

Mild and Phosphine-Free Iron-Catalyzed Cross-Coupling of Non-activated Secondary Alkyl Halides with Alkynyl Grignard Reagents

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General Considerations

General Analytical Information

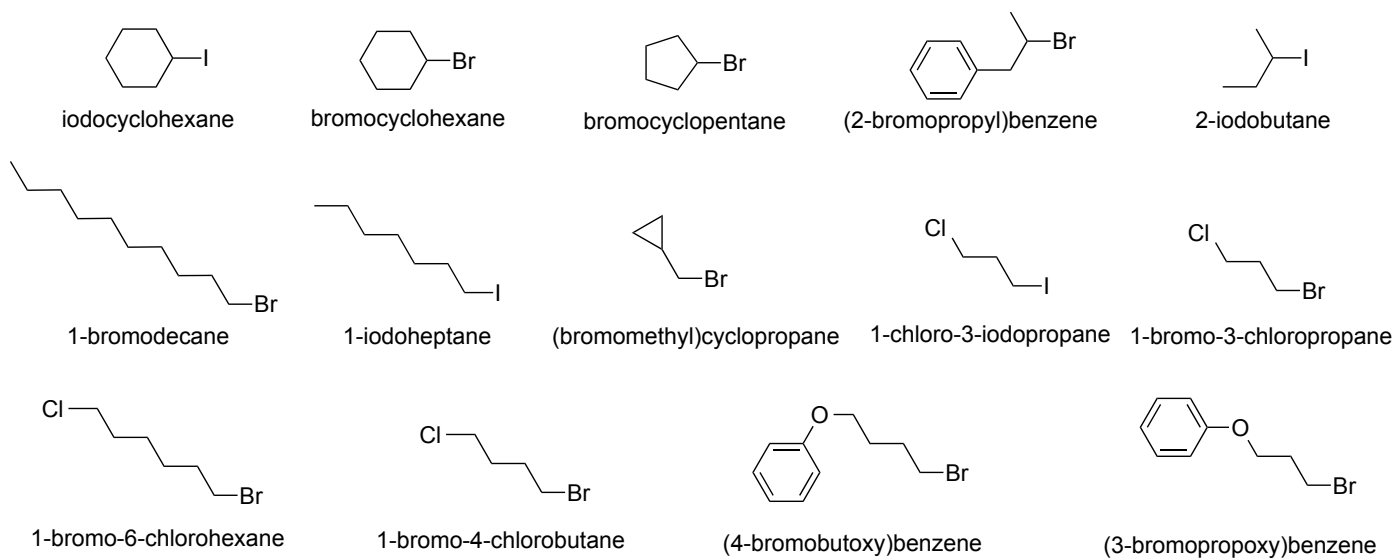
Nuclear Magnetic Resonance spectra were recorded on a Bruker Avance 400 MHz instruments at ambient temperature. All ^1H NMR spectra were measured in part per million (ppm) relative to the signals for tetramethylsilane (TMS) added into the deuterated chloroform (CDCl_3) (0 ppm) unless otherwise stated.^[1] Data for ^1H NMR were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qu = quintet, sex = sextet, m = multiplet, ovrlp = overlap, br = broad), coupling constants, and integration. All ^{13}C NMR spectra were reported in ppm relative to CDCl_3 (77.16 ppm) unless otherwise stated,^[1] and were obtained with complete ^1H decoupling. All GC analyses were performed on a Perkin-Elmer Clarus 400 GC system with a FID detector. All GC-MS analyses were performed on an Agilent Technologies 7890A GC system equipped with a 5975C MS detector. HPLC analyses were performed on an Agilent Technologies 1260 Infinity LC system with CHIRALCEL® OB-H column for the separation of (3-iodobutyl)benzene (**S16**, **S17**) (starting material) and with CHIRALPACK® IB column for the separation of 2-((8-methyl-10-phenyldec-6-yn-1-yl)oxy)tetrahydro-2H-pyran (**3f**) (substituted alkyne product), using a solvent mixture of hexane/isopropanol as an eluent. High-resolution mass spectra (HRMS) by electrospray ionization (ESI) method were performed at the EPFL ISIC Mass Spectroscopy Service with a Micro Mass QTOF Ultima spectrometer. HRMS by atmospheric pressure photoionization (APPI) method were performed on a hybrid linear ion trap Fourier transform ion cyclotron resonance mass spectrometer (LTQ FT-ICR MS, Thermo Scientific, Bremen, Germany) equipped with a 10 T superconducting superconducting agent (Oxford Instruments Nanoscience, Abingdon, UK).

General Reagent Information

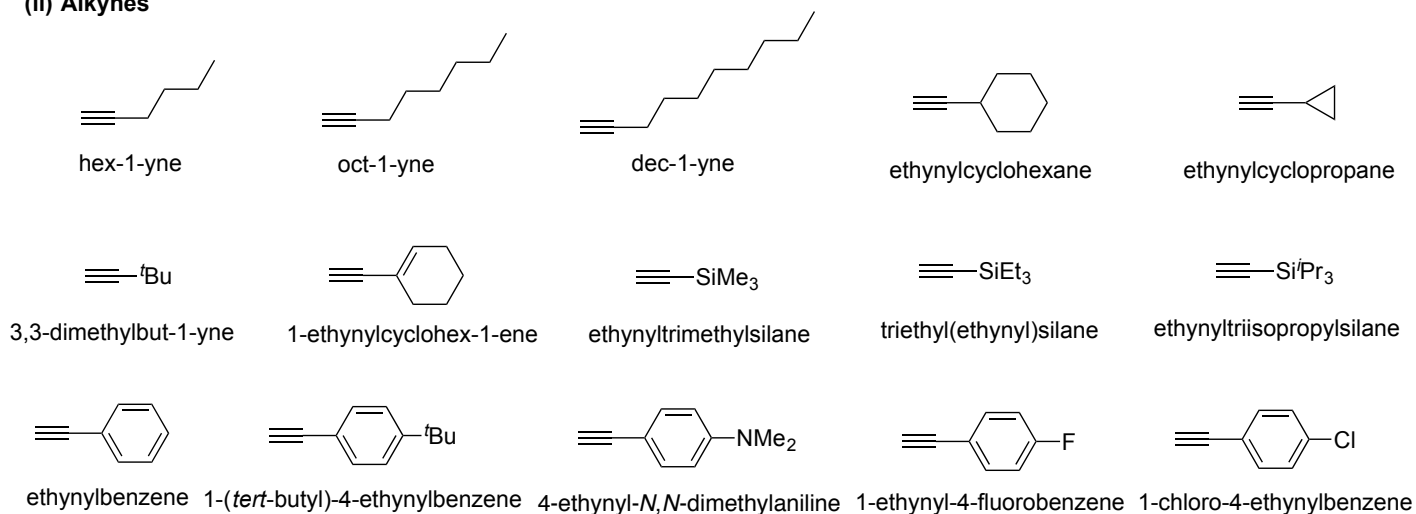
Unless otherwise noted, all chemicals used in the preparations of starting materials and in the iron-catalyzed cross-coupling reactions of alkyl halides with alkynyl Grignard reagents were commercially available and were used as received without further purifications. Solvents (tetrahydrofuran (THF), 1,4-dioxane, acetonitrile (MeCN), dimethyl sulfoxide (DMSO), *N,N*-dimethylformamide (DMF), and dichloromethane (CH_2Cl_2)) were purified and dehydrated using a two-column solid-state purification system (Innovative Technology, NJ, USA) and transferred to the glove box without exposure to air. Anhydrous *N*-methylpyrrolidone (NMP) (99.8% purity) and anhydrous dimethylacetamide (DMA) (99.8% purity) were purchased from Aldrich Chemical Co. or Acros Chemicals in Sure-Seal bottles and stored under nitrogen. Iron(II) bromide (FeBr_2) (98% purity) was purchased from Aldrich Chemical Co. or Acros Chemicals. Iron(II) bromide (FeBr_2) [99.999% purity (containing 0.4-3.2 ppm of Co, Cu, Mn, and Cr), beads, -10 mesh] and 1-propynylmagnesium bromide (0.50 M solution in THF) were purchased from Aldrich Chemical Co.. All the secondary alkyl halides (starting materials) and the corresponding substituted alkyne products were in form of racemic mixtures unless otherwise noted. For the 1,3- and 1,4-di-substituted cyclohexyl halides and substituted alkyne products, only one form of enantiomers was shown to demonstrate the diastereomeric ratios (d.r.).

The following known starting materials (alkyl halides and terminal alkynes) were commercially available and used without further purifications:

(i) Alkyl Halides

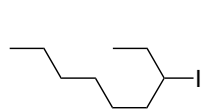


(ii) Alkynes

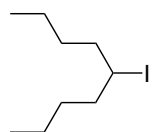


The following known starting materials (alkyl halides and terminal alkynes) were prepared according to the literature procedures:^[2-15]

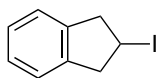
(i) Alkyl Halides



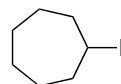
3-iodononane^[2]



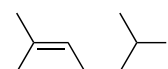
5-iodononane^[2]



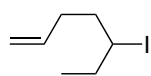
2-iodo-2,3-dihydro-1*H*-indene^[3]



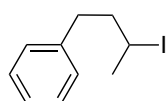
iodocycloheptane^[4]



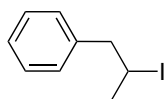
6-iodo-2-methylhept-2-ene^[5]



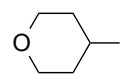
6-iodo-2-methylhept-2-ene^[5]



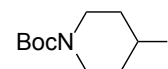
(3-iodobutyl)benzene^[5,6]



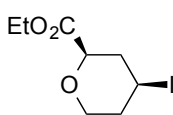
(2-iodobutyl)benzene^[2]



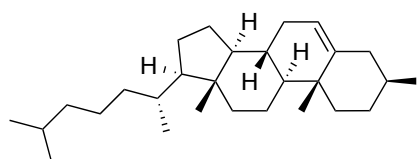
4-iodotetrahydro-2*H*-pyran^[7]



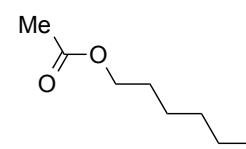
tert-butyl 4-iodopiperidine-1-carboxylate^[5]



ethyl 4-iodotetrahydro-2*H*-pyran-2-carboxylate^[8]
(d.r. = 4.4 : 1)

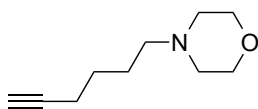


3*beta*-iodo-5-cholestene^[5]

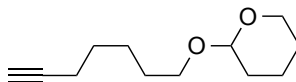


5-iodopentyl acetate^[9]

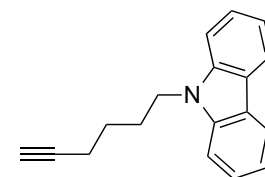
(ii) Alkynes



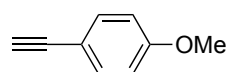
4-(hex-5-yn-1-yl)morpholine^[10]



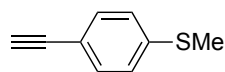
2-(hept-6-yn-1-yloxy)tetrahydro-2*H*-pyran^[11]



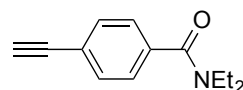
9-(hex-5-yn-1-yl)-9*H*-carbazole^[12]



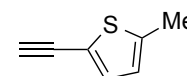
1-ethynyl-4-methoxybenzene^[13]



(4-ethynylphenyl)-(methyl)sulfane^[13]



N,N-diethyl-4-ethynylbenzamide^[13]



2-ethynyl-5-methylthiophene^[13]

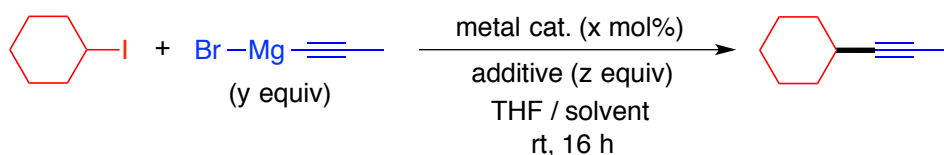
General Manipulation Considerations

All manipulations for the iron-catalyzed cross-coupling reactions of alkyl halides with alkynyl Grignard reagents were set up in a 30 mL Teflon-screw cap test tubes under an inert nitrogen (N₂) atmosphere using glove box techniques. The test tubes were then sealed with air-tight electrical tapes and the reaction mixtures were stirred on bench-top. Flash column chromatography was performed using silica gel (Silicycle, ultra pure grade). The solvent system as an eluent for column chromatography is presented as a ratio of solvent volumes. Yields reported in the publication are of isolated materials. All

new starting materials and substituted alkyne products were characterized by ^1H NMR and ^{13}C NMR spectroscopies and high-resolution mass spectrometry (HRMS). In case the new compounds could not be detected by HRMS, the compounds ([M]) were then detected by GCMS analysis and their purities were further determined by GC-MS analysis. All known starting materials and substituted alkyne products were characterized by ^1H NMR and ^{13}C NMR spectroscopies and the spectra were further compared with the literature values if available.

Supplementary Experimental Results

Table S1. Optimizations of Iron-Catalyzed Cross-Coupling of Non-activated Secondary Alkyl Iodides with Alkynyl Grignard Reagents^[a]



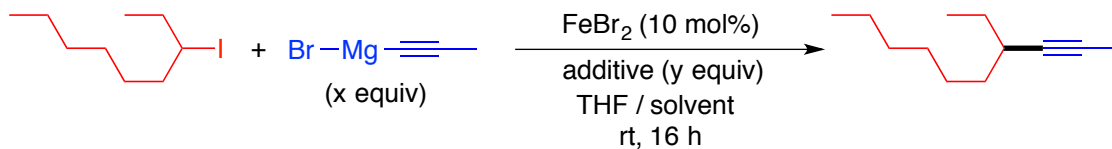
Entry	Metal catalyst (x mol%)	Alkynyl Grignard reagent (y equiv)	Solvent (mL)	Additive (z equiv)	Yield of product (%) ^[b]
1	FeCl ₃ (5)	1.2	NMP (1.5)	---	60
2	Fe ₂ (SO ₄) ₃ (5)	1.2	NMP (1.5)	---	0
3	K ₄ [Fe(CN) ₆].3H ₂ O (5)	1.2	NMP (1.5)	---	0
4	K ₃ [Fe(CN) ₆] (5)	1.2	NMP (1.5)	---	0
5	FeCp ₂ (5)	1.2	NMP (1.5)	---	0
6	Fe(NO ₃) ₃ .9H ₂ O (5)	1.2	NMP (1.5)	---	35
7	Fe(ClO ₄) ₂ .6H ₂ O (5)	1.2	NMP (1.5)	---	38
8	FeSO ₄ (5)	1.2	NMP (1.5)	---	0
9	FeCl ₂ (5)	1.2	NMP (1.5)	---	31
10	FeBr ₂ (5)	1.2	NMP (1.5)	---	64
11	FeI ₂ (5)	1.2	NMP (1.5)	---	49
12	FeF ₂ (10)	1.2	NMP (1.5)	---	0
13	FeBr ₂ (10)	1.2	NMP (1.5)	---	71
14	FeBr ₂ (20)	1.2	NMP (1.5)	---	51
15	FeBr ₂ (10)	1.0	NMP (1.5)	---	64
16	FeBr ₂ (10)	1.5	NMP (1.5)	---	81
17	FeBr ₂ (10)	1.7	NMP (1.5)	---	70
18	FeBr ₂ (10)	3.0	NMP (1.5)	---	33
19	FeBr ₂ (10)	1.5	NMP (2.0)	---	86
20	FeBr ₂ (10)	1.5	NMP (3.0)	---	73
21	FeBr ₂ (0)	1.5	NMP (2.0)	---	0
22	FeBr ₂ (10)	1.2	DMSO (1.5)	---	20
23	FeBr ₂ (10)	1.2	DMA (1.5)	---	55

24	FeBr ₂ (10)	1.5	THF (2.0)	---	1
25	FeBr ₂ (10)	1.5	THF (2.0)	O-TMEDA (2)	26
26	FeBr ₂ (10)	1.5	1,4-dioxane (2.0)	---	0
27	FeBr ₂ (10)	1.5	DMF (2.0)	---	38
28	FeBr ₂ (10)	1.5	MeCN (2.0)	---	4
29	FeBr ₂ (10)	1.2	NMP (1.5)	KI (1)	62
30	FeBr ₂ (10)	1.2	NMP (1.5)	KBr (1)	62
31	FeBr ₂ (10)	1.5	NMP (1.5)	O-TMEDA ^[c] (2)	75
32	FeBr ₂ (10)	1.5	NMP (1.5)	[Me ₂ N(CH ₂) ₂] ₂ NMe (2)	71
33	FeBr ₂ (10)	1.5	NMP (1.5)	[MeO(CH ₂) ₂] ₂ O (2)	75
34	FeBr ₂ (10)	1.5	NMP (1.5)	P(O)Ph ₃ (1)	79
35	FeBr ₂ (10)	1.5	NMP (1.5)	phenanthroline (0.1)	75
36	FeBr ₂ (10)	1.5	NMP (1.5)	TMEDA ^[d] (0.20)	75
37	FeBr ₂ (10)	1.5	NMP (1.5)	pyridine (0.4)	82
38	FeBr ₂ (10)	1.5	NMP (1.5)	P(O)(morpholine) ₃ (1)	68
39	MnCl ₂ ·4H ₂ O (10)	1.5	NMP (2.0)	---	0
40	CoBr ₂ (10)	1.5	NMP (2.0)	---	34
41	NiBr ₂ (10)	1.5	NMP (2.0)	---	5
42	CuBr ₂ (10)	1.5	NMP (2.0)	---	0
43	CuCl (10)	1.5	NMP (2.0)	---	0
44	CuBr (10)	1.5	NMP (2.0)	---	0
45	CuI (10)	1.5	NMP (2.0)	---	0
46	AgNO ₃ (10)	1.5	NMP (2.0)	---	0
47	CrCl ₂ (10)	1.5	NMP (2.0)	---	0
48	Pd(OAc) ₂ (10)	1.5	NMP (2.0)	---	2
49	FeBr ₃ (10)	1.5	NMP (2.0)	---	53

[a] Reaction conditions: iodocyclohexane (0.50 mmol), 1-propynylmagnesium bromide (0.5 M in THF, 0.50-1.5 mmol, 1.0-3.0 mL), metal catalyst (5-20 mol%), solvent (1.5-3.0 mL), and additive (0.05 mmol-1.0 mmol), N₂ atm, rt, 16 h. [b] Calibrated GC yield using *n*-dodecane as internal standard. [c] Bis[2-(*N,N*-dimethylamino)ethyl] ether. [d] Tetramethylethylenediamine.

The conditions for the general Fe-catalyzed cross-coupling of non-activated secondary alkyl iodides with alkynyl Grignard reagents were optimized. Various transition metal catalysts were tested in the cross-coupling of iodocyclohexane with 1-propynylmagnesium bromide in NMP solvent at room temperature. Among a range of iron(III) and iron(II) salts being tested (Table S1, entries 1-12), FeBr₂ was found to be the optimal catalyst (Table S1, entry 10). Further optimization showed that the use of 10 mol% FeBr₂, 1.5 equiv of 1-propynylmagnesium bromide, and 2 mL of NMP solvent afforded the substituted alkyne in the highest yield (Table S1, entry 19). Without FeBr₂ added, no product was obtained (Table S1, entry 21). The variation of other solvents and additives, however, did not further enhance the yield or even decreased the yield (Table S1, entries 22-38). Additionally, the use of transition metal salts other than iron salts did not catalyze the reaction (Table S1, entries 39-48). Furthermore, FeBr₃ did not catalyze the reaction as efficiently as FeBr₂ (Table S1, entry 49). Thus, the conditions of entry 19 were employed for the general Fe-catalyzed cross-coupling of non-activated secondary alkyl iodides with alkynyl Grignard reagents.

Table S2. Optimizations of Iron-Catalyzed Cross-Coupling of Non-activated, Sterically-Hindered Secondary Alkyl Iodides with Alkynyl Grignard Reagents^[a]

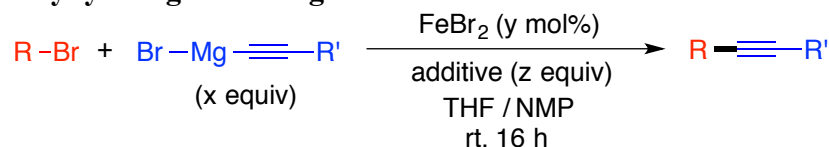


Entry	Alkynyl Grignard reagent (x equiv)	Solvent (mL)	Additive (y equiv)	Yield of product (%) ^[b]
1	1.5	NMP	---	26
2	1.5	THF	---	22
3	1.5	DMF	---	26
4 ^[c]	1.5	NMP	O-TMEDA ^[d] (2)	37
5	3.0	NMP	O-TMEDA ^[d] (2)	19
6 ^[c]	1.5	NMP	TMEDA ^[e] (2)	18
7 ^[c]	1.5	NMP	O-TMEDA (2), Et ₄ Ni (1)	33

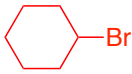
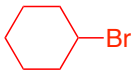
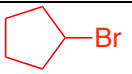
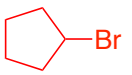
[a] Reaction conditions: 3-iodononane (0.50 mmol), 1-propynylmagnesium bromide (0.5 M in THF, 0.75-1.5 mmol, 1.5-3.0 mL), FeBr₂ (10 mol%), solvent (2.0 mL), and additive (0.5-1.0 mmol), N₂ atm, rt, 16 h. [b] Uncorrected GC yield using *n*-dodecane as internal standard. [c] 6 h. [d] Bis[2-(*N,N*-dimethylamino)ethyl] ether. [e] Tetramethylethylenediamine.

The conditions of Fe-catalyzed cross-coupling of sterically hindered, non-activated secondary alkyl iodides with alkynyl Grignard reagents were optimized. By using 3-iodononane as the model substrate, the general reaction protocol developed in Table S1 was initially employed for the alkylation process. However, only a low yield of substituted product was obtained (Table S2, entry 1). The use of other solvents did not promote the product yield (Table S2, entries 2-3). Further optimizations showed that the addition of O-TMEDA (2 equiv) provided the highest product yield (Table S2, entry 4). Thus, the conditions of entry 4 were employed for the general Fe-catalyzed cross-coupling of non-activated, sterically hindered secondary alkyl iodides with alkynyl Grignard reagents. Additionally, 20 mol% of FeBr₂ was employed in the subsequent scope study to ensure complete conversion of alkyl iodides.

Table S3. Optimizations of Iron-Catalyzed Cross-Coupling of Non-activated Secondary Alkyl Bromides with Alkynyl Grignard Reagents^[a]



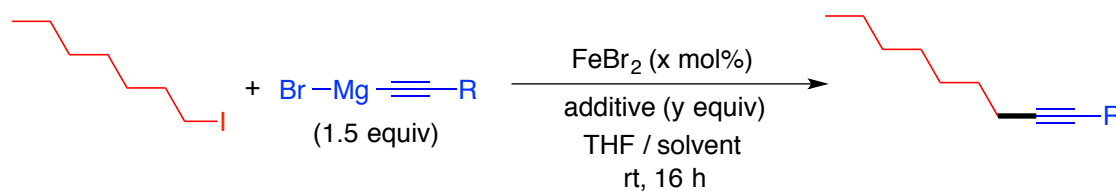
Entry	RBr	R' (x equiv)	FeBr ₂ (y mol%)	Additive (z equiv)	Yield of product (%) ^[b]
1		SiMe ₃ (1.5)	10	---	36
2		SiMe ₃ (1.5)	10	O-TMEDA ^[c] (2)	45

3		SiMe ₃ (1.5)	20	O-TMEDA ^[c] (2)	67
4		SiMe ₃ (2.0)	20	O-TMEDA ^[c] (2)	69
5		Me (1.5)	10	---	14
6		Me (1.5)	10	O-TMEDA ^[c] (2)	42

[a] Reaction conditions: alkyl bromide (0.50 mmol), alkynylmagnesium bromide (0.5 M in THF, 0.75 mmol, 1.5 mL), FeBr₂ (10 or 20 mol%), NMP (2.0 mL), and additive (1.0 mmol), N₂ atm, rt, 16 h. [b] Uncorrected GC yield using *n*-dodecane as internal standard. [c] Bis[2-(*N,N*-dimethylamino)ethyl] ether.

The conditions of Fe-catalyzed cross-coupling of non-activated secondary alkyl bromides with alkynyl Grignard reagents were optimized. By using bromocyclohexane as the model substrate, the general reaction protocol developed in Table S1 was initially employed for the alkylation process. However, only a low yield of substituted product was obtained (Table S3, entry 1). When O-TMEDA (2 equiv) and a higher loading of FeBr₂ (20 mol%) were used, the yield was further enhanced (Table S3, entry 3). The use of O-TMEDA also promoted the yield in the coupling with bromocyclopentane (Table S3, entry 6). Thus, the conditions of entry 3 were employed for the general Fe-catalyzed cross-coupling of non-activated secondary alkyl bromides with alkynyl Grignard reagents.

Table S4. Optimizations of Iron-Catalyzed Cross-Coupling of Non-activated Primary Alkyl Iodides with Alkynyl Grignard Reagents^[a]



Entry	R	FeBr ₂ (x mol%)	Solvent	Additive (y equiv)	Yield of product (%) ^[b]
1	Ph	10	NMP		34
2 ^[c]	Ph	10	NMP	O-TMEDA ^[d] (2)	31
3	Ph	10	THF		23
4	Ph	10	THF	O-TMEDA ^[d] (2)	74
5	Ph	0	THF	O-TMEDA ^[d] (2)	0
6	Me	20	NMP		19
7	Me	20	THF		9
8	Me	20	THF	O-TMEDA ^[d] (2)	30

[a] Reaction conditions: 1-iodoheptane (0.50 mmol), alkynylmagnesium bromide (0.5 M in THF, 0.75 mmol, 1.5 mL), FeBr₂ (10 or 20 mol%), solvent (2.0 mL), and additive (1.0 mmol), N₂ atm, rt, 16 h. [b] Uncorrected GC yield using *n*-dodecane as internal standard. [c] 6 h. [d] Bis[2-(*N,N*-dimethylamino)ethyl] ether.





The conditions of Fe-catalyzed cross-coupling of non-activated primary alkyl iodides with alkynyl Grignard reagents were optimized. By using 1-iodoheptane as the model substrate, the general reaction protocol developed in Table S1 was initially employed for the alkylation process. However, only a

low yield of substituted product was obtained even when O-TMEDA was added (Table S4, entries 1 and 2). When O-TMEDA (2 equiv) in conjunction with THF solvent were employed, the highest yield of substituted alkyne product was obtained (Table S4, entries 4 and 8). Without FeBr₂, no product was obtained (Table S4, entry 5). Thus, the conditions of entry 4 were employed for the Fe-catalyzed cross-coupling of non-activated primary alkyl iodides with alkynyl Grignard reagents.

Table S5. Optimizations of Iron-Catalyzed Cross-Coupling of Non-activated Primary Alkyl Bromides with Alkynyl Grignard Reagents^[a]

$$\text{R-Br} + \text{Br-Mg} \equiv \text{SiMe}_3 \xrightarrow[\text{THF / solvent, rt, 16 h}]{\text{FeBr}_2 (10 \text{ mol}\%), \text{additive (x equiv)}} \text{R} \equiv \text{SiMe}_3$$

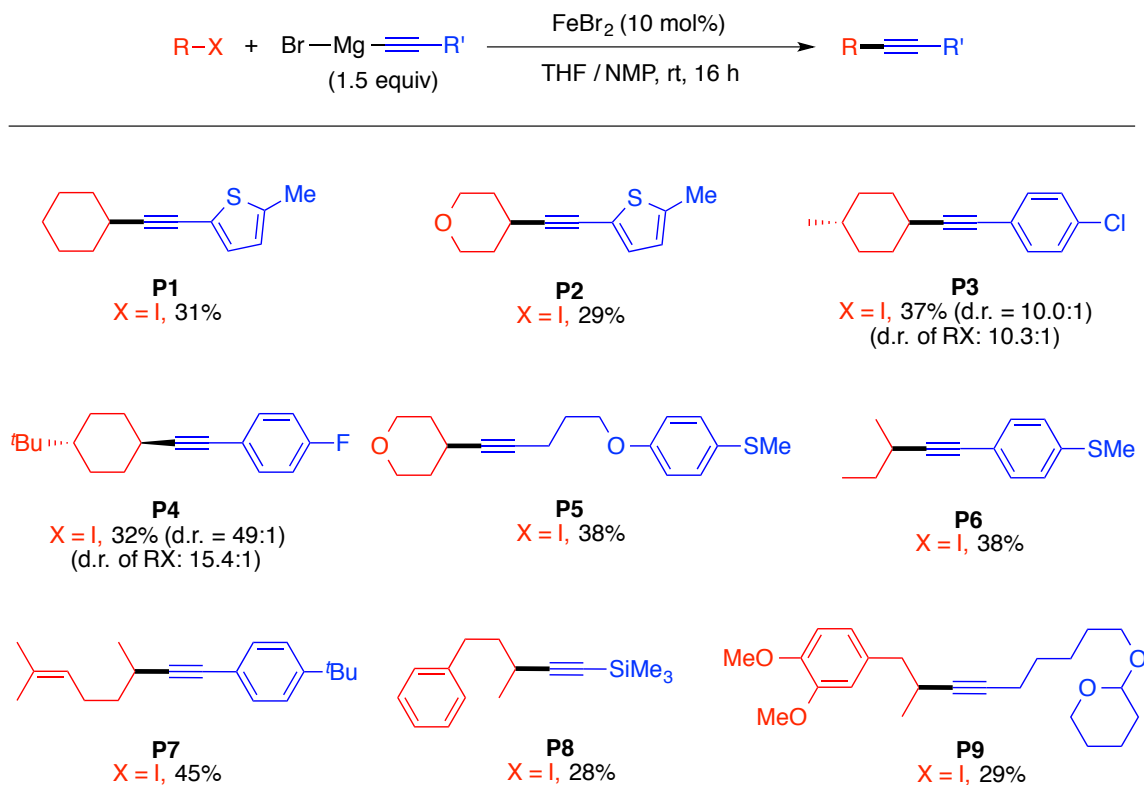
(1.5 equiv)

Entry	RBr	Solvent	Additive (x equiv)	Yield of Product (%) ^[b]
1		NMP	---	40
2		THF	O-TMEDA ^[c] (2)	100
3		NMP	---	34
4		THF	O-TMEDA ^[c] (2)	91

[a] Reaction conditions: 1-bromoalkane (0.50 mmol), alkynylmagnesium bromide (0.5 M in THF, 0.75 mmol, 1.5 mL), FeBr₂ (10 mol%), solvent (2.0 mL), and additive (1.0 mmol), N₂ atm, rt, 16 h. [b] Uncorrected GC yield using *n*-dodecane as internal standard. [c] Bis[2-(*N,N*-dimethylamino)ethyl] ether.

The conditions of Fe-catalyzed cross-coupling of non-activated primary alkyl bromides with alkynyl Grignard reagents were optimized. By using 1-bromooctane and (3-bromopropoxy)benzene as the model substrates, we found that the use of O-TMEDA (2 equiv) in conjunction with THF solvent could provide the highest yield of substituted alkyne products (Table S5, entries 2 and 4). Thus, the conditions of entries 2 and 4 were employed for the Fe-catalyzed cross-coupling of non-activated primary alkyl bromides with alkynyl Grignard reagents. Additionally, 20 mol% of FeBr₂ was employed in the subsequent scope study to ensure complete conversion of alkyl bromides.

Scheme S1. Substrate Scope of Iron-Catalyzed Cross-Coupling of Non-activated Secondary Alkyl Halides with Alkynyl Grignard Reagents: Supplementary Results^[a]



[a] Reaction conditions: alkyl halide (1.0 mmol), alkynylmagnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL), FeBr₂ (10 mol%), and NMP (4.0 mL), N₂ atm, rt, 16 h; yields are of isolated products.

Experimental Section

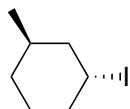
Preparation of Alkyl Halides from Alkyl Alcohols (General Procedure A): A 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with triphenylphosphine (1.4 equiv), imidazole (1.4 equiv), and dichloromethane (300 mL). The reaction mixture was stirred at room temperature until the white solids dissolved to form a clear solution. Iodine (1.4 equiv) were then added slowly in a few portions into the reaction mixture, and the resulting mixture was stirred until all iodine granules dissolved. Alkyl alcohol (1.0 equiv) was then slowly added into the reaction mixture, and the resulting mixture was stirred overnight. The brown mixture was diluted with hexanes and then filtered to remove the solid residues. The filtrate was then concentrated *in vacuo* with the aid of a rotary evaporator. The residue was purified by flash column chromatography with silica gel using hexanes (or a mixture of hexanes and EtOAc) as an eluent to afford the alkyl iodide product.

Preparation of Alkyl Iodides from Benzaldehydes (General Procedure B): A 250 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with benzaldehyde (1.0 equiv), 3-buten-1-ol (2.0 equiv), iodine (1.0 equiv), and dichloromethane (CH_2Cl_2 , 100 mL). The resulting mixture was stirred under reflux until benzaldehyde was consumed as determined by GCMS analysis. After cooling to room temperature, the reaction mixture was washed with additional CH_2Cl_2 (50 mL) and saturated $\text{Na}_2\text{S}_2\text{O}_3$ solution (50 mL). The aqueous solution was further washed with CH_2Cl_2 (2 x 20 mL). The combined organic fractions were concentrated *in vacuo* with the aid of a rotary evaporator. The residue was purified by flash column chromatography with silica gel using a mixture of hexanes and EtOAc as an eluent to afford the alkyl iodide product.

Preparation of Alkyl Iodides from Alkyl Mesylates (General Procedure C): A 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with alkyl alcohol (1.0 equiv), mesyl chloride (1.2-1.5 equiv), triethylamine (1.5 equiv), and dichloromethane (CH_2Cl_2 , 200 mL). The reaction mixture was stirred at room temperature for 2 h, followed by washing with excess CH_2Cl_2 (50 mL) and HCl solution (~1 M (aq), 100 mL). The aqueous solution was further washed with CH_2Cl_2 (2 x 50 mL). The combined organic layers were then dried with anhydrous Na_2SO_4 , filtered, and concentrated with the aid of a rotary evaporator. The residue was dried *in vacuo* to afford a crude product of alkyl mesylate in approximately quantitative yield. Subsequently, a 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with alkyl mesylate (~1.0 equiv), sodium iodide (2.5-3.0 equiv), and solvent (acetone or DMF, 100 mL). The reaction mixture was then stirred at elevated temperature (acetone: 60 °C; DMF: 100 °C) overnight. After cooling to room temperature. After cooling to room temperature, the reaction mixture was washed with CH_2Cl_2 (50 mL) and water (400 mL). The aqueous solution was further washed with CH_2Cl_2 (2 x 50 mL). The combined organic fractions were concentrated *in vacuo* with the aid of a rotary evaporator. The residue was purified by flash column chromatography with silica gel using a mixture of hexanes and EtOAc as an eluent to afford the alkyl iodide product.

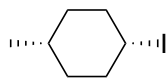
Preparation of Alkyl Iodide from Nitrogen-Containing Heterocycle (General Procedure D): A 500 mL oven-dried round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with N-containing heterocycle (1.0 equiv) and sodium hydride (1.3-1.5 equiv, 60% NaH suspension in oil used). The flask was degassed and refilled with N₂ (this process was repeated for 3 times). Anhydrous DMF (80 mL) was then slowly added into the flask under N₂, and the reaction mixture was stirred at room temperature for 2 h. 1-Bromo-3-chloropropane (1.3-1.5 equiv) was added into the flask under N₂ via syringe, and the reaction mixture was stirred at room temperature overnight. The reaction mixture was then washed with CH₂Cl₂ (50 mL) and water (400 mL). The aqueous solution was further washed with CH₂Cl₂ (2 x 50 mL). The combined organic layer was dried with anhydrous Na₂SO₄, filtered, and concentrated with the aid of a rotary evaporator. The residue was dried *in vacuo* to afford a crude product of 1-chloro-3-(heteroaryl)propane in approximately quantitative yield. Subsequently, a 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with 1-chloro-3-(heteroaryl)propane (~1.0 equiv), sodium iodide (2.5-3.0 equiv), and acetone (100 mL). The reaction mixture was then stirred at elevated temperature at 60 °C overnight. After cooling to room temperature, the reaction mixture was washed with CH₂Cl₂ (50 mL) and water (400 mL). The aqueous solution was further washed with CH₂Cl₂ (2 x 50 mL). The combined organic fractions were concentrated *in vacuo* with the aid of a rotary evaporator. The residue was purified by flash column chromatography with silica gel using a mixture of hexanes and EtOAc as an eluent to afford the alkyl iodide product.

Preparations of Alkynes (General Procedure E): A 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with chloro-substituted terminal alkyne (1.0-1.3 equiv), K₂CO₃ (2 equiv), 4-substituted phenol (1.0-1.3 equiv), sodium iodide (0.2-0.5 equiv), and DMF (60 mL). The reaction mixture was stirred at 70 °C overnight. After cooling to room temperature, the reaction mixture was washed with CH₂Cl₂ (50 mL) and water (400 mL). The aqueous solution was further washed with CH₂Cl₂ (2 x 50 mL). The combined organic fractions were concentrated *in vacuo* with the aid of a rotary evaporator. The residue was purified by flash column chromatography with silica gel using a mixture of hexanes and EtOAc as an eluent to afford the functionalized terminal alkyne product.

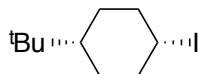


1-Iodo-3-methylcyclohexane (S1).^[5] Following the general procedure A, the title compound was prepared using *cis/trans*-3-methylcyclohexan-1-ol (6.85 g, 60 mmol), triphenylphosphine (22.0 g, 84 mmol), imidazole (5.72 g, 84 mmol), and iodine (21.3 g, 84 mmol). After work up, the crude product was purified by flash chromatography with silica gel using hexanes as an eluent to afford 1-iodo-3-methylcyclohexane (**S1**) as colorless oil (6.50 g, 29 mmol, 48%). The diastereomeric ratio (d.r.: *trans*:*cis* = 6.4:1) of **S1** was determined by ¹H NMR spectroscopy by comparing the integrations of *ipso* C-H protons of both *cis*- and *trans*-isomers.^[14] ¹H NMR (400 MHz, CDCl₃): δ 4.85 (s, 0.9 H), 4.15 (t, *J* = 12.2 Hz, 0.1 H), 2.40-1.96 (m, 3 H), 1.83-1.68 (ovrlp, 2 H), 1.63-1.48 (ovrlp, 2 H), 1.27 (t, *J* = 11.0 Hz, 1 H), 1.03 (t, *J* = 11.2 Hz, 1 H), 0.93-0.88 (ovrlp, 3 H). ¹³C NMR (100 MHz, CDCl₃): δ 49.3, 44.8, 40.3,

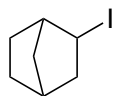
36.6, 36.1, 35.7, 34.4, 33.7, 30.0, 28.9, 28.6, 22.9, 22.3, 21.6 (Observed complexity due to the mixture of diastereoisomers).



1-Iodo-4-methylcyclohexane (S2).^[15] Following the general procedure A, the title compound was prepared using *cis/trans*-4-methylcyclohexan-1-ol (7.99 g, 70 mmol), triphenylphosphine (25.7 g, 98 mmol), imidazole (6.67 g, 98 mmol), and iodine (24.9 g, 98 mmol). After work up, the crude product was purified by flash chromatography with silica gel using hexanes as an eluent to afford 1-iodo-4-methylcyclohexane (**S2**) as colorless oil (5.38 g, 47.2 mmol, 67%). The diastereomeric ratio (d.r.: *cis:trans* = 10.3:1) of **S2** was determined by ¹H NMR spectroscopy by comparing the integrations of *ipso* C-H protons of both *cis*- and *trans*-isomers.^[14] **¹H NMR** (400 MHz, CDCl₃): δ 4.79 (s, 0.9 H), 4.10 (t, *J* = 12.0 Hz, 0.1 H), 2.39 (d, *J* = 11.3 Hz, 0.2 H), 2.07 (d, *J* = 13.5 Hz, 1.8 H), 2.00-1.93 (m, 0.2 H), 1.60-1.44 (ovrlp, 6.8 Hz), 1.06-0.84 (m, 3 H). **¹³C NMR** (major diastereoisomer, 100 MHz, CDCl₃): δ 40.6, 37.5, 36.5, 36.3, 31.8, 31.5, 31.3, 30.6, 22.4, 22.1 (Observed complexity due to the mixture of diastereoisomers).

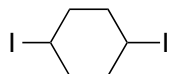


1-(*tert*-Butyl)-4-iodocyclohexane (S3).^[15] Following the general procedure A, the title compound was prepared using *cis/trans*-4-(*tert*-butyl)cyclohexan-1-ol (9.38 g, 60 mmol), triphenylphosphine (22.0 g, 84 mmol), imidazole (5.72 g, 84 mmol), and iodine (21.3 g, 84 mmol). After work up, the crude product was purified by flash chromatography with silica gel using hexanes as an eluent to afford 1-*tert*-butyl-4-iodocyclohexane (**S3**) containing a small amount of dehydrodehalogenation product. The product was heated *in vacuo* to remove the low-boiling impurity. The resulting product was further purified by flash chromatography with silica gel using hexanes as an eluent to afford a pure 1-*tert*-butyl-4-iodocyclohexane (**S3**) as a low-melting, white solid (5.90 g, 22.1 mmol, 37%). The diastereomeric ratio (d.r.: *cis:trans* = 15.4:1) of **S3** was determined by ¹H NMR spectroscopy by comparing the integrations of *ipso* C-H protons of both *cis*- and *trans*-isomers.^[14] **¹H NMR** (400 MHz, CDCl₃): δ 4.88 (s, 0.9 H), 4.09 (t, *J* = 12.2 Hz, 0.1 H), 2.12 (d, *J* = 11.9 Hz, 2 H), 1.65-1.63 (m, 2 H), 1.59-1.46 (ovrlp, 4 H), 1.09-1.04 (m, 1 H), 0.89-0.82 (ovrlp, 9 H). **¹³C NMR** (major diastereoisomer, 100 MHz, CDCl₃): δ 47.9, 38.1, 37.0, 30.4, 27.6, 23.5.

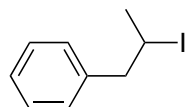


2-Iodobicyclo[2.2.1]heptane [S4].^[15] Following the general procedure A, the title compound was prepared using bicyclo[2.2.1]heptan-2-ol (5.0 g, 44.6 mmol), triphenylphosphine (14.4 g, 62.4 mmol), imidazole (4.25 g, 62.4 mmol), and iodine (15.8 g, 62.4 mmol). After work up, the crude product was purified by flash chromatography with silica gel using hexanes as an eluent to afford 2-iodobicyclo[2.2.1]heptane (**S4**) as colorless oil (7.48 g, 33.7 mmol, 76%). The diastereomeric ratio (d.r.: *exo:endo* = 4.3:1) of **S4** was determined by ¹H NMR spectroscopy of the isolated product. The major *exo*-isomer was determined by comparing the chemical shift of *ipso*-C-H proton of the product with that

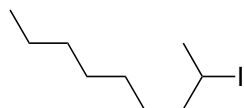
of the reported compound.^[15] $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 4.26-4.24 (m, 0.2 H), 3.98-3.97 (m, 0.8 H), 2.60 (s, 0.8 H), 2.40 (s, 0.2 H), 2.24-2.22 (m, 2 H), 2.12-2.06 (m, 1 H), 1.93-1.82 (m, 1 H), 1.62-1.42 (m, 2 H), 1.40-1.31 (m, 1 H), 1.26-1.22 (m, 1 H), 1.10 (t, $J = 9.4$ Hz, 1 H). $^{13}\text{C NMR}$ (*exo*-isomer (major), 100 MHz, CDCl_3): δ 48.1, 45.3, 38.1, 36.4, 30.4, 28.8, 28.5.



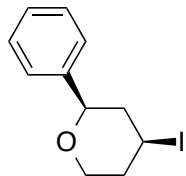
1,4-Diiodocyclohexane (S5).^[16] Following the general procedure A, the title compound was prepared using cyclohexane-1,4-diol (2.32 g, 20 mmol, 1.0 equiv), triphenylphosphine (31.5 g, 120 mmol, 6.0 equiv), imidazole (8.17 g, 120 mmol, 6.0 equiv), and iodine (30.5 g, 120 mmol, 6 equiv). The crude product was purified by flash chromatography with silica gel using hexanes as an eluent to afford 1,4-diiodocyclohexane containing a small amount of impurity. The product was heated *in vacuo* to remove the low-boiling impurity. The resulting product was further purified by flash chromatography with silica gel using hexanes as an eluent to afford a pure 1,4-diiodocyclohexane (**S5**) as a white solid (2.59 g, 7.7 mmol, 39%). The diastereomeric ratio (d.r. = 2.8:1) of **S5** was determined by GCMS analysis. The major diastereoisomer could not be determined due to the broadening and overlapping of the characteristic *ipso*-C-H protons by $^1\text{H NMR}$ spectroscopy. $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 4.51-4.41 (ovrlp, 2 H), 2.28-2.19 (m, 4 H), 2.06-1.96 (m, 4 H). $^{13}\text{C NMR}$ (major diastereoisomer, 100 MHz, CDCl_3): δ 39.0 (br), 37.4, 29.5 (br).



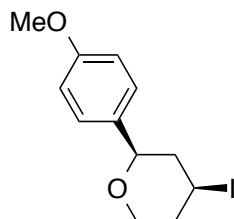
(2-Iodopropyl)benzene (S6).^[17] Following the general procedure A, the title compound was prepared using 1-phenylpropan-2-ol (10.5 g, 76.8 mmol), triphenylphosphine (28.2 g, 107.5 mmol), imidazole (7.32 g, 107.5 mmol), and iodine (27.3 g, 107.5 mmol). The crude product was purified by flash chromatography with silica gel using hexanes as an eluent to afford (2-iodopropyl)benzene (**S6**) as colorless oil (16.6 g, 67.5 mmol, 88%). $^1\text{H NMR}$ (400 MHz, CDCl_3): 7.32-7.24 (ovrlp, 3 H), 7.17 (d, $J = 6.5$ Hz, 2 H), 4.33 (sex, $J = 6.8$ Hz, 1 H), 3.31-3.26 (m, 1 H), 3.08-3.03 (m, 1 H), 1.89 (d, $J = 6.5$ Hz, 3 H).



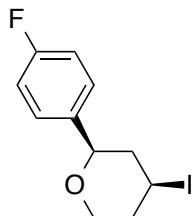
2-Iodononane (S7). Following the general procedure A, the title compound was prepared using 1-phenylpropan-2-ol (10.1 g, 70 mmol), triphenylphosphine (25.7 g, 98 mmol), imidazole (6.67 g, 98 mmol), and iodine (24.9 g, 98 mmol). The crude product was purified by flash chromatography with silica gel using hexanes as an eluent to afford (2-iodopropyl)benzene (**S7**) as colorless oil (15.7 g, 61.7 mmol, 88%). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 4.19 (sex, $J = 6.5$ Hz, 1 H), 1.93 (d, $J = 6.6$ Hz, 3 H), 1.86-1.79 (m, 1 H), 1.65-1.56 (m, 1 H), 1.51-1.24 (ovrlp, 10 H), 0.89 (t, $J = 6.5$ Hz, 3 H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 43.1, 31.9, 31.1, 29.9, 29.3, 29.1, 28.9, 22.8, 14.3. **HRMS:** [M] could not be detected by HRMS (ESI and APPI). **GCMS:** [M] = 254 detected which corresponds to $\text{C}_9\text{H}_{19}\text{I}$; the purity was further confirmed by GCMS.



4-Iodo-2-phenyltetrahydro-2H-pyran (S8).^[18] Following the general procedure B, the title compound was prepared using benaldehyde (4.24 g, 40 mmol), 3-buten-1-ol (5.77 g, 80 mmol), and iodine (10.2 g, 40 mmol). The crude product was purified by flash chromatography with silica gel using hexanes/EtOAc (15:1) as an eluent to afford 4-iodo-2-phenyltetrahydro-2H-pyran (**S8**) as brown oil (6.33 g, 22.0 mmol, 55%). The diastereomeric ratio (d.r.: cis:trans = 15.7:1) of **S8** was determined by ¹H NMR spectroscopy by comparing the integrations of *ipso* C-H protons of both cis- and trans-isomers.^[14] ¹H NMR (400 MHz, CDCl₃): δ 7.35-7.24 (ovrlp, 5 H), 4.92 (s, 0.06 H), 4.84 (d, *J* = 10.2 Hz, 0.06 H), 4.44-4.36 (m, 0.94 H), 4.31 (d, *J* = 10.9 Hz, 0.94 H), 4.05-3.98 (ovrlp, 1 H), 3.61-3.55 (m, 1 H), 2.55 (d, *J* = 12.4 Hz, 1 H), 2.40-1.84 (ovrlp, 3 H). ¹³C NMR (major diastereoisomer, 100 MHz, CDCl₃): δ 141.2, 128.6, 127.9, 125.8, 81.4, 69.6, 47.7, 39.6, 22.1.

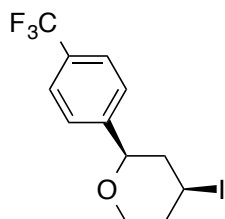


4-Iodo-2-(4-methoxyphenyl)tetrahydro-2H-pyran (S9).^[19] Following the general procedure B, the title compound was prepared using 4-methoxybenaldehyde (5.45 g, 40 mmol), 3-buten-1-ol (5.77 g, 80 mmol), and iodine (10.2 g, 40 mmol). After work up, the crude product was purified by flash chromatography with silica gel using hexanes/EtOAc (10:1) as an eluent to afford 4-iodo-2-(4-methoxyphenyl)tetrahydro-2H-pyran (**S9**) as viscous brown oil (2.35 g, 7.4 mmol, 19%). The diastereomeric ratio (d.r.: cis:trans = 3.0:1) of **S9** was determined by ¹H NMR spectroscopy by comparing the integrations of *ipso* C-H protons of both cis- and trans-isomers.^[14] ¹H NMR (400 MHz, CDCl₃): δ 7.26-7.21 (ovrlp, 2 H), 6.84 (d, *J* = 8.1 Hz, 2 H), 4.87 (s, 0.2 H), 4.76 (d, *J* = 10.3 Hz, 0.2 H), 4.34 (t, *J* = 11.5 Hz, 0.8 H), 4.21 (d, *J* = 10.8 Hz, 0.8 H), 4.03-3.92 (ovrlp, 1.2 H), 3.74 (s, 3 H), 3.51 (t, *J* = 11.2 Hz, 0.8 H), 2.50-1.78 (m, 4 H). ¹³C NMR (major diastereoisomer, 100 MHz, CDCl₃): δ 159.0, 133.3, 127.0, 113.7, 80.7, 69.3, 55.2, 47.4, 39.4, 22.4.

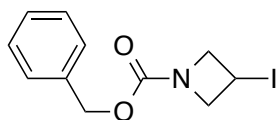


2-(4-Fluorophenyl)-4-iodotetrahydro-2H-pyran (S10). Following the general procedure B, the title compound was prepared using 4-fluorobenzaldehyde (4.96 g, 40 mmol), 3-buten-1-ol (5.77 g, 80 mmol),

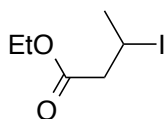
and iodine (10.2 g, 40 mmol). After work up, the crude product was purified by flash chromatography with silica gel using hexanes/EtOAc (15:1) as an eluent to afford 2-(4-fluorophenyl)-4-iodotetrahydro-2*H*-pyran (**S10**) as brown oil (8.21 g, 26.8 mmol, 67%). The diastereomeric ratio (d.r.: cis:trans = 10.1:1) of **S10** was determined by ^1H NMR spectroscopy by comparing the integrations of *ipso* C-H protons of both cis- and trans-isomers.^[14] ^1H NMR (400 MHz, CDCl_3): δ 7.29 (dd, $^3J_{\text{HH}} = 7.8$ Hz, $^4J_{\text{HF}} = 5.8$ Hz, 2 H), 7.02 ($^3J_{\text{HH}} = 8.5$ Hz, $^3J_{\text{HF}} = 8.5$ Hz, 2 H), 4.91 (s, 0.1 H), 4.81 (d, $J = 10.3$ Hz, 0.1 H), 4.42-4.34 (m, 0.9 H), 4.29 (d, $J = 10.8$ Hz, 0.9 H), 4.06-3.97 (ovrlp, 1 H), 3.60-3.54 (m, 1 H), 2.52 (d, $J = 12.8$ Hz, 1 H), 2.39-1.80 (ovrlp, 3 H). ^{13}C NMR (major diastereoisomer, 100 MHz, CDCl_3): δ 162.2 (d, $^1J_{\text{CF}} = 244.4$ Hz), 137.0 (d, $^4J_{\text{CF}} = 3.1$ Hz), 127.5 (d, $^3J_{\text{CF}} = 8.0$ Hz), 115.4 (d, $^2J_{\text{CF}} = 21.2$ Hz), 80.5, 69.5, 47.6, 39.4, 21.7. HRMS (APPI): Calcd for $\text{C}_{11}\text{H}_{11}\text{FIO}$ [M-H]: 304.9834; Found: 304.9833.



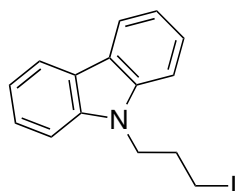
4-Iodo-2-(4-(trifluoromethyl)phenyl)tetrahydro-2*H*-pyran (S11). Following the general procedure B, the title compound was prepared using 4-(trifluoromethyl)benzaldehyde (1.2 g, 8.8 mmol), 3-buten-1-ol (1.27 g, 17.6 mmol), and iodine (2.23 g, 8.8 mmol). After work up, the crude product was purified by flash chromatography with silica gel using hexanes as an eluent to afford 4-iodo-2-(4-(trifluoromethyl)phenyl)tetrahydro-2*H*-pyran (**S11**) as brown oil (981 mg, 2.76 mmol, 31%). The diastereomeric ratio (d.r.: cis:trans = 3.3:1) of **S11** was determined by ^1H NMR spectroscopy by comparing the integrations of *ipso* C-H protons of both cis- and trans-isomers.^[14] ^1H NMR (400 MHz, CDCl_3): δ 7.59 (d, $J = 7.7$ Hz, 2 H), 7.46-7.25 (ovrlp, 2 H), 4.91-4.88 (ovrlp, 0.4 H), 4.43-4.36 (ovrlp, 1.6 H), 4.08-4.00 (ovrlp, 1.2 H), 3.65-3.55 (m, 0.8 H), 2.56 (d, $J = 12.2$ Hz, 0.8 H), 2.36-2.32 (ovrlp, 1.2 H), 2.22-2.13 (ovrlp, 1 H), 1.97 (s, 0.8 H), 1.80 (t, $J = 12.8$ Hz, 0.2 H). ^{13}C NMR (major diastereoisomer, 100 MHz, CDCl_3): δ 145.1, 129.9 (q, $^2J_{\text{CF}} = 32.1$ Hz), 126.0, 125.5 (q, $^3J_{\text{CF}} = 3.4$ Hz), 124.2 (q, $^1J_{\text{CF}} = 270.3$ Hz), 80.4, 69.5, 47.5, 39.4, 21.1. HRMS (APPI): Calcd for $\text{C}_{12}\text{H}_{12}\text{F}_3\text{IO}$ [M]: 355.9853; Found: 355.9879.



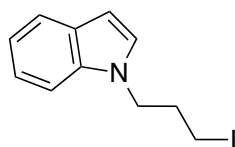
Benzyl 3-iodoazetidine-1-carboxylate (S12).^[5] Following the general procedure C, the title compound was prepared using benzyl 3-iodoazetidine-1-carboxylate (5.05 g, 24.5 mmol), mesyl chloride (4.21 g, 2.8 mL, 36.8 mmol), and triethylamine (3.72 g, 5.1 mL, 36.8 mmol), followed by the iodination of the crude benzyl 3-((methylsulfonyl)oxy)azetidine-1-carboxylate product with sodium iodide (11.0 g, 73.5 mmol) in DMF (Note: No reaction occurred when acetone solvent was used). After work up, the crude product was purified by flash chromatography with silica gel using hexanes/EtOAc (10:1) as an eluent to afford benzyl 3-iodoazetidine-1-carboxylate (**S12**) as brown oil (3.05 g, 9.6 mmol, 39%). ^1H NMR (400 MHz, CDCl_3): 7.36-7.29 (ovrlp, 5 H), 5.08 (s, 2 H), 4.68 (t, $J = 8.4$ Hz, 2 H), 4.43 (qu, $J = 5.2$ Hz, 1 H), 4.34-4.31 (m, 2 H).



Ethyl 3-iodobutanoate (S13).^[20] Following the general procedure C, the title compound was prepared using ethyl 3-hydroxybutanoate (3.97 g, 30 mmol), mesyl chloride (4.12 g, 2.8 mL, 36 mmol), and triethylamine (4.6 g, 6.2 mL, 45 mmol), followed by the iodination of the crude ethyl 3-((methylsulfonyl)oxy)butanoate product with sodium iodide (11.2 g, 75 mmol) in acetone. After work up, the crude product was purified by flash chromatography with silica gel using hexanes/EtOAc (10:1) as an eluent to afford ethyl 3-iodobutanoate (**S13**) as colorless oil (4.62 g, 19.1 mmol, 64%). ¹H NMR (400 MHz, CDCl₃): δ 4.39 (sex, *J* = 7.0 Hz, 1 H), 4.11 (q, *J* = 7.0 Hz, 2 H), 2.96-2.90 (m, 1 H), 2.87-2.81 (m, 1 H), 1.87 (d, *J* = 6.7 Hz, 3 H), 1.21 (t, *J* = 7.0 Hz, 3 H). ¹³C NMR (100 MHz, CDCl₃): δ 170.5, 61.0, 48.0, 28.8, 18.6, 14.3.

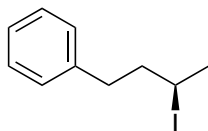


9-(3-Iodopropyl)-9H-carbazole (S14). Following the general procedure D, the title compound was prepared using carbazole (10.0 g, 60 mmol), sodium hydride (2.17 g, 90 mmol, 3.62 g of 60% NaH suspension in oil used), and 1-bromo-3-chloropropane (14.2 g, 8.9 mL, 90 mmol), followed by iodination of the crude 1-(3-chloropropyl)-1H-carbazole product with NaI (23.5 g, 150 mmol). After work up, the crude product was purified by flash chromatography with silica gel using hexanes/EtOAc (15:1) as an eluent to afford 1-(3-iodopropyl)-1H-indole (**S14**) as a pale-yellow solid (18.1 g, 54 mmol, 90%). ¹H NMR (400 MHz, CDCl₃): δ 8.10 (d, *J* = 7.7 Hz, 2 H), 7.50-7.45 (ovrlp, 4 H), 7.27-7.21 (m, 2 H), 4.43 (d, *J* = 6.6 Hz, 2 H), 3.16 (d, *J* = 6.4 Hz, 2 H), 2.41 (qu, *J* = 6.5 Hz, 2 H). ¹³C NMR (100 MHz, CDCl₃): δ 140.3, 125.9, 123.0, 120.5, 119.2, 108.7, 43.1, 32.8, 3.2. HRMS (ESI): Calcd for C₁₅H₁₅IN [M+H]: 336.0249; Found: 366.0257.



1-(3-Iodopropyl)-1H-indole (S15). Following the general procedure D, the title compound was prepared using indole (4.11 g, 35.0 mmol), sodium hydride (1.10 g, 45.5 mmol, 1.83 g of 60% NaH suspension in oil used), and 1-bromo-3-chloropropane (7.16 g, 4.5 mL, 45.5 mmol), followed by iodination of the crude 1-(3-chloropropyl)-1H-indole product with NaI (13.1 g, 87.5 mmol). After work up, the crude product was purified by flash chromatography with silica gel using hexanes/EtOAc (15:1) as an eluent to afford 1-(3-iodopropyl)-1H-indole (**S15**) as pale-yellow oil (3.94 g, 13.8 mmol, 39%). ¹H NMR (400 MHz, CDCl₃): δ 7.61 (d, *J* = 7.6 Hz, 1 H), 7.31 (d, *J* = 8.0 Hz, 1 H), 7.18 (t, *J* = 7.5 Hz, 1 H), 7.11-7.05 (ovrlp, 2 H), 6.46 (s, 1 H), 4.14 (t, *J* = 6.0 Hz, 2 H), 2.95 (t, *J* = 6.2 Hz, 2 H), 2.18 (qu, *J* = 6.2 Hz, 2 H). ¹³C NMR (100 MHz, CDCl₃): δ 135.8, 128.7, 128.0, 121.7, 121.1, 119.6, 109.4, 101.5, 46.1, 33.4, 3.4. HRMS (ESI): Calcd for C₁₁H₁₃IN [M+H]: 286.0093; Found: 286.0080.

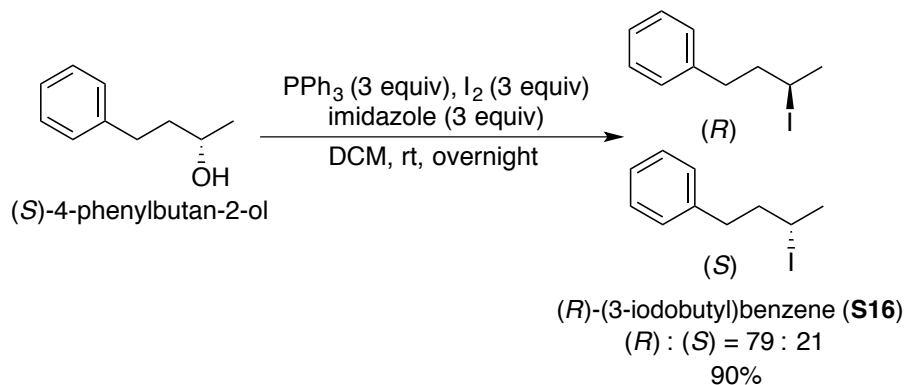
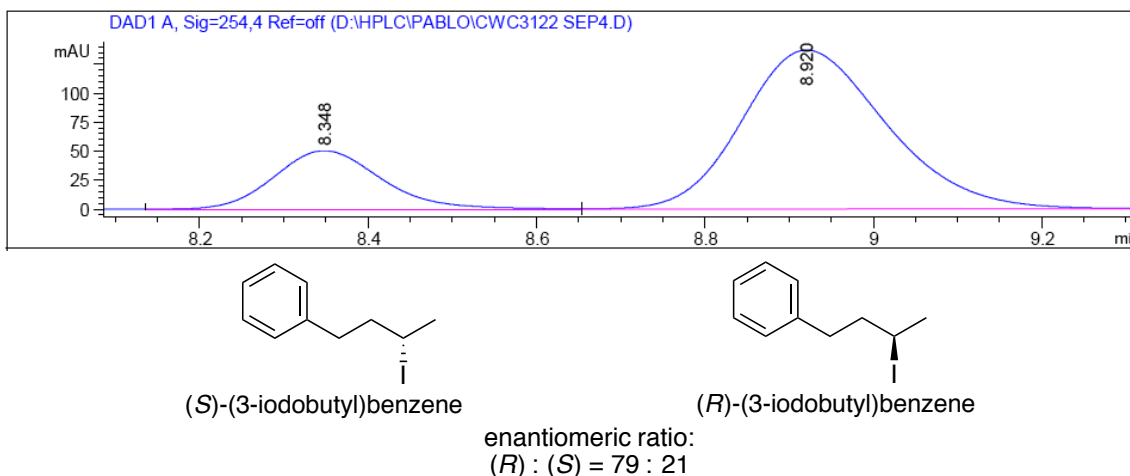
Synthesis of Enantioenriched Alkyl Halides:

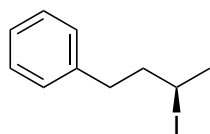


((*R*) : (*S*) = 79 : 21)

(*R*)-(3-Iodobutyl)benzene (S16). Following the general procedure A and the similar literature procedure,^[6] the title compound was prepared using (*S*)-4-phenylbutan-2-ol (185 mg, 1.23 mmol, 1.0 equiv), triphenylphosphine (969 mg, 3.69 mmol, 3.0 equiv), imidazole (251 mg, 3.69 mmol, 3.0 equiv), and iodine (937 mg, 3.69 mmol, 3.0 equiv). The crude product was purified by flash chromatography with silica gel using hexanes as an eluent to afford enantioenriched (*R*)-(3-iodobutyl)benzene (**S16**) (288 mg, 1.11 mmol, 90%). The enantiomeric ratio of (**S16**) ((*R*):(*S*) = 79:21) was determined by HPLC analysis as shown below. The identification and purity of (**S16**) were further determined by GCMS and HPLC analysis by comparing with authentic and racemic (*R*)/(*S*)-(3-iodobutyl)benzene synthesized from (*R*)/(*S*)-phenylbutan-2-ol.^[5] The ¹H NMR of (**S16**) was in agreement with that of (*R*)/(*S*)-(3-iodobutyl)benzene.^[5] The HPLC separation of **S16** was shown below.

HPLC separation of enantio-enriched (*R*)-(3-iodobutyl)benzene

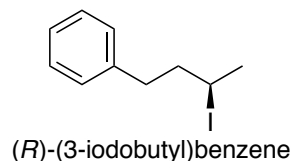
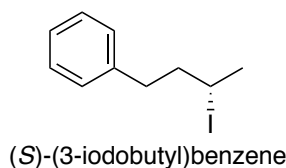
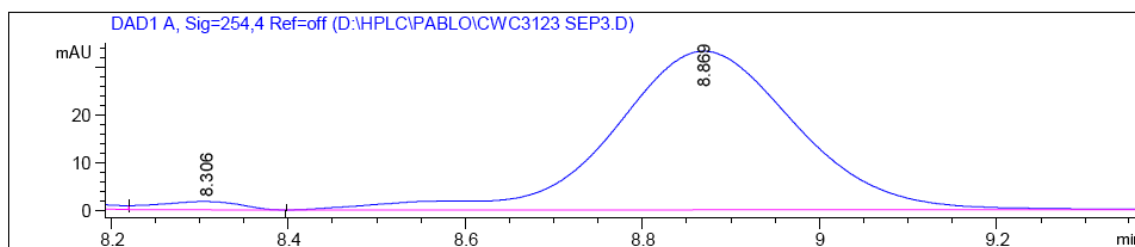




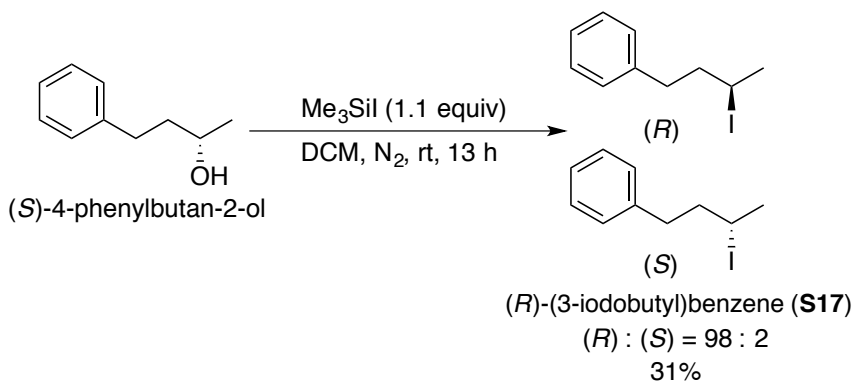
((*R*) : (*S*) = 98 : 2)

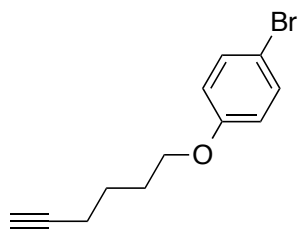
(*R*)-(3-Iodobutyl)benzene (S17). The title compound was prepared according to the literature procedure.^[21] In a nitrogen-filled glovebox, an oven-dried 30 mL re-sealable screw-cap test tube equipped with a Teflon-coated magnetic stirrer bar was charged with (*S*)-4-phenylbutan-2-ol (150 mg, 1.0 mmol, 1.0 equiv), trimethylsilyl iodide (242 mg, 172 μ L, 1.1 mmol, 1.1 equiv), and anhydrous CH_2Cl_2 (10 mL). The reaction mixture was stirred at room temperature for 13 h. The reaction mixture was then washed with CH_2Cl_2 (20 mL) and saturated $\text{Na}_2\text{S}_2\text{O}_3$ solution (20 mL). The aqueous solution was further washed with CH_2Cl_2 (2 x 10 mL). The combined organic fractions were concentrated with the aid of a rotary evaporator. The crude product was purified by flash chromatography with silica gel using hexanes as an eluent to afford enantioenriched (*R*)-(3-iodobutyl)benzene (**S17**) (82 mg, 0.31 mmol, 31%). The enantiomeric ratio of (**S17**) ((*R*):(*S*) = 98:2) was determined by HPLC analysis. The identification and purity of (**S17**) were further determined by GCMS and HPLC analysis by comparing with authentic and racemic (*R*)/(*S*)-(3-iodobutyl)benzene synthesized from (*R*)/(*S*)-phenylbutan-2-ol.^[5] The HPLC separation of **S17** was shown below.

HPLC separation of enantio-enriched (*R*)-(3-iodobutyl)benzene

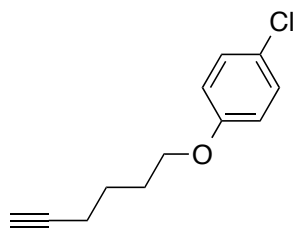


enantiomeric ratio:
(*R*) : (*S*) = 98 : 2

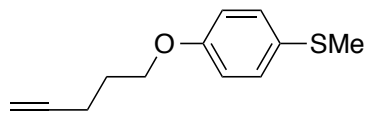




1-Bromo-4-(hex-5-yn-1-yloxy)benzene (S18). Following the general procedure E, the title compound was prepared using 6-chloro-1-hexyne (1.77 g, 15.2 mmol, 1.0 equiv), K_2CO_3 (4.20 g, 30.4 mmol, 2.0 equiv), 4-bromophenol (3.42 g, 19.8 mmol, 1.3 equiv), and sodium iodide (1.14 g, 7.6 mmol, 0.5 equiv). After work up, the crude product was purified by flash chromatography with silica gel using hexanes/EtOAc (20:1) as an eluent to afford 1-bromo-4-(hex-5-yn-1-yloxy)benzene (**S18**) as pale-yellow oil (2.41 g, 9.52 mmol, 63%). 1H NMR (400 MHz, $CDCl_3$): δ 7.34 (d, $J = 8.6$ Hz, 2 H), 6.74 (d, $J = 8.6$ Hz, 2 H), 3.91 (t, $J = 6.1$ Hz, 2 H), 2.27-2.23 (m, $J = 2$ H), 1.98 (s, 1 H), 1.88 (d, $J = 6.7$ Hz, 2 H), 1.69 (d, $J = 7.2$ Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.1, 132.2, 116.3, 112.7, 84.1, 68.9, 67.5, 28.2, 25.0, 18.2. HRMS (ESI): Calcd for $C_{12}H_{13}BrOAg$ [M+Ag]: 358.9201; Found: 358.9230.

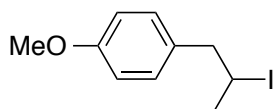


1-Chloro-4-(hex-5-yn-1-yloxy)benzene (S19). Following the general procedure E, the title compound was prepared using 6-chloro-1-hexyne (2.33 g, 20 mmol, 1.0 equiv), K_2CO_3 (5.52 g, 40 mmol, 2.0 equiv), 4-chlorophenol (3.34 g, 26 mmol, 1.3 equiv), and sodium iodide (1.50 g, 10 mmol, 0.5 equiv). After work up, the crude product was purified by flash chromatography with silica gel using hexanes/EtOAc (20:1) as an eluent to afford 1-chloro-4-(hex-5-yn-1-yloxy)benzene (**S19**) as pale-yellow oil (3.37 g, 16.2 mmol, 62%). 1H NMR (400 MHz, $CDCl_3$): δ 7.21 (d, $J = 8.4$ Hz, 2 H), 6.80 (d, $J = 8.4$ Hz, 2 H), 3.93 (t, $J = 6.0$ Hz, 2 H), 2.26 (t, $J = 6.3$ Hz, 2 H), 1.97 (s, 1 H), 1.89 (d, $J = 6.6$ Hz, 2 H), 1.70 (d, $J = 7.1$ Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.7, 129.4, 125.5, 115.8, 84.1, 68.9, 67.7, 28.3, 25.1, 18.2. HRMS: [M] could not be detected by HRMS (ESI). GCMS: [M] = 208 detected which corresponds to $C_{12}H_{13}ClO$; the purity was further confirmed by GCMS.

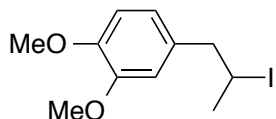


Methyl(4-(pent-4-yn-1-yloxy)phenyl)sulfane (S20). Following the general procedure E, the title compound was prepared using 5-chloro-1-pentyne (4.00 g, 39 mmol, 1.3 equiv), K_2CO_3 (8.29 g, 60 mmol, 2.0 equiv), 4-(methylthio)phenol (4.21 g, 30 mmol, 1.0 equiv), and sodium iodide (900 mg, 6.0 mmol, 0.2 equiv). After work up, the crude product was purified by flash chromatography with silica gel using hexanes/EtOAc (20:1) as an eluent to afford methyl(4-(pent-4-yn-1-yloxy)phenyl)sulfane (**S20**) as pale-yellow oil (4.88 g, 23.7 mmol, 79%). 1H NMR (400 MHz, $CDCl_3$): δ 7.25 (d, $J = 8.3$ Hz, 2 H), 6.84 (d, $J = 8.3$ Hz, 2 H), 4.02 (t, $J = 5.9$ Hz, 2 H), 2.43-2.36 (ovrlp, 5 H), 2.01-1.92 (ovrlp, 3 H). ^{13}C

NMR (100 MHz, CDCl₃): δ 157.5, 130.2, 128.9, 115.3, 83.5, 69.0, 66.3, 28.2, 18.1, 15.2. **HRMS** (ESI): Calcd for C₁₂H₁₄OAg [M+Ag]: 312.9816; Found: 312.9803.

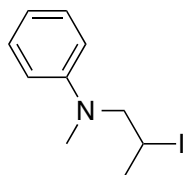


1-(2-Iodopropyl)-4-methoxybenzene (S21). Step (1): A 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with 1-(4-methoxyphenyl)propan-2-one (9.85 g, 60 mmol, 1.0 equiv) and methanol (300 mL). The reaction mixture was cooled in an ice-water bath, and NaBH₄ (6.81 g, 180 mmol, 3.0 equiv) was slowly added into the reaction mixture in a few portions. The resulting reaction mixture was warmed to room temperature and stirred overnight. The reaction mixture was dried *in vacuo* with the aid of a rotary evaporator, and the residue was then washed with water (400 mL) and CH₂Cl₂ (100 mL). The aqueous fraction was further washed with CH₂Cl₂ (2 x 100 mL). The combined organic fractions were dried with anhydrous Na₂SO₄, filtered, and dried with the aid of a rotary evaporator. The residue was dried *in vacuo* to afford a crude 1-(4-methoxyphenyl)propan-2-ol as a viscous, colorless oil. **Step (2):** Following the general procedure A, the title compound was prepared using 1-phenylpropan-2-ol (prepared from the preceding procedure, ~60 mmol), triphenylphosphine (22.0 g, 84 mmol), imidazole (5.72 g, 84 mmol), and iodine (21.3 g, 84 mmol). The crude product was purified by flash chromatography with silica gel using hexanes/EtOAc (10:1) as an eluent to afford 1-(2-iodopropyl)-4-methoxybenzene (**S21**) as colorless oil (11.1 g, 40.2 mmol, 67%). **¹H NMR** (400 MHz, CDCl₃): δ 7.10 (d, *J* = 8.2 Hz, 2 H), 6.84 (d, *J* = 8.2 Hz, 2 H), 4.29 (sex, *J* = 7.0 Hz, 1 H), 3.79 (s, 3 H), 3.25-3.20 (m, 1 H), 3.02-2.96 (m, 1 H), 1.88 (d, *J* = 6.8 Hz, 2 H). **¹³C NMR** (100 MHz, CDCl₃): δ 158.5, 132.0, 130.1, 113.9, 55.3, 48.7, 29.6, 28.0. **HRMS** (APPI): Calcd for C₁₀H₁₃IO [M]: 276.0017; Found: 276.0011.

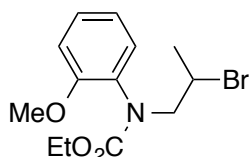


4-(2-Iodopropyl)-1,2-dimethoxybenzene (S22). Step (1): A 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with 1-(3,4-dimethoxyphenyl)propan-2-one (11.7 g, 60 mmol, 1.0 equiv) and methanol (300 mL). The reaction mixture was cooled in an ice-water bath, and NaBH₄ (6.81 g, 180 mmol, 3.0 equiv) was slowly added into the reaction mixture in a few portions. The resulting reaction mixture was warmed to room temperature and stirred overnight. The reaction mixture was dried *in vacuo* with the aid of a rotary evaporator, and the residue was then washed with water (400 mL) and CH₂Cl₂ (100 mL). The aqueous fraction was further washed with CH₂Cl₂ (2 x 100 mL). The combined organic fractions were dried with anhydrous Na₂SO₄, filtered, and dried with the aid of a rotary evaporator. The residue was dried *in vacuo* to afford a crude 1-(3,4-dimethoxyphenyl)propan-2-ol as a white solid. **Step (2):** Following the general procedure A, the title compound was prepared using 1-(3,4-dimethoxyphenyl)propan-2-ol (prepared from the preceding procedure, ~60 mmol), triphenylphosphine (22.0 g, 84 mmol), imidazole (5.72 g, 84 mmol), and iodine (21.3 g, 84 mmol). The crude product was purified by flash chromatography with silica gel using hexanes/EtOAc (10:1) as an eluent to afford 4-(2-iodopropyl)-1,2-dimethoxybenzene (**S22**) as viscous, colorless oil (16.4 g, 53.6 mmol, 89%). **¹H NMR** (400 MHz, CDCl₃): δ 6.81 (d, *J* = 7.9 Hz, 1 H), 6.73-6.71 (ovrlp, 2 H), 4.32 (sex, *J* = 6.9 Hz, 1 H), 3.88 (s, 3 H), 3.86 (s, 3 H), 3.26-3.21 (m, 1 H), 3.02-2.97 (m, 1 H), 1.89 (d, *J* = 6.7 Hz,

3 H). ^{13}C NMR (100 MHz, CDCl_3): δ 148.8, 147.9, 132.3, 121.1, 112.1, 111.0, 55.92, 55.90, 49.1, 29.2, 28.0. HRMS (APPI): Calcd for $\text{C}_{11}\text{H}_{15}\text{IO}_2$ [M]: 306.0114; Found: 306.0117.



***N*-(2-iodopropyl)-*N*-methylaniline (S23).** **Step (1):** A 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer and capped with a rubber septum was charged with *N*-methylaniline (6.43 g, 60.0 mmol, 1.0 equiv), propylene oxide (10.5 g, 12.6 mL 180 mmol, 3.0 equiv), and ethanol (200 mL). The reaction mixture was then heated at 90 °C overnight. The reaction mixture was dried *in vacuo* with the aid of a rotary evaporator, and the residue was then washed with water (400 mL) and CH_2Cl_2 (100 mL). The aqueous fraction was further washed with CH_2Cl_2 (2 x 100 mL). The combined organic fractions were dried with anhydrous Na_2SO_4 , filtered, and dried *in vacuo* with the aid of a rotary evaporator. The residue was dried *in vacuo* to afford a crude 1-(methyl(phenyl)amino)propan-2-ol as a yellow oil. **Step (2):** Following the general procedure A, the title compound was prepared using 1-(methyl(phenyl)amino)propan-2-ol (prepared from the preceding procedure, ~60 mmol), triphenylphosphine (22.0 g, 84 mmol), imidazole (5.72 g, 84 mmol), and iodine (21.3 g, 84 mmol). The crude product was purified by flash chromatography with silica gel using hexanes/EtOAc (8:1) as an eluent to afford *N*-(2-iodopropyl)-*N*-methylaniline (S23) as brown oil (12.5 g, 45.5 mmol, 76%). ^1H NMR (400 MHz, CDCl_3): δ 7.23 (t, $J = 7.5$ Hz, 2 H), 6.72 (t, $J = 7.2$ Hz, 1 H), 6.66 (d, $J = 7.9$ Hz, 2 H), 4.35 (sex, $J = 7.2$ Hz, 1 H), 3.90-3.85 (m, 1 H), 3.52-3.46 (m, 1 H), 3.00 (s, 3 H), 1.85 (d, $J = 6.7$ Hz, 3 H). ^{13}C NMR (100 MHz, CDCl_3): δ 148.2, 129.4, 116.9, 111.8, 63.2, 39.8, 25.9, 25.8. HRMS (ESI): Calcd for $\text{C}_{16}\text{H}_{24}\text{N}$ [M+H]: 230.1909; Found: 230.1913.



Ethyl (2-Bromopropyl)(2-methoxyphenyl)carbamate (S24). **Step (1):** A 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with 2-methoxyaniline (18.5 g, 16.9 mL, 150 mmol, 1.0 equiv), triethylamine (18.2 g, 25.0 mL 180 mmol, 1.2 equiv), and CH_2Cl_2 (200 mL). 2-Bromopropanoyl bromide (32.4 g, 15.7 mL, 150 mmol, 1.0 equiv) was then added dropwise into the reaction mixture, and the resulting mixture was stirred at room temperature overnight. The reaction mixture was washed with aqueous HCl solution (1 M, 300 mL), and the aqueous fraction was further washed with CH_2Cl_2 (2 x 50 mL). The combined organic fractions were then washed with water (200 mL), dried with anhydrous Na_2SO_4 , filtered, and dried *in vacuo* with the aid of a rotary evaporator. The residue was dried *in vacuo* to afford a crude 2-bromo-*N*-(2-methoxyphenyl)propanamide. **Step (2):** A 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer and capped with a rubber septum was charged with 2-bromo-*N*-(2-methoxyphenyl)propanamide (prepared from the preceding procedure) and dry THF (200 mL), and borane-THF solution (1 M in THF, 180 mmol, 180 mL) was then added into the reaction mixture. The resulting solution was stirred at room temperature for 15 min and then heated at 50 °C in an oil bath overnight. After the reaction, water (50 mL) was added and the

reaction mixture was stirred for 15 min to deactivate any unreacted BH_3 . The crude reaction mixture was dried *in vacuo* with the aid of a rotary evaporator, and the residue was then washed with CH_2Cl_2 (200 mL) and water (200 mL). The aqueous fraction was further washed with CH_2Cl_2 (2 x 50 mL). The combined organic fractions were then dried with anhydrous Na_2SO_4 , filtered, and dried *in vacuo* with the aid of a rotary evaporator. The residue was dried *in vacuo* to afford a crude *N*-(2-bromopropyl)-2-methoxyaniline. **Step (3):** A 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with *N*-(2-bromopropyl)-2-methoxyaniline (prepared from the preceding procedure), (~4.88 g, ~20 mmol, ~1.0 equiv), 2,6-lutidine (2.57 g, 2.8 mL, 24 mmol, 1.2 equiv), and diethyl ether (100 mL). Ethyl chloroformate (2.17 g, 1.9 mL, 20 mmol, 1.0 equiv) was then added slowly into the reaction mixture, and the resulting mixture was stirred at room temperature overnight. The reaction mixture was washed with aqueous HCl solution (1 M, 50 mL) and EtOAc (100 mL), and the aqueous fraction was further washed with EtOAc (2 x 50 mL). The combined organic fractions were then washed with water (200 mL), dried with anhydrous Na_2SO_4 , filtered, and dried *in vacuo* with the aid of a rotary evaporator. The crude product was purified by flash chromatography with silica gel using hexanes/EtOAc (20:1) and then hexanes/EtOAc (10:1) as eluents to afford ethyl (2-bromopropyl)(2-methoxyphenyl)carbamate (**S24**) as viscous, colorless oil (3.05 g, 9.6 mmol, 48%, as a mixture of rotamers in a ratio of 2.8:1). ^1H NMR (400 MHz, CDCl_3): δ 7.30-7.23 (ovrlp, 2 H), 6.96-6.92 (ovrlp, 2 H), 4.35-4.05 (ovrlp, 4 H), 3.82 (s, 3 H), 3.74-3.49 (m, 1 H), 1.72 (d, $J = 6.3$ Hz, 3 H), 1.33 (t $J = 6.4$ Hz, 0.8 H), 1.11 (t, $J = 6.8$ Hz, 2.2 H). GCMS: $[M] = 315$ and 317 which corresponds to $\text{C}_{13}\text{H}_{18}\text{BrNO}_3$.

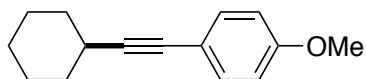
Preparations of Alkynyl Grignard Reagents. Alkynyl Grignard reagents were prepared according to the literature procedure.^[13] In a nitrogen-filled glove box, an oven-dried 30 mL re-sealable screw-cap test tube equipped with a Teflon-coated magnetic stirrer bar was charged with terminal alkynes (1.0 equiv) and THF (1.0 mL of THF was added when 1.0 equiv of terminal alkyne was added), followed by the slow addition of ethylmagnesium bromide via syringe (1.0 M in THF, 1.0 mL of EtMgBr solution was added when 1.0 equiv of terminal alkyne was added) (Caution: exothermic reaction; ethane gas was evolved). The reaction mixture was stirred at room temperature for 15 min to form a clear solution. The reaction mixture was then stirred at 50 °C in an oil bath for 1 h to form an alkynyl Grignard reagent (alkynyl magnesium bromide) solution (0.5 M in THF). The scale of alkynyl Grignard reagent ranged from 3.0 mmol to 7.5 mmol.

Optimizations of Iron-Catalyzed Cross-Coupling of Non-activated Secondary Alkyl Halides with Alkynyl Grignard Reagents (Table 1, Tables S1-S3). An oven-dried 30 mL re-sealable screw-cap test tube equipped with a Teflon-coated magnetic stirrer bar was charged with FeBr_2 (98% purity, 10.8 mg, 0.05 mmol, 0.10 equiv), secondary alkyl halide (0.5 mmol, 1.0 equiv), and NMP solvent (2.0 mL), followed by the addition of alkynyl Grignard reagent solution (0.5 M in THF, 1.5 mL, 1.5 equiv). The reaction mixture was stirred at room temperature for 16 h to form a deep brown or black solution. After the reaction, *n*-dodecane (109 μL , 0.50 mmol, 1.0 equiv) was added into the crude product mixture, and the crude product was washed with EtOAc (5 mL) and water (20 mL). A small portion of the organic fraction was filtered through a plug of silica gel and then subjected to GC analysis to determine the GC yields of alkylated alkyne product using *n*-dodecane as an internal standard.

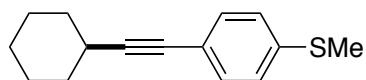
Optimizations of Iron-Catalyzed Cross-Coupling of Non-activated Primary Alkyl Halides with Alkynyl Grignard Reagents (Tables S4-S5). An oven-dried 30 mL re-sealable screw-cap test tube equipped with a Teflon-coated magnetic stirrer bar was charged with FeBr₂ (98% purity, 10.8 mg, 0.05 mmol, 0.10 equiv), primary alkyl halide (0.5 mmol, 1.0 equiv), bis[2-(*N,N*-dimethylamino)ethyl] ether (321 mg, 377 μ L, 1.0 mmol, 2.0 equiv), and THF solvent (2.0 mL), followed by the addition of alkynyl Grignard reagent solution (0.5 M in THF, 1.5 mL, 1.5 equiv). The reaction mixture was stirred at room temperature for 16 h to form a deep brown or black solution. After the reaction, *n*-dodecane (109 μ L, 0.50 mmol, 1.0 equiv) was added into the crude product mixture, and the crude product was washed with EtOAc (5 mL) and water (20 mL). A small portion of the organic fraction was filtered through a plug of silica gel and then subjected to GC analysis to determine the GC yield of substituted alkyne product using *n*-dodecane as an internal standard.

Substrate Scope for Iron-Catalyzed Cross-Coupling of Non-activated Secondary Alkyl Halides with Alkynyl Grignard Reagents (General Procedure F): An oven-dried 30 mL re-sealable screw-cap test tube equipped with a Teflon-coated magnetic stirrer bar was charged with FeBr₂ (98% purity, 22 mg, 0.10 mmol, 0.10 equiv), secondary alkyl halide (1.0 mmol, 1.0 equiv), and NMP solvent (4.0 mL), followed by the addition of alkynyl Grignard reagent solution (0.5 M in THF, 3.0 mL, 1.5 equiv). The reaction mixture was stirred at room temperature for 16 h to form a deep brown or black solution. After the reaction, the crude product was washed with EtOAc (10 mL) and water (30 mL). The aqueous fraction was further washed with EtOAc (2 x 10 mL). The combined organic fractions were concentrated *in vacuo* with the aid of a rotary evaporator. The crude product residue was purified by flash column chromatography with silica gel using a solvent mixture (EtOAc, hexanes) as an eluent to afford the substituted alkylated alkyne product.

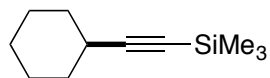
Substrate Scope for Iron-Catalyzed Cross-Coupling of Non-activated Primary Alkyl Halides with Alkynyl Grignard Reagents (General Procedure G). An oven-dried 30 mL re-sealable screw-cap test tube equipped with a Teflon-coated magnetic stirrer bar was charged with FeBr₂ (98% purity, 43 mg, 0.20 mmol, 0.20 equiv), primary alkyl halide (1.0 mmol, 1.0 equiv), bis[2-(*N,N*-dimethylamino)ethyl] ether (O-TMEDA) (321 mg, 377 μ L, 2.0 mmol, 2.0 equiv), and THF solvent (4.0 mL), followed by the addition of alkynyl Grignard reagent solution (0.5 M in THF, 3.0 mL, 1.5 equiv). The reaction mixture was stirred at room temperature for 16 h to form a deep brown or black solution. After the reaction, the crude product was washed with EtOAc (10 mL) and water (30 mL). The aqueous fraction was further washed with EtOAc (2 x 10 mL). The combined organic fractions were concentrated *in vacuo* with the aid of a rotary evaporator. The crude product residue was purified by flash column chromatography with silica gel using a solvent mixture (EtOAc, hexanes) as an eluent to afford the isolated substituted alkyne product.



1-(Cyclohexylethynyl)-4-methoxybenzene (2a).^[22] Following the general procedure F, the title compound was prepared using iodocyclohexane (210 mg, 130 μ L 1.0 mmol) and ((4-methoxyphenyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes/EtOAc (60:1) and then hexanes/EtOAc (40:1) as eluents to afford 1-(cyclohexylethynyl)-4-methoxybenzene (**2a**) as colorless oil (128 mg, 0.60 mmol, 60%). **¹H NMR** (400 MHz, CDCl₃): δ 7.32 (d, J = 8.3 Hz, 2 H), 6.78 (d, J = 8.4 Hz, 2 H), 3.78 (s, 3 H), 2.58-2.52 (m, 1 H), 1.87-1.85 (m, 2 H), 1.78-1.71 (m, 2 H), 1.56-1.48 (ovrlp, 3 H), 1.38-1.30 (ovrlp, 3 H). **¹³C NMR** (100 MHz, CDCl₃): δ 159.1, 132.9, 116.4, 113.8, 92.9, 80.3, 55.3, 33.0, 29.8, 26.1, 25.1.



