

METAL-FREE METHODOLOGY FOR THE PREPARATION
OF YNONES USING POTASSIUM
ALKYNYLTRIFLUOROBORATES AND ITS APPLICATION
TO THE SYNTHESIS OF NATURAL PRODUCTS

by

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ABSTRACT

A straightforward procedure for the preparation of ynones from potassium alkynyltrifluoroborate salts and acyl chlorides or anhydrides has been developed. The one-pot reaction is advantageous in that it does not require exclusion of air or water, is operationally simple, has broad substrate scope, and proceeds rapidly under mild conditions in the presence of a Lewis acid. 2,6-dimethoxy substituted anhydrides afford the corresponding mono-demethylated *o*-alkynoylphenol precursors of aurone and flavone natural product scaffolds in good yields. A variety of flavones were obtained *via* 6-*endo* cyclization of *o*-alkynoylphenol intermediates in the presence of trifluoromethanesulfonic acid (TfOH). Cesium carbonate was discovered to promote the rapid 5-*exo* cyclization of *o*-alkynoylphenols to form aurone products in excellent yields.

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LIST OF ABBREVIATIONS

TfOH	trifluoromethanesulfonic acid
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
TFAA	trifluoroacetic anhydride
TMS	trimethylsilyl
DIEA	N,N-diisopropylethylamine
IPA	isopropyl alcohol
TTN	thallium(III) trinitrate
EtOH	ethanol
PMF	polymethoxyflavones
DMSO	dimethyl sulfoxide
TBDMSCl	<i>tert</i> -butyldimethylsilyl chloride
NBS	<i>N</i> -bromosuccinimide

1. INTRODUCTION

1.1 GENERAL BACKGROUND

Organic chemistry, put simply, is the study of carbon compounds. Carbon is a group 4A element which means that it has the ability to share four valence electrons and form four strong covalent bonds. Carbon atoms are particularly special as a result of their ability to bond to one another, allowing for the formation of long chains and rings. The diversity and quantity of known carbon-based compounds is staggering, ranging from simple single-carbon methane to extremely complex DNA which can have upwards of 100 million carbon atoms.

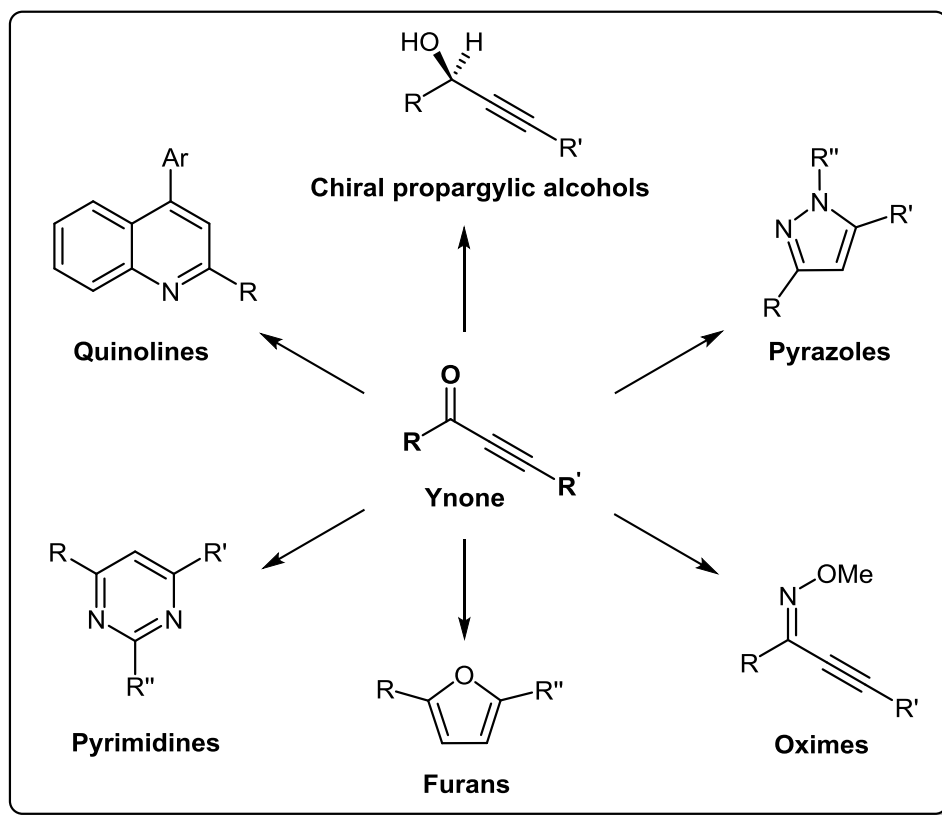
Traditionally, the term organic chemistry has been associated with the study of compounds derived from living organisms. Modern chemistry, however, has made possible the design and synthesis of novel organic compounds in the laboratory. Synthetic organic compounds such as dyes, polymers, and pharmaceuticals have been designed for a variety of practical applications. Due to the extreme diversity of organic compounds, chemists are always seeking new tools for the manipulation of carbon compounds and the formation of new carbon-carbon bonds. Traditional methods for the formation of new carbon-carbon bonds are often associated with limitations such as inadequate functional group tolerance, poor atom economy, the need for harsh reaction conditions, and the use of toxic or costly reagents.

