Regio- and Stereoselective Synthesis of Fluoroalkenes by Directed Au(I) Catalysis

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Supporting Information

I. General Procedures.

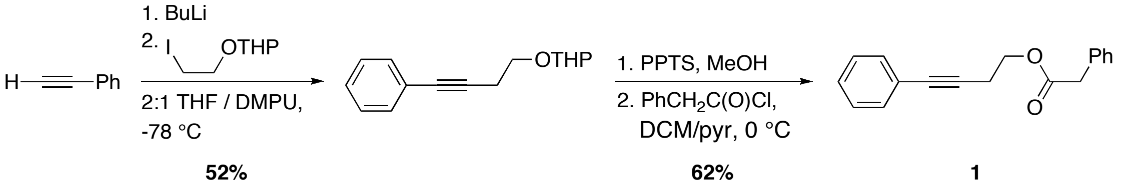
Proton NMR spectra were recorded on a 400 or 500 MHz spectrometer. Proton chemical shifts were reported in ppm (δ) relative to internal tetramethylsilane (TMS, δ 0.00 ppm), or with the solvent reference relative to TMS employed as the internal standard (CDCl$_3$, δ 7.26 ppm; CD$_3$OD, δ 3.30 ppm; CD$_2$Cl$_2$, δ 5.32 ppm). Spectral data are reported as follows: chemical shift (multiplicity [singlet (s), doublet (d), triplet (t), quartet (q), pentet (p), sextet (sext), septet (sept), and multiplet (m)], coupling constants [Hz], integration). Carbon NMR spectra were recorded on a 400 (100) or 500 (125) MHz spectrometer with complete proton decoupling. Carbon chemical shifts are reported in ppm (δ) relative to the residual solvent signal (CDCl$_3$, δ 77.0 ppm; CD$_3$OD, δ 49.0 ppm; CD$_2$Cl$_2$, δ 53.8 ppm). Fluorine NMR spectra were recorded on a 400 (376) MHz spectrometer. Fluorine chemical shifts are reported in ppm (δ) relative to internal tetramethylsilane (TMS, δ 0.00 ppm). NMR data were collected at ambient temperature unless otherwise indicated. Infrared spectra (thin film and attenuated total reflectance (ATR-IR)) were obtained on a Nicolet 6700 FT-IR spectrometer; $\upsilon_{\max}$ (cm^{-1}) are partially reported. Analytical thin-layer chromatography (TLC) was performed using Silica Gel 60 Å F254 pre-coated plates (0.25 mm thickness). TLC R_f values are reported and visualization was accomplished by irradiation with a UV lamp and/or staining with cerium ammonium molybdate (CAM), *p*-anisaldehyde, or KMnO$_4$ solutions. Flash column chromatography was performed using Silica Gel 60 Å (32-63 micron) or using a Biotage SP4 flash purification system. Gradient elution volumes are reported as column volumes, or “CV”. Optical rotations were recorded on a Rudolf Research Analytical Autopol IV Automatic polarimeter at the sodium D line (100 mm path length). High resolution mass spectra were acquired from the Mass Spectrometry Facility of the University of Illinois (Urbana-Champaign, IL) or at the Keck Center of Yale University. The method of ionization is given in parentheses. Chiral analytical normal phase HPLC was performed at a column temperature of 20 °C on a Hewlett-Packard 1100 Series chromatograph equipped with a diode array detector (210 nm, 230 nm or 254 nm).

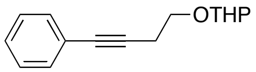
Solvents were purified using a Seca Solvent Purification System by GlassContour. All other chemicals were purchased commercially and used as received unless indicated otherwise.

II. Preparation of Substrates for Hydrofluorination.

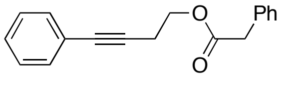
4-Phenylbut-3-ynyl 2-phenylacetate (Scheme 2, compound 1):

This substrate was prepared in three steps from 2-(2-iodoethoxy)tetrahydropyran.[i]





In a flame-dried 50 mL two-neck flask under nitrogen equipped with a stir bar and a septum, phenylacetylene (1.1 mL, 9.8 mmol) was dissolved in 15 mL THF and cooled to -78 ºC. Butyl lithium solution (2.5 M in hexanes, 3.6 mL, 9.3 mmol) was added dropwise via syringe, followed by 7.5 mL DMPU and 2-(2-iodoethoxy)tetrahydropyran[i] (2.256 g, 8.810 mmol). The reaction was allowed to warm to room temperature, and subsequently stirred for 16 hours. Water (25 mL) and Et$_2$O (25 mL) were added. The layers were separated, and the organic layer was washed with 25 mL brine, dried over MgSO$_4$, and filtered. The solvent was removed in vacuo, and the crude residue was purified by flash column chromatography (1 CV hexanes, 2 CV 5% EtOAc/hexanes, 4 CV 10% EtOAc/hexanes) to afford 2-(4-phenylbut-3-ynyloxy)tetrahydro-2*H*-pyran (1.165 g, 52% yield) as a clear oil. **TLC R$_f$** = 0.27 (9:1 hexanes/EtOAc); **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.47 – 7.34 (m, 2H), 7.33 – 7.21 (m, 3H), 4.69 (t, *J* = 3.3, 1H), 4.01 – 3.83 (m, 2H), 3.65 (dtd, *J* = 9.5, 7.1, 1.0, 1H), 3.56 – 3.48 (m, 1H), 2.72 (t, *J* = 7.2, 2H), 1.95 – 1.78 (m, 1H), 1.78 – 1.68 (m, 1H), 1.68 – 1.47 (m, 4H); **^{13}C NMR** (126 MHz, CDCl$_3$) δ 131.5, 128.2, 127.7, 123.7, 98.2, 86.1, 81.0, 65.1, 62.1, 30.6, 25.4, 20.9, 19.4; **IR** (ATR-IR) ν 2943, 2871, 1491, 1442, 1201, 1136, 1122, 1081, 1034, 757, 692 cm^{-1}; **HRMS** calcd for [C$_{15}$H$_{18}$O$_2$ Na]$^+$ requires *m/z* 253.1200; found 253.1200 (ESI+).



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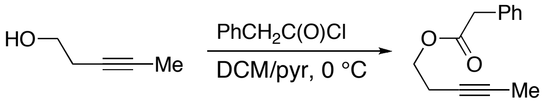
In a 25 mL round bottom flask with a stir bar, 2-(4-phenylbut-3-ynyloxy)tetrahydro-2*H*-pyran (1.165 g, 5.059 mmol) was dissolved in 15 mL of MeOH. Pyridinium *p*-toluenesulfonate (191 mg, 0.760 mmol) was added, and the reaction was stirred under nitrogen for 20 hours. The solvent was removed in vacuo, and the crude residue was dissolved in Et_2O (15 mL) and washed with saturated sodium bicarbonate (15 mL) and brine (15 mL). The organic layer was dried over $MgSO_4$ and filtered. The solvent was removed in vacuo, and 300 mg of the crude residue was dissolved in CH_2Cl_2 (15 mL) and pyridine (5 mL) in a 25 mL round bottom flask. 4-Dimethylaminopyridine (3 mg, 0.02 mmol) was added, followed by phenylacetyl chloride (300 μL, 2.3 mmol). The flask was capped with a septum and stirred under nitrogen for 18 hours. CH_2Cl_2 (10 mL) was added, and the organic layer was washed with saturated sodium bicarbonate (25 mL), saturated $CuSO_4$ (25 mL), water (25 mL), and brine (25 mL). The organic layer was dried over $MgSO_4$ and filtered. The solvent was removed in vacuo, and the crude residue was purified by flash column chromatography (1 CV 10% EtOAc/hexanes, 2 CV 20% EtOAc/hexanes, 2 CV 33% EtOAc/hexanes) to give 4-phenylbut-3-ynyl 2-phenylacetate (338 mg, 62% yield) as a pale yellow oil. **TLC** $\mathbf{R_f}$ = 0.53 (2:1 hexanes/EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 – 7.18 (m, 10H), 4.27 (t, J = 6.8, 2H), 3.65 (s, 2H), 2.73 (t, J = 6.8, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.3, 133.8, 131.6, 129.2, 128.5, 128.2, 127.9, 127.1, 123.3, 85.3, 82.0, 62.7, 41.2, 19.8; **IR** (thin film) ν 3062, 3031, 2962, 1734, 1490, 1454, 1245, 1146, 1025, 1007, 756, 691 cm^{-1}; **HRMS** calcd for $[C_{18}H_{16}O_2\ H]^+$ requires *m/z* 265.1223; found 265.1225 (ESI+).

Pent-3-ynyl 2-phenylacetate (Scheme 2, compound 3):



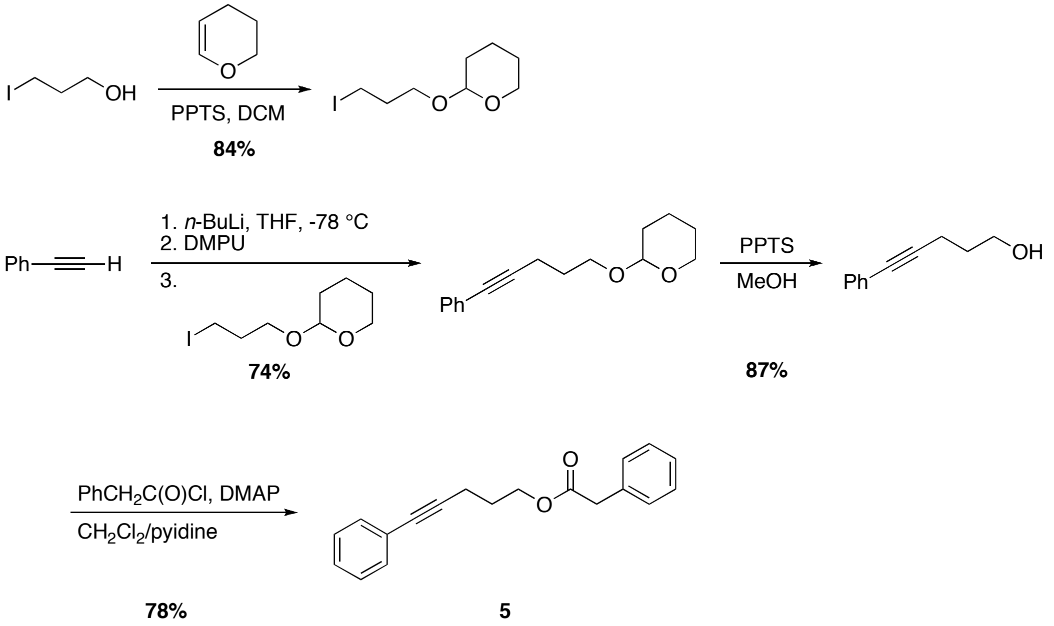
85% **3**

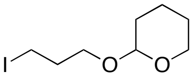
To a 25 mL round bottom flask equipped with a stir bar were added pent-3-yn-1-ol (326 μL, 3.57 mmol), 12 mL CH_2Cl_2, and 3 mL pyridine. Phenylacetyl chloride (455 μL, 3.92 mmol) was added to the stirred solution at 0 ºC under nitrogen. After 5 min, 4-dimethylaminopyridine (5 mg, 0.04 mmol) was added. The reaction was monitored by TLC (2:1 hexanes/EtOAc). After 2.5 hours, phenylacetyl chloride (124 μL, 1.07 mmol) and triethylamine (149 μL, 1.07 mmol) were added. The reaction was deemed complete by TLC after an additional 20 minutes of stirring. CH_2Cl_2 (10 mL) was added, and the solution was washed with saturated aqueous sodium bicarbonate (1 x 25 mL), saturated aqueous $CuSO_4$ (2 x 25 mL), and brine (1 x 25 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude residue was purified by flash column chromatography using a Biotage SP4 flash purification system (0 – 20% EtOAc/hexanes over 3 CV, 20 – 30% EtOAc/hexanes over 3 CV, 30 – 100% EtOAc/hexanes over 3 CV) to afford pent-3-ynyl 2-phenylacetate (616 mg, 85% yield) as a pale yellow oil. **TLC** $\mathbf{R_f}$ = 0.38 (4:1 hexanes/EtOAc); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.36 – 7.23 (m, 5H), 4.15 (t, J = 6.9, 2H), 3.64

(s, 2H), 2.46 (tq, *J* = 6.9, 2.4, 2H), 1.76 (t, *J* = 2.4, 3H); **^{13}C NMR** ($CDCl_3$, 126 MHz) *δ* 171.4, 133.9, 129.3, 128.5, 127.1, 77.3, 74.6, 63.2, 41.2, 19.2, 3.4; **IR** (ATR-IR) ν 3031, 2958, 2920, 1735, 1497, 1454, 1247, 1143, 1011, 696 cm^{-1}; **HRMS** calcd for $[C_{13}H_{14}O_2\ H]^+$ requires *m/z* 203.1067; found 203.1065 (ESI+).

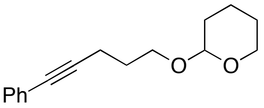
5-Phenylpent-4-ynyl 2-phenylacetate (Scheme 2, compound 5):

This substrate was prepared in 4 steps from 3-iodopropan-1-ol.

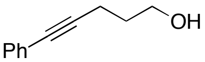




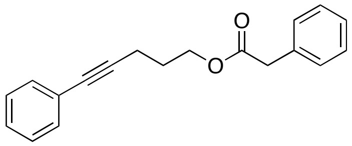
A volume of 20 mL of anhydrous CH_2Cl_2 was added to a 50 mL flask containing a stir bar and pyridinium *p*-toluenesulfonate (405 mg, 1.61 mmol). The mixture was put under nitrogen gas, and iodopropanol (1.0 mL, 11 mmol) and dihydropyran (1.4 mL, 16 mmol) were added. The golden brown reaction was covered by aluminum foil and left to stir at room temperature. The reaction progress was monitored by TLC (30% EtOAc/hexanes). After about 1 hour the reaction was complete and the mixture was concentrated in vacuo. The crude mixture was dry-loaded on silica and purified by column chromatography (5% Et_2O/hexanes) to give 2-(3-iodopropoxy)tetrahydro-2*H*-pyran as a clear oil (2.43 g, 84% yield). The spectral data for this compound matched that which had been previously reported.[ii]



To a flame-dried 50 mL round bottom flask under nitrogen gas containing a stir bar, 15 mL of anhydrous THF and phenyl acetylene (0.71 mL, 6.5 mmol) were added and the mixture was cooled to -78 °C. Butyl lithium solution (2.5 M in hexanes, 2.47 mL, 6.19 mmol) was added to the reaction mixture and left to stir for five minutes. 1,3-Dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (3 mL) was added. The reaction mixture was allowed to warm to room temperature, and then 2-(3-iodopropoxy)tetrahydro-2*H*-pyran (1.592 g, 5.893 mmol) was added with an additional 3 mL of THF. The reaction progress was monitored by ^{1}H NMR. After 12 hours, the reaction mixture was concentrated and purified by silica gel column chromatography in 5% Et_2O/hexanes to give 2-(5-phenylpent-4-ynyloxy)tetrahydro-2*H*-pyran as a yellowish oil (1.061 g, 74% yield). **TLC R$_f$** = 0.27 (9:1 hexanes/EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48 – 7.20 (m, 5H), 4.66 – 4.56 (m, 1H), 3.97 – 3.82 (m, 2H), 3.60 – 3.45 (m, 2H), 2.54 (t, *J* = 7.1, 2H), 2.00 – 1.43 (m, 8H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 131.6, 128.2, 127.5, 124.0, 98.8, 89.6, 80.8, 66.0, 62.2, 30.7, 29.0, 25.5, 19.5, 16.3; **IR** (ATR-IR) ν 3054, 2940, 2869, 1598, 1490, 1440, 1135, 1031, 1019, 991, 868, 754, 691 cm^{-1}; **HRMS** calcd for $[C_{16}H_{20}O_2H]^+$ requires *m/z* 245.1536; found 245.1533 (ESI+).



In a 50 mL round bottom flask containing a stir bar, 2-(5-phenylpent-4-ynyloxy)tetrahydro-2*H*-pyran (960 mg, 3.93 mmol) was dissolved in 25 mL of methanol. Pyridinium *p*-toluenesulfonate (148 mg, 0.589 mmol) was added. The reaction was left to stir at room temperature overnight. ^{1}H NMR of an aliquot of the reaction mixture indicated that the reaction had reached completion. The reaction mixture was diluted with 30 mL of ether and extracted with saturated aqueous NaCl solution. The aqueous layer was further extracted with another 20 mL of ether. The combined ether layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude residue was purified by column chromatography eluting with 40% Et_2O/hexanes to afford 5-phenylpent-4-yn-1-ol as a clear oil (545.2 mg, 87% yield). The spectral data for this compound matched that which had been previously reported.[iii]



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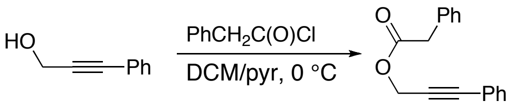
5-Phenylpent-4-yn-1-ol (540 mg, 3.4 mmol) was dissolved in 20 mL of 4:1 CH_2Cl_2/pyridine (v/v) in a 50 mL flask containing a stir bar. 4-Dimethylaminopyridine (3 mg, 0.01 mmol) was added. The reaction mixture was put under nitrogen and cooled to 0 ºC. Phenylacetyl chloride (0.67 mL, 5.1 mmol) was then added and the yellowish reaction mixture was left to stir. A white precipitate gradually formed. The reaction was monitored by TLC (10% MeOH/CH_2Cl_2). After 2 hours, additional phenylacetyl chloride (0.22 mL, 1.7 mmol) was added to drive the reaction to completion. After 30 minutes, the reaction was complete. Dichloromethane (25 mL) was added to the reaction mixture, which was then washed with saturated aqueous $NaHCO_3$ (2 x 25 mL), saturated aqueous $CuSO_4$ solution, and brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo to give a golden brown product. The crude was purified by column chromatography eluting with 5% Et_2O/hexanes to give the title compound as a slightly yellow oil (738.5 mg, 78% yield). **TLC R$_f$** = 0.24 (9:1 hexanes/EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 – 7.26 (m, 10H), 4.25 (t, J = 6.3, 2H), 3.64 (s, 2H), 2.47 (q, J = 7.0, 1H), 1.92 (dq, J = 13.4, 6.7, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.6, 134.1, 131.6, 129.3, 128.6, 128.3, 127.8, 127.1, 123.6, 88.5, 81.3, 63.6, 41.4, 27.8, 16.2; **IR** (ATR-IR) ν 3031, 2957, 1732, 1598, 1490, 1249, 1149, 1029, 755, 690 cm^{-1}; **HRMS** calcd for $[C_{19}H_{18}O_2H]^+$ requires *m/z* 279.1380; found 279.1381 (ESI+).

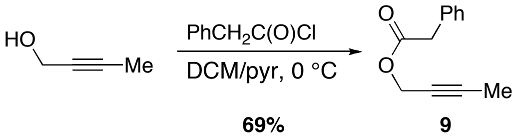
3-Phenylprop-2-ynyl 2-phenylacetate (Scheme 2, compound 7):



56% **7**

A mixture of CH_2Cl_2/pyridine (4:1 v/v, 20 mL) was cooled to 0 ºC in a 50 mL flask containing a stir bar under nitrogen gas. 4-Dimethylaminopyridine (3 mg, 0.01 mmol), 3-phenylprop-2-yn-1-ol (400 mg, 3 mmol), and phenylacetyl chloride (0.60 mL, 4.5 mmol) were added to the flask. The yellowish reaction mixture was left to stir, and the reaction was monitored by TLC (7:3 hexanes/EtOAc). A white precipitate gradually formed. After 2 hours, more phenylacetyl chloride (0.20 mL, 1.5 mmol) was added to drive the reaction to completion. After thirty minutes, the reaction was complete. Dichloromethane (25 mL) was added to the reaction mixture, which was then washed with $NaHCO_3$ (2 x 25 mL), saturated aqueous $CuSO_4$ solution, and brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo to give a golden brown oil. The crude was purified by flash column chromatography using a Biotage SP4 flash purification system (0 – 20% EtOAc/hexanes over 3CV, 20 – 30% EtOAc/hexanes over 3 CV, 30 – 100% EtOAc/hexanes over 3CV) to give the title compound as a slightly yellow oil (453 mg, 56% yield). The spectral data for this compound matched that which had been previously reported.[iv]

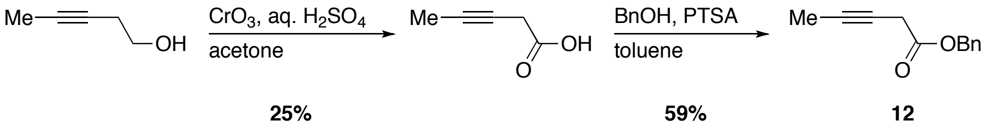
But-2-ynyl 2-phenylacetate (Scheme 2, compound 9):

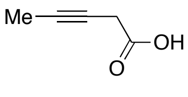


In a 100 mL round bottom flask, 20 mL of CH_2Cl_2/pyridine (4:1 v/v) was cooled to 0 ºC under nitrogen in a 100 mL round bottom flask containing 4-dimethylaminopyridine (5 mg, 0.04 mmol) and a stir bar. But-2-yn-1-ol (0.32 mL, 4.3 mmol) and phenylacetyl chloride (0.62 mL, 4.7 mmol) were added. A white precipitate was observed soon after phenylacetyl chloride addition, which slowly dissolved as the ice bath warmed to room temperature. The progress of the reaction was monitored by TLC (7:3 hexanes/EtOAc). After 3 hours, phenylacetyl chloride (0.28 mL, 2.1 mmol) was added. After an additional 3 hours of stirring, the reaction was complete. The precipitate was redissolved in dichloromethane (10 mL), and the solution was washed with saturated $NaHCO_3$ solution (2x) and brine. The organic layer was dried with $MgSO_4$, filtered, and concentrated in vacuo to give a golden brown oil. The crude was purified by silica gel column chromatography (100% toluene) to give the title compound as a yellow oil (552.7 mg, 69% yield). The spectral data for this compound matched that which had been previously reported.[v]

Benzyl pent-3-ynoate (Scheme 2, compound 12):

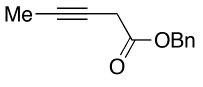
This substrate was prepared in two steps from pent-3-yn-1-ol.





To a 250 mL round bottom flask equipped with a stir bar and a dropping funnel were added pent-3-yn-1-ol (5.00 g, 59.4 mmol) and 20 mL acetone. Jones reagent (50 mL; prepared from 11.78 g

CrO_3, 10.5 mL concentrated H_2SO_4, and 77 mL H_2O) was added dropwise to the stirring solution at 0 ºC, and the reaction progress was monitored by TLC. After 5 hours, an additional 38 mL of Jones reagent was added. The reaction was stirred for an additional 17 hours, after which the reaction was deemed complete by TLC. The reaction mixture was extracted with Et_2O (2 x 100 mL), and the combined organic layers were dried over $MgSO_4$ and filtered. The solvent was removed in vacuo, and the isolated material was subsequently purified using a silica gel plug eluting with 10% $MeOH/CH_2Cl_2$. The solvent was removed in vacuo to give an off-white solid, from which the desired product was recrystallized in 3:1 Et_2O/hexanes. The crystals were washed with cold 3:1 Et_2O/hexanes. A second crop of crystals was similarly obtained from the mother liquor and combined with the first crop to give pent-3-ynoic acid (1.485 g, 25% yield) as white crystals. **TLC R*f*** = 0.41 (9:1 CH_2Cl_2/MeOH); **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 10.35 (br s, 1H), 3.32 (q, *J* = 2.6, 2H), 1.84 (t, *J* = 2.6, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) *δ* 175.2, 80.0, 69.7, 25.8, 3.5; **IR** (ATR-IR) ν 2925 (br), 2748, 2637, 2551, 1724, 1425, 1389, 1376, 1342, 1234, 933, 733, 673 cm^{-1}; **HRMS** calcd for $[(C_5H_6O_2)_2 K]^+$ requires *m/z* 235.0372; found 235.0274 (ESI+).



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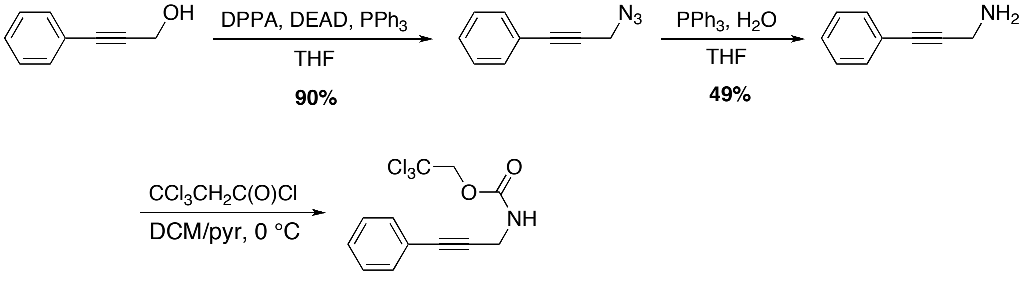
In a 10 mL round bottom flask equipped with a stir bar, pent-3-ynoic acid (300 mg, 3.05 mmol), benzyl alcohol (662 mg, 6.12 mmol), and a few crystals of *p*-toluenesulfonic acid were dissolved in 5 mL toluene. A Dean-Stark trap was attached, and the apparatus was wrapped with glass wool. The reaction was refluxed at 120 ºC for 24 hours, after which the solvent was removed in vacuo. The crude residue was purified by flash column chromatography using a Biotage SP4 flash purification system (hexanes over 5 CV, 0 – 10% EtOAc/hexanes over 10 CV, 10 – 50% EtOAc/hexanes over 5 CV) to afford benzyl pent-3-ynoate (338 mg, 59% yield) as a pale yellow oil. **TLC R*f*** = 0.32 (2:1 hexanes/EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$) *δ* 7.63 – 6.93 (m, 5H), 5.11 (s, 2H), 3.22 (q, *J* = 2.6, 2H), 1.77 (t, *J* = 2.6, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) *δ* 168.4, 135.3, 128.2, 128.0, 127.9, 79.0, 70.3, 66.7, 25.6, 3.1; **IR** (ATR-IR) ν 3034, 2920, 1739, 1455, 1338, 1261, 1163, 1147, 971, 736, 696 cm^{-1}; **HRMS** calcd for $[C_{12}H_{12}O_2\ H]^+$ requires *m/z* 189.0910; found 189.0908 (ESI+).

2,2,2-Trichloroethyl 3-phenylprop-2-ynylcarbamate (Table 1, compound 14):

This substrate was prepared in 3 steps from 3-phenylprop-2-yn-1-ol.



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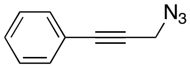
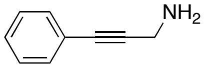
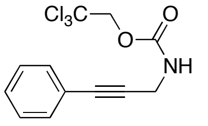


To a 100 mL round bottom flask under nitrogen gas containing a stir bar and triphenylphosphine (2.98 g, 11.3 mmol) was added 20 mL of anhydrous THF. The mixture was stirred at 0 °C. 3-Phenylprop-2-yn-1-ol (750 mg. 5.67 mmol), diethyl azodicarboxylate (1.78 mL, 11.3 mmol) and diphenylphosphoryl azide (2.45 mL, 11.3 mmol) were added. The reaction mixture was stirred at room temperature under nitrogen gas and the reaction progress was monitored by TLC (4:1 hexanes/EtOAc). After three hours, the reaction was complete and was concentrated in vacuo to give a thick, dark brown oil, which was purified by silica gel column chromatography (hexanes) to give (3-azidoprop-1-ynyl)benzene as a yellow oil (802.5 mg, 90% yield). The spectral data for this compound matched that which had been previously reported.[vi]



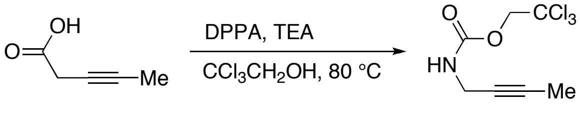
To a solution of (3-azidoprop-1-ynyl)benzene (802 mg, 5.11 mmol) in 60 mL of THF in a 250 mL round bottom flask containing a stir bar was added triphenylphosphine (13.4 g, 51.1 mmol) and water (1.84 mL, 102 mmol). The yellow mixture was refluxed overnight. TLC (4:1 hexanes/EtOAc) showed the reaction had reached completion. The reaction mixture was cooled to room temperature and the solvent was removed in vacuo to give a yellow solid, which was purified by silica gel column chromatography (9:1 hexanes/EtOAc) to afford 3-phenylprop-2-yn-1-amine as a yellow oil (326 mg, 49% yield). Spectral data for this compound matched that which had been previously reported.[vii]



14

3-Phenylprop-2-yn-1-amine (326 mg, 2.48 mmol) was dissolved in 10 mL of dichloromethane in a 50 mL round bottom flask containing a stir bar and the solution was cooled to 0 °C. Pyridine (0.22 mL, 2.7 mmol) and 2,2,2-trichloroethyl chloroformate (0.37 mL, 2.7 mmol) were added. The progress of the reaction was monitored by TLC (9:1 CH_2Cl_2/methanol), and after 1.5 hours the reaction was complete. The reaction mixture was diluted with 20 mL of CH_2Cl_2 and washed with 10% aqueous citric acid solution, saturated aqueous $NaHCO_3$ solution, and brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo to give a brown solid. The crude was purified by silica gel column chromatography (100% toluene) to give the title compound as a white crystalline solid (339 mg, 45% yield). **TLC R$_f$** = 0.30 (toluene); **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.48 – 7.27 (m, 5H), 5.26 (s, 1H), 4.76 (br s, 2H), 4.27 (d, *J* = 5.6, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) *δ* 154.5, 132.2, 129.0, 128.8, 122.7, 95.7, 84.5, 84.4, 75.2, 32.4; **IR** (ATR-IR) ν 3264, 3077, 2965 1703, 1549, 1488, 1425, 1278, 1180, 1030, 685 cm^{-1}; **HRMS** calcd for $[C_{12}H_{10}Cl_3NO_2\ H]^+$ requires *m/z* 305.9850; found 305.9850 (ESI+).

2,2,2-Trichloroethyl but-2-ynylcarbamate (Table 1, compound 16):

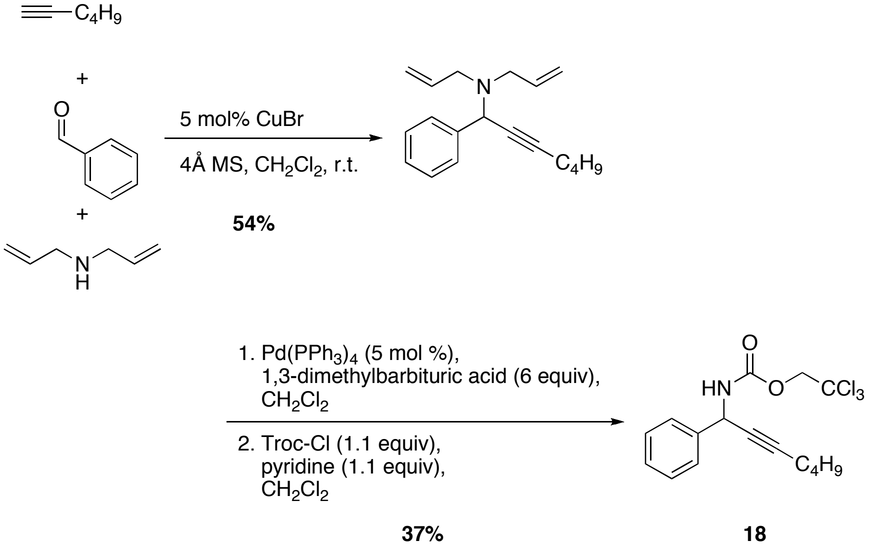


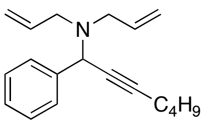
9% **16**

In a 10 mL round bottom flask containing a stir bar, pent-3-ynoic acid (see synthesis of **12** above; 150 mg, 1.53 mmol) was dissolved in 5 mL 2,2,2-trichloroethanol. Diphenylphosphoryl azide (330 μL, 1.53 mmol) and triethylamine (220 μL, 1.60 mmol) were added. The flask was fitted with a reflux condenser, and the reaction was stirred at 80 °C for 17 hours. The reaction was diluted with EtOAc (5 mL) and washed with 10 mL each of 10 % aqueous citric acid, saturated sodium bicarbonate, and brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude isolate was purified by flash column chromatography on silica gel (10% EtOAc/hexanes), followed by reverse phase flash column chromatography using a Biotage SP4 flash purification system (Biotage C18HS 25+S column; 20 – 100% methanol/water over 30 CV) to afford the product (35 mg, 9% yield) as a white crystalline solid. **TLC R$_f$** = 0.38 (9:1 hexanes/EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): *δ* 5.20 (br s, 1H), 4.73 (s, 2H), 3.98 (dq, *J* = 4.8, 2.4, 2H), 1.81 (t, *J* = 2.4, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): *δ* 154.1, 95.3, 80.0, 74.6, 74.1, 31.5, 3.4; **IR** (ATR-IR) ν 3329, 2921, 1713, 1513, 1232, 1127, 1031, 814, 718, 564 cm^{-1}; **HRMS** calcd for $[C_7H_8Cl_3NO_2\ K]^+$ requires *m/z* 281.9258; found 281.9272 (ESI+).

2,2,2-Trichloroethyl 1-phenylhept-2-ynylcarbamate (Table 1, compound 18):

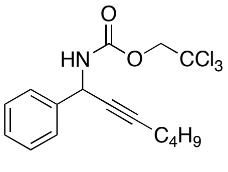
This substrate was prepared using procedures from the literature.[ix, x]





A 100 mL round-bottom flask was charged with 4Å molecular sieves and a stir bar, capped with a septum, flame-dried, and flushed with nitrogen. To the flask was added copper(I) bromide (87 mg, 0.30 mmol) and 50 mL dichloromethane. The mixture was stirred for 1 hour, after which 1-hexyne (1.40 mL, 12.2 mmol), benzaldehyde (1.25 mL, 12.2 mmol), and diallylamine (1.50 mL, 12.2 mmol) were added via syringe. After 2 days of stirring under nitrogen, the reaction mixture was quenched with 20 mL of saturated ammonium chloride, filtered through celite, and poured into a 250 mL separatory funnel. The layers were separated, and the aqueous layer was extracted with dichloromethane (3 x 50 mL). The organic layers were combined and washed with brine. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude residue was purified by flash column chromatography on silica gel (4 CV 5% Et_2O/hexanes) to afford *N*,*N*-diallyl-1-phenylhept-2-yn-1-amine (880 mg, 54% yield) as a yellow oil. **TLC** $\mathbf{R_f}$ = 0.29 (9:1 hexanes/Et_2O); ^{1}**H NMR** (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.3, 2H), 7.32 (t, *J* = 7.5, 2H), 7.24 (t, *J* = 7.3, 1H), 5.81 (dddd, *J* = 17.3, 10.2, 8.2, 4.4, 2H), 5.23 (d, *J* = 17.2, 2H), 5.10 (ddd, *J* = 10.2, 1.8, 1.8, 2H), 4.84 (s, 1H), 3.17 (dddd, *J* = 14.0, 4.2, 1.9, 1.9, 2H), 2.94

(dd, *J* = 14.1, 8.2, 2H), 2.34 (td, *J* = 7.0, 2.1, 2H), 1.77 – 1.10 (m, 4H), 0.96 (t, *J* = 7.3, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) *δ* 140.0, 136.7, 128.3, 127.9, 127.1, 117.0, 88.0, 75.3, 56.1, 53.4, 31.2, 22.0, 18.5, 13.6; **IR** (ATR-IR) ν 3080, 2956, 2931, 2817, 1449, 1418, 1327, 1273, 1256, 1109, 994, 972, 916, 727, 696 cm^{-1}; **HRMS** calcd for $[C_{19}H_{25}N\ H]^+$ requires *m/z* 268.2060; found 268.2052 (ESI+).

