Direct Light Activation of Hypervalent Iodine Reagents: Substrate-Controlled C-C or C-H Alkynylation of Cyclopropanes

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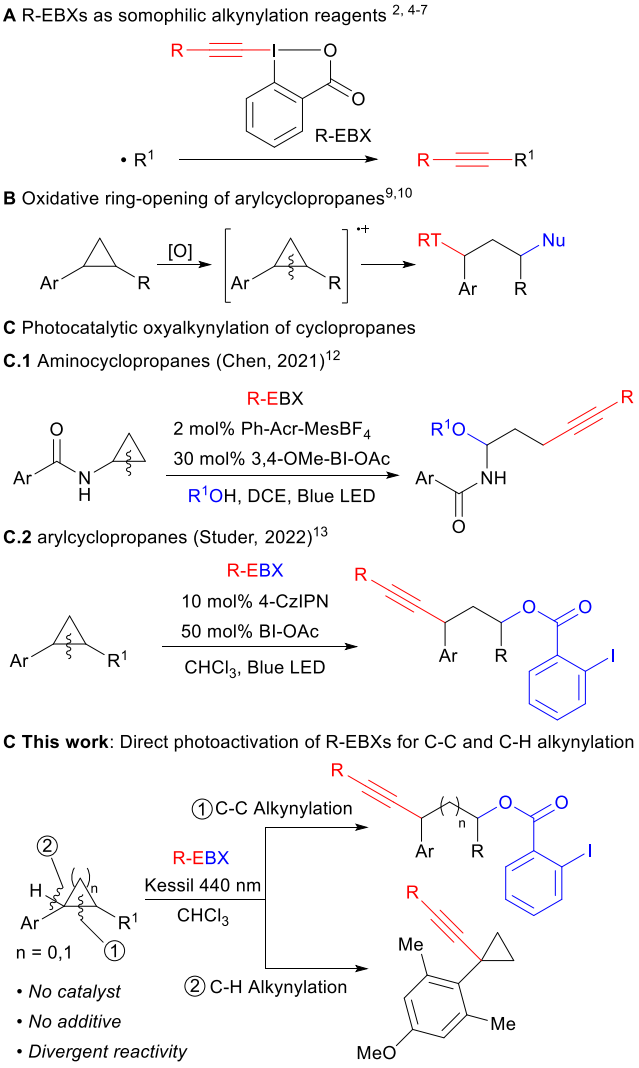
Abstract

We report the direct light activation of ethynylbenziodoxolone (EBX) reagents for the oxyalkynylation of aryl- and amino-cyclopropanes as well as styrenes. Irradiation with visible light at 440 nm promoted the reaction without the need of a photocatalyst. By the choice of the aryl group on the cyclopropane, it was possilbe to completely switch the outcome of the reaction from the oxyalkynylation of the C-C bond to the alkynylation of the C-H bond. This effect has been speculatively attributed to the conformational control induced by the aryl group on the cyclopropane ring

Introduction

Hypervalent iodine reagents are now well-established for the functionalization of nucleophiles under mild conditions due to their unique reactivity.[1] More recently, they have been also successful in the functionalization of radicals. In particular, ethynylbenziodoxolone (EBX) reagents have emerged as excellent radical traps, enabling the synthesis of alkynes otherwise difficult to access (Scheme 1A).[2] Efficient access toward structurally diverse alkynes is urgently needed, due to their numerous applications in synthetic and medicinal chemistry, chemical biology and organic materials.[3] The combination of visible-light photocatalysis and EBX reagents has been especially successful, allowing new processes, such as decarboxylative[4] or deoxygenative alkynylations,[5] as well as alkene[6] and C-H functionalization.[7]

In contrast, the direct alkynylation of inert C-C bonds is more challenging. The use of the ring strain of cyclopropanes is well-established in synthetic chemistry to enable C-C bond cleavage. First applied to more reactive Donor-Acceptor systems,[8] less reactive Donor-only arylcyclopropanes could be also recently functionalized through oxidative activation to give radical cations (Scheme 1B).[9] Photocatalytic methods have further led to new multi-functionalization reactions.[10] However, concerning alkynylation, success has been limited for a long time to cyclopropanols, giving access only to ketones as products.[11] In 2021, Chen and co-workers developed the first photocatalyzed oxyalkynylation of the C-C bond of aminocyclopropanes (Scheme 1C1).[12] During preparation of this manuscript, Studer and co-workers reported in January 2022 the first addition of EBX reagents to the C-C bond of arylcyclopropanes (Scheme 1C2).[13] Both methods required a careful optimization of additives and photocatalyst for success.



Scheme 1 Combining the unique reactivity of hypervalent iodine reagents and ring strain for the synthesis of multi-functionalized alkynes. D = Donor, A = Acceptor, Nu = Nucleophile, RT = radical trap.

Our group recently discovered the direct visible light activation of aryl-substituted EBX reagents.[14] The generated excited species could be used for the oxidative alkynylation of several functional groups and alkenes. A key advantage of this approach is the simplicity of the procedure, requiring only the irradiation of a mixture of substrates and EBX reagents without the need for fine-tuned photocatalysts and additives. We wondered therefore if this approach would be also successful in the case of the oxyalkynylation of the C-C bond of aryl cyclopropanes.

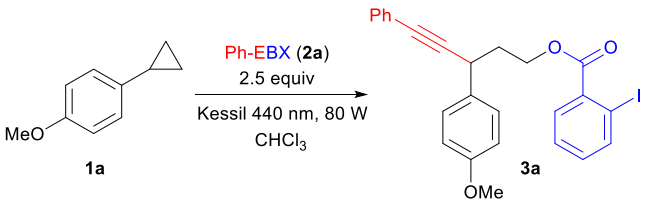
Although the direct light-mediated oxidation of arylcyclopropanes has been reported with nitrogen-based and chloride radicals,[15] alkynylation could not be achieved so far in absence of a photocatalyst.

Herein, we report the first ring-opening oxyalkynylation of aryl cyclopropanes through the direct photoexcitation of EBX reagents (Scheme 1D). The 1,3-oxyalkynylation products were obtained with full regioselectivity, in yields comparable to those of photocatalytic methods. The same conditions were also used for the 1,3-oxyalkynylation of aminocyclopropanes and the 1,2-oxyalkynylation of styrenes. In addition, the reaction outcome could be changed from C-C to C-H alkynylation in dependence of the aryl group on the cyclopropane.

Results and discussion

To start our studies, we choose *para*-methoxybenzene substituted cyclopropane **1a**, as it can be oxidized at a relatively low potential ($E_{1/2}$ = +1.35 V).[15b] As we had estimated the oxidation potential of photoexcited Ph-EBX* (**2a***) to be +1.8 V,[14] the generation of a radical cation should be possible. Indeed, efficient oxyalkynylation to give **3a** was observed (Table 1). The best results were obtained using chloroform as solvent and 2.5 equivalents of **2a**. Under these conditions, **3a** was isolated in 68% yield. The only observed side product was double addition of 2-iodobenzoate in 10% yield, probably resulting from over-oxidation of the benzylic radical to the cation. To obtain reproducible results, thorough degassing of the reaction mixture and purifying Ph-EBX (**2a**) by recrystallization were required (See Supporting Information for details). Product **3a** was also obtained in other chlorinated solvents, but only in moderate yields (entries 2-3). Only very low yields were observed in other solvents (entry 4). Irradiation at 467 nm was less efficient (entry 5). No product was obtained when using a blue LED strip (entry 6). This confirmed that strong irradiation is needed to activate directly aryl EBX reagents. During completion of our work, Zuo and Studer indeed reported that a photocatalyst and BI-OAc as additive are needed with blue LED strips to obtain **3a** in 67% isolated yield.[13] A lower yield was obtained with two equivalents **2a**, and using three equivalents did not improve the yield (entries 7 and 8). This is in agreement with what we observed in our previous work,[14] indicating that one equivalent of **2a** is probably acting as oxidant, and a second one as alkynylation reagent. In contrast to Zuo and Studer's work, no additive was need in the reaction and adding 50% of BI-OAC gave no improvement (entry 9). Finally, no product was obtained when heating the reaction mixture at 50 °C in the dark (entry 10).

Table 1 Optimization of the oxyalkynylation of cyclopropane **1a**.

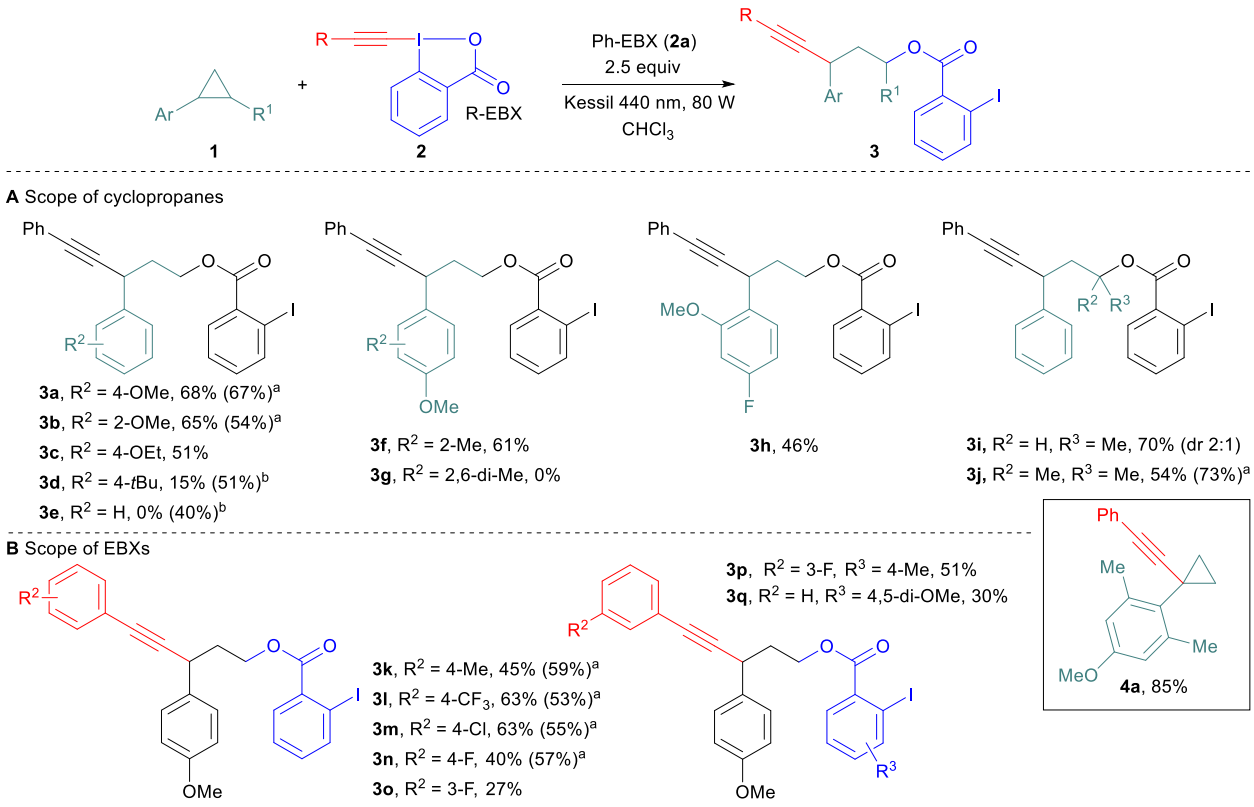


Entry	Deviation from conditions	**Conversion** (%)[a]	**Yield** (%)[a]
1	none	>95	72 (68)
2	In CH_2Cl_2	94	54
3	In DCE	61	20
4	In MeOH, DMF, CH_3CN, THF, EtOAC, DMSO, PhCl	0-74	<14
5	Kessil lamp 467 nm	43	28
6	blue LED strip	6	<5
7	2 equiv Ph-EBX (**2a**)	88	58
8	3 equiv Ph-EBX (**2a**)	>95	73
9	0.5 equiv BI-OAc, 2 equiv **2a**	85	52
10	In the dark at 50 °C	4	<5

Reaction Conditions: 0.2 mmol **1a** (1 equiv), 0.5 mmol **2** (2.5 equiv), two Kessil lamps (440 nm, 2x40 W), in 2 mL $CHCl_3$. [a]^{1}H NMR Yield and conversion were determined with CH_2Br_2 as an internal standard. Isolated yield after chromatography is given in brackets.

With optimized conditions in hand, we studied first the scope of arylcyclopropanes (Scheme 2A). As expected, electron-rich substituents were required to promote the reaction: oxyalkynylation products **3a-c** bearing a methoxy or an ethoxy substituent were obtained in 51-68% yield, whereas a *tert*-butyl substituent gave **3d** in only 15% yield and no product was obtained for an unsubstituted benzene ring (**3e**). For **3a** and **3b**, the yields obtained were comparable or slightly superior to the photocatalytic method developed by Zuo and Studer.[13] However, the photocatalyst approach is superior for less electron-rich substrates not accessible via direct photoexcitation of EBXs: Products **3d** and **3e** where obtained in 52% and 40% respectively using an acridinium dye as photocatalyst. A methyl group in *ortho* position was well tolerated to give product **3f**. However, no product **3g** was obtained with two *ortho* methyl groups. Surprisingly, C-H alkynylation product **4a** was isolated in 85% yield instead. In presence of a methoxy group, an electron-deficient fluoro substituent was tolerated to give product **3h** in 46% yield. Starting from β-substituted cyclopropanes, products **3i** and **3j** were obtained in 70% and 54% yield with selective attack of the iodobenzoate at the most encumbered position.

We then examined the scope of EBX reagents, considering that only aryl-substituted EBXs are photoactive (Scheme 2B).[14] A tolyl-substituted EBX gave **3k** in 45% yield. Introduction of a *para*-trifluoromethyl or a chloro group on the aryl ring of the alkyne led to **3l** and **3m** in 63% yield. Fluoro substituents were also tolerated, but gave only moderate yields of **3n** and **3o**. These results contrasted with our previous work were only Ph- and tolyl-EBX gave useful yields of products.[14]



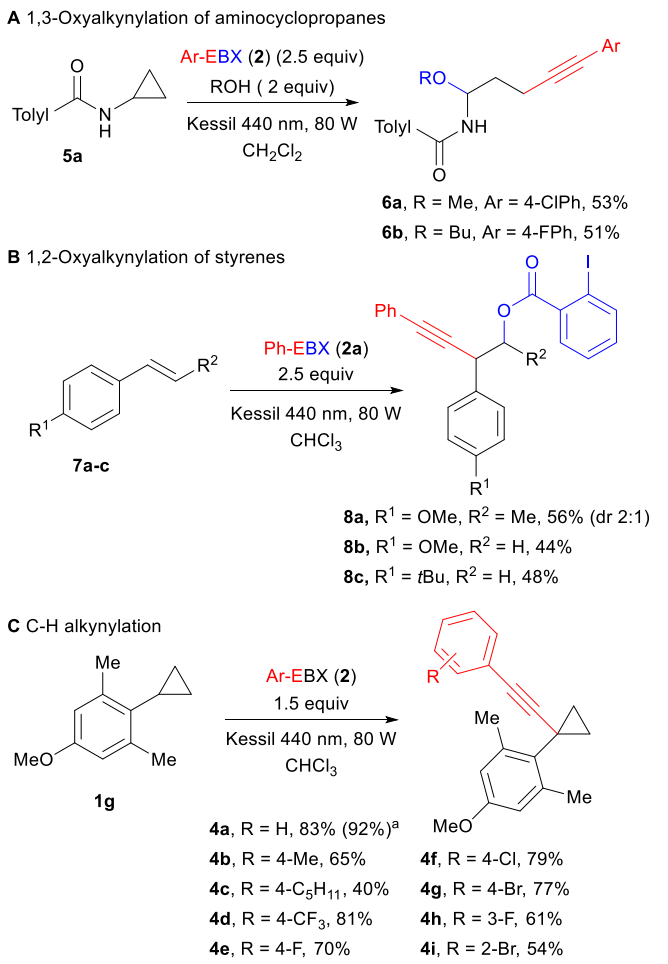
Scheme 2 Scope of the oxyalkynylation of arylcyclopropanes. Reaction Conditions: 0.2 mmol **1a** (1 equiv), 0.5 mmol **2** (2.5 equiv), two Kessil lamps (440 nm, 2x40 W), in 2 mL $CHCl_3$. Isolated yield after column chromatograpy is given. [a] Yield reported in Ref. 13 using 4-CzIPN as photocatalyst and BI-OAc as additive. [b]Yield using Ph-Acr-MesBF_4 as photocatalyst.

Finally, an advantage of EBXs is that the properties can be finely tuned by modification of the 2-iodobenzoic acid core of the reagent. For example the yield of transfer of the 3-F-benzene substituted alkyne could be increased from 27 to 51% by introducing a methyl group *para* to the carboxylic acid (product **3p**). A dimethoxy-substituted reagent could also be used to give **3q** in 30% yield.

Our main goal was the oxyalkynylation of the C-C bond of arylcyclopropanes. However, the same conditions can be also applied to the oxyalkynylation of aminocyclopropane **5a** giving products **6a** and **6b** in 53% and 51% yield (Scheme 3A). As reported by Chen for the photocatalytic reaction,[12] a complete inversion of the regioselectivity can be observed in this case. This is probably due to the lower stability of the radical cation, leading to ring-opening prior to attack of the nucleophile. The oxyalkynylation is not limited to σ-C-C bonds. Indeed, electron-rich styrene derivatives **7a-c** could be converted to products **8a-c** in 44-56% yield with complete regioselectivity via 1,2-oxyalkynylation of the π bond (Scheme 3B). In this case, the same regioselectivity is observed as for enamides.[6b]

Finally, we turned back to the intriguing C-H alkynylation observed in the case of arylcyclopropane **1g**. In fact, 1,1-aryl-alkynyl cyclopropanes are useful building blocks in synthetic and medicinal chemistry.[16] They have never been accessed via C-H alkynylation, which has been realized mostly on unsubstituted positions using directing group mediated transition metal catalysis.[17] We were pleased to see that the Ph-EBX (**2a**) mediated alkynylation of **1g** was surprisingly efficient, with 83% product **4a** isolated after 7 h of irradiation with only 1.5 equivalents of **2a** (Scheme 3C). The reaction was easily scalable and **4a** was obtained in 92% on a 2 mmol scale. The transformation was also successful with functionalized EBX reagents. Alkyl substituents in *para* position on the benzene ring gave products **4b** and **4c** in 65% and 40% yield. A trifluoromethyl group and halogens were well tolerated at this position, giving products **4d-g** in 70-81% yield. Finally, products **4h** and **4i**, bearing a *meta* fluoro and an *ortho* bromo group respectively, were obtained in 61% and 54% yield.

Based on our experimental results and our previous studies,[14] a highly speculative reaction mechanism can be proposed (Scheme 4A). Direct light activation of Ph-EBX (**2a**) would lead to the highly oxidizing species **2a***. Single electron transfer from arylcyclopropane **1** would give then radical anion **I** and radical cation **II**. In a previous work, we showed by computation that **I** was relatively stable to monomolecular decomposition.[18] The major side product observed in the photoactivation of **2a** is diyne **9**, probably formed in either of two bimolecular pathway: Reaction with another molecule of **I** to give **9** and 2 equivalents of 2-iodobenzoate (**10**), or with **2a** to give **9**, **10** and radical **III**.

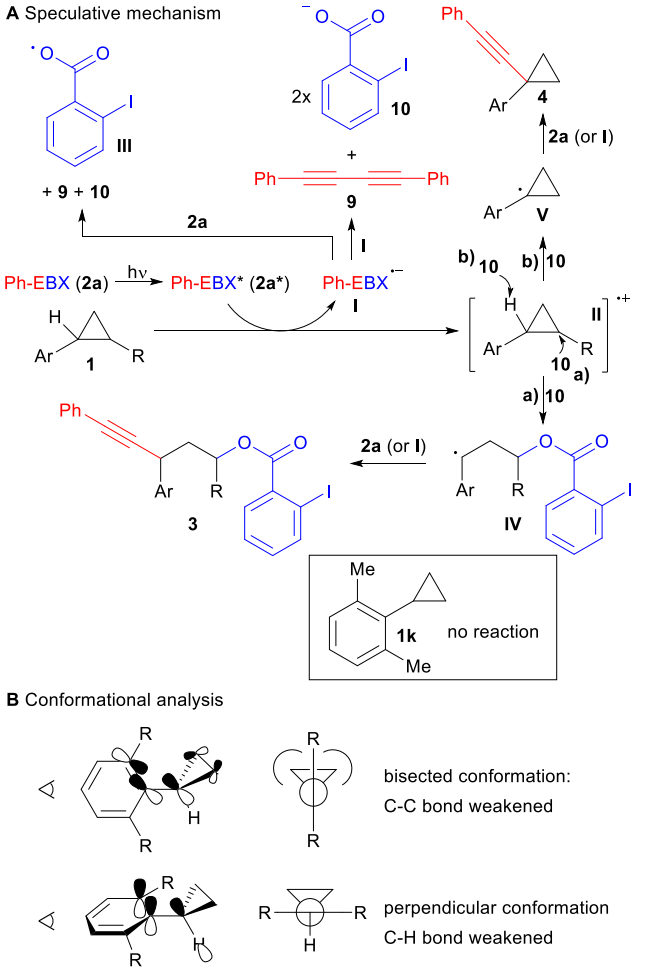


Scheme 3 1,3-Oxyalkynylation of aminocyclopropanes (**A**), 1,2-oxyalkynylation of styrene derivatives (**B**) and C-H alkynylation of arylcyclopropanes (**C**). Isolated yields on 0.2 mmol scale are given, see Supporting Information for detailed experimental procedures. [a]Isolated yield on a 2 mmol scale.

From radical cation **II**, two pathways can be considered. Ring opening with benzoate **10** to give the more stable radical **IV**, followed by reaction with **2a** (or **I**) would lead to the oxyalkynylation product **3** (pathway **a**). Deprotonation with benzoate **10** would give radical **V**, which would be then alkynylated by either **2a** or **I** resulting in the formation of **4** (pathway **b**). In general, we would favour alkynylation with **2a**, as it would be present in higher concentration, but an involvement of **I** cannot be excluded, especially in the case of C-H alkynylation, which is surprisingly efficient. For C-H alkynylation, a radical chain mechanism involving radical **III** should also be considered. In fact, H abstraction from **1** by **III** would give directly radical **V**. However, we think that this mechanism may be less probable, as no alkynylation was observed with arylcyclopropanes lacking the methoxy group such as **1k**, showing that oxidation of the substrate is probably needed for the reaction to occur. Furthermore, direct HAT on cyclopropanes is generally difficult, due to the stronger C-H bond/lower stability of the radical.[19]

A striking result of our studies was the complete switch of chemoselectivity when introducing a second *ortho* methyl group on the arene ring. A tentative explanation may be found in the conformation analysis of the cyclopropane (Scheme 4B).

It is well-known that aryl cyclopropanes favour a bisected conformation to enable overlap between the π-Walsh orbitals and the π* of the benzene ring.[20] Another effect of this interaction is also the weakening of the C-C bond and favour ring-opening. With one *ortho* group, a low energy bisected conformer is still available. However, when a second *ortho* group is present, strong steric interactions with the cyclopropane cannot be avoided anymore. Therefore, the usually less favoured perpendicular conformation becomes lower in energy. In this conformation, there is nearly no effect of the benzene ring on the strength of the C-C bonds. In contrast, one may envision a weakening interaction between the π system of the benzene and the σ* orbital of the C-H bond, favouring deprotonation/H abstraction. Of course, care has to be taken with this simple conformational analysis of the starting material, and future studies will focus on computations involving radical cation **II** and the transition states of the proposed pathways **a** and **b**.



Scheme 4 Speculative mechanism for the C-C oxyalkynylation and the C-H alkynylation reactions (**A**) and conformational analysis of arylcyclopropanes (**B**).

Conclusions

In summary, we have reported a light-mediated oxyalkynylation of the C-C bond of arylcyclopropanes via the direct photoactivation of aryl-EBX reagents with visible light. In contrast to previous works, neither photocatalysts nor additive

were needed. In addition, we discovered a complete switch of the reaction outcome from C-C to C-H alkynylation when using aryl cyclopropanes bearing two *ortho* substituents on the benzene ring. We tentatively attributed this effect to the conformational constrains induced by the aryl ring, and we think this result will pave the way for the development of new selective transformations of cyclopropanes.

Author Contributions

T.V.T. N planned the research and performed all the experiments described, prepared the material for the redaction of the manuscript and the supporting information. J. W. supervised the research, participated to the redaction and finalization of the manuscript, as well as proof-read the supporting information.

Conflicts of interest

There are no conflicts to declare.

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SUPPORTING INFORMATION

Contents

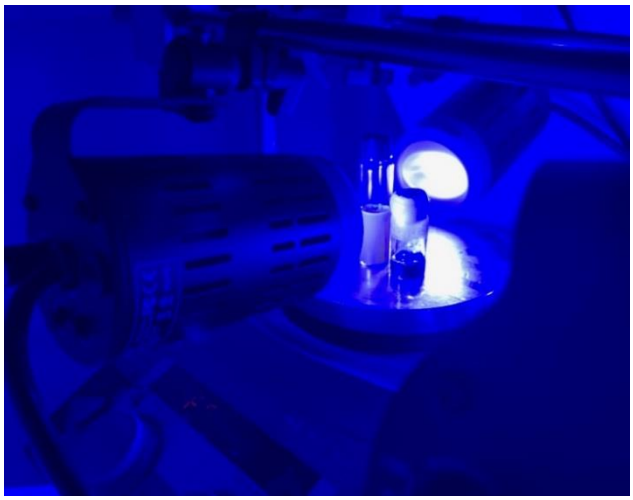
General Methods

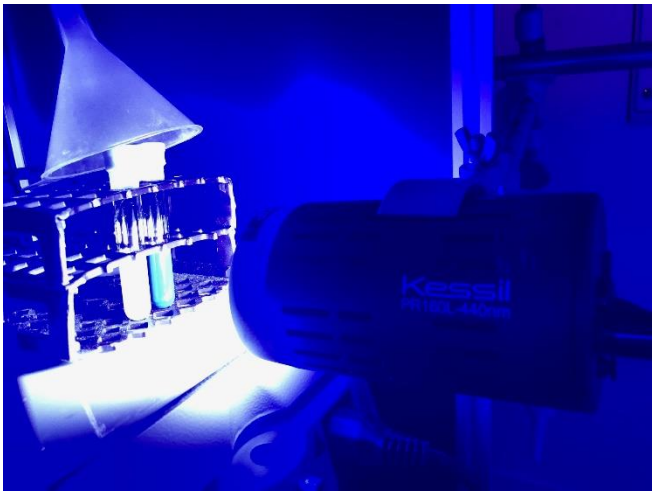
For quantitative flash chromatography, distilled technical grade solvents were used. THF, Et_2O, toluene, hexane and CH_2Cl_2 were dried by passage over activated alumina under nitrogen atmosphere (H_2O content < 7 ppm, Karl-Fischer titration). All chemicals were purchased and used as received unless stated otherwise. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure. TLC was performed on Merck silica gel 60 F254 TLC plastic or aluminium plates and visualized with UV light, permanganate stain. Melting points were measured on a calibrated Büchi B-540 melting point apparatus using open glass capillaries. ^{1}H-NMR spectra were recorded at room temperature on a Brucker DPX-400 400 MHz spectrometer in $CDCl_3$, Acetone-d_6, CD_3CN or CD_3OD, all signals are reported in ppm with the internal chloroform signal at 7.26 ppm, the internal acetone signal at 2.09 ppm, the internal acetonitrile signal at 1.94 ppm and the internal methanol signal at 3.34 ppm as standard. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, p = quintet, m = multiplet or unresolved, br = broad signal, integration, coupling constant(s) in Hz, interpretation). ^{13}C-NMR spectra were recorded with 1H-decoupling on a Brucker DPX-400 101 MHz spectrometer in $CDCl_3$, Acetone-d_6, CD_3CN or CD_3OD, all signals are reported in ppm with the internal chloroform signal at 77.0 ppm, Acetone-d_6 signal at 29.8 ppm, CD_3CN signal at 1.3 ppm or CD_3OD signal at 49.0 ppm as standard. Infrared spectra were recorded on a JASCO FT-IR B4100 or a Bruker Alpha-P spectrophotometer with an ATR device and a ZnSe prism and are reported as cm-1 (w = weak, m = medium, s = strong). High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API. HPLC measurements were done on a Agilent 1260 Infinity autosampler using a CHIRALPAK IA, IB, IC or IF column from DAICEL Chemical. The specific solvents and concentrations (in g/100 mL) are indicated.

All photocatalyzed reactions were carried out in oven dried glassware and under inert atmosphere (freeze pump thaw solvent stored on molecular sieves and under argon for maximum one week) unless specified otherwise. They were placed on a stirring plate with Kessil lamps (440 nm, 40 W) irradiating from both sides (the hood was free and coated with aluminum foil for personal protection). The distance between the Kessil lamps and the vials was approximatively 10 cm. Long irradiation resulted in temperature increasing up to 50 °C during overnight reactions unless a fan was used in which case the temperature raised to 30-35°C.

Photochemical experimental set-up

0.2 mmol scale reactions (both set-up can be used without affecting the yields)



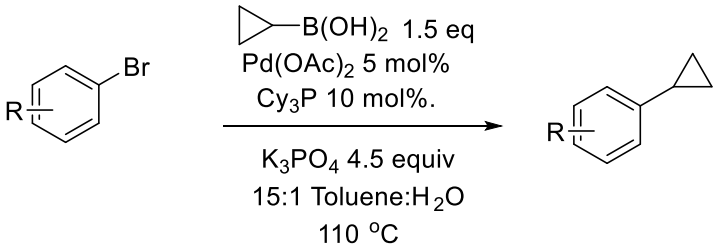


2 mmol scale reactions

Synthesis of aryl cyclopropanes, aminocyclopropanes.

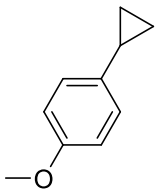
- Compound **1e**, **7a**, **7b**, **7c** are commercially available and were used directly without further purification

General procedure A: Synthesis of aryl cyclopropanes



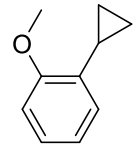
To a solution of aryl bromide (5.00 mmol, 1.00 equiv) in 15:1 toluene:water (32 mL) was added potassium phosphate tribasic potassium (4.78 g, 22.5 mmol, 4.50 equiv), cyclopropylboronic acid (644 mg, 7.50 mmol, 1.50 equiv), 0.5 ml Tricyclohexylphosphine (1M solution in toluene) and palladium(II) diacetate (56.1 mg, 250 µmol, 0.0500 equiv). The resulting mixture was heated to 110 °C. After 12 hours, the reaction mixture was cooled to room temperature, diluted with DCM (100 mL) and washed with water (100 mL). The aqueous layer was extracted with DCM (3 × 100 mL). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 40 g, gradient of pentane: ethyl acetate from 99:1 to 95:5). to obtain the product.

1-Cyclopropyl-4-methoxybenzene (1a)



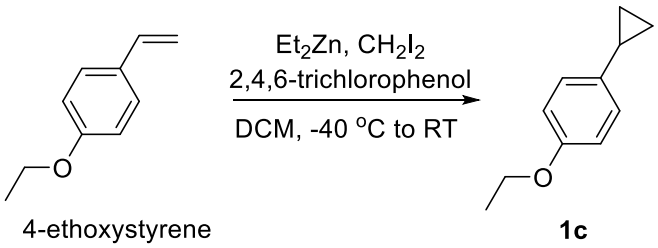
Following the general procedure A, starting from 1-bromo-4-methoxybenzene (935 mg, 5.00 mmol, 1.00 equiv), 1-cyclopropyl-4-methoxybenzene **1a** (580 mg, 3.91 mmol, 78% yield) was obtained as a colorless liquid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.09 – 6.97 (m, 2H, Ar*H*), 6.90 – 6.77 (m, 2H, Ar*H*), 3.78 (s, 3H, O*CH*$_3$), 1.86 (m, 1H, *CH*CH_2), 0.98 – 0.84 (m, 2H, CH*CH*$_2$), 0.71 – 0.57 (m, 2H, CH*CH*$_2$). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 157.7, 136.0, 127.0, 113.9, 55.4, 14.7, 8.6. Consistent with reported data. [1]

1-Cyclopropyl-2-methoxybenzene (1b)



Following the general procedure A, starting from 1-bromo-2-methoxybenzene (935 mg, 5.00 mmol, 1.00 equiv), obtained 1-cyclopropyl-2-methoxybenzene **(1b)** (620 mg, 4.18 mmol, 84% yield) as colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.57 - 7.50 (m, 1H, Ar*H*), 7.37 – 7.17 (m, 3H, Ar*H*), 4.26 (s, 3H, OC*H*$_3$), 2.60 - 2.53 (m, 1H, C*H*CH_2), 1.41 – 1.25 (m, 2H, CHC*H*$_2$), 1.13 – 1.00 (m, 2H, CHC*H*$_2$). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 158.4, 132.1, 126.4, 124.9, 120.7, 110.3, 55.7, 9.4, 7.8. HRMS (APPI/LTQ-Orbitrap) m/z: $[M]^+$ Calcd for $C_{10}H_{12}O^+$ 148.0883; Found 148.0880. Consistent with reported data.[1]

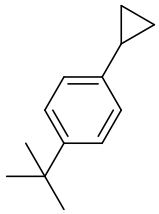
1-cyclopropyl-4-ethoxybenzene (1c)



In a 150 mL oven-dried round-bottom flask with a stirring bar, was added 2,4,6-trichlorophenol (1.18 g, 6.00 mmol, 2.5 equiv) under nitrogen atmosphere. DCM (60 mL, 0.1 M) was added into the flask and the reaction mixture was cooled to -40 °C. $ZnEt_2$ (1.0 M, 6.0 mL, 6.0 mmol,2.5 equiv) was added slowly into the flask by syringe and the reaction mixture was stirred at this temperature for 15 min. CH_2I_2 (2.6 g, 9.6 mmol, 4.0 equiv) was added slowly by syringe and the reaction mixture was stirred at this temperature for another 15 min. Next, the corresponding solution of 4-ethoxystyrene (0.36 g, 2.4 mmol, 1.0 equiv) in DCM (10 mL) was added by syringe and the reaction mixture was allowed to warm to room temperature and stirred for 16 h. After the reaction reached completion (as judged by ^{1}H-NMR), the reaction mixture was quenched with sat. NH_4Cl (30 mL) in 30 minutes and extracted with DCM (100mL) for 3 times. The combined organic layers were washed with aq. NaOH (1.0 M, 30 mL) and brine (20 mL), dried over Na_2SO_4 (20 g) and filtered. The mixture was concentrated under reduced pressure, the crude residue was purified by column chromatography (Pentane: EtOAc = 50: 1 to 10: 1) to afford the desired compound 1-

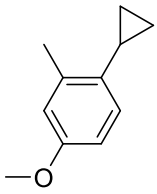
cyclopropyl-4-ethoxybenzene (**1c**) (243 mg, 1.50 mmol 63%) as colorless oil. **Rf** = 0.50 (SiO_2, 40:1 pentane:ethyl acetate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.08 – 6.97 (m, 2H, ArH), 6.86 – 6.77 (m, 2H, ArH), 4.01 (q, *J* = 7.0 Hz, 2H, CH_2O), 1.86 (tt, *J* = 8.5, 5.1 Hz, 1H, ArC*H*), 1.41 (t, *J* = 7.0 Hz, 3H, CH_3), 0.95 – 0.87 (m, 2H, CHC*H*$_2$), 0.63 (dt, *J* = 6.5, 4.5 Hz, 2H, CHC*H*$_2$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.0, 135.8, 126.9, 114.5, 63.6, 15.0, 14.7, 8.6. **HRMS** (APCI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{15}O^+$ 163.1117; Found 163.1113.

1-Tert-butyl-4-cyclopropylbenzene (1d)



Following the general procedure A, starting from 1-bromo-4-tert-butylbenzene (1.07 g, 5.00 mmol, 1.00 equiv), 1-*tert*-butyl-4-cyclopropylbenzene (**1d**) (710 mg, 4.07 mmol, 81% yield) was obtained as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 2H, ArH), 7.07 – 7.00 (m, 2H, ArH), 1.88 (tt, *J* = 8.4, 5.1 Hz, 1H, ArC*H*), 1.31 (s, 9H, $C(CH_3)_3$), 0.97 – 0.89 (m, 2H, CHC*H*$_2$), 0.74 – 0.64 (m, 2H, CHC*H*$_2$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 148.4, 141.0, 125.5, 125.3, 34.5, 31.5, 15.0, 9.1. **HRMS** (APPI/LTQ-Orbitrap) m/z: $[M]^+$ Calcd for $C_{13}H_{18}^+$ 174.1403; Found 174.1400. Consistent with reported data.[2]

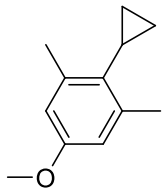
1-bromo-4-methoxy-2-methylbenzene (1f)



Following the general procedure A, starting from 1-bromo-4-methoxy-2-methylbenzene (1.01 g, 5.00 mmol, 1.00 equiv), obtained 1-cyclopropyl-4-methoxy-2-methylbenzene **1f** (622 mg, 3.83 mmol, 77% yield) as colorless oil**. Rf** = 0.44 (SiO_2, 40:1 pentane:ethyl acetate) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.94 (d, *J* = 8.4 Hz, 1H), 6.73 (d, *J* = 2.8 Hz, 1H), 6.66 (dd, *J* = 8.4, 2.8 Hz, 1H, Ar*H*), 3.78 (s, 3H, Ar*H*), 2.41 (s, 3H, ArC*H*$_3$), 1.81 (tt, *J* = 8.4, 5.4 Hz, 1H, C*H*CH_2), 0.99 – 0.79 (m, 2H, CHC*H*$_2$), 0.67 – 0.52 (m, 2H, CHC*H*$_2$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.8, 139.5, 133.6,

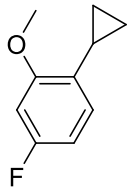
127.2, 115.6, 110.6, 55.3, 19.9, 13.0, 6.5. **HRMS** (APPI/LTQ-Orbitrap) m/z: $[M]^+$ Calcd for $C_{11}H_{14}O^+$ 162.1039; Found 162.1038.

2-Cyclopropyl-5-methoxy-1,3-dimethylbenzene (1g)



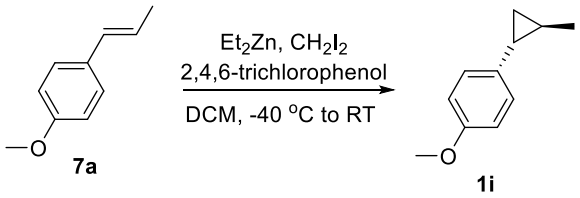
Following the general procedure A, starting from 2-bromo-5-methoxy-1,3-dimethylbenzene (1.08 g, 5.00 mmol, 1.00 equiv), obtained 2-cyclopropyl-5-methoxy-1,3-dimethylbenzene **1g** (630 mg, 3.57 mmol, 71% yield) as a colorless oil. **Rf** = 0.47 (SiO_2, 40:1 pentane:ethyl acetate) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.57 (s, 2H, Ar*H*), 3.77 (s, 3H, OC*H*$_3$), 2.42 (s, 6H, ArC*H*$_3$), 1.71 – 1.58 (m, 1H, ArC*H*CH_2), 1.05 – 0.89 (m, 2H, CHC*H*$_2$), 0.57 – 0.43 (m, 2H, CHC*H*$_2$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.7, 140.4, 131.7, 113.2, 55.2, 21.0, 11.5, 8.2. **HRMS** (APPI/LTQ-Orbitrap) m/z: $[M]^+$ Calcd for $C_{12}H_{16}O^+$ 176.1196; Found 176.1193.

1-cyclopropyl-4-fluoro-2-methoxybenzene (1h)



Following the general procedure A, starting from 1-bromo-4-fluoro-2-methoxybenzene (1.03 g, 5.00 mmol, 1.00 equiv), obtained 1-cyclopropyl-4-fluoro-2-methoxybenzene **1g** (540 mg, 3.25 mmol, 65% yield) as a colorless oil. **Rf** = 0.53 (SiO_2, 40:1 pentane:ethyl acetate). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 6.89 – 6.75 (m, 1H, Ar*H*), 6.64 – 6.52 (m, 2H, Ar*H*), 3.85 (s, 3H, OC*H*$_3$), 2.13 – 1.99 (m, 1H, C*H*CH_2), 0.97 – 0.83 (m, 2H, CHC*H*$_2$), 0.66 – 0.53 (m, 2H, CHC*H*$_2$). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 161.8 (d, *J* = 242.6 Hz), 159.4 (d, *J* = 9.5 Hz), 127.5 (d, *J* = 3.2 Hz), 125.9 (d, *J* = 9.7 Hz), 106.5 (d, *J* = 20.9 Hz), 98.7 (d, *J* = 25.7 Hz), 55.8, 9.3, 7.4. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -115.4. **HRMS (APPI/LTQ-Orbitrap)** m/z: $[M]^+$ Calcd for $C_{10}H_{11}FO^+$ 166.0788; Found 166.0787

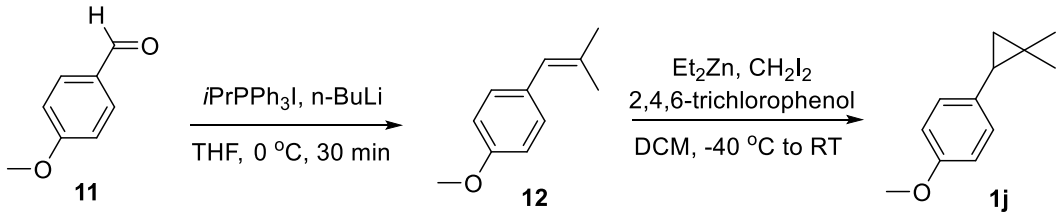
1-methoxy-4-(2-methylcyclopropyl)benzene (1i)



In a 250 mL oven-dried round-bottom flask with a stir bar, was added 2,4,6-trichlorophenol (2.46 g, 12.50 mmol, 2.5 equiv) under nitrogen atmosphere. DCM (120 mL, 0.1 M) was added into the flask and the reaction mixture was cooled to -40 °C. $ZnEt_2$ (1.0 M, 12.5 mL, 12.50 mmol, 2.5 equiv) was added slowly into the flask by syringe and the reaction mixture was stirred at this temperature for 15 min. CH_2I_2 (5.29 g, 20.00 mmol, 4.0 equiv) was added slowly by syringe and the reaction mixture was stirred at this temperature for another 15 min. Next, the corresponding solution of alkene **7a** (741.0 mg, 5.00 mmol, 1.0 equiv) in DCM (20 mL) was added by syringe and the reaction mixture was allowed to warm to room temperatureand stirred for 16 h. After the reaction reached completion (as judged by 1H-NMR), the reaction mixture was quenched with sat. NH_4Cl (60 mL) for 30 minutes and extracted with DCM (100mL) for 3 times. The combined organic layers were washed with aq. NaOH (1.0 M, 60 mL) and brine (40 mL), dried over Na_2SO_4 and filtered. The resulted mixture was concentrated under reduced pressure, the crude residue was purified by column chromatography (Pentane : EtOAc = 50: 1 to 10: 1) to afford the desired compound 1-methoxy-4-(2-methylcyclopropyl)benzene **1i** (389 mg, 2.40 mmol, 48%) as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 – 6.96 (m, 2H, ArH), 6.84 – 6.78 (m, 2H, ArH), 3.80 (s, 3H, OCH_3), 1.60 – 1.51 (m, 1H, ArCHCH$_2$), 1.19 (d, J = 5.9 Hz, 3H, CH$_2$CHCH_3), 1.04 – 0.93 (m, 1H, CHCH$_3$) 0.84 – 0.79 (m, 1H, ArCHCH_2), 0.69 – 0.62 (m, 1H, ArCHCH_2). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.6, 136.1, 126.7, 113.8, 55.4, 23.5, 19.3, 17.3, 16.9. Consistent with reported data.[3]

Synthesis of 1-(2,2-dimethylcyclopropyl)-4-methoxybenzene (1j)



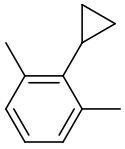
To a 250 mL oven-dried round-bottom flask equiped with a stirring bar, isopropyltriphenylphosphonium iodide (6.0 g, 14 mmol,1.2 equiv) and anhydrous THF (70 mL, 0.2 M) were added. The reaction flaskwas capped with rubber septum and three cycles of evacuate-refill with nitrogen were performed, then the reaction mixture was cooled to 0 °C. n-BuLi (2.5 M, 5.6 mL, 14 mmol, 1.2 equiv) was added dropwise by syringe and the reaction mixture was stirred at this temperature for 30 min. A solution of aldehyde **11** (1577 mg, 11.60 mmol, 1.0 equiv) in THF (20 mL) was added by syringe and the reaction mixture was allowed to warm to room temperature, and then stirred for 16 h. After the reaction reached completion according to the TLC analysis, the reaction mixture was quenched by sat. NH_4Cl (30 mL) and extracted with EtOAc (100mL) for 3 times. The combined organic layers were washed with H_2O_2 (10 wt% in water, 10 mL) and brine (20 mL), dried over Na_2SO_4, and filtered. After that, the mixture was concentrated under reduced pressure, the crude residue was purified by column chromatography (Pentant : EtOAc = 50: 1 to 10: 1) to afford the desired alkene **12** as colorless oil.

