Supporting Information for:

Directed β C-H Amination of Alcohols via Radical Relay Chaperones

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I. General Information

All chemicals and reagents were purchased from Sigma-Aldrich, Alfa Aesar, Acros, TCI, or ChemImplex. Sodium iodide was dried under high vacuum before use. Acetonitrile and triethylamine were distilled over calcium hydride before use. CH_2Cl_2, THF, and DMF were dried and degassed with nitrogen using an Innovative Technology solvent system. Silicycle F60 (230-400 mesh) silica gel was used or a CombiFlash® Automated Flash Chromatograph for flash column chromatography. Thin layer chromatography (TLC) analyses were performed using Merck silica gel 60 F254 plates and visualized under UV (254 nm), $KMnO_4$, or iodine stain. Melting points were determined using an Electrotherman IA9000. ^{1}H, ^{19}F, ^{13}C NMR spectra were recorded using a Bruker AVIII 400 or AVIII 600 MHz NMR spectrometer. ^{1}H NMR and ^{13}C NMR chemical shifts are reported in parts per million and referenced with respect to $CDCl_3$ (^{1}H: residual $CHCl_3$ at δ 7.26, ^{13}C: $CDCl_3$ triplet at δ 77.16). ^{1}H NMR data are reported as chemical shifts (δ ppm), multiplicity (s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet, app t = apparent triplet, app q = apparent quartet, app qd = apparent quartet of doublets), coupling constant (Hz), relative integral. ^{19}F NMR data are reported as chemical shifts (δ ppm). High resolution mass spectra were obtained using Bruker MicrOTOF (ESI). IR spectra were recorded using a Thermo Fisher Nicolet iS10 FT-IR and are reported in terms of frequency of absorption (cm^{-1}).

II. General Procedure:

Trichloroacetimidate Formation; General Procedure (GP1): To a round-bottom flask containing a stir bar, alcohol (1 equiv.), and CH_2Cl_2 (0.1 M) was added trichloroacetonitrile (1.5 equiv.) and DBU (0.1 equiv.). The solution was stirred and monitored by TLC until consumption of alcohol. Upon completion, the solution was concentrated and directly loaded onto silica gel and purified (hexanes with 1% Et_3N to avoid imidate hydrolysis).

Benzimidate Formation; General Procedure (GP2): To a 50 mL round bottom flask was added benzonitrile (1 equiv.), alcohol (12 equiv.), and a stir bar. The solution was cooled to 0 °C, an addition funnel containing acetyl chloride (8 equiv.) was attached, and the apparatus was sealed. The acetyl chloride was added dropwise over a half an hour and then the solution was allowed to warm to room temperature. The reaction was stirred at room temperature for the required amount of time and then evaporated under reduced pressure to yield the imidate-HCl salt. *Free base protocol.* The salt was suspended in Et_2O and a saturated solution of $NaHCO_3$ was added dropwise until the salt dissolved completely. Upon dissolution, the solution was stirred for five minutes and then diluted with H_2O. The organic phase was separated and the aqueous phase was extracted with Et_2O (2 x 10 mL). The combined organic phase was dried over $MgSO_4$ and concentrated.

Transimidation: General Procedure (GP3): To a 2-dram vial equipped with a stir bar was added the trifluoroethyl benzimidate hydrochloride (1 equiv.), the desired alcohol, and MeCN (0.2 M). The reaction was heated to 50 °C and stirred until consumption of starting imidate (monitored by crude ^1H NMR). Upon completion, the solution was concentrated and the resulting crude solid was suspended in dry Et_2O and subjected to the *free base protocol* from **GP2**. The crude reaction mixture was loaded onto silica gel and purified (required eluent with 1% Et_3N).

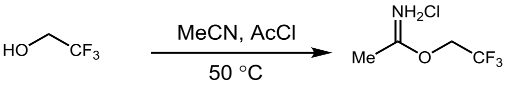
*Note: Transimidation is time sensitive. Long reaction times lead to hydrolysis of the target material to yield the corresponding amide.

C-H Amination; General Procedure (GP4): To a 2-dram vial equipped with PTFE septa cap and magnetic stir bar was added imidate (0.4 mmol), iodobenzene diacetate (1.2 mmol), and NaI (1.2 mmol). This vial was evacuated and backfilled with N_2 (3x). Dry acetonitrile (4 mL) was degassed using a freeze-pump-thaw technique (3x), then added to the vial under N_2. The reaction was irradiated with two 23 W compact fluorescent light bulbs for 2 hours and monitored using TLC. *Hydrolysis and acid/base extraction.* Upon completion, the mixture was concentrated in a round-bottom flask, then methanol (4 mL) and 2M HCl (0.8 mL) was added. After stirring for 2 hours, 25 mL of $CHCl_3$ and 10 mL of H_2O was added. The aqueous layer was washed with $CHCl_3$ (5 x 25 mL). The combined organic fractions were rewashed with H_2O (10 mL). The combined aqueous layer was poured into a round bottom, diluted with $CHCl_3$ (25 mL), and finally 6M NaOH (10 mL) was added and stirred for 30 minutes. The aqueous layer was washed with $CHCl_3$ (5 x 25 mL) and the combined organic solution was dried over $MgSO_4$ and concentrated.

*Note: Sodium iodide must be sufficiently dry to ensure optimum yields in the reaction. Typically, the material was left under high vacuum for at least 24 hours before use.

*Note: If $PhI(OAc)_2$ is wet, $NaHCO_3$ or K_2HPO_4 (2 equiv.) can be added to remove any excess AcOH, which is detrimental to the reaction.

III. Substrate Synthesis



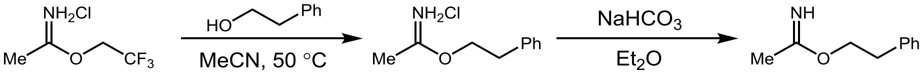
2,2,2-trifluoroethyl acetimidate hydrochloride (S1)

Acetonitrile (0.40 g, 0.5 mL, 9.6 mmol) and trifluoroethanol (7.7 g, 5.54 mL, 77.0 mmol) were combined in a pressure tube. Acetyl chloride (4.53 g, 4.11 mL, 57.7 mmol) was added in one portion and the tube was immediately sealed. During the initial exotherm, the reaction was stirred at room temperature. Once complete, the reaction was warmed to 50 °C and stirred for 48 hours. After 48 hours, the tube was cooled to room temperature and carefully depressurized. (Warning: Excess HCl gas will be released during this process.) The resulting solution was concentrated to yield the hydrogen chloride salt **S1** (0.8 g, 47%) as a white solid.

^{1}H NMR (600 MHz, $(CD_3)_2SO$): δ = 12.41 (bs, 2H), 5.24 (q, $^3J_{HF}$ = 8.5 Hz, 2H), 2.49 (s, 3H).

^{13}C NMR (150 MHz, $(CD_3)_2SO$): δ = 177.4, 122.4 (q, $^1J_{CF}$ = 277.0), 67.1 (m), 18.4 (q, $^5J_{CF}$ = 12.8 Hz).

^{19}F NMR (367 MHz, $(CD_3)_2SO$): δ = – 72.5 (t, $^2J_{FH}$ = 8.4 Hz).



Phenethyl acetimidate (1)

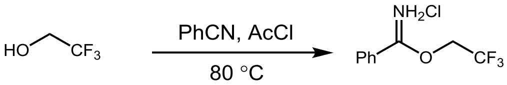
Following GP3, trifluoroethyl acetimidate hydrochloride **S1** (0.2 g, 0.3 mmol) was suspended in MeCN (4 mL) to which 2-phenylethanol (0.15 g, 0.15 mL, 0.3 mmol) was added. After completion and workup, the crude material was purified (silica gel, hexanes with 1% Et_3N) to yield imidate **1** (28 mg) as mixture with 2-phenyethanol and the hydrolyzed ester (1 : 0.18 : 0.16 TM:alcohol:ester).

R_f: 0.08 (20% Ethyl acetate/hexanes)

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.31 (t, J = 7.5 Hz, 2H), 7.27 – 7.22 (m, 3H), 6.90 (bs, 1H), 4.29 (t, J = 6.5 Hz, 2H), 3.00 (t, J = 7.1 Hz, 2H), 2.00 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.8, 138.7, 129.0, 128.5, 126.4, 66.1, 35.2.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{10}H_{14}NO$ $[M+H]^+$ 164.1075, found 164.1087.



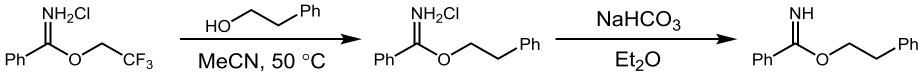
2,2,2-trifluoroethyl benzimidate hydrochloride (S2)

Benzonitrile (1 g, 1 mL, 9.7 mmol) and trifluoroethanol (11.65 g, 8.38 mL, 116 mmol) were combined in a pressure tube. Acetyl chloride (6.09 g, 5.54 mL, 77.6 mmol) was added in one portion and the tube was immediately sealed. During the initial exotherm, the reaction was stirred at room temperature. Once complete, the reaction was warmed to 80 °C and stirred for 48 hours. After 48 hours, the tube was cooled to room temperature and carefully depressurized. (Warning: Excess HCl gas will be released during this process.) The resulting solution was concentrated to yield a crude solid. The solid was washed with hexanes and cold acetonitrile then dried to yield hydrogen chloride salt **S2** (1.78 g, 77%) as a white solid.

^{1}H NMR (600 MHz, $(CD_3)_2SO$): δ = 10.98 (bs, 2H), 8.05 (d, *J* = 7.4 Hz, 2H), 7.75 (t, *J* = 7.4 Hz, 1H), 7.62 (d, *J* = 7.9 Hz, 2H), 5.25 (q, $^3J_{HF}$ = 8.6 Hz, 2H).

^{13}C NMR (150 MHz, $(CD_3)_2SO$): δ = 164.2, 134.1, 129.4, 129.0, 128.8, 123.5 (q, $^1J_{CF}$ = 277.5 Hz), 60.3 (q, $^2J_{CF}$ = 35.2 Hz).

^{19}F NMR (564 MHz, $(CD_3)_2SO$): δ = – 72.3 (t, $^3J_{FH}$ = 8.2 Hz).



Phenethyl benzimidate (2)

Following **GP3**, trifluoroethyl benzimidate hydrochloride **S2** (0.1 g, 0.4 mmol) was suspended in MeCN (2 mL) to which 2-phenylethanol (51 mg, 50 µL, 0.4 mmol) was added. After completion and workup, the crude material was purified (silica gel, hexanes with 1% Et_3N) to yield imidate **2** (46 mg, 49%) as a clear oil.

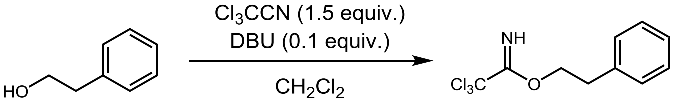
R_f: 0.12 (10% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 – 7.63 (m, 2H), 7.42 – 7.32 (m, 3H), 7.29 – 7.25 (m, 3H), 7.20 – 7.17 (m, 1H), 4.46 (t, *J* = 6.9 Hz, 2H), 3.08 (t, *J* = 6.8 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.9, 138.7, 132.9, 131.0, 129.1, 128.6 (2C), 126.8, 126.5, 66.7, 35.3.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{15}H_{16}NO$ $[M+H]^+$ 226.1232, found 226.1229.

IR (film) cm^{-1}: 3303, 3034, 3024, 2943, 2884, 1631, 1577.



Phenethyl 2,2,2-trichloroacetimidate (3)

Following GP1, phenylethanol (2 g, 1.96 mL, 16.4 mmol) was dissolved in CH_2Cl_2 (50 mL) to which trichloroacetonitrile (3.54 g, 2.46 mL, 24.5 mmol) and 1,8-Diazabicyclo(5.4.0)undec-7-ene (0.26 g, 0.25 mL, 1.7 mmol) were added. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified (hexanes, 1% Et_3N) to yield imidate **3** (4.4 g, 100%) as a white solid.

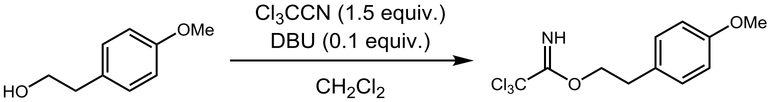
R$_f$: 0.63 (20% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.29 (bs, 1H), 7.33 – 7.22 (m, 5H), 4.50 (t, *J* = 6.9 Hz, 2H), 3.10 (t, *J* = 6.9 Hz, 2H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 163.0, 137.8, 129.2, 128.6, 126.7, 91.6, 70.0, 34.8.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{10}H_{10}Cl_3NONa$ $[M+Na]^+$ 287.9726, found 287.9708.

IR (film) cm^{-1}: 3337, 3025, 2948, 1660, 1602.



4-methoxyphenethyl 2,2,2-trichloroacetimidate (S8)

Following GP1, 4-methoxyphenethyl alcohol (0.1 g, 0.7 mmol) was dissolved in CH_2Cl_2 (10 mL) to which trichloroacetonitrile (0.14 g, 0.1 mL, 0.1 mmol) and 1,8-Diazabicyclo(5.4.0)undec-7-ene (0.01 g, 0.01 mL, 0.07 mmol) were added. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified (hexanes, 1% Et_3N) to yield imidate **S8** (0.18 g, 92%) as a white solid.

R$_f$: 0.25 (10% Ethyl acetate/hexanes)

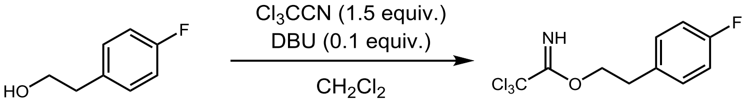
^{1}H NMR (600 MHz, CDCl$_3$): δ = 8.29 (bs, 1H), 7.19 (d, *J* = 7.9 Hz, 2H), 6.84 (d, *J* = 7.3 Hz, 2H), 4.45 (t, *J* = 7.0 Hz, 2H), 3.79 (s, 3H), 3.03 (t, *J* = 6.9 Hz, 2H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 162.9, 158.5, 130.2, 129.8, 114.0, 91.6, 70.2, 55.3, 33.9.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{11}H_{12}Cl_3NONa$ $[M+Na]^+$ 317.9831, found 317.9814.

IR (film) cm^{-1}: 3324, 2936, 2936, 2838, 1658, 1668, 1582.

MP: 54 – 56 °C



4-fluorophenethyl 2,2,2-trichloroacetimidate (S9)

Following GP1, 4-methoxyphenethyl alcohol (0.2 g, 1.4 mmol) was dissolved in CH_2Cl_2 (10 mL) to which trichloroacetonitrile (0.3 g, 0.21 mL, 2.1 mmol) and 1,8-Diazabicyclo(5.4.0)undec-7-ene (0.022 g, 0.022 mL, 0.15 mmol) were added. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified (hexanes, 1% Et_3N) to yield imidate **S9** (0.38 g, 94%) as a colorless oil.

R_f: 0.42 (10% Ethyl acetate/hexanes)

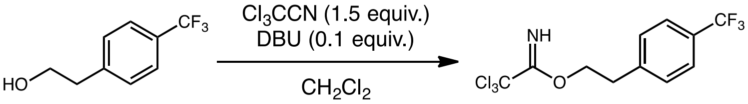
^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.28 (bs, 1H), 7.25 – 7.22 (m, 2H), 7.00 – 6.97 (m, 2H), 4.47 (t, J = 6.6 Hz, 2H), 3.06 (t, J = 6.8 Hz, 2H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 162.9, 161.9 (d, $^1J_{CF}$ = 244.4 Hz), 133.5 (d, $^4J_{CF}$ = 3.2 Hz), 130.7 (d, $^3J_{CF}$ = 7.7 Hz), 115.4 (d, $^2J_{CF}$ = 21.0 Hz), 91.5, 69.9, 34.1.

^{19}F NMR (564 MHz, $CDCl_3$): δ = – 116.57.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{10}H_{10}Cl_3FNO$ $[M+H]^+$ 283.9812, found 283.9817.

IR (film) cm^{-1}: 3651, 3339, 2968, 2881, 1662, 1509, 1304.



4-(trifluoromethyl)phenethyl 2,2,2-trichloroacetimidate (S10)

Following GP1, 2-(4-(trifluoromethyl)phenyl)ethanol (400 mg, 2.1 mmol) was dissolved in CH_2Cl_2 (5 mL) to which trichloroacetonitrile (462 mg, 0.32 mL, 3.2 mmol) and 1,8-Diazabicyclo(5.4.0)undec-7-ene (0.032 g, 31 uL, 0.21 mmol) were added. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified (hexanes, 1% Et_3N) to yield imidate **S10** (660 mg, 93%) as a colorless oil.

R_f: 0.45 (20% Ethyl acetate/hexanes)

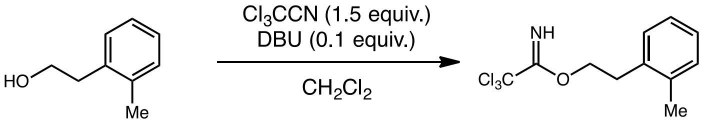
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.32 (bs, 1H), 7.56 (d, J = 8.2 Hz, 2H), 7.40 (t, J = 9.0 Hz, 2H), 4.52 (t, J = 6.5 Hz, 2H), 3.15 (t, J = 6.8 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.8, 142.0, 129.2 (q, $^2J_{CF}$ = 32.4 Hz), 125.5 (q, $^3J_{CF}$ = 3.7 Hz), 124.4 (q, $^1J_{CF}$ = 271.9 Hz), 91.4, 69.3, 34.7.

^{19}F NMR (376MHz, $CDCl_3$): δ = – 62.4.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{11}H_9Cl_3F_3N_2ONa$ $[M+Na]^+$ 355.9600, found 355.9582.

IR (neat) cm^{-1}: 3326, 2980, 2971, 1891, 2360, 2343, 1701, 1662, 1618, 1469, 1393, 1323, 1167, 1132, 1099, 1065, 1001, 942, 849, 802.



2-methylphenethyl 2,2,2-trichloroacetimidate (S11)

Following **GP1**, 2-(2-methylphenyl)ethanol (371 mg, 2.7 mmol) was dissolved in CH_2Cl_2 (5 mL) to which trichloroacetonitrile (0.592 g, 0.852 mL, 4.1 mmol) and 1,8-Diazabicyclo(5.4.0)undec-7-ene (0.042 g, 41 uL, 0.27 mmol) were added. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified (hexanes, 1% Et_3N) to yield imidate **S11** (0.621 g, 82%) as a colorless oil.

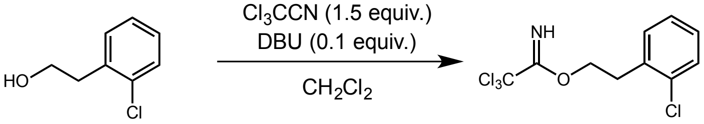
R$_f$: 0.65 (20% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.31 (bs, 1H), 7.25 – 7.15 (m, 4H), 4.49 (t, *J* = 7.2 Hz, 2H), 3.12 (t, *J* = 7.2 Hz, 2H), 2.40 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 163.0, 136.6, 135.8, 130.4, 129.8, 126.9, 126.2, 91.6, 62.2, 32.0, 19.6.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{11}H_{12}Cl_3NONa$ $[M+Na]^+$ 301.9882, found 301.9858.

IR (neat) cm^{-1}: 3339, 2928, 2867, 2360, 2343, 1764, 1659, 1465, 1383, 1303, 1074, 999, 864, 825, 794.



2-chlorophenethyl 2,2,2-trichloroacetimidate (S12)

Following **GP1**, 2-(2-chlorophenyl)ethanol (705 mg, 4.5 mmol) was dissolved in CH_2Cl_2 (5 mL) to which trichloroacetonitrile (0.98 g, 0.68 mL, 6.8 mmol) and 1,8-Diazabicyclo(5.4.0)undec-7-ene (0.069 g, 68 uL, 0.45 mmol) were added. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified (hexanes, 1% Et_3N) to yield imidate **S12** (1.2 g, 90%) as a colorless oil.

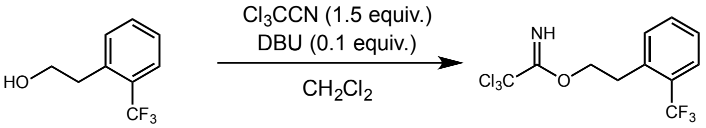
R$_f$: 0.64 (20% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.30 (bs, 1H), 7.38 – 7.16 (m, 4H), 4.53 (t, *J* = 7.0 Hz, 2H), 3.24 (t, *J* = 7.0 Hz, 2H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 162.9, 135.4, 134.3, 131.6, 129.6, 128.3, 126.9, 91.5, 68.3, 32.5.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{10}H_9Cl_4NONa$ [M+Na]$^+$ 321.9336, found 321.9319.

IR (neat) cm^{-1}: 3338, 2957, 2368, 1664, 1474, 1383, 1307, 1080, 1004, 794, 750, 655.



2-(trifluoromethyl)phenethyl 2,2,2-trichloroacetimidate (S13)

Following **GP1**, 2-(2-(trifluoromethyl)phenyl)ethanol (400 mg, 2.1 mmol) was dissolved in CH_2Cl_2 (5 mL) to which trichloroacetonitrile (0.455 g, 0.32 mL, 3.2 mmol) and 1,8-Diazabicyclo(5.4.0)undec-7-ene (0.032 g, 32 uL, 0.21 mmol) were added. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified (hexanes, 1% Et_3N) to yield imidate **S13** (0.267 g, 80%) as a colorless oil.

R$_f$: 0.62 (20% Ethyl acetate/hexanes)

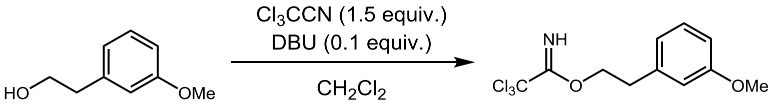
^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.33 (bs, 1H), 7.66 (d, *J* = 7.7 Hz, 1H), 7.49 – 7.48 (m, 2H), 7.37 – 7.31 (m, 1H), 4.52 (t, *J* = 6.3 Hz, 2H), 3.30 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 162.8, 136.3, 132.3, 131.8, 129.1 (q, $^2J_{CF}$ = 26.9 Hz), 126.2 (q, $^3J_{CF}$ = 5.7 Hz), 124.6 (q, $^1J_{CF}$ = 270.7 Hz), 91.5, 69.3, 31.6.

^{19}F NMR (376 MHz, CDCl$_3$): δ = – 59.5.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{11}H_9Cl_3F_3NONa$ [M+Na]$^+$ 333.9780, found 333.9756.

IR (neat) cm^{-1}: 3348, 2964, 2363, 1662, 1449, 1317, 1163, 1107, 1085, 997, 797, 775, 645.



3-methoxyphenethyl 2,2,2-trichloroacetimidate (S14)

Following **GP1**, 4-methoxyphenethyl alcohol (0.2 g, 1.3 mmol) was dissolved in CH_2Cl_2 (10 mL) to which trichloroacetonitrile (0.29 g, 0.2 mL, 2.0 mmol) and 1,8-Diazabicyclo(5.4.0)undec-7-ene (0.02 g, 0.02 mL, 0.13 mmol) were added. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified (hexanes, 1% Et_3N) to yield imidate **S14** (0.37 g, 95%) as a clear colorless oil.

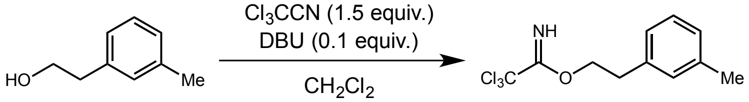
R$_f$: 0.36 (10% Ethyl acetate/hexanes)

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.29 (bs, 1H), 7.22 (t, *J* = 7.9 Hz, 1H), 6.87 (d, *J* = 7.6 Hz, 1H), 6.84 (t, *J* = 1.9 Hz, 1H), 6.78 (dd, *J* = 8.2, 2.6 Hz, 1H), 4.50 (t, *J* = 6.9 Hz, 2H), 3.80 (s, 3H), 3.07 (t, *J* = 6.9 Hz, 2H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 163.0, 159.9, 139.4, 129.6, 121.6, 114.9, 112.3, 91.6, 70.0, 55.3, 34.9.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{11}H_{12}Cl_3NO_2Na$ [M+Na]$^+$ 317.9831, found 317.9819.

IR (film) cm^{-1}: 3331, 2952, 2887, 2832, 1660, 1584.



3-methylphenethyl 2,2,2-trichloroacetimidate (S15)

Following GP1, 2-(3-methylphenyl)ethanol (613 mg, 4.5 mmol) was dissolved in CH_2Cl_2 (5 mL) to which trichloroacetonitrile (0.98 g, 0.68 mL, 6.8 mmol) and 1,8-Diazabicyclo(5.4.0)undec-7-ene (0.069 g, 68 uL, 0.45 mmol) were added. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified (hexanes, 1% Et_3N) to yield imidate **S15** (1.2 g, 95%) as a colorless oil.

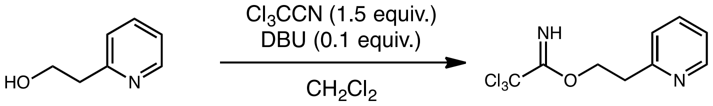
R$_f$: 0.61 (20% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28 (bs, 1H), 7.22 – 7.18 (m, 1H), 7.11 – 7.04 (m, 3H), 4.49 (t, *J* = 7.0 Hz, 2H), 3.06 (t, *J* = 7.0 Hz, 2H), 2.33 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.0, 138.2, 137.6, 130.1, 128.5, 127.5, 126.2, 91.6, 70.1, 34.7, 21.5.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{11}H_{12}Cl_3NONa$ [M+Na]$^+$ 301.9882, found 301.9918.

IR (neat) cm^{-1}: 3345, 2969, 2935, 2886, 1667, 1466, 1376, 1158, 1127, 956, 814.



2-(pyridin-2-yl)ethyl 2,2,2-trichloroacetimidate (S16)

Following GP1, 2-(2-pyridyl)ethanol (0.55 g, 0.51 mL, 4.5 mmol) was dissolved in CH_2Cl_2 (5 mL) to which trichloroacetonitrile (0.98 g, 0.68 mL, 6.8 mmol) and 1,8-Diazabicyclo(5.4.0)undec-7-ene (0.069 g, 68 uL, 0.45 mmol) were added. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified (Hexanes → 40% Ethyl acetate/hexanes) to yield imidate **S16** (1.16 g, 96%) as a yellow oil.

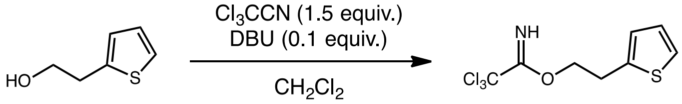
R_f: 0.59 (10% Isopropanol/CH_2Cl_2)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.55 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1H), 8.29 (bs, 1H), 7.61 (td, *J* = 7.7, 1,9 Hz, 2H), 7.25 (d, *J* = 7.7 Hz, 2H), 7.14 (ddd, *J* = 7.6, 4.9, 1.1 Hz, 1H), 4.66 (t, *J* = 6.6 Hz, 2H), 3.25 (t, *J* = 6.6 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.8, 158.0, 149.6, 136.4, 123.8, 121.8, 91.5, 68.7, 37.1.

HRMS (ESI-TOF) *m/z*: calc'd for $C_9H_9Cl_3N_2ONa$ $[M+Na]^+$ 288.9678, found 288.9657.

IR (neat) cm^{-1}: 3339, 2980, 2902, 2360, 2343, 1701, 1655, 1472, 1382, 1301, 1250, 1150, 1079, 1001, 962, 829, 794.



2-(thiophen-2-yl)ethyl 2,2,2-trichloroacetimidate (S17)

Following GP1, 2-(thiophen-2-yl)ethan-1-ol (577 mg, 1.6 mmol) was dissolved in CH_2Cl_2 (5 mL) to which trichloroacetonitrile (0.338 g, 0.23 mL, 2.3 mmol) and 1,8-Diazabicyclo(5.4.0)undec-7-ene (0.024 g, 24 uL, 0.45 mmol) were added. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified (hexanes, 1% Et_3N) to yield imidate **S17** (0.366 g, 86%) as a white solid.

R_f: 0.63 (20% Ethyl acetate/hexanes)

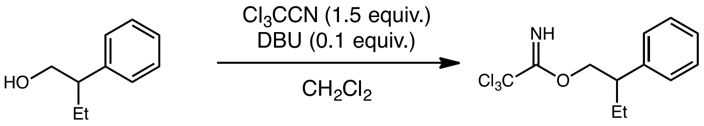
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.32 (bs, 1H), 7.17 (dd, *J* = 5.0, 1.3 Hz, 1H), 6.96 – 6.92 (m, 2H), 4.51 (t, *J* = 6.7 Hz, 2H), 3.31 (t, *J* = 6.7 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.9, 139.7, 127.0, 125.9, 124.2, 91.5, 69.6, 29.0.

HRMS (ESI-TOF) *m/z*: calc'd for $C_8H_8Cl_3NOSNa$ $[M+Na]^+$ 293.9290, found 293.9329.

IR (neat) cm⁻¹: 3323, 2980, 2892, 2360, 2342, 1661, 1470, 1443, 1393, 1308, 1277, 1243, 1090, 1065, 991, 822, 795.

MP: 35 – 36 °C



2-phenylbutyl 2,2,2-trichloroacetimidate (S18)

Following **GP1**, 2-phenylbutan-1-ol (676 mg, 4.5 mmol) was dissolved in CH_2Cl_2 (5 mL) to which trichloroacetonitrile (0.98 g, 0.68 mL, 6.8 mmol) and 1,8-Diazabicyclo(5.4.0)undec-7-ene (0.069 g, 68 uL, 0.45 mmol) were added. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified (hexanes, 1% Et_3N) to yield imidate **S18** (1.26 g, 95%) as a colorless oil.

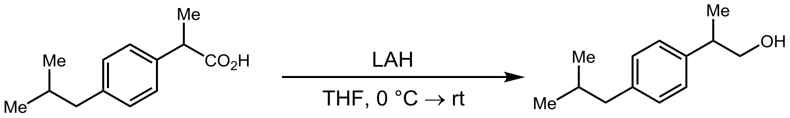
R$_f$: 0.67 (20% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.23 (bs, 1H), 7.33 – 7.20 (m, 5H), 4.45 – 4.36 (m, 2H), 3.03 – 2.96 (m, 1H), 1.99 – 1.88 (m, 1H), 1.78 – 1.67 (m, 1H), 0.88 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 163.1, 141.7, 128.5, 128.2, 126.8, 91.6, 73.2, 46.6, 25.3, 12.0.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{12}H_{14}Cl_3NONa$ $[M+Na]^+$ 316.0039, found 316.0043.

IR (neat) cm⁻¹: 3336, 2967, 2883, 2363, 2336, 1659, 1466, 1376, 1300, 1156, 1129, 951, 819.



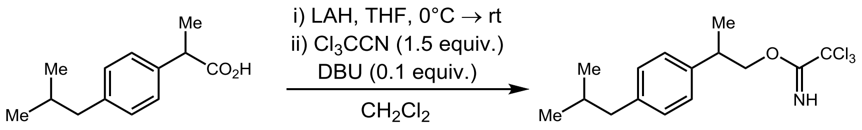
2-(4-isobutylphenyl)propan-1-ol

Lithium aluminum hydride (367 mg, 9.7 mmol) was suspended in dry THF (10 mL) in a 50 mL flask and then cooled to 0 °C. To this flask, was added alcohol (0.5 g, 2.4 mmol) dissolved in THF (10 mL) dropwise. After addition, the solution was warmed to room temperature and allowed to stir for 4 hours. Upon completion, the solution was quenched according to the Fieser workup reproduced here. After cooling the reaction to 0 °C, H_2O (0.37 mL) was added slowly, followed by 15% NaOH (0.37 mL), and finally H_2O (1.11 mL). This solution was warmed to room temperature and allowed to stir for 15 minutes. $MgSO_4$ was added and stirred for an additional 15 minutes. Finally, the solution was filtered and the mixture concentrated to yield the alcohol which was purified column chromatography (silica gel, 10% Ethyl acetate/hexanes) to yield the alcohol as a clear oil (0.48 g, quant.).

R$_f$: 0.24 (20% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.15 – 7.10 (m, 4H), 3.69 (d, *J* = 6.8 Hz, 2H), 2.96 – 2.90 (m, 1H), 2.46 (d, *J* = 7.0 Hz, 2H), 1.90 – 1.81 (m, 1H), 1.35 (bs, 1H), 1.27 (d, *J* = 7.2 Hz, 3H), 0.91 (d, *J* = 6.7 Hz, 6H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 140.9, 140.2, 129.5, 127.3, 68.9, 45.2, 42.2, 30.3, 22.6, 17.8.



2-(4-isobutylphenyl)propyl 2,2,2-trichloroacetimidate (S19)

Carboxylic acid (1 g, 6.4 mmol) was reduced according to the procedure above. After workup the crude material was carried forward without further purification. Crude alcohol was subjected to GP1. After workup and purification, trichloroacetimidate **S19** was isolated as a colorless oil (1.3 g, 80% over 2 steps).

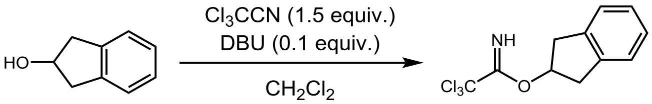
R$_f$: 0.48 (10% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.23 (bs, 1H), 7.19 – 7.17 (m, 2H), 7.09 – 7.07 (m, 2H), 4.39 (dd, *J* = 10.5, 6.1 Hz, 1H), 4.27 (dd, *J* = 10.5, 7.7 Hz, 1H), 3.25 (m, 1H), 2.44 (d, *J* = 7.2 Hz, 2H), 1.89 – 1.79 (m, 1H), 1.39 (d, *J* = 7.0 Hz, 3H), 0.89 (d, *J* = 6.7 Hz, 6H).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 163.1, 140.2, 140.1, 129.3, 127.3, 91.7, 74.6, 45.2, 38.5, 30.4, 22.5, 18.0.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{15}H_{20}Cl_3NONa$ [M+Na]$^+$ 358.0508, found 358.0482.

IR (film) cm^{-1}: 3340, 2952, 2941, 2866, 1662, 1299



4-fluorophenethyl 2,2,2-trichloroacetimidate (S20)

Following GP1, 4-methoxyphenethyl alcohol (0.25 g, 1.9 mmol) was dissolved in CH_2Cl_2 (10 mL) to which trichloroacetonitrile (0.4 g, 0.28 mL, 2.8 mmol) and 1,8-Diazabicyclo(5.4.0)undec-7-ene (0.029 g, 0.028 mL, 0.19 mmol) were added. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified (hexanes, 1% Et_3N) to yield imidate **S20** (0.44 g, 85%) as a colorless oil.

R$_f$: 0.35 (10% Ethyl acetate/hexanes)

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.34 (bs, 1H), 7.26 – 7.24 (m, 2H), 7.21 – 7.18 (m, 2H), 5.70 – 5.67 (m, 1H), 3.43 (dd, *J* = 17.0, 6.7 Hz, 2H), 3.19 (dd, *J* = 17.0, 3.4 Hz, 2H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 162.7, 140.4, 126.9, 124.8, 91.8, 80.1, 39.3.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{11}H_{11}Cl_3NO$ $[M+H]^+$ 277.9906, found 277.9888.

IR (film) cm^{-1}: 3640, 3336, 2978, 2895, 1655, 1302.

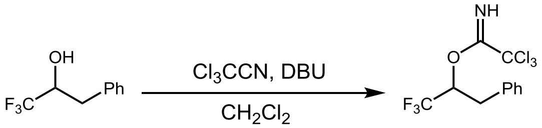
1,1,1-trifluoro-3-phenylpropan-2-ol

Alcohol was synthesized according to the literature.[1] To a solution of 2-phenylacetaldehyde (1.55 g, 1.5 mL, 12.9 mmol) in THF (15 mL) in a sealed round-bottom flask with a stir bar under N_2, was added (trifluoromethyl)trimethylsilane (2.38 g, 2.48 mL, 16.7 mmol) and the mixture was cooled to 0 °C. After 10 minutes, TBAF (1 M in THF, 0.13 mL, 0.13 mmol) was added dropwise and the reaction was stirred at 0 °C for ten minutes and then warmed to room temperature and allowed to stir for 6 hours. Upon completion, the TMS-ether was cleaved by cooling the reaction to 0 °C and adding water (1.27 mL, 56 mmol) and TBAF (1 M in THF, 1.3 mL, 1.3 mmol). The reaction was warmed to room temperature and stirred until completion, then transferred to a separatory funnel and partitioned between brine and Et_2O. The organic layer was isolated and the aqueous layer was washed with Et_2O (3 x 10 mL) and the combined layers were dried over $MgSO_4$, filtered, and concentrated. The crude material was purified (silica gel, 0.5% Ethyl acetate/hexanes) to yield the alcohol (0.92 g, 38%) as a yellow oil.

R_f: 0.23 (10% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 – 7.26 (m, 5H), 4.21 – 4.12 (m, 1H), 3.08 (dd, *J* = 14.2, 2.9 Hz, 1H), 2.86 (dd, *J* = 14.2, 10.1 Hz, 1H), 2.04 (d, *J* = 5.1 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.8, 129.6, 129.0, 127.4, 125.0 (q, $^1J_{CF}$ = 281.7 Hz), 71.6 (q, $^2J_{CF}$ = 30.7 Hz), 36.3 (q, $^3J_{CF}$ = 2.2 Hz).



1,1,1-trifluoro-3-phenylpropan-2-yl 2,2,2-trichloroacetimidate (S21)

Following GP1, 1,1,1-trifluoro-3-phenylpropan-2-ol (0.9 g, 4.7 mmol) was dissolved in CH_2Cl_2 (30 mL) to which trichloroacetonitrile (1.02 g, 0.71 mL, 7.1 mmol) and 1,8-Diazabicyclo(5.4.0)undec-7-ene (0.14 g, 0.14 mL, 0.93 mmol) were added. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified (hexanes, 1% Et_3N) to yield imidate **S21** (0.79 g, 50%) as a yellow oil.

R$_f$: 0.63 (10% Ethyl acetate/hexanes)

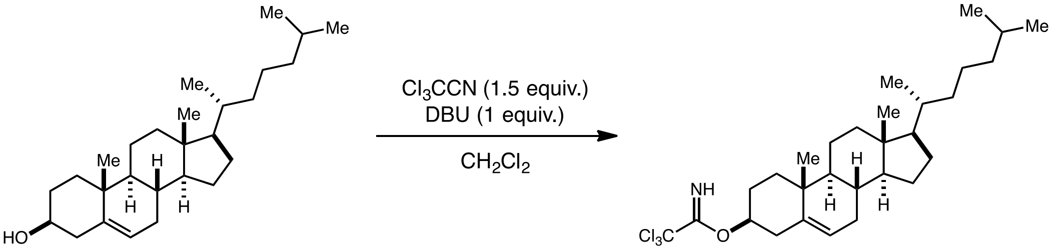
^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.49 (bs, 1H), 7.30 – 7.23 (m, 5H), 5.86 – 5.75 (m, 1H), 3.25 – 3.12 (m, 2H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 161.6, 134.5, 129.6, 128.7, 127.4, 123.7 (q, $^1J_{CF}$ = 282.1 Hz), 90.6, 74.7 (q, $^2J_{CF}$ = 31.8 Hz), 34.4 (q, $^3J_{CF}$ = 1.4 Hz).

^{19}F NMR (376 MHz, CDCl$_3$): δ = – 76.60 (d, $^3J_{HF}$ = 5.6 Hz).

HRMS (ESI-TOF) *m/z*: calc'd for $C_{12}H_{12}Cl_3F_3NO$ [M+H]$^+$ 333.9780, found 333.9777.

IR (film) cm^{-1}: 3341, 2997, 2978, 2878, 1673, 1266.



3-trichloroacetimidatyl cholesterol (S22)

Cholesterol (193 mg, 0.5 mmol) was dissolved in CH_2Cl_2 (1 mL) to which trichloroacetonitrile (0.11 g, 0.75 mL, 0.75 mmol) and 1,8-Diazabicyclo(5.4.0)undec-7-ene (0.069 g, 68 uL, 0.5 mmol) were added. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified (hexanes, 1% Et_3N) to yield imidate **S22** (220 mg, 83%) as a white solid.

R$_f$: 0.72 (20% Ethyl acetate/hexanes)

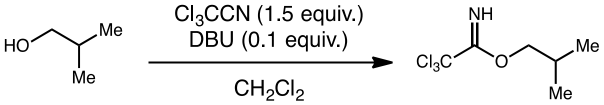
^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.23 (bs, 1H), 5.42 – 5.41 (m, 1H), 4.81 – 4.72 (m, 1H), 2.55 – 2.50 (m, 1H), 2.46 – 2.40 (m, 1H), 2.07 – 0.94 (m, 29H), 0.92 (d, J = 6.6 Hz, 3H), 0.88 (d, J = 1.8 Hz, 3H), 0.86 (d, J = 1.9 Hz, 3H), 0.69 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 162.2, 139.6, 123.1, 92.1, 79.1, 56.9, 56.3, 50.2, 42.5, 39.9, 39.7, 37.5, 37.1, 36.9, 36.4, 35.9, 32.1, 32.0, 28.4, 28.2, 27.2, 24.4, 24.0, 23.0, 22.7, 21.2, 19.5, 18.9, 12.0.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{29}H_{46}Cl_3NONa$ [M+Na]$^+$ 552.2543, found 552.2542.

IR (neat) cm^{-1}: 3340, 2980, 2883, 2360, 2343, 1763, 1654, 1464, 1440, 1382, 1301, 1249, 1135, 1071, 1000, 963, 829, 794.

MP: 158 – 159 °C



isobutyl 2,2,2-trichloroacetimidate (28a)

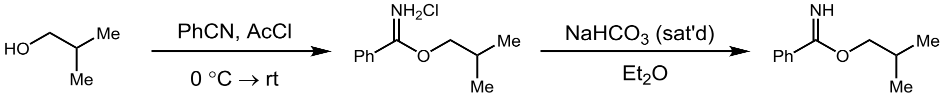
Following GP1, isobutanol **27** (0.815 g, 1.01 mL, 11 mmol) was dissolved in CH_2Cl_2 (20 mL) to which trichloroacetonitrile (2.38 g, 1.65 mL, 16.5 mmol) and 1,8-Diazabicyclo(5.4.0)undec-7-ene (167 mg, 0.165 mL, 1.1 mmol) were added. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified (hexanes, 1% Et_3N) to yield imidate **28a** (2.2 g, 93%) as a yellow oil.
R$_f$: 0.71 (20% Ethyl acetate/hexanes)

^{1}H NMR (600 MHz, CDCl$_3$): δ = 8.20 (bs, 1H), 4.06 (d, *J* = 6.7, 2H), 2.11 (m, *J* = 6.7 Hz, 1H), 1.01 (d, *J* = 6.7 Hz, 6H).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 163.3, 91.9, 75.6, 27.8, 19.1.

HRMS (ESI-TOF) *m/z*: calc'd for $C_6H_{10}Cl_3NONa$ $[M+Na]^+$ 239.9726, found 239.9715.

IR (neat) cm^{-1}: 3346, 2961, 2875, 1733, 1662, 1471, 1379, 1311, 1289, 1077, 1003, 825, 795, 710, 648.



isobutyl benzimidate (28b)

Following GP2, isobutanol **27** (8.64 g, 10.8 mL, 116 mmol) and benzonitrile (1 g, 1 mL, 9.7 mmol) were mixed and acetyl chloride (6.09 g, 5.54 mL, 77.6 mmol) was added dropwise. After 24 hours, the mixture was concentrated yielding a white solid. Upon basic workup, imidate **28b** was isolated as a clear oil (1.17 g, quant.).

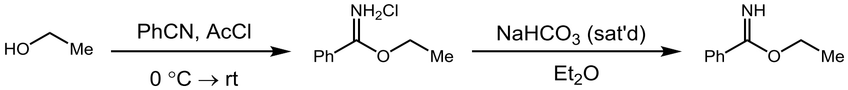
R$_f$: 0.26 (20% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.75 (bs, 3H), 7.48 – 7.40 (m, 3H), 4.04 (t, *J* = 3.4 Hz, 2H), 2.19 – 2.09 (m, 1H), 1.05 (t, *J* = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 168.0, 133.2, 131.0, 128.6, 126.8, 72.4, 28.0, 19.5.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{11}H_{16}NO$ $[M+H]^+$ 178.1232, found 178.1246.

IR (film) cm^{-1}: 3274, 2956, 2871, 1631, 1327.



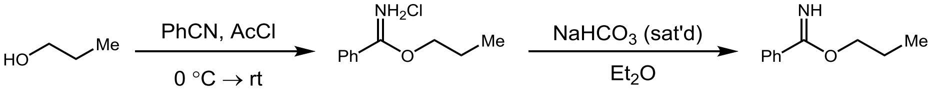
Ethyl benzimidate (S33)

Following **GP2**, ethanol (5.36 g, 6.79 mL, 116 mmol) and benzonitrile (1 g, 1 mL, 9.7 mmol) were mixed and acetyl chloride (6.09 g, 5.54 mL, 77.6 mmol) was added dropwise. After 24 hours, the mixture was concentrated yielding a white solid. This hydrochloride salt (0.5 g) was subjected to basic workup to yield imidate **S33** as a clear oil (0.33 g, 87%).

R_f: 0.21 (20% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 6.9 Hz, 2H), 7.71 (bs, 1H), 7.48 – 7.39 (m, 3H), 4.33 (q, *J* = 6.8 Hz, 2H), 1.43 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.0, 133.2, 130.9, 128.6, 126.8, 61.9, 14.4. Spectroscopic data is consistent with reported literature data.[2]



Propyl benzimidate (S34)

Following **GP2**, propanol (7 g, 8.75 mL, 116 mmol) and benzonitrile (1 g, 1 mL, 9.7 mmol) were mixed and acetyl chloride (6.09 g, 5.54 mL, 77.6 mmol) was added dropwise. After 24 hours, the mixture was concentrated yielding a white solid. Upon basic workup, imidate **S34** was isolated as a clear oil (1.57 g, 99%).

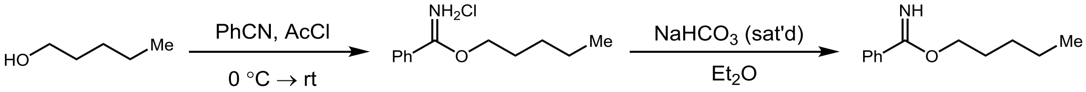
R_f: 0.24 (20% Ethyl acetate/hexanes)

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 5.7 Hz, 2H), 7.71 (bs, 1H), 7.47 – 7.40 (m, 3H), 4.23 (t, *J* = 6.0 Hz, 2H), 1.87 – 1.81 (m, 2H), 1.06 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.1, 133.2, 130.9, 128.6, 126.8, 67.7, 22.2, 10.8.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{10}H_{14}NO$ $[M+H]^+$ 164.1075, found 164.1094.

IR (film) cm^{-1}: 3289, 2965, 2961, 1631, 1326.



Pentyl benzimidate (S35)

Following GP2, pentanol (10.27 g, 12.66 mL, 116 mmol) and benzonitrile (1 g, 1 mL, 9.7 mmol) were mixed and acetyl chloride (6.09 g, 5.54 mL, 77.6 mmol) was added dropwise. After 24 hours, the mixture was concentrated yielding a white solid. Upon basic workup, imidate **S35** was isolated as a clear oil (1.82 g, 98%).

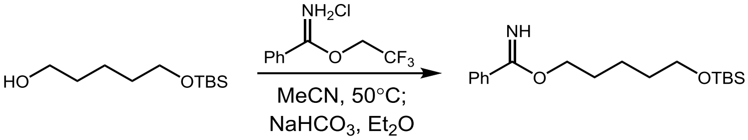
R$_f$: 0.26 (20% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.73 (bs, 3H), 7.48 – 7.39 (m, 3H), 4.28 (bs, 2H), 1.82 (quint, *J* = 7.0 Hz, 2H), 1.51 – 1.36 (m, 4H), 0.94 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 168.7, 133.2, 130.9, 128.6, 126.8, 66.3, 28.6, 28.5, 22.6, 14.1.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{12}H_{18}NO$ [M+H]$^+$ 192.1388, found 192.1402.

IR (film) cm^{-1}: 3275, 2952, 2936, 2856, 1631, 1577.



5-((tert-butyldimethylsilyl)oxy)pentyl benzimidate (S36)

Following GP3, trifluoroethyl benzimidate hydrochloride (0.2 g, 0.8 mmol) was suspended in MeCN (4 mL) to which alcohol (182 mg, 0.8 mmol) was added. After completion and workup, the crude material was purified (silica gel, hexanes with 1% Et$_3$N) to yield imidate **S36** as a clear oil (130 mg, 48%).

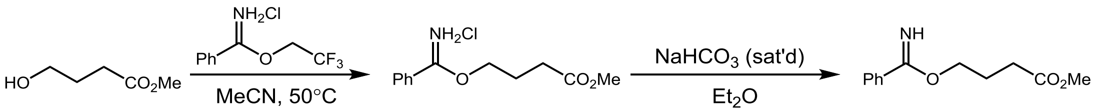
R$_f$: 0.28 (20% Ethyl acetate/hexanes)

^{1}H NMR (600 MHz, CDCl$_3$): δ = 7.76 (bs, 1H), 7.72 (bs, 2H), 7.47 – 7.44 (m, 1H), 7.43 – 7.40 (m, 2H), 4.29 (bs, 2H), 3.65 (t, *J* = 6.3 Hz, 2H), 1.83 (q, *J* = 7.1 Hz, 2H), 1.63 – 1.52 (m, 4H), 0.89 (s, 9H), 0.05 (s, 6H).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 168.1, 133.2, 130.9, 128.6, 126.9, 66.2, 63.2, 32.7, 28.7, 26.1, 22.8, 18.5, – 5.1.

HRMS (ESI-TOF) *m/z*: calc'd $C_{18}H_{32}NO_2Si$ [M+H]$^+$ 322.2202, found 322.2183.

IR (film) cm^{-1}: 3307, 2936, 2926, 2854, 1634, 1578.



Methyl 4-(imino(phenyl)methoxy)butanoate (S37)

Following GP3, trifluoroethyl benzimidate hydrochloride (0.2 g, 0.8 mmol) was suspended in MeCN (4 mL) to which alcohol (98.6 mg, 0.8 mmol) was added. After completion and workup, the crude material was purified (silica gel, 10% ethyl acetate/hexanes with 1% Et_3N) to yield imidate **S37** as a clear oil (52 mg, 28%).

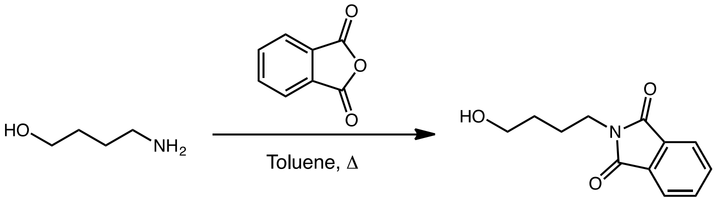
R_f: 0.30 (50% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (bs, 1H), 7.72 (d, *J* = 6.0 Hz, 2H), 7.48 – 7.39 (m, 3H), 4.32 (t, *J* = 5.7 Hz, 2H), 3.68 (s, 3H), 2.53 (t, *J* = 7.5 Hz, 2H), 2.19 – 2.13 (m, 2H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 173.6, 167.8, 132.8, 131.0, 128.6, 126.8, 65.1, 51.7, 31.1, 24.3.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{12}H_{16}NO_3$ $[M+H]^+$ 222.1130, found 222.1137.

IR (film) cm^{-1}: 3305, 2948, 2936, 2846, 1729, 1632, 1577.



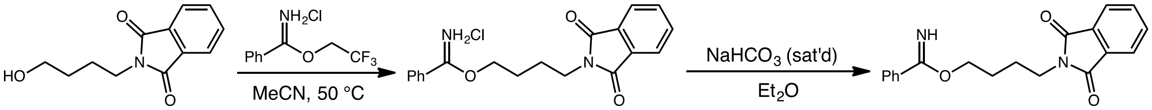
2-(4-hydroxybutyl)isoindoline-1,3-dione

Alcohol was synthesized according to the literature.[3] A mixture of 4-amino-1-butanol (445 mg, 5.0 mmol) and phthalic anhydride (740 mg, 5.0 mmol) in toluene (20 mL) was heated to reflux for 3 h. After cooling and removal of solvent, the crude product was purified (50% Ethyl acetate/hexanes) to yield alcohol as a white crystalline solid (1.1 g, 99% yield).

R_f: 0.24 (50% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (dd, J = 5.5, 3.0 Hz, 2H), 7.70 (dd, J = 5.5, 3.0 Hz, 2H), 3.71 (t, J = 7.0 Hz, 2H), 3.67 (t, J = 6.4 Hz, 2H), 1.94 (bs, 1H), 1.80-1.73 (m, 3H), 1.63-1.56 (m, 2H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 168.6, 134.0, 132.3, 123.3, 62.4, 37.8, 29.9, 25.2.



4-(1,3-dioxoisoindolin-2-yl)butyl benzimidate (S38)

Following GP3, trifluoroethyl benzimididate hydrochloride (575 mg, 2.4 mmol) was suspended in MeCN (2 mL) to which 2-(4-hydroxybutyl)isoindoline-1,3-dione (260 mg, 1.2 mmol) was added. After completion (3 hours) and workup, the crude material was purified (silica gel, hexanes to 30% ethyl acetate in hexanes) to yield imidate **S38** (352 mg, 91%) as a white solid, or the crude material can be purified via trituration in cold hexanes with a slightly lower yield (82%).

R$_f$: 0.27 (50% Ethyl acetate/hexanes)

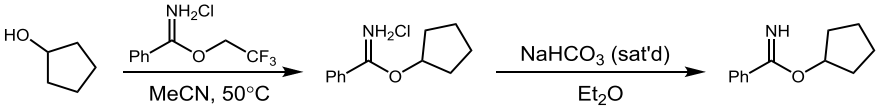
^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.85 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.85 – 7.60 (m, 3H), 7.71 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.47 – 7.38 (m, 3H), 4.31 (bs, 2H), 3.81 – 3.77 (m, 2H), 1.90 – 1.88 (m, 4H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 168.6, 168.0, 134.1, 132.9, 132.3, 131.0, 128.6, 126.8, 123.4, 65.6, 37.9, 26.4, 25.7.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{19}H_{19}N_2O_3$ $[M+H]^+$ 323.1396, found 323.1383.

IR (neat) cm^{-1}: 3314, 2954, 1765, 1702, 1638, 1578, 1468, 1444, 1397, 1323, 1246, 1173, 1077, 948, 860.

MP: 86 °C



Cyclopentyl benzimidate (S39)

Following GP3, trifluoroethyl benzimidate hydrochloride (0.2 g, 0.8 mmol) was suspended in MeCN (4 mL) to which alcohol (72 mg, 76 µL, 0.8 mmol) was added. After completion and workup, the crude material was purified (silica gel, hexanes with 1% Et_3N) to yield imidate **S39** as a clear oil (99 mg, 63%).

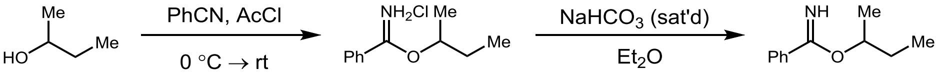
R$_f$: 0.23 (20% Ethyl acetate/hexanes)

^{1}H NMR (600 MHz, CDCl$_3$): δ = 7.73 (d, *J* = 7.0 Hz, 2H), 7.65 (bs, 1H), 7.46 – 7.39 (m, 3H), 5.33 (bs, 1H), 2.00 – 1.94 (m, 2H), 1.92 – 1.88 (m, 2H), 1.84 – 1.78 (m, 2H), 1.68 – 1.63 (m, 2H).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 167.0, 133.7, 130.8, 128.5, 126.9, 78.0, 32.9, 24.1.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{12}H_{16}NO$ $[M+H]^+$ 190.1232, found 190.1241.

IR (film) cm^{-1}: 3275, 2953, 2866, 1628, 1577.



Sec-butyl benzimidate (S40)

Following GP2, *sec*-butanol (8.63 g, 10.66 mL, 116 mmol) and benzonitrile (1 g, 1 mL, 9.7 mmol) were mixed and acetyl chloride (6.09 g, 5.54 mL, 77.6 mmol) was added dropwise. After 24 hours, the mixture was concentrated yielding a white solid. Upon basic workup, imidate **S40** was isolated as a clear oil (0.28 g, 16%)

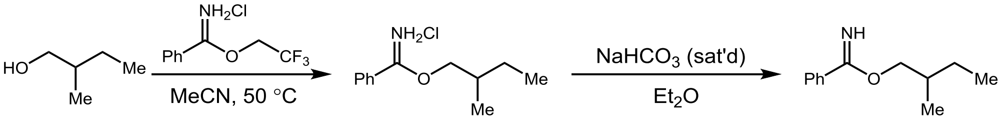
R$_f$: 0.15 (10% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.76 – 7.72 (m, 3H), 7.47 – 7.39 (m, 3H), 5.10 – 5.02 (m, 1H), 1.85 – 1.64 (m, 2H), 1.35 (d, *J* = 6.3 Hz, 3H), 1.00 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 167.5, 133.8, 130.8, 128.5, 126.8, 73.1, 29.1, 19.2, 9.9.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{11}H_{16}NO$ [M+H]$^+$ 178.1232, found 178.1247.

IR (film) cm^{-1}: 3307, 3300, 2936, 2874, 1628, 1577.



2-methylbutyl benzimidate (S41)

Following GP3, trifluoroethyl benzimidate hydrochloride (0.2 g, 0.8 mmol) was suspended in MeCN (4 mL) to which alcohol (74 mg, 90 µL, 0.8 mmol) was added. After completion and workup, the crude material was purified (silica gel, hexanes with 1% Et$_3$N) to yield imidate **S41** as a clear oil (100 mg, 63%).

R$_f$: 0.43 (20% Ethyl acetate/hexanes)

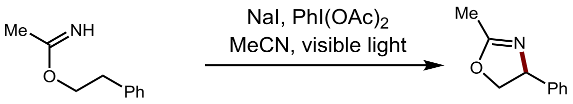
^{1}H NMR (600 MHz, CDCl$_3$): δ = 7.75 (bs, 3H), 7.47 – 7.45 (m, 1H), 7.43 – 7.40 (m, 2H), 4.14 (bs, 1H), 4.07 (bs, 1H), 1.95 – 1.88 (m, 1H), 1.62 – 1.55 (m, 1H), 1.35 – 1.28 (m, 1H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.97 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 168.3, 133.2, 130.9, 128.6, 126.8, 70.9, 34.5, 26.5, 16.8, 11.5.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{12}H_{18}NO$ [M+H]$^+$ 192.1388, found 192.1404.

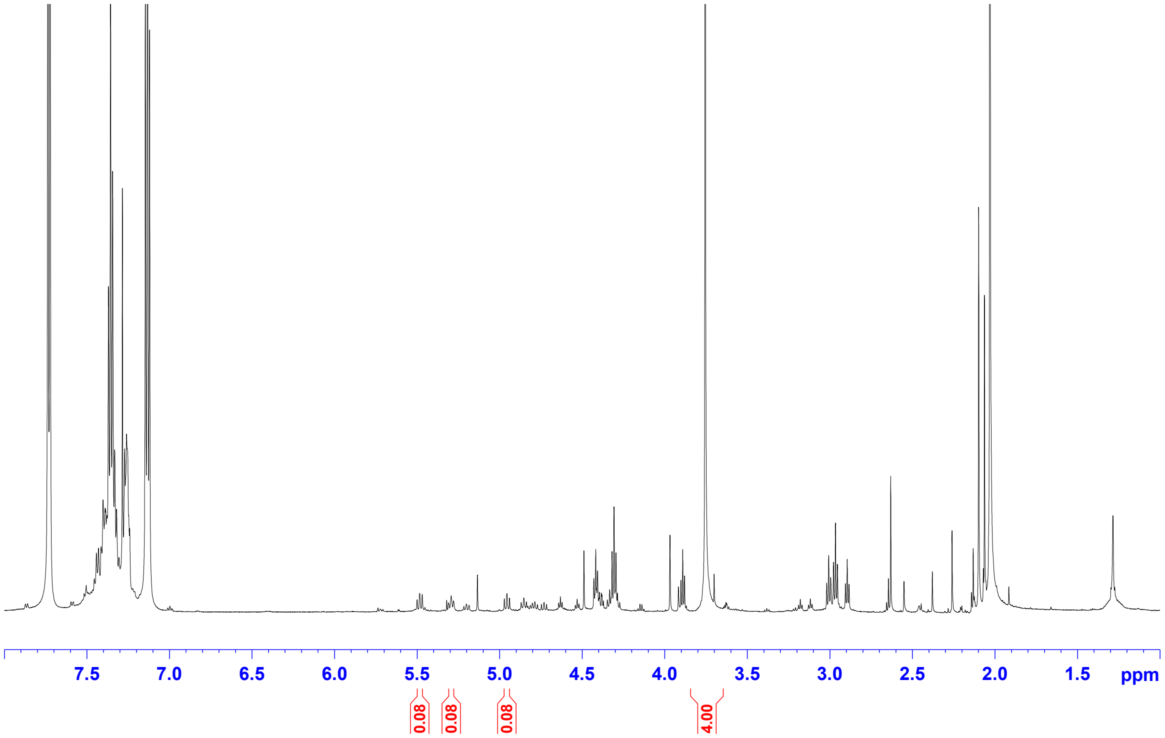
IR (film) cm^{-1}: 3309, 2978, 2877, 1629, 1577.

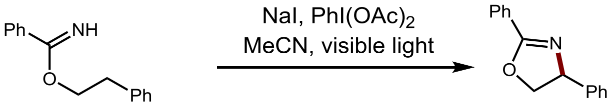
IV. C-H Amination



2-methyl-4-phenyl-4,5-dihydrooxazole

Crude acetimidate **1** (19.0 mg, 0.1 mmol) was subjected to GP4 with the following changes. After six hours, the reaction was removed from the light and concentrated. A crude ^{1}H NMR (1,2 dichloroethane as an internal standard) was taken indicating that less than 10% of the target material was formed based on analogy to ^{1}H spectrum of trichloromethyl oxazoline.





2,4-diphenyl-4,5-dihydrooxazole (5)

Benzimidate **2** (22.5 mg, 0.1 mmol) was subjected to GP4 with the following changes. After two hours, the reaction was removed from the light and concentrated. A crude yield of 71% was determined via ^{1}H NMR (1,2 dichloroethane as an internal standard).

The crude mixture was washed with $Na_2S_2O_3$, extracted with CH_2Cl_2, dried over $MgSO_4$, and concentrated. The crude oil was purified via column chromatography (silica gel, 5% Ethyl Acetate/hexanes) to yield oxazoline **5** (9 mg, 42%) as a clear oil. Oxazoline yield by ^{1}H NMR: 71%.

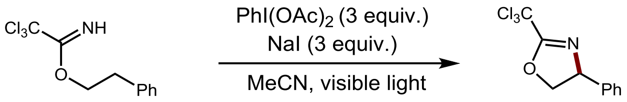
R$_f$: 0.18 (10% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.06 – 8.04 (m, 2H), 7.53 – 7.49 (m, 1H), 7.46 – 7.42 (m, 2H), 7.38 – 7.27 (m, 5H), 5.40 (dd, *J* = 10.0, 8.2 Hz, 1H), 4.80 (dd, *J* = 10.2, 8.3 Hz, 1H), 4.28 (appt, *J* = 8.3 Hz, 1H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 164.9, 142.6, 131.7, 128.9, 128.6, 128.5, 127.8, 127.8, 126.9, 75.0, 70.3.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{15}H_{14}NO$ [M+H]$^+$ 224.1075, found 224.1078.

IR (film) cm^{-1}: 3055, 3026, 2967, 2896, 2891, 1644, 1494.



4-phenyl-2-(trichloromethyl)-4,5-dihydrooxazole (6)

Trichloroacetimidate **3** (106.6 mg, 0.4 mmol) was subjected to GP4 with the following changes. Upon completion, the mixture was poured over 20% $Na_2S_2O_3$ (15 mL) and washed with CH_2Cl_2 (3 x 25 mL). The combined organic layers were dried over $MgSO_4$ and concentrated. The crude material was purified (SiliaFlash® 150 Å, 1% Ethyl acetate/hexanes) to yield oxazoline **6** as a clear oil (93 mg, 88%). Oxazoline yield by ^{1}H NMR: 100%.

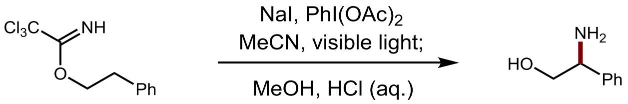
R$_f$: 0.26 (10% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.41 – 7.37 (m, 2H), 7.35 – 7.31 (m, 1H), 7.28 – 7.25 (m, 2H), 5.43 (dd, *J* = 10.1, 8.2 Hz, 1H), 5.00 (dd, *J* = 10.2, 8.6 Hz, 1H), 4.51 (app t, *J* = 8.4 Hz, 1H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 163.8, 140.3, 129.2, 128.4, 126.7, 86.7, 78.4, 70.2.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{10}H_9Cl_3NO$ [M+H]$^+$ 263.9750, found 263.9756.

IR (film) cm^{-1}: 3024, 2936, 2895, 1699, 1658, 1537.



2-amino-2-phenylethan-1-ol (7)

Trichloroacetimidate **3** (106.4 mg, 0.4 mmol) was subjected to GP4. After workup, β-amino alcohol **7** was isolated as a white solid (48.2 mg, 87%). Oxazoline yield by ^{1}H NMR: 100%.

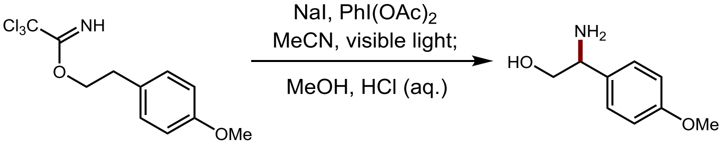
R$_f$: 0.08 (30% Isopropanol/CH_2Cl_2)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 – 7.27 (m, 5H), 4.05 (dd, J = 8.2, 4.4 Hz, 1H), 3.74 (dd, J = 10.7, 4.5 Hz, 1H), 3.55 (dd, J = 10.7, 8.3 Hz, 1H), 1.90 (bs, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ =143.0, 128.8, 127.7, 126.6, 68.2, 57.7.

HRMS (ESI-TOF) *m/z*: calc'd for $C_8H_{12}NO$ $[M+H]^+$ 138.0919, found 138.0944.

IR (film) cm^{-1}: 3363, 3282, 3006, 2896, 2861, 1598, 1555.



2-amino-2-(4-methoxyphenyl)ethan-1-ol (8)

Trichloroacetimidate **S8** (117.8 mg, 0.4 mmol) was subjected to GP4. After workup, β-amino alcohol **8** was isolated as a white solid (54 mg, 80%). Oxazoline yield by ^{1}H NMR: 100%.

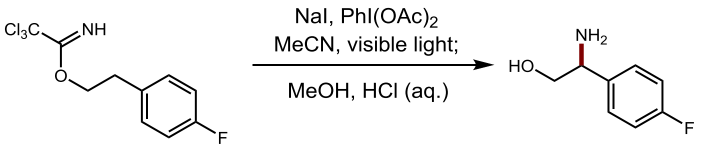
R$_f$: 0.04 (30% Isopropanol/CH_2Cl_2)

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.25 – 7.23 (m, 2H), 6.89 – 6.87 (m, 2H), 3.99 (dd, J = 8.2, 4.4 Hz, 1H), 3.79 (s, 3H), 3.69 (dd, J = 10.4, 3.9 Hz, 1H), 3.52 (dd, J = 10.7, 8.3 Hz, 1H), 2.13 (bs, 3H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 159.1, 135.1, 127.7, 114.2, 68.3, 56.9, 55.4.

HRMS (ESI-TOF) *m/z*: calc'd for $C_9H_{14}NO_2$ $[M+H]^+$ 168.1025, found 168.1040.

IR (film) cm^{-1}: 3316, 3272, 2900, 2833, 1606, 1509.



2-amino-2-(4-fluorophenyl)ethan-1-ol (9)

Trichloroacetimidate **S9** (114 mg, 0.4 mmol) was subjected to GP4. After workup, β-amino alcohol **9** was isolated as a colorless oil that slowly crystallized into a white solid (54.1 mg, 88%).

R_f: 0.05 (30% Isopropanol/CH_2Cl_2)

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.31 – 7.29 (m, 2H), 7.04 – 7.01 (m, 2H), 4.04 (dd, *J* = 8.1, 4.4 Hz, 1H), 3.70 (dd, *J* = 10.8, 4.4 Hz, 1H), 3.52 (dd, *J* = 10.8, 8.2 Hz, 1H), 2.12 (bs, 3H).

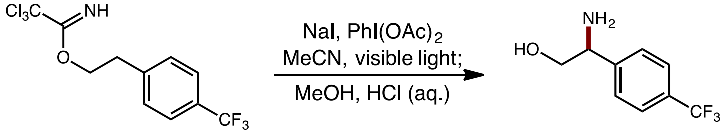
^{13}C NMR (150 MHz, $CDCl_3$): δ = 162.3 ($^{1}J_{CF}$ = 245.4 Hz), 138.6 ($^{4}J_{CF}$ = 3.1 Hz), 128.2 ($^{3}J_{CF}$ = 7.7 Hz), 115.6 ($^{2}J_{CF}$ = 20.9 Hz), 68.2, 56.8.

^{19}F NMR (564 MHz, $CDCl_3$): δ = – 115.2.

HRMS (ESI-TOF) *m/z*: calc'd for $C_8H_{11}FNO$ $[M+H]^+$ 156.0825, found 156.0844.

IR (film) cm^{-1}: 3329, 3273, 3040, 2979, 2903, 2830, 1597.

MP: 104 – 106 °C



2-amino-2-(4-(trifluoromethyl)phenyl)ethan-1-ol (10)

Trichloroacetimidate **S10** (134 mg, 0.4 mmol) was subjected to GP4. After workup, β-amino alcohol **10** was isolated as a white solid (62 mg, 76%). Oxazoline yield by ^{1}H NMR: 98%.

R_f: 0.14 (30% Isopropanol/CH_2Cl_2)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 8.1 Hz, 2H), 7.47 (d, *J* = 8.1 Hz, 2H), 4.14 (dd, *J* = 7.8, 4.3 Hz, 1H), 3.76 (dd, *J* = 10.7, 4.3 Hz, 1H), 3.56 (dd, *J* = 10.6, 7.9 Hz, 1H), 1.89 (bs, 3H).

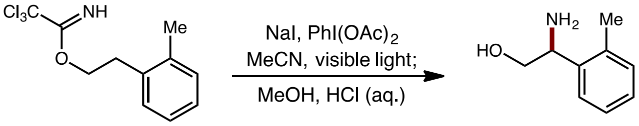
^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.0, 130.0 ($^{2}J_{CF}$ = 32.4 Hz), 127.1, 125.7 ($^{3}J_{CF}$ = 3.8 Hz), 122.9, 68.1, 57.1.

^{19}F NMR (376MHz, $CDCl_3$): δ = – 62.5.

HRMS (ESI-TOF) *m/z*: calc'd for $C_9H_{11}F_3NO$ $[M+H]^+$ 206.0793, found 206.0799

IR (neat) cm^{-1}: 3336, 3283, 3029, 2929, 2818, 1621, 1422, 1322, 1282, 1172, 1123, 1111, 1083, 1061, 1044, 1016, 958, 892, 838

MP: 106 – 109 °C



2-amino-2-(*o*-tolyl)ethan-1-ol (11)

Trichloroacetimidate **S11** (112 mg, 0.4 mmol) was subjected to **GP4**. After workup, β-amino alcohol **11** was isolated as a white solid (53 mg, 89%). Oxazoline yield by ^{1}H NMR: 99%.

R$_f$: 0.03 (30% Isopropanol/CH_2Cl_2)

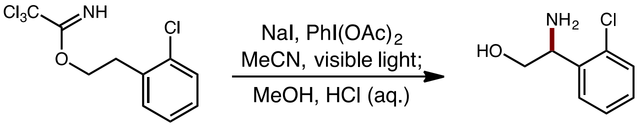
^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.38 (d, *J* = 7.4 Hz, 1H), 7.24 – 7.15 (m, 3H), 4.30 (dd, *J* = 8.3, 4.7 Hz, 1H), 3.70 (dd, *J* = 10.7, 4.0 Hz, 1H), 3.51 (dd, *J* = 10.7, 8.4 Hz, 1H), 2.37 (s, 3H), 2.04 (bs, 3H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 141.0, 135.4, 130.8, 127.3, 126.5, 125.3, 67.2, 53.1, 19.4.

HRMS (ESI-TOF) *m/z*: calc'd for $C_9H_{14}NO$ $[M+H]^+$ 152.1075, found 152.1099.

IR (neat) cm^{-1}: 3334, 3279, 3226, 2918, 2502, 1588, 1487, 1455, 1361, 1093, 1043, 980, 893.

MP: 100 – 102 °C



2-amino-2-(2-chlorophenyl)ethan-1-ol (12)

Trichloroacetimidate **S12** (120 mg, 0.4 mmol) was subjected to **GP4**. After workup, β-amino alcohol **12** was isolated as a white solid (56 mg, 82%). Oxazoline yield by ^{1}H NMR: 100%.

R$_f$: 0.11 (30% Isopropanol/CH_2Cl_2)

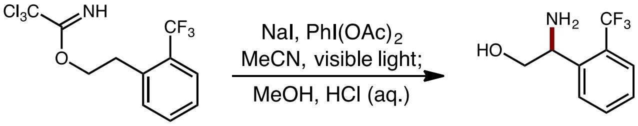
^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.48 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.36 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.30 – 7.26 (m, 1H), 7.20 (dt, *J* = 7.6, 1.6 Hz, 1H), 4.50 (dd, *J* = 8.1, 4.2 Hz, 1H), 3.82 (dd, *J* = 10.7, 4.0 Hz, 1H), 3.57 (dd, *J* = 10.8, 7.8 Hz, 1H), 2.08 (bs, 3H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 140.0, 133.2, 129.9, 128.6, 127.5, 127.3, 66.1, 53.8.

HRMS (ESI-TOF) *m/z*: calc'd for $C_8H_{11}ClNO$ [M+H]$^+$ 172.0529, found 172.0536.

IR (neat) cm^{-1}: 3329, 3277, 2923, 2809, 1589, 1471, 1455, 1435, 1360, 1133, 1102, 1046, 1039, 983, 949, 896, 813, 749.

MP: 76 – 78 °C



2-amino-2-(2-(trifluoromethyl)phenyl)ethan-1-ol (13)

Trichloroacetimidate **S13** (134 mg, 0.4 mmol) was subjected to **GP4**. After workup, β-amino alcohol **13** was isolated as a white solid (61 mg, 74%). Oxazoline yield by ^{1}H NMR: 100%.

R$_f$: 0.31 (30% Isopropanol/CH_2Cl_2)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.67 (dd, *J* = 13.5, 7.9 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 4.47 (dd, *J* = 8.0, 3.8 Hz, 1H), 3.75 (dd, *J* = 10.8, 4.0 Hz, 1H), 3.57 (dd, 10.7, 8.3, 1H), 2.10 (bs, 3H).

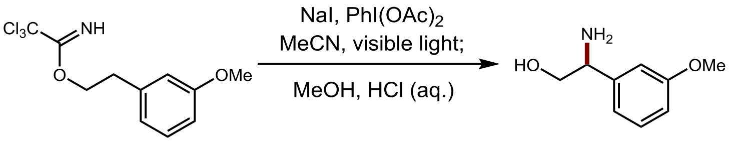
^{13}C NMR (100 MHz, CDCl$_3$): δ = 142.1, 132.4, 128.1 (q, $^2J_{CF}$ = 29.8 Hz), 127.9, 127.6, 126.0, (q, $^3J_{CF}$ = 5.9 Hz), 124.5 (q, $^1J_{CF}$ = 274.1 Hz), 67.4, 52.5 (d, $^4J_{CF}$ = 2.2 Hz).

^{19}F NMR (375 MHz, CDCl$_3$): δ = – 58.4.

HRMS (ESI-TOF) *m/z*: calc'd for $C_9H_{11}F_3NO$ [M+H]$^+$ 206.0793, found 206.0793.

IR (neat) cm^{-1}: 3350, 3281, 3076, 2893, 2828, 1609, 1456, 1311, 1148, 1107, 1044, 989, 899, 771, 757.

MP: 51 – 55 °C



2-amino-2-(3-methoxyphenyl)ethan-1-ol (14)

Trichloroacetimidate **S14** (117.8 mg, 0.4 mmol) was subjected to **GP4**. After workup, β-amino alcohol **14** was isolated as a colorless oil (61.2 mg, 92%). Oxazoline yield by ^{1}H NMR: 92%.

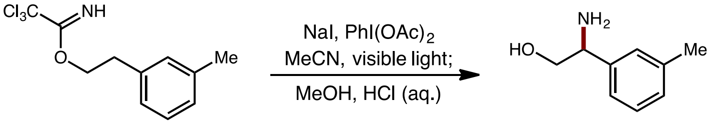
R$_f$: 0.1 (30% Isopropanol/CH_2Cl_2)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.27 – 7.23 (m, 1H), 6.90 – 6.88 (m, 2H), 6.81 – 6.79 (m, 1H), 4.00 (dd, *J* = 8.2, 4.3 Hz, 1H), 3.79 (s, 3H), 3.71 (dd, *J* = 10.8, 4.3 Hz, 1H), 3.54 (dd, *J* = 10.8, 8.2 Hz, 1H), 2.32 (bs, 3H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 159.9, 144.5, 129.7, 118.9, 112.8, 112.4, 68.0, 57.5, 55.3.

HRMS (ESI-TOF) *m/z*: calc'd for $C_9H_{14}NO_2$ [M+H]$^+$ 168.1025, found 168.1040.

IR (film) cm^{-1}: 3326, 3257, 2998, 2877, 2834, 1609, 1581.



2-amino-2-(*m*-tolyl)ethan-1-ol (15)

Trichloroacetimidate **S15** (112 mg, 0.4 mmol) was subjected to **GP4**. After workup, β-amino alcohol **15** was isolated as a white solid (51 mg, 84%). Oxazoline yield by ^{1}H NMR: 97%.

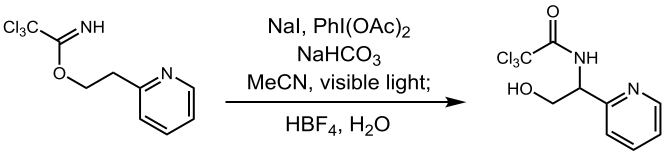
R$_f$: 0.03 (30% Isopropanol/CH_2Cl_2)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.24 – 7.22 (m, 1H), 7.14 – 7.09 (m, 3H), 4.01 (dd, *J* = 8.2, 4.5 Hz, 1H), 3.73 (dd, *J* = 10.6, 4.5 Hz, 1H), 3.55 (dd, *J* = 10.6, 8.3 Hz, 1H), 2.36 (s, 3H), 1.86 (bs, 3H).
^{13}C NMR (100 MHz, CDCl$_3$): δ = 142.9, 138.5, 128.7, 128.4, 127.3, 123.6, 68.2, 57.4, 21.6.

HRMS (ESI-TOF) *m/z*: calc'd for $C_9H_{14}NO$ [M+H]$^+$ 152.1075, found 152.1094.

IR (neat) cm^{-1}: 3190, 3106, 3022, 2949, 2926, 2872, 2672, 2114, 1568, 1445, 1398, 1366, 1315, 1169, 1049, 895, 730.

MP: 84 – 85 °C



2-amino-2-(pyridin-2-yl)ethan-1-ol (16)

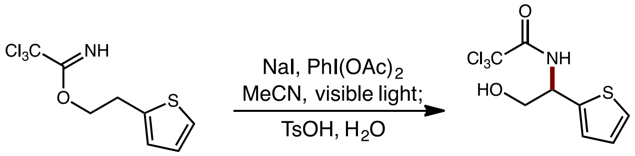
Trichloroacetimidate **S16** (109 mg, 0.4 mmol) was subjected to **GP4**. Upon completion, the mixture was diluted with H_2O (1 mL) and 50% aq. HBF (50 ul, 0.8 mmol) was added and the reaction was allowed to stir for 3 hr. Upon completion, the reaction was poured into a separatory funnel containing a 1:1 mixture of saturated $NaHCO_3$ and 20% $Na_2S_2O_3$ (15 mL). The aqueous phase was washed with ethyl acetate (3 x 15 mL) and the combined organic solution was dried over $MgSO_4$ and concentrated. The crude material was purified (silica gel, Hexanes → 60% Ethyl acetate/hexanes) to yield trichloroacetamide **16** as a white solid (74 mg, 65%). Oxazoline yield by ^{1}H NMR: 97%.

R$_f$: 0.10 (50% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.56 (ddd, *J* = 4.9, 1.6, 0.9, 1H), 8.27 (bs, 1H), 7.74 (td, *J* = 11.6, 1.8, Hz, 1H), 7.43 (d, *J* = 7.8, Hz, 1H), 7.30 (ddd, *J* = 7.6, 4.9, 1.1, 1H), 5.09 – 5.06 (m, 1H), 4.19 – 4.16 (m, 1H), 4.02 – 3.96 (m, 1H), 3.66 (bs, 1H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 162.2, 157.2, 149.2, 137.7, 123.6, 123.3, 92.6, 65.2, 56.0.

HRMS (ESI-TOF) *m/z*: calc'd for $C_9H_9Cl_3N_2O_2Na$ [M+Na]$^+$ 304.9627, found 304.9612.



2-amino-2-(thiophen-2-yl)ethan-1-ol (17)

Trichloroacetimidate **S17** (109 mg, 0.4 mmol) was subjected to **GP4**. Upon completion, the mixture was diluted with H_2O (1 mL) and *p*-toluenesulfonic acid monohydrate (380.4 mg, 2.0 mmol) was added and the reaction was allowed to stir for 1 hr. Upon completion, the reaction was poured into a separatory funnel containing a 1:1 mixture of saturated $NaHCO_3$ and 20% $Na_2S_2O_3$ (15 mL). The aqueous phase was washed with ethyl acetate (3 x 15 mL) and the combined organic solution was dried over $MgSO_4$ and concentrated. The crude material was purified (silica gel, Hexanes → 20% Ethyl acetate/hexanes) to yield trichloroacetamide **17** as a white solid (97 mg, 84%). Oxazoline yield by ^{1}H NMR: 95%.

R$_f$: 0.49 (50% Ethyl acetate/hexanes)

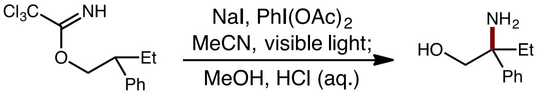
^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.37 (bs, 1H), 7.30 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.08 (td, *J* = 3.5, 1.0 Hz, 1H), 7.02 (dd, *J* = 3.5, 5.1 Hz, 1H), 5.38 – 5.34 (m, 1H), 4.06 (dd, *J* = 6.1, 4.0 Hz, 1H), 1.90 (t, *J* = 6.1 Hz, 1H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 161.7, 140.4, 127.4, 125.8, 125.7, 92.6, 65.4, 52.9.

HRMS (ESI-TOF) *m/z*: calc'd for $C_8H_8Cl_3NO_2SNa$ [M+Na]$^+$ 309.9239, found 309.9227.

IR (neat) cm^{-1}: 3443, 3178, 2981, 2884, 1698, 1545, 1454, 1379, 1278, 1085, 1042, 906, 824.

MP: 127 – 130 °C



2-amino-2-phenylbutan-1-ol (18)

Trichloroacetimidate **S18** (118 mg, 0.4 mmol) was subjected to **GP4** with the following changes: the crude mixture was concentrated in a round-bottom flask, then methanol (4 mL) and 2M HCl (0.8 mL) was added and stirred for 5 hours at 50 °C, after workup, β-amino alcohol **18** was isolated as a white solid (65 mg, 97%). Oxazoline yield by ^{1}H NMR: 97%.

R$_f$: 0.19 (30% Isopropanol/CH_2Cl_2)

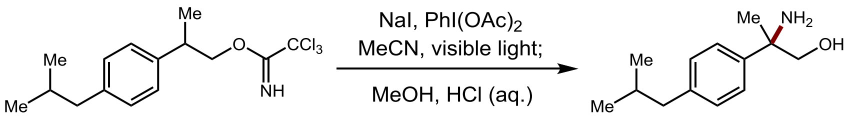
^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.41 – 7.34 (m, 4H), 7.27 – 7.23 (m, 1H), 3.70 – 3.64 (m, 5H), 1.92 – 1.67 (m, 5H), 0.72 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 144.6, 128.6, 126.8, 126.0, 71.1, 59.7, 32.0, 7.9.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{10}H_{16}NO$ [M+H]$^+$ 166.1232, found 166.1246.

IR (neat) cm^{-1}: 3378, 3308, 3057, 2967, 2939, 2876, 1569, 1442, 1307, 1234, 1182, 1067, 1053, 990, 909, 807.

MP: 53 – 54 °C



2-amino-2-(4-isobutylphenyl)propan-1-ol (19)

Trichloroacetimidate **S19** (134.7 mg, 0.4 mmol) was subjected to GP4 with the following changes: the crude mixture was concentrated in a round-bottom flask, then methanol (4 mL) and 2M HCl (0.8 mL) was added and stirred for 2 hours at 50 °C, after workup, β-amino alcohol **19** was isolated as a white solid (69 mg, 83%). Oxazoline yield by ^{1}H NMR: 90%.

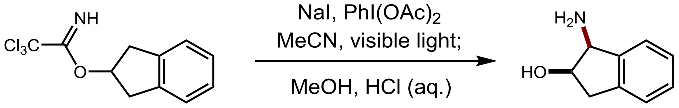
R$_f$: 0.08 (30% Isopropanol/CH_2Cl_2)

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.34 (d, *J* = 8.3 Hz, 2H), 7.13 (d, *J* = 8.3 Hz, 2H), 3.61 (d, *J* = 10.8 Hz, 1H), 3.55 (d, *J* = 10.6 Hz, 1H), 2.46 (d, *J* = 7.1 Hz, 2H), 1.89 – 1.83 (m, 1H), 1.44 (s, 3H), 0.90 (d, *J* = 6.8 Hz, 6H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 143.9, 140.4, 129.3, 125.1, 71.8, 56.0, 45.1, 30.3, 27.2, 22.5.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{13}H_{22}NO$ $[M+H]^+$ 208.1701, found 208.1706.

IR (film) cm^{-1}: 3321, 3266, 2947, 2918, 2863, 1604.



1-amino-2,3-dihydro-1H-inden-2-ol (20)

Trichloroacetimidate **S20** (111.6 mg, 0.4 mmol) was subjected to GP4 with the following changes: the crude mixture was concentrated in a round-bottom flask, then methanol (4 mL) and 6M HCl (0.3 mL) was added and stirred for 5 hours at 50 °C, after workup, β-amino alcohol **20** was isolated as a white solid (48.2 mg, 81%). Oxazoline yield by ^{1}H NMR: 97%.

R$_f$: 0.03 (30% Isopropanol/CH_2Cl_2)

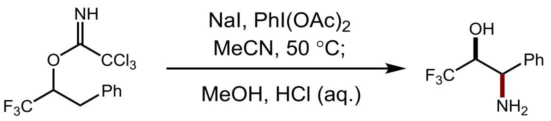
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 – 7.23 (m, 4H), 4.38 (td, *J* = 5.5, 3.0 Hz, 1H), 4.32 (d, *J* = 5.4 Hz, 1H), 3.09 (dd, *J* = 16.5, 5.7 Hz, 1H), 2.94 (dd, *J* = 16.3, 2.9 Hz, 1H), 2.36 (bs, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.1, 141.1, 128.1, 127.1, 125.6, 124.0, 72.8, 58.6, 39.5.

HRMS (ESI-TOF) *m/z*: calc'd for $C_9H_{12}NO$ $[M+H]^+$ 150.0919, found 150.0930.

IR (film) cm^{-1}: 3340, 3265, 3062, 2979, 2898, 2755, 2730, 1580, 1473.

MP: 129 – 130 °C.



cis-3-amino-1,1,1-trifluoro-3-phenylpropan-2-ol (21)

Trichloroacetimidate **S21** (133.6 mg, 0.4 mmol) was subjected to GP4 with the following changes: the reaction was stirred in a heating block at 50 °C for 14 hours. Upon completion, the crude mixture was concentrated in a round-bottom flask and the crude oxazoline yield of 79% was determined by ^{1}H NMR (DCE, 32 µL, as internal standard). The sample was concentrated and then methanol (4 mL) and 2M HCl (0.8 mL) was added and stirred for 12 hours at 50 °C, after workup, β-amino alcohol **21** was isolated as a white solid (46.7 mg, 57%).

R$_f$: 0.46 (10% MeOH/CH_2Cl_2)

^{1}H NMR (600 MHz, CD_3OD): δ = 7.39 – 7.38 (m, 2H), 7.35 – 7.33 (m, 2H), 7.29 – 7.27 (m, 1H), 4.08 (d, J = 5.7 Hz, 1H), 4.00 (dq, J = 5.9, 7.2 Hz, 1H).

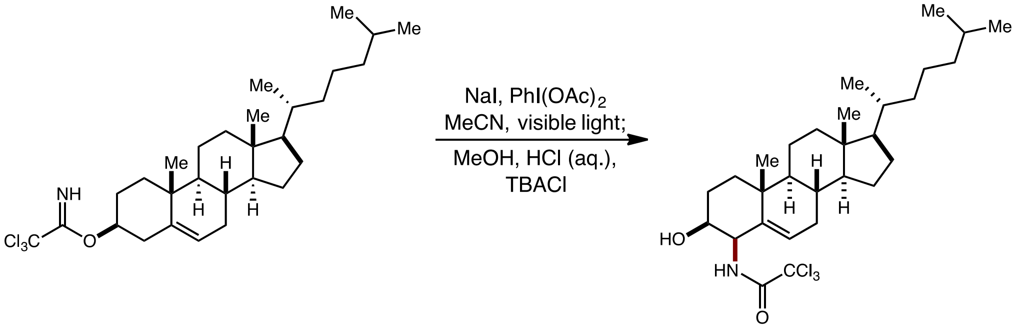
^{13}C NMR (150 MHz, CD_3OD): δ = 142.7, 129.5, 128.8, 128.4, 126.5 (q, $^1J_{CF}$ = 283.2 Hz), 74.5 (q, $^2J_{CF}$ = 28.6 Hz), 56.4.

^{19}F NMR (565 MHz, CD_3OD): δ = – 77.01 (d, $^3J_{HF}$ = 6.1 Hz).

HRMS (ESI-TOF) *m/z*: calc'd for $C_9H_{11}F_3NO$ $[M+H]^+$ 206.0793, found 206.0804.

IR (film) cm^{-1}: 3344, 3289, 2968, 2891, 1766, 1590, 1271.

MP: 115 – 122 °C



4- trichloroacetamidyl cholesterol (22)

To an 10 mL round-bottom flask equipped with septa cap and magnetic stir bar, was added trichloroacetimidate **S22** (212 mg, 0.4 mmol), iodobenzene diacetate (258 mg, 0.8 mmol), and NaI (120 mg, 0.8 mmol). This vial was evacuated and backfilled with N_2 (3x). Dry dicholoromethane (4 mL) was degassed using a freeze-pump-thaw technique (3x), then added to the flask under N_2. The reaction was irradiated with two 23 W compact fluorescent light bulbs for 2 hours and monitored using TLC. *Hydrolysis and acid/base extraction.* Upon completion, the mixture was concentrated, then methanol (4 mL), 2M HCl (0.8 mL), tetrabutylammonium chloride (111 mg, 0.4mmol) were added. After stirring for 24 hours, the reaction was diluted with CH_2Cl_2 (10 mL) and aqueous sodium thiosulfate (20% w/w) was added. The aqueous layer was washed with CH_2Cl_2 (3 x 25 mL). The combined organic layer was dried over $MgSO_4$ and concentrated. The crude product was purified (hexanes, 1% Et_3N) to yield trichloroacetamide **22** (186 mg, 85%) as a white solid. Oxazoline yield by ^1H NMR: 100%.

R_f: 0.26 (20% Ethyl acetate/hexanes)

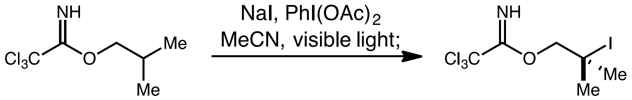
^1H NMR (400 MHz, $CDCl_3$): δ = 7.06 (d, *J* = 6.0 Hz, 1H), 5.88 (dd, *J* = 4.9, 2.2 Hz, 1H), 4.46 (t, *J* = 5.3 Hz, 1H), 3.87 – 3.83 (m, 1H), 2.21 – 2.14 (m, 2H), 2.02 (dt, *J* = 12.6, 3.4 Hz, 1H), 1.88 –1.81 (m, 3H), 1.72 – 1.65 (m, 1H), 1.63 – 0.94 (m, 23H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 1.4 Hz, 3H), 0.86 (d, *J* = 2.8 Hz, 3H), 0.67 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.5, 137.9, 131.7, 93.1, 77.4, 71.1, 60.9, 57.0, 56.2, 50.4, 42.4, 39.7, 39.6, 36.3, 36.1, 35.9, 32.4, 31.8, 28.3, 28.2, 25.7, 24.4, 24.0, 23.0, 22.7, 21.0, 20.7, 18.9, 12.0.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{29}H_{46}Cl_3NO_2Na$ $[M+Na]^+$ 568.2492, found 568.2485.

