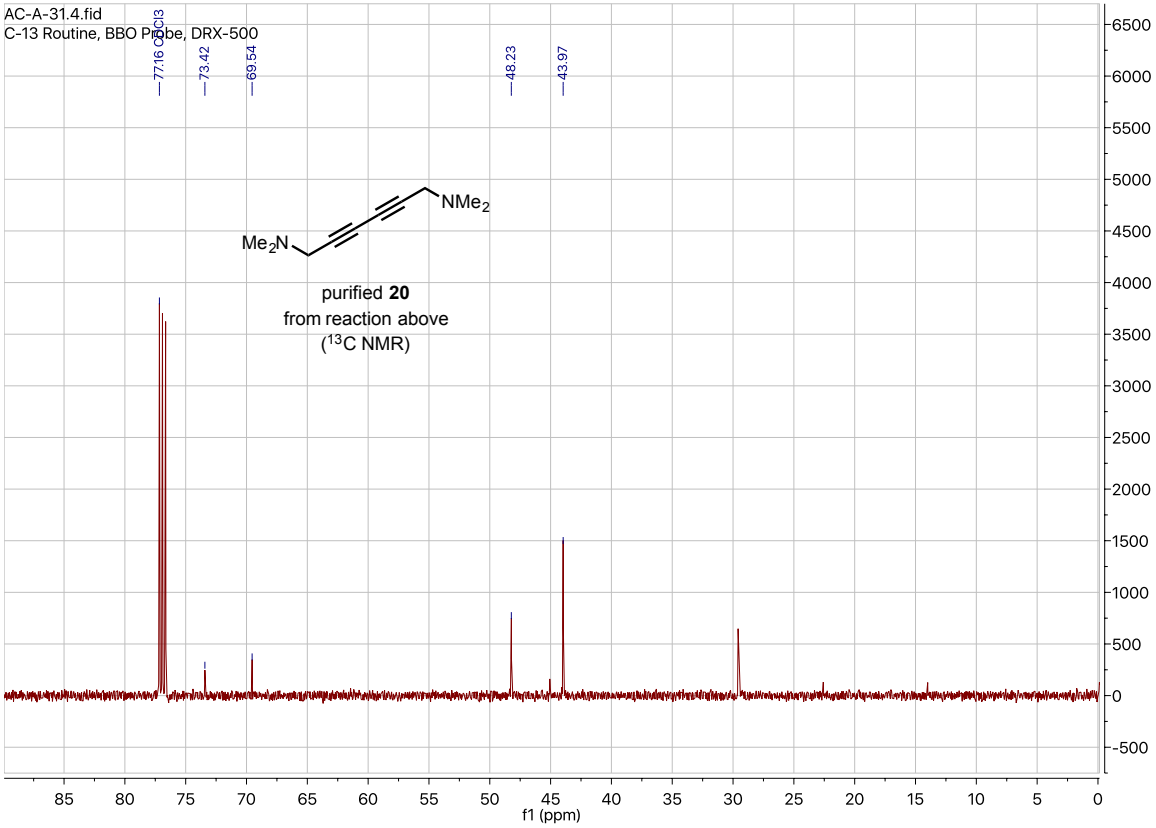
3.35
2.31
NMe2
Me2N
purified 20
from reaction above
(1H NMR)
3.78
12.00
f1 (ppm)


AC-A-31.4.fid
C-13 Routine, BBO Probe, DRX-500
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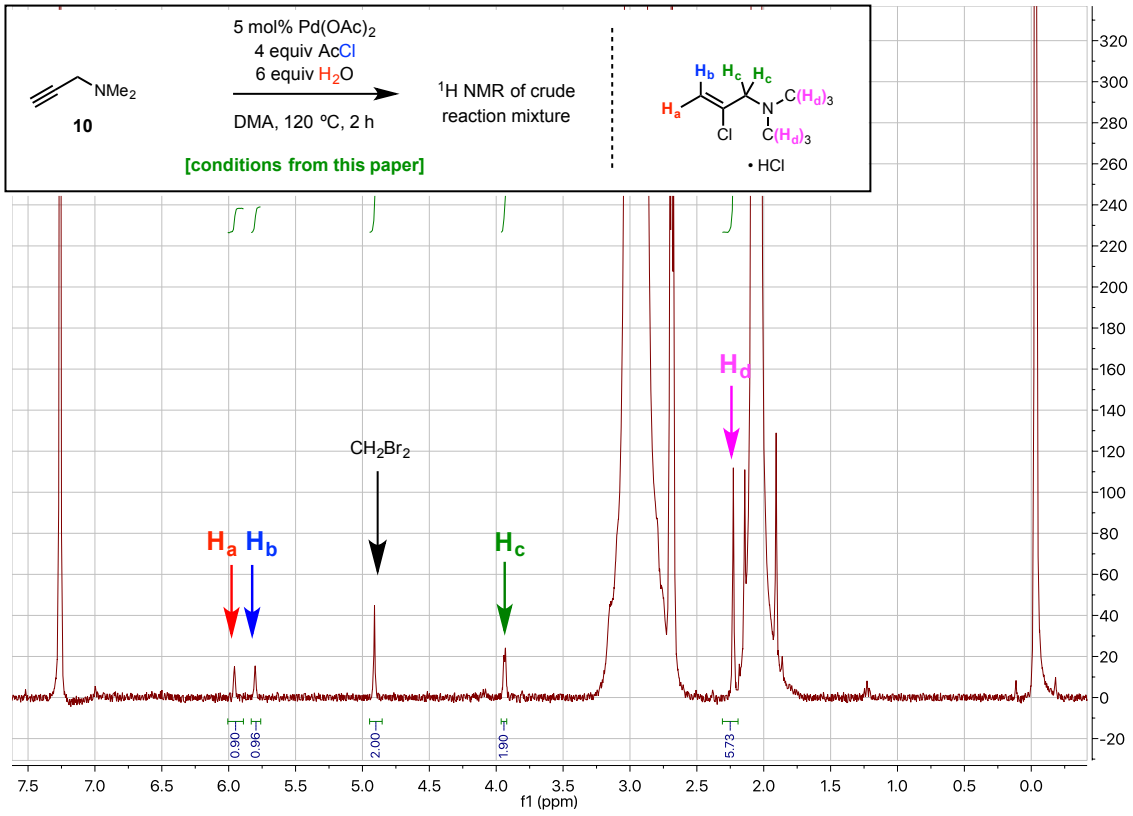
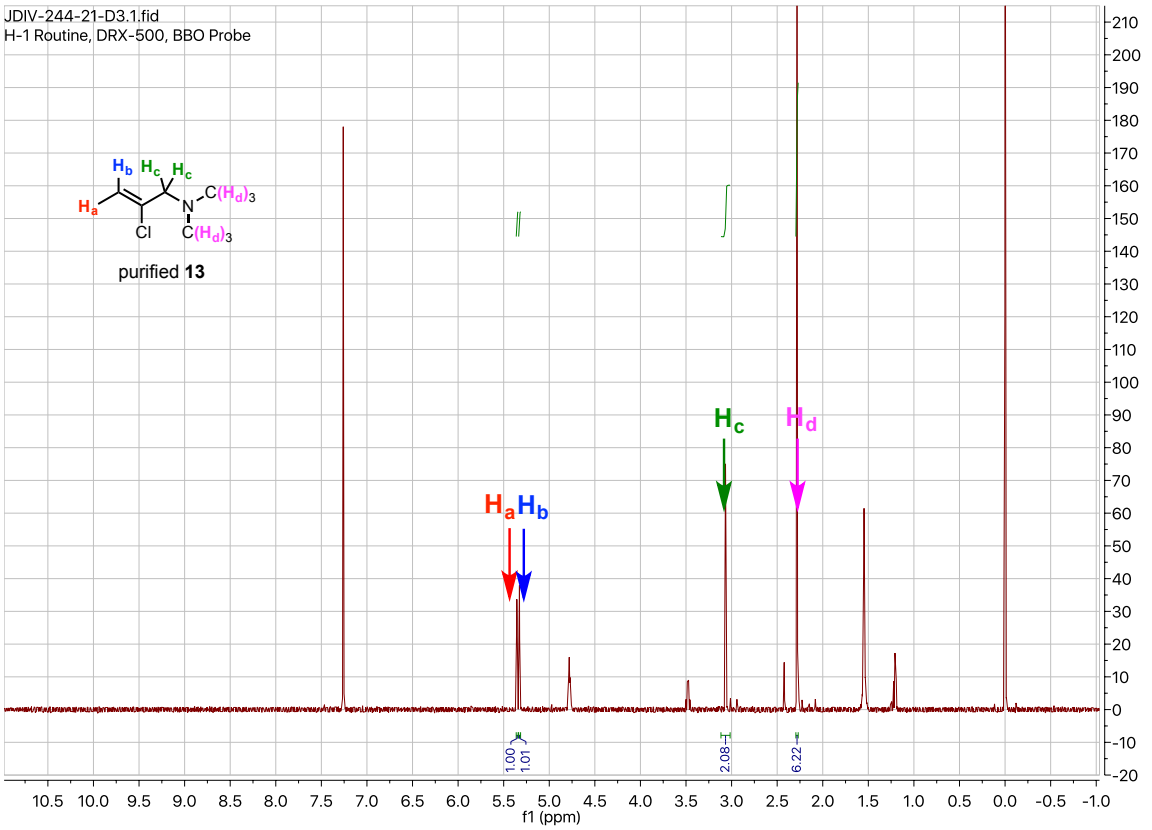
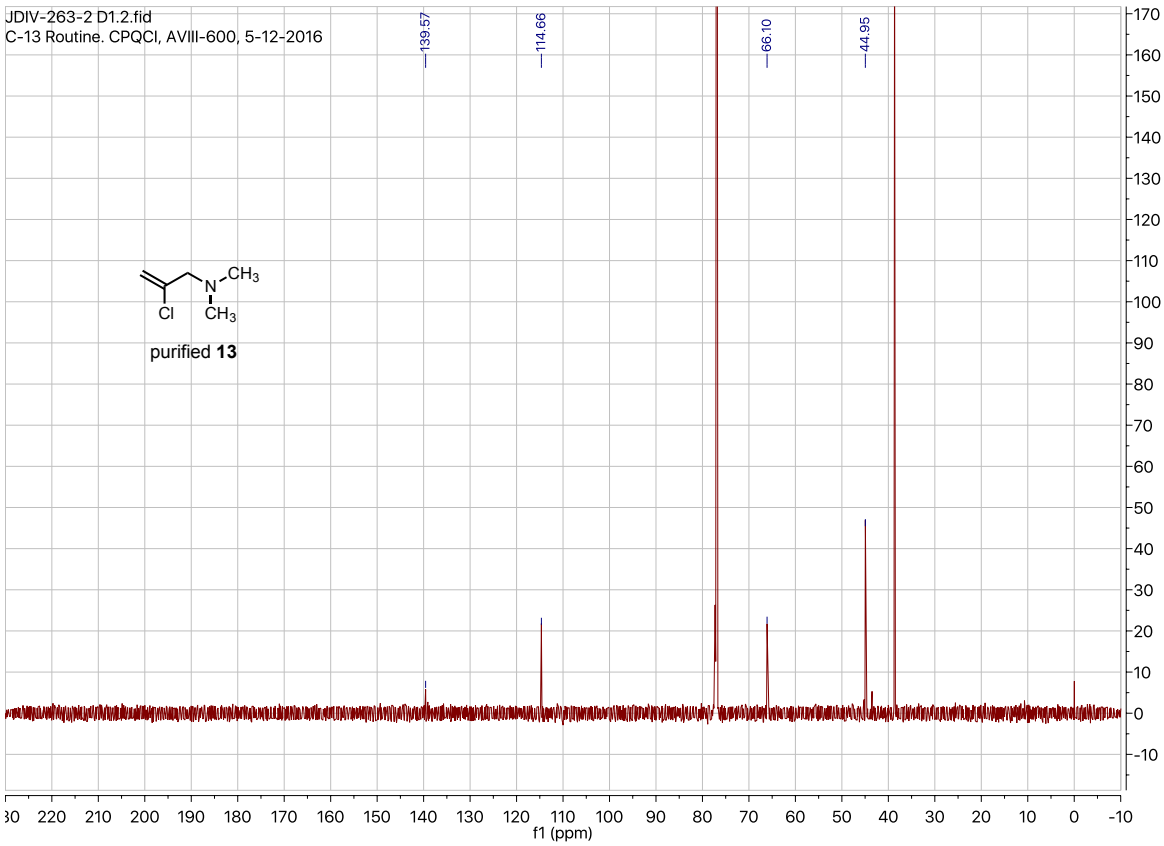
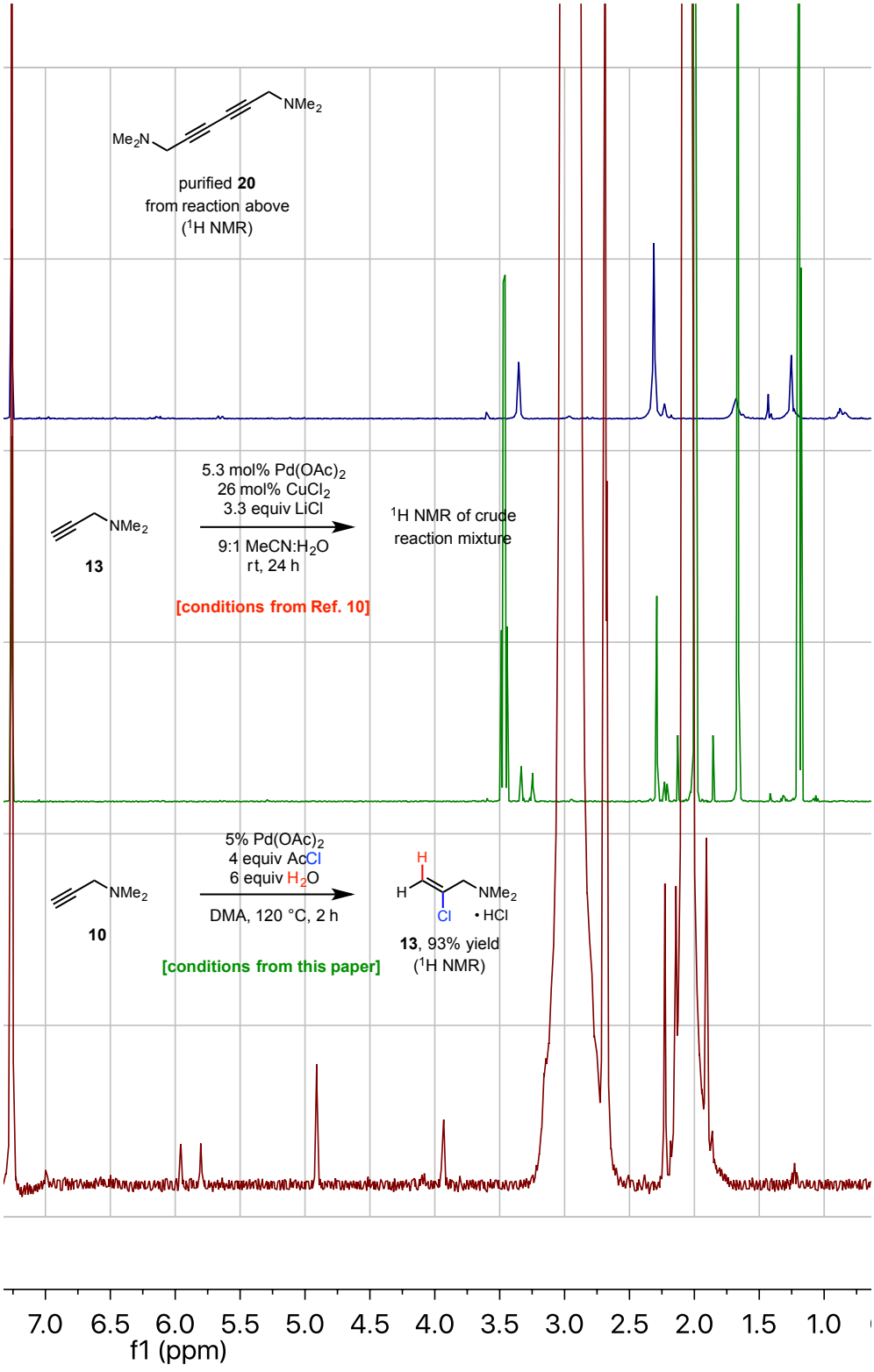
73.42
69.54
48.23
43.97
NMe2
Me2N
purified 20
from reaction above
(13C NMR)
f1 (ppm)


5 mol% Pd(OAc)2
4 equiv AcCl
6 equiv H2O
DMA, 120 °C, 2 h
[conditions from this paper]
NMe2
10
1H NMR of crude reaction mixture
Hb Hc Hc
Ha
Cl
N
C(Hd)3
C(Hd)3
• HCl
Hd
CH2Br2
Ha Hb
Hc
0.90
0.96
2.00
1.90
5.73
f1 (ppm)


JDIV-244-21-D3.1.fid
H-1 Routine, DRX-500, BBO Probe
purified 13
Ha Hb
Hc
Hd
1.00
1.01
2.08
6.22
f1 (ppm)


JDIV-263-2 D1.2.fid
C-13 Routine. CPQCI, AVIII-600, 5-12-2016
139.57
114.66
66.10
44.95
purified 13
f1 (ppm)


NMe2
Me2N
purified 20
from reaction above
(1H NMR)
NMe2
13
5.3 mol% Pd(OAc)2
26 mol% CuCl2
3.3 equiv LiCl
9:1 MeCN:H2O
rt, 24 h
[conditions from Ref. 10]
1H NMR of crude
reaction mixture
NMe2
10
5% Pd(OAc)2
4 equiv AcCl
6 equiv H2O
DMA, 120 °C, 2 h
[conditions from this paper]
H
H
NMe2
Cl
• HCl
13, 93% yield
(1H NMR)
7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
f1 (ppm)

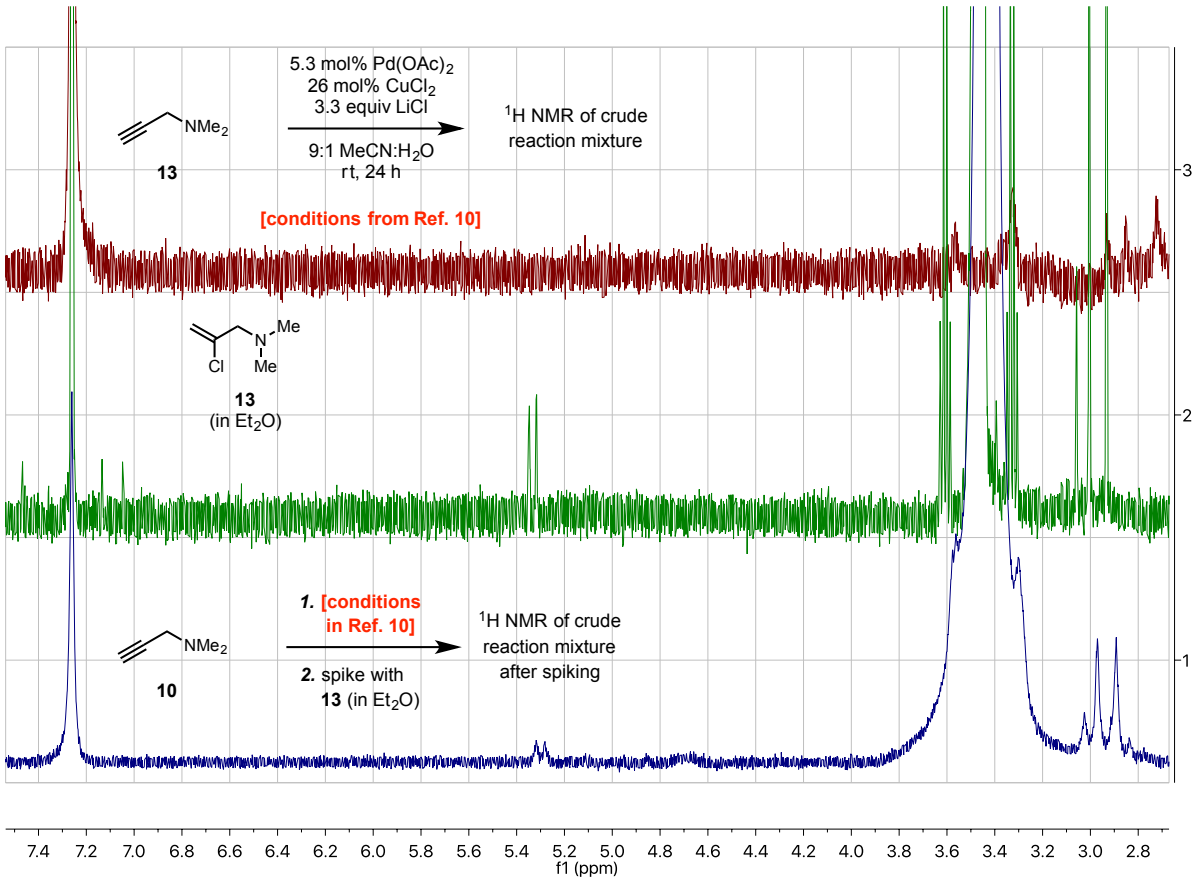
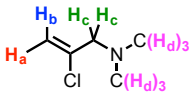
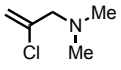



***Table S3.*** Comparison of $^{1}$H NMR shifts of reported **13** (Ref. 10) and authentic **13** from this work.

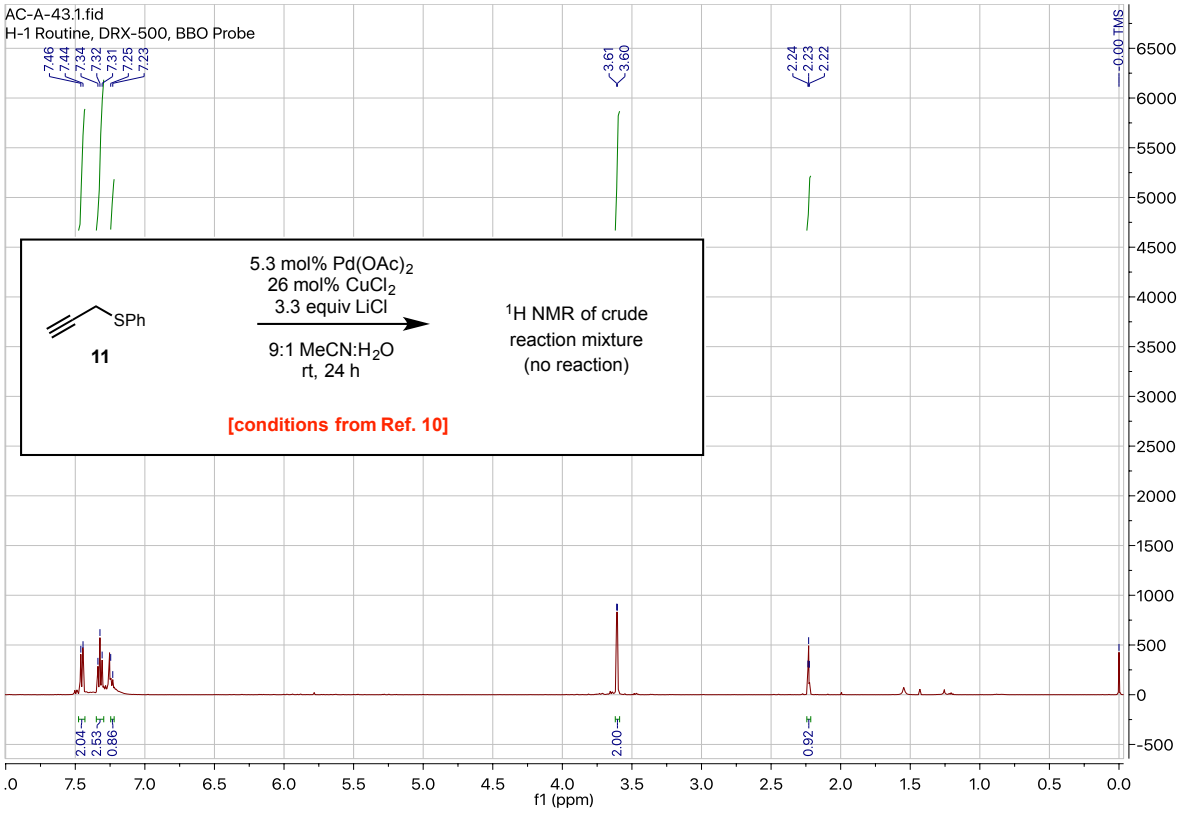


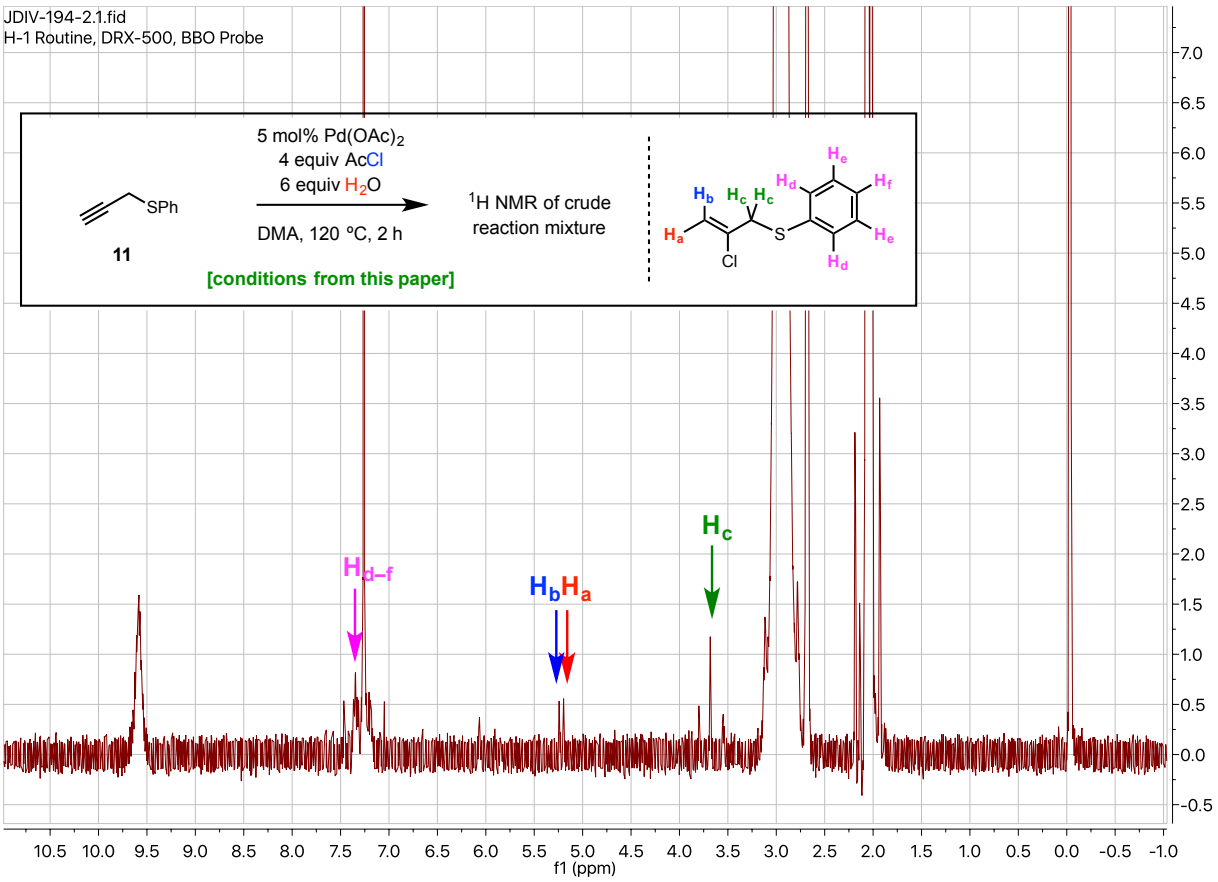

| Compound | $H_a$ | $H_b$ | $H_c$ | $H_d$ |
|---|---|---|---|---|
| **13** (Ref. 10) | 4.77 (bs, 2H) | | 3.34 (s, 2H) | 2.02 (s, 6H) |
| **13**•HCl (this work) | 5.96 (s, 1H) | 5.80 (s, 1H) | 3.93 (s, 2H) | 2.23 (s, 3H) |
| **13** (this work) | 5.36 (s, 1H) | 5.33 (s, 1H) | 3.07 (s, 2H) | 2.23 (s, 3H) |
| **22e** (this work) | 5.45 (s, 1H) | 5.34 (s, 1H) | 4.26 (d, 2H) | --- |

***Table S4.*** Comparison of $^{13}$C NMR shifts of reported **13** (Ref. 10) and authentic **13** from this work.

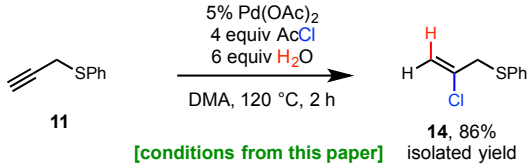



| Compound | $^{13}$C NMR Chemical Shifts (ppm) |
|---|---|
| **13** (Ref. 10) | 138.5, 117.0, 48.5, 44.2 |
| **13** (this work) | 139.6, 114.7, 66.1, 44.9 |

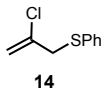

AC-A-43.1.fid
H-1 Routine, DRX-500, BBO Probe
7.46
7.44
7.34
7.32
7.31
7.25
7.23
3.61
3.60
2.24
2.23
2.22
0.00 TMS
SPh
11
5.3 mol% Pd(OAc)2
26 mol% CuCl2
3.3 equiv LiCl
9:1 MeCN:H2O
rt, 24 h
[conditions from Ref. 10]
1H NMR of crude
reaction mixture
(no reaction)
2.04
2.53
0.86
2.00
0.92
f1 (ppm)




In an analogous manner, though we found that that phenyl propargyl sulfide (**11**) was unreactive under the conditions from Ref. 10 (Scheme S14), we found that under our conditions it reacted to provide 86% isolated yield of vinyl chloride **14**, providing an authentic sample for comparison (Table S5). In this case, the $^{1}$H NMR data from Ref. 10 was in better agreement with our data as well as previously published data,[11] except in the aromatic region.

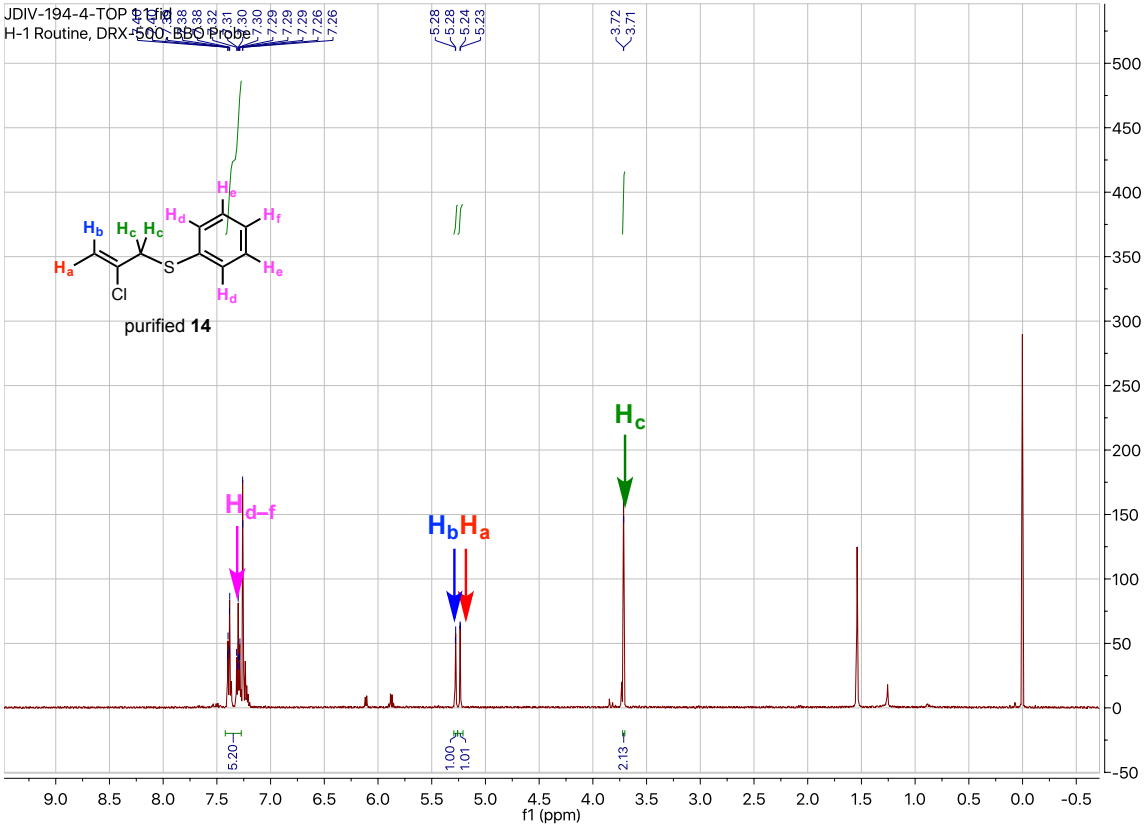



***Scheme S14.*** Hydrochlorination of phenyl propargyl sulfide (**11**) under our optimal reaction conditions from the present paper.




**(2-chloroallyl)(phenyl)sulfane (14):** The title compound was prepared from phenyl propargyl sulfide (14.8 mg, 0.1 mmol) following the standard hydrochlorination procedure. Purification using silica gel flash column chromatography with 5%

EtOAc:hexanes as the eluent gave the product as a colorless oil (13.5 mg, 73% yield). **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.41–7.36 (m, 2H), 7.32–7.26 (m, 2H), 7.25–7.21 (m, 1H), 5.26 (dd, *J* = 21.7, 1.4 Hz, 1H), 3.71 (d, *J* = 1.0 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 131.02, 130.17, 129.17, 127.70, 127.28, 114.98, 42.92; **HRMS** (ESI-TOF) Calcd for C9H9ClS+ [M+H]+ 185.0186, found 185.0182.


JDIV-194-4-TOP P1.fid
H-1 Routine, DRX-500, BBO Probe
purified 14
Hd–f
HbHa
Hc
f1 (ppm)

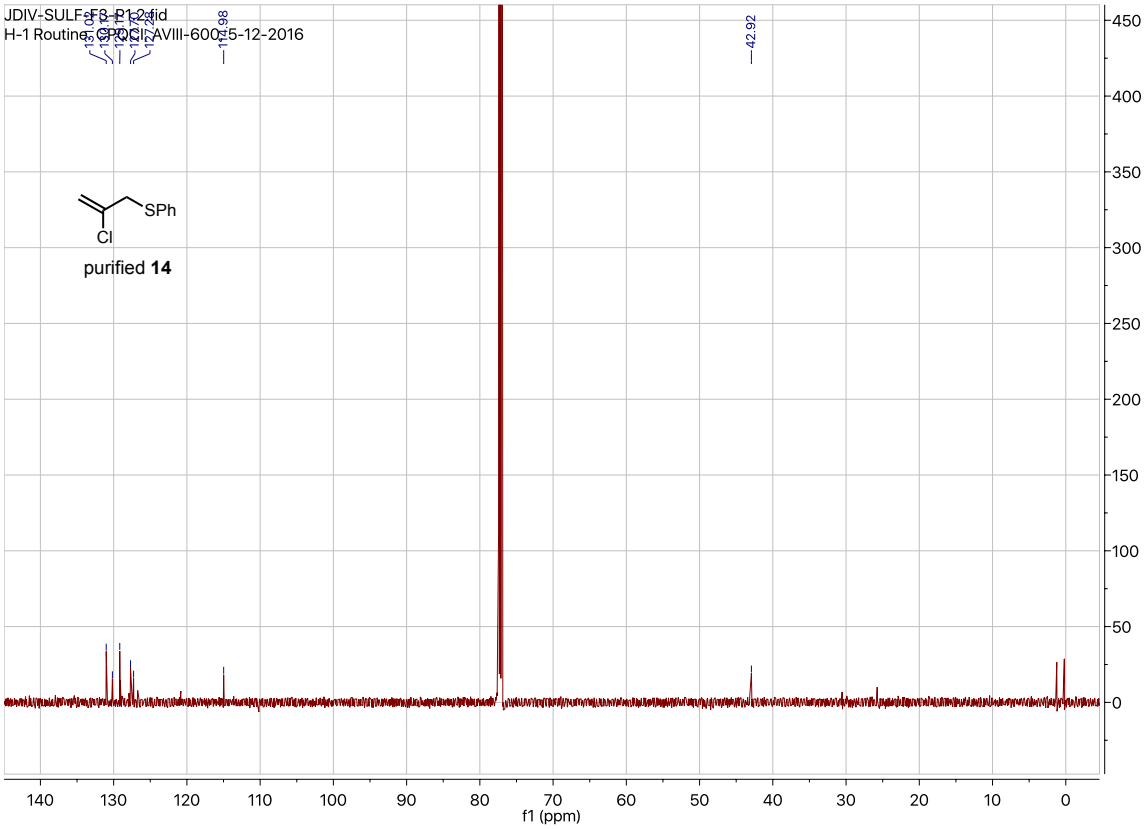
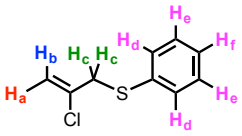
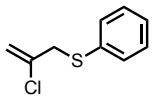

JDIV-SULF-F8-P12.fid
H-1 Routine, CDCl3, AVIII-600-5-12-2016
SPh
Cl
purified 14
f1 (ppm)

***Table S5.*** Comparison of $^{1}$H NMR shifts of reported **14** (Ref. 10), authentic **14** from this work, and previously published spectral data (Ref. 11).




| Compound | $H_a$ | $H_b$ | $H_c$ | $H_{d–f}$ |
|---|---|---|---|---|
| **14** (Ref. 10) | 5.25 (d, 2H) | | 3.69 (s, 2H) | 8.05–7.21 (m, 5H) |
| **14** (this work) | 5.28 (s, 1H) | 5.23 (s, 1H) | 3.72 (s, 2H) | 7.39–7.20 (m, 5H) |
| **14** (Ref. 11) | 5.27 (s, 1H) | 5.19 (s, 1H) | 3.67 (s, 2H) | 7.20 (m, 5H) |

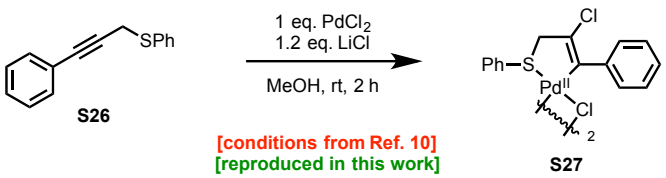
***Table S6.*** Comparison of $^{13}$C NMR shifts of reported **14** (Ref. 10) and authentic **14** from this work.




| Compound | $^{13}$C NMR Chemical Shifts (ppm) |
|---|---|
| **14** (Ref. 10) | 131.17 131.02, 129.17, 127.7, 127.28, 114.98, 42.92 |
| **14** (this work) | 139.5, 136.8, 132.9, 131.9, 129.2, 116.9, 44.8 |

## *Replication of Reported Palladacycle Synthesis and Characterization:*

As the main focus of Ref. 10 was on the preparation of palladacycles via *anti*-chloropalladation, rather than on catalytic hydrochlorination, we next investigated a representative example of stoichiometric *anti*-chloropalladation according to Ref. 10 (Scheme S15). This reaction proceeded as described. After isolation, the $^{1}$H NMR spectra from our sample closely matched the shifts reported in the paper.




***Scheme S15.*** *anti*-Chloropalladation of **S26** according to reported conditions from Ref. 10.

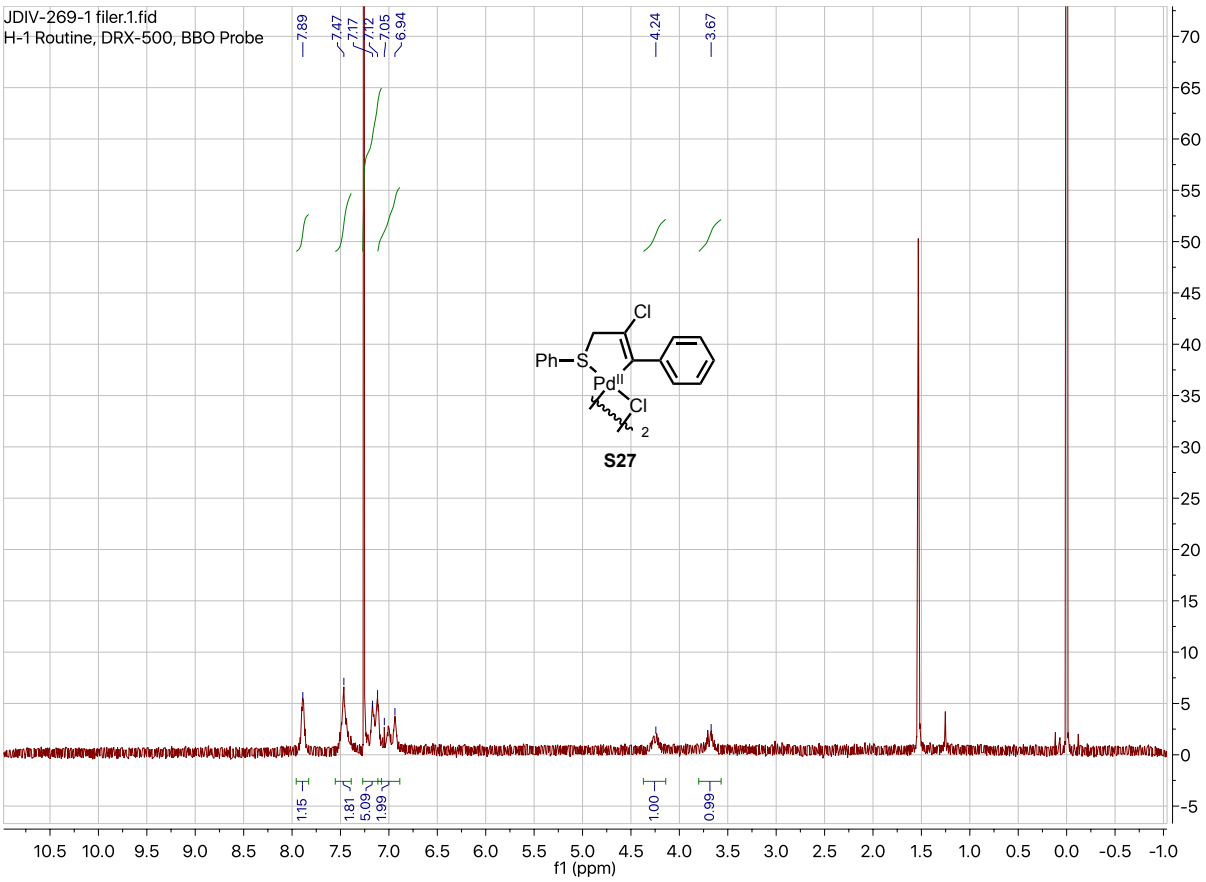
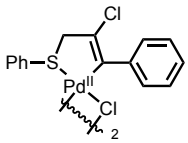


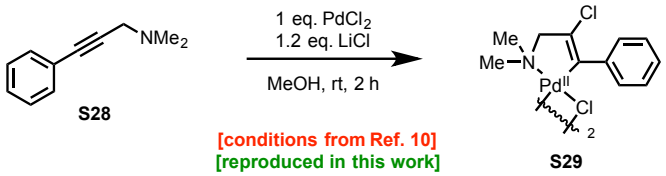

***Table S7.*** Comparison of $^{1}$H NMR shifts of **S27** from Ref. 10 and from this work.




**S27**

| Compound | Solvent | $^{1}$H NMR Chemical Shifts |
|---|---|---|
| **S27** (Ref. 10) | $CDCl_3$ | 7.91–7.03 (m, 10H), 4.27 (d, 1H), 3.70 (d, 1H) |
| **S27** (this work) | $CDCl_3$ | 7.91–6.94 (m, 10H), 4.24 (bs, 1H), 3.67 (bs, 1H) |

***Scheme S16.*** *anti*-Chloropalladation of **S28** according to reported conditions from Ref. 10.



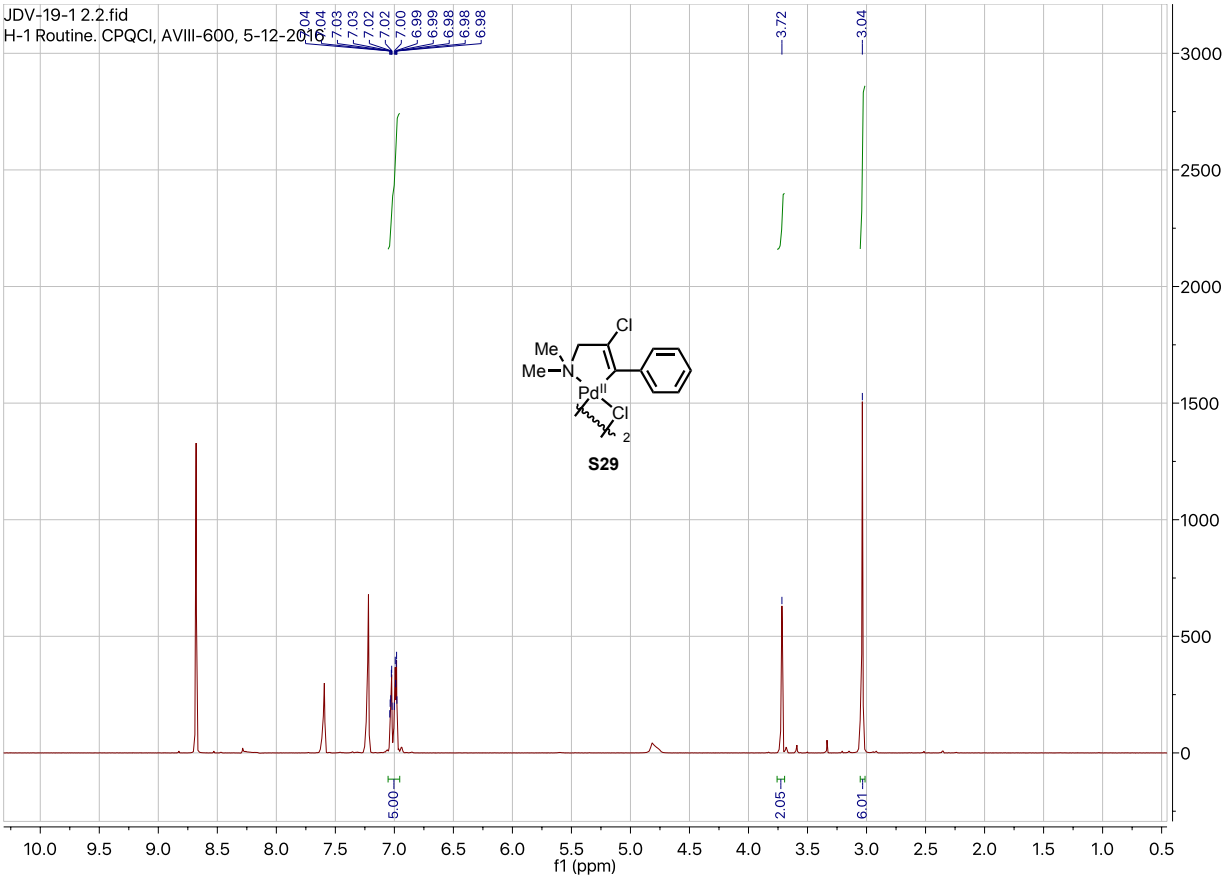
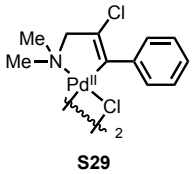
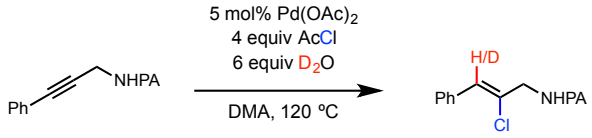




***Table S8.*** Comparison of $^{1}$H NMR shifts of **S29** from Ref. 10 and from this work.




| Compound | Solvent | $^{1}$H NMR Chemical Shifts |
|---|---|---|
| **S27** (Ref. 10) | $CDCl_3$ + $d_5$-pyridine | 6.95-6.85 (m, 5H), 3.71 (d, 2H), 3.05 (s, 6H) |
| **S27** (this work) | $CDCl_3$ + $d_5$-pyridine | 7.04-6.98 (m, 5H), 3.72 (d, 2H), 3.04 (s, 6H) |

*Procedure for Deuterium Incorporation Experiment*

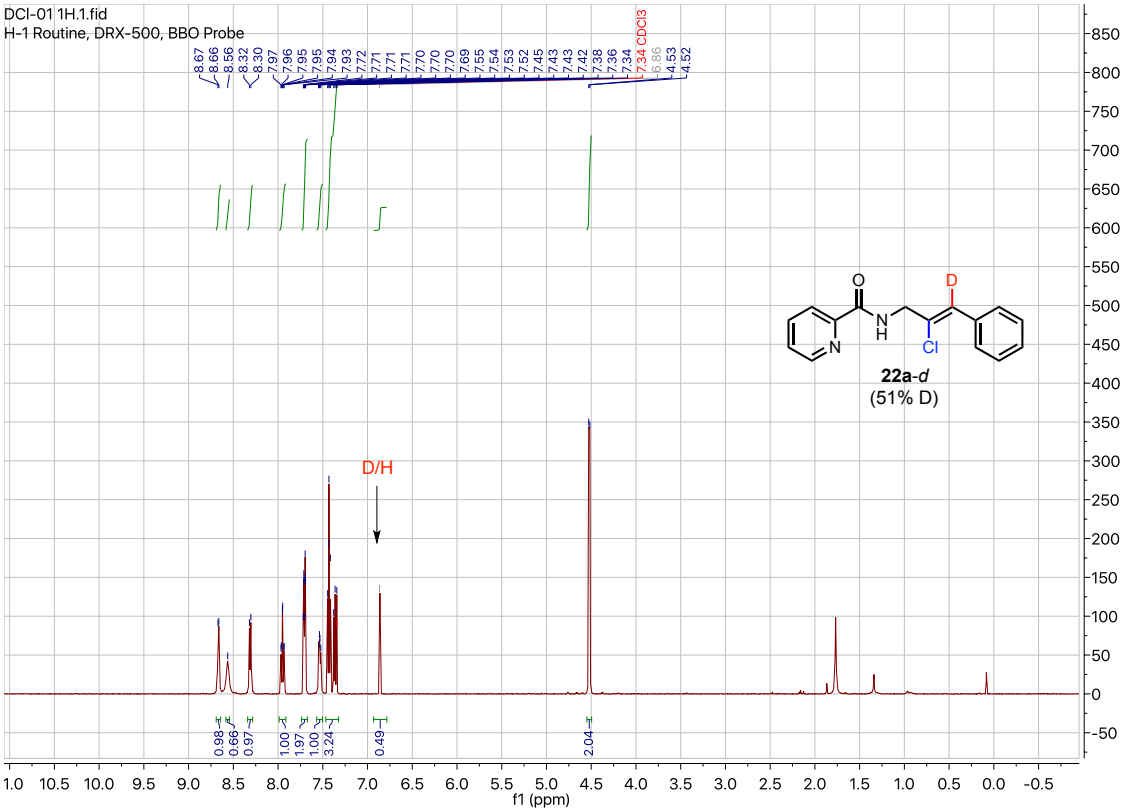


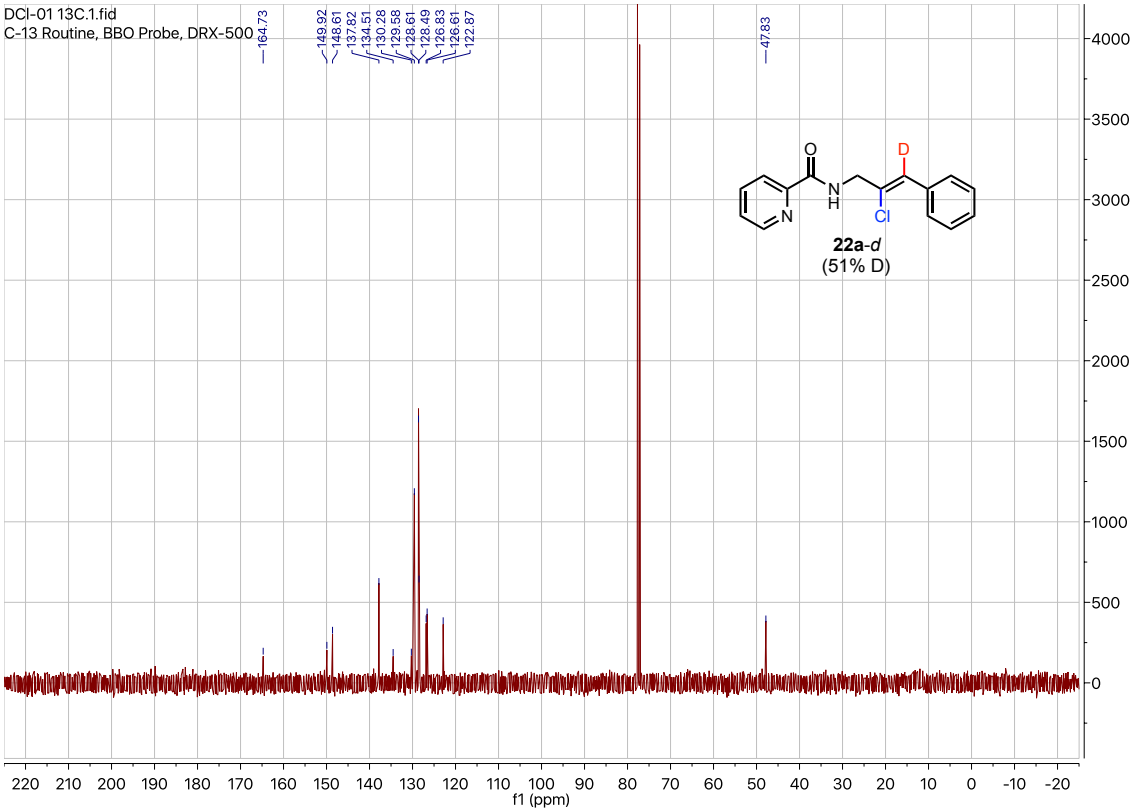

**21a**

**22a-*d*, 92% yield**
**(52% D)**

***Scheme S17:*** Deuterium incorporation experiment with substrate **21a**.

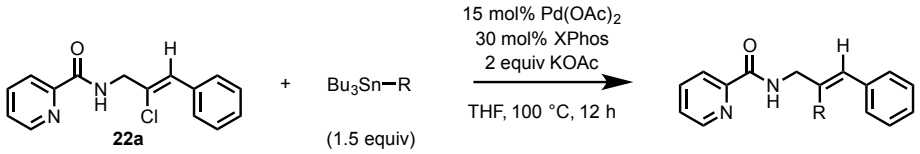
**Deuterium Incorporation Experiment:** To a 5-mL scintillation vial equipped with a Teflon-coated magnetic stir bar were added the propargyl picolinamide **21a** (23.6 mg, 0.1 mmol), acetyl chloride (36 µL, 0.4 mmol), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol, 5 mol %). The vial was sealed with a screw-top septum cap and was then evacuated and backfilled with $N_2$ three times. Under a positive pressure of $N_2$, anhydrous DMA (1.0 mL) was added, followed with $D_2O$ (13.2 µL, 6 equiv). All needle inlets/outlets were removed, and the reaction was allowed to stir at 120 °C for 2 h. After this time, the reaction vial was allowed cooled to room temperature, and the reaction mixture was filtered through a short plug of silica gel (50% EtOAc:hexanes, 10 mL, as eluent). The solvent was removed in *vacuo* to leave a brown residue, which upon purification by silica gel column chromatography, afforded **22a**-*d* (25.6 mg, 92% yield, 51% D).


DCl-01 1H.1.fid
H-1 Routine, DRX-500, BBO Probe
D/H
22a-d
(51% D)
f1 (ppm)

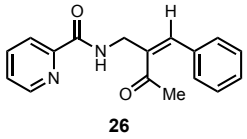

DCl-01 13C.1.fid
C-13 Routine, BBO Probe, DRX-500
22a-d
(51% D)
f1 (ppm)

## *Procedure for Diversification of Alkenyl Chlorides via Stille Coupling*

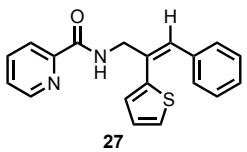
**General Procedure for Stille Coupling:** To an oven-dried 1 dram vial equipped with a Teflon-coated magnetic stir bar were added $Pd(OAc)_2$ (15 mol%), XPhos (30 mol%), anhydrous KOAc (2 eq.), and vinyl chloride substrate, **22a**, (0.1 mmol). Anhydrous THF (0.5 mL) was added and the components were stirred for 1 minute before adding in the appropriate organostannane (1.5 eq.). The reaction vessel was heated to 100 ºC and left to stir for 12 h. Upon completion, the reaction was quenched with $H_2O$ and extracted with EtOAc (5 x 5 mL). Combined organic extracts were dried with $Na_2SO_4$, filtered, and concentrated *in vacuo*. The crude coupling product was purified by silica gel chromatography.




***Scheme S18.*** Diversification of product **22a** by Stille coupling.

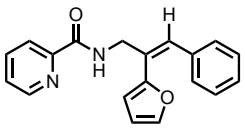



**(*Z*)-*N*-(2-benzylidene-3-oxobutyl)picolinamide (26):** The title compound was prepared from (*Z*)-*N*-(2-chloro-3-phenylallyl)picolinamide (27.2 mg, 0.1 mmol) and tributyl(1-ethoxyvinyl)tin following the general Stille coupling procedure. Purification using silica gel flash column chromatography with 40% EtOAc:hexanes as the eluent gave the product as an off-white solid (20.8 mg, 74% yield). **$^1$H NMR** (500 MHz $CDCl_3$) δ 8.63–8.41 (m, 2H), 8.19 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.83 (td, *J* = 7.7, 1.7 Hz, 1H), 7.70 (s, 1H), 7.62 (d, *J* = 7.4 Hz, 2H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.40 (ddt, *J* = 9.8, 5.2, 2.6 Hz, 2H), 4.55 (d, *J* = 6.0 Hz, 2H), 2.51 (s, 3H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 148.61, 143.62, 139.10, 137.57, 136.81, 130.12, 129.89, 129.24, 128.72, 126.43, 123.96, 122.56, 36.44, 26.38; **HRMS** (ESI-TOF) Calcd for $C_{17}H_{17}N_2O_2^+$ $[M+H]^+$ 281.1285, found 281.1281.



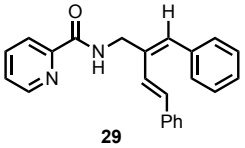

**(*Z*)-*N*-(3-phenyl-2-(thiophen-2-yl)allyl)picolinamide (27):** The title compound was prepared from (*Z*)-*N*-(2-chloro-3-phenylallyl)picolinamide (27.2 mg, 0.1 mmol) and 2-(tributylstannyl)thiophene following the general Stille coupling procedure. Purification using silica gel flash column chromatography with 30% EtOAc:hexanes as the eluent gave the product as a colorless oil (27.0 mg, 84% yield). **$^1$H NMR** (600 MHz $CDCl_3$) δ 8.57 (d, *J* = 4.8 Hz, 1H), 8.38 (d, *J* = 16.1 Hz, 1H), 8.25 (d, *J* = 7.9 Hz, 1H), 7.88 (t, *J* = 7.7 Hz, 1H), 7.46 (tt, *J* = 14.1, 7.9 Hz, 3H), 7.27 (d, *J* = 18.4 Hz, 3H), 7.19 (d, *J* = 7.5 Hz, 2H), 7.07–6.93 (m, 3H), 6.78 (s, 1H), 4.55 (d, *J* = 6.3 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$ δ 148.13, 139.62, 137.35, 136.60, 131.10, 129.59,

129.19, 128.18, 127.30, 126.99, 126.86, 126.23, 125.97, 122.37, 120.23, 47.02; **HRMS** (ESI-TOF) Calcd for $C_{17}H_{19}N_2OS^+$ $[M+H]^+$ 321.1056, found 321.1052.



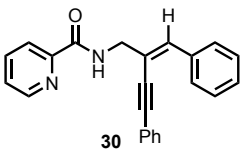
**28**

**(*Z*)-*N*-(2-(furan-2-yl)-3-phenylallyl)picolinamide (28):** The title compound was prepared from (*Z*)-*N*-(2-chloro-3-phenylallyl)picolinamide (27.2 mg, 0.1 mmol) and 2-(tributylstannyl)furan following the general Stille coupling procedure. Purification using silica gel flash column chromatography with 25% EtOAc:hexanes as the eluent gave the product as a yellow oil (26.4 mg, 87% yield). **$^1$H NMR** (500 MHz $CDCl_3$) δ 8.54 (dt, *J* = 4.8, 1.2 Hz, 1H), 8.34 (t, *J* = 6.6 Hz, 1H), 8.27–8.17 (m, 1H), 7.85 (td, *J* = 7.7, 1.8 Hz, 1H), 7.47–7.36 (m, 2H), 7.30 (dd, *J* = 14.9, 3.8 Hz, 2H), 7.23 (q, *J* = 6.9, 5.4 Hz, 3H), 6.70 (s, 1H), 6.43–6.05 (m, 2H), 4.54 (dd, *J* = 6.2, 1.3 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 148.50, 142.12, 137.72, 137.52, 129.21, 128.47, 127.62, 127.43, 126.57, 122.77, 120.62, 111.55, 110.28, 95.95, 44.62; **HRMS** (ESI-TOF) Calcd for $C_{17}H_{19}N_2O_2^+$ $[M+H]^+$ 305.1285, found 305.1289.



**29**

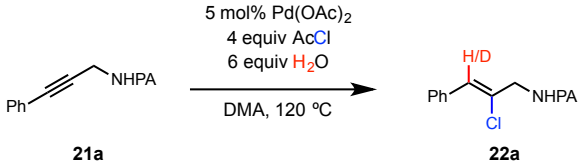
***N*-((*E*)-2-((*E*)-benzylidene)-4-phenylbut-3-en-1-yl)picolinamide (29):** The title compound was prepared from (*Z*)-*N*-(2-chloro-3-phenylallyl)picolinamide (27.2 mg, 0.1 mmol) and tributyl(phenylethenyl}tin following the general Stille coupling procedure. Purification using silica gel flash column chromatography with 10% EtOAc:hexanes as the eluent gave the product as a yellow oil (28.9 mg, 85% yield). **$^1$H NMR** (500 MHz $CDCl_3$) δ 8.51 (ddd, *J* = 4.7, 1.7, 0.9 Hz, 1H), 8.25 (dq, *J* = 7.9, 1.2 Hz, 1H), 8.10 (s, 1H), 7.86 (tt, *J* = 6.0, 1.5 Hz, 1H), 7.48–7.32 (m, 11H), 6.95 (dd, *J* = 16.3, 0.9 Hz, 1H), 6.92 (d, *J* = 3.9 Hz, 1H), 6.82 (d, *J* = 16.3 Hz, 1H), 4.59 (d, *J* = 5.1 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 147.69, 136.86, 136.77, 135.89, 134.86, 134.82, 130.45, 128.71, 128.45, 128.18, 128.13, 127.83, 127.19, 127.14, 126.26, 126.13, 125.72, 121.72, 76.34, 36.26; **HRMS** (ESI-TOF) Calcd for $C_{23}H_{21}N_2O^+$ $[M+H]^+$ 341.1648, found 341.1644.



**30**

**(*E*)-*N*-(2-benzylidene-4-phenylbut-3-yn-1-yl)picolinamide (30):** The title compound was prepared from (*Z*)-*N*-(2-chloro-3-phenylallyl)picolinamide (27.2 mg, 0.1 mmol) and tributyl(phenylethynyl) tin following the general Stille coupling procedure. Purification using silica gel flash column chromatography with 10% EtOAc:hexanes as the eluent gave the product as a yellow oil (27.7 mg, 82% yield). **$^1$H NMR** (500 MHz $CDCl_3$) δ 8.69–8.51 (m, 2H), 8.33 (dt, *J* = 7.8, 1.1 Hz, 1H), 8.02–7.89 (m, 3H), 7.60–7.35 (m, 9H), 6.92 (s, 1H), 4.51 (dd, *J* = 6.2, 1.3 Hz, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 148.55, 137.75, 136.36, 135.71, 132.00, 129.16, 128.94, 128.78, 128.65, 126.63, 123.51, 122.77, 118.64, 97.32, 88.23, 46.30; **HRMS** (ESI-TOF) Calcd for $C_{23}H_{19}N_2O^+$ $[M+H]^+$ 339.1492, found 339.1399.

## *Reaction Progress Kinetic Analysis*




***Scheme S19.*** Standard conditions for reaction investigated in RPKA studies.

**A. Representative aliquot kinetics experiment:** Acetyl chloride (628 mg, 8.00 mmol) was added to a 5-mL volumetric flask and dissolved in dimethylacetamide. Palladium acetate (22.5 mg, 0.100 mmol) and 1,3,5-trimethoxybenzene (111.0 mg, 0.660 mmol) were added to a 5-mL volumetric flask and dissolved in dimethylacetamide. Water (216 mg, 12.00 mmol) was added to a 5-mL volumetric flask and dissolved in dissolved in dimethylacetamide. **21a** (47.2 mg, 0.200 mmol), dimethylacetamide (0.500 mL), palladium stock solution (2.2 mg, 0.01 mmol, 0.500 mL), water stock solution (21.6 mg, 1.200 mmol, 0.500 mL), and a stir bar were added to a 5 $cm^3$ glass vial with a screw cap septum. This mixture was placed in a metal heating block resting on a hot place set for 120 °C and left mixing for 5 min. After this time, acetyl chloride stock solution (62.8 mg, 0.800 mmol, 0.500 mL) was added to the 5 $cm^3$ glass vial. The complete addition of acetyl stock solution was considered t=0 minutes for the kinetic time course. Reaction progress was monitored by removing an aliquot (~15 $mm^3$) from the reaction mixture. Each aliquot was acquired using a new syringe (1 $cm^3$) and hypodermic needle. Each aliquot was quenched upon the moment of collection in a 5 $cm^3$ glass vial containing ethyl acetate (1 mL). The quench solution was plunged in and out of the syringe twice, filtered, and analyzed by an Agilent Technologies 7890A gas chromatography (USA), equipped with a DB-5 column (polyimide coating, 30 mx0.25 mmx0.25µm) manufactured by J&W, and a flame ionization detector (FID) was employed for the separation and quantification of substrates and products. Helium (99.999%) was used as the carrier gas, with a constant flow rate of 6.0 mL/min. The optimized temperature program to be applied in the GC-FID was as follows: It was started from 150 °C, raised to 220 °C by the rate of 14 °C/min, and then raised to 280 °C at 12 °C/min. The temperature of the detector and injector were held at 350 °C and 300 °C respectively. Aliquots were taken at the following time points: 0, 0.5, 5, 10, 15, 20, 25, 30, 40, 50, 60, 90, 120 min.

**B. Experiment conditions (same procedure as above):**

1. Same-excess experiment:

| Same Excess | | | | | | | |
|---|---|---|---|---|---|---|---|
| Substrates: | MW | Mass (mg) | Volume (mL) | Mol (mmol) | Eq. | Conc. (M) | Volume of stock solution (mL) |
| **21a** | 236 | 37.8 | | 0.160 | 1.00 | 0.0800 | N/A |
| $Pd(OAc)_2$ | 224.5 | 2.2 | | 0.010 | 0.06 | 0.0050 | 0.500 |
| AcCl | 78.5 | 59.7 | | 0.760 | 4.75 | 0.3800 | 0.475 |
| 1,3,5-trimethoxybenzene | 168.2 | 11.1 | | 0.066 | 0.41 | 0.0330 | N/A (in Pd stock) |
| $H_2O$ | 18 | 20.9 | | 1.160 | 7.25 | 0.5800 | 0.483 |
| DMA Fill Volume | | | 0.542 | | | | N/A |
| | | Total Volume: | 2.000 | | | | |

2. Same-excess + product experiment:

| Same-excess with Product | | | | | | | |
|---|---|---|---|---|---|---|---|
| Substrates: | MW | Mass (mg) | Volume (mL) | Mol (mmol) | Eq. | Conc. (M) | Volume of stock solution (mL) |
| **21a** | 236 | 47.2 | | 0.200 | 1.00 | 0.1000 | N/A |
| $Pd(OAc)_2$ | 224.5 | 2.2 | | 0.010 | 0.05 | 0.0050 | 0.500 |
| AcCl | 78.5 | 31.4 | | 0.400 | 2.00 | 0.2000 | 0.250 |
| 1,3,5-trimethoxybenzene | 168.2 | 11.1 | | 0.066 | 0.33 | 0.0330 | N/A (in Pd stock) |
| $H_2O$ | 18 | 21.6 | | 1.200 | 6.00 | 0.6000 | 0.500 |
| **22a** | 272 | 10.9 | | 0.040 | 0.25 | 0.0200 | N/A |
| DMA Fill Volume | | | 0.750 | | | | N/A |
| | | Total Volume: | 2.000 | | | | |

3. Pre-mix experiment: see **A** above. A 1 mL aliquot from both the AcCl and $H_2O$ stock solutions were combined and stirred at 120 ºC for one hour. The addition of 1 mL from this new combined stock solution was added to start the experiment.

