Direct Conversion of *N*-Alkylamines to *N*-Propargylamines Through C–H Activation Promoted by Lewis Acid/Organocopper Catalysis: Application to Late-Stage Functionalization of Bioactive Molecules

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1. Procedures, Materials and Instrumentation

General experimental procedures. All reactions were performed in standard, dry glassware fitted with rubber septa under an inert atmosphere of nitrogen unless otherwise described. Stainless steel syringes or cannula were used to transfer air- and moisture-sensitive liquids. Reported concentrations refer to solution volumes at room temperature. Evaporation and concentration *in vacuo* were performed using house vacuum (ca. 40 mm Hg). Column chromatography was performed with SiliaFlash® 60 (40–63 micron) silica gel from Silicycle. Thin layer chromatography (TLC) was used for reaction monitoring and product detection using pre-coated glass plates covered with 0.25 mm silica gel with fluorescent indicator; visualization by UV light (λ_{ex} = 254 nm) or $KMnO_4$ stain.

Materials. Reagents were purchased in reagent grade from commercial suppliers and used without further purification, unless otherwise described. Amines and trimethylsilyl propiolate compounds were prepared according to the procedures reported previously.[1-4] H_2O, in synthetic procedures, refers to distilled water. Tris(pentafluorophenyl)borane, $Cu(MeCN)_4PF_6$, Xantphos, and 1,2-bis(diphenylphosphino)ethane were purchased from TCI and used without further purification. Chiral ligands **L4-7**, **L10**, and **L14-19** were prepared according to the literature procedures.[5-8]

Instrumentation. Proton nuclear magnetic resonance (^{1}H NMR) spectra and proton-decoupled carbon nuclear magnetic resonance (^{13}C {^{1}H} NMR) spectra were recorded at 25 °C (unless stated otherwise) on Inova 600 (600 MHz), Varian Unity/Inova 500 (500 MHz) or Oxford AS400 (400 MHz) spectrometers at the Boston College nuclear magnetic resonance facility. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to 0 ppm. Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent. The peak positions are quoted to one decimal place unless they are indistinguishable. The solvent peak was referenced to 77.0 ppm for ^{13}C for $CDCl_3$. Benzotrifluoride was used as an external standard for ^{19}F NMR and referenced to –63.0 ppm. BF_3•OEt_2 was used as an external standard for ^{11}B NMR and referenced to 0 ppm. Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz).

Infrared spectra were recorded on a Bruker FT-IR Alpha (ATR mode) spectrophotometer. Data are represented as follows: frequency of absorption (cm^{-1}).

High-resolution mass spectrometry was performed on a JEOL AccuTOF-DART (positive mode) at the Mass Spectrometry Facility, Boston College. Chiral HPLC analyses were carried using Agilent 1200 series instruments and Shimadzu chromatograph with Daicel CHIRALPAK® columns or Daicel CHIRALCEL® columns (internal diameter 4.6 mm, column length 250 mm, particle size 5 μm).

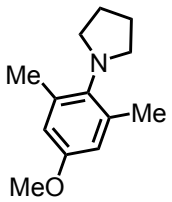
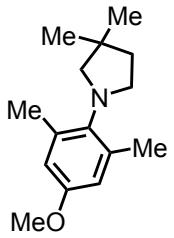
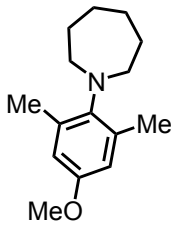
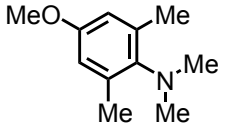
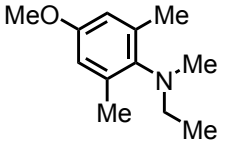
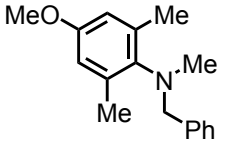
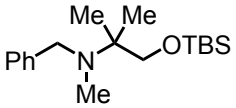
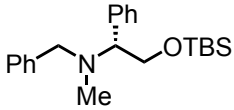
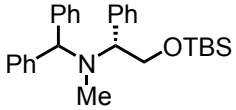
Abbreviations used. Bn = benzyl, COSY = correlated spectroscopy, DART = direct analysis in real time, ESI = electrospray ionization, Et_3N = trimethylamine, EtOAc = ethyl acetate, Et_2O = ethyl ether, HR = high-resolution, HSQC = heteronuclear single quantum coherence, LC = liquid chromatography, MS = mass spectrometry, NOESY = nuclear Overhauser effect spectroscopy, OTf = triflate, PTLC = preparatory thin-layer chromatography, THF = tetrahydrofuran, TLC = thin-layer chromatography, TMS = trimethylsilyl, TBS = *tert*-butyldimethylsilyl, TOF = time-of-flight.

2. Experimental Section

2.1 Substrate Preparation

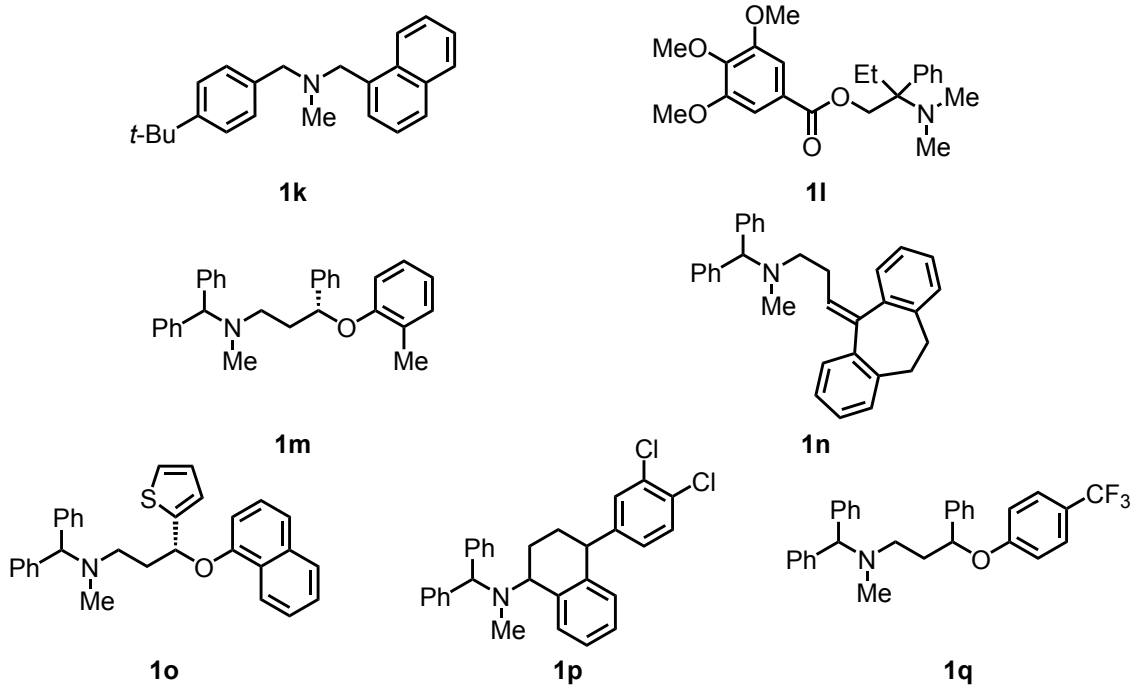
2.1.1 Preparation of Amine Substrates

Table S1-1. List of Amine Substrates (Part 1)

 **1b**	 **1c**	 **1d**
 **1e**	 **1f**	 **1g**
 **1h**	 **1i**	 **1j**

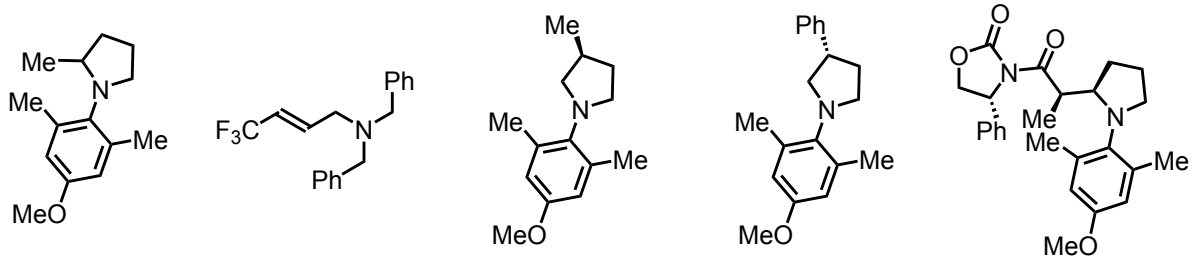
Amines **1b**-**1g** and **1h**-**1j** were prepared according to literature procedures.[1] The spectroscopic data for the amine substrates (**1h**-**1j**) are provided in SI-Section 2.1.

Table S1-2. List of Amine Substrates (Part 2)



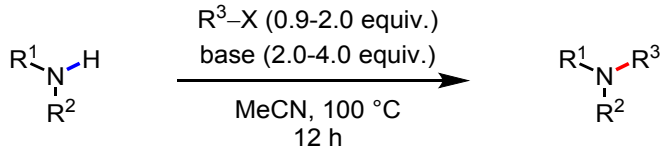
Amines **1m-1q** were prepared according to literature procedures.[2] Amines **1k** and **1l** were obtained by reacting the commercially available amine hydrochloride salt with NaOH (1.0 M aq.). The spectroscopic data for the amine substrates (**1m-1q**) are provided in SI-Section 2.1.

Table S1-3. List of Amine Substrates (Part 3)



Amines listed above were prepared according to literature procedures.[1] The spectroscopic data for the amine substrates (**1s-1u**) are provided in SI-Section 2.1.

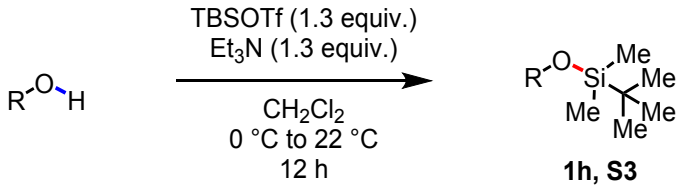
General Procedure for Preparation of Tertiary or Secondary Amines



S1, **S6**, **1m-1q**, **1t-1u**

Amines **S1**, **S6**, **1m-1q** and **1t-1u** were prepared by alkylation of the corresponding primary or secondary amines. To a solution of primary or secondary amine (1.0 equiv.) and K_2CO_3 or Et_3N (2.0-4.0 equiv.) in MeCN was added alkyl halide (R^3–X; 0.9-2.0 equiv.). The reaction mixture was allowed to stir at 100 °C for 12 h. Upon completion (determined by TLC), H_2O was added and the organic material was extracted with EtOAc (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The desired amine products were obtained after purification by flash silica gel column chromatography.

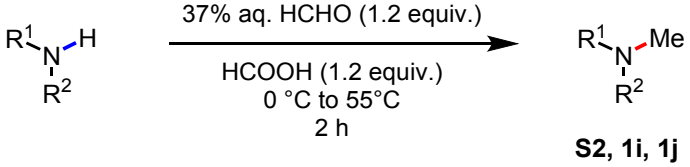
General Procedure for TBS Protection of Alcohols



1h, S3

Substrates **1h** and **S3** were prepared by TBS protection of alcohols. To a solution of alcohol in CH_2Cl_2 at 0 °C, Et_3N (1.3 equiv.) and TBSOTf (1.3 equiv.) were added in a dropwise manner. After the addition, the reaction mixture was allowed to warm to 22 °C and stirred for 12 h. Upon completion (determined by TLC), H_2O was added and the organic material was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The desired silyl ether products were obtained after purification by flash silica gel column chromatography.

General Procedure for *N*-Methylation of Secondary Amines

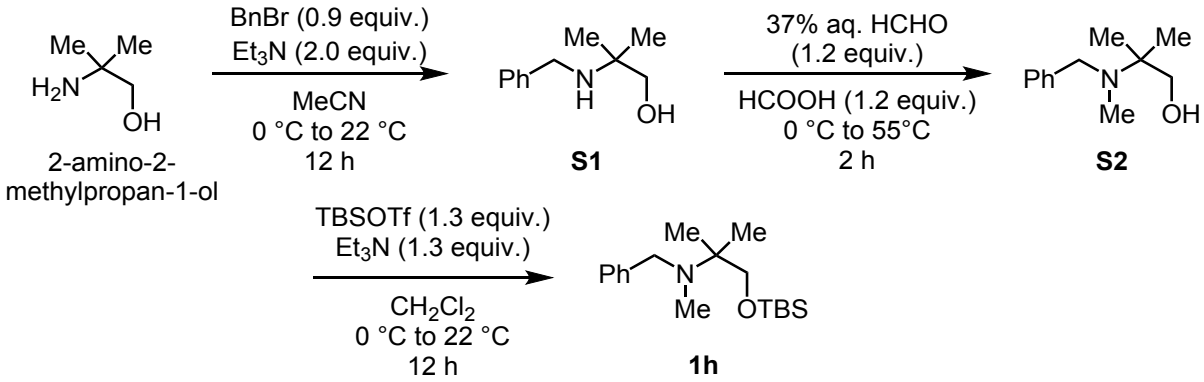


S2, 1i, 1j

Substrates **S2**, **1i**, and **1j** were prepared by *N*-methylation of secondary amines. A solution of amine and formaldehyde (37% aq. solution, 1.2 equiv.) was cooled to 0 °C. To the reaction mixture was added formic acid (1.2 equiv.) in a dropwise manner. The reaction mixture was

allowed to warm to 55 °C and stirred for 2 h. Upon completion (determined by TLC), the reaction mixture was cooled to 0 °C, NaOH (1.0 M aq. solution) was added until the aqueous layer was alkaline. The organic material was extracted with Et_2O (3 x 20 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The desired amine products were obtained after flash silica gel column chromatography.

Procedure for Preparation of *N*-Benzyl-1-((*tert*-butyldimethylsilyl)oxy)-*N*,2-dimethylpropan-2-amine (1h)



2-(Benzylamino)-2-methylpropan-1-ol (S1)

2-(Benzylamino)-2-methylpropan-1-ol was prepared following **General Procedure for Preparation of Secondary Amines** using 2-amino-2-methylpropan-1-ol (69 mmol). The amine product **S1** was obtained after purification by flash silica gel column chromatography (EtOAc:hexanes = 1:1) as a colorless oil (9.0 g, 73% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 – 7.30 (m, 3H), 7.26 (d, *J* = 1.0 Hz, 2H), 3.69 (s, 2H), 3.35 (s, 2H), 1.15 (d, *J* = 1.0 Hz, 6H).

2-(Benzyl(methyl)amino)-2-methylpropan-1-ol (S2)

2-(Benzyl(methyl)amino)-2-methylpropan-1-ol was prepared following **General Procedure for *N*-Methylation of Secondary Amines** using 2-(benzylamino)-2-methylpropan-1-ol (20 mmol). The amine product **S2** was obtained after purification by flash silica gel column chromatography (EtOAc:Et_3N:hexanes = 20:1:79) as a colorless oil (2.0 g, 50% yield).

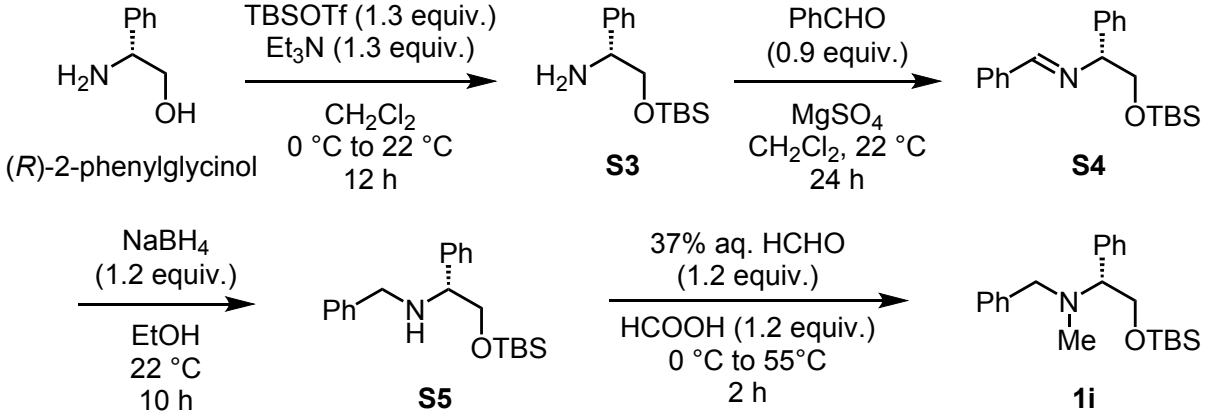
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 1.8 Hz, 1H), 7.26 – 7.20 (m, 4H), 3.52 (s, 2H), 3.44 (s, 2H), 2.09 (s, 3H), 1.13 (s, 6H).

***N*-Benzyl-1-((*tert*-butyldimethylsilyl)oxy)-*N*,2-dimethylpropan-2-amine (1h)**

N-Benzyl-1-((*tert*-butyldimethylsilyl)oxy)-*N*,2-dimethylpropan-2-amine was prepared following **General Procedure for TBS Protection of Alcohols** using 2-(benzyl(methyl)amino)-2-methylpropan-1-ol (10 mmol). The amine product **1h** was obtained after purification by flash silica gel column chromatography (Et_2O:hexanes = 1:9) as a colorless oil (3.0 g, 95% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.24 (m, 4H), 7.24 – 7.17 (m, 1H), 3.63 (s, 2H), 3.56 (s, 2H), 2.15 (s, 3H), 1.11 (s, 6H), 0.91 (s, 9H), 0.06 (s, 6H).

Procedure for Preparation of (*R*)-*N*-Benzyl-2-((*tert*-butyldimethylsilyl)oxy)-*N*-methyl-1-phenylethan-1-amine (1i)



(*R*)-2-((*tert*-Butyldimethylsilyl)oxy)-1-phenylethan-1-amine (S3)

(*R*)-2-((*tert*-Butyldimethylsilyl)oxy)-1-phenylethan-1-amine was prepared following **General Procedure for TBS Protection of Alcohols** using (*R*)-2-amino-2-phenylethan-1-ol (60 mmol). The amine product **S3** was obtained after purification by flash silica gel column chromatography (Et_3N:hexanes = 1:19) as a colorless oil (14.0 g, 93% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.21 (m, 4H), 7.19 – 7.13 (m, 1H), 3.98 (dd, *J* = 8.4, 3.9 Hz, 1H), 3.63 (dd, *J* = 9.8, 3.9 Hz, 1H), 3.43 (dd, *J* = 9.8, 8.3 Hz, 1H), 0.81 (s, 9H), -0.07 (d, *J* = 1.6 Hz, 6H).

(*R,E*)-*N*-(2-((*tert*-Butyldimethylsilyl)oxy)-1-phenylethyl)-1-phenylmethanimine (S4)

To a solution of amine **S1** (33 mmol, 1.1 equiv.) and benzaldehyde (30 mmol, 1.0 equiv.) in CH_2Cl_2, was added $MgSO_4$. The reaction mixture was allowed to stir for 24 h at 22 °C. Upon completion (determined by TLC), the unpurified mixture was filtered over a pad of Celite and rinsed with CH_2Cl_2. The organic layer was concentrated *in vacuo*, and the product obtained

was directly used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.76 – 7.65 (m, 2H), 7.49 – 7.37 (m, 2H), 7.37 – 7.28 (m, 3H), 7.28 – 7.21 (m, 2H), 7.20 – 7.12 (m, 1H), 4.33 (dd, *J* = 8.6, 4.4 Hz, 1H), 3.86 – 3.68 (m, 2H), 0.73 (s, 9H), -0.10 (s, 3H), -0.16 (s, 3H).

(*R*)-*N*-Benzyl-2-((*tert*-butyldimethylsilyl)oxy)-1-phenylethan-1-amine (S5)

To a solution of imine **S4** (30 mmol, 1.0 equiv.) in EtOH, was added $NaBH_4$ (36 mmol, 1.2 equiv.) at 0 °C. The reaction mixture was allowed to stir for 10 h. Upon completion (monitored by TLC), the reaction mixture was diluted with H_2O, and extracted with EtOAc (3 x 20 mL). The combined organic layers were then dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The amine product **S5** was obtained after purification by flash silica gel column chromatography (Et_3N:hexanes = 1:50) as a colorless oil (10 g, 98% yield).

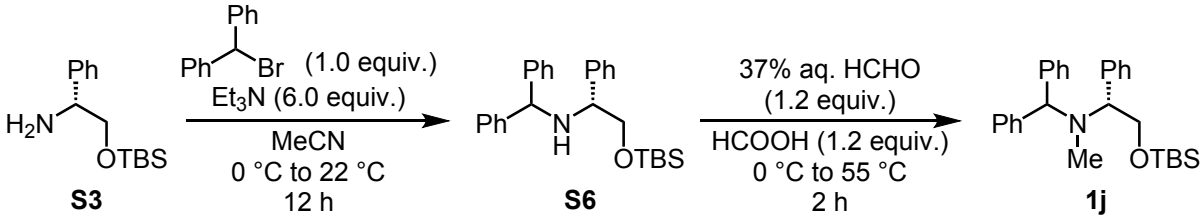
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 2H), 7.24 (ddd, *J* = 7.9, 6.7, 1.6 Hz, 2H), 7.22 – 7.15 (m, 5H), 7.13 (td, *J* = 6.9, 1.7 Hz, 1H), 3.71 (dd, *J* = 9.2, 4.0 Hz, 1H), 3.65 (d, *J* = 13.5 Hz, 1H), 3.56 (dd, *J* = 10.0, 4.0 Hz, 1H), 3.51 – 3.42 (m, 2H), 0.78 (d, *J* = 1.8 Hz, 9H), -0.06 – -0.12 (m, 6H).

(*R*)-*N*-Benzyl-2-((*tert*-butyldimethylsilyl)oxy)-*N*-methyl-1-phenylethan-1-amine (1i)

(*R*)-*N*-Benzyl-2-((*tert*-butyldimethylsilyl)oxy)-*N*-methyl-1-phenylethan-1-amine was prepared using **General Procedure for *N*-Methylation of Secondary Amines** using (*R*)-*N*-benzyl-2-((*tert*-butyldimethylsilyl)oxy)-1-phenylethan-1-amine (21 mmol). The amine product **1i** was obtained after purification by flash silica gel column chromatography (EtOAc: Et_3N: hexanes 20:1:79) as a colorless oil (6.8 g, 93% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.34 (m, 3H), 7.34 – 7.28 (m, 5H), 7.28 – 7.24 (m, 1H), 7.24 – 7.18 (m, 1H), 4.07 (dd, *J* = 10.4, 6.1 Hz, 1H), 3.94 – 3.85 (m, 1H), 3.70 – 3.56 (m, 2H), 3.45 (d, *J* = 13.5 Hz, 1H), 2.19 (s, 3H), 0.83 (s, 9H), -0.06 (d, *J* = 7.9 Hz, 6H); $[\alpha]^{25}_D$ = 1.6° (*c* 1.0, CH_2Cl_2).

Procedure for Preparation of (*R*)-*N*-Benzyl-2-((*tert*-butyldimethylsilyl)oxy)-*N*-methyl-1-phenylethan-1-amine (1j)



(*R*)-*N*-Benzhydryl-2-((*tert*-butyldimethylsilyl)oxy)-1-phenylethan-1-amine (S6)

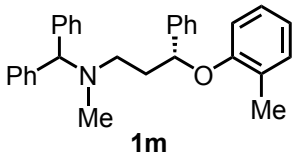
(*R*)-*N*-Benzhydryl-2-((*tert*-butyldimethylsilyl)oxy)-1-phenylethan-1-amine was prepared using **General Procedure for Preparation of Secondary Amines** using (*R*)-2-((*tert*-butyldimethylsilyl)oxy)-1-phenylethan-1-amine (46 mmol). The amine product **S6** was obtained after purification by flash silica gel column chromatography (Et_3N:hexanes = 1:19) as a colorless oil (9.5 g, 49% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.25 (m, 7H), 7.22 (t, J = 6.7 Hz, 6H), 7.19 – 7.10 (m, 2H), 4.62 (s, 1H), 3.68 (dd, J = 8.5, 3.7 Hz, 1H), 3.61 (dd, J = 9.2, 2.3 Hz, 2H), 0.85 (s, 9H), -0.05 (d, J = 11.4 Hz, 6H); $[\alpha]^{25}_D$ = –6.8° (*c* 1.0, CH_2Cl_2).

(*R*)-*N*-Benzyl-2-((*tert*-butyldimethylsilyl)oxy)-*N*-methyl-1-phenylethan-1-amine (1j)

(*R*)-*N*-Benzyl-2-((*tert*-butyldimethylsilyl)oxy)-*N*-methyl-1-phenylethan-1-amine was prepared using **General Procedure for *N*-Methylation of Secondary Amines** using (*R*)-*N*-benzhydryl-2-((*tert*-butyldimethylsilyl)oxy)-1-phenylethan-1-amine (24 mmol). The amine product **1j** was obtained after purification by flash silica gel column chromatography (EtOAc:Et_3N: hexanes 20:1:79) as a colorless oil (10.1 g, 98% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 (ddd, J = 11.6, 8.2, 1.3 Hz, 4H), 7.34 – 7.29 (m, 6H), 7.25 – 7.19 (m, 4H), 7.17 – 7.12 (m, 1H), 4.80 (s, 1H), 4.06 (dd, J = 9.7, 5.9 Hz, 1H), 3.98 – 3.89 (m, 2H), 2.13 (s, 3H), 0.85 (s, 9H), -0.03 (d, J = 6.5 Hz, 6H).



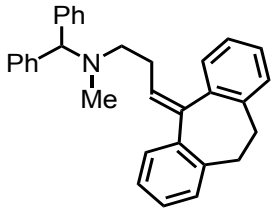
1m

(*R*)-*N*-Benzhydryl-*N*-methyl-3-phenyl-3-(*o*-tolyloxy)propan-1-amine (1m)

(*R*)-*N*-Benzhydryl-*N*-methyl-3-phenyl-3-(*o*-tolyloxy)propan-1-amine was prepared following **General Procedure for Preparation of Tertiary Amines** using (*R*)-*N*-methyl-3-phenyl-3-(o-

tolyloxy)propan-1-amine (1.5 g, 5.9 mmol), (2-bromoethyl)benzene (1.2 equiv.) and K_2CO_3 (1.2 equiv.). The amine product **1m** was obtained after purification by flash silica gel column chromatography (EtOAc:hexanes = 1:19) as a colorless oil (2.0 g, 82%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 (d, *J* = 7.6 Hz, 2H), 7.29 (d, *J* = 4.4 Hz, 6H), 7.23 (t, *J* = 7.3 Hz, 3H), 7.15 (t, *J* = 6.7 Hz, 1H), 7.10 – 7.05 (m, 4H), 6.95 (t, *J* = 7.8 Hz, 1H), 6.75 (t, *J* = 7.5 Hz, 1H), 6.58 (d, *J* = 8.2 Hz, 1H), 5.25 (dd, *J* = 8.9, 3.7 Hz, 1H), 4.33 (s, 1H), 2.72 – 2.65 (m, 1H), 2.48 (ddd, *J* = 12.6, 8.1, 4.5 Hz, 1H), 2.18 (s, 3H), 2.17 – 2.11 (m, 1H), 2.08 – 2.00 (m, 4H).

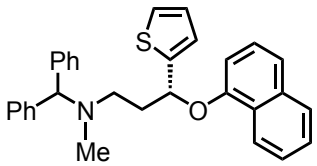


1n

***N*-Benzhydryl-3-(10,11-dihydro-5*H*-dibenzo[*a,d*][7]annulen-5-ylidene)-*N*-methylpropan-1-amine (1n)**

N-Benzhydryl-3-(10,11-dihydro-5*H*-dibenzo[*a,d*][7]annulen-5-ylidene)-*N*-methylpropan-1-amine was prepared following **General Procedure for Preparation of Tertiary Amines** using 3-(10,11-dihydro-5*H*-dibenzo[*a,d*][7]annulen-5-ylidene)-*N*-methylpropan-1-amine (4.3 g, 16 mmol), (bromomethylene)dibenzene (1.2 equiv.) and K_2CO_3 (2.0 equiv.). The amine product **1n** was obtained after purification by flash silica gel column chromatography (Et_2O:hexanes = 1:19) as a colorless oil (6.5 g, 91%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 (d, *J* = 7.5 Hz, 5H), 7.23 (s, 4H), 7.19 (d, *J* = 1.0 Hz, 2H), 7.17 – 7.10 (m, 5H), 7.07 (d, *J* = 7.4 Hz, 1H), 7.03 (d, *J* = 4.1 Hz, 1H), 5.82 (t, *J* = 7.5 Hz, 1H), 4.31 (s, 1H), 3.30 (s, 2H), 2.94 (s, 1H), 2.72 (s, 1H), 2.46 (s, 2H), 2.31 (d, *J* = 7.4 Hz, 2H), 2.07 (s, 3H).

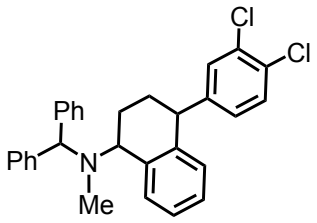


1o

(*R*)-*N*-Benzhydryl-*N*-methyl-3-(naphthalen-1-yloxy)-3-(thiophen-2-yl)propan-1-amine (1o)

(*R*)-*N*-Benzhydryl-*N*-methyl-3-(naphthalen-1-yloxy)-3-(thiophen-2-yl)propan-1-amine was prepared following **General Procedure for Preparation of Tertiary Amines** using (*R*)-*N*-methyl-3-(naphthalen-1-yloxy)-3-(thiophen-2-yl)propan-1-amine (0.9 g, 2.9 mmol), (bromomethylene)dibenzene (1.2 equiv.) and K_2CO_3 (2.0 equiv.). The amine product **1o** was obtained after purification by flash silica gel column chromatography (Et_2O:hexanes = 1:4) as a colorless oil (1.2 g, 90%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.76 (d, *J* = 7.9 Hz, 1H), 7.51 – 7.42 (m, 1H), 7.42 – 7.30 (m, 4H), 7.30 – 7.09 (m, 7H), 7.04 – 6.94 (m, 4H), 6.94 – 6.88 (m, 1H), 6.88 – 6.81 (m, 1H), 5.75 (s, 1H), 4.35 (s, 1H), 2.76 – 2.65 (m, 1H), 2.61 – 2.51 (m, 1H), 2.51 – 2.38 (m, 1H), 2.32 – 2.16 (m, 4H).



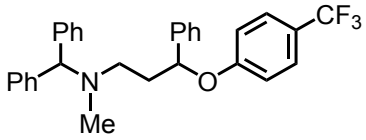
1p

***N*-Benzhydryl-4-(3,4-dichlorophenyl)-*N*-methyl-1,2,3,4-tetrahydronaphthalen-1-amine (1p)**

N-Benzhydryl-4-(3,4-dichlorophenyl)-*N*-methyl-1,2,3,4-tetrahydronaphthalen-1-amine was prepared following **General Procedure for Preparation of Tertiary Amines** using 4-(3,4-dichlorophenyl)-*N*-methyl-1,2,3,4-tetrahydronaphthalen-1-amine (2.9 g, 6.0 mmol), (bromomethylene)dibenzene (1.2 equiv.) and K_2CO_3 (2.0 equiv.). The amine product **1p** was obtained after purification by flash silica gel column chromatography (Et_2O:hexanes = 1:4) as a colorless oil (1.4 g, 49%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.19 – 8.13 (m, 1H), 7.56 (td, *J* = 7.1, 6.3, 1.5 Hz, 4H), 7.38 – 7.33 (m, 1H), 7.29 (ddt, *J* = 7.9, 4.3, 2.0 Hz, 3H), 7.26 – 7.23 (m, 2H), 7.16 (dtd, *J* = 17.5, 7.2, 1.4 Hz, 3H), 7.08 (d, *J* = 1.9 Hz, 1H), 6.87 (d, *J* = 7.6 Hz, 1H), 6.79 (dt, *J* = 8.2, 1.9 Hz, 1H),

4.73 (d, *J* = 1.6 Hz, 1H), 4.08 – 3.99 (m, 2H), 2.04 (d, *J* = 1.7 Hz, 3H), 1.91 (q, *J* = 5.0, 4.5 Hz, 2H), 1.76 – 1.65 (m, 1H), 1.65 – 1.58 (m, 1H).



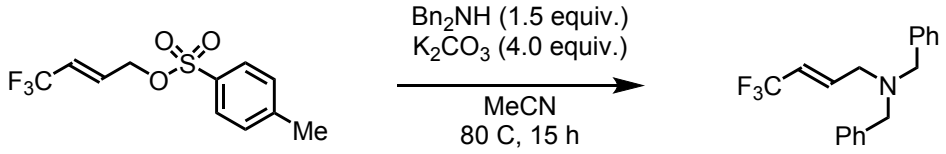
1q

***N*-Benzhydryl-*N*-methyl-3-phenyl-3-(4-(trifluoromethyl)phenoxy)propan-1-amine (1q)**

N-Benzhydryl-*N*-methyl-3-phenyl-3-(4-(trifluoromethyl)phenoxy)propan-1-amine was prepared following **General Procedure for Preparation of Tertiary Amines** using *N*-methyl-3-phenyl-3-(4-(trifluoromethyl)phenoxy)propan-1-amine (2.8 g, 9.0 mmol), (bromomethylene)dibenzene (1.2 equiv.) and K_2CO_3 (2.0 equiv.). The amine product **1q** was obtained after purification by flash silica gel column chromatography (Et_2O:hexanes = 1:9) as a colorless oil (3.0 g, 70%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.4 Hz, 2H), 7.38 – 7.33 (m, 2H), 7.29 (dtd, *J* = 7.3, 5.7, 4.7, 1.6 Hz, 6H), 7.23 (td, *J* = 7.5, 1.7 Hz, 3H), 7.19 – 7.14 (m, 1H), 7.12 – 7.07 (m, 3H), 6.84 – 6.79 (m, 2H), 5.34 – 5.29 (m, 1H), 4.35 (s, 1H), 2.71 (dt, *J* = 13.9, 7.5 Hz, 1H), 2.39 (dt, *J* = 12.2, 5.9 Hz, 1H), 2.18 (d, *J* = 1.6 Hz, 3H), 2.13 (dd, *J* = 13.8, 7.2 Hz, 1H), 2.08 – 1.99 (m, 1H); **^{19}F NMR** (564 MHz, $CDCl_3$) δ -61.51.

Procedure for Preparation of (*E*)-*N,N*-Dibenzyl-4,4,4-trifluorobut-2-en-1-amine (1s)

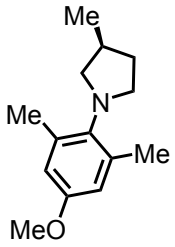


1s

(*E*)-*N,N*-Dibenzyl-4,4,4-trifluorobut-2-en-1-amine (1s)

(*E*)-*N,N*-Dibenzyl-4,4,4-trifluorobut-2-en-1-amine was prepared following the literature previously reported.[2] To a solution of (*E*)-4,4,4-trifluorobut-2-en-1-yl 4-methylbenzenesulfonate (7.0 g, 25 mmol) and K_2CO_3 (13.8 g, 100 mmol) in MeCN (100 mL) was added dibenzylamine (7.4 g, 37.5 mmol). The reaction mixture was then allowed to stir at 80 °C for 15 hours. Upon completion (determined by TLC), the reaction mixture was filtered and concentrated *in vacuo*. The amine product **1s** was obtained after purification by flash silica gel column chromatography (EtOAc:hexanes = 1:20) as a colorless oil (5.9 g, 77%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.29 (m, 8H), 7.28 – 7.22 (m, 2H), 6.51 – 6.30 (m, 1H), 5.85 (ddt, *J* = 15.8, 6.5, 1.7 Hz, 1H), 3.59 (s, 4H), 3.26 – 3.03 (m, 2H); **^{19}F NMR** (470 MHz, $CDCl_3$) δ -63.97 (d, *J* = 6.1 Hz).

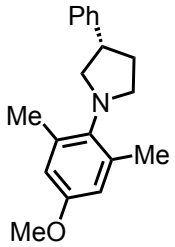


(*S*)-1t

(*S*)-1-(4-Methoxy-2,6-dimethylphenyl)-3-methylpyrrolidine ((*S*)-1t)

(*S*)-1-(4-Methoxy-2,6-dimethylphenyl)-3-methylpyrrolidine was prepared following **General Procedure for Preparation of Tertiary Amines** using 4-methoxy-2,6-dimethylaniline (1.65 g, 10.9 mmol), (*S*)-1,4-dibromo-2-methylbutane (0.9 equiv.) and K_2CO_3 (2.0 equiv.). The amine product **(*S*)-1t** was obtained after purification by flash silica gel column chromatography (Et_2O:hexanes = 1:19) as a colorless oil (1.8 g, 82%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.57 (s, 2H), 3.75 (s, 3H), 3.26 – 3.21 (m, 1H), 3.21 – 3.17 (m, 2H), 2.79 (t, *J* = 7.5 Hz, 1H), 2.39 (dt, *J* = 8.5, 6.8 Hz, 1H), 2.23 (s, 6H), 2.12 – 2.02 (m, 1H), 1.59 (dd, *J* = 11.9, 8.1 Hz, 1H), 1.11 (d, *J* = 6.7 Hz, 3H); $[\alpha]^{25}_D$ = –19.5° (*c* 0.25, CH_2Cl_2).



(*S*)-1u

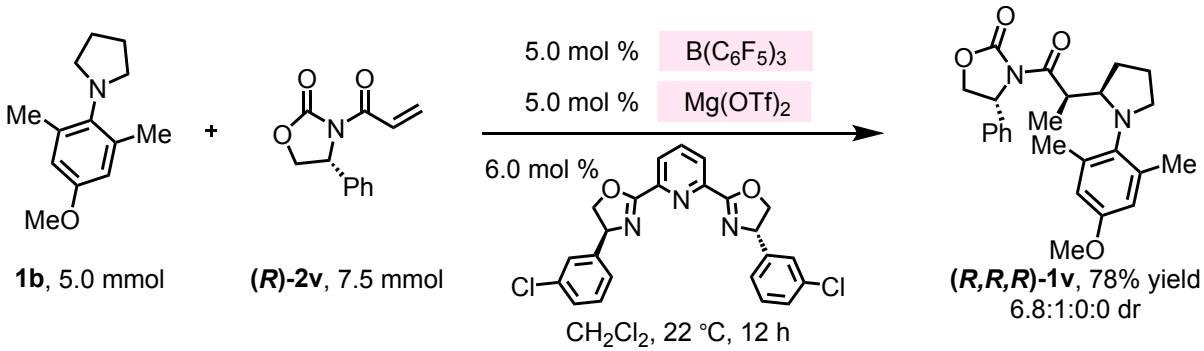
(*S*)-1-(4-Methoxy-2,6-dimethylphenyl)-3-phenylpyrrolidine ((*S*)-1u)

(*S*)-1-(4-Methoxy-2,6-dimethylphenyl)-3-phenylpyrrolidine was prepared following **General Procedure for Preparation of Tertiary Amines** using 4-methoxy-2,6-dimethylaniline (382 mg, 2.5 mmol), (*S*)-(1,4-dibromobutan-2-yl)benzene (0.9 equiv.) and K_2CO_3 (2.0 equiv.). The amine product **(*S*)-1u** was obtained after purification by flash silica gel column chromatography (Et_2O:hexanes = 1:19) as a colorless oil (549 mg, 78%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.29 (m, 4H), 7.24 – 7.17 (m, 1H), 6.60 (s, 2H), 3.76 (s, 3H), 3.63 – 3.45 (m, 2H), 3.40 (t, *J* = 8.0 Hz, 1H), 3.33 (dd, *J* = 13.9, 7.2 Hz, 2H), 2.49 – 2.33

(m, 1H), 2.30 (s, 6H), 2.24 – 2.06 (m, 1H); $[\alpha]^{25}_D = -20.5°$ (*c* 0.25, CH_2Cl_2).

Procedure for Preparation of (*R*)-3-((*R*)-2-((*R*)-1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanoyl)-4-phenyloxazolidin-2-one ((*R,R,R*)-1v)

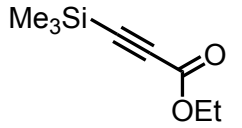
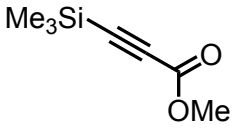
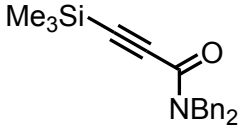
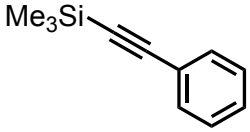
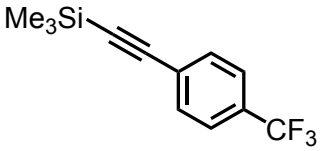
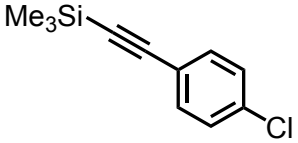
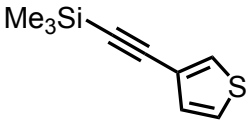
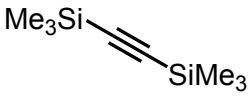
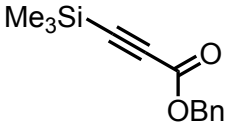


(*R*)-3-((*R*)-2-((*R*)-1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanoyl)-4-phenyloxazolidin-2-one ((*R,R,R*)-1v)

(*R*)-3-((*R*)-2-((*R*)-1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanoyl)-4-phenyloxazolidin-2-one was prepared according to a literature procedure.[1] To a 35 mL oven-dried sealed tube was added $Mg(OTf)_2$ (0.25 mmol), 2,6-bis((*S*)-4-(3-chlorophenyl)-4,5-dihydrooxazol-2-yl)pyridine (0.30 mmol), CH_2Cl_2 (10 mL) under nitrogen atmosphere. The mixture was allowed to stir for 30 min at 22 °C, then (*R*)-3-acryloyl-4-phenyloxazolidin-2-one **(*R*)-2v** (1.3 g, 6.0 mmol), 1-(4-methoxy-2,6-dimethylphenyl)pyrrolidine **1b** (1.02 g, 5.0 mmol), $B(C_6F_5)_3$ (0.25 mmol), and CH_2Cl_2 (5.0 mL) were added to the vessel. The reaction mixture was stirred at 22 °C for 48 h. Upon completion, the solvent was removed *in vacuo*. The diastereomeric ratio was determined to be 6.8:1:0:0 by ^{1}H NMR analysis of the unpurified product mixture. Purification by silica gel column chromatography (Et_2O:hexanes = 1:4) gave the product as a colorless solid as a mixture of diastereomers (1.63 g, 78% yield). Further purification was carried out by silica gel column chromatography (Et_2O:hexanes = 1:4) to obtain the major diastereomer **(*R,R,R*)-1v** in 1.47 g as a colorless oil.

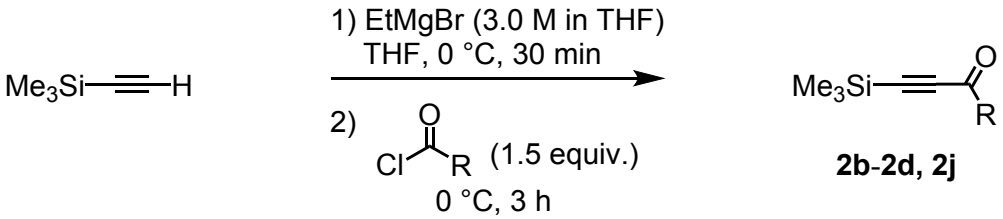
2.1.2. Preparation of Trimethylsilyl Propiolate Substrates

Table S2. List of Trimethylsilyl Propiolate Compounds

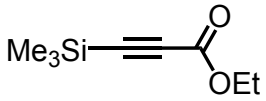
 **2b**	 **2c**	 **2d**
 **2e**	 **2f**	 **2g**
 **2h**	 **2i**	 **2j**

Alkynes **2b**-**2d** and **2j** were prepared according to a literature procedure.[4] Alkyne compounds **2e**-**2i** were obtained from commercial sources and used without further purification.

General Procedure for Preparation of 3-(Trimethylsilyl)propiolates



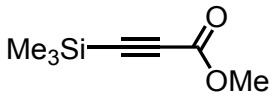
3-(Trimethylsilyl)propiolates **2b**-**2d**, **2j** were prepared according to a literature procedure.[4] To a solution of ethynyltrimethylsilane (20 mmol) in THF (20 mL) was added ethylmagnesium bromide (3.0 M solution in THF) in a dropwise manner at 0 °C. The reaction mixture was allowed to stir for 30 min. The corresponding chloroformate (30 mmol) in THF (30 mL) was added dropwise and the reaction mixture was allowed to stir at 0 °C for 3 h. Upon completion (determined by TLC), H_2O (50 mL) was added and the organic material was extracted using Et_2O (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The desired alkyne products were obtained after purification by flash silica gel column chromatography.



2b

Ethyl 3-(trimethylsilyl)propiolate (**2b**) was prepared according to **General Procedure for Preparation of 3-(Trimethylsilyl)propiolates** using ethyl chloroformate. The propiolate **2b** was obtained after purification by flash silica gel column chromatography (Et_2O:hexanes = 1:99) as a colorless oil (2.7 g, 80%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.23 (q, *J* = 7.2 Hz, 2H), 1.31 (td, *J* = 7.1, 0.9 Hz, 3H), 0.25 (s, 9H).

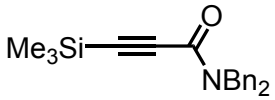


2c

Methyl 3-(trimethylsilyl)propiolate (2c)

Methyl 3-(trimethylsilyl)propiolate was prepared according to **General Procedure for Preparation of 3-(Trimethylsilyl)propiolates** using methyl chloroformate. The propiolate **2c** was obtained after purification by flash silica gel column chromatography (Et_2O:hexanes = 1:99) as a colorless oil (2.6 g, 83%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 3.77 (s, 3H), 0.25 (s, 9H).

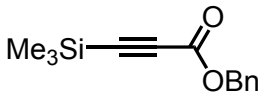


2d

***N,N*-Dibenzyl-3-(trimethylsilyl)propiolamide (2d)**

N,N-Dibenzyl-3-(trimethylsilyl)propiolamide was prepared according to **General Procedure for Preparation of 3-(Trimethylsilyl)propiolates** using *N,N*-dibenzylcarbamoyl chloride. The propiolate **2d** was obtained after purification by flash silica gel column chromatography (Et_2O:hexanes = 1:99) as a colorless oil (3.3 g, 51%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.19 (m, 10H), 4.67 (s, 2H), 4.50 (s, 2H), 0.21 (s, 9H).



2j

Benzyl 3-(trimethylsilyl)propiolate (2j)

Benzyl 3-(trimethylsilyl)propiolate was prepared according to **General Procedure for Preparation of 3-(Trimethylsilyl)propiolates** using benzyl chloroformate. The propiolate **2j** was obtained after purification by flash silica gel column chromatography (Et_2O:hexanes = 1:99) as a colorless oil (3.9 g, 84%).

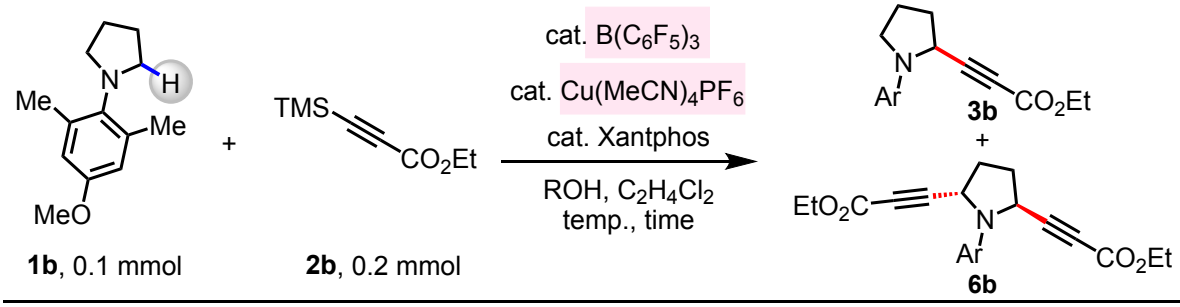
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.81 (s, 2H), 5.11 (hept, *J* = 6.2 Hz, 2H), 1.29 (d, *J* = 6.3 Hz, 12H).

2.2 Optimization Studies for *α*-Alkynylation of *N*-Alkylamines Catalyzed by $B(C_6F_5)_3$ and Organocopper Catalysts

Experimental Procedure for Evaluation of Reaction Conditions (see Table S3)

An oven-dried sealed tube equipped with a magnetic stir bar was used. To the sealed tube were added $Cu(MeCN)_4PF_6$ (0.01 mmol), Xantphos (0.01 mmol), and $C_2H_4Cl_2$ (0.2 mL) under nitrogen atmosphere. The mixture was allowed to stir for 20 minutes at 22 °C, then ethyl 3-(trimethylsilyl)propiolate **2b** (0.2 mmol), alcohol (0.2 mmol), amine **1b** (0.1 mmol), $B(C_6F_5)_3$ (0.01 mmol, 10 mol%), and $C_2H_4Cl_2$ (0.2 mL) were added to the vessel. The reaction mixture was allowed to stir at 80 or 60 °C for 24 or 12 h. Upon completion, the unpurified reaction mixture was filtered through a short plug of Celite and rinsed with CH_2Cl_2. The combined organic material was then concentrated *in vacuo*. Yield values were determined by ^1H NMR analysis of unpurified reaction mixtures using mesitylene as the internal standard.

Table S3. Evaluation of Alcohol Additive and Reaction Conditions



1b, 0.1 mmol **2b**, 0.2 mmol

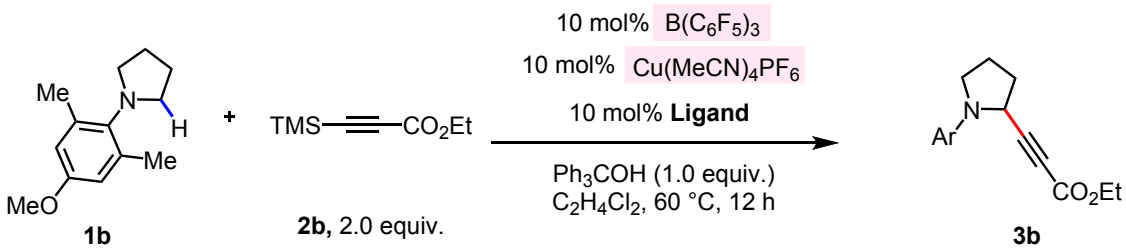
entry	alcohol (equiv.)	Temp. °C	time (h)	yield (%) **3b**	yield (%) **6b**
1	none	80	24	15	0
2	*i*-PrOH (2.0)	80	24	26	0
3	*t*-BuOH (2.0)	80	24	64	5
4	BnOH (2.0)	80	24	34	0
5	Ph_3COH (2.0)	80	24	52	34
6	1-adamantol (2.0)	80	24	93	<5
7	1-adamantol (2.0)	60	24	6	0
8	Ph_3COH (2.0)	60	24	79	19
9	Ph_3COH (1.0)	60	24	83	15
10	Ph_3COH (1.0)	60	12	90	<5

Conditions: *N*-arylpyrrolidine (**1b**, 0.1 mmol), 3-(trimethylsilyl)propiolate (**2b**, 0.2 mmol), $B(C_6F_5)_3$ (10 mol%), $Cu(MeCN)_4PF_6$ (10 mol%), Xantphos (10 mol%), alcohol (0.2 or 0.1 mmol), $C_2H_4Cl_2$ (0.4 mL), under N_2. Yield values were determined by ^1H NMR analysis of unpurified reaction mixtures using mesitylene as the internal standard.

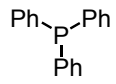
Experimental Procedure for Evaluation of Ligand for 1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine 1b (see Table S4)

An oven-dried sealed tube equipped with a magnetic stir bar was used. To the sealed tube were added $Cu(MeCN)_4PF_6$ (0.01 mmol), ligand (0.01 or 0.02 mmol), and $C_2H_4Cl_2$ (0.2 mL) under nitrogen atmosphere. The mixture was allowed to stir for 20 minutes at 22 °C, then ethyl 3-(trimethylsilyl)propiolate **2b** (0.2 mmol), triphenylmethanol (0.1 mmol), amine **1b** (0.1 mmol), $B(C_6F_5)_3$ (0.01 mmol, 10 mol%), and $C_2H_4Cl_2$ (0.2 mL) were added to the vessel. The reaction mixture was allowed to stir at 60 °C for 12 h. Upon completion, the unpurified reaction mixture was filtered through a short plug of Celite and rinsed with CH_2Cl_2. The combined organic material was then concentrated *in vacuo*. Yield values were determined by ^1H NMR analysis of unpurified reaction mixtures using mesitylene as the internal standard.

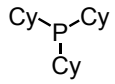
Table S4. Evaluation of Ligand for the Reaction of 1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine **1b** and **2b**



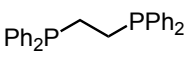
1b + **2b,** 2.0 equiv. → **3b**



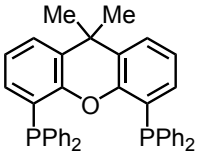
SI-L1
3b, 0% yield[a]



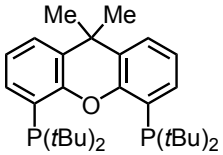
SI-L2
3b, 13% yield[a]



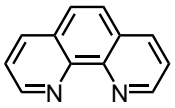
SI-L3
3b, 43% yield



SI-L4
3b, 90% yield



SI-L5
3b, 0% yield



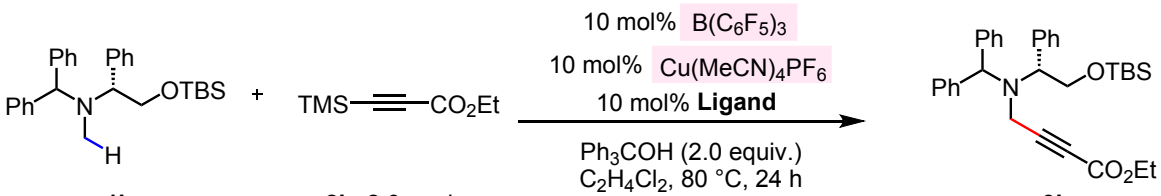
SI-L6
3b, 0% yield

Conditions: *N*-arylpyrrolidine (**1b**, 0.1 mmol), 3-(trimethylsilyl)propiolate (**2b**, 0.2 mmol), $B(C_6F_5)_3$ (10 mol%), $Cu(MeCN)_4PF_6$ (10 mol%), ligand (10 mol%), triphenylmethanol (0.1 mmol), $C_2H_4Cl_2$ (0.4 mL), under N_2, 60 °C, 12 h. Yield values were determined by ^1H NMR analysis of unpurified reaction mixtures using mesitylene as the internal standard. [a]20 mol% ligand was used.

Experimental Procedure for Evaluation of Ligand for (*R*)-*N*-Benzhydryl-2-((*tert*-butyldimethylsilyl)oxy)-*N*-methyl-1-phenylethan-1-amine (1j) (see Table S5)

An oven-dried sealed tube equipped with a magnetic stir bar was used. To the sealed tube were added $Cu(MeCN)_4PF_6$ (0.01 mmol), ligand (0.01 or 0.02 mmol), and $C_2H_4Cl_2$ (0.2 mL) under nitrogen atmosphere. The mixture was allowed to stir for 20 minutes at 22 °C, then ethyl 3-(trimethylsilyl)propiolate **2b** (0.2 mmol), triphenylmethanol (0.1 mmol), amine **1j** (0.1 mmol), $B(C_6F_5)_3$ (0.01 mmol, 10 mol%), and $C_2H_4Cl_2$ (0.2 mL) were added to the vessel. The reaction mixture was allowed to stir at 60 °C for 12 h. Upon completion, the unpurified reaction mixture was filtered through a short plug of Celite and rinsed with CH_2Cl_2. The combined organic material was then concentrated *in vacuo*. Yield values were determined by ^1H NMR analysis of unpurified reaction mixtures using mesitylene as the internal standard.

Table S5. Evaluation of Ligand for the Reaction of (*R*)-*N*-Benzhydryl-2-((*tert*-butyldimethylsilyl)oxy)-*N*-methyl-1-phenylethan-1-amine (**1j**) and **2b**



1j | **2b,** 2.0 equiv. | **3j**

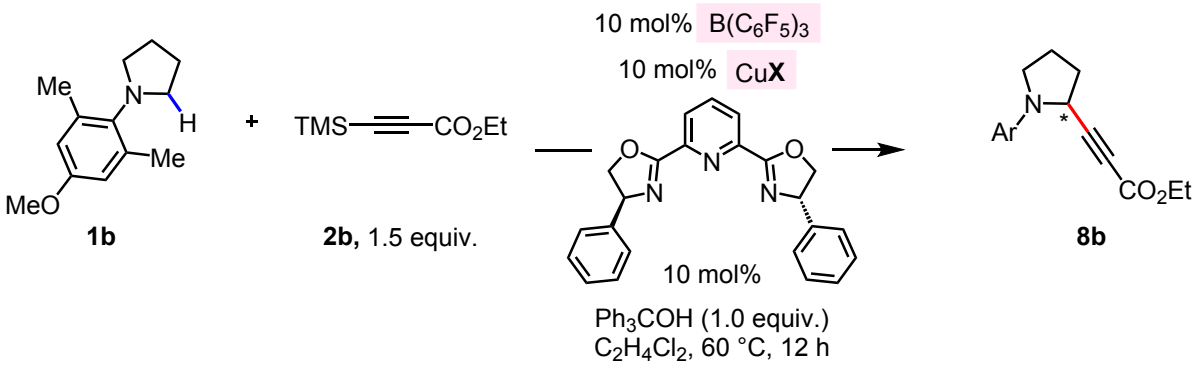
SI-L1 **3j,** 45% yield[a]	**SI-L2** **3j,** 41% yield[a]	**SI-L3** **3j**, 88% yield
SI-L7 **3j**, 45% yield	**SI-L4** **3j,** 45% yield	**SI-L5** **3j,** 9% yield
L1 **3j**, 45% yield	**SI-L8** **3j**, 38% yield	**L3** **3j,** 64% yield

Conditions: *N*-arylpyrrolidine (**1b**, 0.1 mmol), 3-(trimethylsilyl)propiolate (**2b**, 0.2 mmol), $B(C_6F_5)_3$ (10 mol%), $Cu(MeCN)_4PF_6$ (10 mol%), ligand (10 mol%), triphenylmethanol (0.2 mmol), $C_2H_4Cl_2$ (0.4 mL), under N_2, 80 °C, 24 h. Yield values were determined by ^1H NMR analysis of unpurified reaction mixtures with mesitylene as the internal standard. [a]20 mol% ligand was used.

Experimental Procedure for Evaluation of Copper Salt (see Table S6)

An oven-dried sealed tube equipped with a magnetic stir bar was used. To the sealed tube were added CuX (0.01 mmol), (*S*)-Ph-PyBOX (0.01 mmol), and $C_2H_4Cl_2$ (0.2 mL) under nitrogen atmosphere. The mixture was allowed to stir for 20 minutes at 22 °C, then ethyl 3-(trimethylsilyl)propiolate **2b** (0.15 mmol), triphenylmethanol (0.1 mmol), amine **1b** (0.1 mmol), $B(C_6F_5)_3$ (0.01 mmol, 10 mol%), and $C_2H_4Cl_2$ (0.2 mL) were added to the vessel. The reaction mixture was allowed to stir at 60 °C for 12 h. Upon completion, the unpurified reaction mixture was filtered through a short plug of Celite and rinsed with CH_2Cl_2. The combined organic material was then concentrated *in vacuo*. Yield values were determined by ^{1}H NMR analysis of unpurified reaction mixtures using mesitylene as the internal standard. Enantiomeric ratio (er) was determined by HPLC of the purified product.

Table S6. Evaluation of Copper Salt



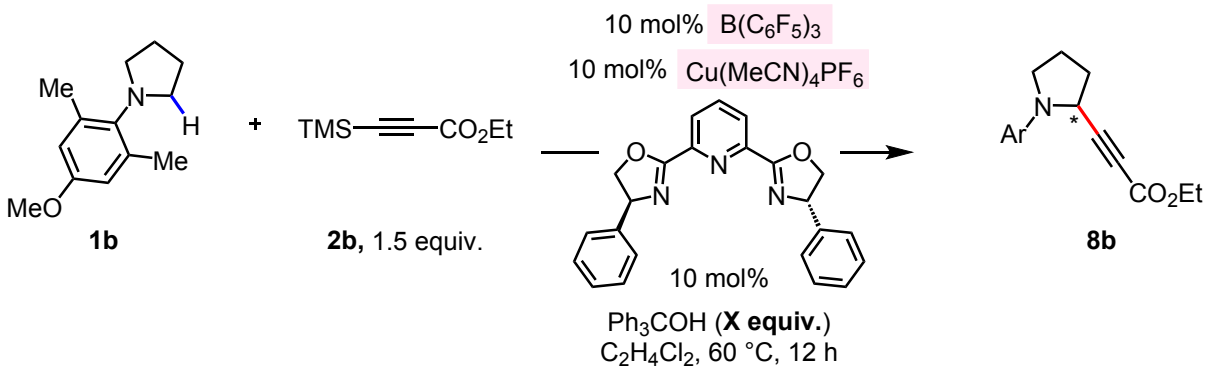
entry	Cu**X**	Yield of **8b** (%)	er of **8b**
1	CuBr	0	nd
2	CuCl	<3	65:35
3	CuI	0	nd
4	CuOTf·Benzene	13	71:29
5	$Cu(OTf)_2$	14	76:24
6	CuOAc	15	62:38
7	$Cu(OAc)_2$	4	62:38
8	$Cu(MeCN)_4PF_6$	69	81:19

Conditions: *N*-arylpyrrolidine (**1b**, 0.1 mmol), 3-(trimethylsilyl)propiolate (**2b**, 0.15 mmol), $B(C_6F_5)_3$ (10 mol%), CuX (10 mol%), (*S*)-PhPyBOX (10 mol%), triphenylmethanol (0.1 mmol), $C_2H_4Cl_2$ (0.4 mL), under N_2, 60 °C, 12 h. Yield values were determined by ^{1}H NMR analysis of unpurified reaction mixtures using mesitylene as the internal standard. Enantiomeric ratio (er) was determined by HPLC of the purified product.

Experimental Procedure for Optimization of Alcohol Additive for the Enantioselective Transformation (see Table S7)

An oven-dried sealed tube equipped with a magnetic stir bar was used. To the sealed tube were added $Cu(MeCN)_4PF_6$ (0.01 mmol), (*S*)-Ph-PyBOX (0.01 mmol), and $C_2H_4Cl_2$ (0.2 mL) under nitrogen atmosphere. The mixture was allowed to stir for 20 minutes at 22 °C, then ethyl 3-(trimethylsilyl)propiolate **2b** (0.15 mmol), triphenylmethanol (0.1 or 0.2 mmol), amine **1b** (0.1 mmol), $B(C_6F_5)_3$ (0.01 mmol, 10 mol%), and $C_2H_4Cl_2$ (0.2 mL) were added to the vessel. The reaction mixture was allowed to stir at 60 °C for 12 h. Upon completion, the unpurified reaction mixture was filtered through a short plug of Celite and rinsed with CH_2Cl_2. The combined organic material was then concentrated *in vacuo*. Yield values were determined by ^1H NMR analysis of unpurified reaction mixtures using mesitylene as the internal standard. Enantiomeric ratio (er) was determined by HPLC of the purified product.

Table S7. Effect of Alcohol Additive for the Enantioselective Transformation



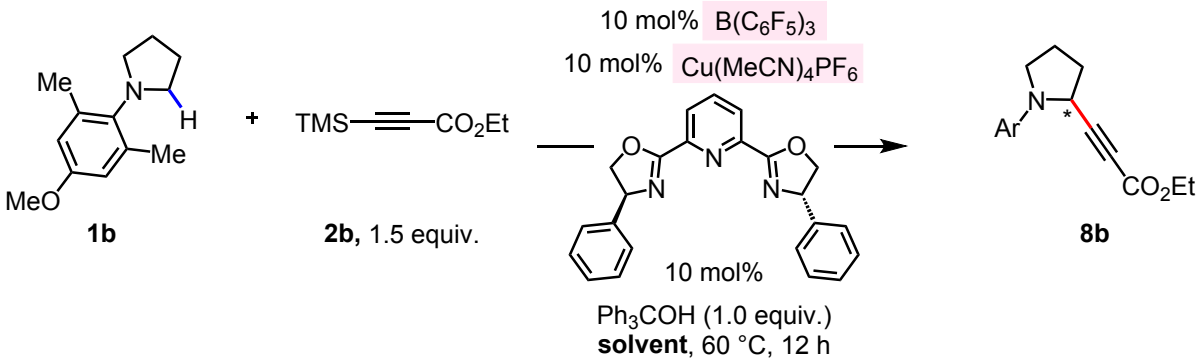
entry	Ph_3COH **(X equiv.)**	Yield of **8b** (%)	er of **8b**
1	1.0	69	81:19
2	2.0	98	77:23

Conditions: *N*-arylpyrrolidine (**1b**, 0.1 mmol), 3-(trimethylsilyl)propiolate (**2b**, 0.15 mmol), $B(C_6F_5)_3$ (10 mol%), $Cu(MeCN)_4PF_6$ (10 mol%), (*S*)-PhPyBOX (10 mol%), triphenylmethanol (0.1 or 0.2 mmol), $C_2H_4Cl_2$ (0.4 mL), under N_2, 60 °C, 12 h. Yield values were determined by ^1H NMR analysis of unpurified reaction mixtures with mesitylene as the internal standard. Enantiomeric ratio (er) was determined by HPLC of the purified product.

Experimental Procedure for Evaluation of Solvent (see Table S8)

An oven-dried sealed tube equipped with a magnetic stir bar was used. To the sealed tube were added $Cu(MeCN)_4PF_6$ (0.01 mmol), (*S*)-Ph-PyBOX (0.01 mmol), and solvent (0.2 mL) under nitrogen atmosphere. The mixture was allowed to stir for 20 minutes at 22 °C, then ethyl 3-(trimethylsilyl)propiolate **2b** (0.15 mmol), triphenylmethanol (0.1 mmol), amine **1b** (0.1 mmol), $B(C_6F_5)_3$ (0.01 mmol, 10 mol%), and solvent (0.2 mL) were added to the vessel. The reaction mixture was allowed to stir at 60 °C for 12 h. Upon completion, the unpurified reaction mixture was filtered through a short plug of Celite and rinsed with CH_2Cl_2. The combined organic material was then concentrated *in vacuo*. Yield values were determined by ^1H NMR analysis of unpurified reaction mixtures using mesitylene as the internal standard. Enantiomeric ratio (er) was determined by HPLC of the purified product.

Table S8. Evaluation of Solvent



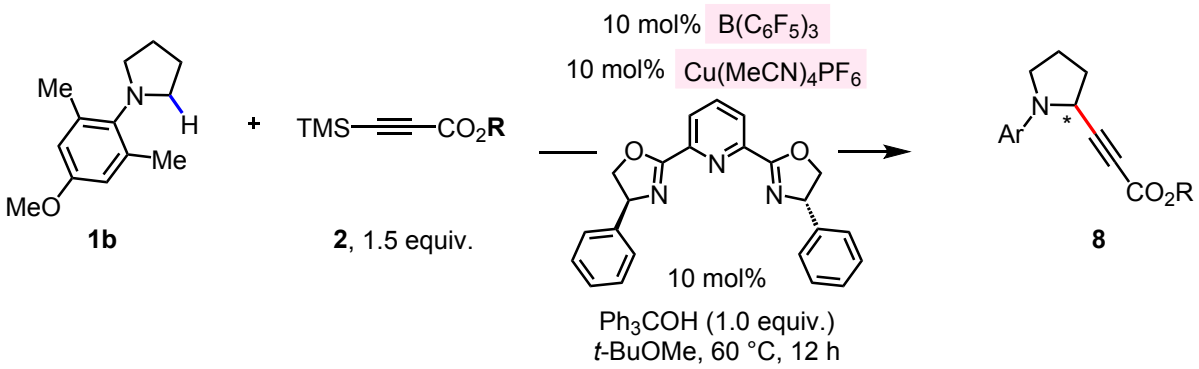
entry	**solvent**	Yield of **8b** (%)	er of **8b**
1	$CHCl_3$	48	59:14
2	CH_2Cl_2	62	78:22
3	$C_2H_4Cl_2$	69	81:19
4	Benzene	43	80:20
5	Toluene	54	71:29
6	THF	63	83:17
7	Et_2O	28	83:17
8	*t*-BuOMe	84	82:18

Conditions: *N*-arylpyrrolidine (**1b**, 0.1 mmol), 3-(trimethylsilyl)propiolate (**2b**, 0.15 mmol), $B(C_6F_5)_3$ (10 mol%), $Cu(MeCN)_4PF_6$ (10 mol%), (*S*)-PhPyBOX (10 mol%), triphenylmethanol (0.1 mmol), solvent (0.4 mL), under N_2, 60 °C, 12 h. Yield values were determined by ^1H NMR analysis of unpurified reaction mixtures with mesitylene as the internal standard. Enantiomeric ratio (er) was determined by HPLC of the purified product.

Experimental Procedure for Evaluation of Alkyne Substrate for the Stereoselective Transformation (see Table S9)

An oven-dried sealed tube equipped with a magnetic stir bar was used. To the sealed tube were added $Cu(MeCN)_4PF_6$ (0.01 mmol), (*S*)-Ph-PyBOX (0.01 mmol), and *t*-BuOMe (0.2 mL) under nitrogen atmosphere. The mixture was allowed to stir for 20 minutes at 22 °C, then 3-(trimethylsilyl)propiolate **2** (0.15 mmol), triphenylmethanol (0.1 mmol), amine **1b** (0.1 mmol), $B(C_6F_5)_3$ (0.01 mmol, 10 mol%), and *t*-BuOMe (0.2 mL) were added to the vessel. The reaction mixture was allowed to stir at 60 °C for 12 h. Upon completion, the unpurified reaction mixture was filtered through a short plug of Celite and rinsed with CH_2Cl_2. The combined organic material was then concentrated *in vacuo*. Yield values were determined by ^1H NMR analysis of unpurified reaction mixtures using mesitylene as the internal standard. Enantiomeric ratio (er) was determined by HPLC of the purified product.

Table S9. Evaluation of Alkyne Substrates



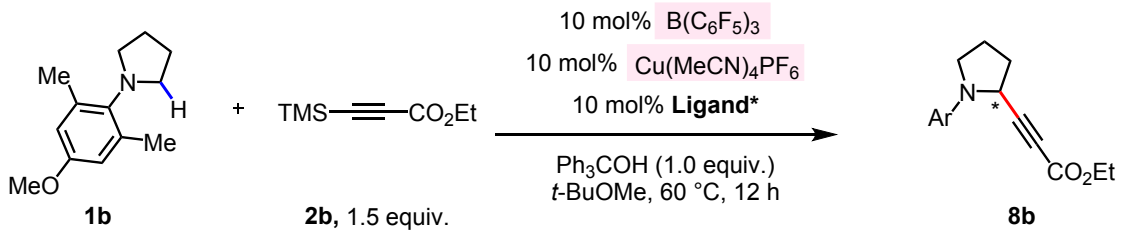
entry	**CO_2R**	Yield of **8** (%)	er of **8**
1	Me	35	82:18
2	Et	84	82:18
3	*i*-Pr	0	nd
4	*i*-Bu	30	62:38
5	*t*-Bu	0	nd
6	Bn	59	64:36

Conditions: *N*-arylpyrrolidine (**1b**, 0.1 mmol), 3-(trimethylsilyl)propiolate (**2**, 0.15 mmol), $B(C_6F_5)_3$ (10 mol%), $Cu(MeCN)_4PF_6$ (10 mol%), (*S*)-PhPyBOX (10 mol%), triphenylmethanol (0.1 mmol), *t*-BuOMe (0.4 mL), under N_2, 60 °C, 12 h. Yield values were determined by ^1H NMR analysis of unpurified reaction mixtures with mesitylene as the internal standard. Enantiomeric ratio (er) was determined by HPLC of the purified product.

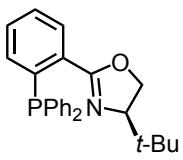
Experimental Procedure for Evaluation of Chiral Ligands (see Table S10)

An oven-dried sealed tube equipped with a magnetic stir bar was used. To the sealed tube were added $Cu(MeCN)_4PF_6$ (0.01 mmol), ligand (0.01 mmol), and *t*-BuOMe (0.2 mL) under nitrogen atmosphere. The mixture was allowed to stir for 20 minutes at 22 °C, then ethyl 3-(trimethylsilyl)propiolate **2b** (0.15 mmol), triphenylmethanol (0.1 mmol), amine **1b** (0.1 mmol), $B(C_6F_5)_3$ (0.01 mmol, 10 mol%), and *t*-BuOMe (0.2 mL) were added to the vessel. The reaction mixture was allowed to stir at 60 °C for 12 h. Upon completion, the unpurified reaction mixture was filtered through a short plug of Celite and rinsed with CH_2Cl_2. The combined organic material was then concentrated *in vacuo*. Yield values were determined by ^1H NMR analysis of unpurified reaction mixtures using mesitylene as the internal standard. Enantiomeric ratio (er) was determined by HPLC of the purified product.

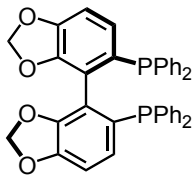
Table S10. Evaluation of Chiral Ligands



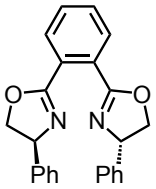
1b **2b,** 1.5 equiv. **8b**



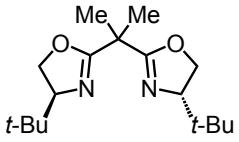
L8
8b, 15% yield
41:59 er



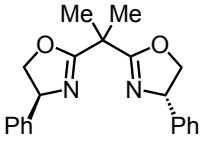
L9
8b, 89% yield
49:51 er



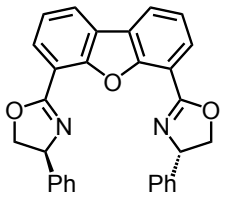
L10
8b, 29% yield
66:34 er



L11
8b, 81% yield
52:48 er



L12
8b, 53% yield
48:52 er



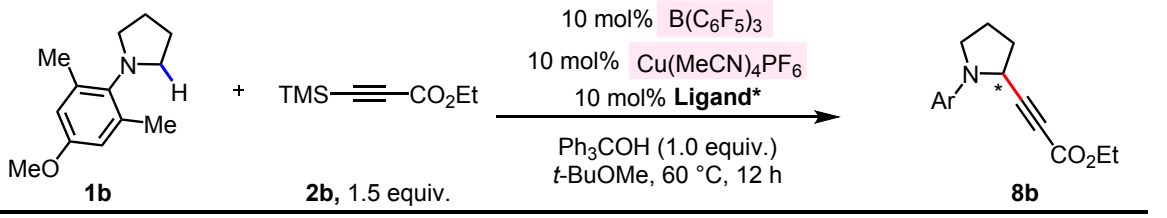
L13
8b, 6% yield
72:28 er

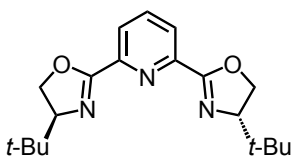
Conditions: *N*-arylpyrrolidine (**1b**, 0.1 mmol), 3-(trimethylsilyl)propiolate (**2b**, 0.15 mmol), $B(C_6F_5)_3$ (10 mol%), $Cu(MeCN)_4PF_6$ (10 mol%), Ligand (10 mol%), triphenylmethanol (0.1 mmol), *t*-BuOMe (0.4 mL), under N_2, 60 °C, 12 h. Yield values were determined by ^1H NMR analysis of unpurified reaction mixtures with mesitylene as the internal standard. Enantiomeric ratio (er) was determined by HPLC of the purified product.

Experimental Procedure for Evaluation of PyBOX Ligands (see Table S11)

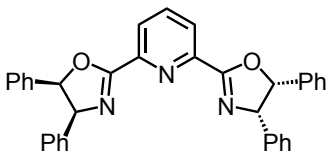
An oven-dried sealed tube equipped with a magnetic stir bar was used. To the sealed tube were added $Cu(MeCN)_4PF_6$ (0.01 mmol), ligand (0.01 mmol), and *t*-BuOMe (0.2 mL) under nitrogen atmosphere. The mixture was allowed to stir for 20 minutes at 22 °C, then ethyl 3-(trimethylsilyl)propiolate **2b** (0.15 mmol), triphenylmethanol (0.1 mmol), amine **1b** (0.1 mmol), $B(C_6F_5)_3$ (0.01 mmol, 10 mol%), and *t*-BuOMe (0.2 mL) were added to the vessel. The reaction mixture was allowed to stir at 60 °C for 12 h. Upon completion, the unpurified reaction mixture was filtered through a short plug of Celite and rinsed with CH_2Cl_2. The combined organic material was then concentrated *in vacuo*. Yield values were determined by ^1H NMR analysis of unpurified reaction mixtures using mesitylene as the internal standard. Enantiomeric ratio (er) was determined by HPLC of the purified product.

Table S11. Evaluation of PyBOX Ligands

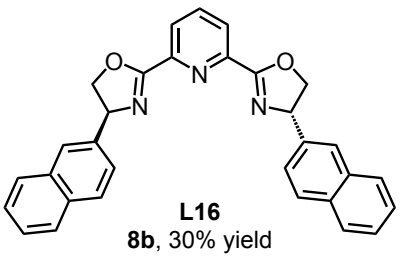




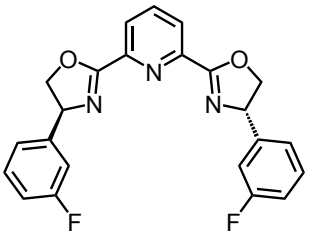
L14
8b, 30% yield
54:46 er



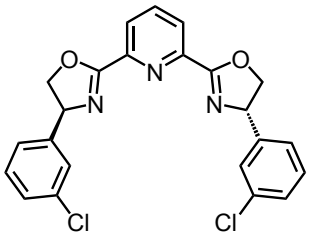
L15
8b, 32% yield
89:11 er



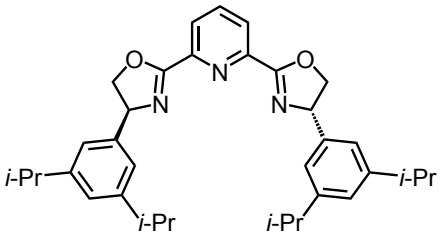
L16
8b, 30% yield
90:10 er



L17
8b, 31% yield
85:15 er



L18
8b, 70% yield
78:22 er



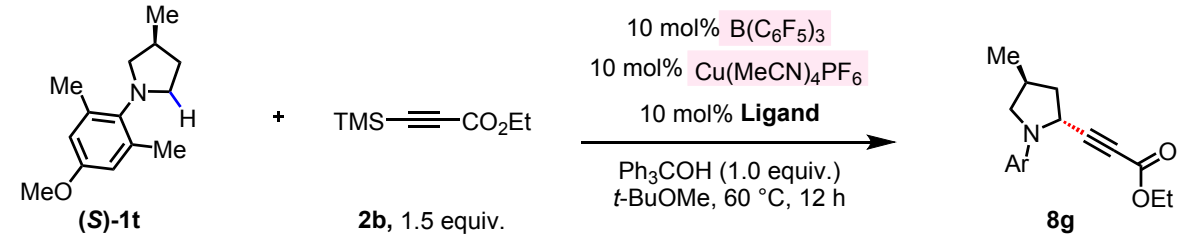
L19
8b, 73% yield
68:32 er

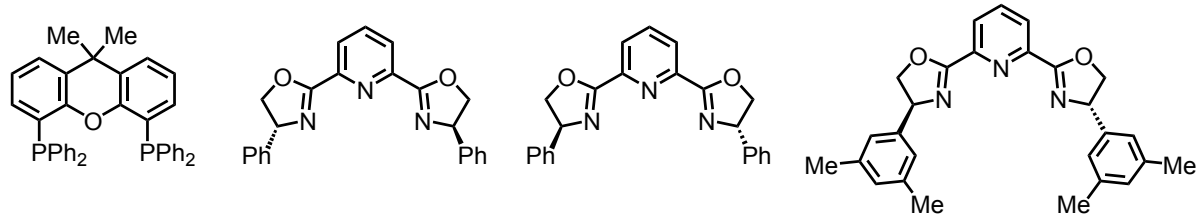
Conditions: *N*-arylpyrrolidine (**1b**, 0.1 mmol), 3-(trimethylsilyl)propiolate (**2b**, 0.15 mmol), $B(C_6F_5)_3$ (10 mol%), $Cu(MeCN)_4PF_6$ (10 mol%), Ligand (10 mol%), triphenylmethanol (0.1 mmol), *t*-BuOMe (0.4 mL), under N_2, 60 °C, 12 h. Yield values were determined by ^1H NMR analysis of unpurified reaction mixtures with mesitylene as the internal standard. Enantiomeric ratio (er) was determined by HPLC of the purified product.

Experimental Procedure for Evaluation of Ligands for Amine (*S*)-1t (see Table S12)

An oven-dried sealed tube equipped with a magnetic stir bar was used. To the sealed tube were added $Cu(MeCN)_4PF_6$ (0.01 mmol), ligand (0.01 mmol), and *t*-BuOMe (0.2 mL) under nitrogen atmosphere. The mixture was allowed to stir for 20 minutes at 22 °C, then 3-(trimethylsilyl)propiolate **2b** (0.15 mmol), triphenylmethanol (0.1 mmol), amine **(*S*)-1t** (0.1 mmol), $B(C_6F_5)_3$ (0.01 mmol, 10 mol%), and *t*-BuOMe (0.2 mL) were added to the vessel. The reaction mixture was allowed to stir at 60 °C for 12 h. Upon completion, the unpurified reaction mixture was filtered through a short plug of Celite and rinsed with CH_2Cl_2. The combined organic material was then concentrated *in vacuo*. Yield values and *trans:cis* ratios were determined by ^1H NMR analysis of unpurified reaction mixtures using mesitylene as the internal standard.