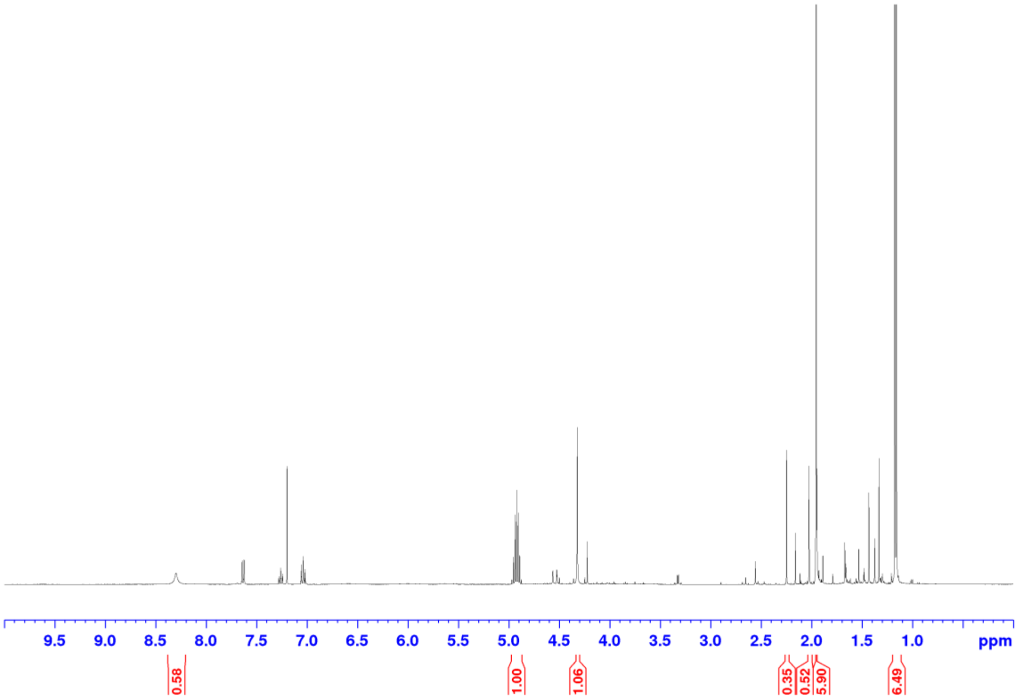
IR (neat) cm^{-1}: 3430, 3380, 2980, 2970, 2938, 2866, 1703, 1500, 1471, 1378, 1247, 1175, 1075, 946, 819, 759.

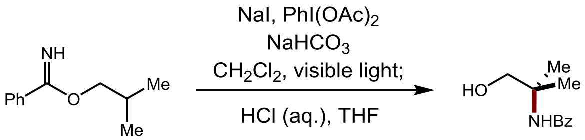
MP: 200.0 °C (decomposed)



2-iodo-2-methylpropyl 2,2,2-trichloroacetimidate (30)

Trichloroacetimidate **28a** (87.4 mg, 0.4 mmol) was subjected to GP4 with the following changes: the crude mixture was concentrated in a round-bottom flask and a crude ^1H NMR was taken (^{i}PrOAc as an internal standard) which indicated a crude yield of 53% of tertiary alkyl iodide imidate by integrating a singlet corresponding to α-oxy methylene around 4.2 ppm (see below for crude ^1H NMR spectra). The presence of alkyl iodide was further confirmed via HRMS.





N-(1-hydroxy-2-methylpropan-2-yl)benzamide (32)

Benzimidate **S28b** (70.4 mg, 0.4 mmol) was subjected to **GP4** with the following changes: solid $NaHCO_3$ (67.2 mg, 0.8 mmol) was added to the reaction mixture. Upon completion (24 hours) the crude mixture was concentrated in a round-bottom flask and a crude ^{1}H NMR was taken (DCE as an internal standard) which indicated a crude oxazoline yield of 62%. THF (4 mL) and 2M HCl (0.8 mL) were added to the crude reaction which was then stirred for 17 hours at 50 °C, after workup, β-amido alcohol **32** was isolated as a white solid (29 mg, 38%).

R_f: 0.24 (50% Ethyl acetate/hexanes)

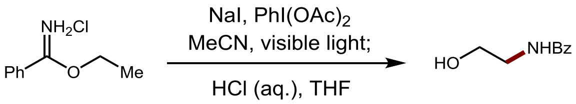
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75 – 7.72 (m, 2H), 7.53 – 7.49 (m, 1H), 7.46 – 7.41 (m, 2H), 6.16 (bs, 1H), 4.64 (t, J = 4.8 Hz, 1H), 3.70 (d, J = 3.8 Hz, 2H), 1.42 (s, 6H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 168.5, 135.1, 131.8, 128.8, 127.0, 70.9, 56.7, 25.0.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{11}H_{16}NO_2$ $[M+H]^+$ 194.1181, found 194.1191.

IR (film) cm^{-1}: 3292, 3158, 3057, 2980, 2899, 2895, 2849, 1626, 1554.

MP: 83 – 85 °C



N-(2-hydroxyethyl)benzamide (33)

Benzimidate hydrochloride **S33** (18.7 mg, 0.1 mmol) was subjected to **GP4** with the following changes: upon completion (24 hours) the crude mixture was concentrated in a round-bottom flask and a crude ^1H NMR was taken (DCE as an internal standard) which indicated a crude oxazoline yield of 45%. MeOH (0.5 mL) and 2M HCl (0.5 mL) were added to the crude reaction which was then stirred for 12 hours at room temperature, after workup, β-amido alcohol **33** was isolated as a white solid (7 mg, 42%).

R$_f$: 0.20 (5% MeOH/CH_2Cl_2)

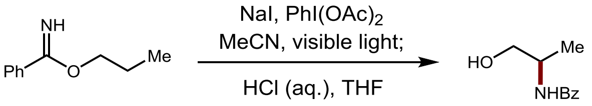
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 – 7.77 (m, 2H), 7.52 – 7.48 (m, 1H), 7.44 – 7.40 (m, 2H), 6.70 (bs, 1H), 3.83 (t, *J* = 5.0 Hz, 2H), 3.63 (appq, *J* = 5.3 Hz, 2H), 2.78 (bs, 1H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 168.7, 134.4, 131.8, 128.7, 127.1, 62.5, 43.0.

HRMS (ESI-TOF) *m/z*: calc'd for $C_9H_{12}NO_2$ $[M+H]^+$ 166.0868, found 166.0878.

IR (film) cm^{-1}: 3327, 3289, 3056, 2969, 2936, 2868, 1632, 1535.

MP: 59 – 61 °C



N-(1-hydroxypropan-2-yl)benzamide (34)

Benzimidate **S34** (64.6 mg, 0.04 mmol) was subjected to **GP4** with the following changes: upon completion (ca 5 hours), the crude mixture was concentrated in a round-bottom flask and a crude ^1H NMR was taken (DCE as an internal standard) which indicated a crude oxazoline yield of 82%. Then THF (2 mL) and 2M HCl (1.0 mL) was added and stirred for 12 hours at room temperature, after workup, β-amido alcohol **34** was isolated as a white solid (50.4 mg, 70%).

R$_f$: 0.09 (50% Ethyl acetate/hexanes)

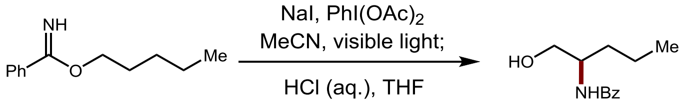
^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.78 – 7.76 (m, 2H), 7.52 – 7.48 (m, 1H), 7.45 – 7.40 (m, 2H), 6.33 (bs, 1H), 4.31 – 4.25 (m, 1H), 3.78 (dd, *J* = 10.8, 3.6 Hz, 1H), 3.65 (dd, *J* = 10.9, 5.8, 1H), 2.80 (bs, 1H), 1.29 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 168.2, 134.5, 131.8, 128.7, 127.1, 67.3, 48.3, 17.3.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{10}H_{13}NO_2Na$ [M+Na]$^+$ 202.0844, found 202.0859.

IR (film) cm^{-1}: 3343, 2971, 2936, 2875, 1629, 1537.

MP: 103 – 105 °C



N-(1-hydroxypentan-2-yl)benzamide (35)

Benzimidate **S35** (75.3 mg, 0.04 mmol) was subjected to **GP4** with the following changes: upon completion (ca 5 hours), the crude mixture was concentrated in a round-bottom flask and a crude ^{1}H NMR was taken (DCE as an internal standard) which indicated a crude oxazoline yield of 79%. Then THF (2 mL) and 2M HCl (1.0 mL) was added and stirred for 12 hours at room temperature, after workup, β-amido alcohol **35** was isolated as a white solid (52 mg, 64%).

R$_f$: 0.13 (50% Ethyl acetate/hexanes)

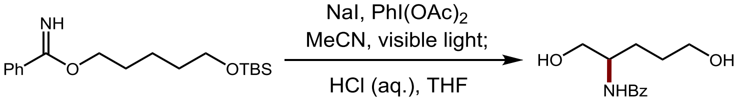
^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.77 – 7.75 (m, 2H), 7.51 – 7.46 (m, 1H), 7.42 – 7.38 (m, 2H), 6.42 (d, *J* = 7.4 Hz, 1H), 4.19 – 4.11 (m, 1H), 3.76 (dd, *J* = 10.9, 3.8 Hz, 1H), 3.66 (dd, *J* = 11.1, 5.4 Hz, 1H), 3.08 (bs, 1H), 1.66 – 1.52 (m, 2H), 1.47 – 1.37 (m, 2H), 0.94 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 168.4, 134.6, 131.7, 128.7, 127.1, 65.7, 52.2, 33.6, 19.5, 14.1.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{12}H_{17}NONa$ [M+Na]$^+$ 230.1157, found 230.1162.

IR (film) cm^{-1}: 3282, 2937, 2936, 2865, 1631, 1530.

MP: 95 – 97 °C



N-(1,5-dihydroxypentan-2-yl)benzamide (36)

Benzimidate **S36** (32.4 mg, 0.2 mmol) was subjected to GP4 with the following changes: upon completion (ca 5 hours), the crude mixture was concentrated in a round-bottom flask and a crude ^{1}H NMR was taken (DCE as an internal standard) which indicated a crude oxazoline yield of 80%. Then THF (1 mL) and 2M HCl (0.5 mL) was added and stirred for 7 hours at room temperature, then saturated $NaHCO_3$ (10 mL) was added and stirred for 12 hours. The crude mixture was extracted with ethyl acetate (4 x 20 mL) and dried over $MgSO_4$. Upon concentration, the crude material was purified via column chromatography (silica gel, 4% → 5% MeOH/CH_2Cl_2) and β-amido alcohol **36** was isolated as a white solid (14 mg, 62%).

R$_f$: 0.20 (10% MeOH/CH_2Cl_2)

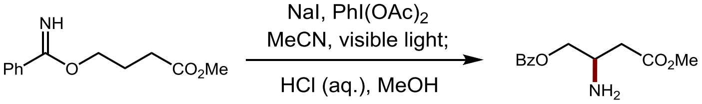
^{1}H NMR (600 MHz, CDCl$_3$): δ = 7.80 – 7.79 (m, 2H), 7.52 – 7.49 (m, 1H), 7.45 – 7.42 (m, 1H), 6.70 (d, *J* = 6.9 Hz, 1H), 4.24 – 4.19 (m, 1H), 3.81 (dd, *J* = 11.1, 3.6 Hz, 1H), 3.77 – 3.71 (m, 3H), 2.78 (bs, 1H), 1.99 (bs, 1H), 1.82 – 1.68 (m, 4H).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 168.5, 134.5, 131.8, 128.8, 127.2, 65.8, 62.7, 52.2, 28.7, 28.1.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{12}H_{18}NO_3$ $[M+H]^+$ 224.1287, found 224.1292.

IR (film) cm^{-1}: 3329, 3275, 3052, 2916, 2853, 1632, 1534.

MP: 87 – 89 °C



Methyl 3-benzamido-4-hydroxybutanoate (37)

Benzimidate **S37** (22.4 mg, 0.1 mmol) was subjected to GP4 with the following changes: upon completion (ca 5 hours), the crude mixture was concentrated in a round-bottom flask and a crude ^{1}H NMR was taken (DCE as an internal standard) which indicated a crude oxazoline yield of 68%. Then MeOH (1 mL) and 2M HCl (0.5 mL) was added and stirred for 3 hours at room temperature, then solid NaOMe (130 mg, 20 equiv.) was added and diluted with 2 mL of $CHCl_3$ and stirred for 6 hours. The crude mixture was extracted with ethyl acetate (4 x 20 mL) and dried over $MgSO_4$. Upon concentration, the crude material was purified via column chromatography (silica gel, 1% → 3% MeOH/CH_2Cl_2) and β-amido alcohol **37** was isolated in low yield and an oily residue.

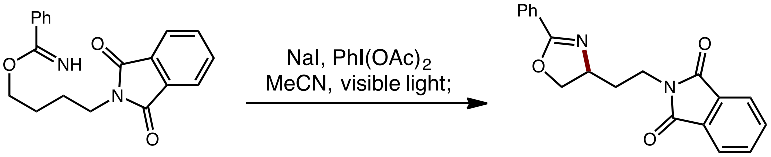
(Note: *Other attempts at hydrolysis yield mixtures of ester and amide. Other basic reaction conditions also yield a mixture of an open amide and ring-closed lactam.)*

R$_f$: 0.49 (10% MeOH/CH_2Cl_2).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.04 – 8.02 (m, 2H), 7.57 – 7.55 (m, 1H), 7.45 – 7.43 (m, 2H), 4.54 – 4.46 (m, 2H), 3.71 – 3.67 (m, 1H), 3.69 (s, 3H), 2.27 – 2.23 (m, 1H), 2.04 – 1.99 (m, 1H), 1.82 (bs, 3H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.4, 133.0, 130.1, 129.6, 128.4, 61.5, 52.1, 51.8, 33.7.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{12}H_{15}NO_4Na$ $[M+Na]^+$ 260.0899, found 260.0897.



(*S*)-2-(2-(2-phenyl-4,5-dihydrooxazol-4-yl)ethyl)isoindoline-1,3-dione

Benzimidate **S38** (64.5 mg, 0.2 mmol) was subjected to **GP4** with the following changes: Upon completion (ca 4 hours), the crude mixture was concentrated in a round-bottom flask and a crude ^{1}H NMR was taken (DCE as an internal standard) which indicated a crude oxazoline yield of 85%. The crude reaction mixture was concentrated and loaded directly onto silica gel and purified (silica gel, Hexanes → 50% Ethyl acetate/hexanes) to yield the target oxazoline **38'** (49 mg, 77%) as an off-white viscous oil.

(Note: *Attempted hydrolysis with HCl led to a complex mixture, due to benzoyl transfer between OH and NH_2. Other hydrolysis condition yield complex mixtures as well. Because of this inconsistent result, we decided to isolate the oxazoline product. Trace amounts of both amide and ester were isolated after hydrolysis. See Section XIII for ^{1}H NMR spectra*)

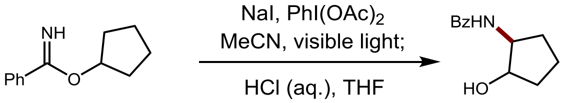
R$_f$: 0.56 (50% Ethyl acetate/hexanes)

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.85 (dd, *J* = 5.7, 3.7, 2H), 7.78 (d, *J* = 8.1, 2H), 7.72 (dd, *J* = 5.4, 3.0, 2H), 7.43 (t, 1H), 7.33 (t, 2H), 4.54 (t, *J* = 9.0 Hz, 1H), 4.34 (q, *J* = 7.8 Hz, 1H), 4.10 (t, *J* = 8.1 Hz, 1H), 3.99 – 3.94 (m, 1H), 3.88 – 3.84 (m, 1H), 2.15 – 2.09 (m, 1H), 1.97 – 1.91 (m, 1H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 168.6, 164.1, 134.0, 132.5, 131.4, 128.4, 128.4, 127.8, 123.4, 72.6, 650, 35.5, 34.6.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{19}H_{17}N_2O_3$ $[M+H]^+$ 321.1239, found 321.1220.

IR (film) cm^{-1}: 3445, 2970, 1738, 1435, 1365, 1228, 1217, 1047.



N-(2-hydroxycyclopentyl)benzamide (39)

Benzimidate **S39** (37.2 mg, 0.2 mmol) was subjected to **GP4** with the following changes: the reaction was run at 50 °C. Upon completion (ca 24 hours), the crude mixture was concentrated in a round-bottom flask, and a crude ^{1}H NMR was taken (DCE as an internal standard) which indicated a crude oxazoline yield of 63%. THF (1 mL) and 2M HCl (0.5 mL) was added and stirred for 24 hours at 50 °C. The crude reaction mixture was purified via column chromatography (silica gel, 20% Ethyl acetate/hexanes) to yield β-amido alcohol **39** as a white solid (18 mg, 45%).

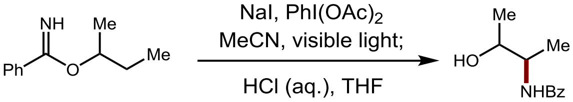
R$_f$: 0.32 (5% MeOH/CH_2Cl_2)

^{1}H NMR (600 MHz, CD_3OD): δ = 7.84 – 7.83 (m, 2H), 7.54 – 7.51 (m, 1H), 7.47 – 7.44 (m, 2H), 4.22 (td, *J* = 4.8, 2.2 Hz, 1H), 4.18 (ddd, *J* = 9.9, 7.9, 4.6 Hz, 1H), 2.05 – 2.00 (m, 1H), 1.98 – 1.85 (m, 2H), 1.80 – 1.71 (m, 1H), 1.67 – 1.59 (m, 1H).

^{13}C NMR (100 MHz, CD_3OD): δ = 170.1, 135.9, 132.6, 129.5, 128.3, 73.2, 56.2, 33.6, 29.4, 21.2.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{12}H_{16}NO_2$ $[M+H]^+$ 206.1181, found 206.1187.

IR (film) cm^{-1}: 3286, 3237, 3065, 2917, 2848, 1628, 1536.



N-(3-hydroxybutan-2-yl)benzamide (40)

Benzimidate **S40** (71.3 mg, 0.4 mmol) was subjected to **GP4** with the following changes: upon completion (ca 12 hours), the crude mixture was concentrated in a round-bottom flask and a crude ^{1}H NMR was taken (DCE as an internal standard) which indicated a crude oxazoline yield of 88%. Methanol (4 mL) and 2M HCl (0.8 mL) were added to the crude reaction which was then stirred for 12 hours at 50 °C, after workup, the crude material was purified via column chromatography (silica gel, 1% → 2% MeOH/CH_2Cl_2) β-amido alcohol **40** was isolated as a white solid and an inseparable mixture of diastereomers (49 mg, 63%, d.r. 1:1).

R$_f$: 0.17 (5% MeOH/CH_2Cl_2)

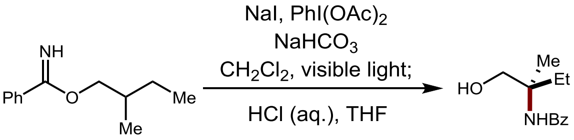
^{1}H NMR (600 MHz, $CDCl_3$): *Diastereomers (a + b)* δ = 7.77 – 7.74 (m, 2Ha), 7.77 – 7.74 (m, 2Hb), 7.50 – 7.45 (m, 1Ha), 7.50 – 7.45 (m, 1Hb), 7.41 – 7.37 (m, 2Ha), 7.41 – 7.37 (m, 2Hb), 6.58 – 6.53 (m, 1Ha), 6.58 – 6.53 (m, 1Hb), 4.22 – 4.14 (m, 1Ha), 4.13 – 4.05 (m, 1Hb), 3.97 – 3.96 (m, 1Ha) 3.85 – 3.82 (m, 1Hb) 3.13 (bs, 1Ha), 2.87 (bs, 1Hb), 1.27 (d, *J* = 6.8 Hz, 3Hb), 1.22 (d, *J* = 6.3 Hz, 3Ha), 1.20 (d, *J* = 6.9 Hz, 3Hb), 1.19 (d, *J* = 6.5 Hz, 3Ha).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 168.0, 167.9, 134.7, 134.6, 131.61, 131.56, 128.6, 127.14, 127.11, 127.08, 70.8, 70.3, 51.1 (2C), 20.8, 19.2, 18.2, 14.3.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{11}H_{15}NO_2Na$ [M+Na]$^+$ 216.1000, found 216.1006.

IR (film) cm^{-1}: 3293, 2970, 2936, 2870, 1627, 1553, 1525.

MP: 84 – 86 °C



N-(1-hydroxy-2-methylbutan-2-yl)benzamide (41)

Benzimidate **S41** (38.3 mg, 0.2 mmol) was subjected to GP4 with the following changes: upon completion (25 hours), the crude mixture was concentrated in a round-bottom flask, and a crude ^{1}H NMR was taken (DCE as an internal standard) which indicated a crude oxazoline yield of 66%. THF (1 mL) and 2M HCl (0.5 mL) was added and stirred for 24 hours at 50 °C. The crude reaction mixture was purified via column chromatography (silica gel, 25% Ethyl acetate/hexanes) to yield β-amido alcohol **41** as a white solid (18 mg, 45%).

R$_f$: 0.29 (50% Ethyl acetate/hexanes)

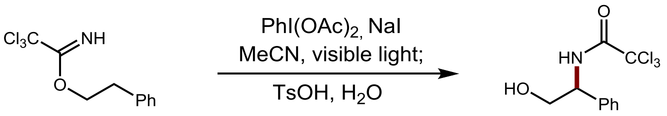
^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.74 – 7.72 (m, 2H), 7.53 – 7.49 (m, 1H), 7.45 – 7.41 (m, 2H), 6.10 (bs, 1H), 4.85 (bs, 1H), 3.74 (q, *J* = 11.0 Hz, 1H), 1.95 – 1.88 (m, 1H), 1.79 – 1.70 (m, 1H), 1.31 (s, 3H), 0.97 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 168.6, 135.1, 131.8, 128.8, 127.0, 69.4, 59.6, 29.4, 22.3, 8.1.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{12}H_{18}NO_2$ [M+H]$^+$ 208.1338, found 208.1343.

IR (film) cm^{-1}: 3369, 3296, 3053, 2938, 2918, 2849, 1639, 1524.

V. Post-Synthetic Functionalization



2,2,2-trichloro-N-(2-hydroxy-1-phenylethyl)acetamide (42)

Trichloroacetimidate **3** (106.6 mg, 0.4 mmol) was subjected to GP4 with the following changes. Upon completion, the mixture was diluted with H_2O (1 mL) and *p*-toluenesulfonic acid monohydrate (380.4 mg, 2.0 mmol) was added and the reaction was allowed to stir for 45 minutes. Upon completion, the reaction was poured into a separatory funnel containing a 1:1 mixture of saturated $NaHCO_3$ and 20% $Na_2S_2O_3$ (15 mL). The aqueous phase was washed with ethyl acetate (3 x 15 mL) and the combined organic solution was dried over $MgSO_4$ and concentrated. The crude material was purified (silica gel, 10 → 20% Ethyl acetate/hexanes) to yield hydroxyacetamide **42** as a white solid (92 mg, 81%).

R_f: 0.32 (25% Ethyl acetate/hexanes)

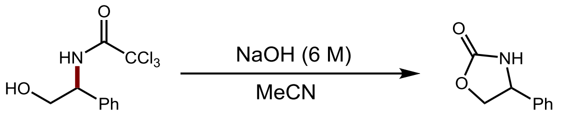
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46 (bs, 1H), 7.43 – 7.38 (m, 2H), 7.36 – 7.32 (m, 3H), 5.06 (dt, *J* = 8.0, 4.0 Hz, 1H), 4.06 – 3.96 (m, 2H), 1.76 (dd, *J* = 6.9, 5.4 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9, 137.6, 129.2, 128.5, 126.6, 92.7, 65.6, 56.8.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{10}H_{13}Cl_3NO_2Na$ $[M+Na]^+$ 303.9675, found 303.9673.

IR (film) cm^{-1}: 3457, 3183, 3021, 2936, 1699, 1540.

MP: 107 – 109 °C



4-phenyloxazolidin-2-one (43)

Hydroxyacetamide **42** (20 mg, 0.7 mmol) was dissolved in MeCN (2 mL) and 6 M NaOH (1.5 mL) was added. The reaction was stirred for three hours and then extracted with CH_2Cl_2., dried over $MgSO_4$, and concentrated to yield oxazolidinone **43** as a white solid (11.6 mg, 100%).

R_f: 0.26 (50% Ethyl acetate/hexanes)

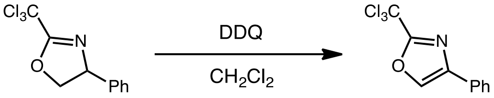
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 – 7.31 (m, 5H), 6.29 (bs, 1H), 4.95 (dd, *J* = 8.0, 7.1 Hz, 1H), 4.72 (t, *J* = 8.7, 1H), 4.17 (dd, *J* = 8.6, 6.8 Hz, 1H).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 160.1, 139.7, 129.3, 128.8, 126.1, 72.3, 56.4.

HRMS (ESI-TOF) *m/z*: calc'd for $C_9H_{10}NO_2$ [M+H]$^+$ 164.0712, found 164.0740.

IR (film) cm^{-1}: 3259, 3148, 2950, 2909, 2840, 1729, 1718, 1595.

MP: 138 – 139 °C



4-phenyl-2-(trichloromethyl)oxazole (44)

To a solution of oxazoline **6** (53 mg, 0.2 mmol) in CH_2Cl_2 was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (182 mg, 0.8 mmol). The reaction mixture was stirred at 50°C for 16 hr. The reaction was concentrated and loaded directly onto silica gel and purified (silica gel, Hexanes → 5% Ethyl acetate/hexanes) to yield the target oxazole **44** (40 mg, 76%) as a white solid.

R$_f$: 0.70 (20% Ethyl acetate/hexanes)

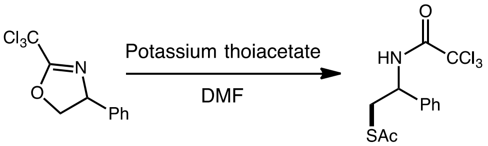
^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.01 (s, 1H), 7.78 – 7.76 (m, 2H), 7.46 – 7.41 (m, 2H), 7.40 – 7.35 (m, 1H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 159.3, 142.1, 135.7, 129.7, 129.1, 129.0, 126.0, 85.7.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{10}H_6Cl_3NONa$ [M+Na]$^+$ 283.9413, found 283.9401.

IR (neat) cm^{-1}: 3146, 3124, 2919, 2850, 1557, 1489, 1448, 1324, 1225, 1118, 1067, 1028, 983, 942, 852, 805, 790.

MP: 84 – 85°C



2-phenyl-2-(2,2,2-trichloroacetamido)ethyl ethanethioate (45)

To a solution of oxazoline **6** (53 mg, 0.2 mmol) in DMF (1 mL) was added potassium thioacetate (46mg, 0.4 mmol). The reaction mixture was stirred at room temperature for 72 hours. The reaction was poured into water and extracted with CH_2Cl_2. The organic layer was concentrated and loaded directly onto silica gel and purified (SiliaFlash® 150 Å, Hexanes → 3% Ethyl acetate/hexanes) to yield the target thioester **45** (39 mg, 57%) as an off-white solid.

(Note: *Potassium thioacetate should be washed thoroughly with hexanes to remove trace amount of thioacetic acid. The reaction does not work in the presence of thioacetic acid.*)

R$_f$: 0.44 (30% Ethyl acetate/hexanes)

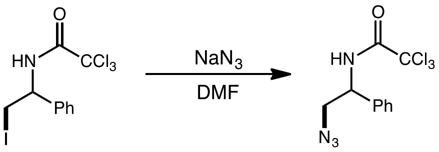
^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.43 (bs, 1H), 7.31 – 7.21 (m, 5H), 4.96 – 4.91 (m, 1H), 3.42 (dd, *J* = 14.6, 10.6 Hz, 1H), 3.06 (dd, *J* = 14.6, 4.0 Hz, 1H), 2.30 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 197.9, 161.8, 139.4, 129.2, 128.6, 126.3, 92.6, 56.8, 34.3, 30.7.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{12}H_{12}Cl_3NO_2SNa$ [M+Na]$^+$ 361.9552, found 361.9521.

IR (neat) cm^{-1}: 3297, 3064, 2980, 2889, 2361, 1693, 1541, 1492, 1398, 1269, 1129, 1093, 1070, 958, 859, 818.

MP: 108– 110 °C



2,2,2-trichloro-N-(2-azido-1-phenylethyl)- acetamide (46)

To a 2-dram vial equipped with PTFE septa cap and magnetic stir bar was added acetamide **47** (39.2 mg, 0.1 mmol), NaN$_3$ (13.0 mg, 0.2 mmol), and DMF (0.5 mL). The reaction was stirred at room temperature for 12 hours. Upon completion (monitored by TLC), the crude reaction was poured into water and extracted with CH_2Cl_2. The organic layer was concentrated and loaded directly onto silica gel and purified (Silica, Hexanes → 10% Ethyl acetate/hexanes) to yield the target azide **46** (26.2 mg, 85%) as a white solid.

R$_f$: 0.48 (20% Ethyl acetate/hexanes)

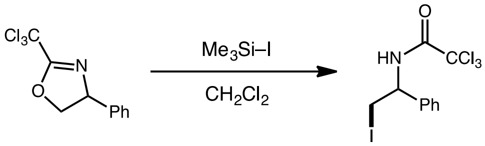
^{1}H NMR (600 MHz, CDCl$_3$): δ = 7.43 – 7.34 (m, 5H), 7.16 (bs, 1H), 5.15 (dt, *J* = 7.8, 5.1 Hz, 1H), 3.83 (dd, *J* = 12.7, 5.0 Hz, 1H), 3.77 (dd, *J* = 12.6, 5.2 Hz, 1H).

^{13}C NMR (125 MHz, CDCl$_3$): δ = 16106, 137.3,, 129.4, 128.9, 126.6, 92.5, 54.9, 54.6.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{10}H_9Cl_3N_4ONa$ [M+Na]$^+$ 328.9740, found 328.9740.

IR (neat) cm^{-1}: 3299, 3068, 2937, 2085, 1688, 1533, 1495, 1445, 1259, 1220, 1097, 820, 762, 701, 637.

MP: 78 – 80 °C



2,2,2-trichloro-*N*-(2-iodo-1-phenylethyl)acetamide (47)

To a 2-dram vial equipped with PTFE septa cap and magnetic stir bar, was added hexamethyldisilane (0.4 mmol) and I_2 (0.4 mmol) under N_2. The reaction was refluxed for 2 hours. After cooling to room temperature, this *in situ* generated $Me_3Si–I$ was added to a solution of oxazoline **6** (53 mg, 0.2 mmol) in CH_2Cl_2 (1 mL) and stirred for 12 hours (99% yield by ^1H NMR: See Sectioni XII). The reaction was concentrated and loaded directly onto silica gel and purified (acidic aluminum oxide, Hexanes → 50% CH_2Cl_2/hexanes) to yield the target iodide **47** (34 mg, 43%) as a white solid.

(Note: *Aluminium oxide, acidic (Brockmann I, 50 – 200 μm,* LOT: A0303504, CAS: 1344-28-1) was used to effectively isolate the desired product. By crude NMR, the reaction yields quantitaive iodide species, however, unknown byproduct (~ 5.9ppm, singlet) co-elutes with both tautomers when silica gel is used. Aluminium oxide avoids this issue)

R_f: 0.49 (20% Ethyl acetate/hexanes)

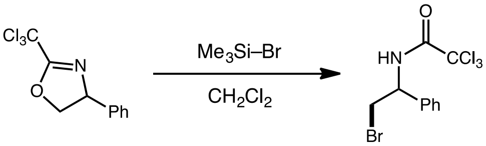
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46 – 7.32 (m, 5H), 7.18 (bs, 1H), 5.11 – 5.06 (m, 1H), 3.69 (dd, J = 10.8, 5.5 Hz, 1H), 3.60 (dd, J = 10.4, 6.1 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.3, 138.3, 129.3, 128.9, 126.2, 92.5, 55.3, 9.9.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{10}H_9Cl_3INONa$ $[M+Na]^+$ 413.8692, found 413.8662.

IR (neat) cm^{-1}: 3246, 3065, 2918, 1673, 1557, 1528, 1495, 1452, 1420, 1339, 1269, 1216, 1179, 1088, 849, 815, 765.

MP: 92 – 94 °C



***N*-(2-bromo-1-phenylethyl)-2,2,2-trichloroacetamide (48)**

To a solution of oxazoline **6** (53 mg, 0.4 mmol) in CH_2Cl_2 was added TMSBr (53 μl, 0.4 mmol). The reaction mixture was stirred at room temperature for 5 min. The reaction was concentrated and loaded directly onto silica gel and purified (silica gel, Hexanes → 20% Ethyl acetate/hexanes) to yield the target bromide **48** (53 mg, 77%) as a white solid.

R_f: 0.44 (20% Ethyl acetate/hexanes)

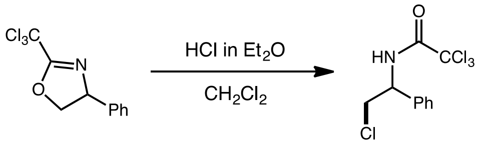
^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.44 – 7.32 (m, 5H), 7.24 (bs, 1H), 5.31 – 5.26 (m, 1H), 3.85 (dd, *J* = 10.8, 4.9 Hz, 1H), 3.77 (dd, *J* = 10.8, 6.0 Hz, 1H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 161.5, 137.4, 129.2, 128.9, 126.4, 92.5, 55.2, 35.8.

HRMS (ESI-TOF) ***m/z***: calc'd for $C_{10}H_9BrCl_3NONa$ [M+Na]$^+$ 365.8831, found 365.8802.

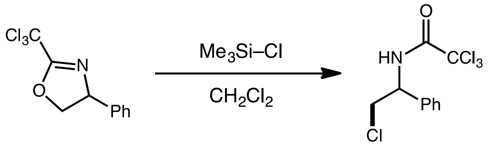
IR (neat) cm^{-1}: 3294, 2980, 2920, 2851, 1691, 1524, 1422, 1266, 1203, 1163, 1024, 971, 861, 840, 822.

MP: 117 – 120 °C



2,2,2-trichloro-*N*-(2-chloro-1-phenylethyl)acetamide (49)

Method A: To a solution of oxazoline **6** (105 mg, 0.4 mmol) in Et$_2$O was added HCl in ether (2M). The reaction mixture was stirred at room temperature for 5 min. The reaction mixture was poured into saturated aqueous NH$_4$Cl and extracted with CH$_2$Cl$_2$ (3 x 25 mL). The organic fraction was dried over MgSO$_4$, concentrated, and purified (silica gel, Hexanes → 10% Ethyl acetate/hexanes) to yield the target chloride **49** (120 mg, 99%) as a white solid.



Method B: To a solution of oxazoline **6** (53 mg, 0.2 mmol) in CH$_2$Cl$_2$ was added Me$_3$Si–Cl (51μl, 0.4 mmol). The reaction mixture was stirred at room temperature for 1 hr. The reaction was concentrated and loaded directly onto silica gel and purified (silica gel, Hexanes → 20% Ethyl acetate/hexanes) to yield the target chloride **49** (51 mg, 85%) as a white solid.

R$_f$: 0.44 (20% Ethyl acetate/hexanes)

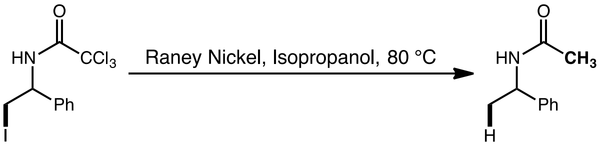
^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.44 – 7.33 (m, 5H), 7.28 (bs, 1H), 5.32 – 5.28 (m, 1H), 3.99 (dd, *J* = 11.6, 4.8 Hz, 1H), 3.91 (dd, *J* = 11.6, 5.7 Hz, 1H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 161.6, 137.0, 129.2, 128.8, 126.6, 92.5, 55.7, 47.1.

HRMS (ESI-TOF) ***m/z***: calc'd for $C_{10}H_9Cl_4NONa$ [M+Na]$^+$ 321.9336, found 321.9316.

IR (neat) cm^{-1}: 3288, 3059, 3030, 2981, 2966, 1692, 1528, 1493, 1428, 1270, 1101, 1051, 879, 822.

MP: 125 – 126 °C



N-(1-phenylethyl)acetamide (50)

To a 2-dram vial equipped with PTFE septa cap and magnetic stir bar, was added the iodide **47** (39.2 mg, 0.1 mmol), excess Raney Nickel (washed with isopropyl alcohol prior to reaction), and isopropyl alcohol (2 mL). The reaction was stirred at 80 °C for 15 min. Upon completion (monitored by TLC), the crude reaction was filtered through a pad of celite and washed thoroughly with ethyl acetate. The filtrate was concentrated to yield acetamide **50** (16.3 mg, quant.) as a white solid.
(Note: *Trichloromethyl is fully reduced to a methyl group.*)

R$_f$: 0.29 (Ethyl acetate)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.35 – 7.23 (m, 5H), 5.87 (bs, 1H), 5.12 (q, *J* = 7.4 Hz, 1H), 1.97 (s, 3H), 1.48 (d, *J* = 6.9 Hz, 3H).

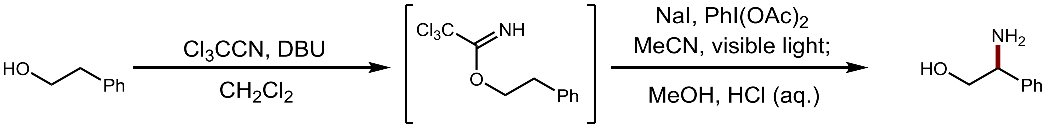
^{13}C NMR (100 MHz, CDCl$_3$): δ = 169.2, 143.3, 128.8, 127.5, 126.3, 48.9, 23.5, 21.8.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{10}H_{13}NONa$ [M+Na]$^+$ 186.0895, found 186.0900.

IR (neat) cm^{-1}: 3258, 3071, 2980, 1639, 1548, 1491, 1443, 1374, 1301, 1279, 1216, 1137, 1027, 741, 701.

MP: 75 – 77 °C

In-situ Imidate Amination

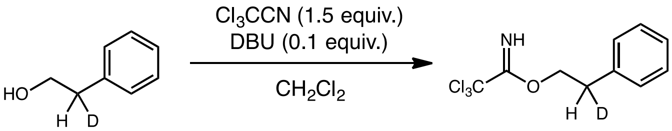


2-amino-2-phenylethan-1-ol (7)

Phenylethanol (49 mg, 48 μL, 0.4 mmol) was subjected to GP1 with the following changes: upon completion of reaction (7 hours), the crude mixture was concentrated and immediately subjected to GP4. After the amination was complete, the crude mixture was concentrated and diluted in hexanes. This solution was passed through a silica plug, eluted (hexanes with 1% Et_3N), and concentrated. The resultant oil was carried forward to the typical acid/base workup which yielded β-amino alcohol **7** as a white solid (44 mg, 80%).

Spectral data matched the above sample.

VI. Kinetic Isotope Effect Experiments



2-phenylethyl-2-*d* 2,2,2-trichloroacetimidate (23)

Following **GP1**, 2-phenylethan-2-*d*-1-ol[4] (86 mg, 0.7mmol) was dissolved in CH_2Cl_2 (0.5 mL) to which trichloroacetonitrile (0.20 g, 0.14 mL, 1.4 mmol) and 1,8-Diazabicyclo(5.4.0)undec-7-ene (10.8 mg, 10.6 uL, 0.07 mmol) were added. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified (hexanes, 1% Et_3N) to yield ***β-d₁*** imidate **23** (131 mg, 70%) as a white solid.

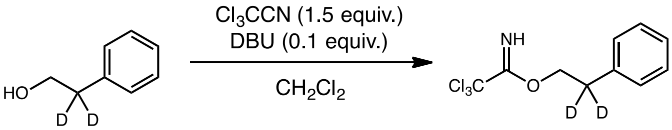
R_f: 0.63 (20% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.26 (bs, 1H), 7.30 – 7.18 (m, 5H), 4.47 (d, *J* = 6.9 Hz, 2H), 3.04 (tt, *J* = 10.4, 1.9 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.0, 137.7, 129.2, 128.6, 126.7, 91.6, 70.0, 34.5 (t, *J* = 19.8 Hz).

HRMS (ESI-TOF) *m/z*: calc'd for $C_{10}H_9DCl_3NONa$ $[M+Na]^+$ 288.9788, found 288.9765.

IR (neat) cm^{-1}: 3341, 3027, 2980, 2889, 2361, 2342, 1661, 1497, 1451, 1381, 1303, 1154, 1074, 997, 825, 794.



2-phenylethyl-2,2-*d*₂ 2,2,2-trichloroacetimidate (25)

Following **GP1**, 2-phenylethan-2-*d*-1-ol[4] (199 mg, 1.6mmol) was dissolved in CH_2Cl_2 (0.5 mL) to which trichloroacetonitrile (0.347 g, 0.241 mL, 2.4 mmol) and 1,8-Diazabicyclo(5.4.0)undec-7-ene (24.3 mg, 23.9 uL, 0.16 mmol) were added. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified (hexanes, 1% Et_3N) to yield ***β-d₂*** imidate **25** (372 mg, 84%) as a white solid.

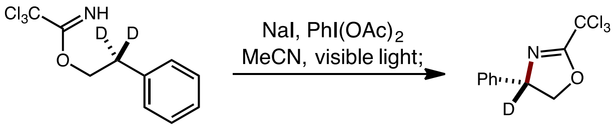
R_f: 0.63 (20% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25 (bs, 1H), 7.30 – 7.18 (m, 5H), 4.46 (s, 2H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 163.0, 137.7, 129.2, 128.6, 126.8, 91.6, 69.9, 34.2 (quint, *J* = 19.6 Hz).

HRMS (ESI-TOF) *m/z*: calc'd for $C_{10}H_8D_2Cl_3NONa$ $[M+Na]^+$ 289.9851, found 289.9824.

IR (neat) cm^{-1}: 3340, 2980, 2889, 2360, 2343, 1661, 1497, 1448, 1379, 1304, 1153, 1070, 1011, 955, 825, 796.



4-phenyl-2-(trichloromethyl)-4,5-dihydrooxazole-4-*d* (26)

β-d$_2$ imidate **25** (53.7 mg, 0.2 mmol) was subjected to GP2. Upon completion, the mixture was poured over 20% $Na_2S_2O_3$ and washed with CH_2Cl_2 (3 x 25 mL). The combined organic layers were dried over $MgSO_4$ and concentrated. The crude material was purified (silica gel, Hexanes → 20% Ethyl acetate/hexanes) to yield ***d$_1$*** oxazoline **26** as a white solid (40 mg, 75%).

R$_f$: 0.26 (10% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.41 – 7.25 (m, 5H), 4.99 (dt, J = 8.6, 1.4 Hz, 1H), 4.51 (d, 1H).

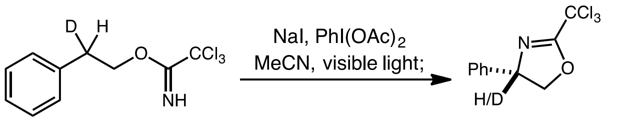
^{13}C NMR (100 MHz, CDCl$_3$): δ = 163.8, 140.3, 129.1, 128.4, 126.7, 86.7, 78.3, 69.9 (t, *J* = 22.3 Hz).

HRMS (ESI-TOF) *m/z*: calc'd for $C_{10}H_7DCl_3NONa$ $[M+Na]^+$ 286..9632, found 286.9624.

IR (neat) cm^{-1}: 3208, 1713, 1655, 1494, 1449, 1352, 1276, 1237, 1060, 992, 946.

Intramolecular Competition

(Note: The rate was significantly influenced by the rate at which reaction was stirred, presumably due to a faster dissolution of sodium iodide and iodobenzene diacetate. To yield consistent kinetic data, the reaction was stirred at 500 rpm, placed 5 cm away from two 23 W CFL bulbs.)

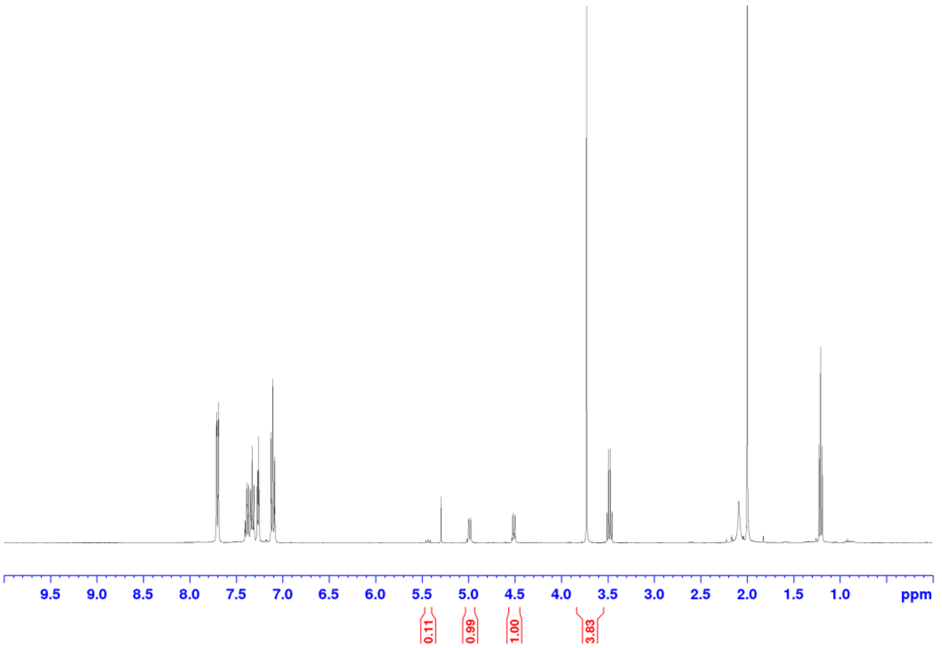


quant., 89%-Deuterium

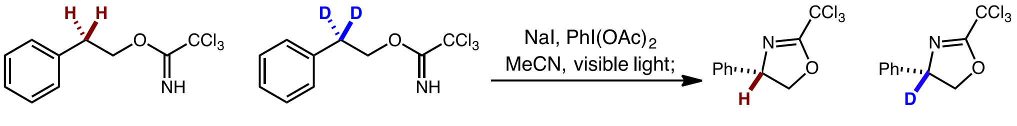
KIE = 8.1

To a 2-dram vial equipped with PTFE septa cap and magnetic stir bar, was added ***β-d_1 phenyethanol imidate*** (0.4 mmol), iodobenzene diacetate (1.2 mmol), and NaI (1.2 mmol). This vial was evacuated and backfilled with N_2 (3x). Dry acetonitrile (4 mL) was degassed using a freeze-pump-thaw technique (3x), then added to the vial under N_2. The reaction was irradiated with two 23 W compact fluorescent light bulbs. After stirring for 2 hours, the crude reaction mixture was poured into 10% $Na_2S_2O_3$ (20 mL), extracted with CH_2Cl_2 (3 x 15 mL), and the combined organic solution was dried over $MgSO_4$ and concentrated. The ^{1}H NMR of crude material (see below) was analyzed for %-deuterium incorporation with 1,2-dichloroethane (0.4 mmol, 1 equiv) as an internal standard (The amination reaction was quantitative).

Note: KIE is calculated by taking the integration of *H/D*-oxazoline (specifically the peak at 5.3 ppm). The integration indicates 89%-deuterium incorporation. The KIE value is calculated by dividing 0.89 by 0.11



Intermolecular Single-Flask Competition



KIE = 4.42

To a 2-dram vial equipped with PTFE septa cap and magnetic stir bar, was carefully added ***β*-H₂ phenyethanol imidate** (0.2 mmol) and ***β*-d₂ phenyethanol imidate** (0.2 mmol). The ratio of two imidates was checked via ^{1}H NMR prior to running the reaction. To this vial, iodobenzene diacetate (1.2 mmol) and NaI (1.2 mmol) were added. The vial was then evacuated and backfilled with N_2 (3x). Dry acetonitrile (4 mL) was degassed using a freeze-pump-thaw technique (3x), and was added to the vial under N_2. The reaction was irradiated with two 23 W compact fluorescent light bulbs. After stirring for 2 min, the crude reaction mixture was poured into 10% $Na_2S_2O_3$ (20 mL), extracted with CH_2Cl_2 (3 x 15 mL), and the combined organic solution was dried over $MgSO_4$ and concentrated. The ^{1}H NMR of crude material was analyzed for product distribution of deuterio and proteo-oxazoline with 1,2-dichloroethane (0.4 mmol, 1 equiv) as an internal standard. The reaction was repeated for 5 more time points (i.e. 5, 10, 20, 30, 60 min).

Table 1: KIE from intermolecular single-flask competition

Time (min)	SM ratio (H_2 to D_2)	*β*-H_2 imidate	*β*-d_2 imidate	*H*-oxazoline	*d*-oxazoline	KIE
2	1 to 0.90	43%	36%	—	—	—
5	1 to 0.94	43%	37%	—	—	—
10	1 to 0.95	45%	48%	8%	2%	4.42
20	1 to 0.96	26%	44%	27%	6%	4.64
30	1 to 0.95	0%	24%	51%	31%	1.62
60	1 to 0.96	0%	1%	51%	52%	0.98

Note: KIE is calculated by taking the ratio of *H*-oxazoline and *d*-oxazoline at each time point. Since the reaction displays pseudo first-order kinetics (see Figure 1) between 10 and 20 min, the KIE value from *t* = 20 min was used for the intermolecular single-flask competition experiment

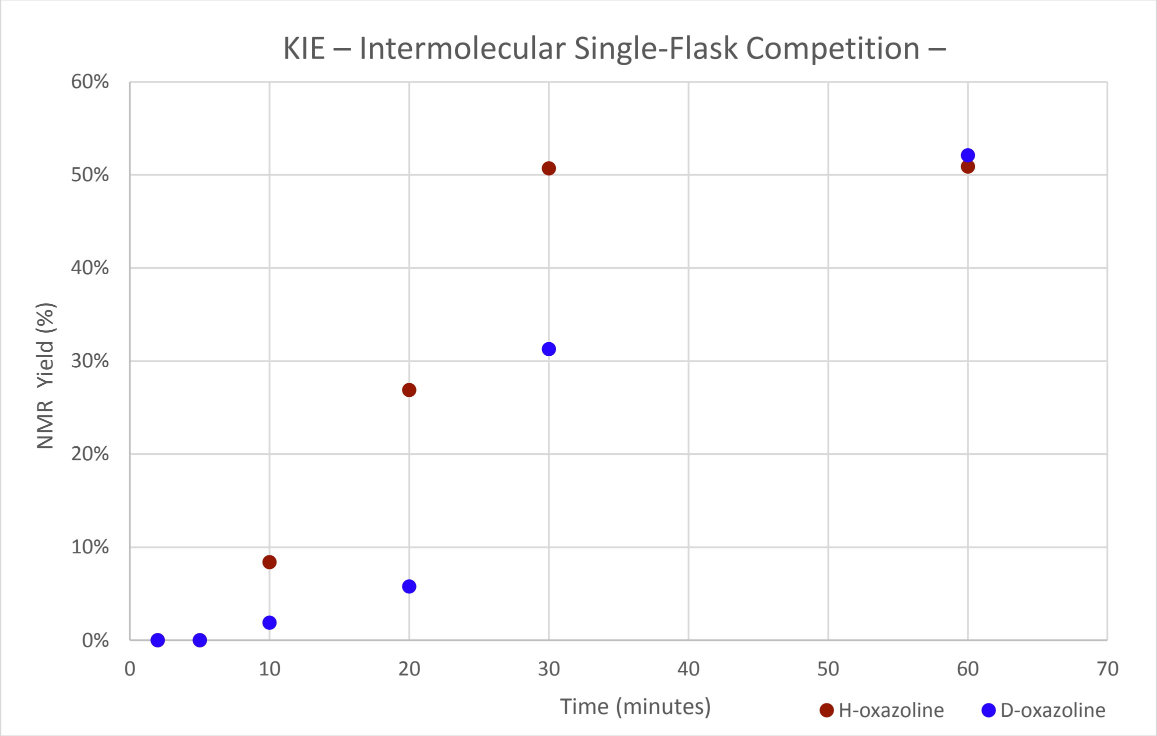
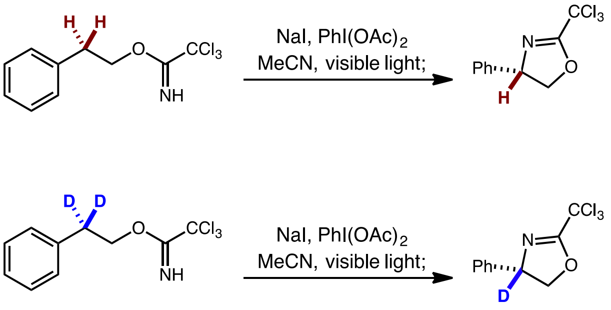


Figure 1: Kinetic profile from intermolecular single-flask competition determined by crude ^{1}H NMR

Intermolecular Parallel Reaction



To a 2-dram vial equipped with PTFE septa cap and magnetic stir bar, was carefully added ***β-H₂ phenyethanol imidate*** (0.2 mmol), iodobenzene diacetate (0.6 mmol), and NaI (0.6 mmol). This vial was evacuated and backfilled with N_2 (3x). Dry acetonitrile (4 mL) was degassed using a freeze-pump-thaw technique (3x), then added to the vial under N_2. The reaction was irradiated with two 23 W compact fluorescent light bulbs. After stirring for 10 min, the crude reaction mixture was poured into 10% $Na_2S_2O_3$

(20 mL), extracted with CH_2Cl_2 (3 x 15 mL), and the combined organic solution was dried over $MgSO_4$ and concentrated. The ^1H NMR of crude material was analyzed using 1,2-dichloroethane (0.4 mmol, 1 equiv) as an internal standard. The reaction was repeated for 3 more time points (i.e. 11, 13, 15 min). The NMR yields of the product were plotted against time in minutes. The slope through four points were utilized as initial rate of the reaction. The procedure was repeated for ***β*-d₂ phenyethanol imidate** (i.e. 10, 11, 13, 15 min). Calculated values are tabulated below.

Initial rates for β-H₂ phenyethanol imidate

Run	H-Initial rate	R^2
1	0.0110	0.999
2	0.0097	0.995
3	0.0104	0.944
Avg.	**0.0103**	

Initial rates for β-d₂ phenyethanol imidate

Run	D-Initial rate	R^2
1	0.0039	0.929
2	0.0042	0.901
3	0.0065	0.949
4	0.0065	0.951
Avg. of 1 & 2	**0.0041**	
Avg. of 3 & 4	**0.0065**	

KIE (using avg. of 1 & 2) = K_H/K_D = 2.5

KIE (using avg. of 3 & 4) = K_H/K_D = 1.6

Average KIE = 2.1

Note: While the yield for ***β*-H₂ phenyethanol imidate** was relatively high (~15%), the yield for ***β*-d₂ phenyethanol imidate** was low (<3%) in the first 15 minutes. Thus, when analyzing via ^1H NMR, the inconsistent integration for deuterio-substrate led to low R^2 values. We obtained two sets of consistent initial rates for ***β*-d₂ phenyethanol imidate**, which are all reported above. The average from both low (Runs 1 & 2) and high (Runs 3 & 4) rates were used to calculate KIE values (2.5 and 1.6, respectively). Then, we took the average of both to determine the KIE value from this parallel reaction, which yielded the final KIE value of 2.1.

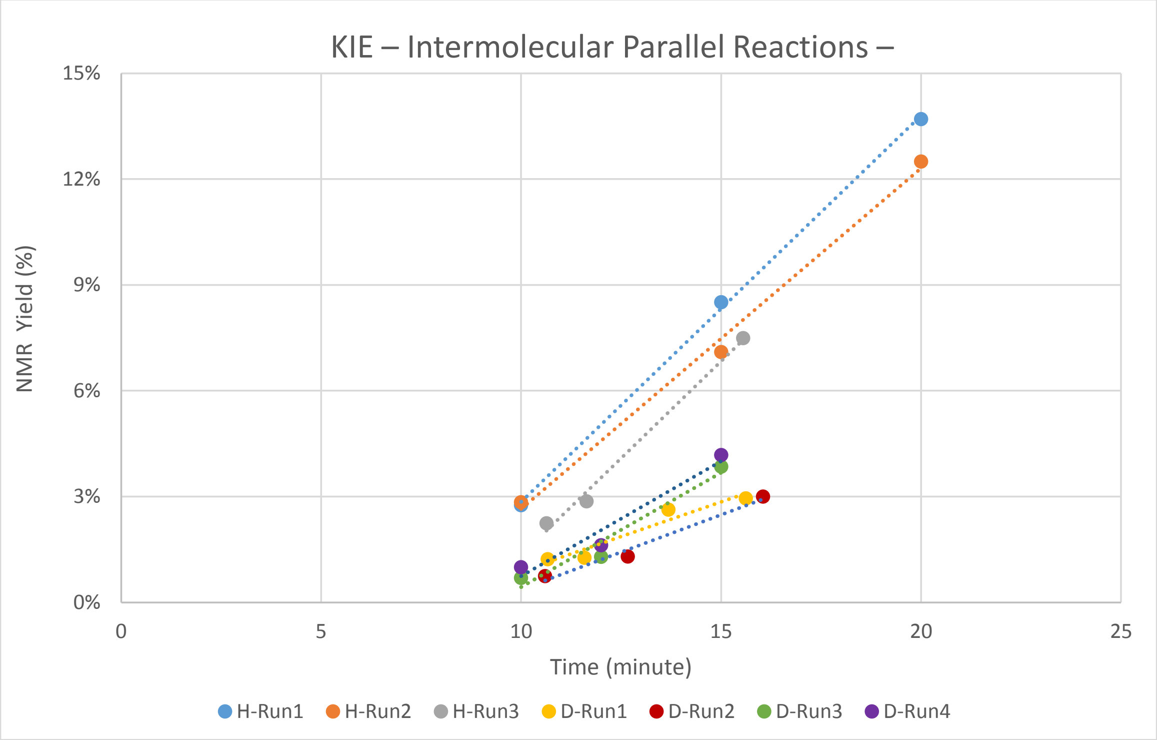
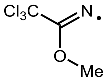
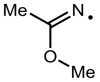
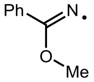
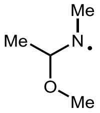
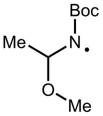
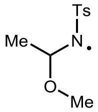


Figure 2: Kinetic profile from intermolecular parallel reaction determined by crude ^{1}H NMR

VII. SOMO Calculations

The structures of various N-centered radicals were optimized using Spartan ’16 (see Section IX for details). We have performed DFT studies of the relative SOMO energies of various N-centered radicals to gain a better understanding of imidate radical reactivity. Comparing these SOMO energies indicates that the R group on the imidate is directly correlated to relative reactivity.

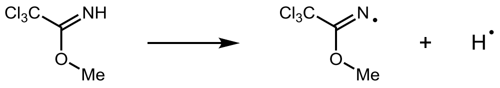
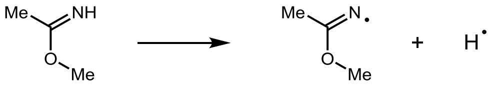
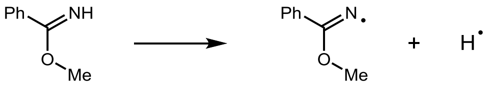
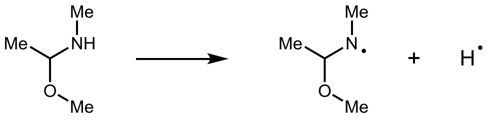
Structure optimization: ωB97X-D/6-31G(D)

N-Centered Radical	E HOMO (eV)	Relative E HOMO
	–10.34	–1.47
	–9.56	–0.69
	–8.89	–0.02
	–8.87	0.00
	–9.30	–0.43
	–9.22	–0.35

VIII. Bond Dissociation Enthalpy (BDE) Calculations

We have performed DFT studies to determine the hemolytic N-H BDEs of various imidates. All imidates have an N-H BDE of 100 – 101 kcal/mol despite the various substituents further supporting the importance of the relative SOMO energies.

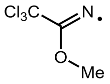
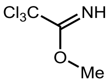
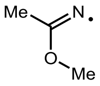
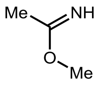
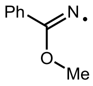
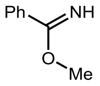
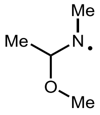
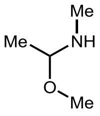
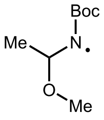
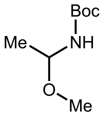
Structure optimization: ωB97X-D/6-31G(D)

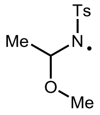
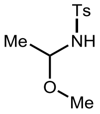
Fragmentation Reaction	BDE (kcal/mol)
	100.6
	101.1
	100.3
	100.0

IX. Computational Studies

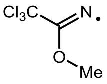
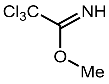
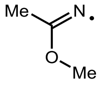
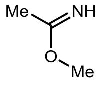
a. Computational Methods

Density functional theory (DFT) calculations were performed using Spartan ‘16[5]. All geometries were optimized at the ωB97X-D/6-31G(D)[6] level of theory and used for the determination of homolytic bond dissociation enthalpies (BDE).

N-Centered Radical	Total Energy (hartrees)
	–1626.456521
	–1627.117406
	–247.753246
	–248.415011
	–439.422545
	–440.082956
	–288.254531
	–288.914502
	–594.683868
	–595.357544

	–1067.747061
	–1068.413078

b. Optimized Cartesian Coordinates

N-Centered Radical	Cartesian Coordinates
	C C1 -0.4206844 0.0000001 0.3357784 O O1 0.5951583 0.0000005 -0.5288722 C C2 0.2190396 0.0000000 -1.9082196 N N1 -1.6473787 -0.0000002 0.0341773 C C3 0.0629285 0.0000000 1.7899272 Cl Cl1 1.0507509 -1.4594757 2.0687192 Cl Cl2 -1.3321472 -0.0000001 2.8889092 Cl Cl3 1.0507510 1.4594756 2.0687194 H H1 -0.3664847 0.8940109 -2.1421046 H H2 1.1545511 0.0000000 -2.4649303 H H3 -0.3664846 -0.8940112 -2.1421040
	N N1 -1.5812450 0.0000000 0.0606202 C C1 -0.3618609 0.0000000 0.3793410 C C2 0.0593077 0.0000000 1.8601633 O O1 0.7384112 0.0000000 -0.3874278 C C3 0.5499423 0.0000000 -1.7926658 Cl Cl1 -1.3421222 0.0000000 2.9369729 Cl Cl2 1.0475191 -1.4611005 2.1721192 Cl Cl3 1.0475191 1.4611005 2.1721192 H H1 -1.7282606 0.0000000 -0.9472399 H H2 0.0105997 0.8979342 -2.1150089 H H3 0.0105997 -0.8979342 -2.1150089 H H4 1.5495900 0.0000000 -2.2239847
	C C1 0.3253905 0.0000000 -1.8112669 C C2 -0.3357848 0.0000000 -0.4609685 N N1 -1.5907631 0.0000000 -0.3048114 O O1 0.5551628 0.0000000 0.5540557 C C3 -0.0136670 0.0000000 1.8601507 H H1 0.9585618 -0.8868048 -1.9067718 H H2 0.9585618 0.8868048 -1.9067718 H H3 -0.4253501 0.0000000 -2.6025300 H H4 -0.6301161 -0.8917165 2.0132330 H H5 -0.6301161 0.8917165 2.0132330 H H6 0.8281202 0.0000000 2.5524480
	C C1 -0.4049045 -0.3030441 -1.7130525 C C2 -0.0848808 -0.3456875 -0.2418623 N N1 -0.0029882 -1.3526060 0.5289654 O O1 0.1280009 0.8998261 0.2202709 C C3 0.4426772 1.0080537 1.6022361 H H1 0.4224802 0.1580812 -2.2605195 H H2 -1.2941974 0.3107889 -1.8834632 H H3 -0.5805005 -1.3057997 -2.1075469 H H4 -0.1923252 -2.2084828 0.0122358

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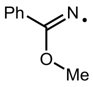
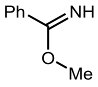
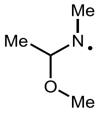
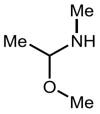
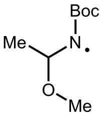
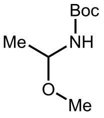
	C C1 0.5166527 0.0000000 1.2607365 N N1 1.6821539 0.0000000 1.7630843 O O1 -0.6040855 0.0000000 2.0143382 C C2 -0.3900074 0.0000000 3.4221825 C C3 0.2556556 0.0000000 -0.2038349 C C4 -0.2104528 0.0000000 -2.9507886 C C5 1.3309566 0.0000000 -1.0969674 C C6 -1.0525029 0.0000000 -0.6896191 C C7 -1.2813276 0.0000000 -2.0620690 C C8 1.0960207 0.0000000 -2.4654600 H H1 0.1669815 0.8918988 3.7267527 H H2 -1.3816870 0.0000000 3.8739683 H H3 0.1669815 -0.8918988 3.7267527 H H4 -0.3923866 0.0000000 -4.0213745 H H5 2.3463068 0.0000000 -0.7126943 H H6 -1.8830274 0.0000000 0.0069132 H H7 -2.3004860 0.0000000 -2.4365408 H H8 1.9342541 0.0000000 -3.1553797
	C C1 0.4694767 0.0000001 1.1284518 N N1 1.6587723 -0.0000001 1.5765356 O O1 -0.6846289 0.0000002 1.8442081 C C2 -0.5882450 0.0000000 3.2527074 C C3 0.1951998 0.0000001 -0.3340946 C C4 -0.2666393 0.0000000 -3.0869650 C C5 1.2697154 0.0000000 -1.2275265 C C6 -1.1108449 0.0000000 -0.8277286 C C7 -1.3388091 0.0000000 -2.2000835 C C8 1.0380852 0.0000000 -2.5968582 H H1 1.7068310 0.0000001 2.5932820 H H2 -0.0713933 0.8954844 3.6183891 H H3 -1.6135000 0.0000001 3.6224772 H H4 -0.0713933 -0.8954846 3.6183890 H H5 -0.4465614 -0.0000001 -4.1581476 H H6 2.2782907 0.0000000 -0.8283321 H H7 -1.9446223 0.0000000 -0.1352013 H H8 -2.3580107 0.0000000 -2.5747268 H H9 1.8782771 0.0000000 -3.2847760
	C C1 -0.2787660 0.4872804 -1.7396912 C C2 -0.1914409 0.2845631 -0.2254138 N N1 0.7800662 -0.7214372 0.1077356 O O1 0.1696328 1.5239413 0.3183320 C C3 0.2901692 -2.0611581 -0.0568486 C C4 0.2109649 1.5228437 1.7255595 H H1 0.7117830 0.7357410 -2.1289406 H H2 -0.6501979 -0.4089606 -2.2433495 H H3 -0.9588196 1.3167473 -1.9469649 H H4 -1.1889990 -0.0106784 0.1670734 H H5 1.0945309 -2.7791485 0.1206587 H H6 -0.5199298 -2.2609821 0.6648705 H H7 -0.1323266 -2.2455340 -1.0578319 H H8 0.4663470 2.5381294 2.0355857 H H9 -0.7689206 1.2545031 2.1531576 H H10 0.9659065 0.8241497 2.1060675

	C C1 -0.6871675 0.0707882 -1.9666158 N N1 0.2439107 -0.3091228 -0.9193241 C C2 -0.0263317 0.2678938 0.3860805 O O1 0.6751181 -0.4317557 1.3810615 C C3 0.2620051 -1.7709759 1.5281849 C C4 0.3748729 1.7309867 0.5334533 H H1 -0.4094706 -0.4353028 -2.8957616 H H2 -1.6932570 -0.2672973 -1.6944793 H H3 -0.7417528 1.1538837 -2.1723870 H H4 1.1982368 -0.0856635 -1.1889606 H H5 -1.1141771 0.1628835 0.5484674 H H6 0.8846840 -2.2085809 2.3114917 H H7 -0.7937152 -1.8278288 1.8377053 H H8 0.3845414 -2.3336925 0.5964867 H H9 1.4586643 1.8298822 0.4079767 H H10 -0.1254683 2.3484484 -0.2191498 H H11 0.1093069 2.1054539 1.5257702
	C C1 -0.1499691 2.2651141 0.5055315 N N1 -0.5424189 1.1114432 1.2779732 C C2 0.1784207 -0.0536581 1.0209543 O O1 1.0711888 -0.4299509 1.7476556 O O2 -0.2924360 -0.6588141 -0.0701875 C C3 0.2549770 -1.9411590 -0.5226624 C C4 1.7282820 -1.7713153 -0.8874444 C C5 0.0417075 -3.0070095 0.5498938 C C6 -0.5801034 -2.2456014 -1.7622410 O O3 -1.0180194 3.3303626 0.7270940 C C7 -2.3423522 3.0752530 0.3141706 C C8 1.2572651 2.7337669 0.8801130 H H1 -0.1762583 1.9708337 -0.5641335 H H2 1.8478704 -0.9627666 -1.6163021 H H3 2.3293508 -1.5478277 -0.0045095 H H4 2.0990880 -2.6963877 -1.3405518 H H5 0.3354525 -3.9836335 0.1516623 H H6 -1.0151369 -3.0552625 0.8307510 H H7 0.6366940 -2.7980954 1.4401095 H H8 -0.2607895 -3.1958651 -2.2008329 H H9 -1.6404046 -2.3193174 -1.5031993 H H10 -0.4592531 -1.4578509 -2.5121199 H H11 -2.7856065 2.2451905 0.8770605 H H12 -2.9109038 3.9874029 0.5030559 H H13 -2.3845913 2.8390403 -0.7604420 H H14 1.2853437 2.9820770 1.9432797 H H15 1.9985224 1.9574955 0.6781214 H H16 1.4940802 3.6265355 0.2971998
	C C1 -1.3156783 1.6872685 -2.8901062 C C2 -0.5968666 1.7564318 -1.5450233 C C3 0.8892053 2.0512407 -1.7448636 C C4 -1.2687193 2.7782318 -0.6287990 O O1 -0.7746660 0.4105384 -1.0176384 C C5 -0.2797759 0.0701062 0.1880320 O O2 0.3426950 0.7960556 0.9332914 N N1 -0.6441033 -1.2318380 0.4495569 C C6 0.0294012 -2.0585711 1.4178909 O O3 1.3080664 -2.3720074 0.8960688 C C7 0.0830490 -1.4385691 2.8098442 C C8 1.9866457 -3.3846226 1.5937538 H H1 -0.8605918 0.9253587 -3.5302982 H H2 -1.2501011 2.6539137 -3.3990840 H H3 -2.3718939 1.4380974 -2.7495453 H H4 1.3481809 1.2741817 -2.3646852 H H5 1.0046360 3.0120838 -2.2574428 H H6 1.4116378 2.0957748 -0.7883608 H H7 -0.7596653 2.8335945 0.3342428 H H8 -2.3164040 2.5061039 -0.4636607

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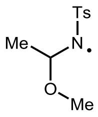
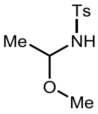
	N N1 -0.0572889 1.3360867 -0.9413513 S S1 -1.1679428 0.8990216 0.2365633 O O1 -2.3807075 0.5550379 -0.4999823 O O2 -1.2066815 1.9003003 1.2957479 C C1 -0.4445164 -0.5814482 0.8840051 C C2 0.7072933 -2.9068818 1.8893987 C C3 0.3032425 -0.5198963 2.0542724 C C4 -0.6362099 -1.7841900 0.2095855 C C5 -0.0582595 -2.9382451 0.7186756 C C6 0.8739725 -1.6868130 2.5486057 C C7 1.3512218 -4.1636958 2.4147676 C C8 -0.3055548 2.6454167 -1.5346638 O O3 0.1016836 2.6232713 -2.8654081 C C9 0.5369001 3.6868552 -0.7993066 C C10 -0.7103126 1.8071636 -3.6855016 H H1 0.4225853 0.4251248 2.5729875 H H2 -1.2408836 -1.8124246 -0.6905526 H H3 -0.2077932 -3.8826505 0.2024619 H H4 1.4550045 -1.6485058 3.4658728 H H5 0.7083862 -5.0351321 2.2585956 H H6 2.2982322 -4.3563748 1.8969736 H H7 1.5681257 -4.0857584 3.4837950 H H8 -1.3753896 2.9093552 -1.4702824 H H9 1.5906855 3.4017491 -0.8435058 H H10 0.2169957 3.7682156 0.2409664 H H11 0.4054810 4.6473699 -1.3038717 H H12 -0.3289519 1.9103414 -4.7025966 H H13 -0.6591436 0.7542276 -3.3818819 H H14 -1.7601741 2.1324796 -3.6543699
	N N1 0.7398024 -0.0420980 1.4309150 C C1 1.0350396 -1.2425210 2.2017900 S S1 -0.8758040 0.2794514 1.0831910 O O1 -1.5854147 -0.9888176 1.1782699 O O2 -1.3000932 1.4520808 1.8320731 C C2 -0.8065915 0.7390067 -0.6348186 C C3 -0.6827553 1.4533026 -3.3254120 C C4 -0.6790438 -0.2553636 -1.6026284 C C5 -0.8811991 2.0788723 -0.9891582 C C6 -0.8178604 2.4266185 -2.3358395 C C7 -0.6168754 0.1087817 -2.9385495 C C8 -0.6198762 1.8250571 -4.7847036 O O3 0.5836181 -1.1090941 3.5299045 C C9 -0.2347883 -2.1682043 3.9813177 C C10 2.5395581 -1.4715312 2.1959586 H H1 1.1529810 0.7890677 1.8479026 H H2 0.5158428 -2.0680997 1.7047446 H H3 -0.6424489 -1.2988499 -1.3076443 H H4 -1.0008844 2.8341618 -0.2197875 H H5 -0.8794332 3.4739033 -2.6184781 H H6 -0.5200838 -0.6618369 -3.6990228 H H7 0.2999983 1.4493133 -5.2458549 H H8 -1.4617894 1.3907228 -5.3349863 H H9 -0.6495785 2.9090386 -4.9243033 H H10 0.3092616 -3.1245093 3.9878984 H H11 -0.5233461 -1.9237013 5.0052760 H H12 -1.1345383 -2.2637218 3.3620274

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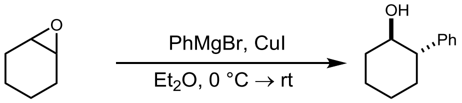
X. Miscellaneous Experiments

a. Stereochemical Probe

To further probe the active intermediates in the reaction, a couple stereochemical probes were synthesized.



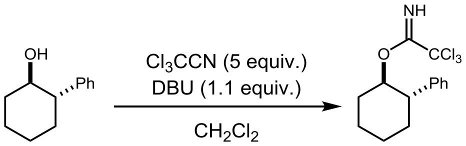
***trans*-2-phenylcyclohexan-1-ol**

Alcohol was synthesized according to the literature.[7] PhMgBr (11.9 mL, 35.6 mmol, 3M in Et_2O) was diluted with 50 mL of dry Et_2O. This solution was cooled to 0 °C followed by the addition of CuI (0.28 g, 1.5 mmol). Cyclohexaneoxide (3 g, 30.6 mmol) was dissolved in 50 mL of Et_2O and added dropwise to the reaction mixture over 30 minutes. The resultant solution was stirred for 7 hours and then quenched with MeOH. The reaction mixture was transferred to a separatory funnel containing 200 mL of water. The organic phase was collected and the aqueous phase was extracted with Et_2O (2 x 50 mL). The combined organic solution was dried over $MgSO_4$ and concentrated. Crude material was purified via column chromatography (silica gel, 5% Ethyl acetate/hexanes) to yield the desired alcohol (1.27 g, 24%) as a white solid. Spectroscopic data matches the literature.

R_f: 0.17 (10% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35 – 7.32 (m, 2H), 7.27 – 7.23 (m, 3H), 3.67 (tdd, *J* = 10.1, 4.1, 2.7 Hz, 1H), 2.43 (ddd, *J* = 12.7, 9.3, 3.3 Hz, 1H), 2.14 – 2.11 (m, 1H), 1.89 – 1.85 (m, 2H), 1.79 – 1.75 (m, 1H), 1.56 – 1.49 (m, 2H), 1.46 – 1.31 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.4, 128.9, 128.1, 127.0, 74.6, 53.4, 34.6, 33.5, 26.2, 25.2.



***trans*-2-phenylcyclohexyl 2,2,2-trichloroacetimidate**

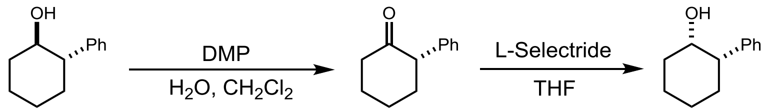
Following GP1, *trans*-2-phenylcyclohexan-1-ol (0.2 g, 1.1 mmol) was dissolved in CH_2Cl_2 (10 mL) to which trichloroacetonitrile (0.82 g, 0.57 mL, 5.7 mmol) and 1,8-Diazabicyclo(5.4.0)undec-7-ene (0.19 g, 0.19 mL, 0.13 mmol) were added. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified (hexanes, 1% Et_3N) to yield imidate (0.12 g, 33%) as a colorless oil.

R$_f$: 0.52 (10% Ethyl acetate/hexanes)

^{1}H NMR (600 MHz, CDCl$_3$): δ = 8.05 (bs, 1H), 7.28 – 7.24 (m, 4H), 7.19 – 7.15 (m, 1H), 5.13 – 5.09 (m, 1H), 2.86 (ddd, *J* = 12.4, 10.8, 3.8 Hz, 1H), 2.40 – 2.37 (m, 1H), 2.02 – 1.98 (m, 1H), 1.94 – 1.91 (m, 1H), 1.85 – 1.82 (m, 1H), 1.64 (app qd, *J* = 13.1, 3.7 Hz, 1H), 1.56 – 1.48 (m, 2H), 1.46 – 1.38 (m, 1H).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 162.3, 143.2, 128.3, 127.8, 126.5, 91.9, 81.5, 50.0, 34.0, 31.0, 26.0, 24.8.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{14}H_{17}Cl_3NO$ [M+H]$^+$ 320.0376, found 320.0399.



cis-2-phenylcyclohexan-1-ol

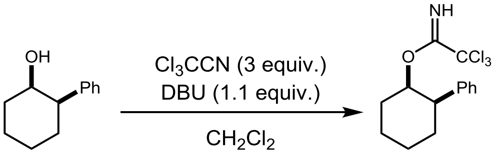
Ketone was synthesized according to the literature.[8] *trans*-2-phenylcyclohexan-1-ol (62 mg, 0.35 mmol) and Dess-Martin Periodinane (0.17 g, 0.4 mmol) were dissolved in dry CH_2Cl_2 (10 mL) and stirred. CH_2Cl_2 was saturated with H_2O (7.6 µL, 0.42 mmol) and added dropwise over 30 minutes as the solution slowly became clear. Upon complete addition, the solution concentrated. The crude reaction was purified via column chromatography (silica gel, 10% ethyl acetate/hexanes) to yield desired ketone as a white solid (52 mg, 78%).

cis-2-phenylcyclohexan-1-ol was synthesized according to the literature.[9] L-selectride (1 M in THF, 0.59 mL, 0.59 mmol) was diluted in dry THF (1 mL). The ketone (51 mg, 0.29 mmol) was dissolve in dry THF (1 mL) and added dropwise via syringe. The reaction was stirred for 1 hour and then quenched by addition of 3 M NaOH (2.5 mL) followed by stirring for 10 minutes and then 30% H_2O_2 (2.5 mL). After stirring for 30 minutes, the mixture was extracted with Et_2O, dried over $MgSO_4$ and concentrated. The crude reaction was purified via column chromatography (silica gel, 10% Ethyl acetate/hexanes) to yield target alcohol as a clear oil (47 mg, 77%).

R$_f$: 0.55 (20% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.36 – 7.33 (m, 2H), 7.29 – 7.22 (m, 3H), 4.02 (bs, 1H), 2.76 (dt, *J* = 12.9, 2.3 Hz, 1H), 2.08 (qd, *J* = 12.9, 3.6 Hz, 1H), 2.01 – 1.97 (m, 1H), 1.93 – 1.87 (m, 1H), 1.77 – 1.61 (m, 3H), 1.57 – 1.53 (m, 1H), 1.41 (qd, *J* = 12.9, 3.7 Hz, 1H), 1.29 (dd, *J* = 2.9, 1.4 Hz, 1H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 144.2, 128.7, 127.9, 126.6, 70.8, 66.0, 48.2, 33.2, 26.4, 24.6, 19.7, 15.4.



cis-2-phenylcyclohexyl 2,2,2-trichloroacetimidate

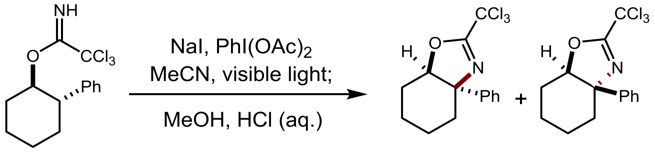
Following **GP1**, *cis*-2-phenylcyclohexan-1-ol (58.6 mg, 0.3 mmol) was dissolved in CH_2Cl_2 (5 mL) to which trichloroacetonitrile (0.14 g, 0.1 mL, 1.0 mmol) and 1,8-Diazabicyclo(5.4.0)undec-7-ene (56 mg, 0.055 mL, 0.4 mmol) were added. Upon completion (monitored by TLC) the reaction was concentrated and loaded directly onto silica gel and purified (hexanes, 1% Et_3N) to yield imidate (8 mg, 8%) as a colorless oil.

R_f: 0.58 (10% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (bs, 1H), 7.33 – 7.15 (m, 5H), 5.27 (bs, 1H), 2.87 (dt, *J* = 12.9, 2.9 Hz, 1H), 2.36 – 2.31 (m, 1H), 2.21 (qd, *J* = 13.0, 3.6 Hz, 1H), 1.98 – 1.92 (m, 1H), 1.84 – 1.80 (m, 1H), 1.75 – 1.46 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.0, 143.1, 128.4, 128.3, 128.1, 126.5, 92.2, 78.8, 47.2, 29.2, 26.2, 26.1, 20.4.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{14}H_{17}Cl_3NO$ $[M+H]^+$ 320.0376, found 320.0399.



cis/trans-2-amino-2-phenylcyclohexan-1-ol

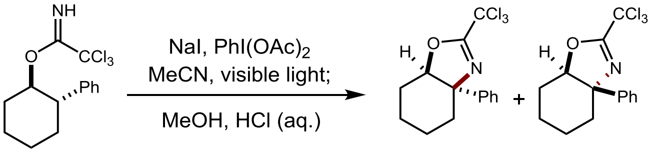
Trichloroacetimidate (128 mg, 0.4 mmol) was subjected to **GP4**. After workup, a separable diastereomeric mixture of oxazoline was isolated as a white solid (102 mg, 80%, dr 2:1).

R_f: 0.44 (*cis* isomer), 0.19 (*trans* isomer) (10% Ethyl acetate/hexanes)

^{1}H NMR (400 MHz, $CDCl_3$): *Major diastereomer (cis)*: δ = 7.44 – 7.41 (m, 2H), 7.39 – 7.36 (m, 2H), 7.31 – 7.27 (m, 1H), 5.03 (t, *J* = 3.5 Hz, 1H), 2.24 – 2.17 (m, 1H), 2.12 – 2.05 (m, 1H), 2.00 – 1.90 (m, 2H), 1.76 – 1.61 (m, 4H). *Minor diastereomer (trans)*: δ = 7.62 – 7.60 (m, 2H), 7.36 – 7.28 (m, 3H), 4.56 – 4.52 (m, 1H), 3.06 – 3.01 (m, 1H), 2.41 – 2.32 (m, 2H), 1.94 – 1.83 (m, 2H), 1.74 – 1.67 (m, 1H), 1.59 – 1.46 (m, 1H), 1.40 – 1.28 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): *Major diastereomer (cis)*: δ = 161.6, 145.6, 128.8, 127.5, 125.4, 88.8, 87.3, 74.3, 34.0, 25.3, 17.8, 16.1. *Minor diastereomer (trans)*: δ = 163.4, 138.4, 129.1, 128.2, 127.3, 94.1, 87.9, 74.4, 34.8, 25.6, 25.0, 22.2.

HRMS (ESI-TOF) *m/z*: calc'd for $C_{14}H_{14}Cl_3NONa$ $[M+Na]^+$ 340.0039, found 340.0032.



cis/trans-2-amino-2-phenylcyclohexan-1-ol

Trichloroacetimidate (8 mg, 0.025 mmol) was subjected to **GP4**. Upon completion, a crude ^{1}H NMR was taken (DCE as internal standard). Analysis revealed less than 5% of the target compounds.

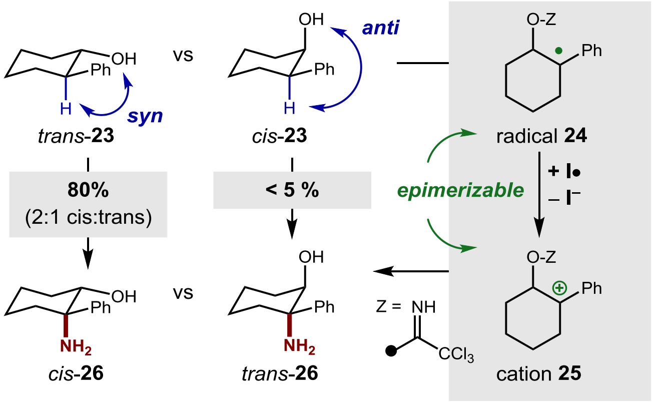


Figure 3: Explanation of the mechanistic pathway leading to diastereomeric products.

After subjecting both diastereomers to the reaction conditions, we found that only the *trans*-imidate cyclized effectively. The *cis*-imidate resulted in a messy mixture of products that resulted in no isolable target material or other compounds. The lack of desired reactivity for the *cis*-imidate is attributed to the relative distance of the N-centered radical from the benzylic C-H bond. Epimerization of the tertiary carbon occurs through either radical inversion which is known to be rapid, or an S_N1 amination of the resultant tertiary, benzyl cation.

