Electronic Supplementary Material (ESI) for Chemical Communications.

Supporting information

Pd-Catalyzed sp-sp^3 Cross-Coupling of Benzyl bromides using Lithium Acetylides

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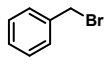
General methods

All reactions were carried out under a nitrogen atmosphere using oven-dried glassware and standard Schlenk techniques. Anhydrous THF and toluene were obtained from solvent purification system were used for all of our reactions. Purifications by automated flash column chromatography were performed using a Grace® Reveleris X2 flash chromatography system used with *EcoFlex silica 50µm irregular column*. Evolution of reactions by thin layer chromatography (TLC) was performed on Merck silica gel 60, 0.25 mm (Kieselguhr F254). Components were visualized by UV and potassium permanganate staining. Mass spectra were recorded on an AEI-MS-902 mass spectrometer (EI+), LTQ Orbitrap XL (ESI+ or ESI-). ^{1}H-,^{13}C-, and ^{19}F-NMR were recorded on a Varian AMX400/600 using $CDCl_3$ as solvent. Chemical shift values are reported in ppm with the solvent resonance as the internal standard ($CHCl_3$: δ 7.26 for ^{1}H, δ 77.0 for ^{13}C). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet, dd = doublet of doublets, dt = doublet of triplets), coupling constants (*J*) are reported in Hertz (Hz), and integration. Metal salts, complexes and ligands were purchased from Sigma-Aldrich and TCI. ^{n}BuLi (1.6M solution in hexane) was purchased from Acros.

Starting materials

Following benzyl bromides are commercially available:



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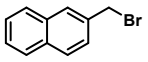

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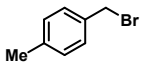

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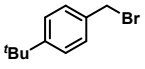

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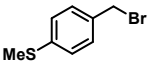

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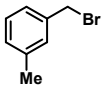

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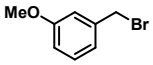

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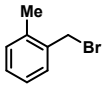

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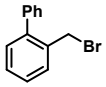

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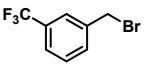

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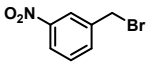

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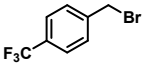

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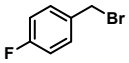

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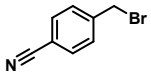

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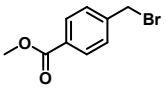

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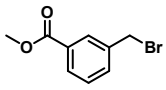

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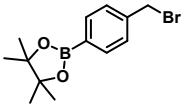

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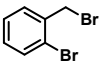

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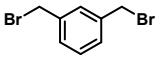

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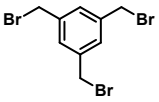

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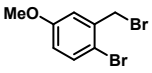
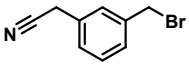
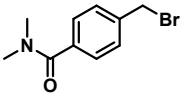


1z

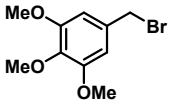
Benzyl bromide **1q**[6], **1v**[1-2], **1x**[3], **1y**[4], **1aa**[5] and were synthetized according to reported procedures:



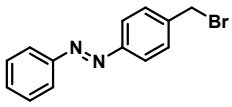
1q



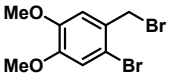
1v



1x

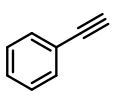


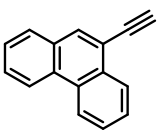
1y



1aa

The following acetylenes are commercially available:





Catalyst [Pd(μ-I)P^{t}Bu$_3$]$_2$ were synthetized according to reported procedures.[7]

General procedures for the cross-coupling

Preparation of 0.5M lithium acetylides (General Procedure-A; GP-A)

In a dry Schlenk tube, the corresponding acetylene (1.3 mmol, 1 eq.) in dry THF (0.65 mL) was stirred at 0 °C and ^{n}BuLi (1.6M in *hexanes*; 1 eq.) was slowly added, resulting in around 0.5M solution, after which the mixture was allowed to warm to RT.

Preparation of 0.35M lithium acetylides (General Procedure-B; GP-B)

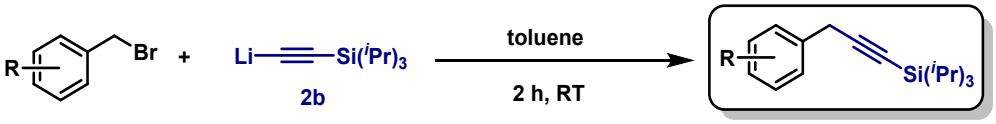
In a dry Schlenk tube, the corresponding acetylene (1.3 mmol, 1 eq.) was added to dry THF (1.2 mL) at 0 °C, followed by ^{n}BuLi (1.37 mmol, 1.05 equiv, 1.6M in hexanes) after which the mixture was allowed to warm up to room temperature and diluted with dry toluene (1.5 mL) to reach a final concentration of around 0.35M.

Synthesis of benzyl alkynes (General Procedure-C; GP-C)

In a dry Schlenk tube $[Pd(\mu\text{-}I)P^{t}Bu_3]_2$ (13.1 mg, 3 mol%) and the corresponding benzyl bromide (0.5 mmol) were added and evacuated and back-filled with nitrogen. Dry toluene (2 mL) was added and the mixture left to stir at RT for 2 min. The organolithium reagent (0.35M) was then added to the reaction mixture over 10 min using a syringe pump. The reaction was quenched* with ^{i}PrOH (1 mL) and all the volatiles were removed under reduced pressure. MeCN (20 mL) was then added to the crude mixture and the solution was passed through a short plug of silica in order to remove remaining catalyst. The filtrate was concentrated under reduced pressure and the residue was subjected to automated flash column chromatography to afford the pure product.

** In case, storage is required before the purification step; the reaction was quenched with sat. aq. NH_4Cl followed by a quick extraction with ethyl acetate, was added and the aqueous phase was extracted with ethyl acetate (3 x 10 mL). The combined organic phases were dried over MgSO4 and all volatiles were removed under reduced pressure to afford crude. This in order to avoid deprotection of silyl protecting group or allene formation.*

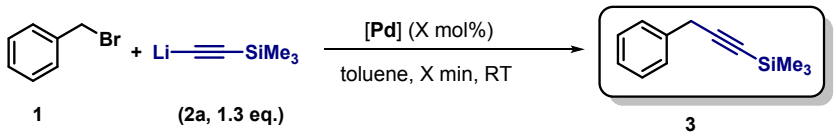
Supplementary table 1. Screening studies without Pd-catalyst



Entry	R	Solvent	Conversion (GC-MS)
1	H	toluene	0
2	H	THF	16
3	H	NMP	0
4	*p*-CF_3	DMPU	0
5	*p*-Me	DMPU	17

Freshly prepared **2b** (1.3 eq.) was added to a solution of corresponding benzyl bromide (0.5 mmol) in anhydrous solvent (2 mL) and stirred for 2 h.

Supplementary table 2. Optimization of Cross–coupling with different Pd-catalyst/reaction conditions



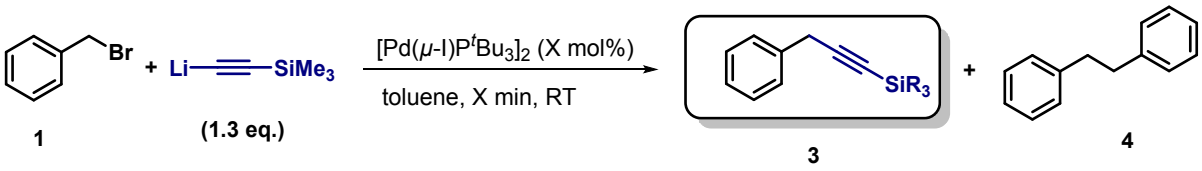
1 (2a, 1.3 eq.) 3

Entry	Solvent	Time (min)	Catalyst loading (Mol%)	[Pd]	Conv to 3 (%)
1	toluene	30	5	$Pd(P^tBu_3)_2/O_2$	98
2	Toluene	15			95
3	toluene	10			93
4	toluene	5			36
5	toluene	10	5	$[Pd(\mu\text{-}I)P^tBu_3]_2$	95
6	**toluene**	**5**	**5**		**95**
7	toluene	1	5		69
8	Neat	15	5	$Pd(P^tBu_3)_2$/under air	48
9	Neat	10	5		50
10	Neat	5	5		75

11	Neat	5	2.5	74
12	**Neat**	**5**	**7.5**	**94**

Freshly prepared **2a** (1.3 eq.; 0.5M) was added to a solution of $[Pd(\mu\text{-I})P^tBu_3]_2$ (2.5-7.5 mol%) and corresponding benzyl bromide (0.5 mmol) in toluene (2 mL) over 1-30 min. 0.5M of **2a** prepared using GP-A.

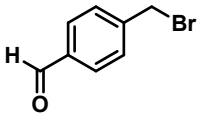
Supplementary table 3. Optimization of reaction condition using $[Pd(\mu\text{-I})P^tBu_3]_2$



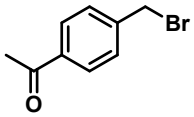
1 (1.3 eq.) 3 4

Entry	Concentration of 1 (M)	Reaction time (min)	Molarity of lithium acetylide (M)	Catalyst loading (Mol%)	1:3:4
1	0.125	5	0.5	2.5	**41:52:7**
2	0.125	15	0.5	2.5	**31:62:7**
3	0.125	5	0.5	3.75	**22:71:6**
4	0.125	10	0.5	3.75	**31:61:6**
5	0.125	10	0.35	3.75	**0:87:13**
6	0.125	10	0.35	2.5	**59:39:2**
7	**0.25**	**10**	**0.35**	**3**	**0:96:4**

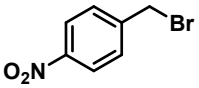
Supplementary table 4. Pd-catalyzed cross-coupling of lithium acetylides with benzyl bromide: limitations



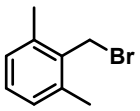
1.05 eq. RLi: 1,2-addition Also at 40 °C, 0 °C



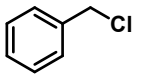
1.05 eq. RLi 1,2-addition Also at 40 °C, 0 °C



Homo-coupling



Homo-coupling

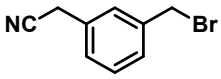


No conversion

Characterization of compounds

Starting materials

2-(3-(Bromomethyl)phenyl)acetonitrile (1q)

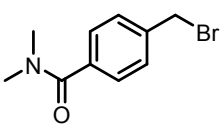


In a flame-dried Schlenk flask under inert atmosphere, 3-methylphenylacetonitrile (1 g, 7.6 mmol) was dissolved in MeCN (48 mL). *N*-Bromosuccinimide (1.1 g, 0.8 eq.) and benzoyl peroxide (0.09 g, 0.05 eq.) were subsequently added, and the solution was heated to reflux for 16 h. After cooling to RT, sat. aq. $NaHCO_3$ solution (300 mL) was added, and the aqueous phase was extracted with EtOAc (3 x 100 mL). The combined organic layers were washed with brine (100 mL), dried over $MgSO_4$, filtered, and dried onto silica. The desired product was obtained as a yellow liquid (0.91 g, 57%) after purification by automated flash column chromatography (Pentane gradient to Pentane/EtOAc 95/5).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.35 (m, 3H), 7.29 – 7.26 (m, 1H), 4.48 (s, 2H), 3.76 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9, 130.6, 129.7, 128.8, 128.6, 128.0, 117.6, 32.0, 23.5.

4-(Bromomethyl)-*N*,*N*-dimethylbenzamide (1v)

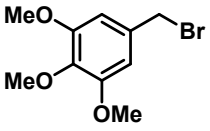


A flame-dried Schlenk flask under inert atmosphere was charged with 4-bromomethylbenzoic acid (1.0 g, 4.7 mmol) and dry toluene (5.0 mL) at room temperature. Thionyl chloride (2.5 mL, 7.5 eq.) was subsequently added, and the mixture was heated to reflux for 16 h. After cooling to RT, the solution was concentrated *in vacuo*. The resulting crude oil was dissolved in toluene (50 mL) and concentrated *in vacuo*. This process was performed three times to afford the desired product as an off-white solid (1.07 g, 99%). n a flame-dried Schlenk flask under inert atmosphere, a solution of dimethylamine (2 M solution in THF; 1.1 mL; 1 eq.) and triethylamine (0.6 mL, 1 eq.) in THF (8.4 mL) was stirred for 10 min. A solution of 4-(bromomethyl)benzoyl chloride (0.5 g, 2.14 mmol) in THF (4.2 mL) was subsequently added, and the reaction mixture was stirred at RT for 16 h. It was then diluted with EtOAc (30 mL), washed with water (3 x 30 mL), and brine (30 mL). The organic phase was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to afford the desired product as an off-white solid (0.22 g, 43%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (s, 4H), 4.60 (s, 2H), 3.11 (s, 3H), 2.98 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 139.8, 136.3, 128.6, 127.5, 45.6.

5-(bromomethyl)-1,2,3-trimethoxybenzene (1x)

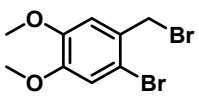


A flame-dried Schlenk flask 3,4,5-trimethoxybenzyl alcohol (2 g, 10.1 mmol, 1.00 equiv.) in Et_2O (200 mL) were added PBr_3 (2.73 g, 10.1 mmol, 1.00 equiv.) and pyridine (40 mg, 0.5 mmol, 0.05 equiv.) slowly at RT. The mixture was heated to reflux for 3 h. Water was added at RT and the aqueous layer extracted with Et_2O.

The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo to give **1x** as a white solid (quant.).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.84 (s, 3H), 3.87 (s, 6H), 4.46 (s, 2H), 6.62 (s, 2H).

1-bromo-2-(bromomethyl)-4,5-dimethoxybenzene (1aa)



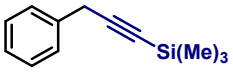
A Schlenk flask under inert atmosphere charged with (3,4-dimethoxyphenyl)methanol (0.86 mL; 5.95 mmol) and anhydrous $CHCl_3$ (10 mL) was cooled to 0 °C. A solution of Br_2 (0.35 mL; 1.15 eq.) in anhydrous $CHCl_3$ (10 mL) was then added dropwise, after which the resulting solution was stirred at RT for 2 h. The reaction was subsequently quenched by addition of sat. aq. $Na_2S_2O_3$ solution (50 mL). The organic phase was separated, washed with brine (50 mL), and dried onto silica. The desired product was obtained as a white solid (1.24 g; 67%) after purification by automated flash column chromatography (Pentane gradient to Pentane/EtOAc 90/10).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (s, 1H), 6.93 (s, 2H), 3.88 (s, 3H), 3.88 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 150.0, 148.8, 128.9, 115.8, 116.1, 113.5, 56.4, 56.3, 34.3.

Coupling products

Trimethyl(3-phenylprop-1-yn-1-yl)silane (3)[8]

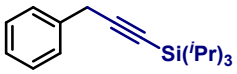


Product **3** was prepared from **1a** (0.5 mmol, 85.5 mg) and **2b** (0.65 mmol, 0.35M) according to **GP-C** and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (Pentane) as a yellow oil (82 mg, 87% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.30 (m, 4H), 7.30 – 7.20 (m, 1H), 3.67 (s, 2H), 0.21 (s, 9H).

^{13}C NMR (151 MHz, CDCl3) δ = 136.4, 128.5, 127.9, 126.6, 104.3, 86.9, 26.2, 0.1.

Triisopropyl(3-phenylprop-1-yn-1-yl)silane (5)[9]

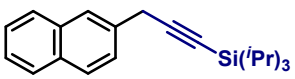


Product **5** was prepared from **1a** (0.5 mmol, 85.5 mg) and **2b** (0.65 mmol, 0.35M) according to **GP-C** and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (Pentane) as a yellow oil (120 mg, 88% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.36 (m, 2H), 7.32 (t, *J* = 7.7 Hz, 2H), 7.23 (d, *J* = 7.4 Hz, 1H), 3.71 (s, 2H), 1.09 (m, 21H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 136.7, 128.4, 127.8, 126.4, 105.7, 82.9, 26.2, 18.6, 11.3.

Triisopropyl(3-(naphthalen-2-yl)prop-1-yn-1-yl)silane (6)[10]



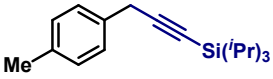
Product **6** was prepared from **1b** (0.5 mmol, 110.5 mg) and **2b** (0.65 mmol, 0.35M) according to **GP-C** and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (flow rate 20 mL/min) (Pentane) as an oil (100 mg, 62% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.84 – 7.78 (m, 3H), 7.49 – 7.43 (m, 3H), 3.86 (s, 2H), 1.27 – 0.89 (m, 21H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 134.2, 133.5, 132.3, 128.0, 127.6, 127.6, 126.4, 126.2, 126.0, 125.5, 105.6, 83.3, 26.4, 18.7, 11.3.

HRMS (ESI-, *m/z*) calculated for $C_{22}H_{29}Si$ $[M-H]^-$: 321.20330; found: 321.20443.

Triisopropyl(3-(p-tolyl)prop-1-yn-1-yl)silane (7)

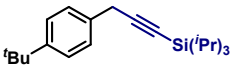


Product **7** was prepared from **1c** (0.5 mmol, 92.5 mg) and **2b** (0.65 mmol, 0.35M) according to **GP-C** and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (flow rate 20 mL/min) (Pentane) as an oil (130 mg, 91 % yield)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 7.9 Hz, 2H), 3.66 (s, 2H), 2.34 (s, 3H), 1.15 – 1.00 (m, 21H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 135.9, 133.6, 129.1, 127.7, 106.0, 82.6, 25.8, 21.0, 18.6, 11.3.

HRMS (ESI-, *m/z*) calculated for $C_{19}H_{29}Si$ $[M-H]^-$: 285.20330; found: 285.20342.

(3-(4-(tert-butyl)phenyl)prop-1-yn-1-yl)triisopropylsilane (8)



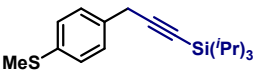
Product **8** was prepared from **1d** (0.5 mmol, 113 mg) and **2b** (0.65 mmol, 0.35M) according to **GP-C** and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (flow rate 20 mL/min) (Pentane/Et_2O 0-1%) as an oil (115mg, 70% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 – 7.31 (m, 4H), 3.71 (s, 2H), 1.42 – 1.27 (m, 9H), 1.12 (m, 21H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 149.3, 133.6, 127.4, 125.3, 105.8, 82.7, 34.4, 31.4, 25.7, 18.7, 11.4.

HRMS (ESI-, *m/z*) calculated for $C_{22}H_{35}Si$ $[M-H]^-$: 327.25025; found: 327.25035.

Triisopropyl(3-(4-(methylthio)phenyl)prop-1-yn-1-yl)silane (9)



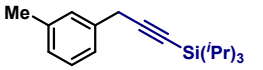
Product **9** was prepared from **1e** (0.5 mmol, 108 mg) and **2b** (0.65 mmol, 0.35M) according to **GP-C** and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (flow rate 20 mL/min) (Pentane) as an oil (126 mg, 81% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 (d, *J* = 7.9 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 3.69 (s, 2H), 2.52 (s, 3H), 1.12 (m, 21H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 136.2, 133.8, 128.3, 127.0, 105.5, 83.0, 25.7, 18.6, 16.2, 11.3.

HRMS (ESI-, *m/z*) calculated for $C_{19}H_{29}SSi$ $[M-H]^-$: 317.17537; found: 317.17512.

Triisopropyl(3-(m-tolyl)prop-1-yn-1-yl)silane (10)



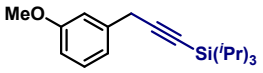
Product **10** was prepared from **1f** (0.5 mmol, 92.5 mg) and **2b** (0.65 mmol, 0.35M) according to GP-C and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (flow rate 20 mL/min) (Pentane) as an oil (120mg, 84% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.24 – 7.16 (m, 3H), 7.04 (d, *J* = 7.3 Hz, 1H), 3.67 (s, 2H), 2.34 (s, 3H), 1.10 (m, 21H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 138.0, 136.6, 128.7, 128.3, 127.1, 124.8, 105.9, 82.8, 26.1, 21.3, 18.6, 11.3.

HRMS (ESI-, *m/z*) calculated for $C_{19}H_{29}Si$ $[M-H]^-$: 285.20330; found: 285.20361.

Triisopropyl(3-(3-methoxyphenyl)prop-1-yn-1-yl)silane (11)



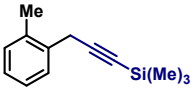
Product **11** was prepared from **1g** (0.5 mmol, 100.5 mg) and **2b** (0.65 mmol, 0.35M) according to **GP-C** and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (flow rate 20 mL/min) (Pentane/EA, 97:3) as an oil (130 mg, 86% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (t, *J* = 7.9 Hz, 1H), 6.99 (s, 1H), 6.93 (d, *J* = 7.6 Hz, 1H), 6.78 (dd, *J* = 8.2, 2.6 Hz, 1H), 3.80 (s, 3H), 3.69 (s, 2H), 1.10 (m, 21H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 159.8, 138.3, 129.3, 120.2, 113.0, 112.5, 105.5, 83.0, 55.2, 26.3, 18.7, 11.3.

HRMS (ESI-, *m/z*) calculated for $C_{19}H_{29}OSi$ $[M-H]^-$: 301.19822; found: 301.19858.

Trimethyl(3-(o-tolyl)prop-1-yn-1-yl)silane (12)[11]

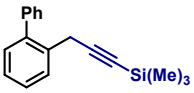


Product **12** was prepared from **1h** (0.5 mmol, 92.5 mg) and **2b** (0.65 mmol, 0.35M) according to **GP-C** and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (flow rate 20 mL/min) (Pentane) as an oil (83 mg, 82% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 – 7.39 (m, 1H), 7.16 (m, 3H), 3.57 (s, 2H), 2.31 (s, 3H), 0.18 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 136.0, 134.6, 130.0, 128.2, 126.8, 126.1, 103.9, 87.0, 24.4, 19.3, 0.1.

(3-([1,1'-biphenyl]-2-yl)prop-1-yn-1-yl)trimethylsilane (13)



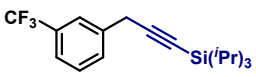
Product **13** was prepared from **1i** (0.5 mmol, 123.5 mg) and **2b** (0.65 mmol, 0.35M) according to **GP-C** and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (flow rate 20 mL/min) (Pentane) as an oil (100 mg, 76% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (dd, *J* = 7.7, 1.4, 1H), 7.46 – 7.20 (m, 8H), 3.54 (s, 2H), 0.16 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 141.4, 141.0, 133.9, 129.9, 129.1, 128.9, 128.2, 127.7, 127.1, 126.7, 105.0, 86.7, 24.6, 0.1.

HRMS (ESI-, *m/z*) calculated for $C_{18}H_{19}OSi$ $[M-H]^-$: 263.12505; found: 263.12514.

Triisopropyl(3-(3-(trifluoromethyl)phenyl)prop-1-yn-1-yl)silane (14)



Product **14** was prepared from **1j** (0.5 mmol, 120 mg) and **2b** (0.65 mmol, 0.35M) according to **GP-C** and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (flow rate 20 mL/min) (Pentane) as an oil (105 mg, 61% yield).

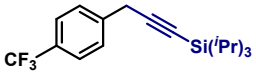
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.50 (d, *J* = 7.8 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 1H), 3.76 (s, 2H), 1.10 (m, 21H).

^{19}F NMR (376 MHz, $CDCl_3$) δ = -62.8.

^{13}C NMR (151 MHz, $CDCl_3$) δ 137.7, 131.2, 130.71 (q, J_{C-F} = 32.2 Hz), 128.8, 124.72 (q, J_{C-F} = 3.8 Hz), 124.72 (q, J_{C-F} = 272.2 Hz), 123.41 (q, J_{C-F} = 3.8 Hz), 104.4, 84.2, 26.1, 18.6, 11.3.

HRMS (ESI-, *m/z*) calculated for $C_{19}H_{27}F_3Si$ $[M-H]^-$: 339.17614; found: 339.17567.

Triisopropyl(3-(4-(trifluoromethyl)phenyl)prop-1-yn-1-yl)silane (15)



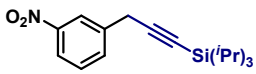
Product **15** was prepared from **1l** (0.5 mmol, 120 mg) and **2b** (0.65 mmol, 0.35M) according to **GP-C** and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (flow rate 20 mL/min) (Pentane) as an oil (128mg, 75% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.1 Hz, 2H), 7.50 (d, *J* = 7.9 Hz, 2H), 3.75 (s, 2H), 1.09 (m, 21H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 140.8, 128.9 (q, J_{C-F} = 32.4 Hz), 128.1, 125.4 (q, J_{C-F} = 3.8 Hz), 124.2 (q, J_{C-F} = 271.7 Hz), 104.3, 84.0, 26.2, 18.6, 11.3.

HRMS (ESI-, *m/z*) calculated for $C_{19}H_{27}F_3Si$ $[M-H]^-$: 339.17614; found: 339.17563.

Triisopropyl(3-(3-nitrophenyl)prop-1-yn-1-yl)silane (17)



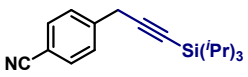
Product **17** was prepared from **1k** (0.5 mmol, 108 mg) and **2b** (0.65 mmol, 0.35M) according to **GP-C** and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (Pentane/EA, 95:5) (70 mg, 45% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (s, 1H), 8.11 (d, *J* = 8.2 Hz, 1H), 7.70 (d, *J* = 7.7 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 1H), 3.80 (s, 2H), 1.10 (m, 21H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 148.7, 139.2, 134.2, 129.5, 123.2, 122.0, 103.9, 85.2, 26.2, 18.9, 11.5.

MS (EI, 70 eV) 317(M^+, 4), 274 ($M-^iPr^+$, 100), 246 (33), 218 (55), 204 (30), 173 (10), 115 (24).

4-(3-(triisopropylsilyl)prop-2-yn-1-yl)benzonitrile (18)



Product **18** was prepared from **1n** (0.5 mmol, 98 mg) and **2b** (0.65 mmol, 0.35M) according to **GP-C** and purified by Grace® Reveleris X2 flash

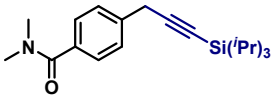
chromatography system with 25g EcoFlex silica 50µm irregular column (Pentane/EtOAc 98/2) as an oil (112 mg, 75% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.0 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H), 3.75 (s, 2H), 1.08 (m, 21H).

^{13}C NMR (101 MHz, $CDCl_3$) δ δ 145.0, 134.9, 131.3, 121.5, 113.2, 106.3, 87.2, 29.1, 21.2, 13.9.

HRMS (ESI-, *m/z*) calculated for $C_{19}H_{26}NSi$ $[M-H]^-$: 296.1840; found: 296.1840.

***N,N*-Dimethyl-4-(3-(triisopropylsilyl)prop-2-yn-1-yl)benzamide (19)**



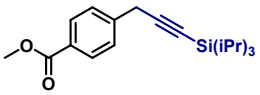
Product **19** was prepared from **1v** (0.5 mmol, 121 mg) and **2b** (0.65 mmol, 0.35M) according to **GP-C** and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (Pentane/EtOAc 98/2) as an oil (122 mg, 71% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 3.71 (s, 2H), 3.10 (s, 3H), 2.99 (s, 3H), 1.08 (m, 21H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 138.5, 134.7, 127.9, 127.5, 105.2, 83.6, 26.3, 18.78, 18.7, 11.4.

HRMS (ESI+, *m/z*) calculated for $C_{21}H_{34}NOSi$ $[M+H]^+$: 344.2404; found: 344.2408.

Methyl 4-(3-(triisopropylsilyl)prop-2-yn-1-yl)benzoate (20)



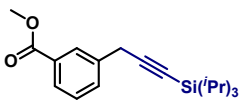
Product **20** was prepared from **1o** (0.5 mmol, 115 mg) and **2b** (0.65 mmol, 0.35M) according to **GP-C** and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (Pentane/EtOAc 98/2) as an oil (111 mg, 67% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.3 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 2H), 3.89 (s, 3H), 3.73 (s, 2H), 1.07 (m, 21H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 142.3, 129.9, 128.7, 128.0, 104.7, 83.9, 52.1, 26.5, 18.8, 11.4.

HRMS (ESI-, *m/z*) calculated for $C_{20}H_{29}O_2Si$ $[M-H]^-$: 329.1942; found: 329.1941.

Methyl 3-(3-(triisopropylsilyl)prop-2-yn-1-yl)benzoate (21)



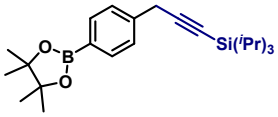
Product **21** was prepared from **1p** (0.5 mmol, 115 mg) and **2b** (0.65 mmol, 0.35M) according to **GP-C** and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (Pentane/EtOAc 98/2) as an oil (124 mg, 76% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.92 (d, J = 7.7 Hz, 1H), 7.57 (d, J = 7.7 Hz, 1H), 7.39 (t, J = 7.7 Hz, 1H), 3.91 (s, 3H), 3.75 (s, 2H), 1.10 (m, 21H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 137.2, 132.5, 130.5, 129.1, 128.6, 128.0, 105.0, 83.91, 52.2, 26.2, 18.8, 11.4.

HRMS (ESI-, *m/z*) calculated for $C_{20}H_{29}O_2Si$ $[M-H]^-$: 329.1942; found: 329.1941.

Triisopropyl (3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)prop-1-yn-1-yl)silane (22)



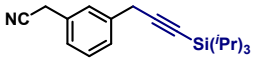
Product **22** was prepared from **1r** (0.5 mmol, 149 mg) and **2b** (0.65 mmol, 0.35M) according to GP-C and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (Pentane/EtOAc 98/2) as an oil (107 mg, 54% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.8 Hz, 2H), 7.40 (d, *J* = 8.0 Hz, 2H), 3.71 (s, 2H), 1.35 (s, 12H), 1.09 (m, 21H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 140.1, 135.1, 127.4, 105.5, 83.9, 83.2, 26.6, 25.0, 18.8, 11.5.

HRMS (ESI-, *m/z*) calculated for $C_{24}H_{38}BO_2Si$ $[M-H]^-$: 397.2740; found: 397.2726.

2-(3-(3-(Triisopropylsilyl)prop-2-yn-1-yl)phenyl)acetonitrile (23)



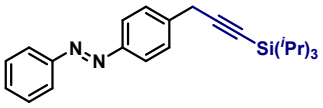
Product **23** was prepared from **1q** (0.5 mmol, 149 mg) and **2b** (0.65 mmol, 0.35M) according to **GP-C** and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (Pentane/EtOAc 98/2) as an oil (105 mg, 47% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.30 (m, 3H), 7.22 – 7.18 (m, 1H), 3.73 (s, 2H), 3.71 (s, 2H), 1.09 (m, 21H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9, 130.2, 129.3, 127.7, 127.6, 126.2, 105.1, 83.7, 26.2, 23.7, 18.7, 11.4. (*One quaternary C missing in the aromatic region probably due to overlapping*)

HRMS (ESI-, *m/z*) calculated for $C_{20}H_{28}NSi$ $[M-H]^-$: 310.1997; found: 310.1999.

(E)-1-phenyl-2-(4-(3-(triisopropylsilyl)prop-2-yn-1-yl)phenyl)diazene (24)



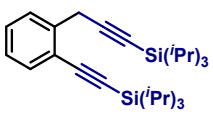
Product **24** was prepared from **1y** (0.5 mmol, 137mg) and **2b** (0.65 mmol, 0.35M) according to **GP-C** and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (flow rate 20 mL/min) (Pentane/EtOAc 98/2) as orange solid (126mg, 67% yield). (The r*eaction was quenched with saturated aq. NH_4Cl solution in order to avoid allene formation*)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94 – 7.88 (m, 4H), 7.56 – 7.50 (m, 4H), 7.47 (t, J = 7.2 Hz, 1H), 3.78 (s, 2H), 1.11 (m, 21H).

^{13}C NMR (151 MHz, $CDCl_3$) δ = 152.7, 151.4, 140.0, 130.9, 129.1, 128.6, 123.0, 122.8, 105.0, 83.6, 26.2, 18.6, 11.3

HRMS (ESI-, m/z) calculated for $C_{24}H_{33}N_2Si$ $[M-H]^-$: 377.24075; found: 377.24136.

Triisopropyl(3-(2-((triisopropylsilyl)ethynyl)phenyl)prop-1-yn-1-yl)silane (25)



In a dry Schlenk tube $[Pd(\mu\text{-}I)P^tBu_3]_2$ (6 mol%) and **1s** (0.5 mmol, 125mg) were added and evacuated back-filled with nitrogen. Dry toluene (4 mL) was added

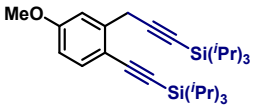
and the mixture left to stir at RT for 2 min. The organolithium reagent (1.3 mmol, 0.35M) was then added to the reaction mixture over 20 min using a syringe pump. The reaction was quenched with ^{i}PrOH and all the volatiles were removed under reduced pressure. The residue was purified using a Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (Pentane) afforded **25** as an oil (112 mg, 50% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 7.8 Hz, 1H), 7.48 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.35 (td, *J* = 7.6, 1.5 Hz, 1H), 7.21 (td, *J* = 7.6, 1.3 Hz, 1H), 3.91 (s, 2H), 1.16 (s, 21H), 1.12 (m, 21H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9, 132.5, 128.8, 127.8, 126.4, 122.6, 105.3, 104.8, 96.0, 83.9, 25.3, 18.9, 18.8, 11.5, 11.5.

HRMS (ESI+, *m/z*) calculated for $C_{21}H_{34}O_3NaSi$ $[M+Na]^+$: 385.2169; found: 385.2176.