Table S12. Evaluation of Ligands for Amine **(*S*)-1t**





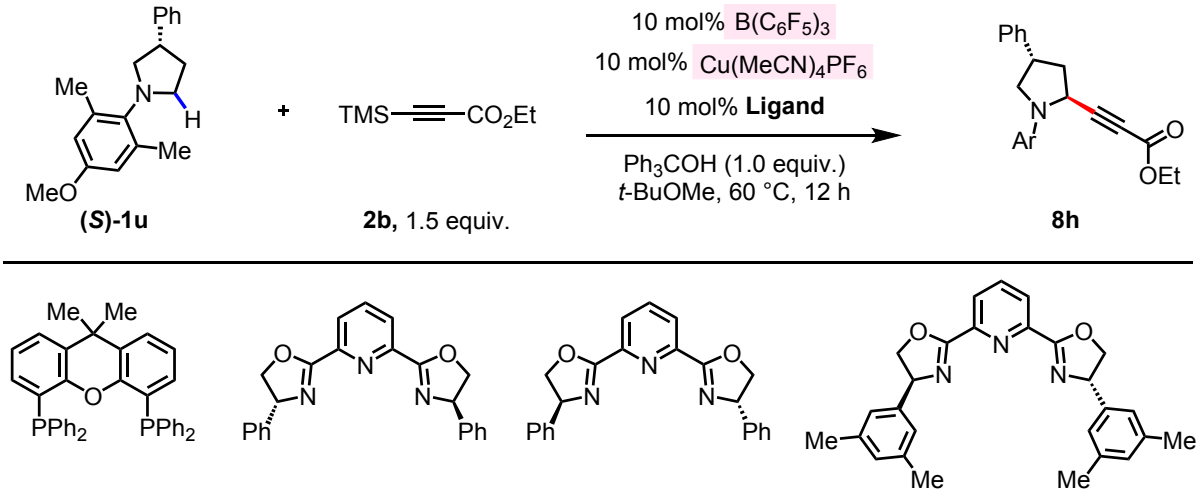
SI-L4	**(*R*)-L3**	**(*S*)-L3**	**L5**
8g, 61% yield	**8g**, 53% yield	**8g**, 34% yield	**8g**, 64% yield
1.8:1 *trans:cis*	5.6:1 *trans:cis*	5.8:1 *trans:cis*	11.8:1 *trans:cis*

Conditions: *N*-arylpyrrolidine (**(*S*)-1t**, 0.1 mmol), 3-(trimethylsilyl)propiolate (**2b**, 0.15 mmol), $B(C_6F_5)_3$ (10 mol%), $Cu(MeCN)_4PF_6$ (10 mol%), ligand (10 mol%), triphenylmethanol (0.1 mmol), *t*-BuOMe (0.4 mL), under N_2, 60 °C, 12 h. Yield values and *trans:cis* ratio were determined by ^1H NMR analysis of the unpurified reaction mixtures with mesitylene as the internal standard.

Experimental Procedure for Evaluation of Ligands for the Reaction of Amine (*S*)-1u and 2b (see Table S13)

An oven-dried sealed tube equipped with a magnetic stir bar was used. To the sealed tube were added $Cu(MeCN)_4PF_6$ (0.01 mmol), ligand (0.01 mmol), and *t*-BuOMe (0.2 mL) under nitrogen atmosphere. The mixture was allowed to stir for 20 minutes at 22 °C, then 3-(trimethylsilyl)propiolate **2** (0.15 mmol), triphenylmethanol (0.1 mmol), amine **(*S*)-1u** (0.1 mmol), $B(C_6F_5)_3$ (0.01 mmol, 10 mol%), and *t*-BuOMe (0.2 mL) were added to the vessel. The reaction mixture was allowed to stir at 60 °C for 12 h. Upon completion, the unpurified reaction mixture was filtered through a short plug of Celite and rinsed with CH_2Cl_2. The combined organic material was then concentrated *in vacuo*. Yield values and *trans:cis* ratios were determined by ^1H NMR analysis of unpurified reaction mixtures using mesitylene as the internal standard.

Table S13. Evaluation of Ligands for Amine **(*S*)-1u**

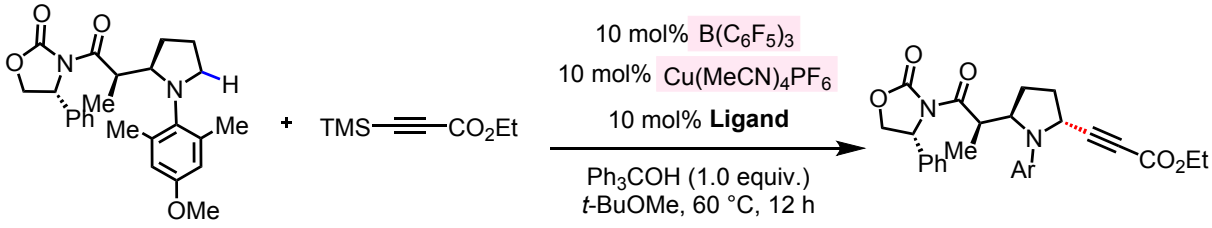


Conditions: *N*-arylpyrrolidine (**(*S*)-1u**, 0.1 mmol), 3-(trimethylsilyl)propiolate (**2b**, 0.15 mmol), $B(C_6F_5)_3$ (10 mol%), $Cu(MeCN)_4PF_6$ (10 mol%), ligand (10 mol%), triphenylmethanol (0.1 mmol), *t*-BuOMe (0.4 mL), under N_2, 60 °C, 12 h. Yield values and *trans:cis* ratio were determined by ^1H NMR analysis of the unpurified reaction mixtures with mesitylene as the internal standard.

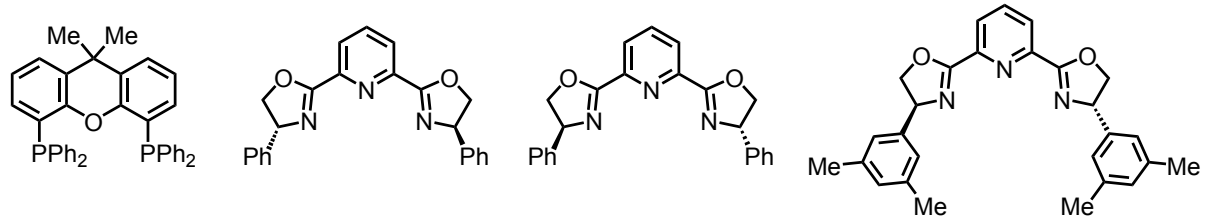
Experimental Procedure for Evaluation of Ligands for the Reaction of Amine (*R,R,R*)-1v and 2b (see Table S14)

An oven-dried sealed tube equipped with a magnetic stir bar was used. To the sealed tube were added $Cu(MeCN)_4PF_6$ (0.01 mmol), ligand (0.01 mmol), and *t*-BuOMe (0.2 mL) under nitrogen atmosphere. The mixture was allowed to stir for 20 minutes at 22 °C, then 3-(trimethylsilyl)propiolate **2b** (0.15 mmol), triphenylmethanol (0.1 mmol), amine **(*R,R,R*)-1v** (0.1 mmol), $B(C_6F_5)_3$ (0.01 mmol, 10 mol%), and *t*-BuOMe (0.2 mL) were added to the vessel. The reaction mixture was allowed to stir at 60 °C for 12 h. Upon completion, the unpurified reaction mixture was filtered through a short plug of Celite and rinsed with CH_2Cl_2. The combined organic material was then concentrated *in vacuo*. Yield values and *trans:cis* ratios were determined by ^{1}H NMR analysis of unpurified reaction mixtures using mesitylene as the internal standard.

Table S14. Evaluation of Ligands for **(*R,R,R*)-1v**



(*R,R,R*)-1v | **2b,** 1.5 equiv. | **8i**

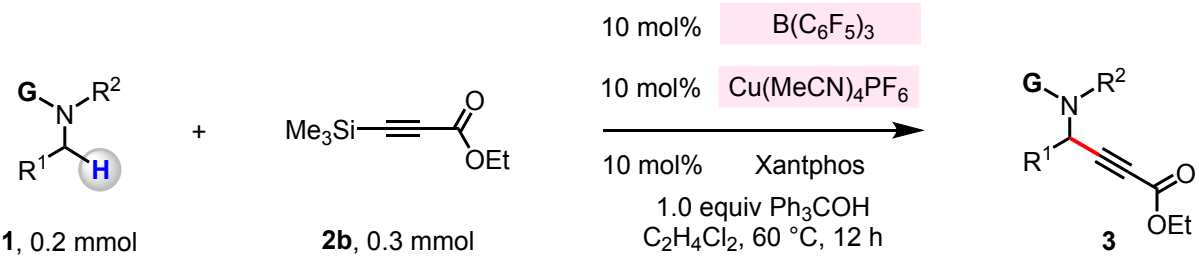


Sl-L4	**(*R*)-L3**	**(*S*)-L3**	**L5**
8i, 54% yield	**8i**, 81% yield	**8i**, 49% yield	**8i**, 93% yield
5.8:1 *trans:cis*	1.9:1 *trans:cis*	7.2:1 *trans:cis*	7.7:1 *trans:cis*

Conditions: *N*-arylpyrrolidine (**(*R,R,R*)-1v**, 0.1 mmol), 3-(trimethylsilyl)propiolate (**2**, 0.15 mmol), $B(C_6F_5)_3$ (10 mol%), $Cu(MeCN)_4PF_6$ (10 mol%), ligand (10 mol%), triphenylmethanol (0.1 mmol), *t*-BuOMe (0.4 mL), under N_2, 60 °C, 12 h. Yield values and *trans:cis* ratio were determined by ^{1}H NMR analysis of the unpurified reaction mixtures with mesitylene as the internal standard.

2.3 General Procedures for α-C–H Alkynylation of *N*-Alkylamines by $B(C_6F_5)_3$ and Organocopper Complex

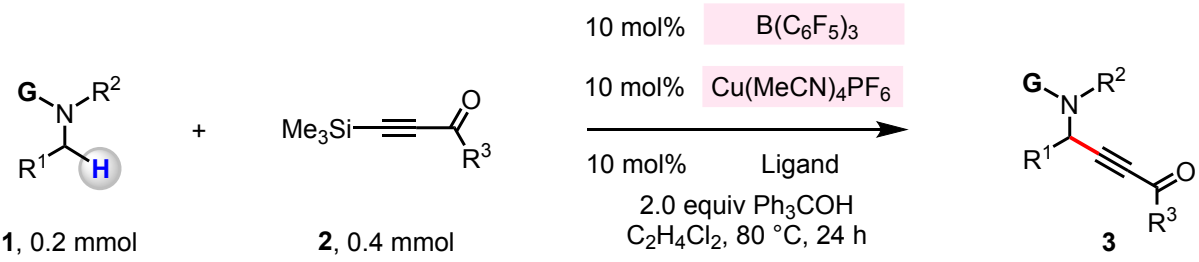
General Procedure A for α-C–H Alkynylation of *N*-Alkylamines Catalyzed by $B(C_6F_5)_3$ and Organocopper Complex (See Table 1 and Figure 2 in the Manuscript)



1, 0.2 mmol **2b**, 0.3 mmol **3**

An oven-dried sealed tube equipped with a magnetic stir bar was used. To the sealed tube were added $Cu(MeCN)_4PF_6$ (0.02 mmol), Xantphos (0.02 mmol), and $C_2H_4Cl_2$ (0.4 mL) under nitrogen atmosphere. The mixture was allowed to stir for 20 minutes at 22 °C, then ethyl 3-(trimethylsilyl)propiolate **2b** (0.3 mmol), triphenylmethanol (0.2 mmol), amine **1** (0.2 mmol), $B(C_6F_5)_3$ (0.02 mmol, 10 mol%), and $C_2H_4Cl_2$ (0.4 mL) were added to the vessel. The reaction mixture was allowed to stir at 60 °C for 12 h. Upon completion, the unpurified reaction mixture was filtered through a short plug of Celite and rinsed with CH_2Cl_2. The combined organic material was then concentrated *in vacuo*. The propargylamine product was purified and isolated by silica gel column chromatography.

General Procedure B for α-C–H Alkynylation of *N*-Alkylamines Catalyzed by $B(C_6F_5)_3$ and Organocopper Complex (See Figures 2-3 in the Manuscript)

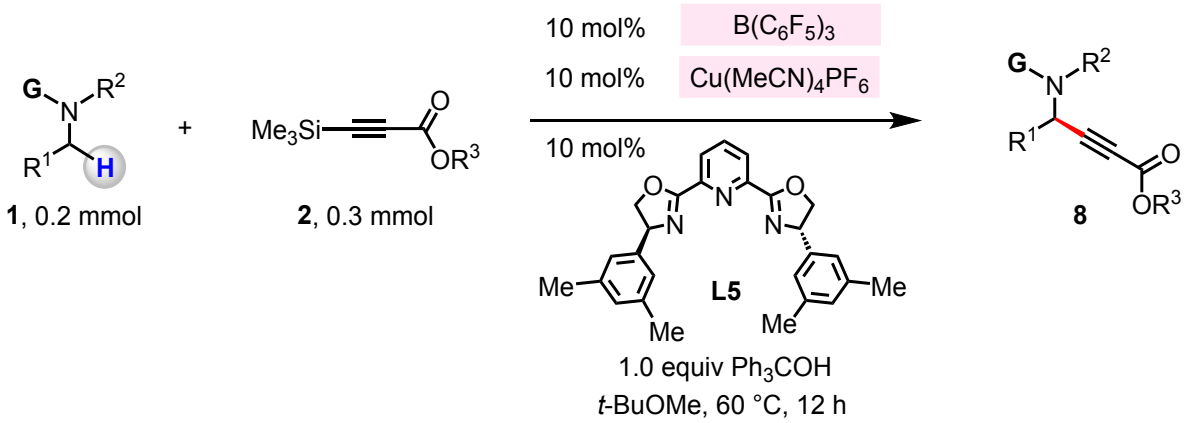


1, 0.2 mmol **2**, 0.4 mmol **3**

An oven-dried sealed tube equipped with a magnetic stir bar was used. To the sealed tube were added $Cu(MeCN)_4PF_6$ (0.02 mmol), ligand (1,2-bis(diphenylphosphino)ethane or (*S*)-PhPyBOX, 0.02 mmol), and $C_2H_4Cl_2$ (0.4 mL) under nitrogen atmosphere. The mixture was allowed to stir for 20 minutes at 22 °C, then (trimethylsilyl)propiolate **2** (0.4 mmol), triphenylmethanol (0.4 mmol), amine **1** (0.2 mmol), $B(C_6F_5)_3$ (0.02, 10 mol%), and $C_2H_4Cl_2$ (0.4 mL) were added to the vessel. The reaction mixture was allowed to stir at 80 °C for 24 h.

Upon completion, the unpurified reaction mixture was filtered through a short plug of Celite and rinsed with CH_2Cl_2. The combined organic material was then concentrated *in vacuo*. The propargylamine product was purified and isolated by silica gel column chromatography.

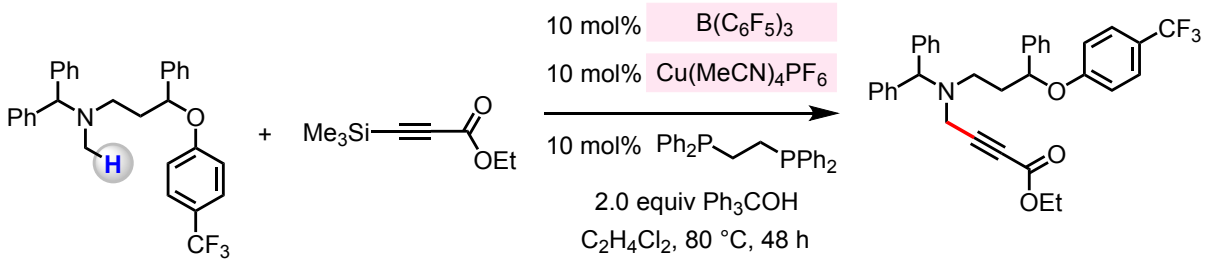
General Procedure C for Stereoselective *α*-C–H Alkynylation of *N*-Alkylamines Catalyzed by $B(C_6F_5)_3$ and Organocopper Complex (See Figure 5 in the Manuscript)



An oven-dried sealed tube equipped with a magnetic stir bar was used. To the sealed tube were added $Cu(MeCN)_4PF_6$ (0.02 mmol), (*S*)-(3,5-dimethylphenyl)PyBOX **L5** (0.02 mmol), and *t*-BuOMe (0.4 mL) under nitrogen atmosphere. The mixture was allowed to stir for 20 minutes at 22 °C, then (trimethylsilyl)propiolate **2** (0.3 mmol), triphenylmethanol (0.2 mmol), amine **1** (0.2 mmol), $B(C_6F_5)_3$ (0.02 mmol, 10 mol%), and solvent (0.4 mL) were added to the vessel. The reaction mixture was allowed to stir at 60 °C for 12 h. Upon completion, the unpurified reaction mixture was filtered through a short plug of Celite and rinsed with Et_2O. The combined organic material was then concentrated *in vacuo*. The propargylamine product was purified isolated by silica gel column chromatography. The er values were determined by HPLC analysis of the isolated product.

2.4 Procedures for Large Scale Reactions

Procedure for Gram-Scale Synthesis of Alkynylated Fluoxetine Derivative 7b



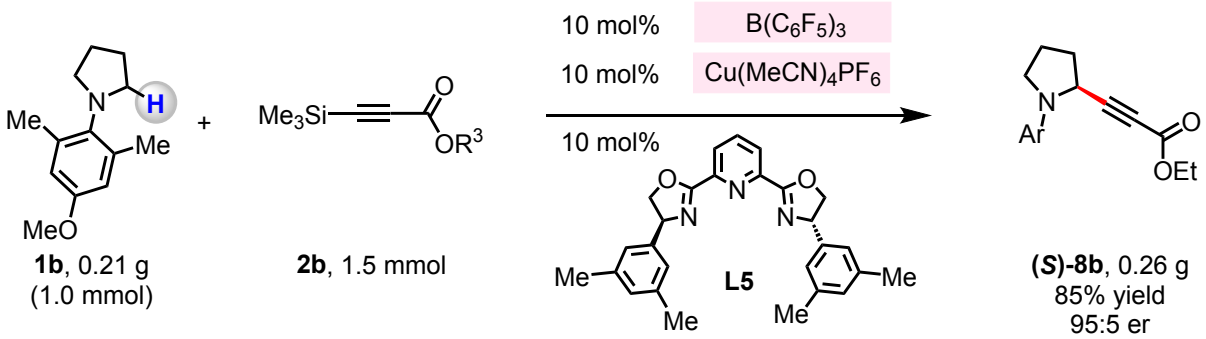
1q, 1.0 g (2.1 mmol)
***N*-Bzh fluoxetine**

2b, 4.2 mmol

7b, 93% yield
1.12 g
fluoxetine derivative

An oven-dried sealed tube equipped with a magnetic stir bar was used. To the sealed tube were added $Cu(MeCN)_4PF_6$ (78 mg, 0.21 mmol), 1,2-bis(diphenylphosphino)ethane (84 mg, 0.21 mmol), and $C_2H_4Cl_2$ (4.0 mL) under nitrogen atmosphere. The mixture was allowed to stir for 30 minutes at 22 °C, then (trimethylsilyl)propiolate **2b** (715 mg, 4.2 mmol), triphenylmethanol (1.1 g, 4.2 mmol), amine **1q** (1.0 g, 2.1 mmol), $B(C_6F_5)_3$ (108 mg, 0.21 mmol), and $C_2H_4Cl_2$ (4.0 mL) were added to the vessel. The reaction mixture was allowed to stir at 80 °C for 48 h. Upon completion, the unpurified reaction mixture was concentrated *in vacuo*. The amine product **7b** was obtained after purification by flash silica gel column chromatography (Et_2O:hexanes = 1:19) as a colorless solid (1.12 g, 93%).

Procedure for Enantioselective *α*-Alkynylation Reaction in 1.0 mmol Scale



1b, 0.21 g
(1.0 mmol)

2b, 1.5 mmol

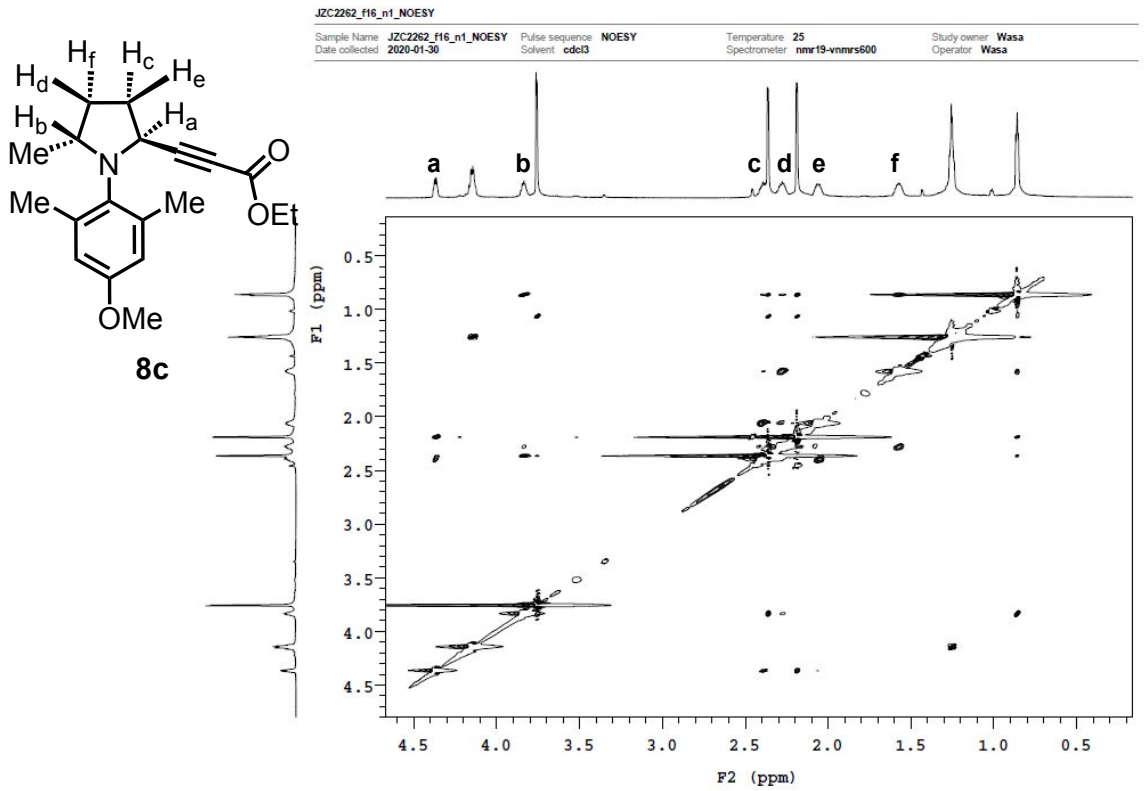
(*S*)-8b, 0.26 g
85% yield
95:5 er

An oven-dried sealed tube equipped with a magnetic stir bar was used. To the sealed tube were added $Cu(MeCN)_4PF_6$ (19 mg, 0.05 mmol), (*S*)-(3,5-dimethylphenyl)PyBOX **L5** (23 mg, 0.05 mmol), and *t*-BuOMe (2.0 mL) under nitrogen atmosphere. The mixture was allowed to stir for 30 minutes at 22 °C, then (trimethylsilyl)propiolate **2b** (255 mg, 1.5 mmol), triphenylmethanol (260 mg, 1.0 mmol), amine **1b** (205 mg, 1.0 mmol), $B(C_6F_5)_3$ (26 mg, 0.05 mmol), and *t*-

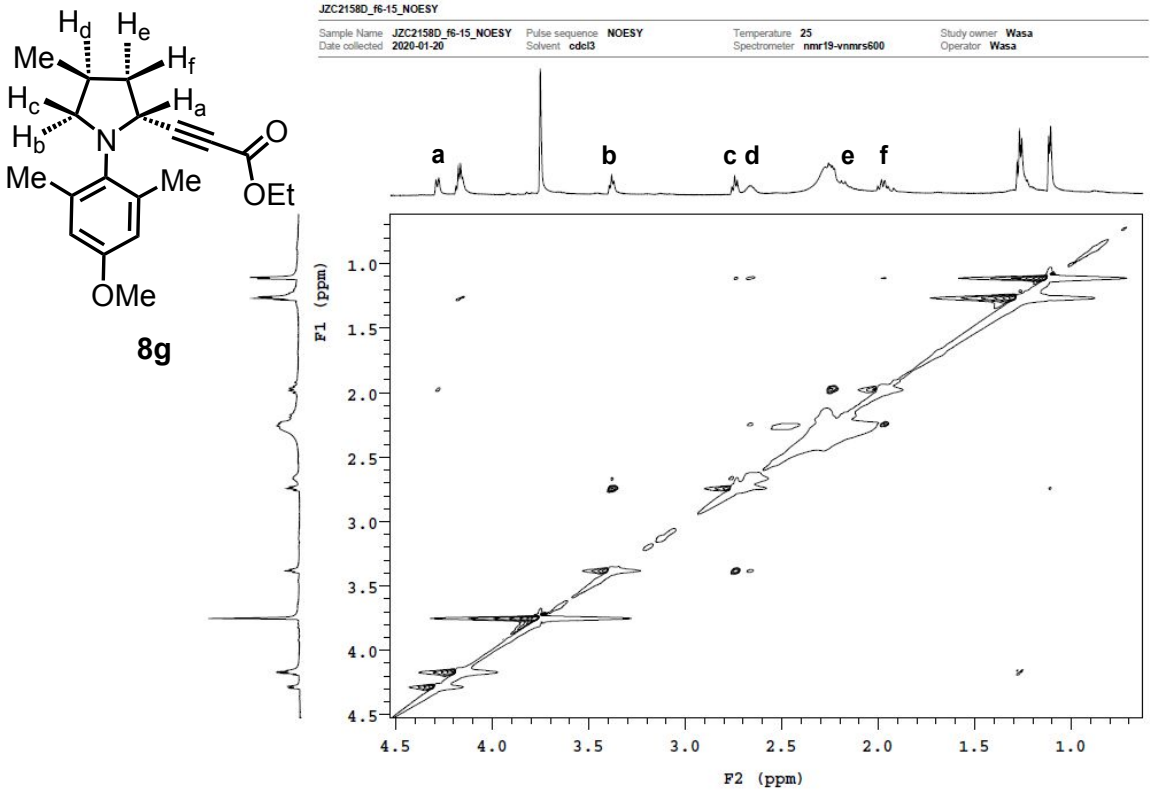
BuOMe (2.0 mL) were added to the vessel. The reaction mixture was allowed to stir at 60 °C for 72 h. Upon completion, the unpurified reaction mixture was concentrated *in vacuo*. The amine product **(*S*)-8b** was obtained after purification by flash silica gel column chromatography (Et_2O:hexanes = 1:19) as a colorless solid (260 mg, 85%).

3. Determination of Relative Configuration

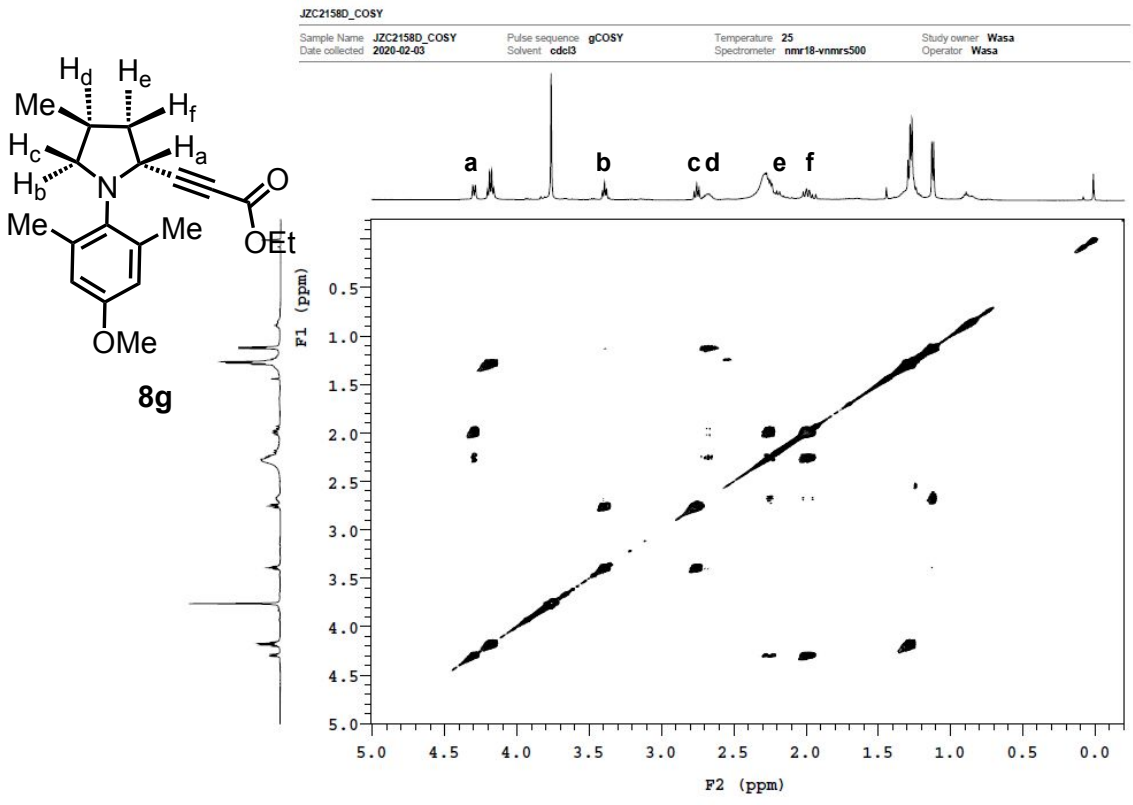
We carried out the following 2D NMR studies in order to determine relative configuration of enantioenriched products **8c, 8g**, **8h**, **8i-*trans***, and **8i-*cis***.



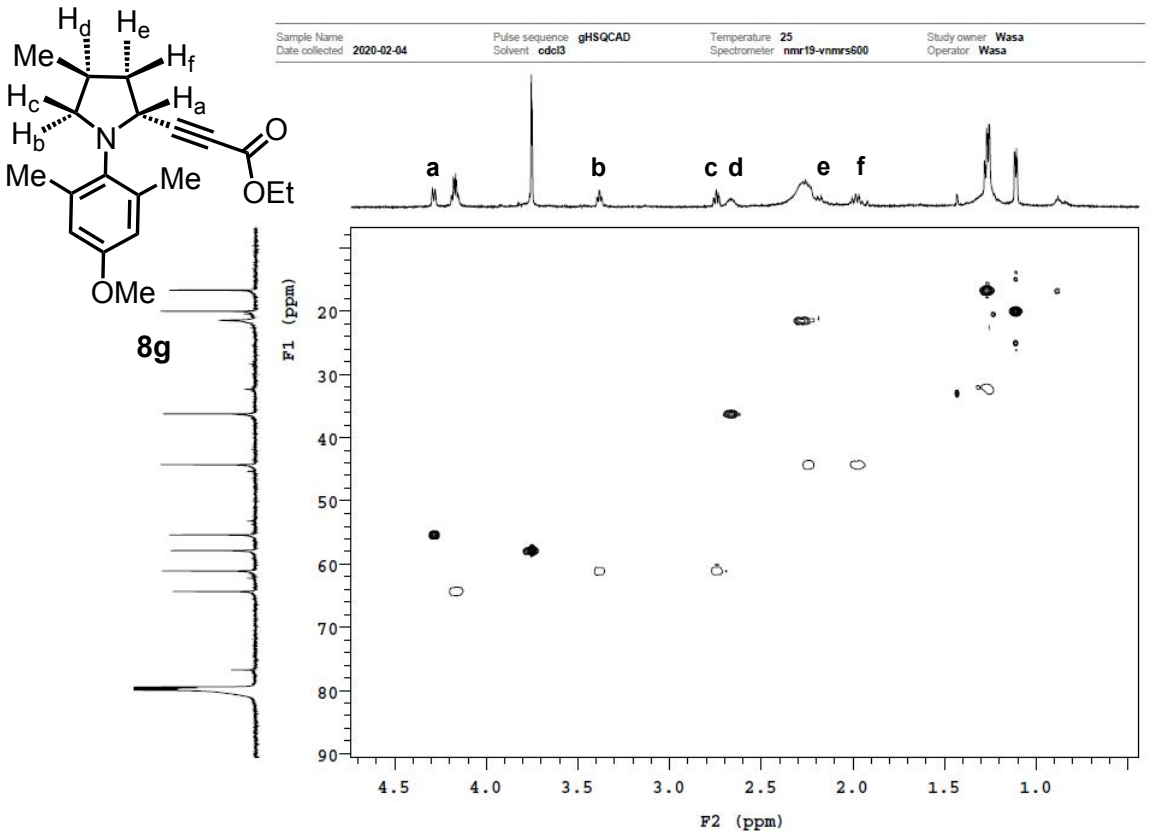
The relative configuration of the major diastereomer of **8c** was assigned to be *trans*.


JZC2158D_f6-15_NOESY
Sample Name JZC2158D_f6-15_NOESY
Date collected 2020-01-20
Pulse sequence NOESY
Solvent cdcl3
Temperature 25
Spectrometer nmr19-vnmrs600
Study owner Wasa
Operator Wasa
a
b
c d
e
f
F1 (ppm)
F2 (ppm)

8g

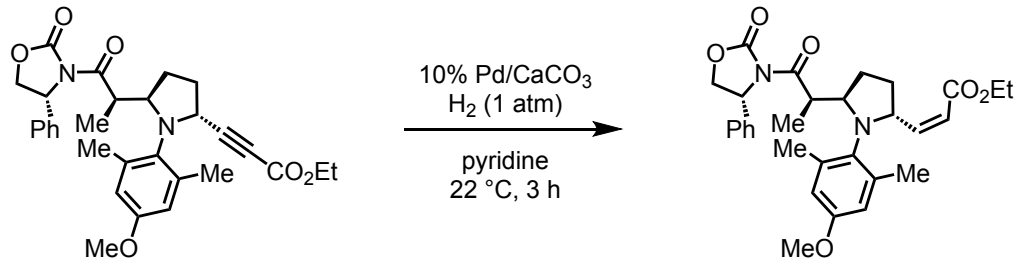

JZC2158D_COSY
Sample Name JZC2158D_COSY
Date collected 2020-02-03
Pulse sequence gCOSY
Solvent cdcl3
Temperature 25
Spectrometer nmr18-vnmrs500
Study owner Wasa
Operator Wasa
a
b
c d
e
f
F1 (ppm)
F2 (ppm)

8g



The relative configuration of the major diastereomer of **8g** was assigned as *trans*. The relative configuration of **8h** was assigned in analogy.

Propargylamine **8i-major** was transformed to **15-major** according to the literature procedure.[9]

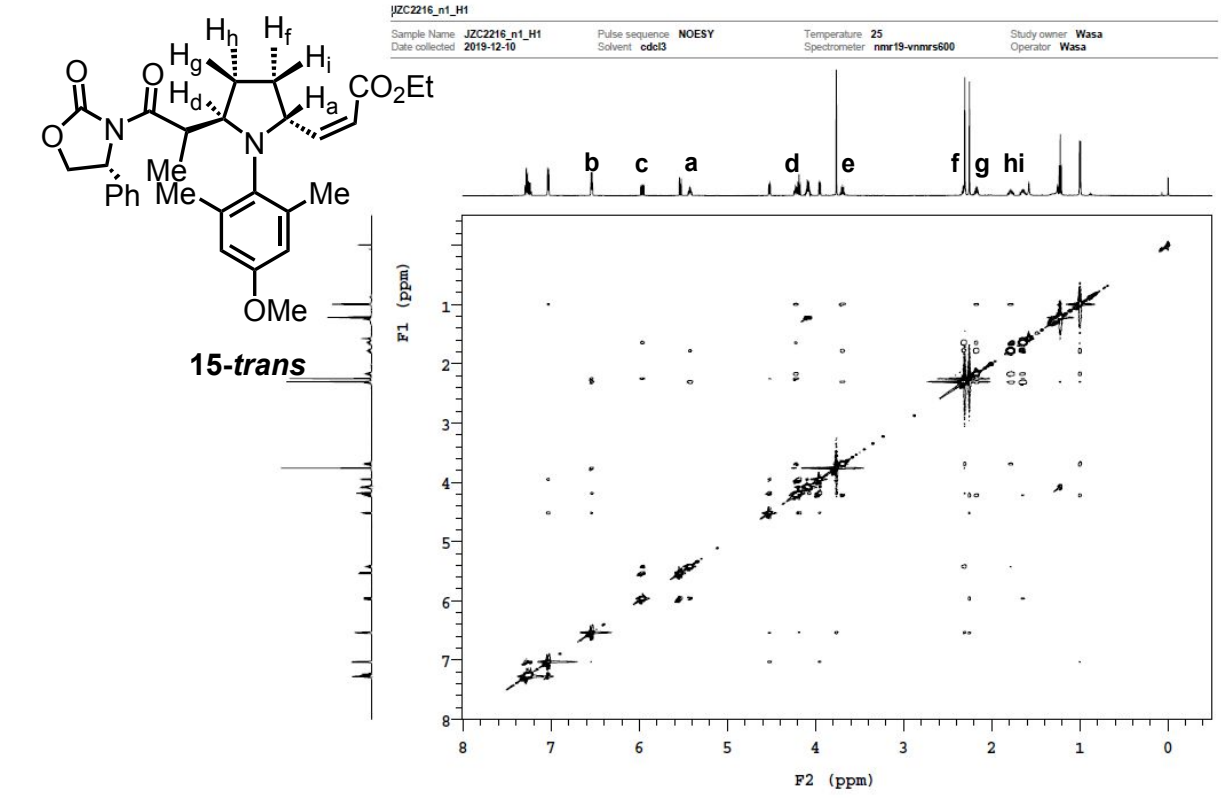


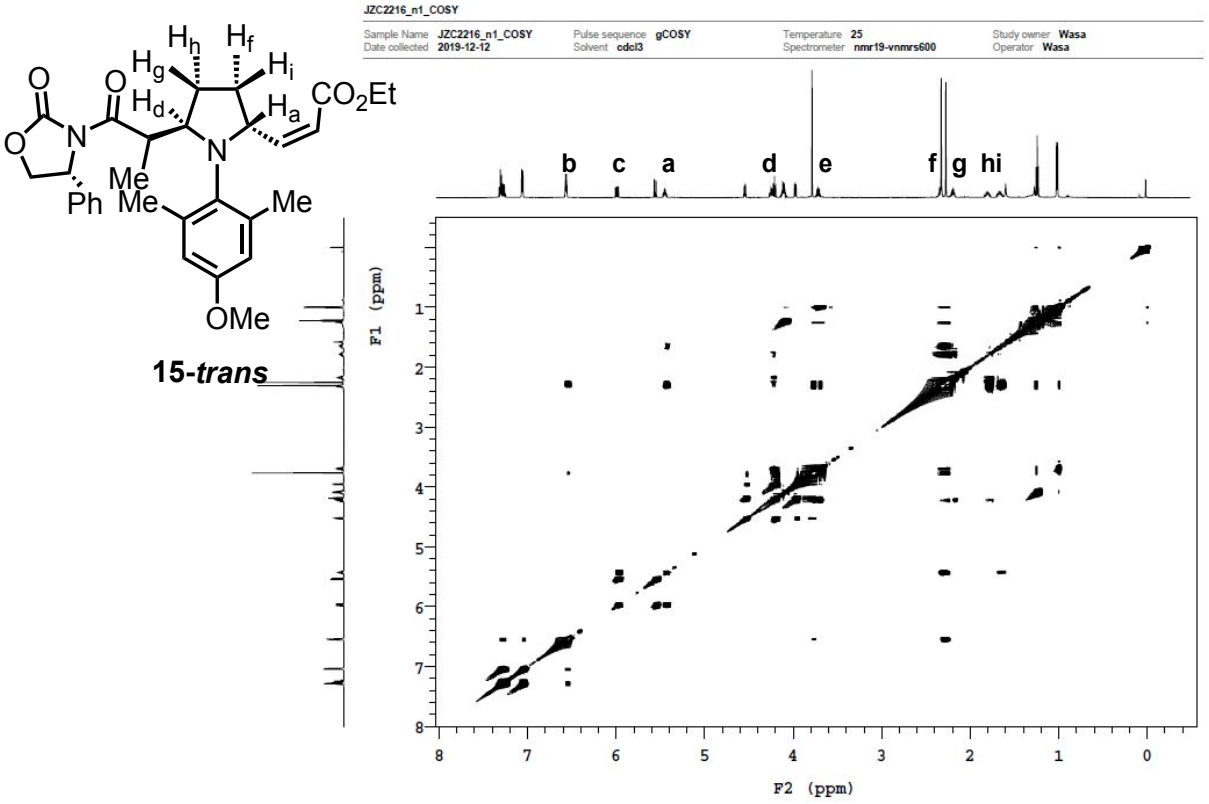
8i-major **15-major**, 98% yield

Ethyl (*Z*)-3-((2*R*,5*R*)-1-(4-methoxy-2,6-dimethylphenyl)-5-((*R*)-1-oxo-1-((*R*)-2-oxo-4-phenyloxazolidin-3-yl)propan-2-yl)pyrrolidin-2-yl)acrylate (15-major)

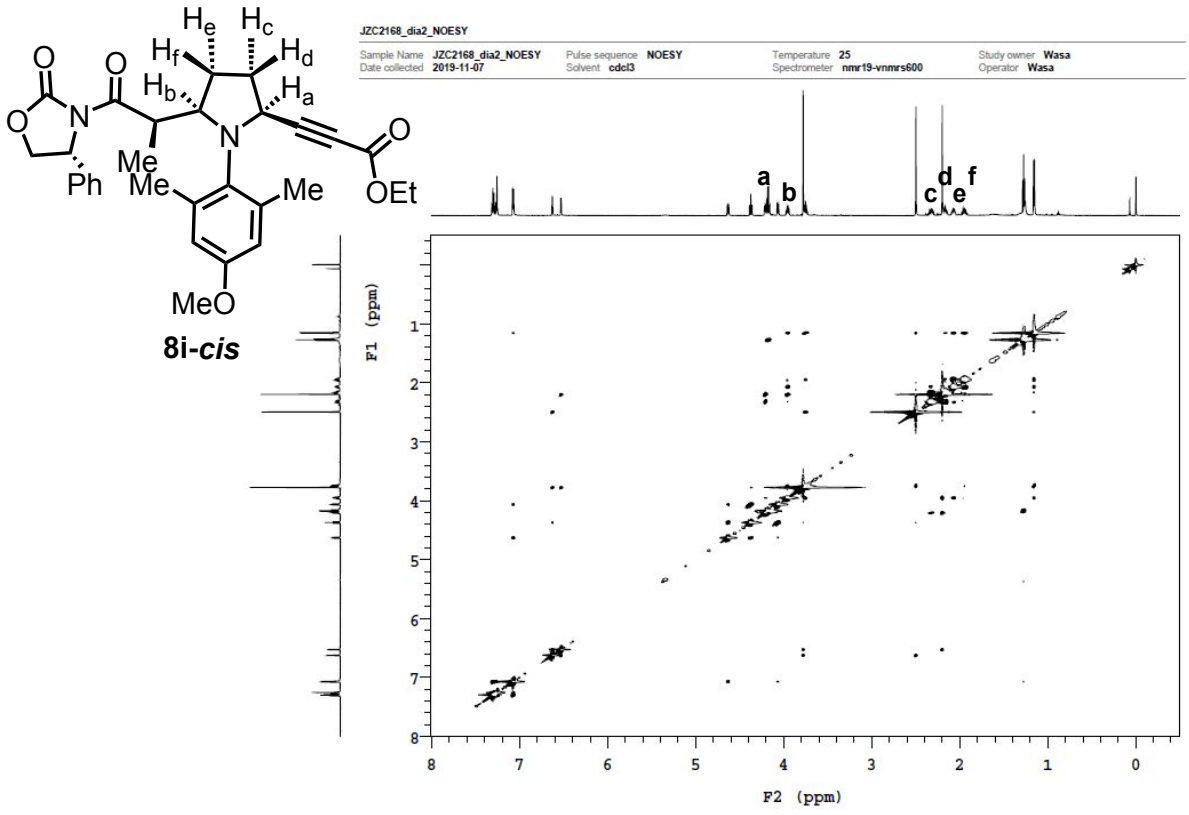
To a solution of **8i-major** (26 mg, 0.05 mmol) in pyridine (0.5 mL) was added $Pd/CaCO_3$ (2.6 mg, 10% wt). The reaction mixture was evacuated and filled with hydrogen gas three times. The reaction mixture was allowed to stir under hydrogen atmosphere at 22 °C for 3 h. Upon completion (determined by TLC), the reaction was filtered through a plug of Celite using EtOAc as the eluent. The amine product **15-major** was obtained after purification by flash silica gel column chromatography (Et_2O:hexanes = 1:4) as a colorless oil (25.5 mg, 98%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31 – 7.22 (m, 3H), 7.06 – 7.02 (m, 2H), 6.57 – 6.50 (m, 2H), 5.97 (ddd, *J* = 11.6, 8.7, 1.0 Hz, 1H), 5.54 (dt, *J* = 11.7, 1.1 Hz, 1H), 5.43 (td, *J* = 8.9, 5.7 Hz, 1H), 4.52 (dd, *J* = 8.5, 2.2 Hz, 1H), 4.23 (dt, *J* = 9.5, 4.7 Hz, 1H), 4.19 (td, *J* = 8.4, 1.1 Hz, 1H), 4.09 (qdd, *J* = 7.1, 3.8, 1.0 Hz, 2H), 3.95 (ddd, *J* = 8.4, 2.4, 1.1 Hz, 1H), 3.77 (d, *J* = 1.0 Hz, 3H), 3.73 – 3.66 (m, 1H), 2.34 – 2.28 (m, 4H), 2.26 (s, 3H), 2.18 (dt, *J* = 11.8, 6.1 Hz, 1H), 1.83 – 1.75 (m, 1H), 1.65 (tdd, *J* = 12.2, 9.2, 6.5 Hz, 1H), 1.58 (s, 1H), 1.22 (td, *J* = 7.1, 1.0 Hz, 3H), 1.00 (dd, *J* = 6.8, 1.0 Hz, 3H); **IR** (neat) 2957, 2926, 2855, 1778, 1713, 1480, 1411, 1182, 1155, 760, 699 cm^{-1}; $[\alpha]^{25}_D$ = –289.9° (*c* 0.5, CH_2Cl_2).



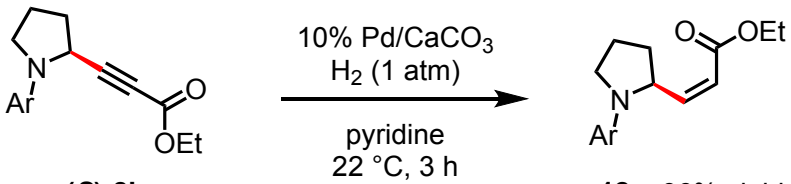


The relative configuration of **15-major** (derivative of **8i-major**) was assigned as *trans*.



The relative configuration of the minor diastereomer of **8i** was assigned as *cis*.

4. Determination of Absolute Configuration and Derivatization Experiments



(*S*)-8b
95:5 er

12a, 96% yield

Ethyl (*S,Z*)-3-(1-(4-methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)acrylate (12a)

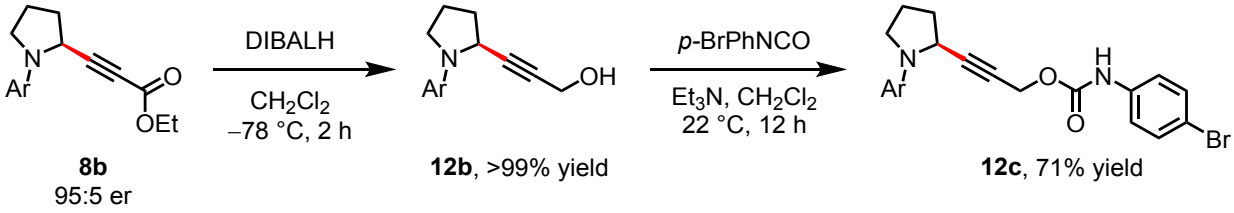
Ethyl (*S,Z*)-3-(1-(4-methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)acrylate (**12a**) was prepared according to the literature procedure.[9]

To a solution of **(*S*)-8b** (30.1 mg, 0.1 mmol) in pyridine (0.5 mL) was added $Pd/CaCO_3$ (3.0 mg, 10% wt). The reaction mixture was evacuated and filled with hydrogen gas three times. The reaction was allowed to stir under hydrogen atmosphere at 22 °C for 3 h. Upon completion (determined by TLC), the reaction was filtered through a plug of Celite using EtOAc as the eluent. The amine product **12a** was obtained after purification by flash silica gel column chromatography (Et_2O:hexanes = 1:19) as a colorless oil (29 mg, 96%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.54 (s, 2H), 6.19 (ddd, J = 11.7, 8.7, 1.2 Hz, 1H), 5.56 (dt, J = 11.6, 1.3 Hz, 1H), 5.26 – 5.16 (m, 1H), 4.06 (qdd, J = 7.0, 5.0, 2.3 Hz, 2H), 3.73 (s, 3H), 3.41 – 3.30 (m, 1H), 3.07 (q, J = 7.6 Hz, 1H), 2.37 – 2.30 (m, 1H), 2.28 (s, 6H), 2.06 – 1.96 (m, 2H), 1.72 (dt, J = 12.1, 6.9 Hz, 1H), 1.20 (td, J = 7.2, 1.2 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.2, 156.6, 154.2, 137.3, 118.8, 59.8, 58.3, 55.1, 51.8, 33.5, 25.5, 19.3, 14.2; **IR** (neat) 2952, 2835, 1715, 1601, 1482, 1317, 1266, 1189, 1154, 1067, 1030, 827 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{18}H_{26}NO_3$ (MH^+): 304.1907; found: 304.1906; $[\alpha]^{25}_D$ = –97.5° (*c* 0.6, CH_2Cl_2).

Determination of Absolute Configuration for 8b

We carried out the following studies in order to determine the absolute configuration of enantioenriched products **8b**, **8d**, and **8e**. The absolute configuration of **(*S*)-8b** was determined by X-ray crystallographic analysis of **12c**. The absolute configuration of **8d** and **8e** were assigned in analogy.



8b
95:5 er

12b, >99% yield

12c, 71% yield

(*S*)-3-(1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)prop-2-yn-1-ol (12b)

(*S*)-3-(1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)prop-2-yn-1-ol (**12b**) was prepared according to the literature procedure.[10] A solution of **8b** (100 mg, 0.3 mmol) in CH_2Cl_2 (5.0 mL) was cooled to −78 °C. DIBAL-H (0.1 mL, 0.5 mmol) was added dropwise. The reaction mixture was allowed to stir for 2 h at −78 °C. Then, potassium sodium tartarate (saturated aqueous solution, 3.0 mL) was added and stirred. The aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The amine product **12b** was obtained after purification by flash silica gel column chromatography (Et_2O:hexanes = 1:1) as a colorless oil (85.7 mg, >99%).

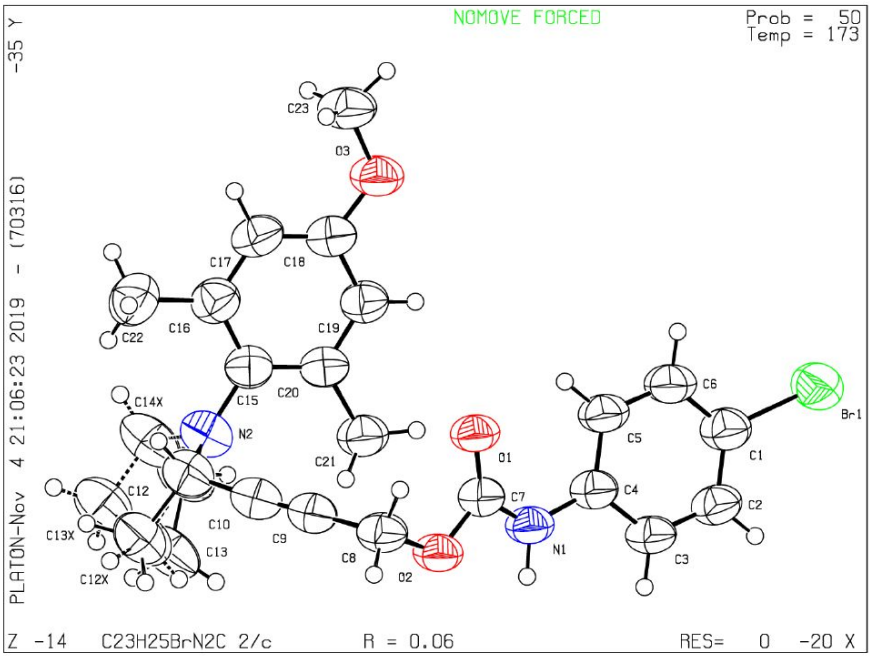
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (s, 2H), 4.22 (ddd, J = 6.7, 4.8, 1.7 Hz, 1H), 4.13 (s, 2H), 3.73 (s, 3H), 3.34 (td, J = 7.6, 4.4 Hz, 1H), 3.06 (q, J = 7.4 Hz, 1H), 2.42 – 2.17 (m, 7H), 2.17 – 2.01 (m, 2H), 1.96 (dtd, J = 11.7, 6.2, 5.8, 3.1 Hz, 1H), 1.70 (d, J = 4.6 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 156.8, 136.4, 113.5, 88.6, 79.5, 55.1, 52.1, 51.2, 50.7, 34.4, 25.3, 19.0; **IR** (neat) 3379, 2939, 2834, 1600, 1482, 1273, 1153, 1066, 925, 835, 571 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{16}H_{22}NO_2$ (MH^+): 260.1645; found: 260.1645.

(*S*)-3-(1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)prop-2-yn-1-yl (4-bromophenyl)carbamate (12c)

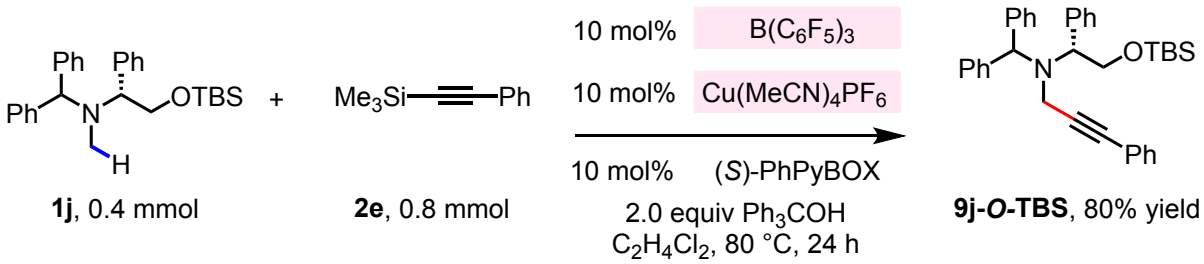
(*S*)-3-(1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)prop-2-yn-1-yl (4-bromophenyl)carbamate was prepared according to the literature procedure.[10] To a solution of **12b** (50 mg, 0.2 mmol) in CH_2Cl_2 (1.0 mL), *p*-bromophenyl isocyanate (113 mg, 0.6 mmol) and Et_3N (96 mg, 1.0 mmol) were added. The reaction mixture was allowed to stir at 22 °C for

12 h. Upon completion (determined by TLC), the reaction mixture was filtered through a short plug of Celite using CH_2Cl_2 as the eluent. The organic layer was concentrated *in vacuo*. The amine product **12c** was obtained after purification by flash silica gel column chromatography (Et_2O:hexanes = 1:1) as a colorless solid (61.3 mg, 71%).

Amine **12c** was recrystallized using the vapor-vapor diffusion method, using Et_2O to dissolve the product in an inner vial, and pentane as the precipitant placed in the outer vial in order for slow diffusion to occur into the inner vial. The solution was cooled to 0 °C, whereupon a crystal was obtained for X-ray crystallography. The X-ray crystallographic analysis revealed that the absolute configuration of **12c** is (*S*), see SI Section 9 for X-ray crystallographic data. The absolute configuration of **8b** is (*S*). The absolute configuration of **8d** and **8e** were assigned in analogy to **8b**.



Procedure for Preparation of Propargylamine 9j-*O*-TBS



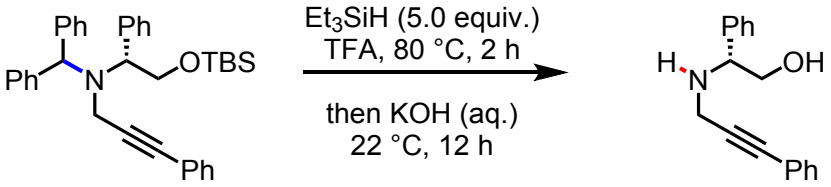
1j, 0.4 mmol **2e**, 0.8 mmol **9j-*O*-TBS**, 80% yield

(*R*)-*N*-Benzhydryl-*N*-(2-((*tert*-butyldimethylsilyl)oxy)-1-phenylethyl)-3-phenylprop-2-yn-1-amine (9j-*O*-TBS)

An oven-dried sealed tube equipped with a magnetic stir bar was used. To the sealed tube were added $Cu(MeCN)_4PF_6$ (0.04 mmol), (*S*)-PhPyBOX, 0.04 mmol), and $C_2H_4Cl_2$ (0.4 mL) under nitrogen atmosphere. The mixture was allowed to stir for 20 minutes at 22 °C, then (trimethylsilyl)propiolate **2e** (0.8 mmol), triphenylmethanol (0.8 mmol), amine **1j** (0.4 mmol), $B(C_6F_5)_3$ (0.04 mmol, 10 mol%), and $C_2H_4Cl_2$ (0.4 mL) were added to the vessel. The reaction mixture was allowed to stir at 80 °C for 24 h. Upon completion, the unpurified reaction mixture was filtered through a short plug of Celite and rinsed with CH_2Cl_2. The combined organic material was then concentrated *in vacuo*. The propargylamine product was purified and isolated by silica gel column chromatography (1:9 CH_2Cl_2:hexane) to afford **9j-*O*-TBS** as a colorless oil (170.2 mg, 80% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69 – 7.58 (m, 6H), 7.47 – 7.33 (m, 12H), 7.33 – 7.24 (m, 2H), 5.40 (s, 1H), 4.38 (dd, J = 10.2, 5.1 Hz, 1H), 4.34 (dd, J = 10.2, 7.3 Hz, 1H), 4.30 (dd, J = 7.2, 5.1 Hz, 1H), 3.75 (d, J = 1.4 Hz, 2H), 0.92 (s, 9H), 0.08 (s, 3H), 0.02 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.6, 142.4, 140.5, 131.5, 128.9, 128.6, 128.5, 128.38, 128.35, 128.07, 128.06, 127.9, 127.7, 127.03, 126.95, 126.9, 123.7, 87.7, 84.4, 69.2, 63.4, 62.8, 37.0, 25.9, 18.2, -5.45, -5.47; **IR** (neat) 3057, 3025, 2924, 2852, 1597, 1488, 1451, 1251, 1095, 835, 813, 744, 699 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{36}H_{42}NOSi$ (MH^+): 532.3030; found: 532.3023; $[\alpha]^{25}_D$ = –25.1° (*c* 1.0, CH_2Cl_2).

Procedure for Deprotection of *N*-Benzhydryl Group



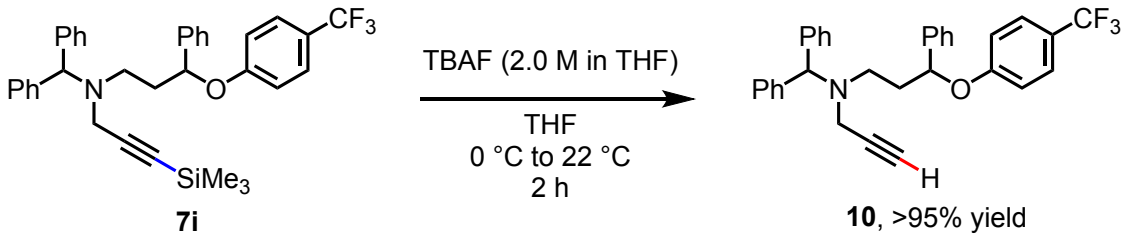
9j-*O*-TBS **9**, 80% yield

(*R*)-2-Phenyl-2-((3-phenylprop-2-yn-1-yl)amino)ethan-1-ol (9)

(*R*)-2-Phenyl-2-((3-phenylprop-2-yn-1-yl)amino)ethan-1-ol was prepared according to the literature procedure.[11] To a solution of **9j-*O*-TBS** (100 mg, 0.2 mmol) in TFA (1.5 mL) was added triethylsilane (0.14 mL, 0.9 mmol). The mixture was allowed to stir at 80 °C for 2 h. The mixture was cooled to 22 °C and KOH (1.0 M, aq.) was added in a dropwise manner until the solution was alkaline. The reaction mixture was allowed to stir at 22 °C for 12 h. CH_2Cl_2 (5 mL) was added and the organic material was extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layers were combined, dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The amine product **9** was obtained after purification by flash silica gel column chromatography (EtOAc:hexanes = 8:2) as a colorless solid (36.2 mg, 80%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 – 7.38 (m, 2H), 7.38 – 7.33 (m, 4H), 7.32 – 7.26 (m, 4H), 4.06 (dd, J = 8.3, 4.4 Hz, 1H), 3.78 (dd, J = 10.9, 4.4 Hz, 1H), 3.68 – 3.60 (m, 2H), 3.45 (d, J = 17.0 Hz, 1H), 2.42 – 2.12 (m, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 139.70, 131.63, 128.66, 128.21, 128.03, 127.81, 127.57, 123.09, 87.29, 83.71, 66.79, 63.22, 36.72; **IR** (neat) 3288, 3056, 2914, 2847, 1488, 1451, 1329, 1026, 754, 690, 526 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{17}H_{18}NO$ (MH^+): 252.1383; found: 252.1379; $[\alpha]^{25}_D$ = 199.1° (*c* 1.0, CH_2Cl_2).

Procedure for Removal of Trimethylsilyl Group



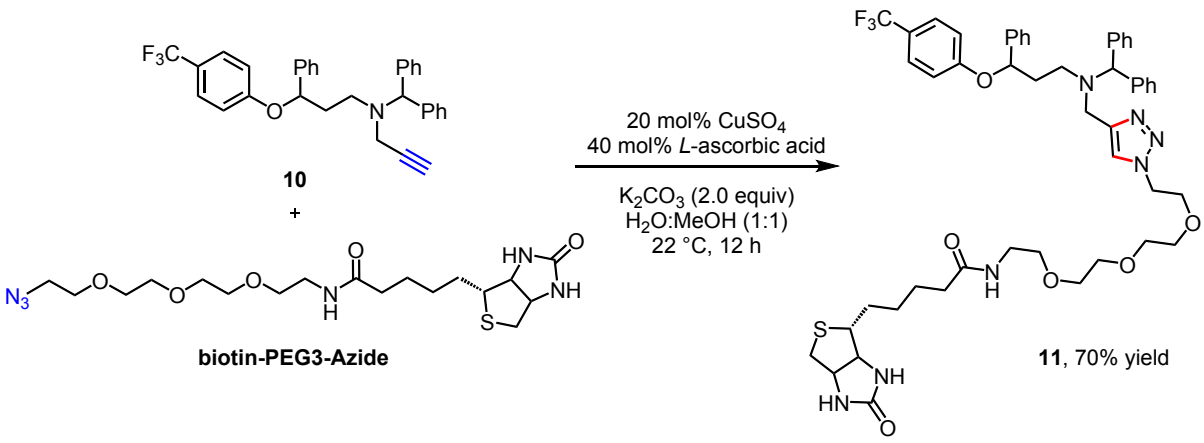
7i **10**, >95% yield

***N*-Benzhydryl-*N*-(3-phenyl-3-(4-(trifluoromethyl)phenoxy)propyl)prop-2-yn-1-amine (10)**

To a solution of **7i** (228 mg, 0.4 mmol) in THF (10 mL) was added TBAF (1.0 mL, 2.0 M in THF) at 0 °C. The reaction mixture was allowed to stir for 2 h at 22 °C. Upon completion (determined by TLC), the reaction mixture was concentrated *in vacuo*. The amine product **10** was obtained after purification by flash silica gel column chromatography (Et_2O:hexane = 1:99) as a colorless solid (200 mg, 99% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 (dd, *J* = 8.4, 3.5 Hz, 4H), 7.34 – 7.30 (m, 2H), 7.28 (d, *J* = 5.9 Hz, 4H), 7.23 (t, *J* = 7.7 Hz, 3H), 7.20 – 7.10 (m, 2H), 7.06 (q, *J* = 7.0, 6.4 Hz, 3H), 6.80 (d, *J* = 8.4 Hz, 2H), 5.26 (d, *J* = 3.8 Hz, 1H), 4.68 (s, 1H), 3.44 (qd, *J* = 17.7, 2.4 Hz, 2H), 2.86 – 2.65 (m, 2H), 2.17 (s, 1H), 2.16 – 1.94 (m, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 160.6, 143.9, 142.6, 142.5, 141.4, 130.0, 129.4, 128.7, 128.6, 128.52, 128.48, 128.44, 128.38, 128.28, 128.25, 128.00, 127.96, 127.93, 127.92, 127.83, 127.80, 127.7, 127.4, 127.24, 127.15, 127.1, 126.96, 126.92, 126.68, 126.65, 126.63, 126.60, 126.3, 125.8, 125.6, 125.5, 125.4, 123.6, 122.6 (q, *J* = 32.7 Hz), 121.8, 115.7, 78.2, 77.8, 73.5, 72.2, 56.8, 46.4, 39.1, 36.8; **^{19}F NMR** (470 MHz, $CDCl_3$) δ -61.34; **IR** (neat) ν 3298, 3060, 3025, 2924, 2831, 1700, 1612, 1515, 1491, 1326, 1250, 1110, 1066, 834, 700 cm^{-1}; **HRMS** (DART) Calcd for $C_{32}H_{29}NOF_3$ (MH^+): 500.2196; found: 500.2183.

Procedure for Organocopper-Catalyzed Alkyne Azide Click Reaction



***N*-(2-(2-(2-(2-(4-((Benzhydryl(3-phenyl-3-(4-(trifluoromethyl)phenoxy)propyl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)ethoxy)ethoxy)ethoxy)ethyl)-5-((4*R*)-2-oxohexahydro-1*H*-thieno[3,4-*d*]imidazol-4-yl)pentanamide (11)**

N-(2-(2-(2-(2-(4-((Benzhydryl(3-phenyl-3-(4-(trifluoromethyl)phenoxy)propyl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)ethoxy)ethoxy)ethoxy)ethyl)-5-((4*R*)-2-oxohexahydro-1*H*-thieno[3,4-*d*]imidazol-4-yl)pentanamide was prepared according to the literature procedure.[12]

To a solution of alkyne **10** (100 mg, 0.2 mmol) in MeOH (2.0 mL) was added K_2CO_3 (55 mg, 0.4 mmol), $CuSO_4$ (6.4 mg, 0.04 mmol), Biotin-PEG3-azide (98 mg, 0.22 mmol), *L*-ascorbic acid (14.1 mg, 0.08 mmol), and H_2O (2.0 mL). The reaction mixture was then allowed to stir for 12 h. Upon completion (determined by TLC), the reaction mixture was concentrated *in vacuo* to remove the organic solvent. EtOAc (3 x 5 mL) was used to extract the organic material. The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The amine product **11** was obtained after purification by flash silica gel column chromatography (MeOH:CH_2Cl_2 = 1:99) as a colorless solid (132 mg, 70%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 – 7.36 (m, 4H), 7.36 – 7.30 (m, 2H), 7.30 – 7.26 (m, 3H), 7.24 (t, *J* = 7.8 Hz, 4H), 7.19 (q, *J* = 7.2, 6.1 Hz, 4H), 6.77 (d, *J* = 8.5 Hz, 2H), 6.64 (s, 1H), 6.57 (s, 1H), 5.63 (s, 1H), 5.23 (dd, *J* = 8.5, 4.2 Hz, 1H), 4.78 (s, 1H), 4.42 (dtt, *J* = 14.3, 10.5, 5.2 Hz, 3H), 4.26 (dd, *J* = 7.8, 4.7 Hz, 1H), 3.94 – 3.74 (m, 4H), 3.54 (d, *J* = 7.2 Hz, 8H), 3.51 (t, *J* = 5.2 Hz, 2H), 3.40 (t, *J* = 5.2 Hz, 2H), 3.10 (td, *J* = 7.3, 4.5 Hz, 1H), 2.85 (dd, *J* = 12.7, 4.9 Hz, 1H), 2.77 – 2.68 (m, 2H), 2.63 (ddd, *J* = 12.9, 7.7, 4.6 Hz, 1H), 2.18 (t, *J* = 7.5 Hz, 2H), 2.12 (dtd, *J* = 14.5, 7.6, 7.0, 3.8 Hz, 2H), 1.78 – 1.56 (m, 4H), 1.46 – 1.34 (m, 2H); **^{13}C NMR**

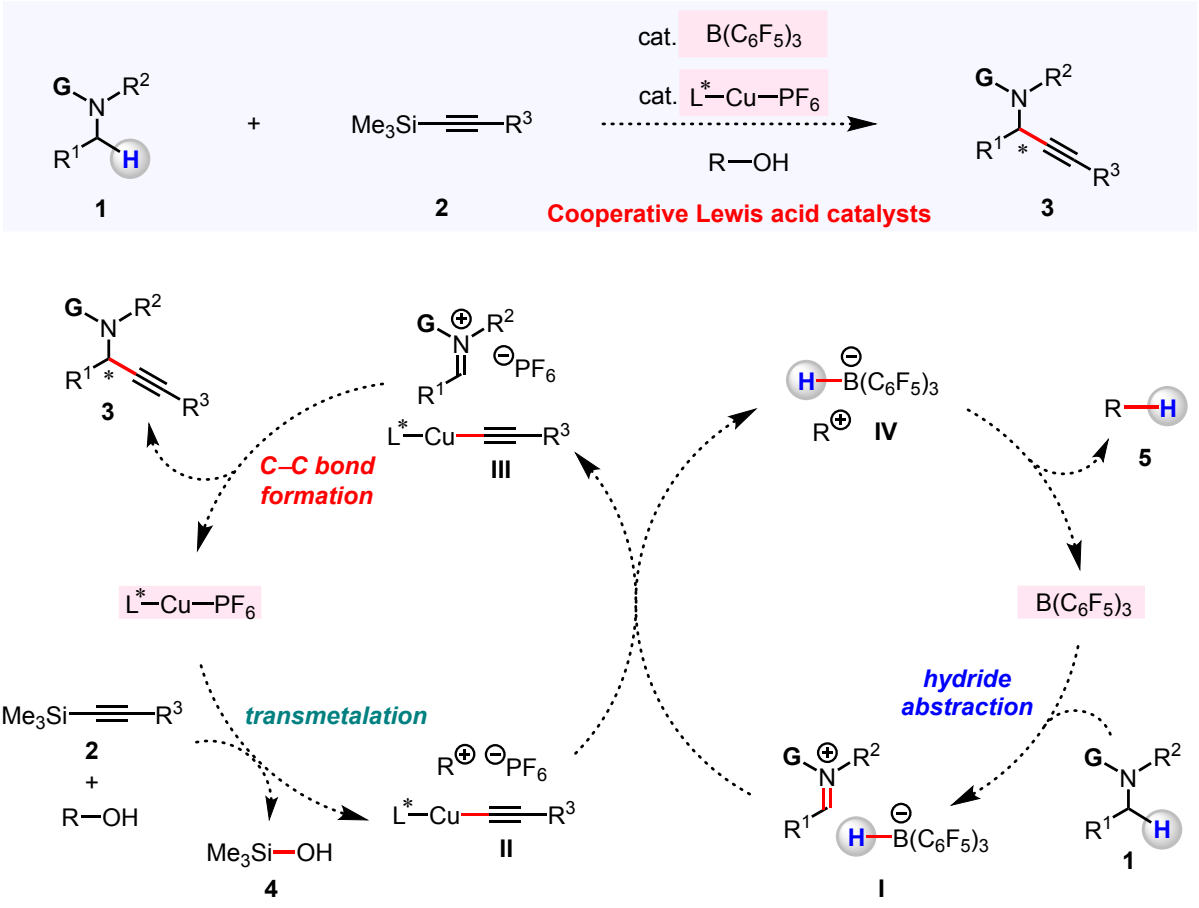
(151 MHz, $CDCl_3$) δ 173.2, 164.0, 160.5, 144.8, 142.2, 141.6, 141.30, 128.6, 128.5, 128.4, 128.34, 128.31, 128.26, 128.1, 127.6, 127.07, 127.00, 126.96, 126.62, 126.60, 126.57, 126.55, 125.7, 125.5, 125.3, 123.5, 122.4 (q, J = 32.5 Hz), 121.9, 115.6, 77.8, 77.2, 77.0, 76.9, 76.8, 70.6, 70.5, 70.4, 70.3, 70.0, 69.9, 69.8, 69.5, 65.8, 61.7, 60.1, 55.6, 50.0, 46.1, 44.9, 40.4, 39.1, 36.1, 35.9, 35.9, 30.3, 29.6, 29.6, 28.2, 28.0, 25.5, 15.2; **^{19}F NMR** (564 MHz, $CDCl_3$) δ -61.44; **IR** (neat) 3287, 2921, 2863, 1698, 1612, 1451, 1325, 1250, 1109, 1066, 835, 734, 701 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{50}H_{61}F_3N_7O_6S$ (MH^+): 944.4278; found: 944.4342.

5. Mechanistic Studies for α-C–H Alkynylation of *N*-Alkylamines Catalyzed by $B(C_6F_5)_3$ and Organocopper Complex

5.1 Kinetic Experiments for the Coupling of 4-Methoxy-*N*,*N*,2,6-tetramethylaniline and Ethyl 3-(trimethylsilyl)propiolate

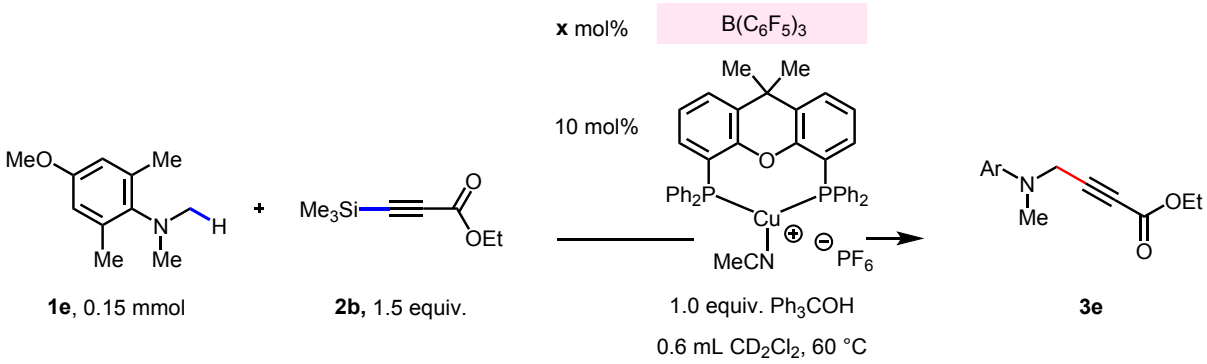
In order to provide evidence for the proposed reaction mechanism, we carried out the following kinetic experiments. We originally proposed (as shown in Figure 1c of the manuscript) that α-alkynylation process is proposed to proceed through $B(C_6F_5)_3$-catalyzed hydride abstraction of the *N*-alkylamine substrate (**1**) to afford an iminium ion (**I**, Scheme S1). Subsequently, the organocopper catalyst can activate the alkyne substrate (**2**) with the aid of alcohol additive to promote transmetallation (**II**), which generates a nucleophilic alkyne that can attack the iminium ion (**III**) to afford the desired propargylamine **3**.

Scheme S1. Proposed Catalytic Cycle



5.1.1 Determination of Reaction Order of $B(C_6F_5)_3$

A kinetic study was conducted following the procedure for time course reaction monitoring by ^1H NMR (using internal standard) while varying the concentration of $B(C_6F_5)_3$ (Figure S1). Initial-rate kinetic analysis, which was determined from the data points in the first 400 seconds, demonstrates half-order kinetics of $B(C_6F_5)_3$ in the reaction between 4-methoxy-*N,N*,2,6-tetramethylaniline **1e** and ethyl 3-(trimethylsilyl)propiolate **2b** (Figure S2).[13]



Procedure for Time Course Reaction Monitoring by *in situ* ^1H NMR

In a nitrogen-filled glove box, previously prepared (Xantphos)Cu(MeCN)PF_6 (41 mg, 0.11 mmol),[14] 4-methoxy-*N,N*,2,6-tetramethylaniline (197 mg, 1.1 mmol), ethyl 3-(trimethylsilyl)propiolate (281 mg, 1.65 mmol) and mesitylene (132 mg, 1.1 mmol) were weighed in an oven-dried 7.0 mL vial and diluted to 2.2 mL with CD_2Cl_2 (**Stock Solution A**). In another oven-dried 7.0 mL vial, $B(C_6F_5)_3$ (63.8 mg, 0.125 mmol) was weighed and diluted to 1.0 mL with CD_2Cl_2 (**Stock Solution B**). In 4 oven-dried 7.0 mL vials, were added triphenylmethanol (39 mg, 0.15 mmol). To each oven-dried vial containing triphenylmethanol was added **Stock Solution A** (0.3 mL), **Stock Solution B** (0.06, 0.12, 0.15 and 0.18 mL) and neat CD_2Cl_2 (0.24, 0.18, 0.15 and 0.12 mL) to prepare reaction mixtures (total 0.6 mL) with 0.150 mmol of 4-methoxy-*N,N*,2,6-tetramethylaniline, 0.225 mmol ethyl 3-(trimethylsilyl)propiolate, 0.150 mmol triphenylmethanol, 10.0 mol% (Xantphos)Cu(MeCN)PF_6, and the following amounts of $B(C_6F_5)_3$ (5.00, 10.0, 12.5 and 15.0 mol%). The reaction mixture was then transferred to a J-Young tube. After the J-Young tube was tightly capped with the Teflon plug, it was taken out of the glove box and ^1H NMR spectra were acquired at 60 °C (preheated) using a pre-acquisition delay in array mode with a spectrum taken every 30 seconds for the length of the experiment. The data were processed using MestReNova and peak integrations were normalized using mesitylene as the internal standard.

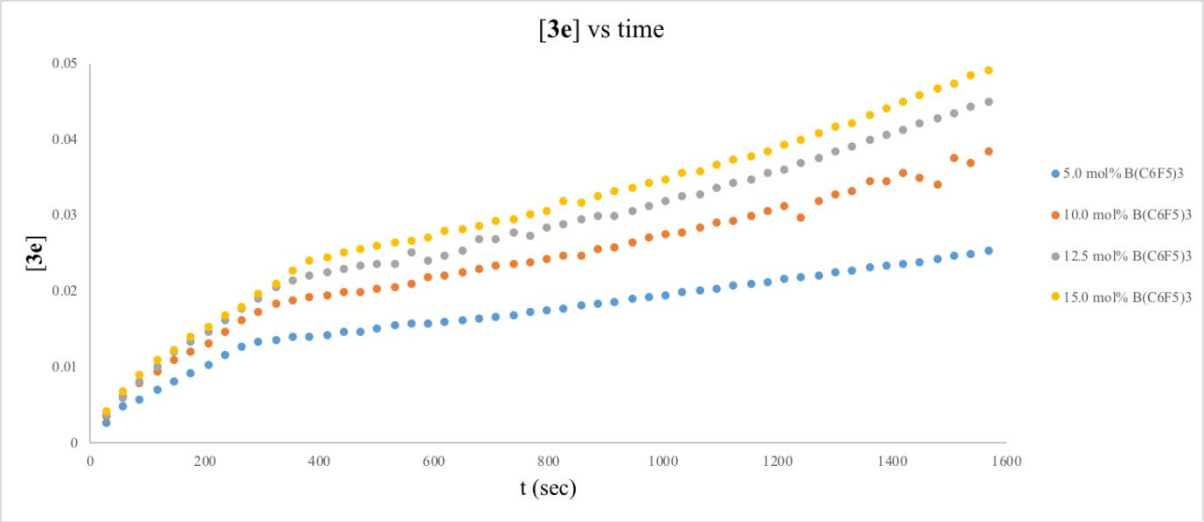


Figure S1. Monitoring the formation of **3e** using different concentrations of $B(C_6F_5)_3$.