In a 150 mL oven-dried round-bottom flask with a stirring bar, was added 2,4,6-trichlorophenol (2.46 g, 12.5 mmol, 2.5 equiv) under nitrogen atmosphere. DCM (120 mL, 0.1 M) was added into the flask and the reaction mixture was cooled to -40 °C. $ZnEt_2$ (1.0 M, 12.5 mL, 12.5 mmol, 2.5 equiv) was added slowly into the flask by syringe and the reaction mixture was stirred at this temperature for 15 min. CH_2I_2 (5.29 g, 20.0 mmol, 4.0 equiv) was added slowly by syringe and the reaction mixture was stirred at this temperature for another 15 min. Next, a solution of alkene **12** (808 mg, 5.00 mmol, 1.0 equiv) in DCM (20 mL) was added by syringe and the reaction mixture was allowed to warm to room temperature and stirred for 16 h. After the reaction reached completion, the reaction mixture was quenched with sat. NH_4Cl (60 mL) in 30 minutes and extracted with DCM (100mL) for 3 times. The combined organic layers were washed with aq. NaOH (1.0 M, 60 mL) and brine, dried over

Na_2SO_4 and filtered. After the volatile materials were removed under reduced pressure, the crude residue was purified by column chromatography (Pentane : EtOAc = 50: 1 to 10: 1) to afford 1-(2,2-dimethylcyclopropyl)-4-methoxybenzene (**1j**) (458 mg, 2.60 mmol, 52%) as colorless oil

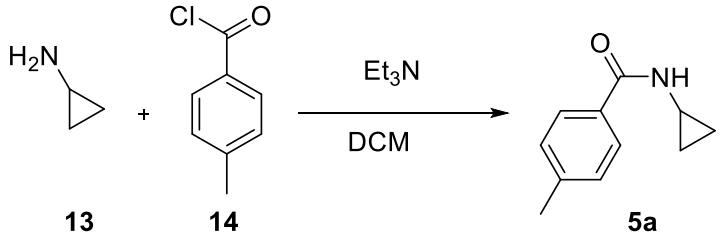
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.1 – 7.0 (m, 2H), 6.9 – 6.8 (m, 2H), 3.8 (d, *J* = 1.6 Hz, 3H), 1.9 – 1.7 (m, 1H), 1.2 (d, *J* = 1.6 Hz, 3H), 0.8 (d, *J* = 1.7 Hz, 3H), 0.8 – 0.6 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.7, 132.6, 130.0, 113.4, 55.4, 29.0, 27.5, 20.6, 18.6, 18.5. Consistent with reported data.[3]

2-Cyclopropyl-1,3-dimethylbenzene (1k)



Following the general procedure D, starting from 2-bromo-1,3-dimethylbenzene (925 mg, 5.00 mmol, 1.00 equiv), 2-cyclopropyl-1,3-dimethylbenzene (**1k**) (530 mg, 3.62 mmol, 72% yield) was obtained as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.09 – 6.95 (m, 3H, Ar*H*), 2.43 (s, 6H, ArCH_3), 1.71 (ddd, *J* = 14.4, 8.4, 6.0 Hz, 1H, ArC*H*CH_3), 1.10 – 0.97 (m, 2H, CH_2), 0.60 – 0.49 (m, 2H, CH_2). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 139.1, 139.0, 127.9, 126.1, 20.7, 12.2, 8.1. **HRMS** (APPI/LTQ-Orbitrap) m/z: $[M]^+$ Calcd for $C_{11}H_{14}^+$ 146.1090; Found 146.1088 Consistent with reported data.[4]

N-cyclopropyl-4- methylbenzamide (5a)



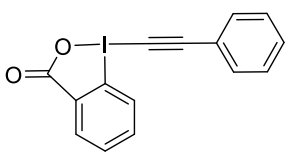
13 **14** **5a**

Following a modified version of a reported procedure,[5] to a solution of cyclopropylamine (**13**) (0.70 mL, 10 mmol, 1.1 equiv.) and triethylamine (1.40 mL, 10.0 mmol, 1.1 equiv.) in dichloromethane (10 mL) was slowly added a solution of 4-methylbenzoyl chloride (**14**) (1.41 g, 9.09 mmol) in dichloromethane (10 mL) at 0 °C. The reaction mixture was stirred at room temperature for 16 hours. Upon completion, the mixture was quenched by the addition of 1

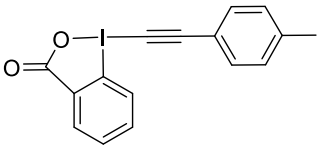
N HCl (10 mL). The aqueous layer was then extracted with dichloromethane. The organic extract was washed with 1 M NaOH (10 mL) and brine (10 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product **5a** was pure enough to be used as such, without further purification.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 – 7.55 (m, 2H, Ar*H*), 7.23 – 7.11 (m, 2H, Ar*H*), 6.33 (d, *J* = 39.2 Hz, 1H, N*H*), 2.88 (tt, *J* = 7.2, 3.5 Hz, 1H, C*H*), 2.37 (d, *J* = 3.1 Hz, 3H, CH_3), 0.92 – 0.75 (m, 2H, CH_2), 0.68 – 0.54 (m, 2H, CH_2). ^{1}H NMR data correspond to the reported values.[6]

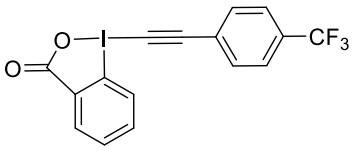
Synthesis of hypervalent iodine reagents



2a



2b



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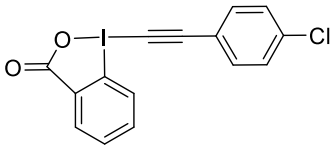

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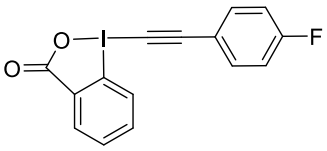
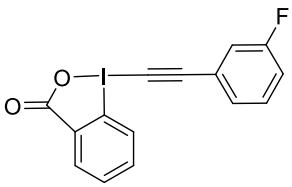
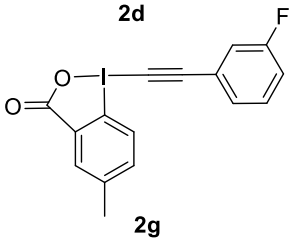


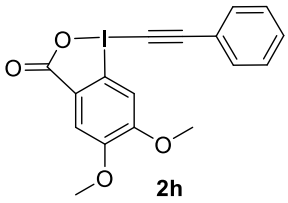
2e



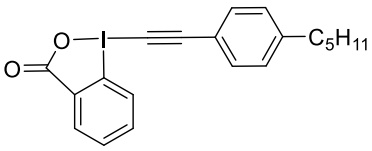
2f



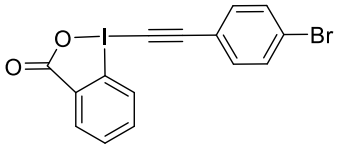
2g



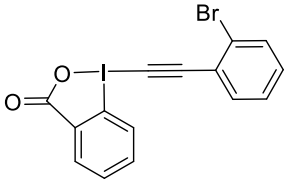
2h



2i

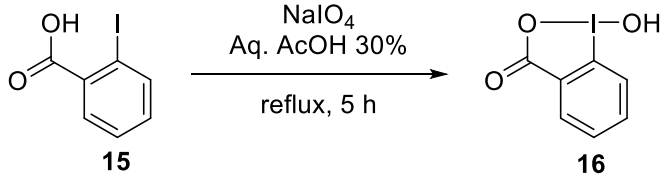


2j



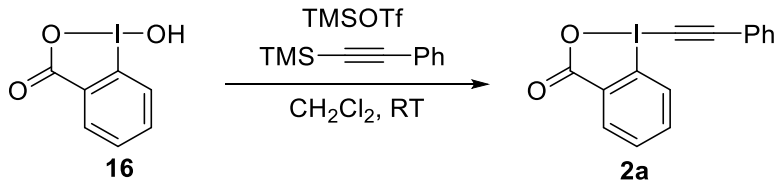
2k

1-Hydroxy-1,2-benziodoxol-3-(1*H*)-one (BIOH, 16)



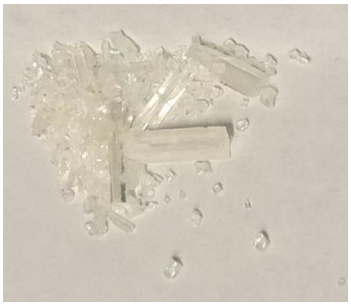
$NaIO_4$ (40.5 g, 189 mmol, 1.05 equiv) and 2-iodobenzoic acid (**15**) (44.8 g, 180 mmol, 1.0 equiv) were suspended in 30% (v:v) aq. AcOH (350 mL). The mixture was vigorously stirred and refluxed for 5 h. The reaction mixture was then diluted with cold water (250 mL) and allowed to cool to rt, protecting it from light. After 1 h, the crude product was collected by filtration, washed on the filter with ice water (3 x 150 mL) and acetone (3 x 150 mL), and air-dried in the dark overnight to afford 1-hydroxy-1,2-benziodoxol-3-(1*H*)-one BIOH (**16**) (44.3 g, 168 mmol, 93% yield) as a white solid. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.02 (dd, *J* = 7.7, 1.4 Hz, 1H, Ar*H*), 7.97 (m, 1H, Ar*H*), 7.85 (dd, *J* = 8.2, 0.7 Hz, 1H, Ar*H*), 7.71 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 167.7, 134.5, 131.5, 131.1, 130.4, 126.3, 120.4. Consistent with reported data[7]

1-[Phenylethynyl]-1,2-benziodoxol-3(1H)-one (PhEBX) (2a)

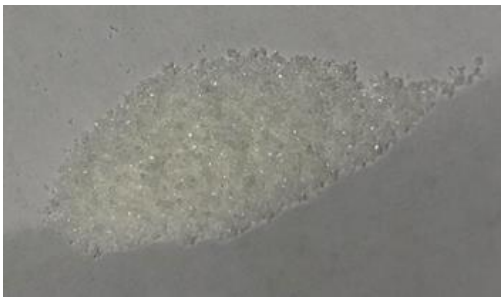


Trimethylsilyltriflate (9.1 mL, 50 mmol, 1.1 equiv) was added dropwise to a suspension of 2-iodosylbenzoic acid (**16**) (12.1 g, 45.8 mmol, 1.0 equiv) in CH_2Cl_2 (120 mL) at 0 °C. The mixture was stirred for 1 h, followed by the dropwise addition of trimethyl(phenylethynyl)silane (8.8 mL, 50 mmol, 1.1 equiv) (slightly exothermic). The resulting suspension was stirred for 6 h at RT, during this time a white solid was formed. A saturated solution of $NaHCO_3$ (120 mL) was added and the mixture was stirred vigorously for 30 min. The mixture was extracted with H_2O and DCM (3x50 mL), washed with brine, then dried over Na_2SO_4, filtered and evaporated under reduced pressure. The resulting solid was recrystalized in EtOAc:MeOH (2:1) (40 mL/grams). **The solution was left to cool to RT overnight**. The slow recrystallization is important to obtain pure product **2a** (photo of crystal obtained below). The crystal formed was filtered and dried under high vacuum to afford PhEBX (**2a**) (5.89 g, 16.95 mmol, 37 %

yield) as colorless crystals.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.46 (m, 1H, Ar*H*), 8.28 (m, 1H, Ar*H*), 7.80 (m, 2H, Ar*H*), 7.63 (m, 2H, Ar*H*), 7.48 (m, 3H, Ar*H*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.9, 134.9, 132.9, 132.5, 131.6, 131.3. 130.8, 128.8, 126.2, 120.5, 116.2, 106.6, 50.2. Consistent with reported data [8]

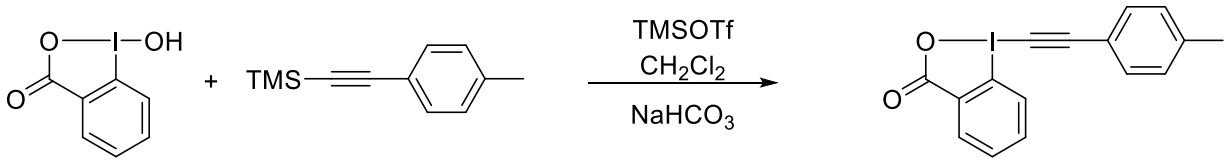


PhEBX with crystallization at RT



PhEBX with fast crystallization in the fridge

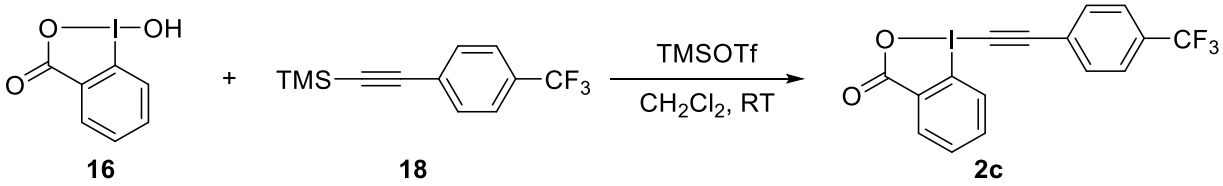
1-(p-Tolylethynyl)-1,2-benziodoxol-3(1H)-one (2b)



16 **17** **2b**

Following a reported procedure,[9] trimethylsilyl triflate (1.0 mL, 5.5 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**16**) (1.32 g, 5.00 mmol, 1.00 equiv) in CH_2Cl_2 (15 mL) at room temperature. The resulting suspension was stirred for 3 h, followed by the drop wise addition of trimethyl(p-tolylethynyl)silane (**17**) (1.04 g, 5.50 mmol, 1.10 equiv). The resulting suspension was stirred for 6 h at room temperature. A saturated solution of $NaHCO_3$ (20 mL) was then added and the mixture was stirred vigorously for 30 minutes. The mixture was extracted with H_2O and DCM (3x20 mL), washed with brine, then dried over Na_2SO_4, filtered and evaporated under reduced pressure. The resulting solid was recrystalized in EtOAc:MeOH (2:1) (40 ml/gram). The solution was left to cool to RT overnight.. The crystal formed was filtered and dried under high vacuum to afford **2b** (0.620 g, 1.71 mmol, 34%) as a white crystals. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.43 (dd, *J* = 6.1, 2.9 Hz, 1H, Ar*H*), 8.30– 8.14 (m, 1H, Ar*H*), 7.77 (dd, *J* = 6.9, 3.1 Hz, 2H, Ar*H*), 7.50 (d, *J* = 7.8 Hz, 2H, Ar*H*), 7.25 (d, *J* = 7.6 Hz, 2H, Ar*H*), 2.43 (s, 3H, ArCH_3).**^{13}C NMR** (100 MHz, CDCl3): δ 166.6, 141.5, 134.9, 132.8, 132.5, 131.6, 131.3, 129.5, 126.2, 117.4, 116.2, 107.25, 49.1, 21.7. Consistent with reported data. [9]

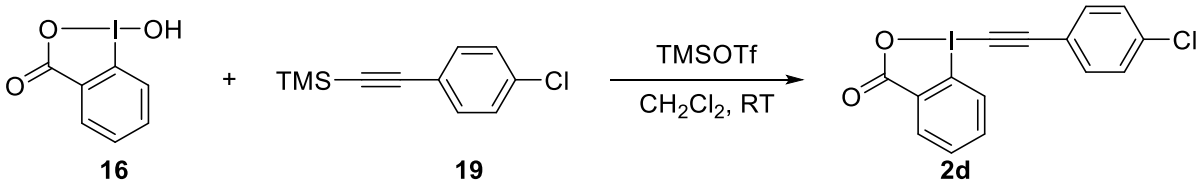
1-(*p*-trifluoromethylethynyl)-1,2-benziodoxol-3(1H)-one (2c)



16 **18** **2c**

Following a reported procedure,[9] trimethylsilyl triflate (1.0 mL, 5.5 mmol, 1.1 equiv) was added to a suspension of BIOH (**16**) (1.3 g, 5.0 mmol, 1.0 equiv) in CH_2Cl_2 (15 mL) at RT The resulting suspension was stirred for 1 h, followed by the dropwise addition of trimethyl((4-(trifluoromethyl)phenyl)ethynyl)silane (**18**) (1.3 mL, 5.5 mmol, 1.1 equiv), which was dissolved in CH_2Cl_2 (1 mL). The resulting suspension was stirred for 6 h at RT. A saturated solution of $NaHCO_3$ (20 mL) was then added and the mixture was stirred vigorously for 30 min, the two layers were separated and the organic layer was washed with sat. $NaHCO_3$ (20 mL), dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting solid was boiled in CH_3CN (20 mL). The mixture was cooled down, filtered and dried under high vacuum to afford **2c** (1.12 g, 2.69 mmol, 54% yield) as a pale yellow solid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.46 – 8.38 (m, 1H, Ar*H*), 8.28 – 8.19 (m, 1H, ArH), 7.84 – 7.74 (m, 2H, Ar*H*), 7.74 – 7.65 (m, 4H, Ar*H*). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 166.6, 135.0, 133.0, 132.6, 132.2 (q, J = 33.0 Hz), 131.7, 131.2, 126.3, 125.7 (q, J = 3.6 Hz), 124.4, 123.4 (q, J = 272.6 Hz), 116.1, 104.2, 53.7. Consistent with reported data.[9]

1-[4-Chlorophenylethynyl]-1,2-benziodoxol-3(1H)-one (2d)

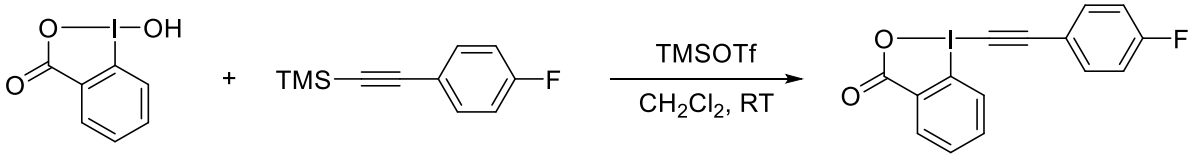


16 **19** **2d**

Following a reported procedure,[10] Trimethylsilyl triflate (1.0 mL, 5.5 mmol, 1.1 equiv) was added to a suspension of BIOH (**16**) (1.32 g, 5.00 mmol, 1.0 equiv) in CH_2Cl_2 (15 mL) at RT. The resulting suspension was stirred for 1 h, followed by the dropwise addition of ((4-Chlorophenyl)ethynyl)trimethylsilane (0.68 mL, 5.00 mmol, 1.0 equiv), which was dissolved in CH_2Cl_2 (5 mL). The resulting suspension was stirred for 6 h at RT. A saturated solution of $NaHCO_3$ (20 mL) was then added and the mixture was stirred vigorously for 30 minutes, the two layers were separated. The mixture was extracted with H_2O and DCM (3x20 mL), washed

with brine, then dried over Na_2SO_4 filtered and evaporated under reduced pressure. The resulting solid was recrystalized in EtOAc:MeOH (2:1) (40 mL/gram). The solution was left to cool to RT overnight. The crystal formed was filtered and dried under high vacuum to afford **(2d)** as a white solid (658 mg, 1.72 mmol, 34%). **^{1}H NMR** (400 MHz, CDCl3) δ 8.41-8.39 (m, 1H, Ar*H*), 8.23-8.21 (m, 1H, Ar*H*), 7.80-7.73 (m, 2H, Ar*H*), 7.54-7.51 (m, 2H, Ar*H*), 7.42-7.38 (m, 2H, Ar*H*). **^{13}C NMR** (100 MHz, CDCl3) δ 166.85, 137.20, 135.07, 134.17, 132.61, 131.74, 131.47, 129.29, 126.48, 119.16, 116.32, 105.22, 51.80. Consistent with reported data.[10]

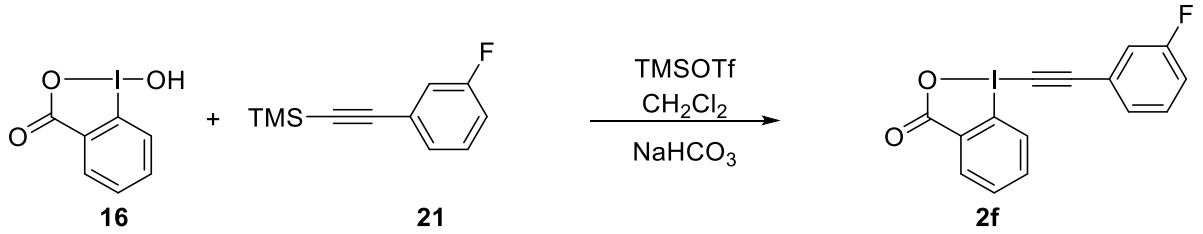
1-[4-Fluorophenylethynyl]-1,2-benziodoxol-3(1H)-one (2e)



16 **20** **2e**

Following a reported procedure,[11] Trimethylsilyl triflate (1.0 mL, 5.5 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**16**) (1.32 g, 5.00 mmol, 1.0 equiv) in CH_2Cl_2 (15 mL) at RT. The resulting suspension was stirred for 1 h, followed by the drop wise addition of ((4-fluorophenyl)ethynyl)trimethylsilane (**20**) (1.1 mL, 5.5 mmol, 1.1 equiv), which was dissolved in CH_2Cl_2 (1 mL). The resulting suspension was stirred for 6 h at RT. A saturated solution of $NaHCO_3$ (20 mL) was then added and the mixture was stirred vigorously for 30 minutes, the two layers were separated. The mixture was extracted with H_2O and DCM (3x20 mL), washed with brine, then dried over Na_2SO_4 filtered and evaporated under reduced pressure. The resulting solid was recrystalized in EtOAc:MeOH (2:1) (40 mL/gram). The solution was left to cool to RT overnight. The crystal formed was filtered and dried under high vacuum to afford product **2e** (739 mg, 2.02 mmol, 40%) as a white solid. **^{1}H NMR** (400 MHz, Chloroform-d) δ 8.48 – 8.34 (m, 1H, ArH), 8.29 – 8.16 (m, 1H, ArH), 7.85 – 7.69 (m, 2H, ArH), 7.68 – 7.53 (m, 2H, ArH), 7.17 – 7.05 (m, 2H, ArH). **^{13}C NMR** (101 MHz, Chloroform-d) δ 166.8, 164.0 (d, J = 253.9 Hz), 135.2 (d, J = 8.8 Hz), 135.0, 132.6, 131.7, 131.50, 126.4, 116.9 (d, J = 3.6 Hz), 116.4 (d, J = 22.4 Hz), 116.3, 105.5, 50.5. Consistent with reported data**.**[11]

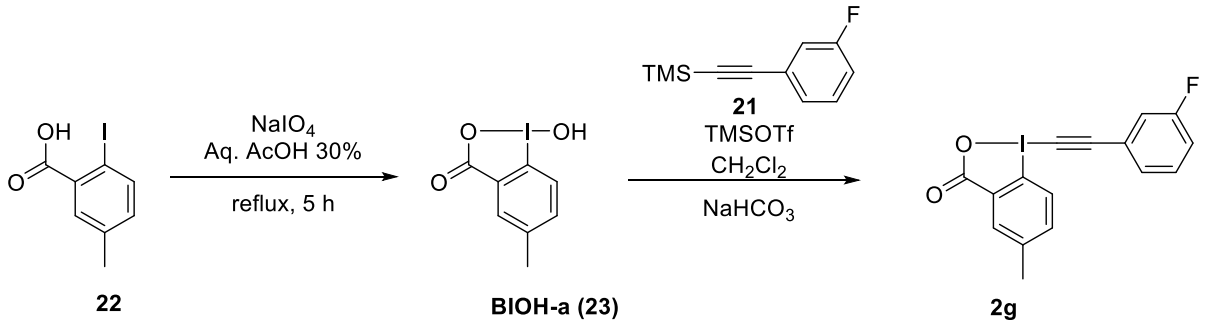
1-[3-Fluorophenylethynyl]-1,2-benziodoxol-3(1H)-one (2f)



16 **21** **2f**

Following reported procedure,[9] Trimethylsilyl triflate (0.44 mL, 2.5 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**16**) (0.589 g, 2.23 mmol, 1.00 equiv) in CH_2Cl_2 (6.8 mL) at RT The resulting suspension was stirred for 1 h, followed by the dropwise addition of ((3-fluorophenyl)ethynyl)trimethylsilane (**21**) (0.50 mL, 2.5 mmol, 1.1 equiv). The resulting suspension was stirred for 6 h at RT. A saturated solution of $NaHCO_3$ (10 mL) was then added and the mixture was stirred vigorously for 30 minutes, resulting in a suspension. The mixture was extracted with H_2O and DCM (3x10 mL), washed with brine, then dried over Na_2SO_4, filtered and evaporated under reduced pressure. The resulting solid was recrystalized in EtOAc:MeOH (2:1) (40 mL/gram). The solution was left to cool to RT and kept in fridge overnight. The crystal formed was filtered and dried under high vacuum to afford product **2f** (384 mg, 1.05 mmol, 47% yield) as colorless crystals. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.33 (dd, *J* = 8.2, 0.8 Hz, 1H, Ar*H*), 8.13 (dd, *J* = 7.4, 1.7 Hz, 1H, Ar*H*), 7.91 (ddd, *J* = 8.2, 7.2, 1.7 Hz, 1H, Ar*H*), 7.81 (td, *J* = 7.3, 0.9 Hz, 1H, Ar*H*), 7.64 – 7.59 (m, 1H, Ar*H*), 7.58 – 7.53 (m, 2H, Ar*H*), 7.47 – 7.37 (m, 1H, Ar*H*). **^{13}C NMR** (101 MHz, DMSO-d_6) 166.3, 161.8 (d, *J* = 245.6 Hz), 135.3, 131.9, 131.3, 131.2 (d, *J* = 8.7 Hz), 129.0 (d, *J* = 2.9 Hz), 127.7, 122.4 (d, *J* = 9.6 Hz), 119.2 (d, *J* = 23.4 Hz), 118.1 (d, *J* = 21.1 Hz), 116.4, 102.5 (d, *J* = 3.3 Hz), 53.8. (One carbon is not resolved) Consistent with reported data.[9]

Synthesis of 2g



22 **BIOH-a (23)** **2g**

$NaIO_4$ (4.05 g, 18.9 mmol, 1.05 equiv) and 2-iodo-5-methylbenzoic acid (**22**) (4.7 g, 18 mmol, 1.0 equiv) were suspended in 30% (v:v) aq. AcOH (35 mL). The mixture was vigorously stirred and refluxed for 5 h. The reaction mixture was then diluted with cold water (25 mL) and allowed to cool to rt, protecting it from light. After 1 h, the crude product was collected by filtration, washed on the filter with ice water (3 x 15 mL) and acetone (3 x 15 mL), and air-dried in the dark overnight to afford **BIOH-a** (**23**) (3.95 g, 14.2 mmol, 79% yield) as a white solid.

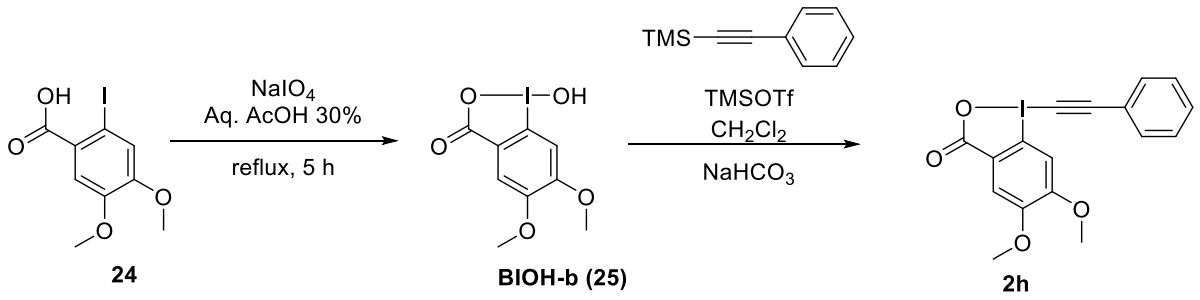
Trimethylsilyl triflate (0.44 mL, 2.5 mmol, 1.1 equiv) was added to a suspension **BIOH-a** (**23**) (0.620 g, 2.23 mmol, 1.00 equiv) in CH_2Cl_2 (6.8 mL) at RT The resulting suspension was stirred for 1 h, followed by the dropwise addition of ((3-fluorophenyl)ethynyl)trimethylsilane (**21**) (0.50 mL, 2.5 mmol, 1.1 equiv). The resulting suspension was stirred for 6 h at RT. A saturated solution of $NaHCO_3$ (10 mL) was then added and the mixture was stirred vigorously for 30 minutes, resulting in a suspension. The mixture was extracted with H_2O and DCM (3x10 mL), washed with brine, then dried over Na_2SO_4, filtered and evaporated under reduced pressure. The resulting solid was recrystalized in EtOAc:MeOH (2:1) (40 mL/gram). The solution was left to cool to RT and kept in fridge overnight. The crystal formed was filtered and dried under high vacuum to afford product **2g** (354 mg, 0.932 mmol, 42% yield) as colorless crystals.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 2.1 Hz, 1H, Ar*H*), 8.05 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.58 (dd, *J* = 8.6, 2.2 Hz, 1H, Ar*H*), 7.45 – 7.35 (m, 2H, Ar*H*), 7.30 – 7.26 (m, 1H, Ar*H*), 7.24 – 7.15 (m, 1H, Ar*H*), 2.51 (s, 3H, ArCH_3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 162.3 (d, *J* = 248.6 Hz), 142.7, 136.0, 133.2, 131.0, 130.5 (d, *J* = 8.5 Hz), 128.7 (d, *J* = 3.3 Hz), 125.9, 122.4 (d, *J* = 9.4 Hz), 119.6 (d, *J* = 23.2 Hz), 118.2 (d, *J* = 21.2 Hz), 112.3, 104.4 (3.3 Hz), 51.8, 20.8.

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{11}FIO_2^+$ 380.9782; Found 380.9784**.**

Synthesis of 2h



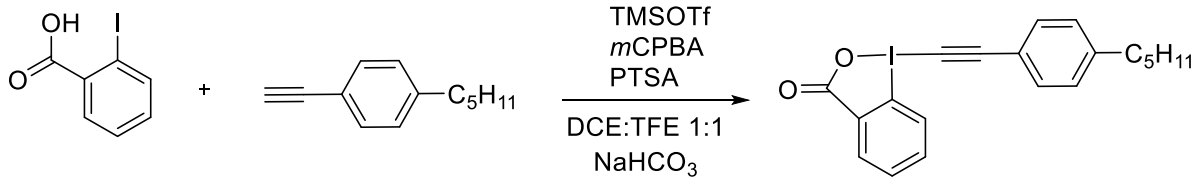
24 **BIOH-b (25)** **2h**

$NaIO_4$ (1.25 g, 5.84 mmol, 1.05 equiv) and 2-iodo 4,5-dimethoxybenzoic acid (**24**) (1.71 g, 5.56 mmol, 1.00 equiv) were suspended in 30% (v:v) aq. AcOH (15 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (40 mL) and allowed to cool to RT, protecting it from light. The crude product was collected by filtration, washed on the filter with ice water (3x4 mL) and acetone (3x4 mL), and air-dried in the dark to give the pure product **BIOH-b** (**25**) (1.51 g, 4.67 mmol, 84%) as a colorless solid.

Following reported procedure,[12] trimethylsilyl triflate (400 µL, 2.20 mmol, 1.10 equiv) was added to a suspension of **BIOH-b** (**25**) (648 mg, 2.00 mmol, 1.00 equiv) in CH_2Cl_2 (10 mL) at RT. The resulting yellow mixture was stirred for 1 h, followed by the dropwise addition of trimethyl(phenylethynyl)silane (430 µL, 2.20 mmol, 1.10 equiv). The resulting suspension was stirred for 6 h at RT, during this time a yellow suspension was formed. A saturated solution of $NaHCO_3$ (10 mL) was then added. The two layers were separated and the aqueous layer was extracted with DCM (10 mL). The combined organic extracts were dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting solid was recrystallized in CH_3CN (50 mL) and a few EtOH to afford **2h** (306 mg, 0.752 mmol, 38%) as a colorless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1 H, Ar*H*), 7.70 (s, 1 H, Ar*H*), 7.60 (m, 2 H, Ar*H*), 7.50 (m, 3 H, Ar*H*), 4.05 (s, 3 H, OC*H*$_3$), 3.98 (s, 3 H; OC*H*$_3$). ^{13}C NMR (101 MHz, CDCl3) δ 166.8, 154.9, 152.2, 132.6, 130.8, 128.9, 124.4, 120.5, 113.3, 107.6, 106.3, 105.3, 56.7, 56.4, 51.2. Consistent with reported data.[12]

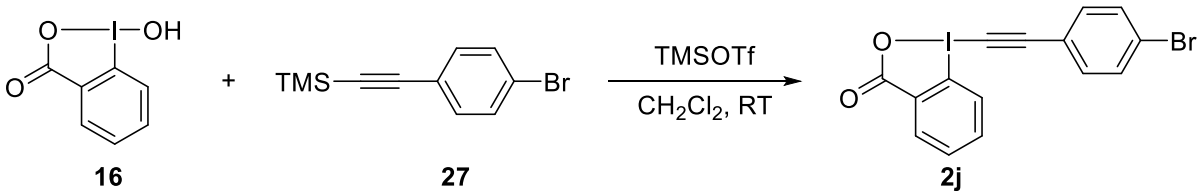
1-[4-Pentylphenylethynyl]-1,2-benziodoxol-3(1H)-one (2i)



15 **26** **2i**

Following a reported procedure,[11] in a sealed tube, 2-iodobenzoic acid (**16**) (1.00 g, 4.03 mmol, 1.00 equiv), 4-methylbenzenesulfonic acid (775 mg, 4.03 mmol, 1.00 equiv) and mCPBA (994 mg, 4.44 mmol, 1.10 equiv) were suspended in DCE:TFE 1:1 (12 mL) and stirred for 1 h at 55 °C. After 1 h, 1-ethynyl-4-pentylbenzene (**26**) (1.1 mL, 5.6 mmol, 1.4 equiv) was added and the reaction was stirred at 55 °C for 24 h. After 24 h, the solvent was evaporated and the residue was redissolved in CH_2Cl_2 (20 mL) and stirred vigorously with $NaHCO_3$ sat. (30 mL). After 1 h, the reaction mixture was transferred into a separating funnel and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2x50 mL). The combined organic layers were washed with sat. $NaHCO_3$, dried over MgSO4, filtered and concentrated under vacuum. The resulting solid was boiled in MeCN (20 mL), then filtered and the collected solid was further purified by column chromatography using pure ethyl acetate. Trituration in pentane afforded **2i** (176 mg, 0.421 mmol, 10%) as a pale yellow solid. **^{1}H NMR** (400 MHz, Chloroform-d) δ 8.45 – 8.40 (m, 1H, Ar*H*), 8.28 – 8.21 (m, 1H, Ar*H*), 7.79 – 7.74 (m, 2H, Ar*H*), 7.56 – 7.48 (m, 2H, Ar*H*), 7.26 – 7.23 (m, 2H, Ar*H*), 2.71 – 2.60 (m, 2H, ArCH_2), 1.69 – 1.54 (m, 2H, ArCH$_2$CH_2), 1.40 – 1.27 (m, 4H, CH_2CH_2CH3), 0.90 (t, *J* = 6.8 Hz, 3H, CH$_2$CH_3). **^{13}C NMR** (101 MHz, Chloroform-d) δ 166.6, 146.7, 135.0, 133.0, 132.6, 131.7, 131.5, 129.0, 126.3, 117.7, 116.4, 107.4, 49.4, 36.2, 31.5, 31.0, 22.6, 14.1. Consistent with reported data. [11]

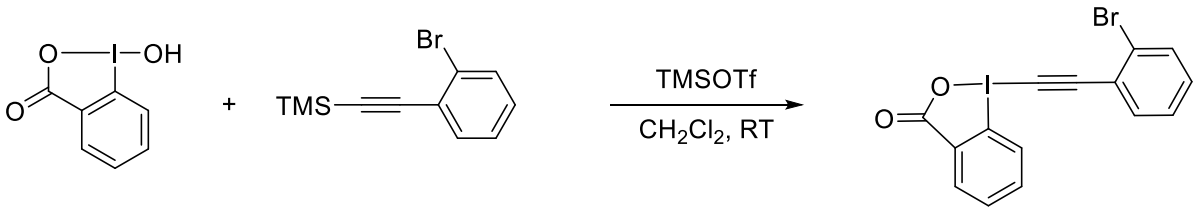
1-[4-Bromophenylethynyl]-1,2-benziodoxol-3(1H)-one (2j)



16 **27** **2j**

Following reported procedure, [7] Trimethylsilyl triflate (1.0 mL, 5.5 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**16**) (1.3 g, 5.0 mmol, 1.0 equiv) in CH_2Cl_2 (15 mL) at RT The resulting suspension was stirred for 1 h, followed by the dropwise addition of ((4 bromophenyl)ethynyl)trimethylsilane (**27**) (1.39 g, 5.5 mmol, 1.1 equiv), which was dissolved in CH_2Cl_2 (1 mL). The resulting suspension was stirred for 6 h at RT A saturated solution of $NaHCO_3$ (20 mL) was then added and the mixture was stirred vigorously for 30 min, the two layers were separated and the organic layer was washed with sat. The mixture was extracted with H_2O and DCM (3x20 mL), washed with brine, then dried over Na_2SO_4, filtered and evaporated under reduced pressure. The resulting solid was recrystalized in EtOAc:MeOH (2:1) (40 mL/gram). The solution was left to cool to RT overnight. The crystal formed was filtered and dried under high vacuum to afford product **2j** (1.35 g, 3.15 mmol, 63% yield) as a pale yellow solid.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.51 – 8.30 (m, 1H, Ar*H*), 8.30 – 8.13 (m, 1H, Ar*H*), 7.84 – 7.72 (m, 2H, Ar*H*), 7.58 (d, 2H, *J* = 8.5 Hz, Ar*H*), 7.46 (d, 2 H, *J* = 8.5 Hz, Ar*H*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.6, 135.1, 134.3, 132.7, 132.3, 131.9, 131.4, 126.3, 125.7, 119.6, 116.3, 105.4, 52.1. Consistent with reported data. [7]

1-[2-Bromophenylethynyl]-1,2-benziodoxol-3(1H)-one (2k)



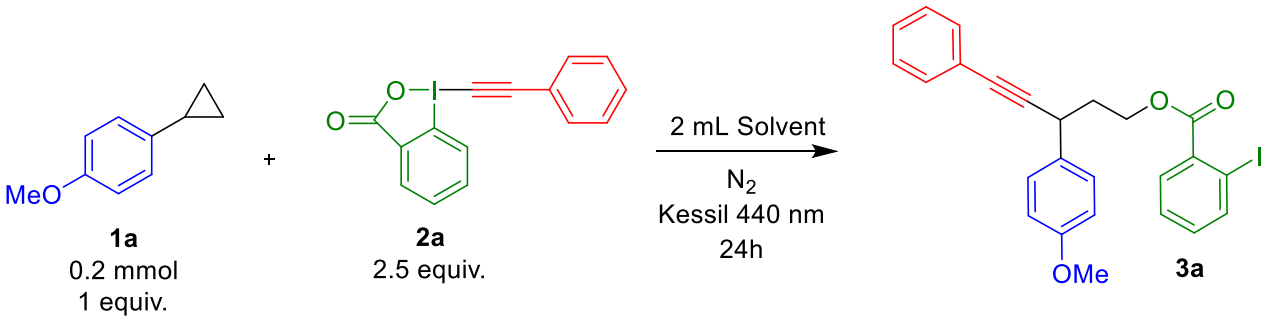
16 **28** **2k**

Following reported procedure,[7] trimethylsilyl triflate (0.42 mL, 2.4 mmol, 1.1 equiv) was added to a suspension of BIOH (**16**) (0.562 g, 2.13 mmol, 1.00 equiv) in CH_2Cl_2 (6 mL) at RT The resulting suspension was stirred for 1 h, followed by the drop wise addition of ((2-bromophenyl)ethynyl)trimethylsilane (**28**) (0.61 g, 2.4 mmol, 1.1 equiv). The resulting

suspension was stirred for 6 h at RT. A saturated solution of $NaHCO_3$ (10 mL) was then added and the mixture was stirred vigorously for 1 h resulting in a persistent emulsion/suspension. The mixture was diluted with $CHCl_3$ (10 mL), water (5 mL) and MeOH (ca. 2 mL) to afford 2 distinct layers. The two layers were separated, and the organic layer was washed with sat. $NaHCO_3$ (5 mL), dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The resulting solid was recrystallized in EtOAc:MeOH (7:3 v:v) (ca. 20 mL). The solution was left to cool to RT then was placed in the freezer (-20 °C) overnight. The crystals were filtered and washed with Et_2O affording **2k** (465 mg, 1.09 mmol, 51% yield) as colorless crystals. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.44 (td, J = 7.3, 2.1 Hz, 2 H, Ar*H*), 7.84 – 7.74 (m, 2 H, Ar*H*), 7.68 (d, J = 1.1 Hz, 1 H, Ar*H*), 7.61 (dd, J = 7.6, 1.7 Hz, 1 H, Ar*H*), 7.36 (m, 2 H, Ar*H*). **^{13}C NMR** (101 MHz, $CDCl_3$) 7 δ 166.6, 135.2, 134.7, 133.0, 132.7 , 131.8, 131.3, 127.6, 126.8, 126.4, 123.2, 116.5, 104.3, 55.4. (One carbon is not resolved). Consistent with reported data.[7]

Optimization

In a 12*75 mm Borosilicate glass tube, **PhEBX 2a** was added. The tube was then closed with a rubber septum and sealed off with parafilm. Three cycles of evacuate-refill with nitrogen were performed to remove O_2 and $CHCl_3$ (0.1M) was added, followed by the addition of **1a**. The reaction mixture was stirred at room temperature with Kessil lamps (440 nm). It should be noted that chloroform can be used from commercially sealed-cap bottle under inert atmosphere or it is recommended to conduct three cycles of Freeze-Pump-Thaw for other sources of chloroform before use. The reaction was monitored by NMR with CH_2Br_2 as internal standard. NMR yield was determined by integration of ArC*H* NMR of products.



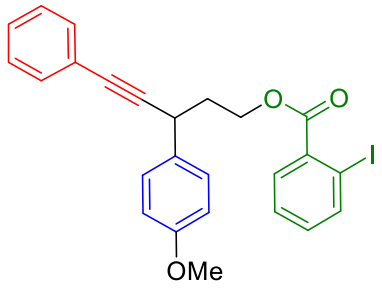
Entry	Variation from standard condition	Conversion (%)	NMR yield (%)
1	$CHCl_3$	100	72
2	DCE	62	20
3	MeOH	64	12
4	CH_3CN/EtOAc	42/19	5/3
5	DMSO or THF	<5	0
8	4 mL $CHCl_3$	100	50
9	1 mL $CHCl_3$	84	63
10	$CHCl_3$, only 1a without 2a	0	0
11	$CHCl_3$, with 1.5 equiv of BIOH	100	63
12	$CHCl_3$, with 1.5 equiv of K_2CO_3	58	24

Synthesis of alkynylated products

General Procedure B (GP B):

In a 12*75 mm Borosilicate glass tube, aryl ethynyl benziodoxolone (0.5 mmol, 2.5 equiv) was added. The tube was then closed with a rubber septum and sealed off with parafilm. Three cycle of evacuate-refill with nitrogen were performed to remove O_2 and $CHCl_3$ (2.0 mL, 0.1M) was added, followed by the addition of starting material (0.2 mmol). The reaction mixture was stirred at room temperature with Kessil lamps (440 nm). It should be noted that chloroform can be used from commercially sealed-cap bottle under inert atmosphere or it is recommended to conduct three cycle of Freeze-Pump-Thaw for other sources of chloroform before use. The reaction was monitored by NMR with CH_2Br_2 as internal standard. Upon completion by either full conversion of starting material or hypervalent iodine reagents, the mixture was concentrated in vacuo and purified by on Biotage (Büchi flashpure cartridge 25 g) to obtained the product.

3-(4-Methoxyphenyl)-5-phenylpent-4-yn-1-yl 2-iodobenzoate (3a)



Following the general procedure B, starting from phenyl ethynyl benziodoxolone (**2a**) (174 mg, 500 µmol, 2.50 equiv) and 1-cyclopropyl-4-methoxybenzene (**1a**) (29.6 mg, 200 µmol, 1.00 equiv). The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of Pentane:EtOAc from 5:95 to 88:12) affording 3-(4-methoxyphenyl)-5-phenylpent-4-yn-1-yl 2-iodobenzoate (**3a**) (67.5 mg, 136 µmol, 68% yield) as pale yellow oil.

Rf = 0.29 (SiO_2, 20:1 Pentane/ethyl acetate).

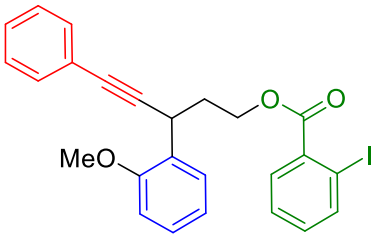
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.77 (dd, *J* = 7.7, 1.9 Hz, 1H, Ar*H*), 7.44 (td, *J* = 4.3, 1.7 Hz, 2H, Ar*H*), 7.40 – 7.34 (m, 3H, Ar*H*), 7.32 – 7.27 (m, 3H, Ar*H*), 7.15 (t, *J* = 7.7 Hz, 1H, Ar*H*), 6.92 – 6.86 (m, 2H, Ar*H*), 4.57 (dt, *J* = 12.7, 6.6 Hz, 1H, OC*H*$_2$CH$_2$), 4.48 (dt, *J* = 11.3, 5.8 Hz, 1H, OC*H*$_2$CH$_2$), 4.11 (t, *J* = 7.4 Hz, 1H, C*H*CH$_2$), 3.81 (s, 3H, OC*H*$_3$), 2.29 (q, *J* = 6.8 Hz, 2H, OCH$_2$C*H*$_2$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 158.8, 141.4, 135.4, 133.2, 132.8, 131.8, 131.2, 128.6, 128.4, 128.1, 128.0, 123.5, 114.2, 94.2, 90.5, 84.0, 63.8, 55.5, 37.3, 34.7.

IR (ν_{max}, cm^{-1}) 2923 (m), 2852 (w), 2358 (w), 1727 (s), 1677 (m), 1601 (s), 1462 (m), 1292 (s), 1250 (s), 1173 (m), 743 (m).

HRMS (APCI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{22}IO_3^+$ 497.0608; Found 497.0604.

3-(2-Methoxyphenyl)-5-phenylpent-4-yn-1-yl 2-iodobenzoate (3b)



Following the general procedure B, starting from 1-cyclopropyl-2-methoxybenzene (**1b**) (29.6 mg, 200 µmol, 1.00 equiv) and phenyl ethynyl benziodoxolone (**2a**) (174 mg, 500 µmol, 2.50 equiv), The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of Pentane:EtOAc from 2:98 to 90:10) affording 3-(2-methoxyphenyl)-5-phenylpent-4-yn-1-yl 2-iodobenzoate (**3b**) (64.7 mg, 130 µmol, 65% yield) as colorless oil.

Rf = 0.59 (SiO_2, 10:1 Pentane/ethyl acetate).

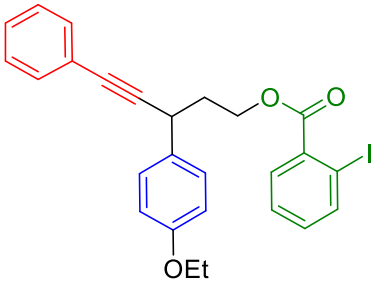
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 8.0, 1.2 Hz, 1H, Ar*H*), 7.79 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.62 (dd, *J* = 7.6, 1.8 Hz, 1H, Ar*H*), 7.44 – 7.38 (m, 2H, Ar*H*), 7.31 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.27 – 7.18 (m, 4H, Ar*H*), 7.09 (td, *J* = 7.6, 1.8 Hz, 1H, Ar*H*), 6.95 (td, *J* = 7.5, 1.1 Hz, 1H, Ar*H*), 6.83 (dd, *J* = 8.2, 1.1 Hz, 1H, Ar*H*), 4.56 (dd, *J* = 8.7, 5.3 Hz, 1H, C*H*CH_2), 4.53 – 4.43 (m, 2H, OC*H*$_2$$CH_2$), 3.78 (s, 3H, OC*H3*), 2.31 (dtd, *J* = 14.0, 7.0, 5.3 Hz, 1H, OCH_2C*H*$_2$), 2.17 (ddt, *J* = 14.3, 8.8, 5.8 Hz, 1H, OCH_2C*H*$_2$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 156.3, 141.5, 135.1, 132.7, 131.8, 131.3, 129.4, 128.7, 128.4, 128.3, 128.3, 128.0, 123.7, 121.0, 110.6, 94.3, 90.7, 83.5, 64.1, 55.5, 35.5, 29.0.

IR (ν_{max}, cm^{-1}) 2925 (w), 2237 (m), 1496 (s), 1487 (m), 1302 (m), 1255 (m), 1234 (m), 1207 (s), 1127 (m), 1114 (m), 1108 (m), 1056 (s), 1046 (m), 755 (s).

HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{21}INaO_3^+$ 519.0428; Found 519.0429.

3-(4-Ethoxyphenyl)-5-phenylpent-4-yn-1-yl 2-iodobenzoate (3c)



Following the general procedure C, starting from 1-cyclopropyl-4-ethoxybenzene (**1c**) (32.4 mg, 200 µmol, 1.00 equiv) and phenyl ethynyl benziodoxolone (**2a**) (174 mg, 500 µmol, 2.50 equiv.). The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of Pentane:EtOAc from 98:2 to 90:10, affording 3-(4-ethoxyphenyl)-5-phenylpent-4-yn-1-yl 2-iodobenzoate (**3c**) (54.1 mg, 103 µmol, 51% yield) as pale yellow oil.

Rf = 0.27 (SiO_2, 20:1 Pentane/ethyl acetate).

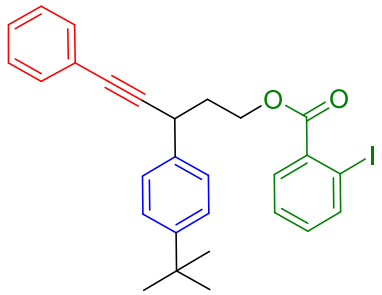
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.77 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.44 (dd, *J* = 6.7, 3.0 Hz, 2H, Ar*H*), 7.40 – 7.33 (m, 3H, Ar*H*), 7.33 – 7.27 (m, 3H, Ar*H*), 7.15 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 6.88 (d, *J* = 8.5 Hz, 2H, Ar*H*), 4.56 (dt, *J* = 11.1, 6.6 Hz, 1H, OC*H*$_2$CH$_2$CH), 4.48 (dt, *J* = 11.4, 5.9 Hz, 1H, OC*H*$_2$CH$_2$CH), 4.10 (t, *J* = 7.4 Hz, 1H, CCC*H*CH$_2$), 4.02 (q, *J* = 7.0 Hz, 2H, OC*H*$_2$CH$_3$), 2.36 – 2.20 (m, 2H, OCH$_2$C*H*$_2$CH), 1.41 (t, *J* = 7.0 Hz, 3H, OCH$_2$C*H*$_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 158.2, 141.4, 135.4, 133.0, 132.8, 131.8, 131.2, 128.6, 128.4, 128.1, 128.0, 123.6, 114.8, 94.2, 90.6, 84.0, 63.8, 63.6, 37.4, 34.7, 15.0.

IR (ν_{max}, cm^{-1}) 2957 (w), 2924 (m), 2227 (w), 1725 (s), 1713 (m), 1508 (m), 1289 (s), 1247 (s), 1205 (m), 1133 (m), 1043 (m), 1013 (m), 758 (m), 741 (m).

HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{26}H_{23}INaO_3^+$ 533.0584; Found 533.0591.

3-(4-(tert-butyl)phenyl)-5-phenylpent-4-yn-1-yl 2-iodobenzoate (3d)



Following the general procedure B, starting from 1-*tert*-butyl-4-cyclopropylbenzene (**1d**) (34.9 mg, 200 µmol, 1.00 equiv), phenyl ethynyl benziodoxolone (**2a**) (139 mg, 400 µmol, 2.00 equiv) and 10-phenyl-9-(2,4,6-trimethylphenyl)acridin-10-ium tetrafluoroborate (1.85 mg, 4.00 µmol, 0.0200 equiv) under kessil lamp 467 nm. The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of Pentane:EtOAc from 99:1 to 92:8) affording 3-(4-(tert-butyl)phenyl)-5-phenylpent-4-yn-1-yl 2-iodobenzoate **(3d)** (53.2 mg, 102 µmol, 51% yield) as pale yellow oil.

R_f: 0.55 (SiO_2, 20:1 Pentane/ethyl acetate).

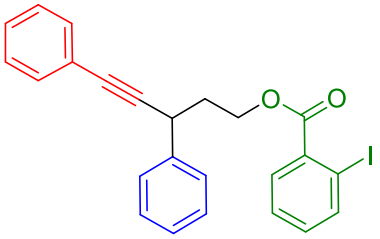
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 7.9, 1.2 Hz, 1H, Ar*H*), 7.81 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.48 – 7.44 (m, 2H, ArH), 7.41 – 7.36 (m, 5H, Ar*H*), 7.33-7.27 (m, 3H, Ar*H*), 7.15 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 4.60 (ddd, *J* = 11.1, 7.4, 6.1 Hz, 1H, OC*H*$_2$CH$_2$), 4.51 (dt, *J* = 11.4, 5.9 Hz, 1H, OC*H*$_2$CH$_2$), 4.18 – 4.11 (m, 1H, C*H*CH$_2$), 2.40 – 2.24 (m, 2H, OCH$_2$C*H*$_2$), 1.33 (s, 9H, C(C*H*$_3$)$_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 150.1, 142.2, 141.4, 138.0, 135.4, 132.7, 131.8, 131.2, 128.9, 128.3, 128.0, 127.3, 125.8, 125.5, 123.6, 94.1, 90.5, 84.0, 63.9, 37.2, 35.0, 34.6, 31.5.

IR (ν_{max}, cm^{-1}) 2953 (m), 2868 (w), 2196 (w), 1711 (s), 1289 (s), 1269 (s), 1249 (s), 1228 (m), 1125 (s), 1105 (s), 1014 (s), 752 (s), 741 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{28}IO_2^+$ 523.1129; Found 523.1136.

3,5-Diphenylpent-4-yn-1-yl 2-iodobenzoate (3e)



Following the general procedure B, starting from cyclopropylbenzene (**1e**) (23.6 mg, 200 µmol, 1.00 equiv), phenyl ethynyl benziodoxolone (**2a**) (139 mg, 400 µmol, 2.00 equiv) and 10-phenyl-9-(2,4,6-trimethylphenyl)acridin-10-ium tetrafluoroborate (1.85 mg, 4.00 µmol, 0.0200 equiv) under kessil lamp 467 nm. The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of Pentane:EtOAc from 99:1 to 92:8) affording 3,5-diphenylpent-4-yn-1-yl 2-iodobenzoate (**3e**) (37.2 mg, 79.8 µmol, 40% yield) as colorless oil.

R_f: 0.46 (SiO_2, 20:1 Pentane/ethyl acetate).

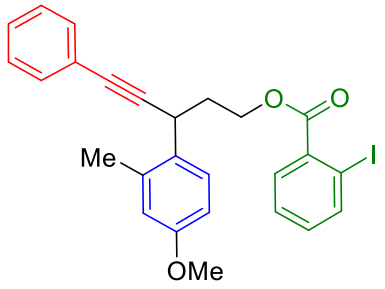
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 8.0, 1.2 Hz, 1H, Ar*H*), 7.77 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.49 (d, *J* = 1.6 Hz, 1H, Ar*H*), 7.47 – 7.43 (m, 3H, Ar*H*), 7.37 (dddd, *J* = 7.8, 5.9, 4.8, 1.4 Hz, 3H, Ar*H*), 7.33 – 7.26 (m, 4H, Ar*H*), 7.15 (td, *J* = 7.6, 1.7 Hz, 1H, Ar*H*), 4.59 (ddd, *J* = 11.2, 7.5, 6.0 Hz, 1H, OC*H*$_2$CH$_2$), 4.50 (dt, *J* = 11.3, 5.9 Hz, 1H, OC*H*$_2$CH$_2$), 4.17 (dd, *J* = 8.5, 6.3 Hz, 1H, C*H*CH$_2$), 2.39 – 2.25 (m, 2H, OCH$_2$C*H*$_2$).

^{13}C NMR (101 MHz, $CDCl_3$): ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 141.4, 141.2, 135.4, 132.8, 131.8, 131.2, 128.9, 128.4, 128.1, 128.0, 127.6, 127.2, 123.5, 94.1, 90.2, 84.2, 63.8, 37.3, 35.5.

IR (ν_{max}, cm^{-1}) 3061 (w), 2957 (w), 2198 (w), 1711 (s), 1706 (m), 1289 (s), 1271 (s), 1249 (s), 1231 (m), 1133 (s), 1102 (m), 1013 (s), 757 (s), 741 (s), 714 (s).

HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{19}INaO_2^+$ 489.0322; Found 489.0331.

3-(4-Methoxy-2-methylphenyl)-5-phenylpent-4-yn-1-yl 2-iodobenzoate (3f)



Following the general procedure B, starting from 1-cyclopropyl-4-methoxy-2-methylbenzene (32.4 mg, 200 µmol, 1.00 equiv) and phenyl ethynyl benziodoxolone (174 mg, 500 µmol, 2.50 equiv), The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of Pentane:EtOAc from 97:3 to 90:10) affording 3-(4-methoxy-2-methylphenyl)-5-phenylpent-4-yn-1-yl 2-iodobenzoate (**3f**) (62.3 mg, 122 µmol, 61% yield) as colorless oil.

Rf = 0.31 (SiO_2, 20:1 Pentane/ethyl acetate).

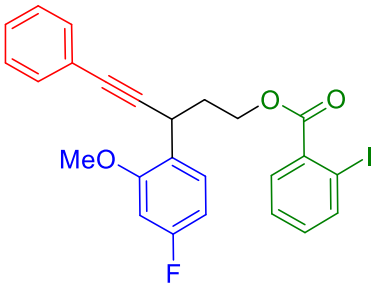
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 7.9, 1.2 Hz, 1H, Ar*H*), 7.79 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.51 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.46 – 7.41 (m, 2H, Ar*H*), 7.38 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.29 (dp, *J* = 4.6, 1.7 Hz, 3H, Ar*H*), 7.15 (td, *J* = 7.6, 1.7 Hz, 1H, Ar*H*), 6.78 (dd, *J* = 8.5, 2.8 Hz, 1H, Ar*H*), 6.72 (d, *J* = 2.8 Hz, 1H, Ar*H*), 4.61 (ddd, *J* = 11.1, 8.0, 5.7 Hz, 1H, OC*H*$_2$CH$_2$), 4.54 (dt, *J* = 11.2, 5.6 Hz, 1H, OC*H*$_2$CH$_2$), 4.27 (dd, *J* = 9.1, 5.6 Hz, 1H, CCC*H*CH$_2$), 3.79 (s, 3H, OC*H*$_3$), 2.39 (s, 3H, ArC*H*$_3$), 2.25 (dqd, *J* = 14.0, 8.4, 5.6 Hz, 2H, OCH$_2$C*H*$_2$CH).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 158.5, 141.5, 136.5, 135.3, 134.2, 132.8, 131.8, 131.6, 131.1, 128.8, 128.4, 128.0, 123.6, 116.3, 111.8, 94.2, 90.9, 83.4, 64.0, 55.4, 36.0, 31.4, 19.7.

IR (ν_{max}, cm^{-1}) 2957 (m), 2363 (w), 1727 (s), 1721 (s), 1609 (m), 1582 (m), 1502 (s), 1288 (s), 1267 (m), 1250 (s), 758 (s), 742 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{24}IO_3^+$ 511.0765; Found 511.0764.