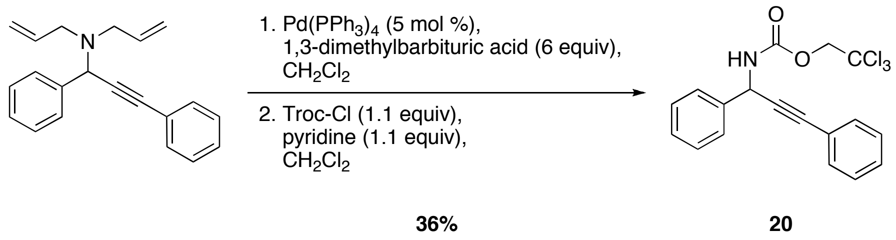


18

In a 100 mL round bottom flask containing a stir bar, tetrakis(triphenylphosphine)palladium(0) (108 mg, 0.935 mmol) and 1,3-dimethylbarbituric acid (1.75 g, 11.2 mmol) were dissolved in 15 mL of dichloromethane. A solution of *N*,*N*-diallyl-1-phenylhept-2-yn-1-amine (500 mg, 1.87 mmol) in 15 mL of dichloromethane was added and the reaction was stirred for 15 hours under nitrogen. The solvent was removed in vacuo and 30 mL of Et_2O was added. The solution was transferred to a separatory funnel and extracted with 2N HCl. The layers were separated, and the aqueous layer was poured into a 250 mL beaker. Diethyl ether (30 mL) was added, and saturated aqueous potassium carbonate was added slowly to pH 10. The mixture was poured into a separatory funnel and the layers were separated. The organic layer was dried over $MgSO_4$ and filtered. The solvent was removed in vacuo, and the crude residue was dissolved in 25 mL of dichloromethane in a 50 mL round bottom flask containing a stir bar. While stirring, 2,2,2-trichloroethyl chloroformate (180 μL, 1.32 mmol) and pyridine (105 μL, 1.32 mmol) were added slowly. The reaction was stirred under nitrogen for 36 hours, after which an additional 50 μL of 2,2,2-trichloroethyl chloroformate was added. After stirring for one hour, the solution was successively washed with 100 mL each of 10% citric acid, saturated aqueous sodium bicarbonate, and brine. The organic layer was dried over $MgSO_4$ and filtered. The solvent was removed in vacuo, and the crude residue was purified by silica gel chromatography (1 CV 20% $CHCl_3$/hexanes, 1 CV 35% $CHCl_3$/hexanes, 1 CV 50% $CHCl_3$/hexanes, 2 CV 66% $CHCl_3$/hexanes) to afford the title compound (251 mg, 37% yield) as a clear, colorless oil. **TLC R$_f$** = 0.54 (4:1 hexanes/EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.50 (d, *J* = 7.2, 2H), 7.42 – 7.26 (m, 3H), 5.69 (d, *J* = 8.6, 1H), 5.56 (d, *J* = 8.6, 1H), 4.73 (s, 2H), 2.25 (dt, *J* = 7.0, 2.1, 2H), 1.52 (tt, *J* = 7.0, 7.0, 2H), 1.41 (tq, *J* = 7.3, 7.3, 2H), 0.91 (t, *J* = 7.3, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) *δ* 153.6, 139.1, 128.6, 128.1, 126.9, 95.4, 86.3, 77.3, 74.7, 47.3, 30.6, 21.9, 18.4, 13.5; **IR**

(ATR-IR) ν 3309, 2956, 2932, 2872, 1712, 1492, 1229, 1181, 1124, 1020, 696 cm^{-1}; **HRMS** calcd for [$C_{16}H_{18}Cl_3NO_2$ Na]$^+$ requires *m/z* 384.0295; found 384.0299 (ESI+).

2,2,2-Trichloroethyl 1,3-diphenylprop-2-ynylcarbamate (Table 1, compound 20):

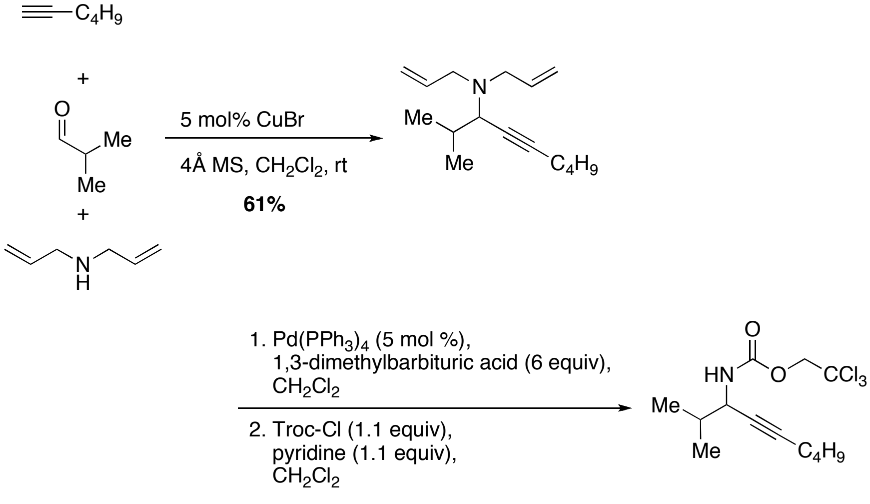


20

In a 50 mL round bottom flask containing a stir bar, tetrakis(triphenylphosphine)palladium(0) (123 mg, 0.107 mmol) and 1,3-dimethylbarbituric acid (2.00 g, 12.8 mmol) were dissolved in 15 mL of dichloromethane. A solution of *N*-allyl-*N*-(1,3-diphenylprop-2-ynyl)prop-2-en-1-amine[viii] (614 mg, 2.14 mmol) in 15 mL of dichloromethane was added and the reaction was stirred for 3 days under nitrogen. The solvent was removed in vacuo and 30 mL of Et_2O was added. The solution was transferred to a separatory funnel and extracted with 2N HCl. The layers were separated, and the aqueous layer was poured into a 250 mL beaker. Dichloromethane (30 mL) was added, and saturated aqueous potassium carbonate was added slowly to pH 10. The mixture was poured into a separatory funnel and the layers were separated. The organic layer was dried over $MgSO_4$ and filtered. The solvent was removed in vacuo, and the 284 mg of the crude residue was dissolved in 25 mL of dichloromethane in a 50 mL round bottom flask containing a stir bar. While stirring, 2,2,2-trichloroethyl chloroformate (200 μL, 1.5 mmol) and pyridine (120 μL, 1.5 mmol) were added slowly. The reaction was stirred under nitrogen for 23 hours, and the solution was successively washed with 100 mL each of 10% citric acid, saturated aqueous sodium bicarbonate, and brine. The organic layer was dried over $MgSO_4$ and filtered. The solvent was removed in vacuo, and the crude material was purified by silica gel chromatography (2 CV hexanes, 5 CV 10% EtOAc/hexanes) to afford the title compound (270 mg, 36% yield) as a clear oil. **TLC R$_f$** = 0.31 (9:1 hexanes/EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.59 (d, J = 7.4, 2H), 7.47 (dd, J = 7.4, 1.9, 2H), 7.43 – 7.37 (m, 2H), 7.37 – 7.29 (m, 4H), 5.95 (d, J = 8.8, 1H), 5.58 (d, J = 8.6, 1H), 4.79 (d, J = 11.9, 1H), 4.76 (d, J = 11.9, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 153.7, 138.5, 131.8, 128.8, 128.7, 128.4, 128.3, 127.0, 122.2, 95.3, 86.3, 85.6, 74.8, 47.7; **IR** (ATR-IR) ν 3405, 3319, 3034, 2954, 1724, 1491, 1229, 1142, 1032, 757, 722, 691 cm^{-1}; **HRMS** calcd for [$C_{18}H_{14}Cl_3NO_2$ H]$^+$ requires *m/z* 382.0163; found 382.0162 (ESI+).

2,2,2-Trichloroethyl 2-methylnon-4-yn-3-ylcarbamate (Table 1, compound 22):

This substrate was prepared using procedures from the literature.[ix, x]



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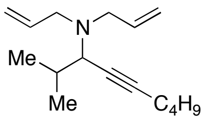
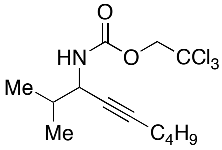


A 100 mL round bottom flask was charged with 4Å molecular sieves and a stir bar, capped with a septum, flame-dried, and flushed with nitrogen. To the flask was added copper(I) bromide (436 mg, 3.04 mmol) and 50 mL dichloromethane. The mixture was stirred for 1 hour, after which freshly distilled 1-hexyne (6.00 mL, 52.2 mmol), freshly distilled isobutyraldehyde (4.77 mL, 52.2 mmol), and diallylamine (6.43 mL, 52.2 mmol) were added via syringe. After 15 hours of stirring under nitrogen, the reaction was poured into a 250 mL separatory funnel and quenched with 20 mL of saturated aqueous ammonium chloride. The layers were separated, and the aqueous layer was extracted with dichloromethane (3 x 50 mL). The organic layers were combined and washed with brine. The combined organic layers were dried over sodium sulfate, filtered, and concentrated in vacuo. The crude residue was purified by flash column chromatography on silica gel (1:1 $CHCl_3$/hexanes) to afford *N*,*N*-diallyl-2-methylnon-4-yn-3-amine (7.369 g, 61% yield) as a clear liquid. **TLC R*f*** = 0.26 (1:1 $CHCl_3$/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.80 (dddd, *J* = 17.3, 10.2, 8.1, 4.2, 2H), 5.19 (dddd, *J* = 17.2, 2.0, 2.0, 1.1, 2H), 5.07 (dddd, *J* = 10.2, 1.5, 1.5, 0.6, 2H), 3.22 (dddd, *J* = 14.3, 4.0, 1.9, 1.9, 2H), 2.96 (dt, *J* = 10.1, 2.1, 1H), 2.82 (dd, *J* = 14.3, 8.1, 2H), 2.22 (td, *J* = 6.9, 2.1, 2H), 1.73 (d sept, *J* = 10.1, 6.6, 1H), 1.55 – 1.39 (m, 4H), 1.00 (d, *J* = 6.6, 3H), 0.94 (d, *J* = 6.6, 3H), 0.92 (t, *J* = 7.2, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 137.2, 116.4, 85.2, 77.4, 59.7, 53.9, 31.4, 31.2, 21.9, 20.8, 19.9, 18.3, 13.6;

IR (thin film) ν 3077, 2958, 2929, 2868, 2811, 1642, 1458, 1095, 997, 915 cm^{-1}; **HRMS** calcd for $[C_{16}H_{27}N\ H]^+$ requires *m/z* 234.2216; found 234.2213 (ESI+).

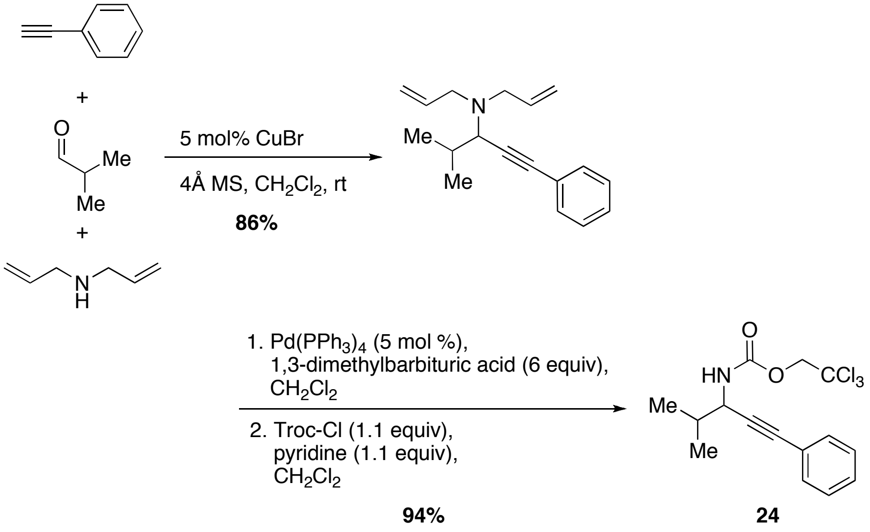


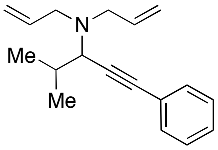
22

In a 100 mL round bottom flask containing a stir bar, tetrakis(triphenylphosphine)palladium(0) (743 mg, 0.642 mmol) and 1,3-dimethylbarbituric acid (12.0 g, 77.1 mmol) were dissolved in 25 mL of dichloromethane. A solution of *N*,*N*-diallyl-2-methylnon-4-yn-3-amine (3.00 g, 12.9 mmol) in 25 mL of dichloromethane was added and the reaction was stirred for 19 hours under nitrogen. The solvent was removed in vacuo and 100 mL of Et_2O was added. The solution was transferred to a separatory funnel and extracted with 2N HCl. The layers were separated, and the aqueous layer was poured into a 500 mL beaker. Dichloromethane (100 mL) was added, and saturated aqueous potassium carbonate was added slowly to pH 10. The mixture was poured into a separatory funnel and the layers were separated. The organic layer was dried over $MgSO_4$ and filtered. The solvent was removed in vacuo, and the crude residue was dissolved in 100 mL of dichloromethane in a 250 mL round bottom flask. A stir bar was added. While stirring, 2,2,2-trichloroethyl chloroformate (1.78 mL, 13.2 mmol) and pyridine (1.07 mL, 13.2 mmol) were added slowly. The reaction was stirred under nitrogen for 19 hours, and the solution was successively washed with 100 mL each of 10% citric acid, saturated aqueous sodium bicarbonate, and brine. The organic layer was dried over $MgSO_4$ and filtered. The solvent was removed in vacuo, and the crude material was purified by silica gel chromatography (1 CV hexanes, 4 CV 10% EtOAc/hexanes) to afford the title compound (3.23 g, 77% yield) as a white crystalline solid. **TLC R*f*** = 0.51 (1:1 $CHCl_3$/hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) *δ* 5.16 (d, *J* = 8.3, 1H), 4.78 (d, *J* = 12.0, 1H), 4.68 (d, *J* = 12.1, 1H), 4.34 (ddd, *J* = 7.3, 4.7, 2.0, 1H), 2.19 (td, *J* = 7.0, 2.1, 2H), 1.99 – 1.87 (m, 1H), 1.54 – 1.34 (m, 4H), 0.99 (d, *J* = 6.8, 6H), 0.91 (t, *J* = 7.2, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) *δ* 153.7, 95.5, 85.0, 76.9, 74.5, 49.9, 33.1, 30.7, 21.9, 18.7, 18.2, 17.5, 13.5. **IR** (thin film) ν 3448, 3330, 2962, 2929, 2872, 1724, 1524, 1467, 1230, 1136, 1029, 821, 727 cm^{-1}; **HRMS** calcd for $[C_{13}H_{20}Cl_3NO_2\ Na]^+$ requires *m/z* 350.0452; found 350.0454 (ESI+).

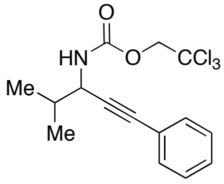
2,2,2-Trichloroethyl 4-methyl-1-phenylpent-1-yn-3-ylcarbamate (Table 1, compound 24):

This substrate was prepared using procedures from the literature.[ix, x]





A 100 mL round bottom flask was charged with 4Å molecular sieves and a stir bar, capped with a septum, flame-dried, and flushed with nitrogen. To the flask was added copper(I) bromide (351 mg, 2.45 mmol) and 50 mL dichloromethane. The mixture was stirred for 1 hour, after which freshly distilled phenylacetylene (5.4 mL, 49 mmol), freshly distilled isobutyraldehyde (4.5 mL, 49 mmol), and diallylamine (6.0 mL, 49 mmol) were added via syringe. After 15 hours of stirring under nitrogen, the reaction was poured into a 250 mL separatory funnel and quenched with 20 mL of saturated aqueous ammonium chloride. The layers were separated, and the aqueous layer was extracted with dichloromethane (3 x 50 mL). The organic layers were combined and washed with brine. The brine wash was extracted with 50 mL dichloromethane, and the combined organic layers were dried over sodium sulfate, filtered, and concentrated in vacuo. The crude residue was purified by flash column chromatography on silica gel (1:1 CHCl$_3$/hexanes) to afford *N*,*N*-diallyl-4-methyl-1-phenylpent-1-yn-3-amine (9.865 g, 86% yield) as a slightly yellow oil. **TLC R$_f$** = 0.31 (1:1 CHCl$_3$/hexanes); **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.47 – 7.39 (m, 2H), 7.34 – 7.27 (m, 3H), 5.84 (dddd, J = 17.3, 10.2, 8.2, 4.2, 2H), 5.23 (d, J = 17.3, 2H), 5.11 (dtd, J = 10.2, 1.9, 0.7, 2H), 3.32 (dddd, J = 14.3, 4.0, 1.9, 1.9, 2H), 3.23 (d, J = 10.2, 1H), 2.94 (dd, J = 14.3, 8.2, 2H), 1.88 (sept d, J = 10.2, 6.6, 1H), 1.09 (d, J = 6.6, 3H), 1.01 (d, J = 6.6, 3H); **^{13}C NMR** (126 MHz, CDCl$_3$) δ 137.2, 131.9, 127.9, 124.0, 117.0, 88.0, 85.7, 77.43, 60.4, 54.3, 31.4, 21.0, 20.2; **IR** (thin film) ν 3706, 2974, 2958, 2921, 2868, 1642, 1487, 1442, 1262, 1160, 1099, 993, 915, 751, 686 cm^{-1}; **HRMS** calcd for $[C_{18}H_{23}N\ H]^+$ requires *m/z* 254.1903; found 254.1900 (ESI+).



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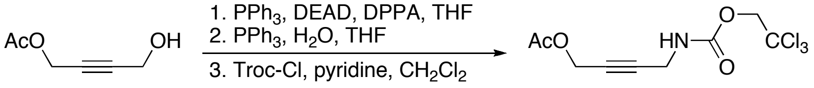
In a 100 mL round bottom flask containing a stir bar, tetrakis(triphenylphosphine)palladium(0) (684 mg, 0.592 mmol) and 1,3-dimethylbarbituric acid (10 g, 64.0 mmol) were dissolved in 25 mL of dichloromethane. A solution of *N*,*N*-diallyl-4-methyl-1-phenylpent-1-yn-3-amine (3.00 g, 11.8 mmol) in 25 mL of dichloromethane was added and the reaction was stirred for 18 hours under nitrogen. The solvent was removed in vacuo and 100 mL of Et_2O was added. The solution was transferred to a separatory funnel and extracted with 2N HCl. The layers were separated, and the aqueous layer was poured into a 500 mL beaker. Dichloromethane (100 mL) was added, and saturated aqueous potassium carbonate was added slowly to pH 10. The mixture was poured into a separatory funnel and the layers were separated. The organic layer was dried over $MgSO_4$ and filtered. The solvent was removed in vacuo, and 2.050 g of the crude residue was dissolved in 100 mL of dichloromethane in a 250 mL round bottom flask containing a stir bar. While stirring, 2,2,2-trichloroethyl chloroformate (1.75 mL, 13.0 mmol) and pyridine (1.05 mL, 13.0 mmol) were added slowly. The reaction was stirred under nitrogen for 15 hours, and the solution was successively washed with 100 mL each of 10% citric acid, saturated aqueous sodium bicarbonate, and brine. The organic layer was dried over $MgSO_4$ and filtered. The solvent was removed in vacuo, and the crude material was purified by silica gel chromatography (1.5 CV 20% EtOAc/hexanes, 5 CV 33% EtOAc/hexanes) to afford the title compound (3.877 g, 94% yield) as a yellow crystalline solid. **TLC R$_f$** = 0.15 (1:1 $CHCl_3$/hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.42 (m, 2H), 7.31 (m, 3H), 5.33 (d, *J* = 8.6, 1H), 4.81 (d, *J* = 12.0, 1H), 4.70 (d, *J* = 12.0, 1H), 4.61 (dd, *J* = 8.6, 5.7, 1H), 2.05 (sept d, *J* = 6.8, 5.7, 1H), 1.07 (d, *J* = 6.8, 6H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 154.0, 131.9, 128.6, 128.5, 122.7, 95.7, 86.5, 84.7, 74.9, 50.5, 33.5, 19.0, 18.0; **IR** (thin film) ν 3432, 3411, 3326, 3056, 2962, 2921, 2868, 1720, 1524, 1230, 1127, 1033, 825, 805, 756, 723, 686 cm^{-1}; **HRMS** calcd for $[C_{15}H_{16}Cl_3NO_2\ Na]^+$ requires *m/z* 370.0139; found 370.0141 (ESI+).

4-((2,2,2-Trichloroethoxy)carbonylamino)but-2-ynyl acetate (Scheme 3, compound 29):



6% **29**

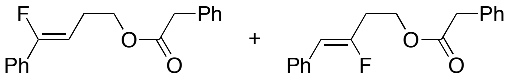
In a 250 mL round bottom flask equipped with a stir bar, 4-hydroxybut-2-ynyl acetate[xi] (1.00 g, 7.80 mmol) was dissolved in THF (150 mL) and cooled to 0 °C under nitrogen. While stirring, triphenylphosphine (4.09 g, 15.6 mmol), diethyl azodicarboxylate (2.50 mL, 15.6 mmol), and diphenylphosphoryl azide (3.40 mL, 15.6 mmol) were added. After 15 hours, the solvent was removed in vacuo and the crude residue was semi-purified by flash column chromatography (1:1 $CHCl_3$/hexanes) to afford 2.637 g of a mixture of 4-azidobut-2-ynyl acetate and triphenylphosphine oxide. Without further purification, 1.195 g of the mixture was dissolved in THF (500 mL) in a 1 L round bottom flask equipped with a stir bar. While stirring, triphenylphosphine (10.2 g, 38.9 mmol) was added, followed by water (6.0 mL). The reaction was refluxed for 12 hours, and the solvent was removed in vacuo. The crude residue was semi-purified by flash column chromatography (10 – 20% MeOH/CH_2Cl_2) to afford 272 mg of a complex mixture of products, which was carried forward without further purification. The mixture was dissolved in dichloromethane (15 mL) and cooled to 0 °C in a 25 mL round bottom flask under nitrogen. Pyridine (190 μL, 2.4 mmol) and 2,2,2-trichloroethyl chloroformate (320 μL, 2.4 mmol) were added, and the reaction was stirred for 36 hours. The solvent was removed in vacuo, and the crude residue was purified by flash column chromatography (2 CV 1% MeOH/CH_2Cl_2, 2 CV 5% MeOH/CH_2Cl_2) to afford the title compound (144 mg, 6% yield) as a brown oil. **TLC R_f** = 0.32 (9:1 CH_2Cl_2/MeOH); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.60 (br s, 1H), 4.82 (t, J = 1.9 Hz, 2H), 4.79 (s, 2H), 4.09 (dt, J = 5.3, 1.9 Hz, 2H), 2.02 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.2, 153.5, 94.3, 84.5, 77.1, 75.7, 56.7, 29.3, 23.0; **IR** (thin film) ν 3273, 3064, 2958, 1765, 1655, 1536, 1438, 1385, 1364, 1275, 1234, 1152, 960, 899, 817, 780, 723 cm^{-1}; **HRMS** calcd for $[C_9H_{10}Cl_3NO_4\,Na]^+$ requires m/z 323.9568; found 323.9562 (ESI+).

III. Synthesis and Characterization of Fluoroalkenes

General Procedure A. To a 2 mL polypropylene microcentrifuge tube were added alkyne substrate (0.40 mmol), $PhNMe_2$•HOTf (11 mg, 0.010 mmol), and a stir bar. In the glove box, 1,3-bis(2,6-di-isopropylphenyl)imidazol-2-ylidenegold(I)chloride (6 mg, 0.010 mmol) and silver tetrafluoroborate (2 mg, 0.011 mmol) were added, and the tube was capped. At the bench, a nitrogen line was inserted through the tube cap using a needle, and 0.75 mL of dichloromethane was added via syringe through the tube cap. After stirring in the dark for 5 minutes, the tube was opened to air, and potassium hydrogen sulfate (40 mg, 0.040 mmol) and triethylamine trihydrogen fluoride (100 μL, 0.060 mmol) were added. The tube was closed with a new cap, and the reaction was stirred in the dark for 15 hours. The tube was opened and the reaction mixture was transferred to a 15 mL polypropylene centrifuge tube. Dichloromethane (5 mL) was added, and the reaction was quenched and washed with 5 mL of saturated aqueous sodium bicarbonate in a separatory funnel. The layers were separated, and the aqueous layer was extracted with 5 mL of dichloromethane. The organic layers were combined, washed with brine, dried over $MgSO_4$, and filtered. The solvent was removed in vacuo. The crude residue was assayed by ^1H and ^{19}F NMR in $CDCl_3$ or CD_2Cl_2 to determine the stereo- and regioisomeric ratios of the products, which were typically inseparable and are reported below as mixtures unless otherwise noted. The minor product (if formed) was not isolated; however, all of its clearly resolved diagnostic resonances in the ^1H and ^{19}F NMR of the product mixtures are listed.

General Procedure B. The reaction was performed per General Procedure A above, except that the reaction was quenched by adding excess Cs_2CO_3 to the diluted reaction mixture until gas evolution ceased. The mixture was filtered through celite, which was subsequently rinsed with dichloromethane (5 mL). The solvent was removed in vacuo. The crude residue was assayed by ^1H and ^{19}F NMR in $CDCl_3$ or CD_2Cl_2 to determine the stereo- and regioisomeric ratios of the products, which were typically inseparable and are reported below as mixtures unless otherwise noted. The minor product (if formed) was not isolated; however, all of its clearly resolved diagnostic resonances in the ^1H and ^{19}F NMR of the product mixtures are listed.

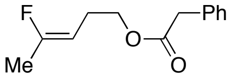
Hydrofluorination of 4-phenylbut-3-ynyl 2-phenylacetate (Scheme 2, Eq 2):



2a **2b**

This reaction was performed using General Procedure A, except that an internal NMR standard solution (C_6F_6 in CD_2Cl_2) was added directly to the reaction mixture immediately upon completion of the reaction (i.e. before workup). The combined yield of the regioisomers (72%, 40:60 **2a**/**2b**) was determined by integration of the peaks in the ^{19}F NMR spectrum of the mixture. (The starting material and products for this reaction were inseparable by column chromatography.) **TLC R_f** = 0.36 (4:1 hexanes/$CHCl_3$); **^{19}F NMR** (376 MHz, CD_2Cl_2) **2a**: δ -103.7 (dt, J = 39.6, 18.4, 1F); **2b**: δ -119.3 (d, J = 37.2, 1F).

Hydrofluorination of pent-3-ynyl 2-phenylacetate (Scheme 2, Eq 2):



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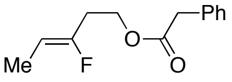
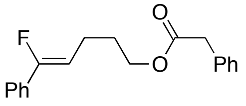


4a **4b**

This reaction was performed using General Procedure A. The crude product was purified by flash column chromatography (10 – 20% EtOAc/hexanes) to give the two regioisomers (91:9 **4a**/**4b**) in 50% combined yield as a clear oil. **TLC R_f** = 0.38 (9:1 hexanes/EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) **4a**: δ 7.43 – 7.19 (m, 5H), 4.43 (dtd, J = 36.7, 7.4, 0.9, 1H), 4.06 (t, J = 6.7, 2H), 3.61 (s, 2H), 2.36 (dt, 6.8, 6.8, 2H), 1.84 (ddd, J = 16.7, 2.1, 1.03, 3H); **4b**: δ 4.58 – 4.35 (dq, J = 37.5, 6.6, 1H, overlapped), 4.20 (t, J = 6.6, 2H), 3.71 (s, 2H), 2.44 (dt, J = 17.9, 6.6, 2H), 1.54 (ddt, J = 6.9, 2.3, 1.1, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) **4a**: δ 171.5, 158.0 (d, J = 253.2), 134.0, 129.2, 128.5, 127.0, 100.6 (d, J = 15.3), 63.9 (d, J = 2.0), 41.3, 23.4 (d, J = 5.3), 17.7 (d, J = 30.2); **^{19}F NMR** (376 MHz, $CDCl_3$) **4a**: δ -100.6 (dqt, J = 36.7, 16.7, 1.7, 1F); **4b**: δ -112.4 (dtq, J = 37.7, 17.8, 2.3, 1F); **IR** (ATR-IR) ν 2924, 1735, 1507, 1210, 1149, 1011, 825, 697, 504 cm^{-1}; **HRMS** calcd for $[C_{13}H_{15}FO_2\,H]^+$ requires *m/z* 223.1129; found 223.1126 (ESI+).

Hydrofluorination of 5-phenylpent-4-ynyl 2-phenylacetate (Scheme 2, Eq 3):



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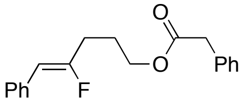
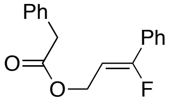


6a **6b**

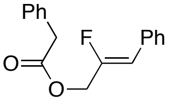
This reaction was performed using General Procedure A. The crude product was purified by flash column chromatography (9:1 hexanes/Et_2O) to give the two regioisomers (19:81 **6a**/**6b**) in 60% combined yield as a yellow oil. **TLC R_f** = 0.15 (9:1 hexanes/EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$) **6a**: δ 5.36 (dt, J = 37.0, 7.7, 1H), 4.15 (t, J = 6.5, 2H); **6b**: δ 7.53 – 7.07 (m, 10H, overlapped), 5.40 (d, J = 39.3, 1H), 4.17 (t, J = 6.3, 2H), 3.63 (s, 2H), 2.34 (dt, J = 18.6, 7.4, 2H), 1.93 (tt, J = 7.4, 6.4, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) **6b**: δ 171.5, 159.5 (d, J = 266.2), 134.1, 133.5, 129.2, 128.6, 128.4, 128.3 (d, J = 7.3), 127.1, 126.8, 106.5 (d, J = 8.6), 63.6, 41.5, 29.7 (d, J = 27.3), 25.5; **^{19}F NMR** (376 MHz, $CDCl_3$) **6a**: δ -120.0 (d, J = 36.8, 1F); **6b**: δ -102.2 (dt, J = 39.3, 18.5, 1F); **IR** (ATR-IR) ν 3030, 2959, 1734, 1690, 1495, 1214, 1146, 1005, 694 cm^{-1}; **HRMS** calcd for $[C_{19}H_{19}FO_2\,Na]^+$ requires *m/z* 321.1261; found 321.1259 (ESI+).

Hydrofluorination of 3-phenylprop-2-ynyl 2-phenylacetate (Scheme 2, Eq 4):



8a

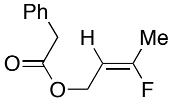
+



8b

This reaction was performed using General Procedure A. The crude product was purified by flash column chromatography (100% toluene) to give the two regioisomers (90:10 **8a**/**8b**) in 34% combined yield as a clear oil. **TLC R$_f$** = 0.42 (toluene); **^{1}H NMR** (400 MHz, CDCl$_3$) **8a**: *δ* 7.60 – 7.20 (m, overlapped, 10H), 5.61 (dt, *J* = 35.2, 7.4, 1H), 4.88 (dd, *J* = 7.4, 2.0, 2H), 3.66 (s, 2H); **8b**: *δ* 5.78 (d, *J* = 37.4, 1H), 4.75 (d, *J* = 17.1, 2H), 3.70 (s, 2H); **^{13}C NMR** (126 MHz, CDCl$_3$) *δ* 171.5, 159.7 (d, *J* = 250.5), 133.8, 129.6, 129.3, 128.6, 128.53, 128.51, 127.1, 124.6 (d, *J* = 7.2), 99.9, 99.8, 58.2, 58.1, 41.2; **^{19}F NMR** (376 MHz, CDCl$_3$) **8a**: *δ* -114.7 (d, *J* = 35.2, 1F); **8b**: *δ* -111.4 (dt, *J* = 37.5, 17.2, 1F); **IR** (ATR-IR) ν 3063, 3031, 2949, 1732, 1682, 1496, 1448, 1240, 1139, 993, 969, 761, 689 cm^{-1}; **HRMS** calcd for $[C_{17}H_{15}FO_2\,Na]^+$ requires *m/z* 293.0948; found 293.0946 (ESI+).

Hydrofluorination of but-2-ynyl 2-phenylacetate (Scheme 2, Eq 5):



10

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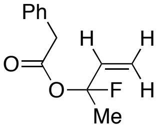
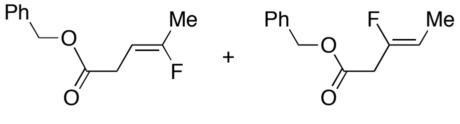


11

The reaction was performed using General Procedure A. The crude product (95:5 **10**/**11**) was purified by flash column chromatography (CHCl$_3$) to give **10** in 49% yield as a clear oil. **TLC R$_f$** = 0.52 (CHCl$_3$); **^{1}H NMR** (400 MHz, CDCl$_3$) **10**: *δ* 7.56 – 6.92 (m, 5H), 4.80 (dt, *J* = 34.5, 7.1, 1H), 4.65 (d, *J* = 8.1, 2H), 3.62 (s, 2H), 1.92 (d, *J* = 16.9, 3H); **11**: *δ* 6.13 (ddd, *J* = 17.5, 13.6, 11.0, 1H), 5.44 (dd, *J* = 17.5, 1.5, 1H), 5.28 (d, *J* = 11.0, 1H), 3.63 (s, 2H), 1.75 (d, *J* = 19.2, 3H); **^{13}C NMR** (126 MHz, CDCl$_3$) **10**: *δ* 171.5, 159.4 (d, *J* = 263.8), 133.9, 129.2, 128.5, 127.1, 100.6 (d, *J* = 12.9), 57.93 (d, *J* = 8.2), 41.2, 17.9 (d, *J* = 28.8); **^{19}F NMR** (376 MHz, CDCl$_3$) **10**: *δ* -96.0 (dqt, *J* = 34.4, 17.5, 1.8, 1F); **11**: *δ* -104.6 (qd, *J* = 19.5, 13.3, 1F); **IR** (ATR-IR) ν 3035, 2924, 1736, 1714, 1497, 1454, 1384, 1244, 1188, 1149, 983, 696 cm^{-1}; **HRMS** calcd for $[C_{12}H_{13}FO_2\,Na]^+$ requires *m/z* 231.0792; found 231.0789 (ESI+).

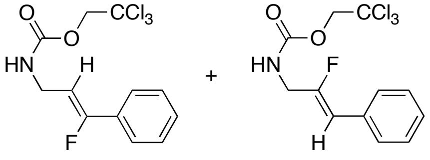
Hydrofluorination of benzyl pent-3-ynoate (Scheme 2, Eq 6):



13a **13b**

This reaction was performed using General Procedure B. The crude product was purified by flash column chromatography using a Biotage SP4 flash purification system (5 CV hexanes, 0 – 15% Et_2O/hexanes over 20 CV) to give the two regioisomers (95:5 **13a**/**13b**) in 26% combined yield as a clear oil. **TLC** $\mathbf{R}_f$ = 0.49 (toluene); ^{1}**H NMR** (400 MHz, $CDCl_3$) **13a**: δ 7.45 – 7.26 (m, 5H), 5.13 (s, 2H), 4.76 (dt, J = 35.8, 7.1, 1H), 3.17 (d, J = 7.2, 2H), 1.91 (d, J = 16.7, 3H); **13b**: δ 7.42 – 7.27 (m, 5H), 5.16 (s, 2H), 4.83 – 4.67 (1H, overlapped), 3.22 (d, J = 18.6, 2H), 1.92 – 1.86 (d, J = 8.7, 3H, overlapped); ^{13}**C NMR** (126 MHz, $CDCl_3$) δ **13a**: δ 171.4, 158.4 (d, J = 254.9), 135.8, 128.5, 128.24, 128.20, 97.5 (d, J = 14.3), 66.5, 29.4 (d, J = 6.0), 17.8 (d, J = 29.5); ^{19}**F NMR** (376 MHz, $CDCl_3$) **13a**: δ -99.09 (dqt, J = 33.6, 16.7, 1.7, 1F), **13b**: δ -109.79 (dtq, J = 36.2, 18.5, 2.3, 1F); **IR** (ATR-IR) ν 3035, 2956, 1737, 1456, 1385, 1348, 1287, 1151, 1002, 940, 752, 698 cm^{-1}; **HRMS** calcd for $[C_{12}H_{13}FO_2\,Na]^+$ requires *m/z* 231.0792; found 231.0789 (ESI+).