Triisopropyl(3-(5-methoxy-2-((triisopropylsilyl)ethynyl)phenyl)prop-1-yn-1-yl)silane (26)



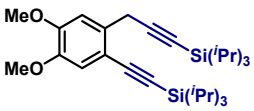
In a dry Schlenk tube $[Pd(\mu\text{-I})P^tBu_3]_2$ (6 mol%) and **1z** (0.5 mmol, 140mg) were added and evacuated and back-filled with nitrogen. Dry toluene (4 mL) was added and the mixture left it to stir at RT for 2 min. The organolithium reagent (1.3 mmol, 0.35M) was then added to the reaction mixture over 20 min using a syringe pump. The reaction was quenched with ^{i}PrOH and all the volatiles were removed under reduced pressure. The residue was purified using Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (Pentane/DCM 90/10) afforded **26** as an oil (134 mg, 52% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ δ 7.38 (d, *J* = 8.5 Hz, 1H), 7.28 (d, *J* = 2.6 Hz, 1H), 6.72 (dd, *J* = 8.5, 2.7 Hz, 1H), 3.87 (s, 2H), 3.81 (s, 3H), 1.12 (s, 21H), 1.11 (m, 21H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 160.1, 140.7, 133.8, 114.8, 113.1, 112.6, 105.2, 104.8, 94.2, 84.1, 55.5, 25.5, 18.9, 18.8, 11.5.

HRMS (ESI+, *m/z*) calculated for $C_{30}H_{51}OSi_2$ $[M+H]^+$: 483.3473; found: 483.3471.

(3-(4,5-Dimethoxy-2-((triisopropylsilyl)ethynyl)phenyl)prop-1-yn-1-yl)triisopropylsilane (27)



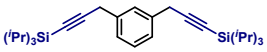
In a dry Schlenk tube $[Pd(\mu\text{-I})P^tBu_3]_2$ (6 mol%) and **1z-1** (0.5 mmol, 155mg) were added and evacuated and back-filled with nitrogen. Dry toluene (4 mL) was added and the mixture left to stir at RT for 2 min. The organolithium reagent (1.3 mmol, 0.35M) was then added to the reaction mixture over 20 min using a syringe pump. The reaction was quenched with ^{i}PrOH and all the volatiles were removed under reduced pressure. The residue was purified using Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (Pentane/EtOAc 95/5) afforded **27** as an oil (124 mg, 48% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (s, 1H), 6.92 (s, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.84 (s, 2H), 1.14 (s, 21H), 1.10 (s, 21H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 149.7, 147.2, 132.4, 114.8, 114.1, 110.9, 105.7, 104.9, 94.2, 83.6, 56.2, 55.9, 24.8, 18.9, 18.8, 11.4, 11.4.

HRMS (ESI+, *m/z*) calculated for $C_{31}H_{53}O_2Si_2$ $[M+H]^+$: 513.3579; found: 513.3575.

1,3-bis(3-(triisopropylsilyl)prop-2-yn-1-yl)benzene (28)



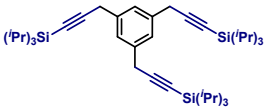
In a dry Schlenk tube [Pd(μ-I)P^{t}Bu$_3$]$_2$ (6 mol%) and **1t** (0.5 mmol, 132.5 mg) were added and evacuated and back-filled with nitrogen. Dry toluene (4 mL) was added and the mixture left to stir at RT for 2 min. The organolithium reagent (1.3 mmol, 0.35M) was then added to the reaction mixture over 20 min using a syringe pump. The reaction was quenched with ^{i}PrOH and all the volatiles were removed under reduced pressure. The residue was purified using Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (flow rate 20 mL/min) (Pentane) afforded **28** as an oil (210 mg, 90% yield).

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.33 (s, 1H), 7.29 (m, 3H), 3.68 (s, 4H), 1.18– 0.92 (m, 42H).

^{13}C NMR (151 MHz, CDCl$_3$) δ = 136.8, 128.5, 127.6, 125.9, 105.7, 82.9, 26.1, 18.6, 11.3.

MS (EI, 70 eV) m/z (%) 466 (M$^+$, 0.1), 423 (M-^{i}Pr$^+$, 42), 381(100), 339 (69), 297 (18), 255 (16), 223 (13), 195 (18), 181 (14), 157 (56), 135 (49), 127 (56), 115 (31), 59 (50)

1,3,5-tris(3-(triisopropylsilyl)prop-2-yn-1-yl)benzene (29)



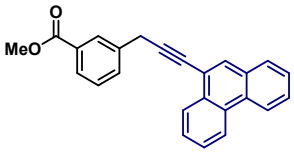
In a dry Schlenk tube [Pd(μ-I)P^{t}Bu$_3$]$_2$ (9 mol%) and **1u** (0.5 mmol, 178.5) were added and evacuated and back-filled with nitrogen. Dry toluene (6 mL) was added and the mixture left to stir at RT for 2 min. The organolithium reagent (1.95 mmol, 0.35M) was then added to the reaction mixture over 30 min using a syringe pump. The reaction was quenched with ^{i}PrOH and all the volatiles were removed under reduced pressure. The residue was purified using Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (flow rate 20 mL/min) (Pentane) afforded **29** as an oil (250 mg, 77% yield).

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.27 (s, 3H), 3.66 (s, 6H), 1.15–1.00 (m, 63H).

^{13}C NMR (151 MHz, CDCl$_3$) δ = 137.1, 125.8, 105.7, 82.9, 26.1, 18.6, 18.6, 11.3.

MS (EI, 70 eV) m/z (%) 660 (M$^+$, 0.13), 617 (M-^{i}Pr$^+$, 30), 575 (55), 449 (8), 375 (9), 333 (10), 266 (12), 207 (11), 157 (100), 73 (81), 59 (84).

Methyl 3-(3-(phenanthren-9-yl)prop-2-yn-1-yl)benzoate (30)



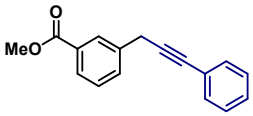
Product **30** was prepared from **1p** (0.5 mmol, 115 mg) and (phenanthren-9-ylethynyl)lithium (0.65 mmol, 0.35M) according to **GP-C** and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (Pentane/EtOAc 94/6) as an oil (80 mg, 46% yield).

^{1}H NMR (600 MHz, CDCl$_3$) δ 8.77 – 8.67 (m, 1H), 8.66 (d, *J* = 8.3 Hz, 1H), 8.48 (dd, *J* = 7.5, 1.8 Hz, 1H), 8.21 (s, 1H), 8.01 (s, 1H), 7.98 (d, *J* = 7.8 Hz, 1H), 7.87 – 7.83 (m, 1H), 7.76 (dt, *J* = 7.6, 1.0 Hz, 1H), 7.72 – 7.63 (m, 3H), 7.62 – 7.56 (m, 1H), 7.48 (t, *J* = 7.7 Hz, 1H), 4.08 (s, 2H), 3.94 (s, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ = 167.0, 137.2, 132.6, 131.7, 131.4, 131.2, 130.5, 130.1, 130.1, 129.2, 128.8, 128.4, 128.1, 127.3, 127.0, 127.0, 126.9, 126.9, 122.7, 122.6, 119.8, 91.3, 81.3, 52.2, 26.0.

HRMS (ESI-, *m/z*) calculated for $C_{25}H_{18}O_2$[M-OMe]$^-$: 319.11174; found: 319.11179.

Methyl 3-(3-phenylprop-2-yn-1-yl)benzoate (31)



Product **31** was prepared from **1p** (0.5 mmol, 115 mg) and (phenylethynyl)lithium (0.65 mmol, 0.5M) according to **GP-C** and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (Pentane/EtOAc 94/6) as an oil (65 mg, 52% yield).

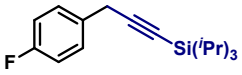
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.94 (d, *J* = 7.8 Hz, 1H), 7.65 (d, *J* = 7.7 1H), 7.46 (dd, *J* = 6.7, 3.1 Hz, 2H), 7.43 (t, *J* = 7.7 Hz, 1H), 7.32 – 7.29 (m, 3H), 3.93 (s, 3H), 3.88 (s, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ = 167.0, 137.2, 132.5, 131.6, 130.4, 129.1, 128.6, 128.2, 128.0, 127.9, 123.4, 86.7, 83.1, 52.1, 25.6.

HRMS (ESI-, *m/z*) calculated for $C_{17}H_{14}O_2$[M-OMe]$^-$: 219.08044; found: 219.08036.

*(Phenylethynyl lithium was prepared in only THF as solvent using **GP-A** due to formation of precipitate upon dilution with toluene, 15% of the homocoupling product was observed)*

(3-(4-fluorophenyl)prop-1-yn-1-yl)triisopropylsilane (32)



Product **32**was prepared from **1m** (0.5 mmol, 95 mg) and **2b** (0.65 mmol, 0.35M) according to **GP-C** and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (flow rate 20 mL/min) (Pentane) as an oil (108 mg, 75% yield).

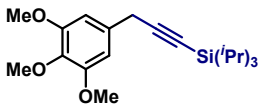
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 – 7.31 (m, 2H), 7.00 (m, 2H), 3.66 (s, 2H), 1.30 – 0.77 (m, 21H).

^{19}F NMR (565 MHz, $CDCl_3$) δ -116.90 (q, *J* = 6.5, 5.7 Hz).

^{13}C NMR (151 MHz, $CDCl_3$) δ δ 161.9 (d, $J_{C\text{-}F}$ = 244.2 Hz), 132.62 (d, $J_{C\text{-}F}$ = 3.2 Hz), 129.48 (d, $J_{C\text{-}F}$ = 8.1 Hz), 115.42 (d, $J_{C\text{-}F}$ = 21.4 Hz), 105.8, 83.4, 25.8, 18.9, 11.5.

HRMS (ESI-, *m/z*) calculated for $C_{18}H_{26}FSi$ [M-H]$^-$: 289.17823; found: 289.17847.

Triisopropyl(3-(3,4,5-trimethoxyphenyl)prop-1-yn-1-yl)silane (34)



Product **34** was prepared from **1x** (0.5 mmol, 131 mg) and **2b** (0.65 mmol, 0.35M) over 30 min according to **GP-C** and purified by Grace® Reveleris X2 flash chromatography system with 25g EcoFlex silica 50µm irregular column (Pentane/EtOAc 95/5) as a brown oil (148 mg, in 82% yield).

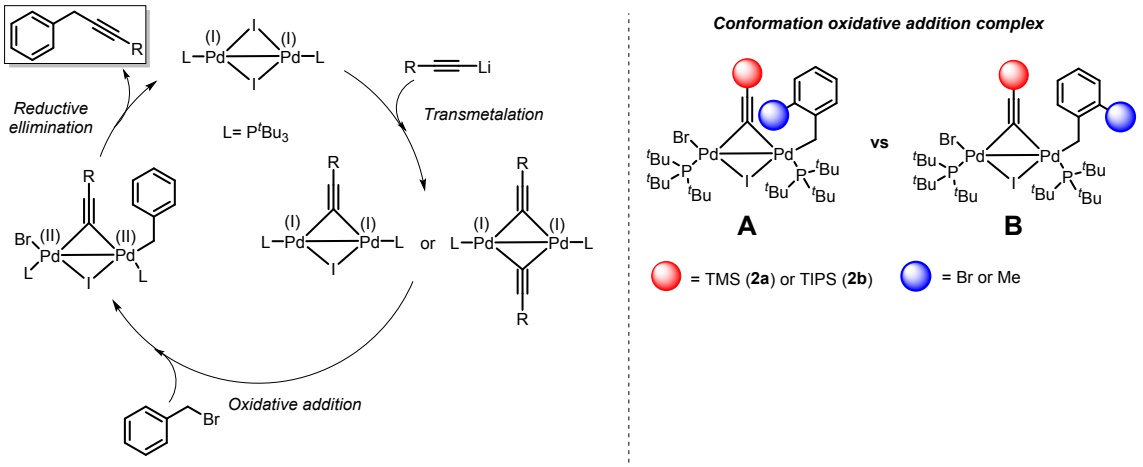
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.63 (s, 2H), 3.85 (s, 6H), 3.83 (s, 3H), 3.67 (s, 2H), 1.09 (s, 21H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.3, 136.6, 132.4, 105.6, 104.7, 83.4, 61.0, 56.1, 26.5, 18.8, 11.4.

HRMS (ESI+, *m/z*): calculated for $C_{21}H_{34}O_3NaSi$ [M+Na]$^+$: 385.2169; found: 385.2176.

Supplementary figure 1. Proposed mechanism[12]

On the basis of computational, spectroscopic, X-ray, and reactivity data the Schoenebeck laboratory suggested dinuclear Pd(I) catalysis to be operative using [Pd(μ-I)P^{t}Bu$_3$]$_2$.[12] In contrary to the 'conventional Pd-catalyzed cross-coupling', in this mechanism a transmetallation precedes the oxidative addition, following a reductive elimination to give the desired benzyl alkyne product.



Reactivity difference of *o*-Me benzyl bromide vs *o*-Br benzyl bromide with triisopropylsilyl lithium acetylide

No productive reaction occurred using *ortho*-methyl substituted benzyl bromide, whereas the reaction did proceed with *ortho*-bromo substituted benzyl bromide, when reacting it with triisopropylsilyl lithium acetylide **2b**. A possible explanation can be formulated by having a closer look at the proposed mechanism for the reaction.

The oxidative addition complex (when formed) as shown above can adopt two conformations which can both be considered sterically demanding (**A** and **B**) and where subtle differences in the size of the *ortho*-substitution might have a pronounced influence on the reaction. In **A** the *ortho*-substituent is in

relatively close proximity to the bulky silyl group, and in **B** the *ortho*-substituent is close to the very bulky ^{t}butyl-group of the phosphine ligand.

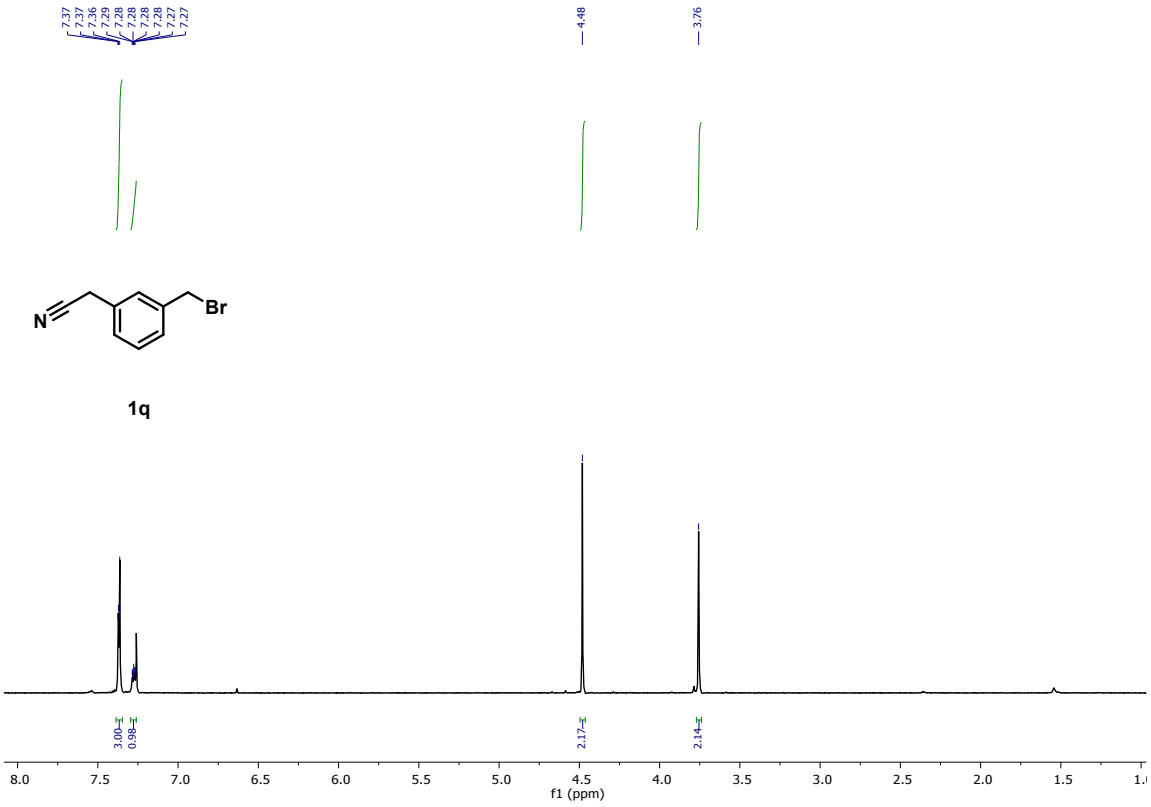
Although bromine is considered a 'large' atom, the chemical literature suggests that the methyl group (CH_3) is bigger than the Br atom. This was shown in a report where the bulkiness parameter (A-value) for –Br, -Me, -Ph, was determined based on the conformational analysis of cyclohexanes. The methyl (1.70)[13] and phenyl (3)[13] are significantly bulkier than bromo (0.43)[14] substituent (greater "A-value" = more "bulky"). Another determining factor of size is the Van der Waals radii, which for Me (2.0 Å)[15] is larger than for Br (1.85 Å).[16]

Taking the aforementioned factors into account we postulate that *ortho*-bromo substituted benzyl bromide is able to undergo an oxidative addition after, transmetallation of $[Pd(\mu\text{-}I)P^tBu_3]_2$ with triisopropylsilyl lithium acetylide **2b**, whereas *ortho*-methyl substituted benzyl bromide cannot. The oxidative addition, however, is possible after transmetallation of $[Pd(\mu\text{-}I)P^tBu_3]_2$ with trimethylsilyl lithium acetylide **2a**. This suggests that in the case of an *ortho*-methyl substituent a conformation as illustrated in oxidative addition complex **B** cannot be adopted, possible due to a steric clash between the Me and ^{t}Bu group. The *ortho*-methyl substituent is therefore 'forced' to adopt a conformation as illustrated oxidative addition complex **A**, with the methyl 'pointing towards' the acetylene moiety. In this case the size of the silyl group on the acetylide matters, which is considerably larger in the case of TIPS vs TMS. This might explain why *ortho*-methyl substituted benzyl bromide does not react with triisopropylsilyl lithium acetylide **2b** but does react with trimethylsilyl lithium acetylide **2a.**

For the *ortho*-bromo substituted benzyl bromide the somewhat smaller bromine atom, compared to CH_3, might be able to adopt a conformation like in oxidative addition complex **B**, or is just small enough to adopt conformation **A** despite the acetylide bearing the large TIPS group.

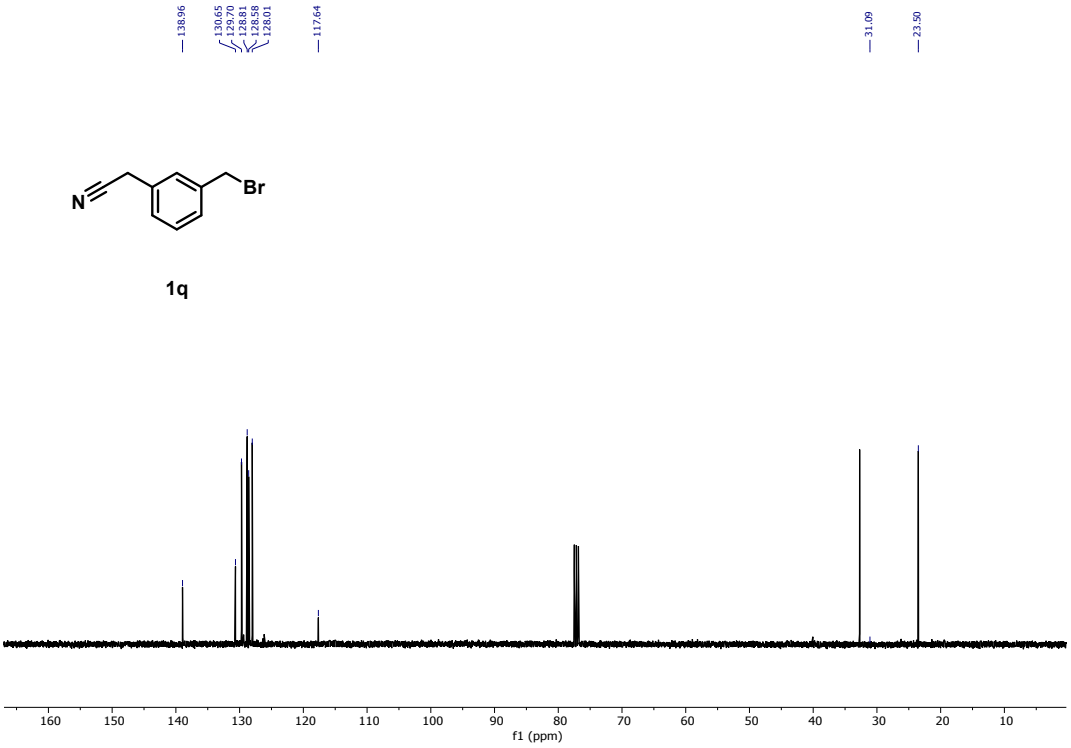
^{1}H and ^{13}C NMR Spectra

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



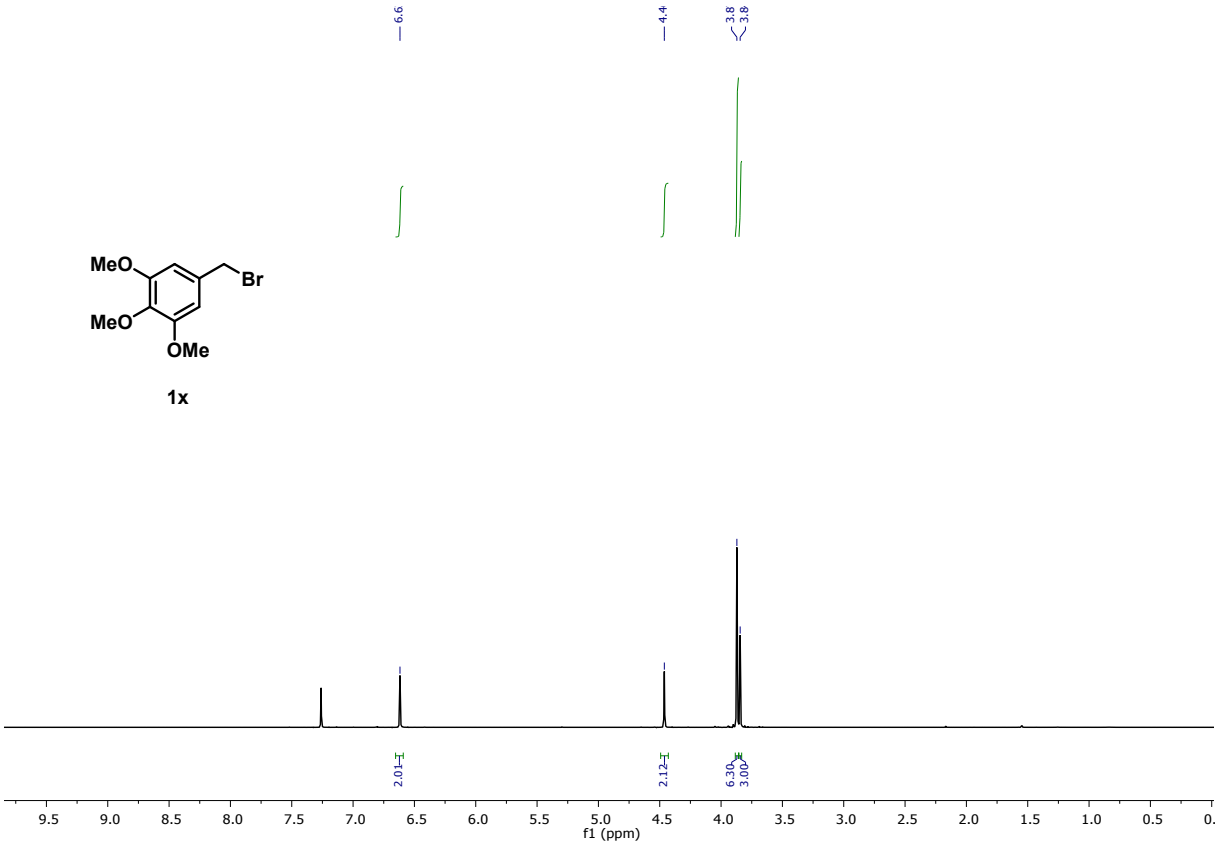
1q

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



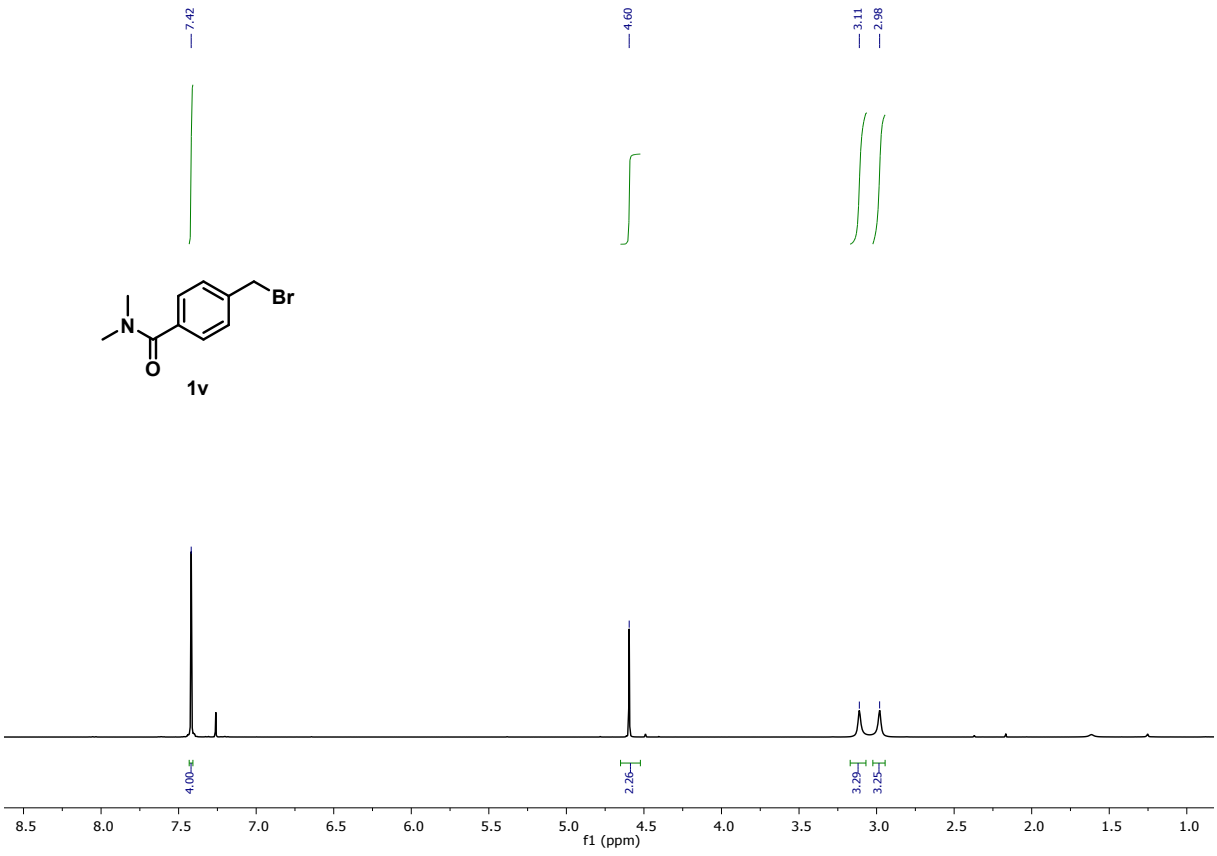
1q

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

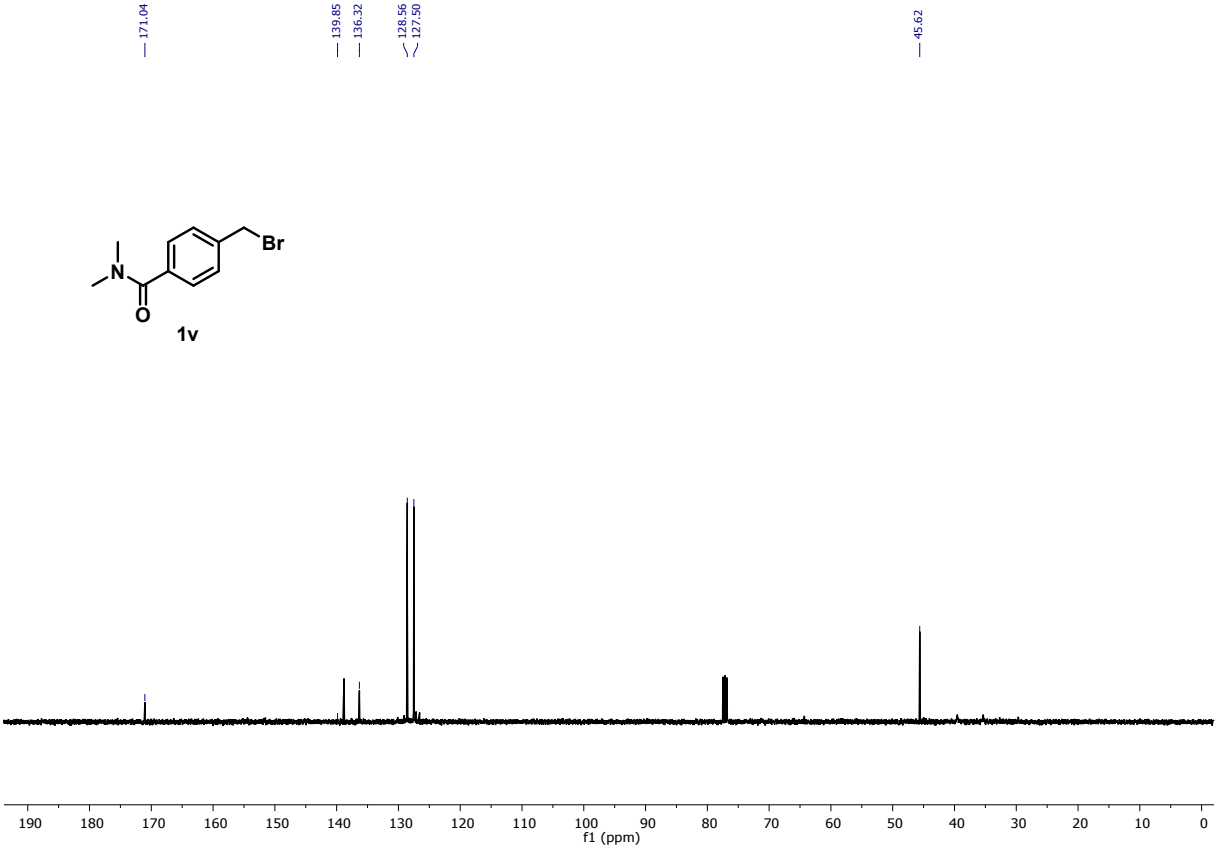


1x

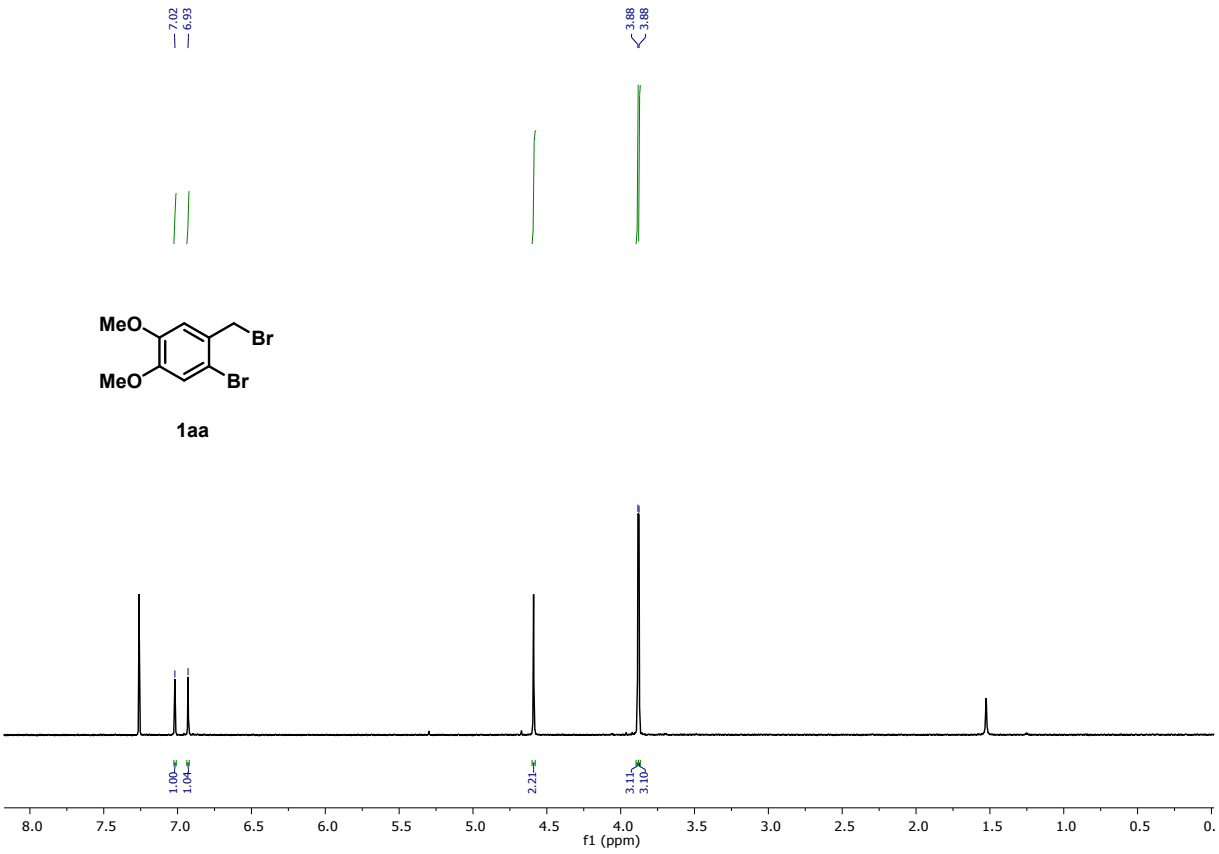
^{1}H NMR (400 MHz, $CDCl_3$)