3-(4-Fluoro-2-methoxyphenyl)-5-phenylpent-4-yn-1-yl 2-iodobenzoate (3h)



Following the general procedure B, starting from 1-cyclopropyl-4-fluoro-2-methoxybenzene (**1h**) (33.2 mg, 200 µmol, 1.00 equiv) and phenyl ethynyl benziodoxolone (**2a**) (174 mg, 500 µmol, 2.50 equiv). The crude mixture was purified by column chromatography on Biotage (Büchi flash pure cartridge 25 g, gradient of Pentane:EtOAc from 95:5 to 88:12) affording 3-(4-fluoro-2-methoxyphenyl)-5-phenylpent-4-yn-1-yl 2-iodobenzoate (**3h**) (47.1 mg, 91.6 µmol, 46% yield) as pale yellow oil.

Rf = 0.33 (SiO_2, 10:1 Pentane/ethyl acetate).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 7.9, 1.2 Hz, 1H, Ar*H*), 7.81 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.59 (dd, *J* = 8.5, 6.7 Hz, 1H, Ar*H*), 7.49 – 7.42 (m, 2H, Ar*H*), 7.36 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.30 (m, 3H, Ar*H*), 7.14 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 6.68 (td, *J* = 8.3, 2.5 Hz, 1H, Ar*H*), 6.60 (dd, *J* = 10.8, 2.5 Hz, 1H, Ar*H*), 4.60 – 4.45 (m, 3H, OC*H*$_2$CH$_2$ and CCC*H*CH$_2$), 3.80 (s, 3H, OC*H*$_3$), 2.30 (m, 1H, CH$_2$C*H*$_2$CH), 2.18 (m, 1H, CH$_2$C*H*$_2$CH).

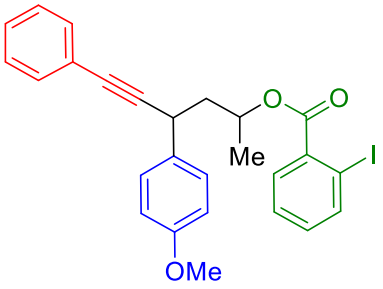
^{13}C NMR δ 166.4, 162.9 (d, J = 245.1 Hz), 157.3 (d, *J* = 9.7 Hz), 141.5, 135.0, 132.8, 131.8, 131.3, 129.7, 129.5 (d, *J* = 9.8 Hz), 128.4, 128.0 (d, *J* = 17.2 Hz), 125.0 (d, *J* = 3.1 Hz), 123.5, 107.1 (d, *J* = 21.2 Hz), 99.0 (d, *J* = 26.0 Hz), 94.4, 90.4, 83.6, 64.0, 55.8, 35.5, 28.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -113.0.

IR (ν_{max}, cm^{-1}) 2957 (w), 2843 (w), 2227 (w), 1724 (s), 1601 (s), 1496 (s), 1282 (s), 1248 (s), 1151 (s), 1133 (s), 1104 (s), 952 (s), 835 (s), 758 (s), 741 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{21}FIO_3^+$ 515.0514; Found 515.0527.

4-(4-Methoxyphenyl)-6-phenylhex-5-yn-2-yl 2-iodobenzoate (3i)



Following the general procedure B, starting from 1-methoxy-4-(2-methylcyclopropyl)benzene (**1i**) (32.4 mg, 200 µmol, 1.00 equiv) and phenyl ethynyl benziodoxolone (**2a**) (174 mg, 500 µmol, 2.50 equiv) The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of Pentane:EtOAc from 95:5 to 90:10) affording 4-(4-methoxyphenyl)-6-phenylhex-5-yn-2-yl 2-iodobenzoate (**3i**) as a colorless oil (mixture of two diastereomers, 71.5 mg, 140 µmol, 70% yield, dr 2:1, the ratio was determined by integration of the ^{1}H NMR signals for the benzylic protons ArC*H*)

Rf = 0.3 (SiO_2, 10:1 Pentane/ethyl acetate).

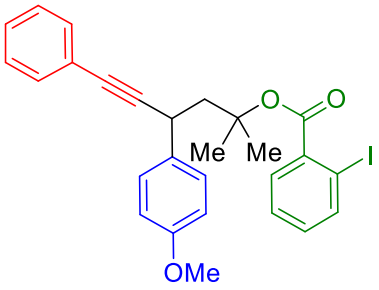
^{1}H NMR (400 MHz, $CDCl_3$ signals for major diastereomer) δ 7.98 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.76 (dd, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 7.48 – 7.43 (m, 2H, Ar*H*), 7.39 – 7.36 (m, 3H, Ar*H*), 7.29 – 7.27 (m, 3H, Ar*H*), 7.16 – 7.13 (m, 1H, Ar*H*), 6.91 – 6.87 (m, 2H, Ar*H*), 5.54 (dqd, *J* = 9.6, 6.2, 3.3 Hz, 1H, OC*H*(CH_3)CH_2), 4.10 (dd, *J* = 10.5, 5.0 Hz, 1H, CH_2C*H*CC), 3.80 (s, 3H, OC*H*$_3$), 2.27 (ddd, *J* = 14.5, 9.7, 5.0 Hz, 1H, CHC*H*$_2$CH(CH_3)), 2.10 – 2.05 (m, 1H, , CHC*H*$_2$CH(CH_3)), 1.47 (d, *J* = 6.2 Hz, 3H,OCHC*H*$_3$).

^{13}C NMR (101 MHz, $CDCl_3$ signals for major diastereomer) δ 166.3, 158.7, 141.3, 136.2, 133.7, 132.5, 131.9, 130.8, 128.7, 128.5, 128.3, 128.0, 123.6, 114.2, 93.9, 90.4, 84.2, 71.5, 55.4, 45.0, 34.7, 20.6.

IR (ν_{max}, cm^{-1}) 2931 (w), 2836 (w), 2250 (w), 1726 (s), 1705 (m), 1511 (s), 1464 (m), 1287 (s), 1249 (s), 1177 (m), 1130 (s), 1101 (m), 1065 (m), 1038 (s), 1014 (m), 829 (m), 758 (s), 740 (s).

HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{26}H_{23}INaO_3^+$ 533.0584; Found 533.0589.

4-(4-Methoxyphenyl)-2-methyl-6-phenylhex-5-yn-2-yl 2-iodobenzoate (3j)



Following the general procedure B, starting from 1-(2,2-dimethylcyclopropyl)-4-methoxybenzene (**1j**) (35.3 mg, 200 µmol, 1.00 equiv) and phenyl ethynyl benziodoxolone (**2a**) (174 mg, 500 µmol, 2.50 equiv). The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of Pentane:EtOAc from 95:5 to 88:12) affording 4-(4-methoxyphenyl)-2-methyl-6-phenylhex-5-yn-2-yl 2-iodobenzoate (**3j**) (56.8 mg, 108 µmol, 54% yield) as colorless oil.

R_f = 0.33 (SiO_2, 20:1 Pentane/ethyl acetate).

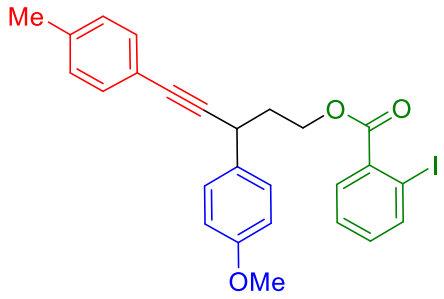
^{1}H NMR : (400 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 7.9, 1.2 Hz, 1H, Ar*H*), 7.69 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.38 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.36 – 7.32 (m, 2H, Ar*H*), 7.31 – 7.26 (m, 3H, Ar*H*), 7.25 (d, *J* = 1.7 Hz, 1H, Ar*H*), 7.09 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 6.89 – 6.84 (m, 2H, Ar*H*), 4.12 – 4.05 (m, 1H, CH_2CHCC), 3.79 (s, 3H, OCH_3), 2.54 – 2.46 (m, 2H, $OCCH_2CH$), 1.82 (s, 3H, $CH_2C(CH_3)_2$), 1.76 (s, 3H, $CH_2C(CH_3)_2$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 158.5, 141.1, 136.7, 134.9, 132.2, 131.6, 131.0, 128.6, 128.3, 127.9, 127.8, 123.8, 114.2, 93.8, 92.5, 84.2, 83.6, 55.4, 49.2, 33.4, 27.2, 26.6.

IR (ν_{max}, cm^{-1}) 2977 (w), 2932 (w), 2835 (w), 2359 (w), 1723 (s), 1610 (w), 1583 (w), 1512 (s), 1299 (s), 1251 (s), 1122 (s), 1103 (m), 758 (m), 741 (s).

HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{27}H_{25}INaO_3^+$ 547.0741; Found 547.0740.

3-(4-Methoxyphenyl)-5-(p-tolyl)pent-4-yn-1-yl 2-iodobenzoate (3k)



Following the general procedure B, starting from 1-cyclopropyl-4-methoxybenzene (**1a**) (29.6 mg, 200 µmol, 1.00 equiv) and 1-(*p*-tolylethynyl)-1,2-benziodoxol-3(1H)-one (**2b**) (181 mg, 500 µmol, 2.50 equiv) The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of Pentane:EtOAc from 99:5 to 88:12) affording 3-(4-methoxyphenyl)-5-(p-tolyl)pent-4-yn-1-yl 2-iodobenzoate (**3k**) (45.8 mg, 89.7 µmol, 45% yield) as pale yellow oil.

R_f: Rf = 0.4 (SiO_2, 10:1 Pentane/ethyl acetate).

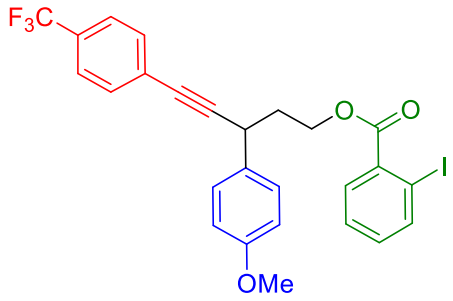
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 7.9, 1.2 Hz, 1H, Ar*H*), 7.77 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.41 – 7.35 (m, 3H, Ar*H*), 7.35 – 7.31 (m, 2H, Ar*H*), 7.15 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 7.12 – 7.08 (m, 2H, Ar*H*), 6.93 – 6.86 (m, 2H, Ar*H*), 4.57 (dt, *J* = 11.1, 6.6 Hz, 1H, OC*H*$_2$CH$_2$), 4.48 (dt, *J* = 11.3, 5.9 Hz, 1H, OC*H*$_2$CH$_2$), 4.10 (dd, *J* = 8.1, 6.7 Hz, 1H, CCC*H*CH$_2$), 3.80 (s, 3H, OC*H*$_3$), 2.34 (s, 3H, ArC*H*$_3$), 2.28 (dtd, *J* = 8.0, 6.1, 1.8 Hz, 2H, CH$_2$C*H*$_2$CH).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 158.8, 141.4, 138.1, 135.4, 133.3, 132.7, 131.7, 131.2, 129.1, 128.6, 128.0, 120.5, 114.2, 94.1, 89.7, 84.1, 63.8, 55.4, 37.4, 34.7, 21.6.

IR (ν_{max}, cm^{-1}) 2956 (w), 2923 (w), 1728 (m), 1610 (w), 1584 (w), 1512 (s), 1462 (m), 1288 (m), 1251 (s), 1133 (m), 820 (m), 743 (m).

HRMS (APPI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{26}H_{24}IO_3^+$ 511.0765; Found 511.0782.

3-(4-Methoxyphenyl)-5-(4-(trifluoromethyl)phenyl)pent-4-yn-1-yl 2-iodobenzoate (3l)

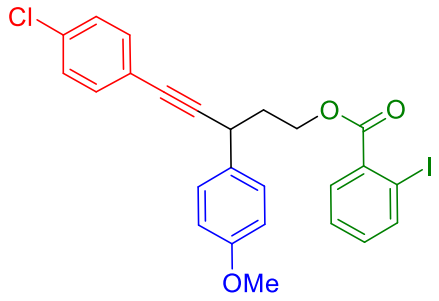


Following the general procedure B, starting from 1-cyclopropyl-4-methoxybenzene (**1a**) (29.6 mg, 200 µmol, 1.00 equiv) and 1-[4-trifluoromethylphenylethynyl]-1,2-benziodoxol-3(1H)-one (**2c**) (208 mg, 500 µmol, 2.50 equiv). The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of Pentane:EtOAc from 97:3 to 88:12) affording 3-(4-methoxyphenyl)-5-(4-(trifluoromethyl)phenyl)pent-4-yn-1-yl 2-iodobenzoate (**3l**) (71.4 mg, 127 µmol, 63% yield) as pale yellow oil.

R_f = 0.29 (SiO_2, 20:1 Pentane/ethyl acetate).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 8.0, 1.2 Hz, 1H, Ar*H*), 7.76 (dd, *J* = 7.8, 1.8 Hz, 1H, Ar*H*), 7.57 – 7.49 (m, 4H, Ar*H*), 7.40 – 7.33 (m, 3H, Ar*H*), 7.16 (dd, *J* = 7.7, 1.8 Hz, 1H, Ar*H*), 6.93 – 6.85 (m, 2H, Ar*H*), 4.56 (dt, *J* = 11.1, 6.6 Hz, 1H, OC*H*$_2$CH$_2$), 4.47 (dt, *J* = 11.4, 5.9 Hz, 1H, OC*H*$_2$CH$_2$), 4.12 (t, *J* = 7.4 Hz, 1H, CCC*H*CH$_2$), 3.81 (s, 3H, OC*H*$_3$), 2.40 – 2.25 (m, 2H, CH$_2$C*H*$_2$CH).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 158.9, 141.5, 135.3, 132.8, 132.6, 132.1, 131.2, 130.0, 129.7, 128.6, 128.0, 127.4, 125.3 (q, *J* = 3.8 Hz), 114.4, 94.2, 93.4, 82.7, 63.6, 55.5, 37.1, 34.7.
^{19}F NMR (377 MHz, $CDCl_3$) δ -62.8.
IR ((ν_{max}, cm^{-1}) 2956 (w), 2932 (w), 2838 (w), 2233 (w), 1511 (m), 1323 (s), 1251 (s), 1176 (m), 1167 (m), 1127 (s), 1105 (m), 1067 (m).
HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{21}F_3IO_3^+$ 565.0482; Found 565.0477.

5-(4-Chlorophenyl)-3-(4-methoxyphenyl)pent-4-yn-1-yl 2-iodobenzoate (3m)



Following the general procedure B, starting from 1-cyclopropyl-4-methoxybenzene (**1a**) (29.6 mg, 200 µmol, 1.00 equiv) and 1-[4-chlorophenylethynyl]-1,2-benziodoxol-3(1H)-one (**2d**) (191 mg, 500 µmol, 2.50 equiv). The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of pentane: ethyl acetate from 95:5 to 85:15) affording 5-(4-chlorophenyl)-3-(4-methoxyphenyl)pent-4-yn-1-yl 2-iodobenzoate (**3m**) (67.2 mg, 127 µmol, 63% yield) as pale yellow oil.

Rf = 0.2 (SiO_2, 10:1 pentane:ethyl acetate).

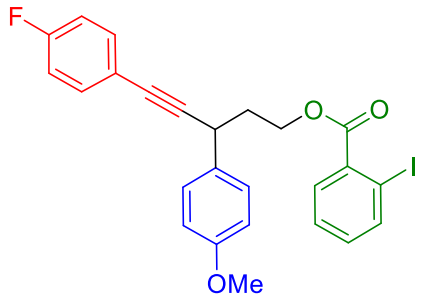
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 7.9, 1.2 Hz, 1H, Ar*H*), 7.76 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.42 – 7.33 (m, 5H, Ar*H*), 7.27 (s, 1H, Ar*H*), 7.25 (d, *J* = 1.7 Hz, 1H, Ar*H*), 7.15 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 6.93 – 6.86 (m, 2H, Ar*H*), 4.55 (dt, *J* = 11.1, 6.6 Hz, 1H, OC*H*$_2$CH$_2$), 4.46 (dt, *J* = 11.4, 5.9 Hz, 1H, OC*H*$_2$CH$_2$), 4.09 (m, 1H, CCC*H*CH$_2$), 3.80 (s, 3H, OC*H*$_3$), 2.36 – 2.21 (m, 2H, CH$_2$C*H*$_2$CH).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 158.8, 141.5, 135.3, 134.0, 133.1, 132.9, 132.8, 131.2, 128.7, 128.6, 128.0, 122.0, 114.3, 94.2, 91.6, 82.9, 63.7, 55.5, 37.2, 34.7.

IR (ν_{max}, cm^{-1}) 2956 (w), 2925 (w), 2838 (w), 2229 (w), 1725 (m), 1512 (m), 1488 (m), 1289 (s), 1250 (s), 1133 (m), 1094 (m), 1014 (m), 829 (m), 742 (m).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{21}ClIO_3^+$ 531.0218; Found 531.0223.

5-(4-Fluorophenyl)-3-(4-methoxyphenyl)pent-4-yn-1-yl 2-iodobenzoate (3n)



Following the general procedure B, starting from 1-cyclopropyl-4-methoxybenzene (**1a**) (29.6 mg, 200 µmol, 1.00 equiv) and 1-[4-fluorophenylethynyl]-1,2-benziodoxol-3(1H)-one (**2e**) (183 mg, 500 µmol, 2.50 equiv). The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of pentane: ethyl acetate from 95:5 to 85:15) affording 5-(4-fluorophenyl)-3-(4-methoxyphenyl)pent-4-yn-1-yl 2-iodobenzoate **(3n)** (41.4 mg, 80.5 µmol, 40% yield) as pale yellow oil.

Rf = 0.29 (SiO_2, 20:1 pentane:ethyl acetate).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 8.0, 1.2 Hz, 1H, Ar*H*), 7.76 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.42 – 7.34 (m, 5H, Ar*H*), 7.15 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 6.98 (t, *J* = 8.7 Hz, 2H, Ar*H*), 6.92 – 6.85 (m, 2H, Ar*H*), 4.55 (dt, *J* = 11.3, 6.6 Hz, 1H, OC*H*$_2$CH$_2$), 4.46 (dt, *J* = 11.3, 5.9 Hz, 1H, OC*H*$_2$CH$_2$), 4.09 (t, *J* = 7.4 Hz, 1H, CCC*H*CH$_2$), 3.80 (s, 3H, OC*H*$_3$), 2.34 – 2.23 (m, 2H, CH$_2$C*H*$_2$CH).

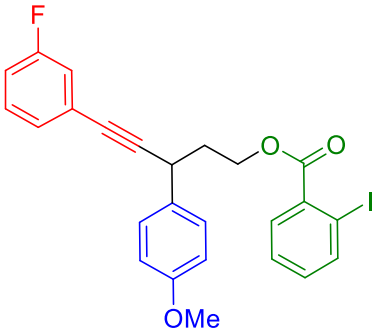
^{13}C NMR (201 MHz, $CDCl_3$) δ 166.6, 162.4 (d, *J* = 248.8 Hz), 158.8, 141.5, 135.4, 133.7 (d, *J* = 8.4 Hz), 133.1, 132.8, 131.2, 128.6, 128.0, 119.6, 115.6 (d, *J* = 22.2 Hz), 114.3, 94.2, 90.2, 82.9, 63.8, 55.5, 37.3, 34.6.

^{19}F NMR (377 MHz, $CDCl_3$) δ -111.6.

IR (ν_{max}, cm^{-1}) 2959 (m), 2929 (w), 2228 (w), 2150 (w), 1721 (m), 1600 (m), 1505 (s), 1288 (s), 1265 (s), 1255 (s), 1249 (s), 1231 (s), 1094 (m), 1030 (m), 1015 (s), 837 (s), 740 (s).

HRMS (APCI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{21}FIO_3^+$ 515.0514; Found 515.0515.

5-(3-Fluorophenyl)-3-(4-methoxyphenyl)pent-4-yn-1-yl 2-iodobenzoate (3o)



Following the general procedure B, starting from 1-cyclopropyl-4-methoxybenzene (**1a**) (29.6 mg, 200 µmol, 1.00 equiv) and 1-[3-fluorophenylethynyl]-1,2-benziodoxol-3(1H)-one (**2f**) (183 mg, 500 µmol, 2.50 equiv). The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of pentane: ethyl acetate from 95:5 to 85:15) affording 5-(3-fluorophenyl)-3-(4-methoxyphenyl)pent-4-yn-1-yl 2-iodobenzoate (**3o**) (28.2 mg, 54.8 µmol, 27% yield) as pale yellow oil.

Rf = 0.26 (SiO_2, 10:1 pentane:ethyl acetate).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 7.9, 1.2 Hz, 1H, Ar*H*), 7.77 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.41 – 7.33 (m, 3H, Ar*H*), 7.26 – 7.19 (m, 2H, Ar*H*), 7.18 – 7.10 (m, 2H, Ar*H*), 7.03 – 6.96 (m, 1H, Ar*H*), 6.93 – 6.87 (m, 2H, Ar*H*), 4.59 – 4.51 (m, 1H, OC*H*$_2$CH$_2$), 4.50 – 4.42 (m, 1H, OC*H*$_2$CH$_2$), 4.10 (t, *J* = 7.4 Hz, 1H, CCC*H*CH$_2$), 3.81 (s, 3H, OC*H*$_3$), 2.29 (dt, *J* = 7.3, 6.2 Hz, 2H, CH$_2$C*H*$_2$CH).

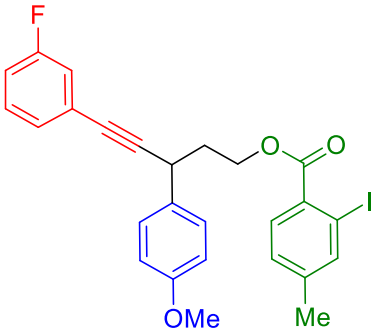
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 162.3 (d, *J* = 246.2 Hz), 158.7, 141.3, 135.2, 134.1, 132.7, 131.1, 129.8 (d, *J* = 8.7 Hz), 128.5, 127.9, 127.6 (d, *J* = 3.2 Hz), 125.2 (d, *J* = 9.5 Hz), 118.5 (d, *J* = 22.6 Hz), 115.3 (d, *J* = 21.2 Hz), 114.2, 94.0, 91.6, 82.7 (d, *J* = 3.4 Hz), 63.5, 55.3, 37.1, 34.5.

^{19}F NMR (377 MHz, $CDCl_3$) δ -113.2.

IR (ν_{max}, cm^{-1}) 2931 (w), 2836 (w), 2229 (w), 1726 (m), 1581 (m), 1510 (s), 1288 (s), 1247 (s), 1176 (m), 1015 (m), 785 (m), 740 (s).

HRMS (APCI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{21}FIO_3^+$ 515.0514; Found 515.0528.

5-(3-Fluorophenyl)-3-(4-methoxyphenyl)pent-4-yn-1-yl 2-iodo-4-methylbenzoate (3p)



Following the general procedure B, starting from 1-cyclopropyl-4-methoxybenzene (**1a**) (29.6 mg, 200 µmol, 1.00 equiv) and 1-[3-fluorophenylethynyl]-5-methyl-1,2-benziodoxol-3(1H)-one (**2g**) (190 mg, 500 µmol, 2.50 equiv). The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of pentane: ethyl acetate from 95:5 to 85:15) affording 5-(3-fluorophenyl)-3-(4-methoxyphenyl)pent-4-yn-1-yl 2-iodo-4-methylbenzoate (**3p**) (54.3 mg, 103 µmol, 51% yield) as pale yellow oil.

Rf = 0.32 (SiO_2, 20:1 pentane:ethyl acetate).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.1 Hz, 1H, Ar*H*), 7.57 (dd, *J* = 2.2, 0.8 Hz, 1H, Ar*H*), 7.40 – 7.33 (m, 2H, Ar*H*), 7.26 – 7.18 (m, 2H, Ar*H*), 7.12 (ddd, *J* = 9.5, 2.6, 1.4 Hz, 1H, Ar*H*), 6.96 – 7.02 (m, 2H, Ar*H*), 6.92 – 6.88 (m, 2H, Ar*H*), 4.54 (dt, *J* = 11.1, 6.7 Hz, 1H, OC*H*$_2$CH$_2$), 4.46 (dt, *J* = 11.3, 6.0 Hz, 1H, OC*H*$_2$CH$_2$), 4.10 (t, *J* = 7.4 Hz, 1H, CCC*H*CH$_2$), 3.80 (s, 3H, OC*H*$_3$), 2.32 (s, 3H, ArC*H*$_3$), 2.32 – 2.26 (m, 2H, CH$_2$C*H*$_2$CH).

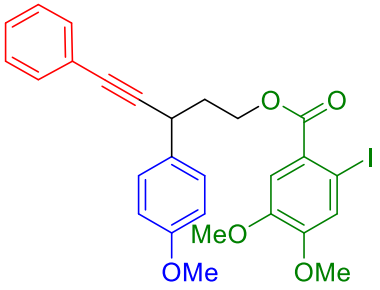
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 162.5 (d, *J* = 246.2 Hz), 158.8, 141.2, 138.3, 135.2, 133.8, 132.8, 131.9, 129.9 (d, *J* = 8.6 Hz), 128.6, 127.7 (d, *J* = 3.0 Hz), 125.4 (d, *J* = 9.4 Hz), 118.6 (d, *J* = 22.7 Hz), 115.4 (d, *J* = 21.3 Hz), 114.3, 91.7, 90.0, 82.8 (d, *J* = 3.3 Hz), 63.6, 55.4, 37.2, 34.6, 20.9.

^{19}F NMR (377 MHz, $CDCl_3$) δ -113.2.

IR (ν_{max}, cm^{-1}) 2958 (w), 2836 (w), 2363 (w), 2232 (w), 1724 (s), 1611 (m), 1579 (m), 1512 (s), 1294 (s), 1249 (s), 1203 (s), 1173 (m), 1108 (m), 1036 (m), 1015 (m), 779 (m).

HRMS (APCI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{23}FIO_3^+$ 529.0670; Found 529.0679.

3-(4-Methoxyphenyl)-5-phenylpent-4-yn-1-yl 2-iodo-4,5-dimethoxybenzoate (3q)



Following the general procedure B, starting from 1-cyclopropyl-4-methoxybenzene (**1a**) (29.6 mg, 200 µmol, 1.00 equiv) and 4,5-dimethoxy-1-[phenylethynyl]-1,2-benziodoxol-3(1H)-one (**2h**) (204 mg, 500 µmol, 2.50 equiv). The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of pentane: ethyl acetate from 85:15 to 70:30) affording 3-(4-methoxyphenyl)-5-phenylpent-4-yn-1-yl 2-iodo-4,5-dimethoxybenzoate **(3q)** (33.7 mg, 60.6 µmol, 30% yield) as colorless oil.

Rf = 0.14 (SiO_2, 10:1 pentane:ethyl acetate).

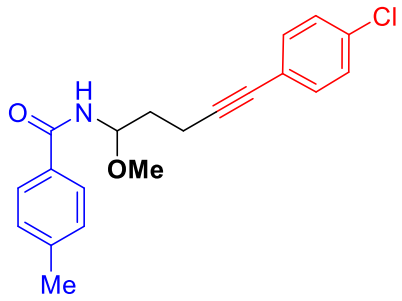
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.41 (m, 3H, Ar*H*), 7.38 (d, *J* = 8.3 Hz, 3H, Ar*H*), 7.32 – 7.27 (m, 3H, Ar*H*), 6.92 – 6.86 (m, 2H, Ar*H*), 4.61 – 4.51 (m, 1H, OC*H*$_2$CH$_2$), 4.51 – 4.43 (m, 1H, OC*H*$_2$CH$_2$), 4.11 (dd, *J* = 8.2, 6.6 Hz, 1H, CCC*H*CH$_2$), 3.92 (s, 3H, OC*H*$_3$), 3.88 (s, 3H, OC*H*$_3$), 3.80 (s, 3H, OC*H*$_3$), 2.35 – 2.22 (m, 2H, CH$_2$C*H*$_2$CH).

^{13}C NMR (201 MHz, $CDCl_3$) δ 165.7, 158.8, 152.0, 148.8, 133.2, 131.8, 128.6, 128.4, 128.1, 126.6, 123.8, 123.5, 114.2, 114.2, 90.6, 84.6, 84.0, 63.7, 56.4, 56.2, 55.5, 37.4, 34.7.

IR (ν_{max}, cm^{-1}) 2960 (m), 2924 (m), 2849 (w), 1720 (m), 1510 (s), 1261 (s), 1246 (s), 1204 (s), 1174 (s), 1111 (m), 1024 (s), 795 (m).

HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{27}H_{25}INaO_5^+$ 579.0639; Found 579.0658.

N-(5-(4-chlorophenyl)-1-methoxypent-4-yn-1-yl)-4-methylbenzamide (6a)



In a 12*75 mm Borosilicate glass tube, **2a** (95.6 mg, 250 µmol, 2.50 equiv) and N-cyclopropyl-4-methylbenzamide (**5a**) (17.5 mg, 100 µmol, 1.00 equiv) were added. The tube was then closed with a rubber septum and sealed off with parafilm. Three cycles of evacuate-refill with nitrogen were performed to remove O_2 and DCM (1.0 mL, 0.1M) was added, followed by the addition of methanol (6.41 mg, 200 µmol, 2.00 equiv). The reaction mixture was stirred at room temperature irradiating with Kessil lamps (440 nm). The reaction was monitored by NMR with CH_2Br_2 as an internal standard. Upon completion by either full conversion of starting material or hypervalent iodine reagents, the mixture was concentrated in vacuo and purified by column chromatography to give product **6a** (18.1 mg, 52.7 µmol, 53% yield) as a white solid

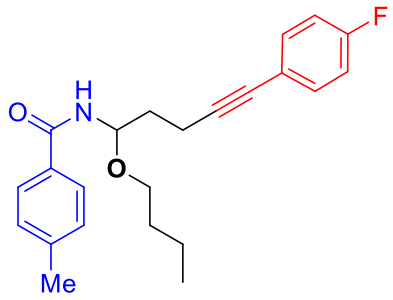
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 8.2 Hz, 2H, Ar*H*), 7.25 (d, J = 8.5 Hz, 2H, Ar*H*), 7.23 (d, J = 8.7 Hz, 2H, Ar*H*), 7.15 (d, J = 8.0 Hz, 2H, Ar*H*) 6.63 (d, *J* = 9.6 Hz, 1H, N*H*), 5.53 (dt, *J* = 9.6, 5.7 Hz, 1H, NHC*H*), 3.43 (s, 3H, OCH_3), 2.65 (dt, *J* = 17.1, 7.0 Hz, 1H, CHCH$_2$CH_2), 2.54 (dt, *J* = 17.1, 6.9 Hz, 1H, CHCH$_2$CH_2), 2.36 (s, 3H, ArCH_3), 2.09 – 1.94 (m, 2H, CHCH_2CH$_2$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 142.6, 133.9, 133.0, 131.0, 129.4, 128.6, 127.2, 127.1, 122.1, 90.4, 80.7, 80.6, 56.3, 34.2, 21.6, 15.0.

HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{20}ClNNaO_2^+$ 364.1075; Found 364.1075

Consistent with reported value.[6]

N-(1-butoxy-5-(4-fluorophenyl)pent-4-yn-1-yl)-4-methylbenzamide (6b)



In a 12*75 mm Borosilicate glass tube, **2a** (91.5 mg, 250 µmol, 2.50 equiv) and N-cyclopropyl-4-methylbenzamide (**5a**) (17.5 mg, 100 µmol, 1.00 equiv) were added. The tube was then closed with a rubber septum and sealed off with parafilm. Three cycles of evacuate-refill with nitrogen were performed to remove O_2 and DCM (1.0 mL, 0.1 M) was added, followed by the addition of methanol (6.41 mg, 200 µmol, 2.00 equiv). The reaction mixture was stirred at room temperature irradiating with Kessil lamps (440 nm). The reaction was monitored by NMR with CH_2Br_2 as an internal standard. Upon completion by either full conversion of starting material or hypervalent iodine reagents, the mixture was concentrated in vacuo and purified by column chromatography to give product **6b** as a white solid (18.7 mg, 50.9 µmol, 51% yield)

^{1}H NMR (400 MHz, $CDCl_3$) δ (d, J = 8.1 Hz, 2H, Ar*H*), 7.35 – 7.29 (m, 2H, Ar*H*), 7.16 (d, J = 8.0 Hz, 2H, Ar*H*), 6.99 – 6.91 (m, 2H, Ar*H*), 6.60 (d, *J* = 9.5 Hz, 1H, N*H*), 5.61 (ddd, *J* = 9.5, 6.3, 5.5 Hz, 1H, NHC*H*), 3.67 (dt, J = 9.5, 6.6 Hz, 1H, OC*H*$_2$CH$_2$), 3.55 (dt, J = 9.6, 6.6 Hz, 1H, OC*H*$_2$CH$_2$), 2.65 (dt, *J* = 17.0, 6.9 Hz, 1H, CHCH$_2$C*H*$_2$), 2.54 (dt, *J* = 17.1, 7.0 Hz, 1H, CHCH$_2$C*H*$_2$), 2.39 (s, 3H, ArC*H*$_3$), 2.12 – 1.93 (m, 2H, CHC*H*$_2$CH$_2$), 1.59 – 1.48 (m, 2H, OCH$_2$C*H*$_2$), 1.46 – 1.32 (m, 2H, OCH$_2$CH$_2$C*H*$_2$), 0.90 (t, *J* = 7.4 Hz, 3H, CH$_2$C*H*$_3$).

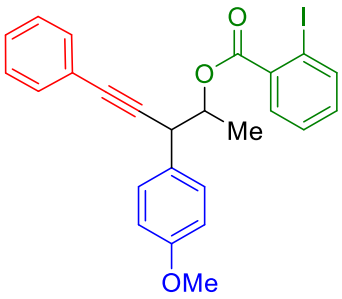
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 162.2 (d, *J* = 248.5 Hz), 142.3, 133.4 (d, *J* = 8.3 Hz), 131.1, 129.3, 127.0, 119.6 (d, *J* = 3.4 Hz), 115.4 (d, *J* = 21.9 Hz), 88.9, 80.3, 79.2, 68.4, 34.4, 31.8, 21.5, 19.4, 15.0, 13.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ -112.0.

HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{26}FNNaO_2^+$ 390.1840; Found 390.1846

Consistent with reported value.[6]

3-(4-Methoxyphenyl)-5-phenylpent-4-yn-2-yl 2-iodobenzoate (8a)



Following the general procedure B, starting from 1-methoxy-4-[(E)-prop-1-enyl]benzene (**7a**) (29.6 mg, 200 µmol, 1.00 equiv) and phenyl ethynyl benziodoxolone (**2a**) (174 mg, 500 µmol, 2.50 equiv). The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of pentane: ethyl acetate from 95:5 to 88:12) affording 3-(4-methoxyphenyl)-5-phenylpent-4-yn-2-yl 2-iodobenzoate (**8a**) as colorless oil (55.8 mg, 112 µmol, 56% yield for two diastereomers combined, dr 2:1, the ratio was determined by integration nof the ^{1}H NMR peaks of the benzylic protons ArC*H*).

Rf = 0.35 (SiO_2, 20:1 pentane:ethyl acetate).

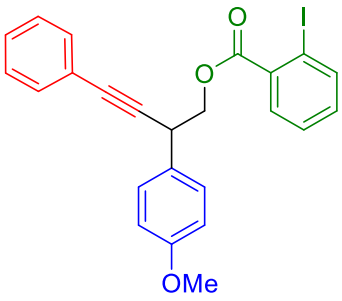
^{1}H NMR (400 MHz, $CDCl_3$, signals for major diastereomer) δ 7.98 (dt, *J* = 7.9, 1.4 Hz, 1H, Ar*H*), 7.78 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.44 – 7.41 (m, 2H, Ar*H*), 7.41 – 7.38 (m, 2H, Ar*H*), 7.36-7.37 (m, 1H, Ar*H*), 7.31 – 7.27 (m, 3H, Ar*H*), 7.13 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 6.93 – 6.86 (m, 2H, Ar*H*), 5.49 (p, *J* = 6.3 Hz, 1H, OC*H*(CH$_3$)CH$_2$), 4.18 (d, *J* = 5.9 Hz, 1H, ArC*H*CH(CH$_3$)), 3.81 (s, 3H, OC*H*$_3$), 1.42 (d, *J* = 6.3 Hz, 3H, CH(CH$_3$)).

^{13}C NMR (101 MHz, $CDCl_3$, signals for major diastereomer) δ 165.8, 159.2, 141.4, 135.3, 132.7, 131.8, 131.1, 129.9, 129.7, 128.4, 128.2, 128.0, 123.4, 114.0, 94.3, 88.3, 84.6, 74.7, 55.4, 43.4, 17.7.

IR (ν_{max}, cm^{-1}) 2987 (w), 2933 (w), 2836 (w), 1738 (m), 1721 (s), 1512 (m), 1289 (s), 1250 (s), 1179 (m), 1129 (m), 1101 (m), 1065 (m), 1057 (m), 1032 (m), 1012 (m), 833 (m), 758 (m), 741 (s).

HRMS (ESI/QTOF) m/z: [M + Na]$^{+}$ Calcd for $C_{25}H_{21}INaO_3^{+}$ 519.0428; Found 519.0436.

2-(4-Methoxyphenyl)-4-phenylbut-3-yn-1-yl 2-iodobenzoate (8b)



Following the general procedure B, starting from 1-ethenyl-4-methoxybenzene (**7b**) (26.8 mg, 200 µmol, 1.00 equiv) and phenyl ethynyl benziodoxolone (**2a**) (174 mg, 500 µmol, 2.50 equiv). The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of pentane: ethyl acetate from 95:5 to 90:10) affording 2-(4-methoxyphenyl)-4-phenylbut-3-yn-1-yl 2-iodobenzoate (**8b**) (42.6 mg, 88.3 µmol, 44% yield) as colorless oil.

Rf = 0.33 (SiO_2, 20:1 pentane:ethyl acetate).

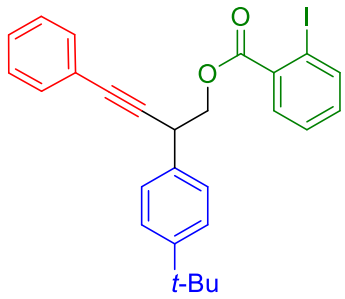
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 7.9, 1.2 Hz, 1H, Ar*H*), 7.81 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.49 – 7.42 (m, 4H, Ar*H*), 7.37 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.33 – 7.27 (m, 3H, Ar*H*), 7.15 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 6.95 – 6.88 (m, 2H, Ar*H*), 4.63 – 4.51 (m, 2H, OC*H*$_2$CH), 4.34 (t, *J* = 7.2 Hz, 1H, OCH_2CHCC). 3.82 (s, 3H, OC*H*$_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 159.2, 141.6, 134.8, 132.9, 131.9, 131.3, 129.7, 129.3, 128.4, 128.3, 128.0, 123.3, 114.3, 94.4, 88.2, 84.4, 69.1, 55.5, 37.6.

IR (IR (ν_{max}, cm^{-1}) 3058 (w), 2954 (w), 2836 (w), 2061 (w), 1728 (s), 1610 (m), 1583 (m), 1511 (s), 1463 (m), 1307 (m), 1287 (m), 1246 (s), 1178 (m), 1132 (m), 1098 (m), 1033 (m), 1013 (m), 830 (m), 758 (m), 740 (s).

HRMS (APPI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{24}H_{20}IO_3^+$ 483.0452; Found 483.0460.

2-(4-(*Tert*-butyl)phenyl)-4-phenylbut-3-yn-1-yl 2-iodobenzoate (8c)



Following the general procedure B, starting from 1-*tert*-butyl-4-ethenylbenzene (**7c**) (32.1 mg, 200 µmol, 1.00 equiv) and phenyl ethynyl benziodoxolone (**2a**) (174 mg, 500 µmol, 2.50 equiv). The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of pentane: ethyl acetate from 99:1 to 90:10) affording 2-(4-(*tert*-butyl)phenyl)-4-phenylbut-3-yn-1-yl 2-iodobenzoate (**8c**) (48.8 mg, 96.0 µmol, 48% yield) as colorless oil.

Rf = 0.55 (SiO_2, 10:1 pentane:ethyl acetate).

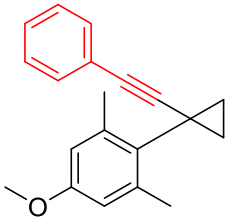
^{1}H NMR : (400 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 7.9, 1.2 Hz, 1H, Ar*H*), 7.80 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.47 (d, *J* = 1.9 Hz, 1H, Ar*H*), 7.46-7.44 (m, 2H, Ar*H*), 7.42 (s, 1H, Ar*H*), 7.40 – 7.34 (m, 3H, Ar*H*), 7.32 – 7.29 (m, 3H, Ar*H*), 7.18 – 7.13 (m, 1H, Ar*H*), 4.59 (d, *J* = 7.2 Hz, 2H, OC*H*$_2$CH$_2$), 4.38 (t, *J* = 7.2 Hz, 1H, CCC*H*CH$_2$), 1.33 (s, 9H, C(C*H*$_3$)$_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 150.8, 141.5, 134.9, 134.6, 132.9, 131.9, 131.4, 128.4, 128.2, 128.0, 127.9, 125.8, 123.4, 94.4, 88.2, 84.4, 69.1, 37.9, 34.7, 31.5.

IR (ν_{max}, cm^{-1}) 2954 (m), 2868 (w), 2200 (w), 1729 (s), 1463 (m), 1288 (s), 1269 (s), 1249 (s), 1134 (s), 1100 (s), 1017 (m), 759 (s), 740 (s).

HRMS (APPI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{27}H_{26}IO_2^+$ 509.0972; Found 509.0986.

5-Methoxy-1,3-dimethyl-2-(1-(phenylethynyl)cyclopropyl)benzene (4a)



Following the general procedure B, starting from **1g** (35.3 mg, 200 µmol, 1.00 equiv) and **2a** (104 mg, 300 µmol, 1.50 equiv). The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of pentane: ethyl acetate from 99:1 to 95:5) affording (**4a**) (46.1 mg, 167 µmol, 83% yield) of off-white amorphous solid.

Rf = 0.55 (SiO_2, 40:1 pentane:ethyl acetate).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.31 (m, 2H, Ar*H*), 7.23 (m, 3H, Ar*H*), 6.59 (s, 2H, Ar*H*), 3.78 (s, 3H, OC*H*$_3$), 2.53 (s, 6H, 2xArC*H*$_3$), 1.55 – 1.49 (m, 2H, , C*H*^{a}H^{b}C*H*^{a}H^b), 1.17 – 1.09 (m, 2H, CH^a*H*^{b}CH^a*H*^{b}).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3, 140.1, 131.8, 131.1, 128.2, 127.4, 124.2, 113.6, 94.5, 75.6, 55.2, 20.9, 19.8, 13.0.

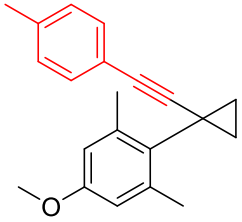
IR (ν_{max}, cm^{-1}) 3005 (w), 2955 (w), 2922 (w), 2836 (w), 2226 (w), 1597 (m), 1484 (m), 1329 (m), 1313 (m), 1158 (s), 1058 (m), 756 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{21}O^+$ 277.1587; Found 277.1587.

***Scale-up experiment**

In a schlenk tube 50 ml, **2a** (5 mmol, 2.5 equiv) was added. The tube was then closed with a rubber septum and sealed off with parafilm. Three cycles of evacuate-refill with nitrogen were performed to remove O_2 and $CHCl_3$ (20 mL, 1 M) was added, followed by three cycles of Freeze Pump Thaw to completely remove O_2. After that, **1f** (353 mg, 2.00 mmol, 1.00 equiv) was added under N_2 atmosphere and the top of the schlenk tube was sealed again with parafilm . The reaction was monitored by NMR with CH_2Br_2 as internal standard. Upon complete conversion of the starting material, the mixture was concentrated in vacuo and purified by column chromatography on Biotage (Büchi flashpure cartridge 40 g, gradient of pentane: ethyl acetate from 99:1 to 95:5) to give product **4a** (511 mg, 1.85 mmol, 92% yield).

5-Methoxy-1,3-dimethyl-2-(1-(p-tolylethynyl)cyclopropyl)benzene (4b)



Following the general procedure B, starting from **1g** (35.3 mg, 200 µmol, 1.00 equiv) and 1-[tolylethynyl]-1,2-benziodoxol-3(1H)-one (**2b**) (109 mg, 300 µmol, 1.50 equiv). The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of pentane: ethyl acetate from 99:1 to 95:5) affording **4b** (37.9 mg, 131 µmol, 65% yield) as pale yellow oil.

Rf = 0.6 (SiO_2, 20:1 pentane:ethyl acetate).

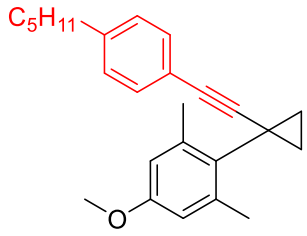
^{1}H NMR : ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.04 (d, *J* = 8.0 Hz, 2H, Ar*H*), 6.58 (s, 2H, Ar*H*), 3.77 (s, 3H, OC*H*$_3$), 2.53 (s, 6H, ArC*H*$_3$), 2.31 (s, 3H), 1.51 (m, 2H, C*H*^{a}H^{b}C*H*^{a}H^b), 1.13 – 1.05 (m, 2H, CH^a*H*^{b}CH^a*H*^{b}).

^{13}C NMR ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3, 140.1, 137.4, 131.7, 131.3, 128.9, 121.1, 113.6, 93.7, 75.6, 55.2, 21.5, 20.9, 19.8, 13.1.

IR (film): IR (ν_{max}, cm^{-1}) 2921 (m), 2838 (w), 2226 (w), 1604 (s), 1507 (m), 1484 (m), 1468 (m), 1462 (m), 1327 (s), 1311 (s), 1193 (m), 1157 (s), 1057 (m), 818 (s).

HRMS (APPI/LTQ-Orbitrap) m/z: $[M]^+$ Calcd for $C_{21}H_{22}O^+$ 290.1665; Found 290.1671.

5-Methoxy-1,3-dimethyl-2-(1-((4-pentylphenyl)ethynyl)cyclopropyl)benzene (4c)



Following the general procedure B, starting from **1g** (35.3 mg, 200 µmol, 1.00 equiv) and 1-[4-*n*-pentylphenylethynyl]-1,2-benziodoxol-3(1H)-one (**2i**) (125 mg, 300 µmol, 1.50 equiv). The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of pentane: ethyl acetate from 99:1 to 95:5) affording **4c** (27.9 mg, 80.5 µmol, 40% yield) as pale yellow oil.

Rf = 0.57 (SiO_2, 40:1 pentane:ethyl acetate).

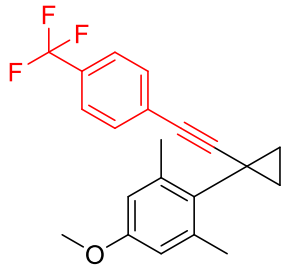
^{1}H NMR : ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.20 (m, 2H, Ar*H*), 7.07 – 7.01 (m, 2H, Ar*H*), 6.58 (s, 2H, Ar*H*), 3.77 (s, 3H, OC*H*$_3$), 2.57 – 2.53 (m, 2H, ArC*H*$_2$CH$_2$), 2.52 (s, 6H, ArC*H*$_3$) 1.61 – 1.54 (m, 2H, ArCH$_2$C*H*$_2$), 1.53 – 1.47 (m, 2H, C*H*^{a}H^{b}C*H*^{a}H^b), 1.35 – 1.23 (m, 4H, ArC$_2$H$_4$C$_2$*H*$_4$), 1.13 – 1.03 (m, 2H, CH^a*H*^{b}CH^a*H*^{b}), 0.87 (t, *J* = 7.0 Hz, 3H, ArC$_4$H$_8$C*H*$_3$).

^{13}C NMR : ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3, 142.5, 140.1, 131.7, 131.3, 128.3, 121.3, 113.5, 93.7, 75.6, 55.2, 35.9, 31.5, 31.1, 22.6, 20.9, 19.8, 14.1, 13.1.

IR (film): IR (ν_{max}, cm^{-1}) 2957 (s), 2924 (s), 2856 (m), 2224 (w), 1604 (s), 1508 (s), 1485 (s), 1462 (m), 1328 (s), 1312 (s), 1155 (s), 1061 (s), 855 (m), 835 (s).

HRMS (APPI/LTQ-Orbitrap) m/z: $[M]^+$ Calcd for $C_{25}H_{30}O^+$ 346.2291; Found 346.2304.

5-Methoxy-1,3-dimethyl-2-(1-((4-(trifluoromethyl)phenyl)ethynyl)cyclopropyl)benzene (4d)



Following the general procedure B, starting from **1g** (35.3 mg, 200 µmol, 1.00 equiv) and 1-[4-trifluoromethylphenylethynyl]-1,2-benziodoxol-3(1H)-one **2c** (124 mg, 300 µmol, 1.50 equiv). The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of pentane: ethyl acetate from 99:1 to 95:5) affording **4d** (55.8 mg, 162 µmol, 81% yield) as pale yellow oil.

Rf = 0.58 (SiO_2, 40:1 pentane:ethyl acetate).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.35 (m, 4H, Ar*H*), 6.60 (s, 2H, Ar*H*), 3.78 (s, 3H, OCH_3), 2.53 (s, 6H, ArCH_3), 1.61 – 1.53 (m, 2H, CH^aH^{b}CH^aH^b), 1.20 – 1.09 (m, 2H, CH^aH^bCH^aH^b).

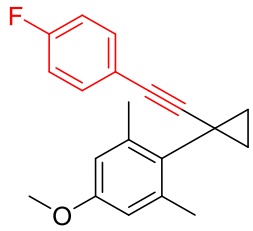
^{13}C NMR (101 MHz, $CDCl_3$) δ 158.5, 140.1, 132.0, 130.6, 129.3, 128.1, 127.4, 125.1 (q, *J* = 3.8 Hz), 113.7, 97.4, 74.5, 55.2, 20.9, 20.0, 13.0.

^{19}F NMR (377 MHz, $CDCl_3$) δ -62.7.

IR (film): IR (ν_{max}, cm^{-1}) 2956 (w), 2925 (w), 2838 (w), 2226 (w), 2118 (w), 1604 (m), 1487 (m), 1322 (s), 1159 (s), 1126 (s), 1066 (s), 842 (m).

HRMS (APPI/LTQ-Orbitrap) m/z: $[M]^+$ Calcd for $C_{21}H_{19}F_3O^+$ 344.1383; Found 344.1386.

2-(1-((4-Fluorophenyl)ethynyl)cyclopropyl)-5-methoxy-1,3-dimethylbenzene (4e)



Following the general procedure B, starting from **1g** (35.3 mg, 200 µmol, 1.00 equiv) and 1-[4-Fluorophenylethynyl]-1,2-benziodoxol-3(1H)-one (**2e**) (110 mg, 300 µmol, 1.50 equiv). The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of pentane: ethyl acetate from 99:1 to 95:5) affording **4e** (41.3 mg, 140 µmol, 70% yield) as pale yellow oil.

Rf = 0.53 (SiO_2, 40:1 pentane:ethyl acetate).

^{1}H NMR : ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 2H, Ar*H*), 6.96 – 6.88 (m, 2H, Ar*H*), 6.58 (s, 2H, Ar*H*), 3.77 (s, 3H, OC*H*$_3$), 2.52 (s, 6H, ArC*H*$_3$), 1.53 – 1.48 (m, 2H, -C*H*^{a}H^{b}C*H*^{a}H^b-), 1.13 – 1.06 (m, 2H, -CH^a*H*^{b}CH^a*H*^{b}-).

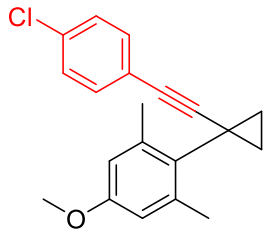
^{13}C NMR : ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1 (d, *J* = 249.5 Hz), 158.4, 140.1, 133.6, 133.6, 131.0, 120.22 (d, *J* = 3.6 Hz), 115.5, 115.3, 113.6, 94.1, 74.5, 55.2, 20.9, 19.8, 13.0.

^{19}F NMR (377 MHz, $CDCl_3$) δ -112.5.

IR (ν_{max}, cm^{-1}) 3002 (w), 2955 (w), 2837 (w), 2228 (w), 1892 (w), 1603 (s), 1505 (s), 1484 (m), 1468 (m), 1329 (m), 1313 (s), 1223 (s), 1192 (m), 1158 (s), 1059 (m), 836 (s).

HRMS (APPI/LTQ-Orbitrap) m/z: $[M]^+$ Calcd for $C_{20}H_{19}FO^+$ 294.1414; Found 294.1429.