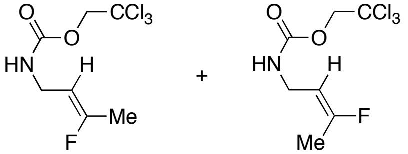
Hydrofluorination of 2,2,2-Trichloroethyl 3-phenylprop-2-ynylcarbamate (Table 1, entry 1):



15 **15b**

The reaction was performed using General Procedure A. The crude product was purified by flash column chromatography (10% EtOAc/hexanes) to give the two regioisomers (92:8 **15**/**15b**) in 73% combined yield as a white crystalline solid. **TLC** $\mathbf{R}_f$ = 0.40 ($CHCl_3$); ^{1}**H NMR** (500 MHz, $CDCl_3$) **15** major rotamer: δ 7.60 – 7.29 (m, 5H, overlapped), 5.55 (dt, J = 36.0, 7.3, 1H), 5.19 (s, 1H), 4.75 (s, 2H), 4.12 (m, J = 13.4, 1.6, 2H, overlapped); **15b**: δ 5.86 (m, 1H), 5.37 (s, 1H), 4.76 (s, 2H), 4.25 – 4.03 (m, 3H); ^{13}**C NMR** (126 MHz, $CDCl_3$) δ 158.8 (d, J = 252.2), 154.6, 131.5 (d, J = 30.3), 129.4, 128.5 (d, J = 1.9), 124.3 (d, J = 7.0), 101.6 (d, J = 15.5), 95.5, 74.6, 35.6; ^{19}**F NMR** (376 MHz, $CDCl_3$) **15** major rotamer: δ -117.2 (d, J = 36.0, 1F); **15b**: δ -110.51 (dt, J = 38.5, 14.7, 1F); **IR** (ATR-IR) ν 3333, 3020, 2958, 1704, 1515, 1490, 1231, 1143, 1034, 985, 815, 716, 689 cm^{-1}; **HRMS** calcd for $[C_{12}H_{11}Cl_3FNO_2\,H]^+$ requires *m/z* 324.9912; found 325.9908 (ESI+).

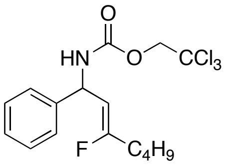
Hydrofluorination of 2,2,2-Trichloroethyl but-2-ynylcarbamate (Table 1, entry 2):



17 **17b**

The reaction was performed using General Procedure B, except that additional Et_3N•3HF (40 μL, 0.24 mmol) was added after 18.5 hours. After an additional 22 hours of stirring, the reaction was deemed complete by TLC. The reaction mixture was assayed by NMR using an internal NMR standard (66% combined yield, 76:24 **17**/**17b**) and worked up per General Procedure B. The crude residue was semi-purified by flash column chromatography using a Biotage SP4 flash purification system (5 CV toluene, 0 – 20% acetone/toluene over 5 CV, 20 – 100% acetone/toluene over 3 CV). A portion of the isolated residue was purified by preparative TLC to give the two stereoisomers (**17** and **17b**) as a yellowish oil. **^{1}H NMR** (400 MHz, $CDCl_3$) **17**: *δ* 4.98 (br s, 1H), 4.72 (s, 2H), 4.72 (dt, *J* = 35.6, 7.2, 1H), 3.88 (dd, *J* = 7.2, 6.6, 2H), 1.91 (d, *J* = 16.9, 3H); **17b**: δ 5.14 (dt, *J* = 19.9, 8.3, 1H), 3.80 (dd, *J* = 7.6, 6.1, 2H), 1.97 (d, *J* = 17.7, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) **17** and **17b**: *δ* 160.4, 154.5, 101.9, 101.8, 95.6, 74.6, 35.2, 17.9, 17.7; **^{19}F NMR** (376 MHz, $CDCl_3$) **17**: *δ* -99.8 (dq, *J* = 34.4, 17.1, 1F); **17b**: *δ* -92.1 (dq, *J* = 18.2, 18.2, 1F); **IR** (ATR-IR) ν 3334, 2950, 1712, 1516, 1242, 1142, 1021, 816, 726 cm^{-1}; **HRMS** calcd for $[C_7H_9Cl_3FNO_2\,H]^+$ requires *m/z* 263.9756; found 263.9767 (ESI+).

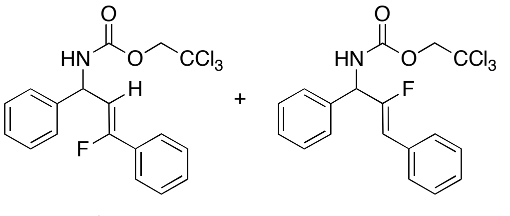
Hydrofluorination of 2,2,2-trichloroethyl 1-phenylhept-2-ynylcarbamate (Table 1, entry 3):



19

This reaction was performed using General Procedure B. The crude product was purified by flash column chromatography using a Biotage SP4 flash purification system (5 CV hexanes, 0 – 20% Et_2O/hexanes over 25 CV) to give the expected product **19** in 60% yield as a white solid. **TLC R*f*** = 0.29 (toluene); **^{1}H NMR** (400 MHz, $CDCl_3$) major rotamer: *δ* 7.39 – 7.26 (m, 5H), 5.72 (dd, *J* = 8.5, 8.5, 1H), 5.38 (d, *J* = 6.4, 1H), 4.81 (dd, *J* = 35.4, 8.9, 1H), 4.74 (d, *J* = 12.0, 1H), 4.72 (d, *J* = 12.0, 1H), 2.21 (dt, *J* = 15.5, 7.5, 2H), 1.54 – 1.45 (m, 2H), 1.40 – 1.30 (m, 2H), 0.91 (t, *J* = 7.3, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) *δ* 161.9 (d, *J* = 261.7), 153.7, 141.0, 128.8, 127.6, 126.2, 105.0, 95.5, 74.6, 50.3, 31.6 (d, *J* = 26.3), 28.0, 22.0, 13.7; **^{19}F NMR** (376 MHz, $CDCl_3$) major rotamer: δ -102.4 (dt, J = 34.9, 17.2, 1F); **IR** (ATR-IR) ν 3345, 2959, 2932, 2872, 1719, 1524, 1236, 1141, 1026, 816, 731, 698 cm^{-1}; **HRMS** calcd for [$C_{16}H_{19}Cl_3FNO_2$ H]$^+$ requires *m/z* 382.0538; found 382.0541 (ESI+).

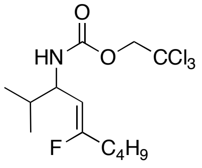
Hydrofluorination of 2,2,2-trichloroethyl 1,3-diphenylprop-2-ynylcarbamate (Table 1, entry 4):



21 **21b**

This reaction was performed using General Procedure A. The crude product was purified by flash column chromatography on silica gel (3 CV hexanes, 3 CV 5% EtOAc/hexanes, 4 CV 10% EtOAc/hexanes) to give the two regioisomers (98:2 **21**/**21b**) in 69% combined yield as a white solid. **TLC R$_f$** = 0.24 (9:1 hexanes/EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) **21** major rotamer: δ 7.64 – 7.13 (m, 10H), 5.94 (dd, J = 8.4, 8.4, 1H), 5.64 (dd, J = 35.3, 8.5, 1H), 5.57 (d, J = 8.4, 1H), 4.76 (d, J = 12.0, 1H), 4.72 (d, J = 12.0, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 158.0 (d, J = 263.9), 153.7, 140.5, 131.3 (d, J = 28.2), 129.5, 128.9, 128.5 (d, J = 1.8), 127.8, 126.3, 124.5 (d, J = 7.2), 105.2 (d, J = 15.5), 95.5, 74.6, 50.6; **^{19}F NMR** (376 MHz, $CDCl_3$) **21** major rotamer: δ -115.0 (d, J = 35.1, 1F); **21b** major rotamer δ -114.1 (dd, J = 38.8, 17.0, 2H); **IR** (ATR-IR) ν 3322, 3062, 3032, 2951, 1708, 1494, 1238, 1143, 1035, 816, 760, 729, 689, 567 cm^{-1}; **HRMS** calcd for [$C_{18}H_{15}Cl_3FNO_2$ Na]$^+$ requires *m/z* 424.0045; found 424.0040 (ESI+).

Hydrofluorination of 2,2,2-trichloroethyl 2-methylnon-4-yn-3-ylcarbamate (Table 1, entry 5):

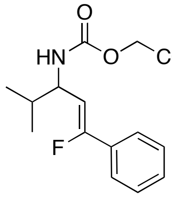


23

This reaction was performed using General Procedure B. The crude product was purified by flash column chromatography using a Biotage SP4 flash purification system (5 CV hexanes, 0 – 20% EtOAc/hexanes over 25 CV) to give **23** in 74% yield as a clear oil. **TLC R$_f$** = 0.67 (4:1 hexanes/EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) major rotamer: δ 5.03 (d, J = 8.7, 1H), 4.77 (d, J

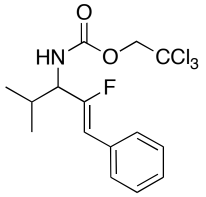
= 11.9, 1H), 4.68 (d, *J* = 12.1, 1H), 4.51 (dd, *J* = 36.4, 9.1, 1H), 4.34 (ddd, *J* = 8.7, 8.7, 7.0, 1H), 2.23 – 2.12 (m, 2H), 1.90 – 1.76 (m, 1H), 1.54 – 1.42 (m, 2H), 1.40 – 1.29 (m, 2H), 0.94 (d, *J* = 6.8, 3H), 0.91 (d, *J* = 6.8, 3H), 0.91 (t, *J* = 7.3, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.8 (d, *J* = 259.2), 153.9, 103.6 (d, *J* = 14.0), 95.7, 74.4, 52.3, 32.7, 31.6 (d, *J* = 27.0), 28.1 (d, *J* = 1.0), 21.9, 18.6, 18.2, 13.7; **^{19}F NMR** (376 MHz, $CDCl_3$) major rotamer: δ -102.8 (dt, *J* = 36.4, 17.6, 1F); **IR** (ATR-IR) ν 3463, 3345, 2961, 2875, 1724, 1508, 1265, 1223, 1120, 815, 732 cm^{-1}; **HRMS** calcd for $[C_{13}H_{21}Cl_3FNO_2\ H]^+$ requires *m/z* 348.0695; found 348.0683 (ESI+).

Hydrofluorination of 2,2,2-trichloroethyl 4-methyl-1-phenylpent-1-yn-3-ylcarbamate (Table 1, entry 6):



25

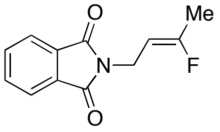
+



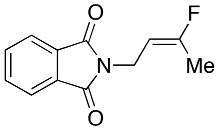
25b

This reaction was performed using General Procedure B. The crude product was purified by flash column chromatography on silica gel (2.5 CV hexanes, 2.5 CV 5% Et_2O/hexanes, 5 CV 10% Et_2O/hexanes) to give each of the two regioisomers (92:8 **25**/**25b**) as white solids in 65% combined yield. **TLC R_f** **25** = 0.50 (4:1 hexanes/EtOAc); **25b** = 0.59 (4:1 hexanes/EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) **25** major rotamer: δ 7.57 – 7.47 (m, 2H), 7.41 – 7.32 (m, 3H), 5.37 (dd, *J* = 36.1, 9.1, 1H), 5.10 (d, *J* = 7.6, 1H), 4.78 (d, *J* = 11.8, 1H), 4.68 (d, *J* = 12.0, 1H), 4.56 (ddd, *J* = 8.9, 8.9, 6.9, 1H), 2.08 – 1.85 (m, 1H), 1.02 (d, *J* = 6.8, 3H), 0.99 (d, *J* = 6.8, 3H); **25b** major rotamer: δ 7.48 (d, *J* = 7.3, 2H), 7.33 (t, *J* = 7.5, 2H), 7.27 – 7.22 (m, 1H), 5.72 (d, *J* = 39.6, 1H), 5.28 (d, *J* = 9.5, 1H), 4.83 (d, *J* = 12.0, 1H), 4.68 (d, *J* = 12.0, 1H), 4.10 (ddd, *J* = 23.3, 9.4, 8.4, 1H), 2.06 (tt, *J* = 13.7, 6.9, 1H), 1.05 (d, *J* = 6.3, 3H), 1.03 (d, *J* = 6.2, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) **25** major rotamer: δ 158.2 (d, *J* = 251.8), 153.9, 131.7 (d, *J* = 29.0), 129.3, 128.5, 124.4 (d, *J* = 7.1), 104.2 (d, *J* = 15.8), 95.6, 74.5, 52.7, 33.0, 18.7, 18.5; **^{19}F NMR** (376 MHz, $CDCl_3$) **25** major rotamer: δ -114.9 (d, *J* = 36.1, 1F); **25b** major rotamer: δ -117.9 (dd, *J* = 39.6, 23.2, 1F); **IR** (ATR-IR) ν 3321, 2962, 2873, 1715, 1527, 1282, 1241, 1126, 816, 763, 730, 690 cm^{-1}; **HRMS** calcd for $[C_{15}H_{17}Cl_3FNO_2\ H]^+$ requires *m/z* 368.0382; found 368.0374 (ESI+).

Hydrofluorination of 2-(but-2-ynyl)isoindoline-1,3-dione (Table 1, entry 8):



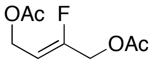
28



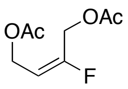
28b

This reaction was performed using General Procedure B with a reaction time of 3 days. The crude product was purified by flash column chromatography using a Biotage SP4 flash purification system (5 CV hexanes, 0 – 10% EtOAc/hexanes over 10 CV, 10 – 50% EtOAc/hexanes over 5 CV) to give the two stereoisomers (85:15 **28**/**28b**) in 53% combined yield as a white solid. **TLC R$_f$** = 0.38 (4:1 hexanes/EtOAc); **^{1}H NMR** (400 MHz, CDCl$_3$) **28**: δ 7.87 – 7.81 (m, 2H), 7.74 – 7.68 (m, 2H), 4.76 (dtq, J = 34.8, 7.0, 0.9, 1H), 4.35 (d, J = 7.0, 2H), 1.89 (ddt, J = 16.8, 0.9, 0.9, 3H); **28b**: δ 7.87 – 7.81 (m, 2H, overlapped), 7.74 – 7.68 (m, 2H, overlapped), 5.24 (dt, J = 19.5, 8.3, 1H), 4.21 (d, J = 8.2, 2H), 2.11 (d, J = 17.9, 3H); **^{13}C NMR** (126 MHz, CDCl$_3$) **28**: δ 167.8, 159.3 (d, J = 258.4), 133.9, 132.2, 123.2, 100.1 (d, J = 13.8), 31.9 (d, J = 8.0), 17.7 (d, J = 29.2); **^{19}F NMR** (376 MHz, CDCl$_3$) **28**: δ -97.2 (dqt, J = 33.5, 16.7, 1.7, 1F); **28b**: δ -89.9 (dq, J = 18.1, 18.1, 1F); **IR** (ATR-IR) ν 3450, 2949, 1702, 1434, 1392, 1326, 1195, 1080, 943, 722, 530 cm^{-1}; **HRMS** calcd for $[C_{12}H_{10}FNO_2\ H]^+$ requires *m/z* 220.0768; found 220.0766 (ESI+).

Hydrofluorination of but-2-yne-1,4-diyl diacetate[xii] (Scheme 3, Eq 8):



31a



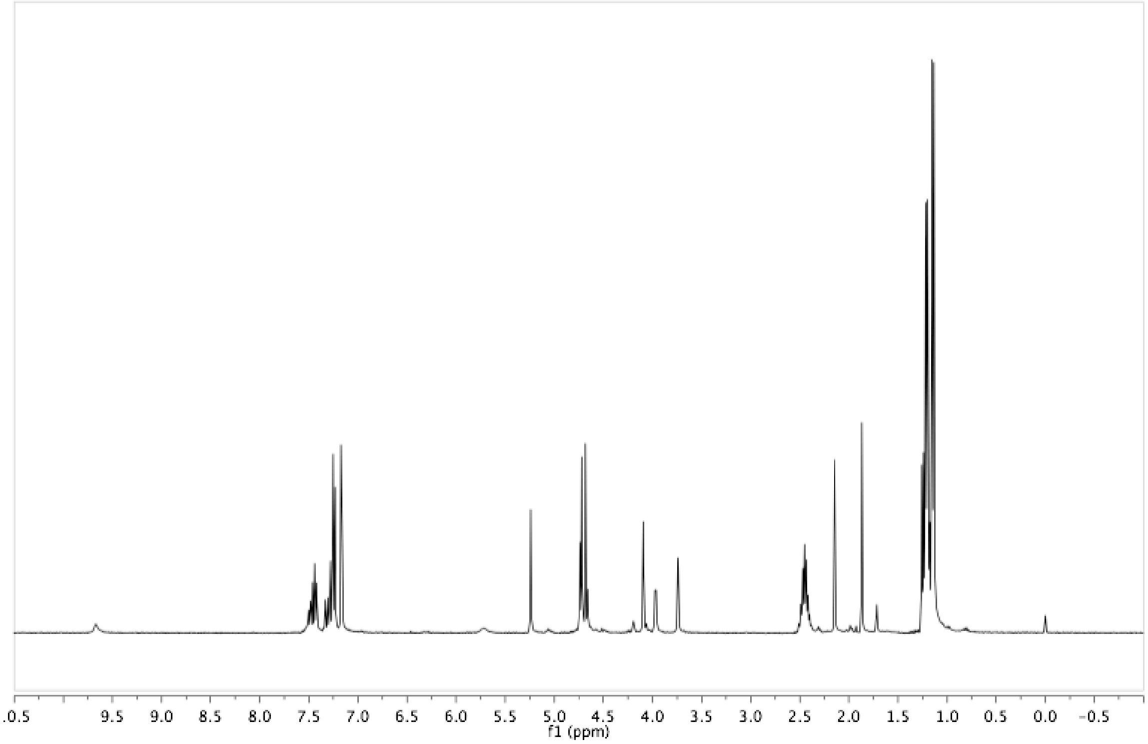
31b

This reaction was performed using General Procedure B, except that an internal NMR standard solution (C_6F_6 in CD_2Cl_2) was added directly to the reaction mixture immediately upon completion of the reaction (i.e. before workup). The combined yield of the regioisomers (19%, 74:60 **31a**/**31b**) was determined by integration of the peaks in the ^{19}F NMR spectrum of the mixture. **^{1}H NMR** (400 MHz, CDCl$_3$) **31a**: δ 5.19 (dt, J = 34.0, 7.2, 1H), 4.69 (dd, J = 7.2, 2.0, 2H), 4.60 (d, J = 15.3, 2H), 2.11 (s, 3H), 2.06 (s, 3H); **31b**: δ 5.52 (dt, J = 17.9, 8.1, 1H), 4.77 (d, J = 20.6, 2H), 4.65 (dd, J = 8.1, 1.4, 2H), 2.11 (s, 3H), 2.06 (s, 3H); **^{19}F NMR** (376 MHz, CDCl$_3$) **31a**: δ -112.4 (dtt, J = 33.0, 15.4, 2.1, 1F); **31b**: δ -104.3 (tdt, J = 20.7, 17.8, 1.6, 1F).

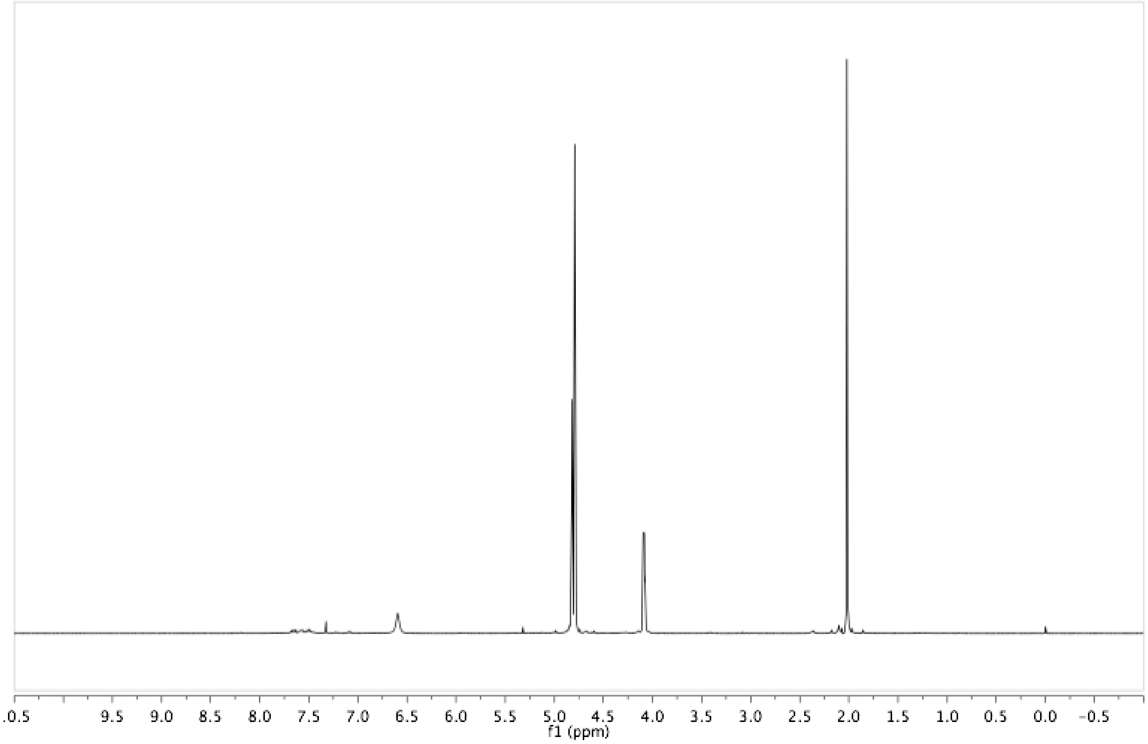
IV. Catalyst Binding Assay.

In the glove box, an NMR tube was charged with 4-((2,2,2-trichloroethoxy)carbonylamino)but-2-ynyl acetate (10 mg, 0.033 mmol), 1,3-bis(2,6-di-isopropylphenyl)imidazol-2-ylidenegold(I)chloride (10 mg, 0.016 mmol) and silver tetrafluoroborate (4 mg, 0.02 mmol). The tube was capped with a septum and wrapped with parafilm. At the bench, a nitrogen line was inserted through the septum with a needle, and 800 μL of CD_2Cl_2 were added. The NMR tube was then shaken several times and wrapped in foil. After 3 hours, a ^1H NMR spectrum was collected (see below.)

^{1}H NMR of catalyst/substrate **29** complex (400 MHz, CD_2Cl_2)

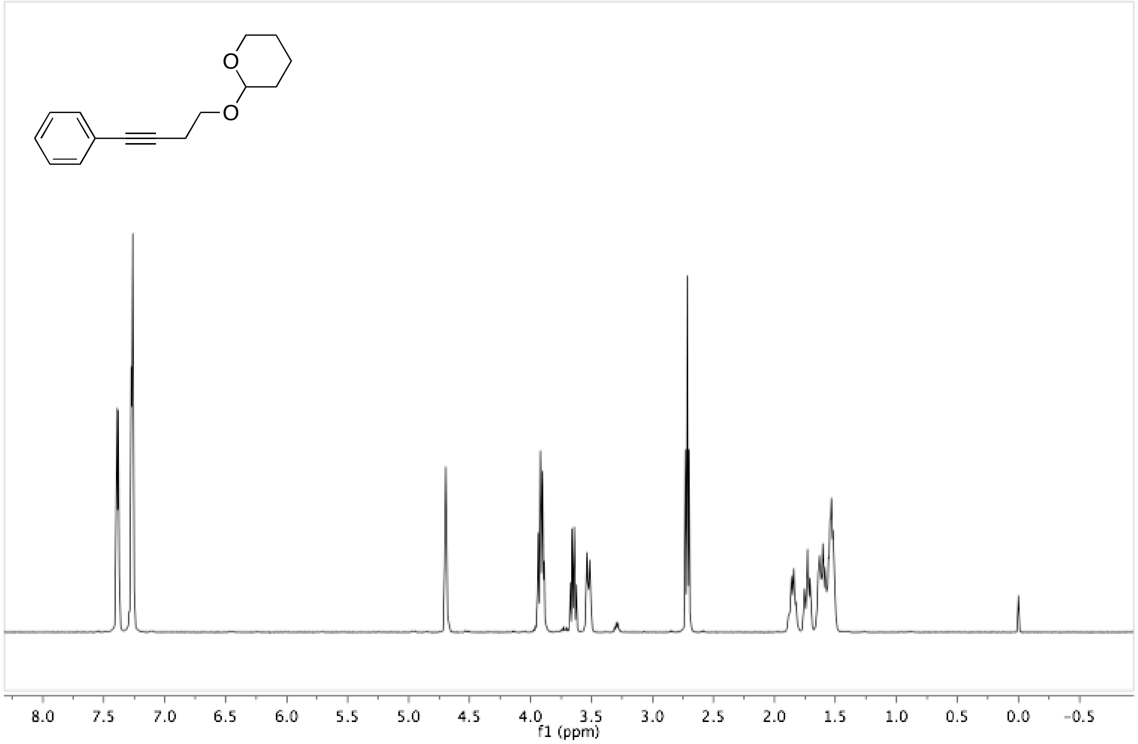


^{1}H NMR of **29** (400 MHz, $CDCl_3$)

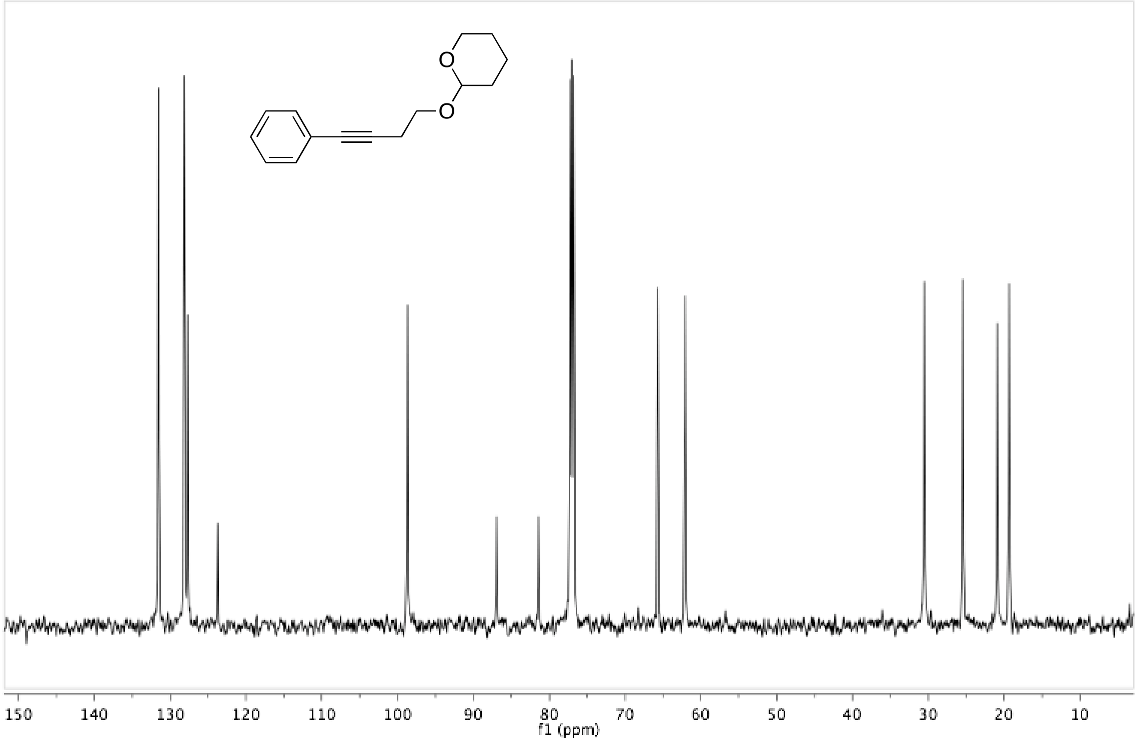


V. ^{1}H NMR, ^{19}F NMR, and ^{13}C NMR Spectra for Characterized Compounds

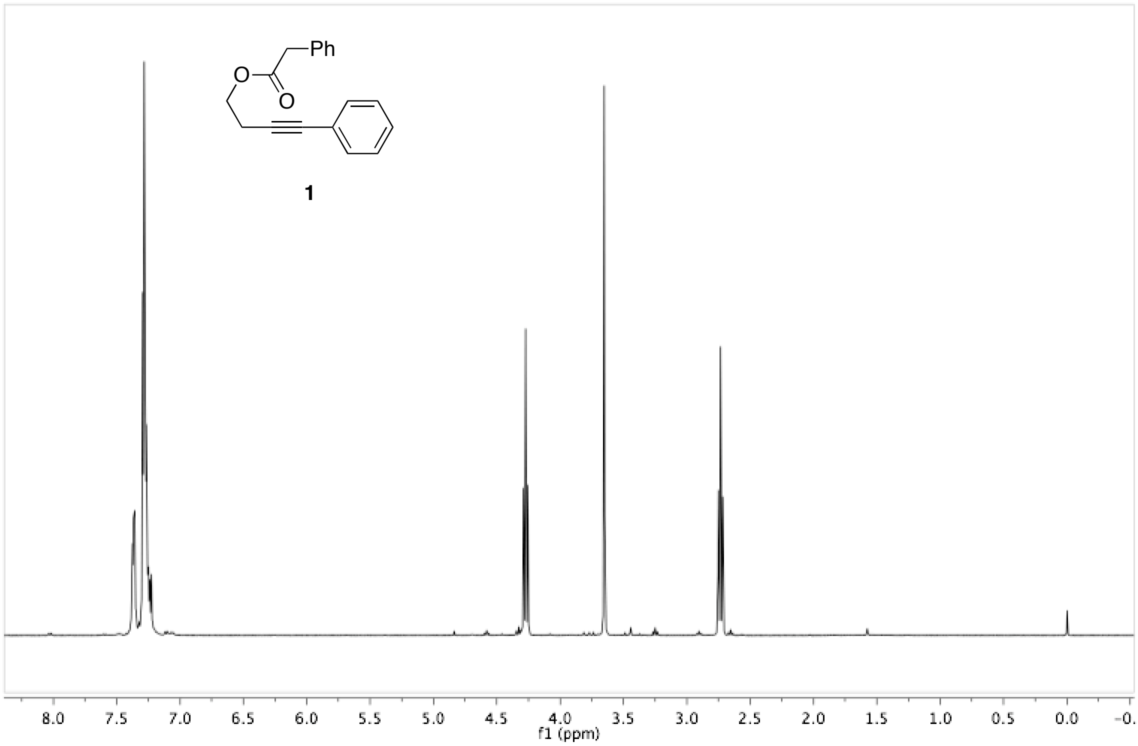
^{1}H NMR (CDCl$_3$, 500 MHz)



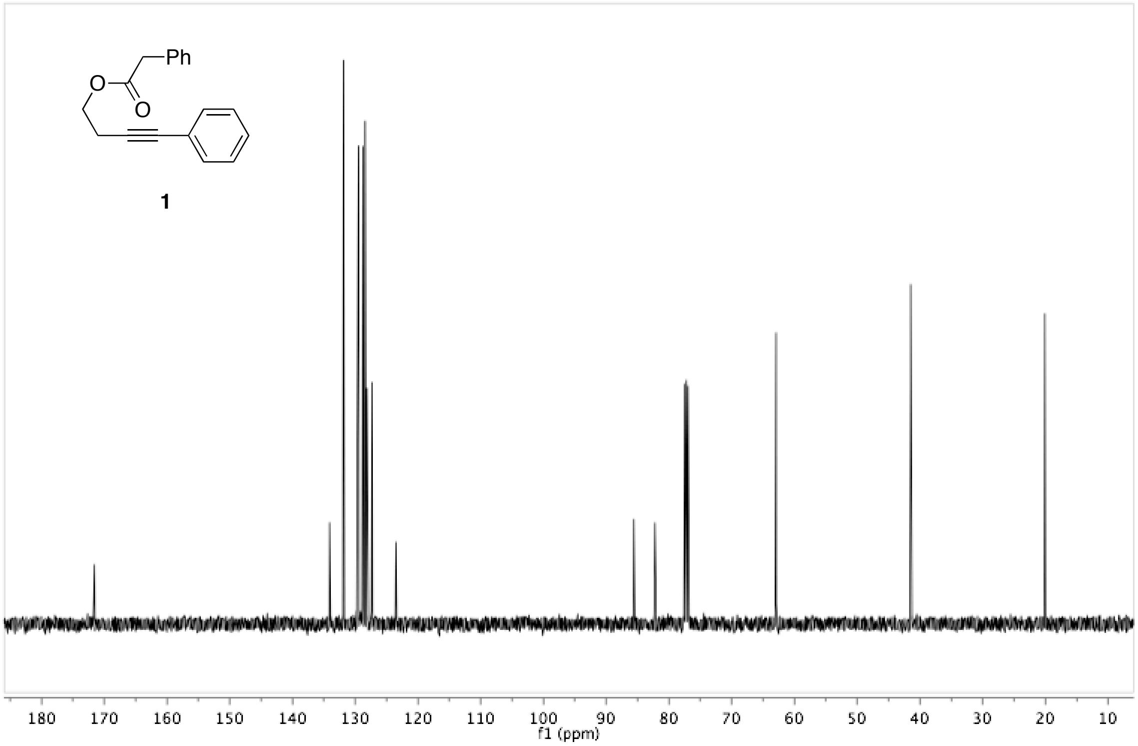
^{13}C NMR (CDCl$_3$, 126 MHz)



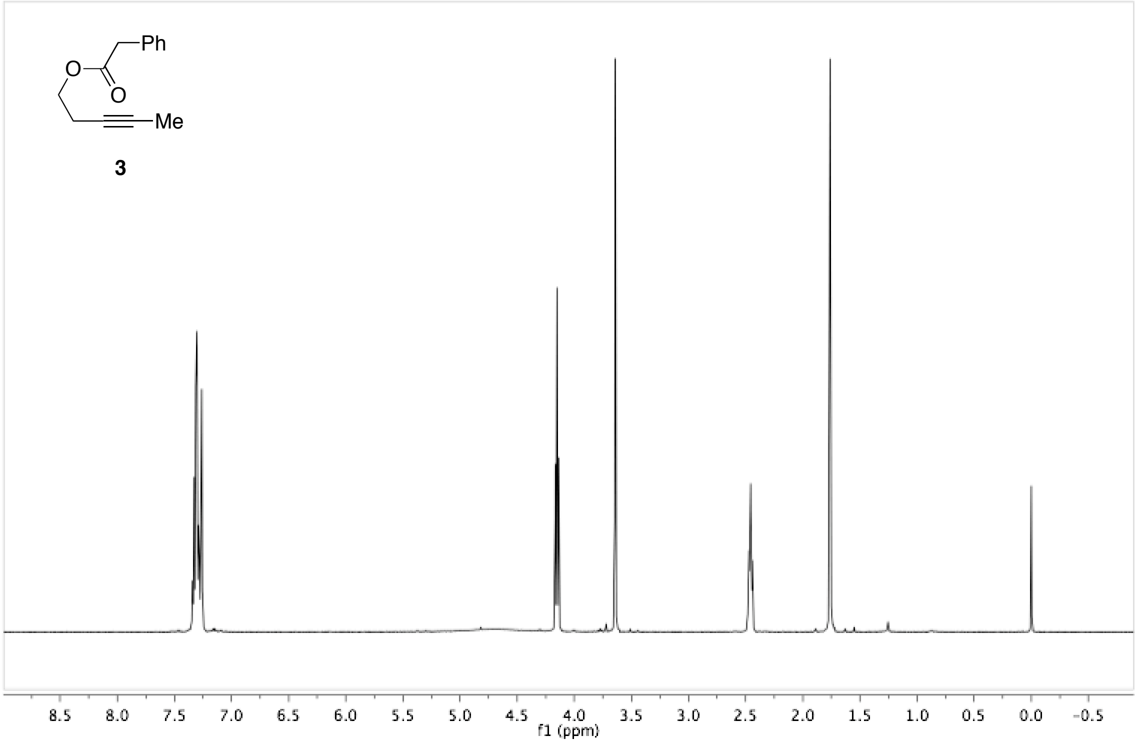
^{1}H NMR (CDCl$_3$, 400 MHz)