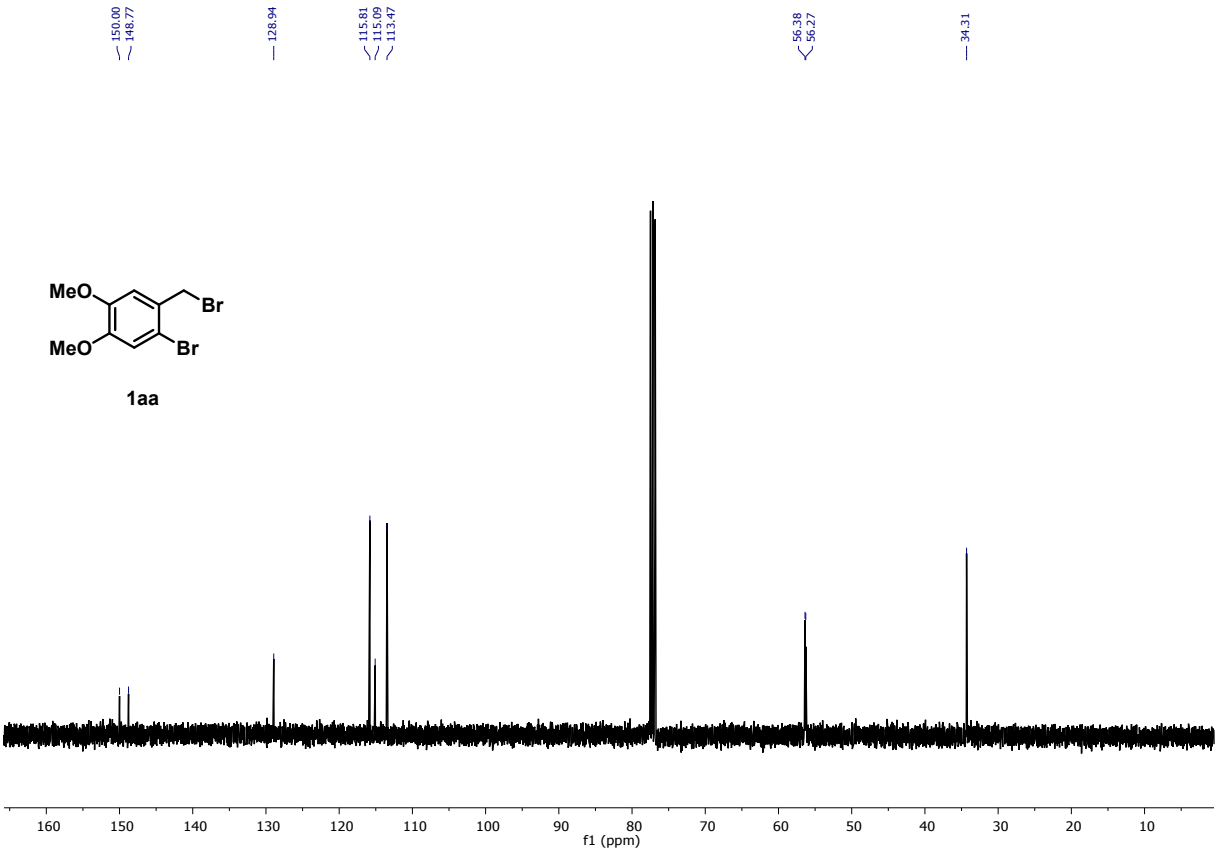
^{13}C NMR (101 MHz, $CDCl_3$)



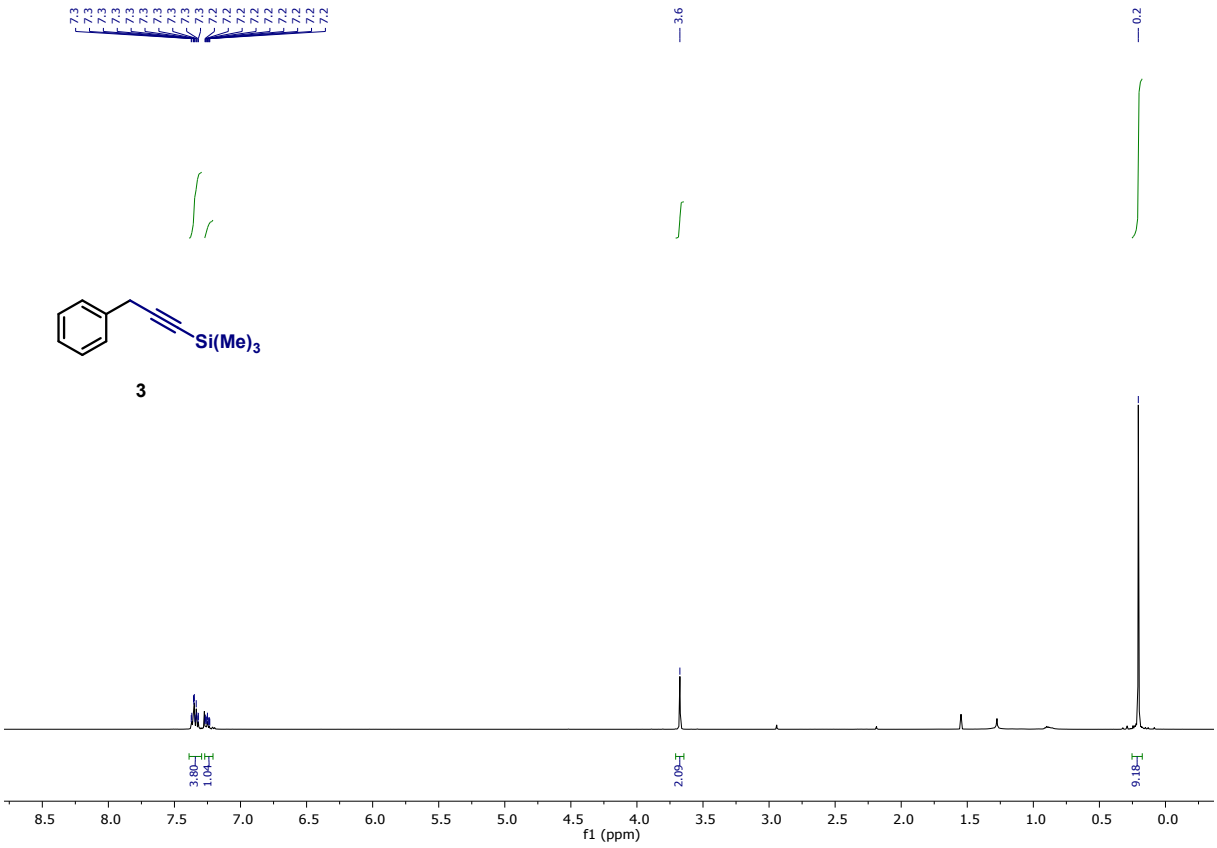
^{1}H NMR (400 MHz, $CDCl_3$)



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

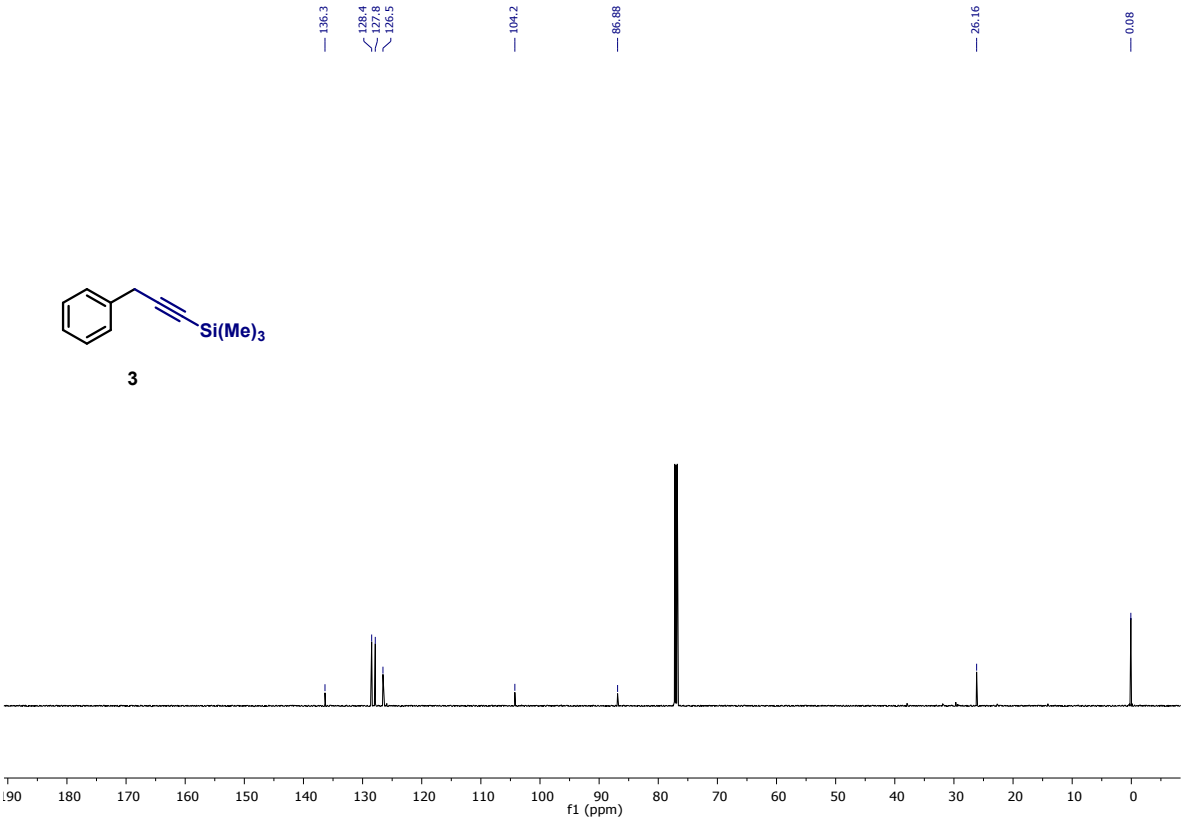


^{1}H NMR (500 MHz, $CDCl_3$)



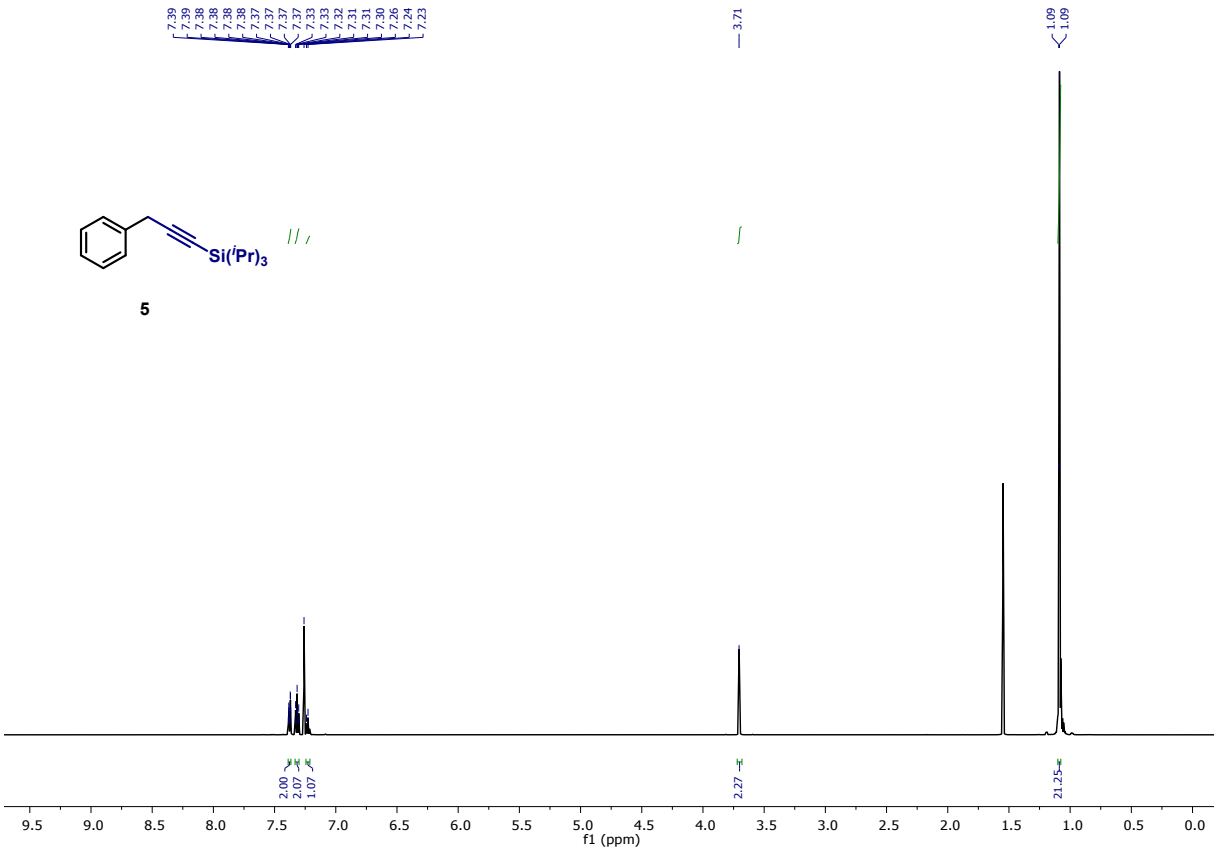
3

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

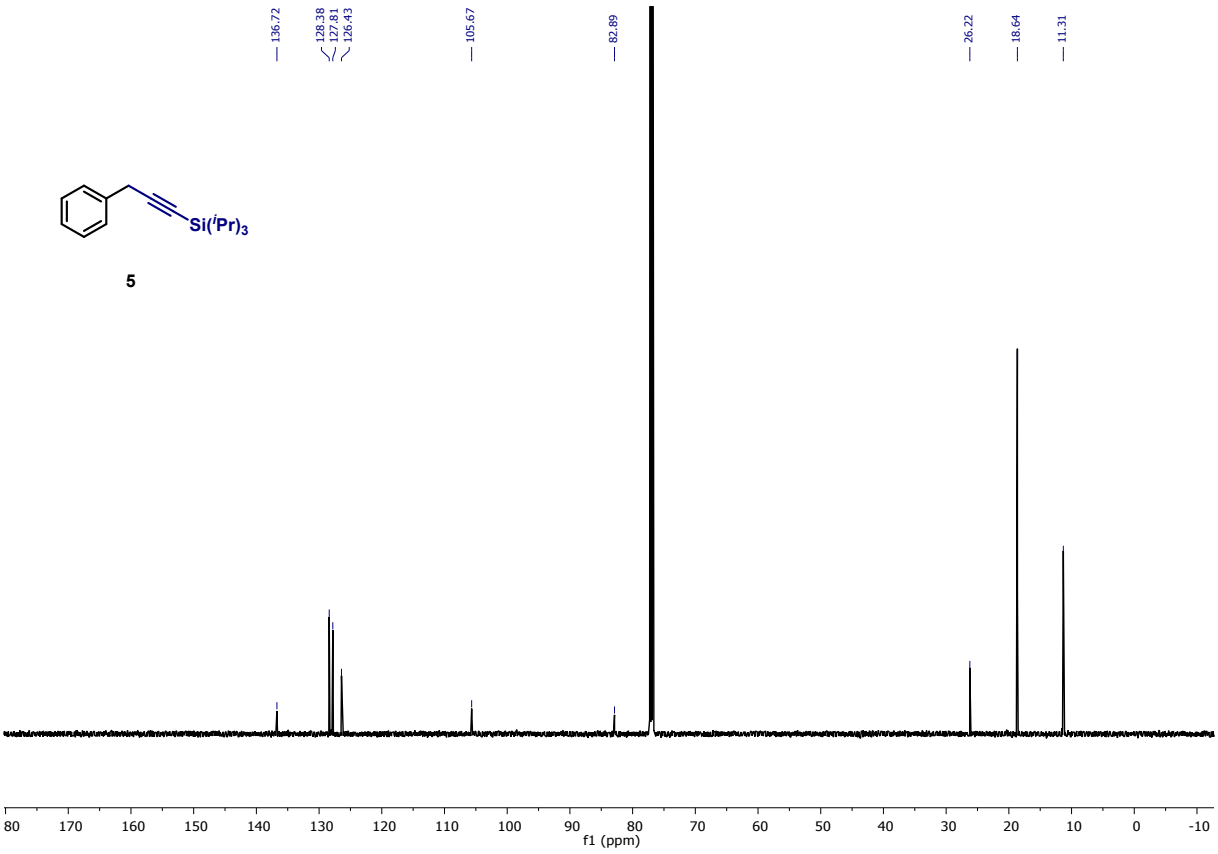


3

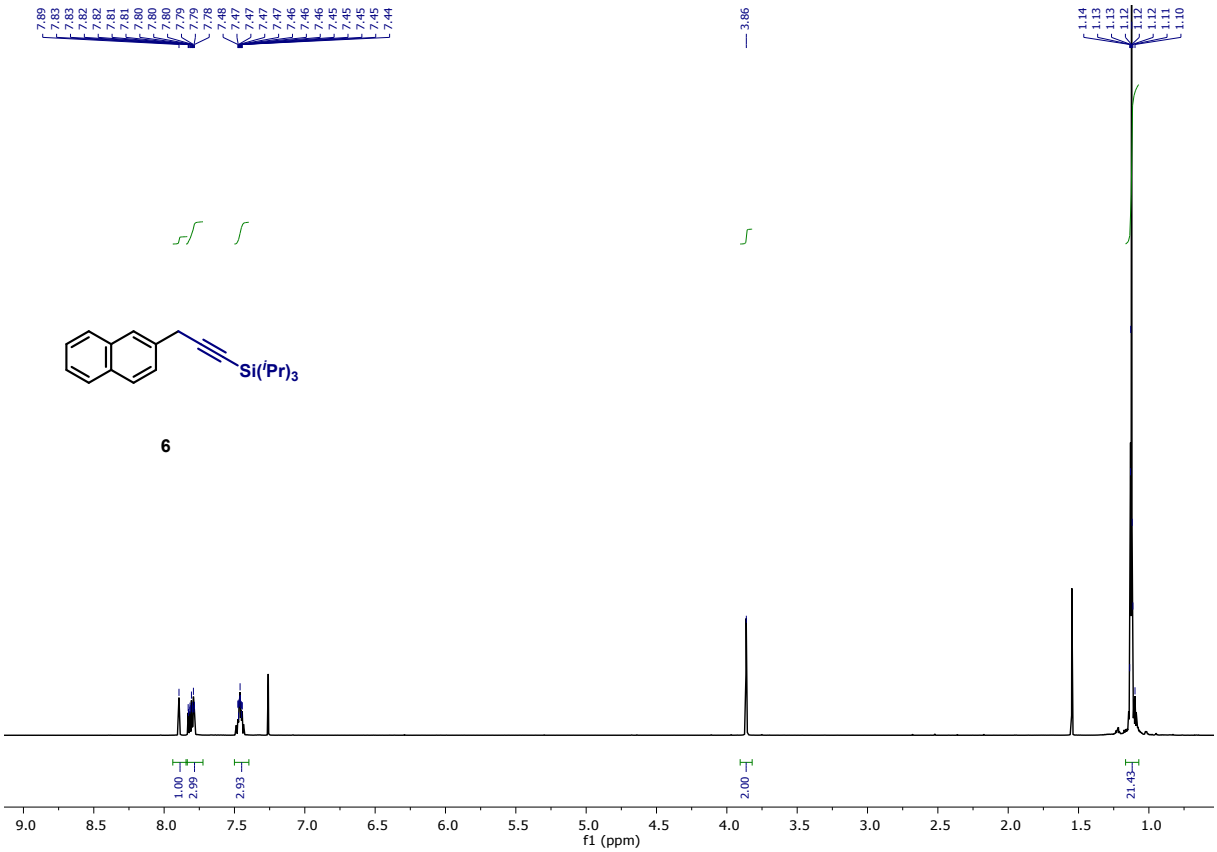
^{1}H NMR (600 MHz, $CDCl_3$)



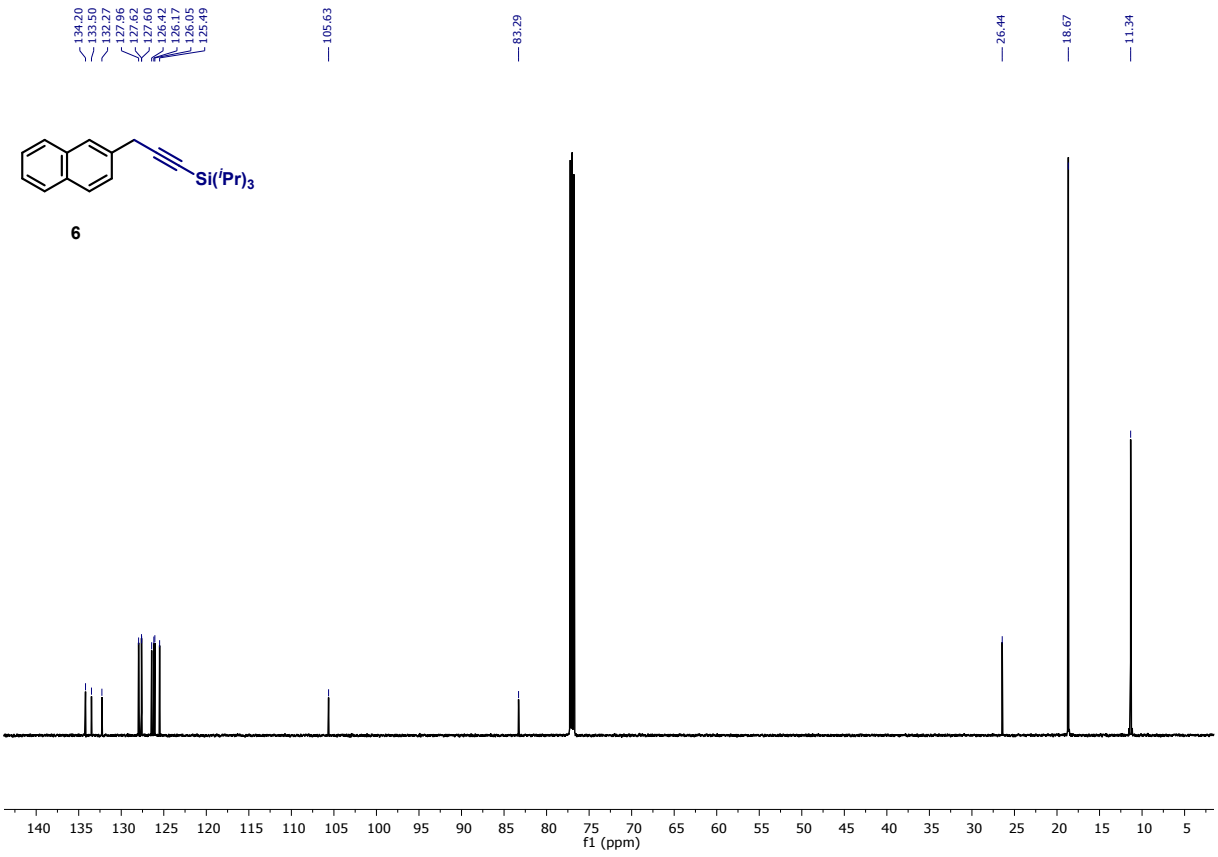
^{13}C NMR (151 MHz, $CDCl_3$)



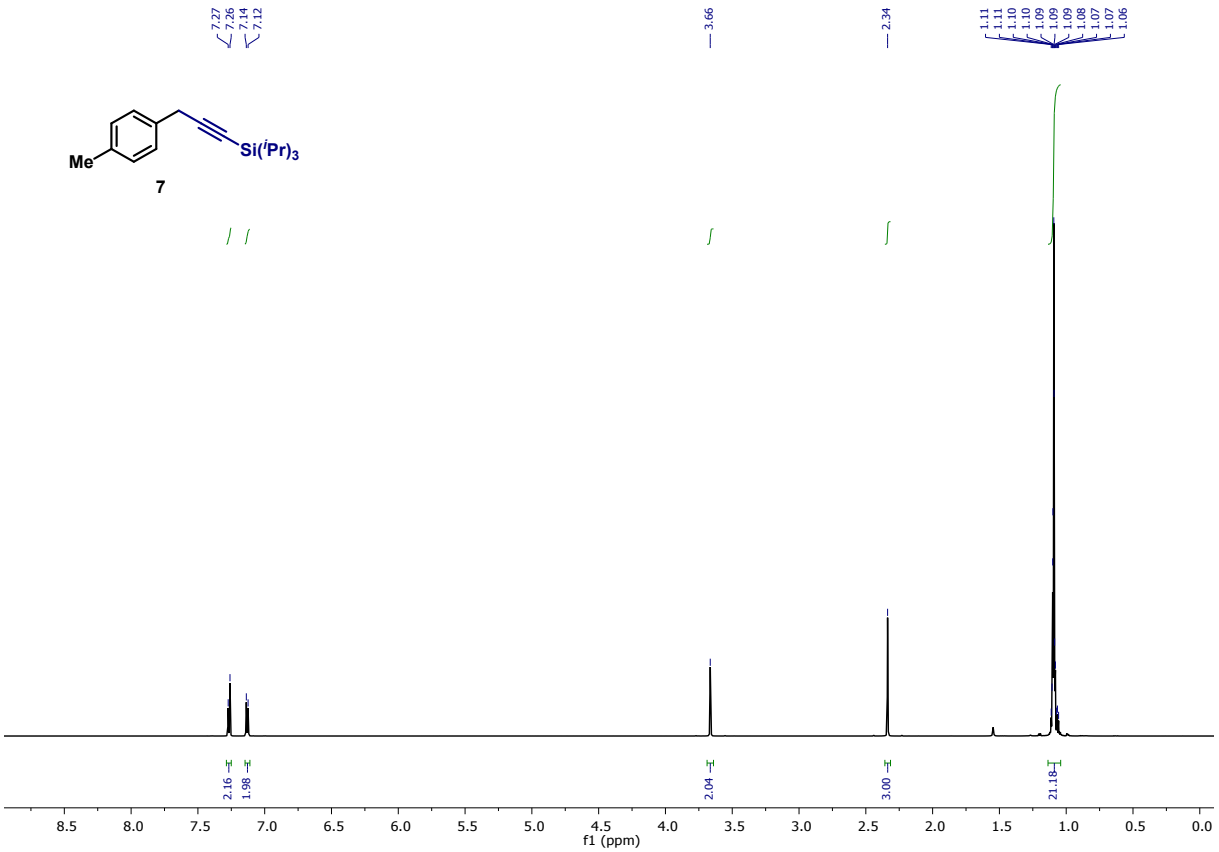
^{1}H NMR (600 MHz, $CDCl_3$)



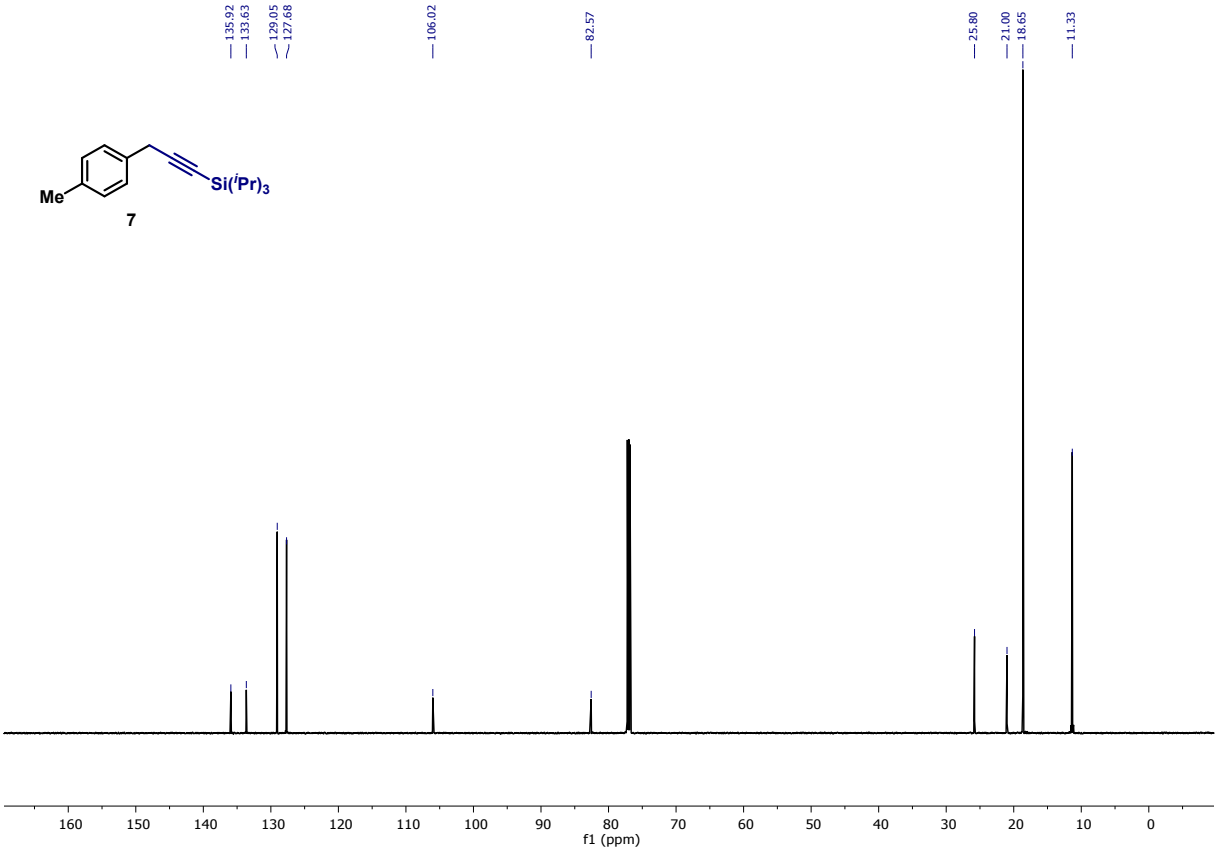
^{13}C NMR (151 MHz, $CDCl_3$)



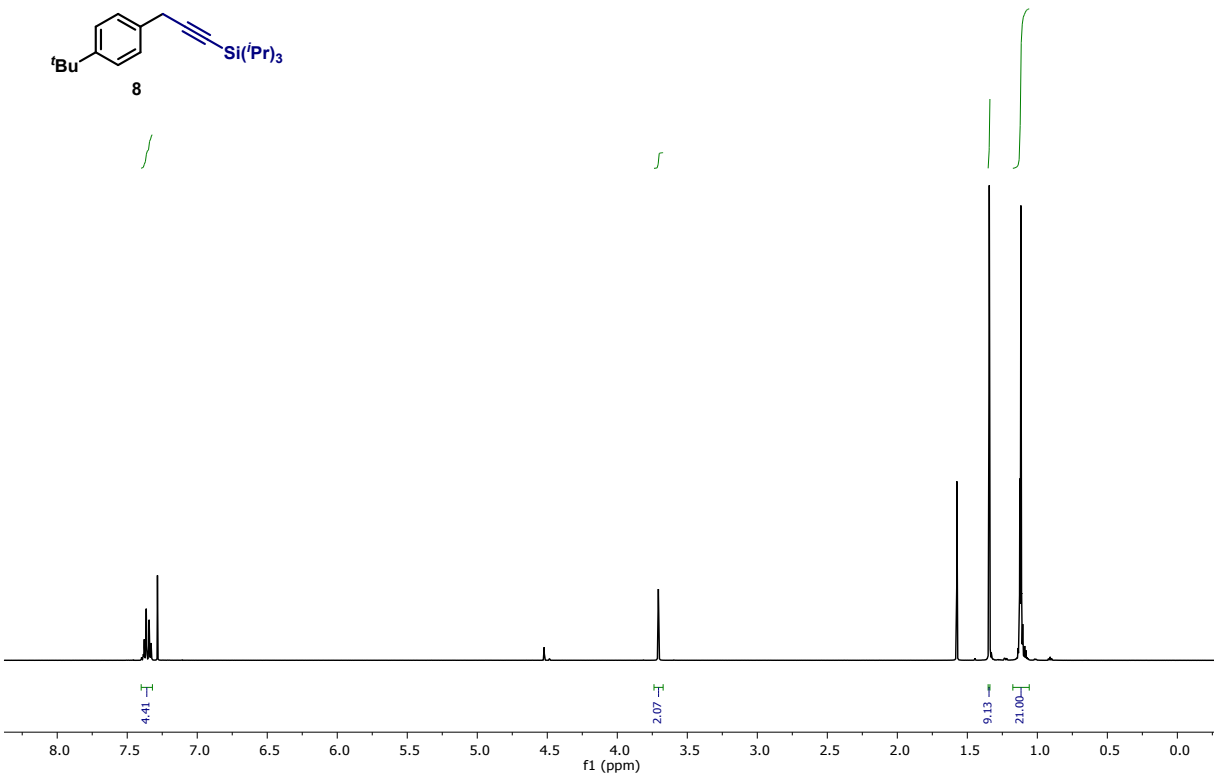
^{1}H NMR (600 MHz, $CDCl_3$)