2-(1-((4-Chlorophenyl)ethynyl)cyclopropyl)-5-methoxy-1,3-dimethylbenzene (4f)



Following the general procedure B, starting from **1g** (35.3 mg, 200 µmol, 1.00 equiv) and 1-1-[4-chlorophenylethynyl]-1,2-benziodoxol-3(1H)-one (**2d**) (115 mg, 300 µmol, 1.50 equiv). The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of pentane: ethyl acetate from 99:1 to 95:5) affording **4f** (49.2 mg, 158 µmol, 79% yield) as pale yellow oil.

Rf = 0.52 (SiO_2, 40:1 pentane:ethyl acetate).

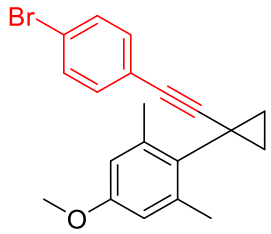
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.16 (m, 4H, Ar*H*), 6.58 (s, 2H, Ar*H*), 3.77 (s, 3H, OC*H*$_3$), 2.52 (s, 6H, ArC*H*$_3$), 1.54 – 1.48 (m, 2H, -C*H*^{a}H^{b}C*H*^{a}H^b-), 1.14 – 1.07 (m, 2H, -CH^a*H*^{b}CH^a*H*^{b}-).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4, 140.1, 133.3, 133.1, 130.8, 128.5, 122.7, 113.6, 95.6, 74.5, 55.2, 20.9, 19.9, 13.0.

IR (ν_{max}, cm^{-1}) 3089 (w), 3003 (m), 2954 (m), 2837 (w), 2226 (m), 1603 (s), 1488 (s), 1314 (s), 1158 (s), 828 (s).

HRMS (APPI/LTQ-Orbitrap) m/z: $[M]^+$ Calcd for $C_{20}H_{19}ClO^+$ 310.1119; Found 310.1133.

2-(1-((4-Bromophenyl)ethynyl)cyclopropyl)-5-methoxy-1,3-dimethylbenzene (4g)



Following the general procedure B, starting from **1g** (35.3 mg, 200 µmol, 1.00 equiv) and 1-[4-bromophenylethynyl]-1,2-benziodoxol-3(1H)-one **2j** (128 mg, 300 µmol, 1.50 equiv). The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of pentane: ethyl acetate from 99:1 to 95:5) affording **4g** (54.8 mg, 154 µmol, 77% yield) as pale yellow oil.

Rf = 0.57 (SiO_2, 20:1 pentane:ethyl acetate).

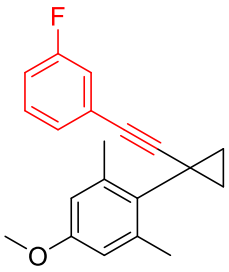
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.33 (m, 2H, Ar*H*), 7.22 – 7.15 (m, 2H, Ar*H*), 6.59 (s, 2H, Ar*H*), 3.77 (s, 3H, OC*H*$_3$), 2.52 (s, 6H, ArC*H*$_3$), 1.55 – 1.48 (m, 2H, -C*H*^{a}H^{b}C*H*^{a}H^b-), 1.16 – 1.08 (m, 2H, CH^a*H*^{b}CH^a*H*^{b}).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4, 140.1, 133.3, 131.4, 130.8, 123.2, 121.5, 113.6, 95.8, 74.6, 55.2, 20.9, 19.9, 13.0.

IR (ν_{max}, cm^{-1}) 3001 (w), 2954 (m), 2837 (w), 2225 (w), 1602 (s), 1484 (s), 1326 (s), 1312 (s), 1157 (s), 1066 (s), 1058 (s), 823 (s).

HRMS (APPI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{20}H_{20}BrO^+$ 355.0692; Found 355.0707.

2-(1-((3-Fluorophenyl)ethynyl)cyclopropyl)-5-methoxy-1,3-dimethylbenzene (4h)



Following the general procedure B, starting from **1g** (35.3 mg, 200 µmol, 1.00 equiv) and 1-[3-fluorophenylethynyl]-1,2-benziodoxol-3(1H)-one **2f** (110 mg, 300 µmol, 1.50 equiv). The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of pentane: ethyl acetate from 99:1 to 95:5) affording **4h** (36.2 mg, 123 µmol, 61% yield) as pale yellow oil.

Rf = 0.3 (SiO_2, 40:1 pentane:ethyl acetate).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (td, *J* = 8.0, 5.9 Hz, 1H, Ar*H*), 7.10 (dt, *J* = 7.7, 1.3 Hz, 1H, Ar*H*), 7.02 (ddd, *J* = 9.8, 2.7, 1.5 Hz, 1H, Ar*H*), 6.96 – 6.89 (m, 1H, Ar*H*), 6.59 (s, 2H, Ar*H*), 3.77 (s, 3H, OC*H*$_3$), 2.52 (s, 6H, ArC*H*$_3$), 1.55 – 1.49 (m, 2H, C*H*^{a}H^{b}C*H*^{a}H^b), 1.15 – 1.09 (m, 2H, CH^a*H*^{b}CH^a*H*^{b}).

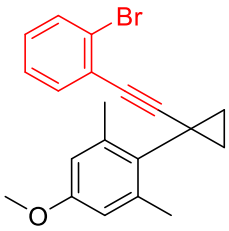
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4 (d, *J* = 245.8 Hz), 158.4, 140.1, 130.8, 129.7 (d, *J* = 8.7 Hz), 127.7 (d, *J* = 2.9 Hz), 126.1 (d, *J* = 9.6 Hz), 118.6 (d, *J* = 22.5 Hz), 114.8 (d, *J* = 21.1 Hz), 113.6, 95.7, 74.5 (d, *J* = 3.4 Hz), 55.2, 20.9, 19.9, 13.0.

^{19}F NMR (377 MHz, $CDCl_3$) δ -113.6.

IR (ν_{max}, cm^{-1}) 2957 (m), 2837 (w), 2220 (m), 1606 (s), 1579 (s), 1487 (s), 1467 (m), 1315 (s), 1159 (s), 1059 (m), 920 (s), 783 (s).

HRMS (APPI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{20}H_{20}FO^+$ 295.1493; Found 295.1489.

2-(1-((2-Bromophenyl)ethynyl)cyclopropyl)-5-methoxy-1,3-dimethylbenzene (4i)



Following the general procedure B, starting from **1g** (35.3 mg, 200 µmol, 1.00 equiv) and 1-[2-bromophenylethynyl]-1,2-benziodoxol-3(1H)-one (**2k**) (128 mg, 300 µmol, 1.50 equiv). The crude mixture was purified by column chromatography on Biotage (Büchi flashpure cartridge 25 g, gradient of pentane: ethyl acetate from 99:1 to 95:5) affording **4i** (38.5 mg, 108 µmol, 54% yield) as pale yellow oil.

Rf = 0.5 (SiO_2, 40:1 pentane:ethyl acetate).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (dd, *J* = 8.0, 1.3 Hz, 1H, Ar*H*), 7.35 (dd, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 7.17 (td, *J* = 7.6, 1.3 Hz, 1H, Ar*H*), 7.07 (ddd, *J* = 8.1, 7.4, 1.7 Hz, 1H, Ar*H*), 6.62 – 6.56 (m, 2H, Ar*H*), 3.77 (s, 3H, OCH_3), 2.54 (s, 6H, ArCH_3), 1.66 – 1.56 (m, 2H, $CH^aH^bCH^aH^b$), 1.20 – 1.09 (m, 2H, $CH^aH^bCH^aH^b$).

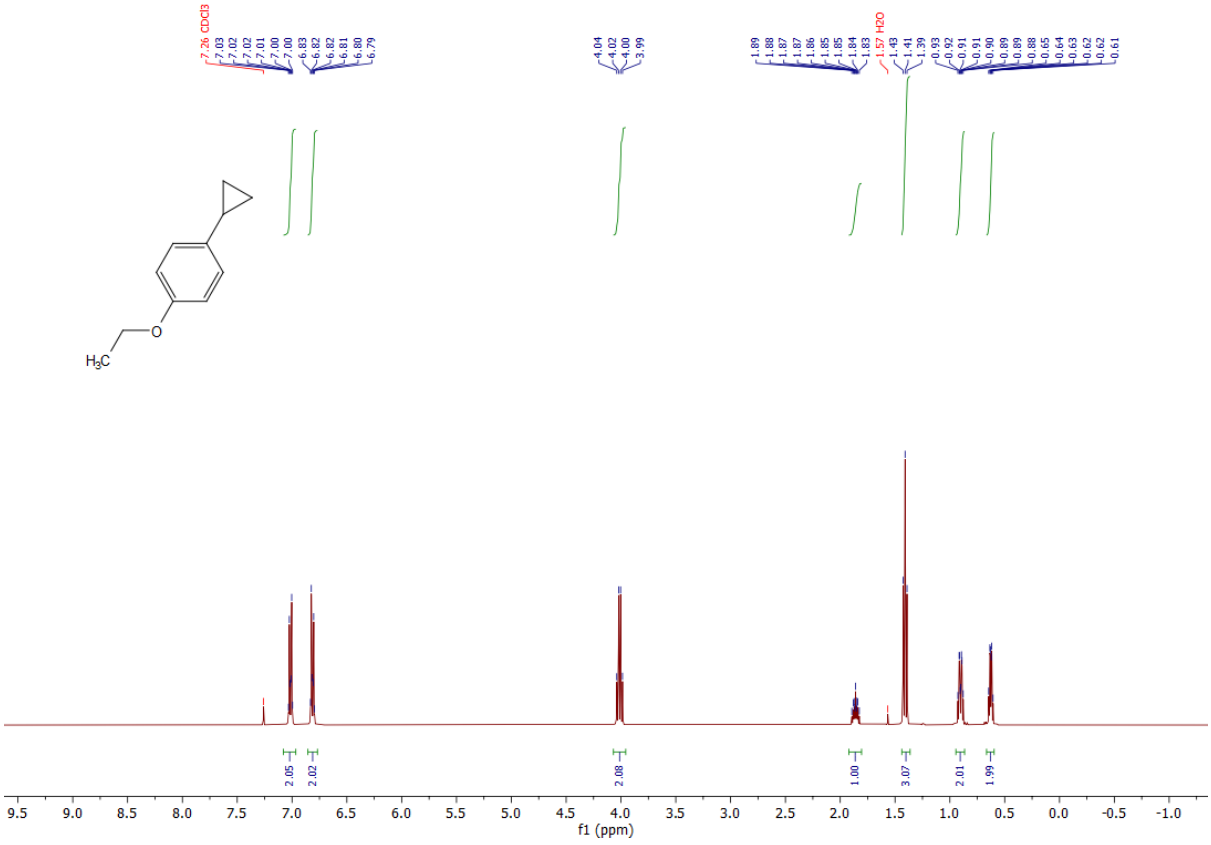
^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4, 140.2, 133.3, 132.3, 130.7, 128.6, 126.9, 126.1, 126.1, 113.6, 99.7, 74.4, 55.2, 20.9, 20.0, 13.2.

IR (ν_{max}, cm^{-1}) 3001 (w), 2955 (w), 2836 (w), 2229 (w), 1750 (w), 1603 (s), 1485 (m), 1467 (s), 1330 (m), 1314 (s), 1158 (s), 1058 (m), 1028 (m), 754 (s).

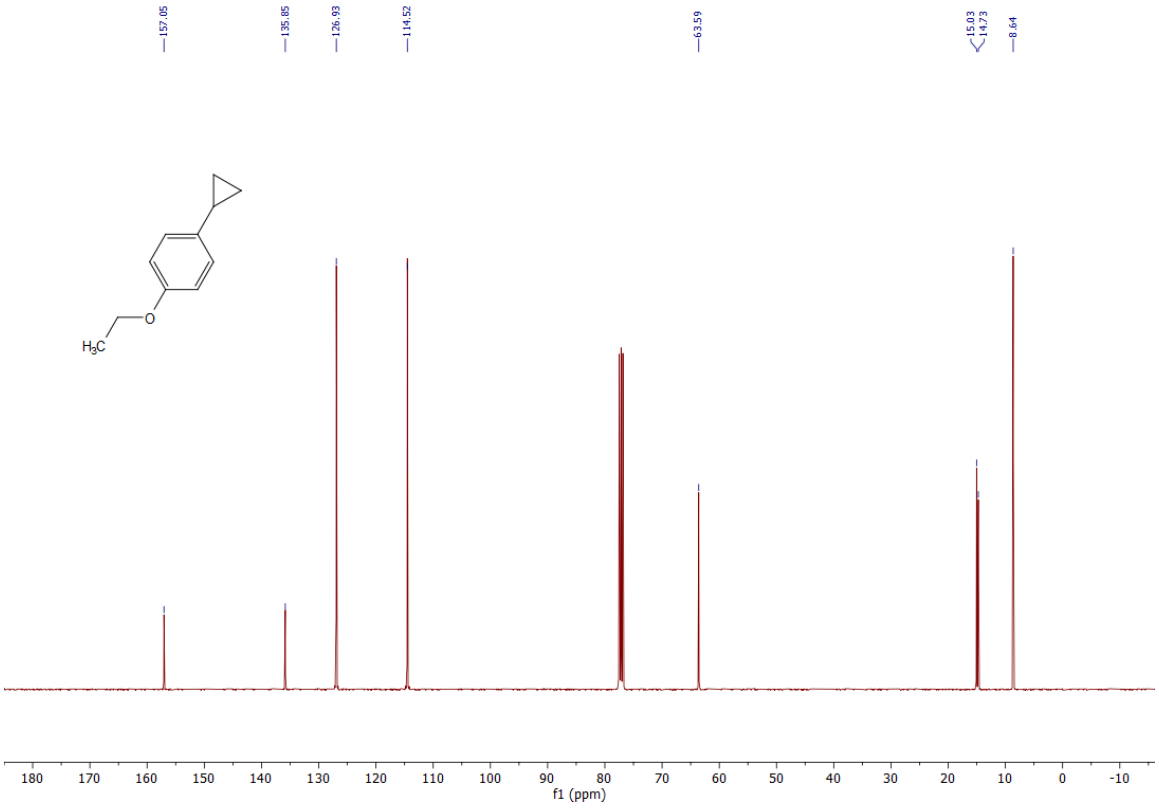
HRMS (APPI/LTQ-Orbitrap) m/z: $[M]^+$ Calcd for $C_{20}H_{19}BrO^+$ 354.0614; Found 354.0630.

NMR spectra

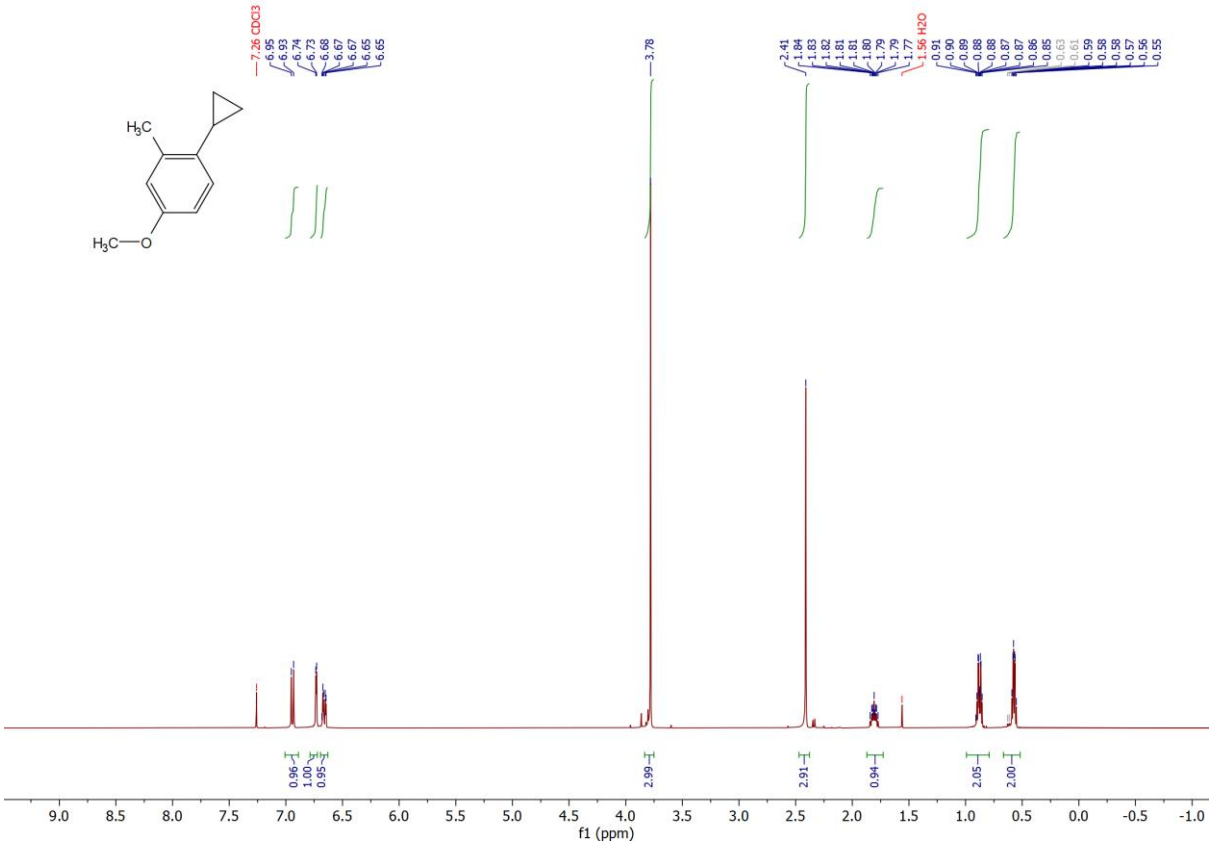
^{1}H-NMR (400 MHz, $CDCl_3$) (1c)



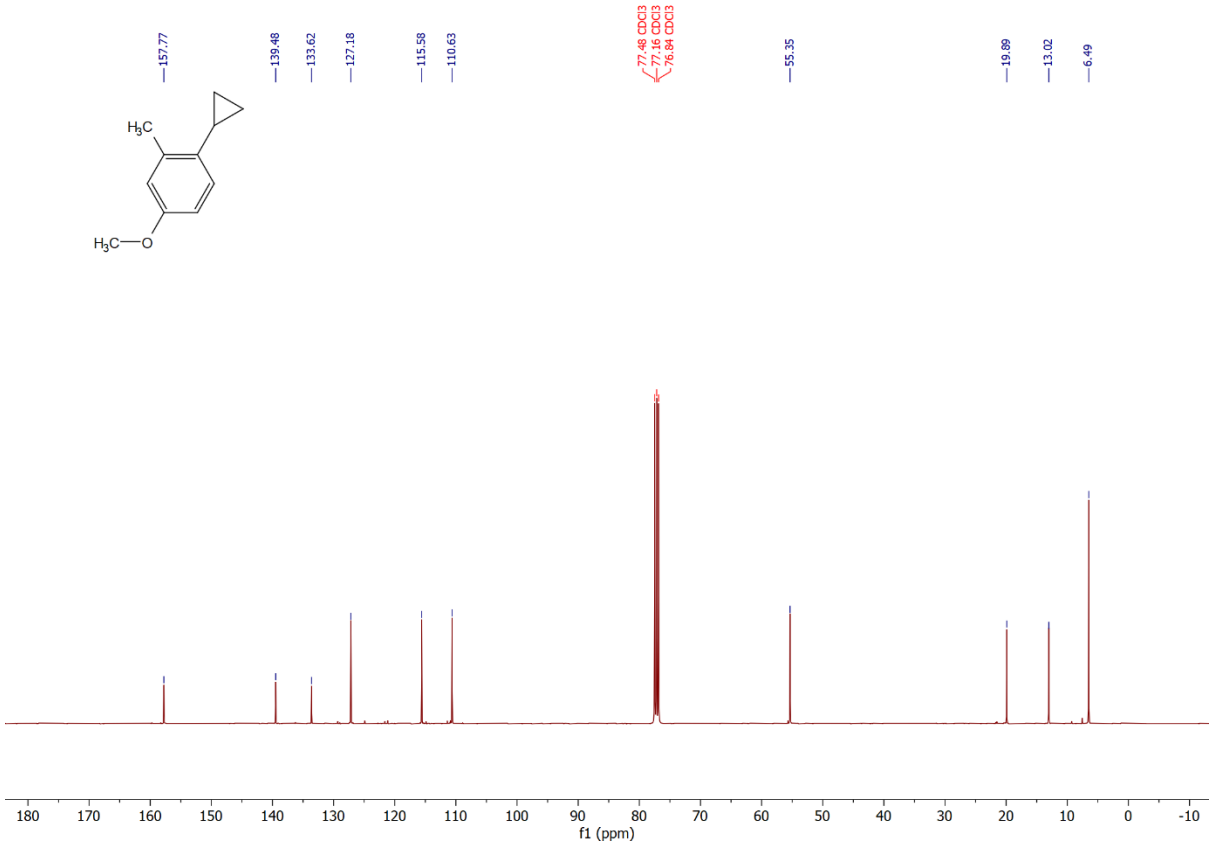
^{13}C NMR (101 MHz, $CDCl_3$) (1c)



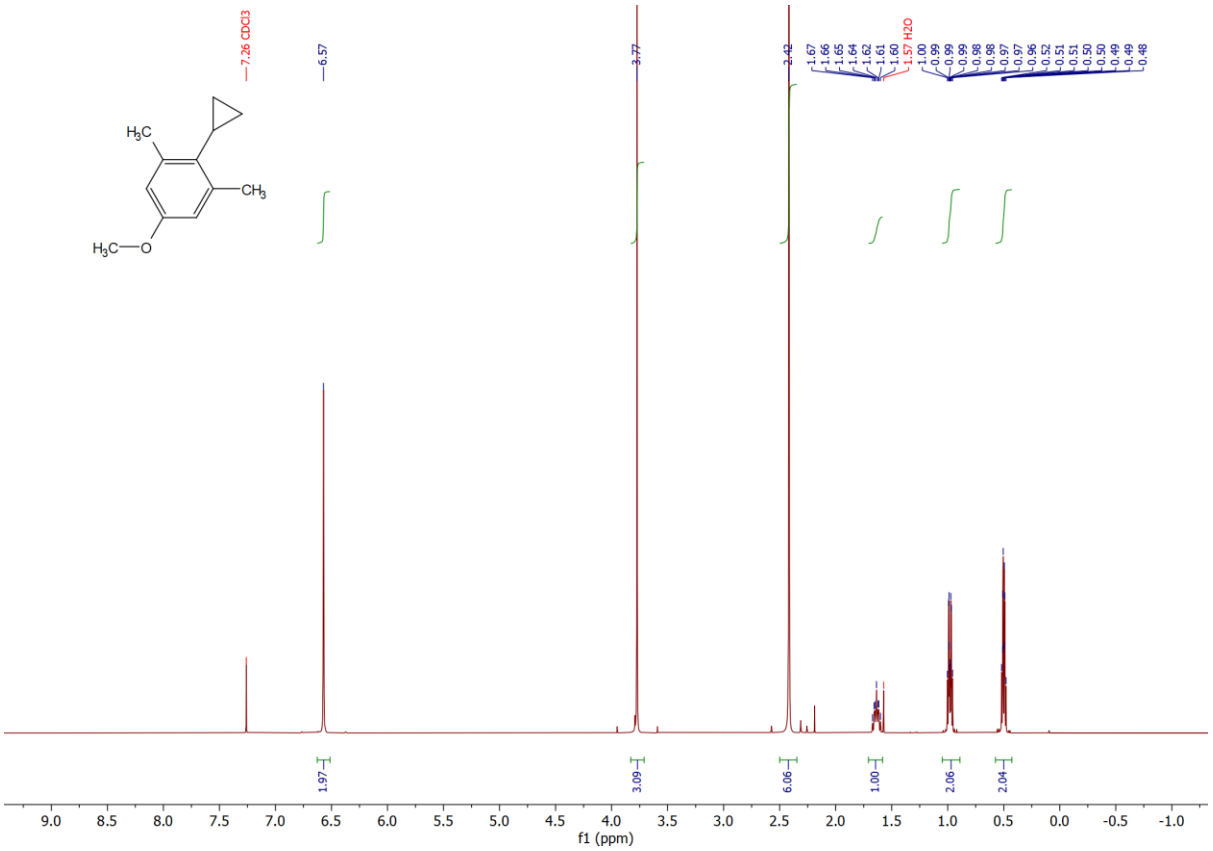
^{1}H-NMR (400 MHz, $CDCl_3$) (1f)



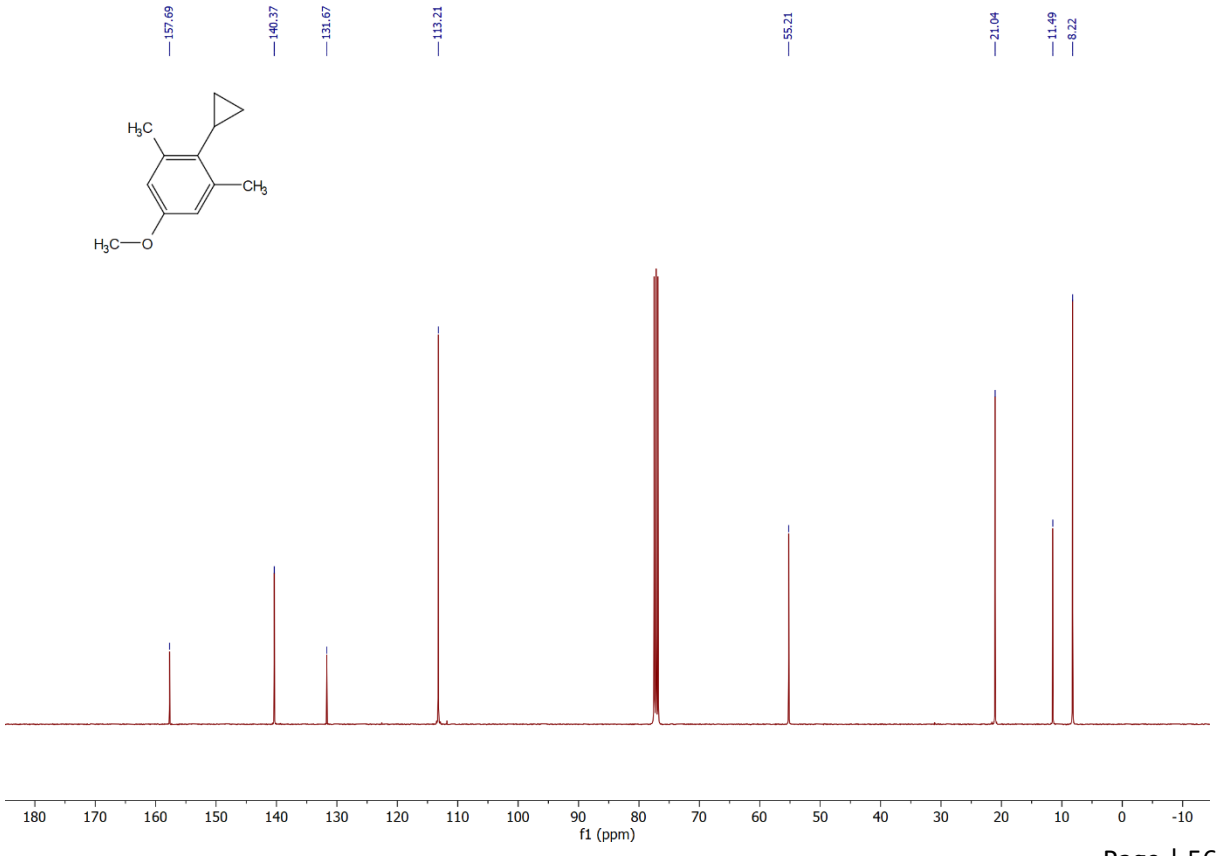
^{13}C NMR (101 MHz, $CDCl_3$) (1f)



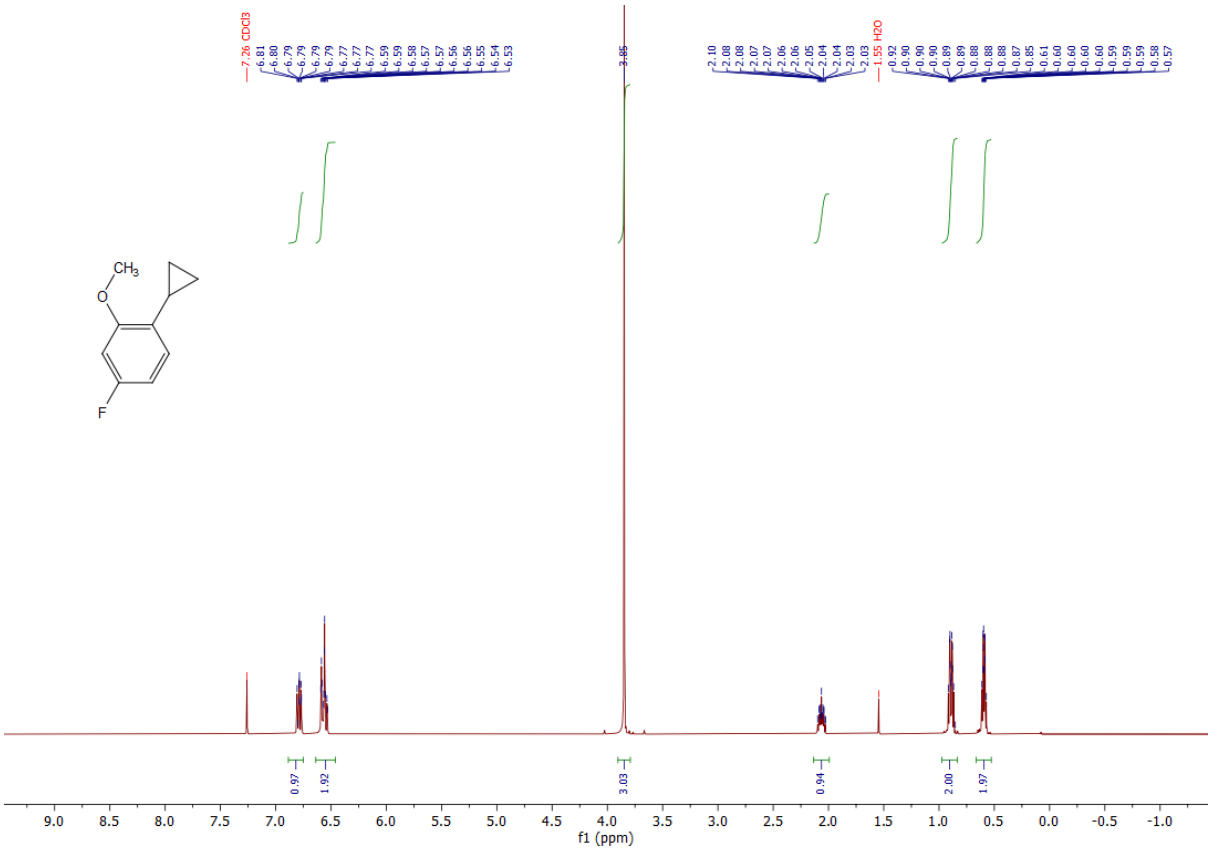
^{1}H-NMR (400 MHz, $CDCl_3$) (1f)



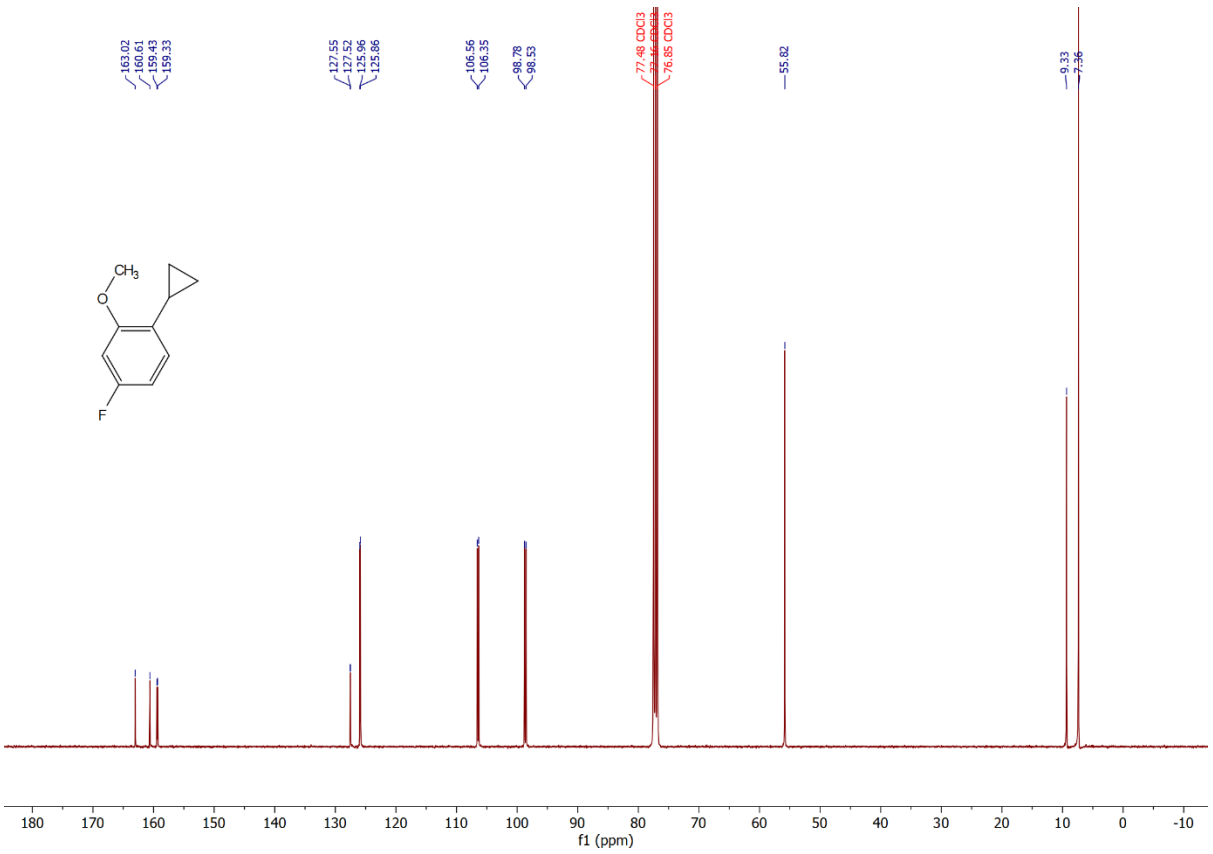
^{13}C NMR (101 MHz, $CDCl_3$) (1f)



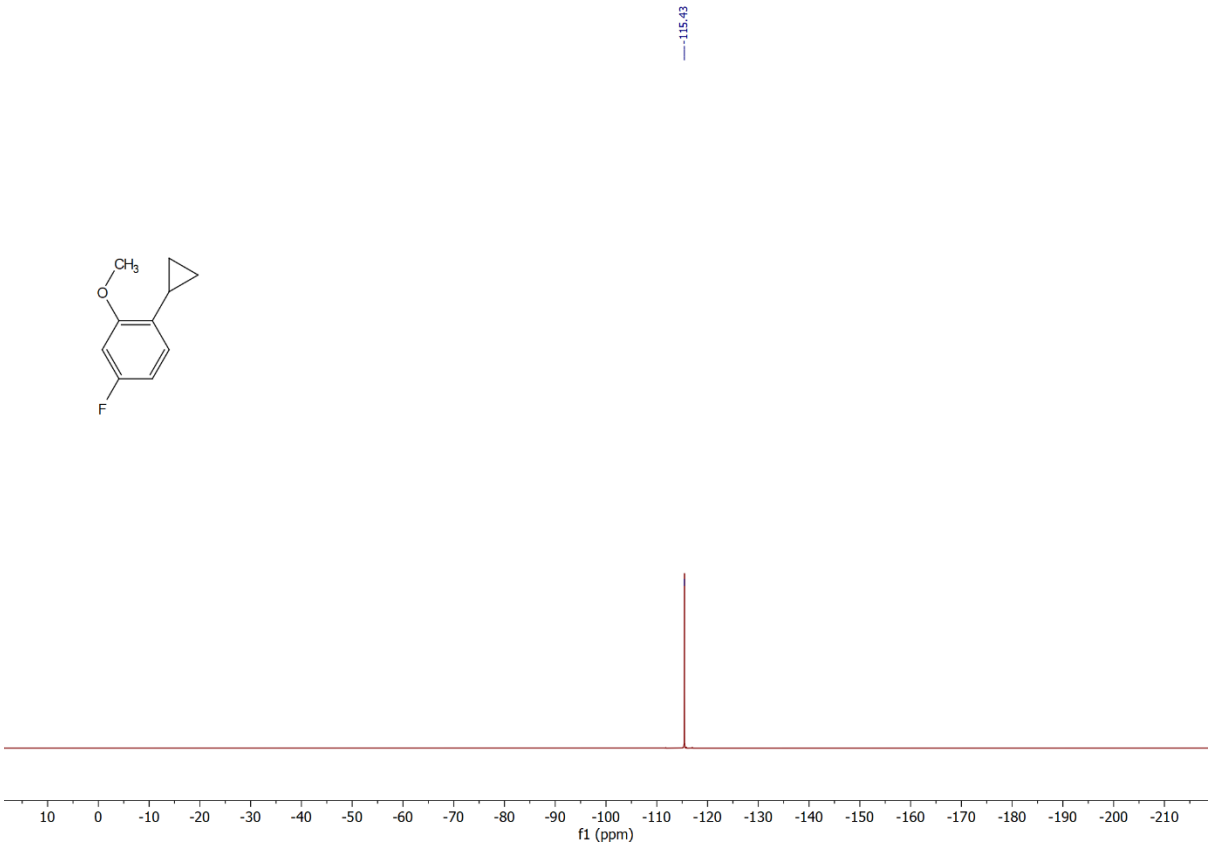
^{1}H-NMR (400 MHz, $CDCl_3$) (1g)



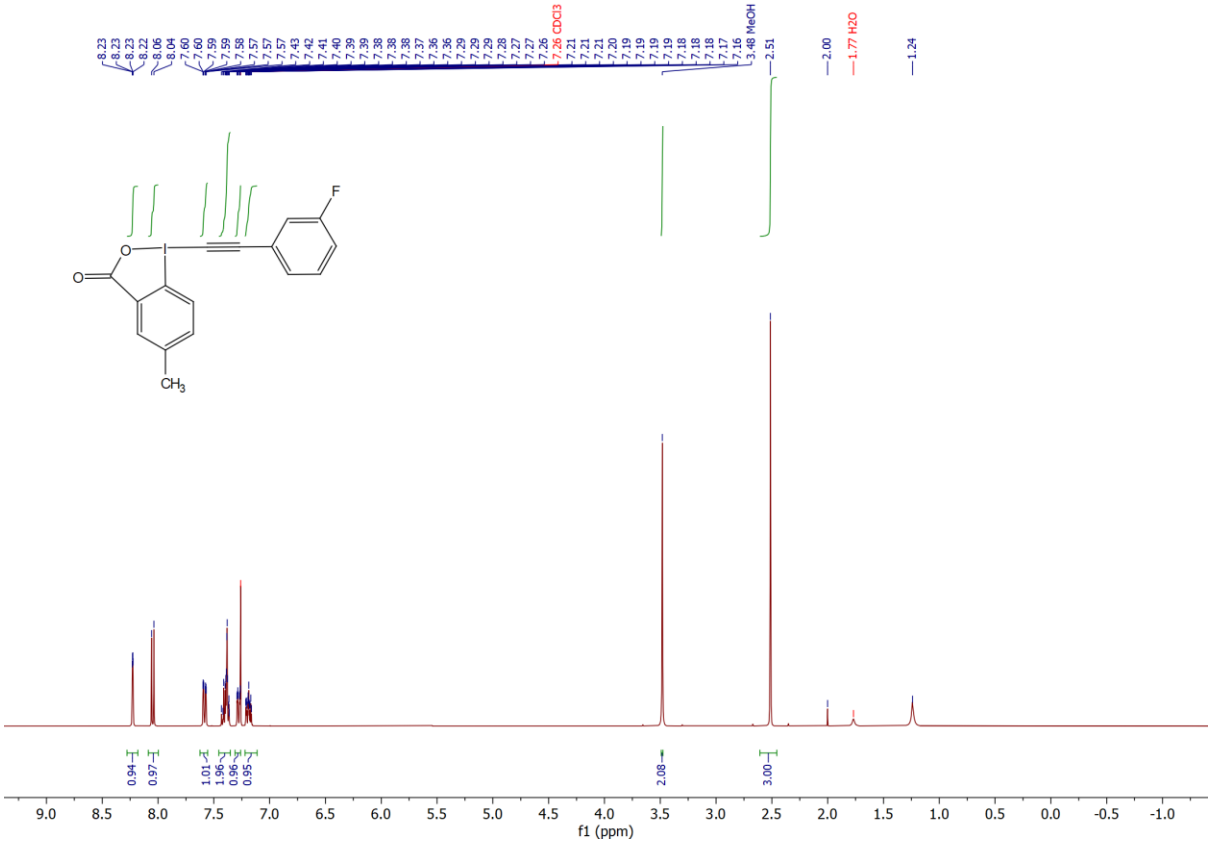
^{13}C NMR (101 MHz, $CDCl_3$) (1g)



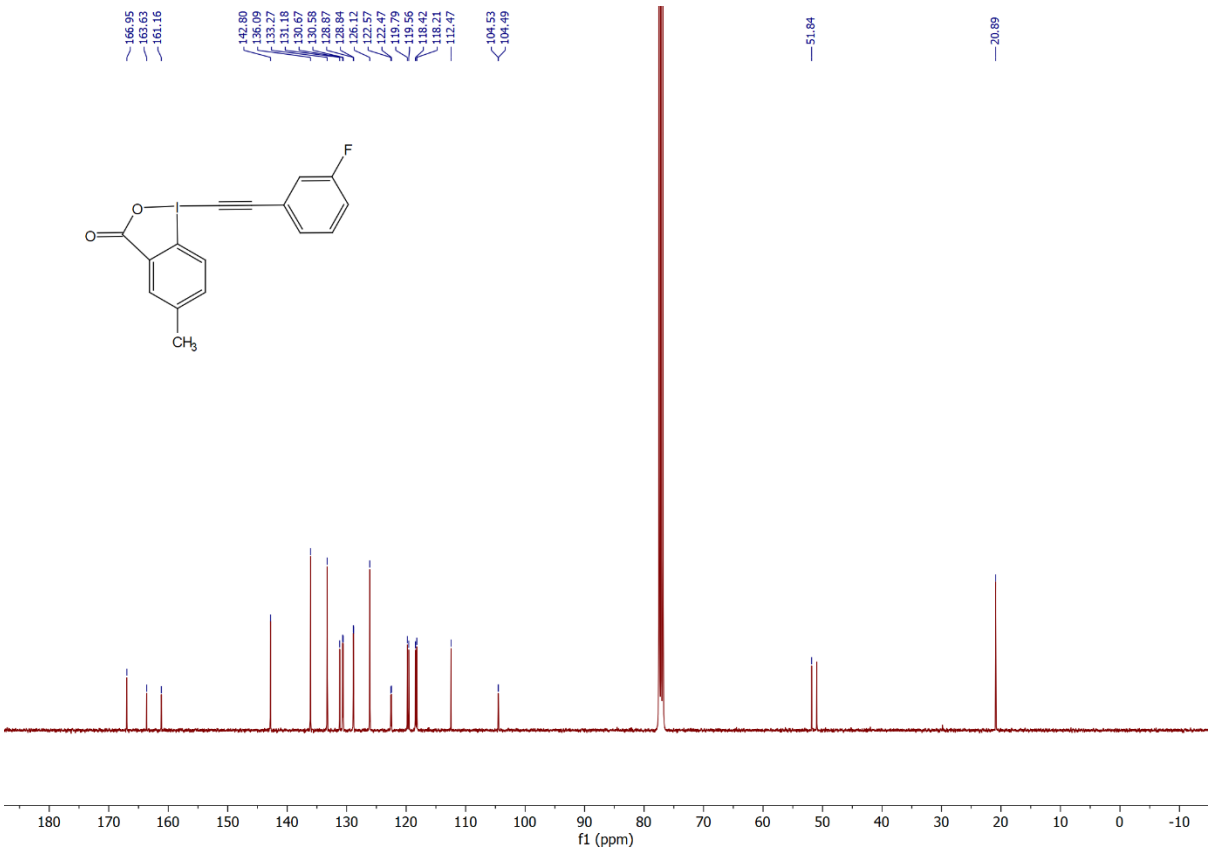
^{19}F NMR (377 MHz, $CDCl_3$) (1h)



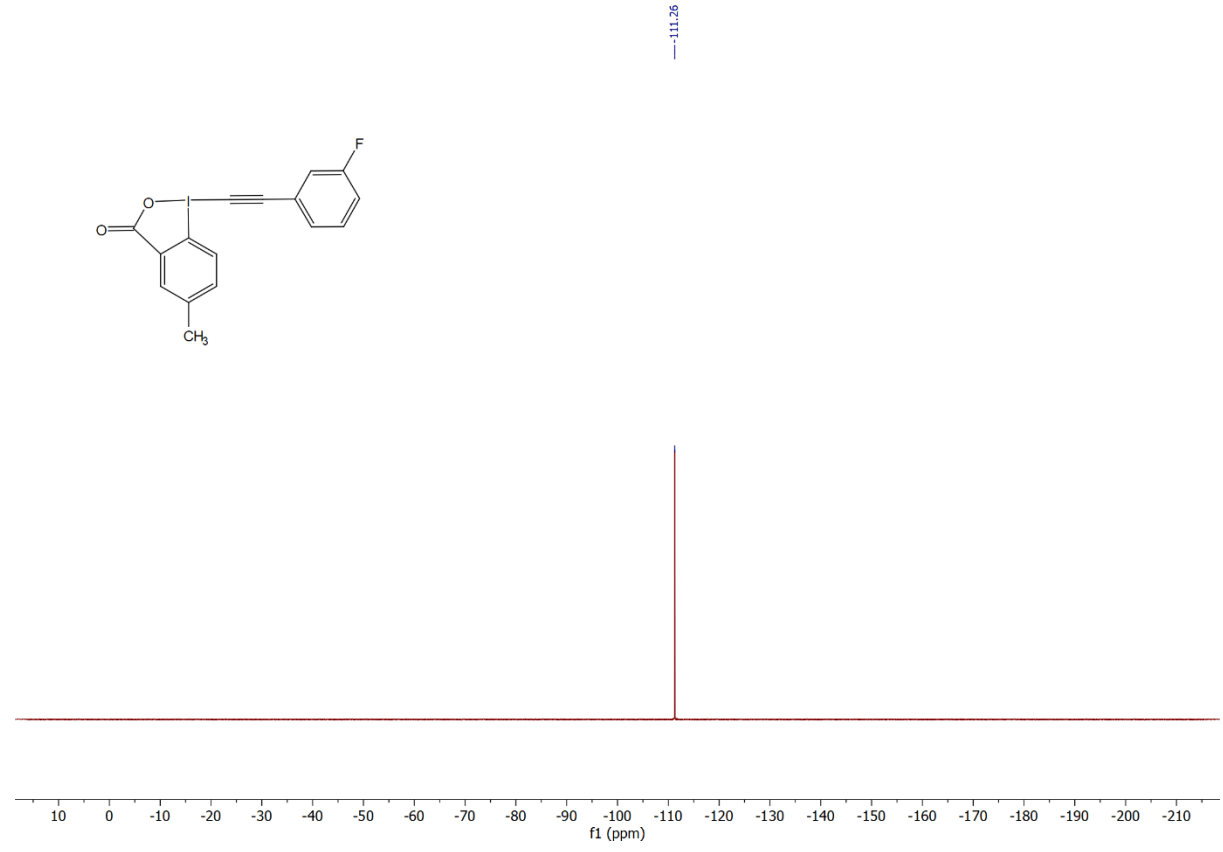
^{1}H-NMR (400 MHz, $CDCl_3$) (2g)



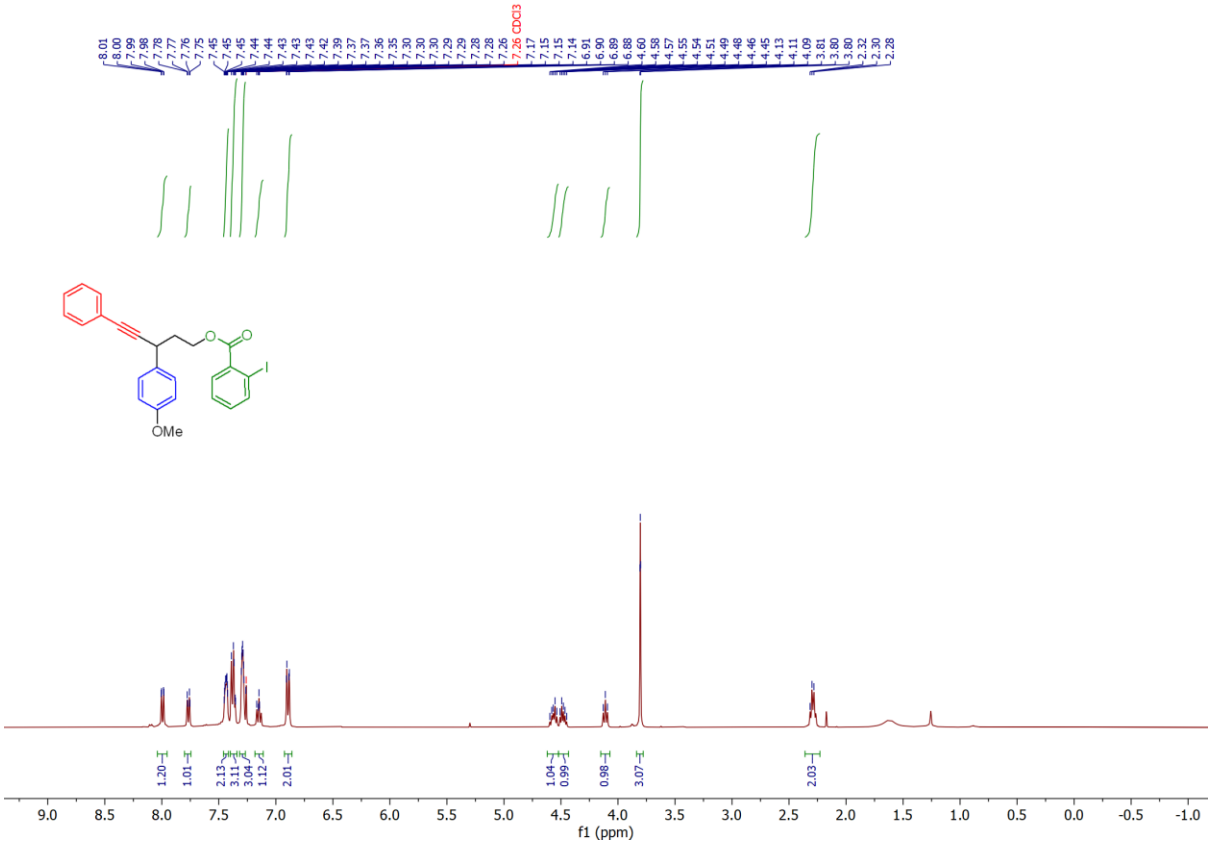
^{13}C NMR (101 MHz, $CDCl_3$) (2g)