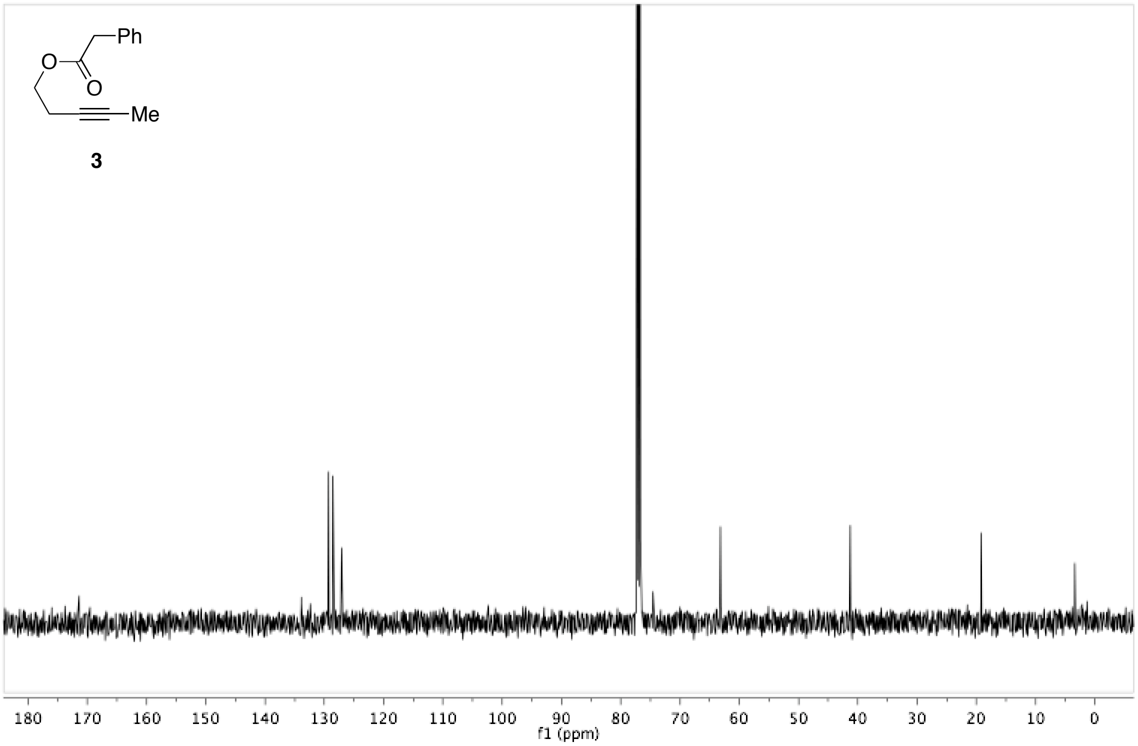
^{13}C NMR (CDCl$_3$, 126 MHz)



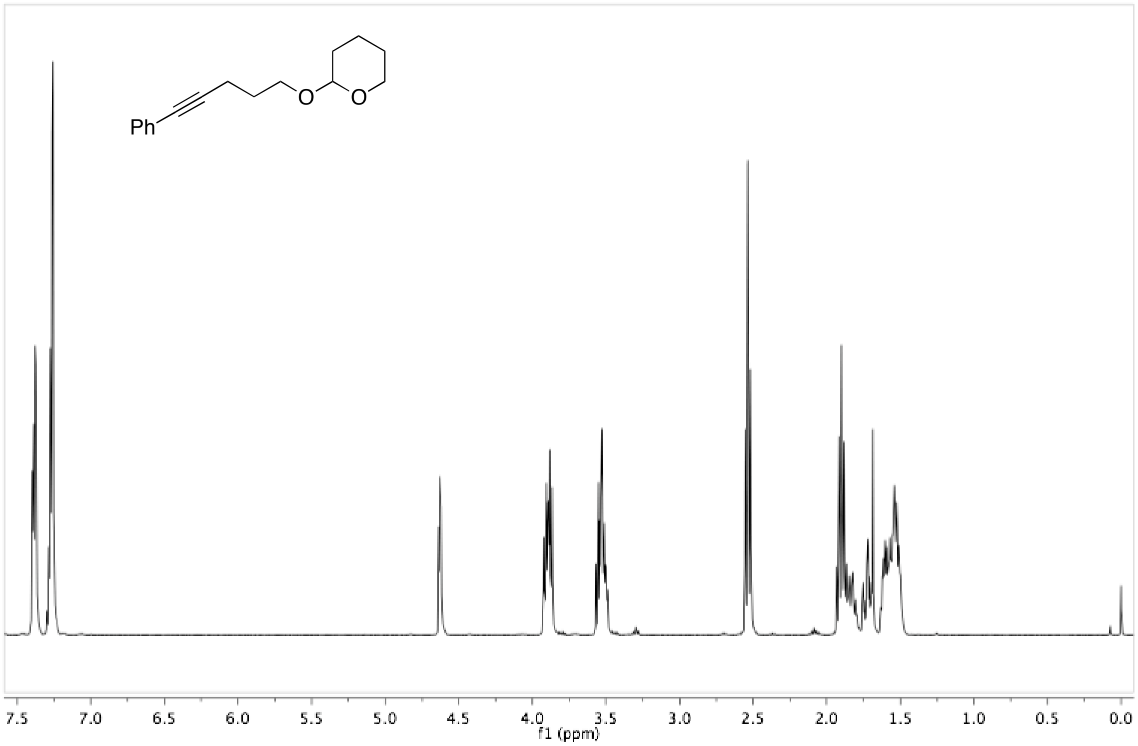
^{1}H NMR ($CDCl_3$, 500 MHz)



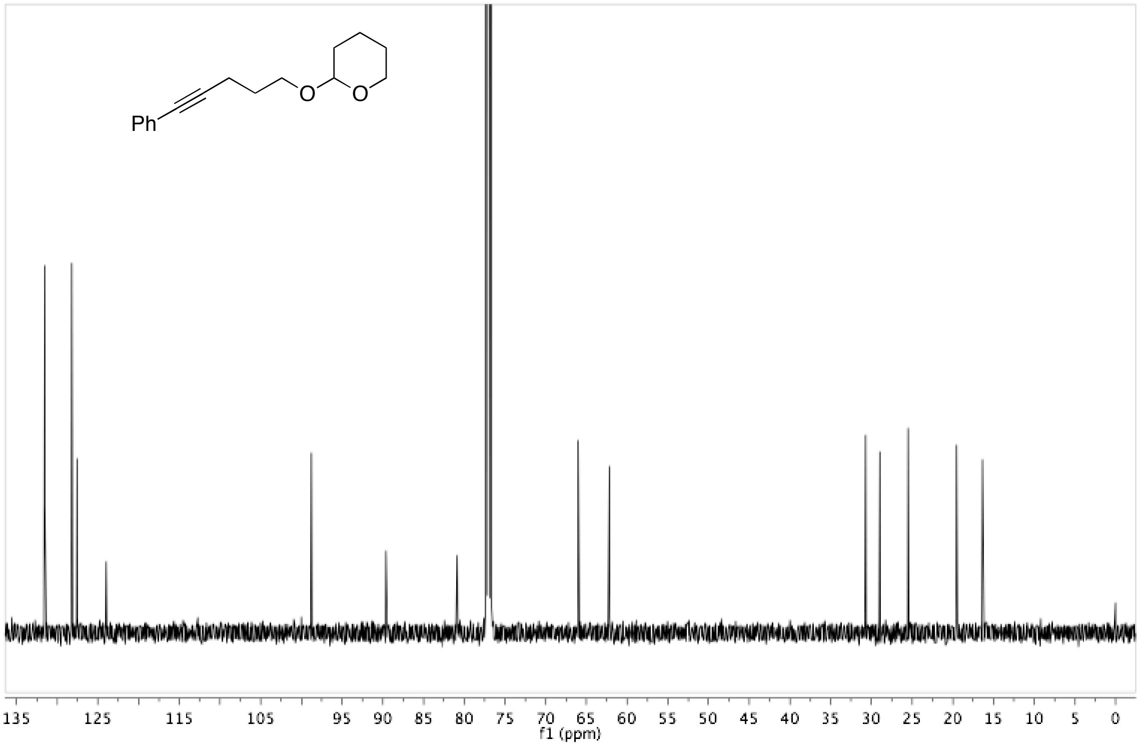
^{13}C NMR ($CDCl_3$, 126 MHz)



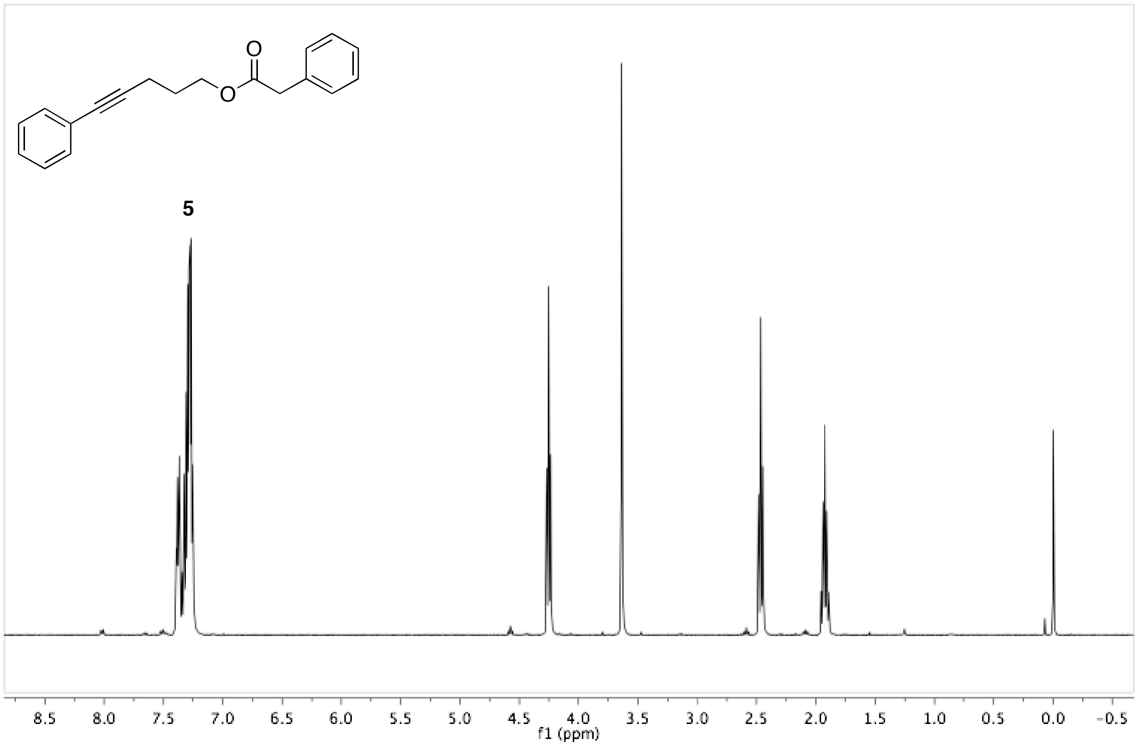
^{1}H NMR (CDCl$_3$, 500 MHz)



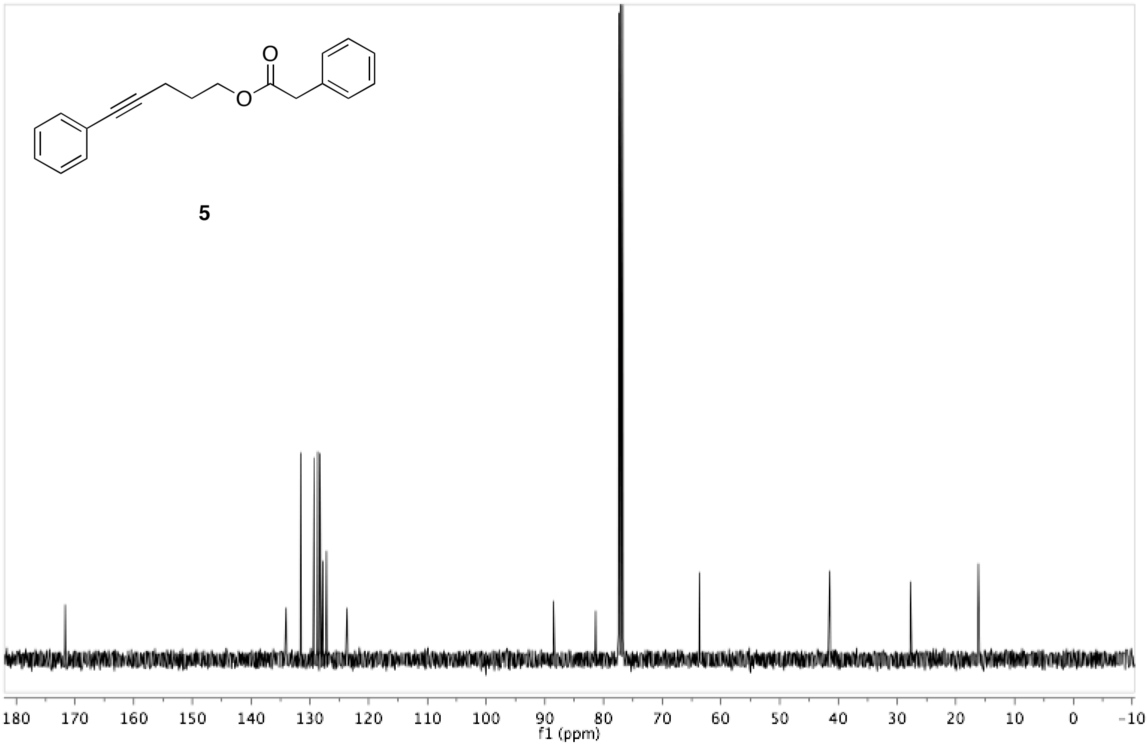
^{13}C NMR (CDCl$_3$, 126 MHz)



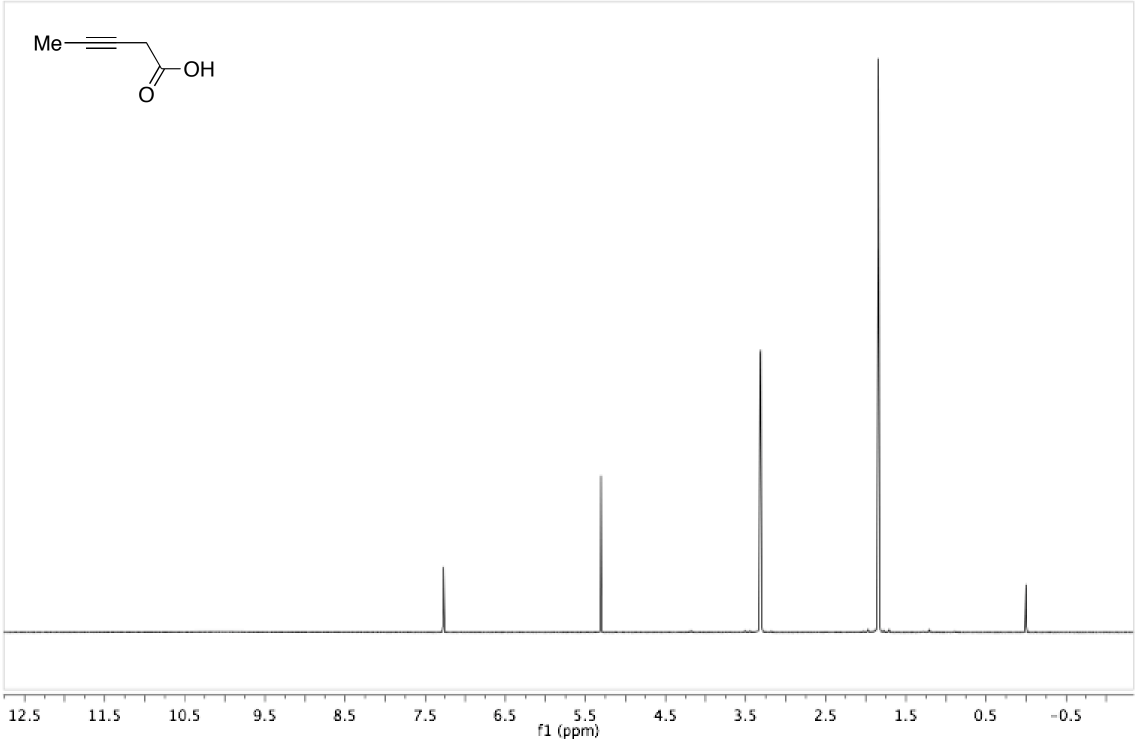
^{1}H NMR ($CDCl_3$, 400 MHz)



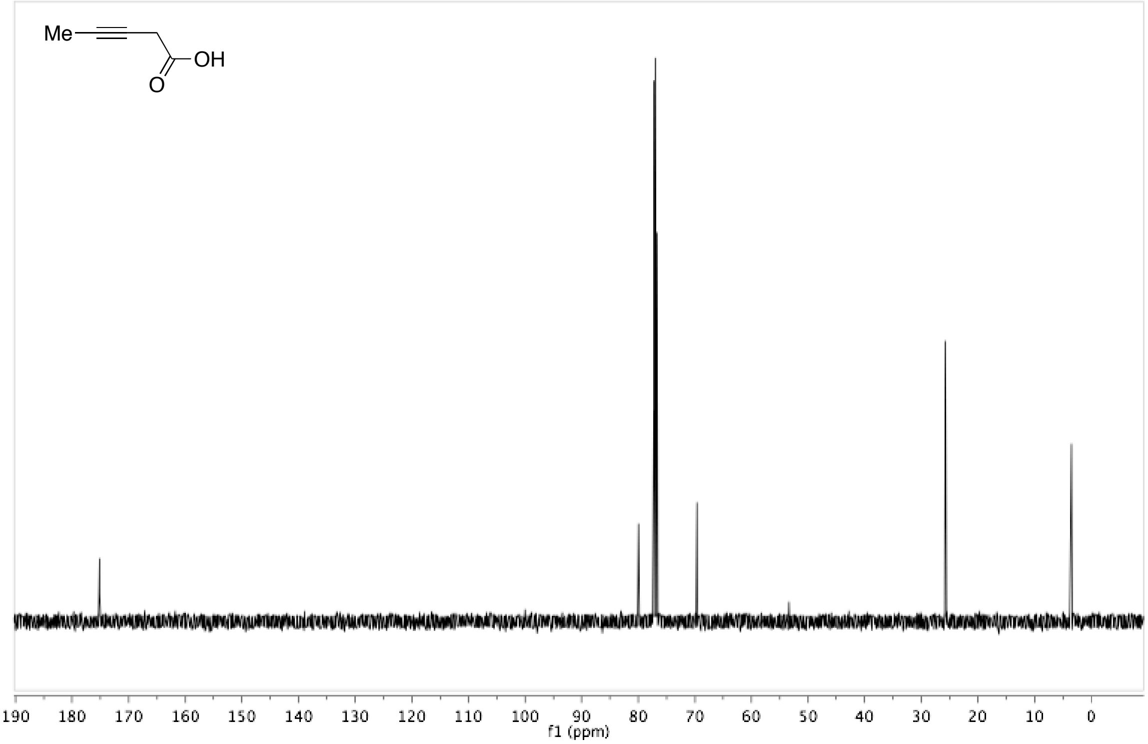
^{13}C NMR ($CDCl_3$, 101 MHz)



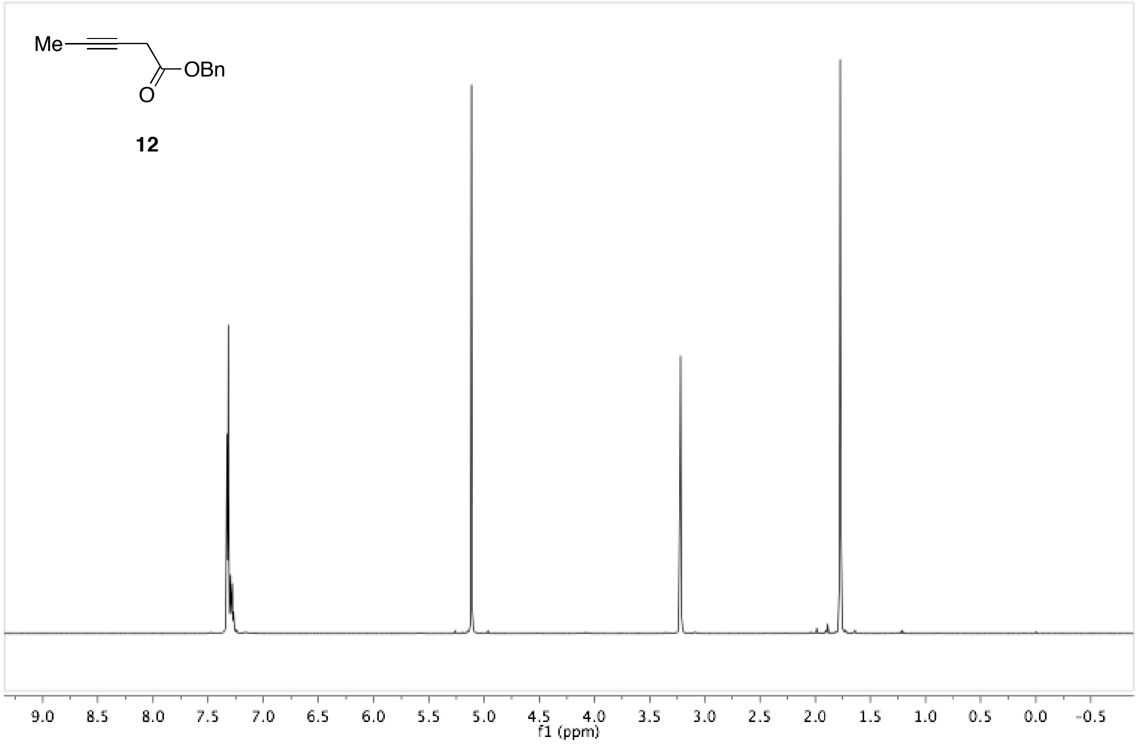
^{1}H NMR (CDCl$_3$, 400 MHz)



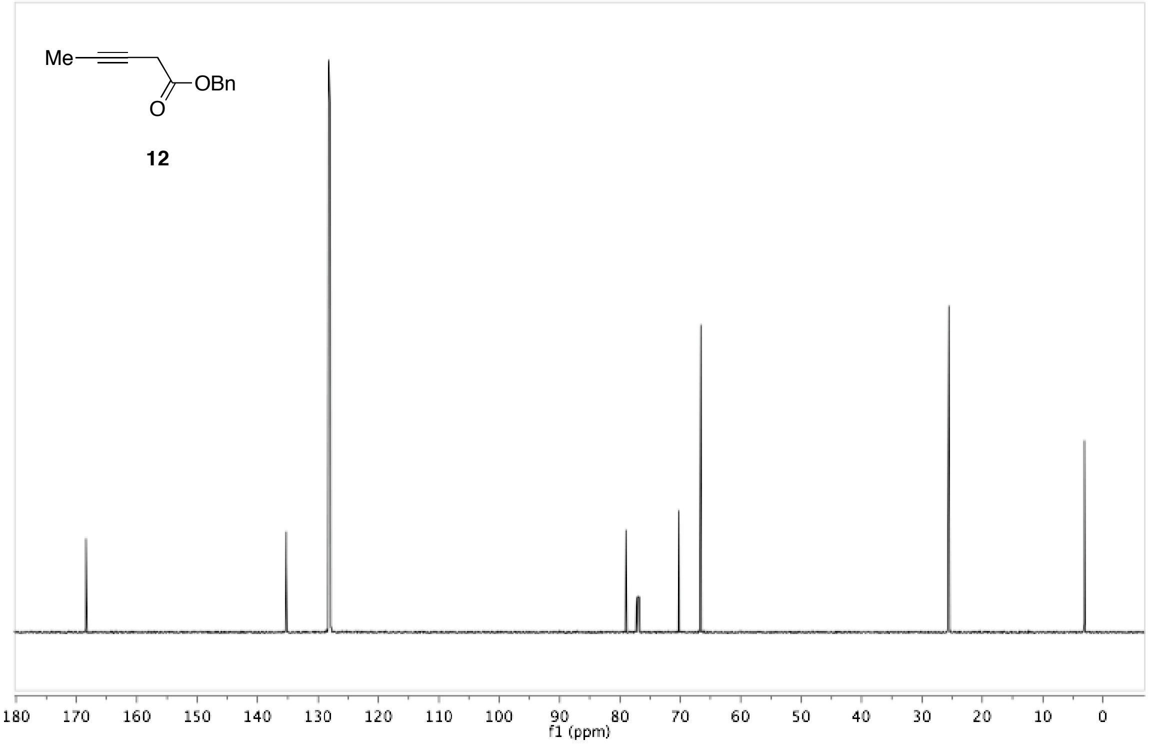
^{13}C NMR (CDCl$_3$, 126 MHz)



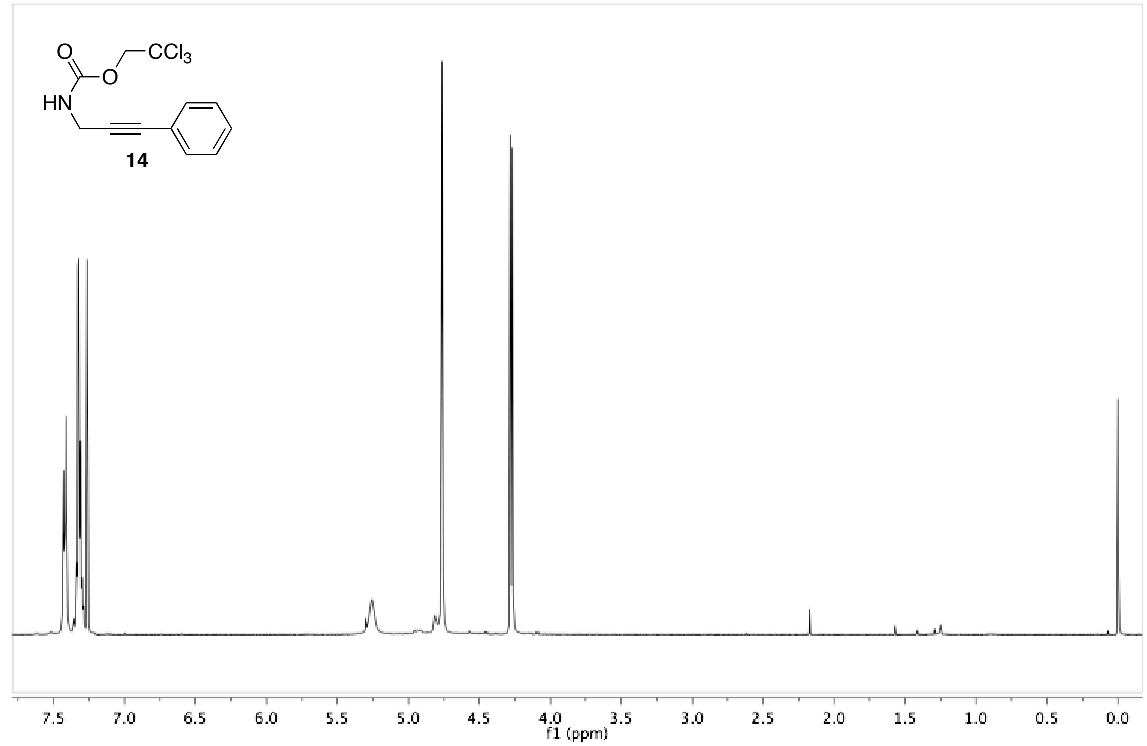
^{1}H NMR (CDCl$_3$, 400 MHz)



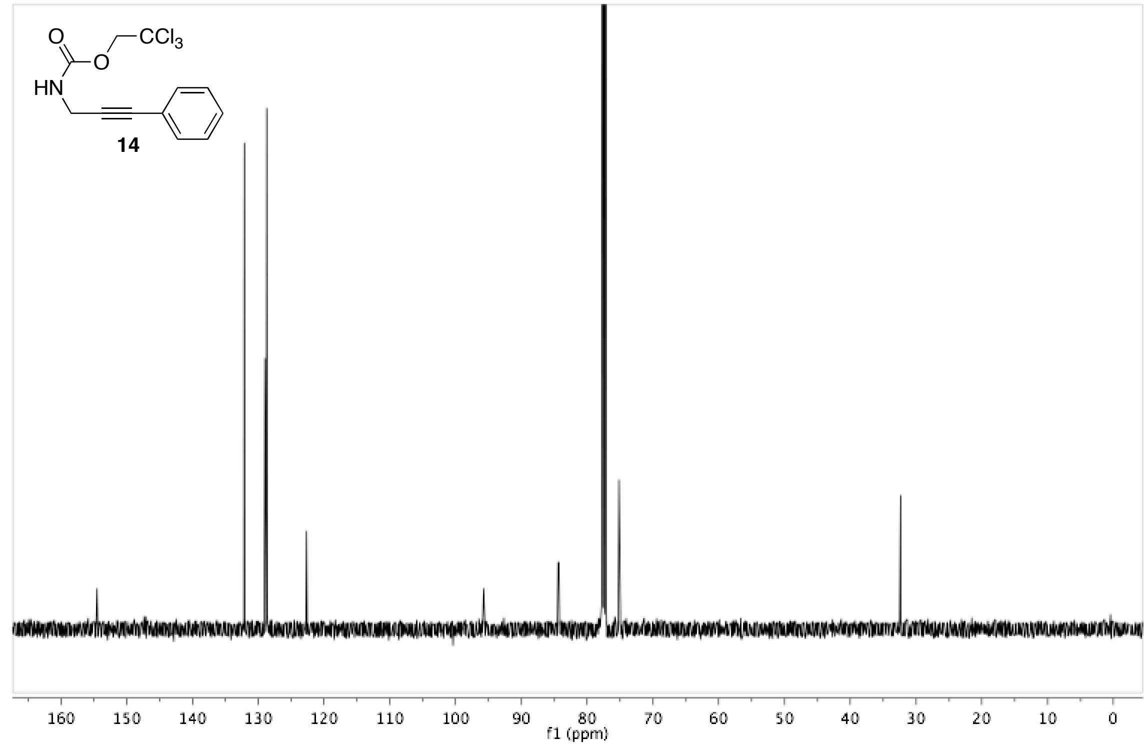
^{13}C NMR (CDCl$_3$, 126 MHz)



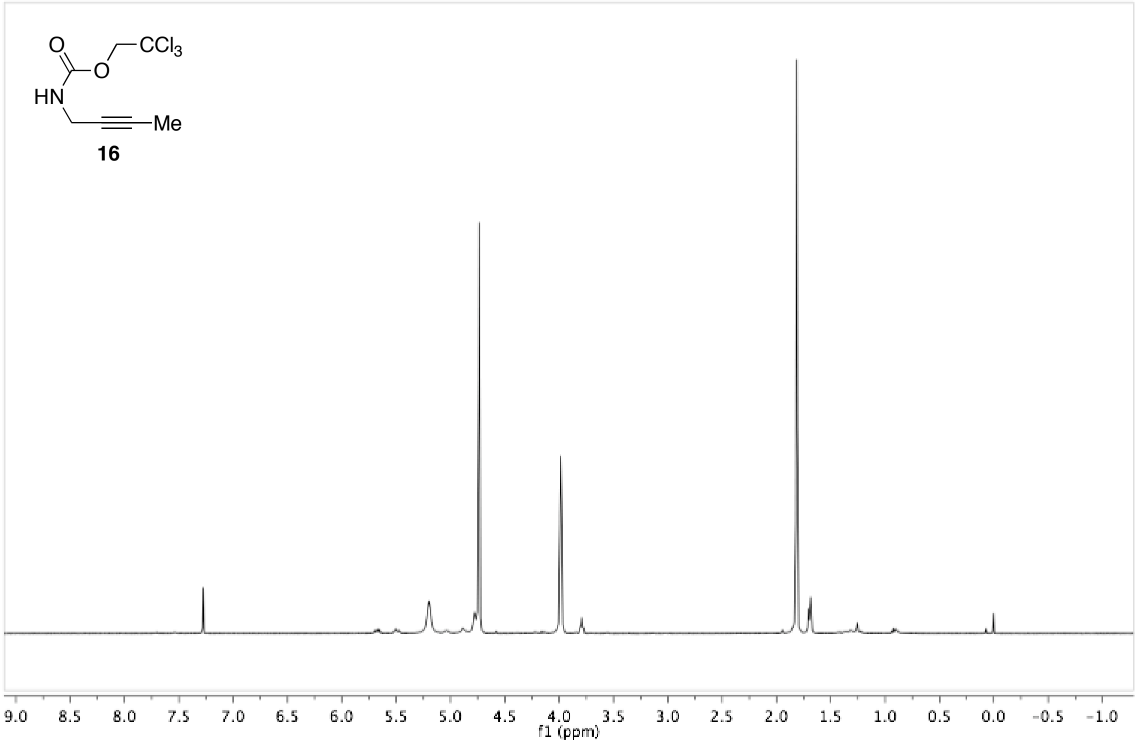
^{1}H NMR ($CDCl_3$, 400 MHz)



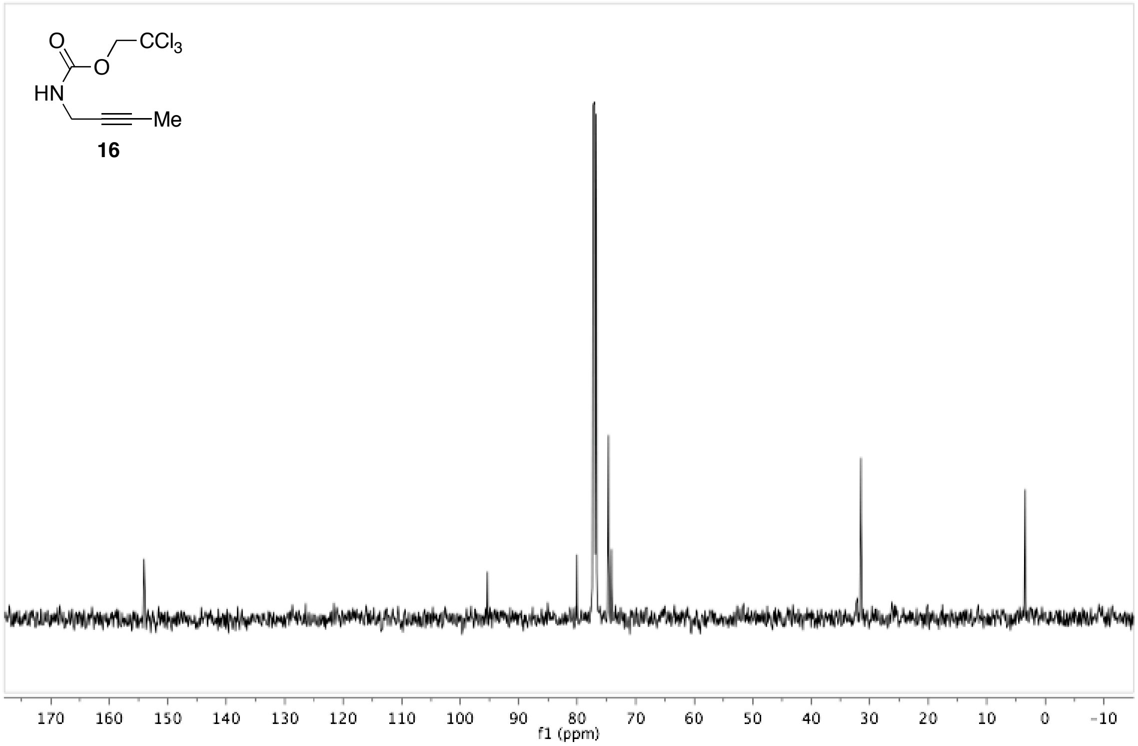
^{13}C NMR ($CDCl_3$, 126 MHz)