XI. References

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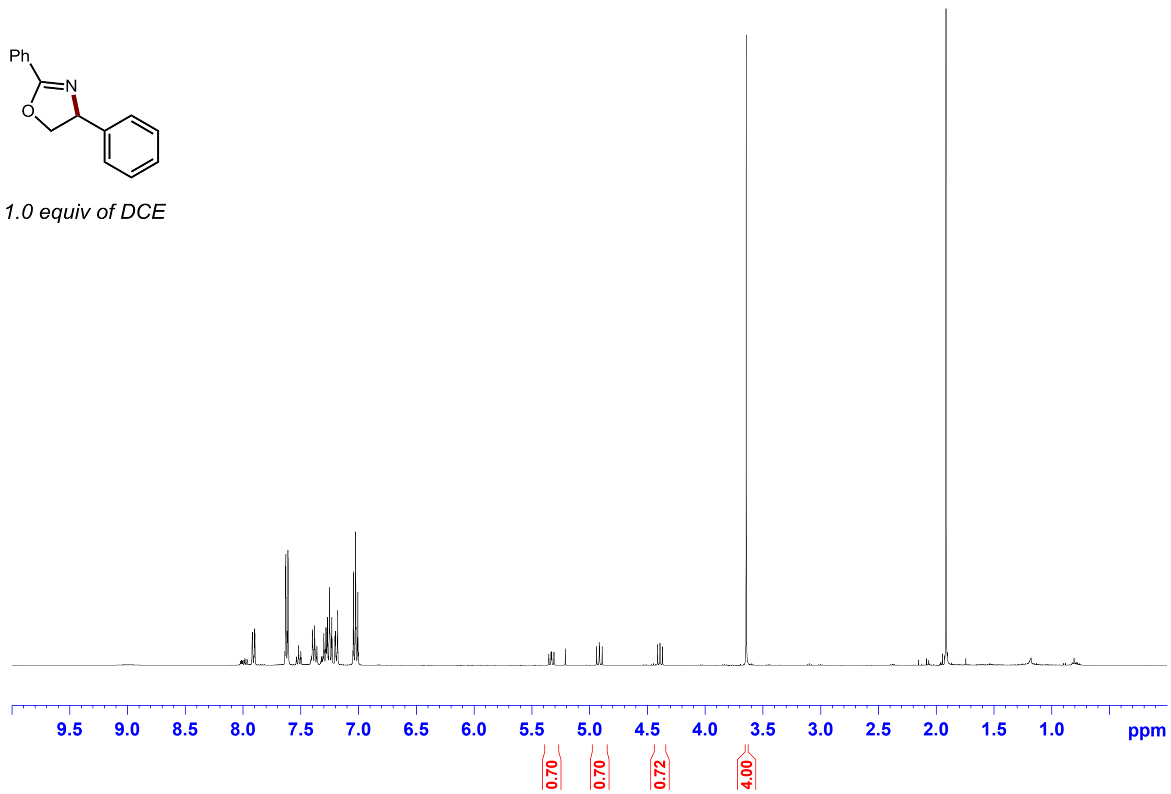
XII. NMR Spectra of Crude Reactions



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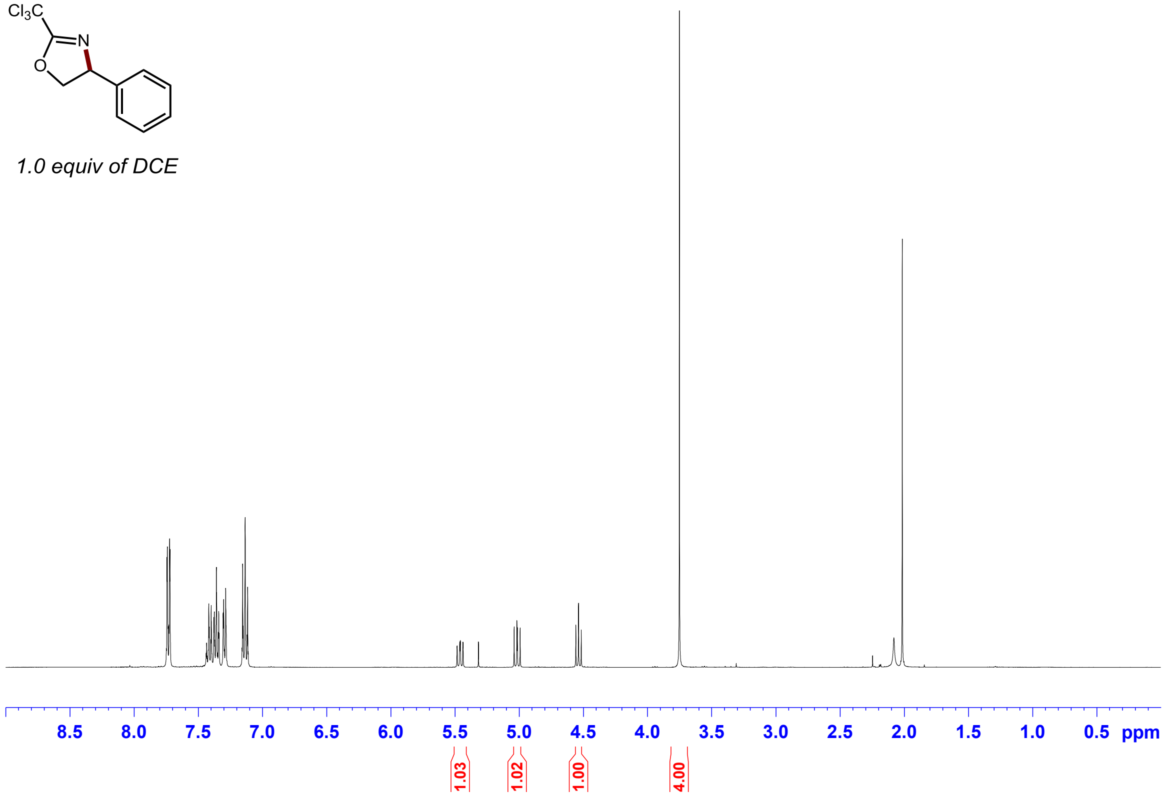

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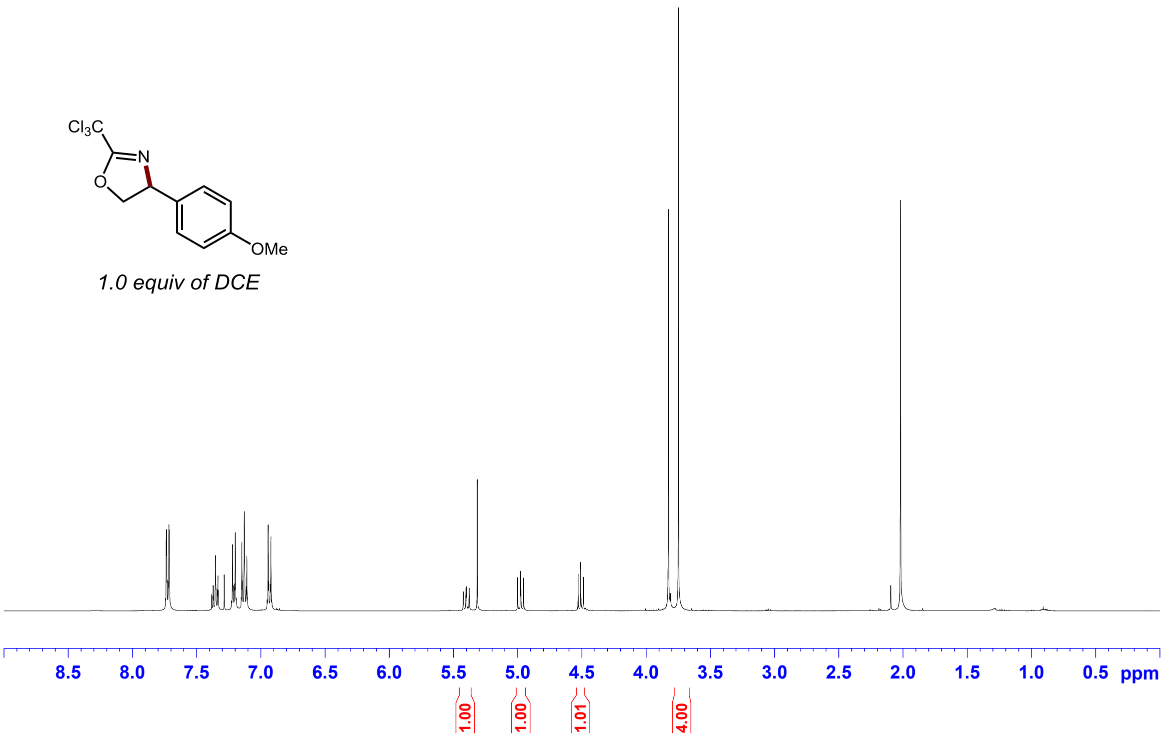
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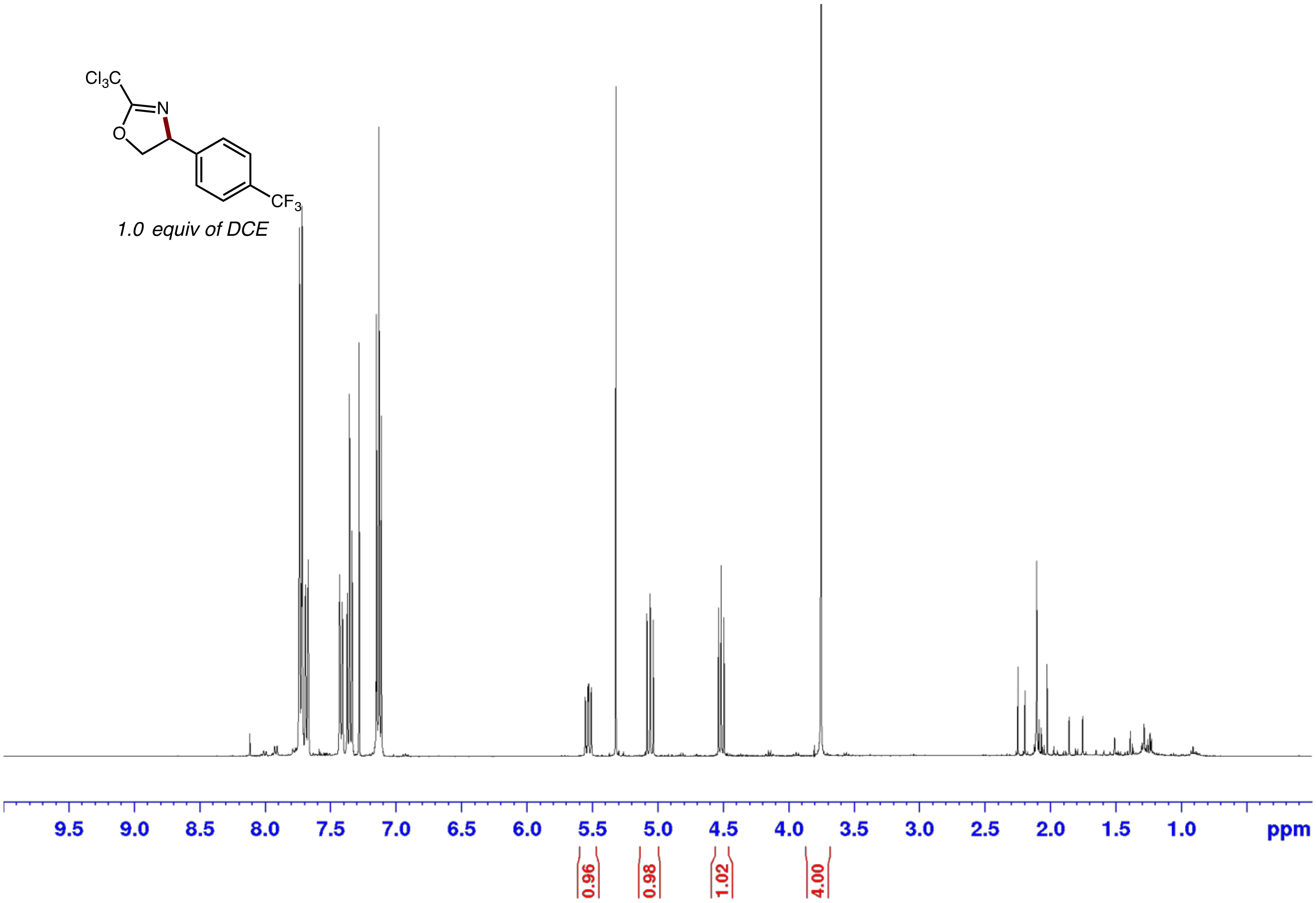
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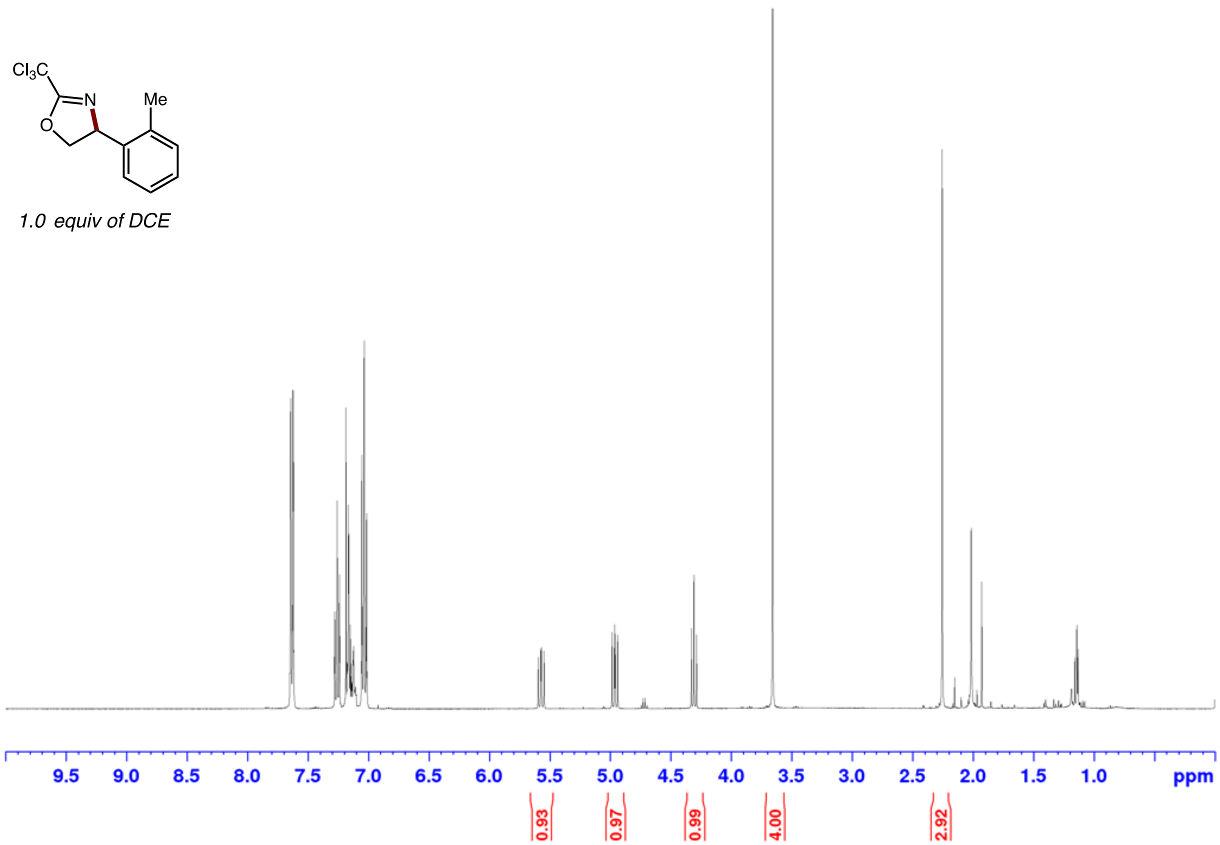
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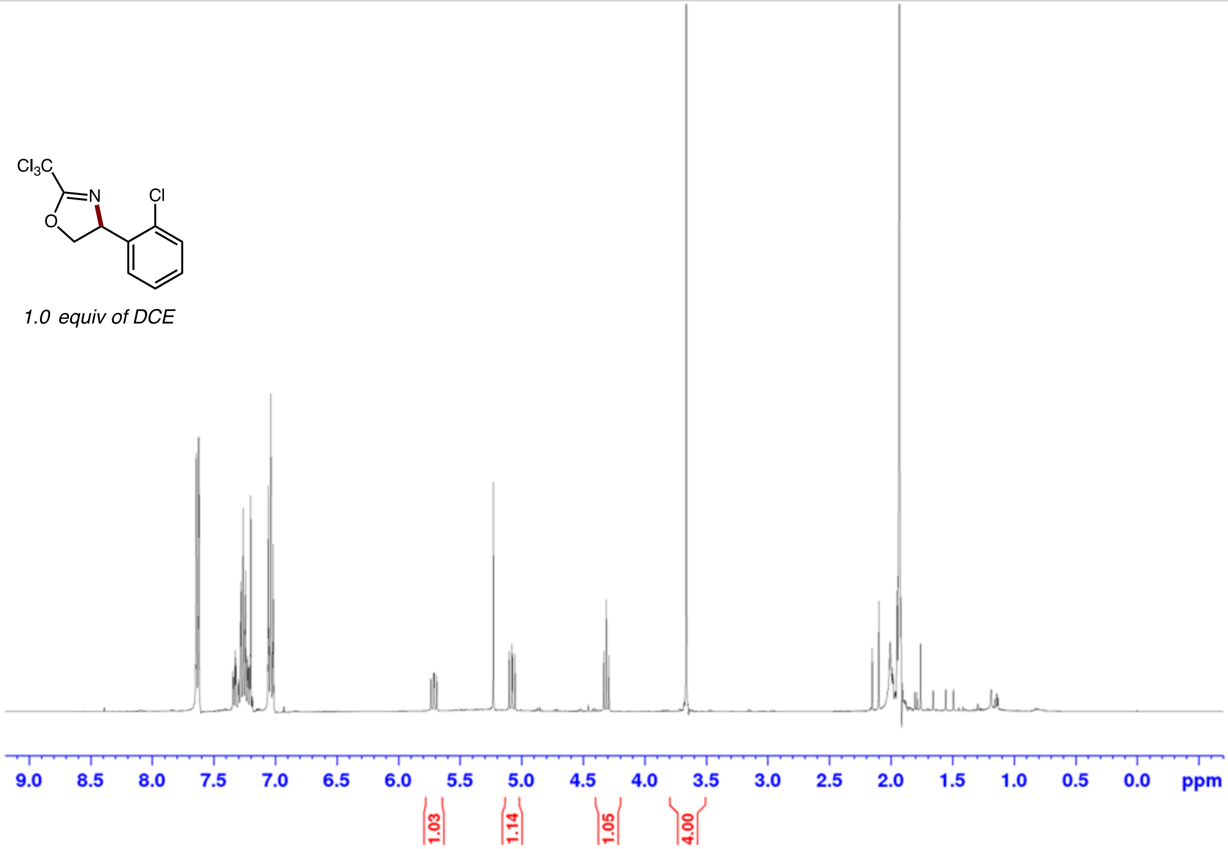
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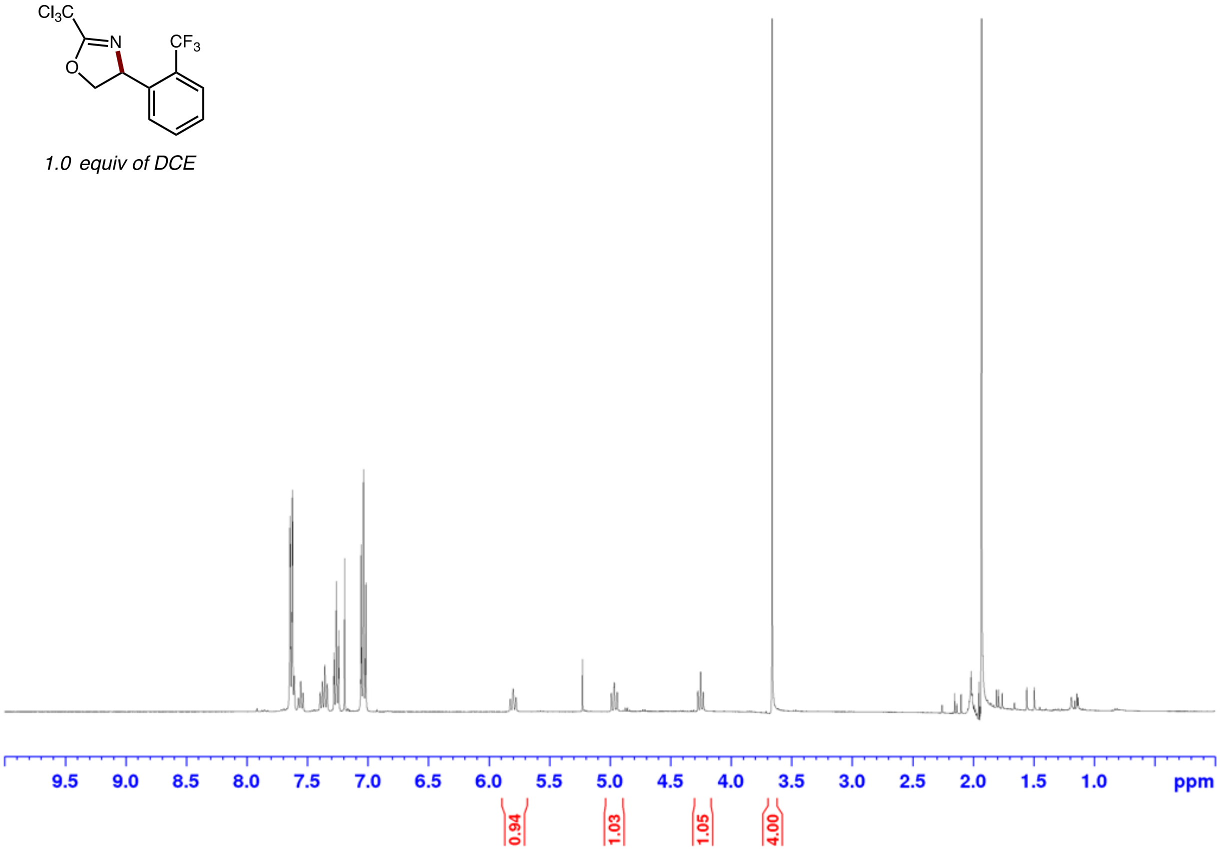
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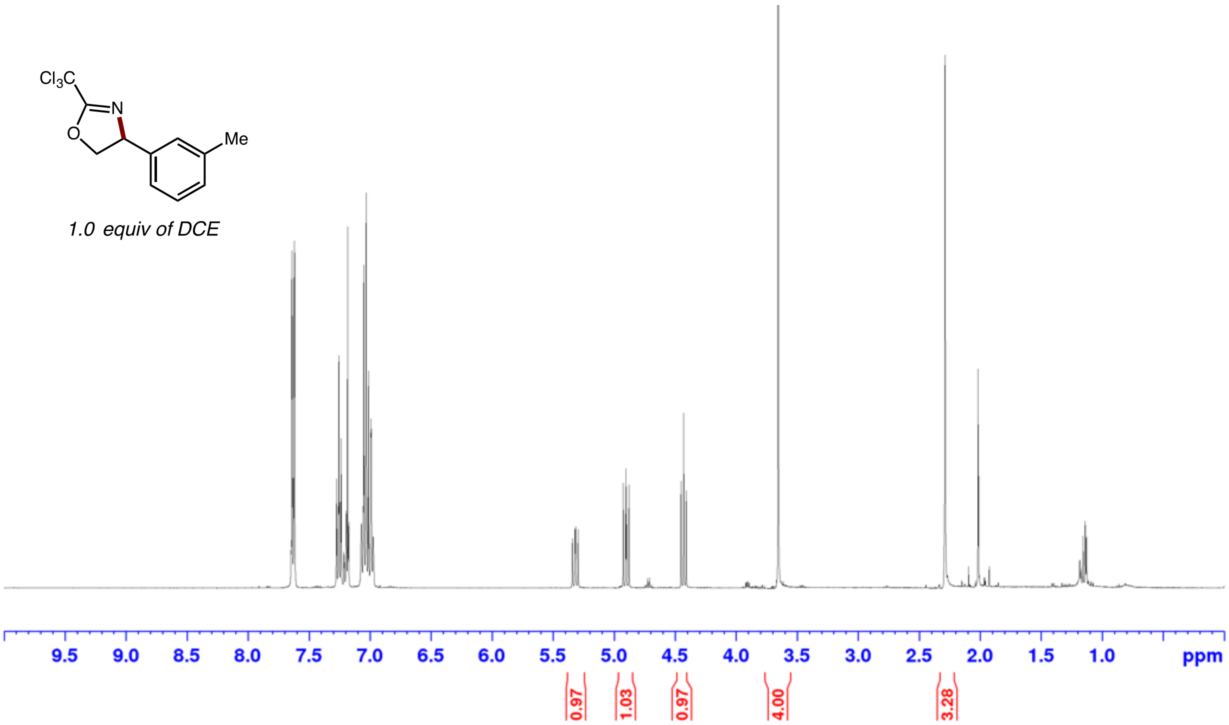
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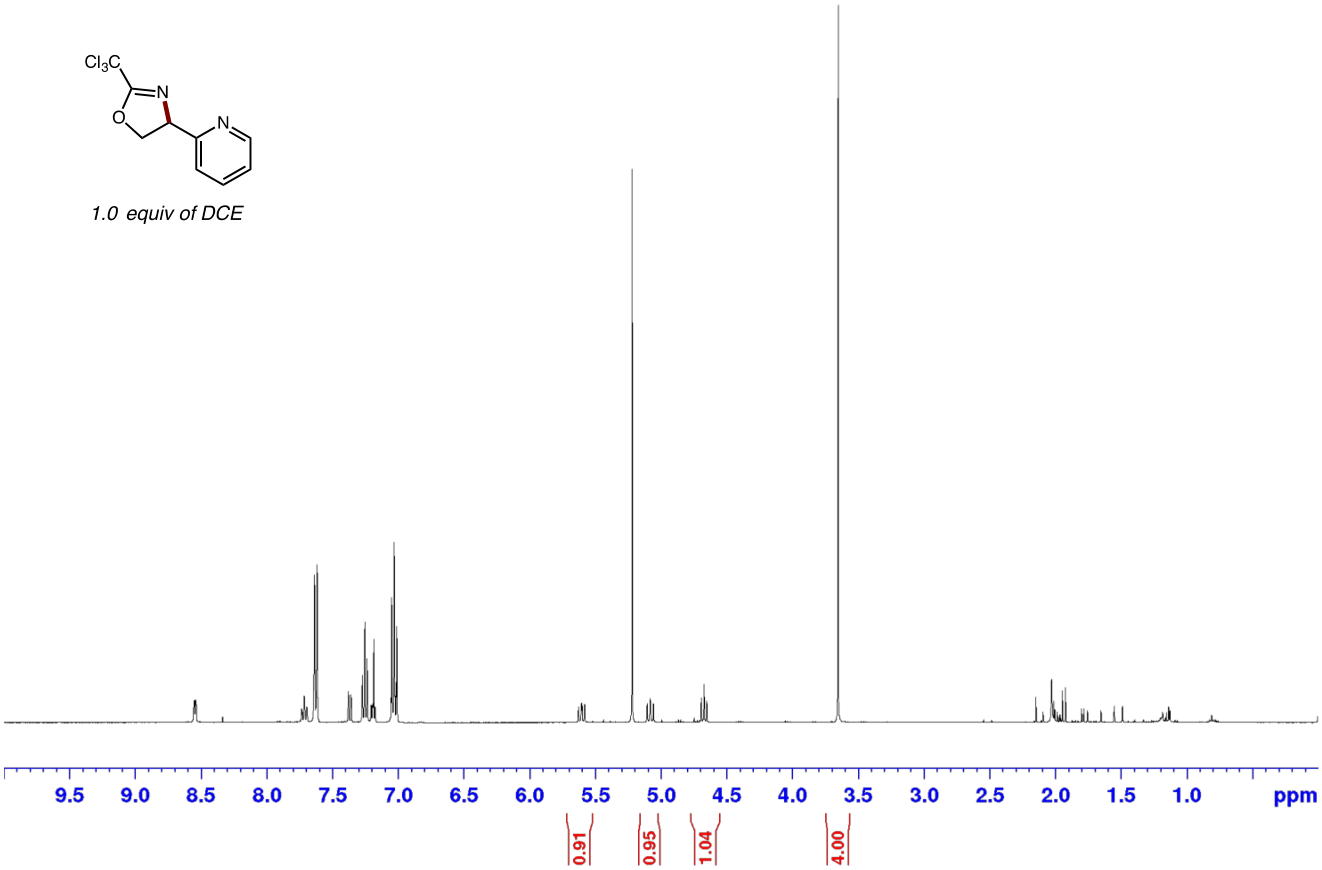
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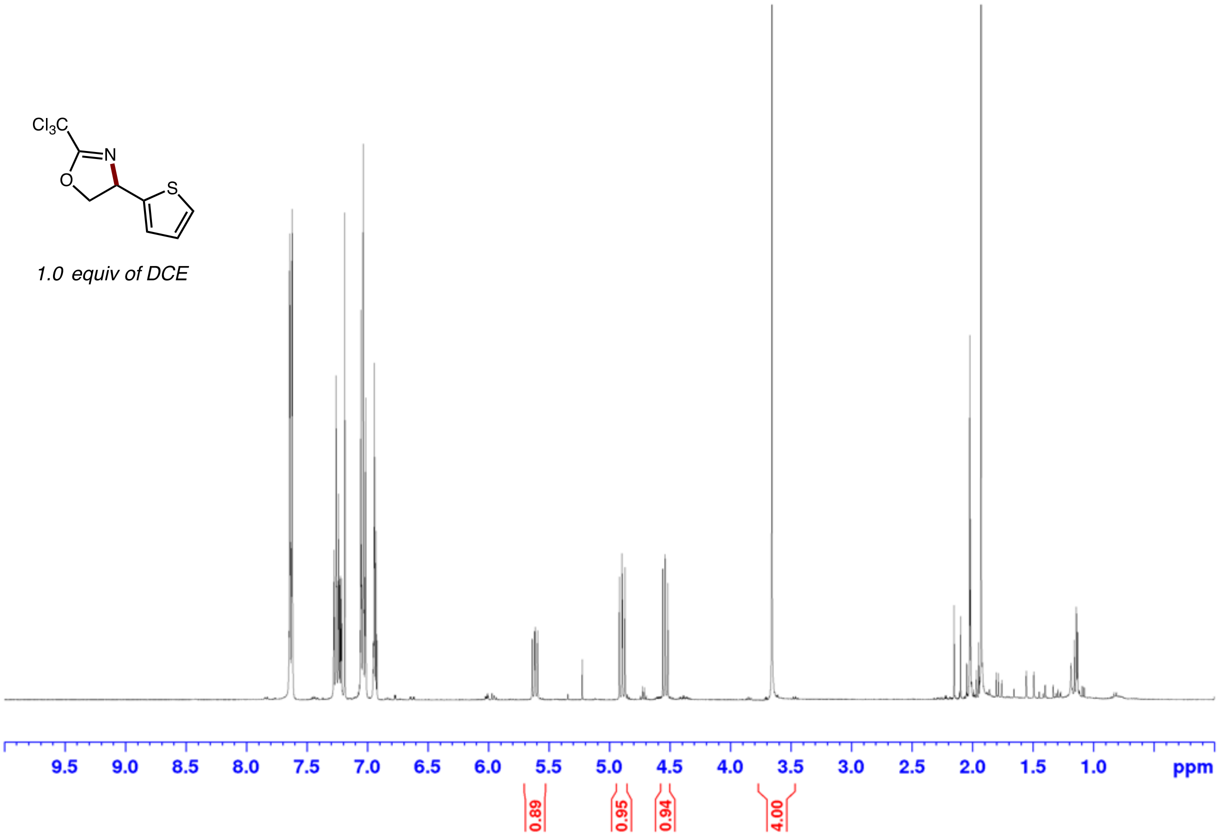
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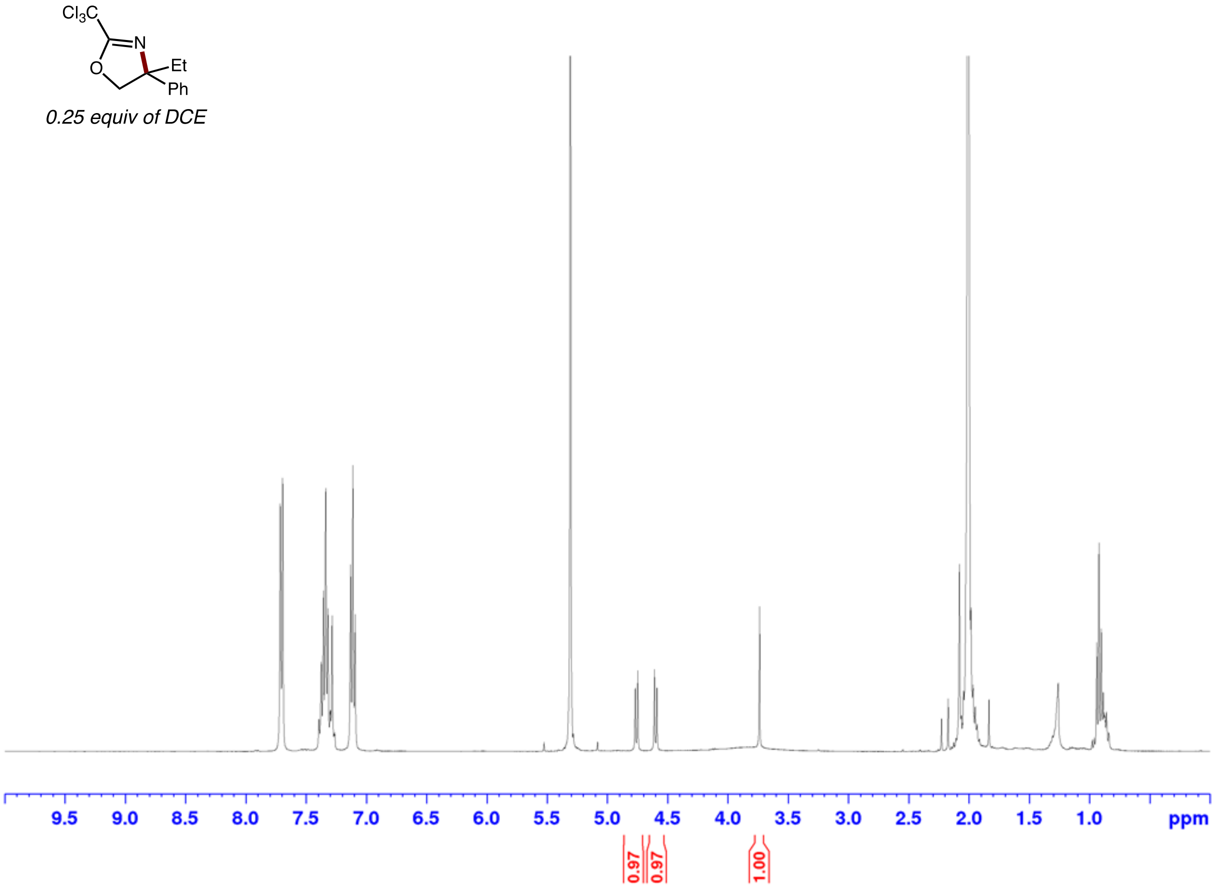
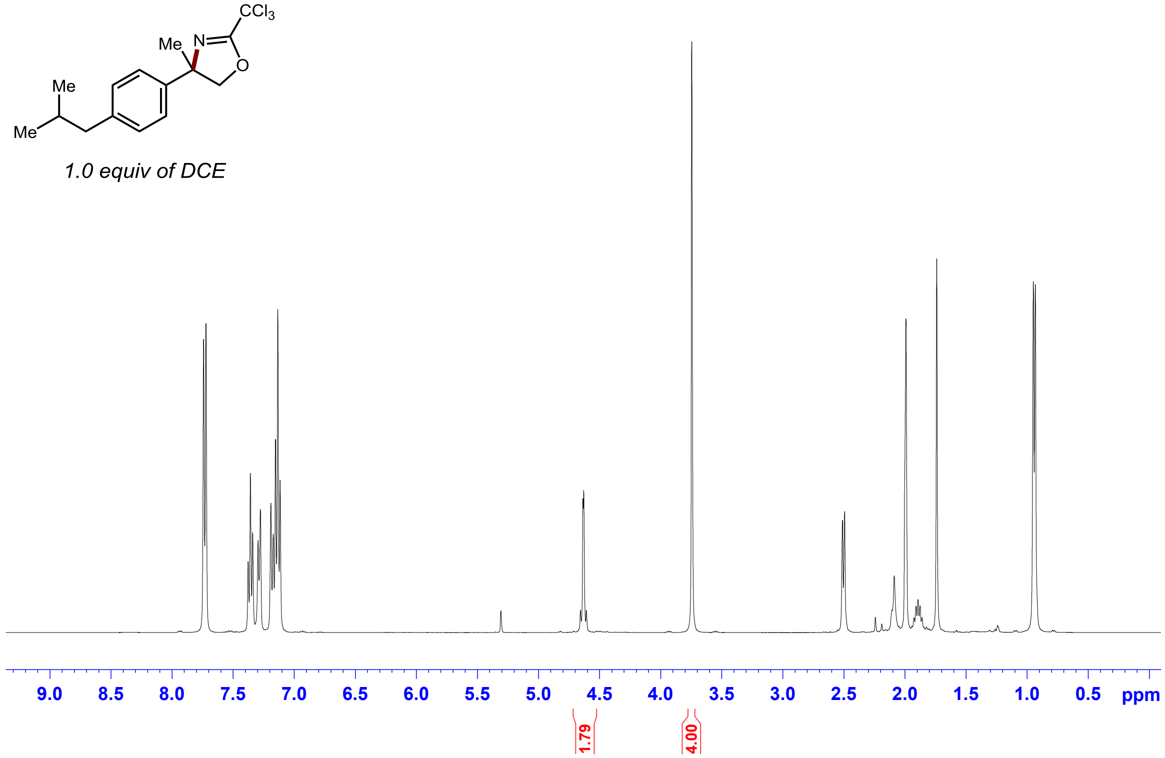
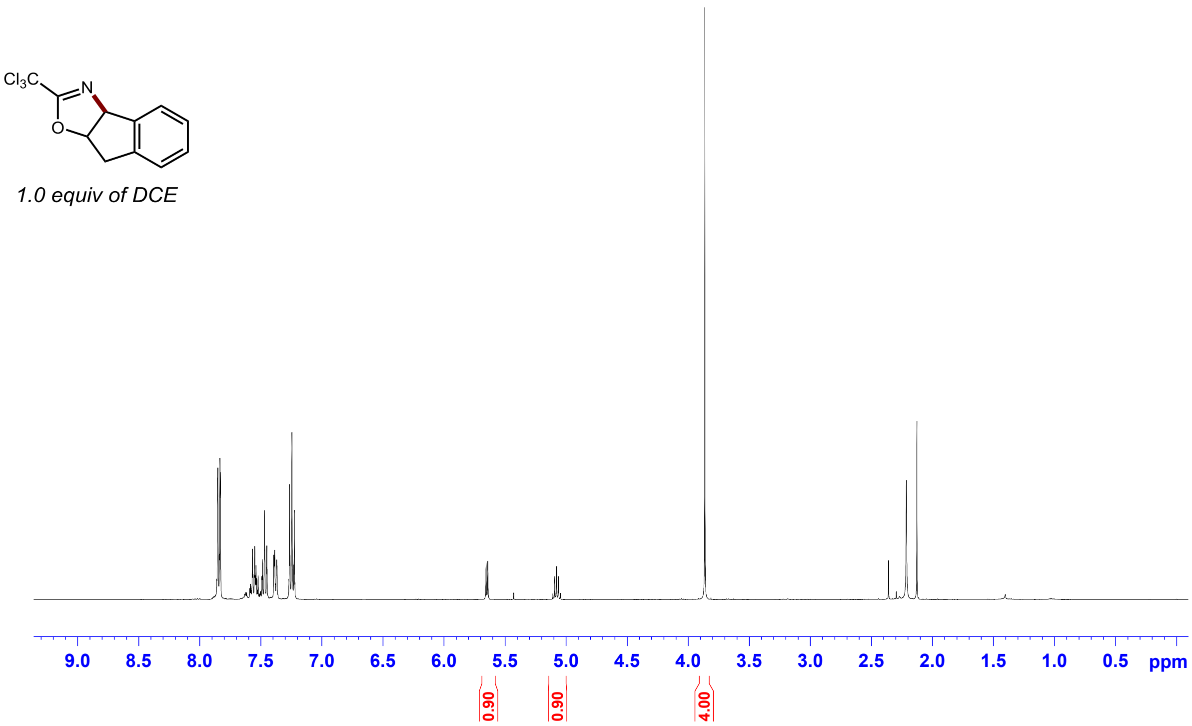
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.89
0.95
0.94
4.00



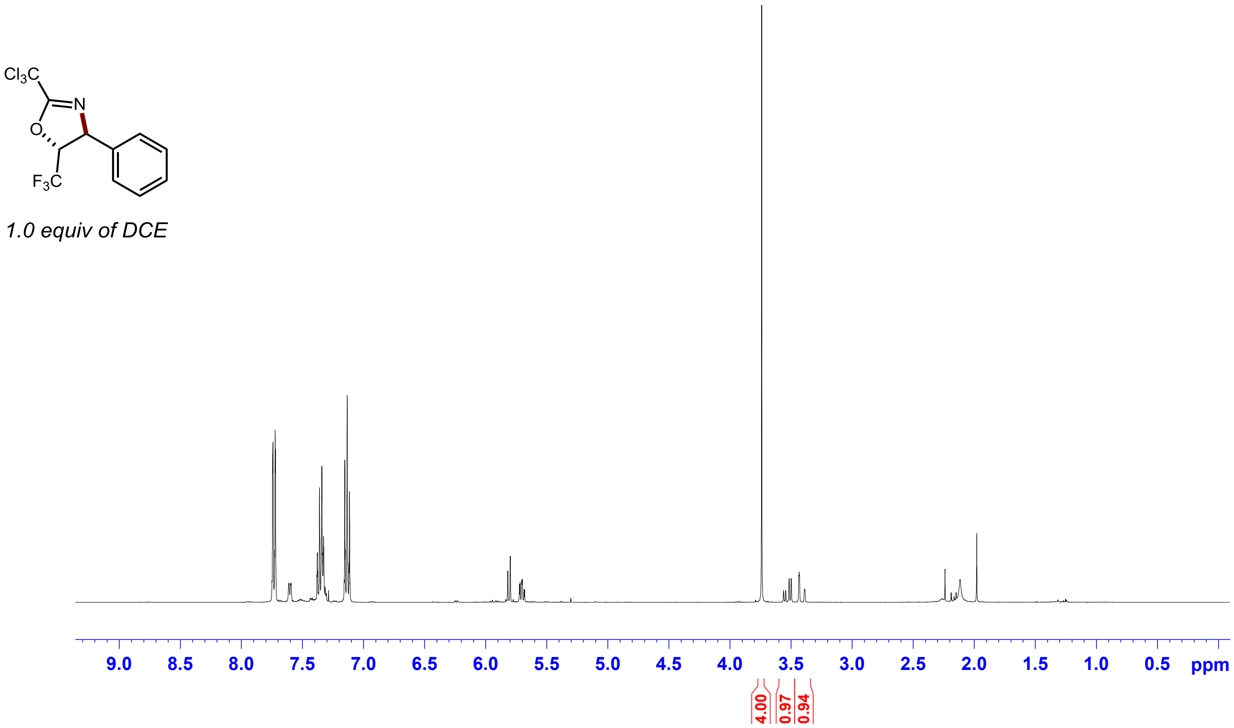
0.25 equiv of DCE



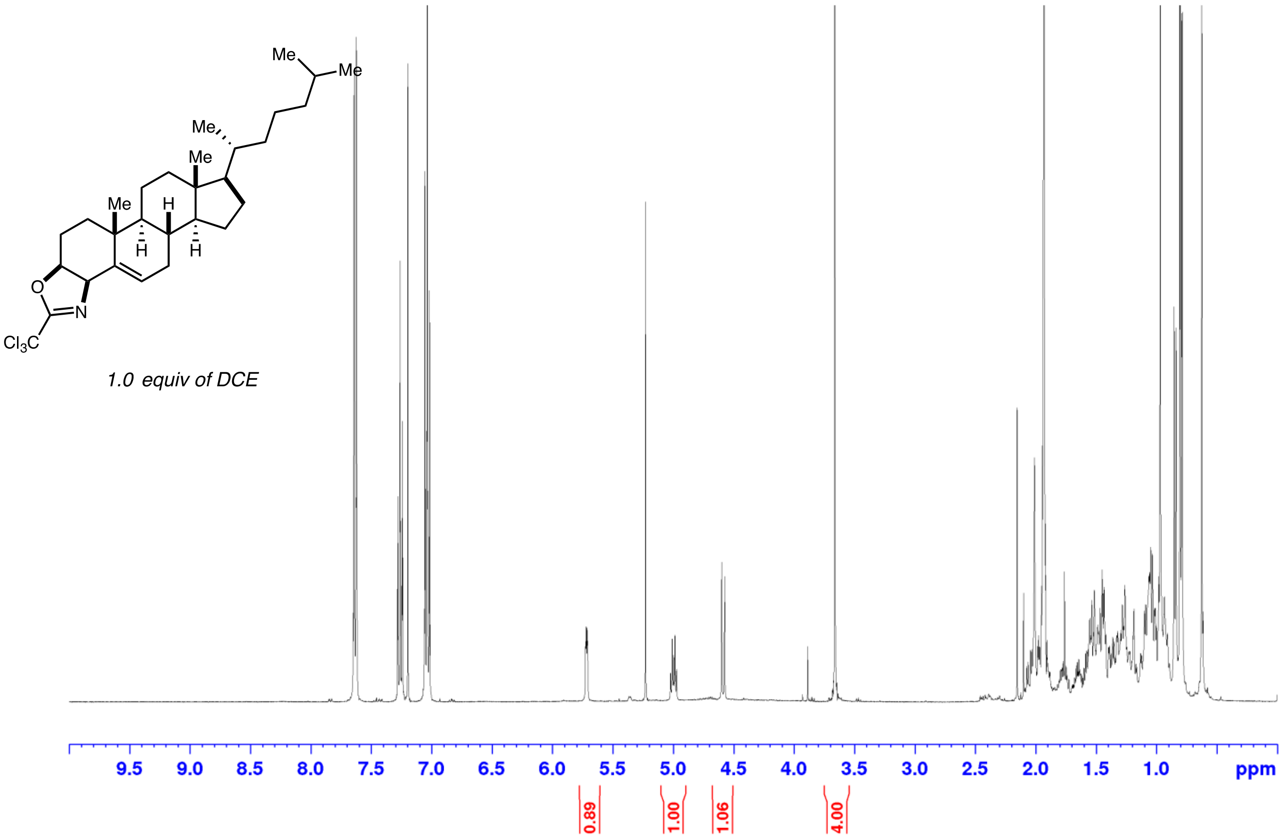
1.0 equiv of DCE

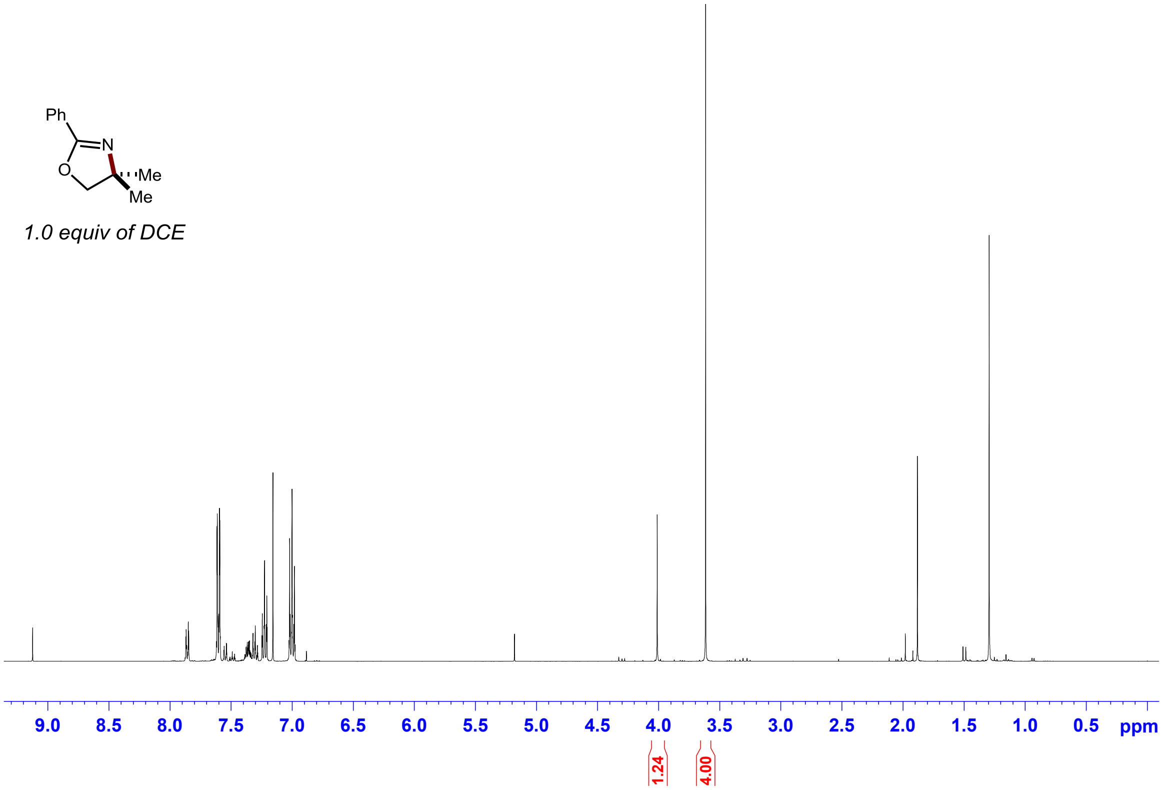


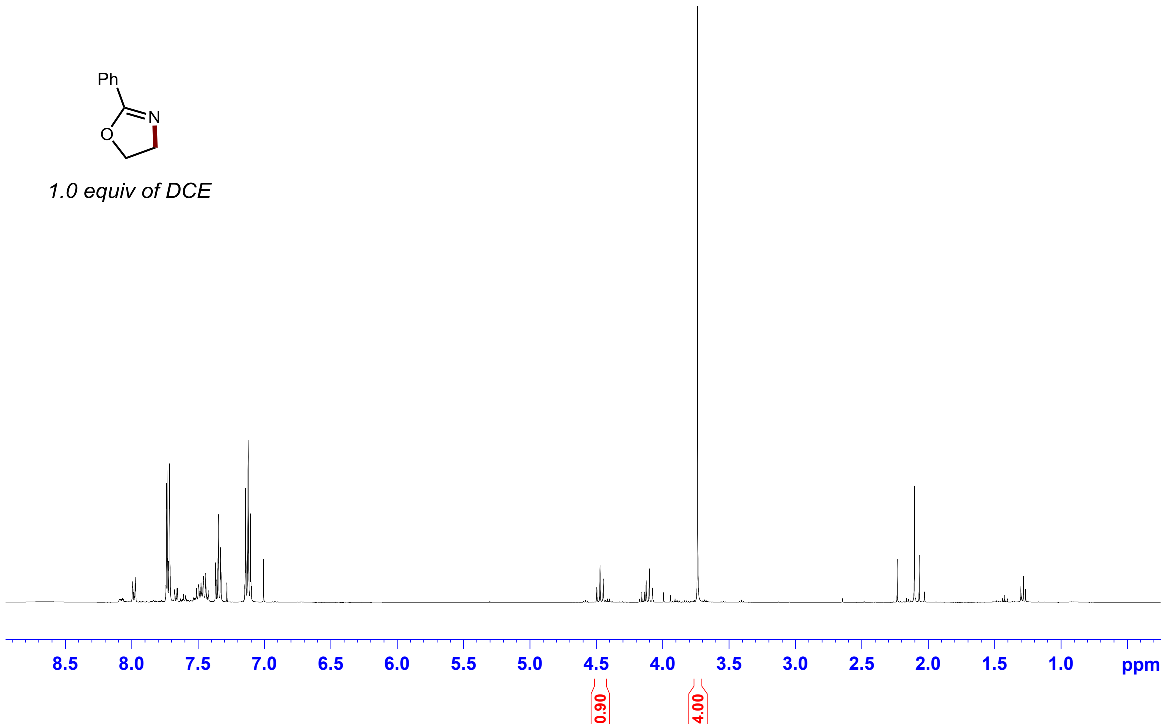
1.0 equiv of DCE

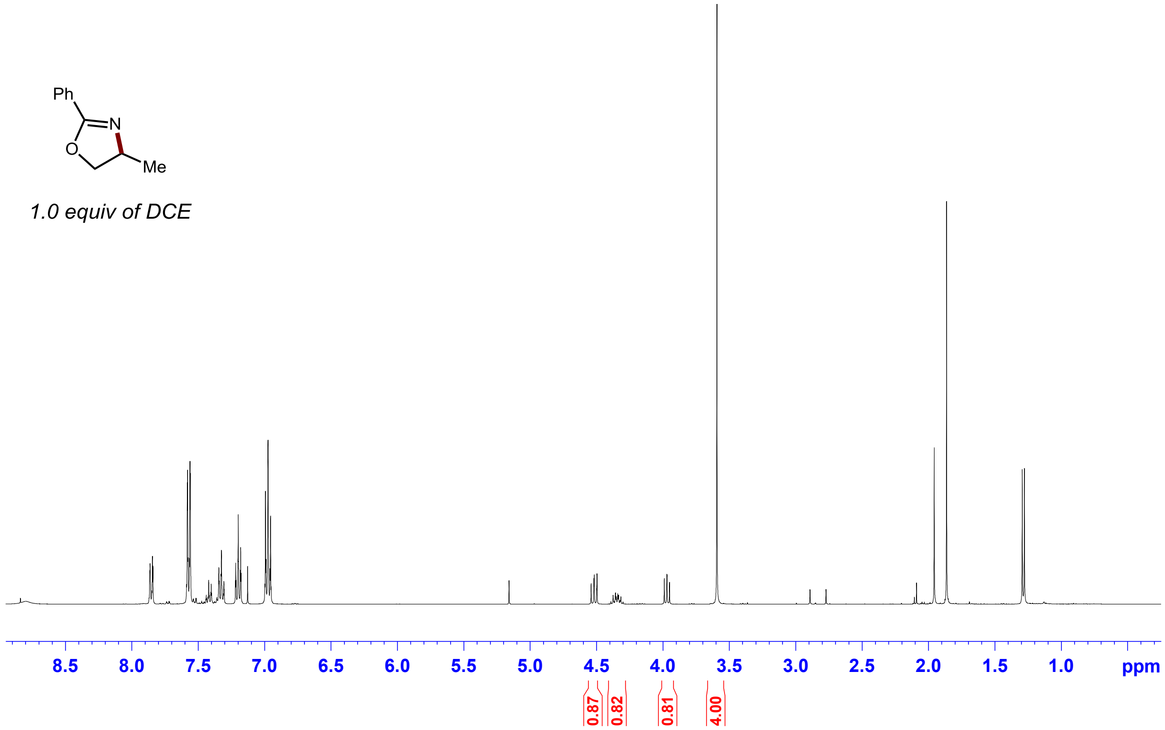


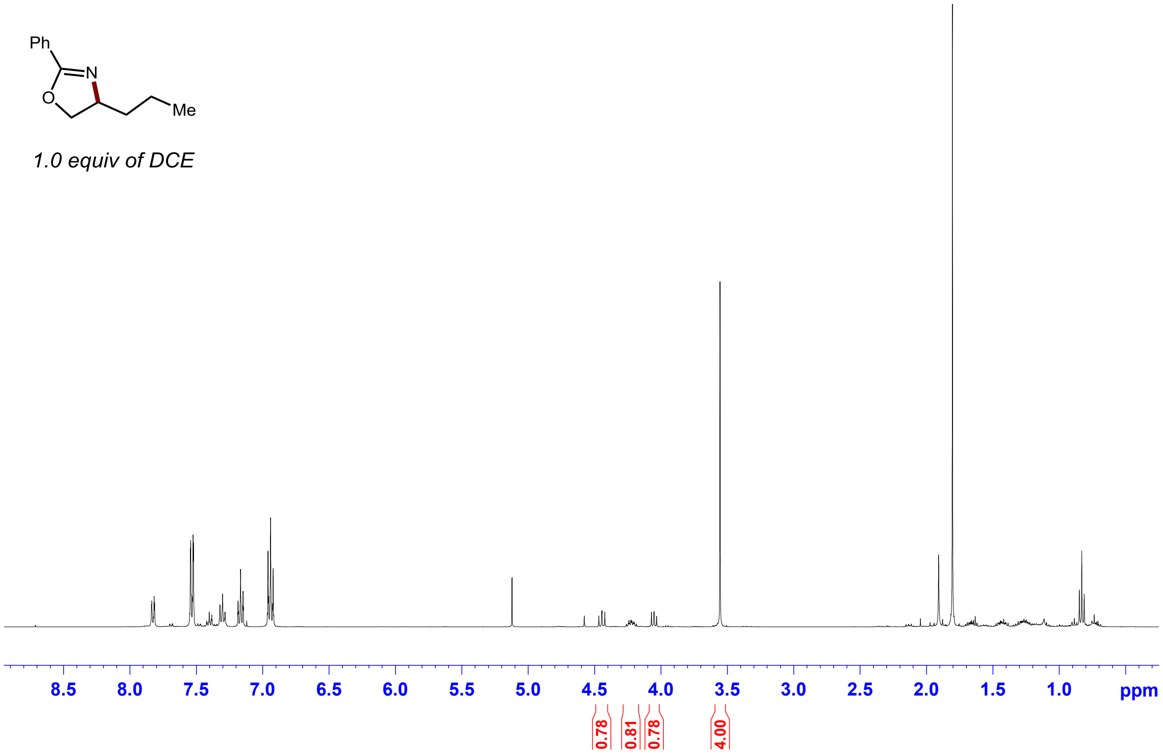
1.0 equiv of DCE


Me
Me
Me
Me
Me
H
H
H
O
N
Cl3C
1.0 equiv of DCE
9.5 9.0 8.5 8.0 7.5 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 ppm
0.89
1.00
1.06
4.00

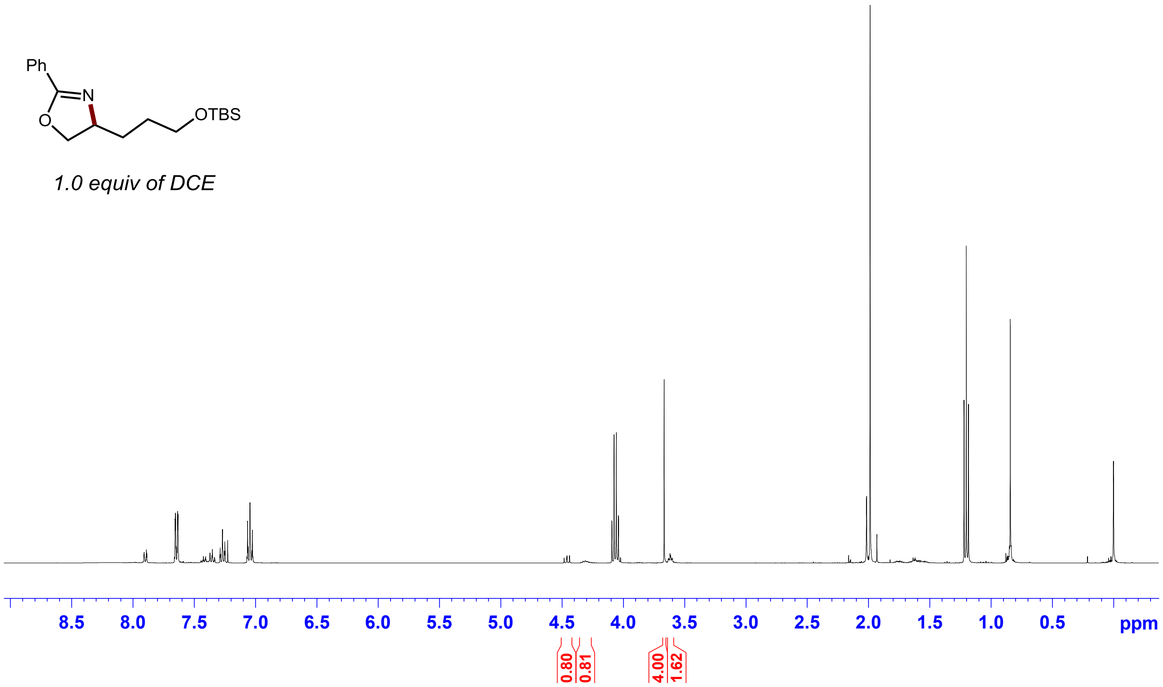

Ph
N
O
Me
Me
1.0 equiv of DCE
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.24
4.00


Ph
N
O
1.0 equiv of DCE
8.5
8.0
7.5
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
ppm
0.90
4.00

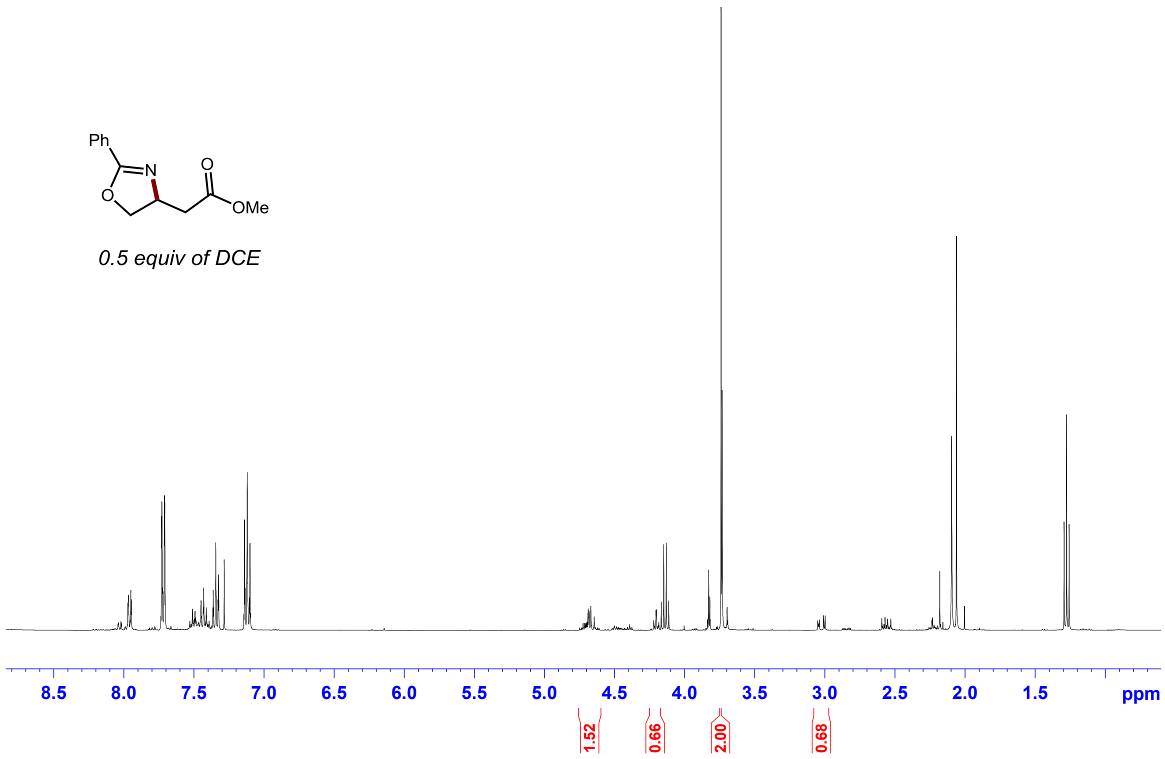

Ph
N
O
Me
1.0 equiv of DCE
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.87
0.82
0.81
4.00

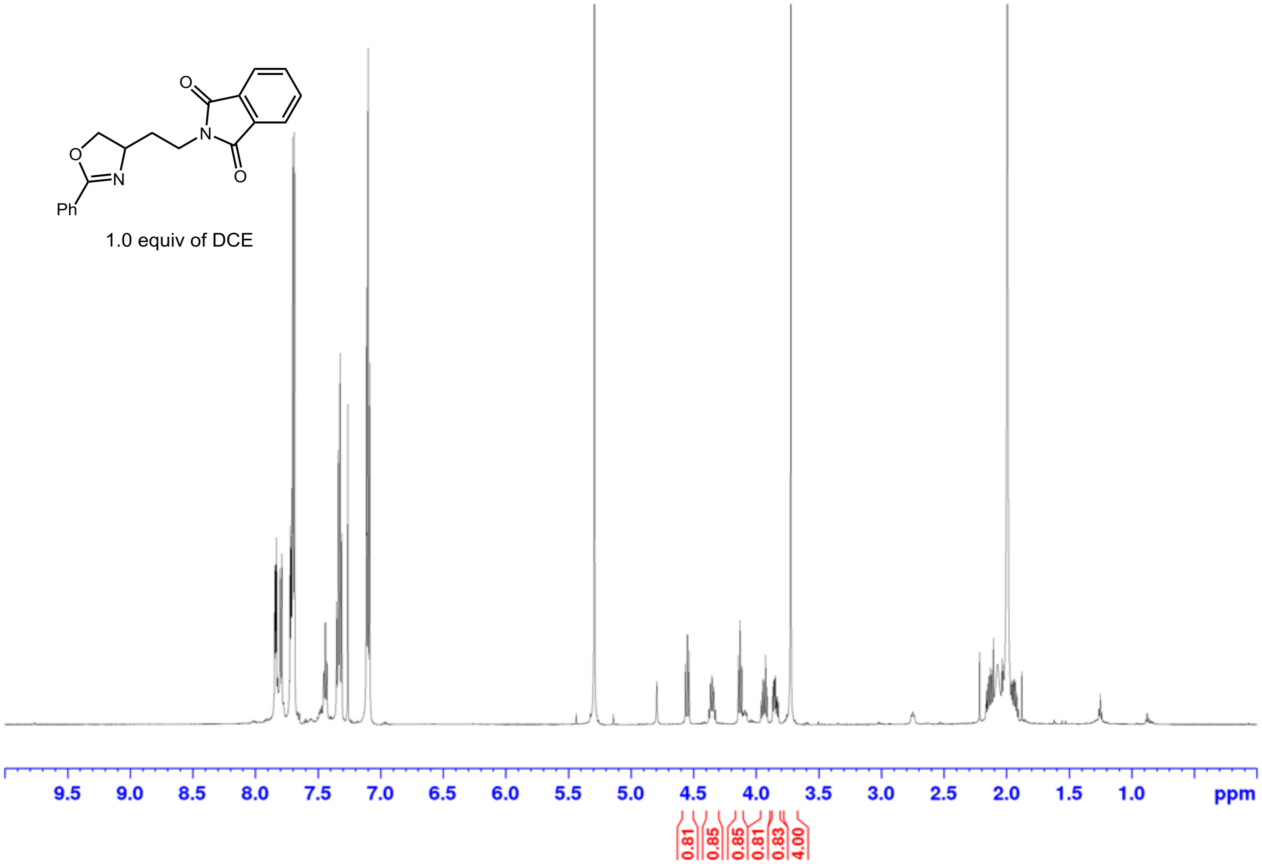


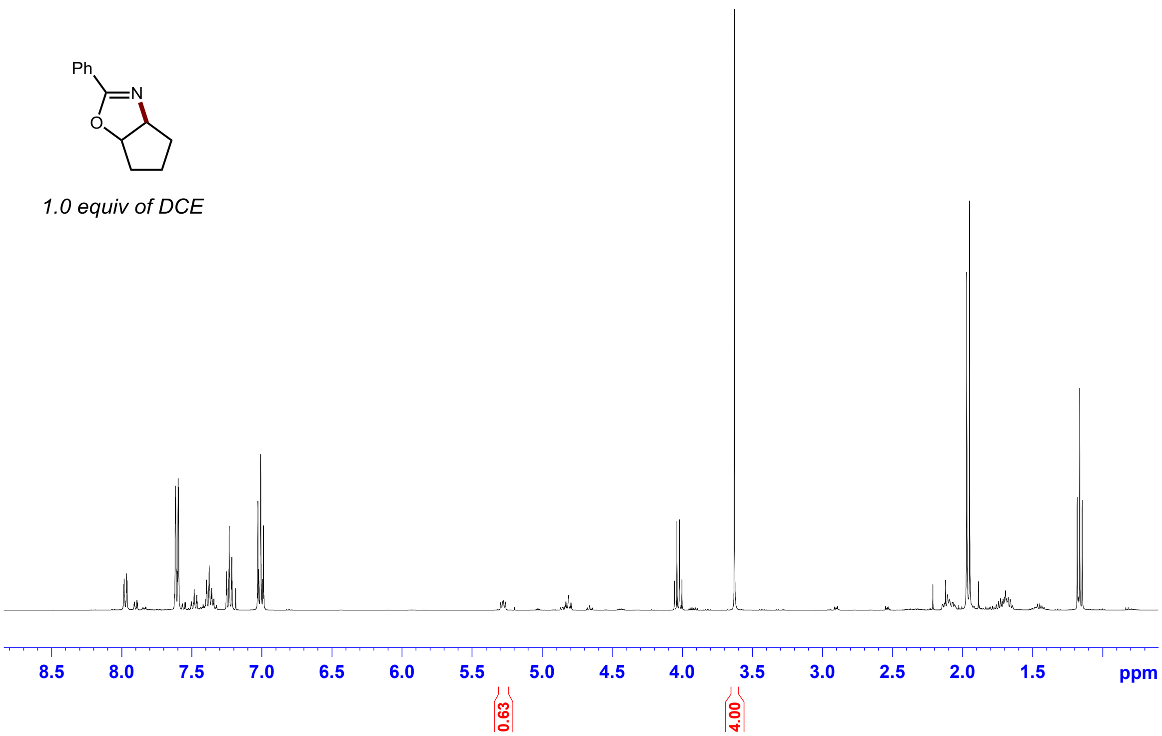
1.0 equiv of DCE

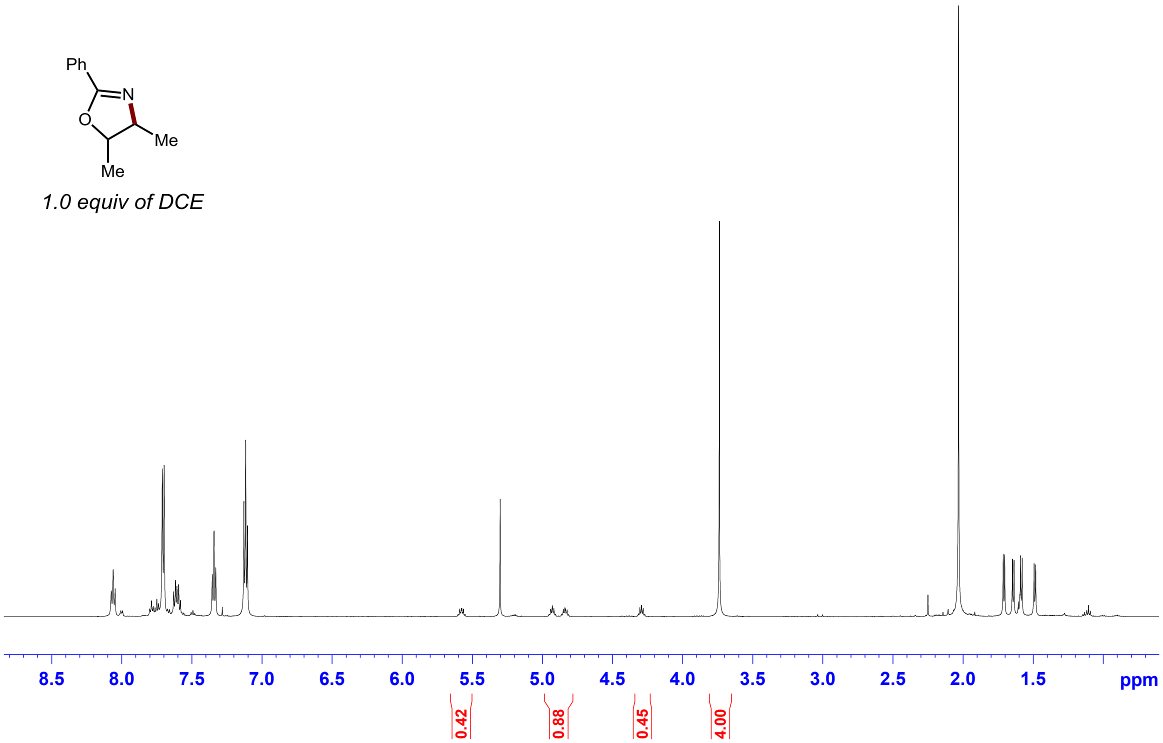


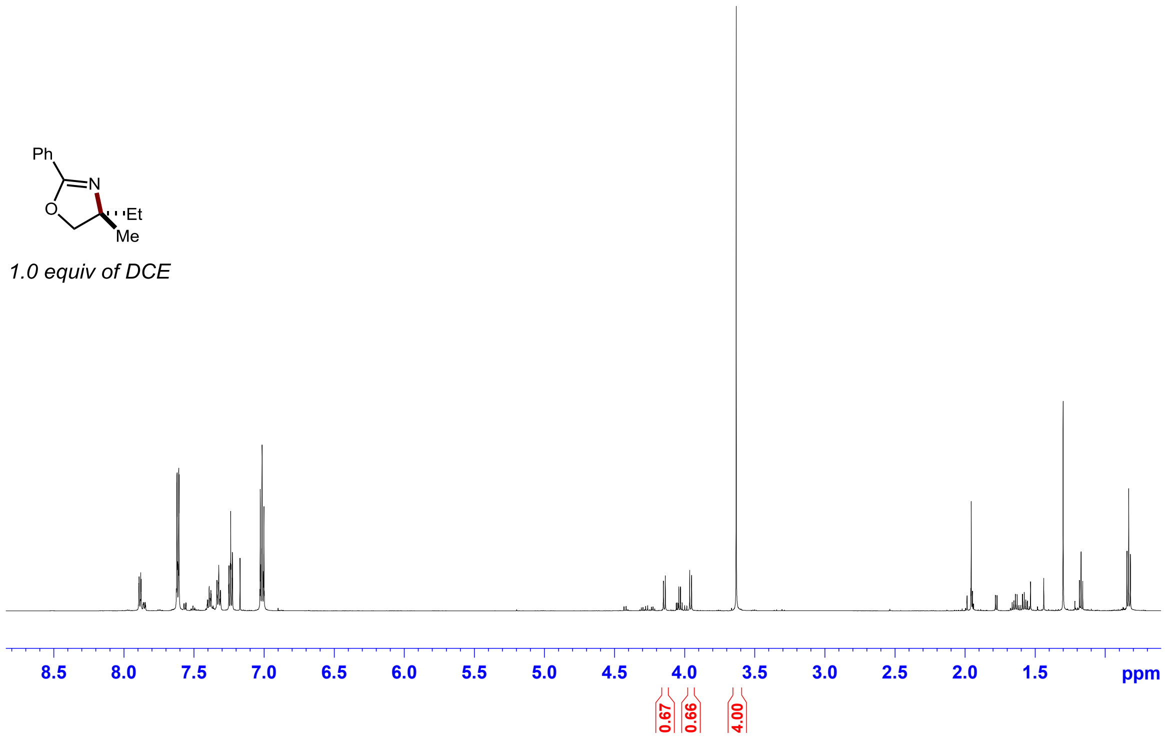
1.0 equiv of DCE


Ph
N
O
O
OMe
0.5 equiv of DCE
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm
1.52
0.66
2.00
0.68

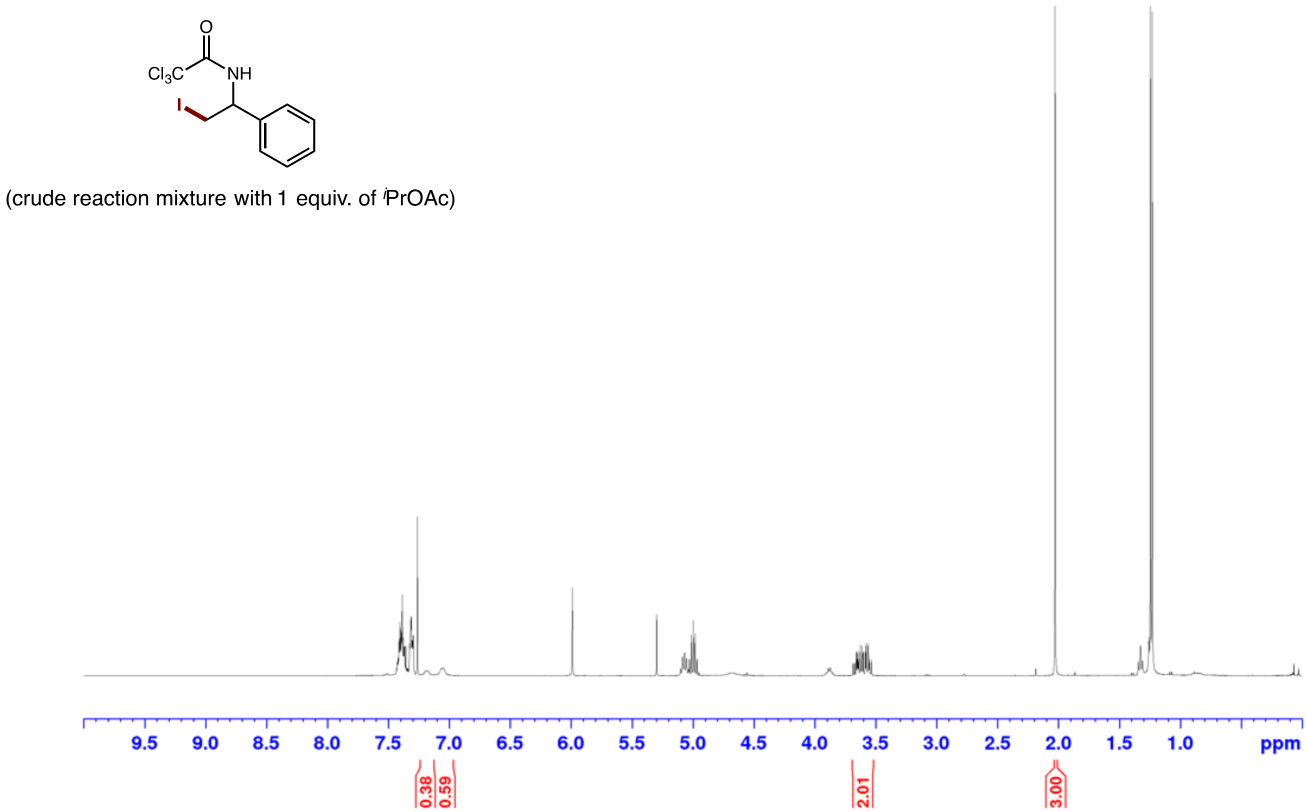

O
N
O
O
N
Ph
1.0 equiv of DCE
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.81
0.85
0.85
0.81
0.83
4.00


Ph
N
O
1.0 equiv of DCE
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm
0.63
4.00


Ph
N
O
Me
Me
1.0 equiv of DCE
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm
0.42
0.88
0.45
4.00

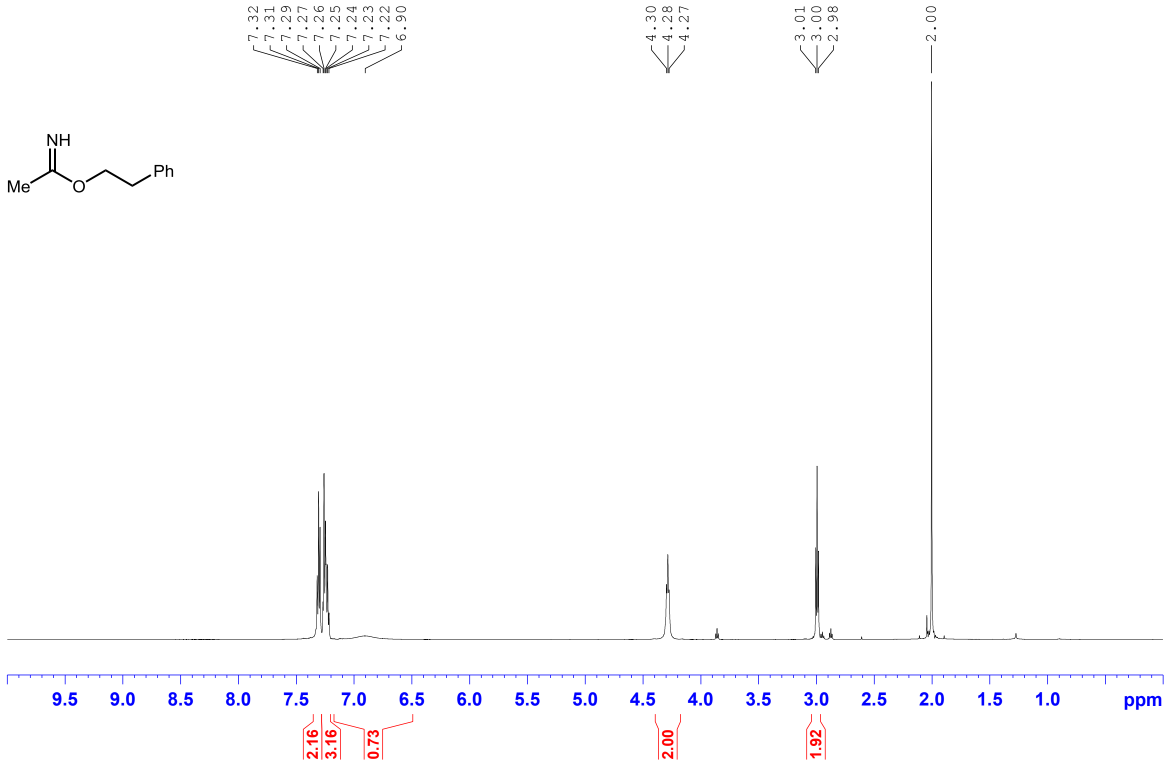


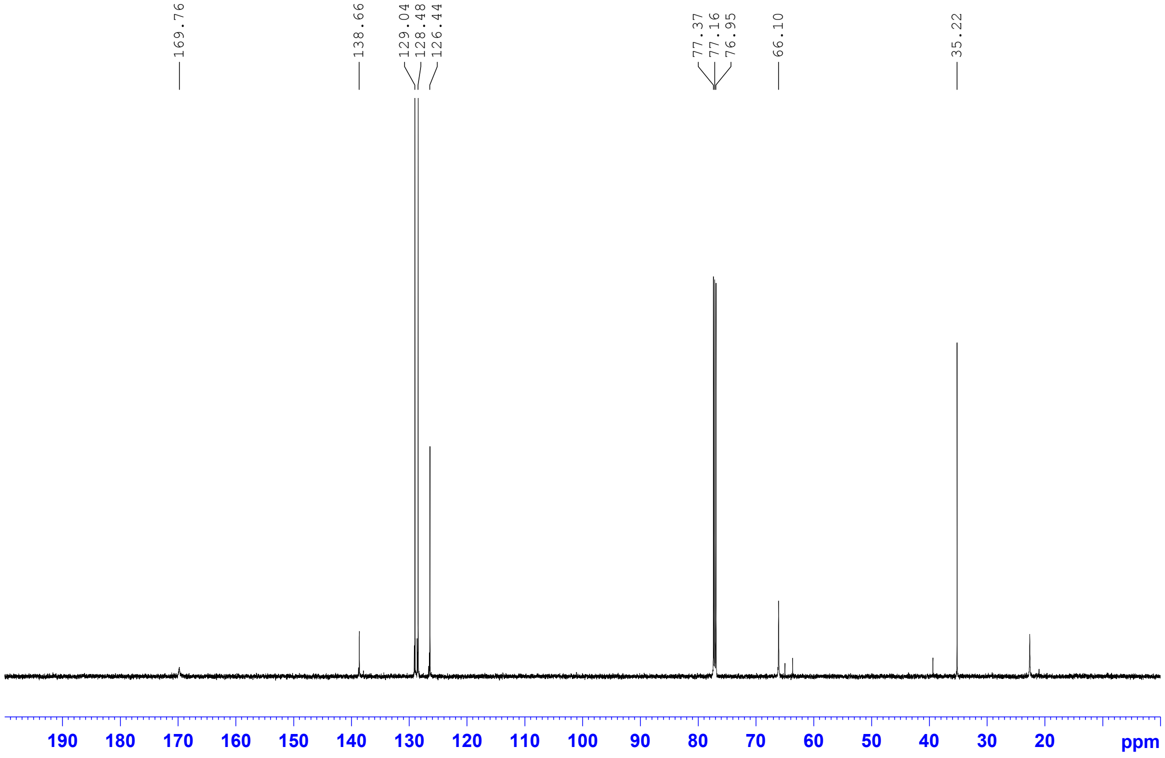
1.0 equiv of DCE

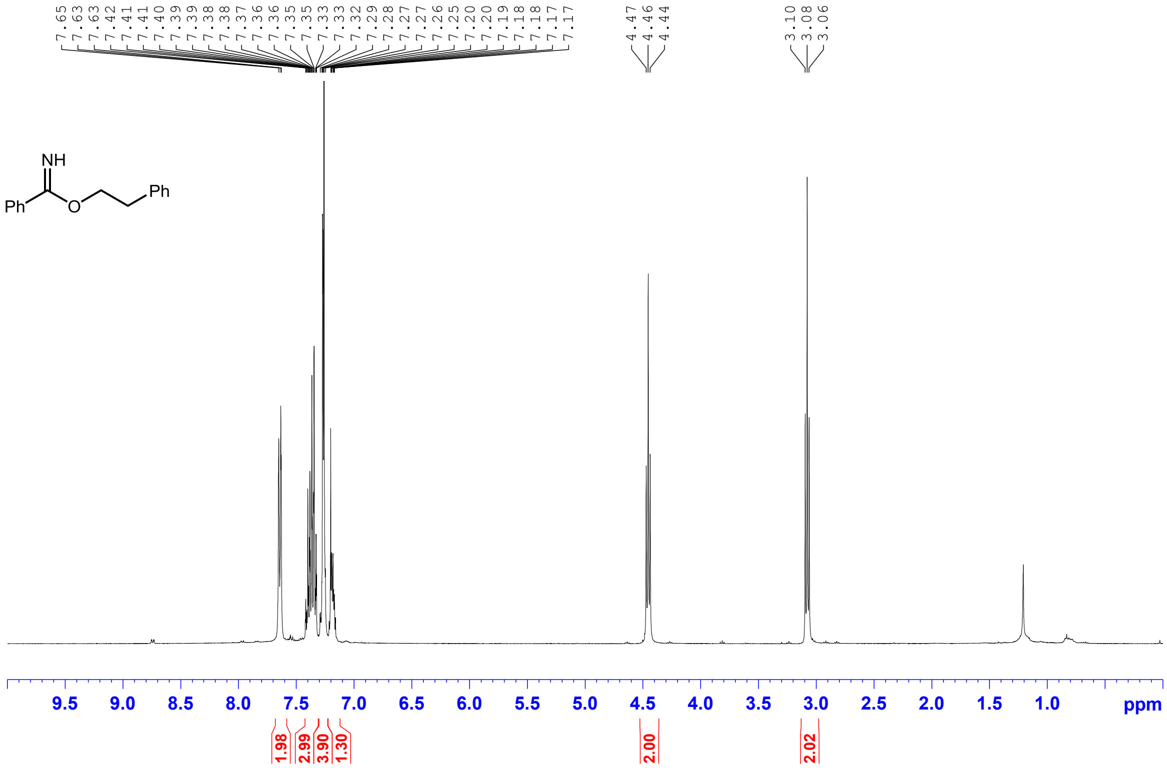


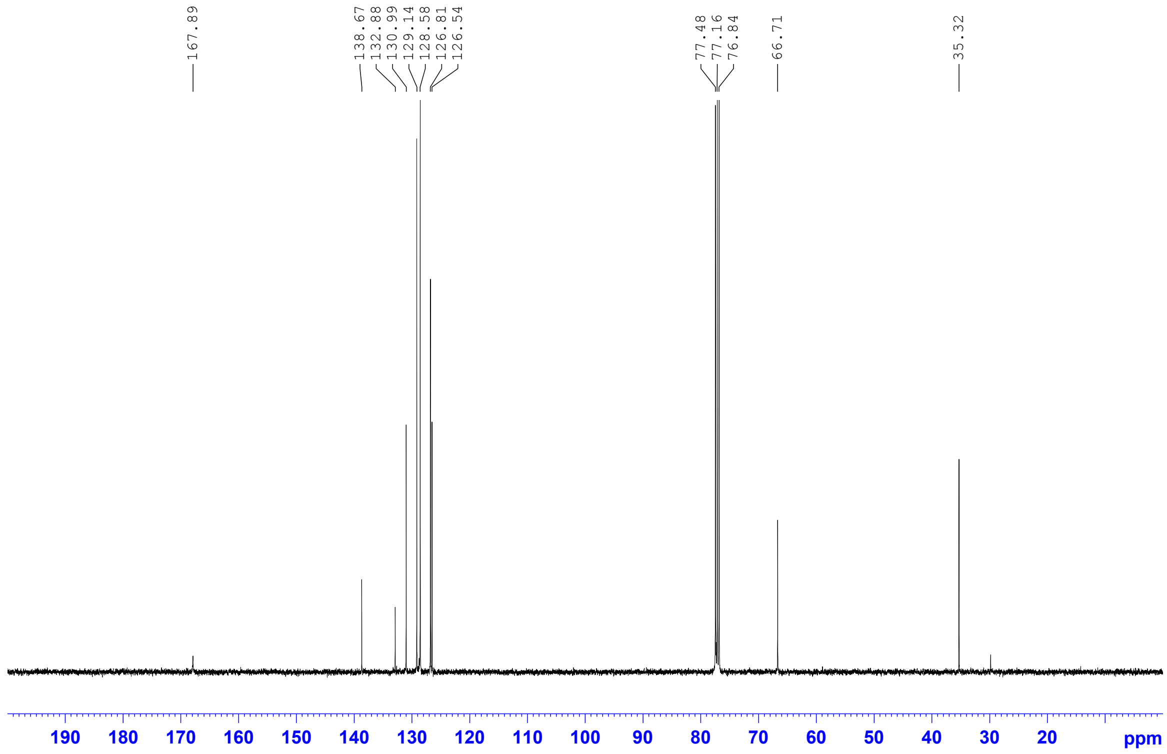
(crude reaction mixture with 1 equiv. of ^{i}PrOAc)

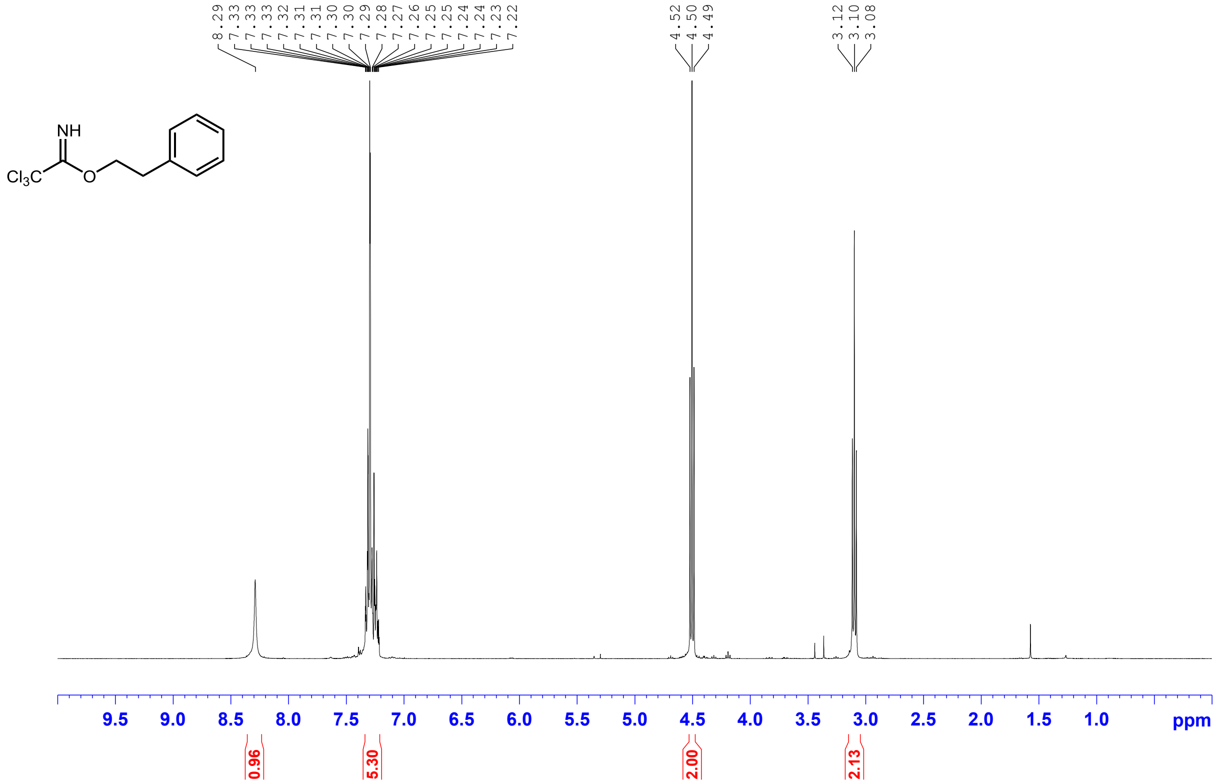
XIII. NMR Spectra of isolated materials

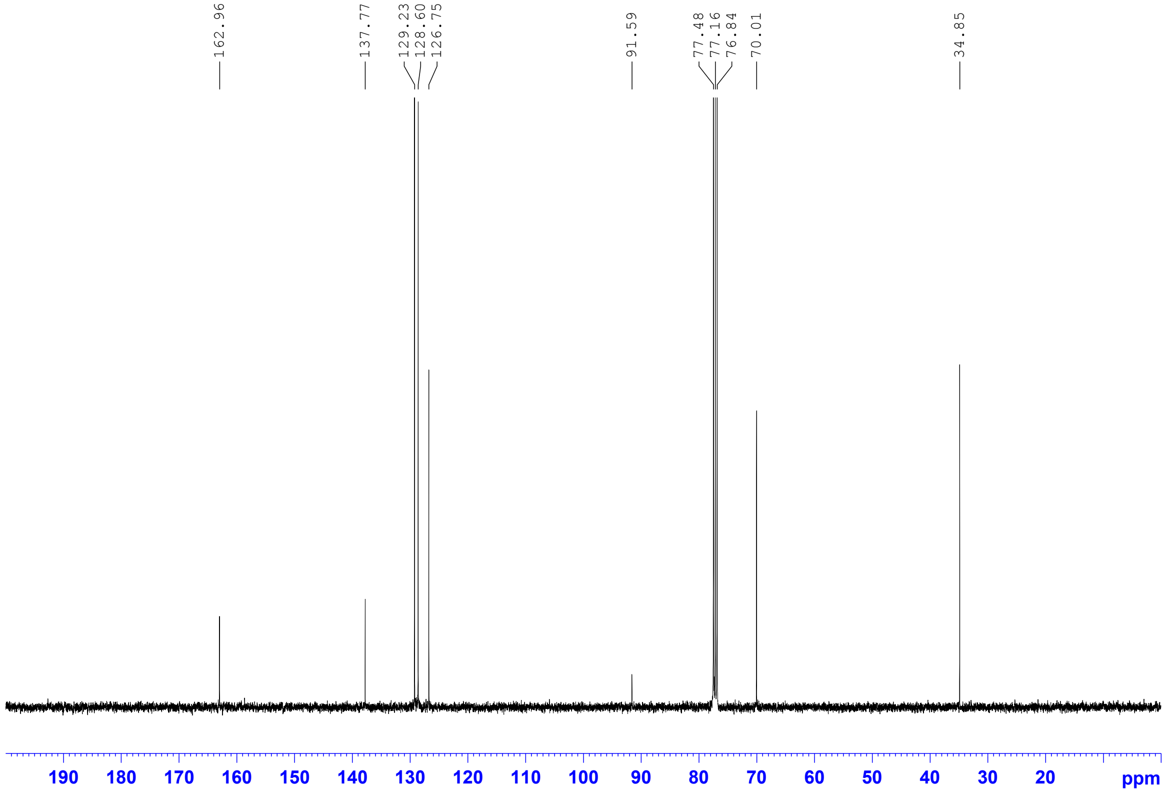


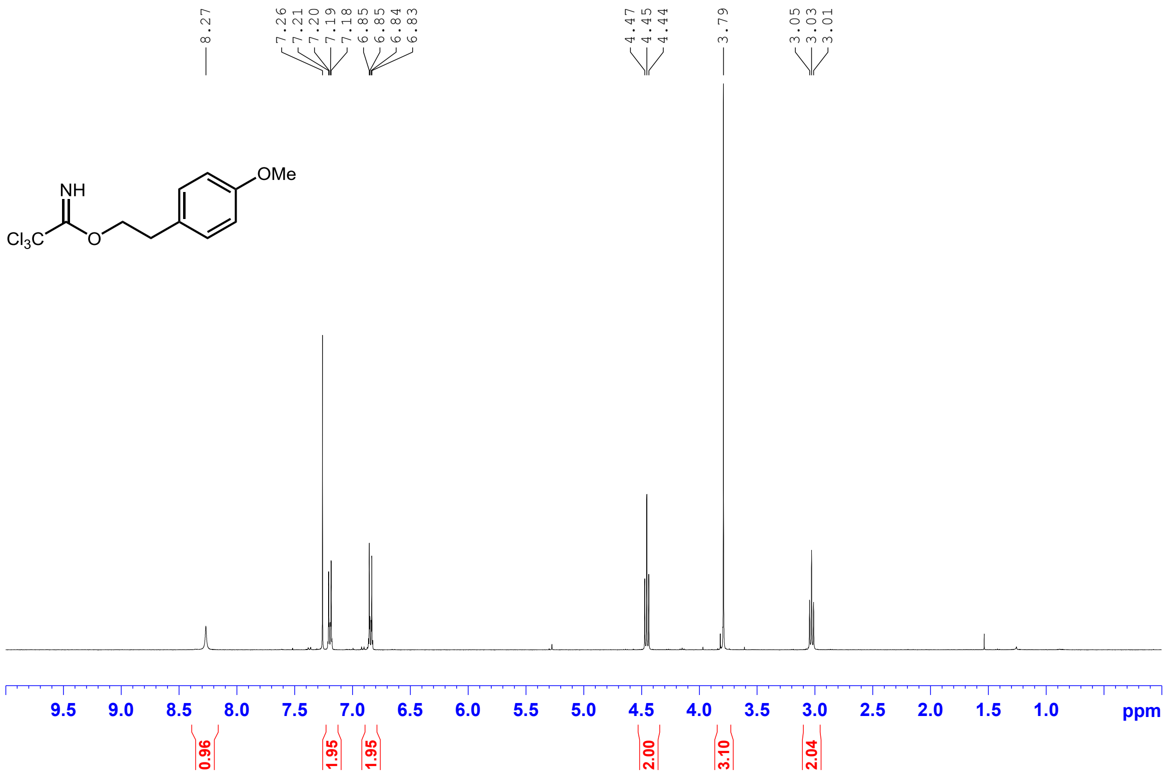


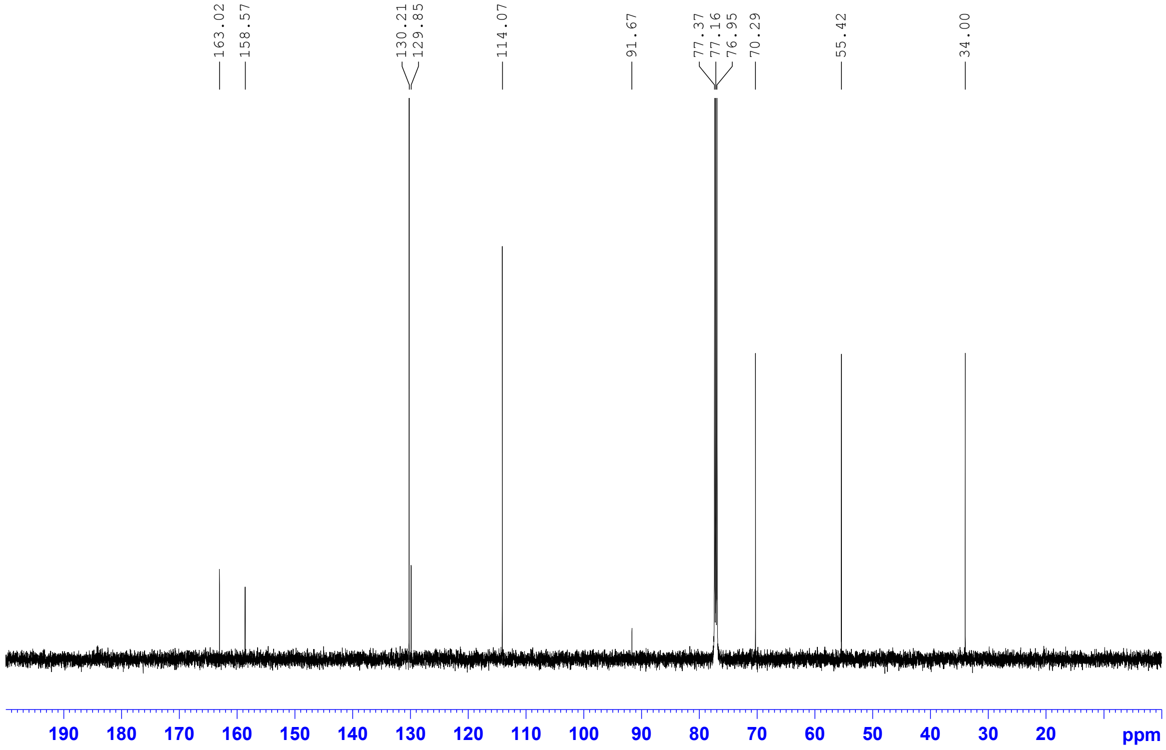

NH
Ph
O
Ph
7.65
7.63
7.63
7.42
7.41
7.41
7.40
7.39
7.39
7.38
7.38
7.37
7.36
7.36
7.35
7.35
7.33
7.33
7.32
7.29
7.28
7.27
7.27
7.26
7.25
7.20
7.20
7.19
7.18
7.18
7.17
7.17
4.47
4.46
4.44
3.10
3.08
3.06
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.98
2.99
3.90
1.30
2.00
2.02