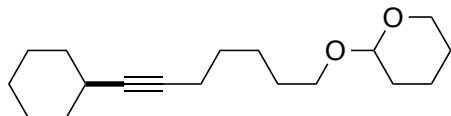
(4-(Cyclohexylethynyl)phenyl)(methyl)sulfane (2b). Following the general procedure F, the title compound was prepared using iodocyclohexane (210 mg, 130 μ L 1.0 mmol) and ((4-(methylthio)phenyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (50:1) as an eluent to afford (4-(cyclohexylethynyl)phenyl)(methyl)sulfane (**2b**) as viscous yellow oil (151 mg, 0.65 mmol, 65%). **¹H NMR** (400 MHz, CDCl₃): δ 7.29 (d, J = 8.1 Hz, 2 H), 7.13 (d, J = 8.1 Hz, 2 H), 2.59-2.53 (m, 1 H), 2.44 (s, 3 H), 1.89-1.83 (m, 2 H), 1.77-1.70 (m, 2 H), 1.56-1.47 (ovrlp, 3 H), 1.38-1.28 (ovrlp, 3 H). **¹³C NMR** (100 MHz, CDCl₃): δ 138.1, 131.9, 126.1, 120.7, 94.6, 80.3, 32.8, 29.8, 26.0, 25.0, 15.7. **HRMS** (ESI): Calcd for C₁₅H₁₈SAg [M+Ag]: 337.0180; Found: 337.0178.



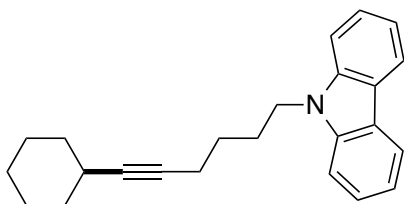
(Cyclohexylethynyl)trimethylsilane (2c).^[23]

(i) From Iodocyclohexane. Following the general procedure F, the title compound was prepared using iodocyclohexane (210 mg, 130 μ L 1.0 mmol) and ((trimethylsilyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes as an eluent to afford (cyclohexylethynyl)trimethylsilane (**2c**) as deep brown oil (93 mg, 0.51 mmol, 51%). **¹H NMR** (400 MHz, CDCl₃): δ 2.41-2.35 (m, 1 H), 1.82-1.76 (m, 2 H), 1.73-1.66 (m, 2 H), 1.53-1.40 (ovrlp, 3 H), 1.32-1.24 (ovrlp, 3 H), 0.14 (s, 9 H). **¹³C NMR** (100 MHz, CDCl₃): δ 112.0, 83.8, 32.8, 30.2, 26.0, 25.0, 0.4.

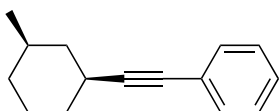
(ii) From Bromocyclohexane. Following the general procedure F, the title compound was prepared using bromocyclohexane (163 mg, 124 μ L 1.0 mmol), ((trimethylsilyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL), FeBr₂ (43 mg, 0.20 mmol), and O-TMEDA (321 mg, 381 μ L). The crude product was purified by flash chromatography using hexanes as an eluent to afford (cyclohexylethynyl)trimethylsilane (**2c**) as brown oil (86 mg, 0.48 mmol, 48%). Spectral and analytical data were identical to those reported for the same compound above.



2-((7-Cyclohexylhept-6-yn-1-yl)oxy)tetrahydro-2H-pyran (2d). Following the general procedure F, the title compound was prepared using iodocyclohexane (210 mg, 130 μ L 1.0 mmol) and 7-((tetrahydro-2H-pyran-2-yl)oxy)hept-1-yn-1-yl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (10:1) as an eluent to afford 2-((7-cyclohexylhept-6-yn-1-yl)oxy)tetrahydro-2H-pyran (**2d**) as colorless oil (186 mg, 0.67 mmol, 67%). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 4.58 (s, 1 H), 3.89-3.85 (m, 1 H), 3.77-3.71 (m, 1 H), 3.53-3.47 (m, 1 H), 3.42-3.36 (m, 1 H), 2.31 (s, 1 H), 2.17 (t, $J = 6.2$ Hz, 2 H), 1.87-1.65 (ovrlp, 6 H), 1.62-1.43 (ovrlp, 11 H), 1.40-1.25 (ovrlp, 5 H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 98.8, 84.8, 79.9, 67.5, 62.3, 33.2, 30.8, 29.4, 29.2, 29.1, 26.0, 25.6, 25.5, 25.0, 19.7, 18.8. **HRMS** (ESI): Calcd for $\text{C}_{18}\text{H}_{31}\text{O}_2$ [M+H]: 279.2324; Found: 279.2326.

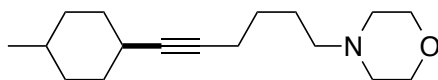


9-(6-Cyclohexylhex-5-yn-1-yl)-9H-carbazole (2e). Following the general procedure F, the title compound was prepared using iodocyclohexane (210 mg, 130 μ L 1.0 mmol) and 6-(9H-carbazol-9-yl)hex-1-yn-1-yl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes/EtOAc (50:1) as an eluent to afford 9-(6-cyclohexylhex-5-yn-1-yl)-9H-carbazole (**2e**) as viscous colorless oil (119 mg, 0.36 mmol, 36%). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 8.09 (d, $J = 7.6$ Hz, 2 H), 7.47-7.40 (ovrlp, 4 H), 7.22 (t, $J = 6.9$ Hz, 2 H), 4.32 (d, $J = 7.0$ Hz, 2 H), 2.33-2.15 (ovrlp, 3 H), 2.00 (qu, $J = 7.3$ Hz, 2 H), 1.77-1.65 (ovrlp, 4 H), 1.60-1.46 (ovrlp, 3 H), 1.39-1.20 (ovrlp, 5 H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 140.5, 125.7, 123.0, 120.4, 118.8, 108.8, 85.6, 79.2, 42.7, 33.2, 29.3, 28.0, 26.7, 26.1, 25.1, 18.6. **HRMS** (ESI): Calcd for $\text{C}_{24}\text{H}_{28}\text{N}$ [M+H]: 330.2222; Found: 330.2220.

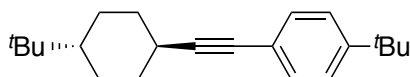


((3-Methylcyclohexyl)ethynyl)benzene (2f). Following the general procedure F, the title compound was prepared using 1-iodo-3-methylcyclohexane (**S1**) (224 mg, 1.0 mmol) and (phenylethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (50:1) as eluents to afford ((3-methylcyclohexyl)ethynyl)benzene (**2f**) as pale-yellow oil (125 mg, 0.63 mmol, 63%). The diastereomeric ratio (d.r.: cis : trans = 9.0:1) of **2f** was determined by $^1\text{H NMR}$ spectroscopy by comparing the integrations of *ipso* C-H protons of both cis- and trans-isomers.^[14] $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.41-7.37 (m, 2 H), 7.28-7.24 (ovrlp, 3 H), 2.99 (s, 0.1 H), 2.44 (t, $J = 11.4$ Hz, 0.9 H), 2.01 (d, $J = 10.4$ Hz, 2 H), 1.81-1.64 (m, 2 H), 1.40-1.23 (ovrlp, 4 H), 1.13-1.04 (m, 1 H), 0.91 (d, $J = 6.4$ Hz, 3 H). $^{13}\text{C NMR}$ (major diastereoisomer, 100 MHz, CDCl_3): δ 131.7, 128.3, 127.5, 124.2, 94.7, 80.0,

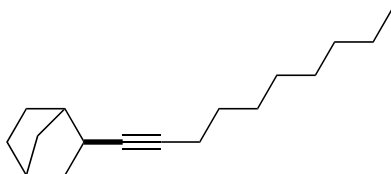
41.8, 34.6, 32.9, 32.5, 30.5, 26.0, 22.7. **HRMS** (APPI): Calcd for C₁₅H₁₈ [M]: 198.1404; Found: 198.1403.



4-(6-(4-Methylcyclohexyl)hex-5-yn-1-yl)morpholine (2g). Following the general procedure F, the title compound was prepared using 1-iodo-4-methylcyclohexane (**S2**) (224 mg, 1.0 mmol) and (6-morpholinohex-1-yn-1-yl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes/EtOAc (2:1) as an eluent to afford 4-(6-(4-methylcyclohexyl)hex-5-yn-1-yl)morpholine (**2g**) as colorless oil (125 mg, 0.54 mmol, 54%). The diastereomeric ratio (d.r. = 1.9:1) of **2g** was determined by GCMS analysis. The major diastereoisomer could not be determined due to the broadening and overlapping of the characteristic *ipso*-C-H proton signals by ¹H NMR spectroscopy. ¹H NMR (400 MHz, CDCl₃): δ 3.71 (br s, 4 H), 2.66 (s, 0.3 H), 2.43 (br s, 4 H), 2.37-2.32 (m, 2 H), 2.19 (qu, *J* = 6.5 Hz, 2 H), 2.09 (t, *J* = 11.5 Hz, 0.7 H), 1.89 (d, *J* = 11.8 Hz, 1 H), 1.62-1.46 (ovrlp, 8 H), 1.34-1.25 (ovrlp, 3 H), 0.92-0.85 (ovrlp, 4 H). ¹³C NMR (100 MHz, CDCl₃): δ 85.2, 84.0, 80.7, 79.2, 67.0, 58.6, 53.8, 34.6, 33.6, 32.1, 32.0, 31.0, 30.8, 29.8, 29.5, 27.2, 27.1, 26.9, 25.7, 22.6, 22.3, 18.7 (Observed complexity due to the mixture of diastereoisomers). **HRMS** (ESI): Calcd for C₁₇H₃₀NO [M+H]: 264.2327; Found: 264.2315.

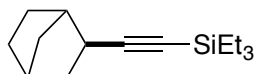


1-(tert-Butyl)-4-((4-(tert-butyl)cyclohexyl)ethynyl)benzene (2h). Following the general procedure F, the title compound was prepared using 1-(*tert*-butyl)-4-iodocyclohexane (**S3**) (266 mg, 1.0 mmol) (**S3**) and ((4-(*tert*-butyl)phenyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (50:1) as eluents to afford 1-(*tert*-butyl)-4-((4-(*tert*-butyl)cyclohexyl)ethynyl)benzene (**2h**) as off-white solid (147 mg, 0.50 mmol, 50%). The diastereomeric ratio (d.r.: trans:cis > 50:1) of **2h** was determined by ¹H NMR spectroscopy by comparing the integrations of *ipso* C-H protons of both cis- and trans-isomers.^[14] ¹H NMR (400 MHz, CDCl₃): δ 7.35-7.25 (ovrlp, 4 H), 2.32 (t, *J* = 11.8 Hz, 1 H), 2.10 (d, *J* = 11.8 Hz, 2 H), 1.82-1.77 (m, 2 H), 1.45-1.35 (m, 2 H), 1.29 (s, 9 H), 1.03-0.98 (ovrlp, 3 H), 0.85 (s, 9 H). ¹³C NMR (major diastereoisomer, 100 MHz, CDCl₃): δ 150.6, 131.4, 125.2, 121.2, 94.1, 80.1, 47.5, 34.8, 33.9, 32.6, 31.3, 30.6, 27.6, 27.1. **HRMS** (APPI): Calcd for C₂₂H₃₂ [M]: 296.2506; Found: 296.2499.

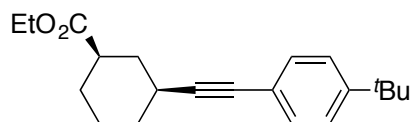


2-(Dec-1-yn-1-yl)bicyclo[2.2.1]heptane (2i). Following the general procedure F, the title compound was prepared using 2-iodobicyclo[2.2.1]heptane (**S4**) (222 mg, 1.0 mmol) and dec-1-yn-1-ylmagnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (100:1) as eluents to afford 2-(dec-1-yn-1-yl)bicyclo[2.2.1]heptane (**2i**) as brown oil (163.3 mg, 0.70 mmol, 70%). The diastereomeric ratio of **2i**

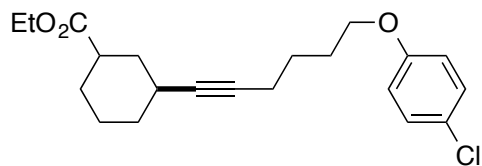
was not determined due to the overlapping of signals in both ^1H NMR spectroscopy and GCMS analysis. ^1H NMR (400 MHz, CDCl_3): δ 2.60-2.11 (ovrlp, 5 H), 1.91-1.58 (m, 2 H), 1.51-1.42 (ovrlp, 4 H), 1.35-1.11 (ovrlp, 14 H), 0.88 (t, $J = 6.0$ Hz, 3 H). ^{13}C NMR (major diastereoisomer, 100 MHz, CDCl_3): δ 86.0, 79.9, 43.9, 39.8, 36.6, 36.3, 33.2, 32.0, 29.4, 29.3, 29.0, 24.1, 22.8, 18.9, 14.2. HRMS (ESI): Calcd for $\text{C}_{17}\text{H}_{28}\text{Ag}$ [$\text{M}+\text{Ag}$]: 339.1242; Found: 339.1255.



((Bicyclo[2.2.1]heptan-2-yl)ethynyl)triethylsilane (2j). Following the general procedure F, the title compound was prepared using 2-iodobicyclo[2.2.1]heptane (**S4**) (222 mg, 1.0 mmol) and ((triethylsilyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes as an eluent to afford ((bicyclo[2.2.1]heptan-2-yl)ethynyl)triethylsilane (**2j**) as brown oil (183 mg, 0.78 mmol, 78%). The diastereomeric ratio (d.r. = 2.8:1) of **2j** was estimated by ^1H NMR spectroscopy and the ratio was found to be comparable to that estimated from the ^{13}C NMR spectroscopy. (Note: The major diastereoisomer could not be determined due to the overlapping of characteristic *ipso* C-H proton signals with other proton signals.) ^1H NMR (400 MHz, CDCl_3): δ 2.65-2.62 (m, 0.3 H), 2.33-2.26 (ovrlp, 2.4 H), 2.21 (s, 0.3 H), 1.95-1.54 (ovrlp, 3 H), 1.48 (s, 1 H), 1.30-1.13 (ovrlp, 4 H), 1.01-0.95 (ovrlp, 9 H), 0.62-0.52 (ovrlp, 6 H). ^{13}C NMR (major diastereoisomer, 100 MHz, CDCl_3): δ 114.6, 80.5, 44.2, 39.8, 36.7, 36.4, 34.2, 28.9, 24.2, 7.7, 4.8. HRMS (ESI): Calcd for $\text{C}_{15}\text{H}_{26}\text{SiAg}$ [$\text{M}+\text{Ag}$]: 341.0855; Found: 341.0855.

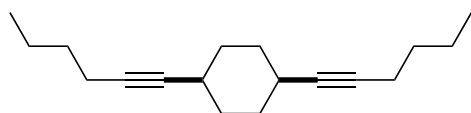


Ethyl 3-((4-(tert-butyl)phenyl)ethynyl)cyclohexane-1-carboxylate (2k). Following the general procedure F, the title compound was prepared using ethyl 3-iodocyclohexane-1-carboxylate (282 mg, 1.0 mmol) and ((4-(tert-butyl)phenyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes/EtOAc (30:1) as an eluent to afford ethyl 3-((4-(tert-butyl)phenyl)ethynyl)cyclohexane-1-carboxylate (**2k**) as viscous, deep-brown oil (284 mg, 0.91 mmol, 91%). The diastereomeric ratio (d.r.: cis:trans = 6.5:1) of **2k** was determined by ^1H NMR spectroscopy by comparing the integrations of *ipso* C-H protons of both cis- and trans-isomers.^[14] ^1H NMR (400 MHz, CDCl_3): δ 7.36-7.25 (m, 4 H), 4.13 (q, $J = 7.0$ Hz, 2 H), 3.05-2.24 (m, 3 H), 2.09-1.53 (ovrlp, 5 H), 1.45-1.38 (m, 2 H), 1.29 (s, 9 H), 1.25 (t, $J = 7.2$ Hz, 3 H). ^{13}C NMR (major diastereoisomer, 100 MHz, CDCl_3): δ 175.3, 150.9, 131.4, 125.3, 120.8, 92.6, 80.7, 60.4, 43.0, 35.2, 34.8, 32.6, 31.3, 29.8, 28.3, 25.1, 14.4. HRMS (ESI): Calcd for $\text{C}_{21}\text{H}_{29}\text{O}_2$ [$\text{M}+\text{H}$]: 313.2168; Found: 313.2163.

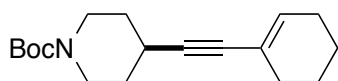


Ethyl 3-(6-(4-chlorophenoxy)hex-1-yn-1-yl)cyclohexane-1-carboxylate (2l). Following the general

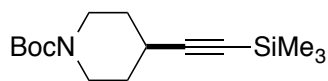
procedure F, the title compound was prepared using ethyl 3-iodocyclohexane-1-carboxylate (282 mg, 1.0 mmol) and (6-(4-chlorophenoxy)hex-1-yn-1-yl)magnesium bromide (synthesized from **S19**, 0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes/EtOAc (30:1) as an eluent to afford ethyl 3-(6-(4-chlorophenoxy)hex-1-yn-1-yl)cyclohexane-1-carboxylate (**2l**) as pale-yellow oil (158 mg, 0.44 mmol, 44%). The diastereomeric ratio (d.r. = 1.9:1) of **2l** was determined by GCMS analysis. (Note: The major diastereoisomer could not be determined by ^1H NMR spectroscopy due to the overlapping of characteristic *ipso* C-H proton signals with other proton signals.) ^1H NMR (400 MHz, CDCl_3): δ 7.21 (d, $J = 8.6$ Hz, 2 H), 6.81 (d, $J = 8.4$ Hz, 2 H), 4.11 (q, $J = 6.7$ Hz, 2 H), 3.94 (d, $J = 5.8$ Hz, 2 H), 2.80-2.16 (ovrlp, 4 H), 1.90-1.80 (ovrlp, 5 H), 1.72-1.50 (ovrlp, 4 H), 1.47-1.39 (m, 1 H), 1.35-1.22 (ovrlp, 5 H). ^{13}C NMR (major diastereoisomer, 100 MHz, CDCl_3): δ 175.3, 157.7, 129.3, 125.4, 115.9, 84.4, 79.7, 67.8, 60.3, 43.0, 35.6, 32.9, 29.3, 28.35, 28.31, 25.6, 25.1, 18.5, 14.3. HRMS (ESI): Calcd for $\text{C}_{21}\text{H}_{27}\text{ClO}_3\text{Ag}$ [$\text{M}+\text{Ag}$]: 469.0700; Found: 469.0710.



1,4-Di(hex-1-yn-1-yl)cyclohexane (2m). Following the general procedure F, the title compound was prepared using 1,4-diiodocyclohexane (**S5**) (336 mg, 1.0 mmol) and hex-1-yn-1-ylmagnesium bromide (0.5 M in THF, 3.0 mmol, 6.0 mL). The crude product was purified by flash chromatography using hexanes/EtOAc (100:1) and then hexanes/EtOAc (50:1) as eluents to afford 1,4-di(hex-1-yn-1-yl)cyclohexane (**2m**) as deep-brown oil (195 mg, 0.80 mmol, 80%). The diastereomeric ratio (d.r. = 2.2:1) of **2m** was determined by GCMS analysis. (Note: The major diastereoisomer could not be determined by ^1H NMR spectroscopy due to the broadening and overlapping of characteristic *ipso* C-H proton signals.) ^1H NMR (400 MHz, CDCl_3): δ 2.41 (s, 0.7 H), 2.26 (s, 1.3 H), 2.18-2.12 (m, 4 H), 1.95-1.88 (m, 2 H), 1.77-1.71 (m, 2 H), 1.63-1.53 (m, 2 H), 1.48-1.26 (ovrlp, 10 H), 0.93-0.88 (ovrlp, 6 H). ^{13}C NMR (100 MHz, CDCl_3): δ 84.1, 83.8, 80.9, 80.3, 32.0, 31.5, 31.4, 30.1, 28.8, 28.2, 22.1, 22.0, 18.6, 18.5, 14.2, 13.7 (Observed complexity due to the mixture of diastereoisomers). HRMS (ESI): Calcd for $\text{C}_{18}\text{H}_{28}\text{Ag}$ [$\text{M}+\text{Ag}$]: 351.1242; Found: 351.1228.



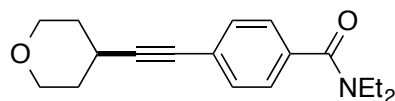
tert-Butyl 4-(cyclohex-1-en-1-ylethynyl)piperidine-1-carboxylate (2n). Following the general procedure F, the title compound was prepared using *tert*-butyl 4-iodopiperidine-1-carboxylate (311 mg, 1.0 mmol) and (cyclohex-1-en-1-ylethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (30:1) as eluents to afford *tert*-butyl 4-(cyclohex-1-en-1-ylethynyl)piperidine-1-carboxylate (**2n**) as viscous brown oil (179 mg, 0.62 mmol, 62%). ^1H NMR (400 MHz, CDCl_3): δ 6.03 (s, 1 H), 3.71-3.65 (m, 2 H), 3.23-3.18 (m, 2 H), 2.71-2.65 (m, 1 H), 2.13-2.04 (ovrlp, 4 H), 1.80-1.73 (m, 2 H), 1.64-1.54 (ovrlp, 6 H), 1.45 (s, 9 H). ^{13}C NMR (100 MHz, CDCl_3): δ 154.9, 133.8, 120.8, 89.0, 83.8, 79.5, 42.4, 31.7, 29.7, 28.6, 27.6, 25.7, 22.5, 21.7. HRMS (ESI): Calcd for $\text{C}_{18}\text{H}_{27}\text{NO}_2\text{Ag}$ [$\text{M}+\text{Ag}$]: 396.1093; Found: 396.1077.



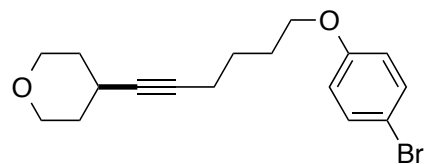
***tert*-Butyl 4-((trimethylsilyl)ethynyl)piperidine-1-carboxylate (**2o**).**

(i) With FeBr₂ (98% purity): Following the general procedure F, the title compound was prepared using *tert*-butyl 4-iodopiperidine-1-carboxylate (311 mg, 1.0 mmol) and ((trimethylsilyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (20:1) as eluents to afford *tert*-butyl 4-((trimethylsilyl)ethynyl)piperidine-1-carboxylate (**2o**) as pale-brown oil (242 mg, 0.86 mmol, 86%). ¹H NMR (400 MHz, CDCl₃): δ 3.67-3.64 (m, 2 H), 3.24-3.18 (m, 2 H), 2.63-2.57 (m, 1 H), 1.77-1.74 (m, 2 H), 1.61-1.53 (m, 2 H), 1.45 (s, 9 H), 0.15 (s, 9 H). ¹³C NMR (100 MHz, CDCl₃): δ 154.6, 108.8, 85.6, 79.2, 41.9, 31.2, 28.4, 27.7, 0.1. HRMS (ESI): Calcd for C₁₅H₂₈NO₂Si [M+H]: 282.1889; 282.1893.

(ii) With FeBr₂ (99.999% purity): Following the general procedure F, the title compound was prepared using *tert*-butyl 4-iodopiperidine-1-carboxylate (311 mg, 1.0 mmol), ((trimethylsilyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL), and FeBr₂ (99.999% purity, 22 mg, 0.10 mmol). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (20:1) as eluents to afford *tert*-butyl 4-((trimethylsilyl)ethynyl)piperidine-1-carboxylate (**2o**) as pale-brown oil (249 mg, 0.88 mmol, 88%). Spectral and analytical data were identical to those reported for the same compound above.

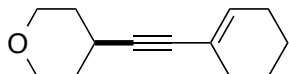


***N,N*-diethyl-4-((tetrahydro-2*H*-pyran-4-yl)ethynyl)benzamide (**2p**).** Following the general procedure F, the title compound was prepared using 4-iodotetrahydro-2*H*-pyran (212 mg, 1.0 mmol) and ((4-(diethylcarbamoyl)phenyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes/EtOAc (2:1) as an eluent to afford *N,N*-diethyl-4-((tetrahydro-2*H*-pyran-4-yl)ethynyl)benzamide (**2p**) as viscous, pale-yellow oil (110 mg, 0.39 mmol, 39%). ¹H NMR (400 MHz, CDCl₃): δ 7.43 (d, *J* = 7.6 Hz, 2 H), 7.30 (d, *J* = 7.7 Hz, 2 H), 3.98-3.92 (m, 2 H), 3.57-5.53 (ovrlp, 4 H), 3.23 (br s, 2 H), 2.88-2.82 (m, 1 H), 1.95-1.88 (m, 2 H), 1.80-1.72 (m, 2 H), 1.25 (br s, 3 H), 1.11 (br s, 3 H). ¹³C NMR (100 MHz, CDCl₃): δ 170.7, 136.5, 131.6, 126.4, 124.6, 93.6, 81.0, 66.4, 43.3, 39.4, 32.3, 26.9, 14.2, 13.0. HRMS (ESI): Calcd for C₁₈H₂₄NO₂ [M+H]: 286.1807; Found: 286.1810.

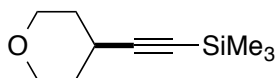


4-(6-(4-bromophenoxy)hex-1-yn-1-yl)tetrahydro-2*H*-pyran (2q**).** Following the general procedure F, the title compound was prepared using 4-iodotetrahydro-2*H*-pyran (212 mg, 1.0 mmol) and (6-(4-bromophenoxy)hex-1-yn-1-yl)magnesium bromide (synthesized from **S20**, 0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes/EtOAc (20:1) as an eluent to afford 4-(6-(4-bromophenoxy)hex-1-yn-1-yl)tetrahydro-2*H*-pyran (**2q**) as viscous, pale-yellow oil (168 mg, 0.50 mmol, 50%). ¹H NMR (400 MHz, CDCl₃): δ 7.35 (d, *J* = 8.6 Hz, 2 H), 6.76 (d, *J* = 8.6

Hz, 2 H), 3.94 (t, $J = 6.2$ Hz, 2 H), 3.90-3.85 (m, 2 H), 3.47 (t, $J = 9.0$ Hz, 2 H), 2.57 (s, 1 H), 2.25 (t, $J = 6.3$ Hz, 2 H), 1.88 (qu, $J = 6.8$ Hz, 2 H), 1.81-1.75 (m, 2 H), 1.70-1.56 (ovrlp, 4 H). ^{13}C NMR (100 MHz, CDCl_3): δ 158.1, 132.3, 116.3, 112.7, 83.3, 80.7, 67.7, 66.5, 32.7, 28.3, 26.3, 25.6, 18.5. HRMS (ESI): Calcd for $\text{C}_{17}\text{H}_{21}\text{BrO}_2\text{Ag}$ [$\text{M}+\text{Ag}$]: 444.9765; Found: 444.9771.



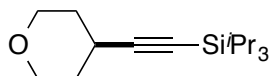
4-(Cyclohex-1-en-1-ylethynyl)tetrahydro-2H-pyran (2r). Following the general procedure F, the title compound was prepared using 4-iodotetrahydro-2H-pyran (212 mg, 1.0 mmol) and (cyclohex-1-en-1-ylethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (20:1) as eluents to afford 4-(cyclohex-1-en-1-ylethynyl)tetrahydro-2H-pyran (**2r**) as brown oil (146 mg, 0.77 mmol, 77%). ^1H NMR (400 MHz, CDCl_3): δ 6.13 (s, 1 H), 4.01-3.98 (m, 2 H), 3.61-3.57 (m, 2 H), 2.85-2.79 (m, 1 H), 2.22-2.15 (ovrlp, 4 H), 1.95-1.90 (m, 2 H), 1.79-1.67 (ovrlp, 6 H). ^{13}C NMR (100 MHz, CDCl_3): δ 133.7, 120.8, 89.3, 83.3, 66.4, 32.5, 29.6, 26.7, 25.8, 22.4, 21.6. HRMS: [M] could not be detected by HRMS (ESI) and HRMS (APPI). GCMS: [M] = 190 detected which corresponds to $\text{C}_{13}\text{H}_{18}\text{O}$; the purity was further confirmed by GCMS.



Trimethyl((tetrahydro-2H-pyran-4-yl)ethynyl)silane (2s).

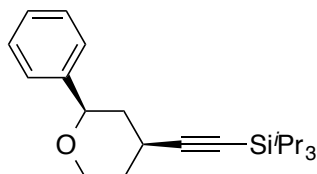
(i) With FeBr_2 (98% purity): Following the general procedure F, the title compound was prepared using 4-iodotetrahydro-2H-pyran (212 mg, 1.0 mmol) and ((trimethylsilyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (20:1) as eluents to afford trimethyl((tetrahydro-2H-pyran-4-yl)ethynyl)silane (**2s**) as brown oil (150 mg, 0.82 mmol, 82%). ^1H NMR (400 MHz, CDCl_3): δ 3.91-3.86 (m, 2 H), 3.51-3.46 (m, 2 H), 2.67-2.61 (m, 1 H), 1.85-1.78 (m, 2 H), 1.69-1.61 (m, 2 H), 0.15 (s, 9 H). ^{13}C NMR (100 MHz, CDCl_3): δ 109.4, 85.3, 66.3, 32.2, 27.2, 0.3. HRMS: [M] could not be detected by HRMS (ESI) and HRMS (APPI). GCMS: [M] = 182 detected which corresponds to $\text{C}_{10}\text{H}_{18}\text{OSi}$; the purity was further confirmed by GCMS.

(ii) With FeBr_2 (99.999% purity): Following the general procedure F, the title compound was prepared using 4-iodotetrahydro-2H-pyran (212 mg, 1.0 mmol), ((trimethylsilyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL), and FeBr_2 (99.999% purity, 22 mg, 0.10 mmol). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (20:1) as eluents to afford trimethyl((tetrahydro-2H-pyran-4-yl)ethynyl)silane (**2s**) as brown oil (147 mg, 0.81 mmol, 81%). Spectral and analytical data were identical to those reported for the same compound above.

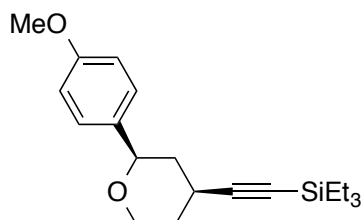


Triisopropyl((tetrahydro-2H-pyran-4-yl)ethynyl)silane (2t).^[24] Following the general procedure F, the title compound was prepared using 4-iodotetrahydro-2H-pyran (212 mg, 1.0 mmol) and ((triisopropylsilyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes/EtOAc (40:1) as an eluent to afford

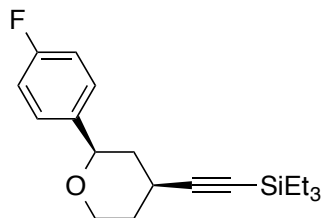
triisopropyl((tetrahydro-2*H*-pyran-4-yl)ethynyl)silane (**2t**) as pale-yellow oil (255 mg, 0.96 mmol, 96%). ¹H NMR (400 MHz, CDCl₃): δ 3.92-3.88 (m, 2 H), 3.56-3.52 (m, 2 H), 2.75-2.69 (m, 1 H), 1.87-1.82 (m, 2 H), 1.70-1.63 (m, 2 H), 1.10-1.01 (ovrlp, 21 H). ¹³C NMR (100 MHz, CDCl₃): δ 111.2, 81.4, 65.9, 32.4, 26.9, 18.7, 11.3. HRMS (ESI): Calcd for C₁₆H₃₀OSiAg [M+Ag]: 373.1117; Found: 273.1109.



Triisopropyl((2-phenyltetrahydro-2*H*-pyran-4-yl)ethynyl)silane (2u**).** Following the general procedure F, the title compound was prepared using 4-iodo-2-phenyltetrahydro-2*H*-pyran (**S8**) (288 mg, 1.0 mmol) and ((triisopropylsilyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes/EtOAc (20:1) as an eluent to afford triisopropyl((2-phenyltetrahydro-2*H*-pyran-4-yl)ethynyl)silane (**2u**) as pale-brown oil (271 mg, 0.79 mmol, 79%). The diastereomeric ratio (d.r.: cis:trans = 24.0:1) of **2u** was determined by ¹H NMR spectroscopy by comparing the integrations of *ipso* C-H protons of both cis- and trans-isomers.^[14] ¹H NMR (400 MHz, CDCl₃): δ 7.33-7.20 (ovrlp, 5 H), 4.85-4.25 (m, 1 H), 4.15-3.99 (m, 1 H), 3.55 (t, *J* = 10.8 Hz, 1 H), 3.07 (s, 0.04 H), 2.69 (t, *J* = 11.6 Hz, 0.96 H), 2.12 (d, *J* = 12.7 Hz, 1 H), 1.89 (d, *J* = 11.8 Hz, 1 H), 1.83-1.75 (m, 1 H), 1.70-1.59 (m, 1 H), 1.12-1.04 (ovrlp, 21 H). ¹³C NMR (major diastereoisomer, 100 MHz, CDCl₃): δ 142.5, 128.5, 127.6, 125.9, 111.4, 80.4, 79.3, 67.9, 40.6, 32.7, 29.0, 18.7, 11.3. HRMS (ESI): Calcd for C₂₂H₃₄OSiAg [M+Ag]: 449.1430; Found: 449.1439.



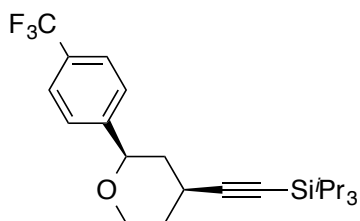
Triethyl((2-(4-methoxyphenyl)tetrahydro-2*H*-pyran-4-yl)ethynyl)silane (2v**).** Following the general procedure F, the title compound was prepared using 4-iodo-2-(4-methoxyphenyl)tetrahydro-2*H*-pyran (**S9**) (318 mg, 1.0 mmol) and ((triethylsilyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes/EtOAc (20:1) as an eluent to afford triethyl((2-(4-methoxyphenyl)tetrahydro-2*H*-pyran-4-yl)ethynyl)silane (**2v**) as brown oil (285 mg, 0.86 mmol, 86%). The diastereomeric ratio (d.r.: cis:trans = 9.4:1) of **2v** was determined by ¹H NMR spectroscopy by comparing the integrations of *ipso* C-H protons of both cis- and trans-isomers.^[14] ¹H NMR (400 MHz, CDCl₃): δ 7.18 (d, *J* = 8.2 Hz, 2 H), 6.78 (d, *J* = 8.3 Hz, 2 H), 4.69-4.12 (m, 1 H), 4.05-3.87 (m, 1 H), 3.69 (s, 3 H), 3.84 (t, *J* = 11.5 Hz, 1 H), 2.98 (s, 0.1 H), 2.59 (t, *J* = 11.8 Hz, 0.9 H), 2.00 (t, *J* = 12.7 Hz, 1 H), 1.80 (t, *J* = 12.7 Hz, 1 H), 1.73-1.66 (m, 1 H), 1.63-1.54 (m, 1 H), 0.98-0.87 (ovrlp, 9 H), 0.58-0.45 (ovrlp, 6 H). ¹³C NMR (major diastereoisomer, 100 MHz, CDCl₃): δ 159.1, 134.7, 127.2, 113.8, 110.9, 81.6, 78.9, 67.9, 55.3, 40.3, 32.6, 28.9, 7.55, 4.61. HRMS (ESI): Calcd for C₂₀H₃₁O₂Si [M+H]: 331.2093; Found: 331.2084.



Triethyl((2-(4-fluorophenyl)tetrahydro-2H-pyran-4-yl)ethynyl)silane (2w).

(i) With FeBr₂ (98% purity): Following the general procedure F, the title compound was prepared using 2-(4-fluorophenyl)-4-iodotetrahydro-2H-pyran (**S10**) (306 mg, 1.0 mmol) and ((triethylsilyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes/EtOAc (20:1) as an eluent to afford triethyl((2-(4-fluorophenyl)tetrahydro-2H-pyran-4-yl)ethynyl)silane (**2w**) as brown oil (295 mg, 0.93 mmol, 93%). The diastereomeric ratio (d.r.: cis:trans = 9.1:1) of **2w** was estimated by ¹H NMR spectroscopy by comparing the integrations of *ipso* C-H protons of both cis- and trans-isomers.^[14] **¹H NMR** (400 MHz, CDCl₃): δ 7.30 (dd, ³J_{HH} = 7.6 Hz, ⁴J_{HF} = 5.8 Hz, 2 H), 7.01 (dd, ³J_{HH} = 8.3 Hz, ³J_{HF} = 8.3 Hz, 2 H), 4.80-4.23 (m, 1 H), 4.14-3.98 (m, 1 H), 3.55 (t, *J* = 11.7 Hz, 1 H), 3.07 (s, 0.1 H), 2.69 (t, *J* = 11.8 Hz, 0.9 H), 2.09 (d, *J* = 13.0 Hz, 1 H), 1.89 (d, *J* = 12.0 Hz, 1 H), 1.81-1.74 (m 1 H), 1.72-1.58 (m, 1 H), 1.06-0.95 (m, 9 H), 0.66-0.53 (m, 6 H). **¹³C NMR** (major diastereoisomer, 100 MHz, CDCl₃): δ 162.3 (d, ¹J_{CF} = 243.9 Hz), 138.2 (d, ⁴J_{CF} = 3.0 Hz), 127.6 (d, ³J_{CF} = 8.0 Hz), 115.3 (d, ²J_{CF} = 21.2 Hz), 110.6, 81.8, 78.6, 67.9, 40.4, 32.5, 28.9, 7.6, 4.6. **HRMS** (ESI): Calcd for C₁₉H₂₇FOSiAg [M+Ag]: 425.0866; Found: 425.0861.

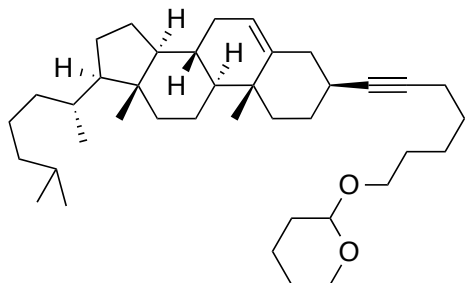
(ii) With FeBr₂ (99.999% purity): Following the general procedure F, the title compound was prepared using 2-(4-fluorophenyl)-4-iodotetrahydro-2H-pyran (**S10**) (306 mg, 1.0 mmol), ((triethylsilyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL), and FeBr₂ (99.999% purity, 22 mg, 0.10 mmol). The crude product was purified by flash chromatography using hexanes/EtOAc (20:1) as an eluent to afford triethyl((2-(4-fluorophenyl)tetrahydro-2H-pyran-4-yl)ethynyl)silane (**2w**) as brown oil (305 mg, 0.96 mmol, 96%). The diastereomeric ratio (d.r.: cis:trans = 9:1) of **2w** was estimated by ¹H NMR spectroscopy by comparing the integrations of *ipso* C-H protons of both cis- and trans-isomers.^[14] Spectral and analytical data were identical to those reported for the same compound above.



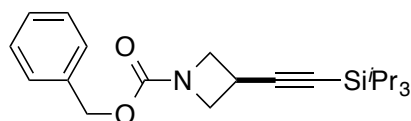
Triisopropyl((2-(4-(trifluoromethyl)phenyl)tetrahydro-2H-pyran-4-yl)ethynyl)silane (2x).

Following the general procedure F, the title compound was prepared using 4-iodo-2-(4-(trifluoromethyl)phenyl)tetrahydro-2H-pyran (**S11**) (356 mg, 1.0 mmol) and ((triisopropylsilyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes/EtOAc (20:1) as an eluent to afford triisopropyl((2-(4-(trifluoromethyl)phenyl)tetrahydro-2H-pyran-4-yl)ethynyl)silane (**2x**) as pale-brown oil (358 mg, 0.87 mmol, 87%). The diastereomeric ratio (d.r.: cis:trans = 24.0:1) of **2x** was determined by ¹H NMR

spectroscopy by comparing the integrations of *ipso* C-H protons of both *cis*- and *trans*-isomers.^[14] **¹H NMR** (400 MHz, CDCl₃): δ 7.59 (d, *J* = 7.6 Hz, 2 H), 7.45 (d, *J* = 7.4 Hz, 2 H), 4.90 (d, *J* = 11.0 Hz, 0.06 H), 4.34 (d, *J* = 11.1 Hz, 0.94 H), 4.16 (d, *J* = 8.7 Hz, 1 H), 4.05 (t, *J* = 11.6 Hz, 0.06 H), 3.57 (t, *J* = 11.8 Hz, 0.94 H), 3.10 (s, 0.06 H), 2.72 (t, *J* = 11.6 Hz, 0.94 H), 2.14 (d, *J* = 12.8 Hz, 1 H), 1.93 (d, *J* = 12.4 Hz, 1 H), 1.84-1.72 (m, 1 H), 1.65-1.55 (m, 1 H), 1.12-1.01 (ovrlp, 21 H). **¹³C NMR** (major diastereoisomer, 100 MHz, CDCl₃): δ 146.5, 129.8 (q, ²*J*_{CF} = 32.2 Hz), 126.1, 125.4 (q, ³*J*_{CF} = 3.6 Hz), 124.3 (q, ¹*J*_{CF} = 270.3 Hz), 110.9, 80.7, 78.5, 67.9, 40.6, 32.8, 28.9, 18.7, 11.3. **HRMS** (ESI): Calcd for C₂₃H₃₄F₃OSi [M+H]: 411.2331; Found: 411.2350.

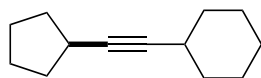


2-((7-((3*S*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl)hept-6-yn-1-yl)oxy)tetrahydro-2*H*-pyran (2y). Following the general procedure F, the title compound was prepared using 3β-iodo-5-cholestene (497 mg, 1.0 mmol) and (7-((tetrahydro-2*H*-pyran-2-yl)oxy)hept-1-yn-1-yl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (10:1) as eluents to afford 2-((7-((3*S*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl)hept-6-yn-1-yl)oxy)tetrahydro-2*H*-pyran (2y) as an off-white, low-melting solid (284 mg, 0.50 mmol, 50%). The diastereomeric ratio (d.r.: major : minor = 7.0:1) of 2y was determined by ¹H NMR spectroscopy by comparing the integrations of olefinic protons of both major and minor isomers. The major isomer was determined by comparing the chemical shift of olefinic C-H proton and *ipso* C-H proton of the major isomer with that of structurally similar and well-defined compound.^[5] **¹H NMR** (400 MHz, CDCl₃): δ 5.30 (s, 0.9 H), 4.96 (s, 0.1 H), 4.58 (s, 1 H), 3.89-3.84 (m, 1 H), 3.77-3.71 (m, 1 H), 3.51-3.49 (m, 1 H), 3.42-3.36 (m, 1 H), 2.77 (s, 0.1 H), 2.46-2.11 (ovrlp, 4.9 H), 2.02-1.26 (ovrlp, 34 H), 1.16-1.07 (ovrlp, 4 H), 0.99 (s, 3 H), 0.91 (d, *J* = 5.6 Hz, 3 H), 0.86 (d, *J* = 5.6 Hz, 6 H), 0.67 (s, 3 H). **¹³C NMR** (major diastereoisomer, 100 MHz, CDCl₃): δ 141.8, 120.6, 98.8, 84.6, 80.0, 67.5, 67.4, 62.3, 56.9, 56.2, 50.3, 42.4, 39.9, 39.7, 39.6, 39.1, 36.8, 36.3, 35.9, 31.92, 31.87, 31.3, 30.8, 29.8, 29.4, 29.1, 28.3, 28.1, 25.61, 25.59, 24.4, 23.9, 22.9, 22.7, 20.9, 19.7, 19.4, 18.8, 11.9. **HRMS** (ESI): Calcd for C₃₉H₆₄O₂Na [M+Na]: 587.4804; Found: 587.4796.

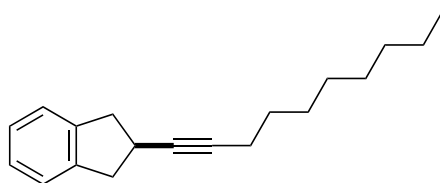


Benzyl 3-((triisopropylsilyl)ethynyl)azetidine-1-carboxylate (3a). Following the general procedure F, the title compound was prepared using benzyl 3-iodoazetidine-1-carboxylate (**S12**) (317 mg, 1.0 mmol) and ((triisopropylsilyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude

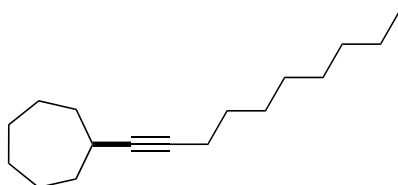
product was purified by flash chromatography using hexanes and then hexanes/EtOAc (20:1) as eluents to afford benzyl 3-((triisopropylsilyl)ethynyl)azetidine-1-carboxylate (**3a**) as pale-brown oil (372 mg, 0.85 mmol, 85%). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.39-7.31 (ovrlp, 5 H), 5.10 (s, 2 H), 4.23 (t, $J = 8.2$ Hz, 2 H), 4.00 (t, $J = 7.2$ Hz, 2 H), 3.41 (qu, $J = 6.6$ Hz, 1 H), 1.11-1.00 (ovrlp, 21 H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 156.1, 136.5, 128.5, 128.1, 128.0, 107.6, 84.5, 66.8, 56.0, 20.6, 18.6, 11.2. **HRMS** (ESI): Calcd for $\text{C}_{22}\text{H}_{34}\text{NO}_2\text{Si}$ [$\text{M}+\text{H}$]: 372.2359; Found: 372.2361.



(Cyclopentylethynyl)cyclohexane (3b). Following the general procedure F, the title compound was prepared using bromocyclopentane (149 mg, 1.0 mmol), (cyclohexylethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL), FeBr_2 (43 mg, 0.20 mmol), and O-TMEDA (321 mg, 381 μL). The crude product was purified by flash chromatography using hexanes as an eluent to afford (cyclopentylethynyl)cyclohexane (**3b**) as pale-yellow oil (123 mg, 0.70 mmol, 70%). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 2.61-2.54 (m, 1 H), 2.32 (s, 1 H), 1.91-1.83 (m, 2 H), 1.79-1.68 (ovrlp, 6 H), 1.58-1.49 (ovrlp, 4 H), 1.42-1.35 (m, 2 H), 1.29-1.26 (ovrlp, 4 H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 84.6, 84.2, 34.4, 33.4, 30.5, 29.3, 26.2, 25.1, 25.0. **HRMS**: [M] could not be detected by HRMS (ESI and APPI). **GCMS**: [M] = 176 detected which corresponds to $\text{C}_{13}\text{H}_{20}$; the purity was further confirmed by GCMS.

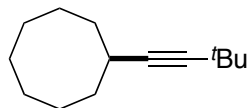


2-(Dec-1-yn-1-yl)-2,3-dihydro-1H-indene (3c). Following the general procedure F, the title compound was prepared using 2-iodo-2,3-dihydro-1H-indene (244 mg, 1.0 mmol) and dec-1-yn-1-ylmagnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (100:1) as eluents to afford 2-(dec-1-yn-1-yl)-2,3-dihydro-1H-indene (**3c**) as pale-brown oil (161 mg, 0.63 mmol, 63%). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.17-7.09 (ovrlp, 4 H), 3.20-3.12 (ovrlp, 3 H), 2.99-2.93 (m, 2 H), 2.15 (t, $J = 6.5$ Hz, 2 H), 1.47 (qu, $J = 6.5$ Hz, 2 H), 1.37-1.20 (ovrlp, 10 H), 0.88 (t, $J = 6.7$ Hz, 3 H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 142.4, 126.5, 124.4, 83.3, 80.6, 40.8, 32.0, 30.6, 29.4, 29.3, 29.2, 29.0, 22.8, 18.9, 14.3. **HRMS** (ESI): Calcd for $\text{C}_{19}\text{H}_{26}\text{Ag}$ [$\text{M}+\text{Ag}$]: 361.1086; Found: 361.1095.

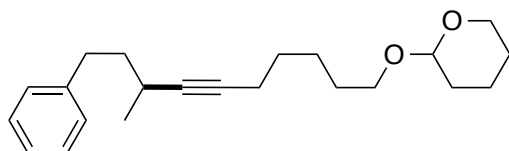


Dec-1-yn-1-ylcycloheptane (3d).^[25] Following the general procedure F, the title compound was prepared using iodocycloheptane (224 mg, 1.0 mmol) and dec-1-yn-1-ylmagnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes as an eluent to afford dec-1-yn-1-ylcycloheptane (**3d**) as pale-brown oil (152 mg, 0.65 mmol, 65%). $^1\text{H NMR}$

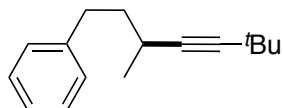
(400 MHz, CDCl₃): δ 2.55 (s, 1 H), 2.15 (t, J = 6.4 Hz, 2 H), 1.83-1.76 (m, 2 H), 1.71-1.60 (ovrlp, 4 H), 1.60-1.44 (ovrlp, 8 H), 1.36-1.23 (ovrlp, 10 H), 0.88 (t, J = 6.5 Hz, 3 H). ¹³C NMR (100 MHz, CDCl₃): δ 85.4, 80.5, 35.3, 32.0, 31.4, 29.42, 29.39, 29.3, 29.0, 28.0, 25.7, 22.8, 18.9, 14.2.



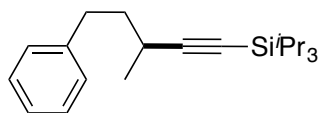
(3,3-Dimethylbut-1-yn-1-yl)cyclooctane (3e). Following the general procedure F, the title compound was prepared using iodocyclooctane (238 mg, 1.0 mmol) and (3,3-dimethylbut-1-yn-1-yl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes as an eluent to afford (3,3-dimethylbut-1-yn-1-yl)cyclooctane (**3e**) as yellow oil (152 mg, 0.65 mmol, 65%). ¹H NMR (400 MHz, CDCl₃): δ 2.52 (s, 1 H), 1.83-1.69 (ovrlp, 4 H), 1.65-1.43 (ovrlp, 10 H), 1.19 (s, 9 H). ¹³C NMR (100 MHz, CDCl₃): δ 89.1, 83.8, 32.4, 31.7, 30.8, 30.2, 27.6, 25.6, 24.6. HRMS (APPI): Calcd for C₁₄H₂₄ [M]: 192.1829; Found: 192.1873.



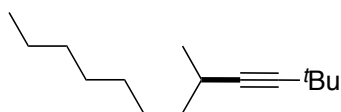
2-((8-Methyl-10-phenyldec-6-yn-1-yl)oxy)tetrahydro-2H-pyran (3f). Following the general procedure F, the title compound was prepared using (3-iodobutyl)benzene (260 mg, 1.0 mmol) and (7-((tetrahydro-2H-pyran-2-yl)oxy)hept-1-yn-1-yl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (15:1) as eluents to afford 2-((8-methyl-10-phenyldec-6-yn-1-yl)oxy)tetrahydro-2H-pyran (**3f**) as pale-yellow oil (202 mg, 0.62 mmol, 62%). ¹H NMR (400 MHz, CDCl₃): δ 7.27 (t, J = 7.2 Hz, 2 H), 7.20-7.15 (ovrlp, 3 H), 4.57 (s, 1 H), 3.86 (t, J = 7.5 Hz, 1 H), 3.75 (q, J = 6.8 Hz, 1 H), 3.51-3.46 (m, 1 H), 3.39 (q, J = 6.2 Hz, 1 H), 2.84-2.77 (m, 1 H), 2.72-2.65 (m, 1 H), 2.39 (sex, J = 6.2 Hz, 1 H), 2.21 (t, J = 6.0 Hz, 2 H), 1.85-1.61 (ovrlp, 6 H), 1.58-1.48 (ovrlp, 8 H), 1.15 (d, J = 6.7 Hz, 3 H). ¹³C NMR (100 MHz, CDCl₃): δ 142.4, 128.6, 128.3, 125.8, 98.9, 84.6, 80.8, 67.6, 62.4, 39.2, 33.8, 30.8, 29.4, 29.1, 25.62, 25.59, 21.6, 19.7, 18.8. HRMS (ESI): Calcd for C₂₂H₃₃O₂ [M+H]: 329.2480; Found: 329.2470.



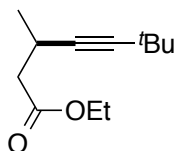
(3,6,6-Trimethylhept-4-yn-1-yl)benzene (3g). Following the general procedure F, the title compound was prepared using (3-iodobutyl)benzene (260 mg, 1.0 mmol) and (3,3-dimethylbut-1-yn-1-yl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (50:1) as eluents to afford (3,6,6-trimethylhept-4-yn-1-yl)benzene (**3g**) as colorless oil (115 mg, 0.54 mmol, 54%). ¹H NMR (400 MHz, CDCl₃): δ 7.27 (t, J = 7.3 Hz, 1 H), 7.21-7.15 (ovrlp, 3 H), 2.83-2.76 (m, 1 H), 2.73-2.65 (m, 1 H), 2.37 (sex, J = 6.9 Hz, 1 H), 1.70-1.64 (m, 2 H), 1.22 (s, 9 H), 1.13 (d, J = 6.8 Hz, 3 H). ¹³C NMR (100 MHz, CDCl₃): δ 142.6, 128.7, 128.4, 125.8, 89.9, 82.7, 39.4, 33.9, 31.7, 27.5, 25.5, 21.7. HRMS (ESI): Calcd for C₁₆H₂₂Ag [M+Ag]: 321.0772; Found: 321.0779.



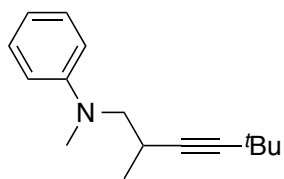
Triisopropyl(3-methyl-5-phenylpent-1-yn-1-yl)silane (3h).^{126l} Following the general procedure F, the title compound was prepared using (3-iodobutyl)benzene (260 mg, 1.0 mmol) and ((triisopropylsilyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (50:1) as eluents to afford triisopropyl(3-methyl-5-phenylpent-1-yn-1-yl)silane (**3h**) as pale-yellow oil (278 mg, 0.88 mmol, 88%). **¹H NMR** (400 MHz, CDCl₃): δ 7.27 (t, *J* = 7.2 Hz, 2 H), 7.21-7.16 (ovrlp, 3 H), 2.89-2.83 (m, 1 H), 2.77-2.70 (m, 1 H), 2.46 (sex, *J* = 6.9 Hz, 1 H), 1.72 (q, *J* = 7.4 Hz, 2 H), 1.19 (d, *J* = 6.7 Hz, 3 H), 1.11-1.06 (ovrlp, 21 H). **¹³C NMR** (100 MHz, CDCl₃): δ 142.4, 128.7, 128.5, 125.9, 113.5, 80.5, 39.2, 33.9, 26.7, 21.5, 18.8, 11.4. **HRMS** (ESI): Calcd for C₂₁H₃₄SiAg [M+Ag]: 421.1481; Found: 421.1487.



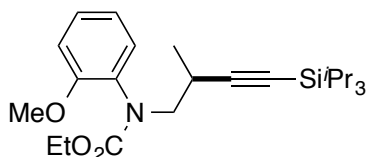
2,2,5-Trimethyldodec-3-yne (3i). Following the general procedure F, the title compound was prepared using 2-iodononane (**S7**) (254 mg, 1.0 mmol) and (3,3-dimethylbut-1-yn-1-yl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (50:1) as eluents to afford 2,2,5-trimethyldodec-3-yne (**3i**) as yellow oil (153 mg, 0.73 mmol, 73%). **¹H NMR** (400 MHz, CDCl₃): δ 2.35 (sex, *J* = Hz, 1 H), 1.43-1.23 (ovrlp, 12 H), 1.19 (s, 9 H), 1.10 (d, *J* = 6.8 Hz, 3 H), 0.89 (t, *J* = 6.6 Hz, 3 H). **¹³C NMR** (100 MHz, CDCl₃): δ 89.1, 83.3, 37.6, 32.0, 31.7, 30.8, 29.6, 29.5, 27.5, 25.9, 22.9, 21.8, 14.3. **HRMS** (ESI): Calcd for C₁₅H₂₈ [M+Ag]: 208.2143; Found: 208.2141.



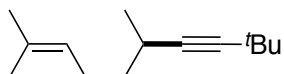
Ethyl 3,6,6-trimethylhept-4-ynoate (3j). Following the general procedure F, the title compound was prepared using ethyl 3-iodobutanoate (**S13**) (242 mg, 1.0 mmol) and (3,3-dimethylbut-1-yn-1-yl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (50:1) as eluents to afford ethyl 3,6,6-trimethylhept-4-ynoate (**3j**) as brown oil (106 mg, 0.54 mmol, 54%). **¹H NMR** (400 MHz, CDCl₃): δ 4.15 (q, *J* = 7.1 Hz, 2 H), 2.90 (sex, *J* = 7.0 Hz, 1 H), 2.49-2.44 (m, 1 H), 2.37-2.32 (m, 1 H), 1.27 (t, *J* = 7.1 Hz, 3 H), 1.18-1.17 (ovrlp, 12 H). **¹³C NMR** (100 MHz, CDCl₃): δ 171.9, 89.6, 81.3, 60.4, 42.5, 31.4, 27.3, 23.0, 21.3, 14.4. **HRMS** (ESI): Calcd for C₁₂H₂₁O₂ [M+H]: 197.1542; Found: 197.1535.



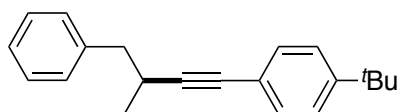
***N*-methyl-*N*-(2,5,5-trimethylhex-3-yn-1-yl)aniline (3k).** Following the general procedure F, the title compound was prepared using *N*-(2-iodopropyl)-*N*-methylaniline (**S23**) (275 mg, 1.0 mmol) and (3,3-dimethylbut-1-yn-1-yl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (20:1) as eluents to afford *N*-methyl-*N*-(2,5,5-trimethylhex-3-yn-1-yl)aniline (**3k**) as brown oil (180 mg, 0.78 mmol, 78%). ¹H NMR (400 MHz, CDCl₃): δ 7.21 (t, *J* = 7.7 Hz, 2 H), 6.68-6.64 (ovrlp, 3 H), 3.40-3.35 (m, 1 H), 3.31-3.26 (m, 1 H), 3.01 (s, 3 H), 2.80 (sex, *J* = 7.0 Hz, 1 H), 1.16 (s, 9 H), 1.12 (d, *J* = 7.0 Hz, 3 H). ¹³C NMR (100 MHz, CDCl₃): δ 149.1, 129.2, 115.9, 111.8, 90.1, 81.4, 59.3, 39.6, 31.4, 27.4, 25.1, 19.3. GCMS: [M] = 275 detected which corresponds to C₁₆H₂₃N; the purity was further confirmed by GCMS.



Ethyl (2-Methoxyphenyl)(2-methyl-4-(triisopropylsilyl)but-3-yn-1-yl)carbamate (3l). Following the general procedure F, the title compound was prepared using ethyl (2-bromopropyl)(2-methoxyphenyl)carbamate (**S24**) (158 mg, 0.50 mmol), ((triisopropylsilyl)ethynyl)magnesium bromide (0.5 M in THF, 0.75 mmol, 1.5 mL), FeBr₂ (22 mg, 0.10 mmol), O-TMEDA (160 mg, 191 μL), and NMP (2.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (10:1) as eluents to afford ethyl (2-methoxyphenyl)(2-methyl-4-(triisopropylsilyl)but-3-yn-1-yl)carbamate (**3l**) as pale yellow oil (181 mg, 0.43 mmol, 87%). ¹H NMR (400 MHz, CDCl₃): δ 7.31-7.22 (ovrlp, 2 H), 6.95-6.90 (ovrlp, 2 H), 4.24-3.94 (ovrlp, 3 H), 3.81 (s, 3 H), 3.45-3.23 (m, 1 H), 2.83-2.55 (m, 1 H), 1.22 (t, *J* = 8.6 Hz, 3 H), 1.12-1.04 (ovrlp, 24 H). ¹³C NMR (100 MHz, CDCl₃): δ 156.6, 155.6, 130.7, 130.2, 130.0, 128.8, 128.6, 120.8, 120.6, 120.4, 112.1, 111.6, 111.4, 81.2, 61.7, 61.5, 55.7, 55.5, 55.0, 54.4, 54.2, 29.8, 26.9, 26.7, 26.6, 18.7, 14.7, 11.3 (observed complexity due to the mixture of 2 rotamers). GCMS: [M] = 417 detected which corresponds to C₂₄H₃₉NO₃Si; the purity was further confirmed by GCMS.



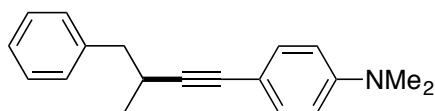
2,6,9,9-Tetramethyldec-2-en-7-yne (3m). Following the general procedure F, the title compound was prepared using 6-iodo-2-methylhept-2-ene (238 mg, 1.0 mmol) and (3,3-dimethylbut-1-yn-1-yl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes as an eluent to afford 2,6,9,9-tetramethyldec-2-en-7-yne (**3m**) as pale yellow oil (138 mg, 0.72 mmol, 72%). ¹H NMR (400 MHz, CDCl₃): δ 5.12 (s, 1 H), 2.37 (sex, *J* = 6.9 Hz, 1 H), 2.16-2.05 (m, 2 H), 1.69 (s, 3 H), 1.63 (s, 3 H), 1.38 (q, *J* = 6.4 Hz, 2 H), 1.19 (s, 9 H), 1.10 (d, *J* = 6.8 Hz, 3 H). ¹³C NMR (100 MHz, CDCl₃): δ 131.8, 124.5, 89.3, 83.1, 37.8, 31.7, 30.8, 26.1, 25.9, 25.5, 21.7, 17.8. HRMS (APPI): Calcd for C₁₄H₂₄ [M]: 192.1874; Found: 192.1873.



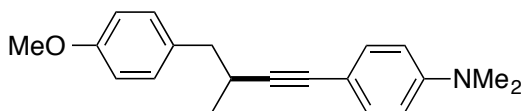
1-(*tert*-Butyl)-4-(3-methyl-4-phenylbut-1-yn-1-yl)benzene (3n).

From (2-iodopropyl)benzene: Following the general procedure F, the title compound was prepared using (2-iodopropyl)benzene (**S6**) (246 mg, 1.0 mmol) and ((4-(*tert*-butyl)phenyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (50:1) as eluents to afford 1-(*tert*-butyl)-4-(3-methyl-4-phenylbut-1-yn-1-yl)benzene (**3n**) as viscous, deep-brown oil (264 mg, 0.95 mmol, 95%). ¹H NMR (400 MHz, CDCl₃): δ 7.30-7.16 (ovrlp, 9 H), 2.87 (d, *J* = 8.2 Hz, 2 H), 2.79-2.70 (m, 1 H), 1.27 (s, 9 H), 1.23 (d, *J* = 5.8 Hz, 3 H). ¹³C NMR (100 MHz, CDCl₃): δ 150.7, 139.8, 131.3, 129.5, 128.2, 126.4, 125.2, 121.1, 93.4, 81.7, 43.4, 34.7, 31.3, 28.7, 20.8. HRMS (ESI): Calcd for C₂₁H₂₄Ag [M+Ag]: 383.0929; Found: 383.0921.

From (2-bromopropyl)benzene: Following the general procedure F, the title compound was prepared using (2-bromopropyl)benzene (199 mg, 1.0 mmol), ((4-(*tert*-butyl)phenyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL), FeBr₂ (43 mg, 0.20 mmol), and O-TMEDA (321 mg, 381 μL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (50:1) as eluents to afford 1-(*tert*-butyl)-4-(3-methyl-4-phenylbut-1-yn-1-yl)benzene (**3i**) as deep-brown oil (229 mg, 0.83 mmol, 83%). Spectral and analytical data were identical to those reported for the same compound above.

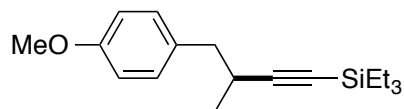


***N,N*-dimethyl-4-(3-methyl-4-phenylbut-1-yn-1-yl)aniline (3o).** Following the general procedure F, the title compound was prepared using (2-iodopropyl)benzene (**S6**) (123 mg, 0.50 mmol), FeBr₂ (11 mg, 0.050 mmol), ((4-(dimethylamino)phenyl)ethynyl)magnesium bromide (0.5 M in THF, 0.75 mmol, 1.5 mL), and NMP (2.0 mL). The crude product was purified by flash chromatography using hexanes/EtOAc (10:1) as an eluent to afford *N,N*-dimethyl-4-(3-methyl-4-phenylbut-1-yn-1-yl)aniline (**3o**) as viscous, pale-yellow oil (86 mg, 0.33 mmol, 65%). ¹H NMR (400 MHz, CDCl₃): δ 7.32-7.19 (ovrlp, 7 H), 6.59 (d, *J* = 8.4 Hz, 2 H), 2.93-2.84 (ovrlp, 8 H), 2.78-2.71 (m, 1 H), 1.23 (d, *J* = 6.0 Hz, 3 H). ¹³C NMR (100 MHz, CDCl₃): δ 149.8, 140.0, 132.6, 129.5, 128.2, 126.3, 112.0, 111.1, 91.6, 82.1, 43.5, 40.4, 28.8, 20.9. HRMS (ESI): Calcd for C₁₉H₂₂N [M+H]: 264.1752; Found: 264.1742.

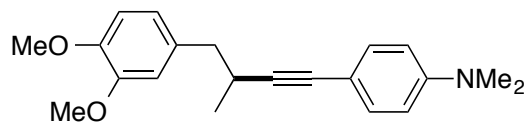


4-(4-(4-methoxyphenyl)-3-methylbut-1-yn-1-yl)-*N,N*-dimethylaniline (3p). Following the general procedure F, the title compound was prepared using 1-(2-iodopropyl)-4-methoxybenzene (**S21**) (138 mg, 0.50 mmol), FeBr₂ (11 mg, 0.050 mmol), ((4-(dimethylamino)phenyl)ethynyl)magnesium bromide (0.5 M in THF, 0.75 mmol, 1.5 mL), and NMP (2.0 mL). The crude product was purified by flash chromatography using hexanes/EtOAc (10:1) as an eluent to afford 4-(4-(4-methoxyphenyl)-3-methylbut-1-yn-1-yl)-*N,N*-dimethylaniline (**3p**) as viscous, pale-yellow oil (72 mg, 0.25 mmol, 50%).

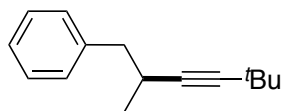
¹H NMR (400 MHz, CDCl₃): 7.24 (d, *J* = 8.2 Hz, 2 H), 7.19 (d, *J* = 8.0 Hz, 2 H), 6.84 (d, *J* = 8.1 Hz, 2 H), 6.60 (d, *J* = 8.3 Hz, 2 H), 3.78 (s, 3 H), 2.93 (s, 6 H), 2.86-2.80 (ovrlp, 2 H), 2.72-2.66 (m, 1 H), 1.22 (d, *J* = 5.8 Hz, 3 H). **¹³C NMR** (100 MHz, CDCl₃): δ 158.1, 149.8, 132.6, 132.1, 130.4, 113.6, 112.0, 111.2, 91.7, 82.1, 55.3, 42.6, 40.4, 29.0, 20.8. **HRMS** (ESI): Calcd for C₂₀H₂₄NO [M+H]: 294.1858; Found: 294.1853.



Triethyl(4-(4-methoxyphenyl)-3-methylbut-1-yn-1-yl)silane (3q). Following the general procedure F, the title compound was prepared using 1-(2-iodopropyl)-4-methoxybenzene (**S21**) (276 mg, 1.0 mmol) and ((triethylsilyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes/EtOAc (20:1) as an eluent to afford triethyl(4-(4-methoxyphenyl)-3-methylbut-1-yn-1-yl)silane (**3q**) as deep-brown oil (271 mg, 0.94 mmol, 94%). **¹H NMR** (400 MHz, CDCl₃): 7.13 (d, *J* = 7.6 Hz, 2 H), 6.81 (d, *J* = 7.6 Hz, 2 H), 3.77 (s, 3 H), 2.76-2.60 (ovrlp, 3 H), 1.15 (d, *J* = 5.2 Hz, 3 H), 0.96 (t, *J* = 7.4 Hz, 9 H), 0.55 (q, *J* = 7.6 Hz, 6 H). **¹³C NMR** (100 MHz, CDCl₃): δ 158.2, 131.8, 130.4, 113.5, 112.7, 82.1, 55.3, 42.3, 29.3, 20.7, 7.58, 4.65. **HRMS** (ESI): Calcd for C₁₈H₂₈OSiAg [M+H]: 395.0960; Found: 395.0968.

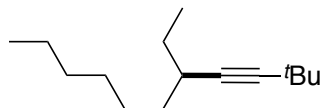


4-(4-(3,4-dimethoxyphenyl)-3-methylbut-1-yn-1-yl)-N,N-dimethylaniline (3r). Following the general procedure F, the title compound was prepared using 4-(2-iodopropyl)-1,2-dimethoxybenzene (**S22**) (153 mg, 0.50 mmol), FeBr₂ (11 mg, 0.050 mmol), ((4-(dimethylamino)phenyl)ethynyl)magnesium bromide (0.5 M in THF, 0.75 mmol, 1.5 mL), and NMP (2.0 mL). The crude product was purified by flash chromatography using hexanes/EtOAc (10:1) as an eluent to afford 4-(4-(3,4-dimethoxyphenyl)-3-methylbut-1-yn-1-yl)-N,N-dimethylaniline (**3r**) as viscous yellow oil (82 mg, 0.25 mmol, 51%). **¹H NMR** (400 MHz, CDCl₃): 7.23 (d, *J* = 8.4 Hz, 2 H), 6.86 (s, 1 H), 6.79 (ovrlp s, 2 H), 6.59 (d, *J* = 8.5 Hz, 2 H), 3.85 (s, 3 H), 3.83 (s, 3 H), 2.93 (s, 6 H), 2.88-2.80 (ovrlp, 2 H), 2.76-2.67 (m, 1 H), 1.24 (d, *J* = 6.2 Hz, 3 H). **¹³C NMR** (100 MHz, CDCl₃): δ 149.7, 148.5, 147.5, 132.6, 132.5, 121.3, 112.7, 111.9, 111.0, 110.9, 91.7, 82.3, 55.9, 55.8, 43.0, 40.4, 29.0, 20.9. **HRMS** (ESI): Calcd for C₂₁H₂₆NO₂ [M+H]: 324.1964; Found: 324.1968.

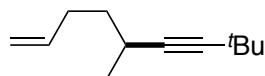


(2-Ethyl-5,5-dimethylhex-3-yn-1-yl)benzene (3s). Following the general procedure F, the title compound was prepared using (2-iodobutyl)benzene (260 mg, 1.0 mmol) and (3,3-dimethylbut-1-yn-1-yl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (50:1) as eluents to afford (2-ethyl-5,5-dimethylhex-3-yn-1-yl)benzene (**3s**) as pale-yellow oil (169 mg, 0.79 mmol, 79%). **¹H NMR** (400 MHz, CDCl₃): δ 7.28-7.16 (ovrlp, 5 H), 2.75-2.65 (m, 2 H), 2.46 (qu, *J* = 5.5 Hz, 1 H), 1.54-1.43 (m, 1 H),

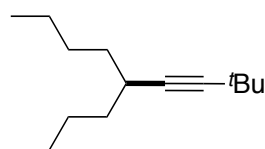
1.40-1.31 (m, 1 H), 1.16 (s, 9 H), 0.99 (t, $J = 7.2$ Hz, 3 H). ^{13}C NMR (100 MHz, CDCl_3): δ 140.3, 129.6, 128.0, 126.1, 91.3, 81.4, 41.7, 35.5, 31.5, 27.9, 27.5, 11.8. HRMS (APPI): Calcd for $\text{C}_{16}\text{H}_{22}$ [M]: 214.1723; Found: 214.1716.



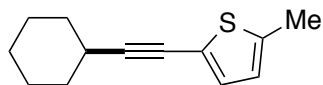
5-Ethyl-2,2-dimethylundec-3-yne (3t). Following the general procedure F, the title compound was prepared using 3-iodononane (254 mg, 1.0 mmol), (3,3-dimethylbut-1-yn-1-yl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL), FeBr_2 (43 mg, 0.20 mmol), and O-TMEDA (321 mg, 381 μL). The crude product was purified by flash chromatography using hexanes as an eluent to afford 5-ethyl-2,2-dimethylundec-3-yne (**3t**) as yellow oil (141 mg, 0.68 mmol, 68%). ^1H NMR (400 MHz, CDCl_3): δ 2.18 (qu, $J = 6.6$ Hz, 1 H), 1.48-1.41 (m, 2 H), 1.39-1.25 (ovrlp, 10 H), 1.19 (s, 9 H), 0.96 (t, $J = 7.3$ Hz, 3 H), 0.89 (t, $J = 6.8$ Hz, 3 H). ^{13}C NMR (100 MHz, CDCl_3): δ 90.3, 81.9, 35.3, 33.4, 32.0, 31.7, 30.5, 29.4, 28.6, 27.5, 22.8, 14.3, 11.9. HRMS (ESI): Calcd for $\text{C}_{15}\text{H}_{28}\text{Ag}$ [M+Ag]: 315.1242; Found: 315.1248.



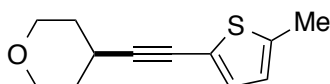
5-Ethyl-8,8-dimethylnon-1-en-6-yne (3u). Following the general procedure F, the title compound was prepared using 5-iodohept-1-ene (224 mg, 1.0 mmol), (3,3-dimethylbut-1-yn-1-yl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL), FeBr_2 (43 mg, 0.20 mmol), and O-TMEDA (321 mg, 381 μL). The crude product was purified by flash chromatography using hexanes as an eluent to afford 5-ethyl-8,8-dimethylnon-1-en-6-yne (**3u**) as volatile, pale-yellow oil (84 mg, 0.47 mmol, 47%). ^1H NMR (400 MHz, CDCl_3): δ 5.88-5.78 (m, 1 H), 5.03 (d, $J = 17.0$ Hz, 1 H), 4.95 (d, $J = 10.0$ Hz, 1 H), 2.24-2.08 (ovrlp, 3 H), 1.50-1.42 (m, 2 H), 1.29-1.23 (m, 2 H), 1.20 (s, 9 H), 0.97 (t, $J = 7.3$ Hz, 3 H). ^{13}C NMR (100 MHz, CDCl_3): δ 139.0, 114.6, 90.8, 81.3, 34.5, 32.9, 31.9, 31.7, 30.8, 28.5, 11.9. HRMS (APPI): Calcd for $\text{C}_{13}\text{H}_{22}$ [M]: 178.1715; Found: 178.1716.



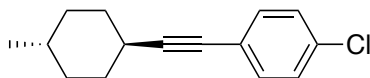
5-Butyl-2,2-dimethylnon-3-yne (3v). Following the general procedure F, the title compound was prepared using 5-iodononane (254 mg, 1.0 mmol), (3,3-dimethylbut-1-yn-1-yl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL), FeBr_2 (43 mg, 0.20 mmol), and O-TMEDA (321 mg, 381 μL). The crude product was purified by flash chromatography using hexanes as an eluent to afford 5-butyl-2,2-dimethylnon-3-yne (**3v**) as volatile, pale-brown oil (152 mg, 0.73 mmol, 73%). ^1H NMR (400 MHz, CDCl_3): δ 2.23 (s, 1 H), 1.47-1.26 (ovrlp, 12 H), 1.19 (s, 9 H), 0.90 (t, $J = 6.4$ Hz, 6 H). ^{13}C NMR (100 MHz, CDCl_3): δ 90.1, 82.2, 35.4, 31.70, 31.65, 29.8, 27.5, 22.8, 14.3. HRMS (ESI): Calcd for $\text{C}_{15}\text{H}_{28}\text{Ag}$ [M+Ag]: 315.1242; Found: 315.1260.



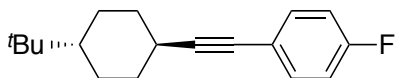
2-(Cyclohexylethynyl)-5-methylthiophene (P1). Following the general procedure F, the title compound was prepared using iodocyclohexane (210 mg, 130 μ L, 1.0 mmol) and ((5-methylthiophen-2-yl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes as an eluent to afford ethyl 2-(cyclohexylethynyl)-5-methylthiophene (**P1**) as pale-brown oil (64 mg, 0.31 mmol, 31%). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 6.90 (d, $J = 3.0$ Hz, 1 H), 6.57 (d, $J = 3.0$ Hz, 1 H), 2.60-2.54 (m, 1 H), 2.43 (s, 3 H), 1.87-1.85 (m, 2 H), 1.77-1.70 (m, 2 H), 1.57-1.47 (ovrlp, 3 H), 1.37-1.29 (ovrlp, 3 H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 140.5, 131.1, 125.0, 121.9, 97.6, 74.0, 32.7, 30.1, 26.0, 25.1, 15.5. **HRMS** (APPI): Calcd for $\text{C}_{13}\text{H}_{16}\text{S}$ [M]: 204.0967; Found: 204.0967.



4-((5-Methylthiophen-2-yl)ethynyl)tetrahydro-2H-pyran (P2). Following the general procedure F, the title compound was prepared using 4-iodotetrahydro-2H-pyran (212 mg, 1.0 mmol) and ((5-methylthiophen-2-yl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes as an eluent to afford 4-((5-methylthiophen-2-yl)ethynyl)tetrahydro-2H-pyran (**P2**) as brown oil (59 mg, 0.29 mmol, 29%). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 6.93 (d, $J = 3.0$ Hz, 1 H), 6.59 (d, $J = 2.8$ Hz, 1 H), 3.96-3.91 (m, 2 H), 3.53 (t, $J = 8.8$ Hz, 2 H), 2.87-2.81 (m, 1 H), 2.33 (s, 3 H), 1.92-1.85 (m, 2 H), 1.78-1.69 (m, 2 H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 141.0, 131.5, 125.1, 121.3, 95.3, 75.0, 66.5, 32.2, 27.2, 15.4. **HRMS** (ESI): Calcd for $\text{C}_{12}\text{H}_{15}\text{OS}$ [M+Ag]: 207.0844; Found: 207.0861.

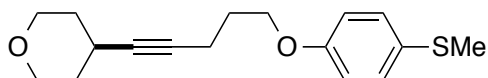


1-Chloro-4-((-4-methylcyclohexyl)ethynyl)benzene (P3). Following the general procedure F, the title compound was prepared using 1-iodo-4-methylcyclohexane (**S2**) (224 mg, 1.0 mmol) and ((4-chlorophenyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (50:1) as eluents to afford 1-chloro-4-((-4-methylcyclohexyl)ethynyl)benzene (**P3**) as an off-white solid (85 mg, 0.37 mmol, 37%). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.34-7.29 (ovrlp, 2 H), 7.26-7.22 (ovrlp, 2 H), 2.90 (s, 0.1 H), 2.35 (t, $J = 11.8$ Hz, 0.9 H), 2.02 (d, $J = 11.8$ Hz, 2 H), 1.85-1.71 (m, 2 H), 1.59-1.36 (ovrlp, 4 H), 0.99-0.88 (ovrlp, 4 H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 133.4, 132.9, 128.6, 122.7, 95.8, 79.1, 34.6, 33.1, 32.0, 30.1, 22.7. **HRMS**: [M] could not be detected by HRMS (ESI). **GCMS**: [M] = 232 detected which corresponds to $\text{C}_{15}\text{H}_{17}^{35}\text{Cl}$; The purity was further confirmed by GCMS.

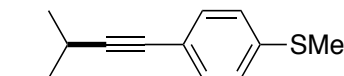


1-((-4-tert-Butyl)cyclohexyl)ethynyl)-4-fluorobenzene (P4). Following the general procedure F, the title compound was prepared using 1-iodo-4-(tert-butyl)cyclohexane (**S3**) (266 mg, 1.0 mmol) and ((4-fluorophenyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was

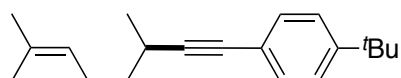
purified by flash chromatography using hexanes as an eluent to afford 1-((4-(*tert*-butyl)cyclohexyl)ethynyl)-4-fluorobenzene (**P4**) as a low-melting, off-white solid (82 mg, 0.32 mmol, 32%). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.36 (dd, $^3J_{\text{HH}} = 7.6$ Hz, $^4J_{\text{HF}} = 5.7$ Hz, 2 H), 6.96 (dd, $^3J_{\text{HH}} = 8.5$ Hz, $^3J_{\text{HF}} = 8.5$ Hz, 2 H), 2.32 (t, $J = 12.0$ Hz, 1 H), 2.09 (d, $J = 12.7$ Hz, 2 H), 1.83-1.78 (m, 2 H), 1.45-1.35 (m, 2 H), 1.03-0.98 (ovrlp, 3 H), 0.85 (s, 9 H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 162.1 (d, $^1J_{\text{CF}} = 246.7$ Hz), 133.5 (d, $^3J_{\text{CF}} = 8.0$ Hz), 120.2 (d, $^4J_{\text{CF}} = 2.9$ Hz), 115.4 (d, $^2J_{\text{CF}} = 21.8$ Hz), 94.4, 79.1, 47.5, 33.8, 32.6, 30.5, 27.6, 27.0. **HRMS** (APPI): Calcd for $\text{C}_{18}\text{H}_{23}\text{F}$ [M]: 258.1780; Found: 258.1778.



4-(5-(4-(Methylthio)phenoxy)pent-1-yn-1-yl)tetrahydro-2H-pyran (P5). Following the general procedure F, the title compound was prepared using 4-iodotetrahydro-2H-pyran (212 mg, 1.0 mmol) and (5-(4-(methylthio)phenoxy)pent-1-yn-1-yl)magnesium bromide (synthesized from (**S20**), 0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (50:1) as eluents to afford 4-(5-(4-(methylthio)phenoxy)pent-1-yn-1-yl)tetrahydro-2H-pyran (**P5**) as an off-white solid (110 mg, 0.38 mmol, 38%). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.18 (d, $J = 8.4$ Hz, 2 H), 6.77 (d, $J = 8.4$ Hz, 2 H), 3.96 (t, $J = 6.1$ Hz, 2 H), 3.82-3.77 (m, 2 H), 3.39 (t, $J = 9.0$ Hz, 2 H), 2.50 (s, 1 H), 2.36 (s, 3 H), 2.30 (t, $J = 6.3$ Hz, 2 H), 1.88 (qu, $J = 6.4$ Hz, 2 H), 1.74-1.67 (m, 2 H), 1.57-1.49 (m, 2 H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 157.7, 130.3, 128.9, 115.4, 83.5, 80.1, 66.7, 66.5, 32.8, 28.8, 26.4, 18.2, 15.6. **HRMS** (ESI): Calcd for $\text{C}_{17}\text{H}_{23}\text{O}_2\text{S}$ [M+H]: 291.1419; Found: 291.1422.

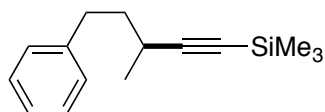


Methyl(4-(3-methylpent-1-yn-1-yl)phenyl)sulfane (P6). Following the general procedure F, the title compound was prepared using 2-iodobutane (184 mg, 1.0 mmol) and ((4-(methylthio)phenyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (50:1) as eluents to afford methyl(4-(3-methylpent-1-yn-1-yl)phenyl)sulfane (**P6**) as yellow oil (77 mg, 0.38 mmol, 38%). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.30 (d, $J = 7.8$ Hz, 2 H), 7.14 (d, $J = 7.8$ Hz, 2 H), 2.57 (sex, $J = 6.6$ Hz, 1 H), 2.46 (s, 3 H), 1.53 (sex, $J = 6.4$ Hz, 2 H), 1.23 (d, $J = 6.8$ Hz, 3 H), 1.04 (t, $J = 7.1$ Hz, 3 H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 138.1, 132.0, 126.2, 120.8, 94.8, 80.6, 30.1, 28.3, 20.8, 15.8, 11.9. **HRMS** (APPI): Calcd for $\text{C}_{13}\text{H}_{17}\text{S}$ [M+H]: 205.1001 Found: 205.1001.

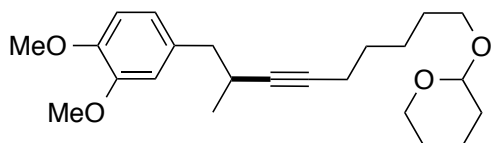


1-(*tert*-Butyl)-4-(3,7-dimethyloct-6-en-1-yn-1-yl)benzene (P7). Following the general procedure F, the title compound was prepared using 6-iodo-2-methylhept-2-ene (184 mg, 1.0 mmol) and ((4-(*tert*-butyl)phenyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes as an eluent to afford 1-(*tert*-butyl)-4-(3,7-dimethyloct-6-en-1-yn-1-yl)benzene (**P7**) as pale-yellow oil (121 mg, 0.45 mmol, 45%). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.33-7.27 (m, 4 H), 5.14 (s, 1 H), 2.63 (sex, $J = 6.4$ Hz, 1 H), 2.21-2.15 (m, 2 H), 1.70 (s, 3 H), 1.65 (s, 3 H), 1.58-1.48 (m, 2 H), 1.29 (s, 9 H), 1.24 (d, $J = 6.7$ Hz, 3 H). $^{13}\text{C NMR}$ (100 MHz,

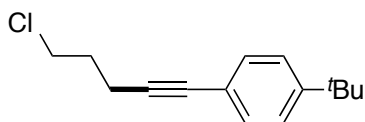
CDCl₃): δ 150.7, 132.1, 131.4, 125.3, 124.2, 121.3, 94.1, 81.0, 37.4, 34.8, 31.4, 26.23, 26.16, 25.9, 21.3, 17.9. **HRMS** (APPI): Calcd for C₂₀H₂₈ [M]: 268.2186; Found: 268.2186.



Trimethyl(3-methyl-5-phenylpent-1-yn-1-yl)silane (P8).^[27] Following the general procedure F, the title compound was prepared using (3-iodobutyl)benzene (260 mg, 1.0 mmol) and ((trimethylsilyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes as an eluent to afford trimethyl(3-methyl-5-phenylpent-1-yn-1-yl)silane (**P8**) as viscous, deep-brown oil (65 mg, 0.28 mmol, 28%). **¹H NMR** (400 MHz, CDCl₃): δ 7.28 (t, J = 7.2 Hz, 2 H), 7.22-7.16 (ovrlp, 3 H), 2.84-2.77 (m, 1 H), 2.74-2.67 (m, 1 H), 2.44 (sex, J = 7.0 Hz, 1 H), 1.79-1.65 (m, 2 H), 1.18 (d, J = 6.8 Hz, 3 H), 0.17 (s, 9 H). **¹³C NMR** (100 MHz, CDCl₃): δ 142.2, 128.6, 128.5, 125.9, 111.7, 84.9, 38.8, 33.8, 26.5, 21.1, 0.44.



2-((9-(3,4-dimethoxyphenyl)-8-methylnon-6-yn-1-yl)oxy)tetrahydro-2H-pyran (P9). Following the general procedure F, the title compound was prepared using 4-(2-iodopropyl)-1,2-dimethoxybenzene (**S22**) (306 mg, 1.0 mmol) and ((4-(dimethylamino)phenyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes/EtOAc (10:1) and then hexanes/EtOAc (6:1) as eluents to afford 2-(((*S*)-9-(3,4-dimethoxyphenyl)-8-methylnon-6-yn-1-yl)oxy)tetrahydro-2H-pyran (**P9**) as viscous, pale-yellow oil (109 mg, 0.29 mmol, 29%). **¹H NMR** (400 MHz, CDCl₃): δ 6.79-6.73 (ovrlp, 3 H), 4.57 (s, 1 H), 3.86 (s, 3 H), 3.85 (s, 3 H), 3.76-3.70 (m, 1 H), 3.52-3.47 (m, 1 H), 3.40-3.35 (m, 1 H), 2.72 (sex, J = 6.2 Hz, 1 H), 2.68-2.56 (ovrlp, 2 H), 2.15 (t, J = 6.0 Hz, 2 H), 1.86-1.79 (m, 1 H), 1.73-1.68 (m, 1 H), 1.63-1.40 (ovrlp, 11 H), 1.13 (d, J = 5.7 Hz, 3 H). **¹³C NMR** (100 MHz, CDCl₃): δ 148.4, 147.3, 132.5, 121.2, 112.4, 110.8, 98.8, 84.4, 80.9, 67.4, 62.2, 55.8, 55.7, 43.1, 30.7, 29.3, 28.9, 28.1, 25.5, 25.4, 20.9, 19.6, 18.7. **GCMS**: [M] = 374 detected which corresponds to C₂₃H₃₄O₄.

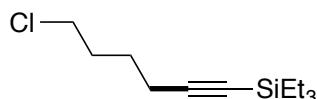


1-(*tert*-Butyl)-4-(5-chloropent-1-yn-1-yl)benzene (4a).

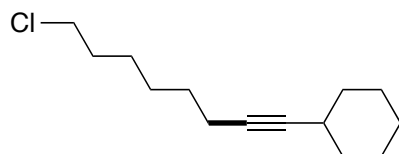
(i) From 1-chloro-3-iodopropane. Following the general procedure G, the title compound was prepared using 1-chloro-3-iodopropane (204 mg, 1.0 mmol), ((4-(*tert*-butyl)phenyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL), and FeBr₂ (22 mg, 0.10 mmol). The crude product was purified by flash chromatography using hexanes/EtOAc (20:1) as an eluent to afford 1-(*tert*-butyl)-4-(5-chloropent-1-yn-1-yl)benzene (**4a**) as deep-brown oil (205 mg, 0.88 mmol, 88%). **¹H NMR** (400 MHz, CDCl₃): δ

7.34-7.29 (ovrlp, 4 H), 3.69 (t, $J = 6.2$ Hz, 2 H), 2.58 (t, $J = 6.6$ Hz, 2 H), 2.03 (qu, $J = 6.5$ Hz, 2 H), 1.29 (s, 9 H). ^{13}C NMR (100 MHz, CDCl_3): δ 151.1, 131.4, 125.3, 120.7, 87.4, 81.7, 43.9, 34.8, 31.7, 31.3, 17.0. HRMS (APPI): Calcd for $\text{C}_{15}\text{H}_{19}\text{Cl}$ [M]: 234.1174; Found: 234.1170.

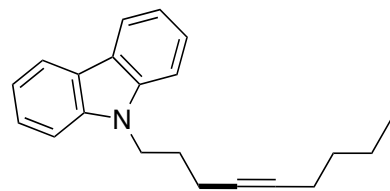
(ii) **From 1-bromo-3-chloropropane.** Following the general procedure G, the title compound was prepared using 1-bromo-3-chloropropane (204 mg, 1.0 mmol) and ((4-(*tert*-butyl)phenyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes/EtOAc (20:1) as an eluent to afford 1-(*tert*-butyl)-4-(5-chloropent-1-yn-1-yl)benzene (**4a**) as deep-brown oil (212 mg, 0.90 mmol, 90%). Spectral and analytical data were identical to those reported for the same compound above.