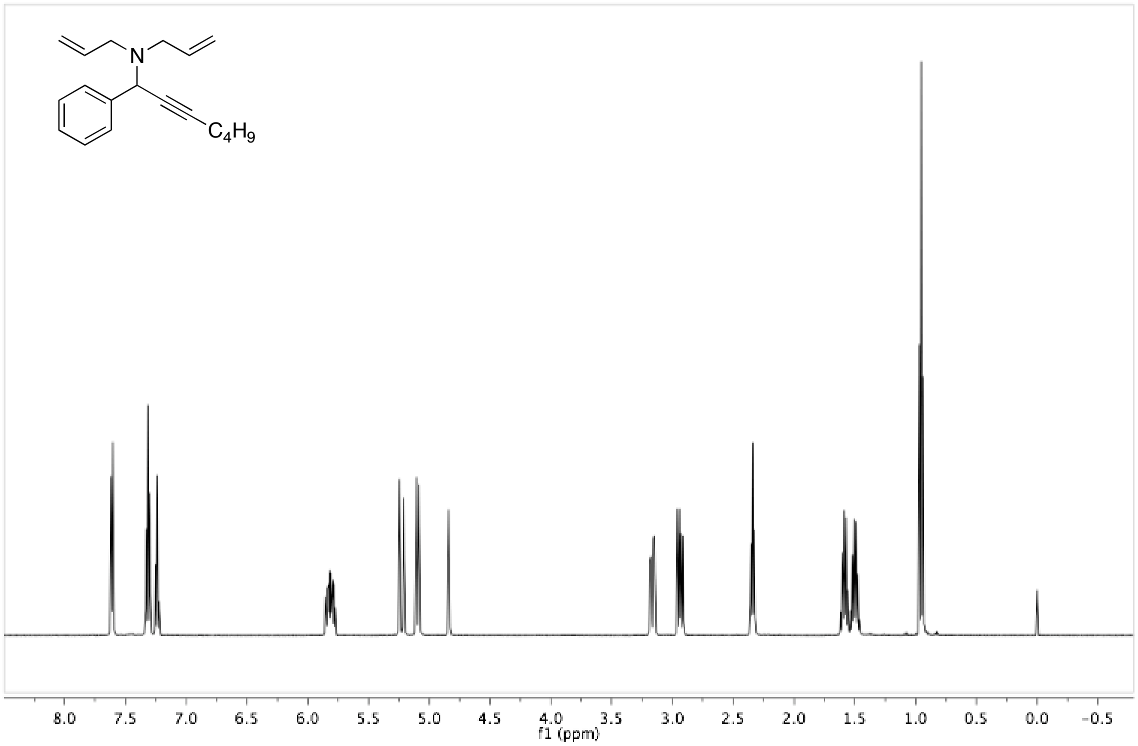
^{1}H NMR (CDCl$_3$, 500 MHz)



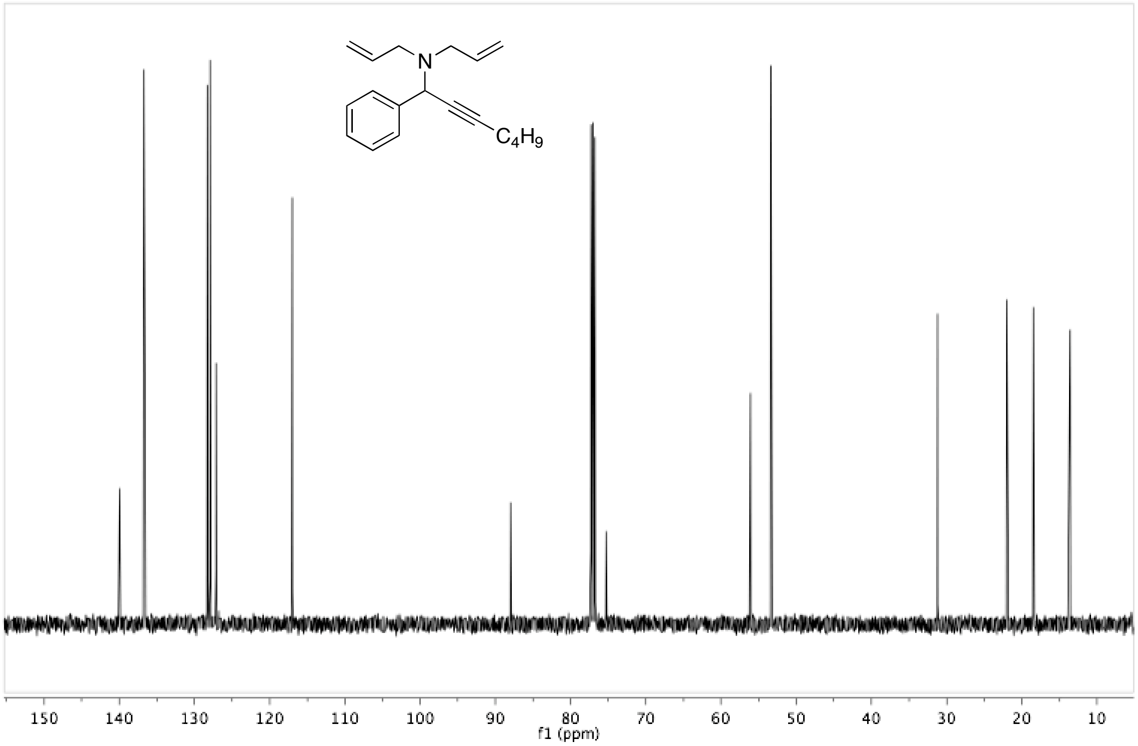
^{13}C NMR (CDCl$_3$, 126 MHz)



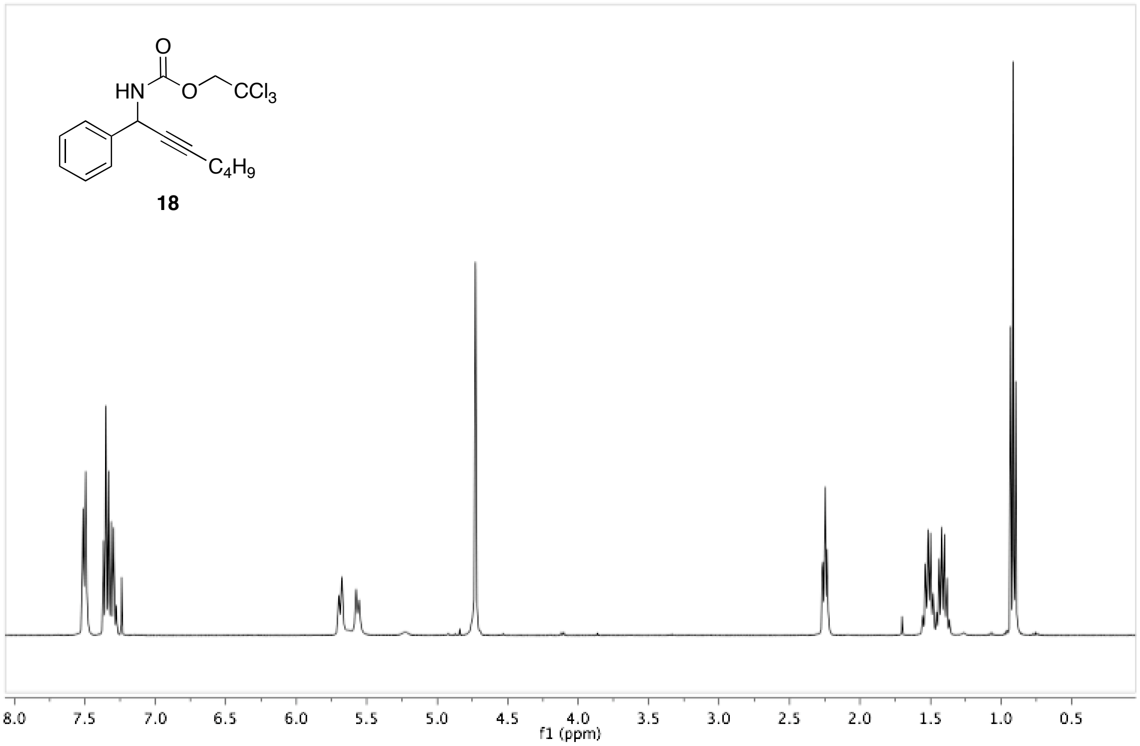
^{1}H NMR ($CDCl_3$, 500 MHz)



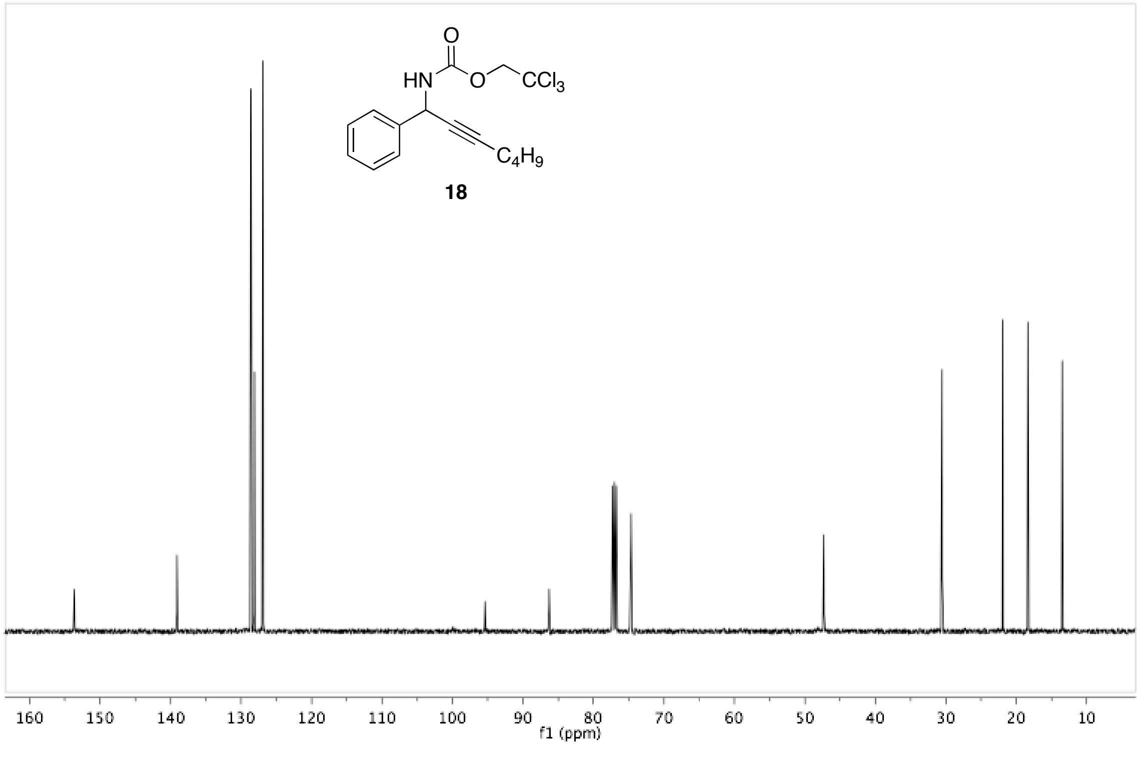
^{13}C NMR ($CDCl_3$, 126 MHz)



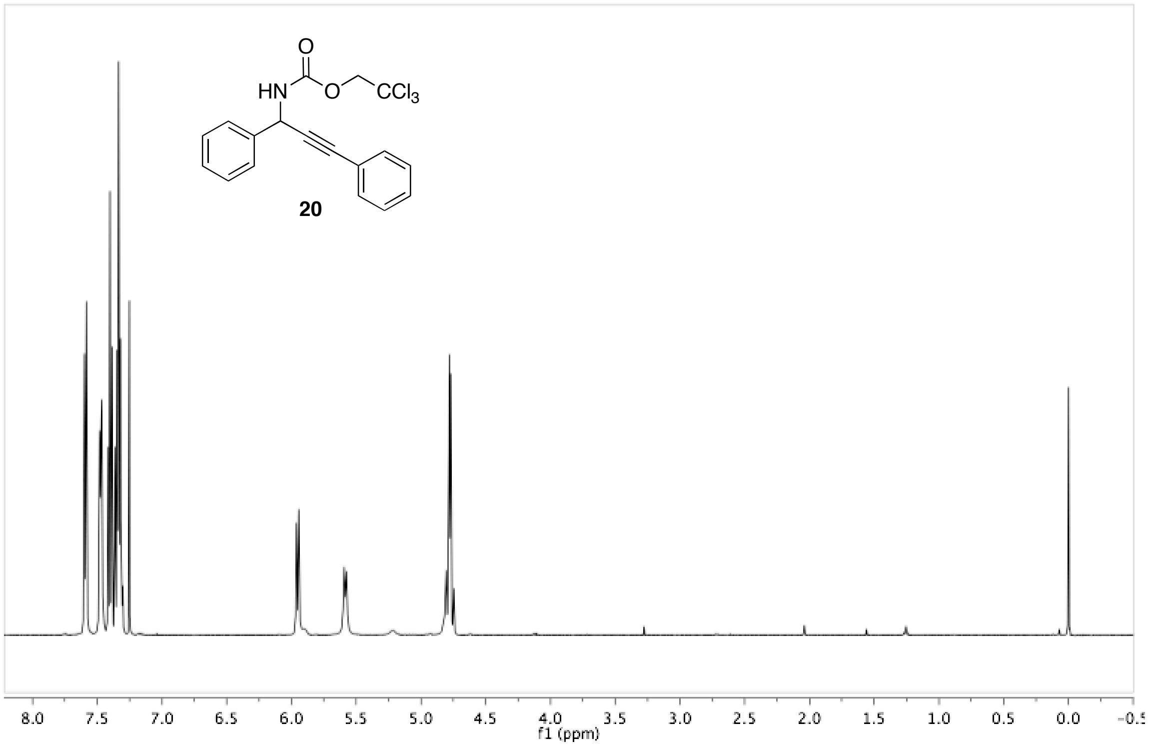
^{1}H NMR (CDCl$_3$, 400 MHz)



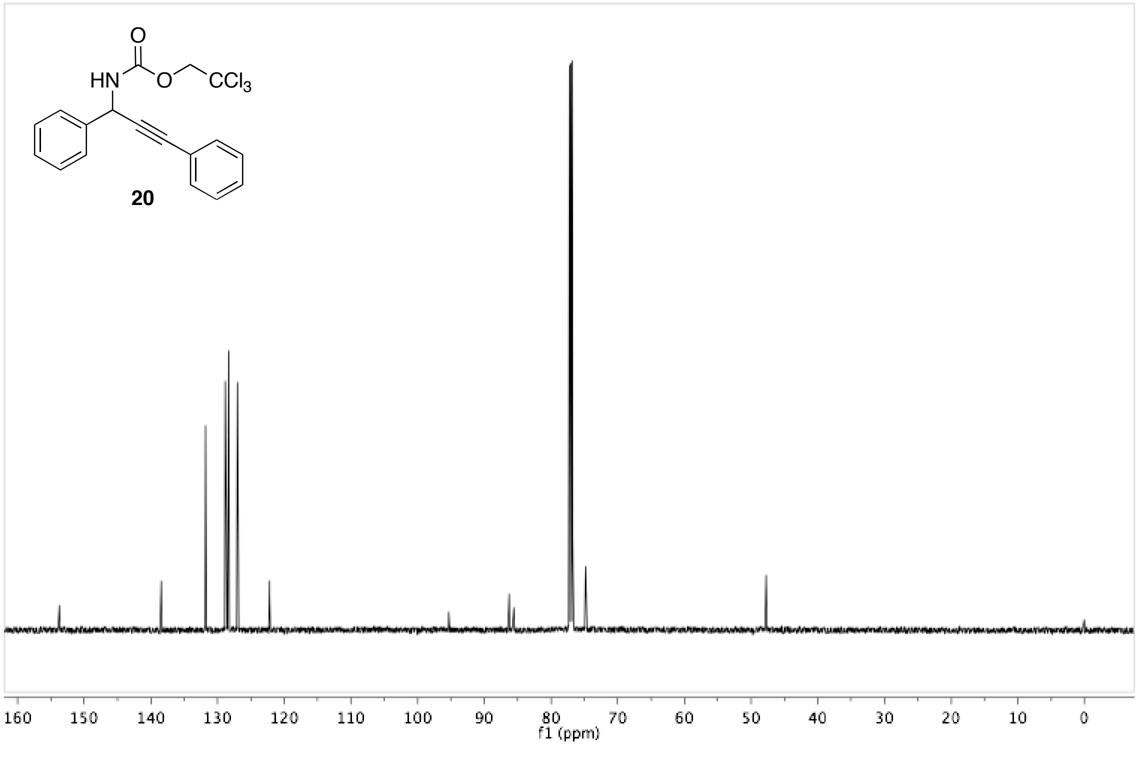
^{13}C NMR (CDCl$_3$, 126 MHz)



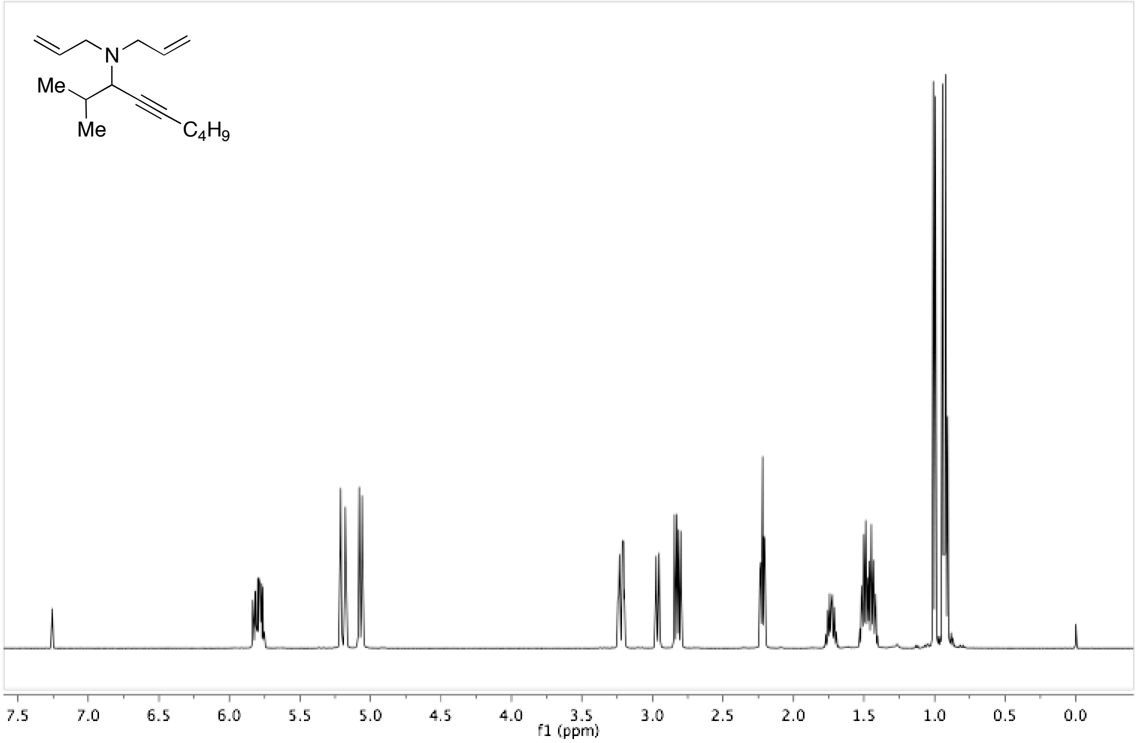
^{1}H NMR ($CDCl_3$, 500 MHz)



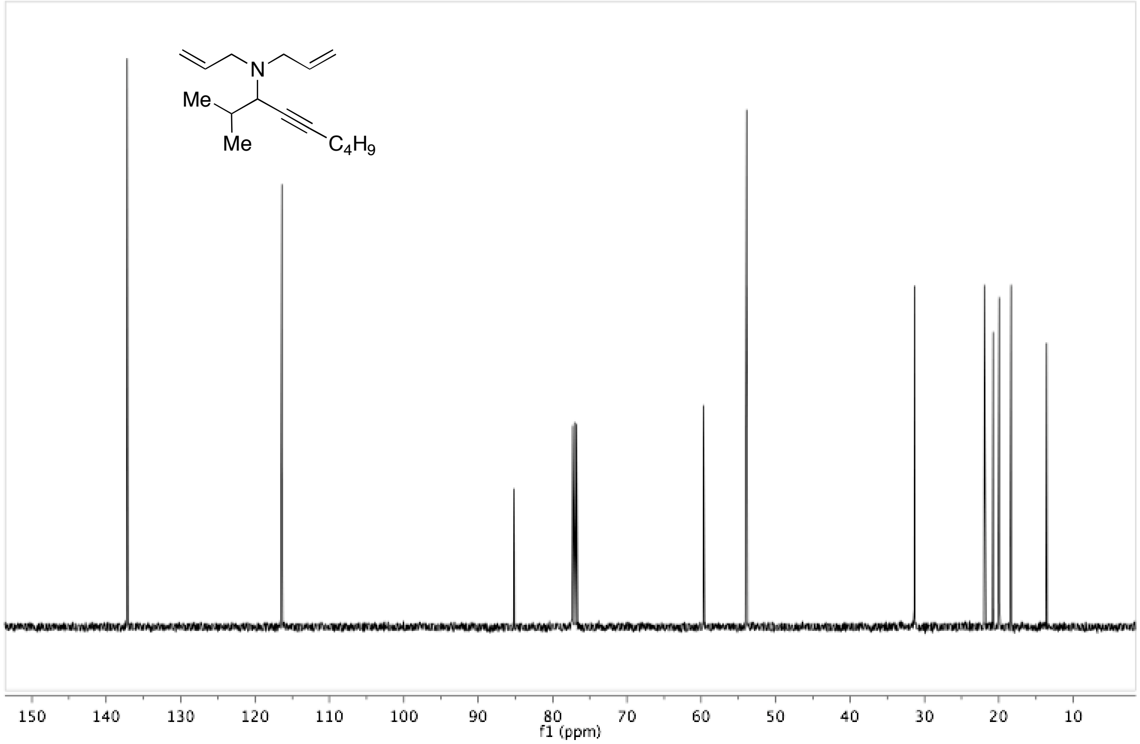
^{13}C NMR ($CDCl_3$, 126 MHz)



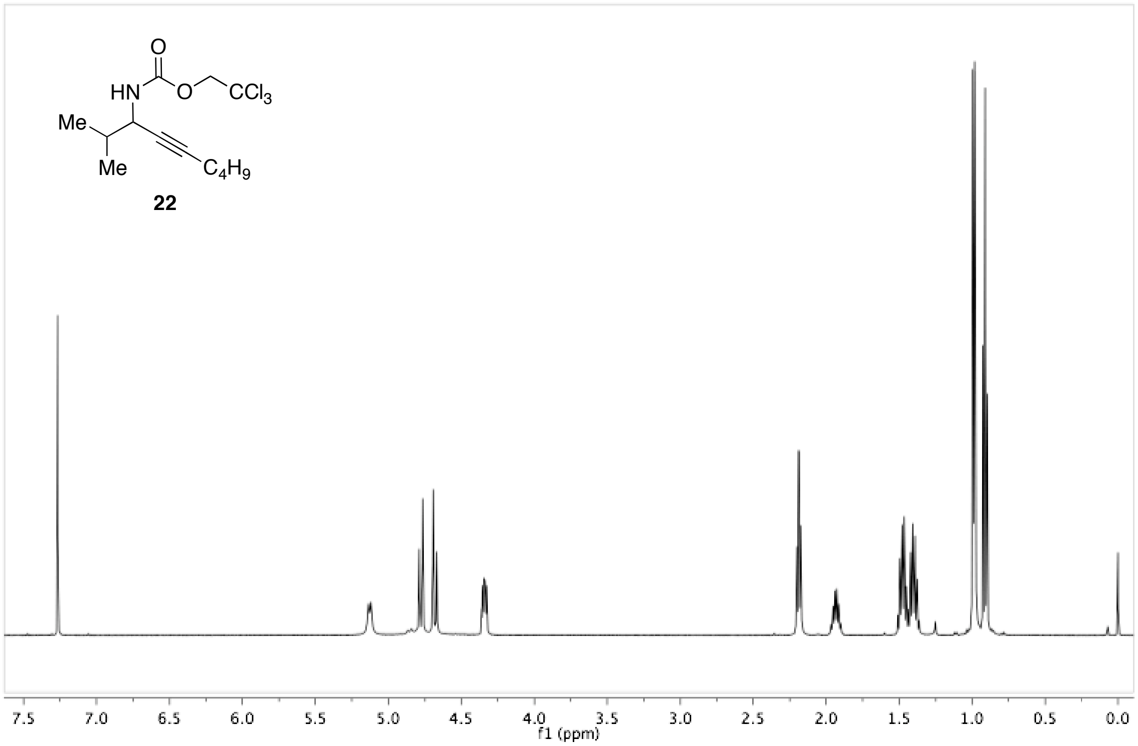
^{1}H NMR (CDCl$_3$, 500 MHz)



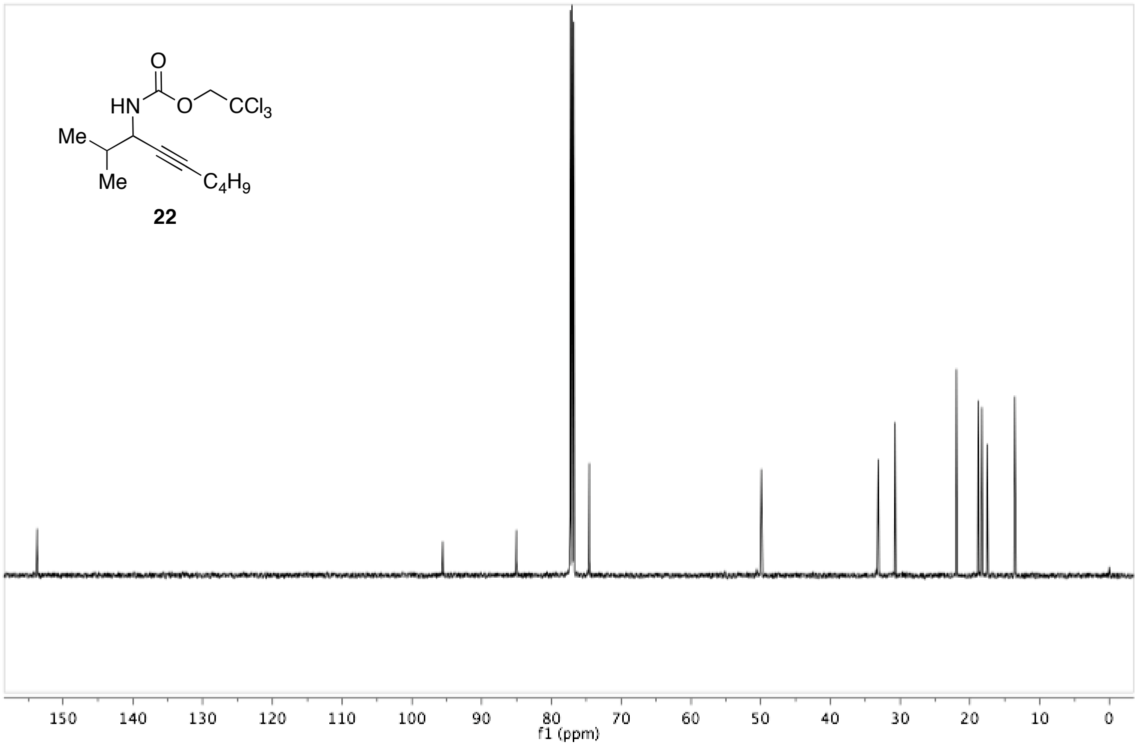
^{13}C NMR (CDCl$_3$, 126 MHz)



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



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



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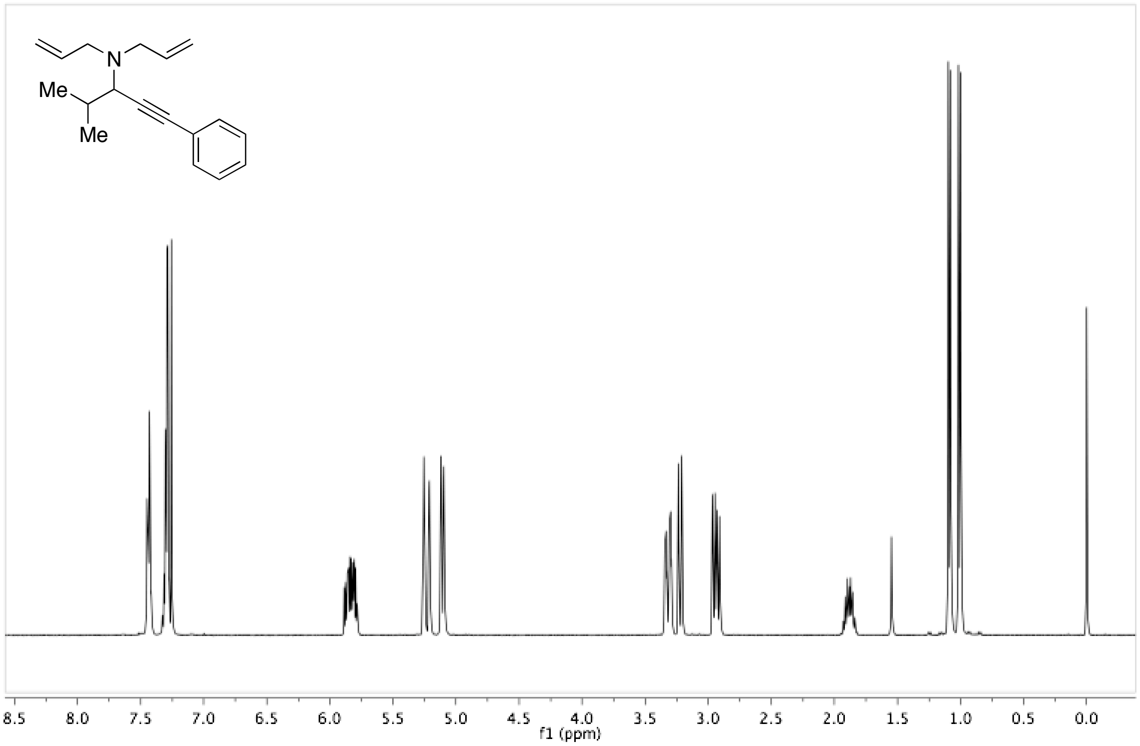

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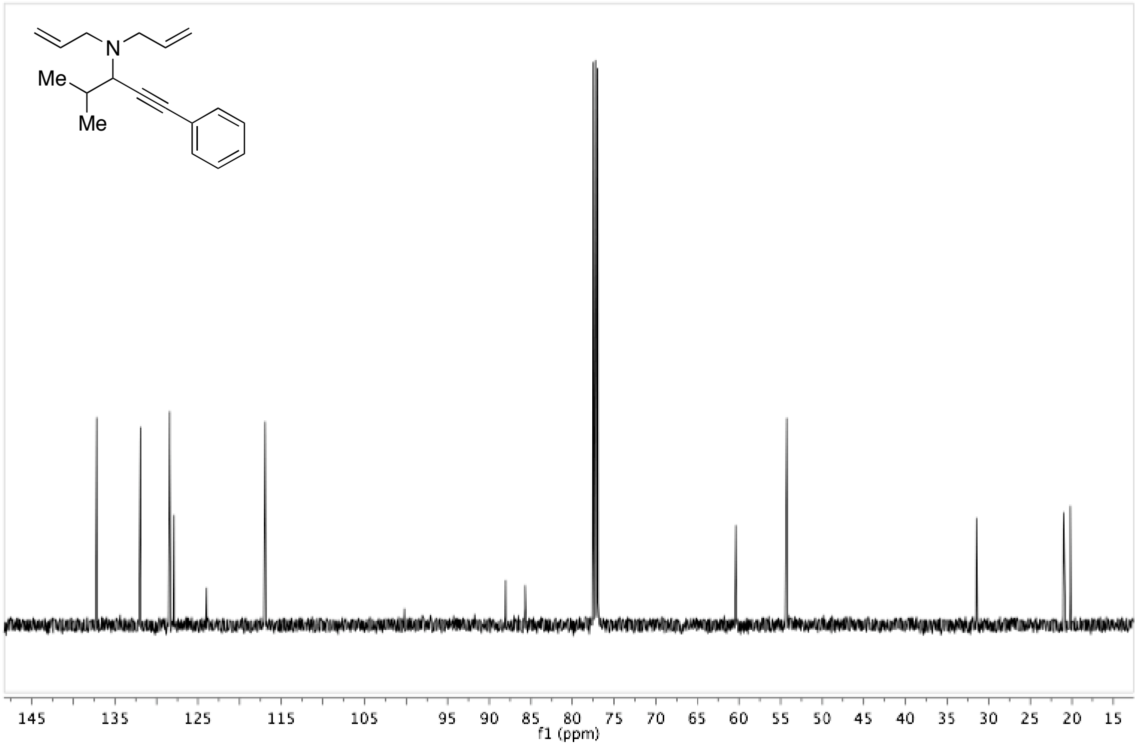

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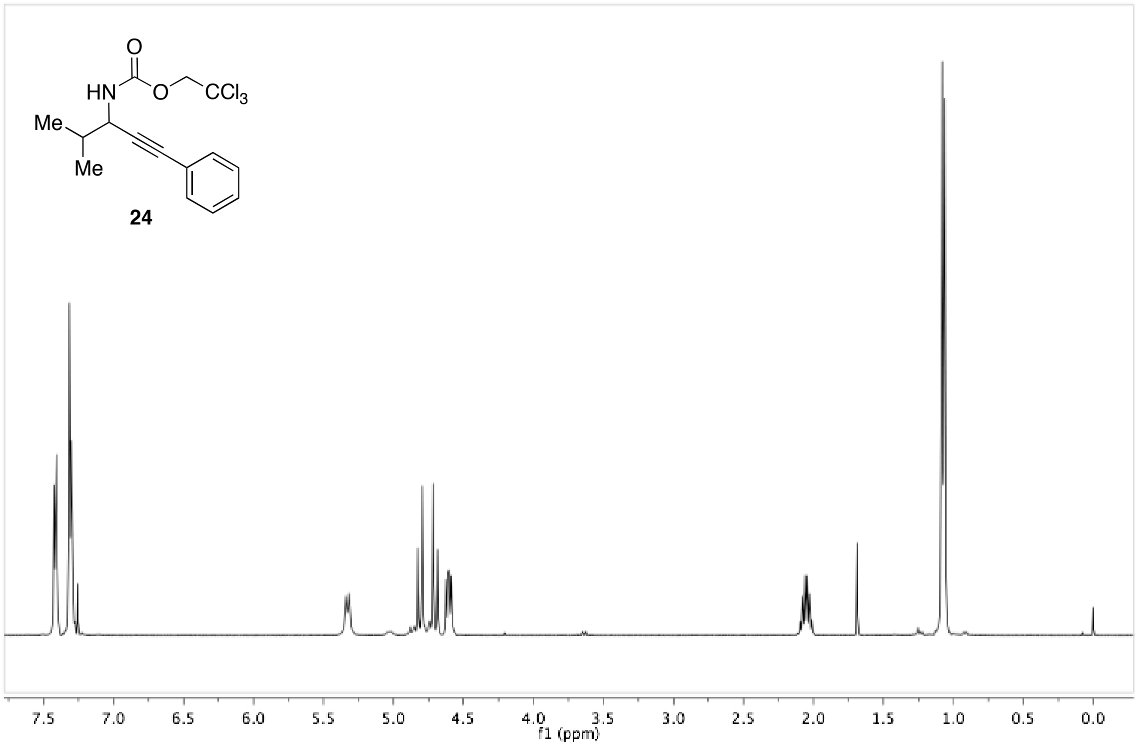

