

Access to Substituted Indenol Ethers via a Regioselective Intermolecular Carbopalladation Cascade

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Access to Substituted Indenol Ethers via a Regioselective Intermolecular Carbopalladation Cascade

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Abstract: Alkyne carbopalladation reactions represent a powerful approach to generating multiple new C–C bonds and substituted alkenes, however regioselectivity is often challenging for intermolecular variants. By utilizing ynl ethers as polarized alkynes we observe complete regiocontrol of migratory insertion with Pd–Ar species. A Heck reaction was used to turn-over the catalytic cycle by intercepting the vinyl-Pd adduct of carbopalladation with a pendant alkene. When using *o*-iodo styrenes substrates the resulting products are oligosubstituted 1-indenol ethers with defined stereochemistry based on the initial alkene geometry. By blocking β -hydride elimination we demonstrated C–H and C–C reductive elimination steps for catalyst turnover. Herein we report the optimization of reaction conditions, scope, and alternative termination steps.

Introduction

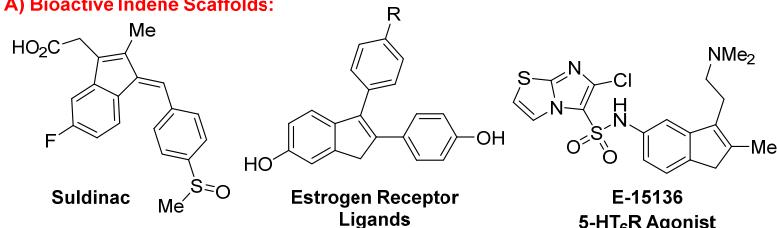
Since the initial demonstration to access polycyclic structures, such as the zipper approach to the A-D rings of a steroid skeleton reported by Negishi in 1990,¹⁻² carbopalladation cascade (or domino) reactions of alkynes represent a powerful class of transformations that can rapidly build multiple new C–C bonds.³ The ability and necessity to intercept the Pd-vinyl adducts of alkyne carbopalladation results in a multitude of options for further functionalization. Variations of this reaction are popular owing to the ability to buildup molecular complexity and that the transformation is robust enough for wide ranging applications including in complex total syntheses.⁴⁻⁷ While many examples within this class of reactions involve intramolecular alkyne carbopalladation, where issues of regioselectivity are not prevalent, the directional control of migratory insertion is certainly a challenge for reactions that involve an intermolecular alkyne carbopalladation step. As a result, many examples involving intermolecular alkyne carbopalladation report only symmetrically substituted alkynes or limited examples of unsymmetrically substituted alkynes, often with incomplete regioselectivity.

Oligosubstituted indenes represent important scaffolds in variety of fields with applications in pharmaceuticals (Figure 1a)⁸⁻¹⁴ and materials research¹⁵⁻¹⁶. Indeed a number of Pd-catalyzed methods involving the intermolecular annulation of alkynes have been developed that result in indene-based products. Heck reported a single example of *o*-iodobenzaldehyde reacting with diphenyl acetylene to provide the indenone product.¹⁷ This work was built on by the Yamamoto group who converted *o*-haloaldehydes to 2-inden-1-ol derivatives with further isomerization to the indanones (Figure 1b).¹⁸

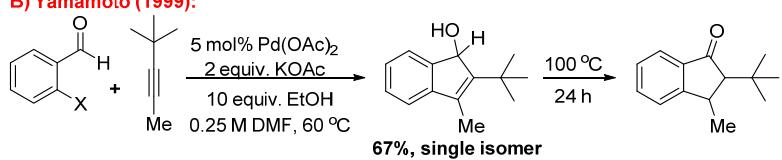
Other notable examples include an enantioselective cationic Pd-catalyzed annulation of *o*-boronate-substituted cinnamic ketones with internal alkynes.¹⁹ Notably only polarized α,β -unsaturated carbonyl alkynes were reported and resulted in single annulation isomers. Additionally, Lautens and coworkers reported that *o*-iodo- α -methyl styrenes participate in a Pd-catalyzed annulation reaction with internal alkynes (Figure 1c).²⁰ Due to the lack of a β -hydrogen the catalytic cycle is turned-over via a C–I reductive elimination in the presence of a bulky phosphine ligand. When an unsymmetrical alkyne was used with electronically disparate arenes (*p*-NO₂ and *p*-OMe, $\Delta\sigma_p = 1.05$)²¹ just a 1.85:1 ratio of regioisomeric products were observed favoring initial C–C bond formation proximal to the more electron rich arene.

Figure 1. Indenes and representative Pd-catalyzed alkyne annulation approaches.

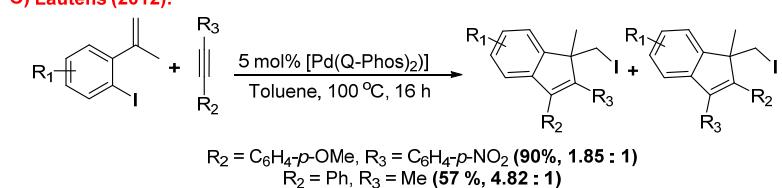
A) Bioactive Indene Scaffolds:



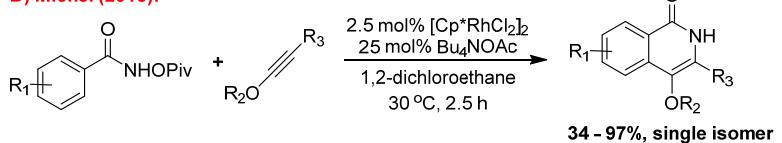
B) Yamamoto (1999):



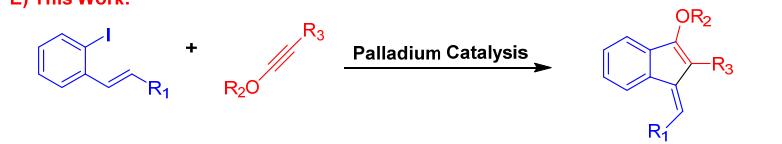
C) Lautens (2012):



D) Michel (2018):



E) This Work:

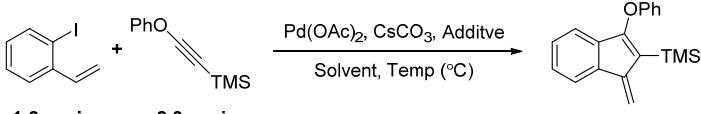


We recently reported the use of ynl ethers as electronically biased alkynes to control the regioselectivity of migratory insertion and annulation processes en route to 4-oxy-substituted isoquinolinones in the context of a Rh catalyzed C–H activation reaction (Figure 1d).²² We hypothesized that ynl ethers could control the intermolecular migratory insertion of a Pd-Aryl species.

The resulting carbopalladation adduct could then be intercepted to generate multisubstituted enol ethers. For initial evaluation, termination of the cascade with a Heck reaction was chosen. Utilizing an *o*-halo styrene this process would allow for rapid access to 1-indenol ether scaffolds with a diverse set of substituted dienol ethers of defined stereochemistry. Herein, we report the regioselective palladium-catalyzed synthesis of oligosubstituted 1-indenol ethers with the catalytic cycle turned over via a Heck reaction along with examples of C–H and C–C reductive eliminations (Figure 1e).

Results and Discussion

Initial optimization efforts utilized *o*-iodosstyrene **1a** and trimethyl(phenoxyethynyl)silane **2a** to evaluate a variety of bases in dioxane with Ph_3P as the ligand (Entries 1-4, Table 1). Knowing that an accumulation of acid would occur *in situ* upon β -hydride elimination and regeneration of the Pd^0 catalyst, we speculated that the identity of base would be essential to obtaining an efficient, high yielding reaction. It was found that Cs_2CO_3 was the optimal base, likely due to the increased solubility of cesium salts in organic solvents over other inorganic salts (Entry 4). While maintaining a 2:1 ligand-to-palladium ratio, we found that the catalyst loading could be reduced from 10 mol% to 5 mol% with limited detriment to reaction efficiency (Entries 4-7). In evaluating phosphine ligands, increased steric demand and bidentate ligands did not improve efficiency over the ubiquitous Ph_3P (Entries 8-10). Increased reaction temperature to 85 °C resulted in a decrease in product yield (Entry 11). Similarly, stirring the reaction mixture for a longer period of time resulted in decreased product yield and this was exacerbated if the reaction was allowed to continue stirring at 85 °C (Entry 12). A slight increase in yield was observed by letting the reaction mixture stir for 3 h at 70 °C, however yields were inconsistent upon scale up to 0.25 mmol (Entry 13). Due to the incomplete solubility of Cs_2CO_3 in dioxane, it was hypothesized that 1.1 equivalents of base was insufficient to quench the acid generated over the course of the reaction, which could cause degradation of the ynl ether substrate or the enol ether product. This was supported by improved yields when increasing the base loadings to 2.0 equivalents relative to the styrene substrate, which resulted in a 92% isolated yield (Entry 14). Expanded optimization results can be found in the SI for solvents and ligand ratios (Tables S1 and S2). The optimized reaction conditions of 5 mol% $\text{Pd}(\text{OAc})_2$, 10 mol% Ph_3P , 2.0 equivalents Cs_2CO_3 in 1,4-dioxane (0.2 M) stirred at 70 °C for 3 h were used going forward.

Table 1. Optimization of Reaction Conditions.


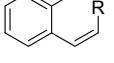
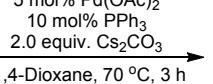
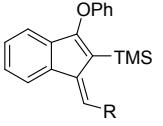
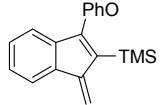
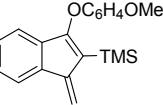
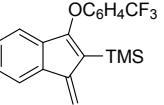
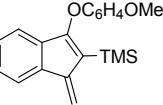
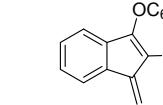
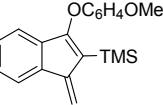
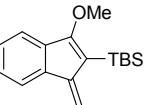
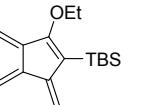
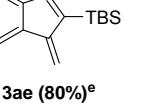
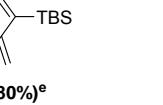
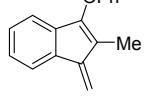
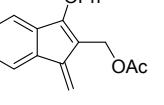
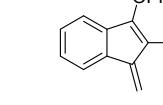
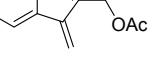
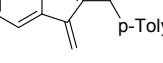
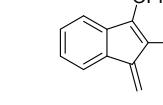
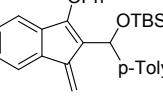
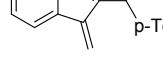
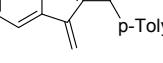
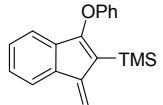
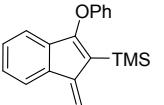
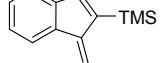
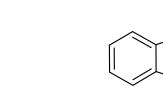
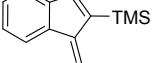
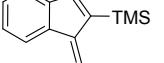
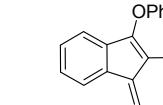
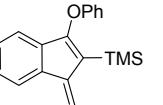
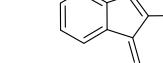
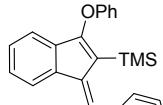
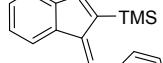
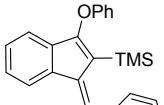
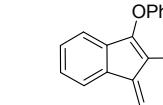
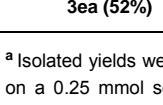
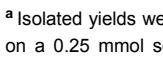
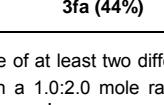
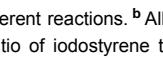
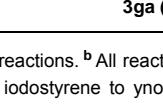
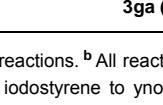
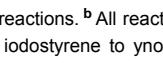
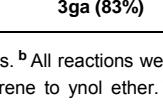
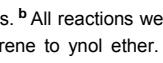
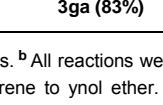
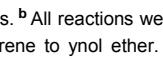
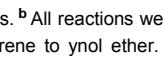
Entry	Pd(OAc) ₂ (mol%)	1.0 equiv		2.0 equiv.		Yield (h)
		Base (equiv.)	Solvent	Temp	Additive (mol%)	
1	10	Et ₃ N (1.1)	Dioxane	70	PPh ₃ (20)	17 (2)
2	10	Bu ₄ NOAc (1.1)	Dioxane	70	PPh ₃ (20)	57 (2)
3	10	CsOAc (1.1)	Dioxane	70	PPh ₃ (20)	54 (2)
4	10	Cs ₂ CO ₃ (1.1)	Dioxane	70	PPh ₃ (20)	100 (2)
5	2.5	Cs ₂ CO ₃ (1.1)	Dioxane	70	PPh ₃ (5)	67 (2)
6	5.0	Cs ₂ CO ₃ (1.1)	Dioxane	70	PPh ₃ (10)	85 (2)
7	20	Cs ₂ CO ₃ (1.1)	Dioxane	70	PPh ₃ (40)	35 (2)
8	5.0	Cs ₂ CO ₃ (1.1)	Dioxane	70	P(o-Tol) ₃ (10)	45 (3)
9	5.0	Cs ₂ CO ₃ (1.1)	Dioxane	70	BINAP (5)	19 (3)
10	5.0	Cs ₂ CO ₃ (1.1)	Dioxane	70	DPPB (5)	27 (3)
11	5.0	Cs ₂ CO ₃ (1.1)	Dioxane	85	PPh ₃ (10)	71 (2)
12	5.0	Cs ₂ CO ₃ (1.1)	Dioxane	85	PPh ₃ (10)	52 (3)
13	5.0	Cs ₂ CO ₃ (1.1)	Dioxane	70	PPh ₃ (10)	87 (3), (68 - 80%) ^b
14	5.0	Cs ₂ CO ₃ (2.0)	Dioxane	70	PPh ₃ (10)	92 (3) ^b

(a) All yields were determined by NMR unless otherwise noted. (b) This reaction was run on a 0.25 mmol scale, and the yield reflects an isolated yield.

With optimized reaction condition in hand, the reaction scale was evaluated at 1.5 mmol of styrene, which provided a 97% isolated yield of **3aa**. The effects of electronically varied substituents off the ynone ether oxygen were evaluated. We were pleased to find that both electron withdrawing and electron donating groups were well tolerated (Table 2, **3ab-3ac**). When the oxygen substituent was changed from phenyl to methyl there was a decrease in yield (Table 2, **3ad**). Here a TBS group was necessitated for the synthesis and isolation of the low molecular weight alkyne. The ethoxy analogue **3ae** was isolated in 65% yield. To further evaluate the other alkyne substituent **2f** was evaluated, which surprisingly led to a significant drop in yield (Table 2, **3af**). However, other alkyl substitutions including a primary propargylic acetate **2g** and a secondary OTBS **2h** resulted in moderate to excellent yields (Table 2, **3ag-3ah**). Next, electron withdrawing moieties were placed at the β -position of the styrene to explore the effect of polarizing the styrene bond. Both a **3b** and **3c** were tolerated providing moderate to good yields of **3ba** and **3ca**. Alkyl substitution in the form of o-iodo- β -methyl styrene provided **3da** in

64% yield. For stilbene derivatives, the more electron poor **3g** (4-NO₂) provided **3ga** in higher yield compared to the relatively neutral substrates **3e** and **3f**.

Table 2. Scope evaluation.

			
1a-g	2a-h		3
			
3aa (97%)^c			
			
3ab (84%)			
			
3ac (89%)			
			
3ad (62%)^d			
			
3ae (80%)^e			
			
3af (17%)			
			
3ag (54%)			
			
			
3ah (94%)			
			
			
3ba^f (83%)			
			
3ca (61%)			
			
			
3da (64%)			
			
			
3ea (52%)			
			
			
3fa (44%)			
			
3ga (83%)			

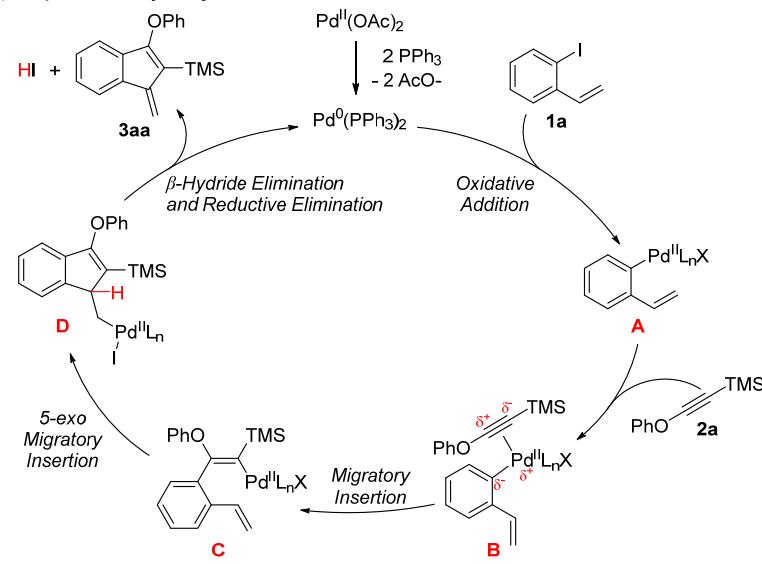
^a Isolated yields were an average of at least two different reactions. ^b All reactions were run on a 0.25 mmol scale, and with a 1.0:2.0 mole ratio of iodostyrene to ynl ether. ^c This reaction was run at 1.50 mmol scale. ^d TBS was used as a protecting group instead of TMS due to challenges with the low molecular weight TMS substrate. ^e single experiment. ^f styrene substrate is a mixture of E/Z isomers, however product is a single isomer as shown.

In all of the above cases, products were only observed to arise from carbopalladation forming the initial C–C bond on the carbon of the alkyne bearing the oxygen substituent. The ability to synthesize these functionalized indenes regioselectively can be better understood by evaluating a proposed catalytic cycle (Scheme 1A). Initial oxidative addition to the Ar–I bond provides an Pd–C adduct **A**, which can subsequently coordinate the π-system of the ynl ether to give the precursor to migratory insertion **B**. Owing to the polarized nature of the alkyne and the moderately polarized Pd–C

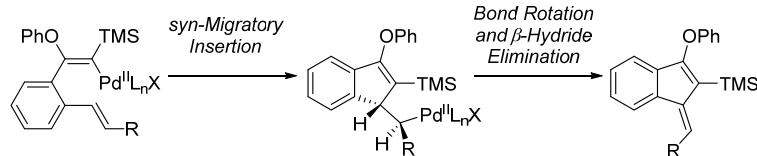
bond, migratory insertion is selective for C–C bond formation proximal to the oxygen. The resultant vinyl–Pd species **C** can undergo a 5-exo-trig cyclization with the pendant alkene to provide **D**. β -hydride elimination provides the dienol ether indene product and ultimately regenerates a Pd^0 species. When a β -substituted styrene is present a predicted isomerization is generally observed. Heck migratory insertion generally occurs via a *syn* carbopalladation, which necessitates a bond rotation to achieve Pd-mediated *syn* β -hydride elimination. Consequently, β -substituted styrenes with a *trans* relationship between the substituents resulted in a product containing a *cis* relationship between these same substituents (Scheme 1B). Notably, the electron withdrawing substrate **3b** actually improves from a starting *E/Z* ratio of ~5.5:1 in the styrene substrate to only a single observed isomer in the product **3ba**. This could be due to alkene isomerization under reaction conditions or the ability of the Pd-enolate intermediate to isomerize from C–Pd to O–Pd with subsequent isomerization prior to β -hydride elimination.

Scheme 1. Mechanistic considerations.

A) Proposed Catalytic Cycle



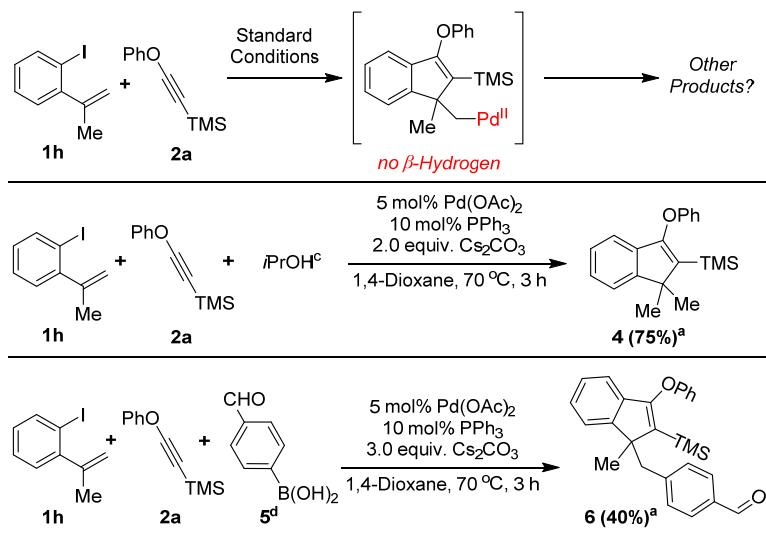
B) Alkene Isomerization



Based on the above proposed mechanism for generating substituted dienol ether we became interested in blocking β -hydride elimination to achieve additional functionalization in lieu of generating a diene. By replacing the α -hydrogen with a methyl group in the styrene no β -hydride elimination is possible; providing a Pd^{II} -alkyl intermediate that could then be intercepted and further functionalized

(Scheme 2). Using styrene **1h** and ynl ether **2a** and the simple addition of 1.1 equivalents of isopropanol generated **4** in 75% isolated yield. It should be noted that no additional changes were made to the reaction conditions and that no other reductive products were observed. Next, we attempted a 3-component coupling, aiming to intercept the Pd^{II} intermediate using 4-formylphenylboronic acid **5**. With an additional equivalent of base, but no other optimization, **6** was isolated in a 40% yield. This final example represents a significant buildup of molecular complexity from relatively simple and readily available substrates. Only a small amount of product resulting from Suzuki-Miyaura cross coupling (i.e. **1h** coupling directly with **5**) was observed. This suggests that the intermolecular then intramolecular carbopalladation cascade is rapid relative to transmetalation processes.

Scheme 2. Intercepting Palladium Intermediates.



^a Isolated yields. ^b All reactions were run on a 0.25 mmol scale, and with a 1.0:2.0 mole ratio of iodostyrene to ynl ether. ^c 1.1 equivalents. ^d 1.0 equivalents.

Conclusion

In summary, we have successfully synthesized diverse indenol ethers utilizing a regioselective carbopalladation cascade. The challenge of facilitating selective alkyne migratory insertion often observed with asymmetrically disubstituted alkynes was overcome by the electronic bias of ynl ethers. The stereochemical information of the alkene is transferred to the product according to a predictable bond rotation. We further demonstrated that if the terminal β -hydride elimination step is blocked by the use of α -methyl-2-iodostyrene, the palladium intermediate can be intercepted for additional functionalization including a selective 3-component coupling. This approach provides direct access to

valuable enol ether or dienol ethers within the privileged indene core containing a range of substitutions.

Methods

General procedure for synthesis of dienol ether products

Pd(OAc)₂ (5 mol%, 0.0125 mmol, 2.8 mg), PPh₃ (10 mol%, 0.025 mmol, 6.6 mg), and Cs₂CO₃ (2.0 equiv., 0.5 mmol, 162.9 mg) were added to a 10 mL rounded bottom flask. Next, a solution containing styrene **1** (0.25 mmol) and ynol ether **2** (0.50 mmol) in 1,4-dioxane (0.2 M) was added to the rounded bottom flask, and the flask was placed under a nitrogen atmosphere. The reaction flask was then heated to 70 °C with stirring. After 3 h the crude reaction mixture was filtered through celite, and concentrated directly onto silica gel. Flash chromatography was performed (Ethyl Acetate in Hexanes) to obtain the purified compound **3**.

All experimental procedures, compound characterization, and supplemental figures can be found in the SI.

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Notes

The authors declare no competing financial interest.

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Access to Substituted Indenol Ethers via Carbopalladati... (306.65 KiB)

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Supporting Information

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General Information

THF was obtained from the Innovative Technologies PureSolv MD 5 solvent purification system and kept under argon. All other solvents were obtained from the from commercial suppliers. Reagents were purchased from Sigma-Aldrich, Fisher Scientific, Alfa Aesar, Acros Organics, and TCI. Reagents were used as received. Reactions were run in dry solvents, with a magnetic stir bar, capped with a rubber septum, and under a nitrogen atmosphere unless otherwise indicated. Heated reactions were performed in temperature-controlled oil baths. Thin-layer chromatography was carried out on EMD Millipore 60 silica gel plates visualized by UV-light (254 nm /365 nm) and treatment with KMnO₄ stain followed by gentle heating utilizing a heat gun. Work-up procedures were completed in ambient conditions. Flash chromatography was performed on RediSep Rf Gold high performance silica gel (12-40 gram) columns. ¹H and ¹³C NMR spectra were recorded with Bruker NMR spectrometer (500 MHz). ¹H NMR spectra were referenced to residual CHCl₃ (7.26 ppm), and reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet). Chemical shifts of the ¹³C NMR spectra were referenced to CDCl₃ (77.2 ppm). Mass spectral data were obtained from the Central Analytical Laboratory at the University of Colorado at Boulder.

Screening Procedures:



Phosphine Screening Procedure

$\text{Pd}(\text{OAc})_2$ (0.01 mmol, 10 mol%), phosphine ligand (0.02 mmol, 20 mol%), and Cs_2CO_3 (0.11 mmol, 1.1 equiv.) were added to a 2 mL autosampler vial with a PTFE septa cap. Next, 2-iodostyrene (0.1 mmol, 1.0 equiv.) and trimethyl(phenoxyethynyl)silane (0.2 mmol, 2.0 equiv.) were added using 0.5 mL of 1,4-dioxane and the reaction vessel was heated to 70 °C until TLC showed consumption of trimethyl(phenoxyethynyl)silane. The reaction mixture was cooled to room temperature, filtered through a celite plug with dichloromethane, and concentrated under reduced pressure. Yields were determined by NMR using 2,4,5-trichloropyrimidine as an internal standard.

Base Screening Procedure

$\text{Pd}(\text{OAc})_2$ (0.01 mmol, 10 mol%), triphenylphosphine (0.02 mmol, 20 mol%), and base (0.11 mmol, 1.1 equiv.) were added to a 2 mL autosampler vial with septa (if the base was a liquid it was added via syringe once 2-iodostyrene and trimethyl(phenoxyethynyl)silane were added). Next, 2-iodostyrene (0.1 mmol, 1.0 equiv.) and trimethyl(phenoxyethynyl)silane (0.2 mmol, 2.0 equiv.) were added using 0.5 mL of 1,4-dioxane and the reaction vessel was heated to 70 °C until TLC showed consumption of trimethyl(phenoxyethynyl)silane. The reaction was cooled to room temperature, filtered through a celite plug with dichloromethane, and concentrated under reduced pressure. Yields were determined by NMR using 2,4,5-trichloropyrimidine as an internal standard.

Catalyst Loading Procedure

$\text{Pd}(\text{OAc})_2$ (2.5 mol% - 20 mol%), triphenylphosphine (5 mol% - 40 mol%), and base (0.11 mmol, 1.1 equiv.) were added to a 2 mL autosampler vial with a PTFE septa cap. Next, 2-iodostyrene (0.1 mmol, 1.0 equiv.) and trimethyl(phenoxyethynyl)silane (0.2 mmol, 2.0 equiv.) were added using 0.5 mL 1,4-dioxane and the reaction vessel was heated to 70 °C until TLC showed consumption of trimethyl(phenoxyethynyl)silane. The reaction was cooled to room temperature, filtered through a celite plug with dichloromethane, and concentrated under reduced pressure. Yields were determined by NMR using 2,4,5-trichloropyrimidine as an internal standard.