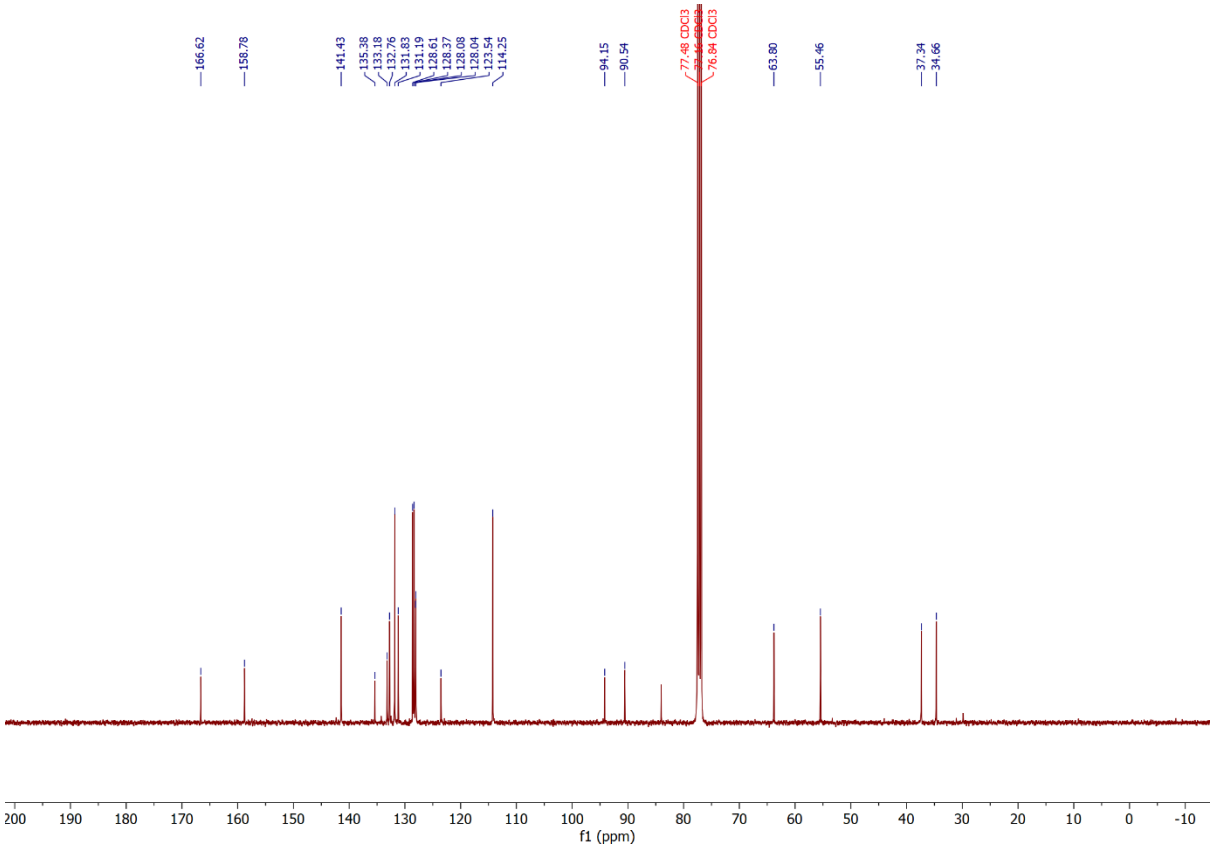
^{19}F NMR (377 MHz, $CDCl_3$) (2g)



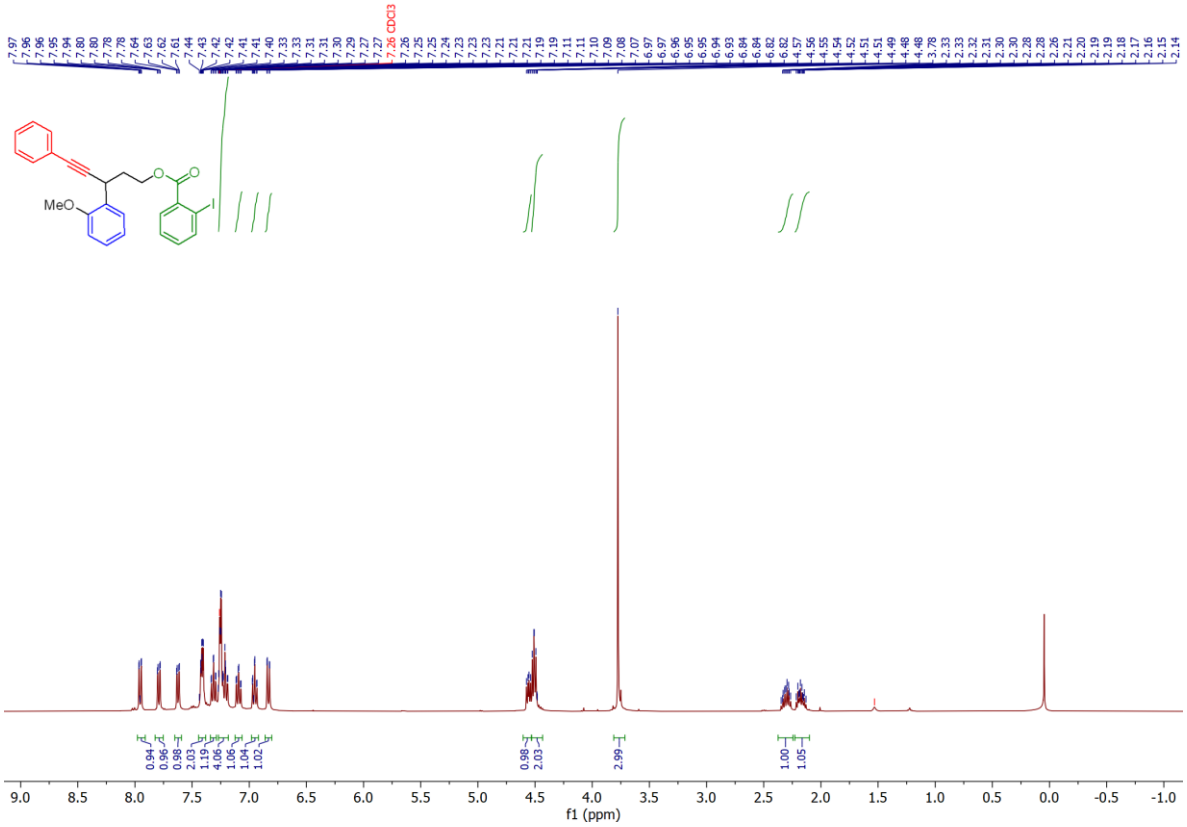
^{1}H NMR (400 MHz, $CDCl_3$) (3a)



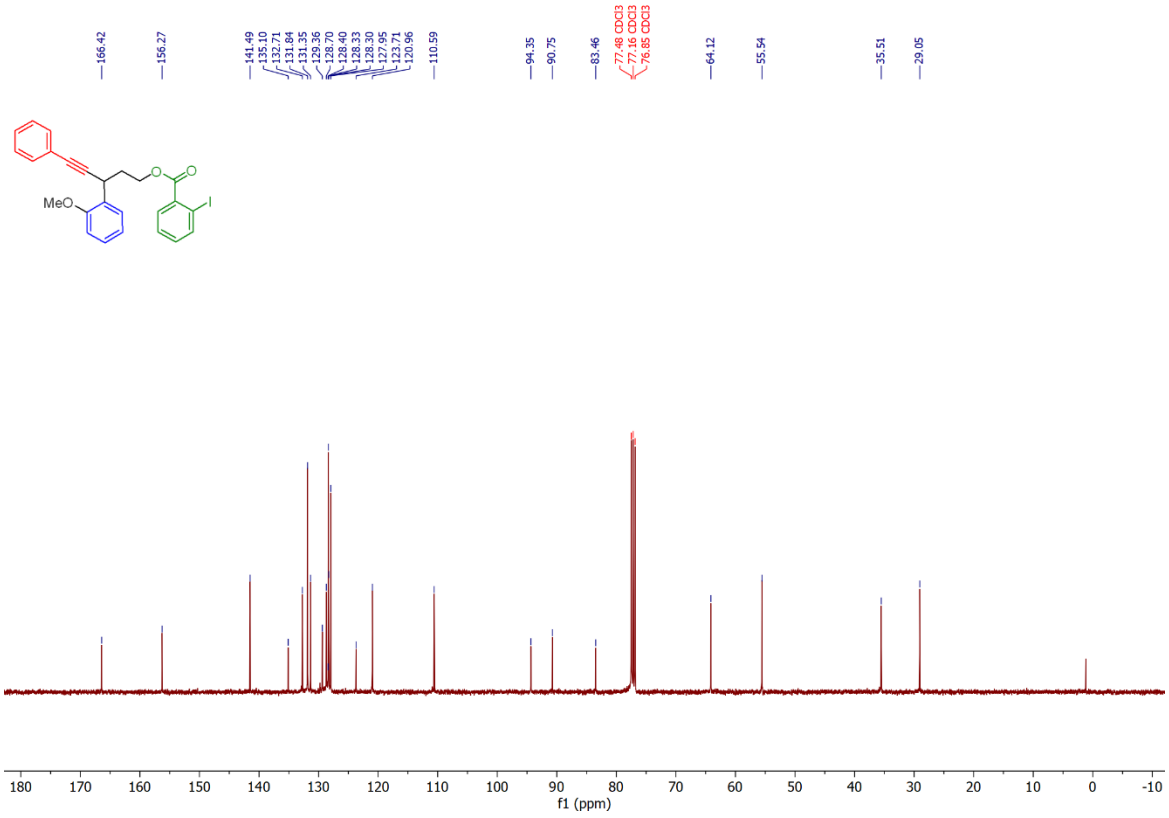
^{13}C NMR (101 MHz, $CDCl_3$) (3a)



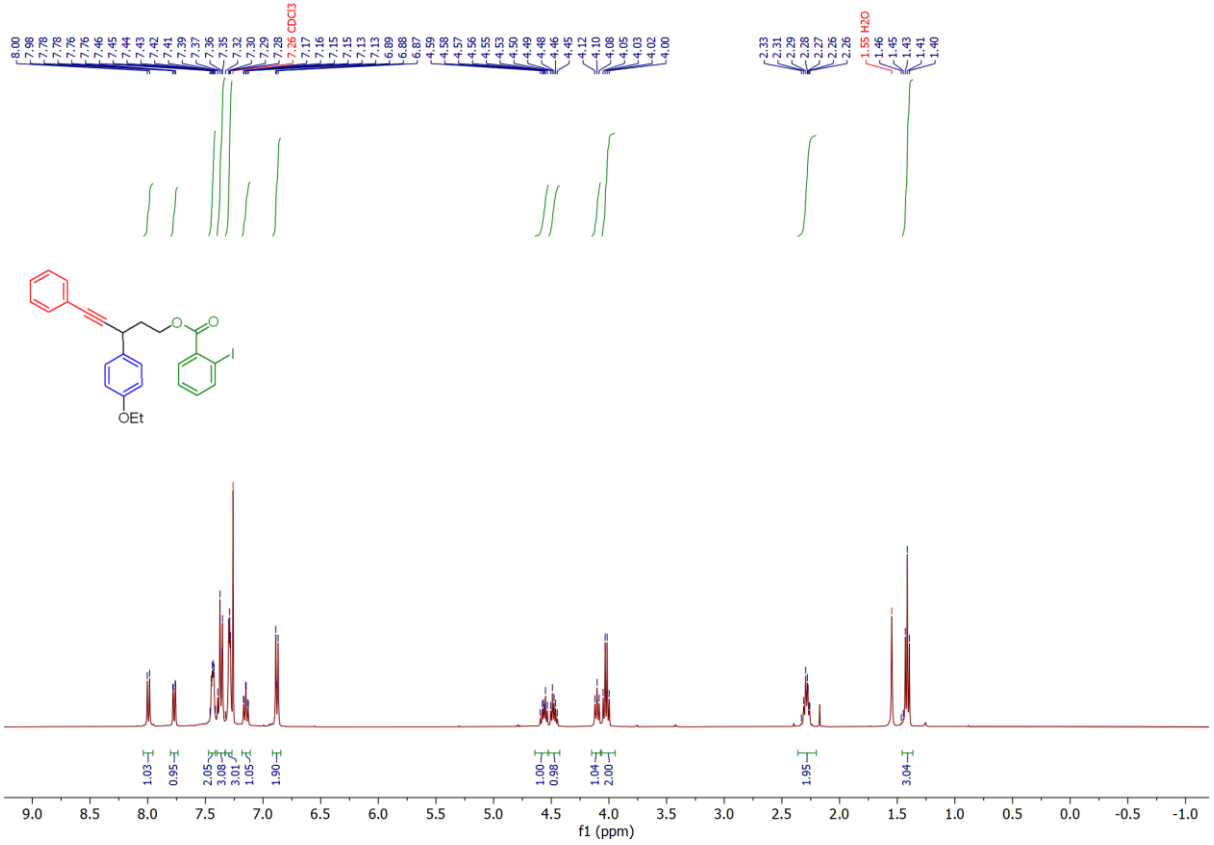
^{1}H NMR (400 MHz, $CDCl_3$) **(3b)**



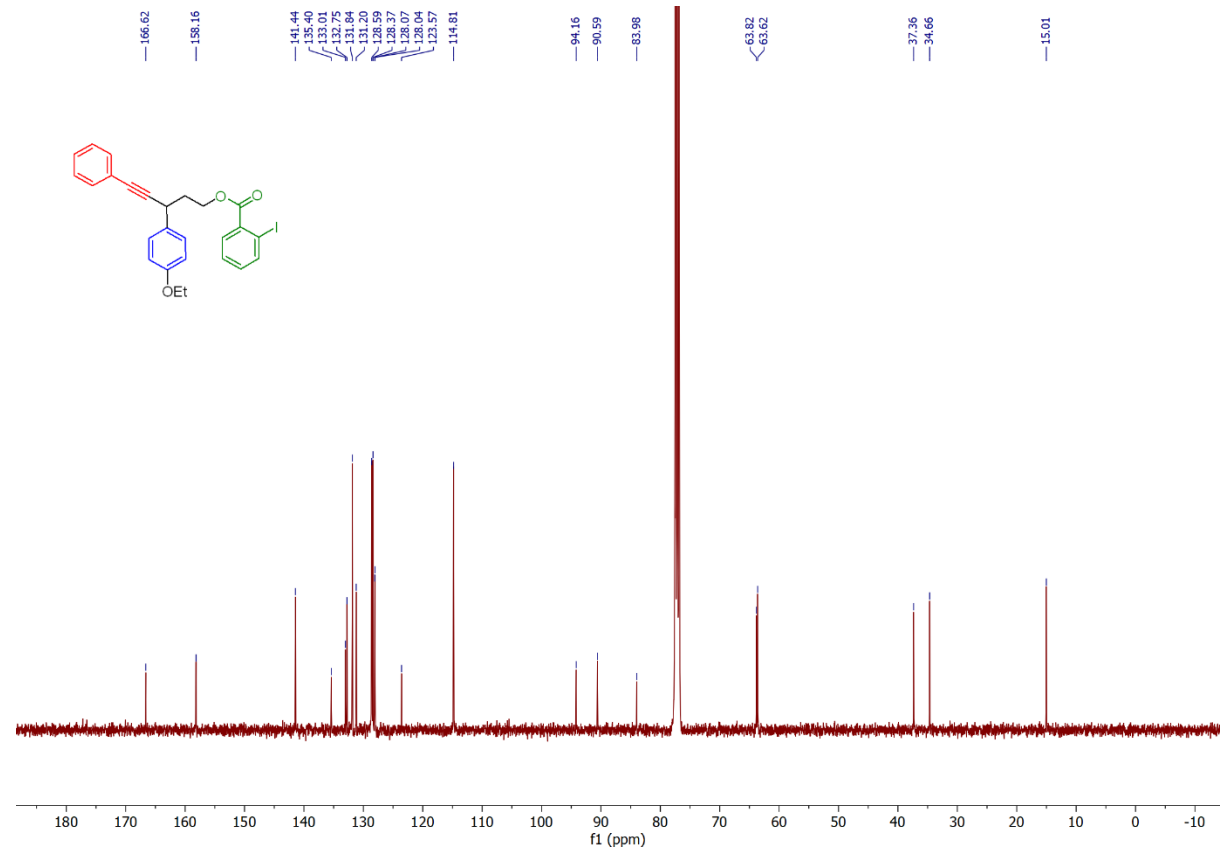
^{13}C NMR (101 MHz, $CDCl_3$) (3b)



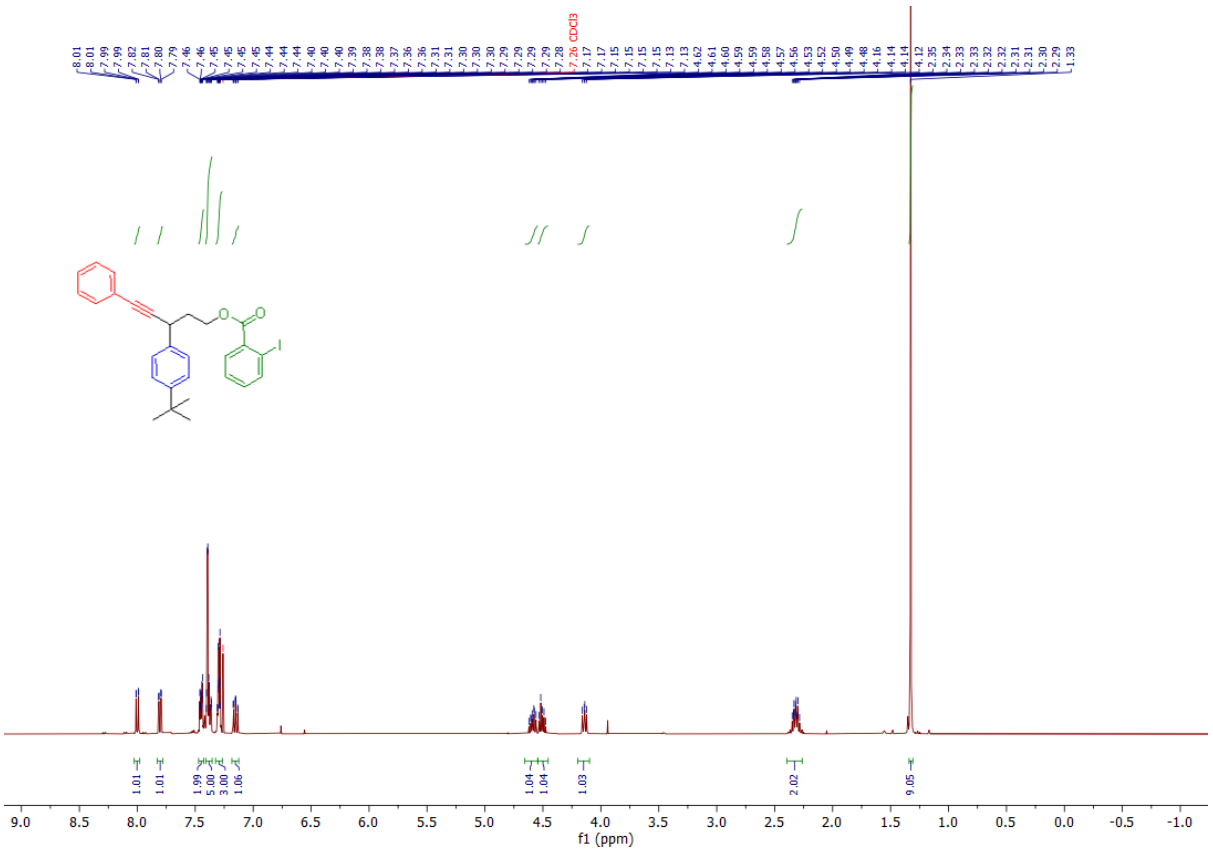
^{1}H NMR (400 MHz, $CDCl_3$) **(3c)**



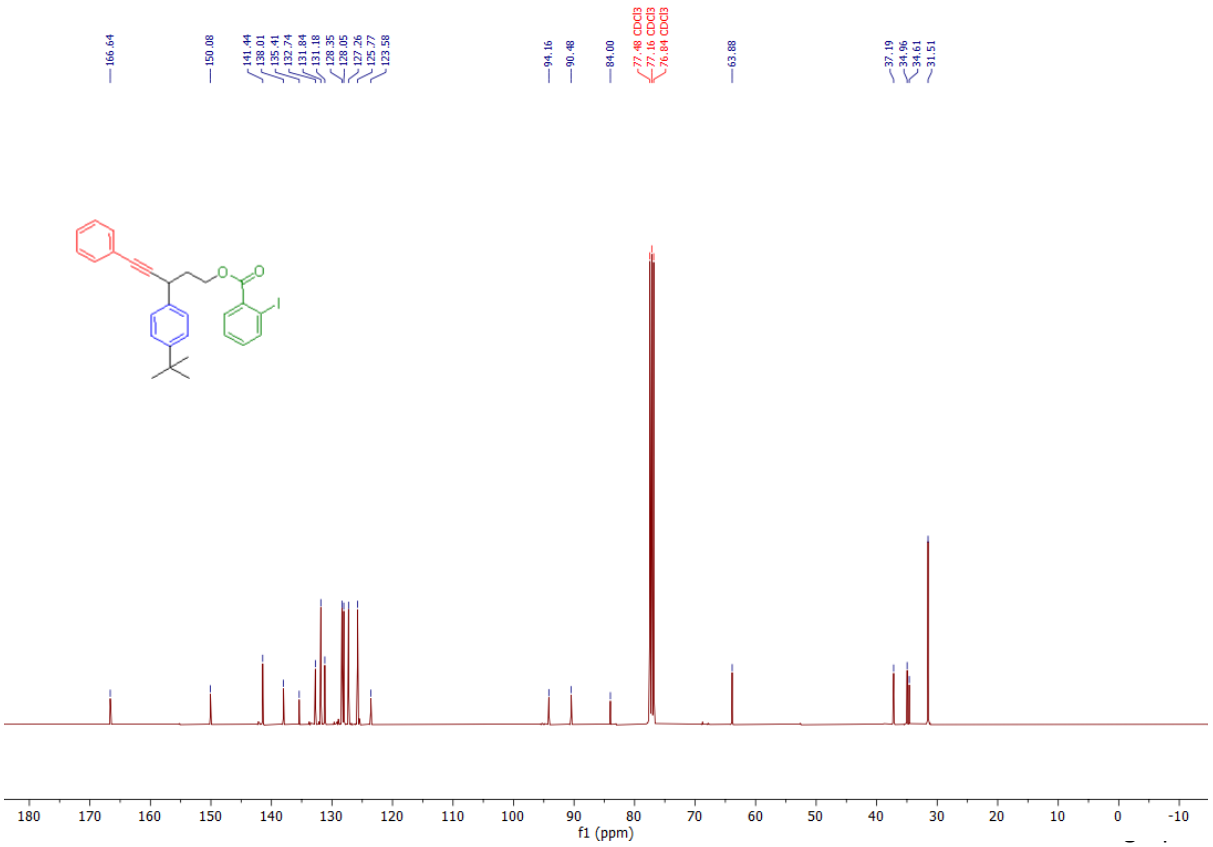
^{13}C NMR (101 MHz, $CDCl_3$) **(3c)**



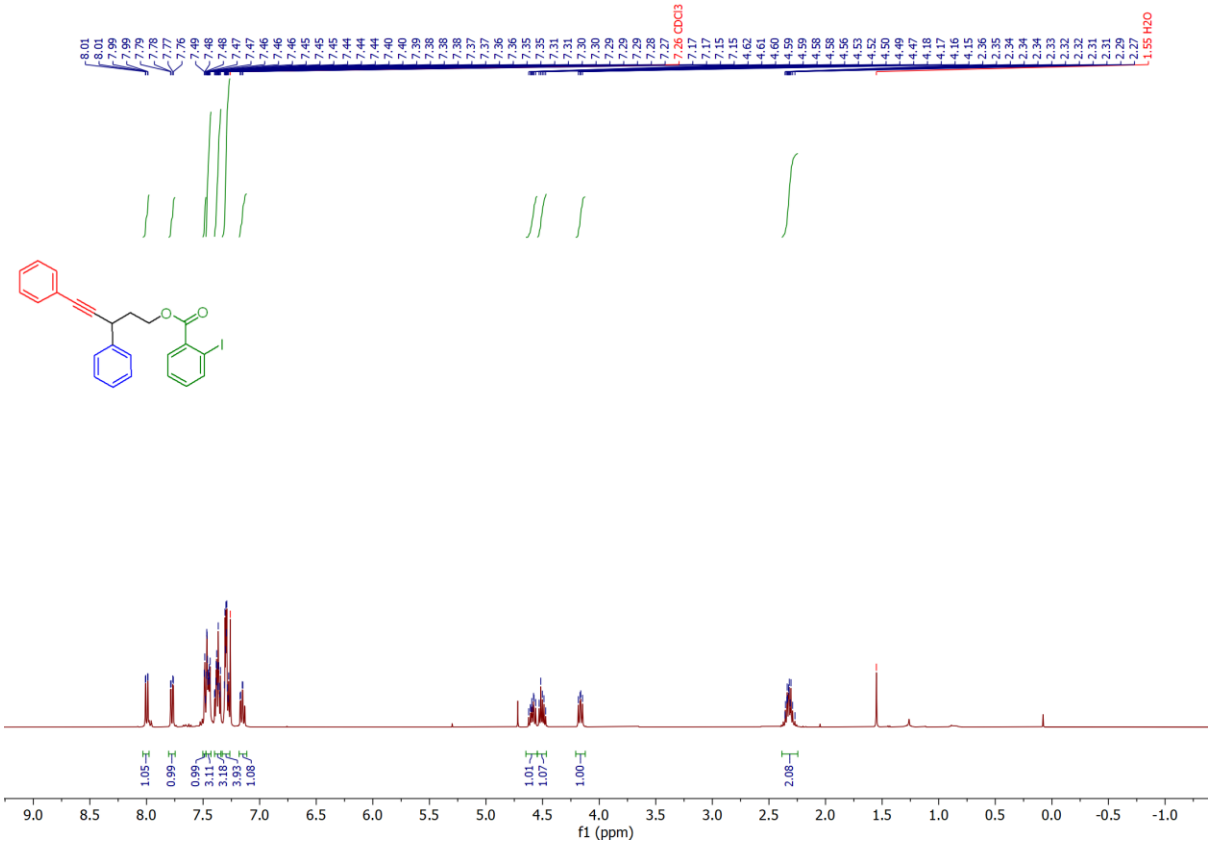
^{1}H NMR (400 MHz, $CDCl_3$) **(3d)**



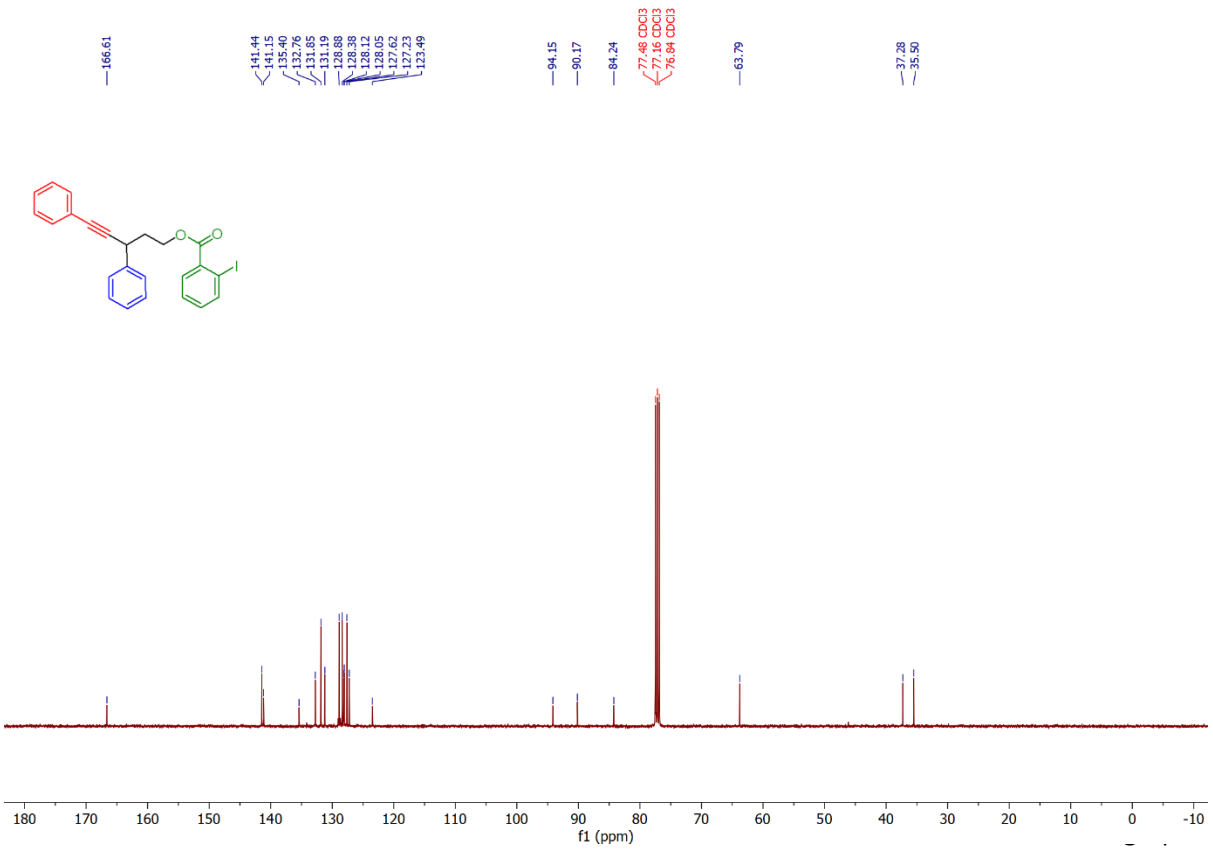
^{13}C NMR (101 MHz, $CDCl_3$) **(3d)**



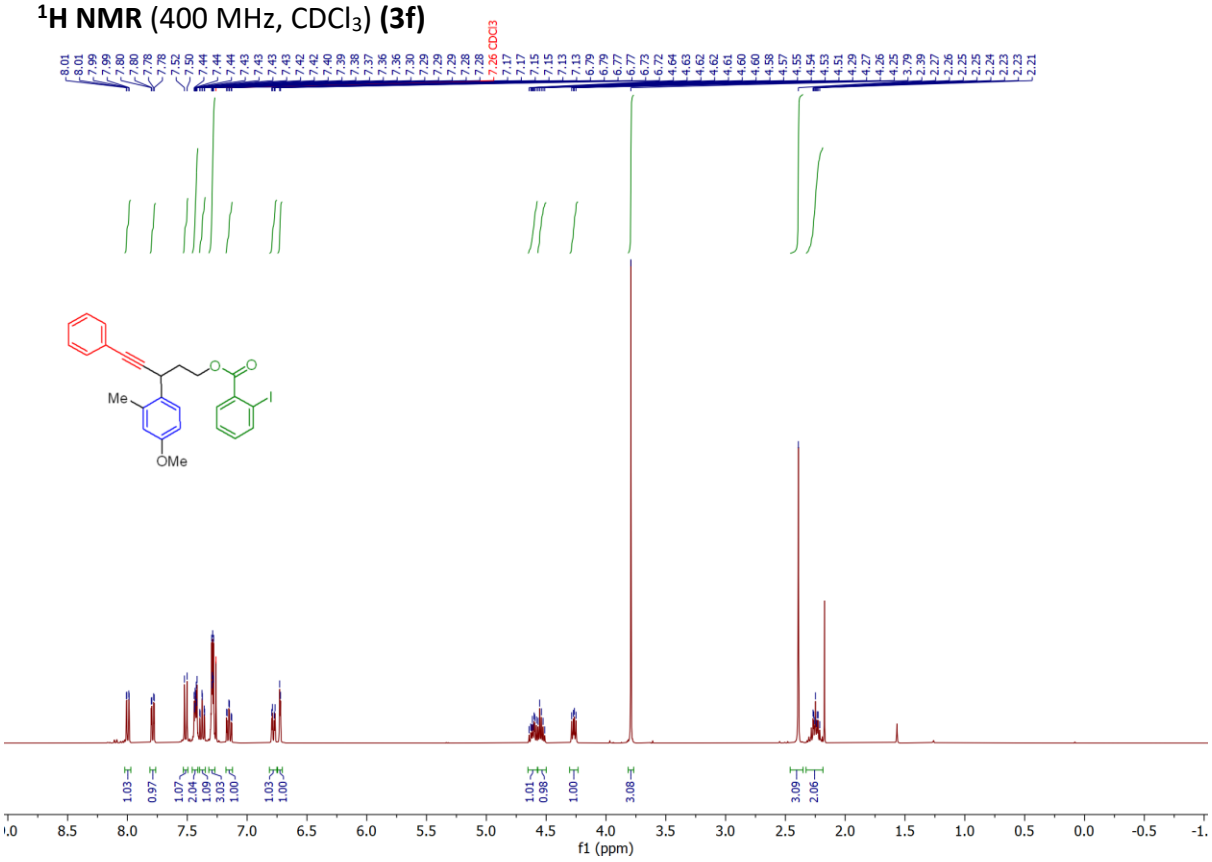
^{1}H NMR (400 MHz, $CDCl_3$) **(3e)**



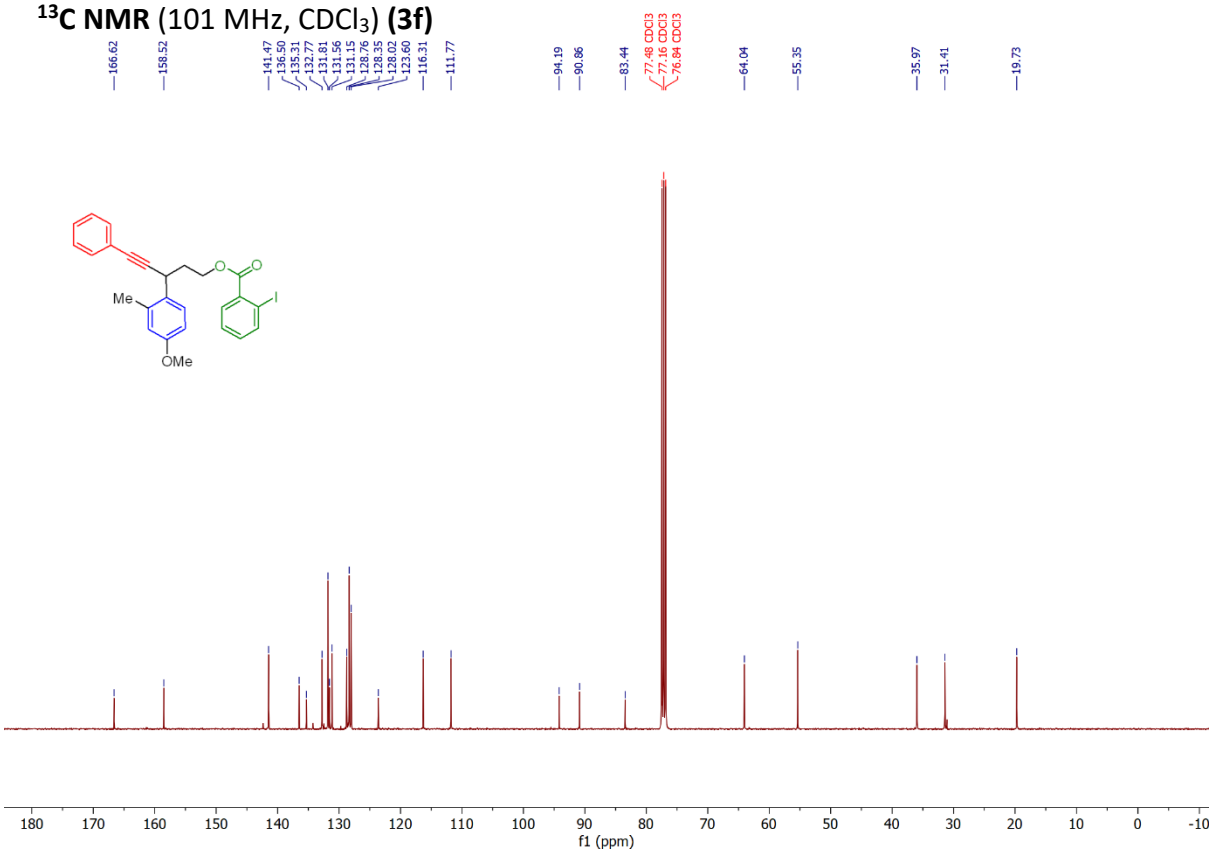
^{13}C NMR (101 MHz, $CDCl_3$): **(3e)**



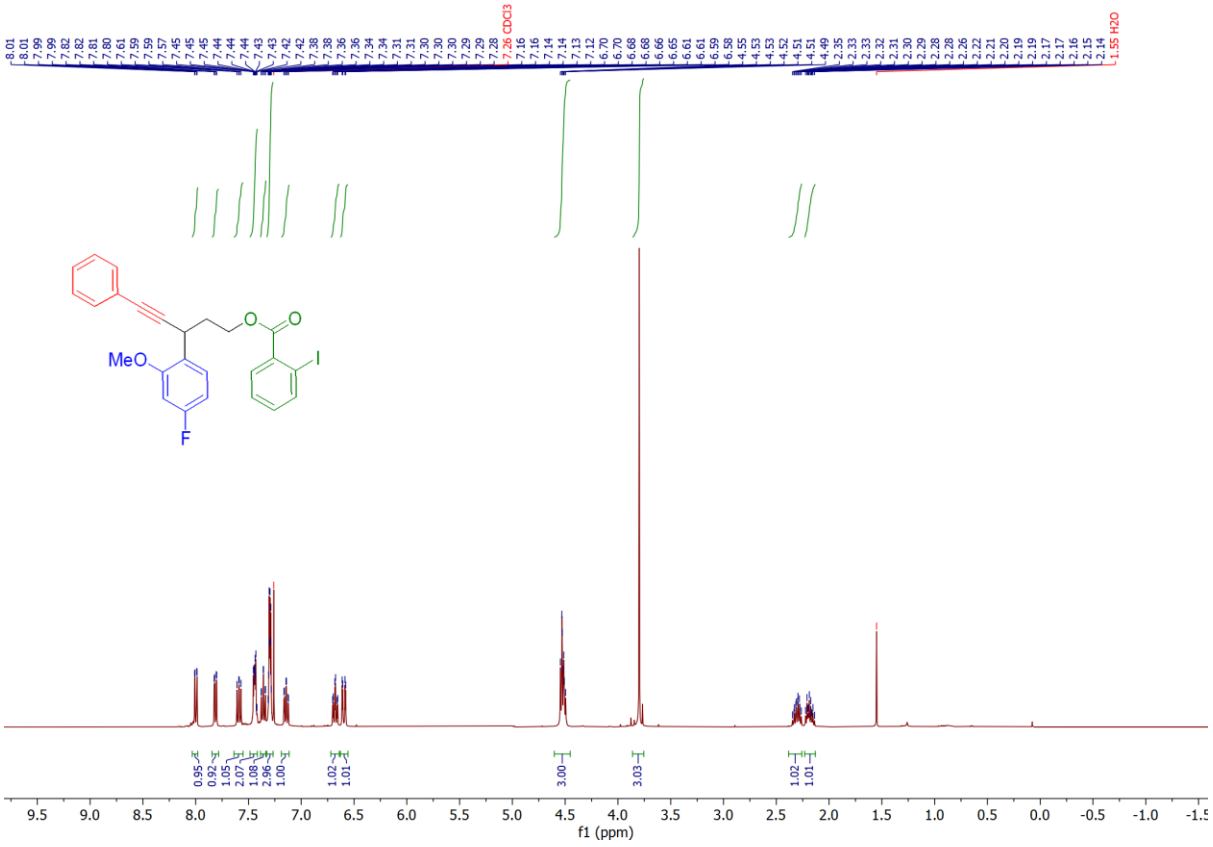
^{1}H NMR (400 MHz, $CDCl_3$) **(3f)**



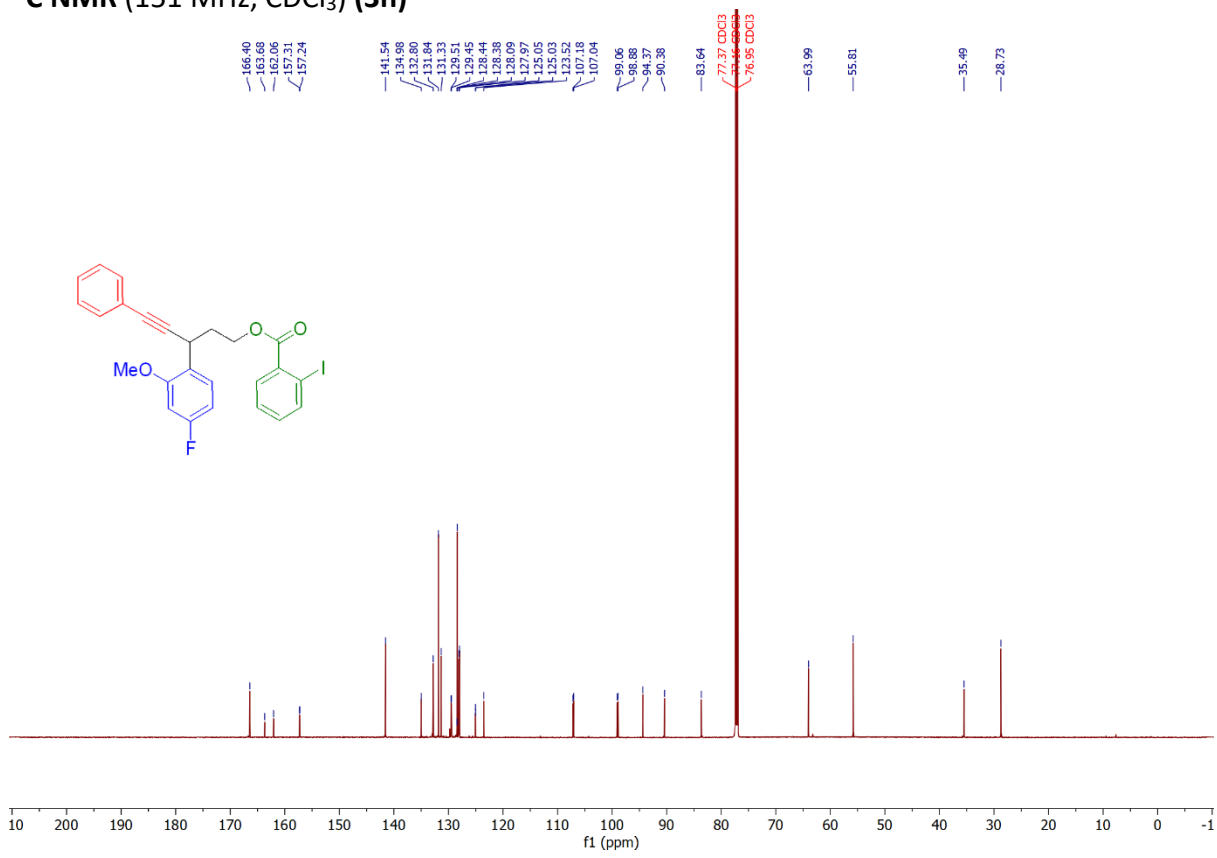
^{13}C NMR (101 MHz, $CDCl_3$) **(3f)**



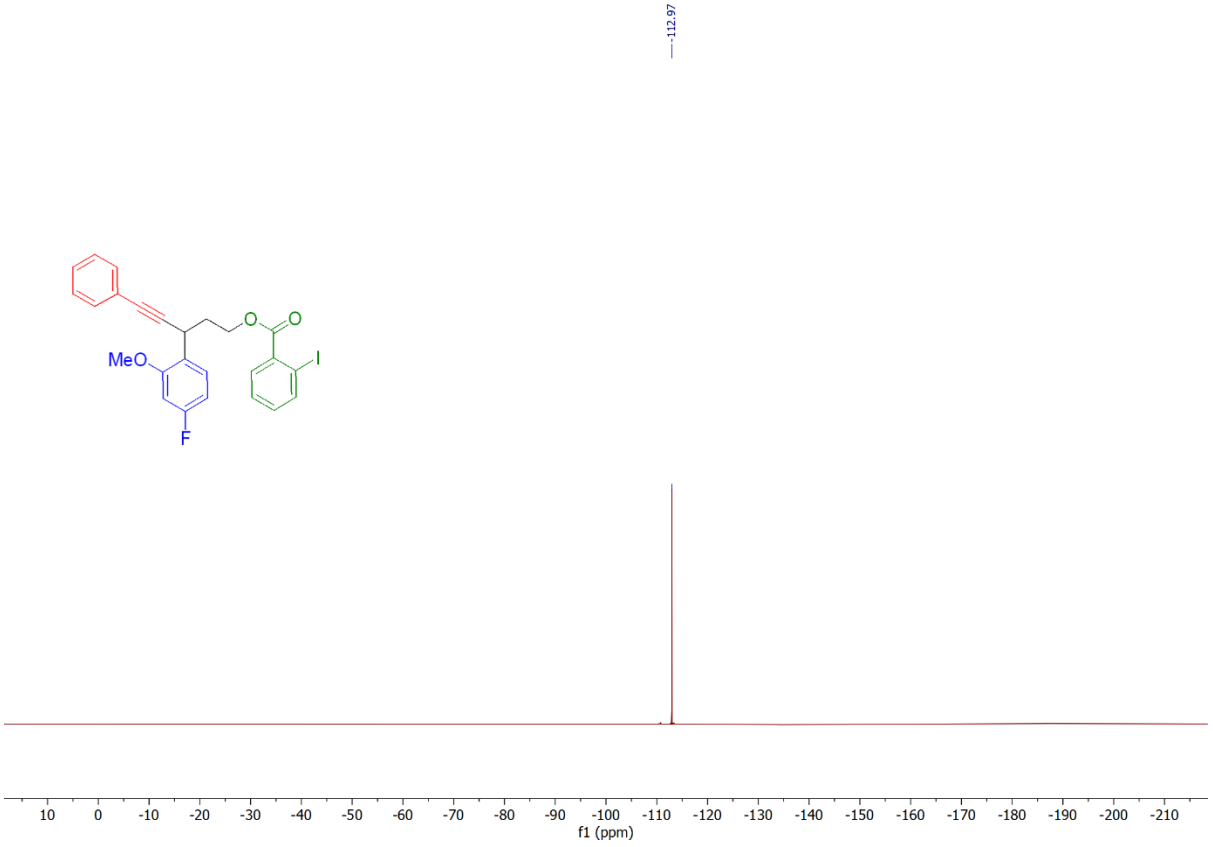
^{1}H NMR (400 MHz, $CDCl_3$) **(3h)**



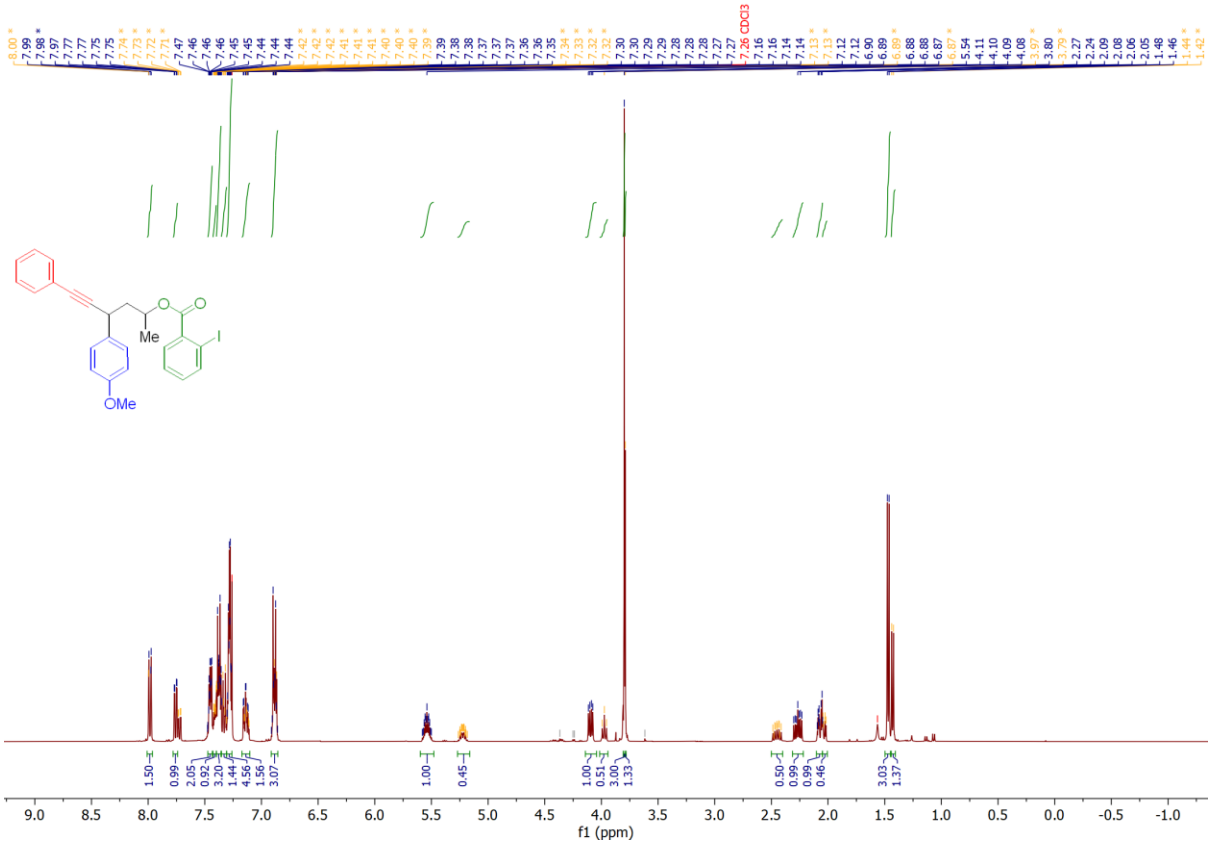
^{13}C NMR (151 MHz, $CDCl_3$) **(3h)**



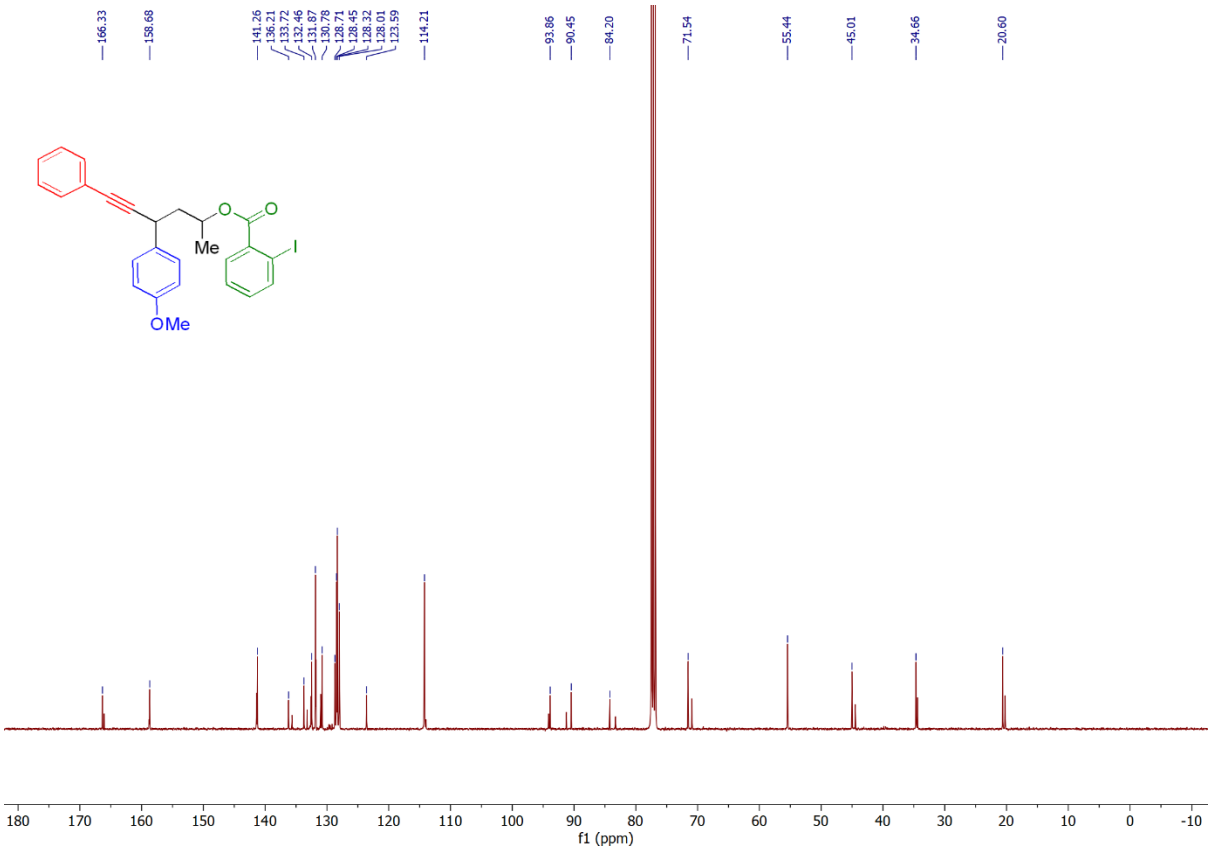
^{19}F NMR (376 MHz, $CDCl_3$) **(3h)**



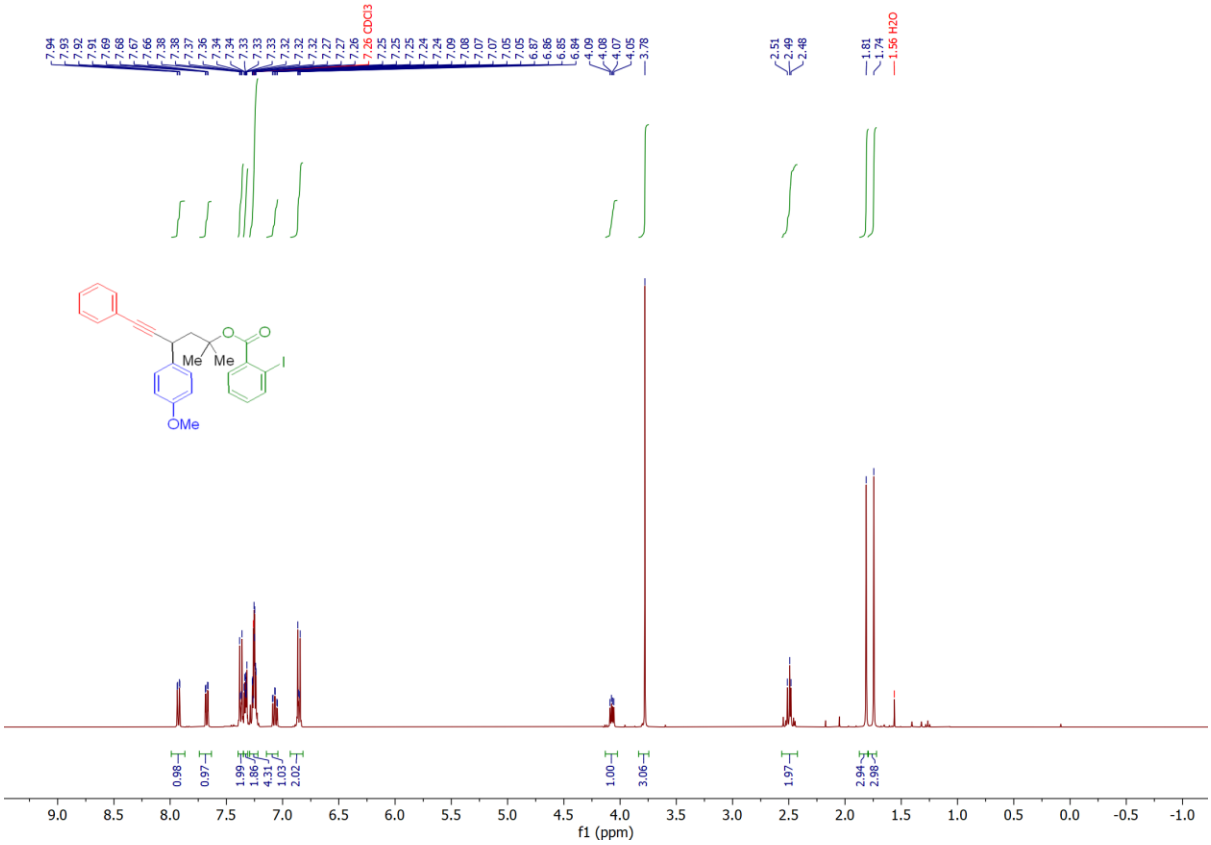
^{1}H NMR (400 MHz, $CDCl_3$) (3i) Blue : major diastereomer. Organe : minor diastereomer