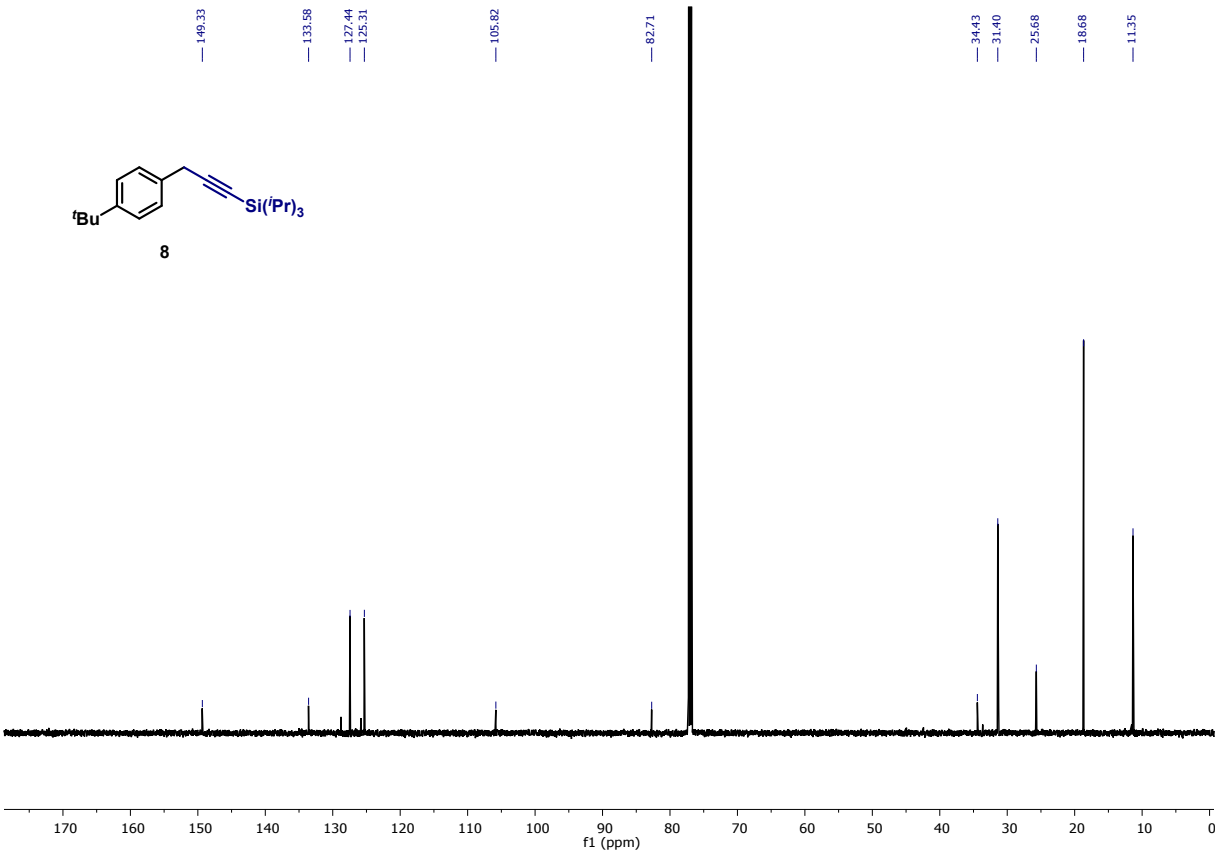
^{13}C NMR (151 MHz, $CDCl_3$)



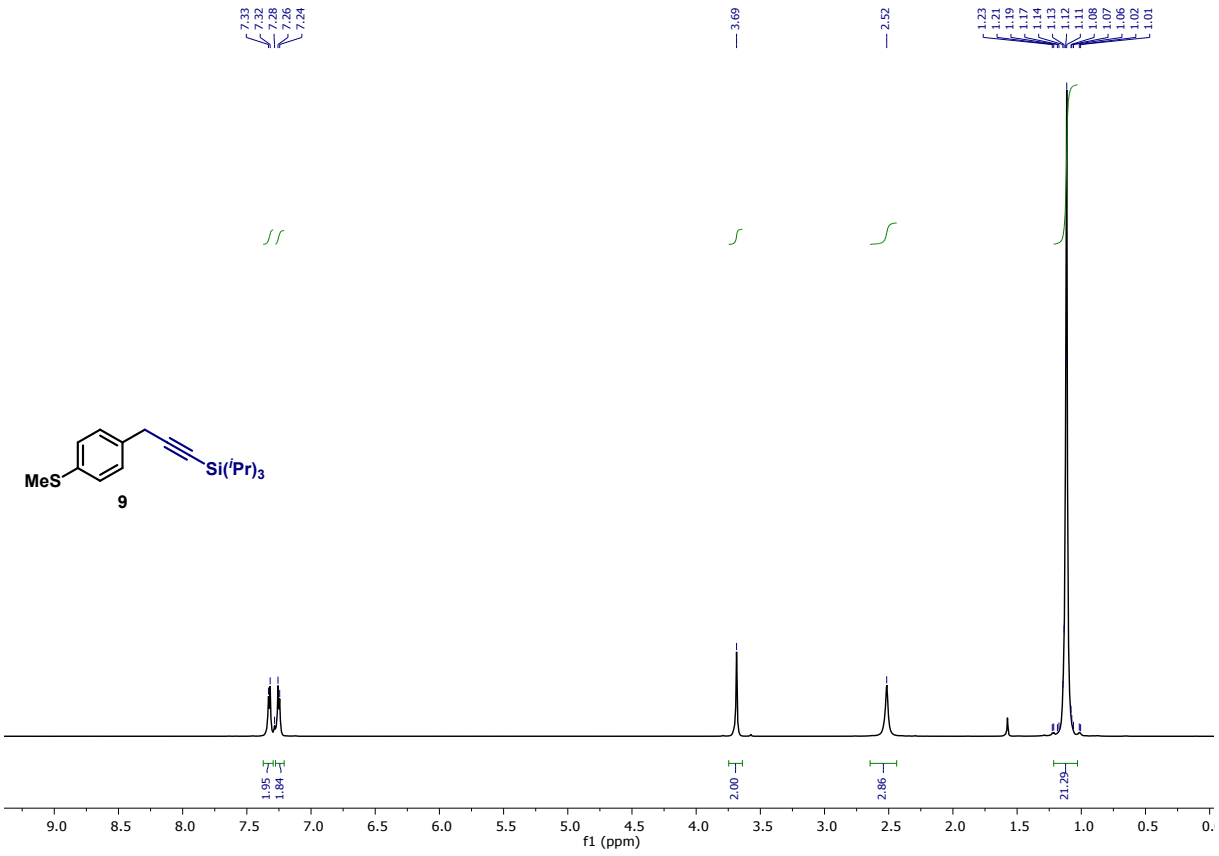
^{1}H NMR (500 MHz, $CDCl_3$)



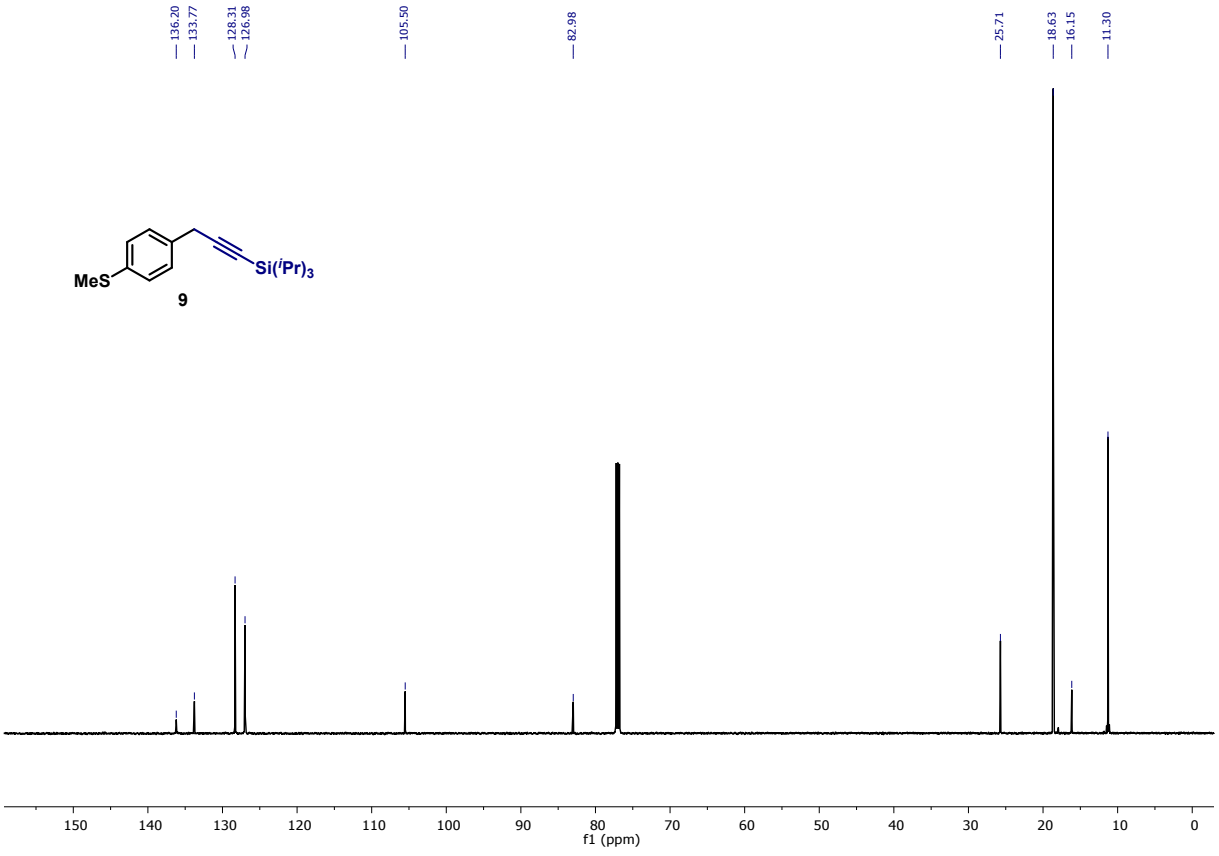
^{13}C NMR (151 MHz, $CDCl_3$)



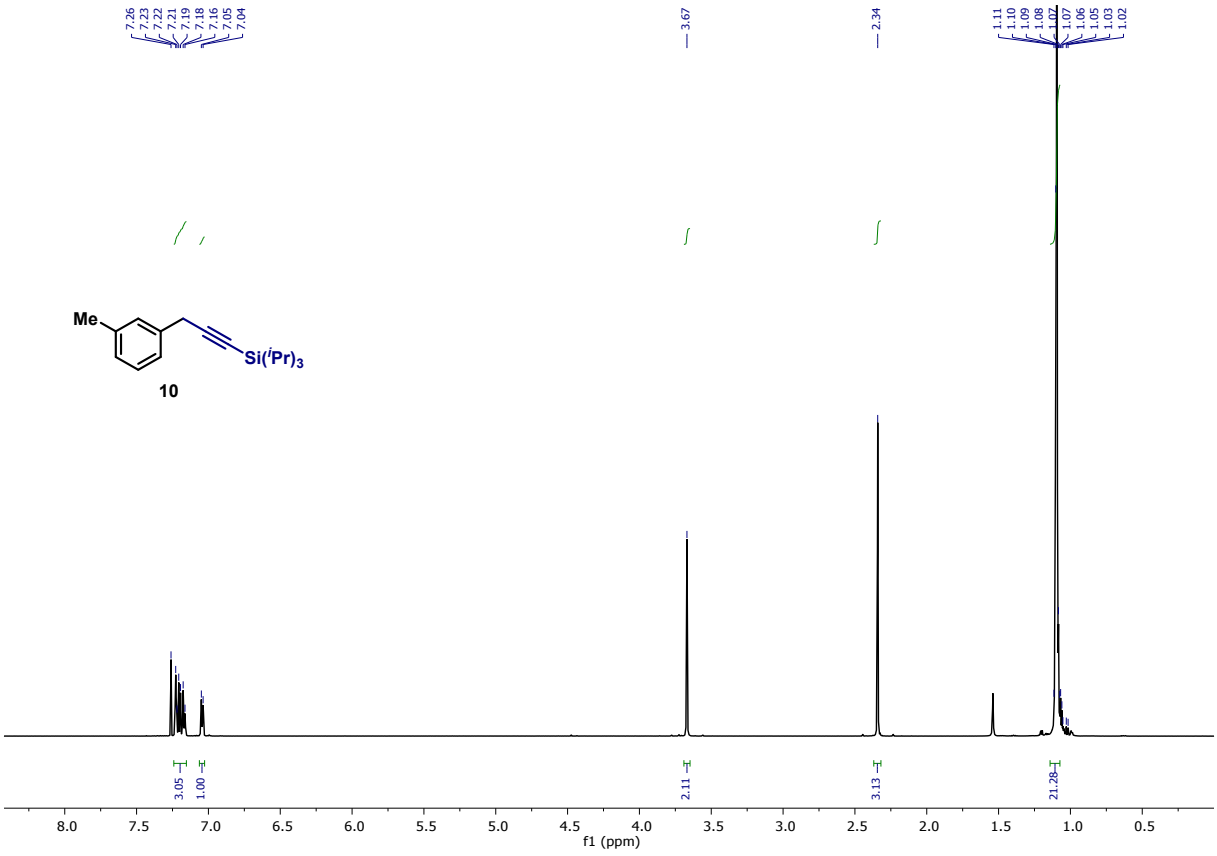
^{1}H NMR (600 MHz, $CDCl_3$)



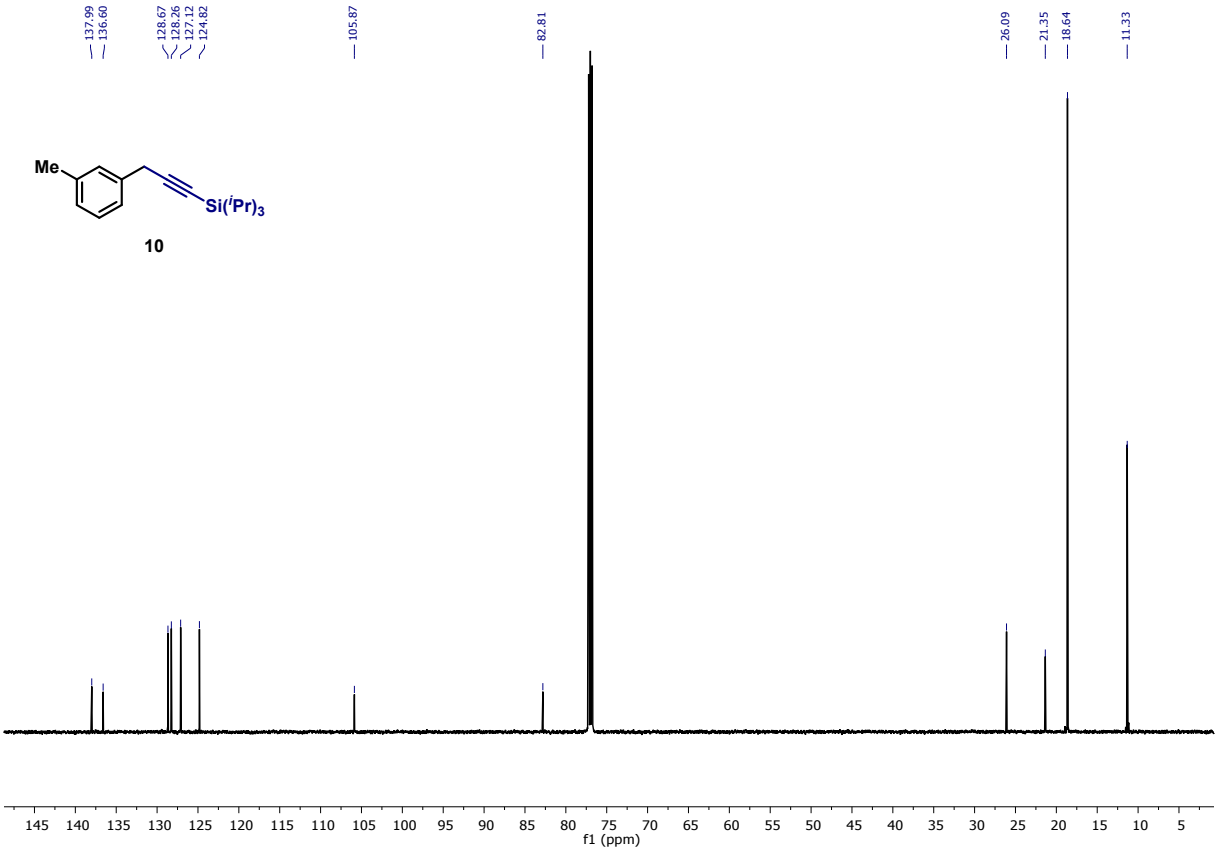
^{13}C NMR (151 MHz, $CDCl_3$)



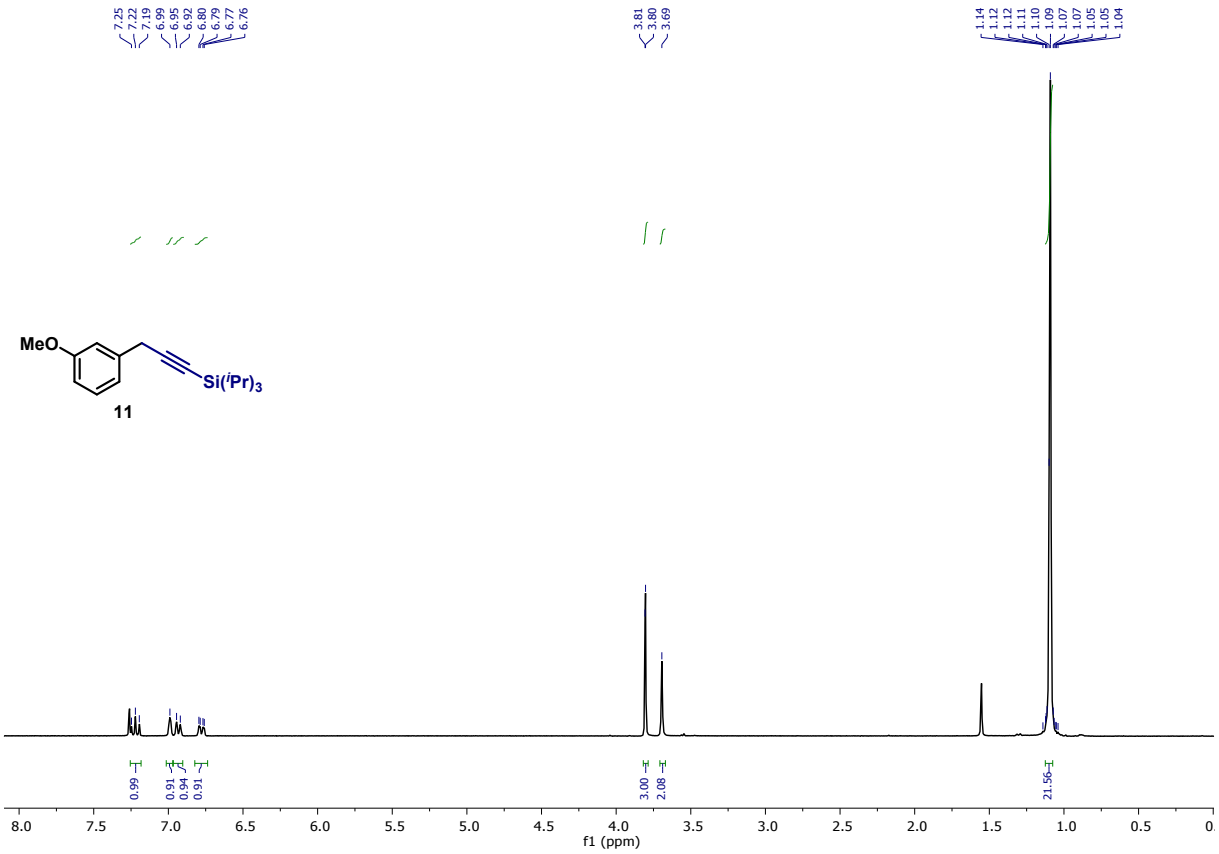
^{1}H NMR (600 MHz, $CDCl_3$)



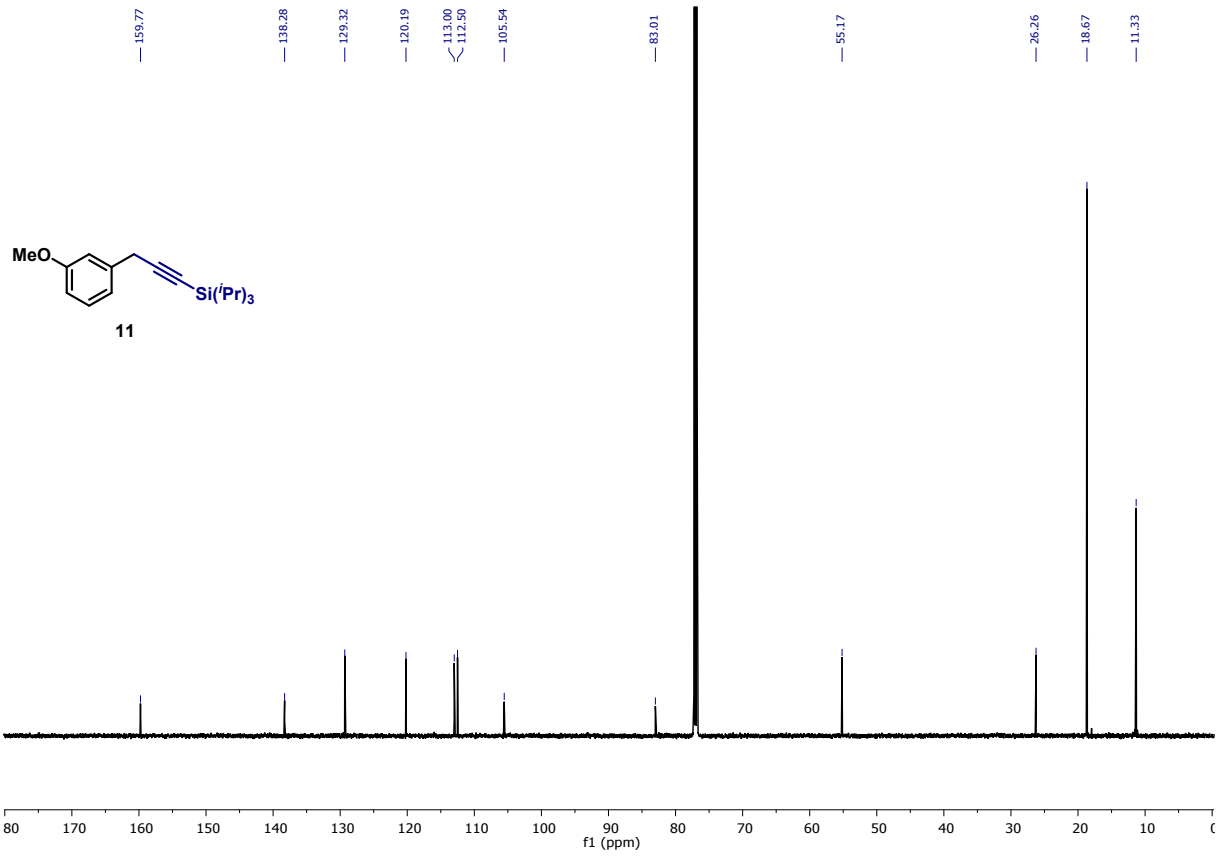
^{13}C NMR (151 MHz, $CDCl_3$)



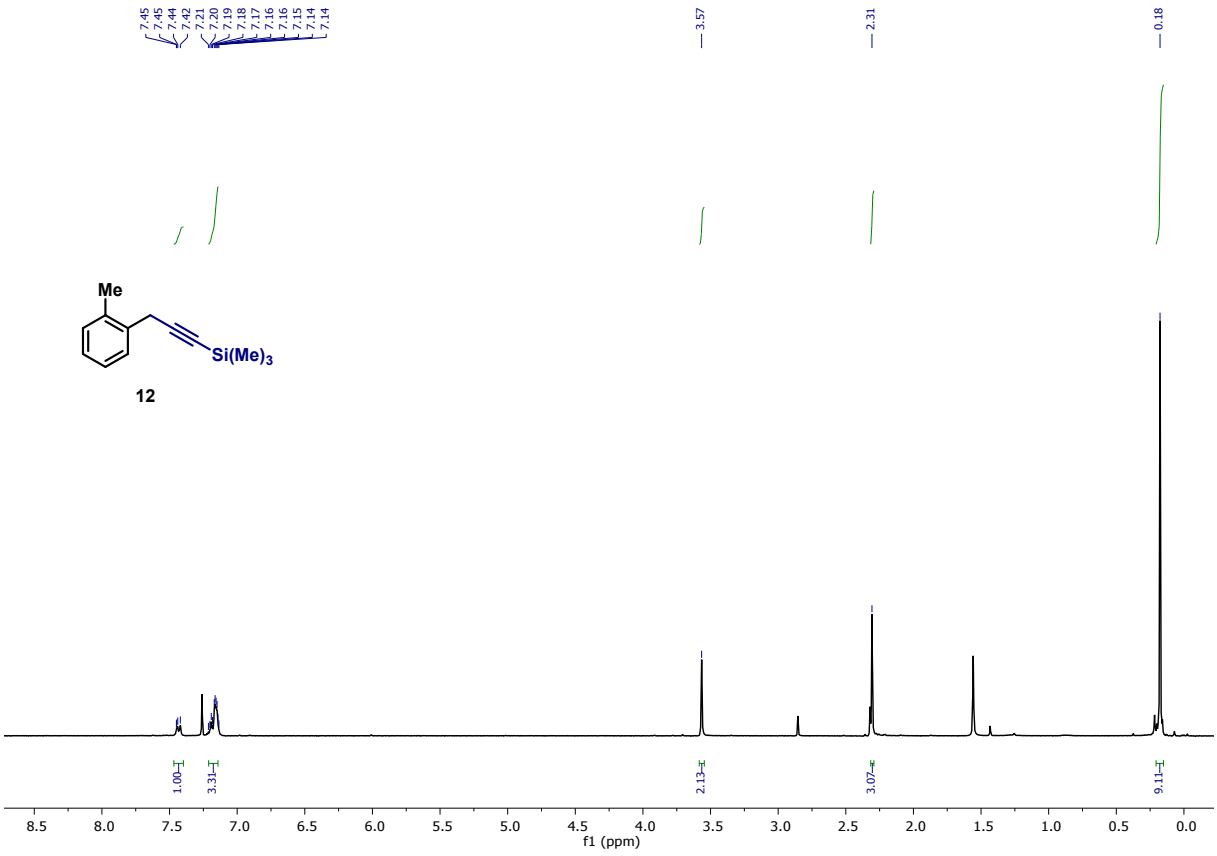
^{1}H NMR (300 MHz, $CDCl_3$)



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

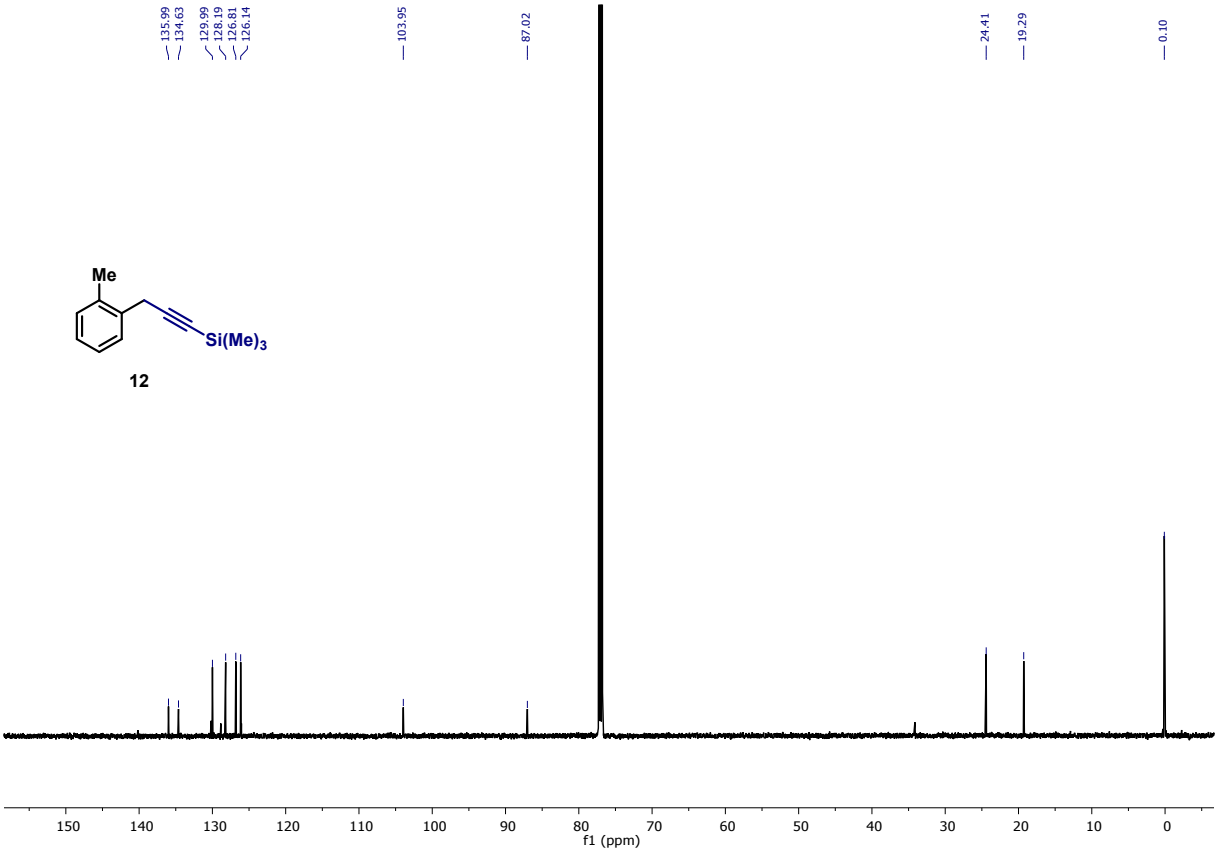


^{1}H NMR (300 MHz, $CDCl_3$)