Final Phosphine Screening

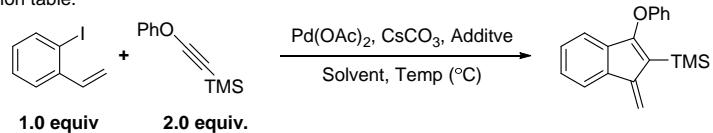
$\text{Pd}(\text{OAc})_2$ (0.05 mmol, 5 mol%), phosphine ligand (0.01 mmol, 10 mol%), and Cs_2CO_3 (0.11 mmol, 1.1 equiv.) were added to a 2 mL autosampler vial with a PTFE septa cap. Next, 2-iodostyrene (0.1 mmol, 1.0 equiv.) and trimethyl(phenoxyethynyl)silane (0.2 mmol, 2.0 equiv.) were added using 0.5 mL of 1,4-dioxane and the reaction vessel was heated to 70 °C until TLC showed consumption of trimethyl(phenoxyethynyl)silane. The reaction was cooled to room temperature, filtered through a celite plug with dichloromethane, and concentrated under reduced pressure. Yields were determined by NMR using 2,4,5-trichloropyrimidine as an internal standard.

NMR Yield Procedure

A solution of a known concentration (10-20 μ M) of 2,4,5-trichloropyrimidine in CDCl_3 was prepared by dissolving 3.6-7.2 mg of trichloropyrimidine per 1 mL of CDCl_3 . A fresh solution was prepared for each set of screening reactions that was performed. 0.5 mL of the fresh 2,4,5-chlorotrichloropyrimidine solution was then added to each concentrated sample from the procedures above. Each yield was determined by comparing the relative integrated values of 2,4,5-trichloropyrimidine (8.60 ppm) and one of the proton of the terminal alkene in the product (~6.1 ppm).

Expanded Optimization Tables:

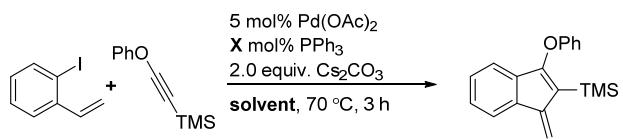
Table S1. Expanded optimization table.



Entry	Pd(OAc) ₂ (mol%)	Base (equiv.)	Solvent	Temperature	Additive (mol%)	Yield (h)
1	10	Cs ₂ CO ₃ (1.1)	Dioxane	70	tBu ₃ PH•BF ₄ (20)	52 (16)
2	10	Cs ₂ CO ₃ (1.1)	Dioxane	70	PCy ₃ (20)	81 (4)
3	10	Cs ₂ CO ₃ (1.1)	Dioxane	70	DPPB (20)	72 (4)
4	10	Cs ₂ CO ₃ (1.1)	Dioxane	70	P(o-Tol) ₃ (20)	89 (4)
5	10	Cs ₂ CO ₃ (1.1)	Dioxane	70	P(o-Tol) ₃ (20)	82 ^b (2)
6	10	Cs ₂ CO ₃ (1.1)	Dioxane	70	P(2-furyl) ₃ (20)	100 (2)
7	10	Cs ₂ CO ₃ (1.1)	Dioxane	70	PPh ₃ (20)	100 (2)
8	10	Et ₃ N (1.1)	Dioxane	70	PPh ₃ (20)	17 (2)
9	10	CsOAc (1.1)	Dioxane	70	PPh ₃ (20)	54 (2)
10	10	Bu ₄ NOAc (1.1)	Dioxane	70	PPh ₃ (20)	57 (2)
11	2.5	Cs ₂ CO ₃ (1.1)	Dioxane	70	PPh ₃ (5)	67 (2)
12	5.0	Cs ₂ CO ₃ (1.1)	Dioxane	70	PPh ₃ (10)	85 (2)
13	20	Cs ₂ CO ₃ (1.1)	Dioxane	70	PPh ₃ (40)	35 (2)
14	5.0	Cs ₂ CO ₃ (1.1)	Dioxane	70	P(o-Tol) ₃ (10)	45 (3)
15	5.0	Cs ₂ CO ₃ (1.1)	Dioxane	70	BINAP (5)	19 (3)
16	5.0	Cs ₂ CO ₃ (1.1)	Dioxane	70	DPPB (5)	27 (3)
17	5.0	Cs ₂ CO ₃ (1.1)	Dioxane	85	PPh ₃ (10)	71 (2)
18	5.0	Cs ₂ CO ₃ (1.1)	Dioxane	85	PPh ₃ (10)	52 (3)
19	5.0	Cs ₂ CO ₃ (1.1)	Dioxane	70	PPh ₃ (10)	92 (3) ^b

(a) All yields were determined by NMR unless otherwise noted. (b) This reaction was run on a 0.25 mmol scale, and the yield reflects an isolated yield.

Table S2. Ligand ratio and solvent recheck with optimized conditions.



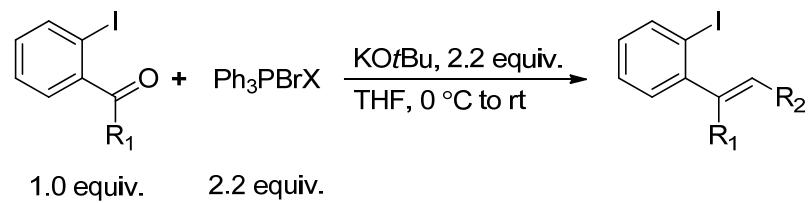
Entry	X mol % PPh ₃	Solvent	Yield (%)
1	5.0	1,4-dioxane	97
2	7.5	1,4-dioxane	91
3	10.0	1,4-dioxane	100
4	20.0	1,4-dioxane	94
5	10.0	Ethanol	13
6	10.0	Toluene	52
7	10.0	DMF	5
8	10.0	DMA	8

All yields were determined by NMR.

Synthesis of Styrenes Substrates:

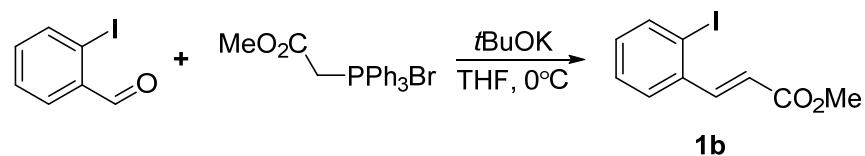
Styrenes **1a**,¹ and **1h**,² and **1g**³ were prepared according to the literature procedures.

General method A: Synthesis of 2-iodostyrenes **1b** and **1e-g**



1,4-dioxane and potassium *tert*-butoxide were added to a rounded-bottom flask. The suspension was cooled to 0 °C and the appropriate triphenylphosphonium salt was added and stirred for 10 minutes. Next, the appropriate 2-iodobenzaldehyde was added and stirred at 0 °C for 5-30 minutes. Once complete, the reaction mixture was filtered through celite using hexanes and the filtrate was concentrated onto silica. Iodo-styrenes were purified via automated flash column chromatograph (Hexanes/Ethyl Acetate). No additive was needed to prevent styrene polymerization unless otherwise noted.

(E/Z)-methyl 3-(2-iodophenyl)acrylate **1b**:



Prepared by general method A. **1b** (*E/Z* = 5.5 : 1.0) (0.454 g, 53%) was isolated.

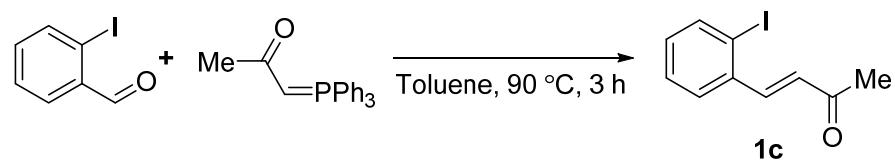
NMR data for major (*E*) isomer:

¹H NMR (500 MHz, CDCl₃): δ 7.94 – 7.87 (m, 2H), 7.56 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.39 – 7.33 (m, 1H), 7.06 (td, *J* = 7.6, 1.7 Hz, 1H), 6.33 (d, *J* = 15.8 Hz, 1H), 3.84 (s, 3H).

¹³C NMR (126 MHz, CDCl₃): δ 166.7, 147.9, 140.0, 137.8, 131.3, 128.6, 127.4, 120.8, 101.2, 51.9.

HR-MS (ESI+): 288.9725 (calculated for M+H) 288.9726 (found)

(E/Z)-4-(2-iodophenyl)but-3-en-2-one **1c** (*E/Z* = 5.5 : 1.0):



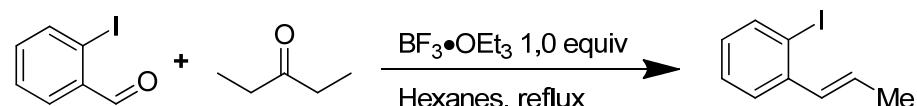
2-iodobenzaldehyde (0.510 g, 2.2 mmol, 1.0 equiv.) and 1-(triphenylphosphoranylidene)propan-2-one (0.891 g, 2.8 mmol, 1.27 equiv.) were added to a 50 mL round-bottomed flask containing 12 mL of toluene. The reaction mixture was stirred for 3 hours at 90 °C. After cooling the reaction flask to room temperature, the toluene was evaporated under reduced pressure, diluted with 50 mL, and the solid

triphenylphosphine oxide was removed via celite filtration. The crude product was purified by flash chromatography (5% Ethyl Acetate in hexanes). (0.558 g, 76%)

¹H NMR (500 MHz, CDCl₃): δ 7.95 – 7.87 (m, 2H), 7.56 (dd, J = 7.8, 1.7 Hz, 1H), 7.39 – 7.34 (m, 1H), 7.06 (td, J = 7.6, 1.7 Hz, 1H), 6.33 (d, J = 15.8 Hz, 1H), 3.84 (s, 3H).

¹³C NMR (126 MHz, CDCl₃): δ 166.7, 147.9, 140.0, 137.8, 131.3, 128.6, 127.4, 120.8, 101.2, 51.9.

(E)-1-iodo-2-(prop-1-en-1-yl)benzene 1d:



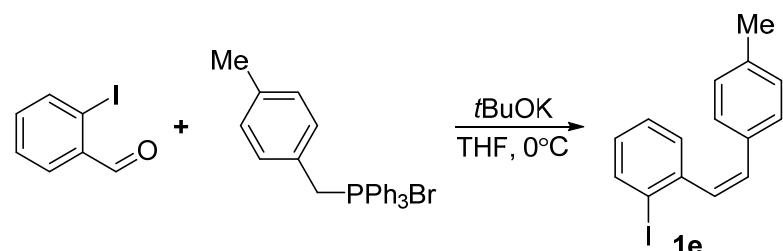
2-iodobenzaldehyde (1.00g, 4.3 mmol, 1.0 equiv.), 3-pentanone (0.414 g, 0.5 mL, 4.8 mmol, 1.12 equiv.), and hexanes (10 mL, 2.3M) were added to a 50 mL rounded-bottom flask. BF₃•OEt₃ (0.610 g, 0.53 mL, 4.3 mmol, 1.0 equiv.) was added dropwise at room temperature, and then the reaction mixture was heated to reflux. The reaction mixture was diluted in hexanes (50 mL) and transferred to a separatory funnel, washed twice with DI H₂O (2 x 50 mL) and once with brine. The organics were dried over anhydrous Na₂SO₄, filtered, concentrated onto silica and purified by flash chromatography (Hexanes) to provide **1d** (0.456 g, 45%).

¹H NMR (500 MHz, CDCl₃): δ 7.84 (dd, J = 7.9, 1.3 Hz, 1H), 7.46 (dd, J = 7.8, 1.7 Hz, 1H), 7.34 – 7.23 (m, 1H), 6.92 (td, J = 7.6, 1.7 Hz, 1H), 6.61 (dd, J = 15.5, 1.8 Hz, 1H), 6.15 (dq, J = 15.5, 6.6 Hz, 1H), 1.96 (dd, J = 6.7, 1.8 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃): δ 141.0, 139.4, 134.8, 129.1, 128.4, 128.3, 126.4, 99.3, 18.6.

HR-MS (ESI+): 244.9827 (calculated for M+H) 244.9811 (found)

(Z)-1-iodo-2-(4-methylstyryl)benzene 1e:

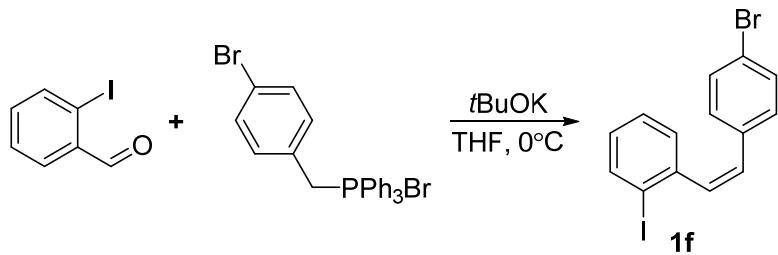


1f was prepared by the general method above with 178 mg (51%) of **1e** was isolated.

¹H NMR (500 MHz, CDCl₃): δ 7.96 – 7.88 (m, 1H), 7.65 (dd, J = 7.8, 1.7 Hz, 1H), 7.56 – 7.47 (m, 2H), 7.38 (td, J = 7.6, 1.3 Hz, 1H), 7.35 – 7.28 (m, 1H), 7.23 (d, J = 7.8 Hz, 2H), 7.02 – 6.93 (m, 2H), 2.42 (s, 3H).

¹³C NMR (126 MHz, CDCl₃): δ 140.5, 139.6, 138.1, 134.2, 131.6, 131.5, 129.5, 128.8, 128.4, 126.8, 126.22, 100.5, 21.4.

(Z)-1-(4-bromostyryl)-2-iodobenzene 1f:

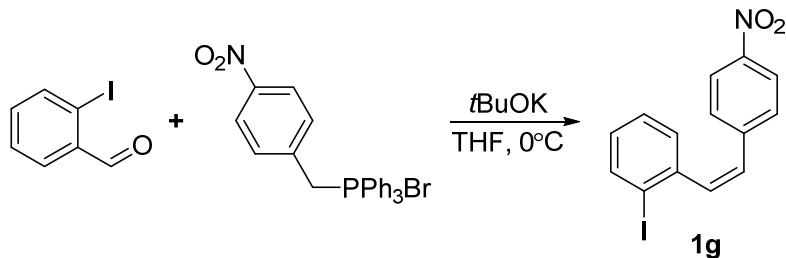


Prepared by the general method A. 210 mg (55%) of **1f** isolated.

¹H NMR (500 MHz, CDCl₃): δ 7.92 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.36 – 7.29 (m, 2H), 7.22 – 7.10 (m, 2H), 7.04 – 6.91 (m, 3H), 6.58 (d, *J* = 1.6 Hz, 2H).

¹³C NMR (126 MHz, CDCl₃): δ 141.3, 139.2, 135.1, 134.4, 131.4, 130.6, 130.1, 129.8, 129.0, 128.1, 121.2, 99.6.

(Z)-1-iodo-2-(4-nitrostyryl)benzene 1g:



Prepared by the general method A. 178 mg (51%) of **1g** was isolated.

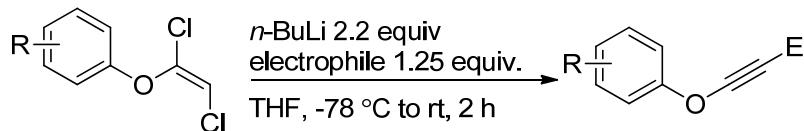
¹H NMR (500 MHz, CDCl₃): δ 8.11 – 8.02 (m, 2H), 7.94 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.32 – 7.24 (m, 2H), 7.20 (td, *J* = 7.5, 1.2 Hz, 1H), 7.07 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.01 (td, *J* = 7.7, 1.7 Hz, 1H), 6.77 (d, *J* = 12.0 Hz, 1H), 6.71 (d, *J* = 12.0 Hz, 1H).

¹³C NMR (126 MHz, CDCl₃): δ 146.5, 143.1, 140.7, 139.4, 137.4, 130.0, 129.7, 129.5, 128.9, 128.3, 123.6, 99.3.

Synthesis of Ynol Ether Substrates:

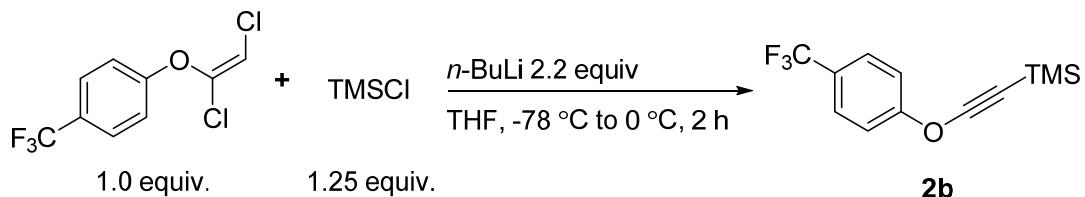
2a was made according to literature procedure.⁴

General Method B: the synthesis of aryl ynol ethers **2b-c, 2f-h.**



A rounded-bottom flask was purged of ambient air and backfilled with N₂ gas (2x). The appropriate aryl dichlorovinyl ether (1.0 equiv.) and THF (0.33 M) were added to a rounded-bottom flask, and the flask was cooled to -78 °C using a dry ice/acetone bath. Once cool, 2.5 M n-butyllithium (2.2 equiv.) was added dropwise and allowed to stir for 30 minutes. Next, the appropriate electrophile (1.25 equiv.) was added at -78 °C and allowed to warm to room temperature over 1 hour. The reaction was quenched with DI water, diluted with 50 mL of diethyl ether, and transferred to a separatory funnel. The mixture was washed water (2 x 50 mL), brine (1 x 50 mL). The organic layer was dried over anhydrous Na₂SO₄, and filtered. The mixture was then concentrated and reconstituted in hexane. Finally, the organic mixture was concentrated onto silica and purified via flash column chromatography (Hexanes/Ethyl Acetate).

Trimethyl((4-(trifluoromethyl)phenoxy)ethynyl)silane **2b:**



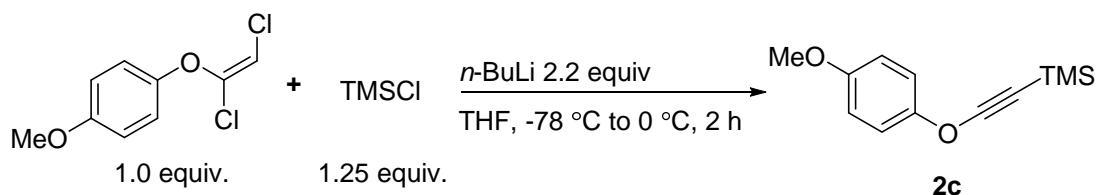
Prepared by general method B. 0.454 g (53%) of **2b** was isolated.

¹H NMR (500 MHz, CDCl₃): δ 7.70 – 7.58 (m, 2H), 7.44 – 7.34 (m, 2H), 0.26 (s, 9H).

¹³C NMR (126 MHz, CDCl₃): δ 157.8, 127.2, 124.9, 116.7, 115.4, 46.1, 0.34.

HR-MS (ESI): 257.0609 (calculated for M+H) 257.0612(found)

((4-methoxyphenoxy)ethynyl)trimethylsilane **2c:**



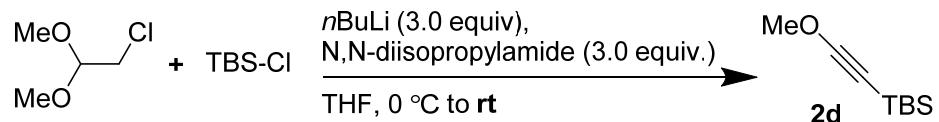
Prepared by general method B. 0.351 g (23%) of **2c** was isolated.

¹H NMR (500 MHz, CDCl₃): δ 7.23 – 7.18 (m, 2H), 6.93 – 6.87 (m, 2H), 3.81 (s, 3H), 0.25 (s, 9H).

¹³C NMR (126 MHz, CDCl₃): δ 156.4, 149.5, 115.8, 114.6, 103.4, 55.7, 43.4, 0.5.

HR-MS (ESI+): 221.0998 (calculated for M+H) 221.0993 (found)

tert-butyl(methoxyethynyl)dimethylsilane 2d:

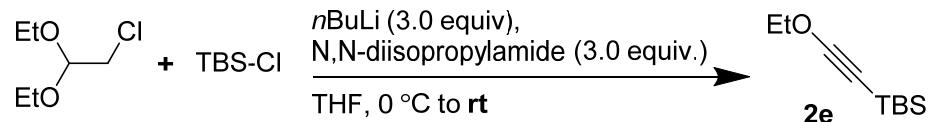


N,N-diisopropylamide (19.5 mmol, 2.7 mL, 3.0 equiv.) and THF (60 mL) were added to a 250 mL round-bottomed flask and placed under an N₂ atmosphere. The reaction mixture was cooled to 0 °C and *n*-butyllithium (2.5 M in hexanes, 8.5 mL, 19.5 mmol, 3.0 equiv.) was added dropwise, and allowed to stir at 0 °C for 10 minutes. Next chloroacetaldehyde dimethyl acetal (0.97 mL, 6.5 mmol, 1.0 equiv) was added, and the mixture was allowed to stir for 30 minutes at 0 °C for 30 minutes. Then, tertbutyldimethylsilyl chloride (1.960 g, 13.0 mmol, 2.0 equiv.) was added, the reaction mixture was warmed to room temperature, and allowed to stir for 1 hour. The reaction was quenched with saturated NH₄Cl and transferred to a separatory funnel. The aqueous layer was removed and the organic layer was washed with DI water (2 x 50 mL), brine (1 x 50 mL). The organic layer dried over anhydrous Na₂SO₄, filtered, concentrated under reduced pressure, and purified via automated flash chromatography (Hexanes) to provide **2d** (0.245 g, 22%).

¹H NMR (500 MHz, CDCl₃): δ 3.92 (s, 3H), 0.94 (s, 9H), 0.09 (s, 6H)

¹³C NMR (126 MHz, CDCl₃): δ 111.25, 65.84, 33.66, 26.10, 16.62, -4.01.

tert-butyl(ethoxyethynyl)dimethylsilane 2e:

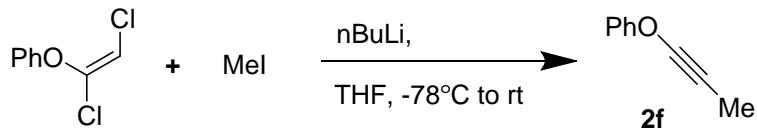


N,N-diisopropylamide (19.5 mmol, 2.7 mL, 3.0 equiv.) and THF (60 mL) were added to a 250 mL round-bottomed flask and placed under an N₂ atmosphere. The reaction mixture was cooled to 0 °C and *n*-butyllithium (2.5 M in hexanes, 8.5 mL, 19.5 mmol, 3.0 equiv.) was added dropwise, and allowed to stir at 0 °C for 10 minutes. Next chloroacetaldehyde diethyl acetal (0.97 mL, 6.5 mmol, 1.0 equiv) was added, and the mixture was allowed to stir for 30 minutes at 0 °C for 30 minutes. Then, tertbutyldimethylsilyl chloride (1.960 g, 13.0 mmol, 2.0 equiv.) was added, the reaction mixture was warmed to room temperature, and allowed to stir for 1 hour. The reaction was quenched with saturated NH₄Cl and transferred to a separatory funnel. The aqueous layer was removed and the organic layer was washed with DI water (2 x 50 mL), brine (1 x 50 mL). The organic layer dried over anhydrous Na₂SO₄, filtered, concentrated under reduced pressure, and purified via automated flash chromatography (Hexanes) to provide **2e** (0.180 g, 19%).

¹H NMR (500 MHz, CDCl₃): δ 4.15 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H), 0.94 (s, 9H), 0.09 (s, 6H).

¹³C NMR (126 MHz, CDCl₃): δ 109.8, 74.8, 34.9, 26.1, 16.7, 14.3, -4.0.

(prop-1-yn-1-yloxy)benzene 2f:

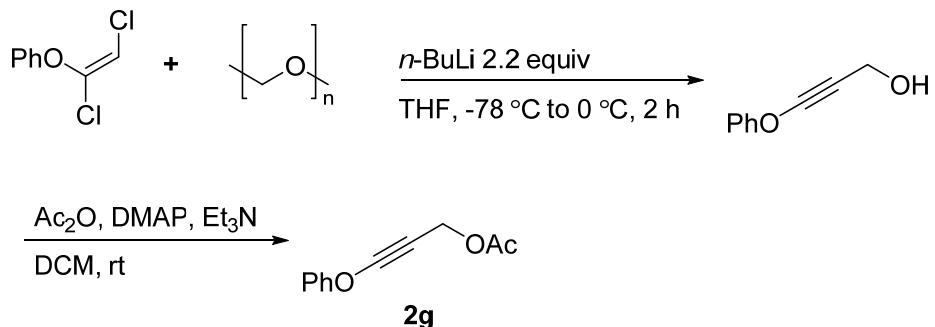


Prepared by general method B. 0.576 g (78%) of **2f** was isolated.

¹H NMR (500 MHz, CDCl₃) δ 7.42 – 7.35 (m, 2H), 7.17 (m, 1H), 7.09 – 7.05 (m, 2H), 2.31 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 154.4, 134.8, 129.7, 124.0, 116.6, 116.4, 21.6.

3-phenoxyprop-2-yn-1-yl acetate 2g:



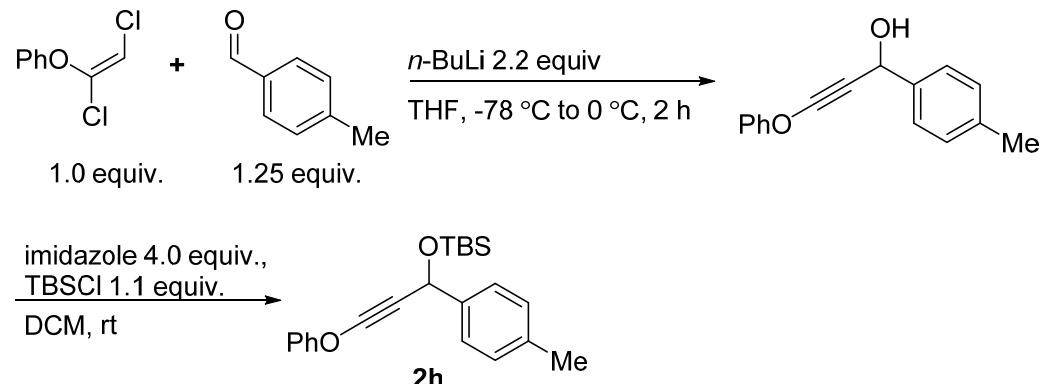
Prepared by a modified procedure of general method B. 0.447 g (23%) of **2g** was isolated.