(6-Chlorohex-1-yn-1-yl)triethylsilane (4b). Following the general procedure G, the title compound was prepared using 1-bromo-4-chlorobutane (172 mg, 1.0 mmol) and ((triethylsilyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and hexanes/EtOAc (50:1) as eluents to afford (6-chlorohex-1-yn-1-yl)triethylsilane (**4b**) as brown oil (183 mg, 0.79 mmol, 79%). ^1H NMR (400 MHz, CDCl_3): δ 3.57 (d, $J = 6.5$ Hz, 2 H), 2.29 (d, $J = 6.8$ Hz, 2 H), 1.91 (qu, $J = 7.0$ Hz, 2 H), 1.68 (d, $J = 7.2$ Hz, 2 H), 0.98 (t, $J = 7.8$ Hz, 9 H), 0.57 (q, $J = 7.9$ Hz, 6 H). ^{13}C NMR (100 MHz, CDCl_3): δ 107.6, 82.4, 44.6, 31.6, 26.0, 19.3, 7.6, 4.7. HRMS (ESI): Calcd for $\text{C}_{12}\text{H}_{23}\text{ClSiAg}$ [M+Ag]: 337.0309; Found: 337.0312.

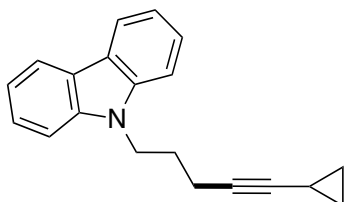


(8-chlorooct-1-yn-1-yl)cyclohexane (4c). Following the general procedure G, the title compound was prepared using 1-bromo-6-chlorohexane (200 mg, 1.0 mmol) and (cyclohexylethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and hexanes/EtOAc (50:1) as eluents to afford (8-chlorooct-1-yn-1-yl)cyclohexane (**4c**) as brown oil (143 mg, 0.63 mmol, 63%). ^1H NMR (400 MHz, CDCl_3): δ 3.53 (t, $J = 6.6$ Hz, 2 H), 2.32 (s, 1 H), 2.17 (t, $J = 6.3$ Hz, 2 H), 1.78-1.69 (ovrlp, 8 H), 1.51-1.38 (ovrlp, 7 H), 1.30-1.26 (ovrlp, 3 H). ^{13}C NMR (100 MHz, CDCl_3): δ 85.0, 79.9, 45.2, 33.3, 32.7, 29.3, 29.1, 28.1, 26.5, 26.1, 25.1, 18.8. HRMS (ESI): Calcd for $\text{C}_{14}\text{H}_{23}\text{ClAg}$ [M+Ag]: 333.0539; Found: 333.0545.

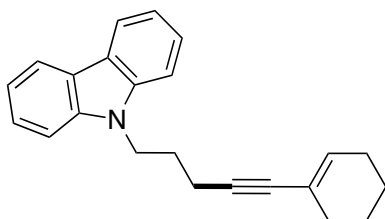


9-(non-4-yn-1-yl)-9H-carbazole (4d). Following the general procedure G, the title compound was prepared using 9-(3-iodopropyl)-9H-carbazole (**S14**) (335 mg, 1.0 mmol), hex-1-yn-1-ylmagnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL), and FeBr_2 (22 mg, 0.10 mmol). The crude product was

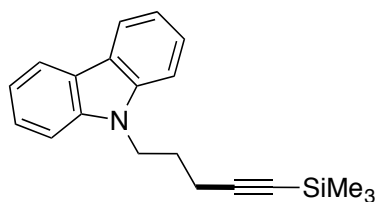
purified by flash chromatography using hexanes and then hexanes/EtOAc (100:1) as eluents to afford 9-(non-4-yn-1-yl)-9*H*-carbazole (**4d**) as brown oil (169 mg, 0.59 mmol, 59%). ¹H NMR (400 MHz, CDCl₃): δ 8.06 (d, *J* = 7.3 Hz, 2 H), 7.44-7.37 (ovrlp, 4 H), 7.22-7.16 (m, 2 H), 4.35 (t, *J* = 6.3 Hz, 2 H), 2.23-2.13 (ovrlp, 4 H), 1.97 (qu, *J* = 6.3 Hz, 2 H), 1.56-1.41 (ovrlp, 4 H), 0.94 (t, *J* = 6.6 Hz, 3 H). ¹³C NMR (100 MHz, CDCl₃): δ 140.6, 125.7, 123.0, 120.4, 118.9, 108.8, 81.6, 79.1, 41.7, 31.3, 28.4, 22.1, 18.6, 16.7, 13.8. HRMS (ESI): Calcd for C₂₁H₂₄N [M+H]: 290.1909; Found: 290.1901.



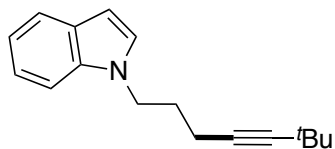
9-(5-Cyclopropylpent-4-yn-1-yl)-9*H*-carbazole (4e**)**. Following the general procedure G, the title compound was prepared using 9-(3-iodopropyl)-9*H*-carbazole (**S14**) (335 mg, 1.0 mmol) and (cyclopropylethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (100:1) as eluents to afford 9-(5-cyclopropylpent-4-yn-1-yl)-9*H*-carbazole (**4e**) as brown oil (116 mg, 0.42 mmol, 42%). ¹H NMR (400 MHz, CDCl₃): δ 8.06 (d, *J* = 7.5 Hz, 2 H), 7.45-7.39 (ovrlp, 4 H), 7.23-7.17 (m, 2 H), 4.36 (t, *J* = 6.6 Hz, 2 H), 2.12 (t, *J* = 5.8 Hz, 2 H), 1.98 (qu, *J* = 6.5 Hz, 2 H), 1.29-1.22 (m, 1 H), 0.76-0.70 (m, 2 H), 0.68-0.64 (m, 2 H). ¹³C NMR (100 MHz, CDCl₃): δ 140.6, 125.7, 123.0, 120.4, 119.0, 108.8, 84.6, 74.5, 41.7, 28.3, 16.6, 8.1, -0.3. HRMS (ESI): Calcd for C₂₀H₂₀N [M+H]: 274.1596; Found: 274.1598.



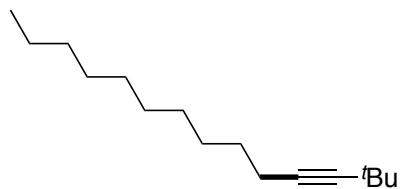
9-(5-(Cyclohex-1-en-1-yl)pent-4-yn-1-yl)-9*H*-carbazole (4f**)**. Following the general procedure G, the title compound was prepared using 9-(3-iodopropyl)-9*H*-carbazole (**S14**) (335 mg, 1.0 mmol), (cyclohex-1-en-1-ylethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL), and FeBr₂ (22 mg, 0.10 mmol). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (200:1) as eluents to afford 9-(5-(cyclohex-1-en-1-yl)pent-4-yn-1-yl)-9*H*-carbazole (**4f**) as viscous brown oil (188 mg, 0.60 mmol, 60%). ¹H NMR (400 MHz, CDCl₃): δ 8.07 (d, *J* = 7.6 Hz, 2 H), 7.47-7.41 (ovrlp, 4 H), 7.21 (t, *J* = 6.5 Hz, 2 H), 6.10 (s, 1 H), 4.41 (t, *J* = 6.6 Hz, 2 H), 2.30 (t, *J* = 6.3 Hz, 2 H), 2.19-2.15 (m, 2 H), 2.11-2.02 (ovrlp, 4 H), 1.68-1.56 (ovrlp, 4 H). ¹³C NMR (100 MHz, CDCl₃): δ 140.6, 133.9, 125.7, 123.0, 121.0, 120.4, 119.0, 108.8, 86.1, 83.7, 41.7, 29.7, 28.2, 25.7, 22.5, 21.7, 17.2. HRMS (ESI): Calcd for C₂₃H₂₄N [M+H]: 314.1909; Found: 314.1921.



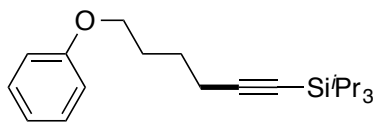
9-(5-(Trimethylsilyl)pent-4-yn-1-yl)-9H-carbazole (4g). Following the general procedure G, the title compound was prepared using 9-(3-iodopropyl)-9H-carbazole (**S14**) (335 mg, 1.0 mmol), ((trimethylsilyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL), and FeBr₂ (22 mg, 0.10 mmol). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (200:1) as eluents to afford 9-(5-(trimethylsilyl)pent-4-yn-1-yl)-9H-carbazole (**4g**) as viscous brown oil (158 mg, 0.52 mmol, 52%). ¹H NMR (400 MHz, CDCl₃): δ 8.09 (d, *J* = 7.5 Hz, 2 H), 7.47-7.42 (ovrlp, 4 H), 7.22 (t, *J* = 6.6 Hz, 2 H), 4.42 (t, *J* = 6.4 Hz, 2 H), 2.23 (t, *J* = 6.1 Hz, 2 H), 2.05 (qu, *J* = 6.3 Hz, 2 H), 0.23 (s, 9 H). ¹³C NMR (100 MHz, CDCl₃): δ 140.6, 125.7, 123.0, 120.5, 119.0, 108.8, 106.4, 86.1, 41.6, 27.8, 17.7, 0.3. HRMS (ESI): Calcd for C₂₀H₂₄NSi [M+H]: 306.1678; Found: 306.1684.



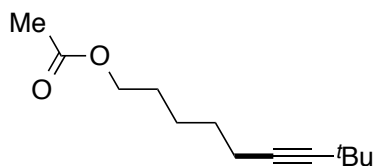
1-(6,6-Dimethylhept-4-yn-1-yl)-1H-indole (4h). Following the general procedure G, the title compound was prepared using 1-(3-iodopropyl)-1H-indole (**S15**) (285 mg, 1.0 mmol), (3,3-dimethylbut-1-yn-1-yl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL), and FeBr₂ (22 mg, 0.10 mmol). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (50:1) as eluents to afford 1-(6,6-dimethylhept-4-yn-1-yl)-1H-indole (**4h**) as brown oil (168 mg, 0.70 mmol, 70%). ¹H NMR (400 MHz, CDCl₃): δ 7.62 (d, *J* = 7.5 Hz, 1 H), 7.39 (d, *J* = 8.0 Hz, 1 H), 7.19 (t, *J* = 7.4 Hz, 1 H), 7.11-7.08 (ovrlp, 2 H), 6.48 (s, 1 H), 4.24 (t, *J* = 6.4 Hz, 2 H), 2.10 (t, *J* = 6.2 Hz, 2 H), 1.95 (qu, *J* = 6.4 Hz, 2 H), 1.25 (s, 9 H). ¹³C NMR (100 MHz, CDCl₃): δ 136.0, 128.7, 128.2, 121.4, 121.0, 119.4, 109.5, 101.1, 90.6, 77.1, 44.8, 31.5, 29.4, 27.6, 16.2. HRMS (ESI): Calcd for C₁₇H₂₂N [M+H]: 240.1752; Found: 240.1750.



2,2-Dimethyltetradec-3-yne (4i). Following the general procedure G, the title compound was prepared using 1-bromodecane (221 mg, 1.0 mmol) and (3,3-dimethylbut-1-yn-1-yl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes as an eluent to afford 2,2-dimethyltetradec-3-yne (**4i**) as pale-brown oil (150 mg, 0.68 mmol, 68%). ¹H NMR (400 MHz, CDCl₃): δ 2.12 (t, *J* = 6.9 Hz, 2 H), 1.46 (qu, *J* = 6.8 Hz, 2 H), 1.35-1.23 (ovrlp, 14 H), 1.19 (s, 9 H), 0.88 (t, *J* = 6.6 Hz, 3 H). ¹³C NMR (100 MHz, CDCl₃): δ 89.1, 78.7, 32.1, 31.6, 30.8, 29.8, 29.7, 29.5, 29.4, 29.3, 29.0, 22.9, 18.8, 14.3. HRMS (APPI): Calcd for C₁₆H₃₀ [M]: 222.2343; Found: 222.2342.



Triisopropyl(6-phenoxyhex-1-yn-1-yl)silane (4j). Following the general procedure G, the title compound was prepared using (4-bromobutoxy)benzene (229 mg, 1.0 mmol) and ((triisopropylsilyl)ethynyl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (50:1) as eluents to afford triisopropyl(6-phenoxyhex-1-yn-1-yl)silane (**4j**) as pale-yellow oil (309 mg, 0.93 mmol, 93%). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.26 (t, $J = 7.6$ Hz, 2 H), 6.93-6.87 (ovrlp, 3 H), 3.98 (t, $J = 6.0$ Hz, 2 H), 2.33 (t, $J = 6.8$ Hz, 2 H), 1.92 (q, $J = 6.8$ Hz, 2 H), 1.72 (q, $J = 7.0$ Hz, 2 H), 1.09-1.00 (ovrlp, 21 H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 159.2, 129.5, 120.7, 114.6, 108.7, 80.7, 67.3, 28.5, 25.7, 19.7, 18.8, 11.5. **HRMS** (ESI): Calcd for $\text{C}_{21}\text{H}_{34}\text{OSiAg}$ [$\text{M}+\text{Ag}$]: 437.1430; Found: 437.1339.



8,8-Dimethylnon-6-yn-1-yl acetate (4k). Following the general procedure G, the title compound was prepared using 5-iodopentyl acetate (256 mg, 1.0 mmol) and (3,3-dimethylbut-1-yn-1-yl)magnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (30:1) as eluents to afford 8,8-dimethylnon-6-yn-1-yl acetate (**4k**) as pale-yellow oil (140 mg, 0.67 mmol, 67%). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 4.00 (t, $J = 6.6$ Hz, 2 H), 2.08 (t, $J = 6.2$ Hz, 2 H), 1.97 (s, 3 H), 1.57 (qu, $J = 6.6$ Hz, 2 H), 1.47-1.35 (ovrlp, 4 H), 1.12 (s, 9 H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 171.3, 89.4, 78.2, 64.6, 31.5, 31.2, 28.8, 28.3, 25.2, 21.1, 18.7. **HRMS** (ESI): Calcd for $\text{C}_{13}\text{H}_{22}\text{O}_2\text{Ag}$ [$\text{M}+\text{Ag}$]: 317.0671; Found: 317.0657.

Large-Scale Synthesis for Iron-Catalyzed Cross-Coupling of Non-activated Secondary Alkyl Halides with Alkynyl Grignard Reagents (General Procedure H). An oven-dried 250 mL round-bottom flask capped with a rubber septum and equipped with a Teflon-coated magnetic stirrer bar was charged with FeBr_2 (98% purity, 0.10 equiv), secondary alkyl halide (1.0 equiv), and NMP solvent, followed by the slow addition of alkynyl Grignard reagent solution (in THF, 1.5 equiv). The reaction mixture was stirred at room temperature for 16 h to form a black solution. After the reaction, the crude product was washed with EtOAc (20 mL) and water (60 mL). The aqueous fraction was further washed with EtOAc (2 x 20 mL). The combined organic fractions were concentrated *in vacuo* with the aid of a rotary evaporator. The crude product residue was purified by flash column chromatography with silica gel using a solvent mixture (EtOAc, hexanes) as an eluent to afford the isolated alkylated alkyne product.

(i) 5 mmol Scale Synthesis. Following the general procedure H, the title compound was prepared using 4-iodotetrahydro-2H-pyran (1.06 g, 5.0 mmol), ((trimethylsilyl)ethynyl)magnesium bromide (0.75 M in

THF, 7.5 mmol, 10 mL) (prepared by ethynyltrimethylsilane (737 mg, 7.5 mmol), ethylmagnesium bromide (1 M in THF, 7.5 mL), and THF (2.5 mL)), FeBr₂ (108 mg, 0.50 mmol), and NMP (20 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (20:1) as eluents to afford trimethyl((tetrahydro-2*H*-pyran-4-yl)ethynyl)silane (**2s**) as brown oil (699 mg, 3.83 mmol, 77%). Spectral and analytical data were identical to those reported for the same compound above based on 1.0 mmol scale.

(ii) 20 mmol Scale Synthesis. Following the general procedure H, the title compound was prepared using 4-iodotetrahydro-2*H*-pyran (4.24 g, 20.0 mmol), ((trimethylsilyl)ethynyl)magnesium bromide (1 M in THF, 30.0 mmol, 30 mL) (prepared by ethynyltrimethylsilane (2.95 g, 30.0 mmol) and ethylmagnesium bromide (1 M in THF, 30 mL)), FeBr₂ (413 mg, 2.0 mmol), and NMP (40 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (20:1) as eluents to afford trimethyl((tetrahydro-2*H*-pyran-4-yl)ethynyl)silane (**2s**) as brown oil (2.68 g, 14.9 mmol, 75%). Spectral and analytical data were identical to those reported for the same compound above based on 1.0 mmol scale.

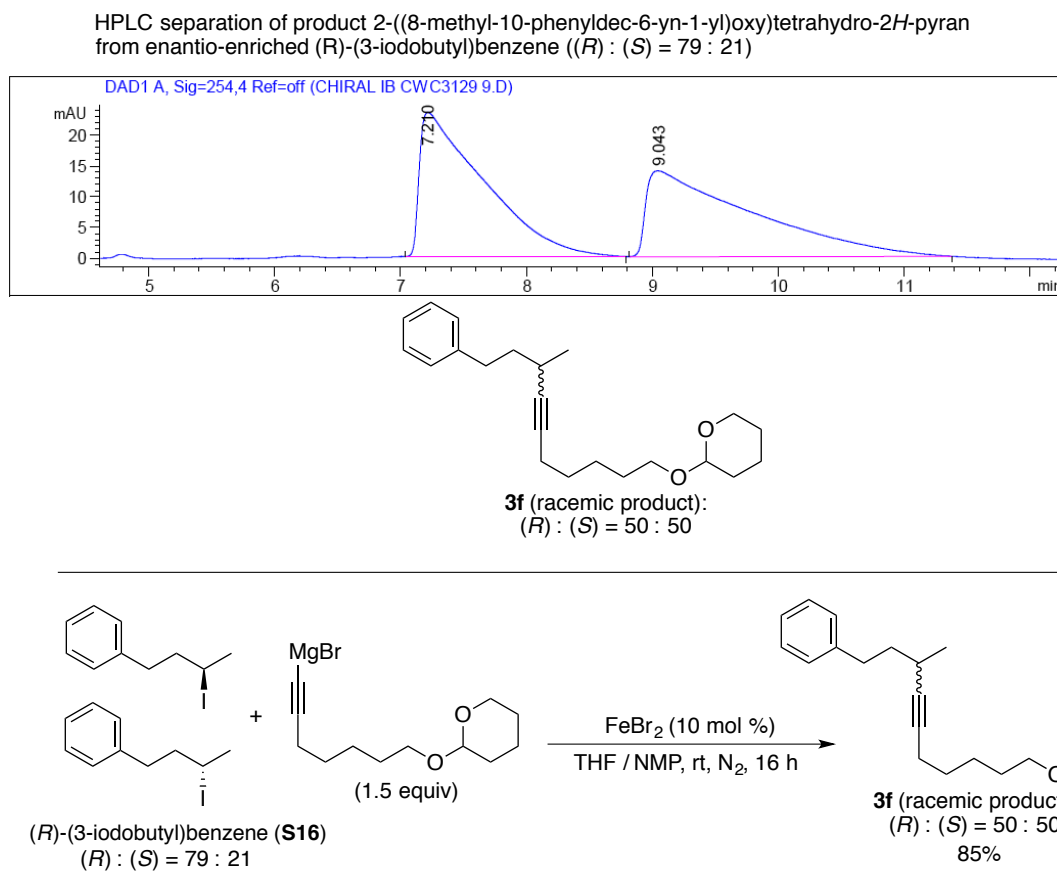
(iii) 10 mmol Scale Synthesis. Following the general procedure H, the title compound was prepared using *tert*-butyl 4-iodopiperidine-1-carboxylate (3.11 g, 10.0 mmol) and ((trimethylsilyl)ethynyl)magnesium bromide (0.75 M in THF, 15.0 mmol, 20 mL) (prepared by ethynyltrimethylsilane (1.47 g, 15.0 mmol), ethylmagnesium bromide (1 M in THF, 15 mL), and THF (5.0 mL)), FeBr₂ (216 mg, 1.0 mmol), and NMP (40 mL). The crude product was purified by flash chromatography using hexanes and then hexanes/EtOAc (20:1) as eluents to afford *tert*-butyl 4-((trimethylsilyl)ethynyl)piperidine-1-carboxylate (**2o**) as pale-brown oil (2.62 g, 9.31 mmol, 93%). Spectral and analytical data were identical to those reported for the same compound above based on 1.0 mmol scale.

Mechanistic Studies on Iron-Catalyzed Cross-Coupling of Non-activated Alkyl Halides with Alkynyl Grignard Reagents

(A) Reaction with Enantioenriched (3-Iodobutyl)benzene (General Procedure I). An oven-dried 30 mL re-sealable screw-cap test tube equipped with a Teflon-coated magnetic stirrer bar was charged with FeBr₂ (98% purity, 0.10 equiv), enantioenriched (3-iodobutyl)benzene (1.0 equiv), and NMP solvent, followed by the addition of (7-((tetrahydro-2*H*-pyran-2-yl)oxy)hept-1-yn-1-yl)magnesium bromide (0.5 M in THF, 1.5 equiv). The reaction mixture was stirred at room temperature for 16 h to form a deep brown solution. After the reaction, the crude product was washed with EtOAc (10 mL) and water (30 mL). The aqueous fraction was further washed with EtOAc (2 x 10 mL). The combined organic fractions were concentrated *in vacuo* with the aid of a rotary evaporator. The crude product residue was purified by flash column chromatography with silica gel using hexanes and then hexanes/EtOAc (10:1) as eluents to afford the isolated substituted alkyne product, 2-((8-methyl-10-phenyldec-6-yn-1-yl)oxy)tetrahydro-2*H*-pyran (**3f**).

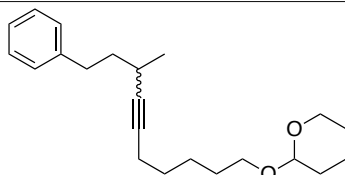
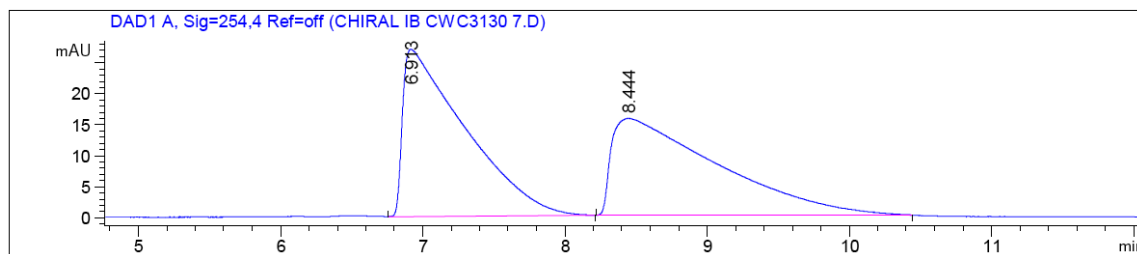
(i) Reaction of (*R*)-(3-iodobutyl)benzene ((*R*):(*S*) = 79:21) (S16). Following the general procedure I, the title compound was prepared using (*R*)-(3-iodobutyl)benzene ((*R*):(*S*) = 79:21) (S16) (130 mg, 0.50

mmol), (7-((tetrahydro-2*H*-pyran-2-yl)oxy)hept-1-yn-1-yl)magnesium bromide (0.5 M in THF, 0.75 mmol, 1.5 mL), FeBr₂ (11 mg, 0.05 mmol), and NMP (2.0 mL). A racemic mixture of 2-((8-methyl-10-phenyldec-6-yn-1-yl)oxy)tetrahydro-2*H*-pyran (**3f**) ((*R*):(*S*) = 50:50) was obtained as pale-yellow oil (140 mg, 0.43 mmol, 85%). The HPLC separation of the racemic product **3f** was shown below and was shown to be similar to that from the reaction of (*R*)/(*S*)-(3-iodobutyl)benzene (Scheme 2, **3f**).

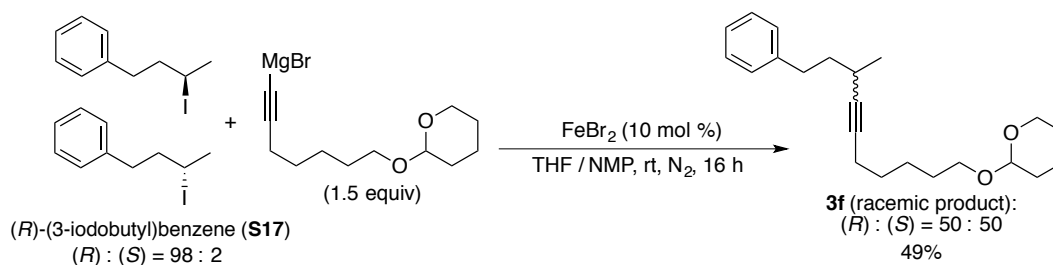


(ii) Reaction of (*R*)-(3-iodobutyl)benzene ((*R*):(*S*) = 98:2) (S17**).** Following the general procedure I, the title compound was prepared using (*R*)-(3-iodobutyl)benzene ((*R*):(*S*) = 98:2) (**S17**) (80 mg, 0.30 mmol), (7-((tetrahydro-2*H*-pyran-2-yl)oxy)hept-1-yn-1-yl)magnesium bromide (0.5 M in THF, 0.45 mmol, 0.90 mL), FeBr₂ (6.5 mg, 0.03 mmol), and NMP (1.2 mL). A racemic mixture of 2-((8-methyl-10-phenyldec-6-yn-1-yl)oxy)tetrahydro-2*H*-pyran (**3f**) ((*R*):(*S*) = 50:50) was obtained as pale-yellow oil (48 mg, 0.15 mmol, 49%). The HPLC separation of the racemic product **3f** was shown below and was shown to be similar to that from the reaction of (*R*)/(*S*)-(3-iodobutyl)benzene (Scheme 2, **3f**).

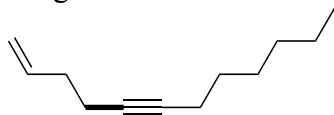
HPLC separation of product 2-((8-methyl-10-phenyldec-6-yn-1-yl)oxy)tetrahydro-2H-pyran from enantio-enriched (*R*)-(3-iodobutyl)benzene (*R*) : (*S*) = 98 : 2)



3f (racemic product):
(*R*) : (*S*) = 50 : 50



(B) Reaction with Radical Clock Substrate. Following the general procedure G, the title compound was prepared using cyclopropylmethyl bromide (135 mg, 1.0 mmol) and oct-1-yn-1-ylmagnesium bromide (0.5 M in THF, 1.5 mmol, 3.0 mL). The crude product was purified by flash chromatography using hexanes as an eluent to afford dodec-1-en-5-yne (**4l**) as pale-brown oil (41 mg, 0.25 mmol, 25%).



Dodec-1-en-5-yne (4l). ¹H NMR (400 MHz, CDCl₃): δ 5.91-5.81 (m, 1 H), 5.07 (d, *J* = 17.4 Hz, 1 H), 5.01 (d, *J* = 10.2 Hz, 1 H), 2.26-2.21 (ovrlp, 4 H), 2.14 (t, *J* = 6.0 Hz, 2 H), 1.47 (qu, *J* = 6.8 Hz, 2 H), 1.41-1.24 (ovrlp, 6 H), 0.89 (t, *J* = 6.7 Hz, 3 H). ¹³C NMR (100 MHz, CDCl₃): δ 137.4, 115.5, 80.9, 79.5, 33.6, 31.5, 29.2, 28.7, 22.7, 18.9, 18.8, 14.2.

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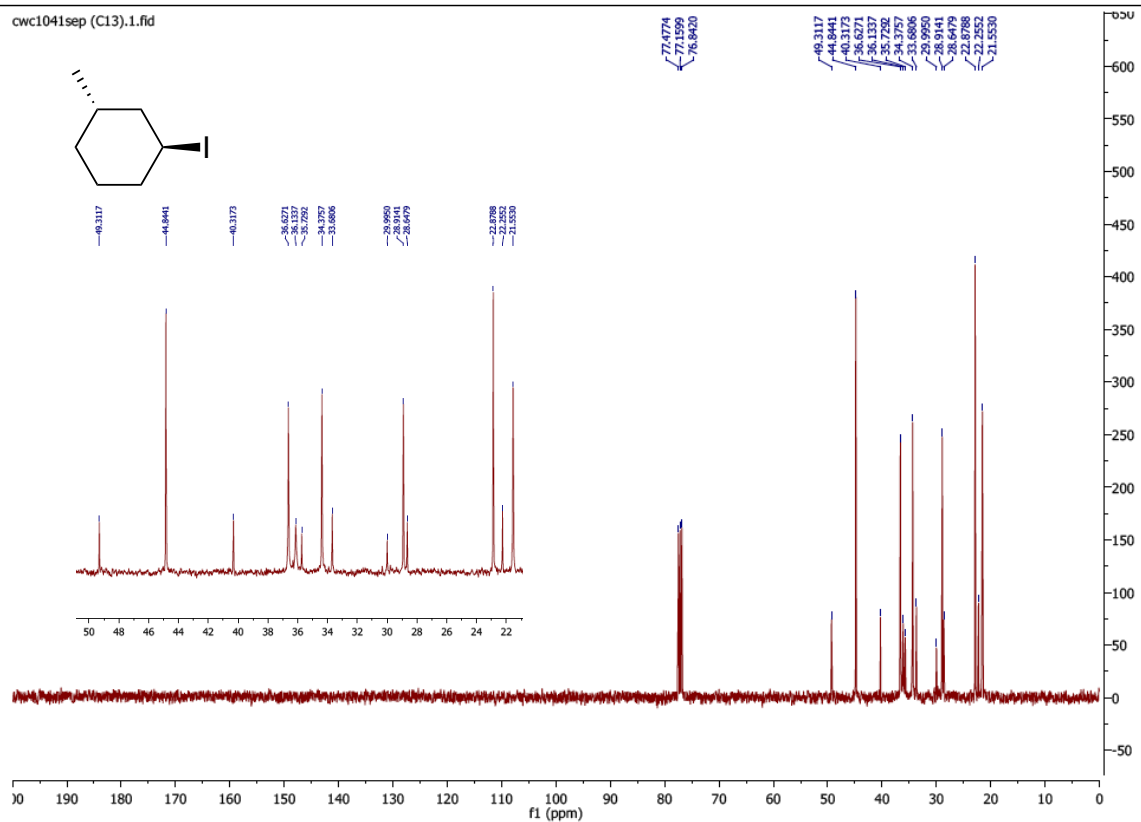
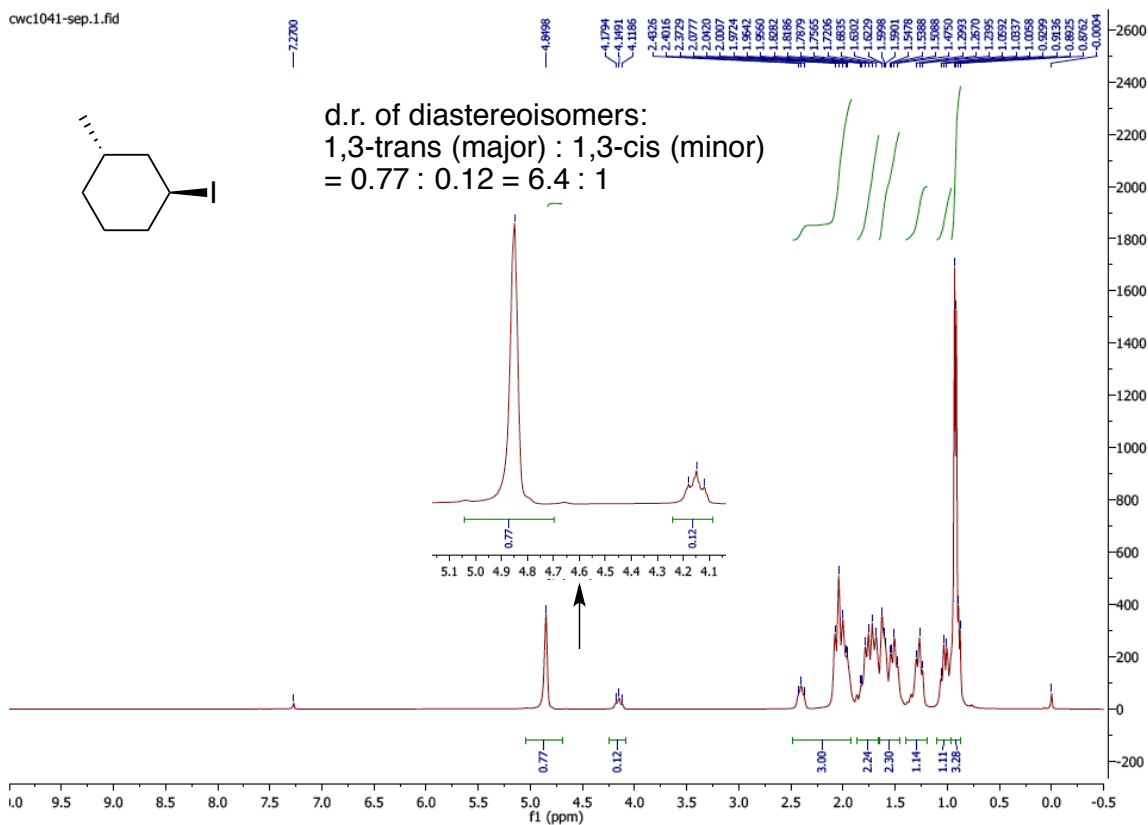
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NMR Spectra

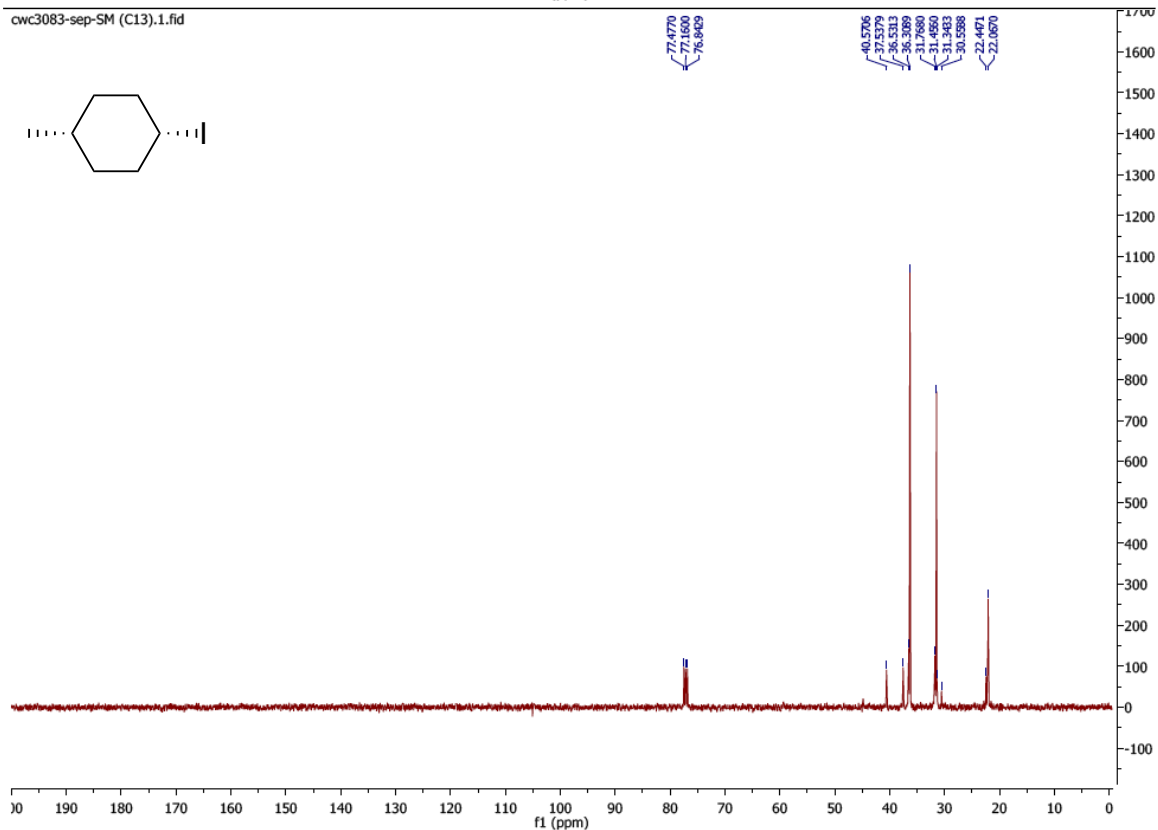
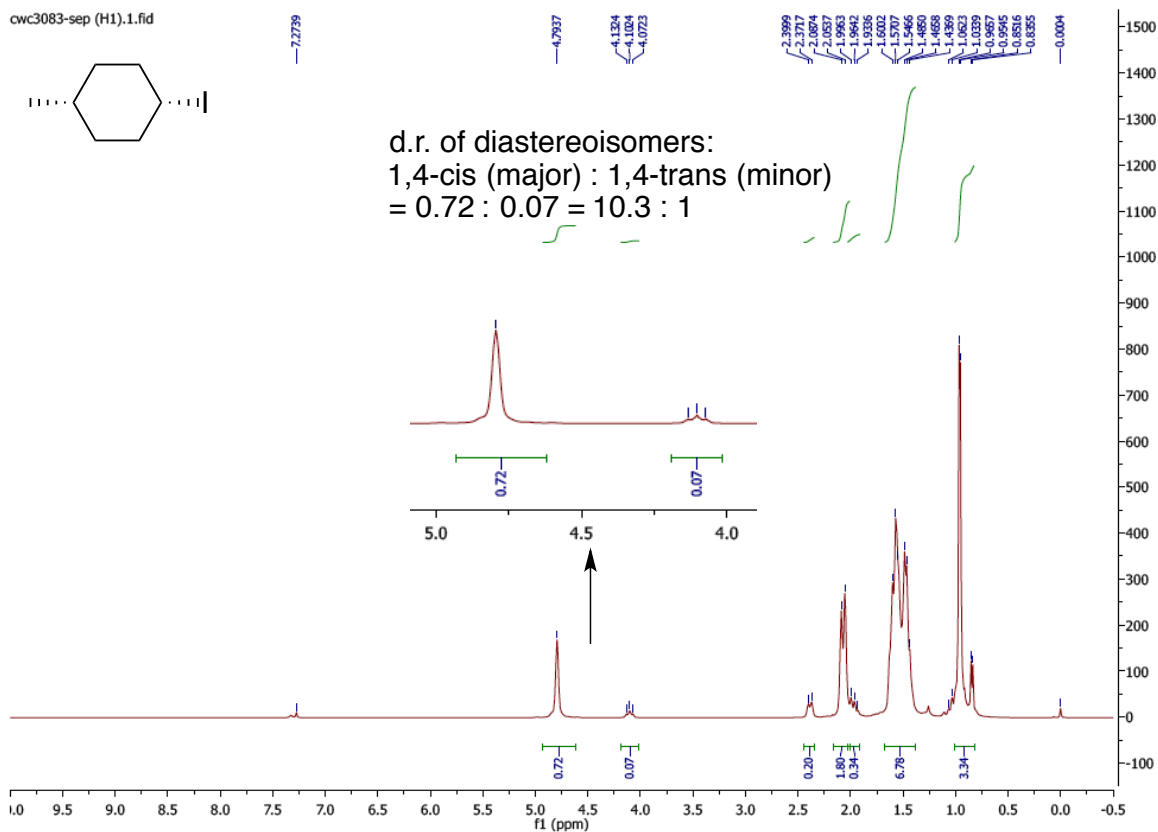
List of Spectra of Compounds

^1H and ^{13}C NMR Spectra	Page no.
Starting Materials – Alkyl Halides and Terminal Alkynes (S1-S23)	S55
Substituted Alkyne Products from Six-Membered Cyclic Alkyl Halides (2a-2y)	S77
Substituted Alkyne Products from Cyclic and Acyclic Alkyl Halides (3a-3u)	S102
Substituted Alkyne Products from Secondary Alkyl Halides (Supplementary Results) (P1-P9)	S124
Substituted Alkyne Products from Primary Alkyl Halides (4a-4l)	S133

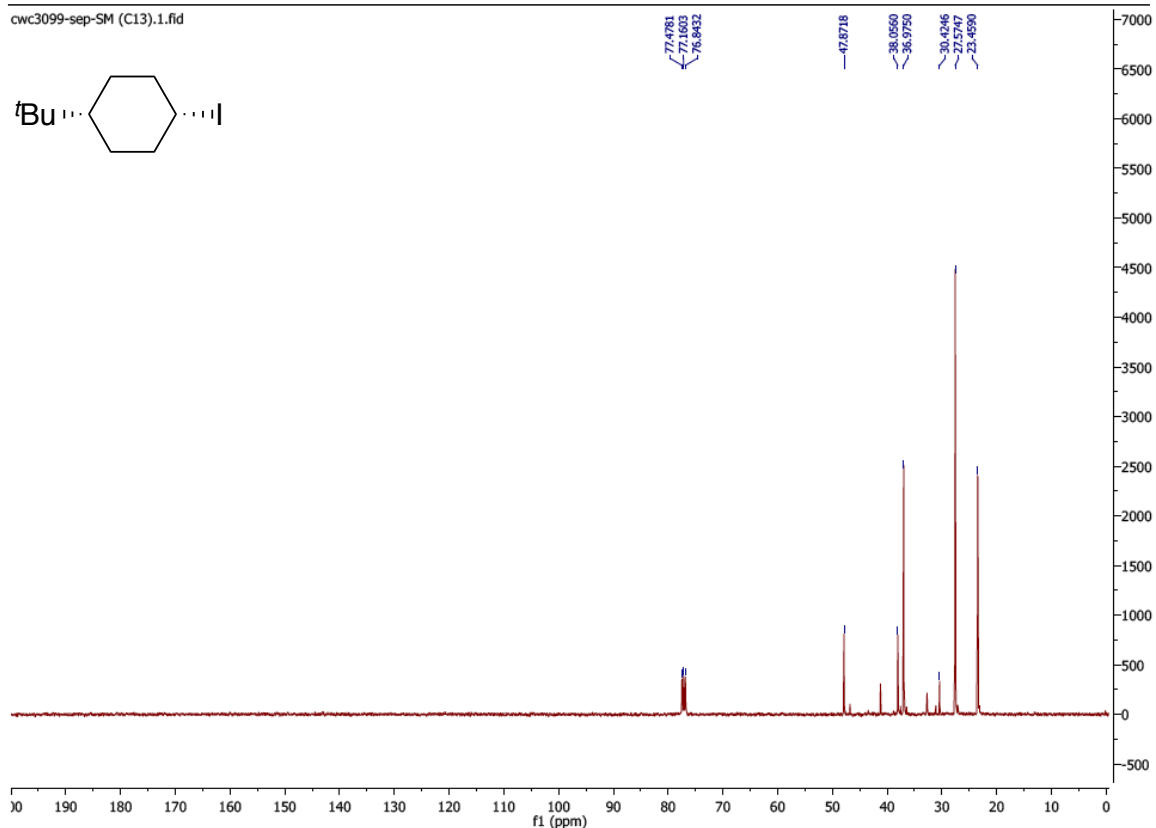
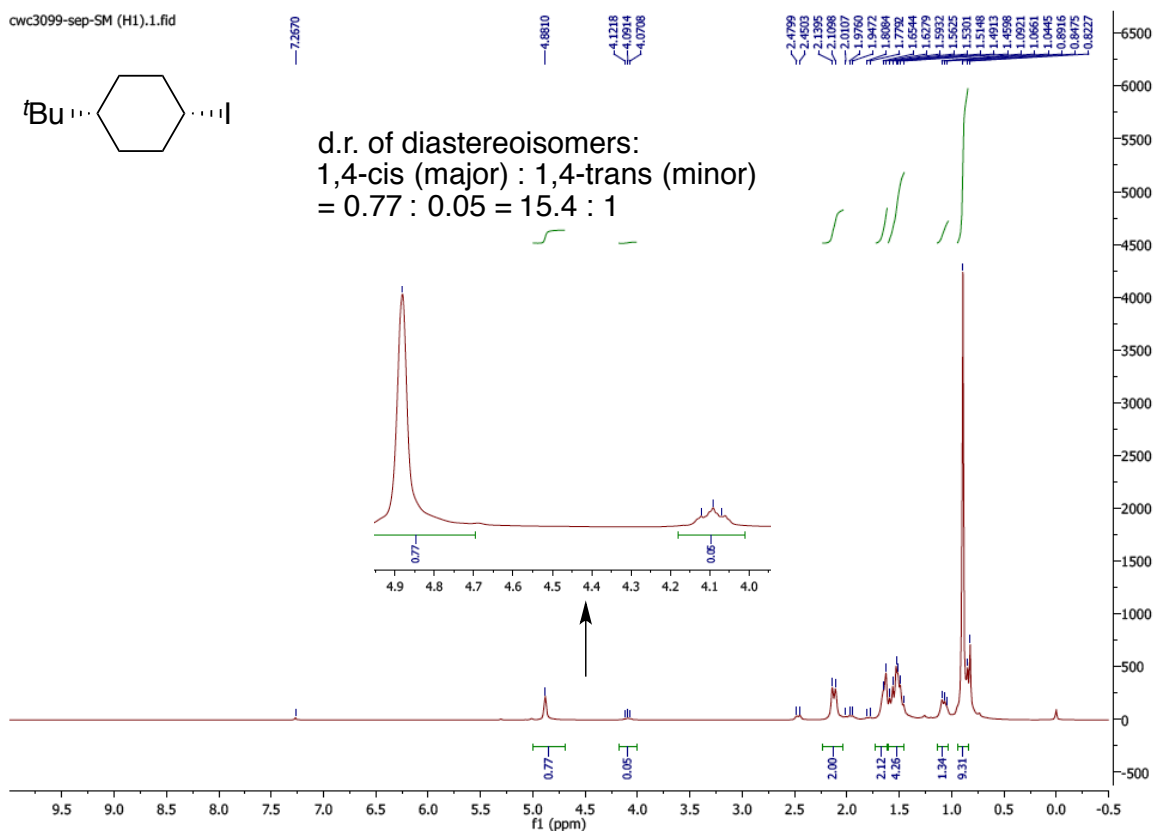
¹H and ¹³C NMR of 1-Iodo-3-methylcyclohexane (S1)



¹H and ¹³C NMR of 1-Iodo-4-methylcyclohexane (S2)

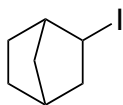


¹H and ¹³C NMR of 1-(*tert*-Butyl)-4-iodocyclohexane (S3)

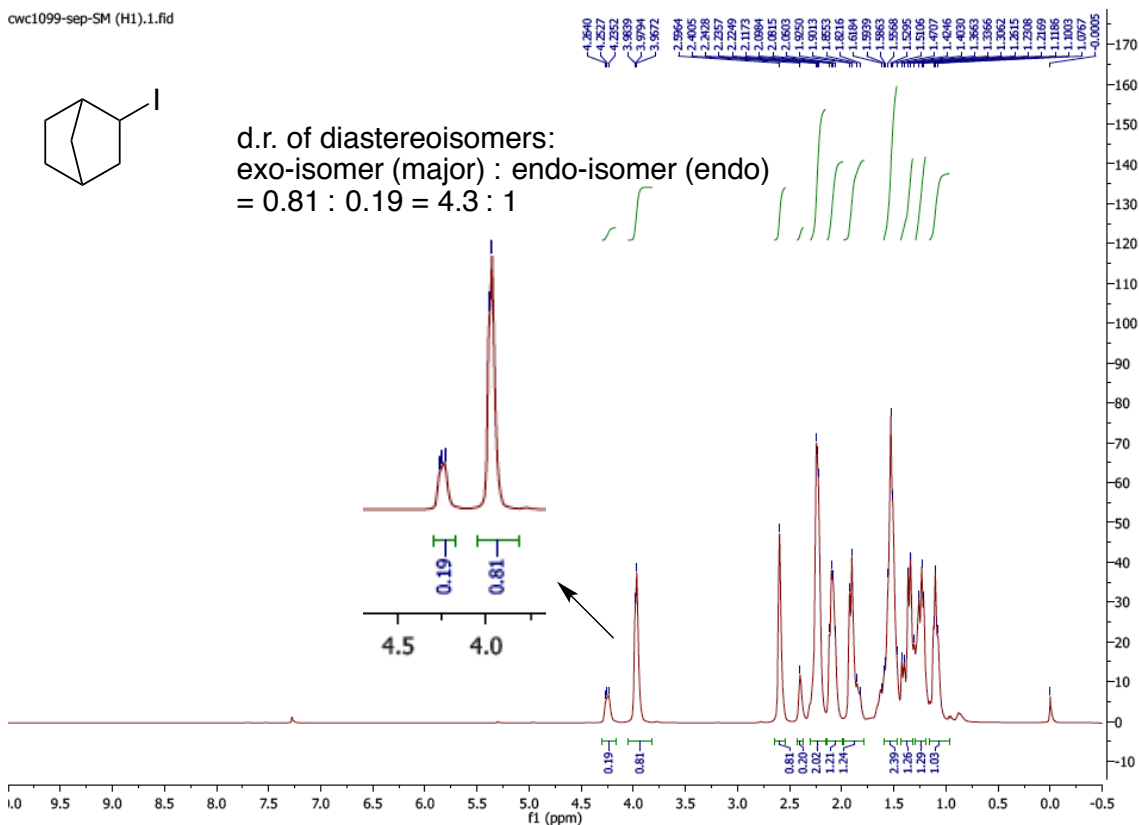


¹H and ¹³C NMR of 2-Iodobicyclo[2.2.1]heptane (S4)

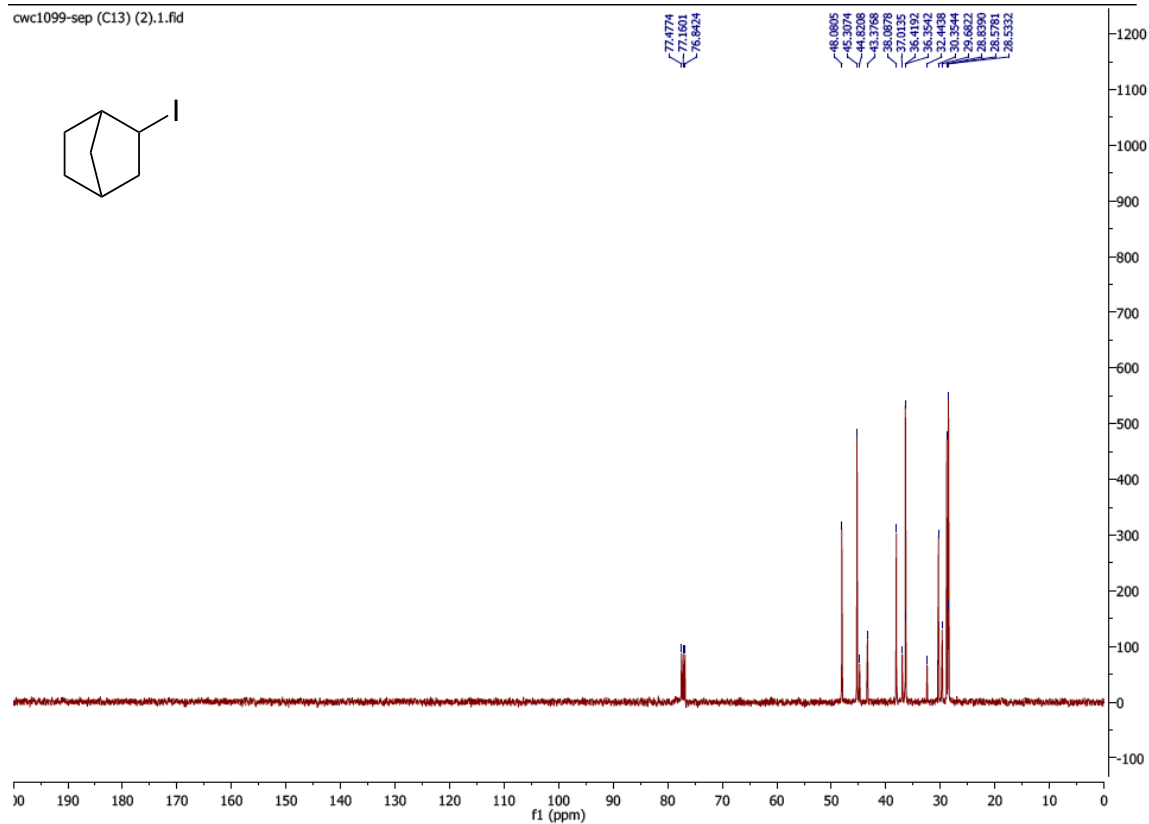
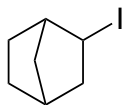
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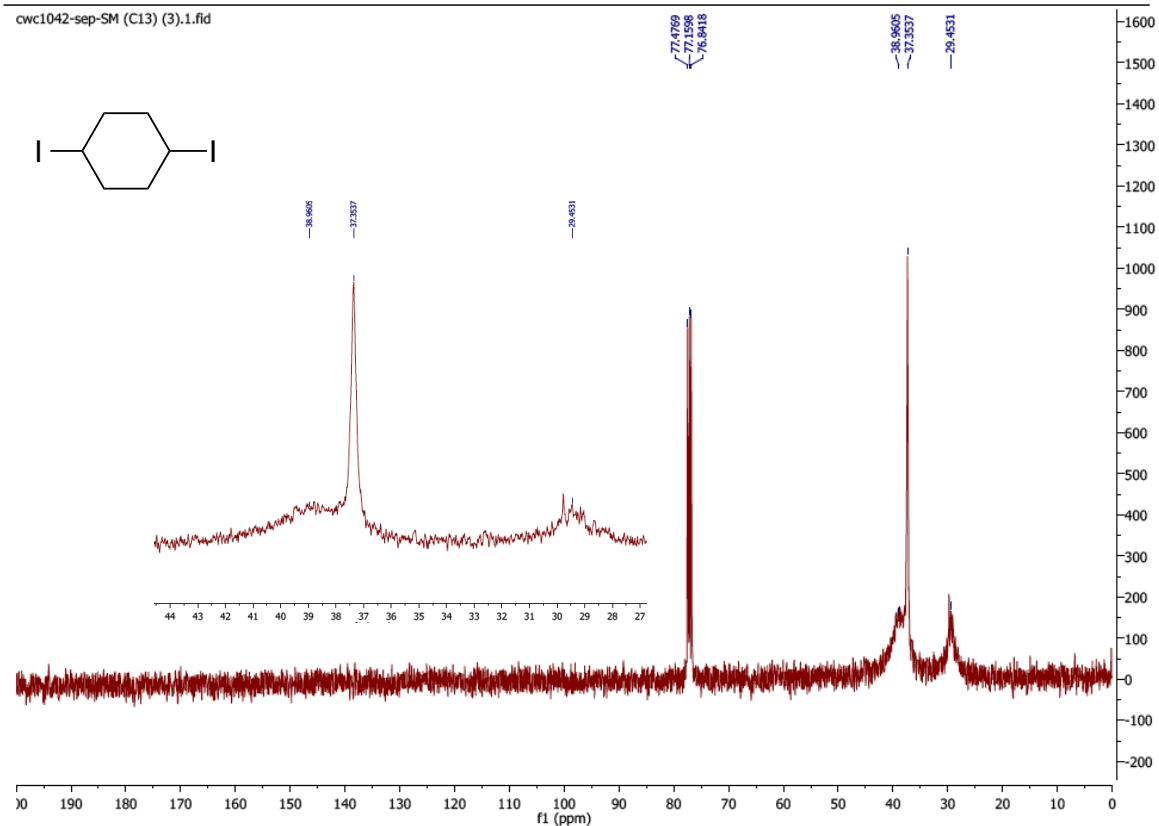
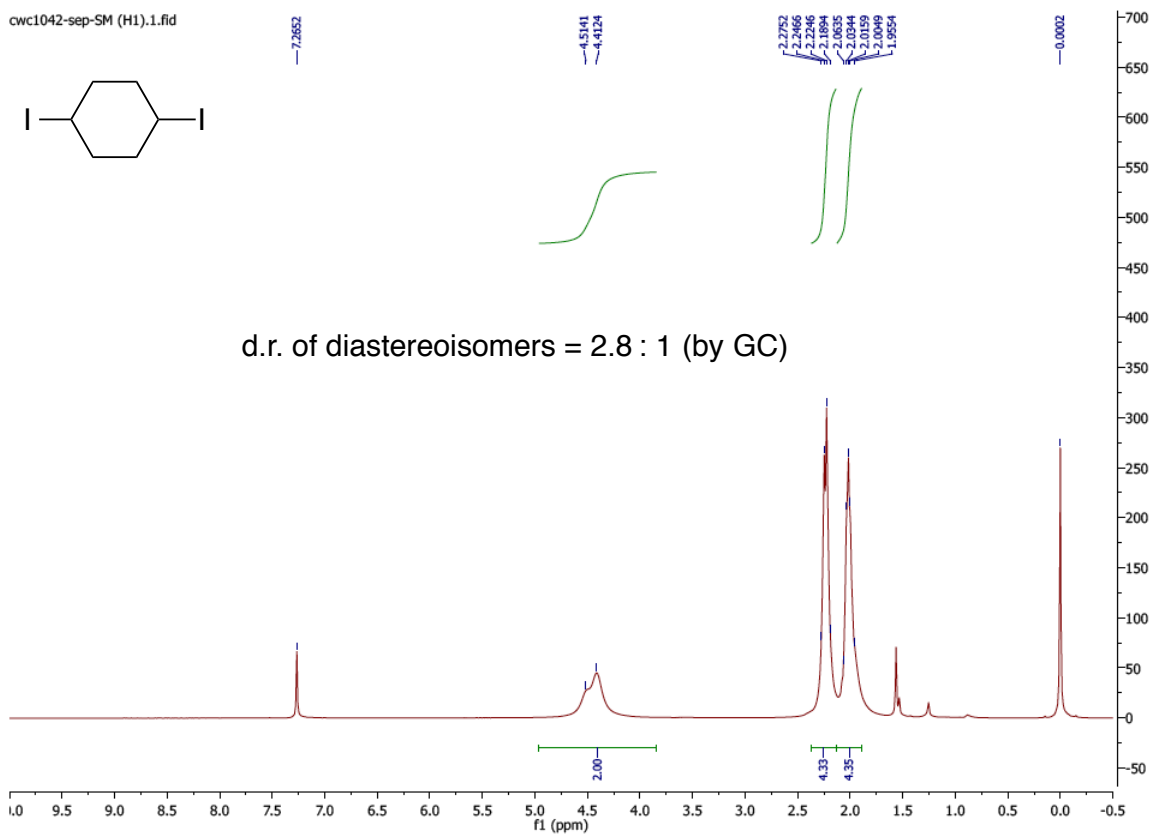
d.r. of diastereoisomers:
 exo-isomer (major) : endo-isomer (endo)
 = 0.81 : 0.19 = 4.3 : 1



cwc1099-sep (C13) (2).1.fid

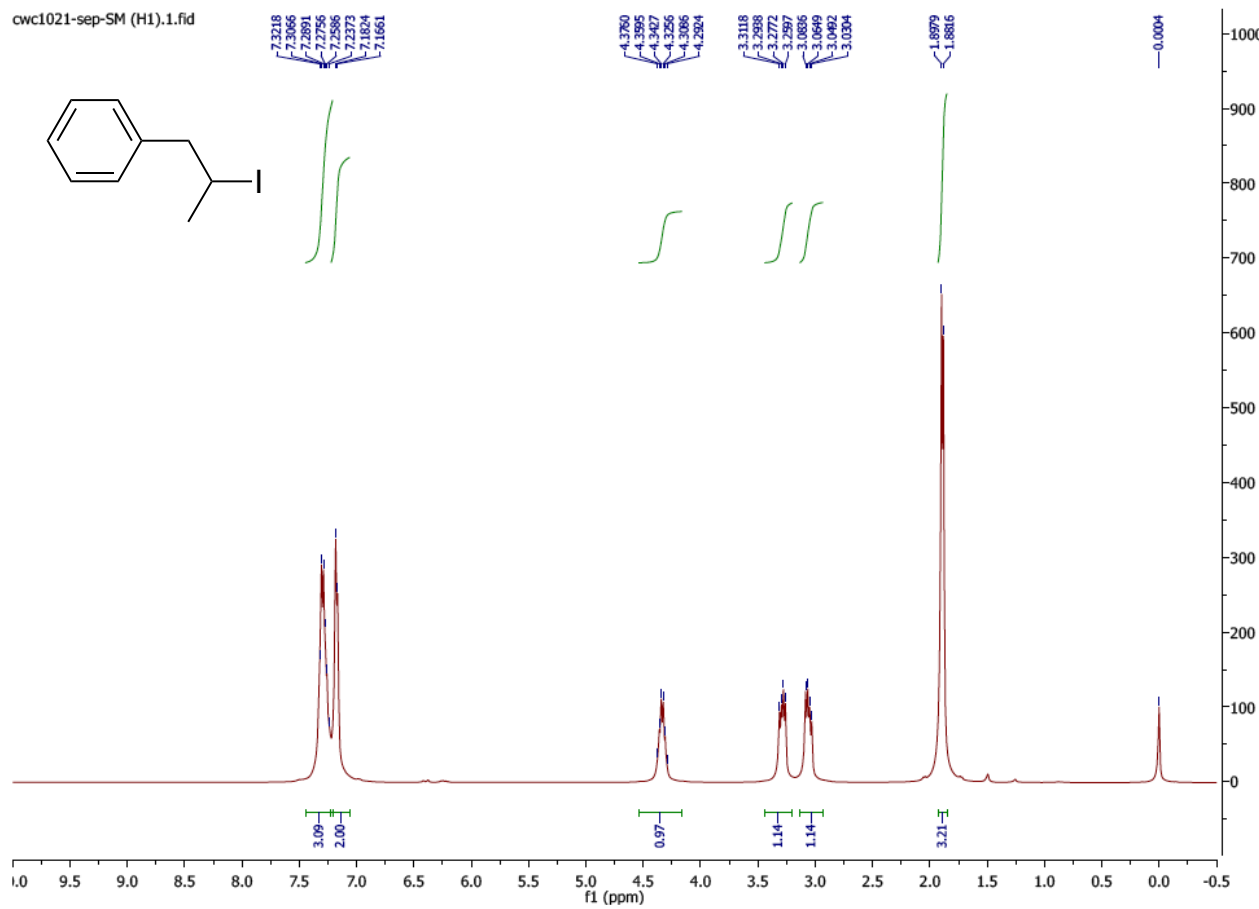


¹H and ¹³C NMR of 1,4-Diiodocyclohexane (S5)

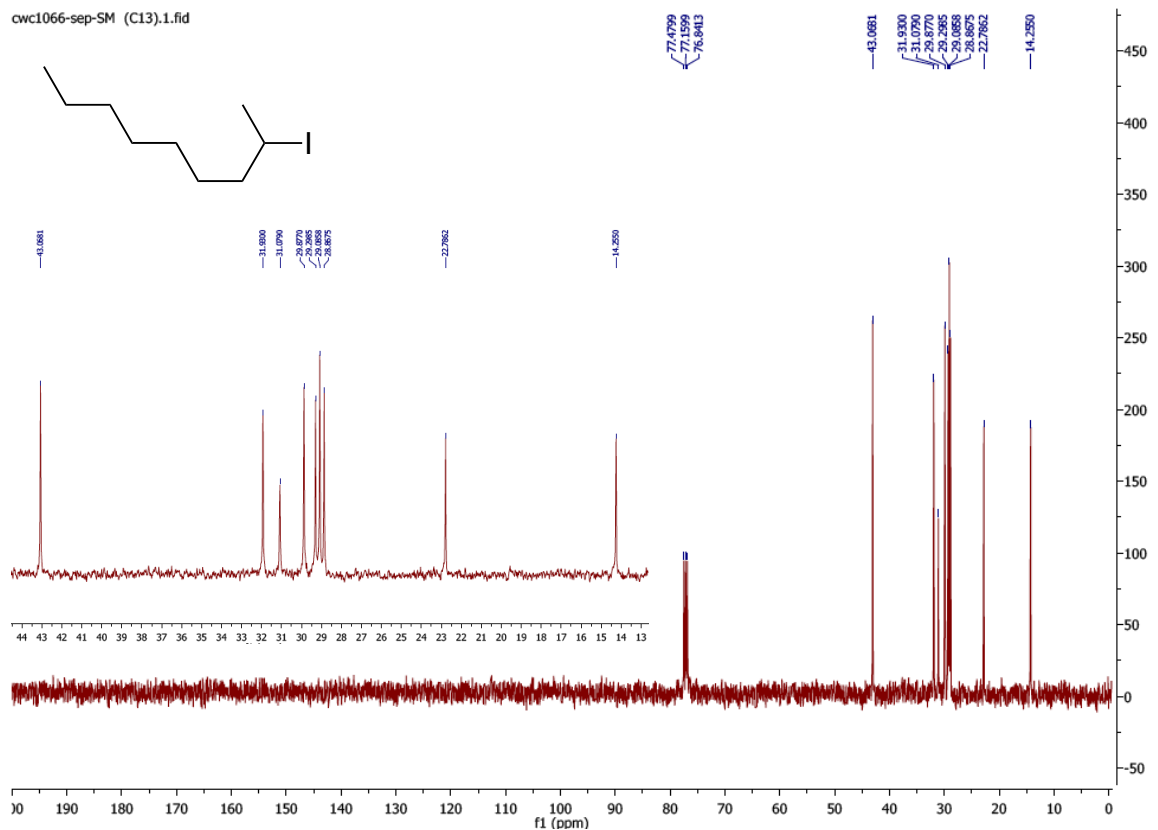
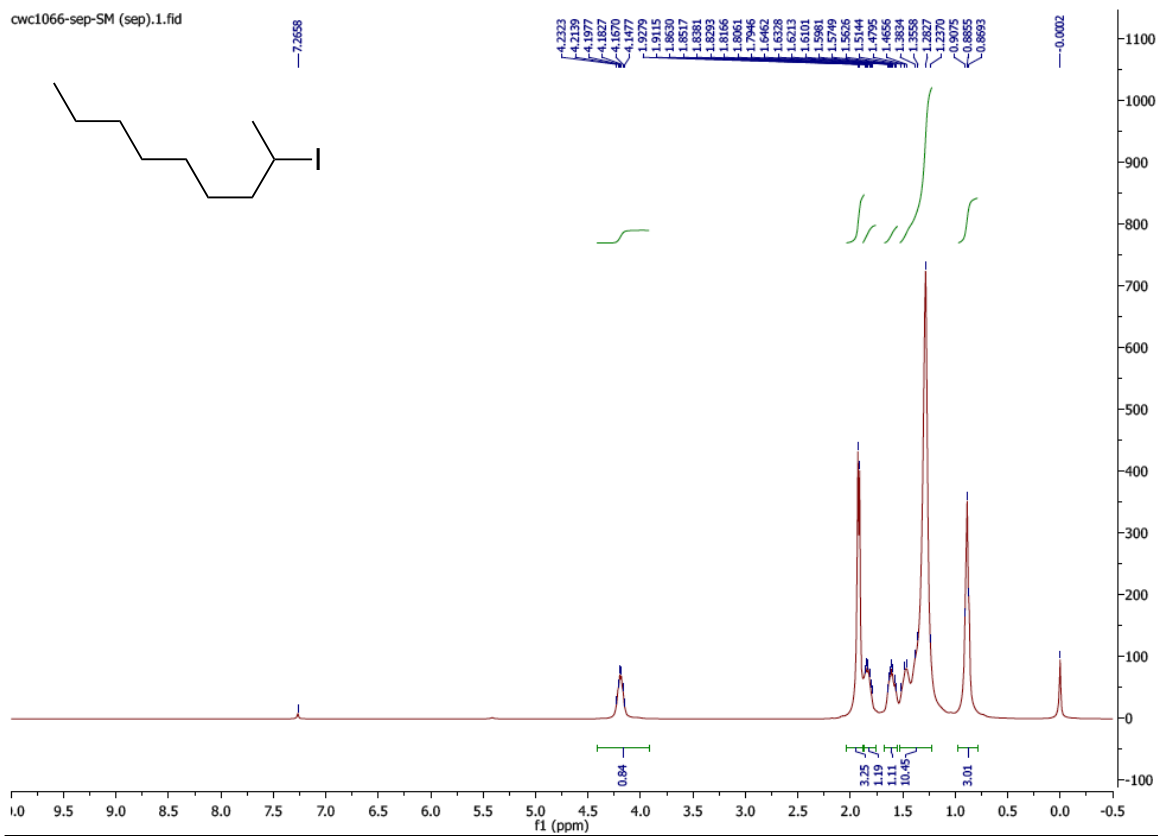


¹H and ¹³C NMR of (2-Iodopropyl)benzene (S6)

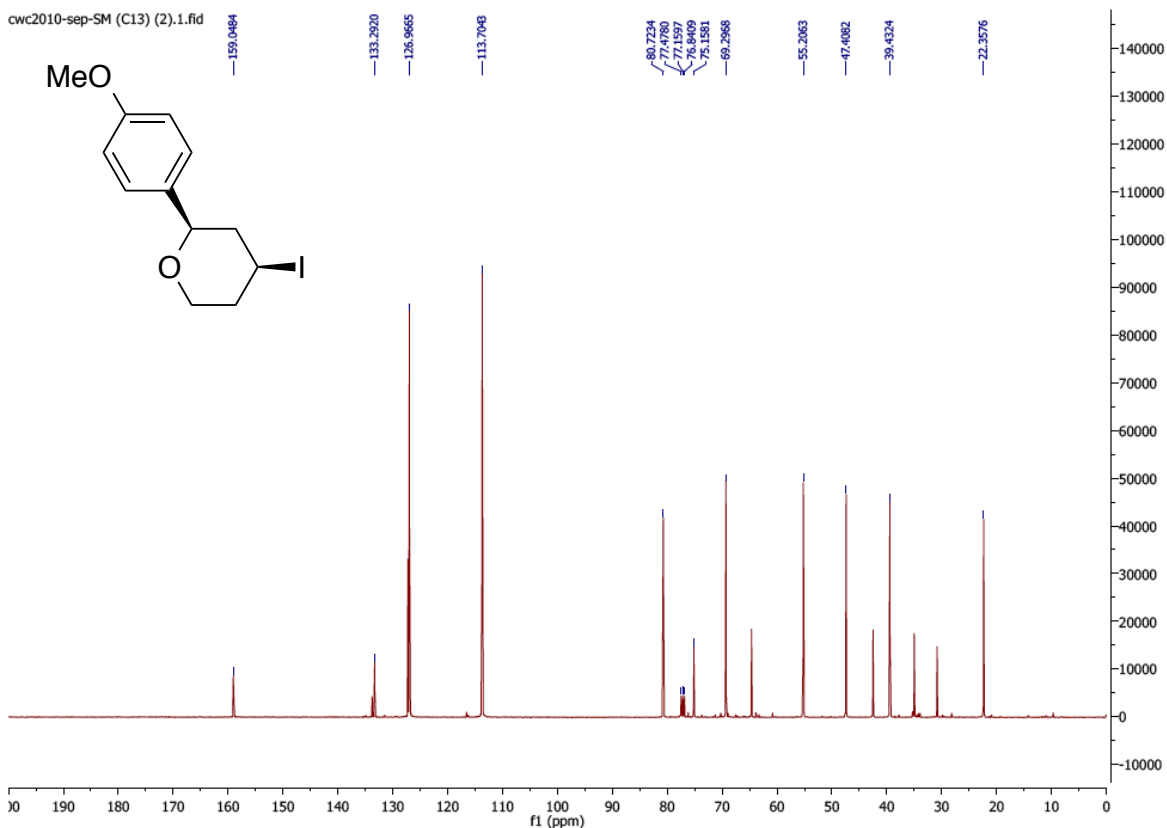
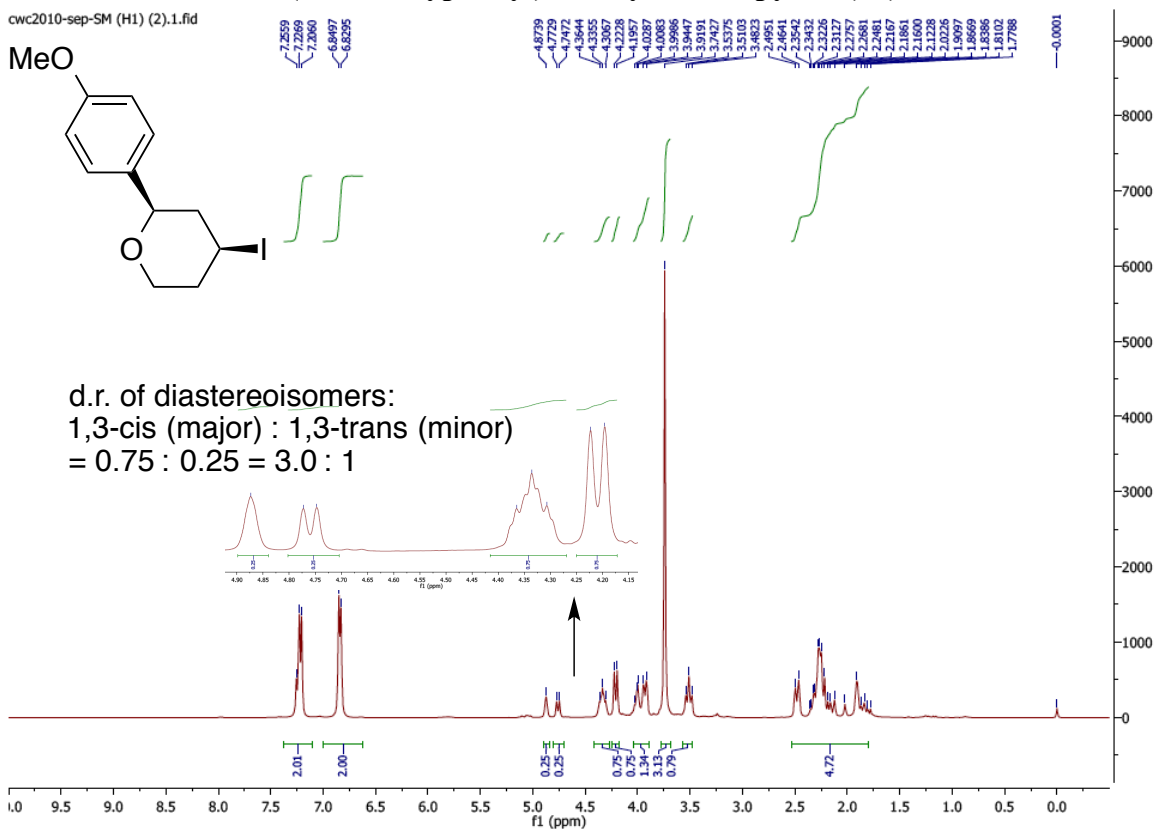
cwc1021-sep-SM (H1).1.fid



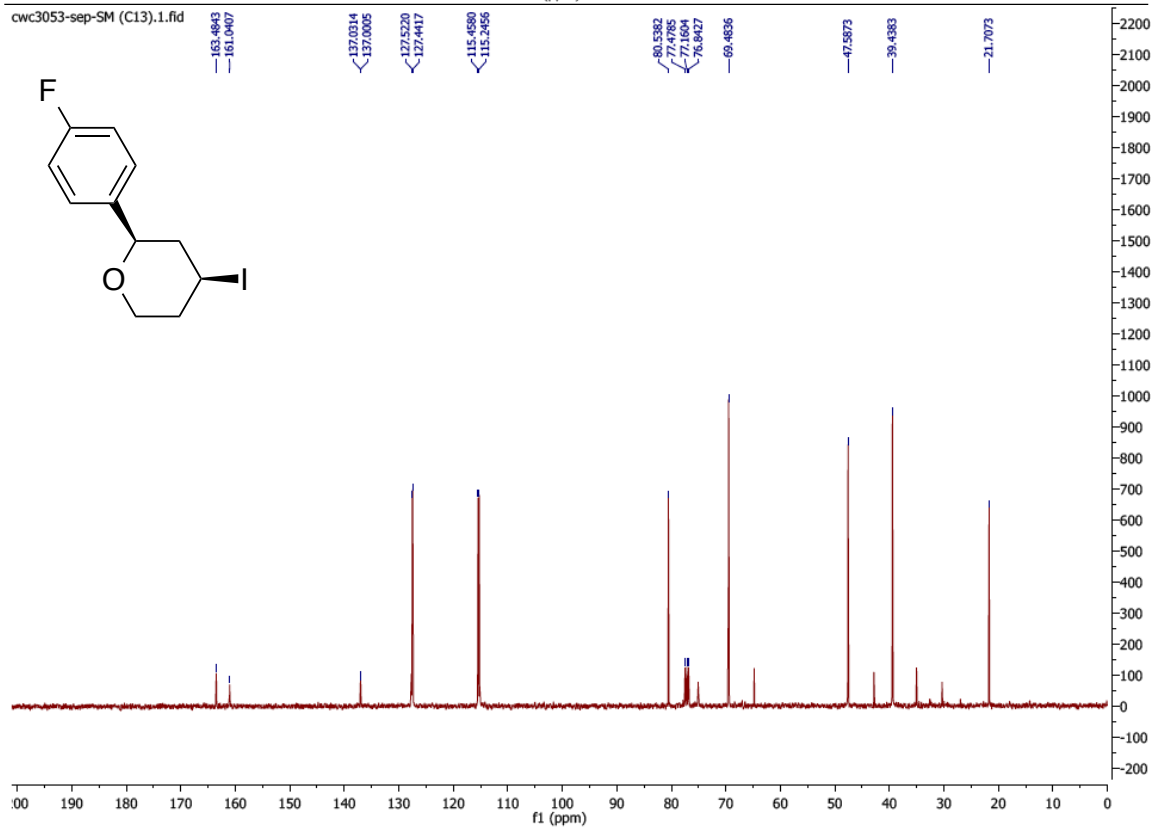
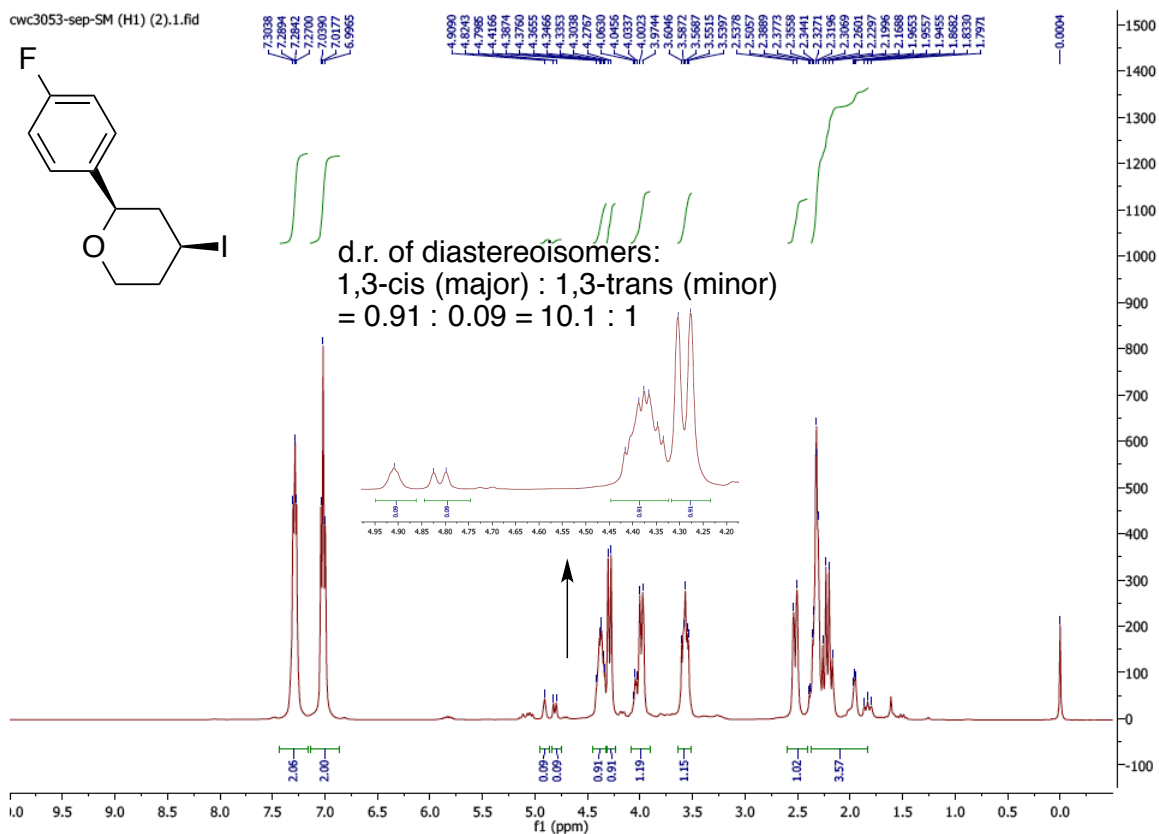
¹H and ¹³C NMR of 2-Iodononane (S7)



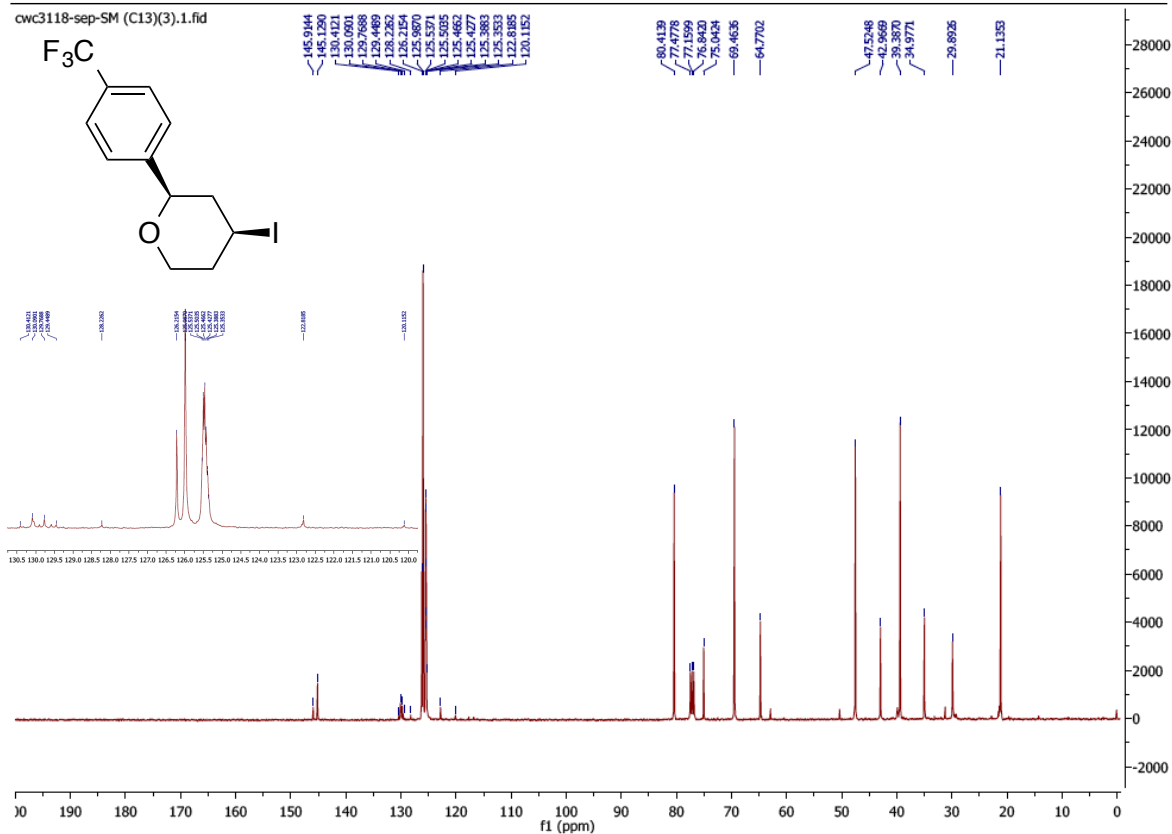
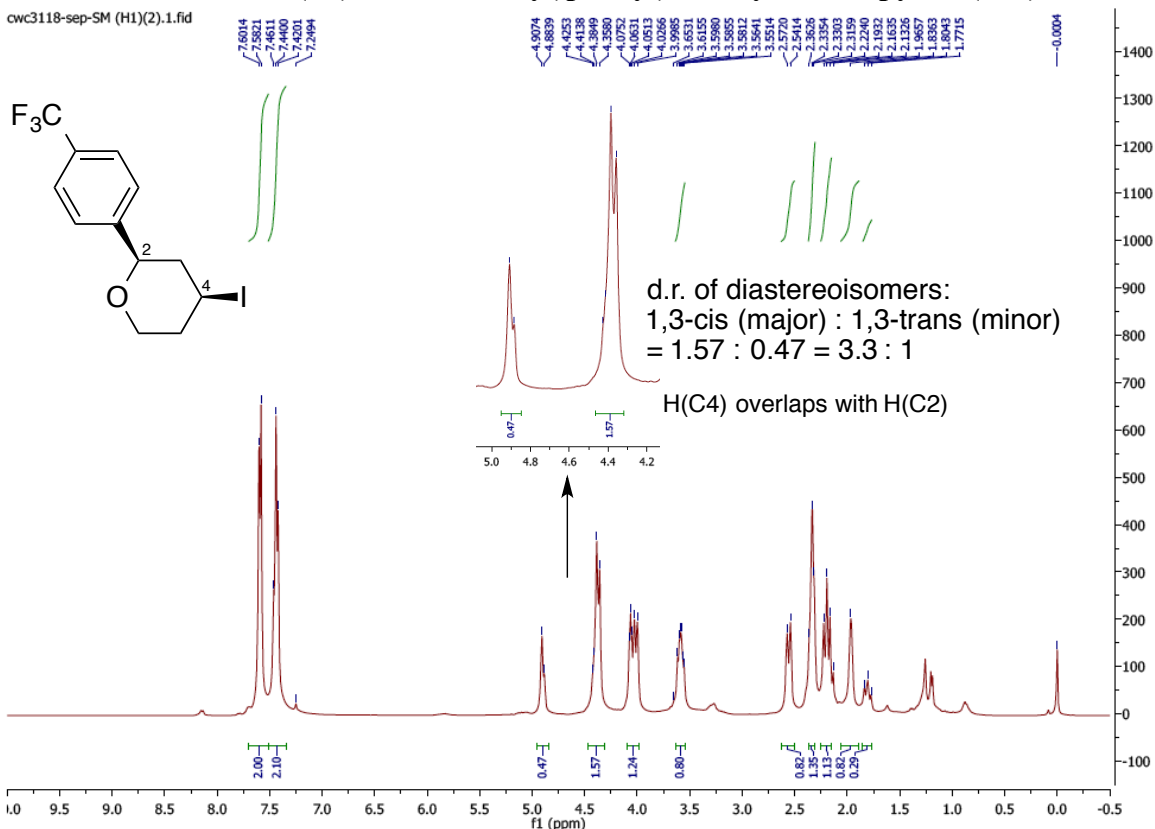
¹H and ¹³C NMR of 4-Iodo-2-(4-methoxyphenyl)tetrahydro-2H-pyran (S9)



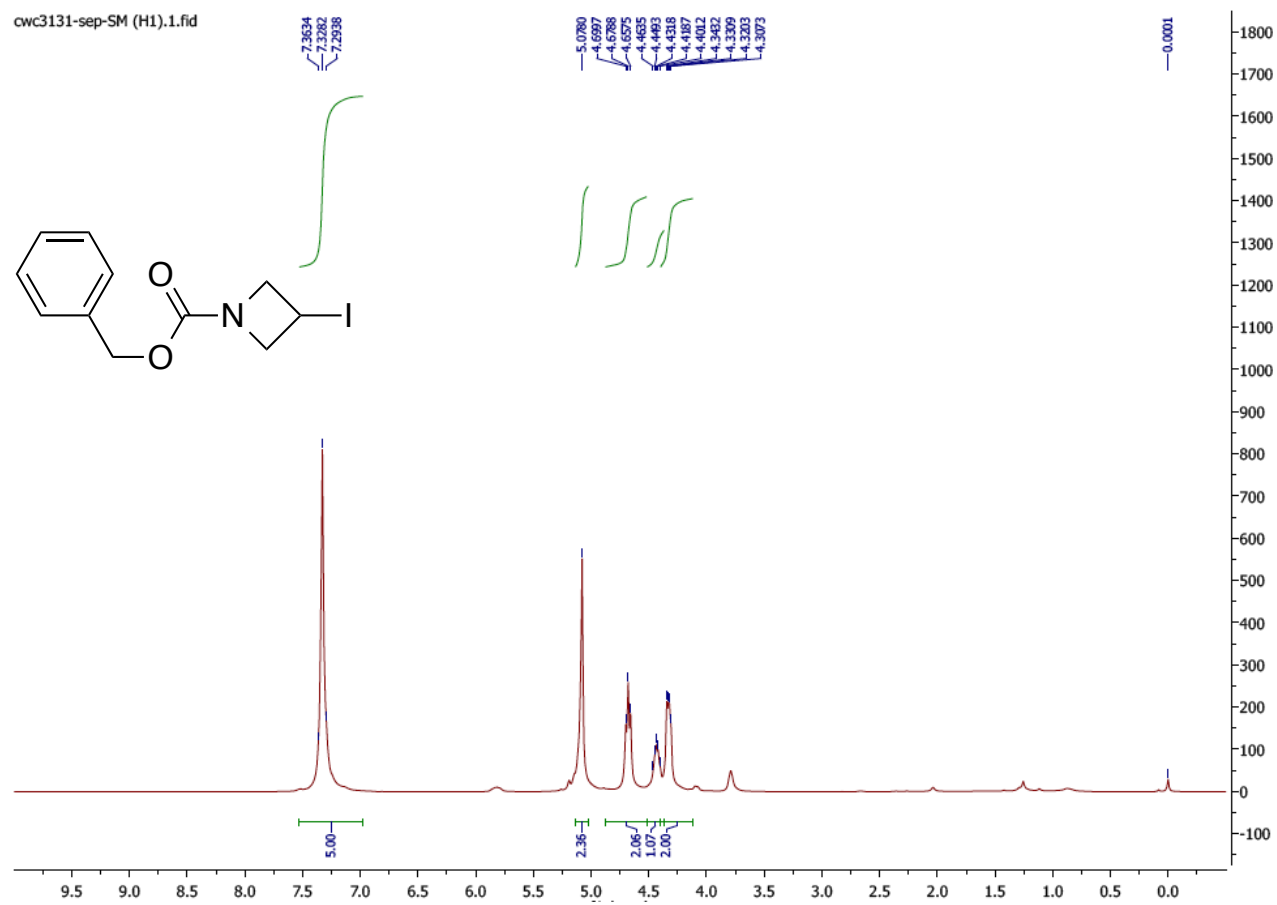
¹H and ¹³C NMR of 2-(4-Fluorophenyl)-4-iodotetrahydro-2H-pyran (S10)



¹H and ¹³C NMR of 4-Iodo-2-(4-(trifluoromethyl)phenyl)tetrahydro-2H-pyran (S11)