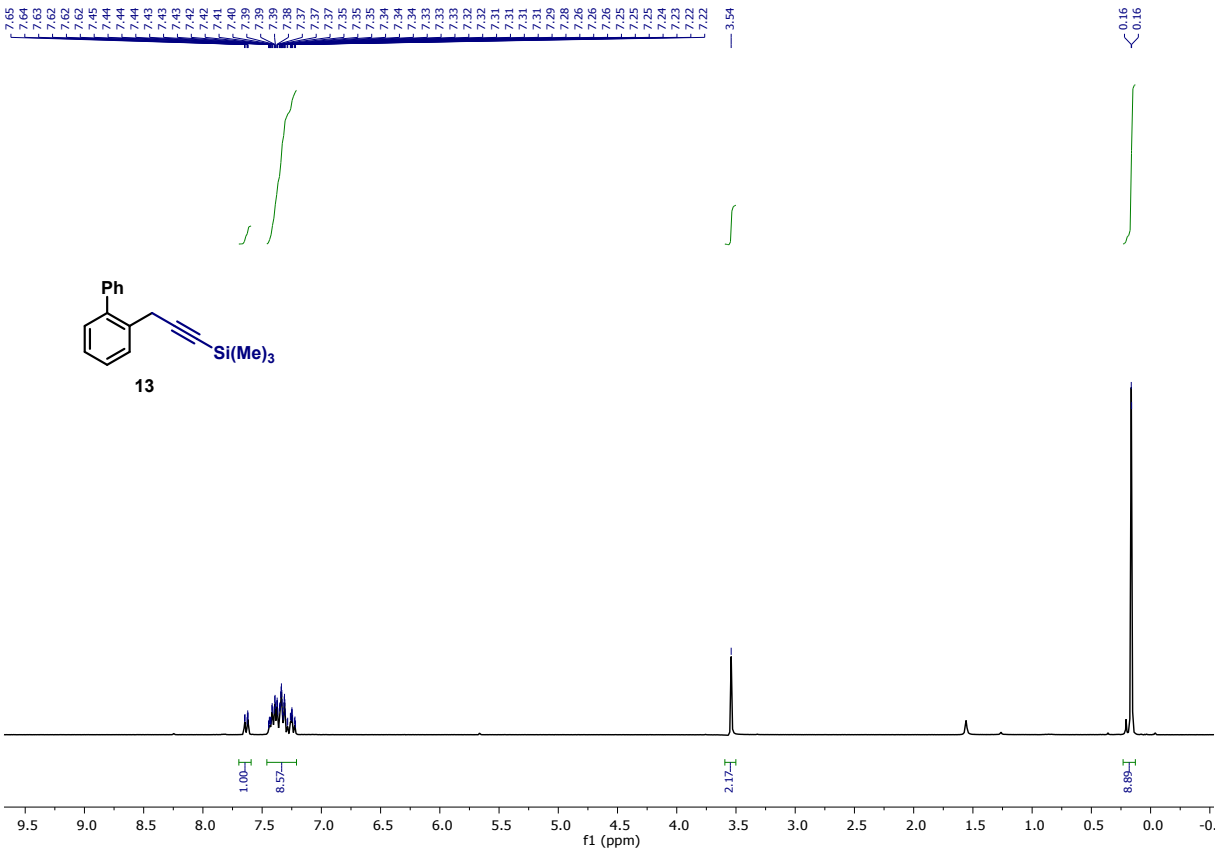
12

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

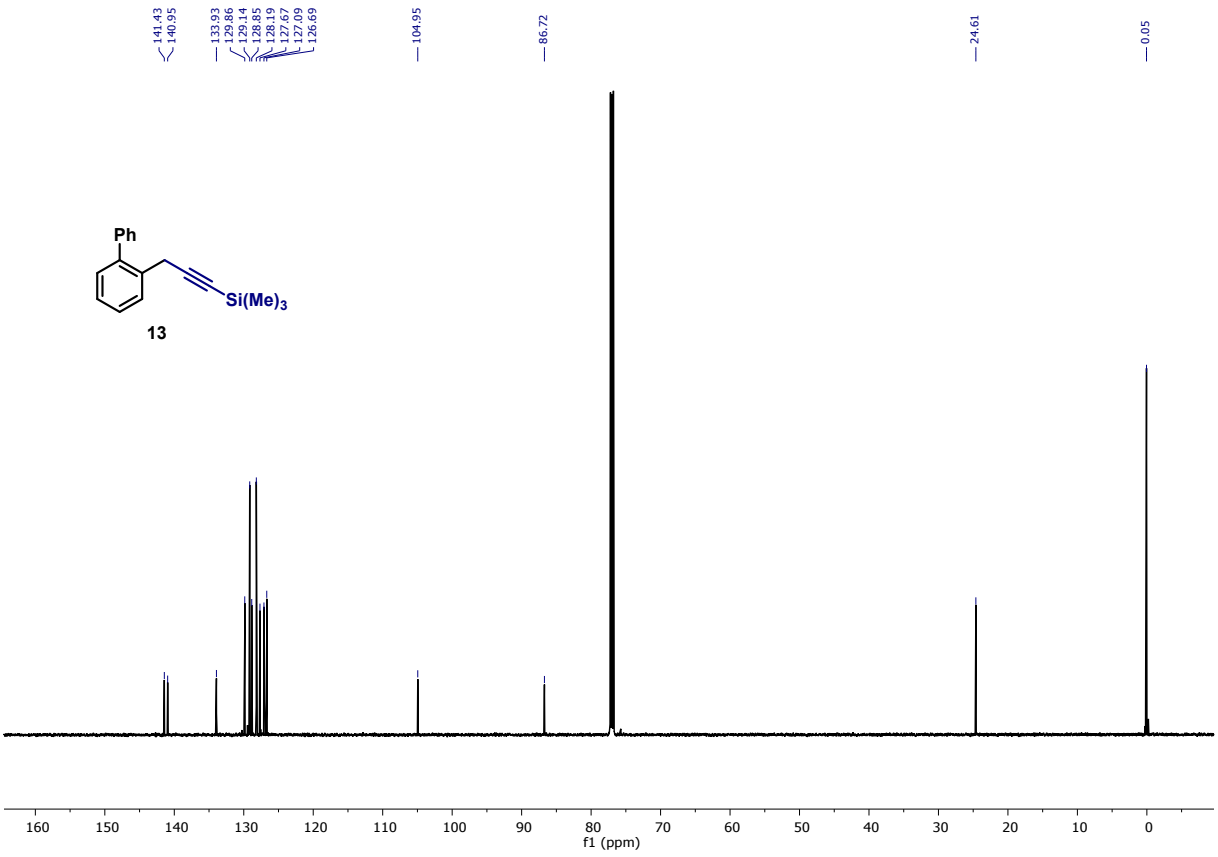


12

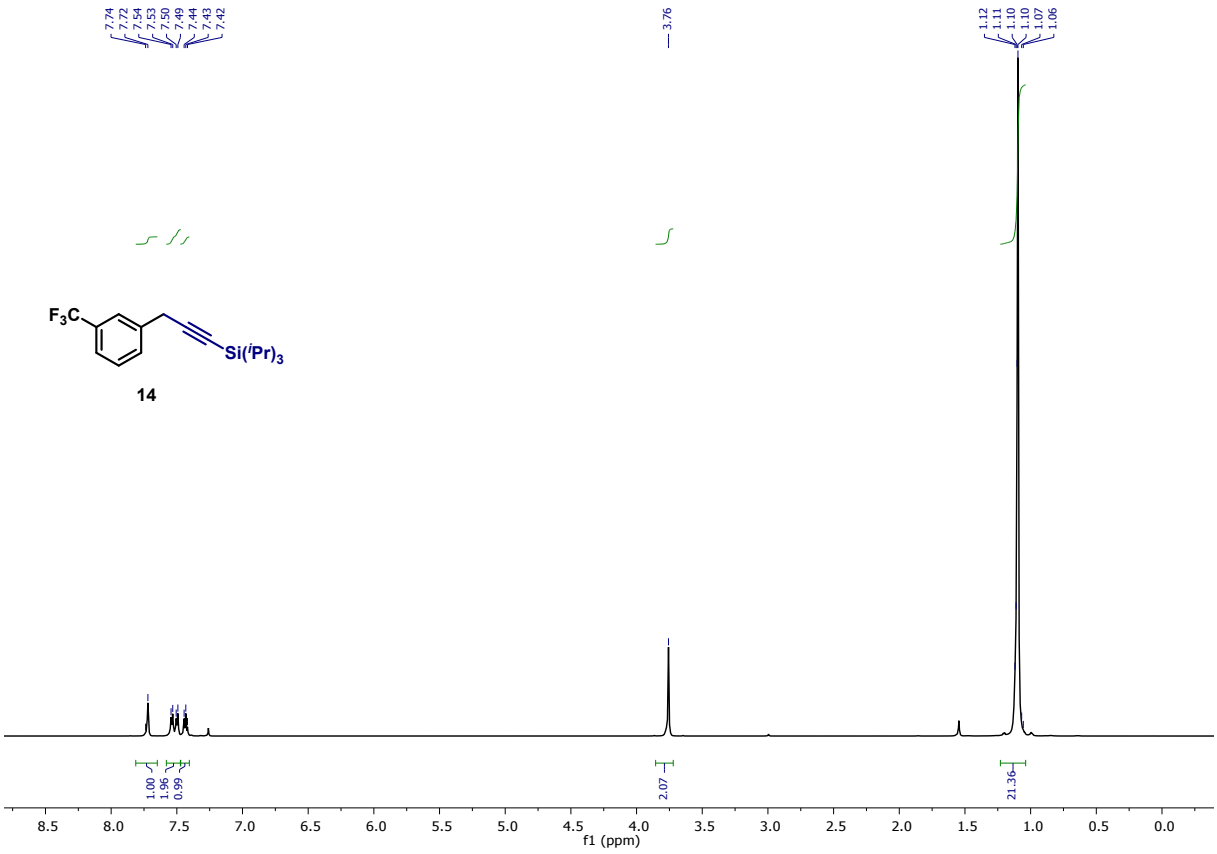
^{1}H NMR (300 MHz, $CDCl_3$)



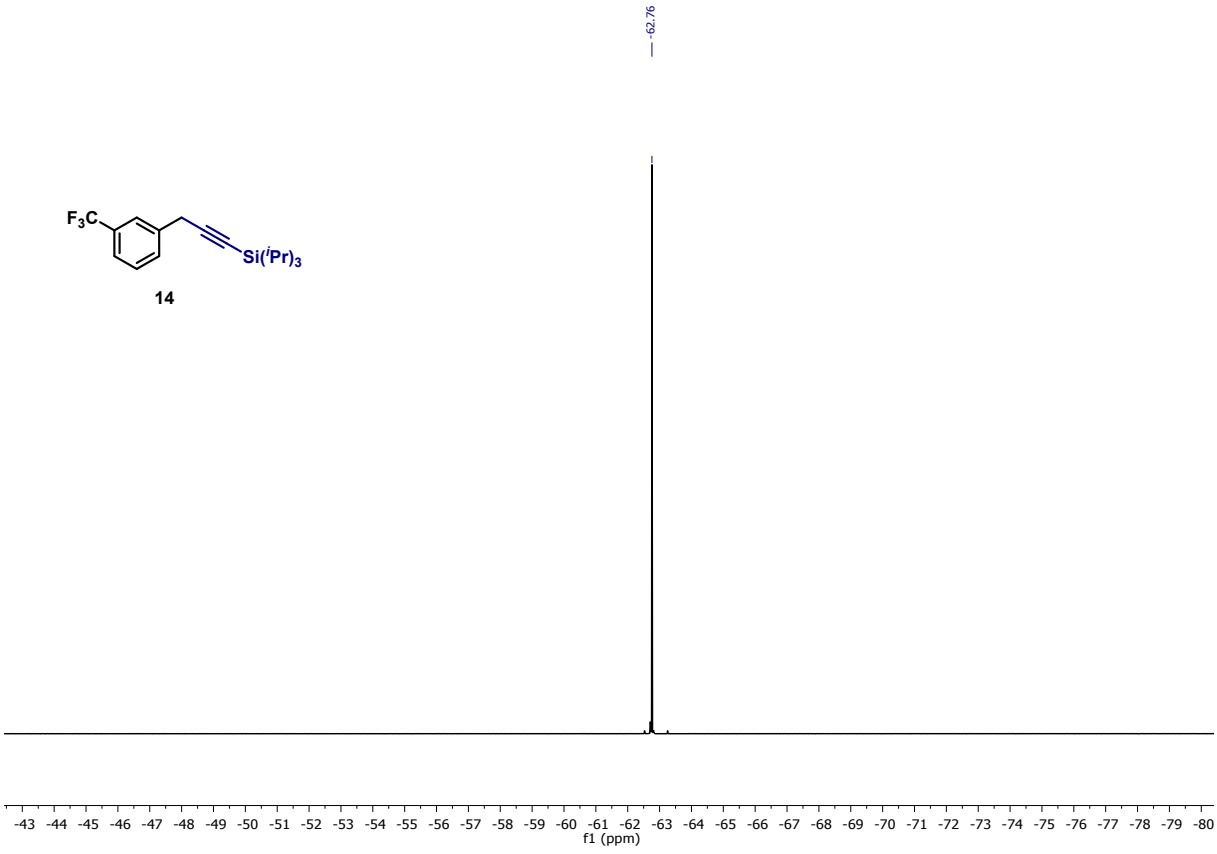
^{13}C NMR (151 MHz, $CDCl_3$)



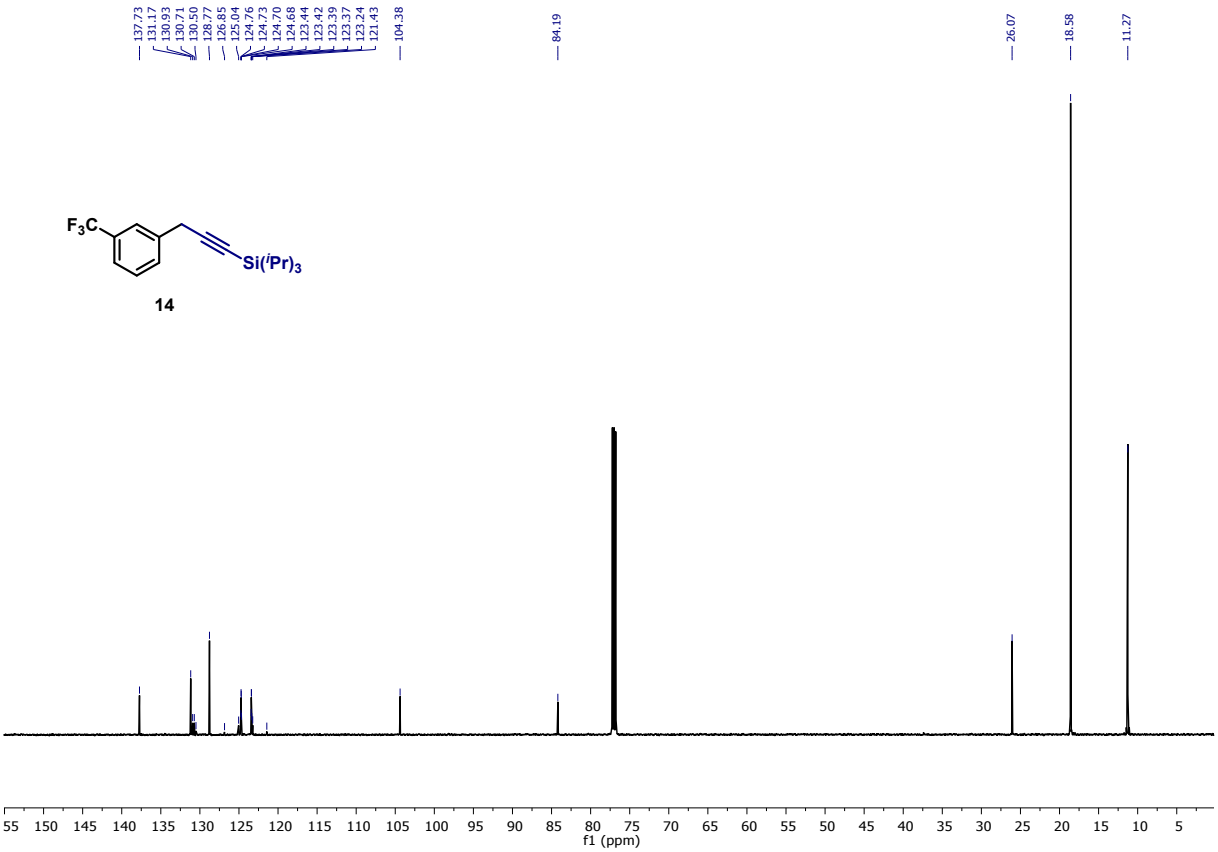
^{1}H NMR (600 MHz, $CDCl_3$)



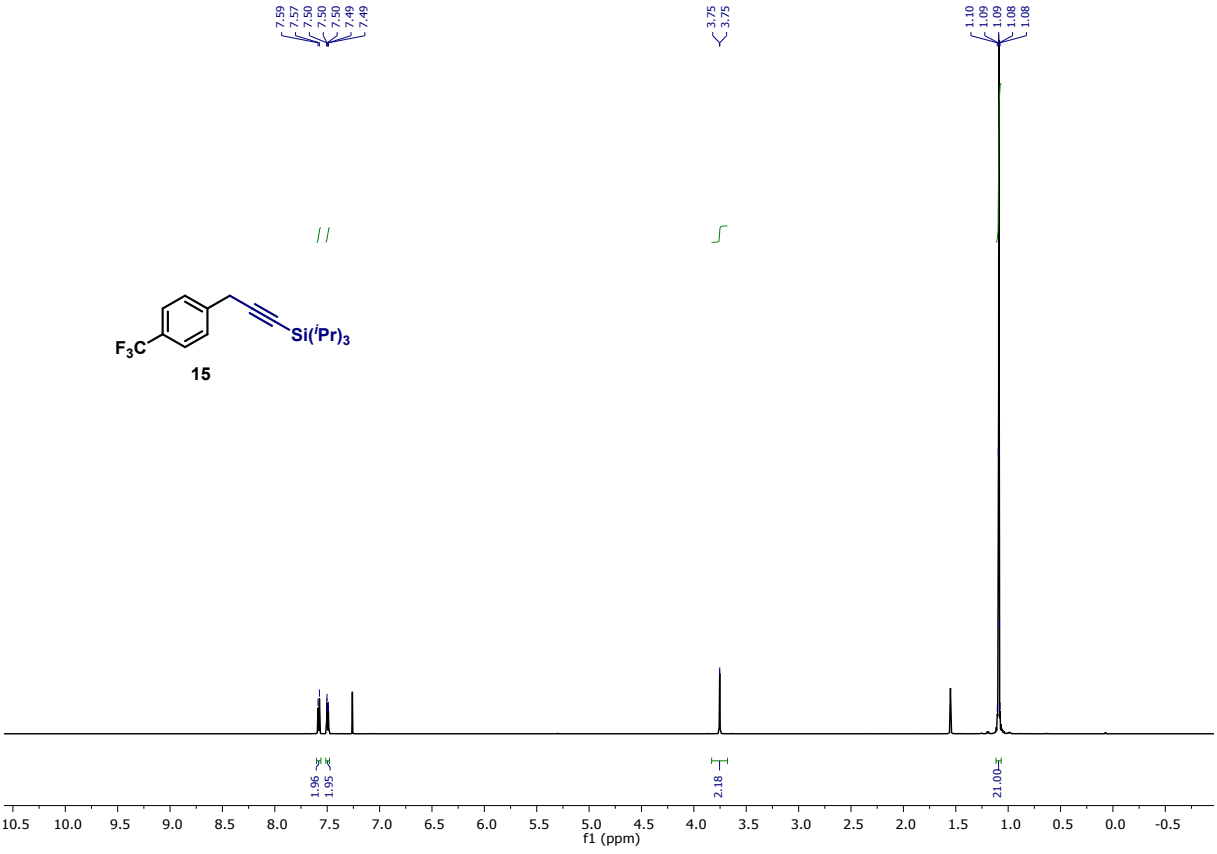
^{19}F NMR (376 MHz, $CDCl_3$)



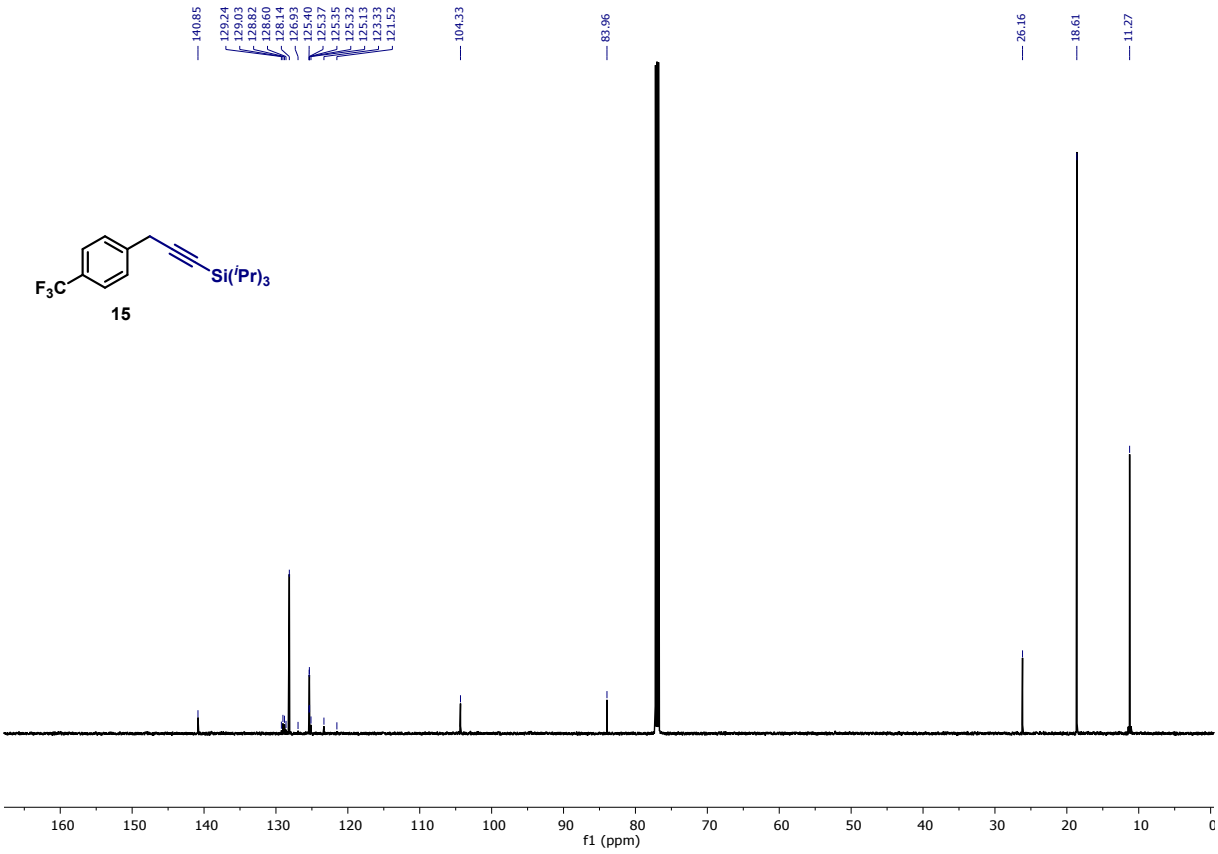
^{13}C NMR (151 MHz, $CDCl_3$)



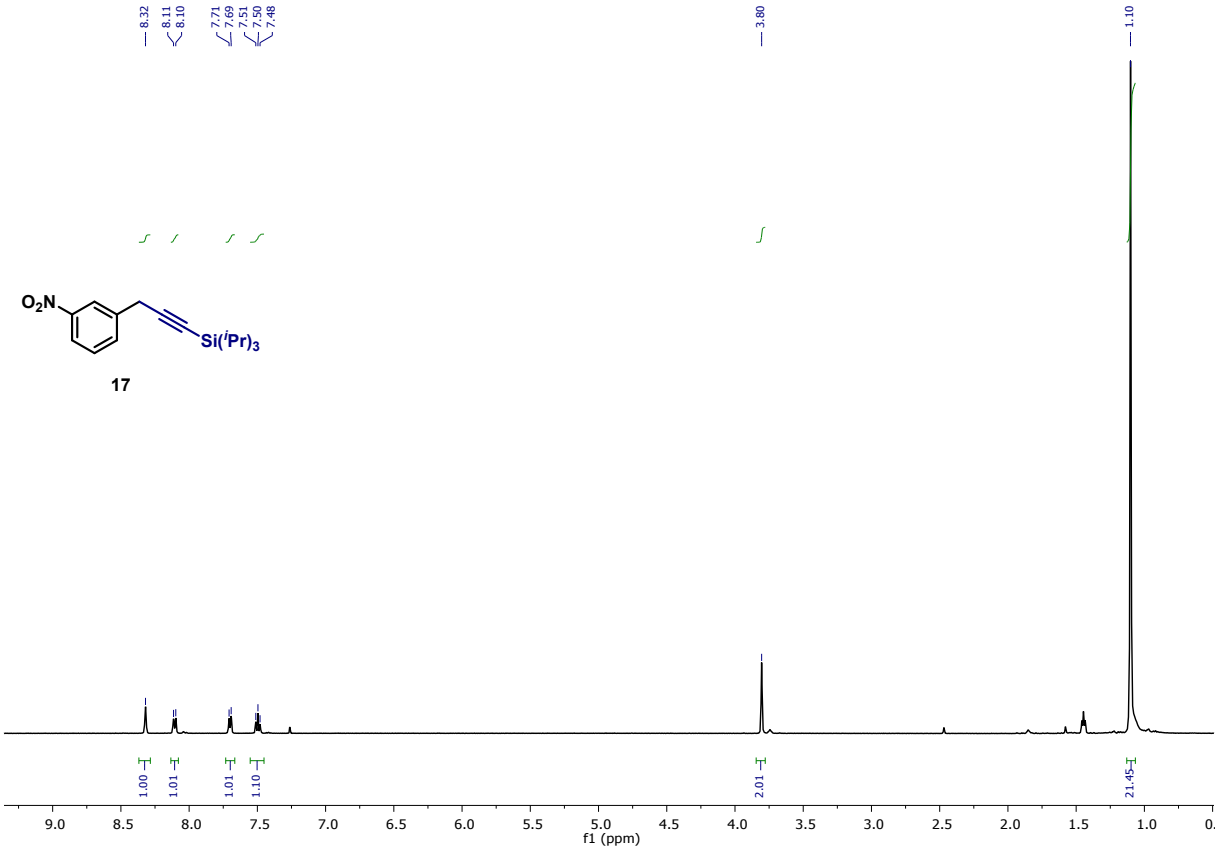
^{1}H NMR (600 MHz, $CDCl_3$)



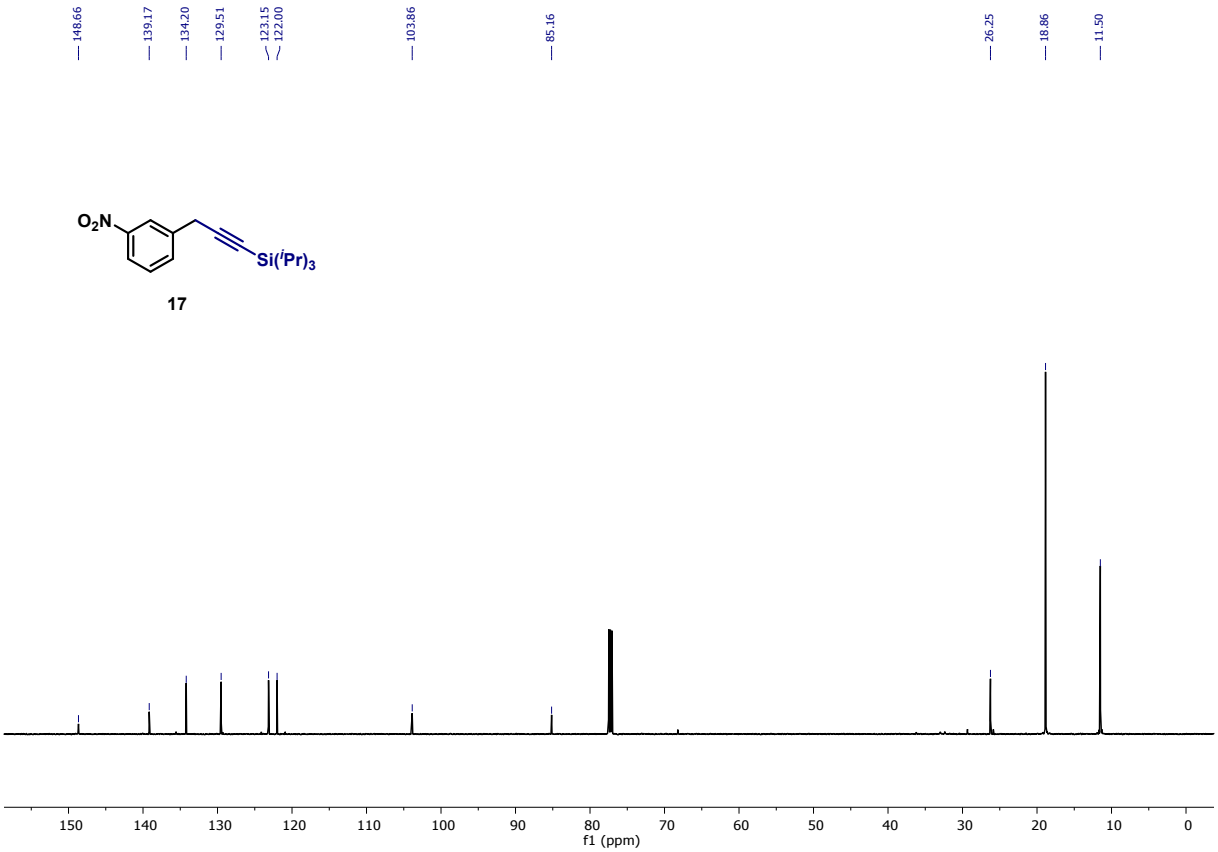
^{13}C NMR (151 MHz, $CDCl_3$)



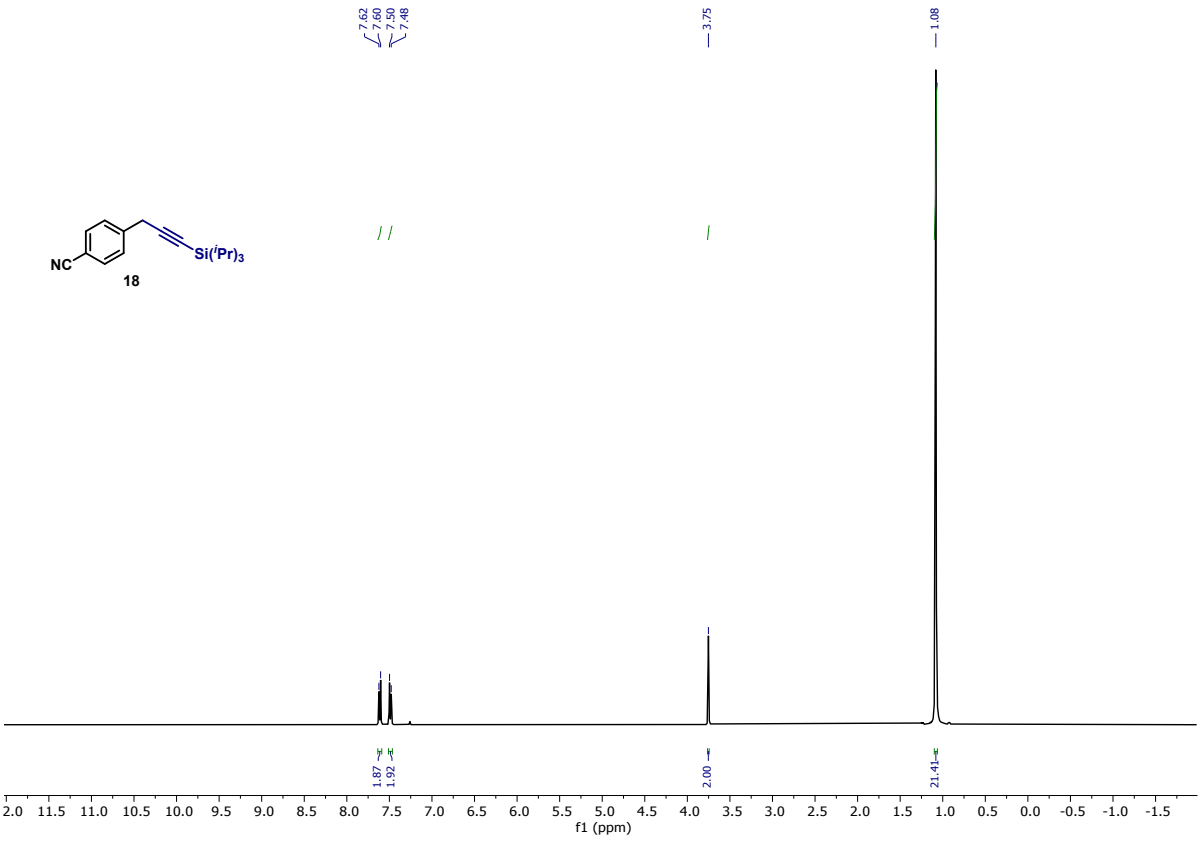
^{1}H NMR (500 MHz, $CDCl_3$)



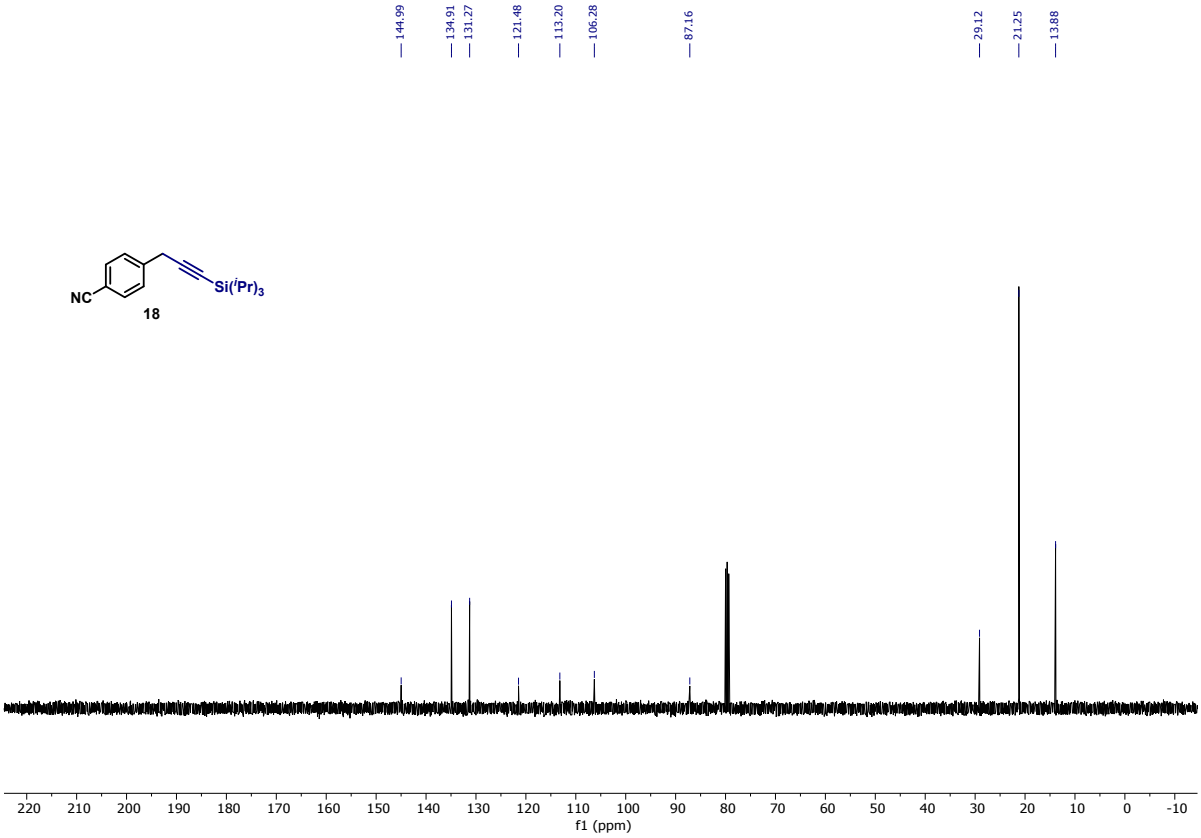
^{13}C NMR (151 MHz, $CDCl_3$)



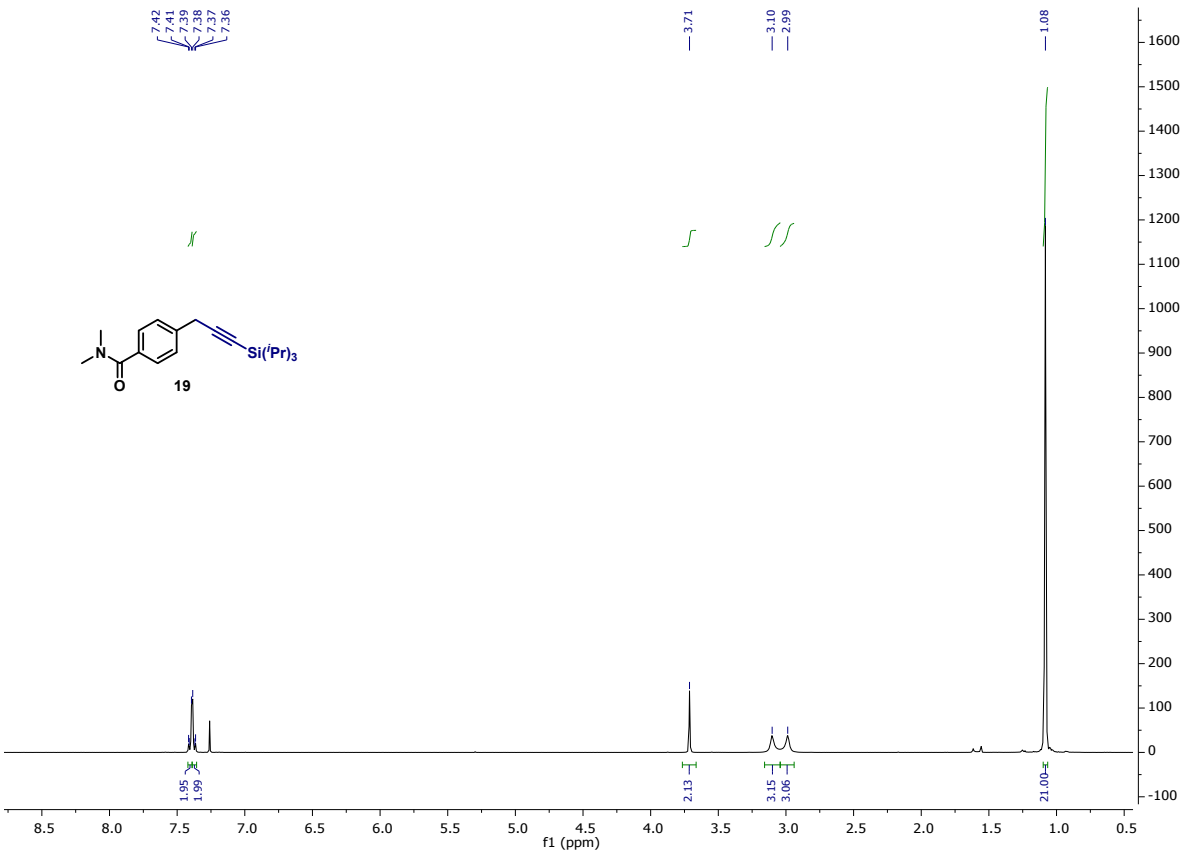
^{1}H NMR (400 MHz, $CDCl_3$)