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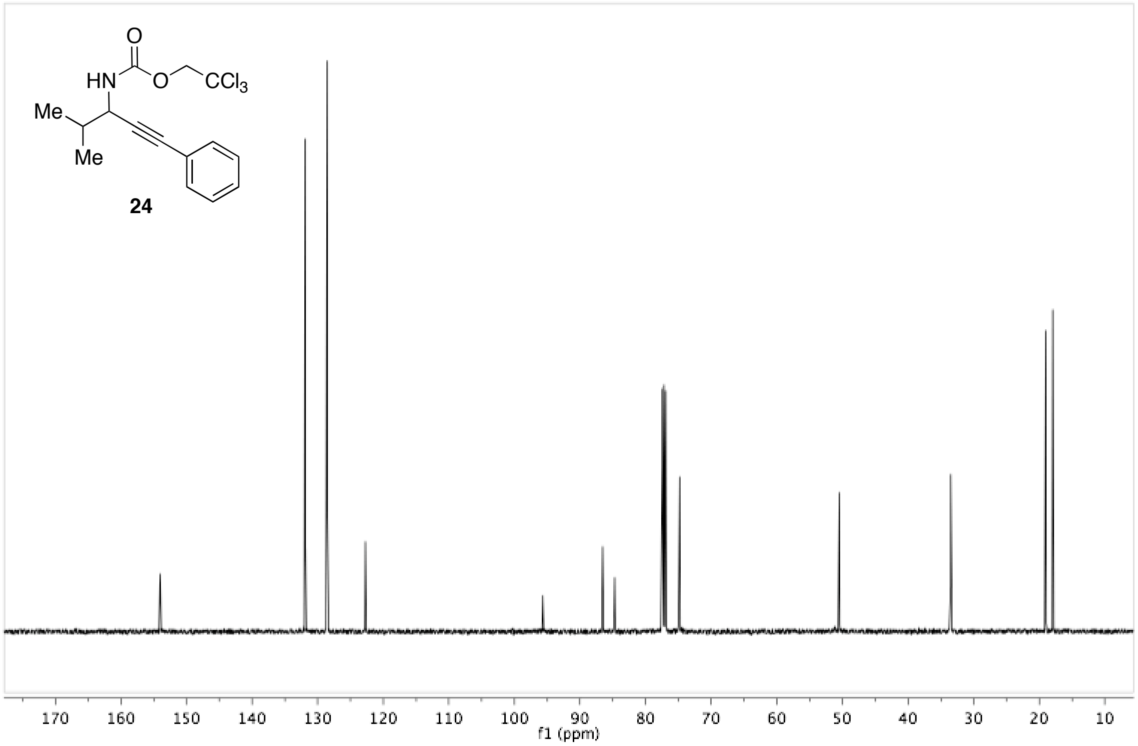

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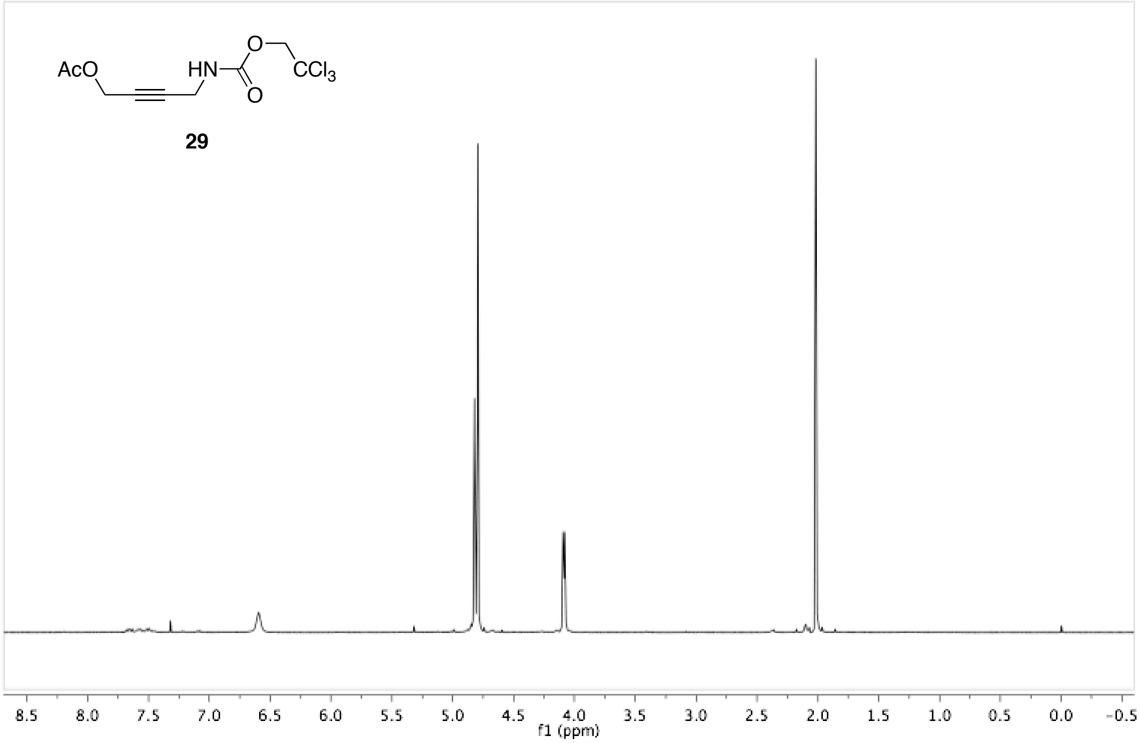

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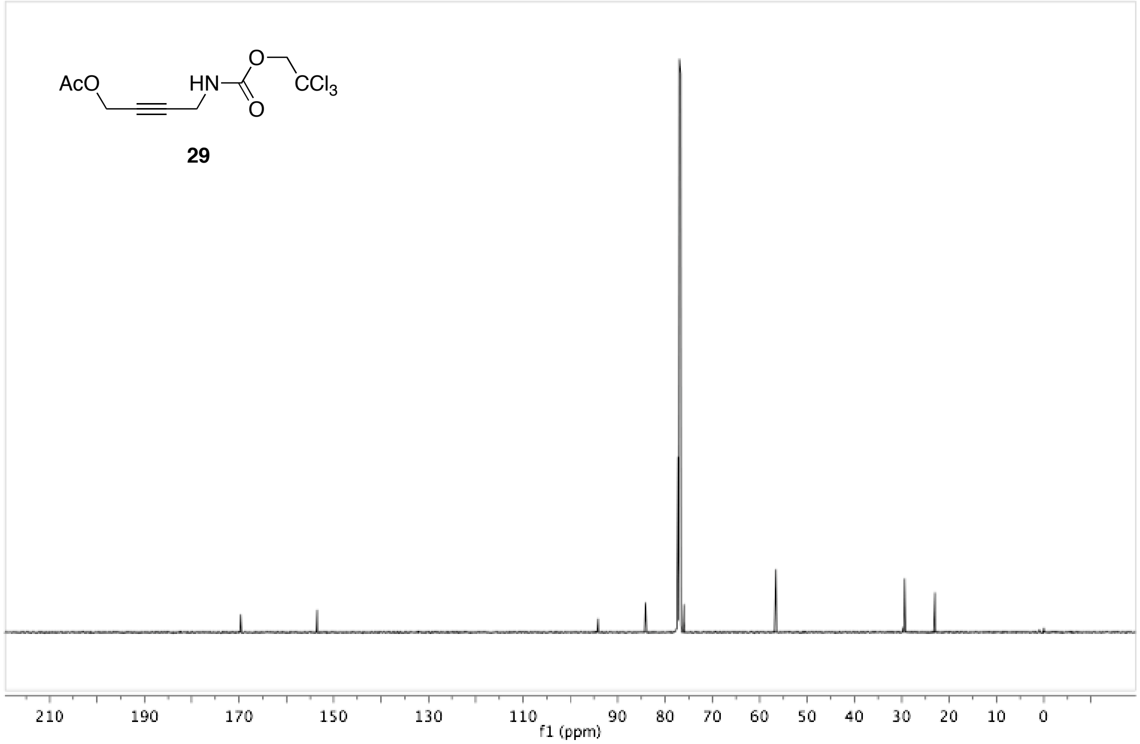
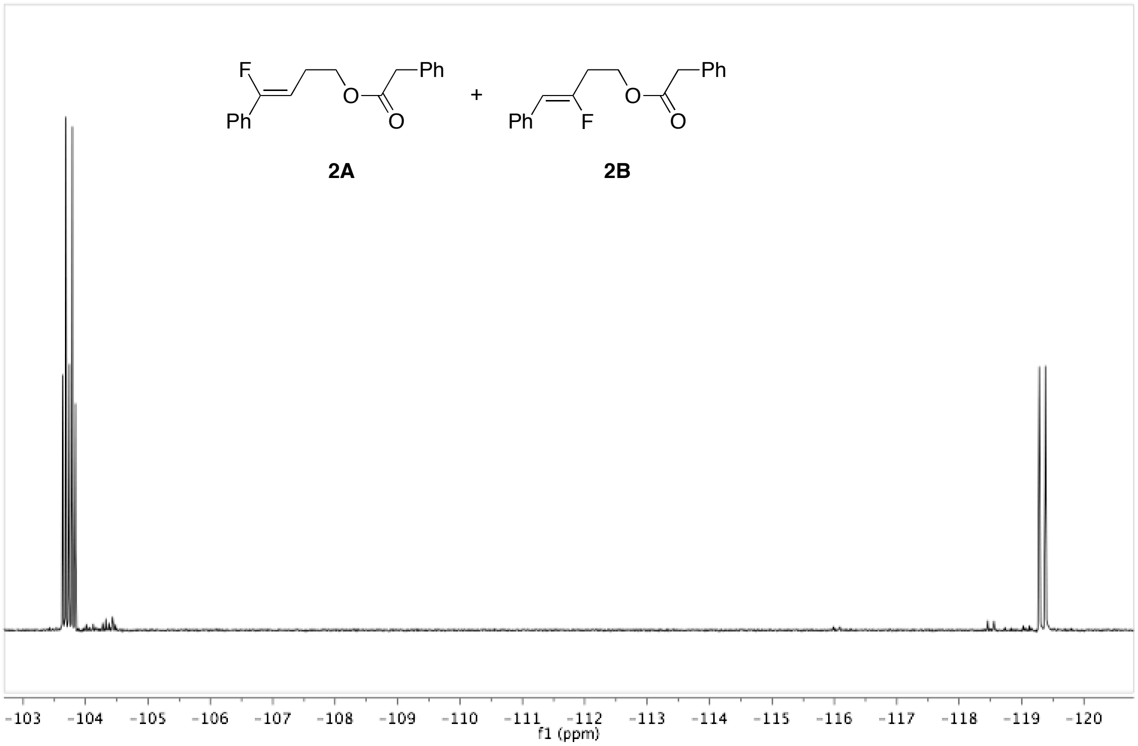


^{19}F NMR (CD_2Cl_2, 376 MHz)



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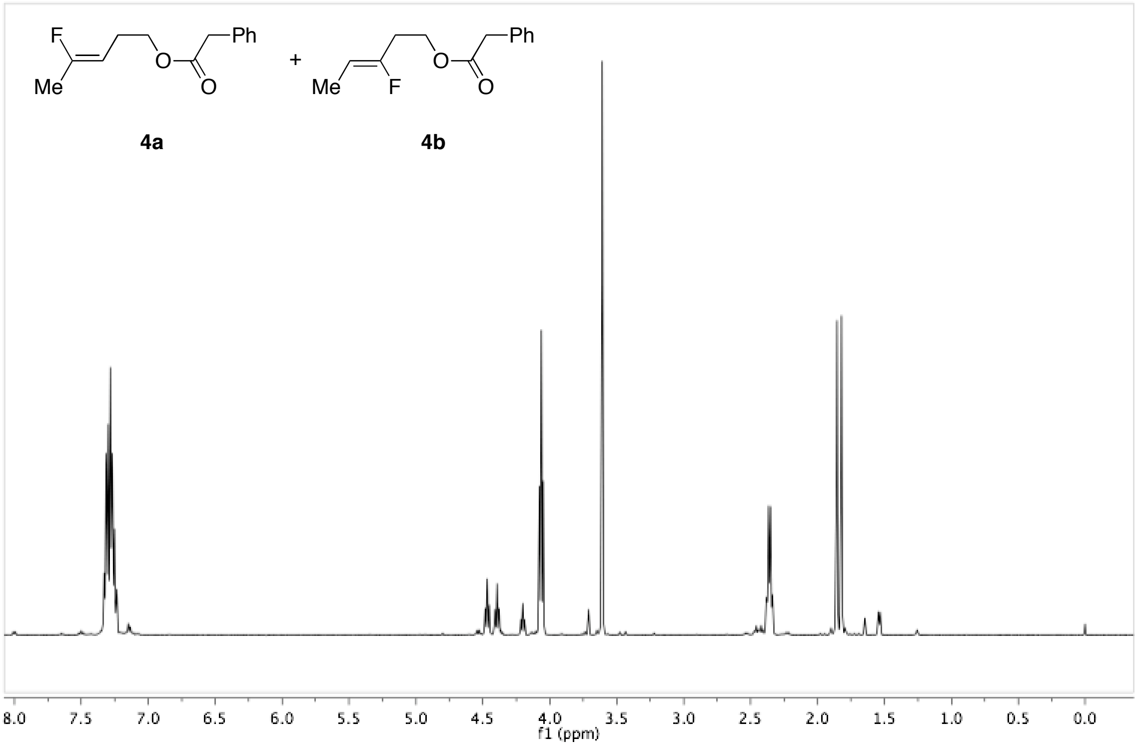

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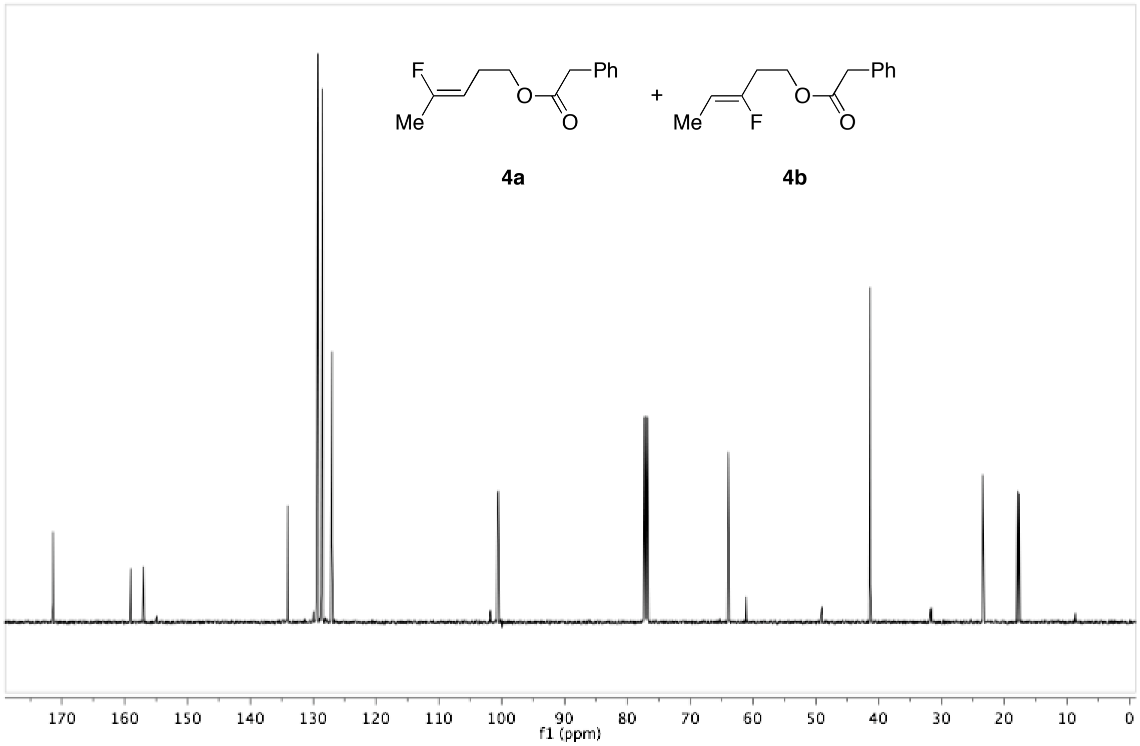

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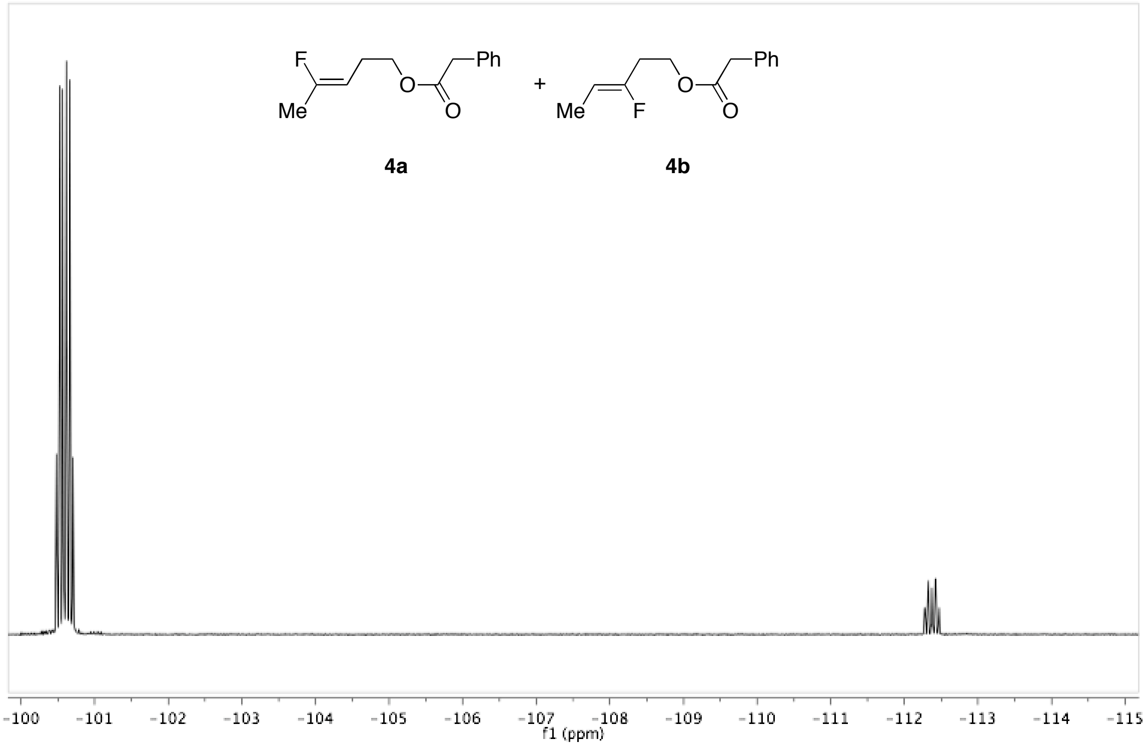
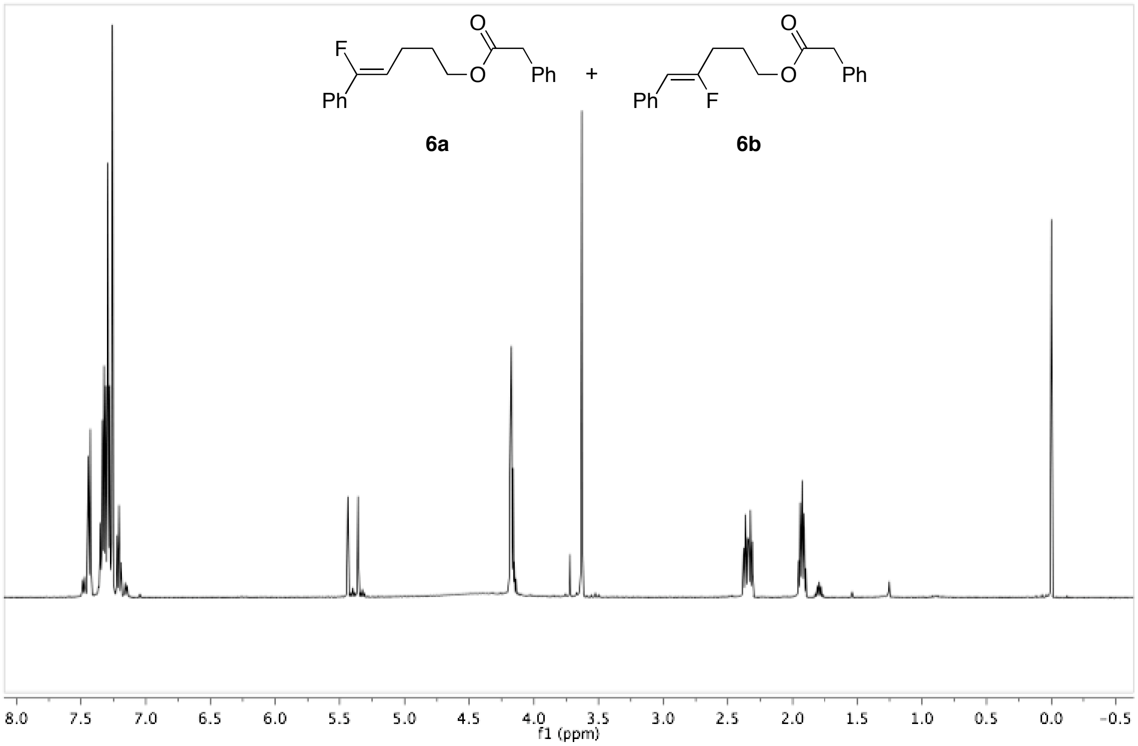


^{1}H NMR (CDCl$_3$, 500 MHz)



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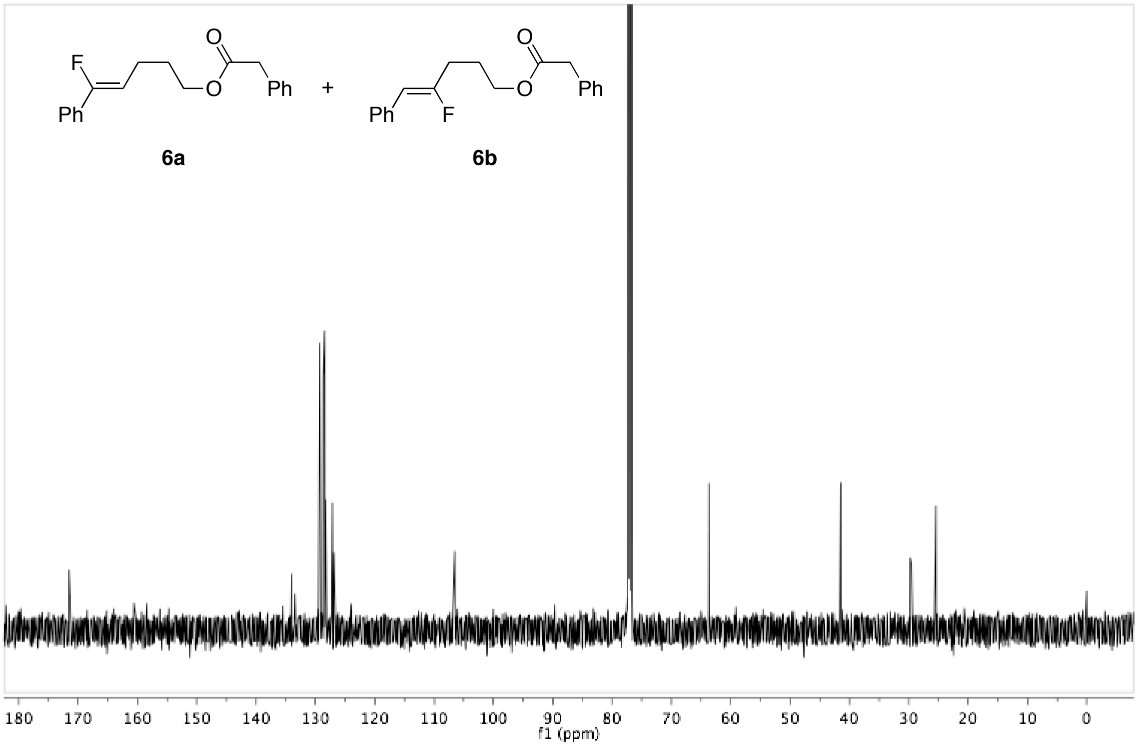

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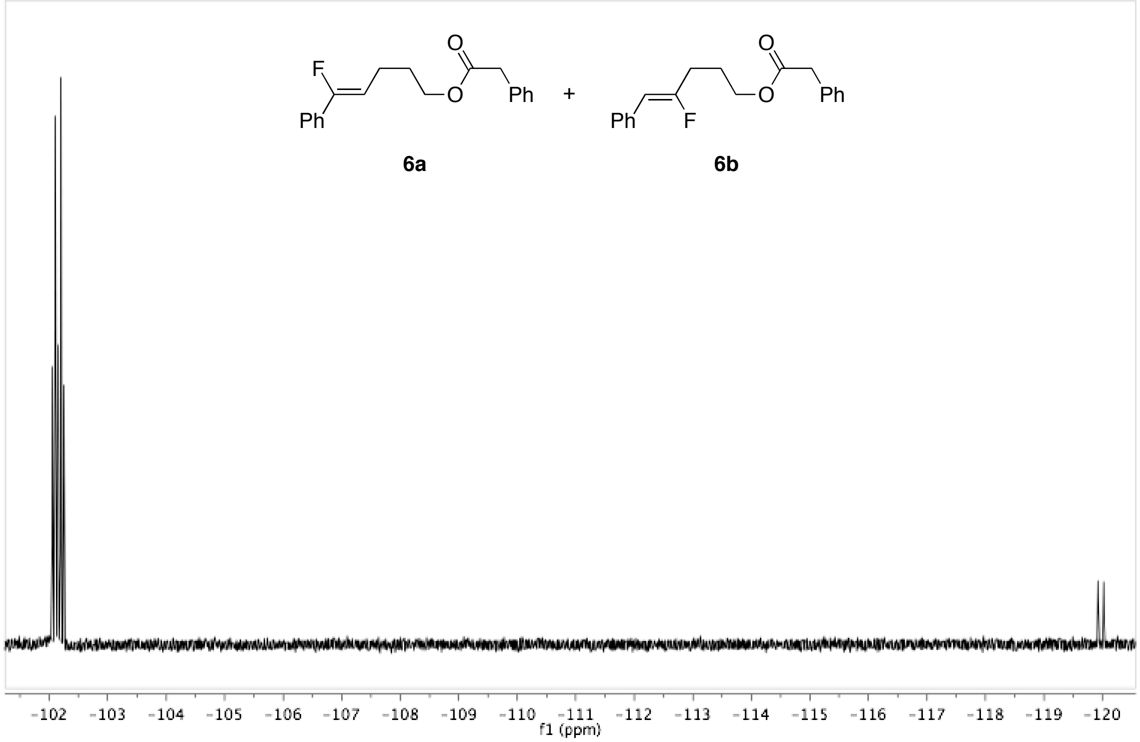

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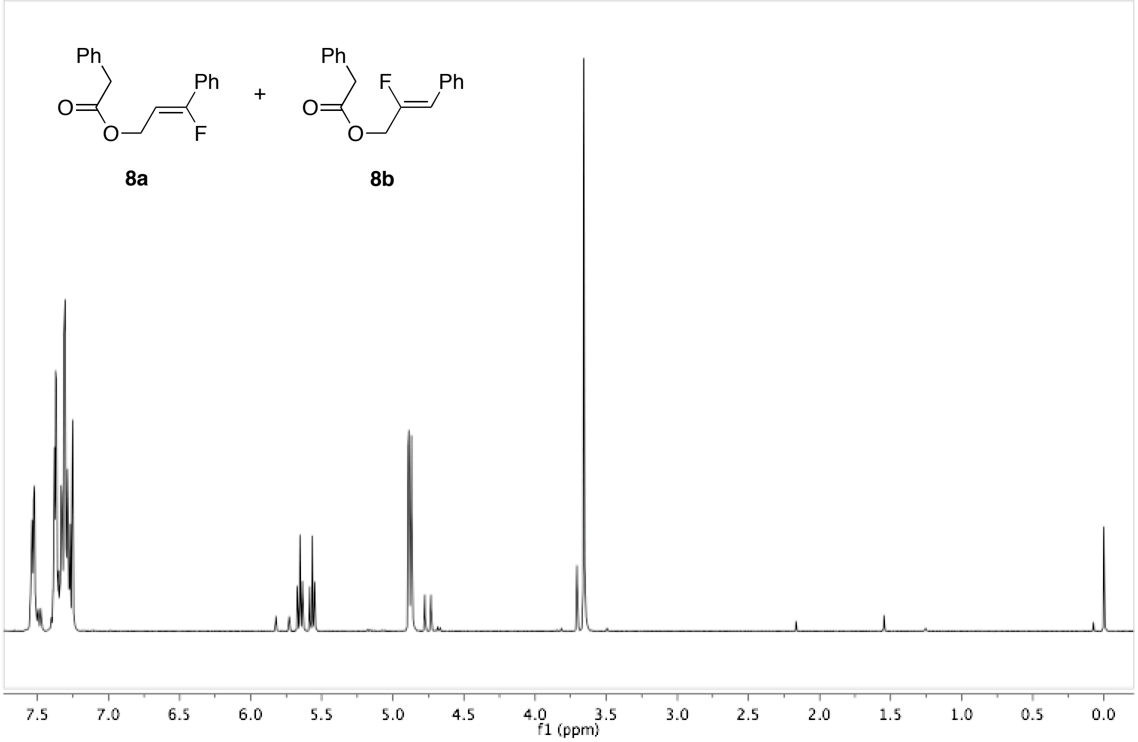

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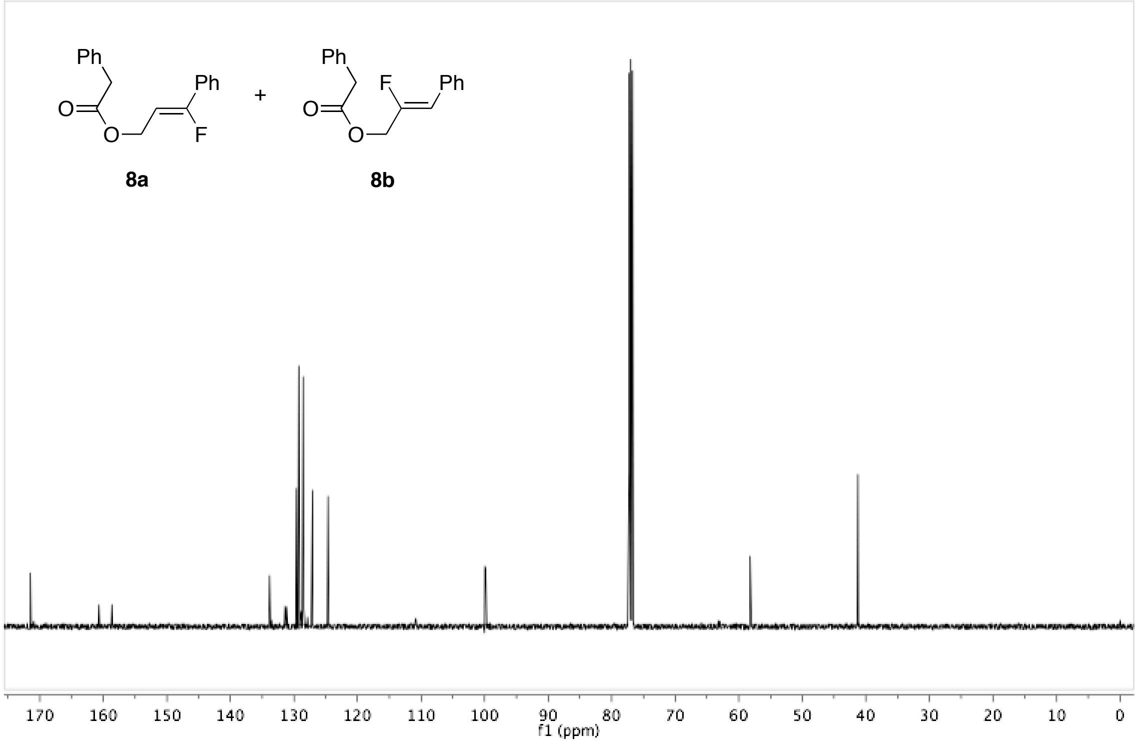

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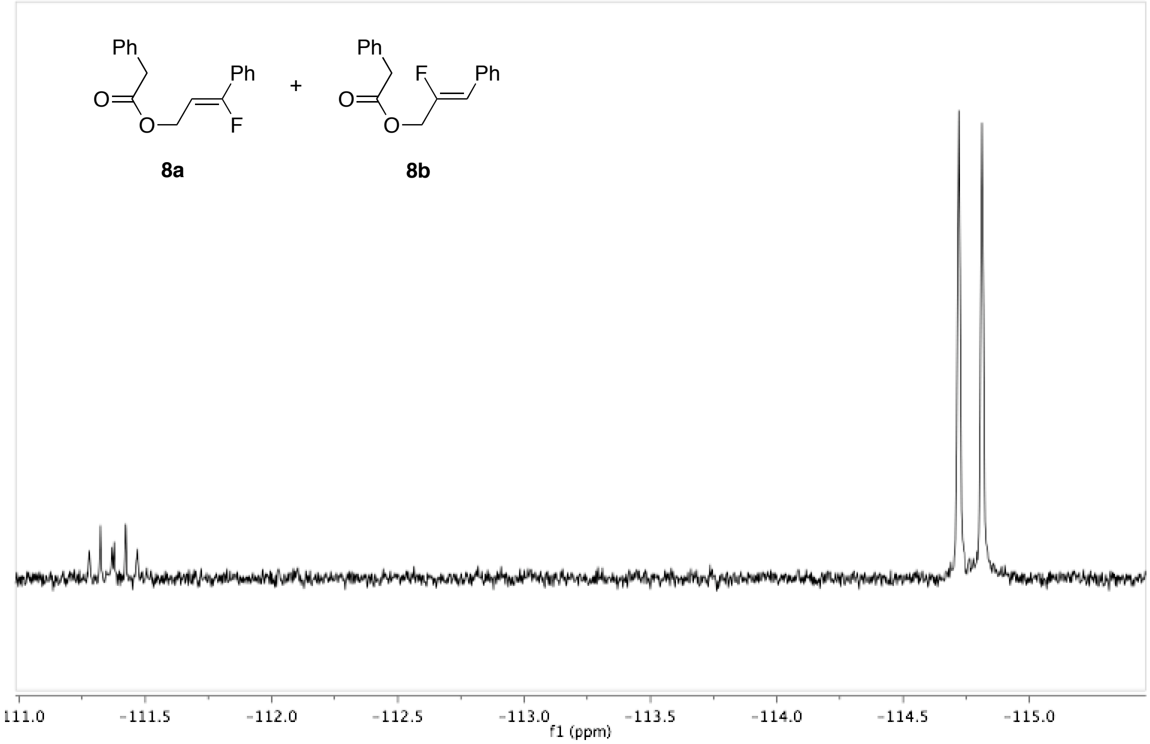