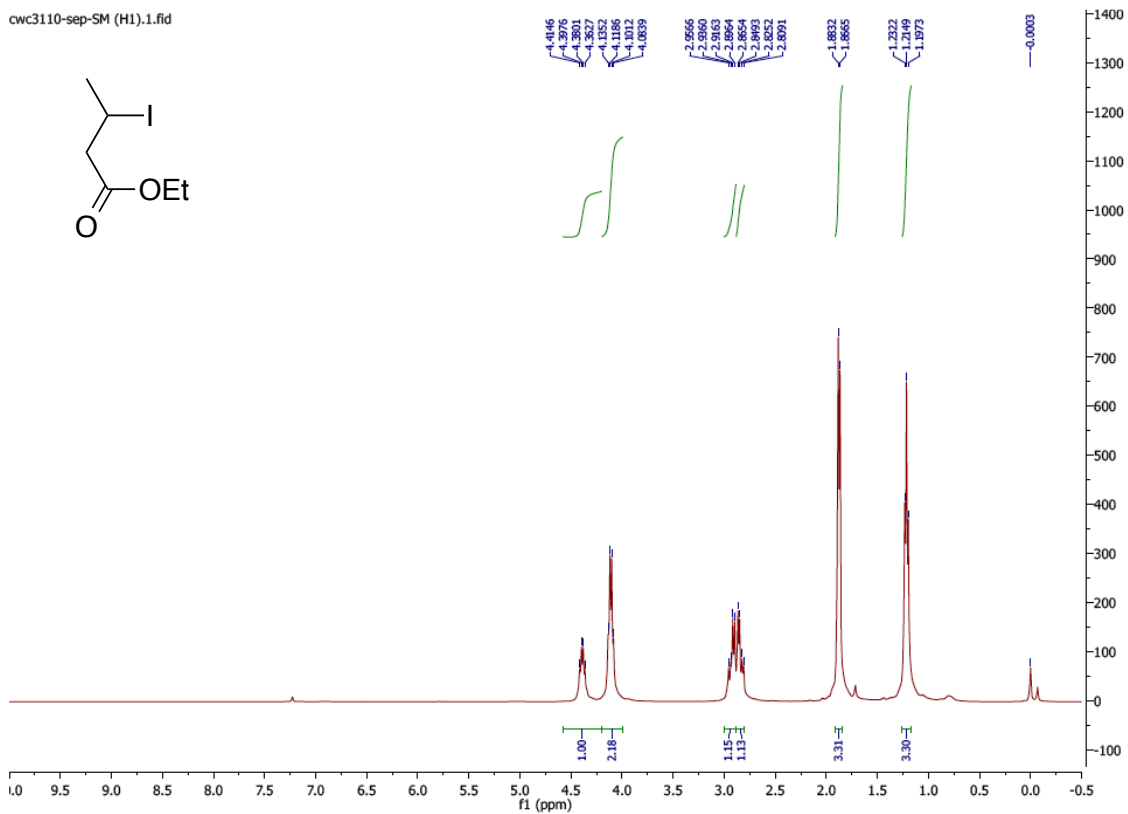


^1H and ^{13}C NMR of Benzyl 3-iodoazetidine-1-carboxylate (S12)

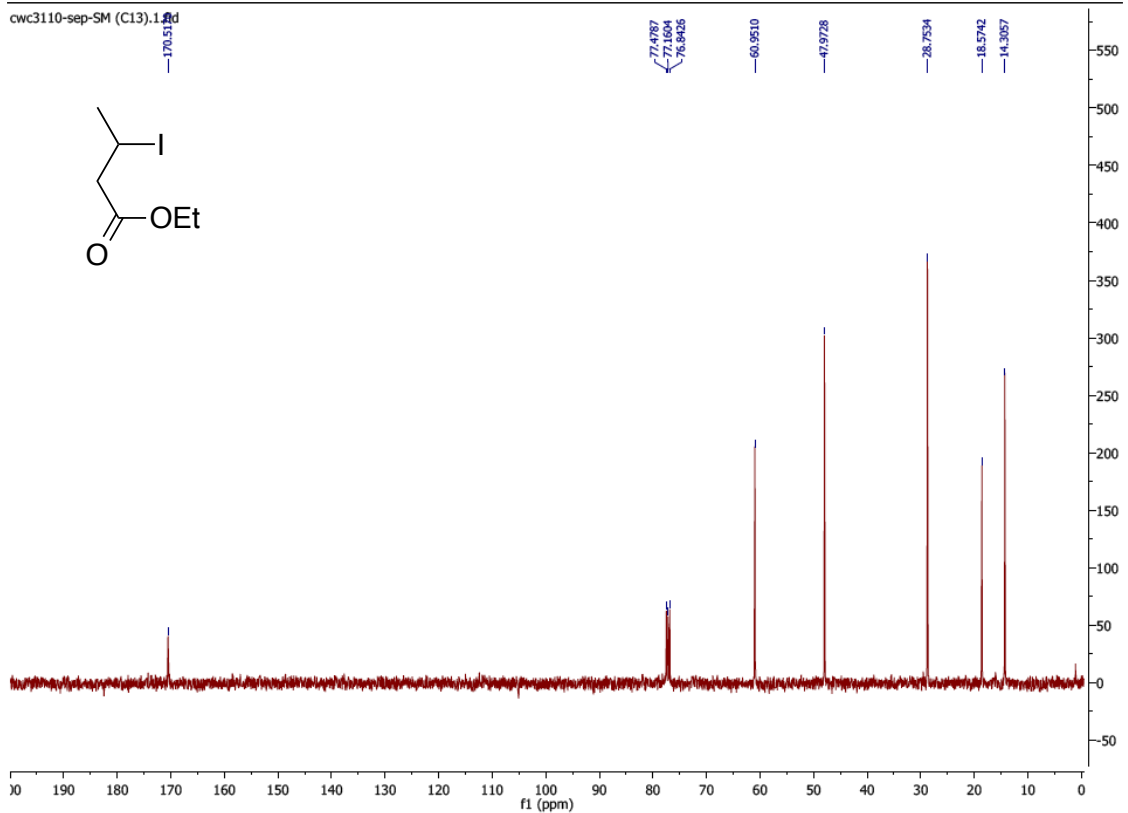


¹H and ¹³C NMR of Ethyl 3-iodobutanoate (S13)

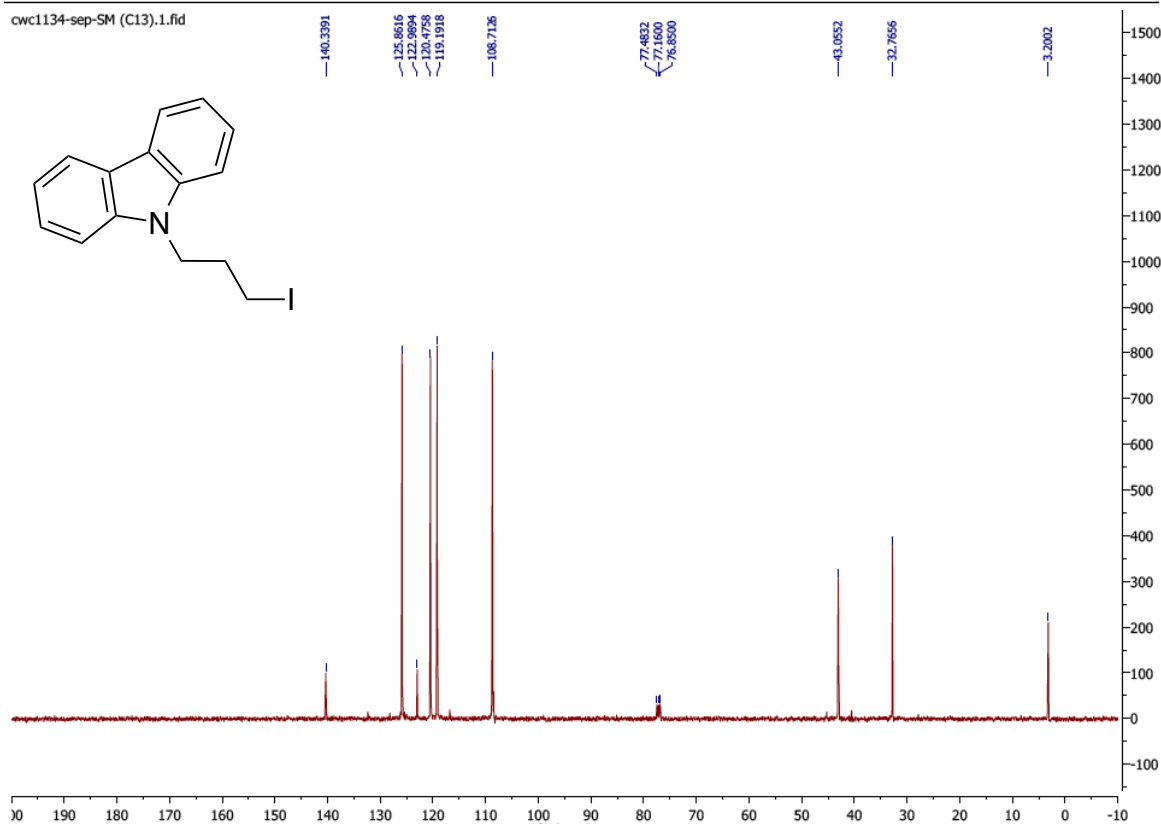
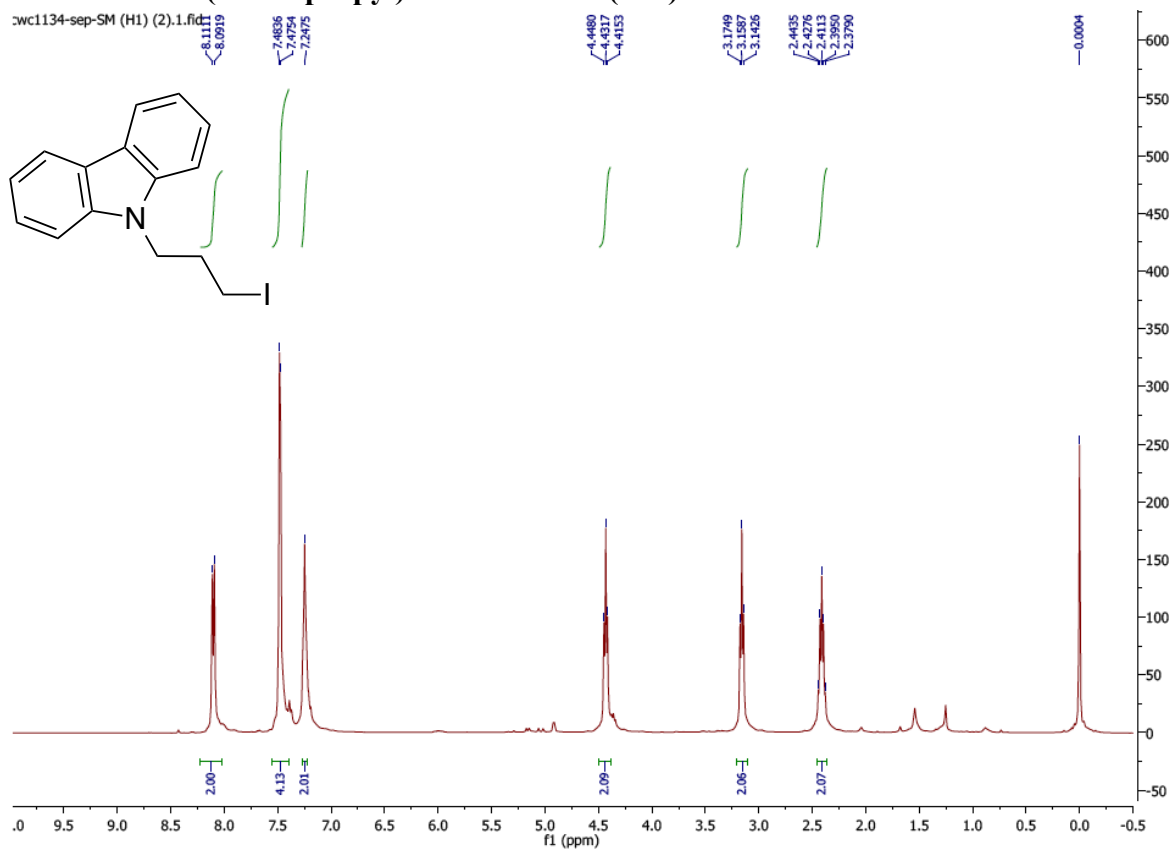
cwc3110-sep-SM (H1).1.fid



cwc3110-sep-SM (C13).1.fid

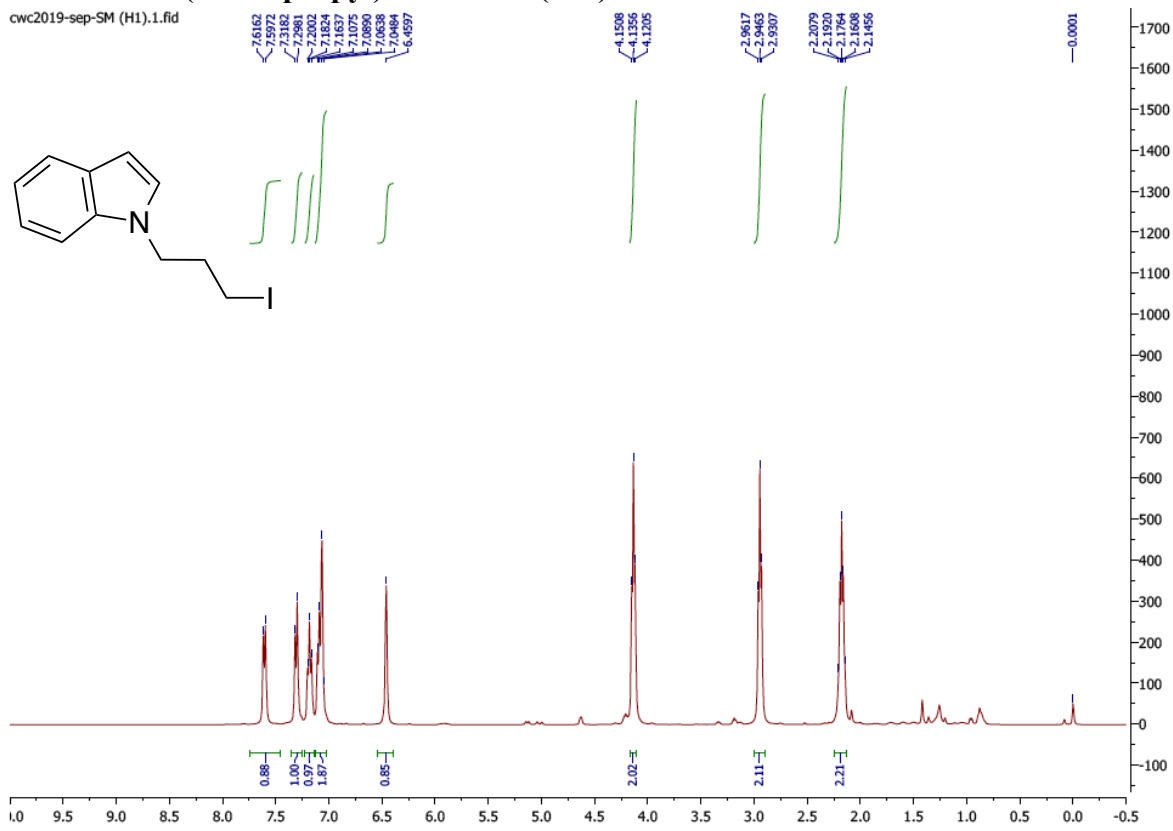


¹H and ¹³C NMR of 9-(3-Iodopropyl)-9H-carbazole (S14)

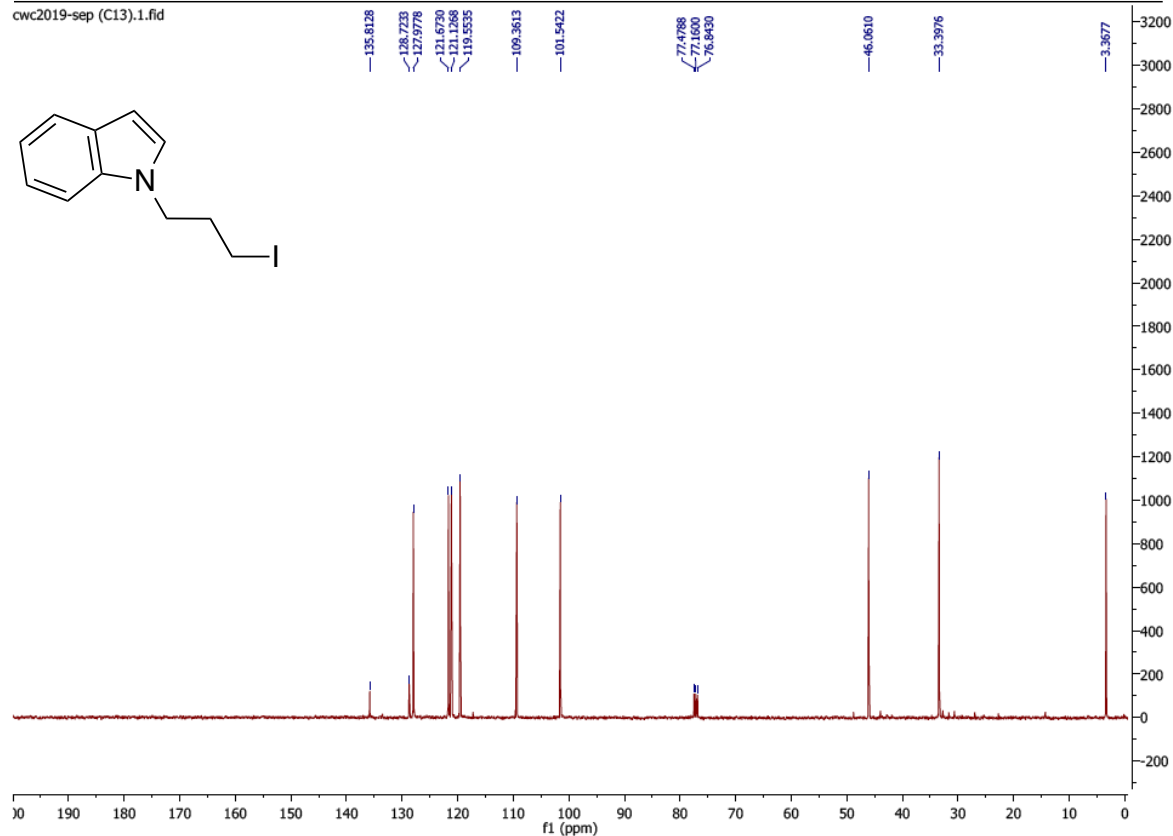


¹H and ¹³C NMR of 1-(3-Iodopropyl)-1H-indole (S15)

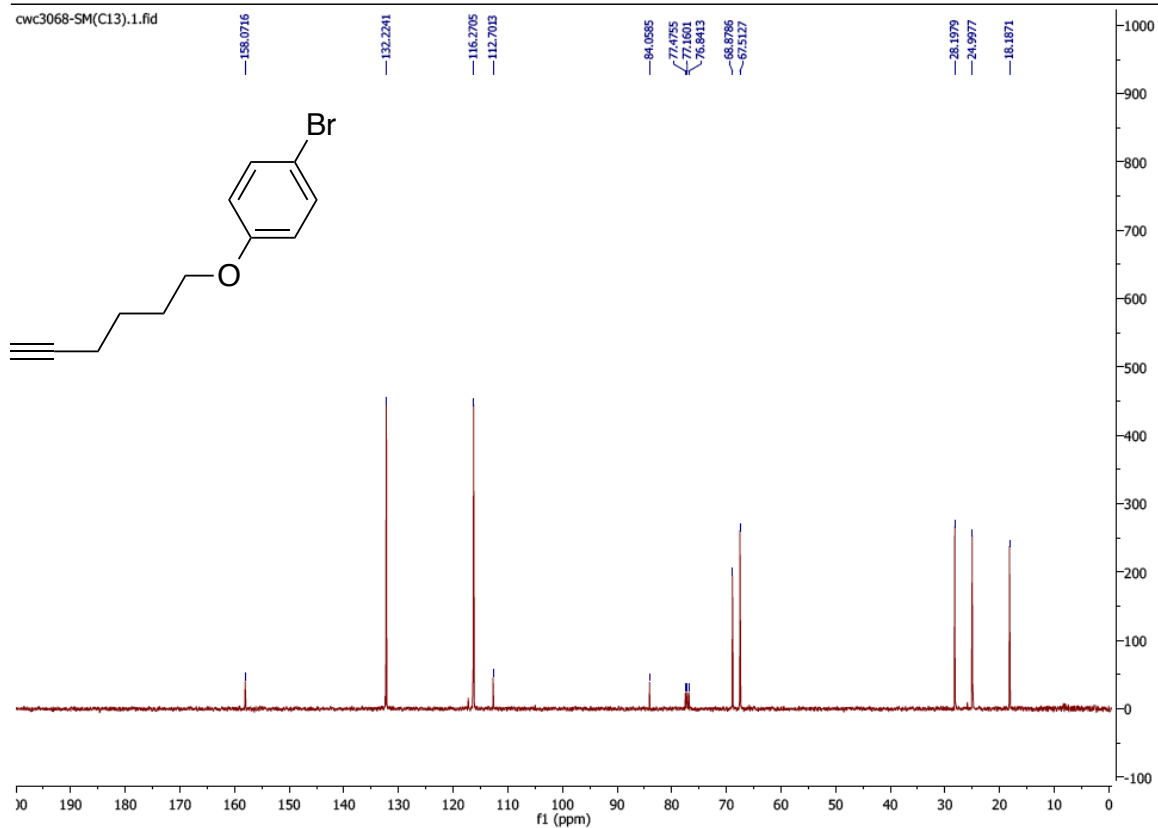
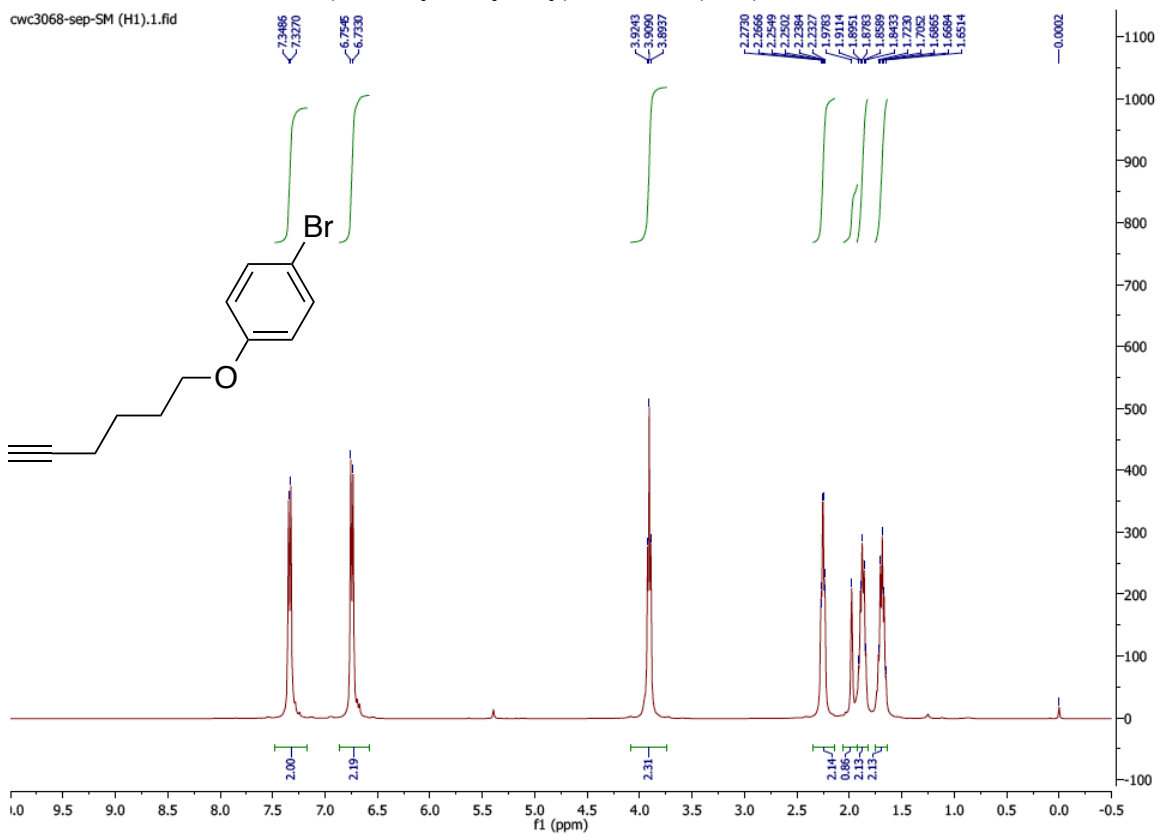
cwc2019-sep-SM (H1).1.fid



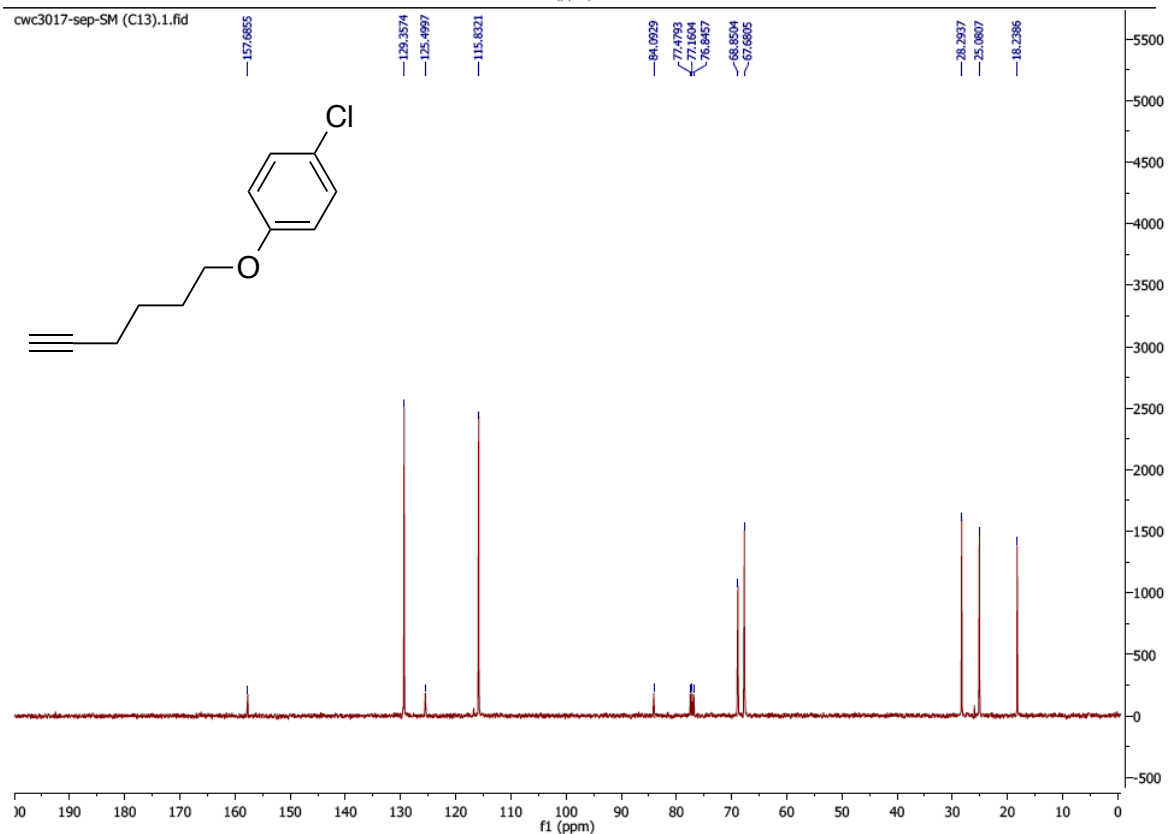
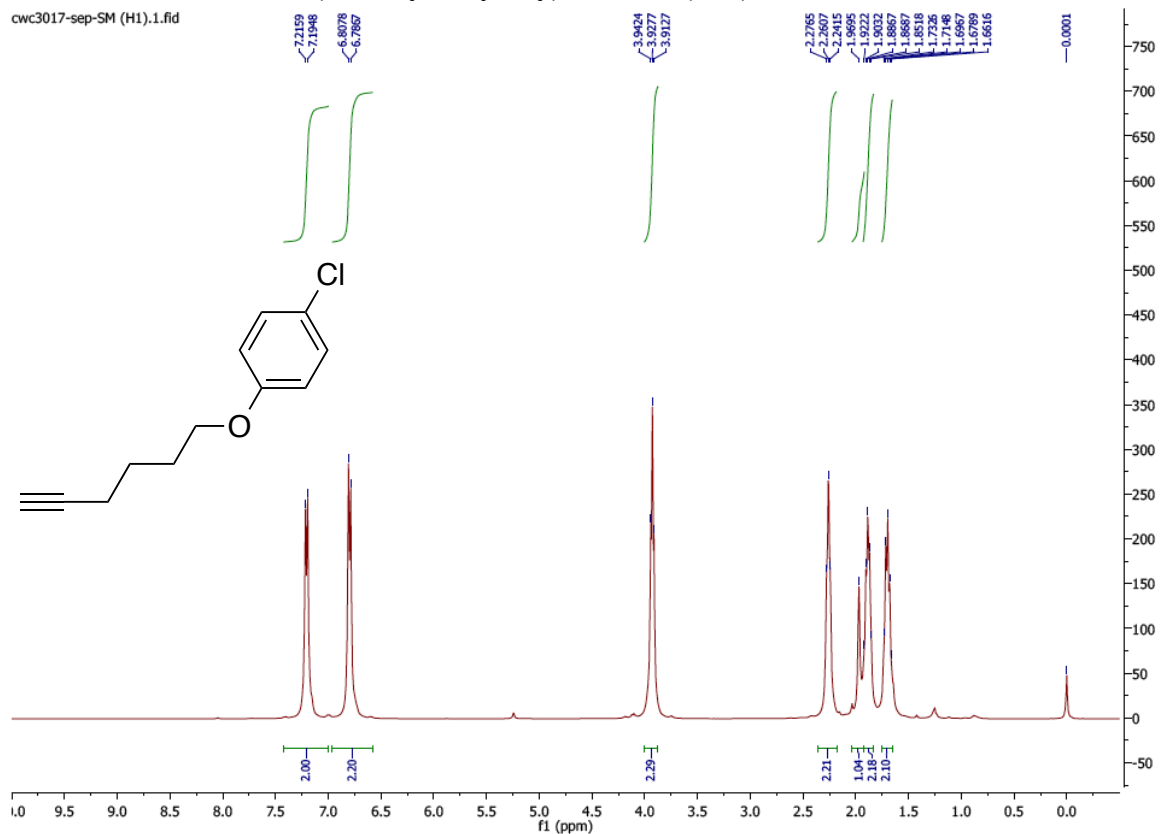
cwc2019-sep (C13).1.fid



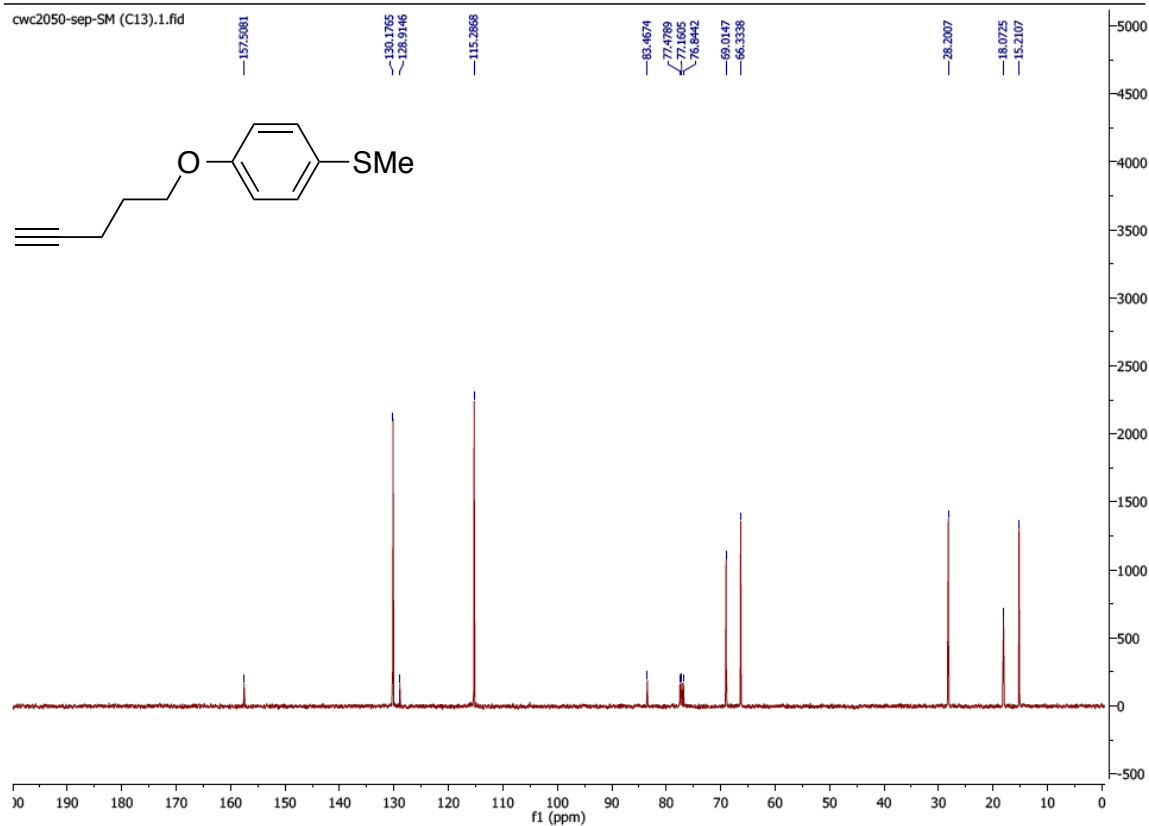
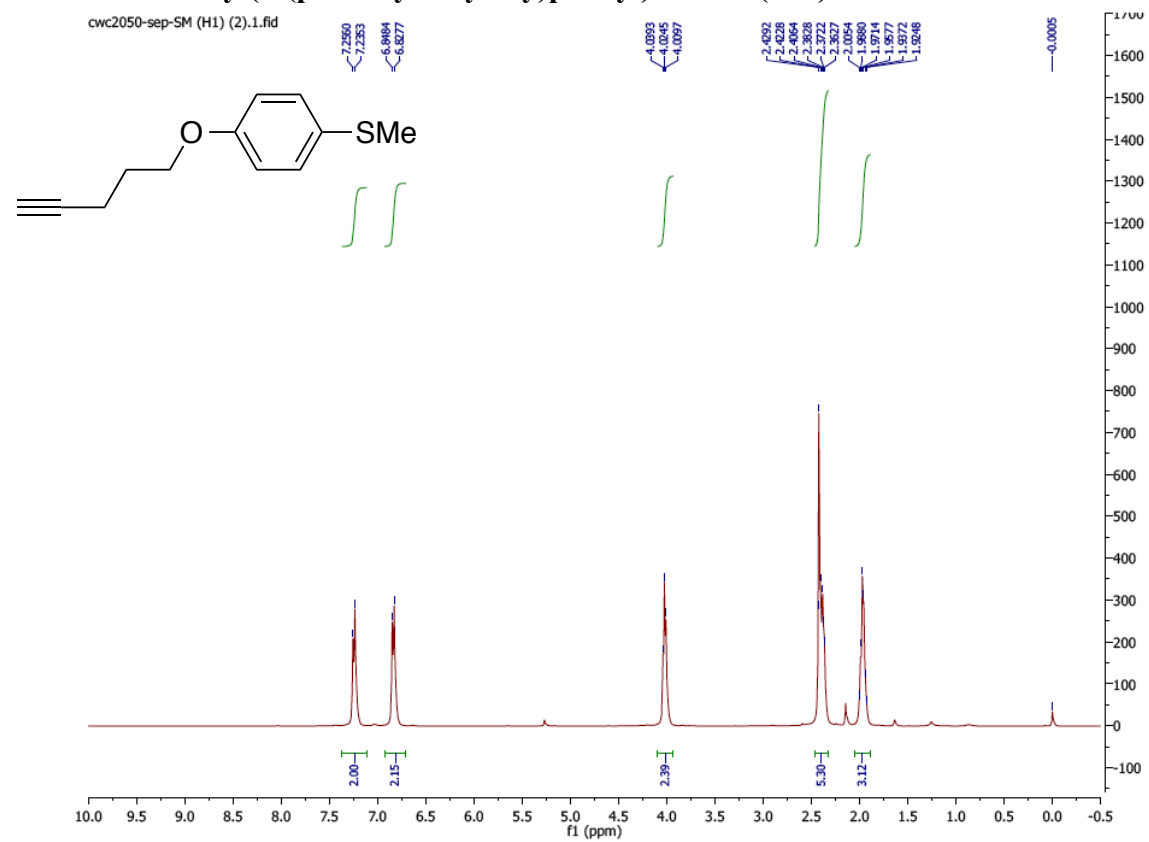
¹H and ¹³C NMR of 1-Bromo-4-(hex-5-yn-1-yloxy)benzene (S18)



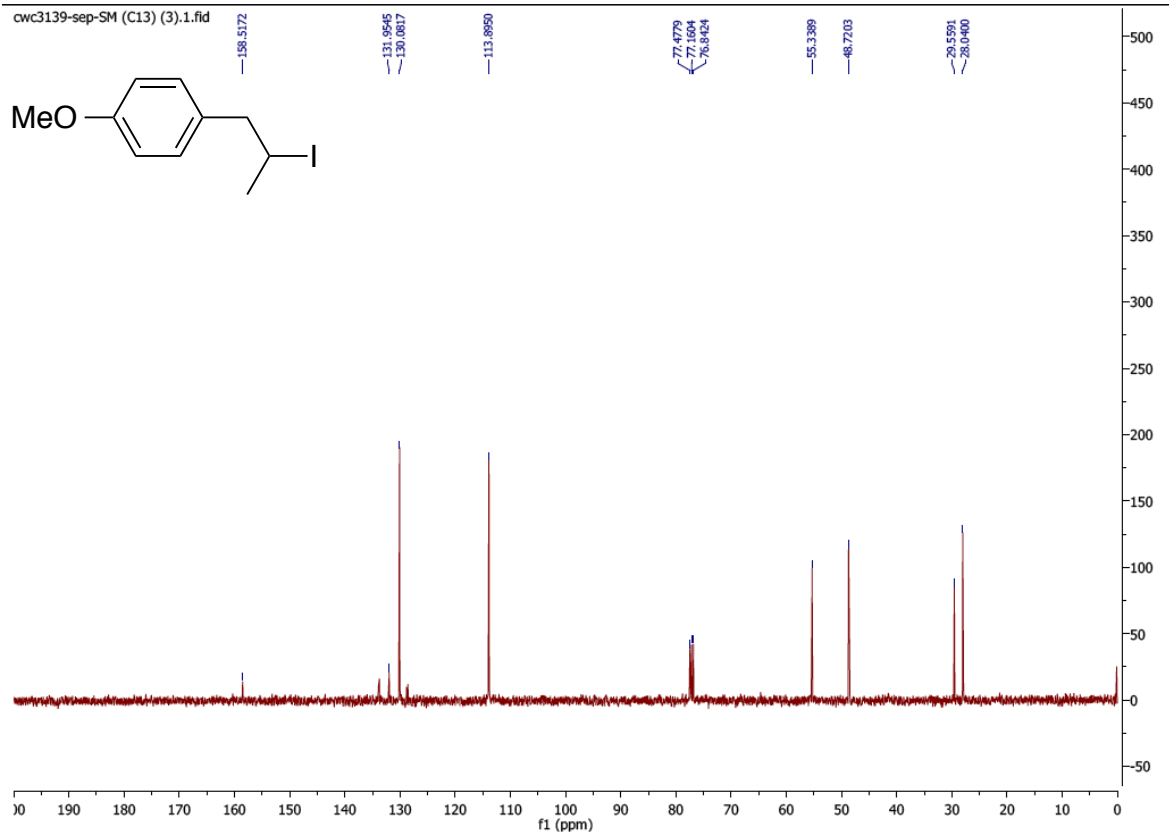
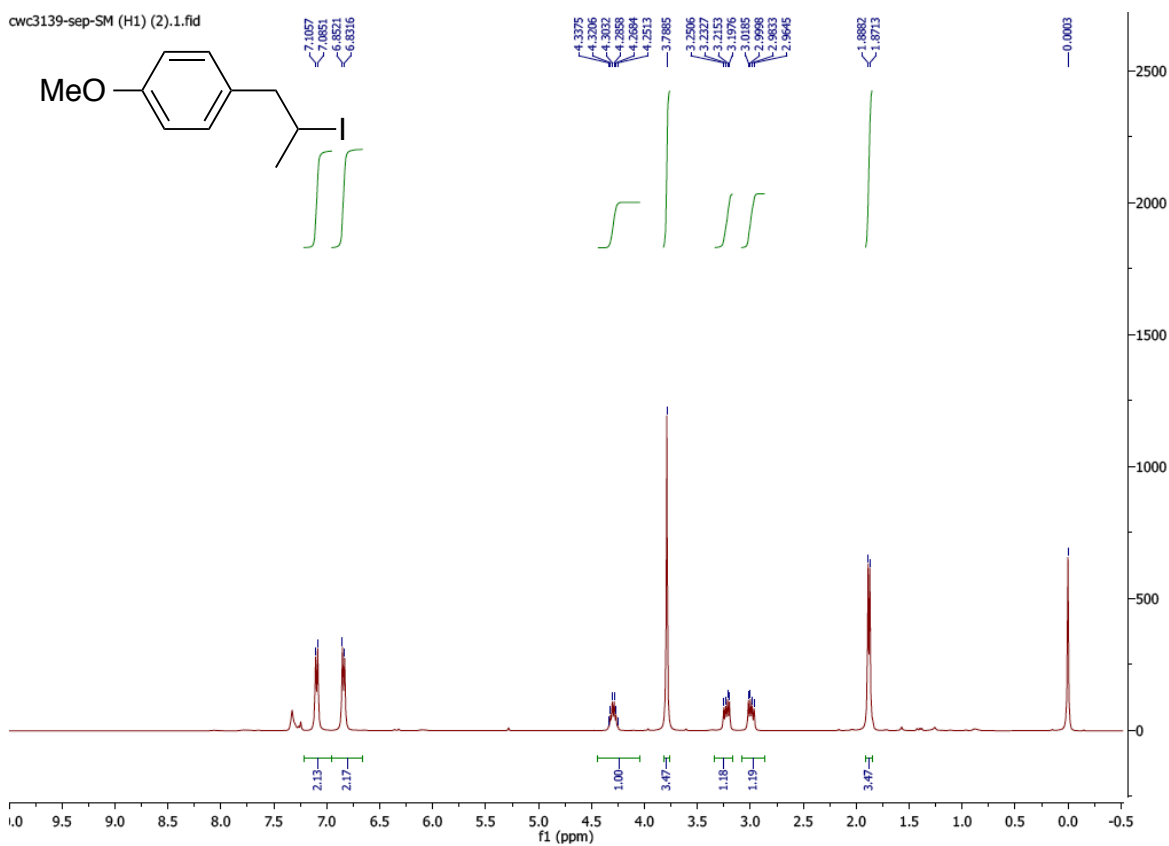
¹H and ¹³C NMR of 1-Chloro-4-(hex-5-yn-1-yloxy)benzene (S19)



¹H and ¹³C NMR of Methyl(4-(pent-4-yn-1-yloxy)phenyl)sulfane (S20)

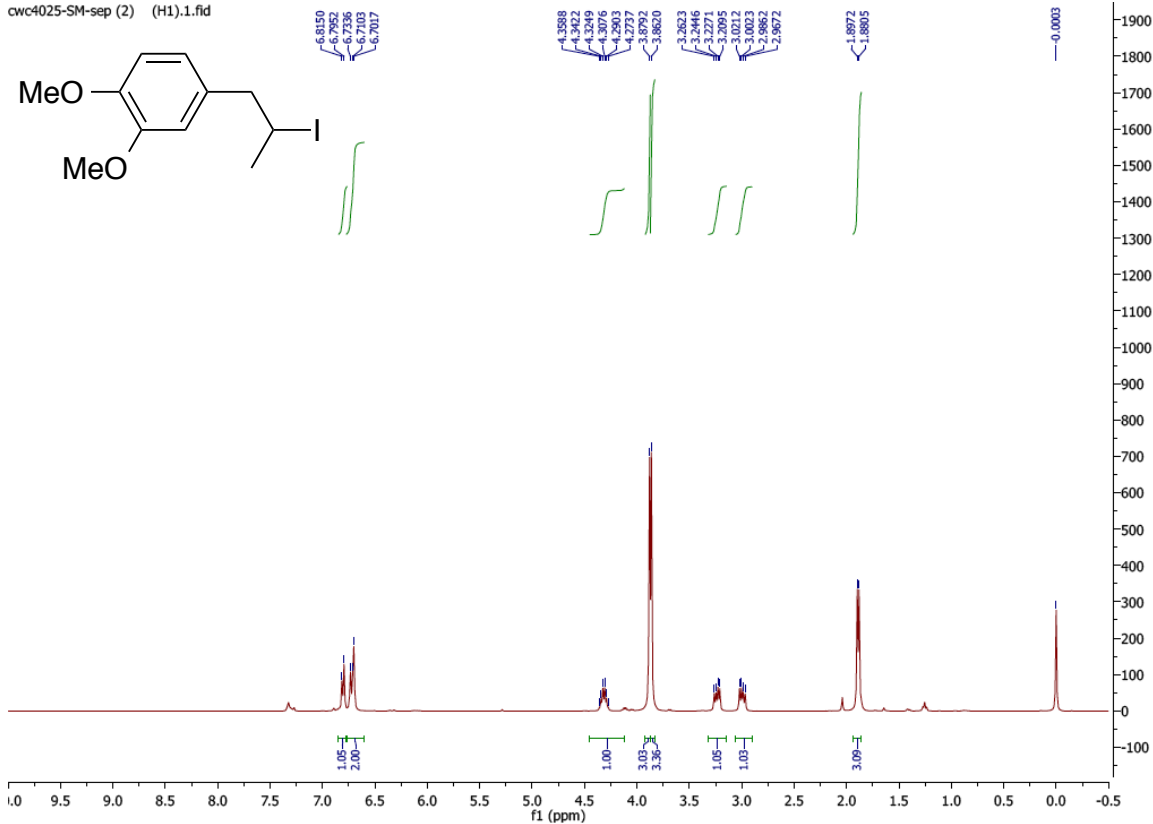


¹H and ¹³C NMR of 1-(2-Iodopropyl)-4-methoxybenzene (S21)

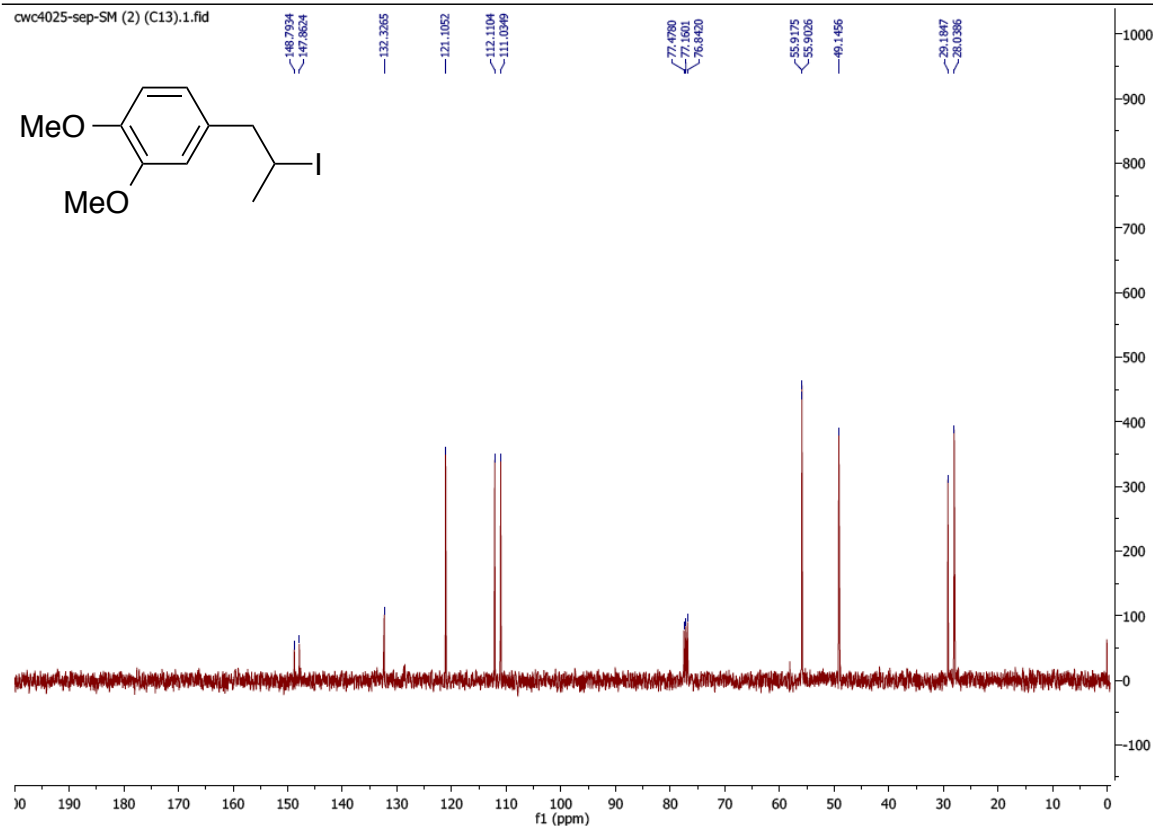


¹H and ¹³C NMR of 4-(2-Iodopropyl)-1,2-dimethoxybenzene (S22)

cwc4025-SM-sep (2) (H1).1.fid

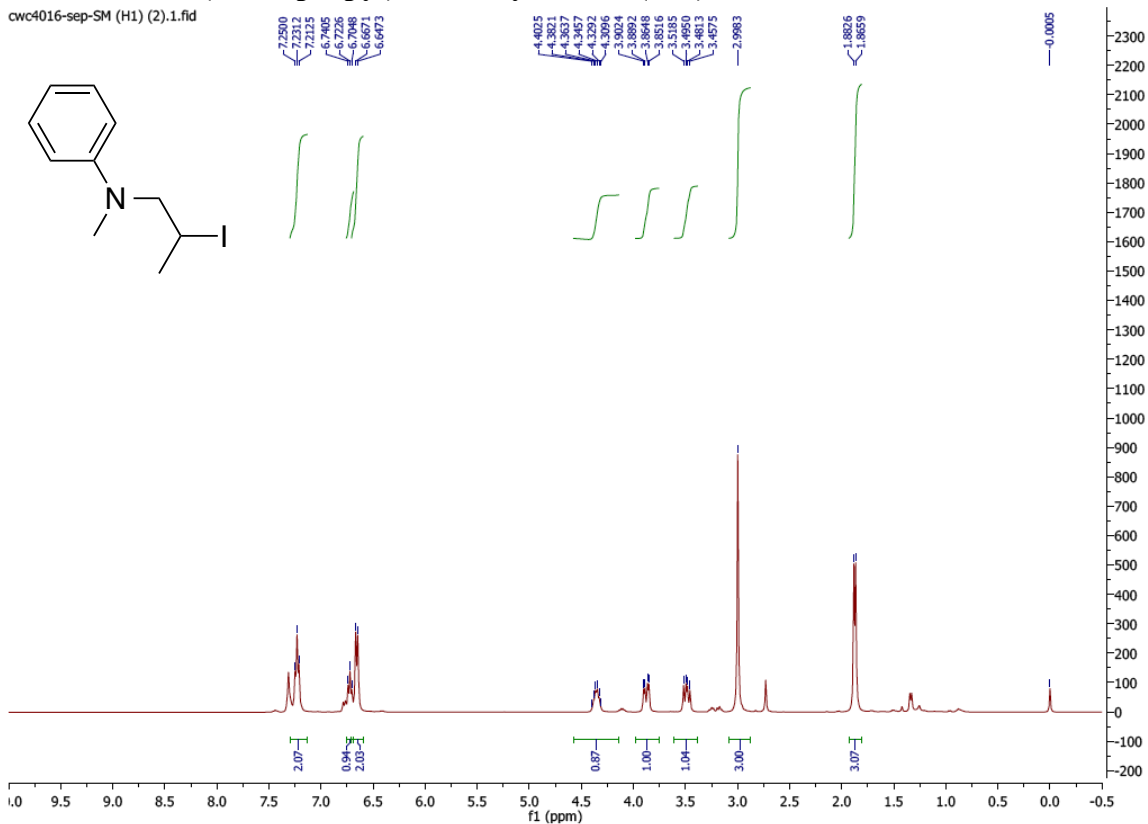


cwc4025-sep-SM (2) (C13).1.fid

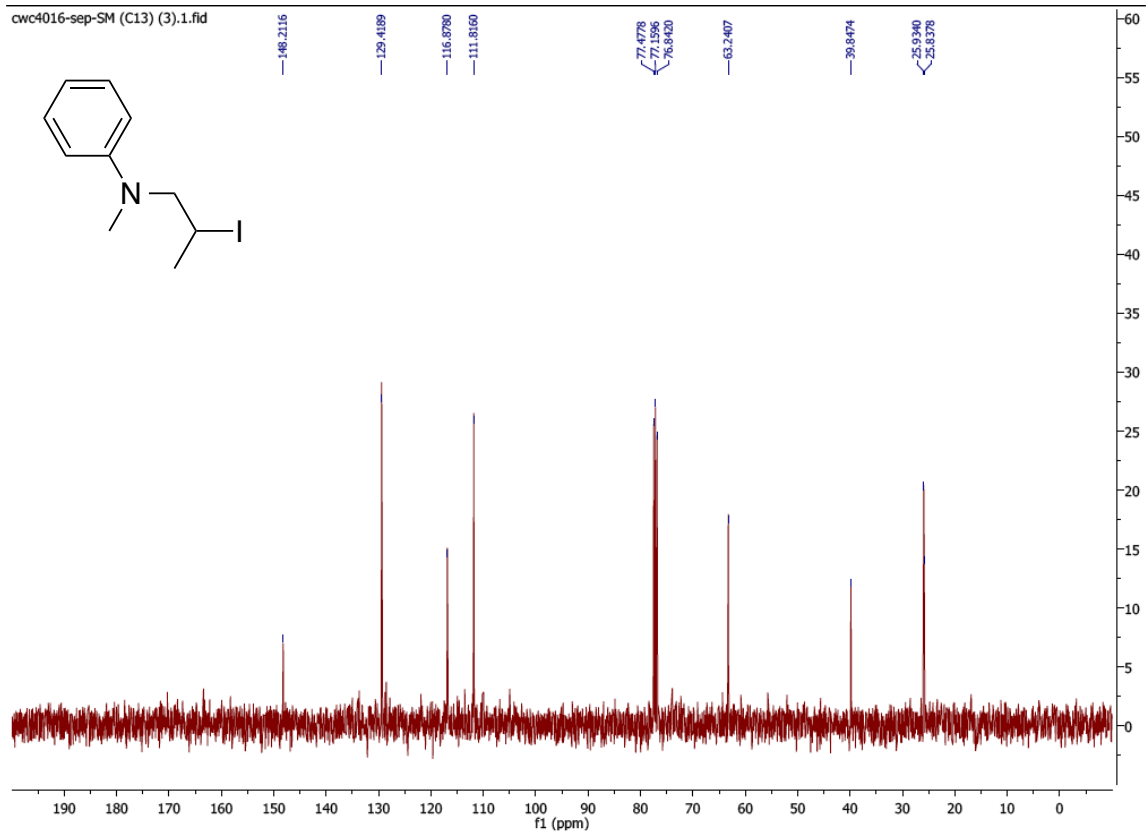


¹H and ¹³C NMR of *N*-(2-iodopropyl)-*N*-methylaniline (S23)

cwc4016-sep-SM (H1) (2).1.fid

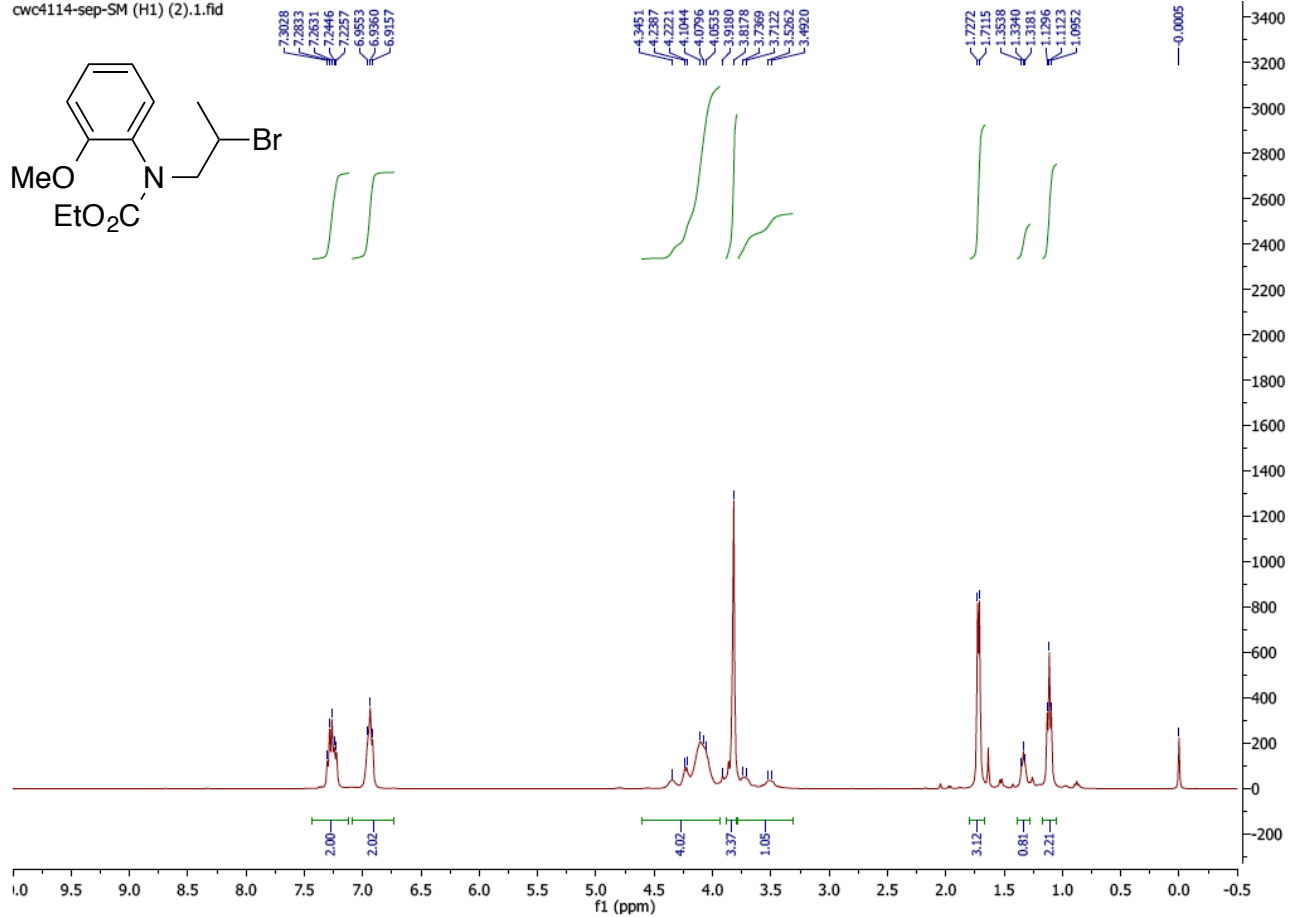


cwc4016-sep-SM (C13) (3).1.fid

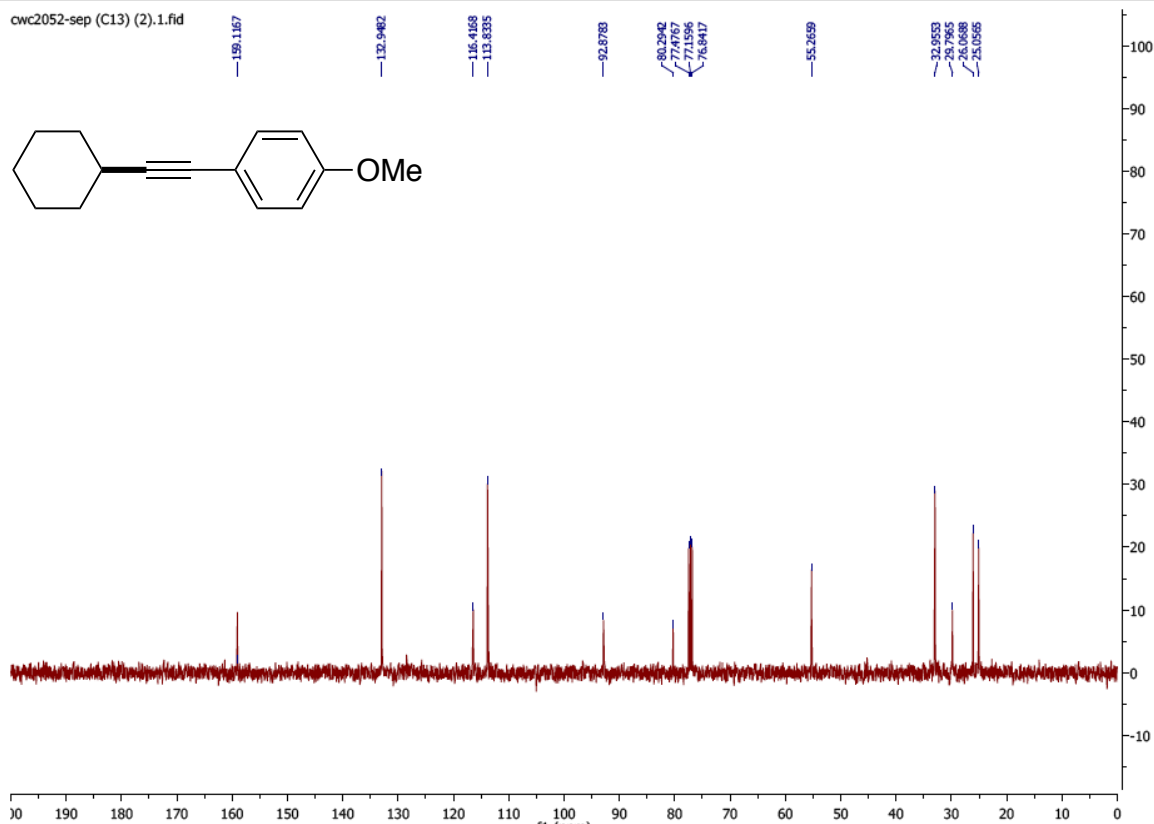
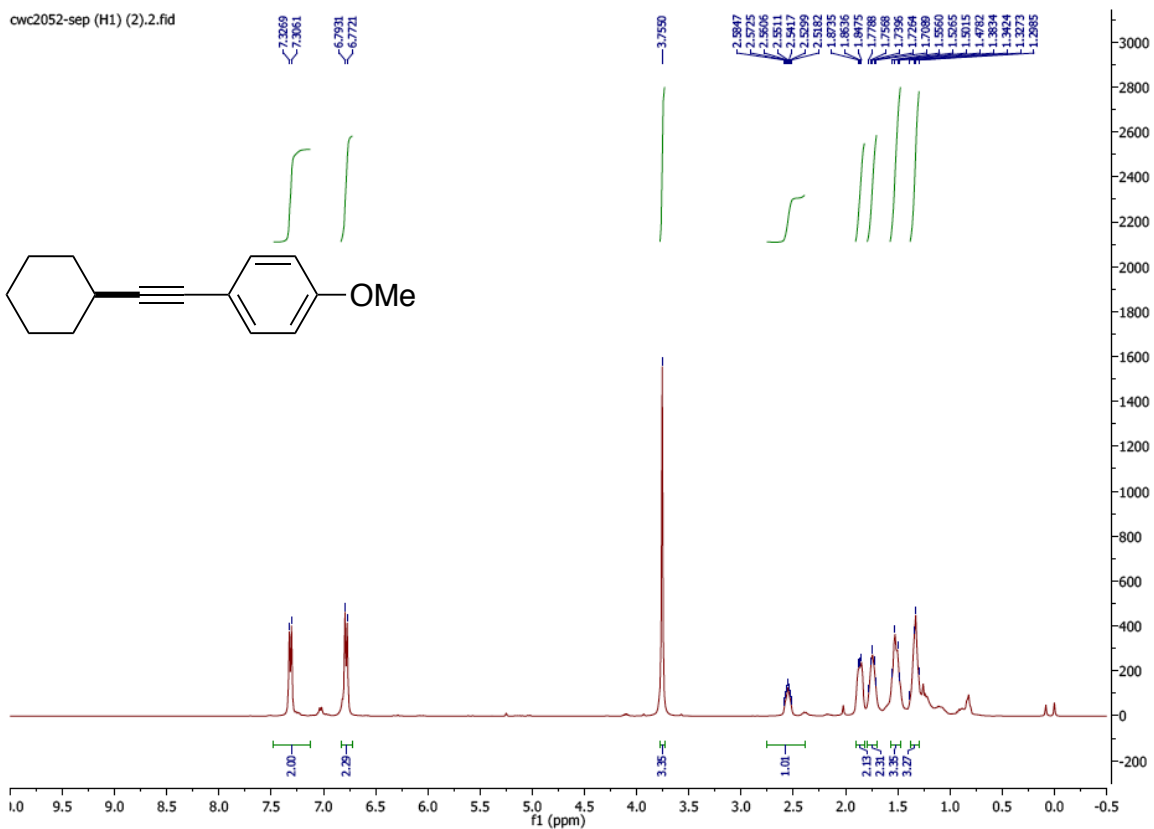


¹H and ¹³C NMR of Ethyl (2-Bromopropyl)(2-methoxyphenyl)carbamate (S24)

cwc4114-sep-SM (H1) (2).1.fid

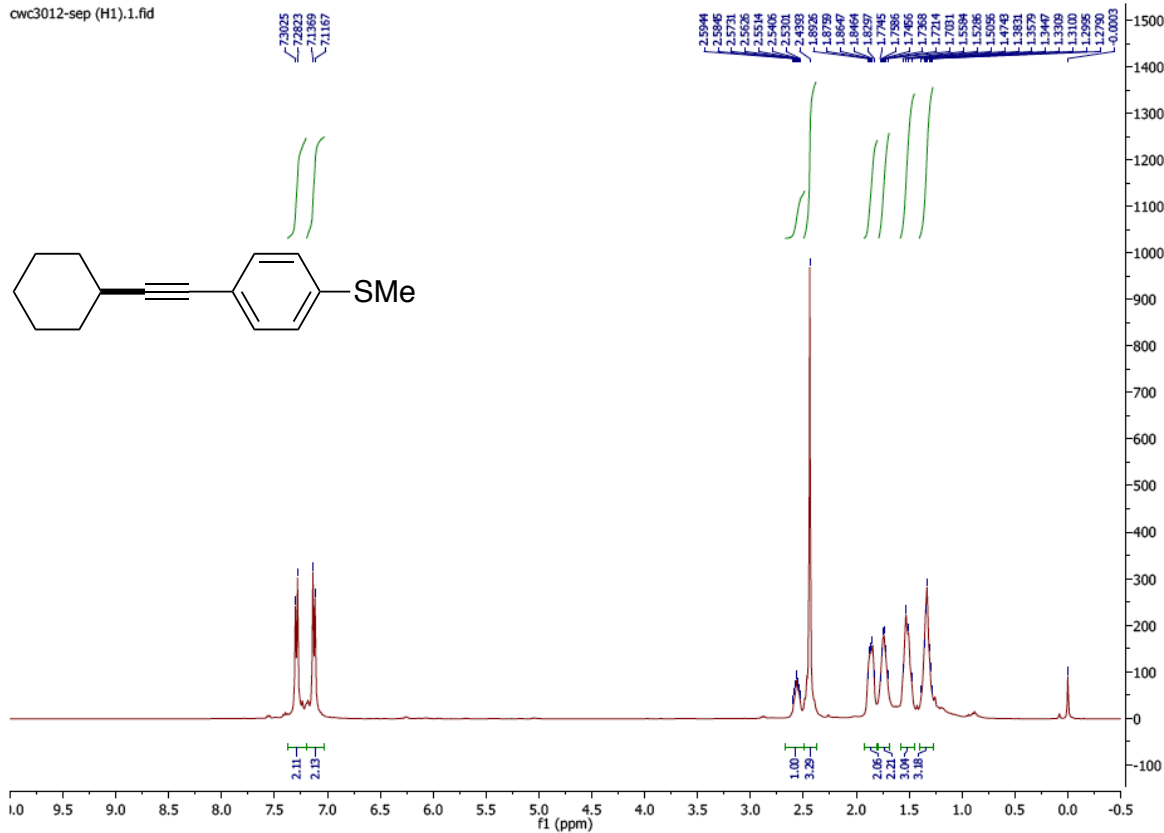


^1H and ^{13}C NMR of 1-(Cyclohexylethynyl)-4-methoxybenzene (2a)

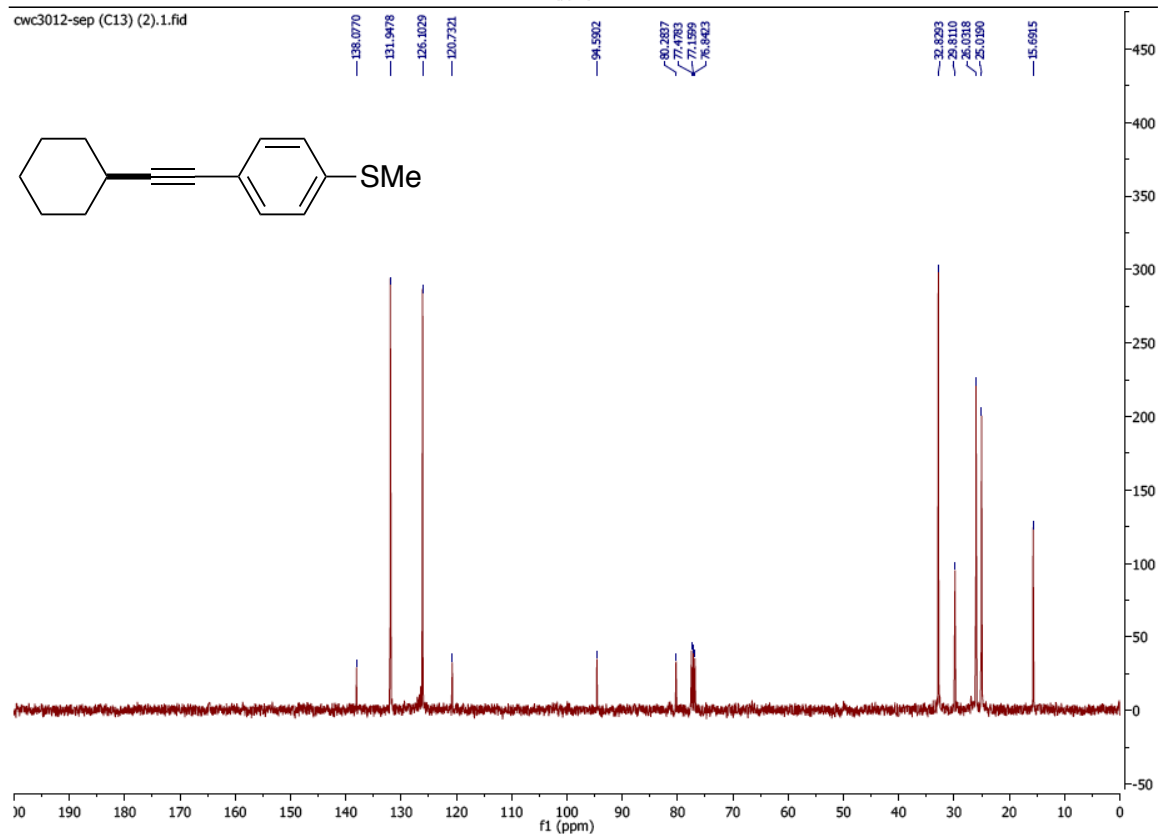


¹H and ¹³C NMR of (4-(Cyclohexylethynyl)phenyl)(methyl)sulfane (2b)

cwc3012-sep (H1).1.fid

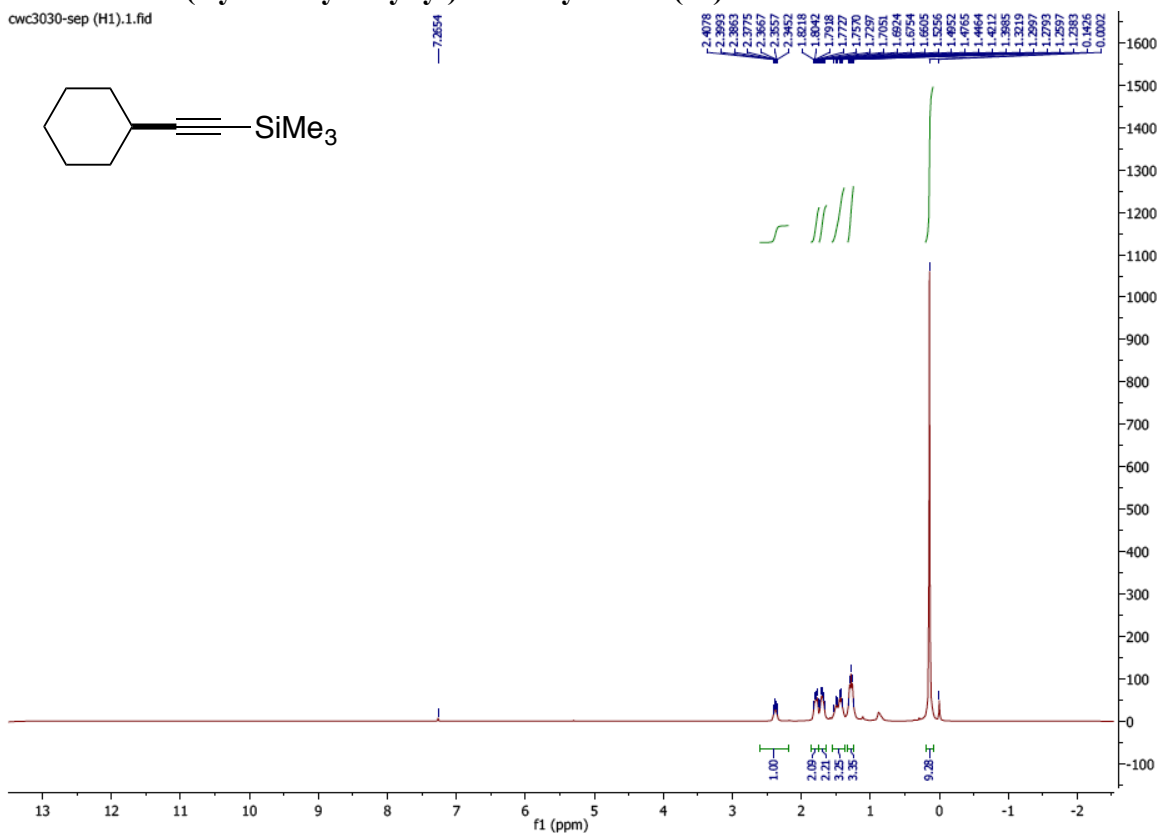
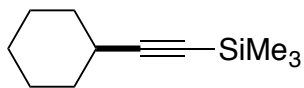


cwc3012-sep (C13) (2).1.fid

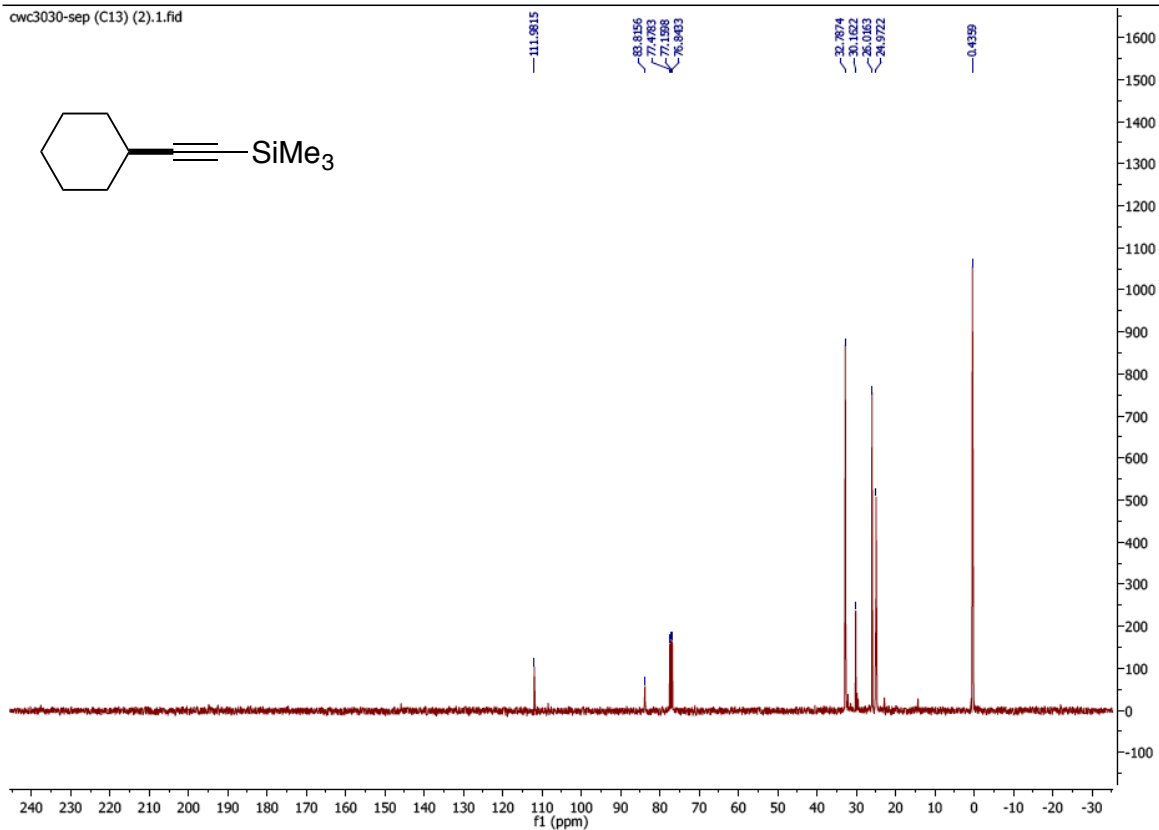
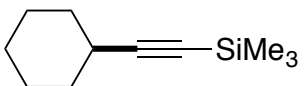


¹H and ¹³C NMR of (Cyclohexylethynyl)trimethylsilane (2c)

cwc3030-sep (H1).1.fid

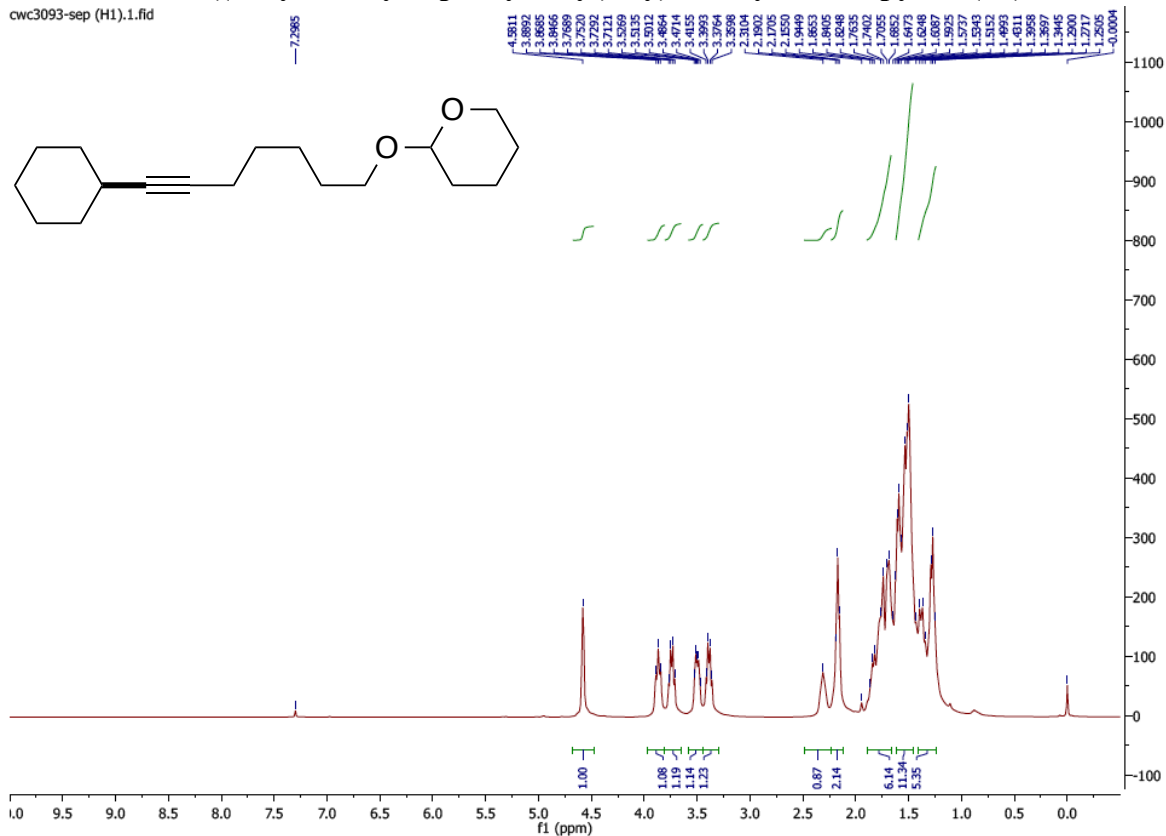


cwc3030-sep (C13) (2).1.fid

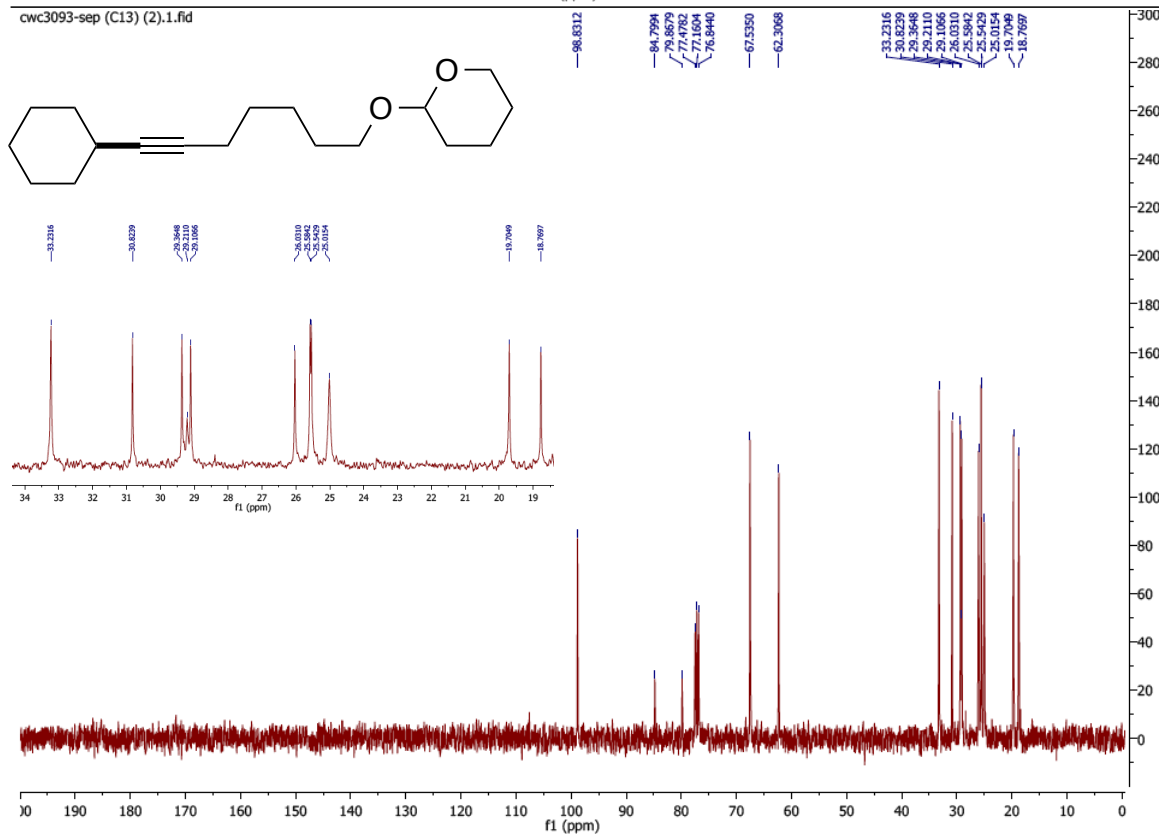


¹H and ¹³C NMR of 2-((7-Cyclohexylhept-6-yn-1-yl)oxy)tetrahydro-2H-pyran (2d)

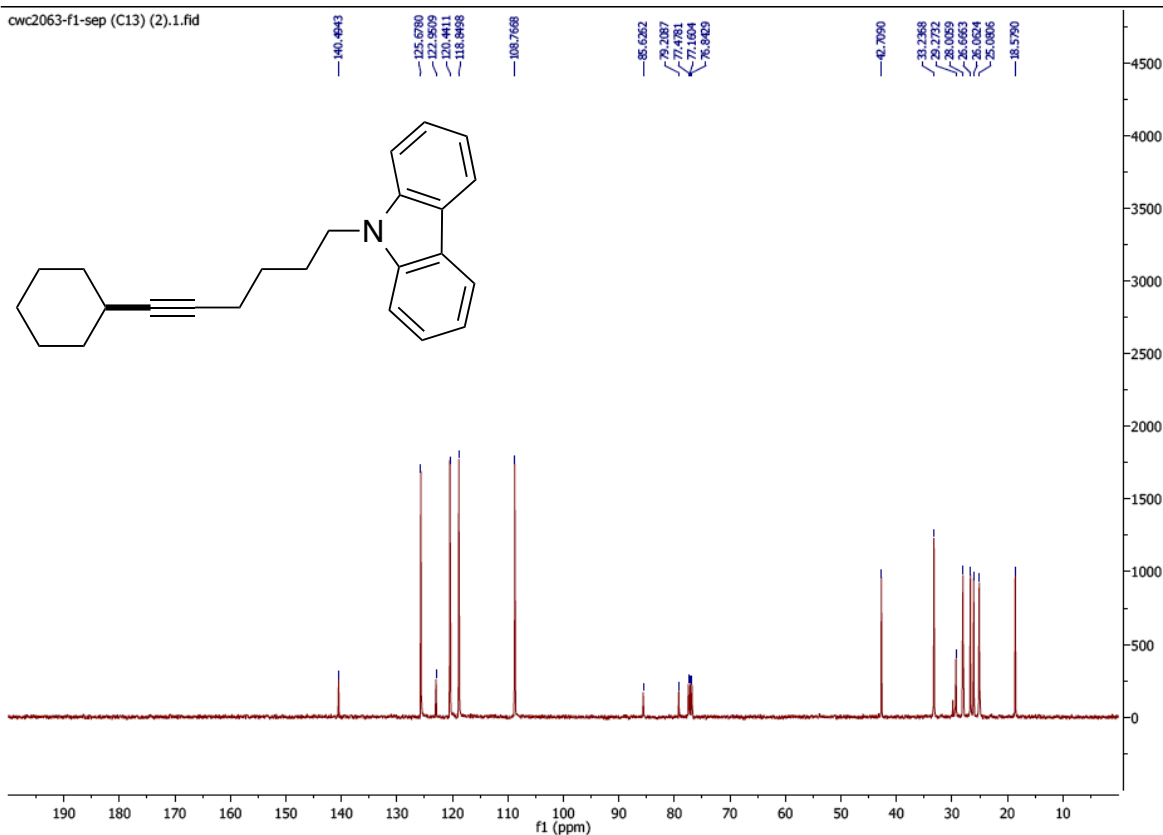
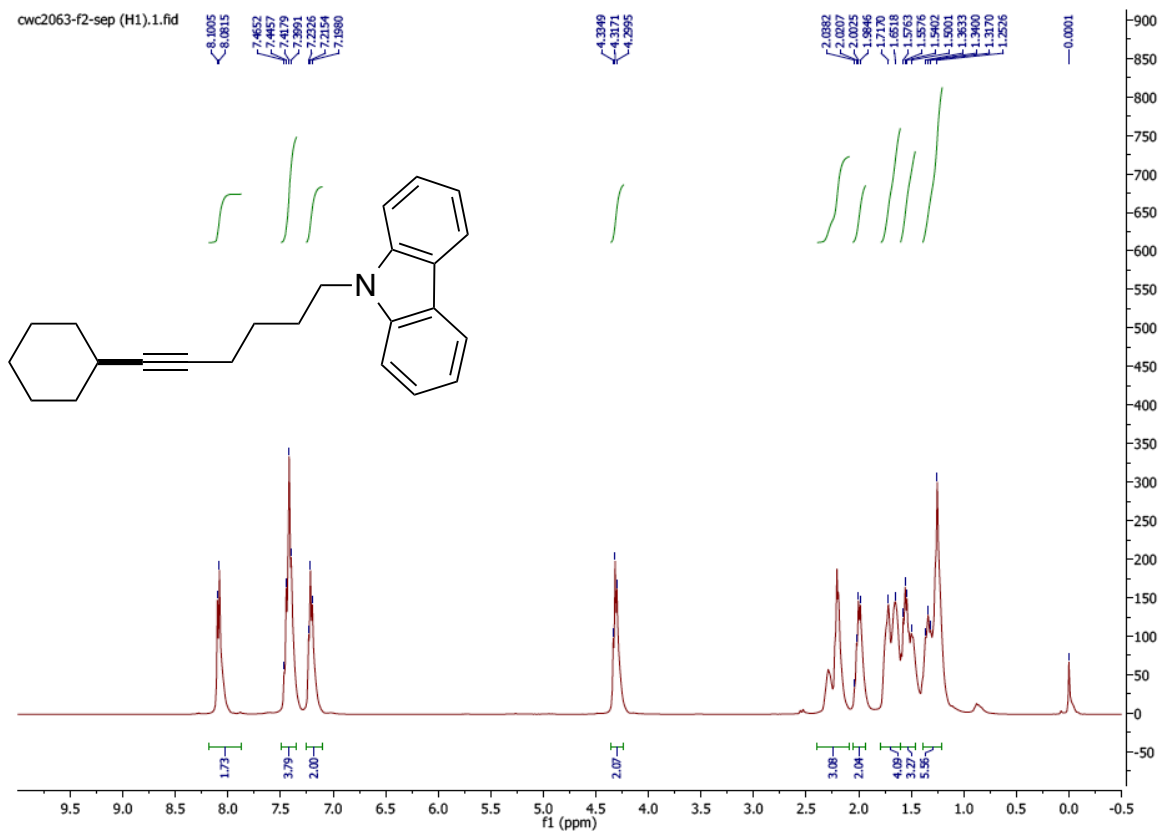
cwc3093-sep (H1).1.fid