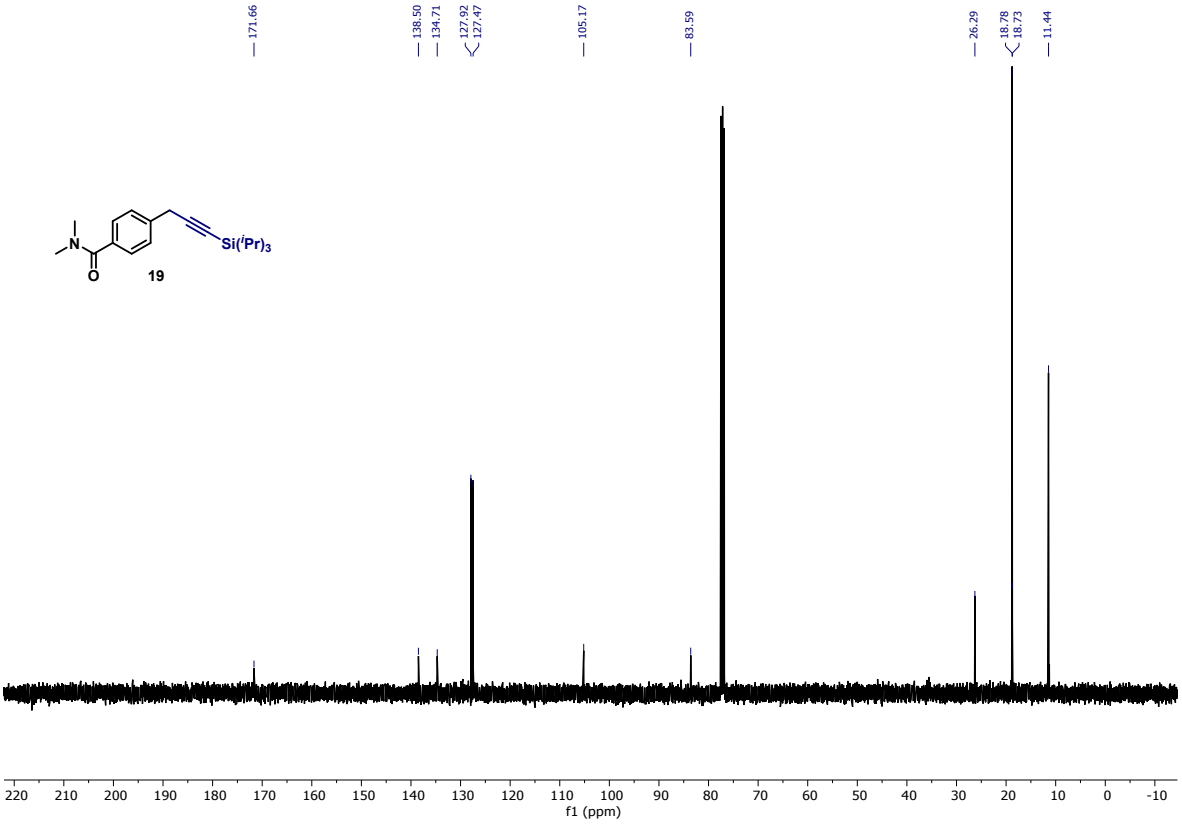
^{13}C NMR (101 MHz, $CDCl_3$)



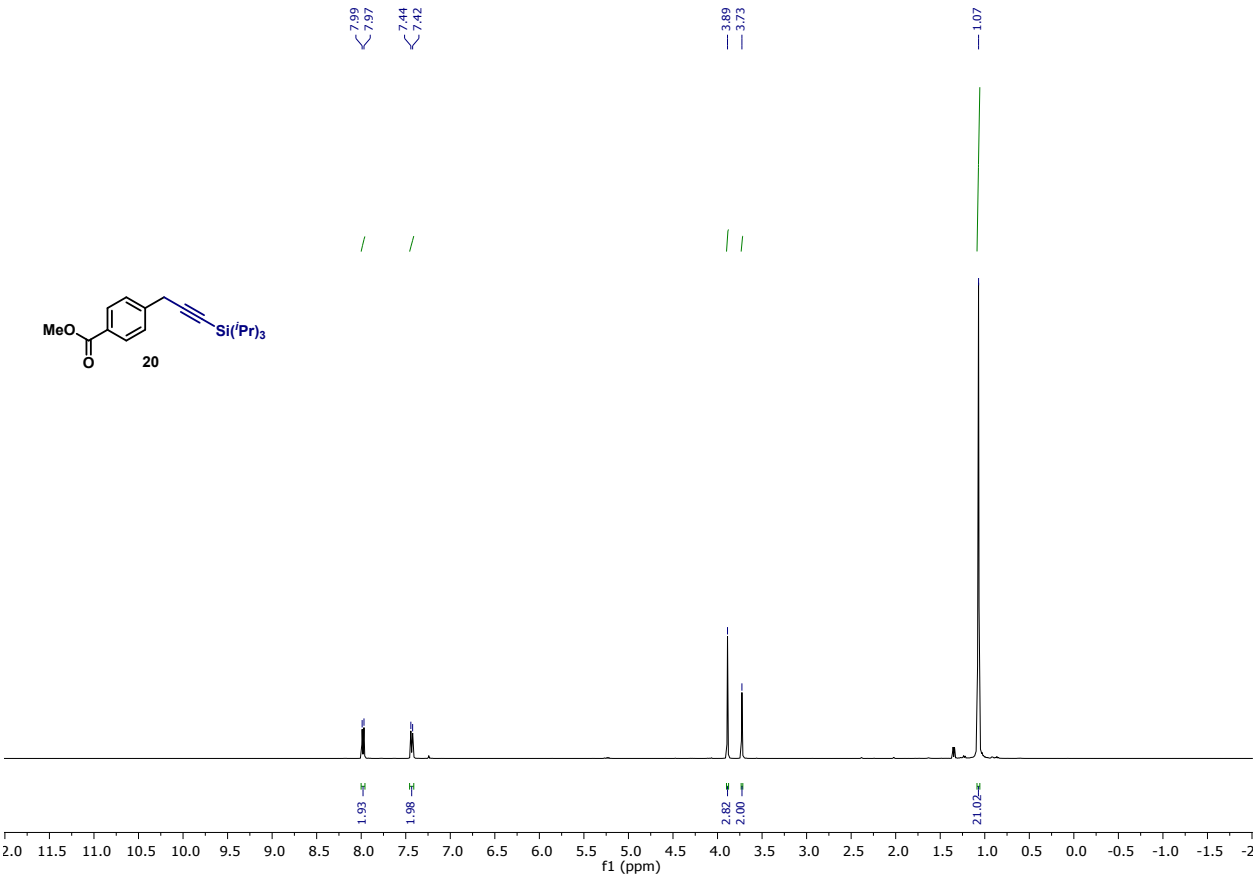
^{1}H NMR (400 MHz, $CDCl_3$)



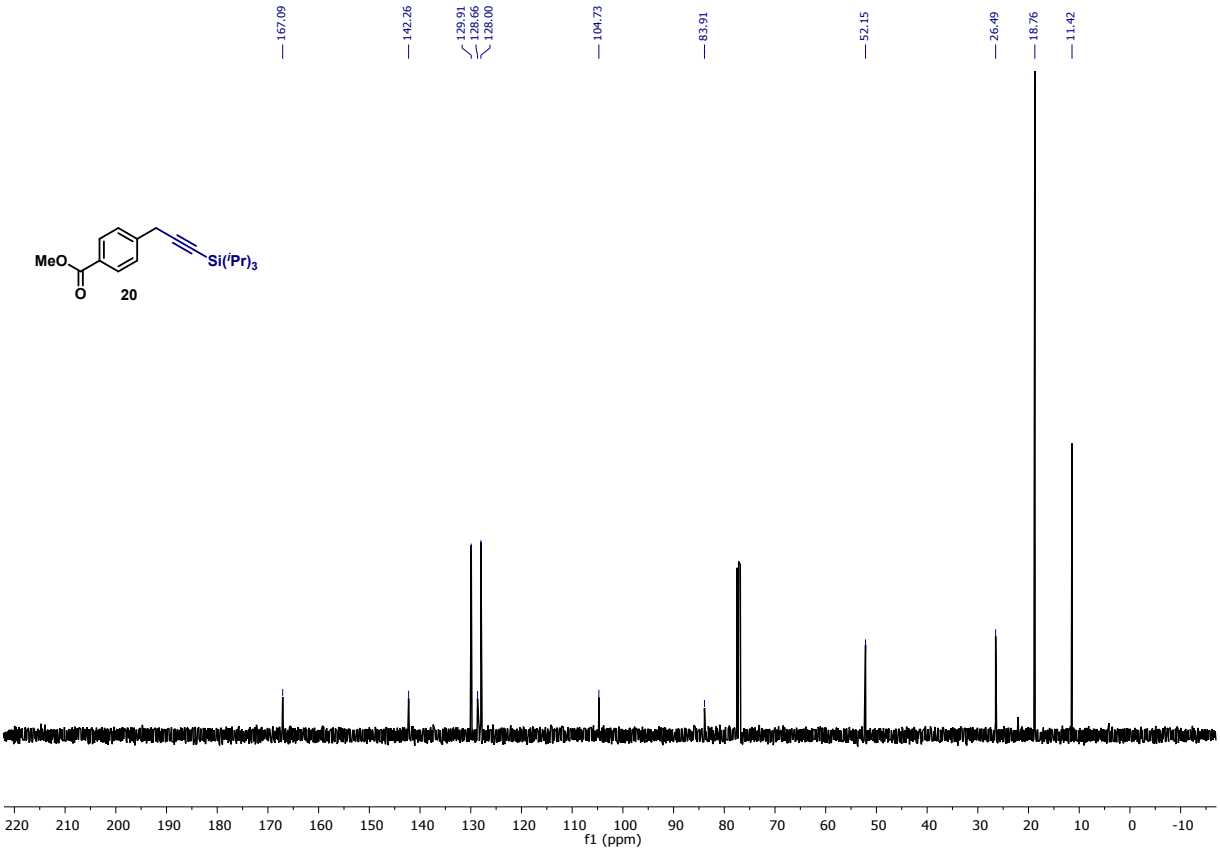
^{13}C NMR (101 MHz, $CDCl_3$)



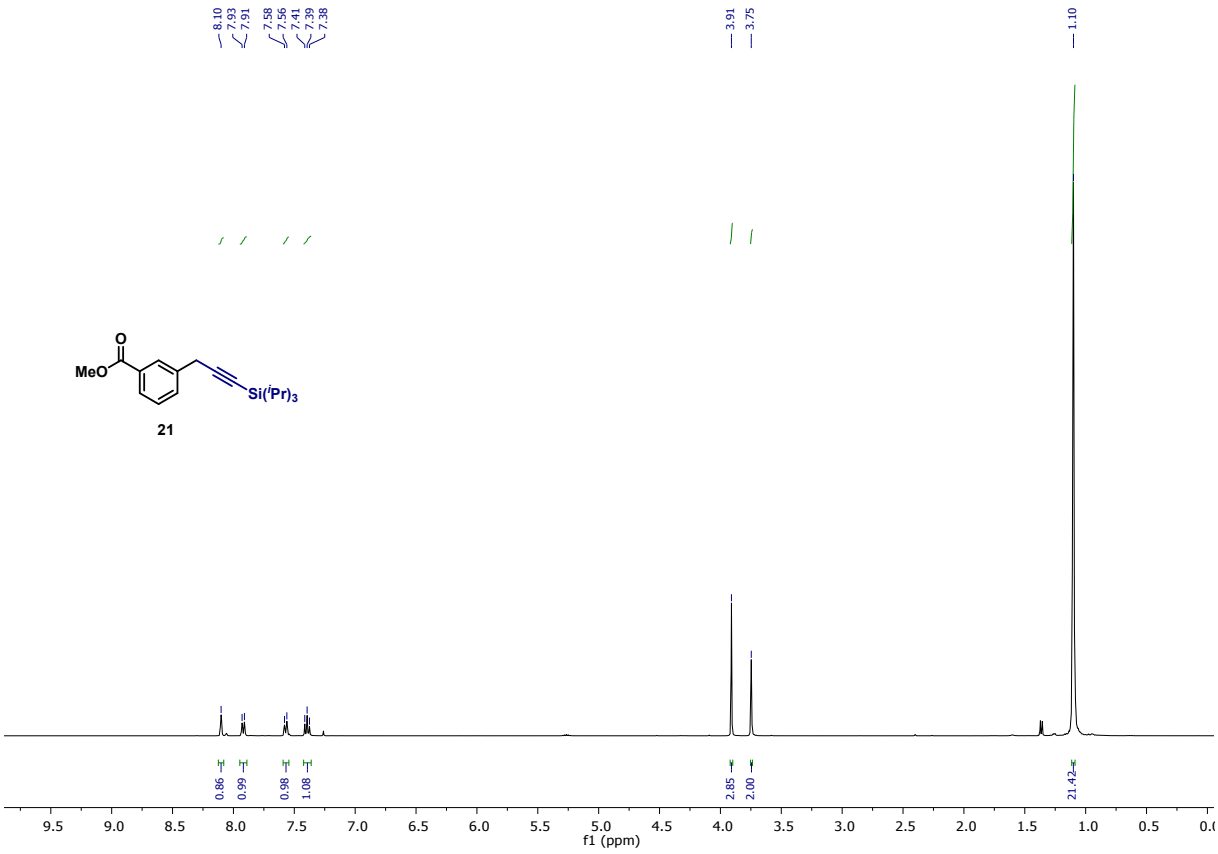
^{1}H NMR (400 MHz, $CDCl_3$)



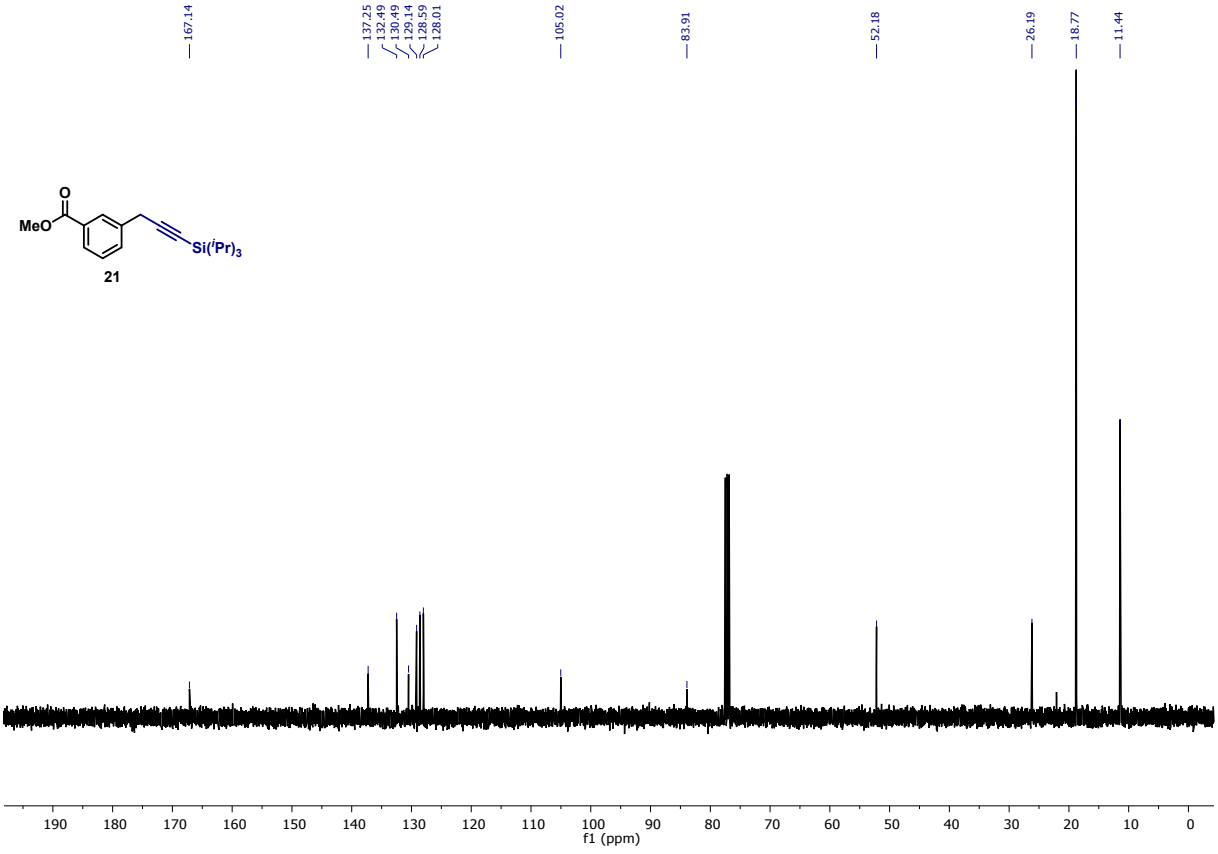
^{13}C NMR (101 MHz, $CDCl_3$)



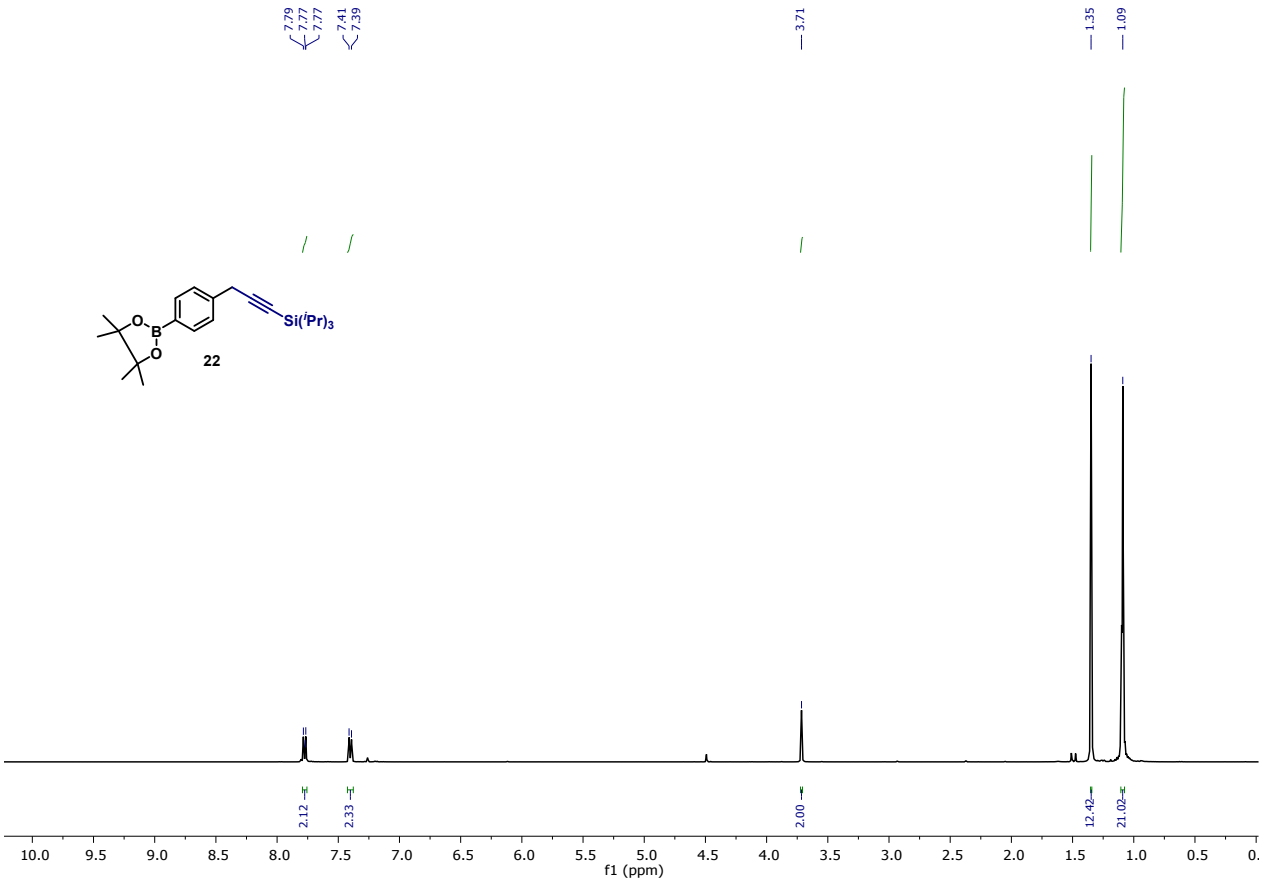
^{1}H NMR (400 MHz, $CDCl_3$)



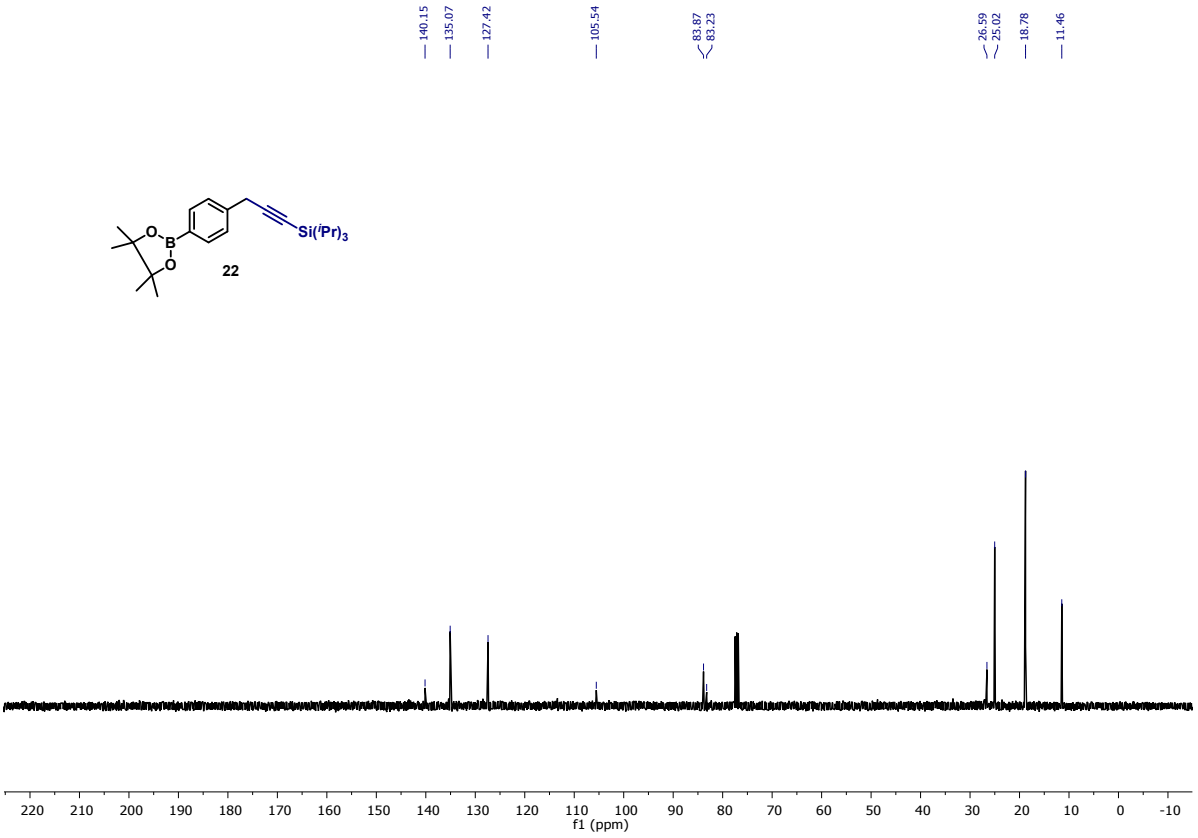
^{13}C NMR (101 MHz, $CDCl_3$)



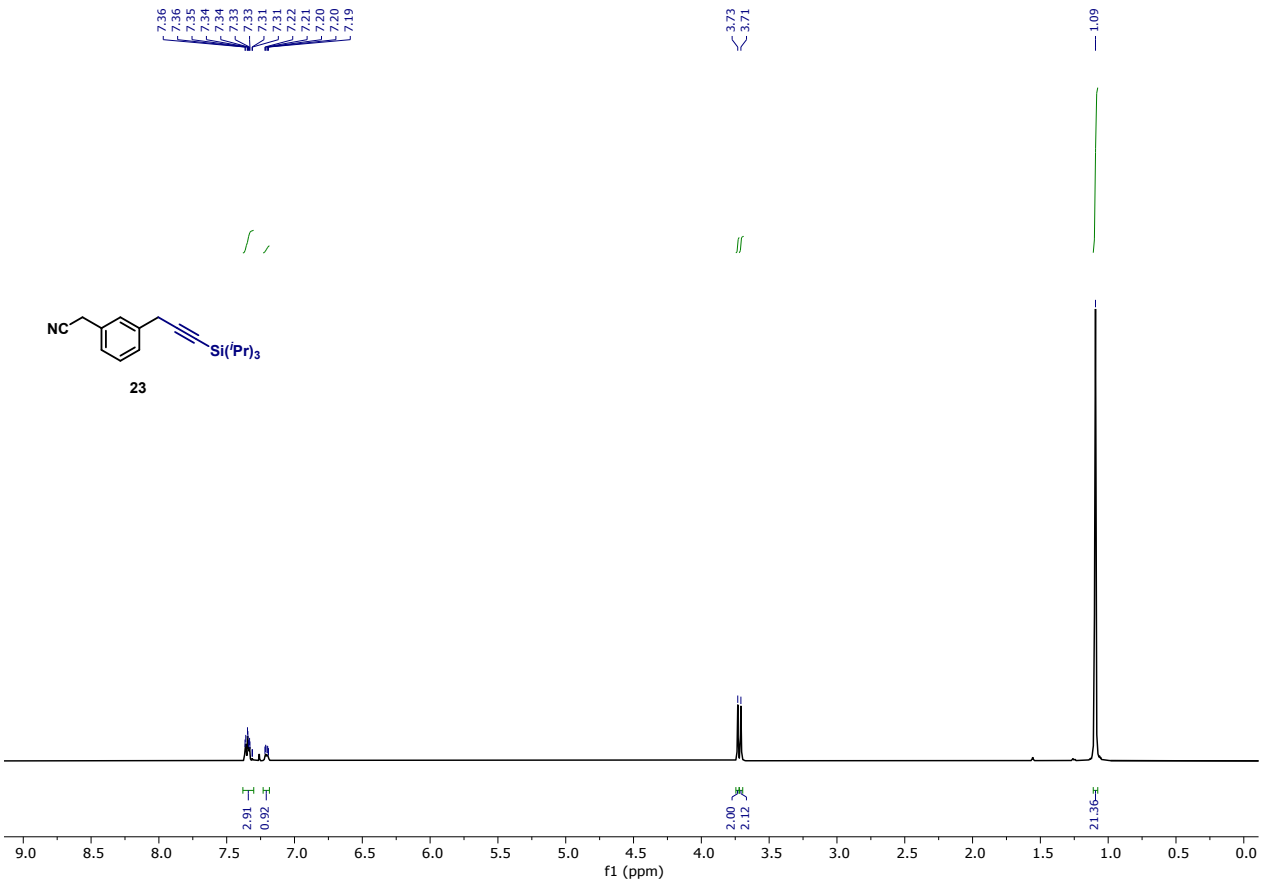
^{1}H NMR (400 MHz, $CDCl_3$)



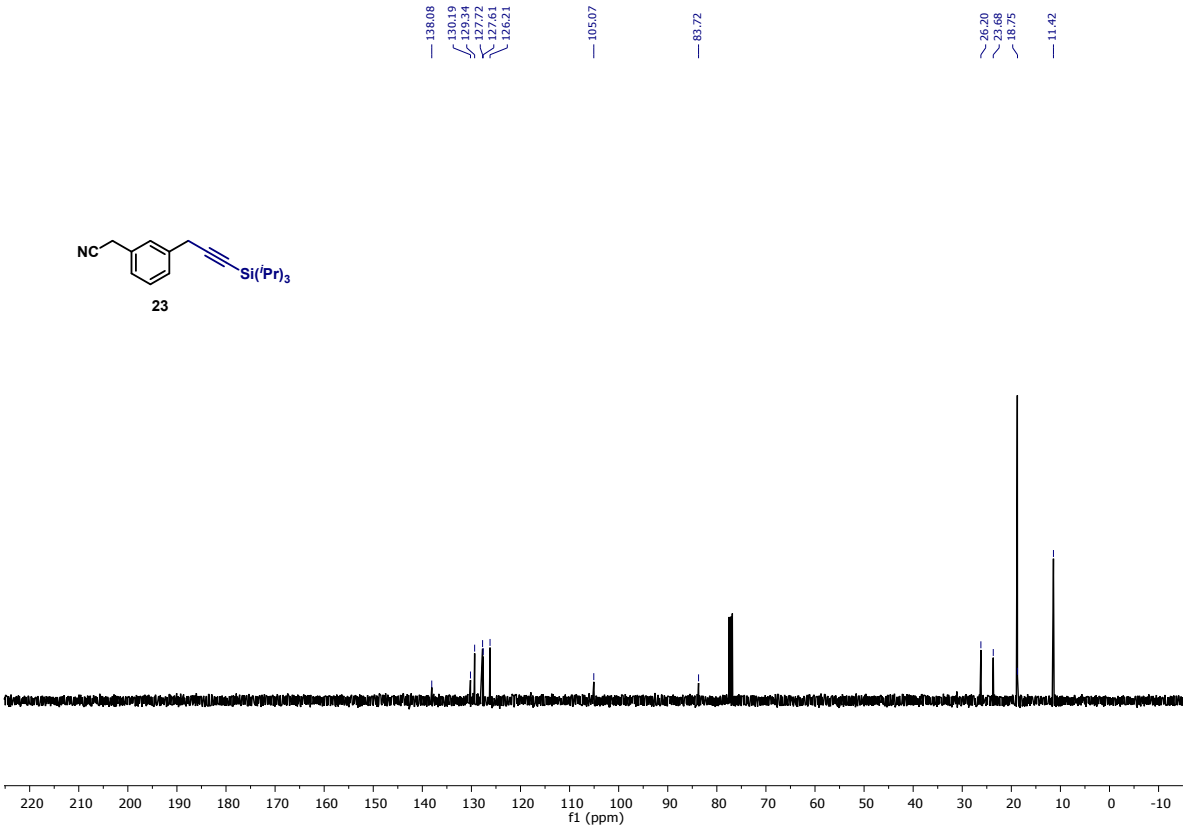
^{13}C NMR (101 MHz, $CDCl_3$)



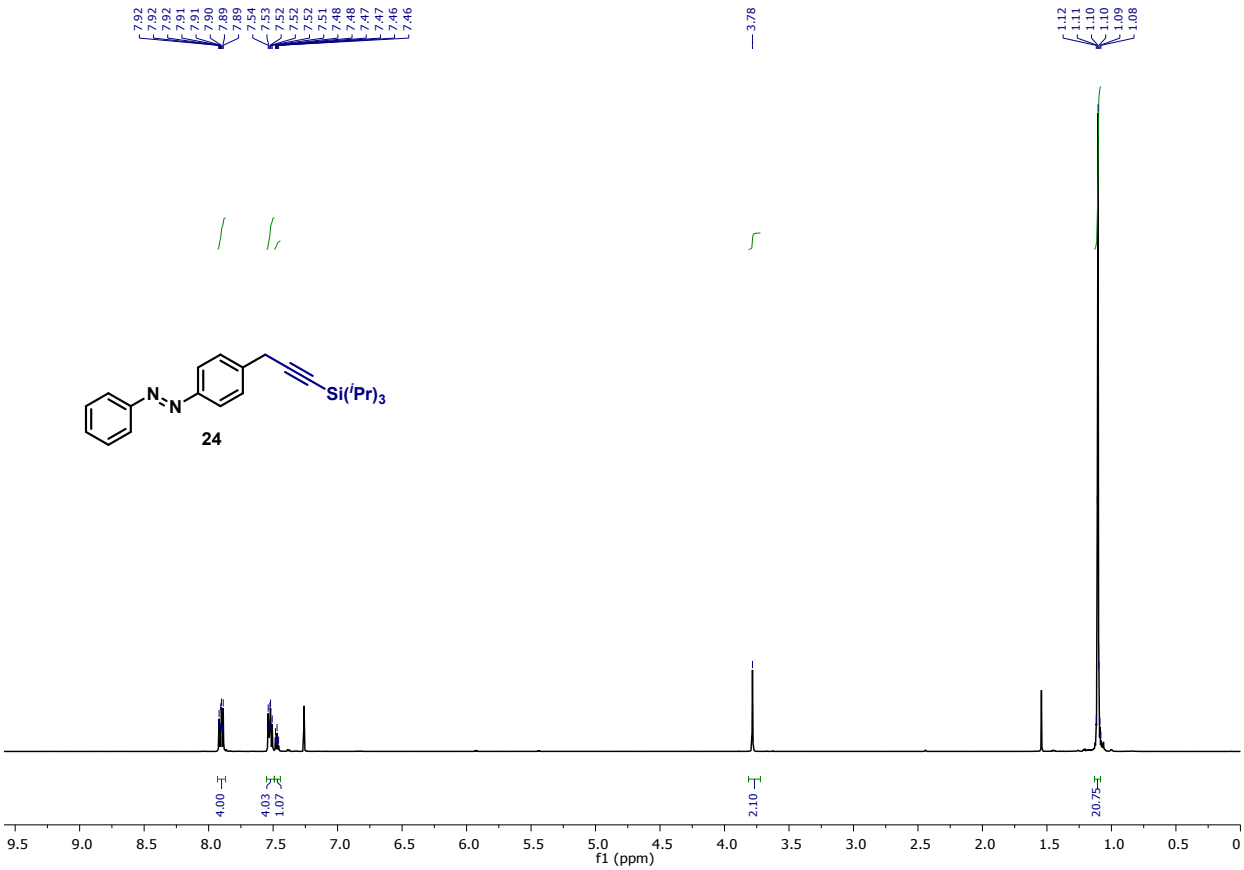
^{1}H NMR (400 MHz, $CDCl_3$)