- (1) (1,2-dichlorovinyl)oxybenzene (1.790 g, 10 mmol, 1.0 equiv.) and 30 mL THF were added to a dried, purged (N₂) round-bottomed flask. The mixture was cooled to -78 °C in a dry ice acetone bath and *n*-butyllithium (2.5 M in Hexanes, 8.8 mL, 22 mmol, 2.2 equiv.) was added dropwise over 5 minutes and stirred for 30 minutes at that temperature. Next, paraformaldehyde (0.600 g, 20 mmol, 2.0 equiv.) was added and the reaction mixture was allowed to warm to room temperature over 1 hour. The reaction mixture was quenched with 30 mL of saturated and aqueous NH₄Cl and transferred to a separatory funnel. The aqueous layer was removed and the top organic layer was washed with DI water (1 x 50 mL) and Brine (1 x 50 mL). The dried organic layer was dried with anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure.
- (2) The concentrated crude material was diluted in 10 mL of dichloromethane. Next, triethylamine (1.210 g, 1.7 mL, 12.0 mmol, 1.2 equiv.), a catalytic amount of N,N-dimethylaminopyridine (2.2 mg), and acetic anhydride (2.040 g, 20 mmol, 2.0 equiv.) were added to the reaction mixture and allowed to stir for 2 hours at room temperature. The crude reaction mixture was diluted with dichloromethane, washed once with DI water, once with brine, and dried over anhydrous Na₂SO₄. The organic material was concentrated under reduced pressure and purified by flash chromatography (25% Ethyl Acetate/Hexanes) to provide **2f** (0.447g, 23%) over two steps.

¹H NMR (500 MHz, CDCl₃) δ 7.43 – 7.35 (m, 2H), 7.29 (m, 2H), 7.21 – 7.13 (m, 1H), 4.85 (s, 2H), 2.13 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 170.5, 155.7, 129.7, 124.7, 115.0, 88.7, 52.3, 39.8, 20.9.

tert-butyldimethyl((3-phenoxy-1-(p-tolyl)prop-2-yn-1-yl)oxy)silane 2h:



Prepared by a modified procedure of general method B. 0.810 g (34%) of **2h** was isolated.

(1) ((1,2-dichlorovinyl)oxy)benzene (1.790 g, 10 mmol, 1.0 equiv.) and 30 mL THF were added to a dried, purged (N_2) round-bottomed flask. The mixture was cooled to -78 °C and *n*-butyllithium (2.5 M in Hexanes, 8.8 mL, 22 mmol, 2.2 equiv.) was added dropwise over 5 minutes and was allowed to stir for 30 minutes at that temperature. Next, tolualdehyde (1.5 mL, 12.5 mmol, 1.25 equiv.) was added and the reaction mixture was allowed to warm to room temperature over 1 hour. The reaction mixture was quenched with 30 mL of saturated and aqueous NH_4Cl and transferred to a separatory funnel. The aqueous layer was removed and the top organic layer was washed with DI water (1 x 50 mL) and Brine (1 x 50 mL). The dried organic layer was dried with anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. Due to difficulties separating the product from a minor impurity via flash chromatography the 3-phenoxy-1-(p-tolyl)prop-2-yn-1-ol was protected as the tert-butyldimethylsilyl ether.

Synthesis of tert-butyldimethyl((3-phenoxy-1-(p-tolyl)prop-2-yn-1-yl)oxy)silane

(2) The crude 3-phenoxy-1-(p-tolyl)prop-2-yn-1-ol isolated from step 1 was diluted in dichloromethane (30 mL). Next, imidazole (1.36 g, 20 mmol, 2.0 equiv.) and tert-butyldimethylsilyl chloride (2.26 g, 15 mmol, 1.5 equiv.) were added and the reaction mixture stirred at room temperature for 3 hours. The reaction mixture was quenched with 30 mL of saturated and aqueous NH_4Cl and transferred to a separatory funnel. The aqueous layer was removed and the top organic layer was washed with DI water (1 x 50 mL) and Brine (1 x 50 mL). The dried organic layer was dried with anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. (5% Ethyl Acetate/Hexanes) (0.810 g, 2-step yield 34%).

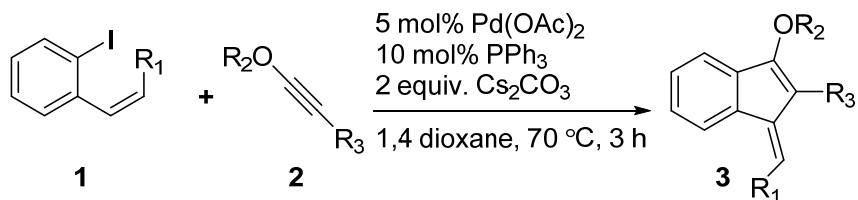
1H NMR (500 MHz, $CDCl_3$): δ 7.46 – 7.40 (m, 2H), 7.40 – 7.33 (m, 2H), 7.29 – 7.20 (m, 3H), 7.17 (m, 1H), 7.07 – 6.91 (m, 2H), 6.08 (d, J = 3.8 Hz, 1H), 2.40 (d, J = 2.6 Hz, 3H), 1.01 (d, J = 3.9 Hz, 9H), 0.20 (dd, J = 30.5, 3.8 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 154.1, 137.9, 137.5, 134.8, 129.7, 128.9, 1255, 124.9, 124.3, 116.8, 71.6, 25.8, 21.2, 18.2, -4.9.

HR-MS (ESI+): 353.1937 (calculated for $M+H$) 353.1933 (found)

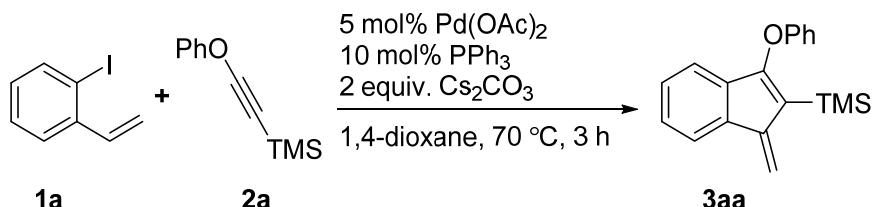
General Procedure C: Synthesis of Indenes:

Synthesis of indenes **3**.



$\text{Pd}(\text{OAc})_2$ (5 mol%), PPh_3 (10 mol%), and Cs_2CO_3 (2.0 equiv.) were added to a 10 mL rounded bottom flask. Next, a solution containing styrene **1** (0.25 mmol) and ynone ether **2** (0.50 mmol) in 1,4-dioxane (0.2 M) was added to the rounded bottom flask, and the flask was placed under a nitrogen atmosphere. The reaction flask was then heated to 70 °C for 3 hours. After the reaction was complete, the crude reaction mixture was filtered through celite, and concentrated directly onto silica. Flash chromatography was performed (5% Ethyl Acetate/Hexanes) to obtain the purified compound **3**.

1-methylene-2-trimethylsilyl-3-phenoxyindene 3aa:



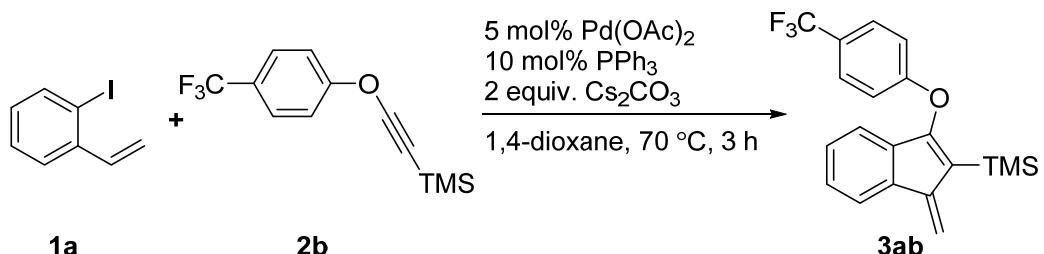
3aa was prepared by general method C on a 1.5 mmol scale (0.424 g, 97%). When run on a 0.25 mmol scale the reaction yielded (68.1 mg and 65.8 mg, 92%).

^1H NMR (500 MHz, CDCl_3): δ 7.69 (d, J = 7.5 Hz, 1H), 7.33 (dd, J = 8.7, 7.5 Hz, 2H), 7.25 (m, 1H), 7.18 – 7.00 (m, 4H), 6.79 (d, J = 7.5 Hz, 1H), 6.18 (s, 1H), 5.87 (s, 1H), 0.35 (s, 9H).

^{13}C NMR (126 MHz, CDCl_3): δ 164.8, 157.0, 147.3, 139.0, 136.7, 129.6, 127.5, 126.2, 122.6, 122.4, 119.3, 119.2, 116.5, 113.2, 0.4.

HR-MS (ESI+): 293.1362 (calculated for $\text{M}+\text{H}$) 293.1355 (found)

trimethyl(1-methylene-3-(4-(trifluoromethyl)phenoxy)-1H-inden-2-yl)silane 3ab:



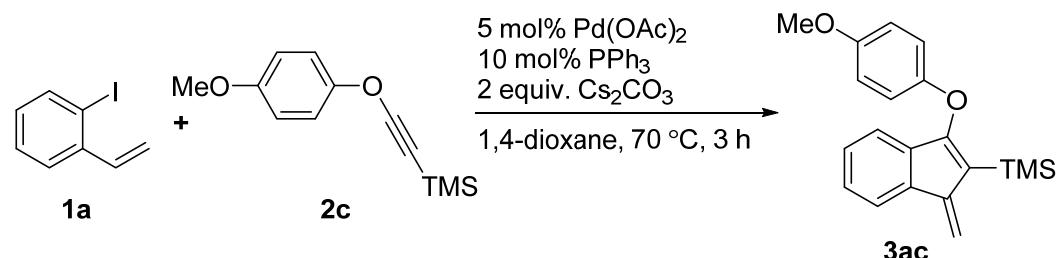
3ab was prepared by general method C (74.7 mg and 76.1 mg, 84%).

¹H NMR (500 MHz, CDCl₃): δ 7.70 (d, J = 7.6 Hz, 1H), 7.59 (d, J = 8.8 Hz, 2H), 7.28 (dd, J = 7.5 Hz, 1.1 Hz, 1H), 7.18 (dd, J = 7.5, 1.0 Hz, 1H), 7.10 (d, J = 8.6 Hz, 2H), 6.80 (d, J = 7.5 Hz, 1H), 6.23 (s, 1H), 5.91 (s, 1H), 0.33 (s, 9H).

¹³C NMR (126 MHz, CDCl₃): δ 163.7, 159.6, 147.0, 138.7, 136.1, 127.7, 127.1 (q, J = 3.7 Hz), 126.6, 123.8, 119.5, 118.7, 116.2, 114.4, 0.4.

HR-MS (ESI+): 361.1236 (calculated for M+H) 361.1223 (found)

1-methylene-2-trimethylsilyl-3-(4-methoxyphenoxy)indene 3ac:



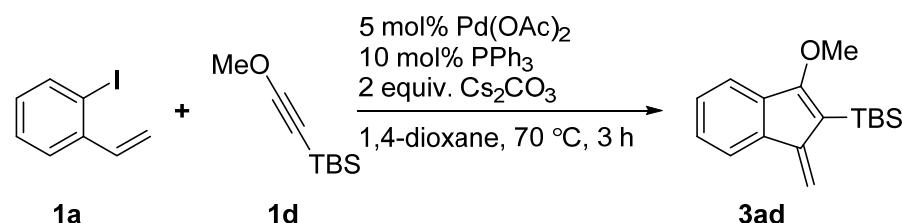
3ac was prepared by general method C (68.2 mg and 75.0 mg, 89%).

¹H NMR (500 MHz, CDCl³): δ 7.65 (d, J = 7.5 Hz, 1H), 7.22 (m, 1H), 7.11 (m, 1H), 6.97 (d, J = 9.1 Hz, 2H), 6.85 (d, J = 9.1 Hz, 1H), 6.72 (d, J = 7.6 Hz, 1H), 6.13 (s, 1H), 5.83 (s, 1H), 3.81 (s, 3H), 0.34 (s, 9H).

¹³C NMR (126 MHz, CDCl₃): δ 165.3, 155.1, 150.8, 147.3, 139.1, 1367, 127.4, 126.1, 121.7, 119.3, 119.18, 117.5, 114.6, 112.8, 55.6, 0.4.

HR-MS (ESI-): 321.1311 (calculated for M-) 321.1326 (found)

1-methylene-2-*tert*-butyldimethylsilyl-3-phenoxyindene 3ad:

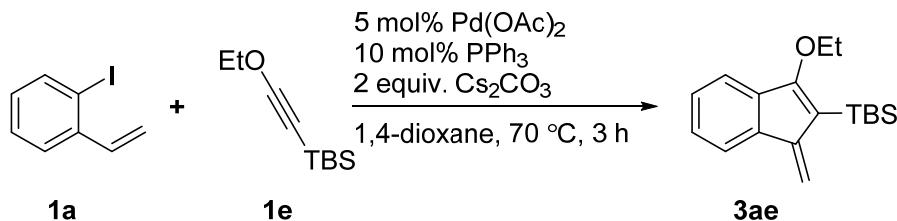


3ad was prepared by general method C (45.0 mg and 39.9 mg, 64%).

¹H NMR (500 MHz, CDCl₃) δ 7.71 – 7.62 (m, 1H), 7.50 – 7.40 (m, 1H), 7.34 – 7.21 (m, 2H), 6.05 (s, 1H), 5.71 (s, 1H), 4.04 (s, 3H), 0.95 (s, 9H), 0.34 (s, 6H).

¹³C NMR (126 MHz, CDCl₃) δ 171.7, 148.0, 139.8, 136.9, 127.4, 126.1, 119.2, 118.8, 116.18, 112.66, 59.22, 26.90, 17.77, -3.51.

tert-butyl(3-ethoxy-1-methylene-1H-inden-2-yl)dimethylsilane 3ae:

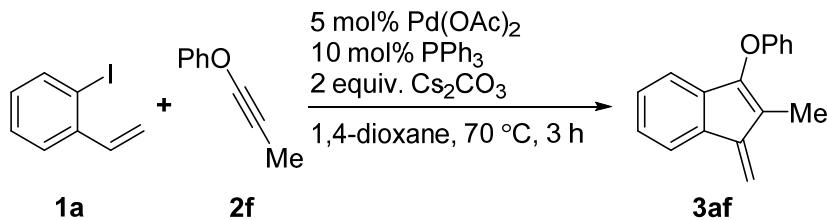


3ae was prepared by general method C (57.5 mg, 80%).

¹H NMR (500 MHz, CDCl₃): δ 7.67 – 7.61 (m, 1H), 7.43 – 7.38 (m, 1H), 7.34 – 7.20 (m, 2H), 6.03 (s, 1H), 5.70 (s, 1H), 4.35 (q, J = 7.0 Hz, 2H), 1.48 (t, J = 7.0 Hz, 3H), 0.96 (s, 9H), 0.35 (s, 6H).

¹³C NMR (126 MHz, CDCl₃): δ 170.9, 148.1, 139.9, 137.2, 127.3, 126.0, 119.1, 119.0, 115.5, 112.2, 67.2, 27.0, 17.9, -3.3.

2-methyl-1-methylene-3-phenoxy-1H-indene 3af:



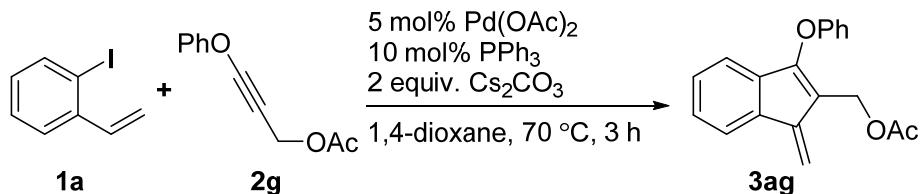
3af was prepared by general method C (10.0 mg and 10.2 mg, 17%).

¹H NMR (500 MHz, CDCl₃) δ 7.71 – 7.52 (m, 1H), 7.32 (dd, J = 8.7, 7.4 Hz, 2H), 7.16 (m, 2H), 7.10 – 7.02 (m, 3H), 6.86 – 6.80 (m, 1H), 6.04 (s, 1H), 5.70 (s, 1H), 2.03 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 156.9, 152.6, 145.3, 137.0, 1350, 129.6, 127.7 125.3, 122.4, 121.0, 119.20, 118.0, 116.4, 109.7, 8.0.

HR-MS (ESI+): 235.1123 (calculated for M+H) 235.1116 (found)

(1-methylene-3-phenoxy-1H-inden-2-yl)methyl acetate 3ag

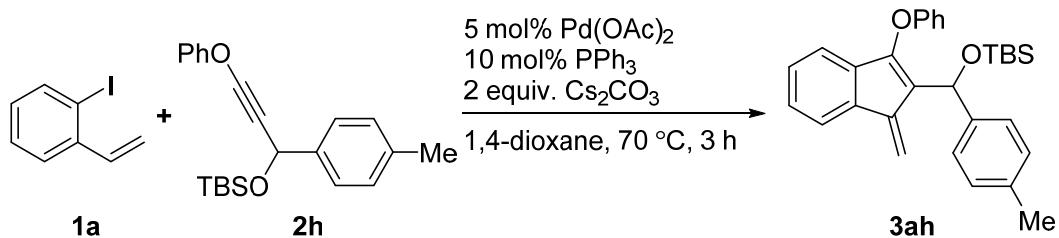


3ag was prepared by general method C (43.8 mg and 35.2 mg, 54%).

¹H NMR (500 MHz, CDCl₃) δ 7.67 (d, J = 7.5 Hz, 1H), 7.34 (dd, J = 8.7, 7.4 Hz, 2H), 7.30 – 7.25 (m, 2H), 7.20 – 7.03 (m, 4H), 6.86 (m, 1H), 6.13 (s, 1H), 5.83 (s, 1H), 5.07 (s, 2H), 2.05 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 170.9, 156.6, 156.5, 142.9, 135.5, 135.4, 129.6, 1278, 126.8, 123.4, 119.68, 119.7, 117.7, 117.2, 111.1, 55.4, 21.0.

tert-butyldimethyl((1-methylene-3-phenoxy-1H-inden-2-yl)(p-tolyl)methoxy)silane 3ah:



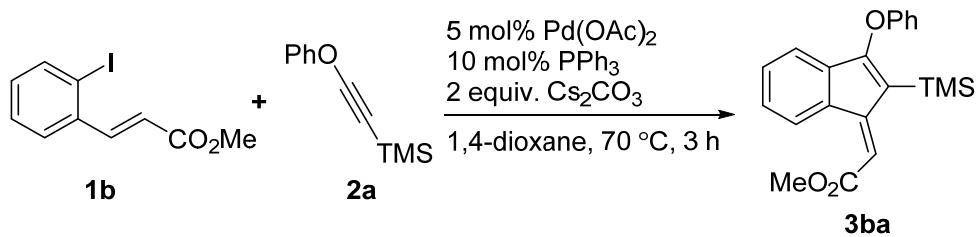
3ah was prepared by general method C (105.6mg and 107.6 mg, 94%).

¹H NMR (500 MHz, CDCl₃): δ 7.56 (d, J = 7.4 Hz, 1H), 7.42 – 7.32 (m, 4H), 7.22 – 7.04 (m, 7H), 6.73 (d, J = 7.5 Hz, 1H), 6.17 (s, 1H), 6.05 (s, 2H), 2.34 (s, 3H), 0.97 (s, 9H).

¹³C NMR (126 MHz, CDCl₃): δ 156.7, 152.2, 141.5, 140.9, 136.1, 136.0, 135.1, 129.7, 128.8, 127.3, 127.1, 126.1, 125.5, 123.0, 119.5, 119.4, 117.1, 114.8, 67.9, 26.0, 21.2, 18.4, -5.0

HR-MS (ESI+): 461.2489 (calculated for M-Li⁺) 461.2489 (found)

(E/Z)-methyl 2-(3-phenoxy-2-(trimethylsilyl)-1H-inden-1-ylidene)acetate 3ba:



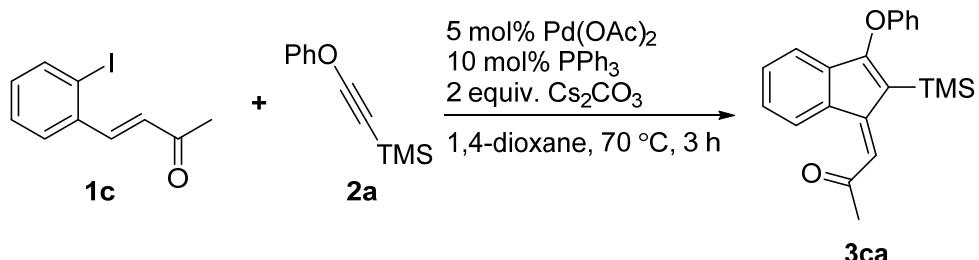
3ba was prepared by general method C (75.0 mg and 70.3 mg, 83%). Note: the starting 2-iodostyrene had a stereoisomeric ratio *E/Z* = 5.5:1.0.

¹H NMR (500 MHz, Chloroform-d) δ 8.66 (d, J = 7.7 Hz, 1H), 7.33 (dd, J = 8.6, 7.3 Hz, 2H), 7.29 – 7.23 (m, 1H), 7.17 – 7.07 (m, 2H), 7.04 (m, 2H), 6.70 (m, 1H), 6.49 (s, 1H), 3.90 (s, 3H), 0.36 (s, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 167.4, 166.7, 156.6, 153.2, 138.5, 135.6, 129.7, 129.2, 127.8, 127.2, 124.4, 122.8, 119.4, 118.8, 116.5, 51.8, 0.6.

HR-MS (ESI+): 351.1416 (calculated for M+H) 351.1415 (found)

(E/Z)-1-(3-phenoxy-2-(trimethylsilyl)-1H-inden-1-ylidene)propan-2-one 3ca:

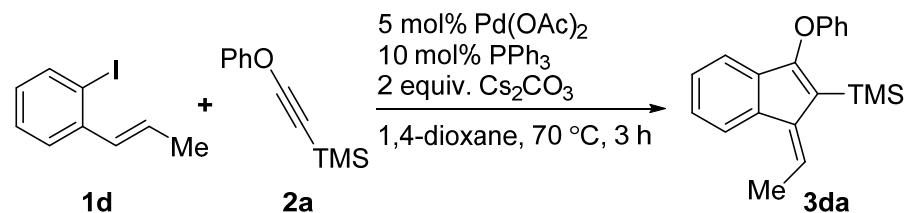


3ca was prepared by general method C (49.1 mg and 52.9 mg, 61%).

¹H NMR (500 MHz, CDCl₃): δ 8.42 (dt, J = 7.7, 0.9 Hz, 1H), 7.32 (dd, J = 8.6, 7.4 Hz, 2H), 7.22 (td, J = 7.6, 1.2 Hz, 1H), 7.11 (m, 2H), 7.05 – 6.94 (m, 2H), 6.77 (s, 1H), 6.67 (dt, J = 7.5, 0.9 Hz, 1H), 2.48 (s, 3H), 0.34 (s, 9H).

¹³C NMR (126 MHz, CDCl₃): δ 199.2, 168.0, 156.6, 150.5, 138.3, 135.7, 129.7, 129.4, 128.0, 127.1, 126.4, 124.2, 122.9, 119.5, 116.5, 32.2, 0.6.

(E)-(1-ethylidene-3-phenoxy-1H-inden-2-yl)trimethylsilane 3da:



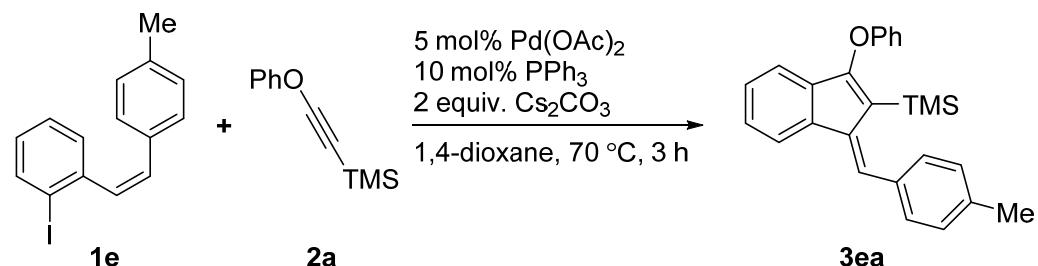
3da was prepared by general method C (45.9 mg and 51.7 mg, 64%).

¹H NMR (500 MHz, CDCl₃): δ 7.85 (d, J = 7.7 Hz, 1H), 7.31 (dd, J = 8.7, 7.3 Hz, 2H), 7.27 (td, J = 7.7, 1.3 Hz, 1H), 7.16 (td, J = 7.4, 1.0 Hz, 1H), 7.09 – 6.99 (m, 3H), 6.91 (dt, J = 7.5, 1.0 Hz, 1H), 6.60 (q, J = 7.5 Hz, 1H), 2.45 (d, J = 7.5 Hz, 3H), 0.33 (s, 9H).

¹³C NMR (126 MHz, CDCl₃): δ 161.4, 157.6, 141.7, 138.1, 137.6, 131.4, 129.6, 126.7, 126.0, 125.0, 124.1, 122.0, 119.1, 116.0, 16.4, 0.8.

HR-MS (ESI+): 307.1518 (calculated for M+H) 307.1513 (found)

(Z)-trimethyl(1-(4-methylbenzylidene)-3-phenoxy-1H-inden-2-yl)silane 3ea

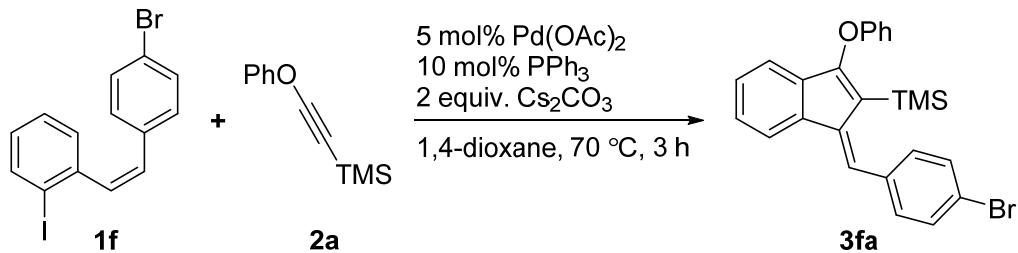


3ea was prepared by general method C (50.1 mg and 79.3 mg, 68%).

¹H NMR (500 MHz, CDCl₃): δ 7.51 (d, J = 7.8 Hz, 2H), 7.47 (d, J = 7.7 Hz, 1H), 7.44 (s, 1H), 7.38 – 7.29 (m, 4H), 7.11 – 7.05 (m, 5H), 7.00 (td, J = 7.5, 1.2 Hz, 1H), 6.85 (d, J = 7.5 Hz, 1H), 2.49 (s, 3H), 0.41 (s, 9H).

¹³C NMR (126 MHz, Chloroform-d): δ 162.8, 157.4, 141.4, 138.2, 137.9, 137.0, 134.6, 133.8, 129.6, 129.4, 129.2, 127.3, 125.8, 125.1, 123.6, 122.2, 119.0, 116.2, 21.5, 0.9.

(Z)-(1-(4-bromobenzylidene)-3-phenoxy-1H-inden-2-yl)trimethylsilane 3fa:

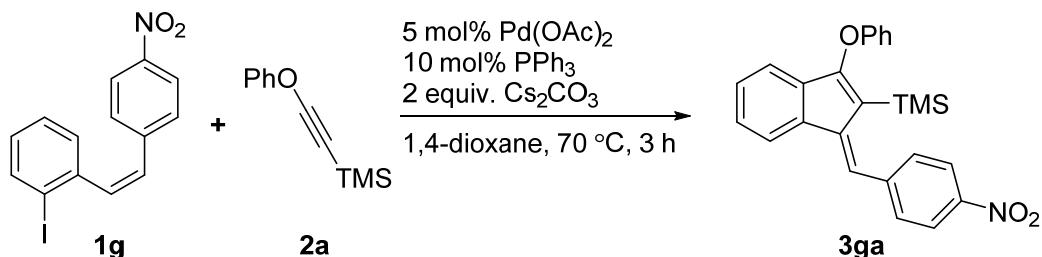


3fa was prepared by general method C (57.5 mg and 40.1 mg, 44%).