4. Different-excess experiments:

| Different Excess AcCl | | | | | | | |
|---|---|---|---|---|---|---|---|
| Substrates: | MW | Mass (mg) | Volume (mL) | Mol (mmol) | Eq. | Conc. (M) | Volume of stock solution (mL) |
| **21a** | 236 | 47.2 | | 0.200 | 1.00 | 0.1000 | N/A |
| $Pd(OAc)_2$ | 224.5 | 2.2 | | 0.010 | 0.05 | 0.0050 | 0.500 |
| AcCl | 78.5 | 31.4 | 0.02844203 | 0.400 | 2.00 | 0.2000 | 0.250 |
| 1,3,5-trimethoxybenzene | 168.2 | 11.1 | | 0.066 | 0.33 | 0.0330 | N/A (in Pd stock) |
| $H_2O$ | 18 | 21.6 | | 1.200 | 6.00 | 0.6000 | 0.500 |
| DMA Fill Volume | | | 0.750 | | | | N/A |
| | | Total Volume: | 2.000 | | | | |

| Different Excess $H_2O$ | | | | | | | |
|---|---|---|---|---|---|---|---|
| Substrates: | MW | Mass (mg) | Volume (mL) | Mol (mmol) | Eq. | Conc. (M) | Volume of stock solution (mL) |
| **21a** | 236 | 47.2 | | 0.200 | 1.00 | 0.1000 | N/A |
| $Pd(OAc)_2$ | 224.5 | 2.2 | | 0.010 | 0.05 | 0.0050 | 0.500 |
| AcCl | 78.5 | 62.8 | | 0.800 | 4.00 | 0.4000 | 0.500 |
| 1,3,5-trimethoxybenzene | 168.2 | 11.1 | | 0.066 | 0.33 | 0.0330 | N/A (in Pd stock) |
| $H_2O$ | 18 | 10.8 | | 0.600 | 3.00 | 0.3000 | 0.250 |
| DMA Fill Volume | | | 0.750 | | | | N/A |
| | | Total Volume: | 2.000 | | | | |

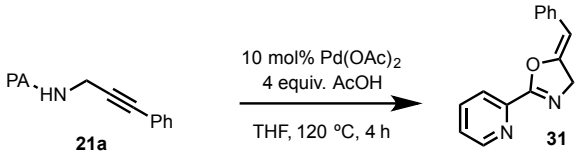
| Different Excess **21a** | | | | | | | |
|---|---|---|---|---|---|---|---|
| Substrates: | MW | Mass (mg) | Volume (mL) | Mol (mmol) | Eq. | Conc. (M) | Volume of stock solution (mL) |
| **21a** | 236 | 37.8 | | 0.160 | 1.00 | 0.0800 | N/A |
| $Pd(OAc)_2$ | 224.5 | 2.2 | | 0.010 | 0.05 | 0.0050 | 0.500 |
| AcCl | 78.5 | 31.4 | | 0.400 | 2.00 | 0.2000 | 0.500 |
| 1,3,5-trimethoxybenzene | 168.2 | 11.1 | | 0.066 | 0.33 | 0.0330 | N/A (in Pd stock) |
| $H_2O$ | 18 | 21.6 | | 1.200 | 6.00 | 0.6000 | 0.500 |
| DMA Fill Volume | | | 0.500 | | | | N/A |
| | | Total Volume: | 2.000 | | | | |

5. KIE experiment (all stock solutions prepared in anhydrous DMA):

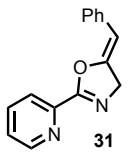
| KIE | | | | | | | |
|---|---|---|---|---|---|---|---|
| Substrates: | MW | Mass (mg) | Volume (mL) | Mol (mmol) | Eq. | Conc. (M) | Volume of stock solution (mL) |
| **21a** | 236 | 47.2 | | 0.200 | 1.00 | 0.1000 | N/A |
| $Pd(OAc)_2$ | 224.5 | 2.2 | | 0.010 | 0.05 | 0.0050 | 0.500 |
| AcCl | 78.5 | 62.8 | | 0.800 | 4.00 | 0.4000 | 0.500 |
| 1,3,5-trimethoxybenzene | 168.2 | 11.1 | | 0.066 | 0.33 | 0.0330 | N/A (in Pd stock) |
| $D_2O$ | 20 | 12.0 | | 0.600 | 3.00 | 0.3000 | 0.500 |
| DMA Fill Volume | | | 0.500 | | | | N/A |
| | | Total Volume: | 2.000 | | | | |

## *General Procedure for Oxazoline Synthesis*|

**General Procedure for Oxazoline Synthesis:** To an oven-dried 1 dram vial equipped with a Teflon-coated magnetic stir bar were added $Pd(OAc)_2$ (10 mol%), AcOH (4 eq.), and alkyne substrate **21a** (0.1 mmol). Anhydrous THF (0.5 mL) was added and the vessel was heated to 120 ºC and left to stir for 4 h. Upon completion, the reaction was quenched with $H_2O$ and extracted with EtOAc (5 x 5 mL). Combined organic extracts were dried with $Na_2SO_4$, filtered, and concentrated *in vacuo*. The crude oxazoline product was purified by preparative TLC.




***Scheme S20.*** Formation of oxazoline **31** from alkyne substrate **21a**.




**(*E*)-5-benzylidene-2-(pyridin-2-yl)-4,5-dihydrooxazole (31):** The title compound was prepared from alkyne substrate **21a** (23.6 mg, 0.1 mmol) following the standard oxazoline synthesis procedure. Purification using silica gel flash column chromatography with 66% EtOAc:hexanes as the eluent gave the product as an orange oil (15.1 mg, 64% yield). **$^1$H NMR** (600 MHz $CDCl_3$) δ 8.71 (dt, *J* = 5.0, 1.2 Hz, 1H), 8.09 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.78 (d, *J* = 1.8 Hz, 1H), 7.36–7.25 (m, 6H), 6.88 (s, 1H), 4.13 (s, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ 160.01, 153.17, 149.90, 146.29, 136.89, 136.27, 128.81, 128.73, 126.99, 125.41, 124.36, 121.77, 32.25; **HRMS** (ESI-TOF) Calcd for $C_{15}H_{13}N_2O^+$ $[M+H]^+$ 237.1022, found 237.1029.

*X-ray Crystallography Data*

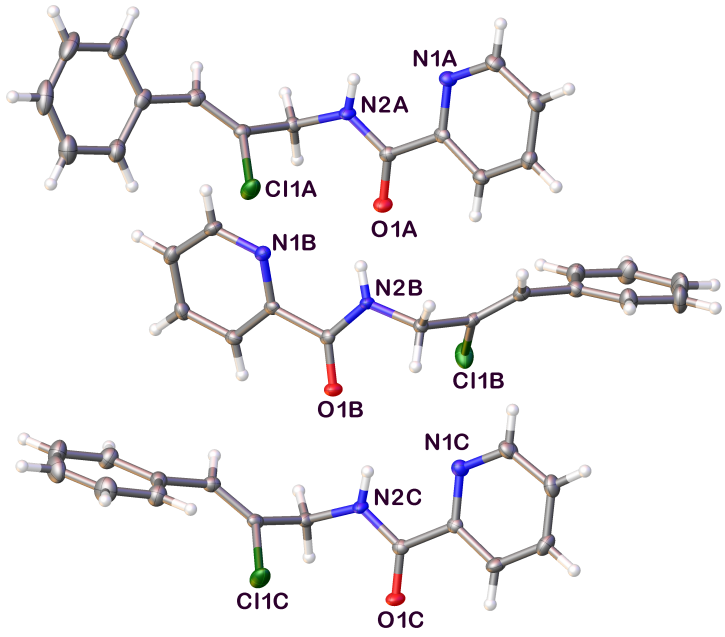



***Table S9.*** Crystal data and structure refinement for **22a** (engle17_a).

| | | |
|---|---|---|
| Identification code | HCl-01 | |
| Empirical formula | C15 H13 Cl N2 O | |
| Formula weight | 272.72 | |
| Temperature | 100 K | |
| Wavelength | 0.71073 Å | |
| Crystal system | Monoclinic | |
| Space group | P 21/c | |
| Unit cell dimensions | a = 13.195(4) Å | α= 90°. |
| | b = 28.087(7) Å | β= 96.998(7)°. |
| | c = 10.834(3) Å | γ = 90°. |
| Volume | 3985.3(18) $Å^3$ | |
| Z, Z' | 12, 3 | |
| Density (calculated) | 1.364 $Mg/m^3$ | |
| Absorption coefficient | 0.280 $mm^{-1}$ | |
| F(000) | 1704 | |
| Crystal size | 0.27 x 0.13 x 0.08 $mm^3$ | |
| Theta range for data collection | 1.716 to 26.375°. | |
| Index ranges | -16<=h<=15, -35<=k<=34, -13<=l<=13 | |

| | |
|---|---|
| Reflections collected | 25934 |
| Independent reflections | 8145 [R(int) = 0.0582] |
| Completeness to theta = 26.000° | 99.8 % |
| Absorption correction | Semi-empirical from equivalents |
| Max. and min. transmission | 0.2602 and 0.2142 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 8145 / 0 / 514 |
| Goodness-of-fit on $F^2$ | 1.016 |
| Final R indices [I>2sigma(I)] | R1 = 0.0464, wR2 = 0.0926 |
| R indices (all data) | R1 = 0.0859, wR2 = 0.1092 |
| Extinction coefficient | n/a |
| Largest diff. peak and hole | 0.303 and -0.292 e.$Å^{-3}$ |

***Table S10.*** Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($Å^2$x $10^3$) for **22a** (engle17_a). U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| Cl(1A) | 7469(1) | 4552(1) | 8629(1) | 27(1) |
| Cl(1B) | 2636(1) | 6194(1) | 6225(1) | 27(1) |
| Cl(1C) | 7106(1) | 7826(1) | 8450(1) | 29(1) |
| O(1B) | 5115(1) | 6415(1) | 6485(1) | 20(1) |
| O(1C) | 4516(1) | 8070(1) | 8154(1) | 22(1) |
| O(1A) | 4881(1) | 4758(1) | 8183(1) | 21(1) |
| N(2C) | 4973(1) | 7329(1) | 7573(2) | 15(1) |
| N(2B) | 4721(1) | 5662(1) | 7036(2) | 14(1) |
| N(2A) | 5417(1) | 4010(1) | 7791(2) | 16(1) |
| N(1A) | 4139(1) | 3642(1) | 9317(2) | 17(1) |
| N(1C) | 3694(1) | 6931(1) | 9041(2) | 18(1) |
| N(1B) | 6157(1) | 5311(1) | 5678(2) | 16(1) |
| C(5B) | 5930(2) | 5777(1) | 5564(2) | 14(1) |
| C(5A) | 4216(2) | 4117(1) | 9270(2) | 14(1) |
| C(10B) | 1114(2) | 5572(1) | 7593(2) | 19(1) |
| C(7A) | 6078(2) | 4154(1) | 6878(2) | 16(1) |
| C(9B) | 2230(2) | 5565(1) | 7951(2) | 16(1) |
| C(6C) | 4460(2) | 7632(1) | 8220(2) | 15(1) |
| C(4C) | 3310(2) | 7693(1) | 9870(2) | 20(1) |
| C(6A) | 4867(2) | 4324(1) | 8355(2) | 15(1) |
| C(8C) | 6759(2) | 7440(1) | 7206(2) | 16(1) |
| C(8A) | 7190(2) | 4157(1) | 7391(2) | 16(1) |
| C(6B) | 5212(2) | 5981(1) | 6411(2) | 14(1) |
| C(11B) | 671(2) | 5537(1) | 6363(2) | 25(1) |
| C(5C) | 3784(2) | 7405(1) | 9074(2) | 14(1) |
| C(7B) | 4063(2) | 5805(1) | 7953(2) | 15(1) |
| C(3A) | 3213(2) | 4229(1) | 10926(2) | 20(1) |
| C(8B) | 2947(2) | 5807(1) | 7468(2) | 15(1) |
| C(7C) | 5649(2) | 7484(1) | 6695(2) | 16(1) |
| C(4B) | 6316(2) | 6076(1) | 4719(2) | 16(1) |

| | | | | |
|---|---|---|---|---|
| C(3B) | 6987(2) | 5889(1) | 3959(2) | 20(1) |
| C(9C) | 7417(2) | 7147(1) | 6776(2) | 17(1) |
| C(2A) | 3117(2) | 3743(1) | 10981(2) | 21(1) |
| C(11C) | 9120(2) | 6934(1) | 6242(2) | 25(1) |
| C(10C) | 8519(2) | 7068(1) | 7153(2) | 19(1) |
| C(1C) | 3104(2) | 6733(1) | 9826(2) | 22(1) |
| C(4A) | 3766(2) | 4423(1) | 10043(2) | 17(1) |
| C(3C) | 2694(2) | 7482(1) | 10666(2) | 24(1) |
| C(9A) | 7902(2) | 3886(1) | 6985(2) | 19(1) |
| C(2B) | 7235(2) | 5413(1) | 4066(2) | 20(1) |
| C(15B) | 476(2) | 5619(1) | 8516(2) | 26(1) |
| C(15C) | 8988(2) | 7105(1) | 8378(2) | 26(1) |
| C(14C) | 10031(2) | 7022(1) | 8656(2) | 32(1) |
| C(2C) | 2588(2) | 6993(1) | 10638(2) | 23(1) |
| C(12B) | -379(2) | 5562(1) | 6069(2) | 29(1) |
| C(1A) | 3589(2) | 3463(1) | 10167(2) | 22(1) |
| C(1B) | 6800(2) | 5138(1) | 4925(2) | 20(1) |
| C(13C) | 10610(2) | 6900(1) | 7734(2) | 34(1) |
| C(12C) | 10156(2) | 6854(1) | 6524(2) | 32(1) |
| C(13B) | -1003(2) | 5623(1) | 6989(2) | 33(1) |
| C(10A) | 9014(2) | 3857(1) | 7382(2) | 22(1) |
| C(15A) | 9616(2) | 4247(1) | 7766(2) | 27(1) |
| C(14B) | -576(2) | 5650(1) | 8214(2) | 33(1) |
| C(11A) | 9486(2) | 3413(1) | 7347(2) | 32(1) |
| C(14A) | 10654(2) | 4193(1) | 8159(2) | 35(1) |
| C(12A) | 10514(2) | 3359(1) | 7754(3) | 41(1) |
| C(13A) | 11092(2) | 3748(1) | 8163(2) | 39(1) |

***Table S11.*** Bond lengths [Å] and angles [°] for **22a** (engle17_a).

| | |
|---|---|
| Cl(1A)-C(8A) | 1.745(2) |
| Cl(1B)-C(8B) | 1.740(2) |
| Cl(1C)-C(8C) | 1.746(2) |
| O(1B)-C(6B) | 1.230(3) |
| O(1C)-C(6C) | 1.234(3) |
| O(1A)-C(6A) | 1.232(3) |
| N(2C)-H(2C) | 0.8800 |
| N(2C)-C(6C) | 1.338(3) |
| N(2C)-C(7C) | 1.448(3) |
| N(2B)-H(2B) | 0.8800 |
| N(2B)-C(6B) | 1.336(3) |
| N(2B)-C(7B) | 1.453(3) |
| N(2A)-H(2A) | 0.8800 |
| N(2A)-C(7A) | 1.453(3) |
| N(2A)-C(6A) | 1.338(3) |
| N(1A)-C(5A) | 1.339(3) |
| N(1A)-C(1A) | 1.340(3) |
| N(1C)-C(5C) | 1.337(3) |
| N(1C)-C(1C) | 1.340(3) |
| N(1B)-C(5B) | 1.343(3) |
| N(1B)-C(1B) | 1.338(3) |
| C(5B)-C(6B) | 1.510(3) |
| C(5B)-C(4B) | 1.385(3) |
| C(5A)-C(6A) | 1.506(3) |
| C(5A)-C(4A) | 1.383(3) |
| C(10B)-C(9B) | 1.477(3) |
| C(10B)-C(11B) | 1.392(3) |
| C(10B)-C(15B) | 1.390(3) |
| C(7A)-H(7AA) | 0.9900 |
| C(7A)-H(7AB) | 0.9900 |
| C(7A)-C(8A) | 1.504(3) |
| C(9B)-H(9B) | 0.9500 |
| C(9B)-C(8B) | 1.323(3) |

| | |
|---|---|
| C(6C)-C(5C) | 1.504(3) |
| C(4C)-H(4C) | 0.9500 |
| C(4C)-C(5C) | 1.386(3) |
| C(4C)-C(3C) | 1.388(3) |
| C(8C)-C(7C) | 1.505(3) |
| C(8C)-C(9C) | 1.322(3) |
| C(8A)-C(9A) | 1.325(3) |
| C(11B)-H(11B) | 0.9500 |
| C(11B)-C(12B) | 1.385(3) |
| C(7B)-H(7BA) | 0.9900 |
| C(7B)-H(7BB) | 0.9900 |
| C(7B)-C(8B) | 1.502(3) |
| C(3A)-H(3A) | 0.9500 |
| C(3A)-C(2A) | 1.375(3) |
| C(3A)-C(4A) | 1.384(3) |
| C(7C)-H(7CA) | 0.9900 |
| C(7C)-H(7CB) | 0.9900 |
| C(4B)-H(4B) | 0.9500 |
| C(4B)-C(3B) | 1.385(3) |
| C(3B)-H(3B) | 0.9500 |
| C(3B)-C(2B) | 1.377(3) |
| C(9C)-H(9C) | 0.9500 |
| C(9C)-C(10C) | 1.478(3) |
| C(2A)-H(2AA) | 0.9500 |
| C(2A)-C(1A) | 1.384(3) |
| C(11C)-H(11C) | 0.9500 |
| C(11C)-C(10C) | 1.390(3) |
| C(11C)-C(12C) | 1.383(3) |
| C(10C)-C(15C) | 1.398(3) |
| C(1C)-H(1C) | 0.9500 |
| C(1C)-C(2C) | 1.385(3) |
| C(4A)-H(4A) | 0.9500 |
| C(3C)-H(3C) | 0.9500 |
| C(3C)-C(2C) | 1.381(3) |
| C(9A)-H(9A) | 0.9500 |

| | |
|---|---|
| C(9A)-C(10A) | 1.480(3) |
| C(2B)-H(2BA) | 0.9500 |
| C(2B)-C(1B) | 1.387(3) |
| C(15B)-H(15B) | 0.9500 |
| C(15B)-C(14B) | 1.390(3) |
| C(15C)-H(15C) | 0.9500 |
| C(15C)-C(14C) | 1.392(3) |
| C(14C)-H(14C) | 0.9500 |
| C(14C)-C(13C) | 1.373(4) |
| C(2C)-H(2CA) | 0.9500 |
| C(12B)-H(12B) | 0.9500 |
| C(12B)-C(13B) | 1.379(3) |
| C(1A)-H(1A) | 0.9500 |
| C(1B)-H(1B) | 0.9500 |
| C(13C)-H(13C) | 0.9500 |
| C(13C)-C(12C) | 1.379(3) |
| C(12C)-H(12C) | 0.9500 |
| C(13B)-H(13B) | 0.9500 |
| C(13B)-C(14B) | 1.379(3) |
| C(10A)-C(15A) | 1.389(3) |
| C(10A)-C(11A) | 1.397(3) |
| C(15A)-H(15A) | 0.9500 |
| C(15A)-C(14A) | 1.391(3) |
| C(14B)-H(14B) | 0.9500 |
| C(11A)-H(11A) | 0.9500 |
| C(11A)-C(12A) | 1.383(3) |
| C(14A)-H(14A) | 0.9500 |
| C(14A)-C(13A) | 1.377(4) |
| C(12A)-H(12A) | 0.9500 |
| C(12A)-C(13A) | 1.374(4) |
| C(13A)-H(13A) | 0.9500 |

| | |
|---|---|
| C(6C)-N(2C)-H(2C) | 118.5 |
| C(6C)-N(2C)-C(7C) | 123.0(2) |
| C(7C)-N(2C)-H(2C) | 118.5 |

| | |
|---|---|
| C(6B)-N(2B)-H(2B) | 119.1 |
| C(6B)-N(2B)-C(7B) | 121.86(19) |
| C(7B)-N(2B)-H(2B) | 119.1 |
| C(7A)-N(2A)-H(2A) | 119.0 |
| C(6A)-N(2A)-H(2A) | 119.0 |
| C(6A)-N(2A)-C(7A) | 122.0(2) |
| C(5A)-N(1A)-C(1A) | 116.8(2) |
| C(5C)-N(1C)-C(1C) | 116.8(2) |
| C(1B)-N(1B)-C(5B) | 116.6(2) |
| N(1B)-C(5B)-C(6B) | 117.58(19) |
| N(1B)-C(5B)-C(4B) | 123.8(2) |
| C(4B)-C(5B)-C(6B) | 118.6(2) |
| N(1A)-C(5A)-C(6A) | 117.53(19) |
| N(1A)-C(5A)-C(4A) | 123.7(2) |
| C(4A)-C(5A)-C(6A) | 118.7(2) |
| C(11B)-C(10B)-C(9B) | 122.6(2) |
| C(15B)-C(10B)-C(9B) | 119.0(2) |
| C(15B)-C(10B)-C(11B) | 118.4(2) |
| N(2A)-C(7A)-H(7AA) | 109.0 |
| N(2A)-C(7A)-H(7AB) | 109.0 |
| N(2A)-C(7A)-C(8A) | 112.88(17) |
| H(7AA)-C(7A)-H(7AB) | 107.8 |
| C(8A)-C(7A)-H(7AA) | 109.0 |
| C(8A)-C(7A)-H(7AB) | 109.0 |
| C(10B)-C(9B)-H(9B) | 115.6 |
| C(8B)-C(9B)-C(10B) | 128.9(2) |
| C(8B)-C(9B)-H(9B) | 115.6 |
| O(1C)-C(6C)-N(2C) | 124.5(2) |
| O(1C)-C(6C)-C(5C) | 120.2(2) |
| N(2C)-C(6C)-C(5C) | 115.4(2) |
| C(5C)-C(4C)-H(4C) | 120.6 |
| C(5C)-C(4C)-C(3C) | 118.7(2) |
| C(3C)-C(4C)-H(4C) | 120.6 |
| O(1A)-C(6A)-N(2A) | 124.4(2) |
| O(1A)-C(6A)-C(5A) | 120.1(2) |

| | |
|---|---|
| N(2A)-C(6A)-C(5A) | 115.5(2) |
| C(7C)-C(8C)-Cl(1C) | 112.67(16) |
| C(9C)-C(8C)-Cl(1C) | 122.38(17) |
| C(9C)-C(8C)-C(7C) | 125.0(2) |
| C(7A)-C(8A)-Cl(1A) | 113.11(16) |
| C(9A)-C(8A)-Cl(1A) | 121.82(18) |
| C(9A)-C(8A)-C(7A) | 125.1(2) |
| O(1B)-C(6B)-N(2B) | 124.8(2) |
| O(1B)-C(6B)-C(5B) | 119.6(2) |
| N(2B)-C(6B)-C(5B) | 115.6(2) |
| C(10B)-C(11B)-H(11B) | 119.7 |
| C(12B)-C(11B)-C(10B) | 120.5(2) |
| C(12B)-C(11B)-H(11B) | 119.7 |
| N(1C)-C(5C)-C(6C) | 117.63(19) |
| N(1C)-C(5C)-C(4C) | 123.6(2) |
| C(4C)-C(5C)-C(6C) | 118.8(2) |
| N(2B)-C(7B)-H(7BA) | 108.8 |
| N(2B)-C(7B)-H(7BB) | 108.8 |
| N(2B)-C(7B)-C(8B) | 113.77(17) |
| H(7BA)-C(7B)-H(7BB) | 107.7 |
| C(8B)-C(7B)-H(7BA) | 108.8 |
| C(8B)-C(7B)-H(7BB) | 108.8 |
| C(2A)-C(3A)-H(3A) | 120.7 |
| C(2A)-C(3A)-C(4A) | 118.6(2) |
| C(4A)-C(3A)-H(3A) | 120.7 |
| C(9B)-C(8B)-Cl(1B) | 120.96(17) |
| C(9B)-C(8B)-C(7B) | 125.3(2) |
| C(7B)-C(8B)-Cl(1B) | 113.66(16) |
| N(2C)-C(7C)-C(8C) | 112.59(17) |
| N(2C)-C(7C)-H(7CA) | 109.1 |
| N(2C)-C(7C)-H(7CB) | 109.1 |
| C(8C)-C(7C)-H(7CA) | 109.1 |
| C(8C)-C(7C)-H(7CB) | 109.1 |
| H(7CA)-C(7C)-H(7CB) | 107.8 |
| C(5B)-C(4B)-H(4B) | 120.8 |

| | |
|---|---|
| C(3B)-C(4B)-C(5B) | 118.3(2) |
| C(3B)-C(4B)-H(4B) | 120.8 |
| C(4B)-C(3B)-H(3B) | 120.6 |
| C(2B)-C(3B)-C(4B) | 118.9(2) |
| C(2B)-C(3B)-H(3B) | 120.6 |
| C(8C)-C(9C)-H(9C) | 114.2 |
| C(8C)-C(9C)-C(10C) | 131.5(2) |
| C(10C)-C(9C)-H(9C) | 114.2 |
| C(3A)-C(2A)-H(2AA) | 120.4 |
| C(3A)-C(2A)-C(1A) | 119.1(2) |
| C(1A)-C(2A)-H(2AA) | 120.4 |
| C(10C)-C(11C)-H(11C) | 119.3 |
| C(12C)-C(11C)-H(11C) | 119.3 |
| C(12C)-C(11C)-C(10C) | 121.4(2) |
| C(11C)-C(10C)-C(9C) | 118.1(2) |
| C(11C)-C(10C)-C(15C) | 118.0(2) |
| C(15C)-C(10C)-C(9C) | 123.9(2) |
| N(1C)-C(1C)-H(1C) | 118.2 |
| N(1C)-C(1C)-C(2C) | 123.7(2) |
| C(2C)-C(1C)-H(1C) | 118.2 |
| C(5A)-C(4A)-C(3A) | 118.5(2) |
| C(5A)-C(4A)-H(4A) | 120.8 |
| C(3A)-C(4A)-H(4A) | 120.8 |
| C(4C)-C(3C)-H(3C) | 120.8 |
| C(2C)-C(3C)-C(4C) | 118.4(2) |
| C(2C)-C(3C)-H(3C) | 120.8 |
| C(8A)-C(9A)-H(9A) | 114.6 |
| C(8A)-C(9A)-C(10A) | 130.9(2) |
| C(10A)-C(9A)-H(9A) | 114.6 |
| C(3B)-C(2B)-H(2BA) | 120.6 |
| C(3B)-C(2B)-C(1B) | 118.8(2) |
| C(1B)-C(2B)-H(2BA) | 120.6 |
| C(10B)-C(15B)-H(15B) | 119.6 |
| C(14B)-C(15B)-C(10B) | 120.8(2) |
| C(14B)-C(15B)-H(15B) | 119.6 |

| | |
|---|---|
| C(10C)-C(15C)-H(15C) | 119.8 |
| C(14C)-C(15C)-C(10C) | 120.3(2) |
| C(14C)-C(15C)-H(15C) | 119.8 |
| C(15C)-C(14C)-H(14C) | 119.7 |
| C(13C)-C(14C)-C(15C) | 120.5(2) |
| C(13C)-C(14C)-H(14C) | 119.7 |
| C(1C)-C(2C)-H(2CA) | 120.6 |
| C(3C)-C(2C)-C(1C) | 118.8(2) |
| C(3C)-C(2C)-H(2CA) | 120.6 |
| C(11B)-C(12B)-H(12B) | 119.7 |
| C(13B)-C(12B)-C(11B) | 120.6(2) |
| C(13B)-C(12B)-H(12B) | 119.7 |
| N(1A)-C(1A)-C(2A) | 123.2(2) |
| N(1A)-C(1A)-H(1A) | 118.4 |
| C(2A)-C(1A)-H(1A) | 118.4 |
| N(1B)-C(1B)-C(2B) | 123.5(2) |
| N(1B)-C(1B)-H(1B) | 118.2 |
| C(2B)-C(1B)-H(1B) | 118.2 |
| C(14C)-C(13C)-H(13C) | 120.1 |
| C(14C)-C(13C)-C(12C) | 119.9(2) |
| C(12C)-C(13C)-H(13C) | 120.1 |
| C(11C)-C(12C)-H(12C) | 120.1 |
| C(13C)-C(12C)-C(11C) | 119.9(2) |
| C(13C)-C(12C)-H(12C) | 120.1 |
| C(12B)-C(13B)-H(13B) | 120.3 |
| C(14B)-C(13B)-C(12B) | 119.5(2) |
| C(14B)-C(13B)-H(13B) | 120.3 |
| C(15A)-C(10A)-C(9A) | 123.6(2) |
| C(15A)-C(10A)-C(11A) | 118.2(2) |
| C(11A)-C(10A)-C(9A) | 118.2(2) |
| C(10A)-C(15A)-H(15A) | 119.6 |
| C(10A)-C(15A)-C(14A) | 120.7(3) |
| C(14A)-C(15A)-H(15A) | 119.6 |
| C(15B)-C(14B)-H(14B) | 119.9 |
| C(13B)-C(14B)-C(15B) | 120.2(2) |

| | |
|---|---|
| C(13B)-C(14B)-H(14B) | 119.9 |
| C(10A)-C(11A)-H(11A) | 119.6 |
| C(12A)-C(11A)-C(10A) | 120.8(3) |
| C(12A)-C(11A)-H(11A) | 119.6 |
| C(15A)-C(14A)-H(14A) | 120.1 |
| C(13A)-C(14A)-C(15A) | 119.9(3) |
| C(13A)-C(14A)-H(14A) | 120.1 |
| C(11A)-C(12A)-H(12A) | 120.0 |
| C(13A)-C(12A)-C(11A) | 120.0(3) |
| C(13A)-C(12A)-H(12A) | 120.0 |
| C(14A)-C(13A)-H(13A) | 119.9 |
| C(12A)-C(13A)-C(14A) | 120.3(3) |
| C(12A)-C(13A)-H(13A) | 119.9 |

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Symmetry transformations used to generate equivalent atoms:

***Table S12.*** Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **22a** (engle17_a). The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ \ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| Cl(1A) | 21(1) | 30(1) | 28(1) | -14(1) | 2(1) | 1(1) |
| Cl(1B) | 21(1) | 34(1) | 28(1) | 16(1) | 5(1) | 5(1) |
| Cl(1C) | 22(1) | 30(1) | 34(1) | -18(1) | 2(1) | -1(1) |
| O(1B) | 24(1) | 11(1) | 25(1) | -1(1) | 9(1) | 0(1) |
| O(1C) | 29(1) | 10(1) | 28(1) | 1(1) | 12(1) | 1(1) |
| O(1A) | 26(1) | 13(1) | 25(1) | 3(1) | 8(1) | 2(1) |
| N(2C) | 18(1) | 9(1) | 20(1) | 2(1) | 7(1) | 2(1) |
| N(2B) | 15(1) | 10(1) | 18(1) | -2(1) | 5(1) | 0(1) |
| N(2A) | 20(1) | 10(1) | 18(1) | 2(1) | 5(1) | 1(1) |
| N(1A) | 20(1) | 14(1) | 17(1) | 2(1) | 3(1) | 0(1) |
| N(1C) | 20(1) | 18(1) | 17(1) | -1(1) | 4(1) | -2(1) |
| N(1B) | 15(1) | 14(1) | 19(1) | -1(1) | 2(1) | 0(1) |
| C(5B) | 12(1) | 13(1) | 16(1) | -3(1) | -1(1) | -1(1) |
| C(5A) | 12(1) | 14(1) | 16(1) | 2(1) | -3(1) | 0(1) |
| C(10B) | 18(1) | 17(1) | 22(1) | 0(1) | 2(1) | -1(1) |
| C(7A) | 17(1) | 15(1) | 16(1) | 1(1) | 4(1) | -1(1) |
| C(9B) | 18(1) | 15(1) | 16(1) | -2(1) | 2(1) | 2(1) |
| C(6C) | 15(1) | 14(1) | 15(1) | 1(1) | -1(1) | 2(1) |
| C(4C) | 25(1) | 14(1) | 22(1) | 0(1) | 5(1) | 4(1) |
| C(6A) | 16(1) | 14(1) | 15(1) | 0(1) | 0(1) | 1(1) |
| C(8C) | 20(1) | 13(1) | 14(1) | 0(1) | 5(1) | -3(1) |
| C(8A) | 19(1) | 13(1) | 15(1) | 1(1) | 3(1) | 0(1) |
| C(6B) | 11(1) | 14(1) | 16(1) | -1(1) | -1(1) | 1(1) |
| C(11B) | 21(1) | 28(2) | 27(1) | -6(1) | 5(1) | -1(1) |
| C(5C) | 13(1) | 14(1) | 14(1) | 2(1) | -1(1) | 1(1) |
| C(7B) | 16(1) | 13(1) | 17(1) | 1(1) | 5(1) | 0(1) |
| C(3A) | 16(1) | 23(2) | 20(1) | -1(1) | 3(1) | 2(1) |
| C(8B) | 18(1) | 13(1) | 14(1) | -1(1) | 3(1) | 4(1) |
| C(7C) | 20(1) | 13(1) | 17(1) | 1(1) | 7(1) | 0(1) |
| C(4B) | 17(1) | 14(1) | 19(1) | 1(1) | 1(1) | -1(1) |

| | | | | | | |
|---|---|---|---|---|---|---|
| C(3B) | 18(1) | 23(2) | 19(1) | 1(1) | 6(1) | -4(1) |
| C(9C) | 20(1) | 15(1) | 17(1) | -1(1) | 2(1) | 0(1) |
| C(2A) | 21(1) | 23(2) | 20(1) | 6(1) | 4(1) | -2(1) |
| C(11C) | 23(1) | 27(2) | 25(1) | -2(1) | 2(1) | 4(1) |
| C(10C) | 18(1) | 17(1) | 23(1) | 2(1) | 5(1) | 0(1) |
| C(1C) | 25(1) | 20(2) | 22(1) | 4(1) | 6(1) | -4(1) |
| C(4A) | 16(1) | 15(1) | 21(1) | 2(1) | 2(1) | 0(1) |
| C(3C) | 24(1) | 27(2) | 20(1) | -1(1) | 6(1) | 9(1) |
| C(9A) | 24(1) | 18(1) | 17(1) | 2(1) | 3(1) | 1(1) |
| C(2B) | 17(1) | 24(2) | 20(1) | -6(1) | 4(1) | 1(1) |
| C(15B) | 20(1) | 35(2) | 24(1) | -2(1) | 4(1) | -2(1) |
| C(15C) | 24(1) | 28(2) | 26(1) | 0(1) | 5(1) | 2(1) |
| C(14C) | 24(1) | 41(2) | 29(2) | 1(1) | -4(1) | 2(1) |
| C(2C) | 18(1) | 31(2) | 20(1) | 4(1) | 6(1) | -2(1) |
| C(12B) | 21(1) | 37(2) | 28(1) | -7(1) | -1(1) | -1(1) |
| C(1A) | 25(1) | 18(1) | 23(1) | 4(1) | 3(1) | -2(1) |
| C(1B) | 21(1) | 15(1) | 24(1) | -4(1) | 5(1) | 2(1) |
| C(13C) | 18(1) | 40(2) | 43(2) | 11(1) | 1(1) | 2(1) |
| C(12C) | 24(1) | 40(2) | 34(2) | 1(1) | 10(1) | 7(1) |
| C(13B) | 15(1) | 42(2) | 41(2) | -7(1) | 1(1) | -1(1) |
| C(10A) | 23(1) | 27(2) | 16(1) | 4(1) | 8(1) | 6(1) |
| C(15A) | 22(1) | 31(2) | 29(1) | 3(1) | 9(1) | 3(1) |
| C(14B) | 20(1) | 48(2) | 32(2) | -5(1) | 10(1) | -2(1) |
| C(11A) | 32(2) | 31(2) | 35(2) | 4(1) | 15(1) | 7(1) |
| C(14A) | 23(1) | 53(2) | 30(2) | 1(1) | 7(1) | 0(1) |
| C(12A) | 35(2) | 44(2) | 47(2) | 16(2) | 20(1) | 22(2) |
| C(13A) | 21(1) | 68(3) | 30(2) | 17(2) | 9(1) | 12(2) |

***Table S13.*** Hydrogen coordinates ( x $10^4$) and isotropic displacement parameters ($Å^2$x 10 $^3$) for **22a** (engle17_a).

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(2C) | 4895 | 7022 | 7685 | 18 |
| H(2B) | 4797 | 5357 | 6887 | 17 |
| H(2A) | 5378 | 3706 | 7980 | 19 |
| H(7AA) | 5879 | 4477 | 6573 | 19 |
| H(7AB) | 5976 | 3934 | 6160 | 19 |
| H(9B) | 2466 | 5359 | 8619 | 20 |
| H(4C) | 3405 | 8028 | 9871 | 24 |
| H(11B) | 1092 | 5496 | 5720 | 30 |
| H(7BA) | 4263 | 6129 | 8254 | 18 |
| H(7BB) | 4174 | 5586 | 8672 | 18 |
| H(3A) | 2905 | 4429 | 11483 | 24 |
| H(7CA) | 5498 | 7820 | 6469 | 19 |
| H(7CB) | 5518 | 7291 | 5929 | 19 |
| H(4B) | 6125 | 6402 | 4663 | 20 |
| H(3B) | 7270 | 6084 | 3374 | 24 |
| H(9C) | 7131 | 6953 | 6105 | 21 |
| H(2AA) | 2732 | 3600 | 11569 | 25 |
| H(11C) | 8811 | 6897 | 5409 | 30 |
| H(1C) | 3037 | 6397 | 9824 | 27 |
| H(4A) | 3835 | 4758 | 9969 | 21 |
| H(3C) | 2354 | 7670 | 11218 | 28 |
| H(9A) | 7659 | 3676 | 6327 | 23 |
| H(2BA) | 7697 | 5275 | 3560 | 24 |
| H(15B) | 762 | 5631 | 9364 | 32 |
| H(15C) | 8594 | 7188 | 9023 | 31 |
| H(14C) | 10344 | 7050 | 9490 | 38 |
| H(2CA) | 2168 | 6838 | 11166 | 27 |
| H(12B) | -671 | 5536 | 5226 | 35 |
| H(1A) | 3519 | 3127 | 10215 | 26 |

| | | | | |
|---|---|---|---|---|
| H(1B) | 6967 | 4809 | 4982 | 23 |
| H(13C) | 11323 | 6847 | 7930 | 40 |
| H(12C) | 10554 | 6768 | 5886 | 39 |
| H(13B) | -1722 | 5647 | 6780 | 39 |
| H(15A) | 9317 | 4555 | 7761 | 32 |
| H(14B) | -1003 | 5690 | 8853 | 39 |
| H(11A) | 9096 | 3144 | 7039 | 38 |
| H(14A) | 11059 | 4462 | 8424 | 42 |
| H(12A) | 10821 | 3053 | 7752 | 49 |
| H(13A) | 11797 | 3710 | 8448 | 47 |

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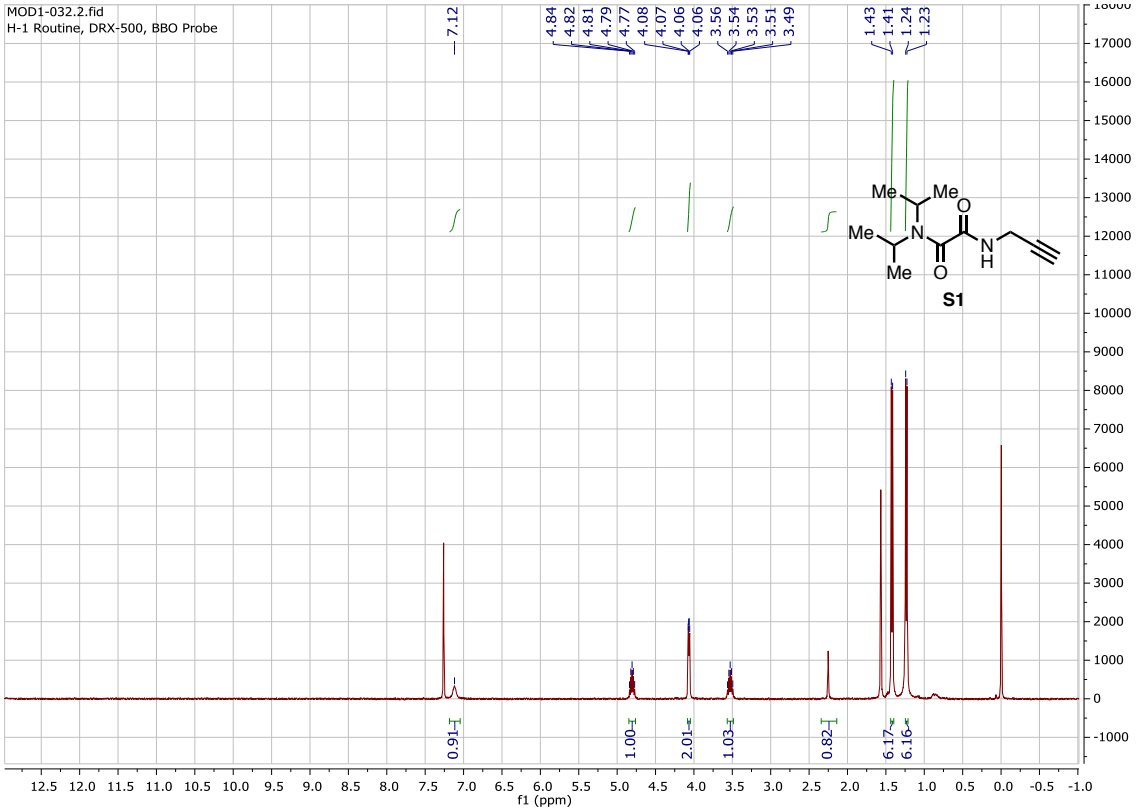
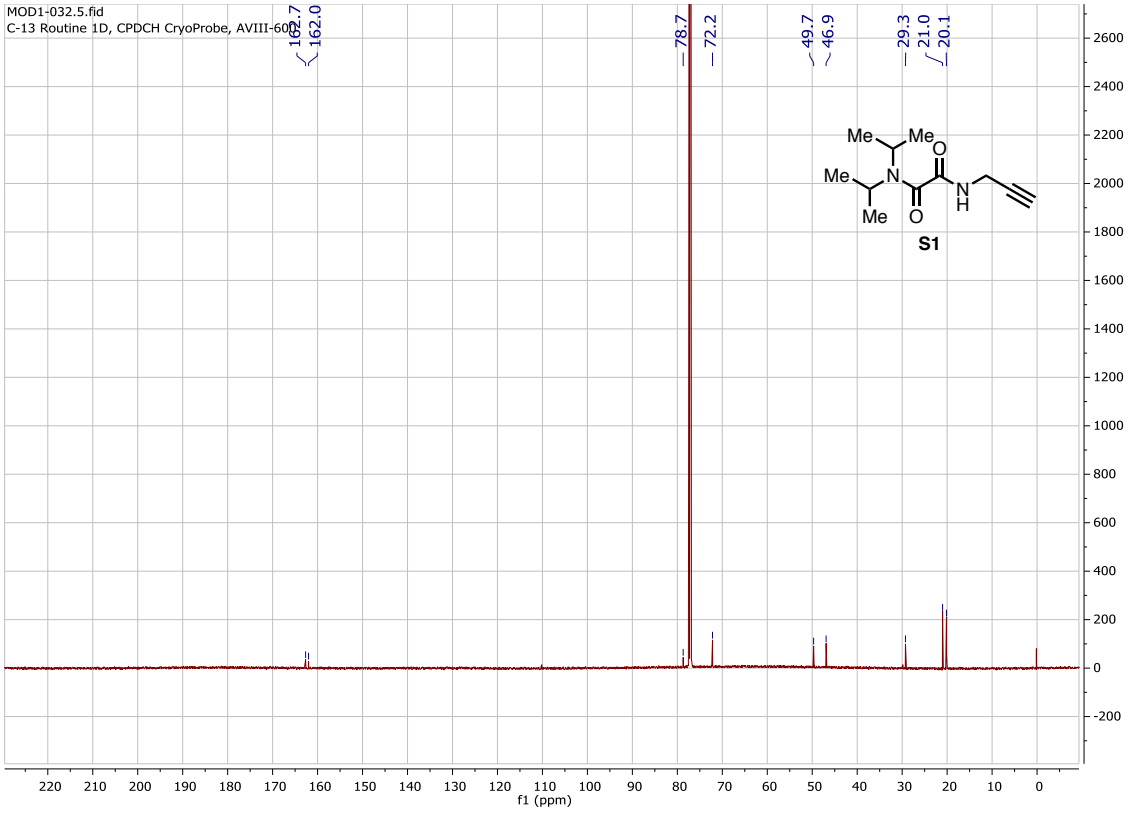
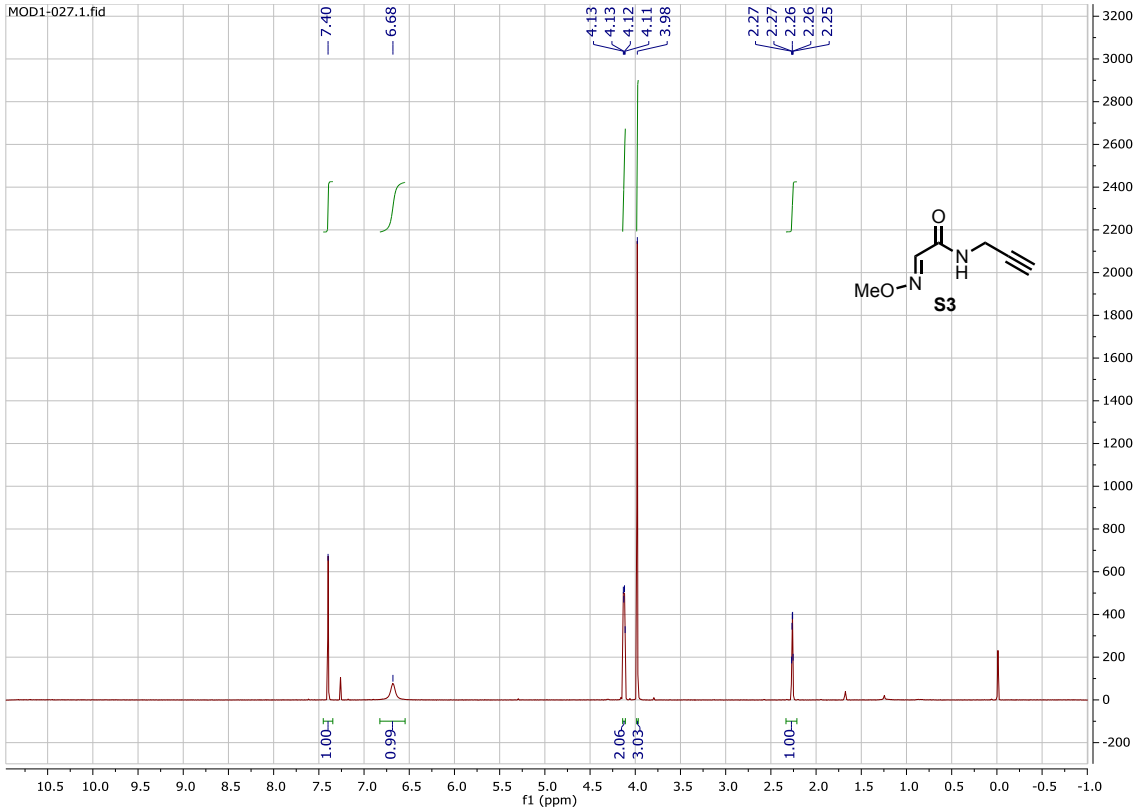
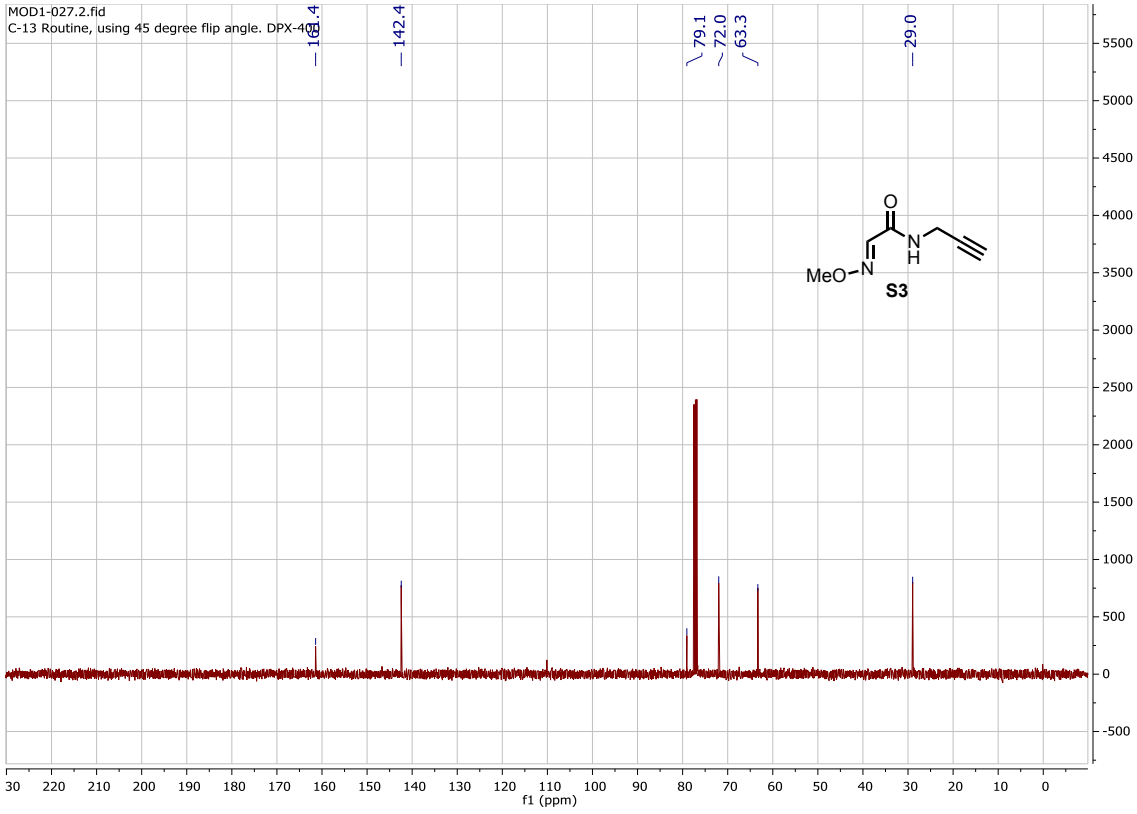
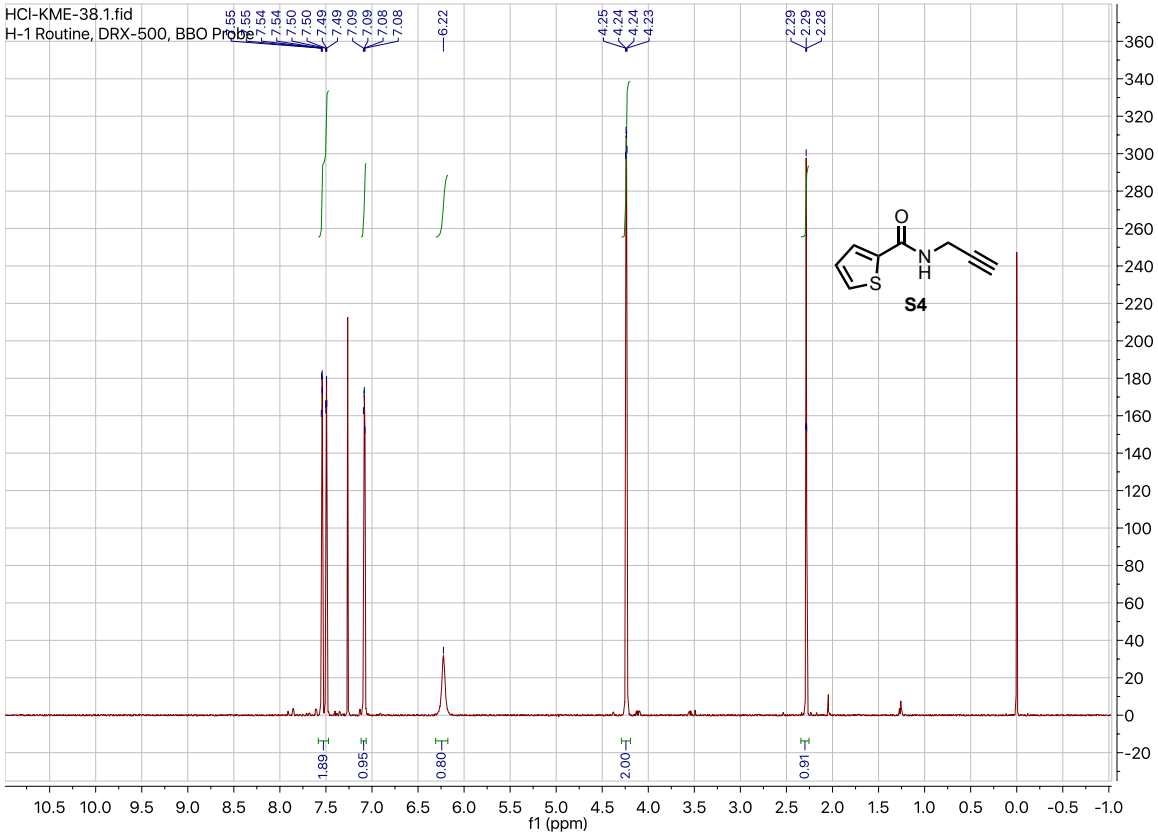
# NMR SPECTRA

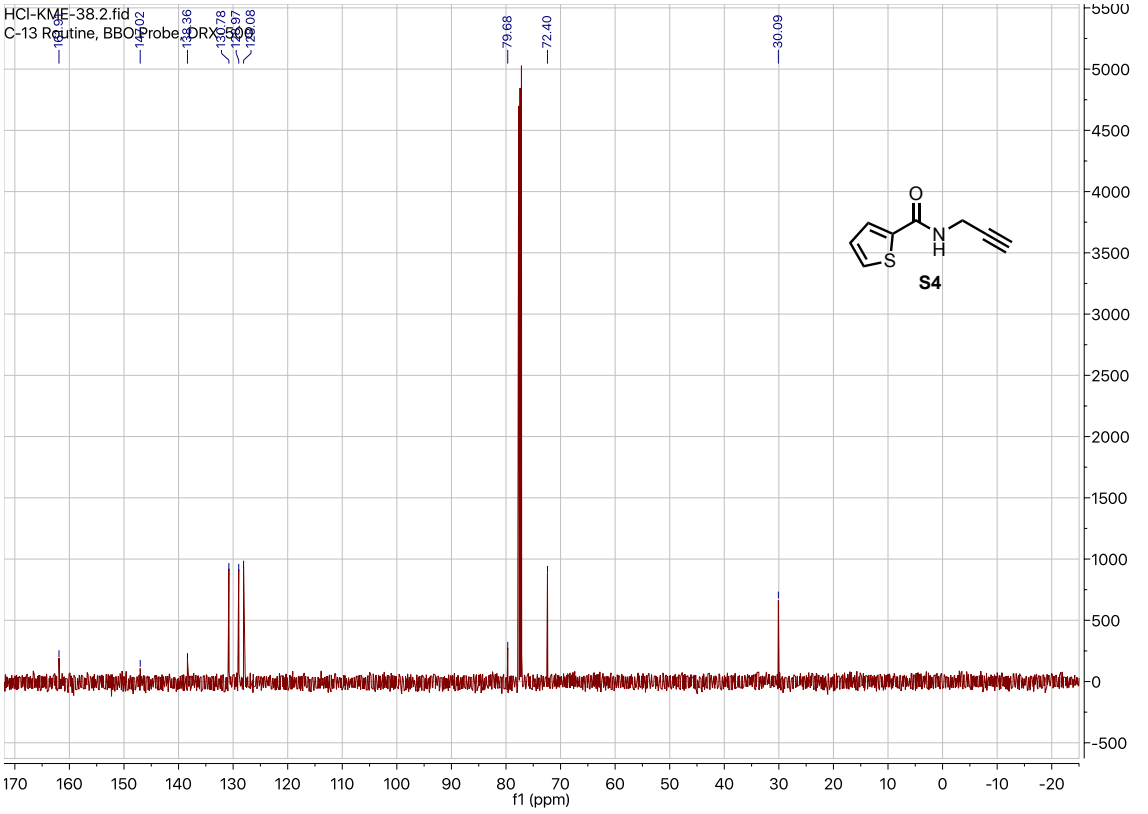

MOD1-032.2.fid
H-1 Routine, DRX-500, BBO Probe
7.12
4.84
4.82
4.81
4.79
4.77
4.08
4.07
4.06
4.06
3.56
3.54
3.53
3.51
3.49
1.43
1.41
1.24
1.23
Me
Me
Me
N
O
O
N
H
Me
S1
0.91
1.00
2.01
1.03
0.82
6.17
6.16
f1 (ppm)

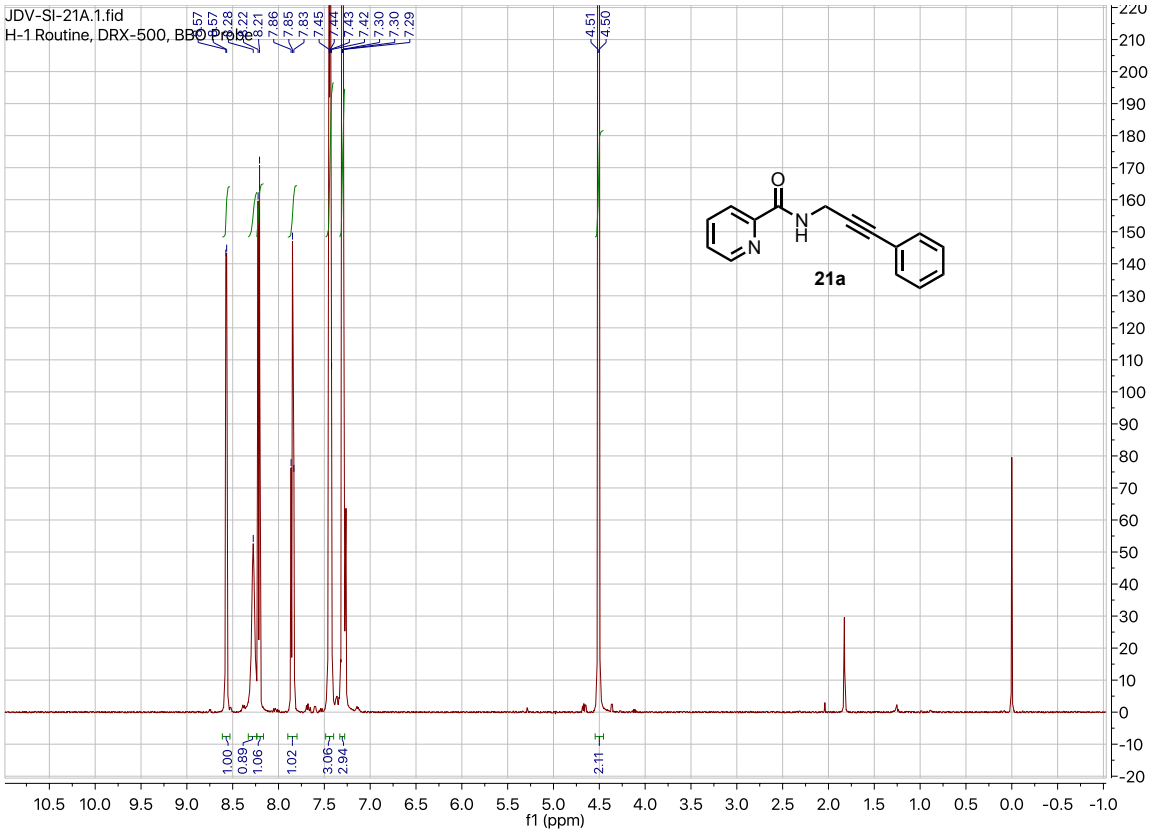

MOD1-032.5.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
162.7
162.0
78.7
72.2
49.7
46.9
29.3
21.0
20.1
Me
Me
Me
N
O
O
N
H
Me
S1
f1 (ppm)

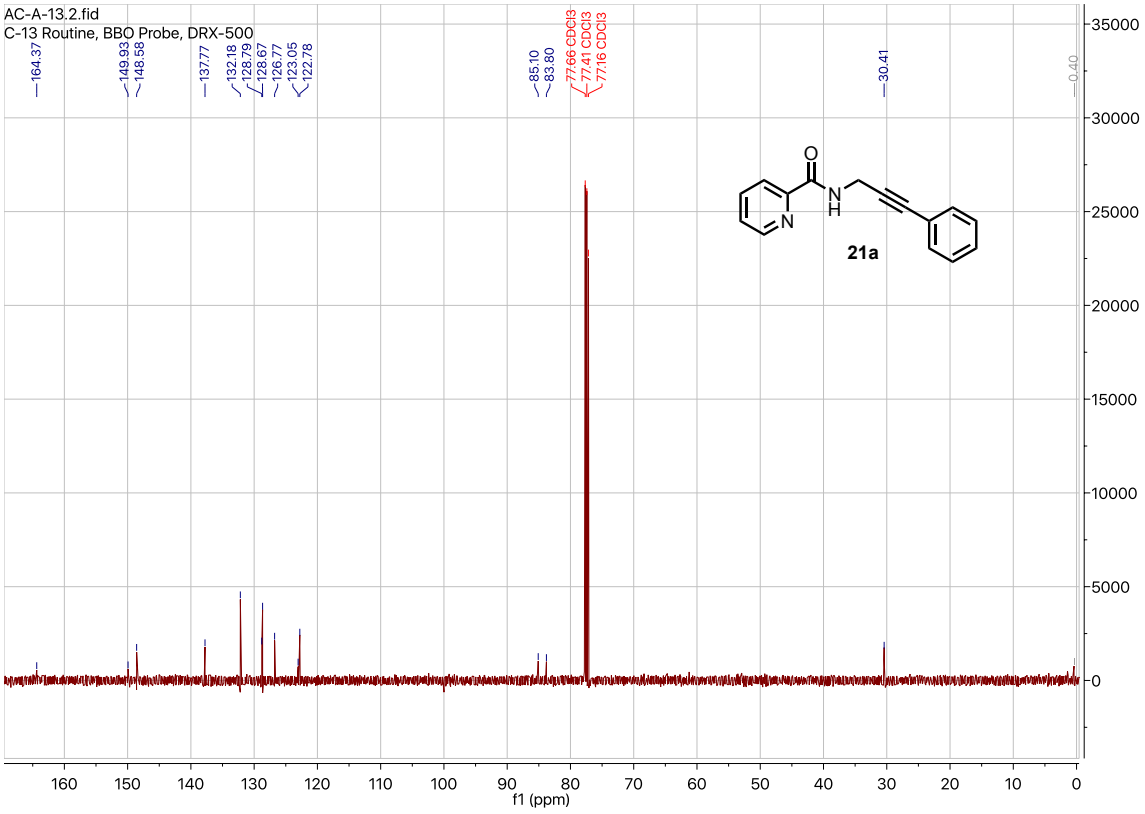

MOD1-027.1.fid
7.40
6.68
4.13
4.13
4.12
4.11
3.98
2.27
2.27
2.26
2.26
2.25
1.00
0.99
2.06
3.03
1.00
MeO
N
O
N
H
S3
f1 (ppm)

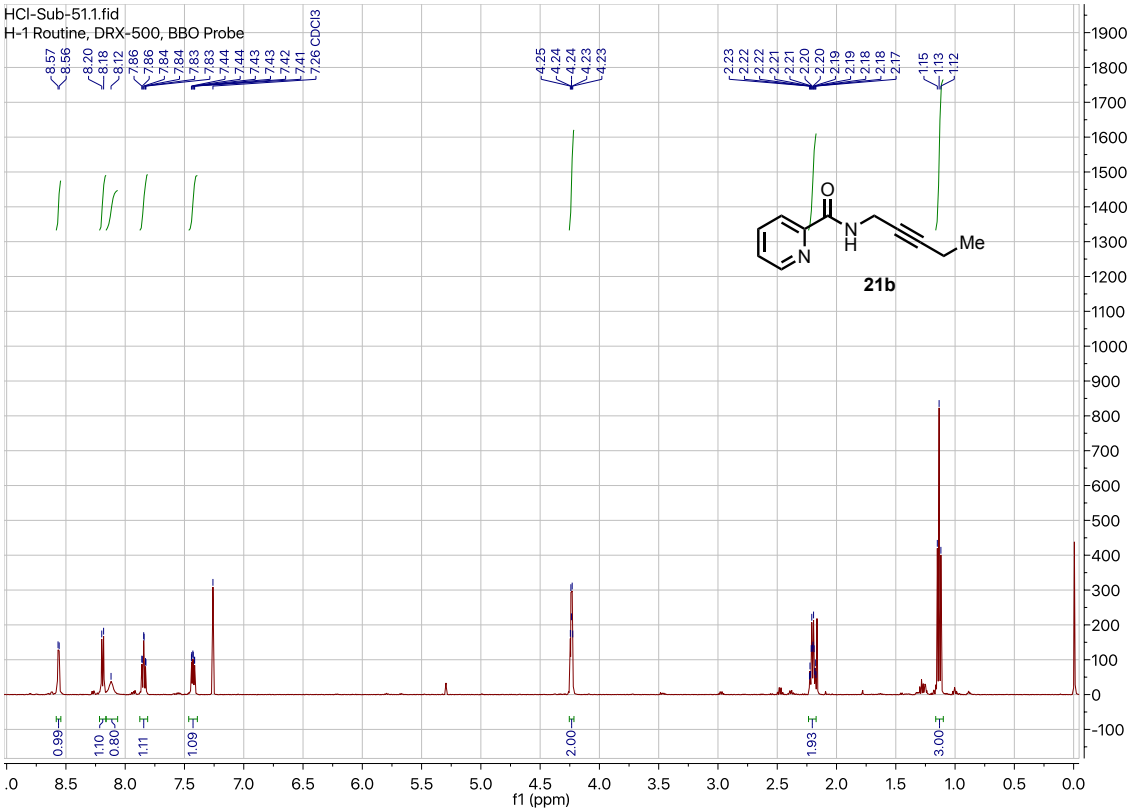

MOD1-027.2.fid
C-13 Routine, using 45 degree flip angle. DPX-400
159.4
142.4
79.1
72.0
63.3
29.0
MeO
N
O
N
H
S3
f1 (ppm)


HCl-KME-38.1.fid
H-1 Routine, DRX-500, BBO Probe
7.55
7.55
7.54
7.54
7.50
7.50
7.49
7.49
7.09
7.09
7.08
7.08
6.22
4.25
4.24
4.24
4.23
2.29
2.29
2.28
1.89
0.95
0.80
2.00
0.91
O
N
H
S
S4
f1 (ppm)


HCl-KME-38.2.fid
C-13 Routine, BBO Probe, DRX-500
79.68
72.40
30.09
O
N
H
S
S4
f1 (ppm)


JDV-SI-21A.1.fid
H-1 Routine, DRX-500, BBO Probe
21a
f1 (ppm)


AC-A-13.2.fid
C-13 Routine, BBO Probe, DRX-500
77.66 CDCl3
77.41 CDCl3
77.16 CDCl3
21a
f1 (ppm)