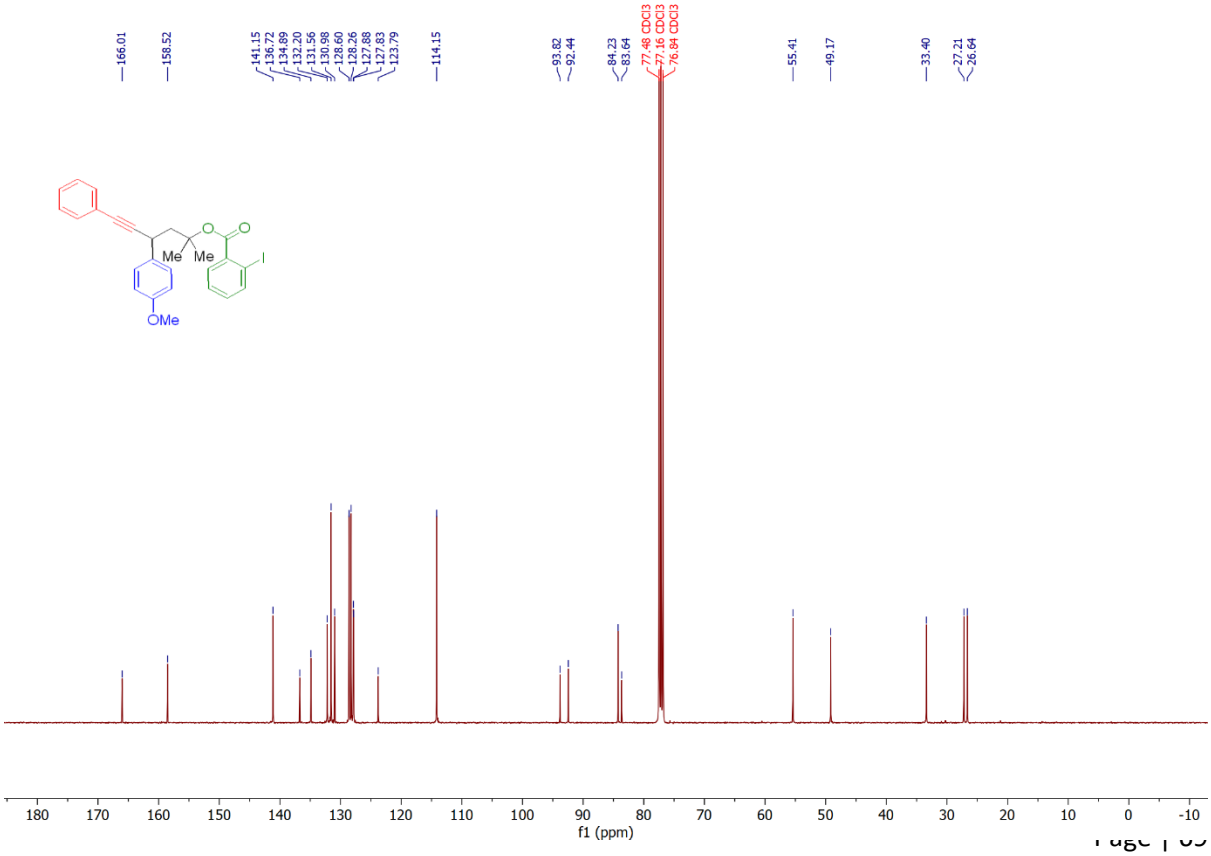
^{13}C NMR (101 MHz, $CDCl_3$) **(3i)**



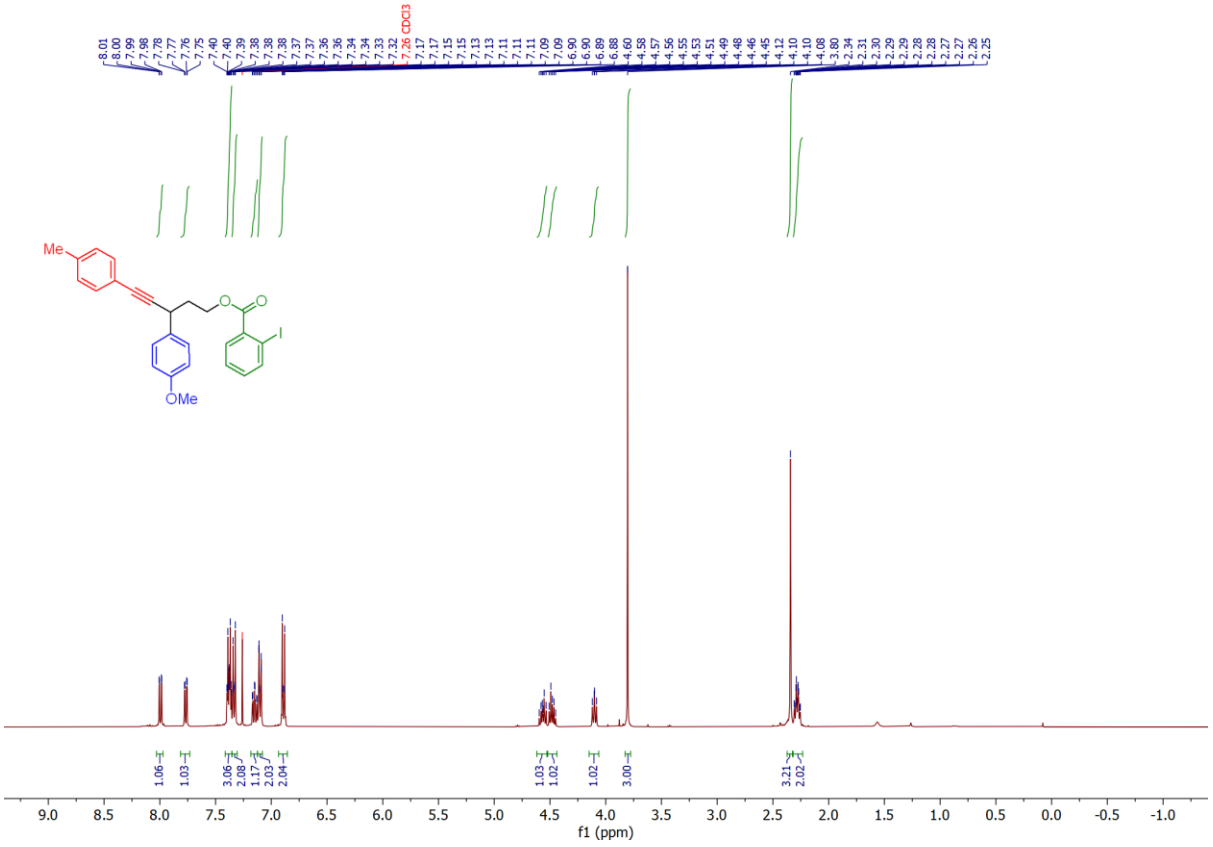
^{1}H NMR (400 MHz, $CDCl_3$) (3j)



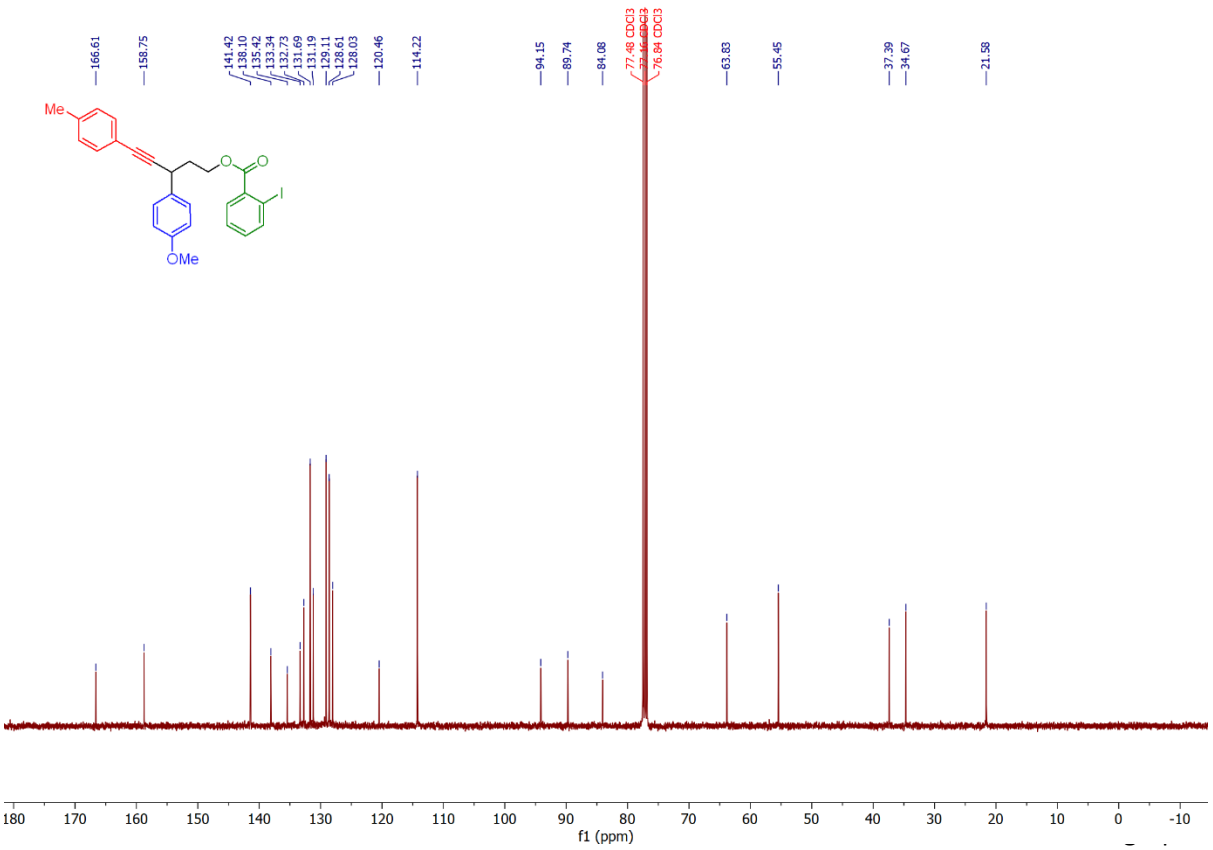
^{13}C NMR ^{13}C NMR (101 MHz, $CDCl_3$) **(3j)**



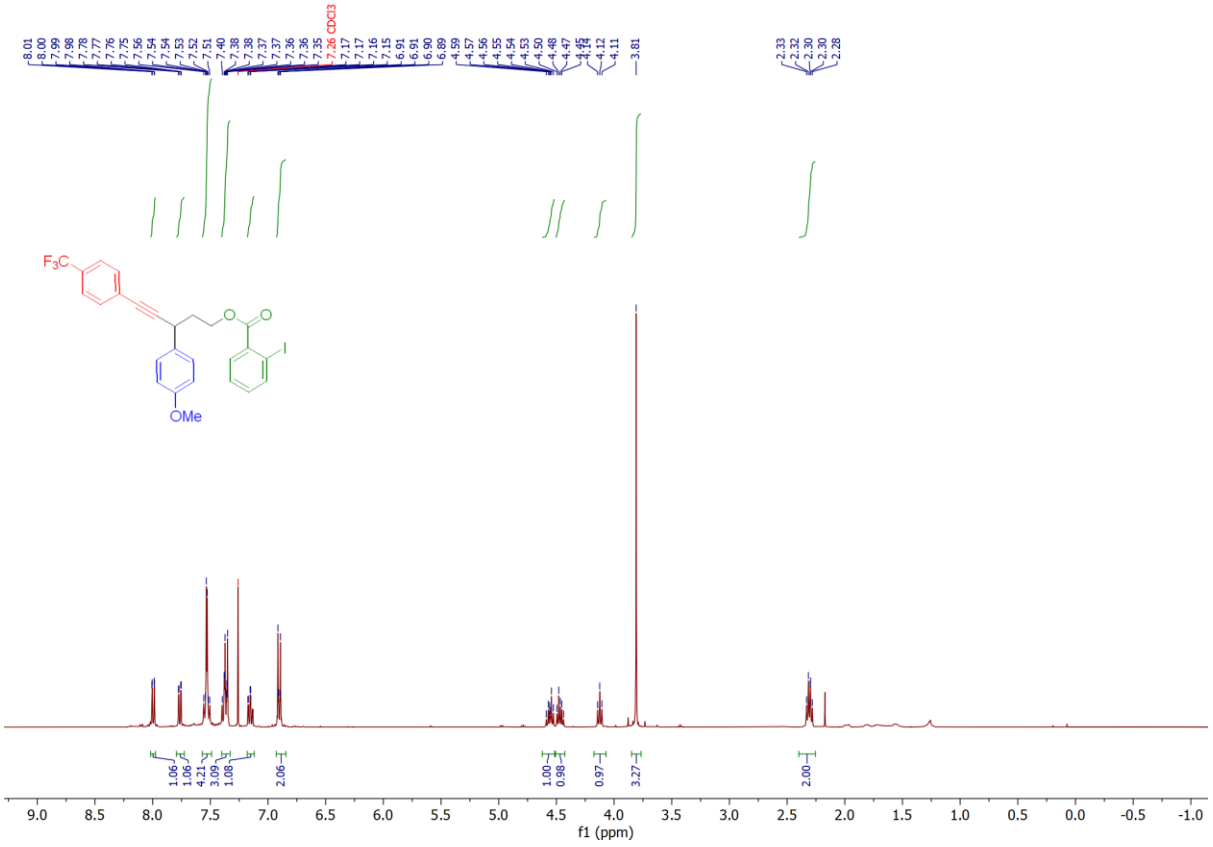
^{1}H NMR (400 MHz, $CDCl_3$) **(3k)**



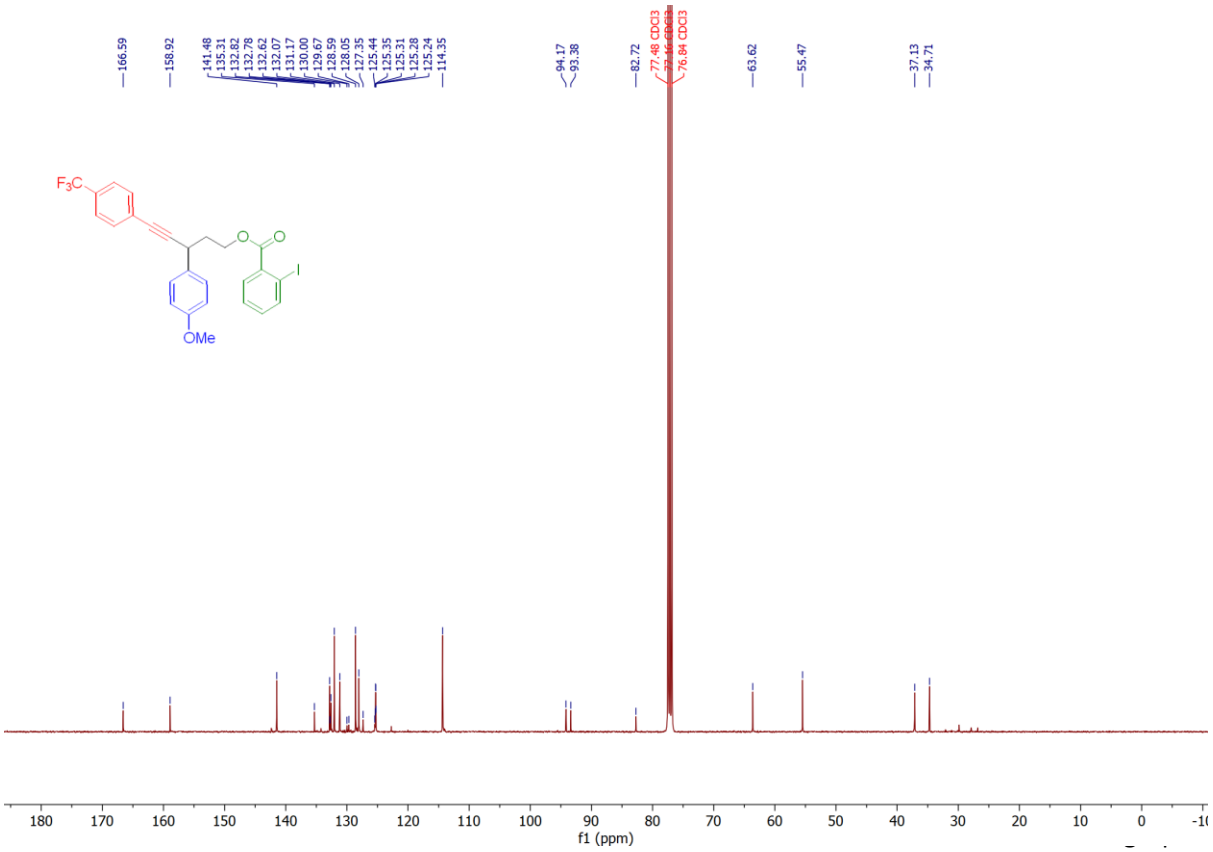
^{13}C NMR (101 MHz, $CDCl_3$) **(3k)**



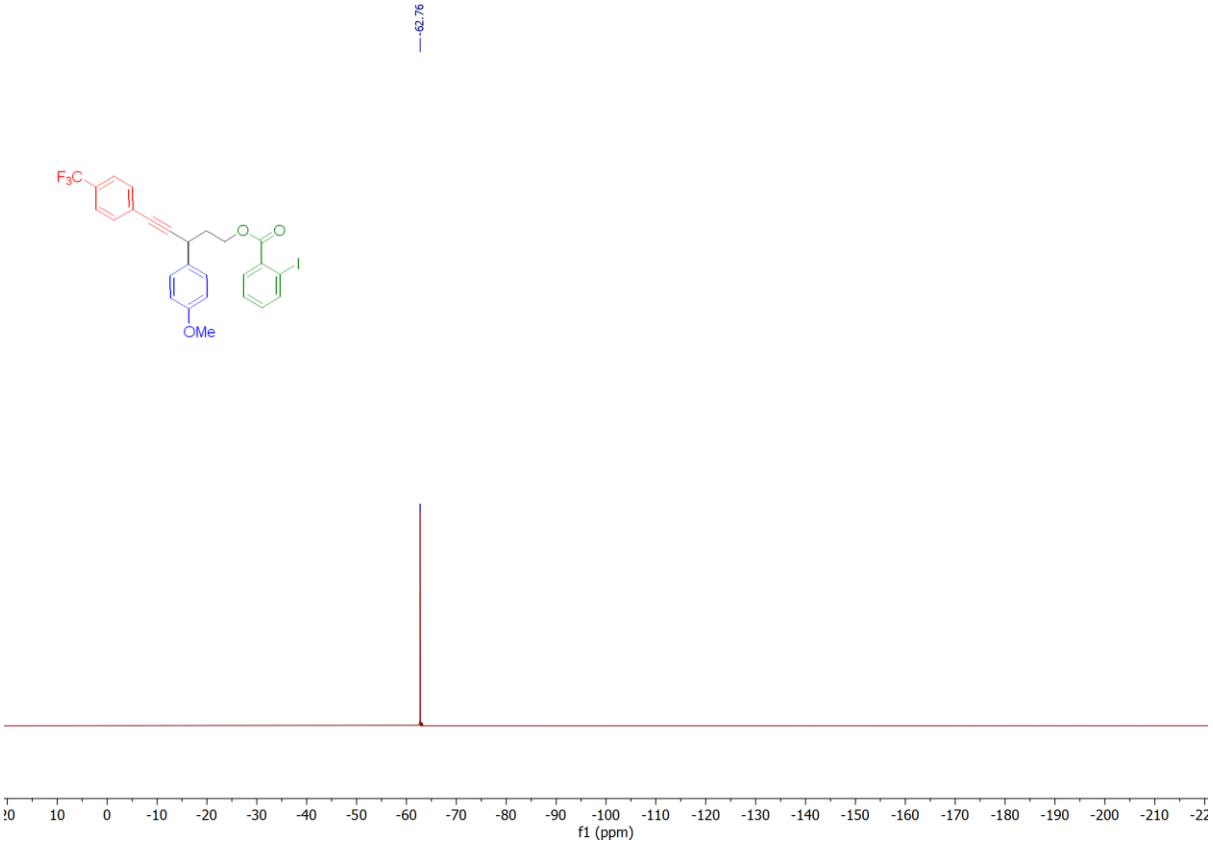
^{1}H NMR (400 MHz, $CDCl_3$) (3l)



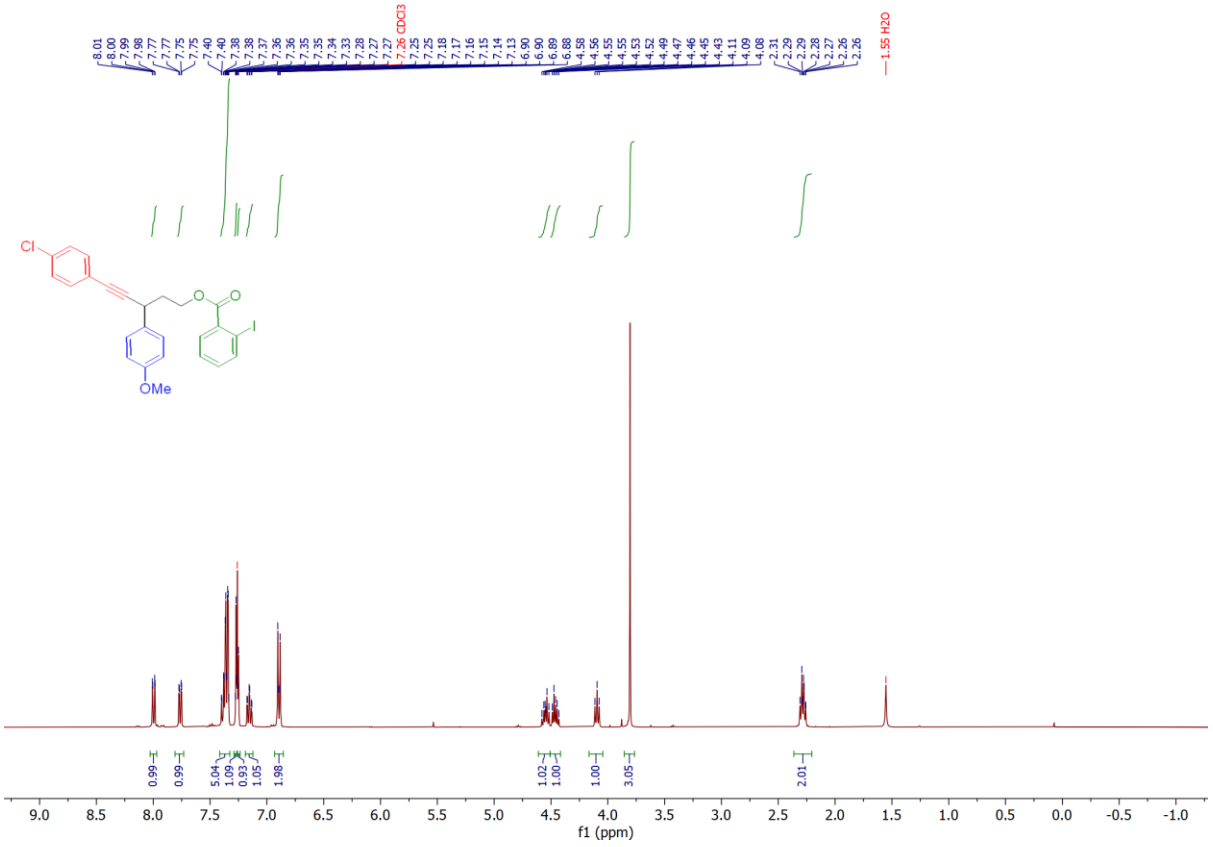
^{13}C NMR (101 MHz, $CDCl_3$) (3l)



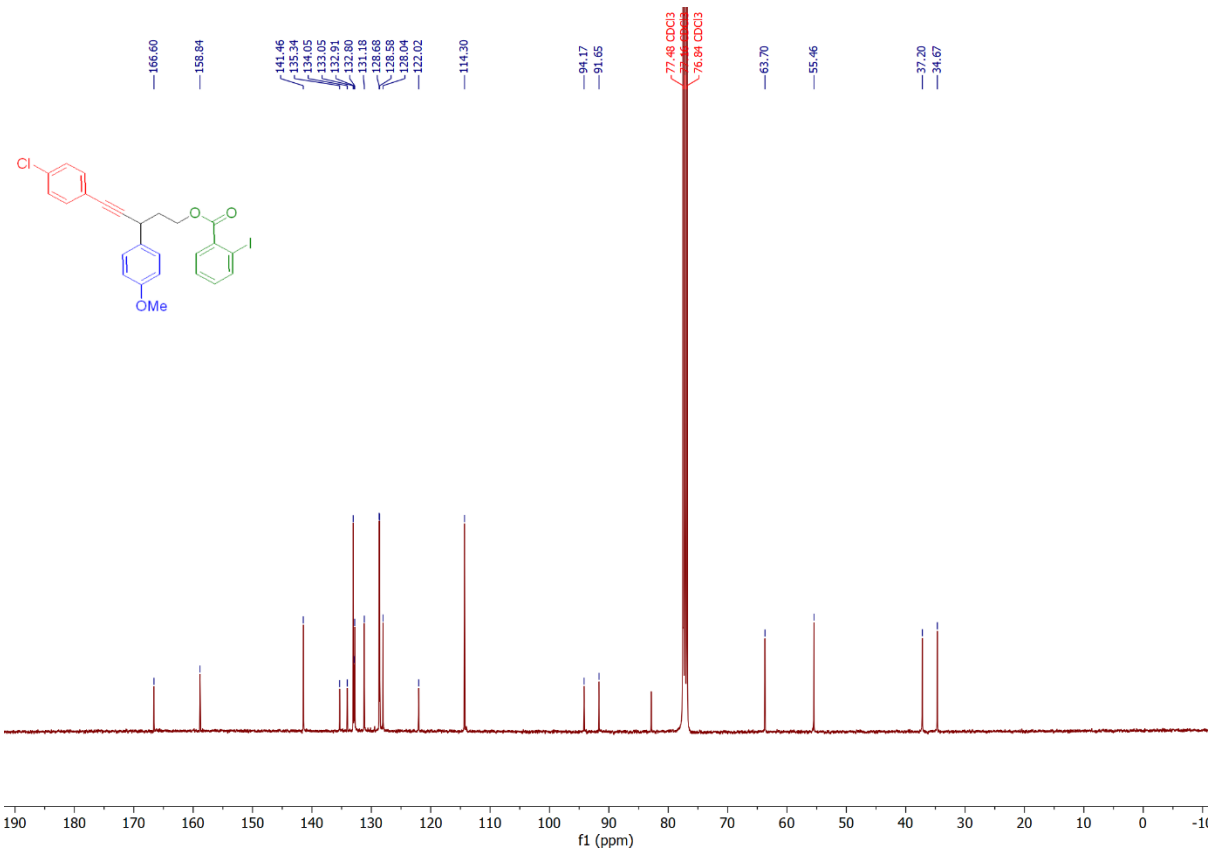
^{19}F NMR (377 MHz, $CDCl_3$) (3l)



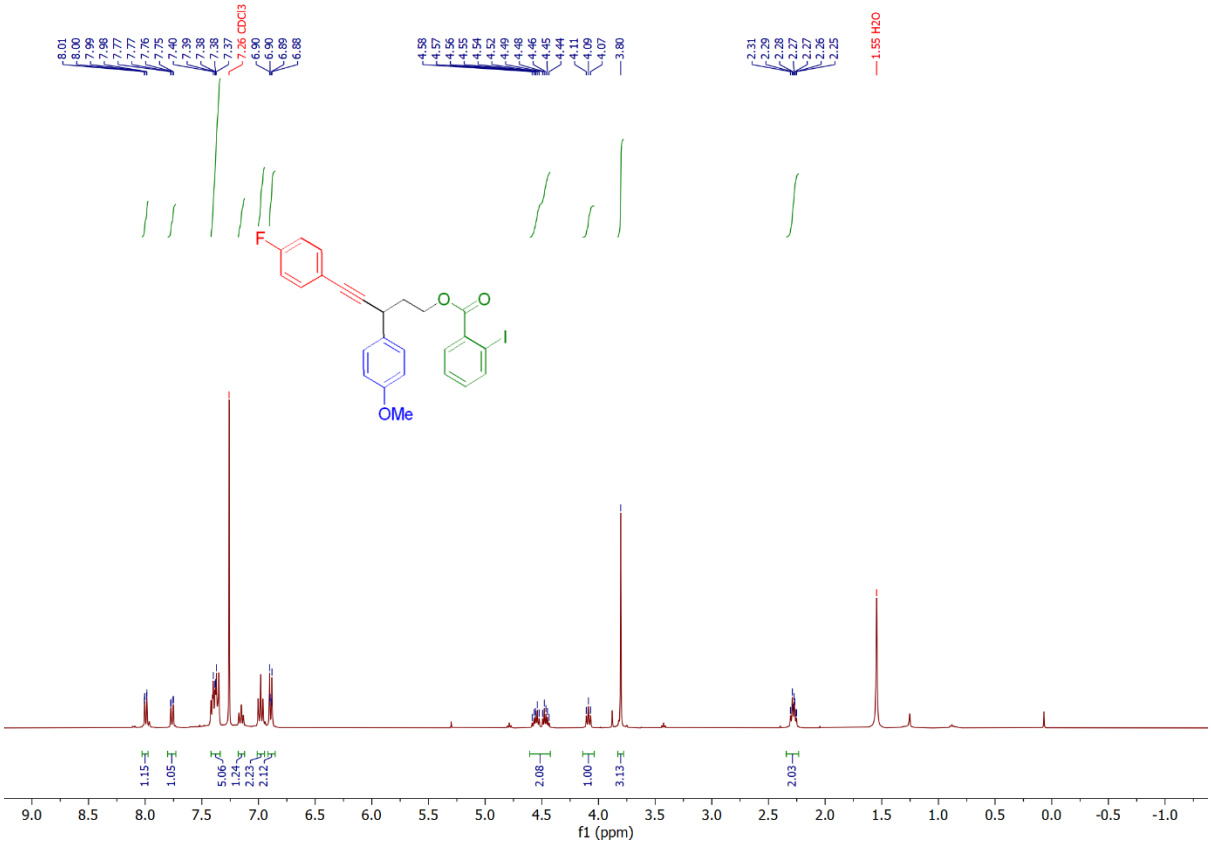
^{1}H NMR (400 MHz, $CDCl_3$) (3m)



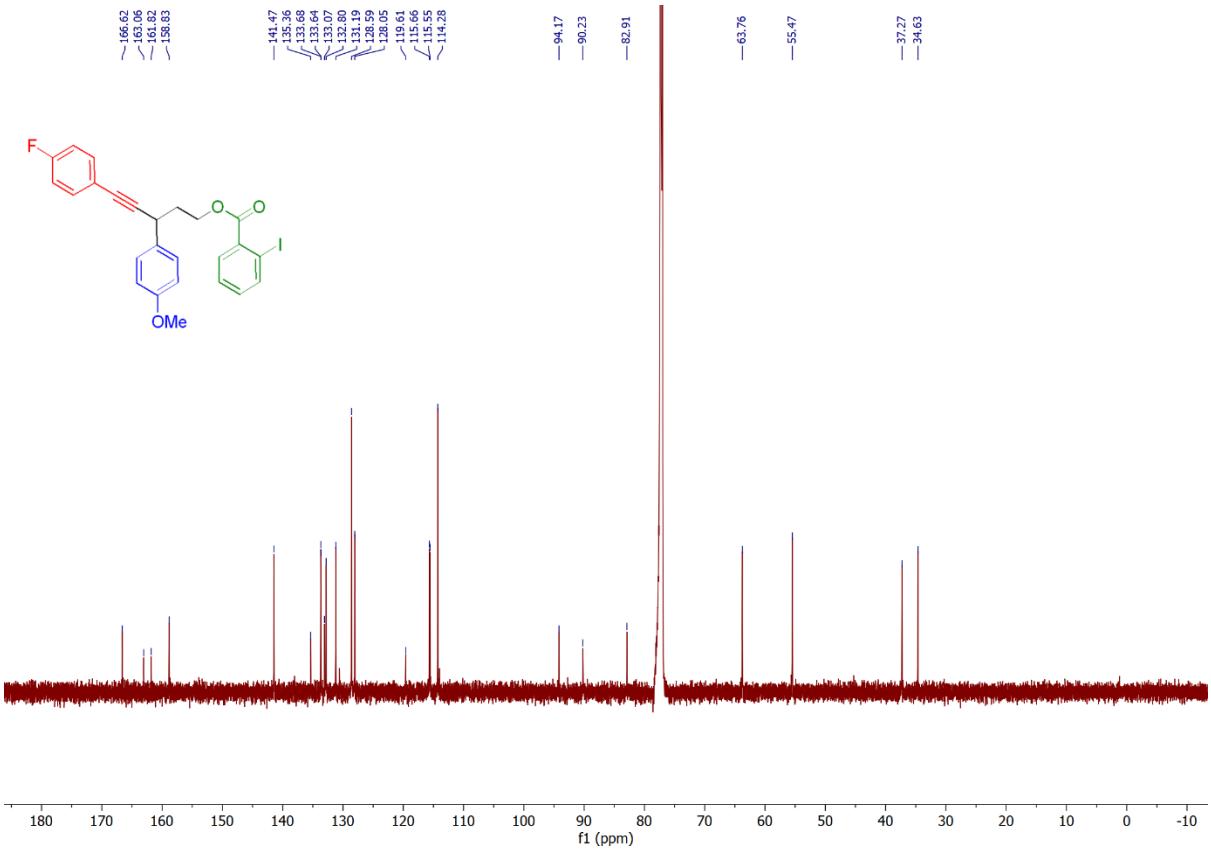
^{13}C NMR (101 MHz, $CDCl_3$) (3m)



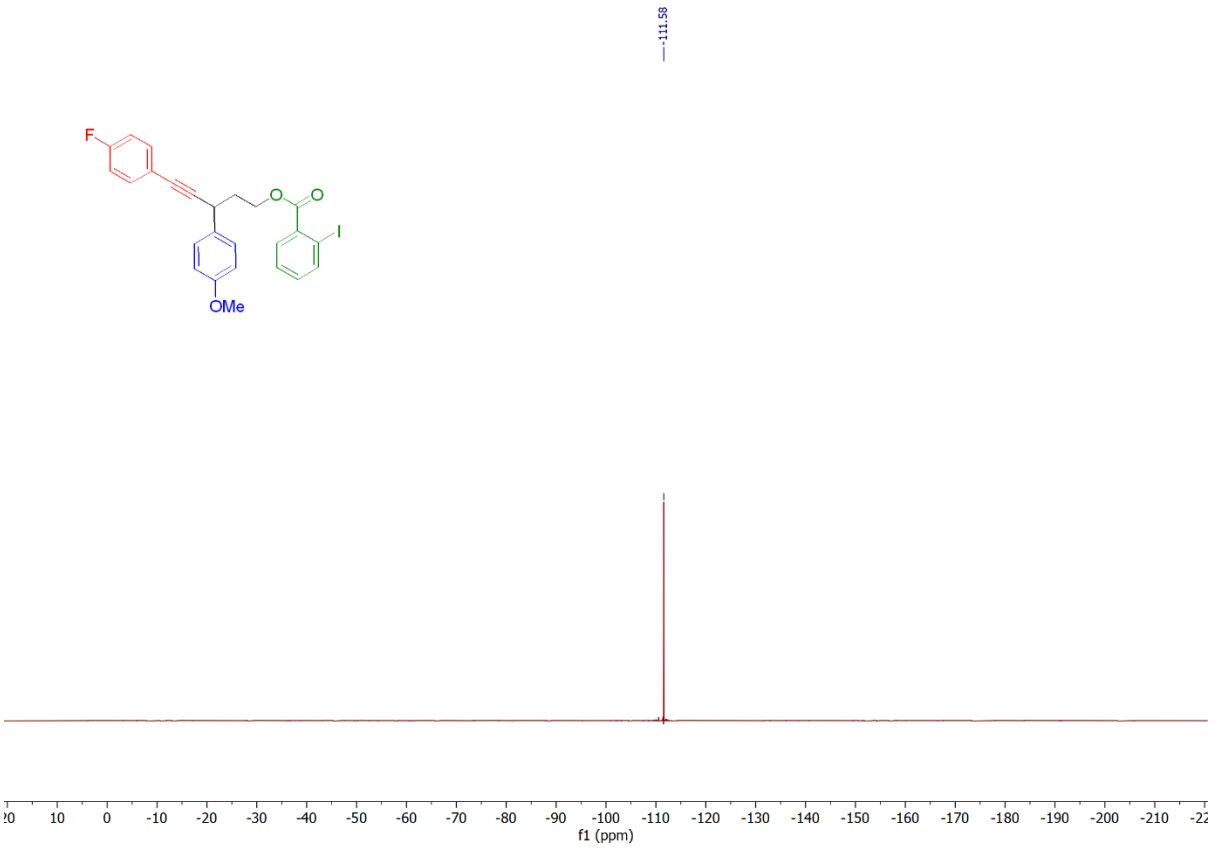
^{1}H NMR (400 MHz, $CDCl_3$) (3n)



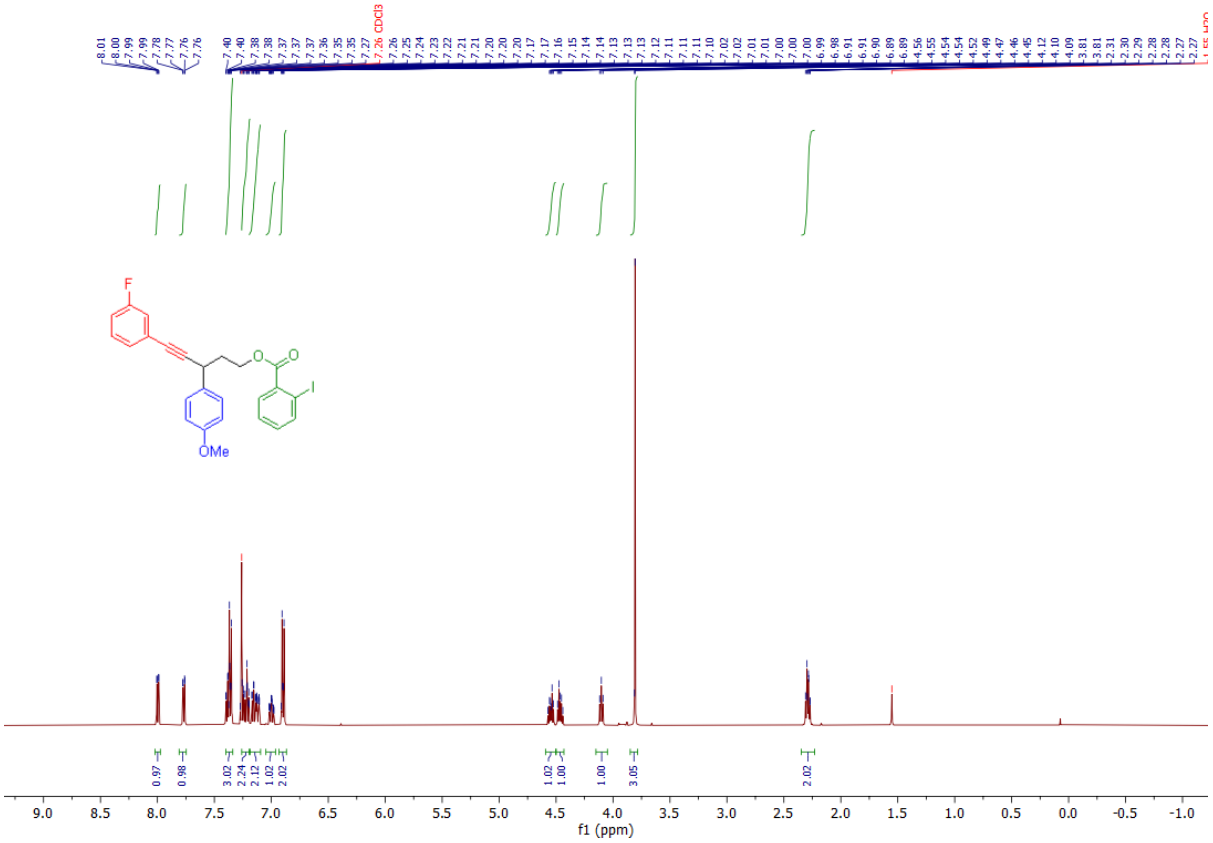
^{13}C NMR (201 MHz, $CDCl_3$) (3n)



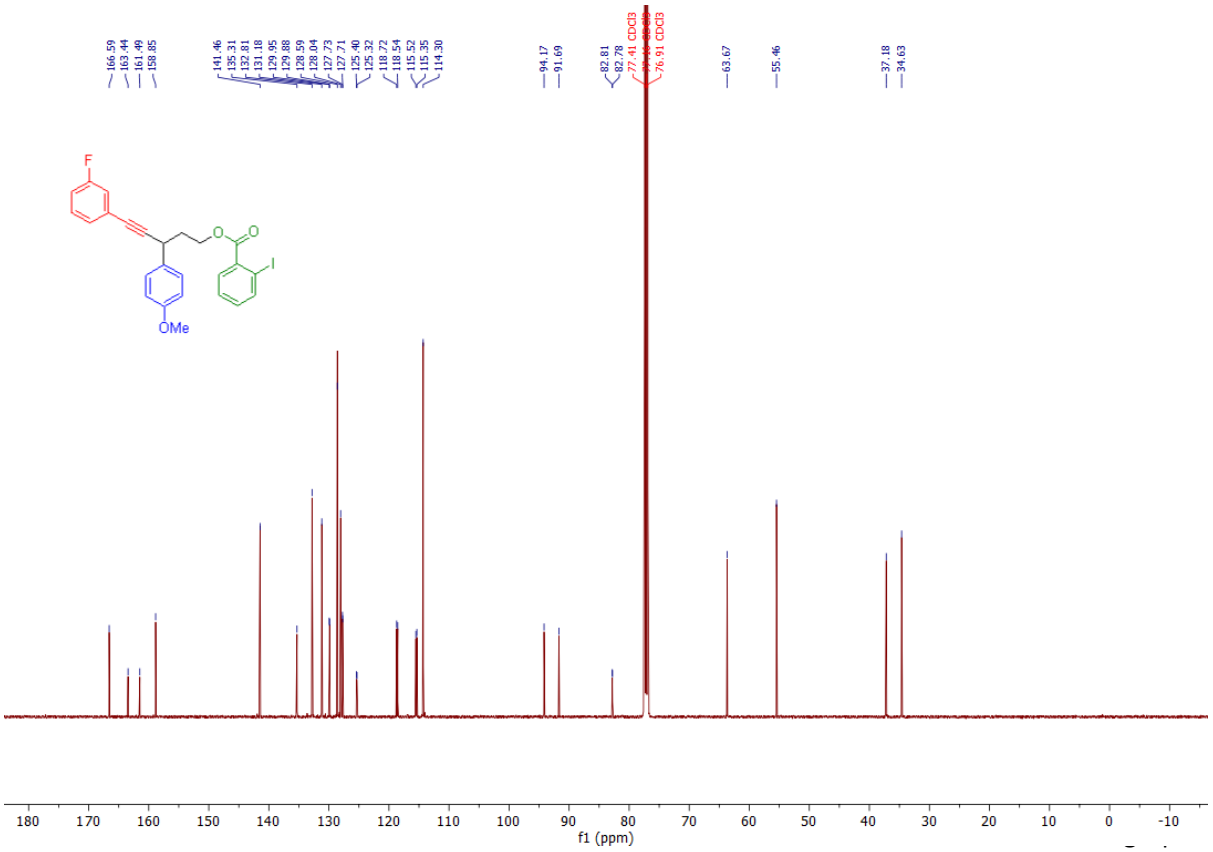
^{19}F NMR (377 MHz, $CDCl_3$) (3n)



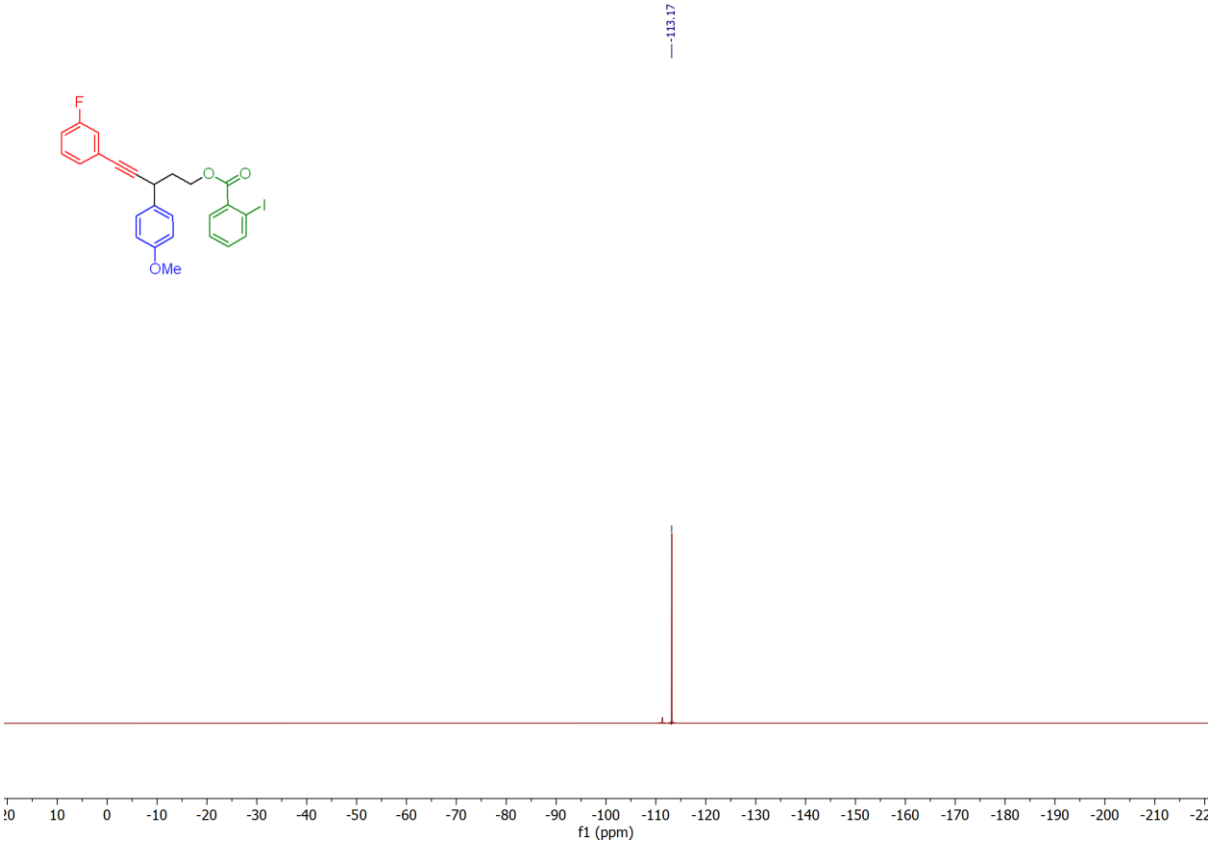
^{1}H NMR (400 MHz, $CDCl_3$) (3o)



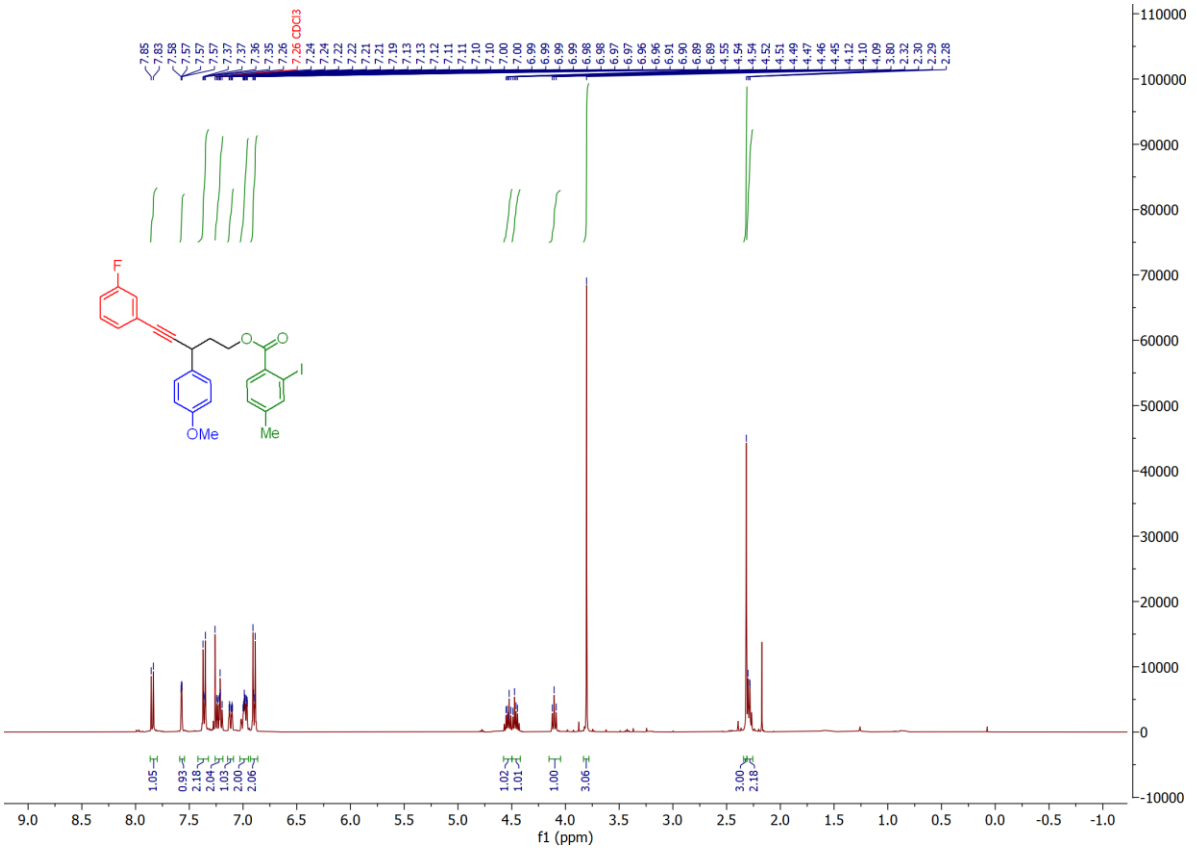
^{13}C NMR (101 MHz, $CDCl_3$) (3o)