¹H NMR (500 MHz, CDCl₃): δ 7.75 (d, J = 7.6 Hz, 1H), 7.67 – 7.53 (m, 3H), 7.39 – 7.32 (m, 4H), 7.27 (td, J = 7.5, 1.1 Hz, 1H), 7.17 – 7.06 (m, 4H), 6.81 – 6.71 (m, 1H), -0.04 (s, 9H).

¹³C NMR (126 MHz, CDCl₃): δ 168.5, 156.8, 141.6, 141.2, 137.9, 135.0, 132.4, 131.6, 129.6, 127.2, 126.9, 126.2, 122.8, 122.2, 120.3, 119.5, 118.8, 117.2, 0.8.

(Z)-trimethyl(1-(4-nitrobenzylidene)-3-phenoxy-1H-inden-2-yl)silane 3ga:

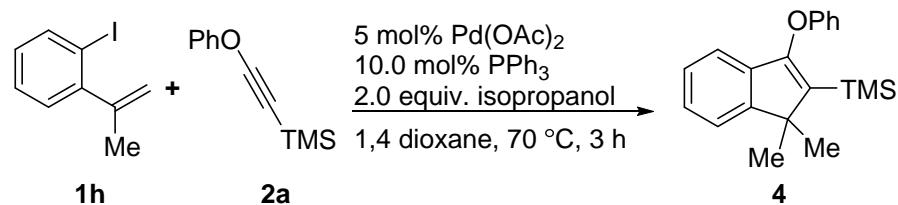


3ga was prepared by general method C (91.8 mg and 78.9 mg, 83%).

¹H NMR (500 MHz, CDCl₃): δ 8.30 (d, J = 8.7 Hz, 1H), 7.74 (dt, J = 7.7, 0.9 Hz, 1H), 7.62 (d, J = 8.6 Hz, 3H), 7.36 (dd, J = 8.6, 7.4 Hz, 2H), 7.31 – 7.23 (m, 2H), 7.17 – 7.03 (m, 4H), 6.70 (dd, J = 7.6, 0.9 Hz, 1H), -0.07 (s, 9H).

¹³C NMR (126 MHz, CDCl₃): δ 169.9, 156.5, 147.0, 145.7, 144.0, 141.0, 135.0, 131.5, 129.6, 127.5, 126.6, 125.1, 123.7, 123.2, 119.9, 119.5, 119.0, 117.4, 0.8.

(1,1-dimethyl-3-phenoxy-1H-inden-2-yl)trimethylsilane 4:

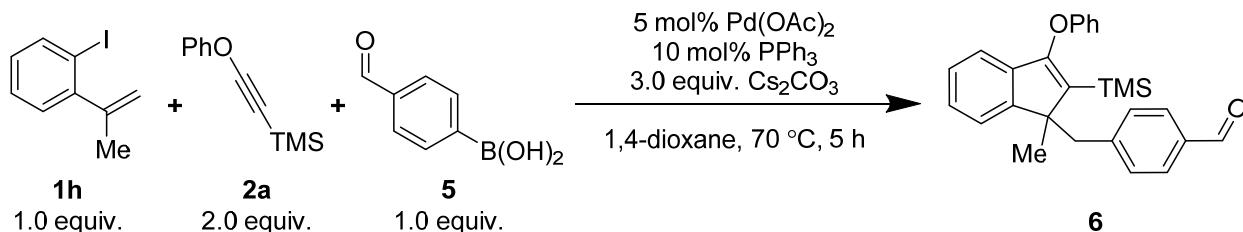


Pd(OAc)₂ (5 mol%), PPh₃ (10 mol%), and Cs₂CO₃ (2.0 equiv.) were added to a 10 mL rounded bottom flask. Next, a solution containing α -methyl-2-iodostyrene **1h** (0.25 mmol) and ynl ether **2a** (0.50 mmol) in 1,4-dioxane (0.2M) was added to the rounded bottom flask, and the flask was placed under a nitrogen atmosphere. Next, isopropyl alcohol (38 μ L, 0.5 mmol, 2.0 equiv.) was added and the reaction flask was then heated to 70 °C for 3 hours. After the reaction was complete, the crude reaction mixture was filtered through celite, and concentrated directly onto silica. Flash chromatography was performed (5% Ethyl Acetate/Hexanes) to obtain the purified compound **4** (57.7 mg, 75%).

¹H NMR (500 MHz, CDCl₃): δ 7.40 (dt, *J* = 7.6, 0.9 Hz, 1H), 7.34 – 7.28 (m, 2H), 7.24 (td, *J* = 7.4, 1.1 Hz, 1H), 7.10 (td, *J* = 7.5, 1.1 Hz, 1H), 7.05 (m, 1H), 7.03 – 6.95 (m, 2H), 6.83 (dt, *J* = 7.6, 1.0 Hz, 1H), 1.52 (s, 7H), 0.28 (s, 9H).

¹³C NMR (126 MHz, CDCl₃): δ 158.7, 157.3, 156.5, 138.9, 136.8, 129.5, 126.1, 126.1, 121.9, 121.1, 119.8, 116.0, 50.5, 25.6, 0.4.

4-((1-methyl-3-phenoxy-2-(trimethylsilyl)-1H-inden-1-yl)methyl)benzaldehyde 6

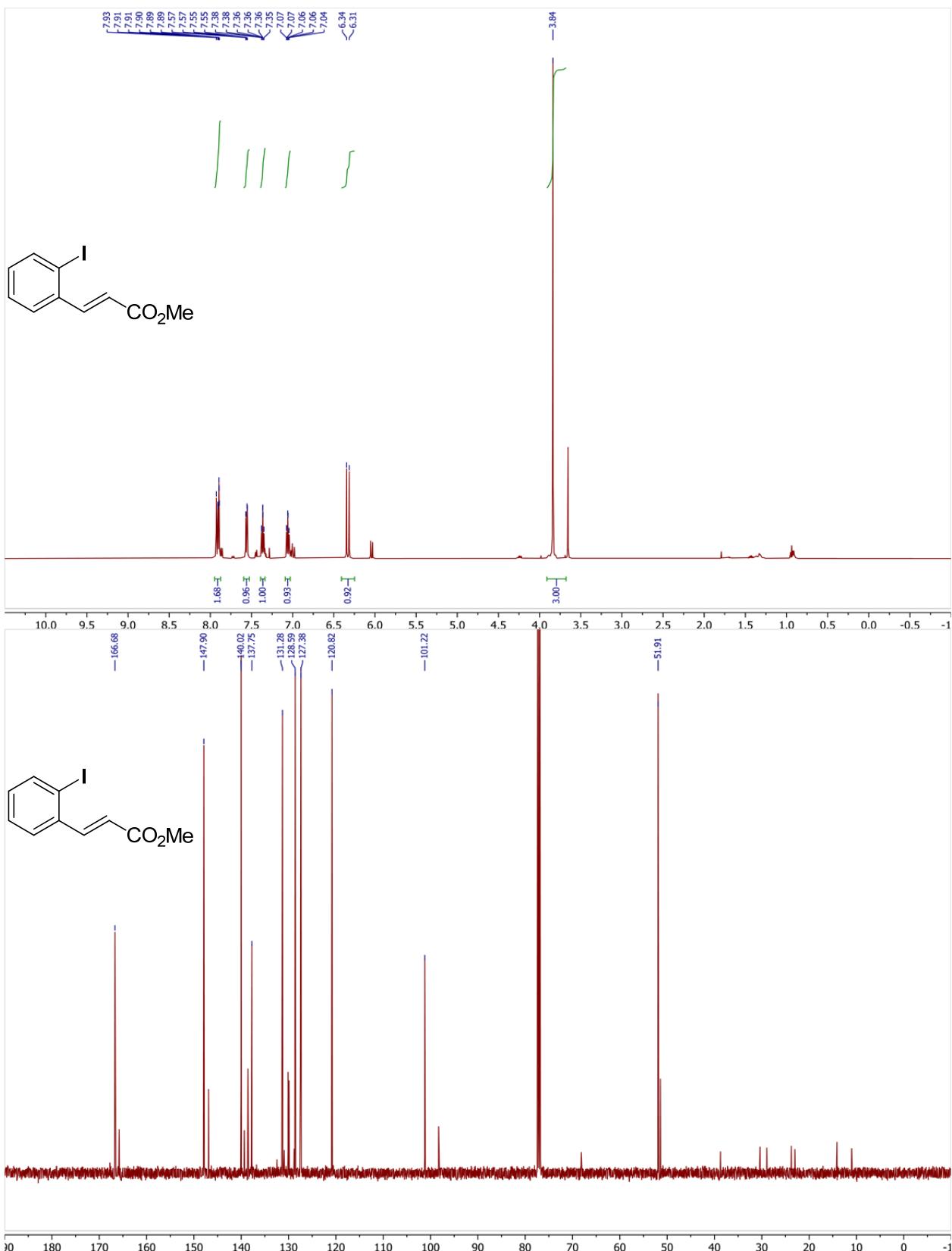


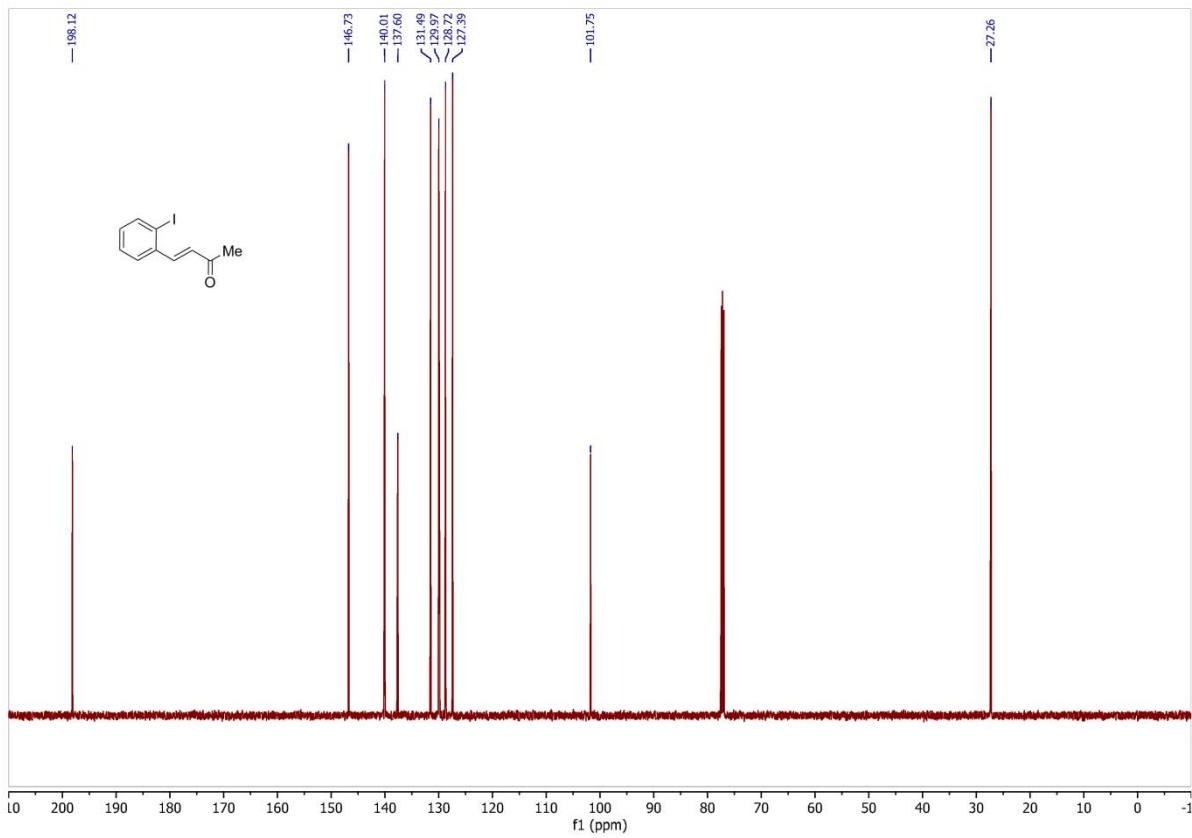
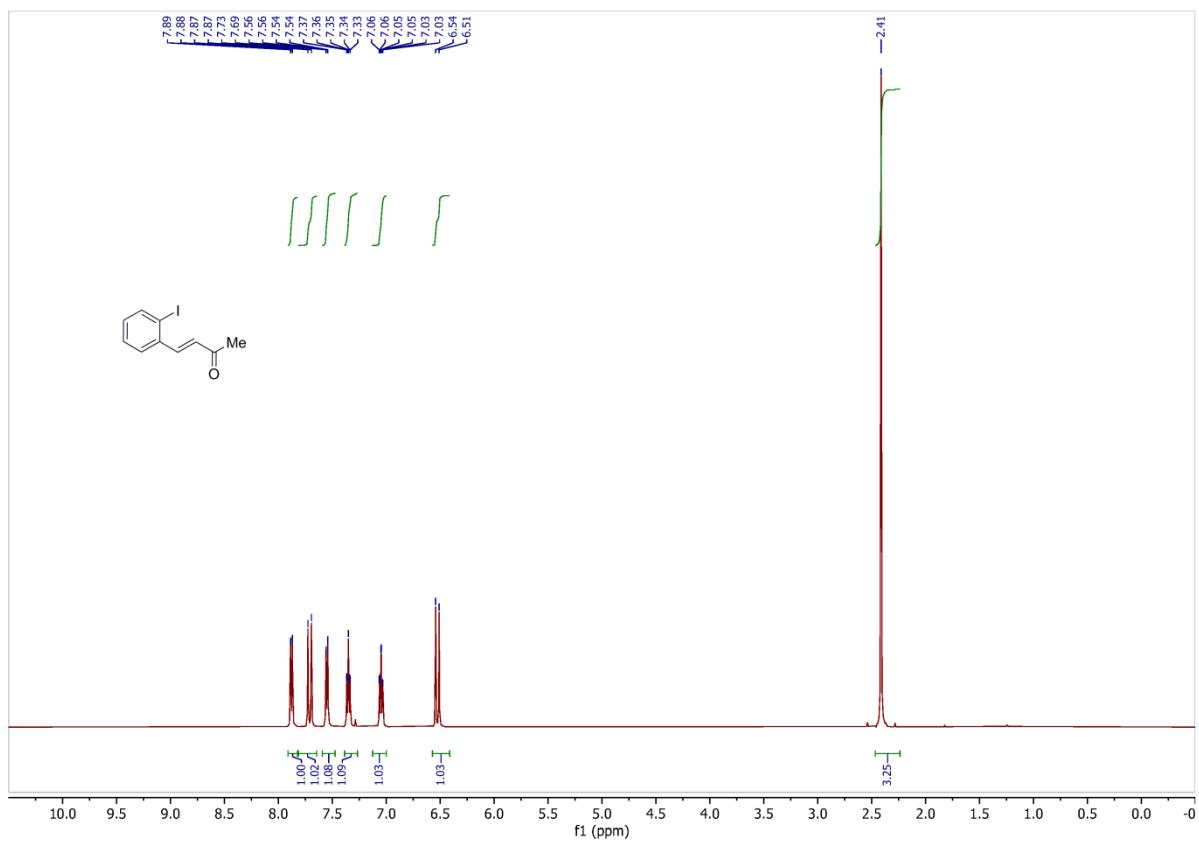
$\text{Pd}(\text{OAc})_2$ (2.8 mg, 0.013 mmol, 5 mol%), PPh_3 (6.6 mg, 0.025 mmol, 10 mol%), 4-formylphenylboronic acid **5** (37.5 mg, 0.25 mmol, 1.0 equiv.) and Cs_2CO_3 (244.4 mg, 0.75 mmol, 3.0 equiv.) were added to a 10 mL rounded bottom flask. Next, a solution containing α -methyl-2-iodostyrene **1h** (0.25 mmol) and ynl ether **2a** (0.50 mmol) in 1,4-dioxane (0.2M) was added to the rounded bottom flask, and the flask was placed under a nitrogen atmosphere. The reaction flask was then heated to 70 °C for 3 hours. After the reaction was complete, the crude reaction mixture was filtered through celite, and concentrated directly onto silica. Flash chromatography was performed (5% Ethyl Acetate/Hexanes) to obtain the purified compound **6** (42.0 mg, 40 %).

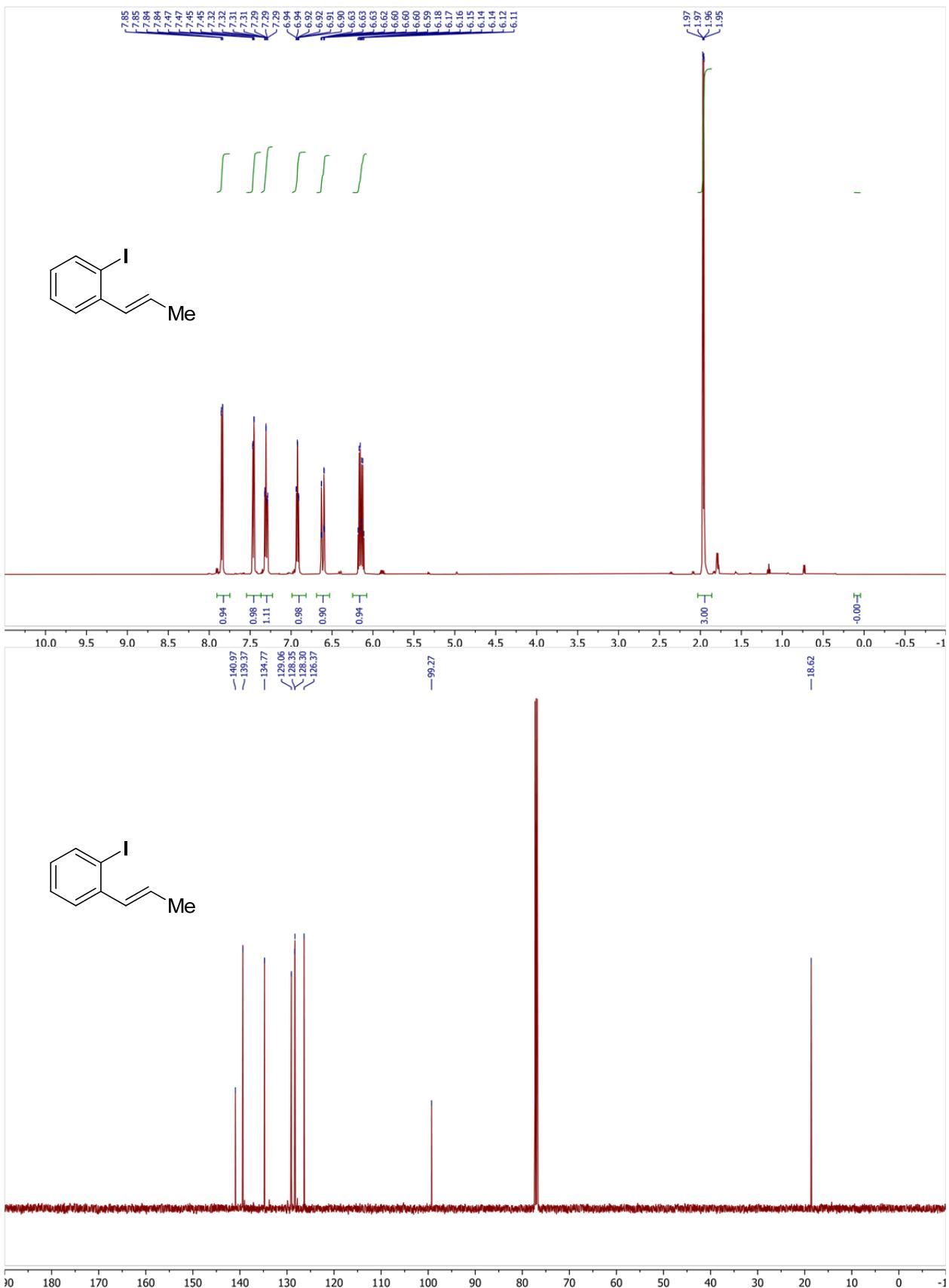
^1H NMR (500 MHz, CDCl_3): δ 9.86 (s, 1H), 7.75 (dd, J = 7.7, 1.6 Hz, 1H), 7.45 (td, J = 7.5, 1.6 Hz, 1H), 7.39 (td, J = 7.5, 1.3 Hz, 1H), 7.23 – 7.19 (m, 3H), 7.08 – 6.98 (m, 3H), 6.88 – 6.85 (m, 1H), 6.68 – 6.62 (m, 3H), 3.92 (d, J = 13.6 Hz, 1H), 3.40 (d, J = 13.6 Hz, 1H), 1.61 (s, 3H), 0.34 (s, 9H).

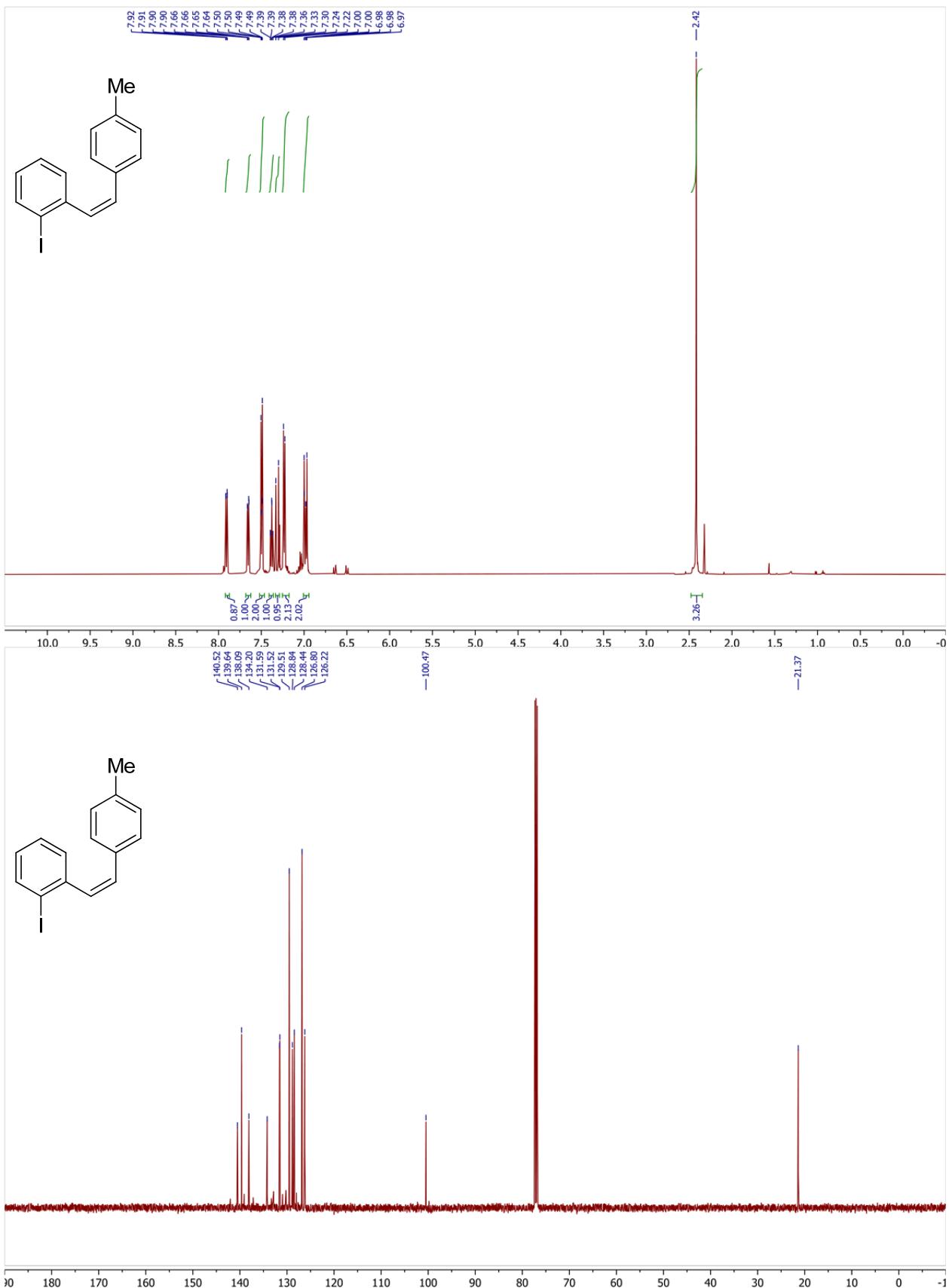
^{13}C NMR (126 MHz, CDCl_3): δ 191.2, 160.0, 156.9, 152.1, 140.8, 137.6, 137.1, 132.8, 132.6, 123.0, 129.4, 126.9, 126.7, 125.5, 123.0, 121.9, 119.9, 116.0, 55.1, 38.6, 24.0, 0.5.