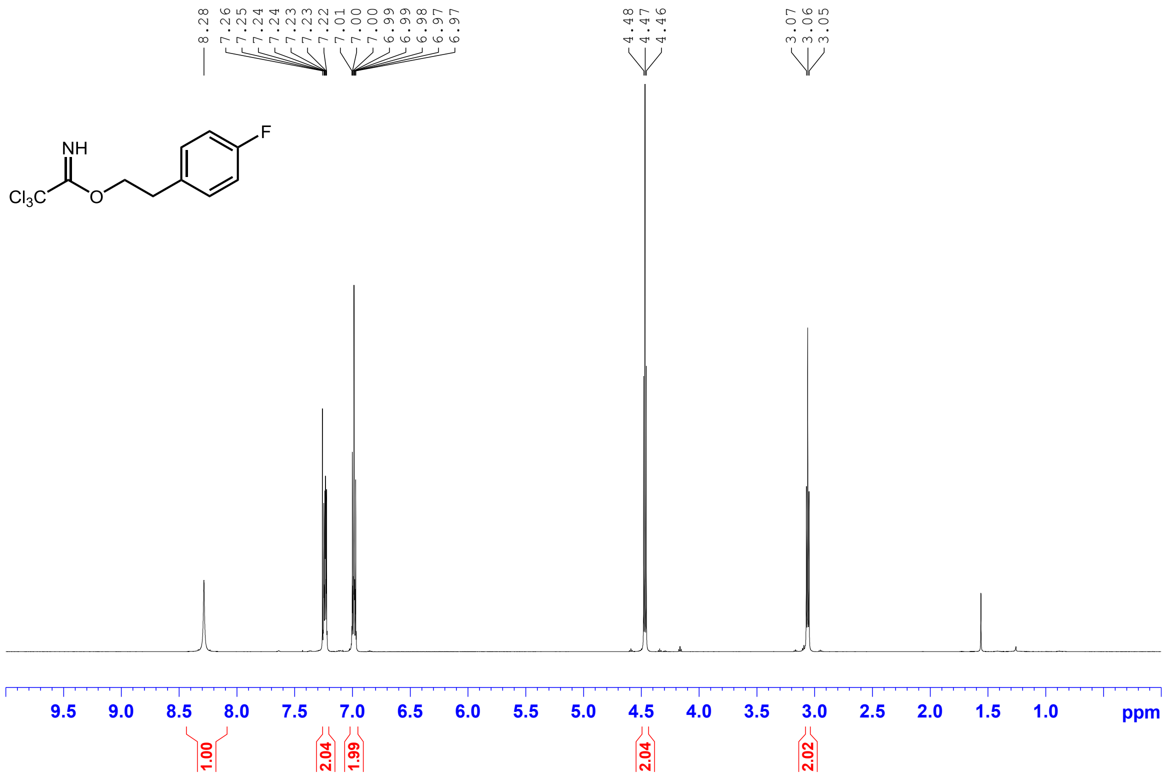

167.89
138.67
132.88
130.99
129.14
128.58
126.81
126.54
77.48
77.16
76.84
66.71
35.32
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

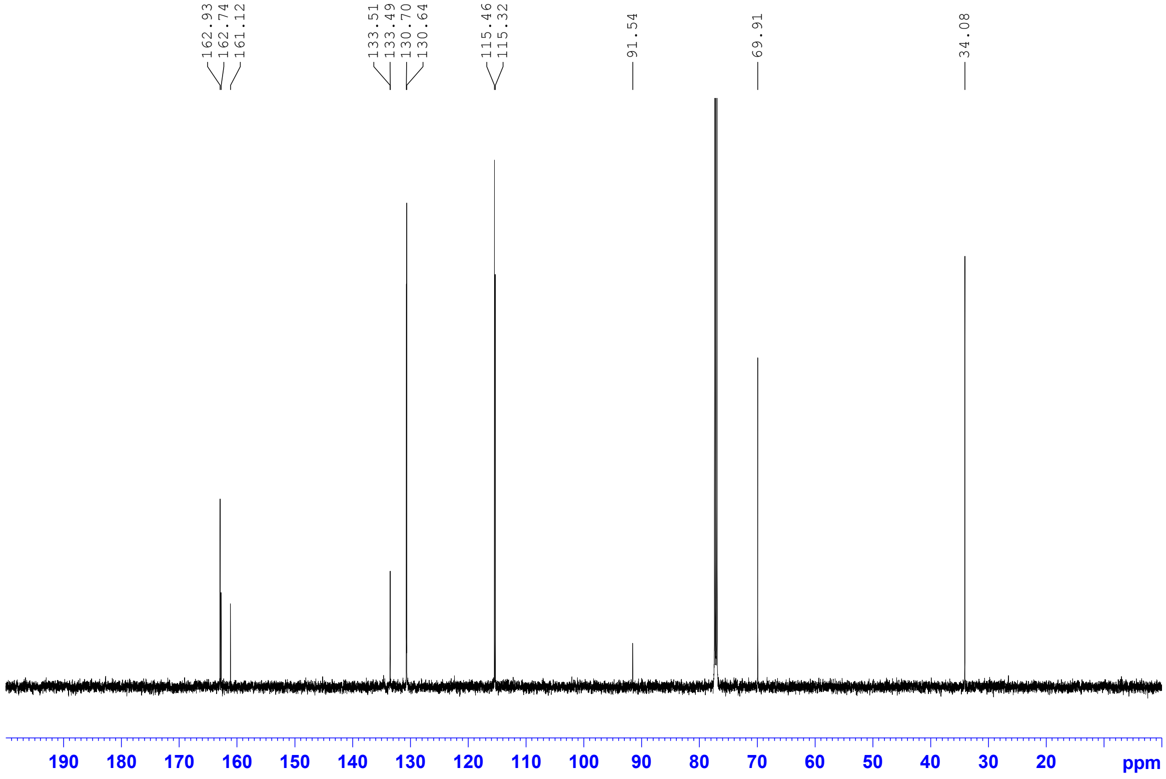

NH
Cl3C
O
8.29
7.33
7.33
7.33
7.32
7.31
7.31
7.30
7.30
7.29
7.28
7.27
7.26
7.25
7.25
7.24
7.24
7.23
7.22
4.52
4.50
4.49
3.12
3.10
3.08
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.96
5.30
2.00
2.13

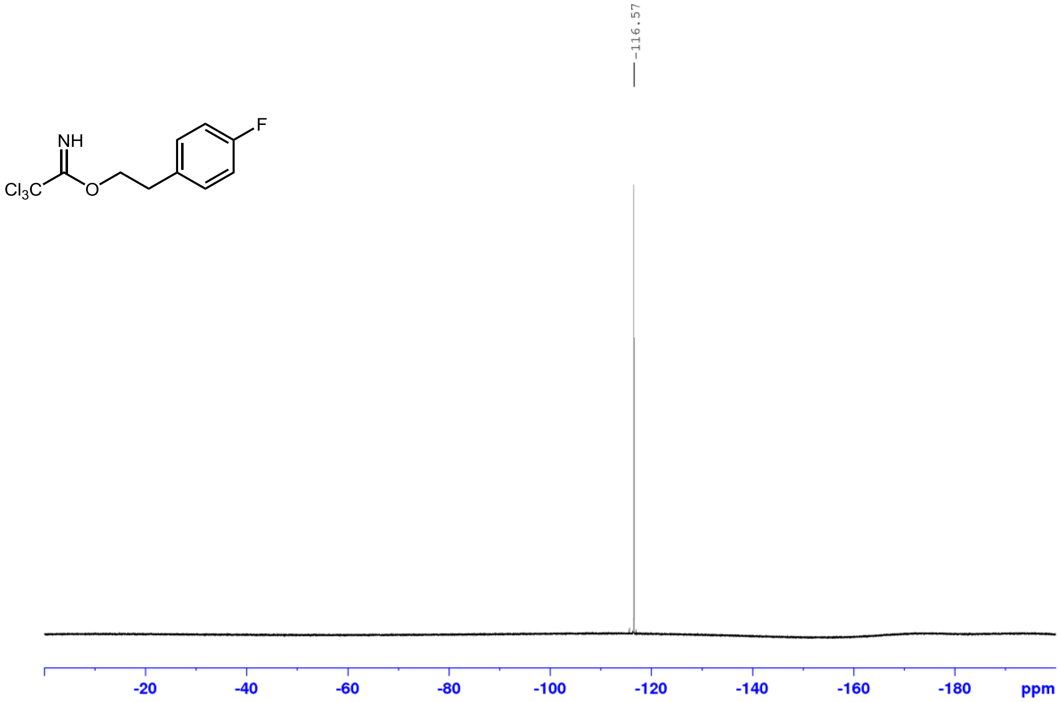

162.96
137.77
129.23
128.60
126.75
91.59
77.48
77.16
76.84
70.01
34.85
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

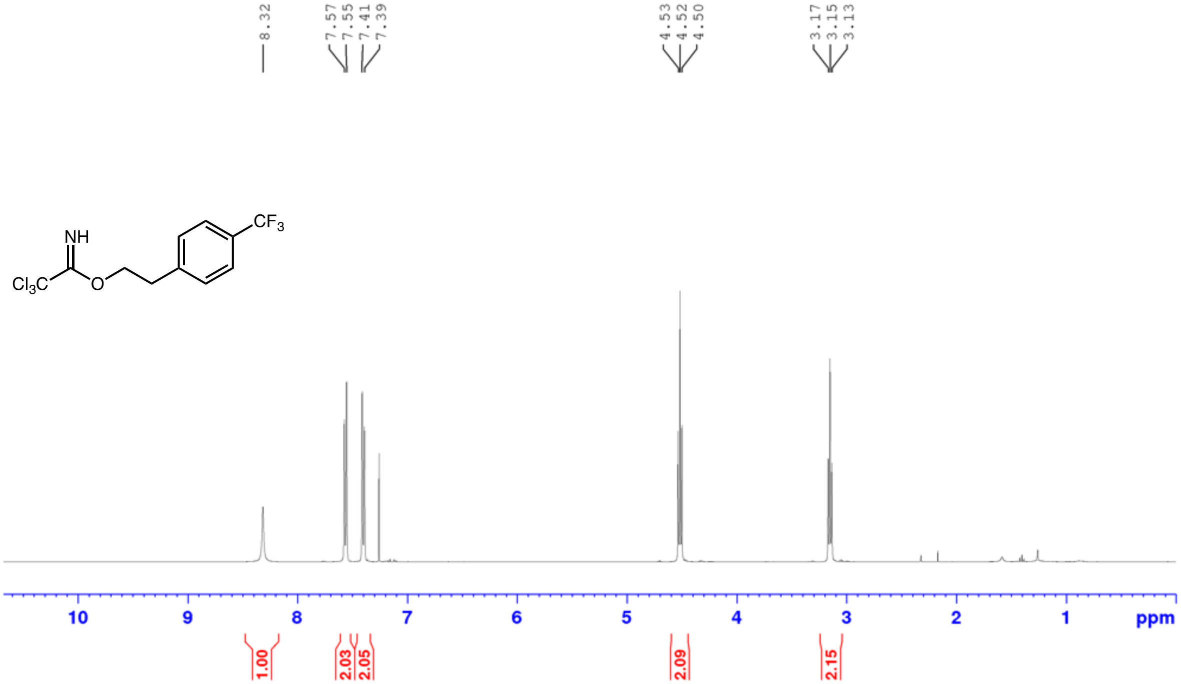

8.27
7.26
7.21
7.20
7.19
7.18
6.85
6.85
6.84
6.83
4.47
4.45
4.44
3.79
3.05
3.03
3.01
NH
OMe
Cl3C
O
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.96
1.95
1.95
2.00
3.10
2.04

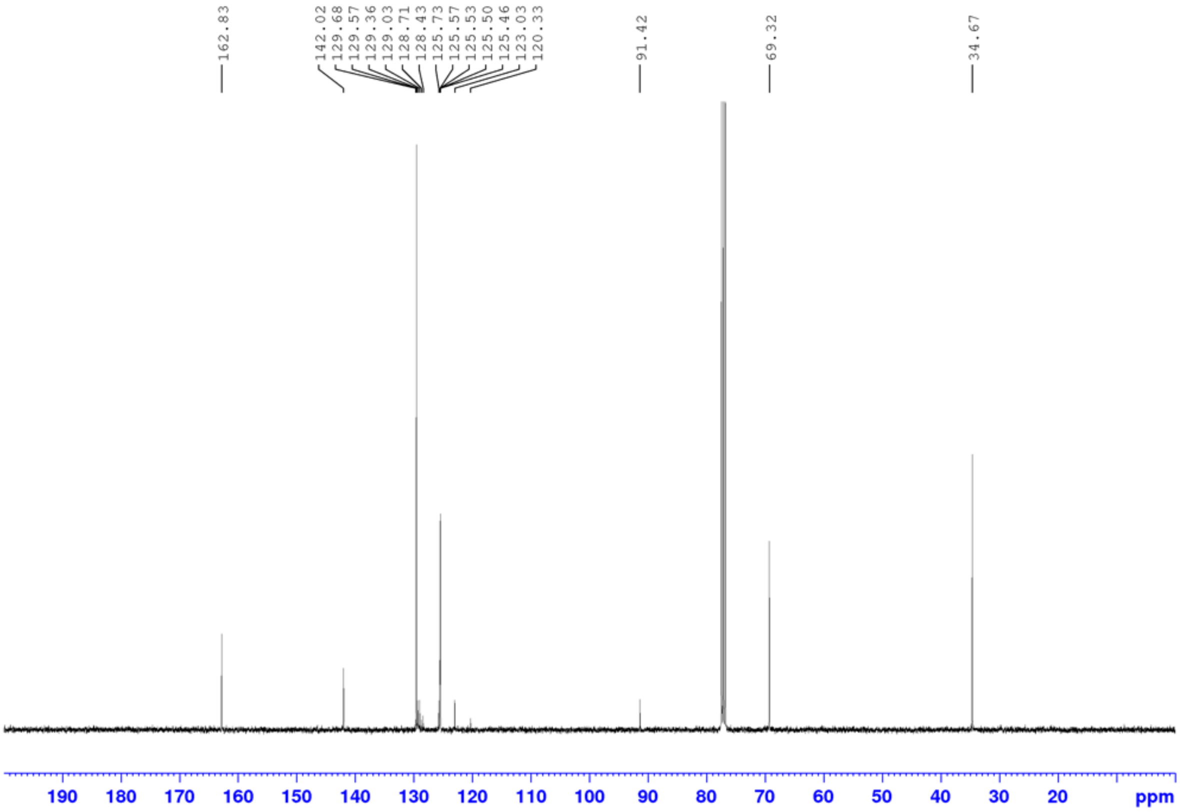

163.02
158.57
130.21
129.85
114.07
91.67
77.37
77.16
76.95
70.29
55.42
34.00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

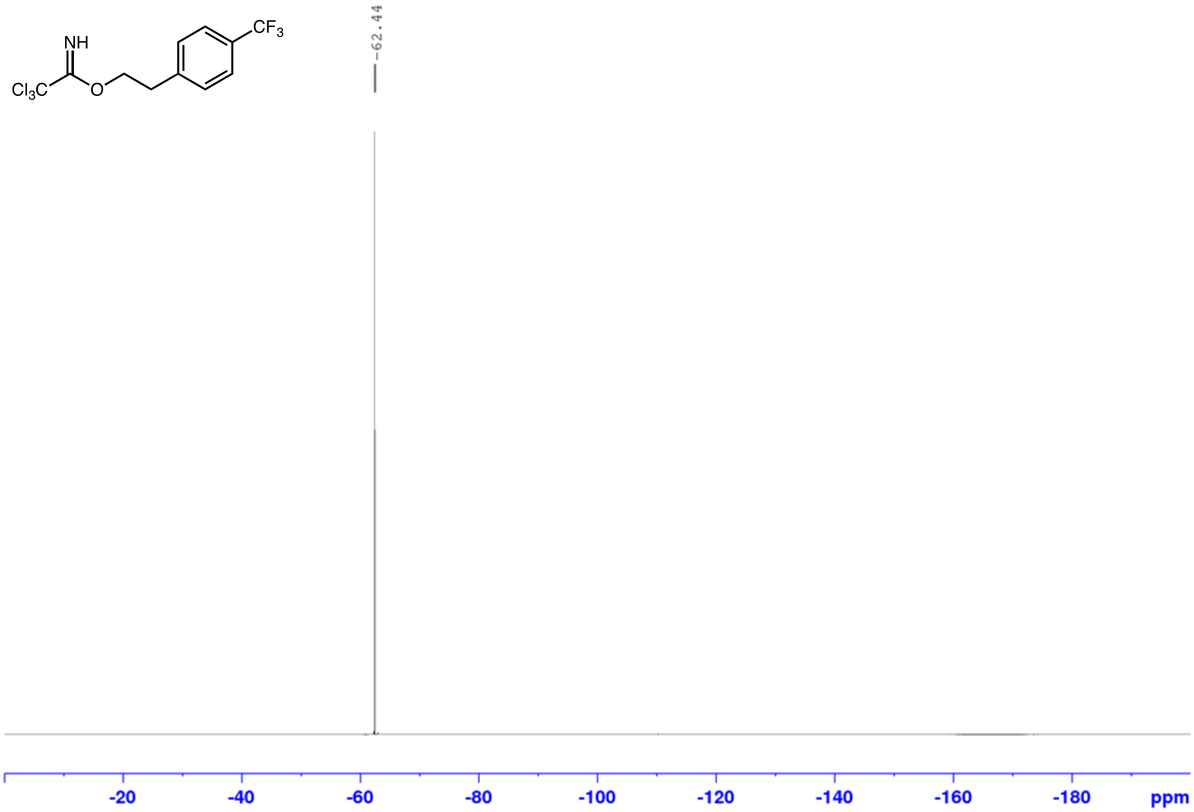

8.28
7.26
7.25
7.24
7.24
7.23
7.23
7.22
7.01
7.00
7.00
6.99
6.99
6.98
6.97
6.97
4.48
4.47
4.46
3.07
3.06
3.05
NH
F
Cl3C
O
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.00
2.04
1.99
2.04
2.02

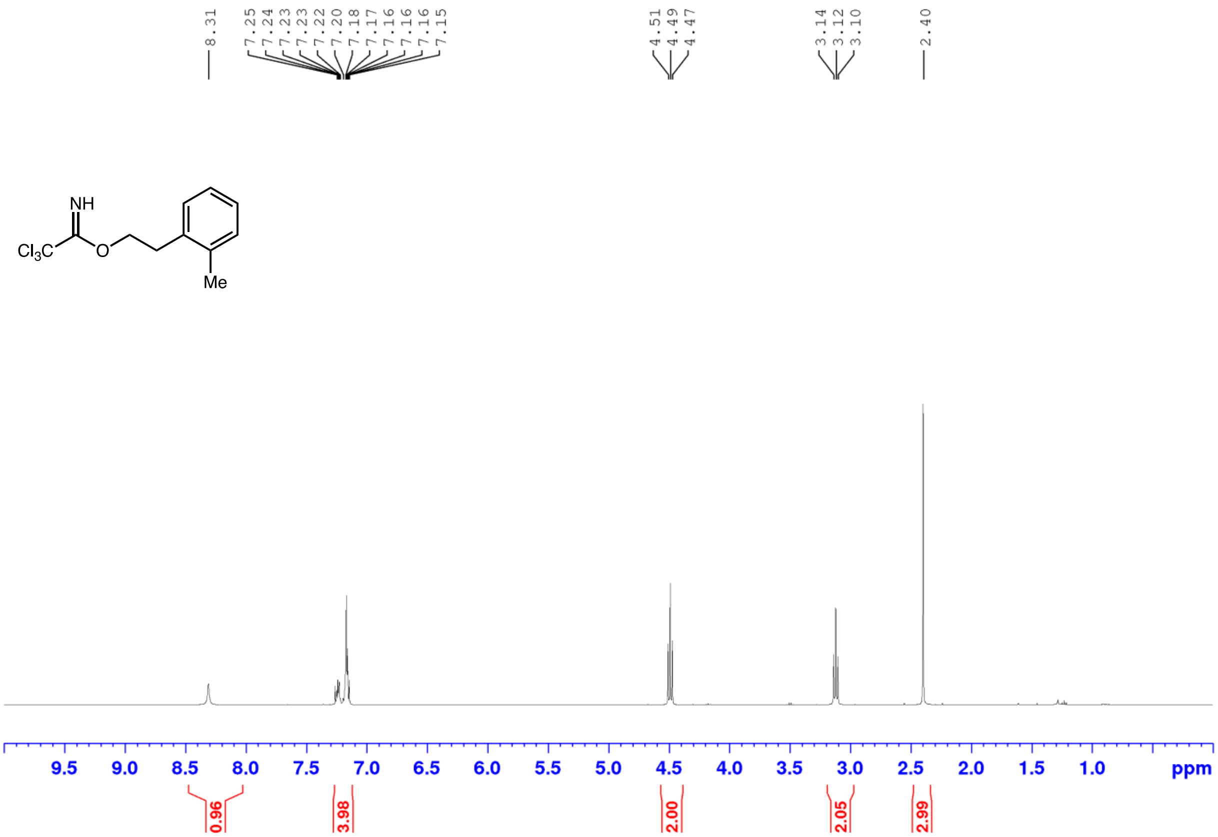

162.93
162.74
161.12
133.51
133.49
130.70
130.64
115.46
115.32
91.54
69.91
34.08
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

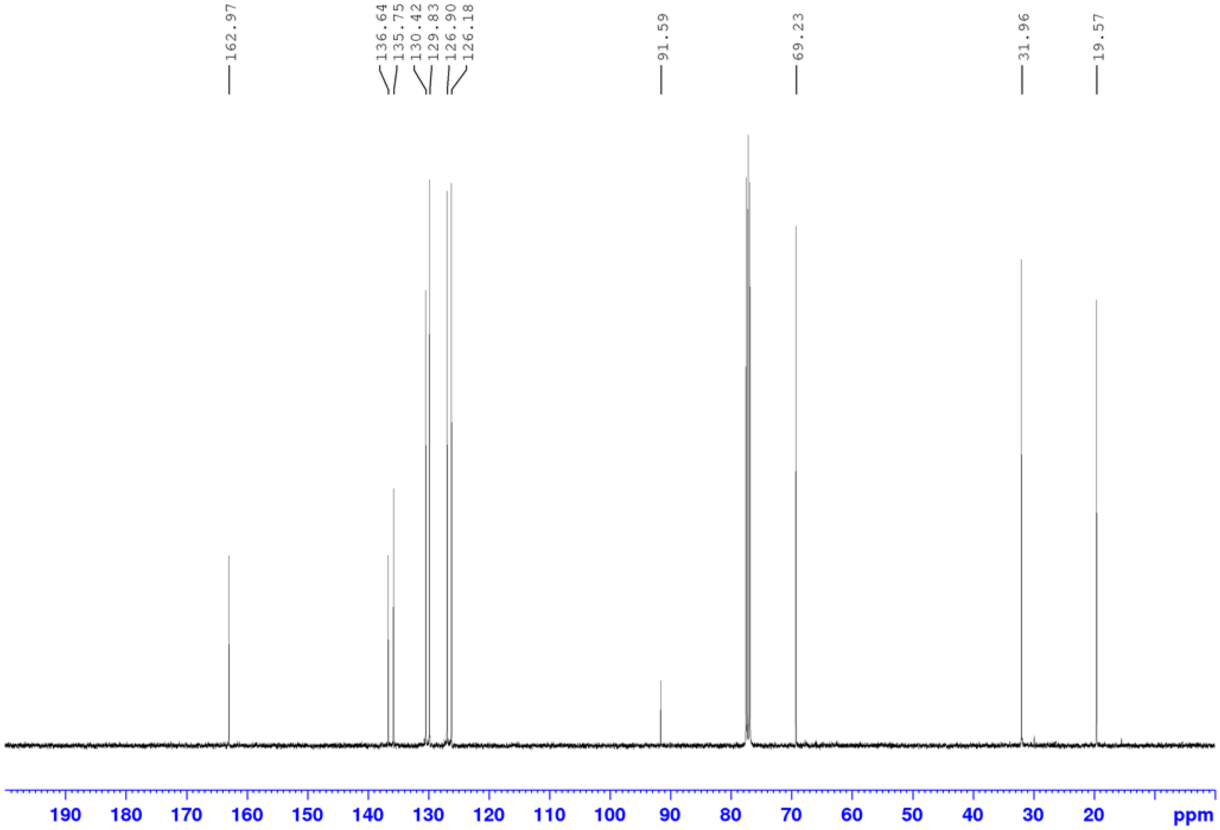

-116.57
NH
F
Cl3C
O
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

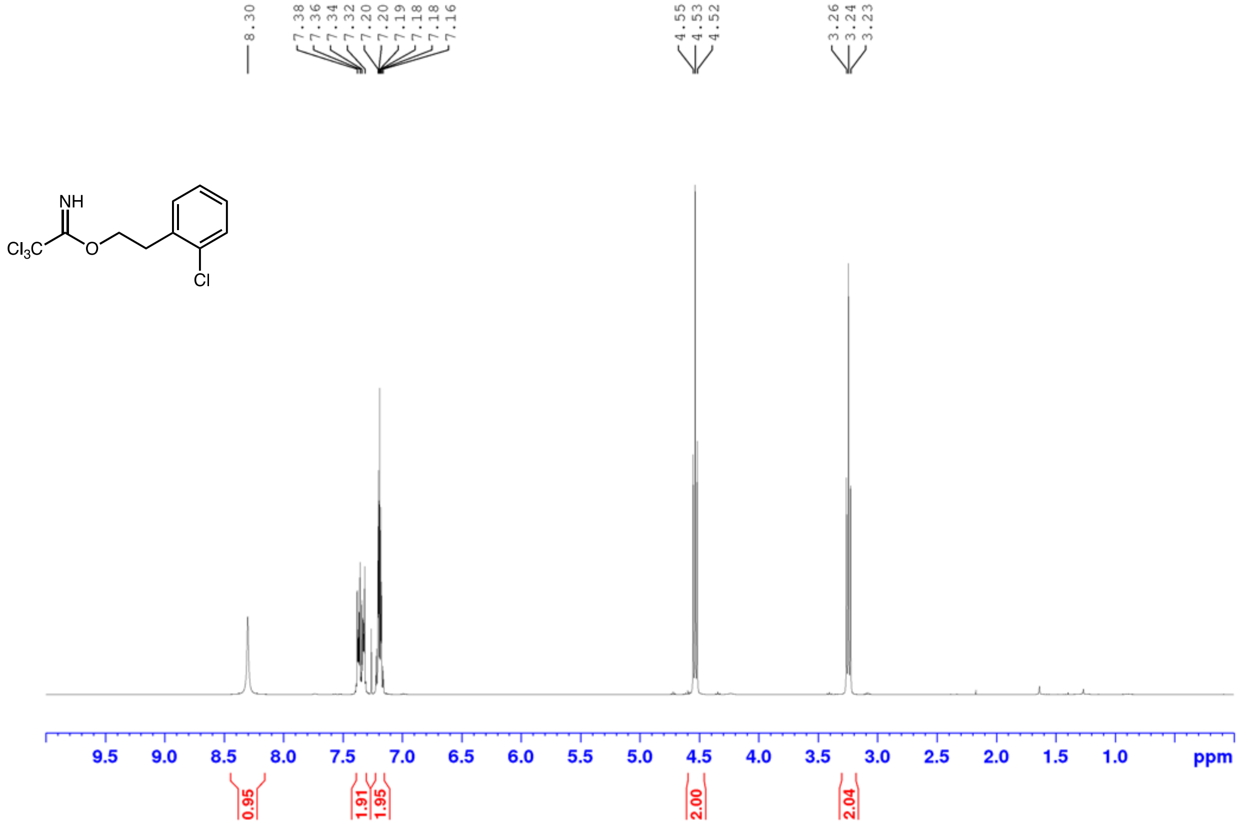

8.32
7.57
7.55
7.41
7.39
4.53
4.52
4.50
3.17
3.15
3.13
NH
CF3
Cl3C
O
10
9
8
7
6
5
4
3
2
1
ppm
1.00
2.03
2.05
2.09
2.15

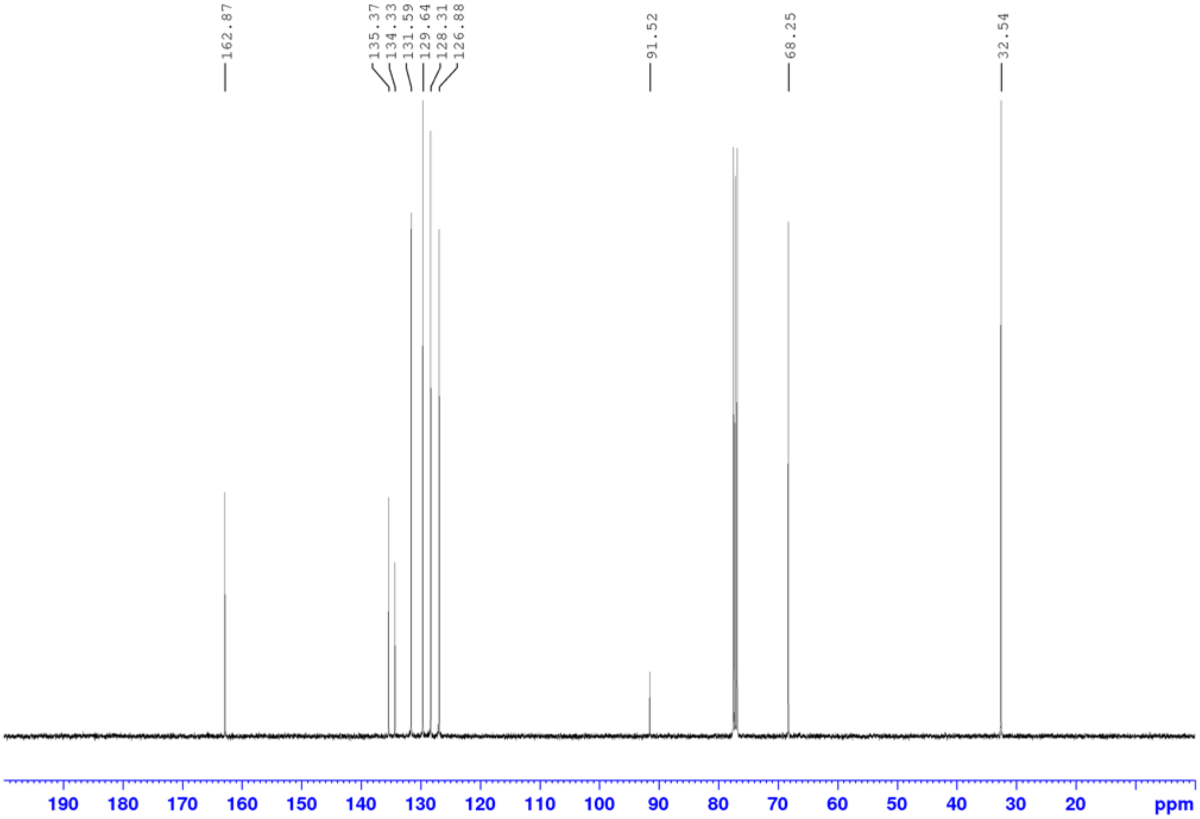

162.83
142.02
129.68
129.57
129.36
129.03
128.71
128.43
125.73
125.57
125.53
125.50
125.46
123.03
120.33
91.42
69.32
34.67
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

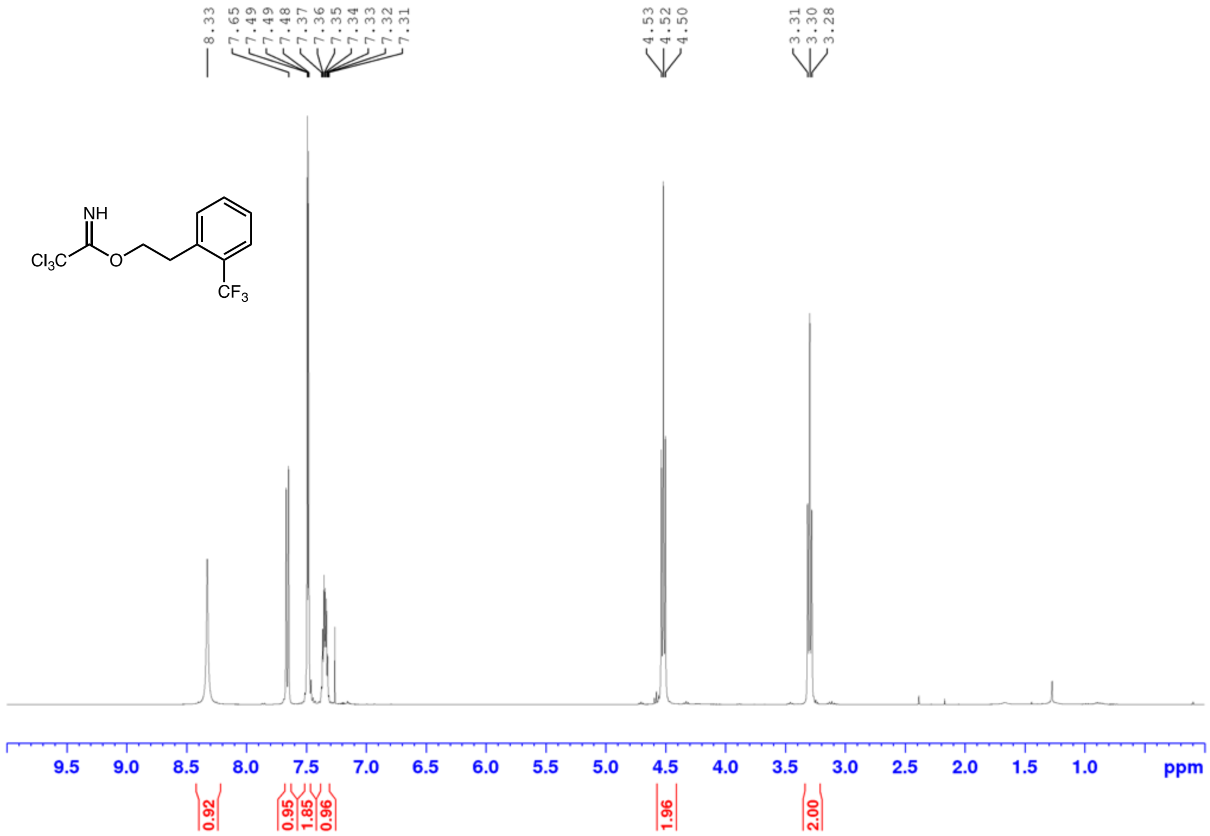

NH
Cl3C
O
CF3
-62.44
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

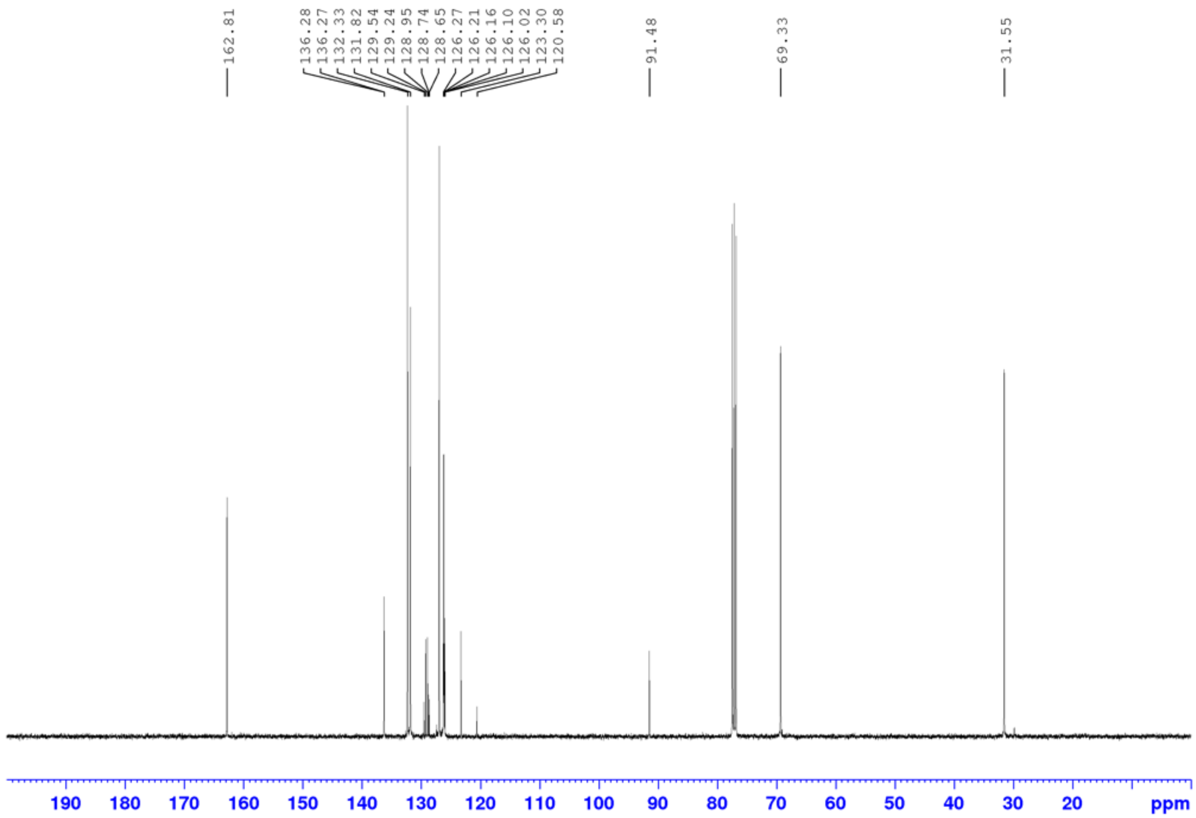

8.31
7.25
7.24
7.23
7.23
7.22
7.20
7.18
7.17
7.16
7.16
7.16
7.15
4.51
4.49
4.47
3.14
3.12
3.10
2.40
NH
Cl3C
O
Me
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.96
3.98
2.00
2.05
2.99

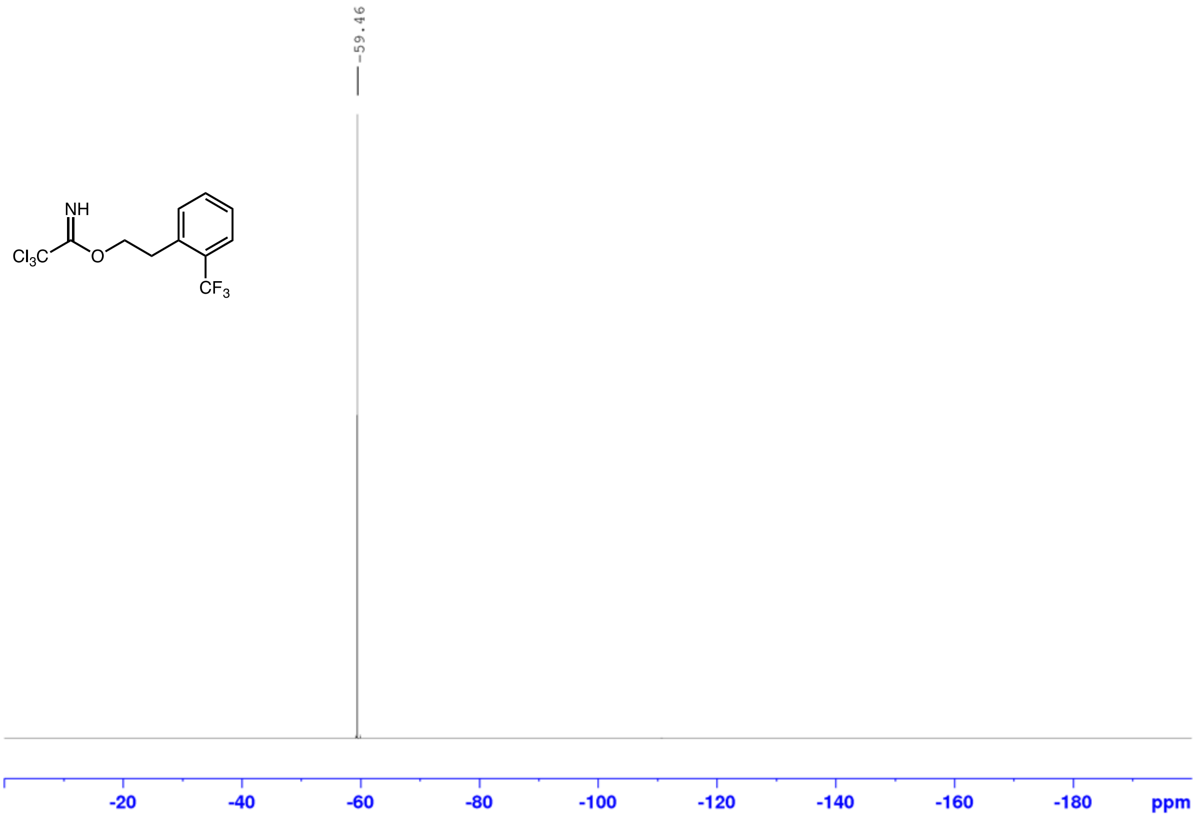

162.97
136.64
135.75
130.42
129.83
126.90
126.18
91.59
69.23
31.96
19.57
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

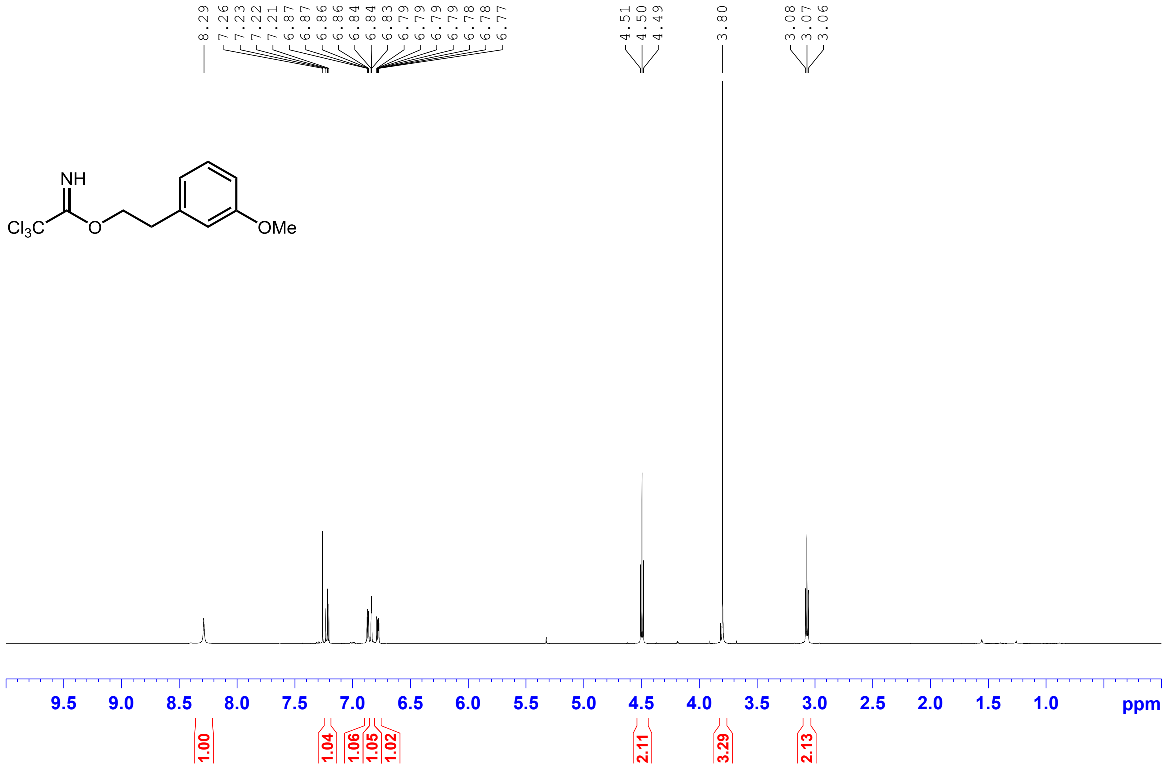

8.30
7.38
7.36
7.34
7.32
7.20
7.20
7.19
7.18
7.18
7.16
4.55
4.53
4.52
3.26
3.24
3.23
NH
Cl3C
O
Cl
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.95
1.91
1.95
2.00
2.04


162.87
135.37
134.33
131.59
129.64
128.31
126.88
91.52
68.25
32.54
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


8.33
7.65
7.49
7.49
7.48
7.37
7.36
7.35
7.34
7.33
7.32
7.31
4.53
4.52
4.50
3.31
3.30
3.28
NH
Cl3C
O
CF3
9.5
9.0
8.5
8.0
7.5
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
ppm
0.92
0.95
1.85
0.96
1.96
2.00


162.81
136.28
136.27
132.33
131.82
129.54
129.24
128.95
128.74
128.65
126.27
126.21
126.16
126.10
126.02
123.30
120.58
91.48
69.33
31.55
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