HCl-Sub-51.1.fid
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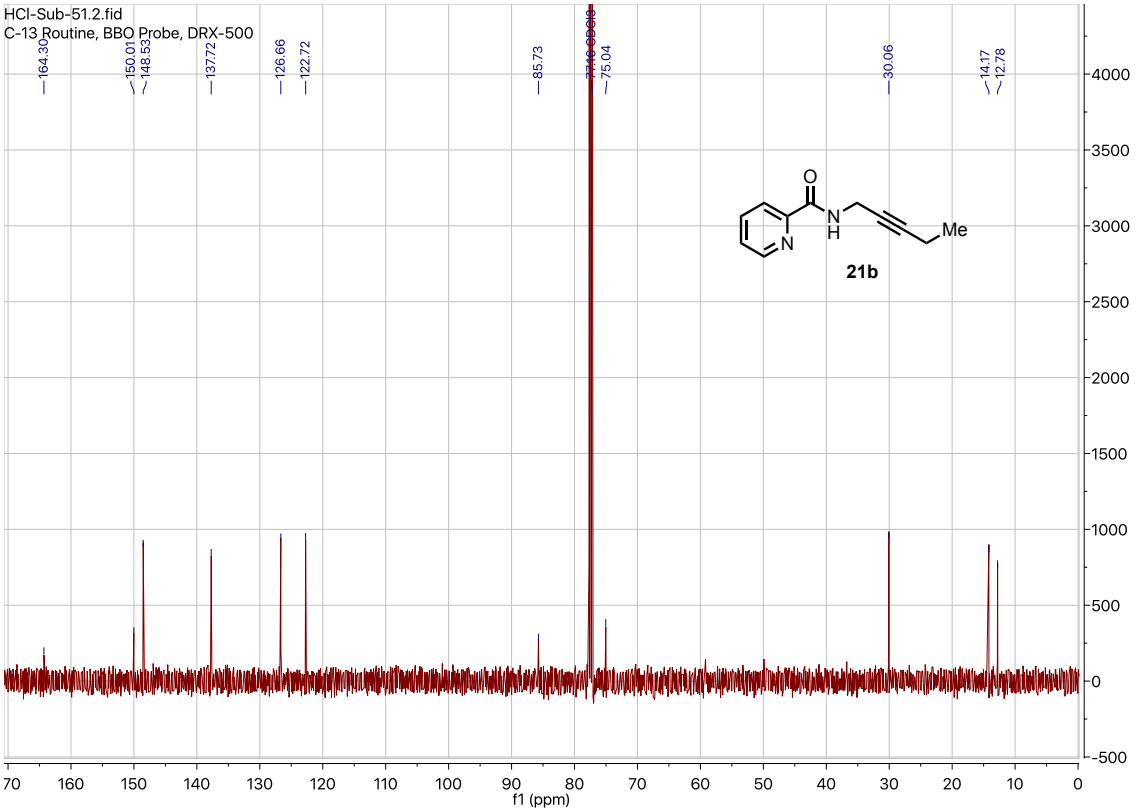
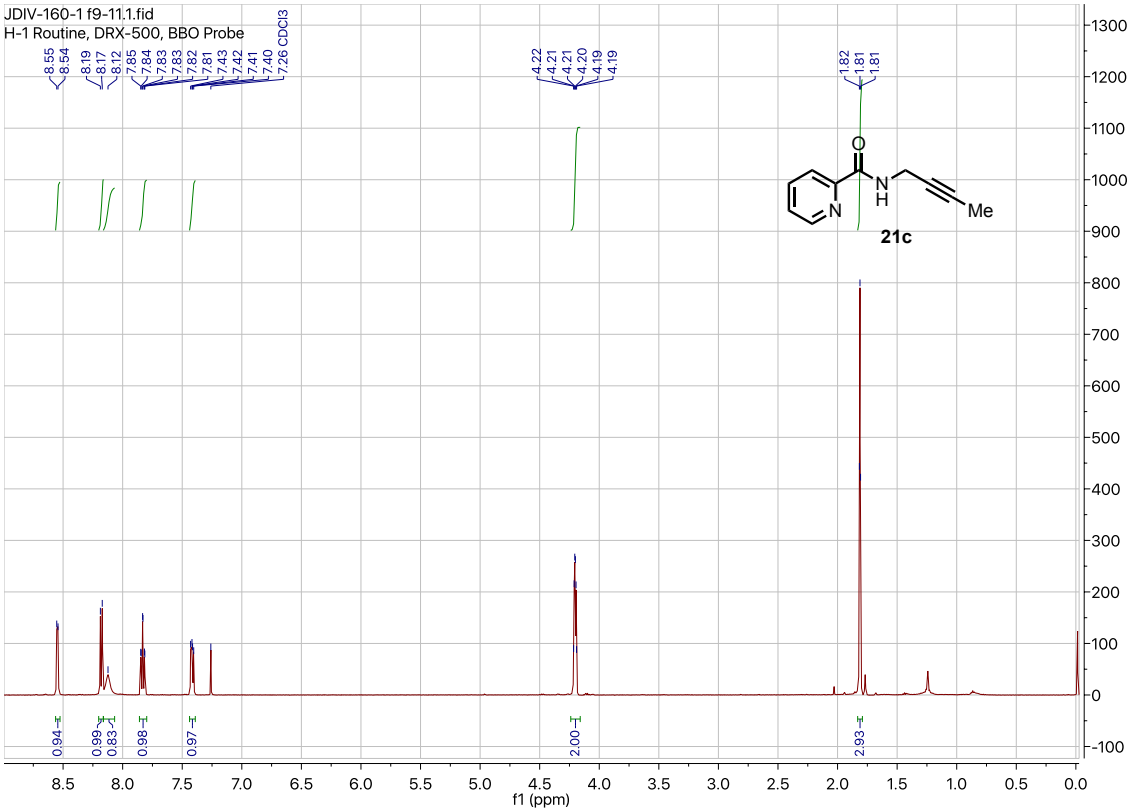
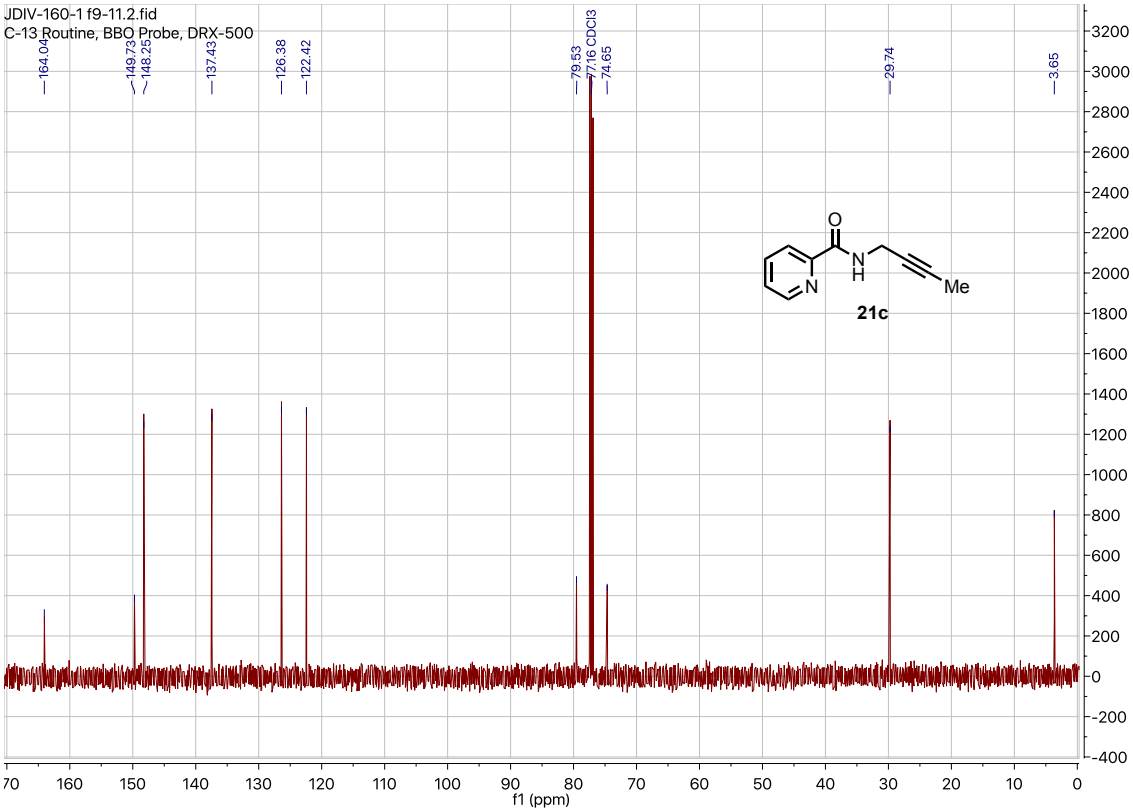
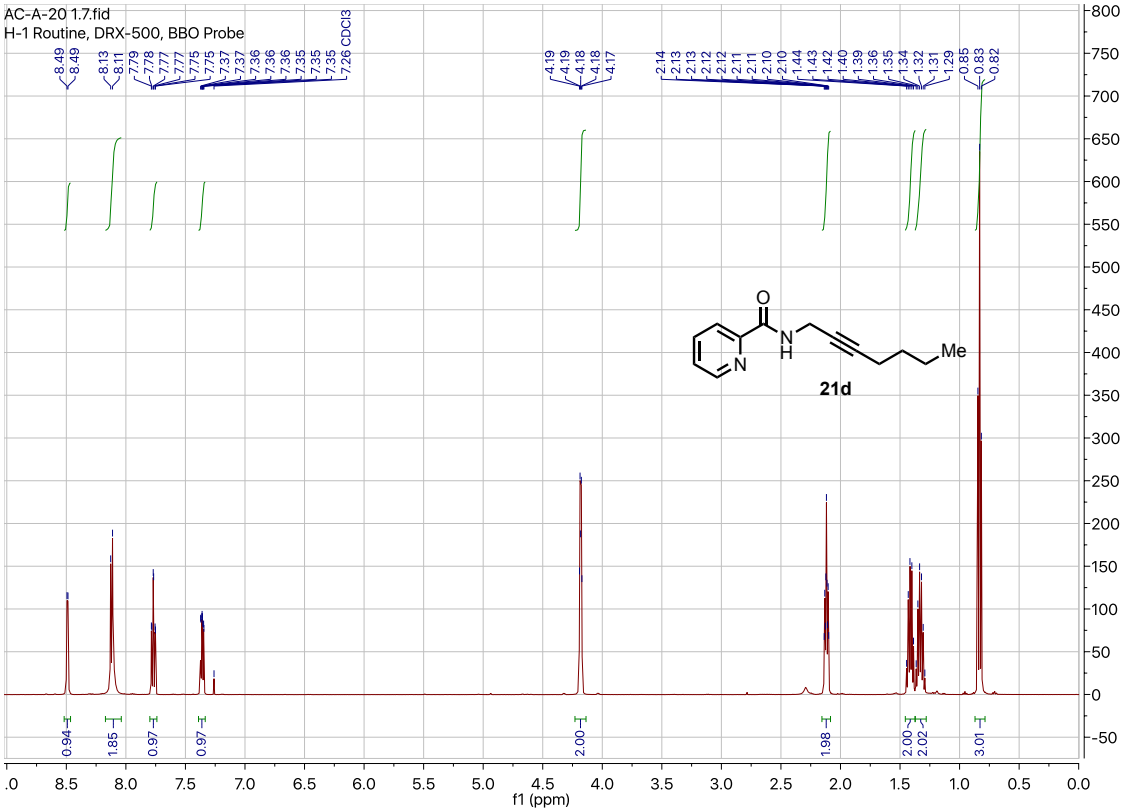
8.57
8.56
8.20
8.18
8.12
7.86
7.86
7.84
7.84
7.83
7.83
7.44
7.44
7.43
7.43
7.42
7.41
7.26 CDCl3
4.25
4.24
4.24
4.23
4.23
2.23
2.22
2.22
2.21
2.21
2.20
2.20
2.19
2.19
2.18
2.18
2.17
1.15
1.13
1.12
O
N
H
N
Me
21b
0.99
1.10
0.80
1.11
1.09
2.00
1.93
3.00
f1 (ppm)


HCl-Sub-51.2.fid
C-13 Routine, BBO Probe, DRX-500
164.30
150.01
148.53
137.72
126.66
122.72
85.73
77.16 CDCl3
75.04
30.06
14.17
12.78
O
N
H
N
Me
21b
f1 (ppm)


JDIV-160-1 f9-11.1.fid
H-1 Routine, DRX-500, BBO Probe
8.55
8.54
8.19
8.17
8.12
7.85
7.84
7.83
7.82
7.81
7.43
7.42
7.41
7.40
7.26 CDCl3
4.22
4.21
4.21
4.20
4.19
4.19
1.82
1.81
1.81
0.94
0.99
0.83
0.98
0.97
2.00
2.93
O
N
H
N
Me
21c
f1 (ppm)


JDIV-160-1 f9-11.2.fid
C-13 Routine, BBO Probe, DRX-500
164.04
149.73
148.25
137.43
126.38
122.42
79.53
77.16 CDCl3
74.65
29.74
3.65
O
N
H
N
Me
21c
f1 (ppm)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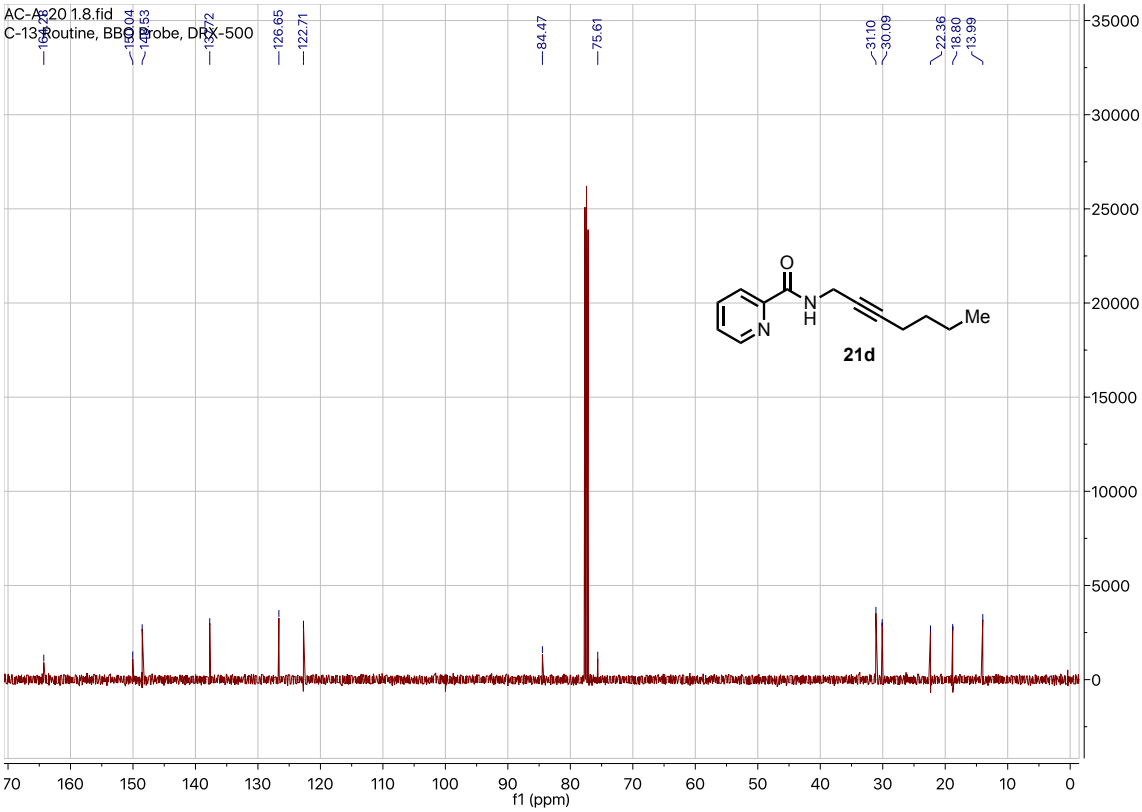
8.49
8.49
8.13
8.11
7.79
7.78
7.77
7.77
7.77
7.75
7.75
7.37
7.37
7.36
7.36
7.36
7.35
7.35
7.35
7.26 CDCl3
4.19
4.19
4.18
4.18
4.17
2.14
2.13
2.13
2.12
2.12
2.11
2.11
2.10
2.10
1.44
1.43
1.42
1.40
1.39
1.36
1.35
1.34
1.32
1.31
1.29
0.85
0.83
0.82
O
N
H
N
Me
21d
0.94
1.85
0.97
0.97
2.00
1.98
2.00
2.02
3.01
f1 (ppm)


AC-A-20 1.8.fid
C-13 Routine, BBO Probe, DRX-500
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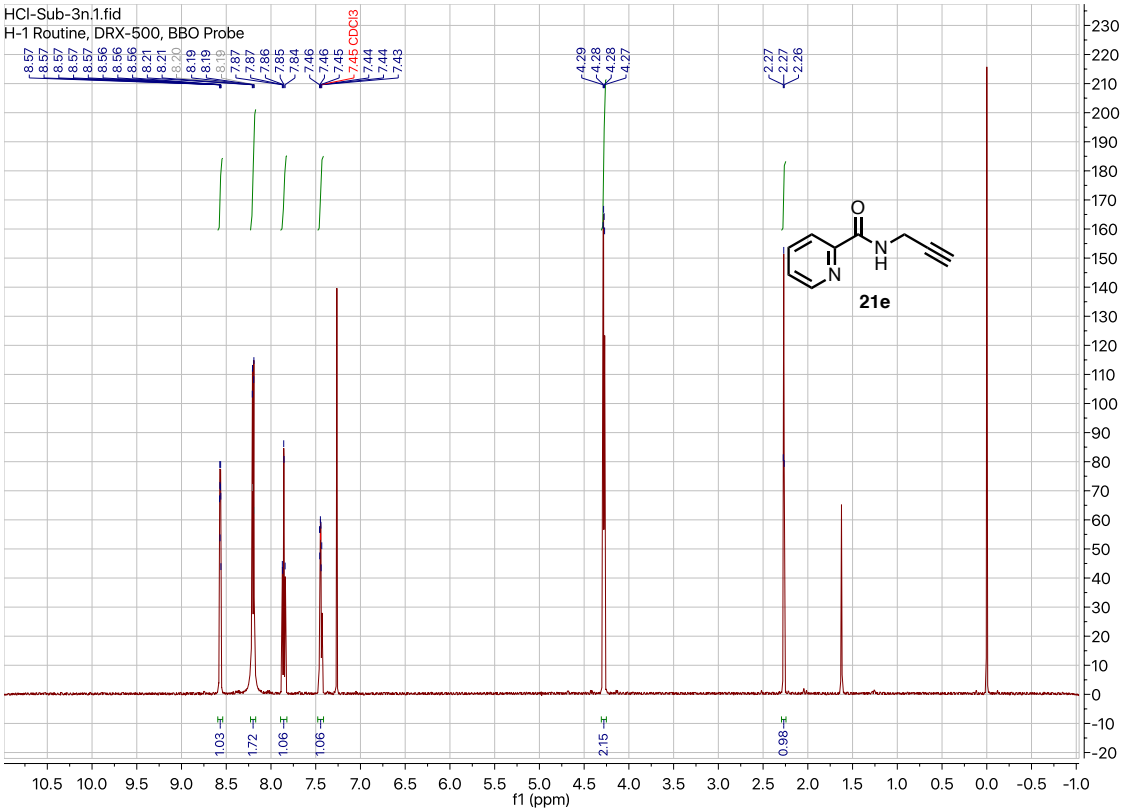
147.53
137.72
126.65
122.71
84.47
75.61
31.10
30.09
22.36
18.80
13.99
O
N
H
N
Me
21d
f1 (ppm)


HCl-Sub-3n.1.fid
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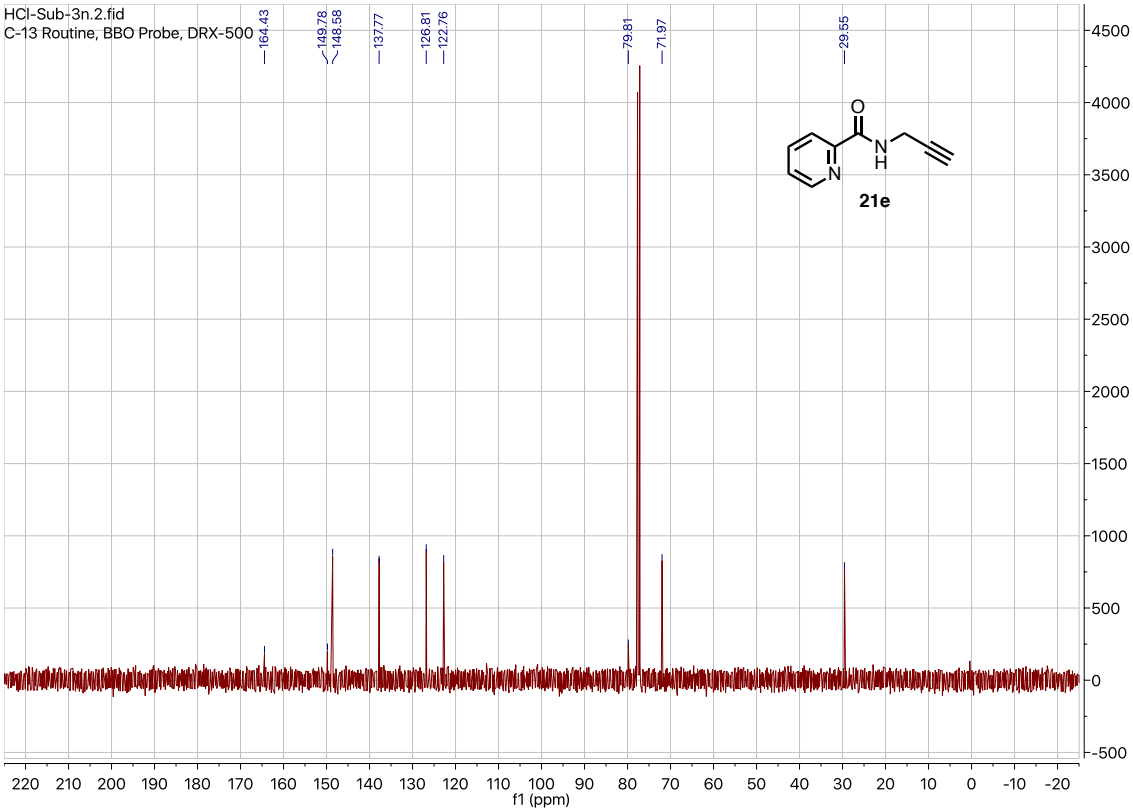
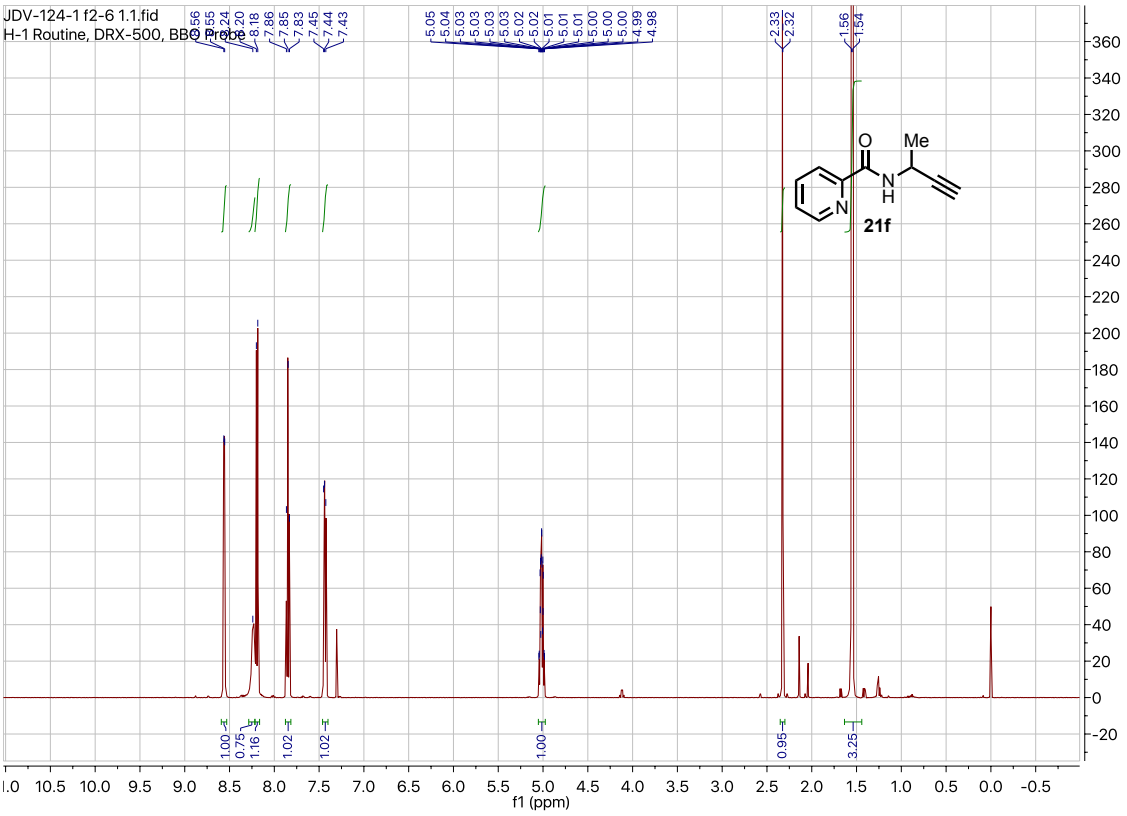
8.57
8.57
8.57
8.57
8.56
8.56
8.56
8.21
8.21
8.20
8.19
8.19
8.19
7.87
7.87
7.86
7.85
7.84
7.46
7.46
7.45
7.45 CDCl3
7.44
7.44
7.43
4.29
4.28
4.28
4.27
2.27
2.27
2.26
1.03
1.72
1.06
1.06
2.15
0.98
21e
f1 (ppm)


HCl-Sub-3n.2.fid
C-13 Routine, BBO Probe, DRX-500
164.43
149.78
148.58
137.77
126.81
122.76
79.81
71.97
29.55
21e
f1 (ppm)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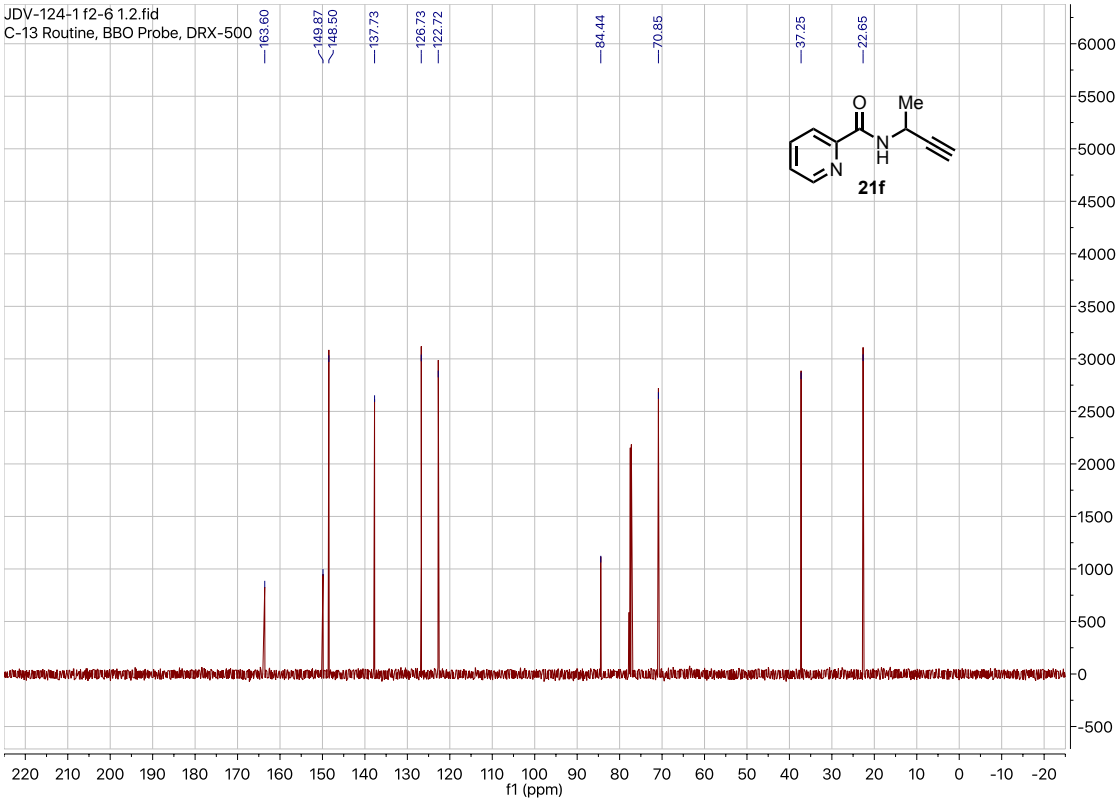
21f
f1 (ppm)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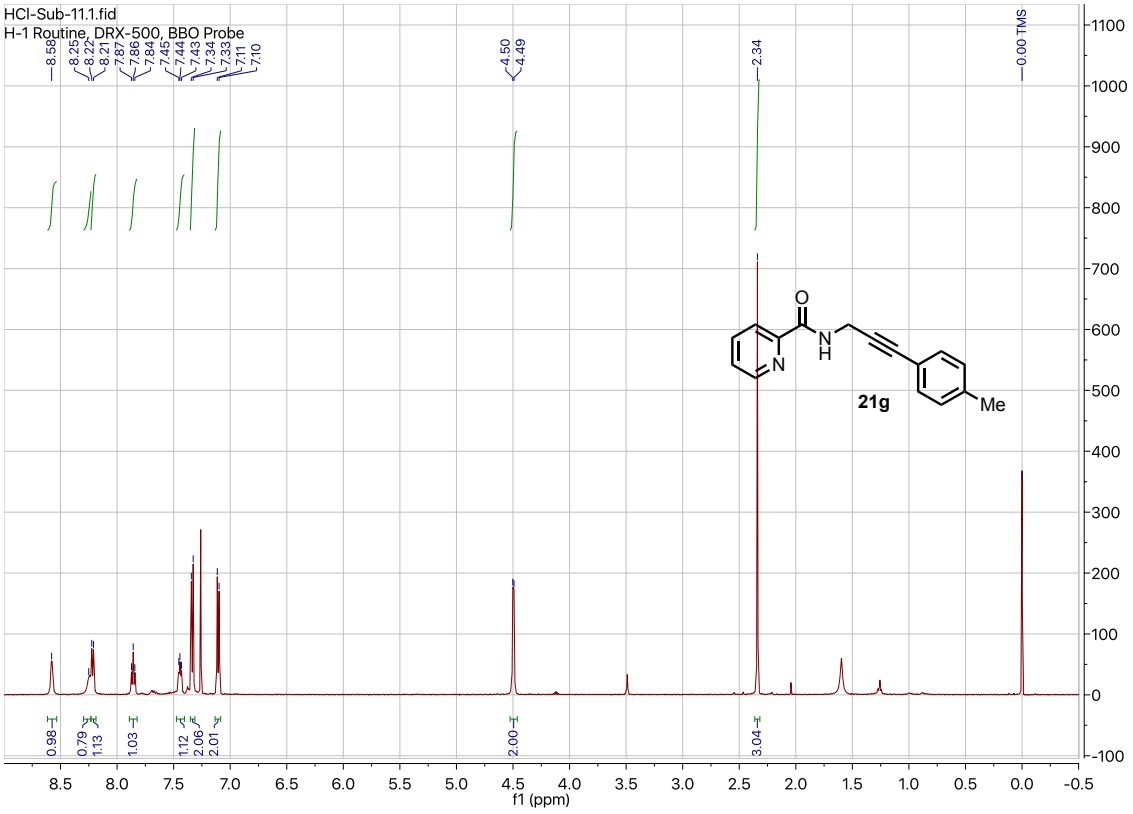
C-13 Routine, BBO Probe, DRX-500
21f
f1 (ppm)


HCl-Sub-11.1.fid
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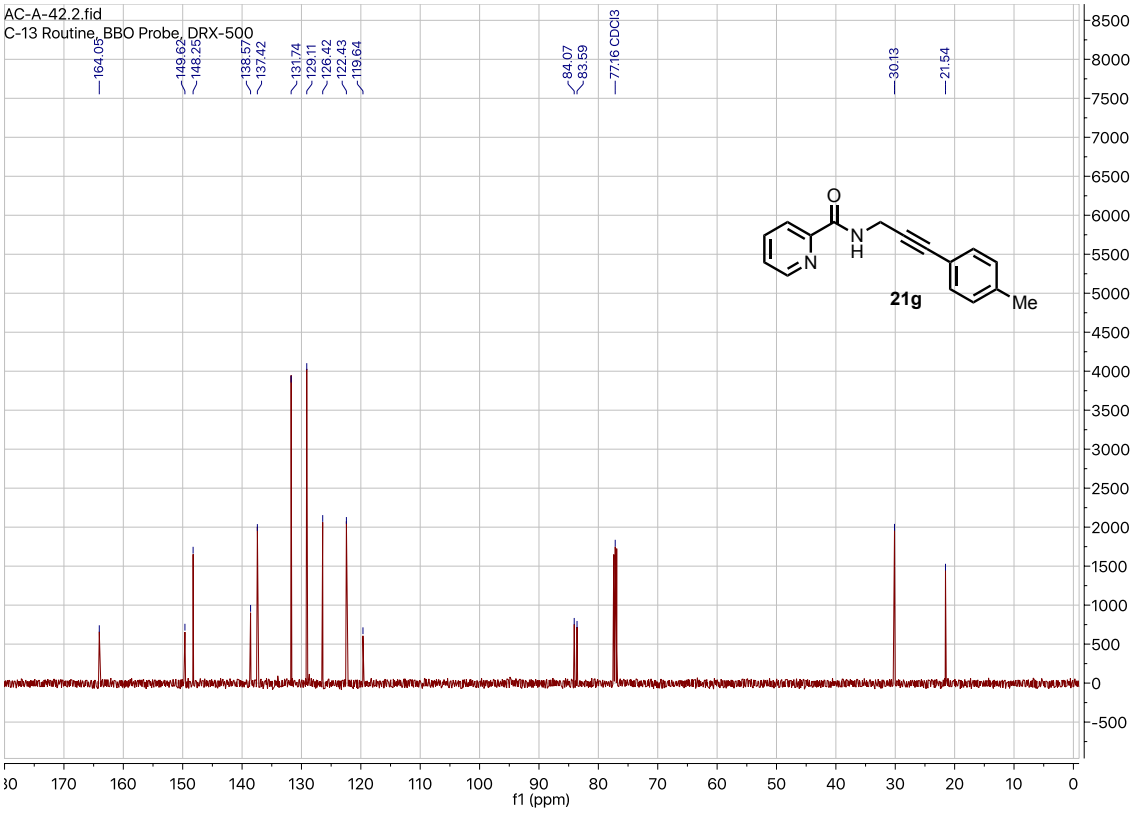
8.25
8.22
8.21
7.87
7.86
7.84
7.45
7.44
7.43
7.34
7.33
7.11
7.10
4.50
4.49
2.34
0.00 TMS
0.98
0.79
1.13
1.03
1.12
2.06
2.01
2.00
3.04
f1 (ppm)
21g
Me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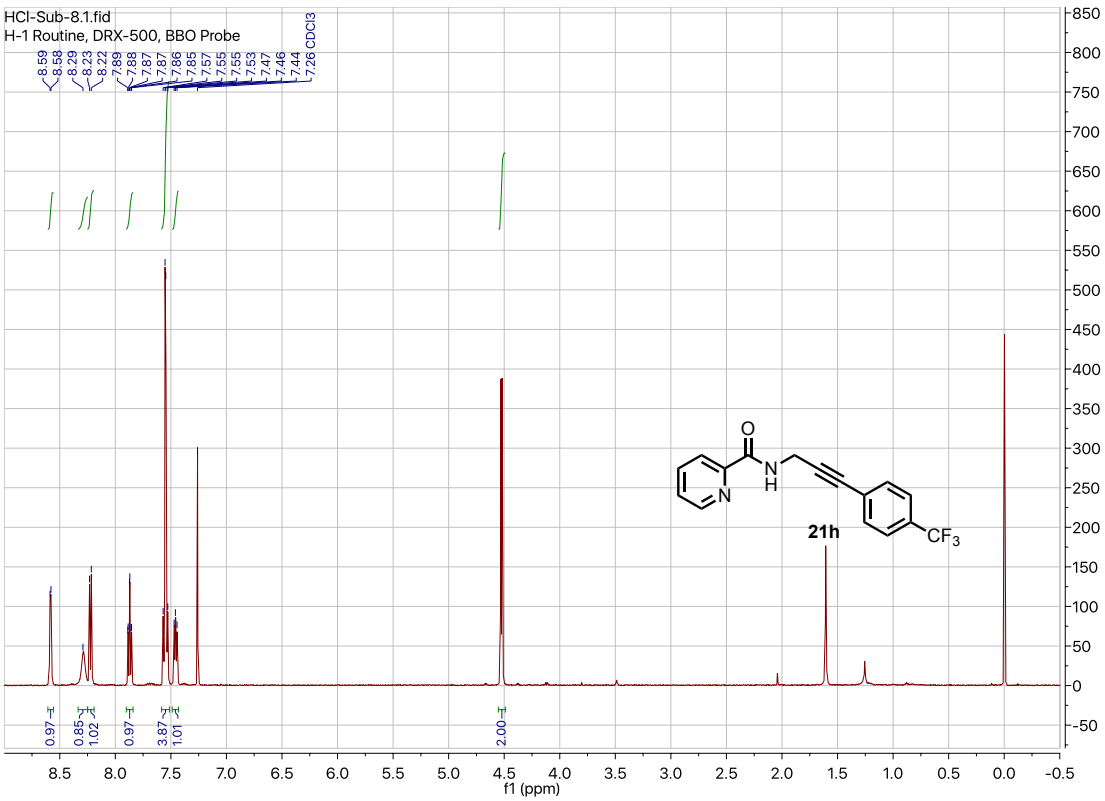
149.62
148.25
138.57
137.42
131.74
129.11
126.42
122.43
119.64
84.07
83.59
77.16 CDCl3
30.13
21.54
f1 (ppm)
21g
Me


HCl-Sub-8.1.fid
H-1 Routine, DRX-500, BBO Probe
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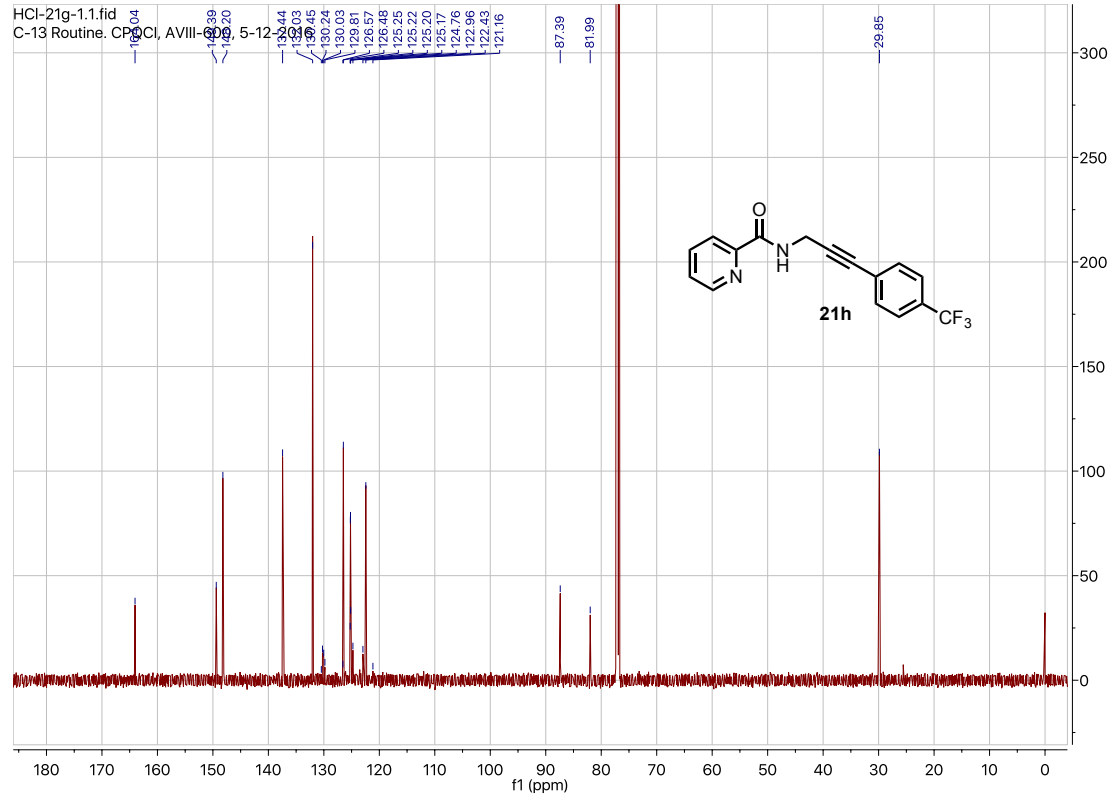
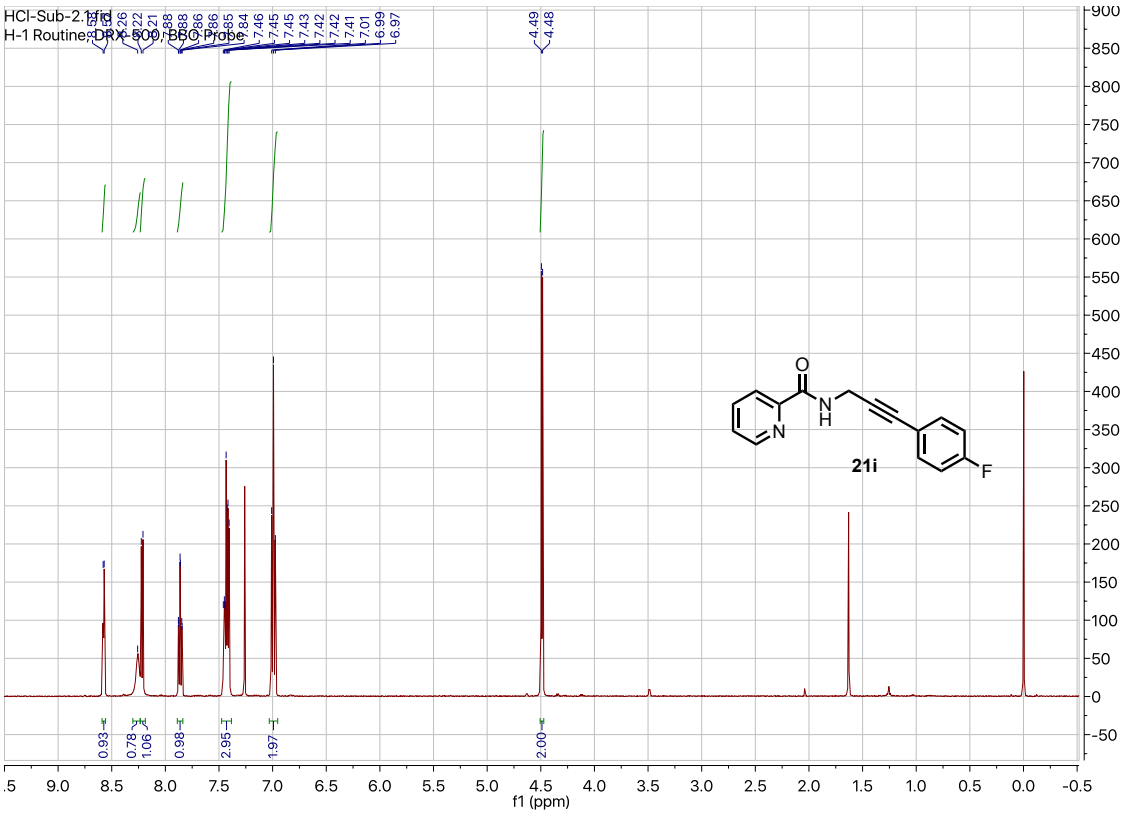
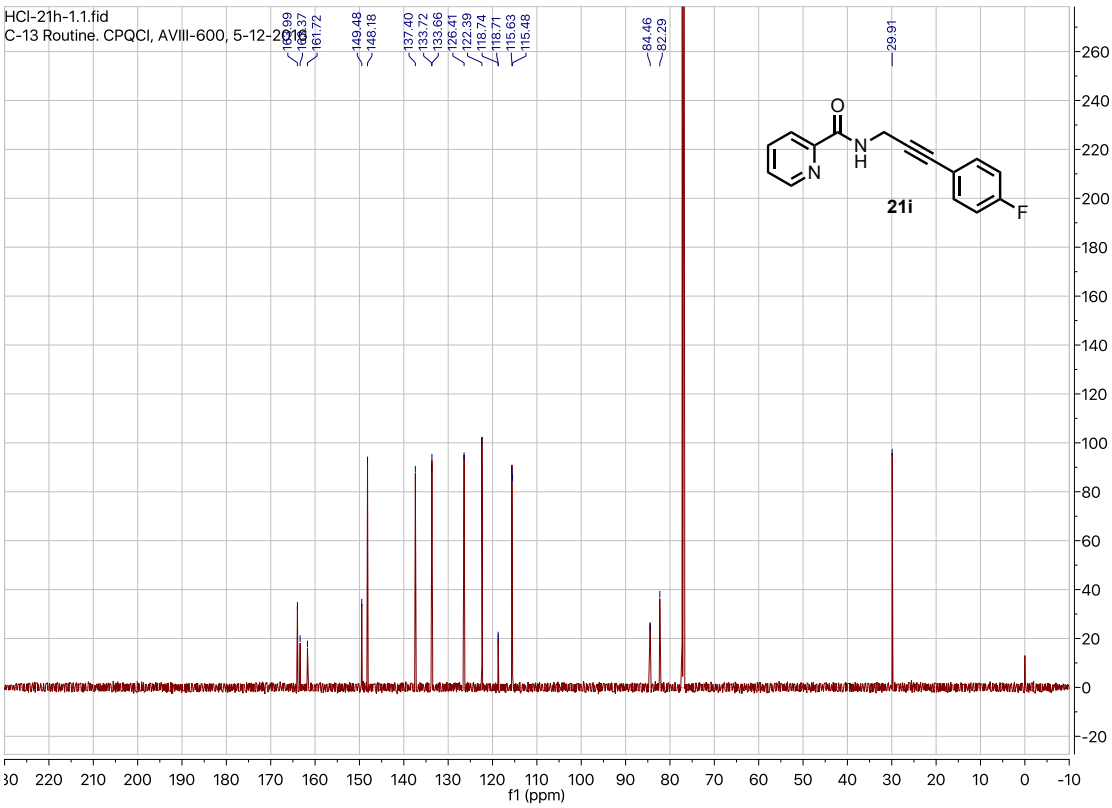
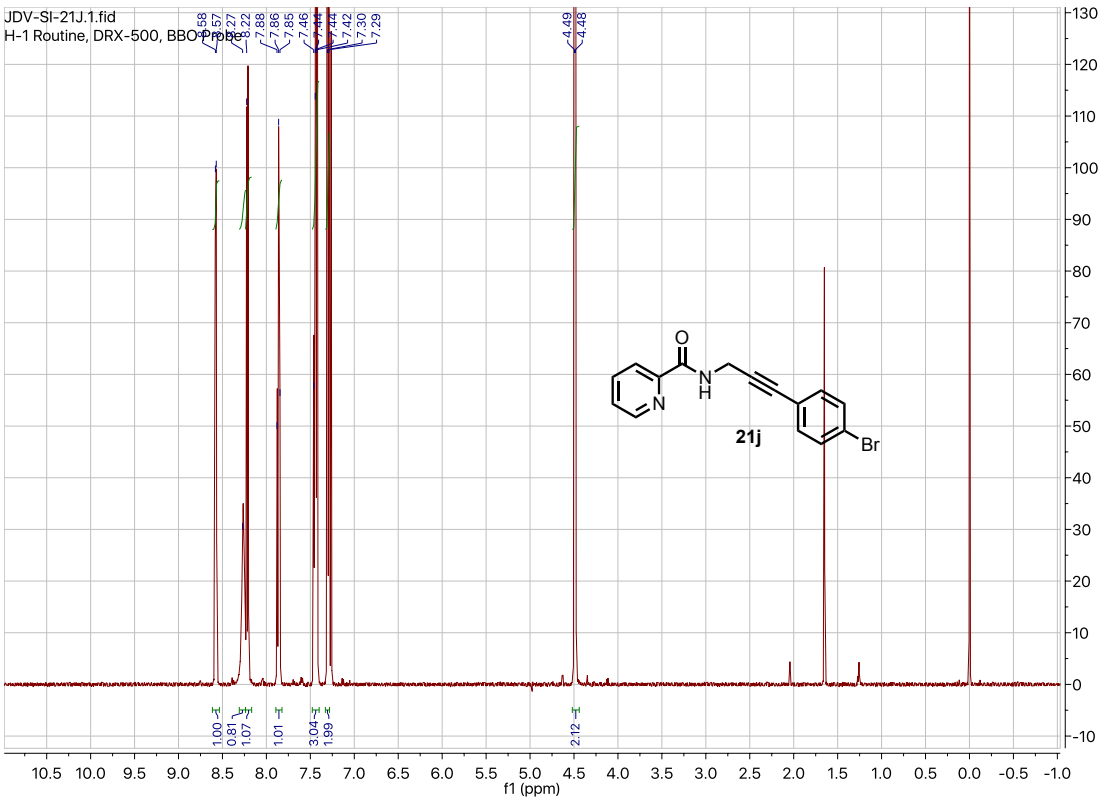
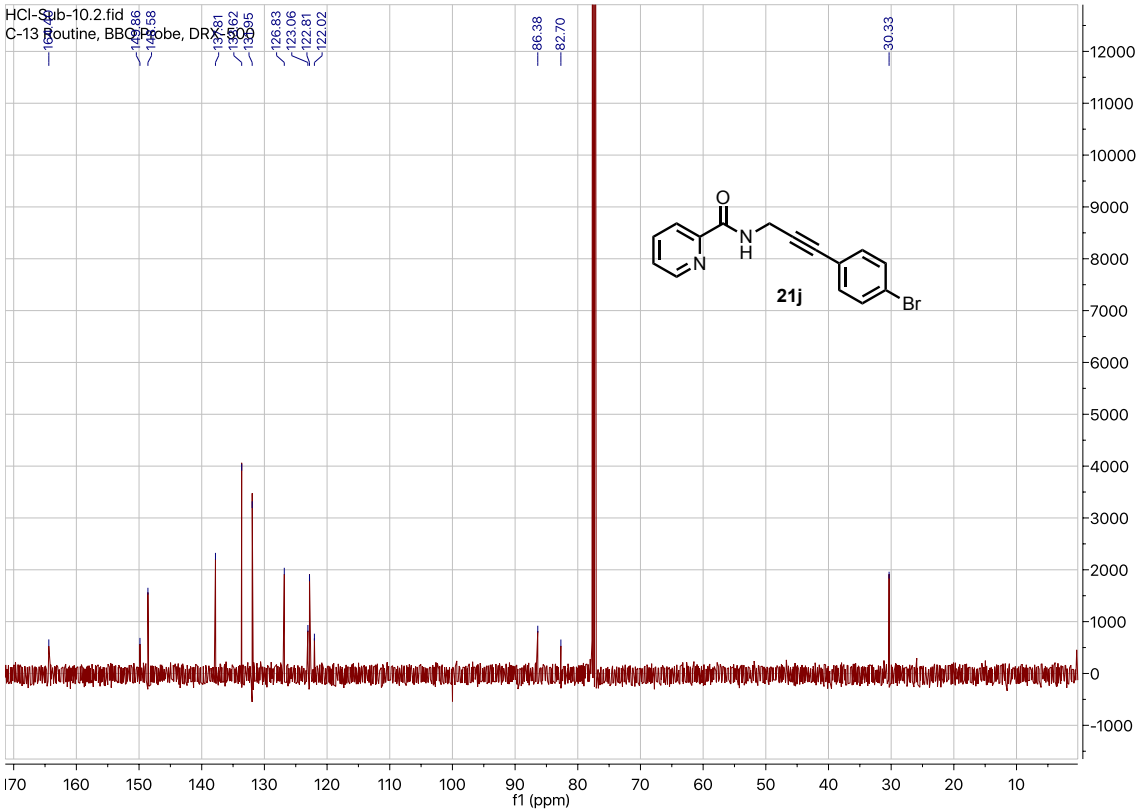
8.58
8.29
8.23
8.22
7.89
7.88
7.87
7.87
7.86
7.85
7.57
7.55
7.55
7.53
7.47
7.46
7.44
7.26 CDCl3
0.97
0.85
1.02
0.97
3.87
1.01
2.00
O
N
H
N
21h
CF3
f1 (ppm)

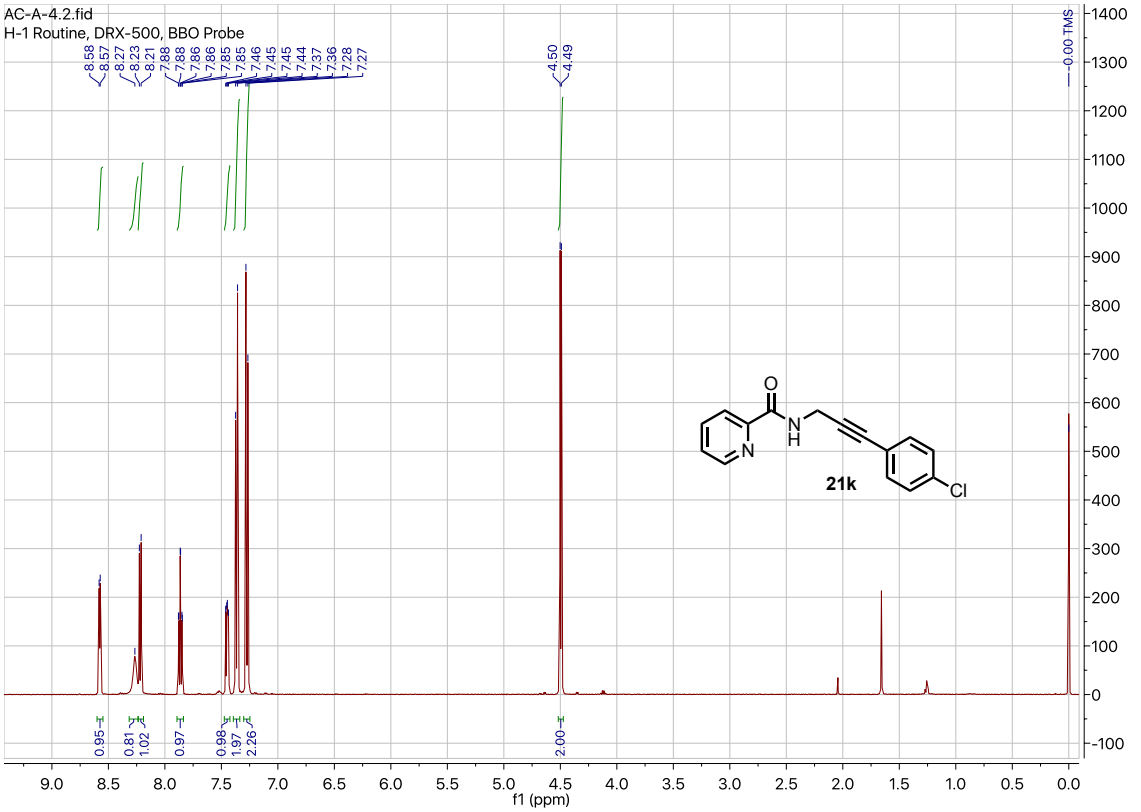

HCl-21g-1.1.fid
C-13 Routine. CDCl, AVIII-600, 5-12-2016
150.04
147.39
147.20
137.44
137.03
136.45
130.24
130.03
129.81
126.57
126.48
125.25
125.22
125.20
125.17
124.76
122.96
122.43
121.16
87.39
81.99
29.85
O
N
H
N
21h
CF3
f1 (ppm)

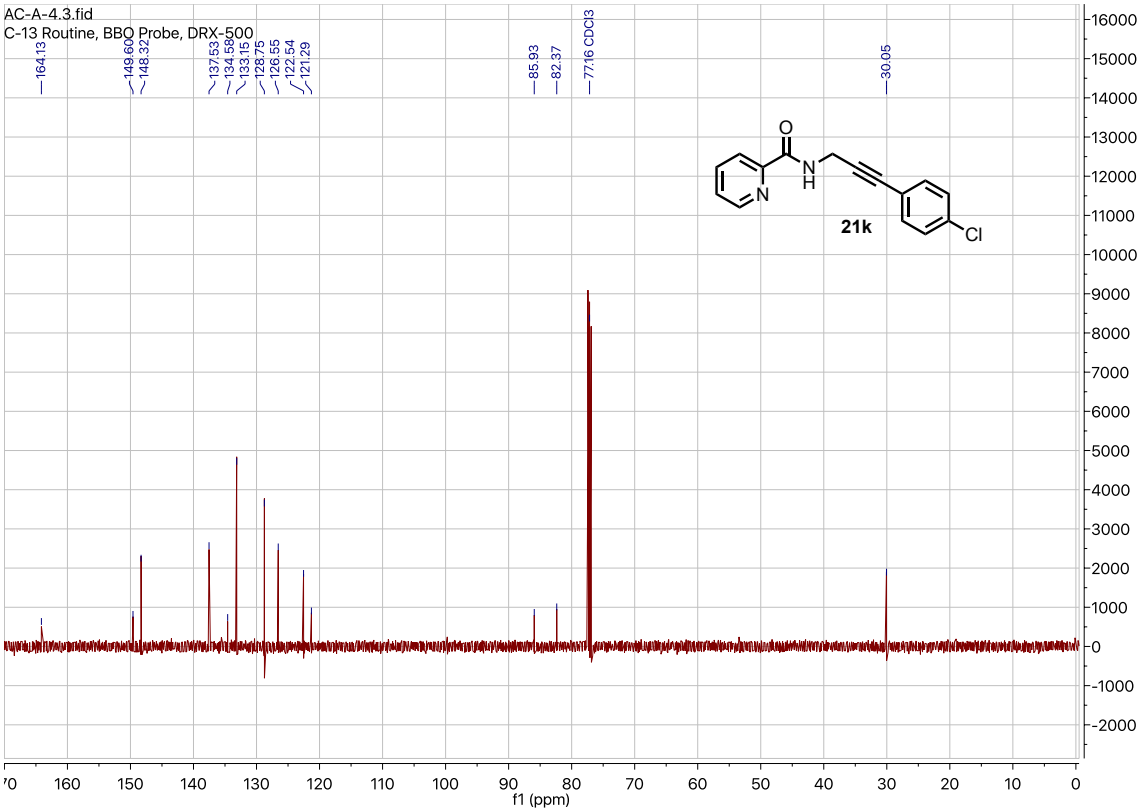

HCl-Sub-2.1.fid
H-1 Routine, DRX-500, BBO Probe
8.26
8.22
8.21
7.88
7.88
7.86
7.86
7.85
7.84
7.46
7.45
7.45
7.43
7.42
7.42
7.41
7.01
6.99
6.97
4.49
4.48
0.93
0.78
1.06
0.98
2.95
1.97
2.00
O
N
H
N
F
21i
f1 (ppm)

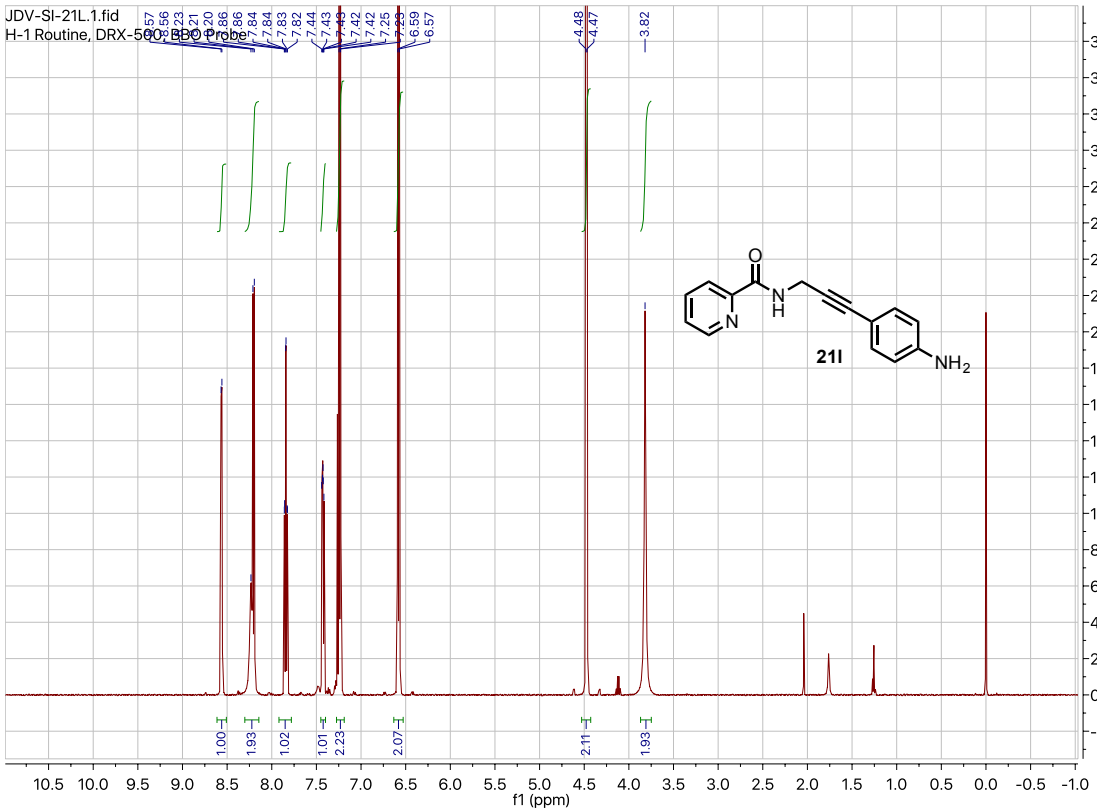

HCl-21h-1.1.fid
C-13 Routine. CPQCI, AVIII-600, 5-12-2016
163.99
163.37
161.72
149.48
148.18
137.40
133.72
133.66
126.41
122.39
118.74
118.71
115.63
115.48
84.46
82.29
29.91
O
N
H
N
F
21i
f1 (ppm)

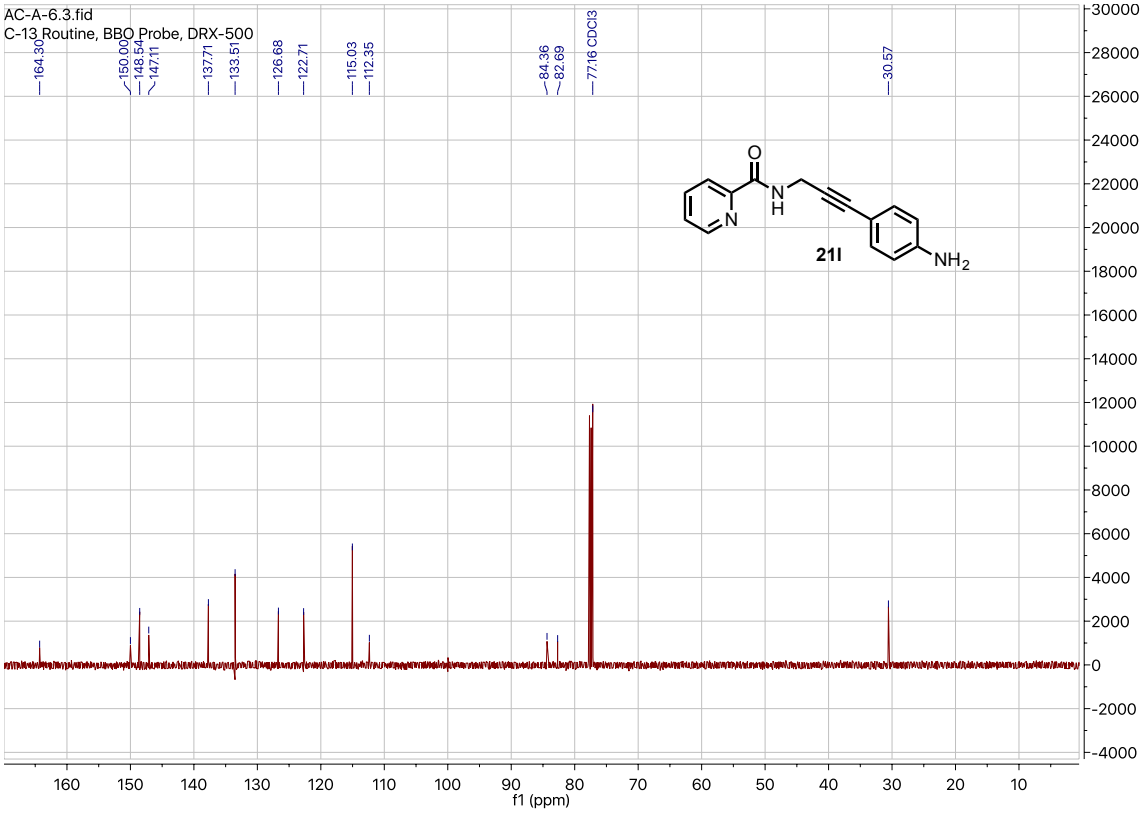

JDV-SI-21J.1.fid
H-1 Routine, DRX-500, BBO Probe
8.58
8.57
8.27
8.22
7.88
7.86
7.85
7.46
7.44
7.42
7.30
7.29
4.49
4.48
1.00
0.81
1.07
1.01
3.04
1.99
2.12
21j
Br
f1 (ppm)

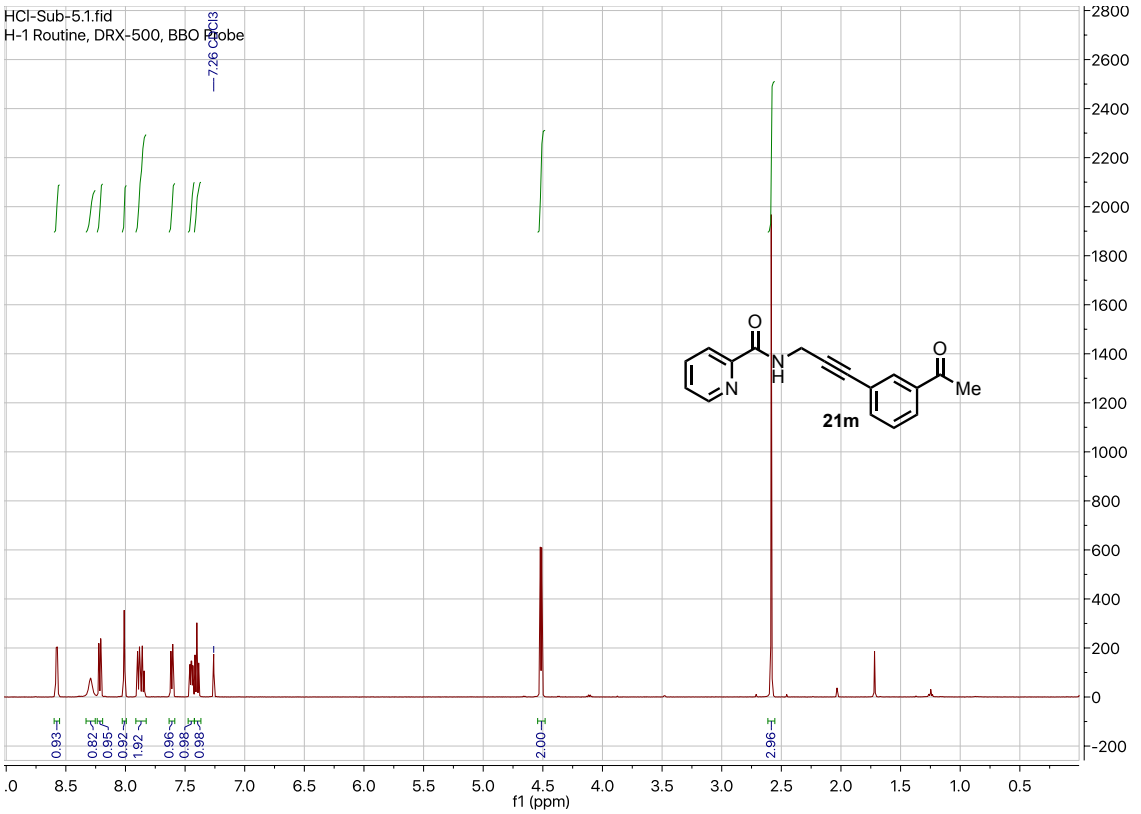

HCl-Sub-10.2.fid
C-13 Routine, BBO Probe, DRX-500
164.84
149.86
149.58
138.81
138.62
138.95
126.83
123.06
122.81
122.02
86.38
82.70
30.33
21j
Br
f1 (ppm)

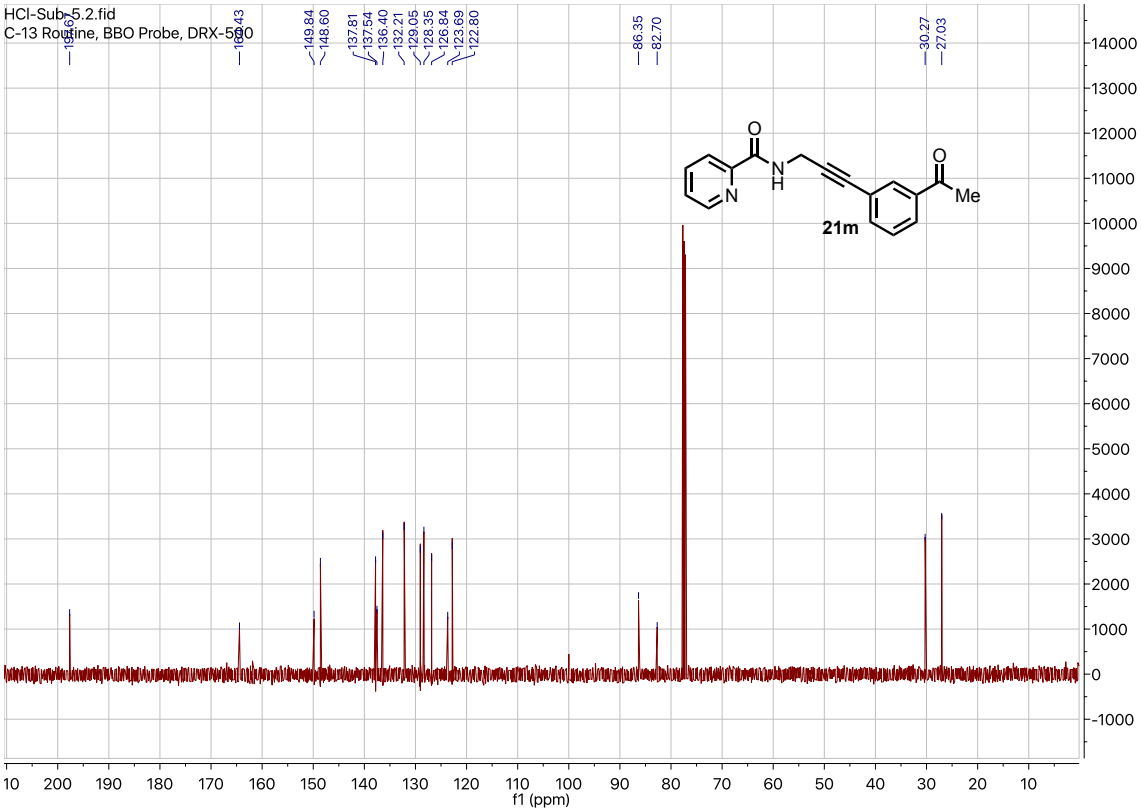

AC-A-4.2.fid
H-1 Routine, DRX-500, BBO Probe
8.58
8.57
8.27
8.23
8.21
7.88
7.88
7.86
7.86
7.85
7.85
7.46
7.45
7.45
7.44
7.37
7.36
7.28
7.27
4.50
4.49
0.00 TMS
0.95
0.81
1.02
0.97
0.98
1.97
2.26
2.00
O
N
H
N
Cl
21k
f1 (ppm)

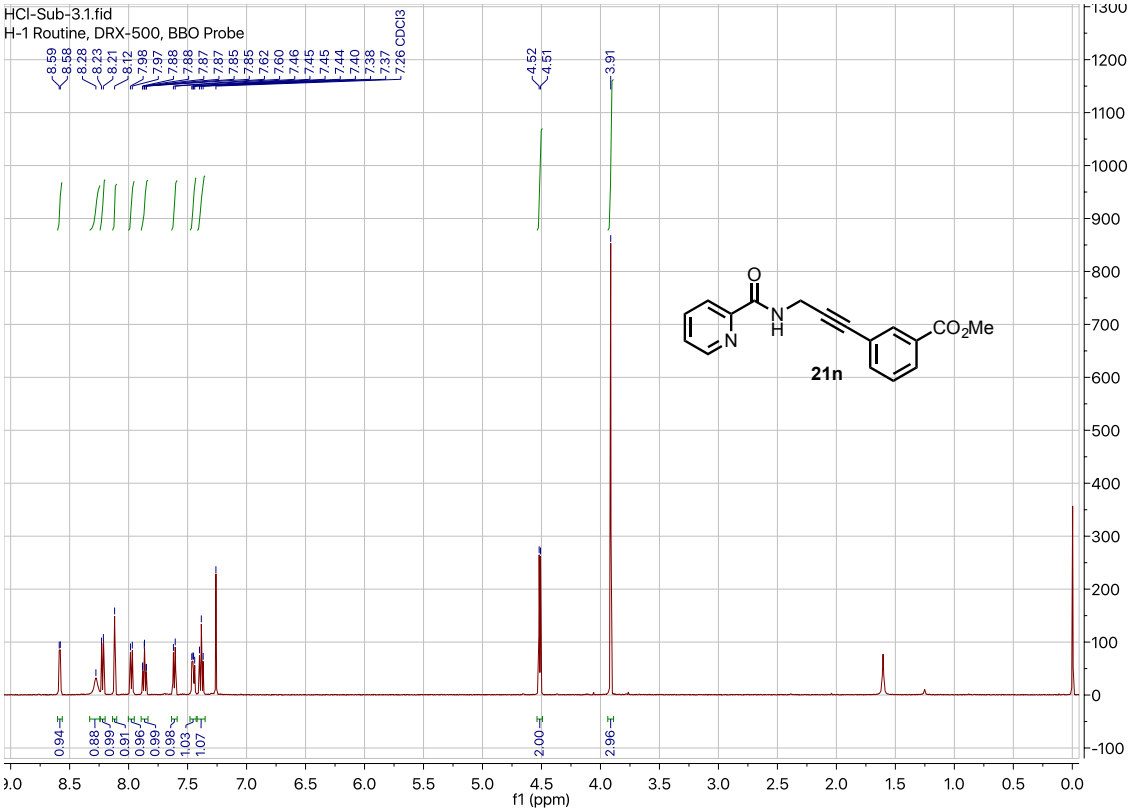

AC-A-4.3.fid
C-13 Routine, BBO Probe, DRX-500
164.13
149.60
148.32
137.53
134.58
133.15
128.75
126.55
122.54
121.29
85.93
82.37
77.16 CDCl3
30.05
O
N
H
N
Cl
21k
f1 (ppm)

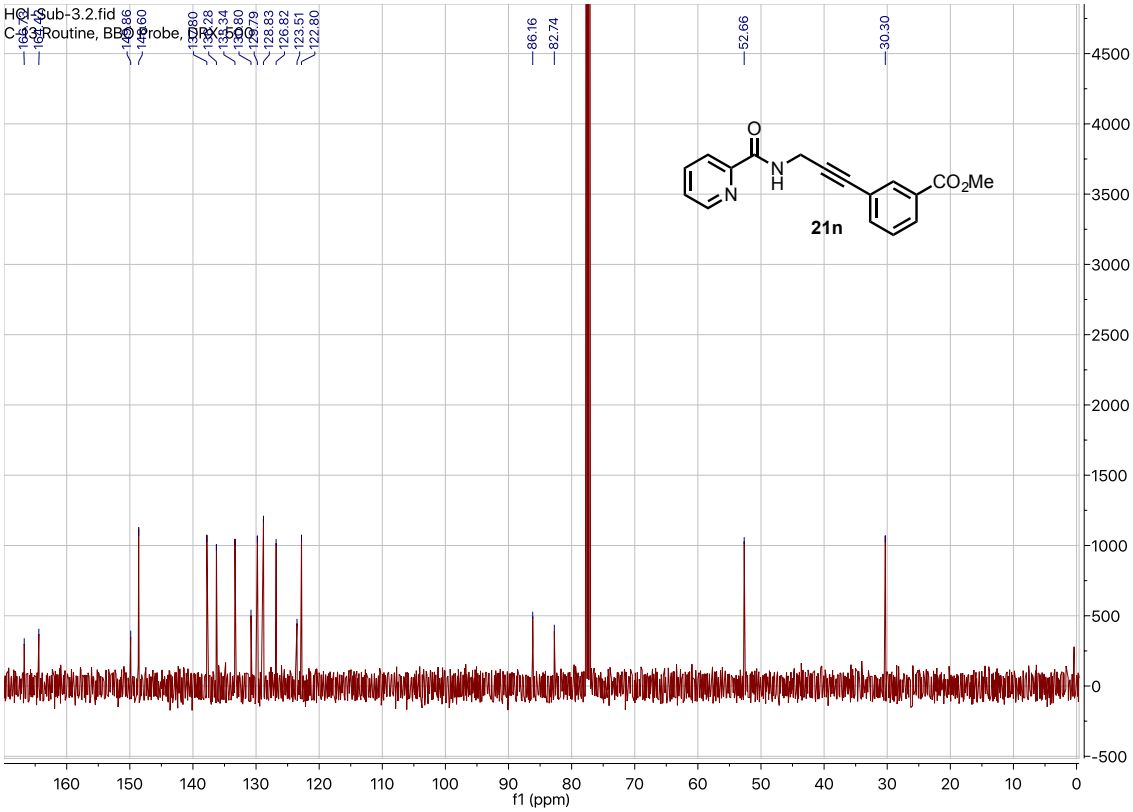

JDV-SI-21L.1.fid
H-1 Routine, DRX-500, BBO Probe
8.57
8.56
8.23
8.21
8.20
7.86
7.86
7.84
7.84
7.83
7.82
7.44
7.43
7.43
7.42
7.42
7.25
6.59
6.57
4.48
4.47
3.82
1.00
1.93
1.02
1.01
2.23
2.07
2.11
1.93
21l
NH2
f1 (ppm)