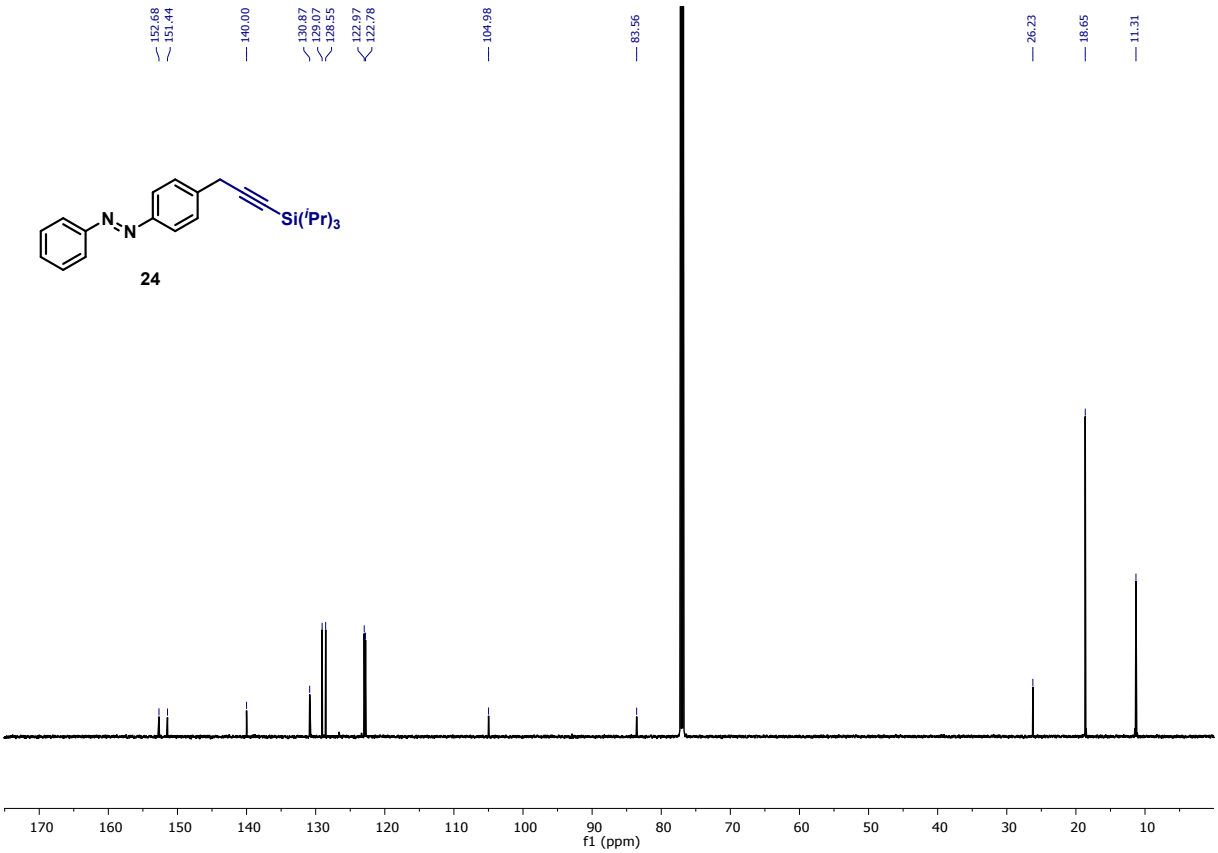
^{13}C NMR (101 MHz, $CDCl_3$)



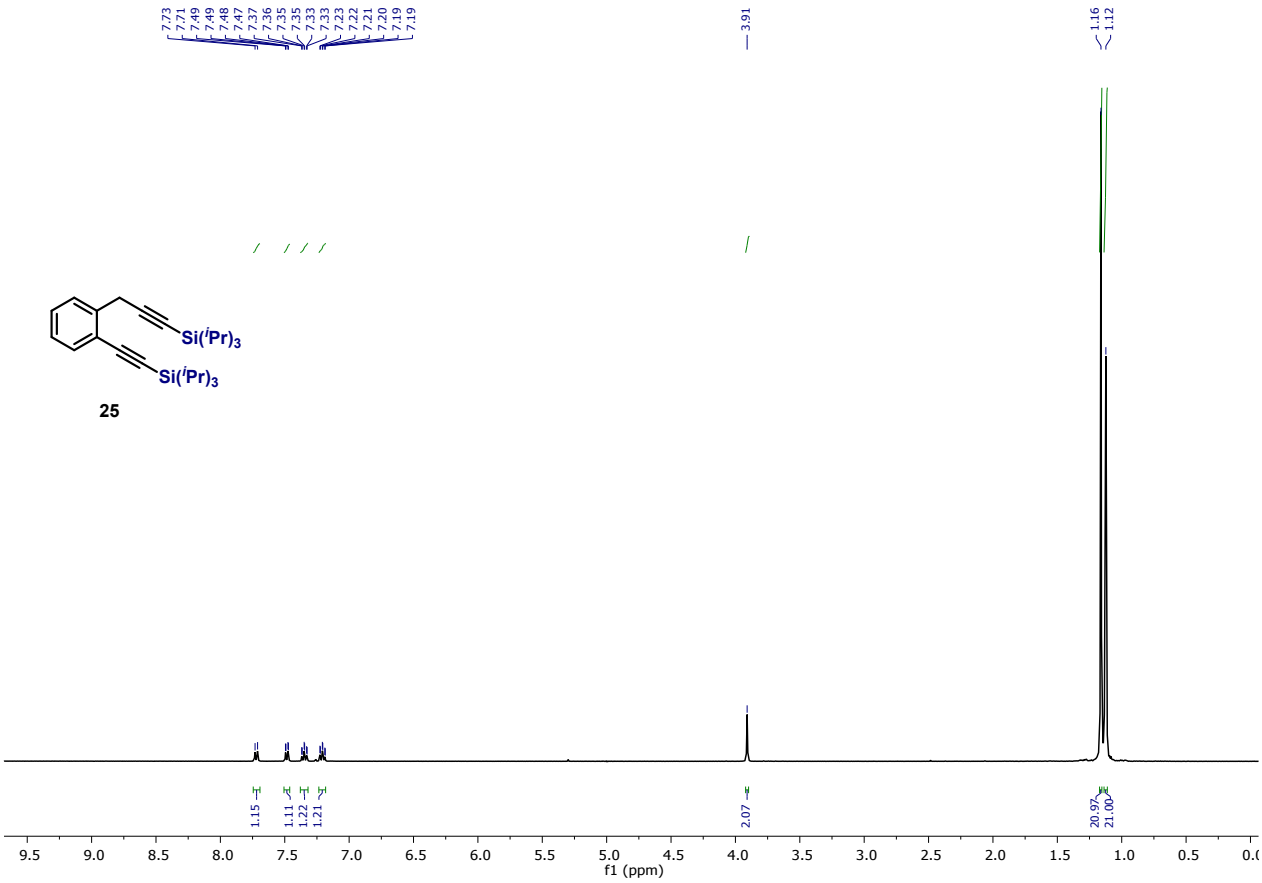
^{1}H NMR (600 MHz, $CDCl_3$)



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

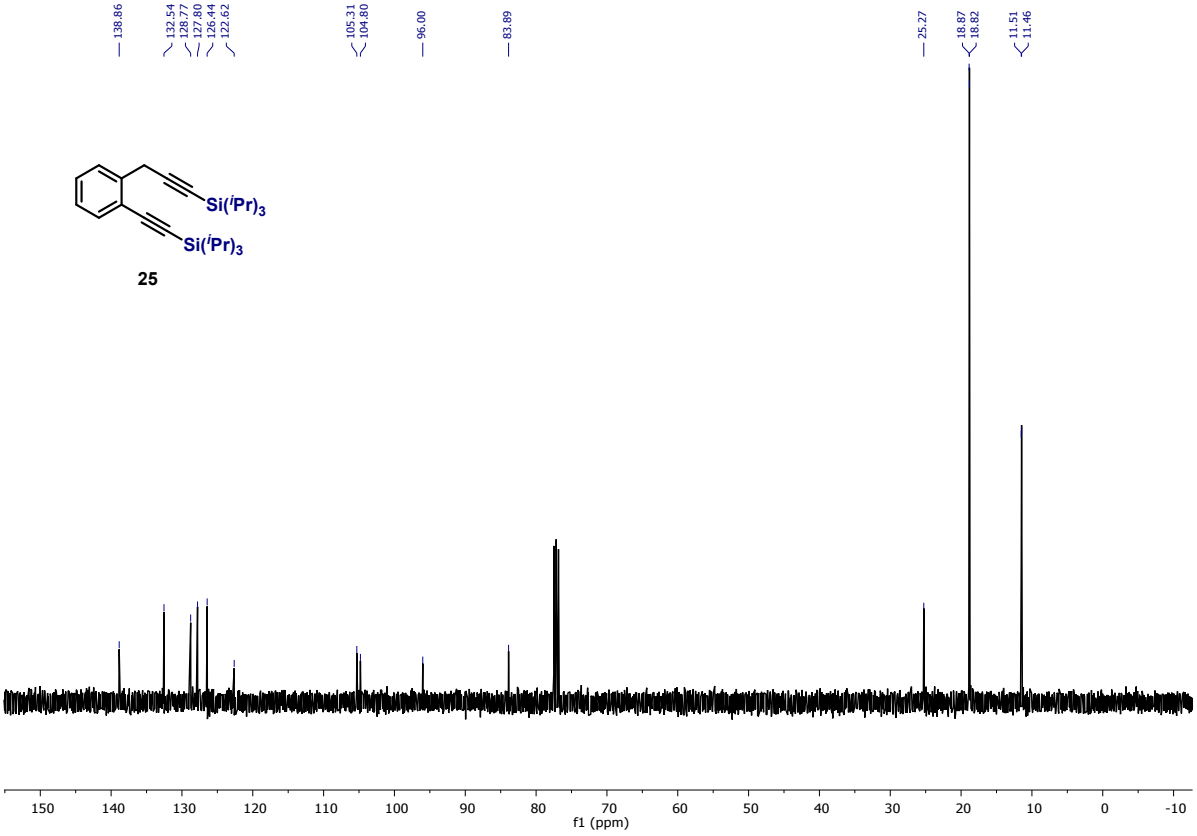


^{1}H NMR (400 MHz, $CDCl_3$)



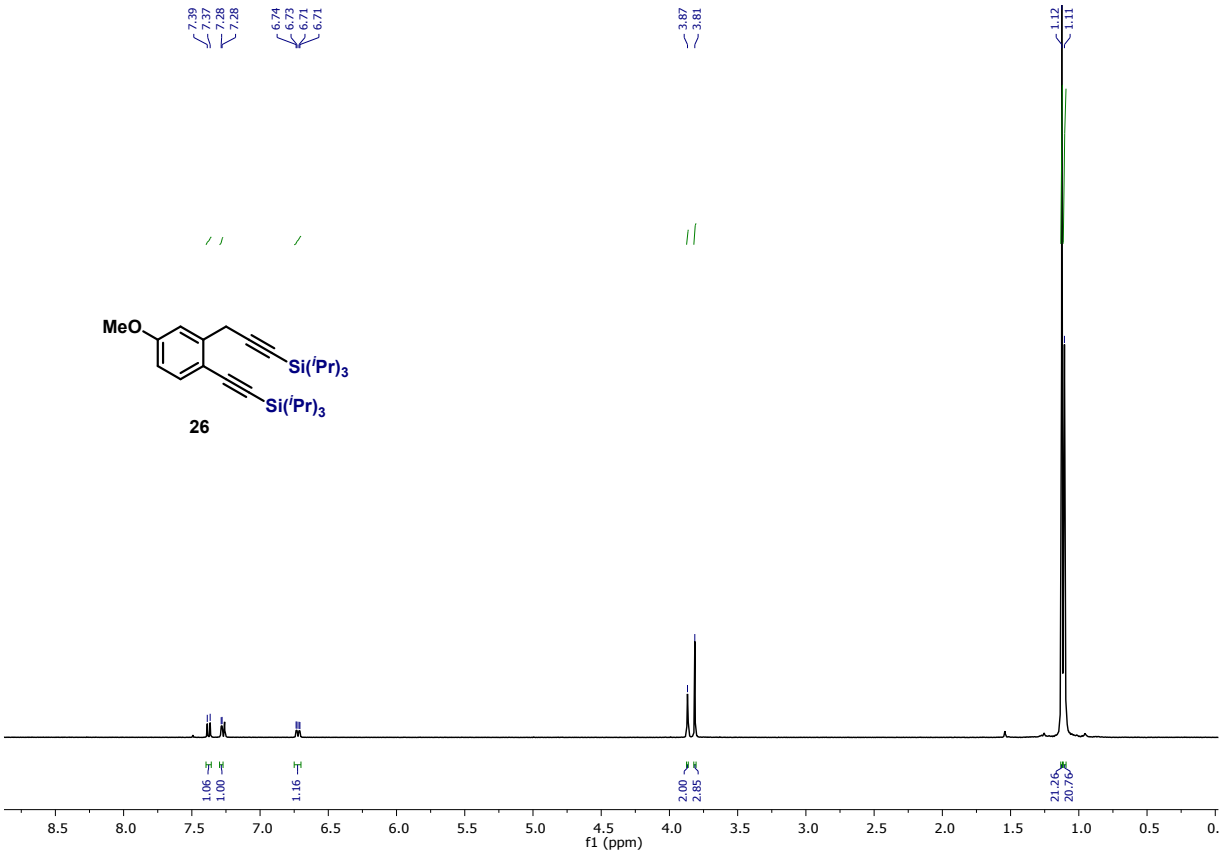
25

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

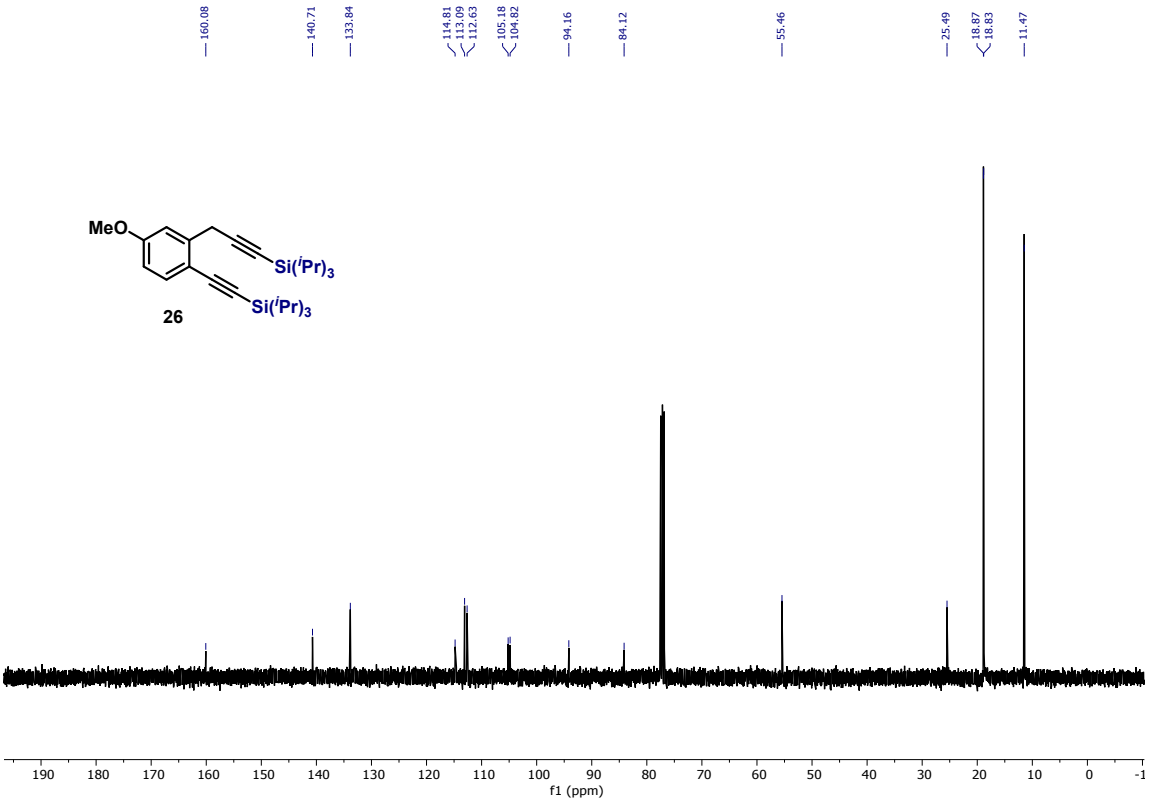


25

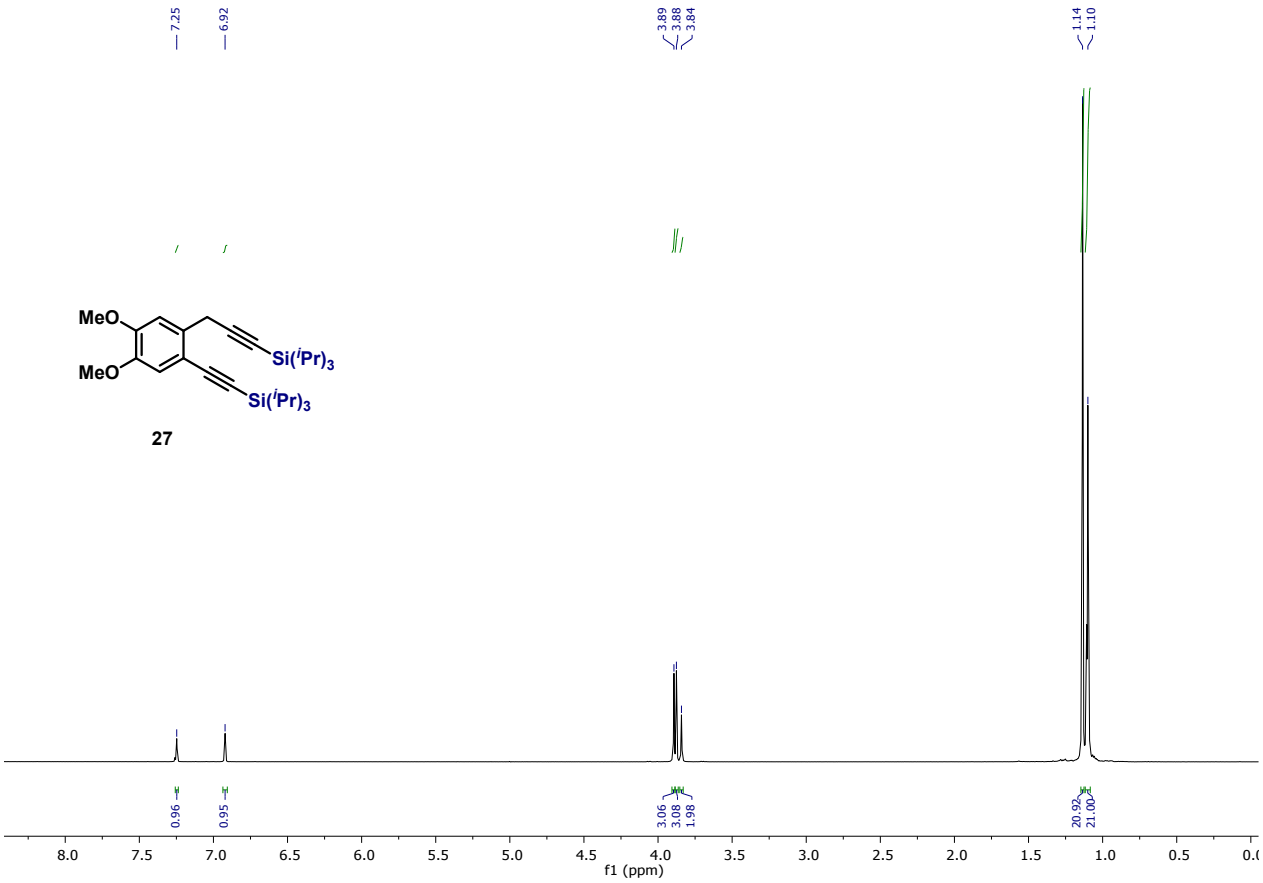
^{1}H NMR (400 MHz, $CDCl_3$)



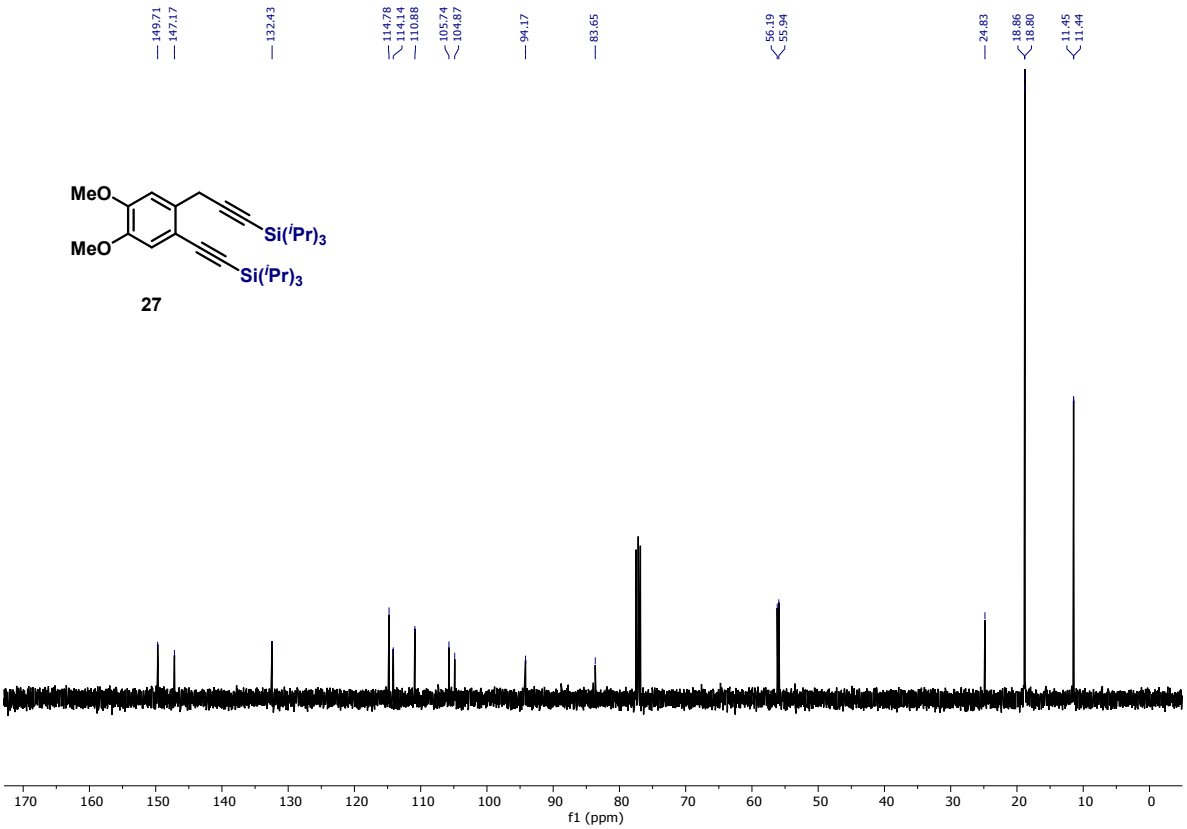
^{13}C NMR (101 MHz, $CDCl_3$)



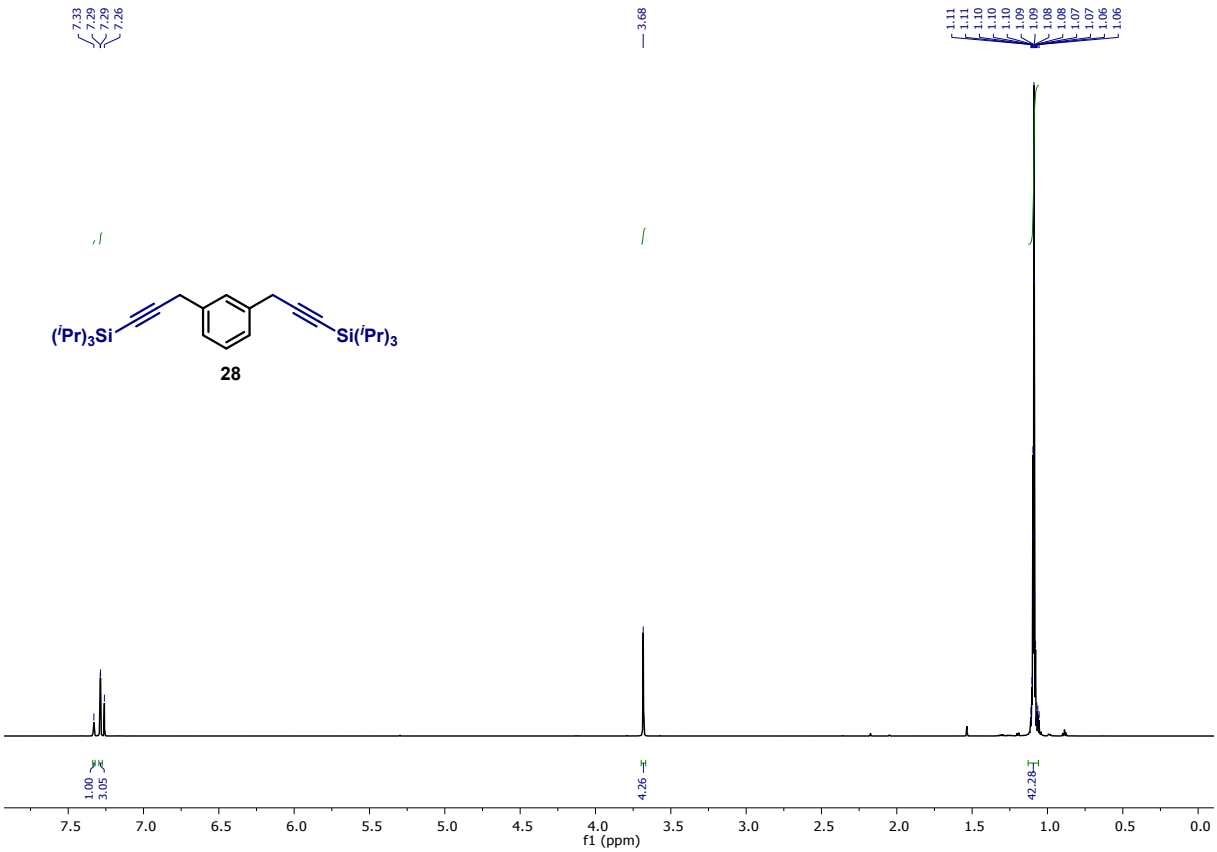
^{1}H NMR (400 MHz, $CDCl_3$)



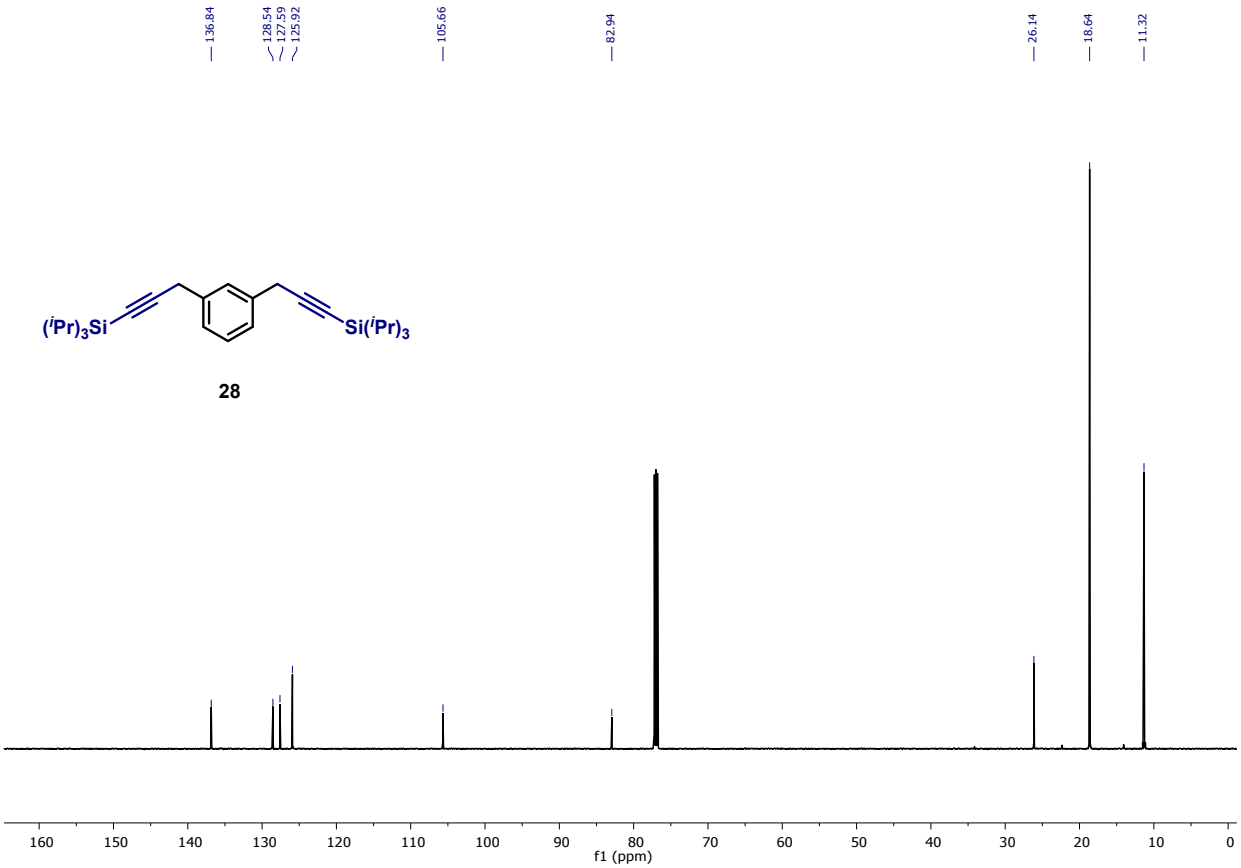
^{13}C NMR (101 MHz, $CDCl_3$)



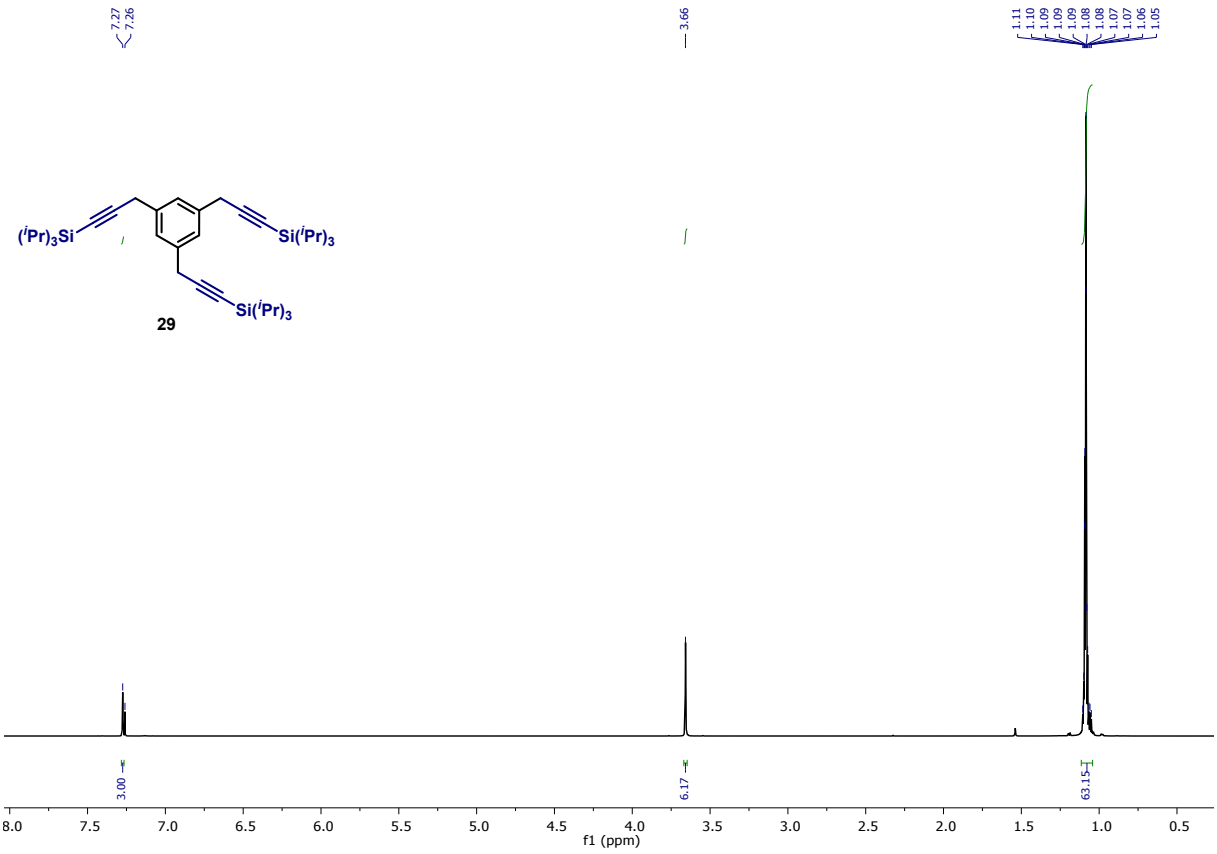
^{1}H NMR (600 MHz, $CDCl_3$)