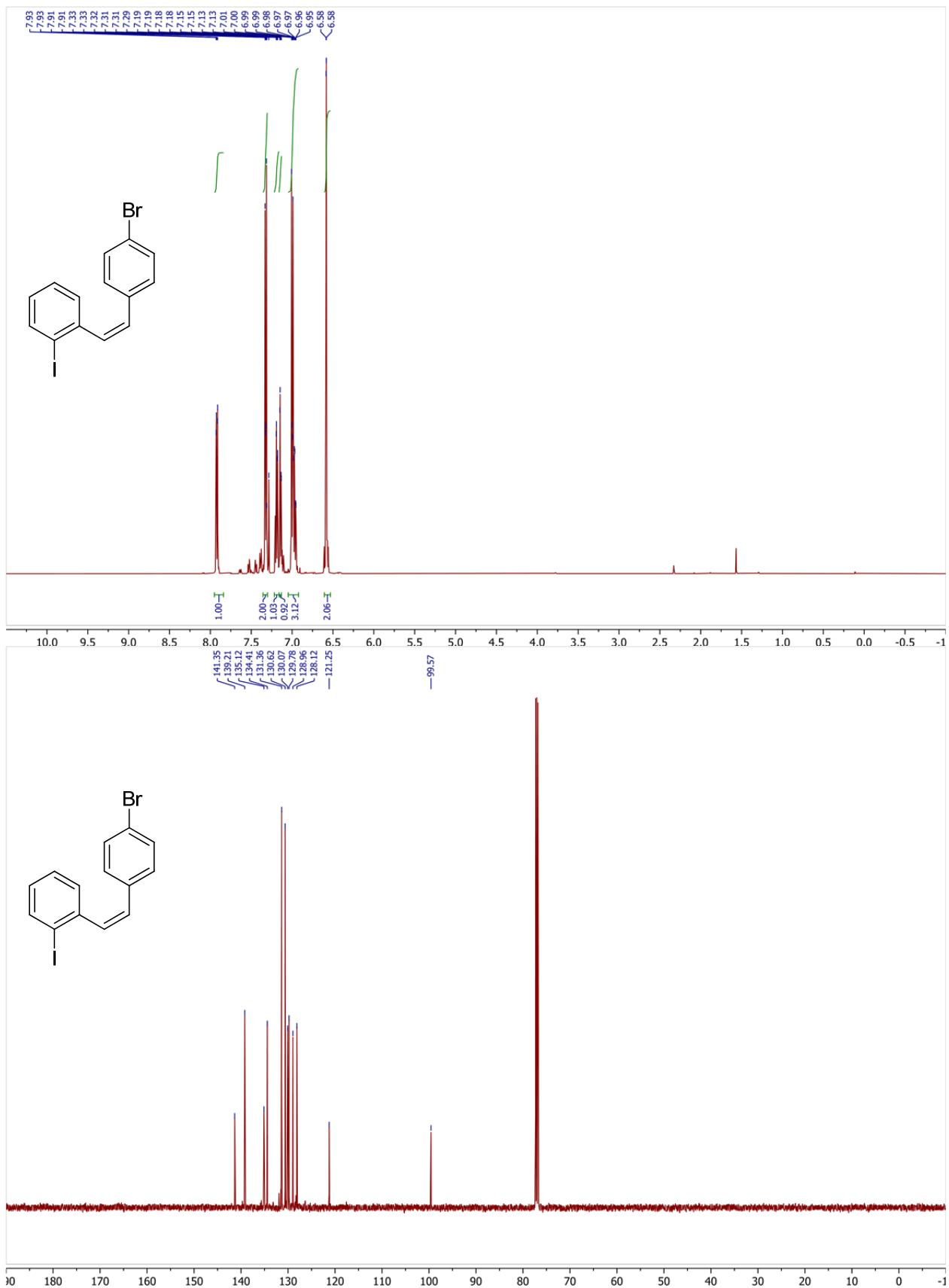
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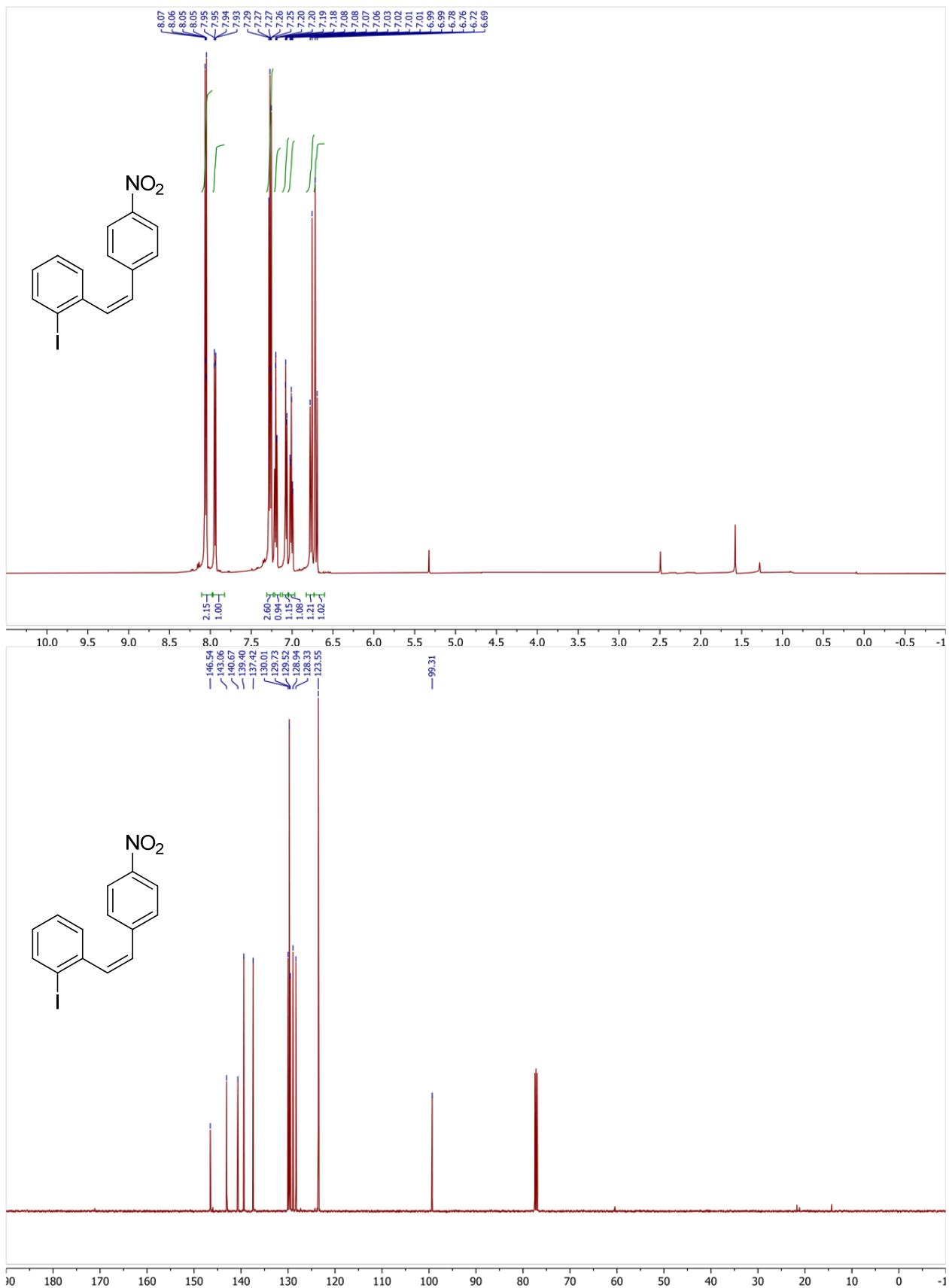