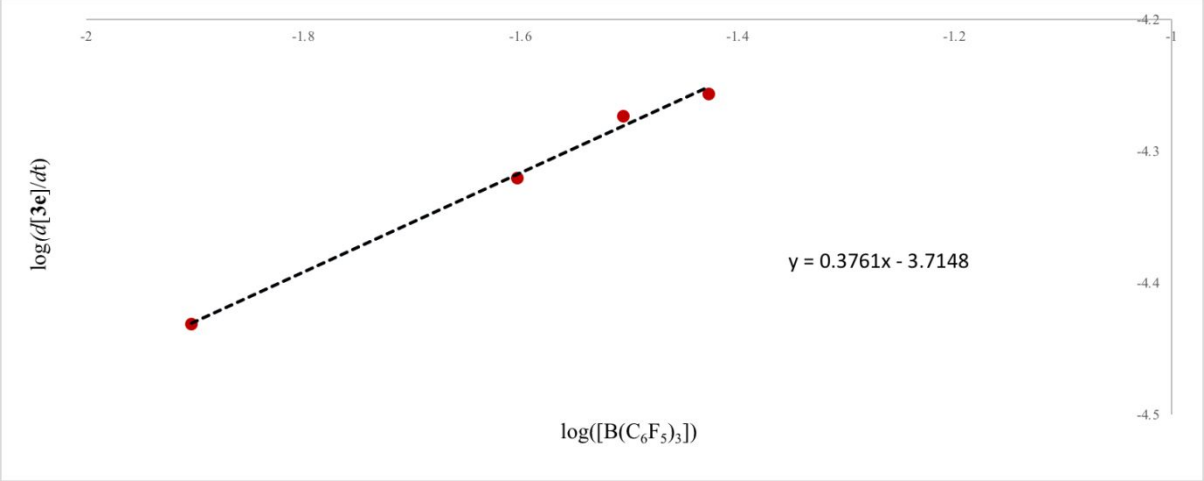
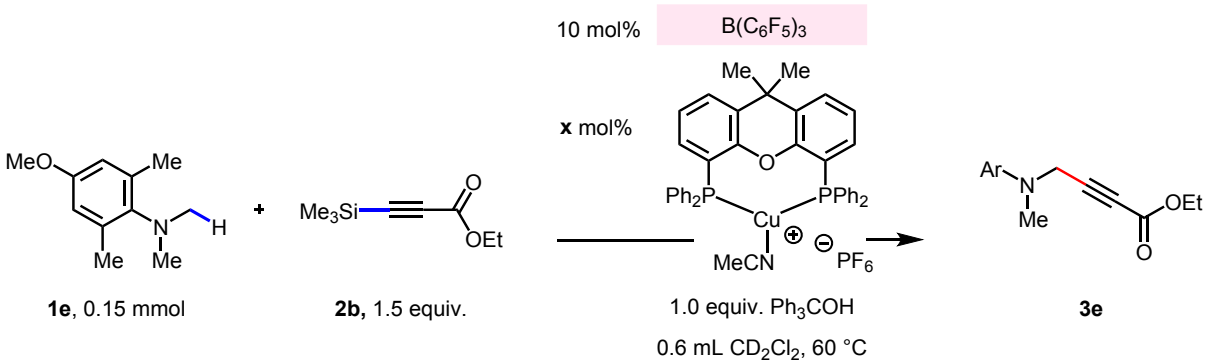


Figure S2. Log(rate) *vs* Log[$B(C_6F_5)_3$] plot is employed to determine the reaction order for $B(C_6F_5)_3$**.** The result suggests that there is approximately 0.5-order dependency on the concentration of $B(C_6F_5)_3$.

5.1.2 Determination of Reaction Order of (Xantphos)Cu(MeCN)PF_6

A kinetic study was conducted following the procedure for time course reaction monitoring by ^{1}H NMR (using internal standard) while varying the concentration of (Xantphos)Cu(MeCN)PF_6 (Figure S3). Initial-rate kinetic analysis, which was determined from the data points in the first 400 seconds, demonstrates zero-order kinetics of (Xantphos)Cu(MeCN)PF_6 in the reaction between 4-methoxy-*N,N*,2,6-tetramethylaniline **1e** and ethyl 3-(trimethylsilyl)propiolate **2b** (Figure S4).[13]



In a nitrogen-filled glove box, $B(C_6F_5)_3$ (56.3 mg, 0.11 mmol), 4-methoxy-*N,N*,2,6-tetramethylaniline (197 mg, 1.10 mmol), ethyl 3-(trimethylsilyl)propiolate (281 mg, 1.65 mmol) and mesitylene (132 mg, 1.10 mmol) were weighed in an oven-dried 7.0 mL vial and diluted to 2.2 mL with CD_2Cl_2 (**Stock Solution A**). In another oven-dried 7.0 mL vial, (Xantphos)Cu(MeCN)PF_6 (103.5 mg, 0.125 mmol)[14] was weighed and diluted to 2.00 mL with CD_2Cl_2 (**Stock Solution B**). In 5 oven-dried 7.0 mL vials, were added triphenylmethanol (39 mg, 0.15 mmol). To each oven-dried vial containing triphenylmethanol was added **Stock Solution A** (0.30 mL), **Stock Solution B** (0.06, 0.12, 0.24, 0.30 and 0.36 mL) and neat CD_2Cl_2 (0.30, 0.24, 0.12, 0.06 and 0.00 mL) to prepare reaction mixtures (total 0.62 mL) with 0.150 mmol of 4-methoxy-*N,N*,2,6-tetramethylaniline, 0.225 mmol ethyl 3-(trimethylsilyl)propiolate, 0.15 mmol triphenylmethanol, 10.0 mol% $B(C_6F_5)_3$, and the following amounts of (Xantphos)Cu(MeCN)PF_6 (2.5, 5.0, 10.0, 12.5 and 15.0 mol%). The reaction mixture was then transferred to a J-Young tube. After the J-Young tube was tightly capped with the Teflon plug, it was taken out of the glove box and ^{1}H NMR spectra were acquired at 60 °C (preheated) using a pre-acquisition delay in array mode with a spectrum taken every 30 seconds for the length of the experiment. The data were processed using MestReNova and peak integrations were normalized using mesitylene as the internal standard.

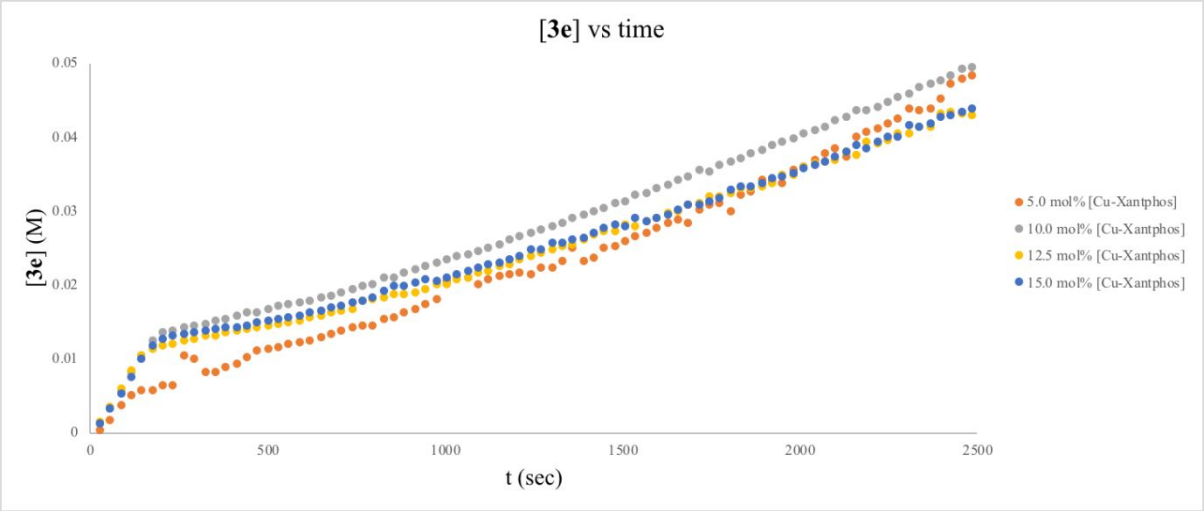


Figure S3. Monitoring the formation of **3e** using different concentrations of (Xantphos)Cu(MeCN)(PF_6).

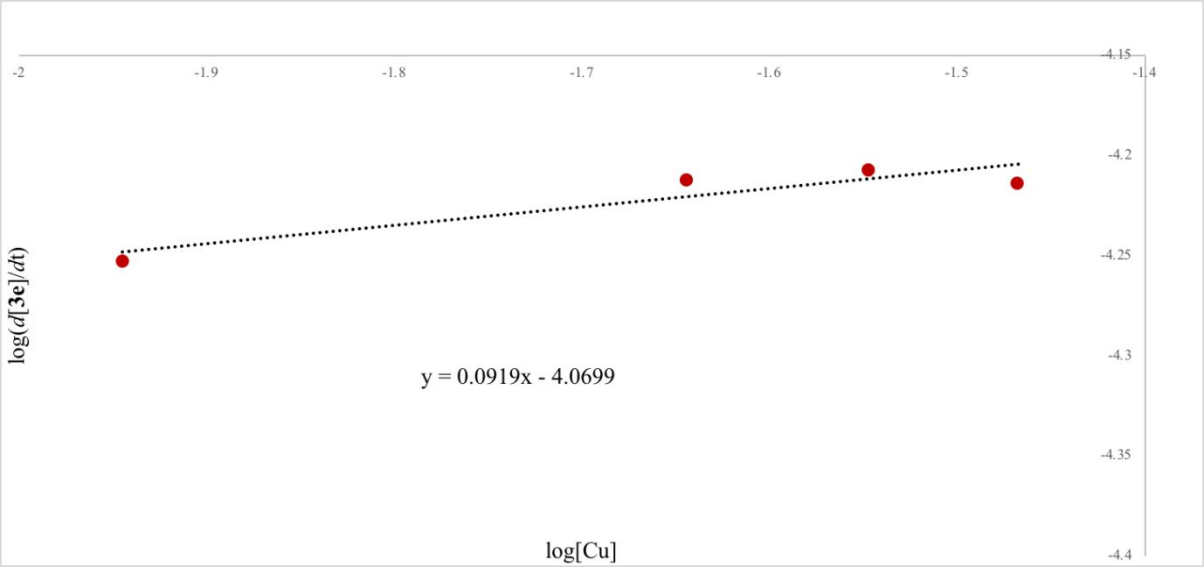
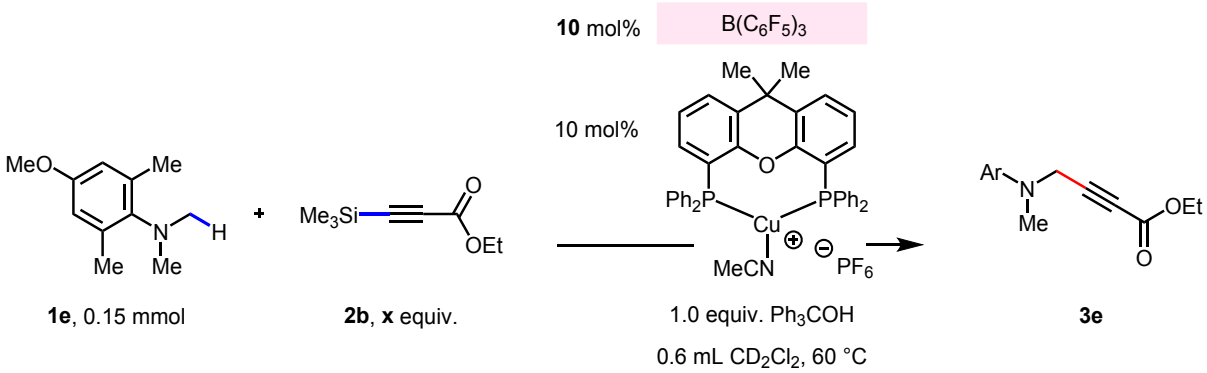


Figure S4. Log(rate) *vs* Log[(Xantphos)Cu(MeCN)(PF_6)] plot is employed to determine the initial reaction order for (Xantphos)Cu(MeCN)(PF_6)**.** The result suggests that there is 0-order dependency on the concentration of (Xantphos)Cu(MeCN)(PF_6).

5.1.3 Determination of Reaction Order of Ethyl 3-(trimethylsilyl)propiolate 2b

A kinetic study was conducted following the procedure for time course reaction monitoring by ^{1}H NMR (using internal standard) while varying the concentration of ethyl 3-(trimethylsilyl)propiolate **2b** (Figure S5). Initial-rate kinetic analysis, which was determined from the data points in the first 400 seconds, demonstrates zero-order kinetics of ethyl 3-

(trimethylsilyl)propiolate in the reaction between 4-methoxy-*N,N*,2,6-tetramethylaniline **1e** and ethyl 3-(trimethylsilyl)propiolate **2b** (Figure S6).[13]



Procedure for Time Course Reaction Monitoring by *in situ* ^{1}H NMR

In a nitrogen-filled glove box, (Xantphos)Cu(MeCN)PF_6 (103.5 mg, 0.11 mmol),[14] $B(C_6F_5)_3$ (56.3 mg, 0.11 mmol), 4-methoxy-*N,N*,2,6-tetramethylaniline (197 mg, 1.10 mmol), and mesitylene (132 mg, 1.10 mmol) were weighed in an oven-dried 7.0 mL vial and diluted to 2.20 mL with CD_2Cl_2 (**Stock Solution A**). In another oven-dried 7.0 mL vial, (ethyl 3-(trimethylsilyl)propiolate (623 mg, 3.66 mmol) was weighed and diluted to 1.30 mL with CD_2Cl_2 (**Stock Solution B**). In 5 oven-dried 7.0 mL vials, were added triphenylmethanol (39 mg, 0.15 mmol). To each oven-dried vial containing triphenylmethanol was added **Stock Solution A** (0.30 mL), **Stock Solution B** (0.04, 0.08, 0.12, 0.16 and 0.24 mL) and neat CD_2Cl_2 (0.28, 0.24, 0.18, 0.14 and 0.08 mL) to prepare reaction mixtures (total 0.60 mL) with 0.15 mmol of 4-methoxy-*N,N*,2,6-tetramethylaniline, 0.15 mmol triphenylmethanol, 10.0 mol% $B(C_6F_5)_3$, 10.0 mol% (Xantphos)Cu(MeCN)PF_6 and the following amounts of ethyl 3-(trimethylsilyl)propiolate (0.75, 1.50, 2.25, 3.00 and 4.50 equiv.). The reaction mixture was then transferred to a J-Young tube. After the J-Young tube was tightly capped with the Teflon plug, it was taken out of the glove box and ^{1}H NMR spectra were acquired at 60 °C (preheated) using a pre-acquisition delay in array mode with a spectrum taken every 30 seconds for the length of the experiment. The data were processed using MestReNova and peak integrations were normalized using mesitylene as the internal standard.

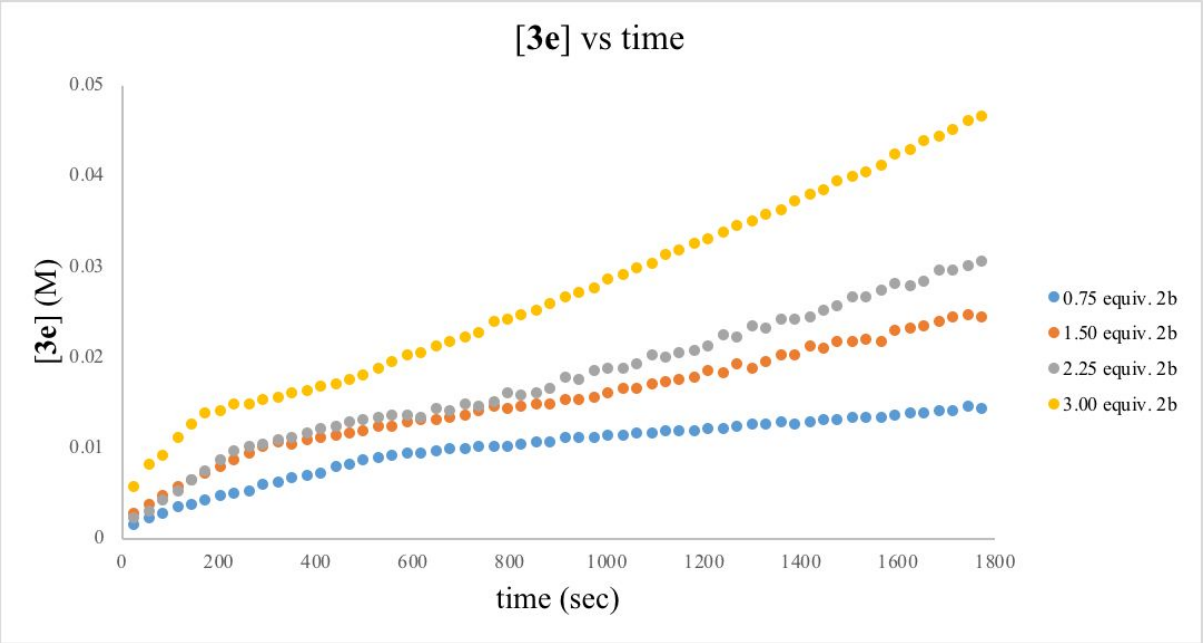


Figure S5. Monitoring the formation of **3e** using different concentrations of **2b**.

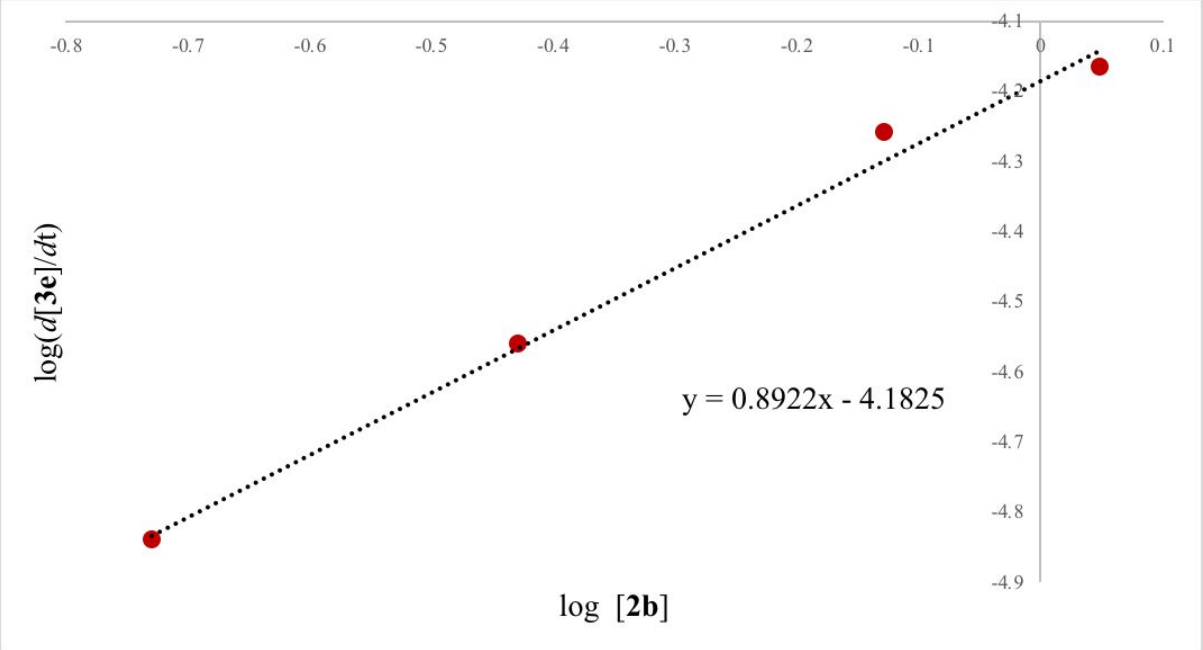
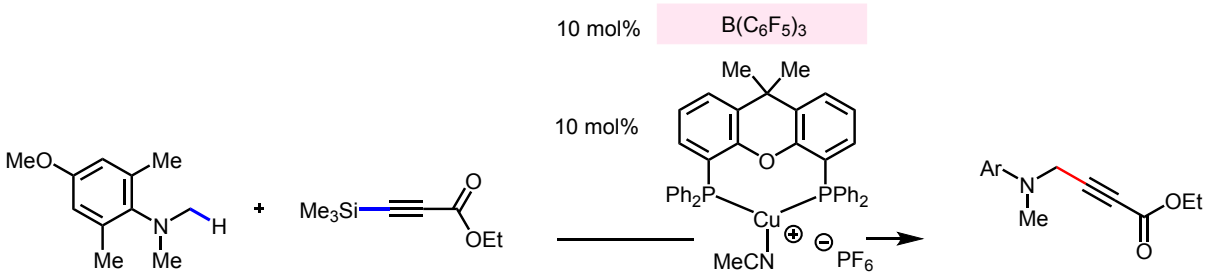


Figure S6. Log(rate) *vs* Log[**2b**] plot is employed to determine the initial reaction order for **2b**. The result suggests that there is 1.0-order dependency on the concentration of **2b**.

5.1.4 Determination of Reaction Order of Ph_3COH

A kinetic study was conducted following the procedure for time course reaction monitoring by ^1H NMR (using internal standard) while varying the concentration of trityl alcohol (Figure S7). Initial-rate kinetic analysis, which was determined from the data points in

the first 400 seconds, demonstrates zero-order kinetics of trityl alcohol in the reaction between 4-methoxy-*N,N*,2,6-tetramethylaniline **1e** and ethyl 3-(trimethylsilyl)propiolate **2b** (Figure S8).[13]



In a nitrogen-filled glove box, (Xantphos)Cu(MeCN)PF_6 (91.2 mg, 0.11 mmol),[14] $B(C_6F_5)_3$ (56.3 mg, 0.11 mmol), 4-methoxy-*N,N*,2,6-tetramethylaniline (197 mg, 1.1 mmol), ethyl 3-(trimethylsilyl)propiolate (281 mg, 1.65 mmol) and mesitylene (132 mg, 1.1 mmol) were weighed in an oven-dried 7.0 mL vial and diluted to 2.2 mL with CD_2Cl_2 (**Stock Solution A**). In 5 oven-dried 7.0 mL vials, were added triphenylmethanol (19.5 mg, 39.0 mg, 52.0 mg, 64.7 mg and 78.0 mg). To each oven-dried vial containing triphenylmethanol was added **Stock Solution A** (0.3 mL) and neat CD_2Cl_2 (0.3 mL) to prepare reaction mixtures (total 0.6 mL) with 0.15 mmol of 4-methoxy-*N,N*,2,6-tetramethylaniline, 0.22 mmol ethyl 3-(trimethylsilyl)propiolate, 10.0 mol% $B(C_6F_5)_3$, and the following amounts of (Xantphos)Cu(MeCN)PF_6 (10.0 mol%) and triphenylmethanol (0.5, 1.0, 1.3, 1.7 and 2.0 equiv.). The reaction mixture was then transferred to a J-Young tube. After the J-Young tube was tightly capped with the Teflon plug, it was taken out of the glove box and ^{1}H NMR spectra were acquired at 60 °C (preheated) using a pre-acquisition delay in array mode with a spectrum taken every 30 seconds for the length of the experiment. The data were processed using MestReNova and peak integrations were normalized using mesitylene as the internal standard.

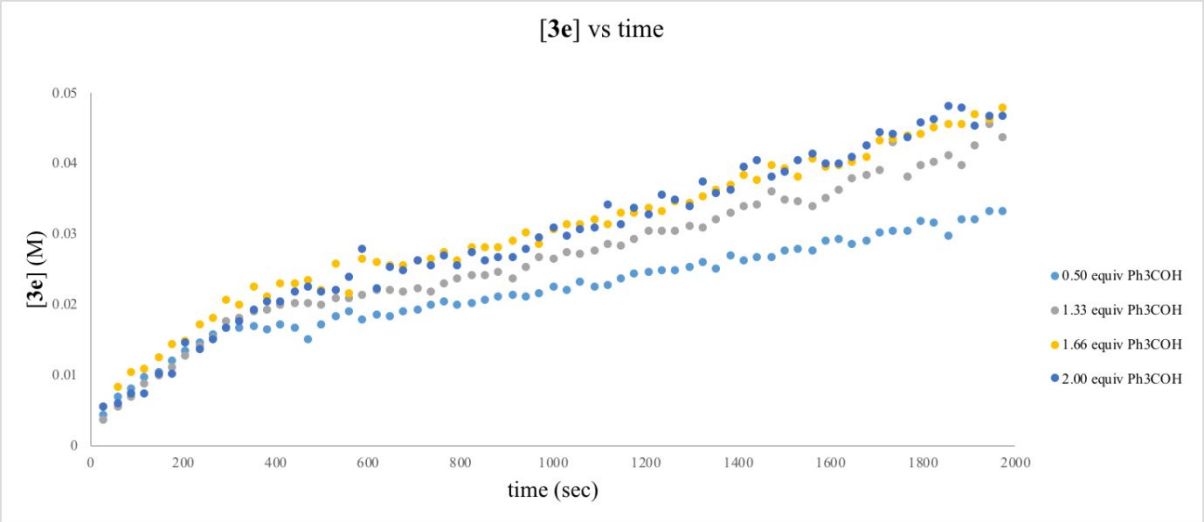


Figure S7. Monitoring the formation of **3e** using different concentrations of Ph_3COH.

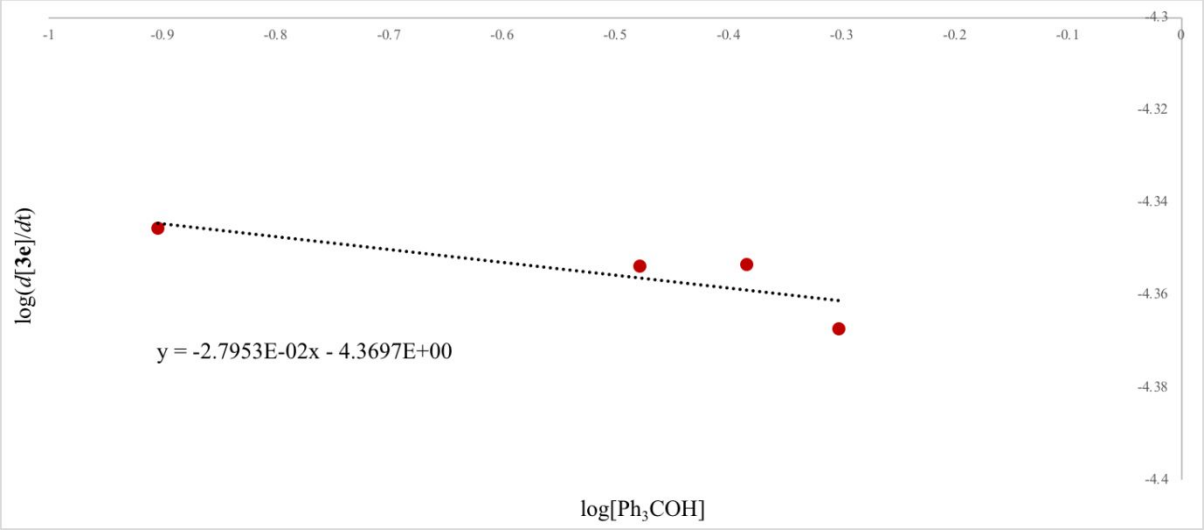
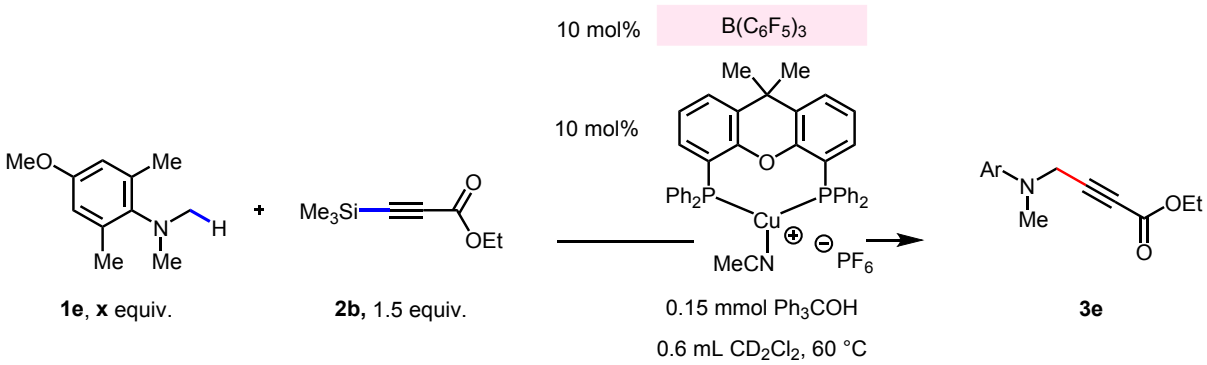


Figure S8. Log(rate) *vs* Log[Ph_3COH] plot is employed to determine the initial reaction order for Ph_3COH. The result suggests that there is 0-order dependency on the concentration of Ph_3COH.

5.1.5 Determination of Reaction Order in Ethyl 4-methoxy-*N,N*,2,6-tetramethylaniline 1e

A kinetic study was conducted following the procedure for time course reaction monitoring by ^{1}H NMR (using internal standard) while varying the concentration of 4-methoxy-*N,N*,2,6-tetramethylaniline **1e** (Figure S9). Initial-rate kinetic analysis, which was determined from the data points in the first 400 seconds, demonstrates zero-order kinetics of 4-methoxy-*N,N*,2,6-tetramethylaniline **1e** (Figure S10).[13]



In a nitrogen-filled glove box, $B(C_6F_5)_3$ (56.3 mg, 0.11 mmol), (Xantphos)Cu(MeCN)PF_6 (91.2 mg, 0.11 mmol),[14] ethyl 3-(trimethylsilyl)propiolate (281.0 mg, 1.65 mmol) and mesitylene (132 mg, 1.10 mmol) were weighed in an oven-dried 7.0 mL vial and diluted to 2.20 mL with CD_2Cl_2 (**Stock Solution A**). In another oven-dried 7.0 mL vial, 4-methoxy-*N,N*,2,6-tetramethylaniline (436.9 mg, 2.44 mmol) was weighed and diluted to 1.30 mL with CD_2Cl_2 (**Stock Solution B**). In 5 oven-dried 7.0 mL vials, were added triphenylmethanol (39 mg, 0.15 mmol). To each oven-dried vial containing triphenylmethanol was added **Stock Solution A** (0.3 mL), **Stock Solution B** (0.04, 0.06, 0.08, 0.16 and 0.24 mL) and neat CD_2Cl_2 (0.28, 0.26, 0.24, 0.16 and 0.08 mL) to prepare reaction mixtures (total 0.62 mL) with 0.225 mmol ethyl 3-(trimethylsilyl)propiolate, 0.15 mmol triphenylmethanol, 10.0 mol% $B(C_6F_5)_3$, 10.0 mol% (Xantphos)Cu(MeCN)PF_6 and the following amounts of 4-methoxy-*N,N*,2,6-tetramethylaniline (0.50, 0.75, 1.00, 2.00 and 3.00 equiv). The reaction mixture was then transferred to a J-Young tube. After the J-Young tube was tightly capped with the Teflon plug, it was taken out of the glove box and ^{1}H NMR spectra were acquired at 60 °C (preheated) using a pre-acquisition delay in array mode with a spectrum taken every 30 seconds for the length of the experiment. The data were processed using MestReNova and peak integrations were normalized using mesitylene as the internal standard.

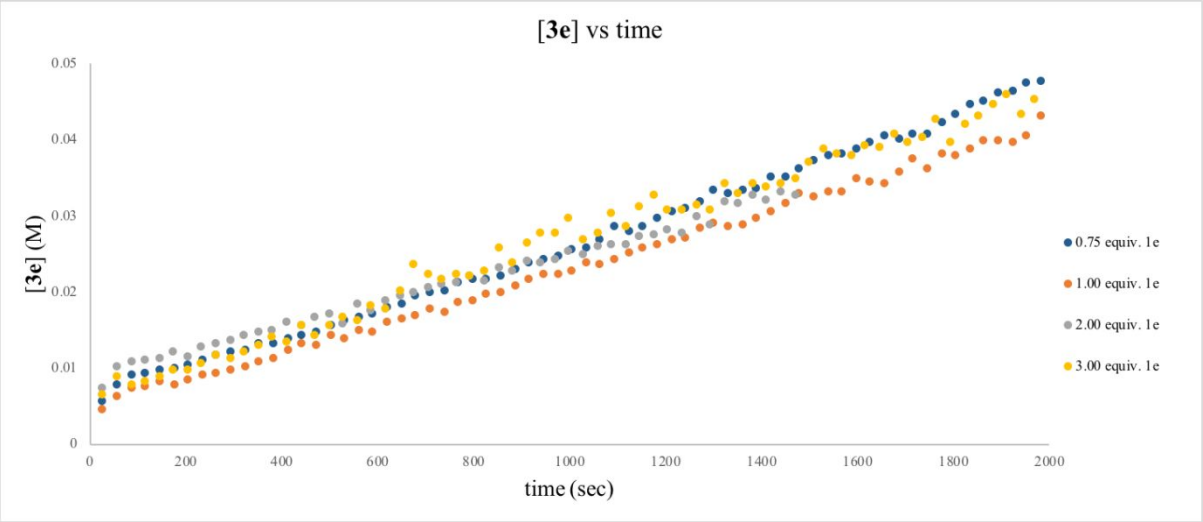


Figure S9. Monitoring the formation of **3e** using different concentrations of amine **1e**.

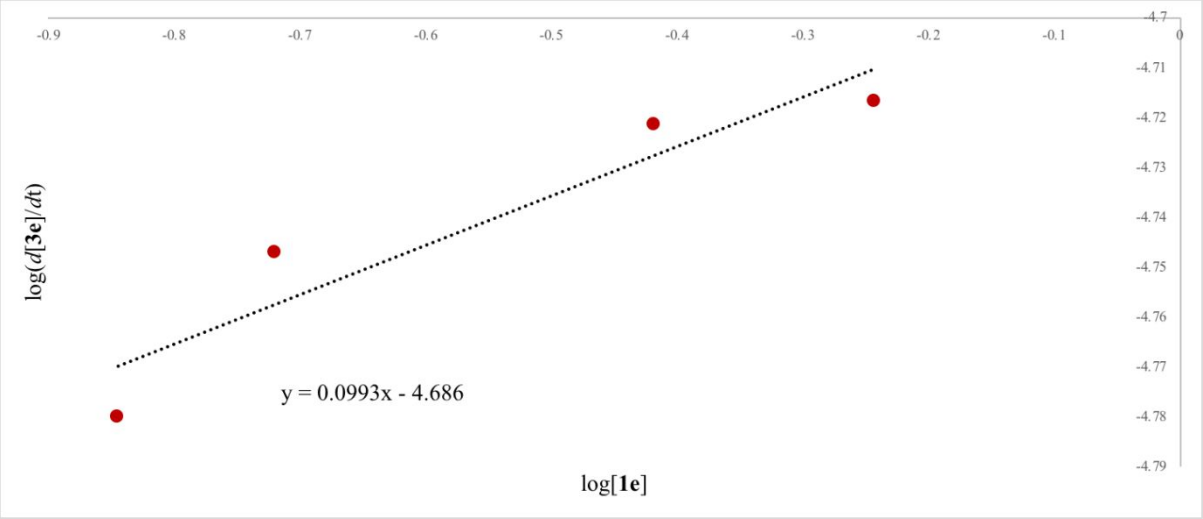


Figure S10. Log(rate) *vs* Log[**1e**] plot is employed to determine the initial reaction order for amine **1e.** The result suggests that there is 0-order dependency on the concentration of **1e**.

5.2 Parallel and Intermolecular Competition Kinetic Isotope Effect Experiments

5.2.1 Measurements of the Parallel Kinetic Isotope Effect

A parallel kinetic isotope effect study was conducted following the procedure for time course reaction monitoring by ^{1}H NMR (using internal standard). Kinetic analysis based on the initial rates of the product formation (Figure S11) demonstrates no kinetic isotope effect (k_H/k_D = 1.02 ± 0.02, average of 2 reactions) in the reaction between *N*-benzyl-4-methoxy-*N*,2,6-trimethylaniline **1g** or *N*-benzyl-4-methoxy-2,6-dimethyl-*N*-(methyl-d_3)aniline **1g-*d*** and ethyl 3-(trimethylsilyl)propiolate **2b**.[13,15]

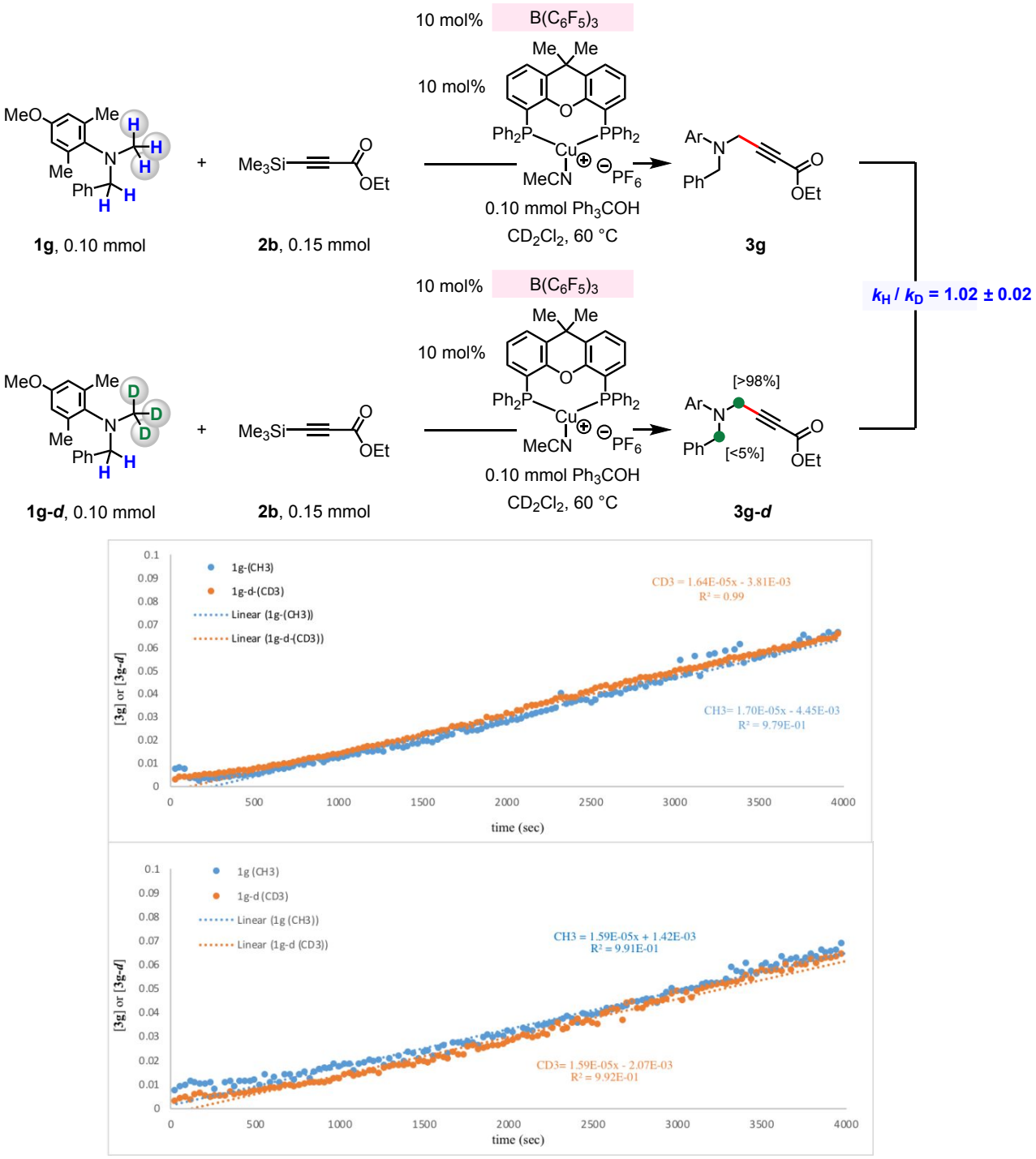


Figure S11. Parallel kinetic isotope effect experiments. The rate of the reaction is unaffected when amine **1g** or **1g-*d*** are employed as both have similar reaction time course plots. From the set of two parallel KIE experiments, the KIE value of 1.02 ± 0.02 was found.

Experimental Procedure for Measuring the Parallel Kinetic Isotope Effect

To an oven-dried 7.0 mL vial were added (Xantphos)Cu(MeCN)PF_6 (0.01 mmol), ethyl 3-(trimethylsilyl)propiolate **2b** (0.15 mmol), triphenylmethanol (0.10 mmol), amine **1g** (0.10 mmol) or amine **1g-*d*** (0.10 mmol), $B(C_6F_5)_3$ (0.01 mmol, 10 mol%), mesitylene (0.10 mmol). This mixture was then diluted to 0.40 mL with CD_2Cl_2 and transferred into a J-Young tube. After the J-Young tube was tightly capped with the Teflon plug, it was taken out of the glove box and ^{1}H NMR spectra were acquired at 60 °C (preheated) using a pre-acquisition delay in array mode with a spectrum taken every 30 seconds for the length of the experiment. The data were processed using MestReNova and peak integrations were normalized using mesitylene as the internal standard.

5.2.2 Intermolecular Competition Kinetic Isotope Effect Experiment

An intermolecular competition kinetic isotope effect study was conducted between *N*-benzyl-4-methoxy-*N*,2,6-trimethylaniline **1g** and *N*-benzyl-4-methoxy-2,6-dimethyl-*N*-(methyl-d_3)aniline **1g-*d***. Upon analysis of the unpurified reaction mixture by ^{1}H NMR spectroscopy, 27% conversion to both **3g** and **3g-*d*** was detected where 22% conversion of **3g** was detected. This ratio was further verified by studying the ^{2}H NMR spectrum; it revealed that approximately 5% of **3g-*d*** is formed.

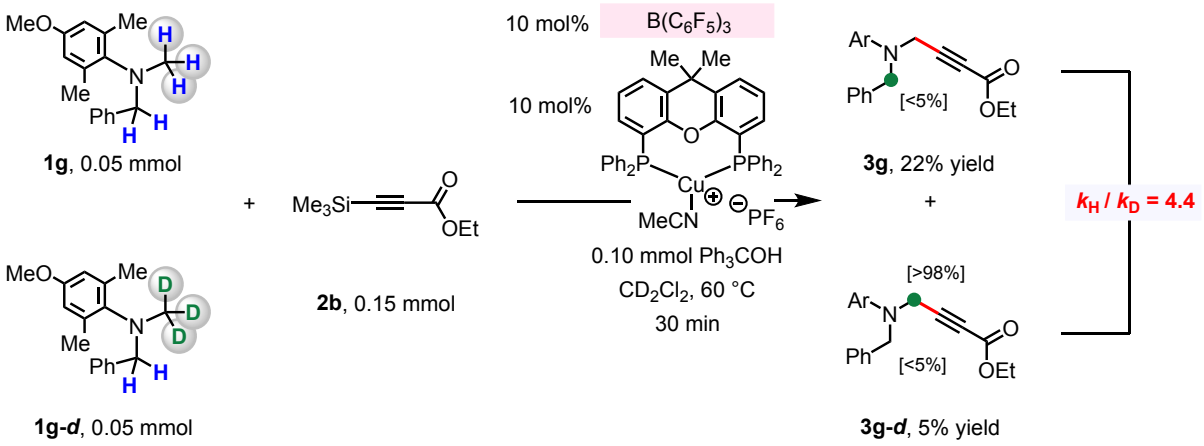


Figure S12. Intermolecular Competition Kinetic Isotope Effect Experiment. The result suggests hydride abstraction step is irreversible.

Experimental Procedure for Measuring the Intermolecular Competition Kinetic Isotope Effect

An oven-dried 7.0 mL vial equipped with a magnetic stir bar was used. To the vial were added (Xantphos)Cu(MeCN)PF_6 (0.01 mmol), ethyl 3-(trimethylsilyl)propiolate **2b** (0.15 mmol), triphenylmethanol (0.10 mmol), amine **1g** (0.05 mmol), amine **1g-*d*** (0.05 mmol), $B(C_6F_5)_3$ (0.01 mmol, 10 mol%), mesitylene (0.10 mmol), benzene-d_6 (0.05 mmol), and CD_2Cl_2 (0.40 mL). The reaction mixture was then transferred to a J-Young tube and was allowed to heat at 60 °C for 2 h. After 2 h, the reaction mixture was allowed to cool and NMR spectroscopy was obtained. The conversion values were determined by ^{1}H and ^{2}H NMR (Figure S13) analysis of the unpurified reaction mixture using mesitylene and benzene-d_6 as internal standards.

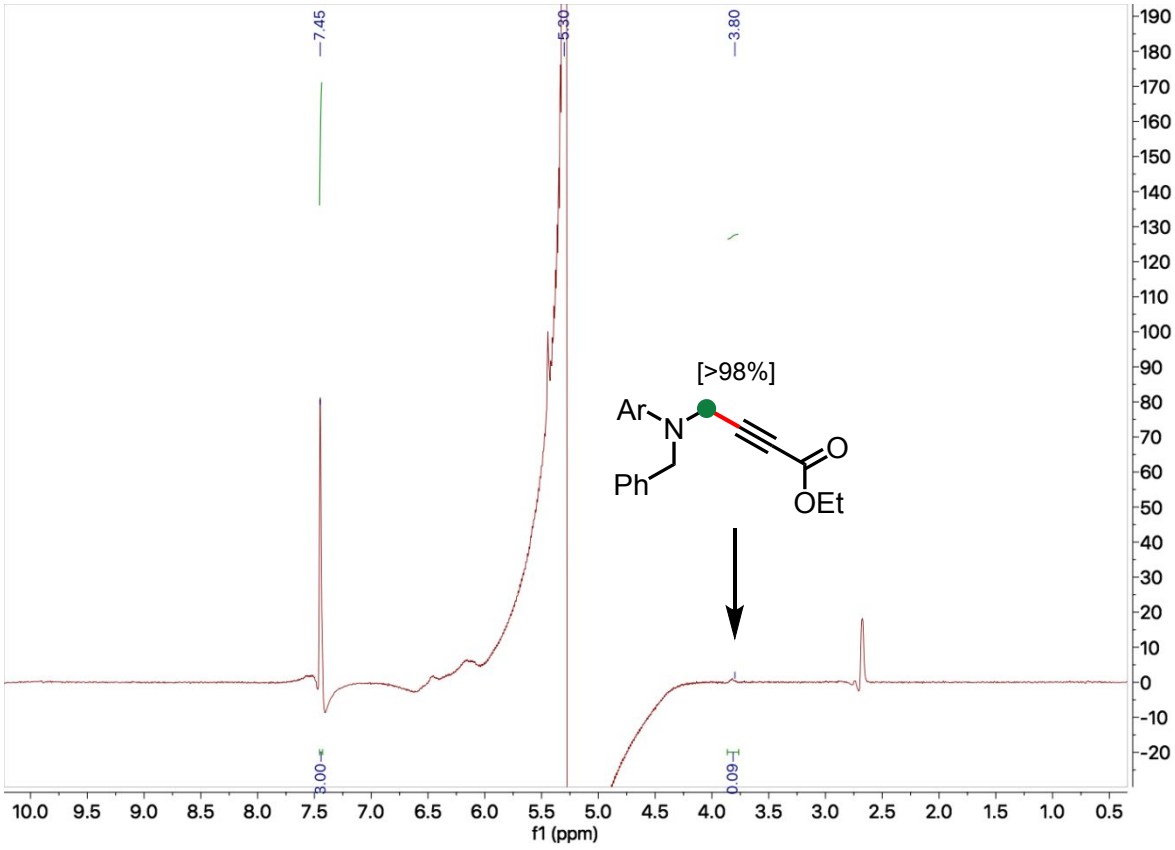


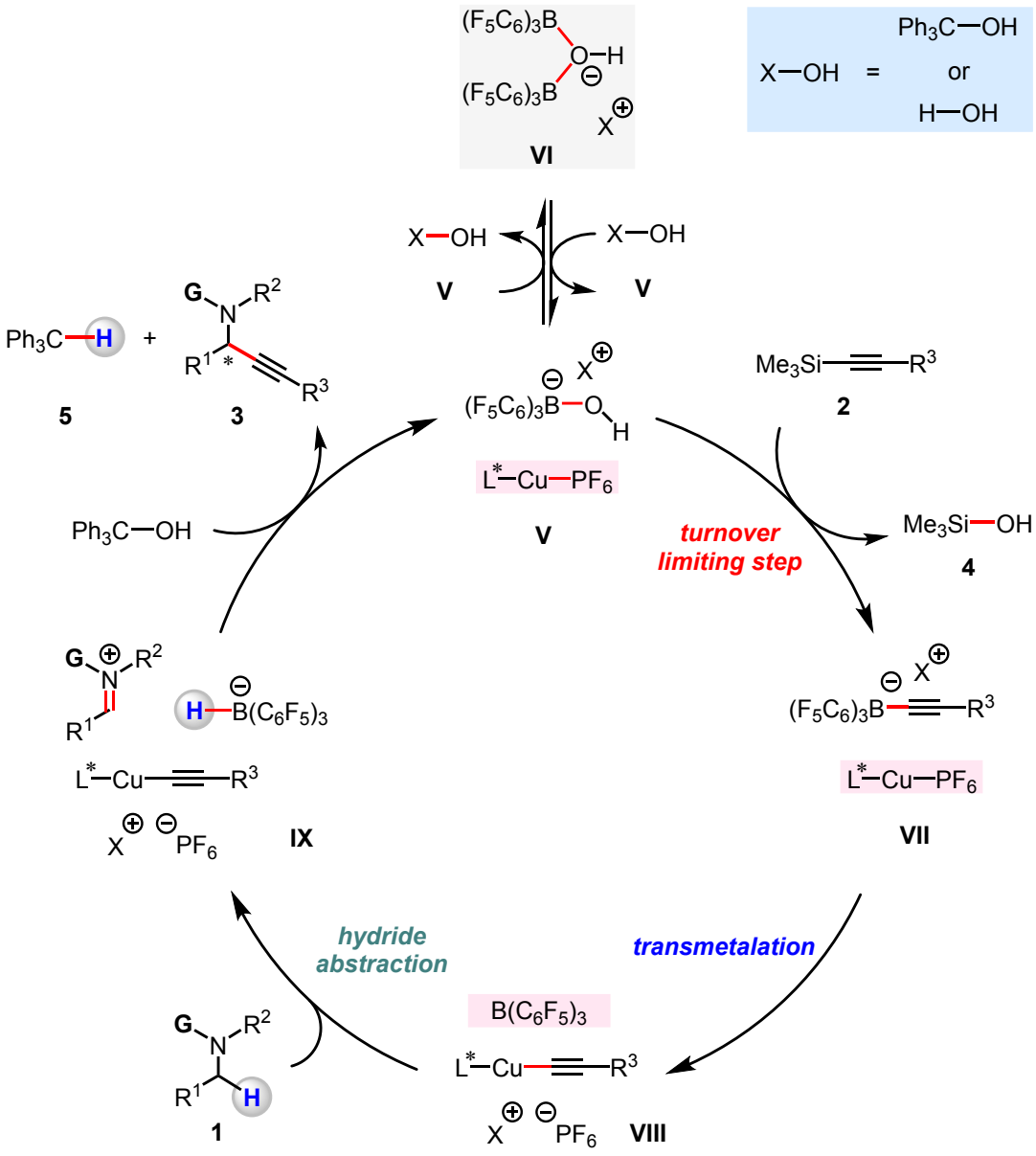
Figure S13: ^{2}H NMR spectrum for intermolecular competition kinetic isotope effect study.

5.3 NMR Experiments for Detection of Proposed Intermediates and the Resting State

5.3.1 Demonstration of Chemical Competency of the Proposed Intermediate VII

Based on the kinetic studies as described above, we propose that borate anion **V** (Scheme S2) reacts with trimethylsilylacetylene **2** to afford $[(F_5C_6)_3B–alkyne]^-$ $[X]^+$ (**VII**). To demonstrate the competency of **VII** as an intermediate to afford the propargylamine product **3**, we prepared a sample of $[(F_5C_6)_3B–C{\equiv}C–CO_2Et]^-[H–NR_3]^+$ (NR_3 = **1e**) following a procedure reported previously in the literature.[16]

Scheme S2. Proposed Mechanism



Experimental Procedure for the Preparation of $[(F_5C_6)_3B–C\equiv C–CO_2Et]^-[H–1e]^+$

An oven-dried 7.0 mL vial equipped with a magnetic stir bar was used. To the vial were added ethyl propiolate (0.10 mmol), amine **1e** (0.15 mmol), $B(C_6F_5)_3$ (0.10 mmol, 100 mol%), mesitylene (0.10 mmol), trifluorotoluene (0.10 mmol) and CD_2Cl_2 (0.60 mL) under nitrogen atmosphere. The mixture was then transferred to a J-Young tube and NMR spectroscopy was obtained. Analysis of the ^1H NMR spectra of unpurified mixture with mesitylene as the internal standard revealed that ethyl propiloate was fully consumed (Figure S14) and $[(F_5C_6)_3B–C\equiv C–CO_2Et]^-[H–1e]^+$ (**VII)** was formed (Figure S15) which was indicated by a characteristic sharp singlet at -21.5 ppm on ^{11}B NMR (Figure S16).[16]

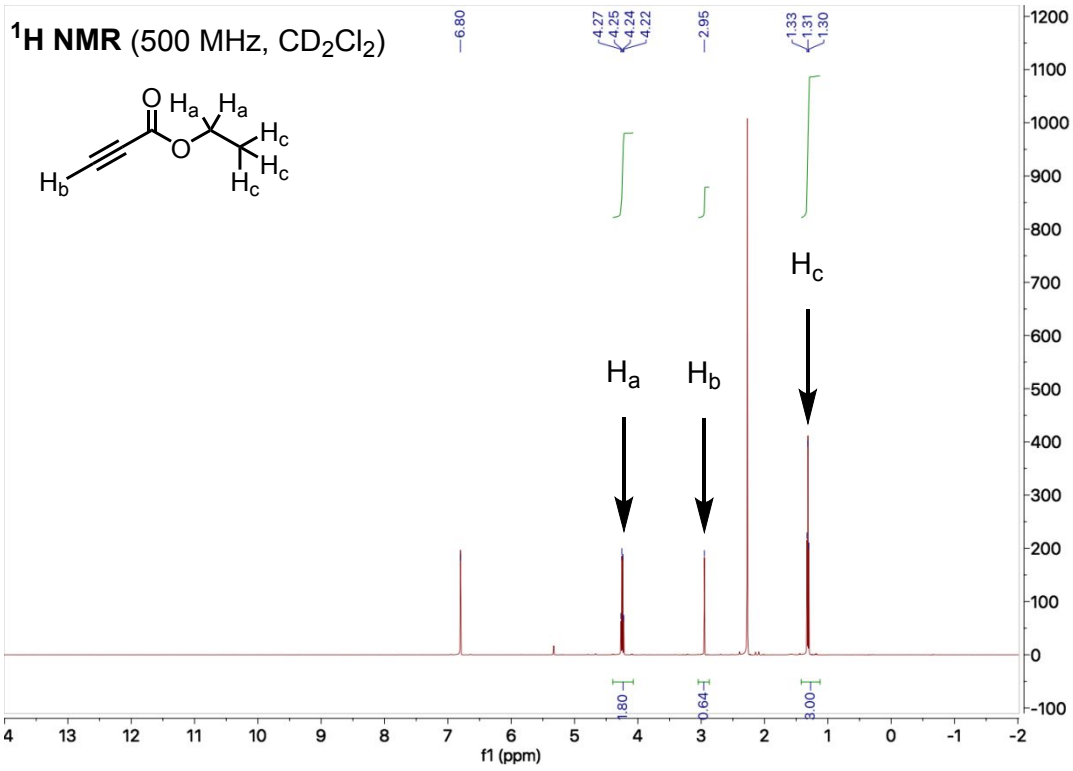


Figure S14. ^1H NMR spectrum of ethyl propiolate.

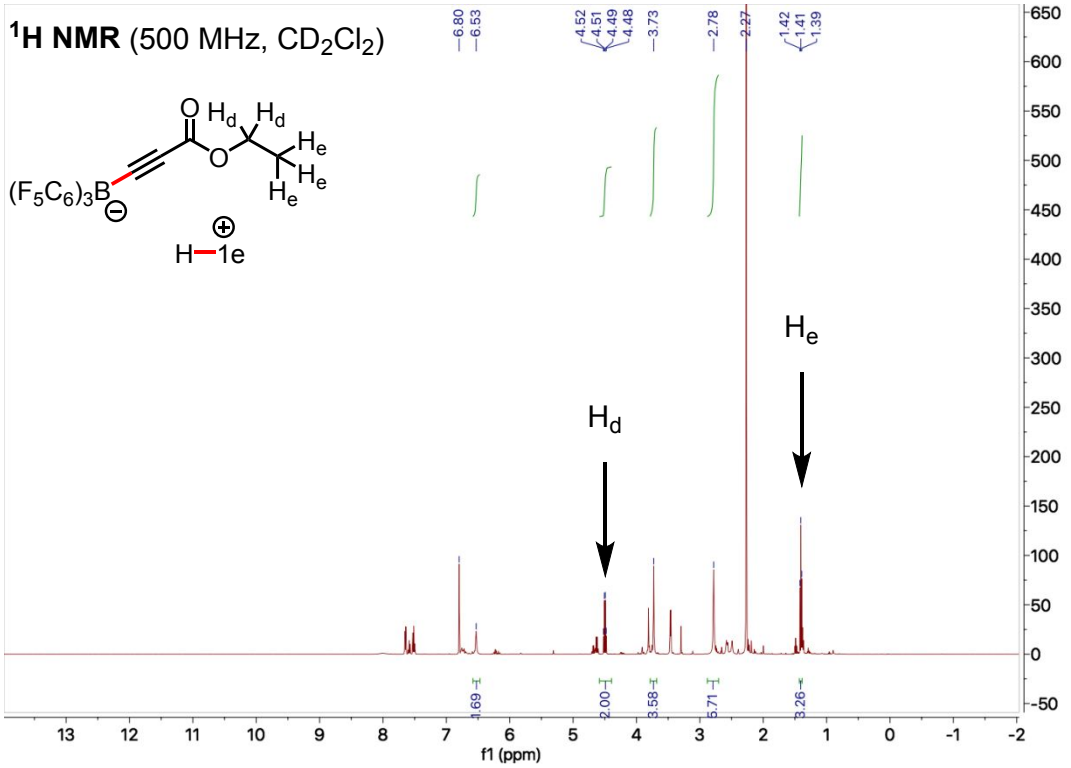


Figure S15. ^{1}H NMR spectrum of unpurified reaction mixture of $[(F_5C_6)_3B–C{\equiv}C–CO_2Et]^-[H–1e]^+$.

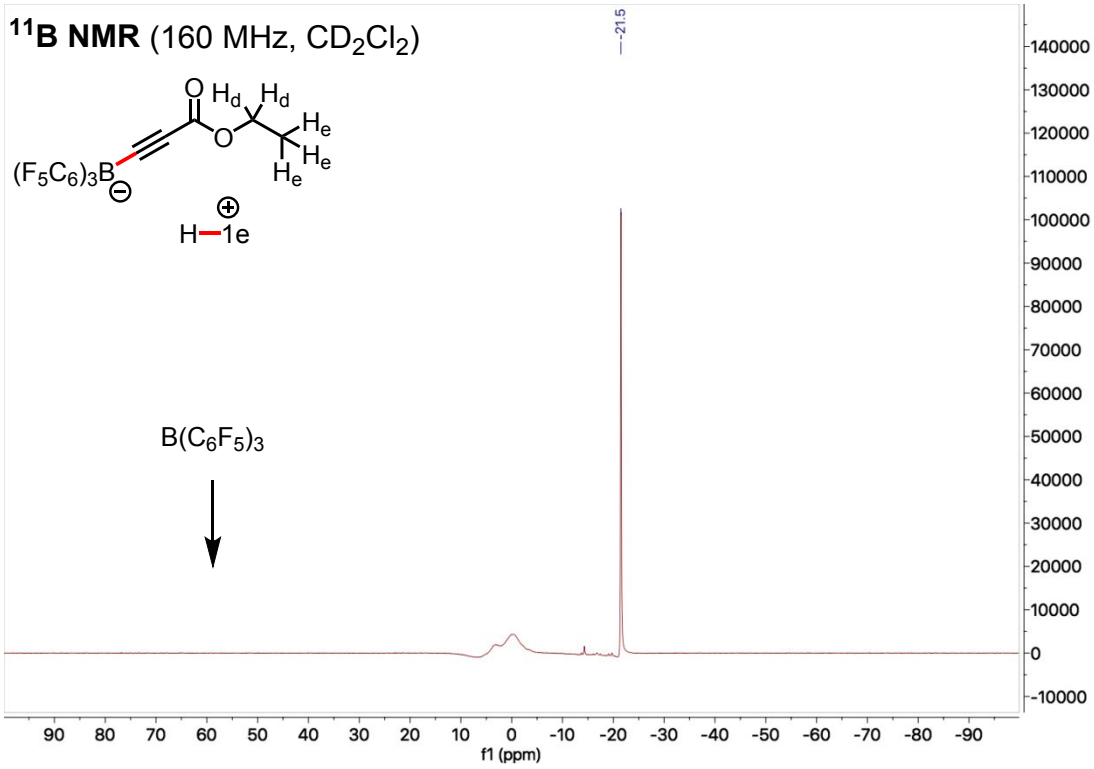


Figure S16. ^{11}B NMR spectrum of unpurified reaction mixture of $[(F_5C_6)_3B–C{\equiv}C–CO_2Et]^-[H–1e]^+$.

To this unpurified reaction mixture was added (Xantphos)Cu(MeCN)PF_6 (0.10 mmol). The reaction mixture was allowed to stir at 60 °C for 1 h. Then, the reaction mixture was cooled down to 22 °C and a ^{1}H NMR spectrum was obtained (Figure 17). Analysis of the ^{1}H spectrum of unpurified mixtures with mesitylene as the internal standard revealed that **3e** was formed in 24% under this reaction conditions, thereby demonstrating competency of the proposed intermediate **VII** in the alkyne incorporation process.

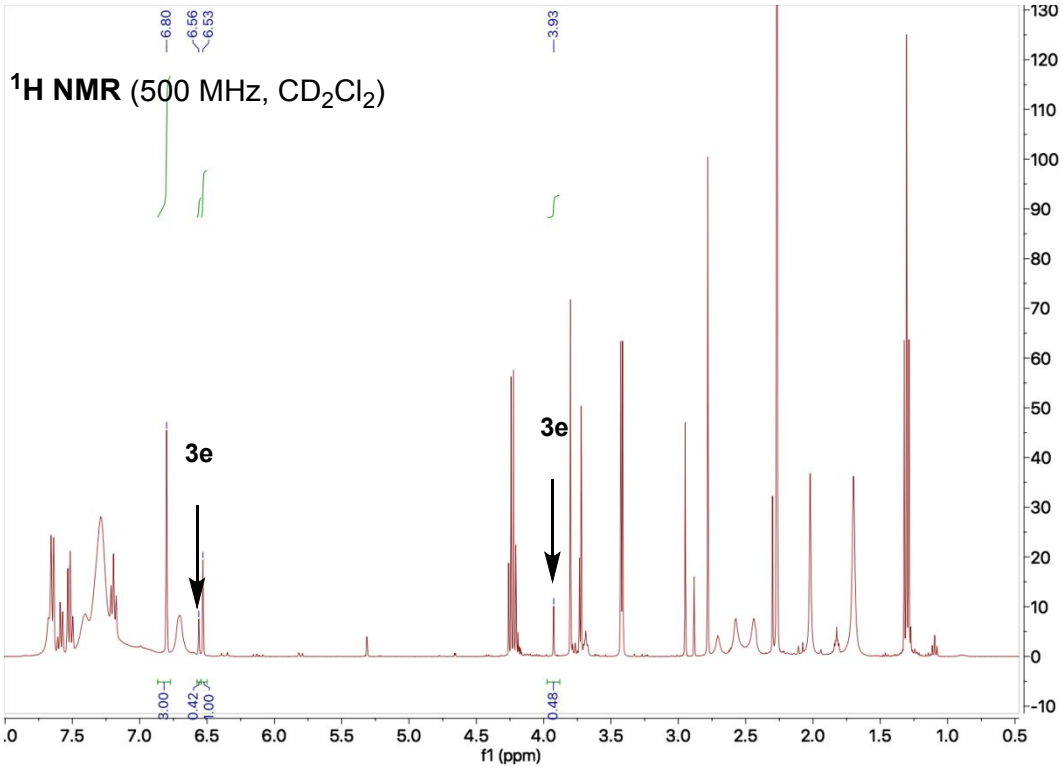
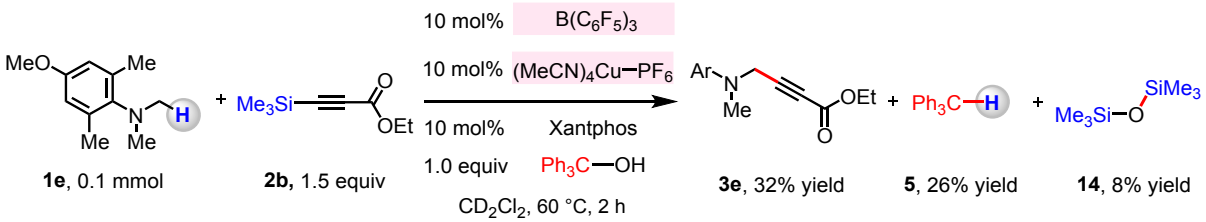


Figure S17. ^{1}H NMR spectrum of unpurified reaction mixture of **VII** and 100 mol % of (Xantphos)Cu(MeCN)PF_6.

5.3.2 NMR Experiments for Detection of Byproducts

The reaction between 4-methoxy-*N,N*,2,6-tetramethylaniline **1e** and ethyl 3-(trimethylsilyl)propiolate **2b** was monitored by ^{1}H NMR spectroscopy (Figure S18–S20). This study revealed that Ph_3C–H **5** and Me_3Si–O–$SiMe_3$ **14** are the stable byproducts of this α-alkynylation reaction (Scheme S2 and S3).

Scheme S3. Formation of Stable Byproducts **5** and **14**



Experimental Procedure for the α-Alkynylation of 4-Methoxy-*N,N*,2,6-tetramethylaniline and Ethyl 3-(trimethylsilyl)propiolate

An oven-dried 7.0 mL vial equipped with a magnetic stir bar was used. To the vial were added $Cu(MeCN)_4PF_6$ (0.010 mmol), Xantphos (0.01 mmol), and CD_2Cl_2 (0.2 mL) under nitrogen atmosphere. The mixture was allowed to stir for 20 minutes at 22 °C, then ethyl 3-(trimethylsilyl)propiolate **2b** (0.15 mmol), triphenylmethanol (0.1 mmol), amine **1e** (0.10 mmol), mesitylene (0.10 mmol), $B(C_6F_5)_3$ (0.01 mmol, 10 mol%), and CD_2Cl_2 (0.20 mL) were added to the vial. The reaction mixture was then transferred to a J-Young tube and was allowed to heat at 60 °C for 1 h. After 1 h, the reaction mixture was allowed to cool and NMR spectroscopy was obtained. Upon analysis of the ^{1}H NMR of the unpurified reaction mixture, triphenylmethane **5** and 1,1,1,3,3,3-hexamethyldisiloxane **14** was detected (Figure S18).

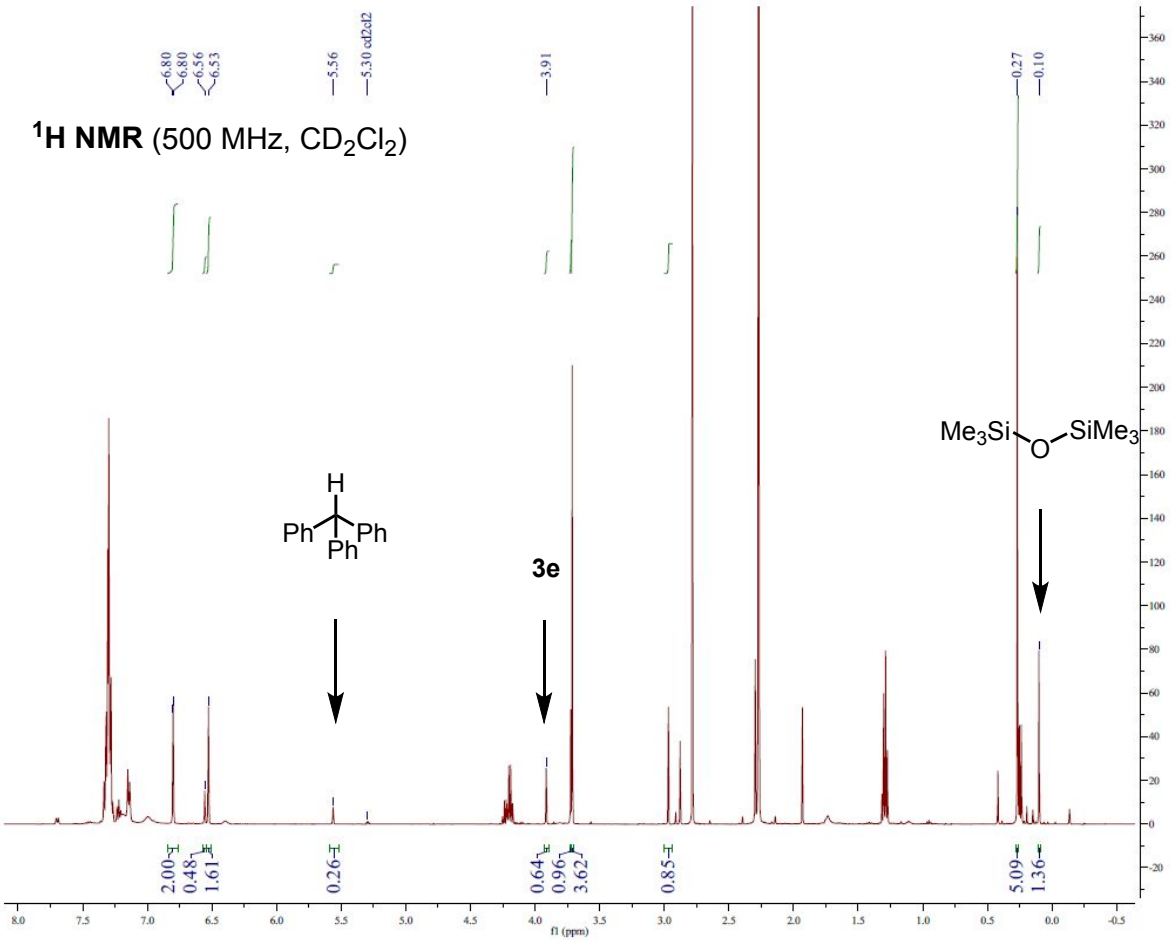


Figure S18. ^{1}H NMR spectrum of unpurified reaction mixture of **1e** and **2b** under α-alkynylation condition.

To this unpurified reaction mixture was added $Me_3Si–O–SiMe_3$ **14** obtained from a commercial source (Figure S19).

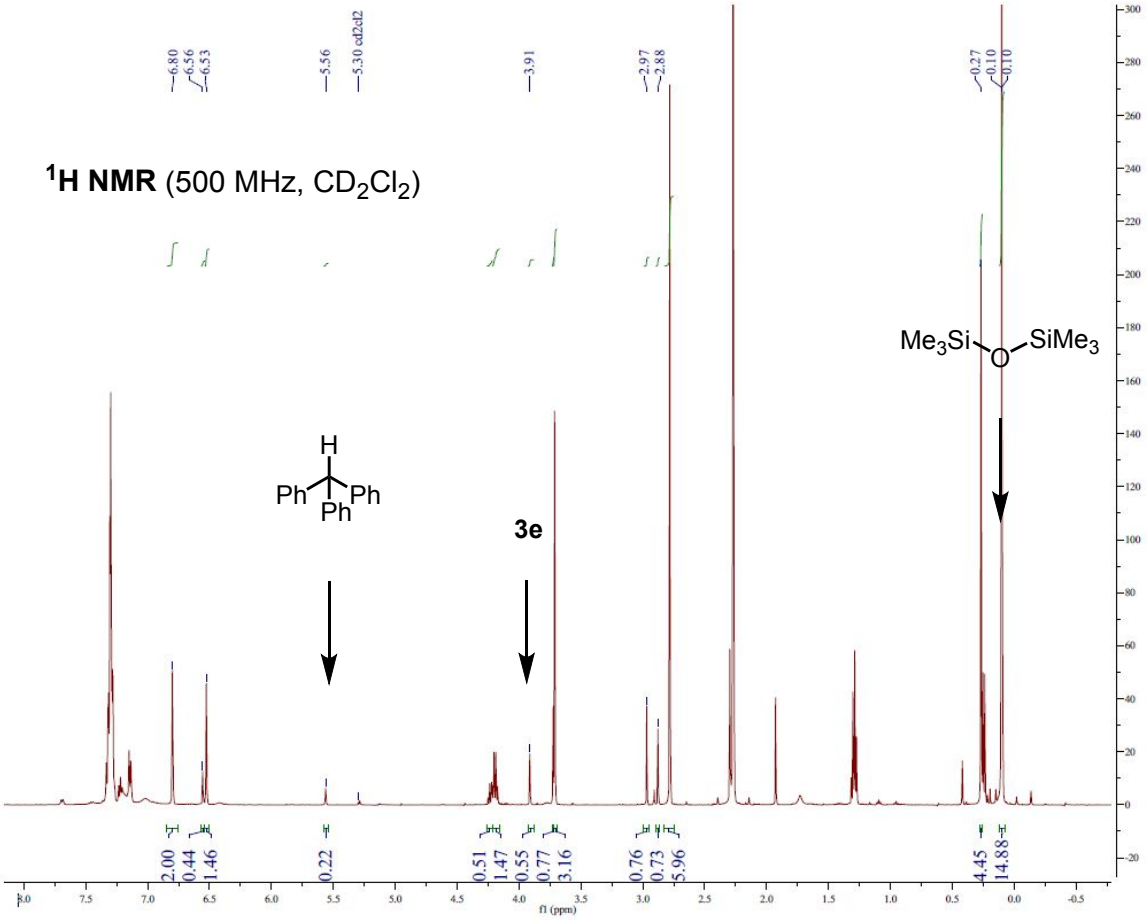


Figure S19. ^{1}H NMR spectrum of the unpurified reaction mixture of **1e** and **2b** under α-alkynylation conditions, where $Me_3Si–O–SiMe_3$ **14** was added to the cooled reaction mixture after 1 h.

In order to determine the fate of the hydride abstracted from the amine substrates by $B(C_6F_5)_3$, we carried out the transformation between 4-methoxy-2,6-dimethyl-*N,N*-bis(methyl-d_3)aniline **1e-*d*** and ethyl 3-(trimethylsilyl)propiolate **2b** in the presence of $Ph_3C–OH$ (Figure 20). Upon analysis of the ^{1}H NMR of the unpurified product mixture, it was found that deuteride is trapped by in situ generated Ph_3C^+ to produce (methanetriyl-*d*)tribenzene **5-*d*** (Figure S20). The yield of **3e-*d***, **5-*d*** and **14** were determined based on the amount of mesitylene added as an internal standard.

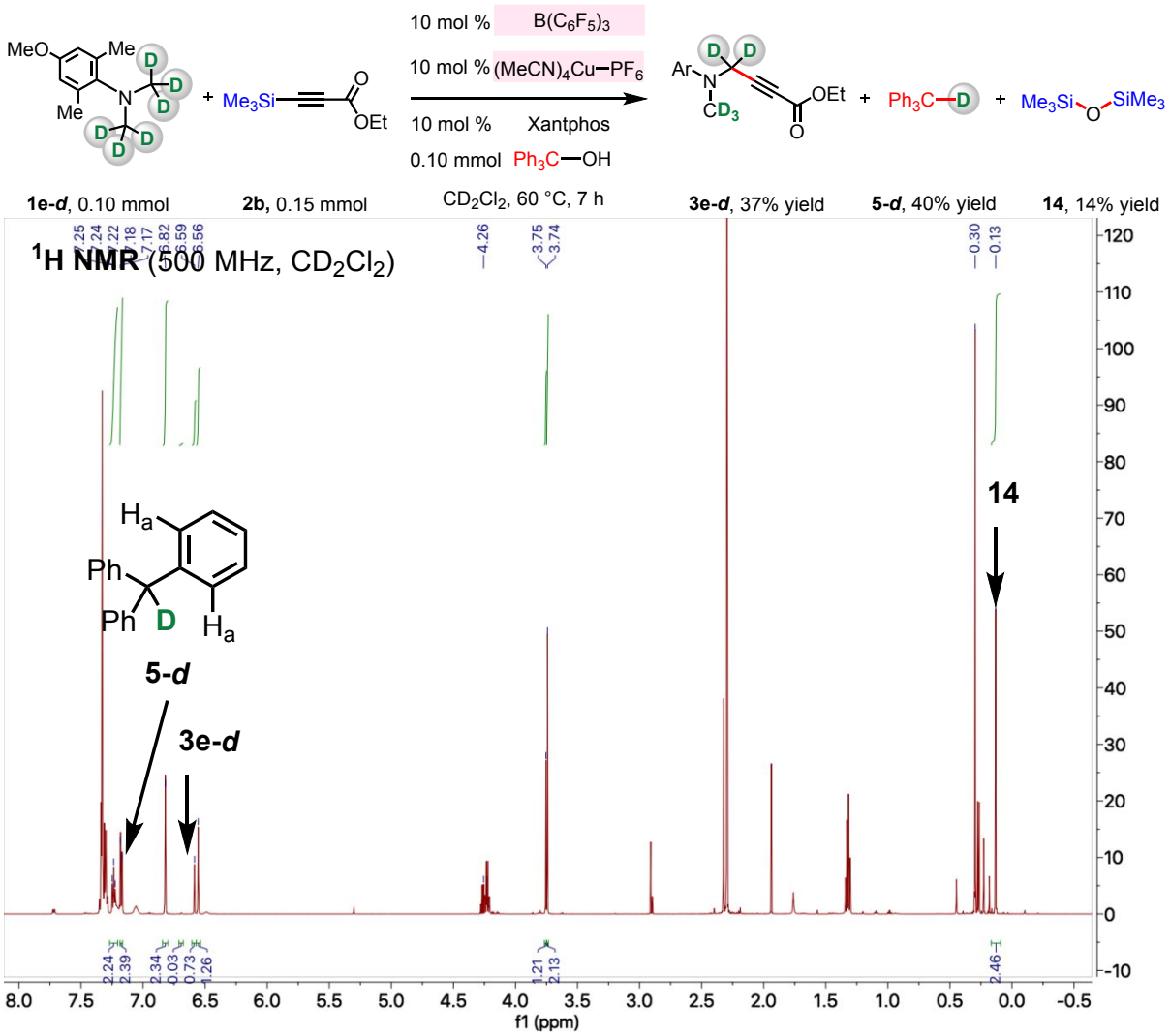


Figure S20. ^{1}H NMR spectrum of unpurified reaction mixture of **1e-*d*** and **2b** under *α*-alkynylation conditions.

5.3.3 NMR Experiments for the Detection of the Resting State Complex Containing $B(C_6F_5)_3$

We embarked on a study to identify the structure of a resting state complex which contains $B(C_6F_5)_3$. Previously, the groups of Pinkas and Resconi have independently reported that a borate anion $[(C_6F_5)_3B(\mu\text{-}OH)B(C_6F_5)_3]^-$ can be formed through the reaction of $B(C_6F_5)_3$ and Ph_3COH,[17] and by reacting $B(C_6F_5)_3$, H_2O and an amine.[18] Since the $B(C_6F_5)_3$/organocopper co-catalyzed transformation of C–H bonds was found to have a *0.5 order dependency* with respect to the concentration of $B(C_6F_5)_3$, we surmised that $[(C_6F_5)_3B(\mu\text{-}OH)B(C_6F_5)_3]^-$ containing two molecules of $B(C_6F_5)_3$ could be its resting state.

We first acquired a ^{1}H NMR spectrum of a sample containing $B(C_6F_5)_3$ and Ph_3COH in CD_2Cl_2 (Figure S21) and compared that to the spectra reported by Pinkas.[17] Based on this analysis, we concluded that $[(F_5C_6)_3B(\mu\text{-}OH)B(C_6F_5)_3]^-[CPh_3]^+$ is generated.

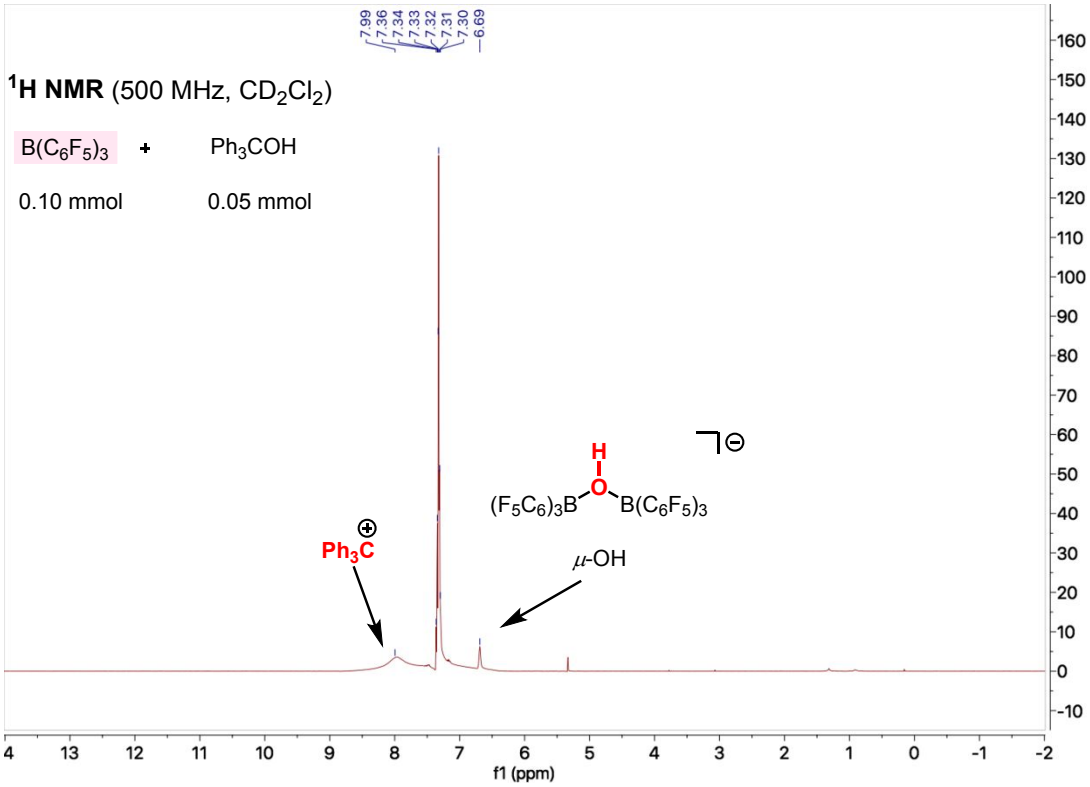


Figure S21. ^{1}H NMR of $B(C_6F_5)_3$ and Ph_3COH in CD_2Cl_2.