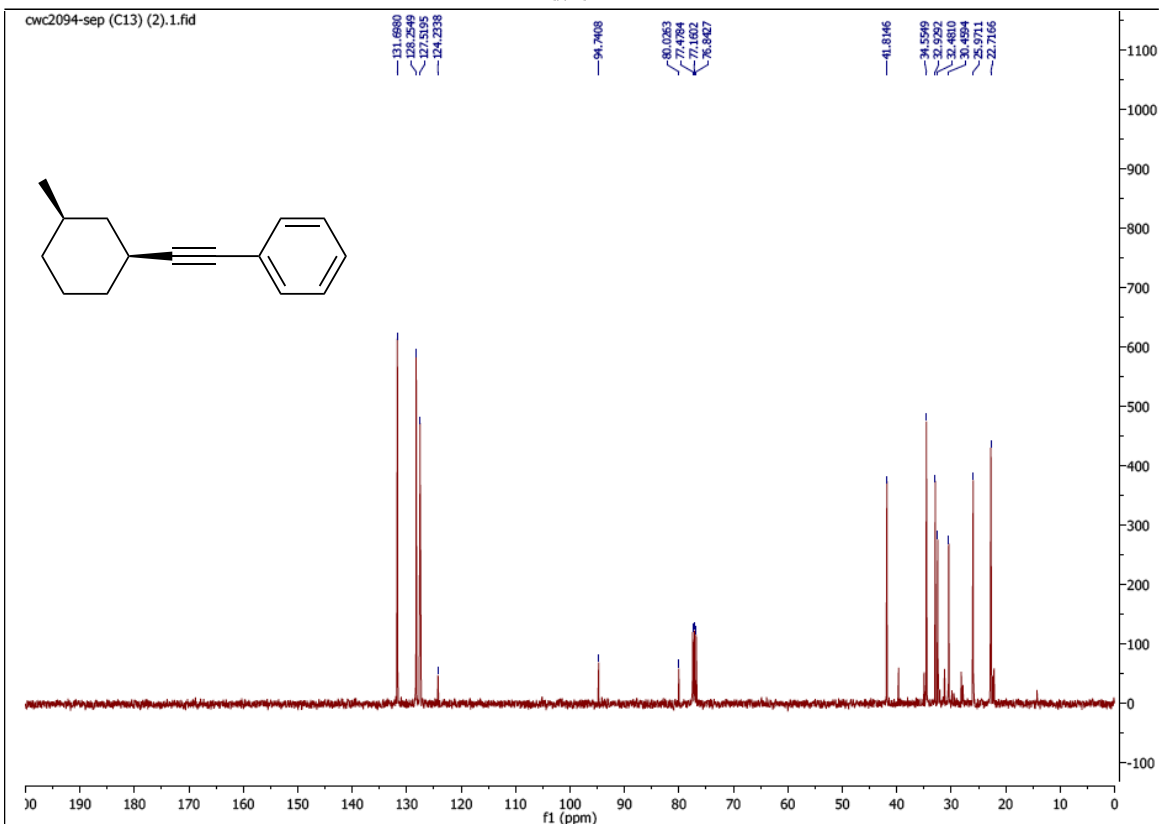
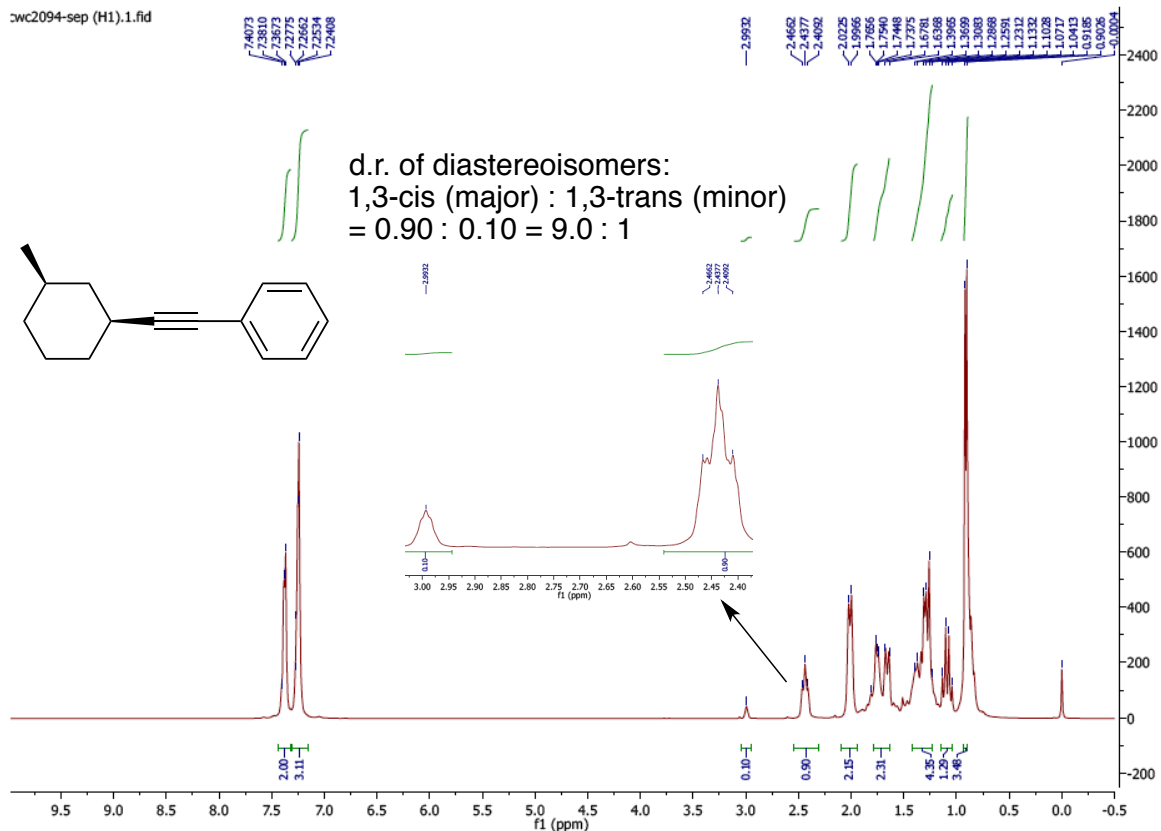
cwc3093-sep (C13) (2).1.fid



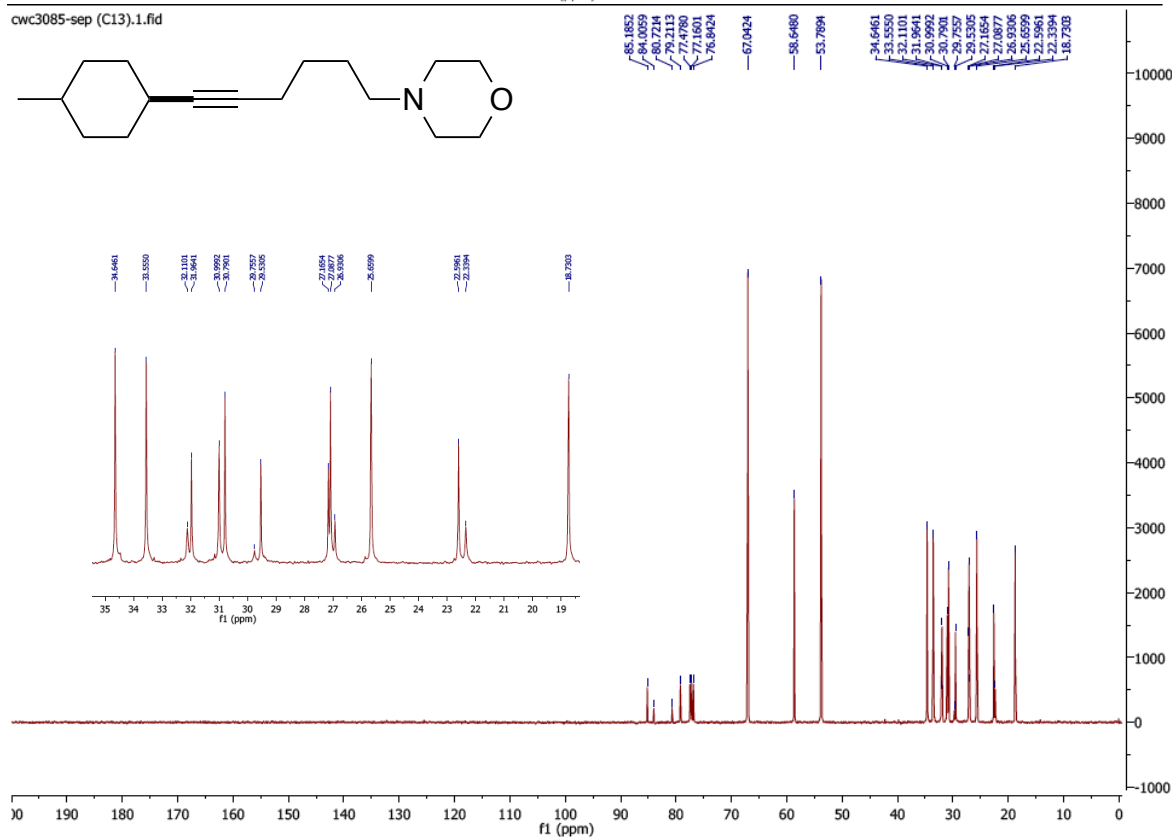
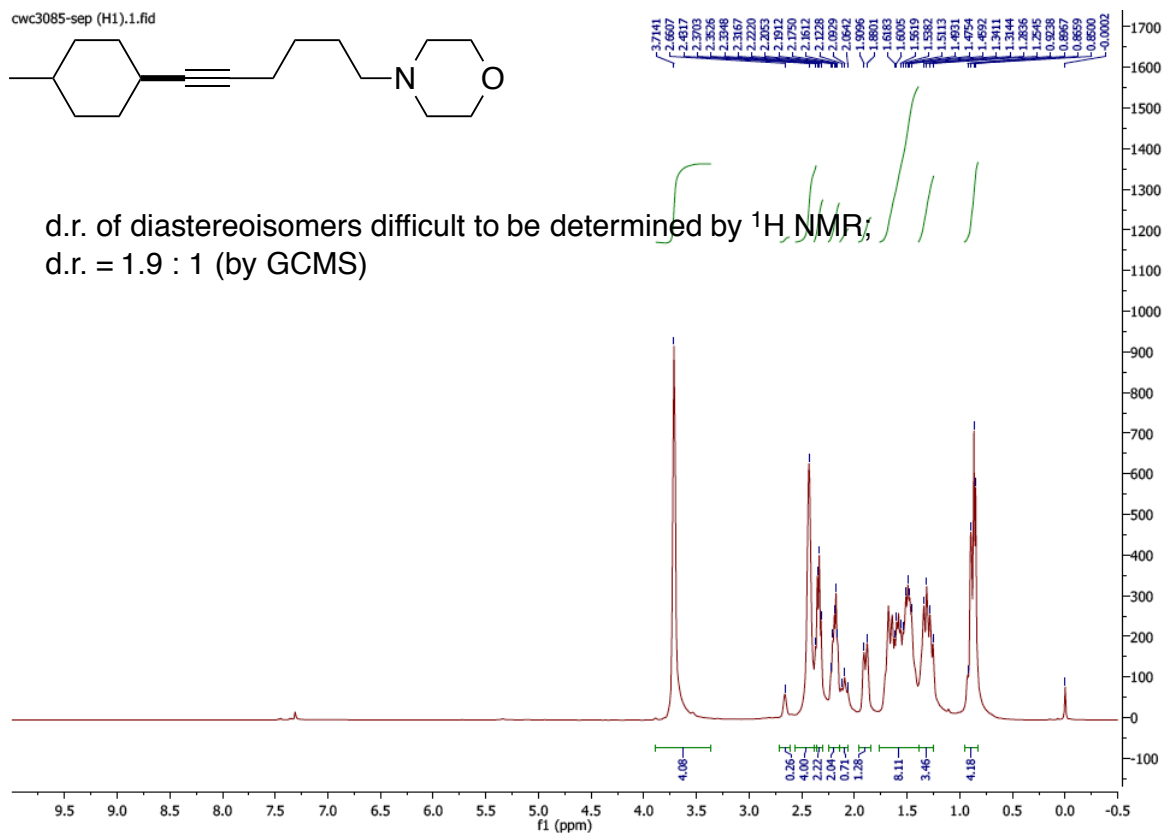
¹H and ¹³C NMR of 9-(6-Cyclohexylhex-5-yn-1-yl)-9H-carbazole (2e)



¹H and ¹³C NMR of ((3-Methylcyclohexyl)ethynyl)benzene (2f)

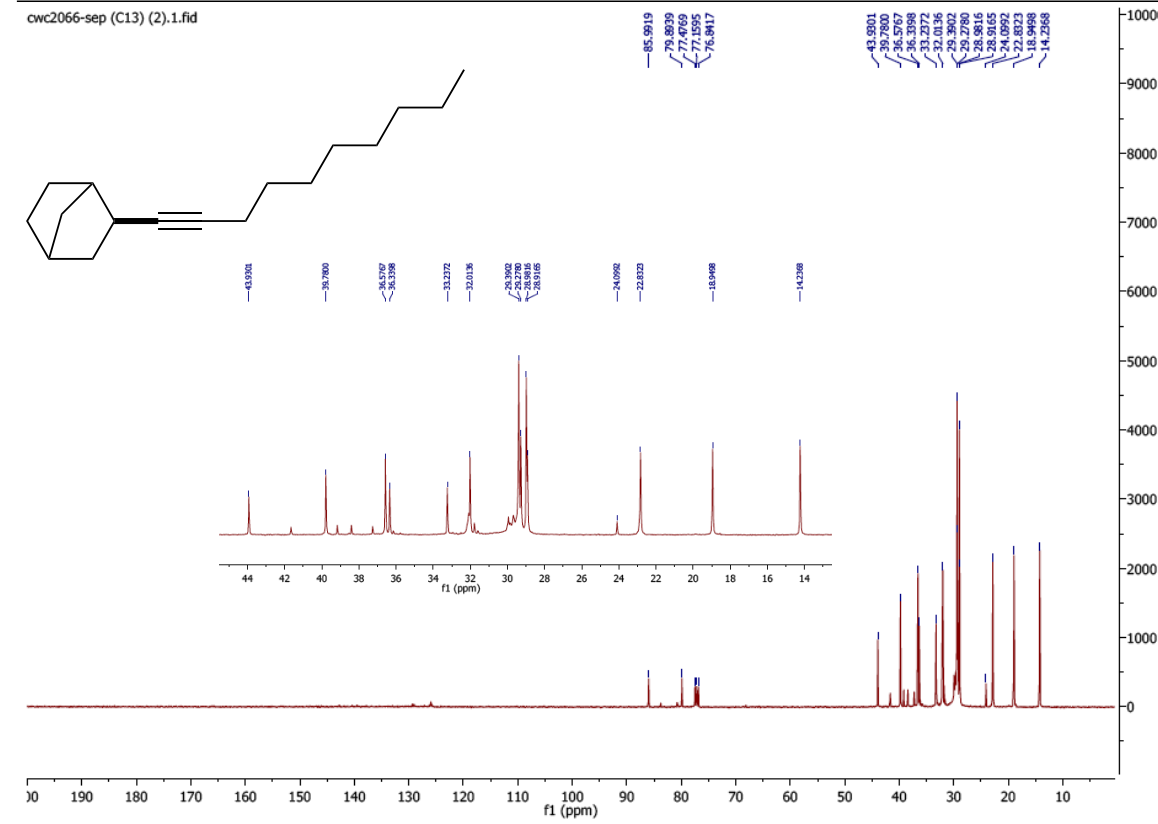
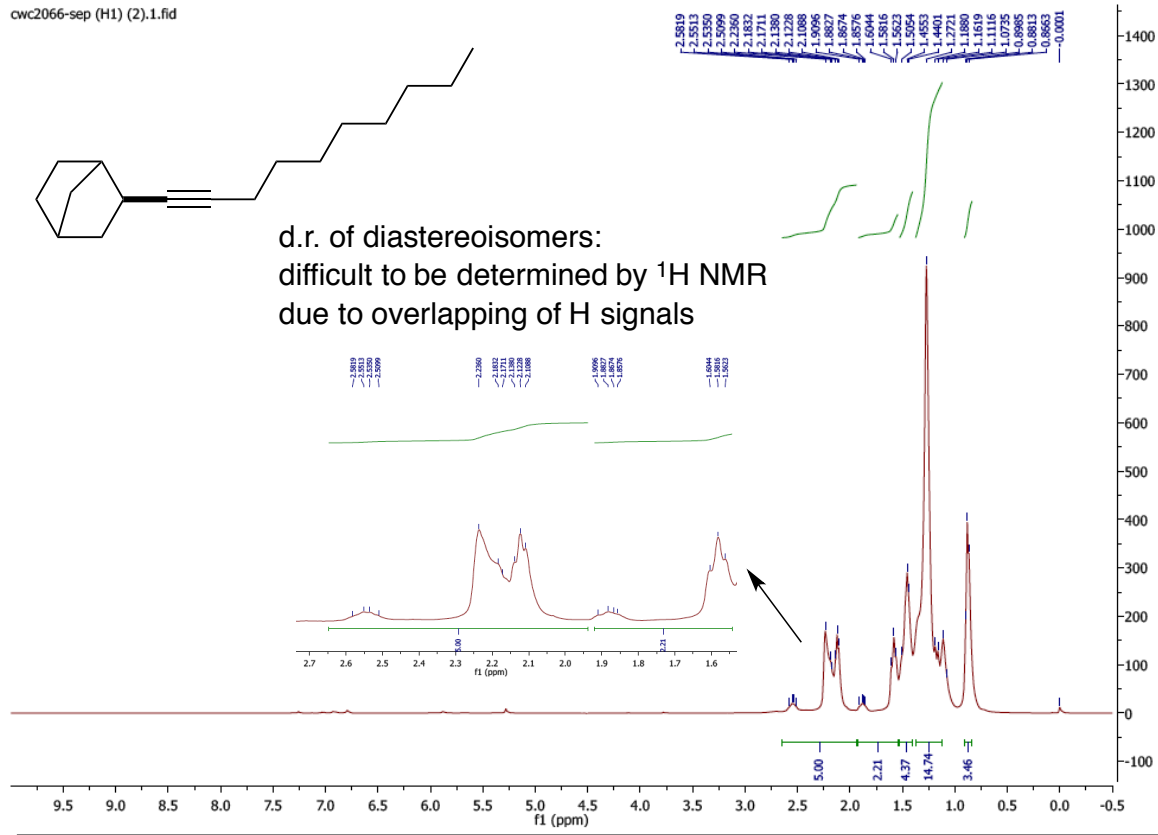


¹H and ¹³C NMR of 4-(6-(4-Methylcyclohexyl)hex-5-yn-1-yl)morpholine (2g)

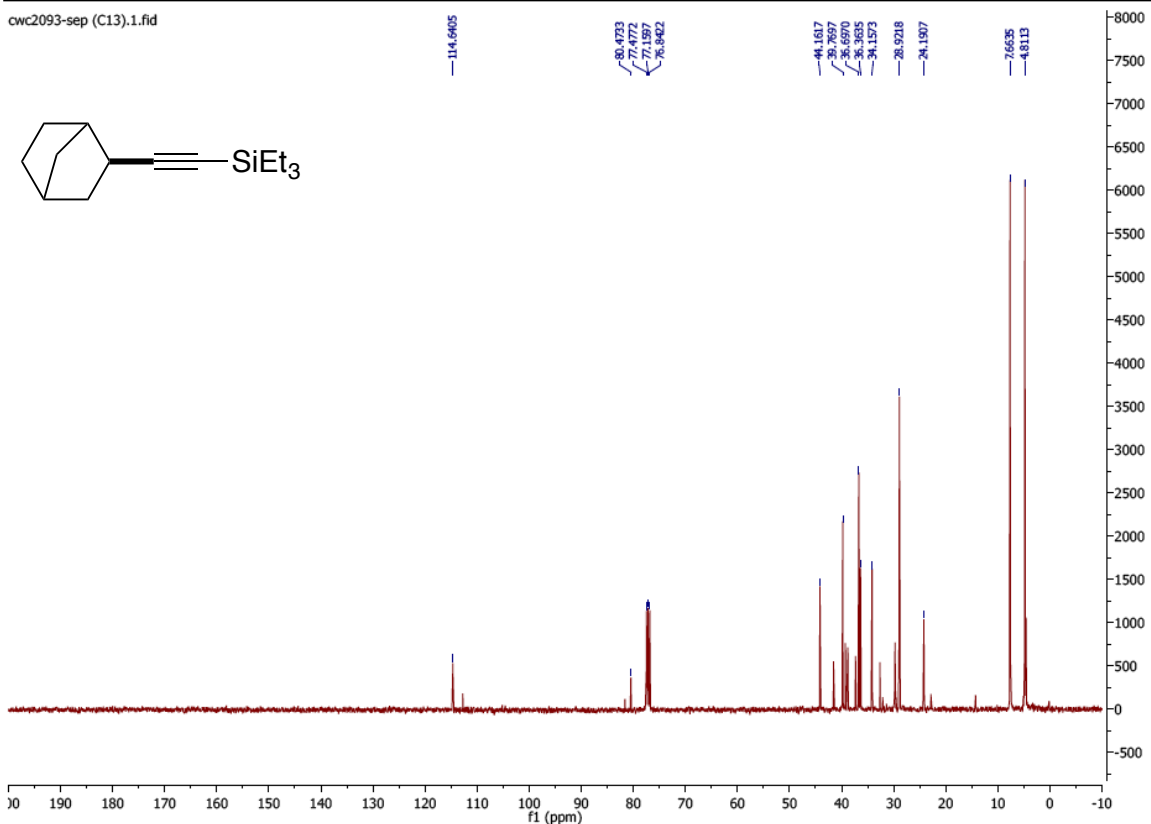
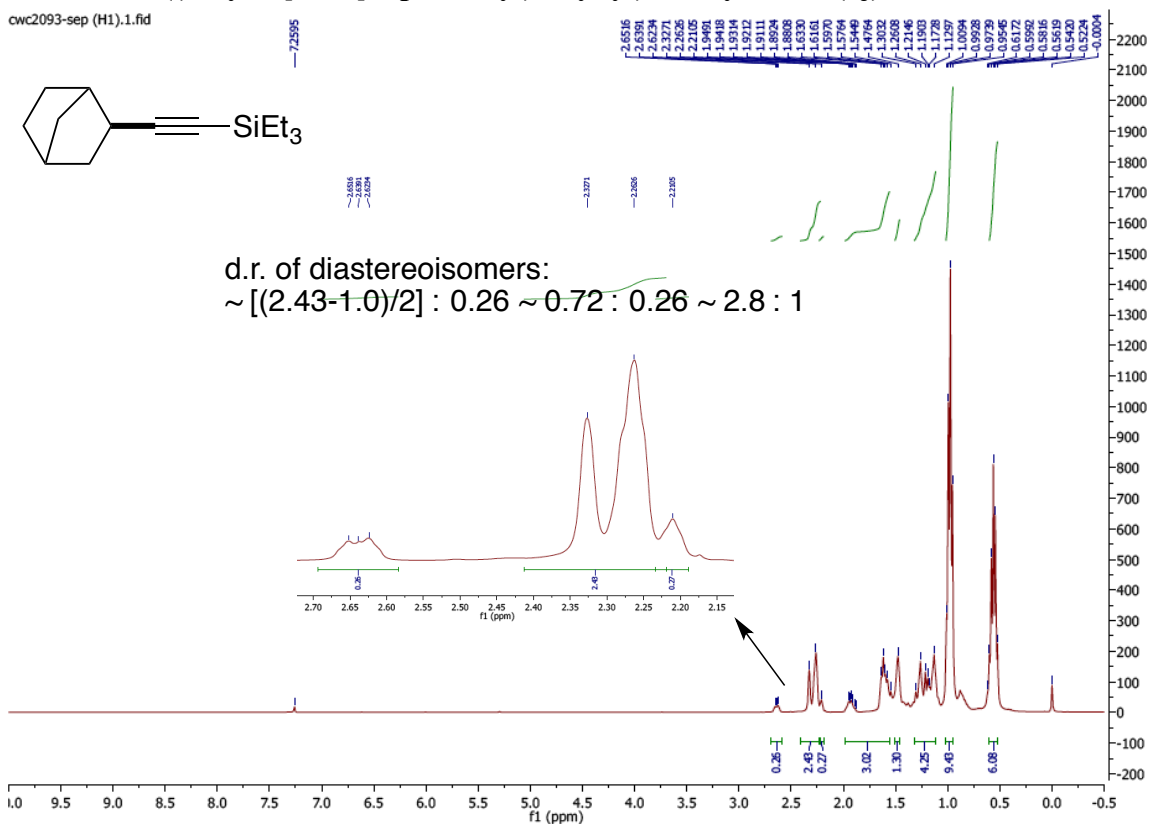


¹H and ¹³C NMR of 2-(Dec-1-yn-1-yl)bicyclo[2.2.1]heptane (2i)

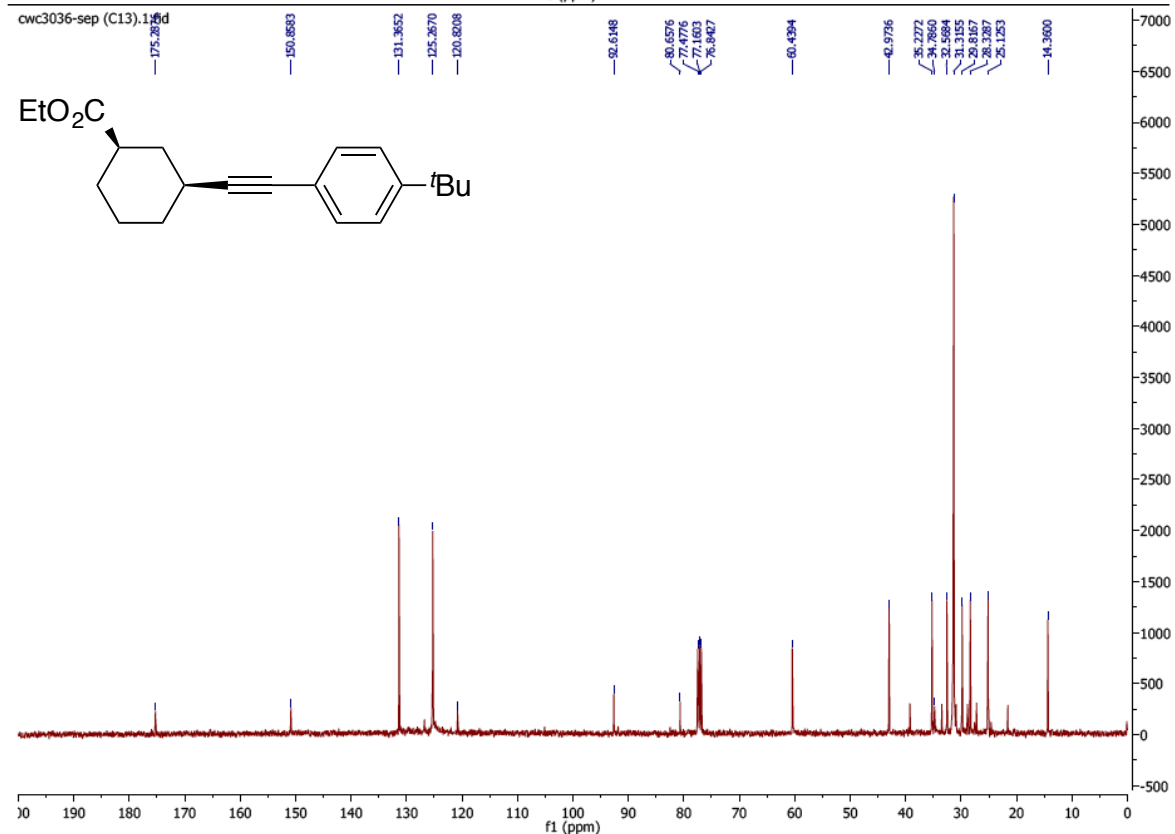
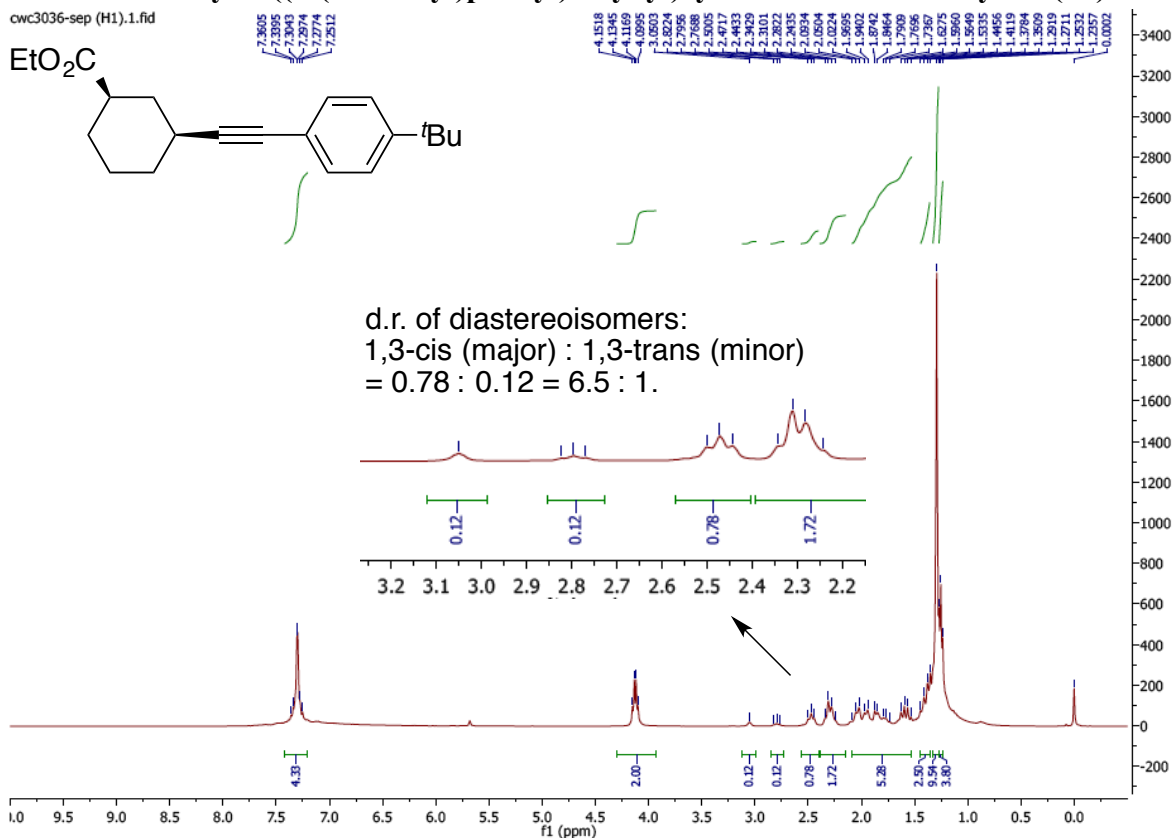
cwc2066-sep (H1) (2).1.fid



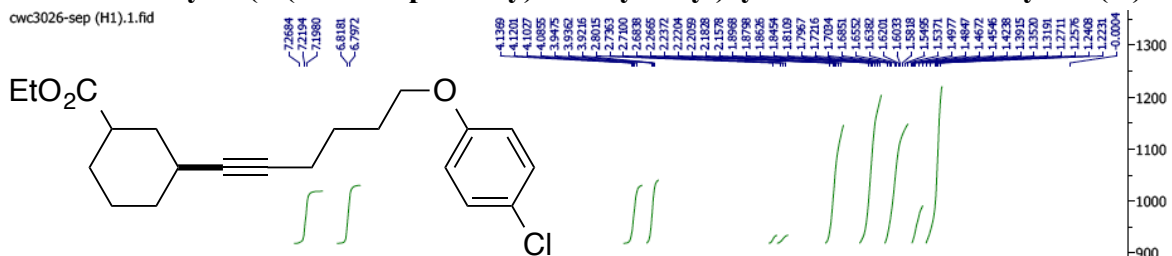
¹H and ¹³C NMR of ((Bicyclo[2.2.1]heptan-2-yl)ethynyl)triethylsilane (2j)



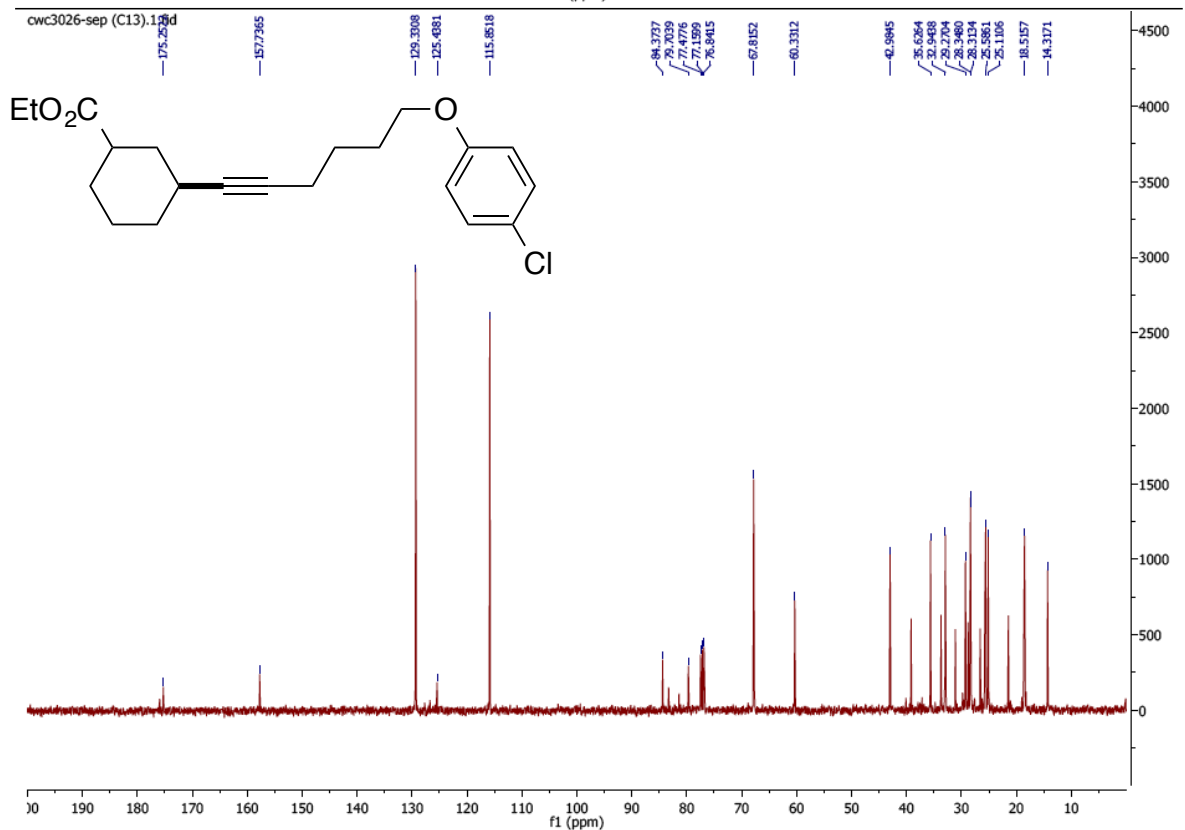
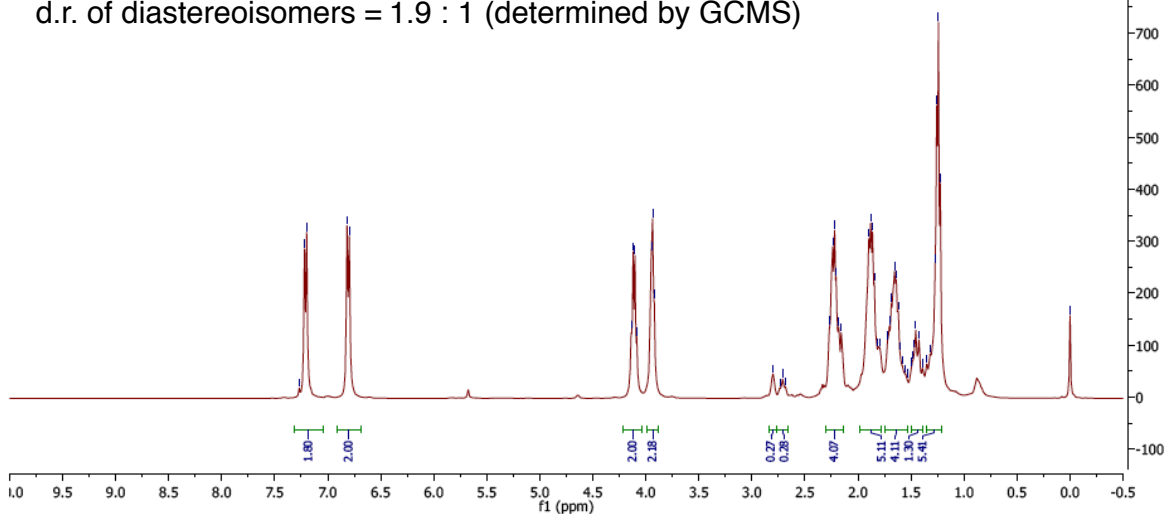
¹H and ¹³C NMR of Ethyl 3-((4-(*tert*-butyl)phenyl)ethynyl)cyclohexane-1-carboxylate (2k)



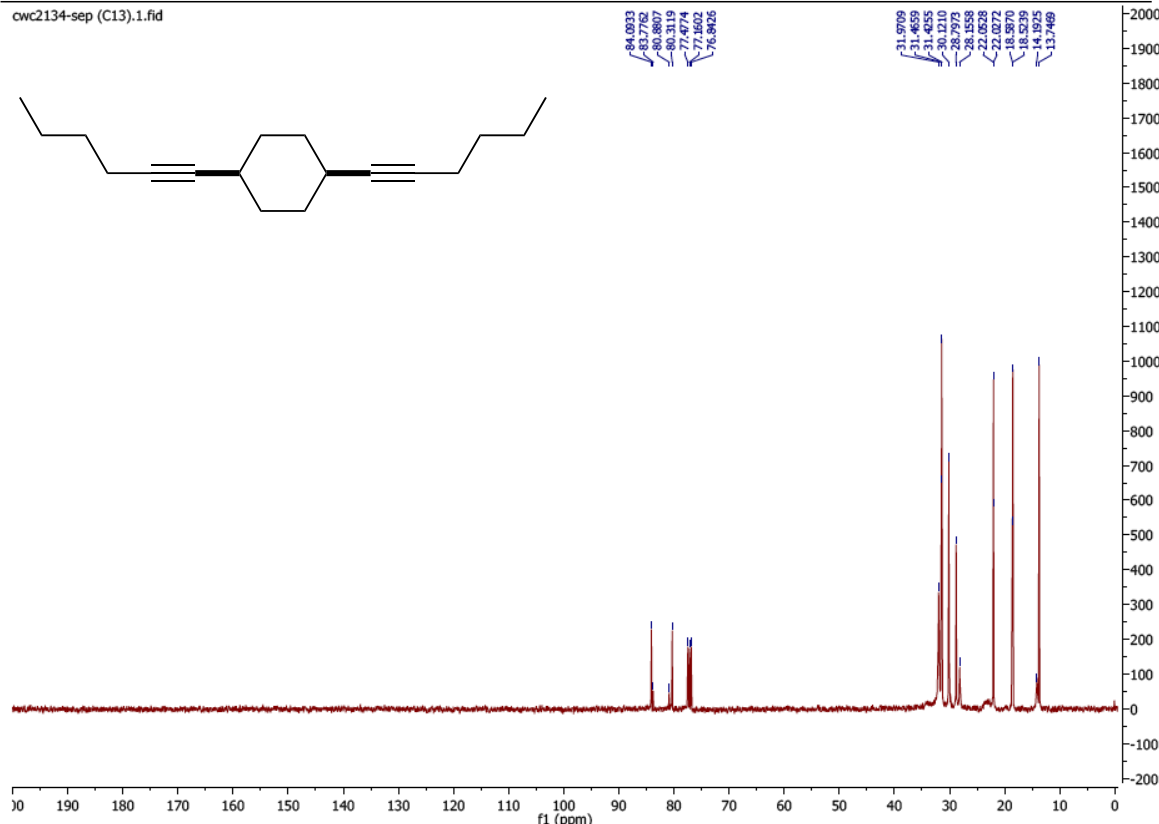
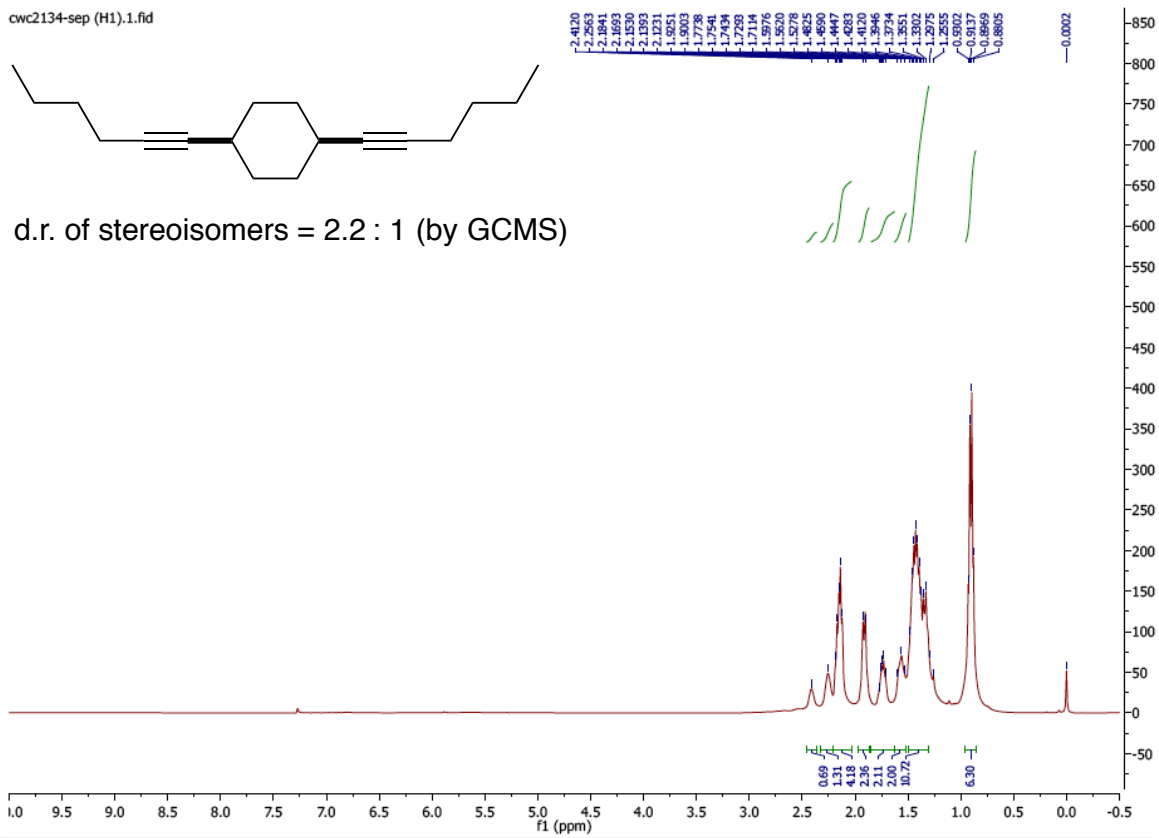
¹H and ¹³C NMR of Ethyl 3-(6-(4-chlorophenoxy)hex-1-yn-1-yl)cyclohexane-1-carboxylate (2l)



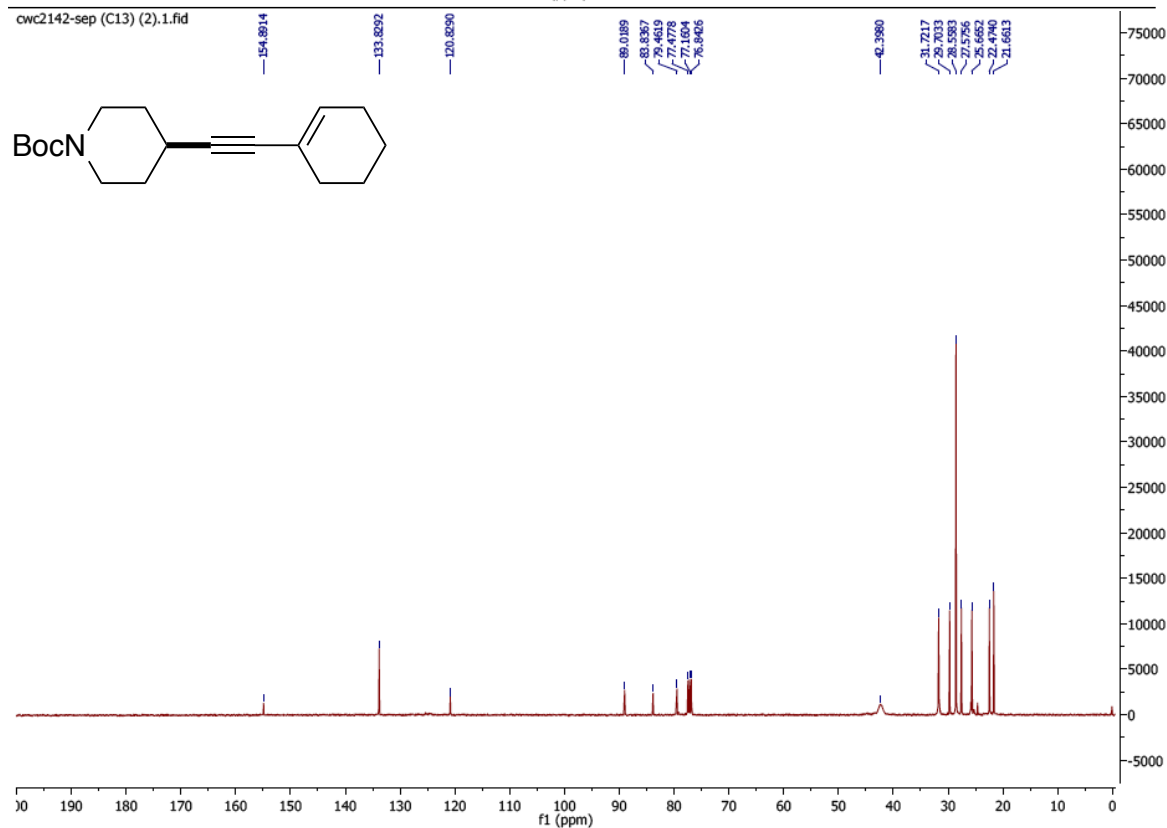
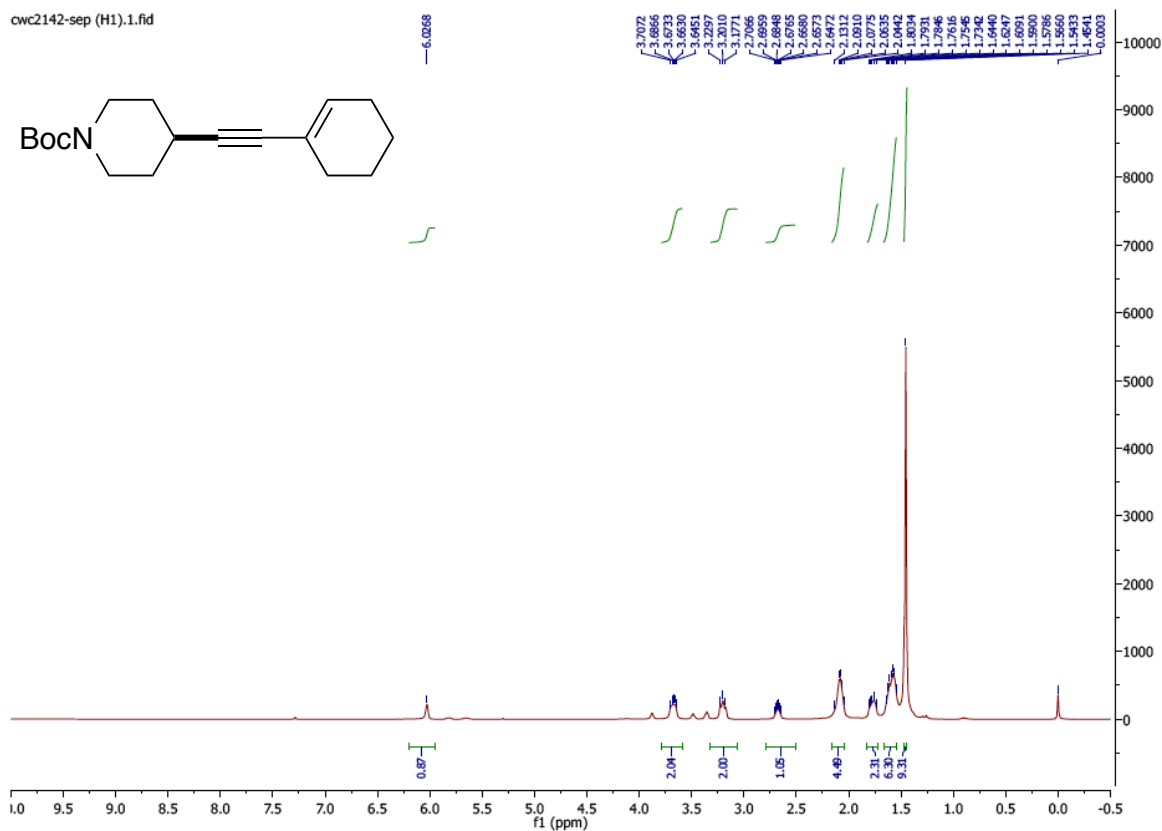
d.r. of diastereoisomers difficult to be determined by ¹H NMR.
 d.r. of diastereoisomers = 1.9 : 1 (determined by GCMS)



¹H and ¹³C NMR of 1,4-Di(hex-1-yn-1-yl)cyclohexane (2m)

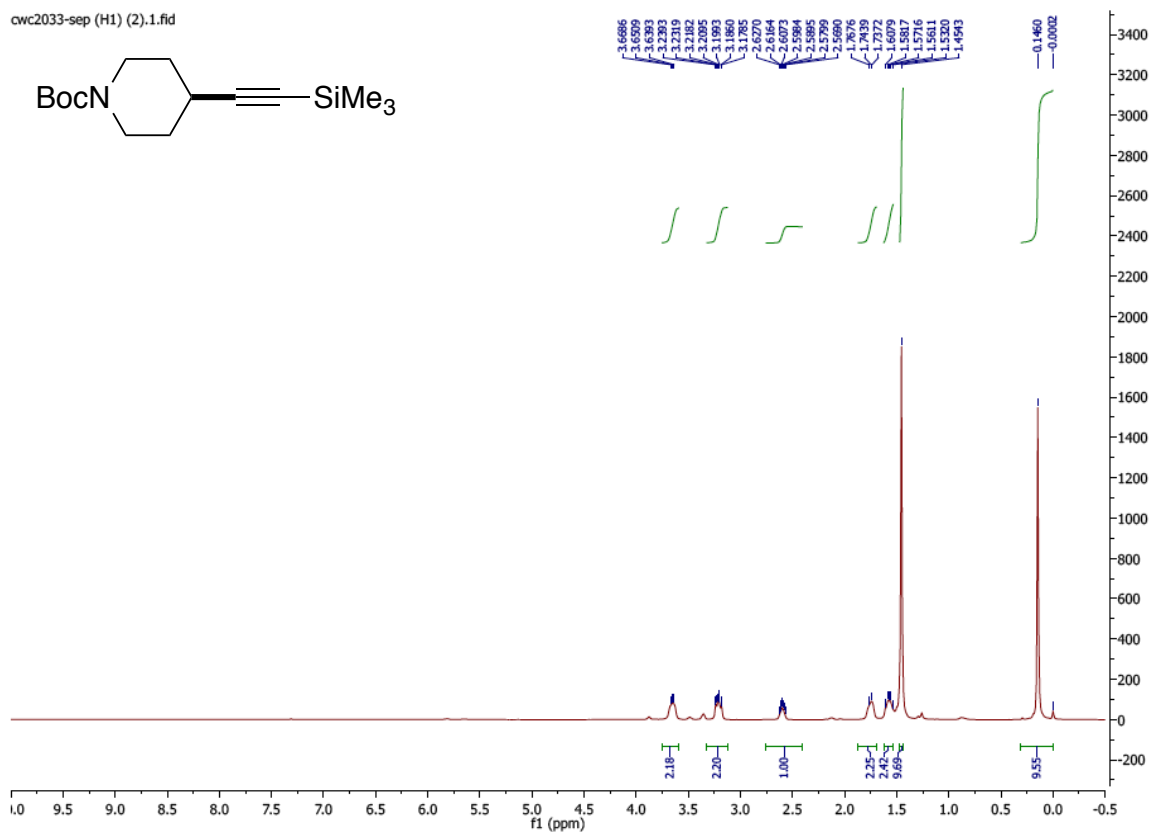
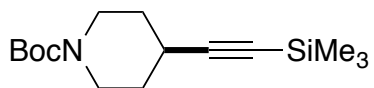


¹H and ¹³C NMR of *tert*-Butyl 4-(cyclohex-1-en-1-ylethynyl)piperidine-1-carboxylate (2n)

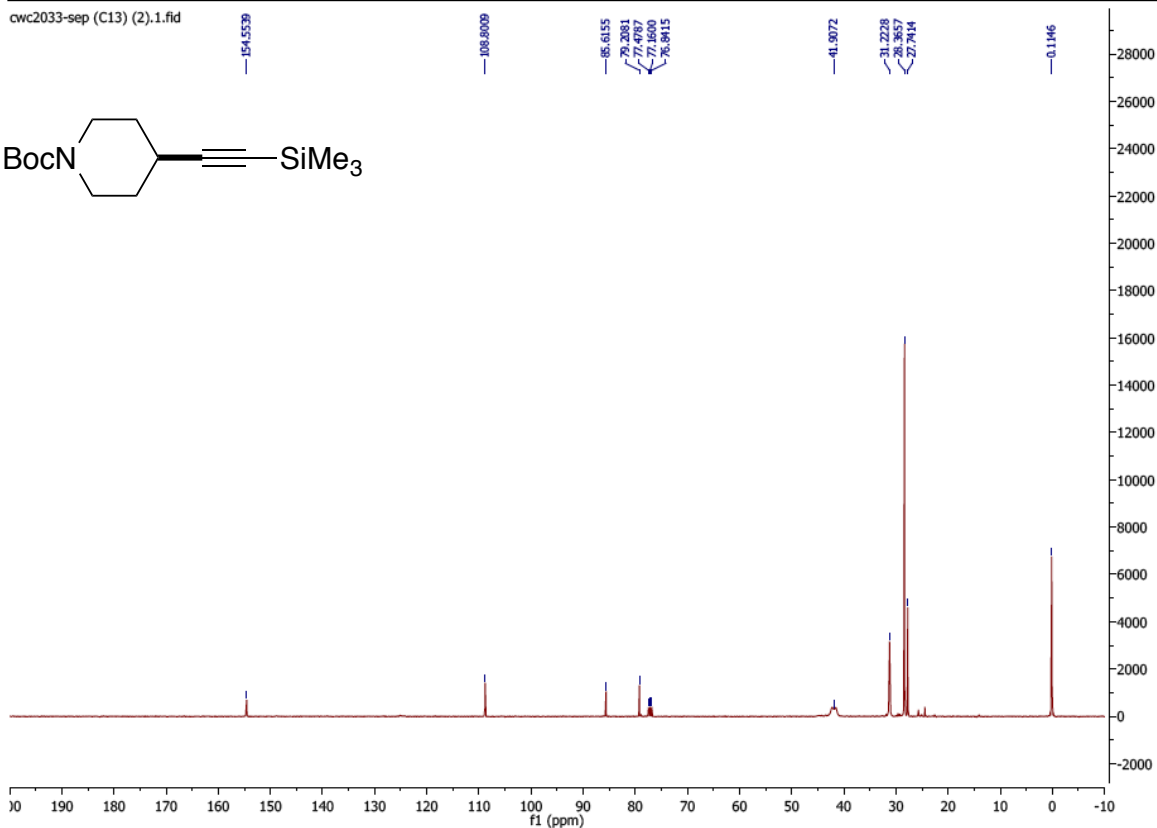
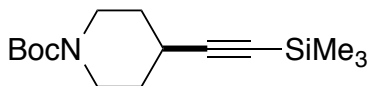


¹H and ¹³C NMR of *tert*-Butyl 4-((trimethylsilyl)ethynyl)piperidine-1-carboxylate (2o)

cwc2033-sep (H1) (2).1.fid

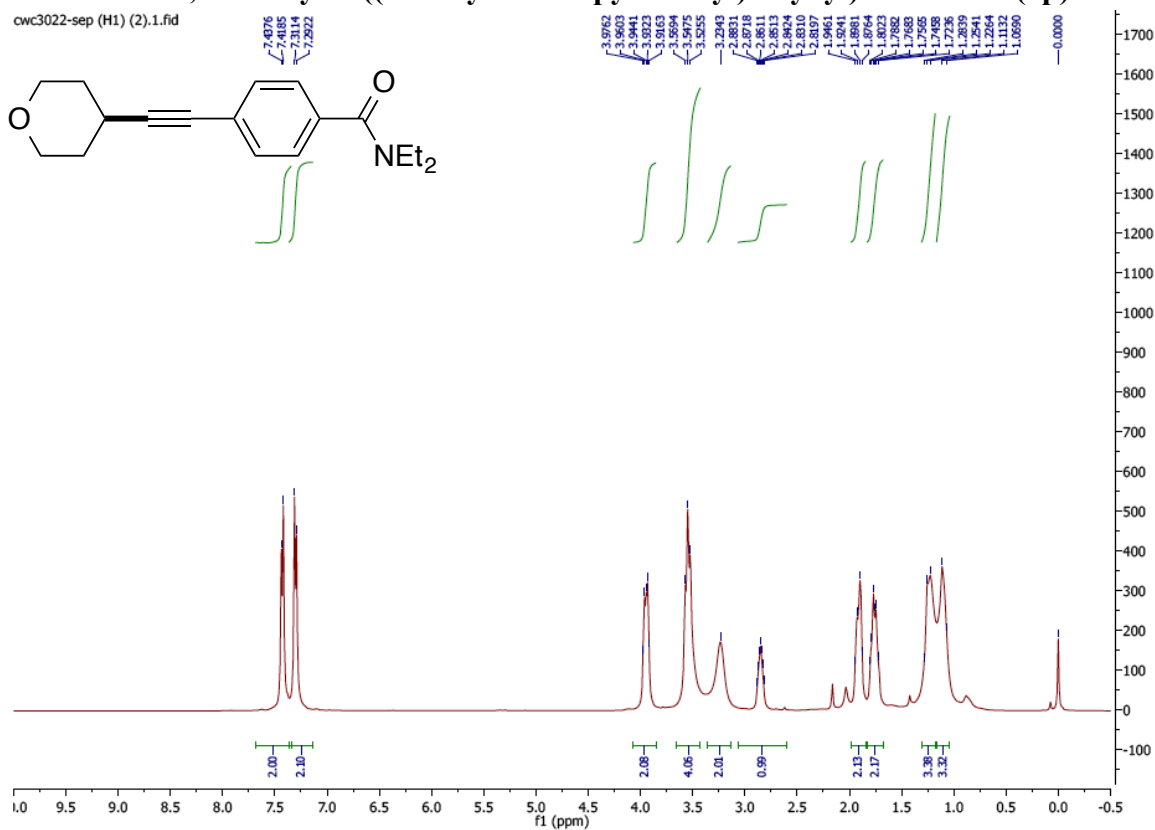


cwc2033-sep (C13) (2).1.fid

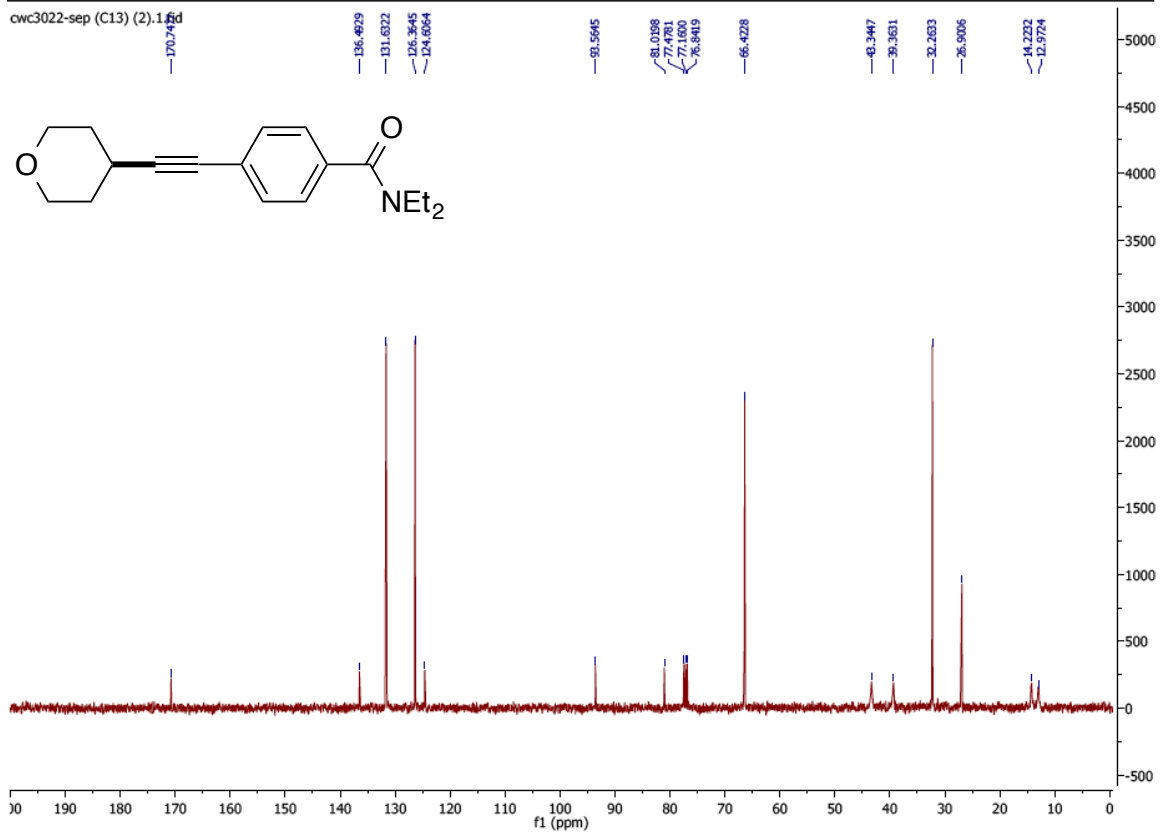


¹H and ¹³C NMR of *N,N*-diethyl-4-((tetrahydro-2*H*-pyran-4-yl)ethynyl)benzamide (2p)

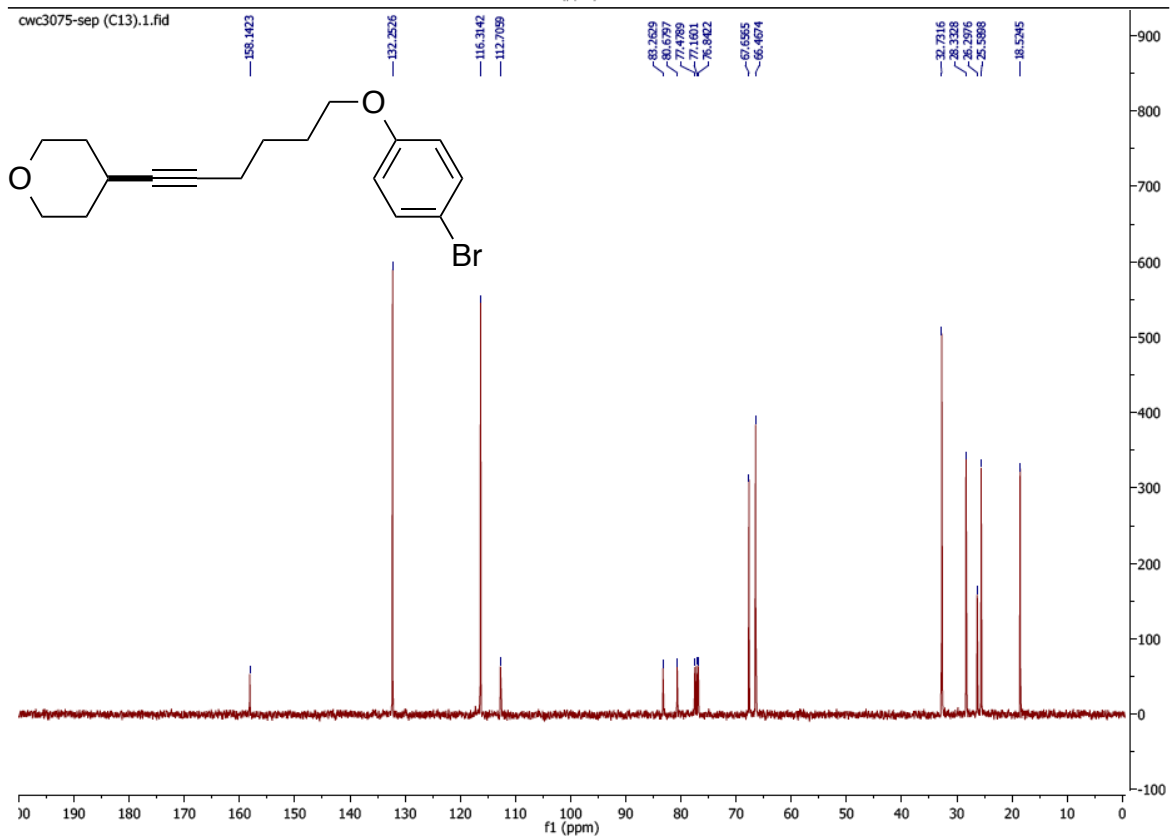
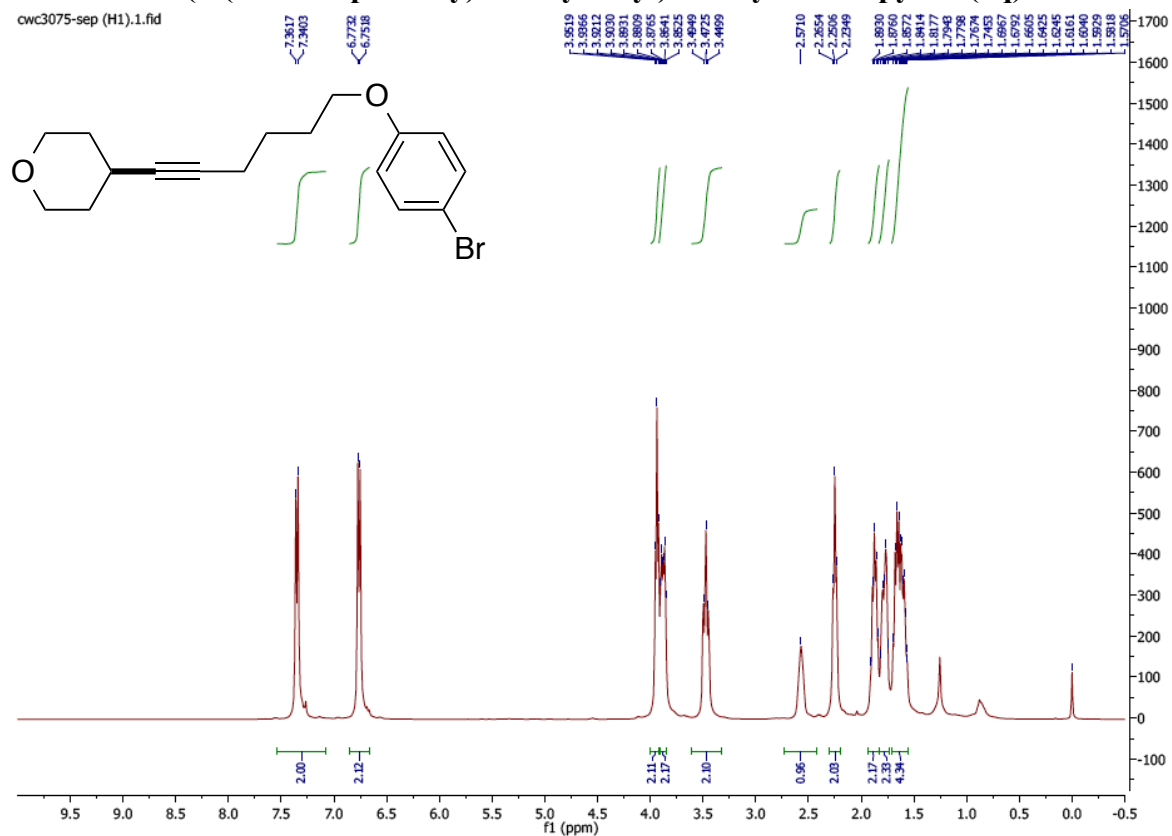
cwc3022-sep (H1) (2).1.fid



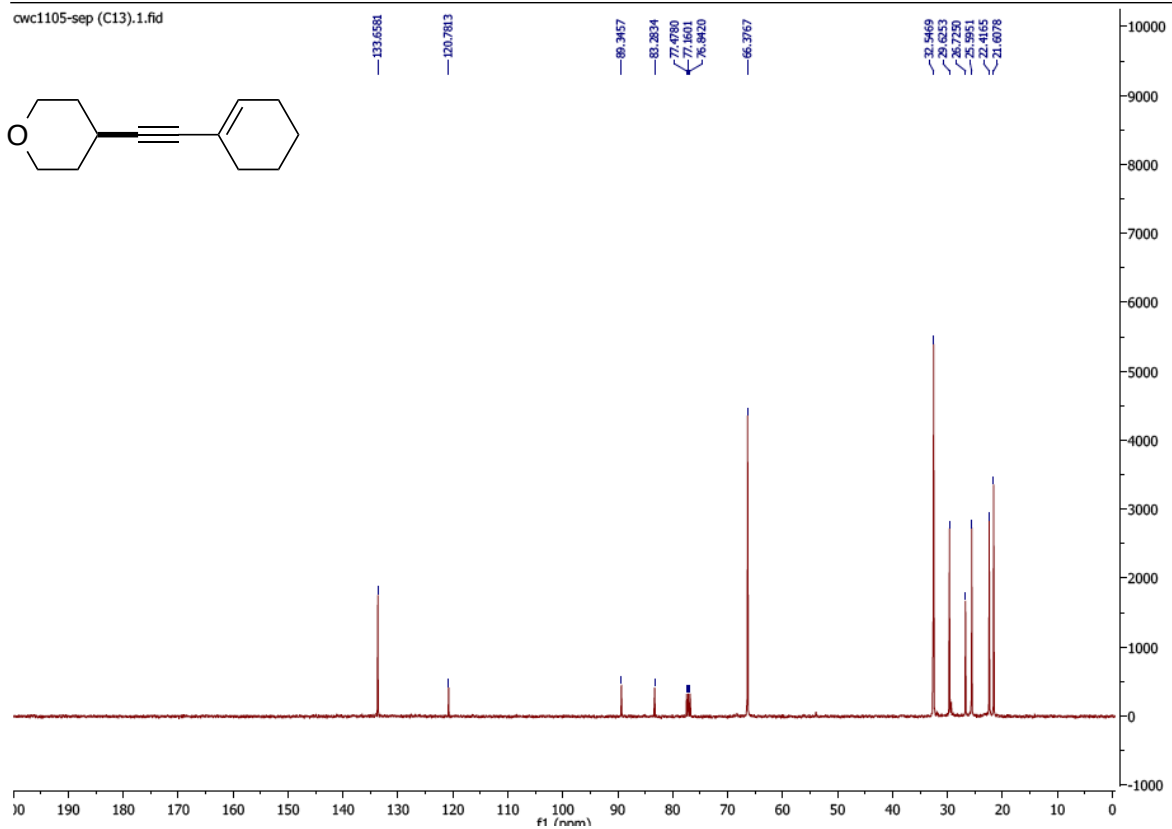
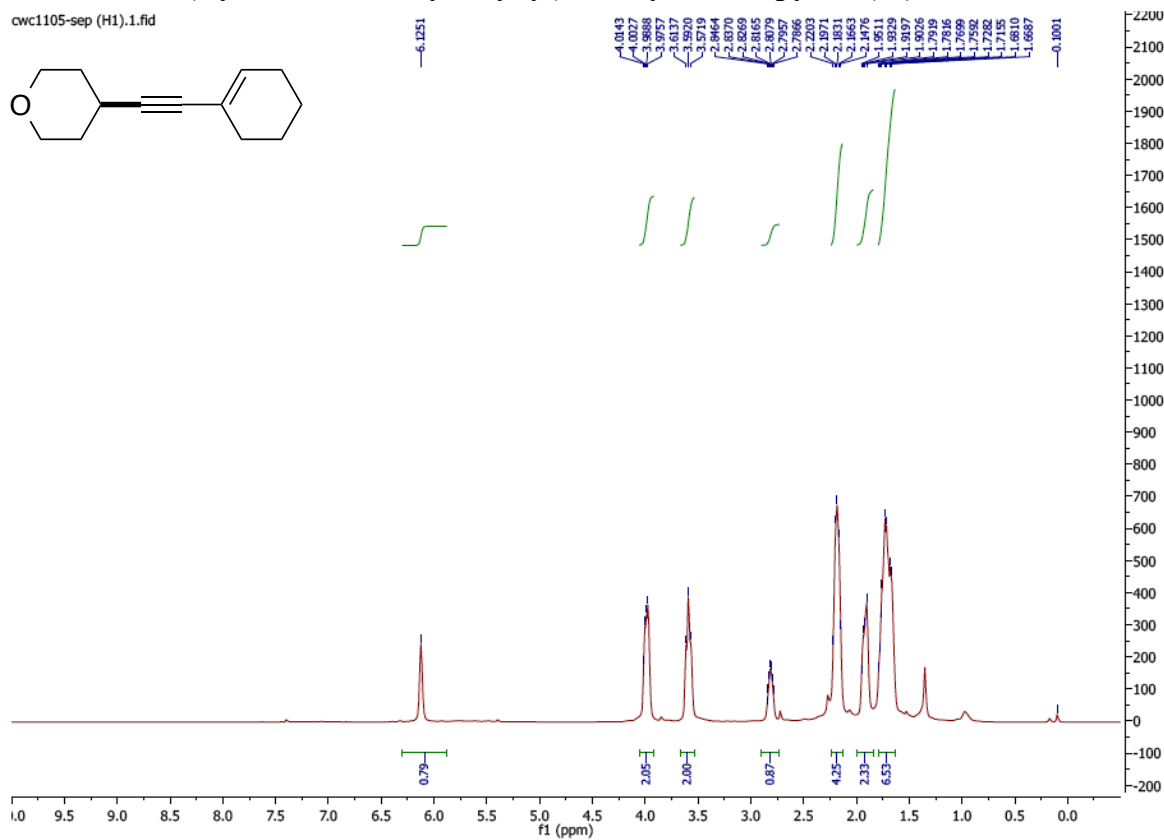
cwc3022-sep (C13) (2).1.fid



¹H and ¹³C NMR of 4-(6-(4-bromophenoxy)hex-1-yn-1-yl)tetrahydro-2H-pyran (2q)

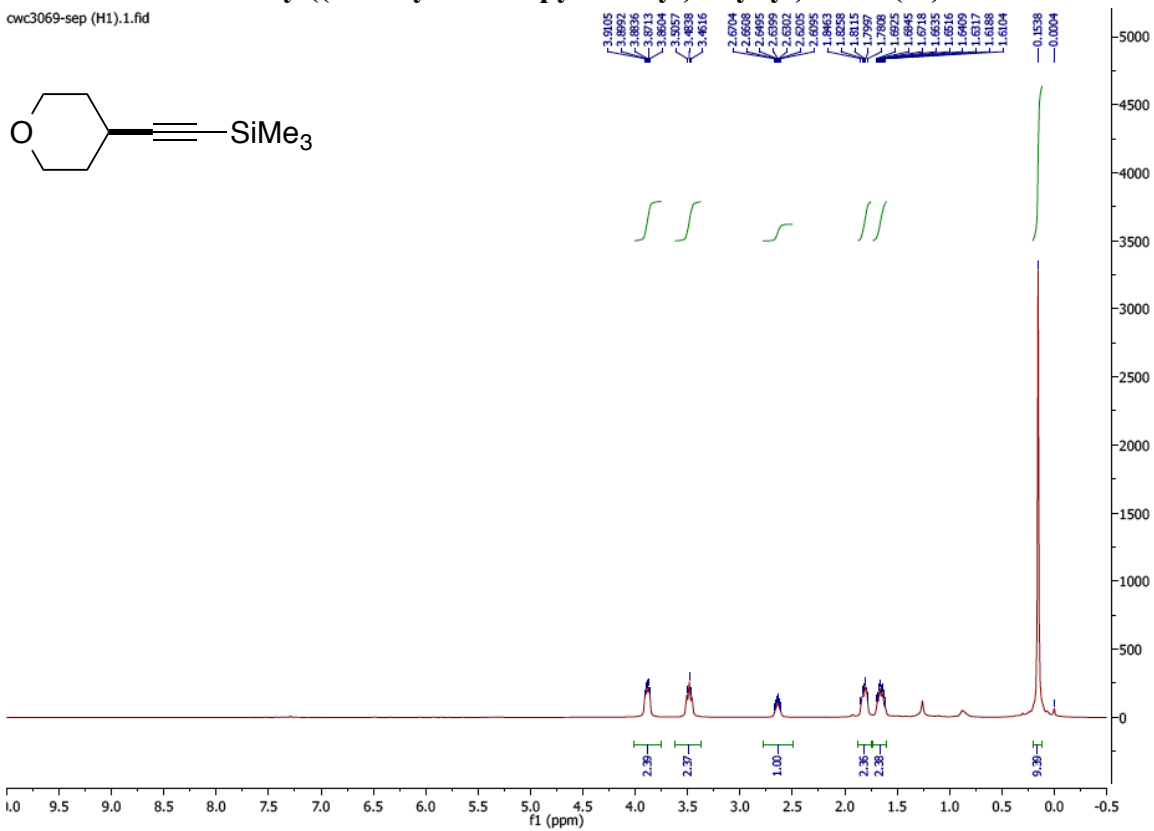


¹H and ¹³C NMR of 4-(Cyclohex-1-en-1-ylethynyl)tetrahydro-2H-pyran (2r)

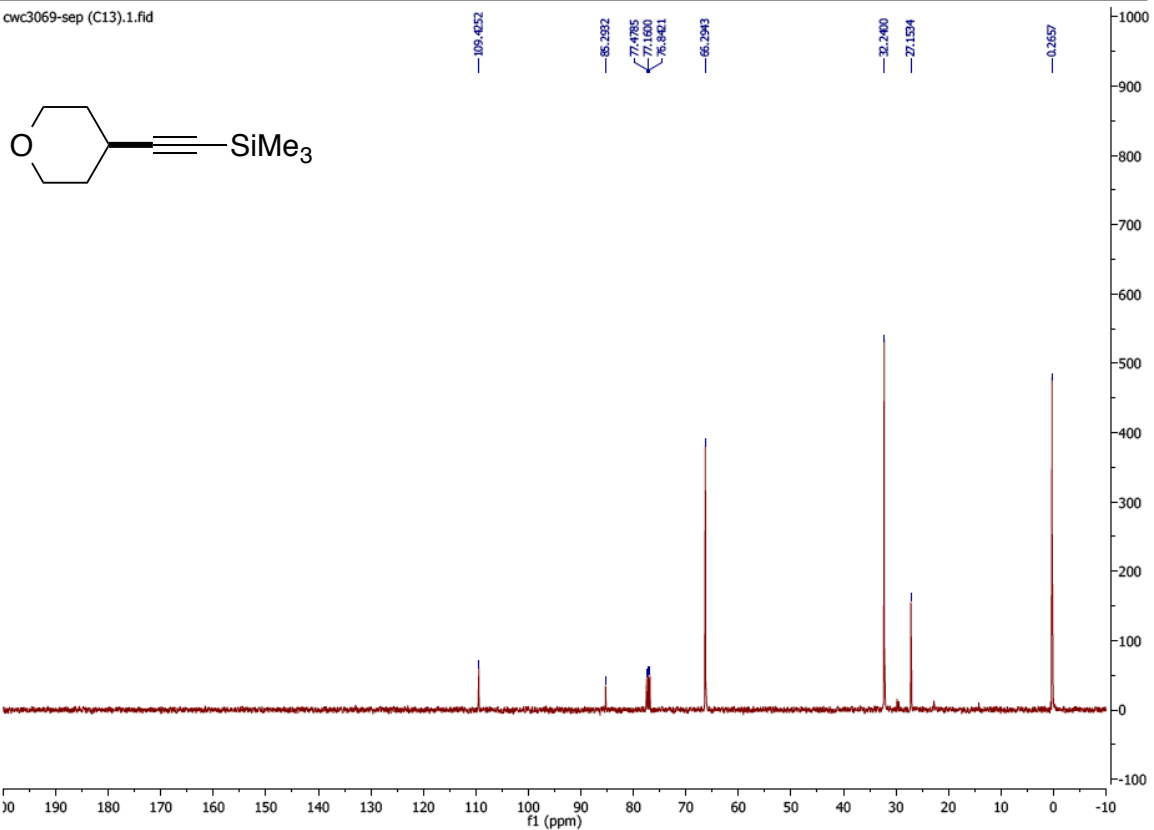


¹H and ¹³C NMR of Trimethyl((tetrahydro-2H-pyran-4-yl)ethynyl)silane (2s)

cwc3069-sep (H1).1.fid

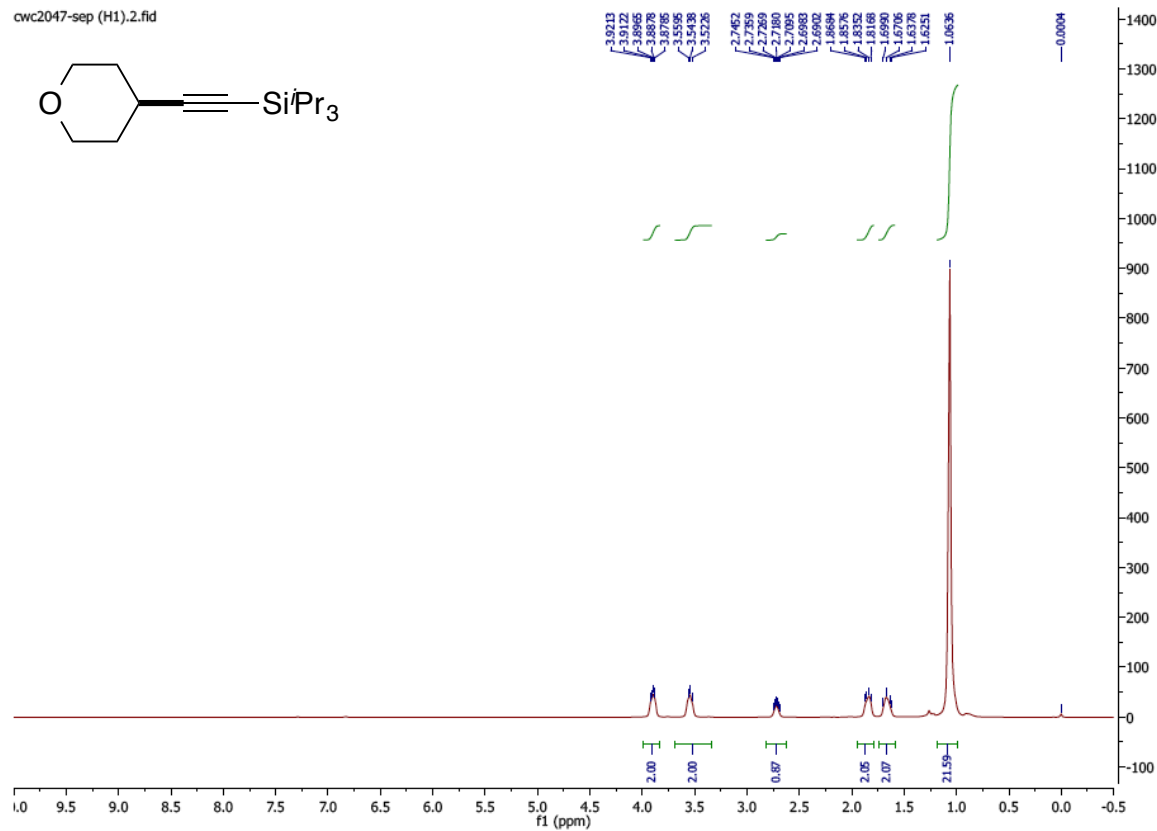


cwc3069-sep (C13).1.fid

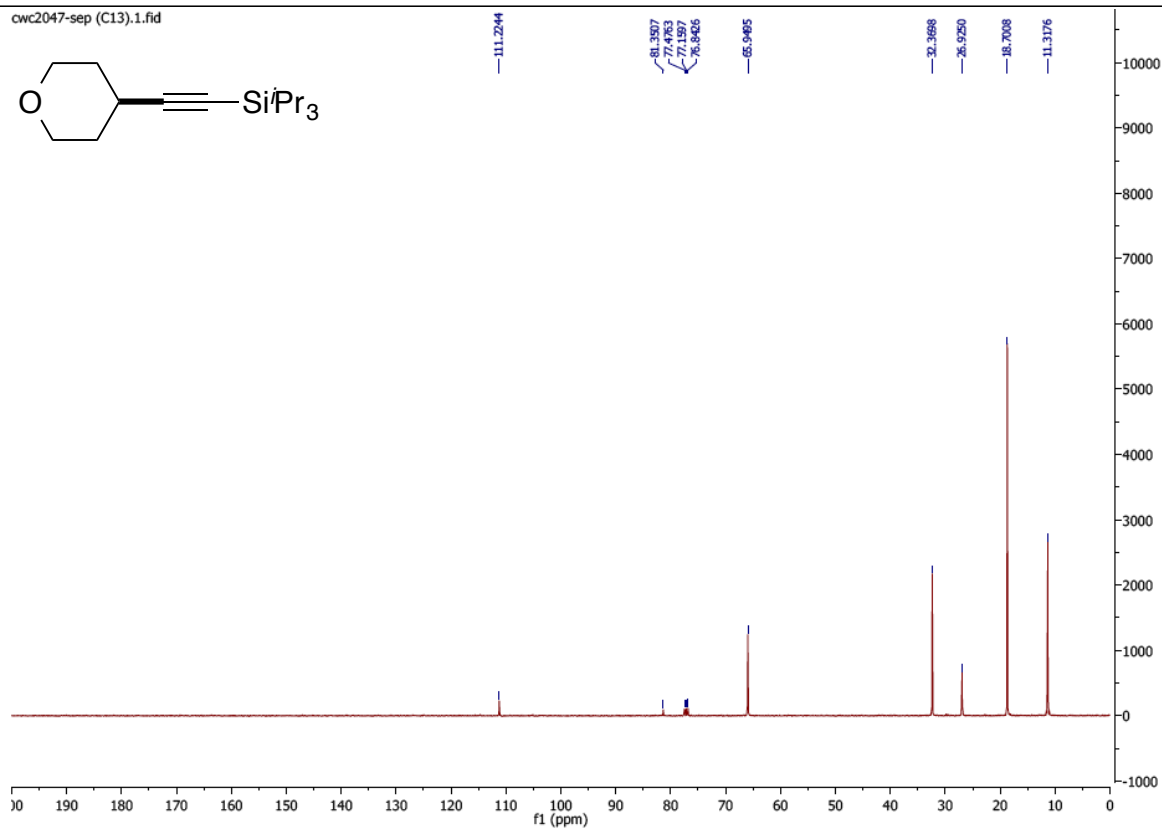


¹H and ¹³C NMR of triisopropyl((tetrahydro-2H-pyran-4-yl)ethynyl)silane (2t)

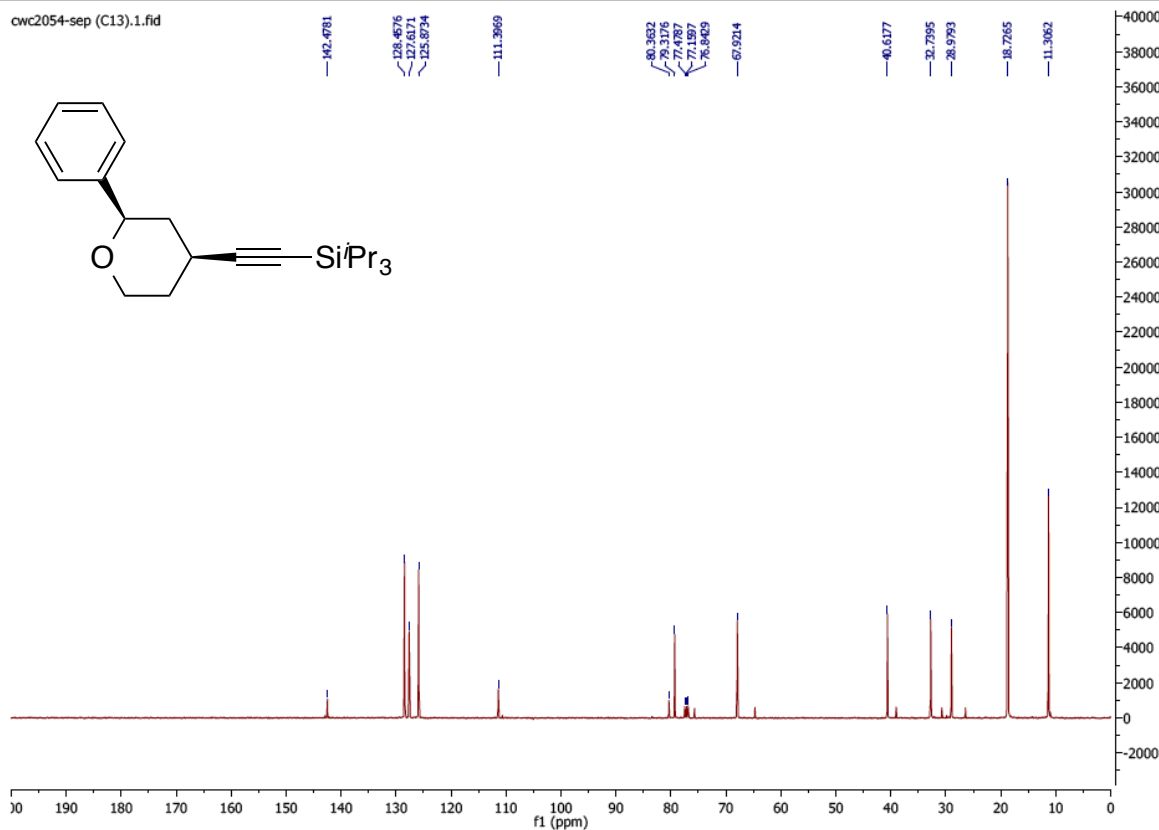
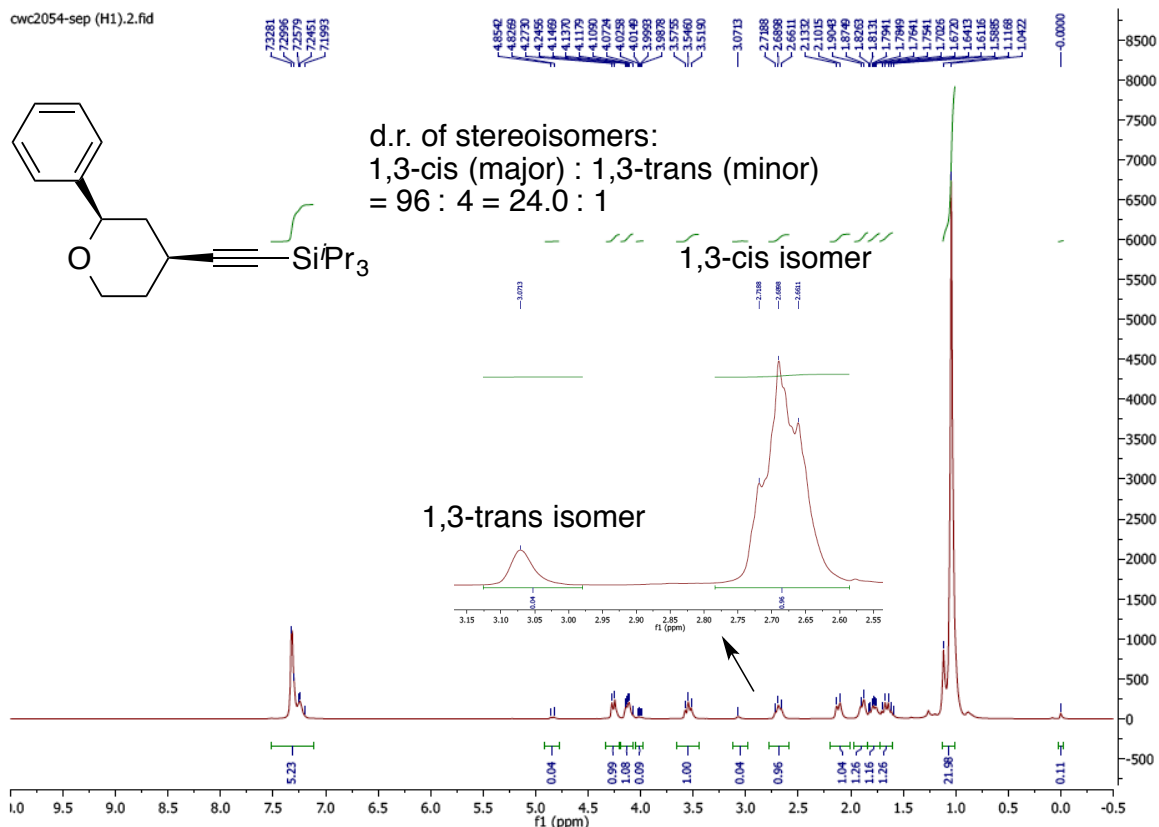
cwc2047-sep (H1).2.fid