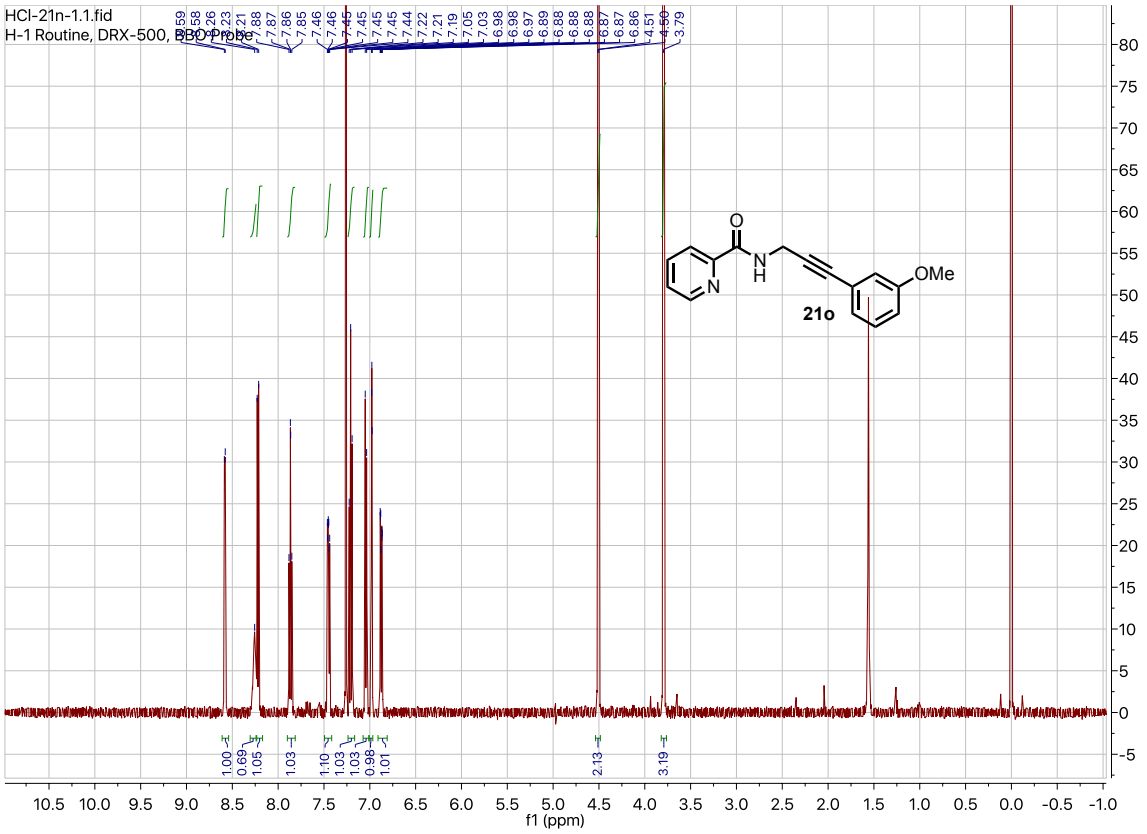

AC-A-6.3.fid
C-13 Routine, BBO Probe, DRX-500
164.30
150.00
148.54
147.11
137.71
133.51
126.68
122.71
115.03
112.35
84.36
82.69
77.16 CDCl3
30.57
21l
NH2
f1 (ppm)

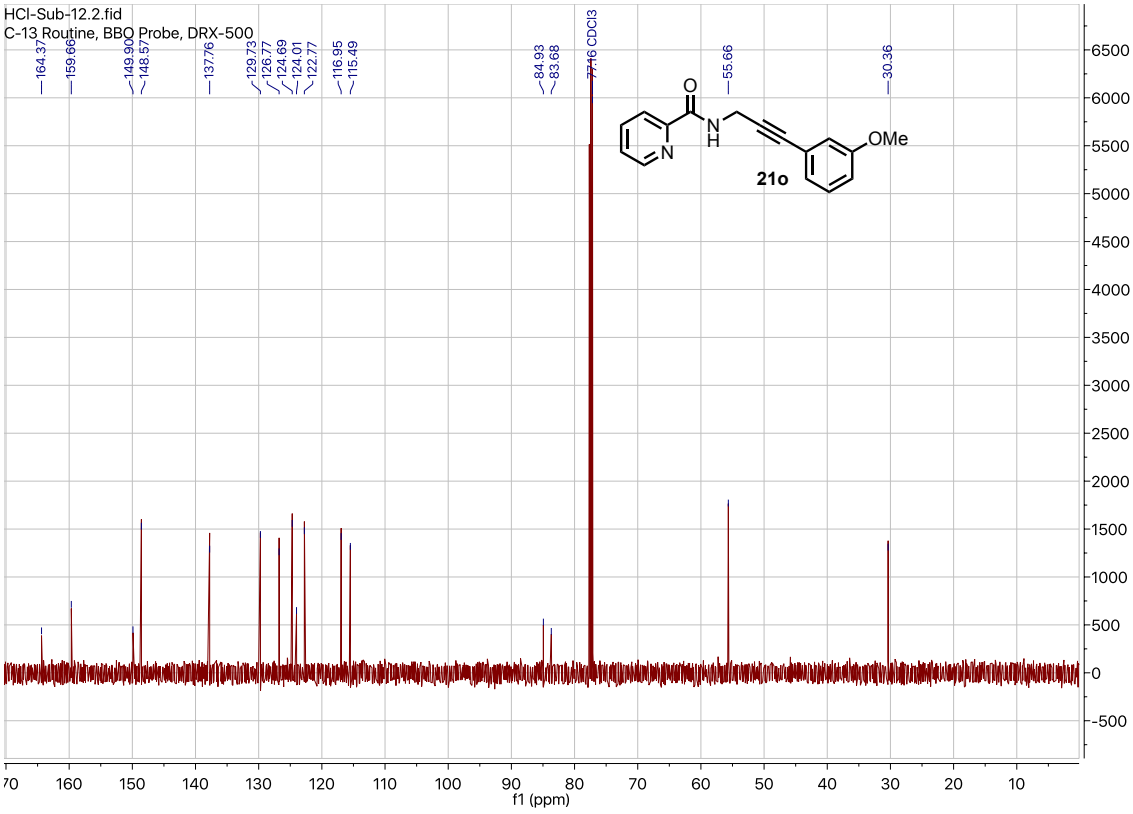

HCl-Sub-5.1.fid
H-1 Routine, DRX-500, BBO Probe
7.26 CDCl3
0.93
0.82
0.95
0.92
1.92
0.96
0.98
0.98
2.00
2.96
f1 (ppm)
21m

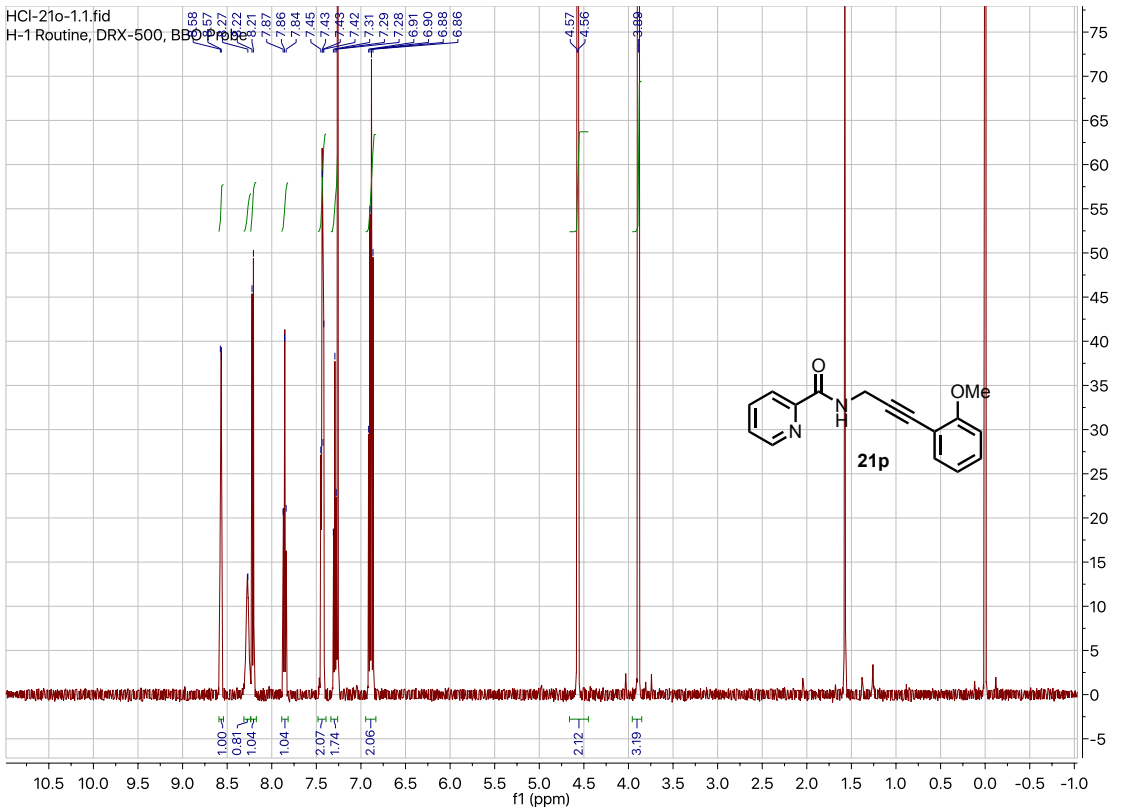

HCl-Sub-5.2.fid
C-13 Routine, BBO Probe, DRX-500
151.67
149.84
148.60
137.81
137.54
136.40
132.21
129.05
128.35
126.84
123.69
122.80
86.35
82.70
30.27
27.03
f1 (ppm)
21m

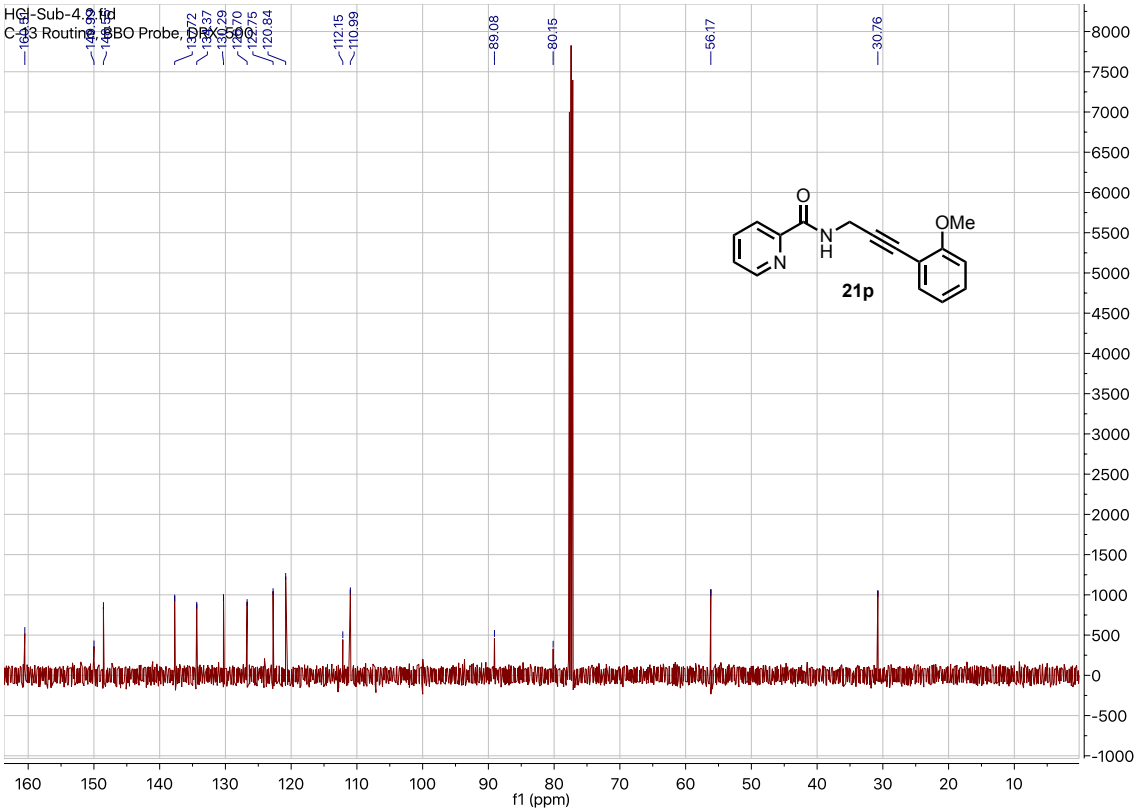

HCl-Sub-3.1.fid
H-1 Routine, DRX-500, BBO Probe
8.59
8.58
8.28
8.23
8.21
8.12
7.98
7.97
7.88
7.88
7.87
7.87
7.85
7.85
7.62
7.60
7.46
7.45
7.45
7.44
7.40
7.38
7.37
7.26 CDCl3
4.52
4.51
3.91
0.94
0.88
0.99
0.91
0.96
0.99
0.98
1.03
1.07
2.00
2.96
f1 (ppm)
21n

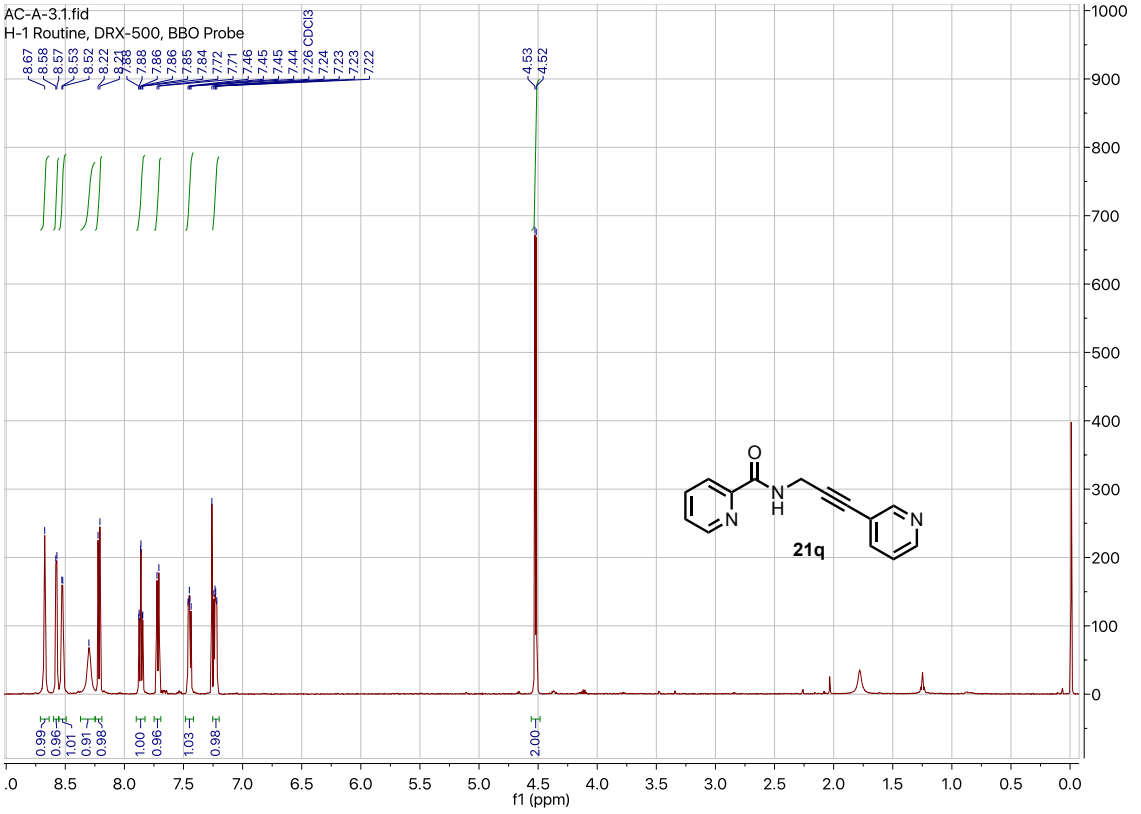

HCl-Sub-3.2.fid
C-13 Routine, BBO Probe, DRX-500
164.76
164.47
146.86
146.60
138.80
138.28
135.34
130.80
129.79
128.83
126.82
123.51
122.80
86.16
82.74
52.66
30.30
f1 (ppm)
21n

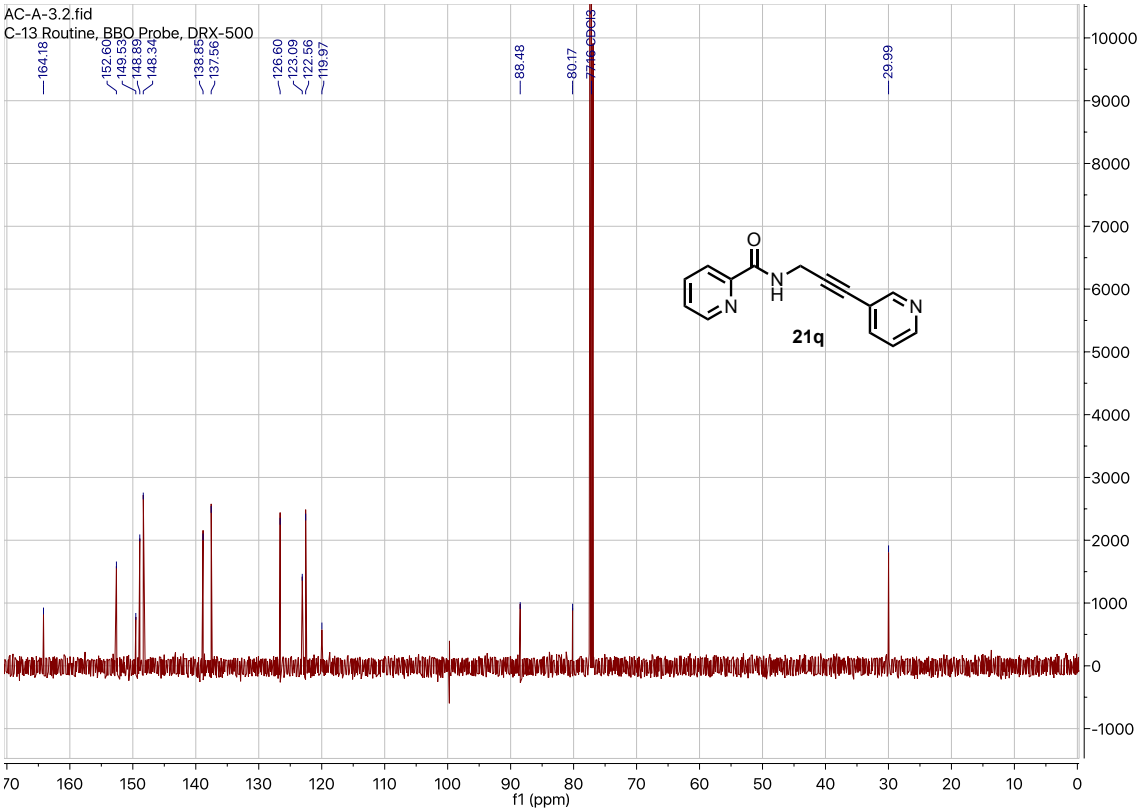

HCl-21n-1.1.fid
H-1 Routine, DRX-500, BBO Probe
21o
f1 (ppm)

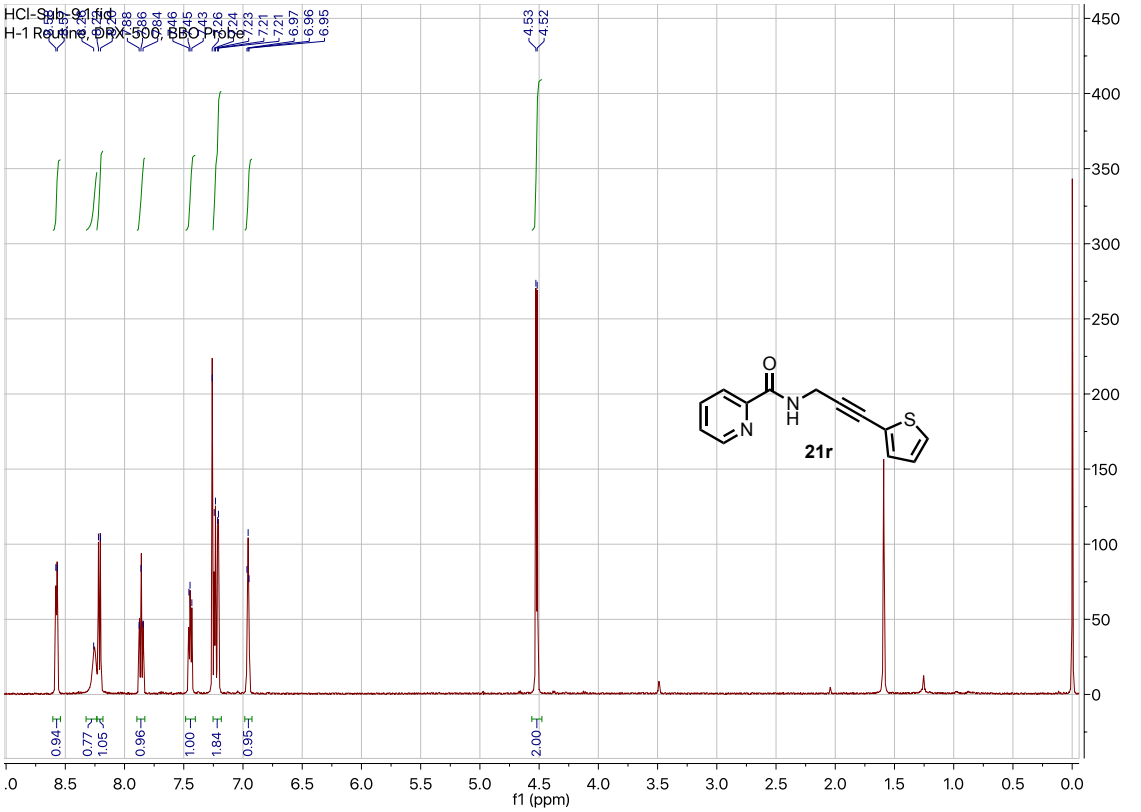

HCl-Sub-12.2.fid
C-13 Routine, BBO Probe, DRX-500
164.37
159.66
149.90
148.57
137.76
129.73
126.77
124.69
124.01
122.77
116.95
115.49
84.93
83.68
77.16 CDCl3
55.66
30.36
21o
f1 (ppm)

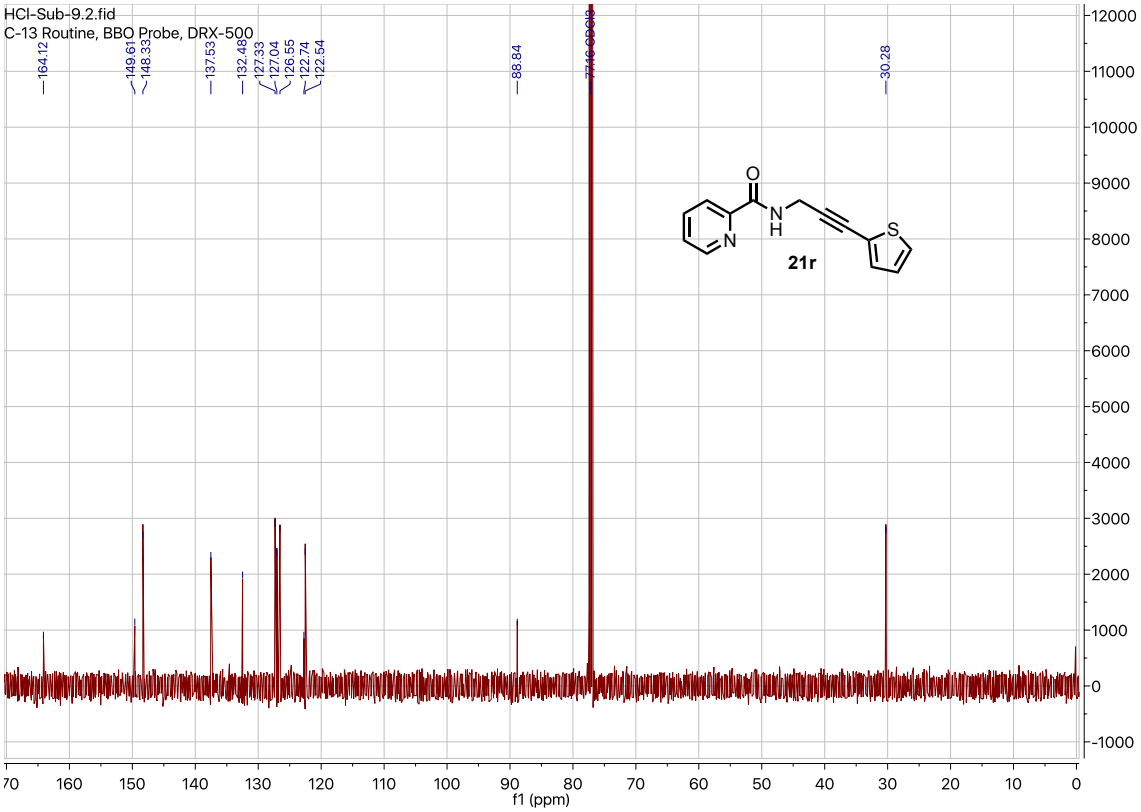

HCl-21o-1.1.fid
H-1 Routine, DRX-500, BBO Probe
21p
f1 (ppm)

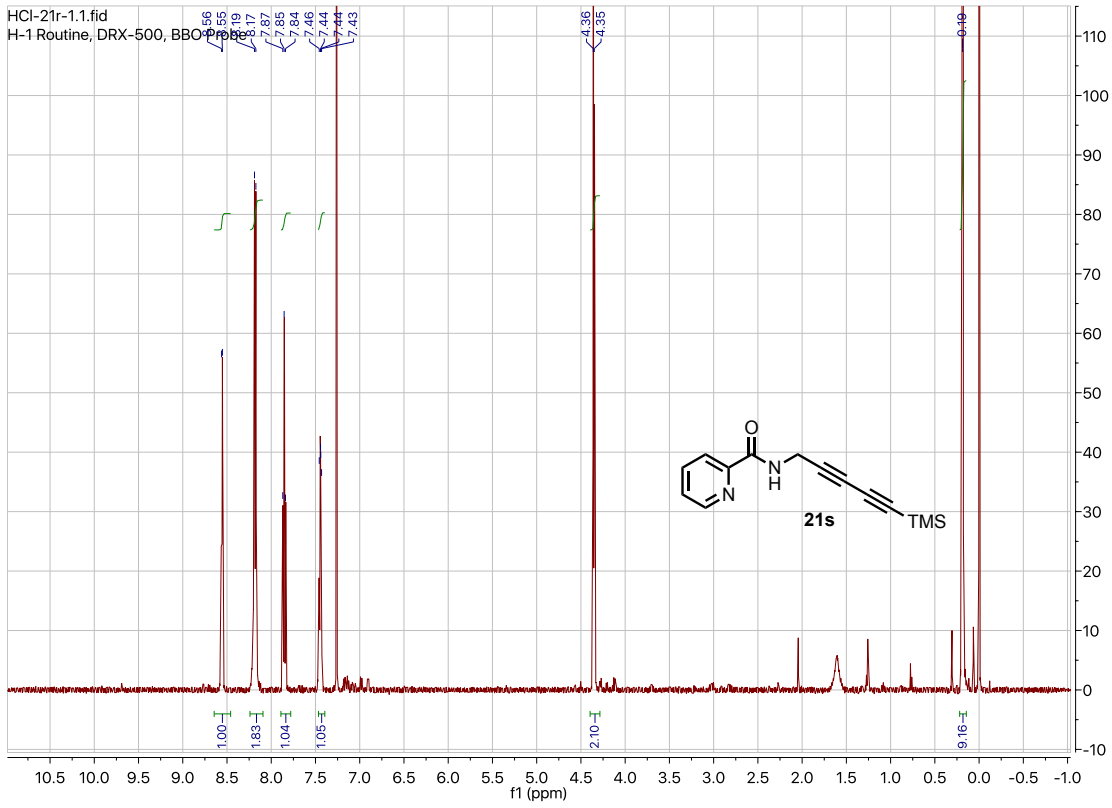

HCl-Sub-4.2.fid
C-13 Routine, BBO Probe, DRX-500
21p
f1 (ppm)

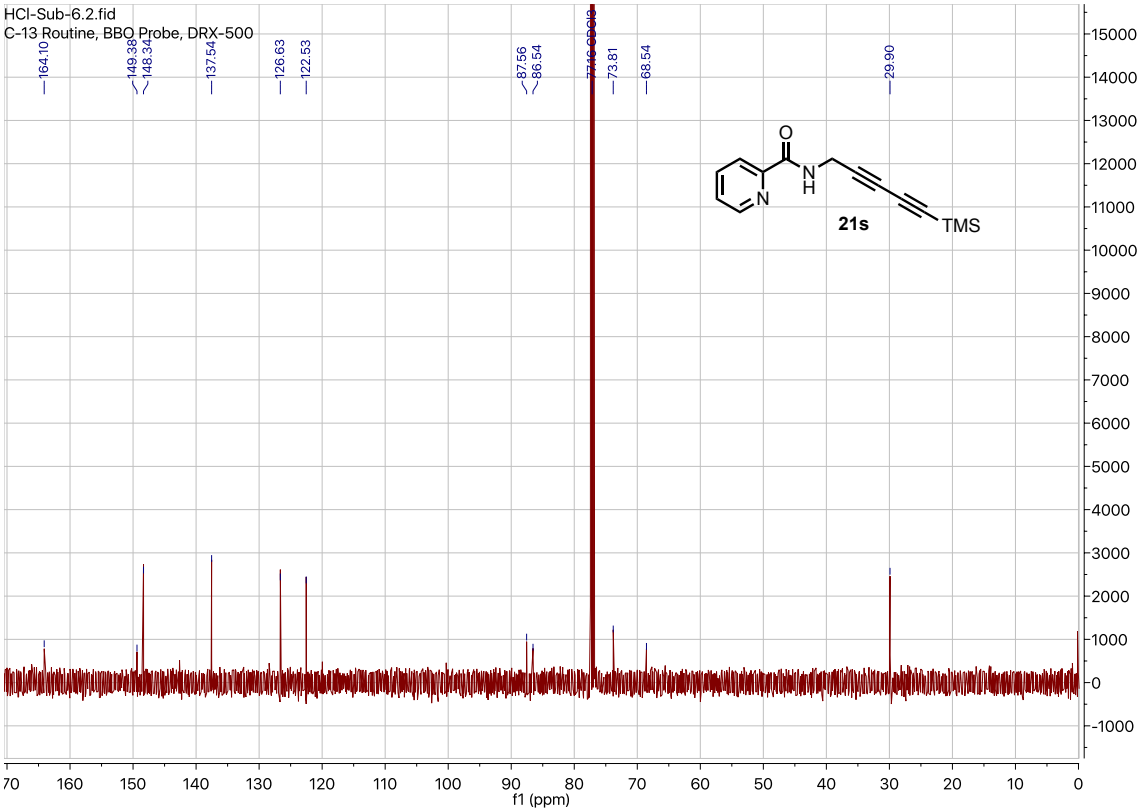

AC-A-3.1.fid
H-1 Routine, DRX-500, BBO Probe
8.67
8.58
8.57
8.53
8.52
8.22
7.88
7.86
7.86
7.85
7.84
7.72
7.71
7.46
7.45
7.44
7.26 CDCl3
7.24
7.23
7.23
7.22
4.53
4.52
0.99
0.96
1.01
0.91
0.98
1.00
0.96
1.03
0.98
2.00
21q
f1 (ppm)

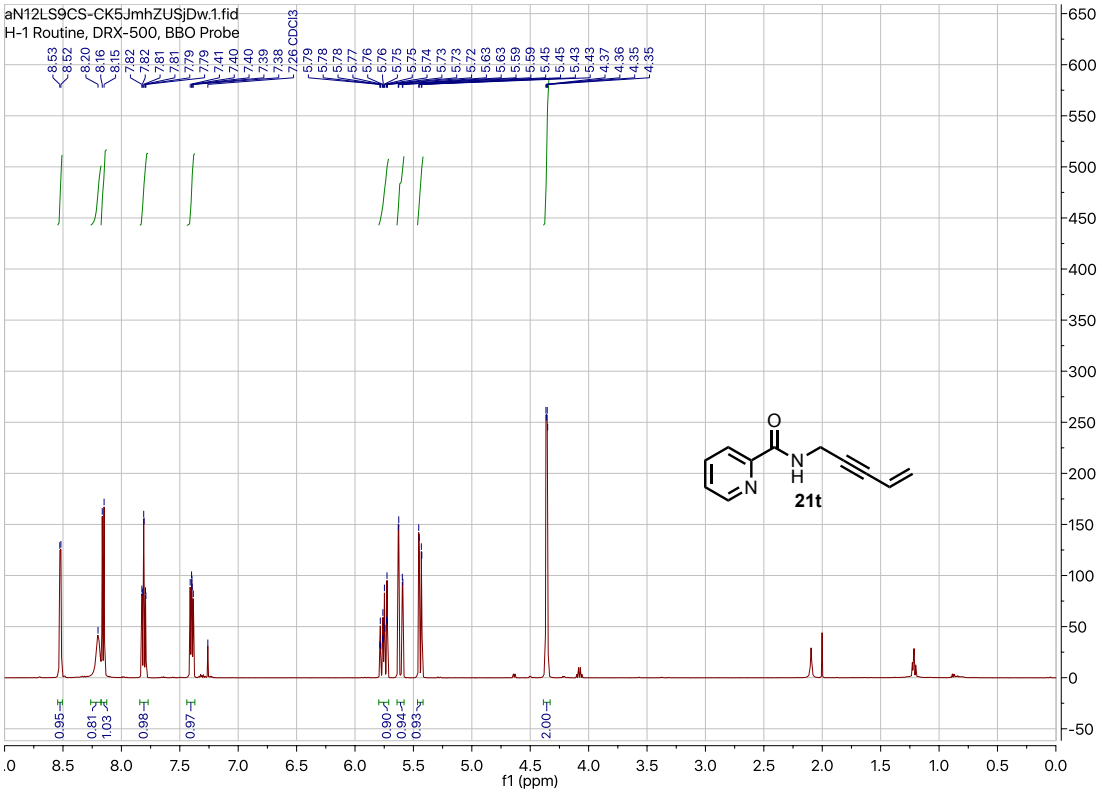

AC-A-3.2.fid
C-13 Routine, BBO Probe, DRX-500
164.18
152.60
149.53
148.89
148.34
138.85
137.56
126.60
123.09
122.56
119.97
88.48
80.17
77.46 CDCl3
29.99
21q
f1 (ppm)

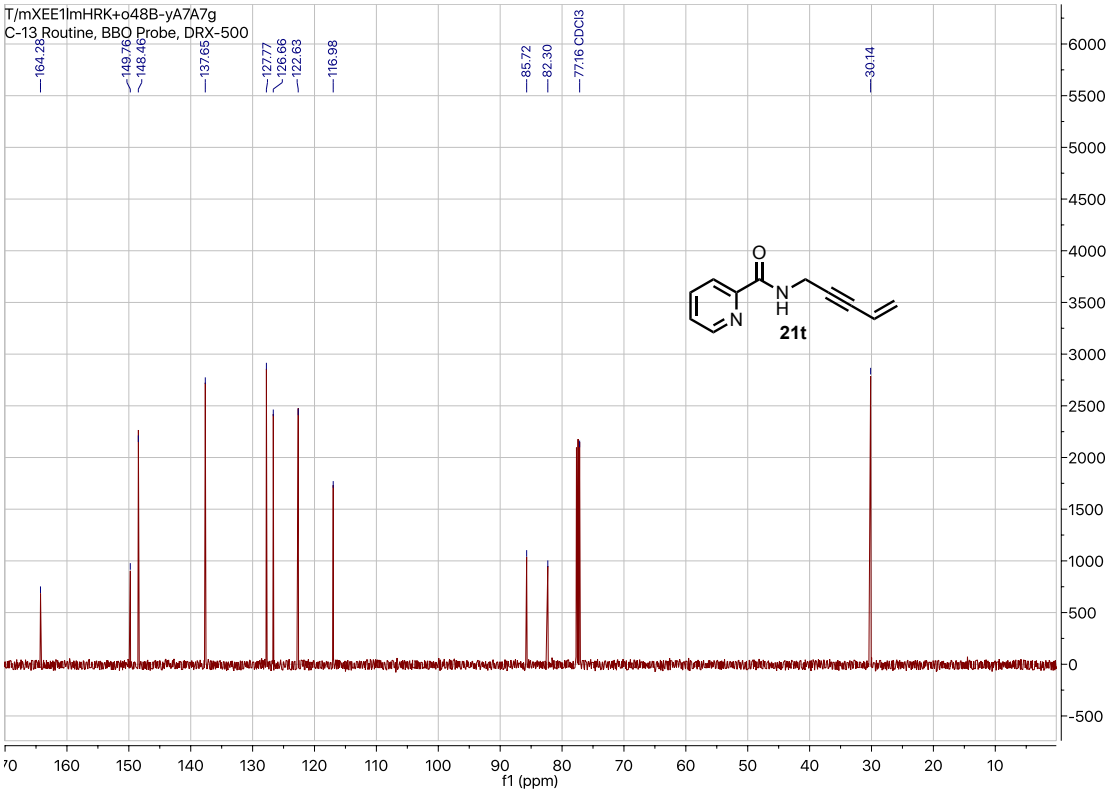

HCl-Sub-9.1.fid
H-1 Routine, DRX-500, BBO Probe
4.53
4.52
7.88
7.86
7.84
7.46
7.45
7.43
7.26
7.24
7.23
7.21
7.21
6.97
6.96
6.95
0.94
0.77
1.05
0.96
1.00
1.84
0.95
2.00
f1 (ppm)
21r

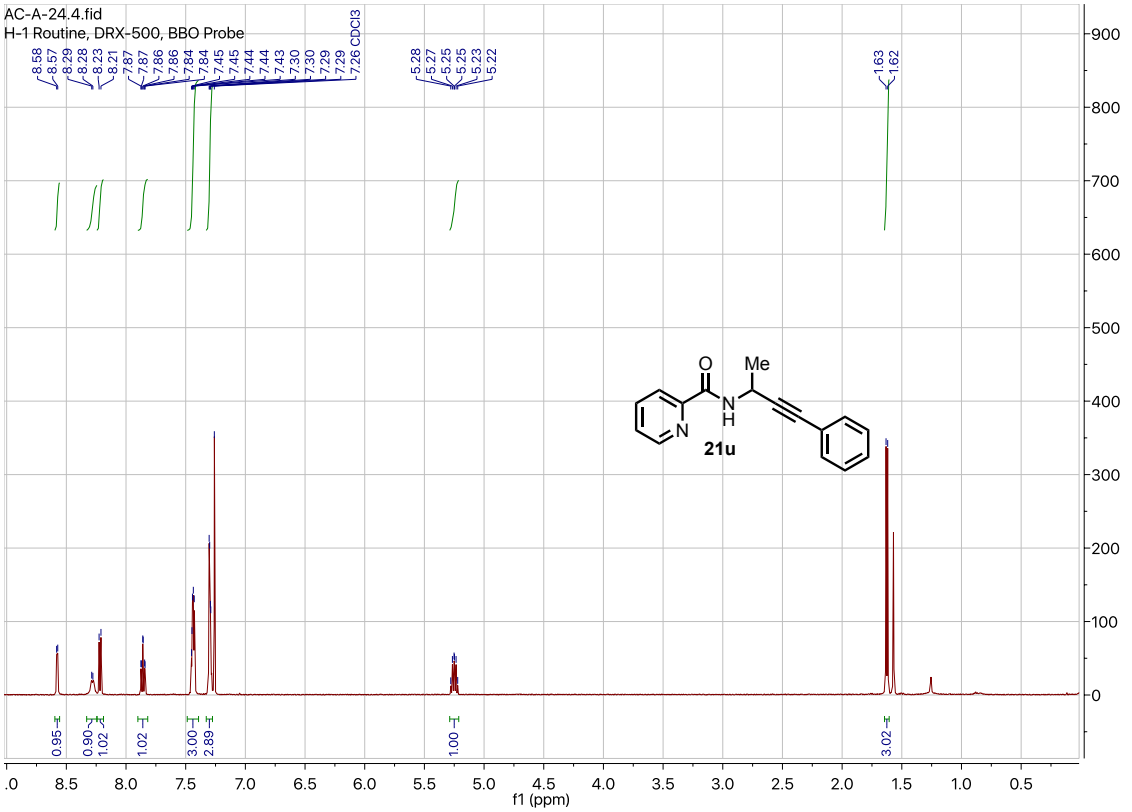

HCl-Sub-9.2.fid
C-13 Routine, BBO Probe, DRX-500
164.12
149.61
148.33
137.53
132.48
127.33
127.04
126.55
122.74
122.54
88.84
77.16
30.28
f1 (ppm)
21r

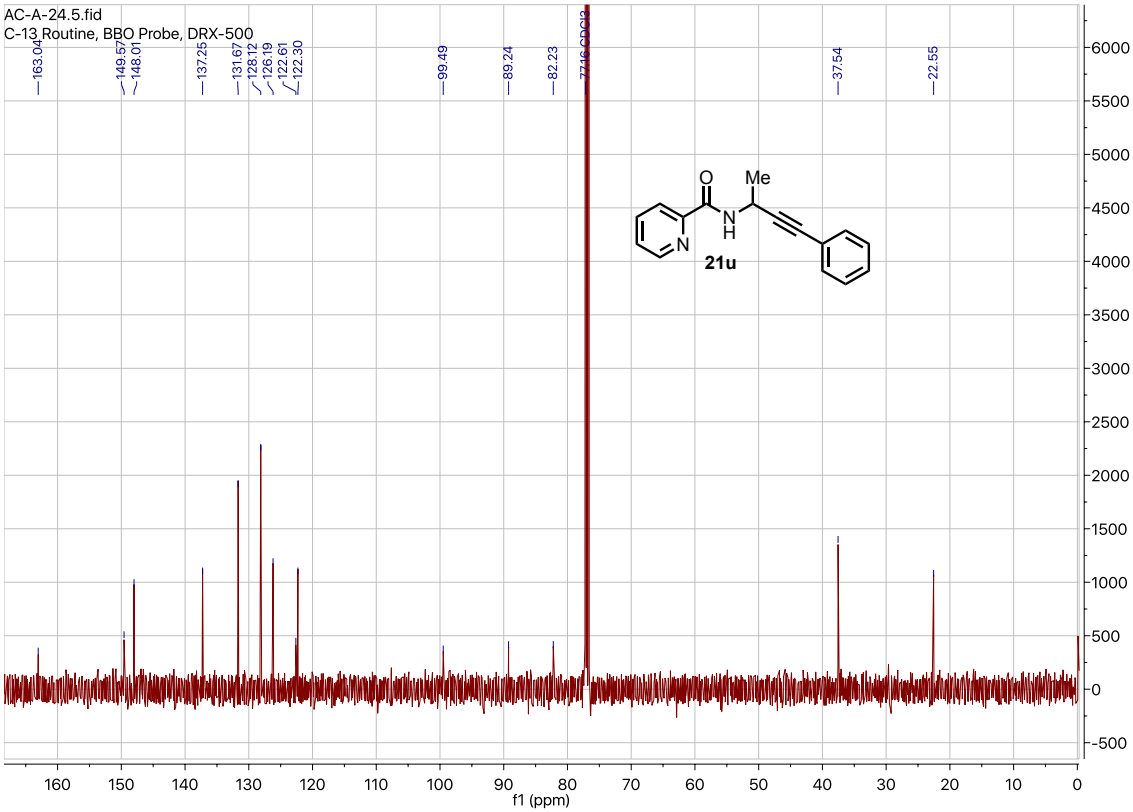

HCl-21r-1.1.fid
H-1 Routine, DRX-500, BBO Probe
8.56
8.55
8.19
8.17
7.87
7.85
7.84
7.46
7.44
7.44
7.43
4.36
4.35
0.19
1.00
1.83
1.04
1.05
2.10
9.16
O
N
H
N
21s
TMS
f1 (ppm)

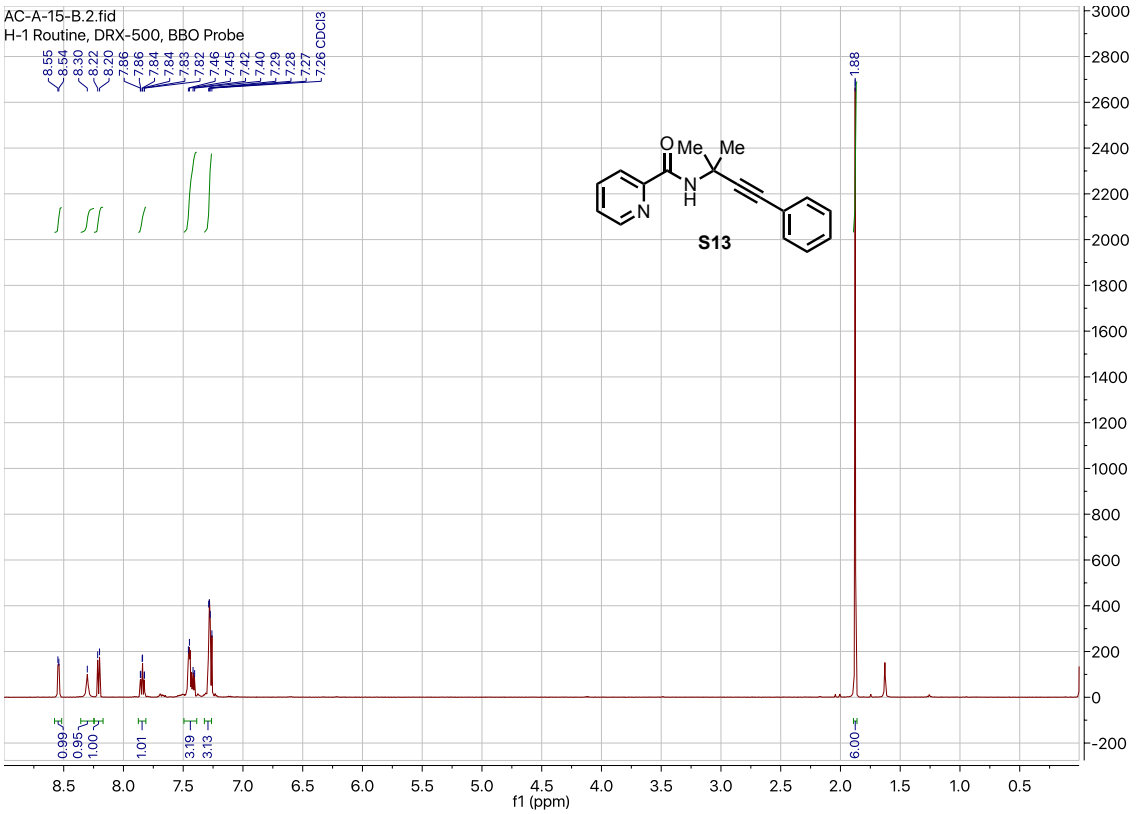

HCl-Sub-6.2.fid
C-13 Routine, BBO Probe, DRX-500
164.10
149.38
148.34
137.54
126.63
122.53
87.56
86.54
77.16 CDCl3
73.81
68.54
29.90
O
N
H
N
21s
TMS
f1 (ppm)

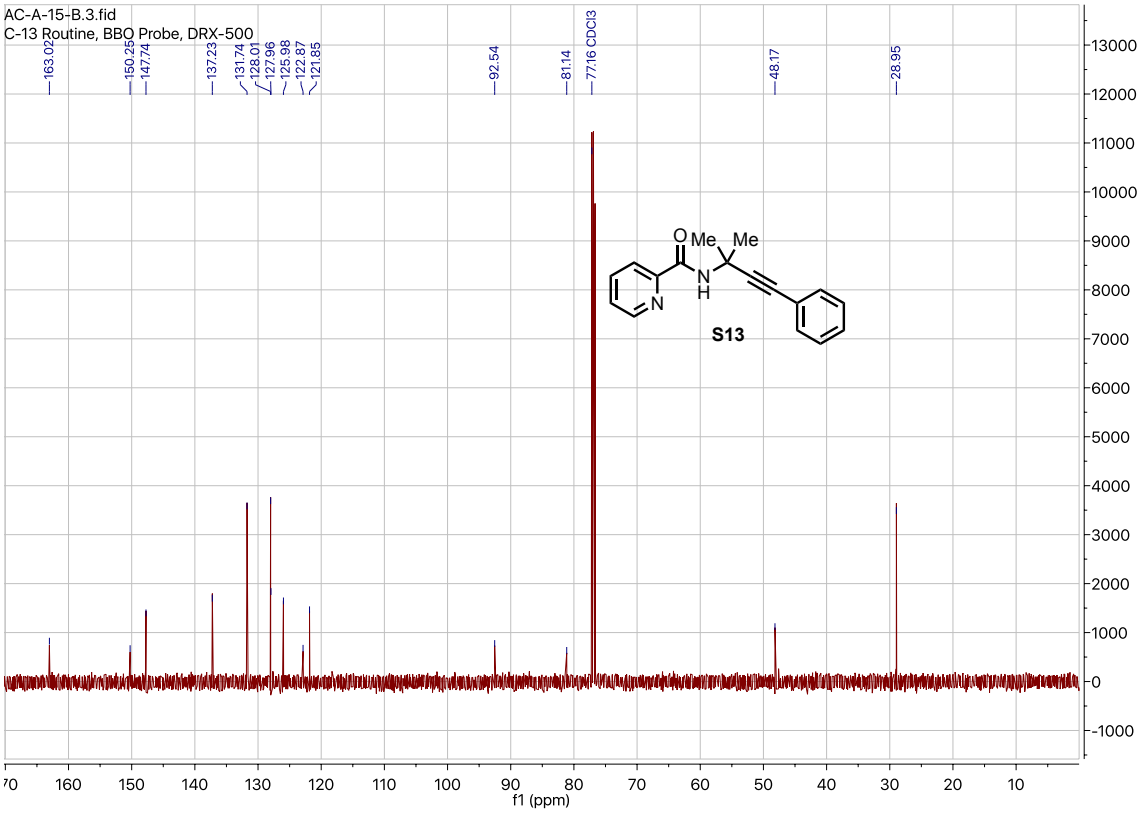

aN12LS9CS-CK5JmhZUSjDw.1.fid
H-1 Routine, DRX-500, BBO Probe
8.53
8.52
8.20
8.16
8.15
7.82
7.82
7.81
7.81
7.79
7.79
7.41
7.40
7.40
7.39
7.38
7.26 CDCl3
5.79
5.78
5.78
5.77
5.76
5.76
5.75
5.75
5.74
5.73
5.73
5.72
5.63
5.63
5.59
5.59
5.45
5.45
5.43
5.43
4.37
4.36
4.35
4.35
0.95
0.81
1.03
0.98
0.97
0.90
0.94
0.93
2.00
21t
f1 (ppm)

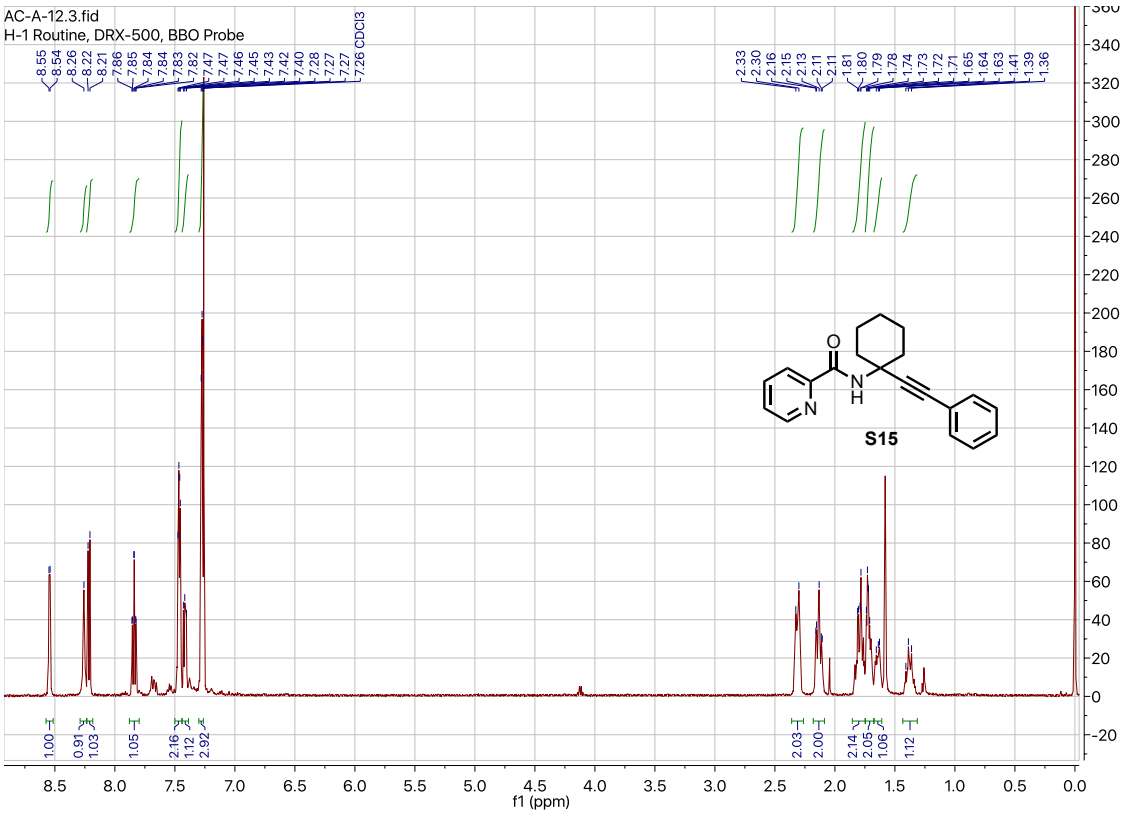

T/mXEE1lmHRK+o48B-yA7A7g
C-13 Routine, BBO Probe, DRX-500
164.28
149.76
148.46
137.65
127.77
126.66
122.63
116.98
85.72
82.30
77.16 CDCl3
30.14
21t
f1 (ppm)

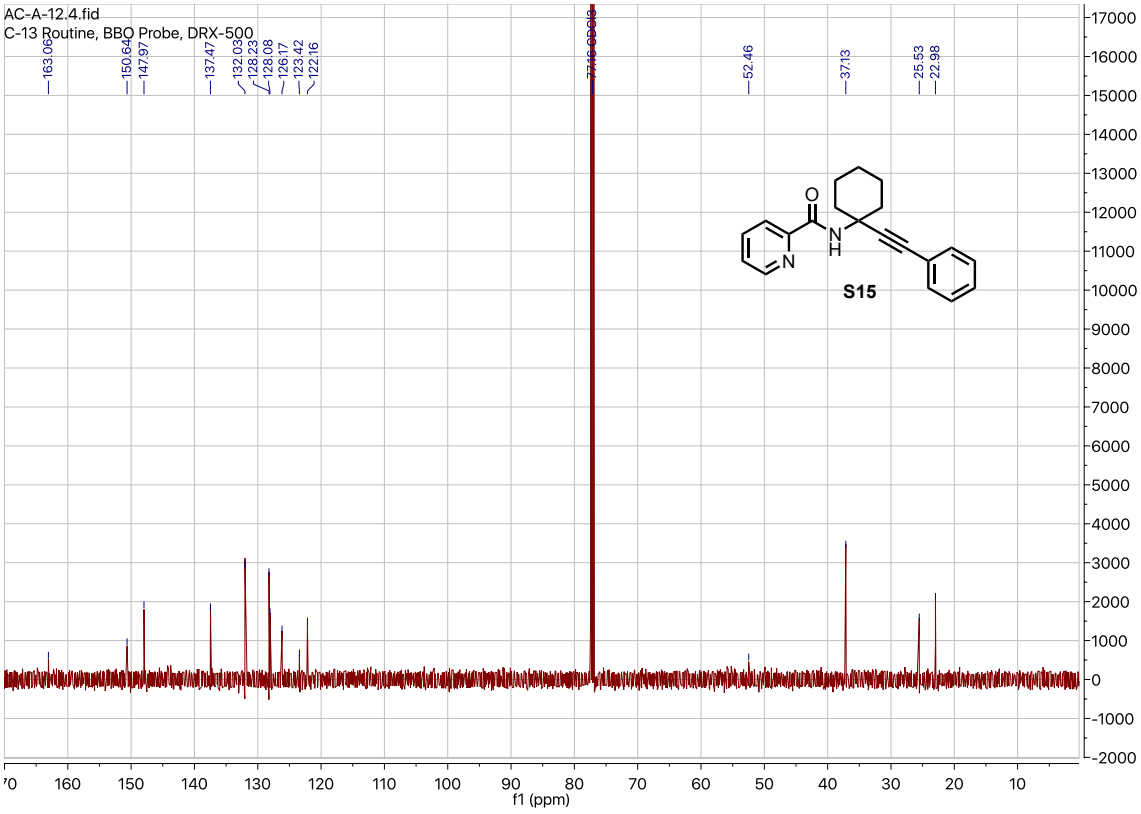

AC-A-24.4.fid
H-1 Routine, DRX-500, BBO Probe
8.58
8.57
8.29
8.28
8.23
8.21
7.87
7.87
7.86
7.86
7.84
7.84
7.45
7.45
7.44
7.44
7.43
7.30
7.30
7.29
7.29
7.26 CDCl3
5.28
5.27
5.25
5.25
5.23
5.22
1.63
1.62
O
Me
N
H
N
21u
0.95
0.90
1.02
1.02
3.00
2.89
1.00
3.02
f1 (ppm)

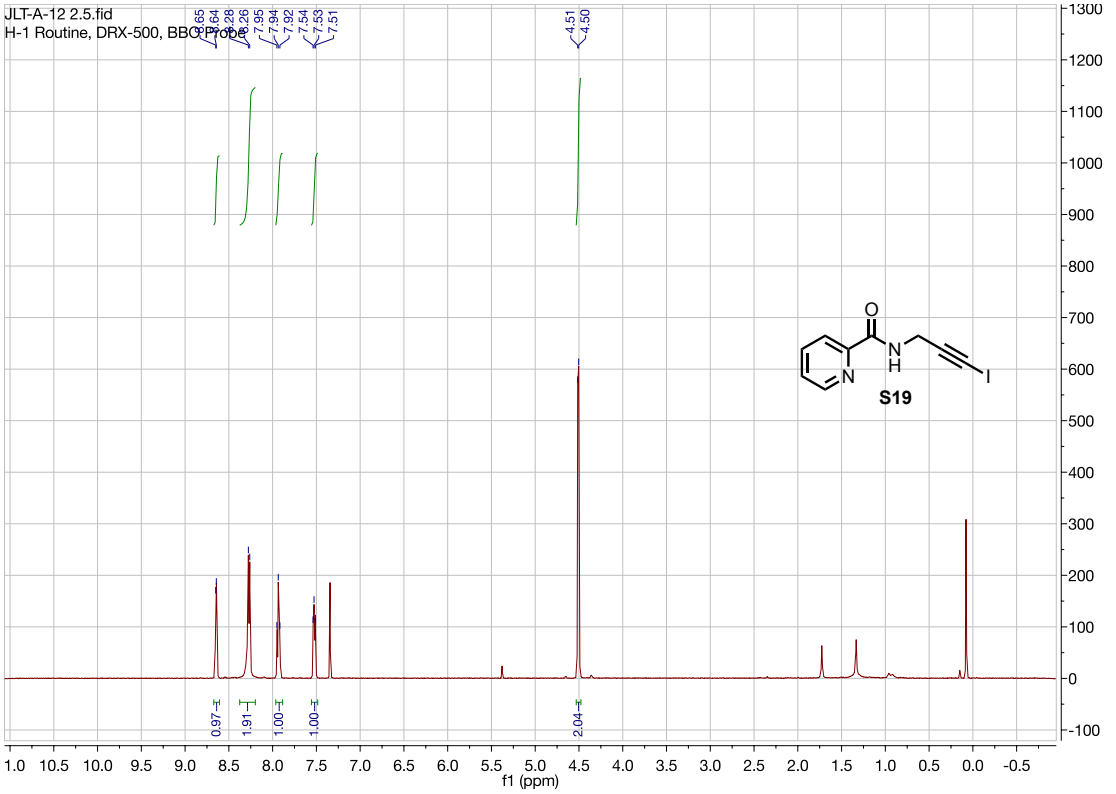

AC-A-24.5.fid
C-13 Routine, BBO Probe, DRX-500
163.04
149.57
148.01
137.25
131.67
128.12
126.19
122.61
122.30
99.49
89.24
82.23
77.16 CDCl3
37.54
22.55
O
Me
N
H
N
21u
f1 (ppm)

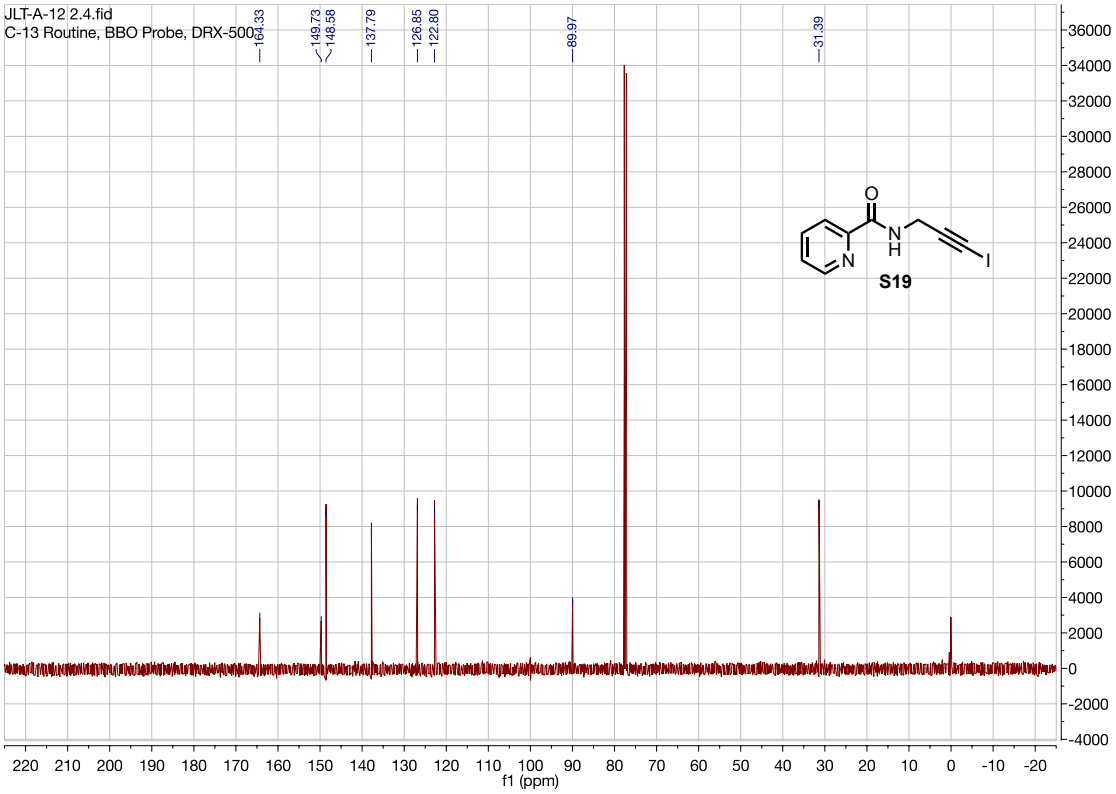

AC-A-15-B.2.fid
H-1 Routine, BBO Probe, DRX-500
8.55
8.54
8.30
8.22
8.20
7.86
7.86
7.84
7.84
7.83
7.82
7.46
7.45
7.42
7.40
7.29
7.28
7.27
7.26 CDCl3
1.88
Me
Me
O
N
H
N
S13
0.99
0.95
1.00
1.01
3.19
3.13
6.00
f1 (ppm)

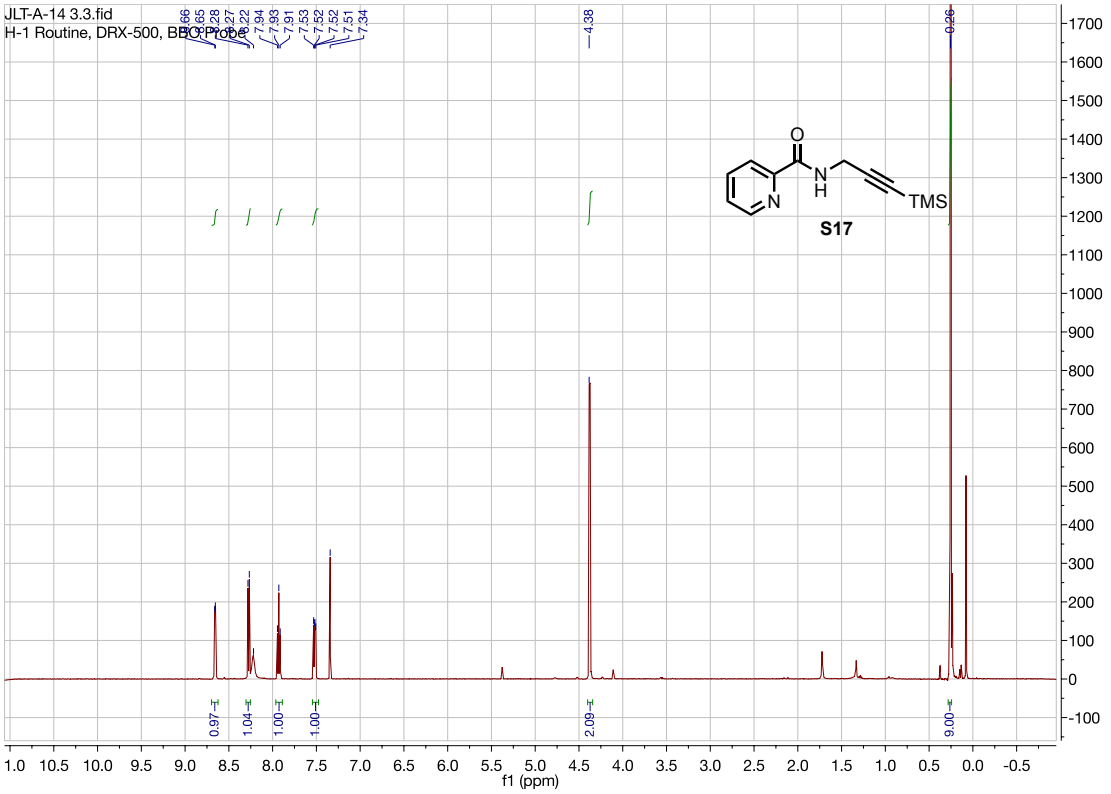

AC-A-15-B.3.fid
C-13 Routine, BBO Probe, DRX-500
163.02
150.26
147.74
137.23
131.74
128.01
127.96
125.98
122.87
121.85
92.54
81.14
77.16 CDCl3
48.17
28.95
Me
Me
O
N
H
N
S13
f1 (ppm)

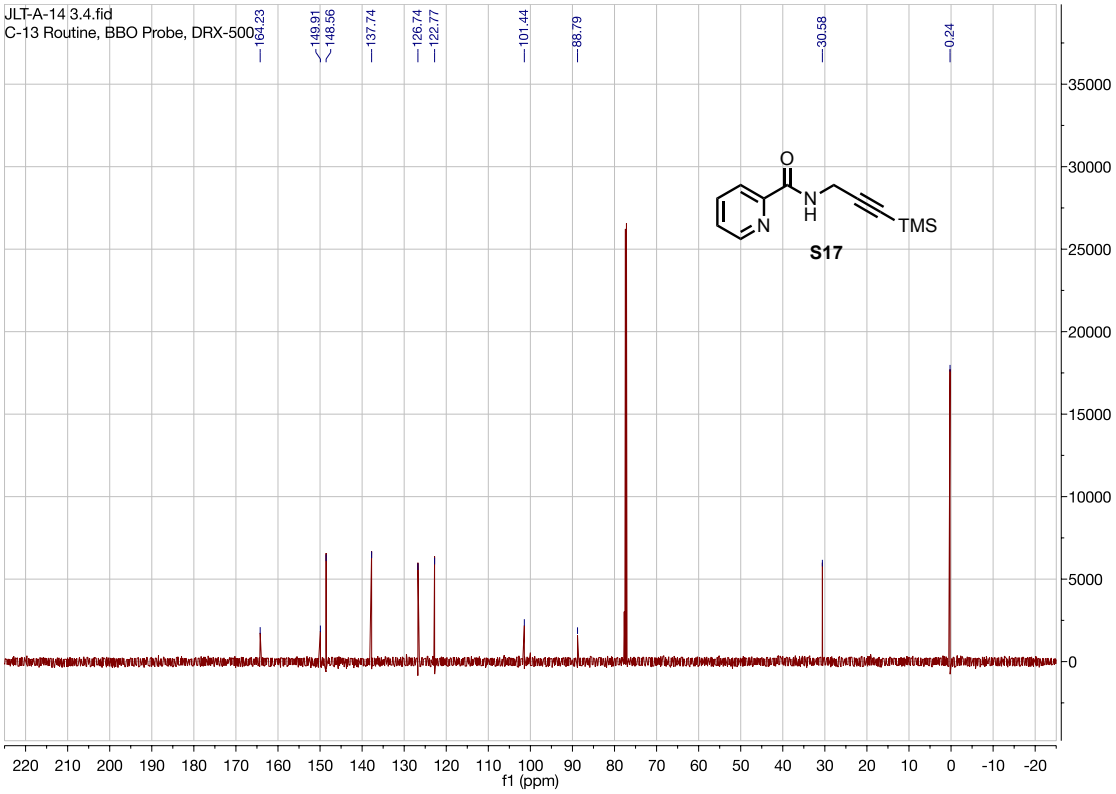

AC-A-12.3.fid
H-1 Routine, DRX-500, BBO Probe
S15
f1 (ppm)