Next, we obtained the ^{11}B and/or ^{19}F NMR spectra of:

Figures S22–S23: the sample containing $[(F_5C_6)_3B(\mu\text{-}OH)B(C_6F_5)_3]^-[CPh_3]^+$ prepared as described above,

and compared those to the spectra we obtained for:

Figures S24-25: $B(C_6F_5)_3$ only

Figures S26-27: a mixture of $B(C_6F_5)_3$, [Cu(Xantphos)(MeCN)][PF_6], 4-methoxy-*N*,*N*,2,6-tetramethylaniline **1e**, 3-(triemthylsilyl)propiolate **2b**, Ph_3COH in CD_2Cl_2 at 22 °C, and

Figure S28: a mixture of $B(C_6F_5)_3$, [Cu(Xantphos)(MeCN)][PF_6], 4-methoxy-*N*,*N*,2,6-tetramethylaniline **1e**, 3-(triemthylsilyl)propiolate **2b**, Ph_3COH in CD_2Cl_2 at 60 °C.

The analyses of Figures S26–S28 revealed that there is no free $B(C_6F_5)_3$ remaining in the reaction mixture (characteristic peak at 58.7 ppm corresponding to $B(C_6F_5)_3$ in Figure 24 is not observed in Figure S26).

The comparison of ^{19}F NMR spectra for the authentic sample of $[(F_5C_6)_3B(\mu\text{-}OH)B(C_6F_5)_3]^-$

$[CPh_3]^+$ (Figure 23) with those acquired for the actual reaction mixture (Figures S27 and S28) revealed that there are consistent peaks at −135.94, −160.88 and −165.53 ppm.

Furthermore, the comparison of ^{11}B NMR spectrum we acquired for the sample of $[(F_5C_6)_3B(\mu\text{-}OH)B(C_6F_5)_3]^-[CPh_3]^+$ (Figure S22) with the one for the reaction mixture (Figure 26) also showed that there are common peaks at 0.8 and −3.7 ppm.

These results serve as evidences to support the formation of $[(F_5C_6)_3B(\mu\text{-}OH)B(C_6F_5)_3]^-$ anion under the reaction conditions for $B(C_6F_5)_3$/[Cu(Xantphos)(MeCN)][PF_6] co-catalyzed C–H functionalization.

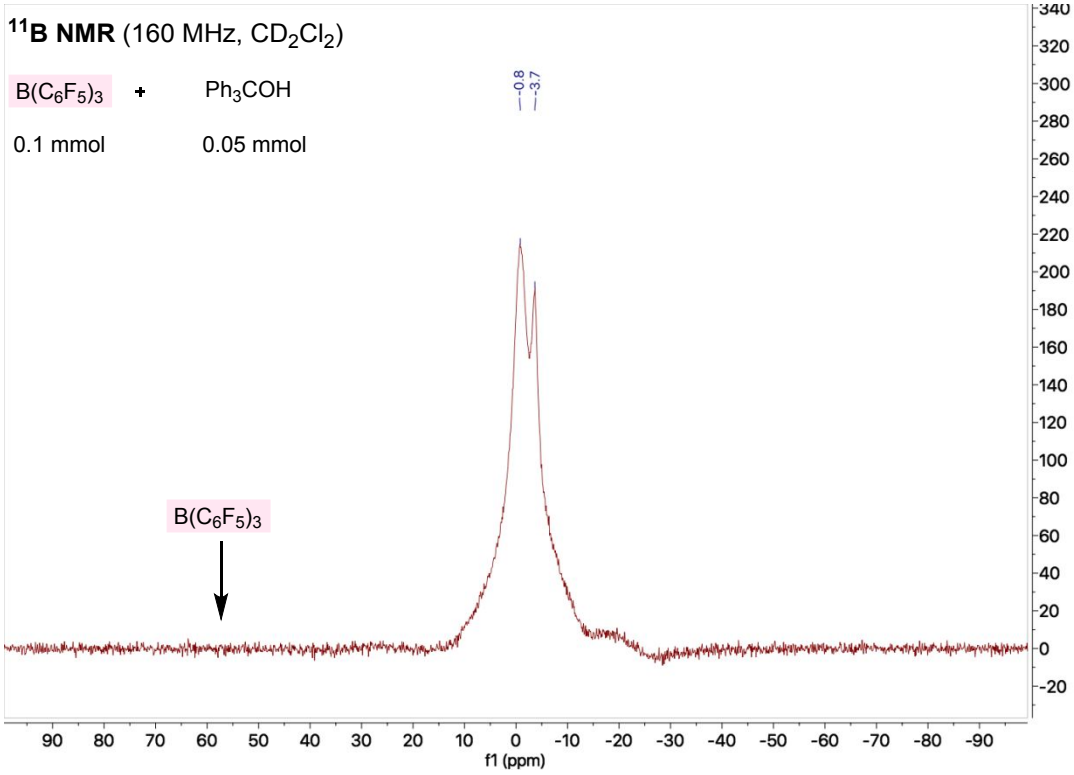


Figure S22. ^{11}B NMR spectrum of a sample containing $B(C_6F_5)_3$ and Ph_3COH in CD_2Cl_2

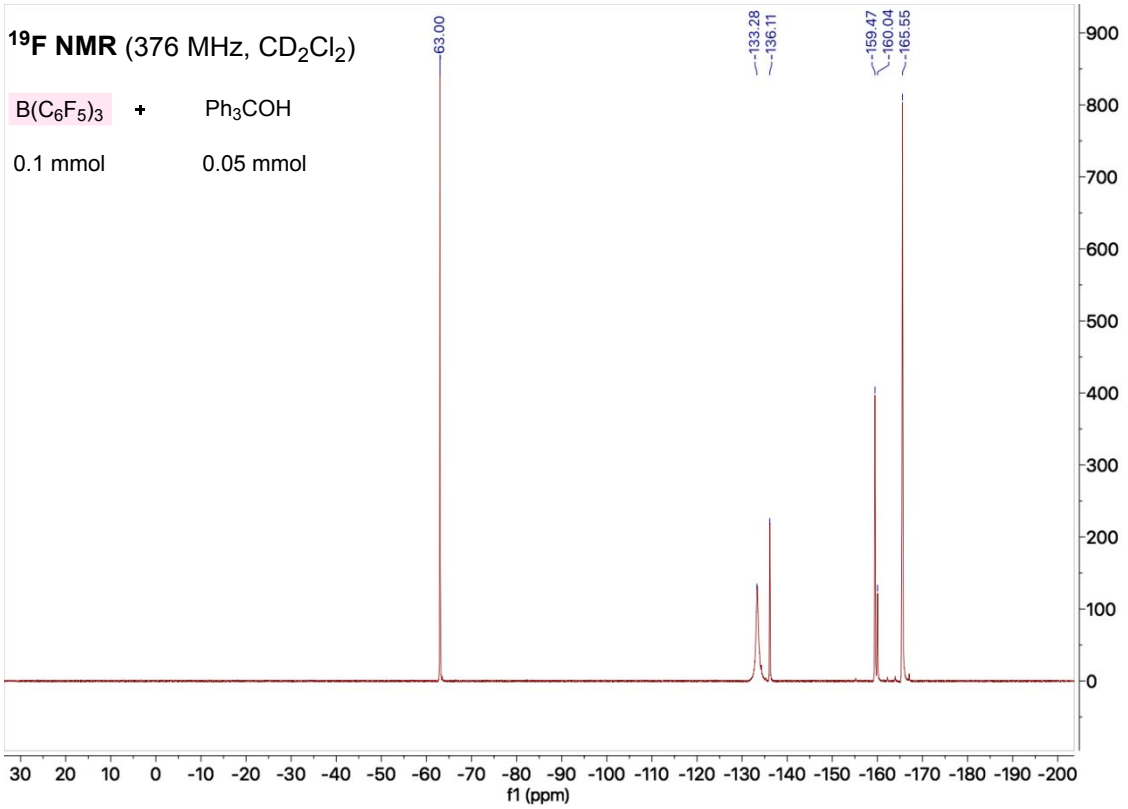


Figure S23. ^{19}F NMR spectrum of a sample containing $B(C_6F_5)_3$ and Ph_3COH in CD_2Cl_2.

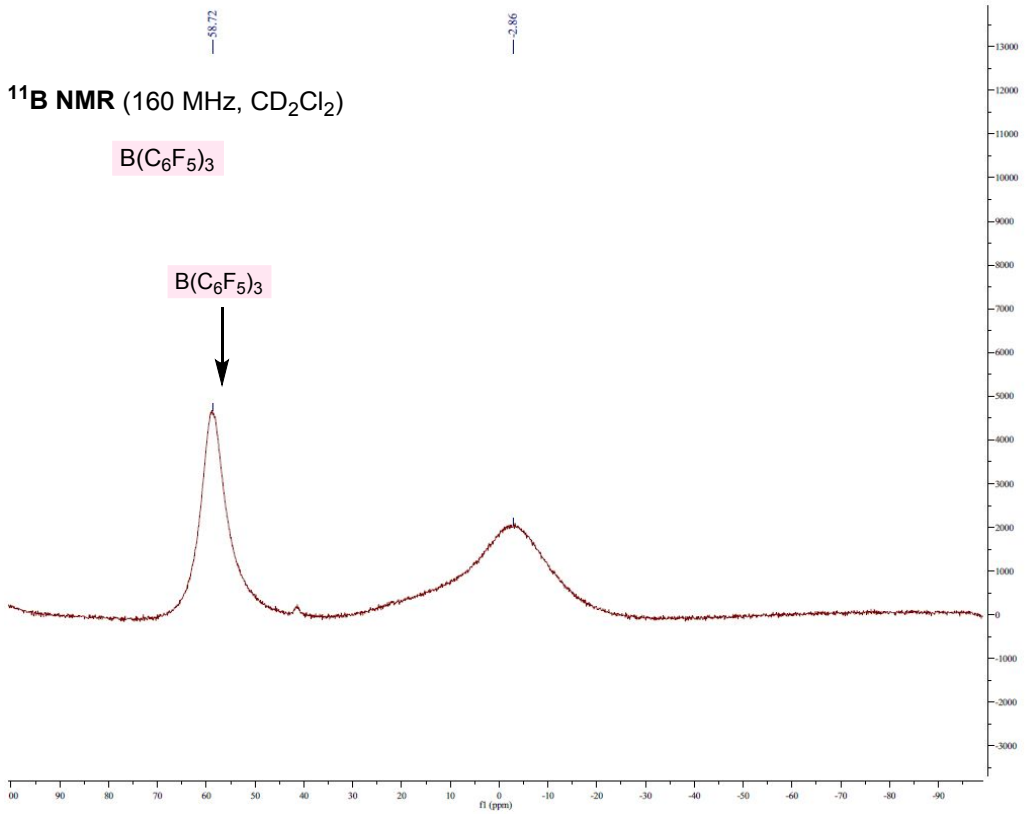


Figure S24. ^{11}B NMR spectrum of $B(C_6F_5)_3$ in CD_2Cl_2.

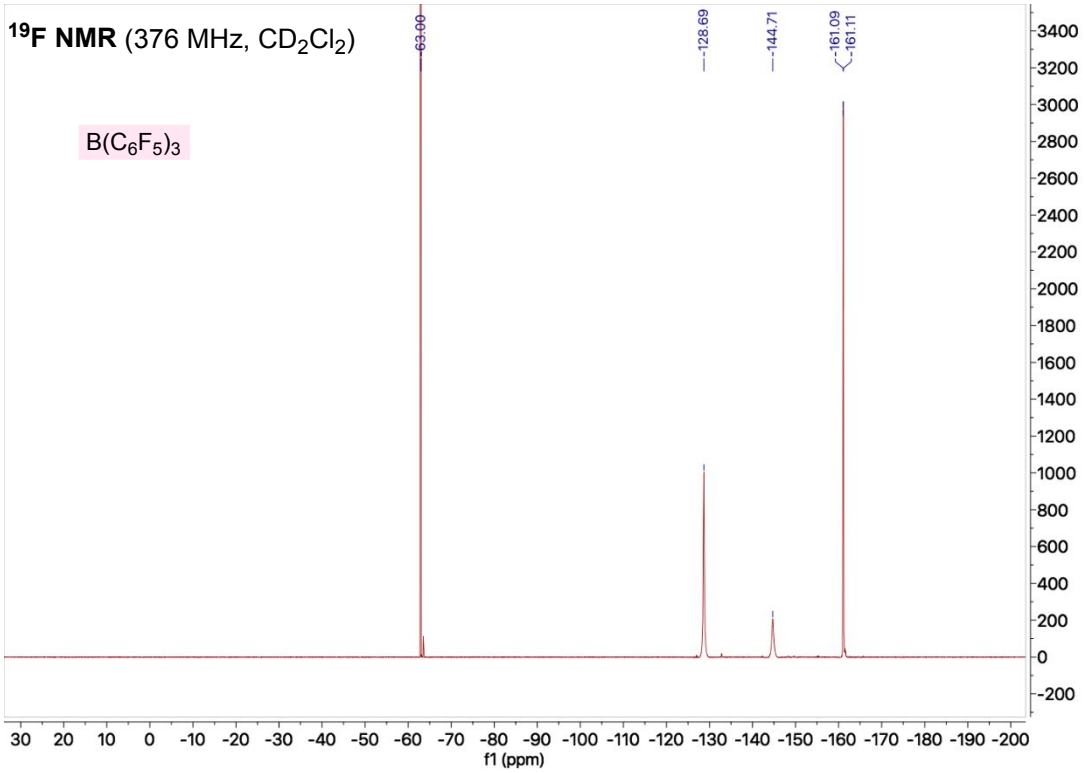


Figure S25. ^{19}F NMR spectrum of $B(C_6F_5)_3$ in CD_2Cl_2.

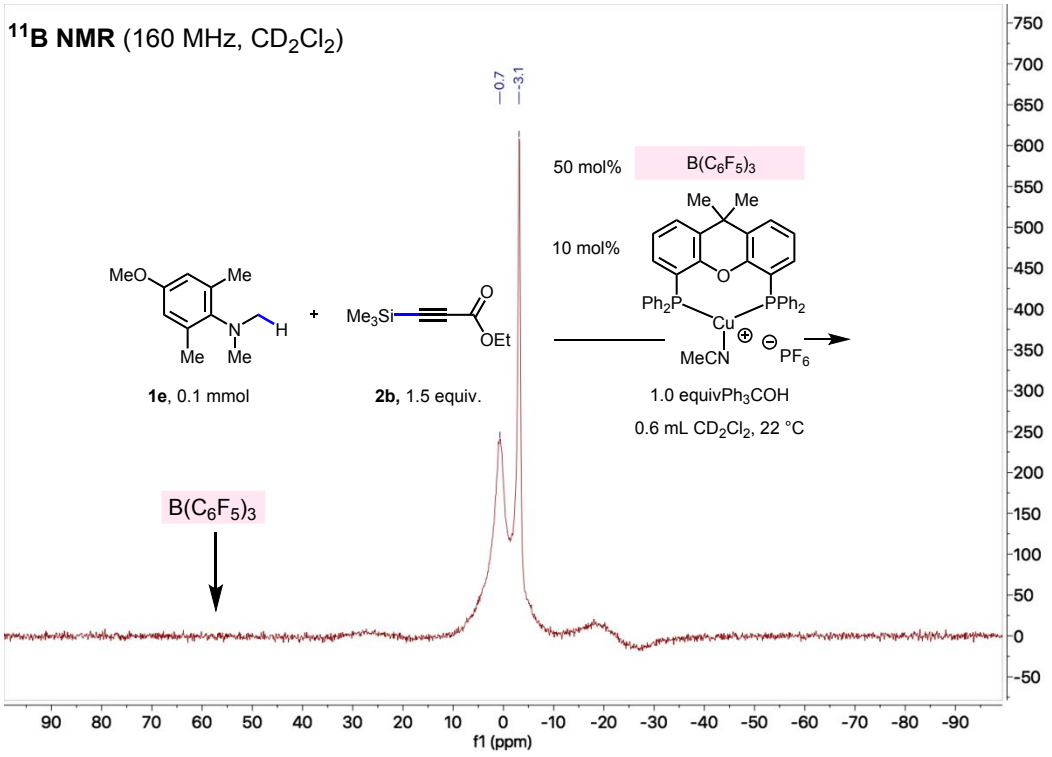


Figure S26. ^{11}B NMR spectrum of α-alkynylation reaction between **1e** and **2b** with 50 mol% $B(C_6F_5)_3$ at 22 °C.

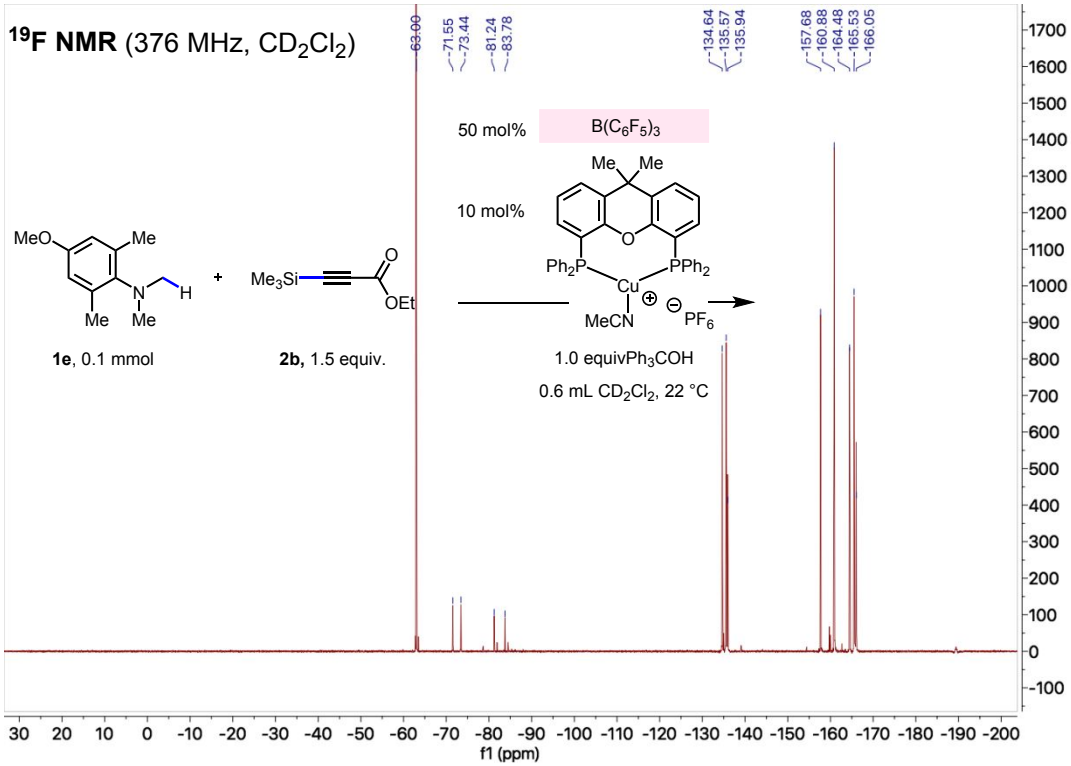


Figure S27. ^{19}F NMR spectrum of α-alkynylation reaction of amine **1e** with 50 mol% $B(C_6F_5)_3$ at 22 °C.

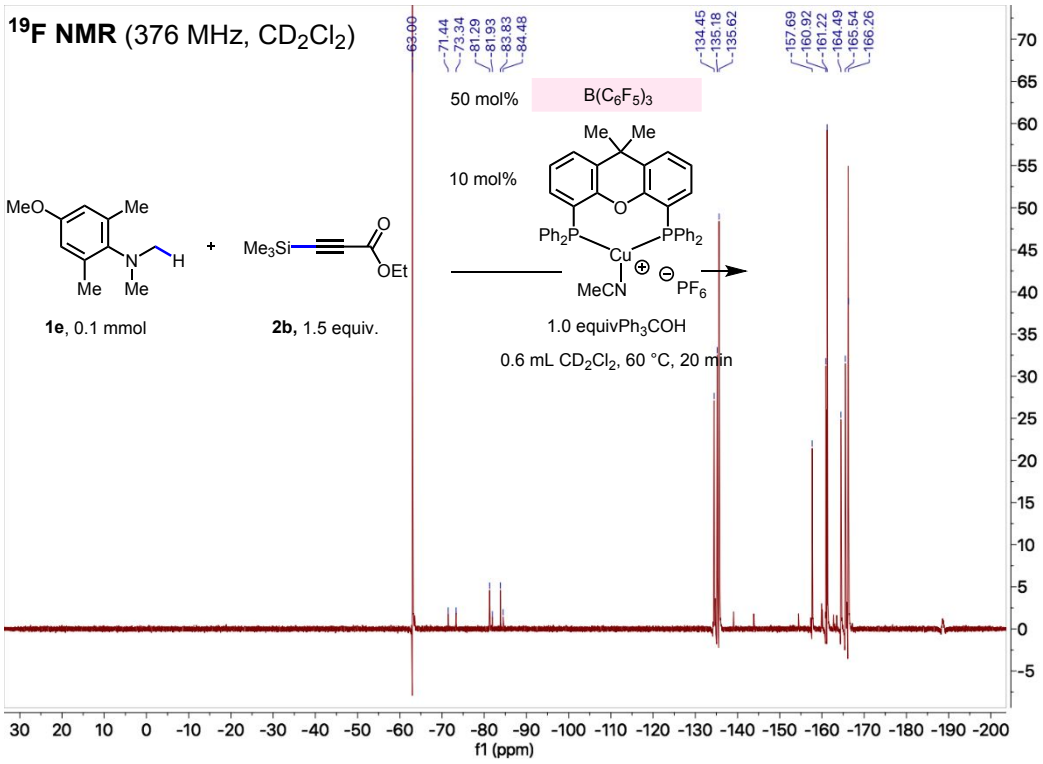


Figure S28. ^{19}F NMR spectrum of α-alkynylation reaction between **1e** and **2b** using 50 mol% $B(C_6F_5)_3$ at 22 °C.

As reported by the group of Resconi, the reaction of $B(C_6F_5)_3$ and H_2O may result in the formation of $[(F_5C_6)_3B(\mu\text{-}OH)B(C_6F_5)_3]^-[H{-}NR_3]^+$.[18] To probe if this can occur under our reaction conditions, we acquired the following spectra:

Figures S29: ^{11}B spectrum for a mixture of $B(C_6F_5)_3$, H_2O and **1e**, and

Figures S26: ^{11}B NMR spectra for a mixture of $B(C_6F_5)_3$, [Cu(Xantphos)(MeCN)][PF_6], 4-methoxy-*N*,*N*,2,6-tetramethylaniline **1e**, 3-(triemthylsilyl)propiolate **2b**, Ph_3COH in CD_2Cl_2 at 22 °C.

Resconi *et al.*[18] reported that ^{11}B NMR spectrum for $[(F_5C_6)_3B(\mu\text{-}OH)B(C_6F_5)_3]^-$ contains a characteristic singlet peak at –1 ppm (298 K). The ^{11}B NMR spectra we acquired (Figures S26 and S29) both possess a singlet at – 3.7 ppm, therefore suggesting that the formation of $[(F_5C_6)_3B(\mu\text{-}OH)B(C_6F_5)_3]^-$ anion is possible.

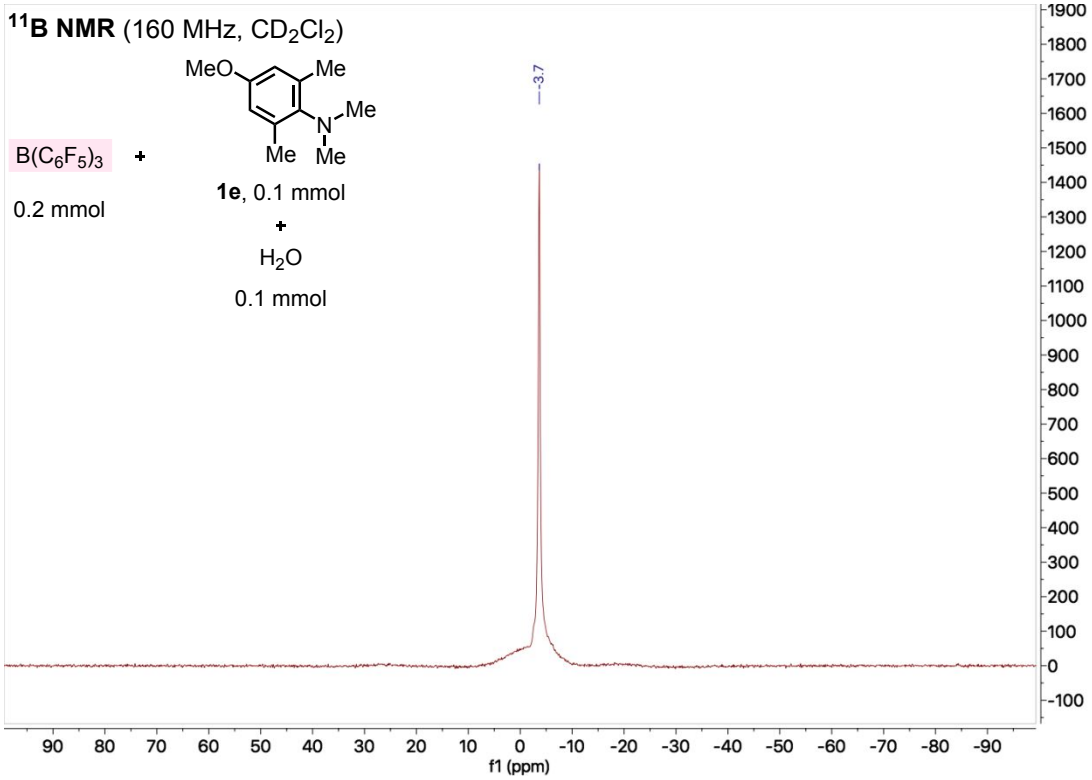


Figure S29. ^{11}B NMR spectrum of a sample containing $B(C_6F_5)_3$, H_2O and amine **1e** in CD_2Cl_2.

As reported by the group of Basset,[19] a tertiary amine and $B(C_6F_5)_3$ could form an ionic complex containing an iminium ion and $[(F_5C_6)_3B{-}H]^-$. In the ^{11}B NMR spectrum, $[(F_5C_6)_3B{-}H]^-$ has been reported to have a characteristic peak at –23.6 ppm.[19] To probe if the related ion pairs are formed in our system, we prepared the following sample and obtained their ^1H, ^{11}B and ^{19}F NMR spectra:

Figures S30-32: a reaction mixture containing 0.1 mmol $B(C_6F_5)_3$ and 0.1 mmol of 4-methoxy-*N,N*,2,6-tetramethylaniline **1e** in CD_2Cl_2.

Figure S33: 4-methoxy-*N,N*,2,6-tetramethylaniline **1e** in CD_2Cl_2 only.

The comparison of the ^1H NMR spectra (Figure S30 versus Figure 33) suggests that, even in the presence of a stoichiometric quantity of $B(C_6F_5)_3$, amine **1e** is recovered in full and that the formation of corresponding iminium ion cannot be detected.

The analysis of the ^{11}B NMR spectrum (Figure S31) and its comparison to S24 (standard spectrum for $B(C_6F_5)_3$ only) indicates that there is free $B(C_6F_5)_3$ (characteristic peaks at 59.5 ppm was observed in both Figures S24 and S31). In addition, generation of a small quantity of $B(C_6F_5)_3$•**1e** adduct was observed (characteristic peak at −1.2 ppm was found in S31).

In agreement with the observations mentioned above, the ^{19}F NMR spectrum (Figure S32) contains peaks corresponding to both free $B(C_6F_5)_3$ and the adduct $B(C_6F_5)_3$•**1e**.

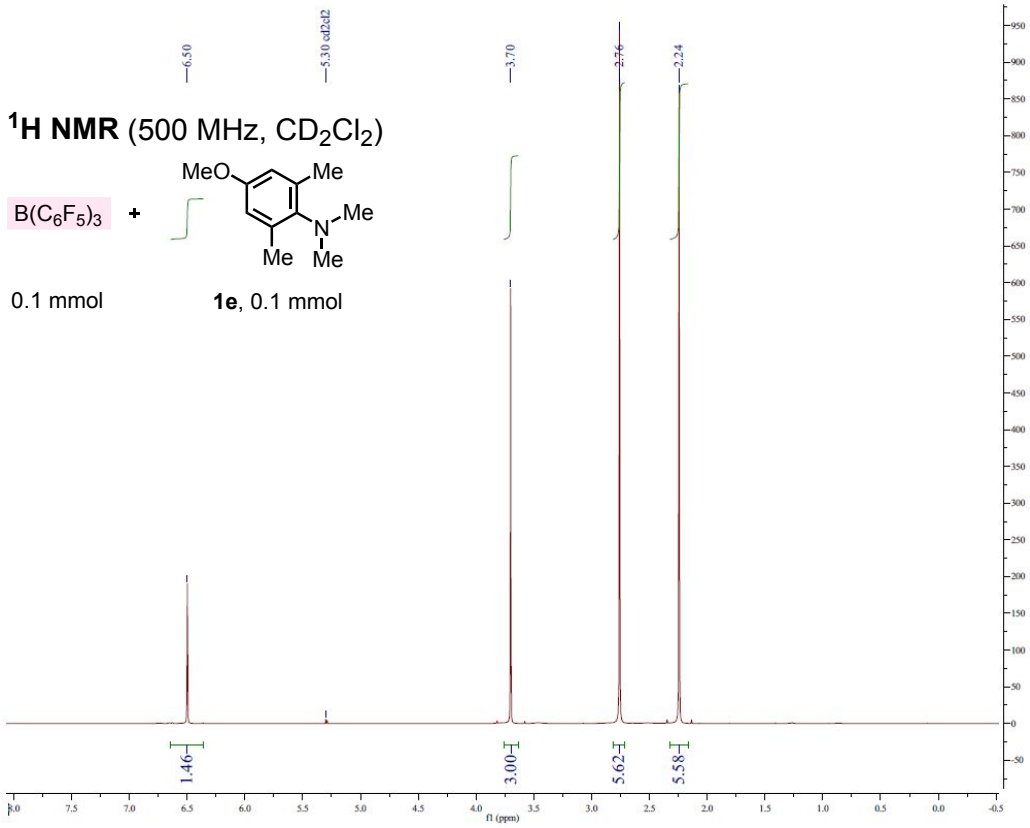


Figure S30. ^1H NMR of spectrum of a sample containing $B(C_6F_5)_3$ and amine **1e** in CD_2Cl_2.

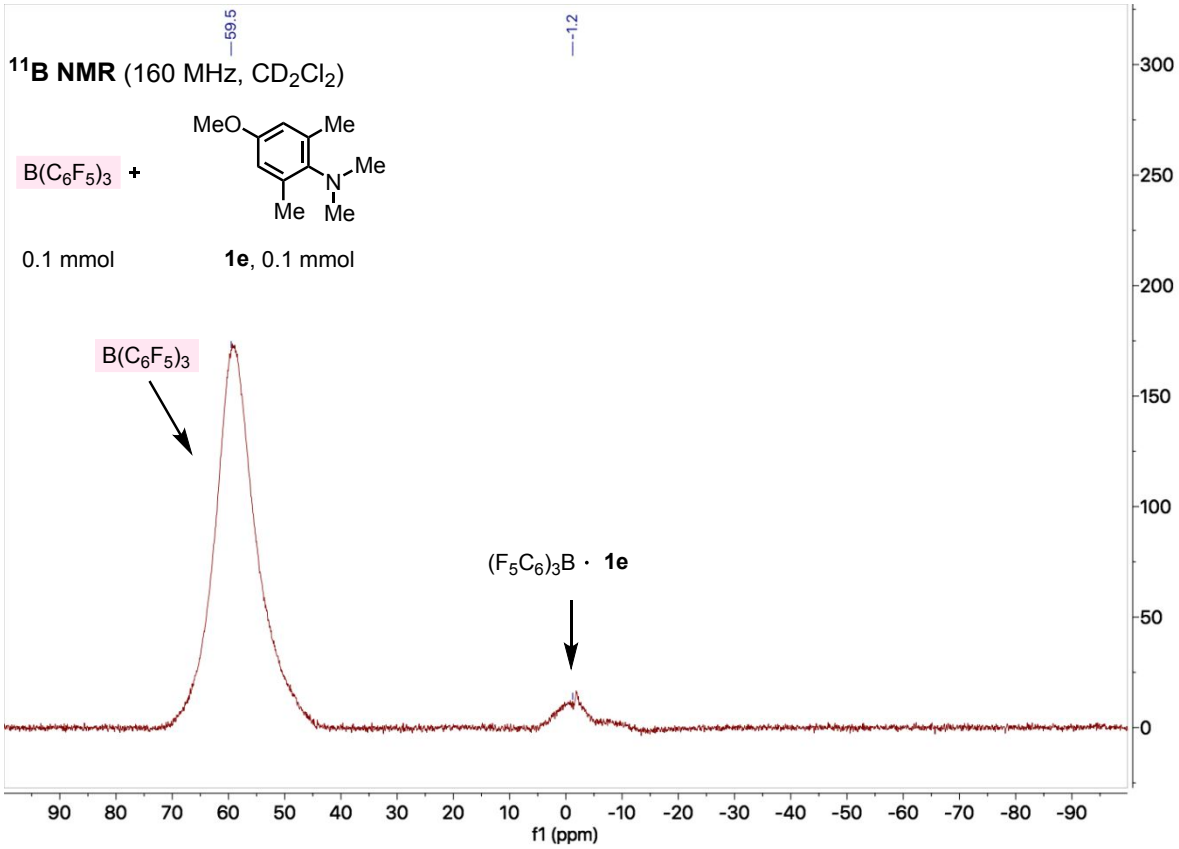


Figure S31. ^{11}B NMR spectrum of a sample containing $B(C_6F_5)_3$ and amine **1e** in CD_2Cl_2.

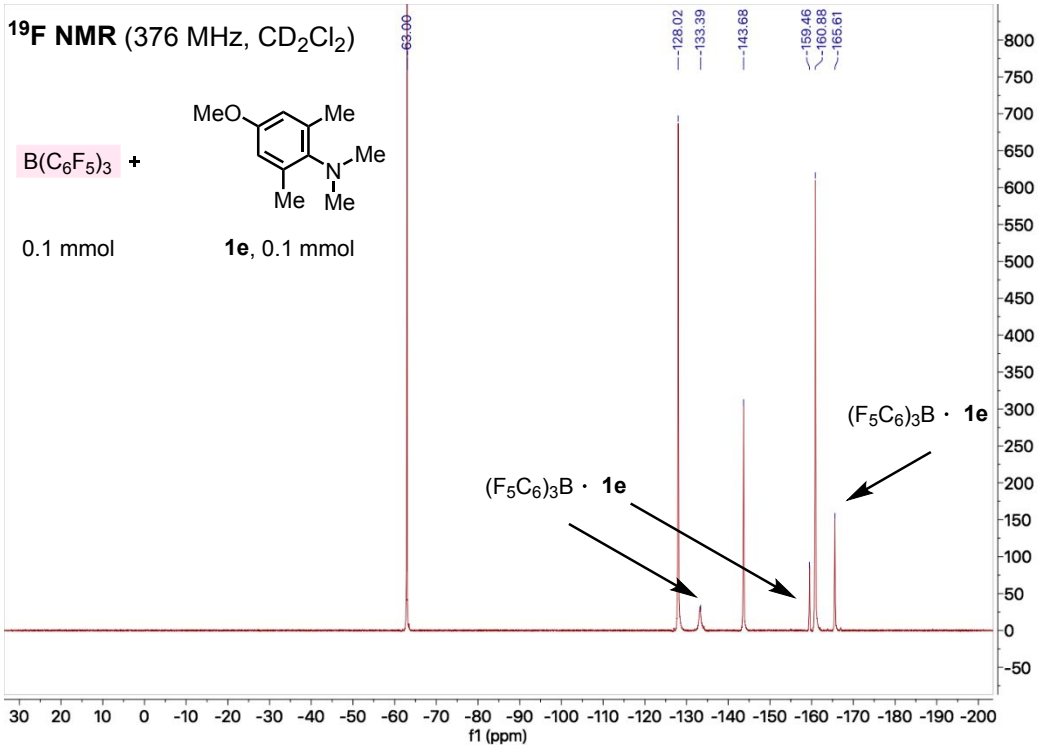


Figure S32. ^{19}F NMR spectrum of a sample containing $B(C_6F_5)_3$ and amine **1e** in CD_2Cl_2

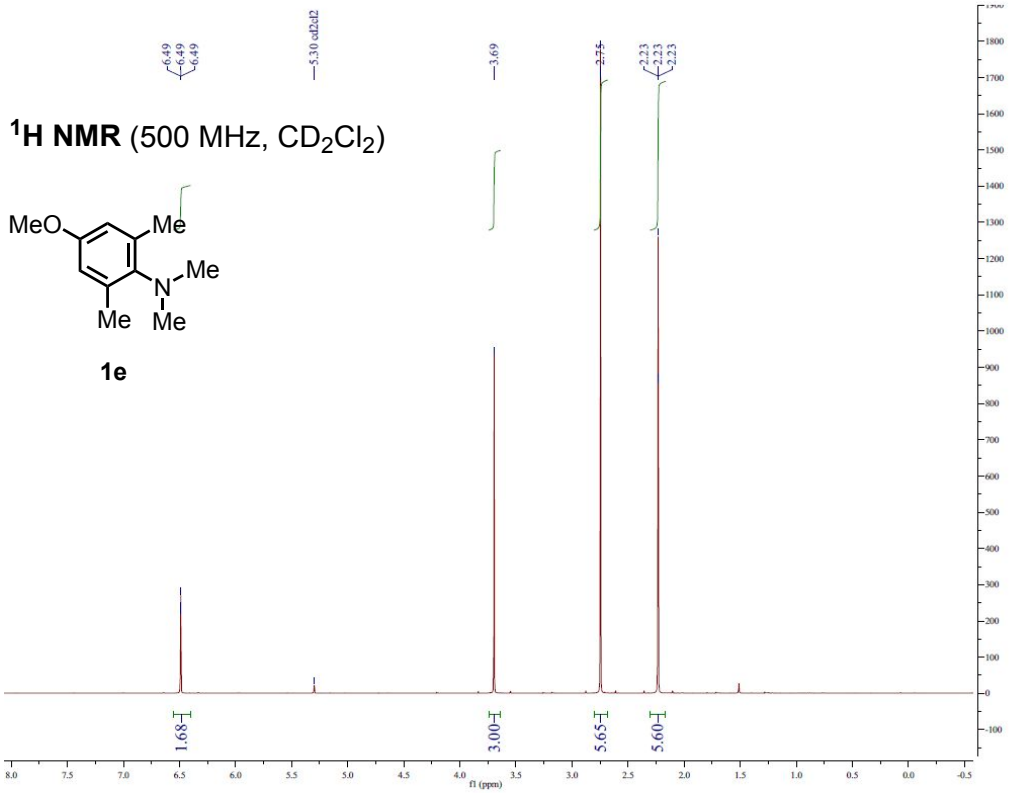


Figure S33. ^{1}H NMR spectrum of amine **1e** in CD_2Cl_2.

Next, we attempted to detect a Lewis acid/Lewis base adduct that may form between the carbonyl unit of alkynylsilane **2b** and $B(C_6F_5)_3$.[20] The ^{11}B and ^{19}F NMR spectra were obtained for:

Figures S34 – S35: the sample containing 0.1 mmol of $B(C_6F_5)_3$ and 0.1 mmol of **2b**.

It was found through studying the ^{11}B NMR spectrum of the sample (Figure S34) that $B(C_6F_5)_3$ forms the adduct with **2b** (a characteristic peak was observed at –2.1 ppm), and that $B(C_6F_5)_3$ is consumed.

Furthermore, we detected peaks at –134.14, –157.49 and –164.44 ppm in the ^{19}F NMR spectrum (Figure S35) that may correspond to the adduct formed while $B(C_6F_5)_3$ was fully consumed.

In order to determine if the adduct may also be generated in under the standard reaction conditions for catalytic C–H functionalization, ^{19}F NMR spectrum (Figure S35) was compared to those obtained for the unpurified reaction mixtures (Figures S27–S28). In Figures S27–S28, there were peaks at –134.64, –157.68 and –164.48 ppm (vs those at –134.14, –157.49 and –164.44 ppm found in S35), thereby suggesting that the adduct may be present in the unpurified reaction mixture.

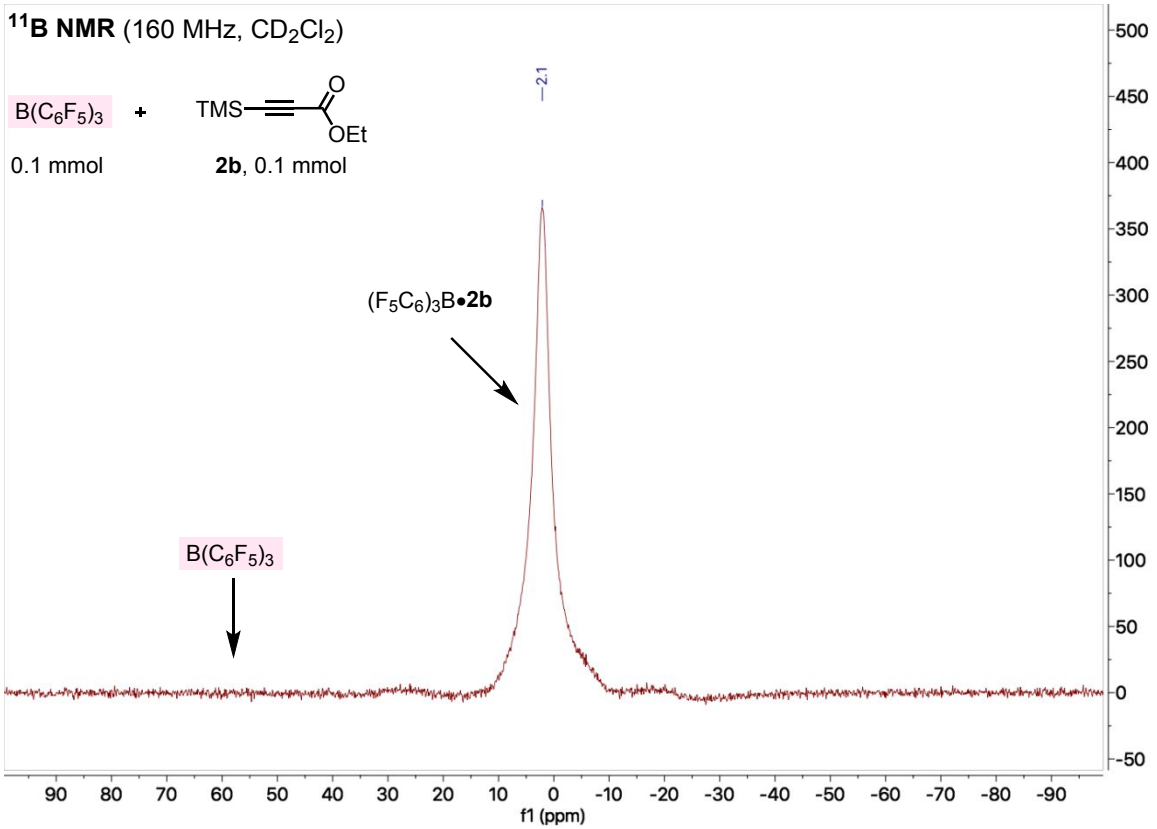


Figure S34. ^{11}B NMR spectrum of a sample containing $B(C_6F_5)_3$ and alkyne **2b** in CD_2Cl_2.

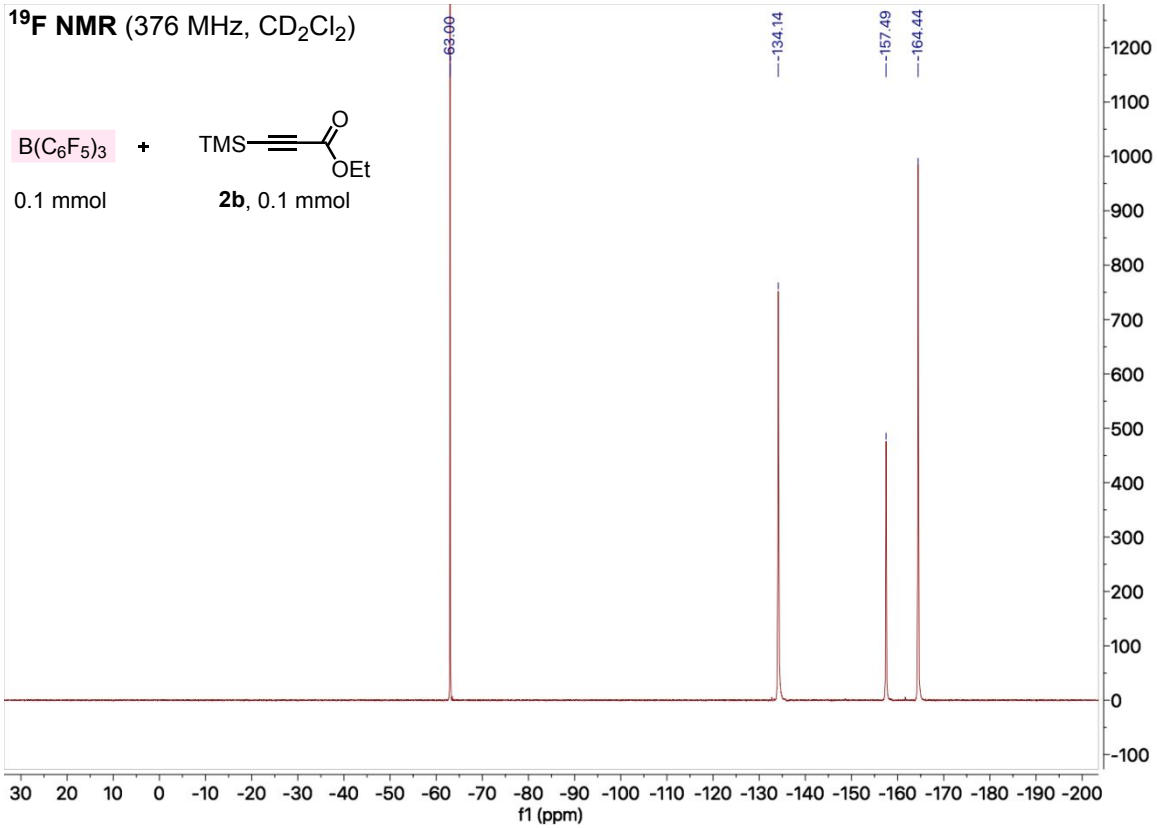
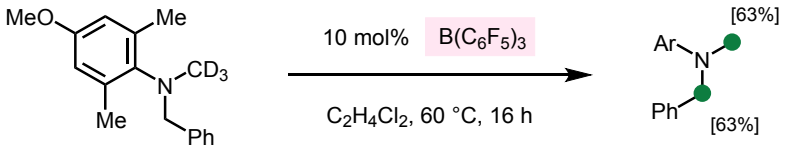


Figure S35. ^{19}F NMR spectrum of a sample containing $B(C_6F_5)_3$ and alkyne **2b** in CD_2Cl_2.

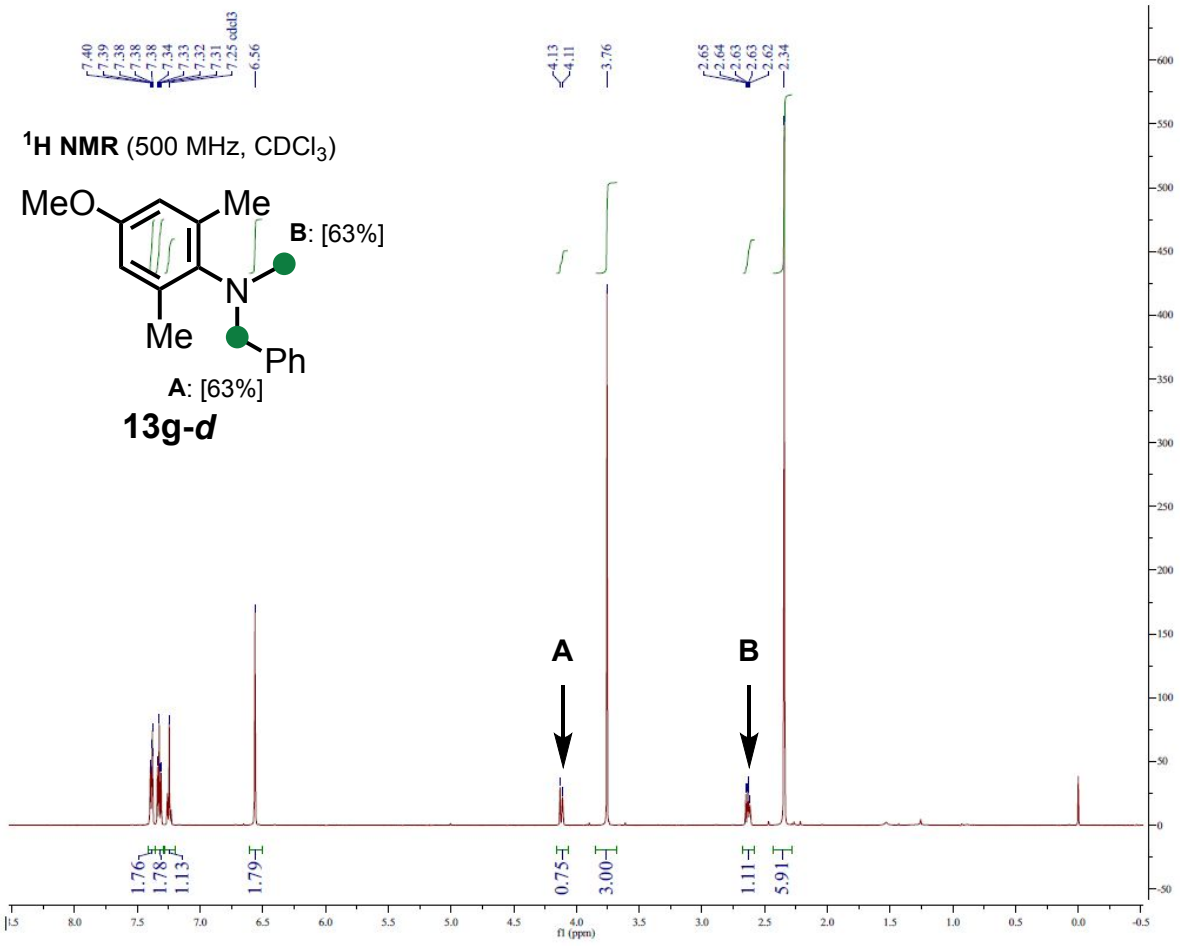
5.4. Experiments Involving *N*-Benzyl-4-methoxy-2,6-dimethyl-*N*-(methyl-d_3)aniline



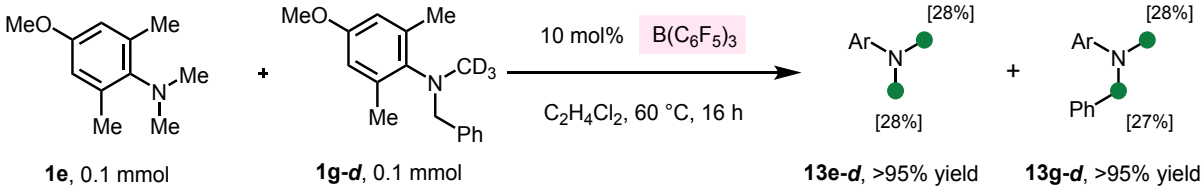
1g-*d*, 0.1 mmol **13g-*d***, >95% yield

Experimental Procedure for the Isotope Exchange of *N*-Benzyl-4-methoxy-2,6-dimethyl-*N*-(methyl-d_3)aniline

An oven-dried sealed tube equipped with a magnetic stir bar was used. To the sealed tube were added amine **1g-*d*** (0.1 mmol), $B(C_6F_5)_3$ (0.01 mmol, 10 mol%), and $C_2H_4Cl_2$ (0.4 mL) were added to the vessel. The reaction mixture was allowed to stir at 60 °C for 16 h. Upon completion, the unpurified reaction mixture was filtered through a short plug of Celite and rinsed with CH_2Cl_2. The combined organic material was then concentrated *in vacuo*. The unpurified mixture was purified by silica gel column chromatography (Et_2O:hexanes = 1:19), to afford **13g-*d*** as a colorless oil (>95% yield). Deuterium or proton incorporation values were determined based on analysis of the ^{1}H NMR spectrum of the purified product.



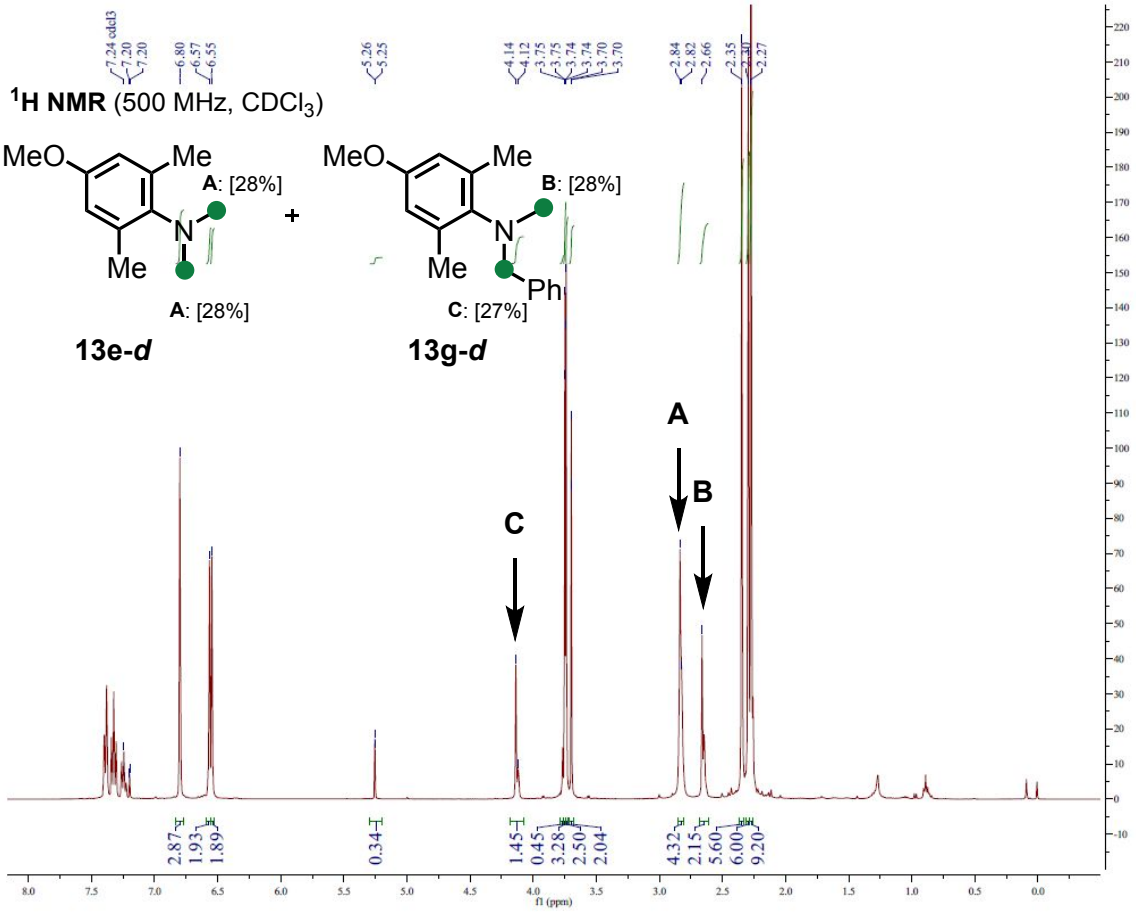
Intermolecular Isotope Exchange Experiment Between *N*-Benzyl-4-methoxy-2,6-dimethyl-*N*-(methyl-d_3)aniline and 4-Methoxy-*N*,*N*,2,6-tetramethylaniline

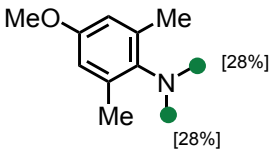


1e, 0.1 mmol **1g-*d***, 0.1 mmol **13e-*d***, >95% yield **13g-*d***, >95% yield

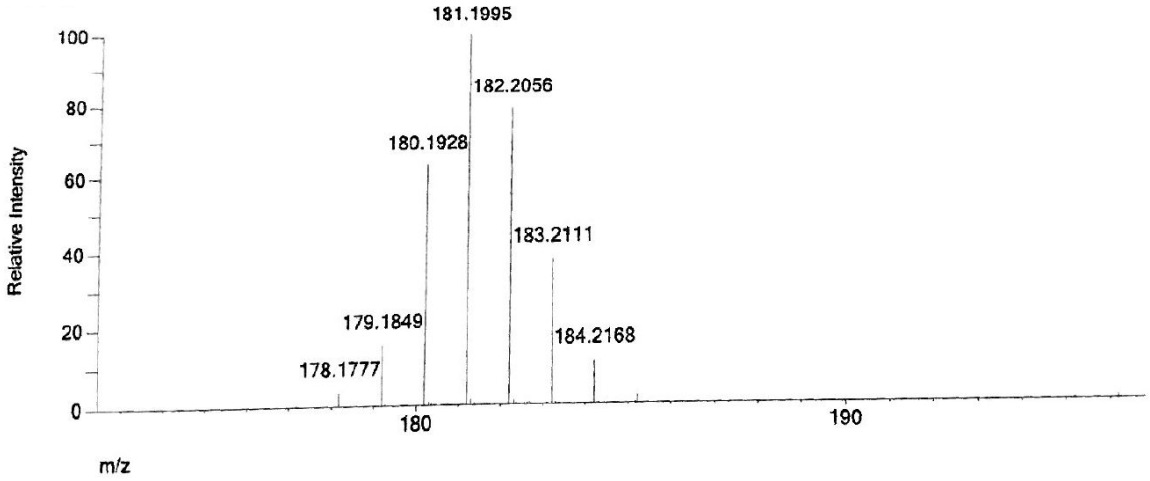
Experimental Procedure for the Isotope Exchange Between of *N*-Benzyl-4-methoxy-2,6-dimethyl-*N*-(methyl-d_3)aniline and 4-Methoxy-*N*,*N*,2,6-tetramethylaniline

An oven-dried sealed tube equipped with a magnetic stir bar was used. To the sealed tube were added amine **1e** (0.1 mmol), amine **1g-*d*** (0.1 mmol), $B(C_6F_5)_3$ (0.02 mmol, 10 mol%), and $C_2H_4Cl_2$ (0.4 mL) were added to the vessel. The reaction mixture was allowed to stir at 60 °C for 16 h. Upon completion, the unpurified reaction mixture was filtered through a short plug of Celite and rinsed with CH_2Cl_2. The combined organic material was then concentrated *in vacuo*. Deuterium incorporation values were determined based on analysis of the ^{1}H NMR and HRMS spectra of the purified product.




MeO
Me
N
[28%]
Me
[28%]

13e-*d*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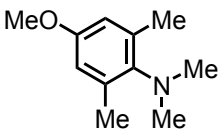
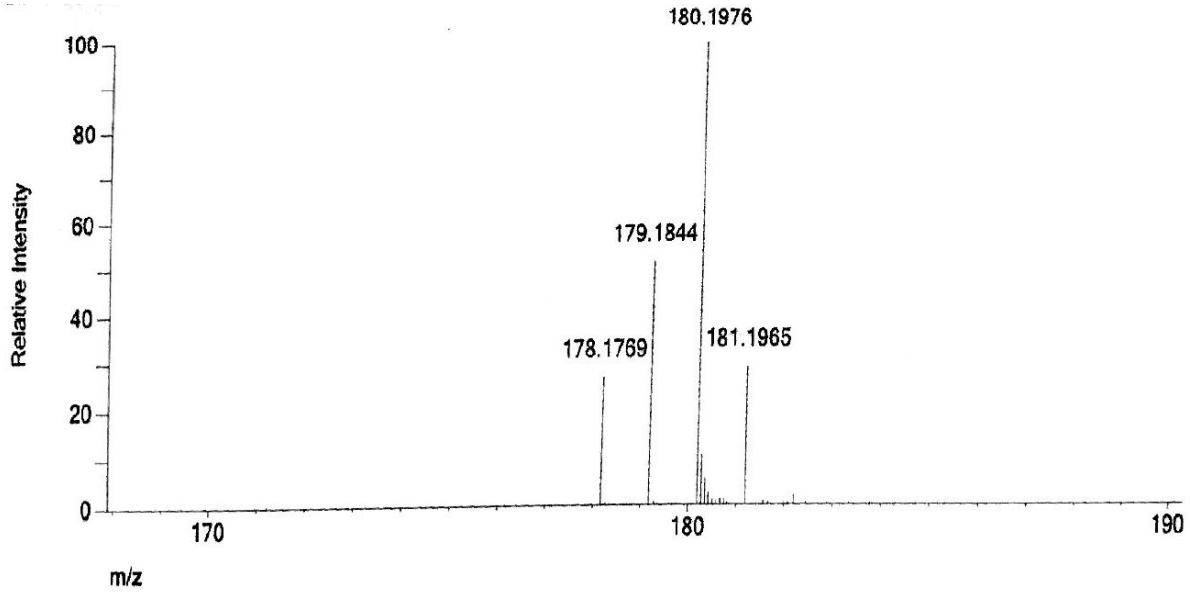
182.2056
180.1928
183.2111
179.1849
184.2168
178.1777
Relative Intensity
100
80
60
40
20
0
180
190
m/z


MeO
Me
N
Me
Me
Me

1e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178.1769
181.1965
Relative Intensity
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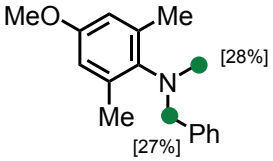
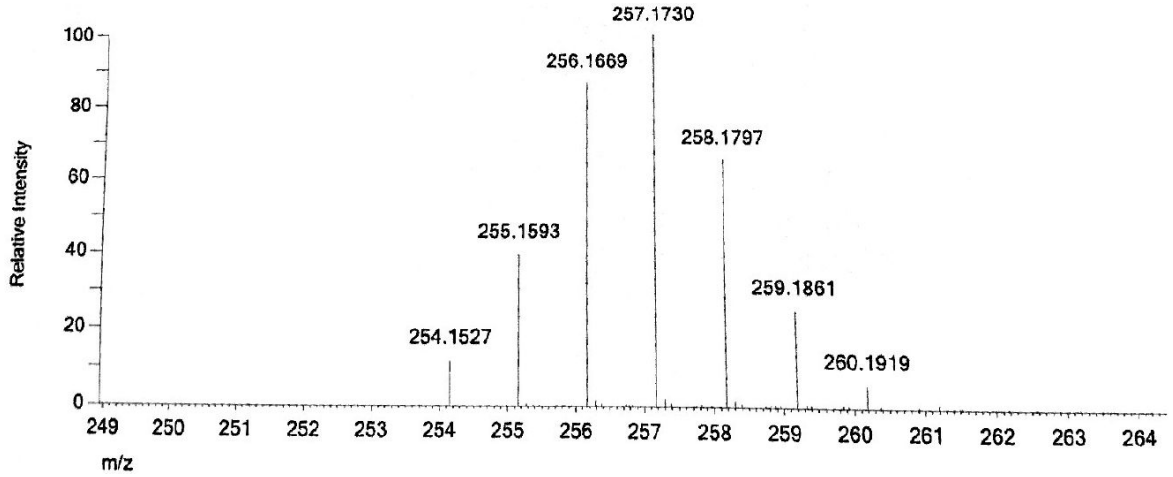
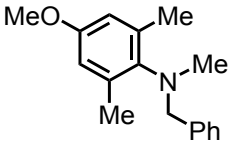
190
m/z

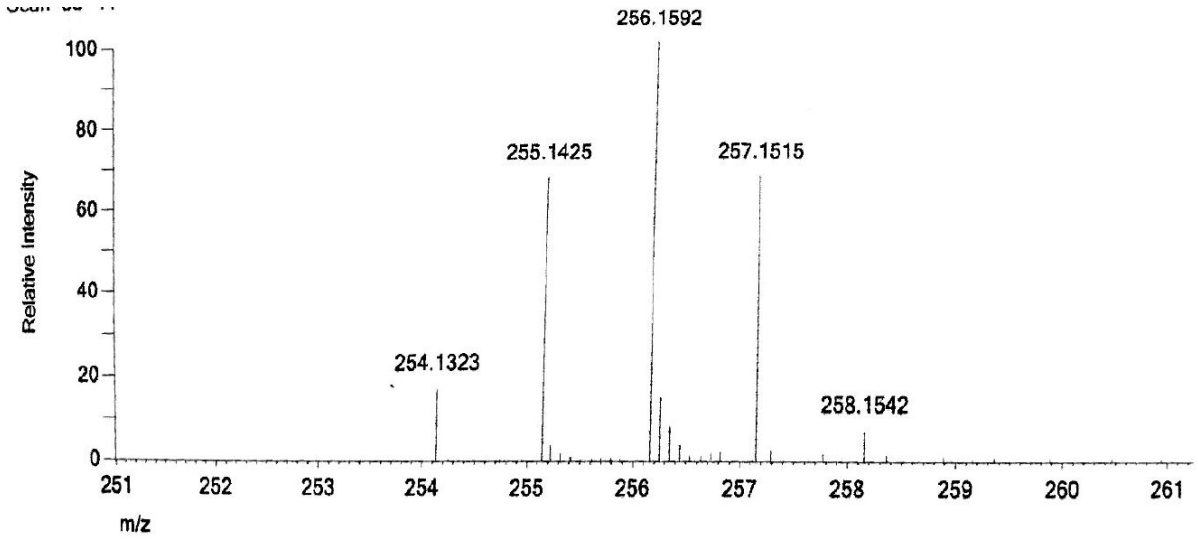


13g-*d*



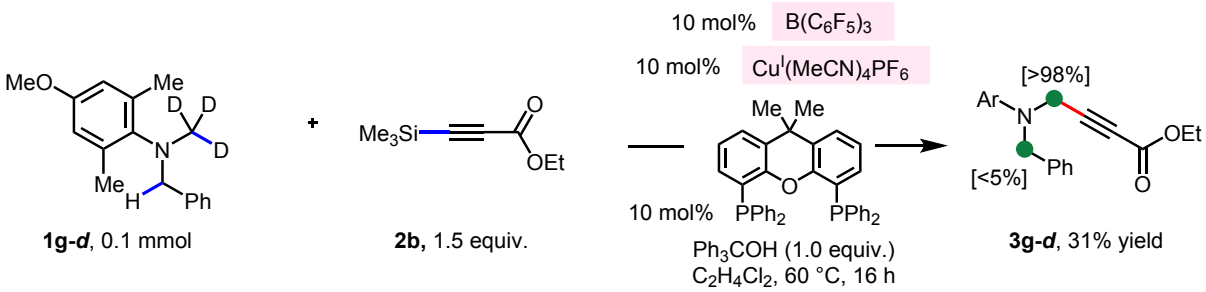


1g



Experiments Involving *N*-Benzyl-4-methoxy-2,6-dimethyl-*N*-(methyl-d_3)aniline

We investigated if the H/D exchange reaction may take place under the standard conditions for $B(C_6F_5)_3$ and organocopper co-catalyzed α-amino C–H alkynylation reaction with 0.10 mmol of *N*-benzyl-4-methoxy-2,6-dimethyl-*N*-(methyl-*d3*)aniline **1g-*d***, 0.15 mmol of 3-(trimethylsilyl)propiolate **2b** and 0.10 mmol of Ph_3COH.

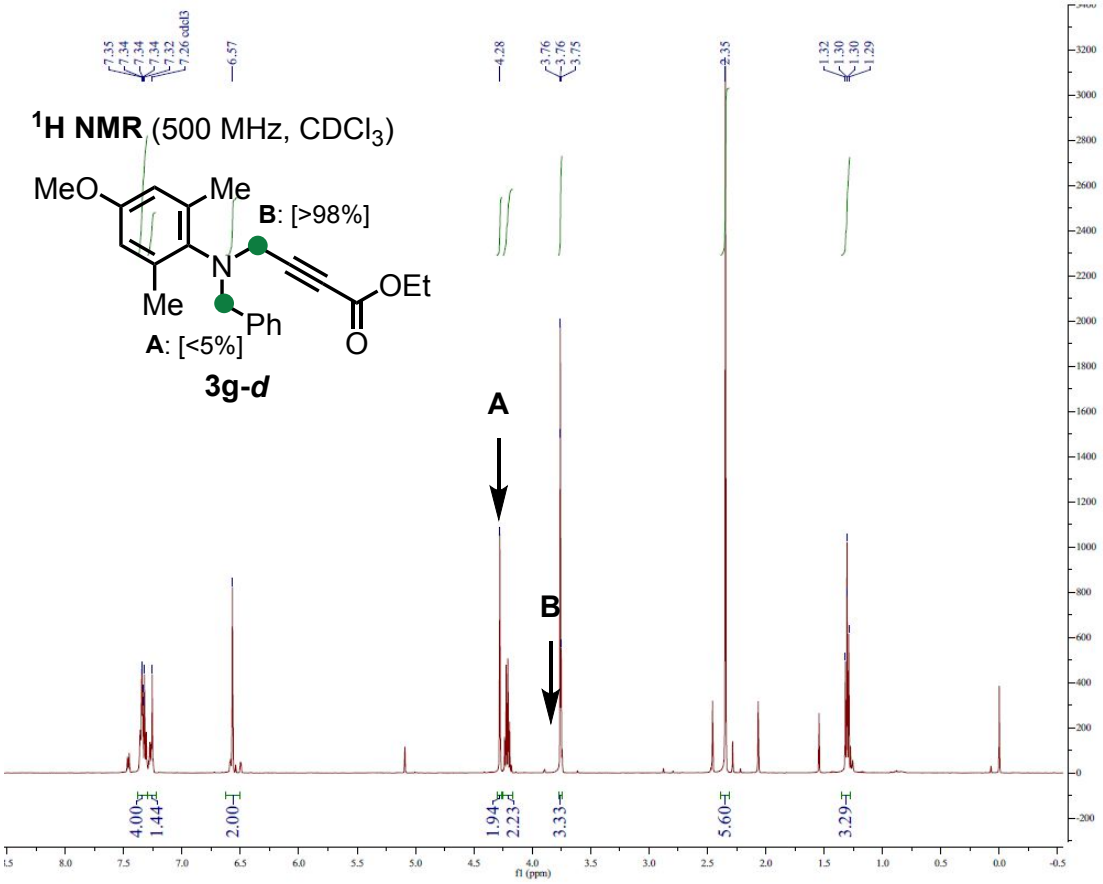


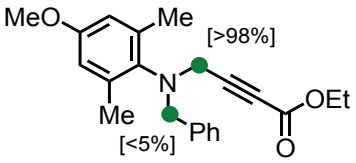
The ^{1}H NMR and HRMS spectrum of the isolated and purified product **3g-*d*** showed that there was 19% deuterium incorporation at the benzylic position of **3g-*d*.**

Experimental Procedure for the *α*-Alkynylation of *N*-Benzyl-4-methoxy-2,6-dimethyl-*N*-(methyl-*d*$_3$)aniline

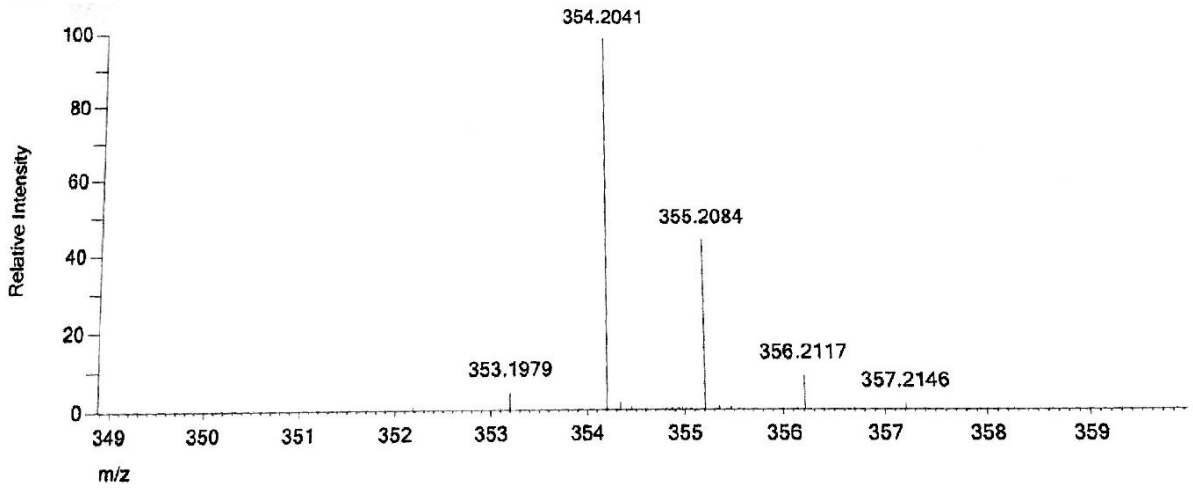
An oven-dried sealed tube equipped with a magnetic stir bar was used. To the sealed tube were added $Cu(MeCN)_4PF_6$ (0.01 mmol), Xantphos (0.01 mmol), and $C_2H_4Cl_2$ (0.2 mL) under nitrogen atmosphere. The mixture was allowed to stir for 20 minutes at 22 °C, then ethyl 3-(trimethylsilyl)propiolate **2b** (0.15 mmol), triphenylmethanol (0.1 mmol), amine **1g-*d*** (0.1 mmol), $B(C_6F_5)_3$ (0.01 mmol, 10 mol%), and $C_2H_4Cl_2$ (0.2 mL) were added to the vessel. The reaction mixture was allowed to stir at 60 °C for 16 h. Upon completion, the unpurified reaction mixture was filtered through a short plug of Celite and rinsed with CH_2Cl_2. The combined organic material was then concentrated *in vacuo*. The propargylamine product was purified and isolated by silica gel column chromatography (Et_2O:hexanes = 1:9), **3g-*d*** was obtained as a colorless liquid (12.7 mg, 36%). Deuterium incorporation values were determined based on analysis of the ^{1}H NMR and HRMS spectra of the purified product.

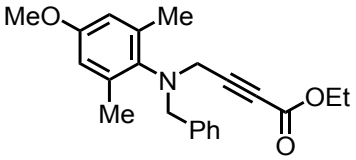
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 4H), 7.29 – 7.23 (m, 1H), 6.57 (s, 2H), 4.28 (s, 2H), 4.22 (qd, J = 7.1, 0.9 Hz, 2H), 3.76 (s, 3H), 2.35 (s, 6H), 1.30 (dd, J = 7.8, 6.9 Hz, 3H).


1H NMR (500 MHz, CDCl3)
MeO
Me
Me
N
Ph
OEt
O
B: [>98%]
A: [<5%]
3g-d
A
B
7.35
7.34
7.34
7.34
7.32
7.26 cdcl3
6.57
4.28
3.76
3.76
3.75
2.35
1.32
1.30
1.30
1.29
4.00
1.44
2.00
1.94
2.23
3.33
5.60
3.29
f1 (ppm)

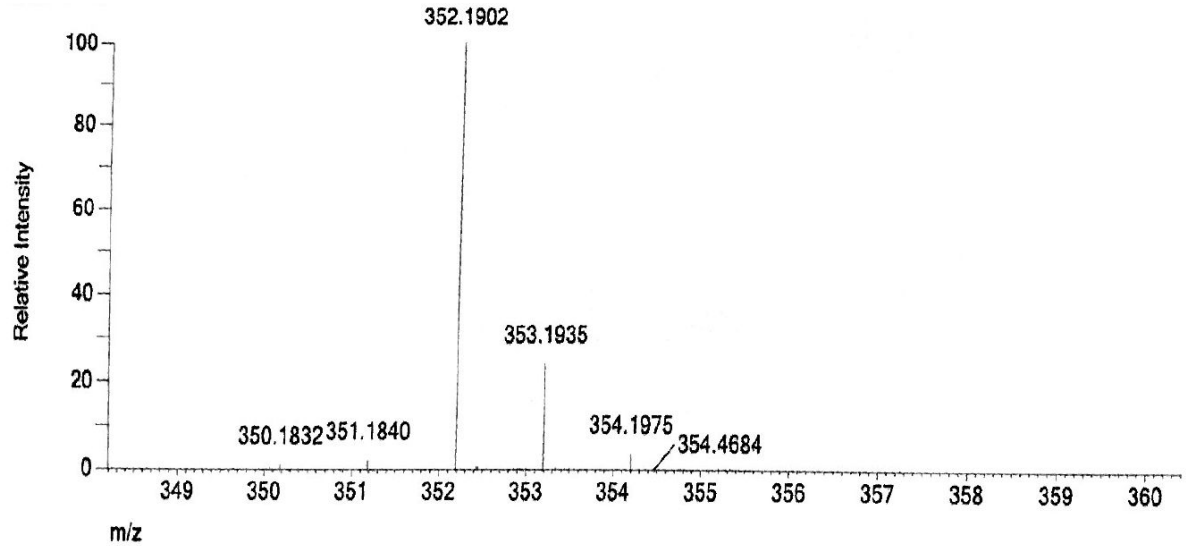

MeO
Me
[>98%]
N
OEt
Me
Ph
[<5%]
O

3g-*d*

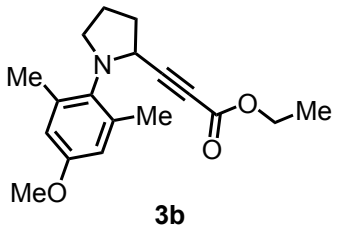

354.2041
355.2084
356.2117
353.1979
357.2146
Relative Intensity
m/z


MeO
Me
N
OEt
Me
Ph
O

3g


352.1902
353.1935
350.1832
351.1840
354.1975
354.4684
Relative Intensity
m/z

6. Analytical Data

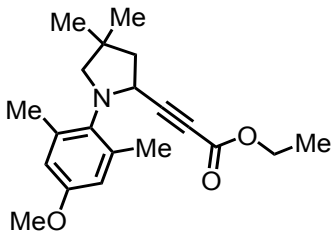


3b

Ethyl 3-(1-(4-methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propiolate (3b)

1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine **1b** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure A**. After purification by column chromatography (Et_2O:hexanes = 1:19), **3b** was obtained as a colorless liquid (54 mg, 90%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.58 (s, 2H), 4.27 (ddd, *J* = 7.8, 3.5, 1.3 Hz, 1H), 4.17 (qd, *J* = 7.2, 1.3 Hz, 2H), 3.75 (s, 3H), 3.43 – 3.31 (m, 1H), 3.09 (q, *J* = 6.9 Hz, 1H), 2.47 – 2.22 (m, 6H), 2.22 – 2.10 (m, 3H), 2.09 – 1.94 (m, 1H), 1.27 (td, *J* = 7.2, 1.4 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.2, 153.3, 136.6, 113.2, 91.5, 73.9, 63.3, 55.9, 52.3, 51.0, 35.8, 26.7, 18.4, 15.1; **IR** (neat) ν 2967, 2837, 2224, 1707, 1599, 1476, 1366,1244, 1153, 1067, cm^{-1}; **HRMS** (DART) Calcd for $C_{18}H_{24}NO_3$ (MH^+): 302.1751; found: 302.1755.

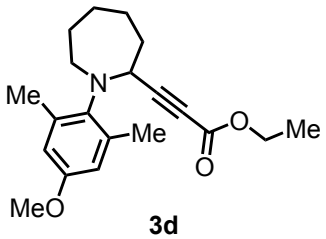


3c

Ethyl 3-(1-(4-methoxy-2,6-dimethylphenyl)-3,3-dimethylpyrrolidin-2-yl)propiolate (3c)

1-(4-Methoxy-2,6-dimethylphenyl)-3,3-dimethylpyrrolidine **1c** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure A**. After purification by column chromatography (Et_2O:hexanes = 1:19), **3c** was obtained as a colorless liquid (51 mg, 77%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.57 (s, 2H), 4.41 (dd, *J* = 9.0, 3.8 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.75 (s, 3H), 3.07 (d, *J* = 7.9 Hz, 1H), 2.95 (d, *J* = 7.8 Hz, 1H), 2.37 (s, 5H), 2.19 (dd, *J* = 12.5, 9.0 Hz, 2H), 1.98 (dd, *J* = 12.5, 3.9 Hz, 1H), 1.37 (s, 3H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.15 (d, *J* = 1.0 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.2, 153.8, 135.4, 113.7, 91.0, 74.3, 64.5, 61.6, 55.2, 51.9, 47.0, 39.1, 27.8, 27.2, 14.0; **IR** (neat) ν 2954, 2864, 2228, 1707, 1601, 1465, 1243, 1094, 1023, 751 cm^{-1}; **HRMS** (DART) Calcd for $C_{20}H_{28}NO_3$ (MH^+): 330.2063; found: 330.2069.

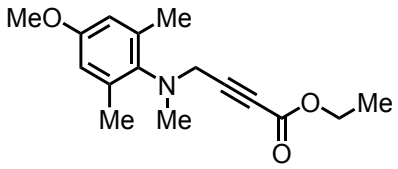


3d

Ethyl 3-(1-(4-methoxy-2,6-dimethylphenyl)azepan-2-yl)propiolate (3d)

1-(4-Methoxy-2,6-dimethylphenyl)azepane **1d** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure A**. After purification by column chromatography (Et_2O:hexanes = 1:19), **3d** was obtained as a colorless liquid (51 mg, 77%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (d, *J* = 13.4 Hz, 2H), 4.18 (d, *J* = 7.1 Hz, 2H), 4.06 (d, *J* = 2.7 Hz, 1H), 3.75 (s, 3H), 3.32 (d, *J* = 9.1 Hz, 1H), 3.08 (d, *J* = 11.1 Hz, 1H), 2.42 (s, 3H), 2.29 (s, 3H), 2.19 (d, *J* = 1.5 Hz, 1H), 1.95 – 1.85 (m, 2H), 1.85 – 1.79 (m, 1H), 1.79 – 1.70 (m, 2H), 1.57 (s, 2H), 1.28 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.4, 153.8, 140.9, 139.7, 137.9, 114.1, 113.6, 90.3, 75.6, 59.4, 55.6, 53.0, 51.3, 34.8, 31.4, 28.9, 25.2, 20.1, 19.6, 14.0; **IR** (neat) ν 2926, 2845, 2221, 1707, 1598, 1474, 1309, 1240, 1065, 853 cm^{-1}; **HRMS** (DART) Calcd for $C_{20}H_{28}NO_3$ (MH^+): 330.2063; found: 330.2061.