-59.46
NH
Cl3C
O
CF3
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm


8.29
7.26
7.23
7.22
7.21
6.87
6.86
6.86
6.84
6.84
6.83
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6.79
6.79
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3.07
3.06
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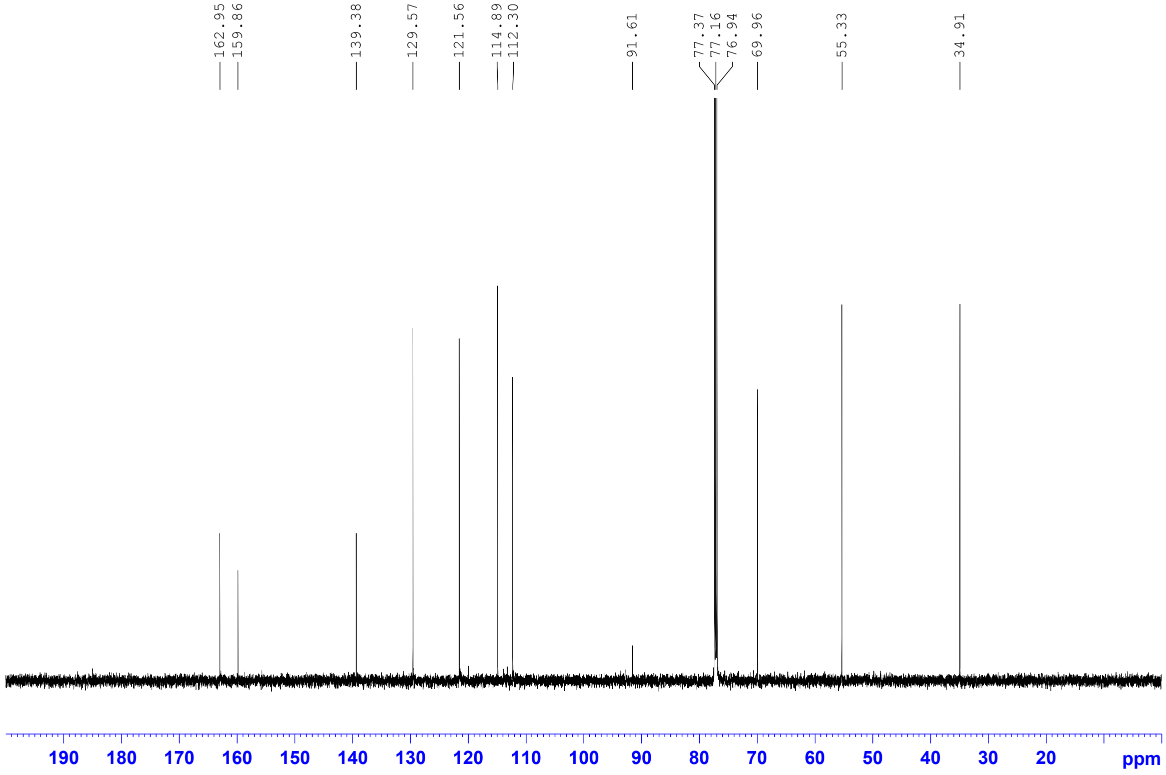
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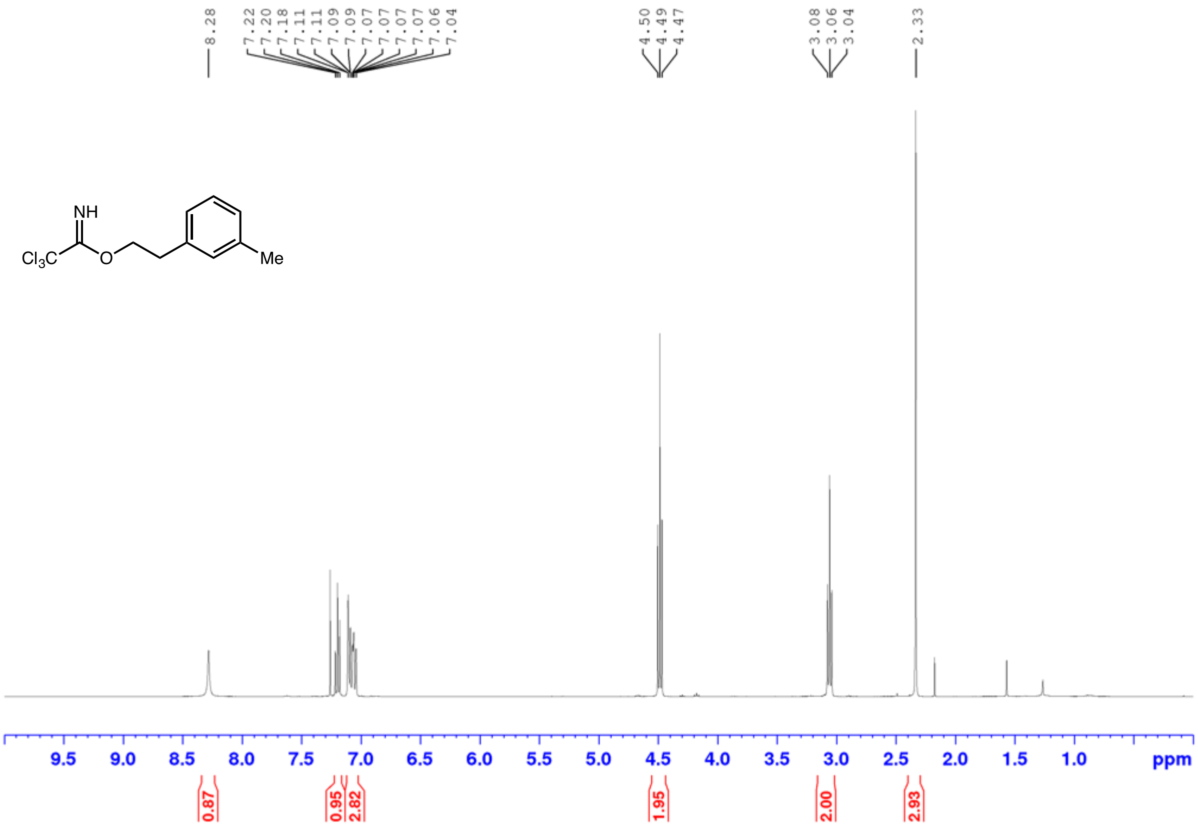
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3.06
3.04
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O
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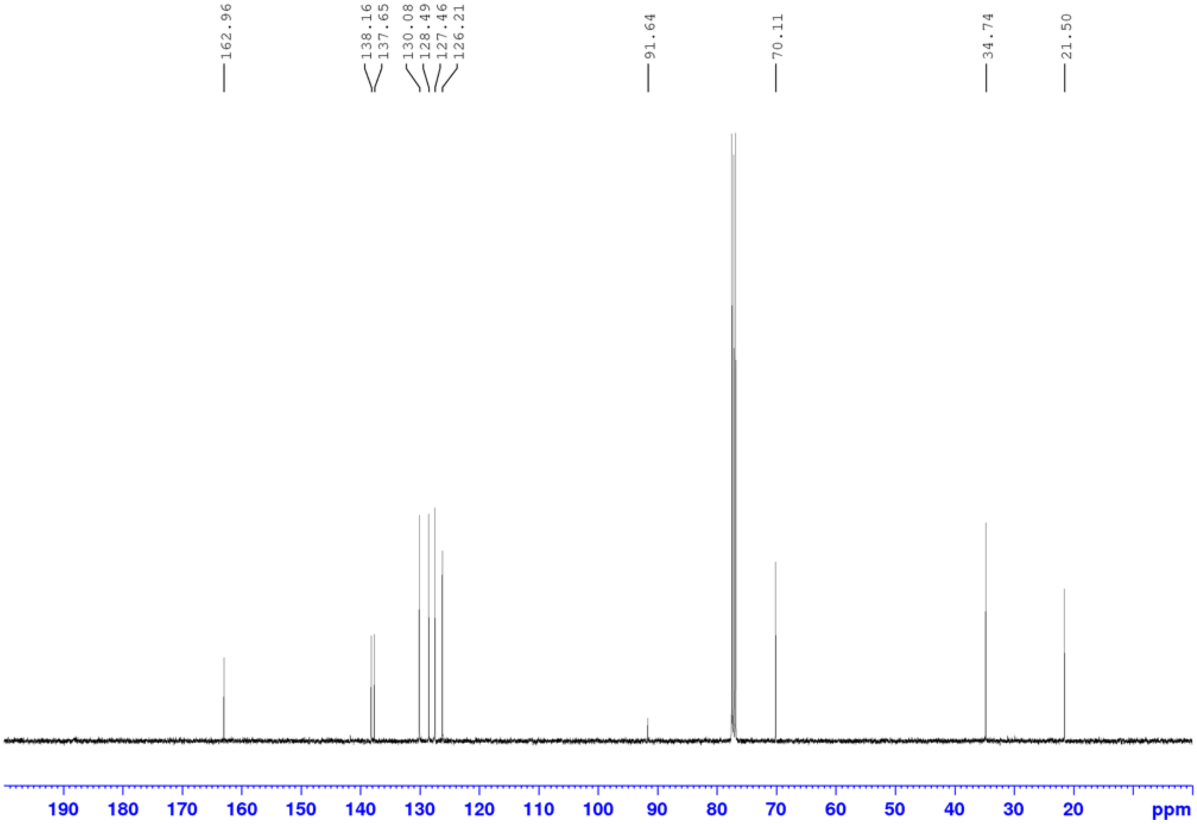
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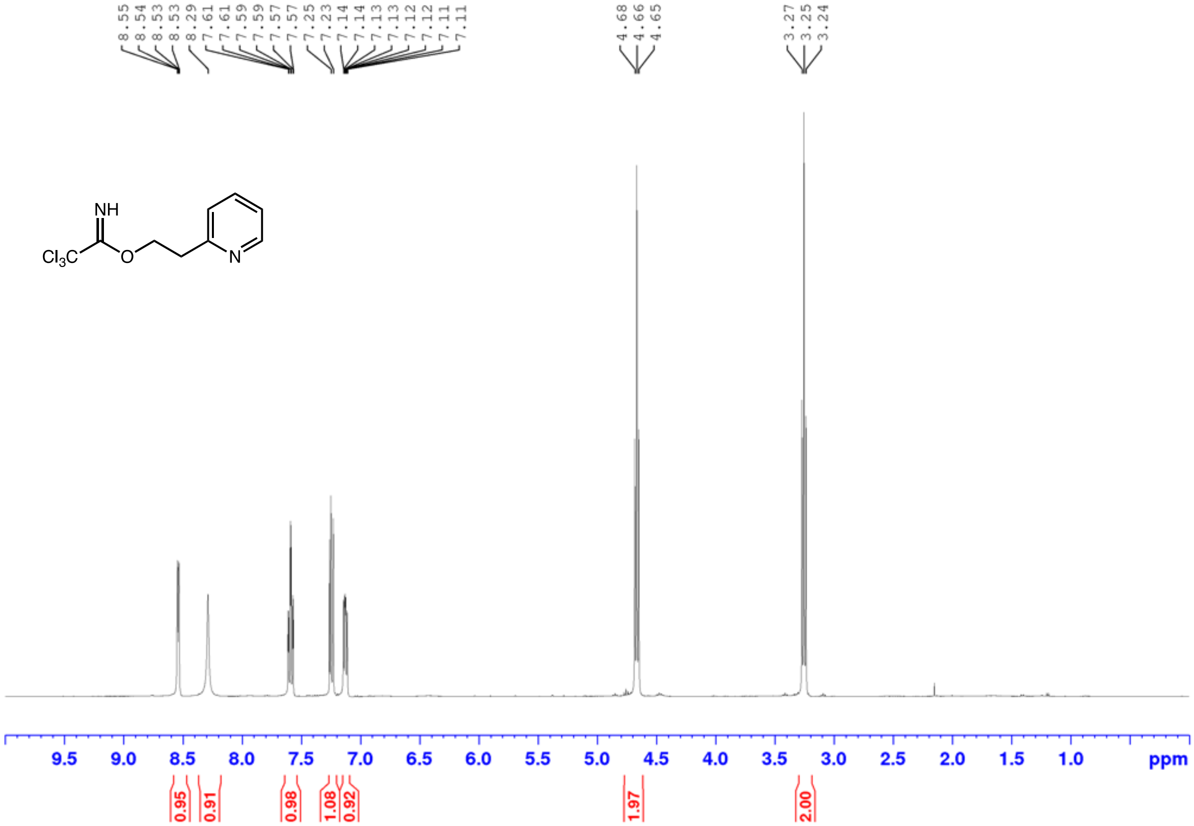
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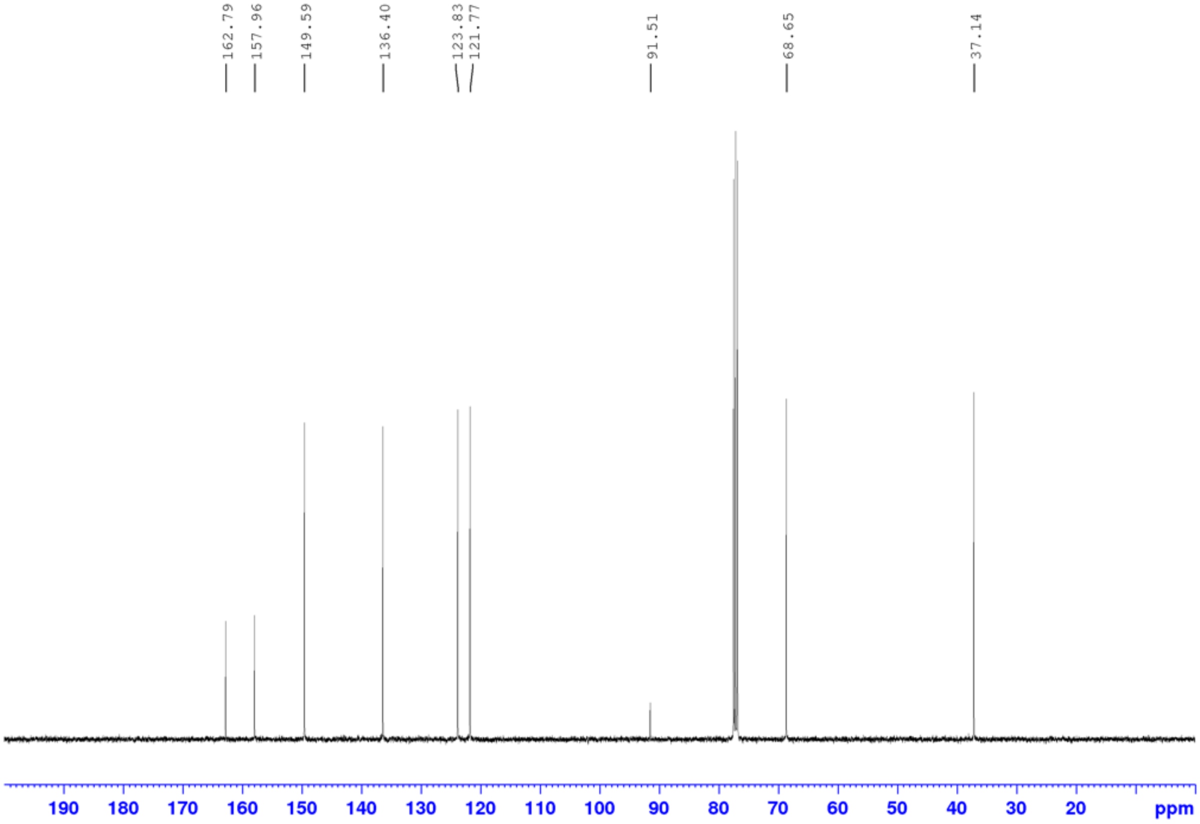
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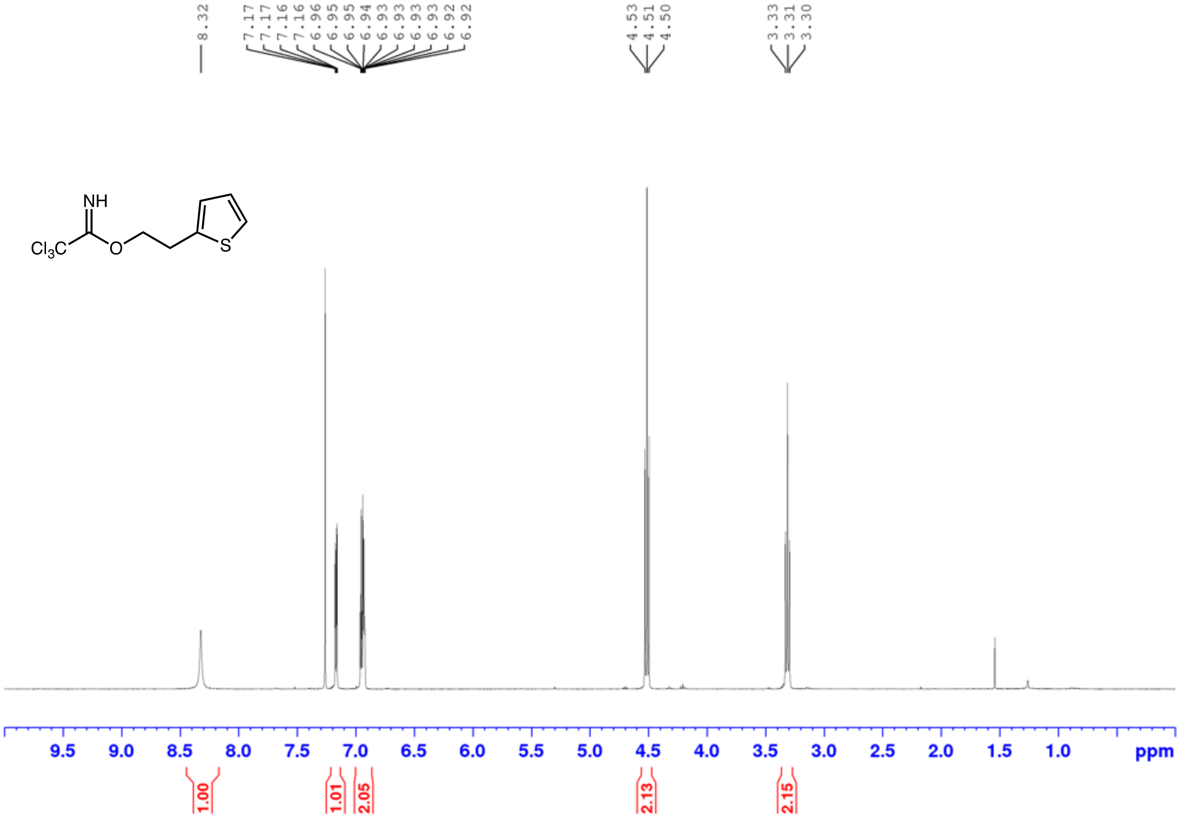
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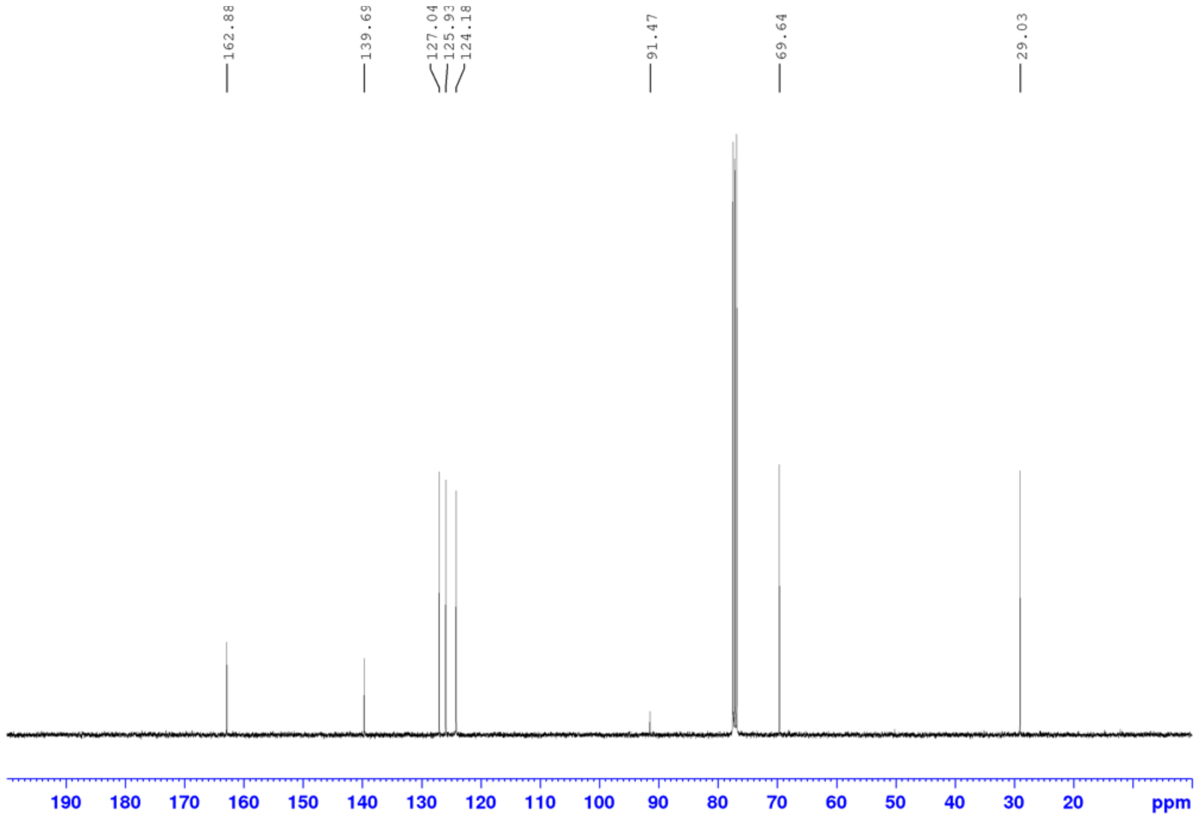
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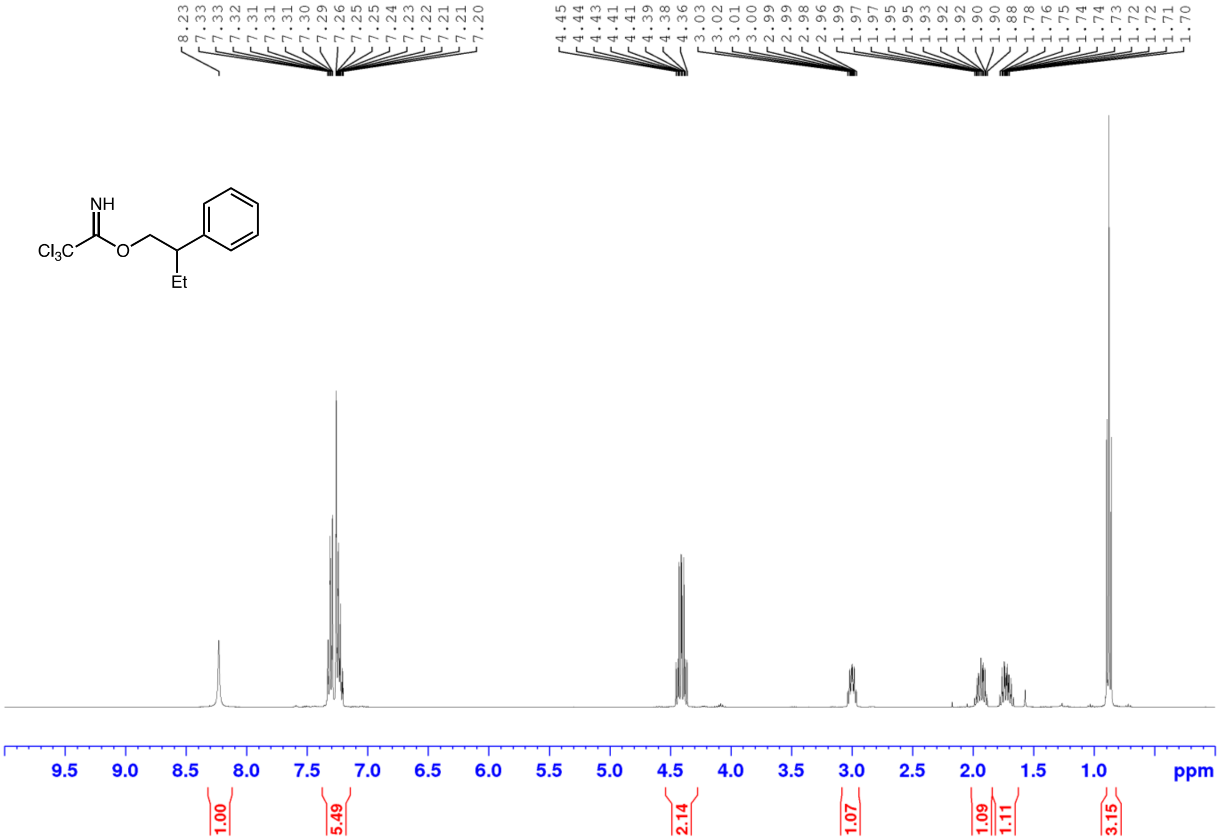
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7.21
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4.44
4.43
4.41
4.41
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4.38
4.36
3.03
3.02
3.01
3.00
2.99
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Cl3C
O
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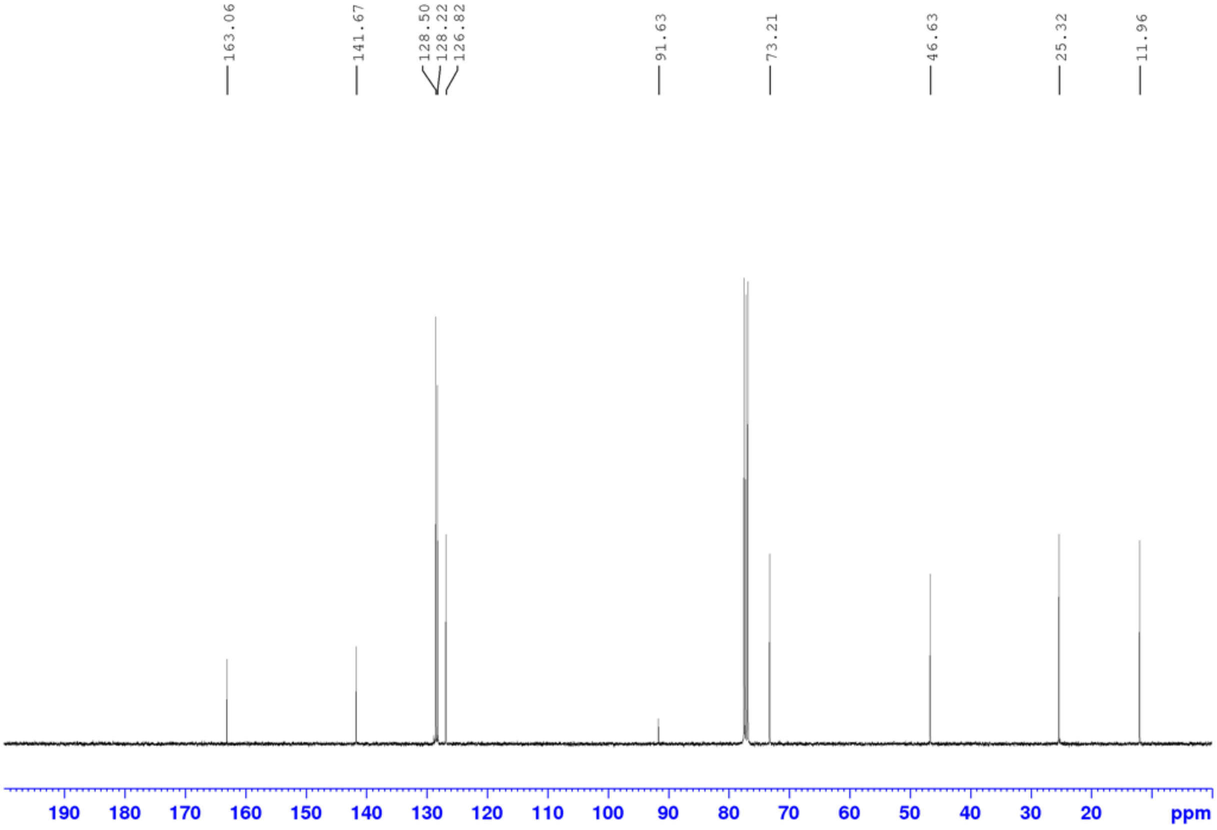
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40
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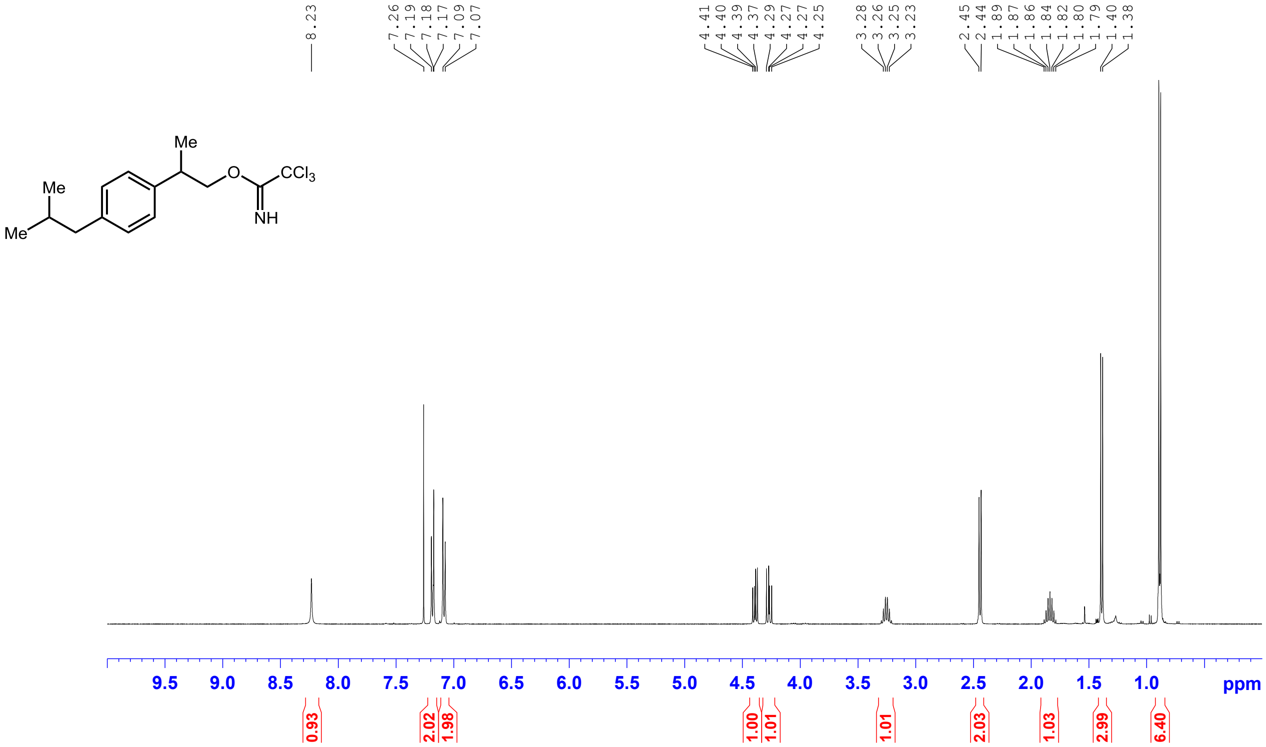
ppm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4.39
4.37
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4.27
4.27
4.25
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3.23
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4.0
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3.0
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1.03
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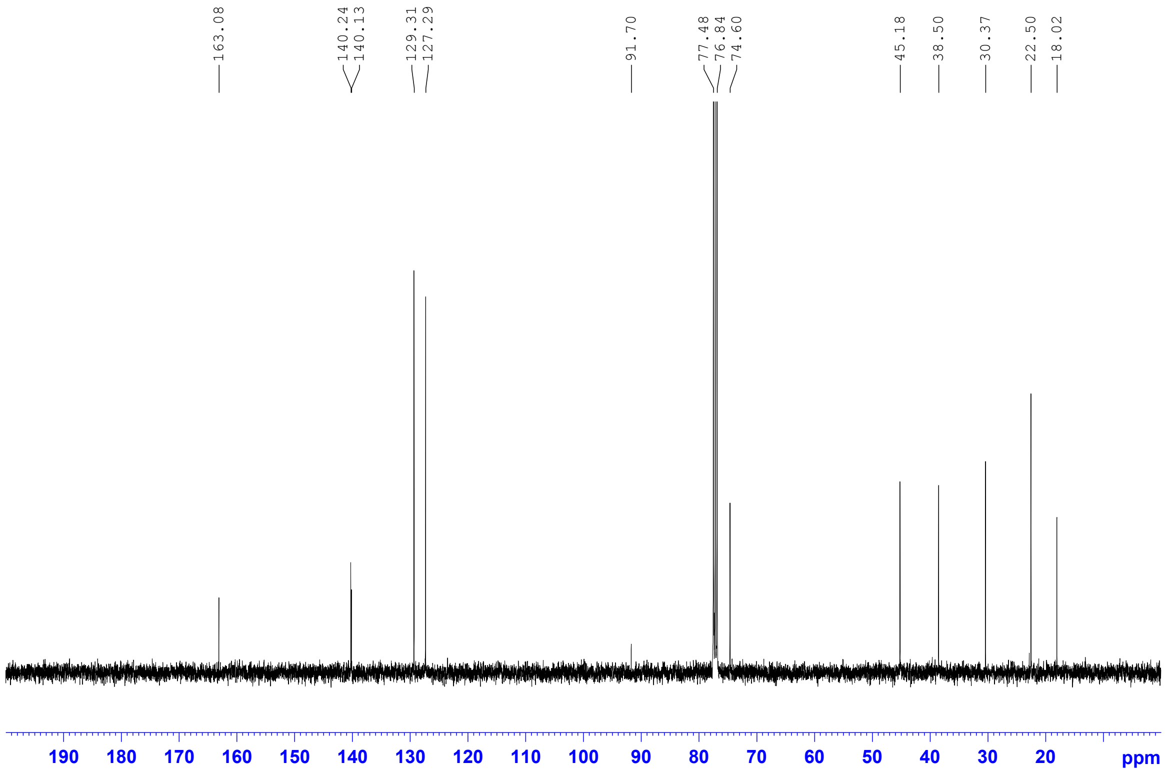
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22.50
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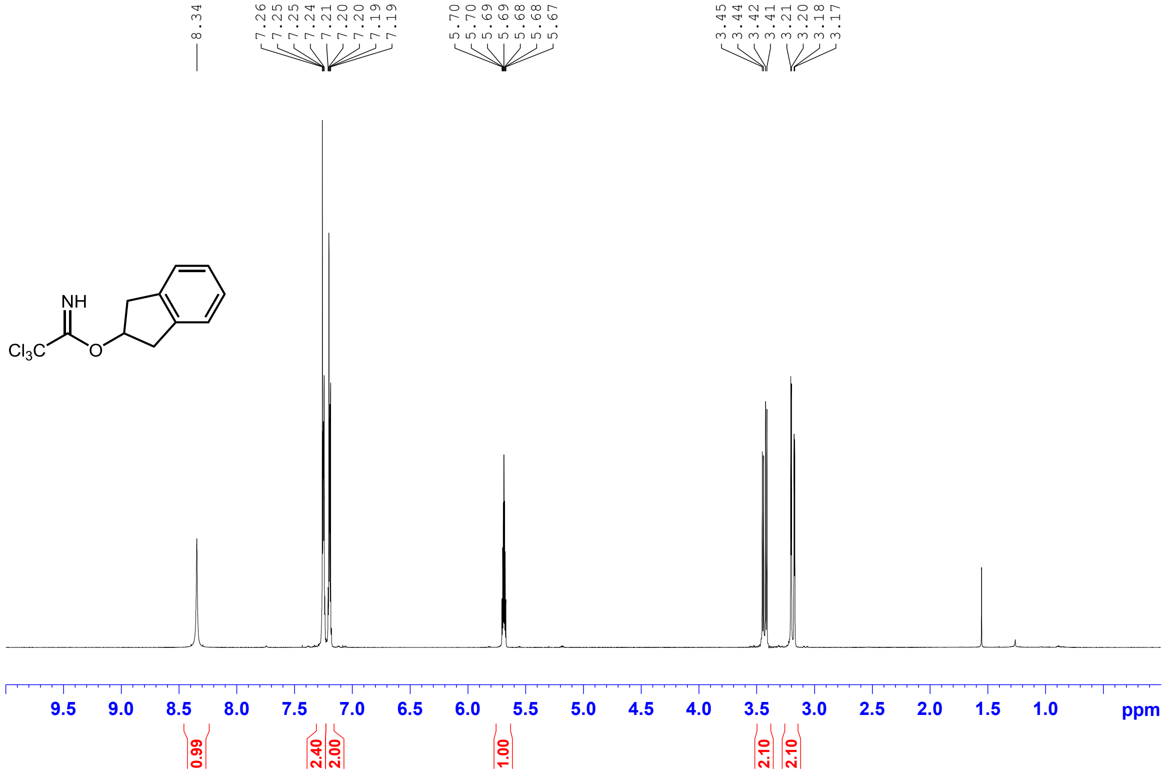
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7.19
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5.69
5.68
5.68
5.67
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3.44
3.42
3.41
3.21
3.20
3.18
3.17
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Cl_3C
O
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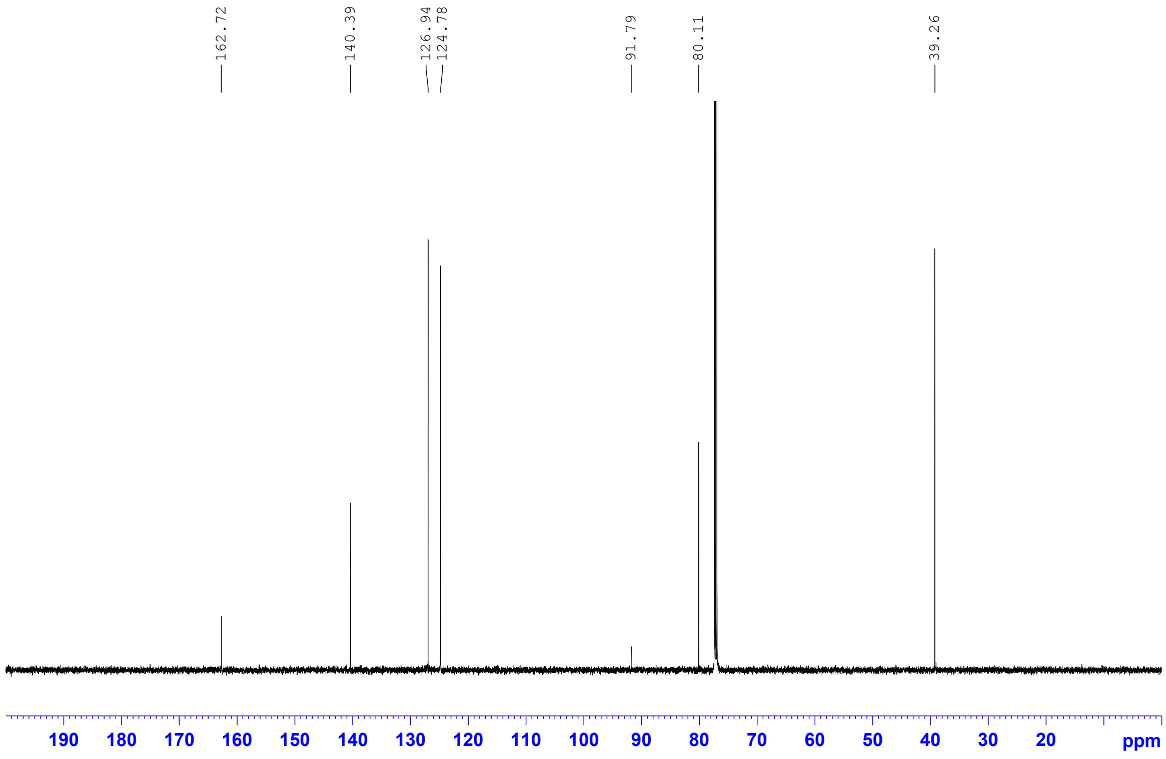
2.10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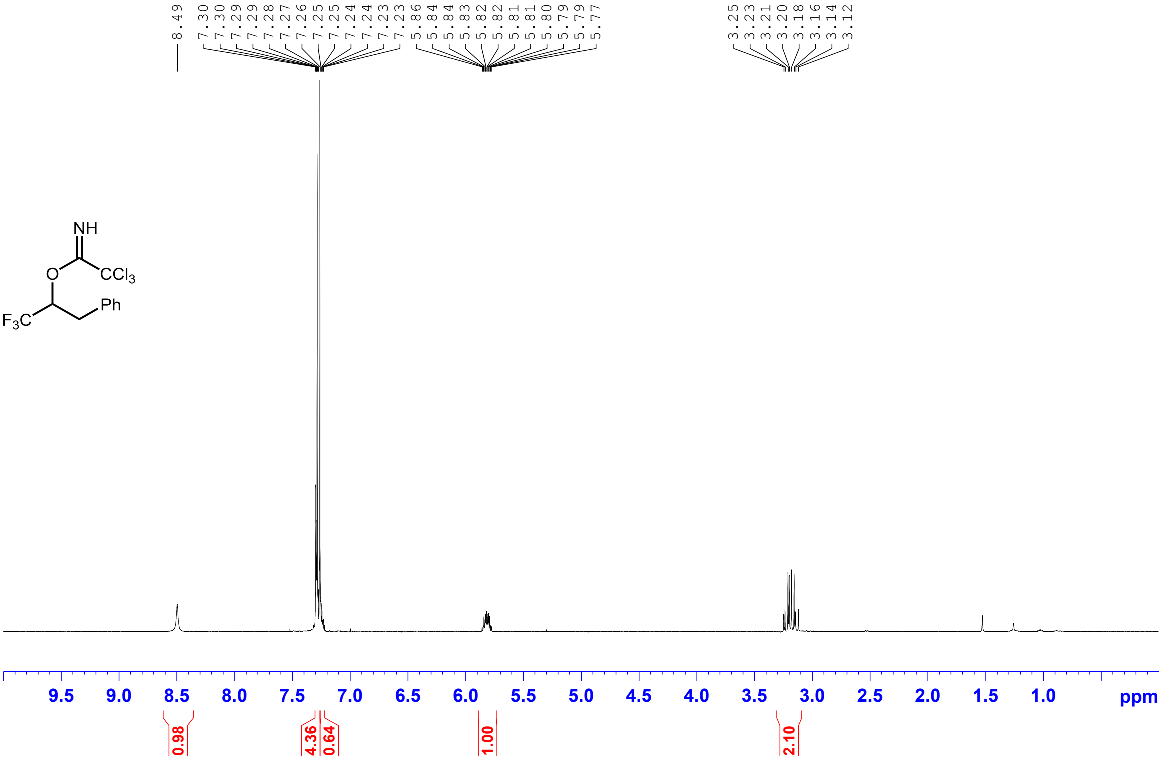
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CCl$_3$
F$_3$C
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7.25
7.25
7.24
7.24
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7.23
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5.82
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5.77
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3.18
3.16
3.14
3.12
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7.5
7.0
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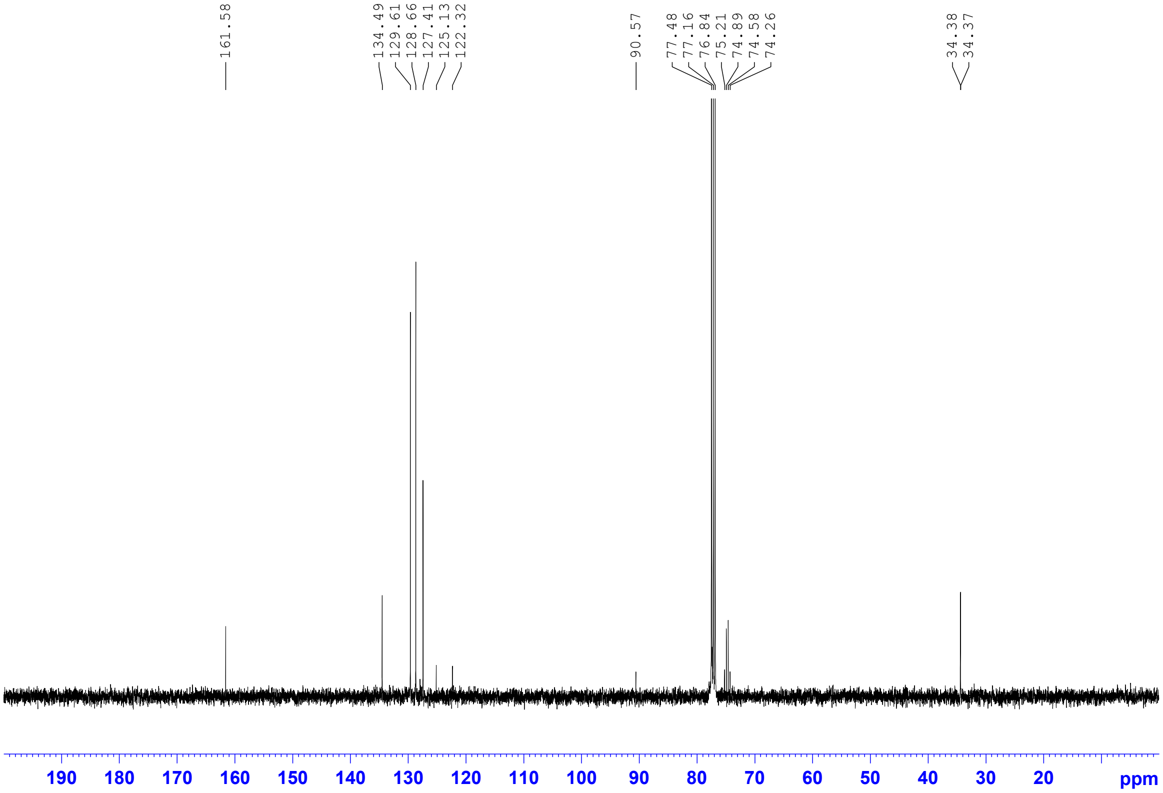
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74.26
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150
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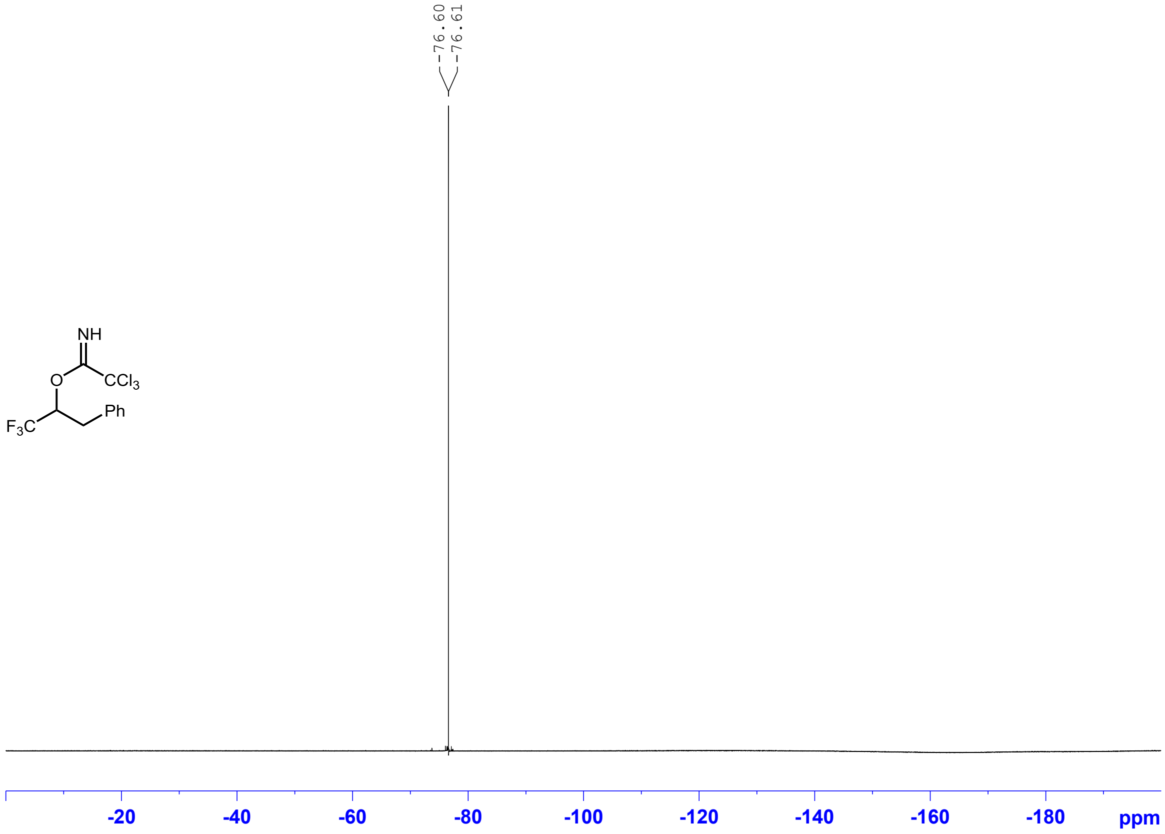
ppm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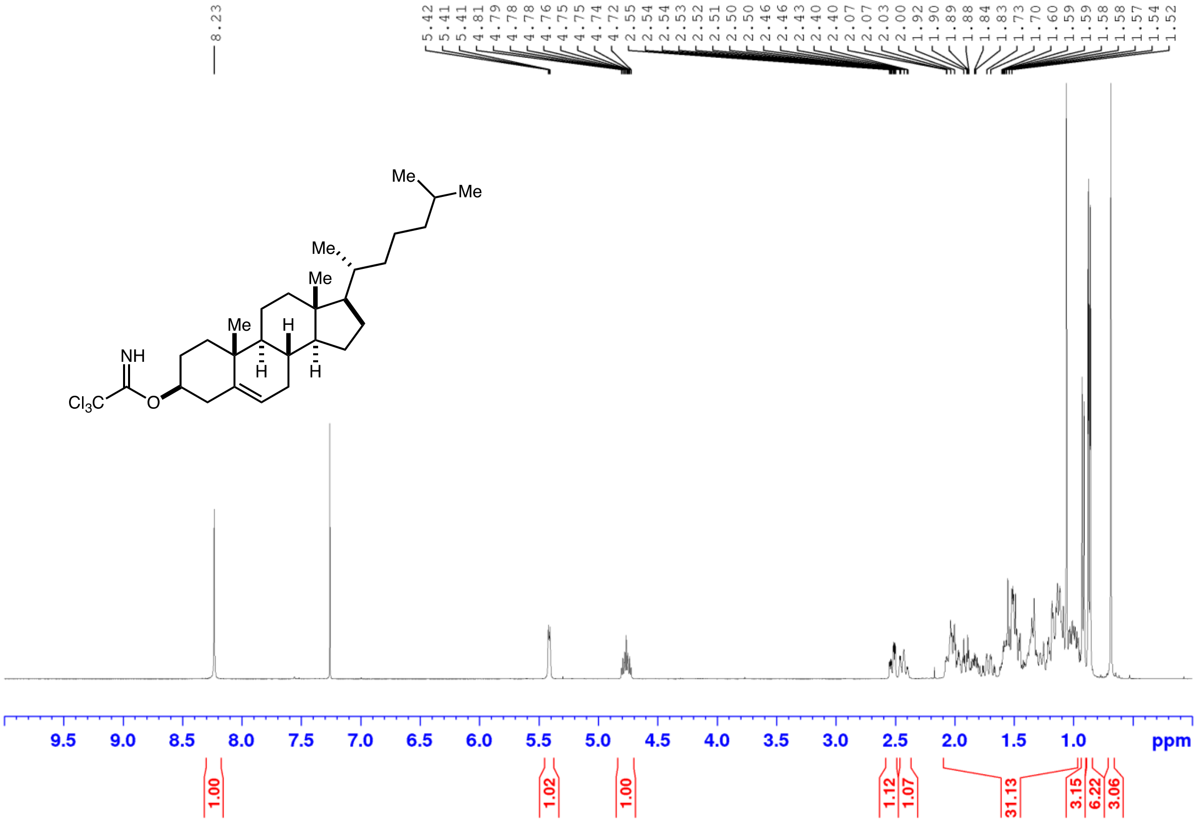
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2.40
2.07
2.07
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Me
Me
Me
Me
H
H
H
NH
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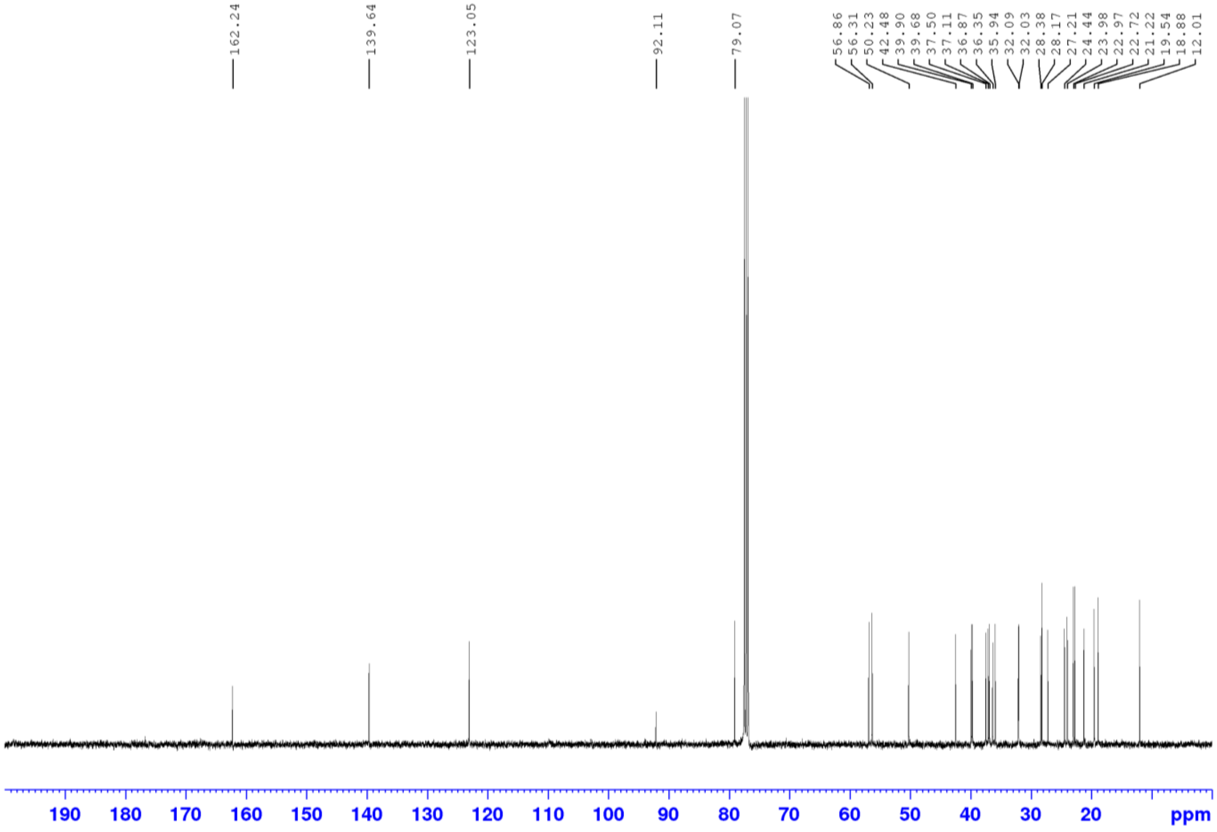
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36.35
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32.03
28.38
28.17
27.21
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22.97
22.72
21.22
19.54
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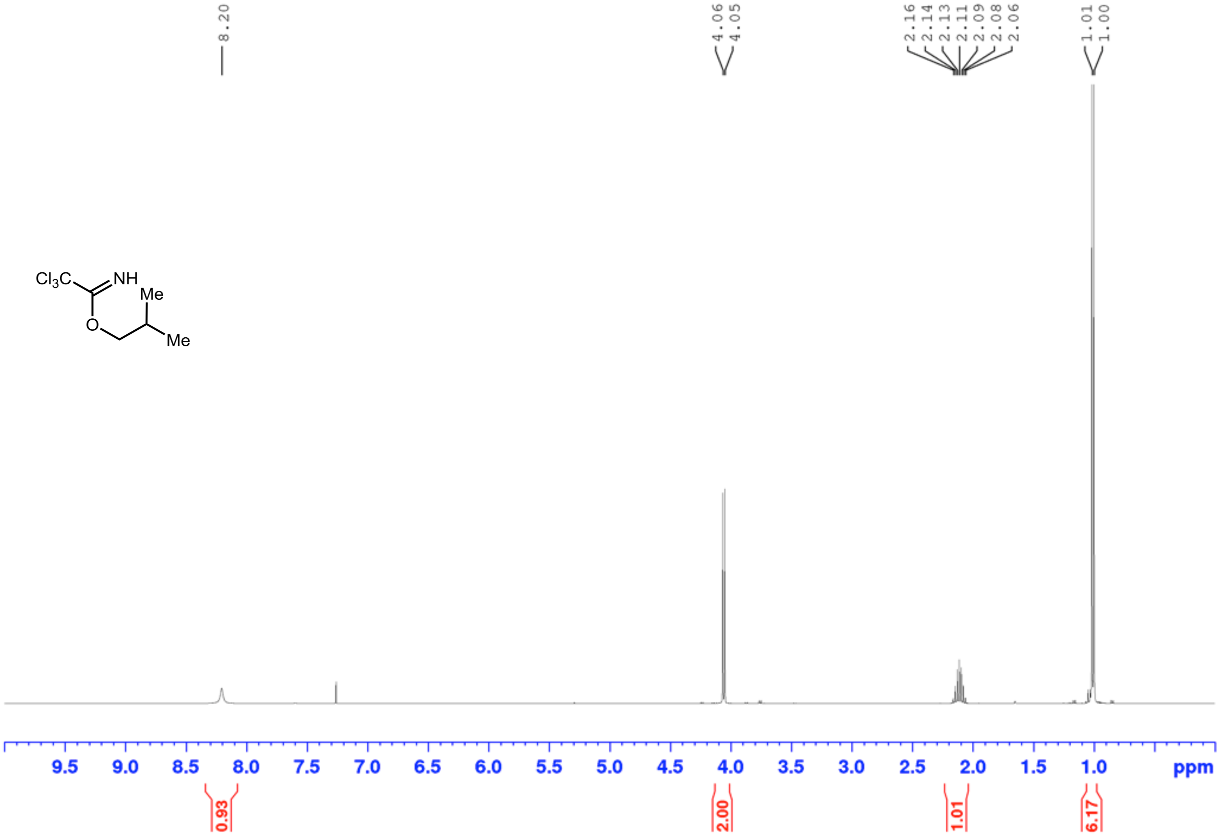
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2.08
2.06
1.01
1.00
Cl3C
NH
O
Me
Me
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
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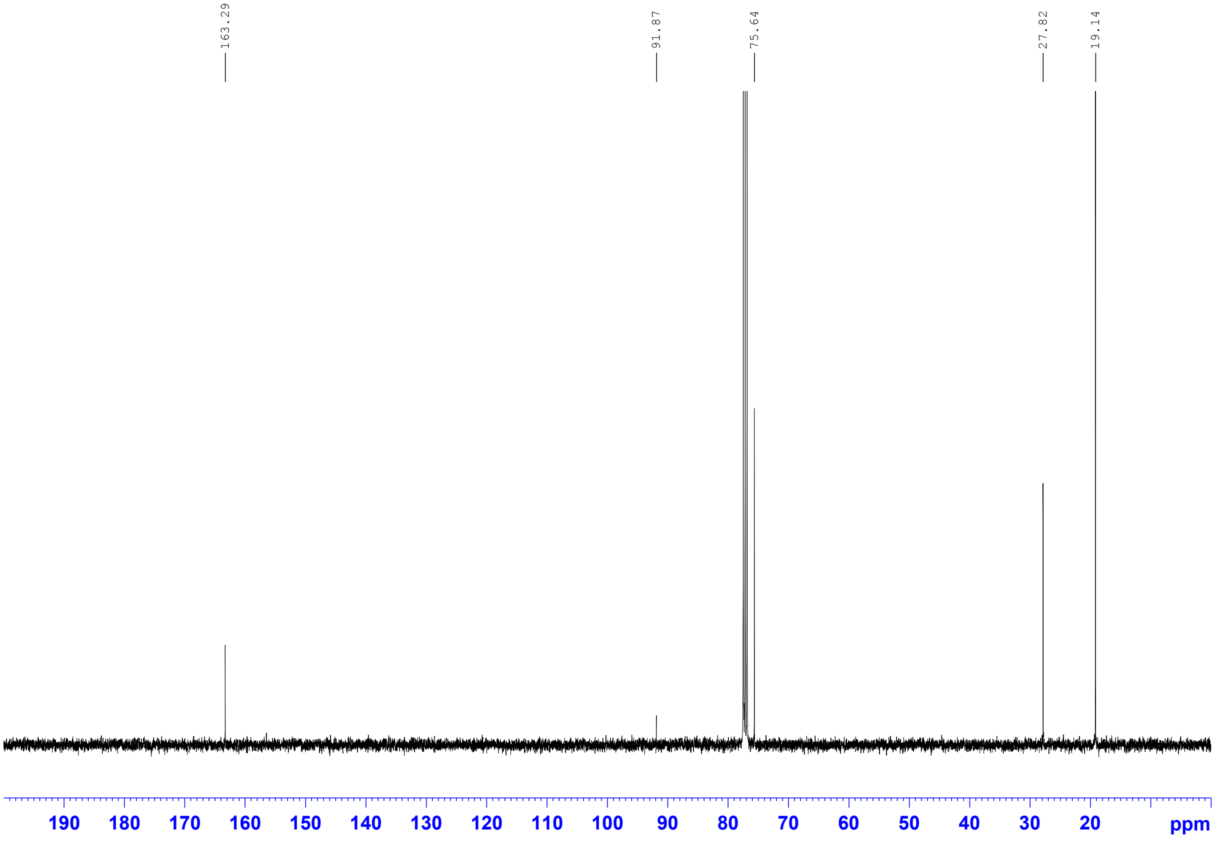
6.17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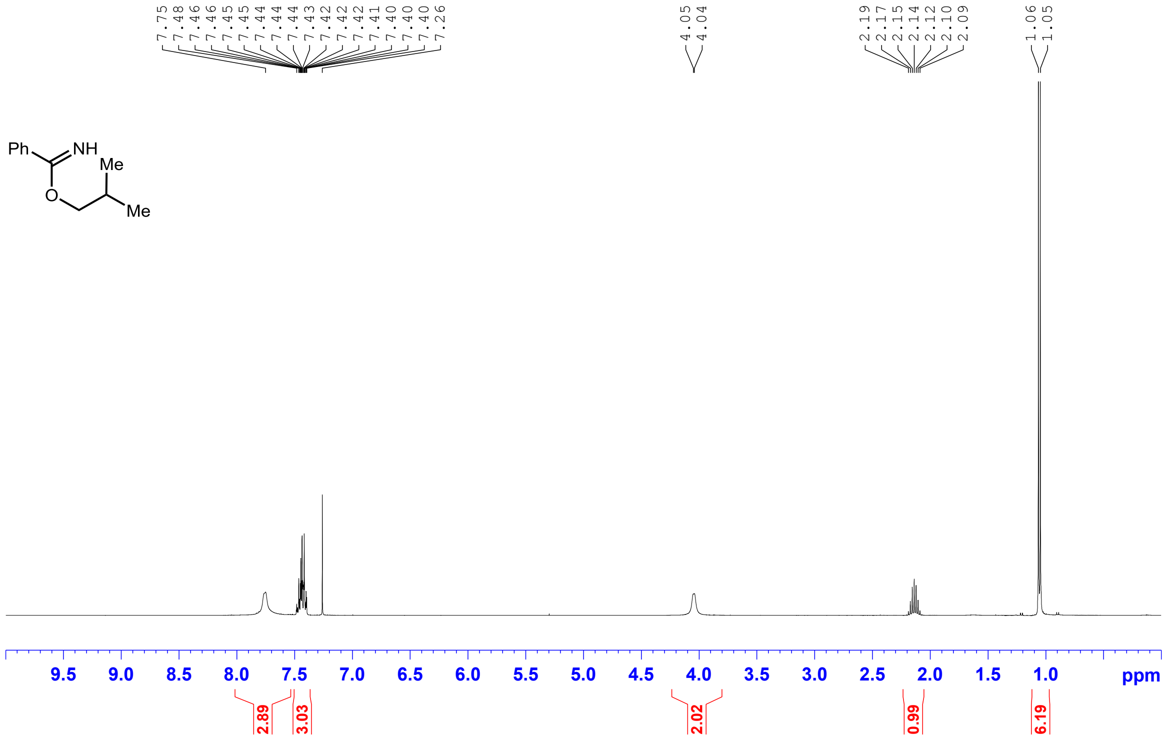
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7.42
7.42
7.41
7.40
7.40
7.40
7.26
4.05
4.04
2.19
2.17
2.15
2.14
2.12
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2.09
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1.05
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8.0
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7.0
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6.0
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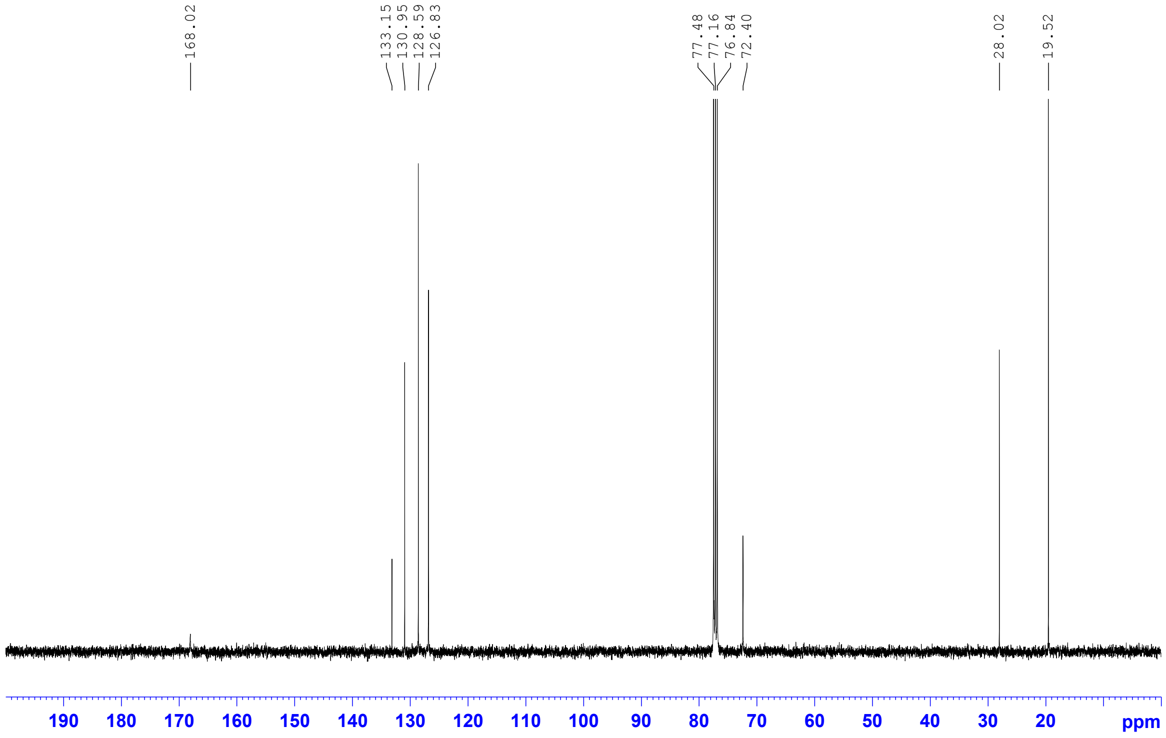
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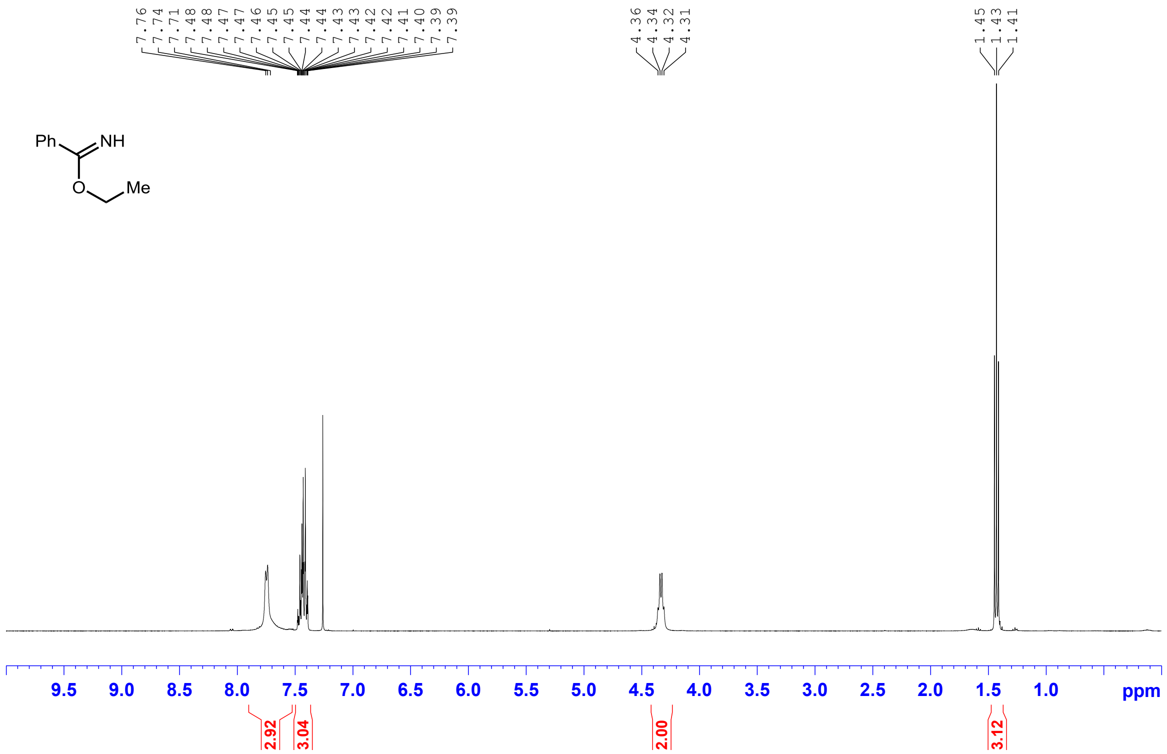
ppm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7.42
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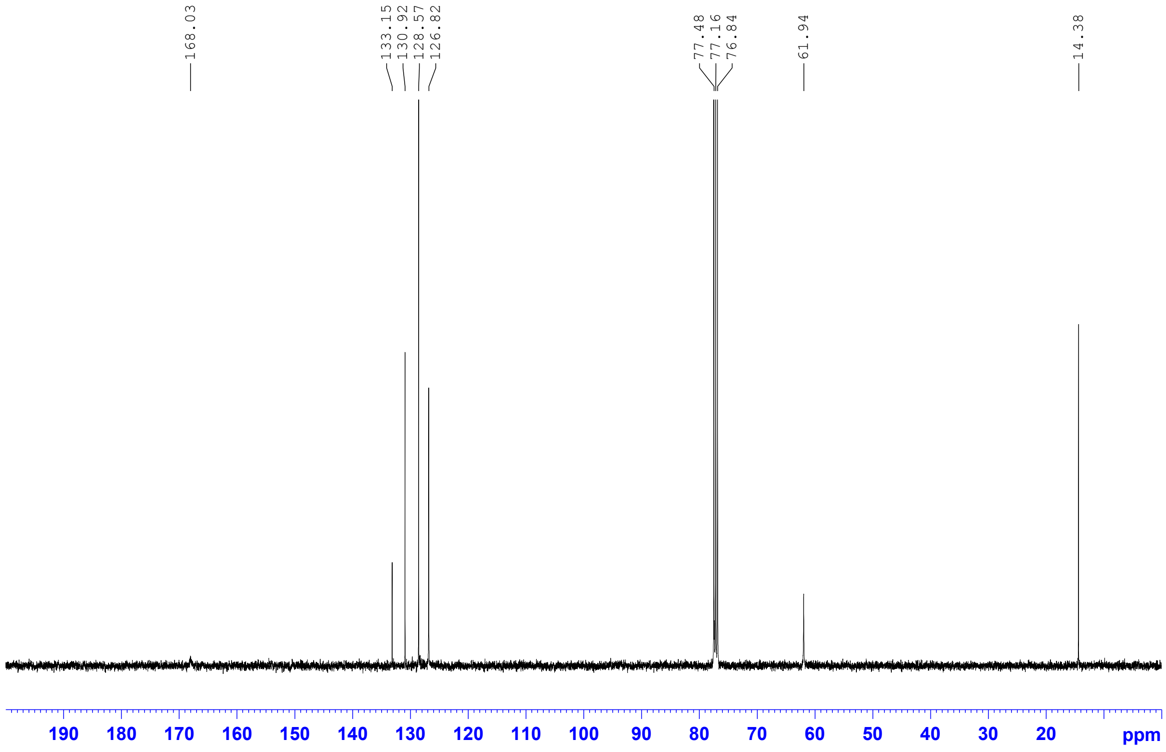
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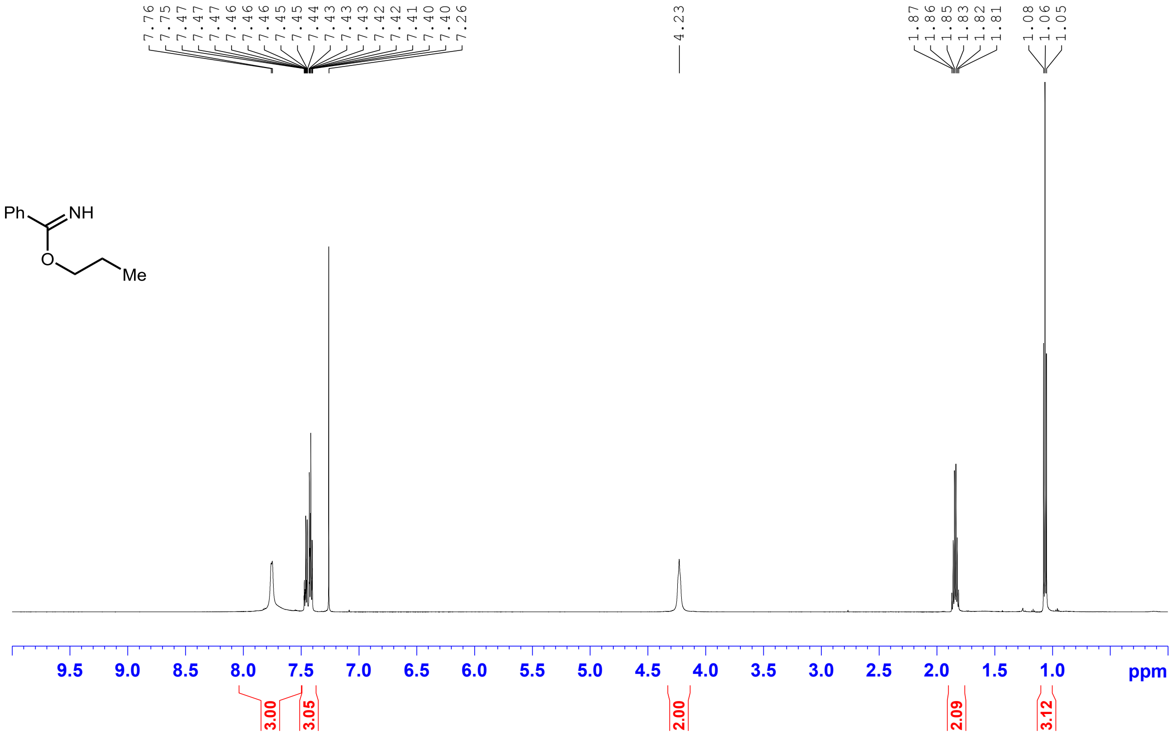
ppm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7.42
7.42
7.41
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7.40
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1.83
1.83
1.82
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1.08
1.06
1.05
Ph
NH
O
Me
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5.5
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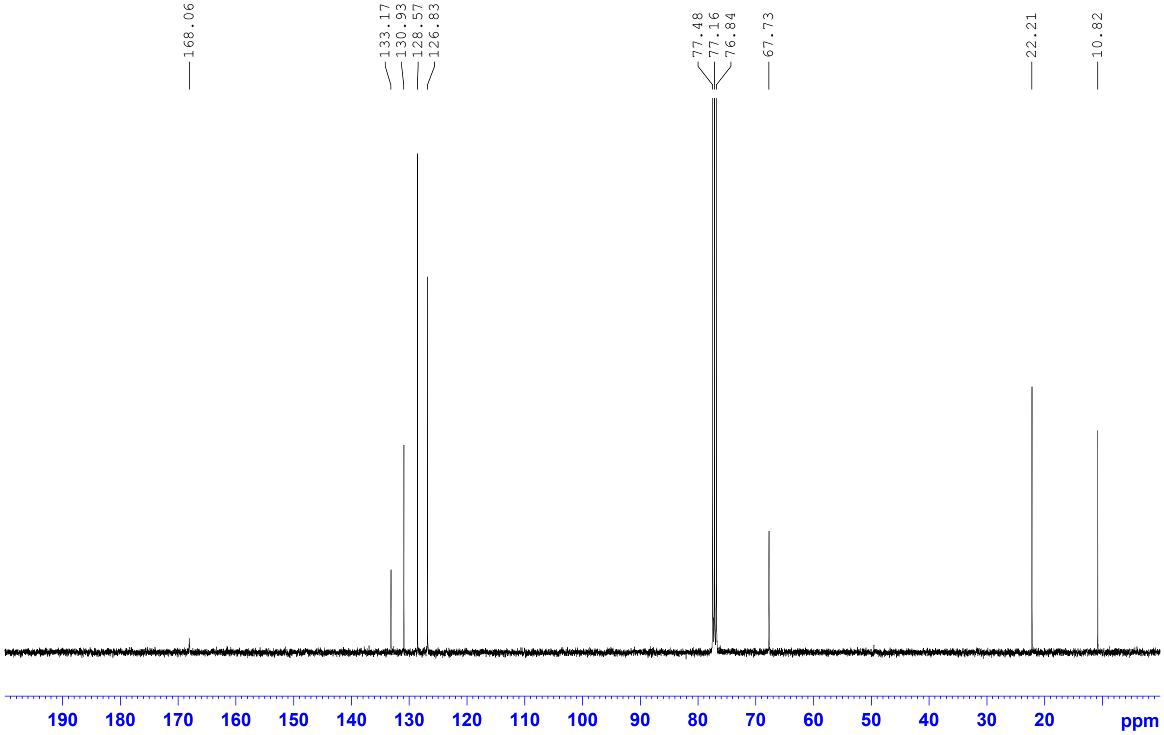
3.12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22.21
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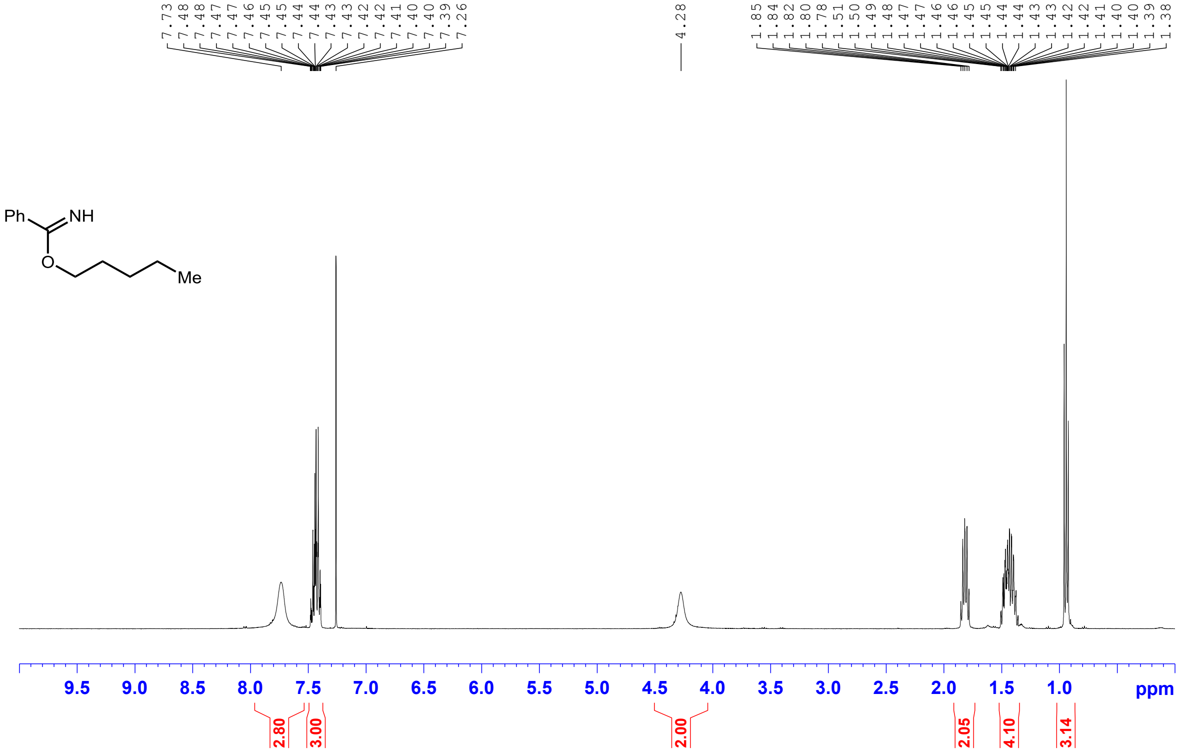
ppm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7.40
7.40
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7.26
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1.78
1.51
1.50
1.49
1.48
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1.44
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1.40
1.39
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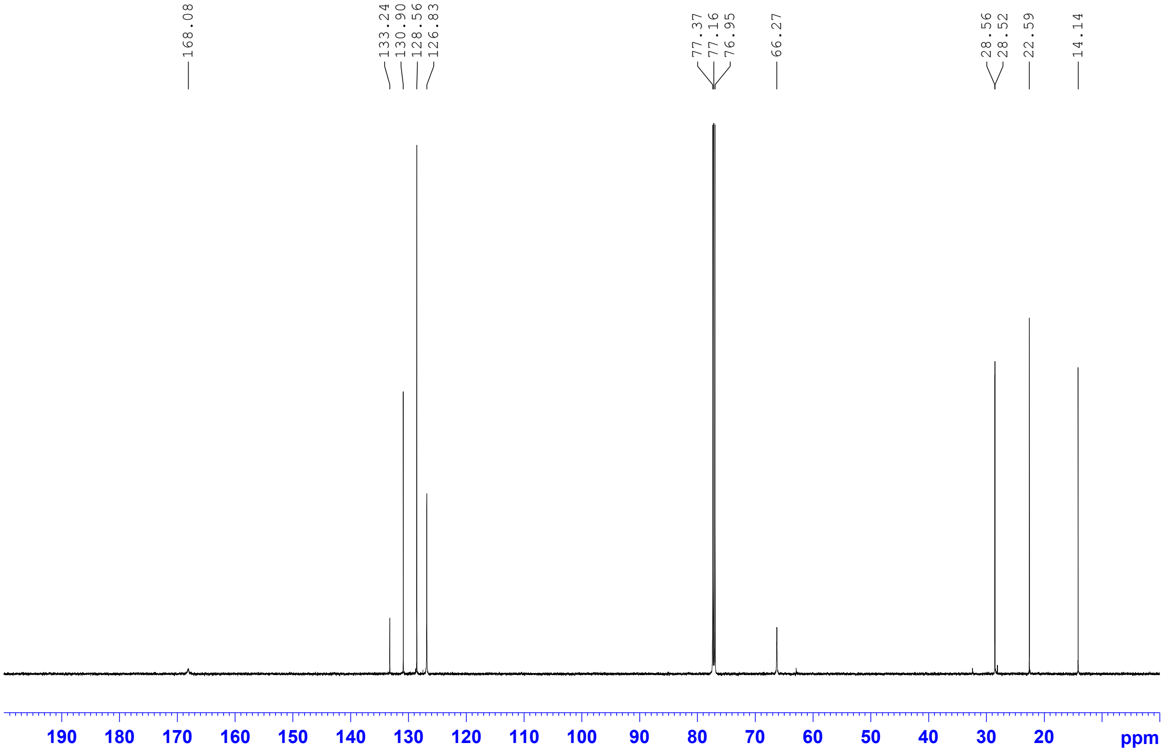
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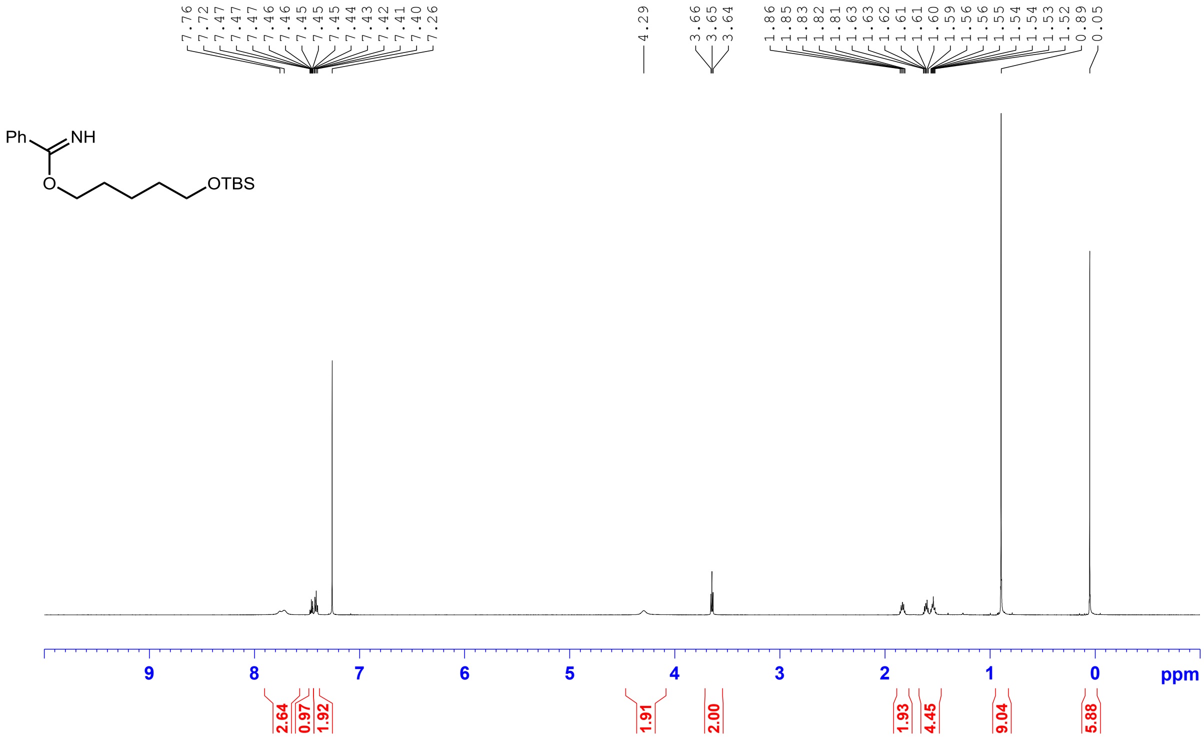
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7.44
7.43
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3.65
3.64
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1.83
1.82
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1.63
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1.60
1.59
1.56
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1.54
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1.53
1.52
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6
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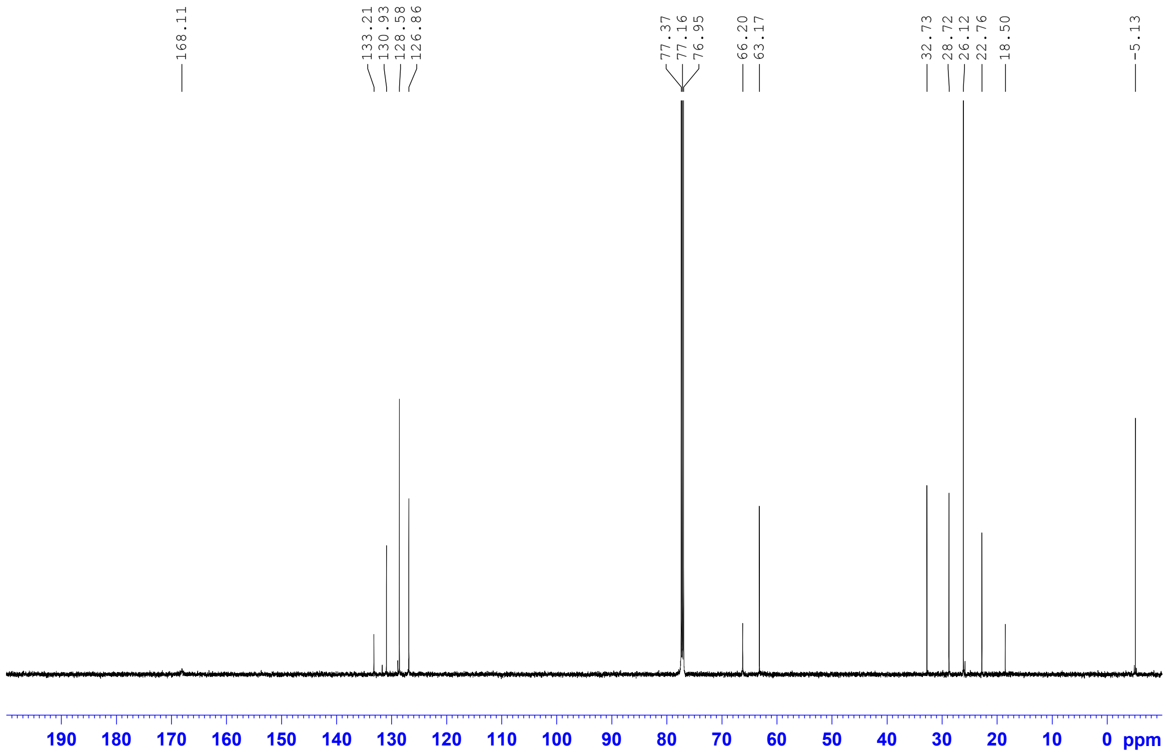
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22.76
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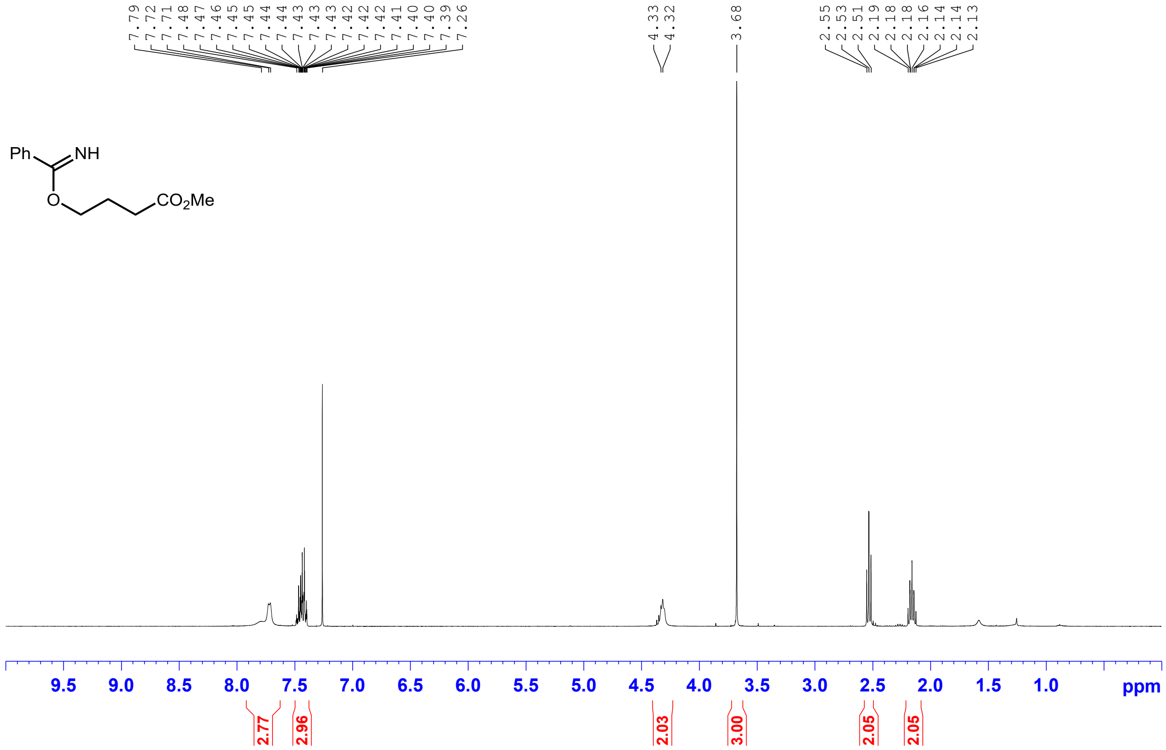
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7.39
7.26
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4.32
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2.53
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2.18
2.16
2.14
2.14
2.13
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O
CO2Me
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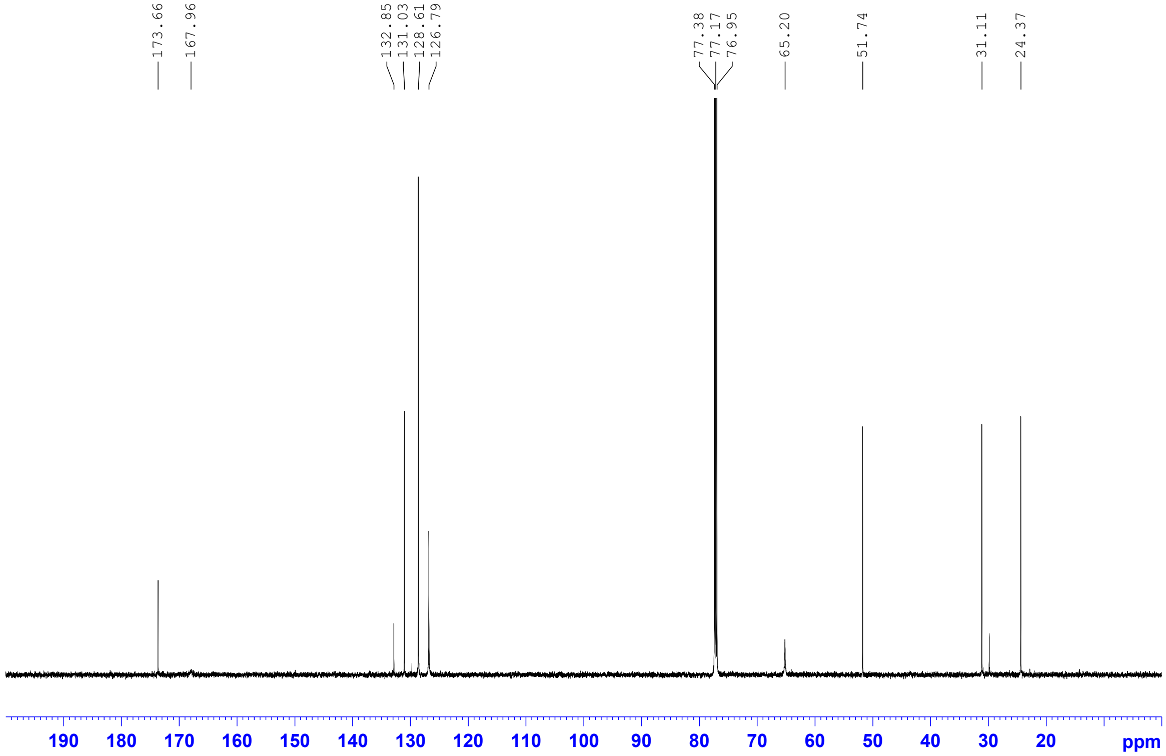
2.05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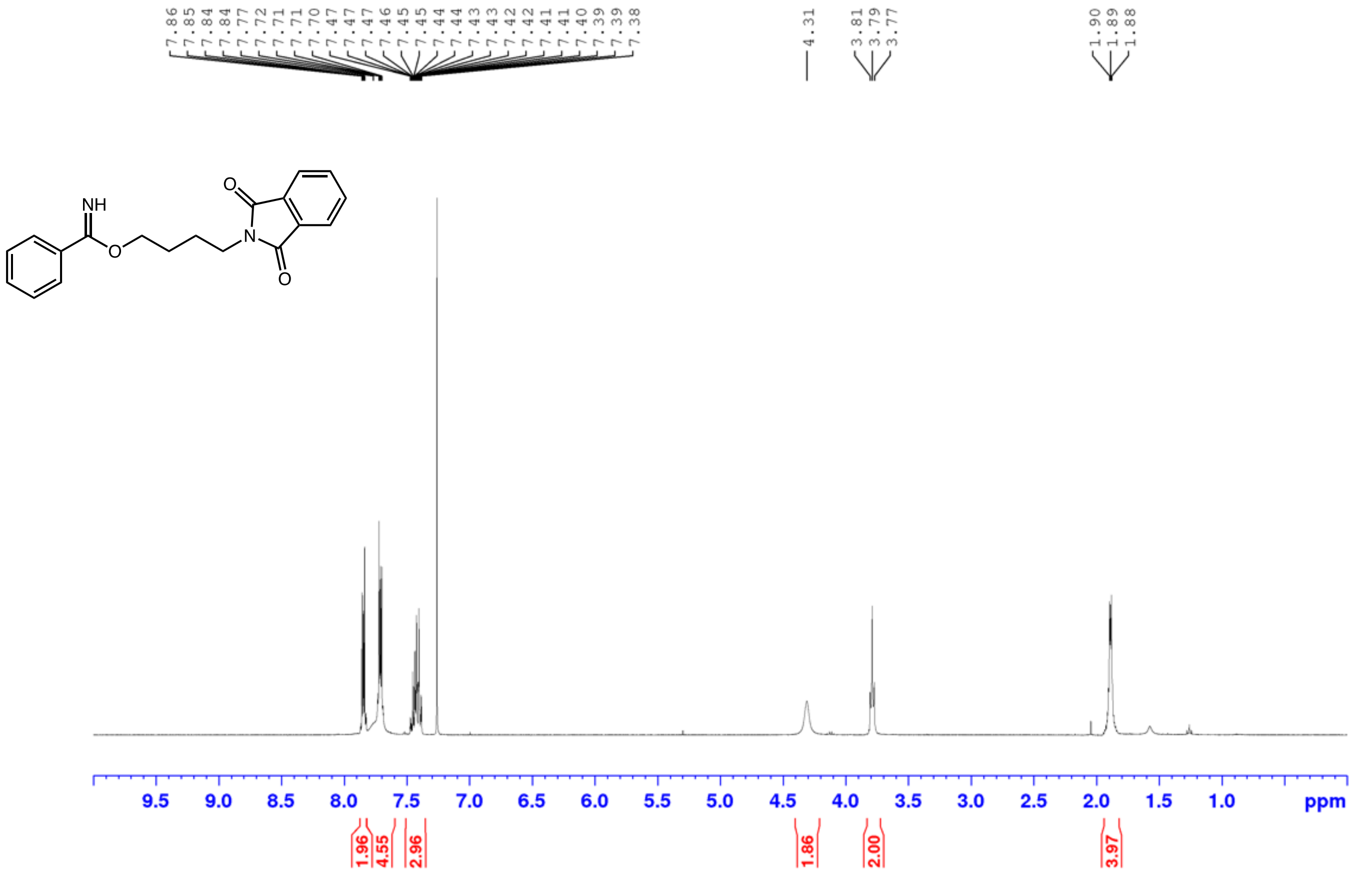
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7.45
7.44
7.44
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7.43
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7.42
7.41
7.41
7.40
7.39
7.39
7.38
4.31
3.81
3.79
3.77
1.90
1.89
1.88
NH
O
N
O
O
9.5
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8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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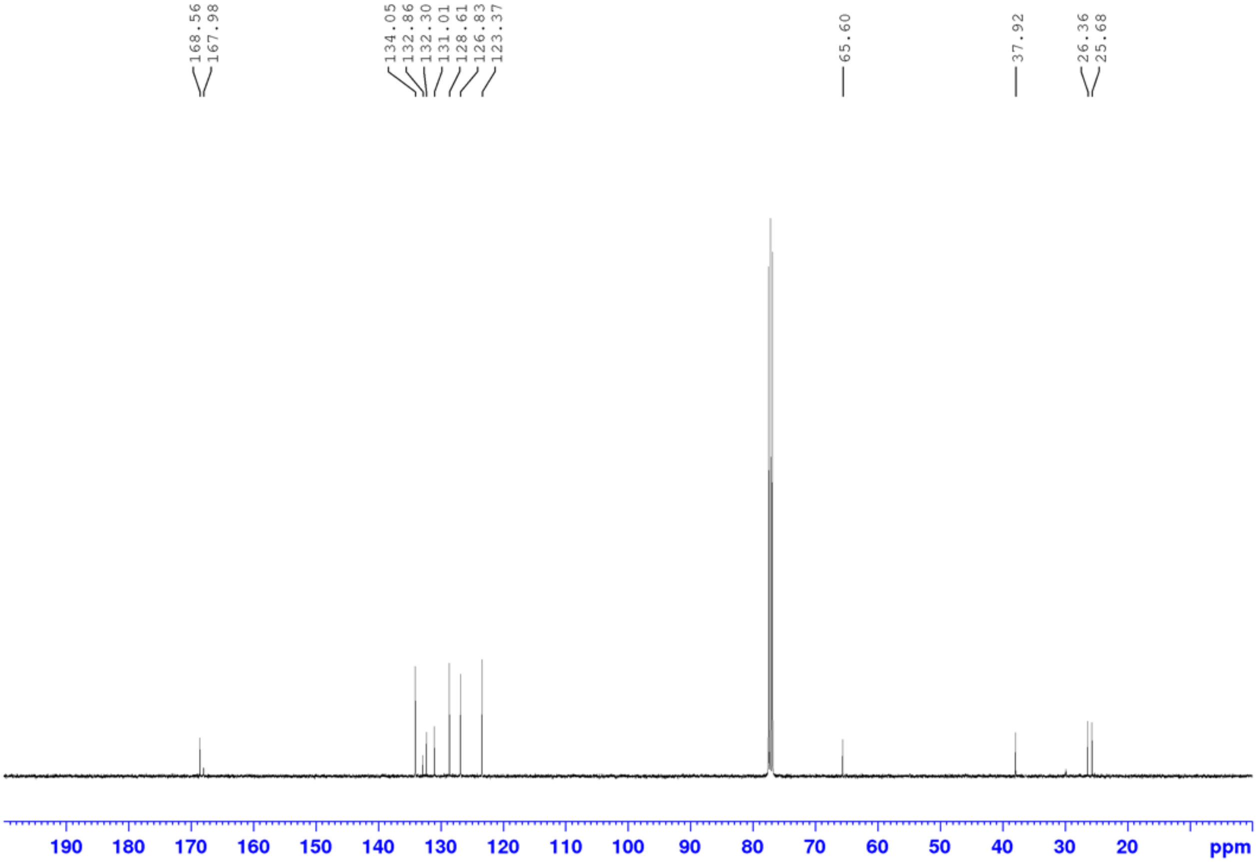
3.97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150
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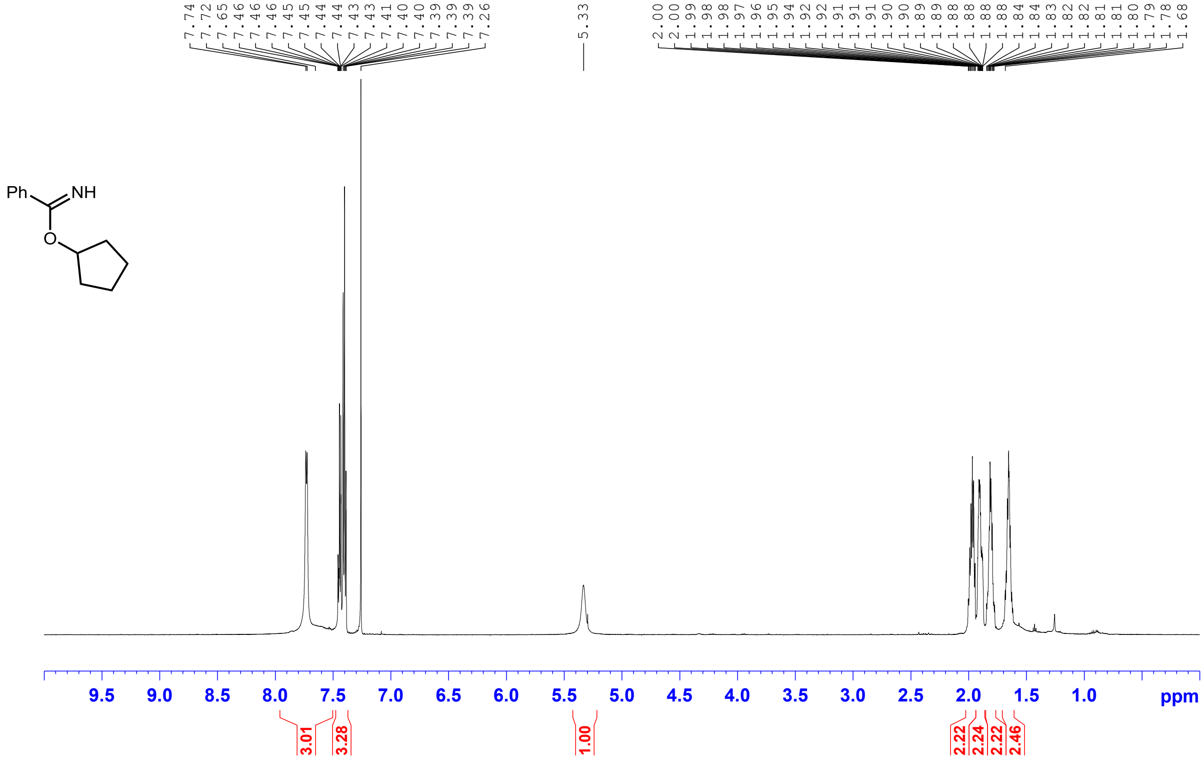
ppm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O
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5.33
2.00 2.00 1.99 1.98 1.98 1.97 1.96 1.95 1.94 1.92 1.92 1.91 1.91 1.91 1.90 1.89 1.89 1.88 1.88 1.88 1.88 1.84 1.84 1.83 1.82 1.82 1.81 1.81 1.80 1.79 1.78 1.68
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
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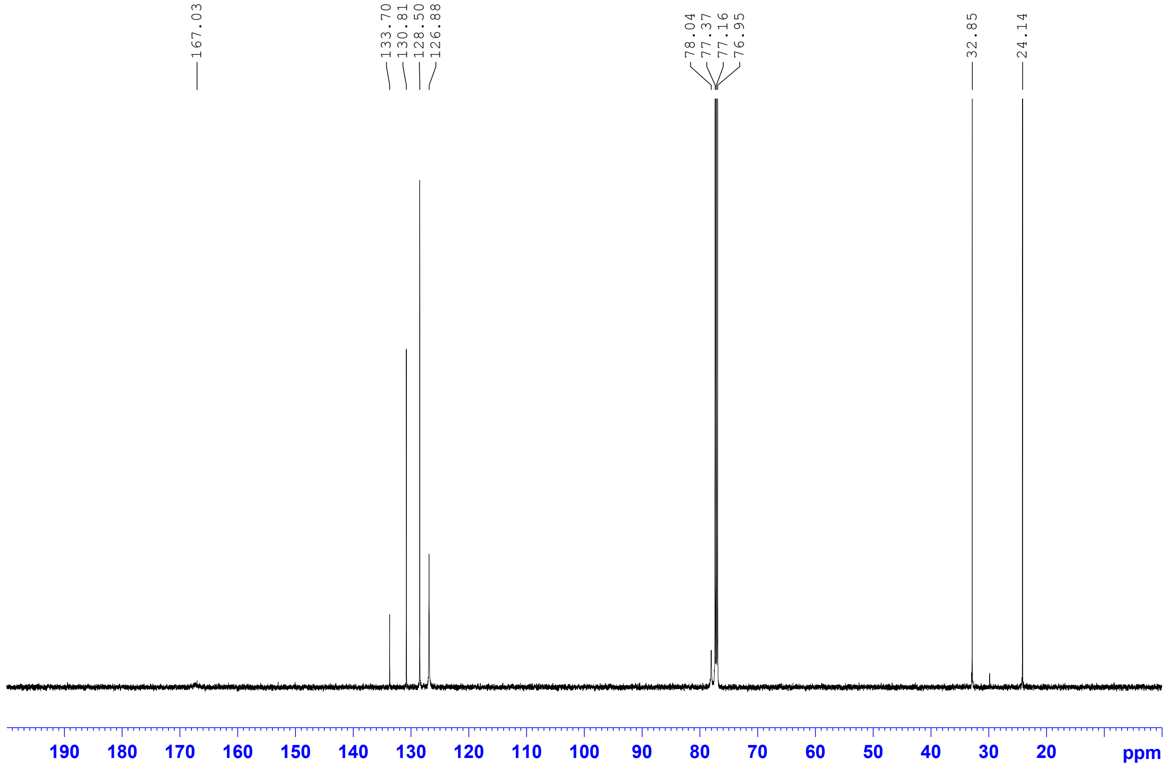
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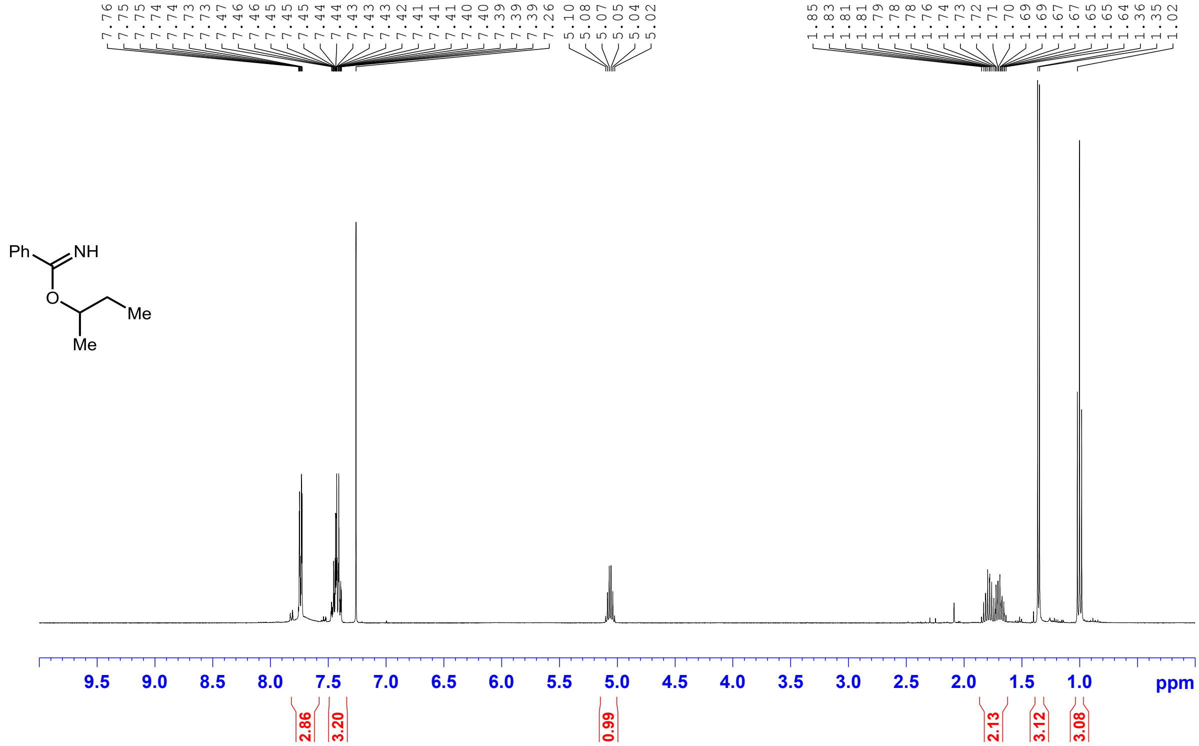
133.70 130.81 128.50 126.88
78.04 77.37 77.16 76.95
32.85
24.14
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