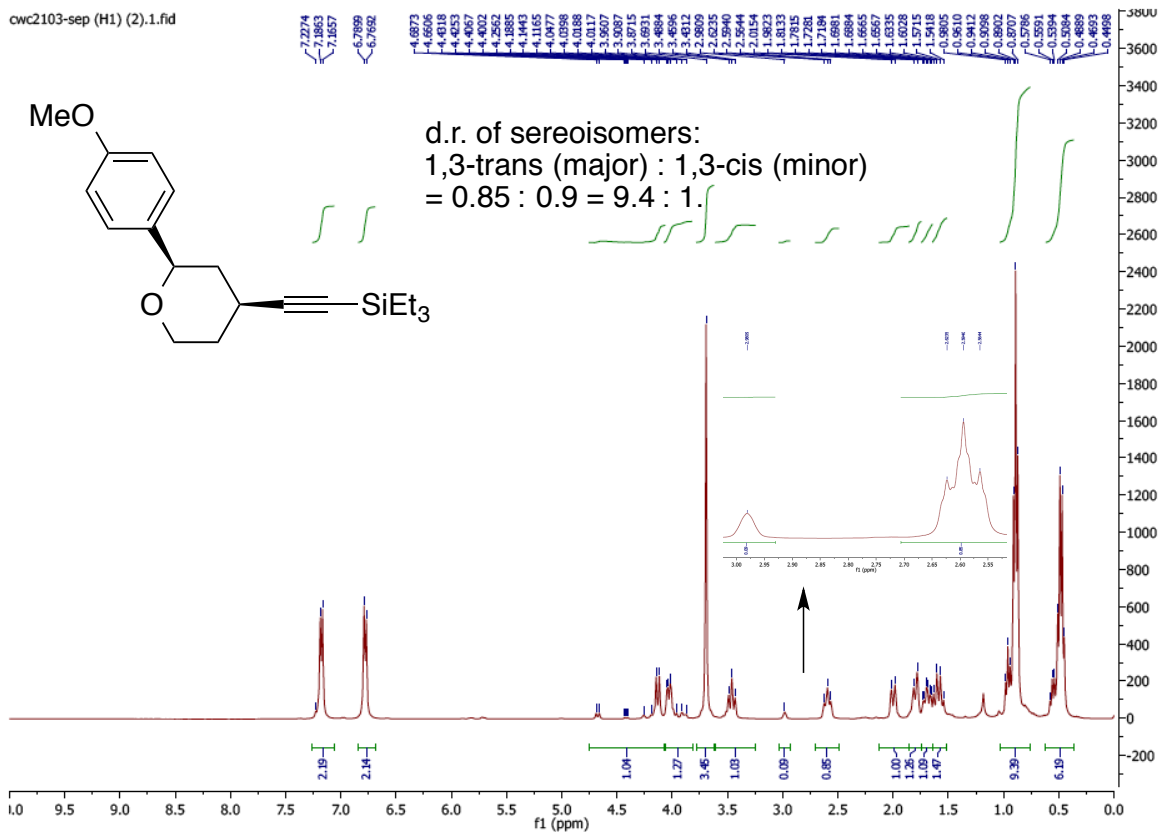
cwc2047-sep (C13).1.fid



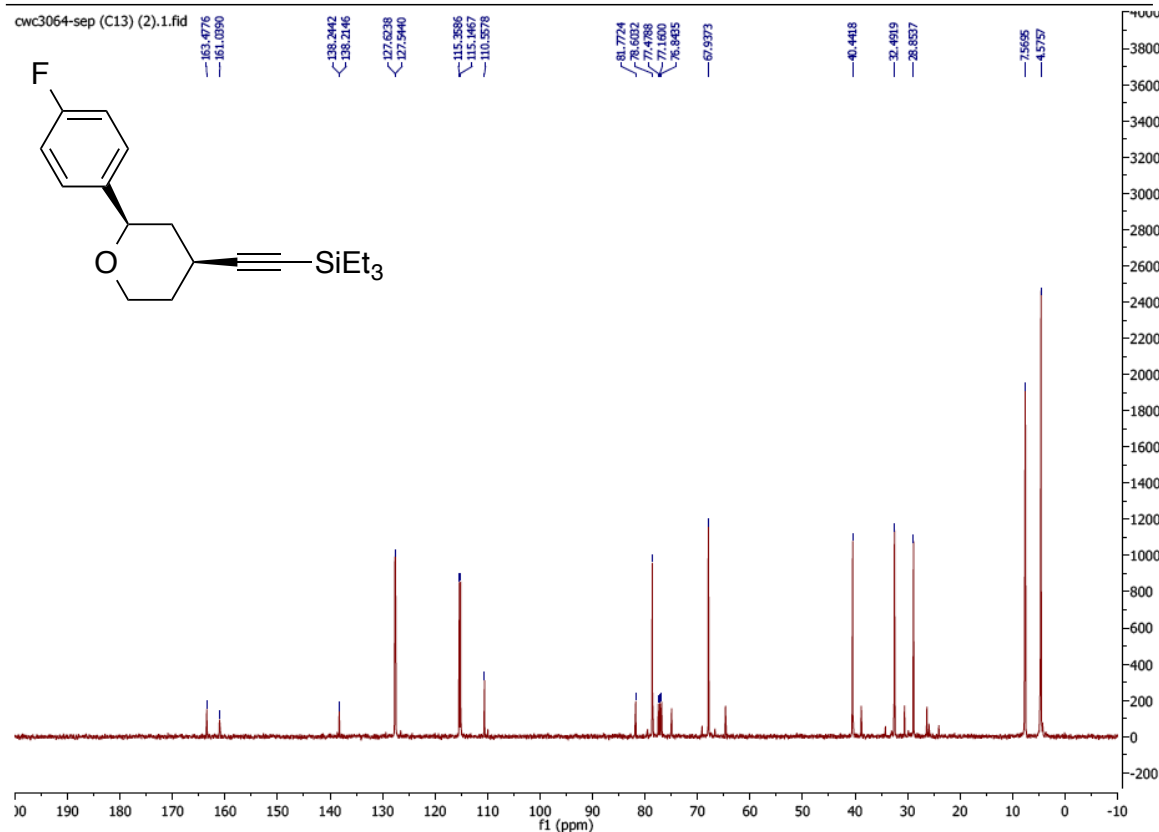
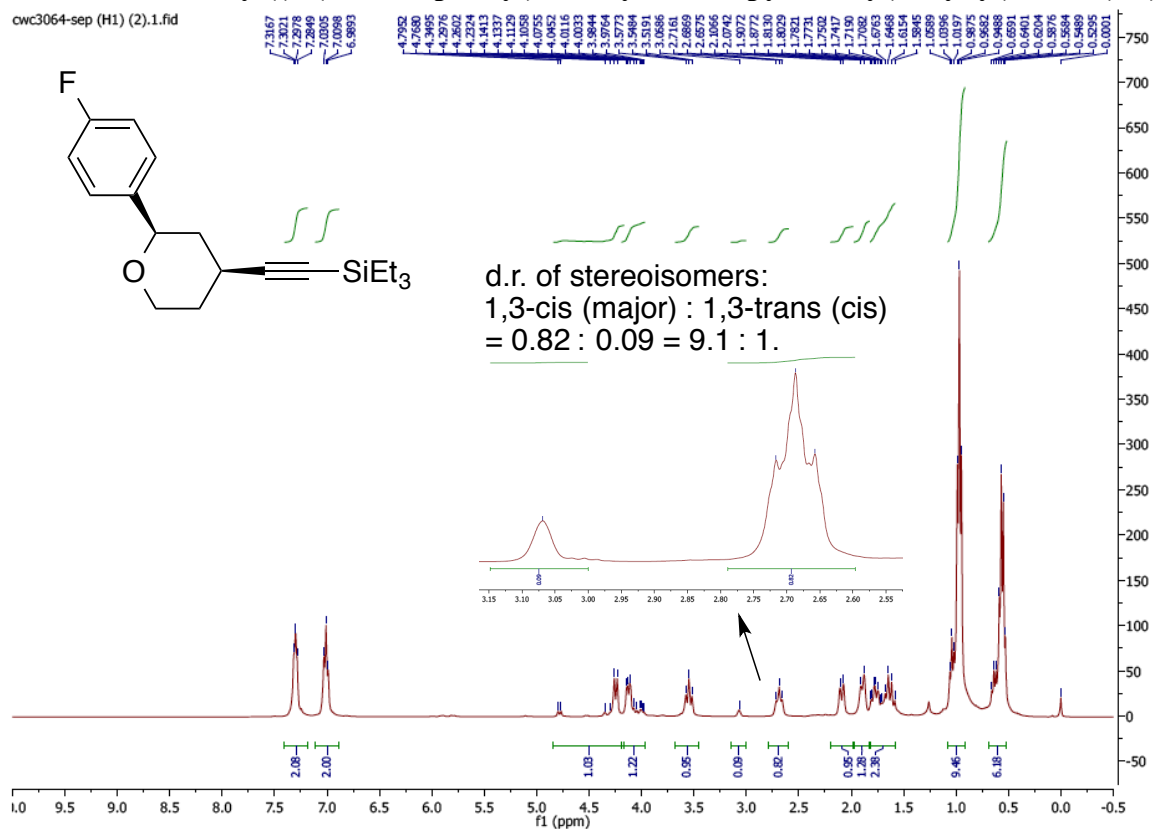
¹H and ¹³C NMR of Triisopropyl((2-phenyltetrahydro-2H-pyran-4-yl)ethynyl)silane (**2u**)



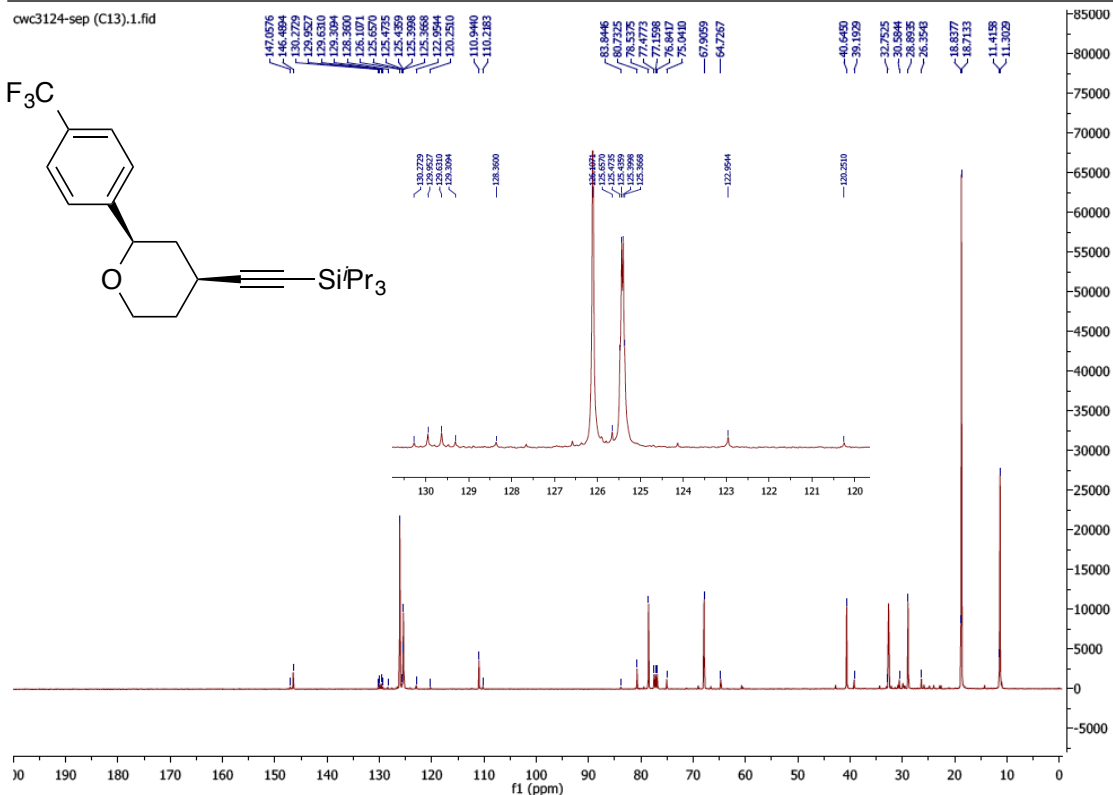
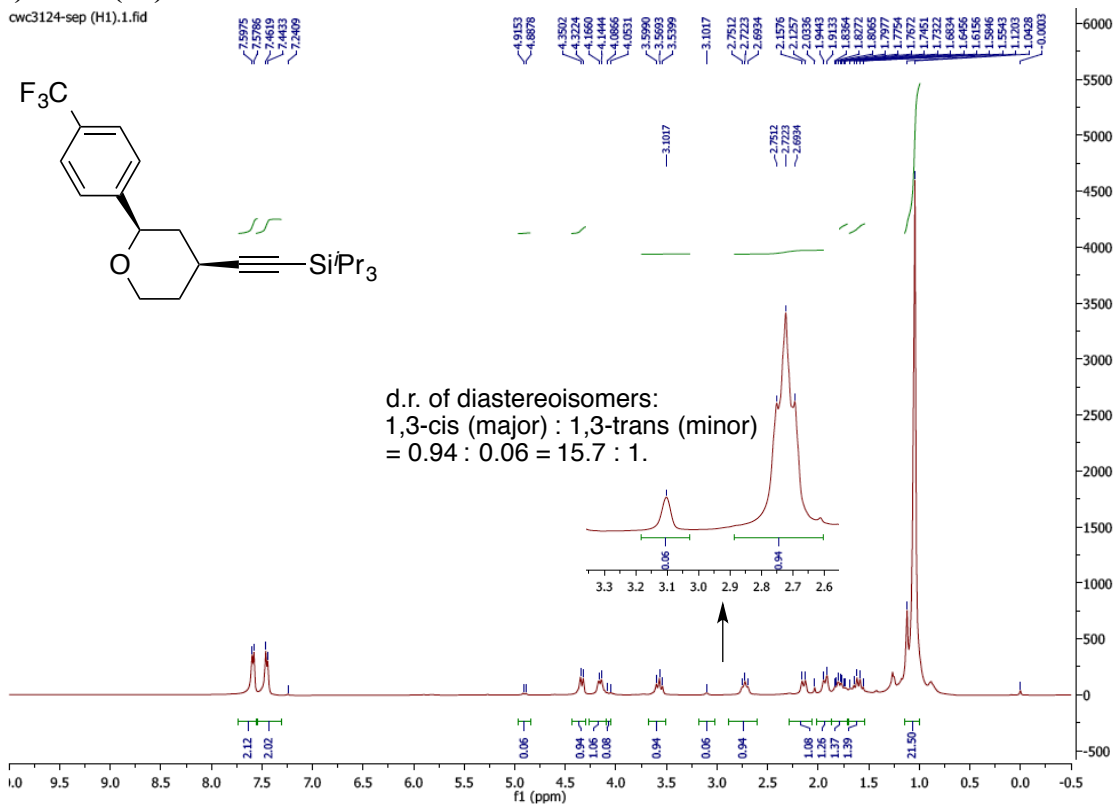
¹H and ¹³C NMR of Triethyl((2-(4-methoxyphenyl)tetrahydro-2H-pyran-4-yl)ethynyl)silane (2v)



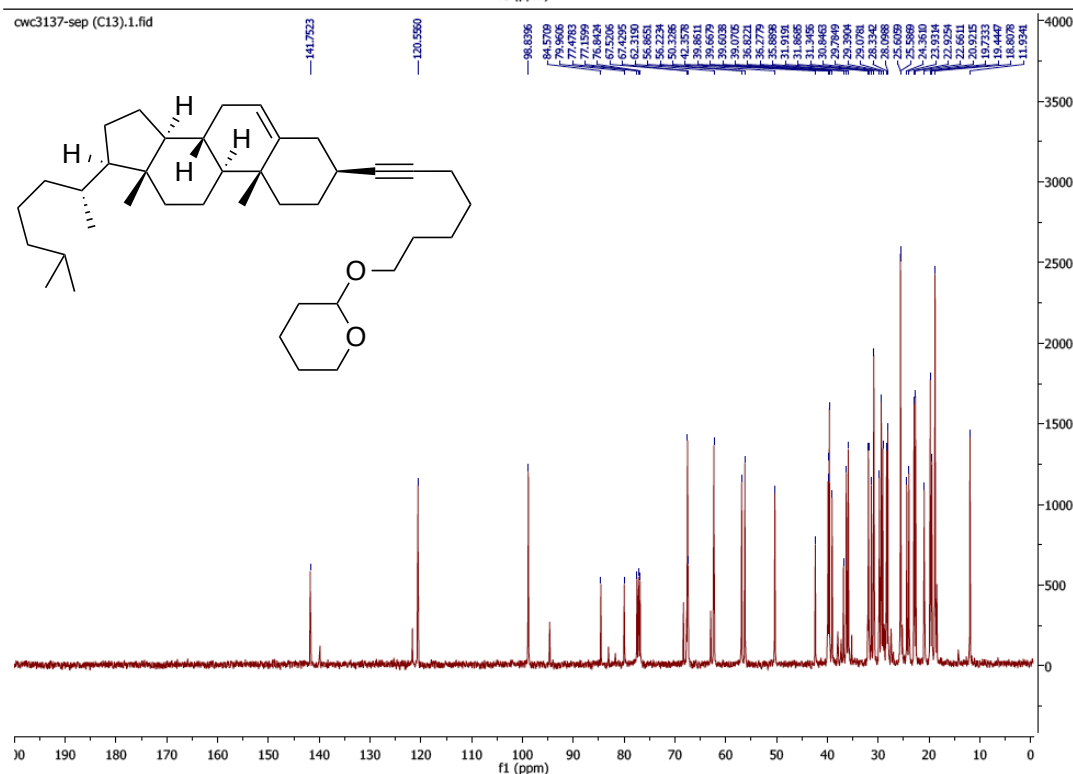
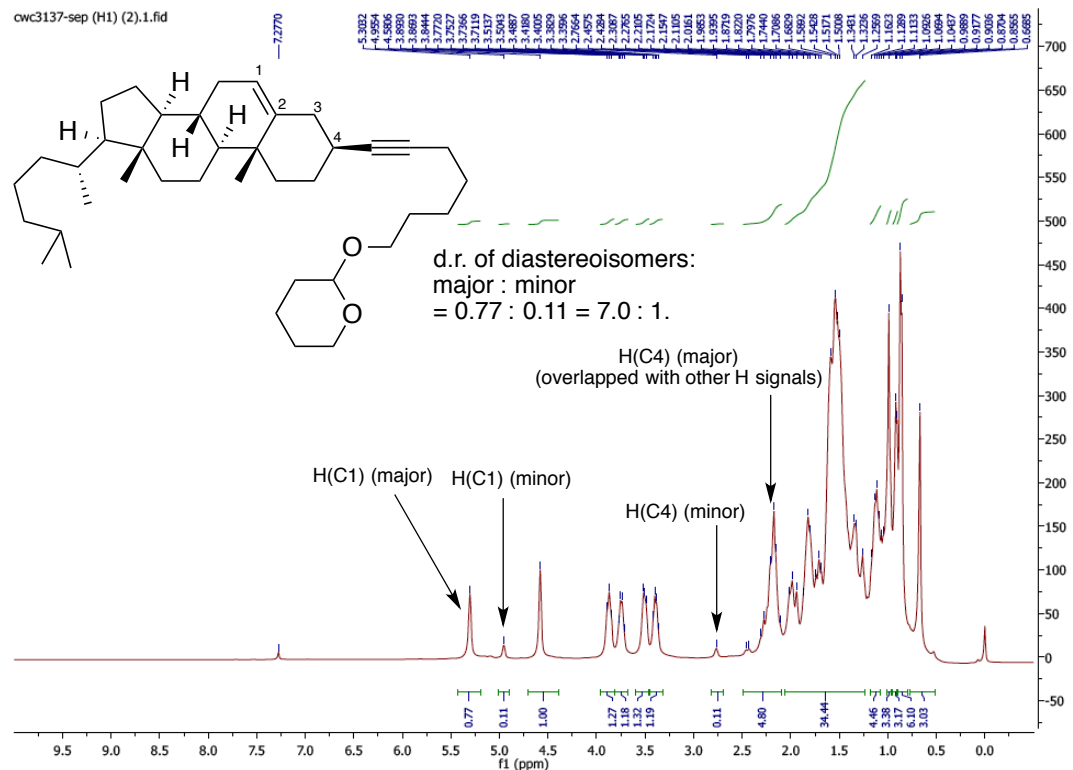
¹H and ¹³C NMR of Triethyl((2-(4-fluorophenyl)tetrahydro-2H-pyran-4-yl)ethynyl)silane (2w)



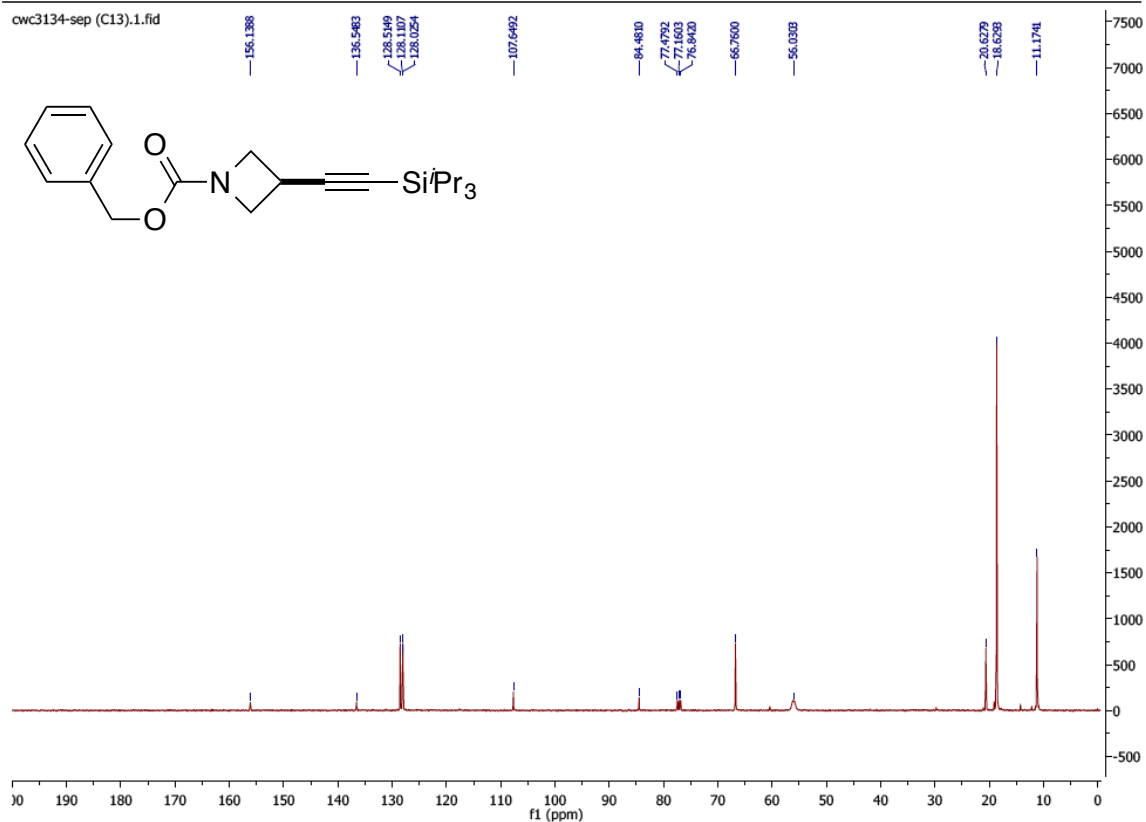
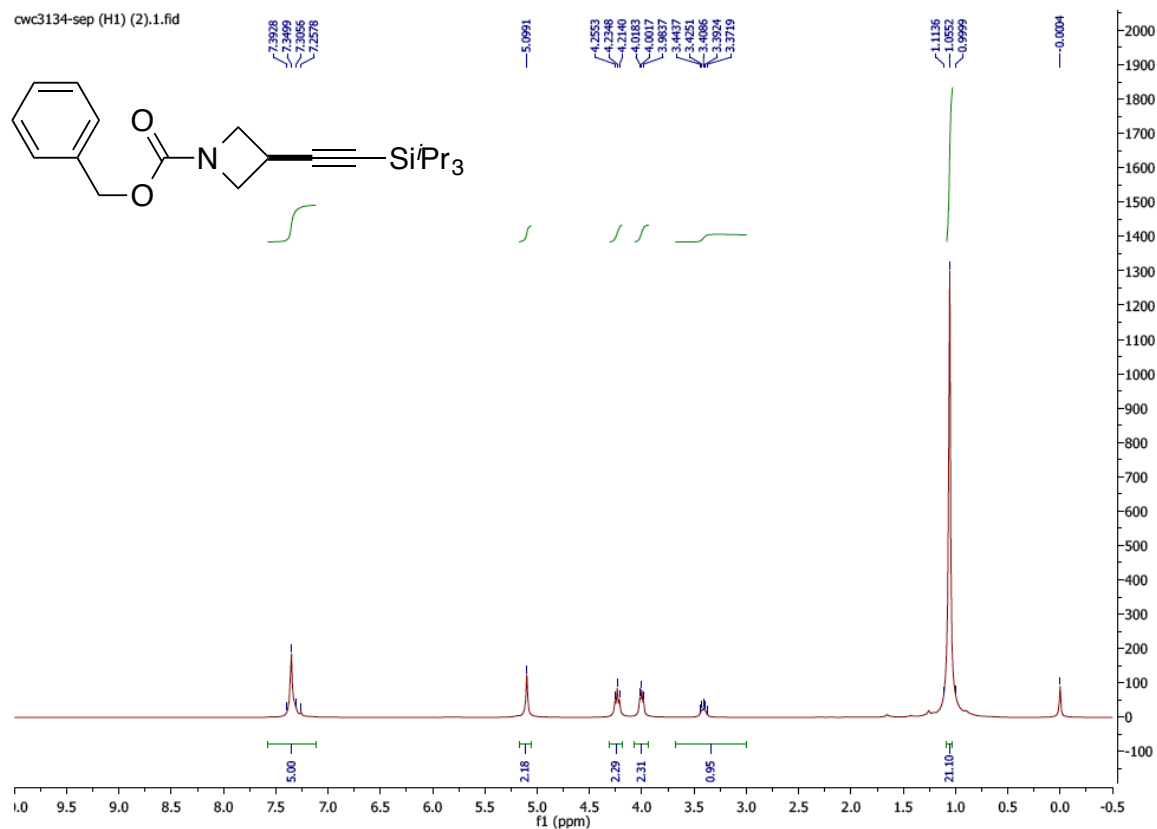
¹H and ¹³C NMR of Triisopropyl((2-(4-(trifluoromethyl)phenyl)tetrahydro-2H-pyran-4-yl)ethynyl)silane (2x)



¹H and ¹³C NMR of 2-((7-((3*S*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl)hept-6-yn-1-yl)oxy)tetrahydro-2*H*-pyran (2y)

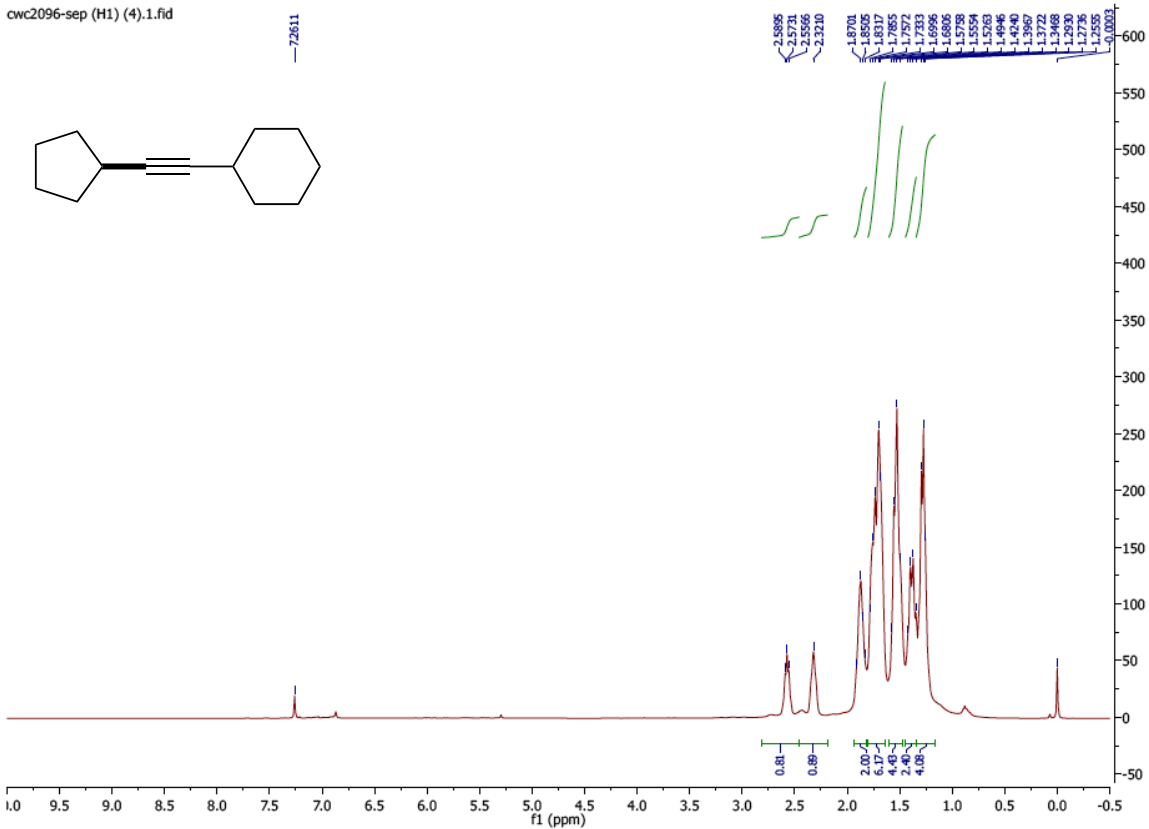


¹H and ¹³C NMR of Benzyl 3-((triisopropylsilyl)ethynyl)azetidine-1-carboxylate (3a)

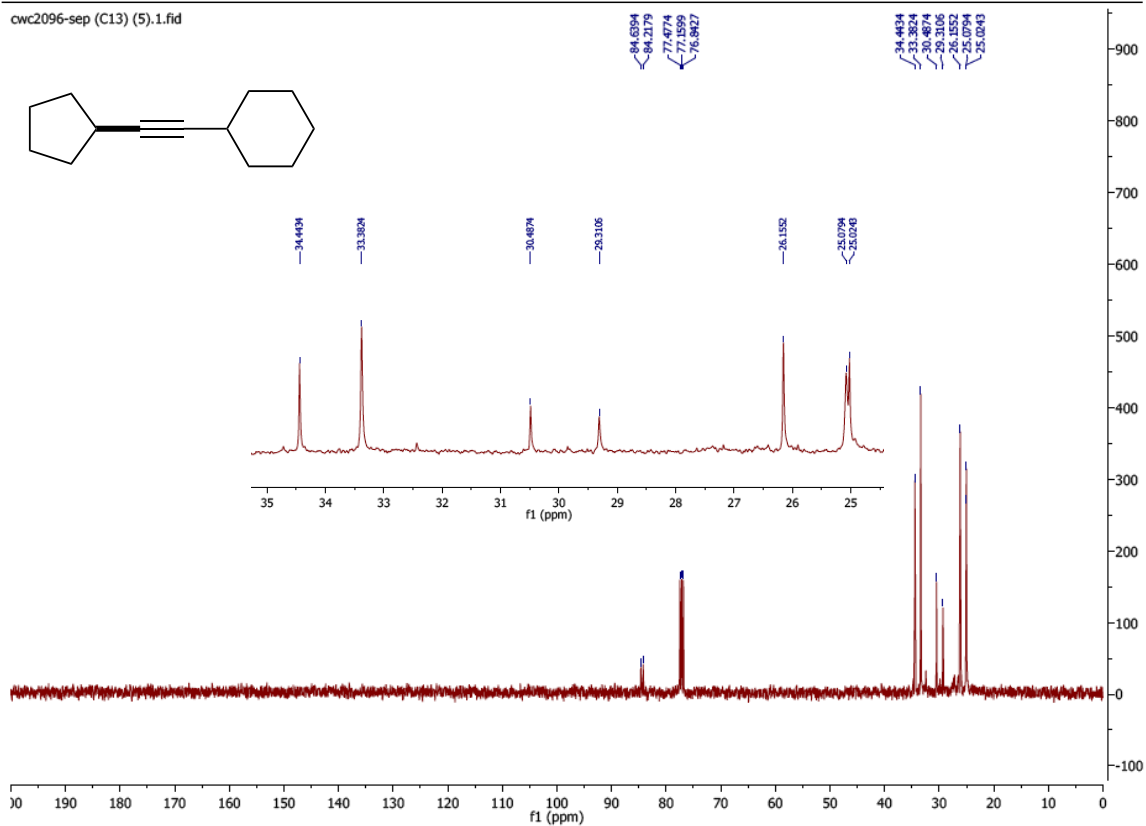


^1H and ^{13}C NMR of (Cyclopentylethynyl)cyclohexane (3b)

cwc2096-sep (H1) (4).1.fid

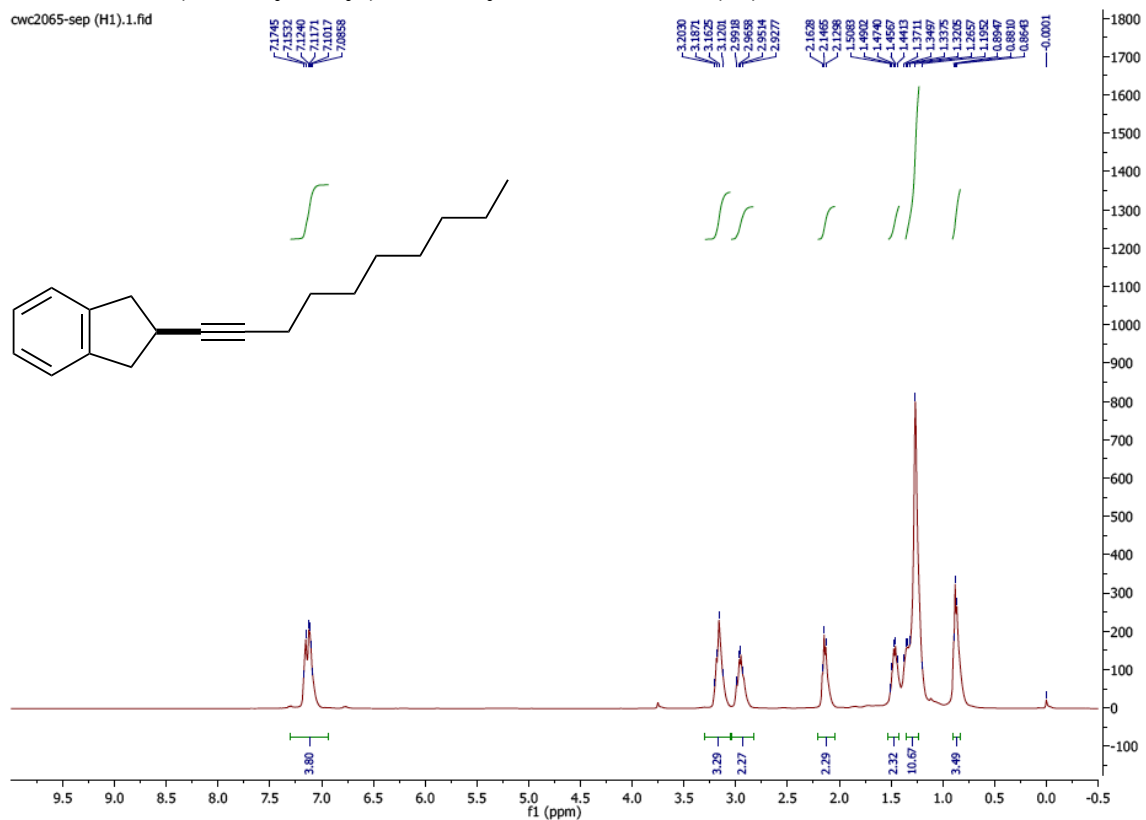


cwc2096-sep (C13) (5).1.fid

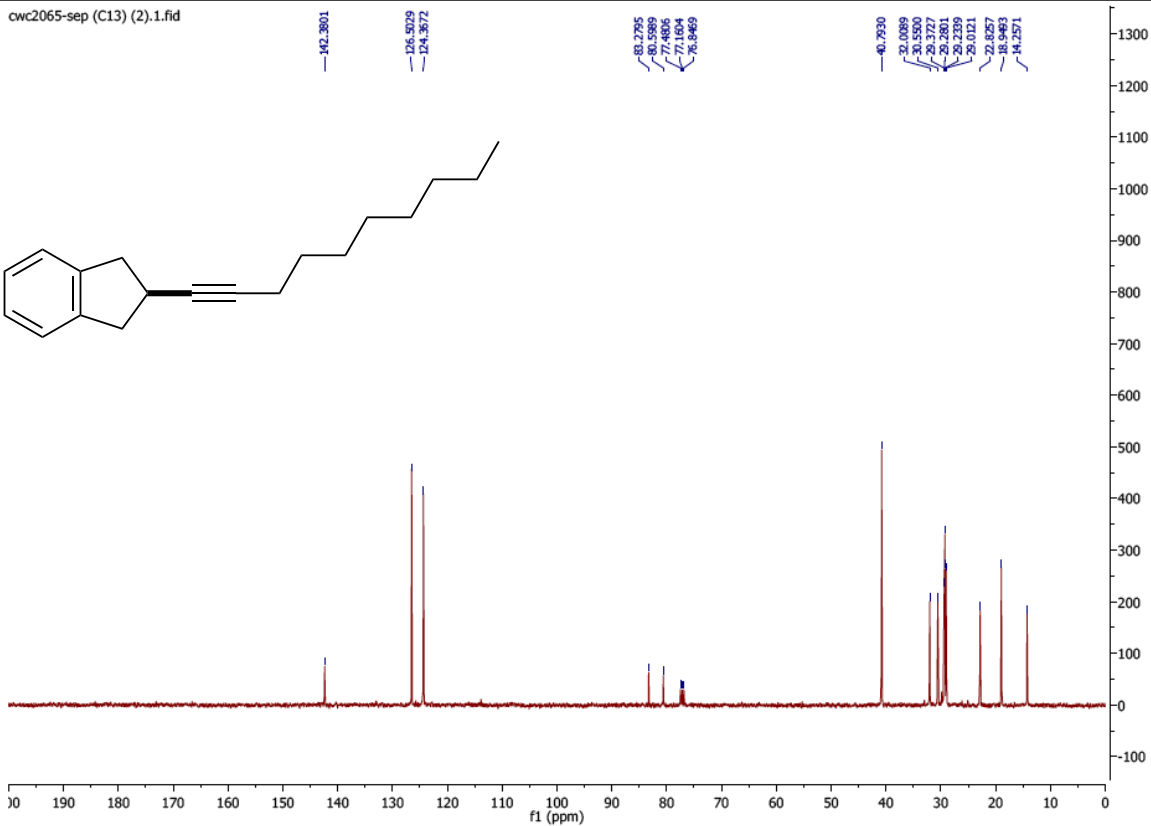


^1H and ^{13}C NMR of 2-(Dec-1-yn-1-yl)-2,3-dihydro-1H-indene (3c)

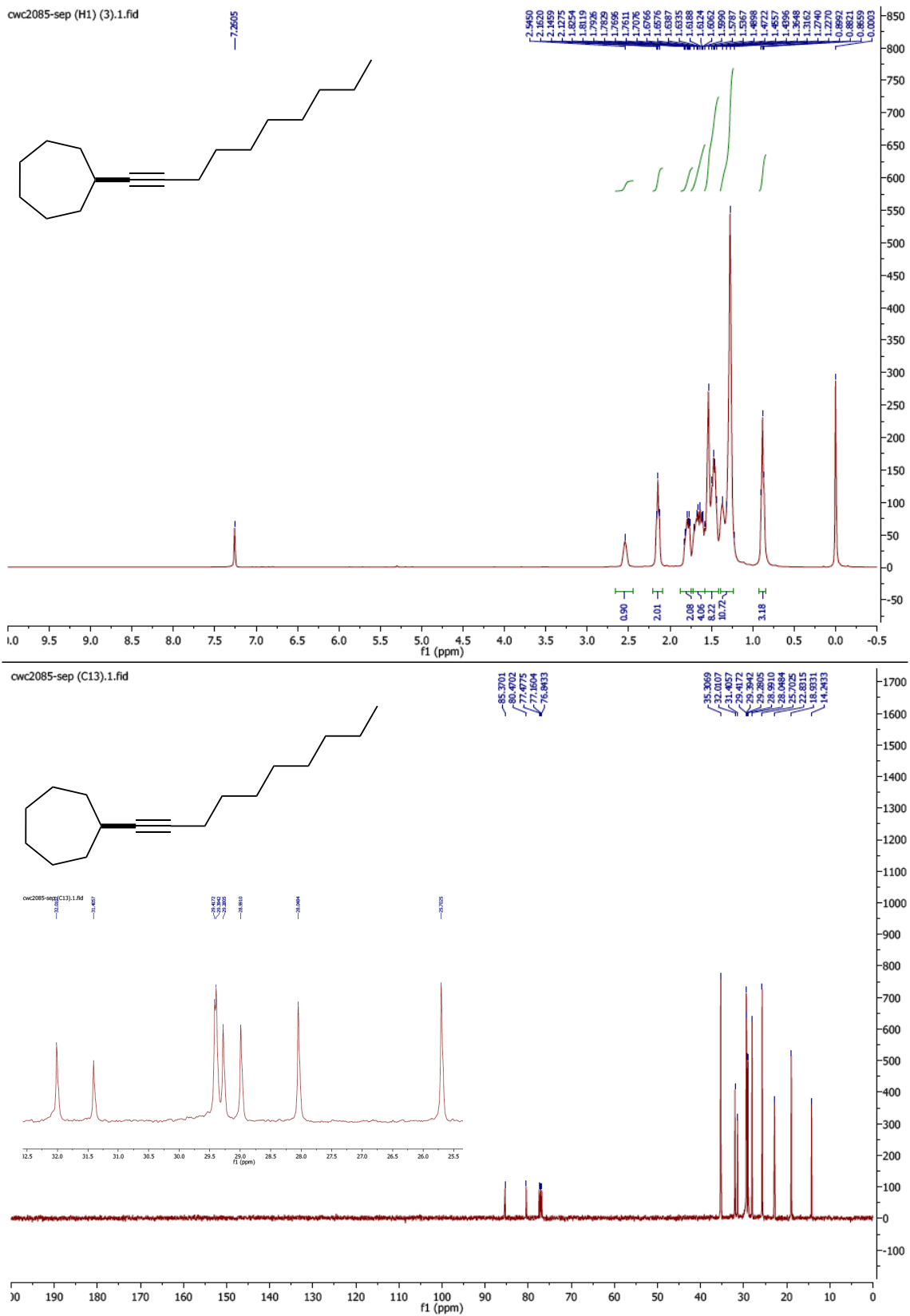
cwc2065-sep (H1).1.fid



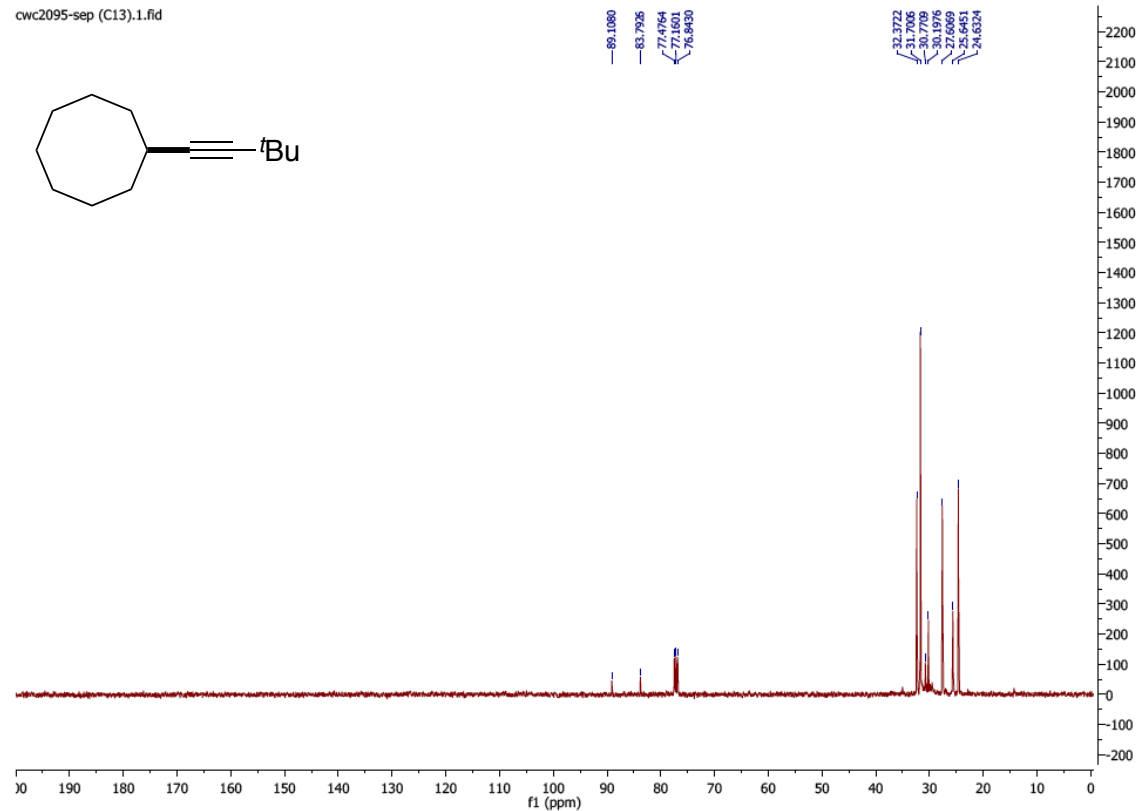
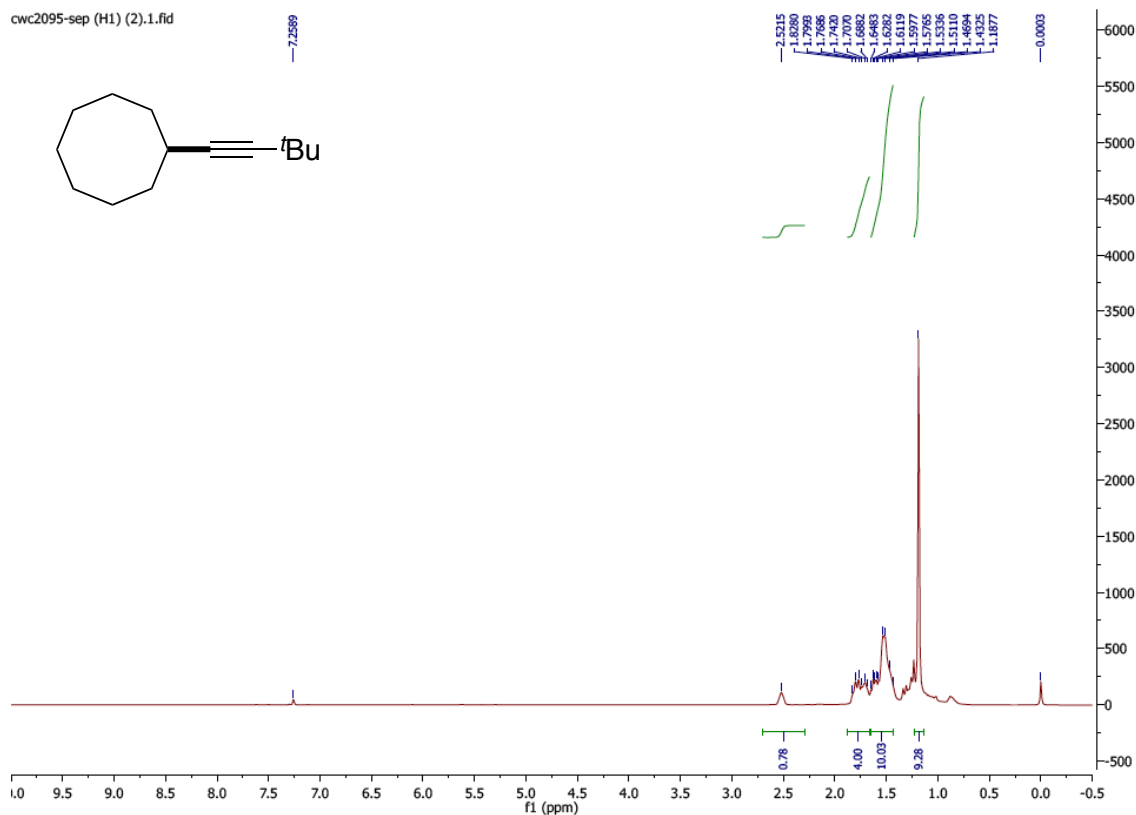
cwc2065-sep (C13) (2).1.fid



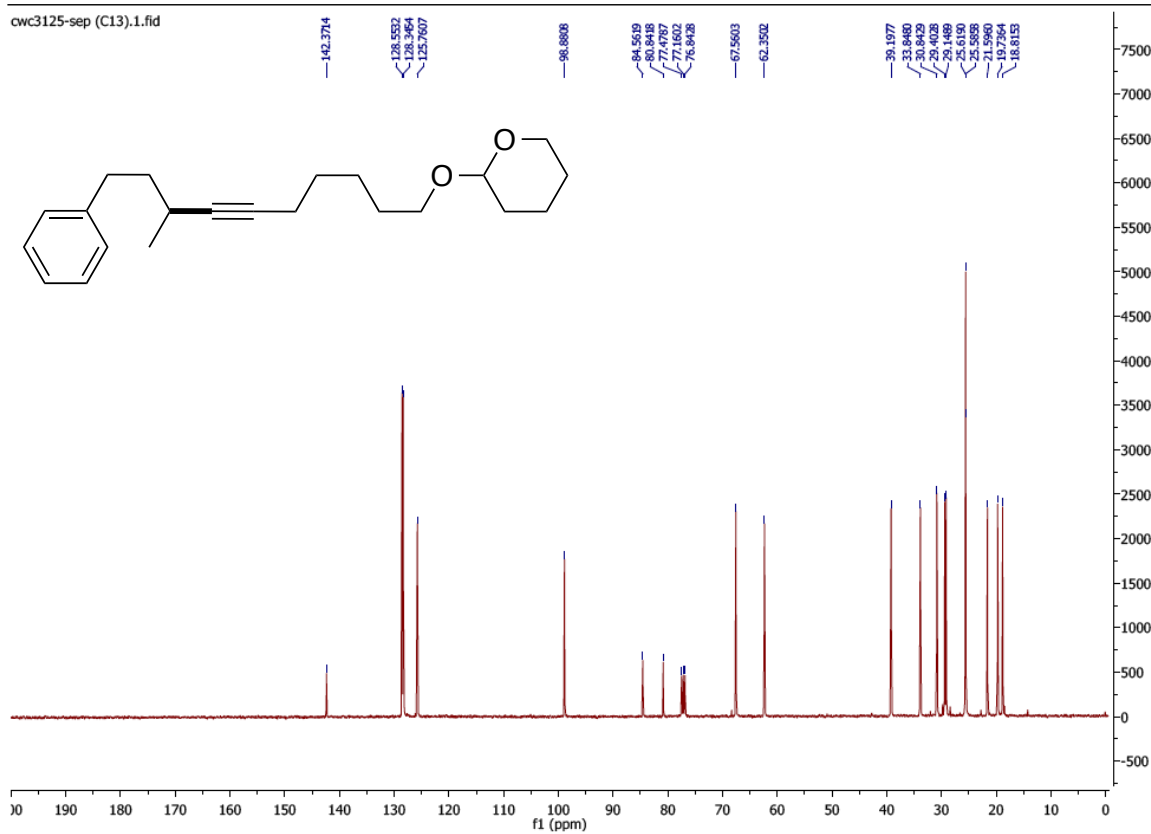
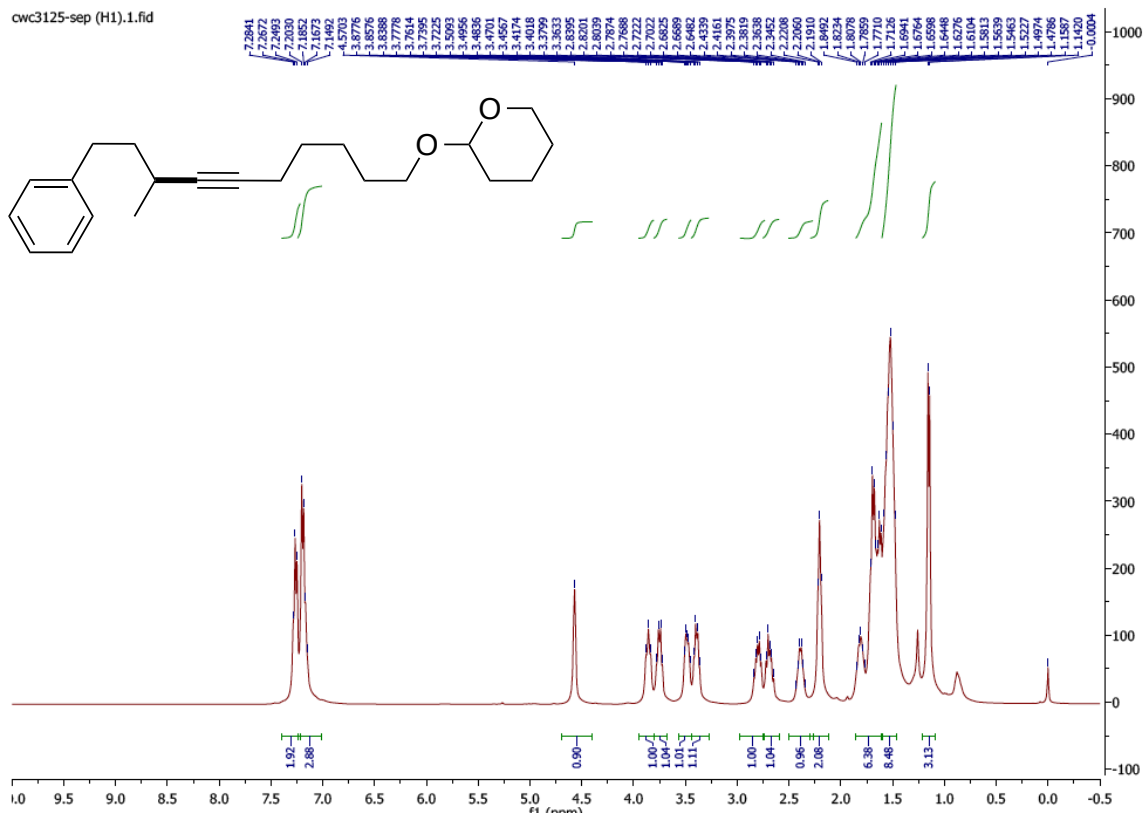
¹H and ¹³C NMR of Dec-1-yn-1-ylcycloheptane (3d)



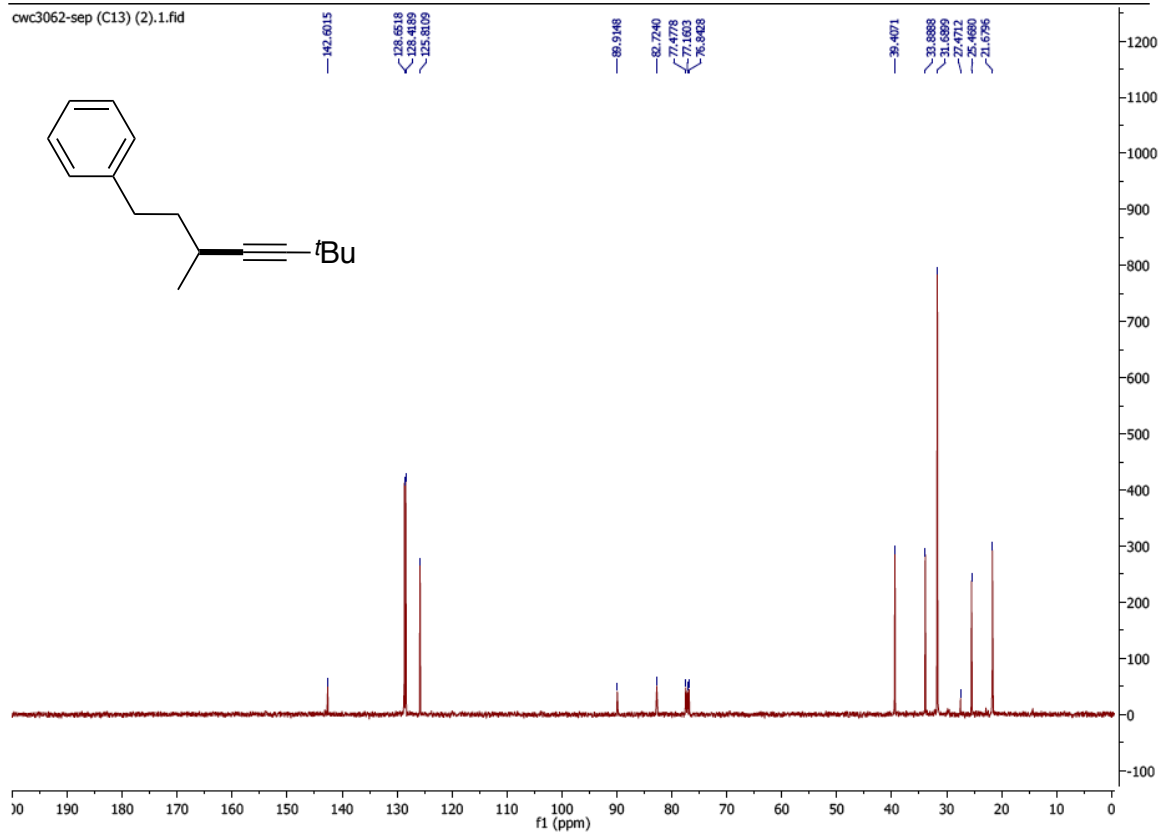
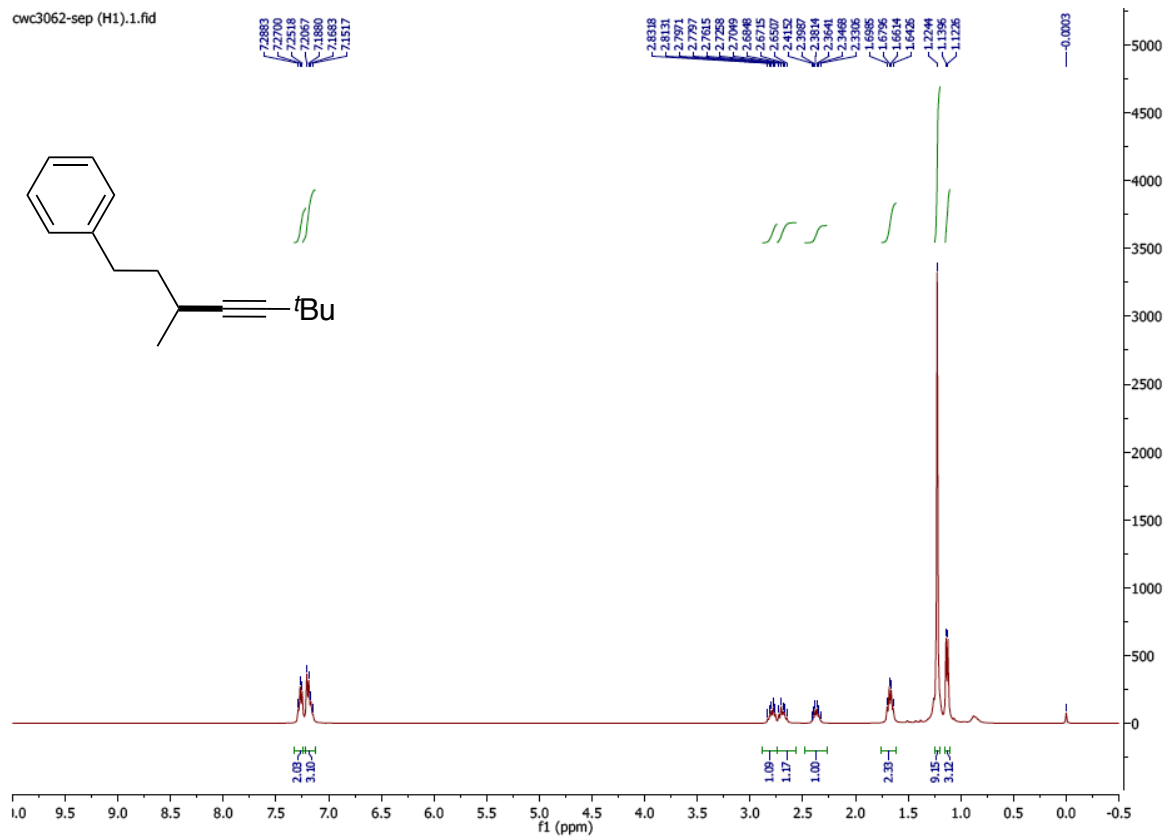
¹H and ¹³C NMR of (3,3-Dimethylbut-1-yn-1-yl)cyclooctane (3e)



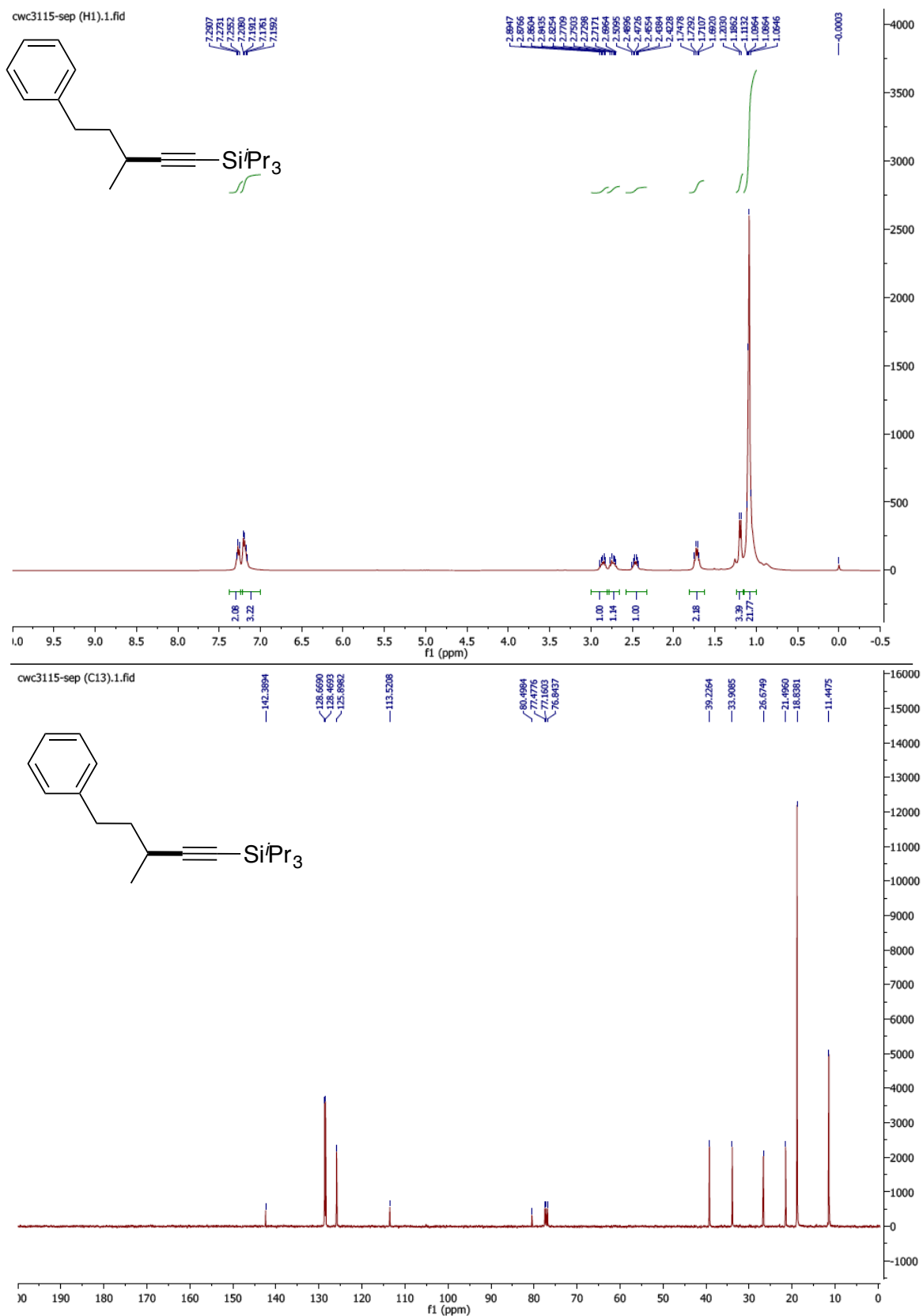
¹H and ¹³C NMR of 2-((8-Methyl-10-phenyldec-6-yn-1-yl)oxy)tetrahydro-2H-pyran (3f)



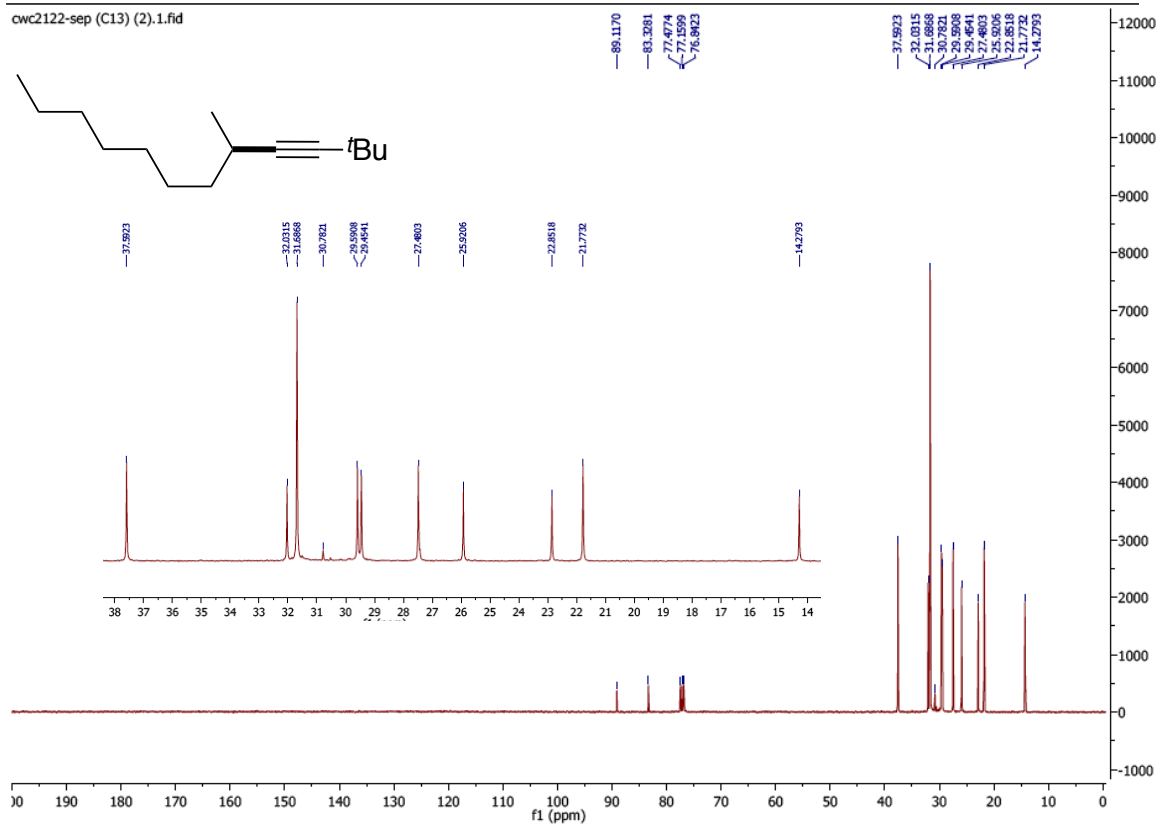
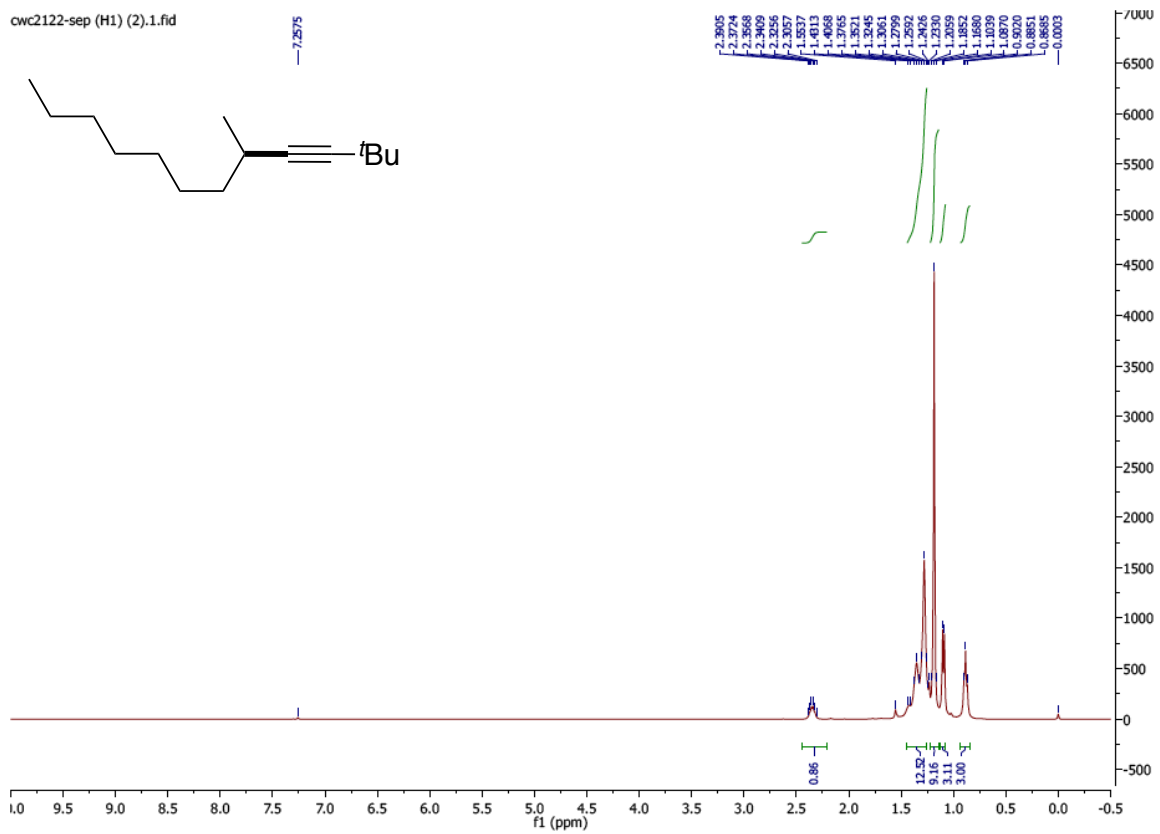
^1H and ^{13}C NMR of (3,6,6-Trimethylhept-4-yn-1-yl)benzene (3g)



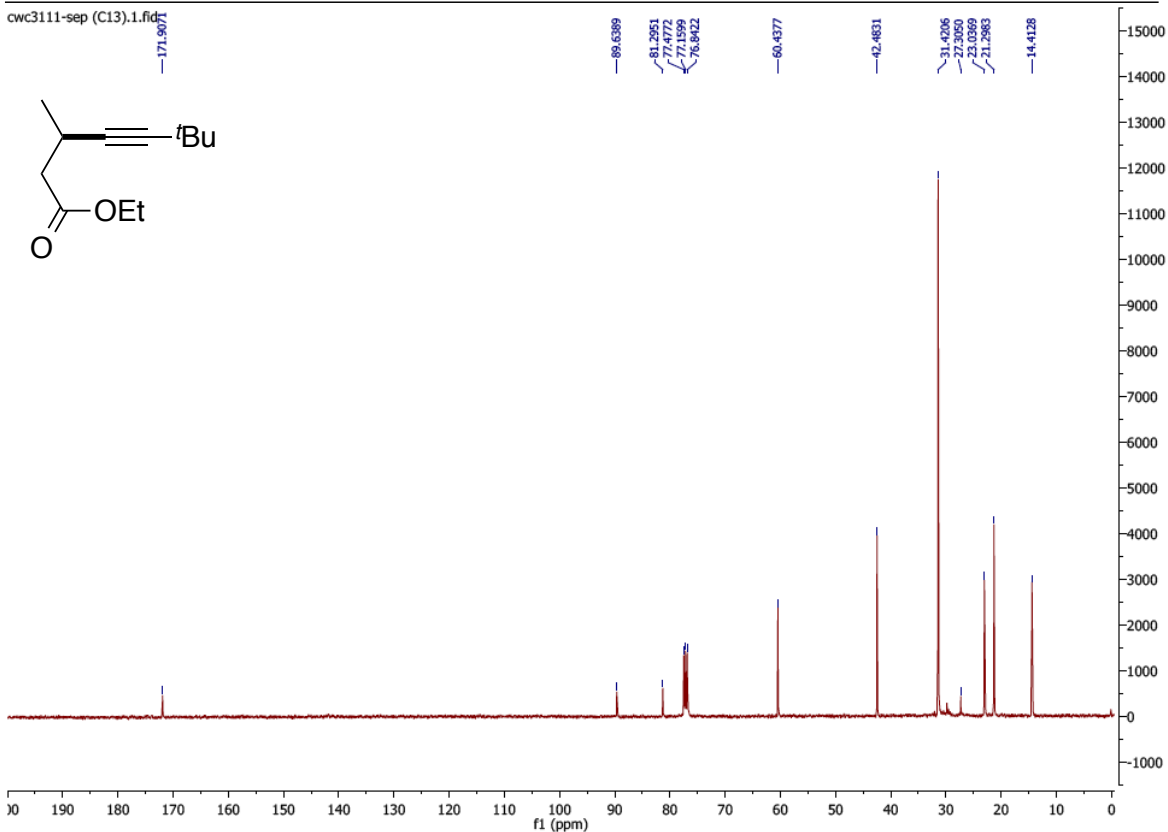
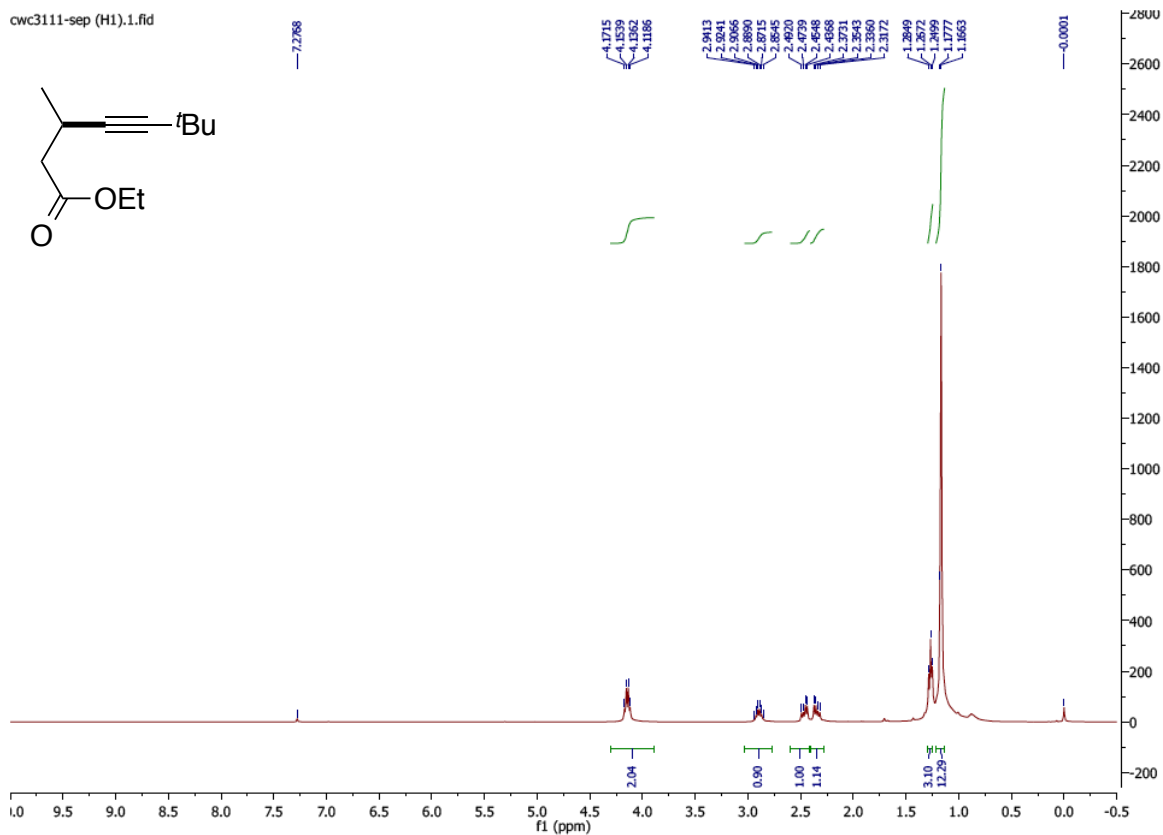
¹H and ¹³C NMR of Triisopropyl(3-methyl-5-phenylpent-1-yn-1-yl)silane (3h)



¹H and ¹³C NMR of 2,2,5-Trimethyldodec-3-yne (3i)

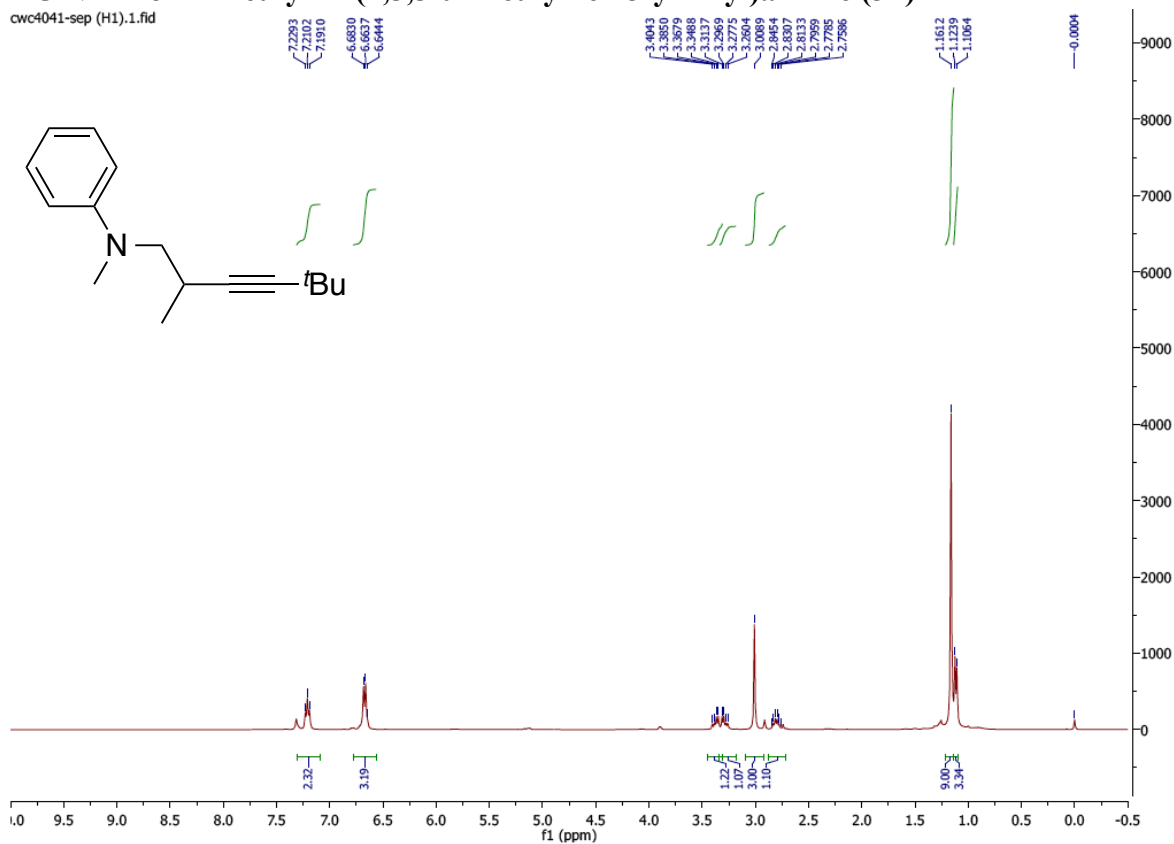


¹H and ¹³C NMR of Ethyl 3,6,6-trimethylhept-4-ynoate (3j)

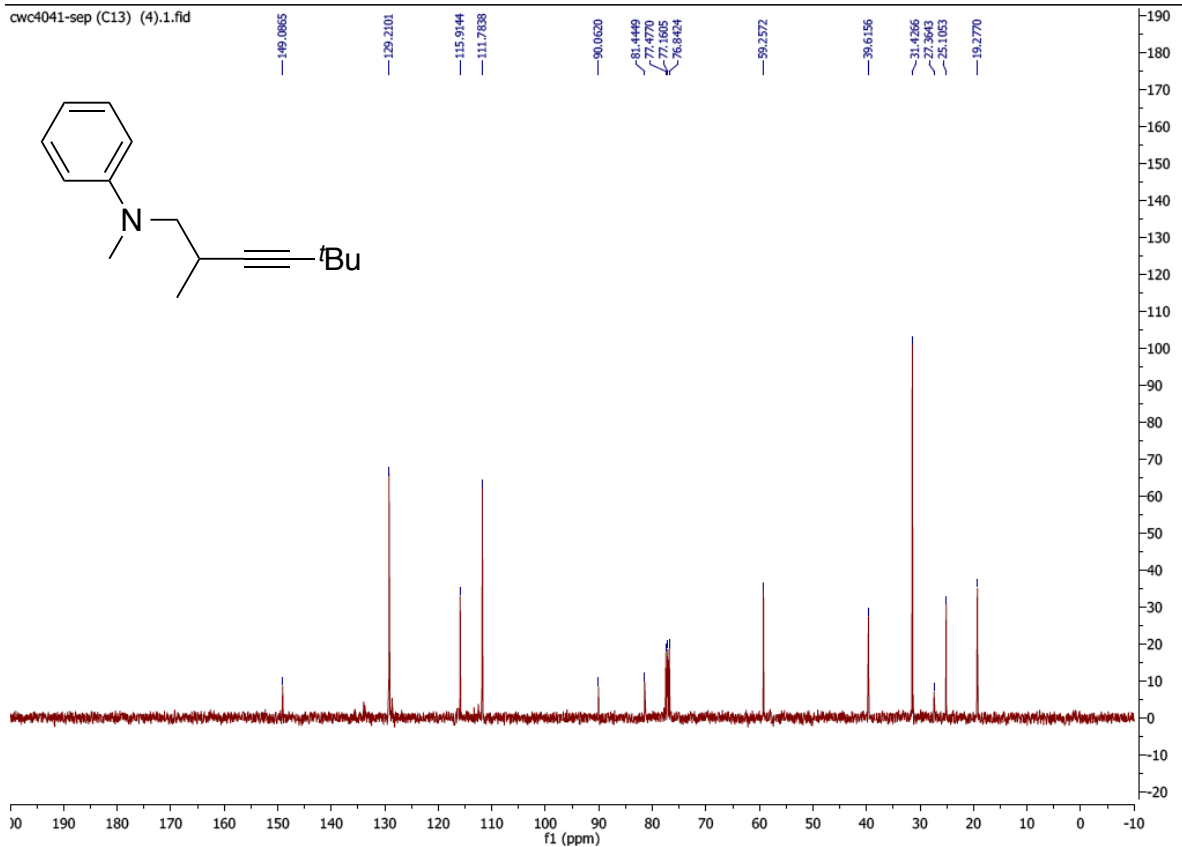


¹H and ¹³C NMR of *N*-methyl-*N*-(2,5,5-trimethylhex-3-yn-1-yl)aniline (3k)