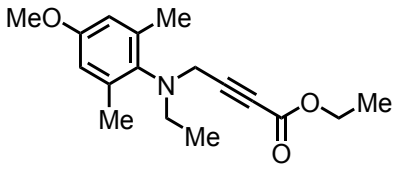


3e

Ethyl 4-((4-methoxy-2,6-dimethylphenyl)(methyl)amino)but-2-ynoate (3e)

4-Methoxy-*N,N*,2,6-tetramethylaniline **1e** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure A**. After purification by column chromatography (Et_2O:hexanes = 1:19), **3e** was obtained as a colorless liquid (50 mg, 90%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.54 (s, 2H), 4.23 (q, *J* = 7.1, 1.5 Hz, 2H), 3.89 (s, 2H), 3.74 (s, 3H), 2.88 (s, 3H), 2.29 (s, 6H), 1.31 (t, *J* = 7.1, 1.5 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.3, 153.6, 140.9, 138.7, 112.8, 86.1, 75.6, 61.8, 55.2, 44.8, 40.1, 19.4, 13.9; **IR** (neat) ν 2933, 2228, 1707, 1598, 1480, 1309, 1244, 1155, 1060, 855 cm^{-1}; **HRMS** (DART) Calcd for $C_{16}H_{22}NO_3$ (MH^+): 276.1594; found: 276.1609.

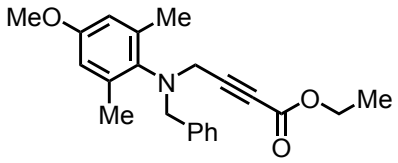


3f

Ethyl 4-(ethyl(4-methoxy-2,6-dimethylphenyl)amino)but-2-ynoate (3f)

N-Ethyl-4-methoxy-*N*,2,6-trimethylaniline **1f** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure A**. After purification by column chromatography (Et_2O:hexanes = 1:19), **3f** was obtained as a colorless liquid (24 mg, 42%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.56 (s, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.92 (s, 2H), 3.76 (s, 3H), 3.21 (q, *J* = 7.2 Hz, 2H), 2.30 (s, 6H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.04 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 156.8, 153.7, 139.5, 139.3, 113.6, 86.7, 75.5, 61.8, 55.2, 47.2, 42.9, 19.6, 14.3, 14.0; **IR** (neat) ν 2933, 2230, 1707, 1598, 1490, 1309, 1254, 1120, 1060, 840 cm^{-1}; **HRMS** (DART) Calcd for $C_{17}H_{24}NO_3$ (MH^+): 290.1751; found: 290.1755.

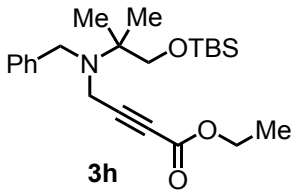


3g

Ethyl 4-(benzyl(4-methoxy-2,6-dimethylphenyl)amino)but-2-ynoate (3g)

N-Benzyl-4-methoxy-*N*,2,6-trimethylaniline **1g** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure A**. After purification by column chromatography (Et_2O:hexanes = 1:19), **3g** was obtained as a colorless liquid (51 mg, 72%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 4H), 7.28 – 7.23 (m, 1H), 6.57 (s, 2H), 4.28 (s, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.78 (s, 2H), 3.76 (s, 3H), 2.34 (s, 6H), 1.30 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.8, 153.5, 140.6, 139.0, 138.5, 128.9, 128.4, 127.2, 113.4, 85.4, 75.3, 61.8, 58.5, 55.2, 41.5, 19.9, 13.2; **IR** (neat) ν 2927, 2841, 2230, 1708, 1598, 1479, 1312, 1245, 1065, 855 cm^{-1}; **HRMS** (DART) Calcd for $C_{22}H_{26}NO_3$ (MH^+): 352.1907; found: 352.1895.

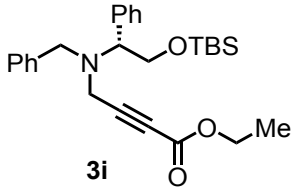


3h

Ethyl 4-(benzyl(1-((*tert*-butyldimethylsilyl)oxy)-2-methylpropan-2-yl)amino)but-2-ynoate (3h)

N-Benzyl-1-((*tert*-butyldimethylsilyl)oxy)-*N*,2-dimethylpropan-2-amine **1h** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure B** using 1,2-bis(diphenylphosphino)ethane as the ligand. After purification by column chromatography (Et_2O:hexanes = 1:19), **3h** was obtained as a colorless liquid (61 mg, 76%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (dt, *J* = 6.6, 1.1 Hz, 2H), 7.32 – 7.27 (m, 2H), 7.24 – 7.20 (m, 1H), 4.23 (q, *J* = 7.2 Hz, 2H), 3.91 (s, 2H), 3.60 (s, 2H), 3.51 (s, 2H), 1.31 (t, *J* = 7.1, 0.8 Hz, 3H), 1.23 (s, 6H), 0.91 (s, 9H), 0.06 (s, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 153.6, 140.3, 128.4, 128.2, 126.9, 87.6, 76.7, 69.7, 61.8, 58.6, 51.4, 36.7, 25.9, 22.9, 18.2, 14.1, -5.6; **IR** (neat) ν 2949, 2855, 2221, 1708, 1463, 1364, 1237, 1092, 840, 774 cm^{-1}; **HRMS** (DART) Calcd for $C_{23}H_{38}NO_3Si$ (MH^+): 404.2615; found: 404.2610.

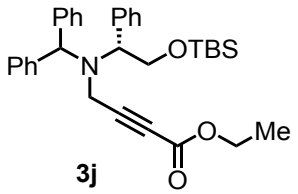


3i

Ethyl (*R*)-4-(benzyl(2-((*tert*-butyldimethylsilyl)oxy)-1-phenylethyl)amino)but-2-ynoate (3i)

(*R*)-*N*-Benzyl-2-((*tert*-butyldimethylsilyl)oxy)-*N*-methyl-1-phenylethan-1-amine **1i** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure B** using 1,2-bis(diphenylphosphino)ethane as the ligand. After purification by column chromatography (Et_2O:hexanes = 1:19), **3i** was obtained as a colorless liquid (78 mg, 86%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.5 Hz, 2H), 7.37 – 7.20 (m, 8H), 4.26 (q, *J* = 7.1, 2.1 Hz, 2H), 3.94 (dd, *J* = 7.3, 4.9 Hz, 2H), 3.82 (d, *J* = 2.0 Hz, 1H), 3.74 (d, *J* = 2.1 Hz, 1H), 3.70 – 3.60 (m, 2H), 3.37 – 3.28 (m, 1H), 1.34 (t, *J* = 2.0 Hz, 3H), 0.83 (s, 9H), -0.09 (d, *J* = 5.7, 2.1 Hz, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 153.6, 141.1, 138.8, 128.9, 128.5, 128.30, 128.26, 127.4, 127.1, 84.5, 77.84, 67.6, 65.9, 61.9, 55.1, 39.1, 25.8, 18.2, 14.1, -0.01, -5.67, -5.69; **IR** (neat) ν 2923, 2853, 2222, 1709, 1458, 1365, 1239, 1095, 870, 698 cm^{-1}; **HRMS** (DART) Calcd for $C_{27}H_{38}NO_3Si$ (MH^+): 452.2615; found: 452.2612; $[\alpha]^{25}_D$ = 36.7° (*c* 0.2, CH_2Cl_2).

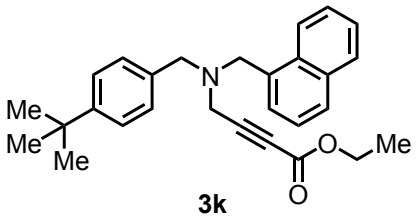


3j

Ethyl (*R*)-4-(benzhydryl(2-((*tert*-butyldimethylsilyl)oxy)-1-phenylethyl)amino)but-2-ynoate (3j)

(*R*)-*N*-Benzhydryl-2-((*tert*-butyldimethylsilyl)oxy)-*N*-methyl-1-phenylethan-1-amine **1j** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure B** using 1,2-bis(diphenylphosphino)ethane as the ligand. After purification by column chromatography (Et_2O:hexanes = 1:19), **3j** was obtained as a colorless liquid (102 mg, 97%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 – 7.46 (m, 4H), 7.42 (dt, *J* = 8.1, 1.1 Hz, 2H), 7.35 – 7.14 (m, 9H), 5.23 (s, 1H), 4.24 – 4.06 (m, 5H), 3.55 (s, 2H), 1.31 (t, *J* = 7.1, 3H), 0.82 (s, 9H), -0.04 (d, *J* = 20.0, 6H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 153.4, 142.0, 141.9, 139.8, 128.7, 128.6, 128.49, 128.47, 128.39, 128.1, 127.24, 127.15, 86.5, 76.6, 69.2, 63.1, 62.9, 61.6, 36.6, 25.9, 18.2, 14.1, -5.55, -5.57; **IR** (neat) ν 3026, 2930, 2855, 2224, 1708, 1456, 1362, 1243,1095, 837 cm^{-1}; **HRMS** (DART) Calcd for $C_{33}H_{42}NO_3Si$ (MH^+): 528.2928; found: 528.2922; $[\alpha]^{25}_D$ = −16.2° (*c* 0.8, CH_2Cl_2).

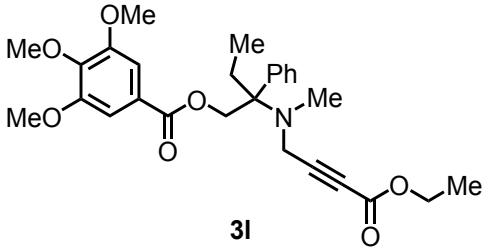


3k

Ethyl 4-((4-(*tert*-butyl)phenyl)(naphthalen-1-ylmethyl)amino)but-2-ynoate (3k)

4-(*tert*-Butyl)-*N*-methyl-*N*-(naphthalen-1-ylmethyl)aniline **1k** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure B** using 1,2-bis(diphenylphosphino)ethane as the ligand. After purification by column chromatography (Et_2O:hexanes = 1:19), **3k** was obtained as a colorless liquid (63 mg, 76%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, *J* = 7.4 Hz, 1H), 7.86 – 7.80 (m, 1H), 7.77 (d, *J* = 8.2 Hz, 1H), 7.55 – 7.45 (m, 3H), 7.40 (dd, *J* = 8.6, 6.6 Hz, 1H), 7.36 – 7.27 (m, 4H), 4.30 (q, *J* = 7.2 Hz, 2H), 4.15 (s, 2H), 3.78 (s, 2H), 3.35 (s, 2H), 1.37 (t, *J* = 7.1 Hz, 4H), 1.30 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 153.6, 150.3, 135.1, 133.9, 133.7, 132.5, 128.9, 128.4, 128.3, 127.8, 125.8, 125.7, 125.3, 125.2, 124.9, 83.6, 78.3, 62.0, 57.7, 56.2, 40.9, 34.5, 31.4, 14.1; **IR** (neat) ν 2957, 2825, 2220, 1707, 1597, 1509, 1239, 1107, 1050, 791 cm^{-1}; **HRMS** (DART) Calcd for $C_{28}H_{32}NO_2$ (MH^+): 414.2428; found: 414.2429.

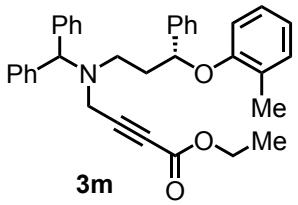


3l

2-((4-Ethoxy-4-oxobut-2-yn-1-yl)(methyl)amino)-2-phenylbutyl 3,4,5-trimethoxybenzoate (3l)

2-(Dimethylamino)-2-phenylbutyl 3,4,5-trimethoxybenzoate **1l** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure B** using 1,2-bis(diphenylphosphino)ethane as the ligand. After purification by column chromatography (Et_2O:hexanes = 1:2), **3l** was obtained as a colorless liquid (69 mg, 71%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 – 7.46 (m, 2H), 7.40 – 7.33 (m, 2H), 7.29 – 7.22 (m, 1H), 7.18 (d, *J* = 1.4 Hz, 2H), 4.89 (dd, *J* = 12.1, 1.3 Hz, 1H), 4.74 (dd, *J* = 12.0, 1.3 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.89 (s, 3H), 3.82 (s, 6H), 3.63 (d, *J* = 17.6 Hz, 1H), 3.48 (d, *J* = 17.6 Hz, 1H), 2.63 (s, 3H), 1.95 – 1.78 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 2H), 0.69 (t, *J* = 7.3 Hz, 4H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.8, 153.5, 152.9, 142.3, 141.7, 128.2, 127.3, 126.9, 124.8, 106.8, 86.2, 75.5, 65.7, 64.8, 61.8, 60.8, 56.1, 42.1, 35.8, 30.1, 13.9, 8.5; **IR** (neat) ν 2939, 2231, 1709, 1586, 1498, 1331, 1239, 1123, 1006, 756 cm^{-1}; **HRMS** (DART) Calcd for $C_{27}H_{34}NO_7$ (MH^+): 484.2330; found: 484.2322.

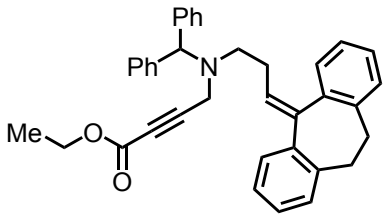


3m

Ethyl (*R*)-4-(benzhydryl(3-phenyl-3-(*o*-tolyloxy)propyl)amino)but-2-ynoate (3m)

(*R*)-*N*-Benzhydryl-*N*-methyl-3-phenyl-3-(*o*-tolyloxy)propan-1-amine **1m** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure B** using 1,2-bis(diphenylphosphino)ethane as the ligand. After purification by column chromatography (Et_2O:hexanes = 1:19), **3m** was obtained as a colorless liquid (58 mg, 56%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 – 7.40 (m, 2H), 7.35 – 7.13 (m, 10H), 7.07 (qt, *J* = 5.7, 1.3 Hz, 4H), 6.94 (td, *J* = 7.8, 1.8 Hz, 1H), 6.75 (td, *J* = 7.4, 1.1 Hz, 1H), 6.57 – 6.52 (m, 1H), 5.19 (dd, *J* = 9.2, 3.4 Hz, 1H), 4.66 (s, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.63 – 3.50 (m, 2H), 2.86 – 2.77 (m, 2H), 2.13 (dddd, *J* = 19.3, 9.2, 7.5, 5.6 Hz, 1H), 2.02 (s, 3H), 2.02 – 1.95 (m, 1H), 1.34 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 155.9, 153.4, 142.33, 142.26, 142.24, 130.5, 128.64, 128.57, 128.54, 127.91, 127.88, 127.72, 127.4, 127.20, 127.15, 127.1, 126.4, 125.8, 120.0, 112.3, 83.5, 77.9, 76.9, 72.6, 61.9, 47.3, 39.5, 37.2, 16.3, 14.1; **IR** (neat) ν 3025, 2933, 2831, 2220, 1707, 1594, 1490, 1240, 1049, 749 cm^{-1}; **HRMS** (DART) Calcd for $C_{35}H_{36}NO_3$ (MH^+): 518.2689; found: 518.2691.

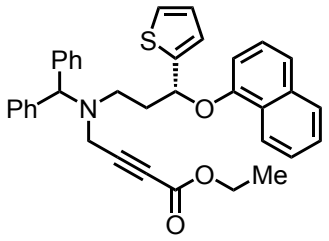


3n

Ethyl 4-(benzhydryl(3-(10,11-dihydro-5*H*-dibenzo[*a,d*][7]annulen-5-ylidene)propyl)amino)but-2-ynoate (3n)

N-Benzhydryl-3-(10,11-dihydro-5*H*-dibenzo[*a,d*][7]annulen-5-ylidene)-*N*-methylpropan-1-amine **1n** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure B** using 1,2-bis(diphenylphosphino)ethane as the ligand. After purification by column chromatography (Et_2O:hexanes = 1:4), **3n** was obtained as a colorless liquid (79 mg, 74%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 – 7.39 (m, 4H), 7.30 – 7.22 (m, 5H), 7.22 – 7.12 (m, 7H), 7.10 – 7.02 (m, 2H), 5.84 (t, *J* = 7.5, 1.5 Hz, 1H), 4.67 (s, 1H), 4.27 (q, *J* = 7.1, 1.5 Hz, 2H), 3.47 – 3.19 (m, 4H), 2.97 (s, 1H), 2.67 (t, *J* = 7.2 Hz, 3H), 2.30 (q, *J* = 7.2 Hz, 2H), 1.36 (t, *J* = 7.1, 1.4 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 153.4, 143.8, 142.4, 141.2, 139.9, 139.3, 137.0, 129.9, 128.9, 128.6, 128.51, 128.48, 128.2, 128.0, 127.9, 127.4, 127.1, 126.9, 125.9, 125.8, 83.7, 77.8, 72.3, 61.9, 50.3, 39.3, 33.7, 31.9, 27.6, 14.1; **IR** (neat) ν 3020, 2922, 2836, 2224, 1707, 1484, 1448, 1365, 11243, 751 cm^{-1}; **HRMS** (DART) Calcd for $C_{37}H_{36}NO_2$ (MH^+): 526.2740; found: 526.2751.

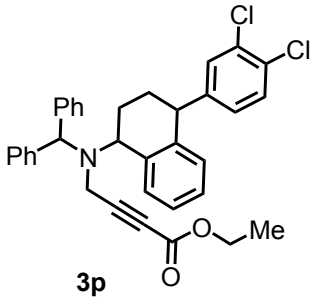


3o

Ethyl (*R*)-4-(benzhydryl(3-(naphthalen-1-yloxy)-3-(thiophen-2-yl)propyl)amino)but-2-ynoate (3o)

(*R*)-*N*-Benzhydryl-*N*-methyl-3-(naphthalen-1-yloxy)-3-(thiophen-2-yl)propan-1-amine **1o** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure B** using 1,2-bis(diphenylphosphino)ethane as the ligand. After purification by column chromatography (Et_2O:hexanes = 1:19), **3o** was obtained as a colorless liquid (76 mg, 68%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.3 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.46 (t, *J* = 7.3 Hz, 1H), 7.40 (dd, *J* = 19.1, 7.8 Hz, 4H), 7.27 (dt, *J* = 25.2, 7.3 Hz, 5H), 7.17 (q, *J* = 5.5 Hz, 2H), 7.01 – 6.91 (m, 4H), 6.89 (t, *J* = 4.4 Hz, 1H), 6.81 (d, *J* = 7.6 Hz, 1H), 5.69 (dd, *J* = 8.5, 4.3 Hz, 1H), 4.67 (s, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.59 (d, *J* = 4.6 Hz, 2H), 2.86 (d, *J* = 7.7 Hz, 2H), 2.49 – 2.11 (m, 2H), 1.32 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 153.4, 153.3, 145.3, 142.3, 141.9, 134.5, 128.7, 128.5, 127.9, 127.7, 127.3, 127.2, 126.9, 126.5, 126.2, 126.1, 125.6, 125.1, 124.6, 124.5, 122.2, 120.5, 106.4, 83.4, 78.1, 73.9, 72.5, 61.9, 53.4, 47.1, 39.7, 37.2, 14.0; **IR** (neat) ν 3055, 2926, 2837, 2220, 1707, 1579, 1453, 1243, 1092, 702 cm^{-1}; **HRMS** (DART) Calcd for $C_{36}H_{34}NO_3S$ (MH^+): 560.2254; found: 560.2239.

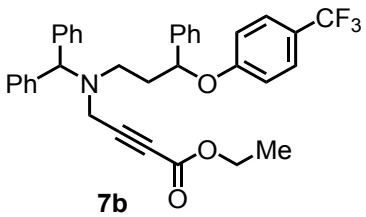


3p

Ethyl 4-(benzhydryl(4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydronaphthalen-1-yl)amino)but-2-ynoate (3p)

N-Benzhydryl-4-(3,4-dichlorophenyl)-*N*-methyl-1,2,3,4-tetrahydronaphthalen-1-amine **1p** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure B** using 1,2-bis(diphenylphosphino)ethane as the ligand. After purification by column chromatography (Et_2O:hexanes = 1:19), **3p** was obtained as a colorless liquid (76 mg, 67%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.1 Hz, 1H), 7.72 – 7.56 (m, 4H), 7.42 – 7.07 (m, 10H), 6.85 (dd, *J* = 69.9, 8.1 Hz, 2H), 5.31 – 5.17 (m, 1H), 4.28 – 4.11 (m, 3H), 4.05 (s, 1H), 3.53 (s, 2H), 2.06 (t, *J* = 12.1 Hz, 1H), 2.00 – 1.75 (m, 3H), 1.27 (t, *J* = 7.1, 3.2 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 153.3, 147.2, 142.24, 142.18, 139.1, 138.6, 132.2, 130.7, 130.04, 129.99, 129.87, 128.8, 128.74, 128.70, 128.5, 128.3, 128.2, 128.1, 127.93, 127.91, 127.58, 127.56, 127.45, 127.38, 127.3, 127.2, 127.0, 86.3, 77.5, 69.1, 61.7, 57.8, 43.4, 36.2, 30.3, 17.5, 13.9; **IR** (neat) ν 3023, 2931, 2860, 2221, 1706, 1592, 1459, 1241, 1117, 1052 cm^{-1}; **HRMS** (DART) Calcd for $C_{35}H_{32}NO_2Cl_2$ (MH^+): 568.1805; found: 568.1799.

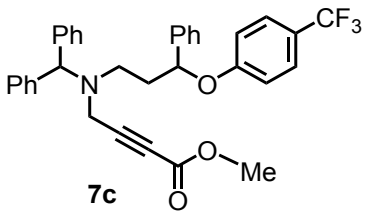


7b

Ethyl 4-(benzhydryl(3-phenyl-3-(4-(trifluoromethyl)phenoxy)propyl)amino)but-2-ynoate (7b)

N-Benzhydryl-*N*-methyl-3-phenyl-3-(4-(trifluoromethyl)phenoxy)propan-1-amine **1q** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure B** using 1,2-bis(diphenylphosphino)ethane as the ligand. After purification by column chromatography (Et_2O:hexanes = 1:19), **7b** was obtained as a colorless liquid (94 mg, 82%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 – 7.39 (m, 4H), 7.35 – 7.22 (m, 10H), 7.18 (tt, J = 7.4, 1.5 Hz, 1H), 7.14 – 7.04 (m, 3H), 6.83 – 6.77 (m, 2H), 5.28 – 5.19 (m, 1H), 4.67 (s, 1H), 4.26 (q, J = 7.2, 2.4 Hz, 2H), 3.64 – 3.50 (m, 2H), 2.88 – 2.78 (m, 1H), 2.78 – 2.68 (m, 1H), 2.19 – 2.08 (m, 1H), 2.04 – 1.94 (m, 1H), 1.34 (t, J = 7.2, 2.4 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.5, 153.4, 142.13, 142.08, 141.2, 128.8, 128.6, 128.5, 127.9, 127.8, 127.3, 127.1, 126.7 (d, J_{CF} = 3.3 Hz), 125.6, 124.4 (d, J_{CF} = 271.1 Hz), 122.7 (q, J_{CF} = 32.7 Hz), 115.7, 83.3, 78.0, 77.7, 72.5, 61.9, 46.9, 39.5, 36.8, 14.0; **^{19}F NMR** (470 MHz, $CDCl_3$) δ -61.53; **IR** (neat) ν 3028, 2930, 2834, 2221, 1708, 1612, 1513, 1451, 1324, 1246, 1114 cm^{-1}; **HRMS** (DART) Calcd for $C_{35}H_{33}NO_3F_3(MH^+)$: 572.2407; found: 572.2402.

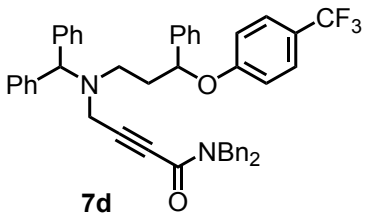


7c

Methyl 4-(benzhydryl(3-phenyl-3-(4-(trifluoromethyl)phenoxy)propyl)amino)but-2-ynoate (7c)

N-Benzhydryl-*N*-methyl-3-phenyl-3-(4-(trifluoromethyl)phenoxy)propan-1-amine **1q** was reacted with methyl 3-(trimethylsilyl)propiolate **2c** following **General Procedure B** using 1,2-bis(diphenylphosphino)ethane as the ligand. After purification by column chromatography (Et_2O:hexanes = 1:19), **7c** was obtained as a colorless liquid (76 mg, 68%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 – 7.37 (m, 4H), 7.36 – 7.21 (m, 9H), 7.18 (tt, *J* = 7.1, 1.5 Hz, 1H), 7.12 – 7.05 (m, 3H), 6.80 (d, *J* = 8.4 Hz, 2H), 5.23 (dd, *J* = 9.1, 3.6 Hz, 1H), 4.66 (s, 1H), 3.80 (s, 3H), 3.57 (d, *J* = 10.6 Hz, 2H), 2.88 – 2.67 (m, 2H), 2.20 – 1.95 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.5, 153.8, 142.11, 142.05, 141.2, 128.8, 128.7, 128.6, 127.9, 127.79, 127.75, 127.3, 127.2, 126.7 (d, J_{CF} = 3.8 Hz), 125.6, 124.4 (d, J_{CF} = 271.3 Hz), 122.7 (q, J_{CF} = 32.5 Hz), 115.7, 83.7, 77.7, 72.5, 53.4, 52.7, 46.9, 39.5, 36.8; **^{19}F NMR** (470 MHz, $CDCl_3$) δ -61.50; **IR** (neat) ν 3028, 2946, 2832, 2226, 1713, 1513, 1445, 1324, 1249, 1114 cm^{-1}; **HRMS** (DART) Calcd for $C_{34}H_{31}NO_3F_3$ (MH^+): 558.2251; found: 558.2246.

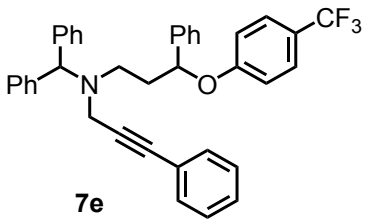


7d

4-(Benzhydryl(3-phenyl-3-(4-(trifluoromethyl)phenoxy)propyl)amino)-*N*,*N*-dibenzylbut-2-ynamide (7d)

N-Benzhydryl-*N*-methyl-3-phenyl-3-(4-(trifluoromethyl)phenoxy)propan-1-amine **1q** was reacted with *N,N*-dibenzyl-3-(trimethylsilyl)propiolamide **2d** following **General Procedure B** using (*S*)-PhPyBOX as the ligand. After purification by column chromatography (Et_2O:hexanes = 1:4), **7d** was obtained as a colorless liquid (116 mg, 80%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.0 Hz, 4H), 7.35 (t, *J* = 7.5 Hz, 3H), 7.31 (d, *J* = 6.8 Hz, 1H), 7.27 (d, *J* = 7.4 Hz, 4H), 7.23 (t, *J* = 9.3 Hz, 7H), 7.17 (t, *J* = 7.5 Hz, 2H), 7.15 – 7.10 (m, 3H), 7.06 (t, *J* = 7.3 Hz, 1H), 7.01 (t, *J* = 7.4 Hz, 2H), 6.75 (d, *J* = 8.4 Hz, 2H), 5.16 (dd, *J* = 9.0, 3.7 Hz, 1H), 4.78 – 4.65 (m, 2H), 4.55 (q, *J* = 14.8 Hz, 2H), 4.46 (s, 1H), 3.61 (q, *J* = 18.3 Hz, 2H), 2.75 – 2.57 (m, 2H), 2.13 – 1.90 (m, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 160.5, 154.7, 142.13, 142.06, 141.1, 136.2, 135.9, 129.0, 128.8, 128.7, 128.6, 128.5, 128.0, 127.8, 127.7, 127.6, 127.24, 127.20, 127.1, 126.6 (d, J_{CF} = 3.0 Hz), 125.6, 124.4 (d, J_{CF} = 271.1 Hz), 122.7 (q, J_{CF} = 32.7 Hz), 115.7, 87.7, 78.9, 77.7, 72.6, 51.3, 46.9, 46.5, 39.6, 36.9; **^{19}F NMR** (470 MHz, $CDCl_3$) δ -61.48; **IR** (neat) ν 3028, 2925, 2830, 2221, 1628, 1324, 1245, 1162, 1113, 700 cm^{-1}; **HRMS** (DART) Calcd for $C_{47}H_{42}N_2O_2F_3$ (MH^+): 723.3193; found: 723.3167.

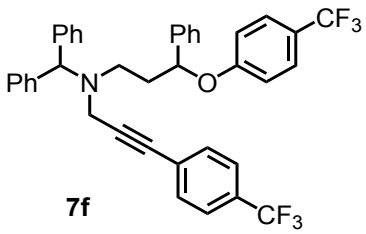


7e

***N*-Benzhydryl-3-phenyl-*N*-(3-phenyl-3-(4-(trifluoromethyl)phenoxy)propyl)prop-2-yn-1-amine (7e)**

N-Benzhydryl-*N*-methyl-3-phenyl-3-(4-(trifluoromethyl)phenoxy)propan-1-amine **1q** was reacted with trimethyl(phenylethynyl)silane **2e** following **General Procedure B** using (*S*)-PhPyBOX as the ligand. After purification by column chromatography (Et_2O:hexanes = 1:49), **7e** was obtained as a colorless liquid (86 mg, 75%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 – 7.38 (m, 6H), 7.37 – 7.14 (m, 13H), 7.08 (d, J = 6.6 Hz, 3H), 6.81 (d, J = 8.4 Hz, 2H), 5.30 (dd, J = 9.0, 3.8 Hz, 1H), 4.74 (s, 1H), 3.72 – 3.56 (m, 2H), 2.91 – 2.70 (m, 2H), 2.24 – 2.00 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.6, 142.8, 142.7, 141.4, 131.7, 128.7, 128.5, 128.4, 128.3, 128.1, 127.9, 127.7, 127.1, 126.9, 126.6 (d, J_{CF} = 3.1 Hz), 125.7, 124.5 (d, J_{CF} = 271.5 Hz), 123.3, 122.6 (q, J_{CF} = 32.6 Hz), 115.7, 85.9, 84.2, 77.9, 72.6, 46.7, 39.9, 36.9; **^{19}F NMR** (470 MHz, $CDCl_3$) δ -61.49; **IR** (neat) ν 3060, 2927, 2829, 2096, 1513, 1491, 1324, 1249, 1162, 1114, 698 cm^{-1}; **HRMS** (DART) Calcd for $C_{38}H_{33}NOF_3$ (MH^+): 576.2509; found: 576.2504.

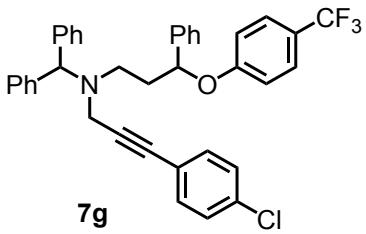


7f

***N*-Benzhydryl-*N*-(3-phenyl-3-(4-(trifluoromethyl)phenoxy)propyl)-3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-amine (7f)**

N-Benzhydryl-*N*-methyl-3-phenyl-3-(4-(trifluoromethyl)phenoxy)propan-1-amine **1q** was reacted with trimethyl((4-(trifluoromethyl)phenyl)ethynyl)silane **2f** following **General Procedure B** using (*S*)-PhPyBOX as the ligand. After purification by column chromatography (Et_2O:hexanes = 1:19), **7f** was obtained as a colorless liquid (106 mg, 82%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 8.4, 4.1 Hz, 2H), 7.48 (dd, *J* = 8.1, 4.1 Hz, 2H), 7.43 (ddd, *J* = 13.0, 8.0, 4.1 Hz, 4H), 7.35 (tt, *J* = 4.9, 2.2 Hz, 2H), 7.29 (d, *J* = 4.8 Hz, 4H), 7.28 – 7.22 (m, 3H), 7.19 (td, *J* = 7.1, 4.4 Hz, 1H), 7.10 (p, *J* = 5.2 Hz, 3H), 6.81 (dd, *J* = 9.0, 4.0 Hz, 2H), 5.30 (dt, *J* = 8.5, 4.0 Hz, 1H), 4.73 (d, *J* = 4.2 Hz, 1H), 3.73 – 3.60 (m, 2H), 2.97 – 2.70 (m, 2H), 2.25 – 2.00 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.6, 142.6, 142.5, 141.3, 132.4, 132.2 (d, J_{CF} = 293.4 Hz), 129.8 (q, J_{CF} = 32.6 Hz), 128.8, 128.6, 128.5, 128.0, 127.9, 127.8, 127.2, 127.1, 126.7 (d, J_{CF} = 2.9 Hz), 125.7, 125.2 (d, J_{CF} = 2.8 Hz), 124.2 (d, J_{CF} = 211.0 Hz), 122.7 (q, J_{CF} = 32.5 Hz), 115.7, 87.1, 84.6, 77.9, 72.6, 46.8, 40.0, 36.9; **^{19}F NMR** (470 MHz, $CDCl_3$) δ -61.45, -62.75; **IR** (neat) ν 3027, 2931, 2829, 1612, 1513, 1450, 1322, 1249, 1116, 701 cm^{-1}; **HRMS** (DART) Calcd for $C_{39}H_{32}NOF_6$ (MH^+): 644.2383; found: 644.2365.

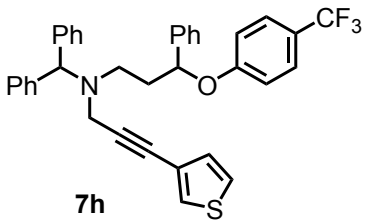


7g

***N*-Benzhydryl-3-(4-chlorophenyl)-*N*-(3-phenyl-3-(4-(trifluoromethyl)phenoxy)propyl)prop-2-yn-1-amine (7g)**

N-Benzhydryl-*N*-methyl-3-phenyl-3-(4-(trifluoromethyl)phenoxy)propan-1-amine **1q** was reacted with ((4-chlorophenyl)ethynyl)trimethylsilane **2g** following **General Procedure B** using (*S*)-PhPyBOX as the ligand. After purification by column chromatography (Et_2O:hexanes = 1:19), **7g** was obtained as a colorless liquid (98 mg, 80%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 – 7.37 (m, 4H), 7.29 (dddd, *J* = 22.3, 20.6, 9.1, 7.4 Hz, 13H), 7.18 (ddd, *J* = 7.4, 6.1, 1.4 Hz, 1H), 7.13 – 7.03 (m, 3H), 6.81 (d, *J* = 8.4 Hz, 2H), 5.29 (dd, *J* = 9.0, 3.8 Hz, 1H), 4.71 (s, 1H), 3.63 (q, *J* = 17.7 Hz, 2H), 2.93 – 2.65 (m, 2H), 2.25 – 1.97 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.6, 142.7, 142.5, 141.4, 134.0, 132.9, 128.7, 128.6, 128.53, 128.45, 128.0, 127.9, 127.7, 127.1, 127.0, 126.7 (d, J_{CF} = 2.6 Hz), 125.7, 124.4 (d, J_{CF} = 271.1 Hz), 122.6 (q, J_{CF} = 32.8 Hz), 121.8, 115.7, 85.3, 84.7, 77.9, 72.6, 46.7, 40.0, 36.9; **^{19}F NMR** (470 MHz, $CDCl_3$) δ -61.50; **IR** (neat) ν 3055, 2928, 2832, 2223, 1707, 1608, 1488, 1245, 1113, 701 cm^{-1}; **HRMS** (DART) Calcd for $C_{38}H_{32}NOF_3Cl$ (MH^+): 610.2119; found: 610.2125.

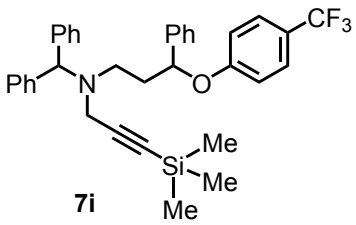


7h

***N*-Benzhydryl-*N*-(3-phenyl-3-(4-(trifluoromethyl)phenoxy)propyl)-3-(thiophen-3-yl)prop-2-yn-1-amine (7h)**

N-Benzhydryl-*N*-methyl-3-phenyl-3-(4-(trifluoromethyl)phenoxy)propan-1-amine **1q** was reacted with trimethyl(thiophen-3-ylethynyl)silane **2h** following **General Procedure B** using (*S*)-PhPyBOX as the ligand. After purification by column chromatography (Et_2O:hexanes = 1:49), **7h** was obtained as a colorless liquid (86 mg, 74%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 (dt, *J* = 8.9, 5.0 Hz, 4H), 7.38 (d, *J* = 2.9 Hz, 1H), 7.34 (dd, *J* = 6.2, 3.4 Hz, 2H), 7.29 (t, *J* = 3.4 Hz, 4H), 7.25 (ddq, *J* = 9.9, 7.1, 4.3, 3.5 Hz, 4H), 7.18 (dt, *J* = 7.8, 3.8 Hz, 1H), 7.08 (dt, *J* = 8.8, 4.2 Hz, 4H), 6.81 (dd, *J* = 8.8, 2.5 Hz, 2H), 5.30 (dd, *J* = 9.1, 3.9 Hz, 1H), 4.72 (s, 1H), 3.62 (q, *J* = 17.8 Hz, 2H), 2.80 (ddt, *J* = 50.2, 12.0, 6.5 Hz, 2H), 2.12 (dt, *J* = 55.1, 12.1 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 160.6, 142.7, 142.6, 141.4, 130.0, 128.7, 128.5, 128.4, 128.3, 128.0, 127.9, 127.7, 127.1, 126.9, 126.7 (d, J_{CF} = 3.6 Hz), 124.7 (d, J_{CF} = 267.9 Hz), 125.7, 122.6 (d, J_{CF} = 32.9 Hz), 122.3, 115.7, 83.8, 80.8, 77.8, 72.5, 46.6, 39.9, 36.9; **^{19}F NMR** (470 MHz, $CDCl_3$) δ -61.41; **IR** (neat) ν 3026, 2929, 2829, 2166, 1514, 1450, 1324,1249, 1114, 700 cm^{-1}; **HRMS** (DART) Calcd for $C_{36}H_{31}NOF_3S$ (MH^+): 582.2073; found: 582.2074.

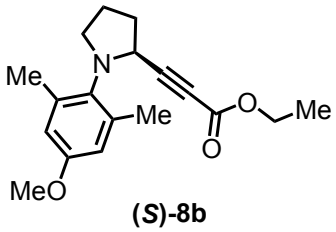


7i

***N*-Benzhydryl-*N*-(3-phenyl-3-(4-(trifluoromethyl)phenoxy)propyl)-3-(trimethylsilyl)prop-2-yn-1-amine (7i)[21]**

N-Benzhydryl-*N*-methyl-3-phenyl-3-(4-(trifluoromethyl)phenoxy)propan-1-amine **1q** was reacted with 1,2-bis(trimethylsilyl)ethyne **2i** following **General Procedure B** using (*S*)-PhPyBOX as the ligand. After purification by column chromatography (Et_2O:hexanes = 1:19), **7i** was obtained as a colorless liquid (99 mg, 87%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 (dd, *J* = 20.0, 8.2 Hz, 4H), 7.32 – 7.27 (m, 6H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 7.5 Hz, 2H), 7.10 – 7.05 (m, 3H), 6.80 (d, *J* = 8.4 Hz, 2H), 5.25 (dd, *J* = 9.2, 3.4 Hz, 1H), 4.64 (s, 1H), 3.42 (q, *J* = 17.9 Hz, 2H), 2.80 – 2.66 (m, 2H), 2.13 – 1.98 (m, 2H), 0.20 (s, 9H); **^{13}C** NMR;[21] ^{19}F **NMR** (470 MHz, $CDCl_3$) δ -61.50; **IR** (neat) ν 3059, 2951, 2848, 2160, 1612, 1324, 1250, 1116, 840, 700 cm^{-1}; **HRMS** (DART) Calcd for $C_{35}H_{37}NOF_3Si(MH^+)$: 572.2591; found: 572.2579.



(*S*)-8b

Ethyl (*S*)-3-(1-(4-methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propiolate ((*S*)-8b)

1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine **1b** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure C**. After purification by column chromatography (Et_2O:hexanes = 1:19), **(*S*)-8b** was obtained as a colorless liquid (45 mg, 75%). The absolute configuration of **(*S*)-8b** was assigned as (*S*) as described in SI Section 4.