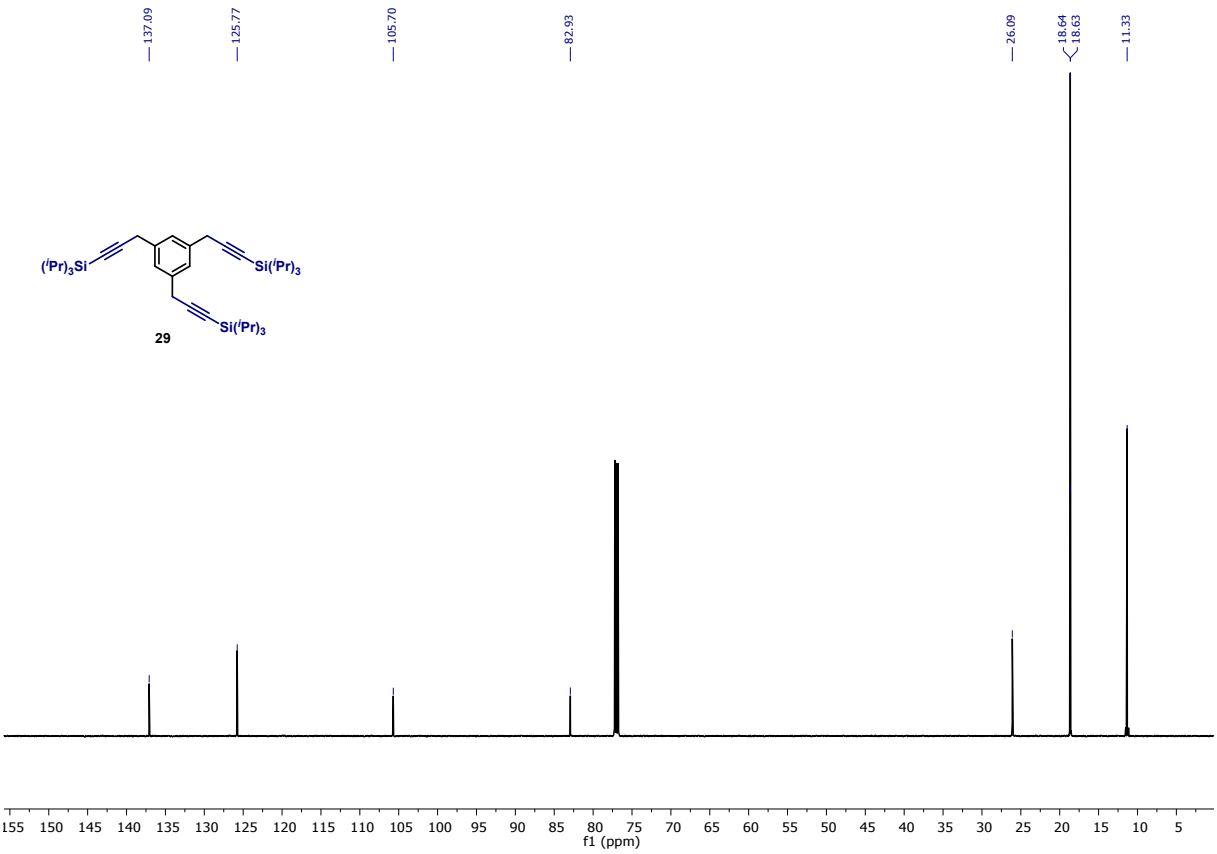
^{13}C NMR (151 MHz, $CDCl_3$)



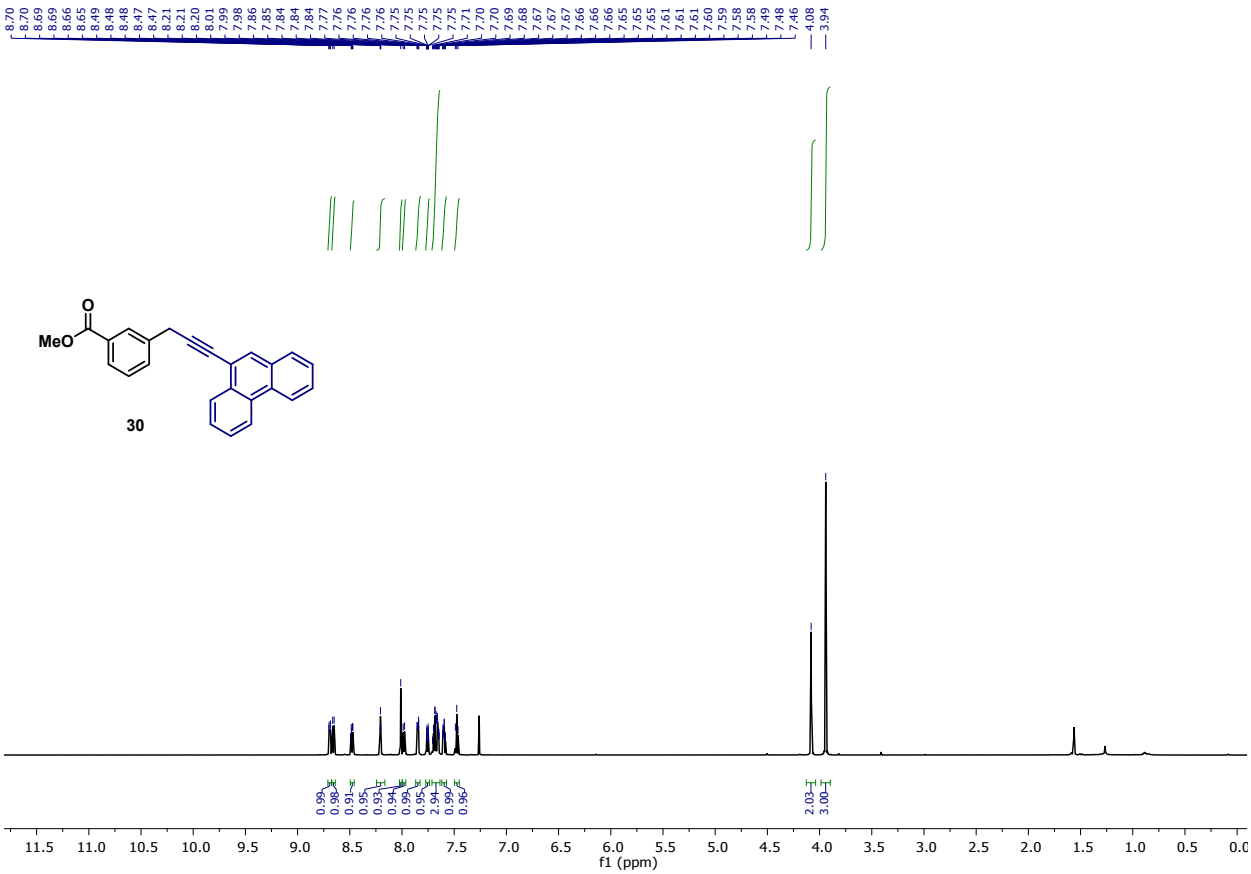
^{1}H NMR (600 MHz, $CDCl_3$)



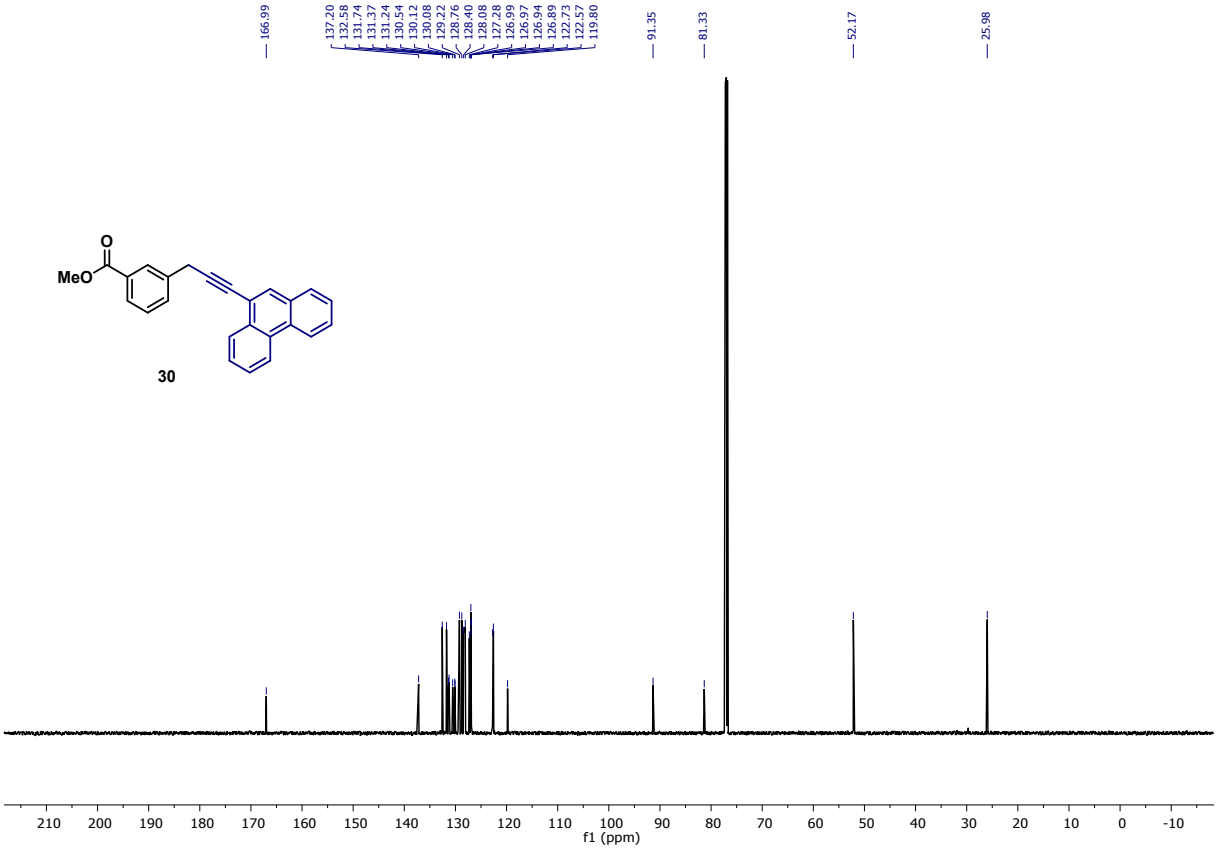
^{13}C NMR (151 MHz, $CDCl_3$)



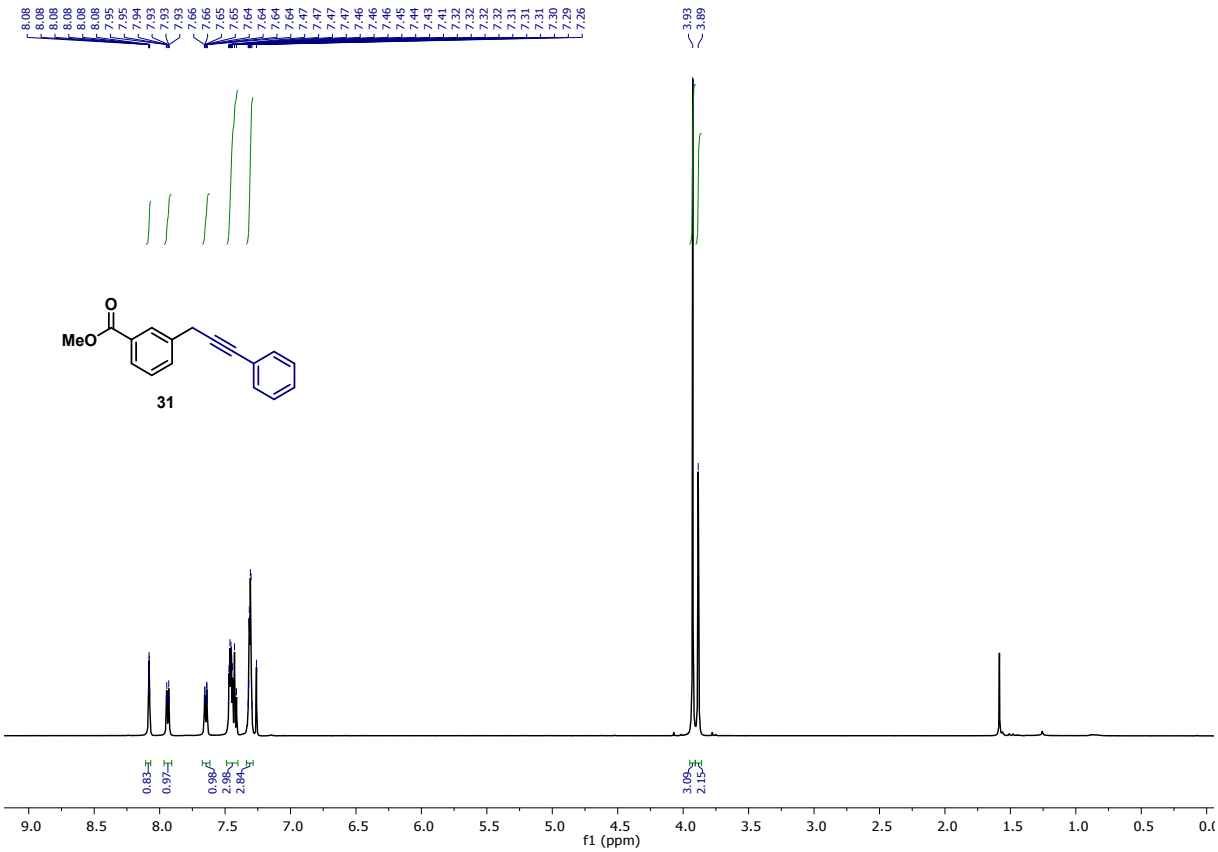
^{1}H NMR (600 MHz, $CDCl_3$)



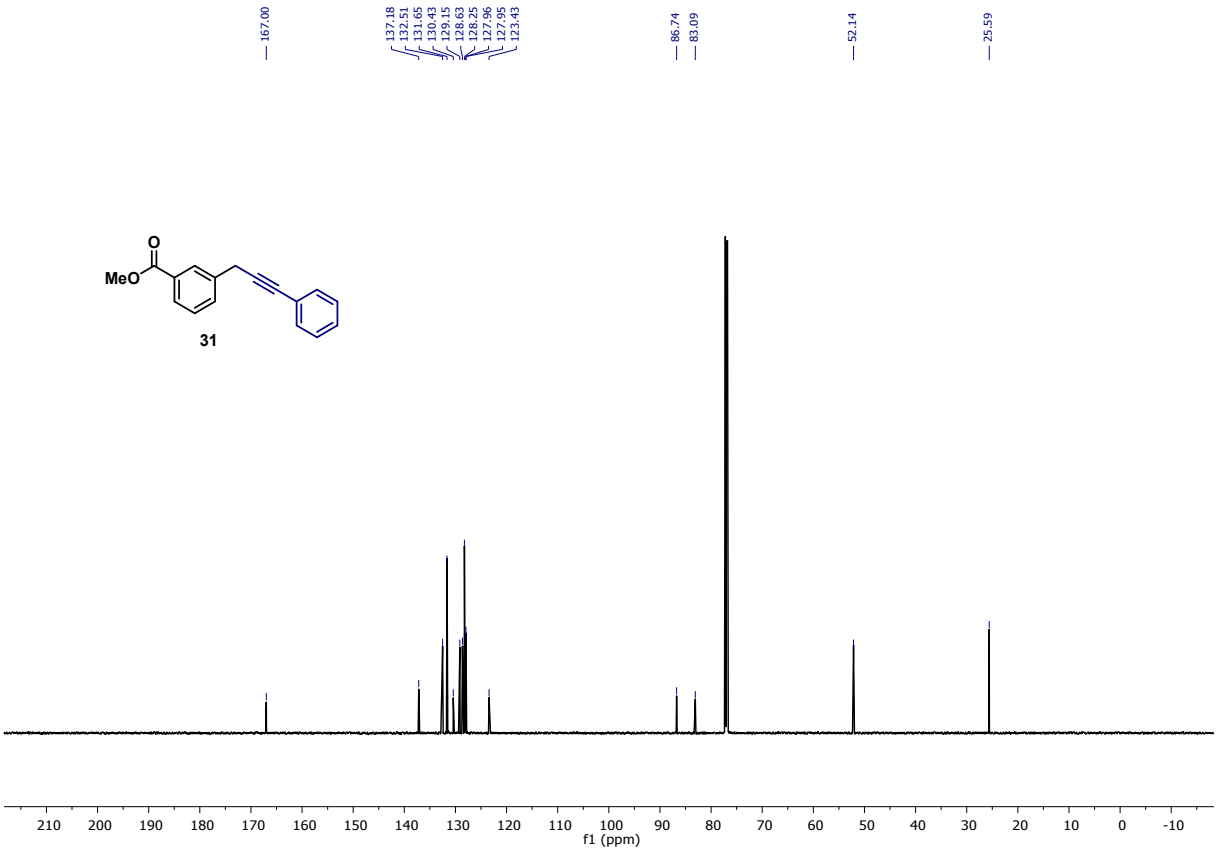
^{13}C NMR (151 MHz, $CDCl_3$)



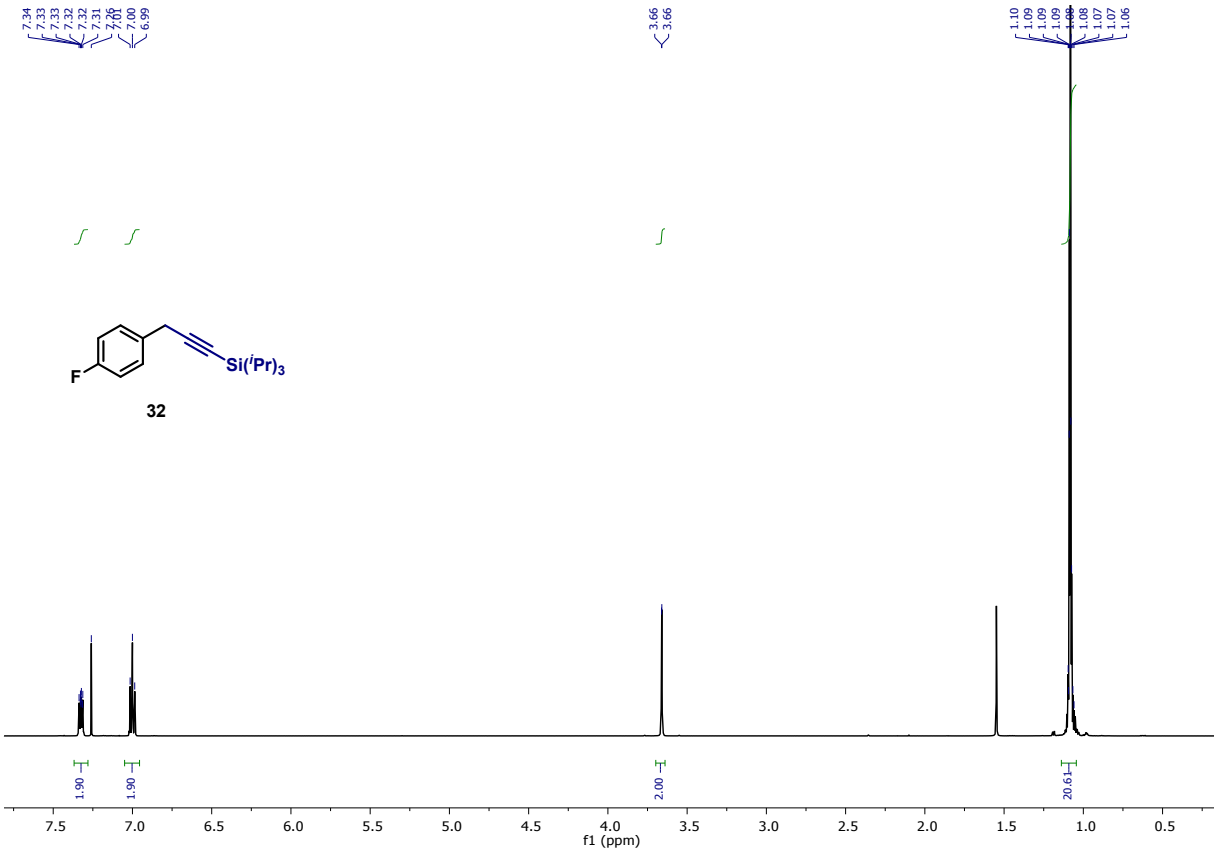
^{1}H NMR (600 MHz, $CDCl_3$)



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

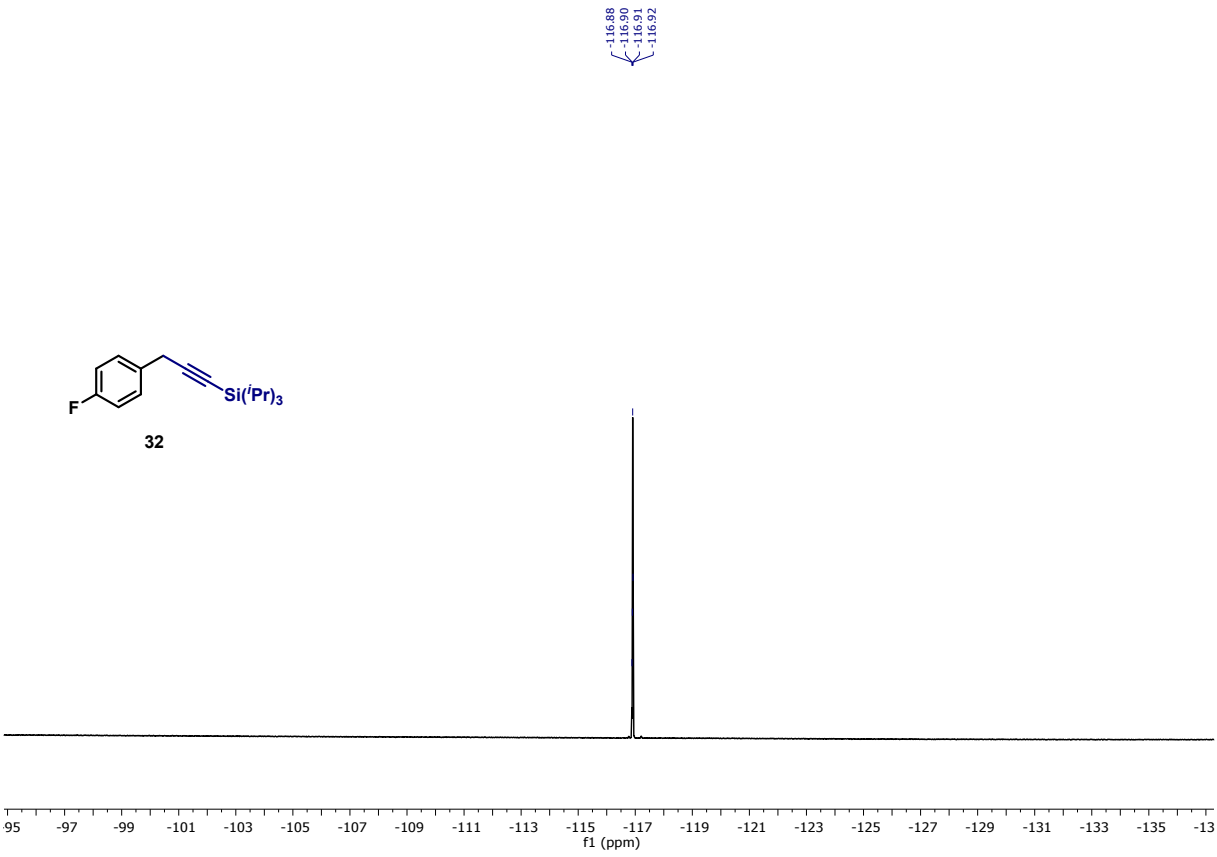


^{1}H NMR (600 MHz, $CDCl_3$)



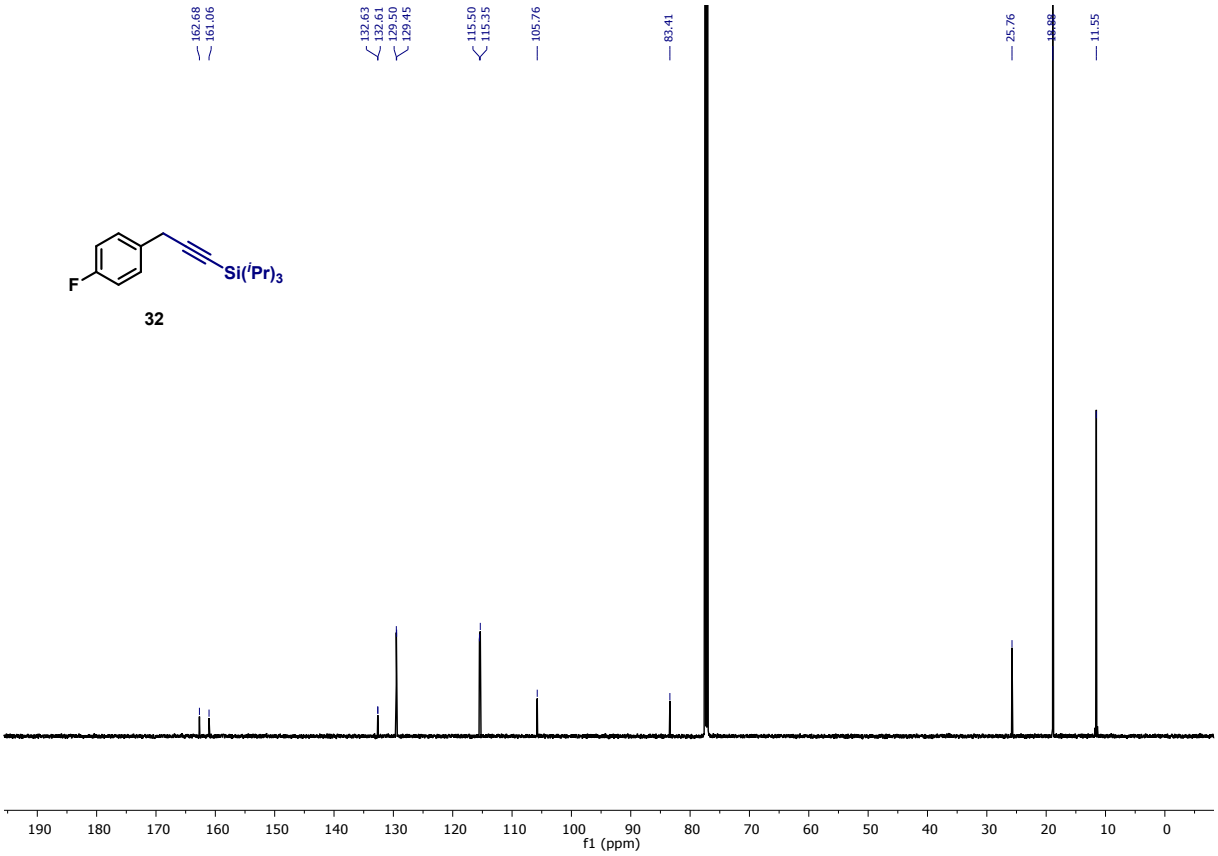
32

^{19}F NMR (565 MHz, $CDCl_3$)

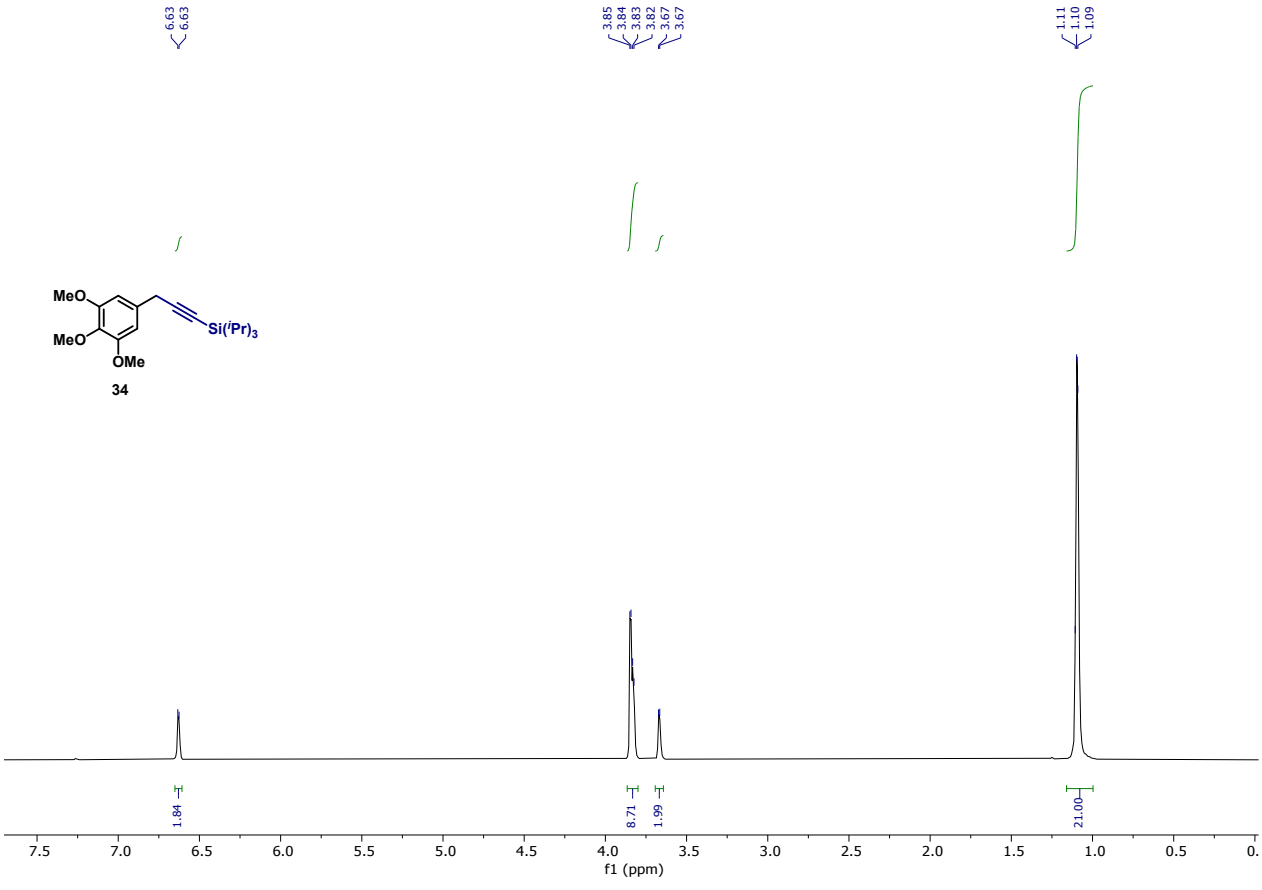


32

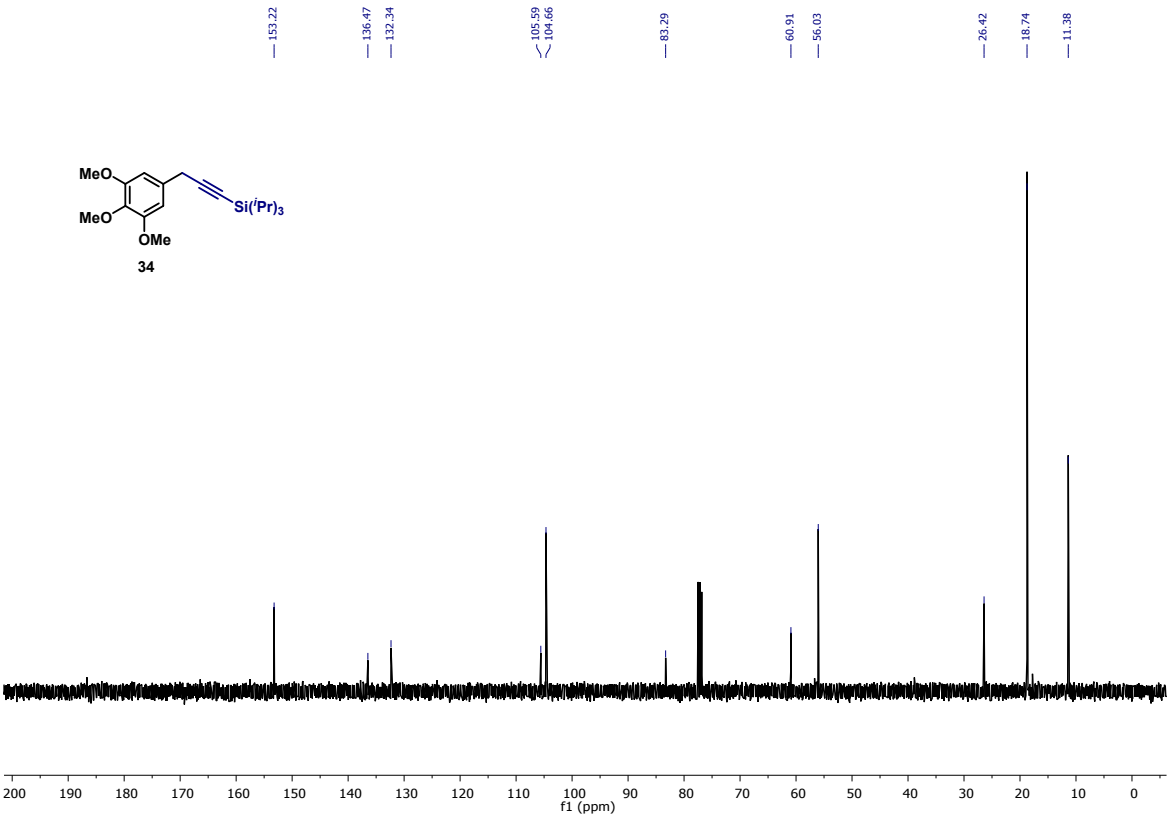
^{13}C NMR (151 MHz, $CDCl_3$)



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



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



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