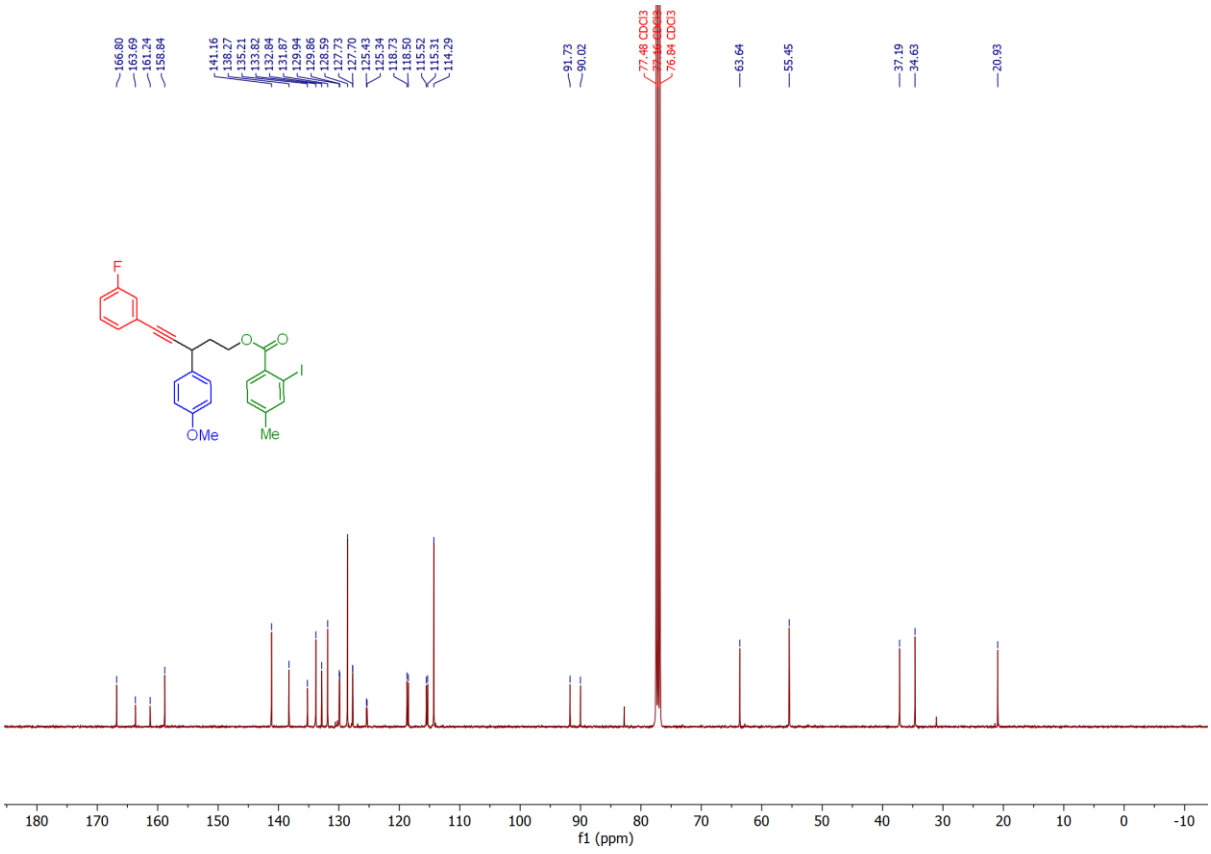
^{19}F NMR (377 MHz, $CDCl_3$) (3o)



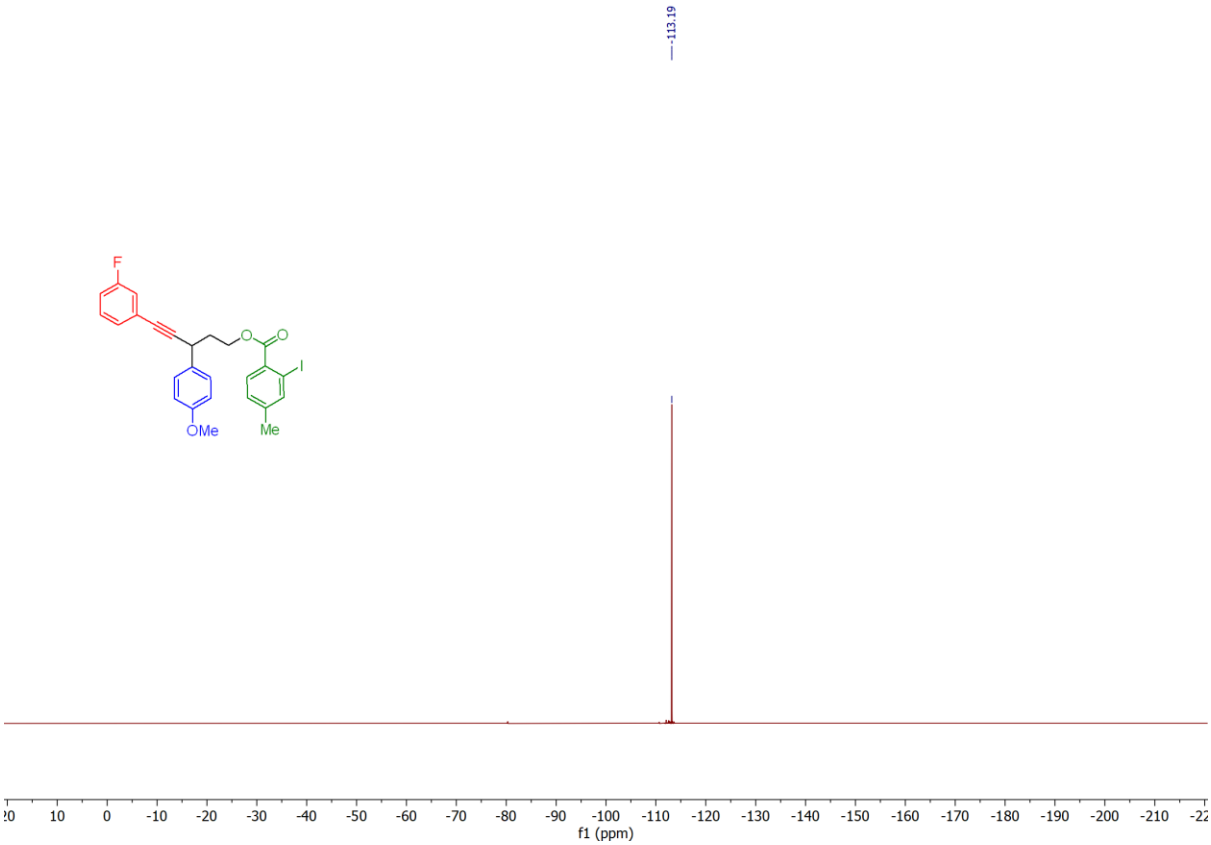
^{1}H NMR (400 MHz, $CDCl_3$) (3p)



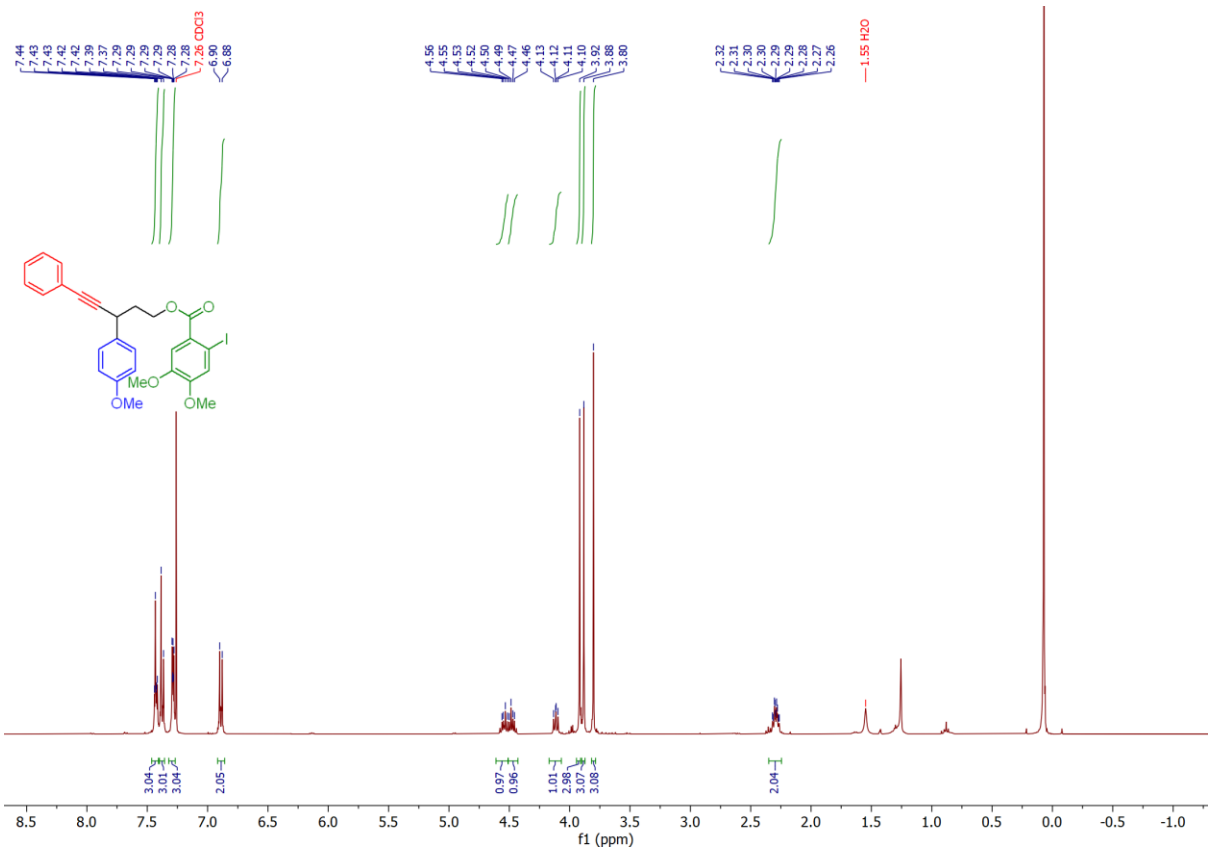
^{13}C NMR (101 MHz, $CDCl_3$) (3p)



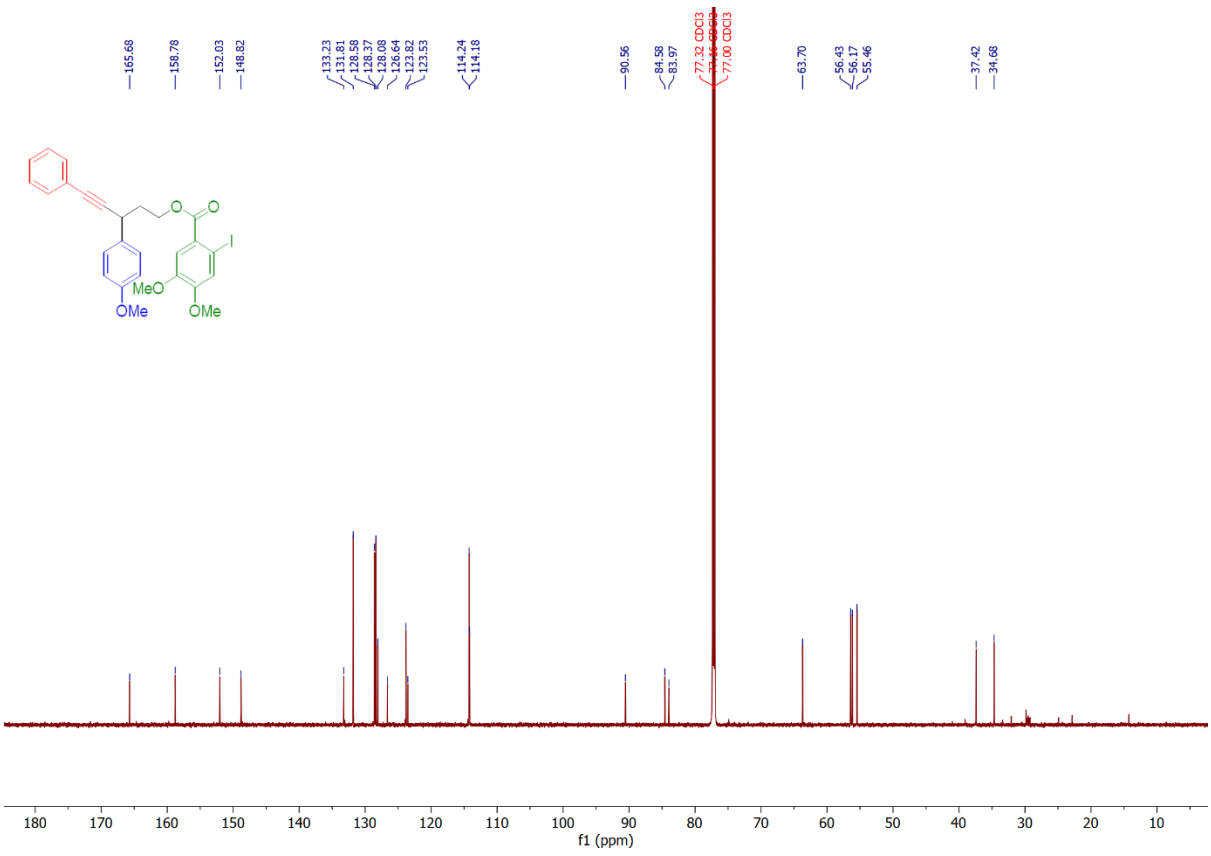
^{19}F NMR (377 MHz, $CDCl_3$) (3p)



^{1}H NMR (400 MHz, $CDCl_3$) (3q)

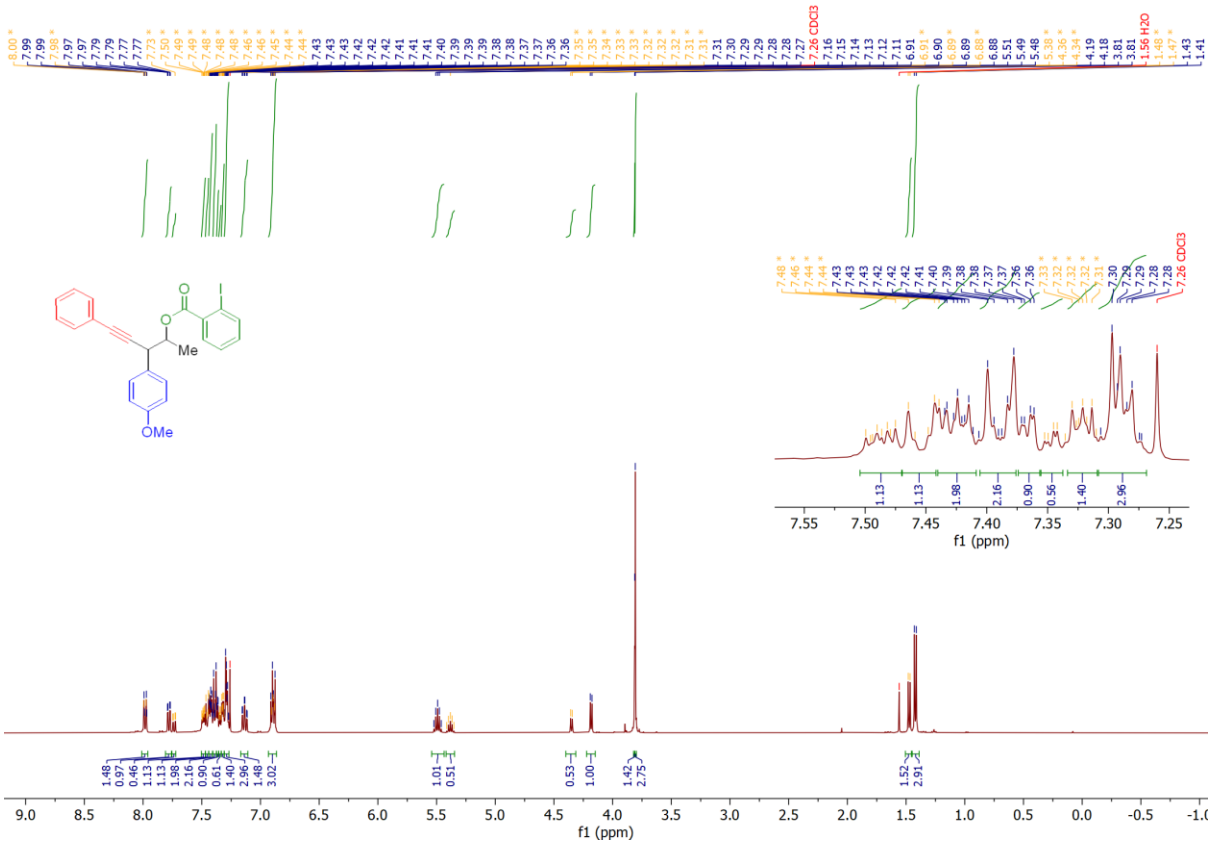


^{13}C NMR (201 MHz, $CDCl_3$) (3q)

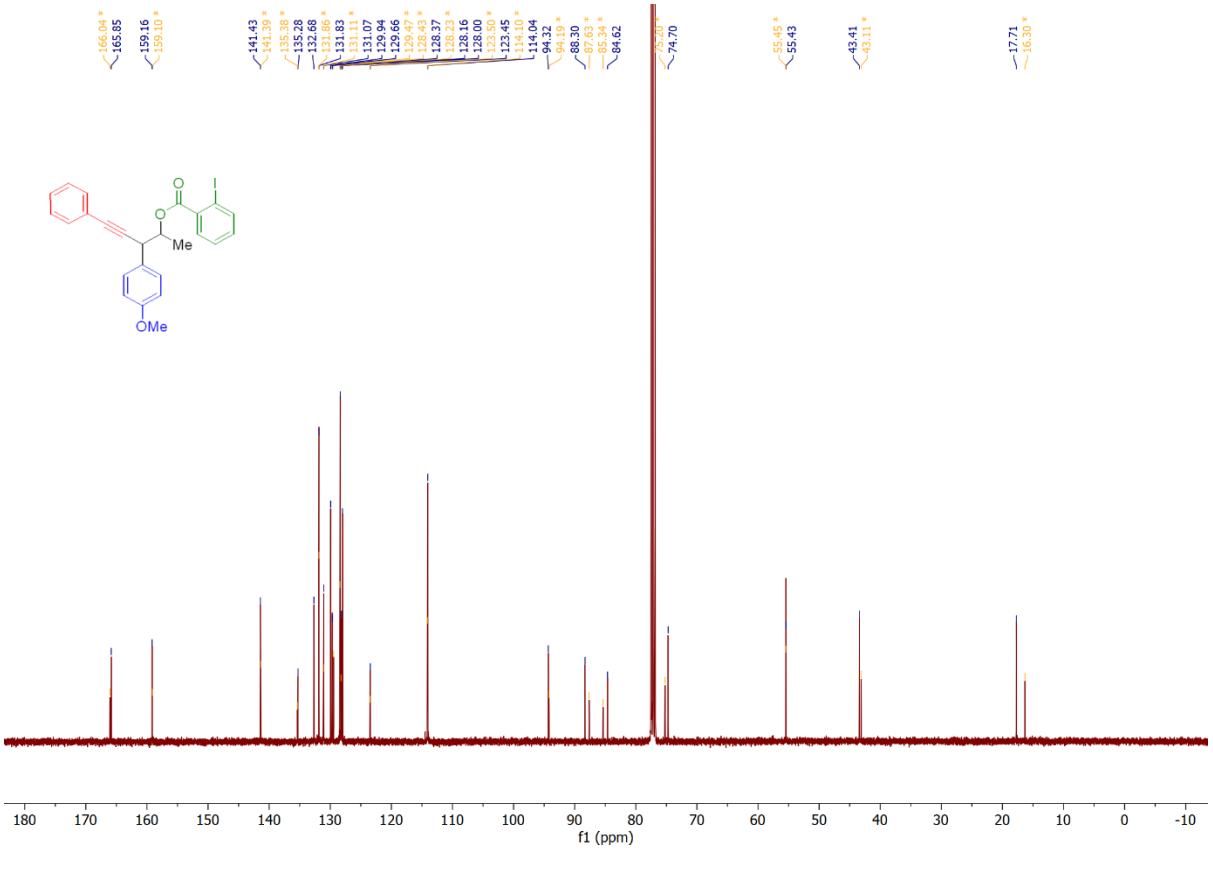


Blue: Major diastereomer, *Orange : Minor diastereomer

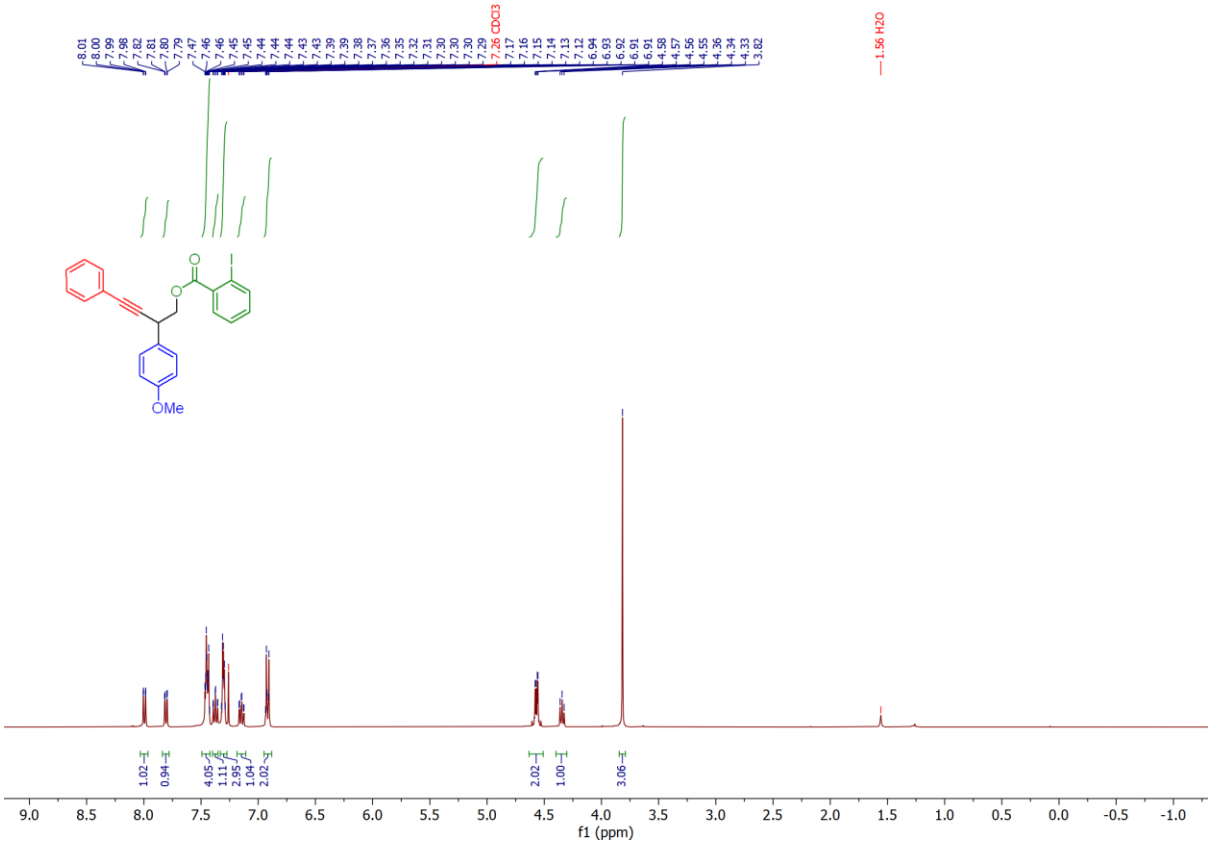
^{1}H NMR (400 MHz, $CDCl_3$ (8a)



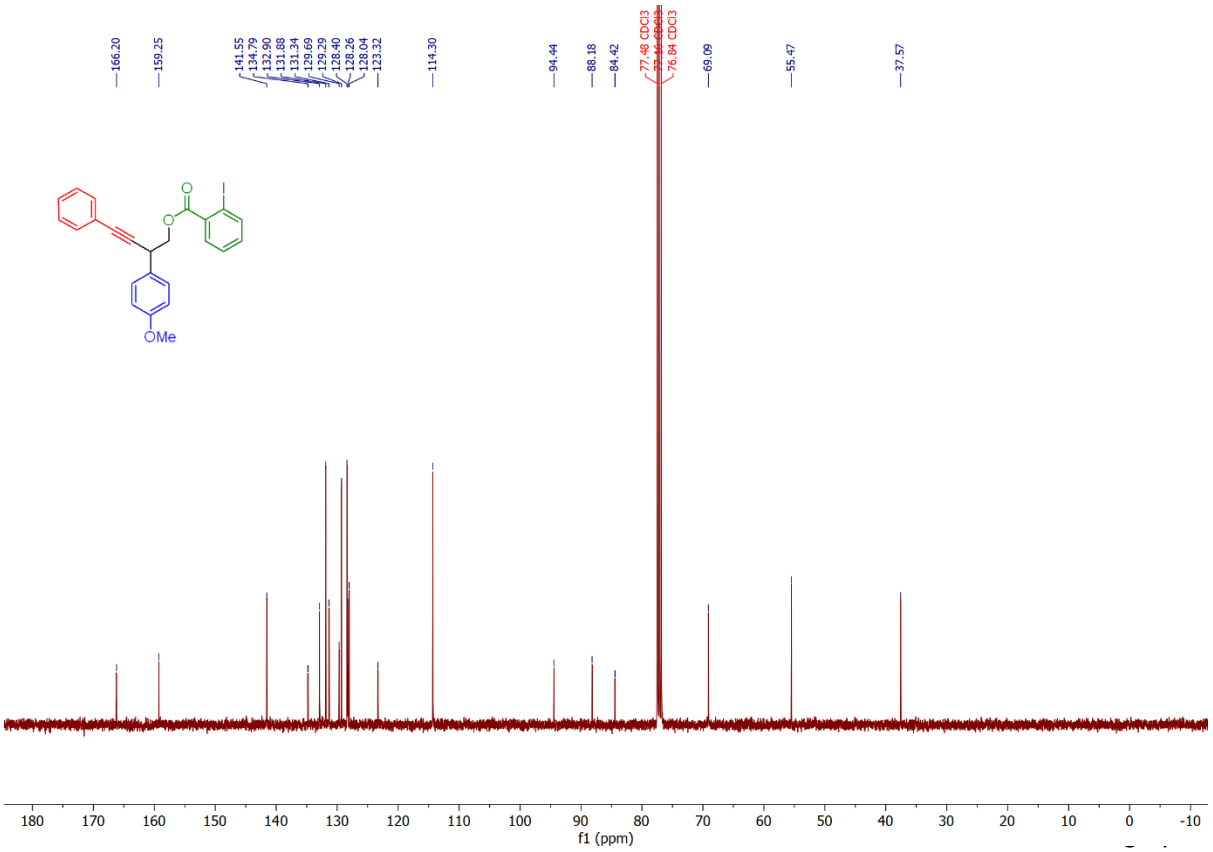
^{13}C NMR (101 MHz $CDCl_3$ (8a)



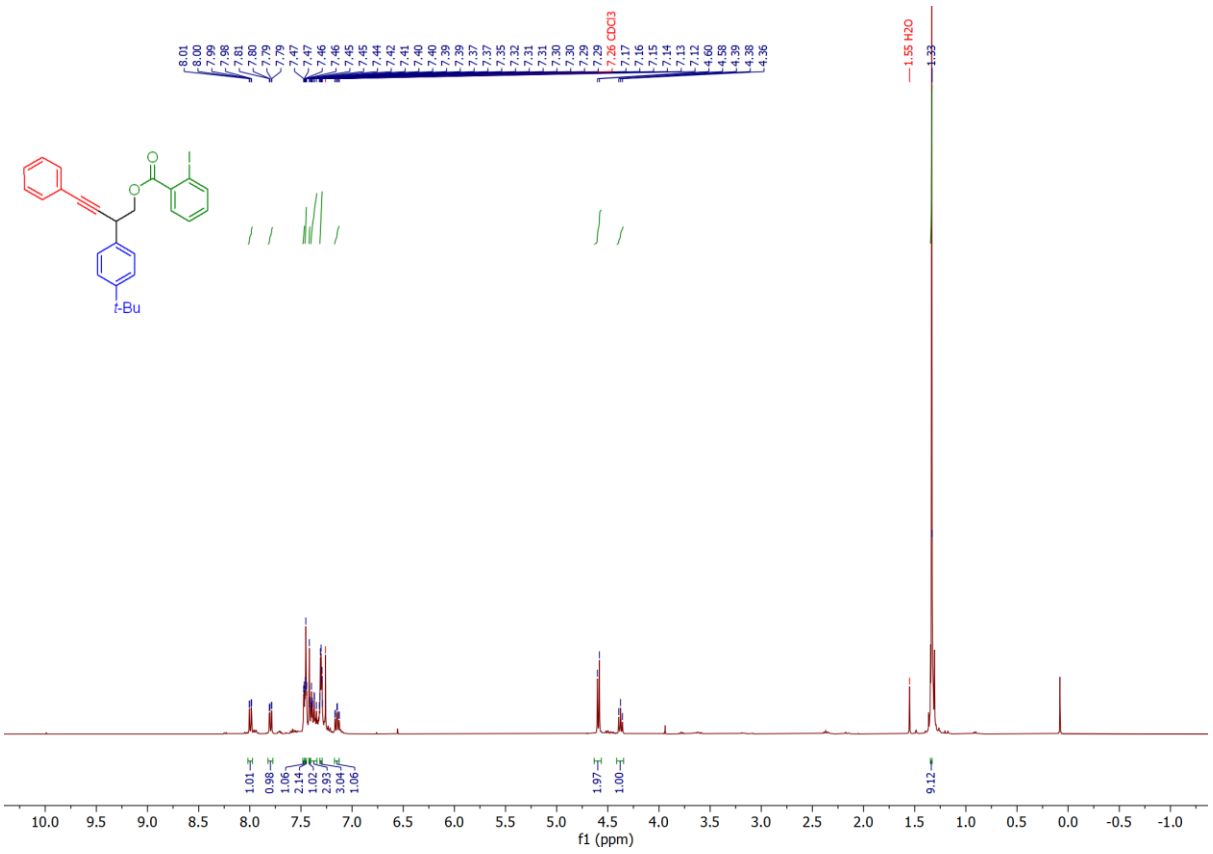
^{1}H NMR (400 MHz, $CDCl_3$) (8b)



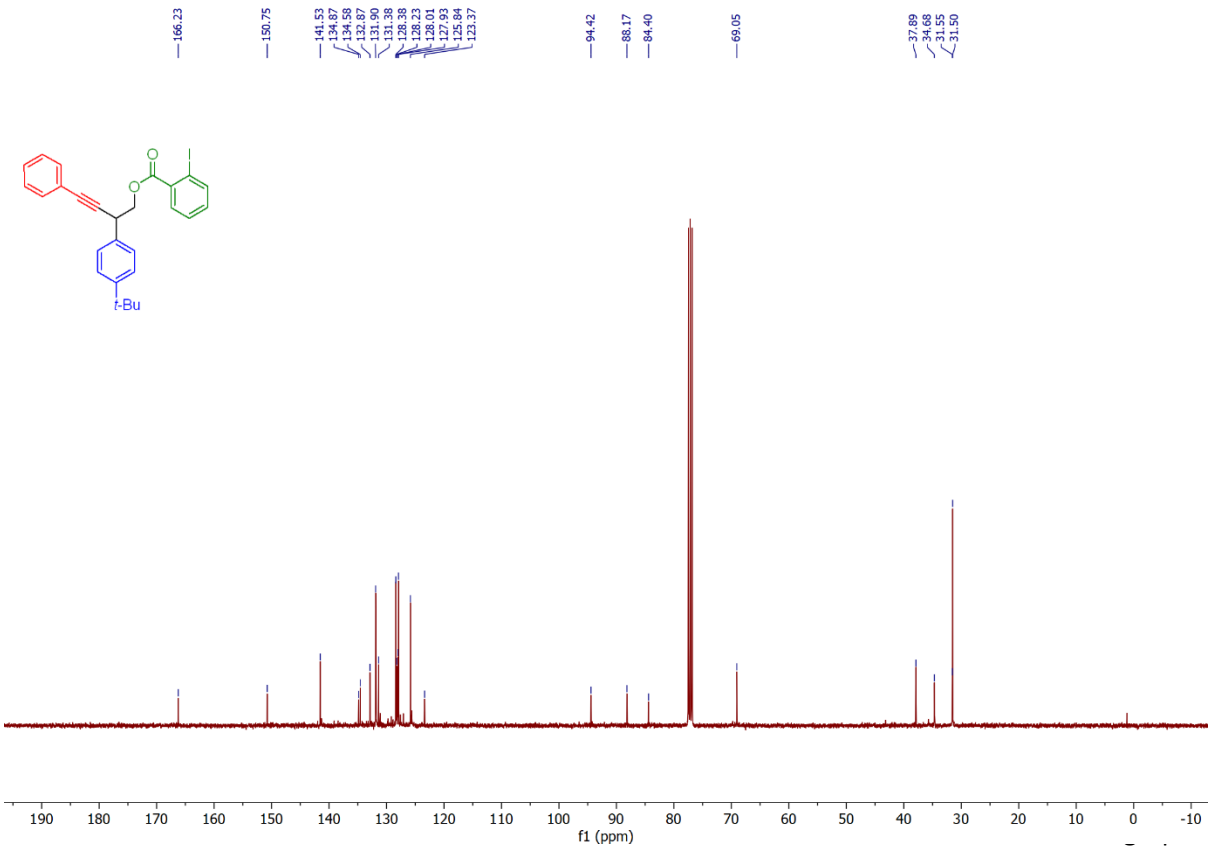
^{13}C NMR (101 MHz, $CDCl_3$) (8b)



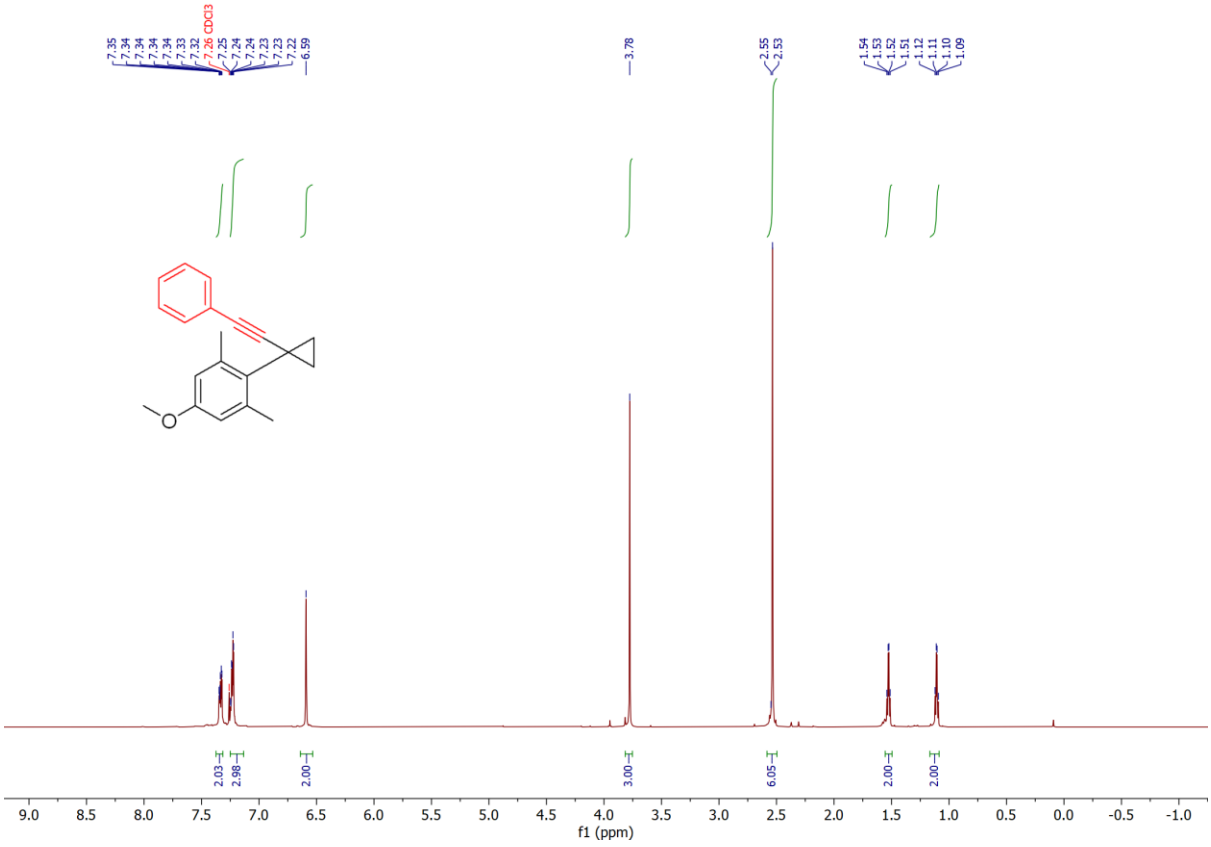
^{1}H NMR (400 MHz, $CDCl_3$ (8c)



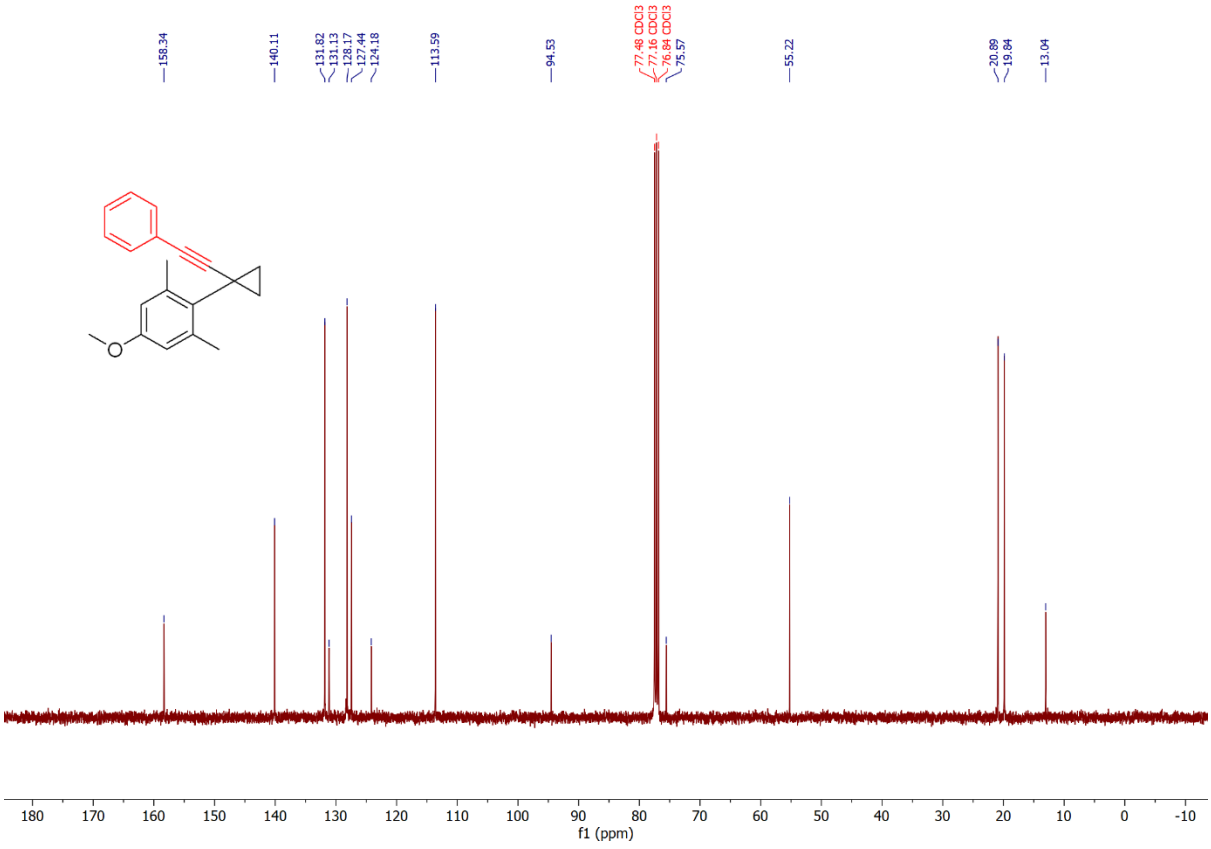
^{13}C NMR (101 MHz, $CDCl_3$) (8c)



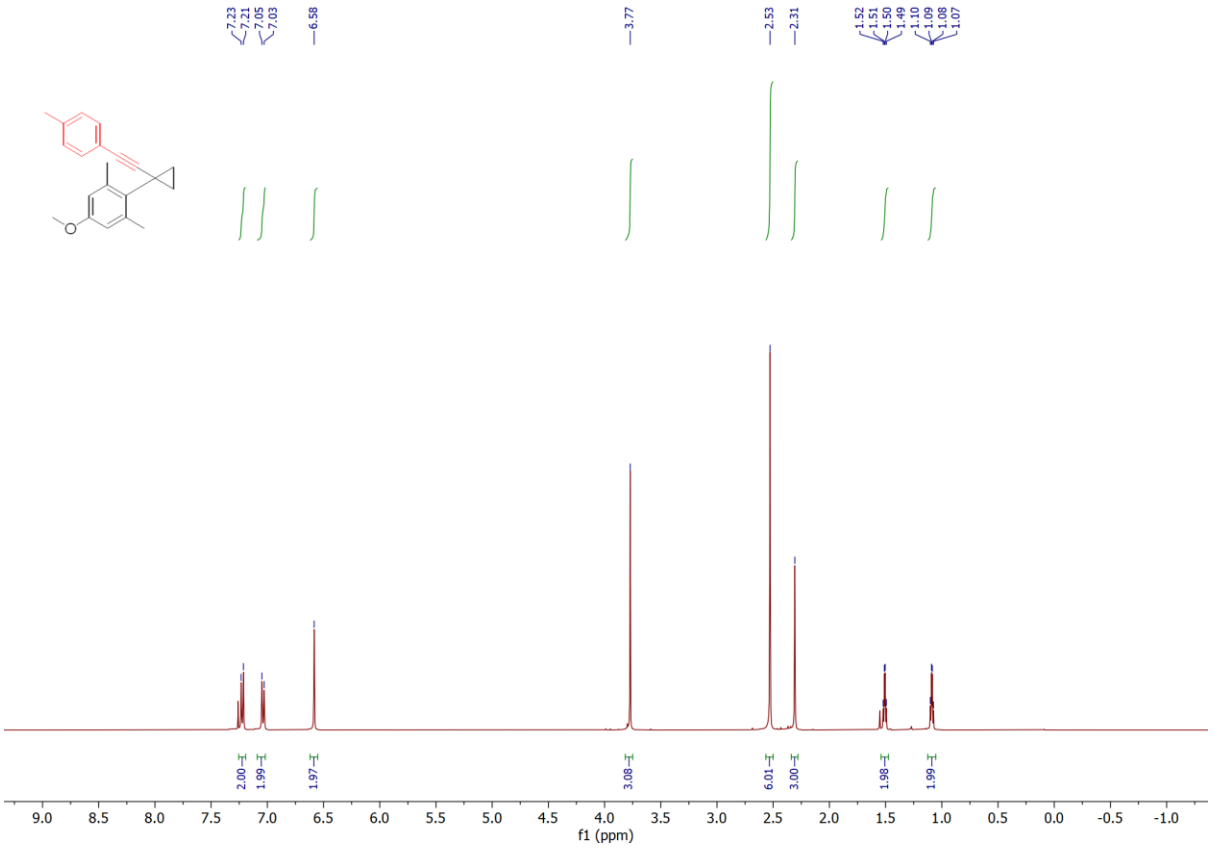
^{1}H NMR (400 MHz, $CDCl_3$) (4a)



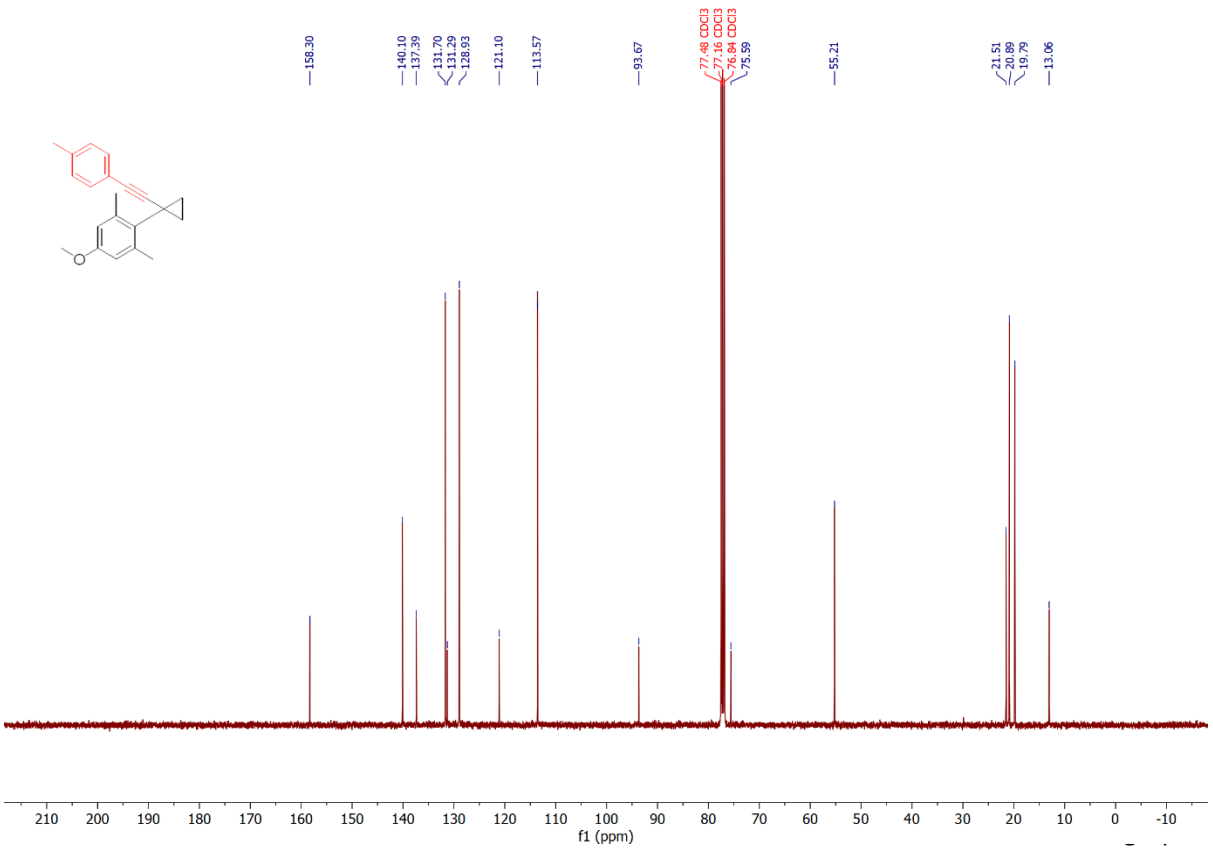
^{13}C NMR (101 MHz, $CDCl_3$) (4a)



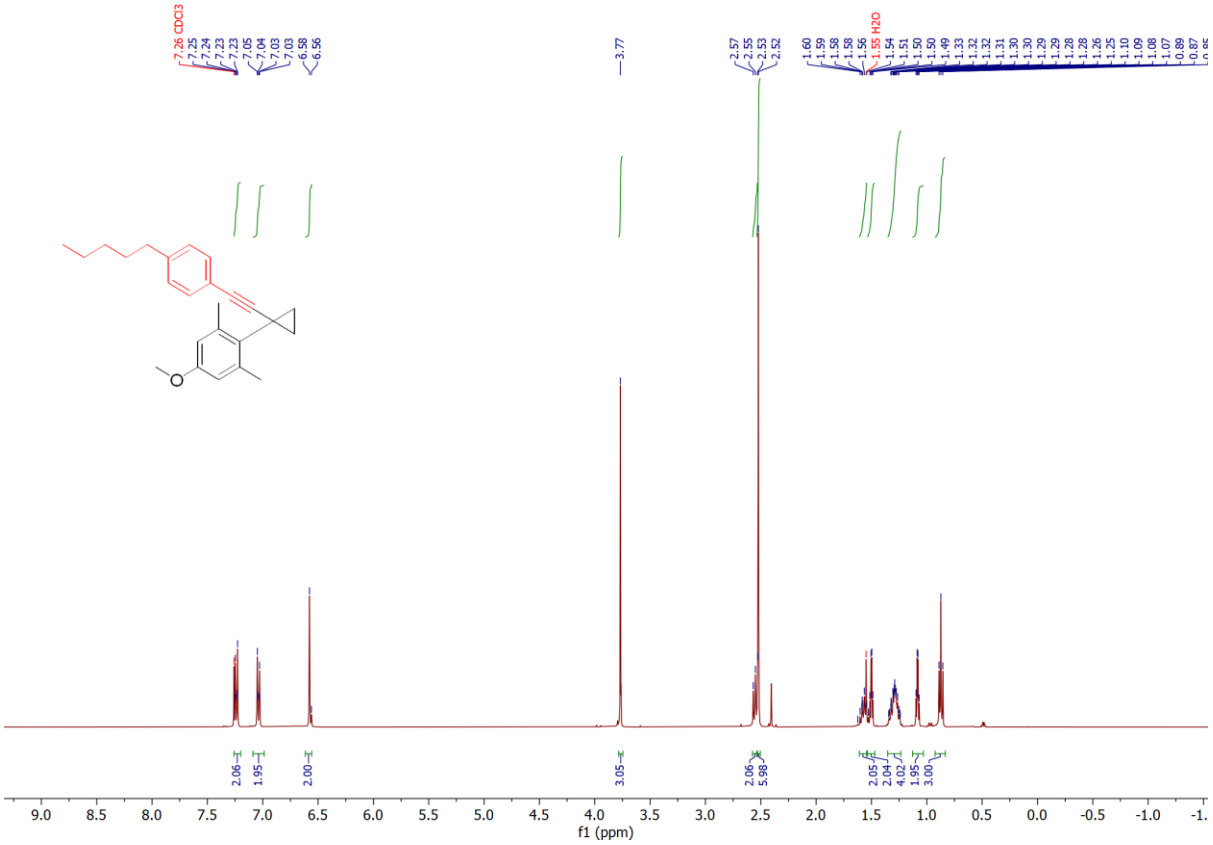
^{1}H NMR (400 MHz, $CDCl_3$) (4b)