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.58 (s, 2H), 4.27 (ddd, *J* = 7.8, 3.5, 1.3 Hz, 1H), 4.17 (qd, *J* = 7.2, 1.3 Hz, 2H), 3.75 (s, 3H), 3.43 – 3.31 (m, 1H), 3.09 (q, *J* = 6.9 Hz, 1H), 2.47 – 2.22 (m, 6H), 2.22 – 2.10 (m, 3H), 2.09 – 1.94 (m, 1H), 1.27 (td, *J* = 7.2, 1.4 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.2, 153.3, 136.6, 113.2, 91.5, 73.9, 63.3, 55.9, 52.3, 51.0, 35.8, 26.7, 18.4, 15.1; **IR** (neat) ν 2967, 2837, 2224, 1707, 1599, 1476, 1366,1244, 1153, 1067, cm^{-1}; **HRMS** (DART) Calcd for $C_{18}H_{24}NO_3$ (MH^+): 302.1751; found: 302.1755; $[\alpha]^{25}_D$ = 76.2° (*c* 1.0, CH_2Cl_2); **HPLC** (Chiralcel OJ-H; 95:5 hexane:isopropanol, 1.0 mL/min; **(*S*)-8b:** tr = 6.5 min (major), 9.5 min (minor); 95:5 er.

```
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Acq. Instrument : Wasa_LC1                         Location :   52
Injection Date  : 12/12/2019 7:06:12 PM                Inj :   1
                                                 Inj Volume : 4.000 µl
Method          : C:\Chem32\1\Data\JOE 2019-12-12 19-05-00\column4 5%IPA 95% hexane 30min-1.
                  0mL.M (Sequence Method)
Last changed    : 12/12/2019 7:05:05 PM by SYSTEM
Method Info     : Column4 60min-1% iPrOH 99% hexane-1.0mL
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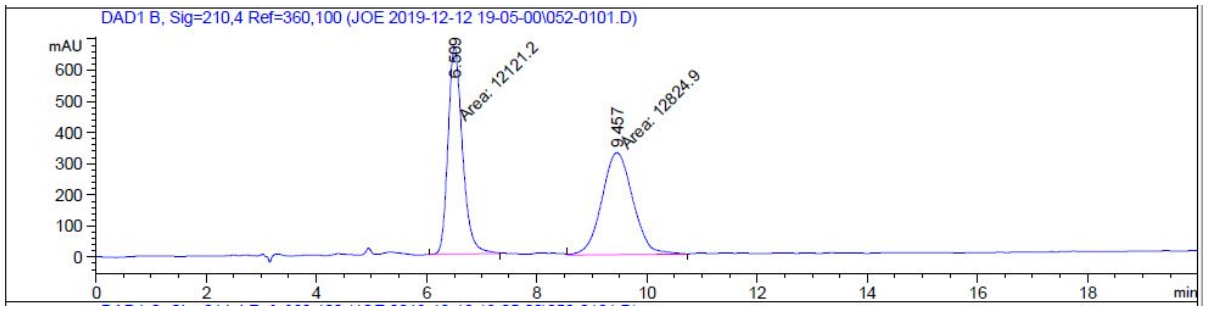
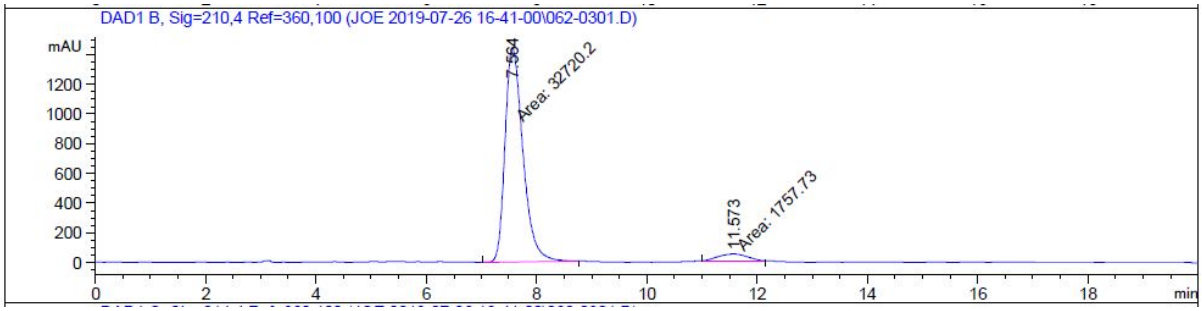


Signal 2: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.509	MM	0.3045	1.21212e4	663.55304	48.5896
2	9.457	MM	0.6531	1.28249e4	327.28235	51.4104

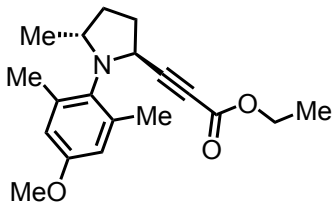
==========

Acq. Operator : SYSTEM Seq. Line : 3
Acq. Instrument : Wasa_LC1 Location : 62
Injection Date : 7/26/2019 5:44:53 PM Inj : 1
Inj Volume : 4.000 µl
Method : C:\Chem32\1\Data\JOE 2019-07-26 16-41-00\column4 5%IPA 95% hexane 30min-1.0mL.M (Sequence Method)
Last changed : 7/26/2019 4:41:04 PM by SYSTEM
Method Info : Column4 60min-1% iPrOH 99% hexane-1.0mL



Signal 2: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.564	MM	0.3774	3.27202e4	1445.16772	94.9019
2	11.573	MM	0.6270	1757.73438	46.72317	5.0981



8c

Ethyl 3-((2*S*,5*R*)-1-(4-methoxy-2,6-dimethylphenyl)-5-methylpyrrolidin-2-yl)propiolate (8c)

1-(4-Methoxy-2,6-dimethylphenyl)-2-methylpyrrolidine ***rac*-1r** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure C**. The *trans*:*cis* ratio was determined to be 6.3:1 by ^{1}H NMR analysis of the unpurified reaction mixtures. After purification by column chromatography (Et_2O:hexanes = 1:19), **8c** was obtained as a yellow oil (42 mg, 66%). The relative configuration of **8c** was assigned by NOESY analysis as described in SI Section 3.

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.58 (d, *J* = 1.2 Hz, 2H), 4.37 (dd, *J* = 7.7, 4.1 Hz, 1H), 4.15 (qd, *J* = 7.1, 0.8 Hz, 2H), 3.84 (q, *J* = 6.1 Hz, 1H), 3.76 (s, 3H), 2.43 – 2.37 (m, 1H), 2.36 (s, 3H), 2.32 – 2.25 (m, 1H), 2.19 (s, 3H), 2.09 – 2.02 (m, 1H), 1.61 – 1.55 (m, 1H), 1.25 (d, *J* = 0.9 Hz, 3H), 0.86 (d, *J* = 6.2 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.8, 153.8, 140.2, 139.7, 133.6, 113.9, 113.2, 91.0, 74.6, 61.7, 55.2, 55.1, 52.2, 33.2, 31.4, 20.3, 19.9, 19.0, 14.0; **IR** (neat) ν 2956, 2222, 1705, 1597, 1471, 1368, 1234, 1152, 1065, 852 cm^{-1}; **HRMS** (DART) Calcd for $C_{19}H_{26}NO_3$ (MH^+): 316.1907; found: 316.1905; $[\alpha]^{25}_D$ = 12.1° (*c* 0.3, CH_2Cl_2); **HPLC** (Chiralpak AD-H; 99.7:0.3 hexane:isopropanol, 0.3 mL/min; **8c:** tr = 36.9 min (minor), 46.7 min (major); 83:17 er.

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Sample ID	: 8b_rac1_aMe_f6_AD-H_inst4_0.3mL		
Data Filename	: 8b_rac1_aMe_f6_AD-H_inst4_0.3mL_3.lcd		
Method Filename	: 99.7_0.3_60min_0.3mL.lcm		
Batch Filename	: batch9.lcb		
Vial #	: 1-20	Sample Type	: Unknown
Injection Volume	: 30 uL		
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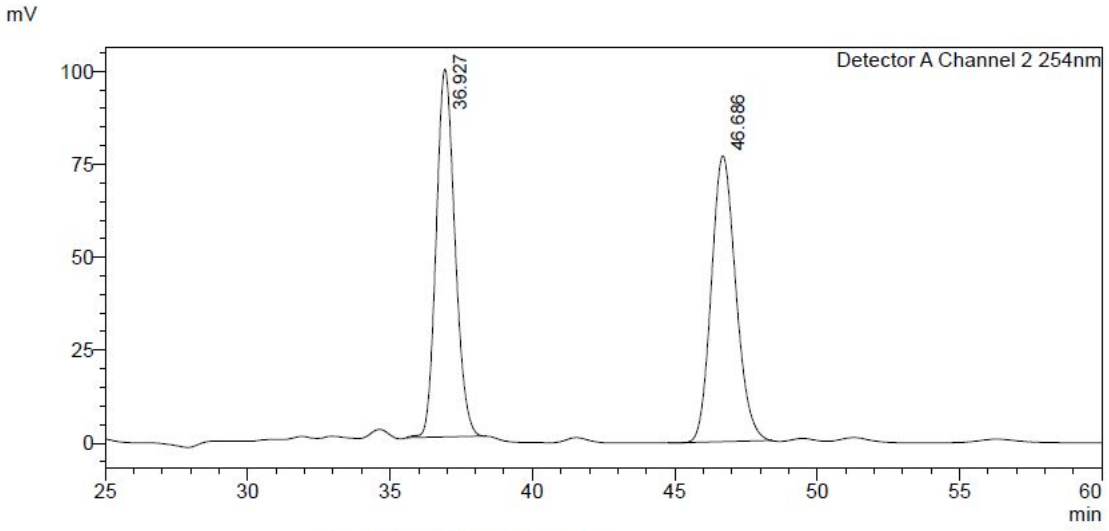
Date Processed	: 2/13/2020 11:43:41 PM	Processed by	: System Administrator



Detector A Channel 2 254nm

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2	46.686	4589671	50.359
Total		9113925	100.000

Sample Name	: 8b_ee2_JZC2264_f9_AD-H_inst4_0.3mL		
Sample ID	: 8b_ee2_JZC2264_f9_AD-H_inst4_0.		
Data Filename	: 8b_ee2_JZC2264_f9_AD-H_inst4_0.3mL.lcd		
Method Filename	: 99.7_0.3_60min_0.3mL.lcm		
Batch Filename	: batch9.lcb		
Vial #	: 1-21	Sample Type	: Unknown
Injection Volume	: 20 uL		
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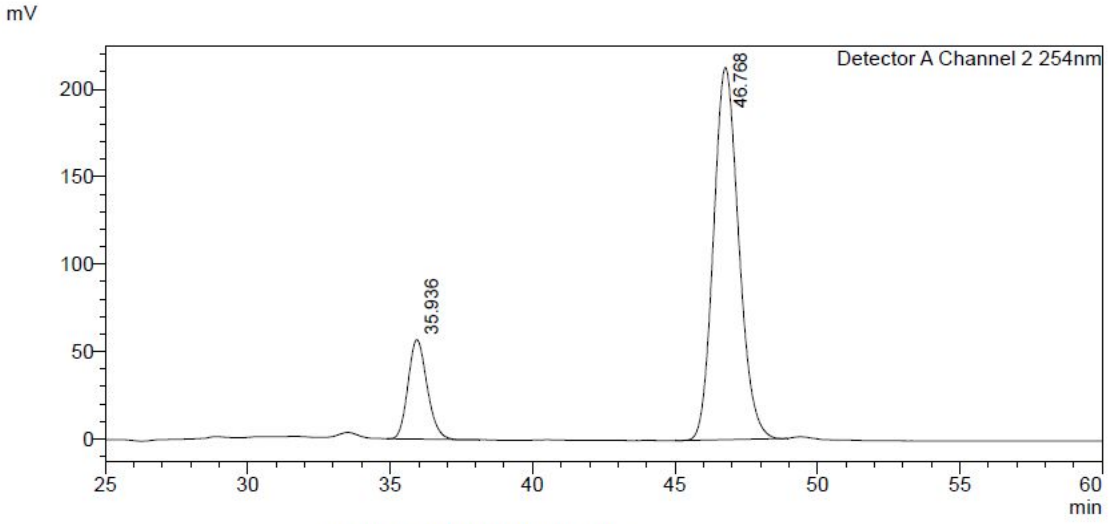
Date Processed	: 2/13/2020 8:34:17 PM	Processed by	: System Administrator



Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
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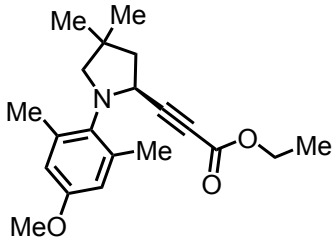
2	46.768	13116228	83.186
Total		15767359	100.000



8d

Ethyl (*S*)-3-(1-(4-methoxy-2,6-dimethylphenyl)-4,4-dimethylpyrrolidin-2-yl)propiolate (8d)

1-(4-Methoxy-2,6-dimethylphenyl)-3,3-dimethylpyrrolidine **1c** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure C**. After purification by column chromatography (Et_2O:hexanes = 1:19), **8d** was obtained as a yellow oil (45 mg, 69%). The absolute configuration of **8d** was assigned in analogy to **(*S*)-8b** (see SI Section 4).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.57 (s, 2H), 4.41 (dd, J = 9.0, 3.8 Hz, 1H), 4.15 (q, J = 7.1 Hz, 2H), 3.75 (s, 3H), 3.07 (d, J = 7.9 Hz, 1H), 2.95 (d, J = 7.8 Hz, 1H), 2.37 (s, 5H), 2.19 (dd, J = 12.5, 9.0 Hz, 2H), 1.98 (dd, J = 12.5, 3.9 Hz, 1H), 1.37 (s, 3H), 1.26 (t, J = 7.2 Hz, 3H), 1.15 (d, J = 1.0 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.2, 153.8, 135.4, 113.7, 91.0, 74.3, 64.5, 61.6, 55.2, 51.9, 47.0, 39.1, 27.8, 27.2, 14.0; **IR** (neat) ν 2954, 2864, 2228, 1707, 1601, 1465, 1243, 1094, 1023, 751 cm^{-1}; **HRMS** (DART) Calcd for $C_{20}H_{28}NO_3$ (MH^+): 330.2063; found: 330.2069; $[\alpha]^{25}_D$ = 20.5° (*c* 0.3, CH_2Cl_2); **HPLC** (Chiralpak AY-3; 99.9:0.1 hexane:isopropanol, 0.3 mL/min; **8d:** tr = 27.4 min (major), 38.1 min (minor); 93:7 er.

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Data Filename	: 8c_rac5_JZC2152A_n2n1_AY-3_2-10.lcd		
Method Filename	: 99.9_0.1_60min_0.3mL.lcm		
Batch Filename	: batch8.lcb		
Vial #	: 1-24	Sample Type	: Unknown
Injection Volume	: 10 uL		
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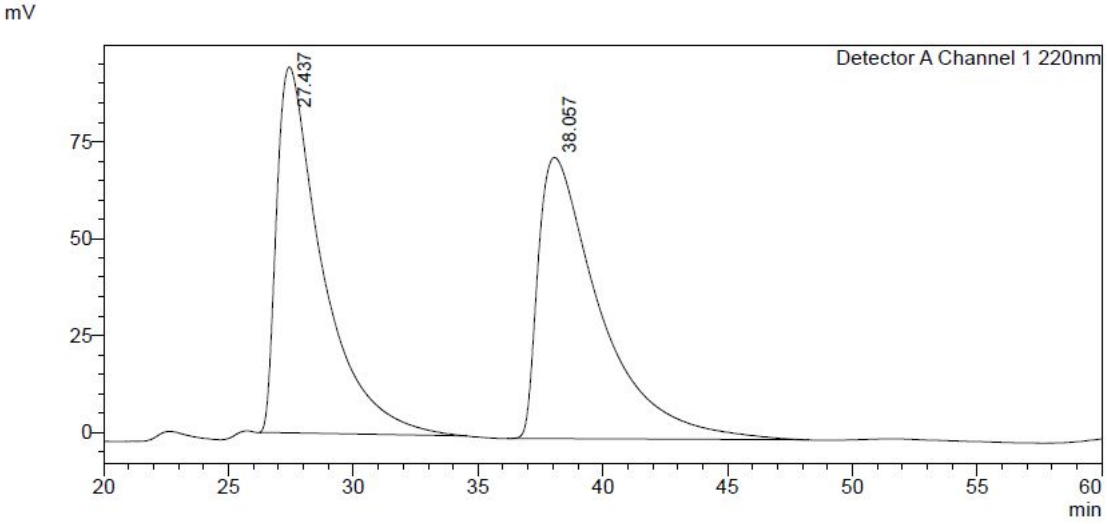
Date Processed	: 2/11/2020 10:17:04 AM	Processed by	: System Administrator



Detector A Channel 1 220nm

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2	38.057	12512111	51.047
Total		24511111	100.000

Sample Name	: 8c_ee4_JZC2101A_AY-3_2-10		
Sample ID	: 8c_ee4_JZC2101A_AY-3_2-10		
Data Filename	: 8c_ee4_JZC2101A_AY-3_2-10.lcd		
Method Filename	: 99.9_0.1_60min_0.3mL.lcm		
Batch Filename	: batch8.lcb		
Vial #	: 1-25	Sample Type	: Unknown
Injection Volume	: 4 uL		
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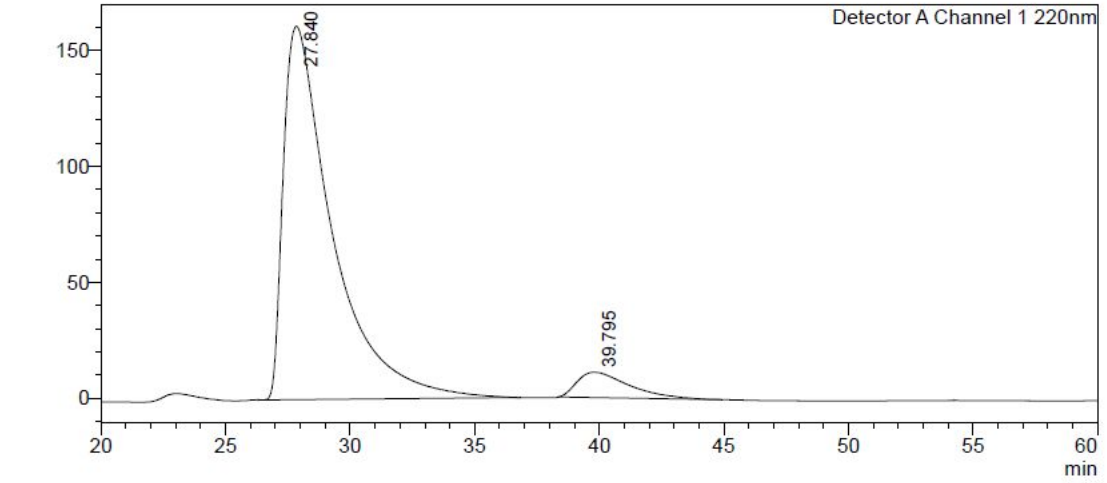
Date Processed	: 2/12/2020 4:33:05 PM	Processed by	: System Administrator



Detector A Channel 1 220nm

Peak#	Ret. Time	Area	Area%
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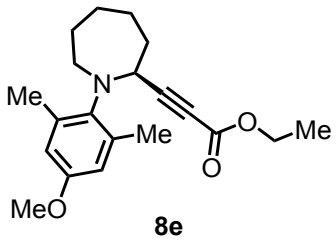
Total		23599165	100.000



8e

Ethyl (*S*)-3-(1-(4-methoxy-2,6-dimethylphenyl)azepan-2-yl)propiolate (8e)

1-(4-Methoxy-2,6-dimethylphenyl)azepane **1d** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure C**. After purification by column chromatography (Et_2O:hexanes = 1:19), **8e** was obtained as a colorless liquid (42 mg, 64%). The absolute configuration of **8e** was assigned in analogy to **(*S*)-8b** (see SI Section 4).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (d, J = 13.4 Hz, 2H), 4.18 (d, J = 7.1 Hz, 2H), 4.06 (d, J = 2.7 Hz, 1H), 3.75 (s, 3H), 3.32 (d, J = 9.1 Hz, 1H), 3.08 (d, J = 11.1 Hz, 1H), 2.42 (s, 3H), 2.29 (s, 3H), 2.19 (d, J = 1.5 Hz, 1H), 1.95 – 1.85 (m, 2H), 1.85 – 1.79 (m, 1H), 1.79 – 1.70 (m, 2H), 1.57 (s, 2H), 1.28 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.4, 153.8, 140.9, 139.7, 137.9, 114.1, 113.6, 90.3, 75.6, 59.4, 55.6, 53.0, 51.3, 34.8, 31.4, 28.9, 25.2, 20.1, 19.6, 14.0; **IR** (neat) ν 2926, 2845, 2221, 1707, 1598, 1474, 1309, 1240, 1065, 853 cm^{-1}; **HRMS** (DART) Calcd for $C_{20}H_{28}NO_3$ (MH^+): 330.2063; found: 330.2061; $[\alpha]^{25}_D$ = 30.1° (c 1.0, CH_2Cl_2); **HPLC** (Chiralcel OJ-H; 98.5:1.5 hexane:isopropanol, 0.5 mL/min; **8e:** tr = 14.8 min (major), 17.4 min (minor); 95:5 er.

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                                                 Inj Volume : 4.000 µl
Acq. Method     : C:\Chem32\1\Data\JOE 2019-06-06 11-04-24\column4 1.5%IPA 98.5% hexane 60min
                  -0.5mL.M
Last changed    : 6/6/2019 11:04:28 AM by SYSTEM
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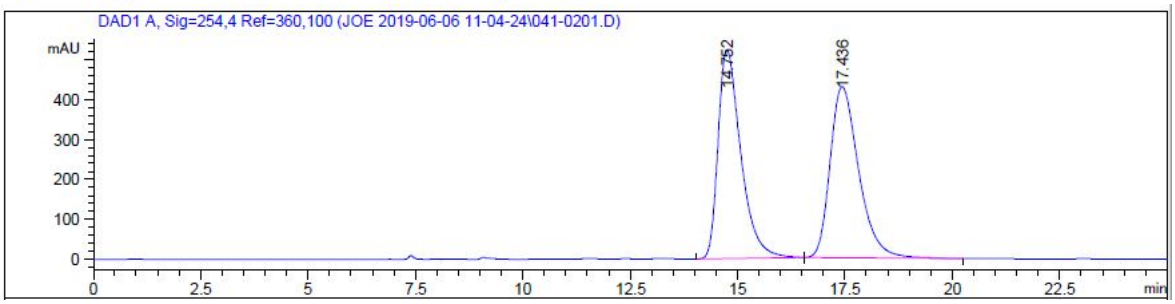

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.752	BB	0.5570	1.92070e4	522.36609	49.2058
2	17.436	BB	0.7122	1.98270e4	428.21890	50.7942

Acq. Operator : SYSTEM
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Inj : 1
Inj Volume : 4.000 µl
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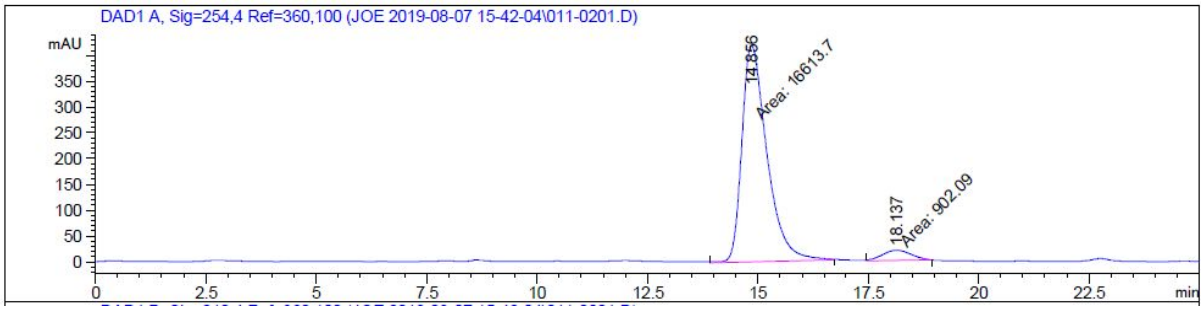
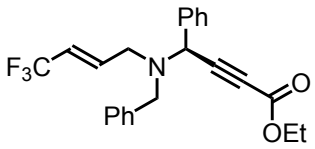
Last changed : 8/7/2019 3:42:08 PM by SYSTEM



Signal 2: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.856	MM	0.6745	9.39466e4	2321.40063	95.4662
2	18.137	MM	0.6770	4461.63379	109.84474	4.5338



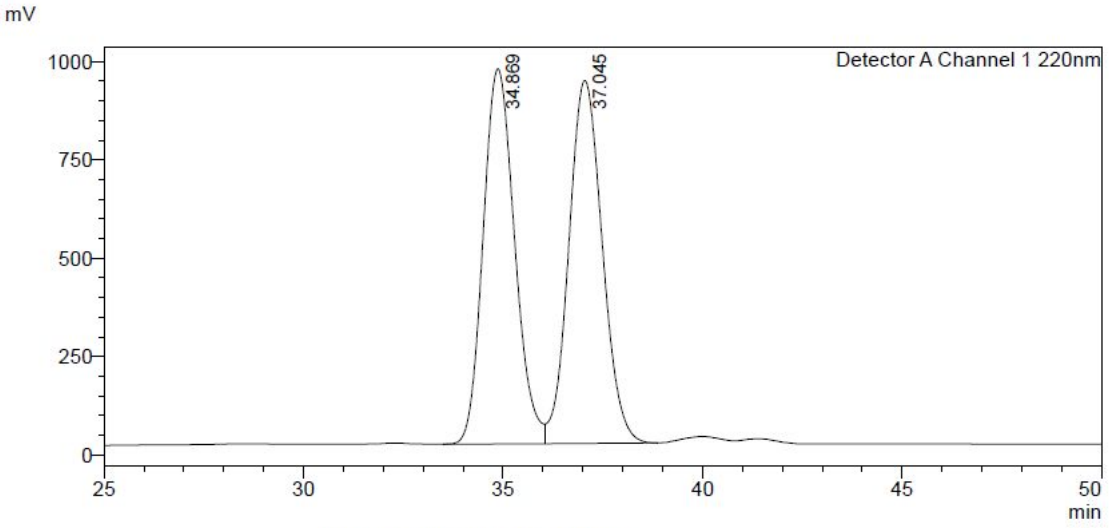
8f

Ethyl (*S,E*)-4-(benzyl(4,4,4-trifluorobut-2-en-1-yl)amino)-4-phenylbut-2-ynoate (8f)

(*E*)-*N,N*-Dibenzyl-4,4,4-trifluorobut-2-en-1-amine **1s** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure C** using (*S*)-PhPyBOX as the ligand. After purification by column chromatography (Et_2O:hexanes = 1:19), **8f** was obtained as a colorless liquid (36 mg, 45%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 (dt, *J* = 8.1, 1.1 Hz, 2H), 7.40 – 7.31 (m, 7H), 7.31 – 7.25 (m, 1H), 6.33 (dddd, *J* = 15.8, 7.5, 4.2, 2.1 Hz, 1H), 5.94 – 5.84 (m, 1H), 4.87 (s, 1H), 4.32 (q, *J* = 7.1 Hz, 2H), 3.83 (d, *J* = 13.5 Hz, 1H), 3.54 (d, *J* = 13.5 Hz, 1H), 3.28 (dq, *J* = 15.6, 3.2 Hz, 1H), 3.21 – 3.14 (m, 1H), 1.38 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 153.4, 138.1, 138.03, 137.99, 137.95, 137.93, 136.5, 128.84, 128.81, 128.68, 128.65, 128.60, 128.57, 128.5, 128.42, 128.36, 128.3, 128.2, 128.0, 127.9, 127.6, 127.21, 127.16, 123.7, 121.9, 120.7, 120.5, 120.3, 120.0, 82.8, 80.5, 62.3, 58.3, 56.3, 55.4, 53.5, 50.6, 14.1; **^{19}F NMR** (564 MHz, $CDCl_3$) δ -64.07, -64.08, -64.08, -64.09, -64.09, -64.10; **IR** (neat) ν 2925, 2222, 1711, 1492, 1450, 1242, 1119, 749, 698 cm^{-1}; **HRMS** (DART) Calcd for $C_{23}H_{23}NO_2F_3$ (MH^+): 402.1675; found: 402.1667; $[\alpha]^{25}_D$ = –45.3° (*c* 1.0, CH_2Cl_2); **HPLC** (Chiralcel AD-H; 99.5:0.5 hexane:isopropanol, 0.3 mL/min; **8f:** tr = 34.9 min (minor), 37.0 min (major); 84:16 er.

Sample Name	: 8e_rac3_JZC2017H2_AD-H_0.3mL		
Sample ID	: 8e_rac3_JZC2017H2_AD-H_0.3mL		
Data Filename	: 8e_rac3_JZC2017H2_AD-H_0.3mL.lcd		
Method Filename	: 995_05_60min_03mL.lcm		
Batch Filename	: batch9.lcb		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 4 uL		
Date Acquired	: 2/9/2020 5:43:00 PM	Acquired by	: System Administrator
Date Processed	: 2/10/2020 9:51:53 AM	Processed by	: System Administrator



Detector A Channel 1 220nm

Peak#	Ret. Time	Area	Area%
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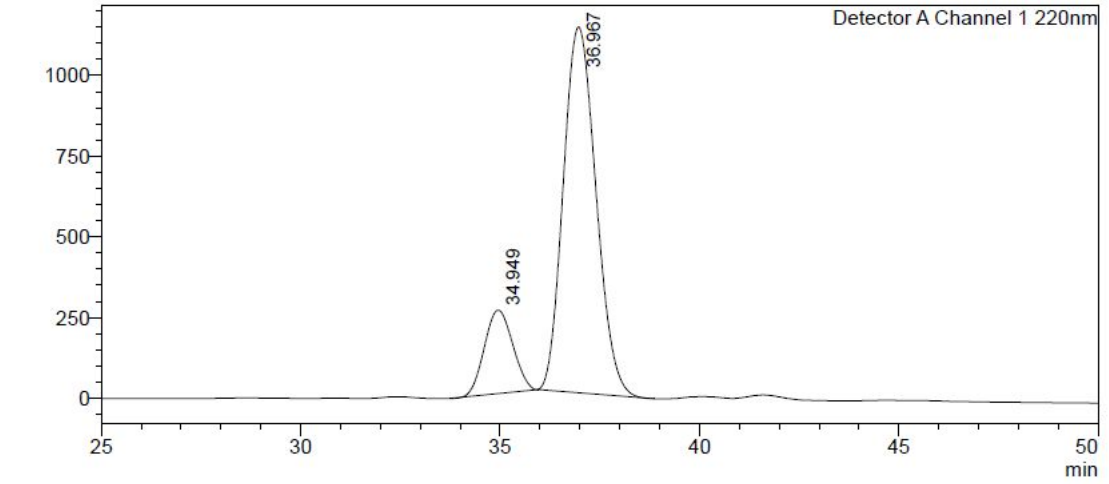
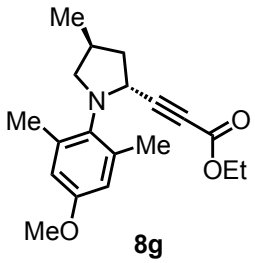
2	37.045	53800949	50.728
Total		106058696	100.000

Sample Name	: 8e_ee3_JZC2187BC_n1n1_AD-H_0.3mL		
Sample ID	: 8e_ee3_JZC2187BC_n1n1_AD-H_0.3m		
Data Filename	: 8e_ee3_JZC2187BC_n1n1_AD-H_0.3mL.lcd		
Method Filename	: 995_05_60min_03mL.lcm		
Batch Filename	: batch9.lcb		
Vial #	: 1-5	Sample Type	: Unknown
Injection Volume	: 4 uL		
Date Acquired	: 2/9/2020 6:43:34 PM	Acquired by	: System Administrator
Date Processed	: 2/10/2020 9:40:28 AM	Processed by	: System Administrator



Detector A Channel 1 220nm

Peak#	Ret. Time	Area	Area%
1	34.949	12756097	16.485
2	36.967	64623088	83.515
Total		77379185	100.000



8g

Ethyl 3-((2*R*,4*S*)-1-(4-methoxy-2,6-dimethylphenyl)-4-methylpyrrolidin-2-yl)propiolate (8g)

(*S*)-1-(4-Methoxy-2,6-dimethylphenyl)-3-methylpyrrolidine **(*S*)-1t** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure C**. The *trans*:*cis* ratio was determined to be 11.8:1 by ^{1}H NMR analysis of the unpurified reaction mixtures. After purification by column chromatography (Et_2O:hexanes = 1:19), **8g** was obtained as a colorless liquid (40 mg, 64%). The relative configuration of **8g** was assigned by NOESY, COSY, and HSQC analysis (see SI Section 3).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.58 (s, 2H), 4.29 (dd, *J* = 8.6, 1.8 Hz, 1H), 4.17 (qd, *J* = 7.1, 1.0 Hz, 2H), 3.75 (d, *J* = 1.0 Hz, 3H), 3.38 (t, *J* = 7.2 Hz, 1H), 2.74 (dd, *J* = 8.8, 7.8 Hz, 1H), 2.71 – 2.62 (m, 1H), 2.42 – 2.18 (m, 7H), 2.03 – 1.94 (m, 1H), 1.27 (td, *J* = 7.1, 0.9 Hz, 3H), 1.11 (dd, *J* = 6.5, 0.9 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.1, 153.9, 135.8, 113.6, 91.2, 74.1, 61.7, 58.4, 55.2, 52.7, 41.6, 33.6, 18.8, 17.3, 14.0; **IR** (neat) ν 2954, 2924, 1708, 1601, 1484, 1465, 1244, 1154, 1066 cm^{-1}; **HRMS** (DART) Calcd for $C_{19}H_{26}NO_3$ (MH^+): 316.1907; found: 316.1904; $[\alpha]^{25}_D$ = 63.0° (*c* 0.2, CH_2Cl_2); **HPLC** (Chiralpak IA; 97.5:2.5 hexane:isopropanol, 0.2 mL/min; **8g:** tr = 23.0 min (major), 24.0 min (minor); 97:3 er.

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                                                  Inj Volume : 4.000 µl
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                  -0.2mL.M
Last changed    : 2/13/2020 5:34:32 PM by SYSTEM
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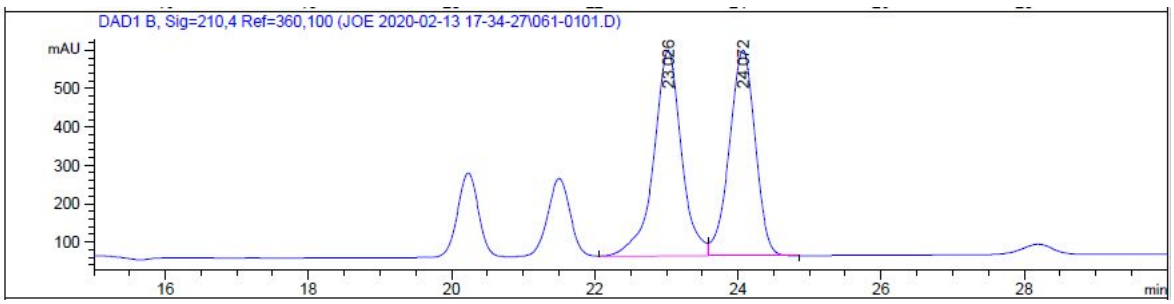
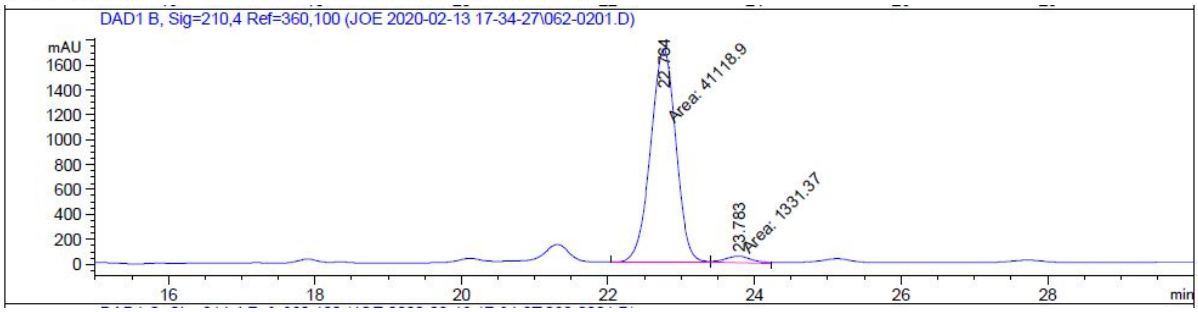


Signal 2: DAD1 B, Sig=210,4 Ref=360,100

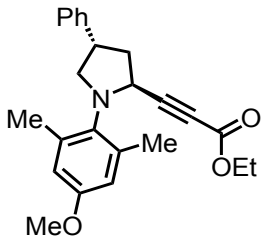
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.026	VV	0.4035	1.44252e4	536.82739	51.7382
2	24.072	VB	0.3885	1.34559e4	536.65869	48.2618

Acq. Operator : SYSTEM
Seq. Line : 2
Acq. Instrument : Wasa_LC1
Location : 62
Injection Date : 2/13/2020 6:16:42 PM
Inj : 1
Inj Volume : 4.000 µl