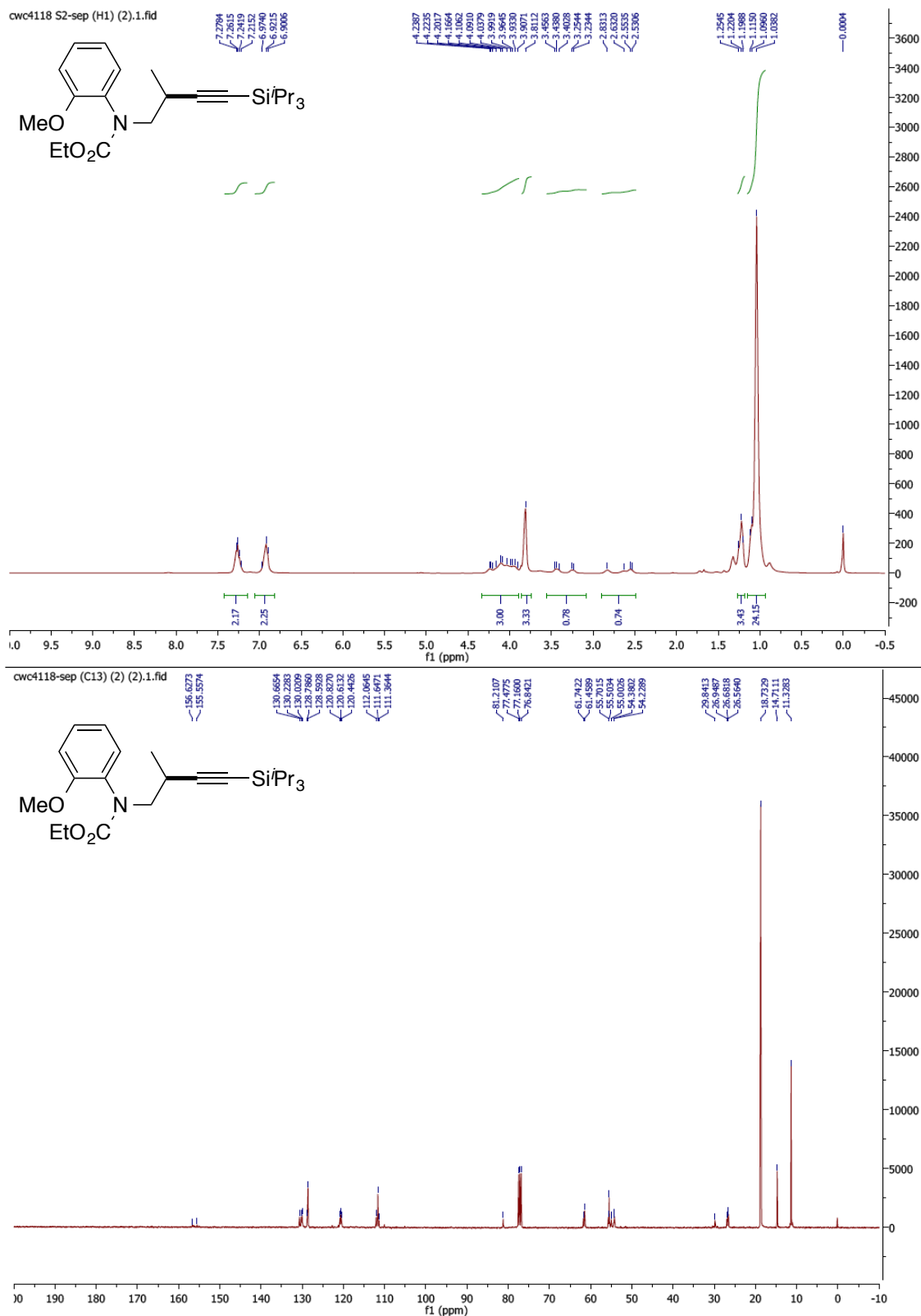
cwc4041-sep (H1).1.fid



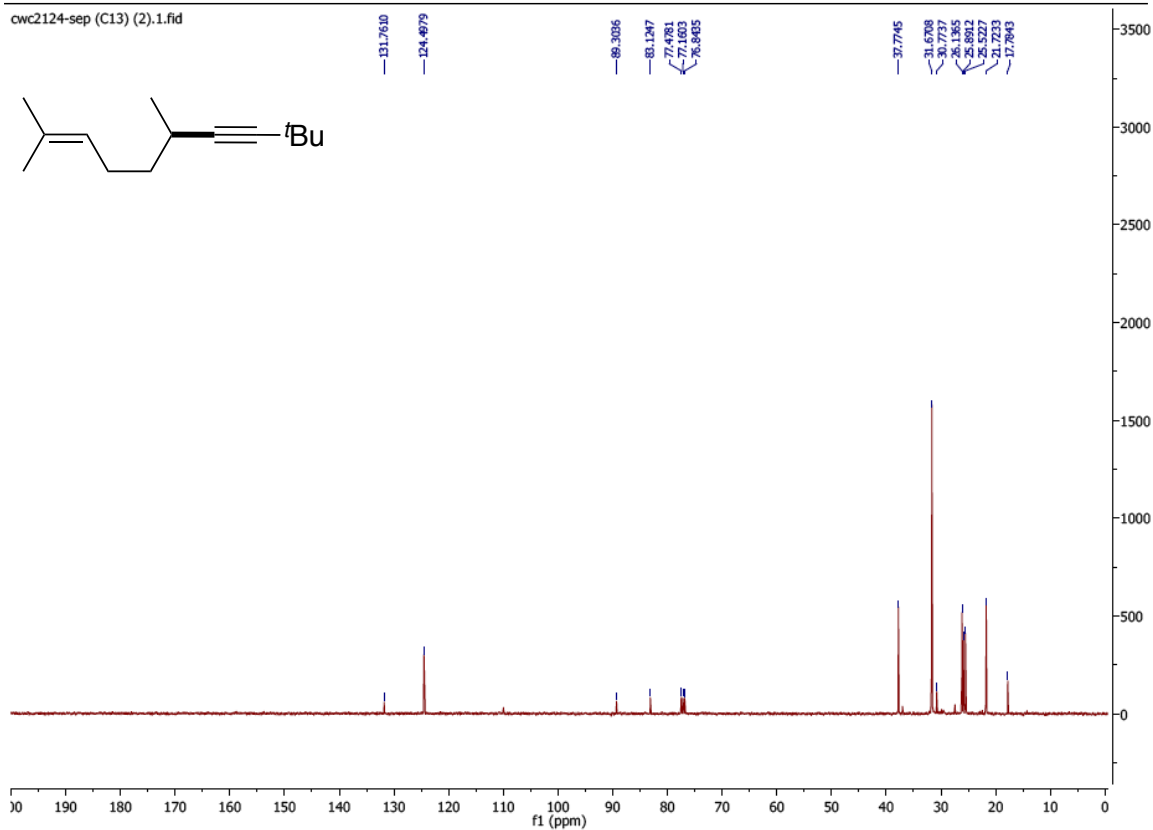
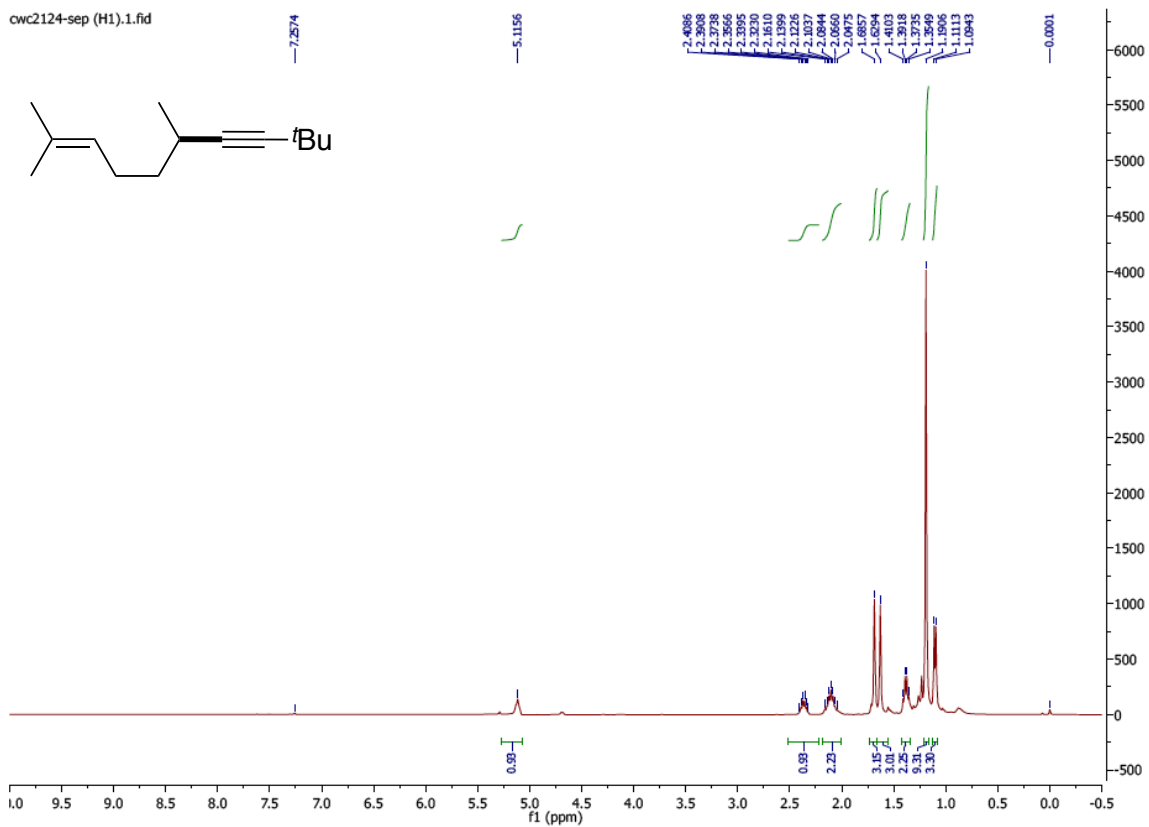
cwc4041-sep (C13) (4).1.fid



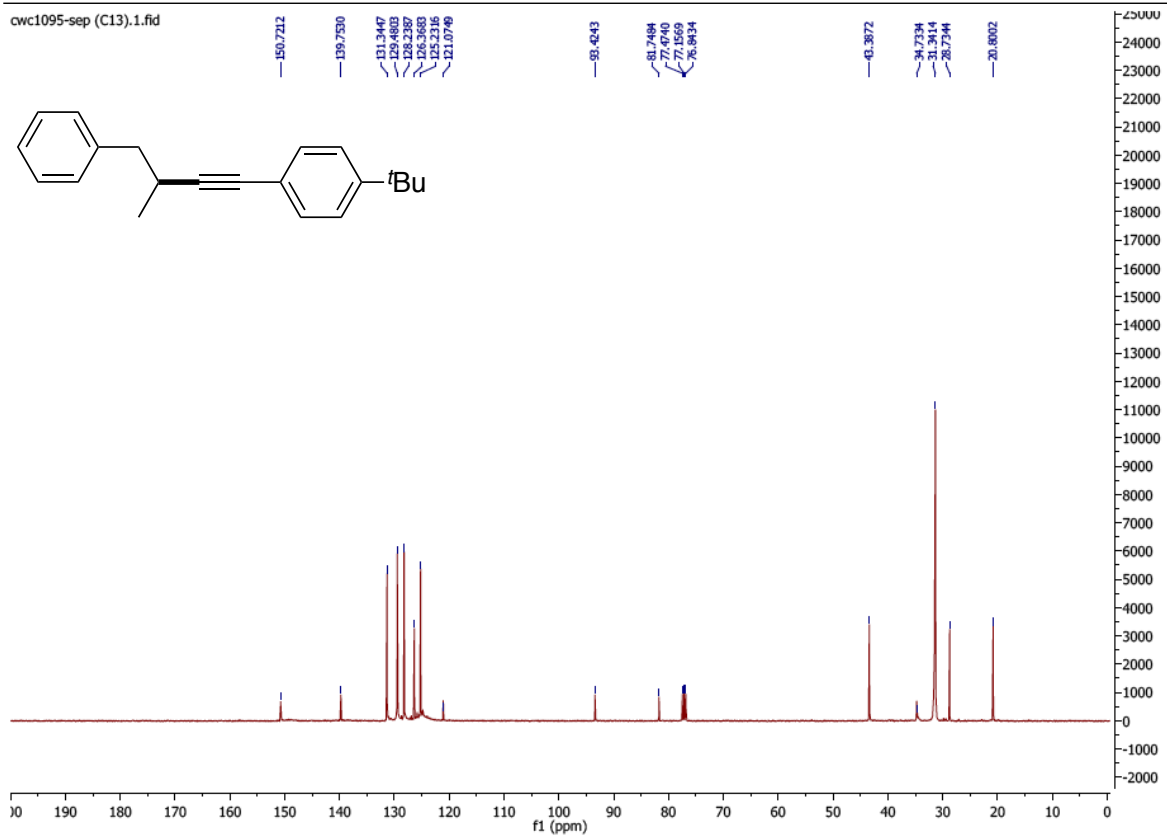
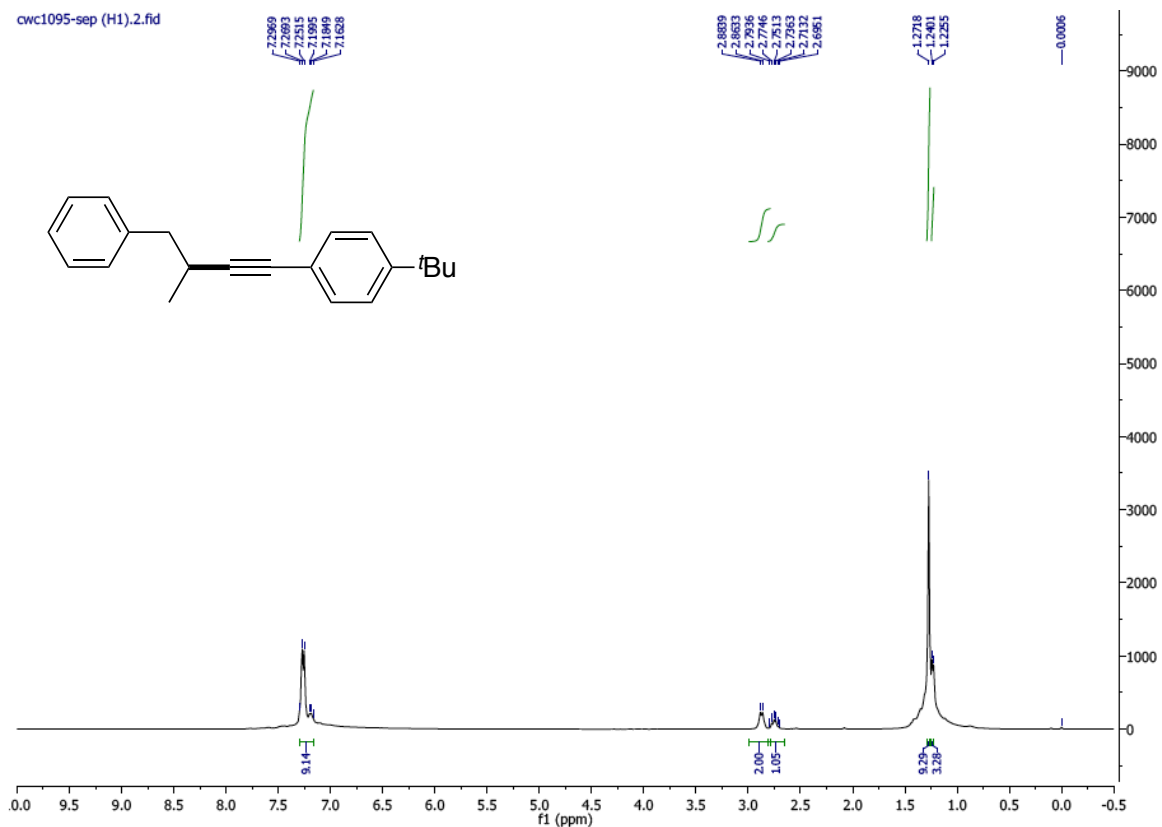
¹H and ¹³C NMR of Ethyl (2-Methoxyphenyl)(2-methyl-4-(triisopropylsilyl)but-3-yn-1-yl)carbamate
(3)



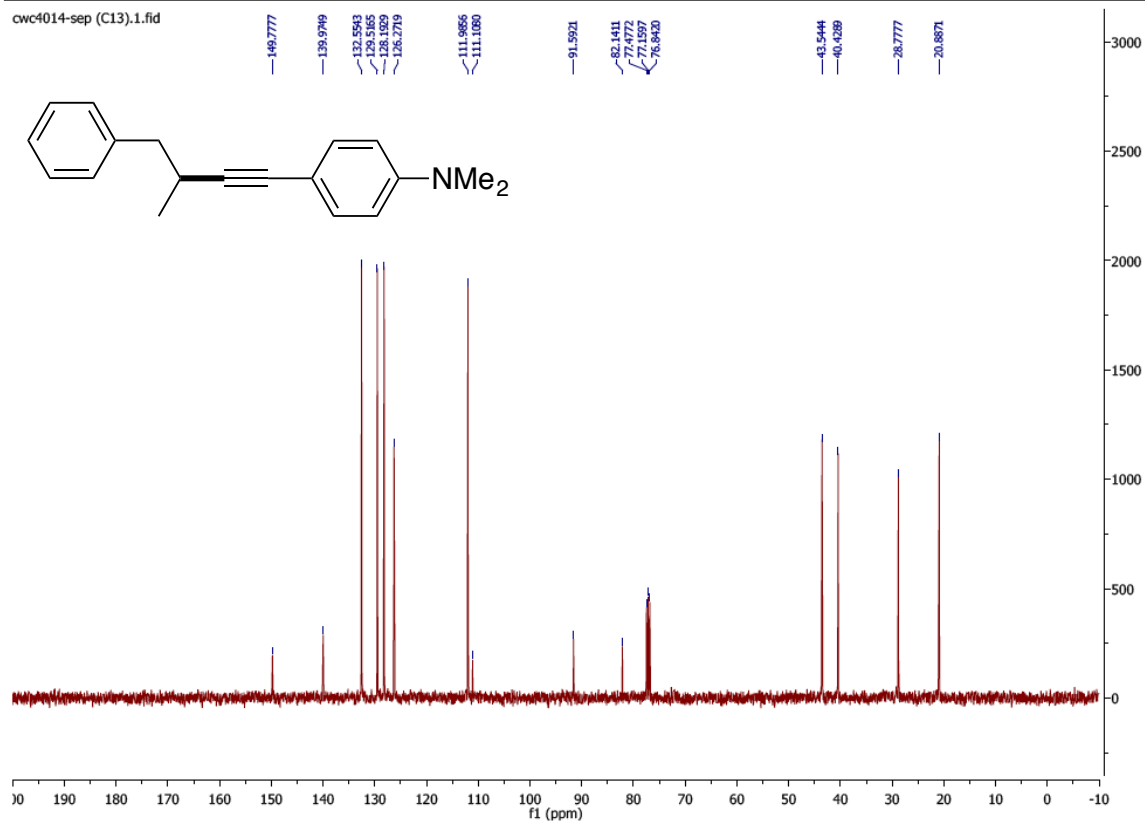
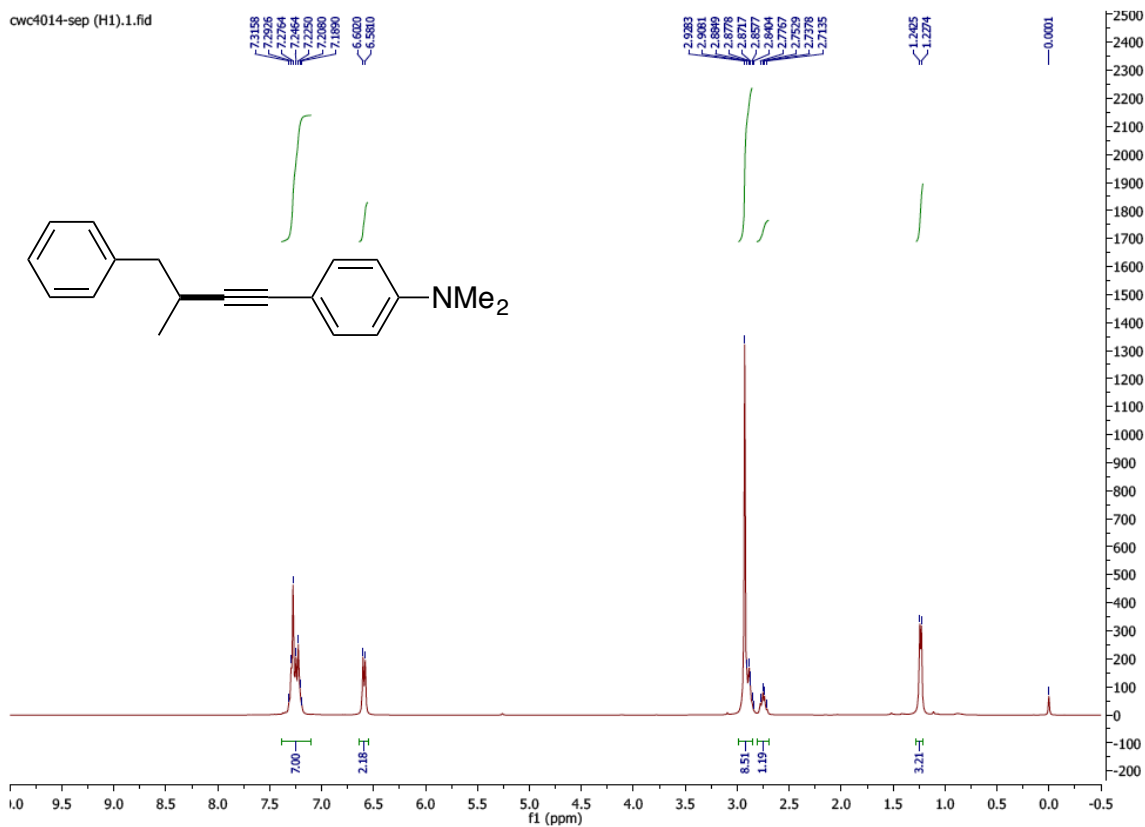
¹H and ¹³C NMR of 2,6,9,9-Tetramethyldec-2-en-7-yne (3m)



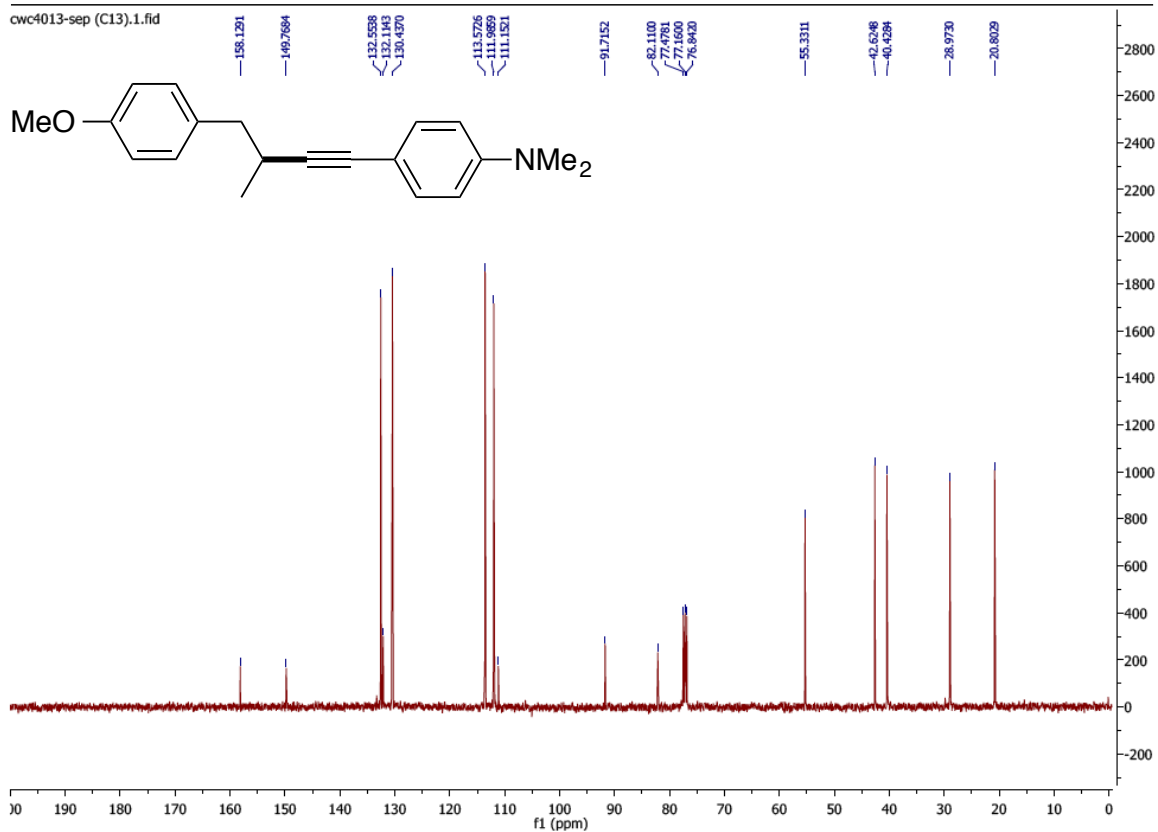
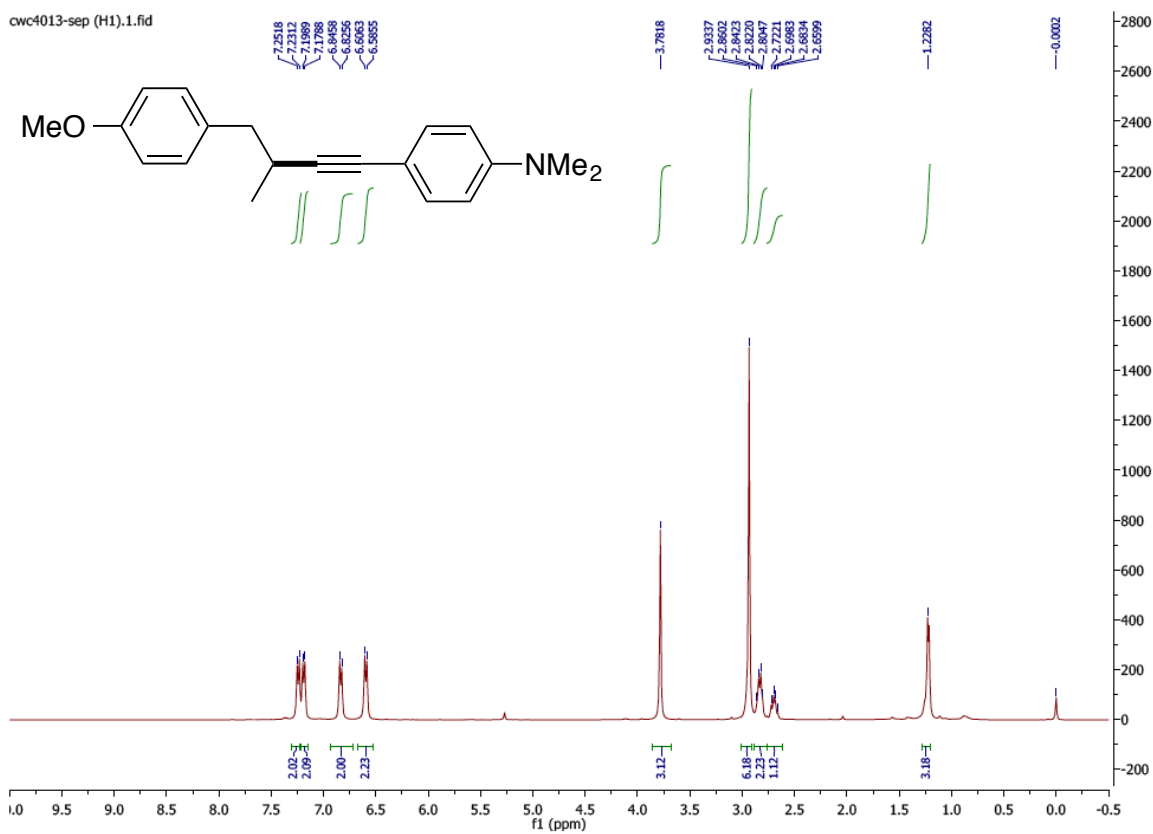
¹H and ¹³C NMR of 1-(*tert*-Butyl)-4-(3-methyl-4-phenylbut-1-yn-1-yl)benzene (3n)



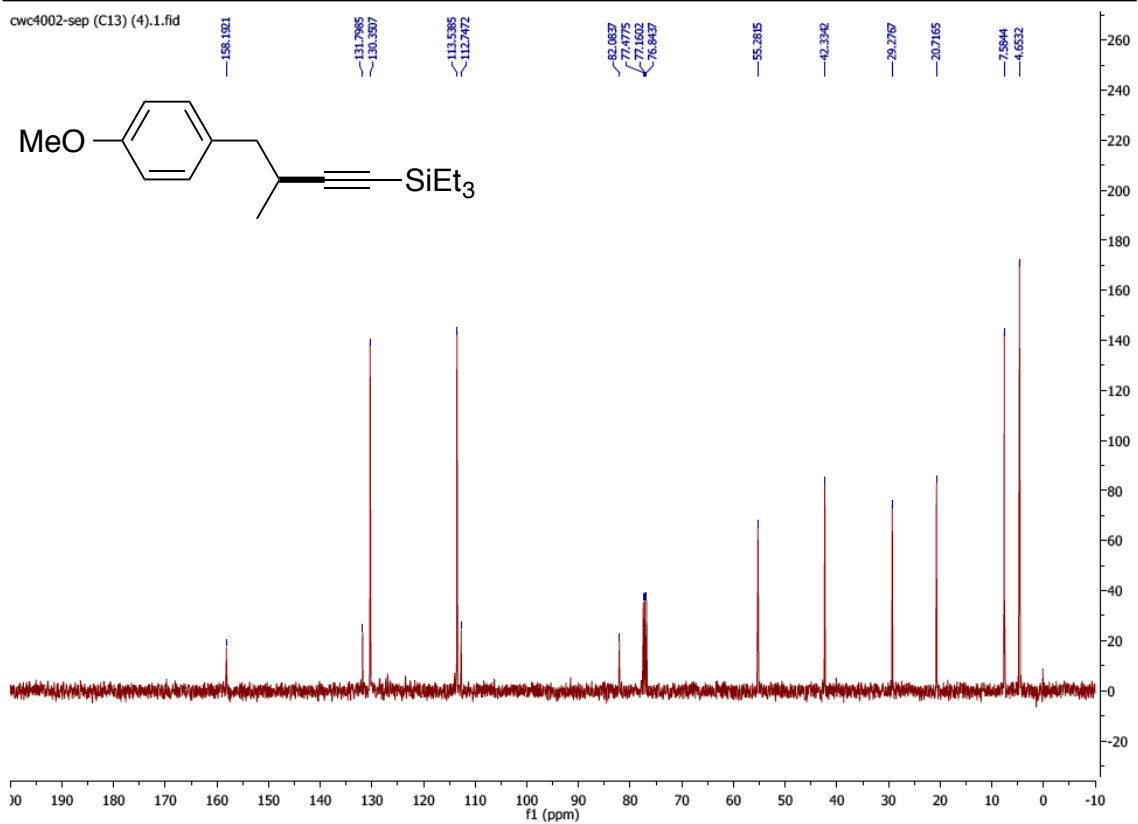
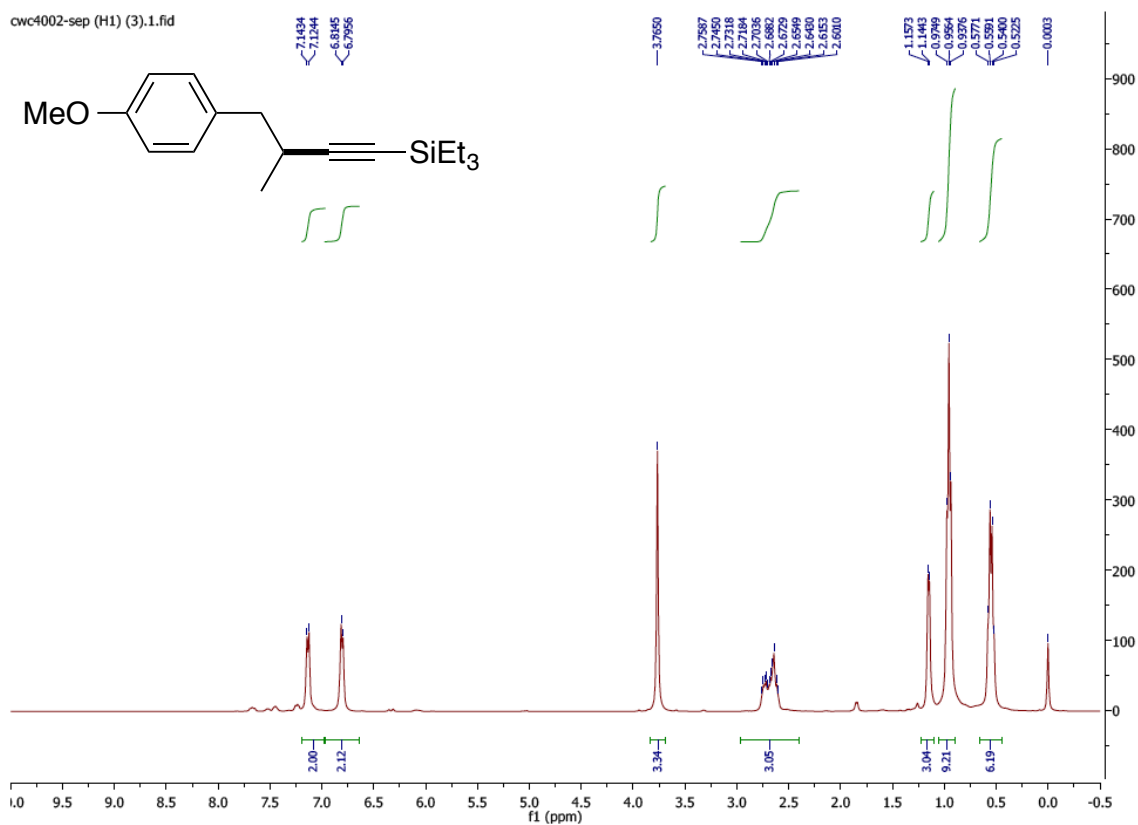
¹H and ¹³C NMR of *N,N*-dimethyl-4-(3-methyl-4-phenylbut-1-yn-1-yl)aniline (3o)



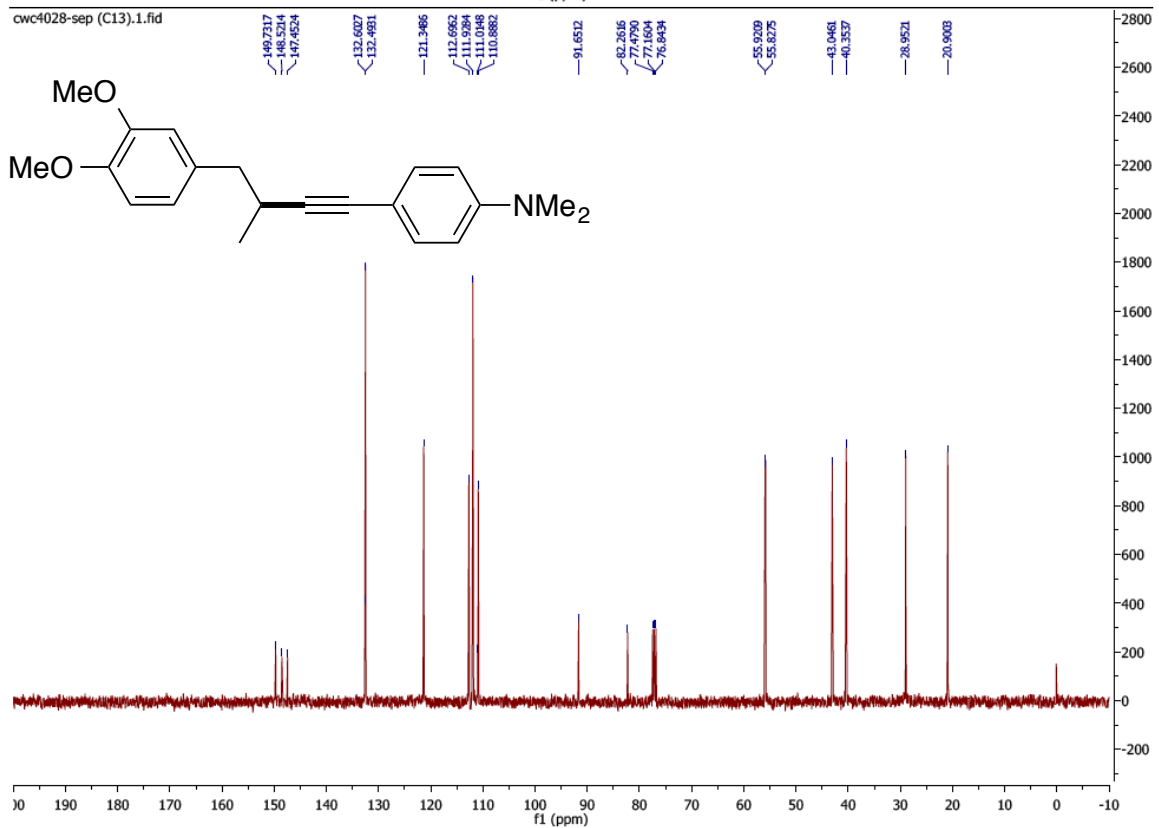
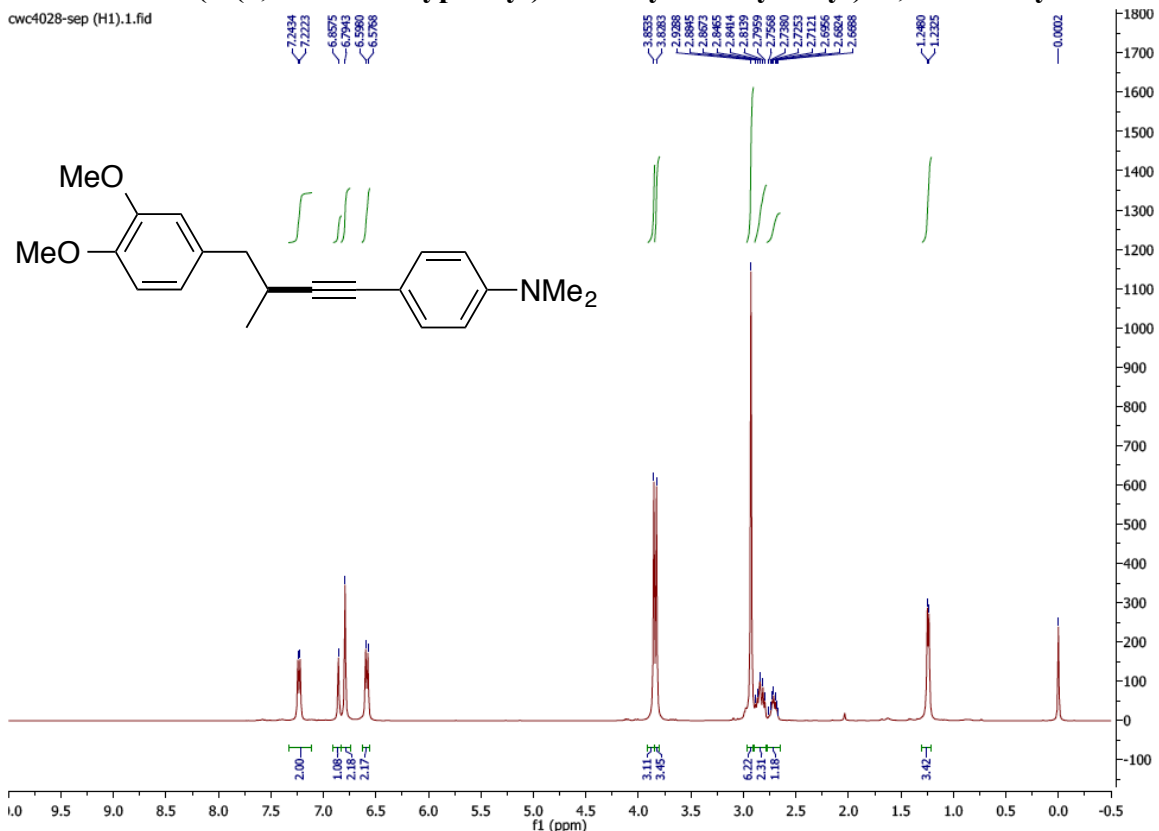
¹H and ¹³C NMR of 4-(4-(4-methoxyphenyl)-3-methylbut-1-yn-1-yl)-*N,N*-dimethylaniline (3p)



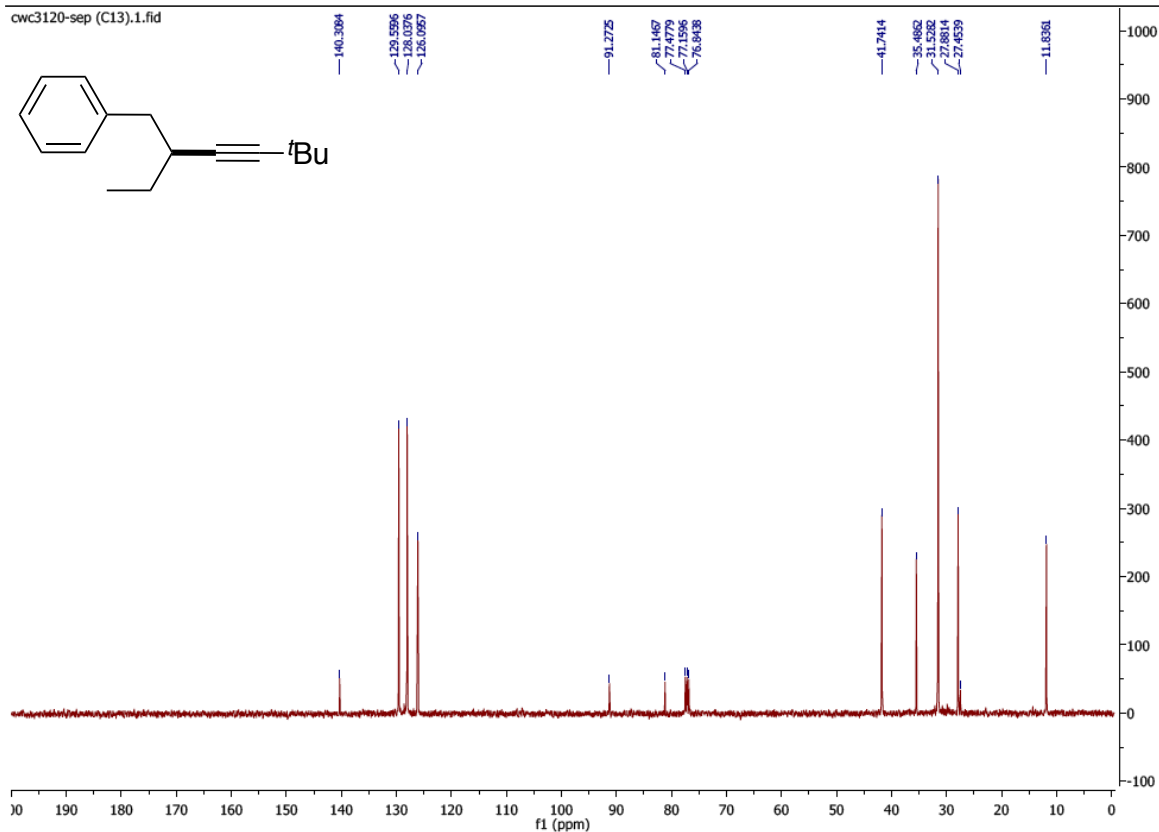
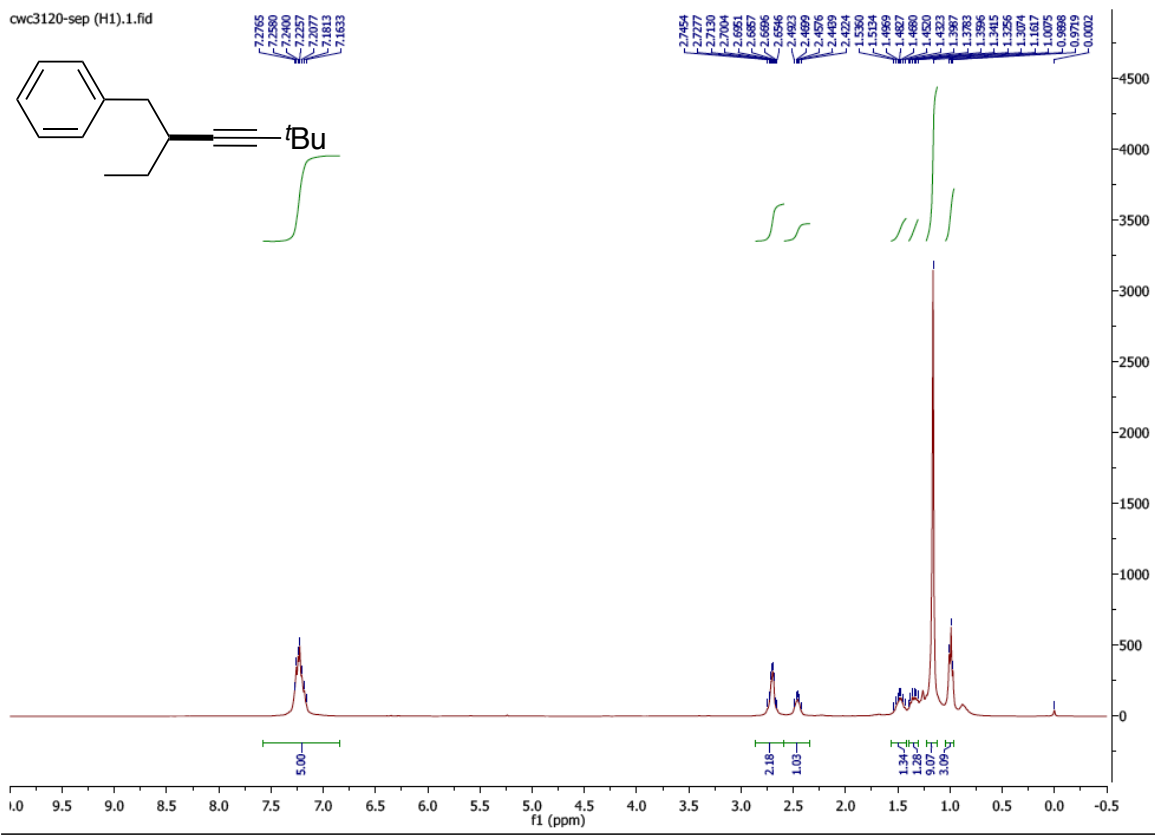
¹H and ¹³C NMR of Triethyl(4-(4-methoxyphenyl)-3-methylbut-1-yn-1-yl)silane (3q)



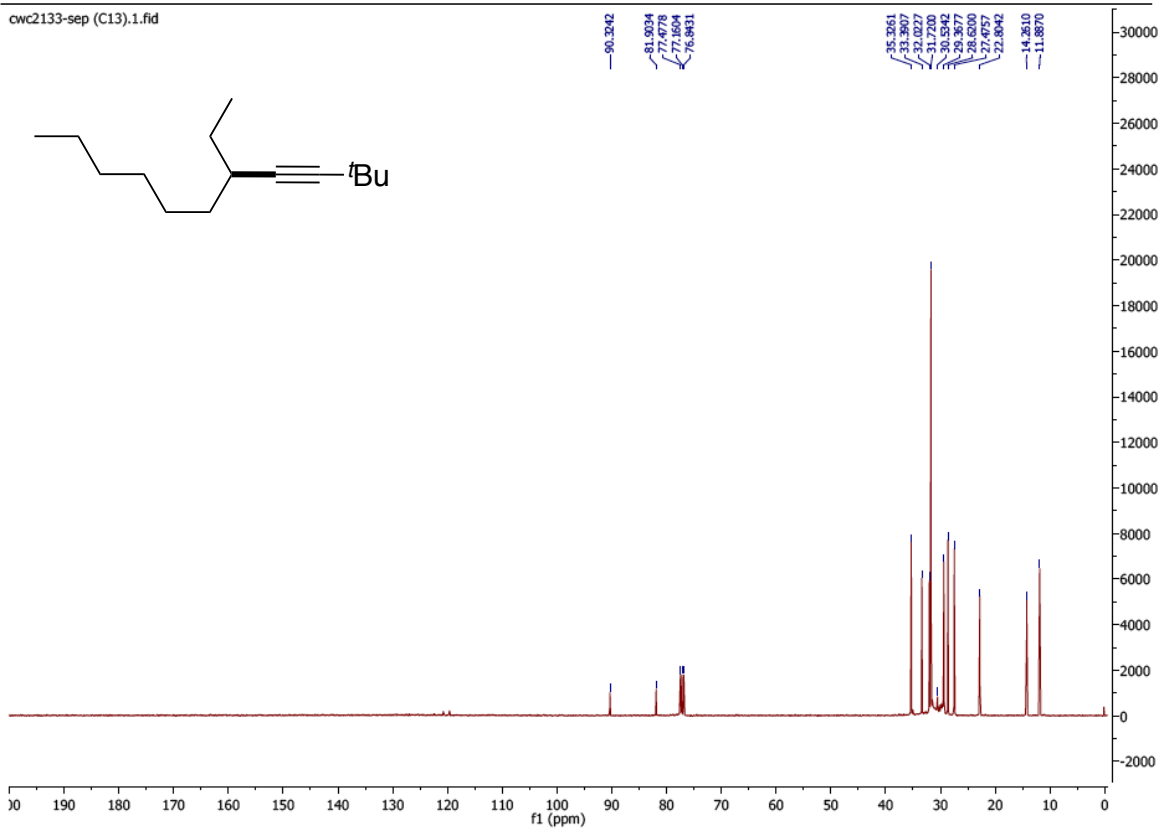
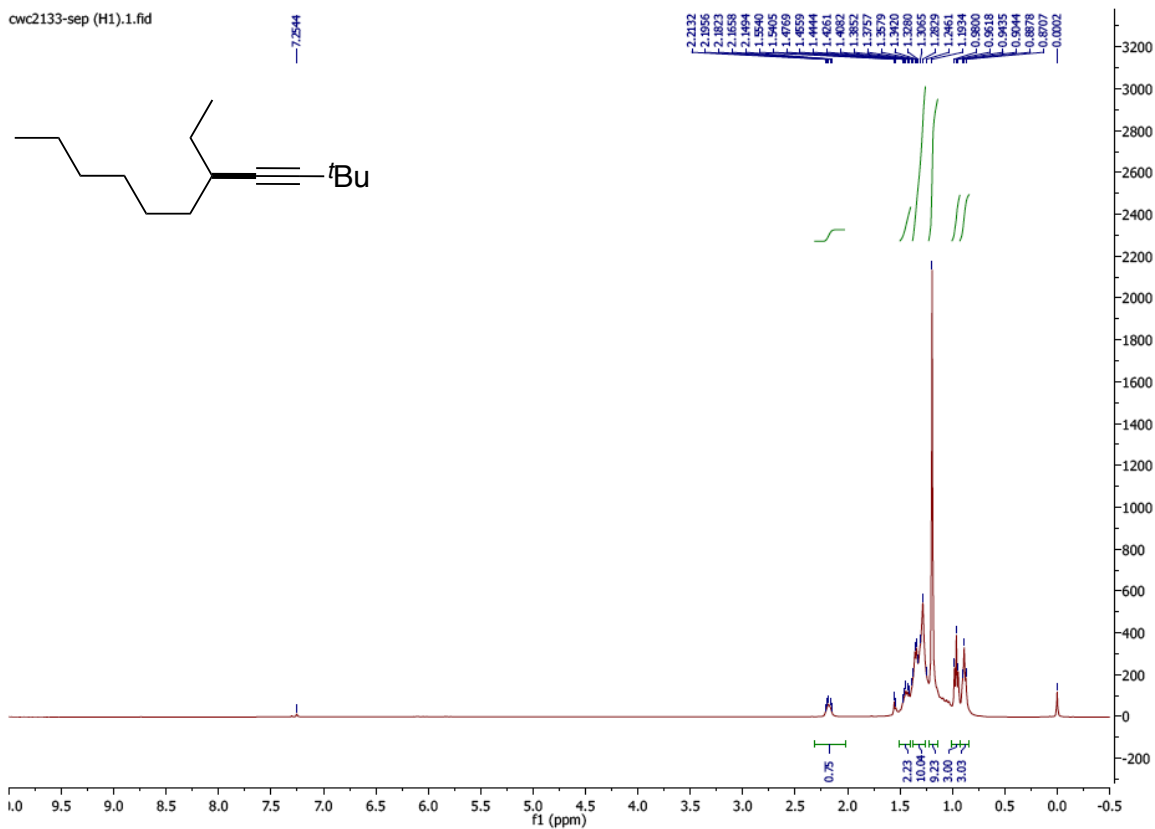
¹H and ¹³C NMR of 4-(4-(3,4-dimethoxyphenyl)-3-methylbut-1-yn-1-yl)-N,N-dimethylaniline (3r)



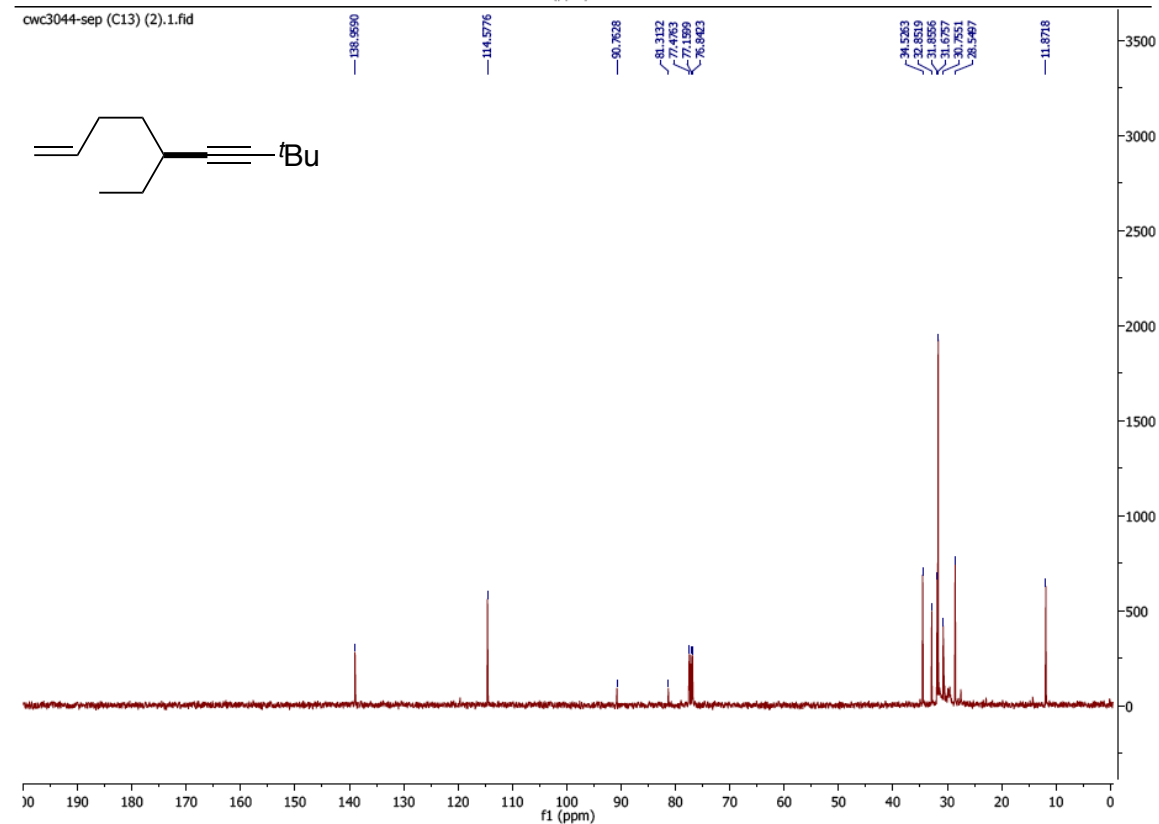
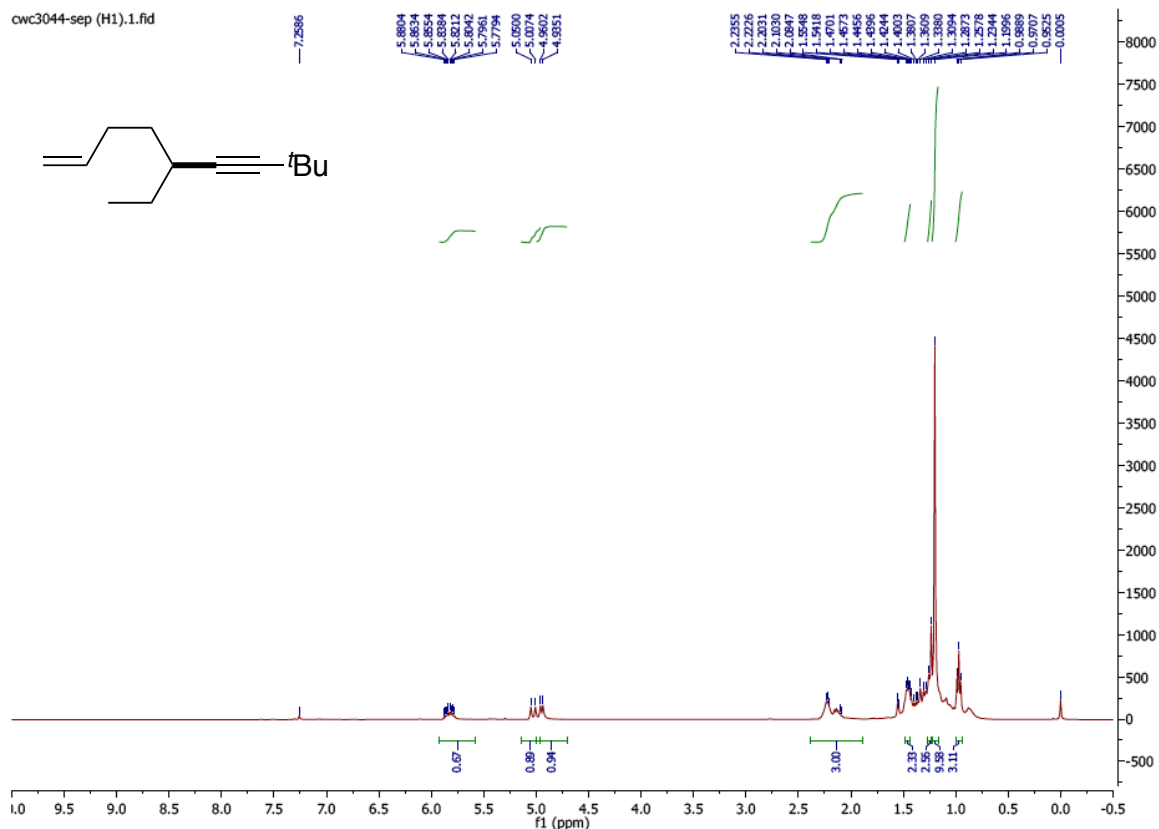
¹H and ¹³C NMR of (2-Ethyl-5,5-dimethylhex-3-yn-1-yl)benzene (3s)



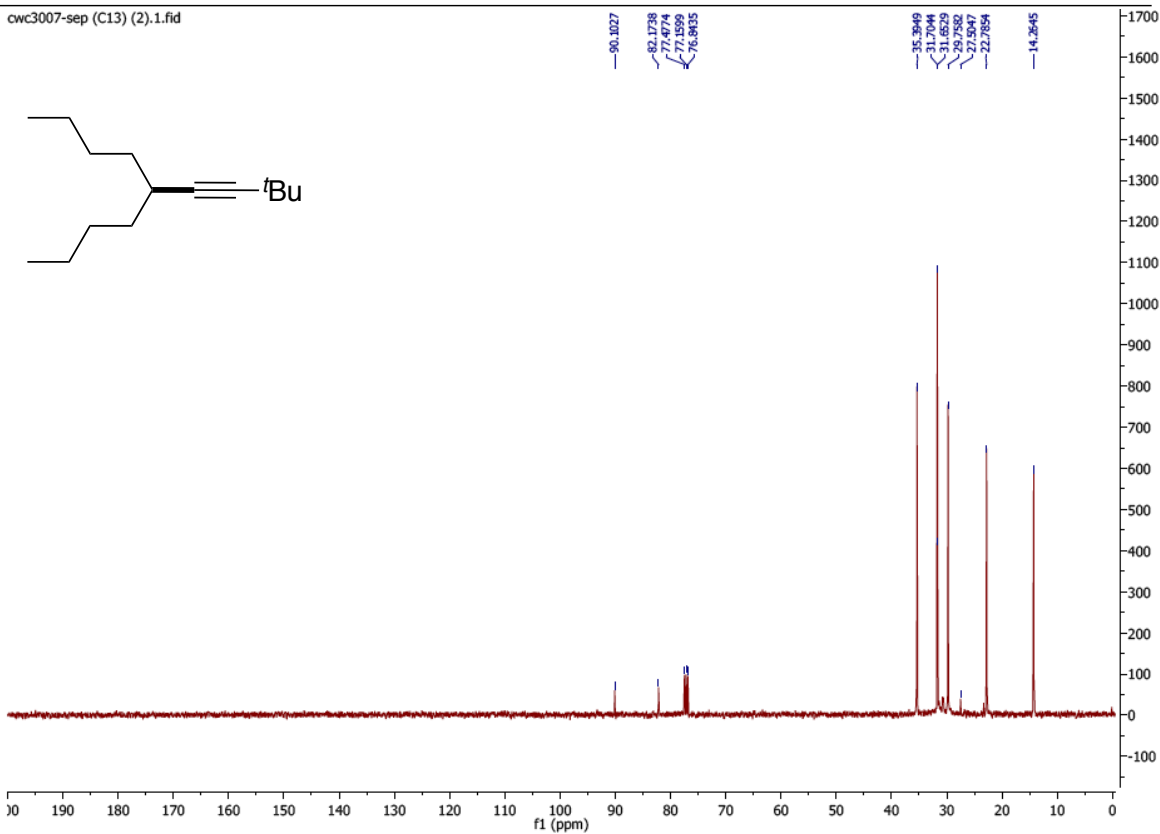
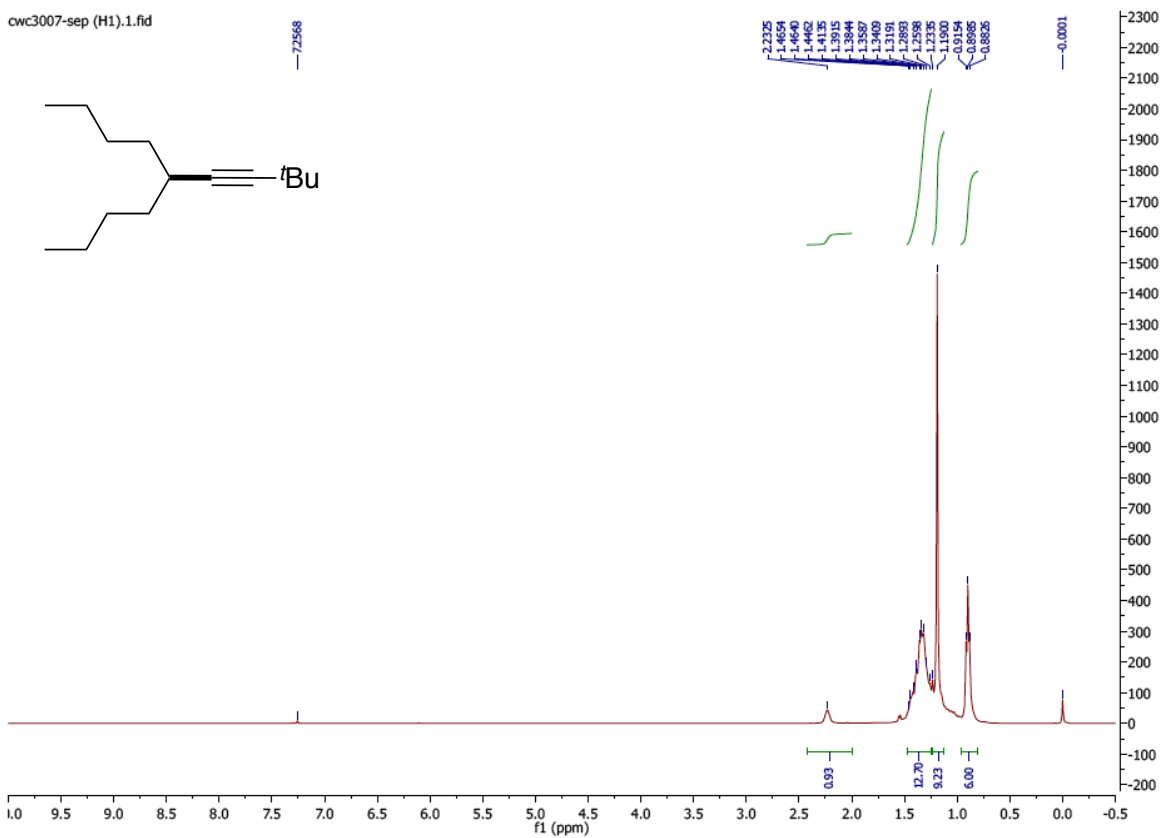
¹H and ¹³C NMR of 5-Ethyl-2,2-dimethylundec-3-yne (3t)



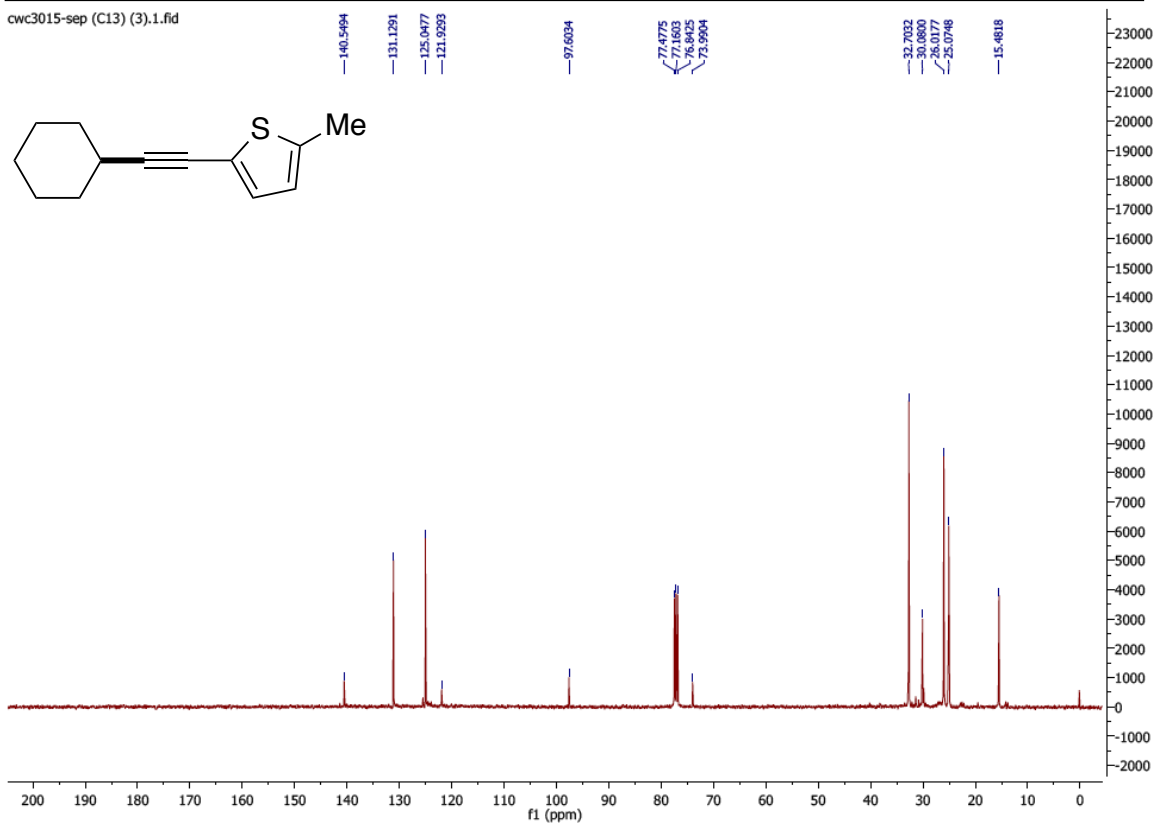
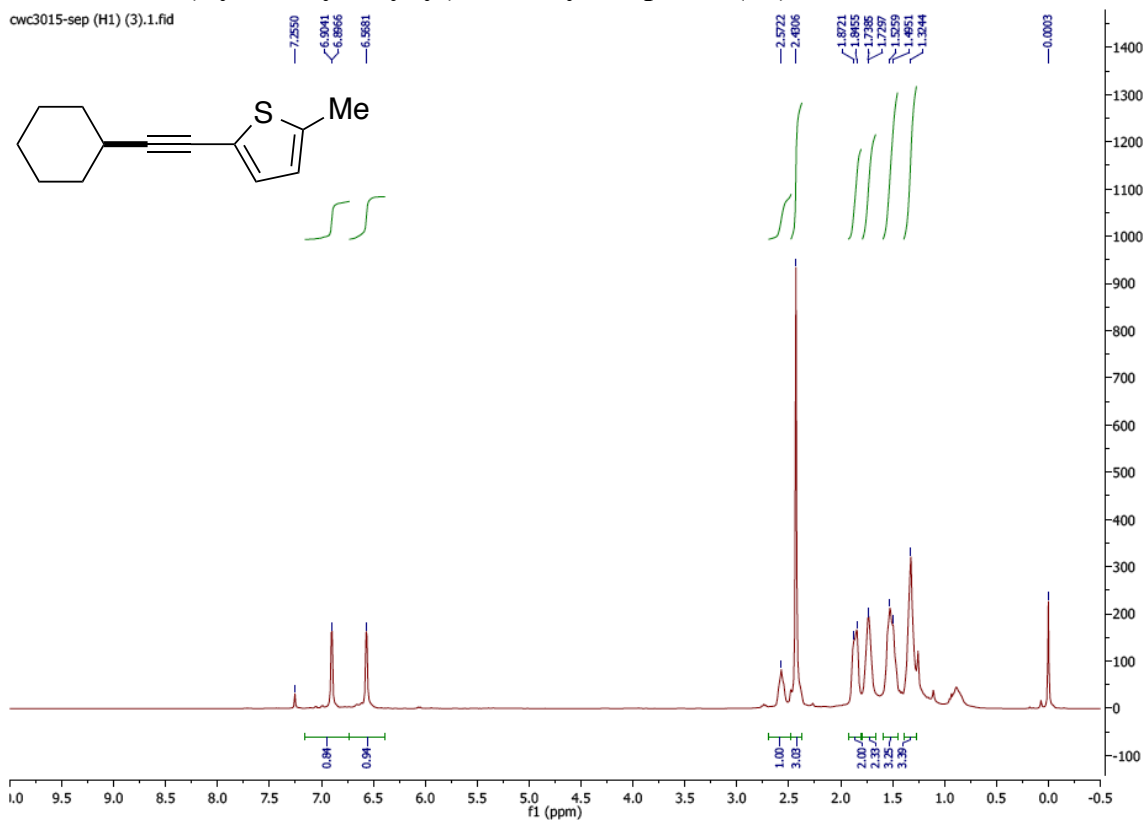
¹H and ¹³C NMR of 5-Ethyl-8,8-dimethylnon-1-en-6-yne (3u)



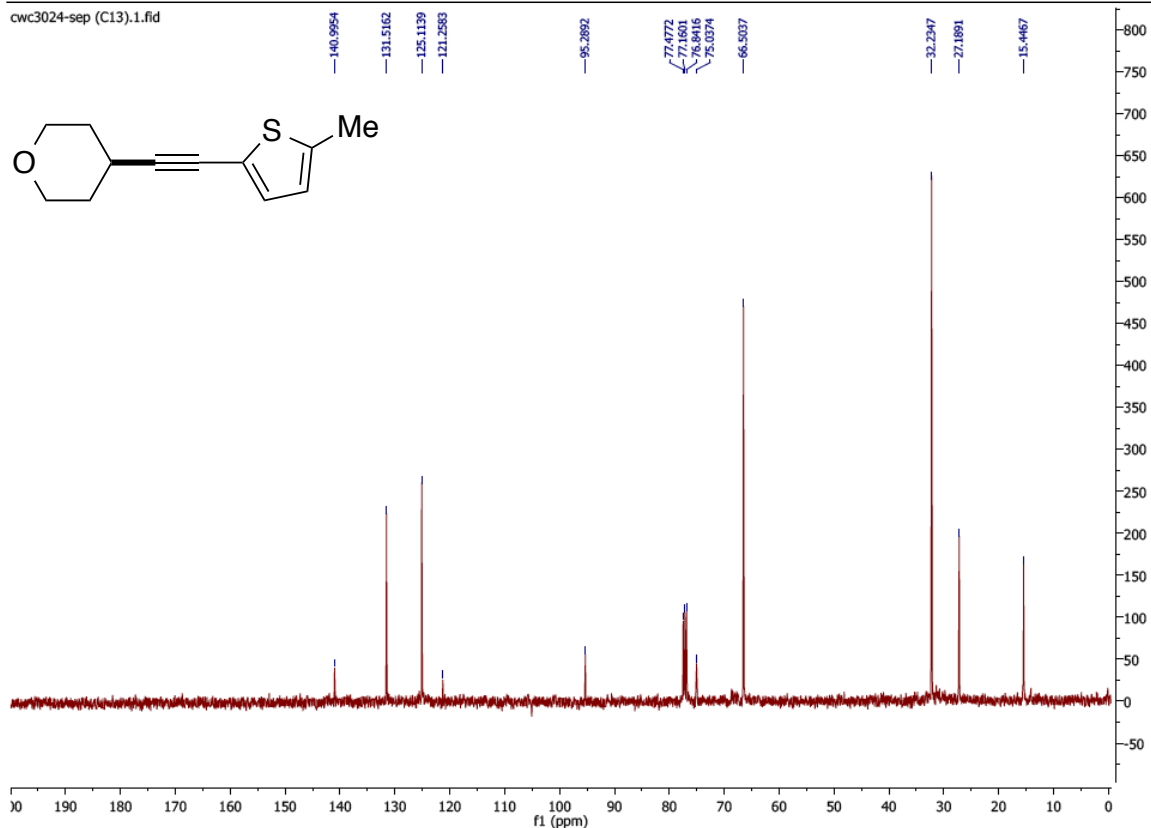
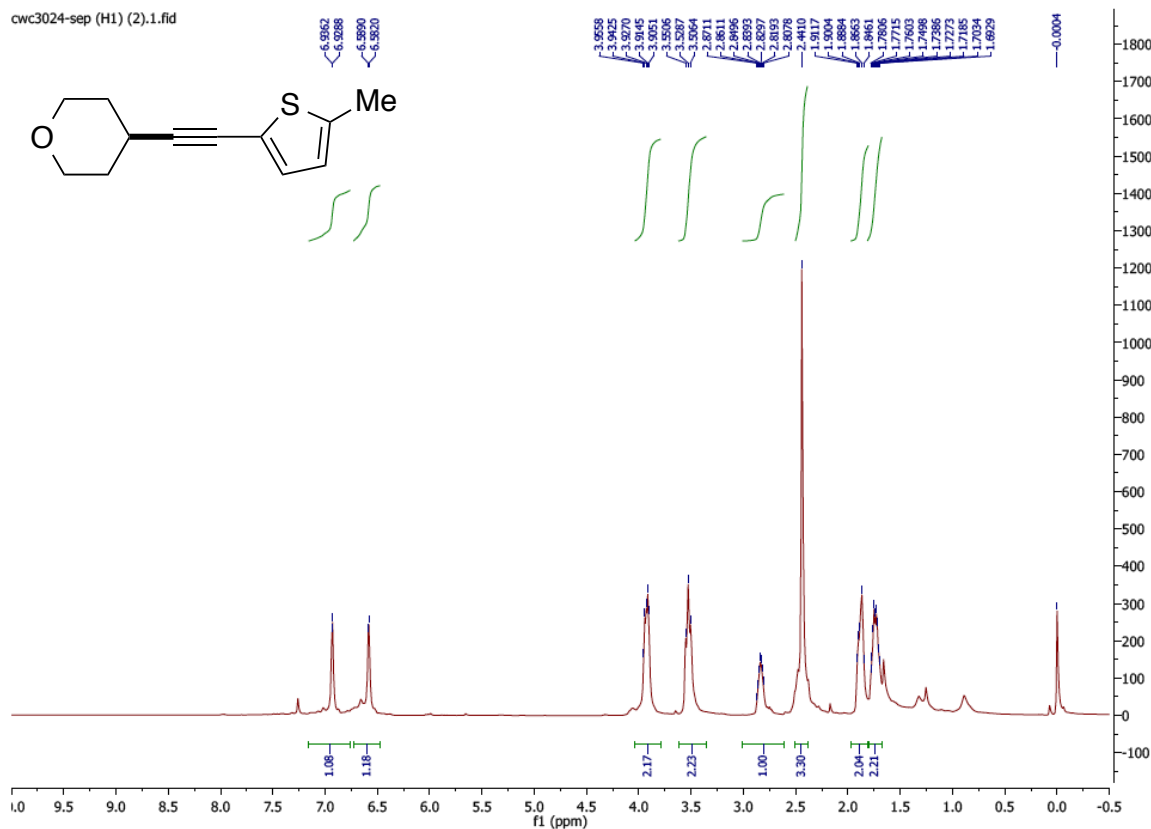
¹H and ¹³C NMR of 5-Butyl-2,2-dimethylnon-3-yne (3v)



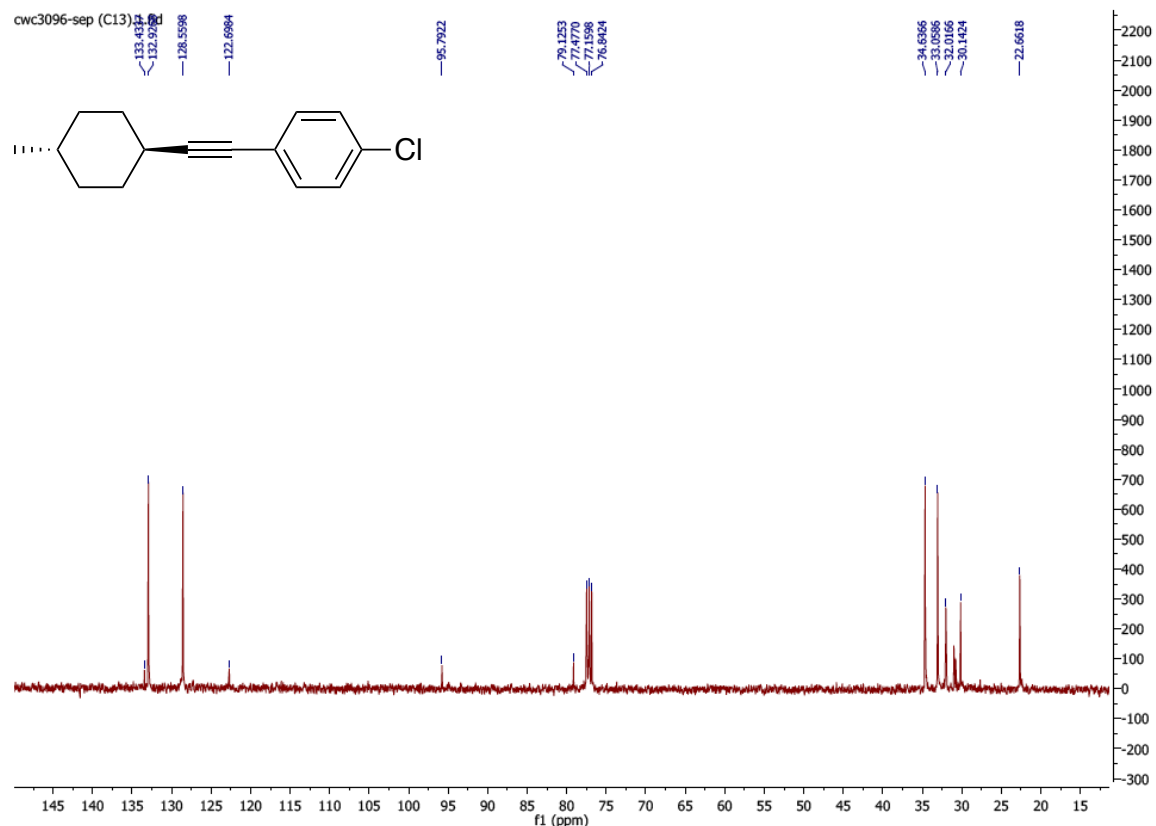
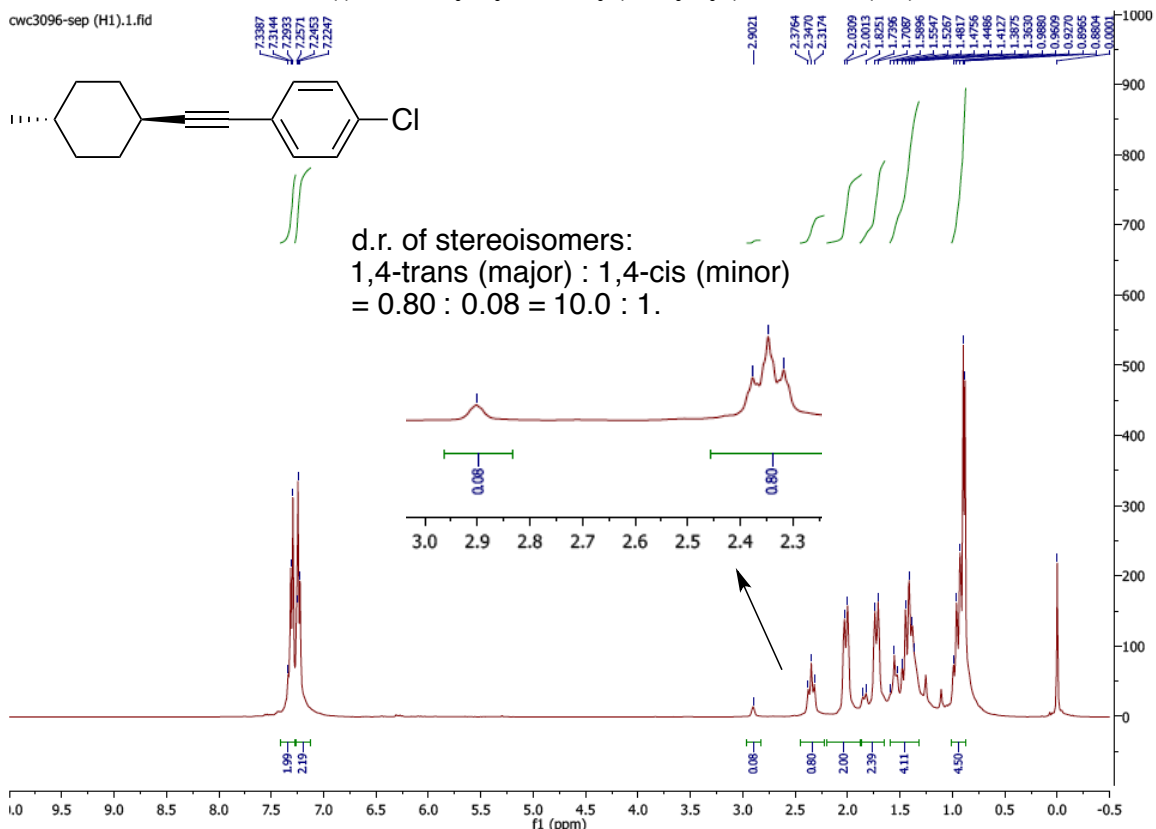
¹H and ¹³C NMR of 2-(Cyclohexylethynyl)-5-methylthiophene (P1)



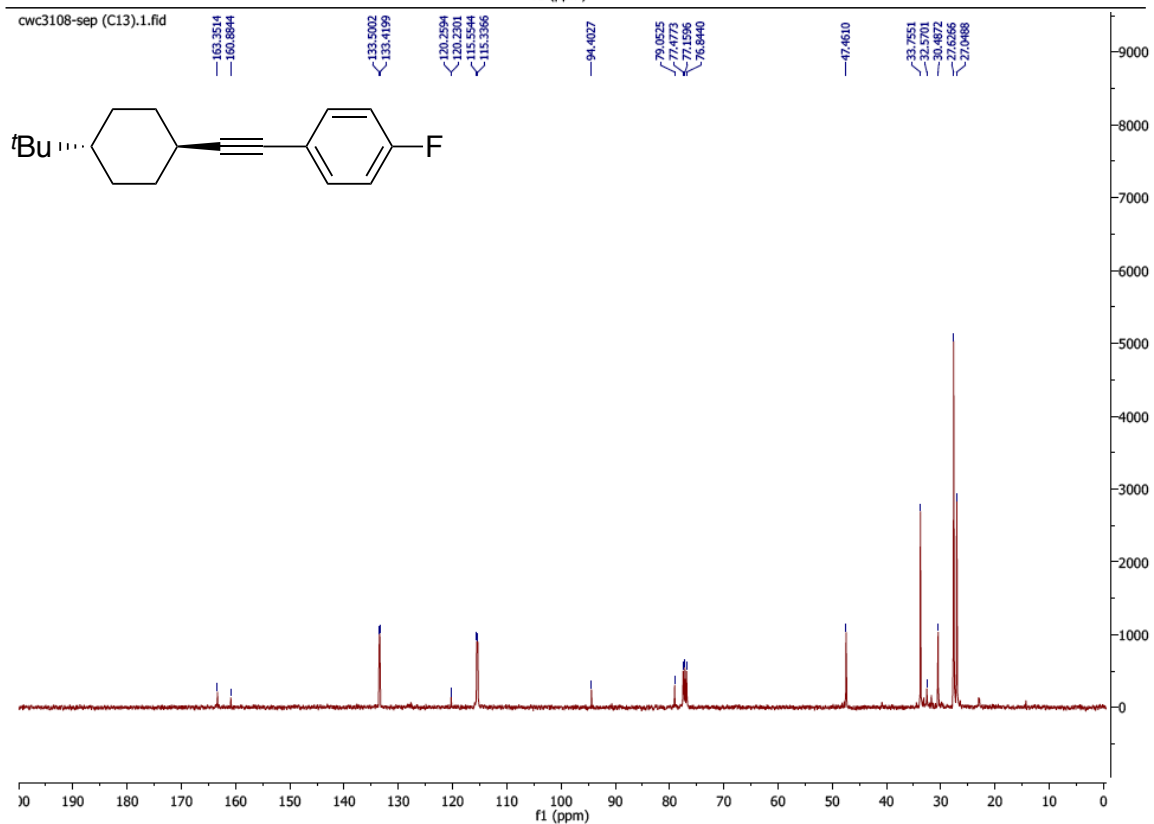
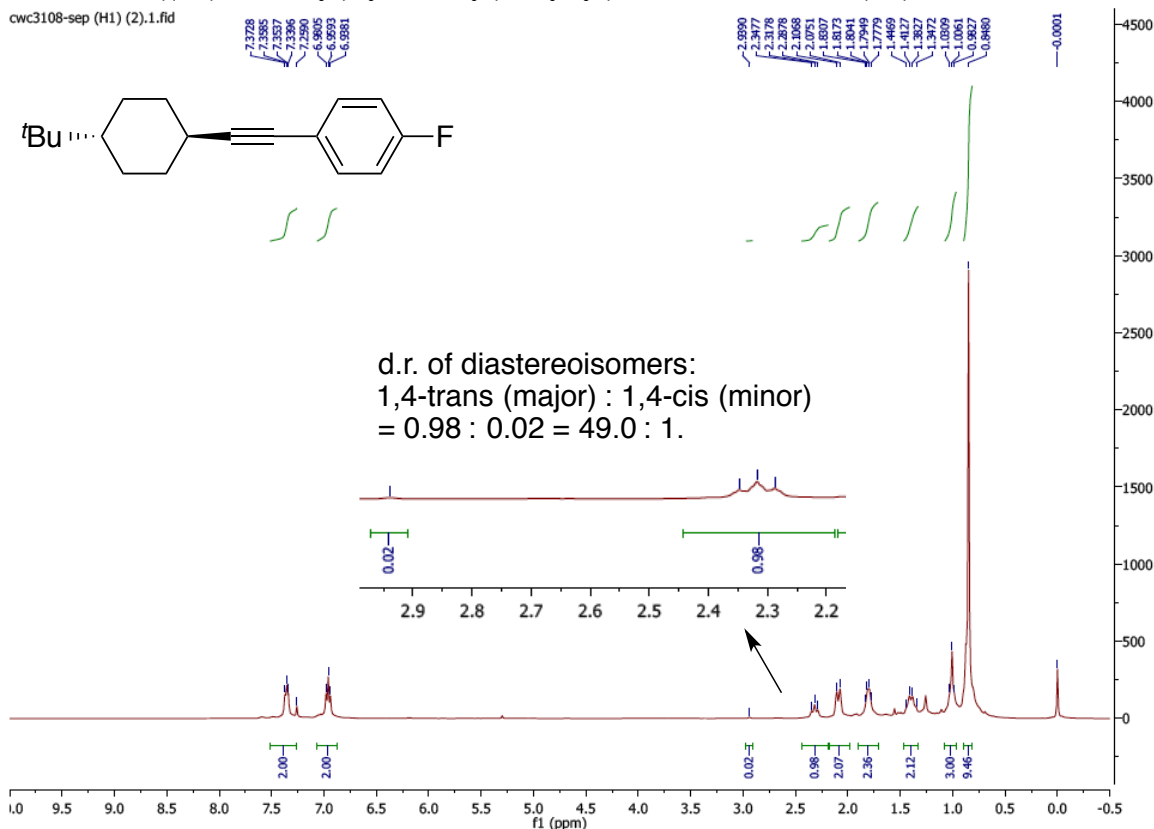
¹H and ¹³C NMR of 4-((5-Methylthiophen-2-yl)ethynyl)tetrahydro-2H-pyran (P2)



¹H and ¹³C NMR of 1-Chloro-4-((-4-methylcyclohexyl)ethynyl)benzene (P3)

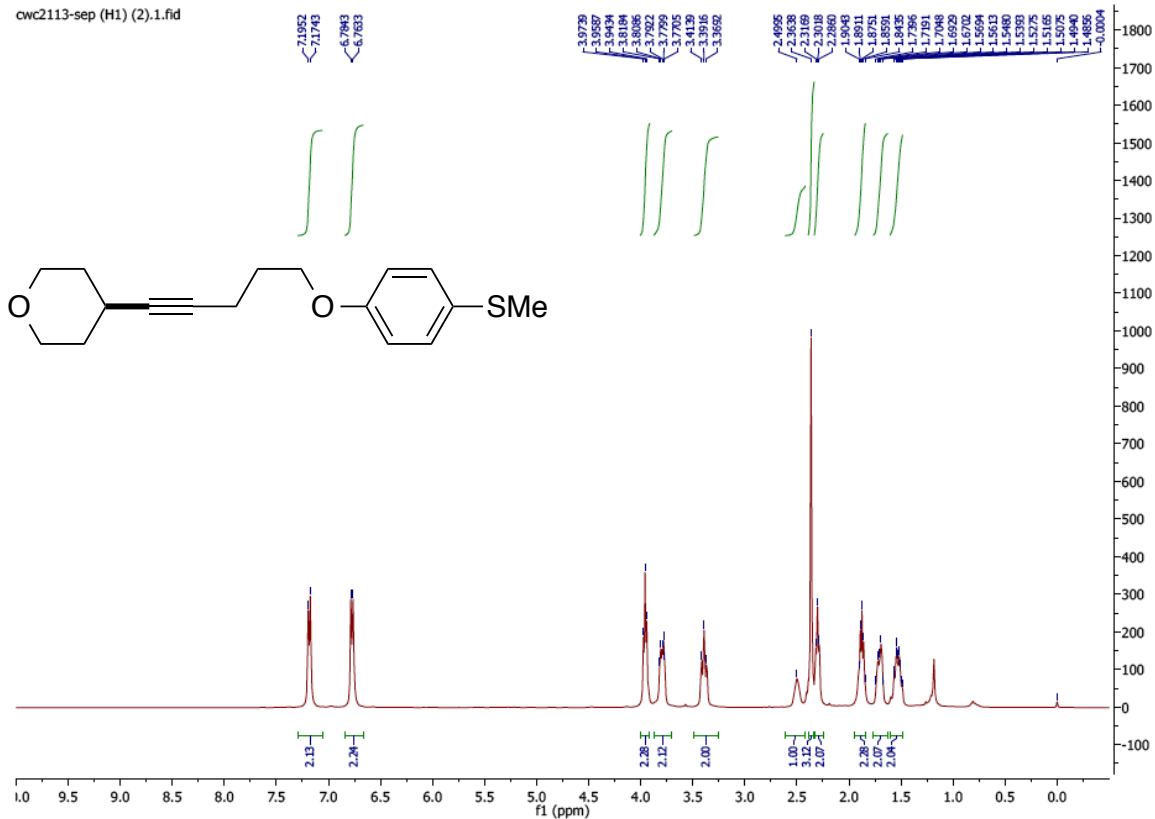


¹H and ¹³C NMR of 1-((4-*tert*-Butyl)cyclohexyl)ethynyl)-4-fluorobenzene (P4)

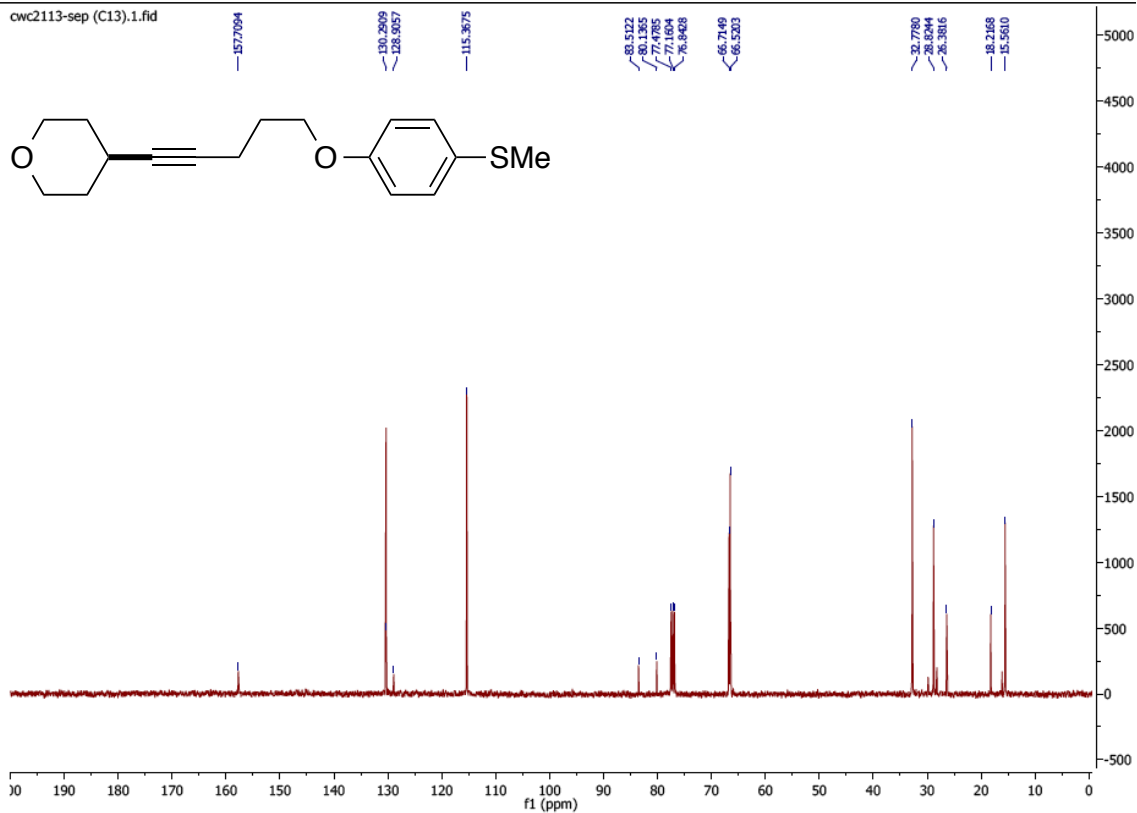


¹H and ¹³C NMR of 4-(5-(4-(Methylthio)phenoxy)pent-1-yn-1-yl)tetrahydro-2H-pyran (P5)