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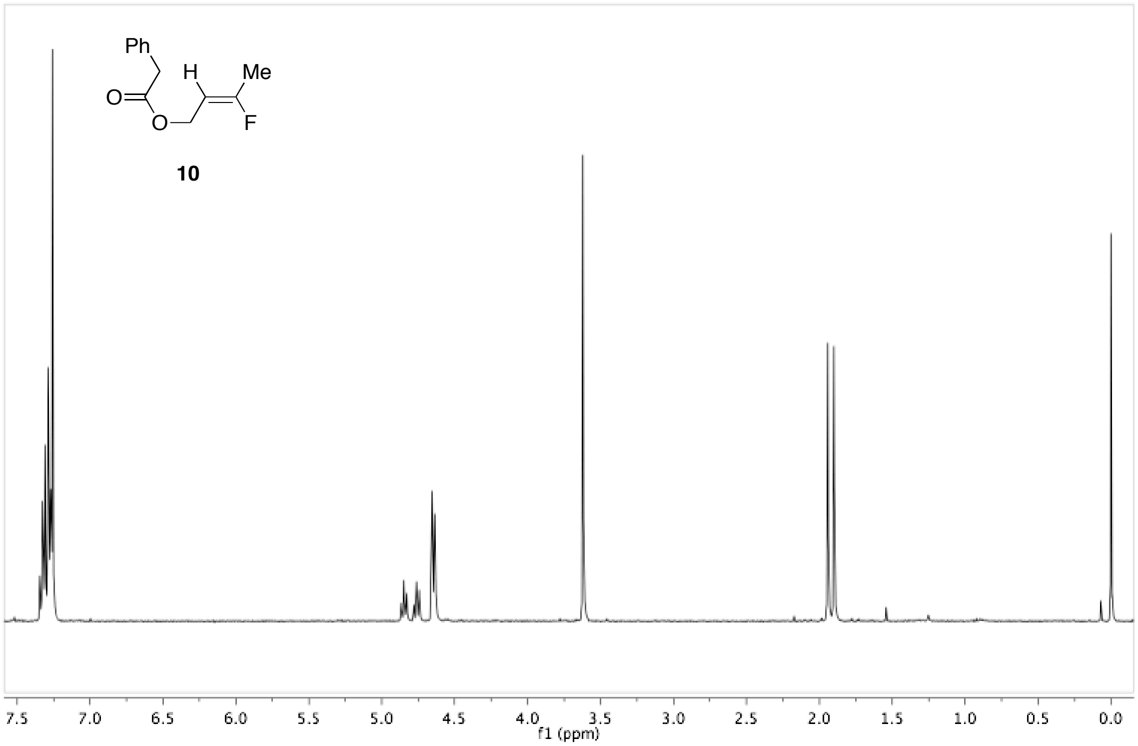

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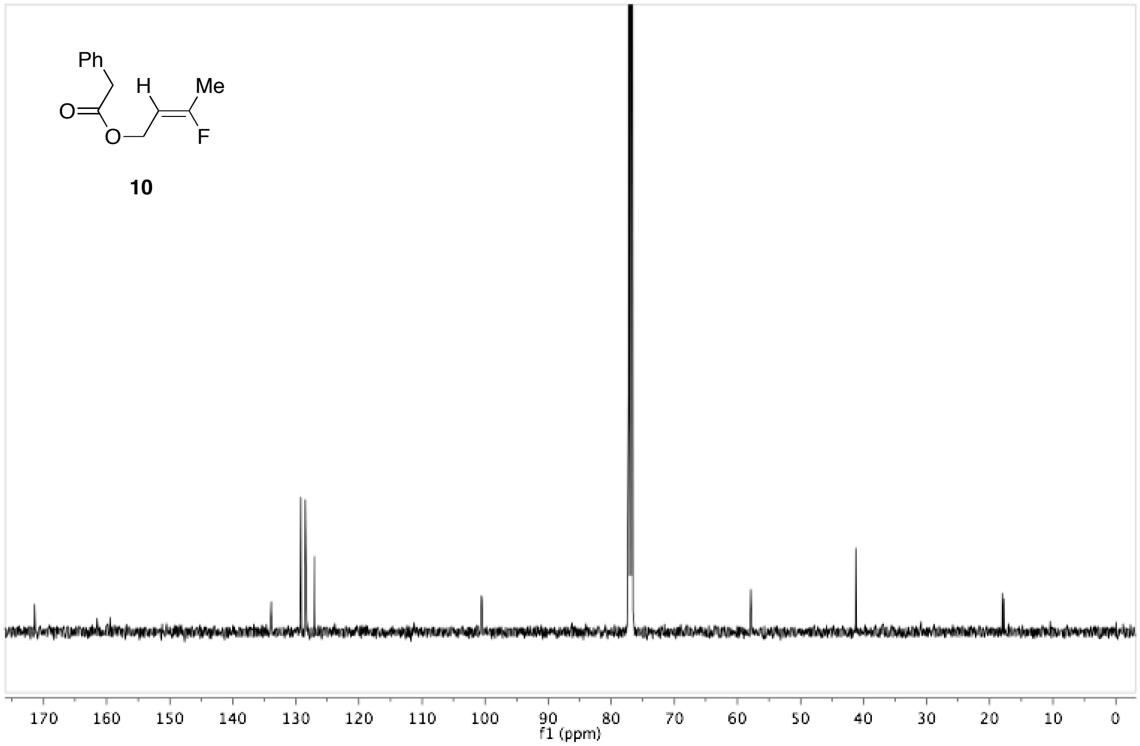

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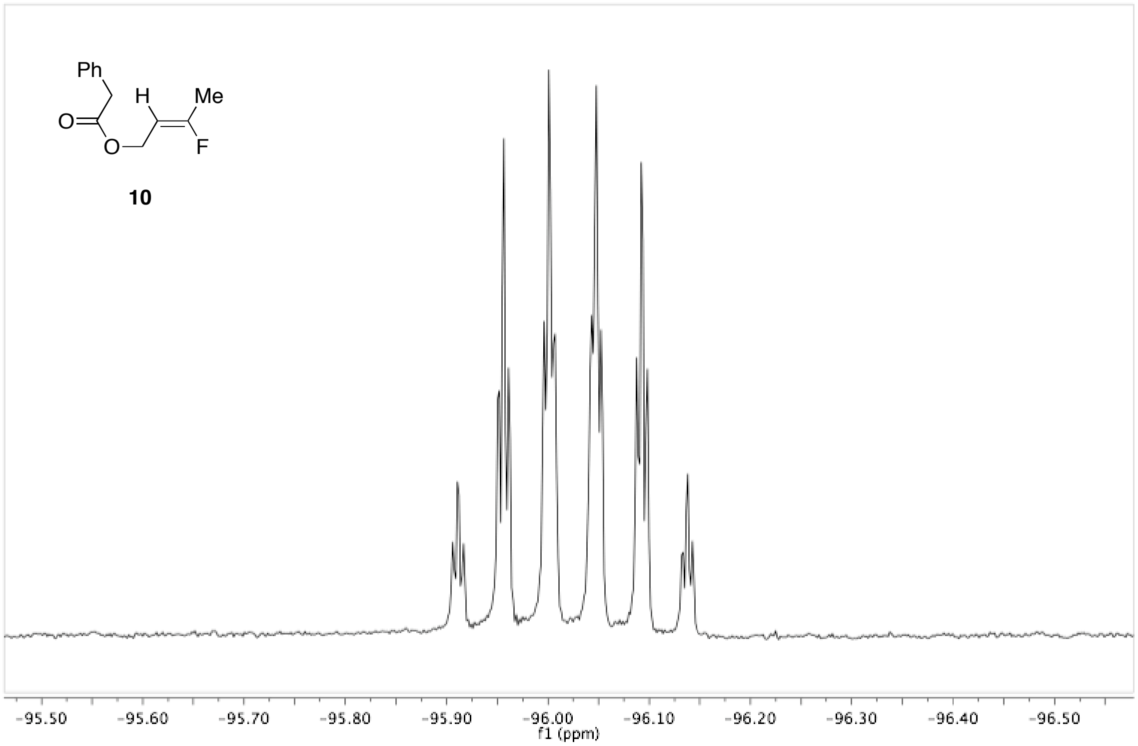

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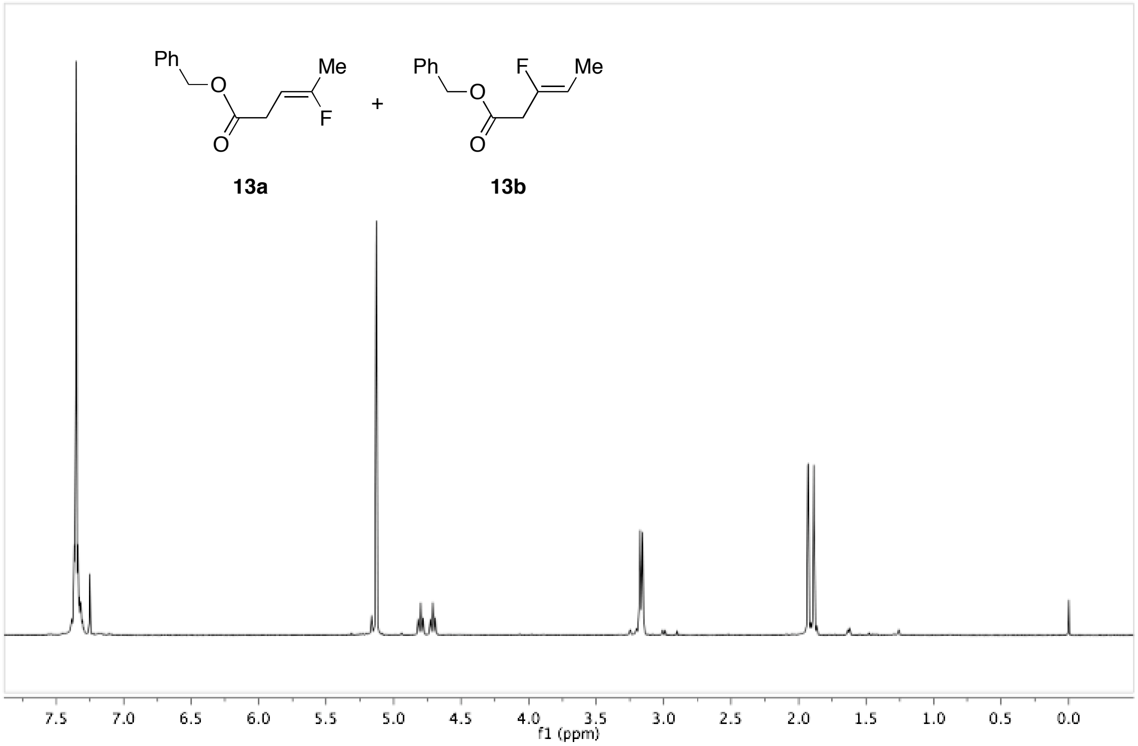

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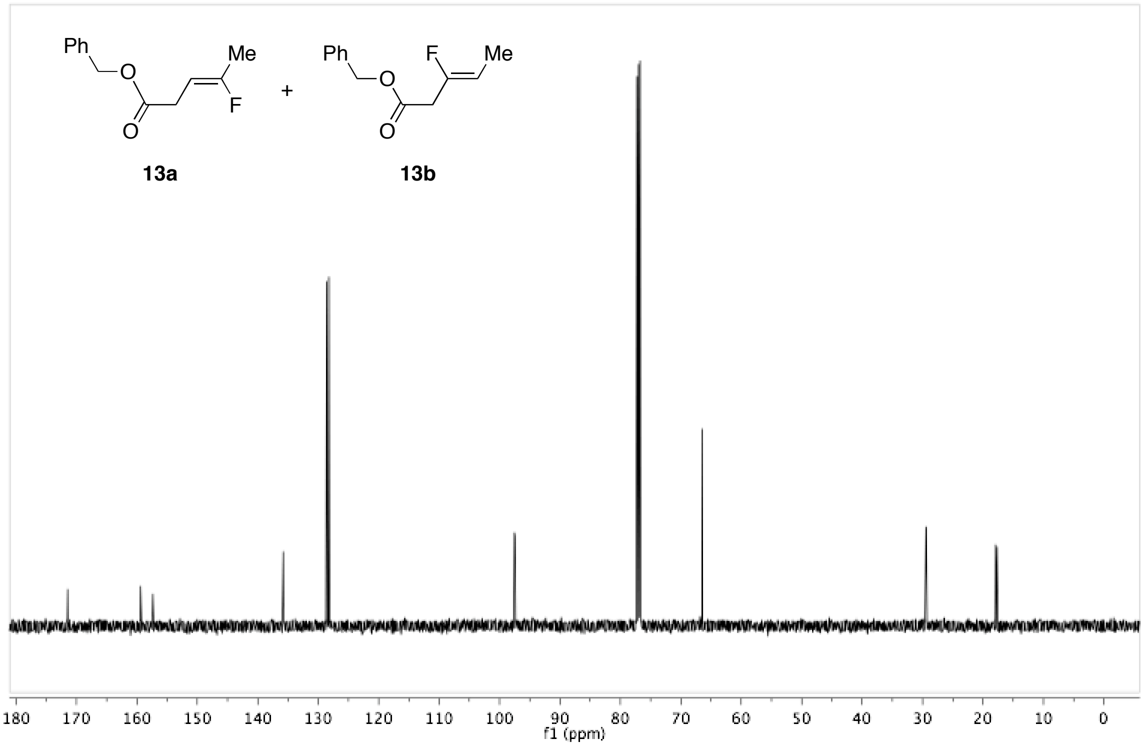

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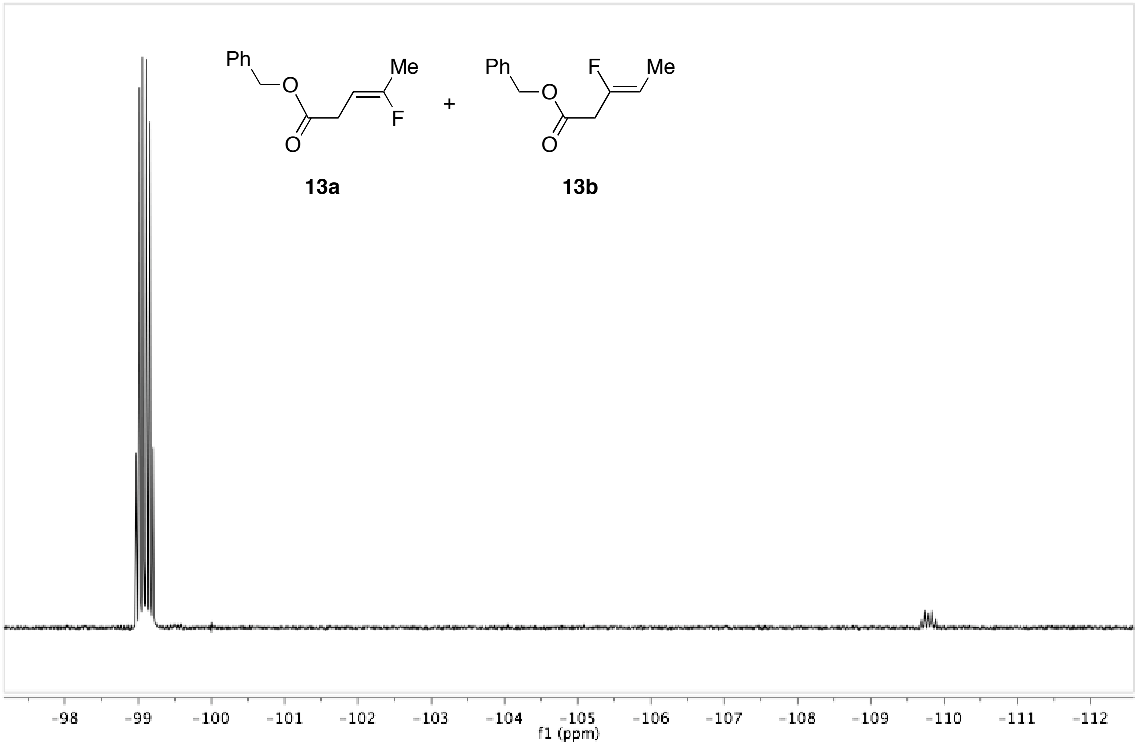

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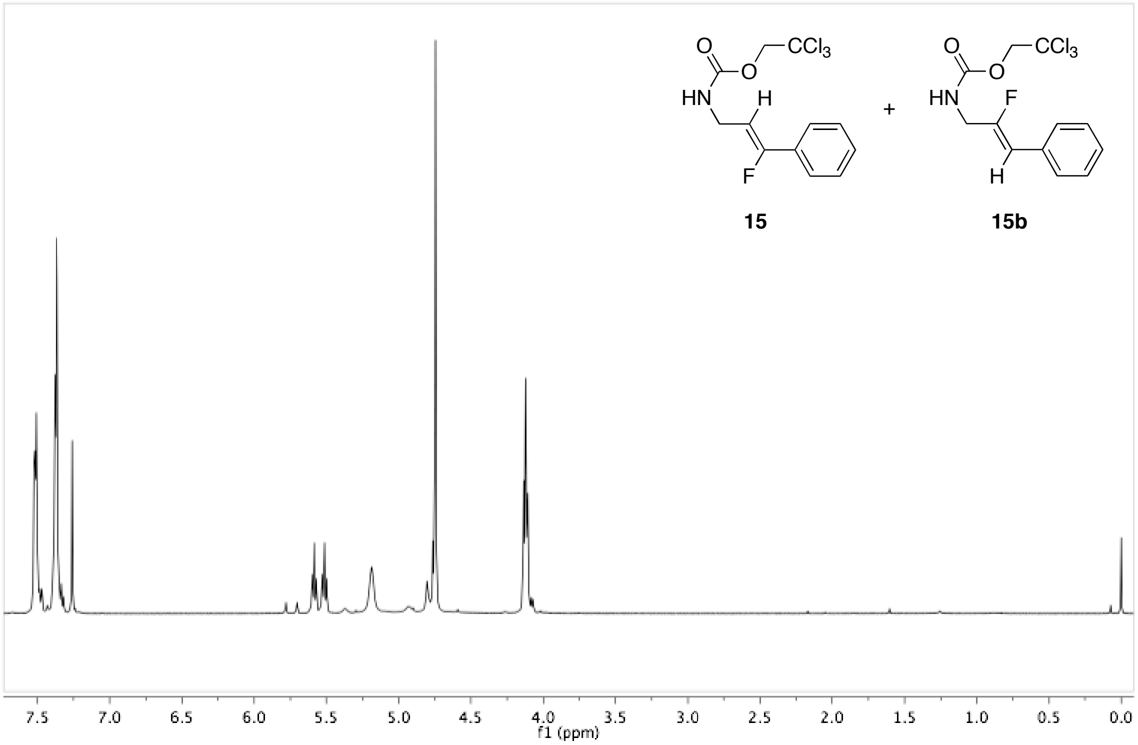

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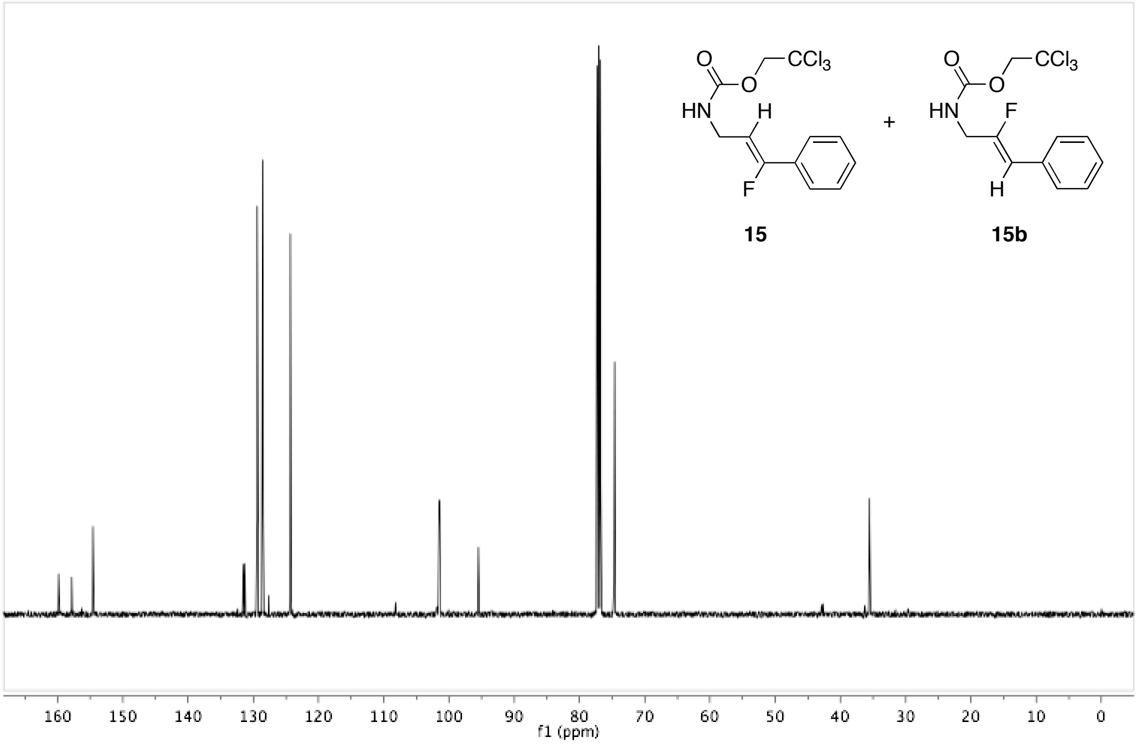

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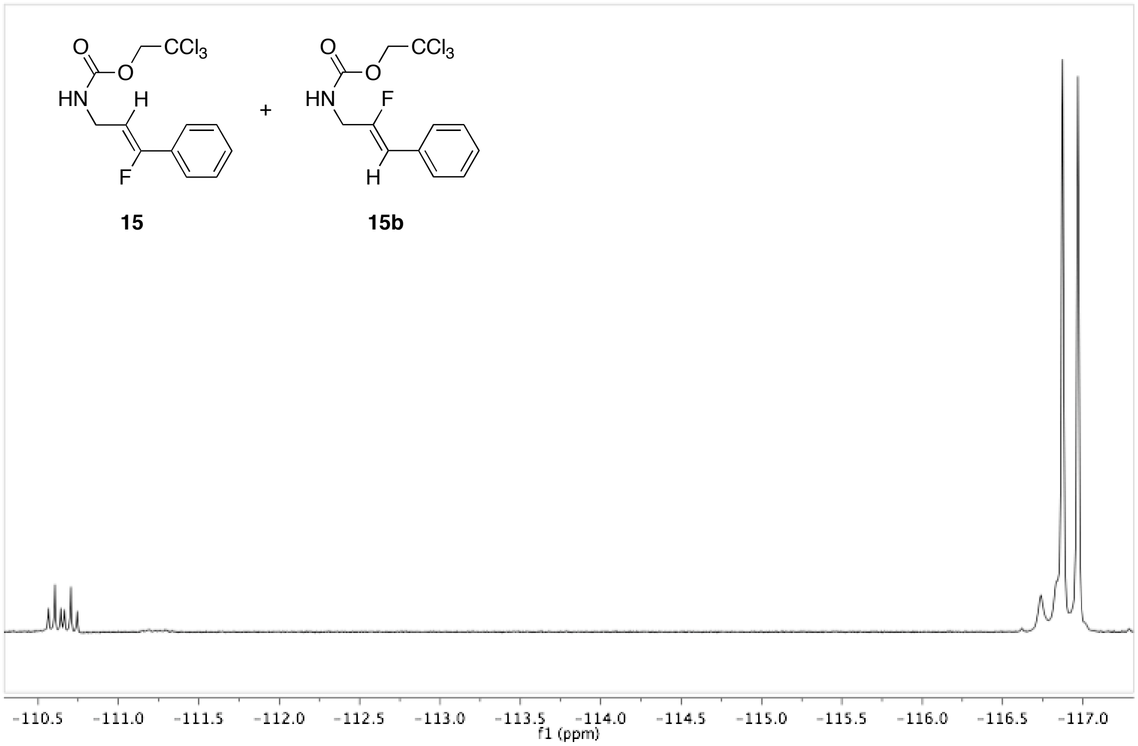

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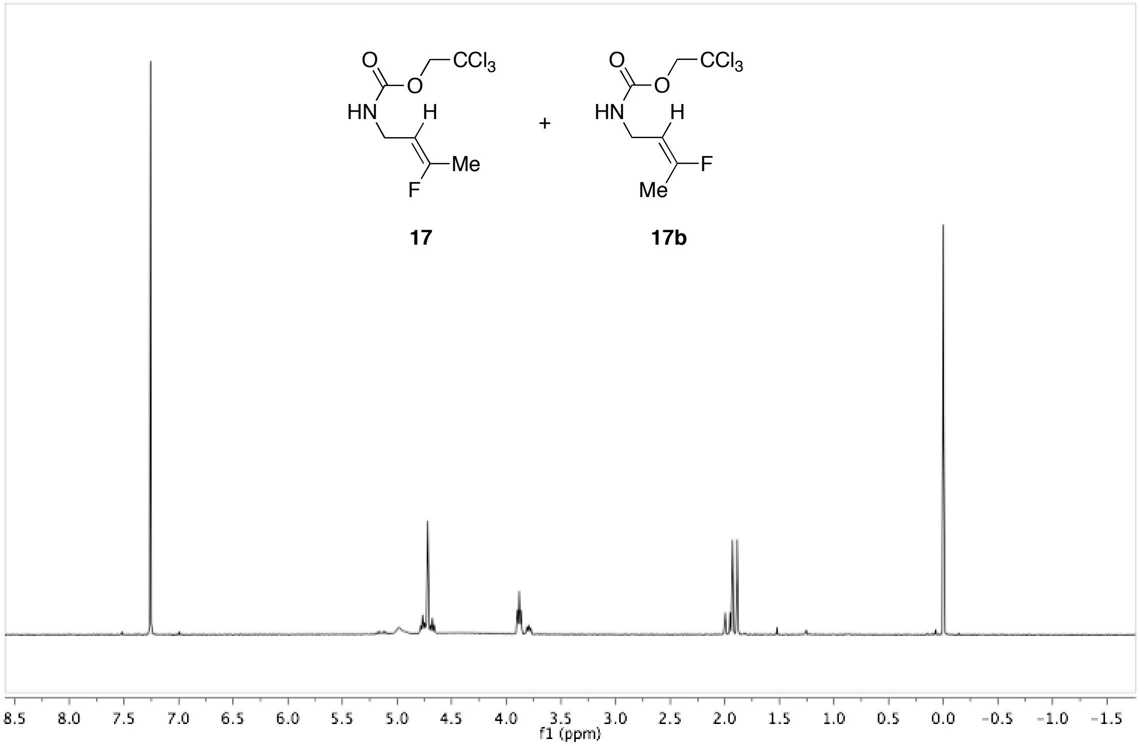

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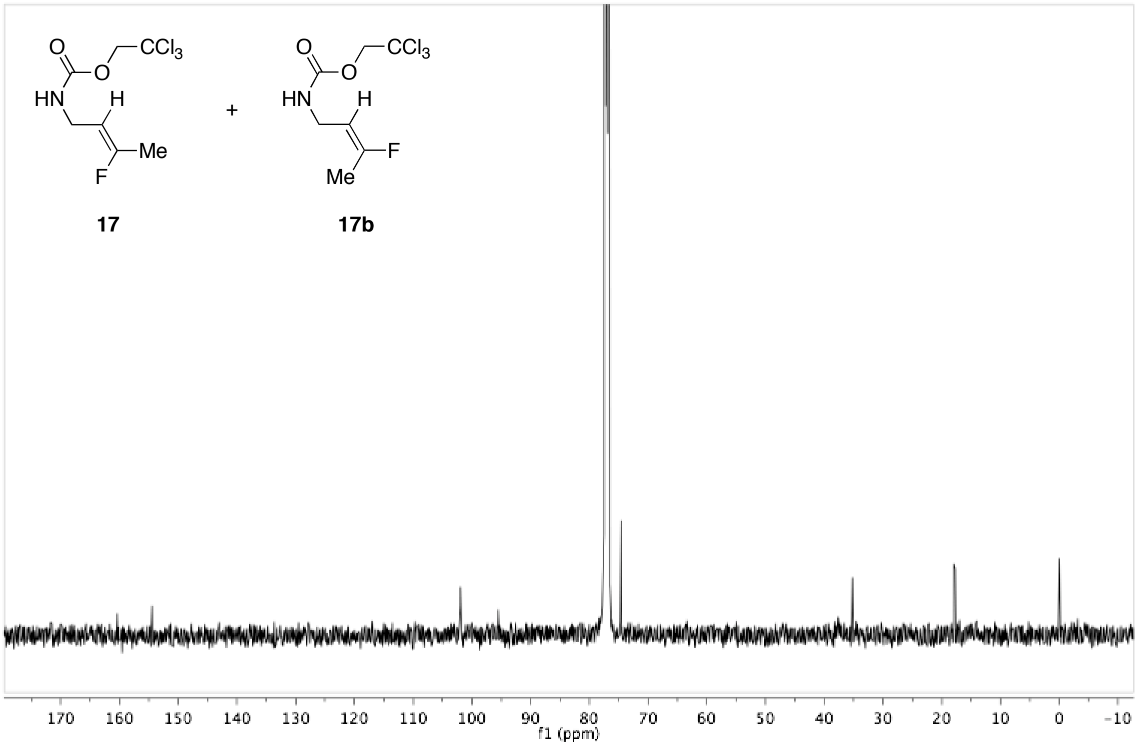

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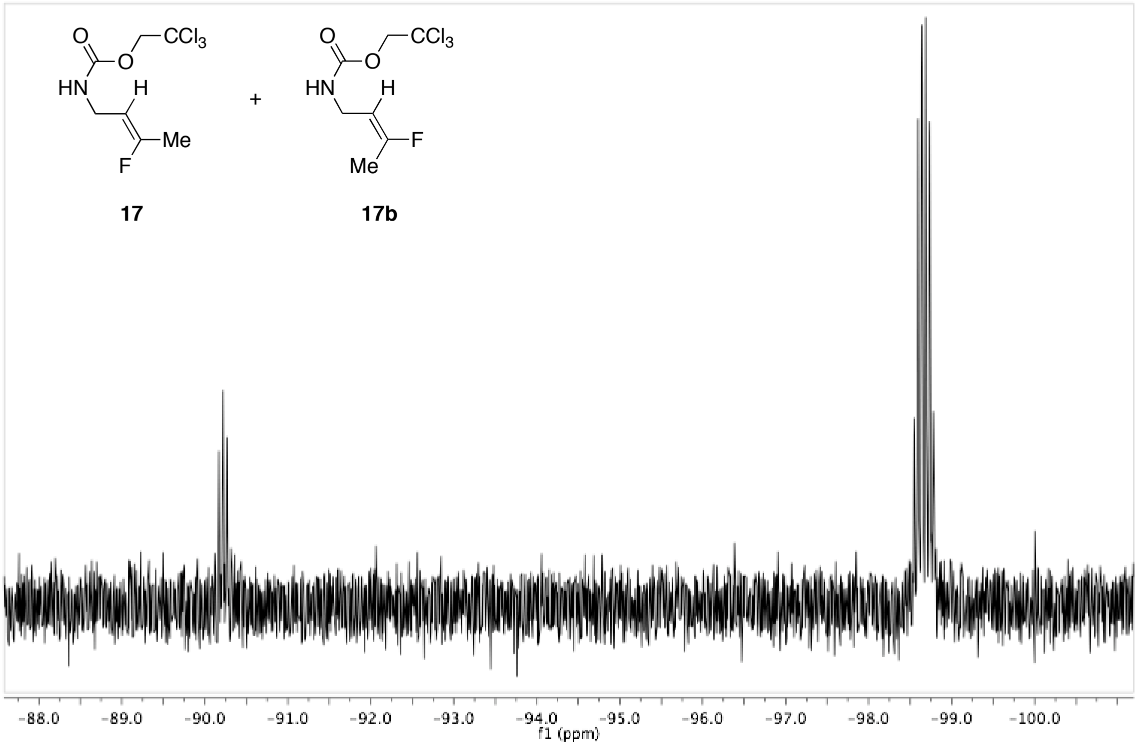

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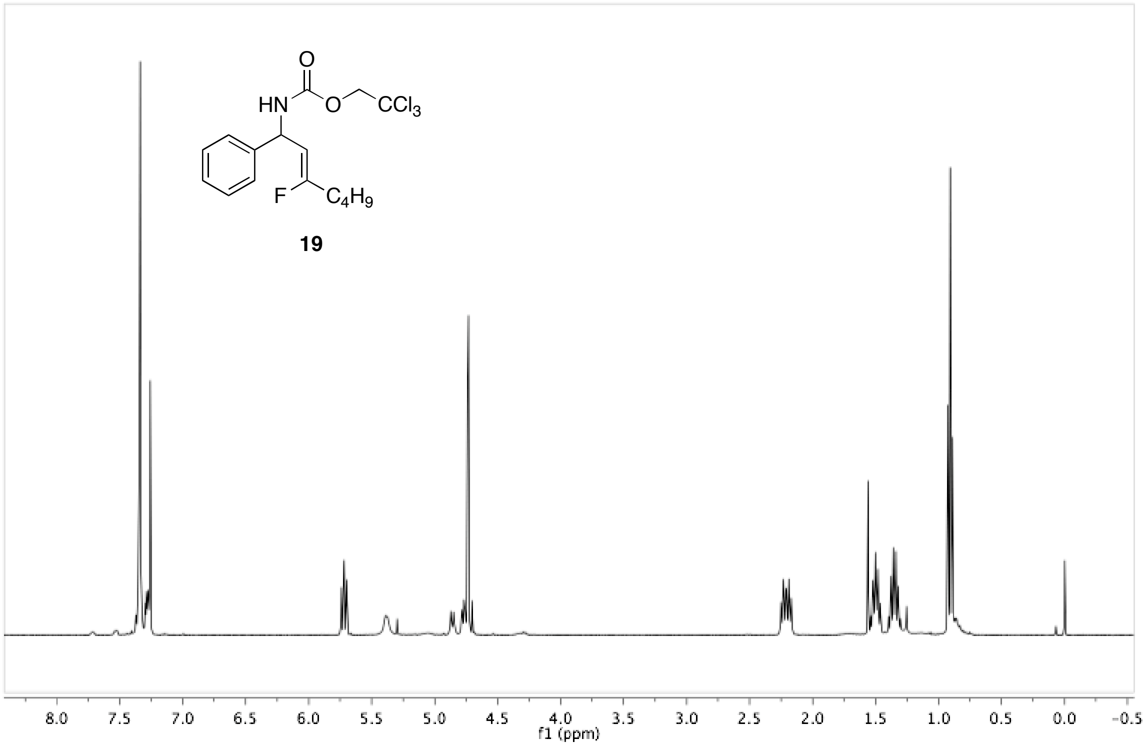

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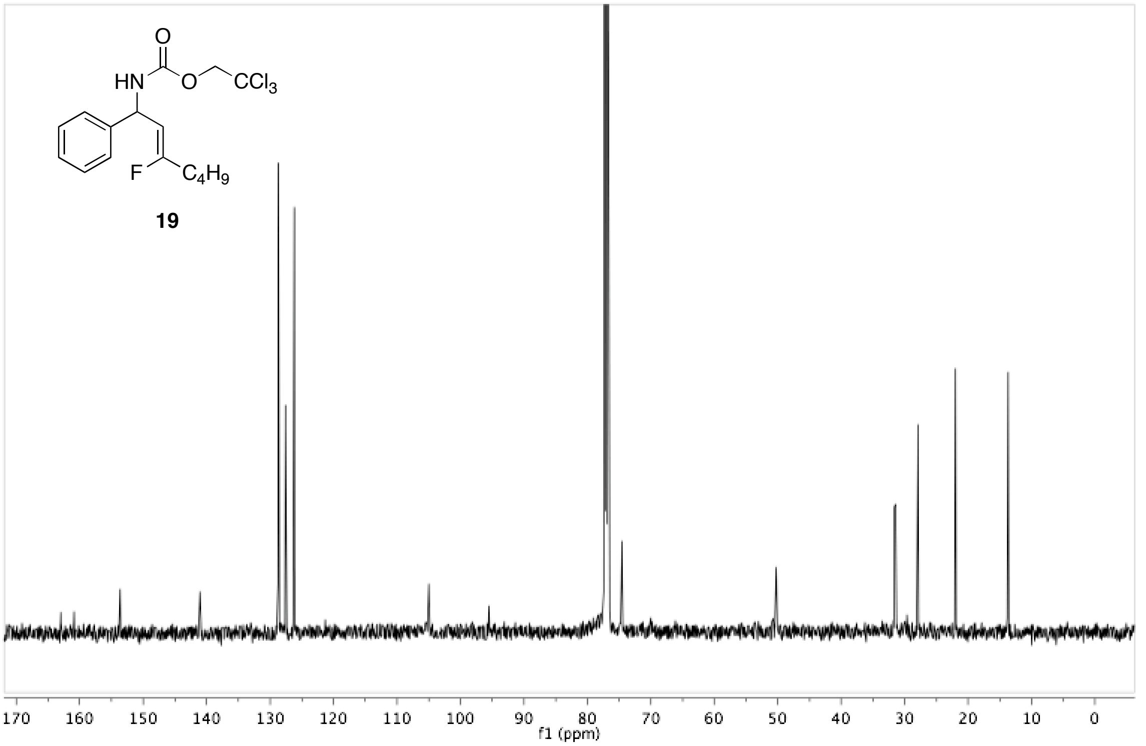