Acq. Method : C:\Chem32\1\Data\JOE 2020-02-13 17-34-27\column6 2.5%IPA 97.5% hexane 40min -0.2mL.M
Last changed : 2/13/2020 5:34:32 PM by SYSTEM



Signal 2: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.764	MM	0.3995	4.11189e4	1715.43152	96.8637
2	23.783	MM	0.4273	1331.37109	51.93531	3.1363



8h

Ethyl 3-((2*S*,4*S*)-1-(4-methoxy-2,6-dimethylphenyl)-4-phenylpyrrolidin-2-yl)propiolate (8h)

(*S*)-1-(4-Methoxy-2,6-dimethylphenyl)-3-phenylpyrrolidine **(*S*)-1u** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure C**. The *trans*:*cis* ratio was determined to be 10.1:1 by ^{1}H NMR analysis of the unpurified product mixtures. After purification by column chromatography (Et_2O:hexanes = 1:19), **8h** was obtained as a colorless liquid (51 mg, 68%). The absolute and relative configuration of **8h** was assigned in analogy to **8g** (see SI Section 3).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 (t, *J* = 7.6 Hz, 2H), 7.31 – 7.27 (m, 2H), 7.24 (dt, *J* = 6.8, 1.7 Hz, 1H), 6.61 (s, 2H), 4.44 (dd, *J* = 7.3, 2.8 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.84 (ddd, *J* = 17.7, 10.2, 7.5 Hz, 1H), 3.76 (s, 3H), 3.64 (t, *J* = 7.6 Hz, 1H), 3.25 (dd, *J* = 10.0, 8.0 Hz, 1H), 2.56 – 2.50 (m, 2H), 2.50 – 2.14 (m, 6H), 1.29 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ157.4, 153.9, 141.1, 135.5, 128.6, 127.9, 127.2, 126.7, 113.7, 90.6, 74.4, 61.8, 57.7, 55.2, 52.9, 44.1, 40.5, 18.9, 14.0; **IR** (neat) ν 2196, 2847, 2226, 1701,1601, 1485, 1243, 1153, 1037, 699 cm^{-1}; **HRMS** (DART) Calcd for $C_{24}H_{28}NO_3$ (MH^+): 378.2064; found: 378.2063; $[\alpha]^{25}_D$ = –25.5° (*c* 0.6, CH_2Cl_2); **HPLC** (Chiralpak AY-3; 99.5:0.5 hexane:isopropanol, 0.5 mL/min; **8h:** tr = 14.9 min (minor), 21.6 min (major); 88:12 er.

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Sample ID	: 8g_rac1_JZC2137C_n1_AY-3_2		
Data Filename	: 8g_rac1_JZC2137C_n1_AY-3_2.lcd		
Method Filename	: 995_05_40min_05mL.lcm		
Batch Filename	: batch8.lcb		
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Injection Volume	: 10 uL		
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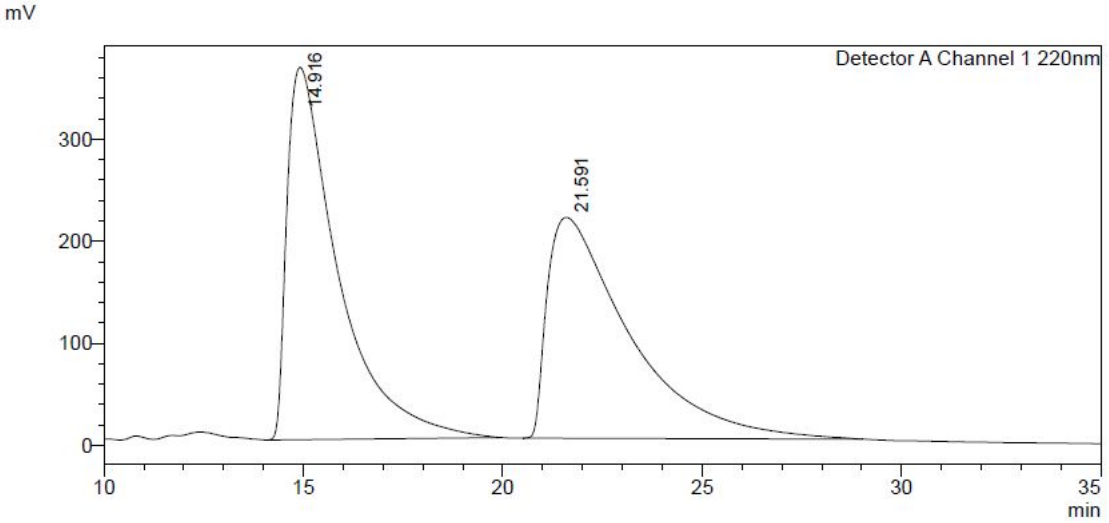
Date Processed	: 2/12/2020 4:14:36 PM	Processed by	: System Administrator



Detector A Channel 1 220nm

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2	21.591	31028467	48.950
Total		63388699	100.000

Sample Name	: 8g_ee2_JZC2194B_AY-3_4		
Sample ID	: 8g_ee2_JZC2194B_AY-3_4		
Data Filename	: 8g_ee2_JZC2194B_AY-3_4.lcd		
Method Filename	: 995_05_40min_05mL.lcm		
Batch Filename	: batch8.lcb		
Vial #	: 1-21	Sample Type	: Unknown
Injection Volume	: 10 uL		
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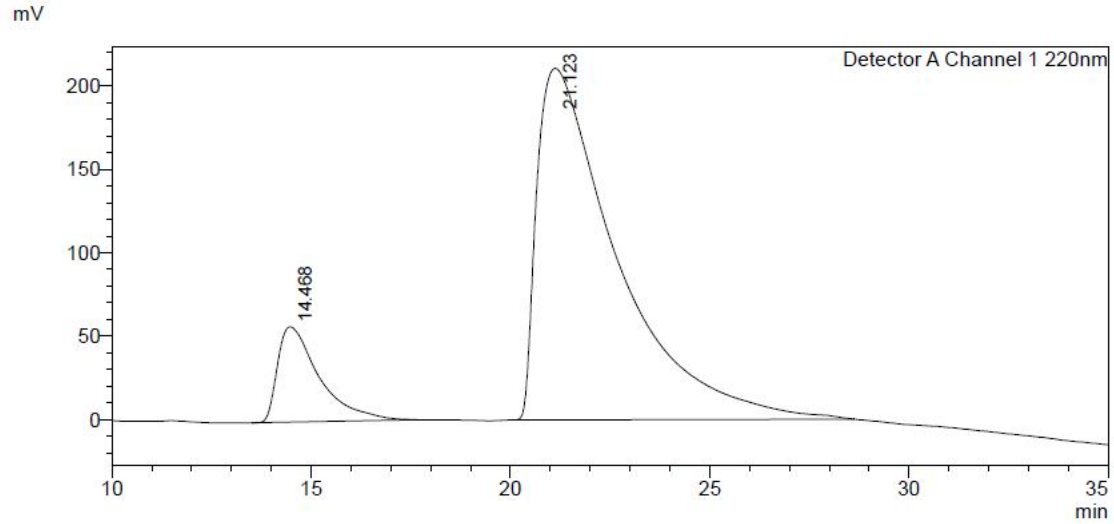
Date Processed	: 2/12/2020 4:18:29 PM	Processed by	: System Administrator



Detector A Channel 1 220nm

Peak#	Ret. Time	Area	Area%
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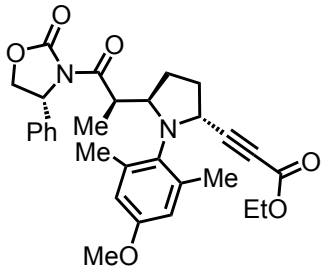
2	21.123	29460297	87.669
Total		33604042	100.000

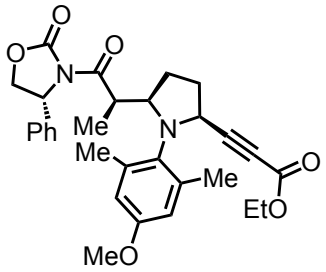


8i-*trans*

Ethyl 3-((2*R*,5*R*)-1-(4-methoxy-2,6-dimethylphenyl)-5-((*R*)-1-oxo-1-((*R*)-2-oxo-4-phenyloxazolidin-3-yl)propan-2-yl)pyrrolidin-2-yl)propiolate (8i-*trans*)

(*R*)-3-((*R*)-2-((*R*)-1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanoyl)-4-phenyloxazolidin-2-one **(*R,R,R*)-1v** was reacted with ethyl 3-(trimethylsilyl)propiolate **2b** following **General Procedure C**. The *trans*:*cis* ratio was determined to be 7.7:1 by ^{1}H NMR analysis of the unpurified reaction mixtures. After purification by column chromatography (Et_2O:hexanes = 1:4), **8i-*trans*** was obtained as a colorless liquid (96 mg, 93%). The relative configuration of **8i-*trans*** was assigned by NOESY and COSY analysis (see SI Section 3).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.21 (m, 3H), 7.07 – 7.02 (m, 2H), 6.59 (q, *J* = 3.1 Hz, 2H), 4.56 (dd, *J* = 8.4, 2.4 Hz, 1H), 4.47 (t, *J* = 7.0 Hz, 1H), 4.21 (dt, *J* = 12.7, 8.5 Hz, 2H), 4.13 (q, *J* = 7.1 Hz, 2H), 3.98 (dd, *J* = 8.4, 2.4 Hz, 1H), 3.79 (s, 3H), 3.71 (dq, *J* = 9.0, 6.9 Hz, 1H), 2.42 (dtd, *J* = 12.3, 7.0, 3.8 Hz, 1H), 2.34 (s, 3H), 2.26 (s, 3H), 2.21 (dtd, *J* = 12.2, 6.3, 3.8 Hz, 1H), 2.11 (ddt, *J* = 12.3, 10.1, 7.0 Hz, 1H), 1.76 (ddt, *J* = 11.9, 9.8, 7.4 Hz, 1H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.02 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.2, 157.2, 153.6, 153.1, 143.7, 140.6, 139.5, 133.2, 128.9, 128.3, 125.1, 113.8, 112.4, 89.6, 74.8, 69.7, 62.4, 61.7, 57.4, 55.21, 55.20, 52.5, 42.1, 32.2, 30.3, 20.1, 19.5, 15.9, 13.9; **IR** (neat) ν 2960, 2847, 2226, 2172, 1775, 1699, 1597, 1380, 1240, 1039, 699 cm^{-1}; **HRMS** (DART) Calcd for $C_{30}H_{35}N_2O_6$ (MH^+): 519.2489; found: 519. 2475; $[\alpha]^{25}_D$ = –62.2° (*c* 0.5, CH_2Cl_2).



8i-*cis*

Ethyl 3-((2*S*,5*R*)-1-(4-methoxy-2,6-dimethylphenyl)-5-((*R*)-1-oxo-1-((*R*)-2-oxo-4-phenyloxazolidin-3-yl)propan-2-yl)pyrrolidin-2-yl)propiolate (8i-*cis*)

The relative configuration of **8i-*cis*** was assigned by NOESY analysis (see SI Section 3).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.21 (m, 3H), 7.08 (dt, *J* = 7.2, 2.3 Hz, 2H), 6.62 (d, *J* = 3.1 Hz, 1H), 6.53 (d, *J* = 3.2 Hz, 1H), 4.63 (dt, *J* = 8.7, 2.9 Hz, 1H), 4.37 (td, *J* = 8.5, 3.0 Hz, 1H), 4.19 (dtt, *J* = 17.6, 7.4, 3.7 Hz, 3H), 4.07 (dt, *J* = 10.5, 2.8 Hz, 1H), 3.95 (q, *J* = 8.7 Hz, 1H), 3.83 – 3.67 (m, 4H), 2.50 (d, *J* = 3.0 Hz, 3H), 2.32 (tt, *J* = 12.3, 4.6 Hz, 1H), 2.25 – 2.12 (m, 4H), 2.07 (dh, *J* = 13.2, 3.5 Hz, 1H), 1.94 (ddd, *J* = 11.9, 7.8, 2.8 Hz, 1H), 1.27 (tt, *J* = 9.0, 4.2 Hz, 4H), 1.15 (dd, *J* = 7.2, 3.0 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.8, 157.5, 153.7, 153.1, 142.8, 140.8, 139.3, 134.7, 129.1, 129.0, 128.4, 125.2, 114.5, 112.8, 90.0, 74.4, 69.9, 63.8, 61.7, 57.4, 55.3, 53.9, 42.0, 32.2, 29.0, 19.9, 19.4, 14.9, 14.0; **IR** (neat) ν 2876, 2848, 2232, 1779, 1704, 1600, 1465, 1382, 1246, 1194, 1066, 1041, 702 cm^{-1}; **HRMS** (DART) Calcd for $C_{30}H_{35}N_2O_6$ (MH^+): 519.2489; found: 519. 2483; $[\alpha]^{25}_D$ = –108.6° (*c* 0.4, CH_2Cl_2).

7. References

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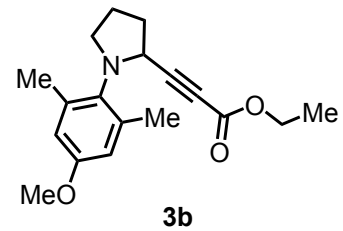
(21) **7i** required longer ^{13}C NMR acquisition during which trimethylsilyl group was fallen off to afford **10**. For corresponding ^{13}C NMR, *see: N*-Benzhydryl-*N*-(3-phenyl-3-(4-(trifluoromethyl)phenoxy)propyl)prop-2-yn-1-amine (p45)

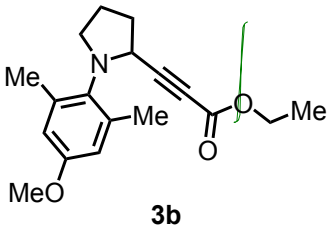
8. NMR Spectra

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



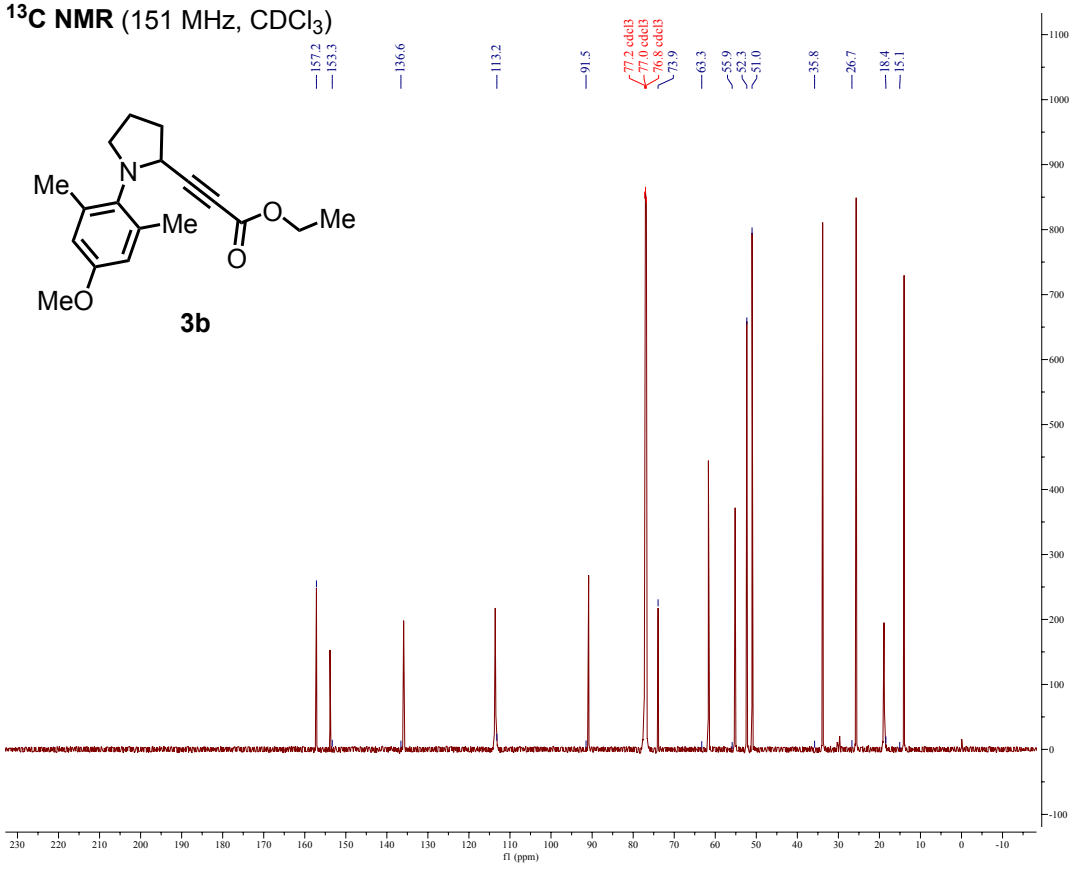
3b

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



3b

^{13}C NMR (151 MHz, $CDCl_3$)



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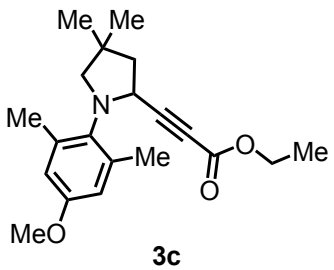

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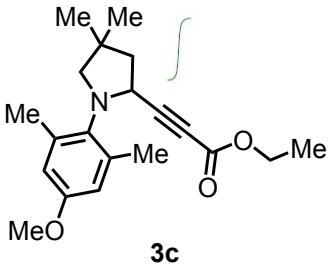

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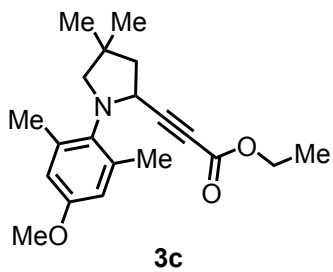

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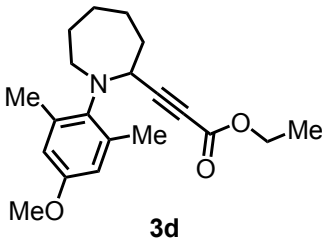

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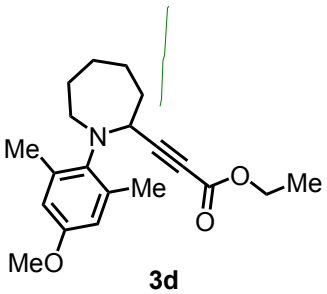

3d

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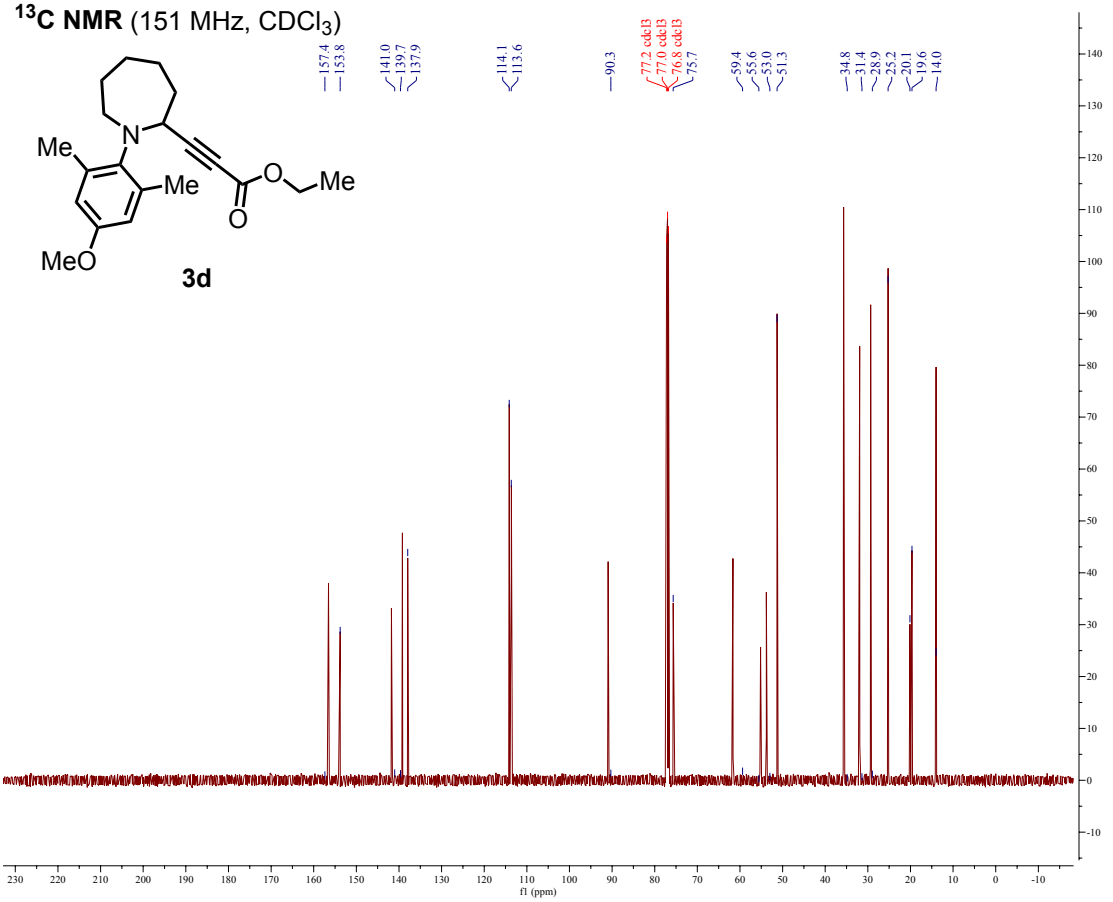

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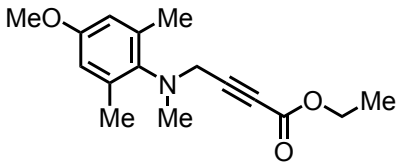

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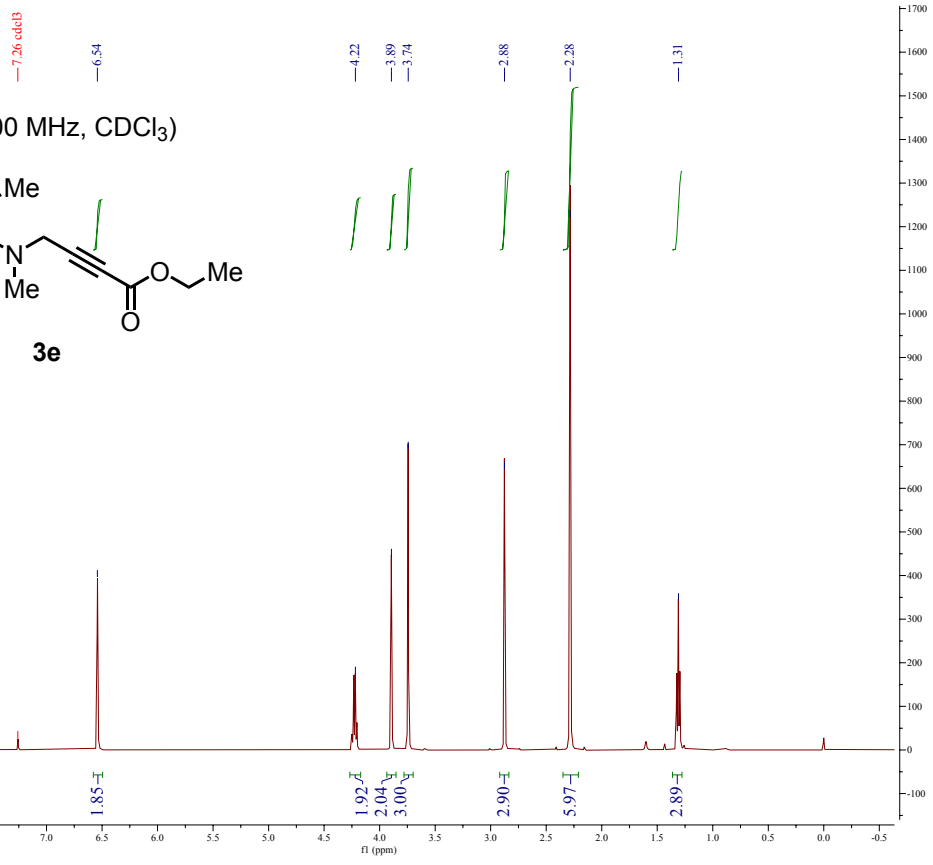
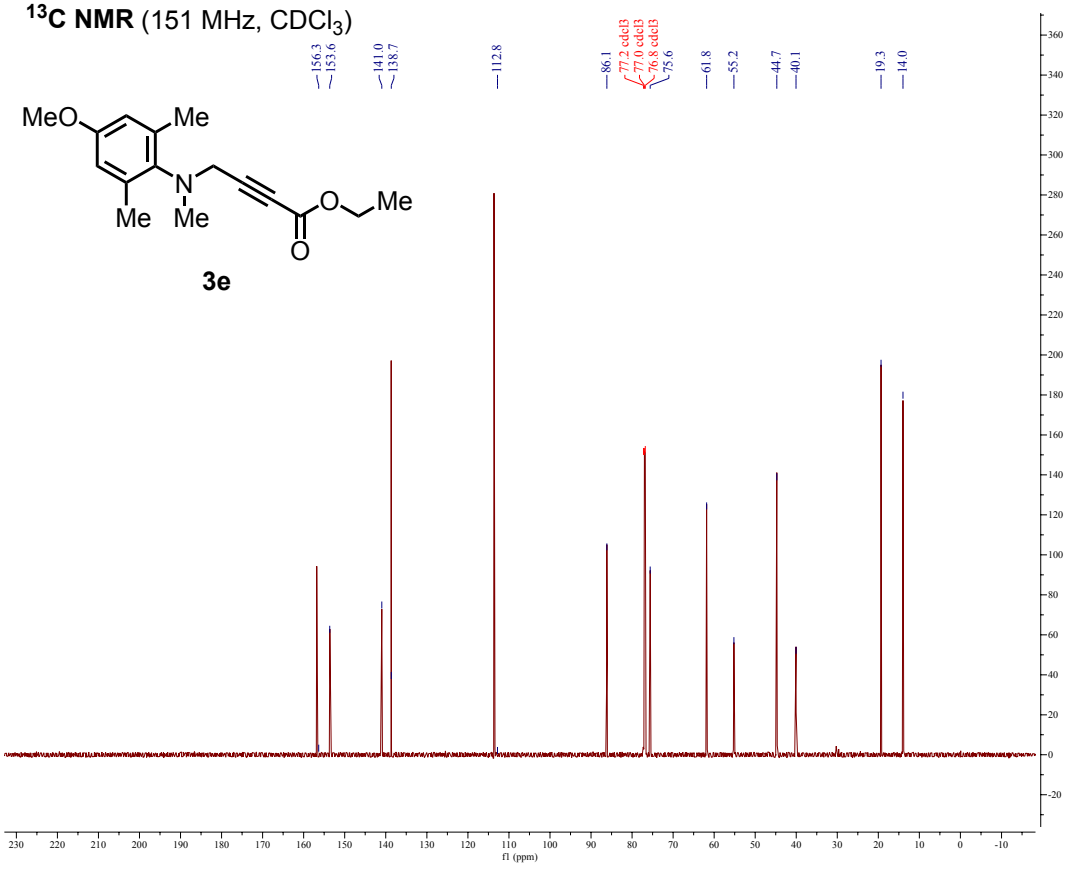


^{1}H NMR (500 MHz, $CDCl_3$)

3e

^{13}C NMR (151 MHz, $CDCl_3$)



3e

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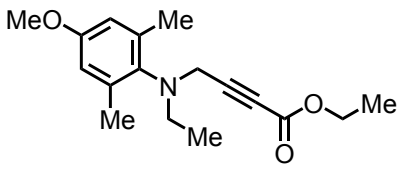

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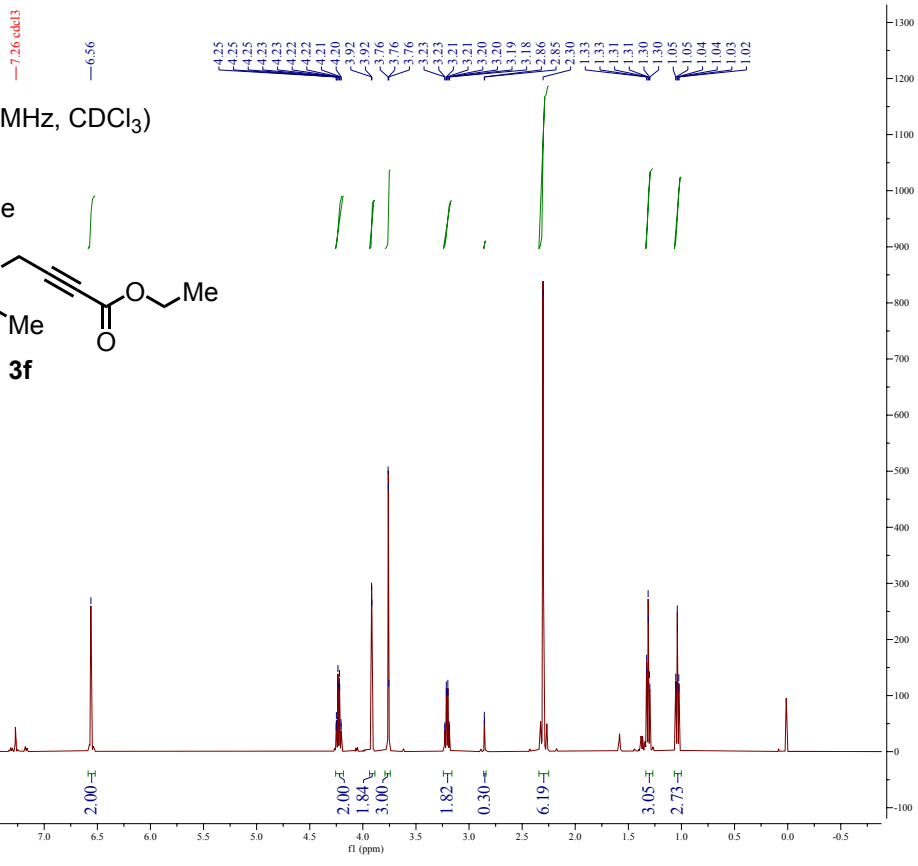
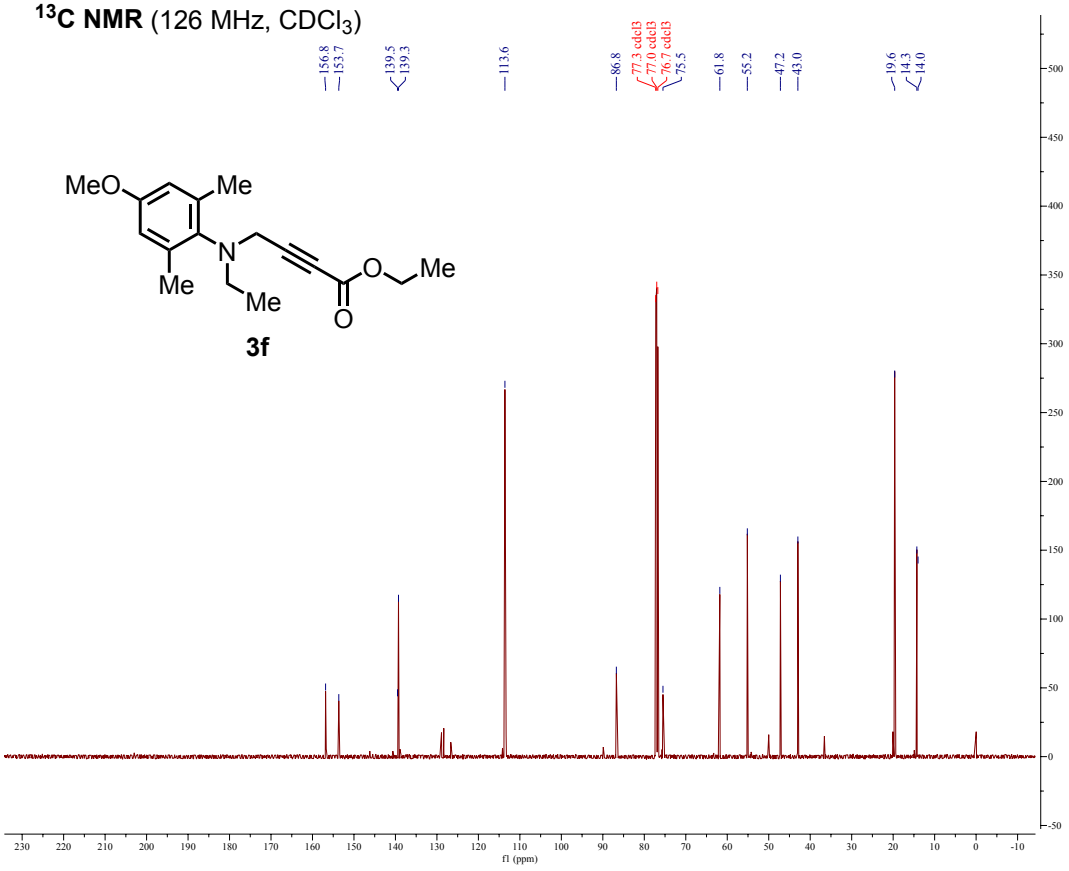


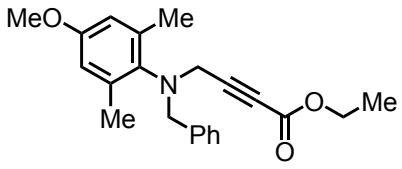
^{1}H NMR (500 MHz, $CDCl_3$)

3f

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



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



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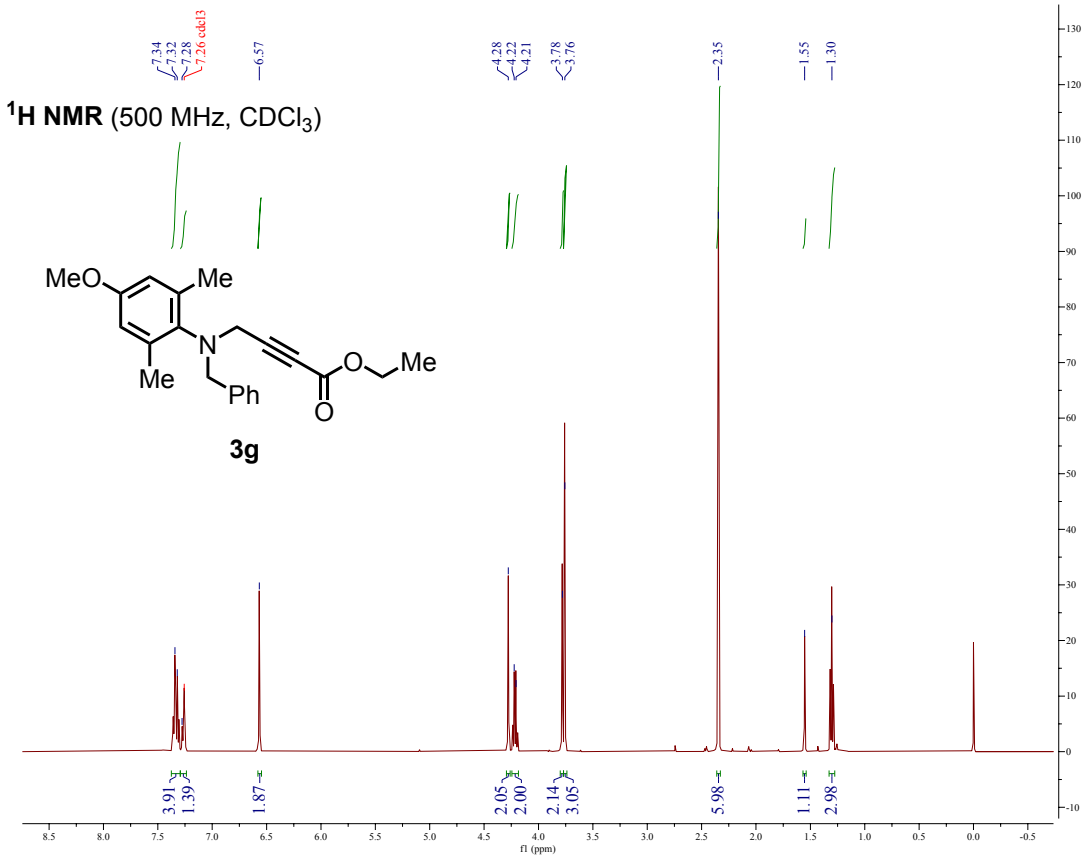
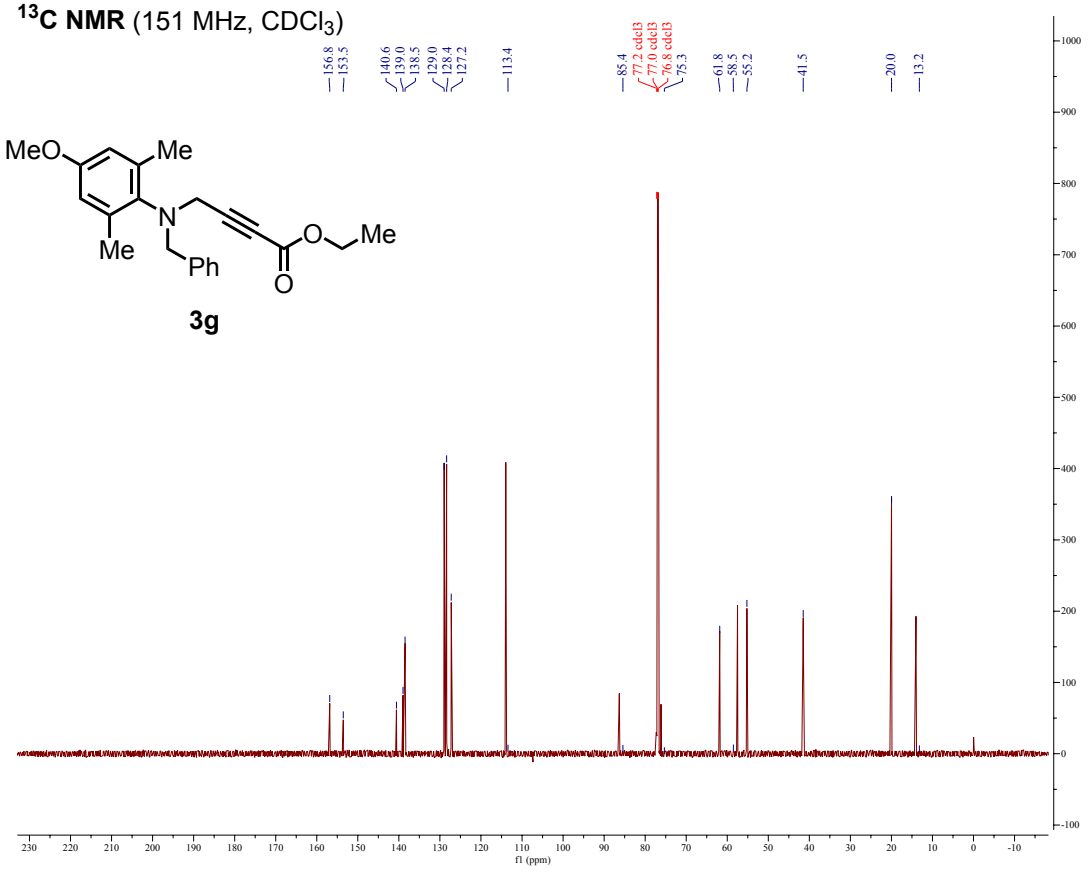


^{1}H NMR (500 MHz, $CDCl_3$)

3g

^{13}C NMR (151 MHz, $CDCl_3$)



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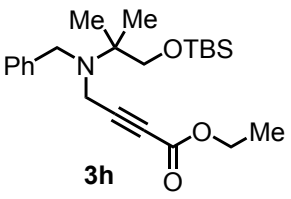
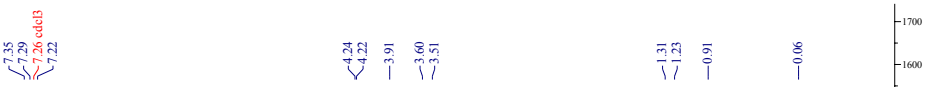


3h



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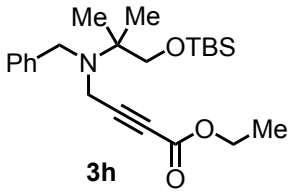
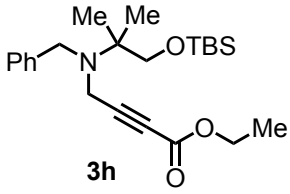


3h

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



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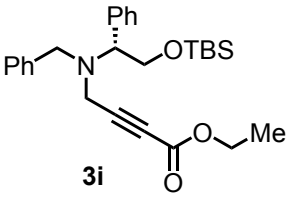

3i

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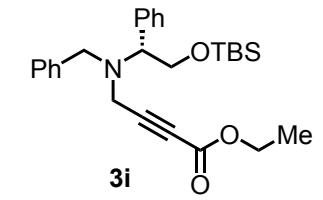

3i

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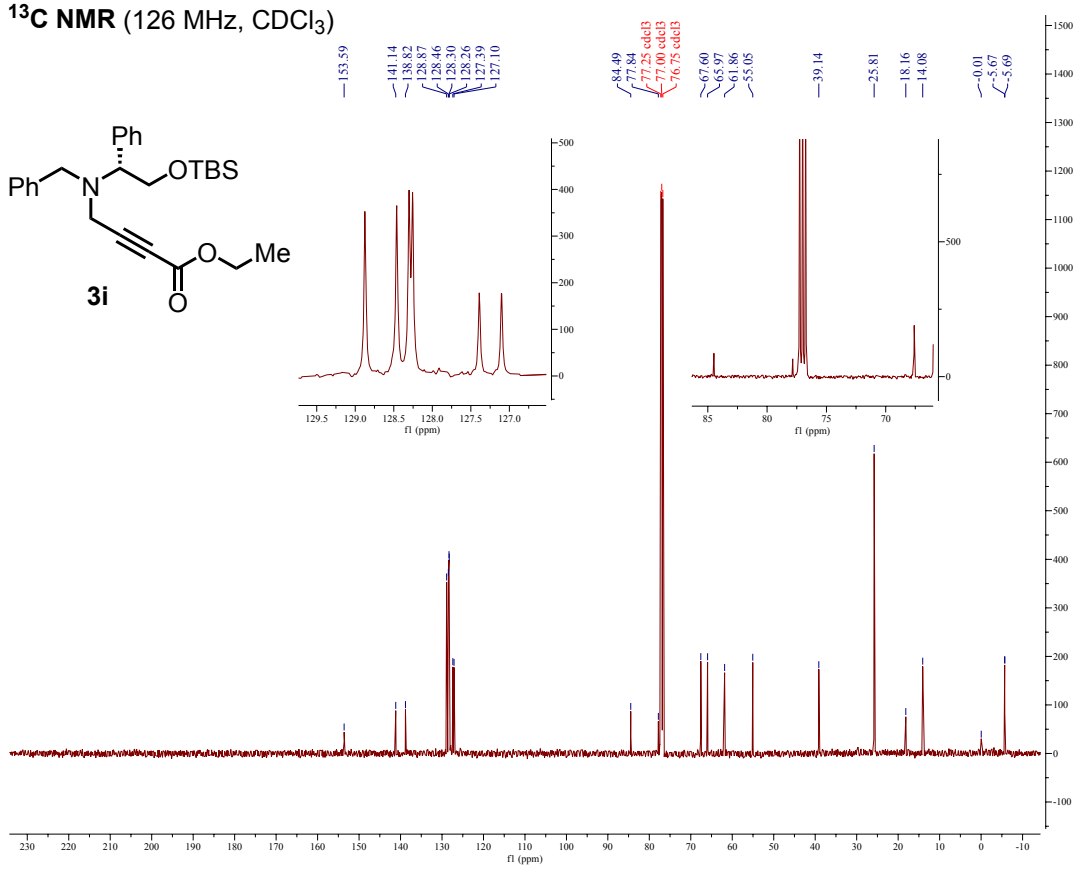

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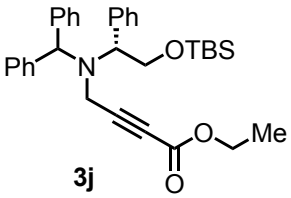

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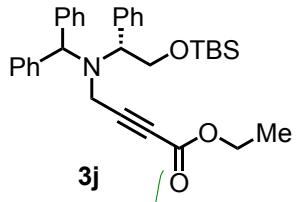

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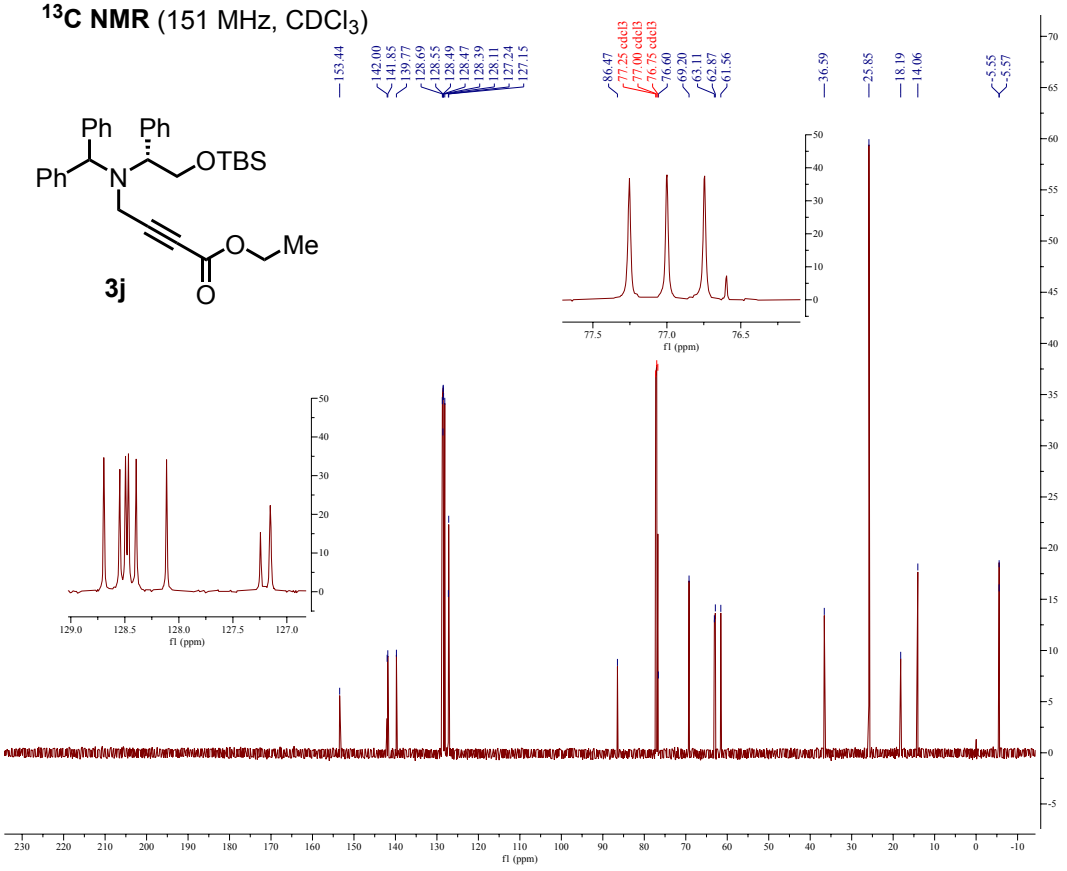
^{13}C NMR (151 MHz, $CDCl_3$)



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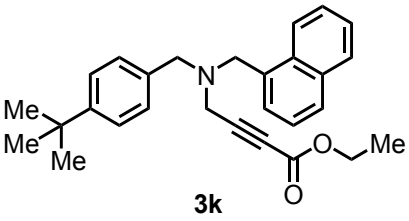

3k

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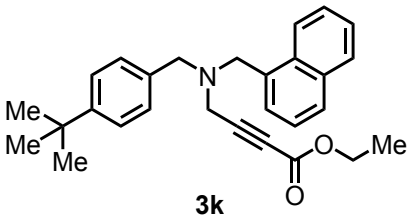

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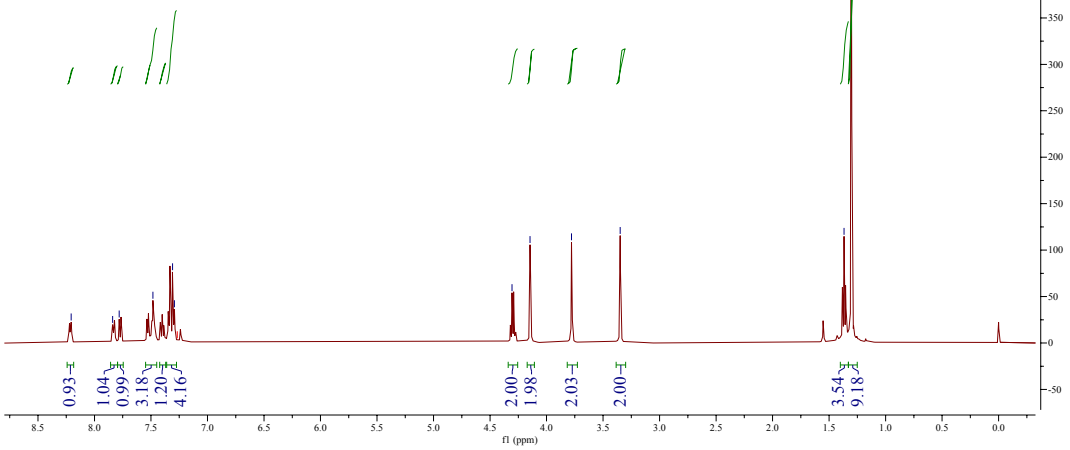
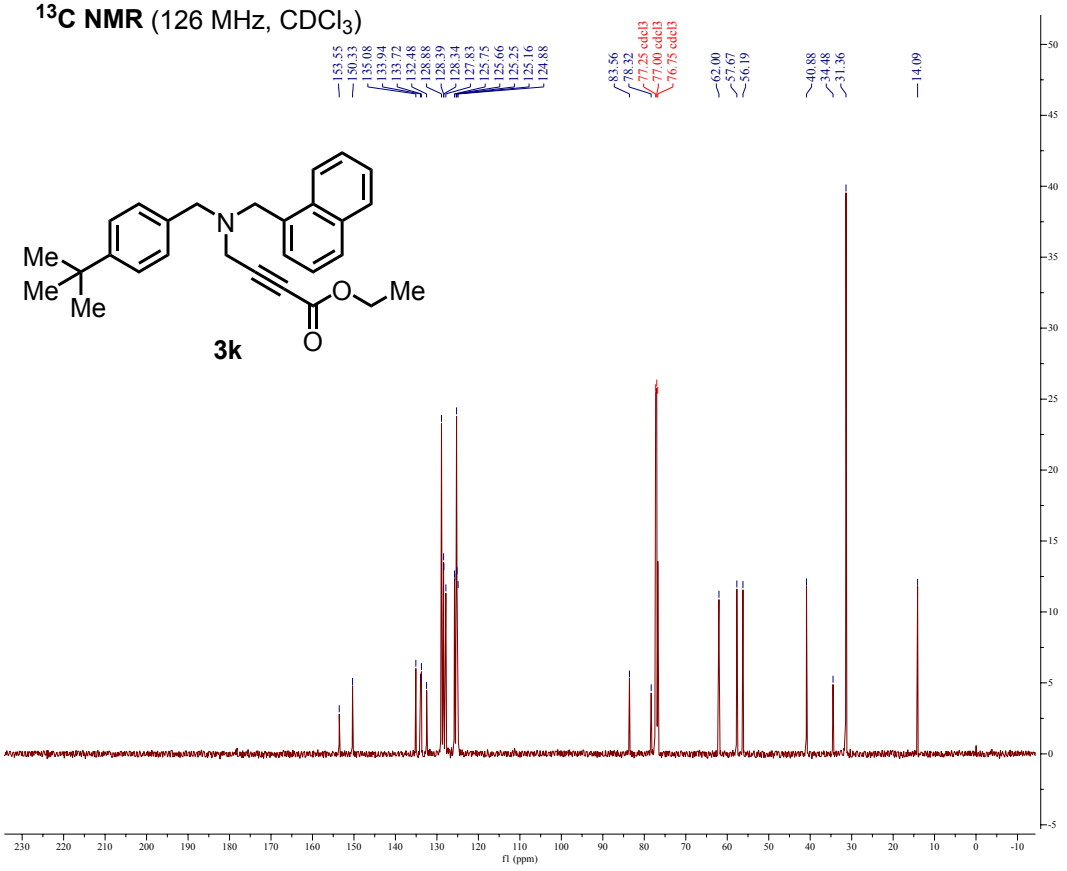


^{13}C NMR (126 MHz, $CDCl_3$)



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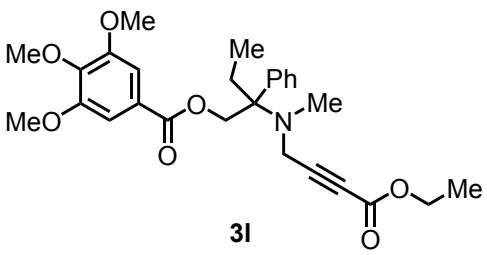

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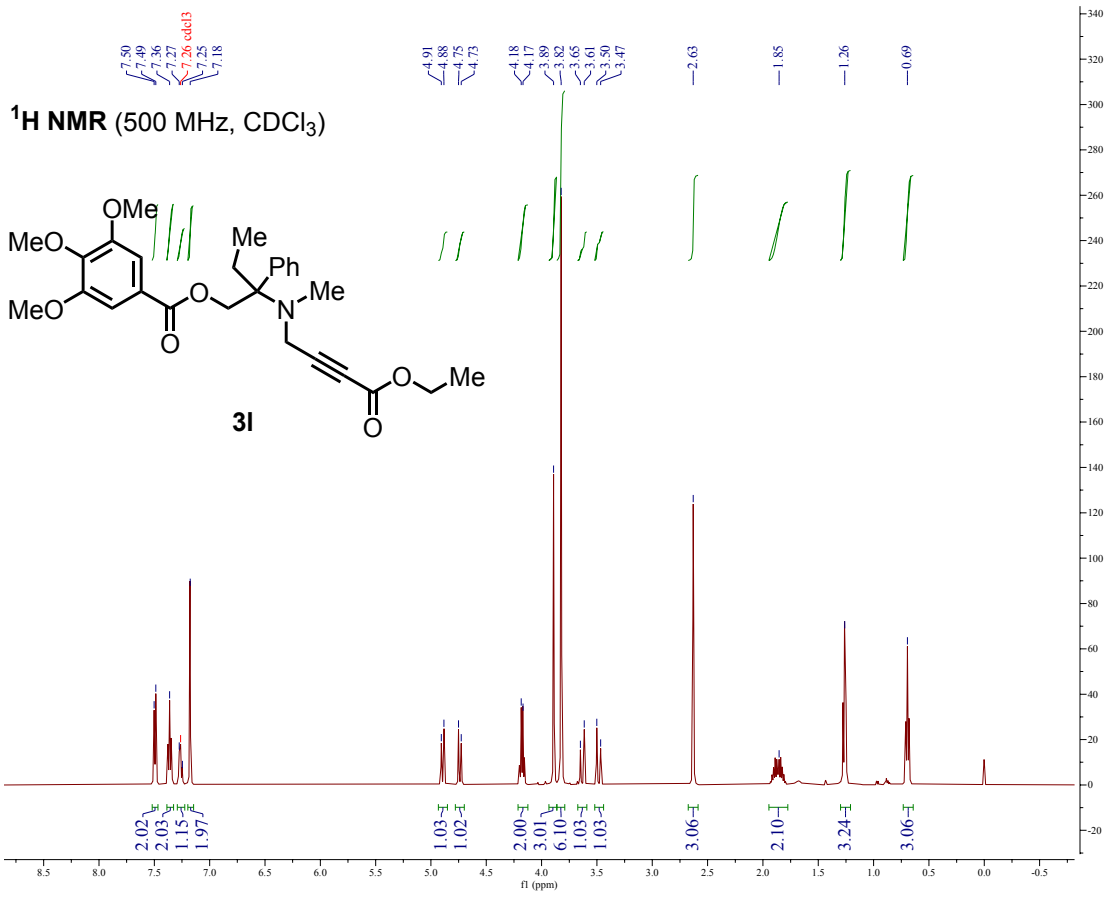
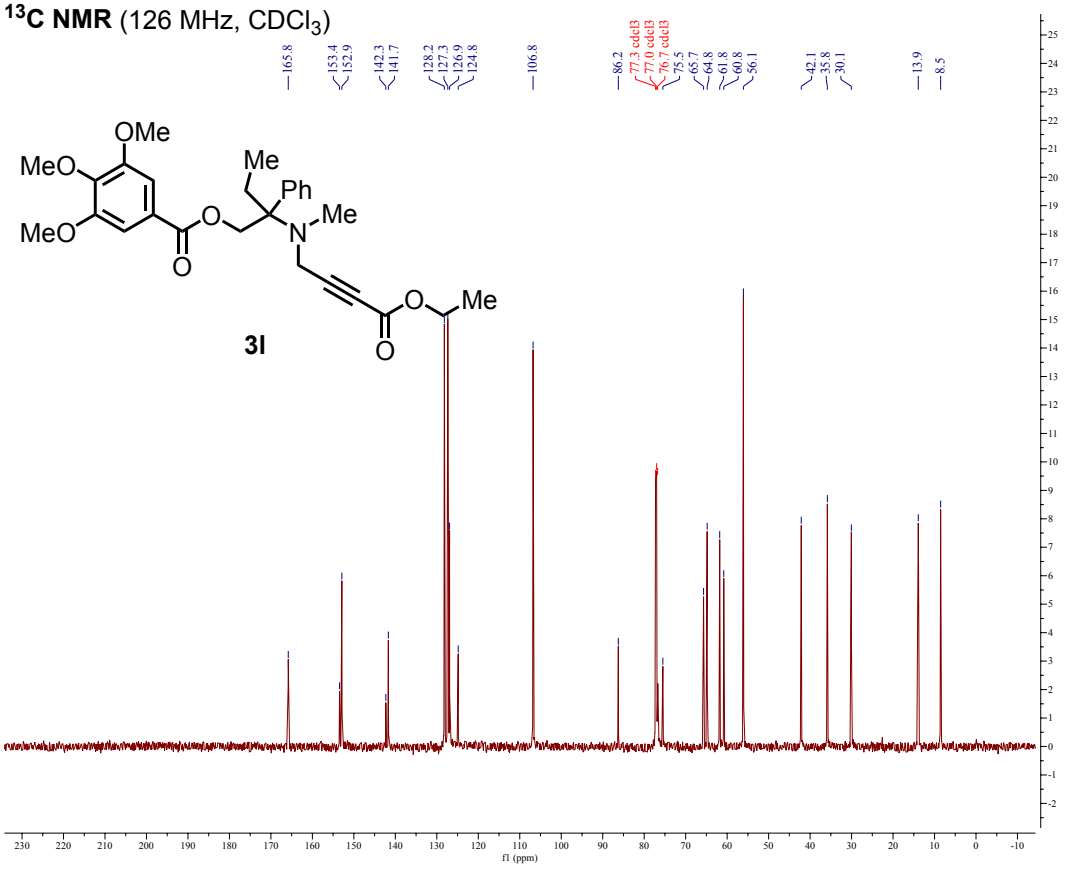


^{1}H NMR (500 MHz, $CDCl_3$)

3l

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



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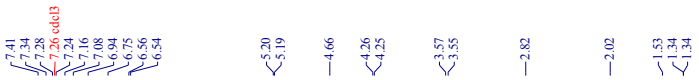

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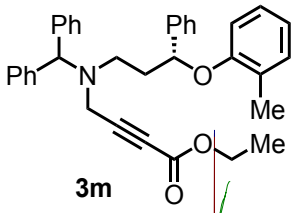
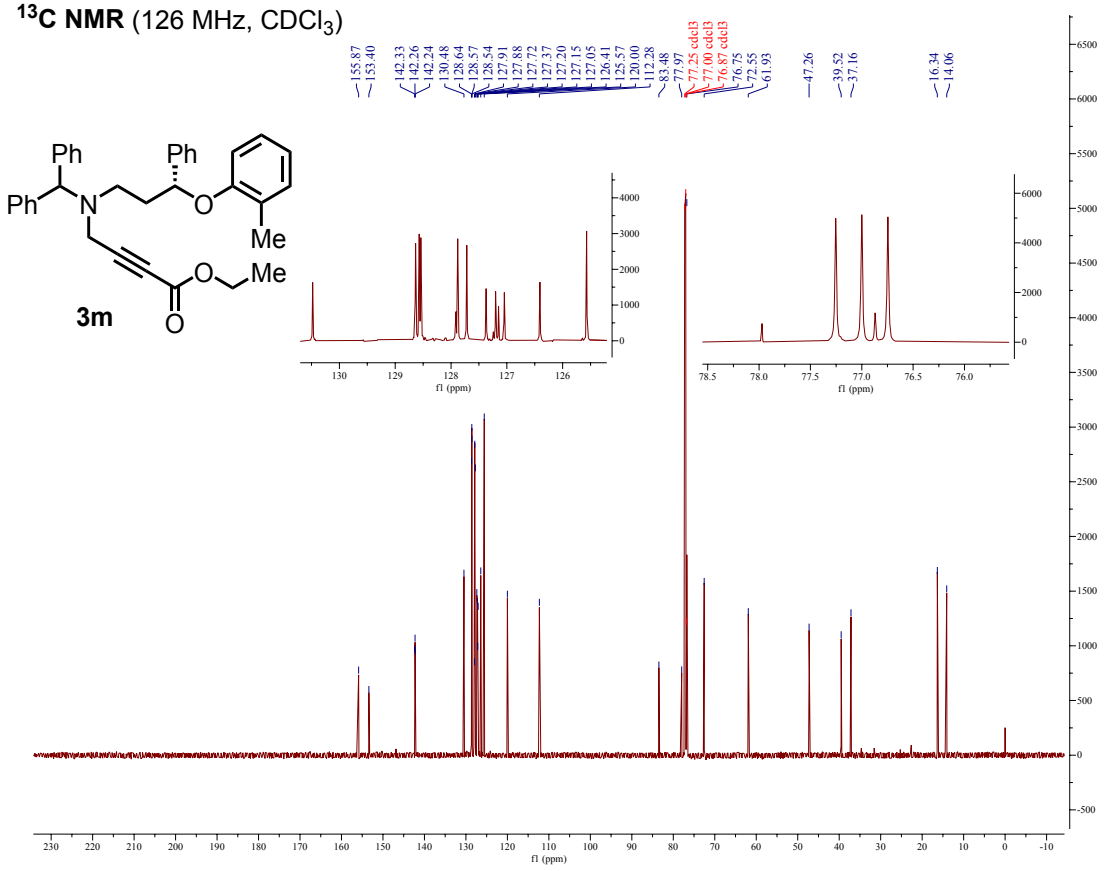
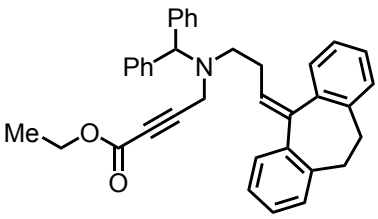


^{13}C NMR (126 MHz, $CDCl_3$)

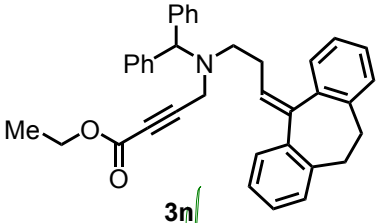


^{1}H NMR (500 MHz, $CDCl_3$)



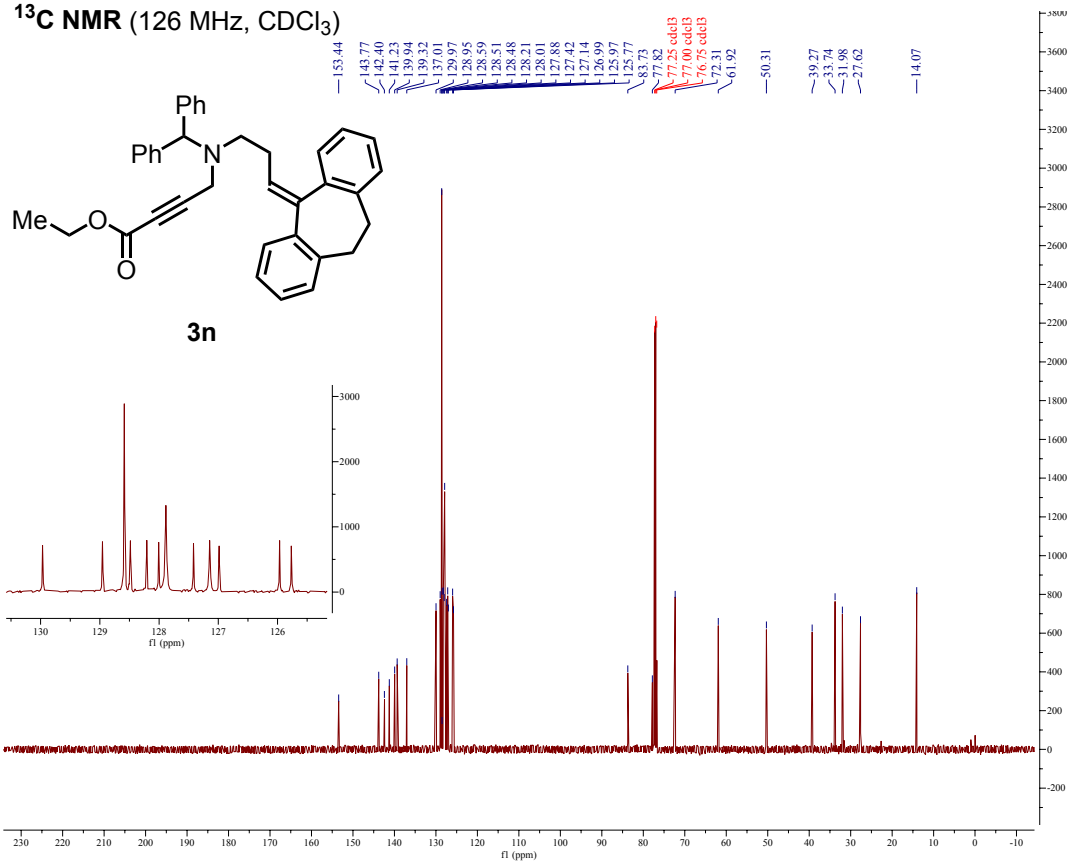
3n

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



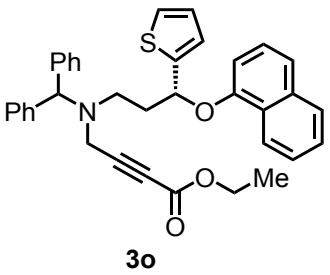
3n

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

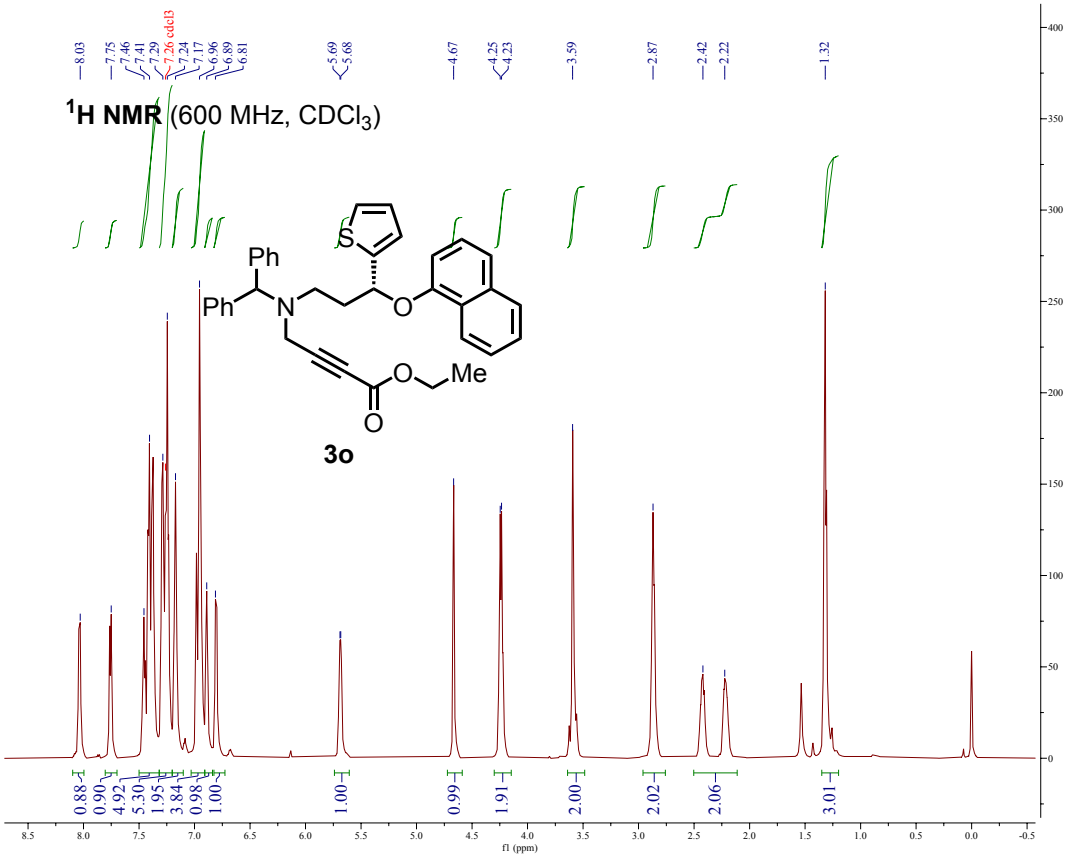


3n

^{1}H NMR (600 MHz, $CDCl_3$)



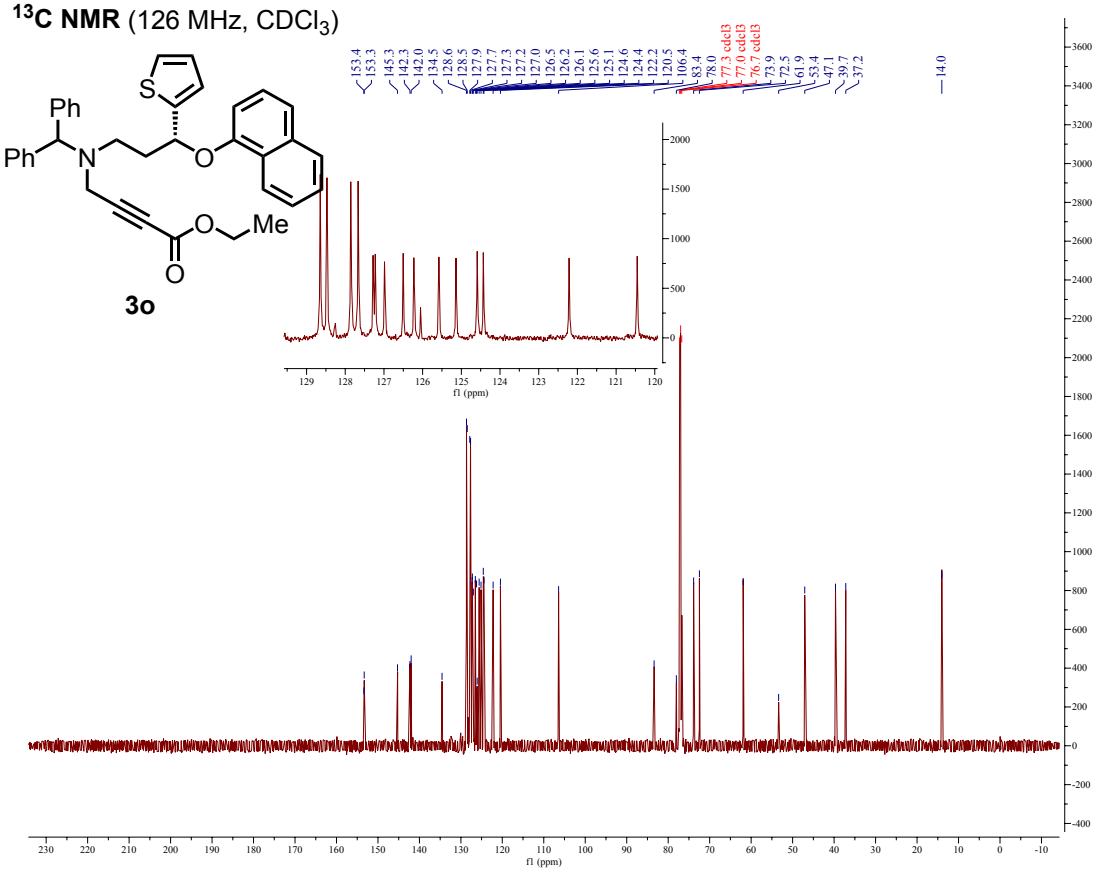
3o



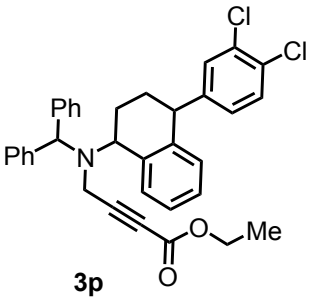
^{1}H NMR (600 MHz, $CDCl_3$)

3o

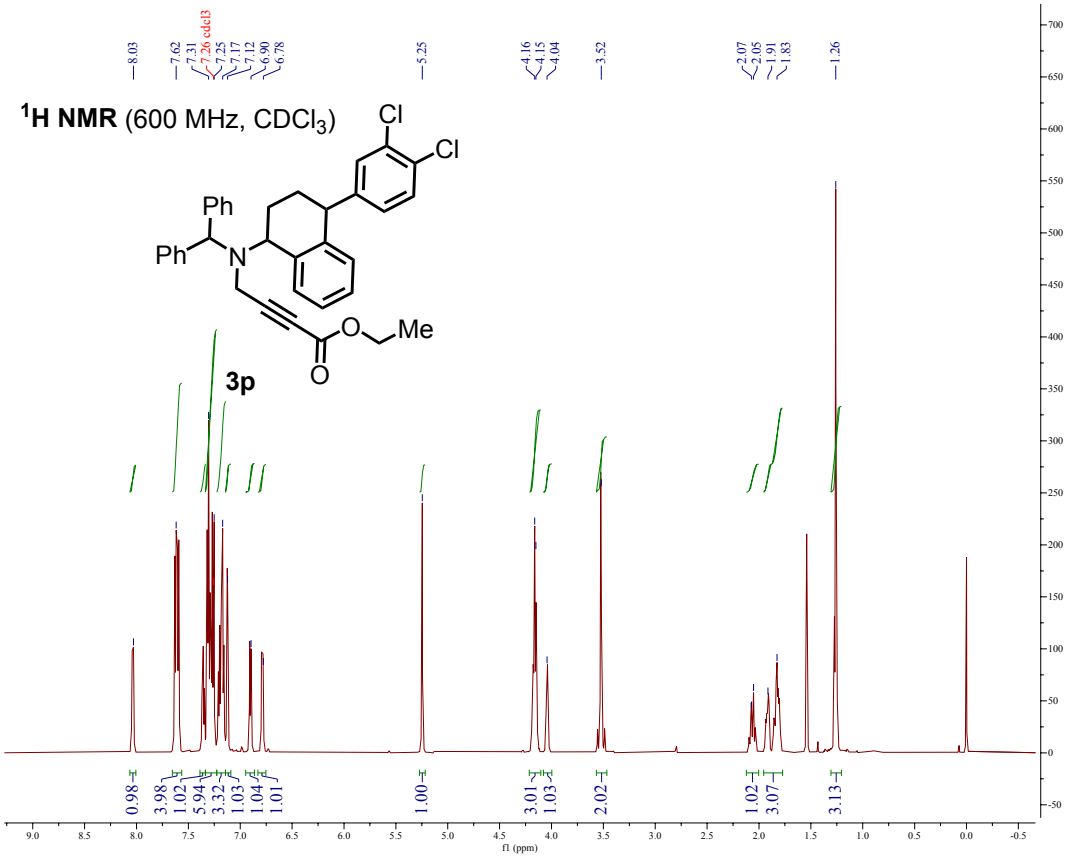
^{13}C NMR (126 MHz, $CDCl_3$)



^{1}H NMR (600 MHz, $CDCl_3$)



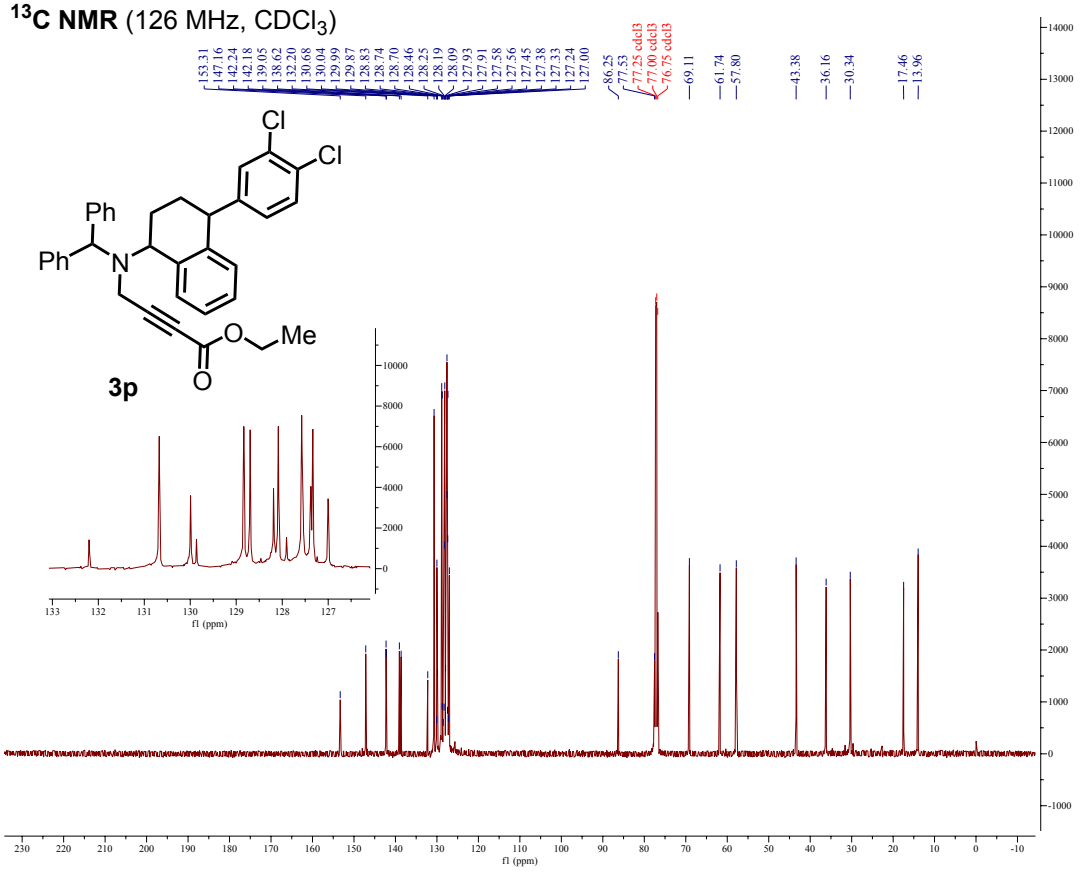
3p



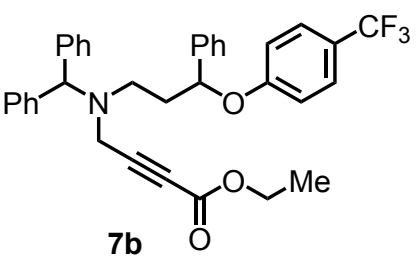
^{1}H NMR (600 MHz, $CDCl_3$)

3p

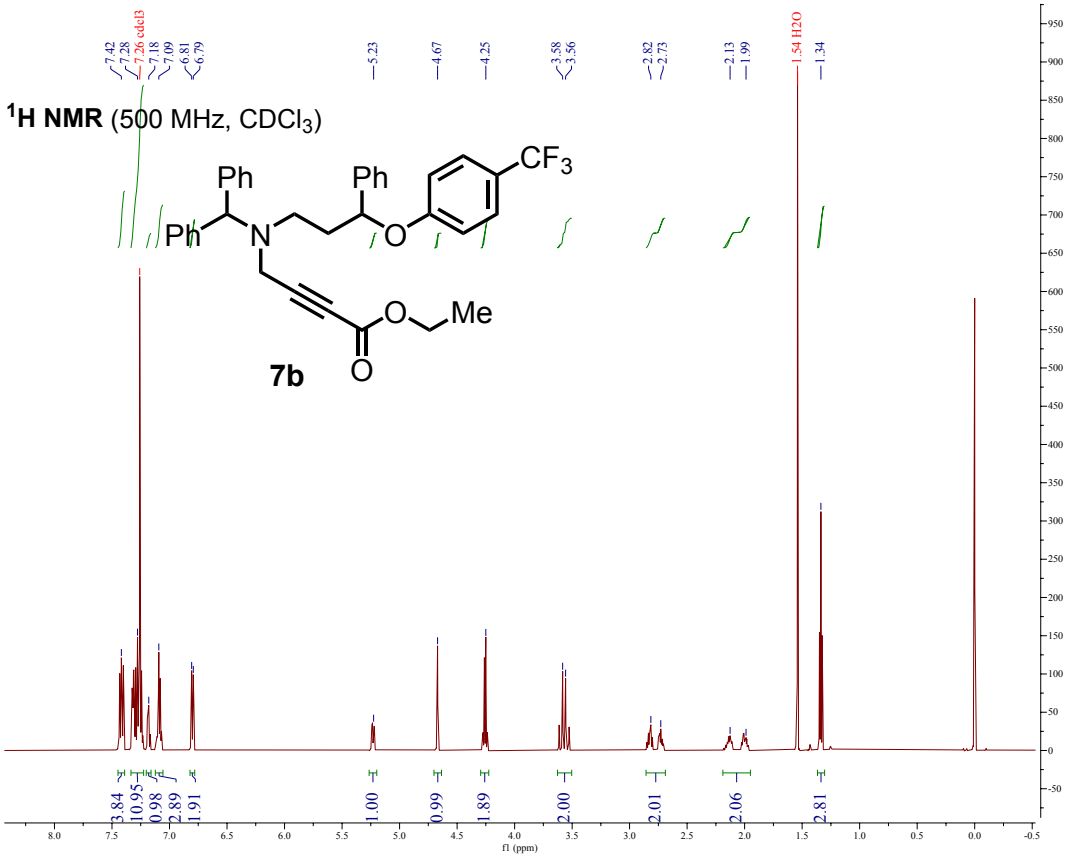
^{13}C NMR (126 MHz, $CDCl_3$)



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



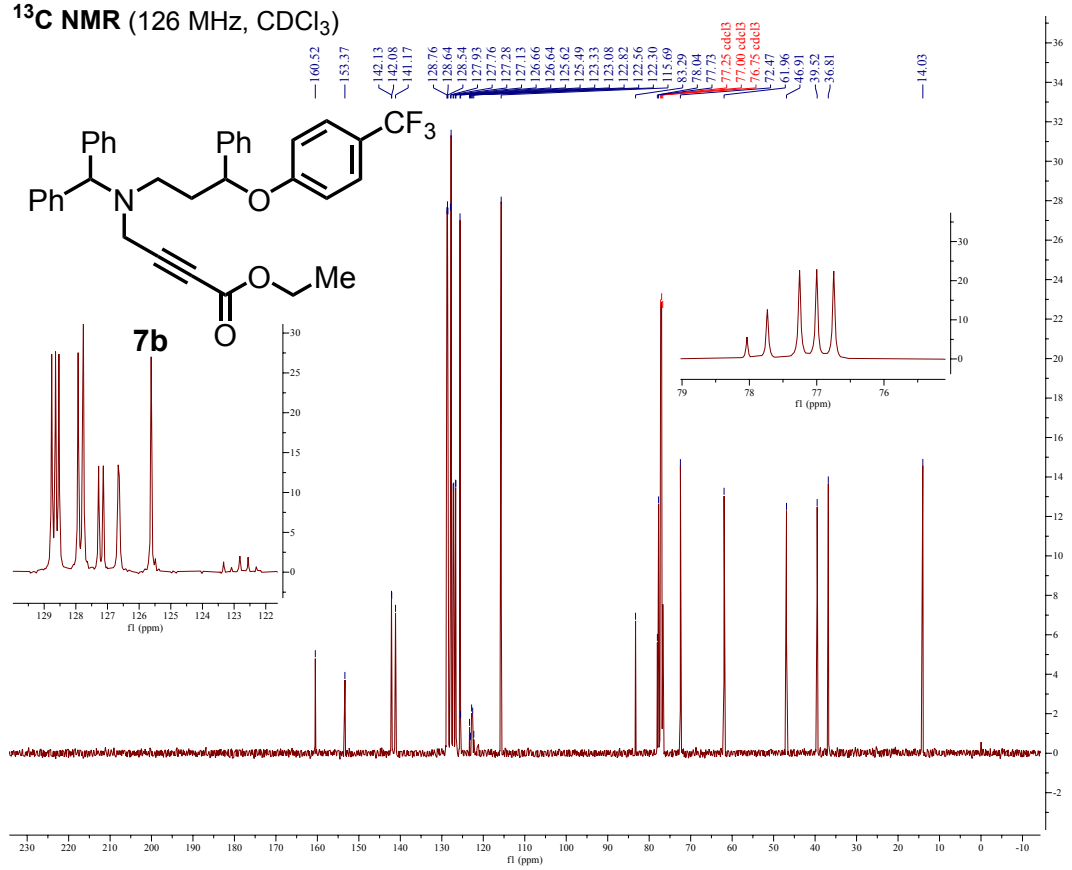
7b



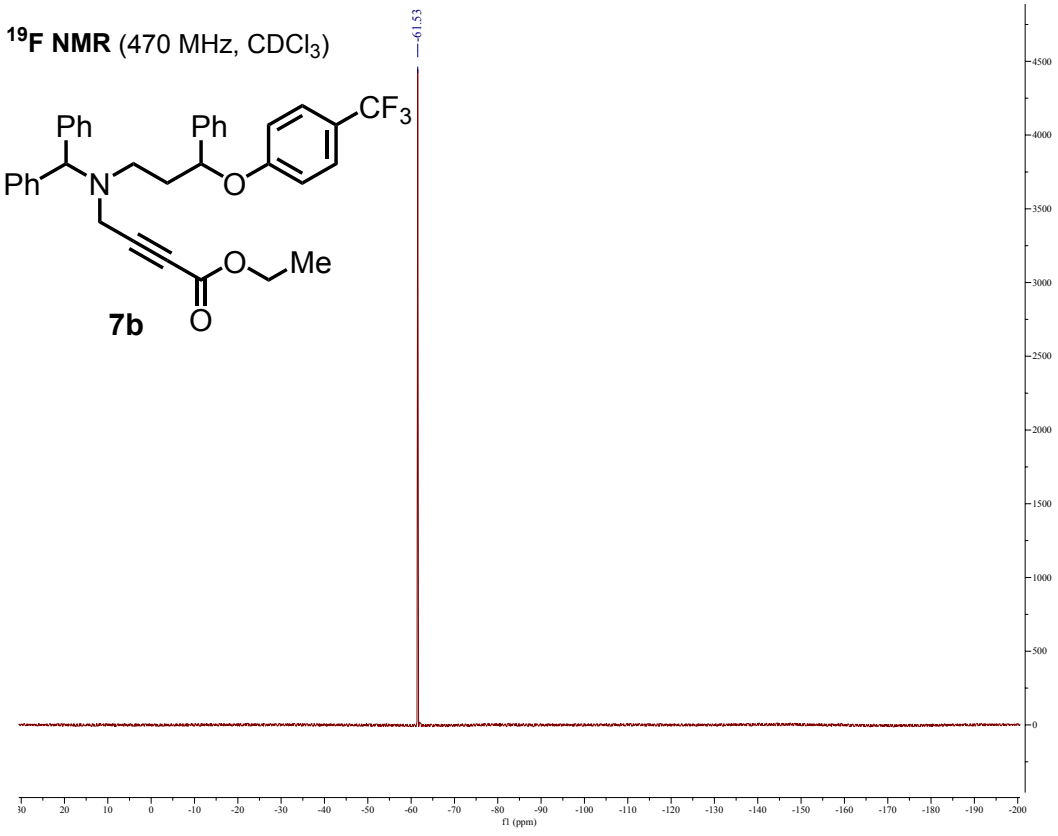
^{1}H NMR (500 MHz, $CDCl_3$)

7b

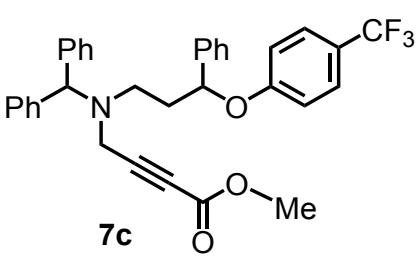
^{13}C NMR (126 MHz, $CDCl_3$)



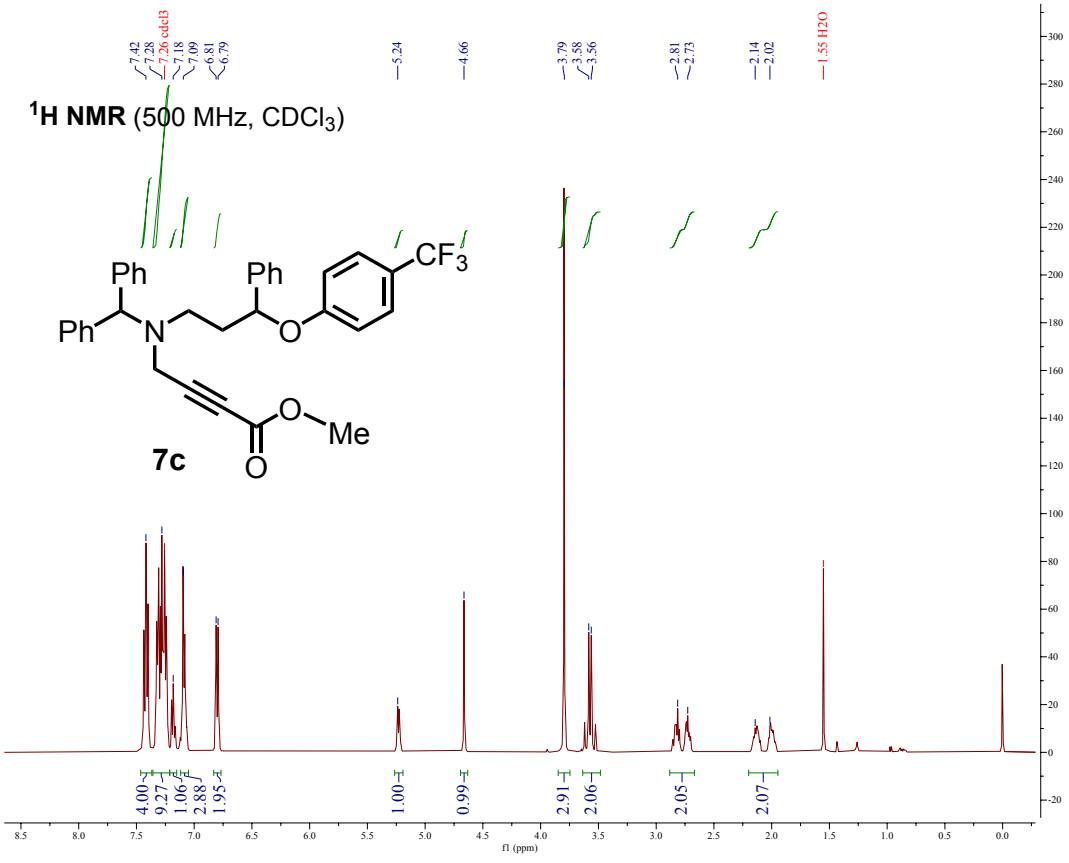
^{19}F NMR (470 MHz, $CDCl_3$)



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



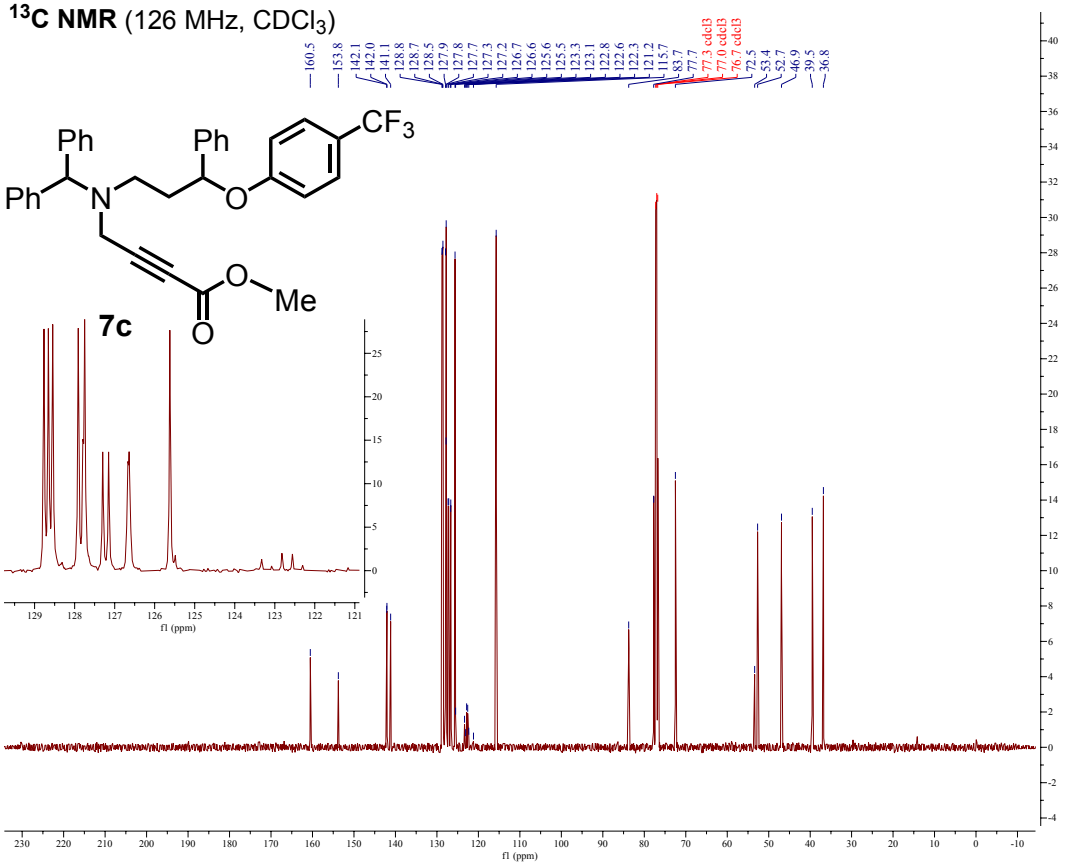
7c



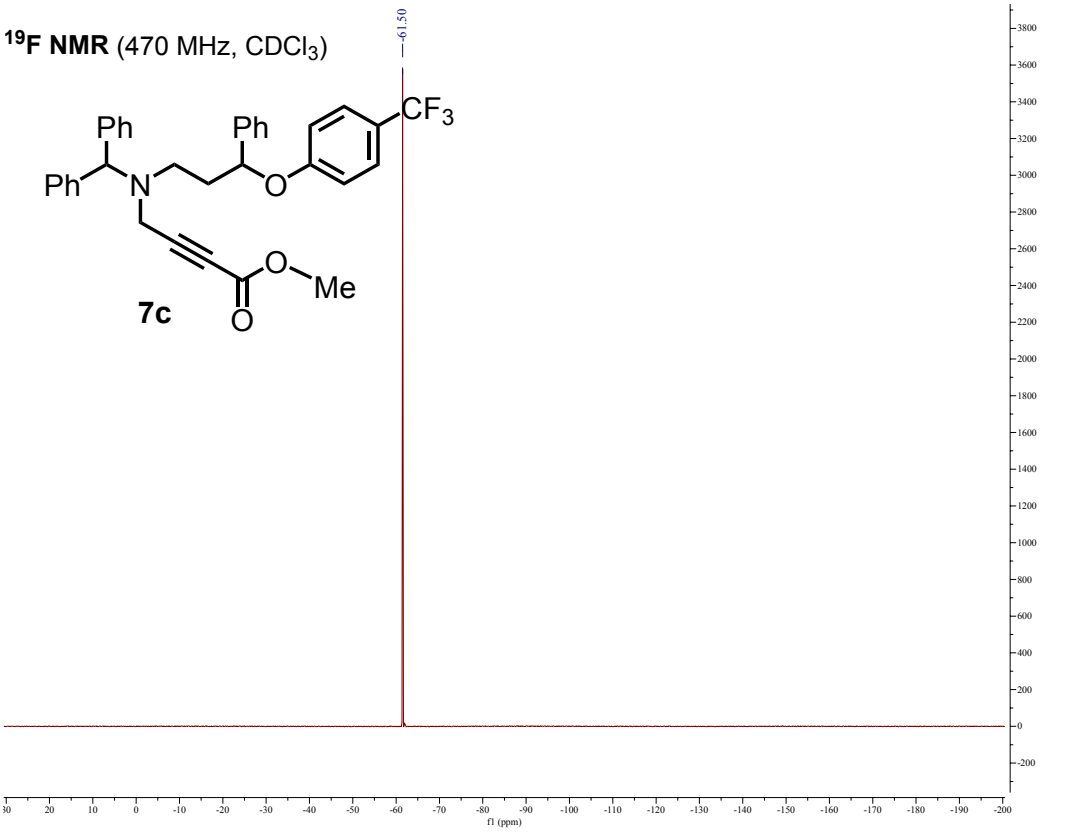
^{1}H NMR (500 MHz, $CDCl_3$)

7c

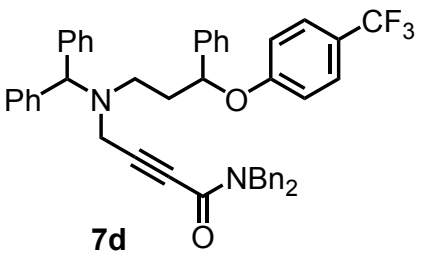
^{13}C NMR (126 MHz, $CDCl_3$)



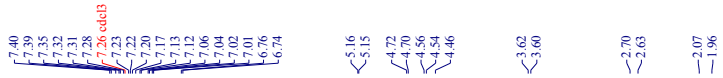
^{19}F NMR (470 MHz, $CDCl_3$)



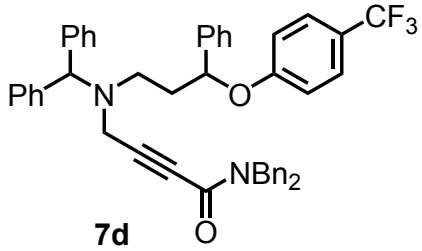
^{1}H NMR (600 MHz, $CDCl_3$)



7d

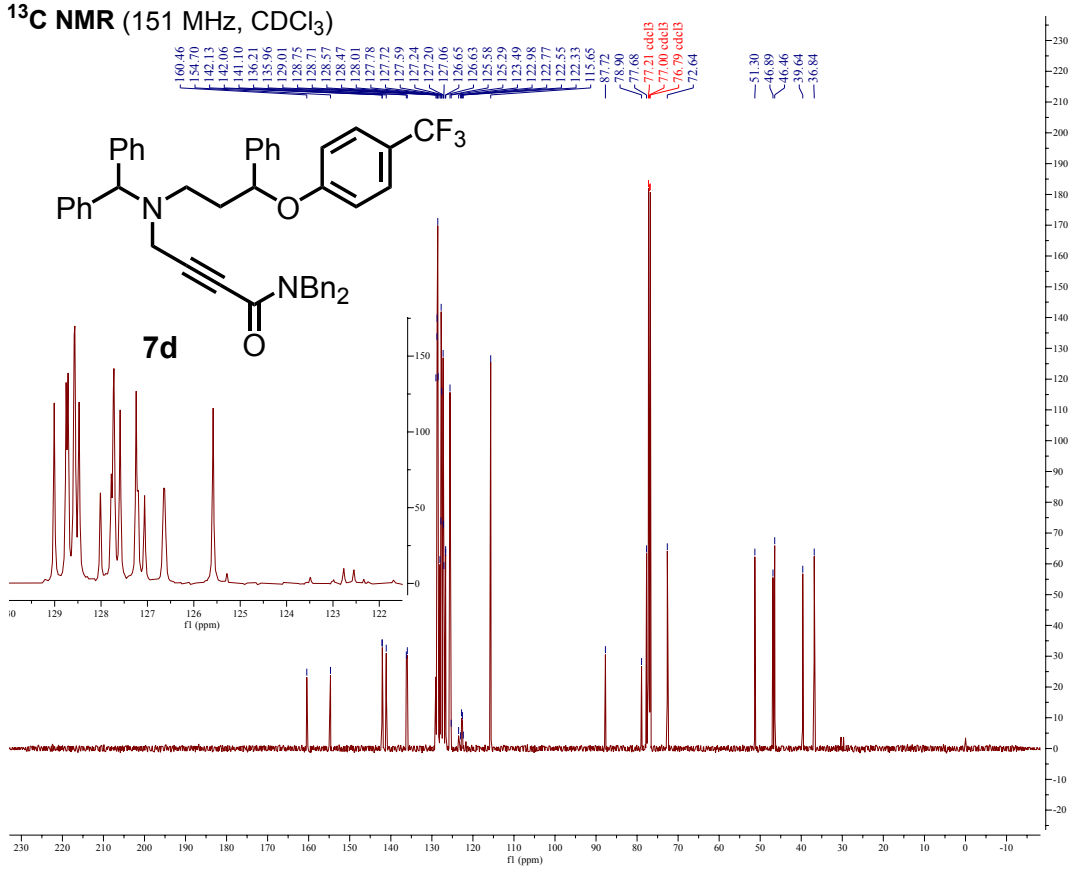


^{1}H NMR (600 MHz, $CDCl_3$)

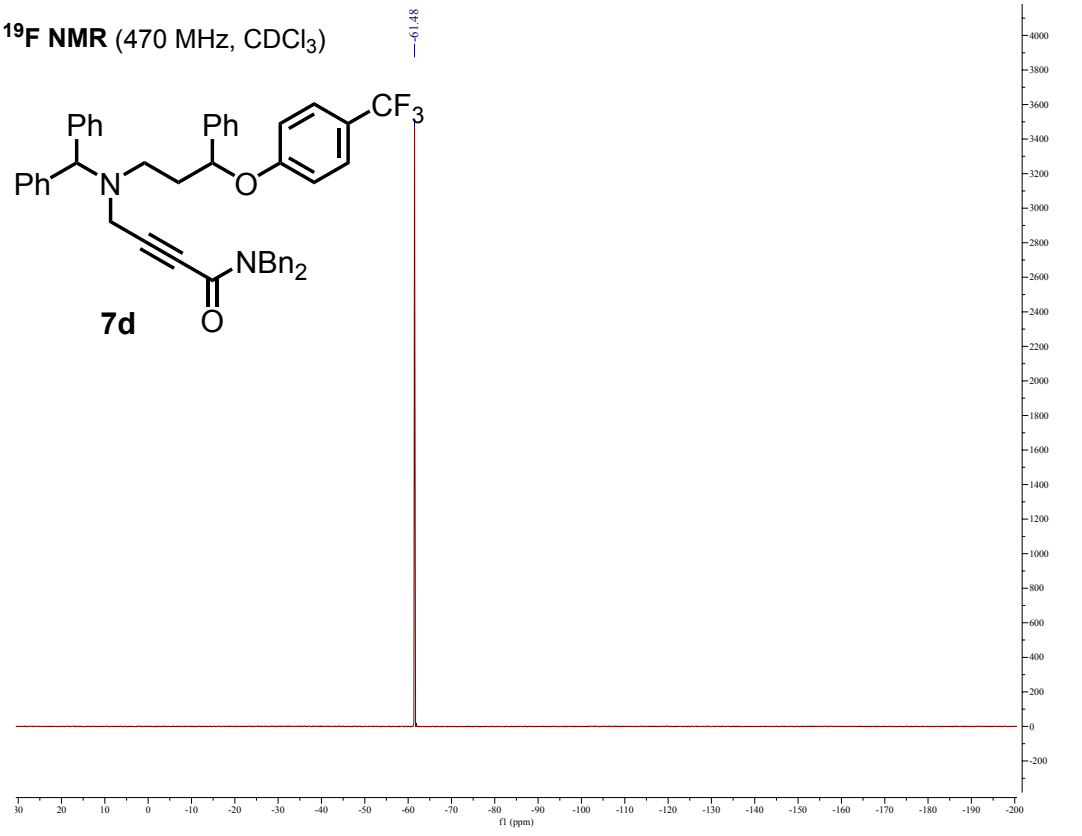


7d

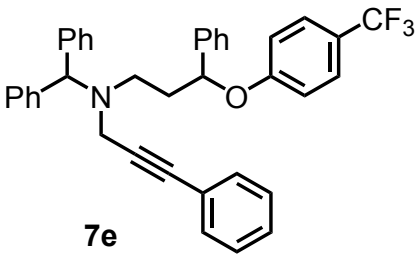
^{13}C NMR (151 MHz, $CDCl_3$)



^{19}F NMR (470 MHz, $CDCl_3$)

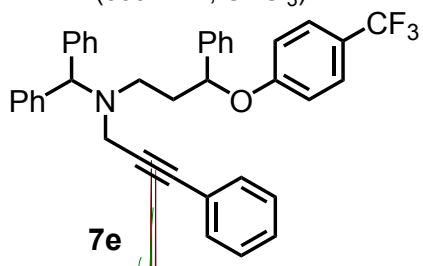


^{1}H NMR (500 MHz, $CDCl_3$)



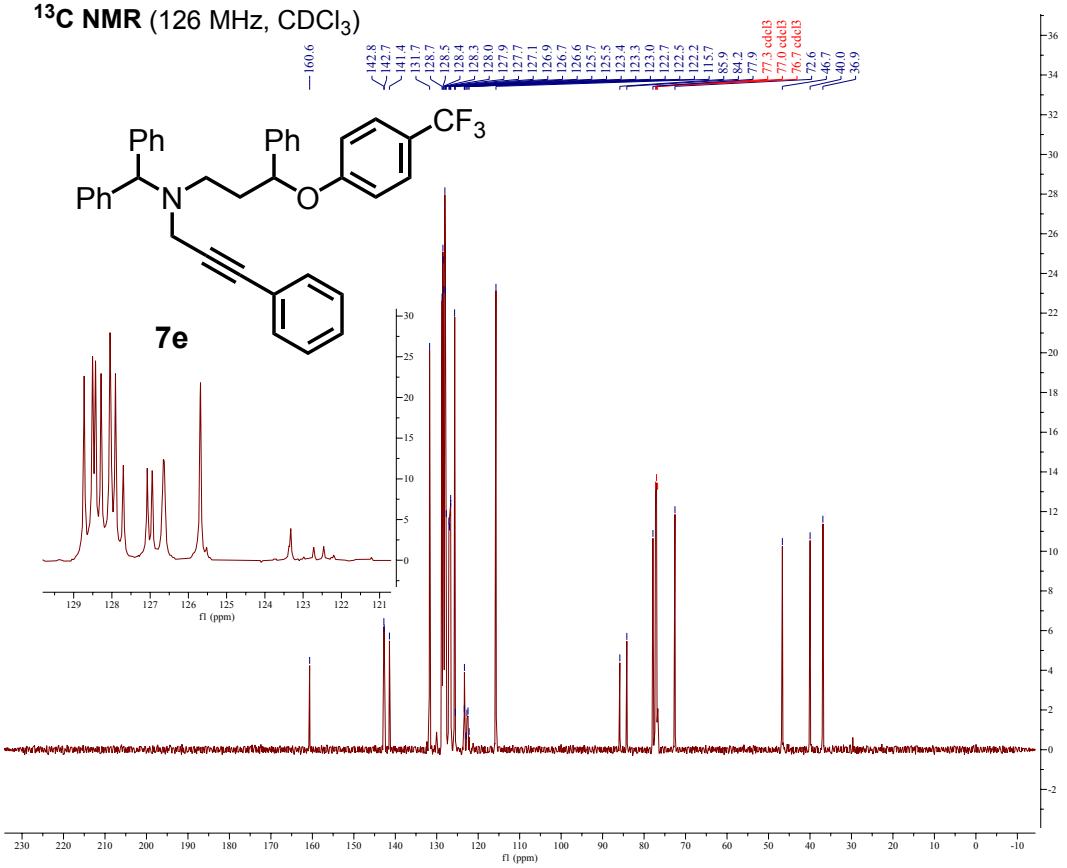
7e

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

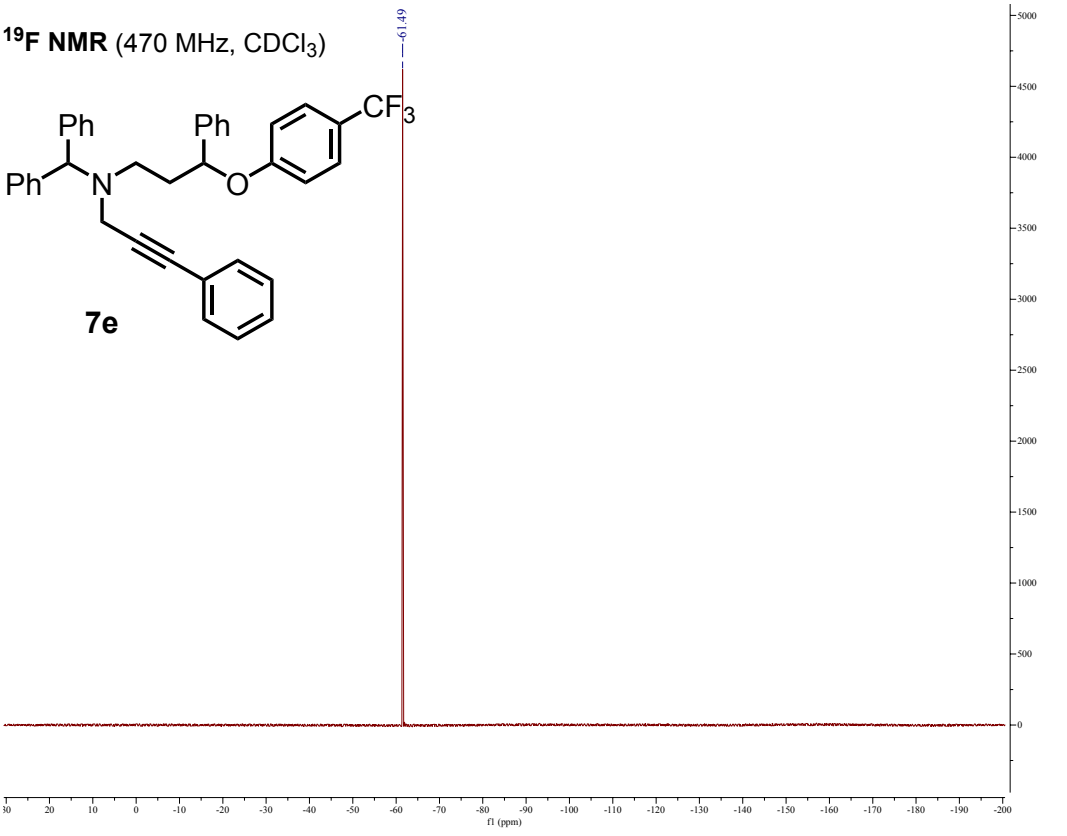


7e

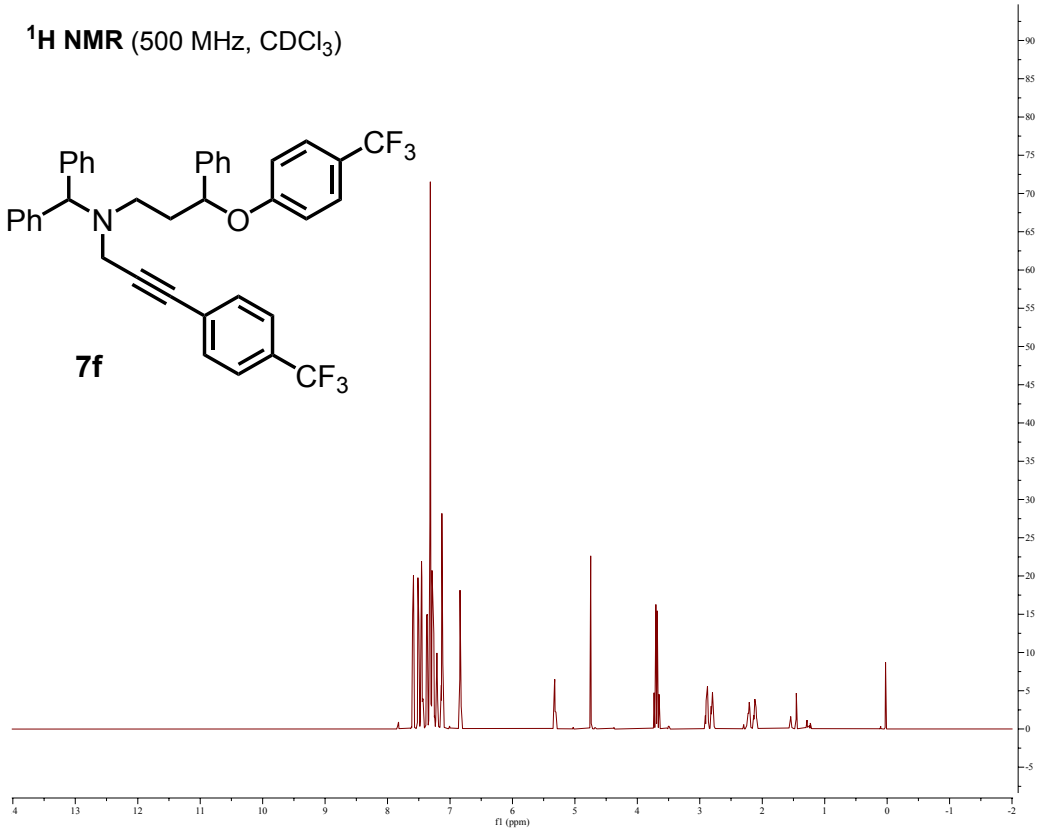
^{13}C NMR (126 MHz, $CDCl_3$)



^{19}F NMR (470 MHz, $CDCl_3$)

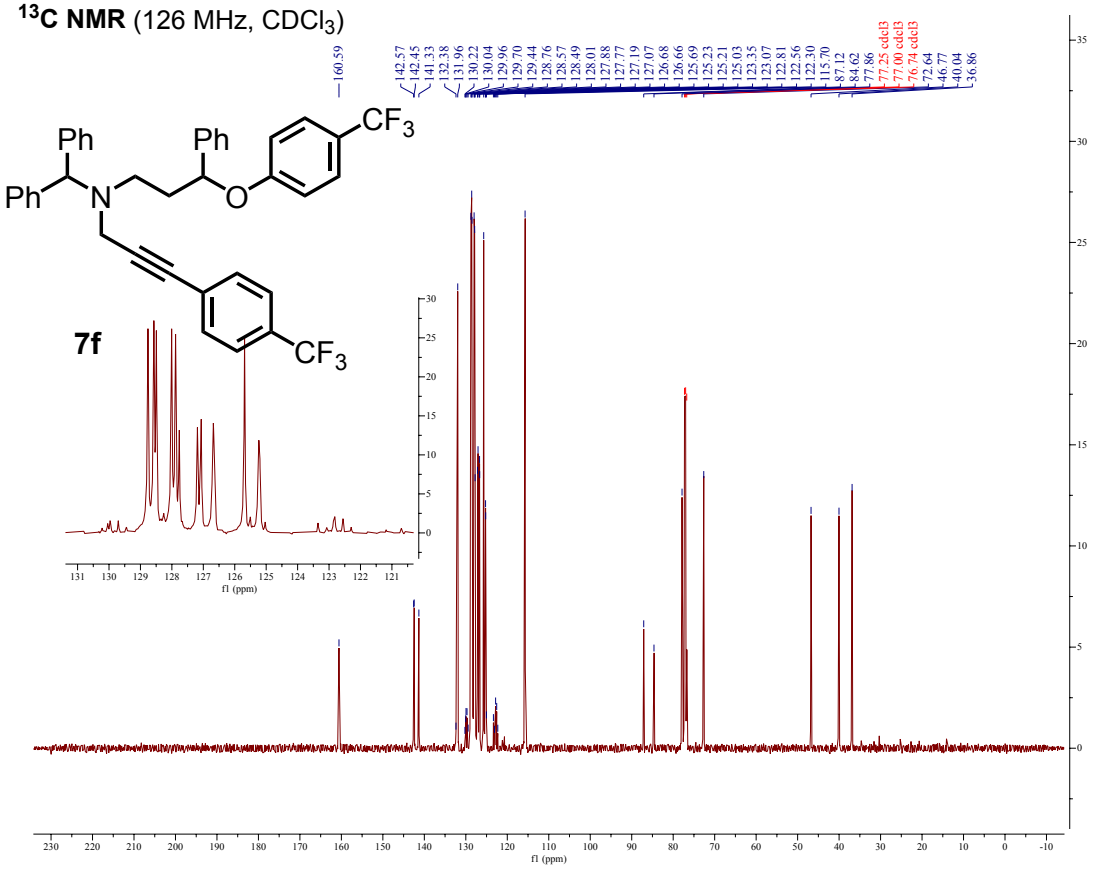


^{1}H NMR (500 MHz, $CDCl_3$)

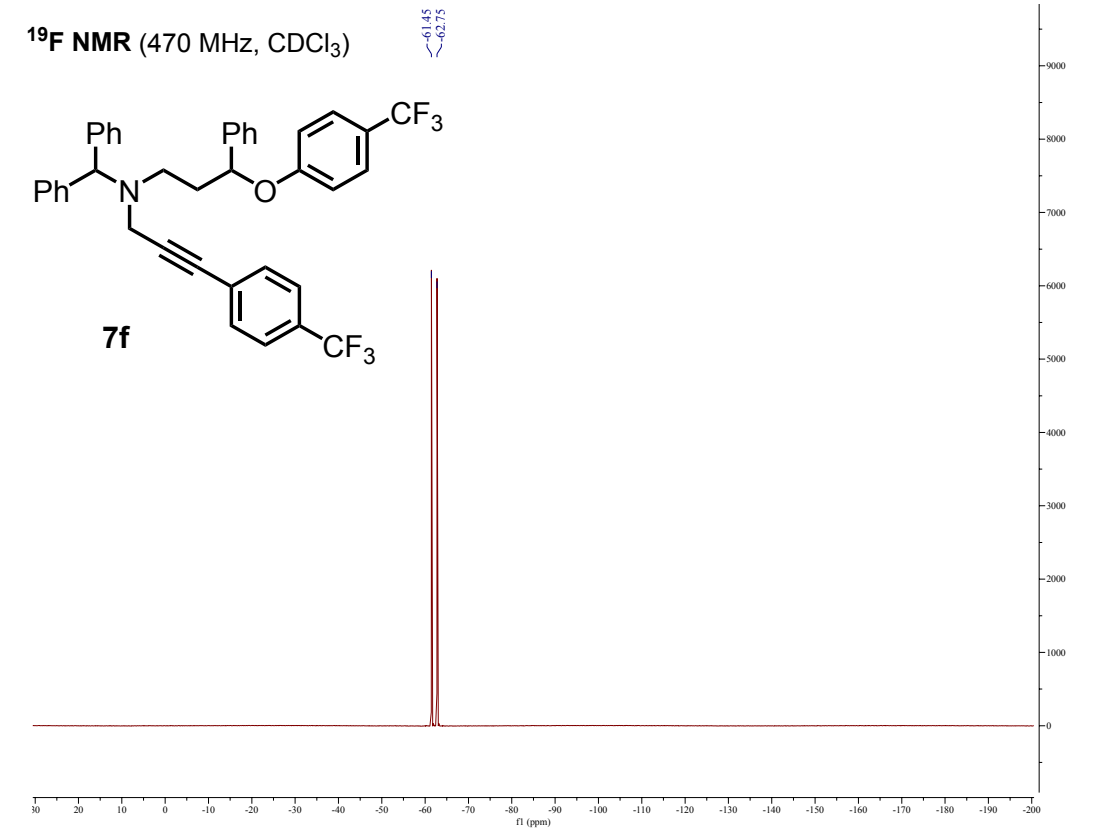


^{1}H NMR (500 MHz, $CDCl_3$)

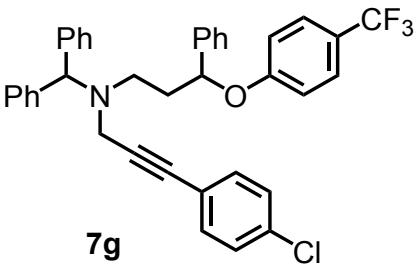
^{13}C NMR (126 MHz, $CDCl_3$)



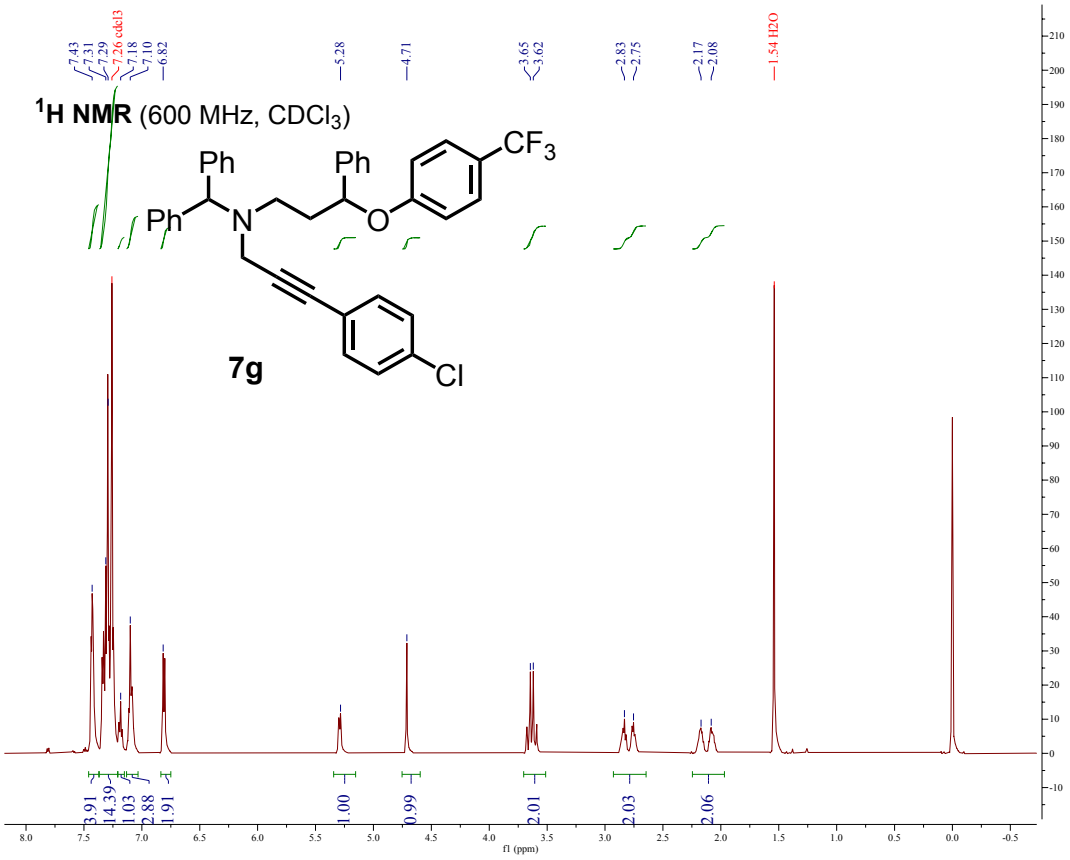
^{19}F NMR (470 MHz, $CDCl_3$)



^{1}H NMR (600 MHz, $CDCl_3$)



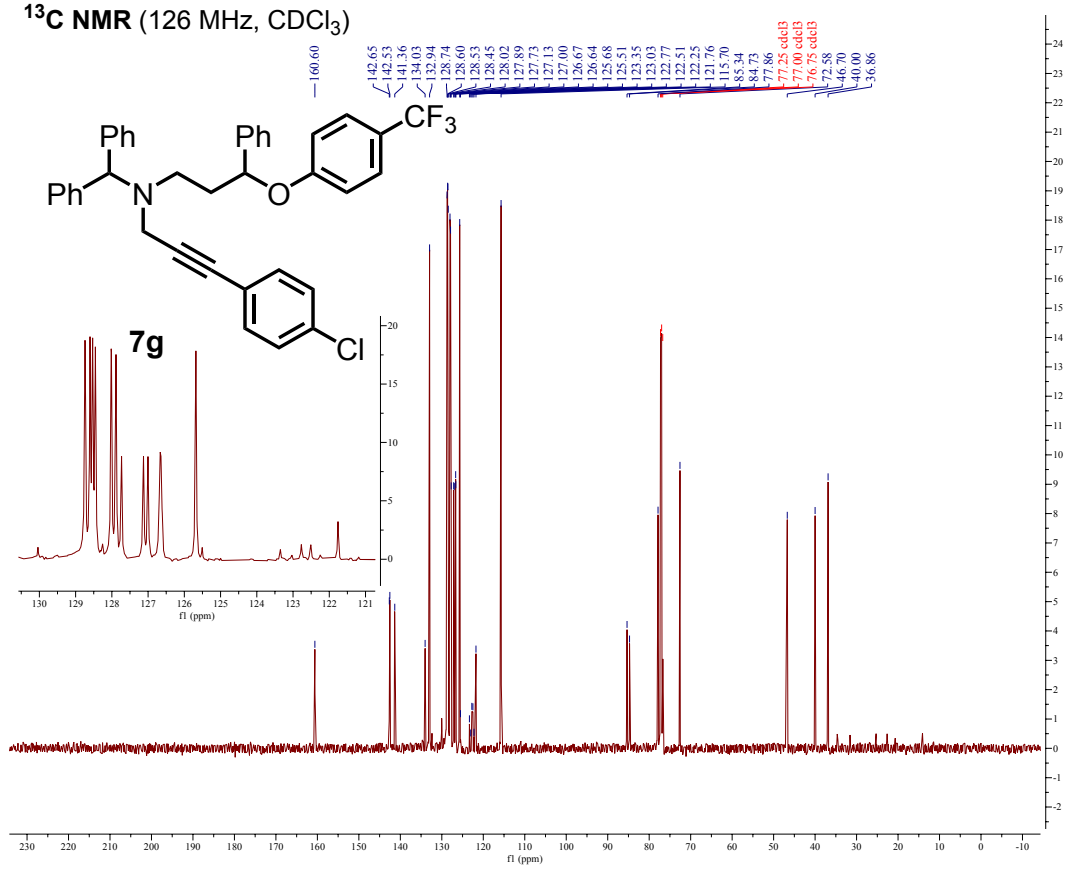
7g



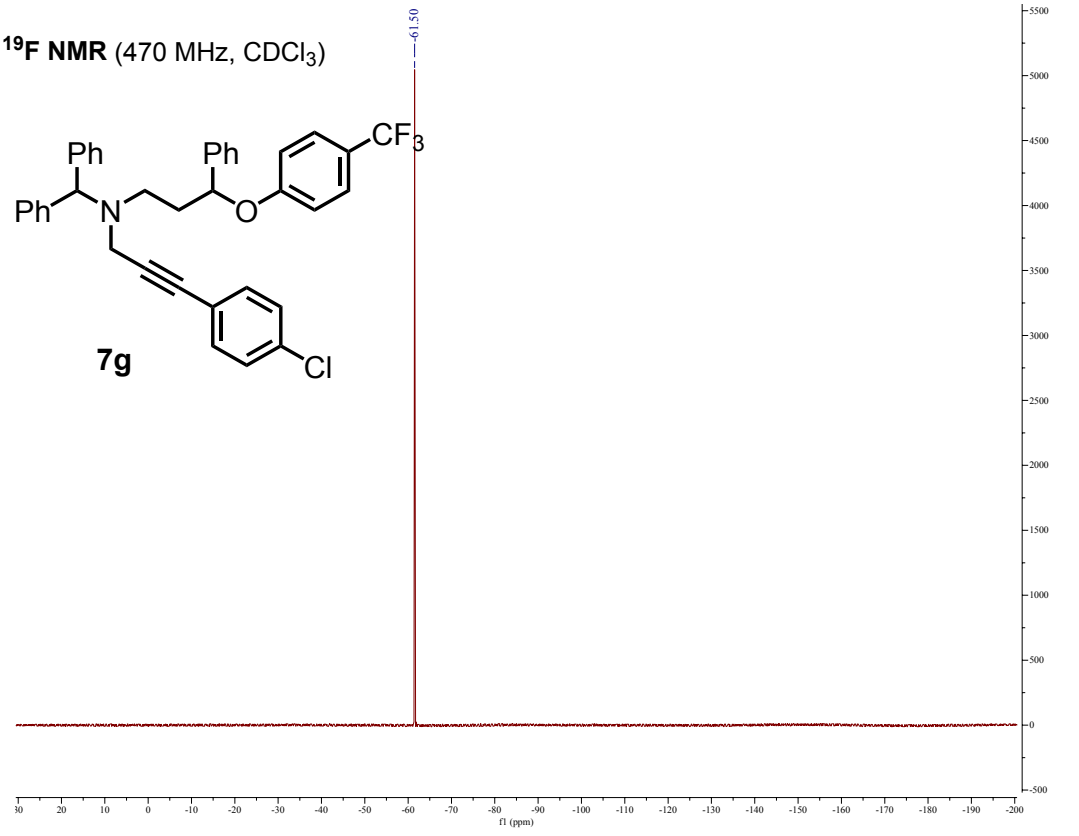
^{1}H NMR (600 MHz, $CDCl_3$)

7g

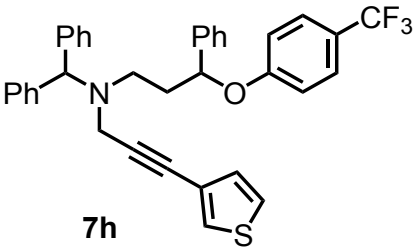
^{13}C NMR (126 MHz, $CDCl_3$)



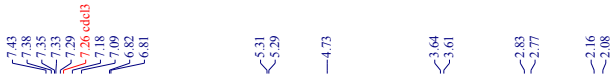
^{19}F NMR (470 MHz, $CDCl_3$)



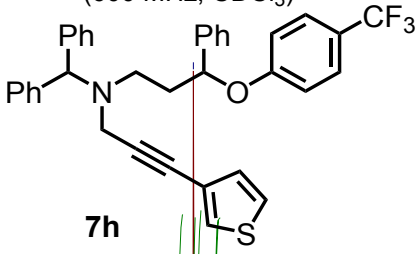
^{1}H NMR (600 MHz, $CDCl_3$)



7h

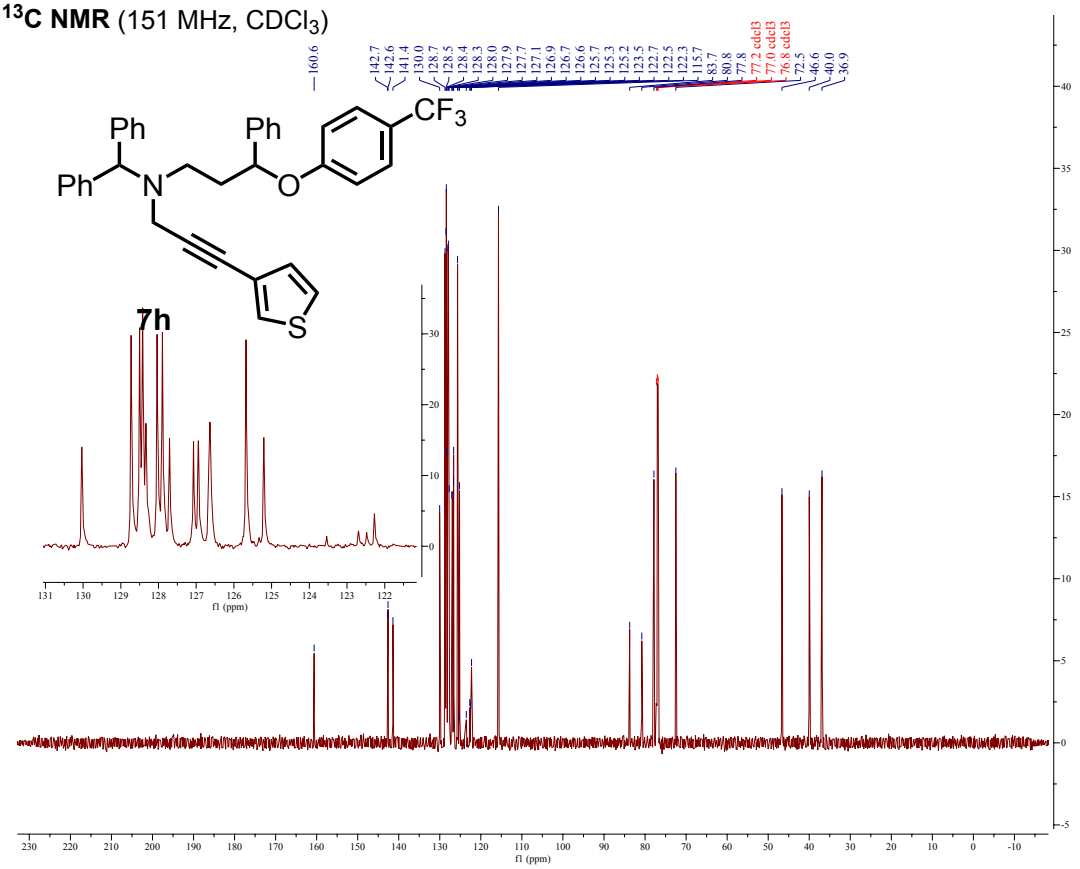


^{1}H NMR (600 MHz, $CDCl_3$)

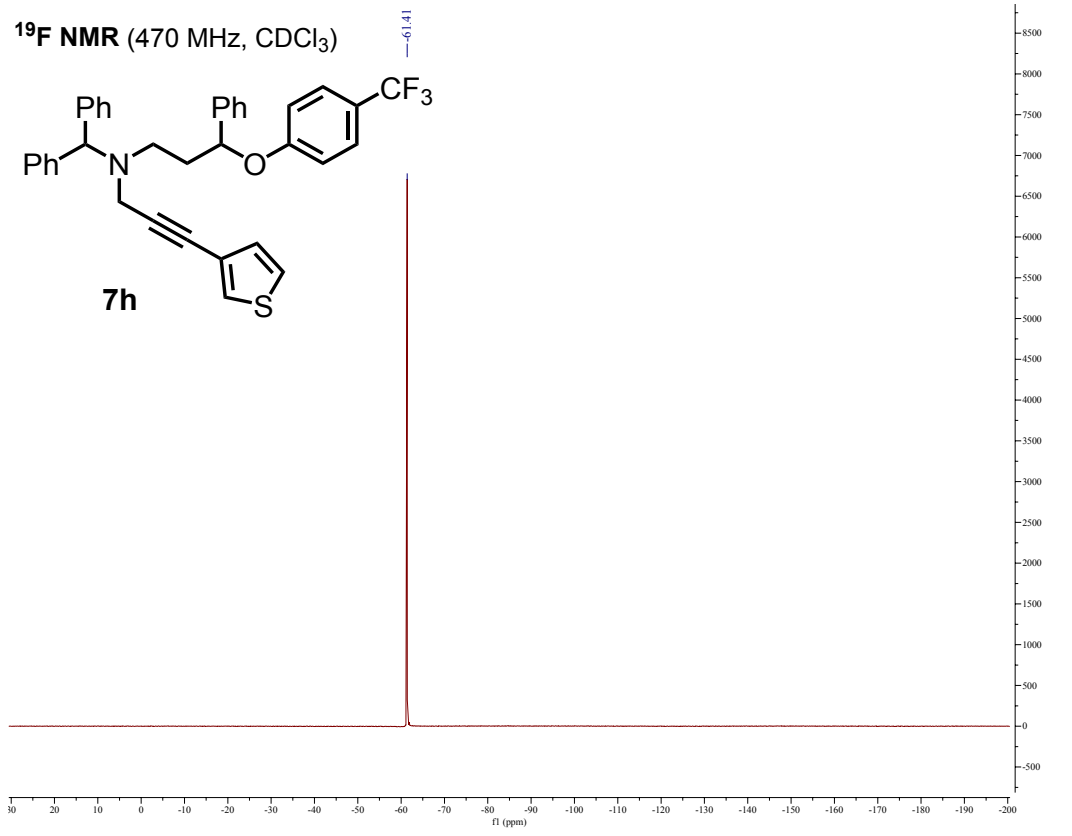


7h

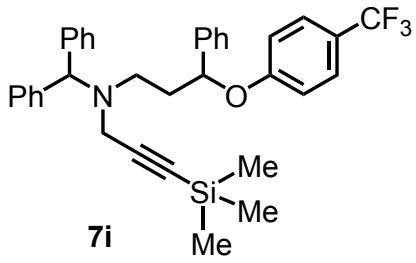
^{13}C NMR (151 MHz, $CDCl_3$)



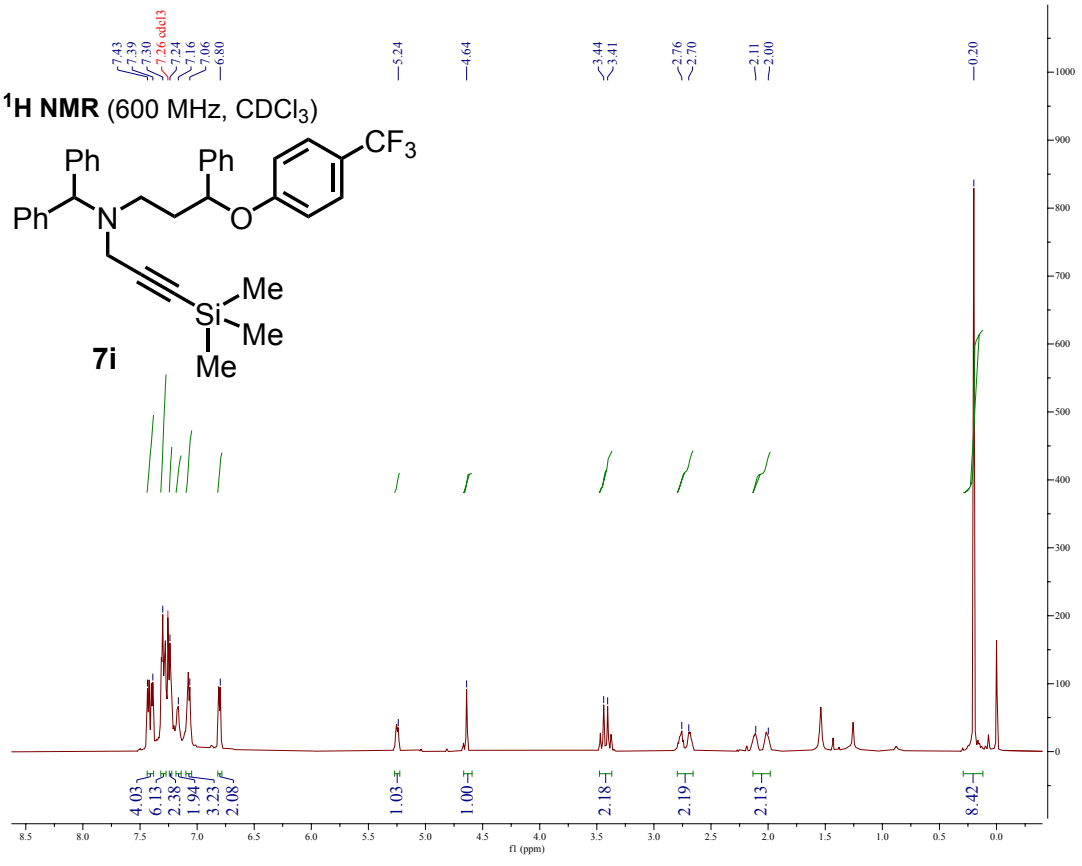
^{19}F NMR (470 MHz, $CDCl_3$)



^{1}H NMR (600 MHz, $CDCl_3$)



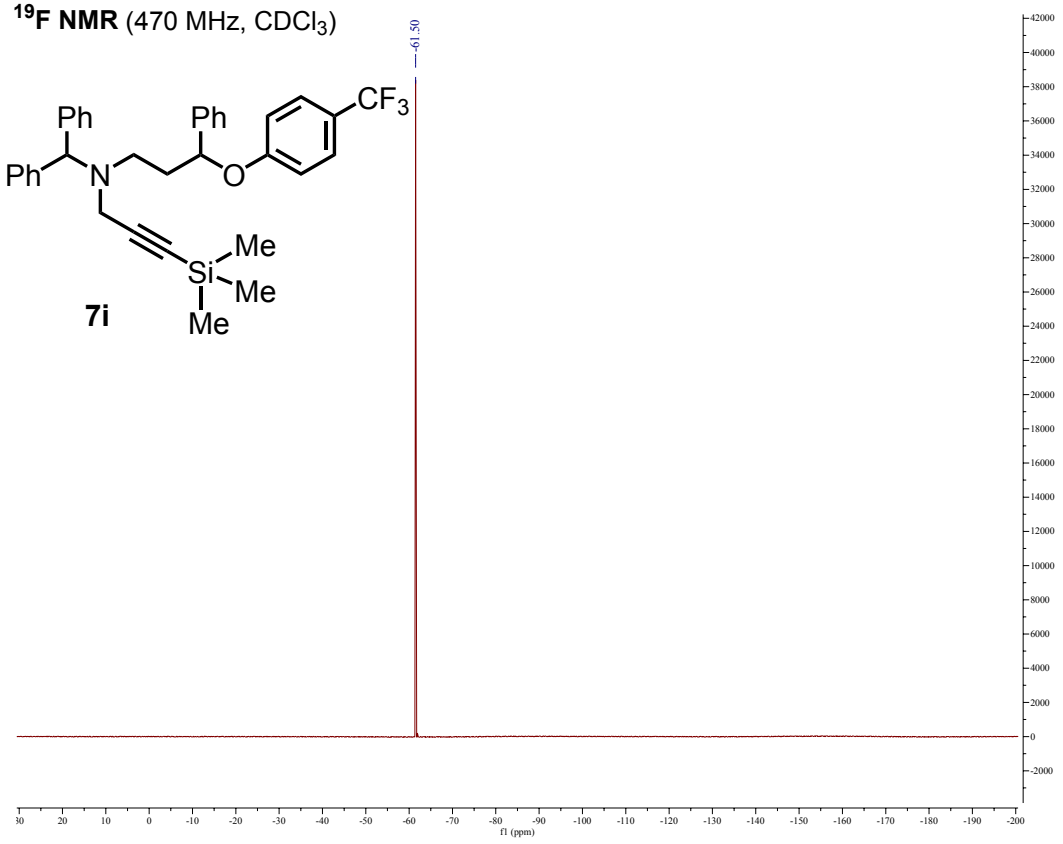
7i



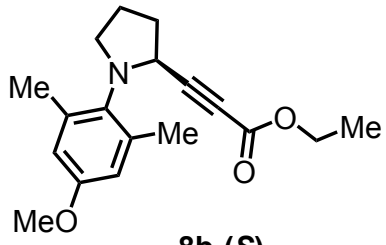
^{1}H NMR (600 MHz, $CDCl_3$)

7i

^{19}F NMR (470 MHz, $CDCl_3$)

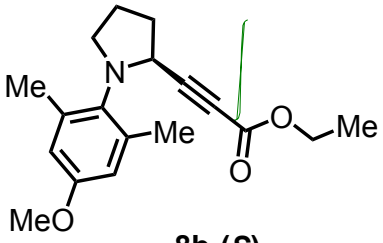


^{1}H NMR (500 MHz, $CDCl_3$)



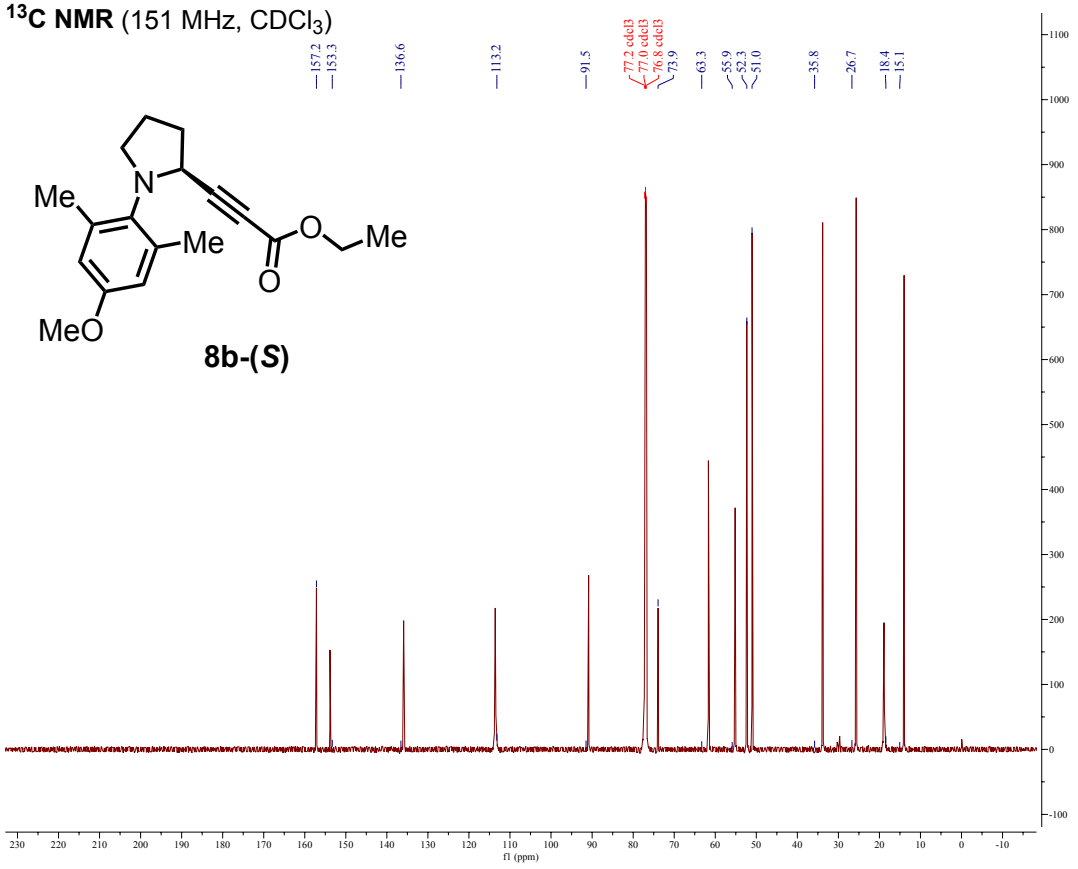
8b-(*S*)

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



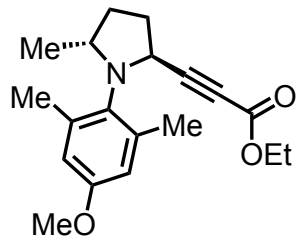
8b-(*S*)

^{13}C NMR (151 MHz, $CDCl_3$)

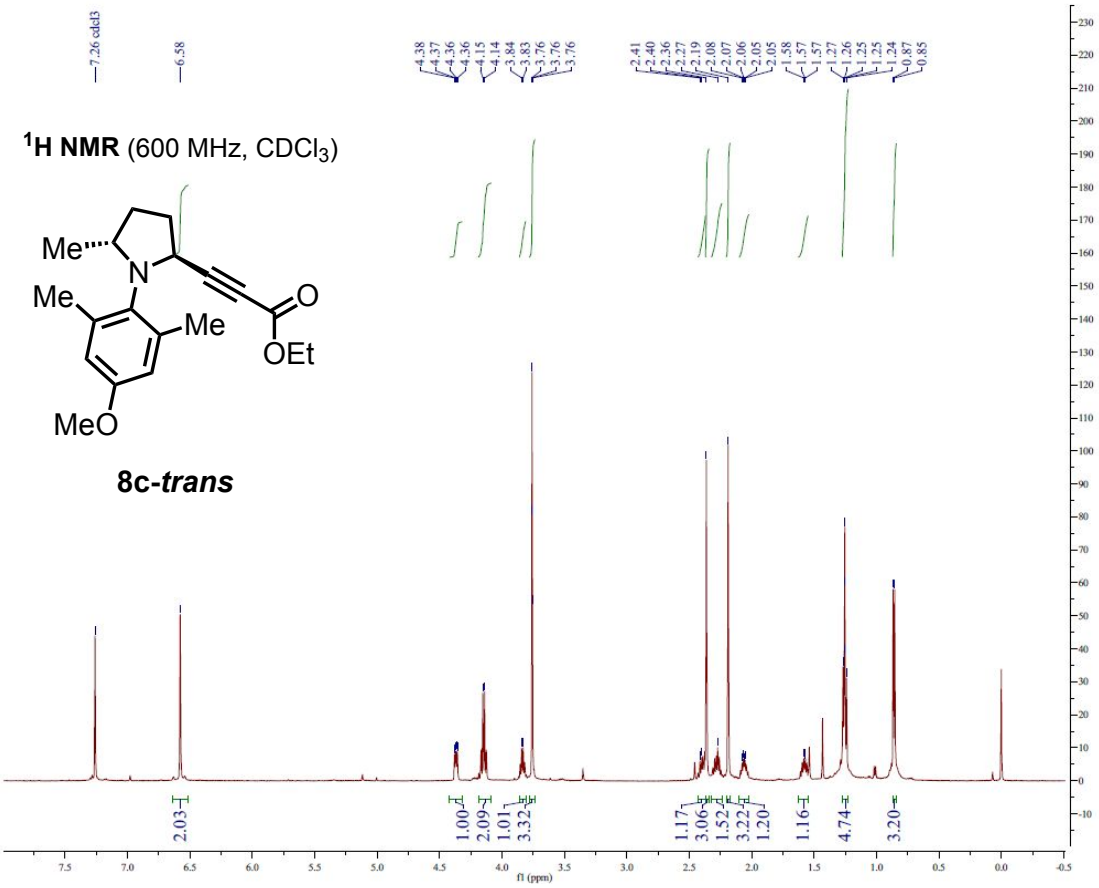


8b-(*S*)

^{1}H NMR (600 MHz, $CDCl_3$)



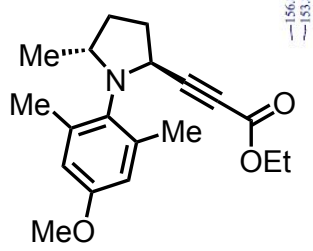
8c-*trans*



^{1}H NMR (600 MHz, $CDCl_3$)

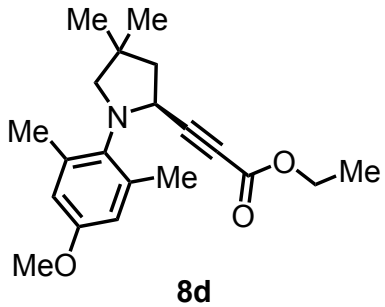
8c-*trans*

^{13}C NMR (151 MHz, $CDCl_3$)



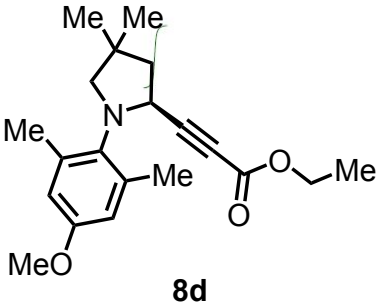
8c-*trans*

^{1}H NMR (600 MHz, $CDCl_3$)



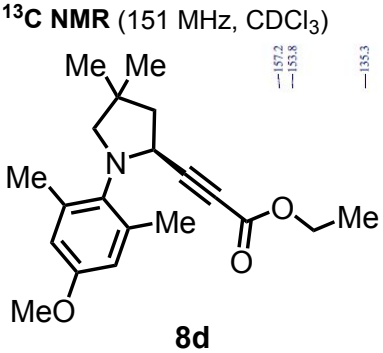
8d

^{1}H NMR (600 MHz, $CDCl_3$)



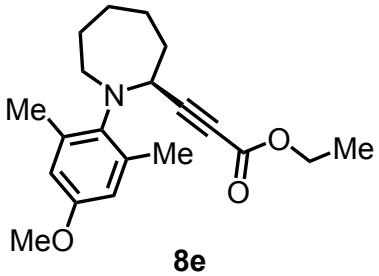
8d

^{13}C NMR (151 MHz, $CDCl_3$)



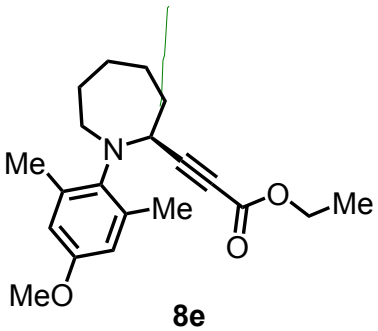
8d

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



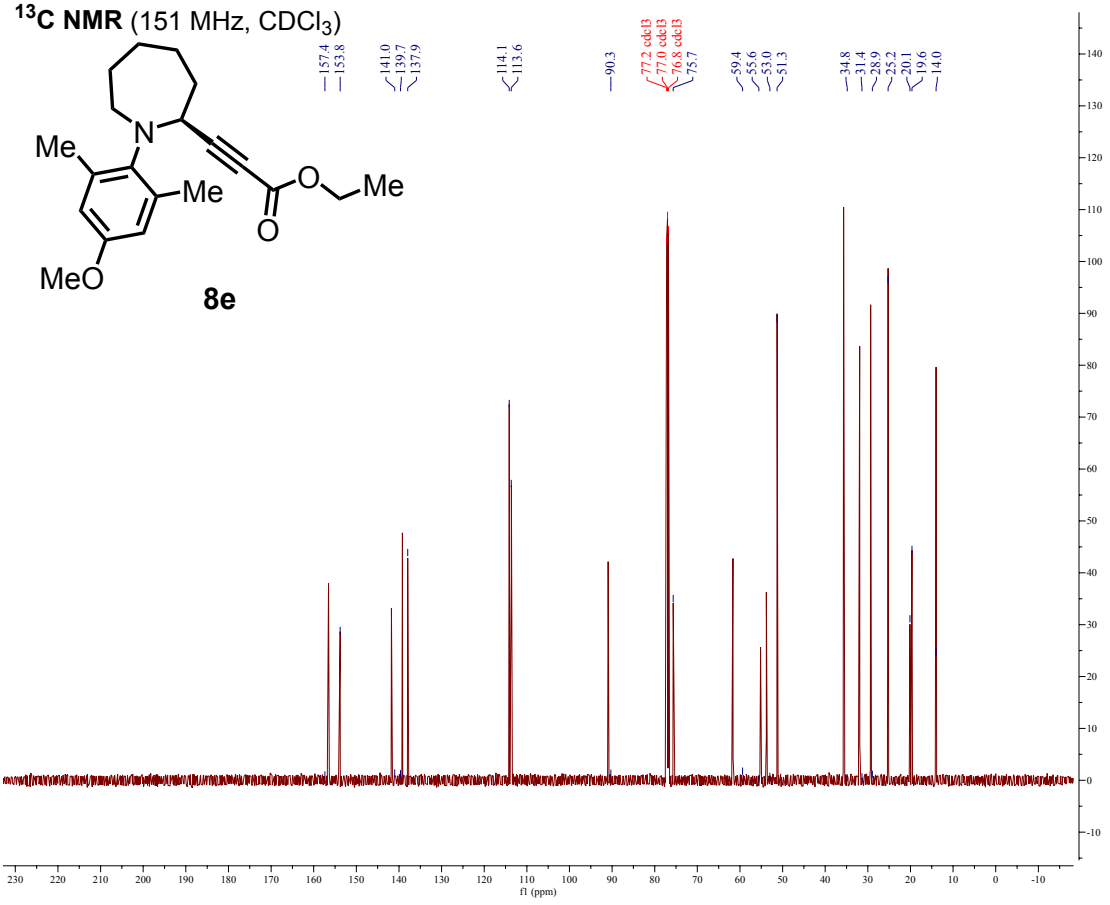