Ph
NH
O
Me
Me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7.43
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7.39
7.39
7.39
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1.70
1.69
1.69
1.67
1.67
1.65
1.65
1.64
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1.35
1.02
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7.0
6.5
6.0
5.5
5.0
4.5
4.0
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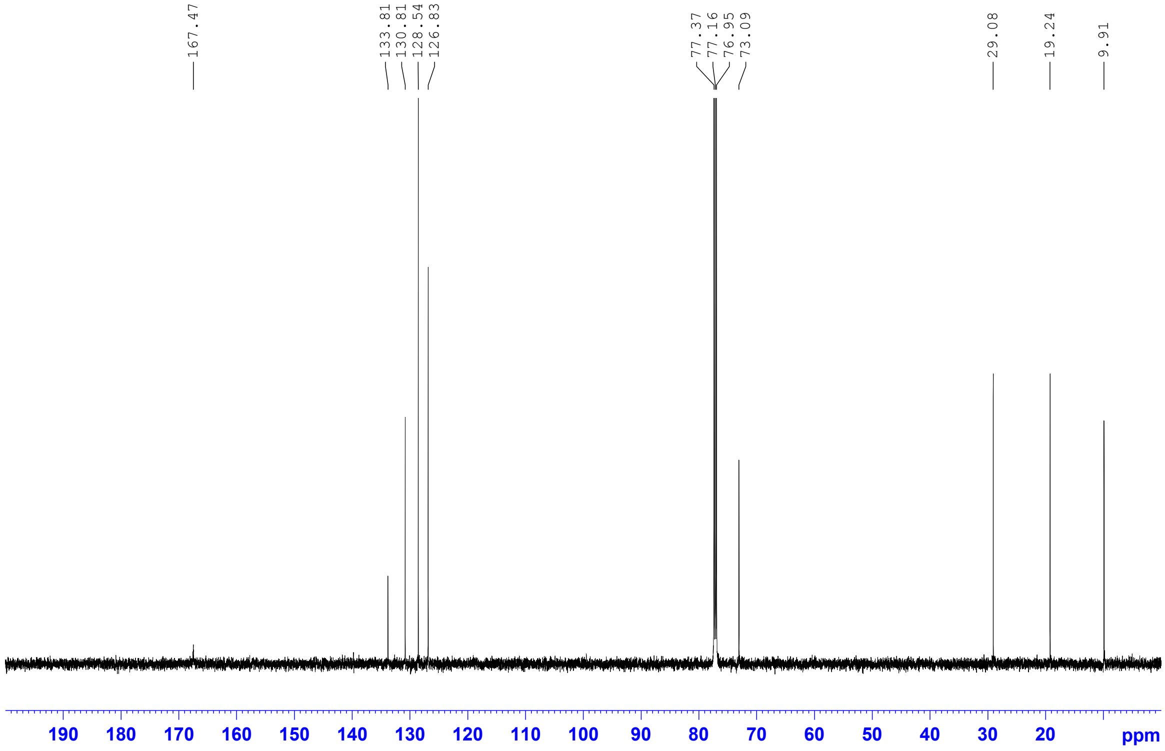
3.08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29.08
19.24
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160
150
140
130
120
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100
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80
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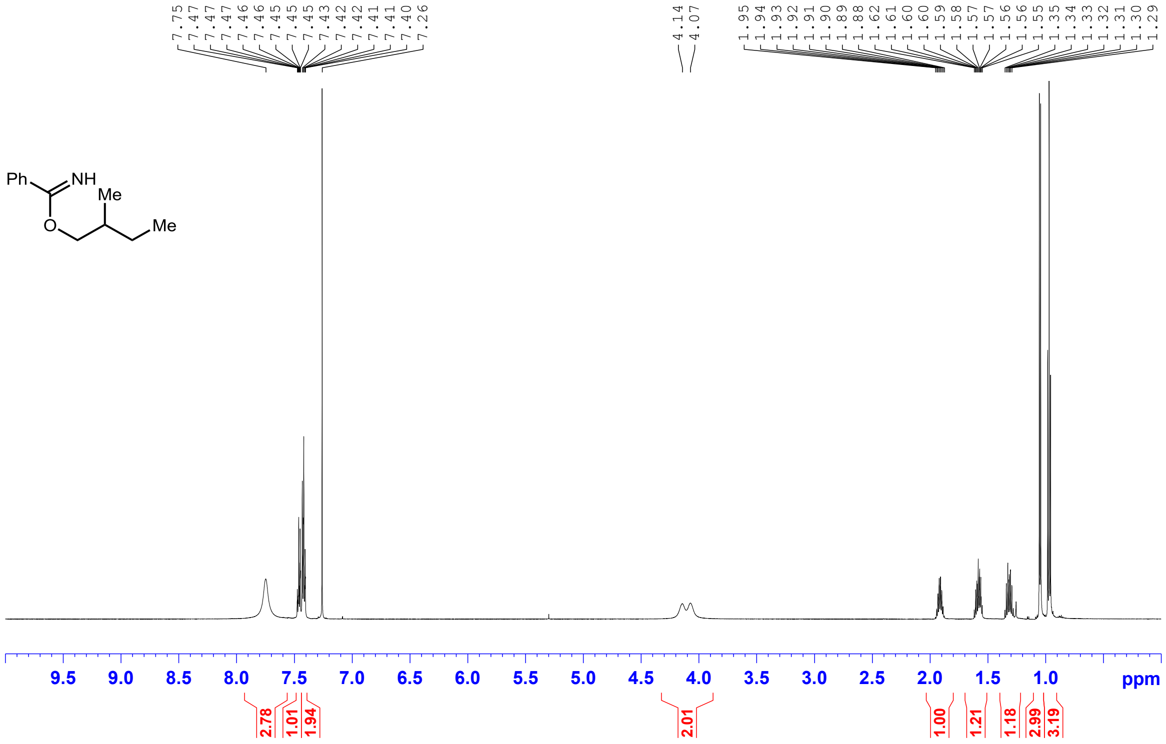
50
40
30
20
ppm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Me
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7.43
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7.42
7.41
7.41
7.40
7.26
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4.07
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1.93
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1.91
1.90
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1.57
1.56
1.56
1.55
1.35
1.34
1.33
1.32
1.31
1.30
1.29
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3.0
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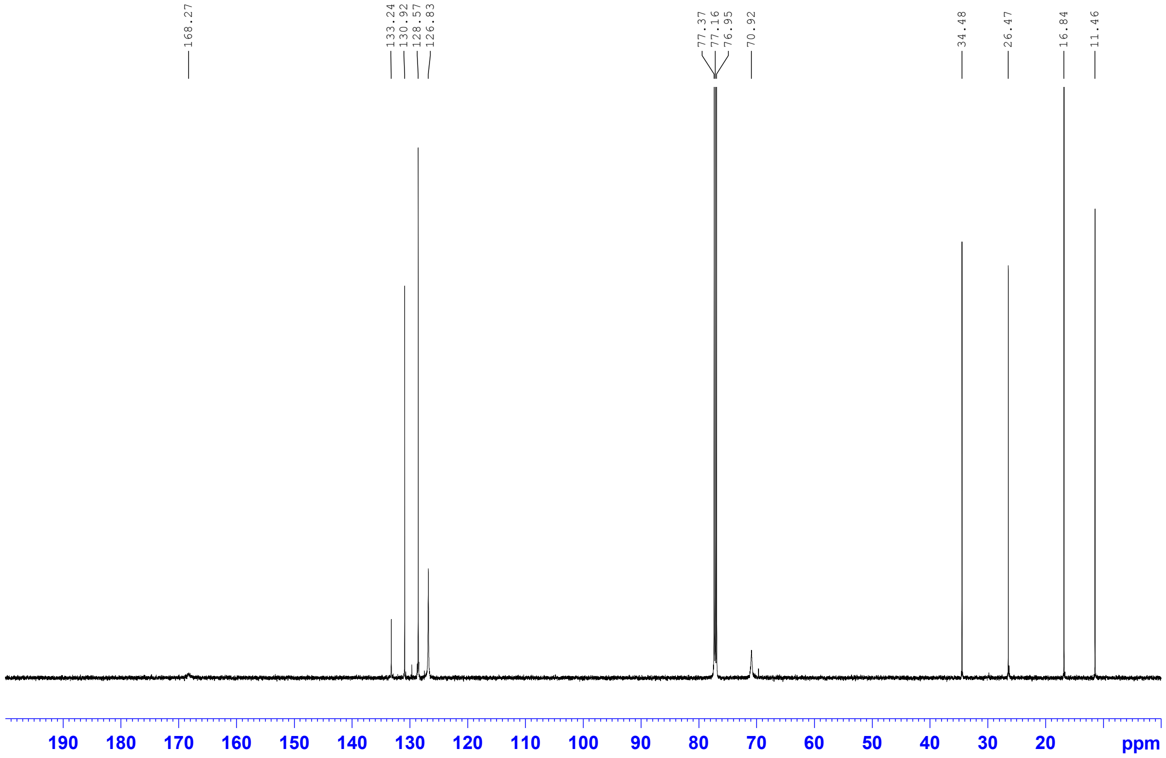
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160
150
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120
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80
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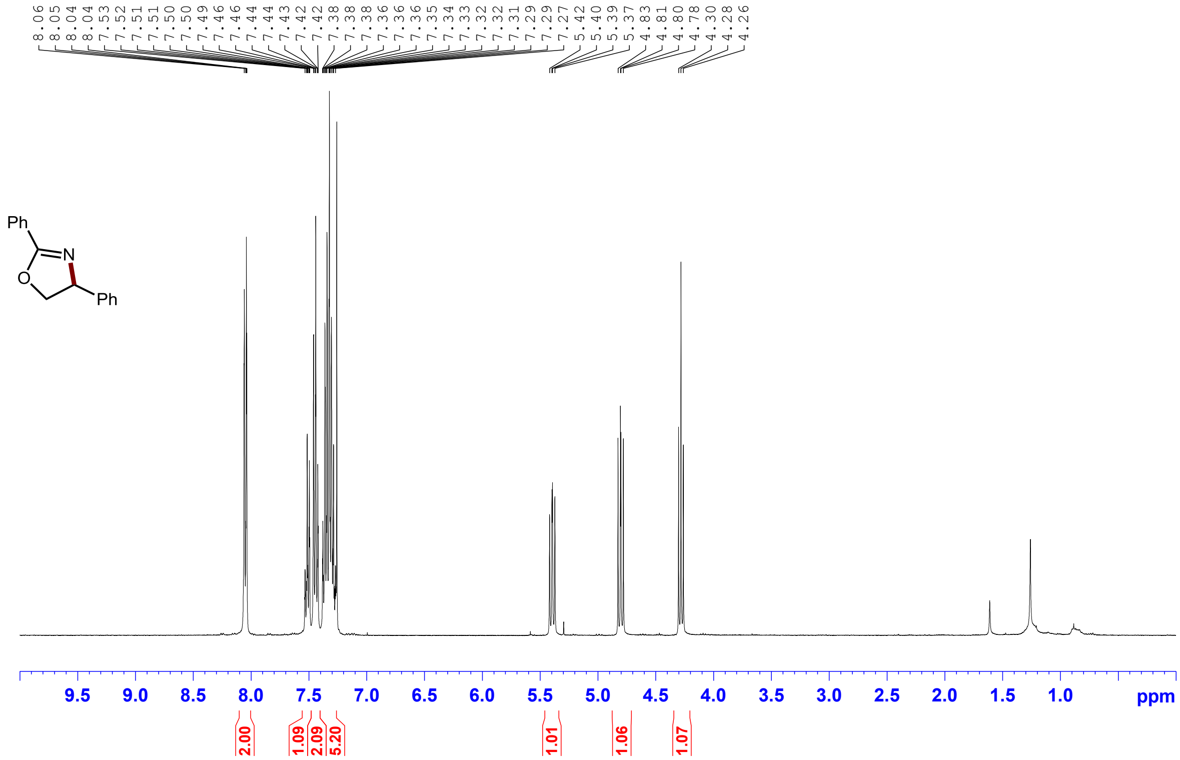
30
20
ppm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7.44
7.43
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7.42
7.38
7.38
7.38
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7.36
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7.34
7.33
7.32
7.32
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5.37
4.83
4.81
4.80
4.78
4.30
4.28
4.26
Ph
N
O
Ph
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8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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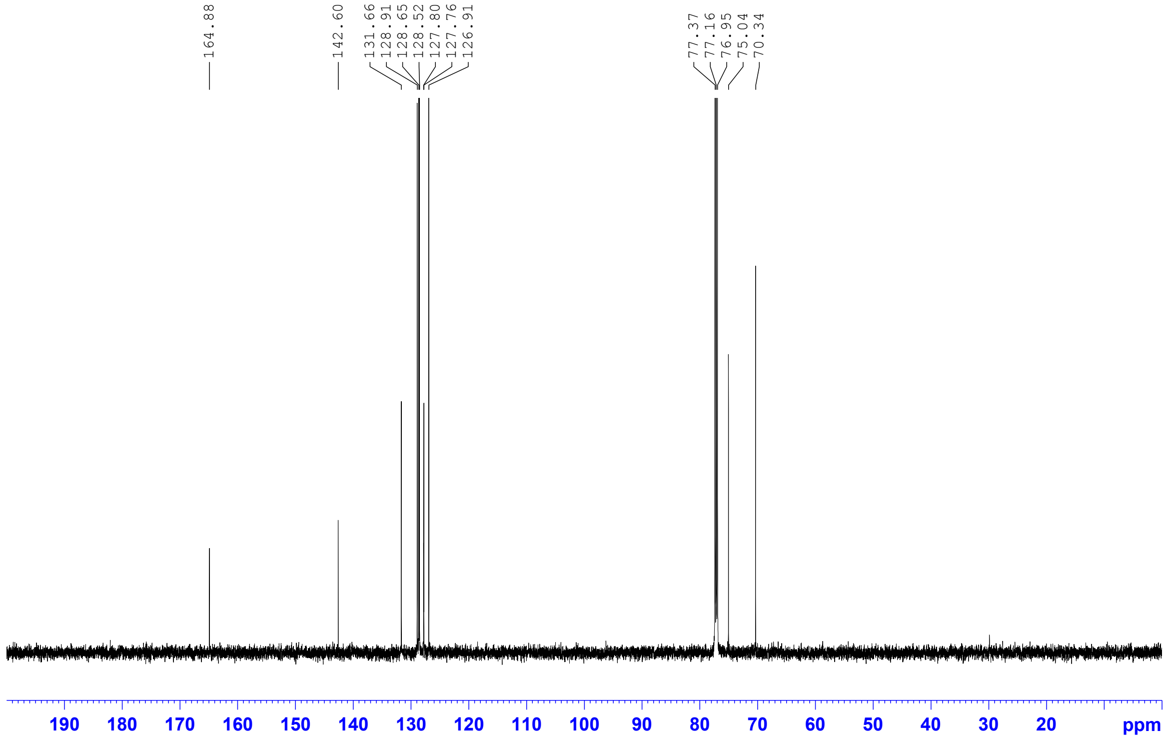
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75.04
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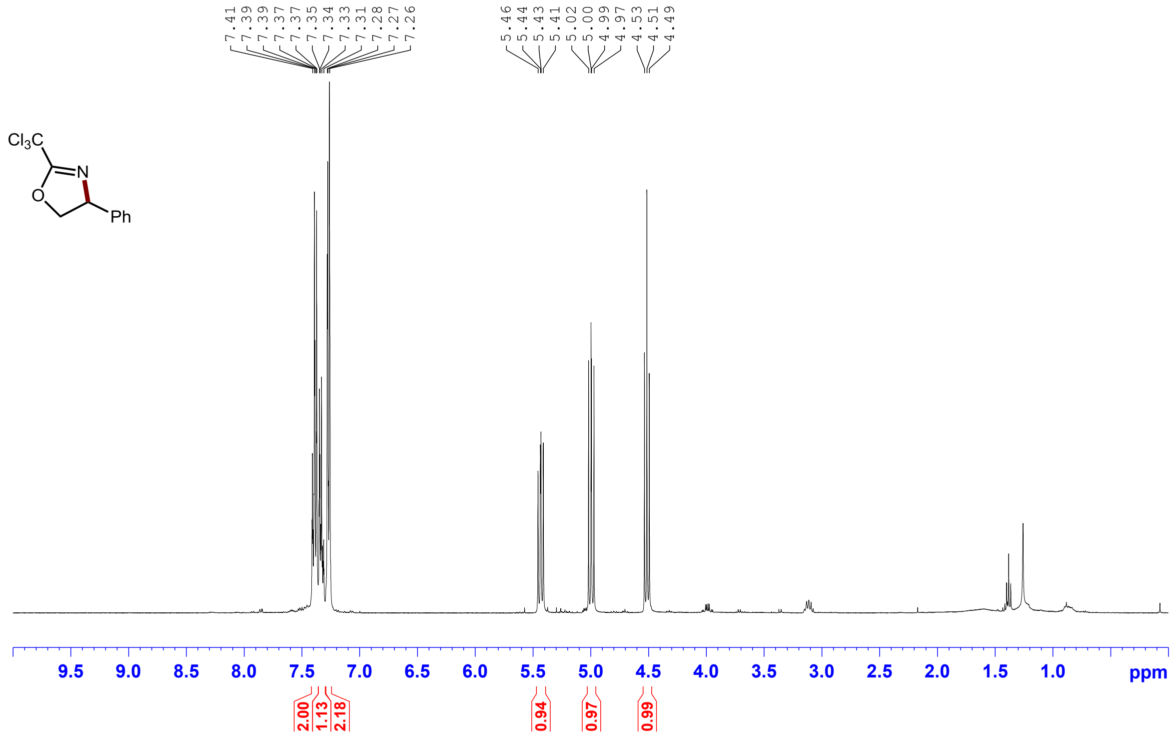
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5.44
5.43
5.41
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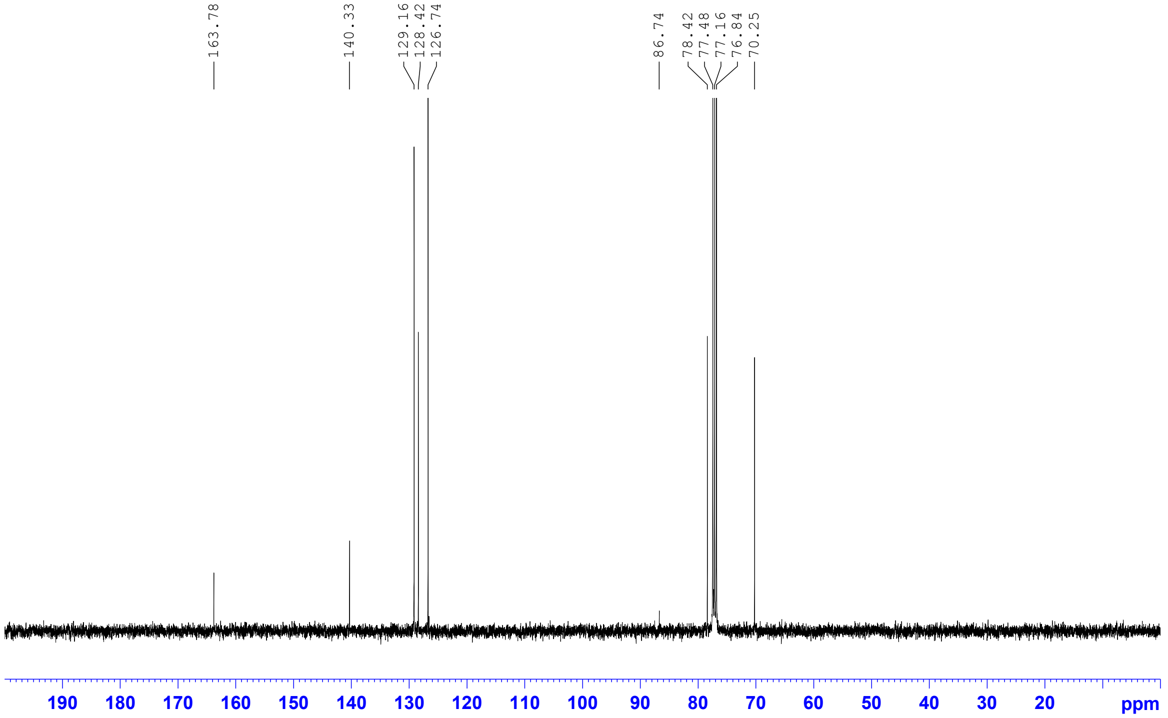
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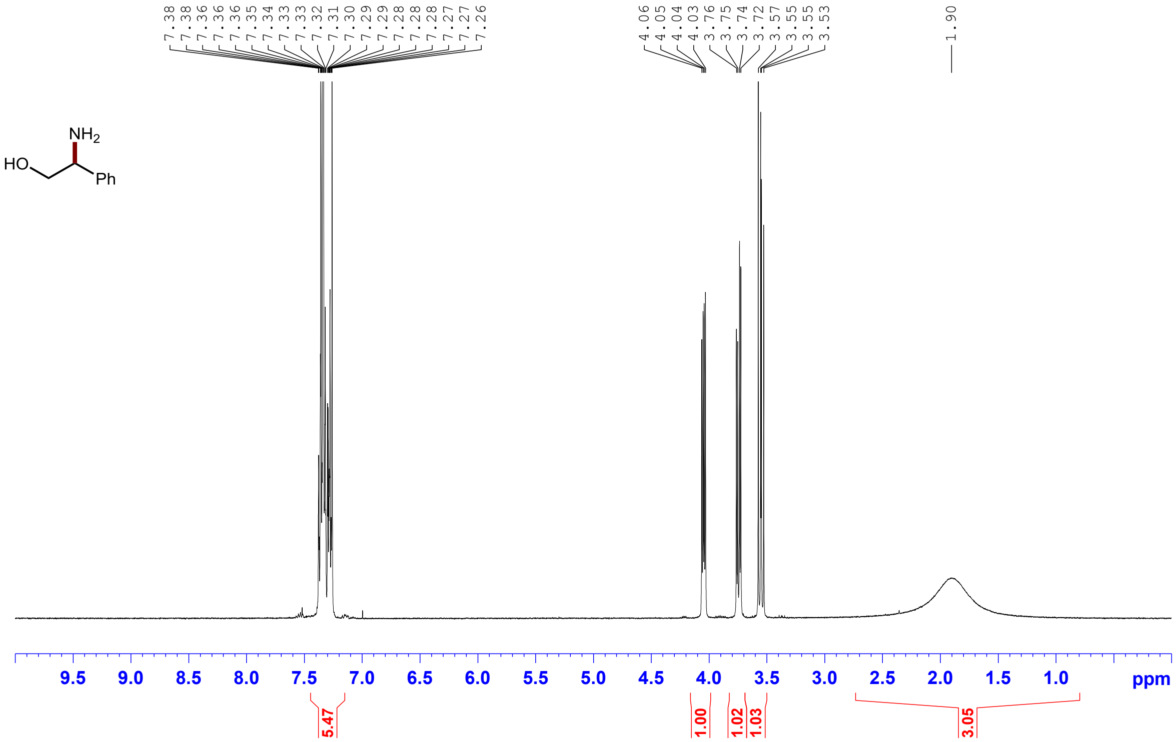
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Ph
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7.28
7.28
7.27
7.27
7.26
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4.05
4.04
4.03
3.76
3.75
3.74
3.72
3.57
3.55
3.55
3.53
1.90
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8.5
8.0
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7.0
6.5
6.0
5.5
5.0
4.5
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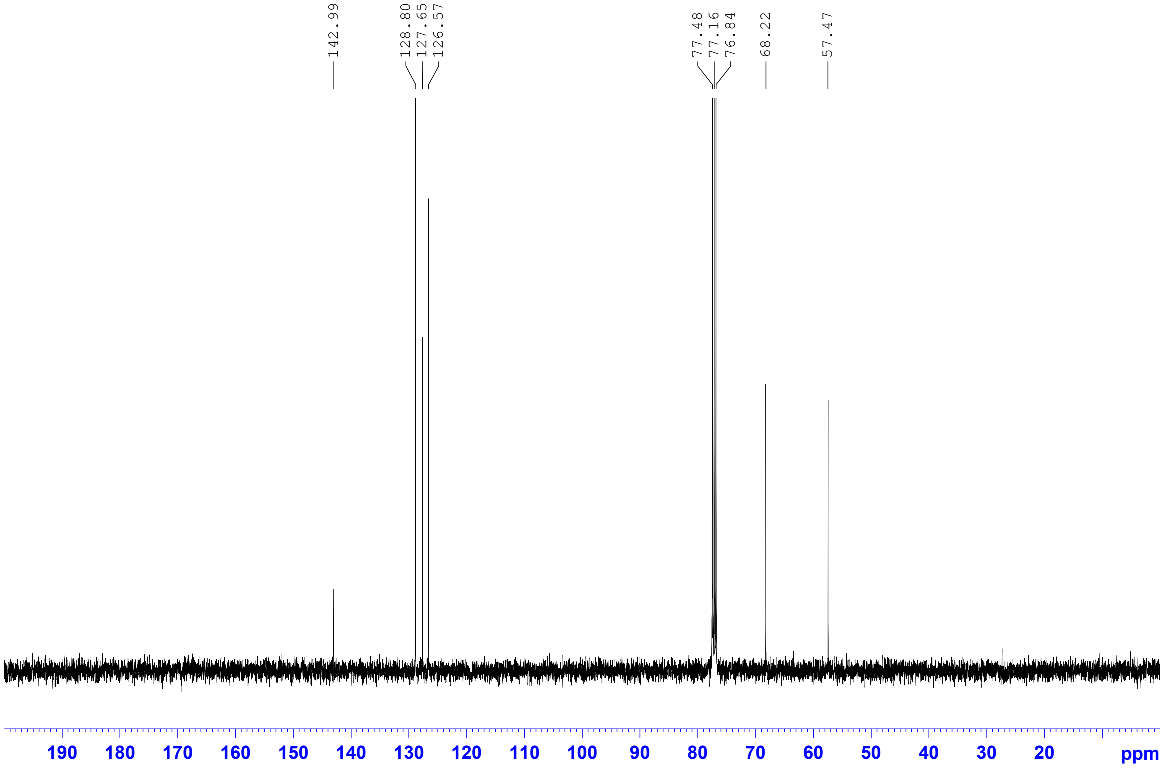
1.03
3.05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130
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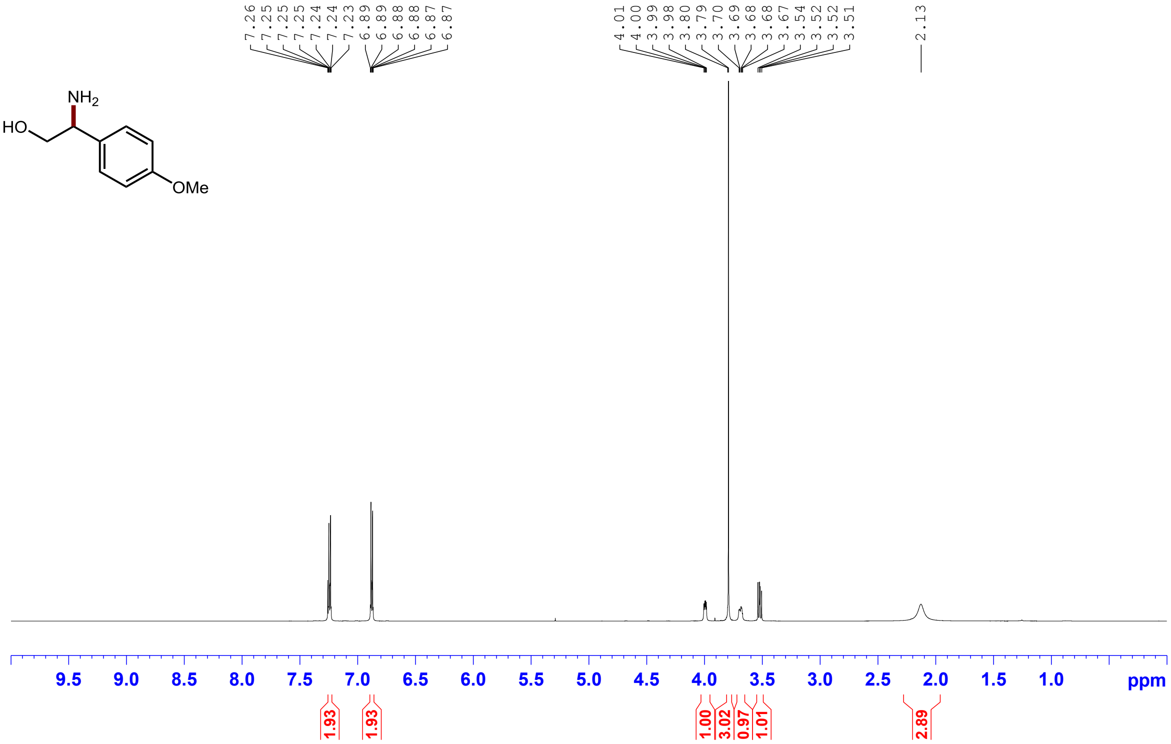
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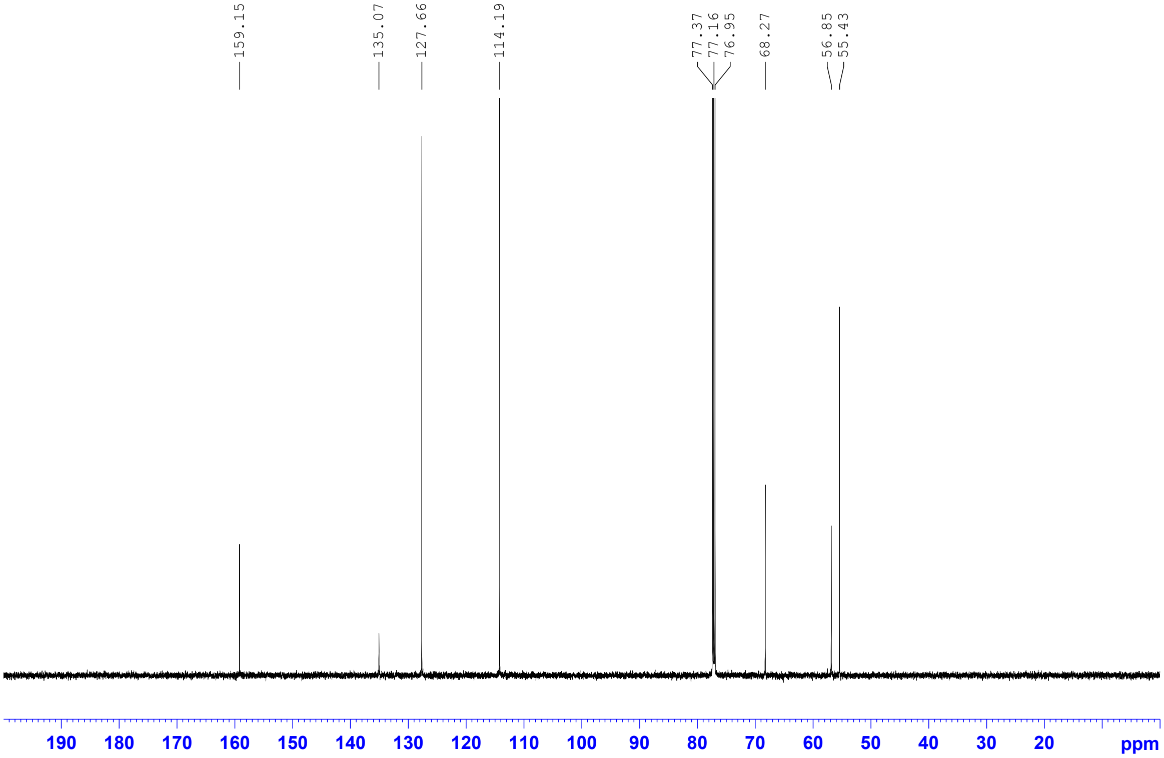
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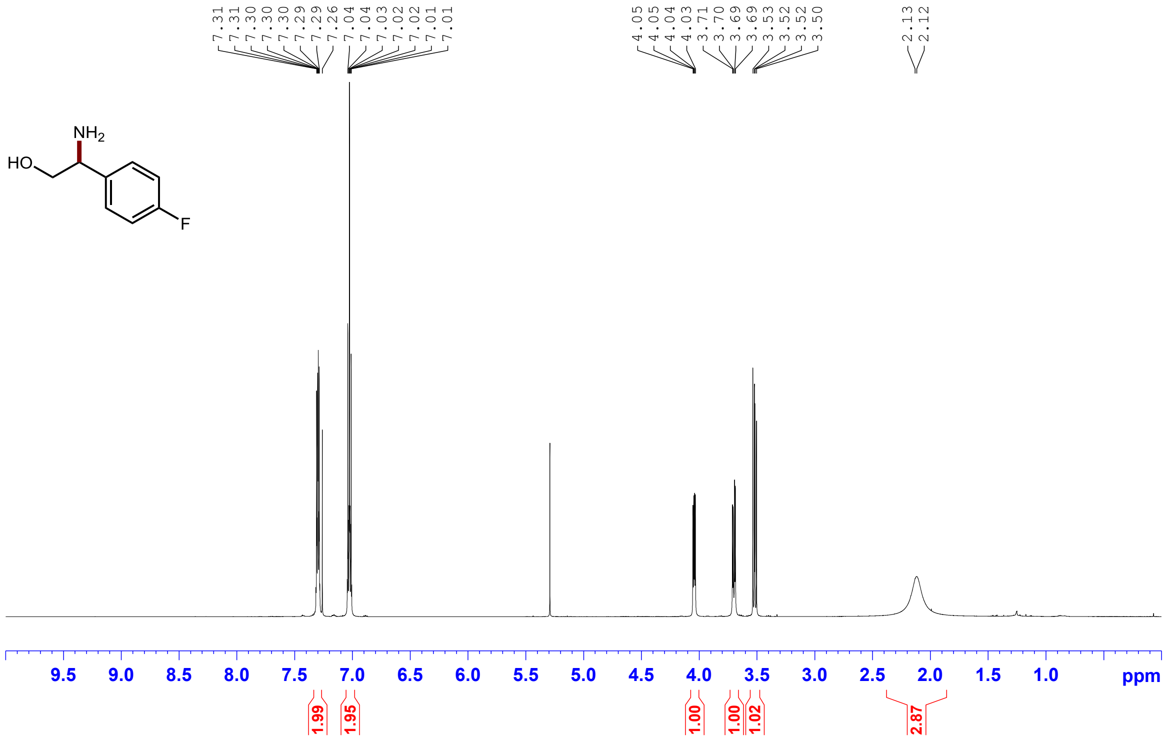
20
ppm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7.29
7.26
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7.02
7.01
7.01
4.05
4.05
4.04
4.03
3.71
3.70
3.69
3.69
3.53
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3.52
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NH2
HO
F
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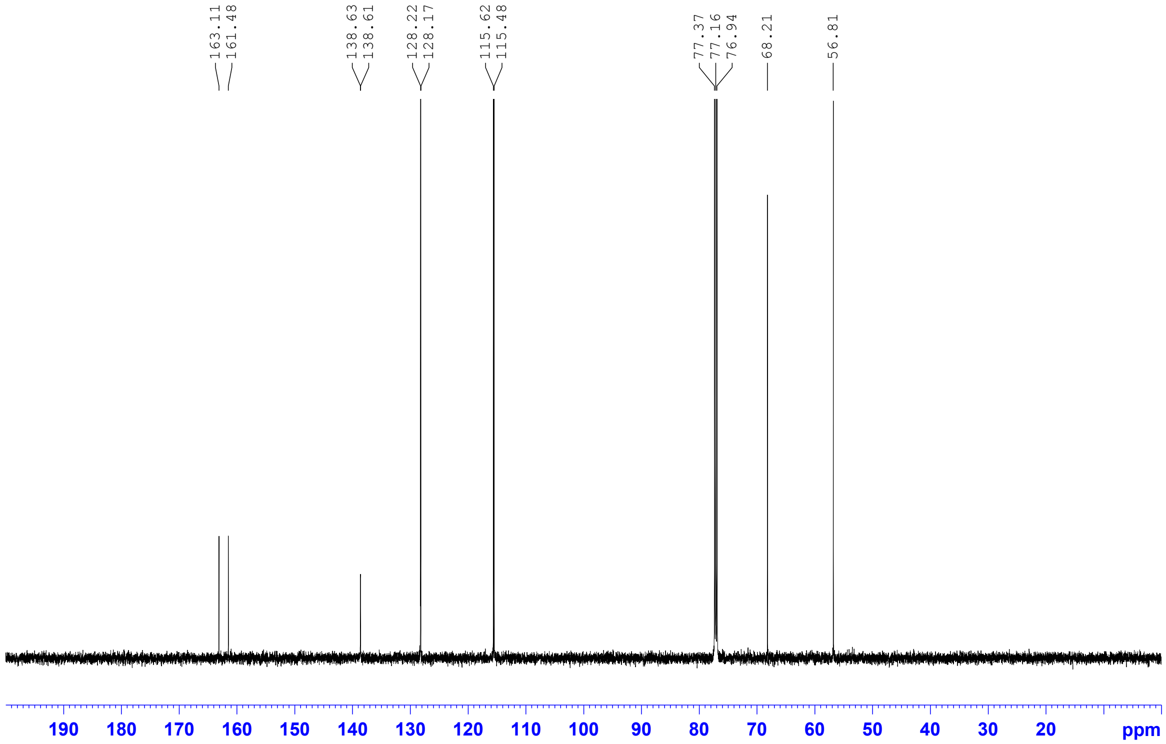
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77.16
76.94
68.21
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150
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130
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80
70
60
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40
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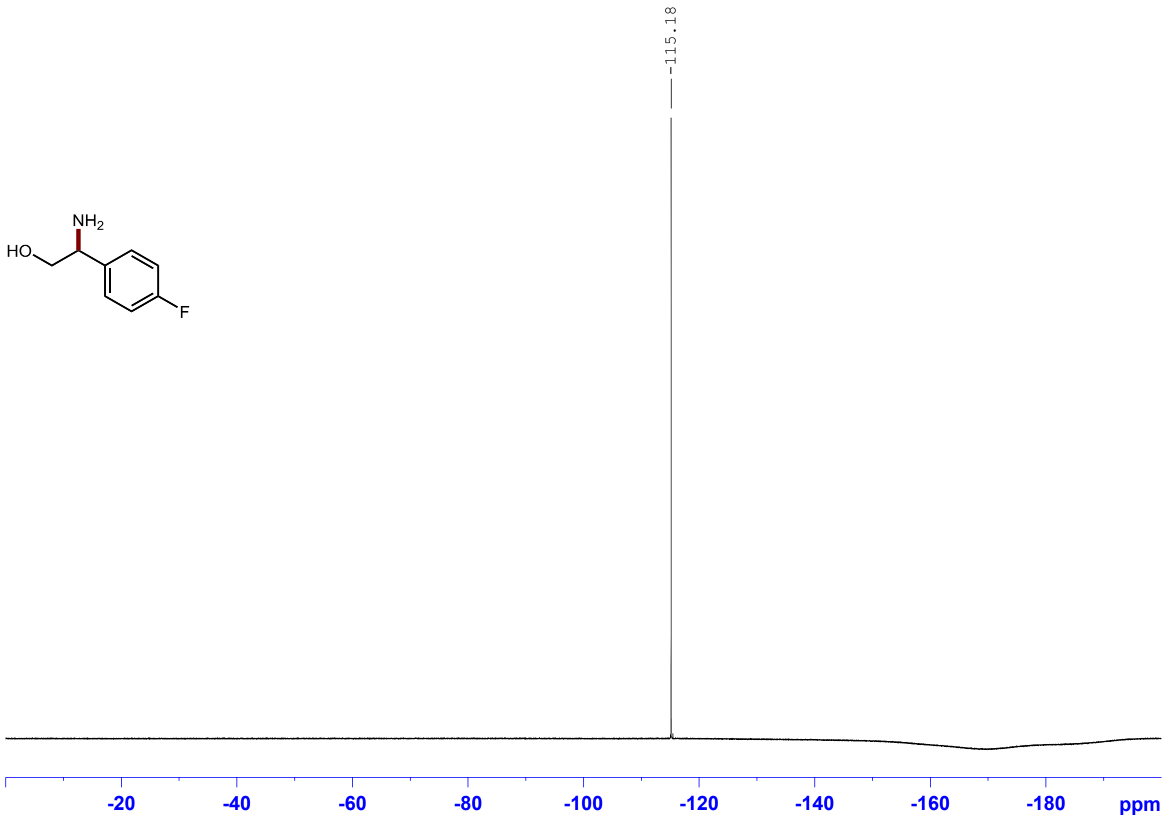
20
ppm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-180
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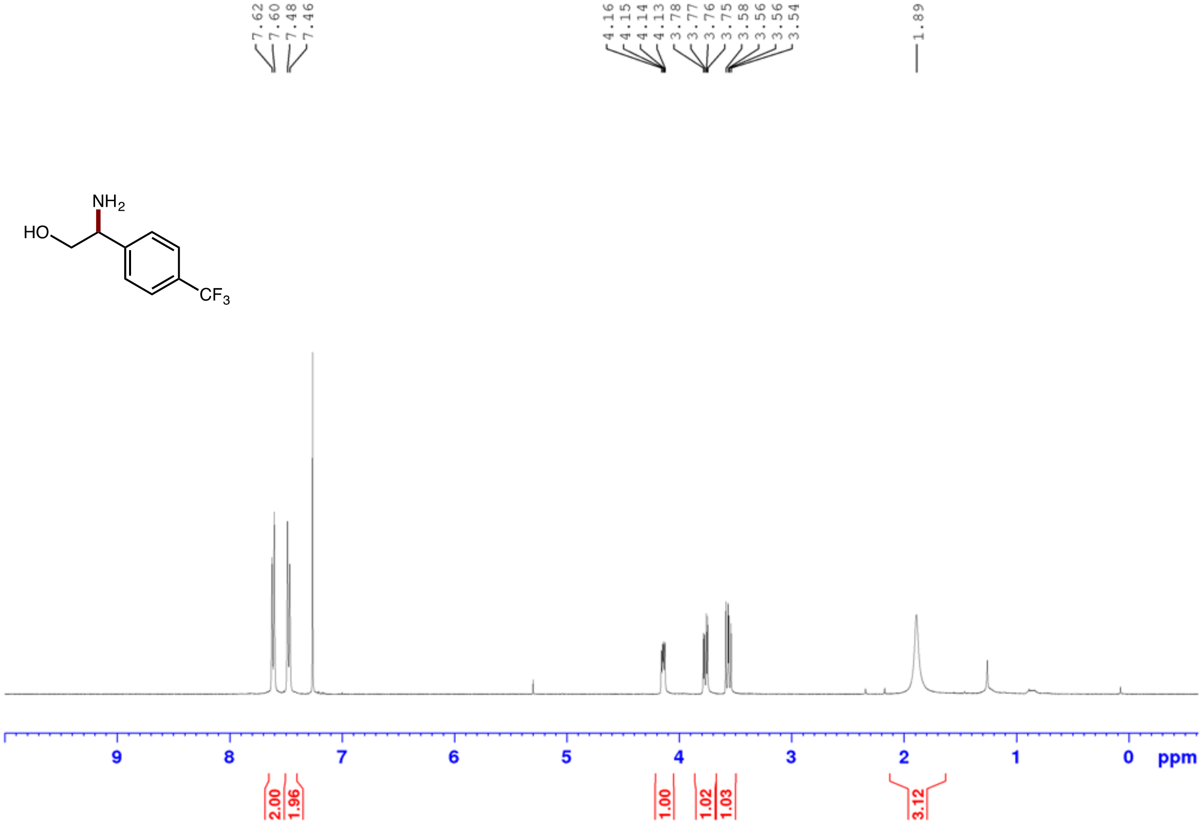
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3.76
3.75
3.58
3.56
3.56
3.54
1.89
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8
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4
3
2
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ppm
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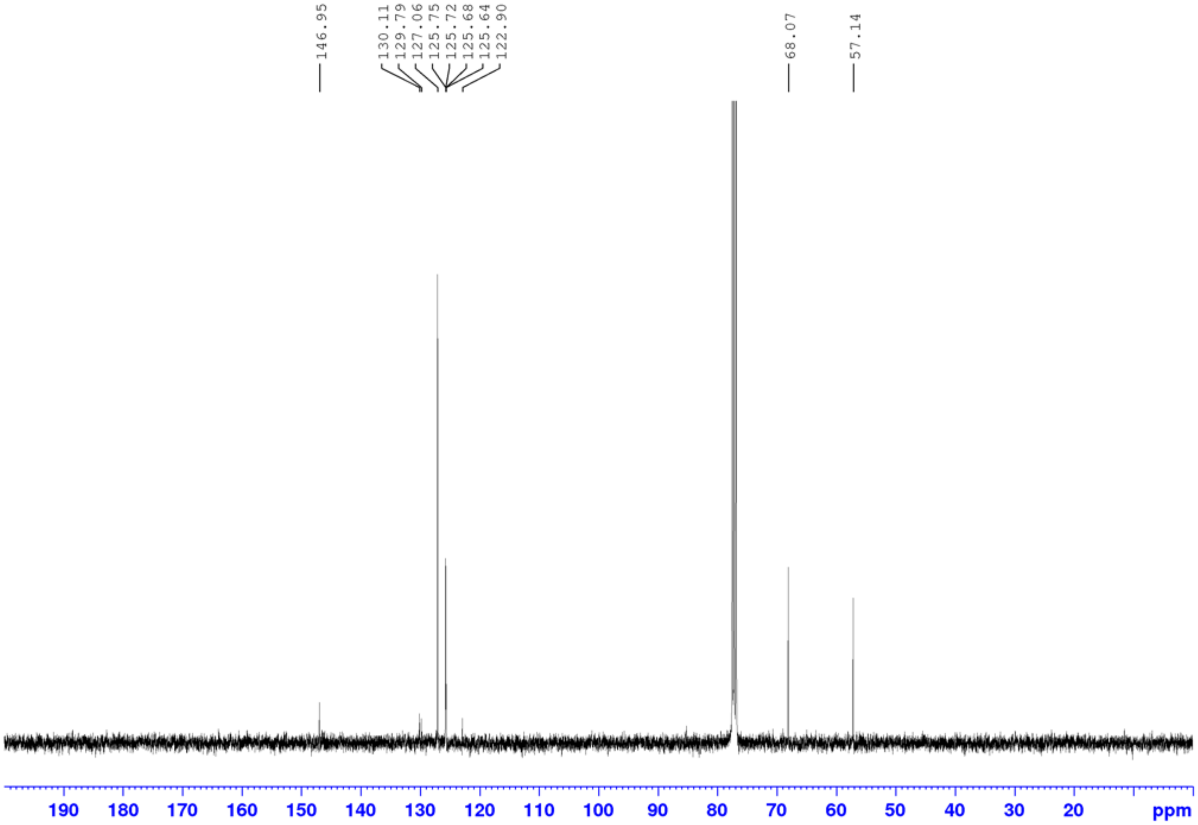
1.02
1.03
3.12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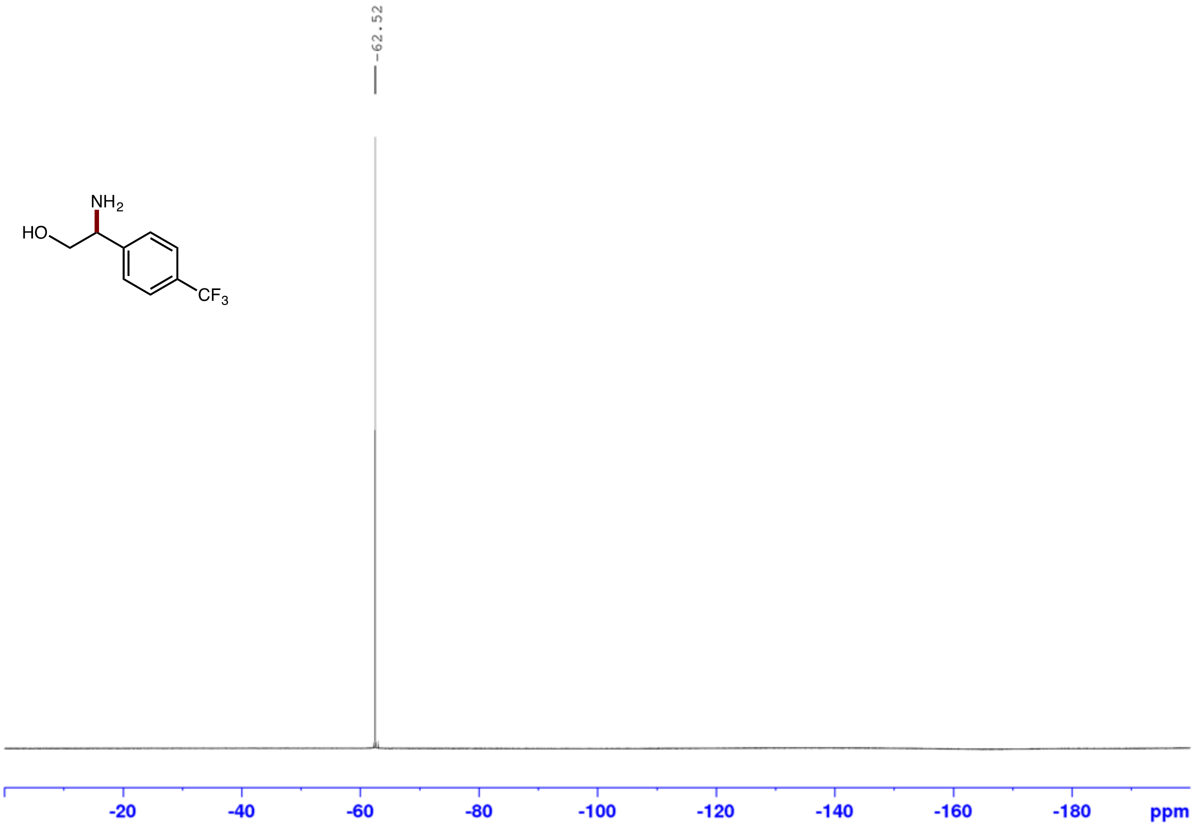
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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NH2
HO
CF3
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-40
-60
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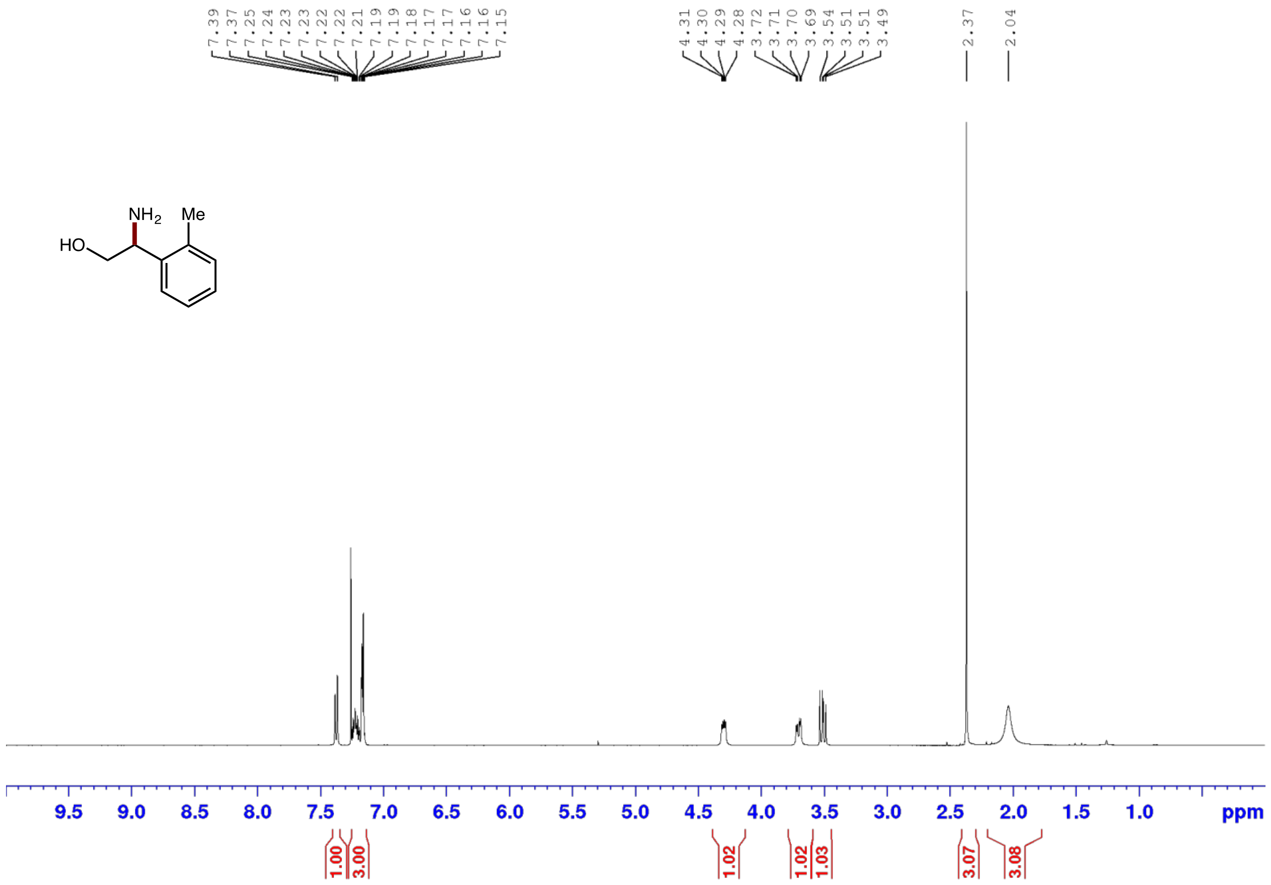
-120
-140
-160
-180
ppm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7.37
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7.23
7.22
7.22
7.21
7.19
7.19
7.18
7.17
7.17
7.16
7.15
4.31
4.30
4.29
4.28
3.72
3.71
3.70
3.69
3.54
3.51
3.51
3.49
2.37
2.04
NH2
Me
HO
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
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1.0
ppm
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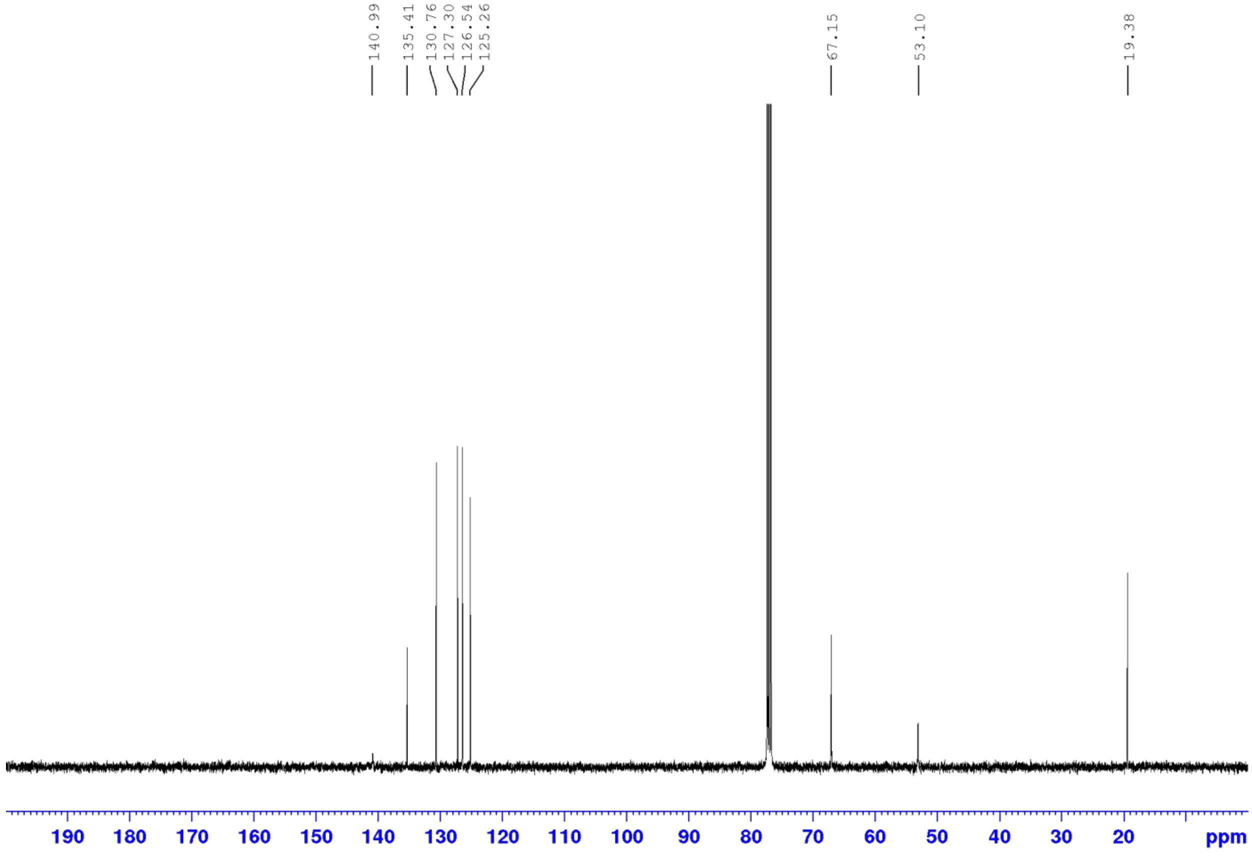
3.00
1.02
1.02
1.03
3.07
3.08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135.41
130.76
127.30
126.54
125.26
67.15
53.10
19.38
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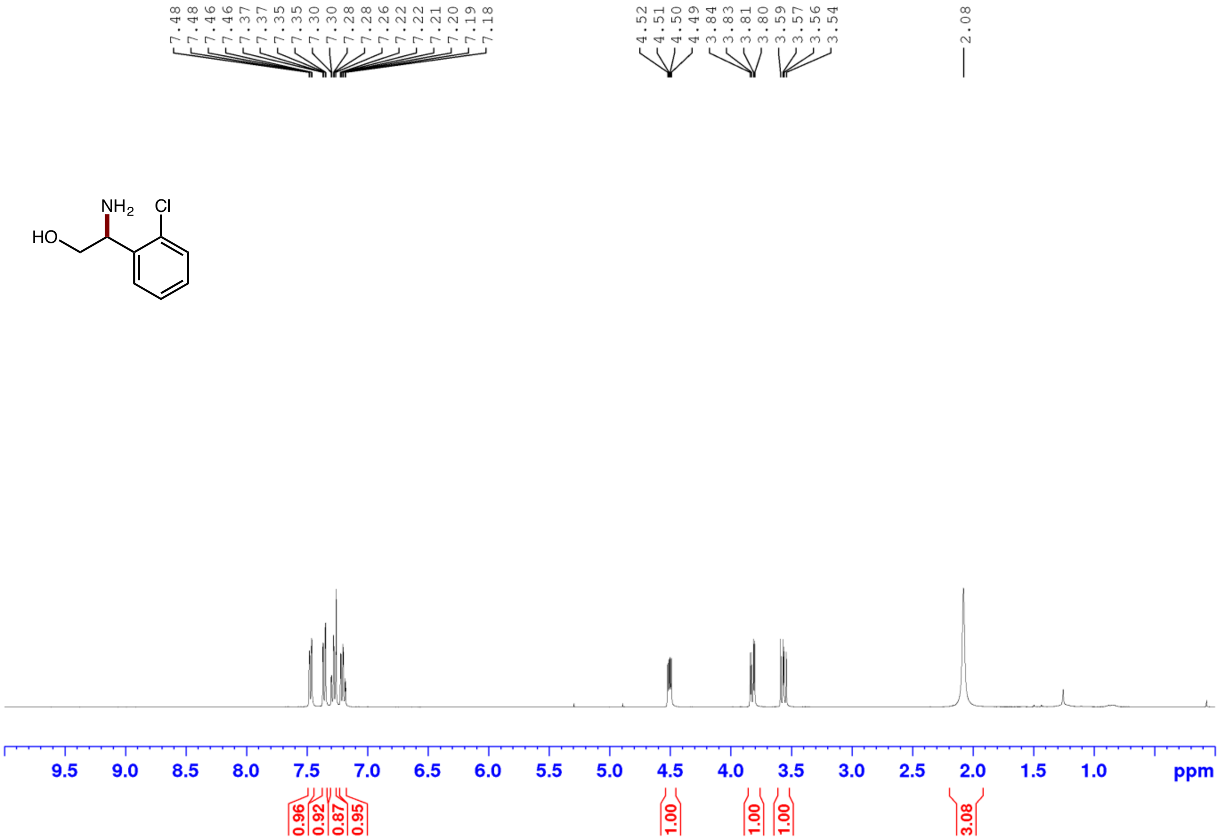
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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Cl
HO
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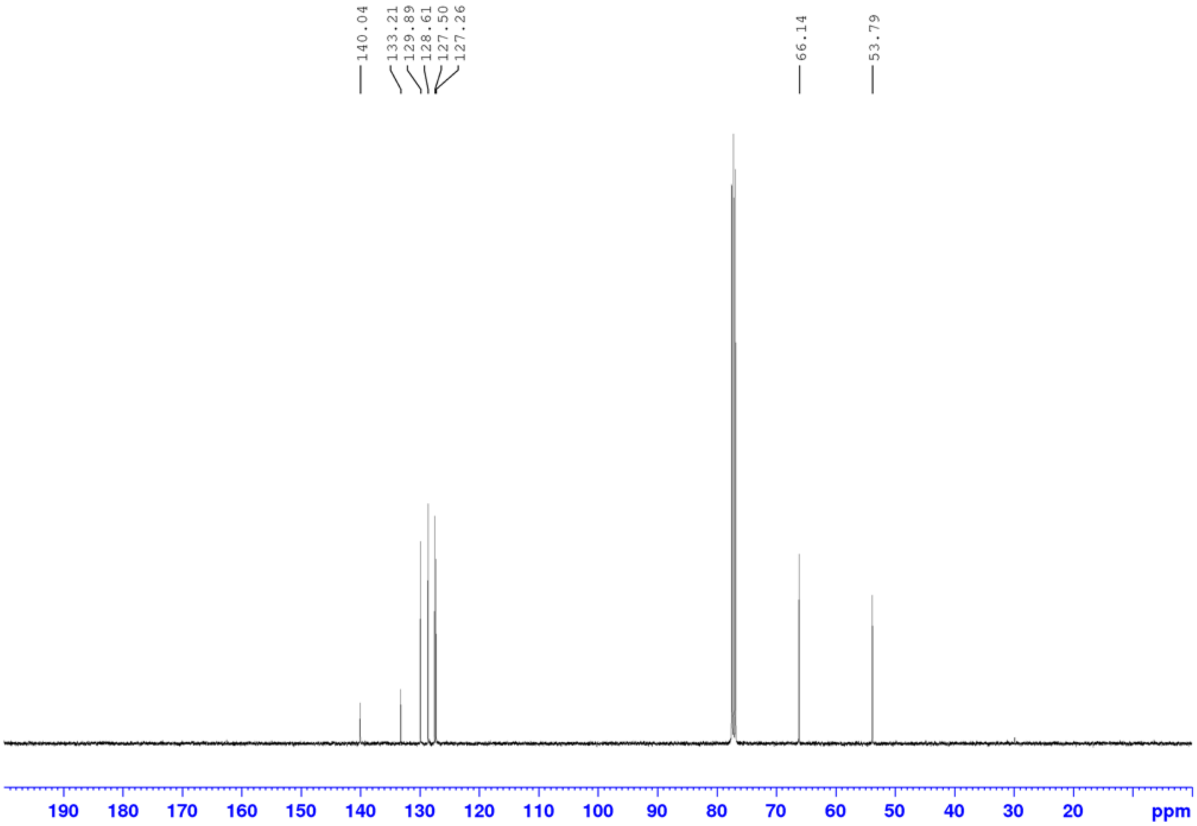
7.48
7.46
7.46
7.37
7.37
7.35
7.35
7.30
7.30
7.28
7.28
7.26
7.22
7.22
7.21
7.20
7.19
7.18
4.52
4.51
4.50
4.49
3.84
3.83
3.81
3.80
3.59
3.57
3.56
3.54
2.08
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.96
0.92
0.87
0.95
1.00
1.00
1.00
3.08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133.21
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127.50
127.26
66.14
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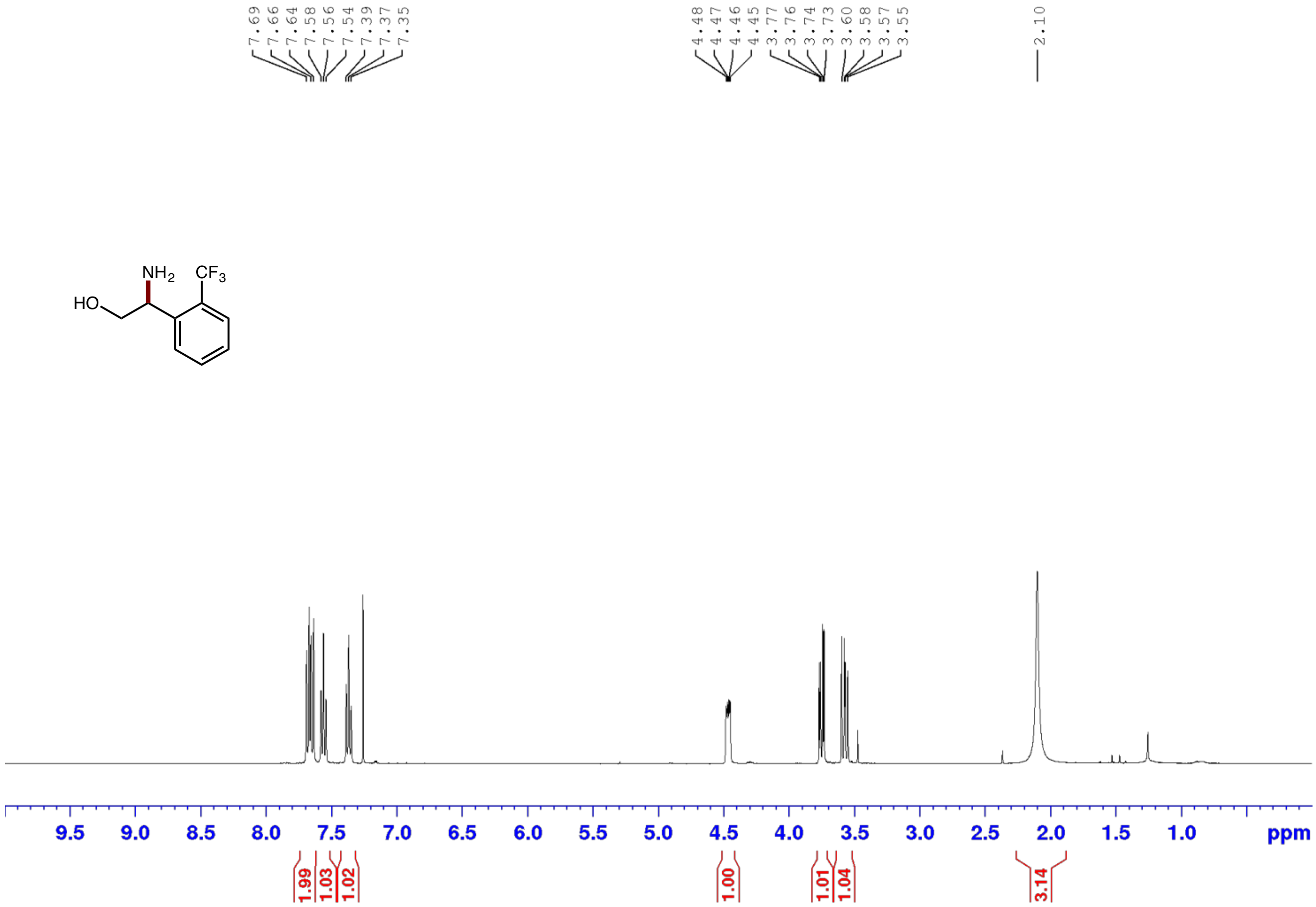
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


7.69
7.66
7.64
7.58
7.56
7.54
7.39
7.37
7.35
4.48
4.47
4.46
4.45
3.77
3.76
3.74
3.73
3.60
3.58
3.57
3.55
2.10
NH2
CF3
HO
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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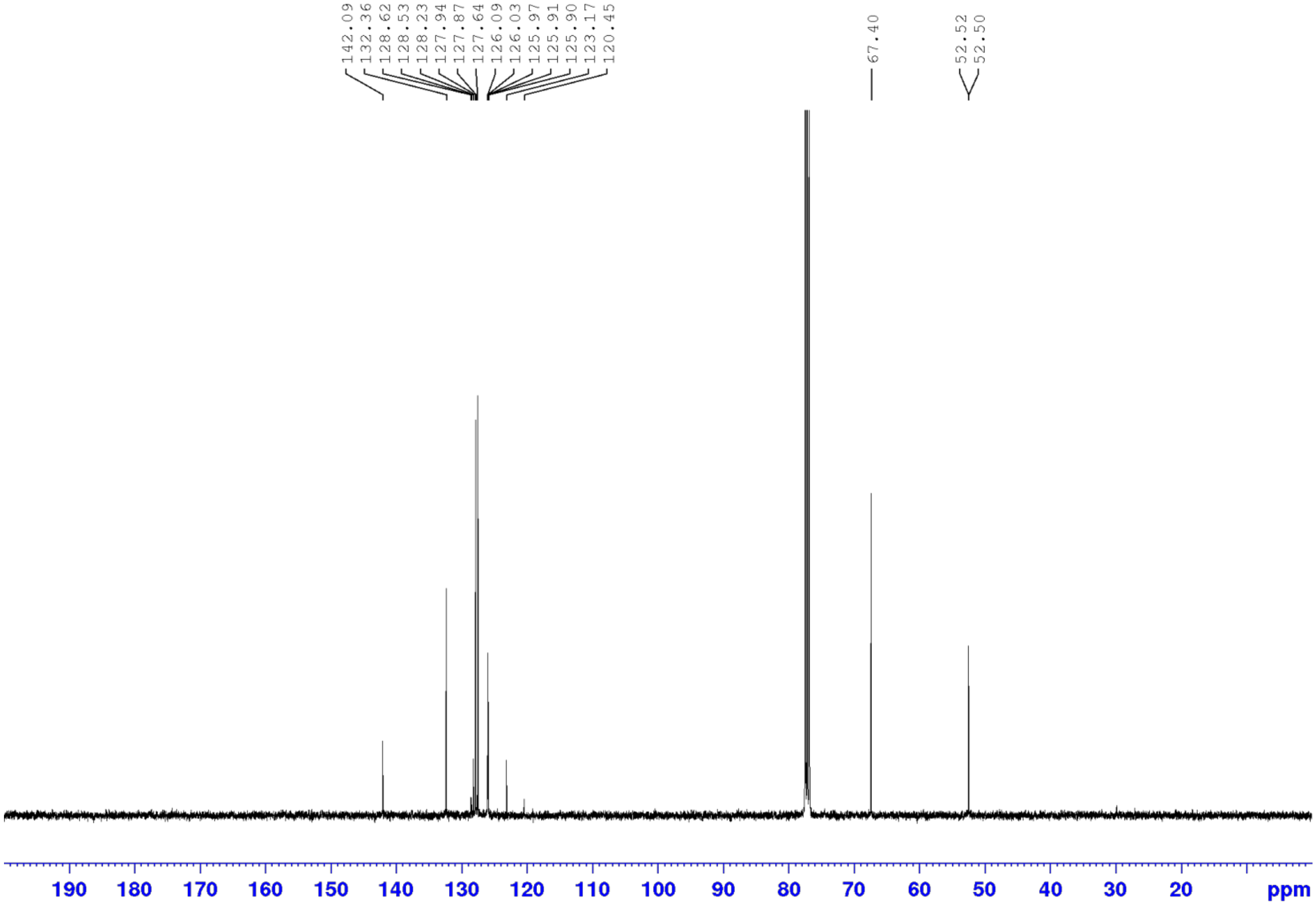
1.5
1.0
ppm
1.99
1.03
1.02
1.00
1.01
1.04
3.14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132.36
128.62
128.53
128.23
127.94
127.87
127.64
126.09
126.03
125.97
125.91
125.90
123.17
120.45
67.40
52.52
52.50
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180
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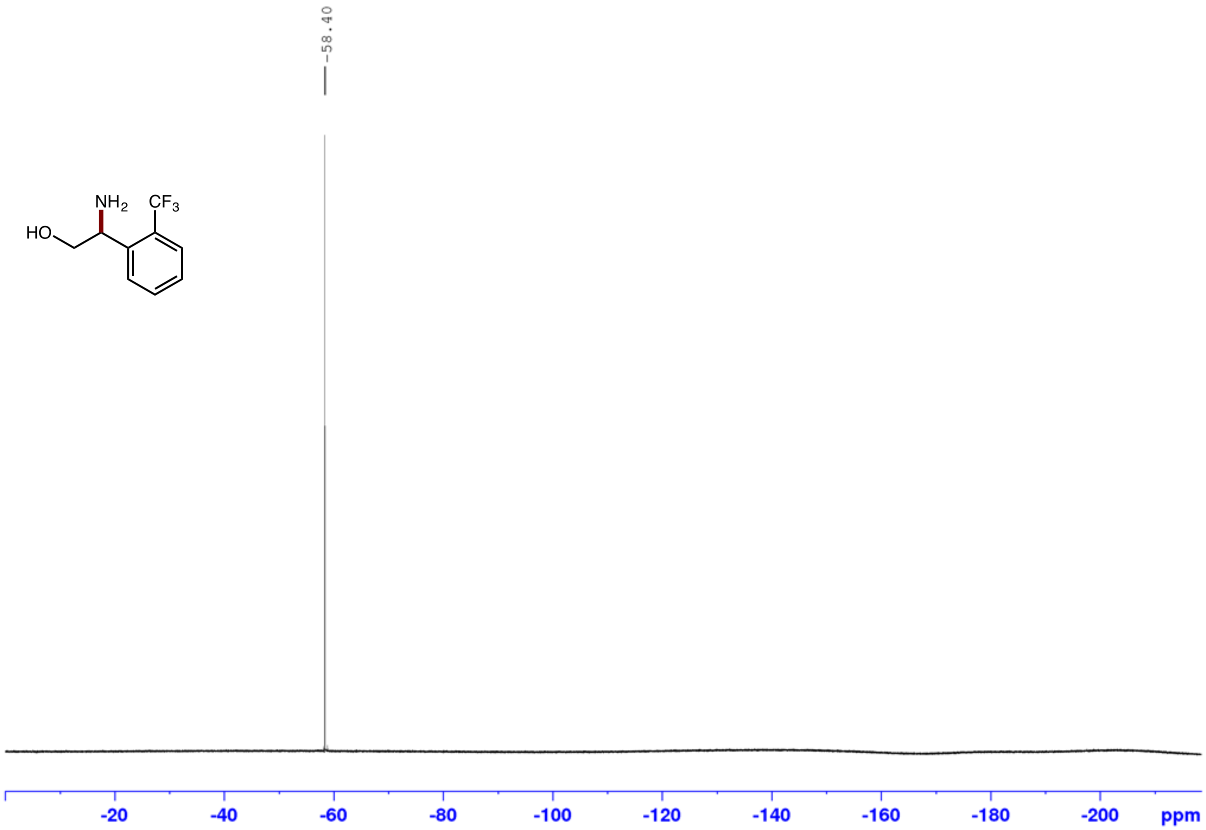
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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CF3
HO
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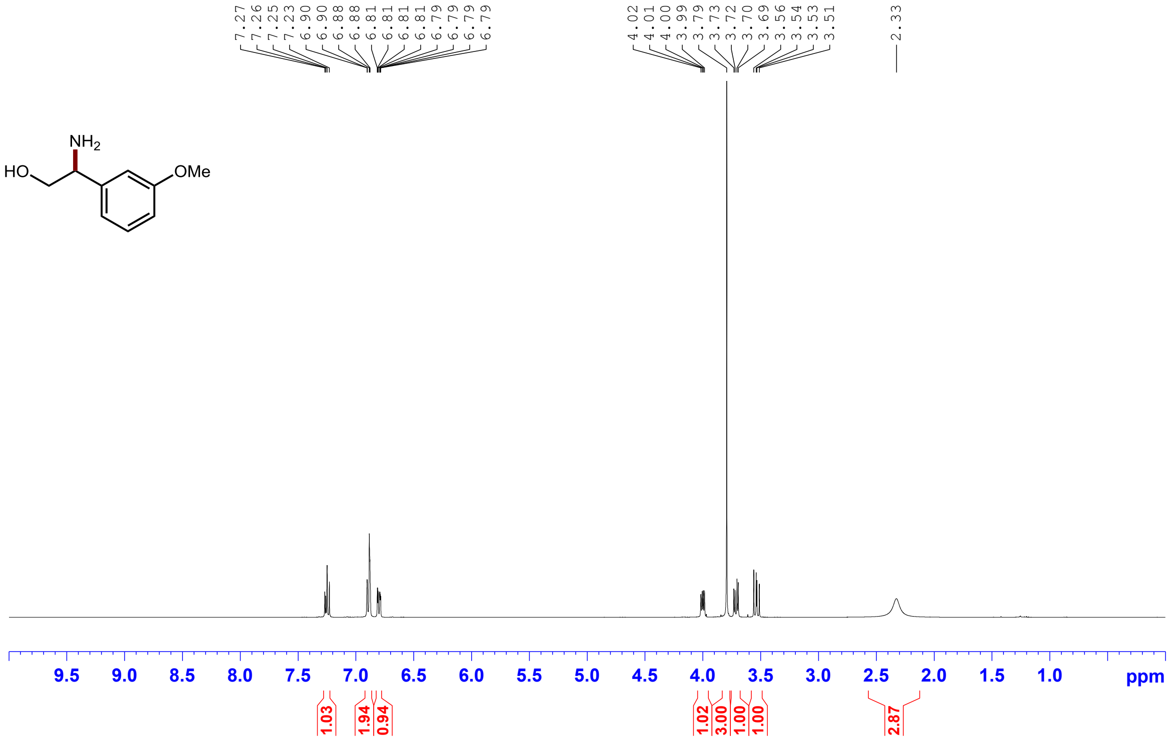
-120
-140
-160
-180
-200
ppm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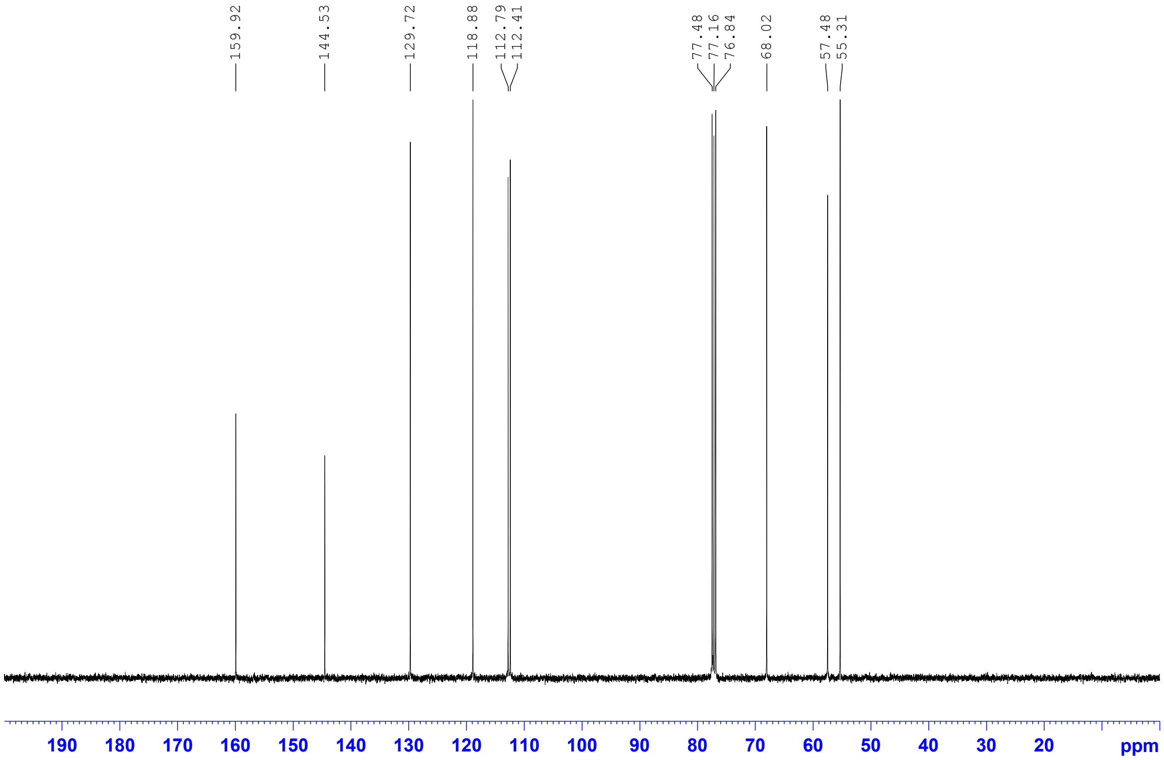
7.26
7.25
7.23
6.90
6.88
6.81
6.81
6.81
6.81
6.79
6.79
6.79
6.79
4.02
4.01
4.00
3.99
3.79
3.73
3.72
3.70
3.69
3.56
3.54
3.53
3.51
2.33
NH$_2$
HO
OMe
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.03
1.94
0.94
1.02
3.00
1.00
1.00
2.87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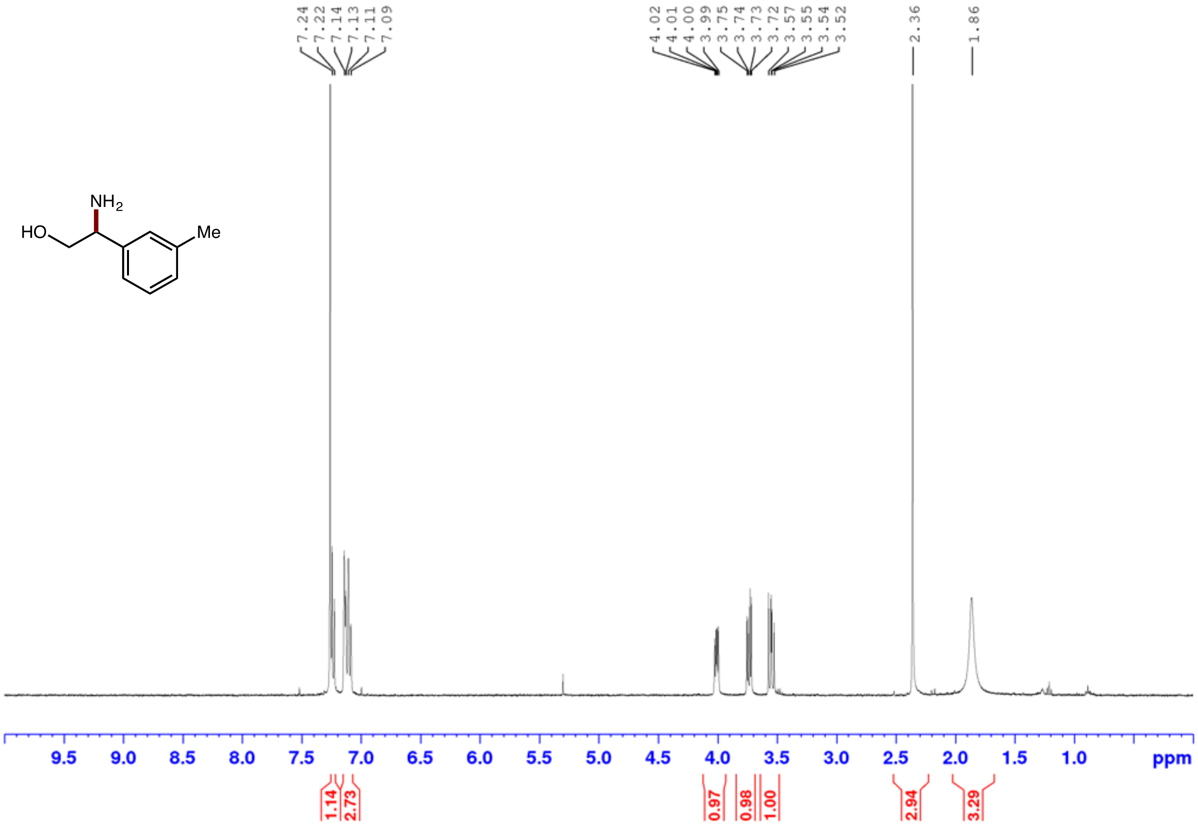
144.53
129.72
118.88
112.79
112.41
77.48
77.16
76.84
68.02
57.48
55.31
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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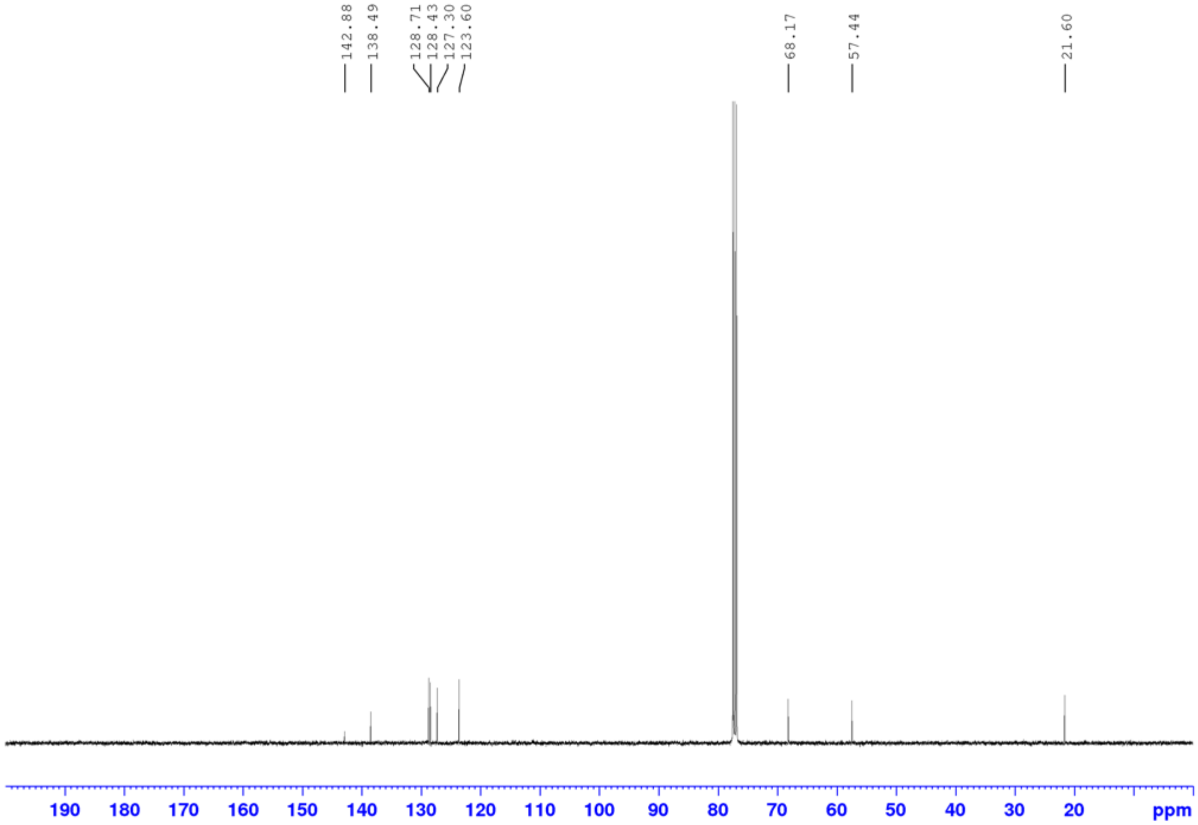
7.22
7.14
7.13
7.11
7.09
4.02
4.01
4.00
3.99
3.75
3.74
3.73
3.72
3.57
3.55
3.54
3.52
2.36
1.86
NH2
HO
Me
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.14
2.73
0.97
0.98
1.00
2.94
3.29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128.71
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123.60
68.17
57.44
21.60
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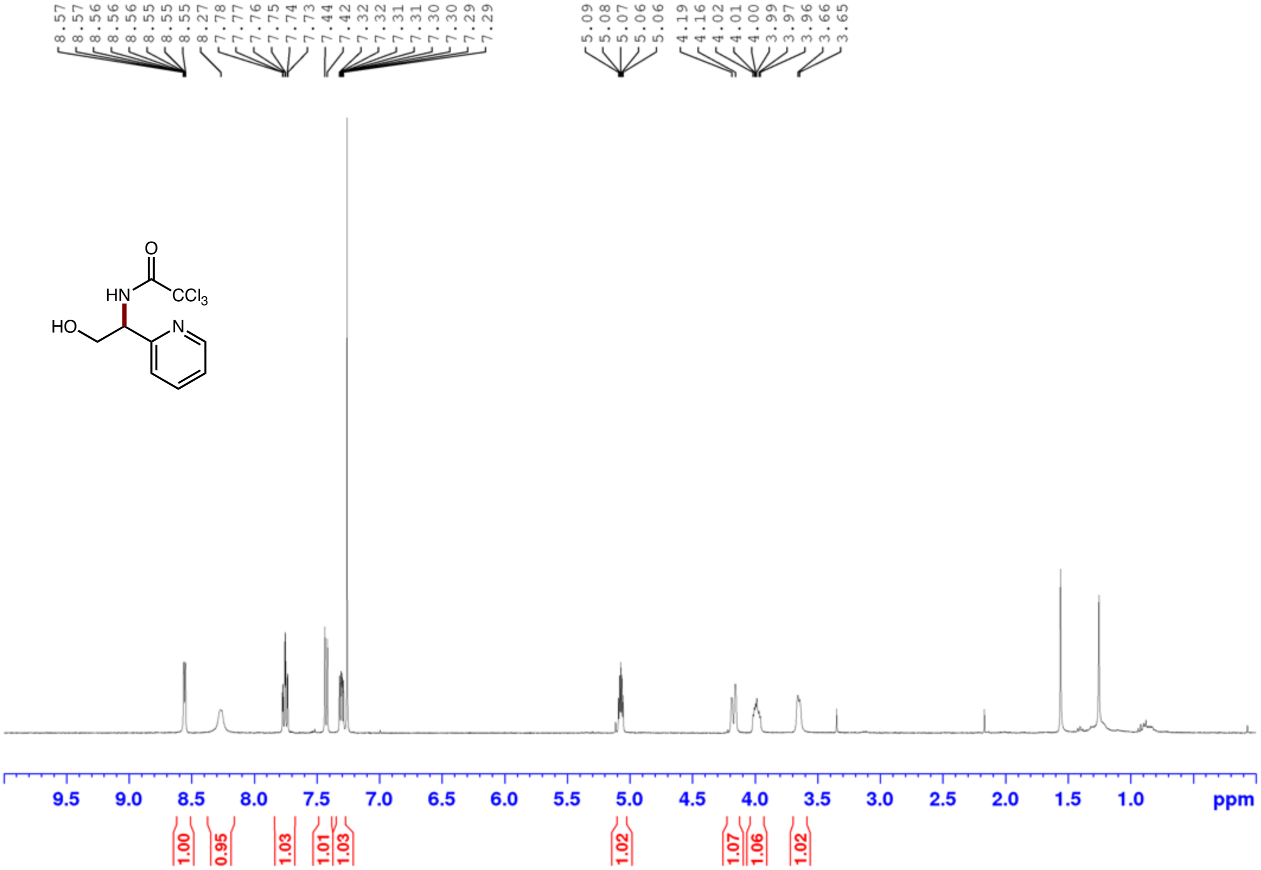
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


8.57
8.57
8.56
8.56
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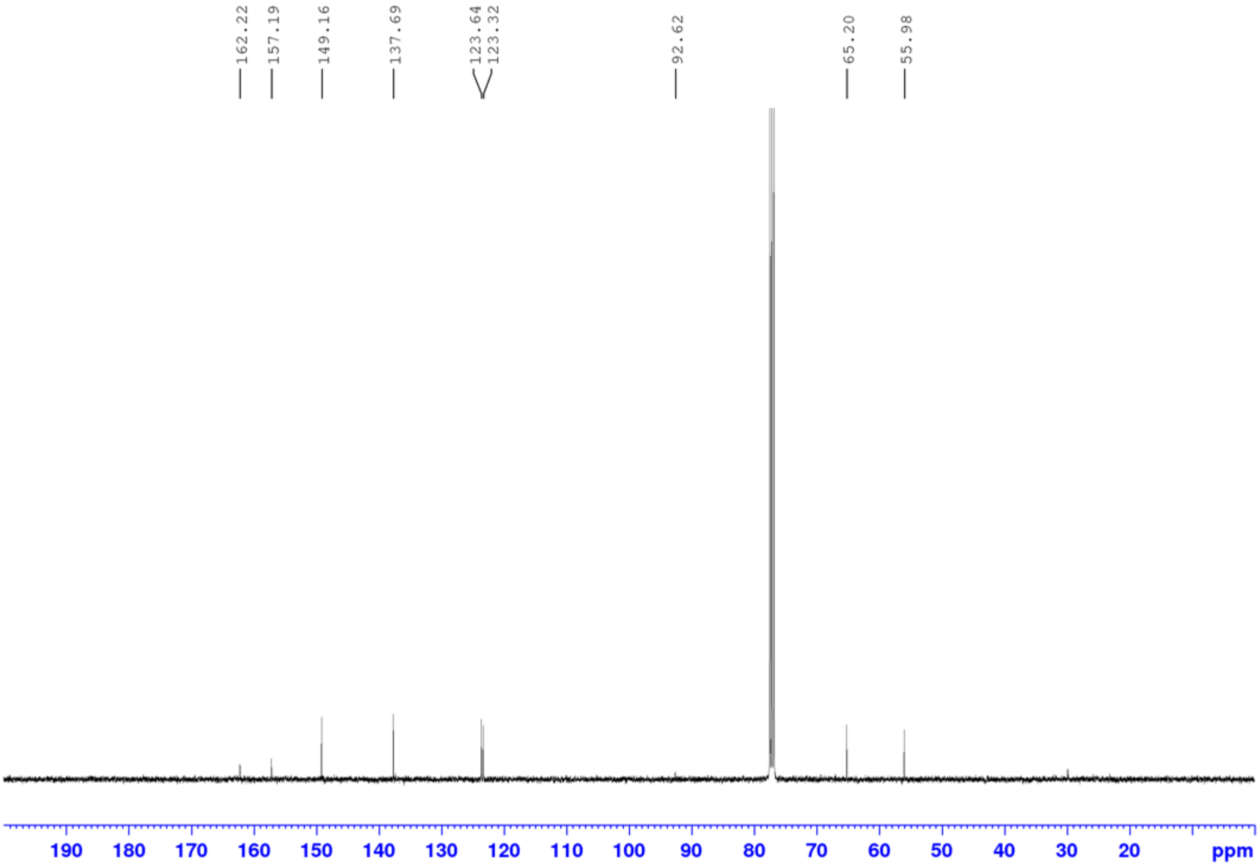
8.55
8.55
8.55
8.27
7.78
7.77
7.76
7.75
7.74
7.73
7.44
7.42
7.32
7.32
7.31
7.31
7.30
7.30
7.29
7.29
5.09
5.08
5.07
5.06
5.06
4.19
4.16
4.02
4.01
4.00
3.99
3.97
3.96
3.66
3.65
O
HN
CCl3
HO
N
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.00
0.95
1.03
1.01
1.03
1.02
1.07
1.06
1.02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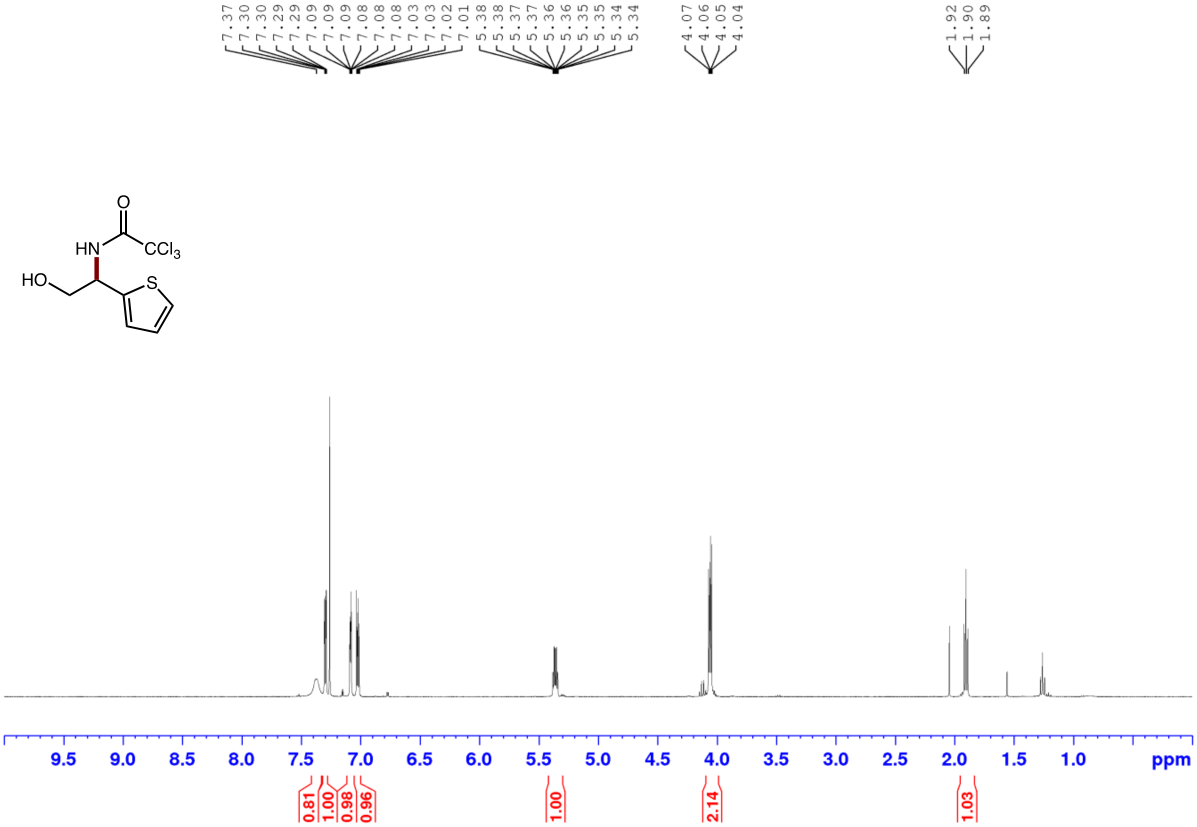
157.19
149.16
137.69
123.64
123.32
92.62
65.20
55.98
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

O
HN
CCl3
HO
S


7.37
7.30
7.30
7.29
7.29
7.09
7.09
7.09
7.08
7.08
7.08
7.03
7.02
7.01
5.38
5.38
5.37
5.37
5.36
5.36
5.35
5.35
5.34
5.34
4.07
4.06
4.05
4.04
1.92
1.90
1.89
9.5
9.0
8.5
8.0
7.5
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
ppm
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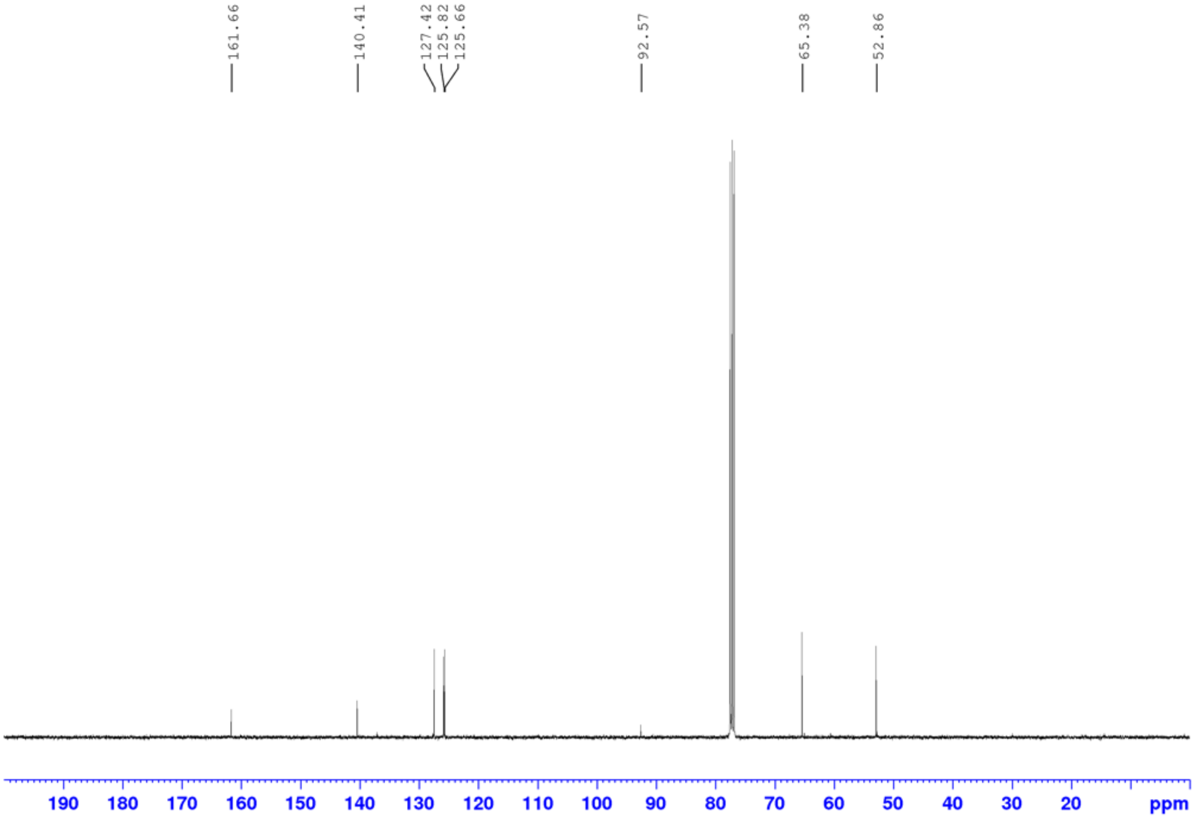
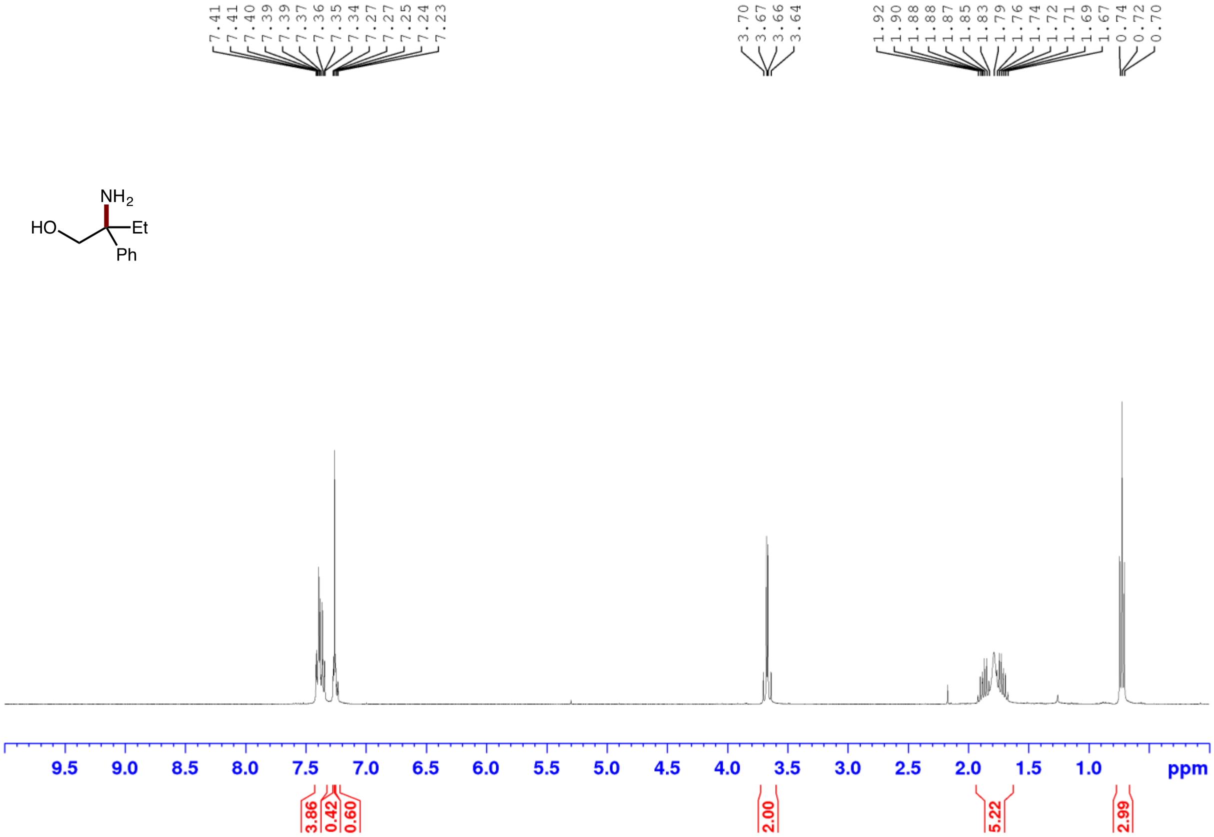
1.00
0.98
0.96
1.00
2.14
1.03


161.66
140.41
127.42
125.82
125.66
92.57
65.38
52.86
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


NH$_2$
HO
Et
Ph

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7.41
7.40
7.39
7.39
7.37
7.36
7.35
7.34
7.27
7.27
7.25
7.24
7.23
3.70
3.67
3.66
3.64
1.92
1.90
1.88
1.88
1.87
1.85
1.83
1.79
1.76
1.74
1.72
1.71
1.69
1.67
0.74
0.72
0.70
9.5
9.0
8.5
8.0
7.5
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
ppm
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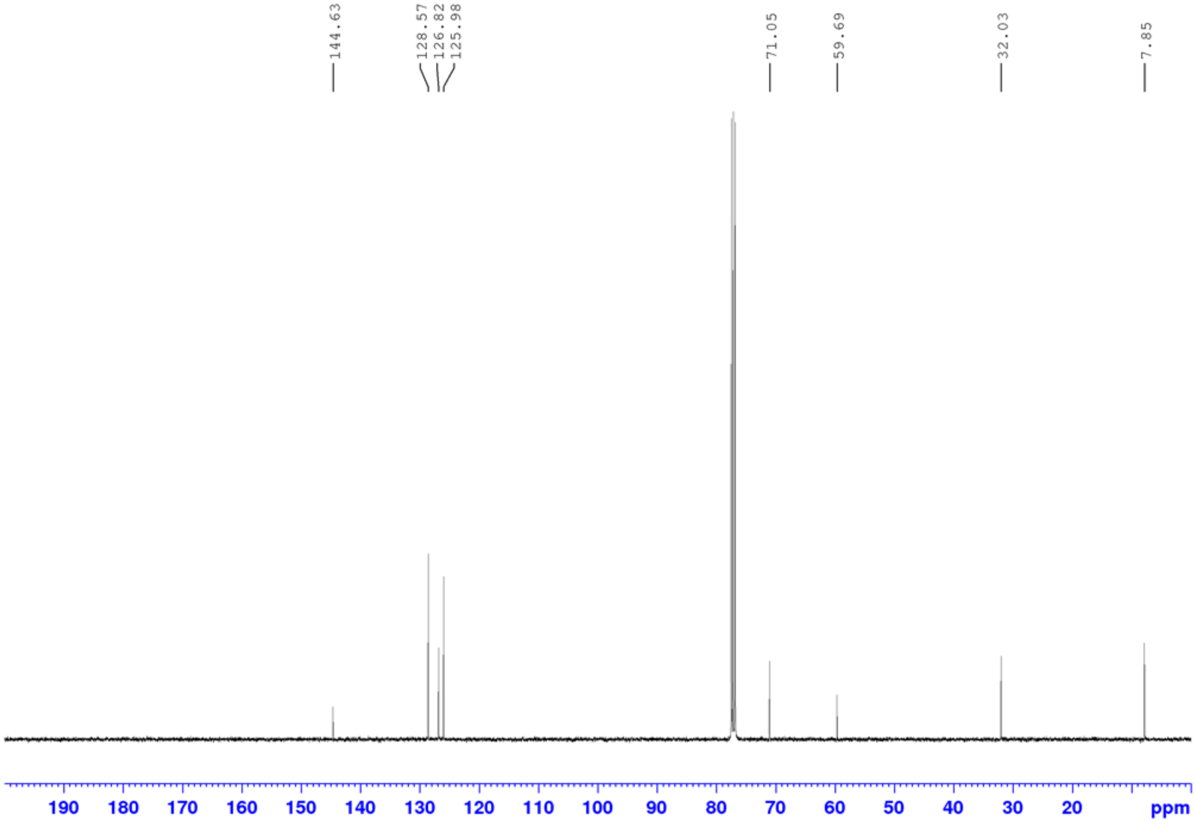
0.60
2.00
5.22
2.99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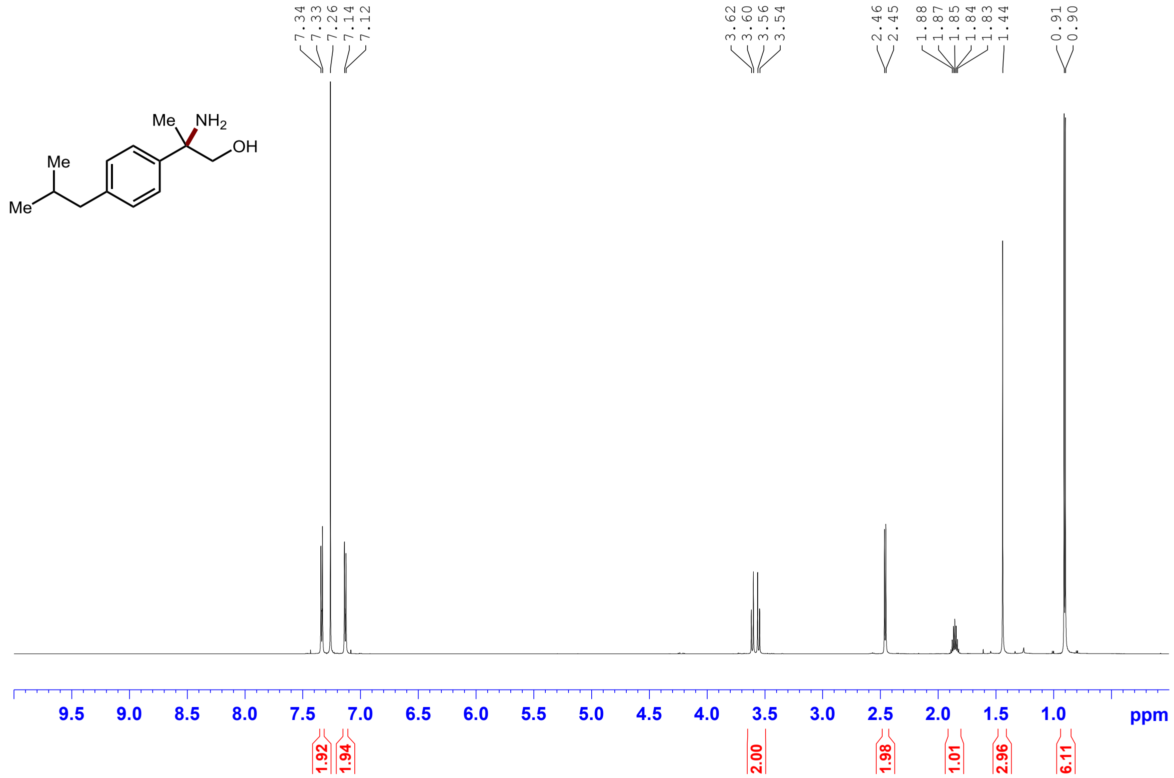
128.57
126.82
125.98
71.05
59.69
32.03
7.85
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


Me
NH2
OH
Me
Me
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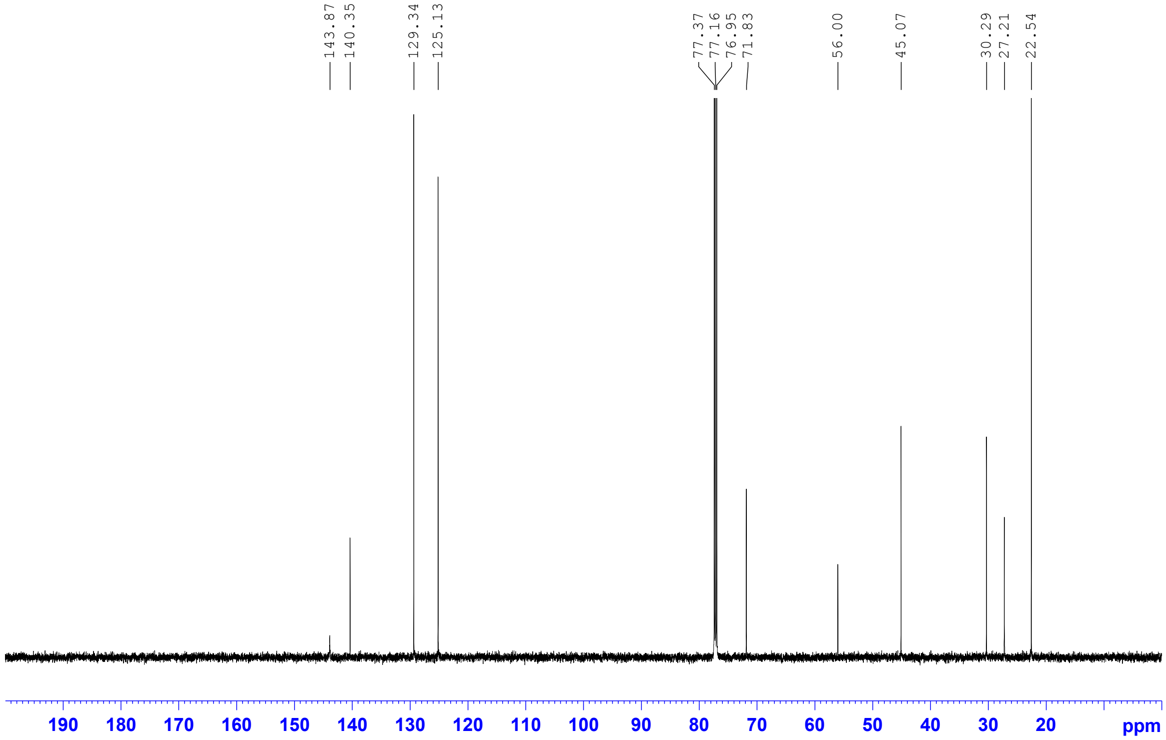
7.26
7.14
7.12
3.62
3.60
3.56
3.54
2.46
2.45
1.88
1.87
1.85
1.84
1.83
1.44
0.91
0.90
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.92
1.94
2.00
1.98
1.01
2.96
6.11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129.34
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77.37
77.16
76.95
71.83
56.00
45.07
30.29
27.21
22.54
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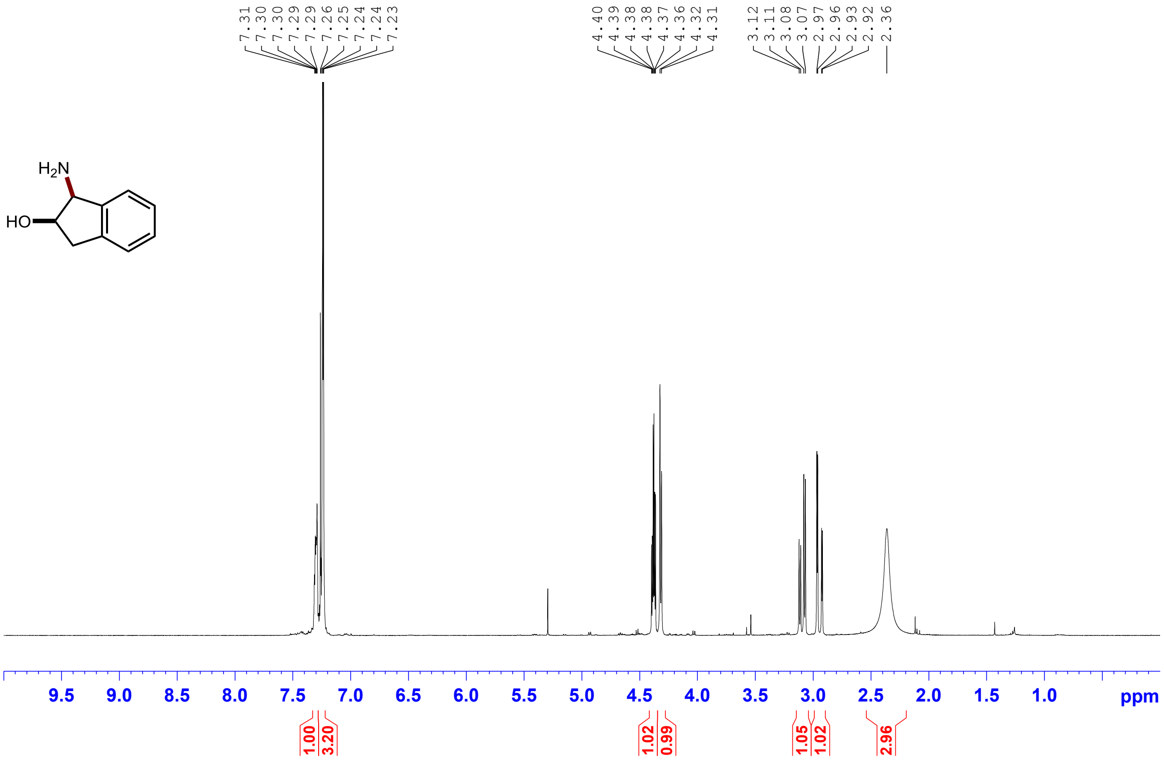
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