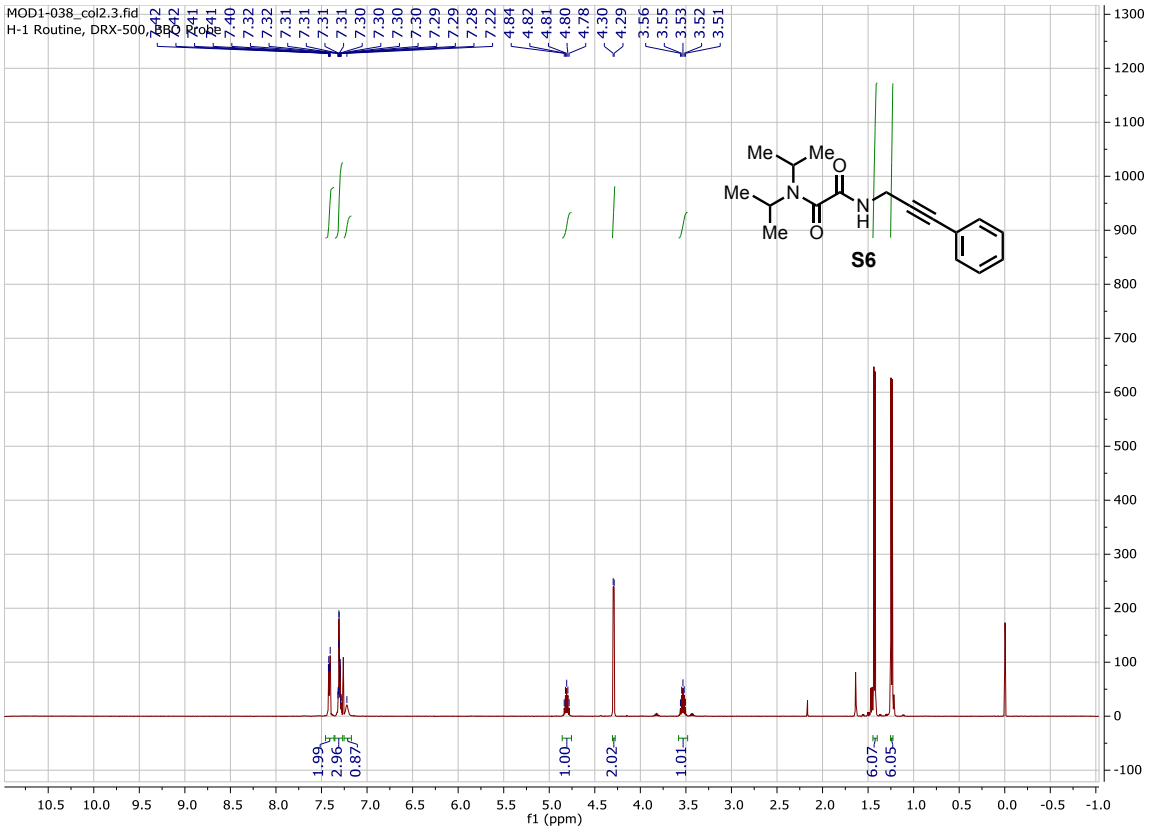

AC-A-12.4.fid
C-13 Routine, BBO Probe, DRX-500
S15
f1 (ppm)

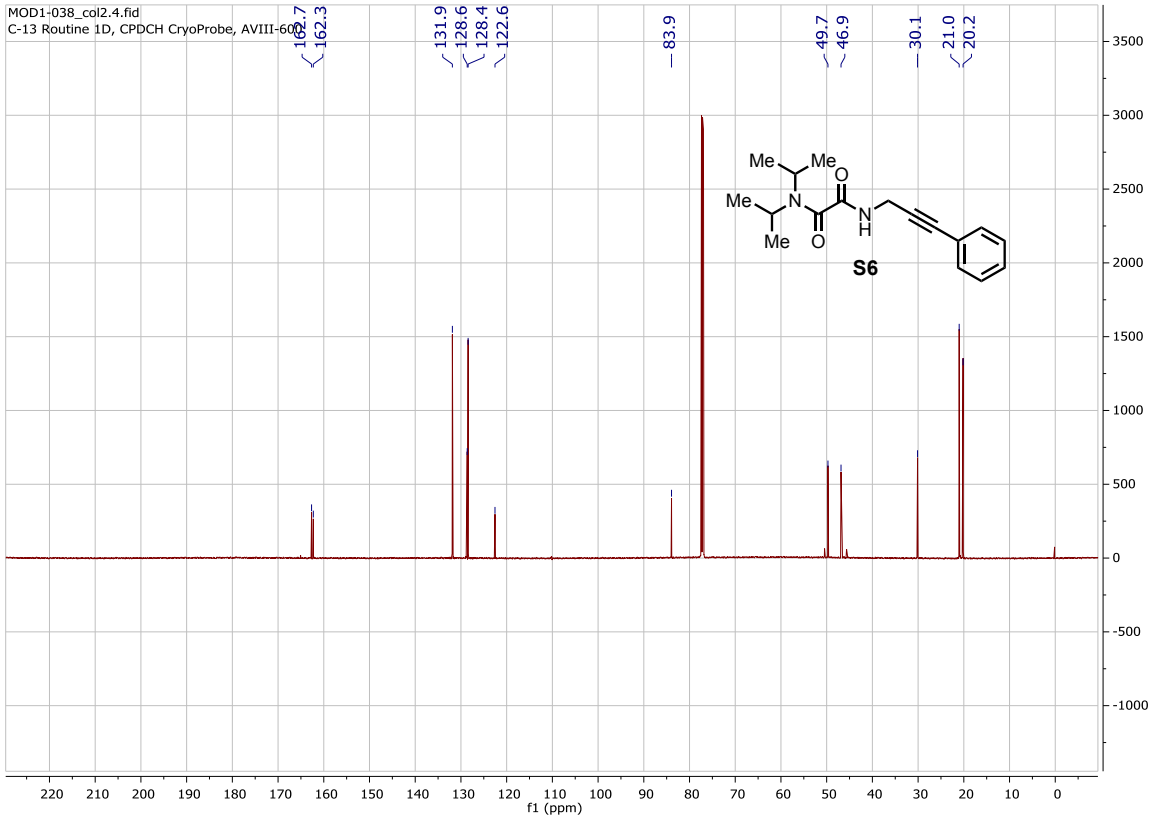

JLT-A-12 2.5.fid
H-1 Routine, DRX-500, BBO Probe
8.65
8.64
8.28
8.26
7.95
7.94
7.92
7.54
7.53
7.51
4.51
4.50
0.97
1.91
1.00
1.00
2.04
S19
f1 (ppm)

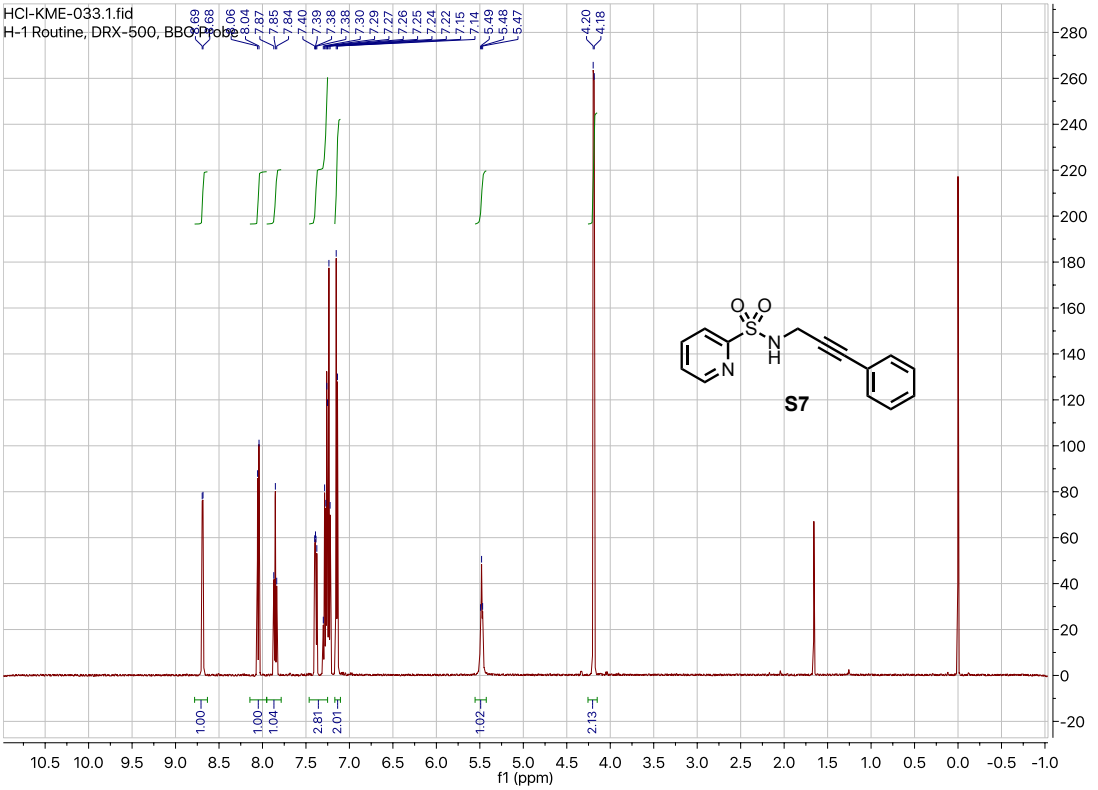

JLT-A-12 2.4.fid
C-13 Routine, BBO Probe, DRX-500
164.33
149.73
148.58
137.79
126.85
122.80
89.97
31.39
S19
f1 (ppm)

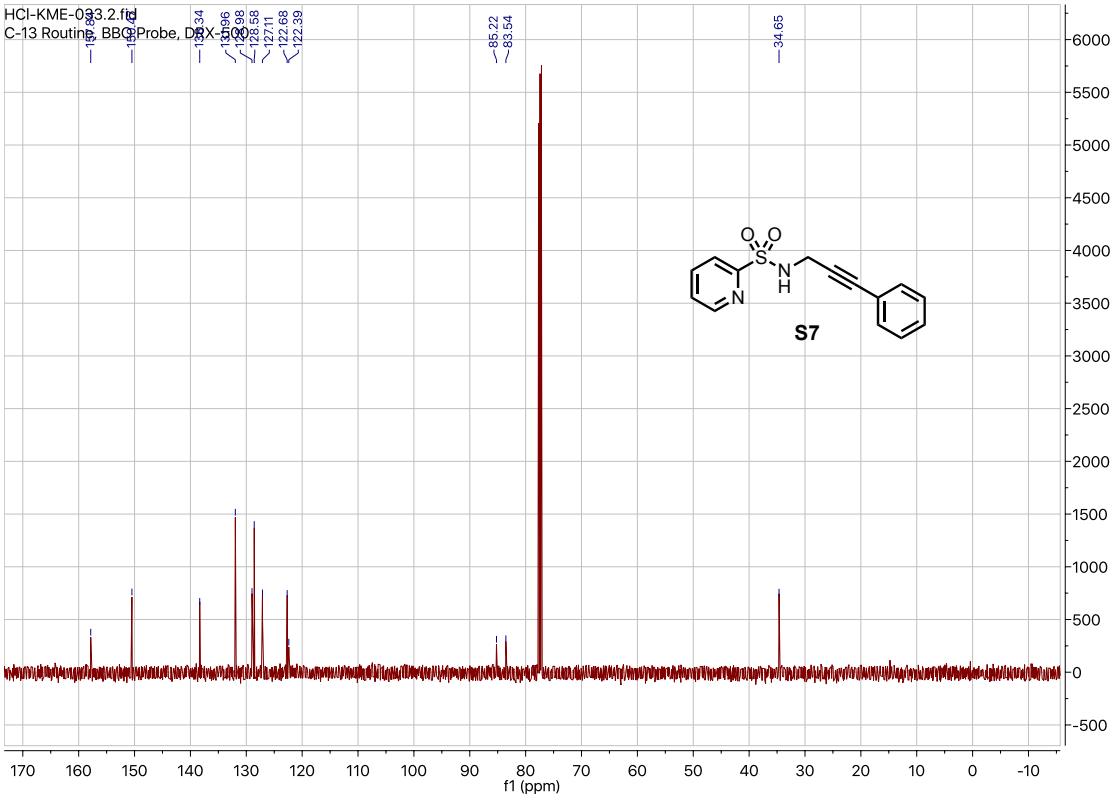

JLT-A-14 3.3.fid
H-1 Routine, DRX-500, BBO Probe
8.66
8.65
8.28
8.27
8.22
7.94
7.93
7.91
7.53
7.52
7.52
7.51
7.34
4.38
0.26
0.97
1.04
1.00
1.00
2.09
9.00
f1 (ppm)
S17

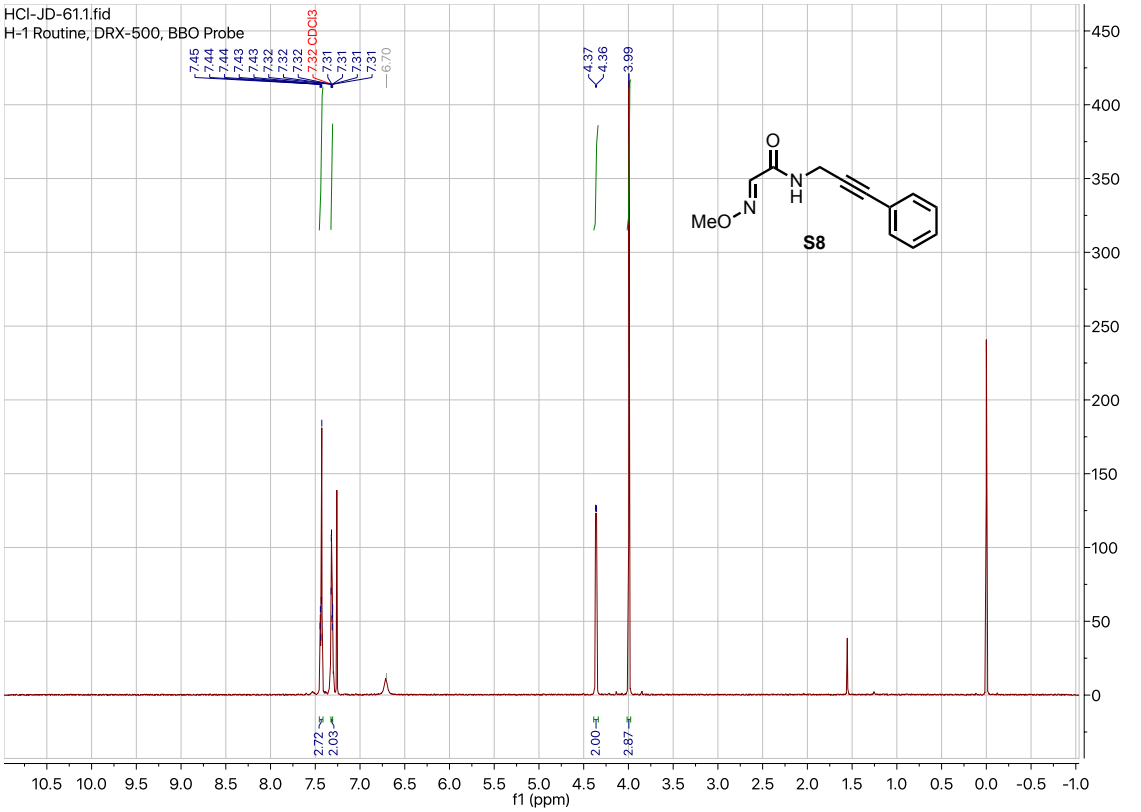

JLT-A-14 3.4.fid
C-13 Routine, BBO Probe, DRX-500
164.23
149.91
148.56
137.74
126.74
122.77
101.44
88.79
30.58
0.24
f1 (ppm)
S17

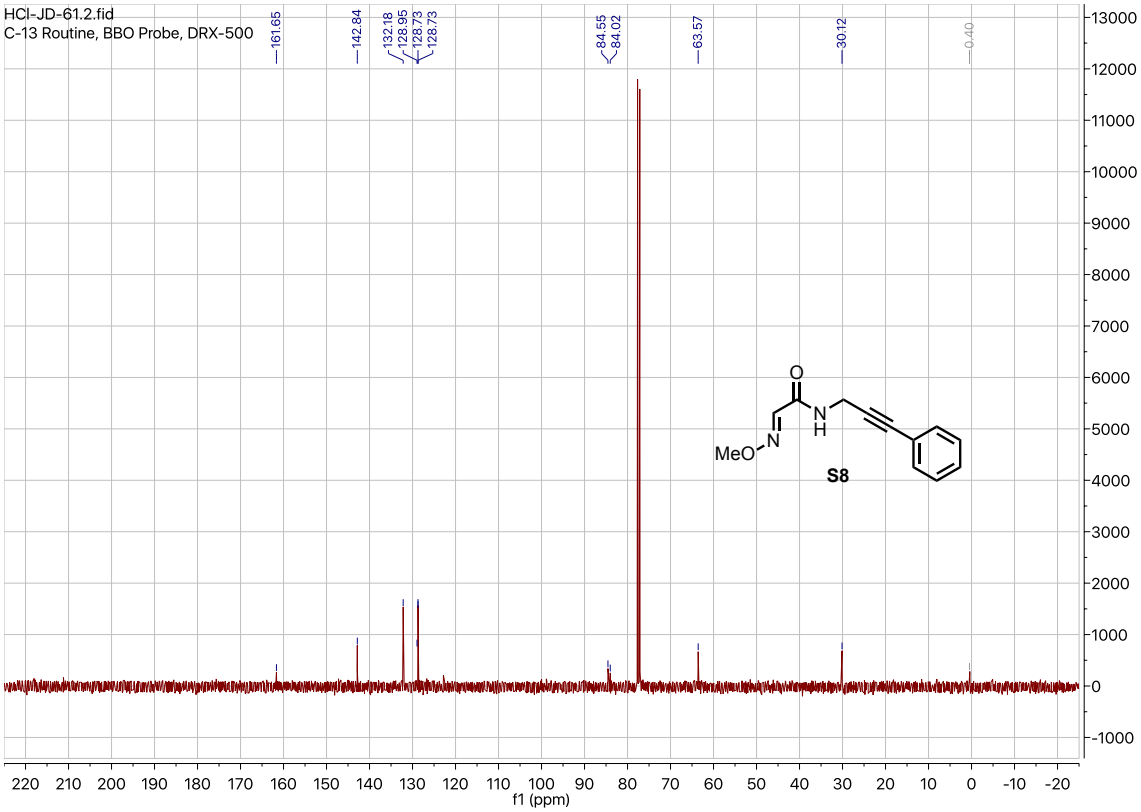

MOD1-038_col2.3.fid
H-1 Routine, DRX-500_CBO Probe
S6

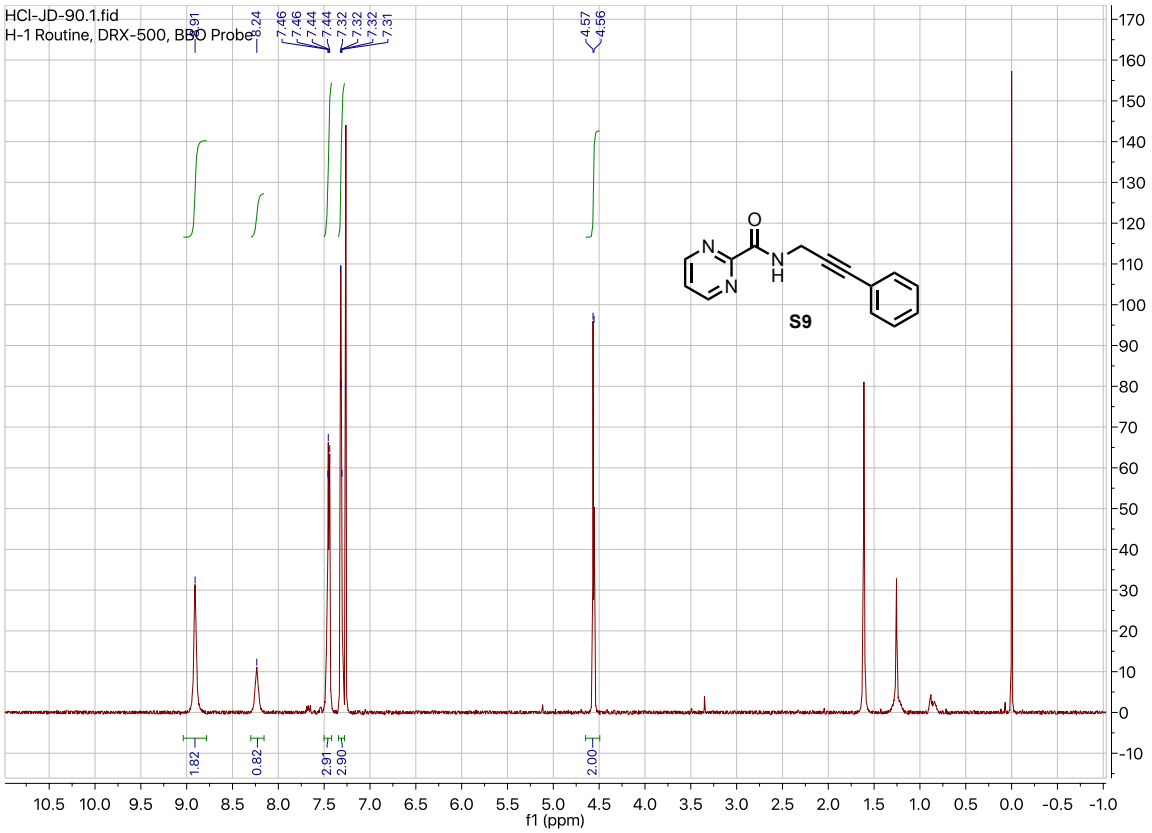

MOD1-038_col2.4.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
S6

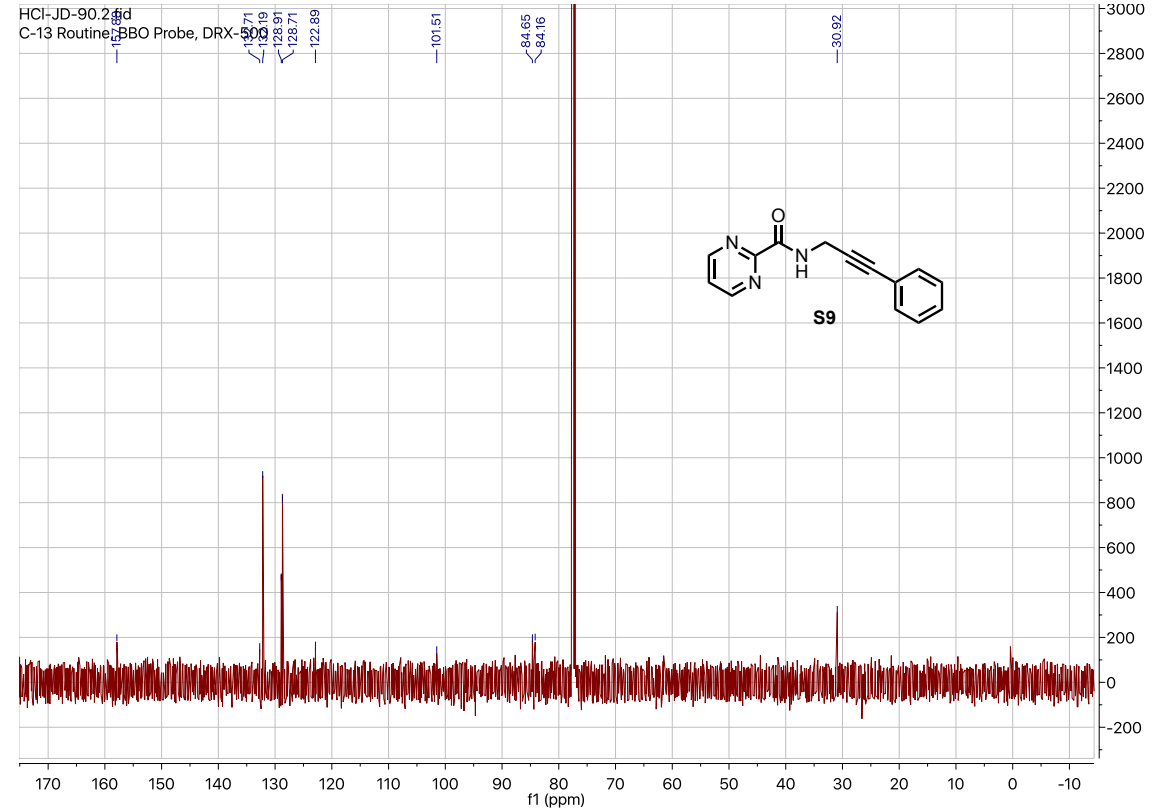

HCl-KME-033.1.fid
H-1 Routine, DRX-500, BBO Probe
S7
f1 (ppm)

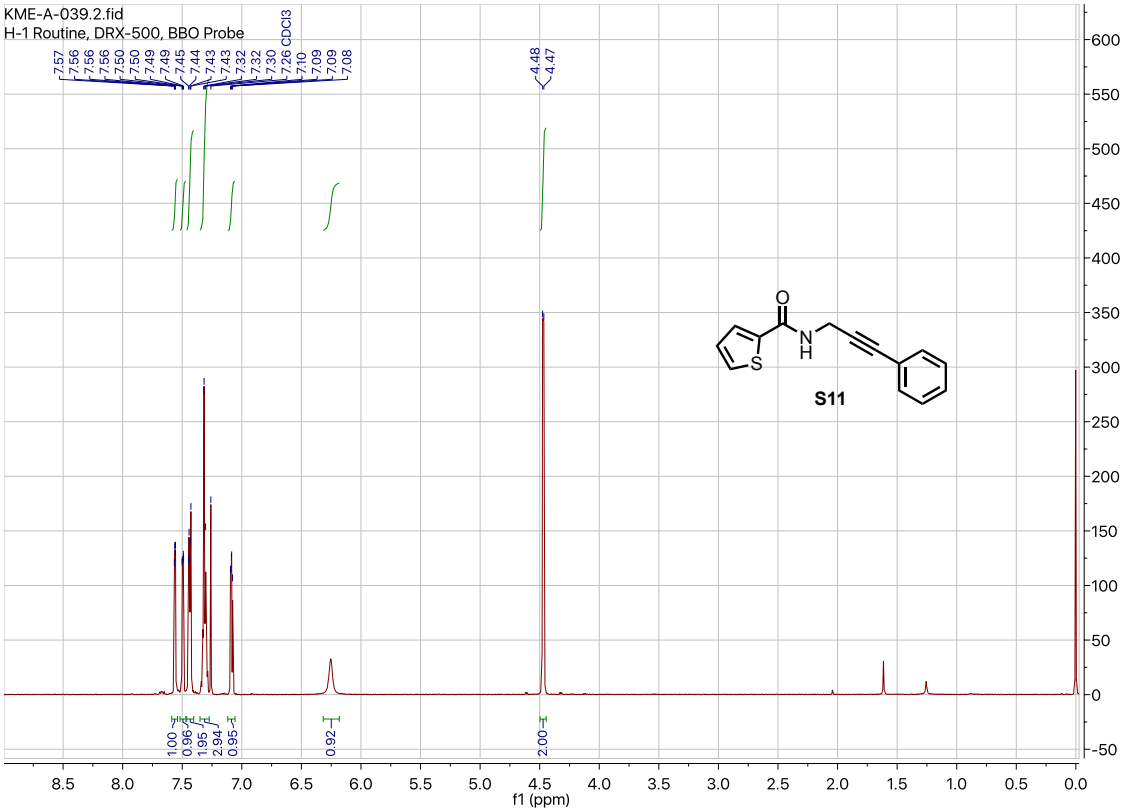

HCl-KME-033.2.fid
C-13 Routine, BBO Probe, DRX-500
S7
f1 (ppm)

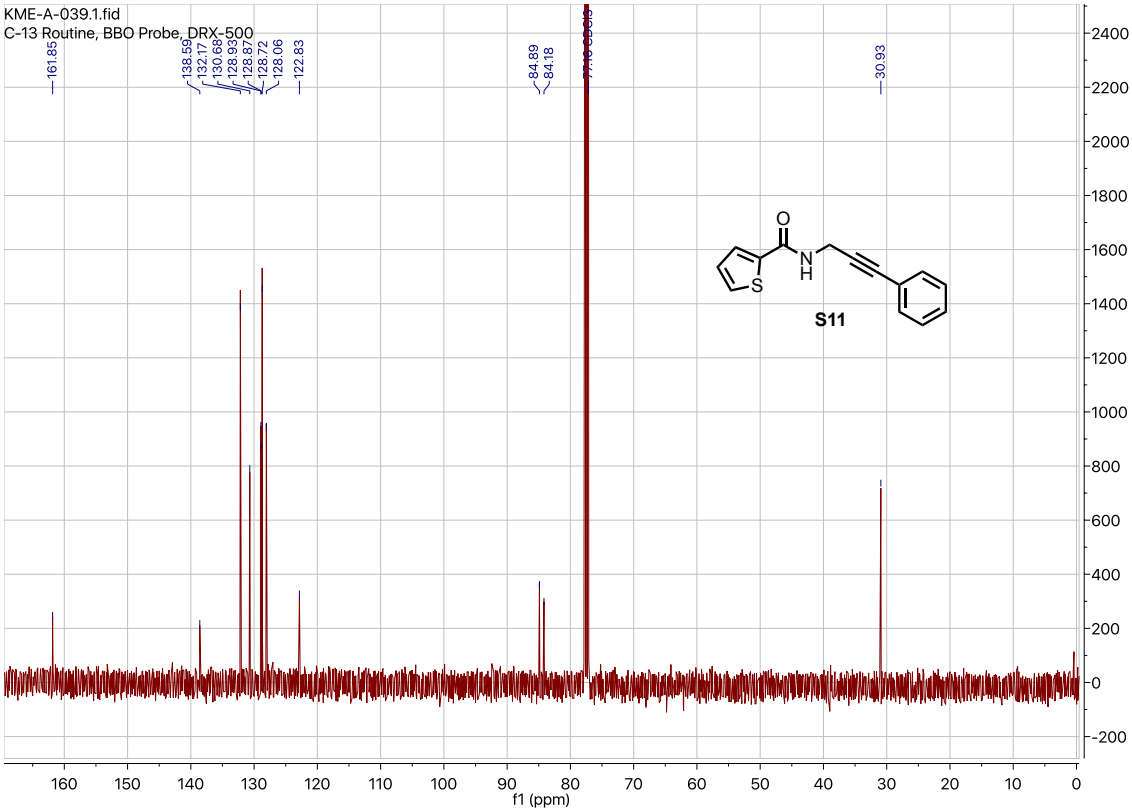

HCl-JD-61.1.fid
H-1 Routine, DRX-500, BBO Probe
7.45
7.44
7.44
7.43
7.43
7.32
7.32
7.32
7.32 CDCl3
7.31
7.31
7.31
7.31
6.70
4.37
4.36
3.99
2.72
2.03
2.00
2.87
MeO
N
O
N
H
S8
f1 (ppm)

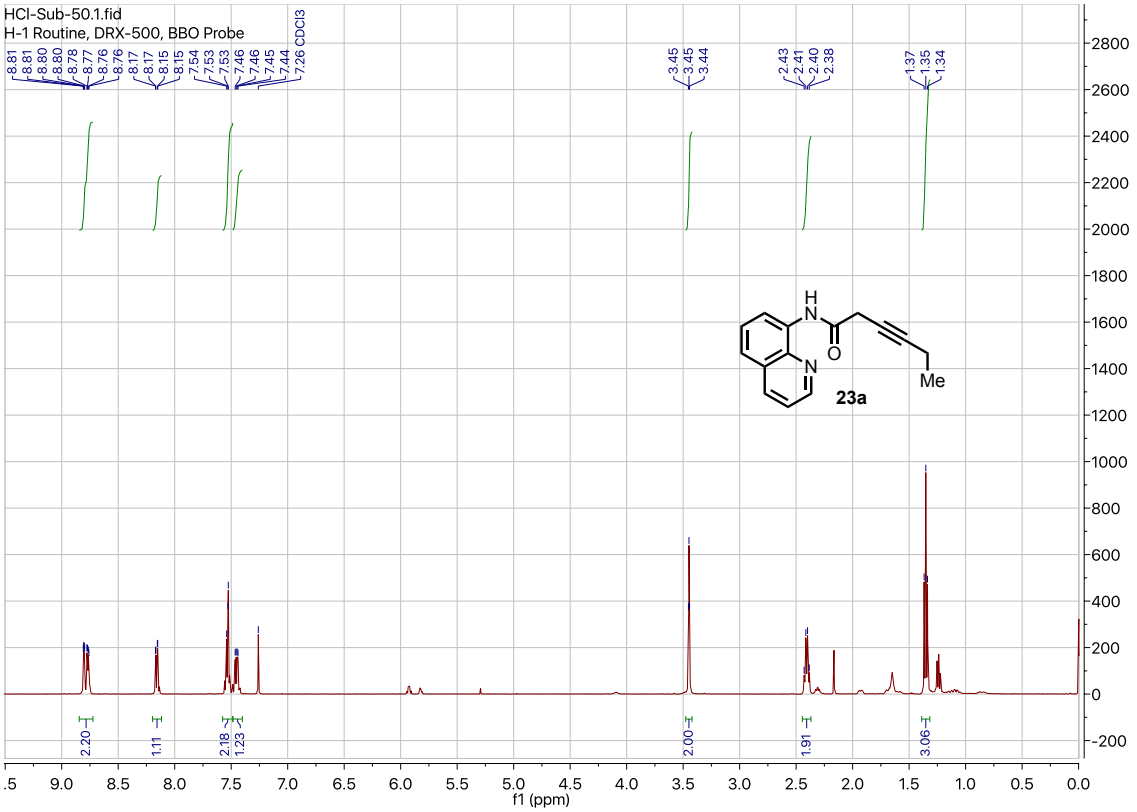

HCl-JD-61.2.fid
C-13 Routine, BBO Probe, DRX-500
161.65
142.84
132.18
128.95
128.73
128.73
84.55
84.02
63.57
30.12
0.40
MeO
N
O
N
H
S8
f1 (ppm)

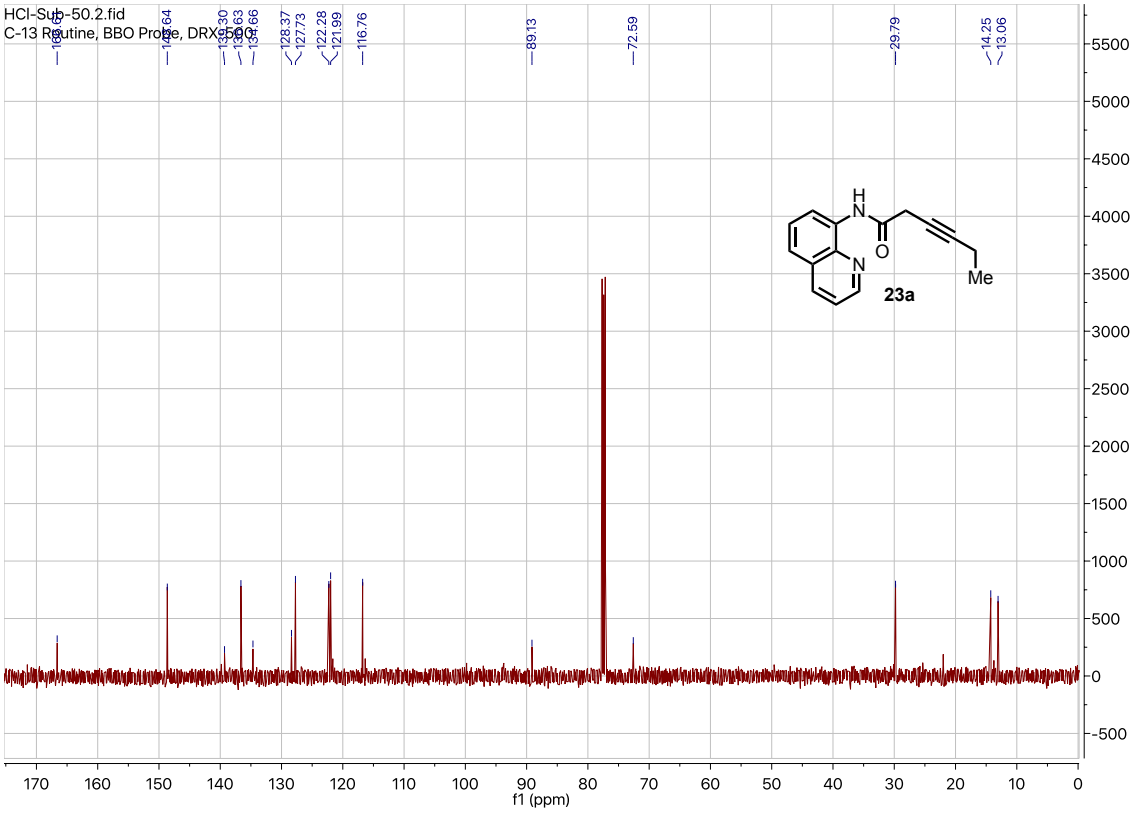

HCl-JD-90.1.fid
H-1 Routine, DRX-500, BBO Probe
8.91
8.24
7.46
7.46
7.44
7.44
7.32
7.32
7.32
7.31
4.57
4.56
1.82
0.82
2.91
2.90
2.00
S9
f1 (ppm)

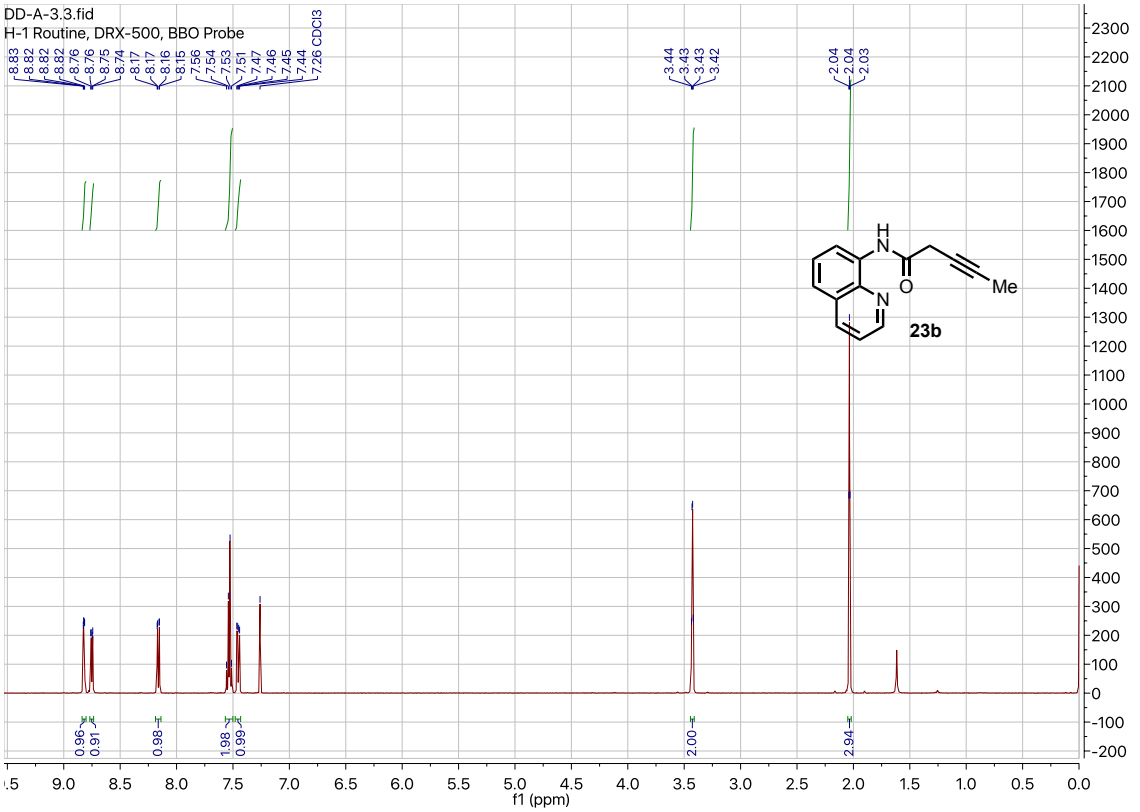

HCl-JD-90.2.fid
C-13 Routine, BBO Probe, DRX-500
157.71
132.19
128.91
128.71
122.89
101.51
84.65
84.16
30.92
S9
f1 (ppm)

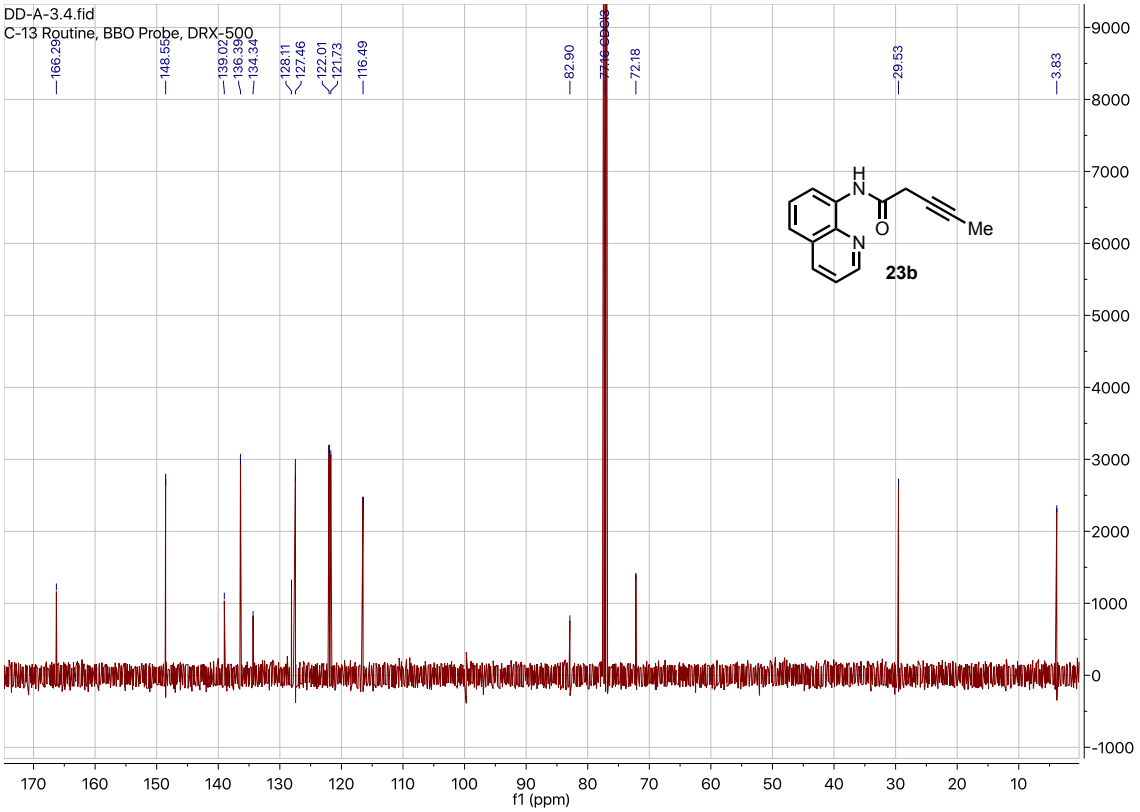

KME-A-039.2.fid
H-1 Routine, DRX-500, BBO Probe
7.57
7.56
7.56
7.56
7.50
7.50
7.49
7.49
7.45
7.44
7.43
7.43
7.32
7.32
7.30
7.26 CDCl3
7.10
7.09
7.09
7.08
4.48
4.47
1.00
0.96
1.95
2.94
0.95
0.92
2.00
S11
f1 (ppm)

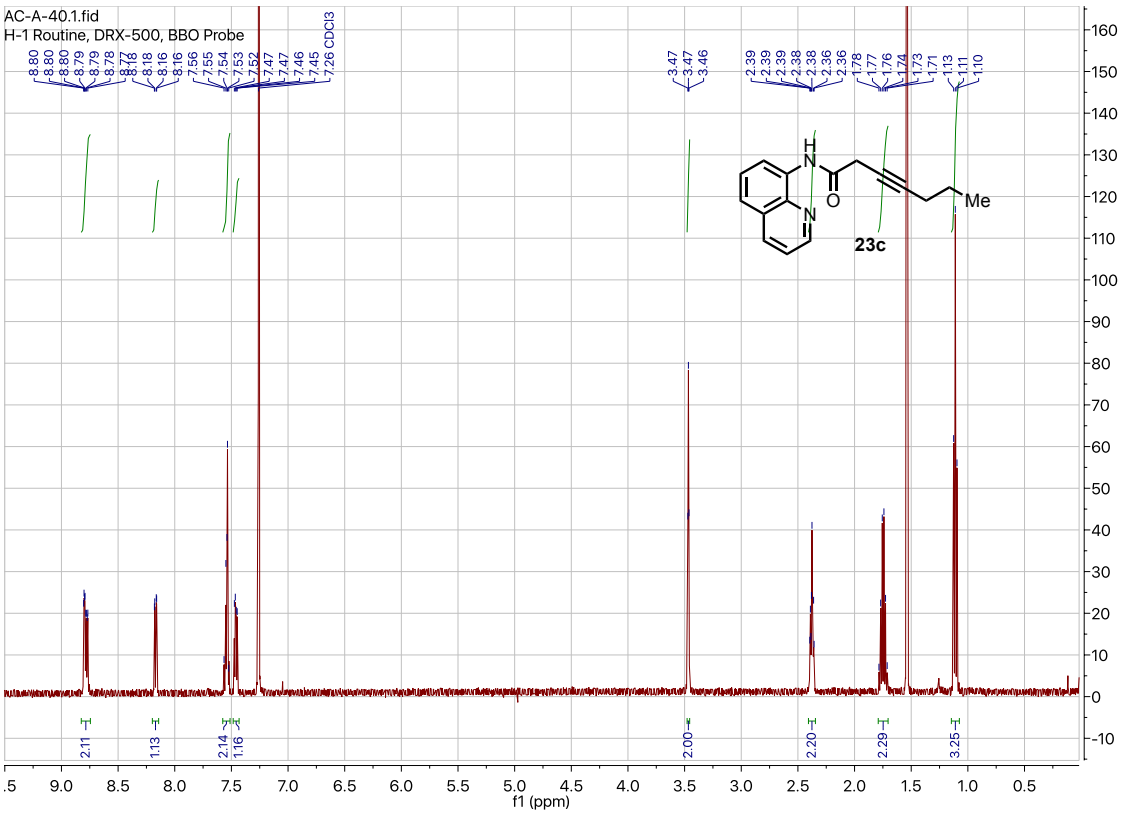

KME-A-039.1.fid
C-13 Routine, BBO Probe, DRX-500
161.85
138.59
132.17
130.68
128.93
128.87
128.72
128.06
122.83
84.99
84.18
77.16 CDCl3
30.93
S11
f1 (ppm)

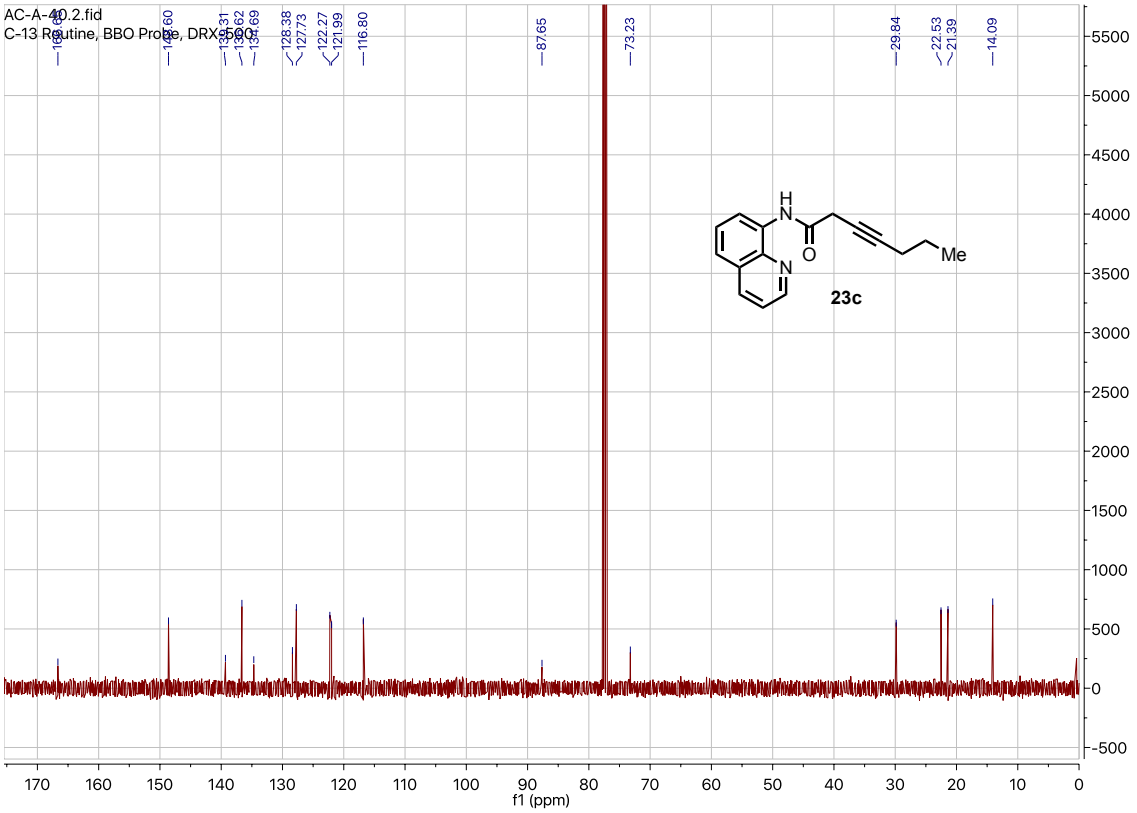

HCl-Sub-50.1.fid
H-1 Routine, DRX-500, BBO Probe
8.81
8.81
8.80
8.80
8.78
8.77
8.76
8.76
8.17
8.17
8.15
8.15
7.54
7.53
7.53
7.46
7.46
7.45
7.44
7.26 CDCl3
3.45
3.45
3.44
2.43
2.41
2.40
2.38
1.37
1.35
1.34
2.20
1.11
2.18
1.23
2.00
1.91
3.06
f1 (ppm)
H
N
O
N
Me
23a

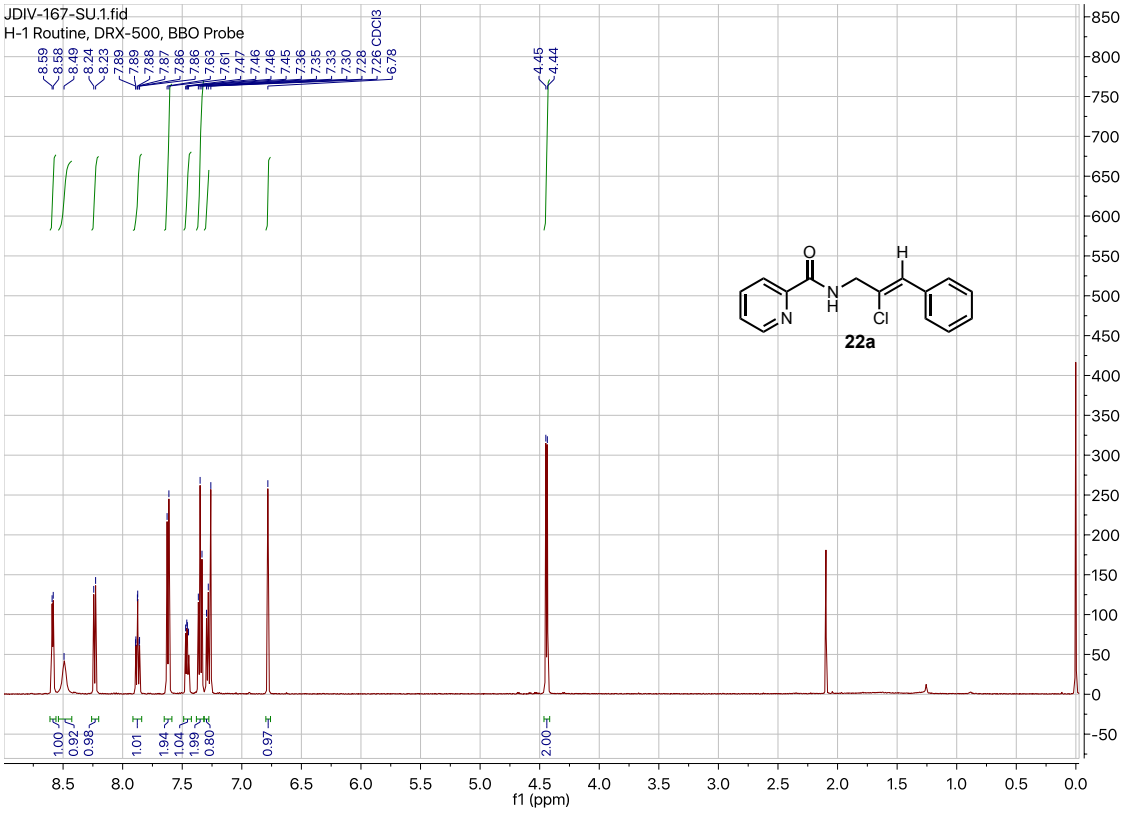

HCl-Sub-50.2.fid
C-13 Routine, BBO Probe, DRX-500
164.64
134.30
133.63
134.66
128.37
127.73
122.28
121.99
116.76
89.13
72.59
29.79
14.25
13.06
f1 (ppm)
H
N
O
N
Me
23a

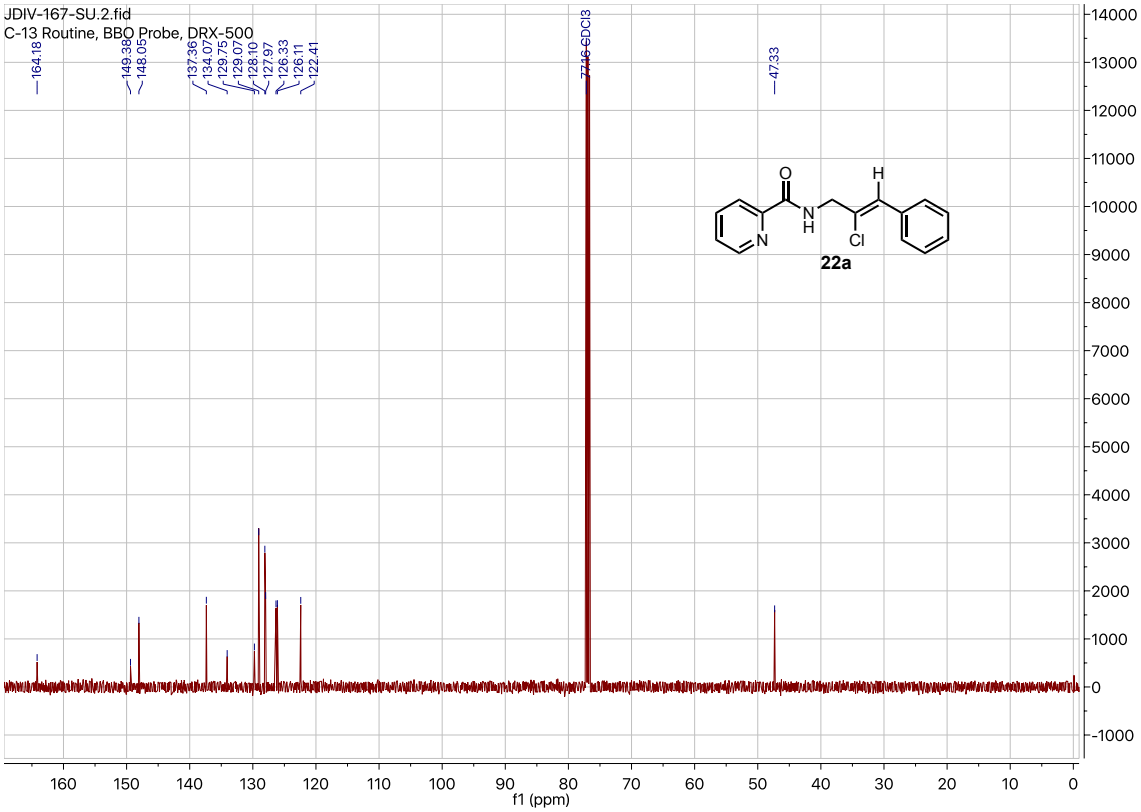

DD-A-3.3.fid
H-1 Routine, DRX-500, BBO Probe
8.83
8.82
8.82
8.82
8.76
8.76
8.75
8.74
8.17
8.17
8.16
8.15
7.56
7.54
7.53
7.51
7.47
7.46
7.45
7.44
7.26 CDCl3
3.44
3.43
3.43
3.42
2.04
2.04
2.03
0.96
0.91
0.98
1.98
0.99
2.00
2.94
H
N
O
N
Me
23b
f1 (ppm)

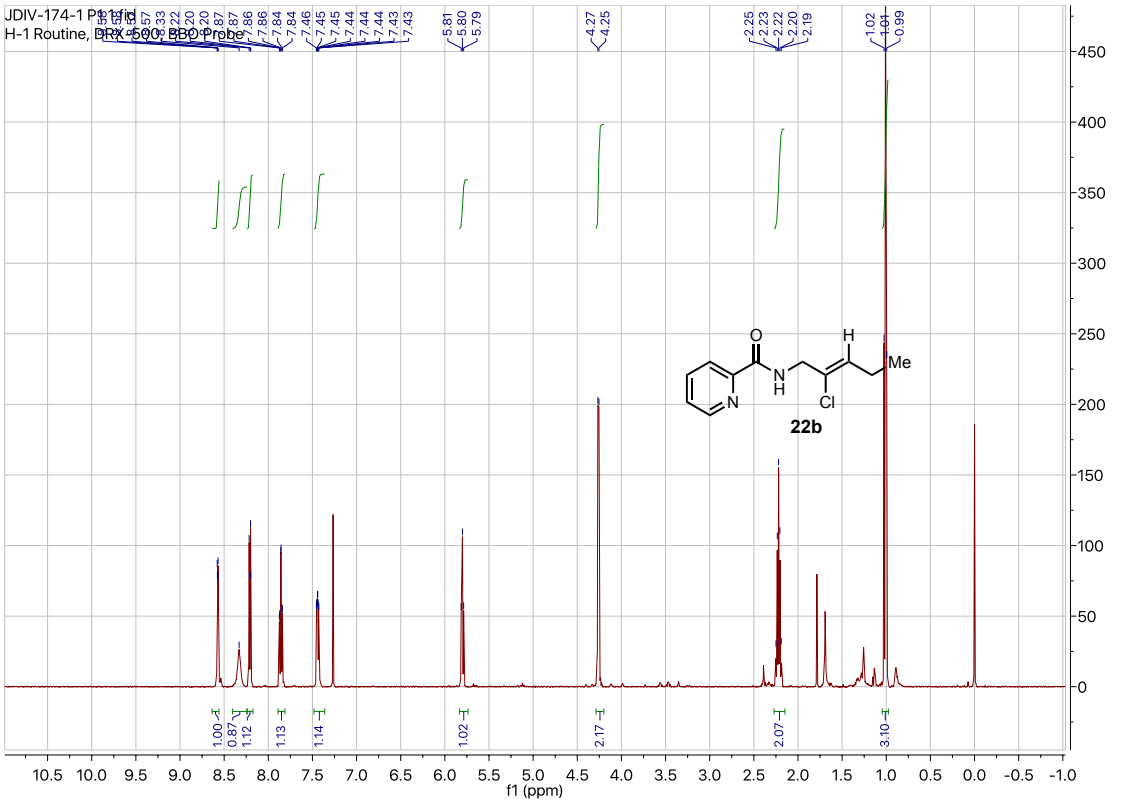

DD-A-3.4.fid
C-13 Routine, BBO Probe, DRX-500
166.29
148.55
139.02
136.39
134.34
128.11
127.46
122.01
121.73
116.49
82.90
77.16 CDCl3
72.18
29.53
3.83
H
N
O
N
Me
23b
f1 (ppm)

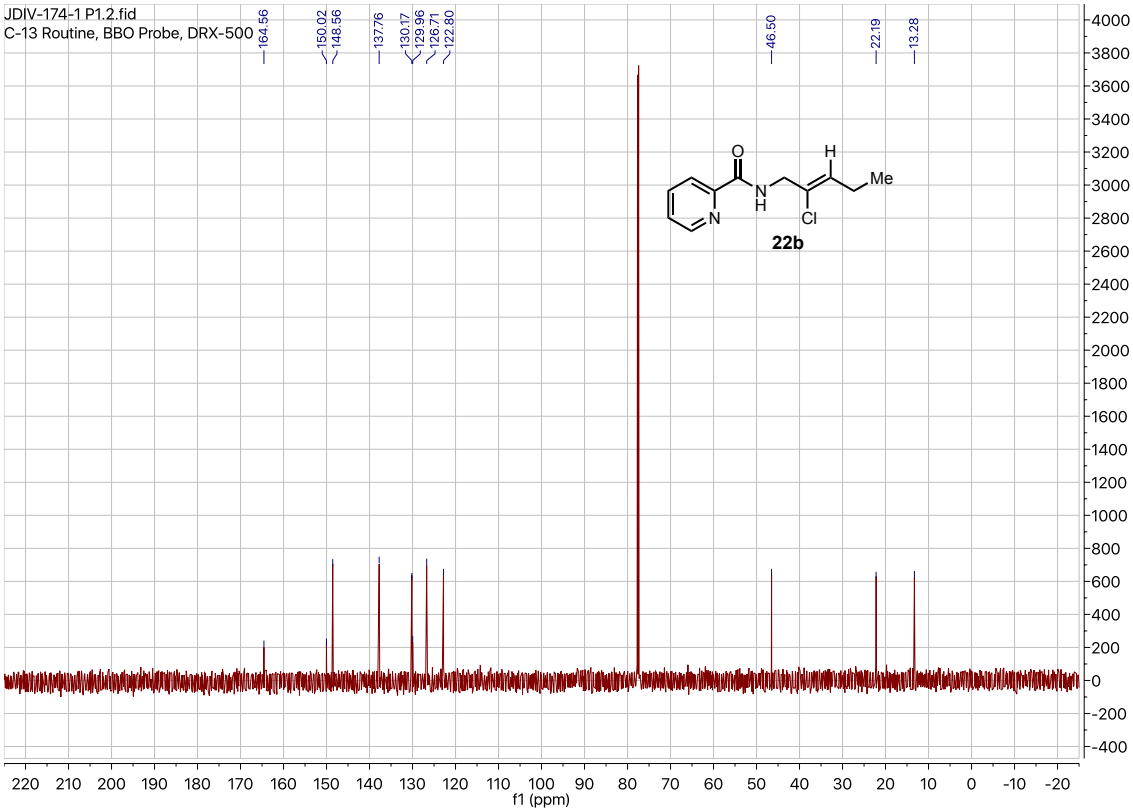

AC-A-40.1.fid
H-1 Routine, DRX-500, BBO Probe
8.80
8.80
8.80
8.79
8.79
8.78
8.77
8.18
8.18
8.16
8.16
7.56
7.55
7.54
7.53
7.52
7.47
7.47
7.46
7.45
7.26 CDCl3
3.47
3.47
3.46
2.39
2.39
2.39
2.38
2.38
2.36
2.36
1.78
1.77
1.76
1.74
1.73
1.71
1.13
1.11
1.10
2.11
1.13
2.14
1.16
2.00
2.20
2.29
3.25
f1 (ppm)
H
N
O
N
Me
23c

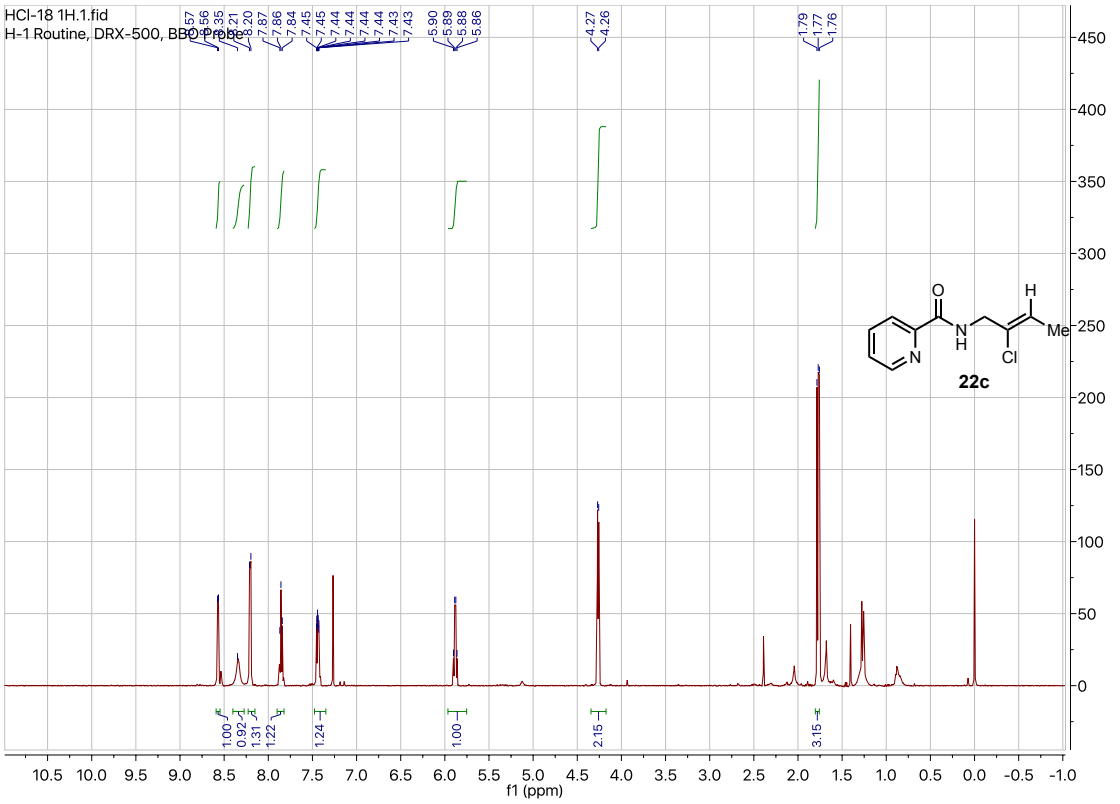

AC-A-40.2.fid
C-13 Routine, BBO Probe, DRX-500
160.60
147.31
139.62
134.69
128.38
127.73
122.27
121.99
116.80
87.65
73.23
29.84
22.53
21.39
14.09
f1 (ppm)
H
N
O
N
Me
23c

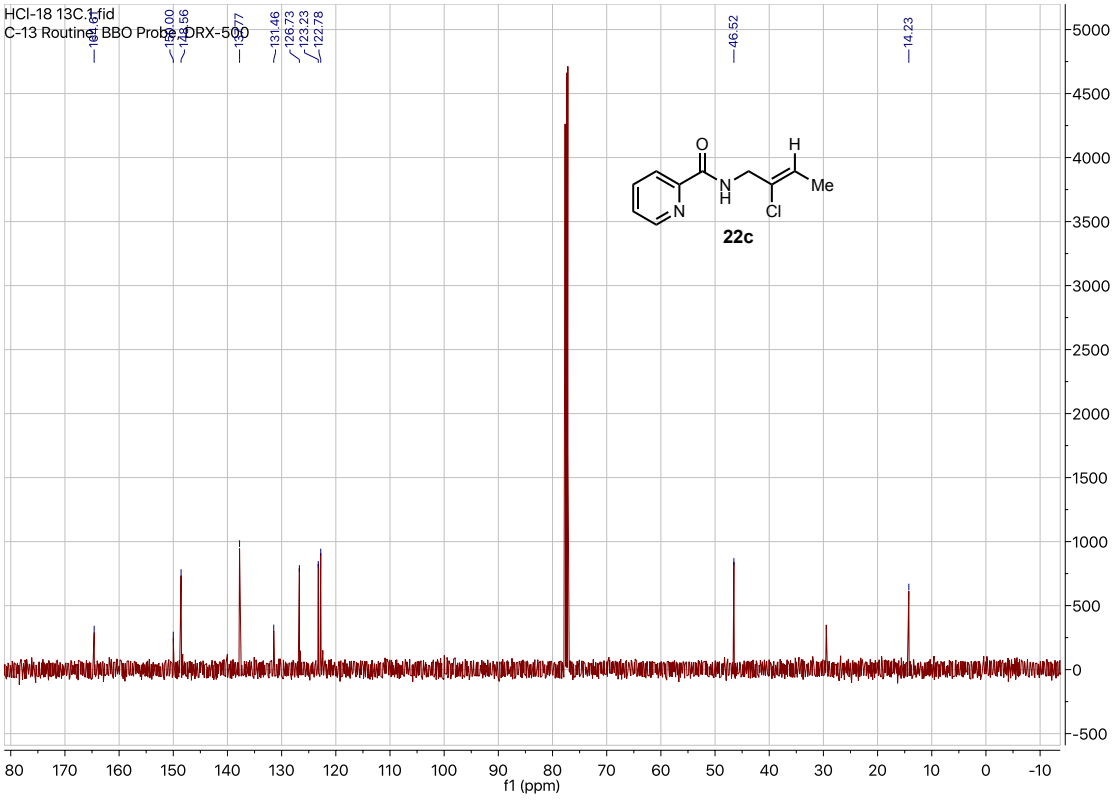

JDIV-167-SU.1.fid
H-1 Routine, DRX-500, BBO Probe
8.59
8.58
8.49
8.24
8.23
7.89
7.88
7.87
7.86
7.86
7.63
7.61
7.47
7.46
7.46
7.45
7.36
7.35
7.33
7.30
7.28
7.26 CDCl3
6.78
4.46
4.44
1.00
0.92
0.98
1.01
1.94
1.04
1.99
0.80
0.97
2.00
f1 (ppm)
22a