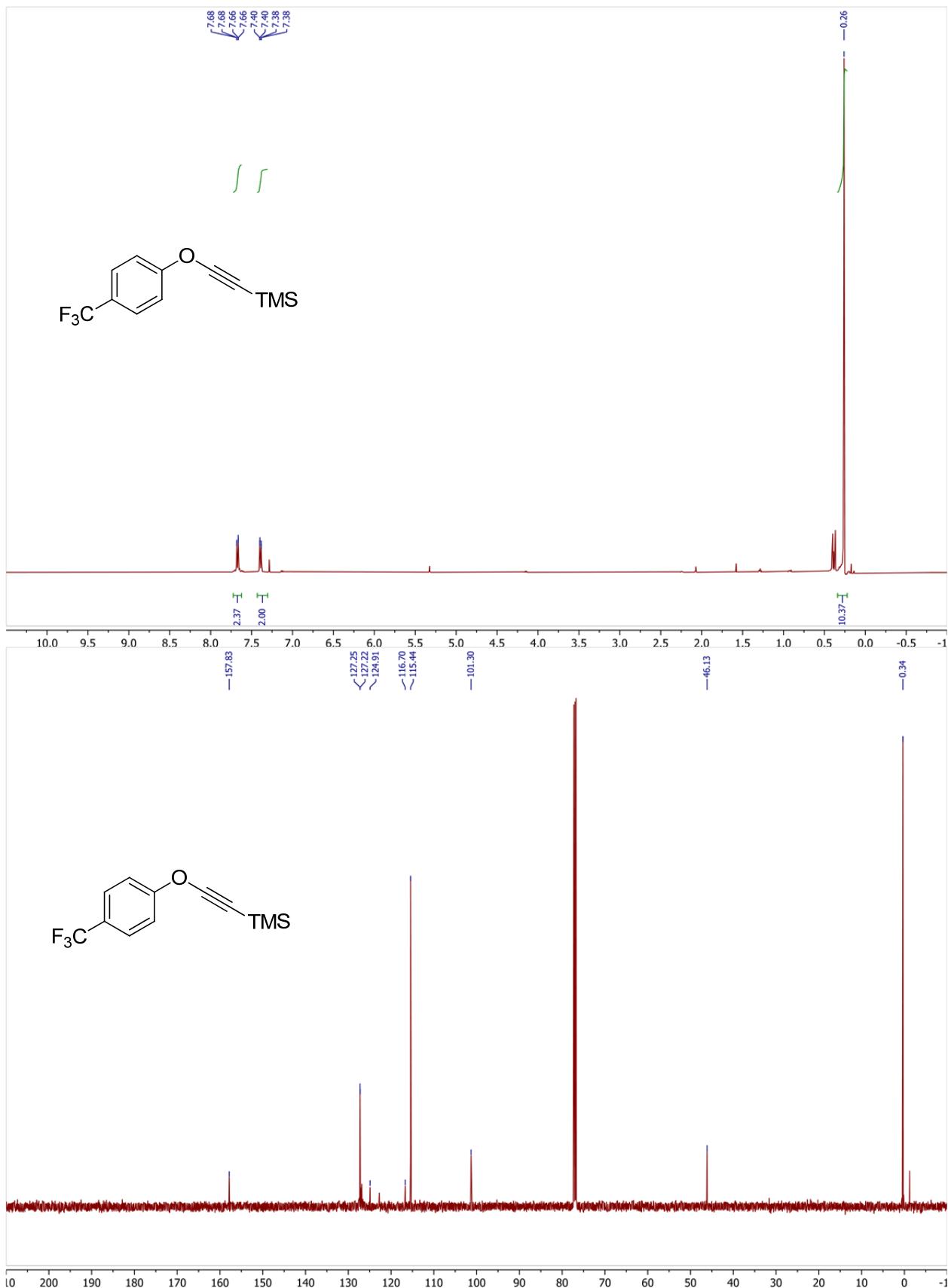


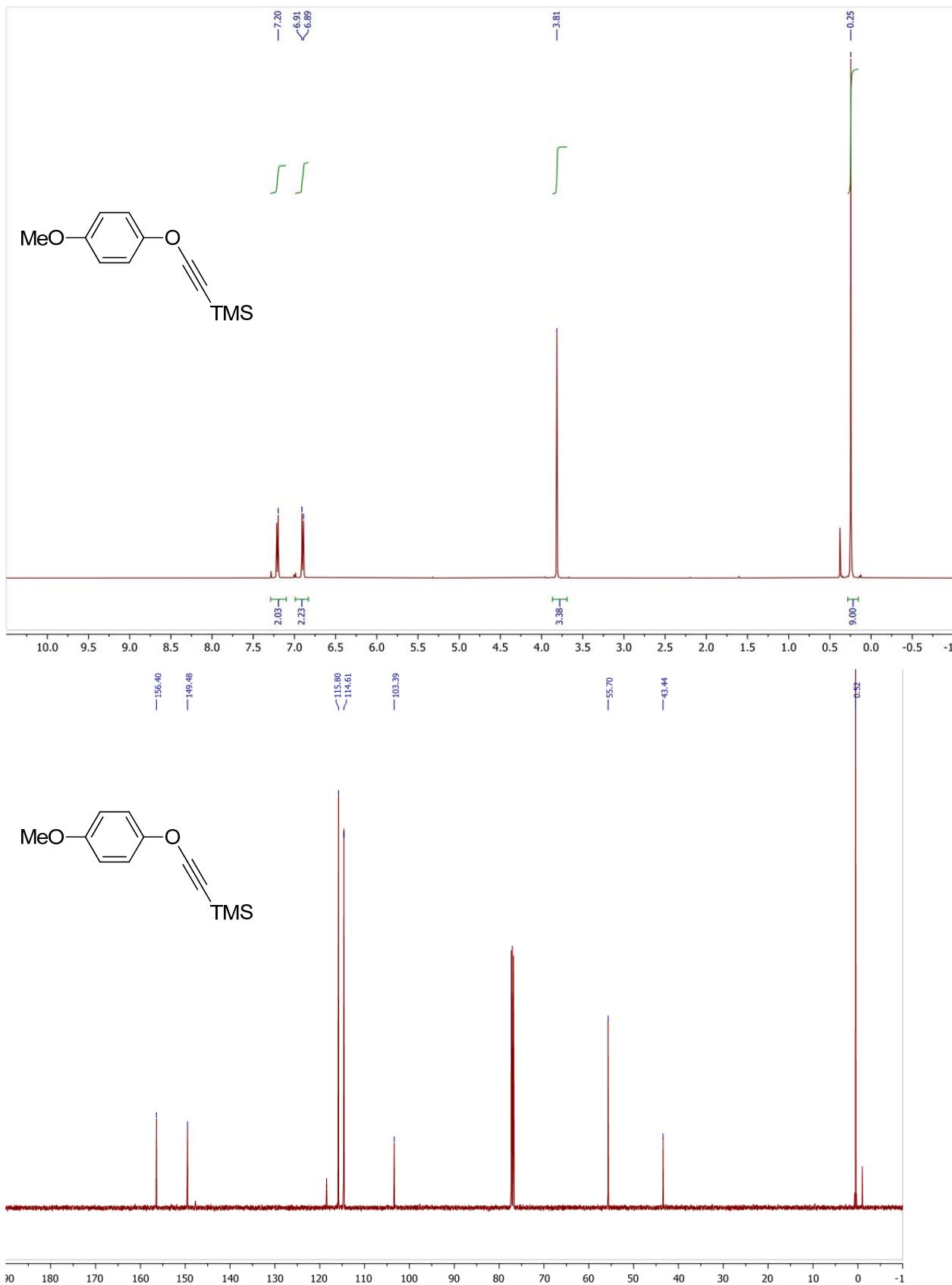


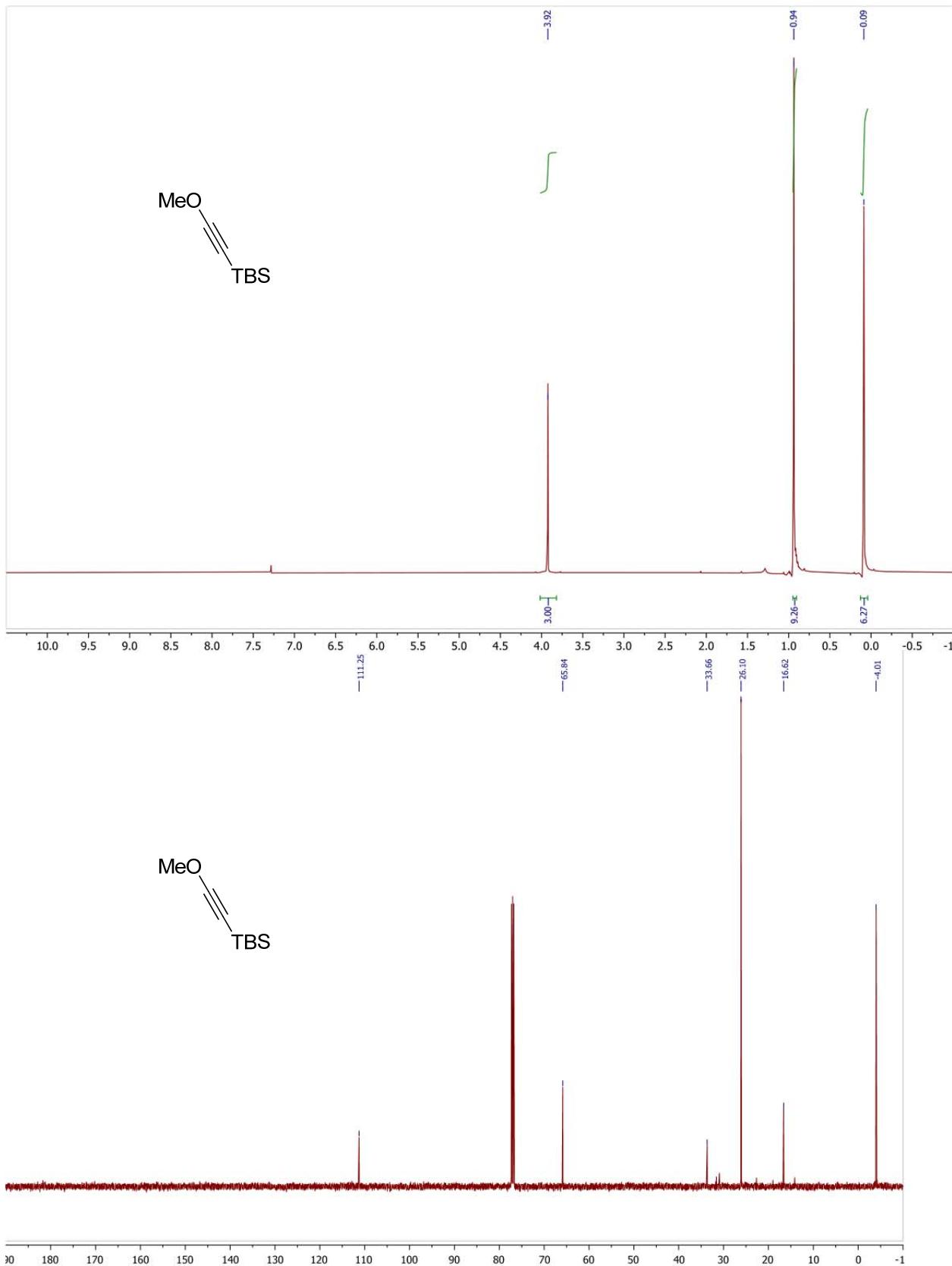


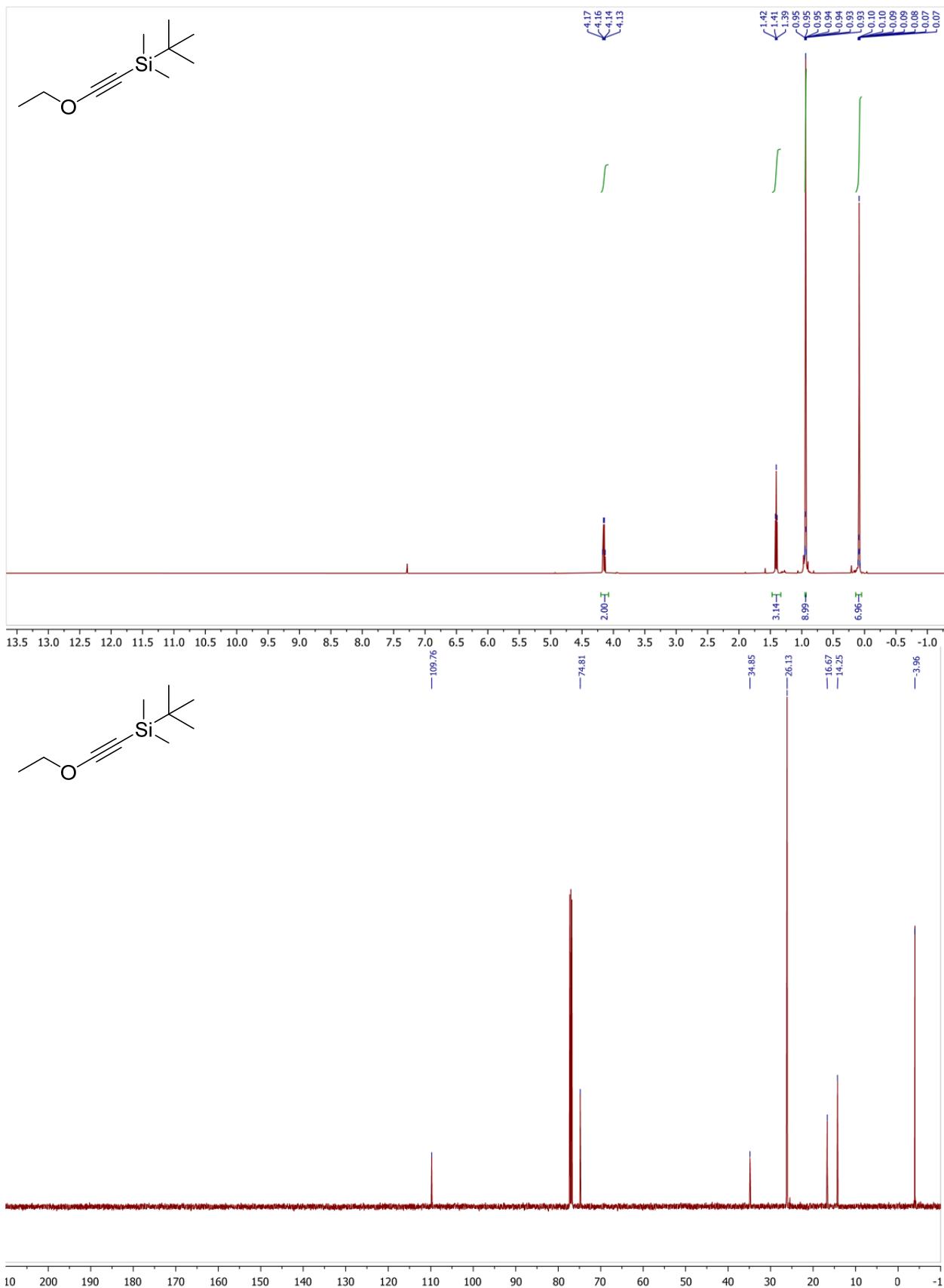


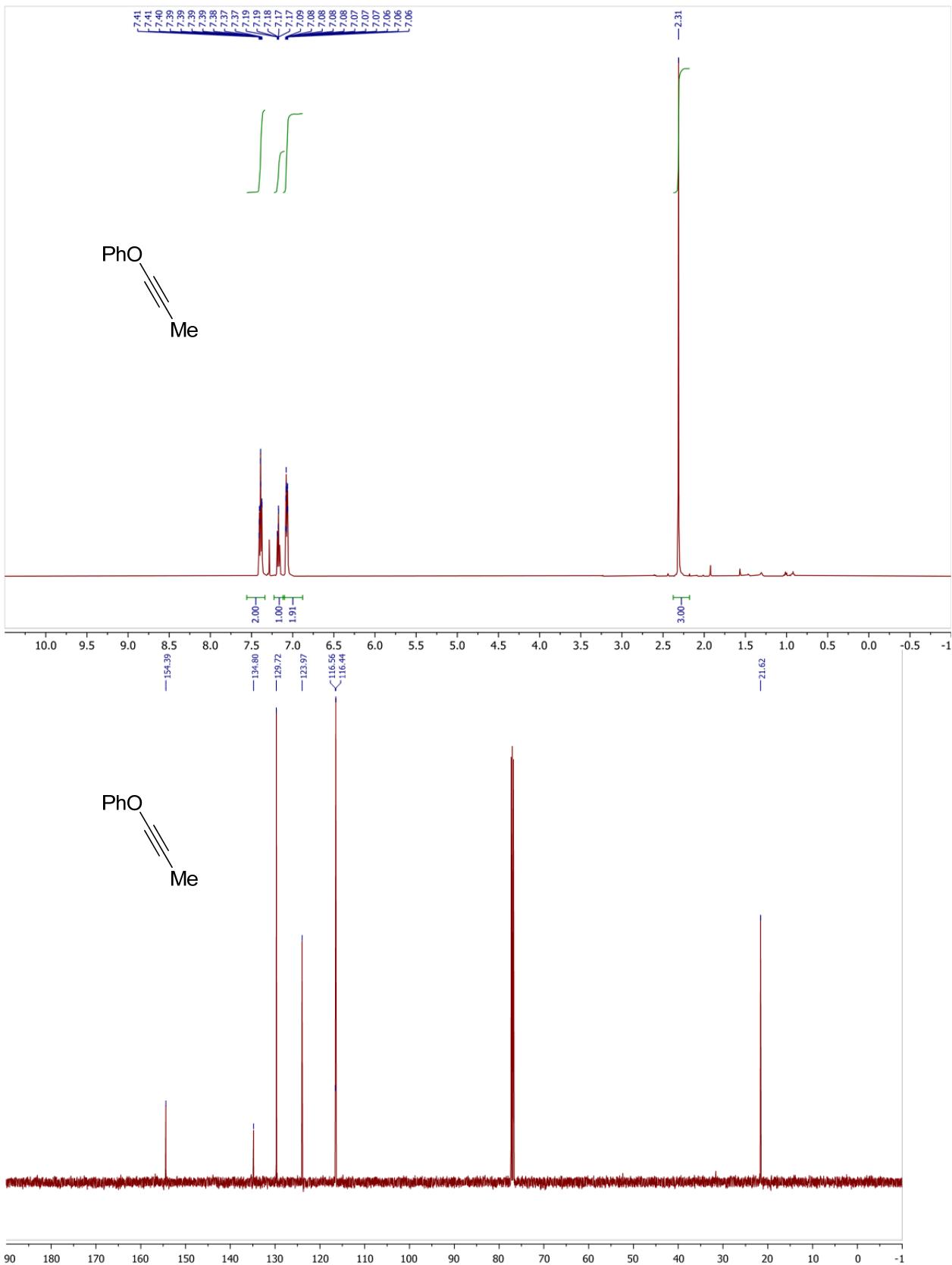


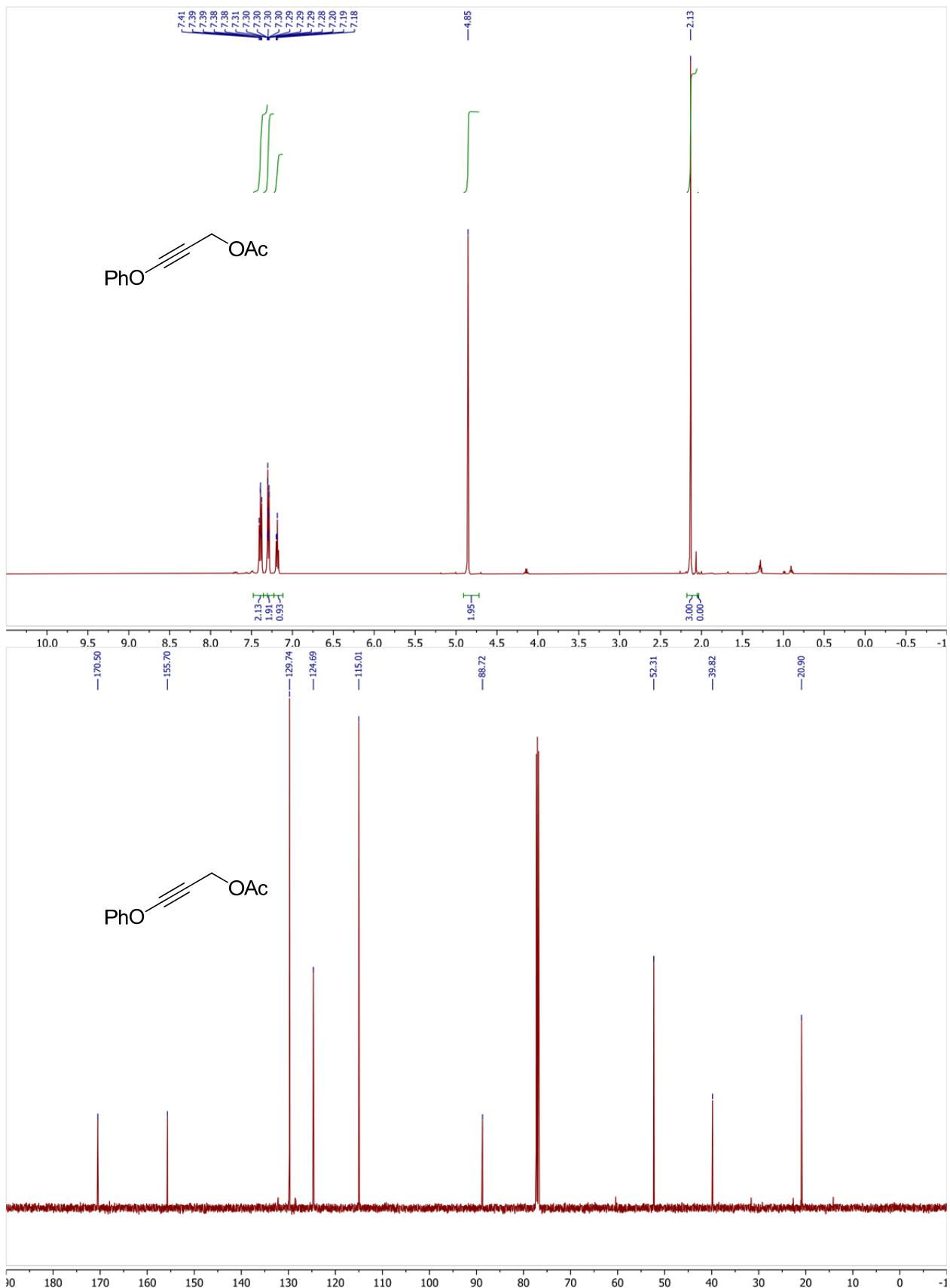


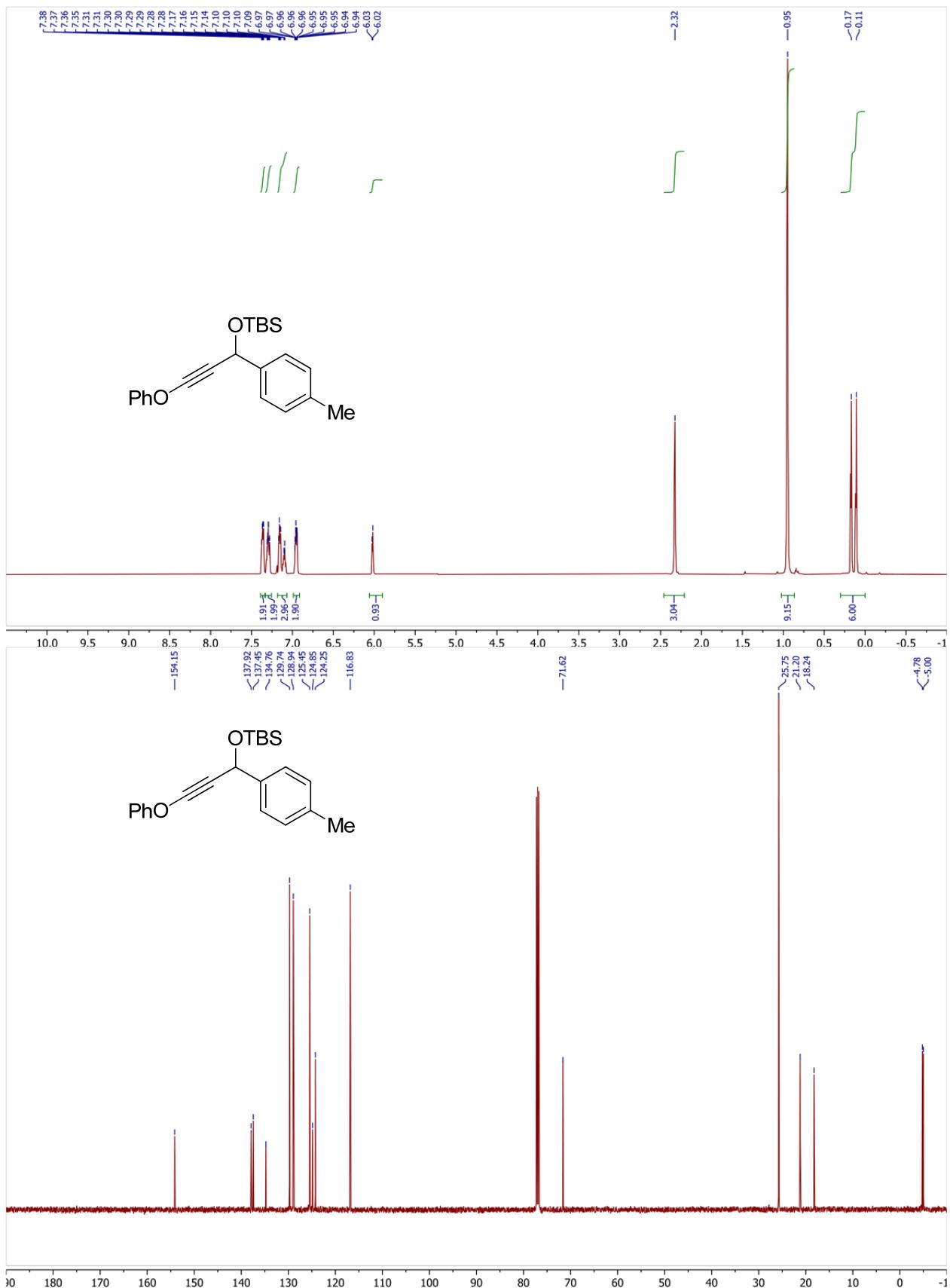


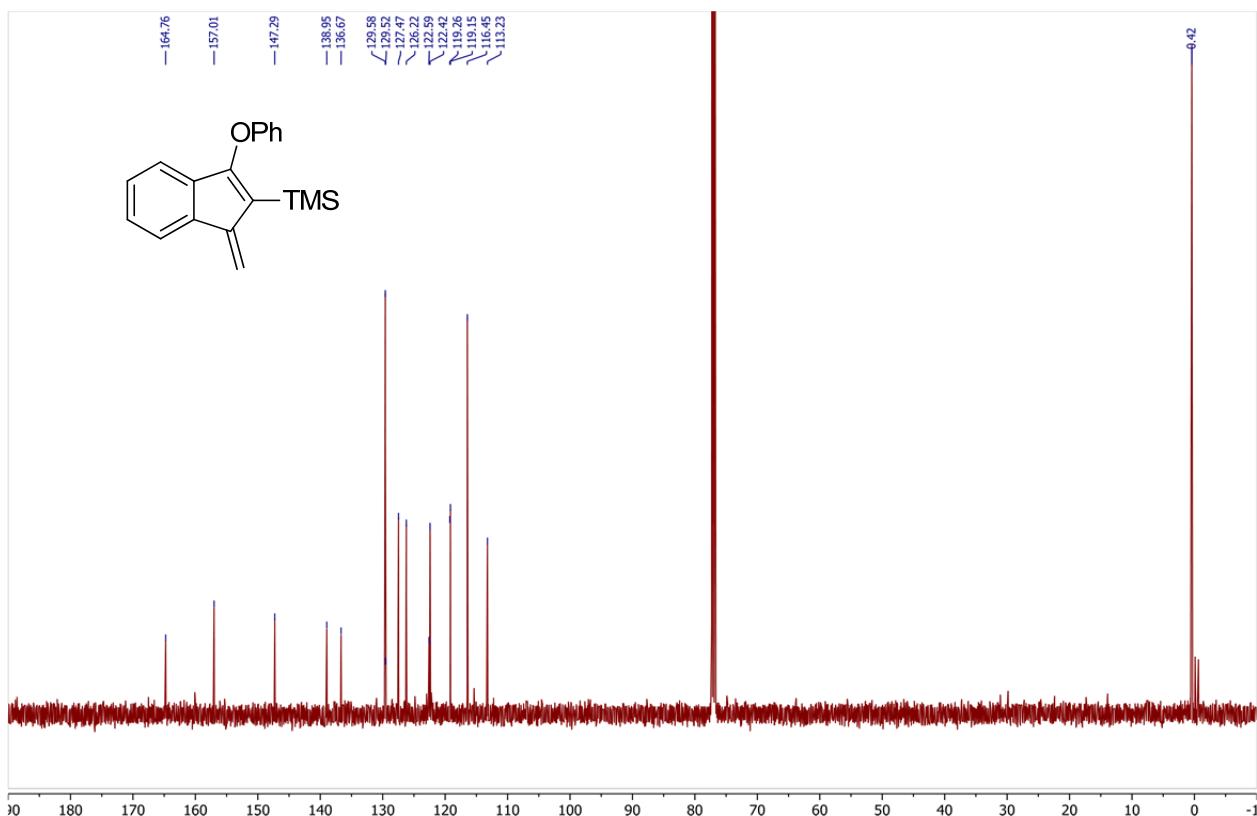
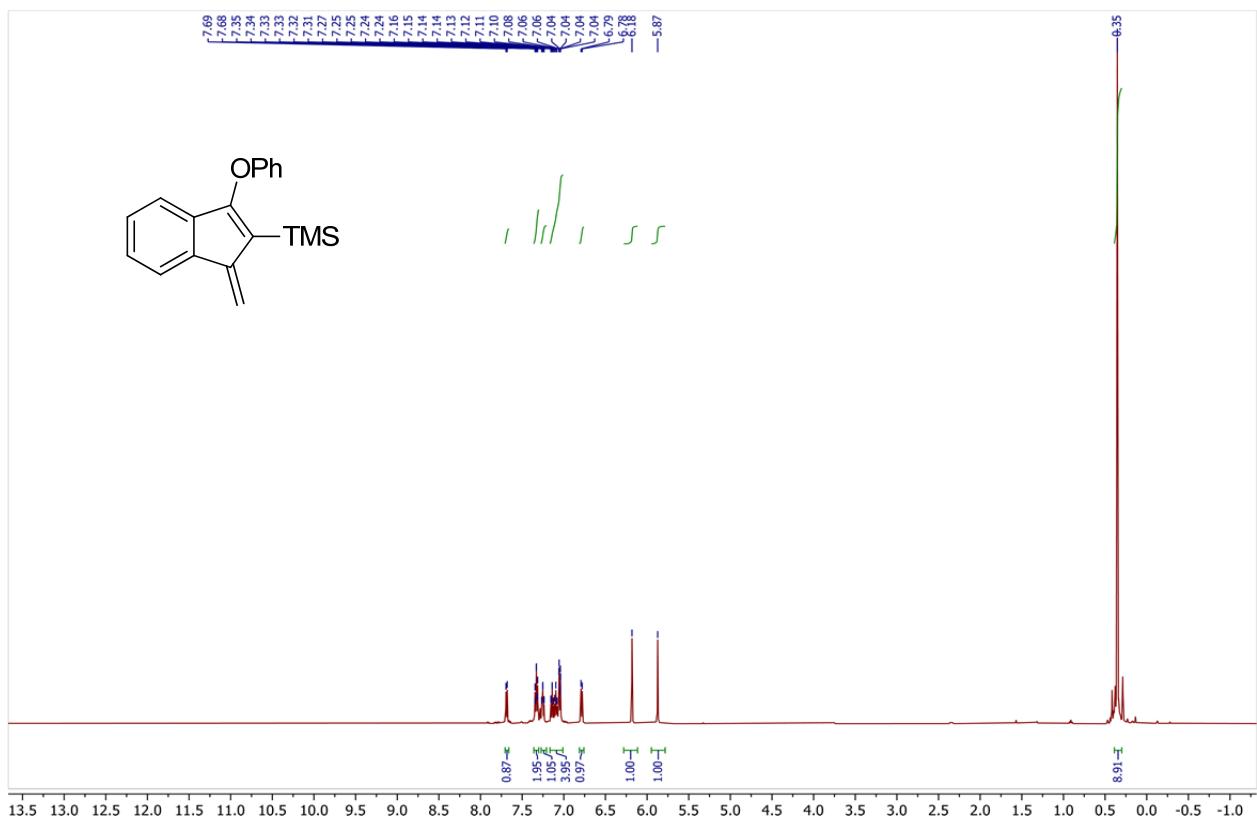


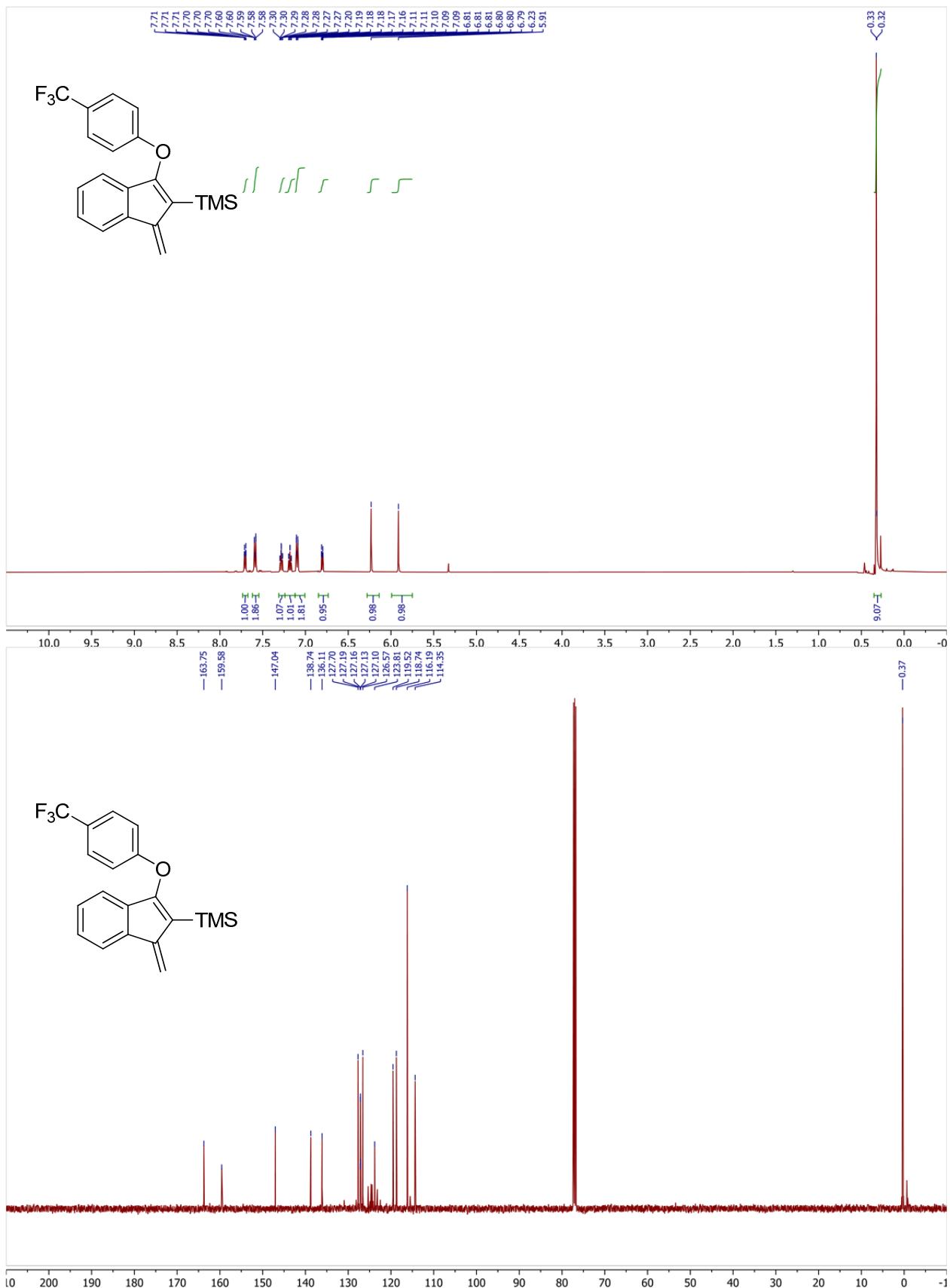


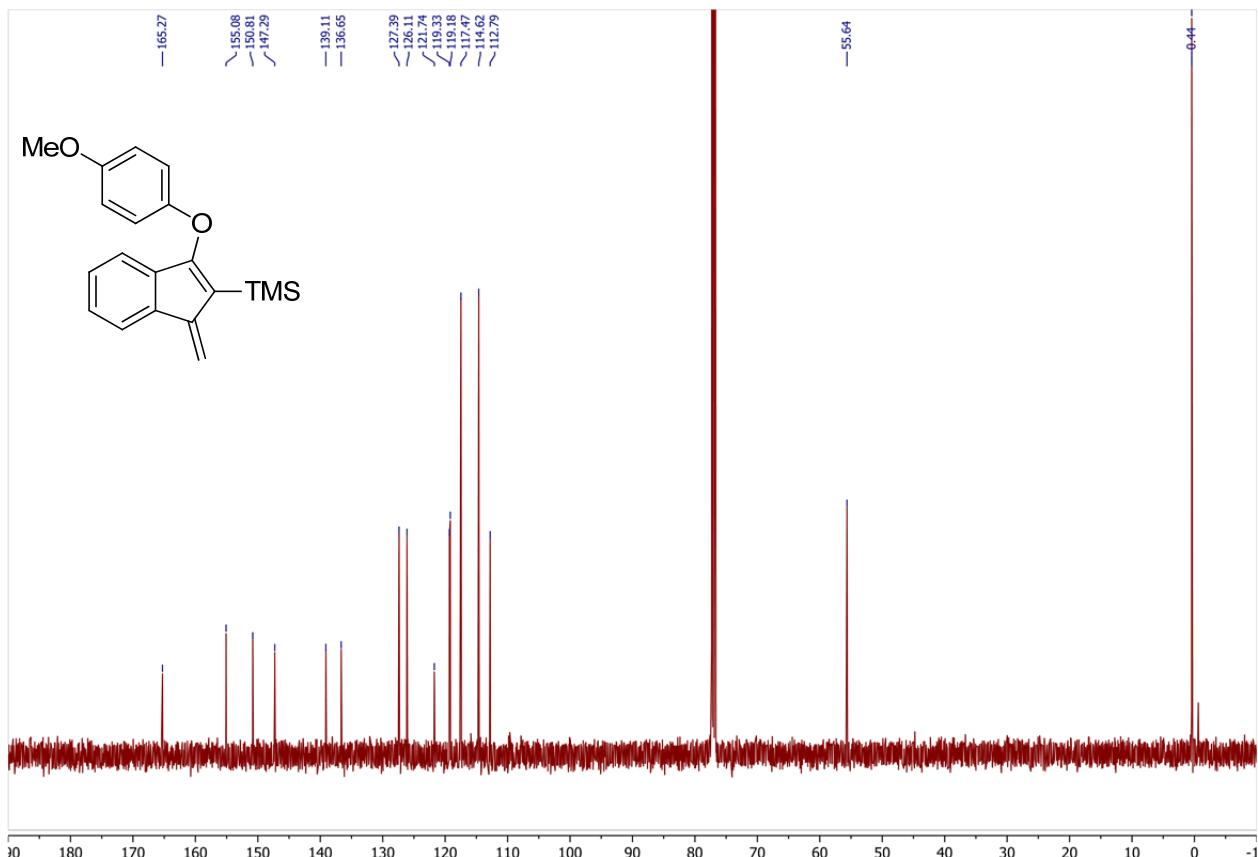
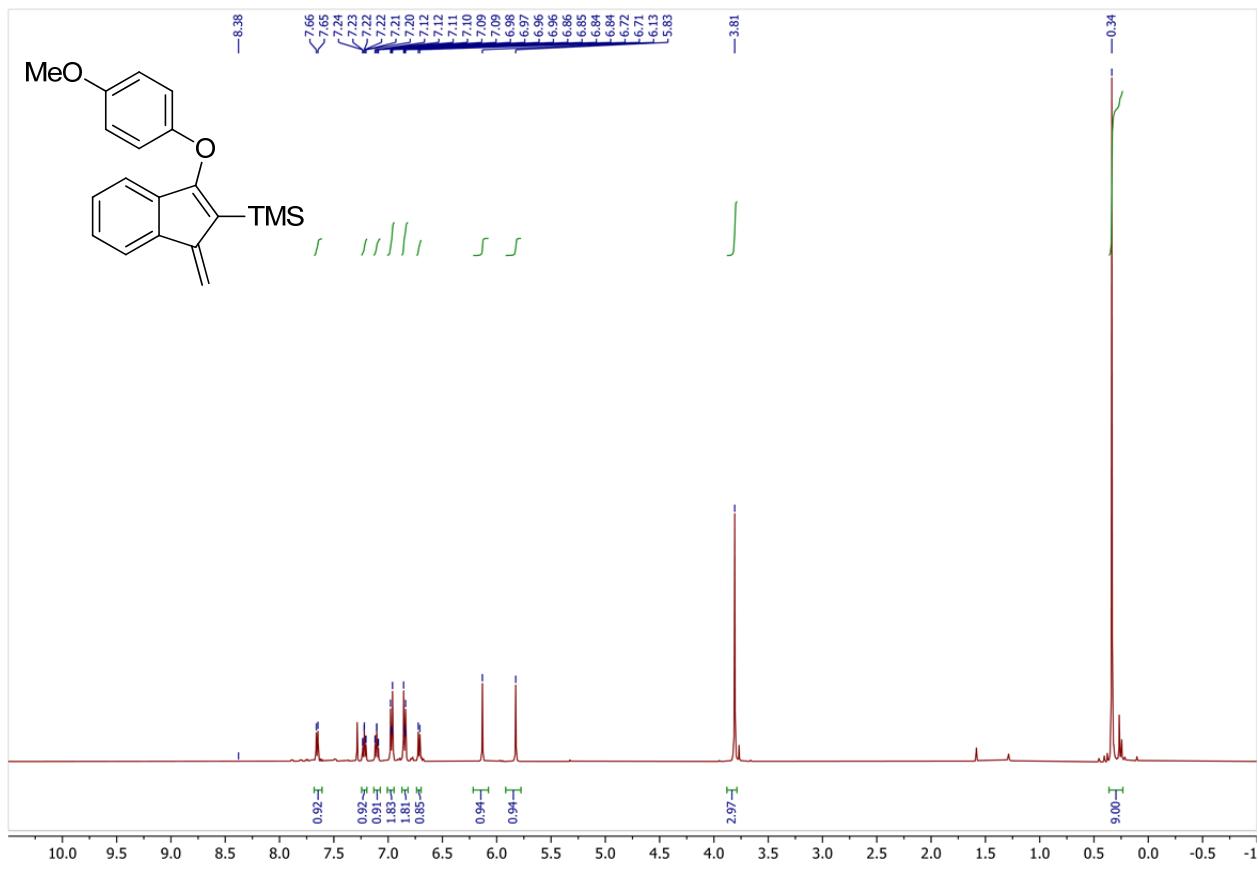


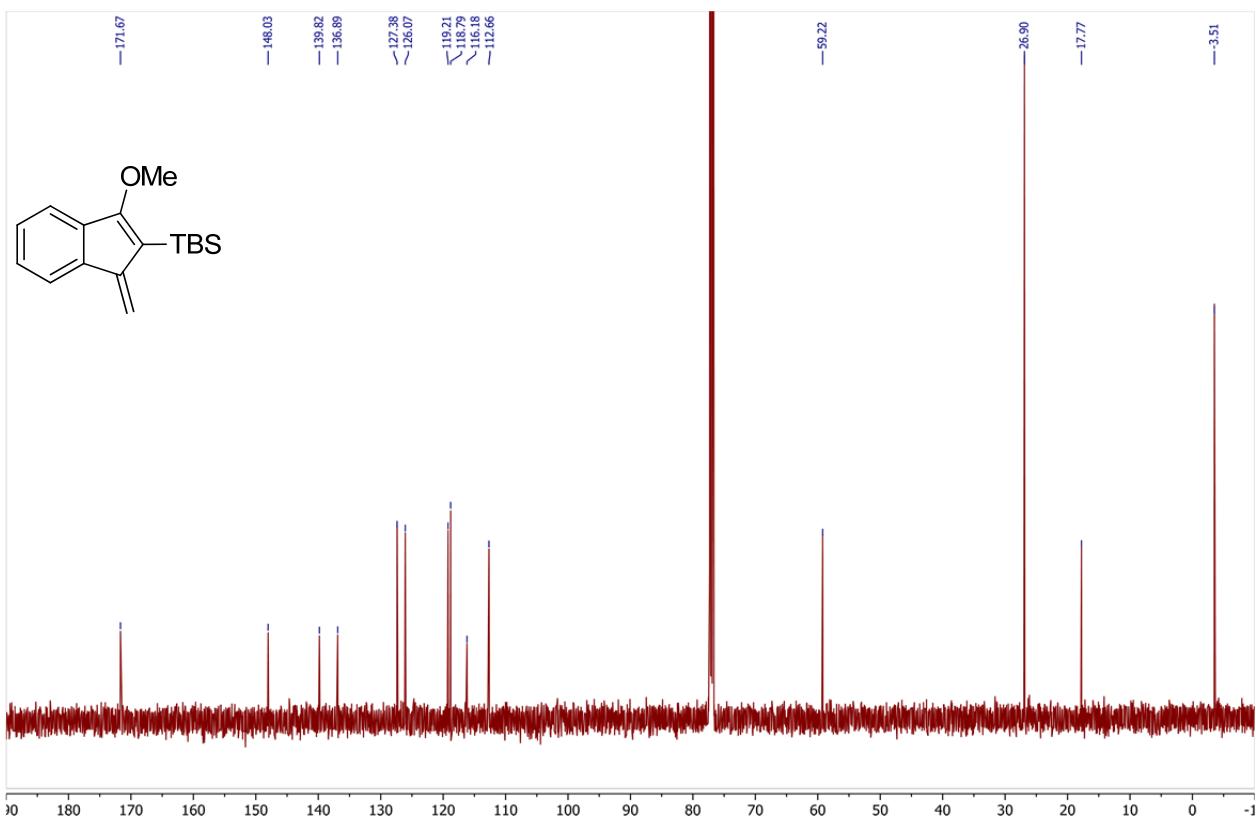
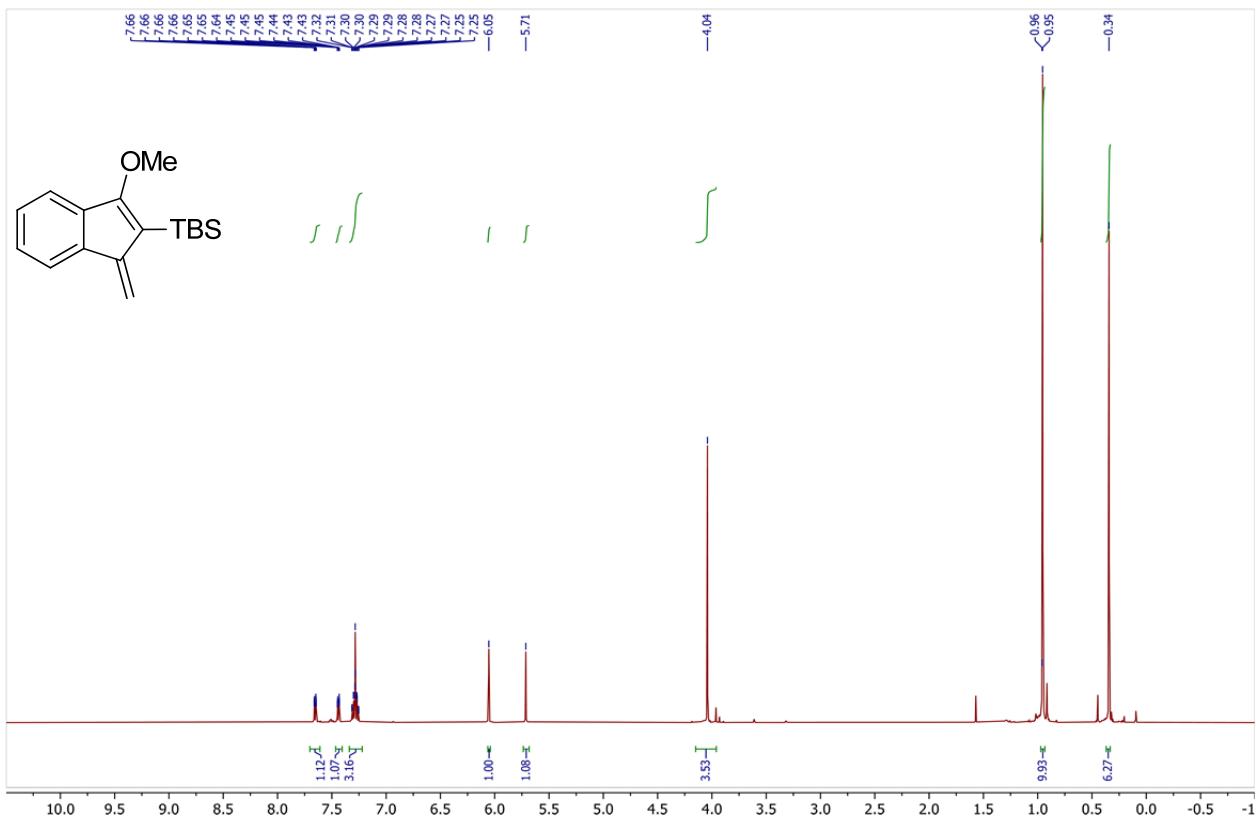