8e

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



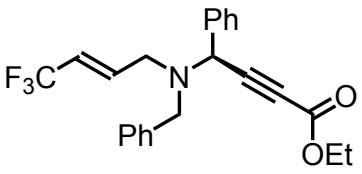
8e

^{13}C NMR (151 MHz, $CDCl_3$)

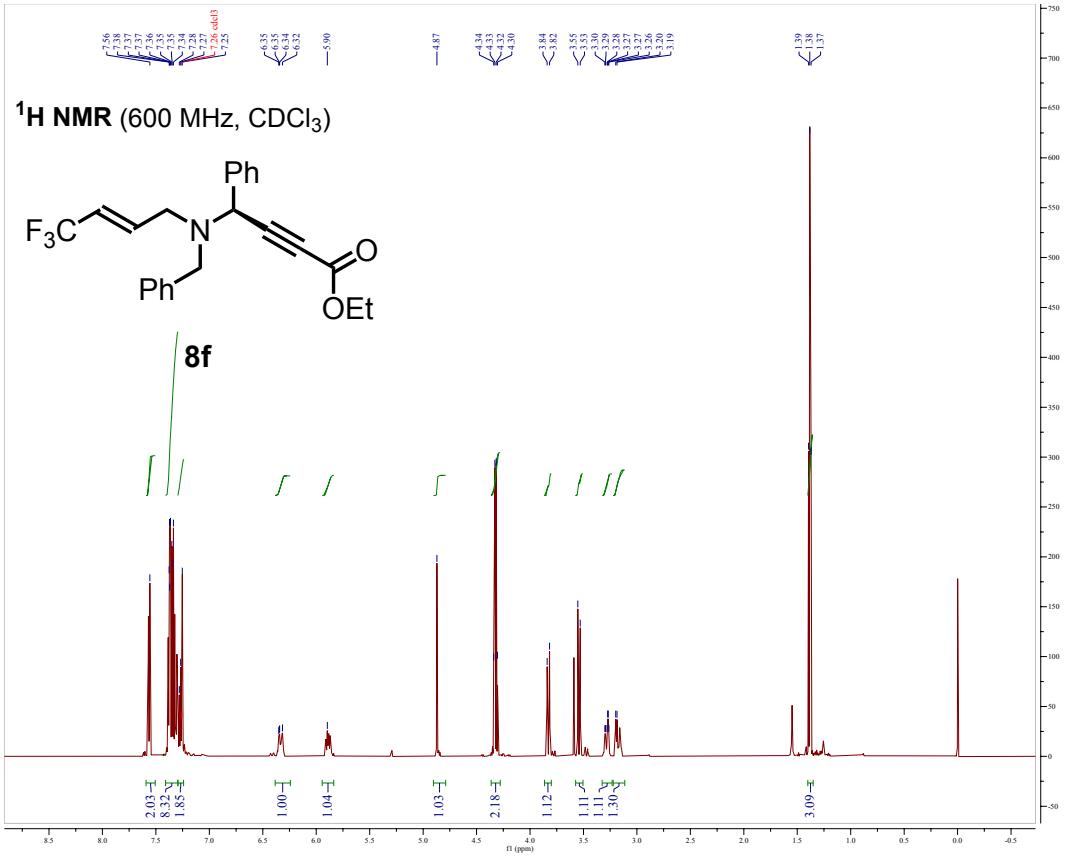


8e

^{1}H NMR (600 MHz, $CDCl_3$)



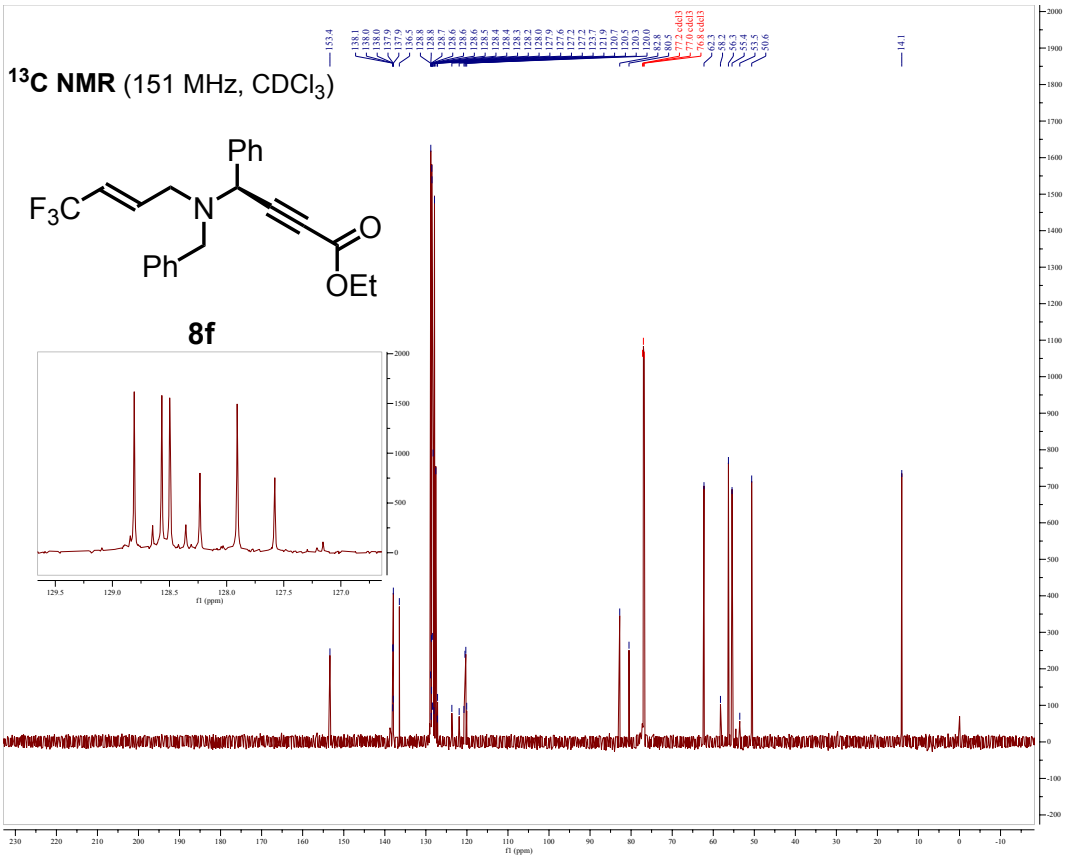
8f



^{1}H NMR (600 MHz, $CDCl_3$)

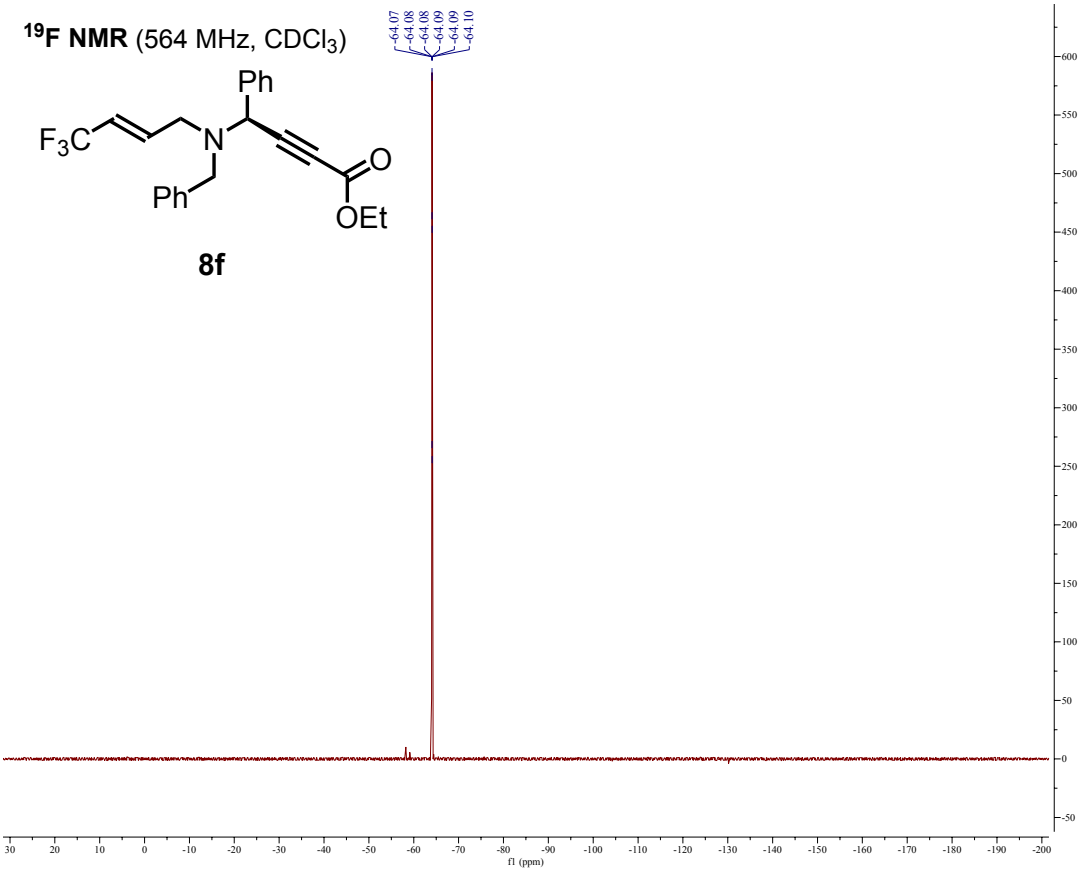
8f

^{13}C NMR (151 MHz, $CDCl_3$)



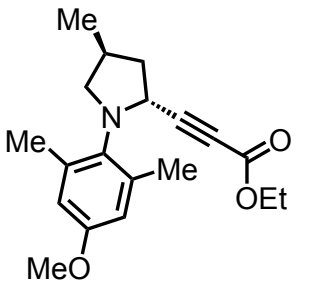
8f

^{19}F NMR (564 MHz, $CDCl_3$)



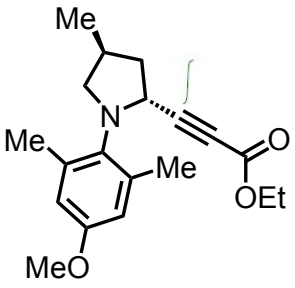
8f

^{1}H NMR (600 MHz, $CDCl_3$)



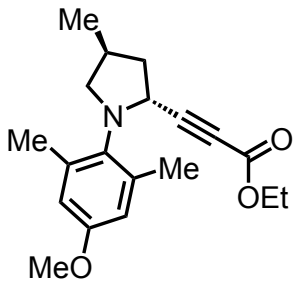
8g-*trans*

^{1}H NMR (600 MHz, $CDCl_3$)



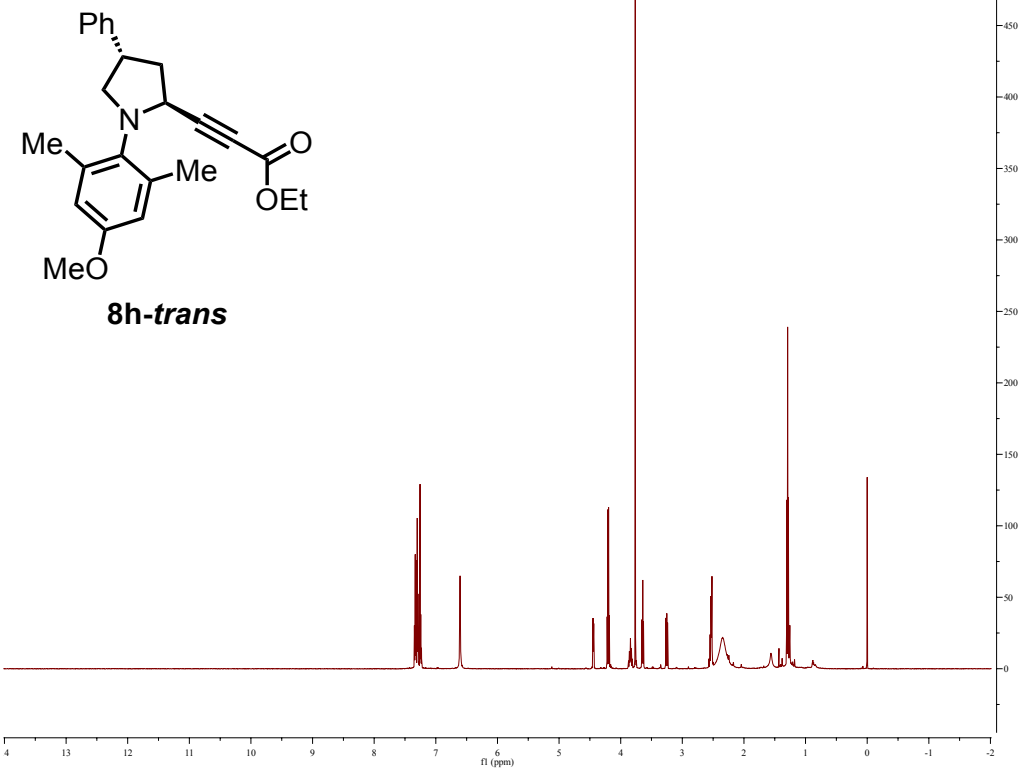
8g-*trans*

^{13}C NMR (151 MHz, $CDCl_3$)



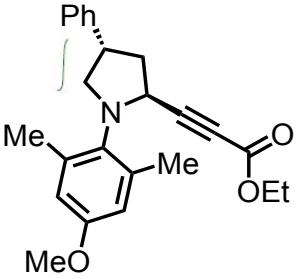
8g-*trans*

^{1}H NMR (600 MHz, $CDCl_3$)



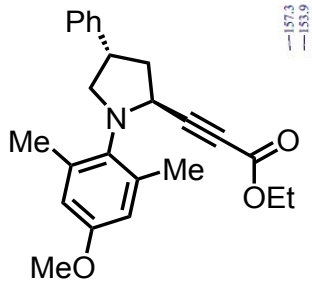
8h-*trans*

^{1}H NMR (600 MHz, $CDCl_3$)



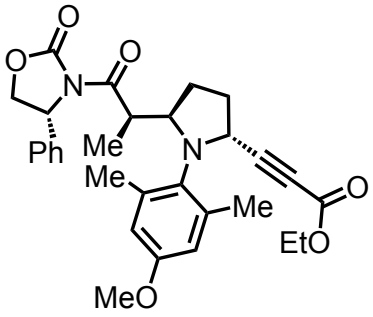
8h-*trans*

^{13}C NMR (151 MHz, $CDCl_3$)

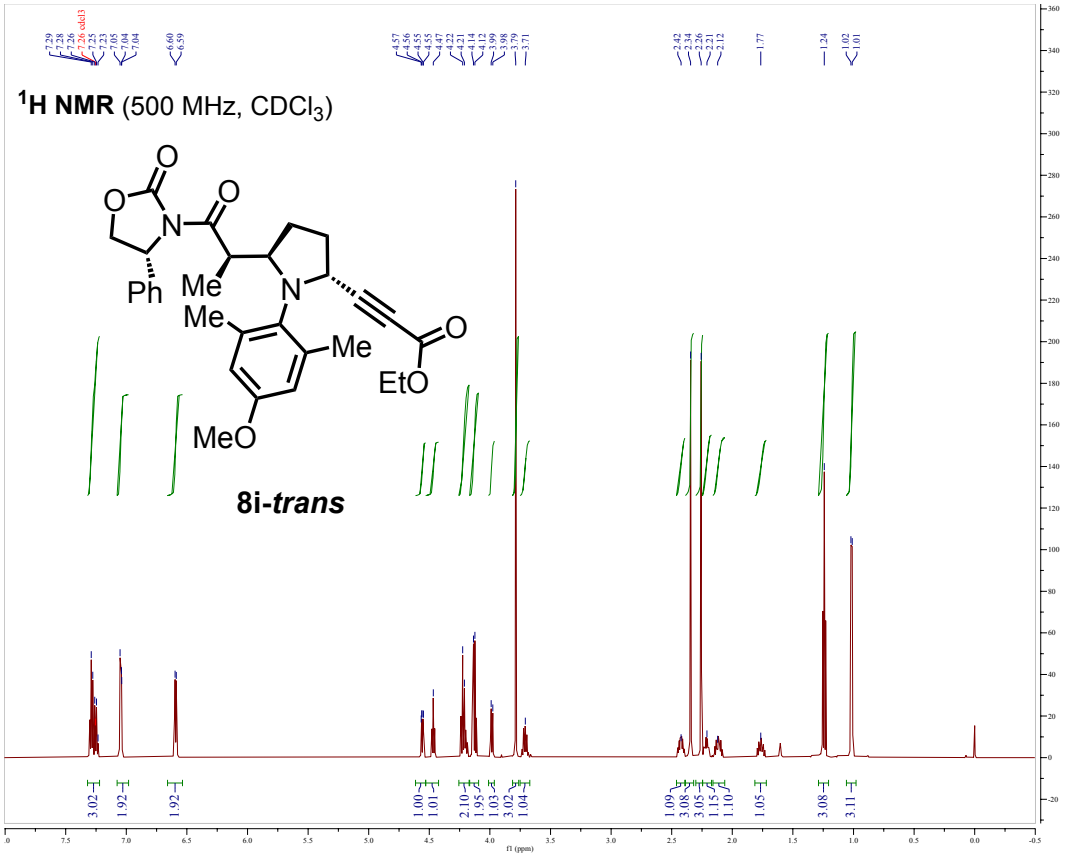


8h-*trans*

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

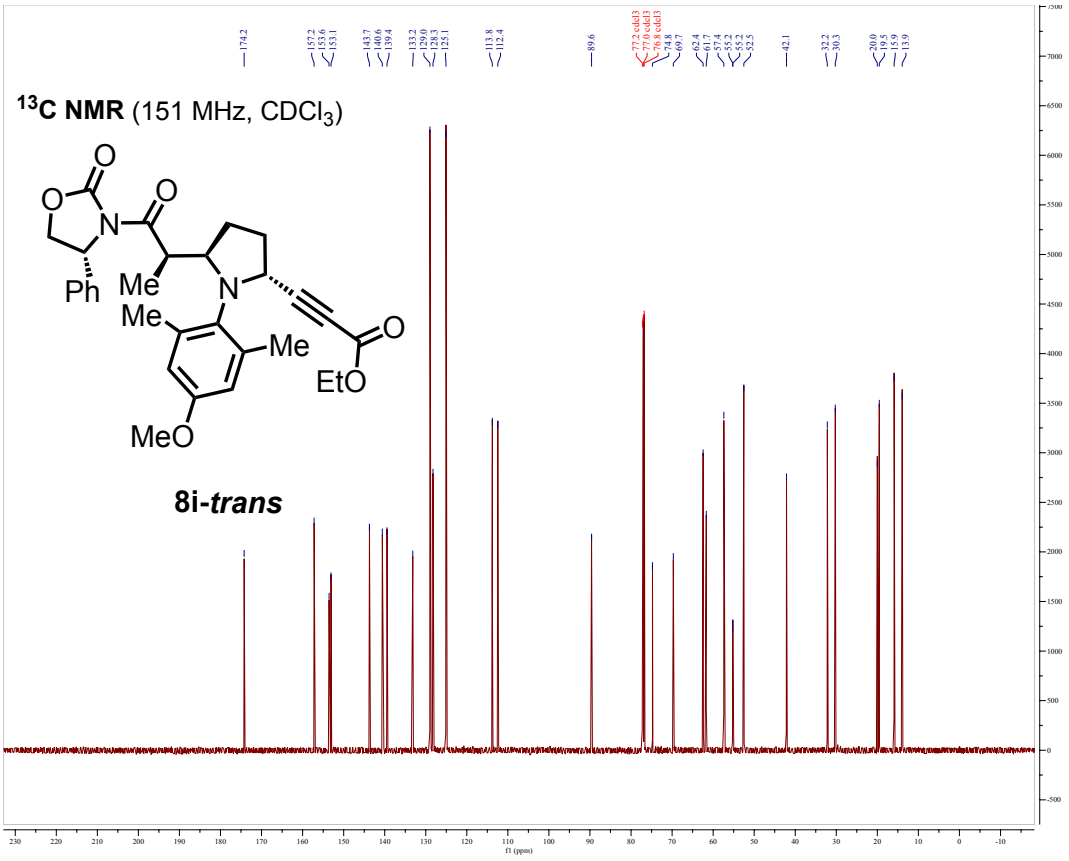


8i-*trans*

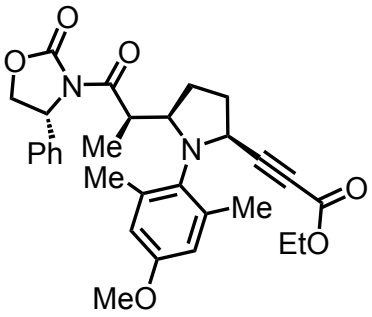


^{1}H NMR (500 MHz, $CDCl_3$)

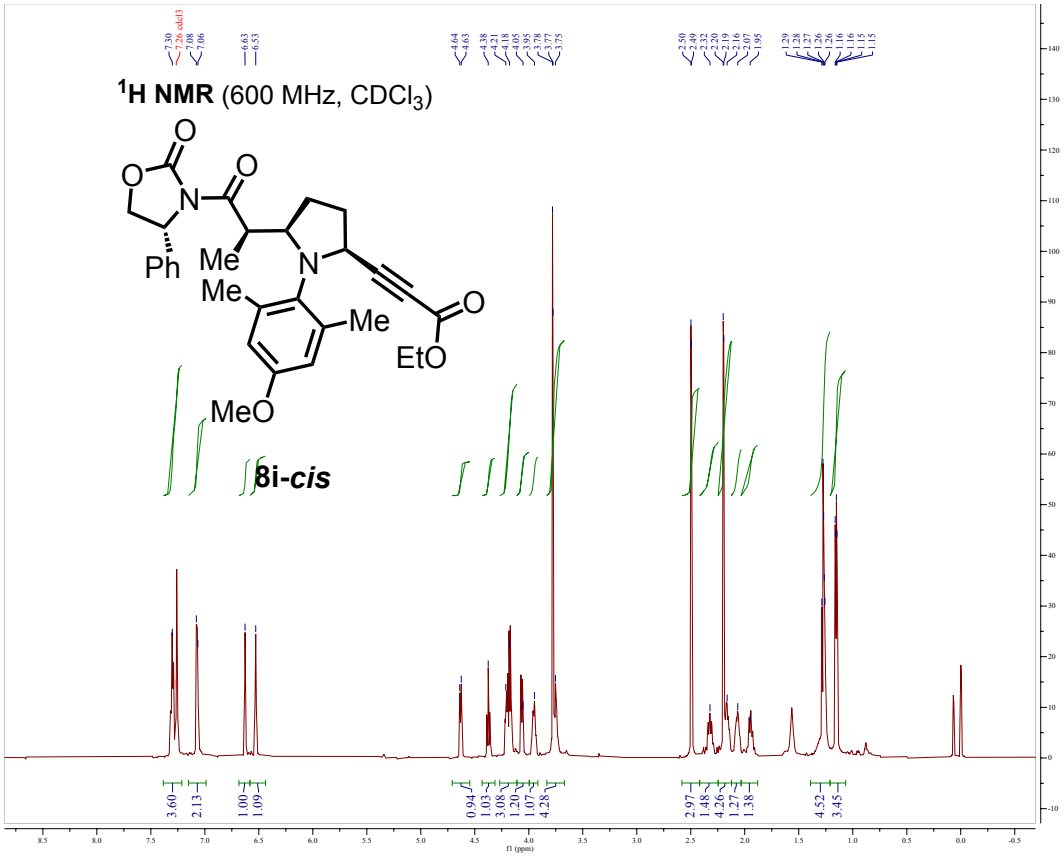
8i-*trans*


174.2
157.2
153.6
153.1
143.7
140.6
139.4
133.2
129.0
128.3
125.1
113.8
112.4
89.6
77.2 cdcl3
77.0 cdcl3
76.8 cdcl3
74.8
69.7
62.4
61.7
57.4
55.7
55.2
52.5
42.1
32.2
30.3
20.0
19.5
15.9
13.9
13C NMR (151 MHz, CDCl3)
O
O
N
O
Ph
Me
N
Me
Me
O
EtO
MeO
8i-trans
f1 (ppm)

^{1}H NMR (600 MHz, $CDCl_3$)

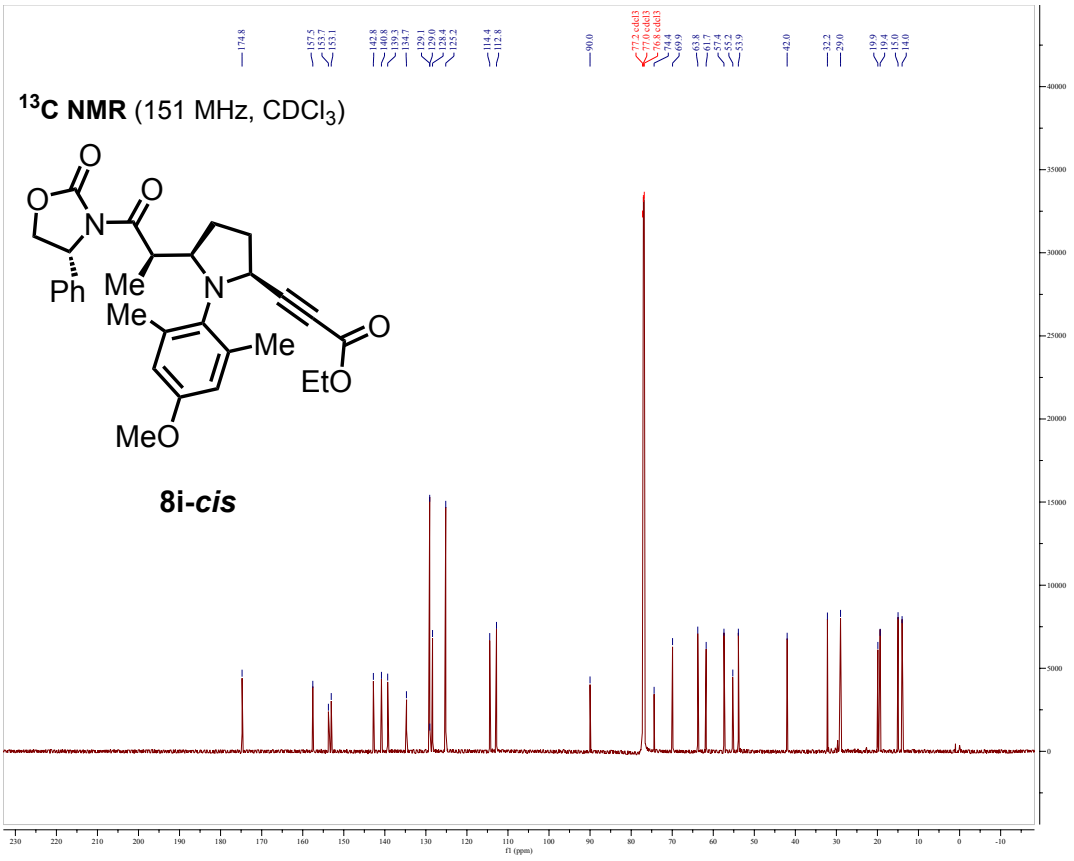


8i-*cis*

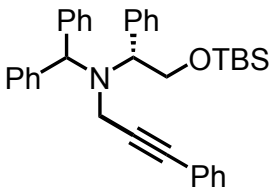


^{1}H NMR (600 MHz, $CDCl_3$)

8i-*cis*

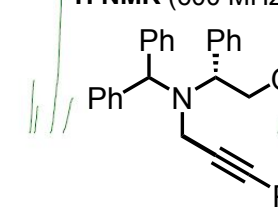

13C NMR (151 MHz, CDCl3)
O
O
N
O
Ph
Me
N
Me
Me
O
EtO
MeO
8i-cis

^{1}H NMR (600 MHz, $CDCl_3$)



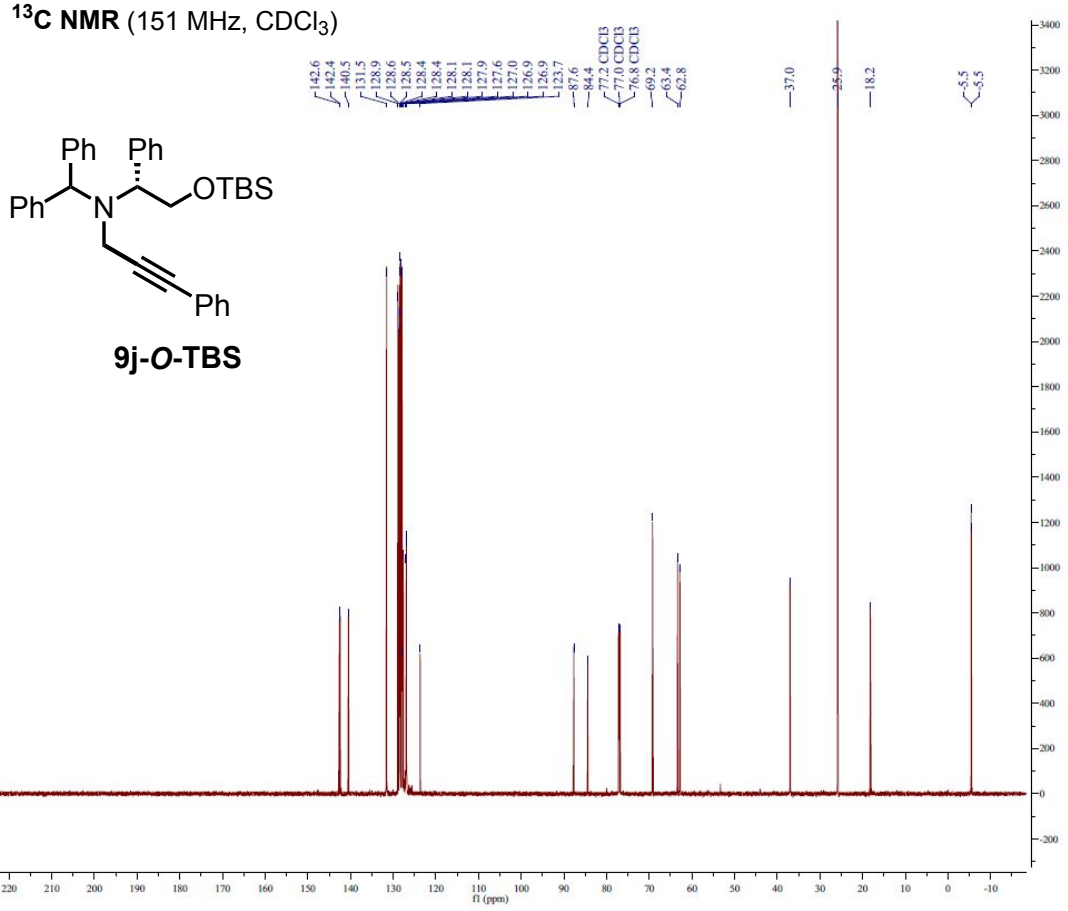
9j-*O*-TBS

^{1}H NMR (600 MHz, $CDCl_3$)



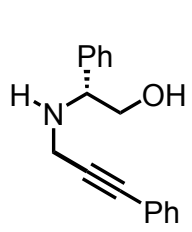
9j-*O*-TBS

^{13}C NMR (151 MHz, $CDCl_3$)

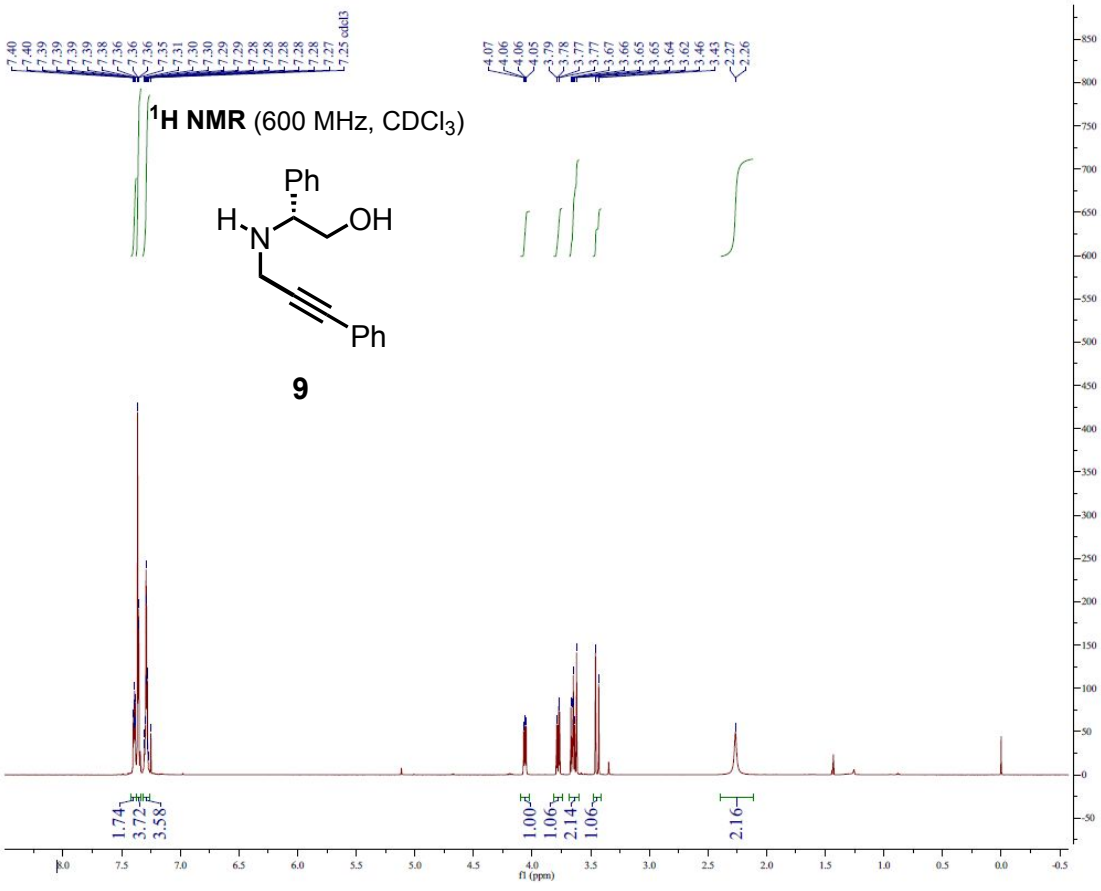


9j-*O*-TBS

^{1}H NMR (600 MHz, $CDCl_3$)



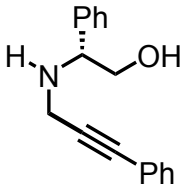
9



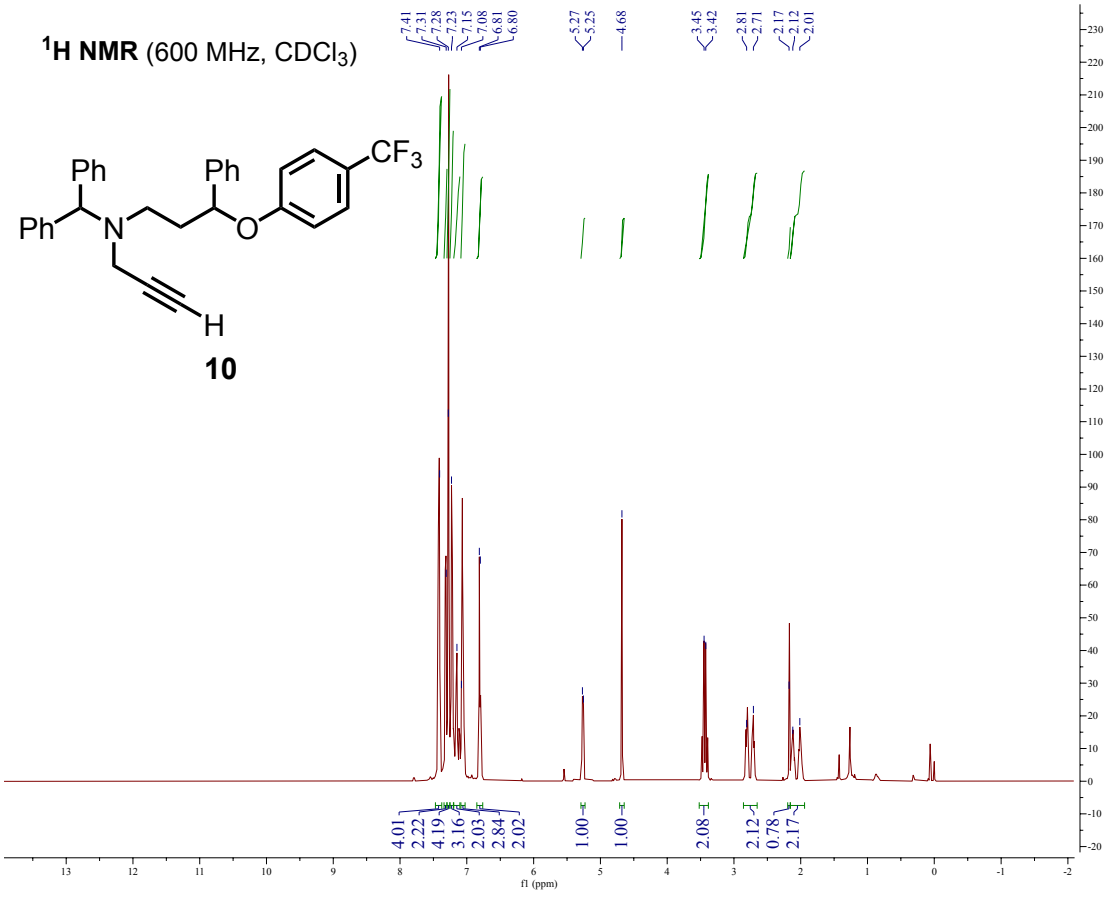
^{1}H NMR (600 MHz, $CDCl_3$)

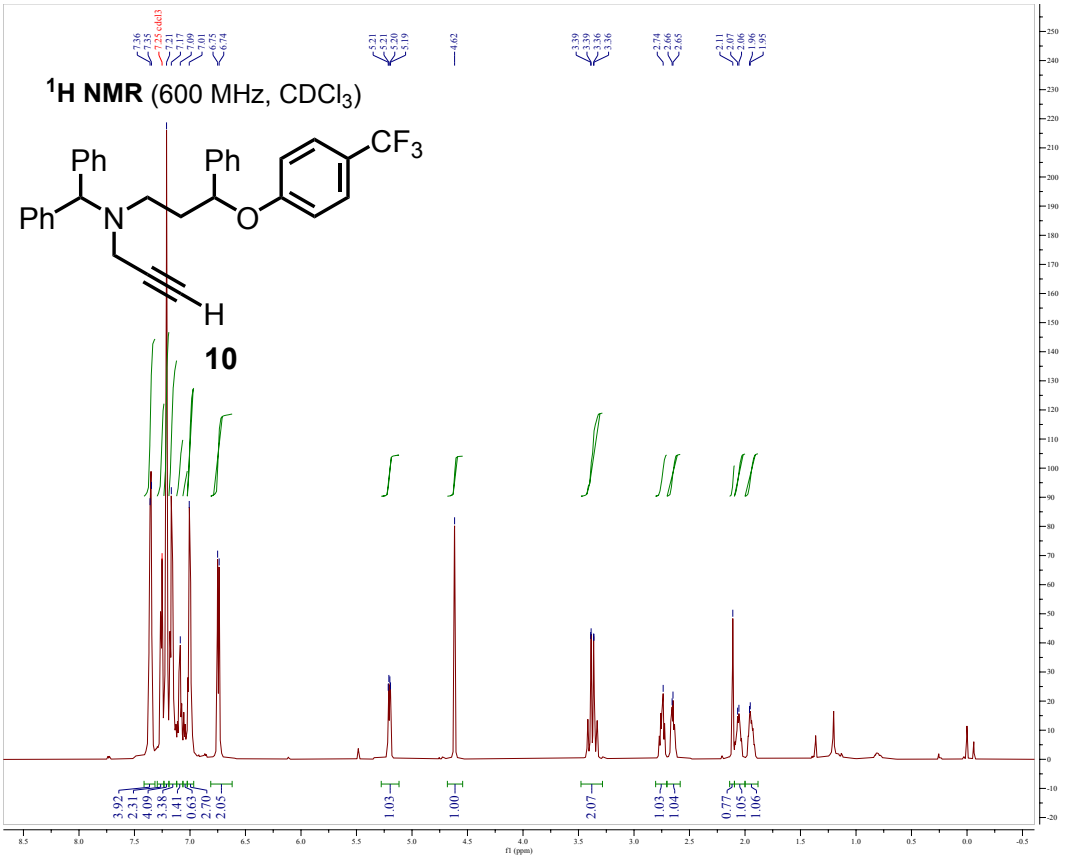
9

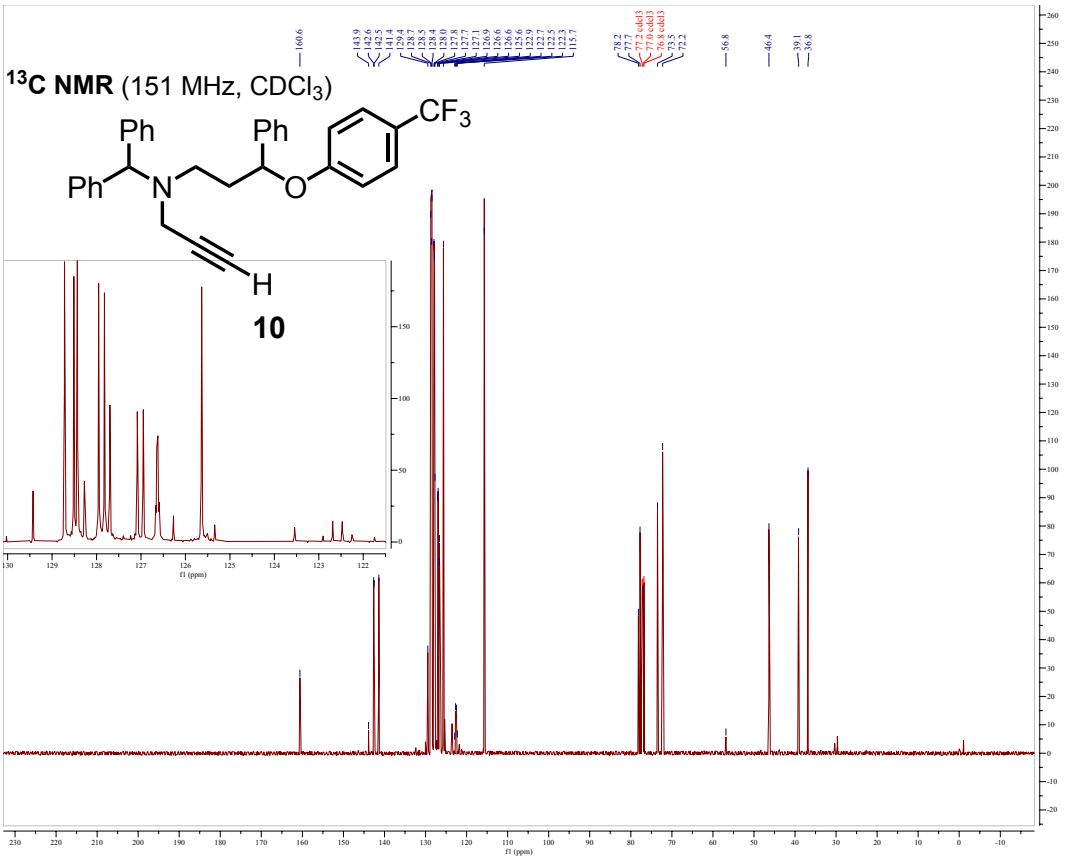
^{13}C NMR (151 MHz, $CDCl_3$)

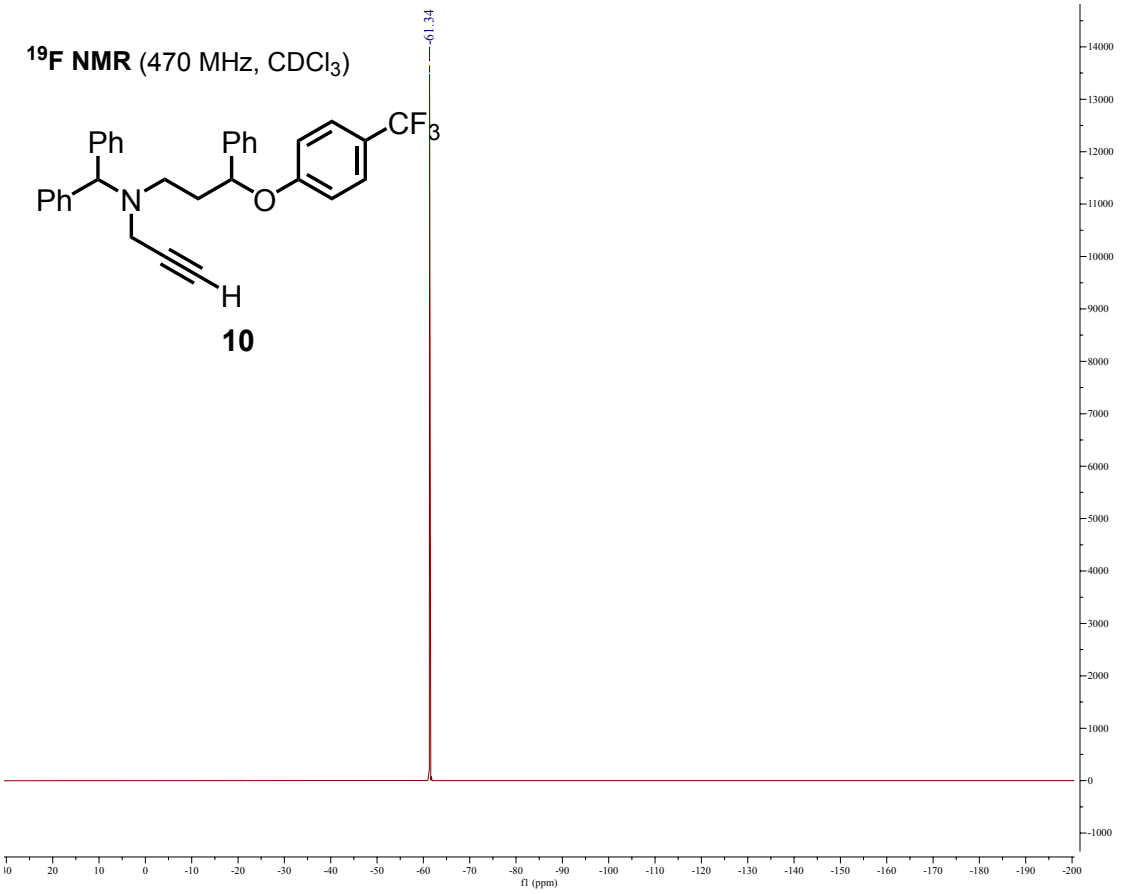


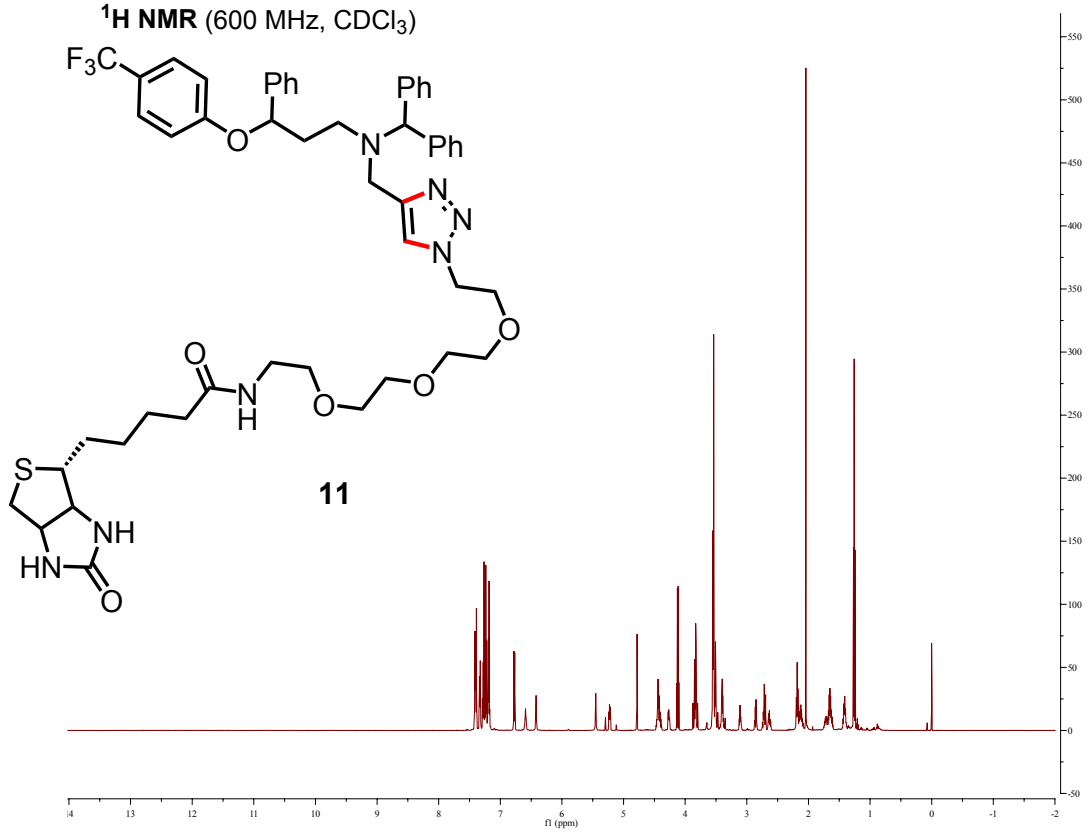
9

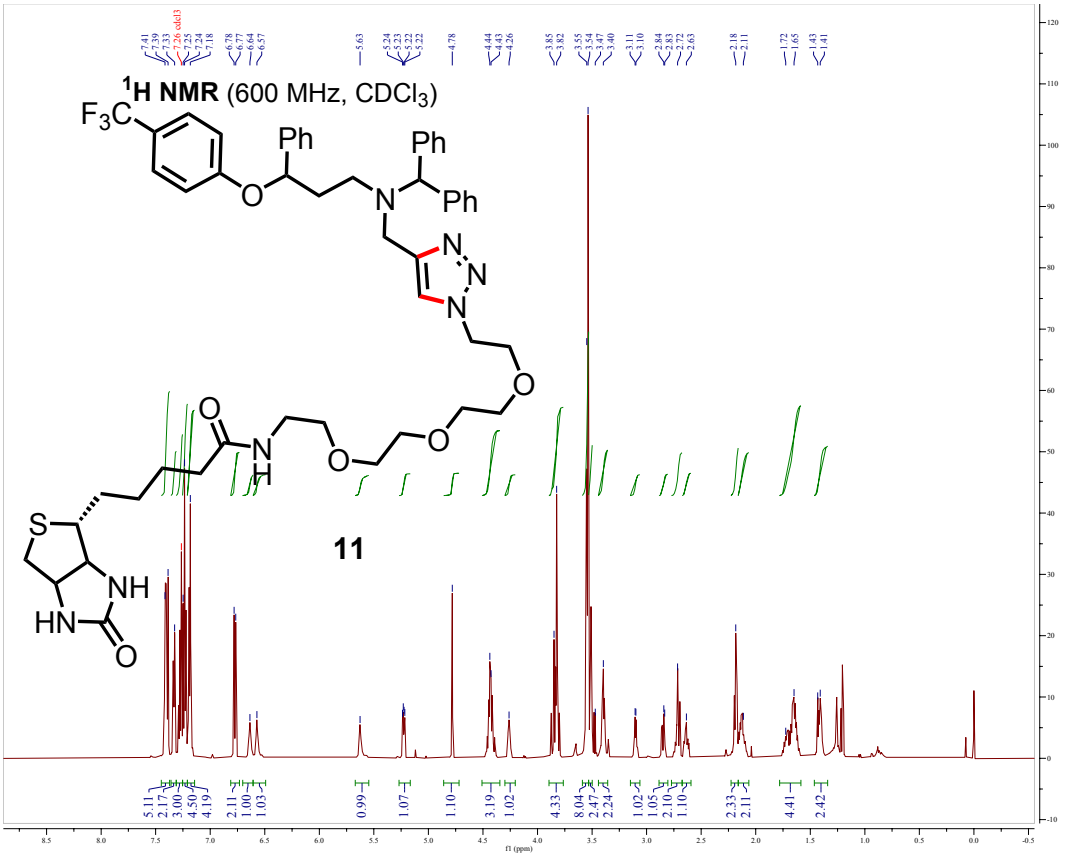

1H NMR (600 MHz, CDCl3)
Ph
Ph
Ph
N
O
CF3
H
10
7.41
7.31
7.28
7.23
7.15
7.08
6.81
6.80
5.27
5.25
4.68
3.45
3.42
2.81
2.71
2.17
2.12
2.01
4.01
2.22
4.19
3.16
2.03
2.84
2.02
1.00
1.00
2.08
2.12
0.78
2.17
f1 (ppm)


1H NMR (600 MHz, CDCl3)
Ph
Ph
Ph
N
O
CF3
H
10
7.36
7.35
7.25 cdcl3
7.21
7.17
7.09
7.01
6.75
6.74
5.21
5.21
5.20
5.19
4.62
3.39
3.39
3.36
3.36
2.74
2.66
2.65
2.11
2.07
2.06
1.96
1.95
3.92
2.31
4.09
3.38
1.41
0.63
2.70
2.05
1.03
1.00
2.07
1.03
1.04
0.77
1.05
1.06
f1 (ppm)

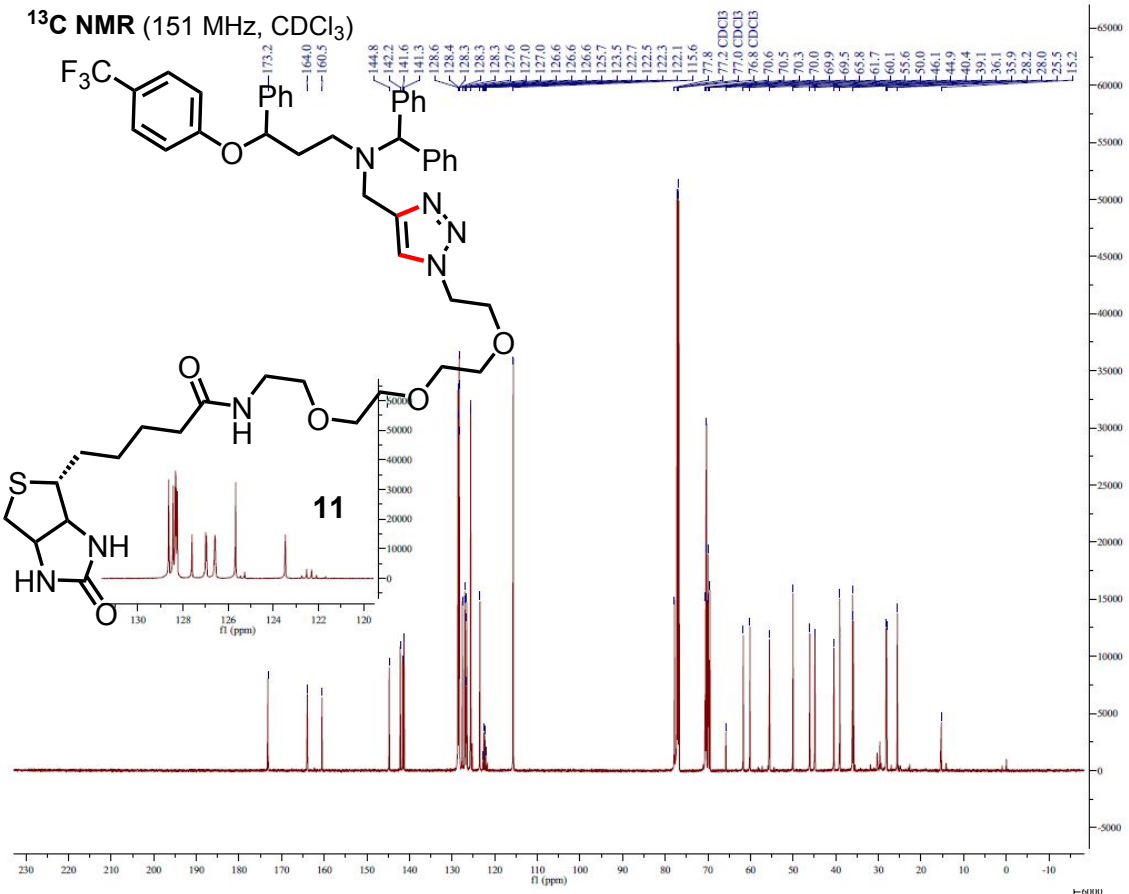

13C NMR (151 MHz, CDCl3)
Ph
Ph
Ph
N
O
CF3
H
10


19F NMR (470 MHz, CDCl3)
-61.34
Ph
Ph
Ph
N
O
CF3
H
10
f1 (ppm)

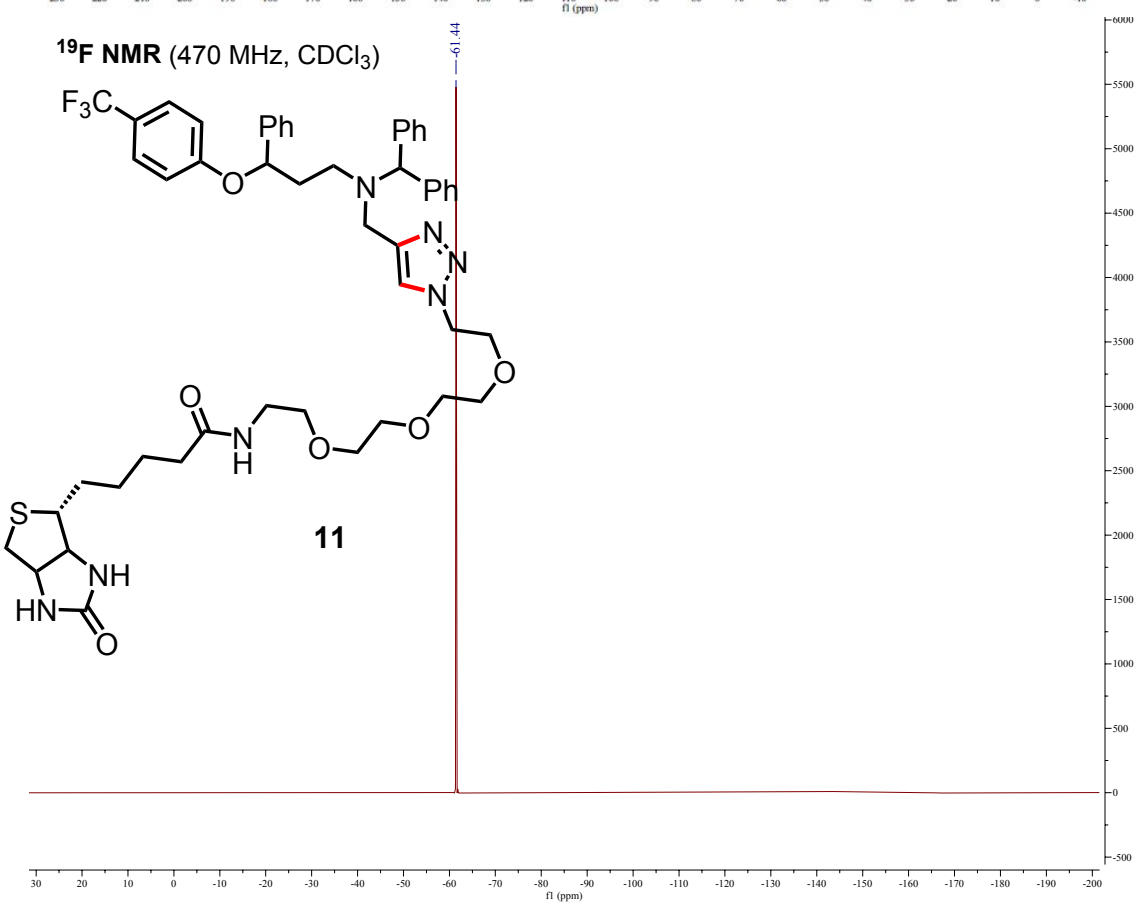

^{1}H NMR (600 MHz, $CDCl_3$)
11
f1 (ppm)


^{1}H NMR (600 MHz, $CDCl_3$)
11
f1 (ppm)

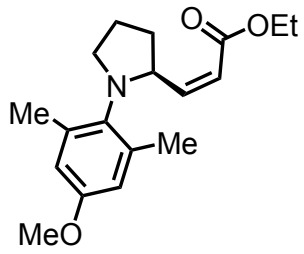
^{13}C NMR (151 MHz, $CDCl_3$)



^{19}F NMR (470 MHz, $CDCl_3$)

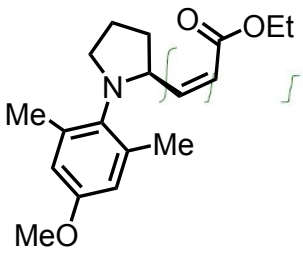


^{1}H NMR (600 MHz, $CDCl_3$)



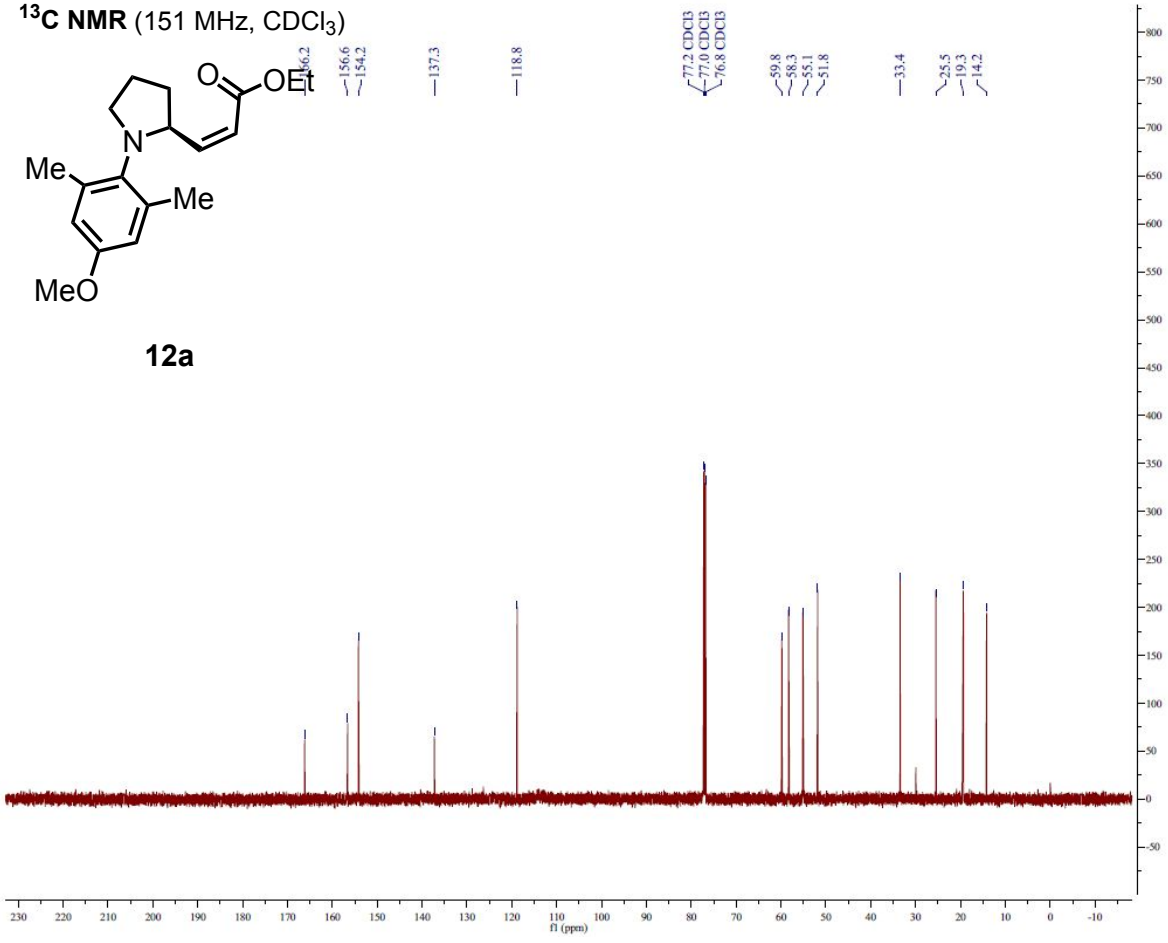
12a

^{1}H NMR (600 MHz, $CDCl_3$)



12a

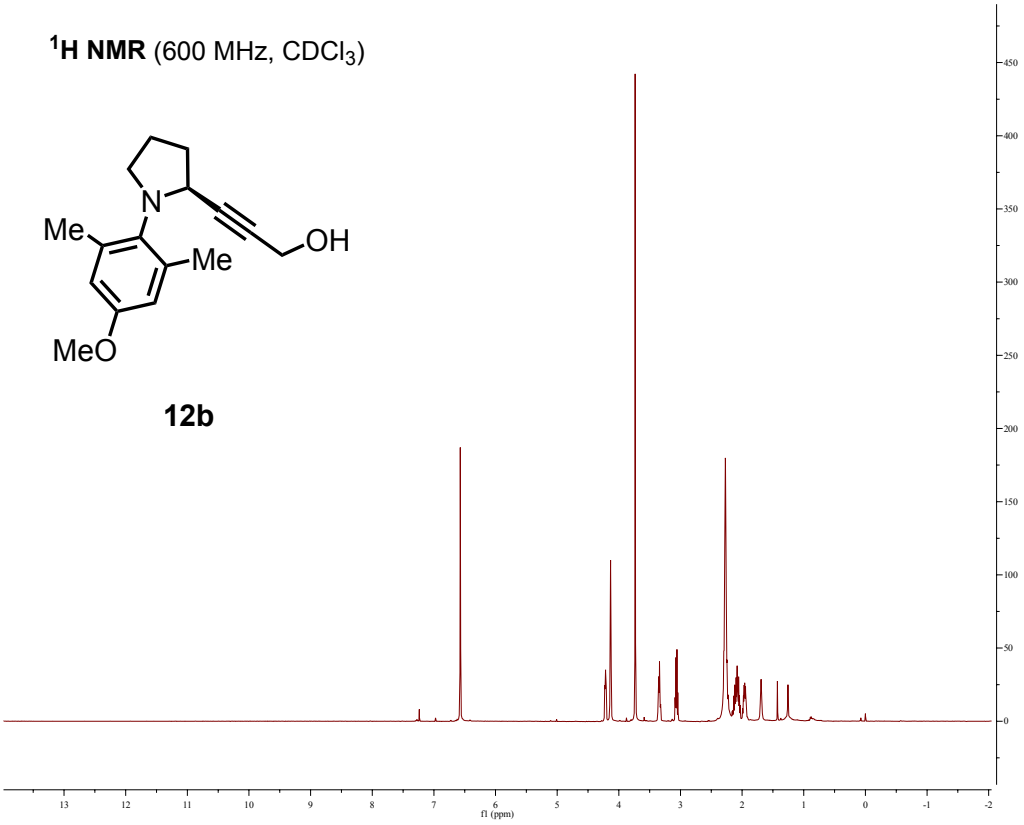
^{13}C NMR (151 MHz, $CDCl_3$)



12a

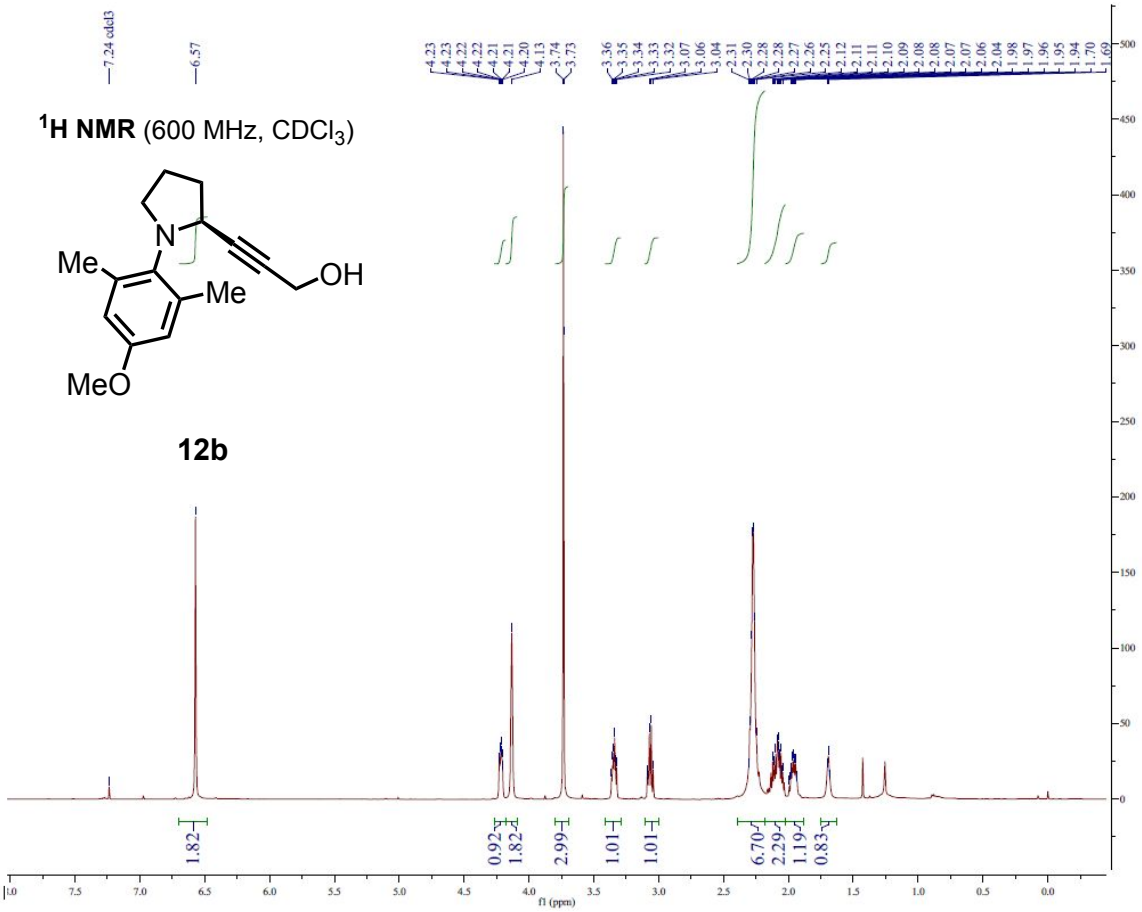
^{1}H NMR (600 MHz, $CDCl_3$)

12b

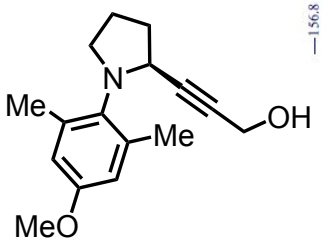


^{1}H NMR (600 MHz, $CDCl_3$)

12b

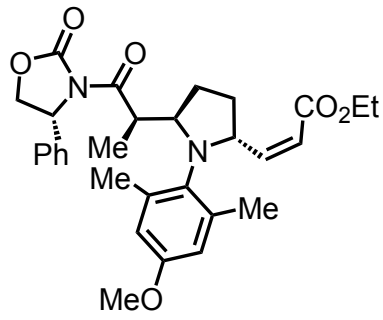


^{13}C NMR (126 MHz, $CDCl_3$)



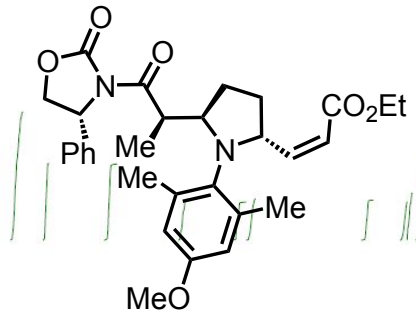
12b

^{1}H NMR (600 MHz, $CDCl_3$)



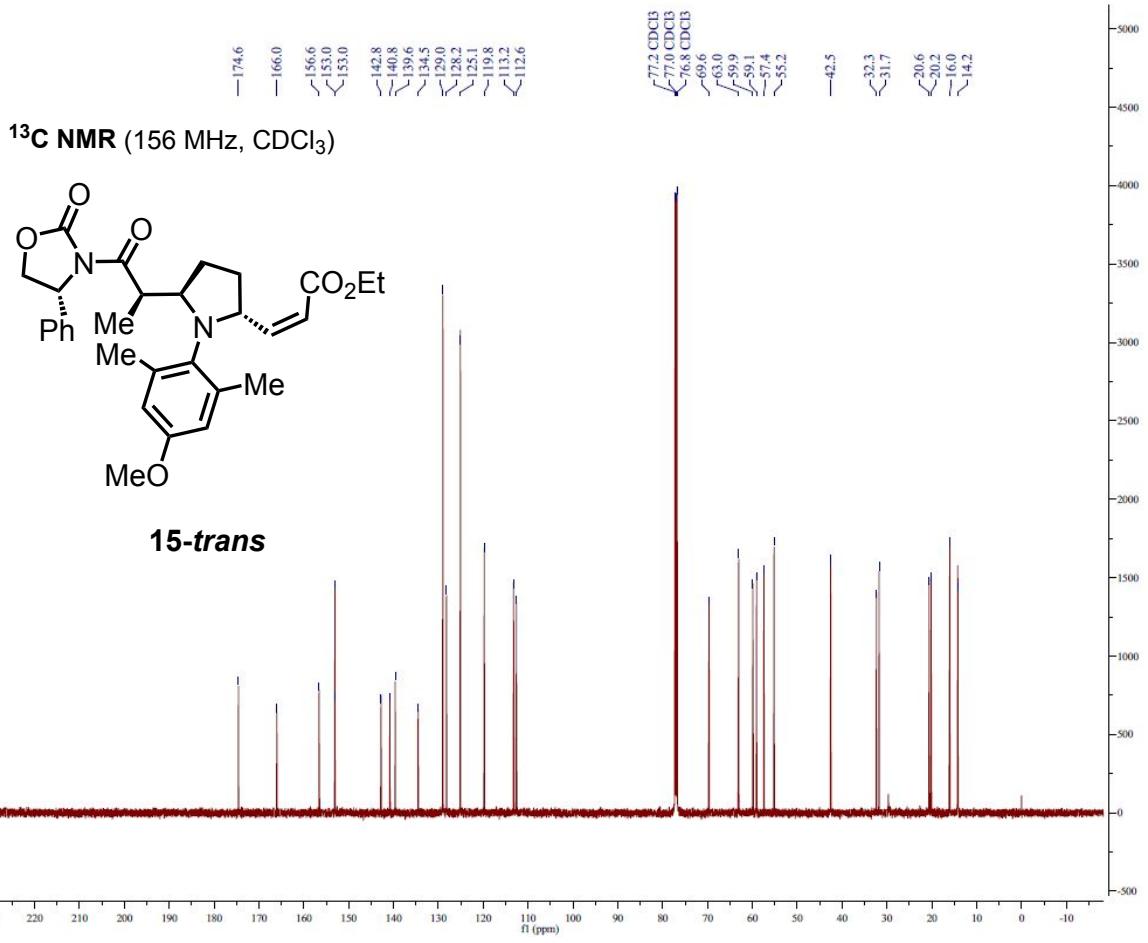
15-*trans*

^{1}H NMR (600 MHz, $CDCl_3$)



15-*trans*

^{13}C NMR (156 MHz, $CDCl_3$)



15-*trans*

9. X-Ray Crystallography Data

Table S15. Crystal data and structure refinement for $C_{23}H_{25}BrN_2O_3$.

Identification code	$C_{23}H_{25}BrN_2O_3$	
Empirical formula	C23 H25 Br N2 O3	
Formula weight	457.36	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	C2/c	
Unit cell dimensions	a = 31.9630(17) Å	α= 90°.
	b = 9.8050(5) Å	β= 112.711(3)°.
	c = 15.0555(8) Å	γ = 90°.
Volume	4352.5(4) $Å^3$	
Z	8	
Density (calculated)	1.396 Mg/m^3	
Absorption coefficient	2.783 mm^{-1}	
F(000)	1888	
Crystal size	0.480 x 0.180 x 0.100 mm^3	
Theta range for data collection	2.997 to 66.526°.	
Index ranges	-37<=h<=34, 0<=k<=11, 0<=l<=17	
Reflections collected	3790	
Independent reflections	3790 [R(int) = 0.1009]	
Completeness to theta = 66.526°	98.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7528 and 0.4332	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3790 / 258 / 278	
Goodness-of-fit on F^2	1.071	
Final R indices [I>2sigma(I)]	R1 = 0.0611, wR2 = 0.1753	
R indices (all data)	R1 = 0.0826, wR2 = 0.1919	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.704 and -0.647 $e.Å^{-3}$	

Table S16. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for $C_{23}H_{25}BrN_2O_3$. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	4645(1)	4818(1)	8410(1)	102(1)
O(1)	2346(1)	5189(2)	7608(2)	72(1)
O(2)	2035(1)	3146(2)	7683(2)	72(1)
O(3)	2085(1)	9312(3)	5196(2)	83(1)
N(1)	2703(1)	3164(3)	7568(3)	70(1)
C(1)	4033(2)	4296(4)	8101(3)	78(1)
C(2)	3927(2)	2965(4)	8208(3)	74(1)
C(3)	3484(1)	2620(4)	8017(3)	69(1)
C(4)	3143(1)	3597(4)	7716(3)	67(1)
C(5)	3255(2)	4934(4)	7597(4)	79(1)
C(6)	3703(2)	5272(4)	7804(4)	85(1)
C(7)	2366(1)	3966(4)	7629(3)	66(1)
C(8)	1644(1)	3829(4)	7738(3)	70(1)
C(9)	1294(2)	4050(4)	6781(3)	70(1)
C(10)	1015(2)	4204(4)	5999(4)	80(1)
N(2)	914(2)	4846(4)	4377(3)	81(1)
C(11)	686(2)	4496(5)	5009(4)	87(1)
C(12)	391(8)	3269(17)	4511(10)	96(2)
C(13)	668(3)	2606(8)	4006(6)	109(2)
C(14)	859(3)	3808(9)	3636(6)	99(2)
C(12X)	430(30)	3200(50)	4500(20)	96(2)
C(13X)	297(7)	3530(20)	3435(13)	99(2)
C(14X)	656(9)	4490(30)	3374(12)	109(2)
C(15)	1209(1)	5996(4)	4559(3)	69(1)
C(16)	1027(2)	7312(5)	4359(3)	76(1)
C(17)	1316(2)	8433(4)	4562(3)	77(1)
C(18)	1776(2)	8273(4)	4965(3)	72(1)
C(19)	1959(1)	6967(4)	5150(3)	68(1)
C(20)	1682(1)	5831(4)	4961(3)	66(1)
C(21)	1900(2)	4441(4)	5148(4)	79(1)
C(22)	518(2)	7512(6)	3924(5)	105(2)

C(23)	1917(2)	10679(5)	5077(4)	93(1)

Table S17. Bond lengths [Å] and angles [°] for $C_{23}H_{25}BrN_2O_3$.

Br(1)-C(1)	1.898(5)
O(1)-C(7)	1.200(4)
O(2)-C(7)	1.356(4)
O(2)-C(8)	1.449(5)
O(3)-C(18)	1.367(5)
O(3)-C(23)	1.430(5)
N(1)-C(7)	1.364(5)
N(1)-C(4)	1.404(5)
N(1)-H(1N)	0.93(5)
C(1)-C(6)	1.366(6)
C(1)-C(2)	1.373(6)
C(2)-C(3)	1.373(6)
C(2)-H(2)	0.9500
C(3)-C(4)	1.389(5)
C(3)-H(3)	0.9500
C(4)-C(5)	1.387(5)
C(5)-C(6)	1.384(7)
C(5)-H(5)	0.9500
C(6)-H(6)	0.9500
C(8)-C(9)	1.460(7)
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900
C(9)-C(10)	1.181(6)
C(10)-C(11)	1.482(8)
N(2)-C(15)	1.428(5)
N(2)-C(11)	1.445(6)
N(2)-C(14)	1.470(7)
C(11)-C(12)	1.534(8)
C(11)-H(11)	1.0000
C(12)-C(13)	1.52(2)
C(12)-H(12A)	0.9900

C(12)-H(12B)	0.9900
C(13)-C(14)	1.527(10)
C(13)-H(13A)	0.9900
C(13)-H(13B)	0.9900
C(14)-H(14A)	0.9900
C(14)-H(14B)	0.9900
C(15)-C(16)	1.400(6)
C(15)-C(20)	1.403(6)
C(16)-C(17)	1.391(6)
C(16)-C(22)	1.514(7)
C(17)-C(18)	1.366(6)
C(17)-H(17)	0.9500
C(18)-C(19)	1.390(5)
C(19)-C(20)	1.383(5)
C(19)-H(19)	0.9500
C(20)-C(21)	1.508(6)
C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800
C(21)-H(21C)	0.9800
C(22)-H(22A)	0.9800
C(22)-H(22B)	0.9800
C(22)-H(22C)	0.9800
C(23)-H(23A)	0.9800
C(23)-H(23B)	0.9800
C(23)-H(23C)	0.9800

C(7)-O(2)-C(8)	116.1(3)
C(18)-O(3)-C(23)	117.8(4)
C(7)-N(1)-C(4)	125.8(3)
C(7)-N(1)-H(1N)	114(3)
C(4)-N(1)-H(1N)	117(3)
C(6)-C(1)-C(2)	120.7(4)
C(6)-C(1)-Br(1)	118.9(3)
C(2)-C(1)-Br(1)	120.4(3)
C(3)-C(2)-C(1)	119.4(4)
C(3)-C(2)-H(2)	120.3
C(1)-C(2)-H(2)	120.3

C(2)-C(3)-C(4)	120.9(4)
C(2)-C(3)-H(3)	119.6
C(4)-C(3)-H(3)	119.6
C(5)-C(4)-C(3)	119.1(4)
C(5)-C(4)-N(1)	123.8(4)
C(3)-C(4)-N(1)	117.1(3)
C(6)-C(5)-C(4)	119.5(4)
C(6)-C(5)-H(5)	120.2
C(4)-C(5)-H(5)	120.2
C(1)-C(6)-C(5)	120.4(4)
C(1)-C(6)-H(6)	119.8
C(5)-C(6)-H(6)	119.8
O(1)-C(7)-O(2)	124.1(3)
O(1)-C(7)-N(1)	127.5(4)
O(2)-C(7)-N(1)	108.4(3)
O(2)-C(8)-C(9)	111.1(3)
O(2)-C(8)-H(8A)	109.4
C(9)-C(8)-H(8A)	109.4
O(2)-C(8)-H(8B)	109.4
C(9)-C(8)-H(8B)	109.4
H(8A)-C(8)-H(8B)	108.0
C(10)-C(9)-C(8)	178.4(5)
C(9)-C(10)-C(11)	175.3(5)
C(15)-N(2)-C(11)	121.7(4)
C(15)-N(2)-C(14)	124.7(4)
C(11)-N(2)-C(14)	113.1(4)
N(2)-C(11)-C(10)	111.4(4)
N(2)-C(11)-C(12)	103.7(5)
C(10)-C(11)-C(12)	113.8(9)
N(2)-C(11)-H(11)	109.3
C(10)-C(11)-H(11)	109.3
C(12)-C(11)-H(11)	109.3
C(13)-C(12)-C(11)	102.2(10)
C(13)-C(12)-H(12A)	111.3
C(11)-C(12)-H(12A)	111.3
C(13)-C(12)-H(12B)	111.3
C(11)-C(12)-H(12B)	111.3

H(12A)-C(12)-H(12B)	109.2
C(12)-C(13)-C(14)	104.2(7)
C(12)-C(13)-H(13A)	110.9
C(14)-C(13)-H(13A)	110.9
C(12)-C(13)-H(13B)	110.9
C(14)-C(13)-H(13B)	110.9
H(13A)-C(13)-H(13B)	108.9
N(2)-C(14)-C(13)	101.9(5)
N(2)-C(14)-H(14A)	111.4
C(13)-C(14)-H(14A)	111.4
N(2)-C(14)-H(14B)	111.4
C(13)-C(14)-H(14B)	111.4
H(14A)-C(14)-H(14B)	109.3
C(16)-C(15)-C(20)	119.2(4)
C(16)-C(15)-N(2)	119.9(4)
C(20)-C(15)-N(2)	120.9(4)
C(17)-C(16)-C(15)	119.7(4)
C(17)-C(16)-C(22)	120.3(4)
C(15)-C(16)-C(22)	120.0(4)
C(18)-C(17)-C(16)	121.0(4)
C(18)-C(17)-H(17)	119.5
C(16)-C(17)-H(17)	119.5
C(17)-C(18)-O(3)	125.1(4)
C(17)-C(18)-C(19)	119.5(4)
O(3)-C(18)-C(19)	115.4(4)
C(20)-C(19)-C(18)	120.9(4)
C(20)-C(19)-H(19)	119.6
C(18)-C(19)-H(19)	119.6
C(19)-C(20)-C(15)	119.6(4)
C(19)-C(20)-C(21)	118.4(4)
C(15)-C(20)-C(21)	121.9(4)
C(20)-C(21)-H(21A)	109.5
C(20)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
C(20)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5

C(16)-C(22)-H(22A)	109.5
C(16)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
C(16)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5
O(3)-C(23)-H(23A)	109.5
O(3)-C(23)-H(23B)	109.5
H(23A)-C(23)-H(23B)	109.5
O(3)-C(23)-H(23C)	109.5
H(23A)-C(23)-H(23C)	109.5
H(23B)-C(23)-H(23C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table S18. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for $C_{23}H_{25}BrN_2O_3$. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	80(1)	77(1)	152(1)	7(1)	50(1)	-1(1)
O(1)	79(2)	45(1)	97(2)	6(1)	39(2)	3(1)
O(2)	78(2)	47(1)	96(2)	1(1)	41(2)	-1(1)
O(3)	93(2)	52(1)	112(2)	1(1)	47(2)	-1(1)
N(1)	79(2)	45(2)	87(2)	3(1)	35(2)	2(1)
C(1)	83(3)	61(2)	99(3)	5(2)	46(2)	4(2)
C(2)	84(3)	53(2)	93(3)	7(2)	42(2)	11(2)
C(3)	85(2)	46(2)	84(3)	1(2)	41(2)	3(2)
C(4)	77(2)	51(2)	78(3)	3(2)	35(2)	1(2)
C(5)	82(3)	50(2)	111(4)	11(2)	44(3)	6(2)
C(6)	86(3)	52(2)	123(4)	10(2)	46(3)	1(2)
C(7)	74(2)	52(2)	73(2)	2(2)	30(2)	-1(2)
C(8)	84(2)	52(2)	84(3)	-3(2)	44(2)	0(2)
C(9)	79(2)	56(2)	82(3)	-2(2)	39(2)	-6(2)
C(10)	88(3)	63(2)	91(3)	-1(2)	38(2)	-12(2)

N(2)	90(2)	75(2)	83(2)	-8(2)	40(2)	-14(2)
C(11)	85(3)	84(3)	95(3)	1(2)	39(2)	-11(2)
C(12)	89(5)	98(4)	101(3)	-7(3)	37(3)	-25(3)
C(13)	111(5)	95(4)	131(5)	-37(4)	56(4)	-40(4)
C(14)	107(5)	99(4)	101(4)	-33(3)	52(4)	-28(4)
C(12X)	89(5)	98(4)	101(3)	-7(3)	37(3)	-25(3)
C(13X)	107(5)	99(4)	101(4)	-33(3)	52(4)	-28(4)
C(14X)	111(5)	95(4)	131(5)	-37(4)	56(4)	-40(4)
C(15)	77(2)	65(2)	69(2)	2(2)	32(2)	-1(2)
C(16)	78(2)	73(2)	83(3)	8(2)	39(2)	5(2)
C(17)	90(3)	60(2)	90(3)	11(2)	44(2)	14(2)
C(18)	86(2)	57(2)	81(3)	5(2)	39(2)	2(2)
C(19)	77(2)	59(2)	74(3)	0(2)	35(2)	3(2)
C(20)	81(2)	57(2)	67(2)	2(2)	37(2)	1(2)
C(21)	88(3)	58(2)	95(3)	5(2)	39(2)	2(2)
C(22)	81(3)	100(4)	133(4)	26(3)	39(3)	17(3)
C(23)	114(4)	55(2)	120(4)	1(2)	56(3)	2(2)

Table S19. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for $C_{23}H_{25}BrN_2O_3$.

	x	y	z	U(eq)
H(1N)	2658(15)	2230(50)	7620(30)	84
H(2)	4157	2289	8411	89
H(3)	3410	1701	8092	83
H(5)	3025	5611	7376	95
H(6)	3782	6190	7738	102
H(8A)	1738	4718	8067	84
H(8B)	1518	3270	8124	84
H(11)	486	5270	5029	104
H(12A)	349	2642	4986	115
H(12B)	90	3564	4045	115
H(13A)	475	2024	3467	131
H(13B)	916	2044	4460	131
H(14A)	1153	3575	3598	118
H(14B)	644	4114	2995	118
H(12C)	626	2389	4691	115
H(12D)	157	3049	4649	115
H(13C)	287	2681	3068	118
H(13D)	-6	3962	3166	118
H(14C)	850	4033	3087	131
H(14D)	516	5309	2989	131
H(17)	1191	9324	4419	93
H(19)	2279	6854	5409	82
H(21A)	1899	4062	4544	119
H(21B)	1731	3836	5406	119
H(21C)	2214	4521	5614	119
H(22A)	409	7687	4438	158
H(22B)	373	6688	3571	158
H(22C)	443	8290	3481	158
H(23A)	1743	10860	4393	140
H(23B)	2172	11317	5324	140
H(23C)	1720	10798	5434	140

Table S20. Torsion angles [°] for $C_{23}H_{25}BrN_2O_3$.

C(6)-C(1)-C(2)-C(3)	-0.3(7)
Br(1)-C(1)-C(2)-C(3)	177.4(3)
C(1)-C(2)-C(3)-C(4)	0.2(6)
C(2)-C(3)-C(4)-C(5)	0.8(6)
C(2)-C(3)-C(4)-N(1)	-177.9(4)
C(7)-N(1)-C(4)-C(5)	-24.6(6)
C(7)-N(1)-C(4)-C(3)	154.0(4)
C(3)-C(4)-C(5)-C(6)	-1.6(7)
N(1)-C(4)-C(5)-C(6)	177.0(4)
C(2)-C(1)-C(6)-C(5)	-0.5(8)
Br(1)-C(1)-C(6)-C(5)	-178.2(4)
C(4)-C(5)-C(6)-C(1)	1.5(8)
C(8)-O(2)-C(7)-O(1)	-1.3(5)
C(8)-O(2)-C(7)-N(1)	-179.2(3)
C(4)-N(1)-C(7)-O(1)	17.4(7)
C(4)-N(1)-C(7)-O(2)	-164.8(4)
C(7)-O(2)-C(8)-C(9)	90.8(4)
C(15)-N(2)-C(11)-C(10)	-60.4(6)
C(14)-N(2)-C(11)-C(10)	111.7(6)
C(15)-N(2)-C(11)-C(12)	176.9(11)
C(14)-N(2)-C(11)-C(12)	-11.1(13)
N(2)-C(11)-C(12)-C(13)	30.5(14)
C(10)-C(11)-C(12)-C(13)	-90.7(10)
C(11)-C(12)-C(13)-C(14)	-39.1(14)
C(15)-N(2)-C(14)-C(13)	158.8(6)
C(11)-N(2)-C(14)-C(13)	-13.0(9)
C(12)-C(13)-C(14)-N(2)	32.0(11)
C(11)-N(2)-C(15)-C(16)	-76.4(6)
C(14)-N(2)-C(15)-C(16)	112.5(7)
C(11)-N(2)-C(15)-C(20)	102.0(5)
C(14)-N(2)-C(15)-C(20)	-69.1(7)
C(20)-C(15)-C(16)-C(17)	-0.2(6)

N(2)-C(15)-C(16)-C(17)	178.2(4)
C(20)-C(15)-C(16)-C(22)	179.9(4)
N(2)-C(15)-C(16)-C(22)	-1.7(6)
C(15)-C(16)-C(17)-C(18)	-0.6(7)
C(22)-C(16)-C(17)-C(18)	179.2(5)
C(16)-C(17)-C(18)-O(3)	-179.5(4)
C(16)-C(17)-C(18)-C(19)	1.8(7)
C(23)-O(3)-C(18)-C(17)	5.1(6)
C(23)-O(3)-C(18)-C(19)	-176.2(4)
C(17)-C(18)-C(19)-C(20)	-2.2(6)
O(3)-C(18)-C(19)-C(20)	179.0(4)
C(18)-C(19)-C(20)-C(15)	1.3(6)
C(18)-C(19)-C(20)-C(21)	178.2(4)
C(16)-C(15)-C(20)-C(19)	-0.1(6)
N(2)-C(15)-C(20)-C(19)	-178.5(4)
C(16)-C(15)-C(20)-C(21)	-176.8(4)
N(2)-C(15)-C(20)-C(21)	4.8(6)

Symmetry transformations used to generate equivalent atoms:

Table S21. Hydrogen bonds for $C_{23}H_{25}BrN_2O_3$ [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1N)...O(1)#1	0.93(5)	2.03(5)	2.928(4)	160(4)

Symmetry transformations used to generate equivalent atoms:
#1 -x+1/2,y-1/2,-z+3/2