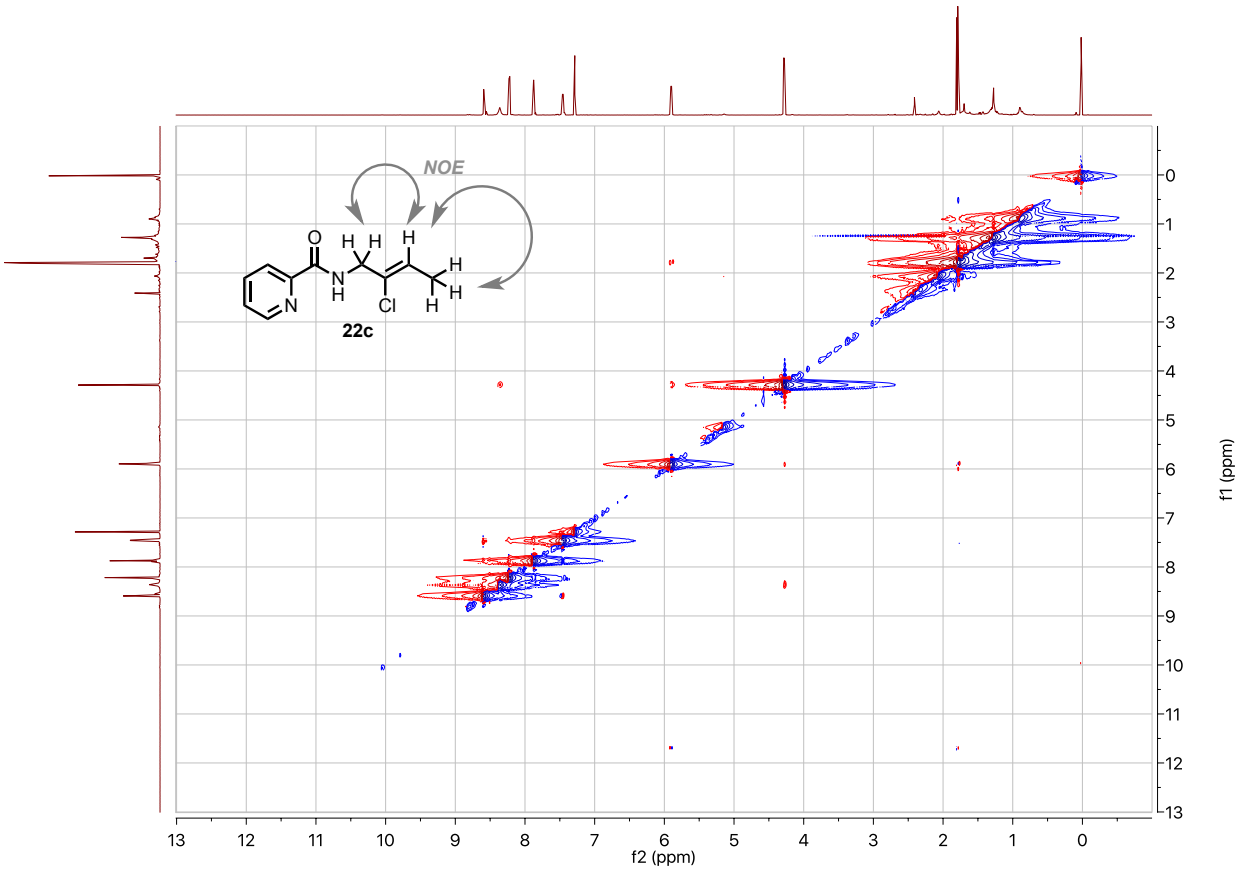

JDIV-167-SU.2.fid
C-13 Routine, BBO Probe, DRX-500
164.18
149.38
148.05
137.36
134.07
129.75
129.07
128.10
127.97
126.33
126.11
122.41
77.16 CDCl3
47.33
f1 (ppm)
22a

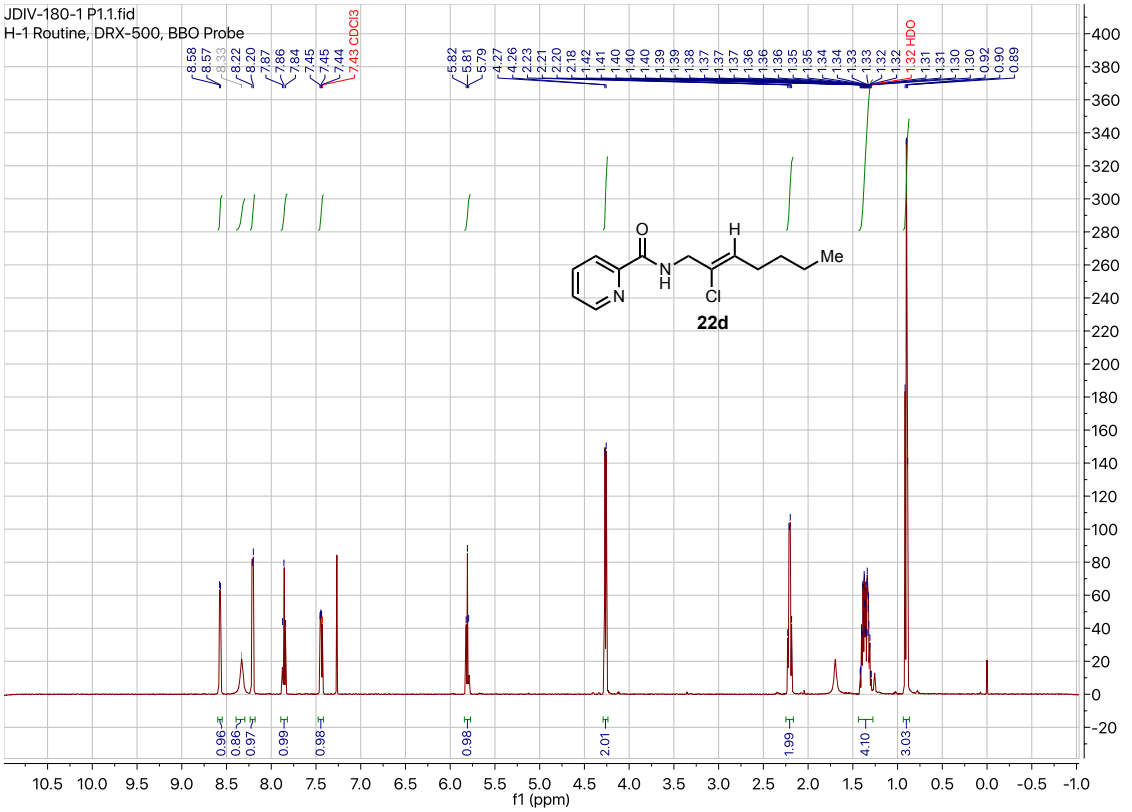

JDIV-174-1 P1.1.fid
H-1 Routine, DRX-500, BBO Probe
22b
f1 (ppm)

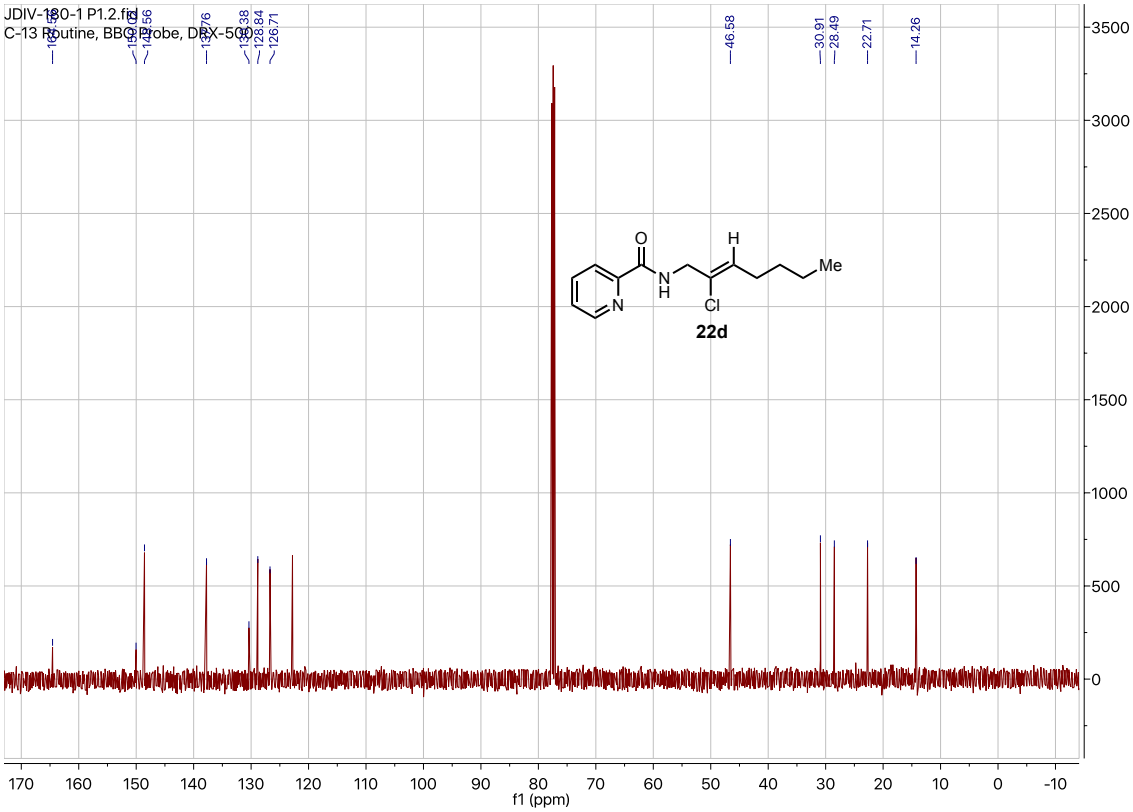

JDIV-174-1 P1.2.fid
C-13 Routine, BBO Probe, DRX-500
22b
f1 (ppm)

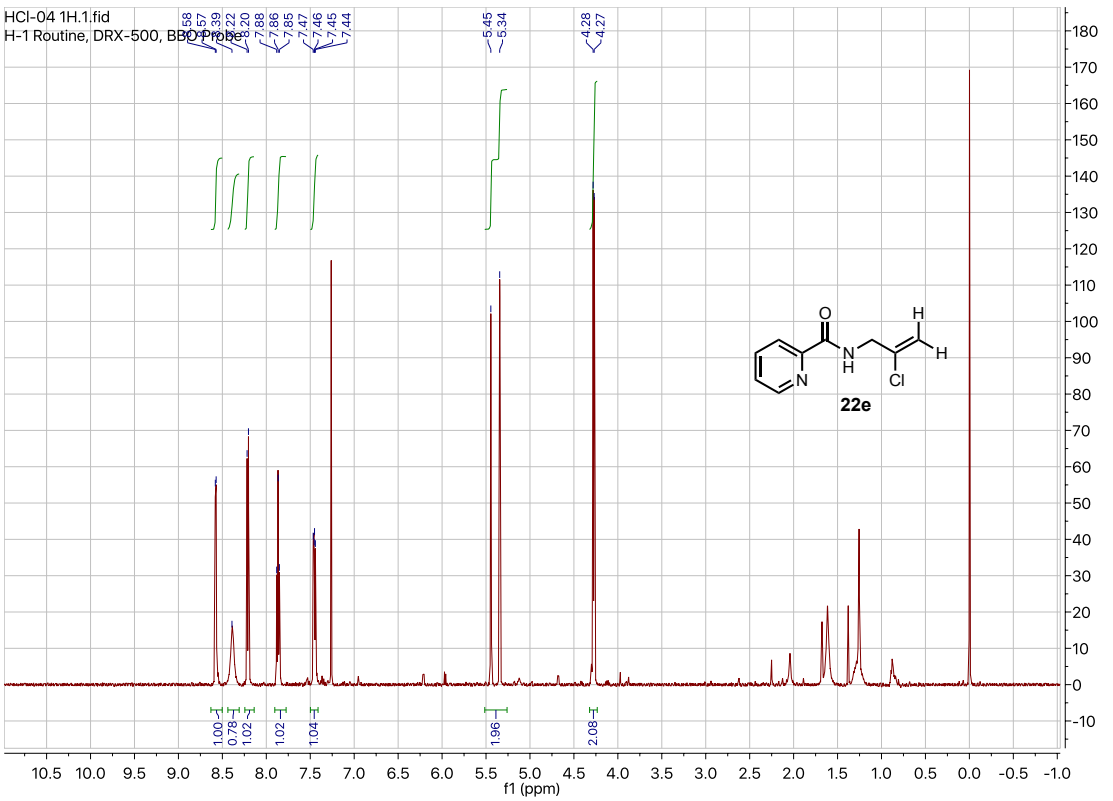

HCl-18 1H.1.fid
H-1 Routine, DRX-500, BBO Probe
8.57
8.56
8.35
8.21
8.20
7.87
7.86
7.84
7.45
7.45
7.44
7.44
7.44
7.44
7.43
7.43
5.90
5.89
5.88
5.86
4.27
4.26
1.79
1.77
1.76
1.00
0.92
1.31
1.22
1.24
1.00
2.15
3.15
O
H
N
H
Me
N
Cl
22c
f1 (ppm)

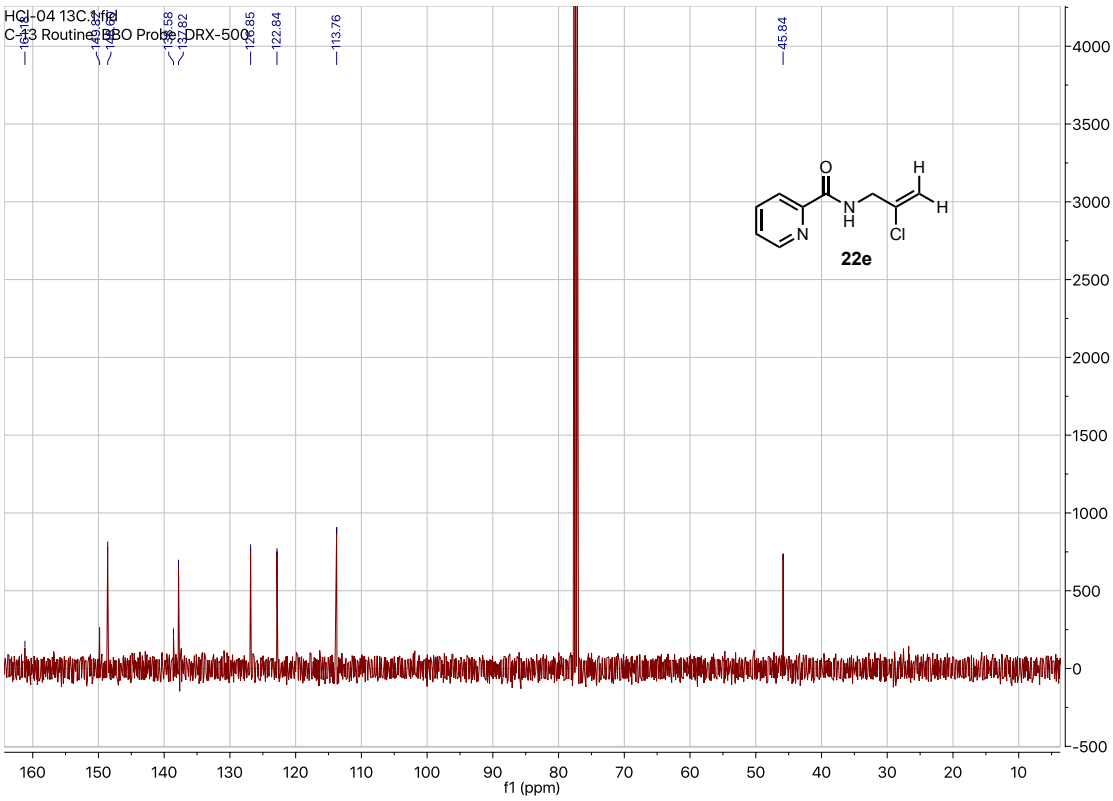

HCl-18 13C.1.fid
C-13 Routine, BBO Probe, DRX-500
161.65
150.00
149.56
137.77
131.46
126.73
123.23
122.78
46.52
14.23
O
H
N
H
Me
N
Cl
22c
f1 (ppm)

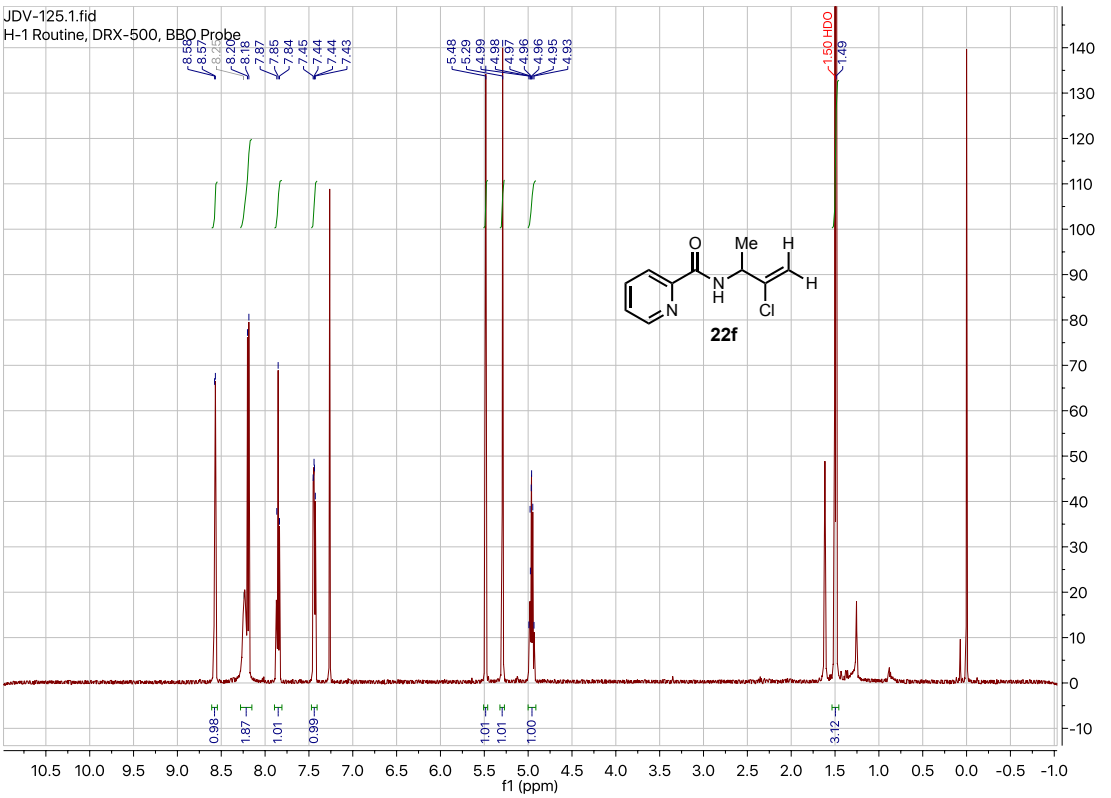

NOE
22c
f2 (ppm)
f1 (ppm)

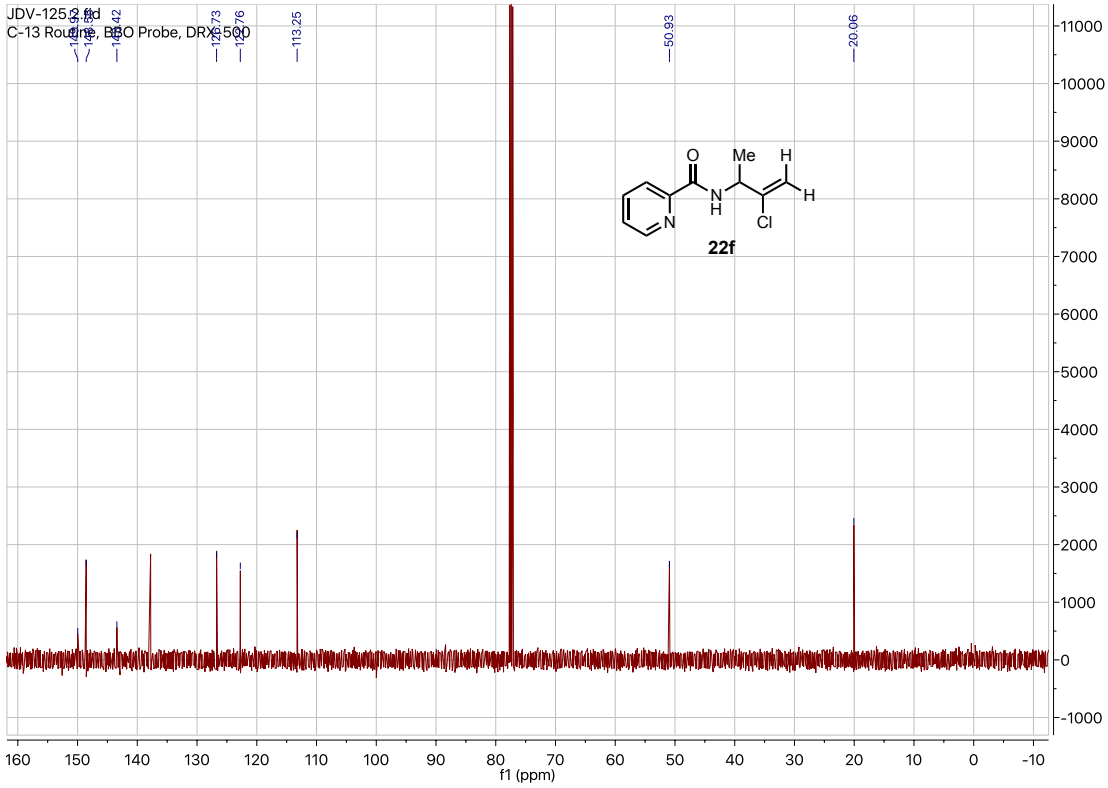

JDIV-180-1 P1.1.fid
H-1 Routine, DRX-500, BBO Probe
22d
f1 (ppm)

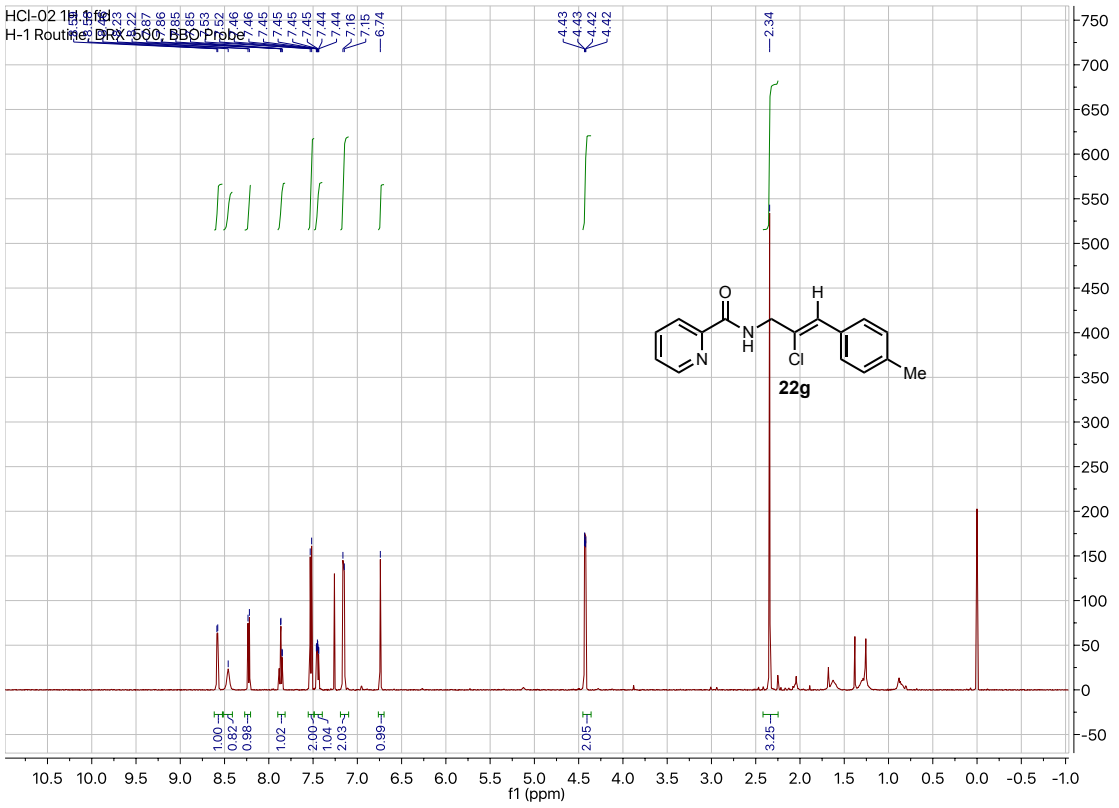

JDIV-180-1 P1.2.fid
C-13 Routine, BBO Probe, DRX-500
22d
f1 (ppm)

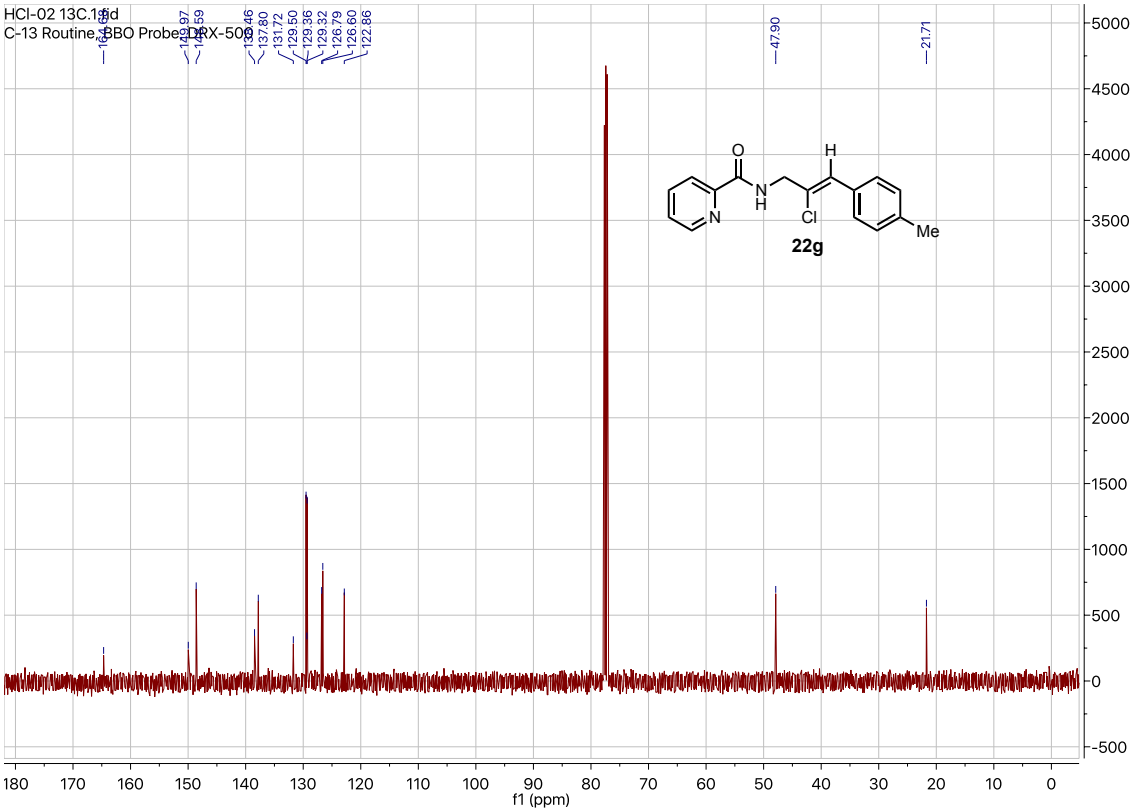

HCl-04 1H.1.fid
H-1 Routine, DRX-500, BBO Probe
8.58
8.57
8.39
8.22
8.20
7.88
7.86
7.85
7.47
7.46
7.45
7.44
5.45
5.34
4.28
4.27
1.00
0.78
1.02
1.02
1.04
1.96
2.08
f1 (ppm)
22e

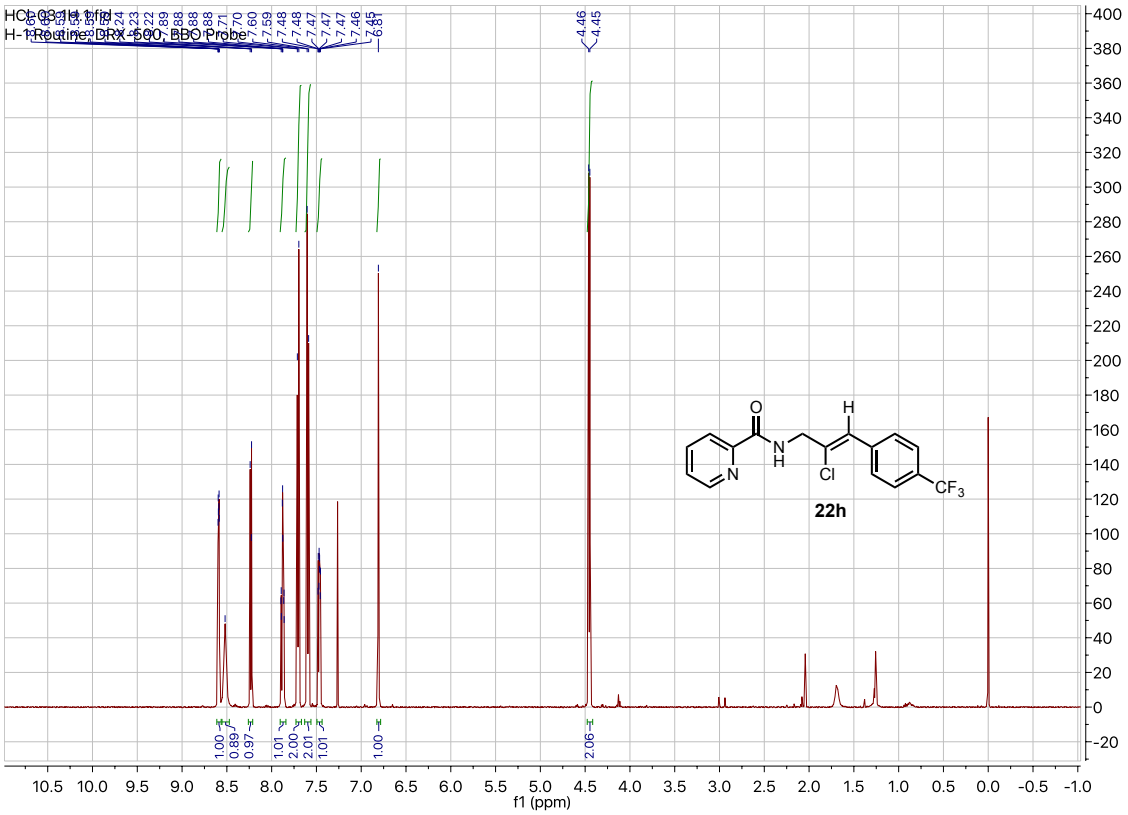

HCl-04 13C.1.fid
C-13 Routine, BBO Probe, DRX-500
164.41
149.32
148.16
138.58
132.82
126.85
122.84
113.76
45.84
f1 (ppm)
22e

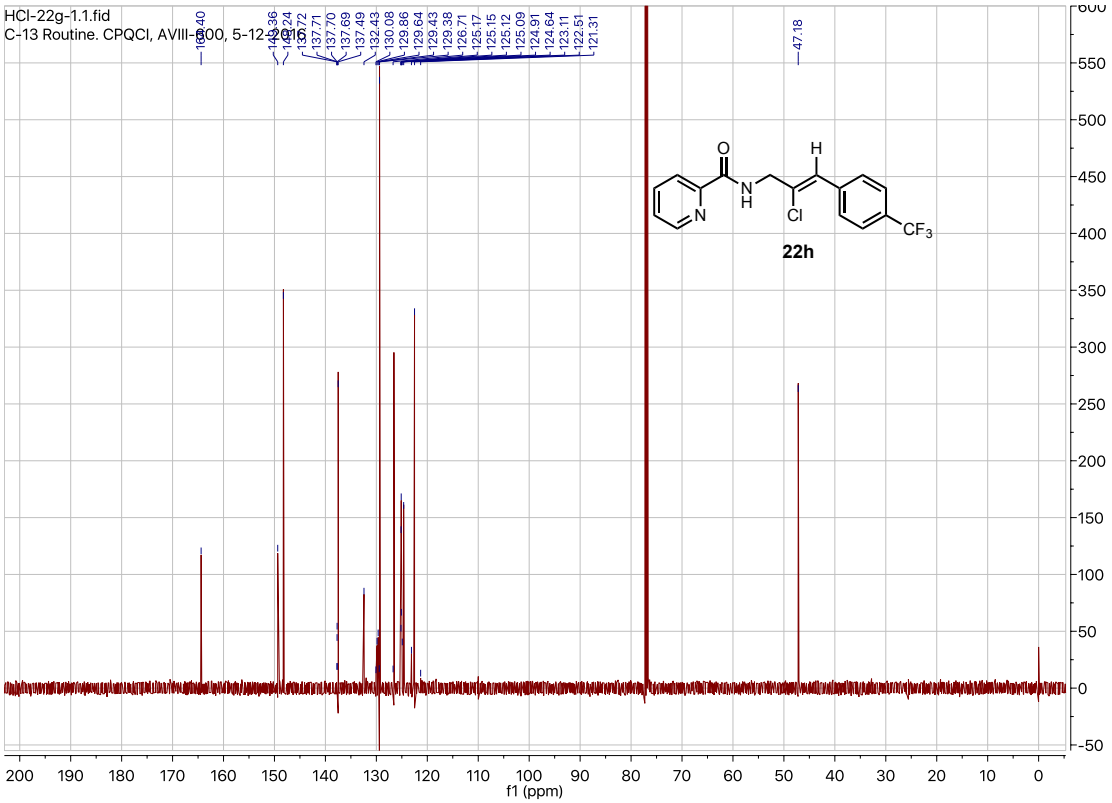

JDV-125.1.fid
H-1 Routine, DRX-500, BBO Probe
8.59
8.57
8.20
8.18
7.87
7.85
7.84
7.45
7.44
7.44
7.44
7.43
5.48
5.29
4.99
4.98
4.97
4.96
4.96
4.95
4.93
1.50 HDO
1.49
0.98
1.87
1.01
0.99
1.01
1.01
1.00
3.12
O
Me
H
N
H
H
N
Cl
22f
f1 (ppm)

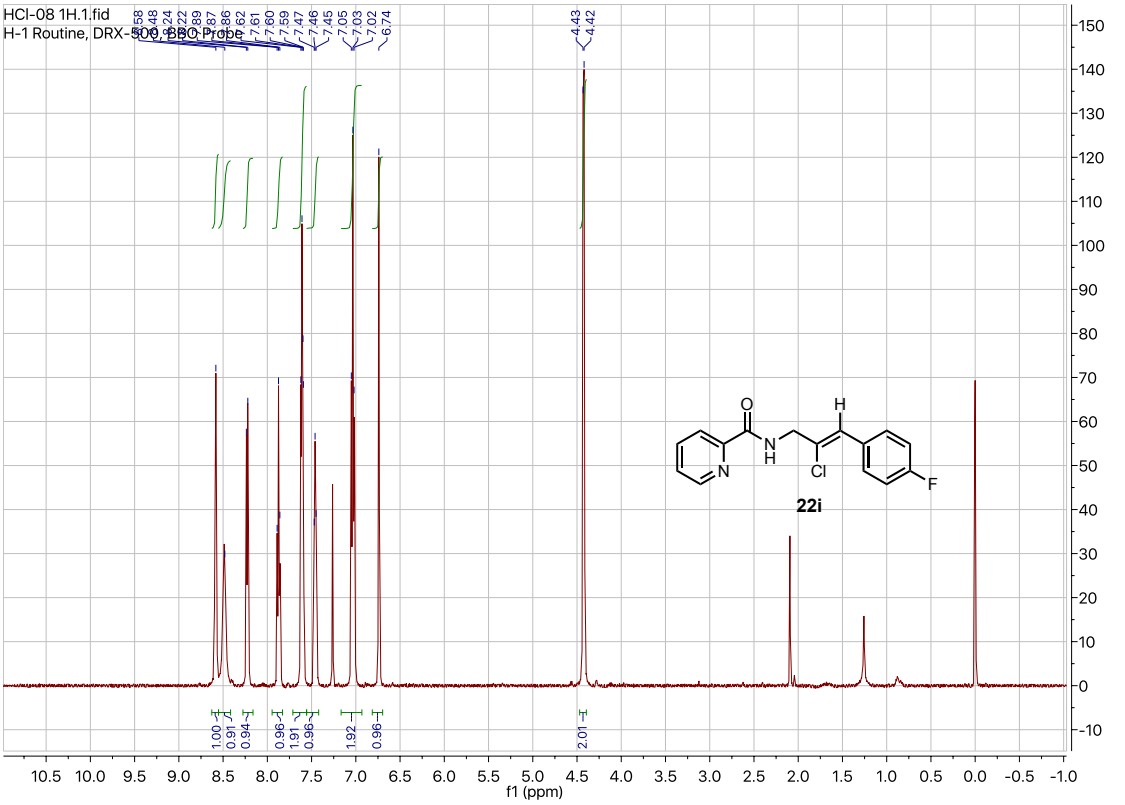

JDV-125.2.fid
C-13 Routine, BBO Probe, DRX-500
150.15
149.42
142.42
126.73
125.76
113.25
50.93
20.06
O
Me
H
N
H
H
N
Cl
22f
f1 (ppm)

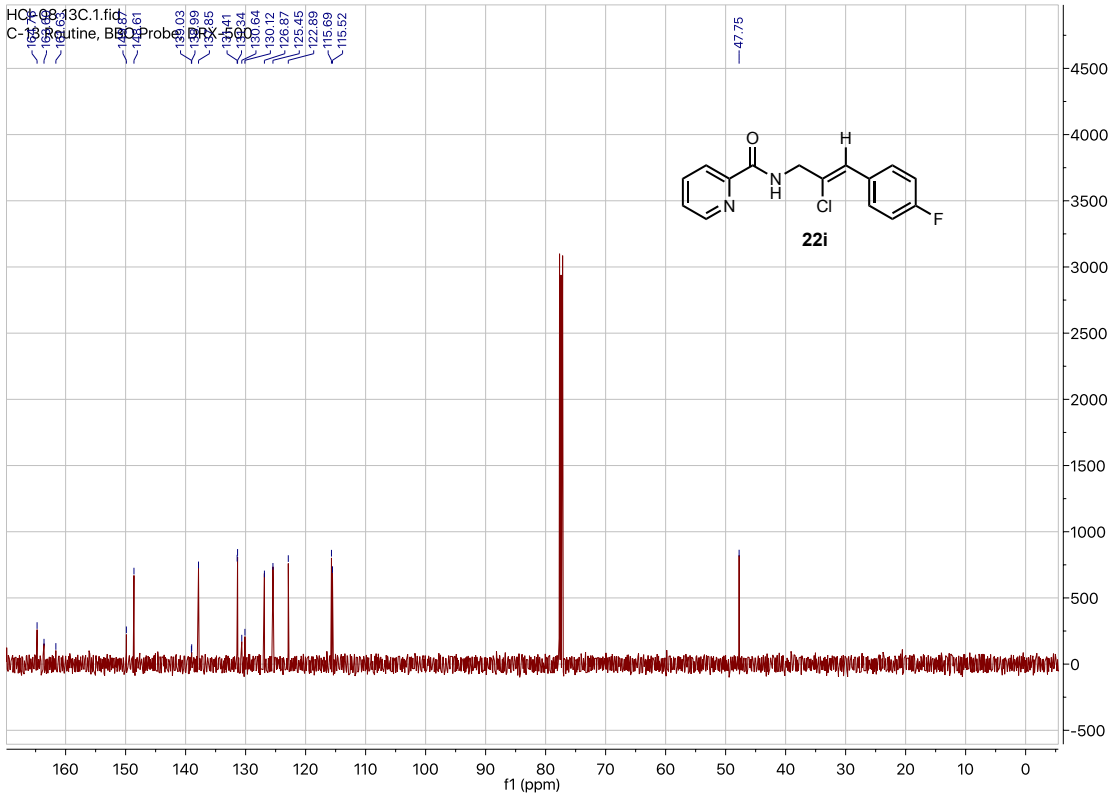

HCl-02 1H 1.fid
H-1 Routine, DRX-500, BBO Probe
22g
f1 (ppm)

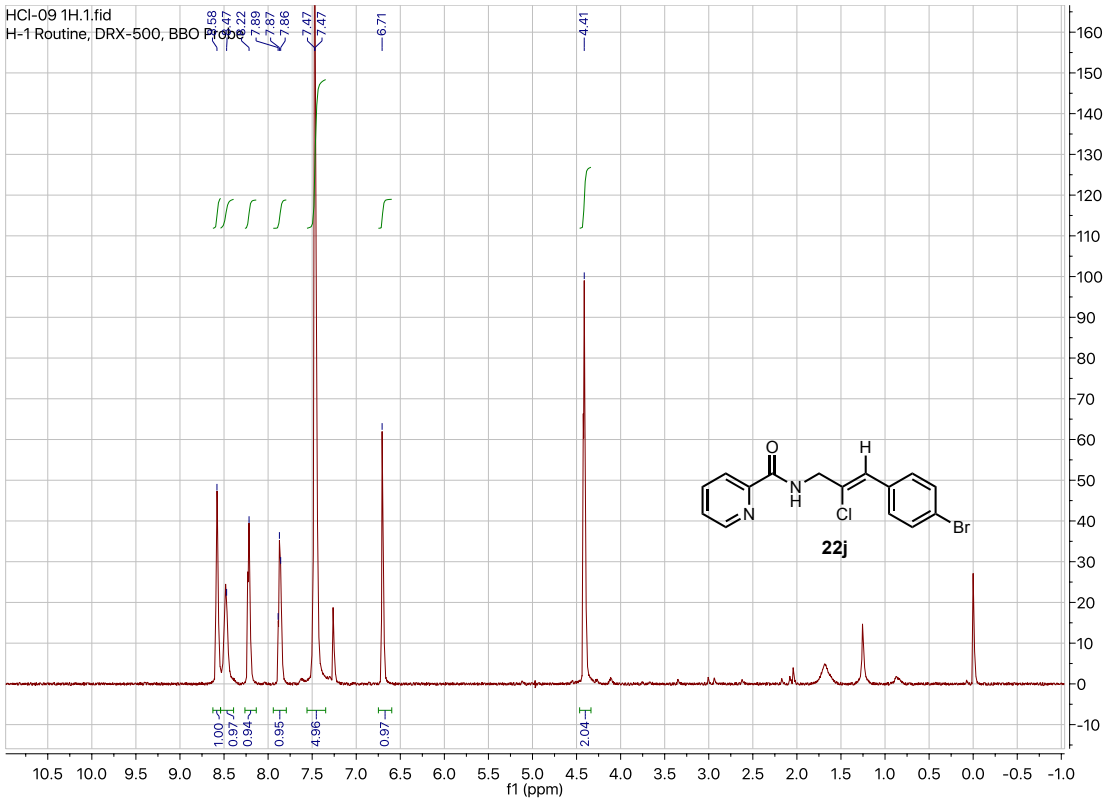

HCl-02 13C.1.fid
C-13 Routine, BBO Probe, DRX-500
22g
f1 (ppm)

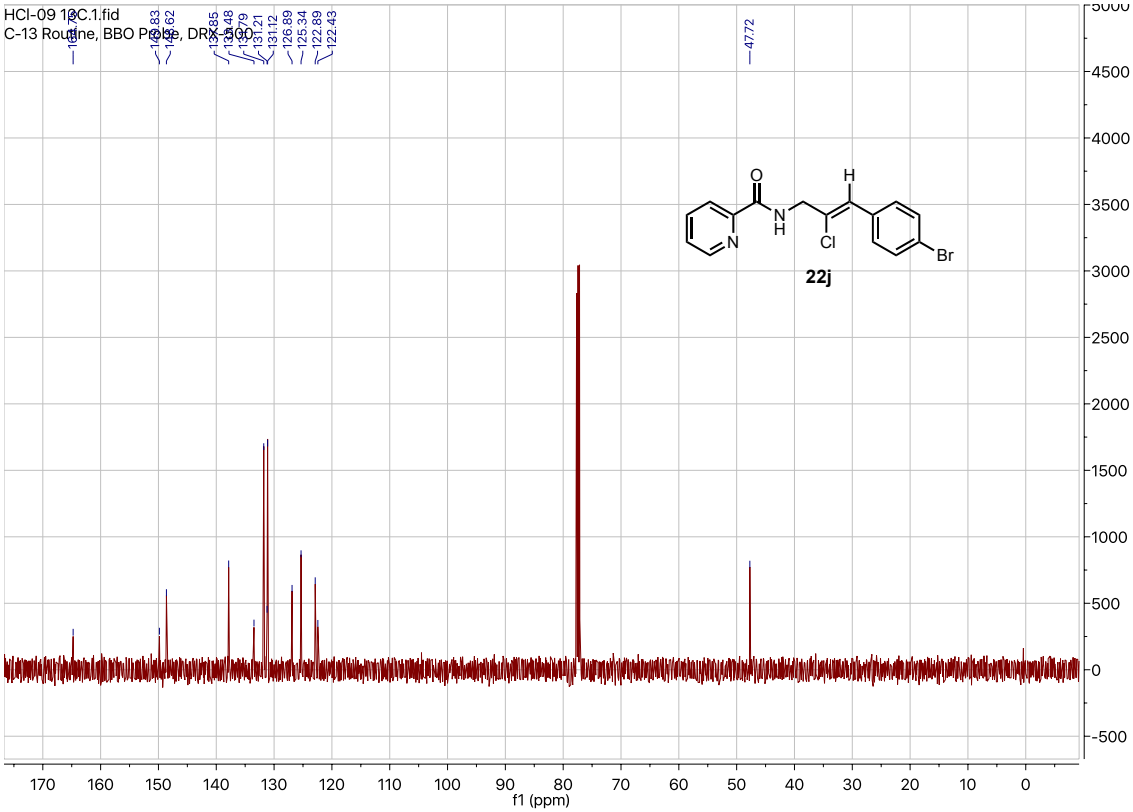

HCl-03-14-1.fid
H-1 Routine. DRX-500, BBO Probe
22h
f1 (ppm)

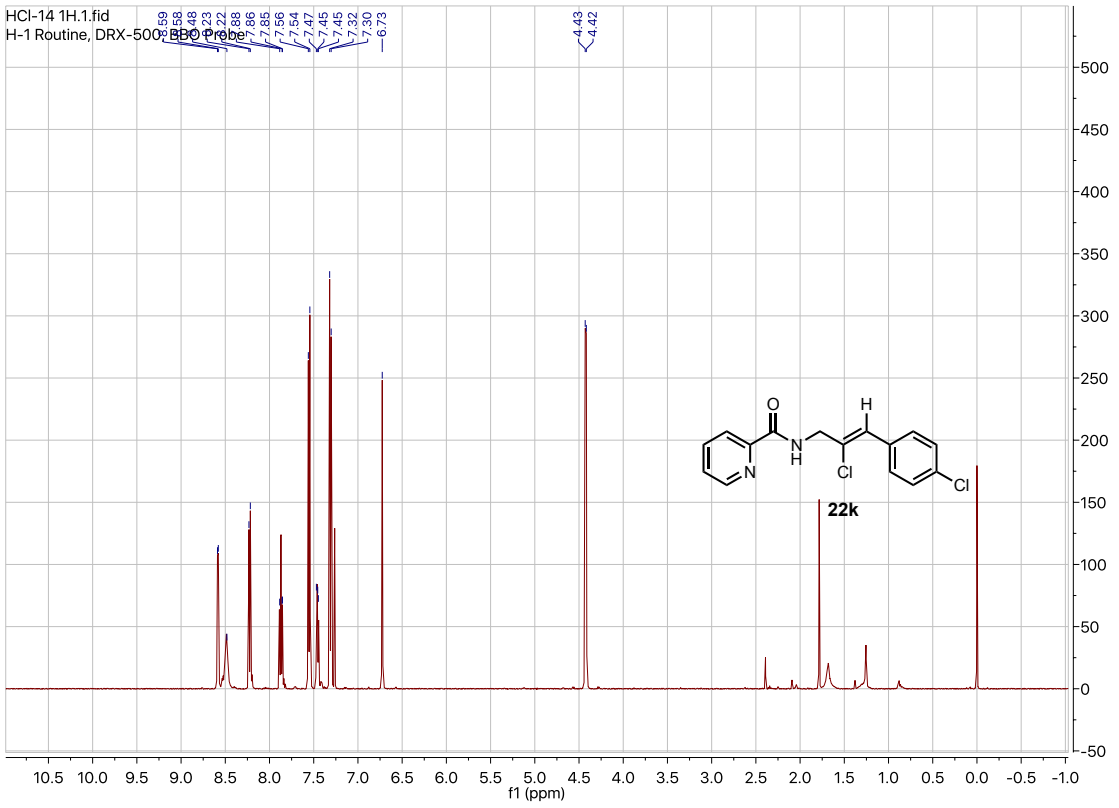

HCl-22g-1.1.fid
C-13 Routine. CPQCI, AVIII-600, 5-12-2016
22h
f1 (ppm)

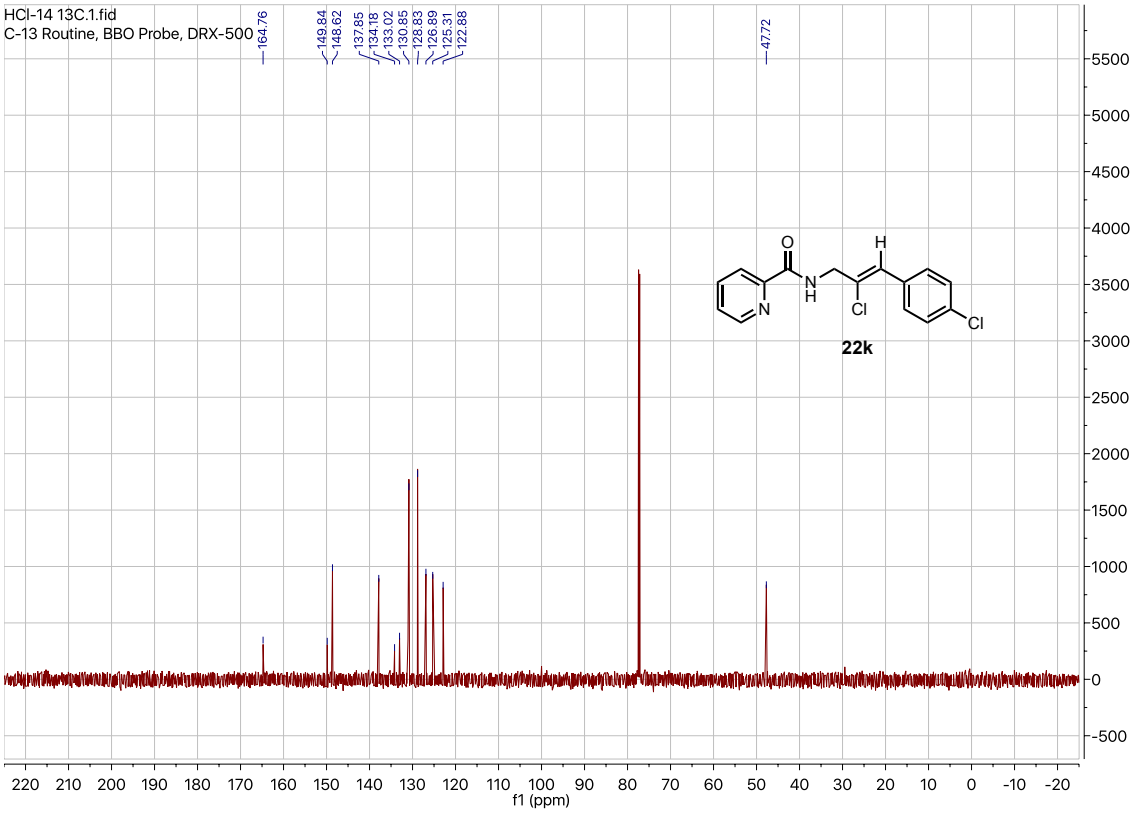

HCl-08 1H.1.fid
H-1 Routine, DRX-500, BBO Probe
22i
f1 (ppm)

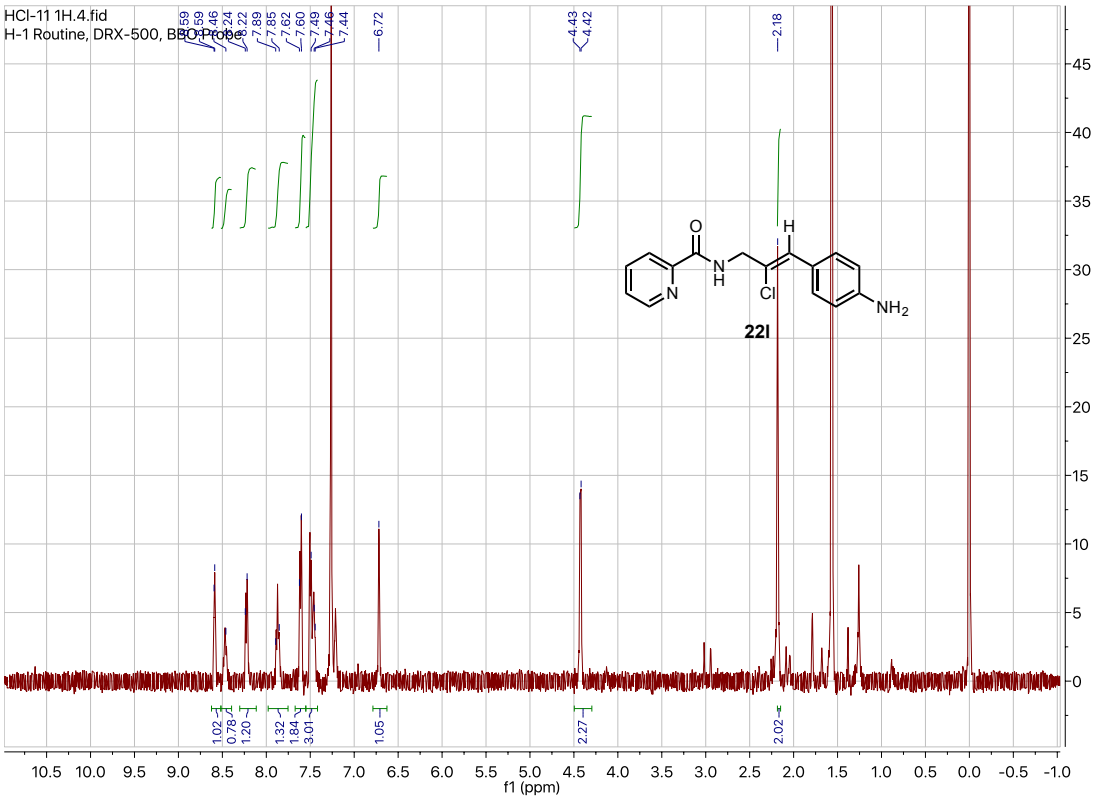

HCl-08-13C.1.fid
C-13 Routine, BBO Probe, DRX-500
22i
f1 (ppm)

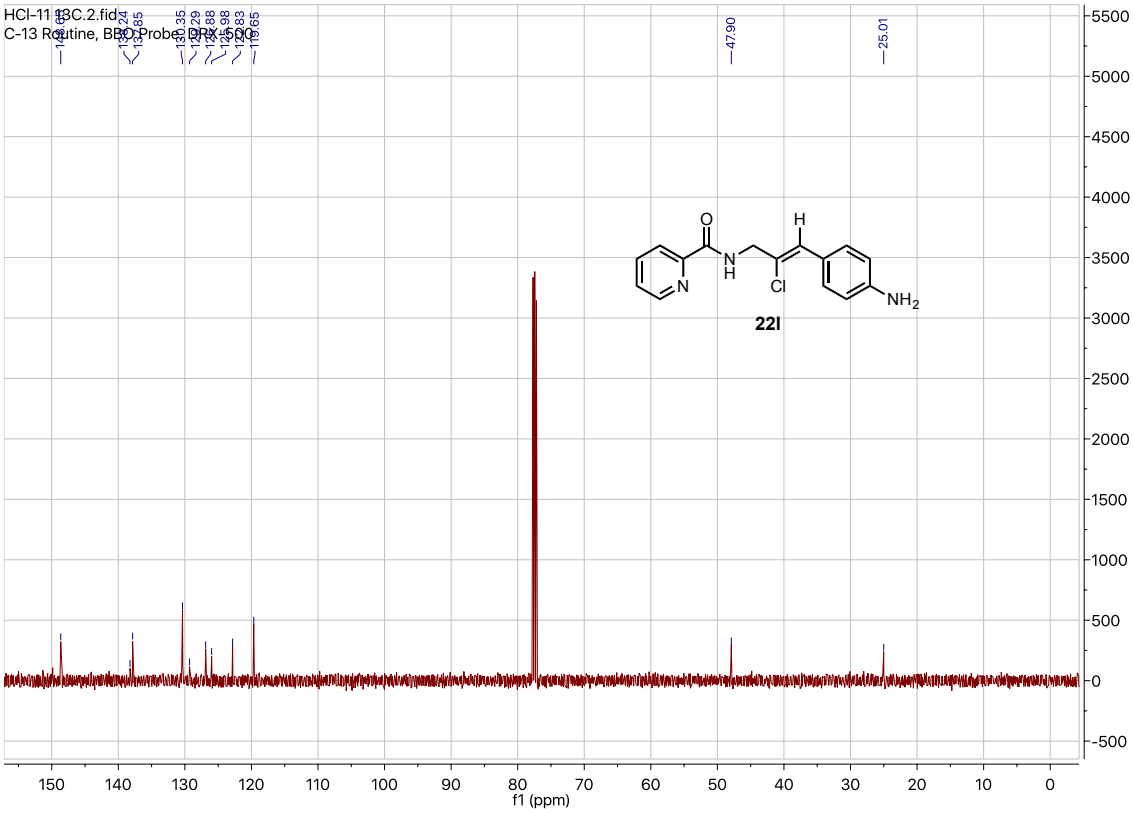

HCl-09 1H.1.fid
H-1 Routine, DRX-500, BBO Probe
8.58
8.47
8.22
7.89
7.87
7.86
7.47
7.47
6.71
4.41
1.00
0.97
0.94
0.95
4.96
0.97
2.04
f1 (ppm)
22j

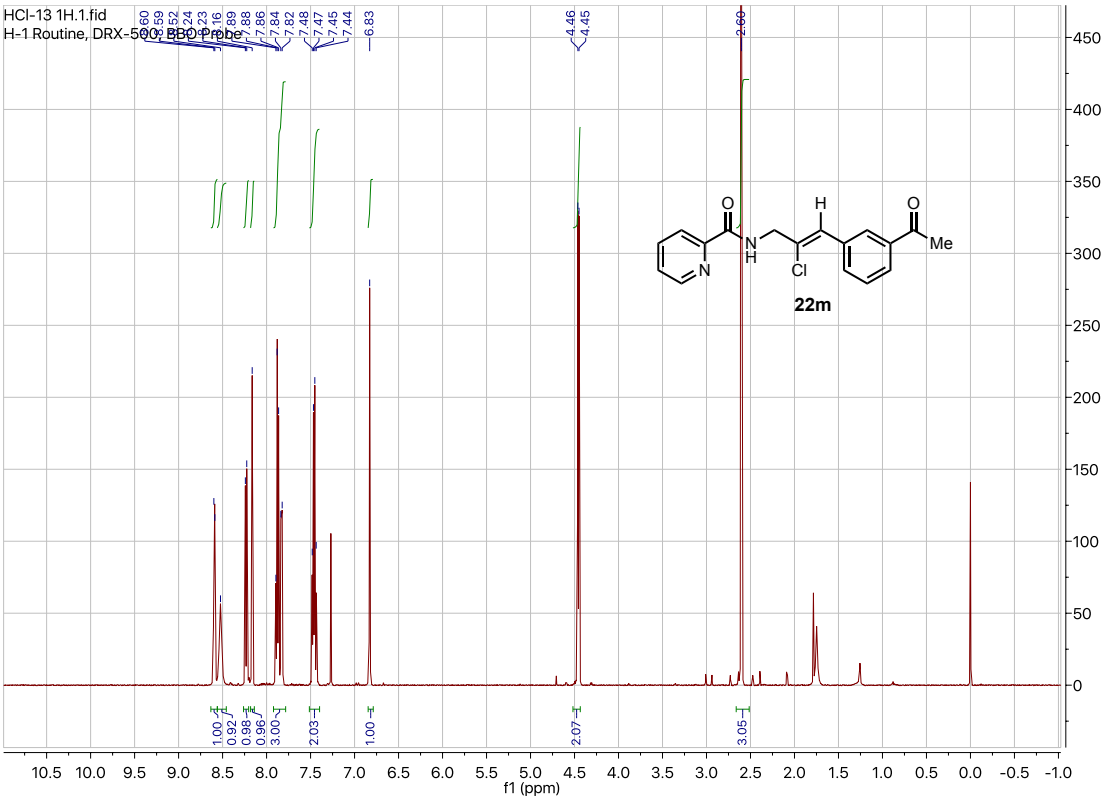

HCl-09 13C.1.fid
C-13 Routine, BBO Probe, DRX-500
149.83
148.62
138.85
138.48
137.79
131.21
131.12
126.89
125.34
122.89
122.43
47.72
f1 (ppm)
22j

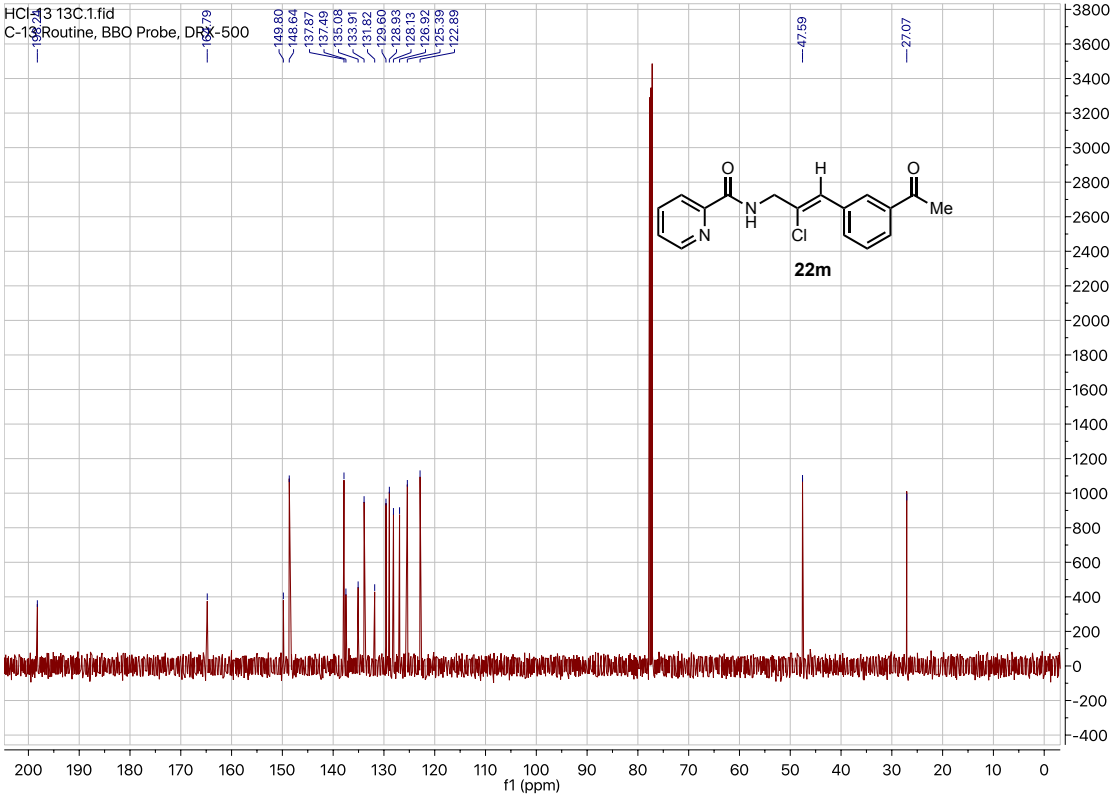

HCl-14 1H.1.fid
H-1 Routine, DRX-500, BBO Probe
8.59
8.58
8.48
8.23
8.22
7.88
7.86
7.85
7.56
7.54
7.47
7.45
7.45
7.32
7.30
6.73
4.43
4.42
22k
f1 (ppm)

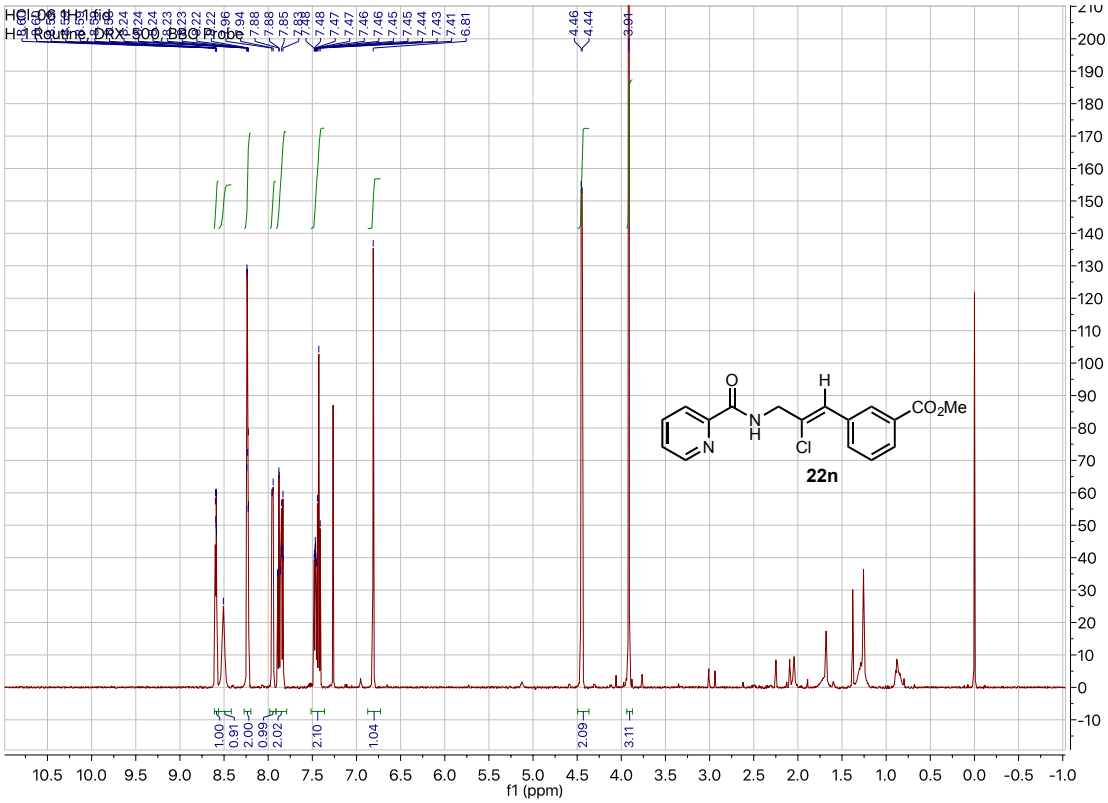

HCl-14 13C.1.fid
C-13 Routine, BBO Probe, DRX-500
164.76
149.84
148.62
137.85
134.18
133.02
130.85
128.83
126.89
125.31
122.88
47.72
22k
f1 (ppm)

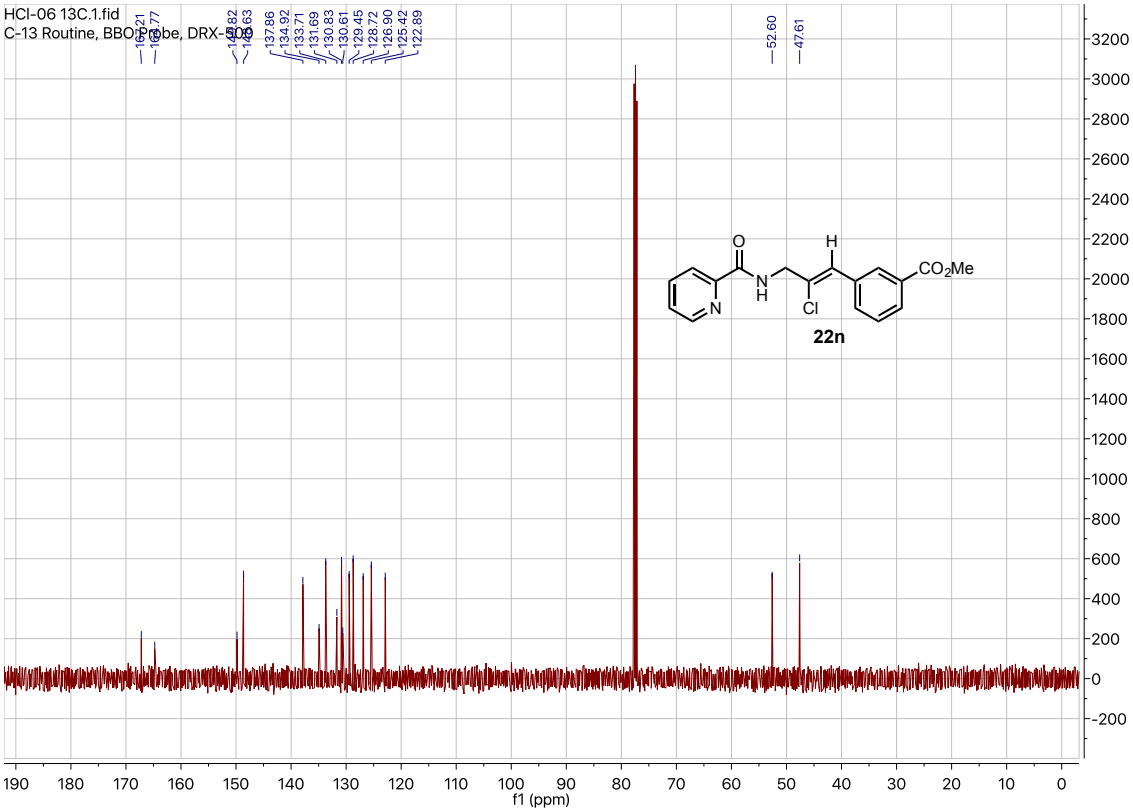

HCl-11 1H.4.fid
H-1 Routine, DRX-500, BBO Probe
22l
f1 (ppm)

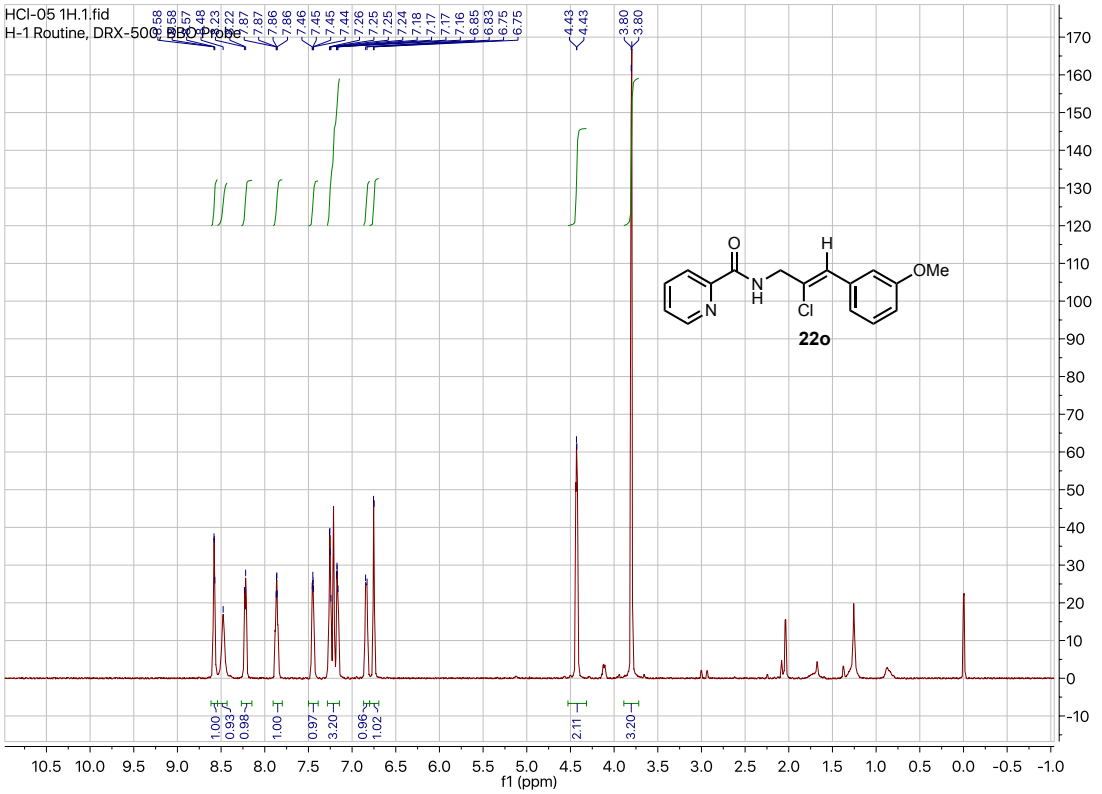

HCl-11 13C.2.fid
C-13 Routine, BBO Probe, DRX-500
22l
f1 (ppm)