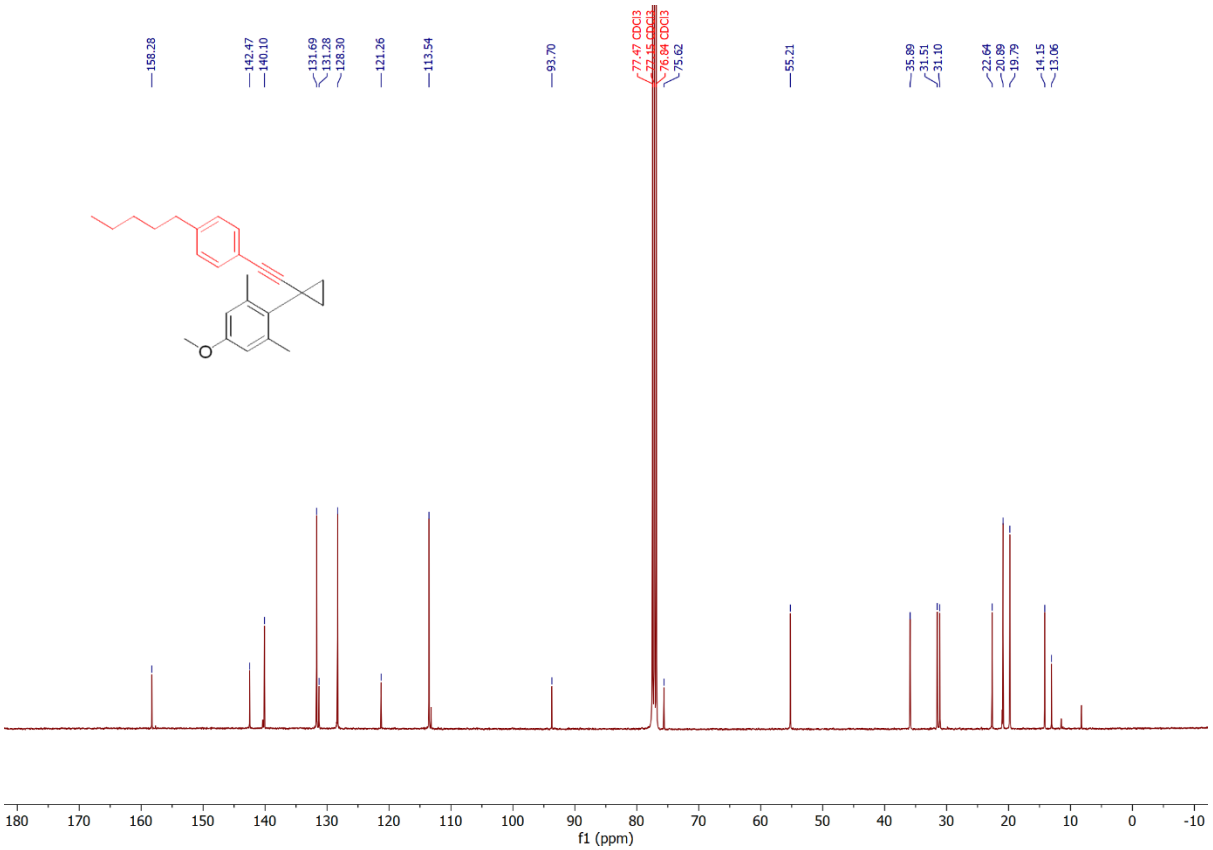
^{13}C NMR (101 MHz, $CDCl_3$) (4b)



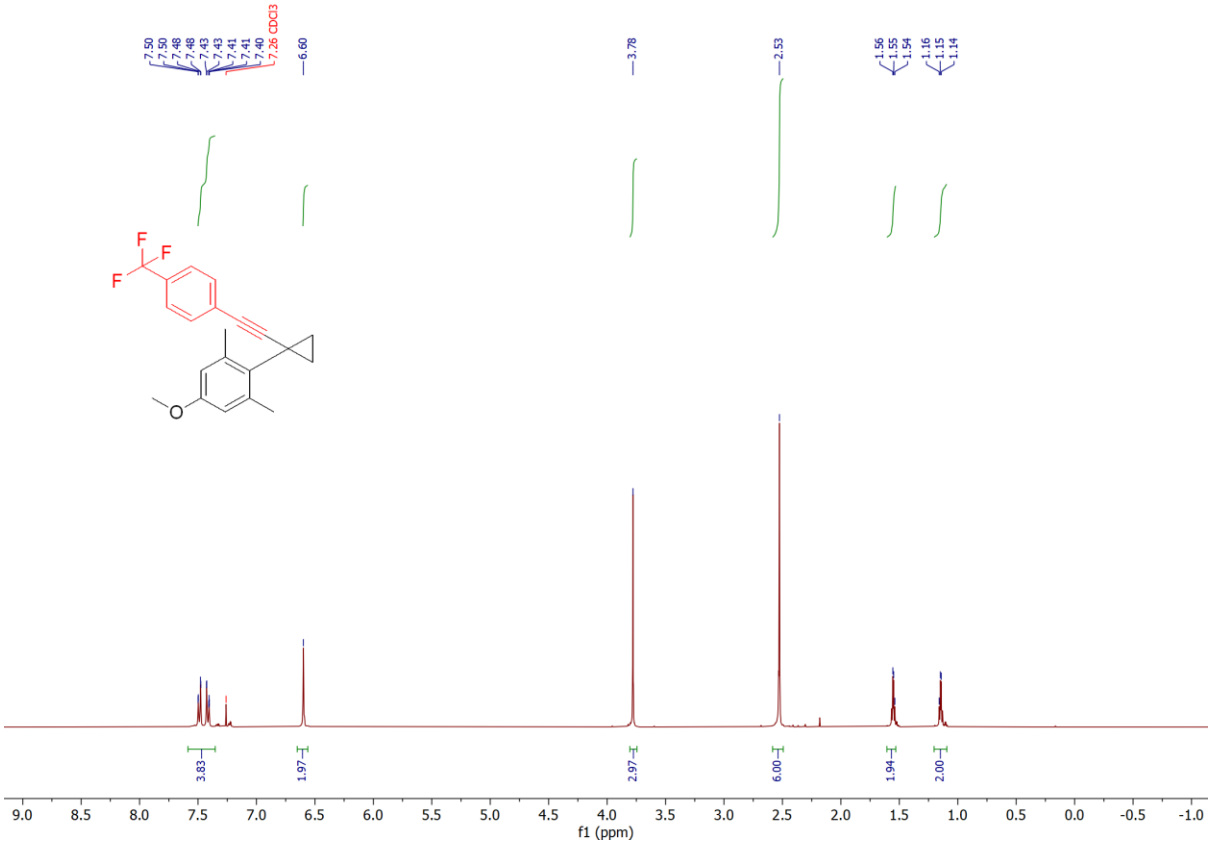
^{1}H NMR (400 MHz, $CDCl_3$) (4c)



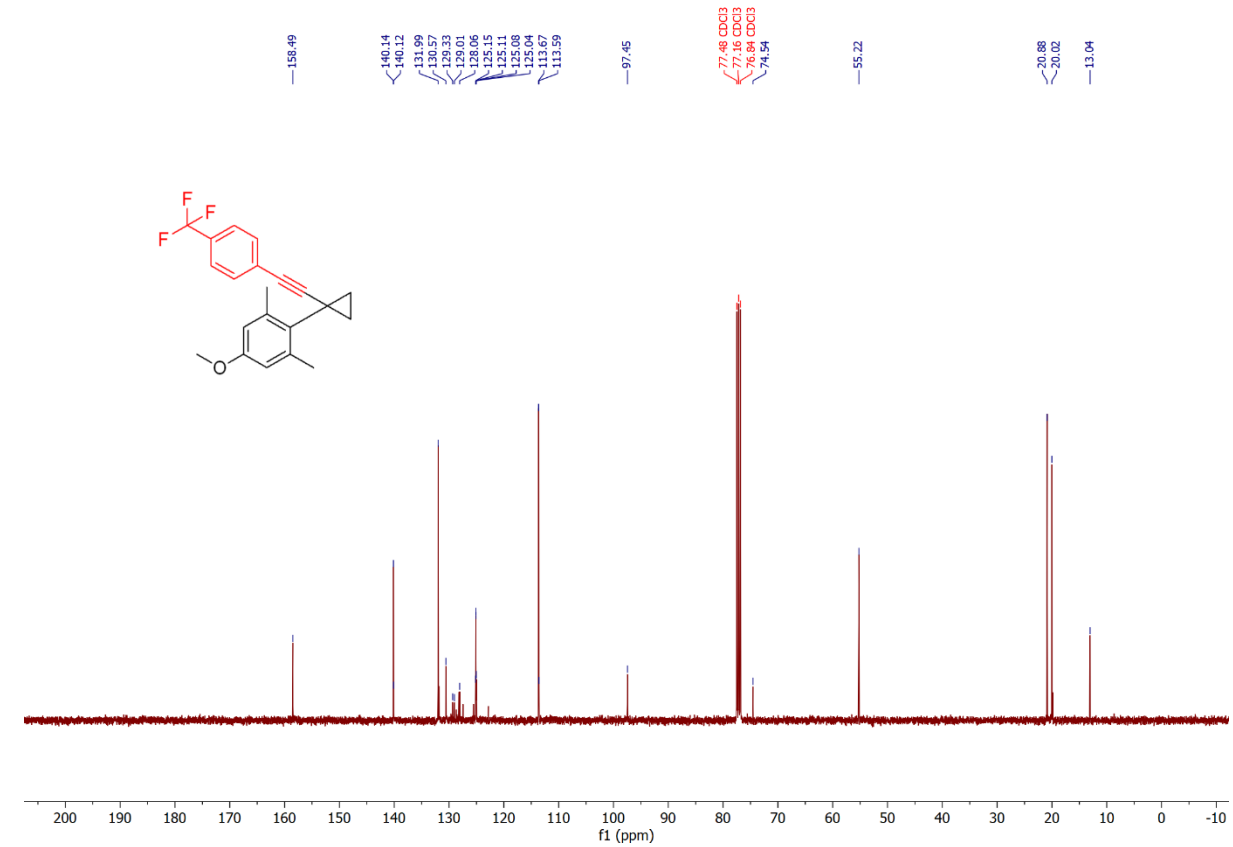
^{13}C NMR (101 MHz, $CDCl_3$) (4c)



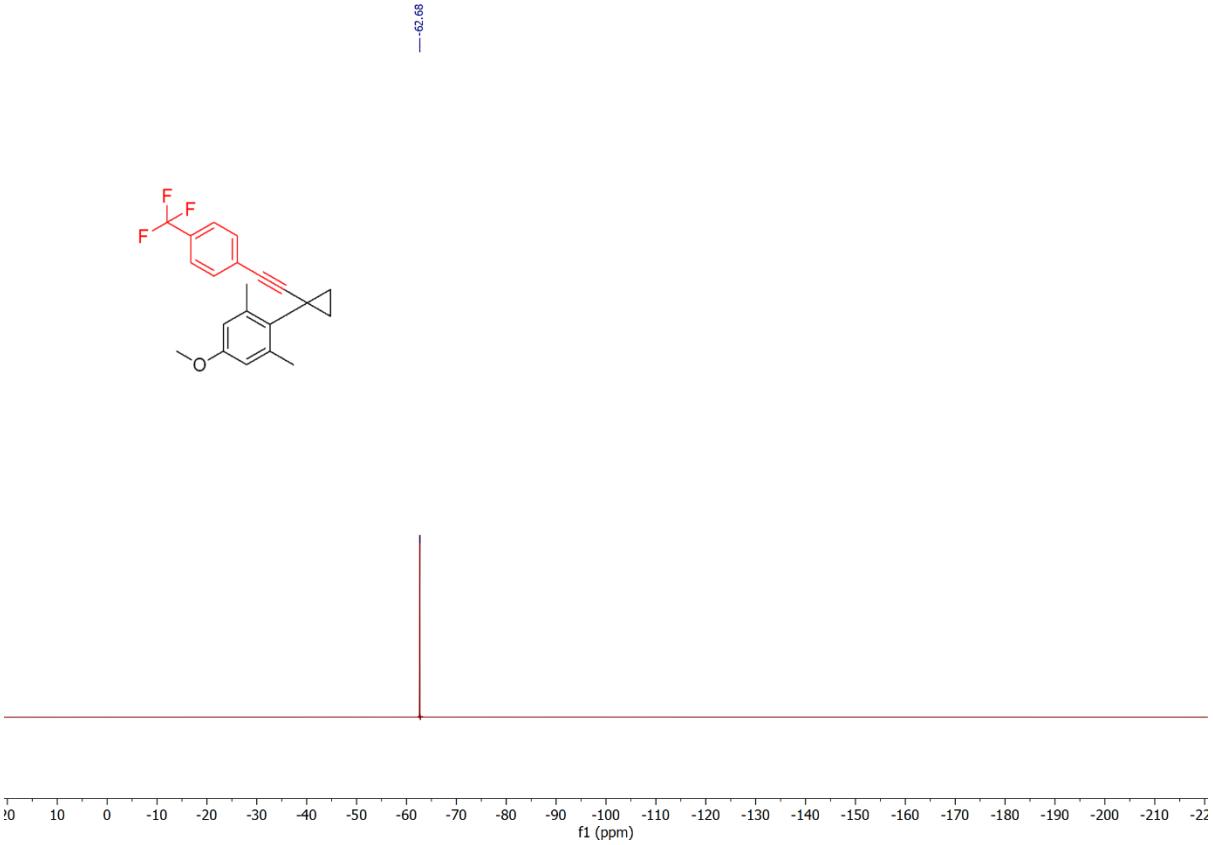
^{1}H NMR (400 MHz, $CDCl_3$) (4d)



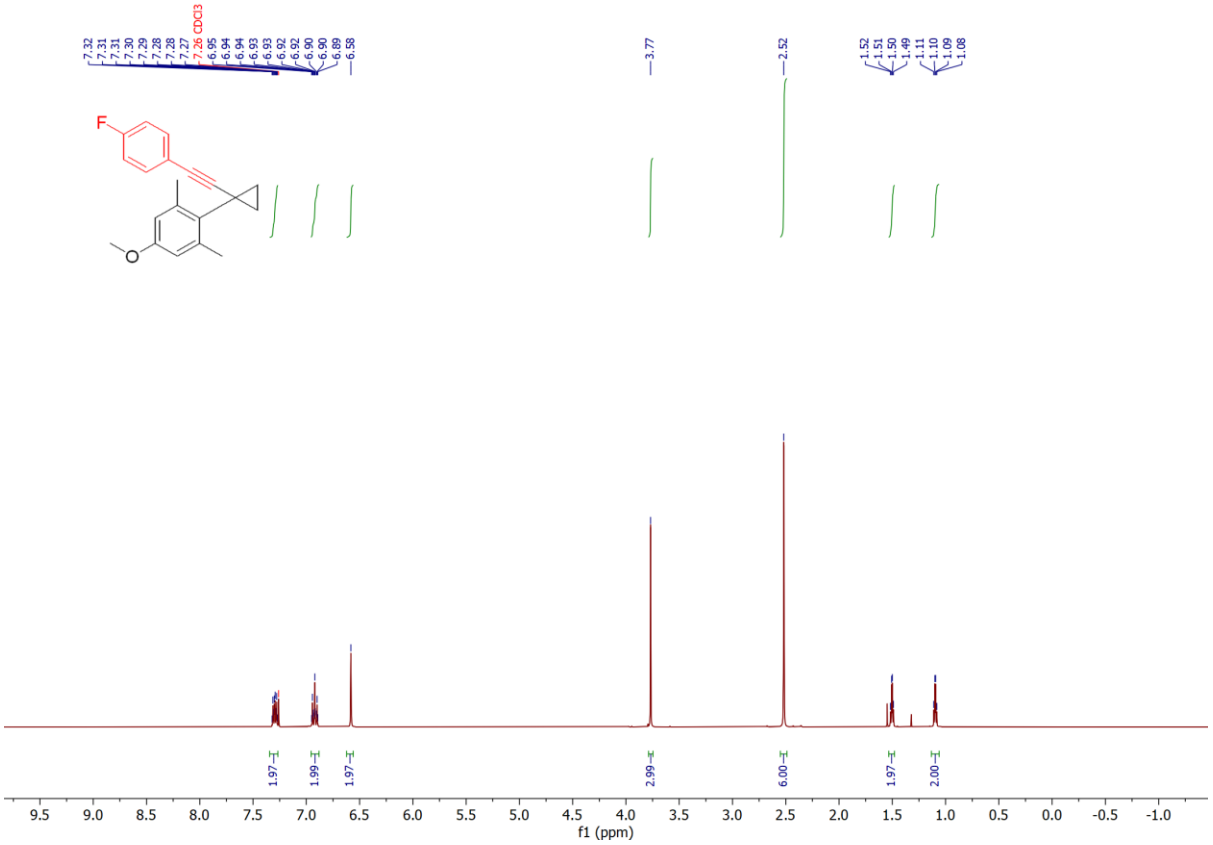
^{13}C NMR (101 MHz, $CDCl_3$) (4d)



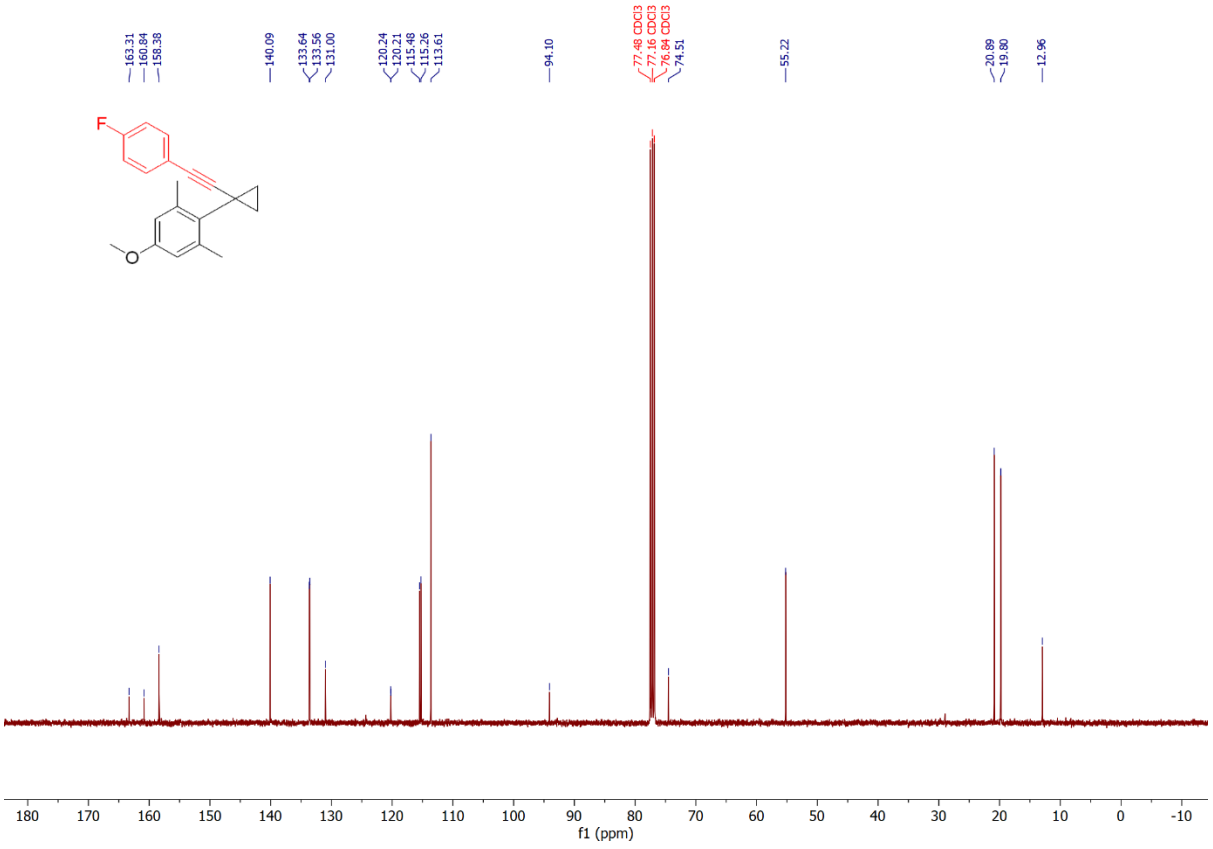
^{19}F NMR (377 MHz, $CDCl_3$) (4d)



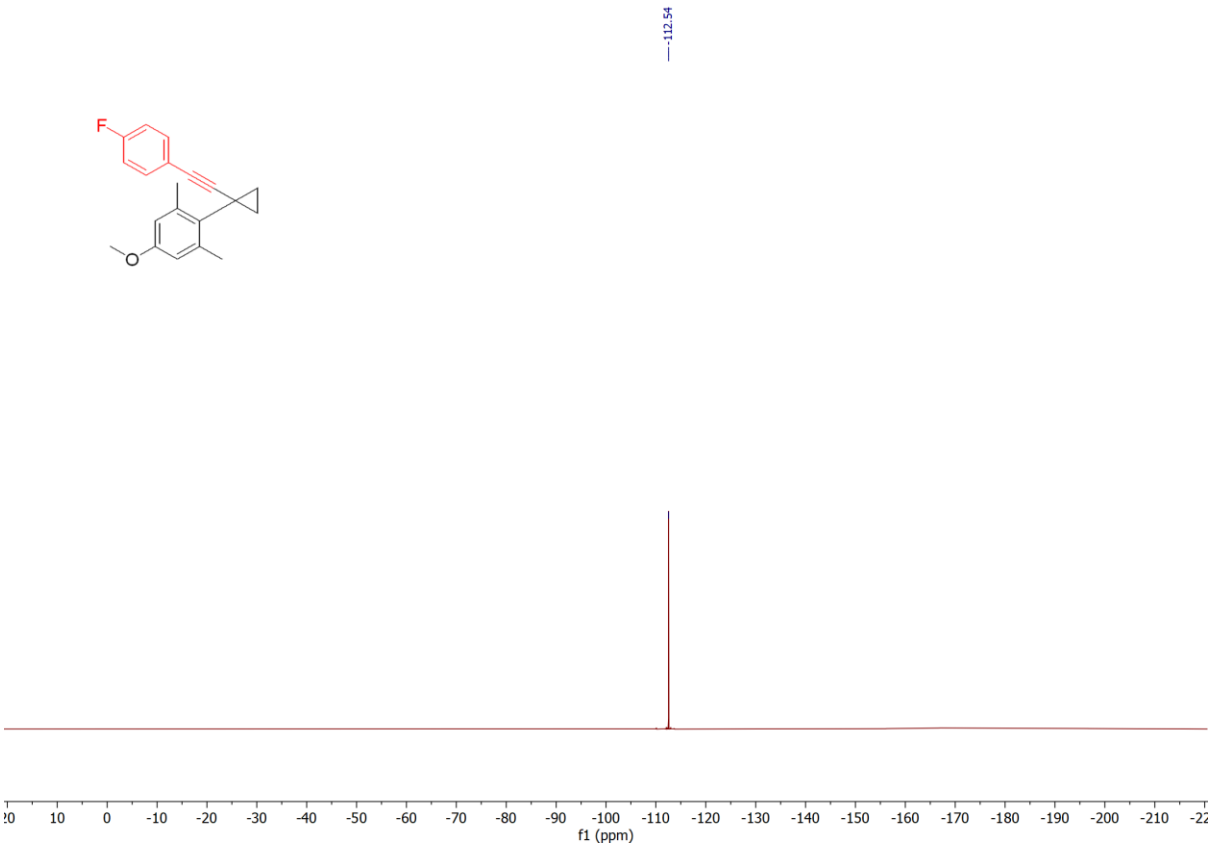
^{1}H NMR (400 MHz, $CDCl_3$) (4e)



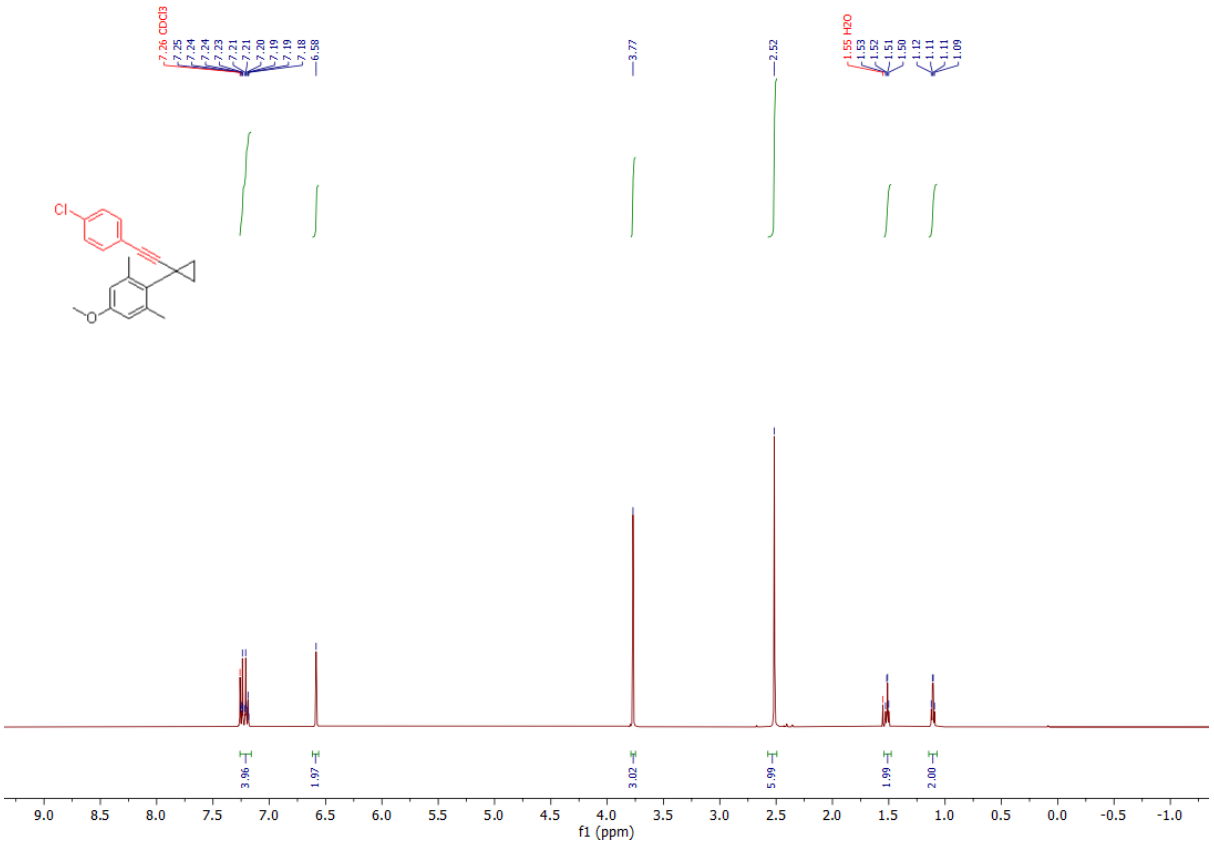
^{13}C NMR (101 MHz, $CDCl_3$) (4e)



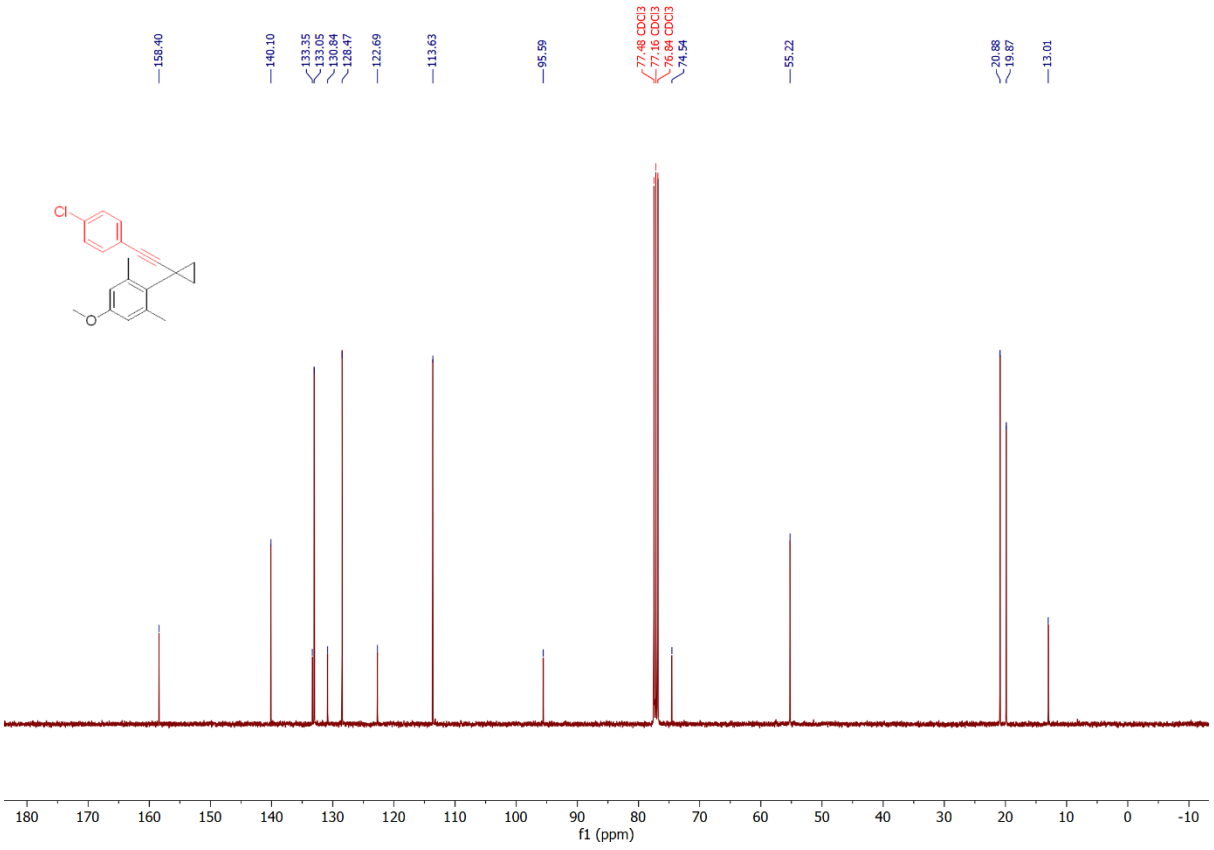
^{19}F NMR (377 MHz, $CDCl_3$) **(4e)**



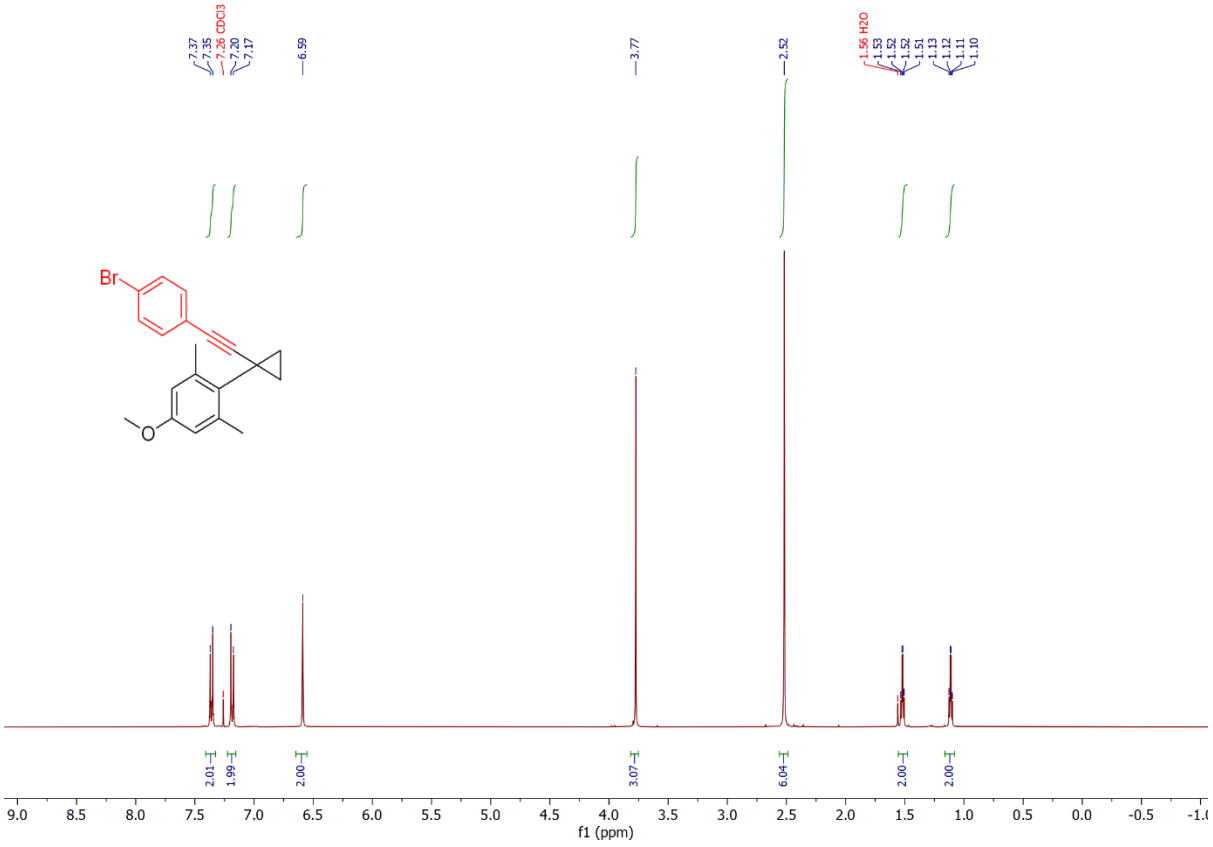
^{1}H NMR (400 MHz, $CDCl_3$) (4f)



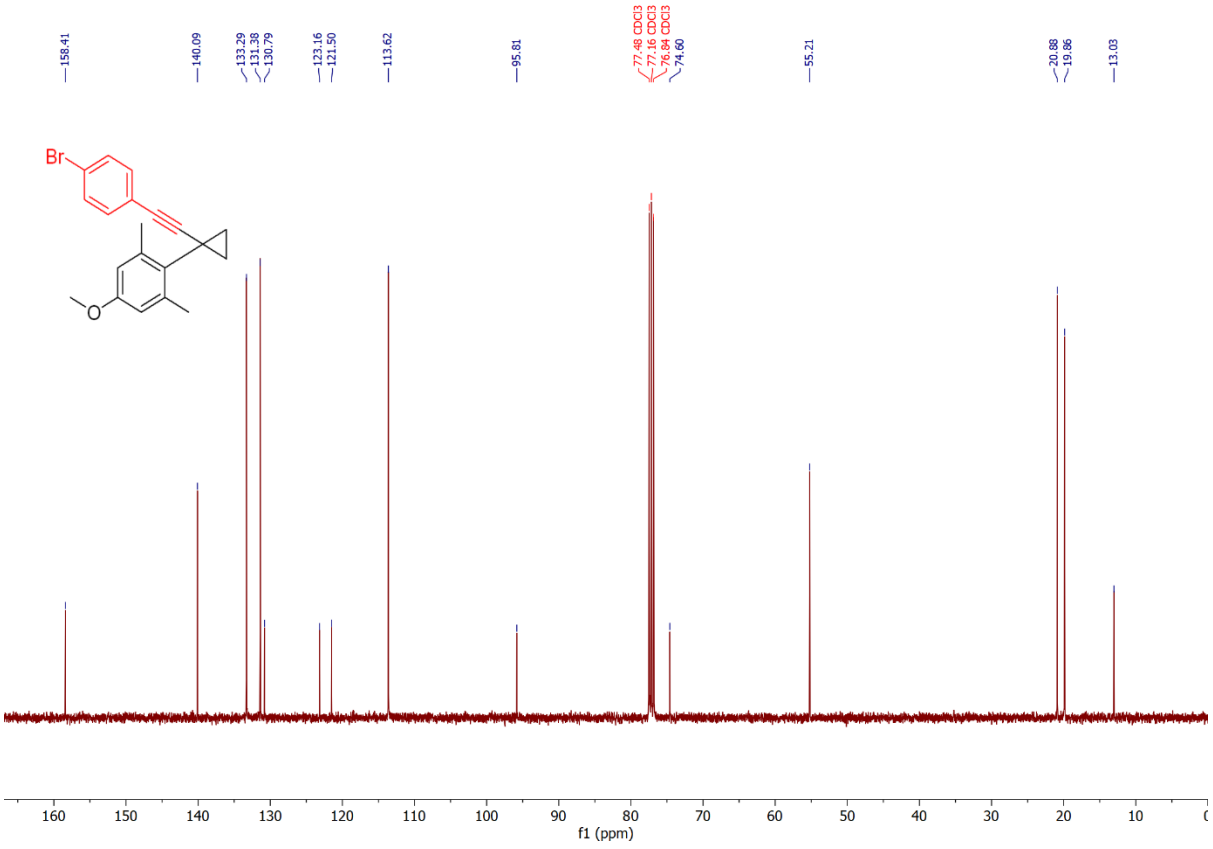
^{13}C NMR (101 MHz, $CDCl_3$) (4f)



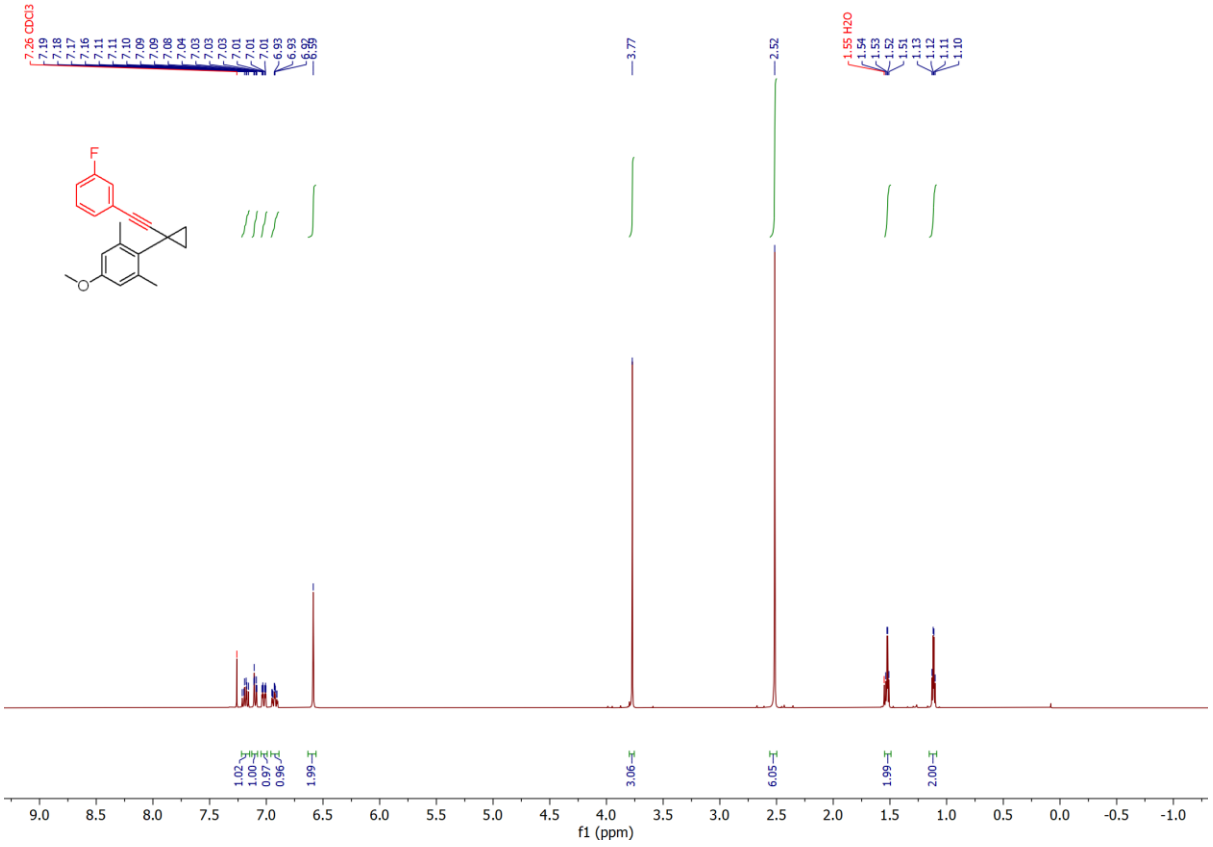
^{1}H NMR (400 MHz, $CDCl_3$) (4g)



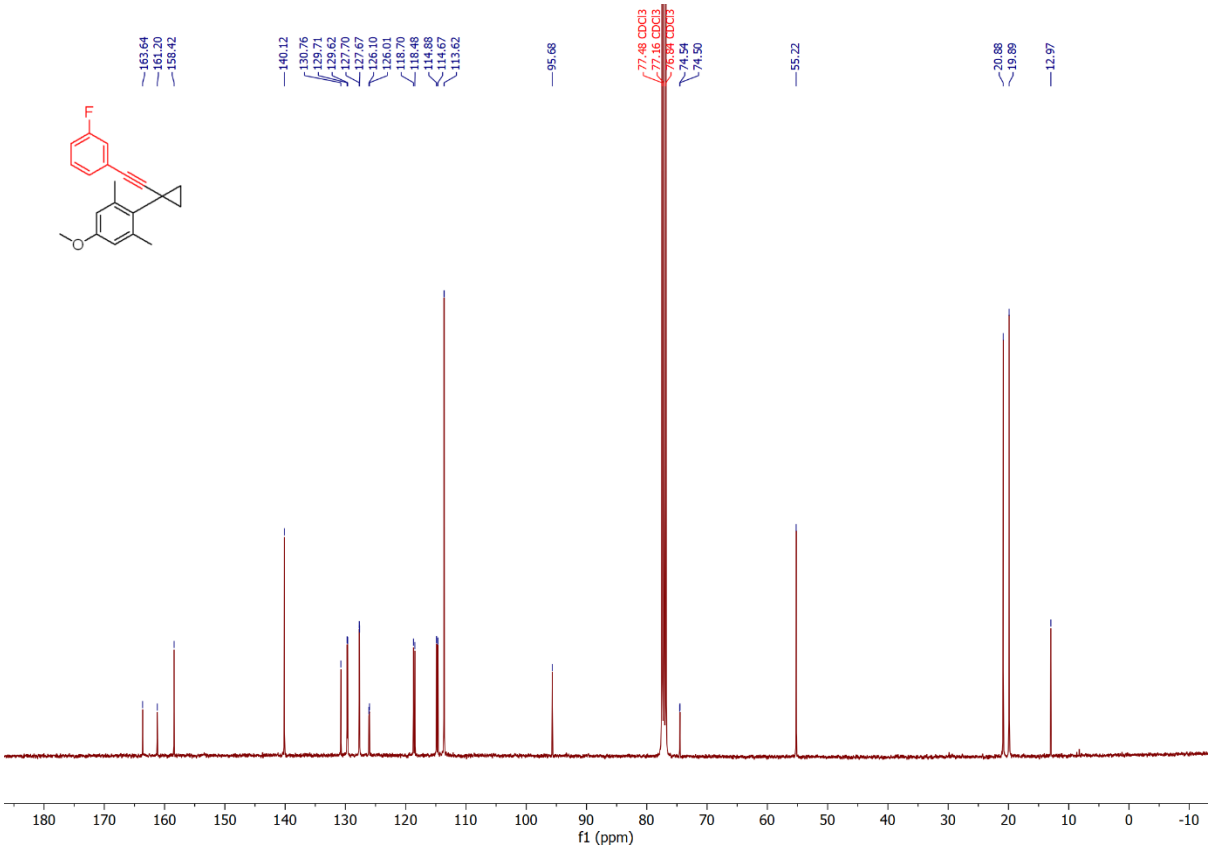
^{13}C NMR (101 MHz, $CDCl_3$) (4g)



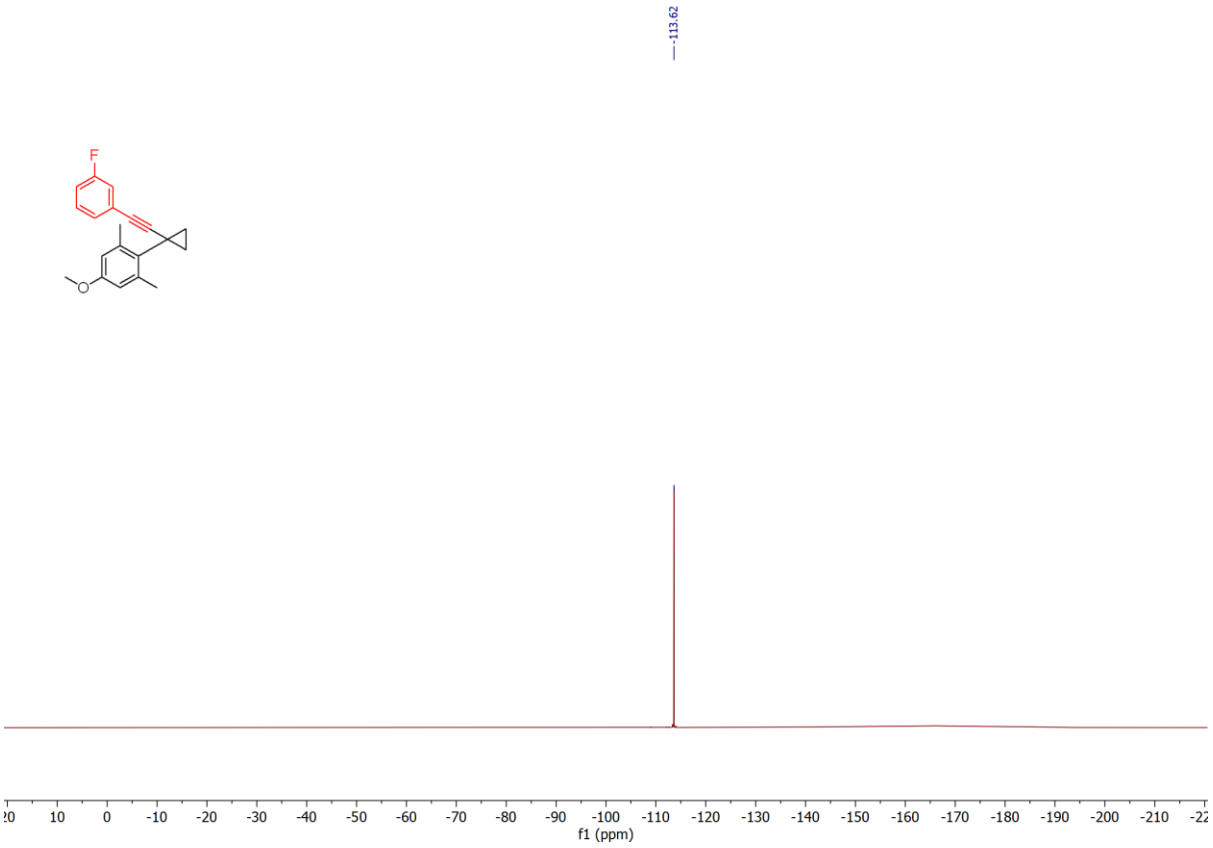
^{1}H NMR (400 MHz, $CDCl_3$) (4h)



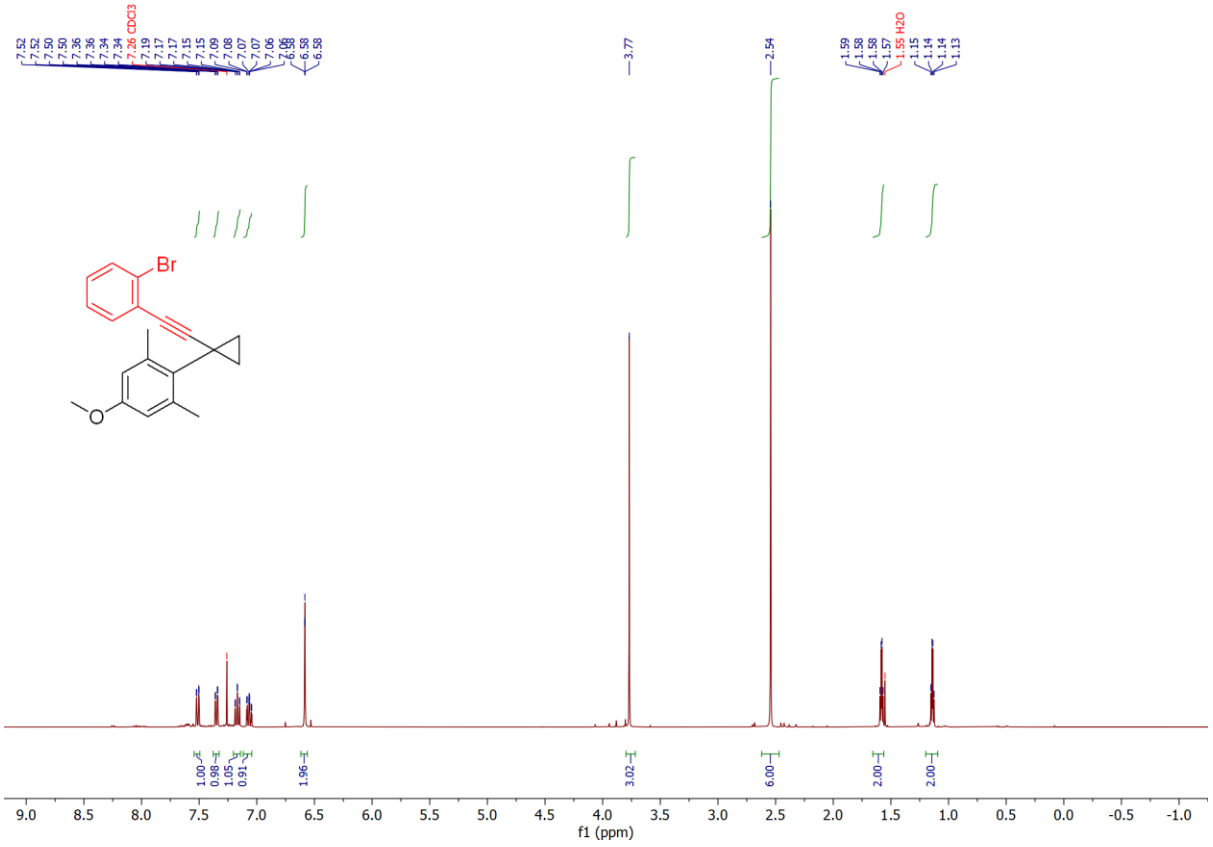
^{13}C NMR (101 MHz, $CDCl_3$) (4h)



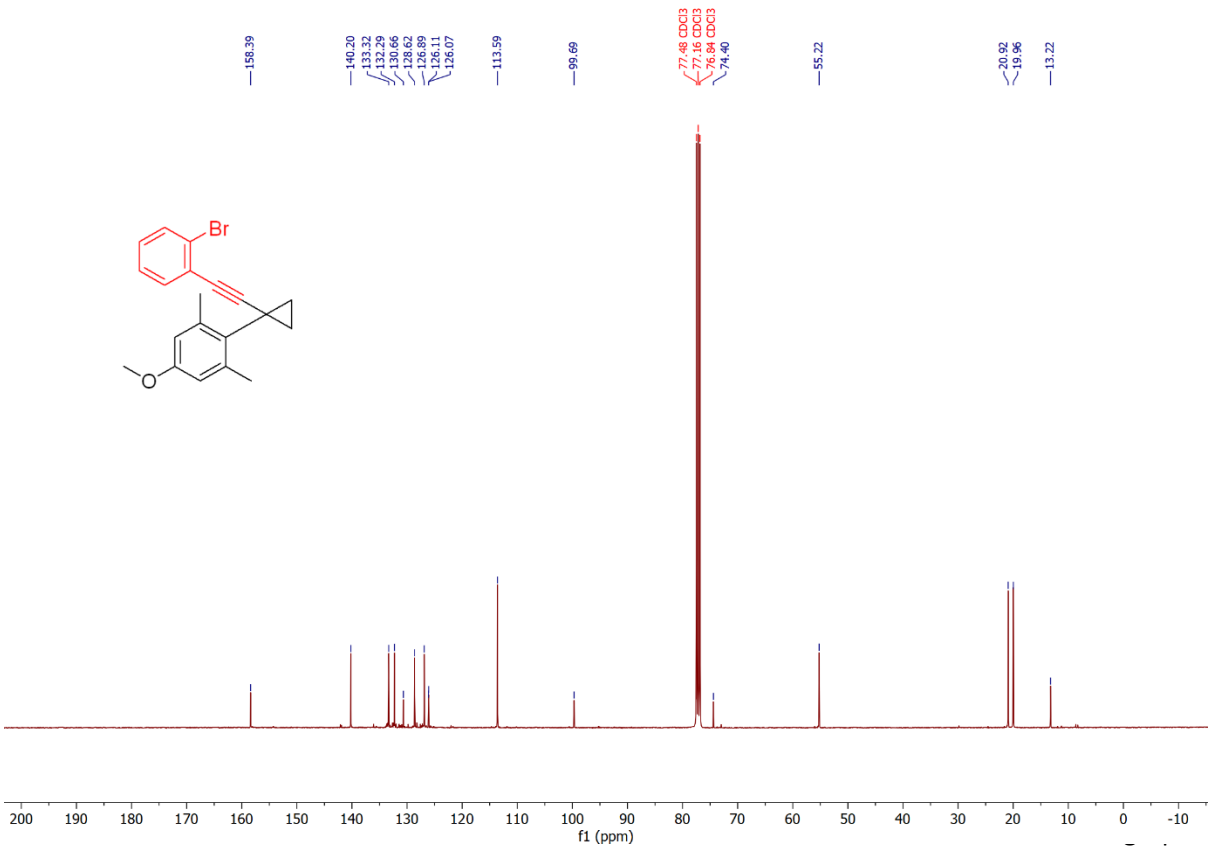
^{19}F NMR (377 MHz, $CDCl_3$) (4h)



^{1}H NMR (400 MHz, $CDCl_3$) (4i)



^{13}C NMR (101 MHz, $CDCl_3$) (4i)



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