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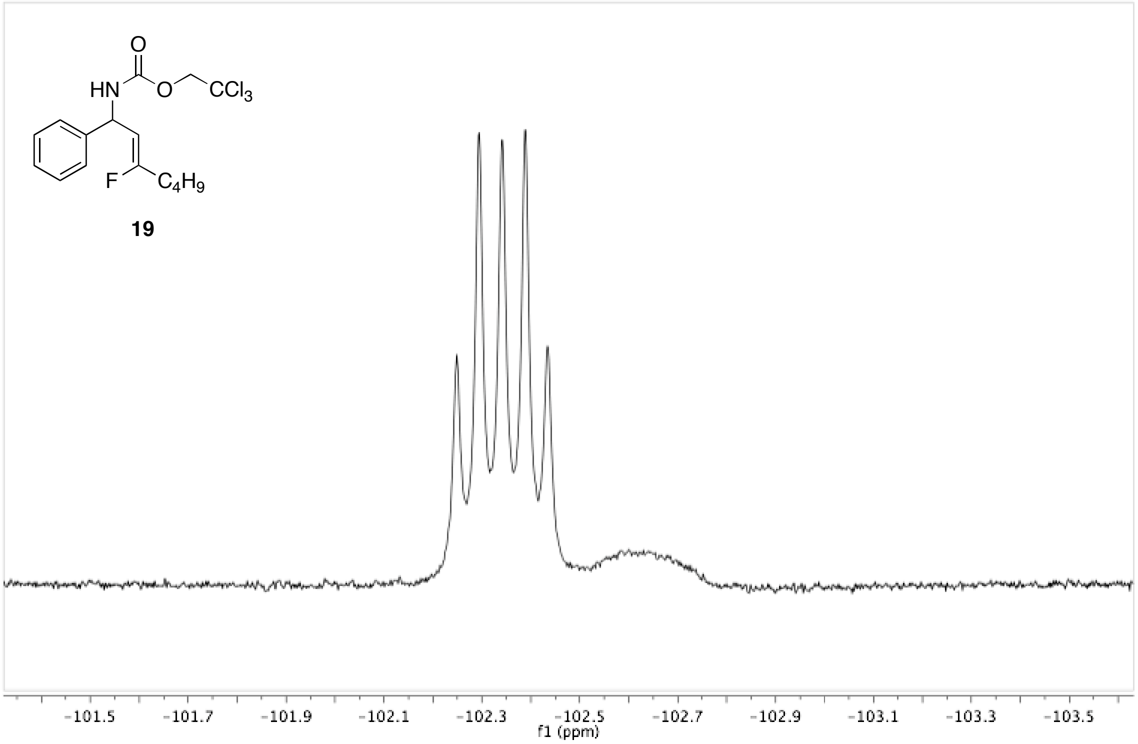

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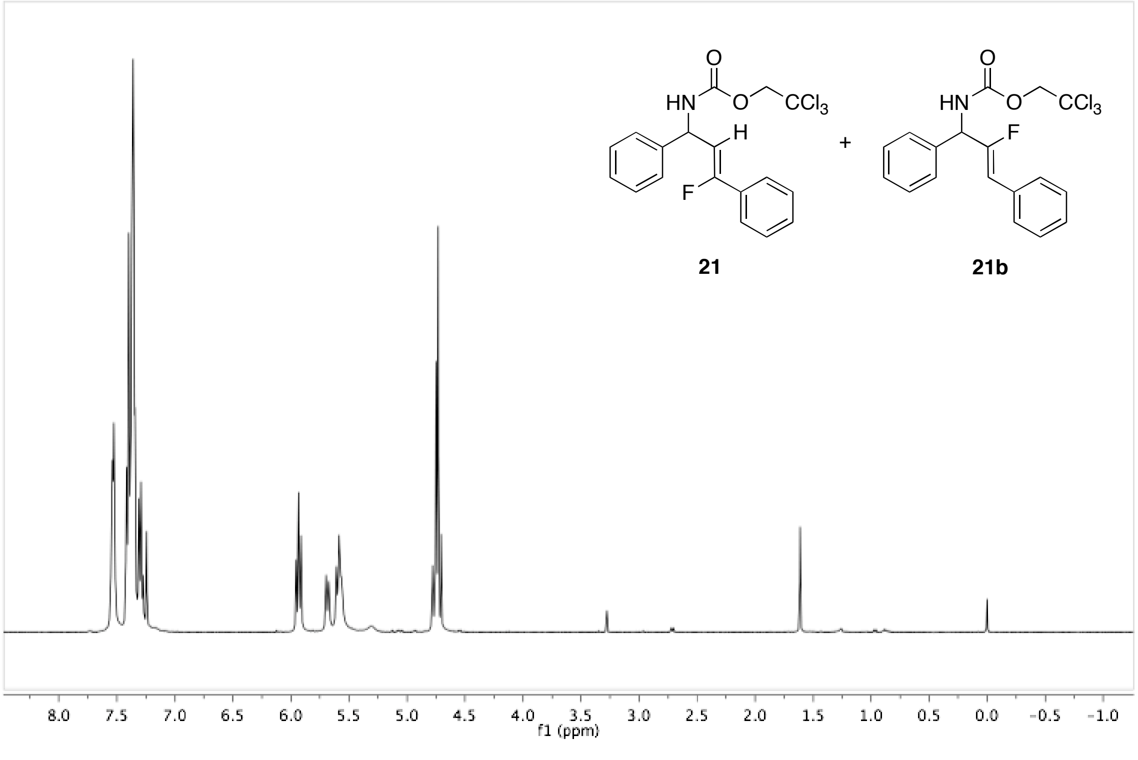

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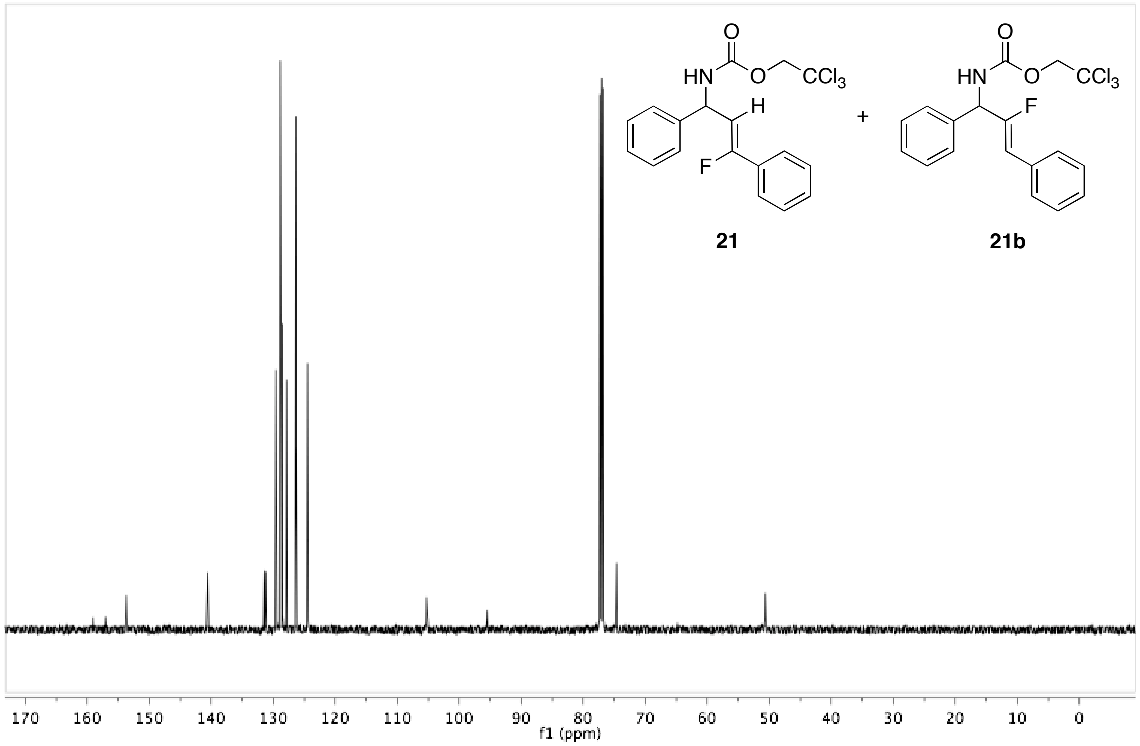

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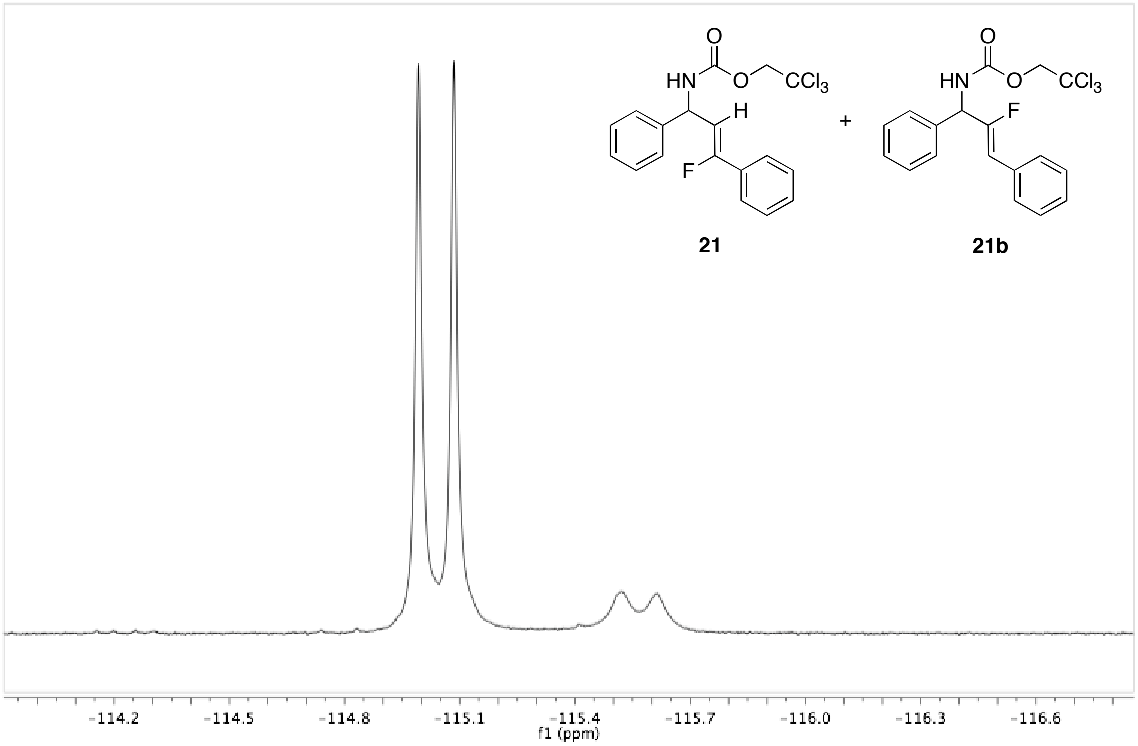

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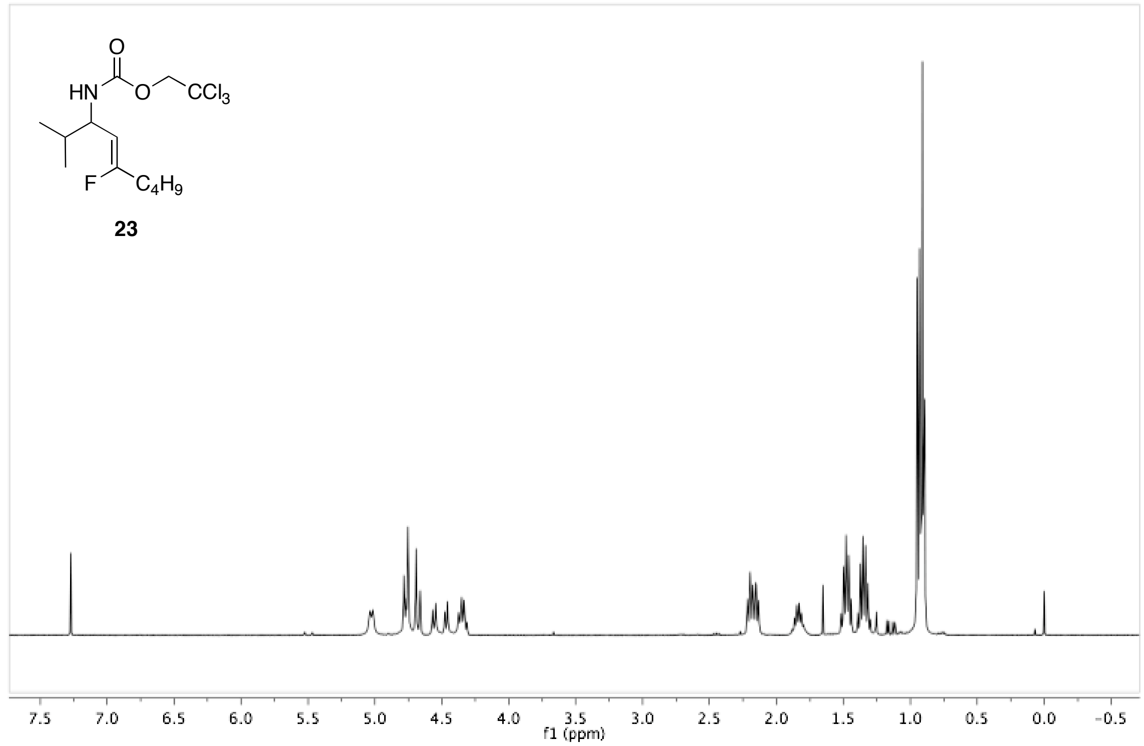

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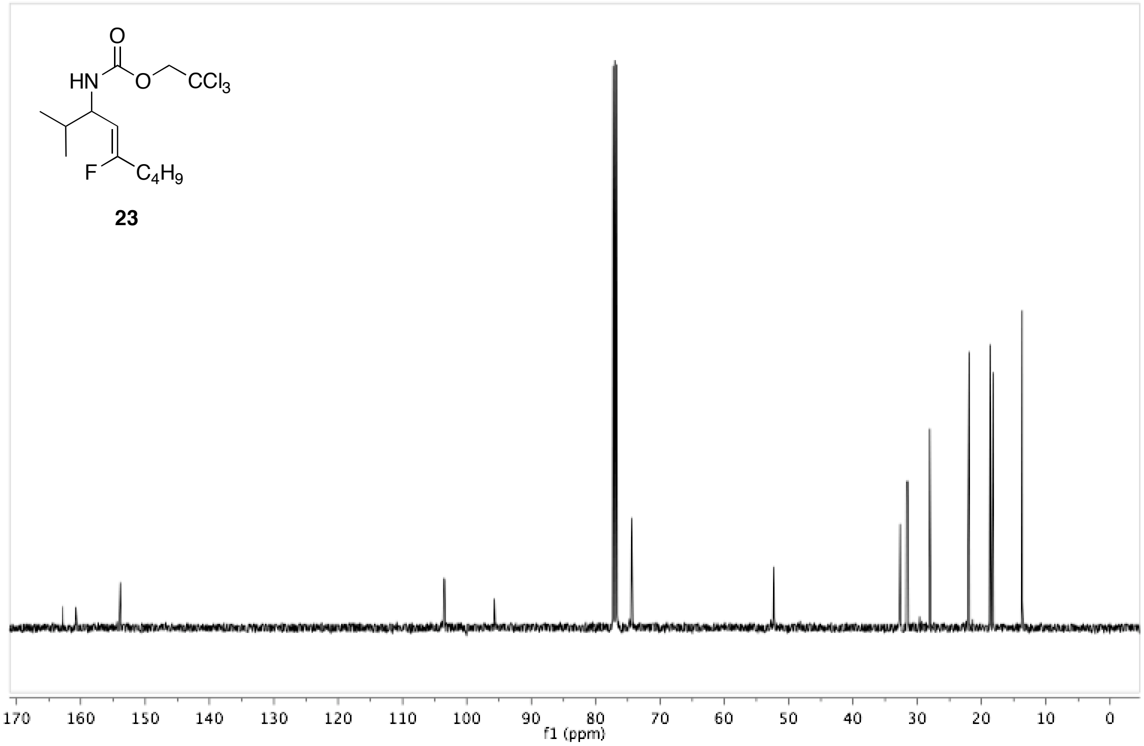

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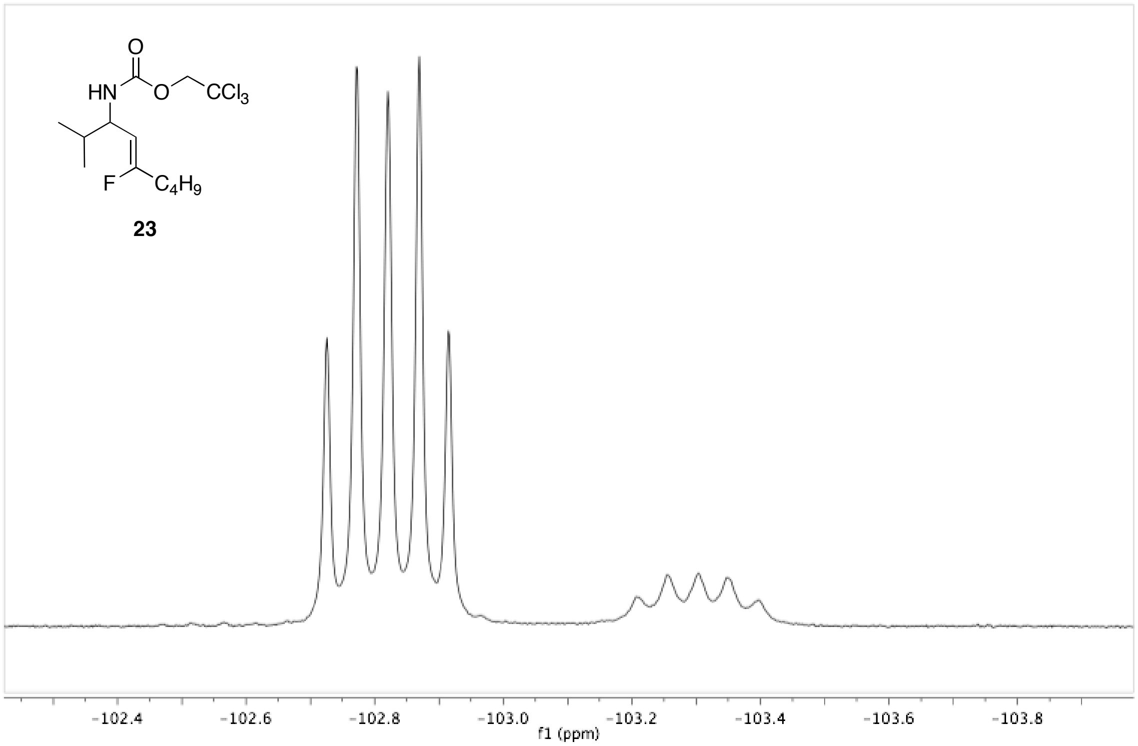

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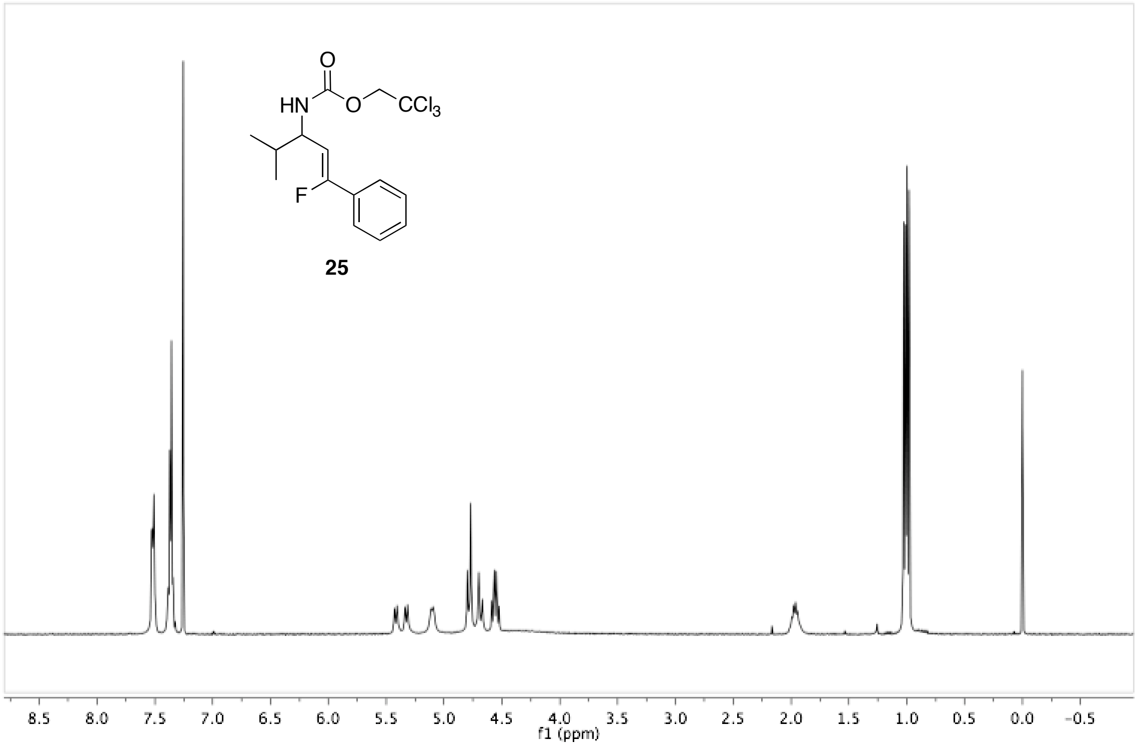

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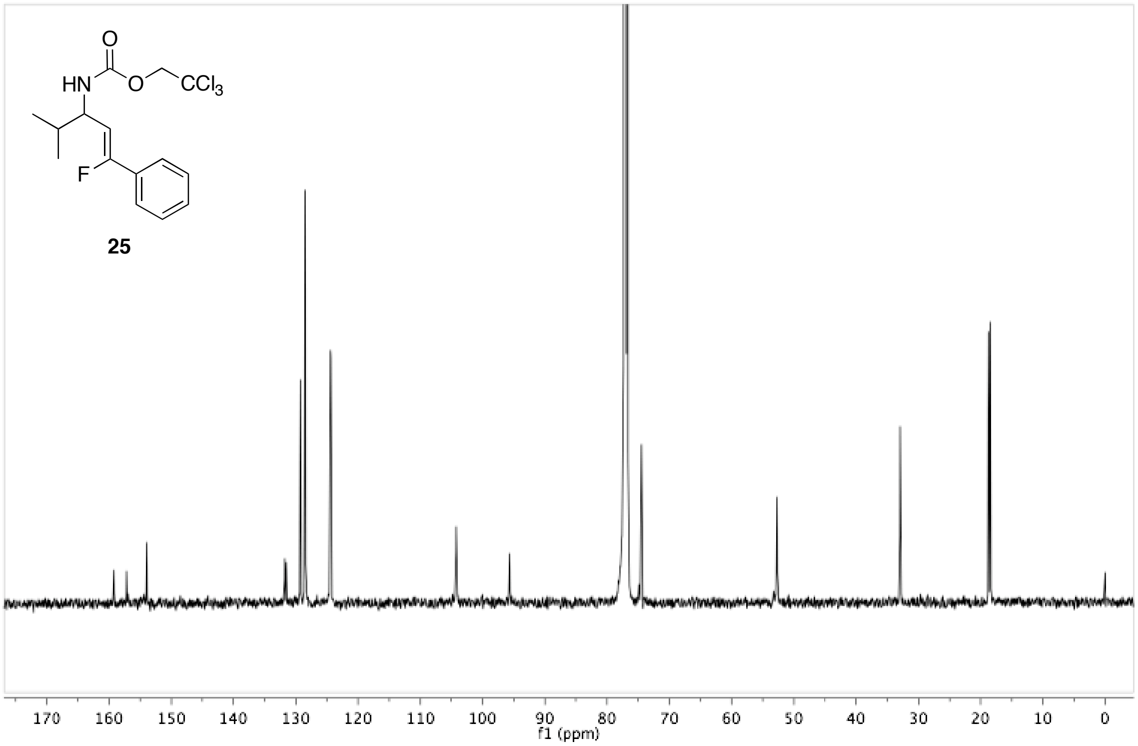

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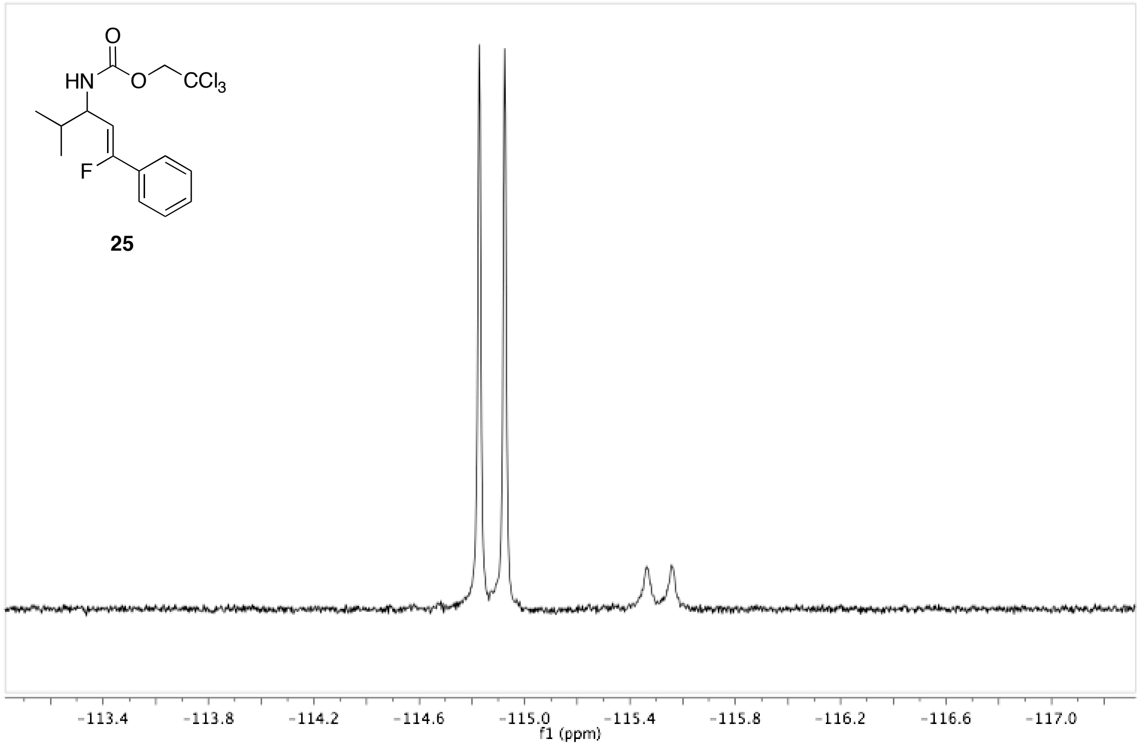

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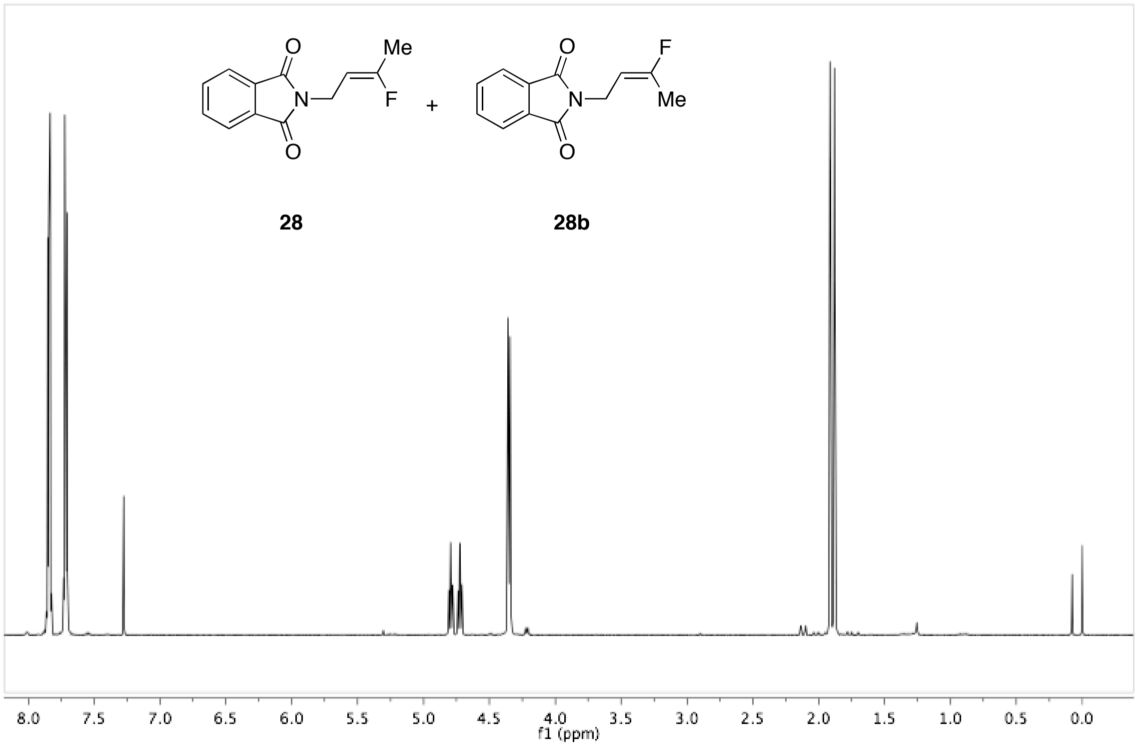

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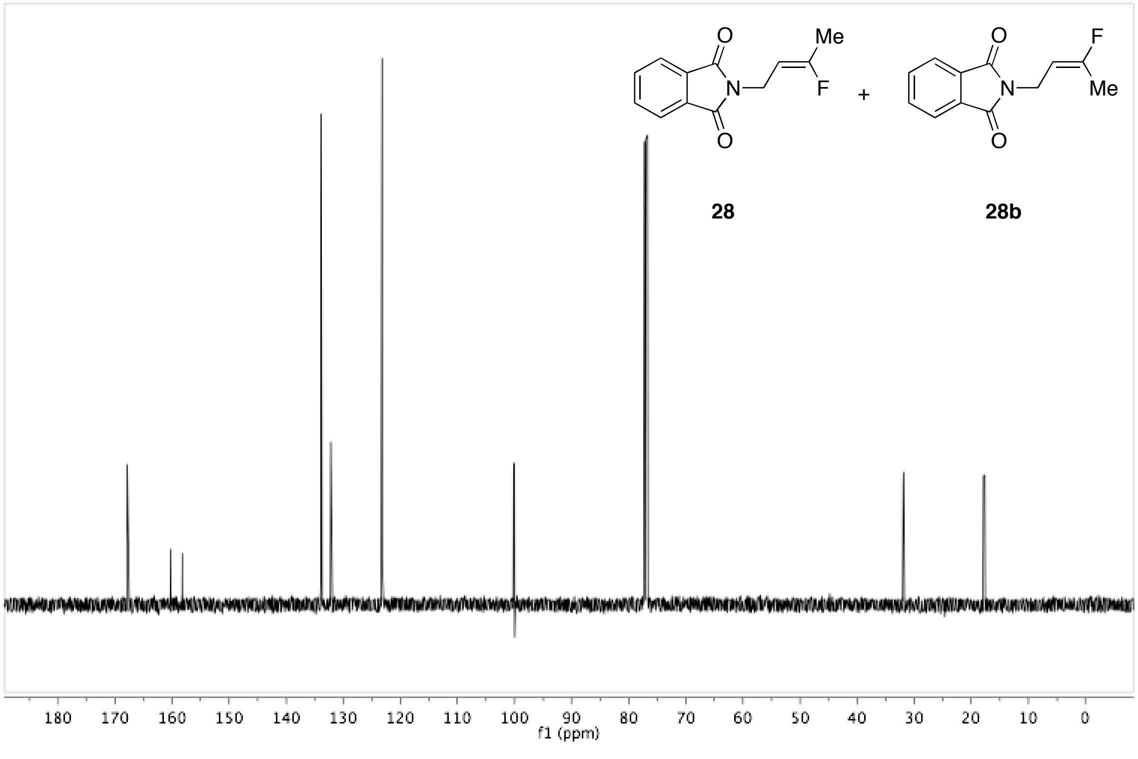

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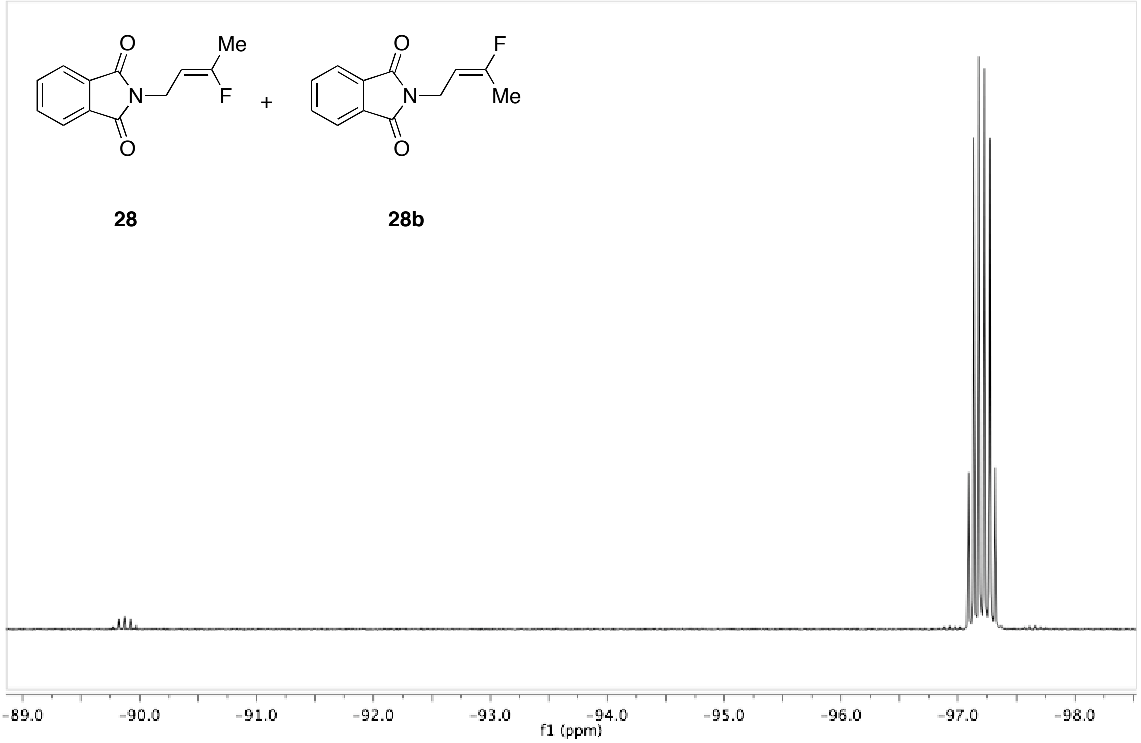

VI. References

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