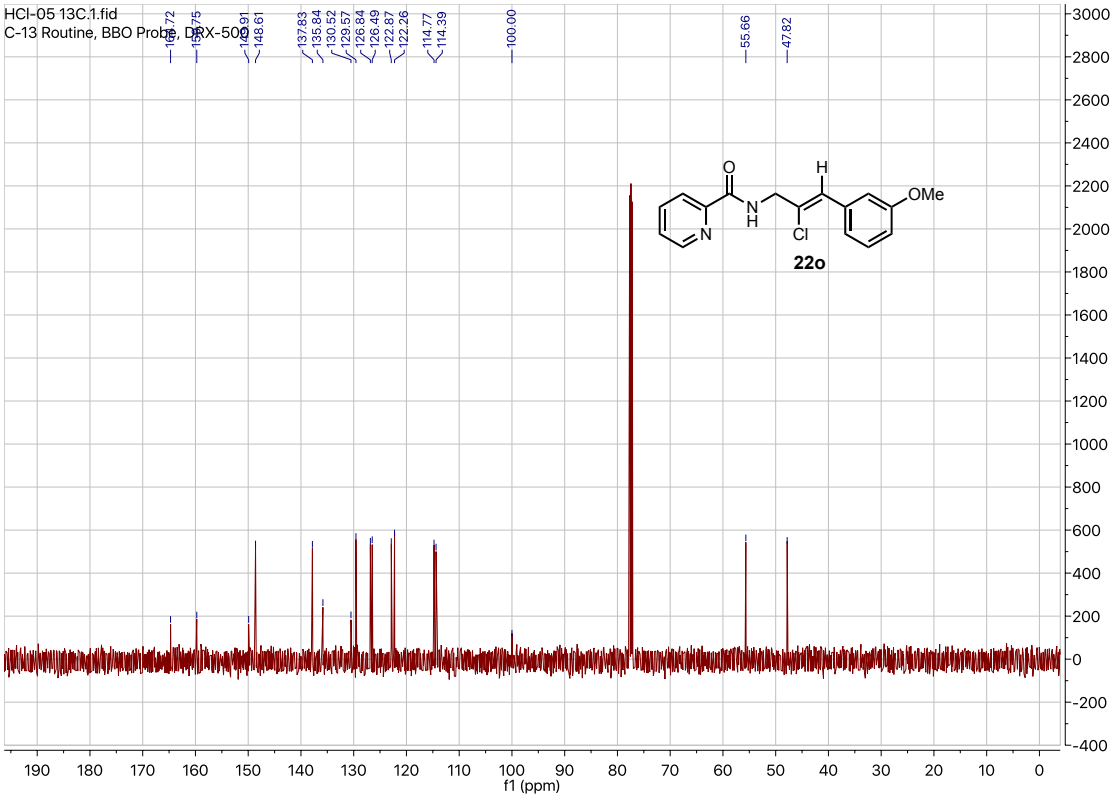

HCl-13 1H.1.fid
H-1 Routine, DRX-500, BBO Probe
22m
f1 (ppm)

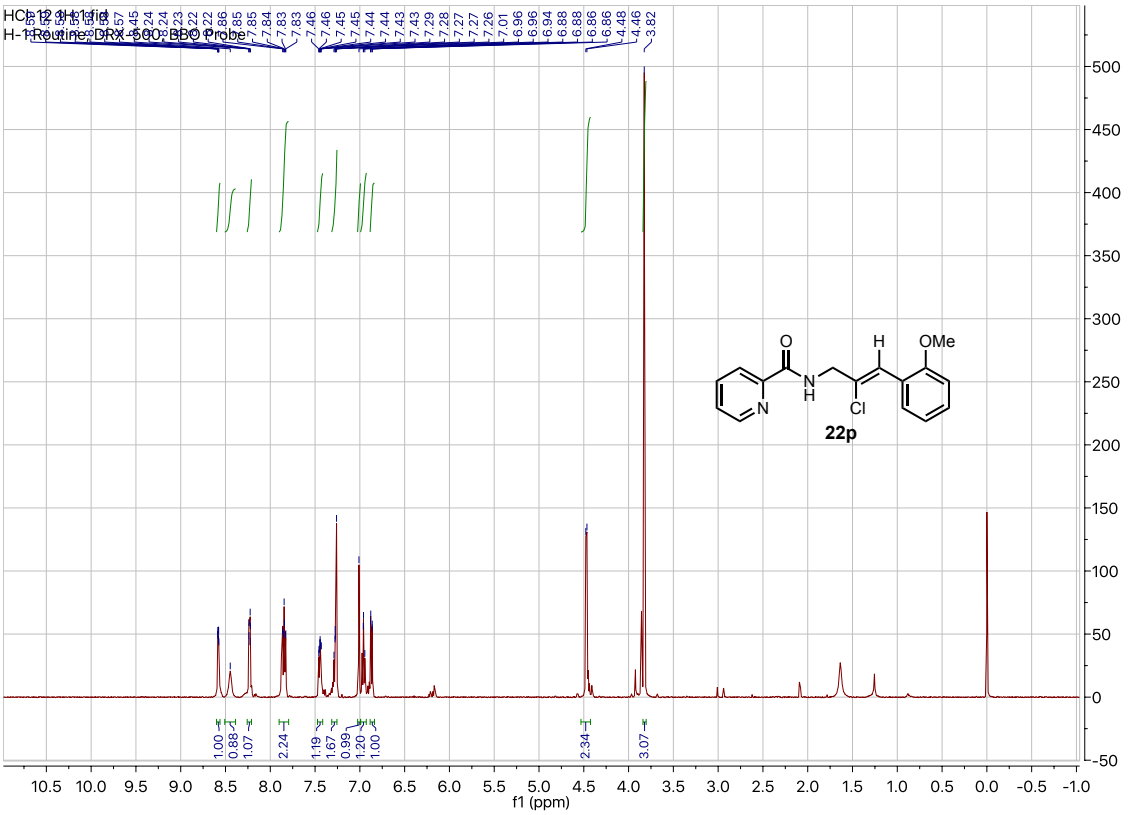

HCl-13 13C.1.fid
C-13 Routine, BBO Probe, DRX-500
22m
f1 (ppm)

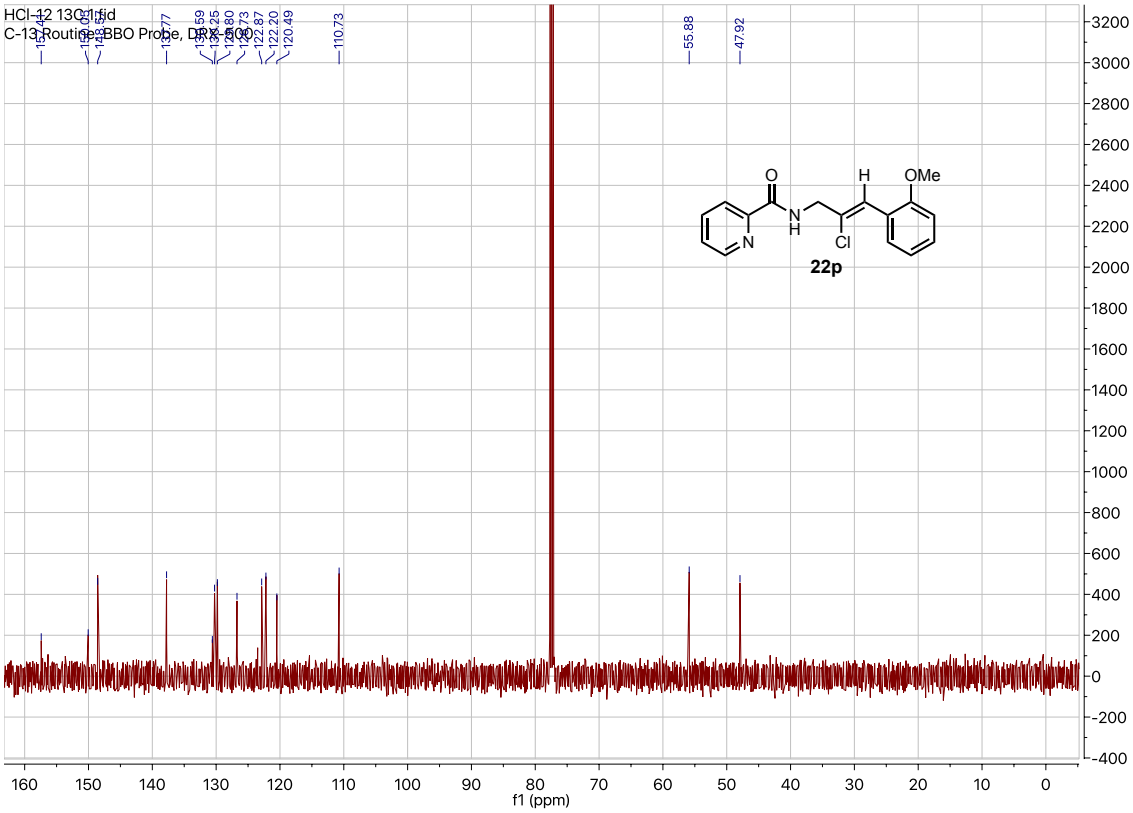

HCl-06 1H.1.fid
H-1 Routine, DRX-500, BBO Probe
4.46
4.44
3.91
7.96
7.94
7.88
7.85
7.83
7.48
7.47
7.47
7.46
7.46
7.45
7.45
7.44
7.43
7.41
6.81
1.00
0.91
2.00
0.99
2.02
2.10
1.04
2.09
3.11
O
H
N
H
N
Cl
CO2Me
22n
f1 (ppm)

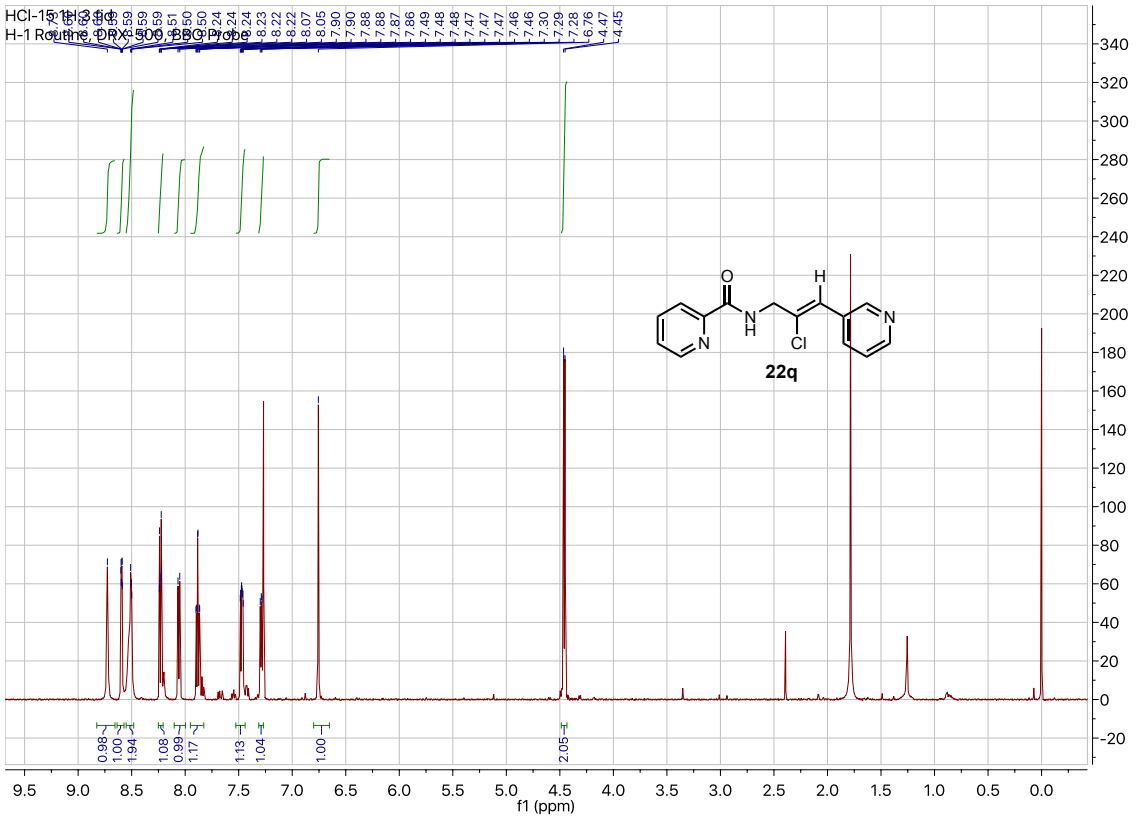

HCl-06 13C.1.fid
C-13 Routine, BBO Probe, DRX-500
164.21
163.77
149.82
149.63
137.86
134.92
133.71
131.69
130.83
130.61
129.45
128.72
126.90
125.42
122.89
52.60
47.61
O
H
N
H
N
Cl
CO2Me
22n
f1 (ppm)

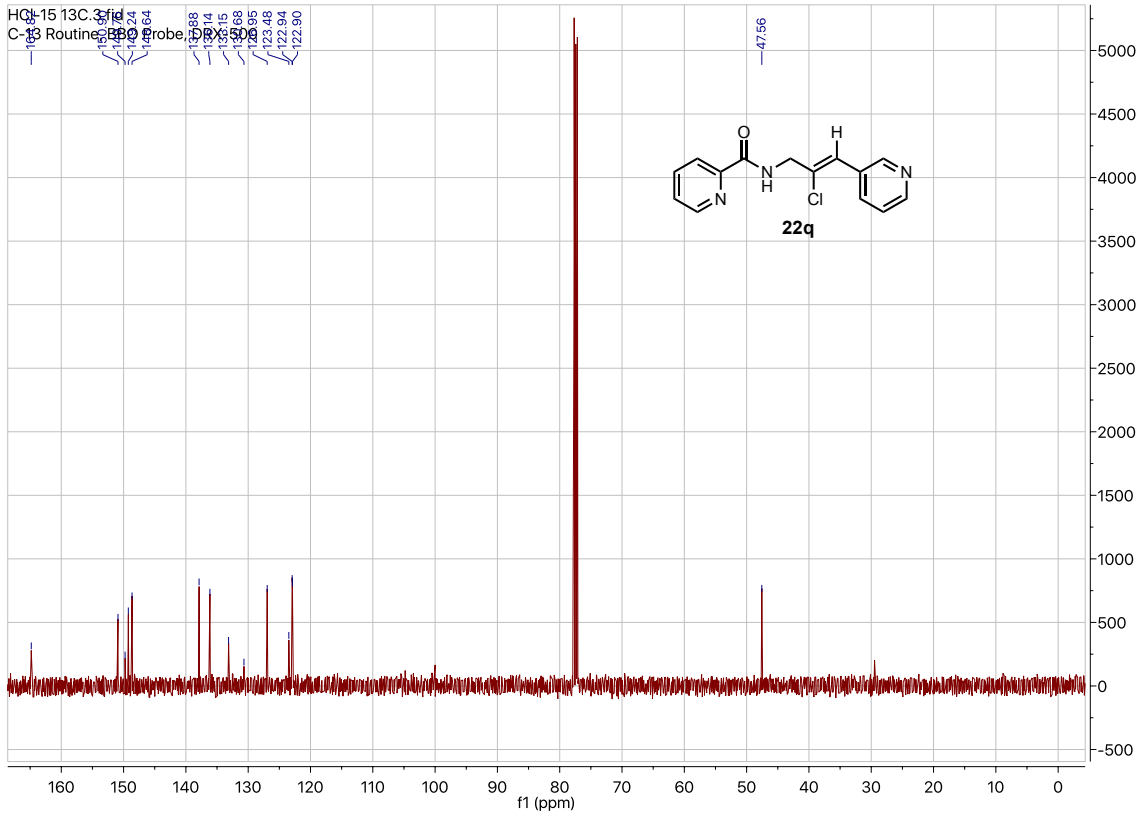

HCl-05 1H.1.fid
H-1 Routine, DRX-500, BBO Probe
22o

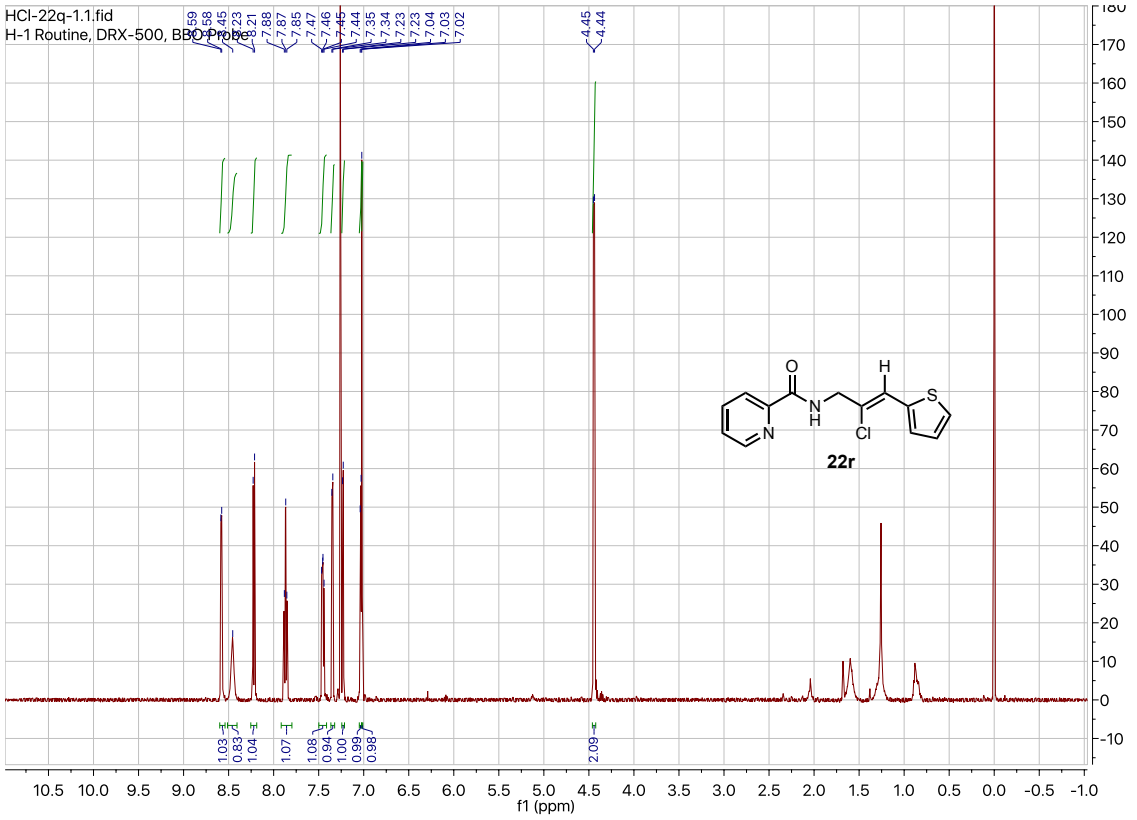

HCl-05 13C.1.fid
C-13 Routine, BBO Probe, DRX-500
22o

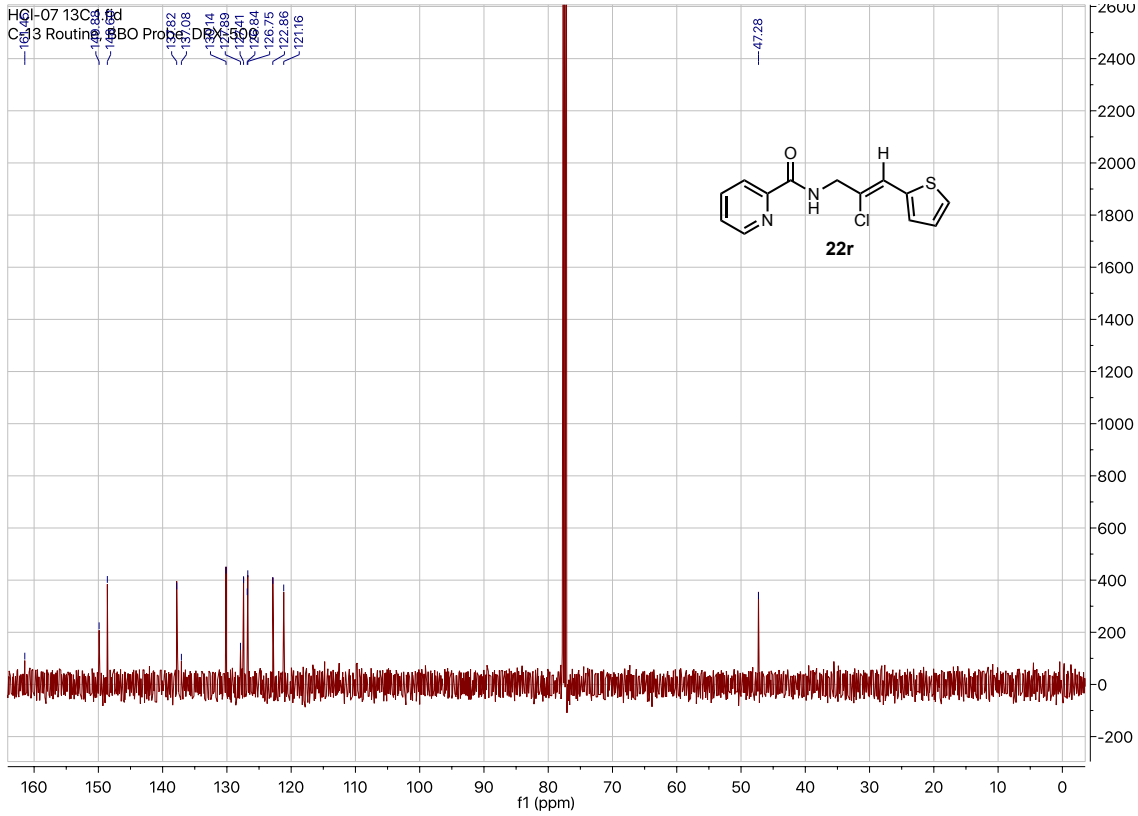

HCl-12 1H 1.fid
H-1 Routine, DRX-500, BBO Probe
22p
f1 (ppm)

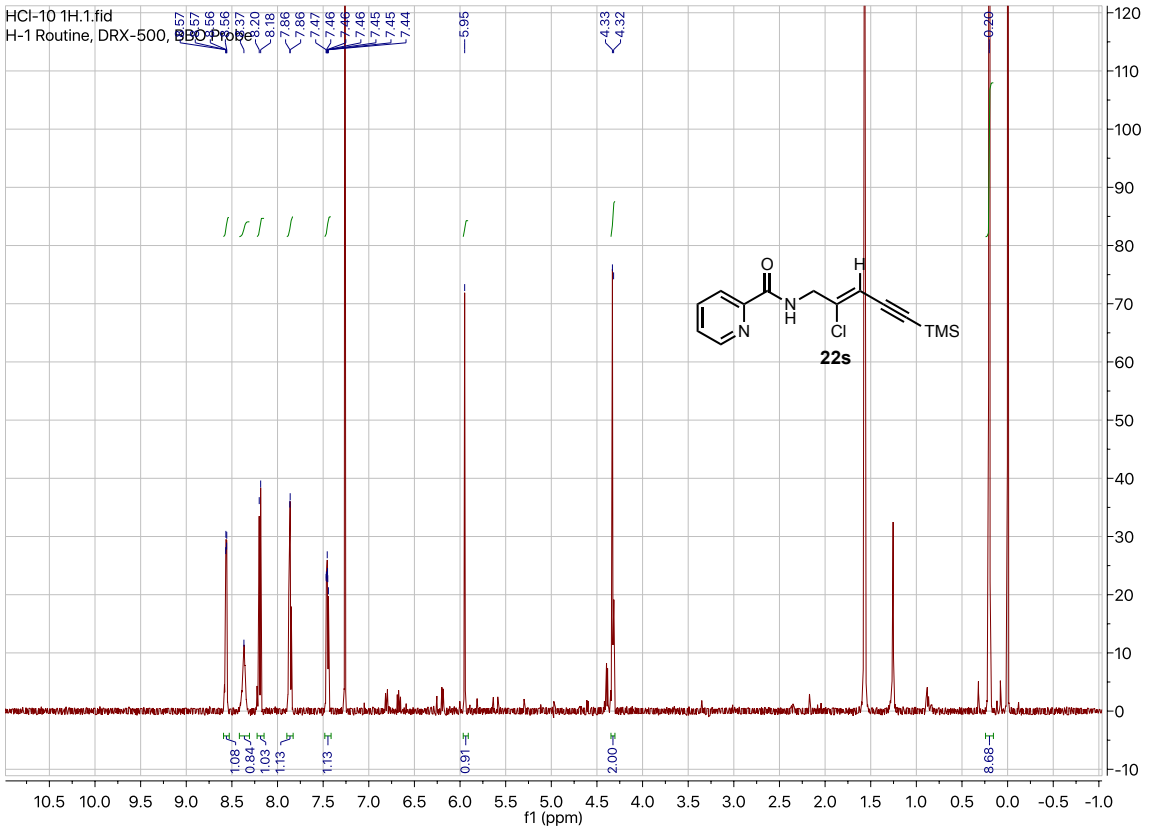

HCl-12 13C 1.fid
C-13 Routine, BBO Probe, DRX-500
22p
f1 (ppm)

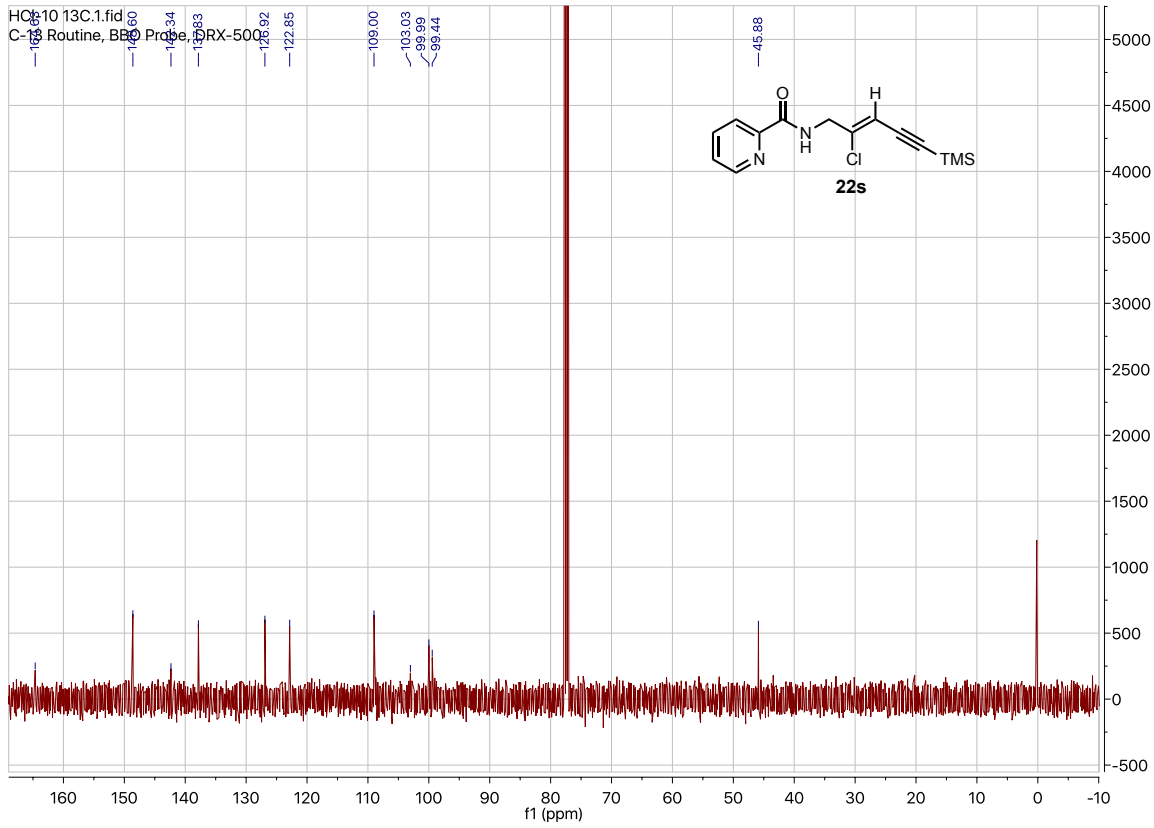

HCl-15 1H 3.fid
H-1 Routine, DRX-500, BBO Probe
22q
f1 (ppm)

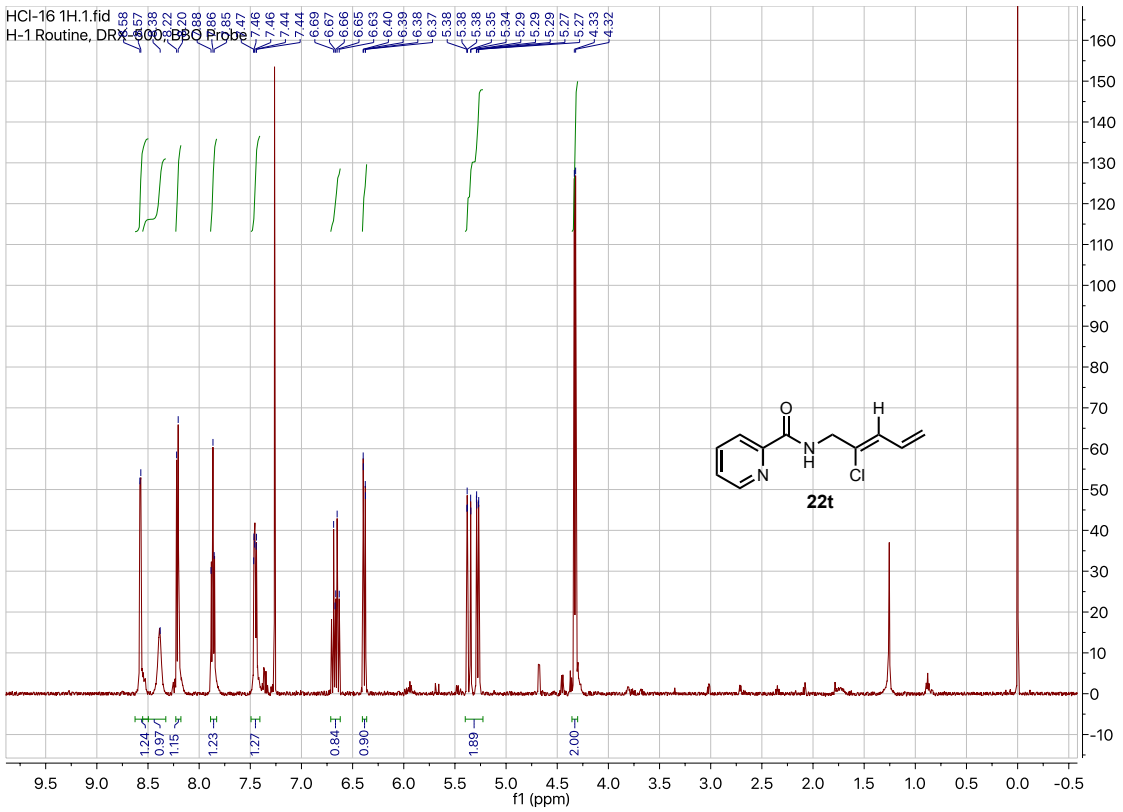

HCl-15 13C 3.fid
C-13 Routine, BBO Probe, DRX-500
22q
f1 (ppm)

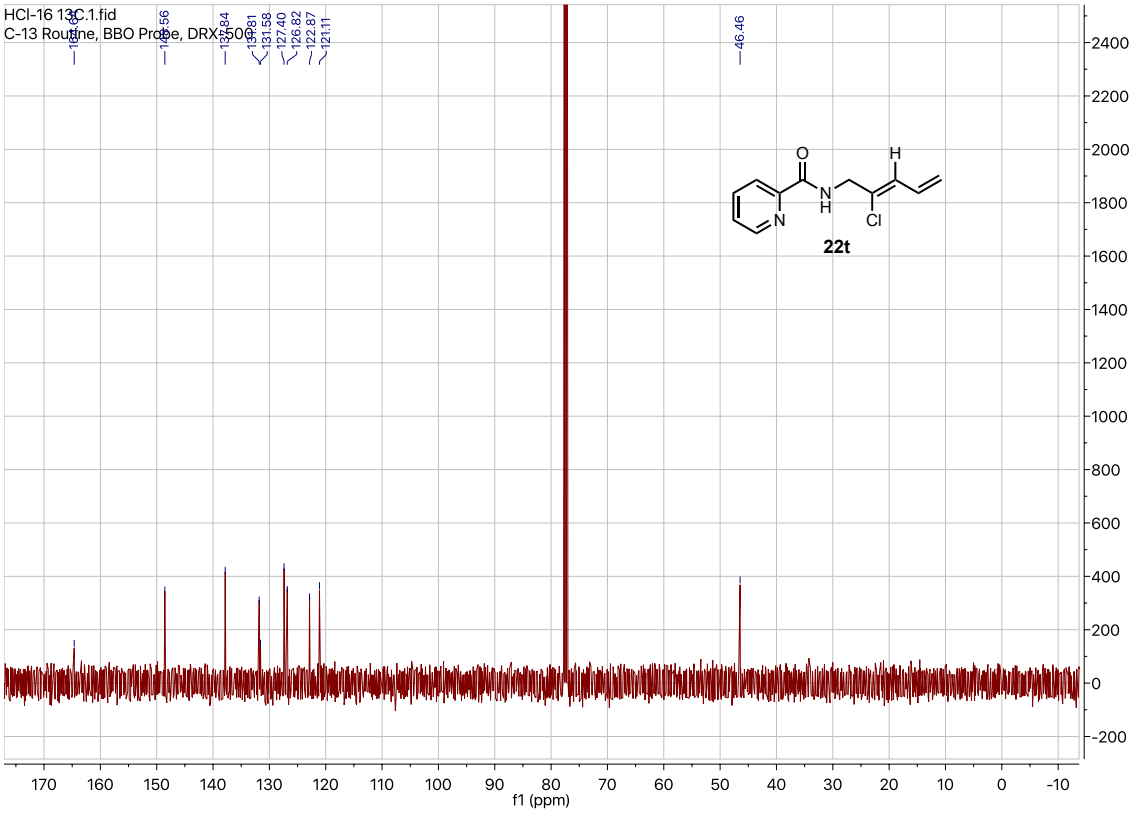

HCl-22q-1.1.fid
H-1 Routine, DRX-500, BBO Probe
22r
f1 (ppm)

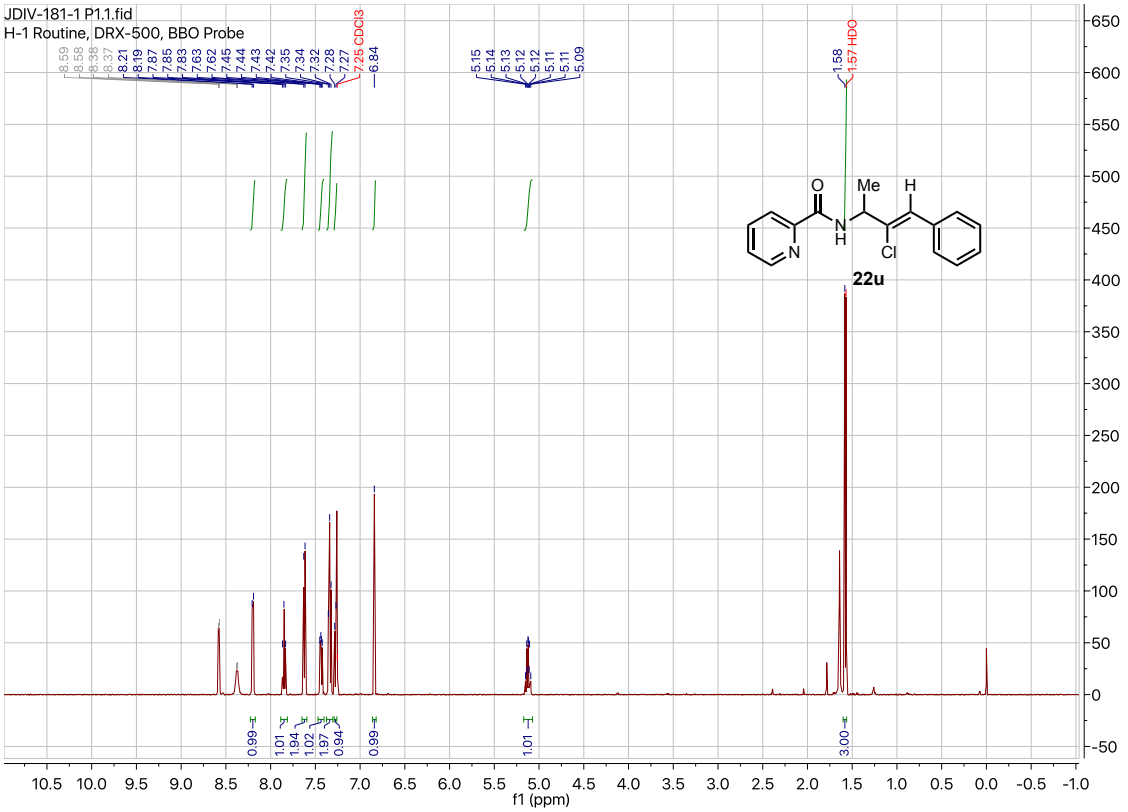

HCl-07 13C-1.fid
C13 Routine, BBO Probe, DRX-500
22r
f1 (ppm)

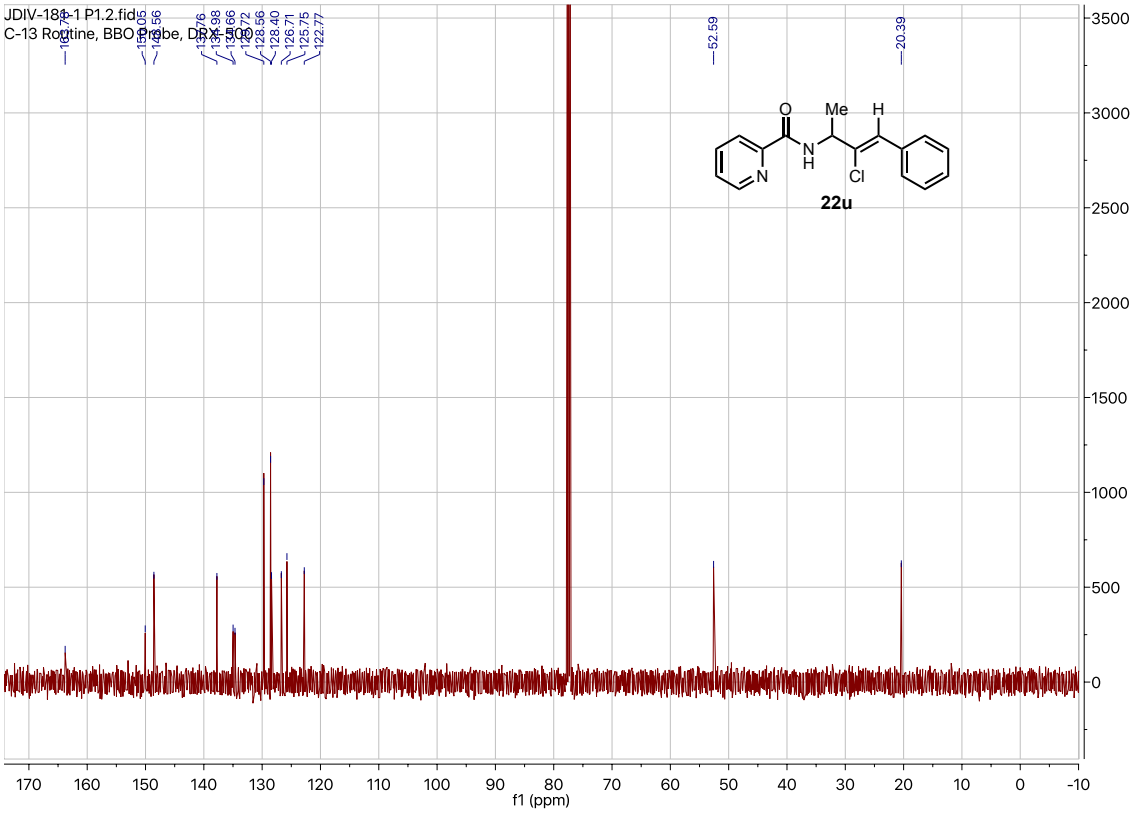

HCl-10 1H.1.fid
H-1 Routine, DRX-500, BBO Probe
8.57
8.57
7.56
7.56
8.37
8.20
8.18
7.86
7.86
7.47
7.46
7.46
7.46
7.45
7.45
7.44
5.95
4.33
4.32
0.20
1.08
0.84
1.03
1.13
1.13
0.91
2.00
8.68
O
H
N
H
N
Cl
TMS
22s
f1 (ppm)

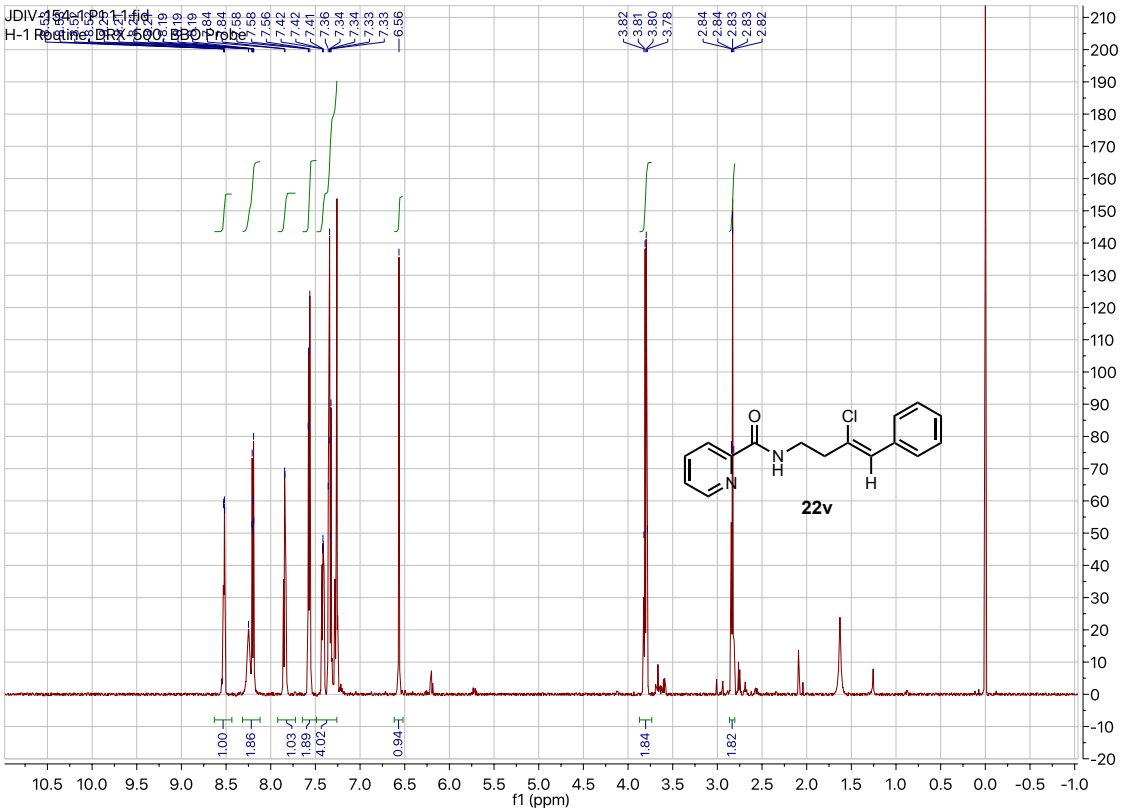

HCl-10 13C.1.fid
C-13 Routine, BBO Probe, DRX-500
163.66
149.60
149.34
137.83
126.92
122.85
109.00
103.03
99.99
99.44
45.88
O
H
N
H
N
Cl
TMS
22s
f1 (ppm)

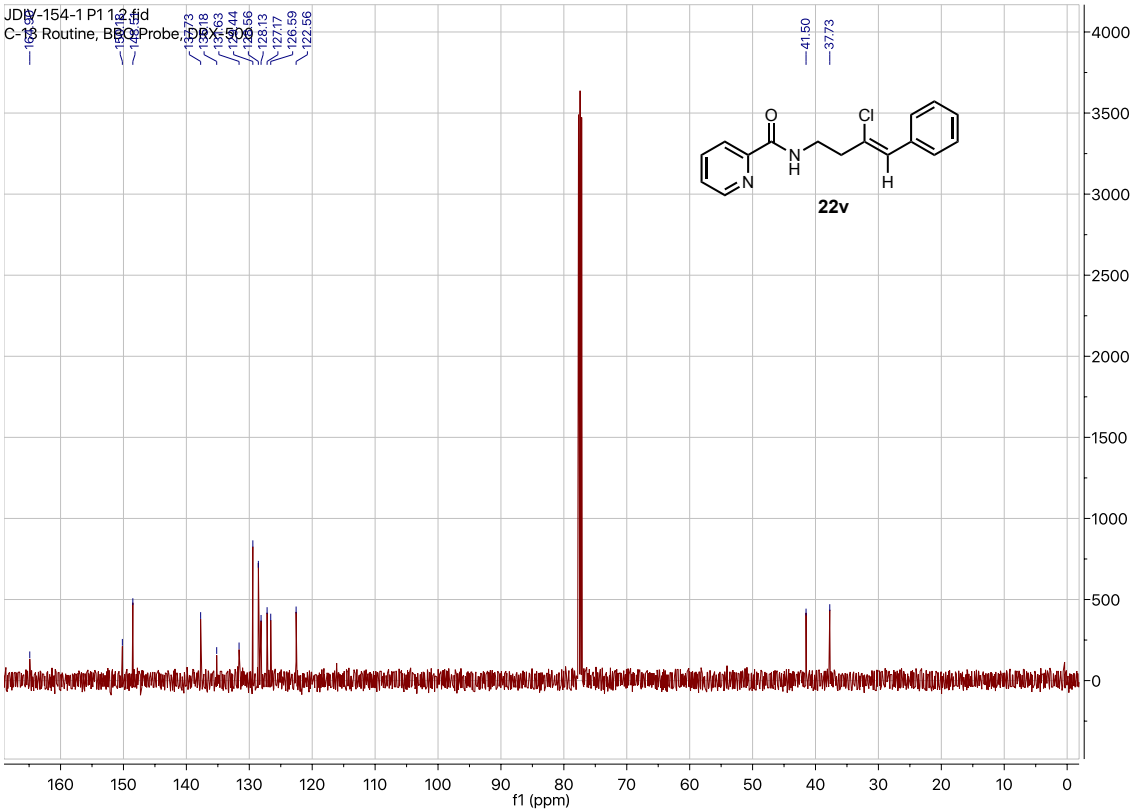

HCl-16 1H.1.fid
H-1 Routine, DRX-600, BBO Probe
22t
f1 (ppm)

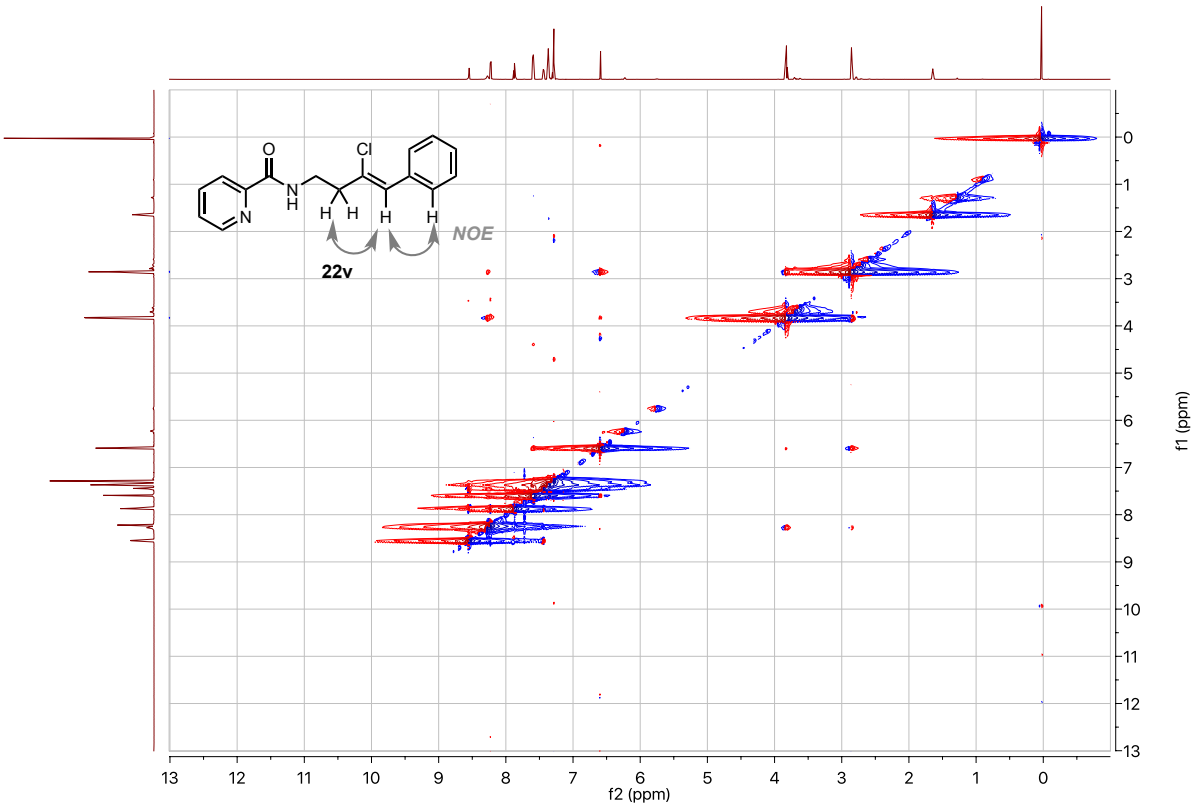

HCl-16 13C.1.fid
C-13 Routine, BBO Probe, DRX-500
22t
f1 (ppm)

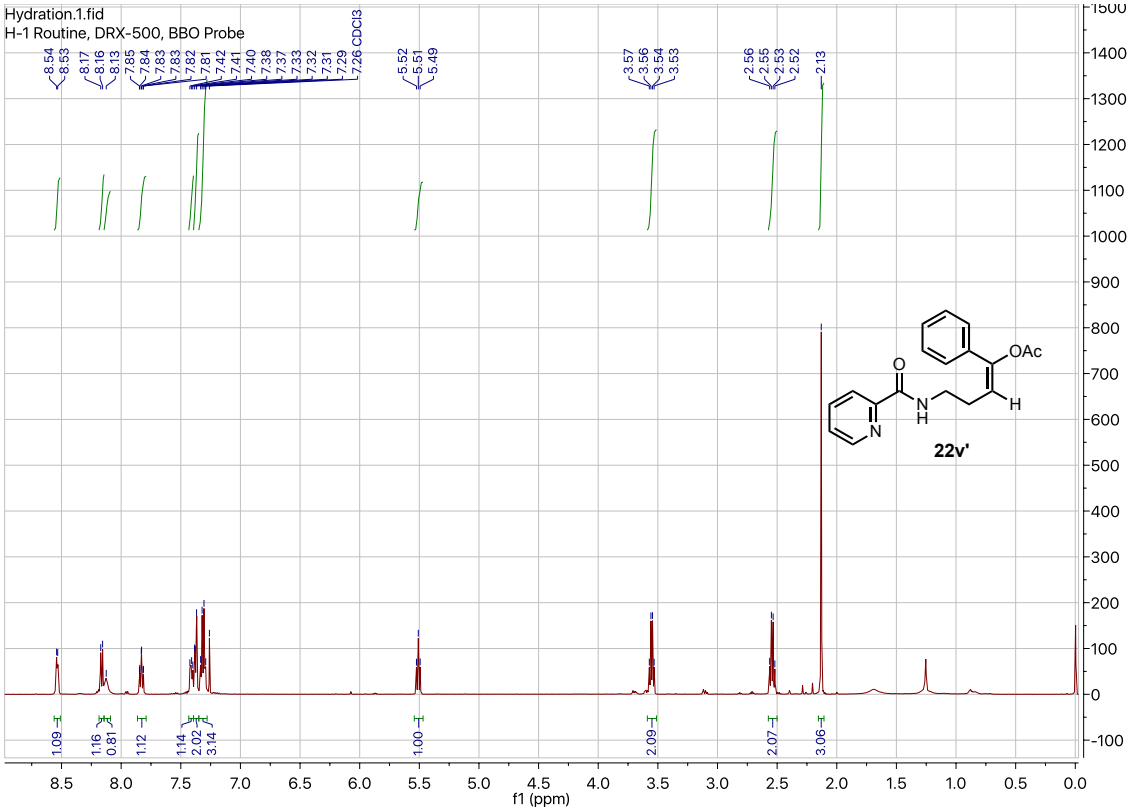

JDIV-181-1 P1.1.fid
H-1 Routine, DRX-500, BBO Probe
22u
f1 (ppm)

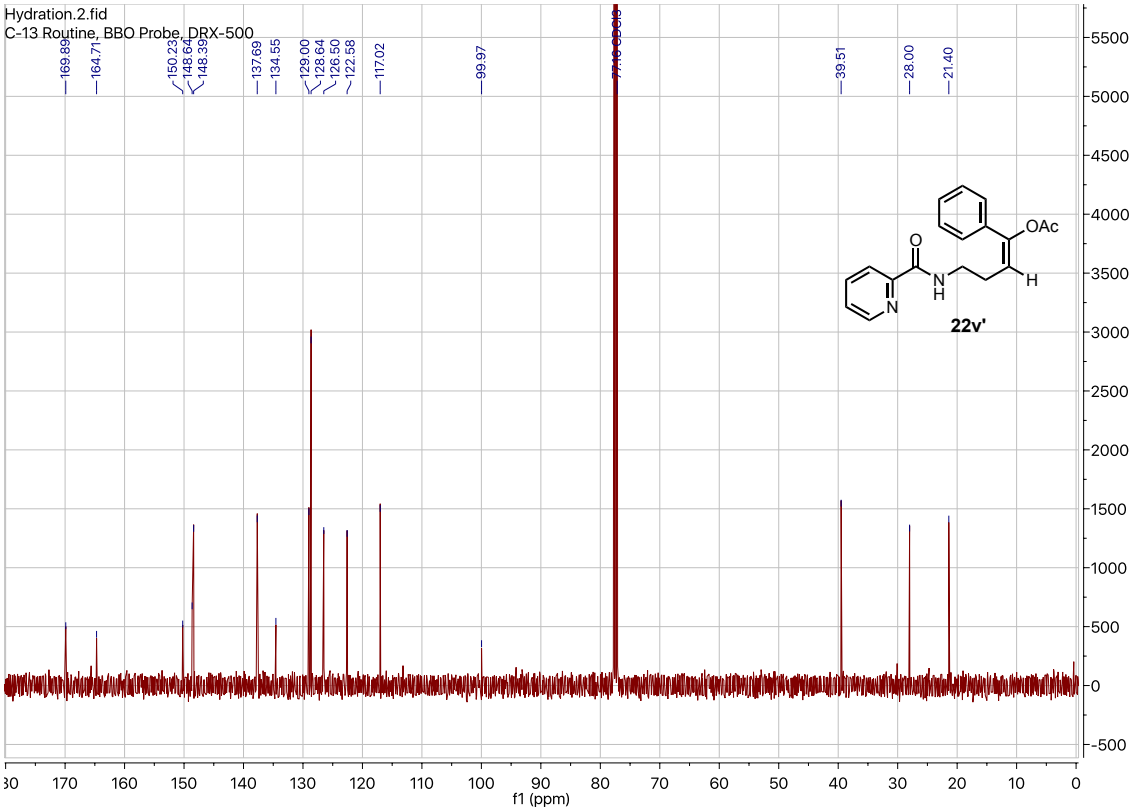

JDIV-181-1 P1.2.fid
C-13 Routine, BBO Probe, DRX-500
22u
f1 (ppm)

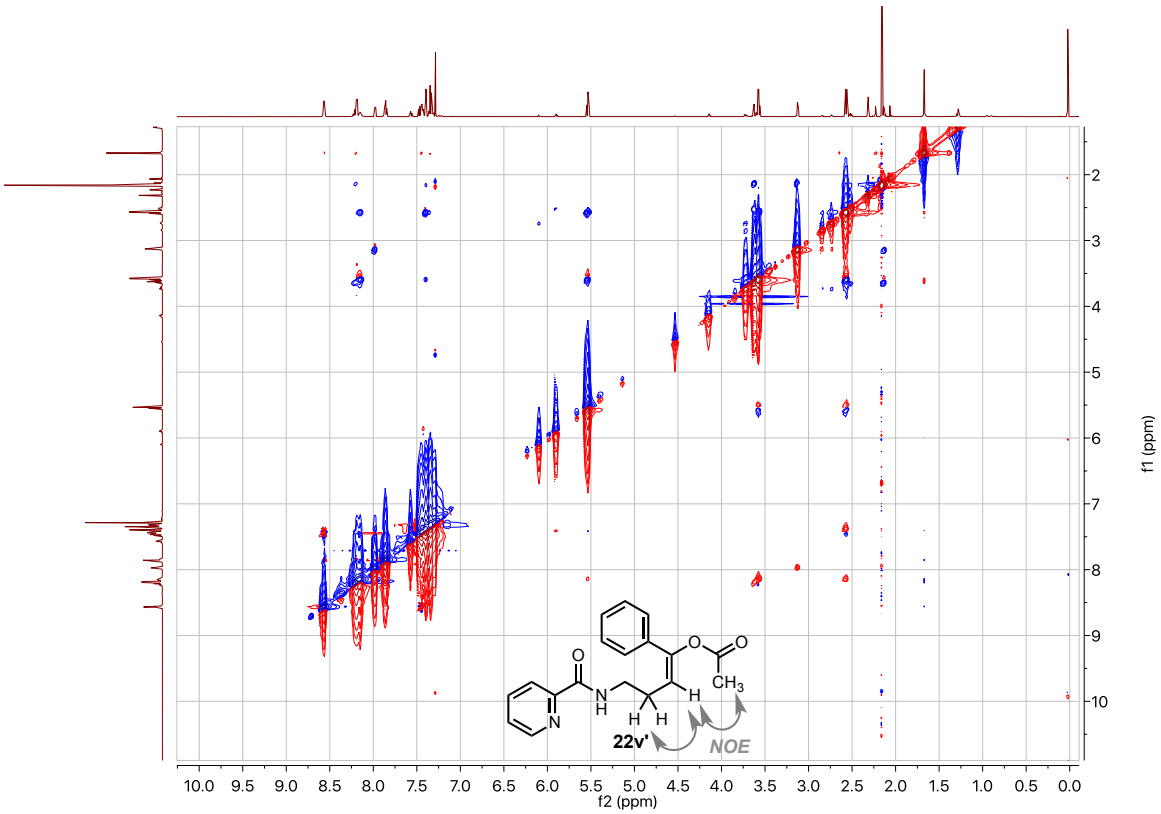

JDIV-154-1-P1-1-1.fid
H-1 Routine, DRX-500, BBO Probe
3.82
3.81
3.80
3.78
2.84
2.84
2.83
2.83
2.82
7.36
7.34
7.34
7.33
7.33
6.56
1.00
1.86
1.03
1.89
4.02
0.94
1.84
1.82
O
N
H
Cl
H
N
22v
f1 (ppm)

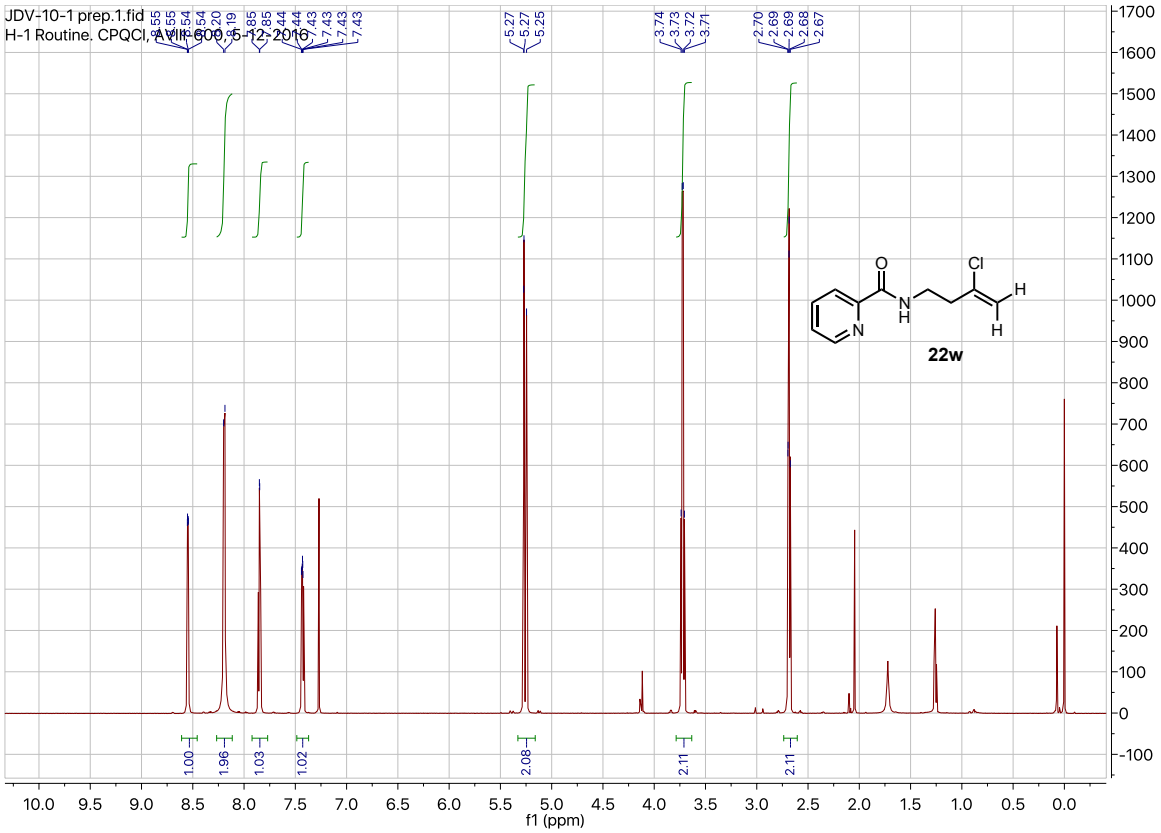

JDIV-154-1 P1 1a-2.fid
C-13 Routine, BBO Probe, DRX-500
41.50
37.73
O
N
H
Cl
H
N
22v
f1 (ppm)

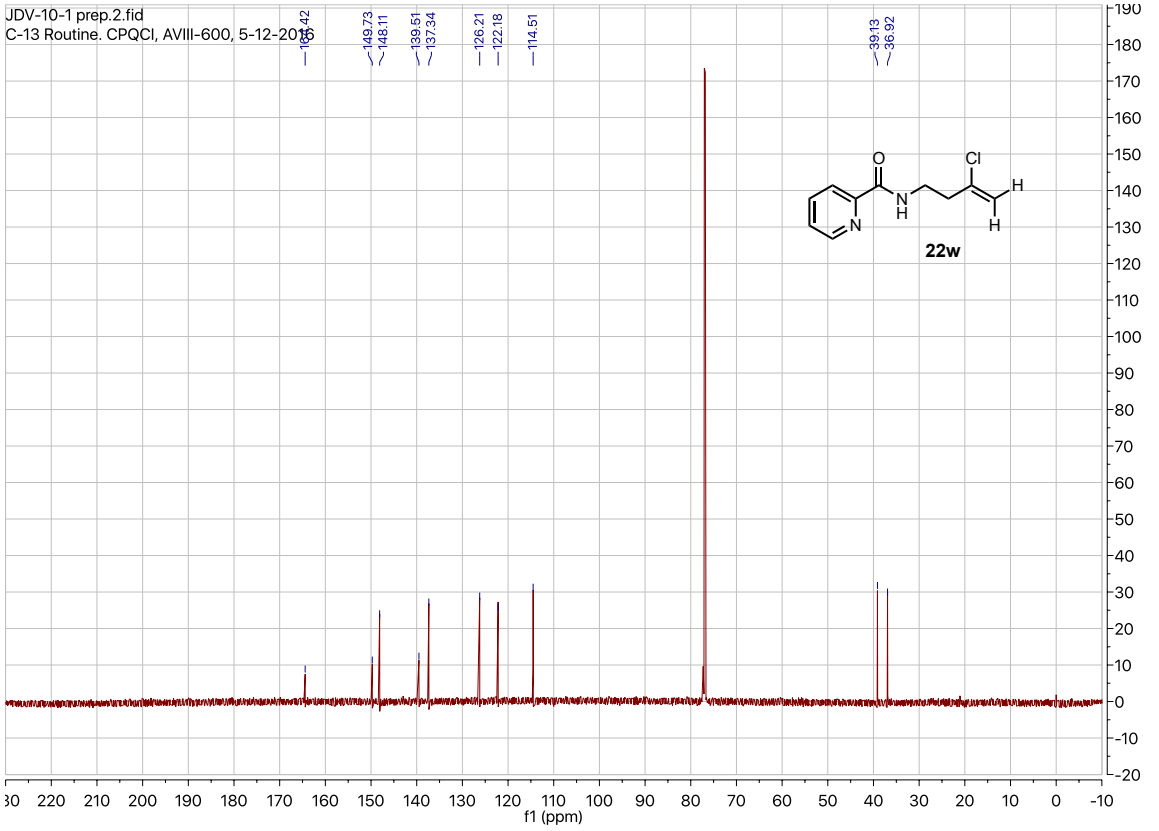

O
Cl
N
H
N
H H H H
NOE
22v
f2 (ppm)
f1 (ppm)

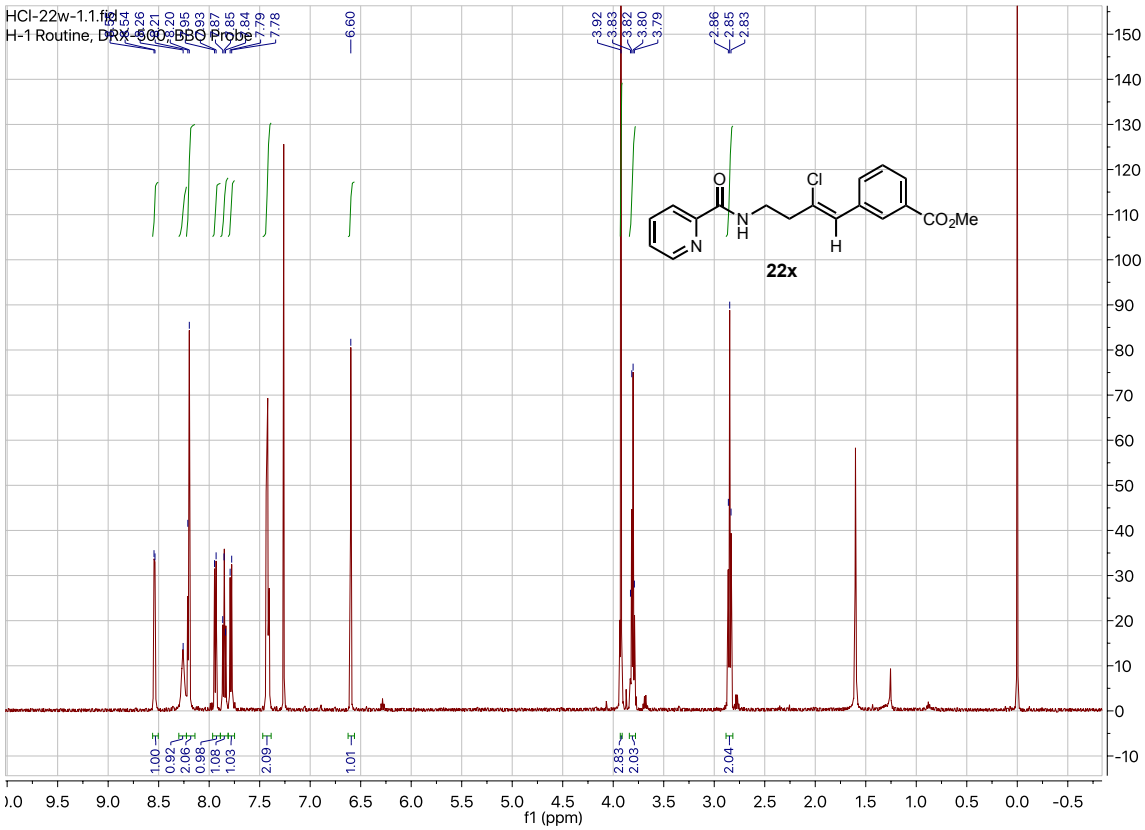

Hydration.1.fid
H-1 Routine, DRX-500, BBO Probe
8.54
8.53
8.17
8.16
8.13
7.85
7.84
7.83
7.83
7.82
7.81
7.42
7.41
7.40
7.38
7.37
7.33
7.32
7.31
7.29
7.26 CDCl3
5.52
5.51
5.49
3.57
3.56
3.54
3.53
2.56
2.55
2.53
2.52
2.13
1.09
1.16
0.81
1.12
1.14
2.02
3.14
1.00
2.09
2.07
3.06
f1 (ppm)
OAc
O
N
H
H
N
22v'