H2N
HO
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7.30
7.30
7.29
7.29
7.26
7.25
7.24
7.24
7.23
4.40
4.39
4.38
4.38
4.37
4.36
4.32
4.31
3.12
3.11
3.08
3.07
2.97
2.96
2.93
2.92
2.36
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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1.5
1.0
ppm
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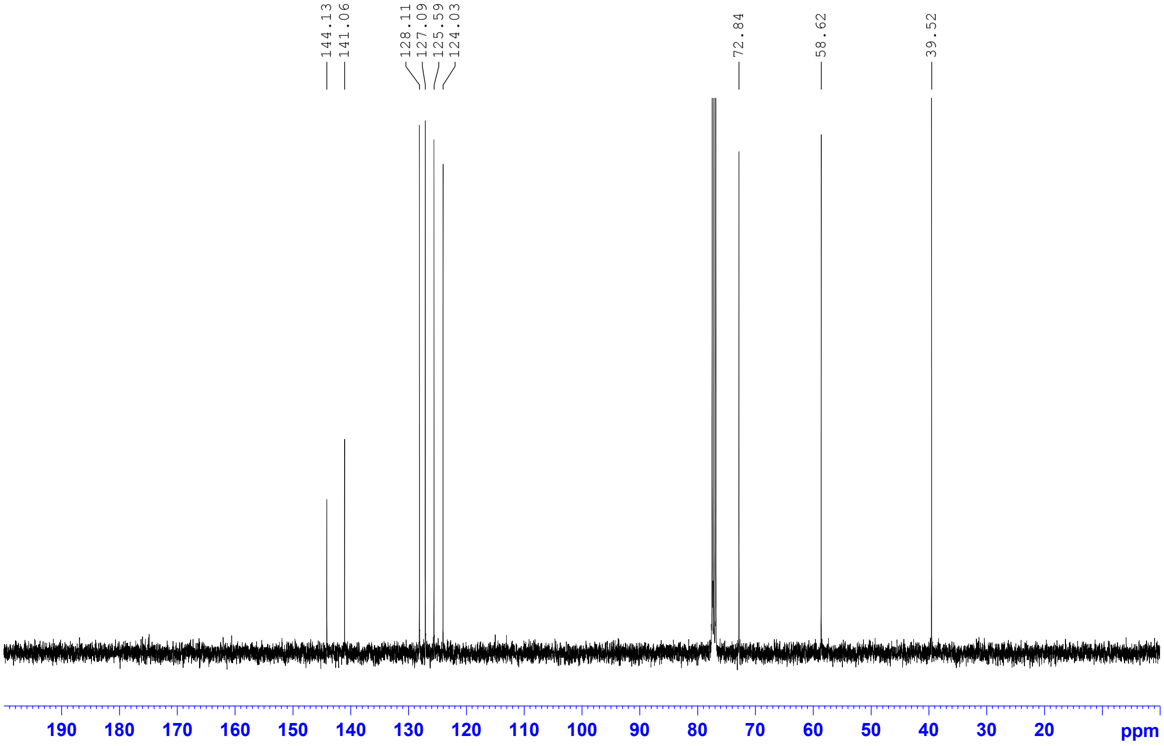
3.20
1.02
0.99
1.05
1.02
2.96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124.03
72.84
58.62
39.52
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180
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160
150
140
130
120
110
100
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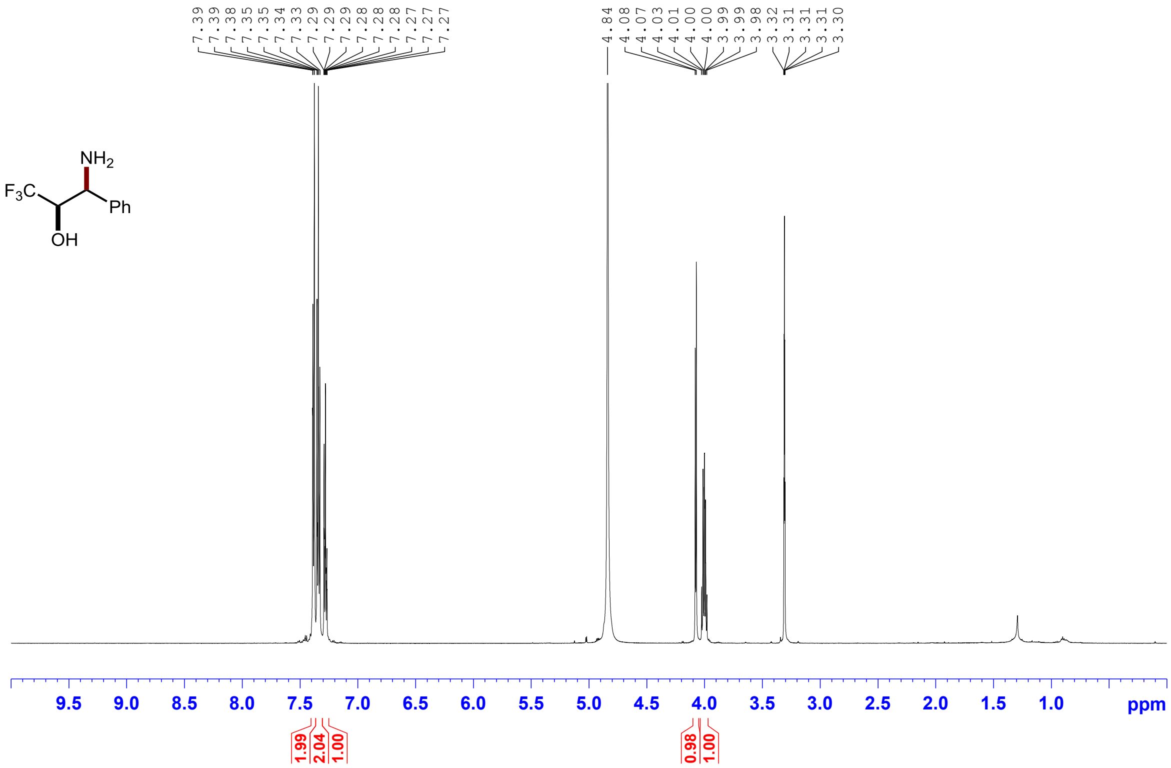
80
70
60
50
40
30
20
ppm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7.38
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7.35
7.34
7.33
7.29
7.29
7.29
7.28
7.28
7.28
7.27
7.27
7.27
4.84
4.08
4.07
4.03
4.01
4.00
4.00
3.99
3.99
3.98
3.32
3.31
3.31
3.31
3.30
NH2
F3C
Ph
OH
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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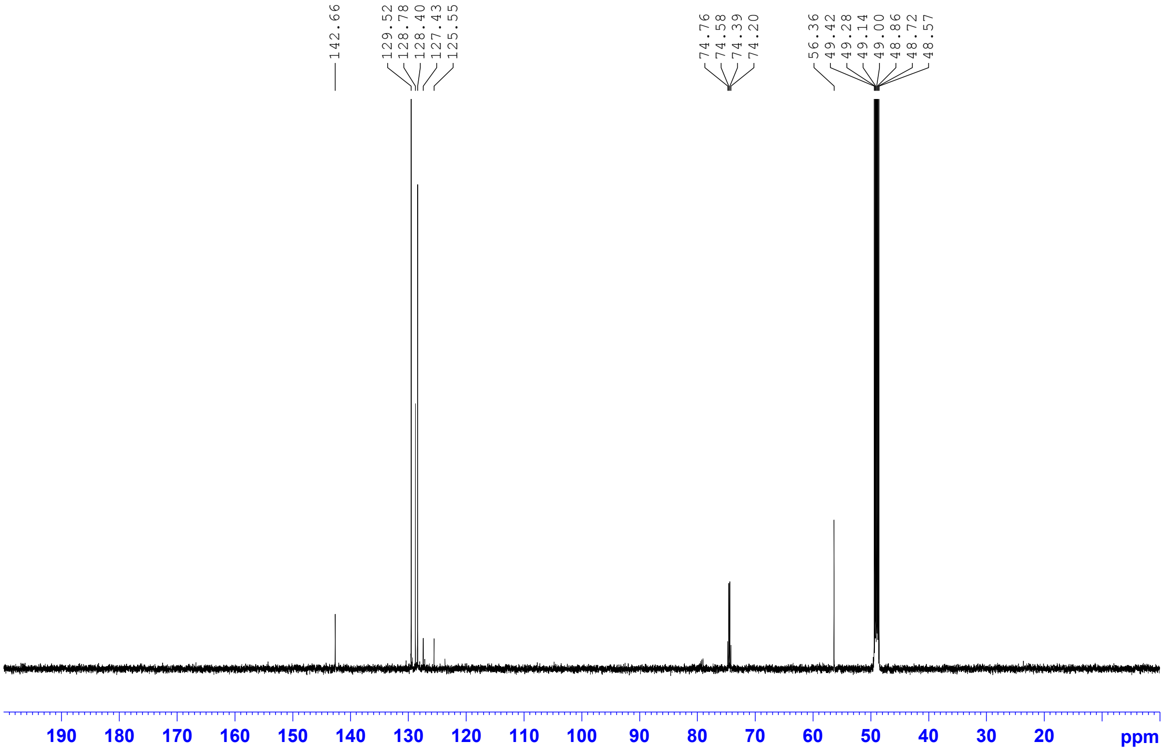
1.00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74.58
74.39
74.20
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49.42
49.28
49.14
49.00
48.86
48.72
48.57
190
180
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160
150
140
130
120
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100
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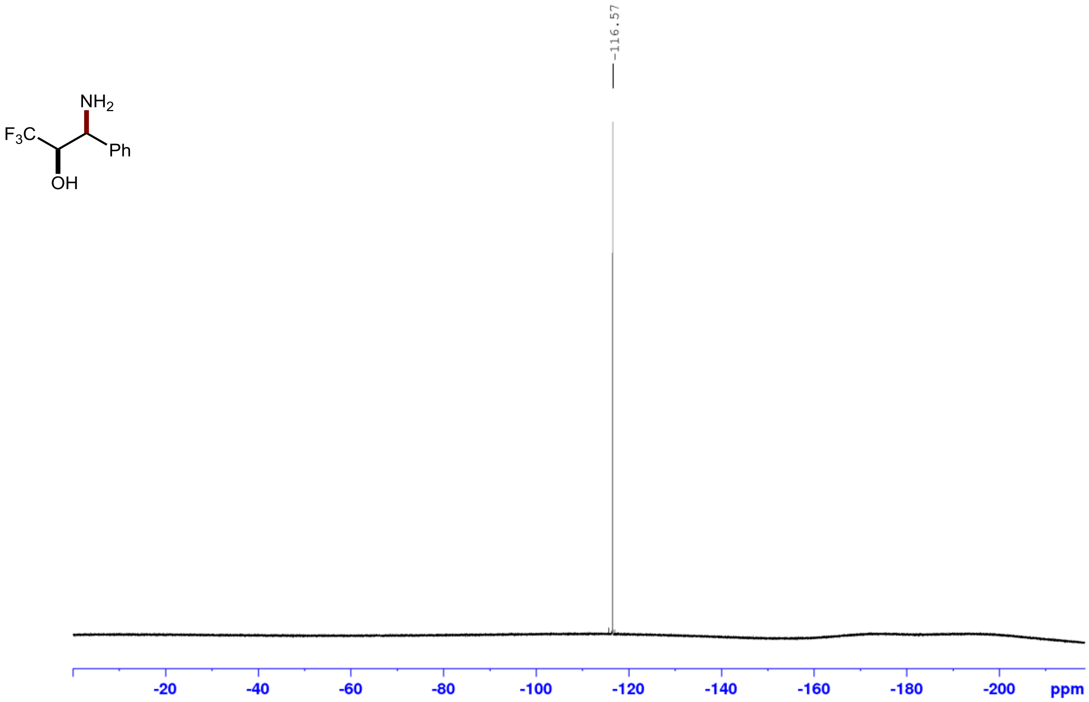
80
70
60
50
40
30
20
ppm


NH$_2$
F$_3$C
Ph
OH
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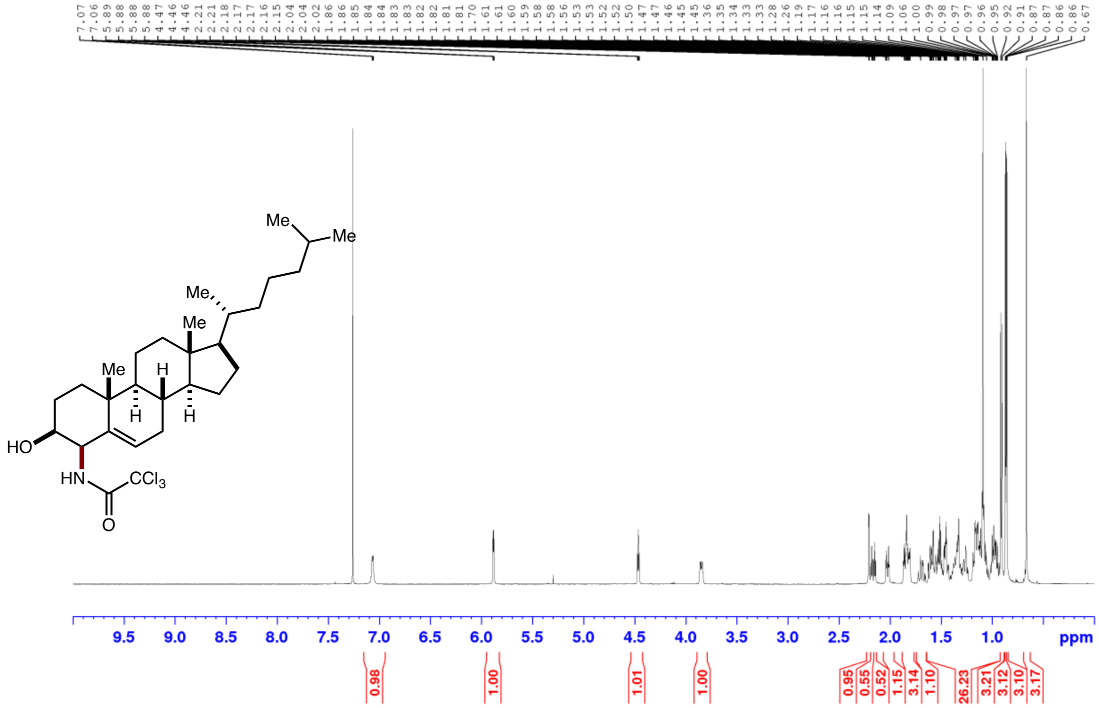
-160
-180
-200
ppm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4.46
4.46
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2.21
2.18
2.17
2.17
2.16
2.15
2.04
2.04
2.02
1.86
1.86
1.85
1.84
1.84
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1.81
1.70
1.61
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1.60
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1.58
1.58
1.56
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1.53
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1.52
1.50
1.47
1.47
1.46
1.45
1.45
1.36
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1.34
1.33
1.33
1.28
1.26
1.19
1.17
1.16
1.16
1.15
1.15
1.14
1.09
1.06
1.00
0.99
0.98
0.97
0.97
0.96
0.95
0.92
0.91
0.87
0.87
0.86
0.86
0.67
Me
Me
Me
Me
Me
H
H
H
HO
HN
CCl3
O
9.5
9.0
8.5
8.0
7.5
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
ppm
0.98
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26.23
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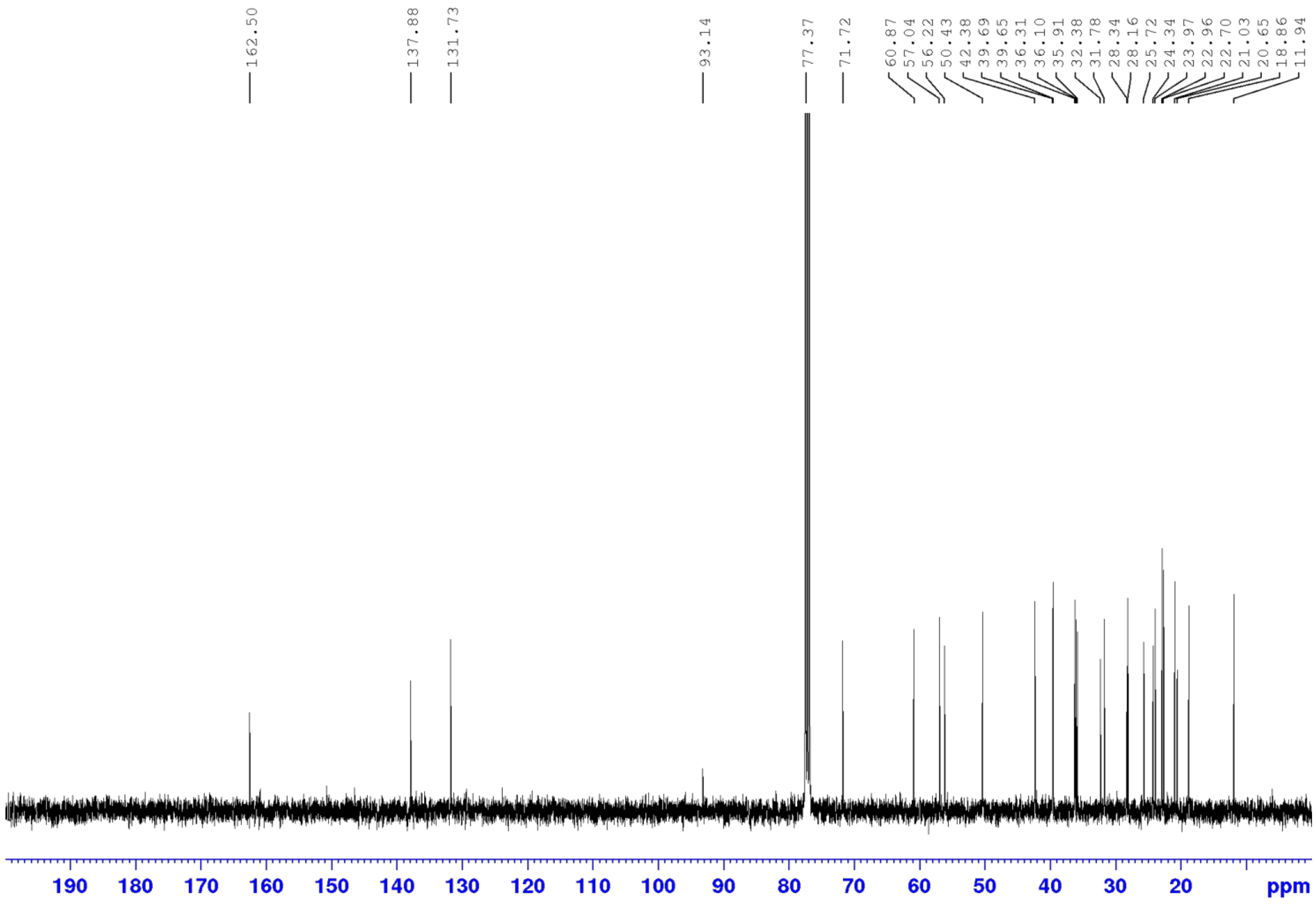
3.10
3.17


162.50
137.88
131.73
93.14
77.37
71.72
60.87
57.04
56.22
50.43
42.38
39.69
39.65
36.31
36.10
35.91
32.38
31.78
28.34
28.16
25.72
24.34
23.97
22.96
22.70
21.03
20.65
18.86
11.94
190
180
170
160
150
140
130
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110
100
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80
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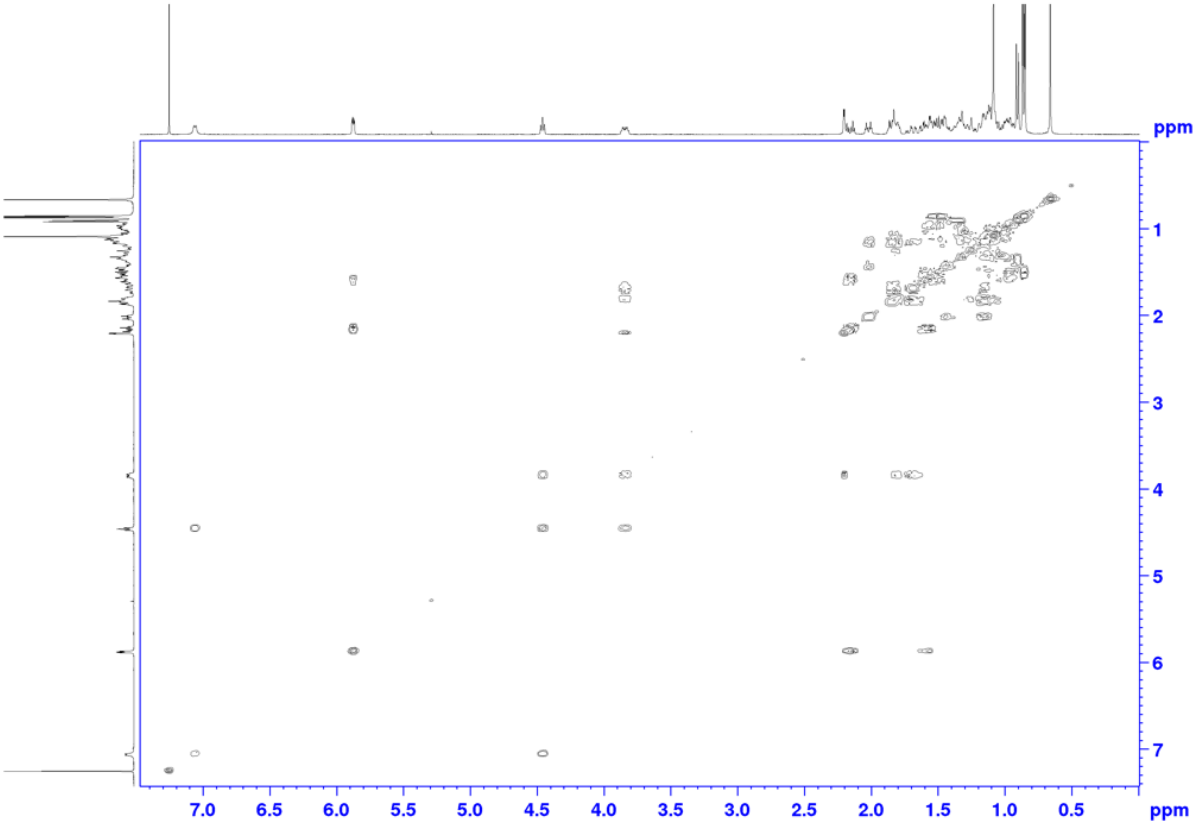
20
ppm

COSY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1.0
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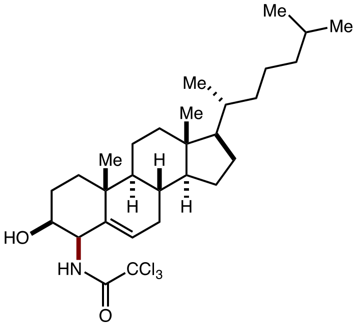
ppm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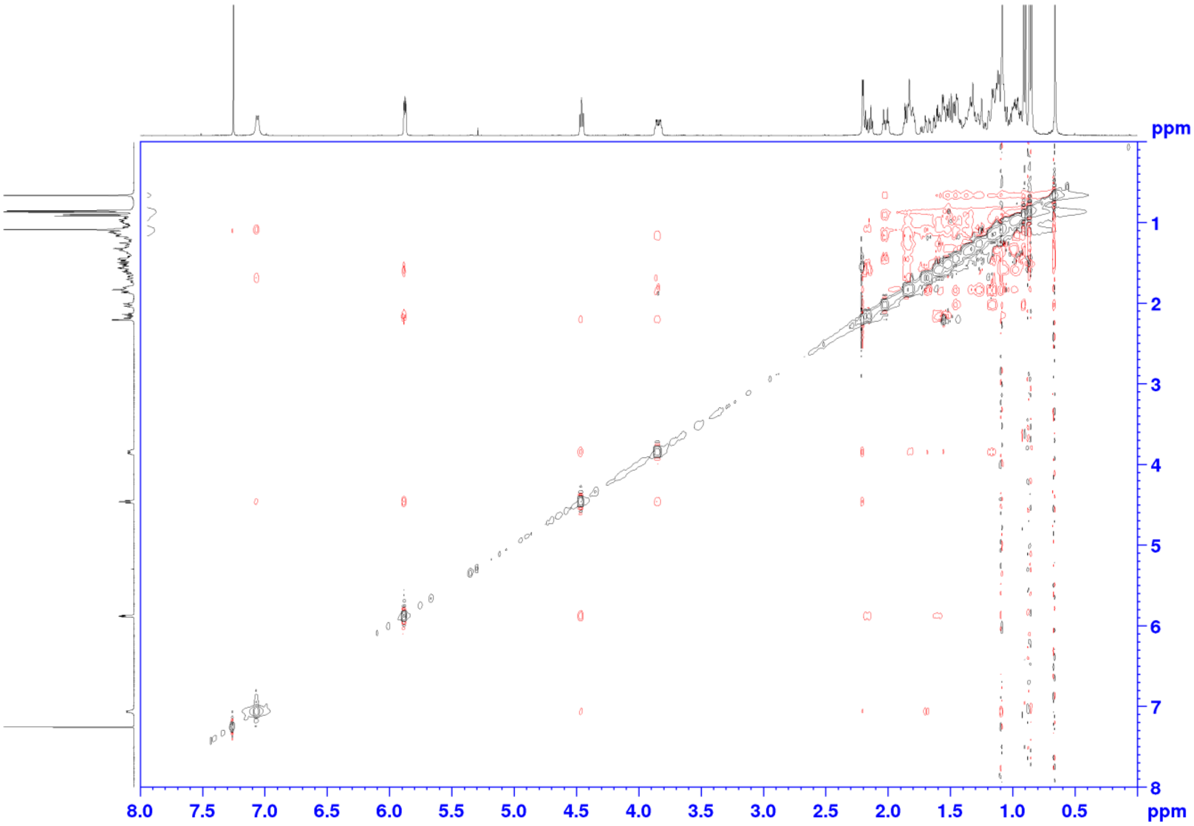
Me
Me
Me
H
H
H
HO
HN
CCl3
O

NOESY


ppm
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6
7
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ppm
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4.5
4.0
3.5
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2.0
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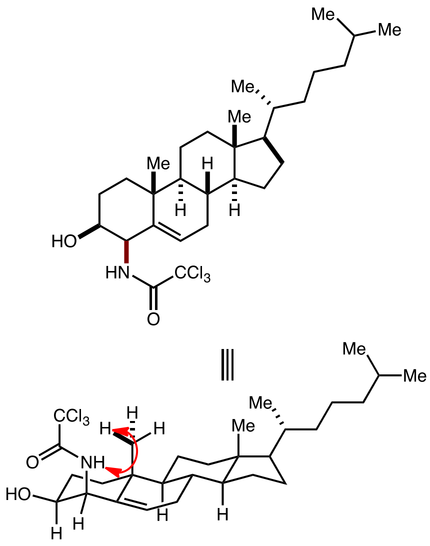
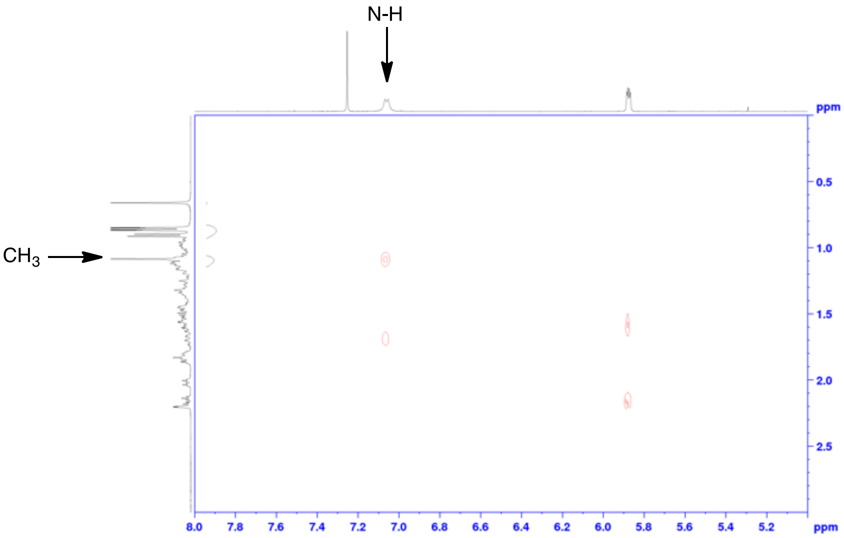
1.0
0.5
ppm


Me
Me
Me
Me
Me
H
H
H
HO
HN
CCl3
O
≡
Me
Me
Me
Me
CCl3
H
H
H
O
NH
HO
H
H
H
H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CH3
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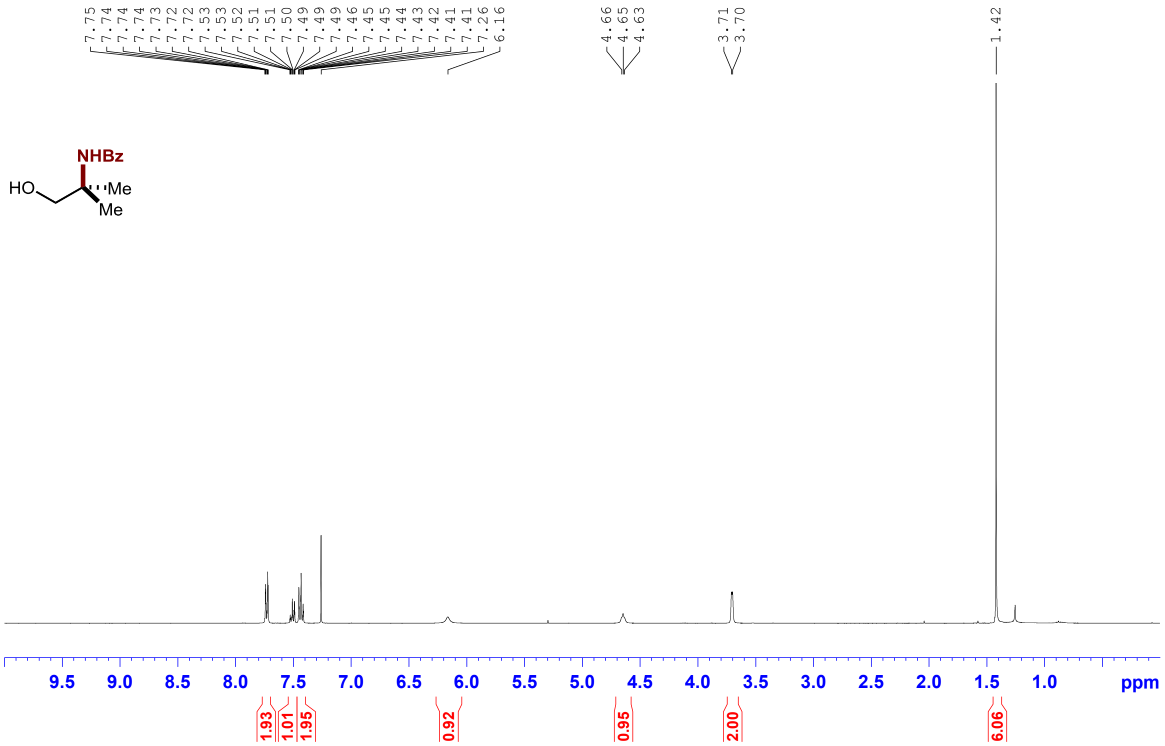
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
ppm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7.53
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7.49
7.49
7.49
7.46
7.45
7.45
7.44
7.43
7.43
7.42
7.41
7.41
7.26
6.16
4.66
4.65
4.63
3.71
3.70
1.42
NHBz
HO
Me
Me
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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ppm
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1.95
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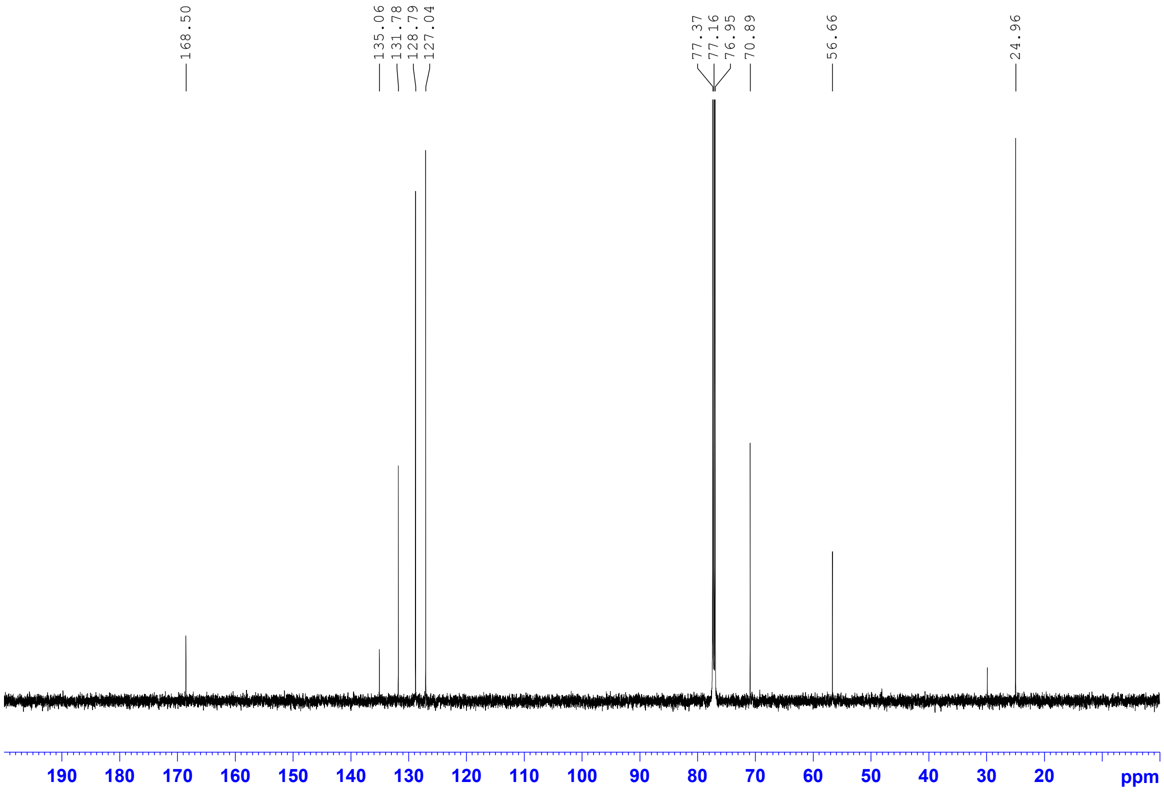
2.00
6.06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127.04
77.37
77.16
76.95
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56.66
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180
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160
150
140
130
120
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80
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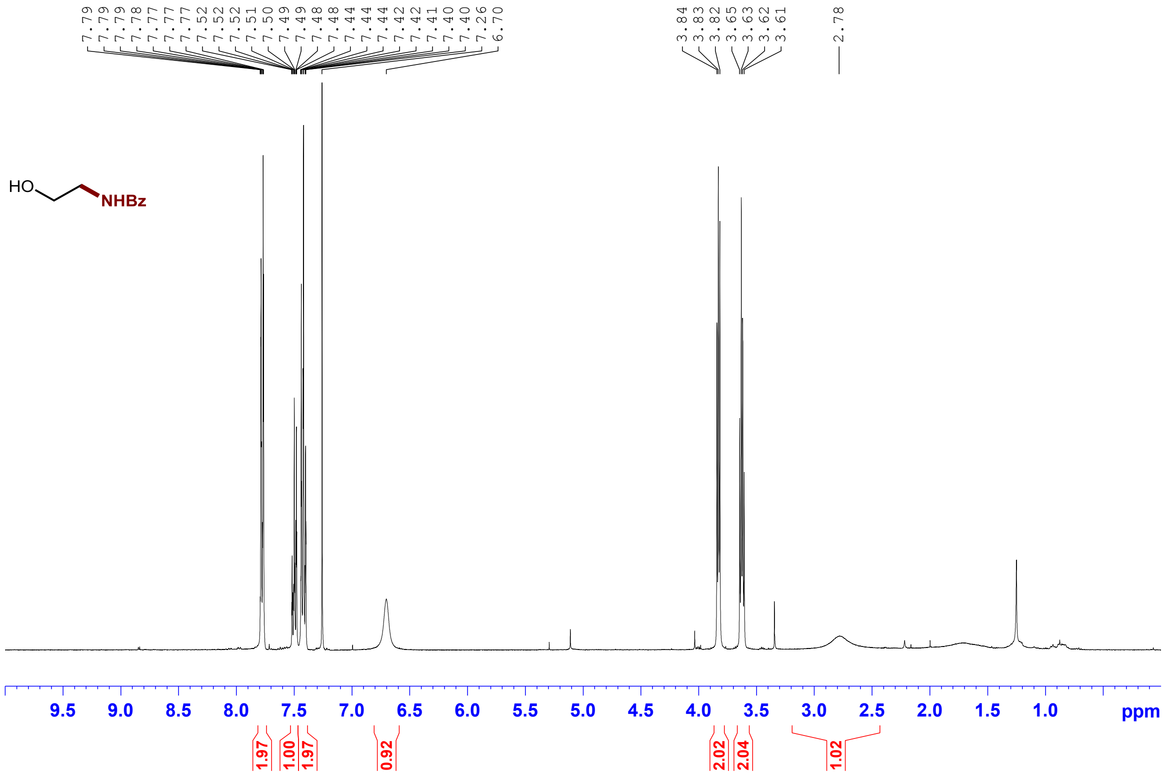
50
40
30
20
ppm



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7.49
7.48
7.48
7.44
7.44
7.44
7.42
7.42
7.41
7.40
7.40
7.26
6.70
3.84
3.83
3.82
3.65
3.63
3.62
3.61
2.78
HO
NHBz
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
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1.5
1.0
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1.97
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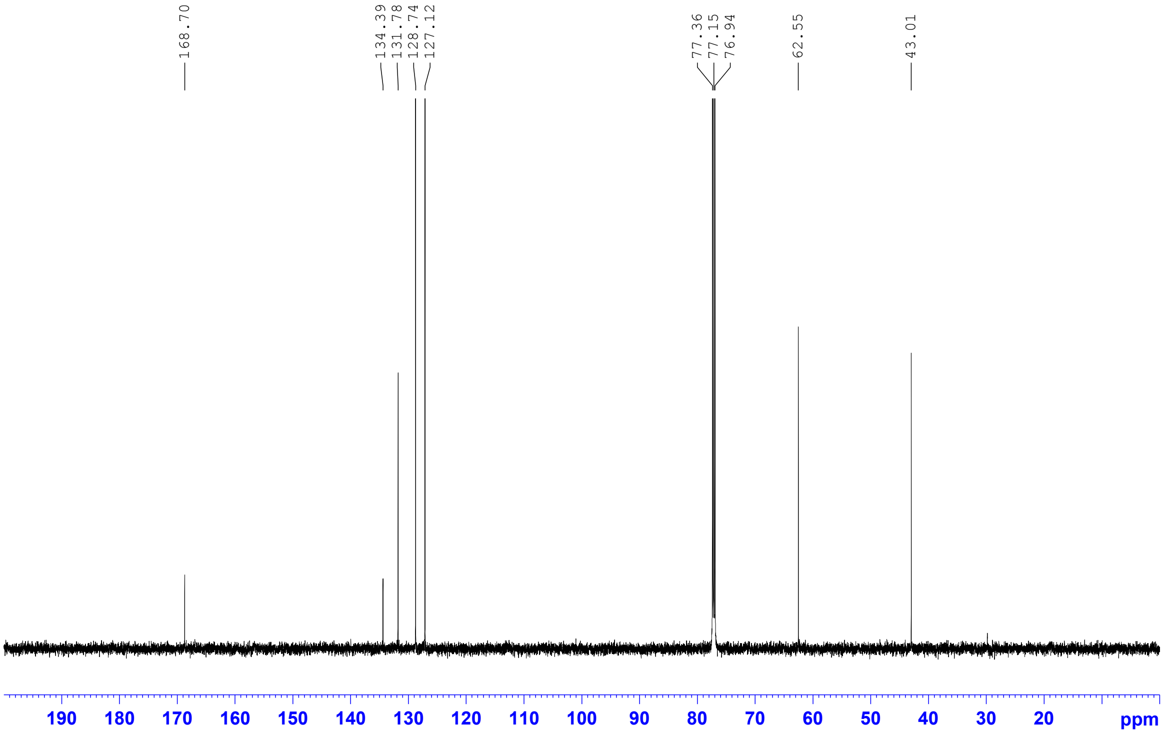
2.04
1.02



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77.15
76.94
62.55
43.01
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160
150
140
130
120
110
100
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80
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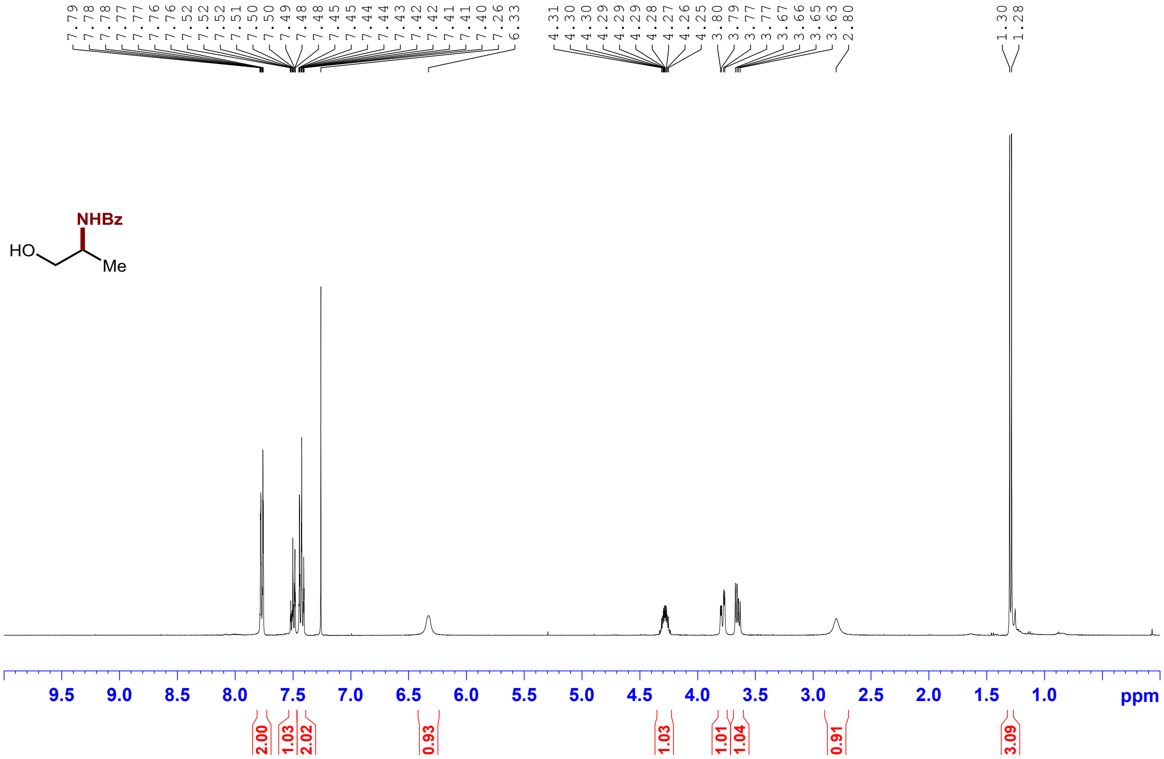
40
30
20
ppm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7.78
7.78
7.77
7.77
7.76
7.76
7.52
7.52
7.52
7.51
7.50
7.50
7.49
7.48
7.48
7.45
7.45
7.44
7.44
7.43
7.42
7.42
7.41
7.41
7.40
7.26
6.33
4.31
4.30
4.30
4.29
4.29
4.29
4.28
4.27
4.26
4.25
3.80
3.79
3.77
3.77
3.67
3.66
3.65
3.63
2.80
1.30
1.28
NHBz
HO
Me
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9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
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2.02
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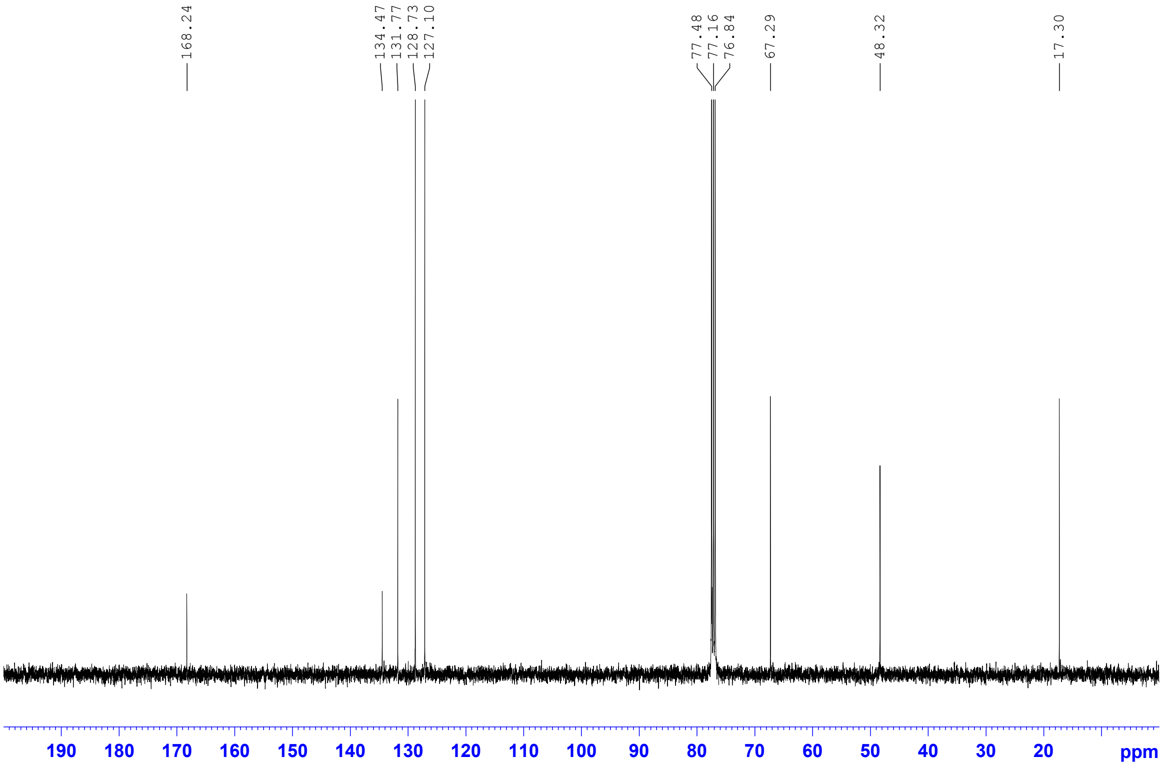
1.03
1.01
1.04
0.91
3.09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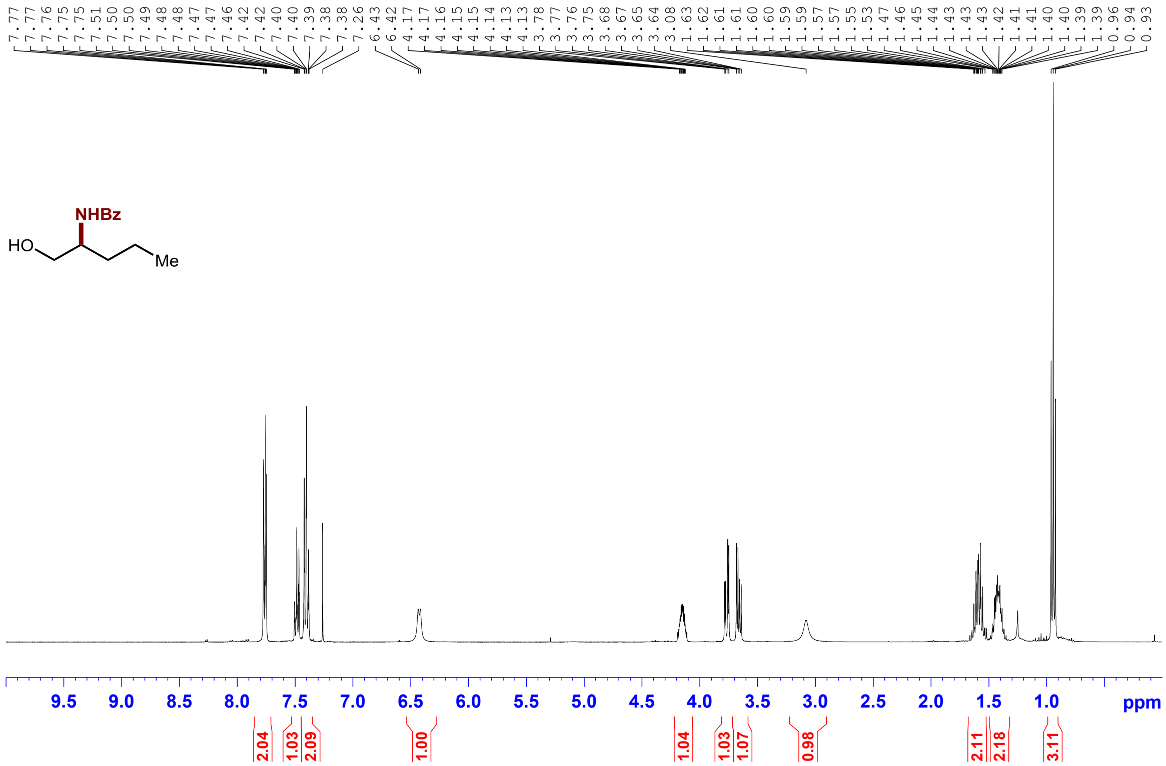
30
20
ppm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7.48
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7.47
7.47
7.46
7.42
7.42
7.40
7.40
7.39
7.38
7.38
7.26
6.43
6.42
4.17
4.17
4.16
4.15
4.15
4.14
4.13
4.13
3.78
3.77
3.76
3.75
3.68
3.67
3.65
3.64
3.08
1.63
1.62
1.61
1.61
1.60
1.60
1.59
1.59
1.57
1.57
1.55
1.53
1.47
1.46
1.45
1.44
1.43
1.43
1.43
1.42
1.41
1.41
1.40
1.40
1.39
1.39
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0.94
0.93
NHBz
HO
Me
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
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2.09
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1.04
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1.07
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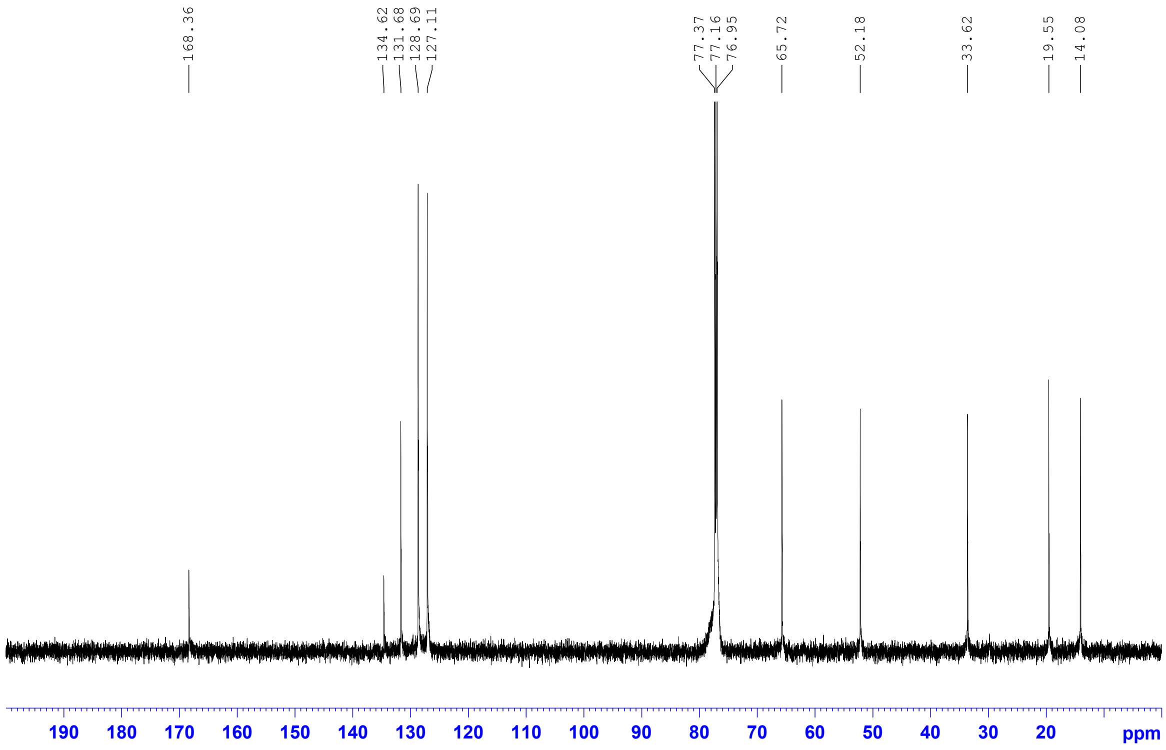
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52.18
33.62
19.55
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150
140
130
120
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80
70
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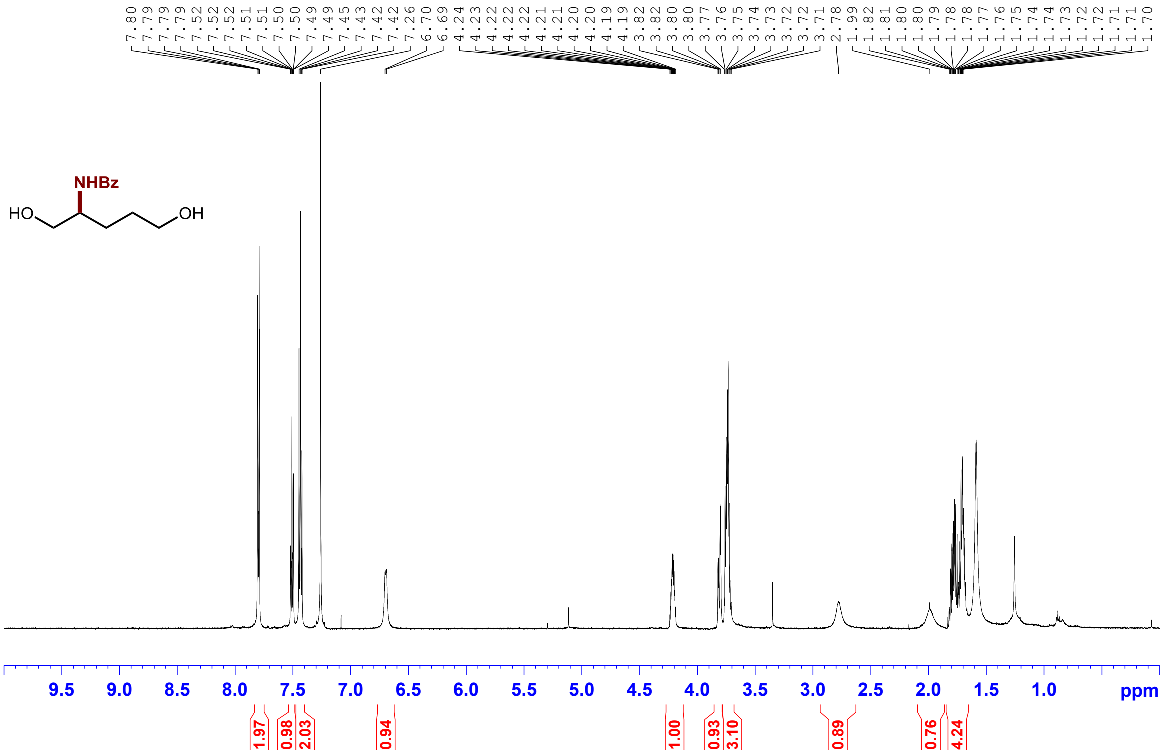
50
40
30
20
ppm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7.50
7.50
7.49
7.49
7.45
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7.42
7.42
7.26
6.70
6.69
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4.23
4.22
4.22
4.22
4.21
4.21
4.20
4.20
4.19
4.19
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3.80
3.80
3.77
3.76
3.75
3.74
3.73
3.72
3.72
3.71
2.78
1.99
1.82
1.81
1.80
1.80
1.79
1.78
1.78
1.77
1.76
1.75
1.74
1.74
1.73
1.72
1.72
1.71
1.71
1.70
NHBz
HO
OH
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9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
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0.98
2.03
0.94
1.00
0.93
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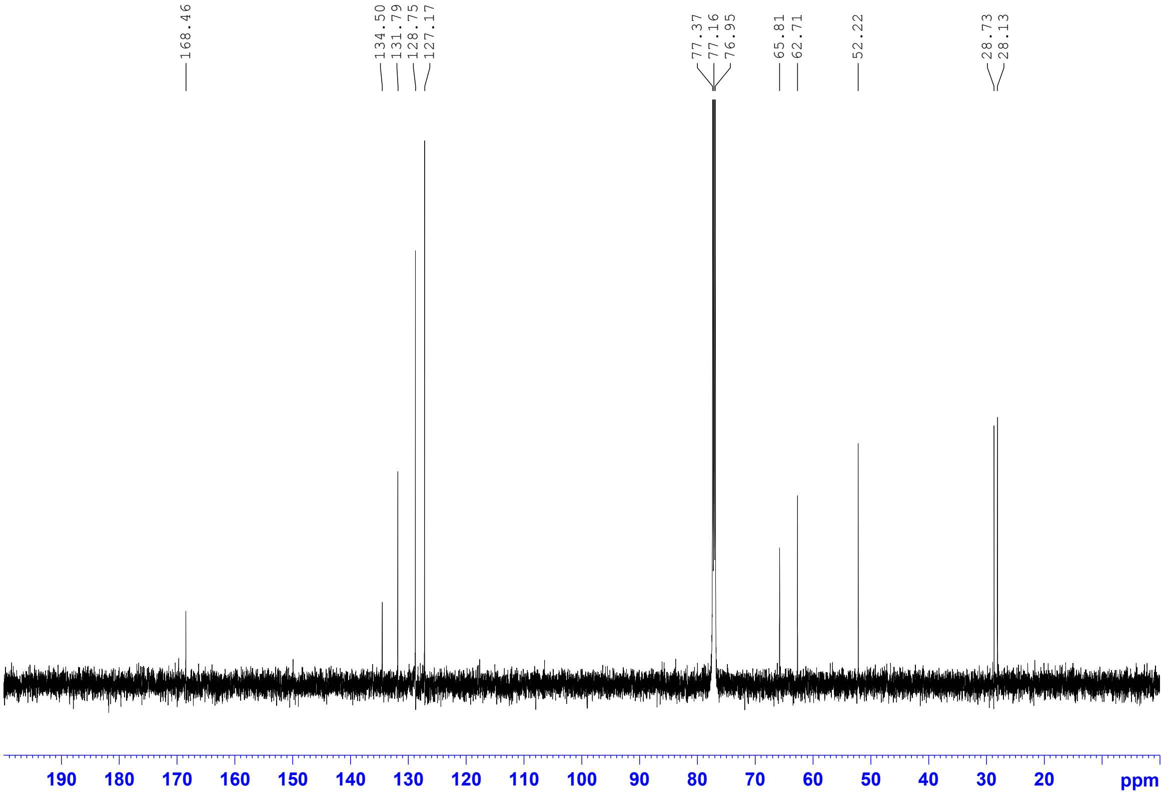
0.76
4.24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77.16
76.95
65.81
62.71
52.22
28.73
28.13
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180
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160
150
140
130
120
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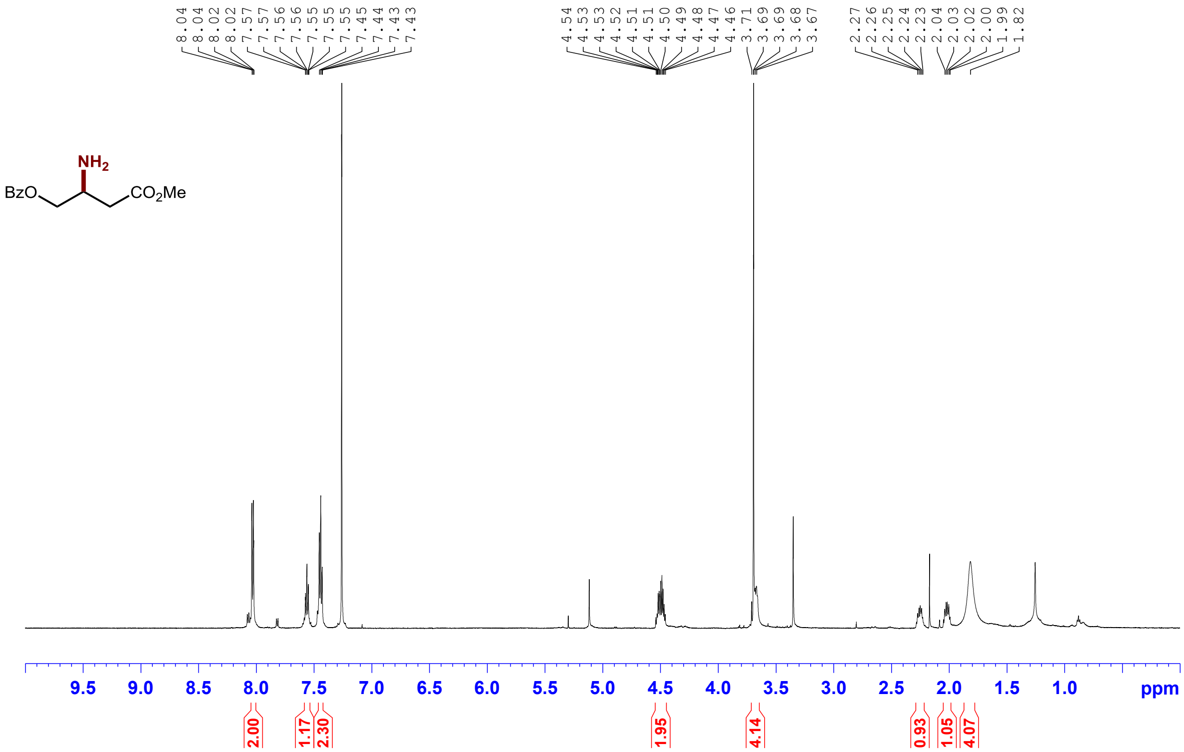
100
90
80
70
60
50
40
30
20
ppm


BzO
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CO2Me
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7.57
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7.55
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7.55
7.45
7.44
7.43
7.43
4.54
4.53
4.53
4.52
4.51
4.51
4.50
4.49
4.48
4.47
4.46
3.71
3.69
3.69
3.68
3.67
2.27
2.26
2.25
2.24
2.23
2.04
2.03
2.02
2.00
1.99
1.82
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
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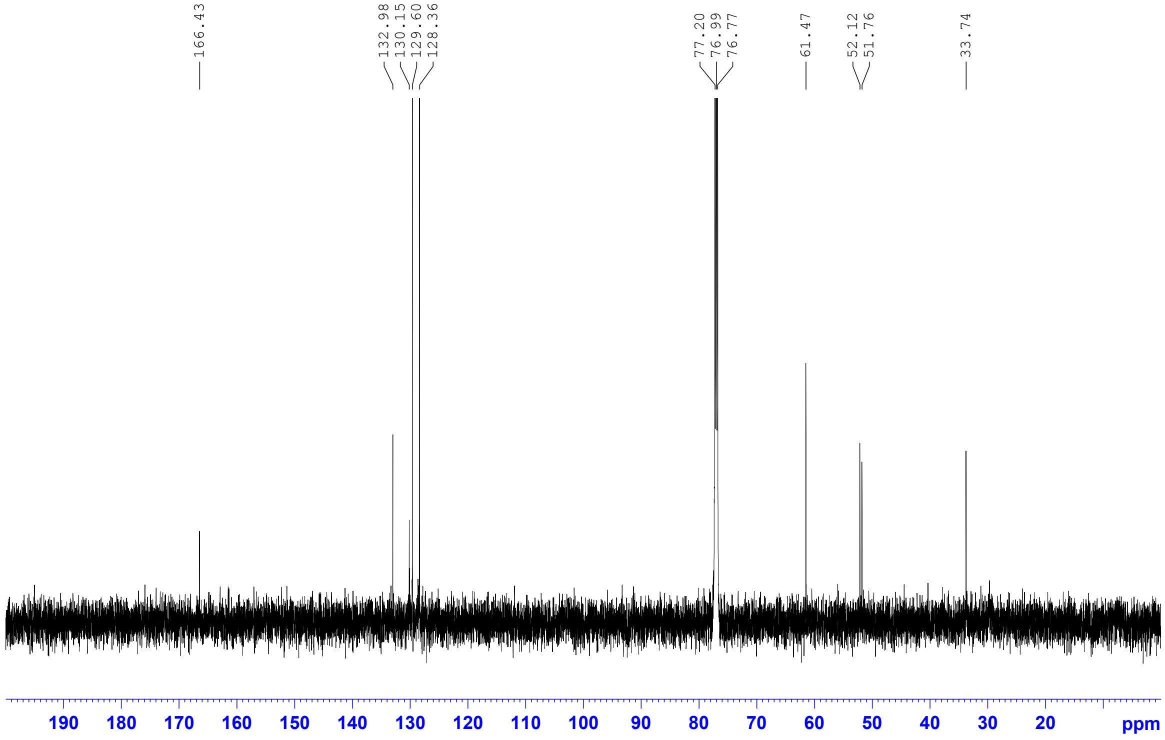
1.05
4.07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76.77
61.47
52.12
51.76
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160
150
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80
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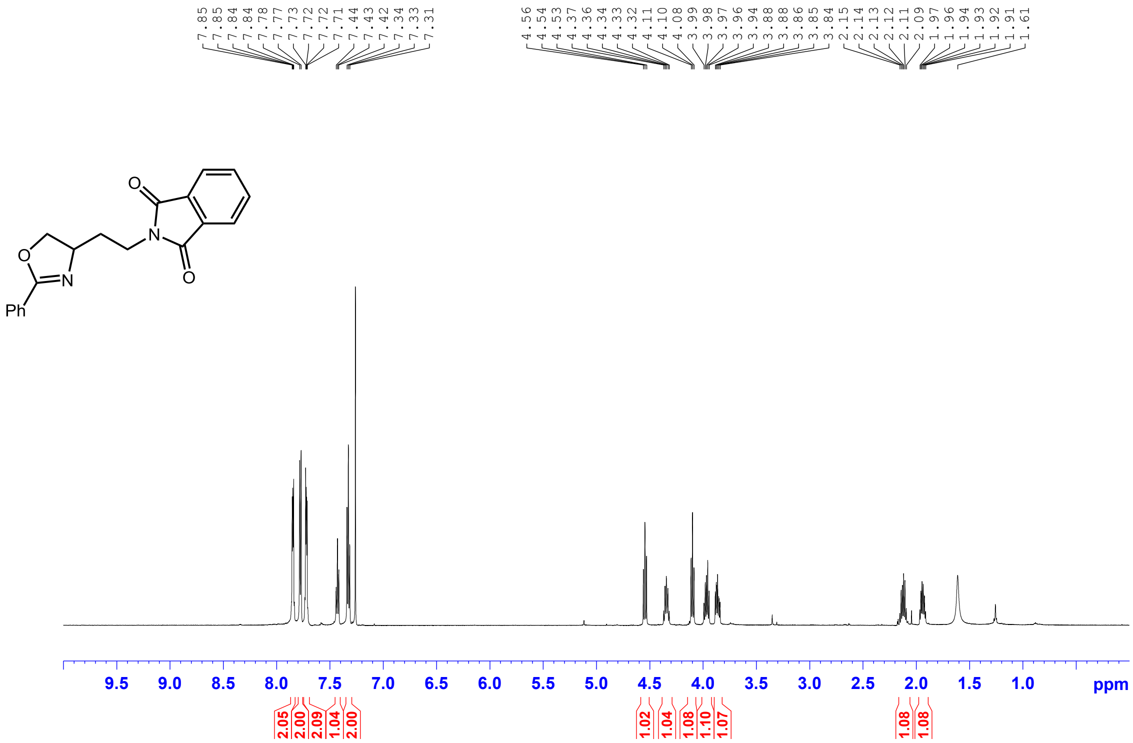
20
ppm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7.71
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7.43
7.42
7.34
7.33
7.31
4.56
4.54
4.53
4.37
4.36
4.34
4.33
4.32
4.11
4.10
4.08
3.99
3.98
3.97
3.96
3.94
3.88
3.88
3.86
3.85
3.84
2.15
2.14
2.13
2.12
2.11
2.09
1.97
1.96
1.94
1.93
1.92
1.91
1.61
O
O
O
N
N
Ph
9.5
9.0
8.5
8.0
7.5
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
ppm
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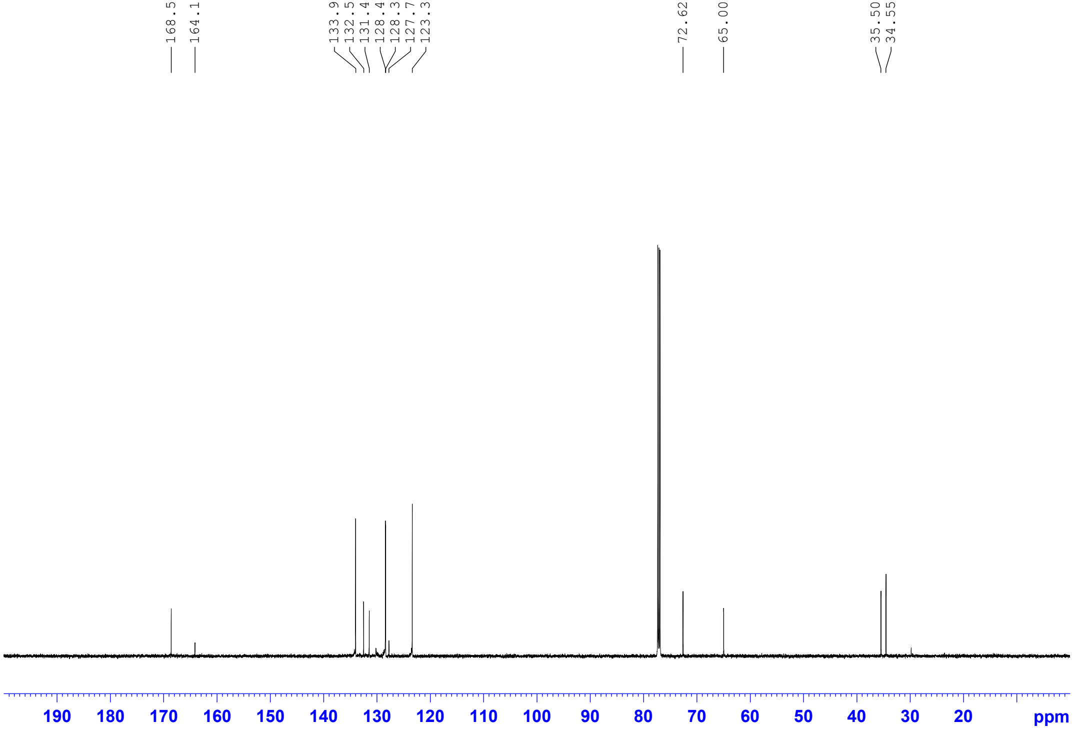
2.00
2.09
1.04
2.00
1.02
1.04
1.08
1.10
1.07
1.08
1.08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128.42
128.35
127.75
123.38
72.62
65.00
35.50
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190
180
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160
150
140
130
120
110
100
90
80
70
60
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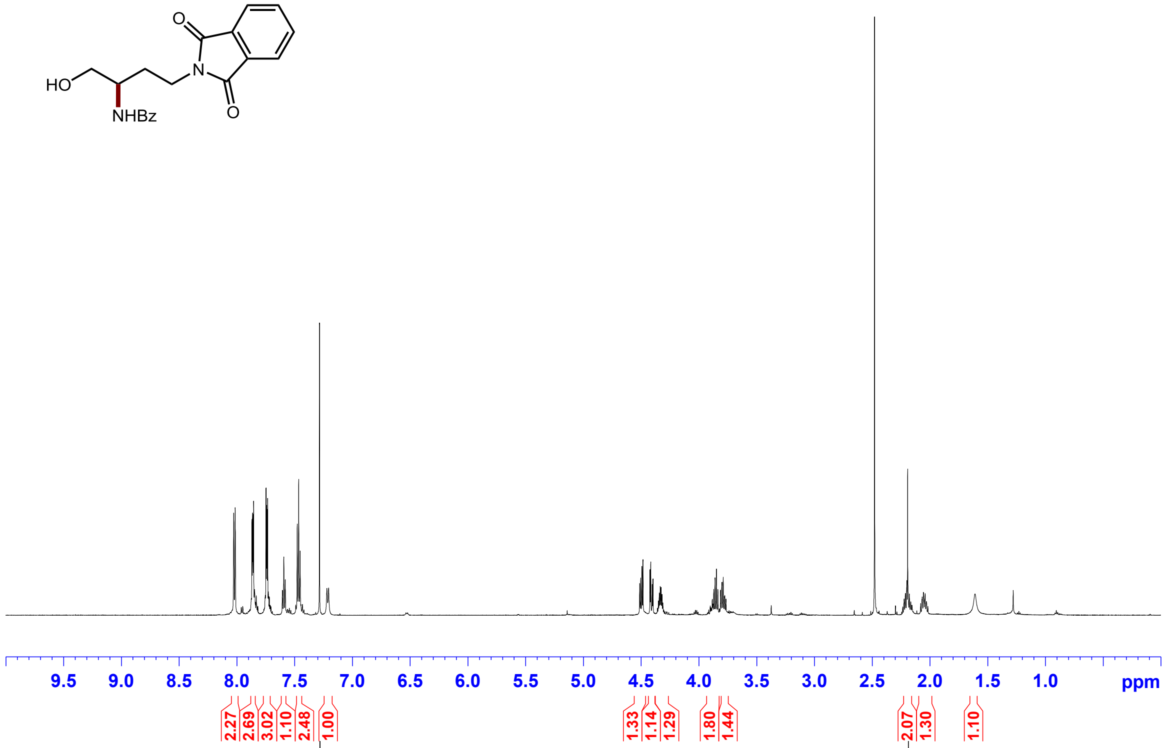
40
30
20
ppm


O
HO
N
NHBz
O
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7.5
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
ppm
2.27
2.69
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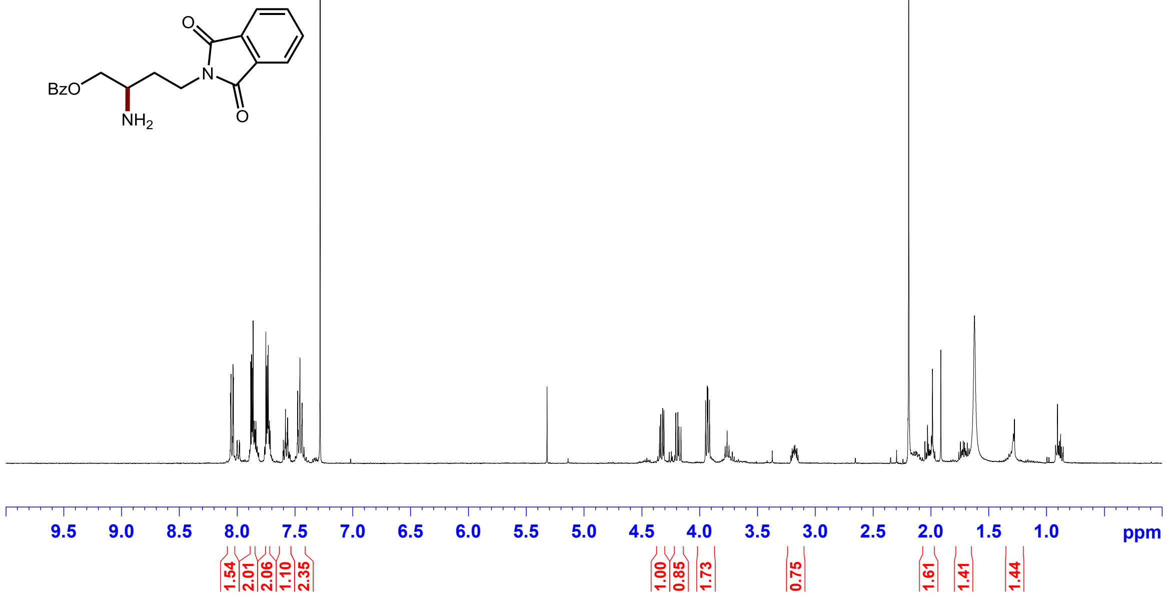
1.00
1.33
1.14
1.29
1.80
1.44
2.07
1.30
1.10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BzO
N
NH2
O
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7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
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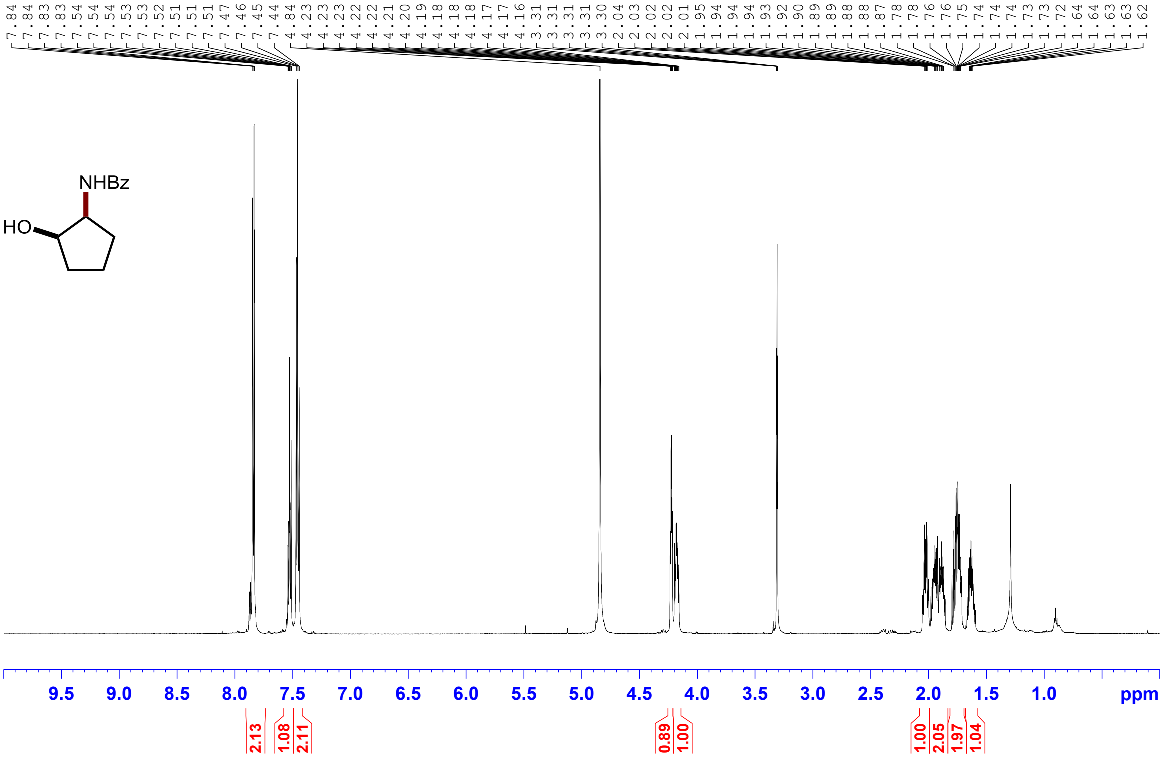
1.41
1.44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7.51
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7.45
7.44
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4.23
4.23
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4.22
4.21
4.20
4.19
4.18
4.18
4.18
4.17
4.17
4.16
3.31
3.31
3.31
3.31
3.30
2.04
2.03
2.02
2.02
2.01
1.95
1.94
1.94
1.94
1.93
1.92
1.90
1.89
1.89
1.88
1.88
1.87
1.78
1.78
1.76
1.76
1.75
1.74
1.74
1.74
1.73
1.73
1.72
1.64
1.64
1.63
1.63
1.62
NHBz
HO
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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ppm
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0.89
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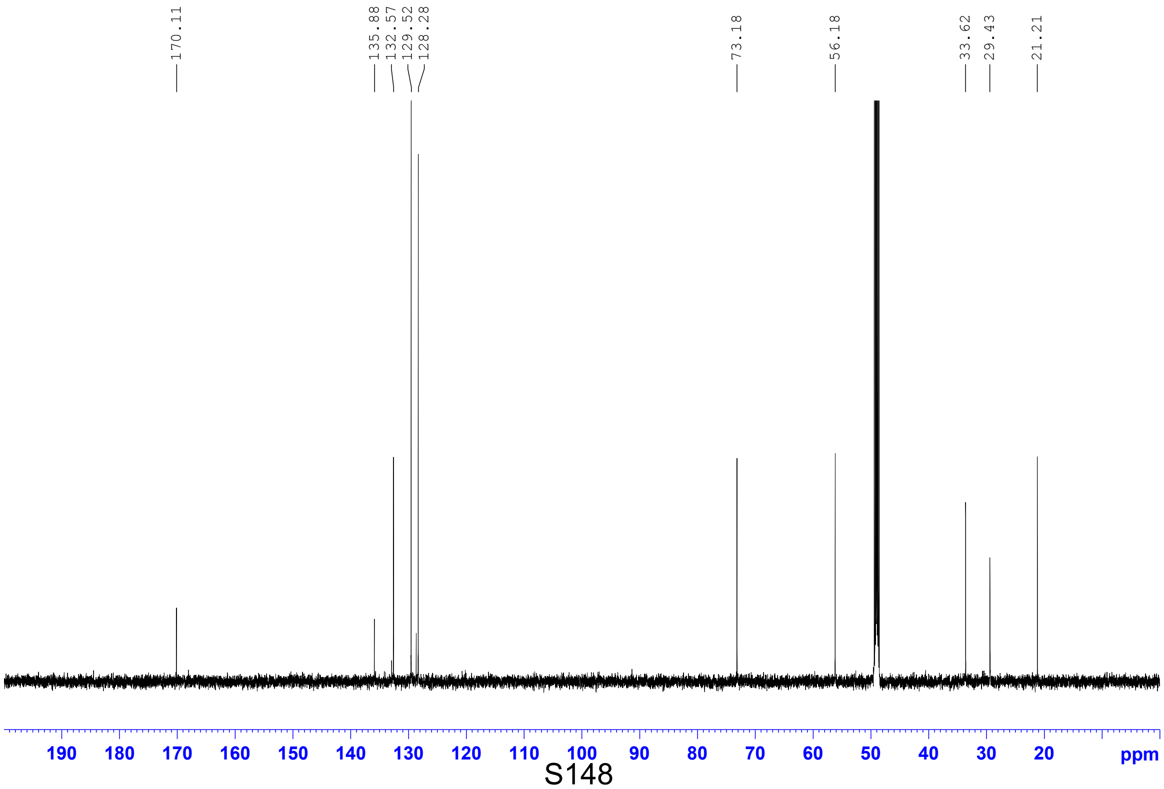
1.04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73.18
56.18
33.62
29.43
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160
150
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120
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80
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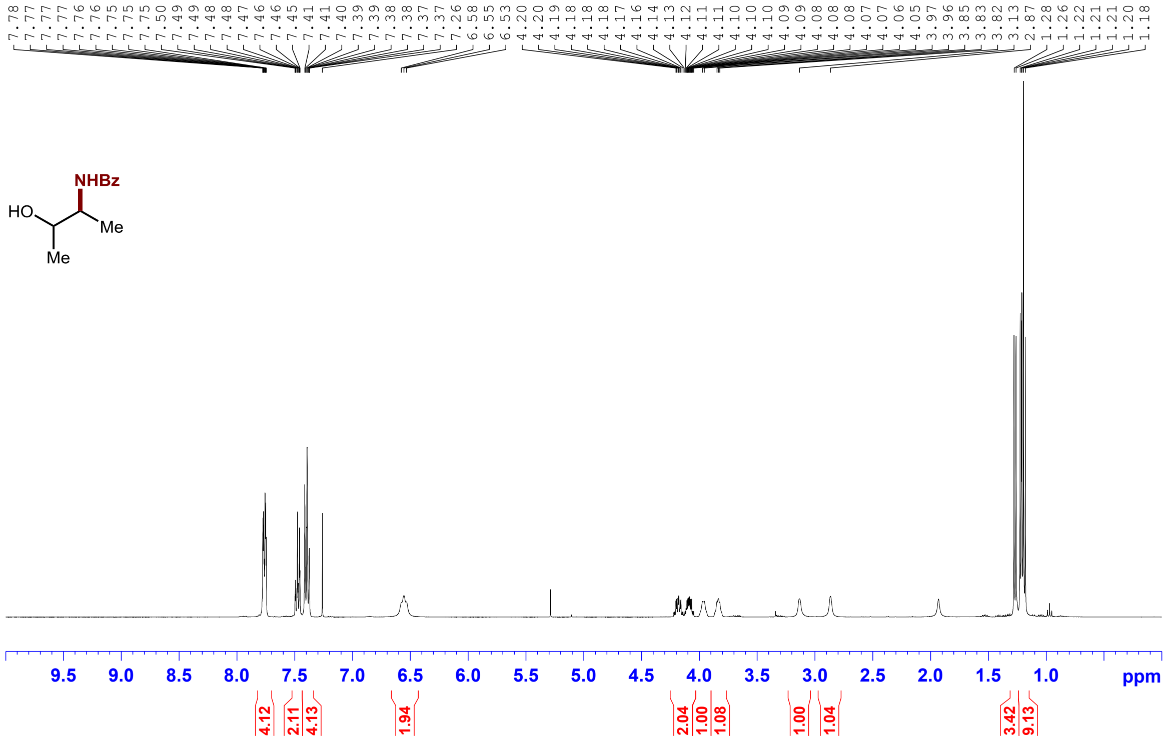
40
30
20
ppm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7.77
7.77
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7.48
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7.47
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7.46
7.45
7.41
7.41
7.40
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7.38
7.37
7.37
7.26
6.58
6.55
6.53
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4.18
4.18
4.18
4.17
4.16
4.14
4.13
4.12
4.11
4.11
4.10
4.10
4.10
4.09
4.09
4.08
4.08
4.08
4.07
4.07
4.06
4.05
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3.96
3.85
3.83
3.82
3.13
2.87
1.28
1.26
1.22
1.21
1.21
1.20
1.18
NHBz
HO
Me
Me
9.5
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8.5
8.0
7.5
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
ppm
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4.13
1.94
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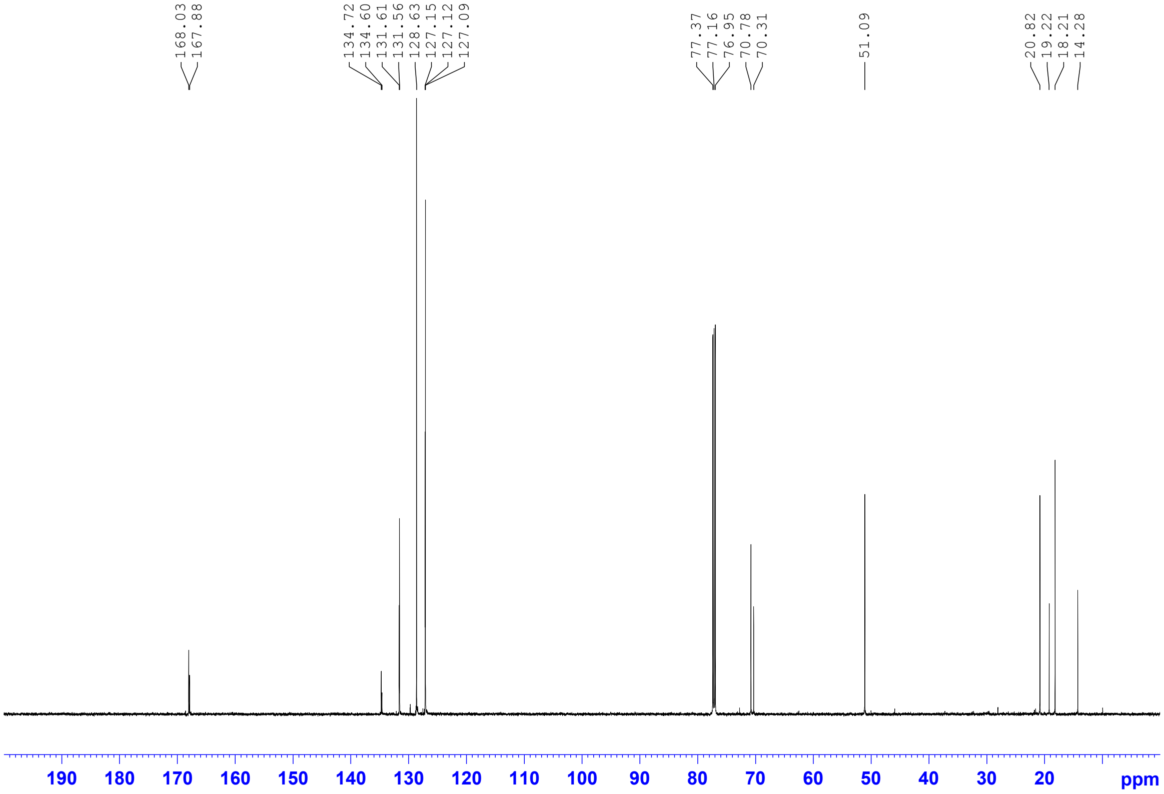
1.00
1.08
1.00
1.04
3.42
9.13


168.03
167.88
134.72
134.60
131.61
131.56
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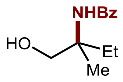
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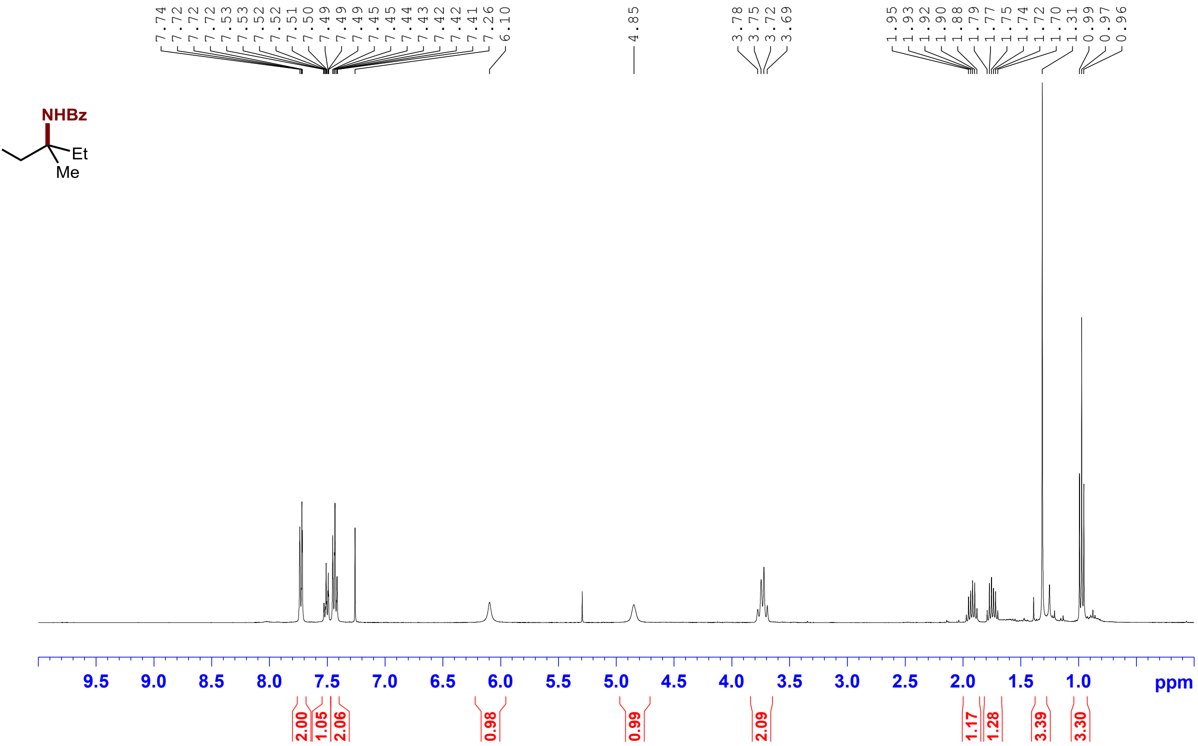
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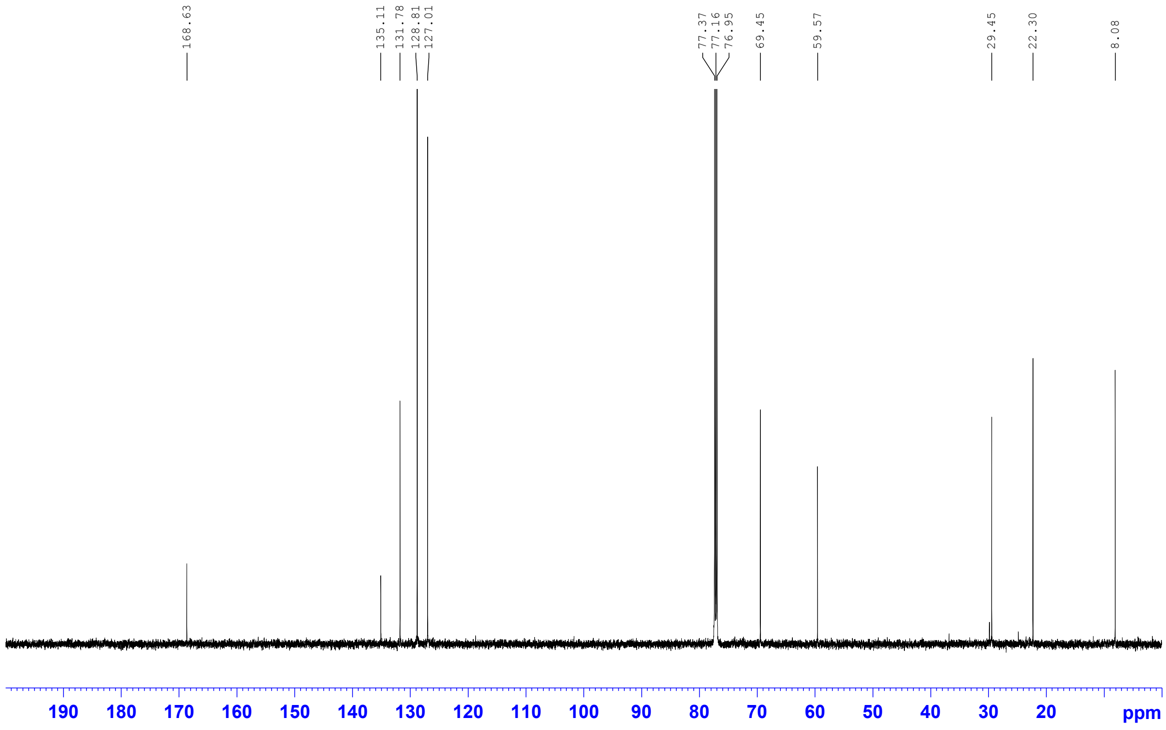
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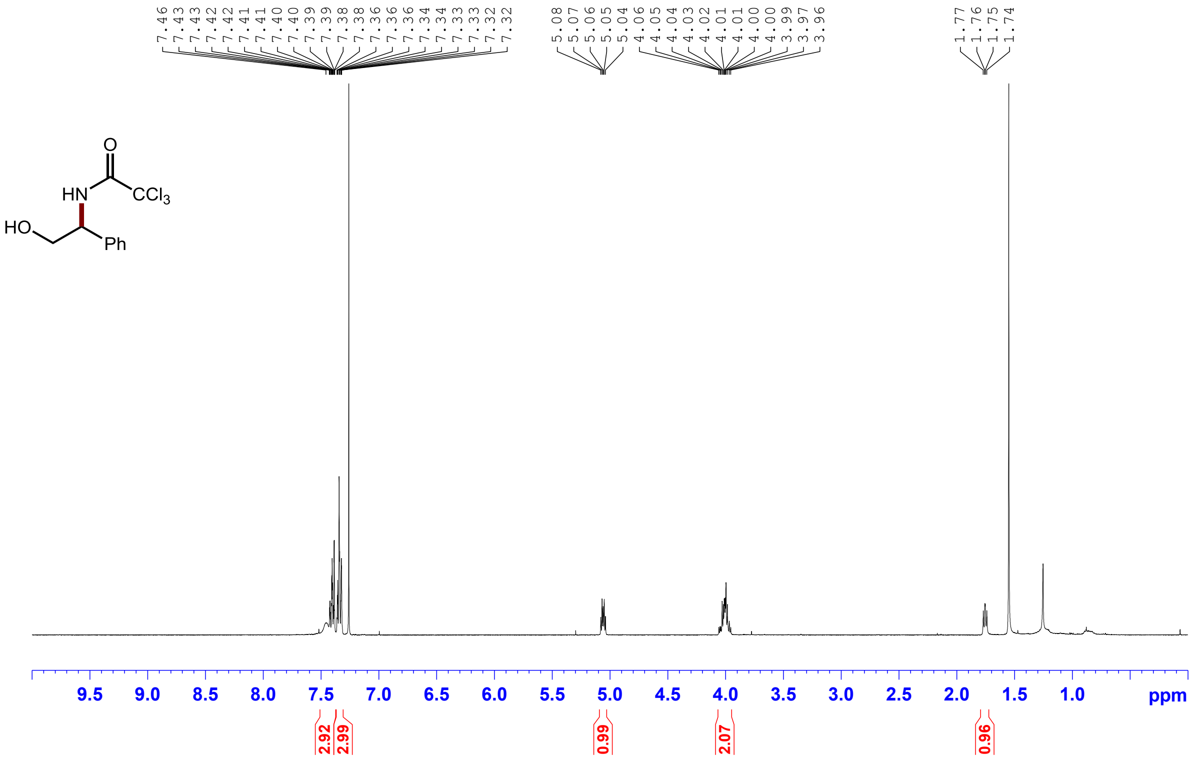
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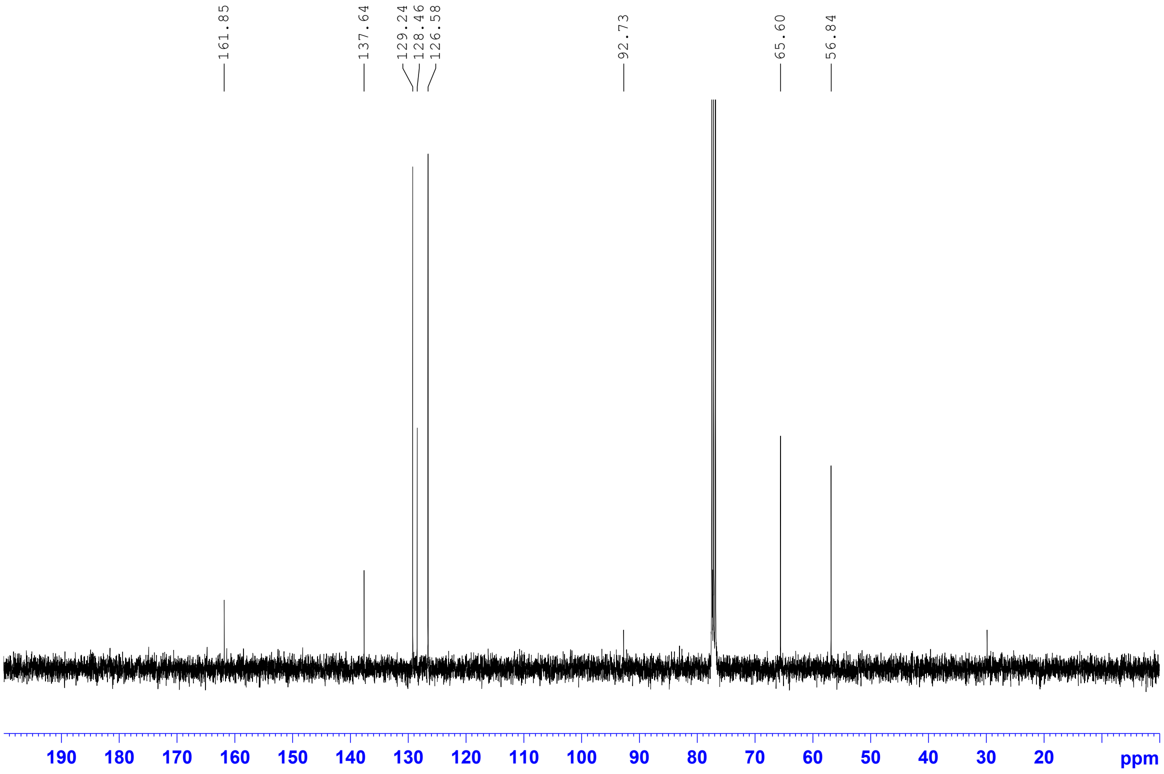
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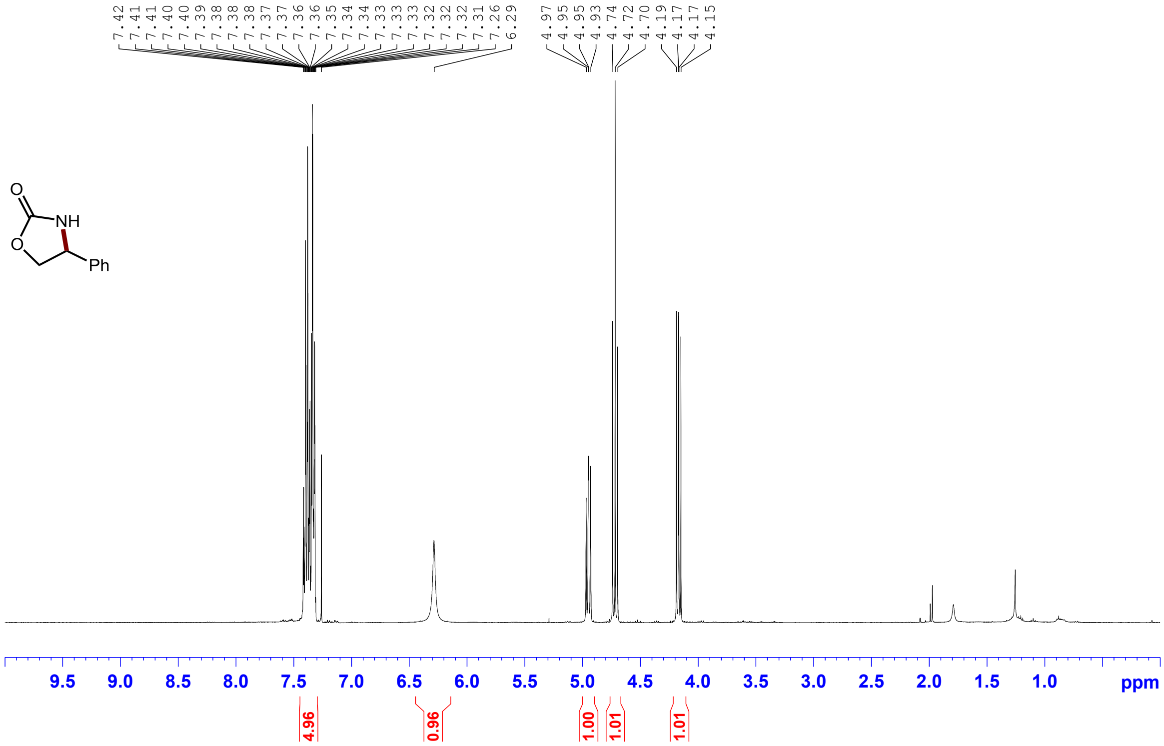