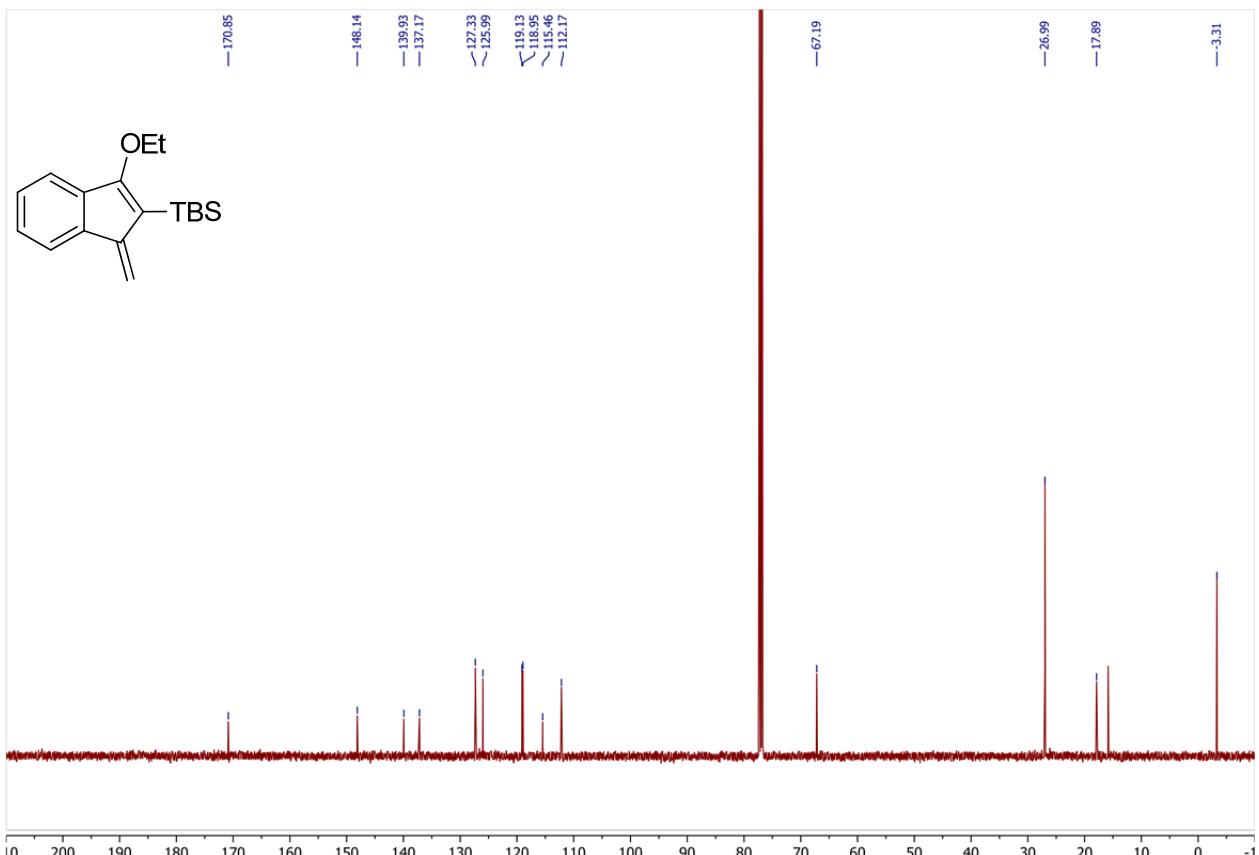
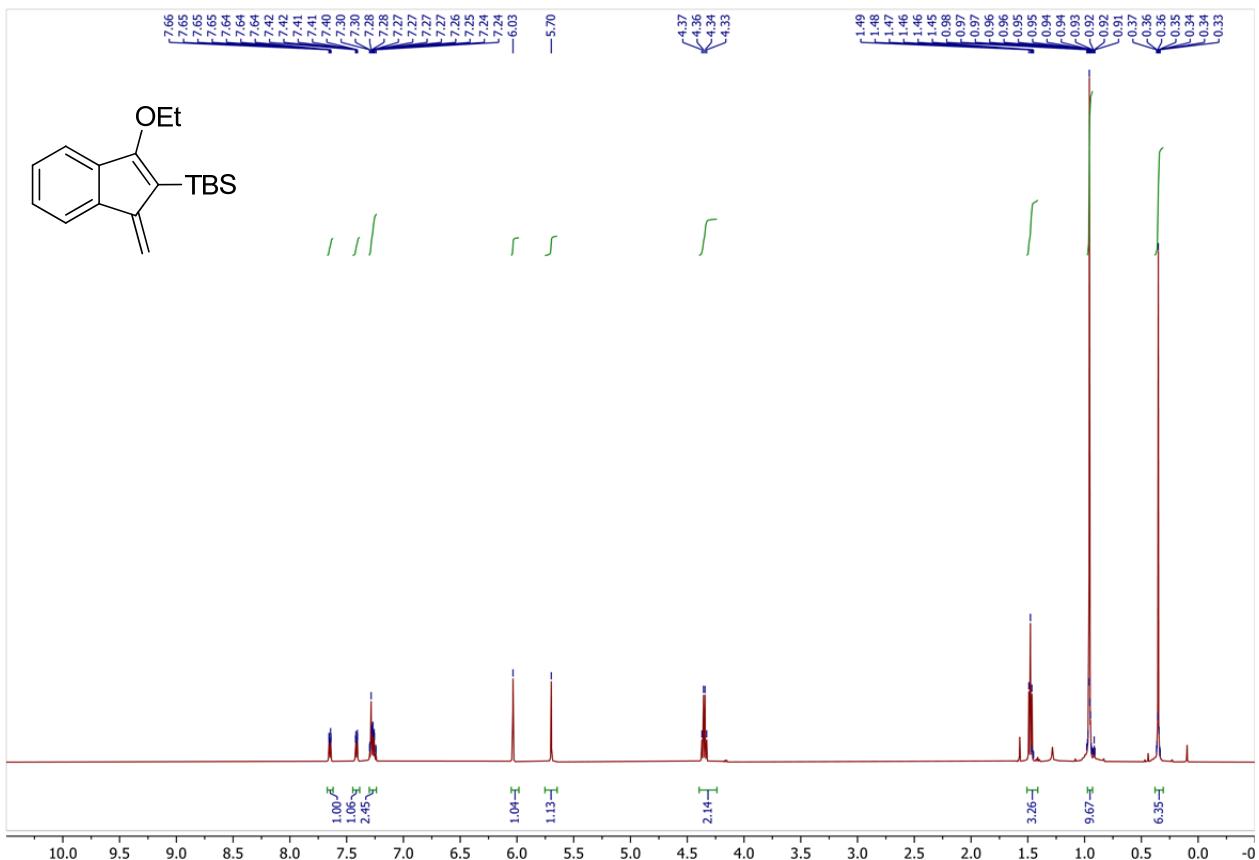


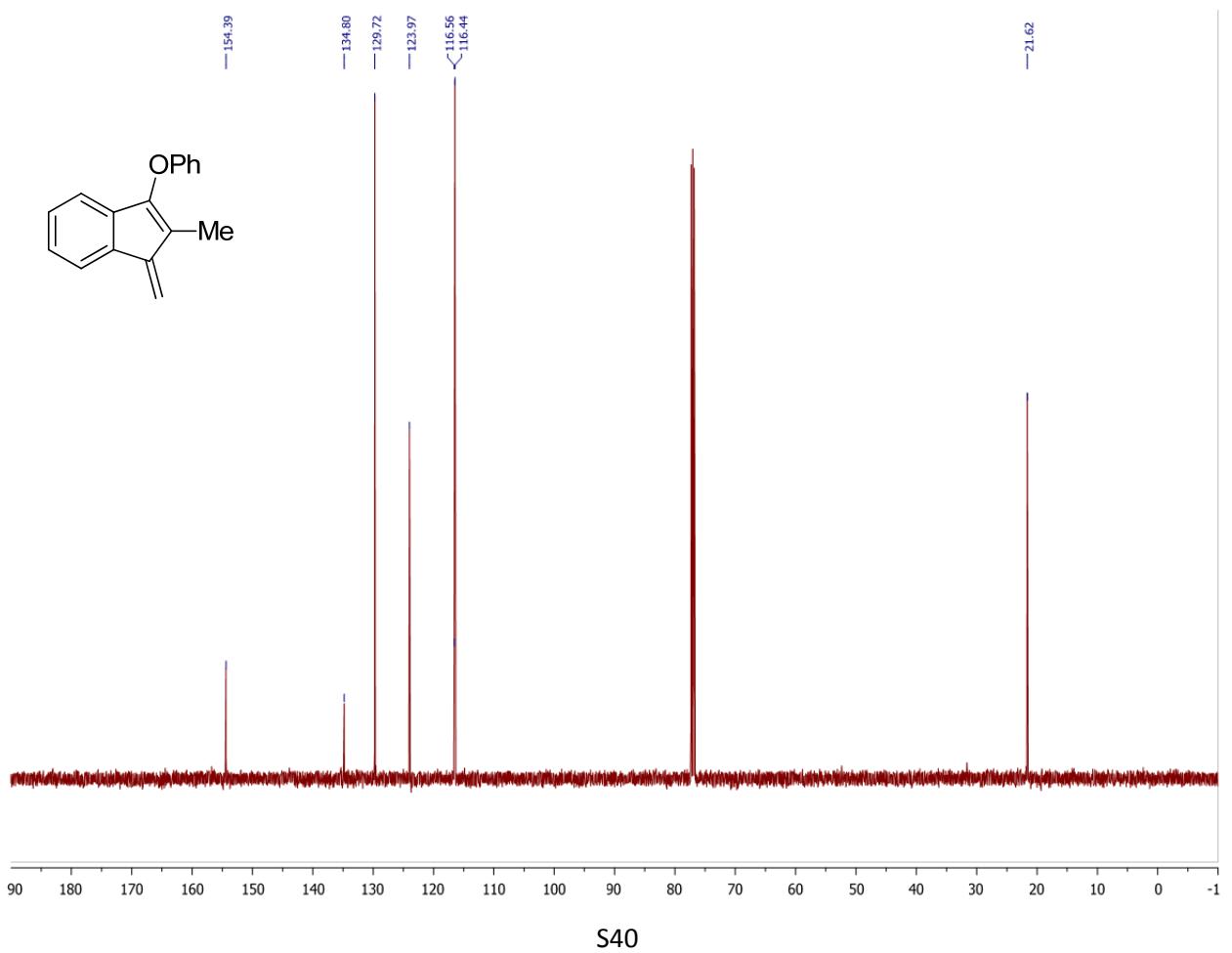
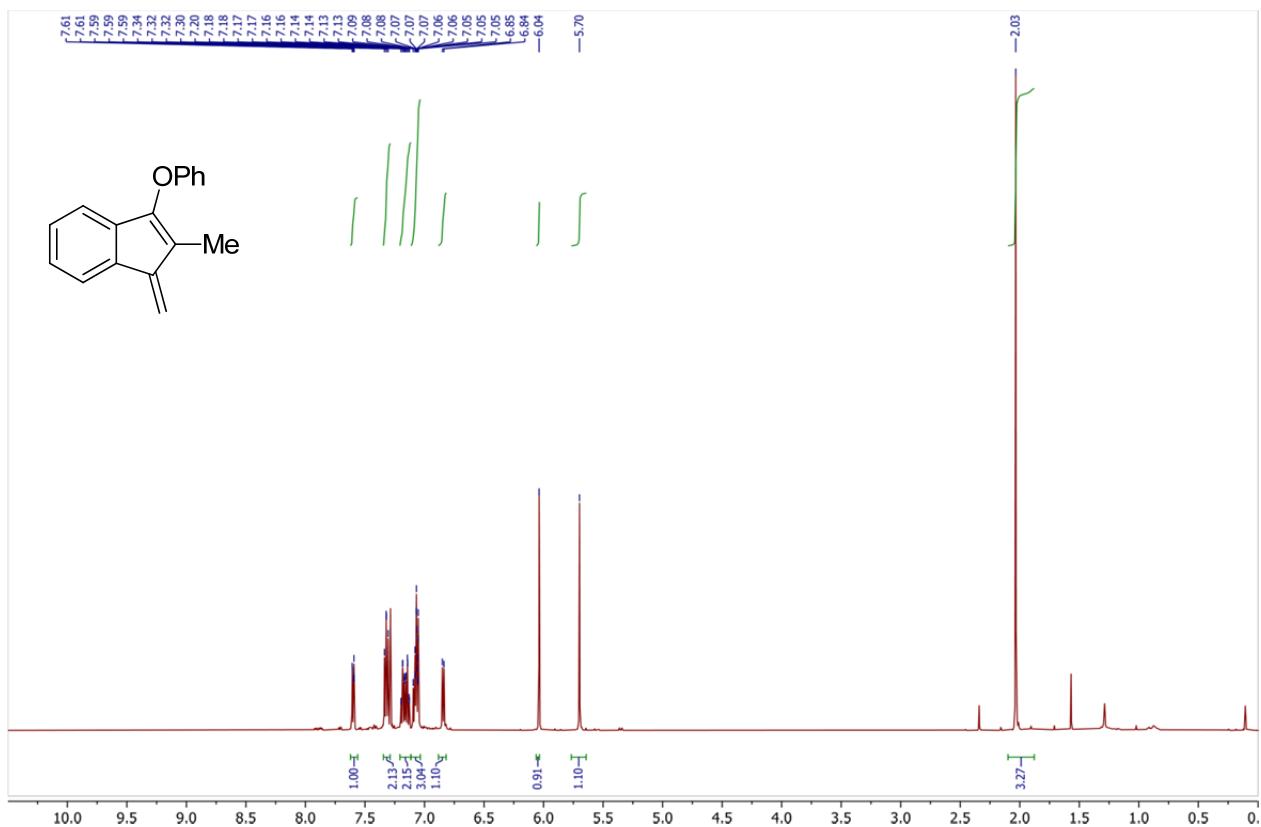


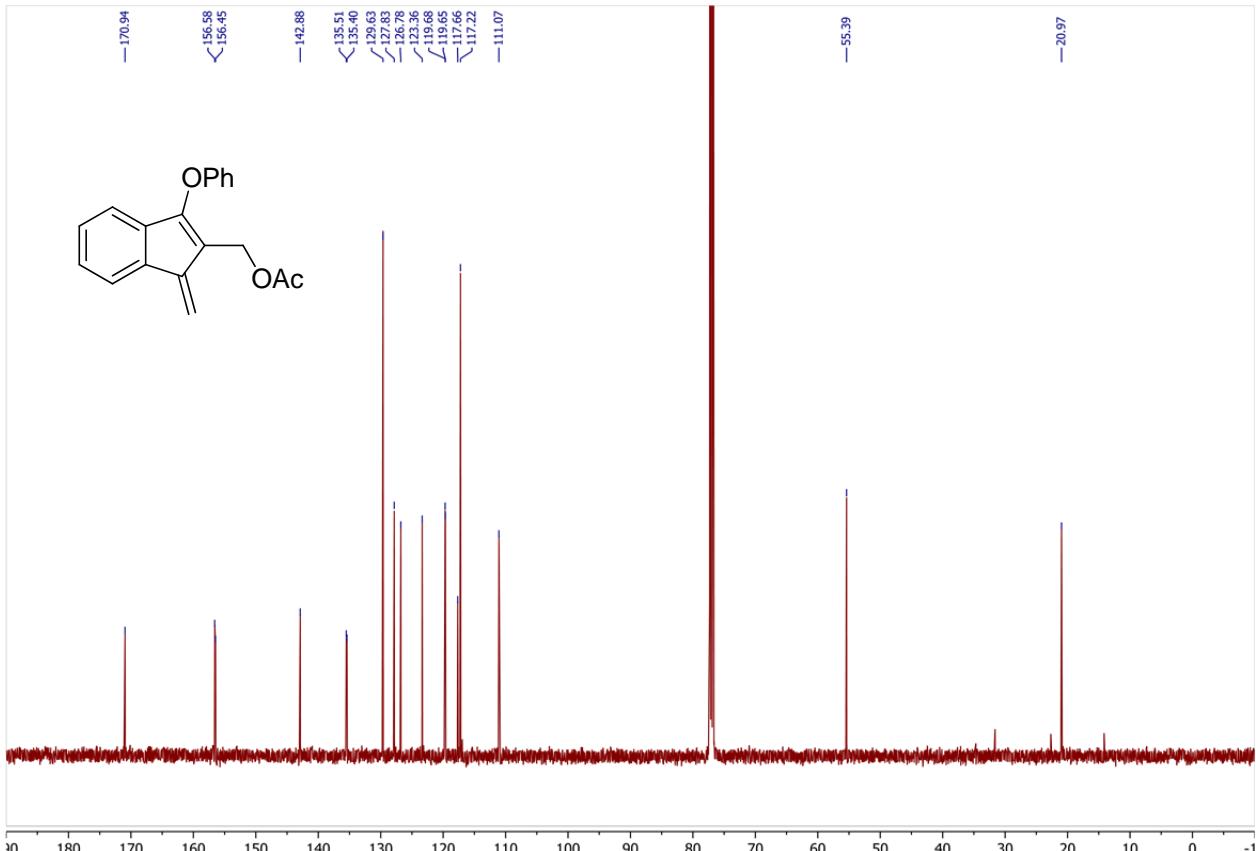
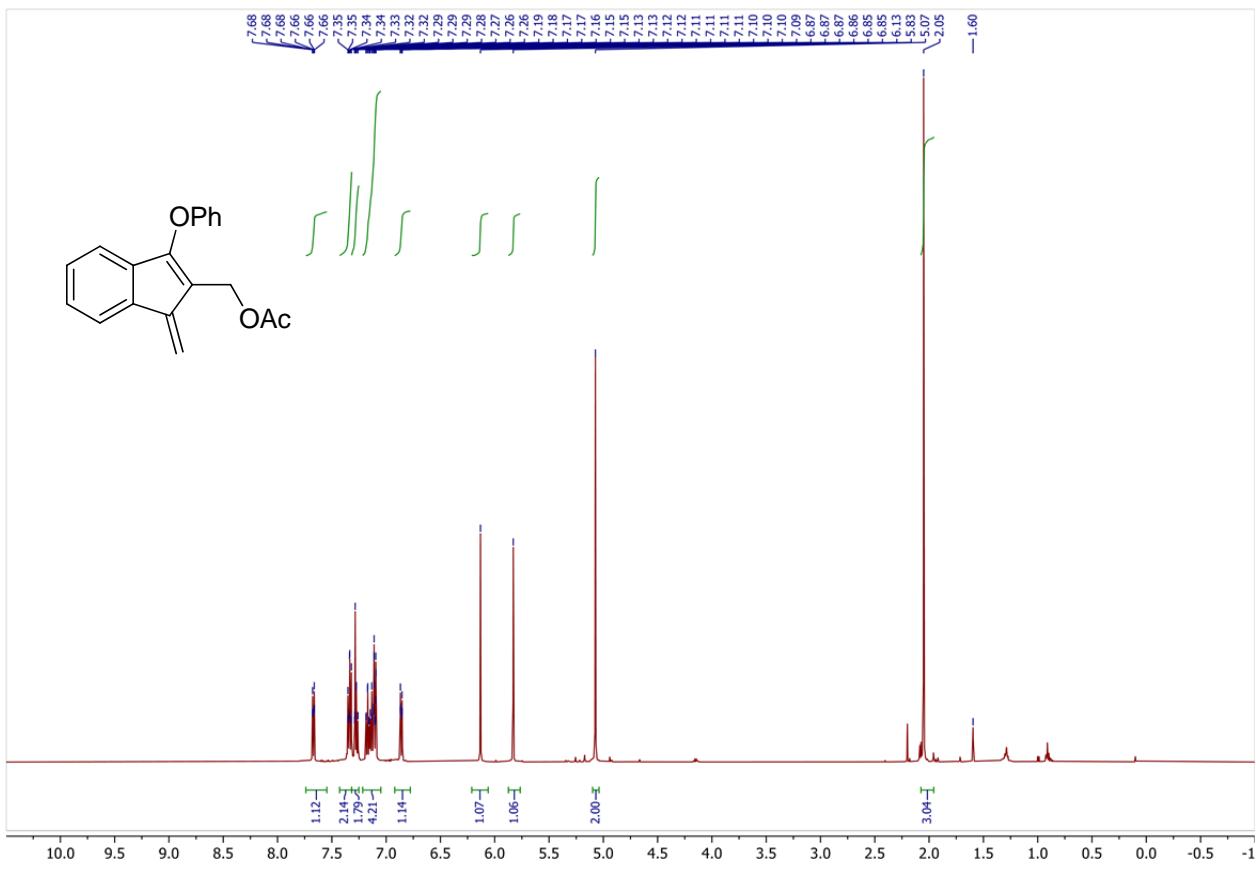