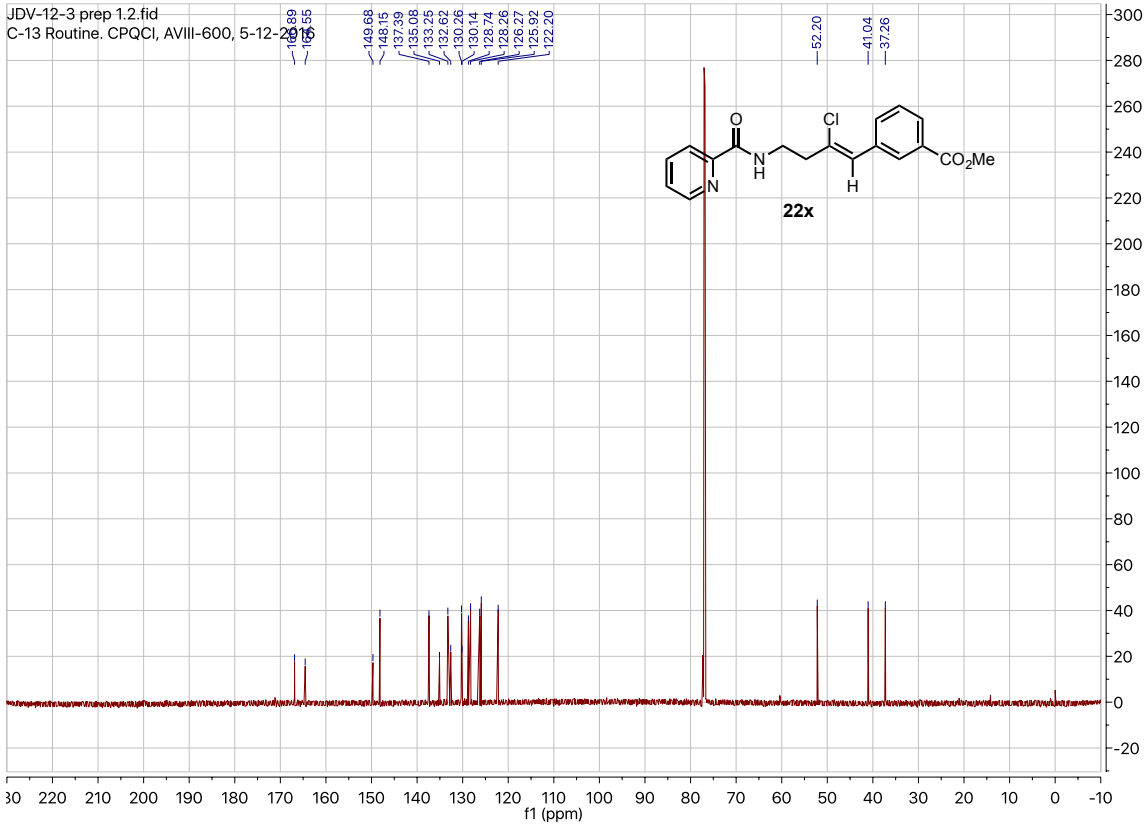

Hydration.2.fid
C-13 Routine, BBO Probe, DRX-500
169.89
164.71
150.23
148.64
148.39
137.69
134.55
129.00
128.64
126.50
122.58
117.02
99.97
39.51
28.00
21.40
f1 (ppm)
OAc
O
N
H
H
N
22v'

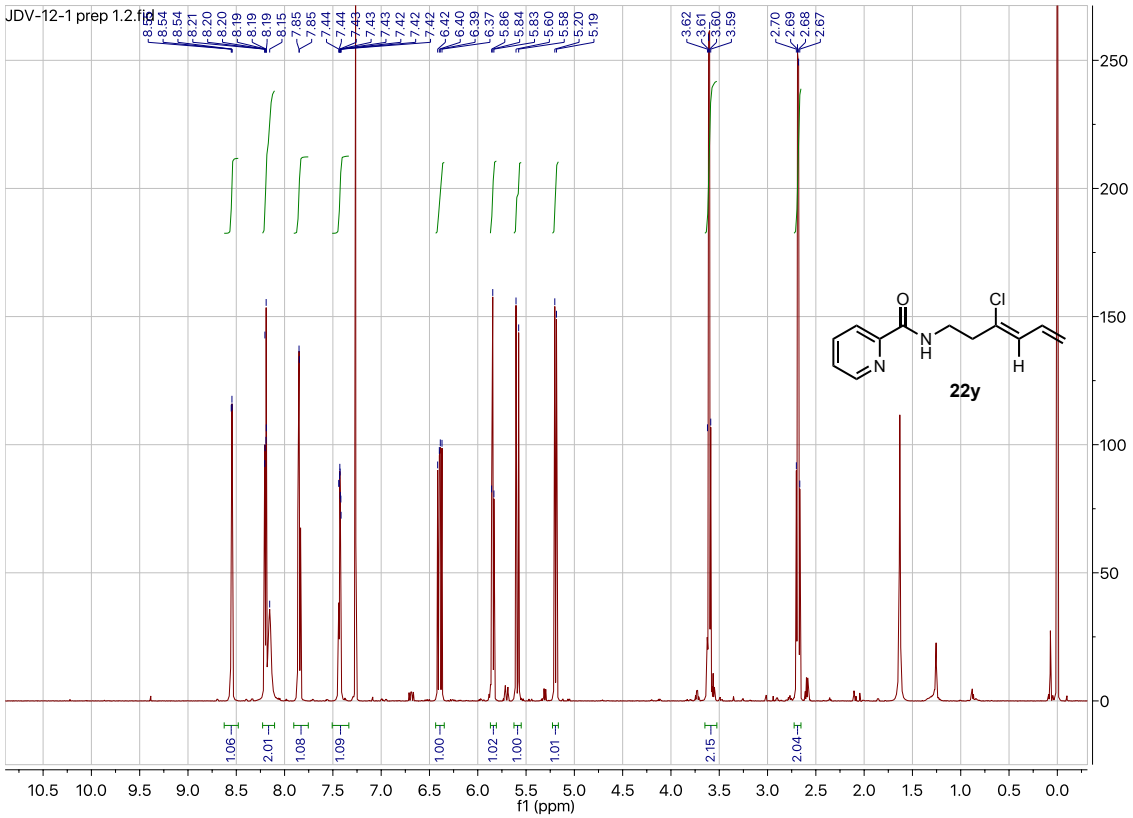

f2 (ppm)
f1 (ppm)
22v'
NOE

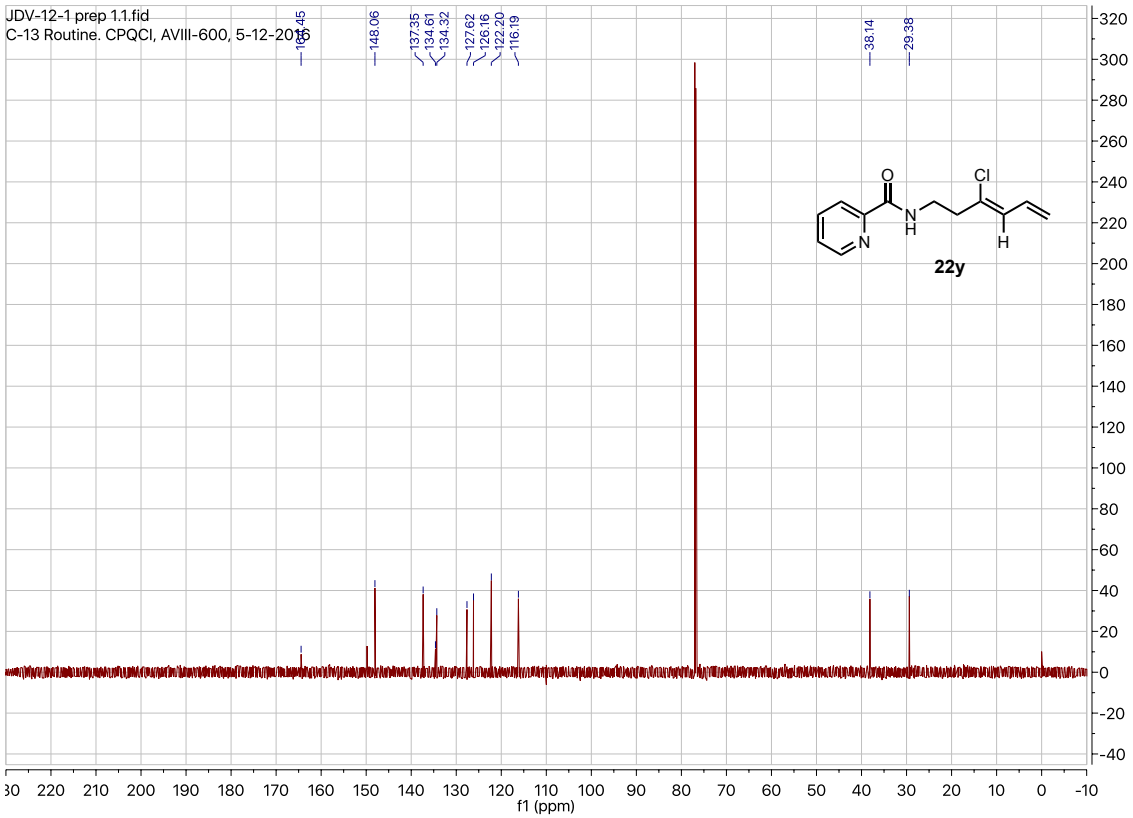

JDV-10-1 prep.1.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
8.55
8.55
8.54
8.54
8.20
8.19
7.85
7.85
7.44
7.44
7.43
7.43
7.43
7.43
5.27
5.27
5.25
3.74
3.73
3.72
3.71
2.70
2.69
2.69
2.68
2.67
1.00
1.96
1.03
1.02
2.08
2.11
2.11
O
Cl
H
N
H
N
H
22w
f1 (ppm)

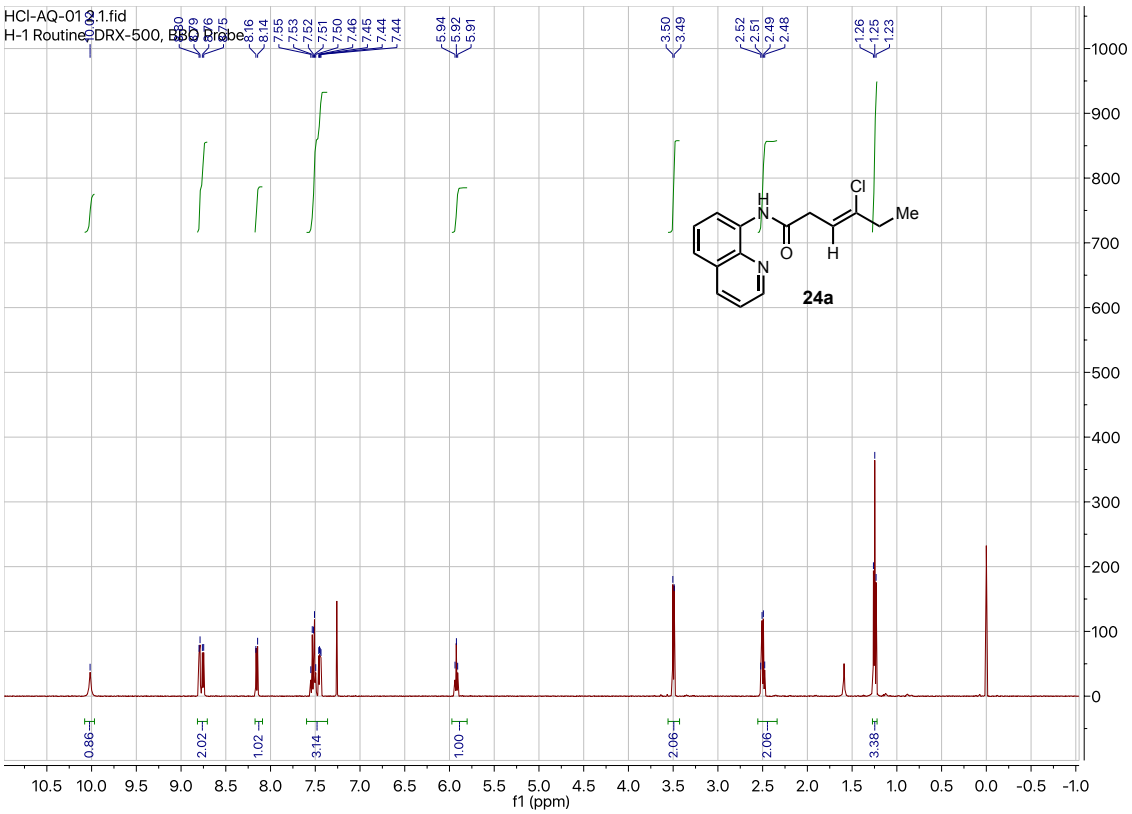

JDV-10-1 prep.2.fid
C-13 Routine. CPQCI, AVIII-600, 5-12-2016
164.42
149.73
148.11
139.51
137.34
126.21
122.18
114.51
39.13
36.92
O
Cl
H
N
H
N
H
22w
f1 (ppm)

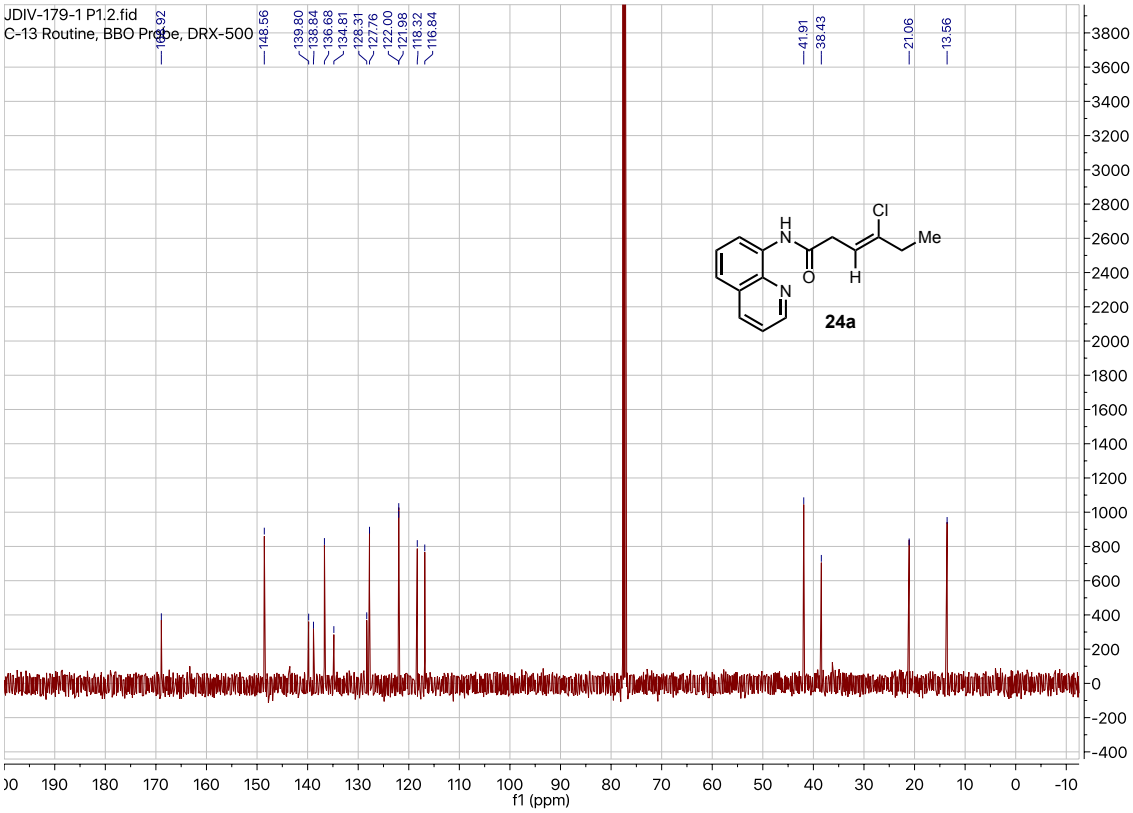

HCl-22w-1.1.fid
H-1 Routine, DRX-600 BBO Probe
6.60
3.92
3.83
3.82
3.80
3.79
2.86
2.85
2.83
7.78
7.79
7.84
7.85
7.87
7.93
8.20
8.21
8.26
8.54
8.64
1.00
0.92
2.06
0.98
1.08
1.03
2.09
1.01
2.83
2.03
2.04
O
N
H
N
Cl
H
CO2Me
22x
f1 (ppm)

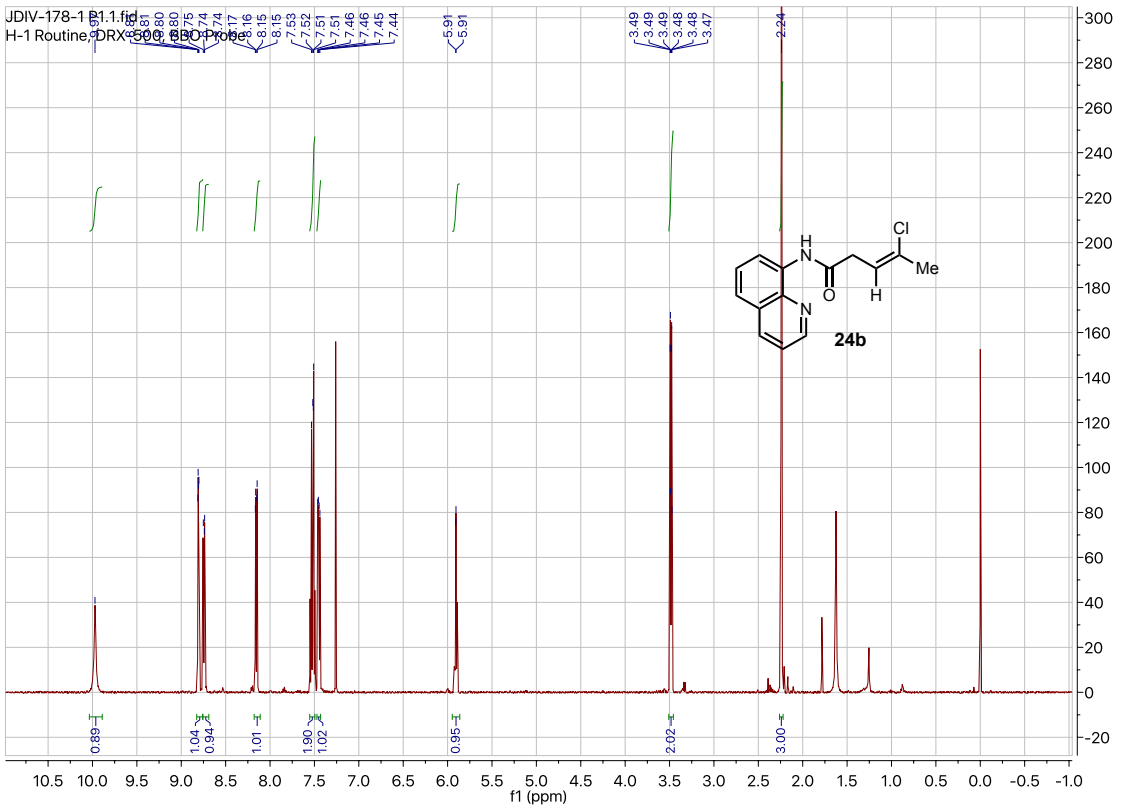

JDV-12-3 prep 1.2.fid
C-13 Routine. CPQCI, AVIII-600, 5-12-2016
165.89
165.55
149.68
148.15
137.39
135.08
133.25
132.62
130.26
130.14
128.74
128.26
126.27
125.92
122.20
52.20
41.04
37.26
O
N
H
N
Cl
H
CO2Me
22x
f1 (ppm)

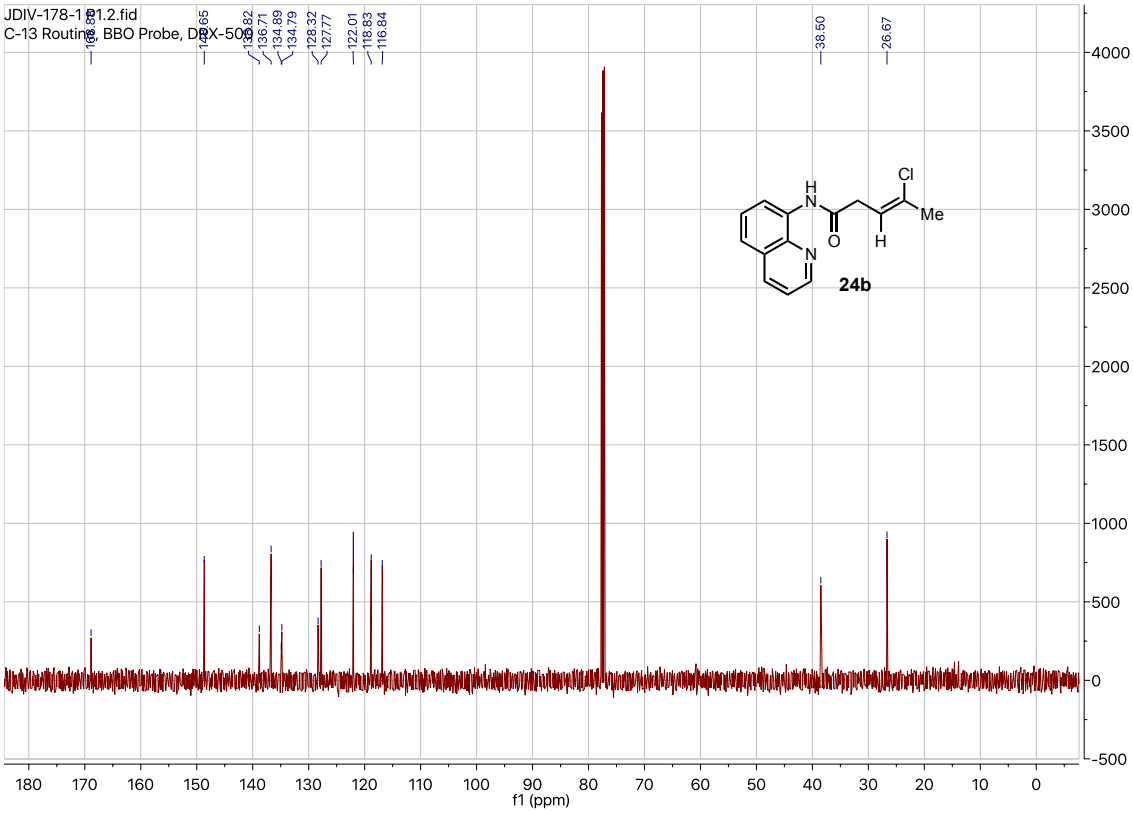

JDV-12-1 prep 1.2.fid
22y
f1 (ppm)

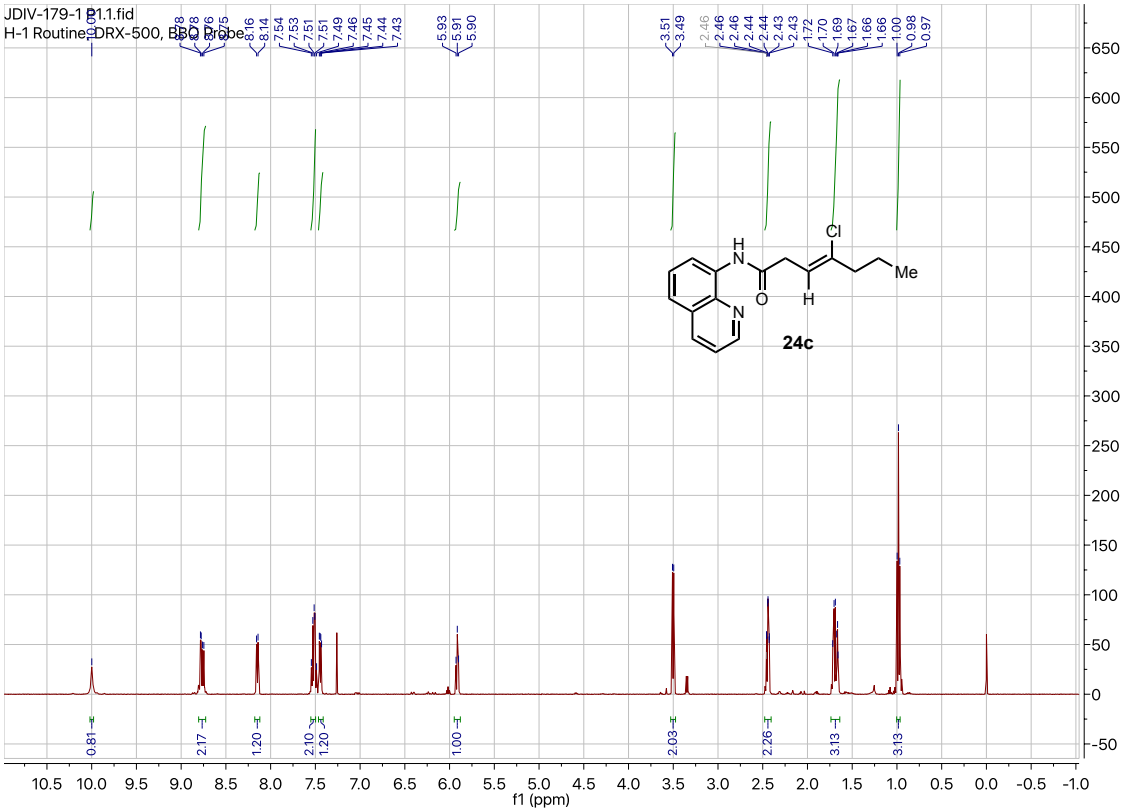

JDV-12-1 prep 1.1.fid
C-13 Routine. CPQCI, AVIII-600, 5-12-2015
22y
f1 (ppm)

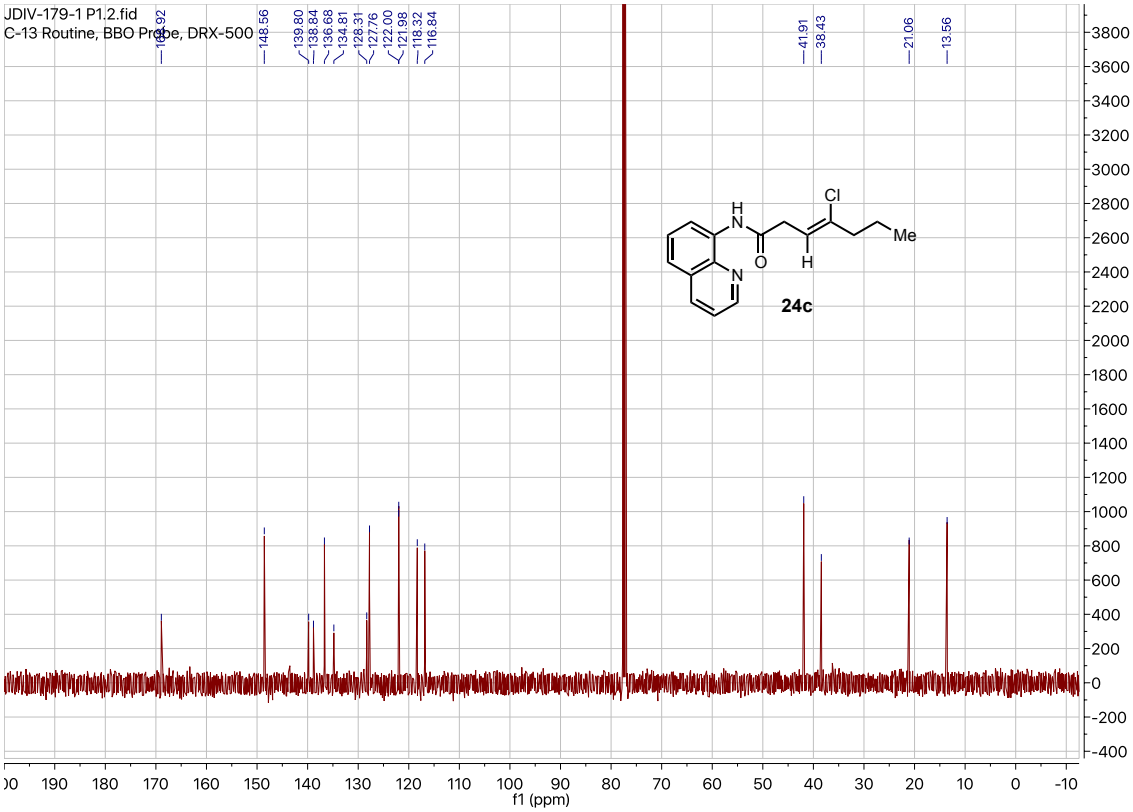

HCl-AQ-01 2.1.fid
H-1 Routine, DRX-500, BBO Probe
10.00
8.30
8.29
8.26
8.25
8.16
8.14
7.55
7.53
7.52
7.51
7.50
7.46
7.45
7.44
7.44
5.94
5.92
5.91
3.50
3.49
2.52
2.51
2.49
2.48
1.26
1.25
1.23
0.86
2.02
1.02
3.14
1.00
2.06
2.06
3.38
f1 (ppm)
Cl
Me
H
N
O
H
N
24a

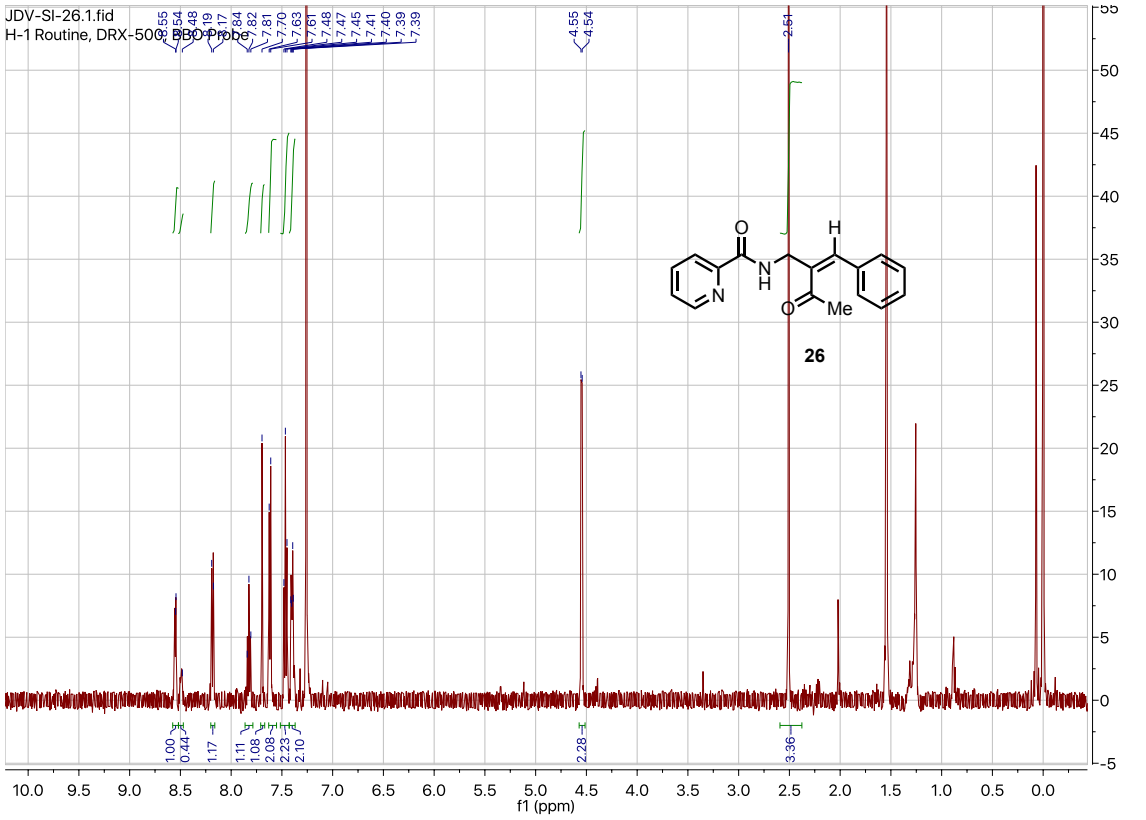

JDIV-179-1 P1.2.fid
C-13 Routine, BBO Probe, DRX-500
169.92
148.56
139.80
136.84
136.68
134.81
128.31
127.76
122.00
121.98
118.32
116.84
41.91
38.43
21.06
13.56
f1 (ppm)
Cl
Me
H
N
O
H
N
24a

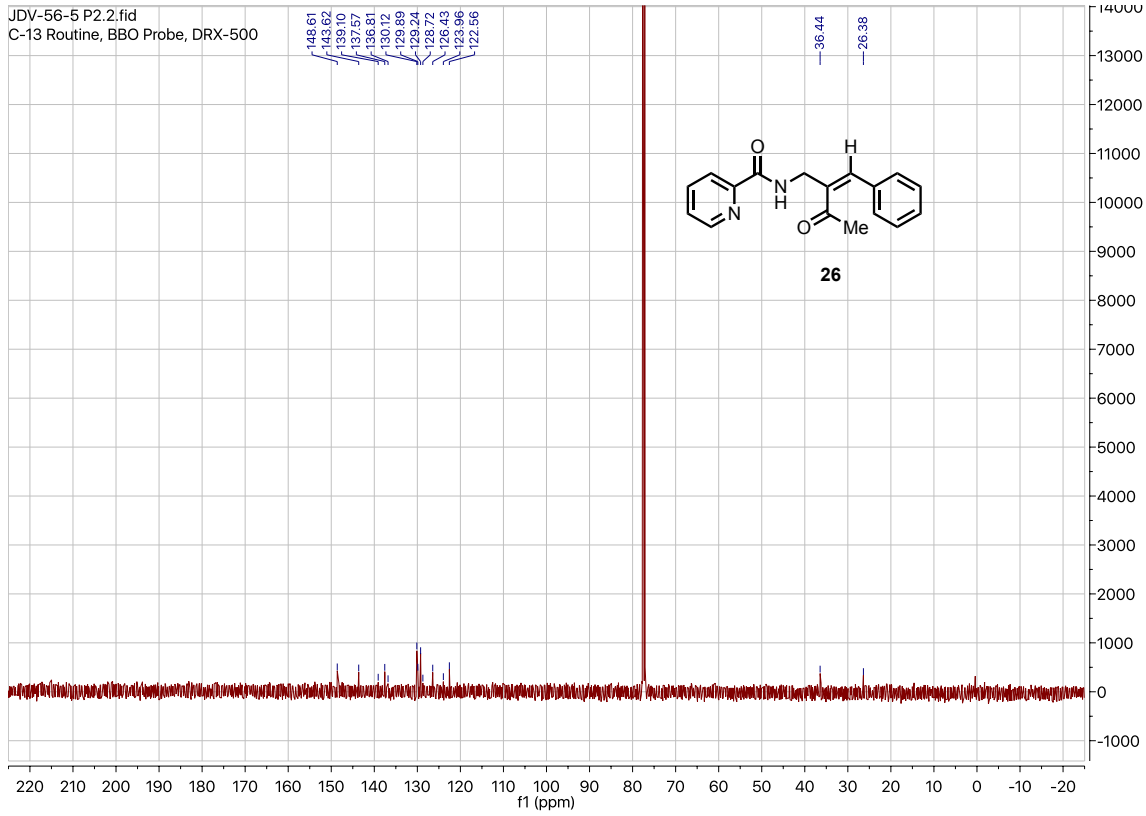

JDIV-178-1 P1.1.fid
H-1 Routine, DRX-500, BBO Probe
9.99
9.81
9.80
9.75
7.74
8.17
8.16
8.15
7.53
7.52
7.51
7.51
7.46
7.46
7.45
7.44
5.91
5.91
3.49
3.49
3.49
3.48
3.48
3.47
2.24
0.89
1.04
0.94
1.01
1.90
1.02
0.95
2.02
3.00
Cl
Me
H
N
O
H
N
24b
f1 (ppm)

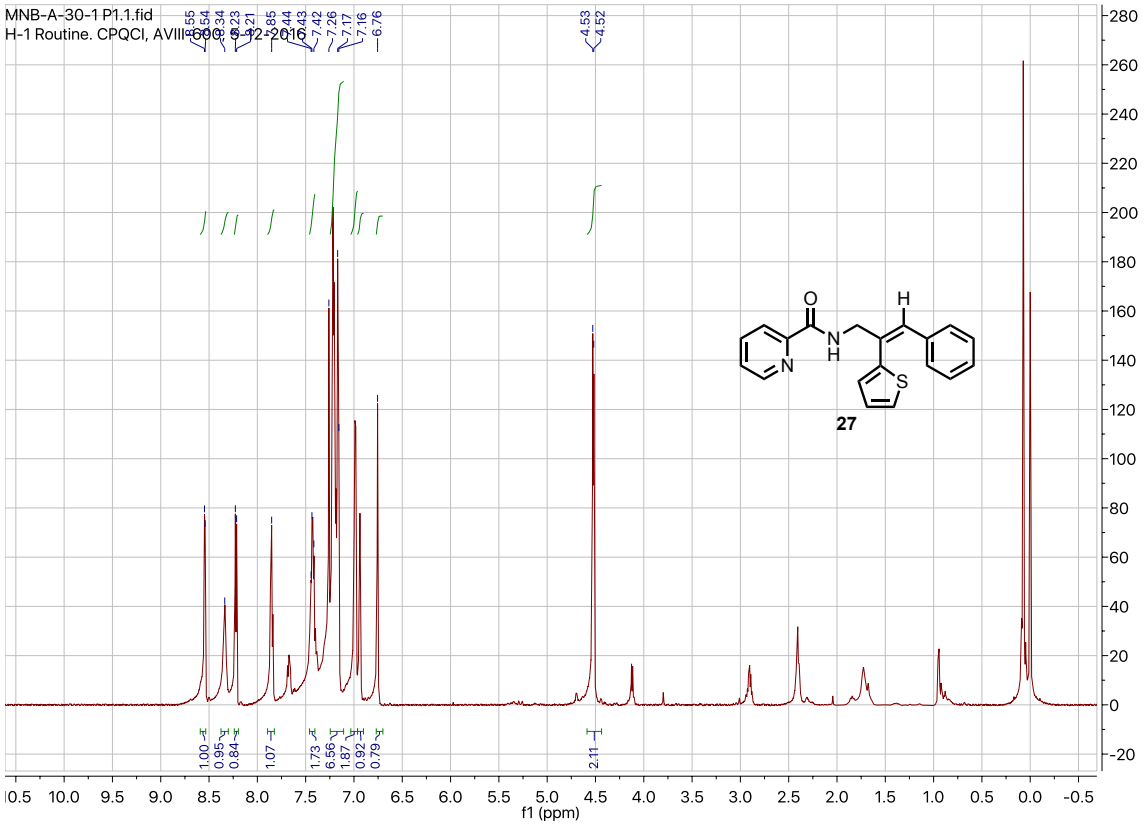

JDIV-178-1 P1.2.fid
C-13 Routine, BBO Probe, DRX-500
169.88
149.65
138.82
136.71
134.89
134.79
128.32
127.77
122.01
118.83
116.84
38.50
26.67
Cl
Me
H
N
O
H
N
24b
f1 (ppm)

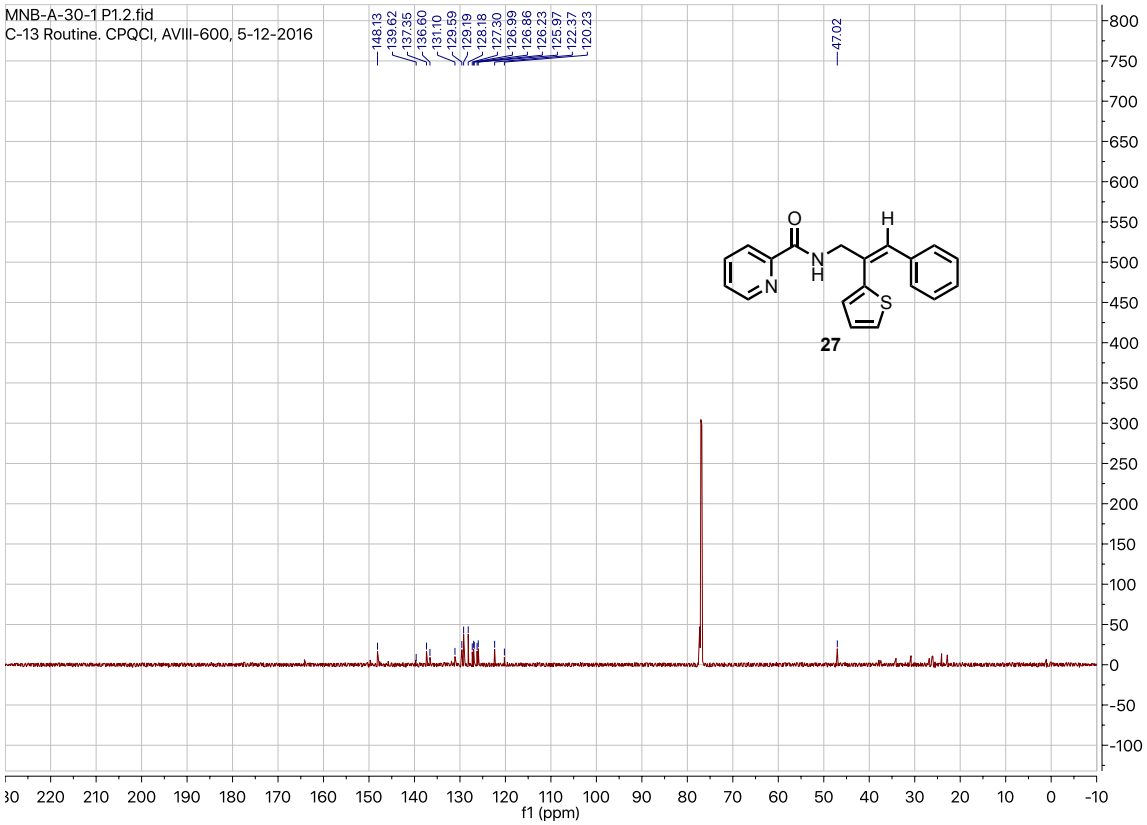

JDIV-179-1 P1.1.fid
H-1 Routine, DRX-500, BBO Probe
10.01
8.18
8.16
8.14
7.54
7.53
7.51
7.51
7.49
7.46
7.45
7.44
7.43
5.93
5.91
5.90
3.51
3.49
2.46
2.46
2.44
2.44
2.43
2.43
1.72
1.70
1.69
1.67
1.66
1.66
1.00
0.98
0.97
0.81
2.17
1.20
2.10
1.20
1.00
2.03
2.26
3.13
3.13
f1 (ppm)
Cl
H
N
O
H
Me
N
24c

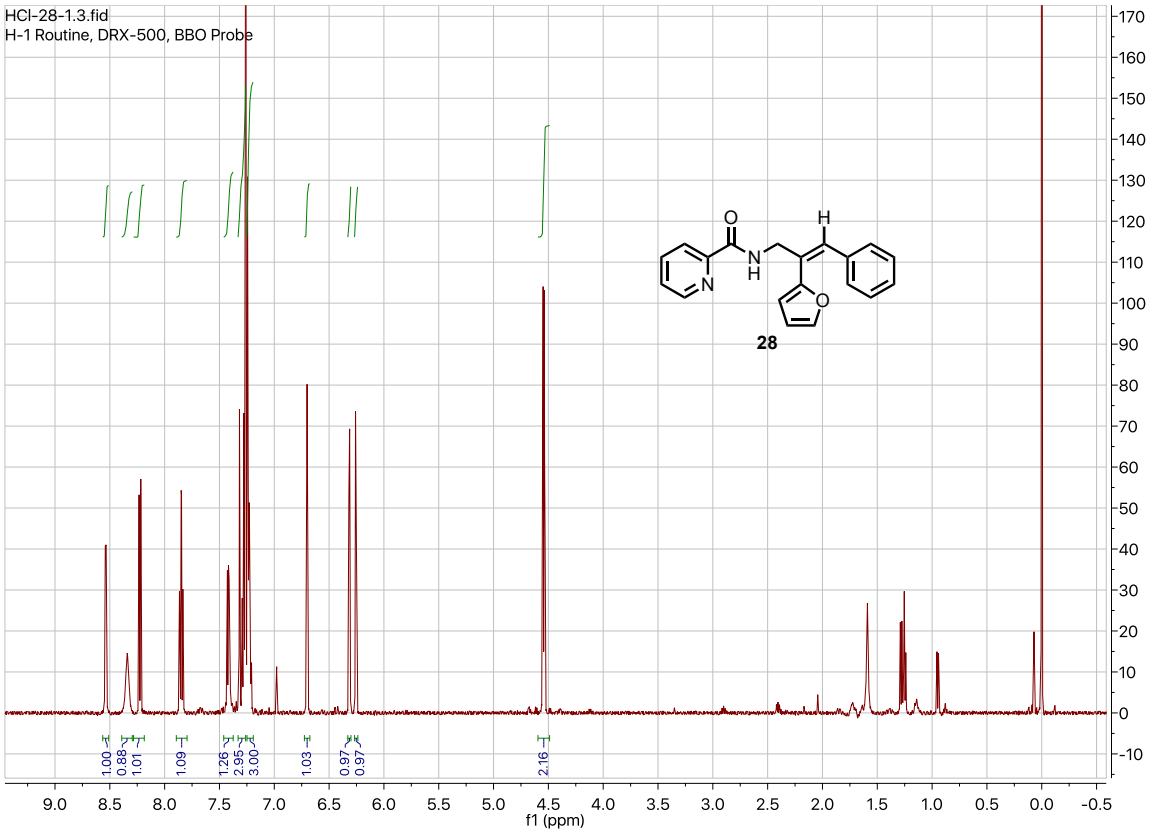

JDIV-179-1 P1.2.fid
C-13 Routine, BBO Probe, DRX-500
169.92
148.56
139.80
138.84
136.68
134.81
128.31
127.76
122.00
121.98
118.32
116.84
41.91
38.43
21.06
13.56
f1 (ppm)
Cl
H
N
O
H
Me
N
24c

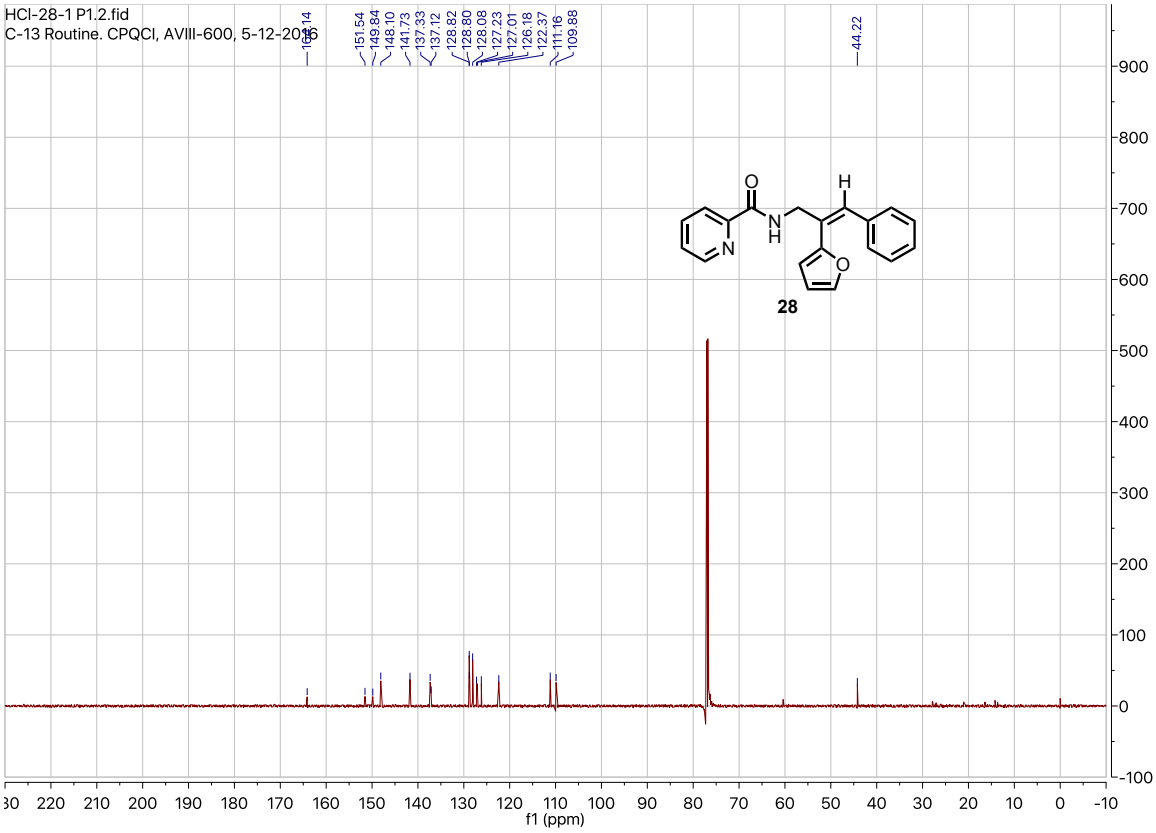

JDV-SI-26.1.fid
H-1 Routine, DRX-500, BBO Probe
8.55
8.54
8.48
8.19
8.17
7.84
7.82
7.81
7.70
7.63
7.61
7.48
7.47
7.45
7.41
7.40
7.39
7.39
4.55
4.54
2.61
1.00
0.44
1.17
1.11
1.08
2.08
2.23
2.10
2.28
3.36
O
H
N
N
H
O
Me
26
f1 (ppm)

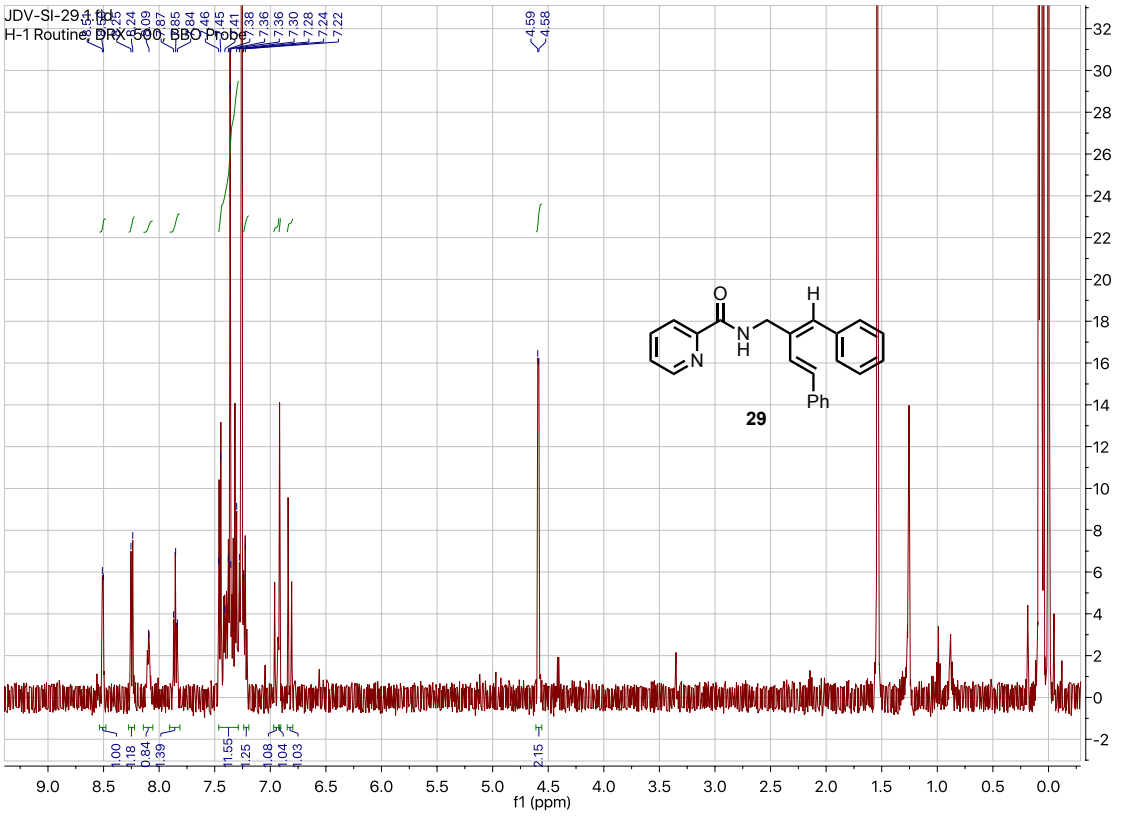

JDV-56-5 P2.2.fid
C-13 Routine, BBO Probe, DRX-500
148.61
143.62
139.10
137.57
136.81
130.12
129.89
129.24
128.72
126.43
123.96
122.56
36.44
26.38
O
H
N
N
H
O
Me
26
f1 (ppm)

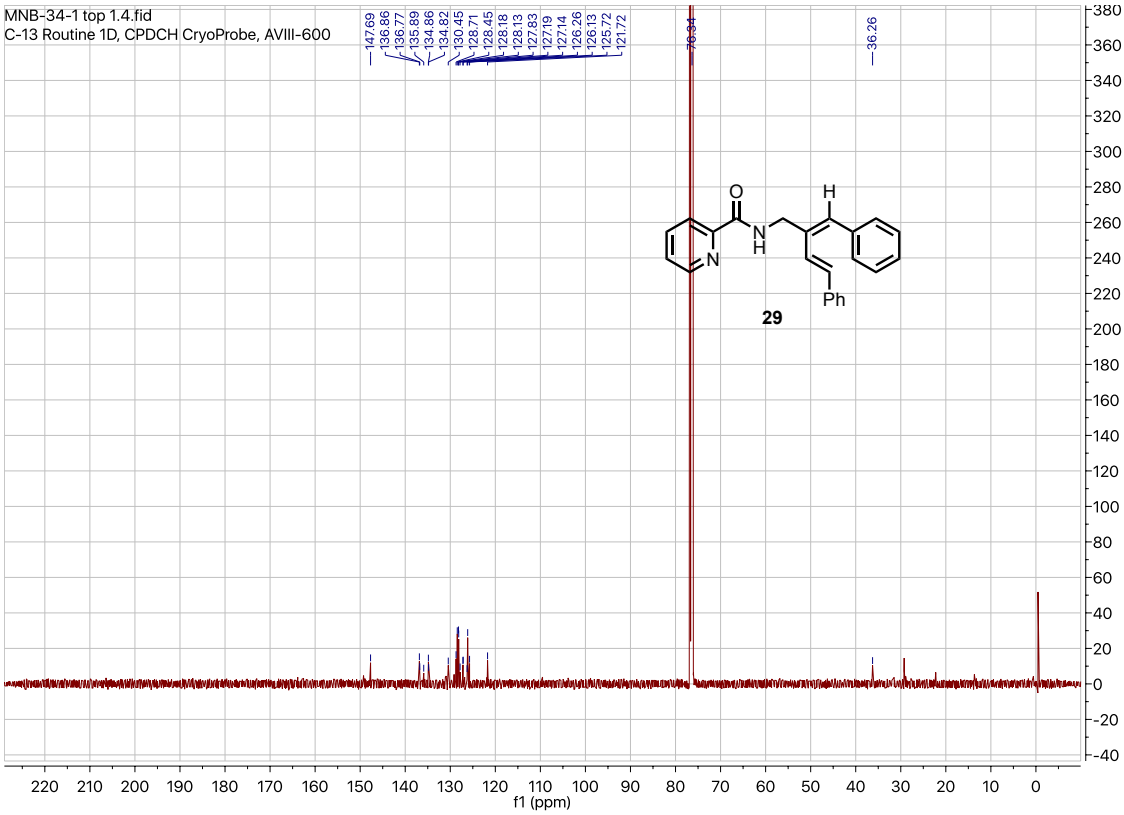

MNB-A-30-1 P1.1.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
8.55
8.54
8.34
8.23
8.21
7.85
7.44
7.43
7.42
7.26
7.17
7.16
6.76
4.53
4.52
1.00
0.95
0.84
1.07
1.73
6.56
1.87
0.92
0.79
2.11
f1 (ppm)
O
H
N
H
N
S
27

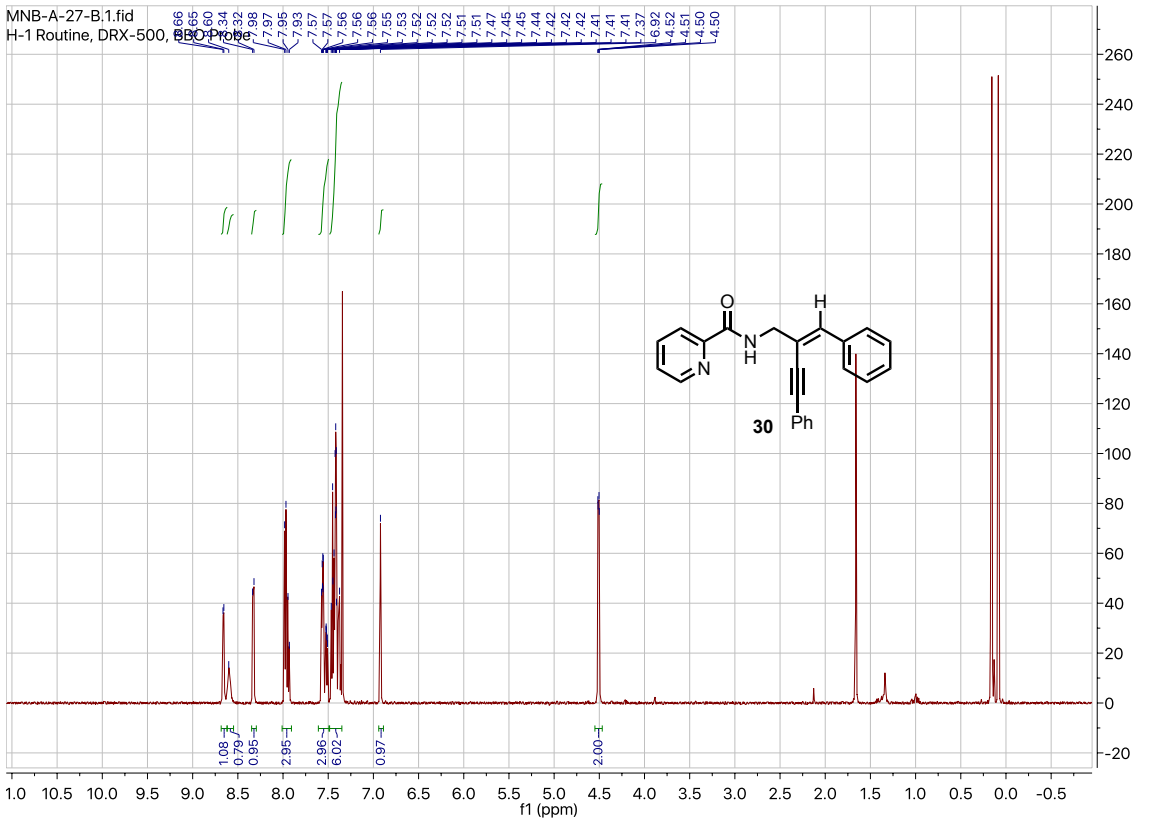

MNB-A-30-1 P1.2.fid
C-13 Routine. CPQCI, AVIII-600, 5-12-2016
148.13
139.62
137.35
136.60
131.10
129.59
129.19
128.18
127.30
126.99
126.86
126.23
125.97
122.37
120.23
47.02
f1 (ppm)
O
H
N
H
N
S
27

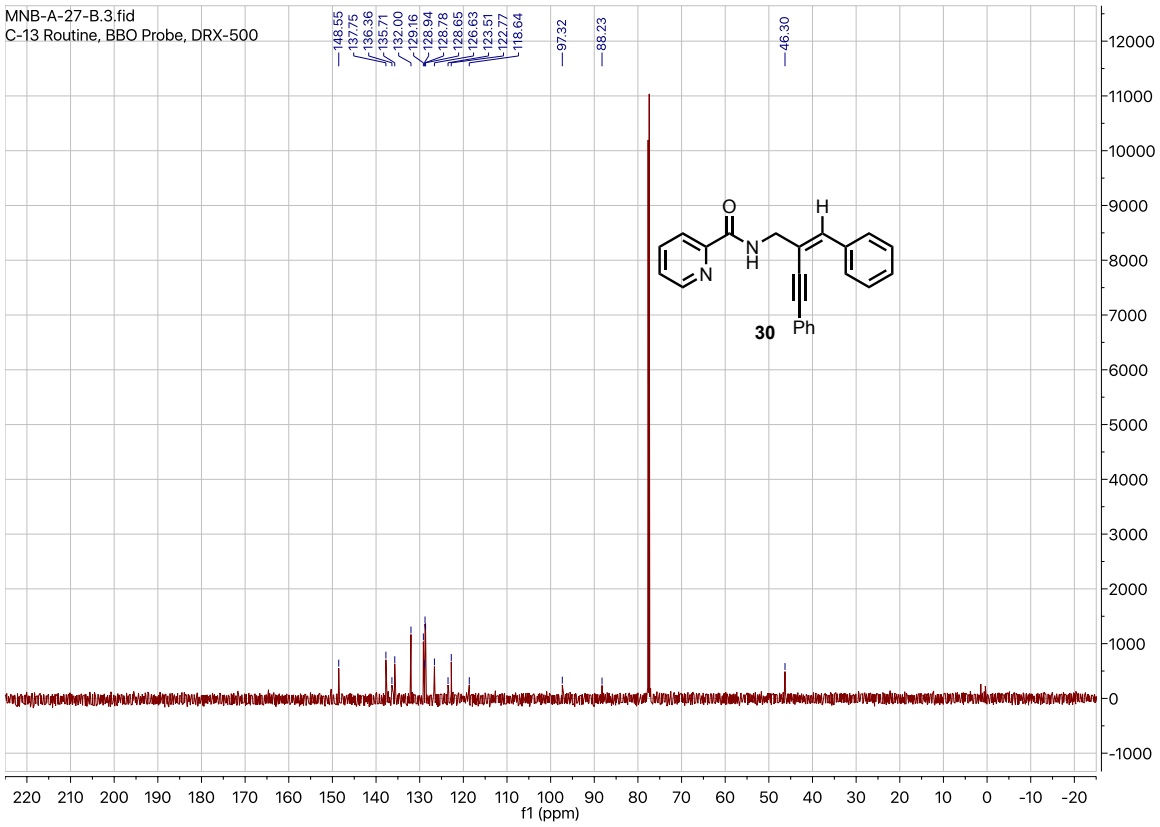

HCl-28-1.3.fid
H-1 Routine, DRX-500, BBO Probe
28
1.00
0.88
1.01
1.09
1.26
2.95
3.00
1.03
0.97
0.97
2.16
f1 (ppm)

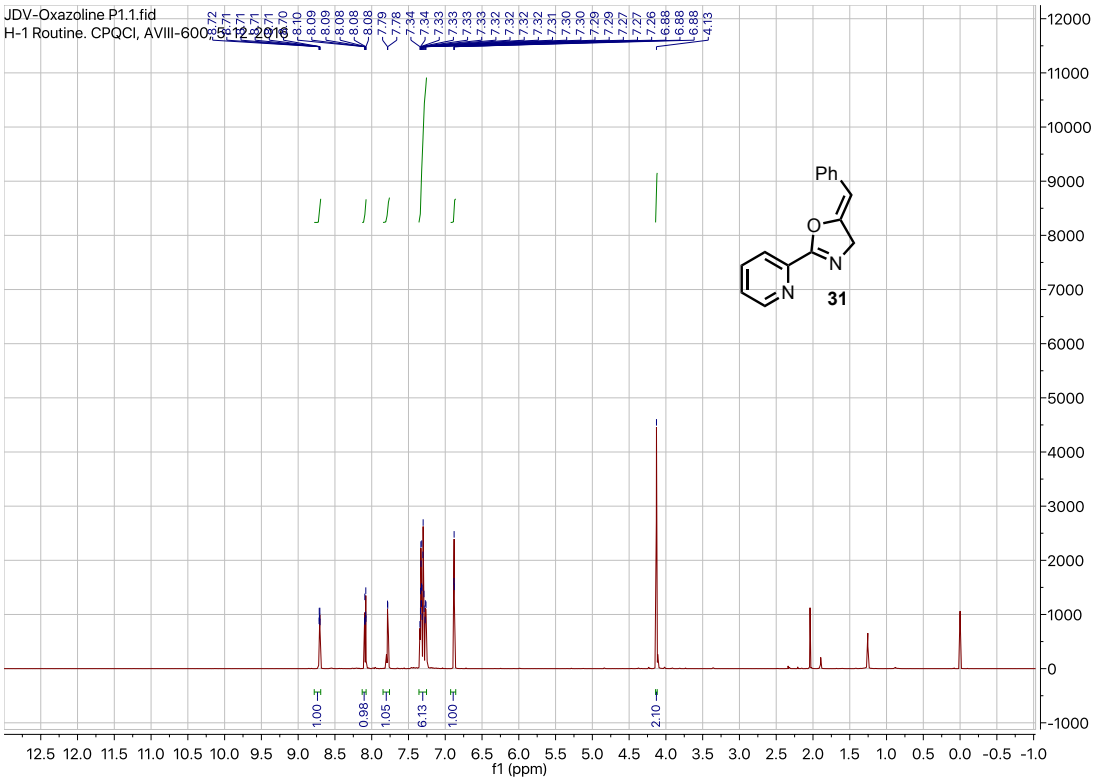

HCl-28-1 P1.2.fid
C-13 Routine. CPQCI, AVIII-600, 5-12-2016
166.14
151.54
149.84
148.10
141.73
137.33
137.12
128.82
128.80
128.08
127.23
127.01
126.18
122.37
111.16
109.88
44.22
28
f1 (ppm)

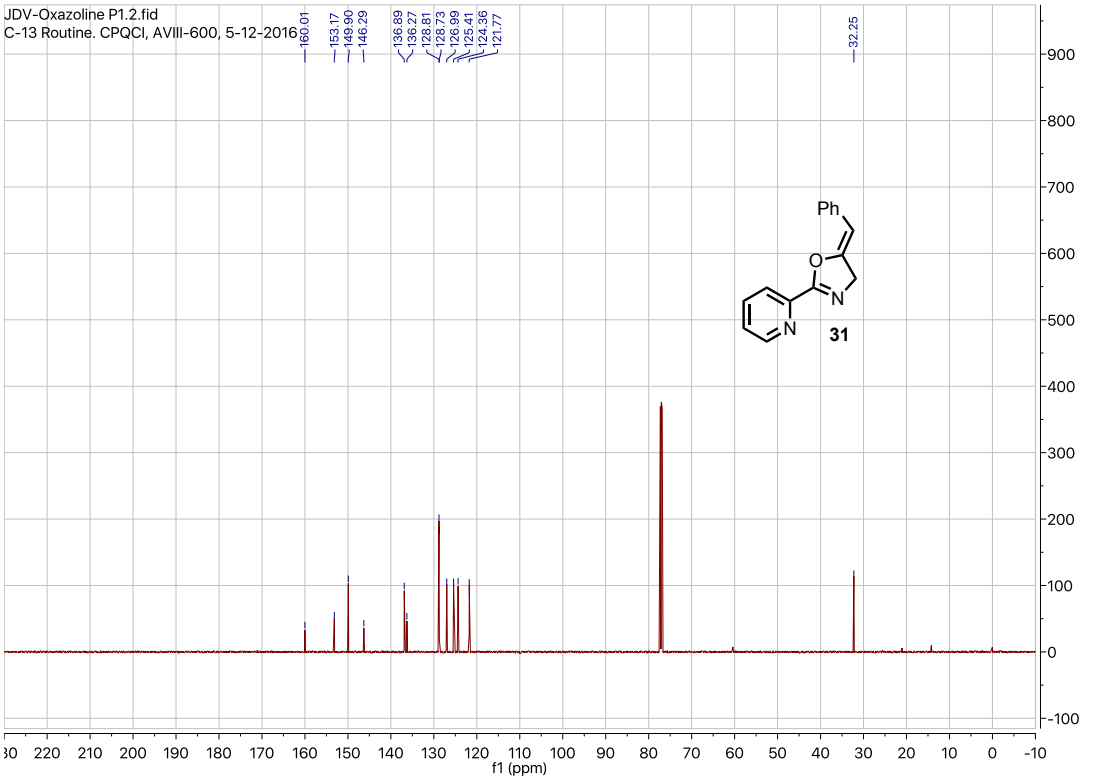

JDV-SI-29-1.fid
H-1 Routine, DRX-500, BBO Probe
f1 (ppm)
29

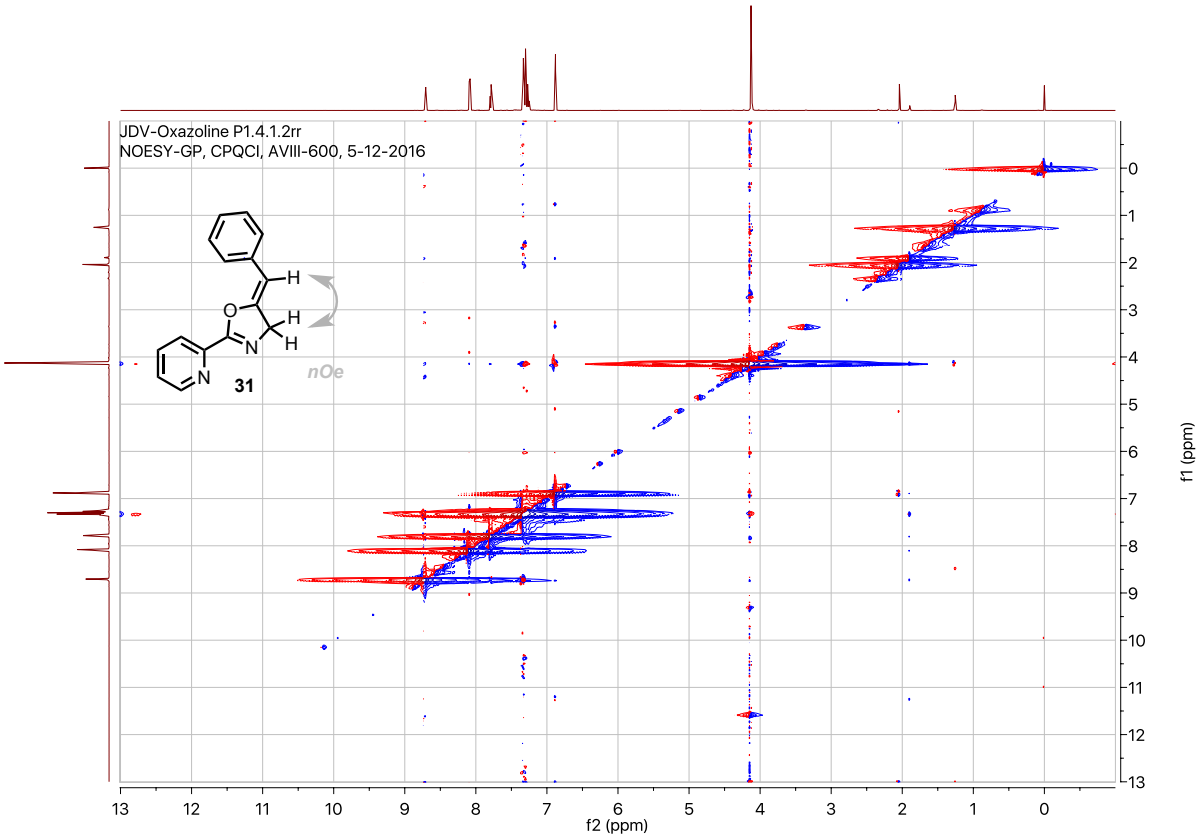

MNB-34-1 top 1.4.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
f1 (ppm)
29


MNB-A-27-B.1.fid
H-1 Routine, DRX-500, BBO Probe
30
Ph
f1 (ppm)


MNB-A-27-B.3.fid
C-13 Routine, BBO Probe, DRX-500
30
Ph
f1 (ppm)


JDV-Oxazoline P1.1.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
Ph
O
N
N
31
1.00
0.98
1.05
6.13
1.00
2.10
f1 (ppm)


JDV-Oxazoline P1.2.fid
C-13 Routine. CPQCI, AVIII-600, 5-12-2016
160.01
153.17
149.90
146.29
136.89
136.27
128.81
128.73
126.99
125.41
124.36
121.77
32.25
Ph
O
N
N
31
f1 (ppm)


JDV-Oxazoline P1.4.1.2rr
NOESY-GP, CPQCI, AVIII-600, 5-12-2016
H
H
H
O
N
N
31
nOe
f2 (ppm)
f1 (ppm)