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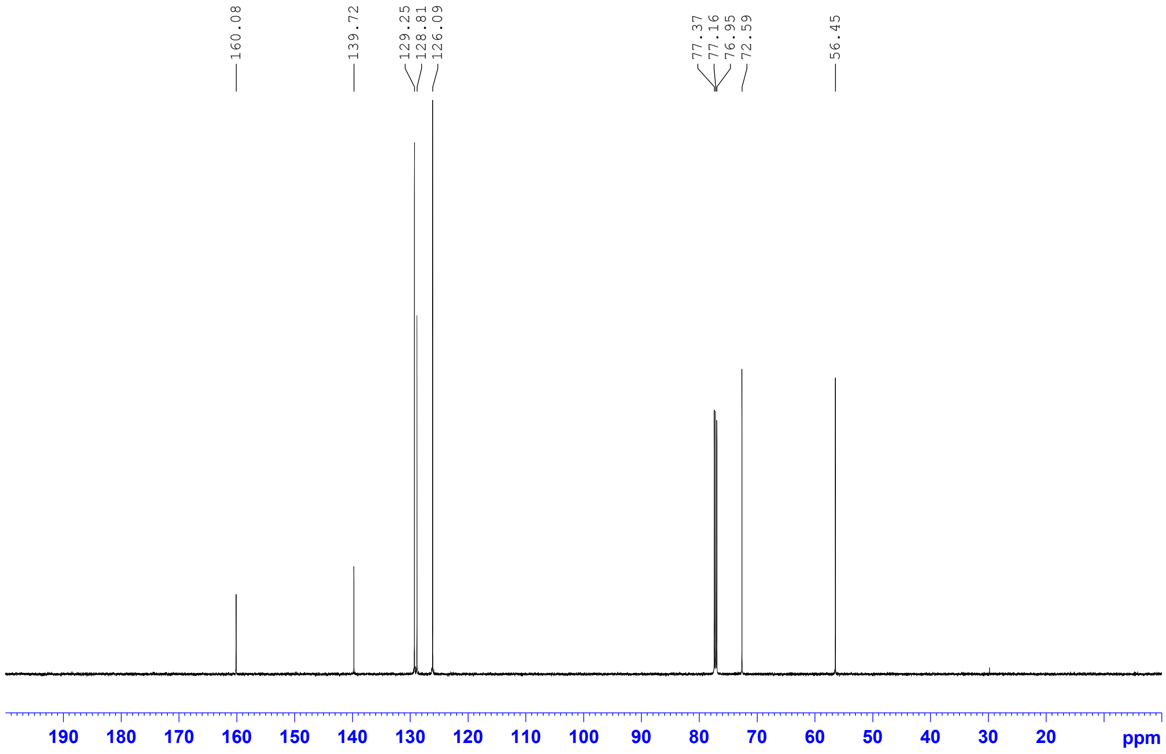

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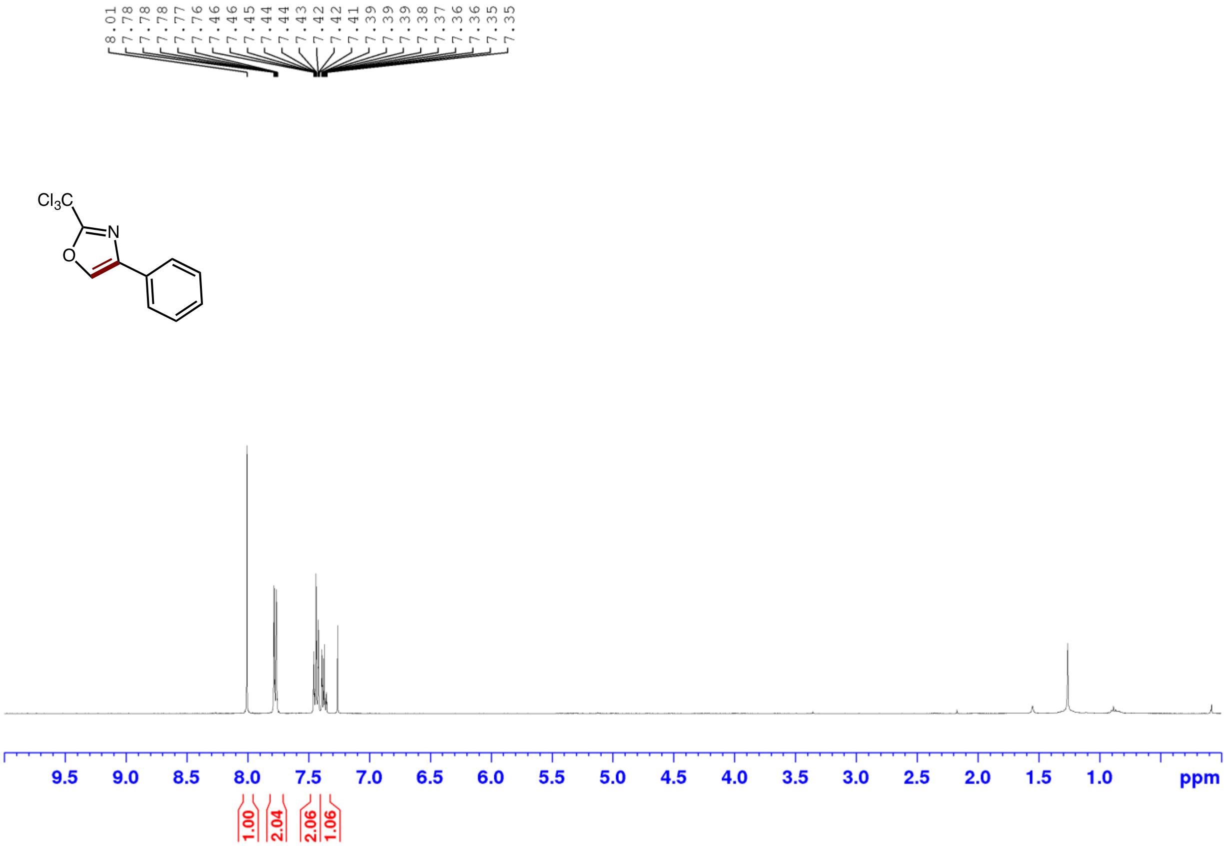
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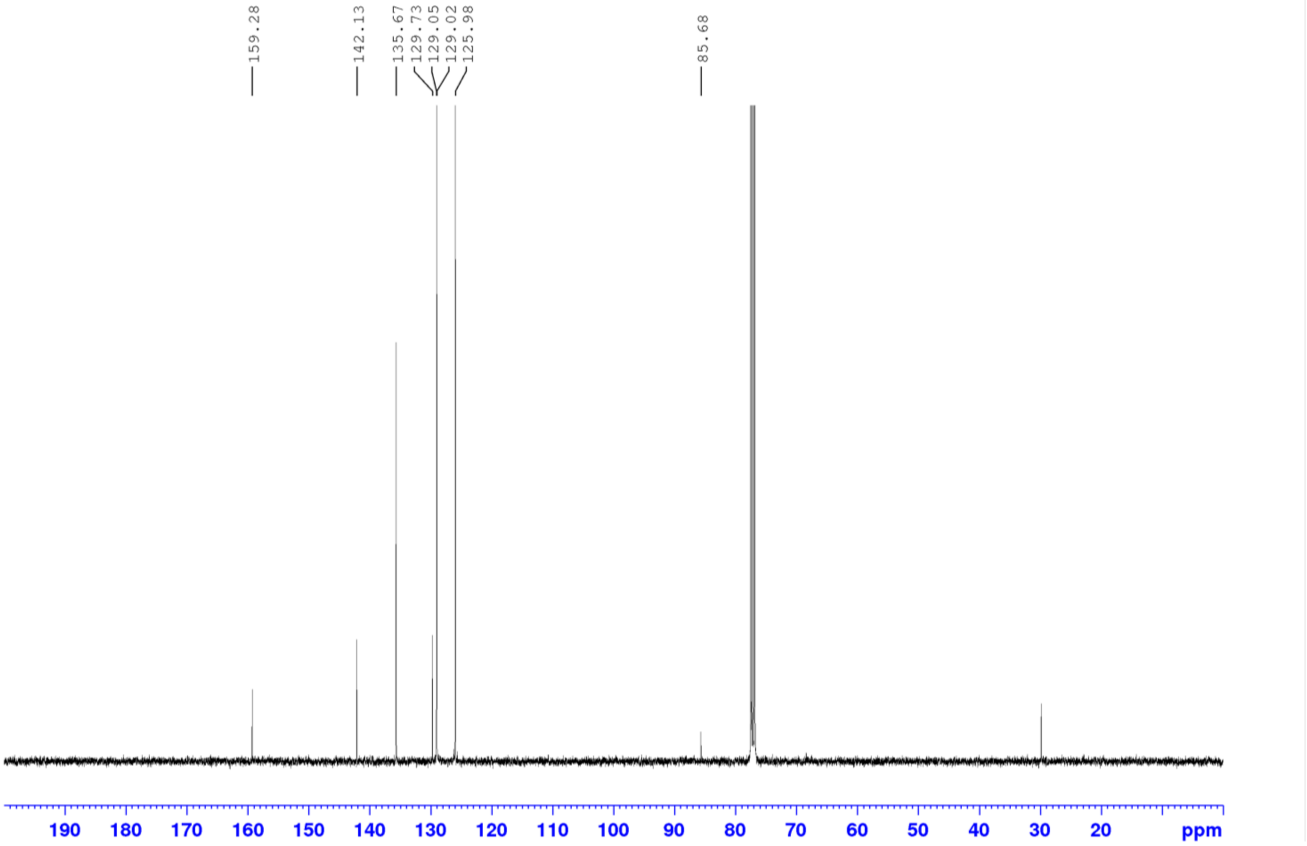
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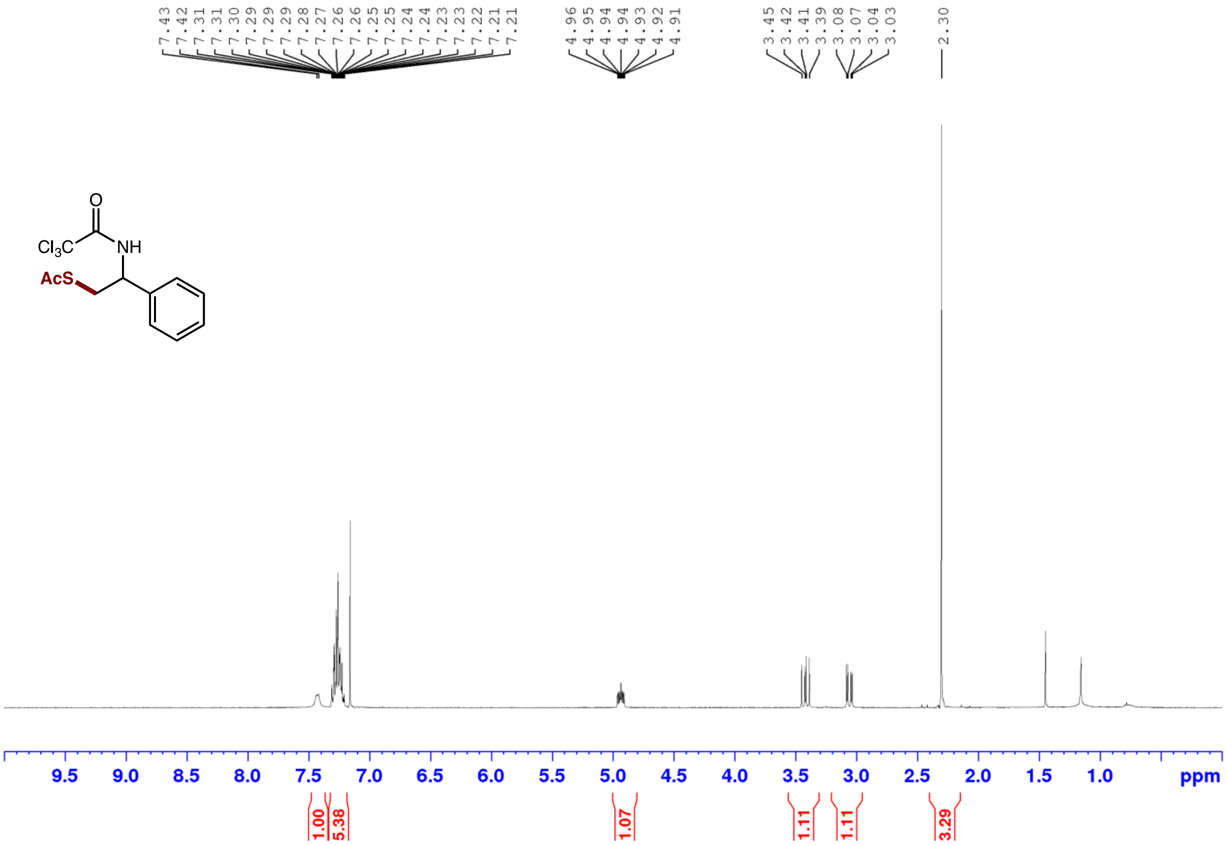
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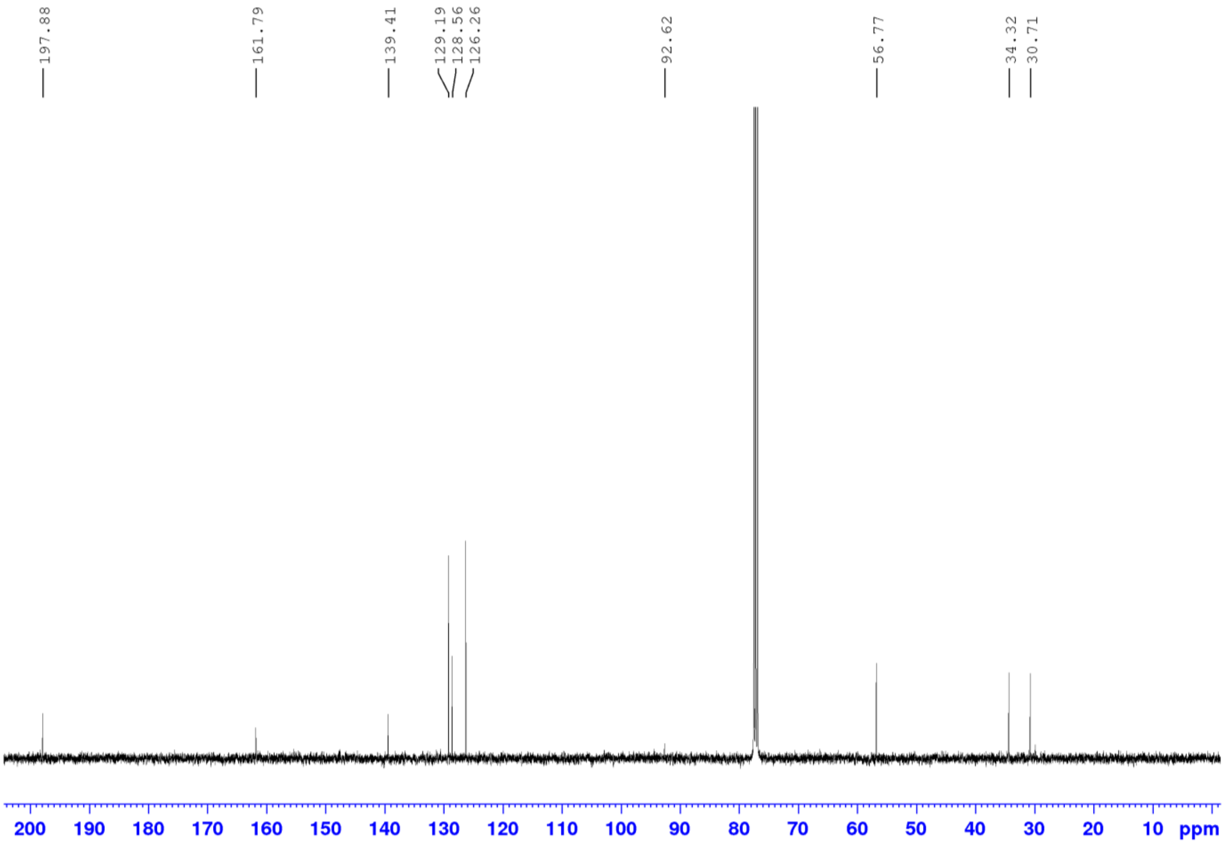
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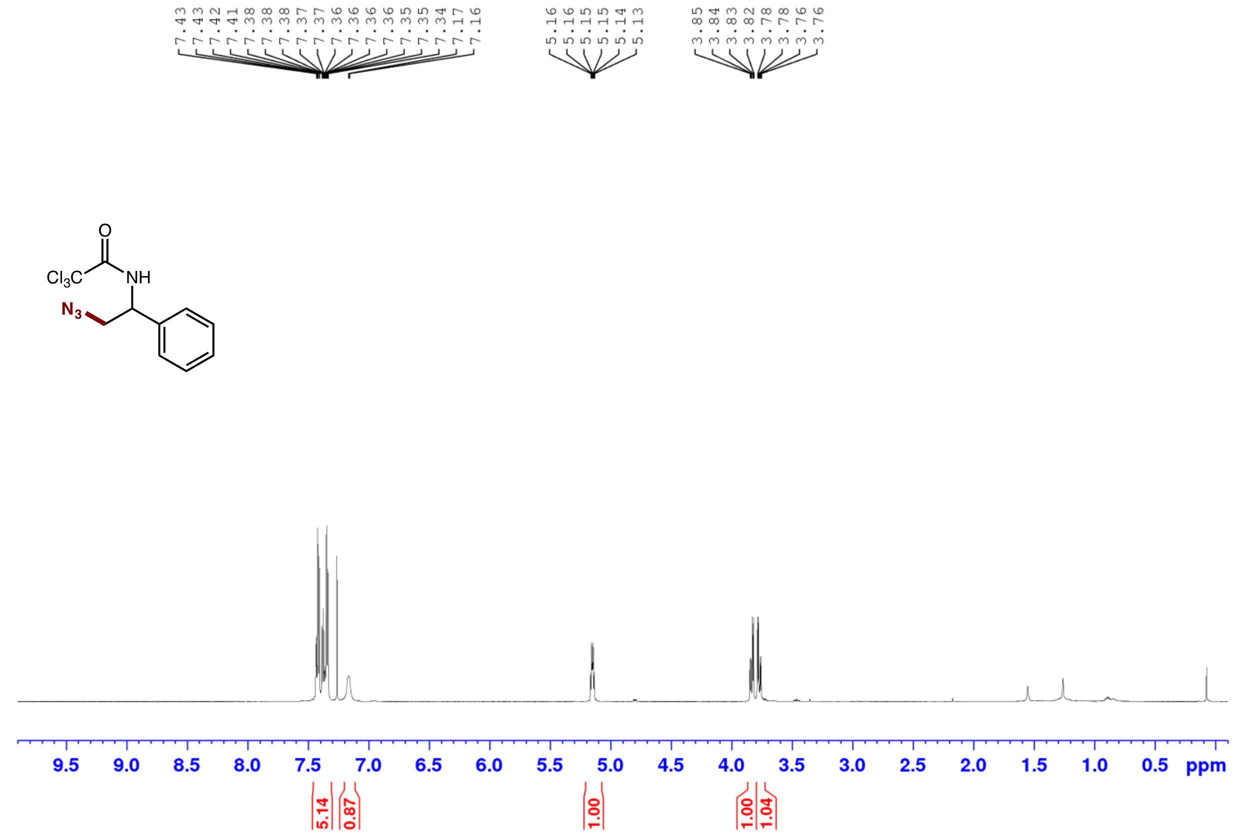
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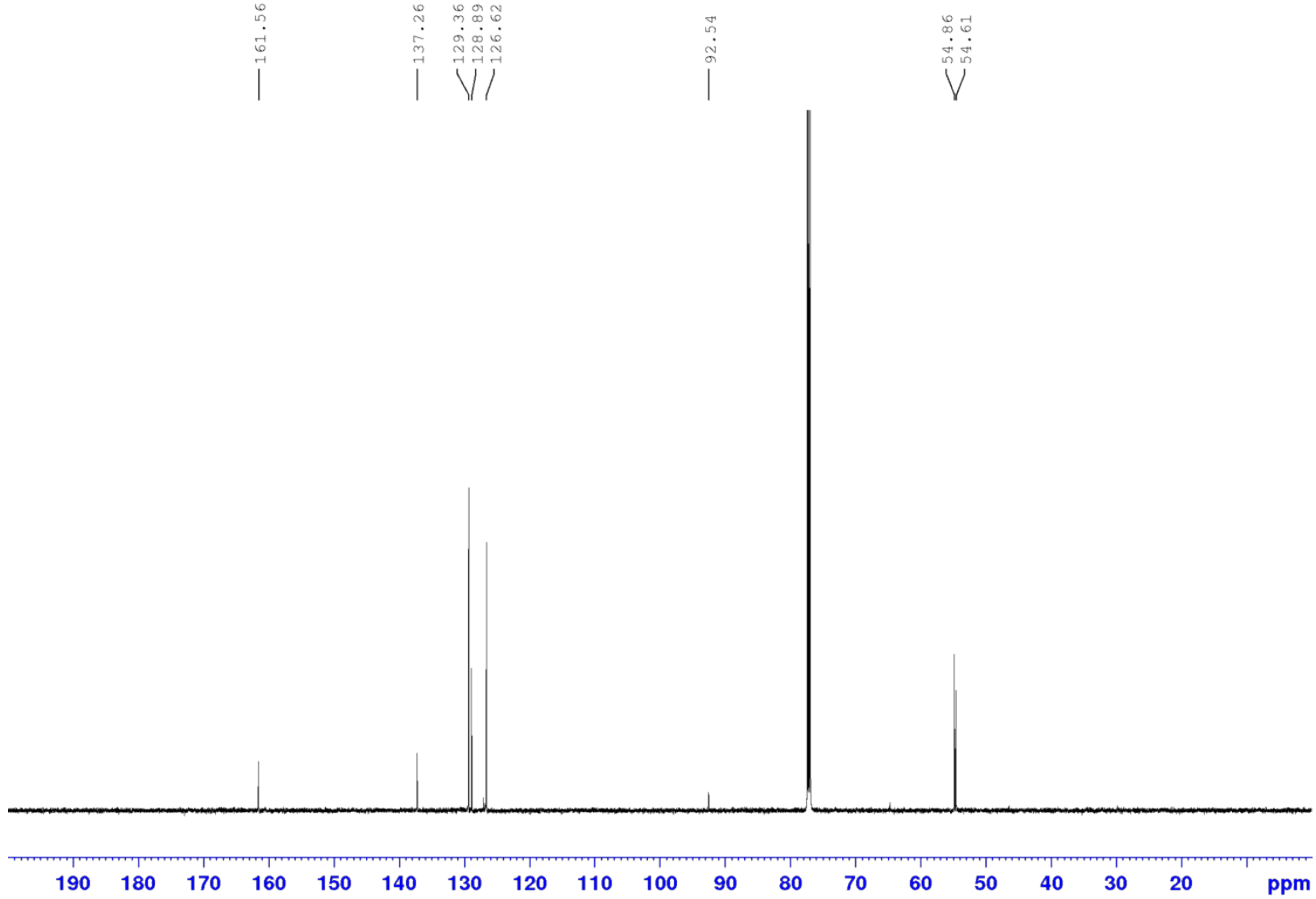
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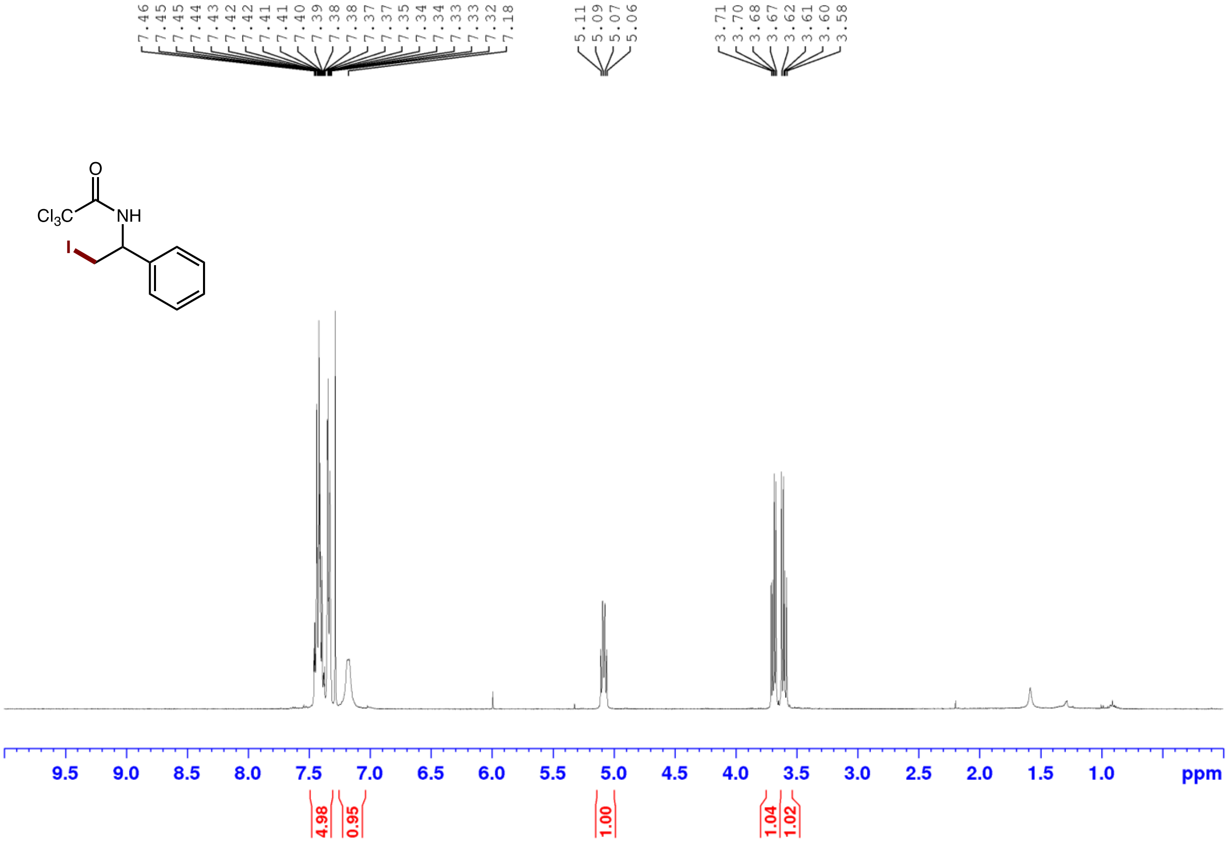

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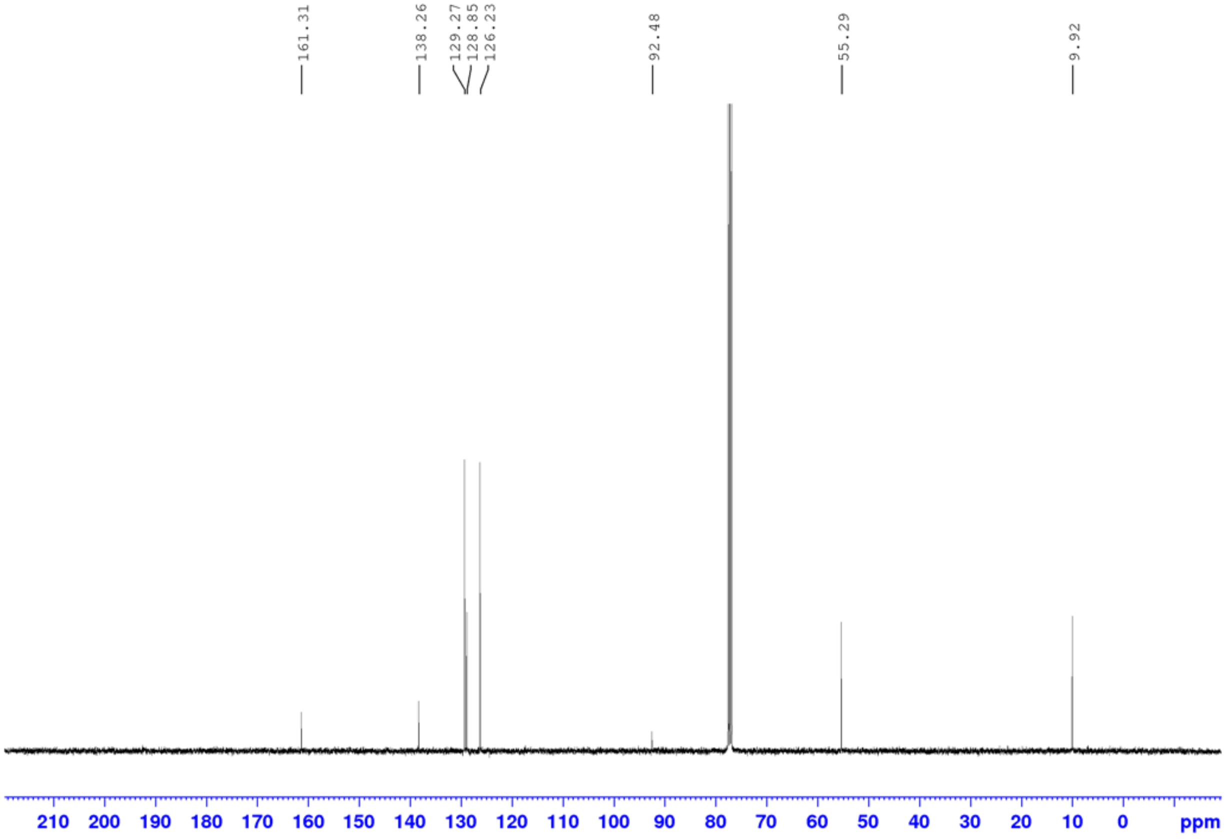

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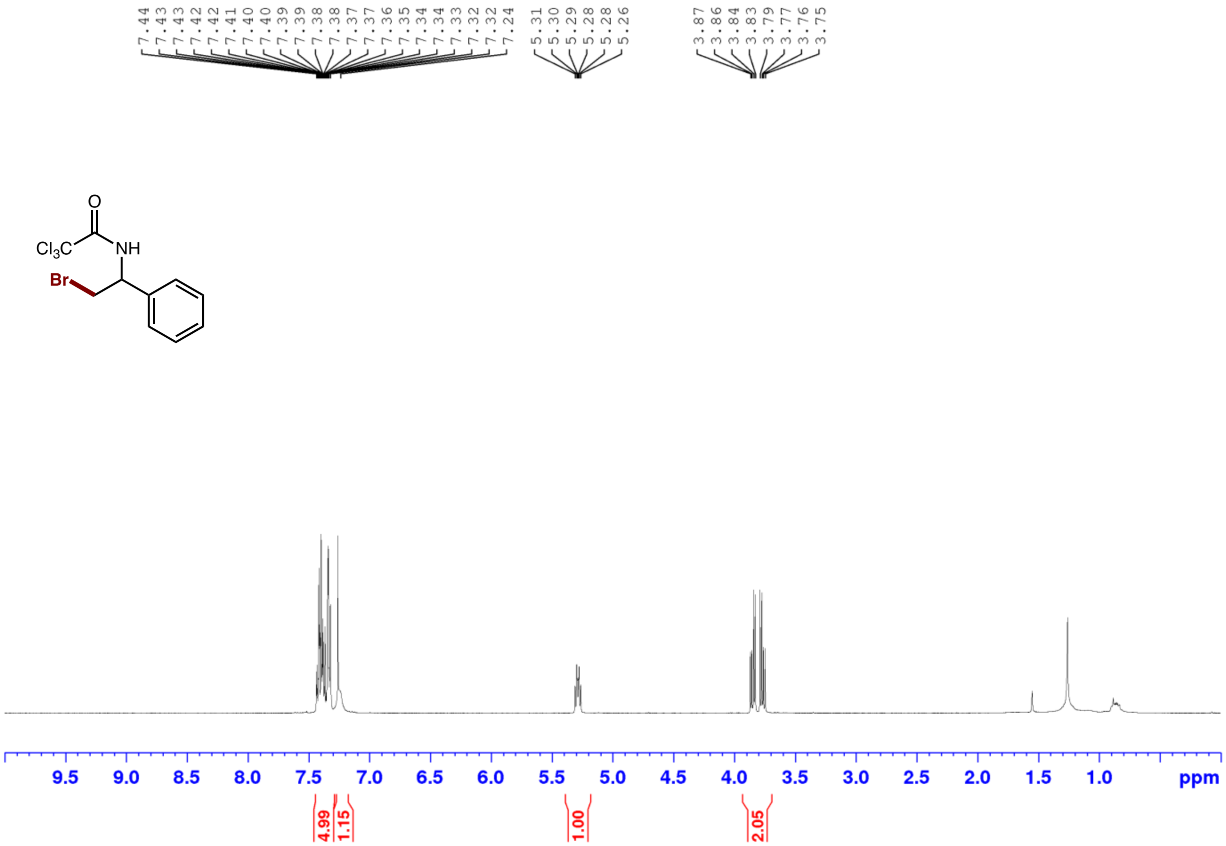
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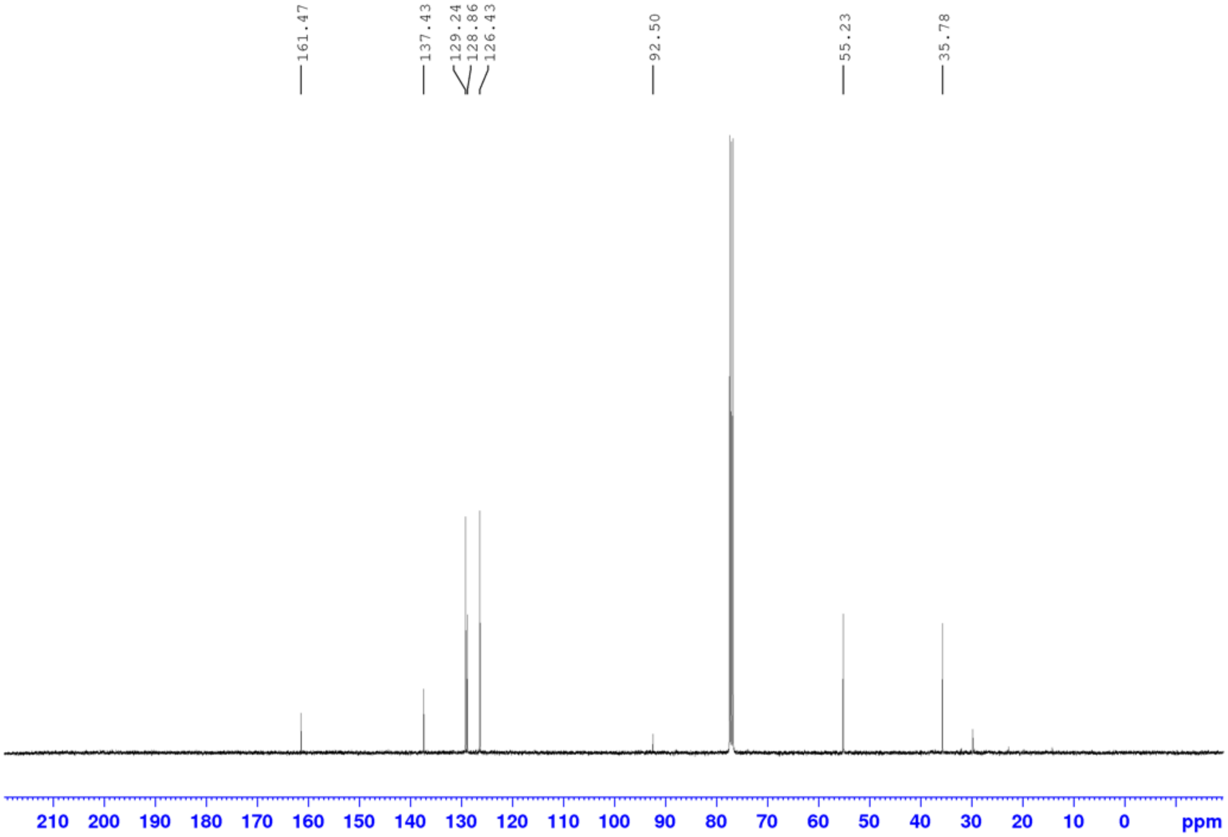
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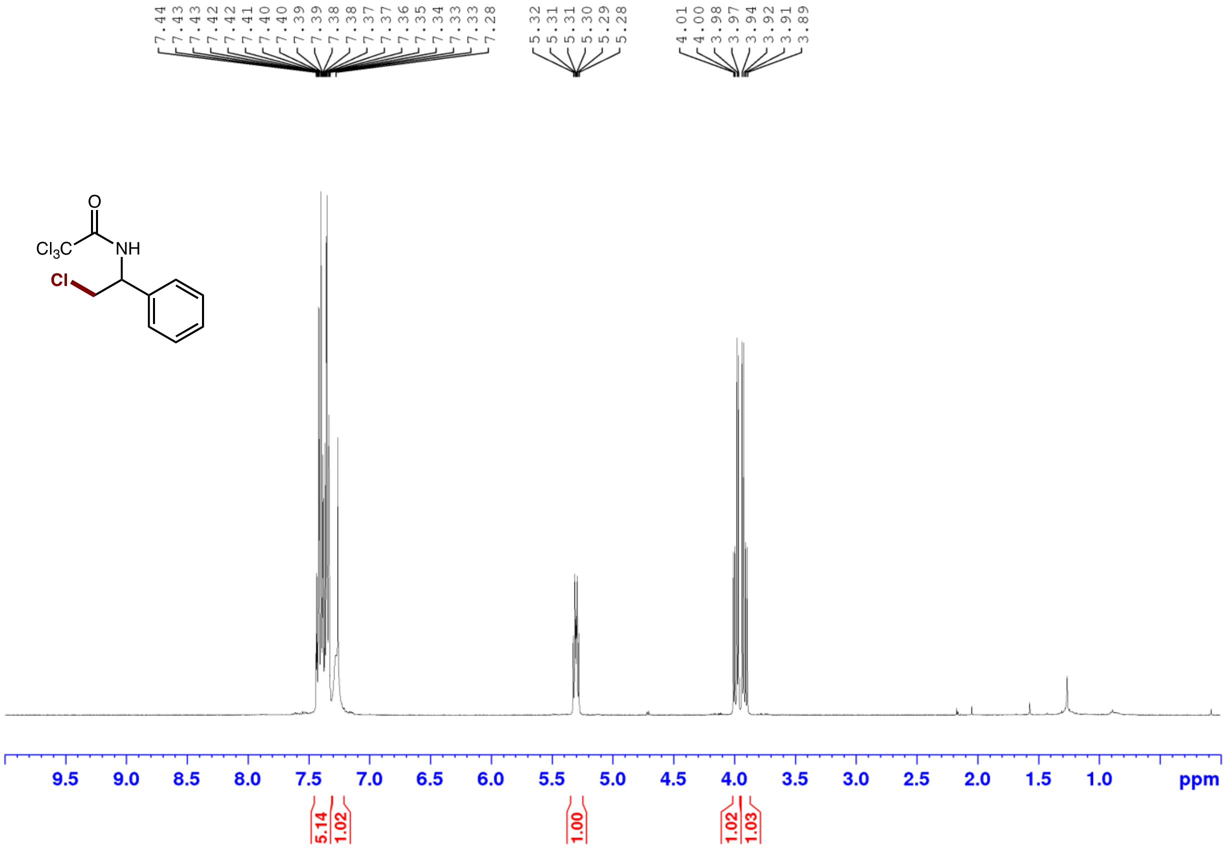
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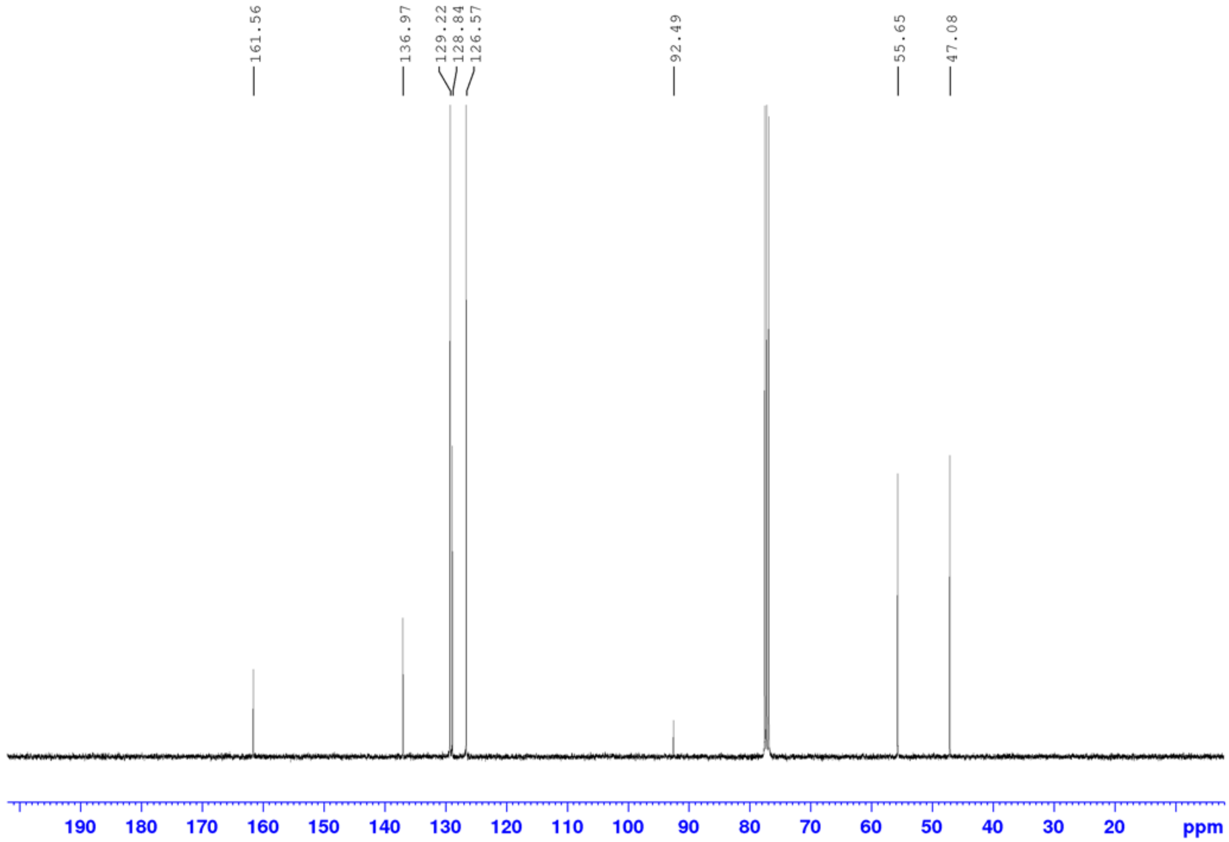
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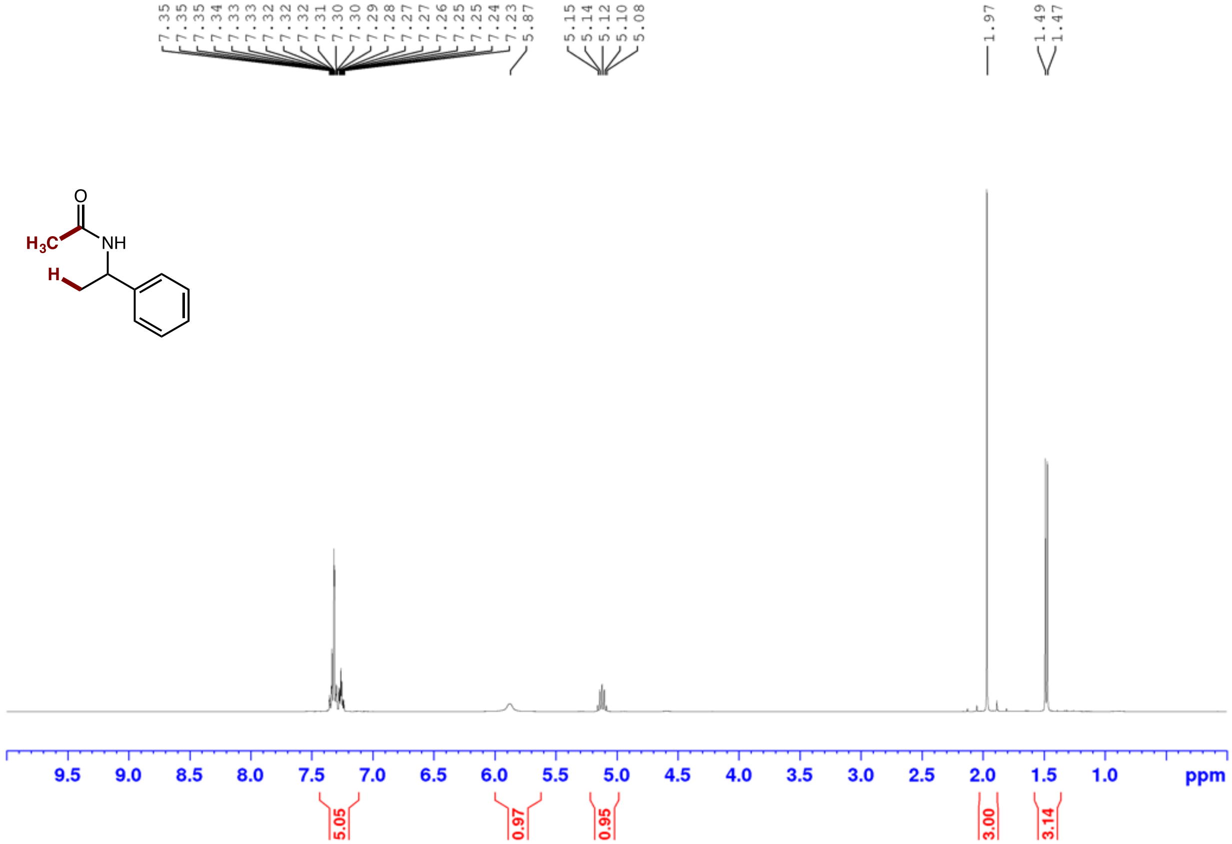
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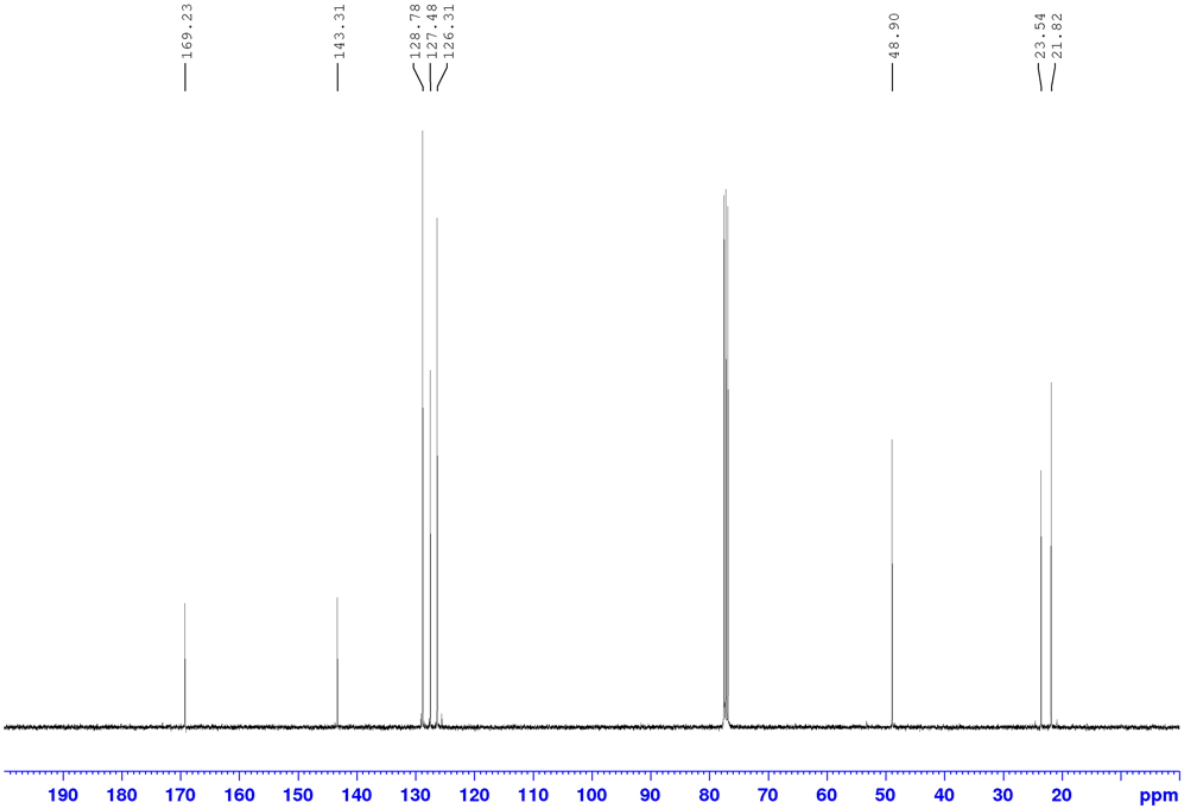
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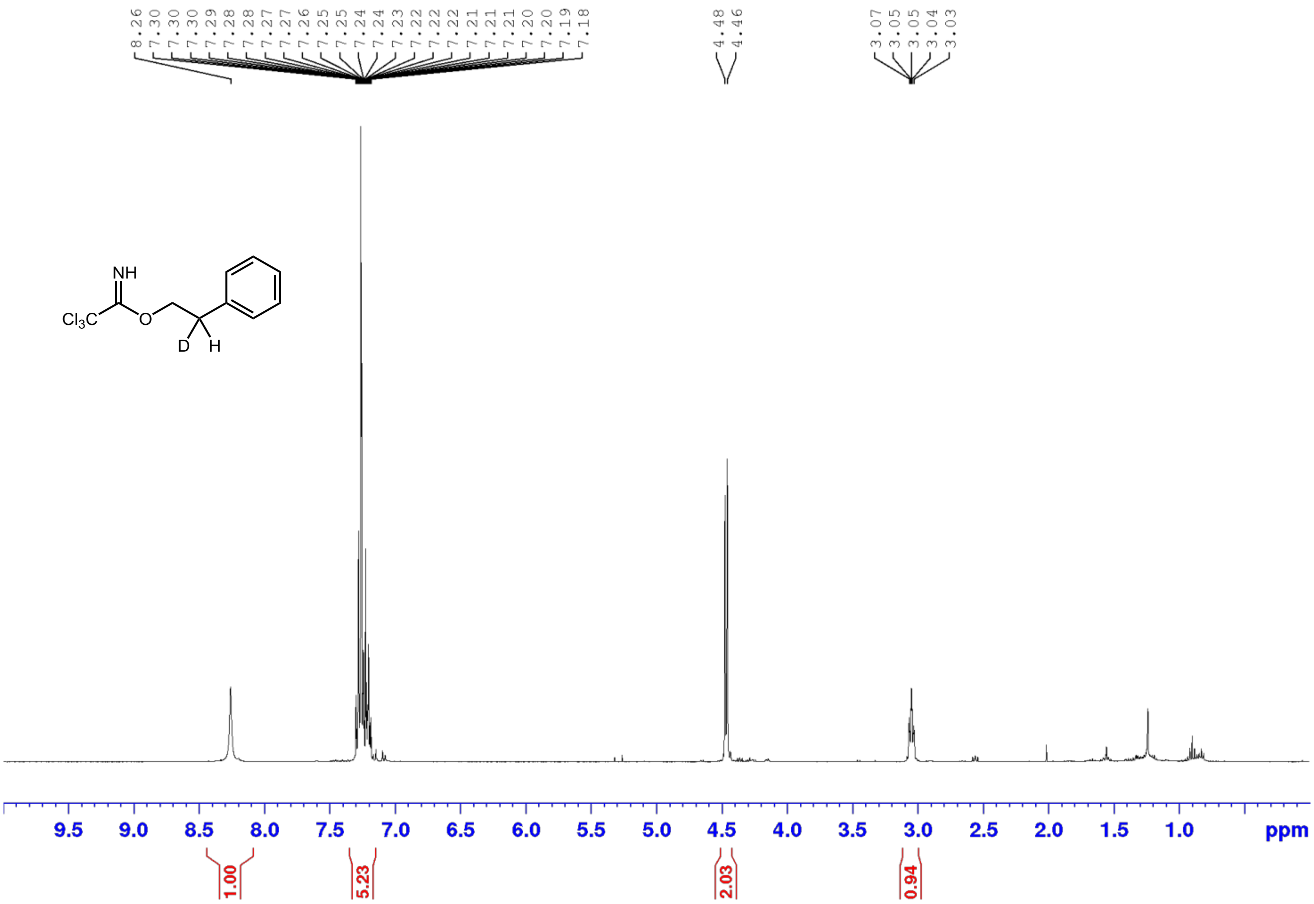
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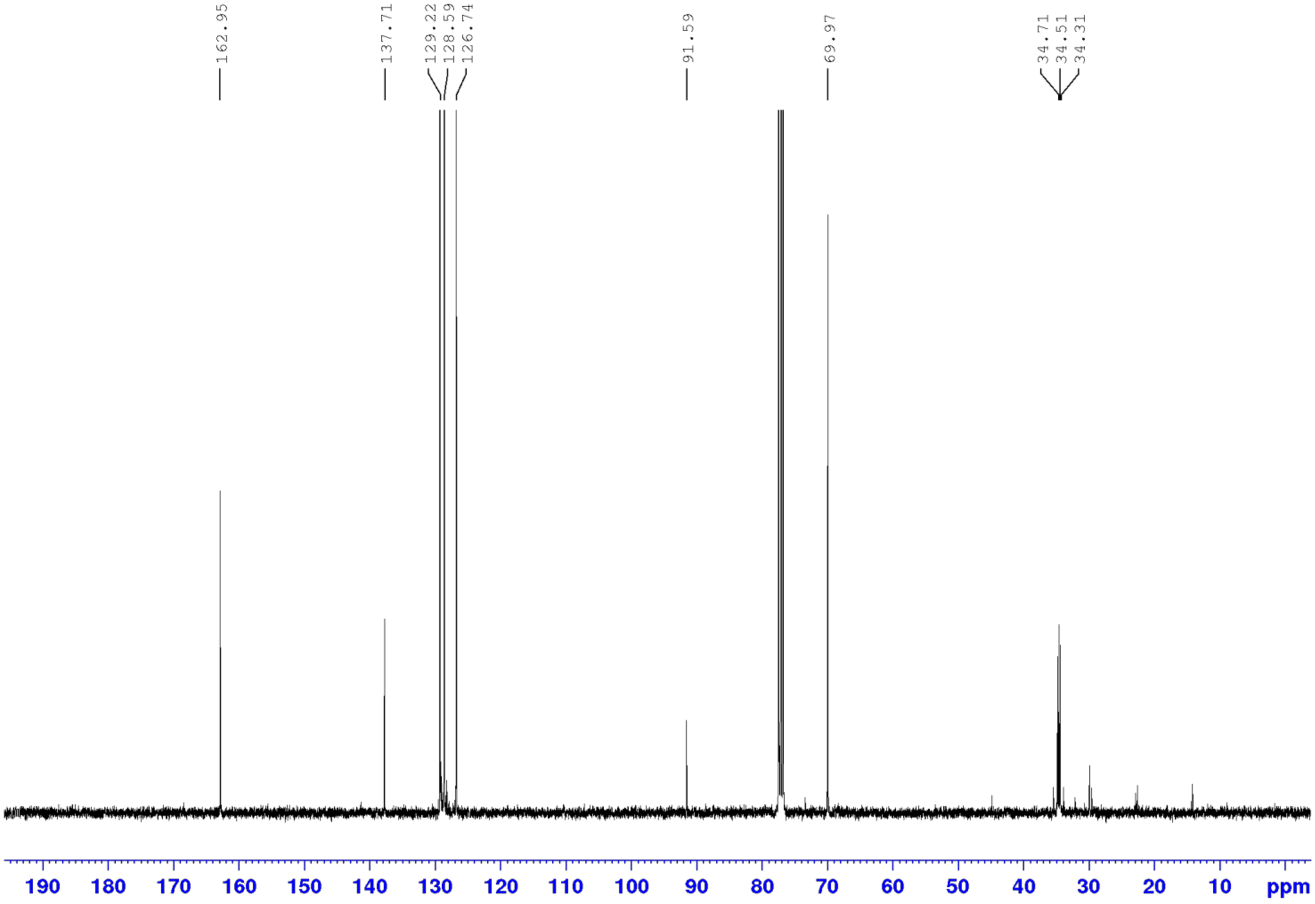
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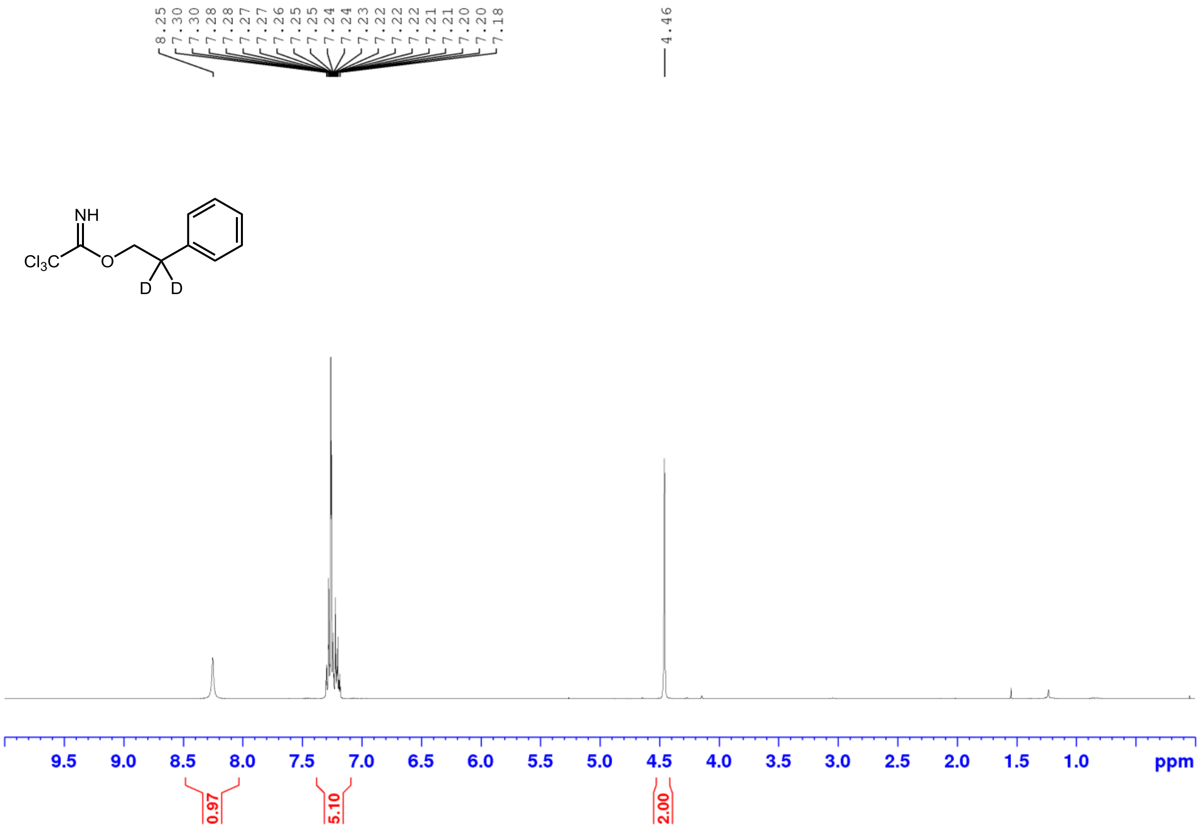
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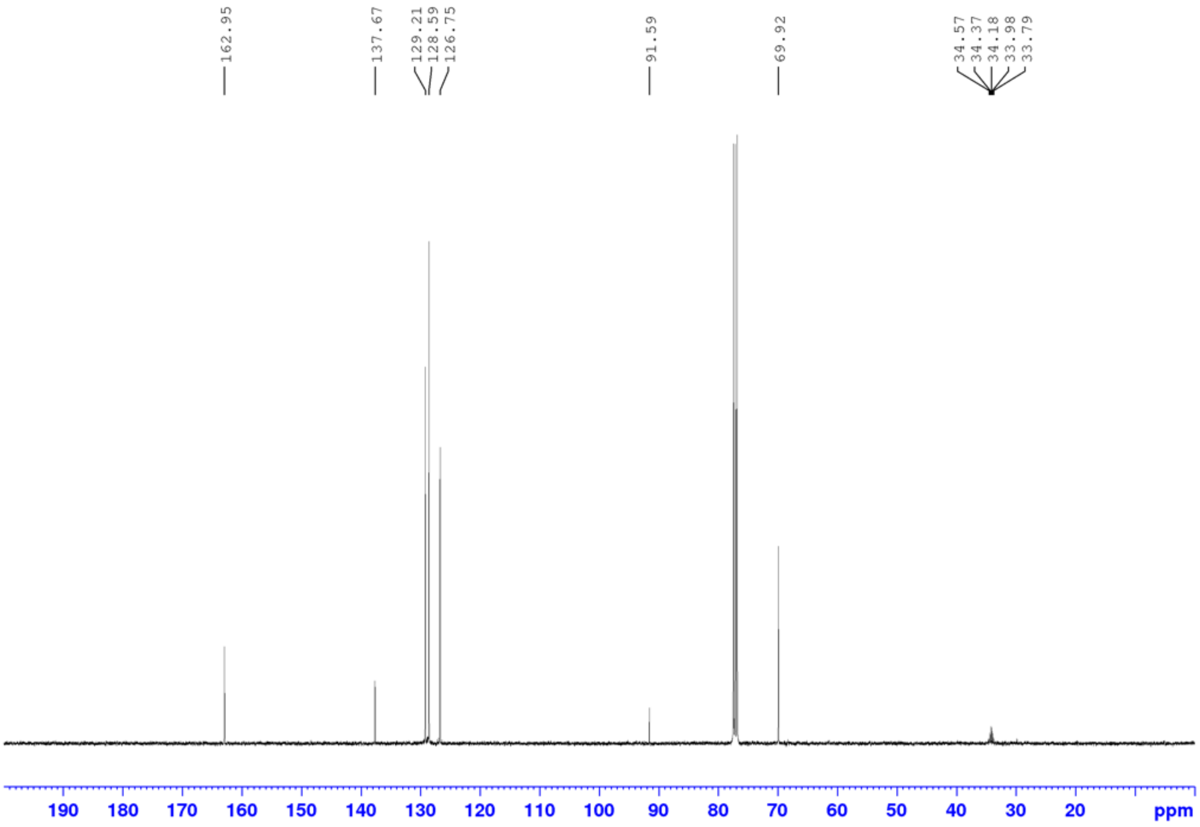
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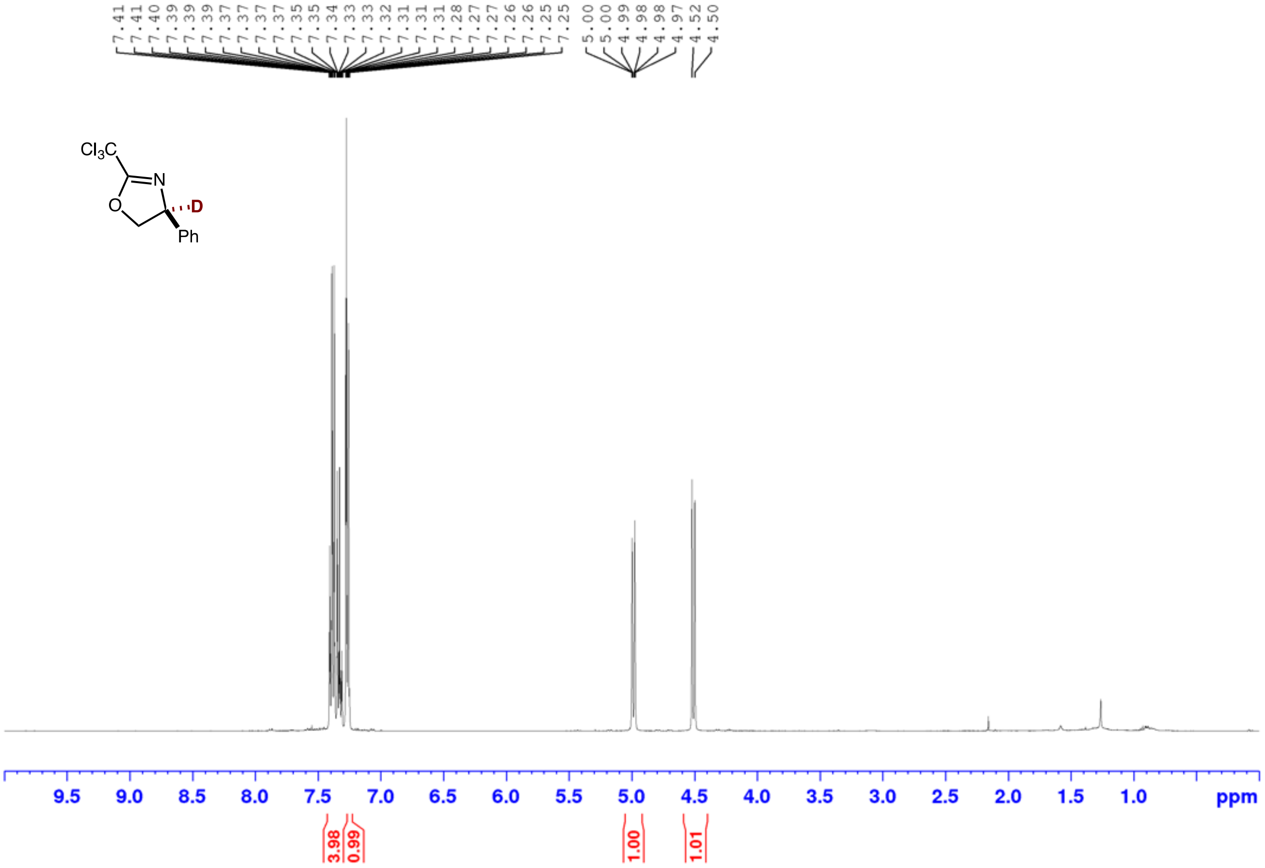
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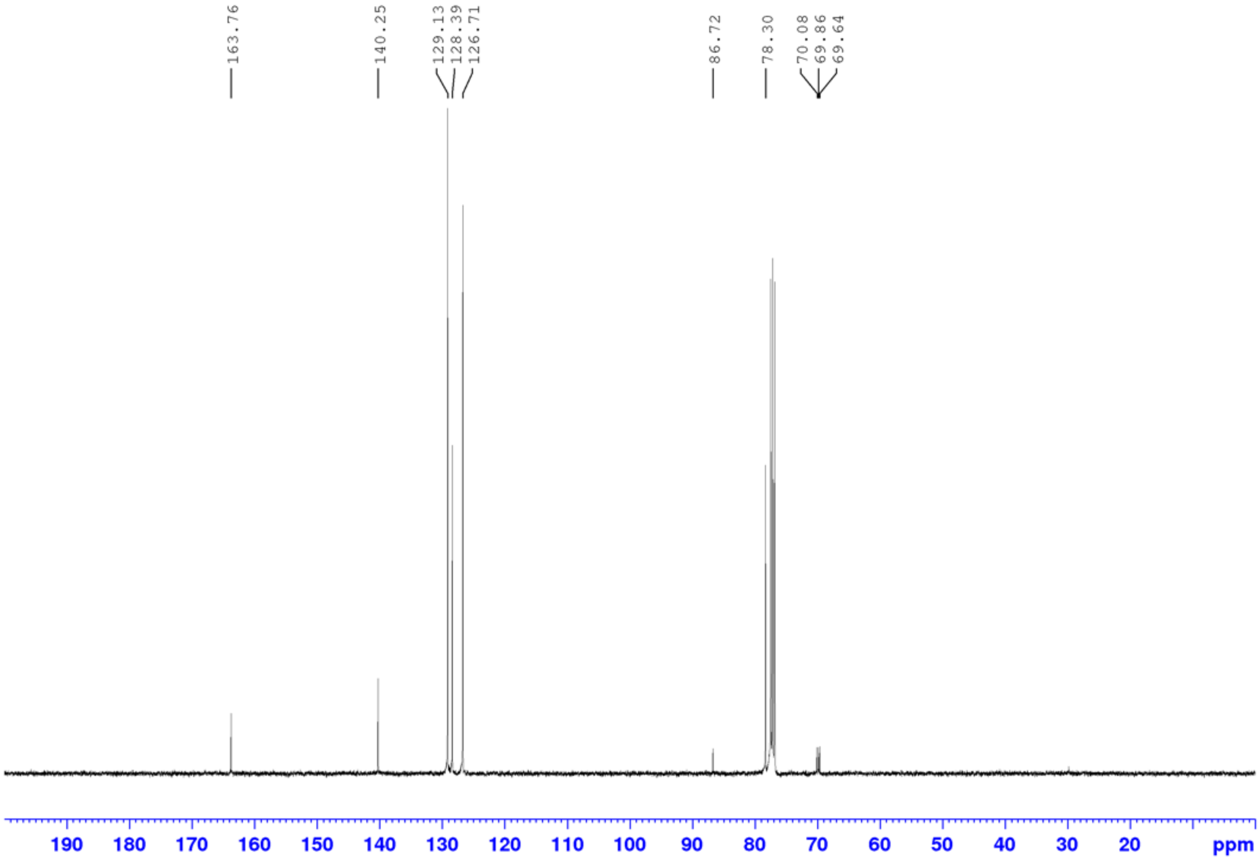
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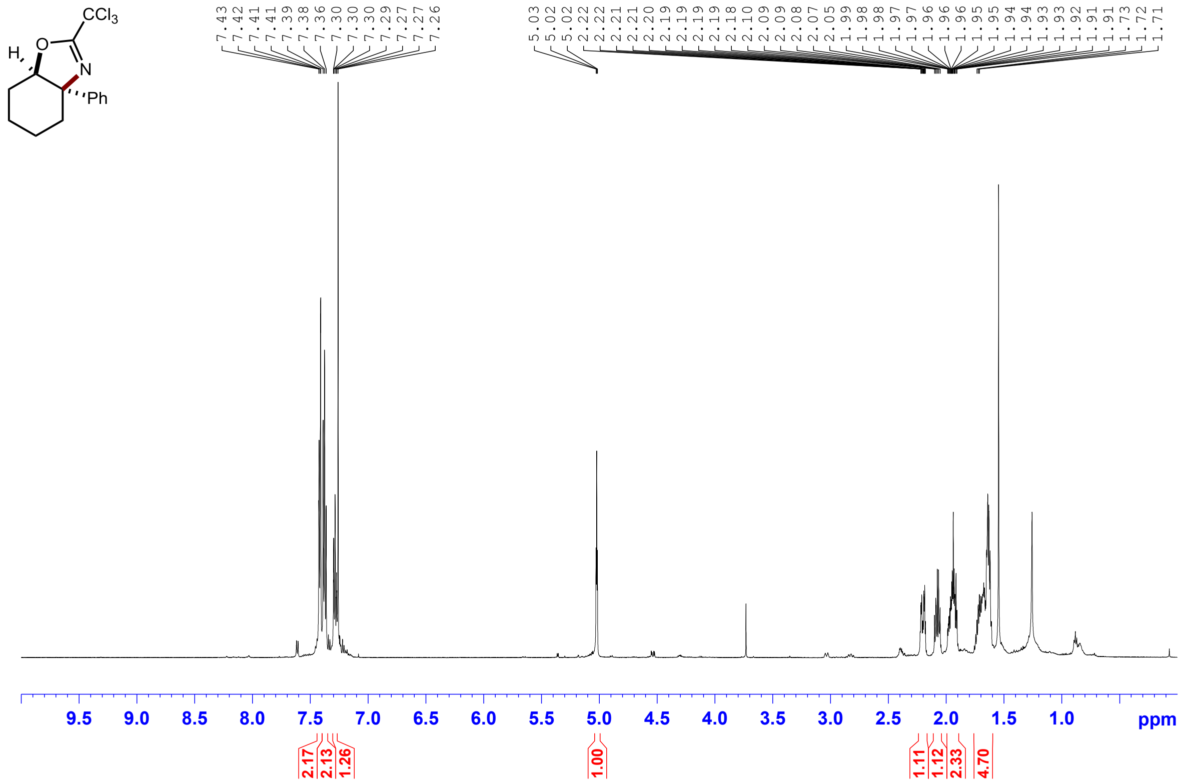
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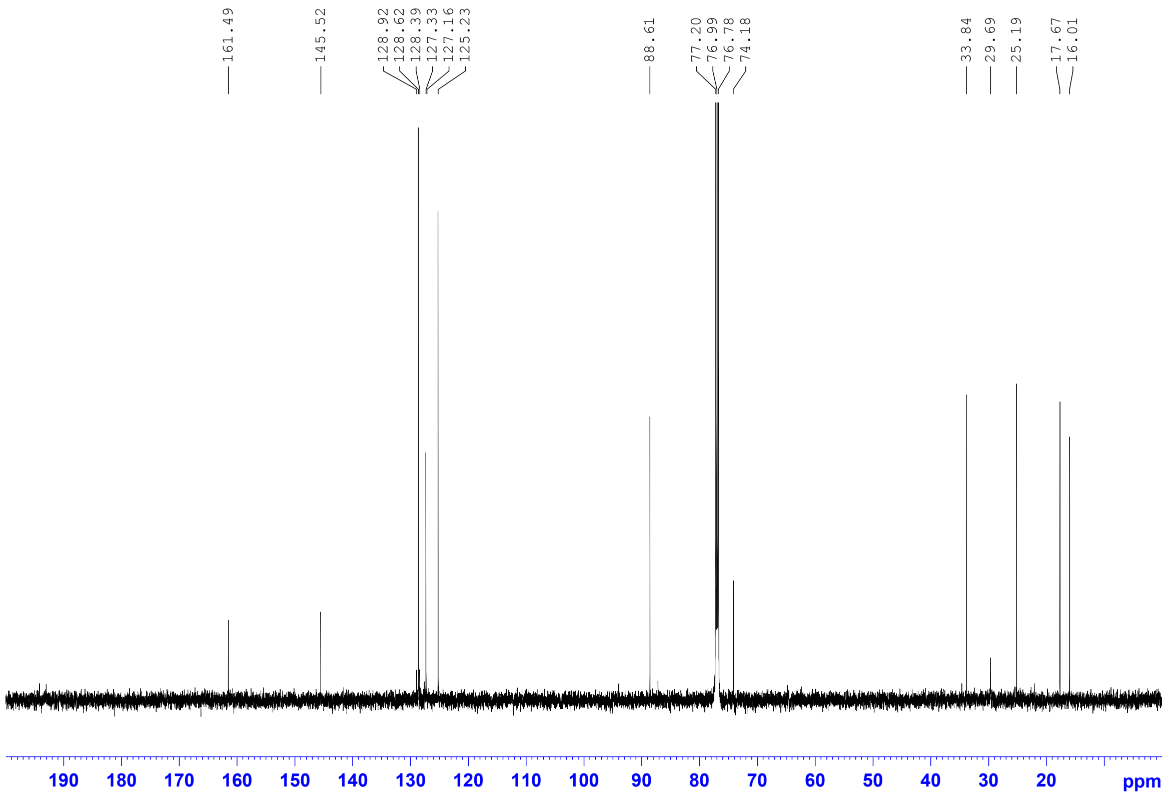
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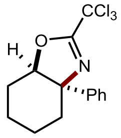
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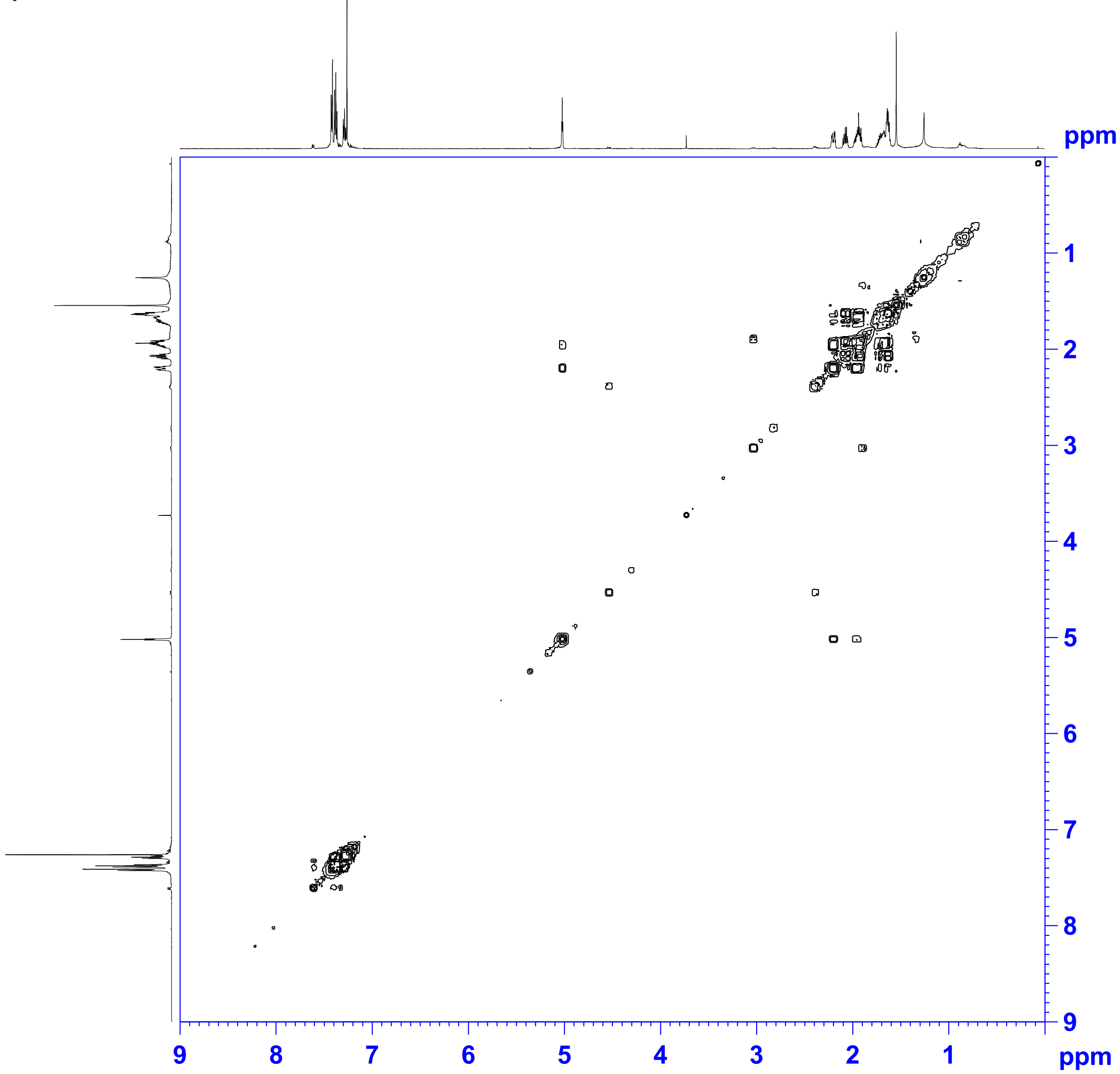
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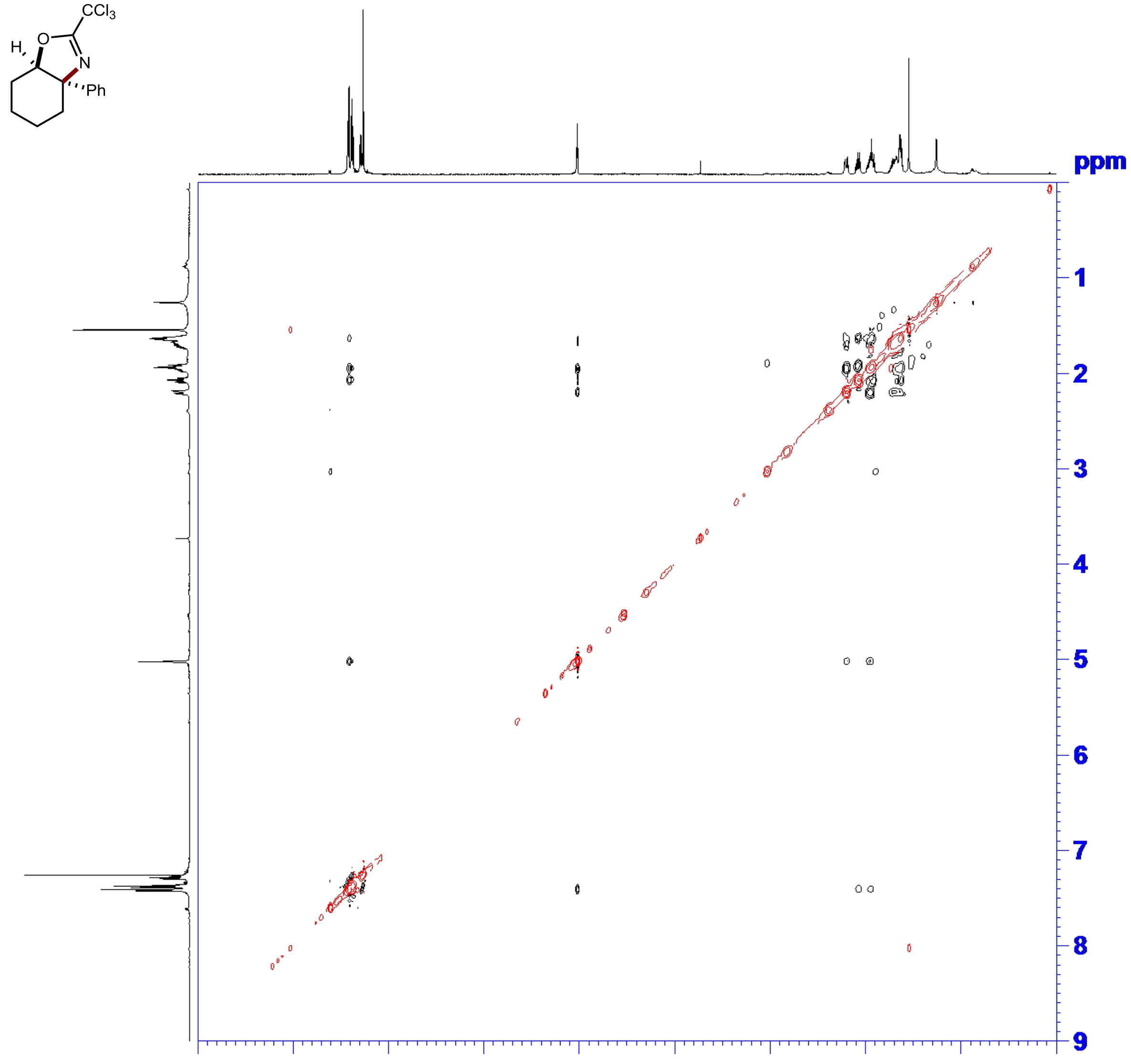
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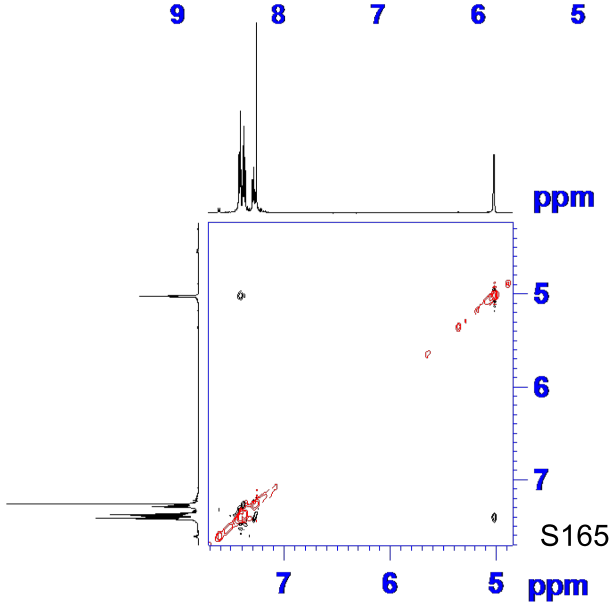
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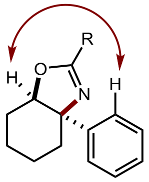
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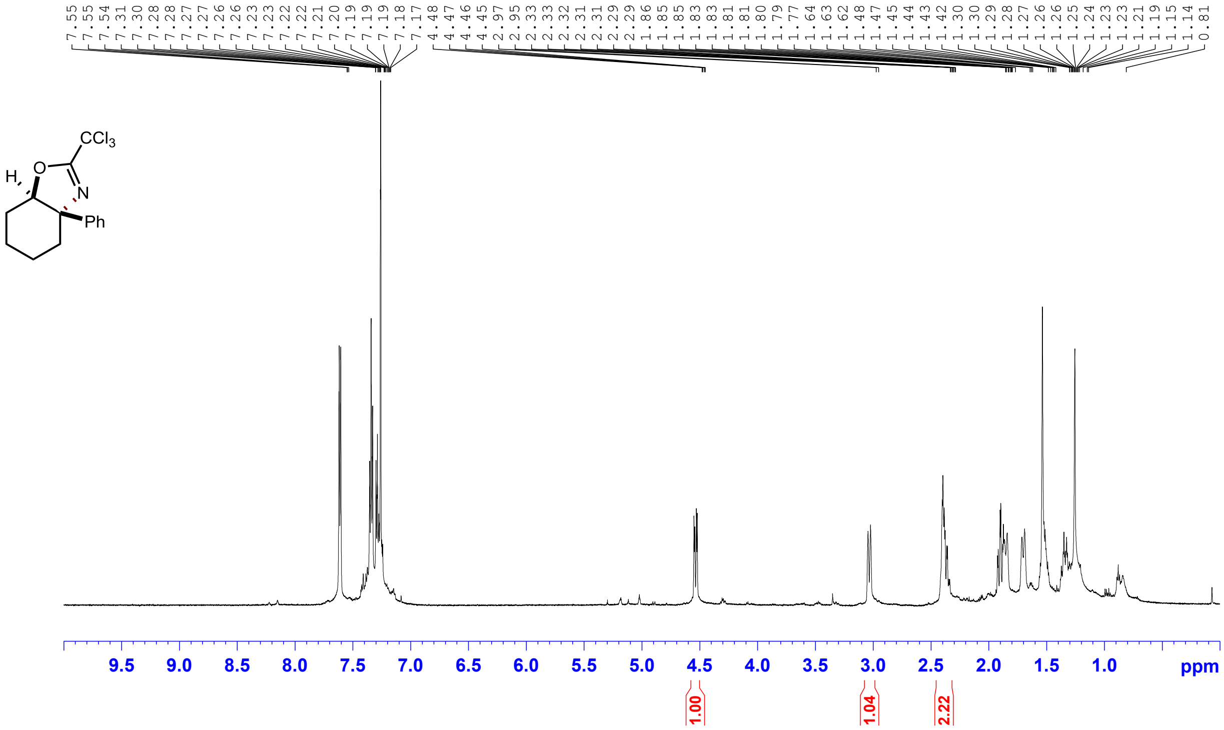
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O
N
H
Ph
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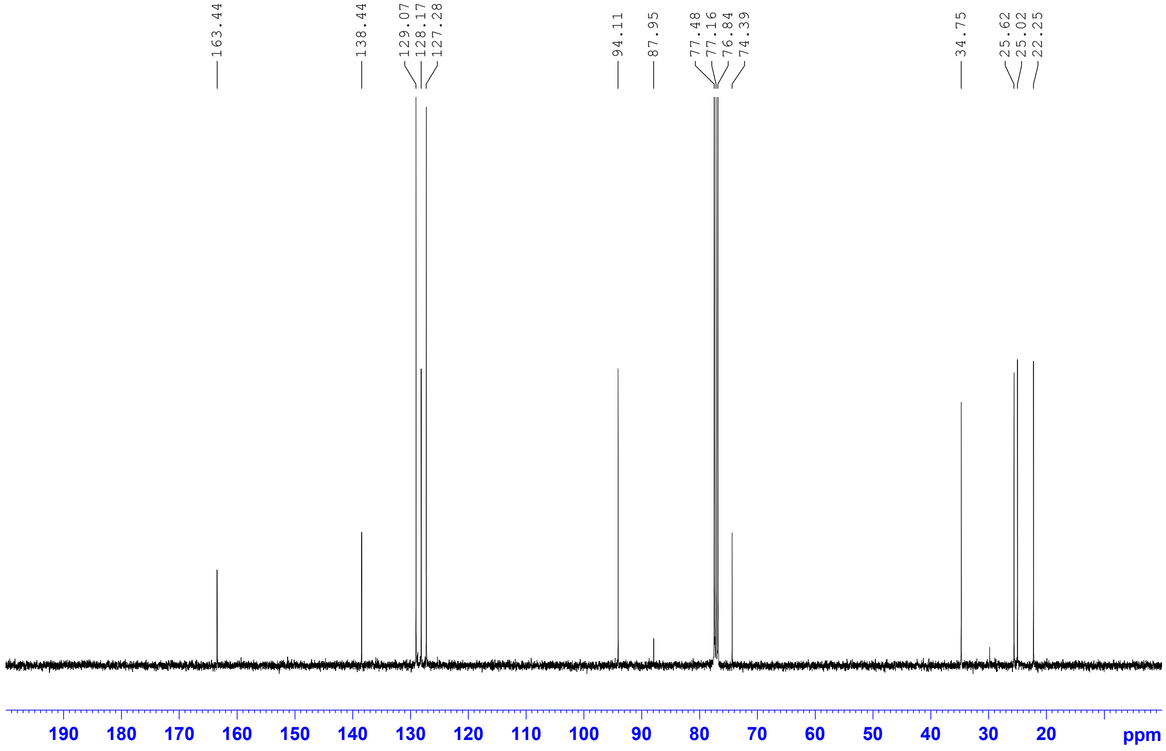
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25.02
22.25
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120
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30
20
ppm