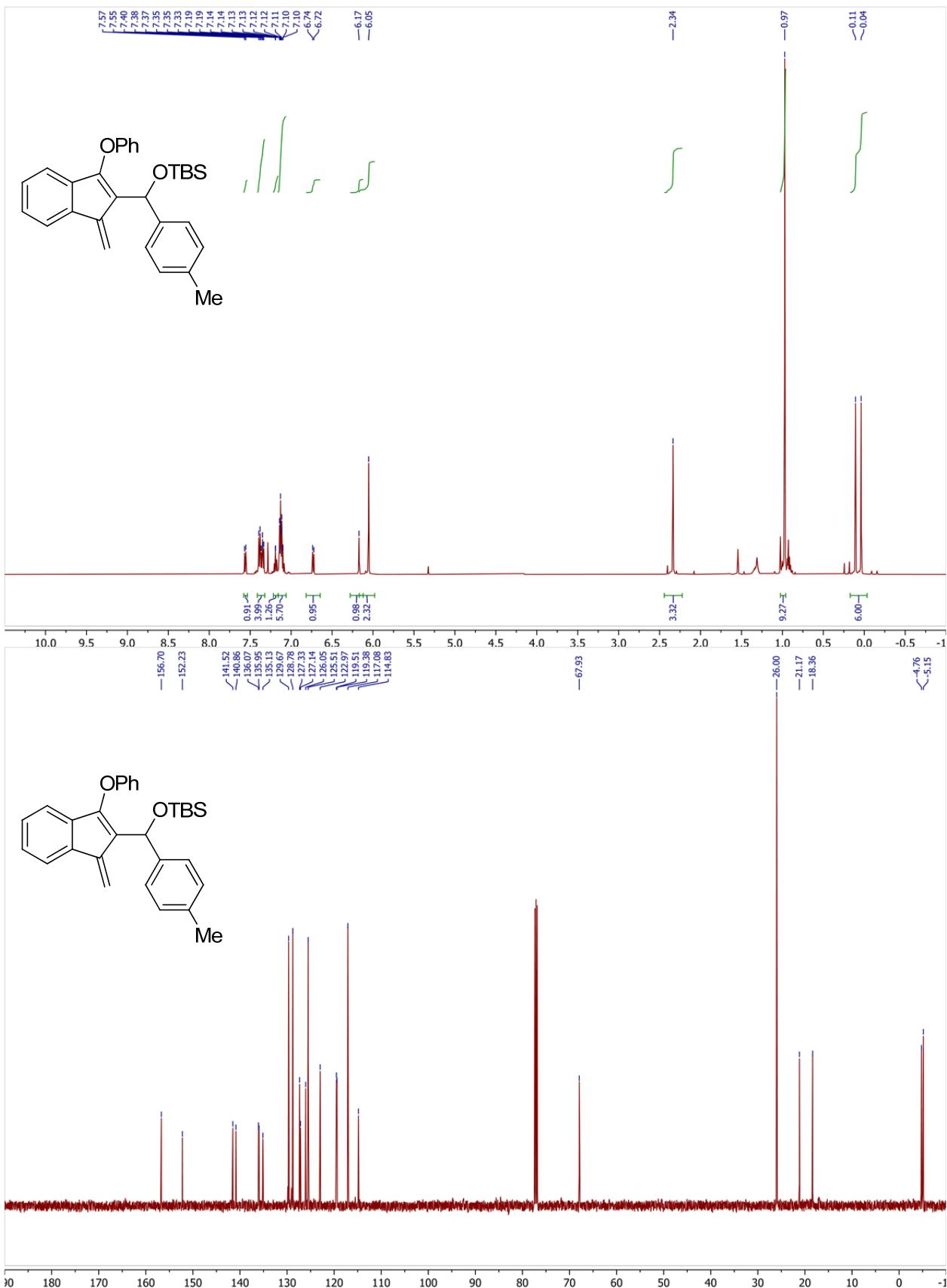


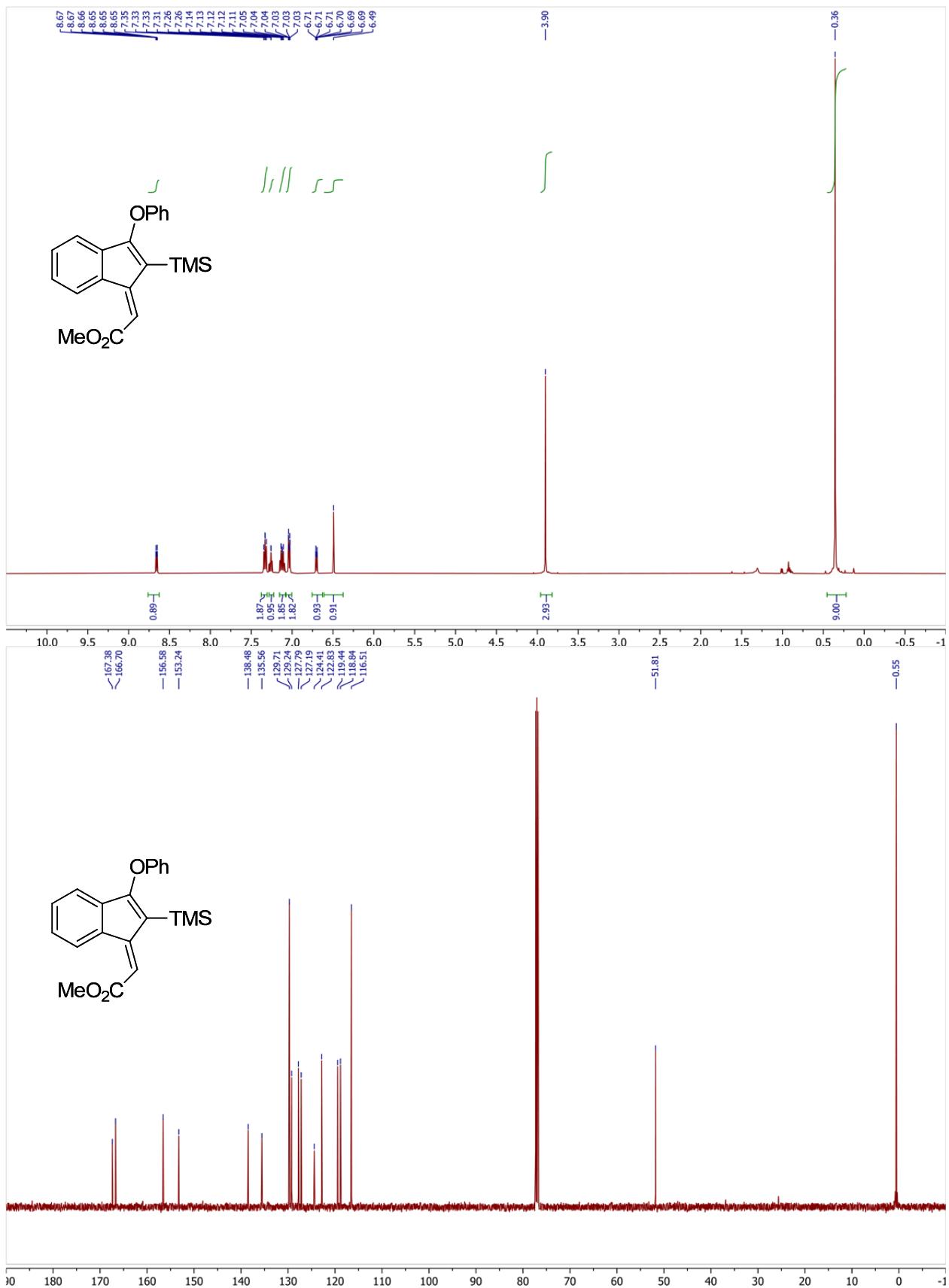


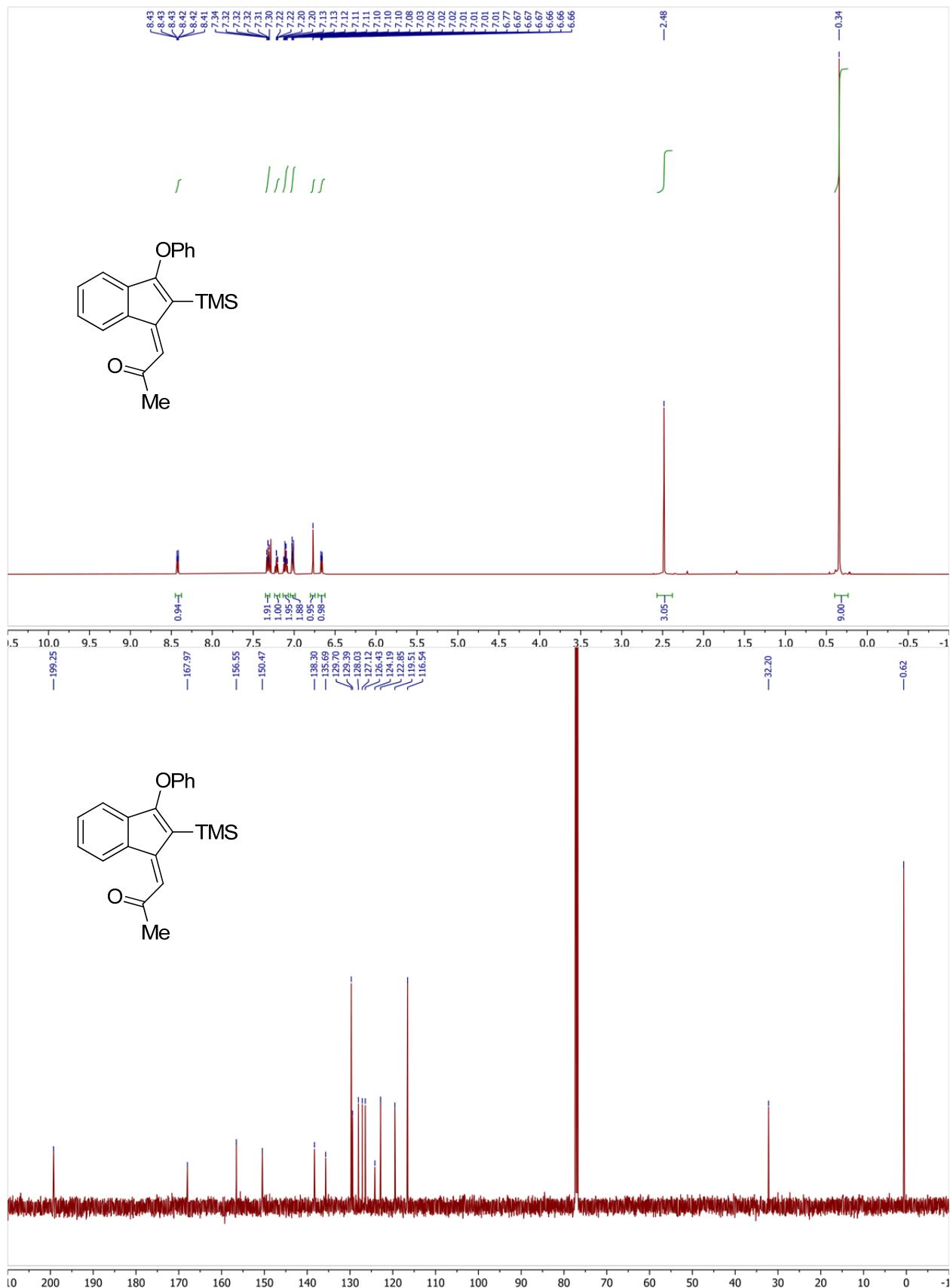


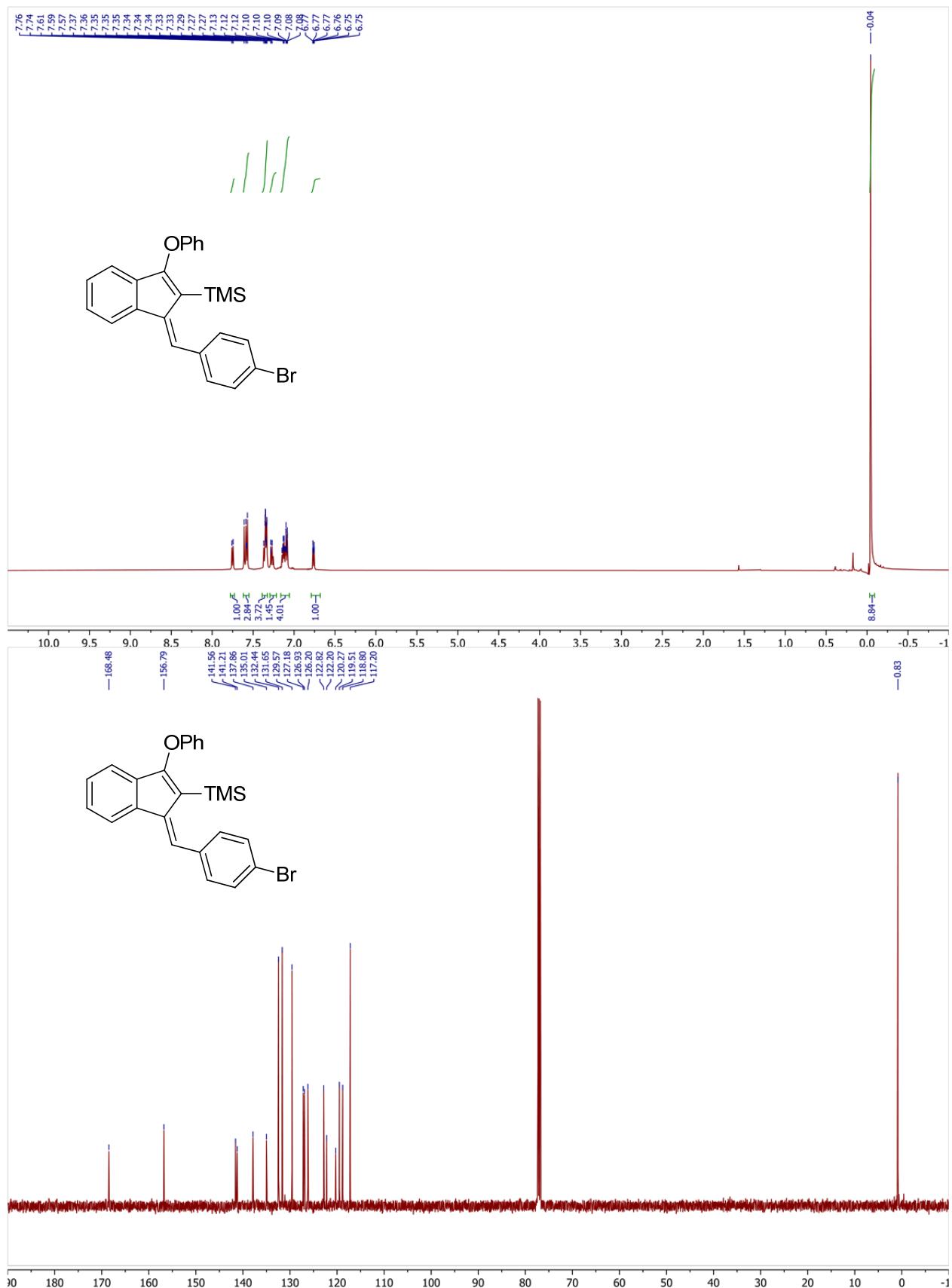


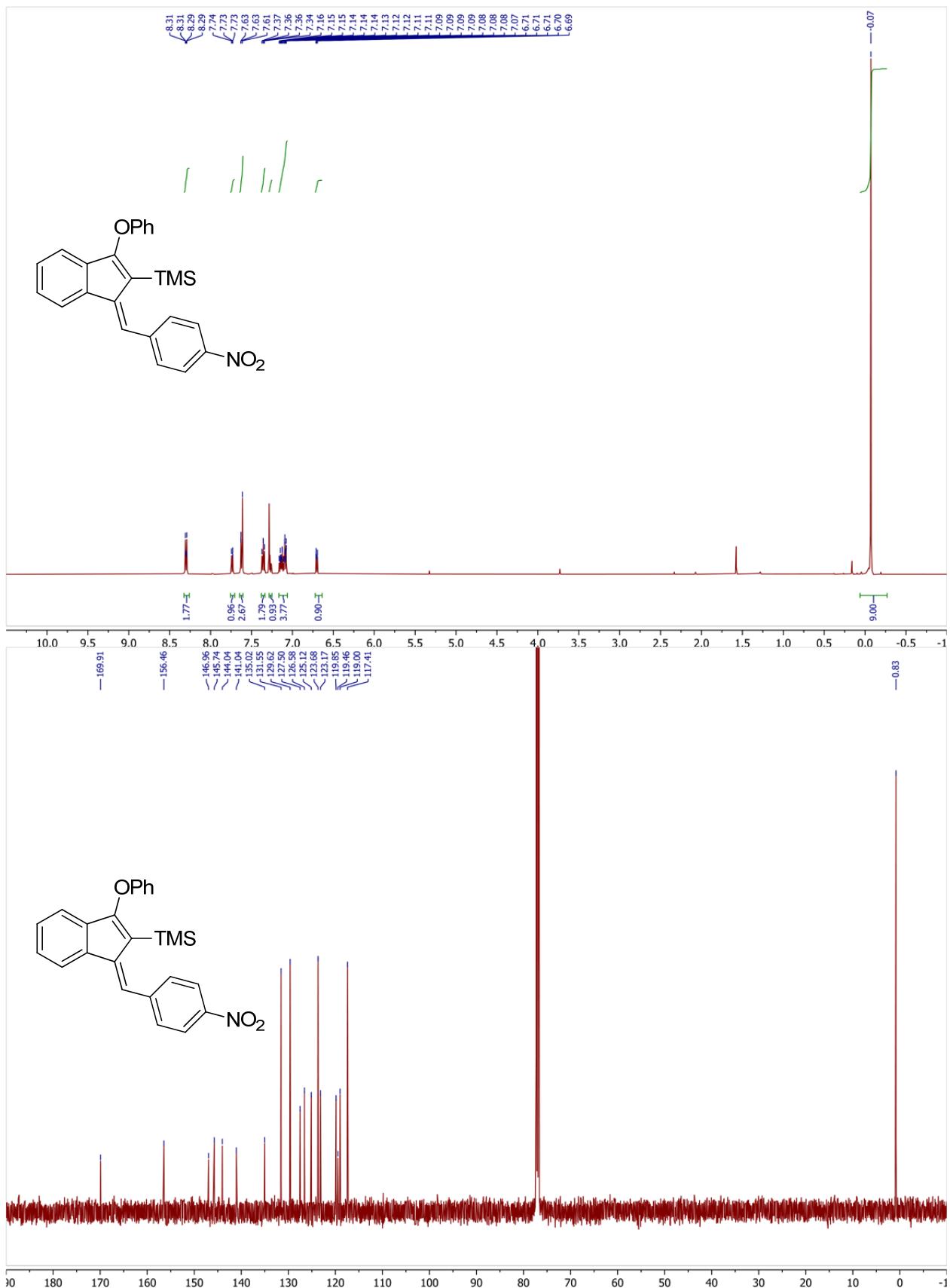


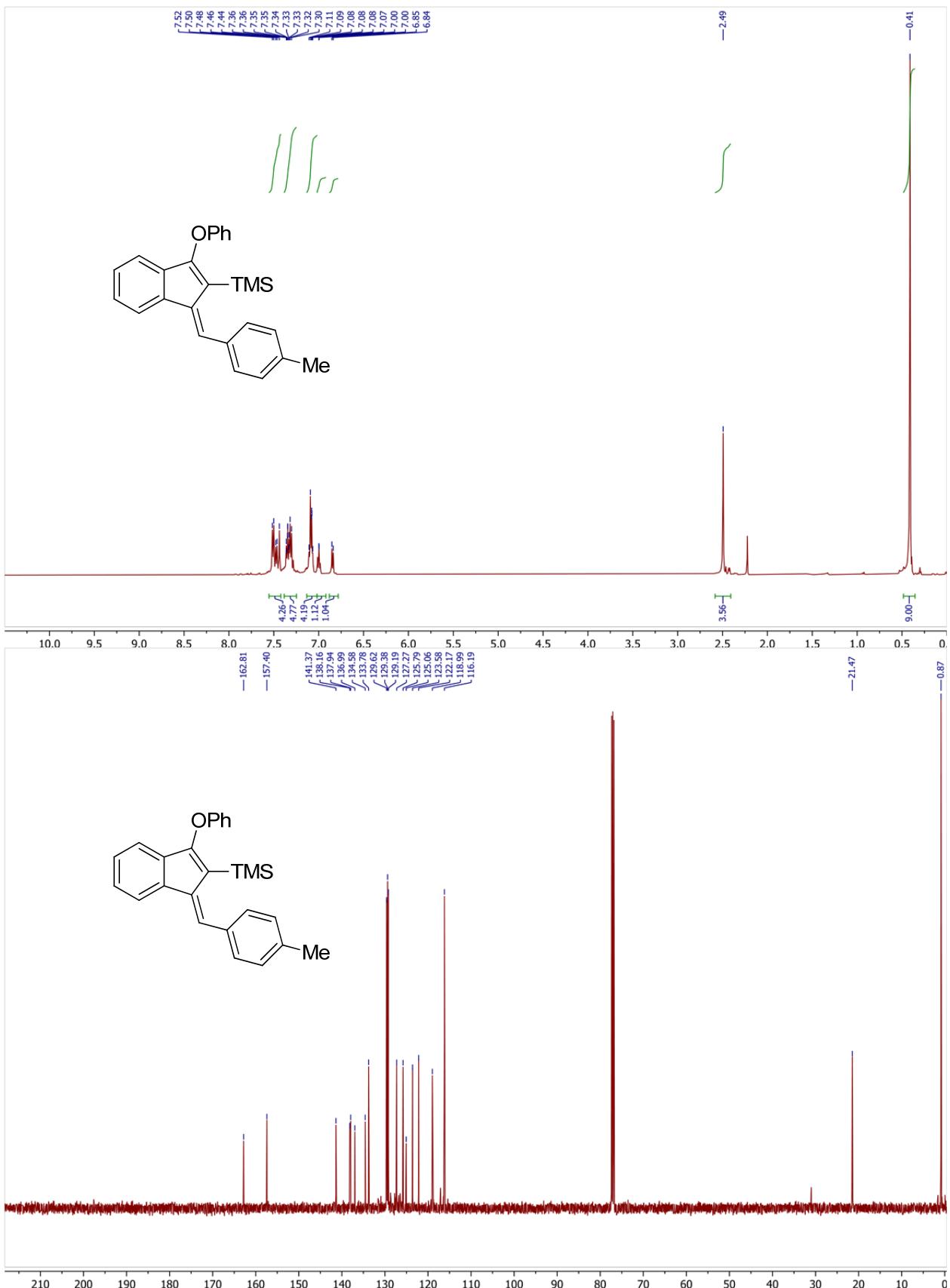


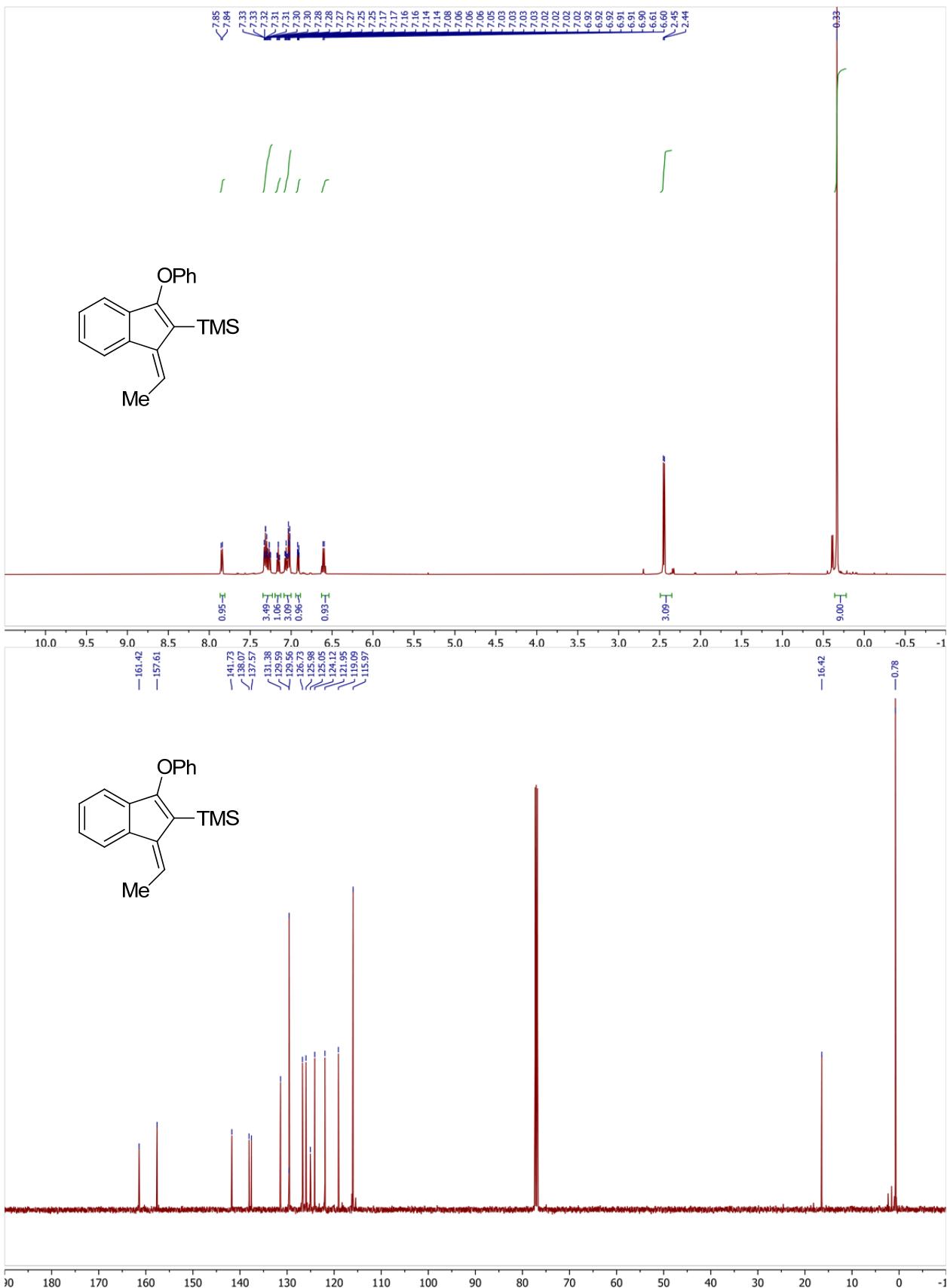


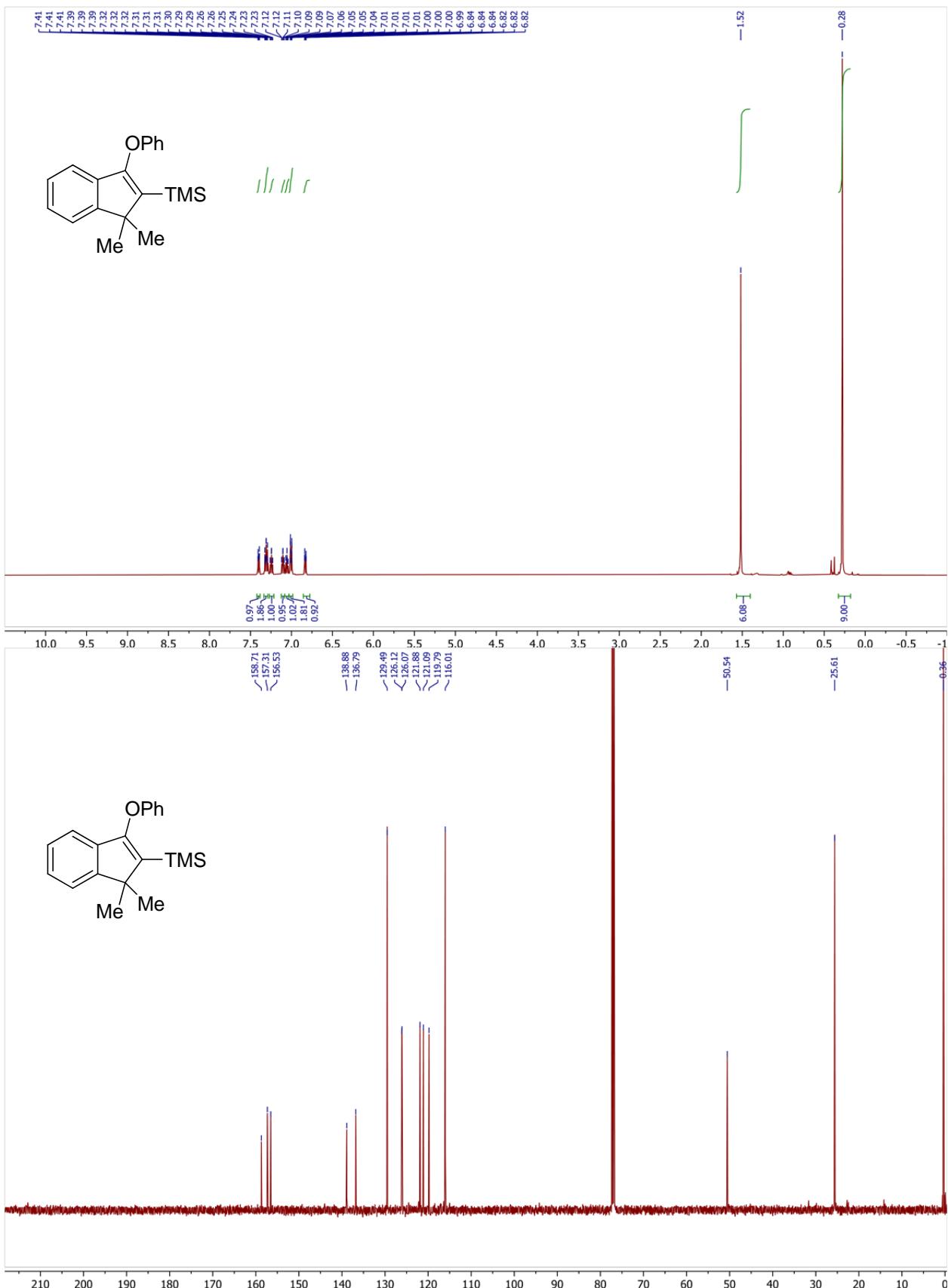


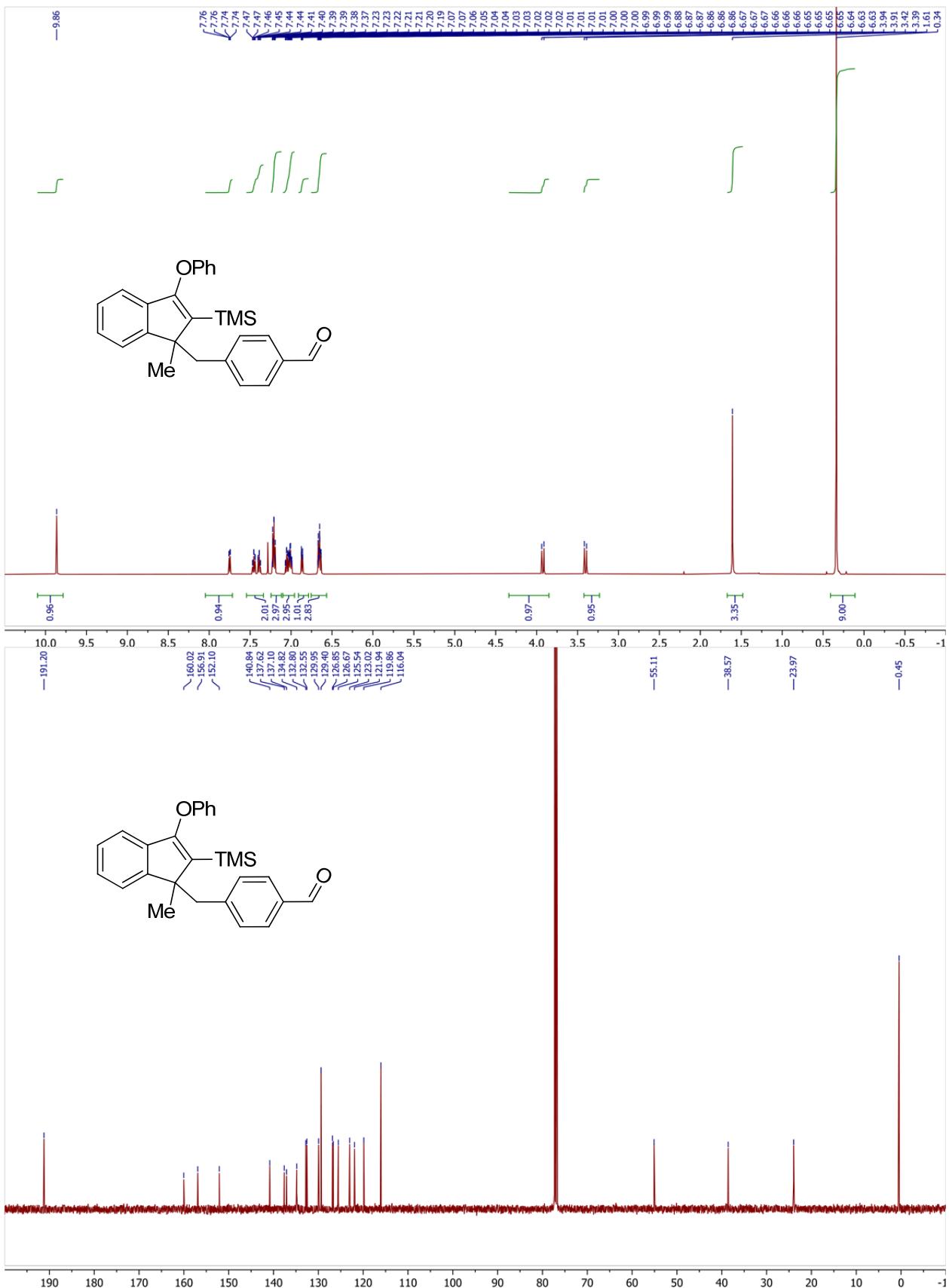












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- (4) Coles-Taylor, B. L.; McCallum, M. S.; Lee, J. S.; Michel, B. W. "Accessing 4-oxy-substituted isoquinolinones via C-H activation and regioselective migratory insertion with electronically biased ynl ethers." *Organic & Biomolecular Chemistry*, **2018**, *16*, 8639-8646.

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