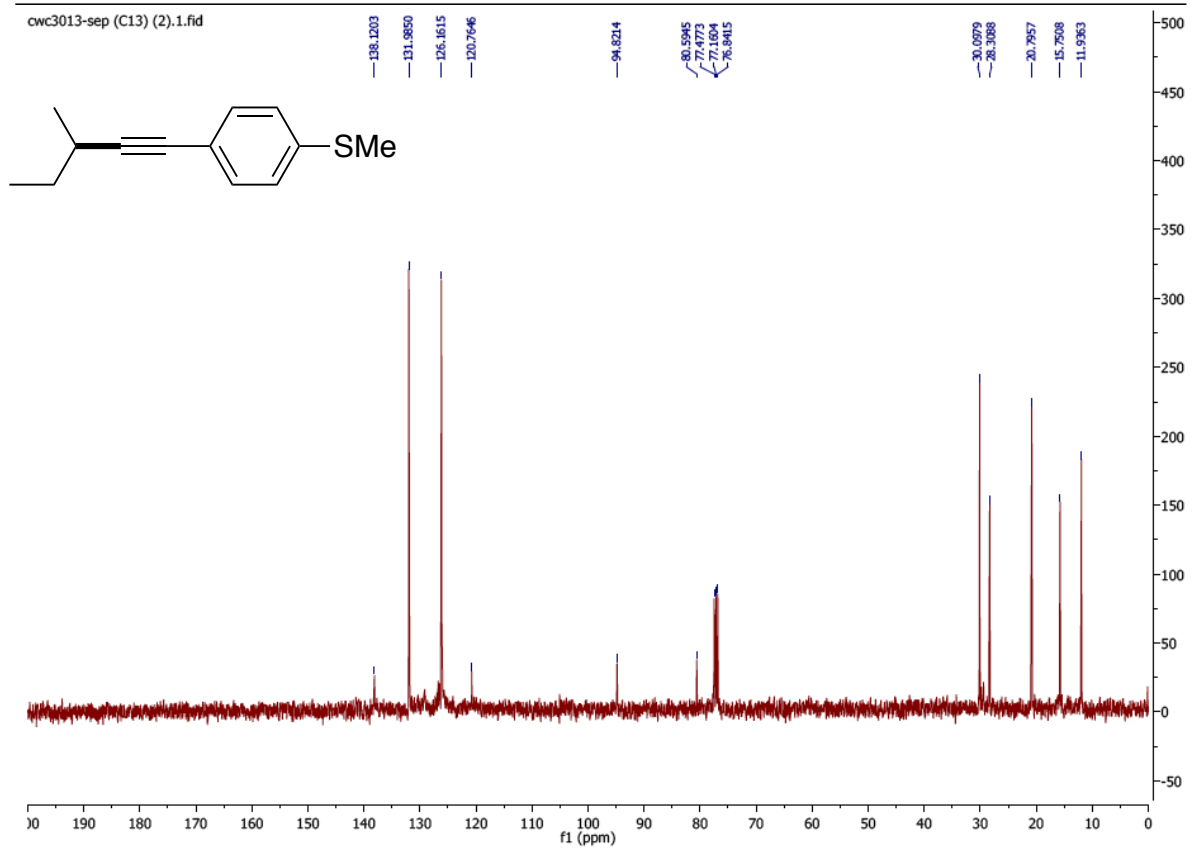
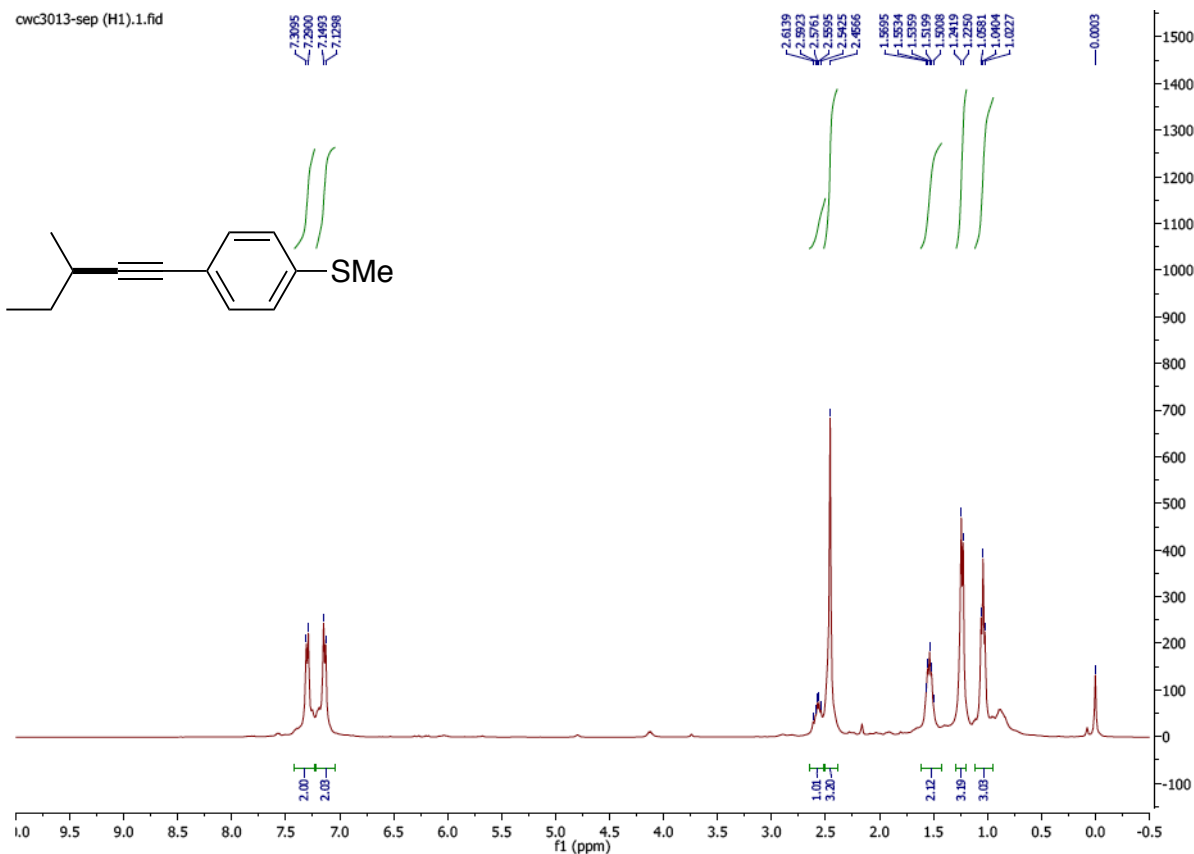
cwc2113-sep (H1) (2).1.fid



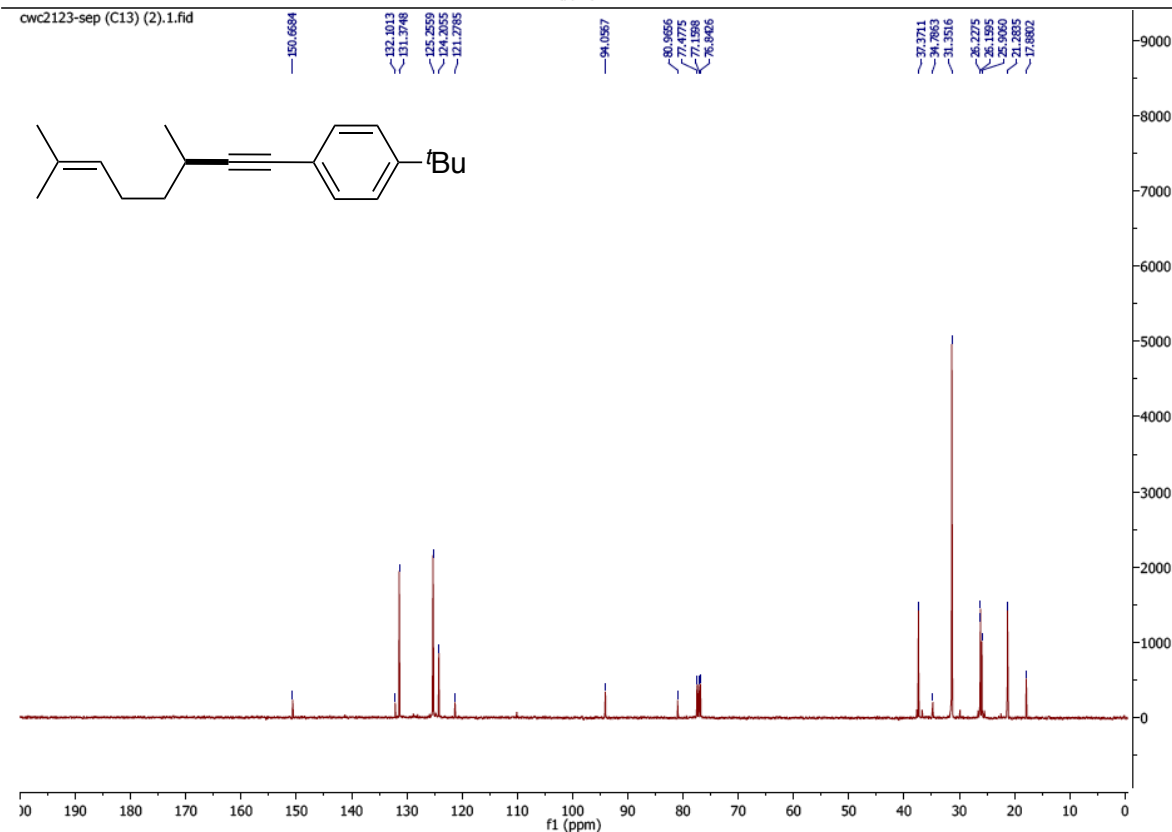
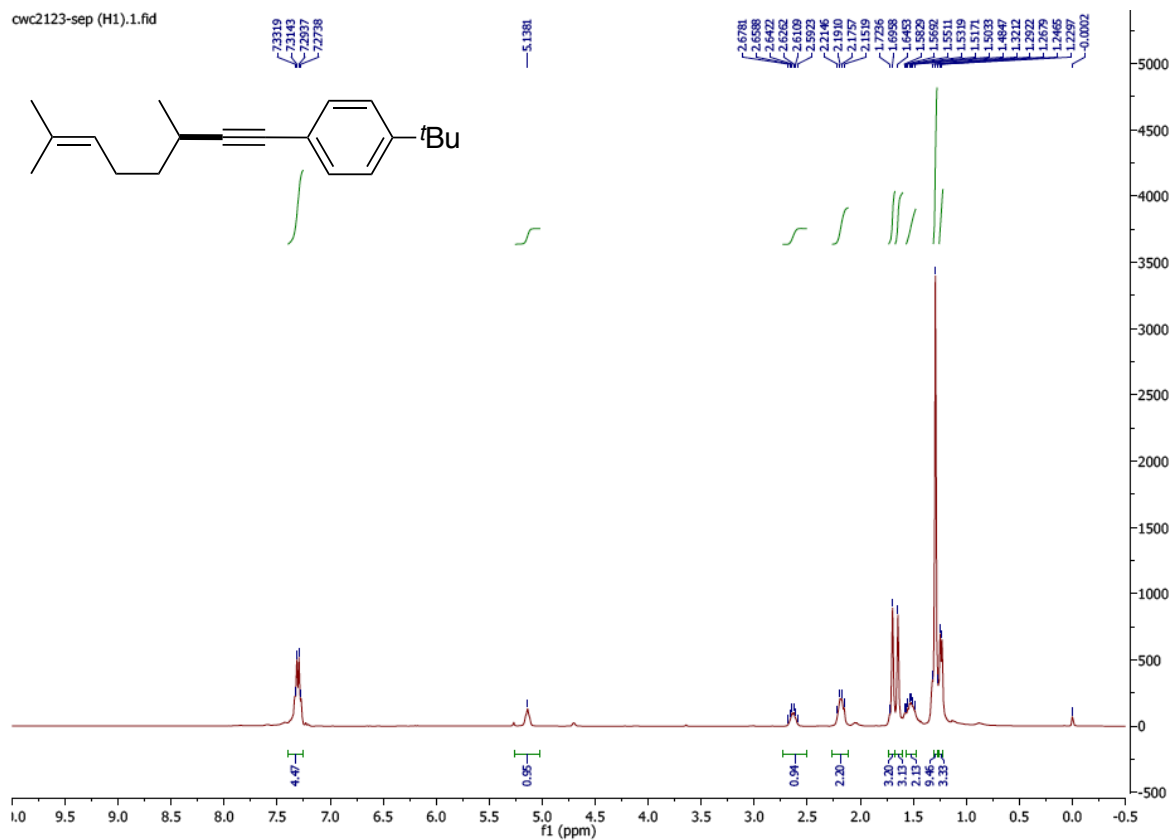
cwc2113-sep (C13).1.fid



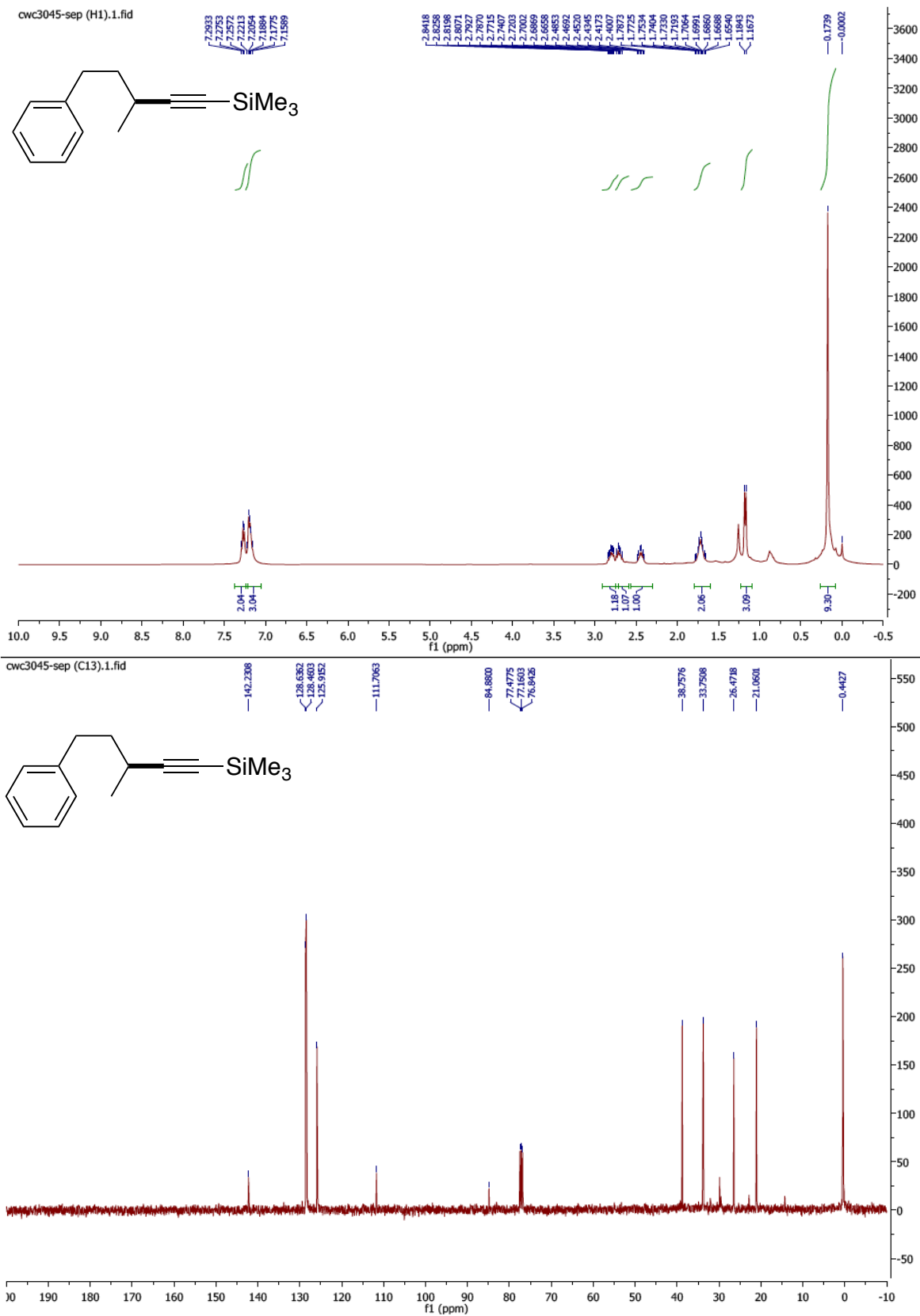
^1H and ^{13}C NMR of Methyl(4-(3-methylpent-1-yn-1-yl)phenyl)sulfane (P6)



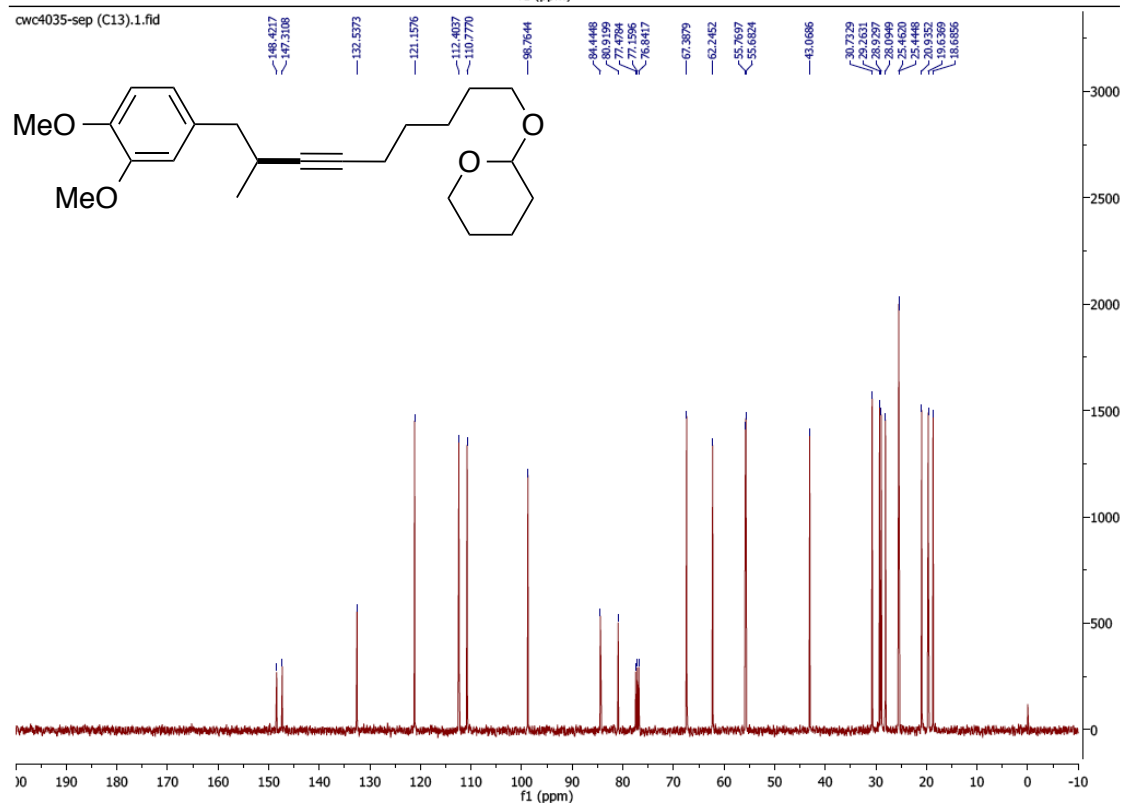
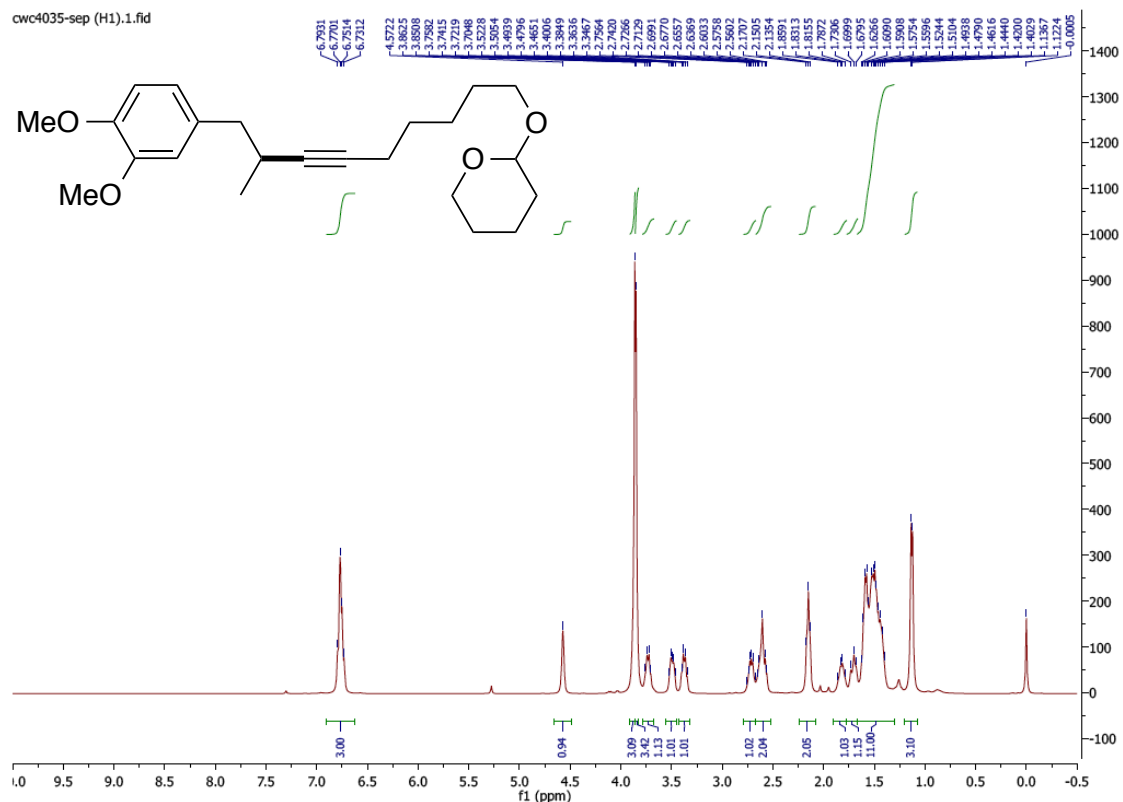
^1H and ^{13}C NMR of 1-(*tert*-Butyl)-4-(3,7-dimethyloct-6-en-1-yn-1-yl)benzene (P7)



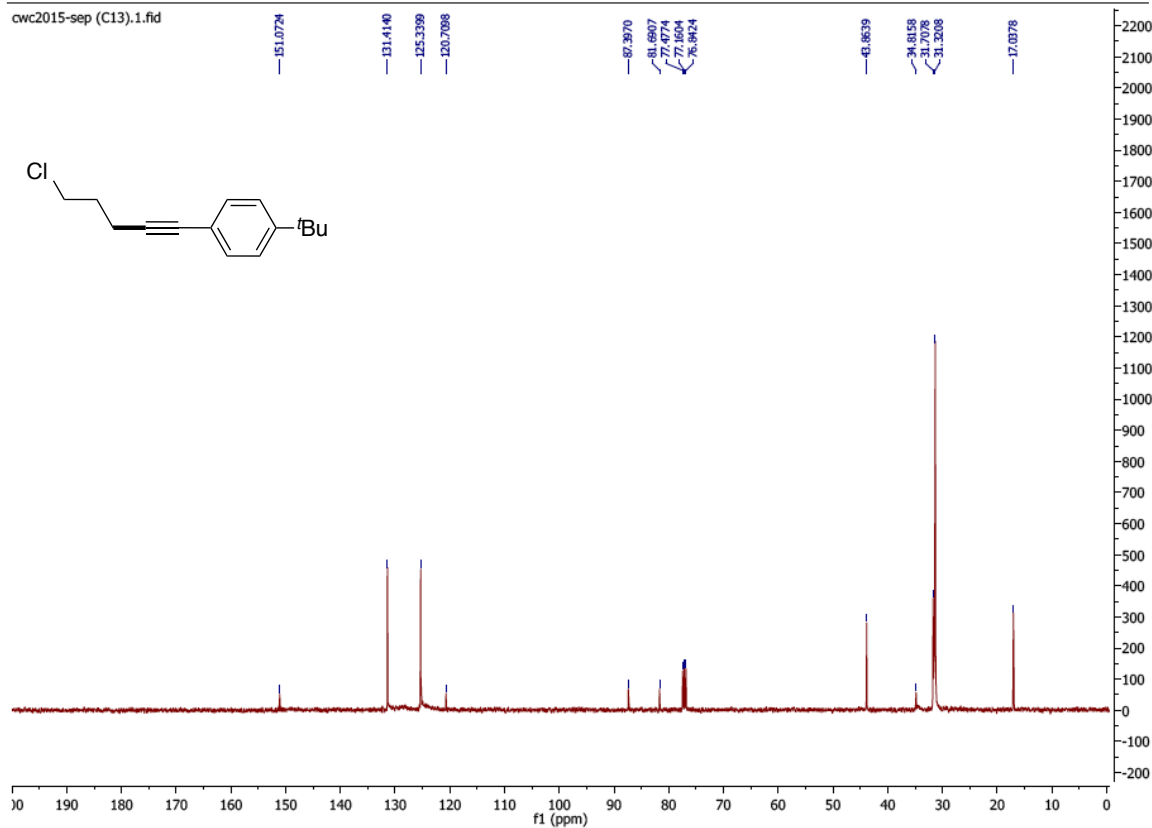
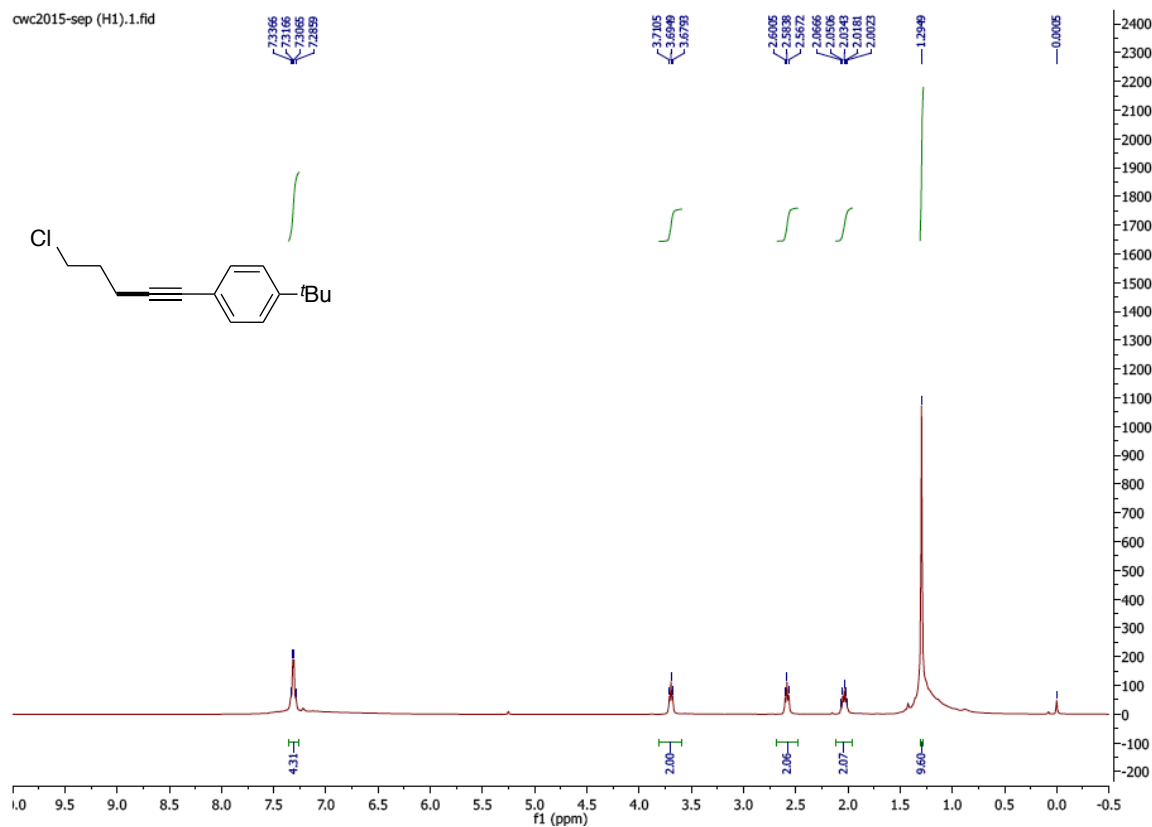
¹H and ¹³C NMR of Trimethyl(3-methyl-5-phenylpent-1-yn-1-yl)silane (P8)



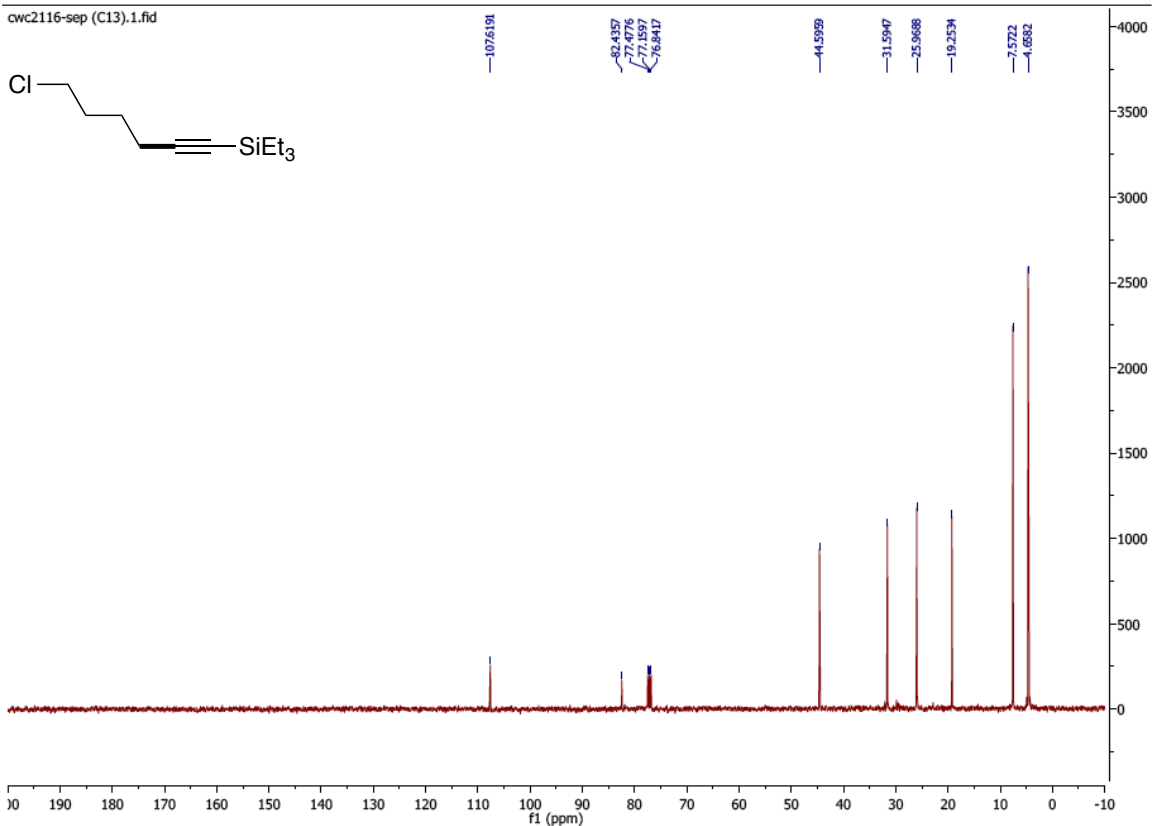
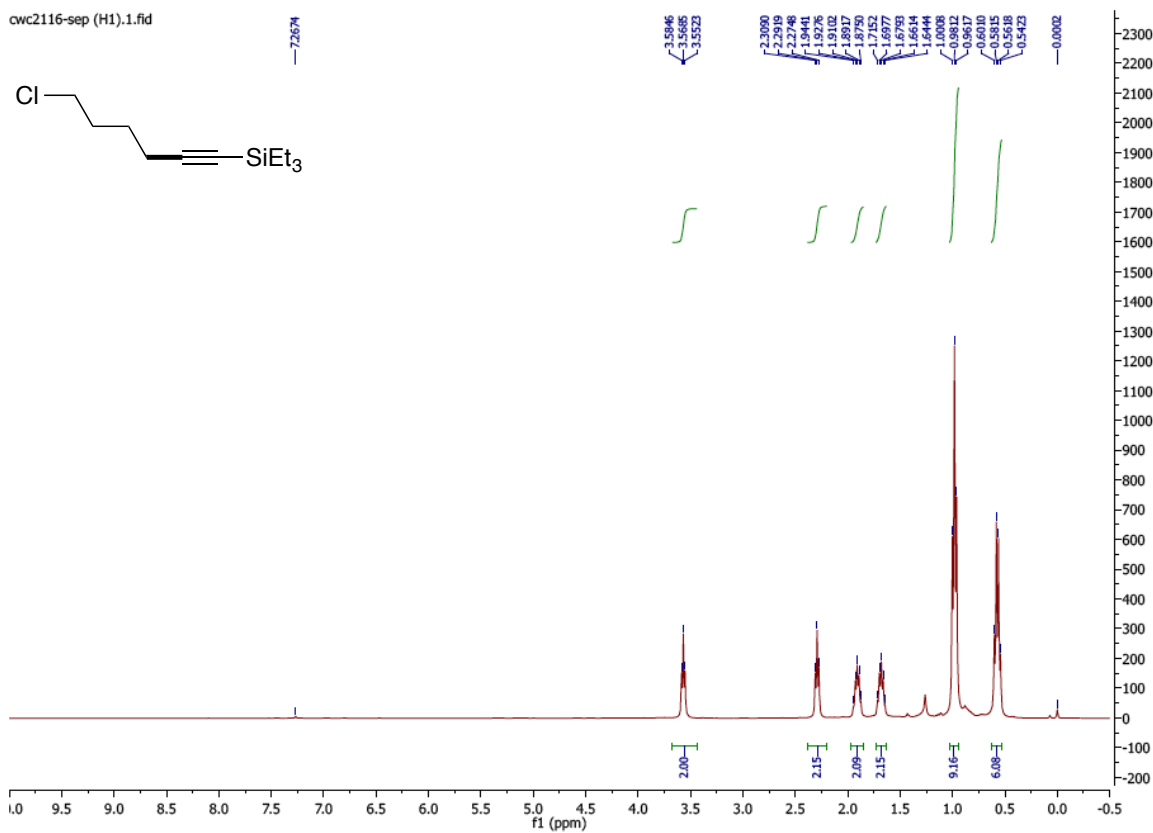
¹H and ¹³C NMR of 2-((9-(3,4-dimethoxyphenyl)-8-methylnon-6-yn-1-yl)oxy)tetrahydro-2H-pyran (P9)



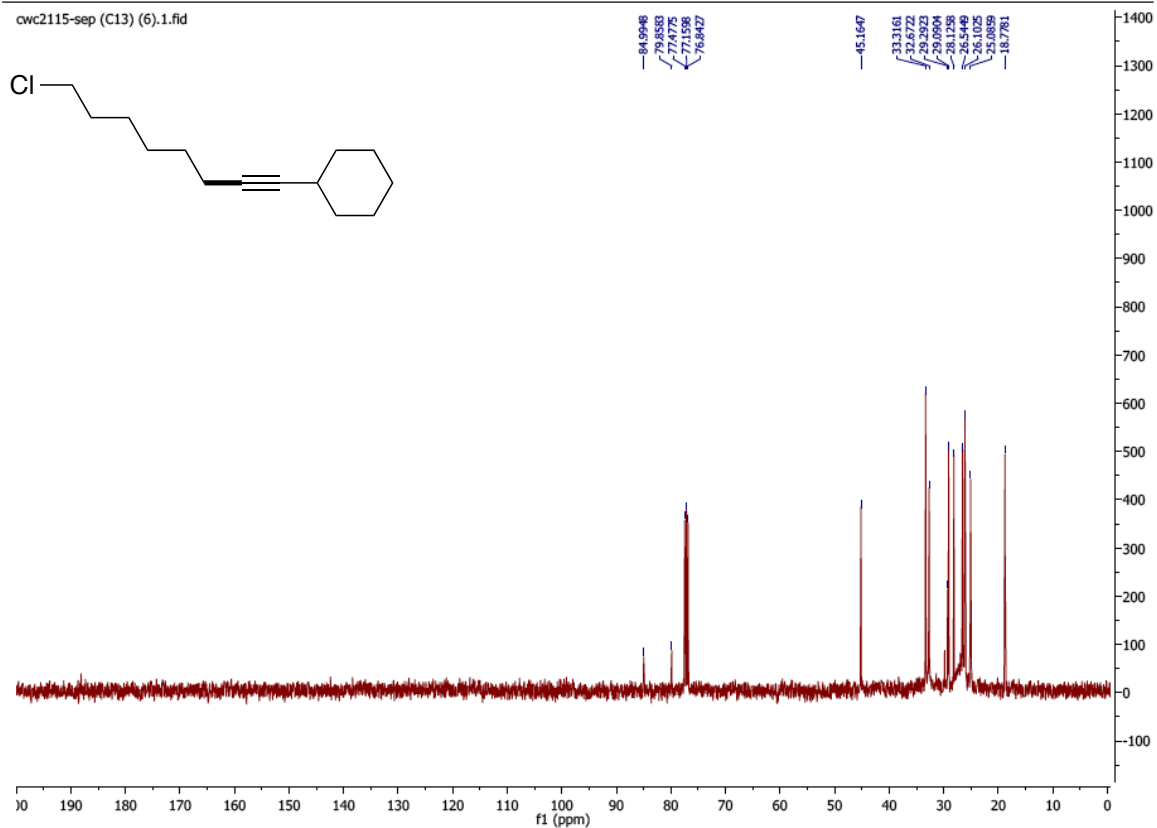
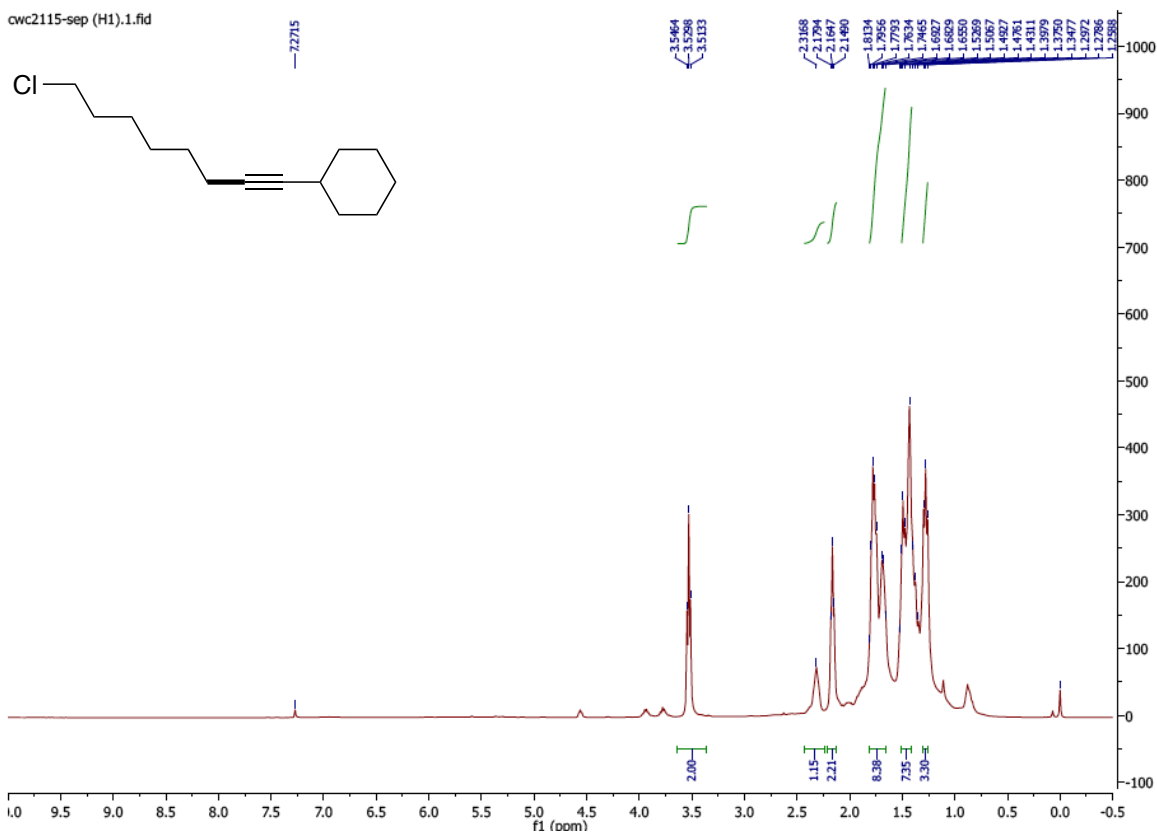
¹H and ¹³C NMR of 1-(*tert*-Butyl)-4-(5-chloropent-1-yn-1-yl)benzene (4a)



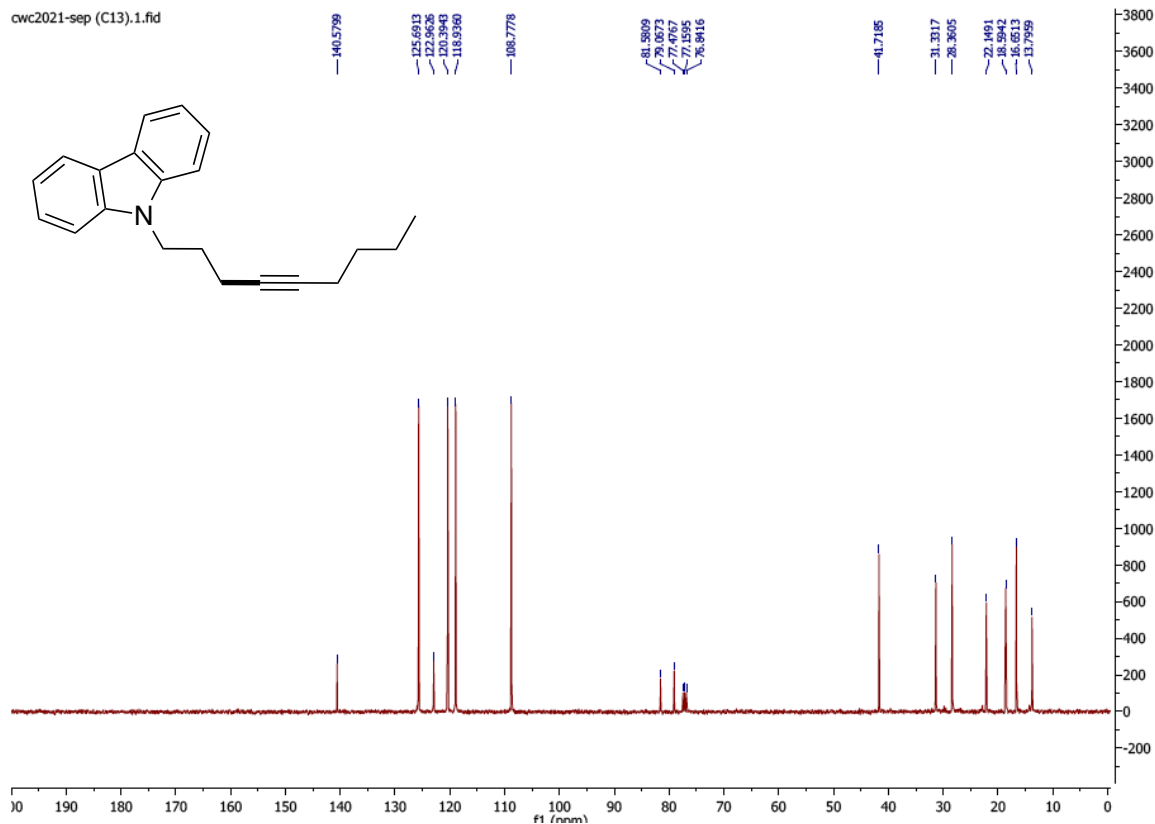
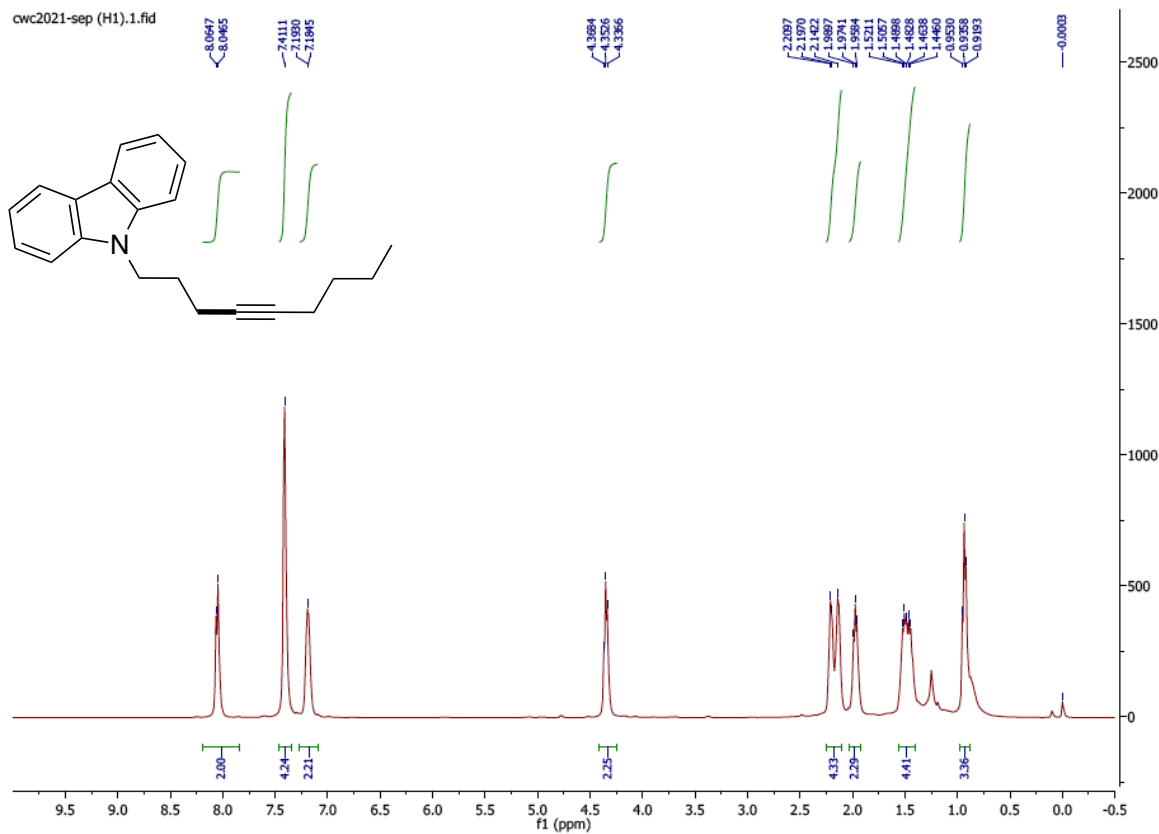
¹H and ¹³C NMR of (6-Chlorohex-1-yn-1-yl)triethylsilane (4b)



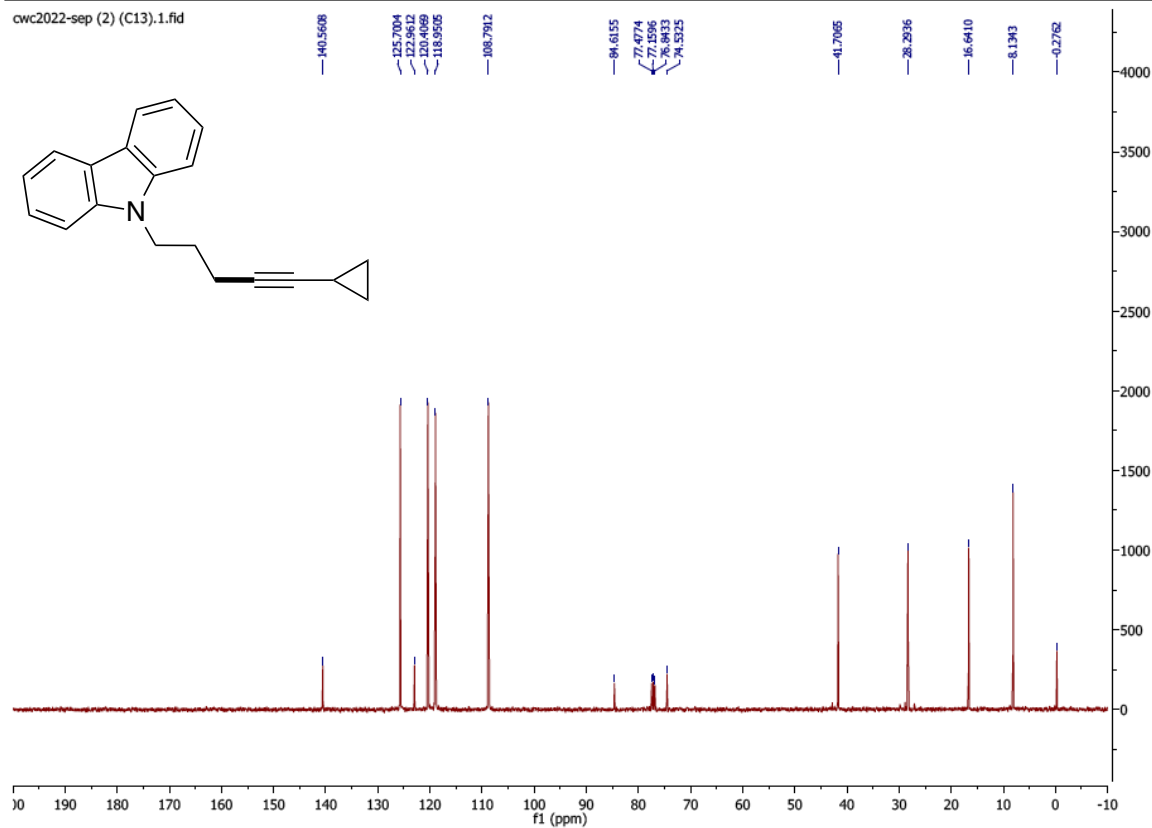
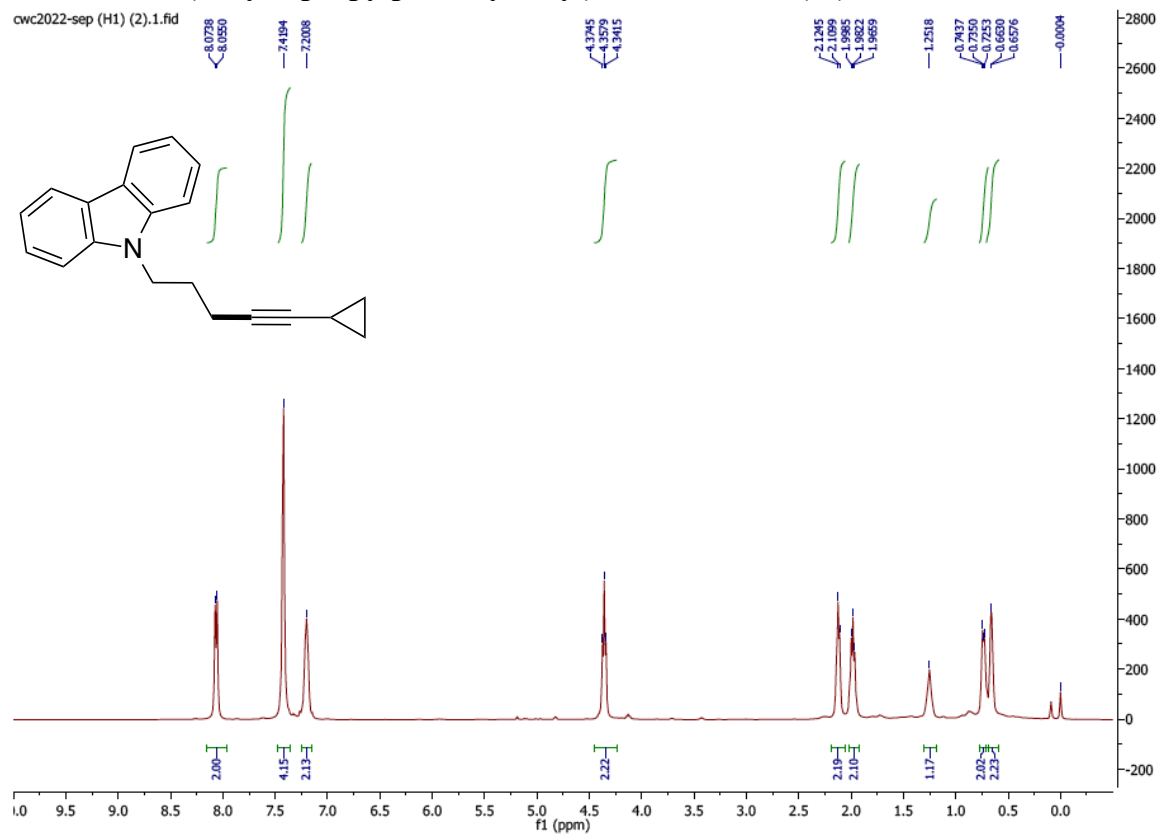
¹H and ¹³C NMR of (8-chlorooct-1-yn-1-yl)cyclohexane (4c)



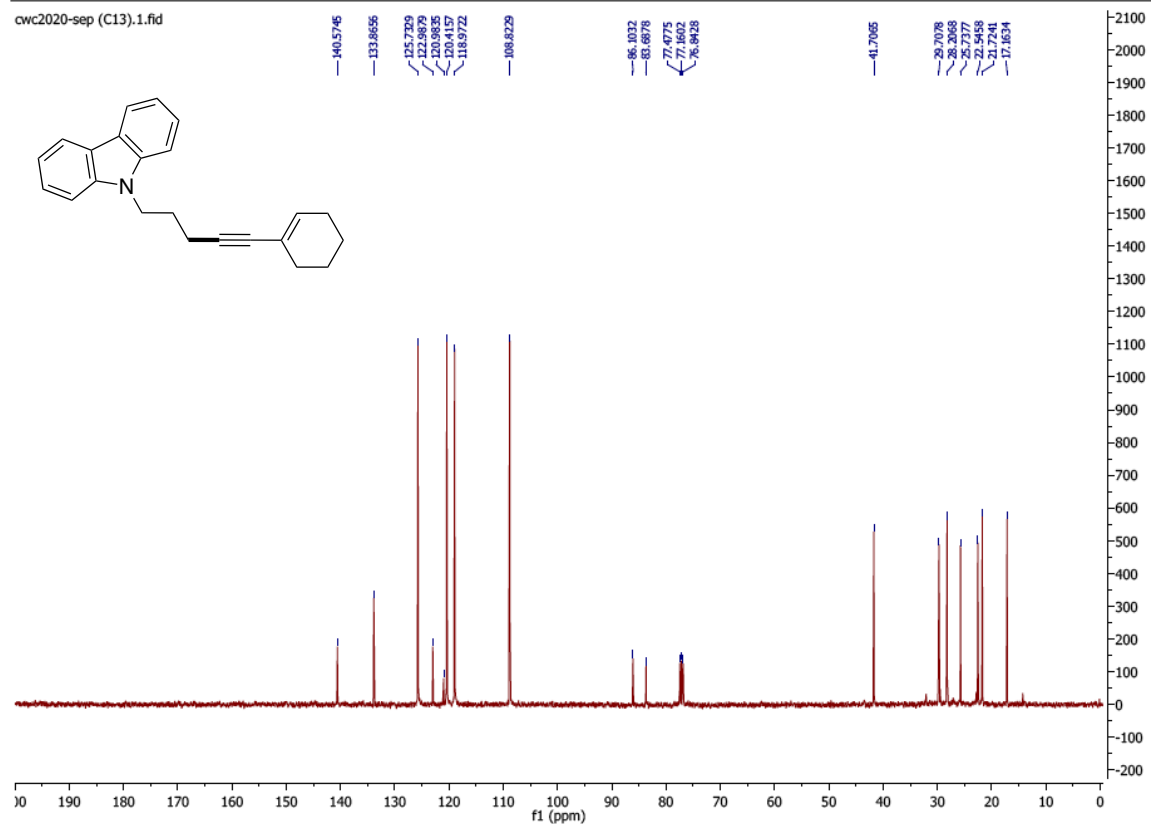
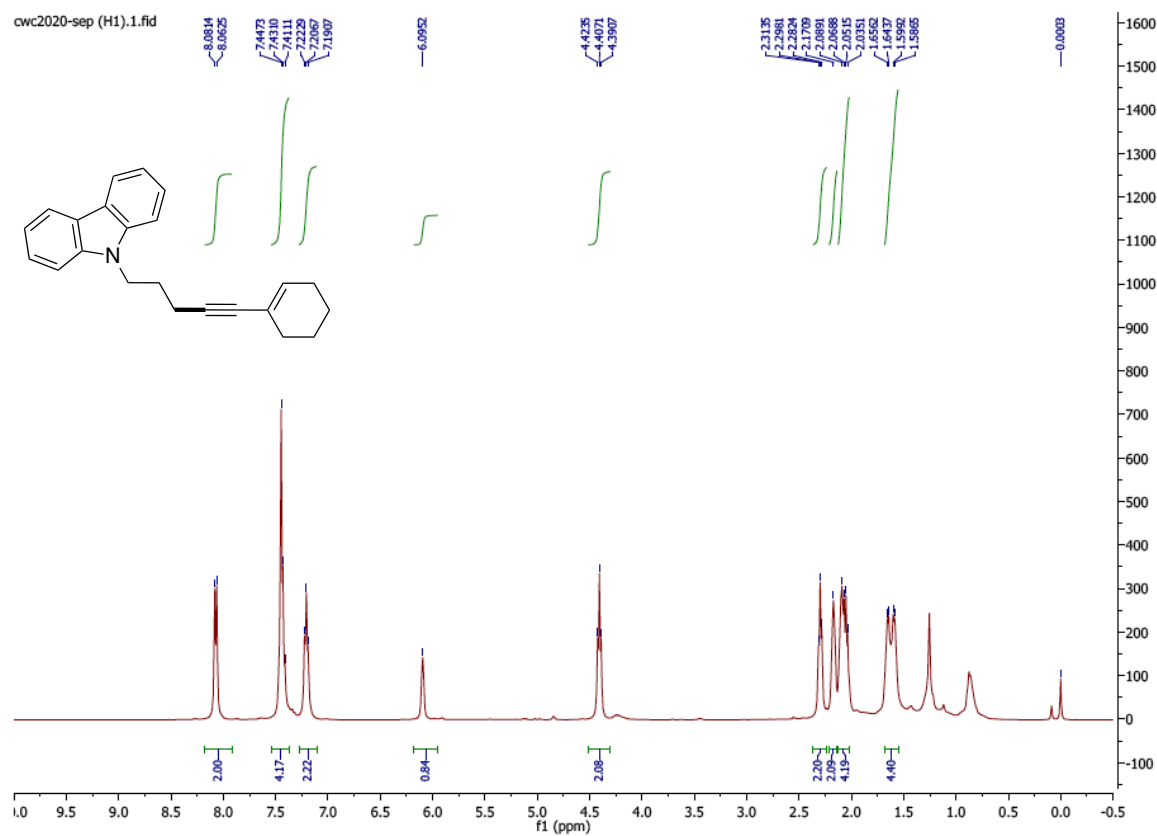
¹H and ¹³C NMR of 9-(non-4-yn-1-yl)-9H-carbazole (4d)



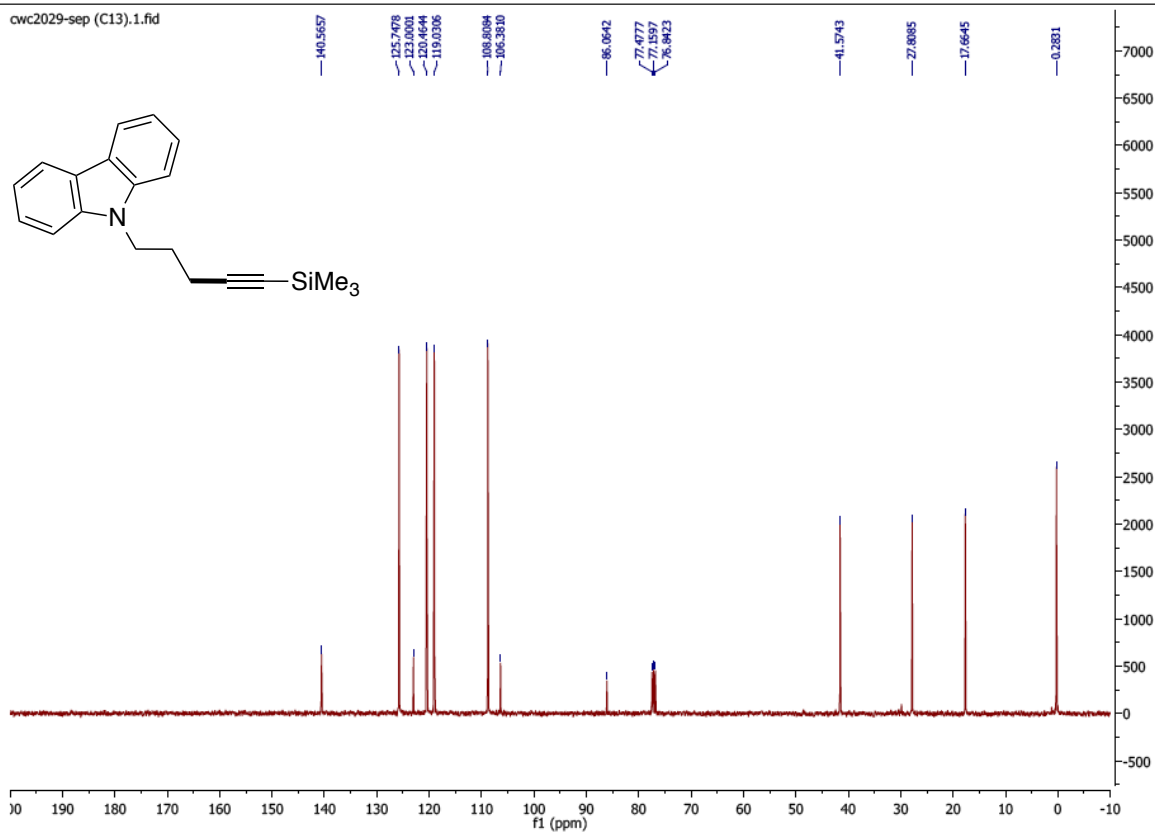
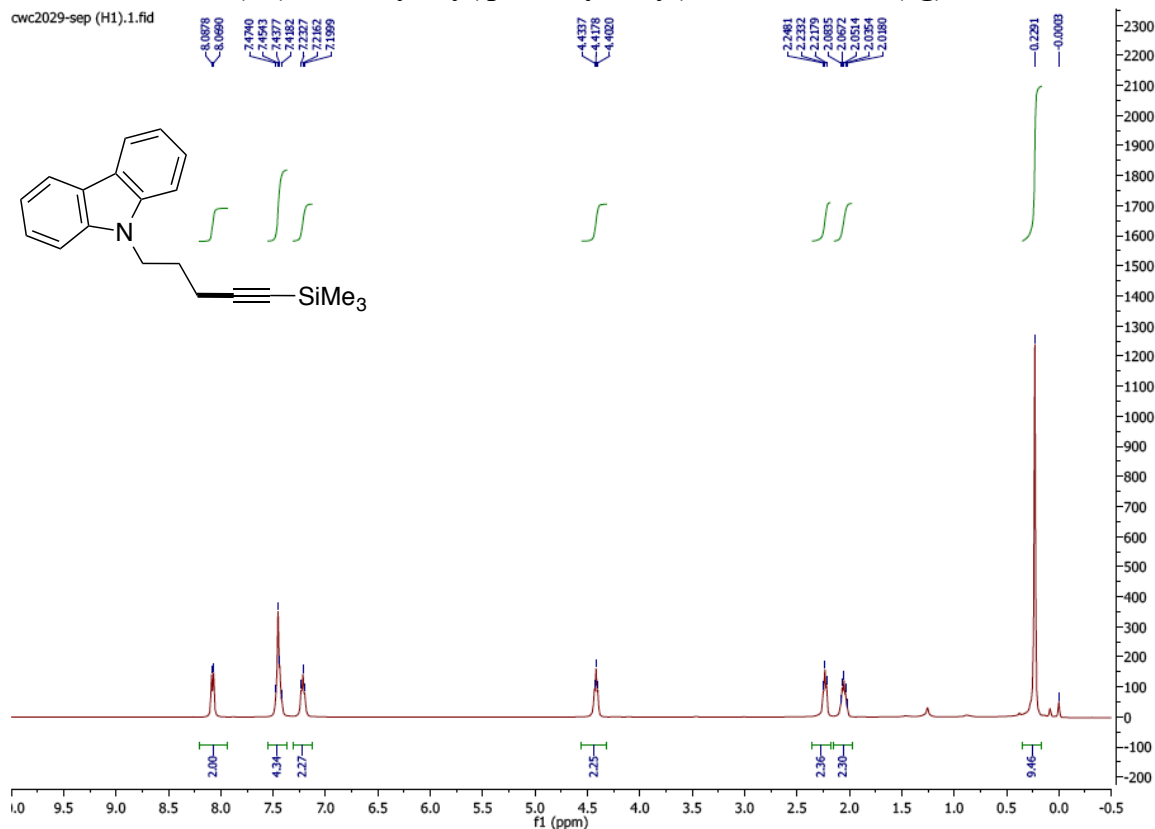
¹H and ¹³C NMR of 9-(5-Cyclopropylpent-4-yn-1-yl)-9H-carbazole (4e)



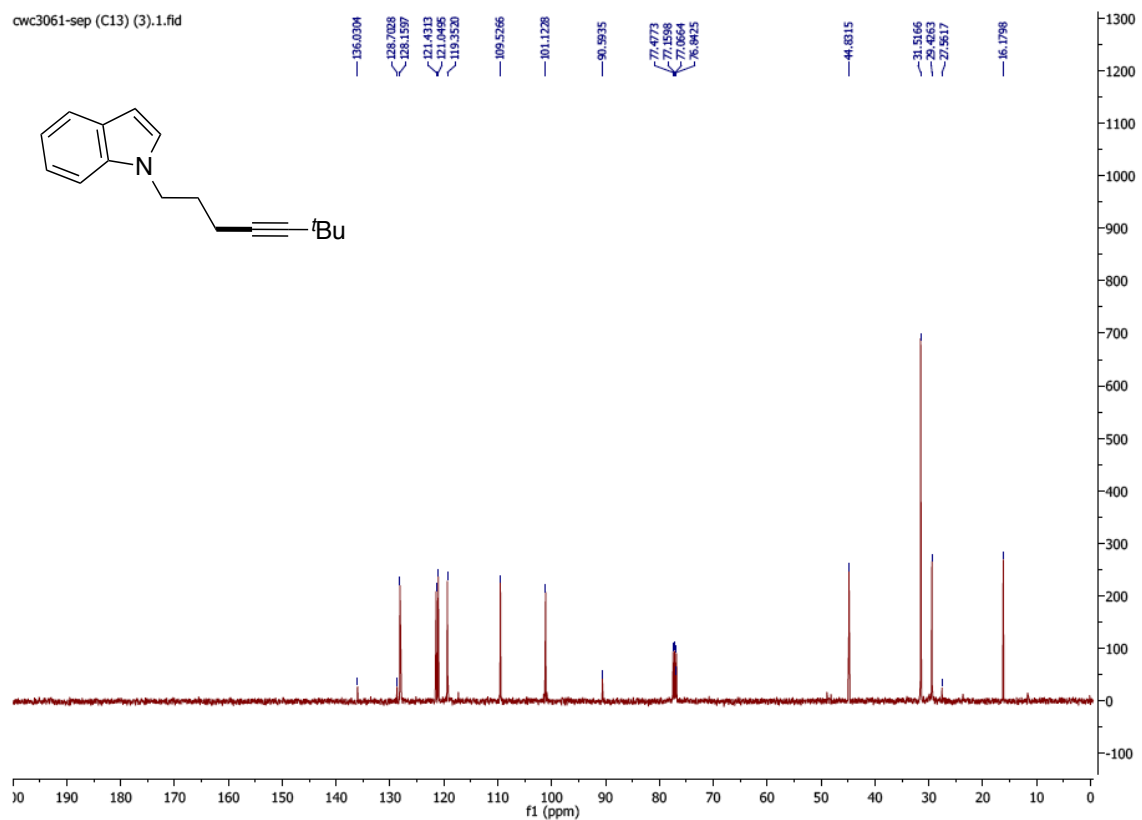
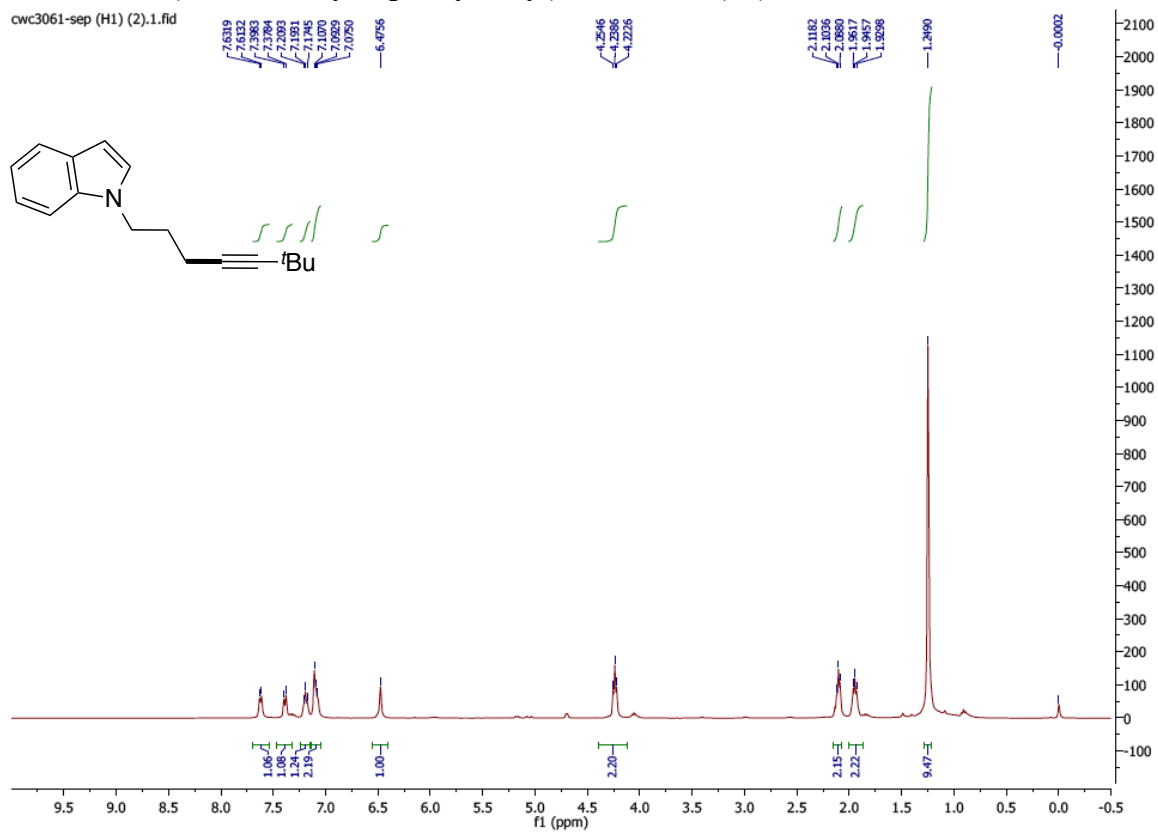
¹H and ¹³C NMR of 9-(5-(Cyclohex-1-en-1-yl)pent-4-yn-1-yl)-9H-carbazole (4f)



¹H and ¹³C NMR of 9-(5-(Trimethylsilyl)pent-4-yn-1-yl)-9H-carbazole (4g)

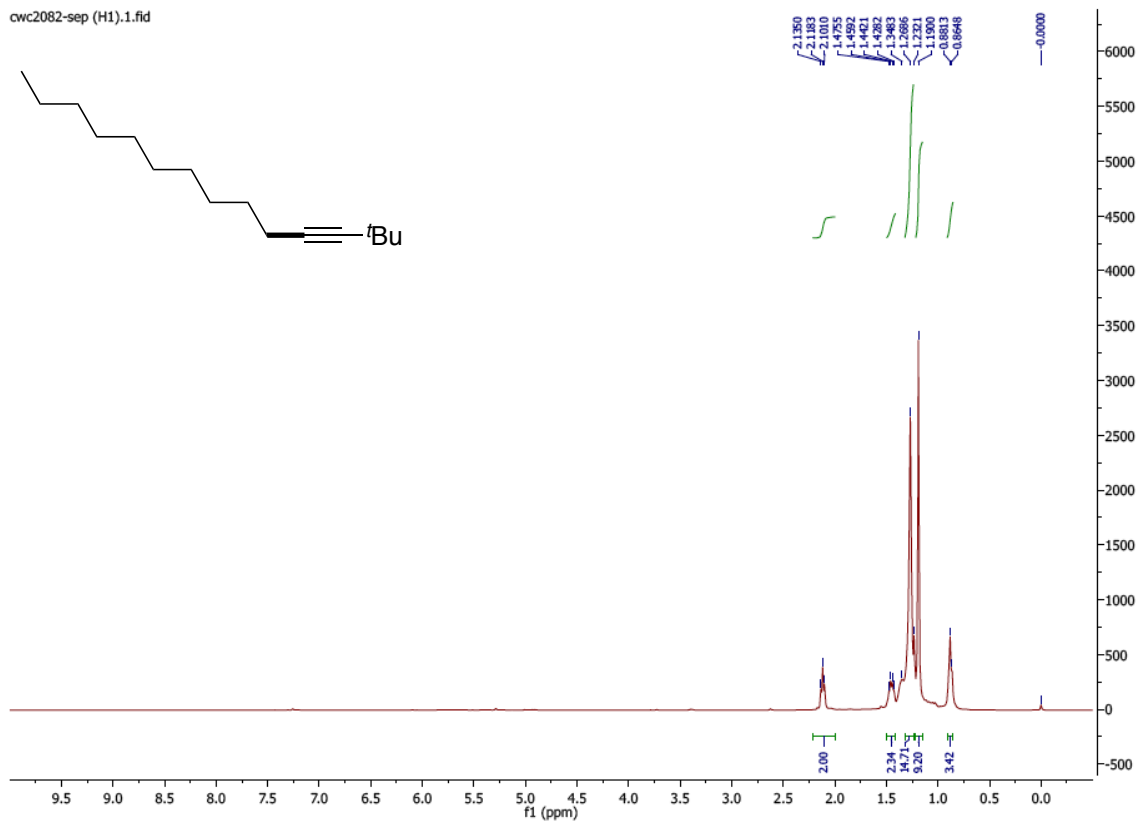


¹H and ¹³C NMR of 1-(6,6-Dimethylhept-4-yn-1-yl)-1H-indole (4h)

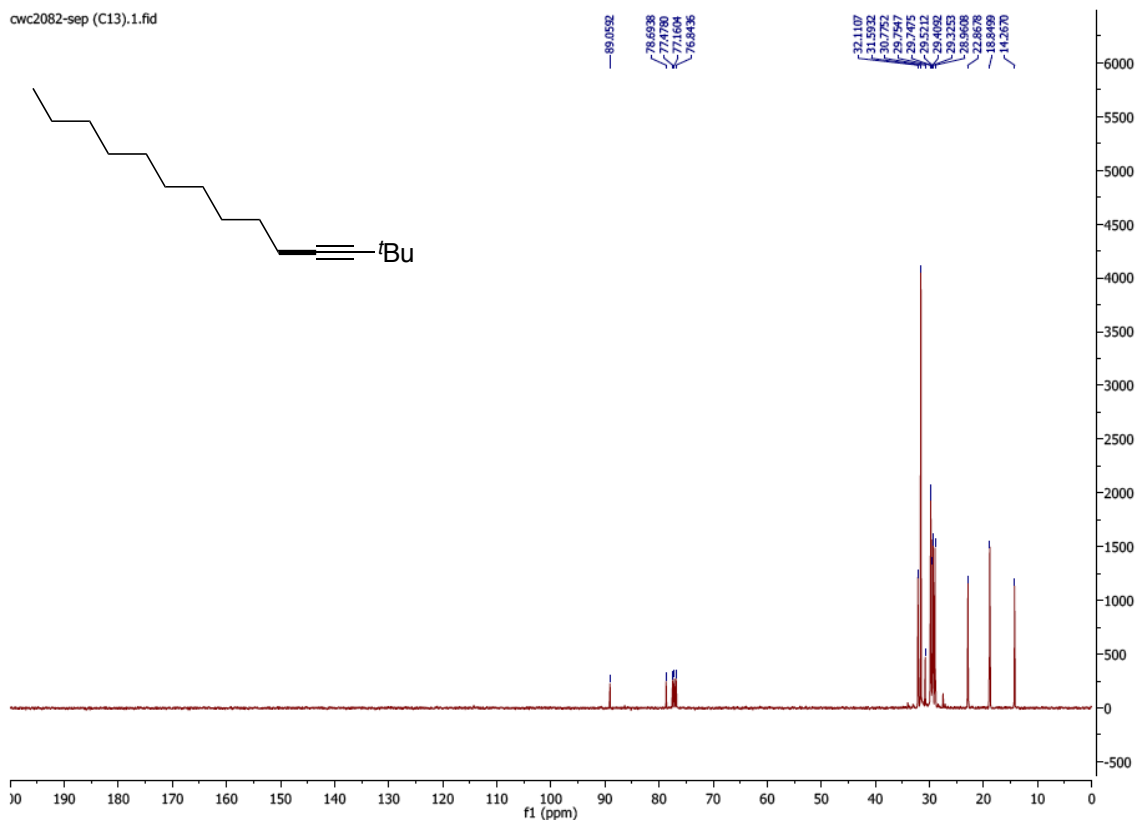


¹H and ¹³C NMR of 2,2-Dimethyltetradec-3-yne (4i)

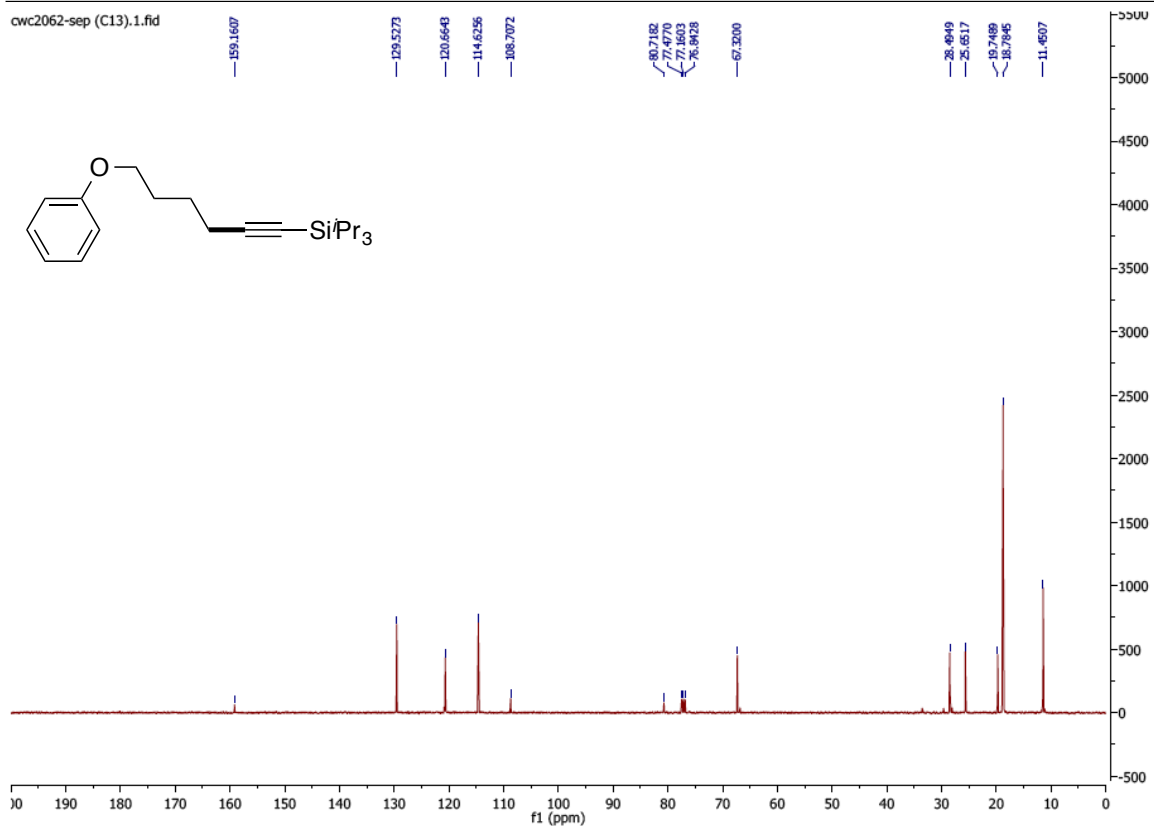
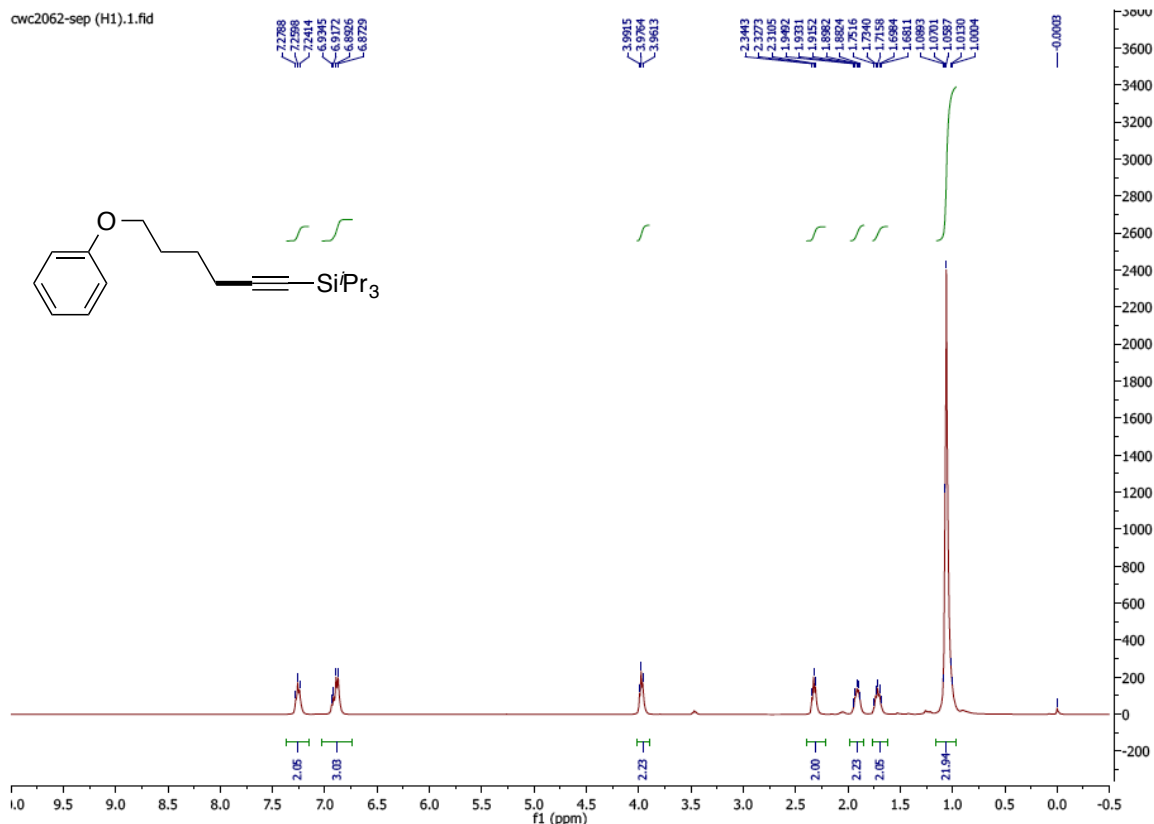
cwc2082-sep (H1).1.fid



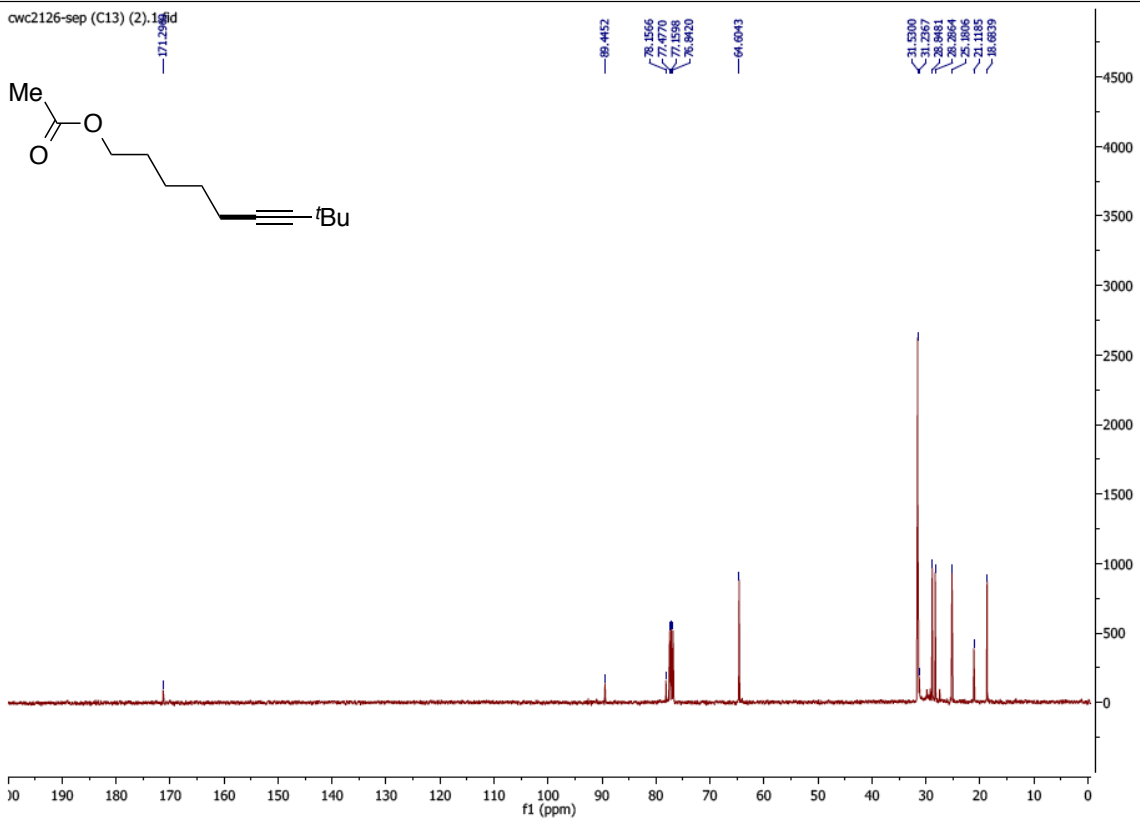
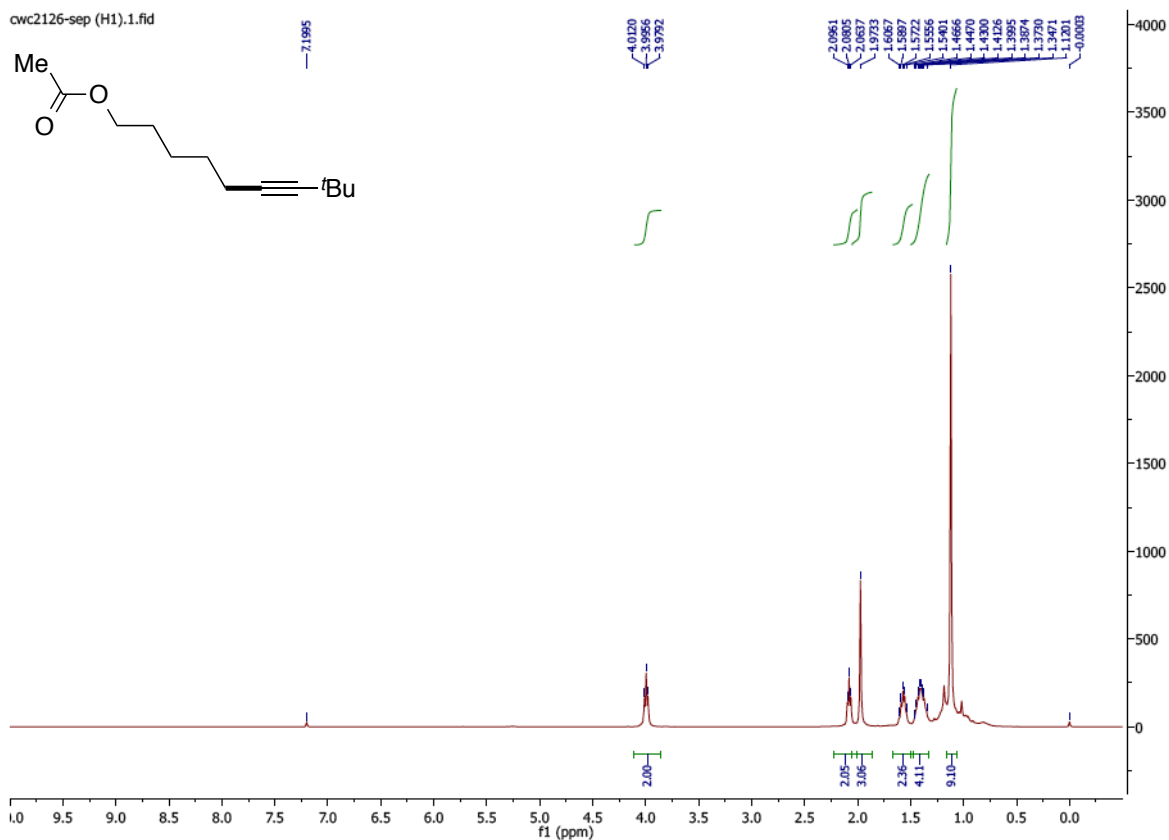
cwc2082-sep (C13).1.fid



¹H and ¹³C NMR of Triisopropyl(6-phenoxyhex-1-yn-1-yl)silane (4j)



¹H and ¹³C NMR of 8,8-Dimethylnon-6-yn-1-yl acetate (4k)



^1H and ^{13}C NMR of Dodec-1-en-5-yne (4l)