The focus of this project has been the development and optimization of a novel, convenient methodology for the formation of an important class of organic functional group, specifically the ynone. The new method for the preparation of this valuable type of carbon-carbon bond has a number of advantages over traditional methods including good functional group tolerance and operational simplicity. This method has been applied toward the synthesis of a library of biologically relevant aurone and flavone natural product scaffolds.

1.2 YNONES

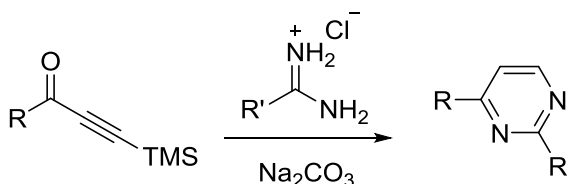
1.2.1 UTILITY OF YNONES AS SYNTHETIC BUILDING BLOCKS

Ynones are characterized by a ketone functional group with a carbon-carbon triple bond *alpha* to the carbonyl carbon. Ynones are valuable building blocks that have been applied toward the synthesis of a number of biomedically significant natural and unnatural products.^[1] As illustrated by Scheme 1, ynones are precursors to a number of useful organic functional groups including pyrimidines,^[2] quinolines,^[3] furans,^[4] pyrazoles,^[5] oximes,^[6] and chiral propargylic alcohols.^[7] Additionally, *ortho*-hydroxyl substituted ynones are intermediates in the synthesis of aurone and flavone natural product scaffolds. These functional groups are of particular interest and will be discussed in detail in section 1.4 Natural products.



Scheme 1: Ynones are precursors to a variety of valuable organic scaffolds

Pyrimidines are a class of heterocycles widely recognised to have pharmacological activity.^[8] Gleevec is an example of an FDA approved pharmaceutical for the treatment of several cancers which contains a pyrimidine scaffold.^[9] The straightforward preparation of pyrimidines in modest to excellent yields from TMS-ynones is possible by addition of amidinium or guanidinium salts with sodium carbonate (Scheme 2).^[2]



Scheme 2: Preparation of pyrimidines from TMS-ynones

Quinoline scaffolds are important substructures found in natural and designed compounds with valuable pharmacological activities.^[10] Quinoline functionalities are prevalent in a variety of compounds with antibacterial and antimicrobial activities.^[11] Specifically, quinoline-containing drugs are used in the treatment of malaria^[12] and tuberculosis (Figure 1)^[13]. Quinoline derivatives have also found application in materials science as ligands,^[14] chemosensors for fluoride ions,^[15] and as fluorescent sensors for selective metal ion recognition in aqueous solution.^[16]

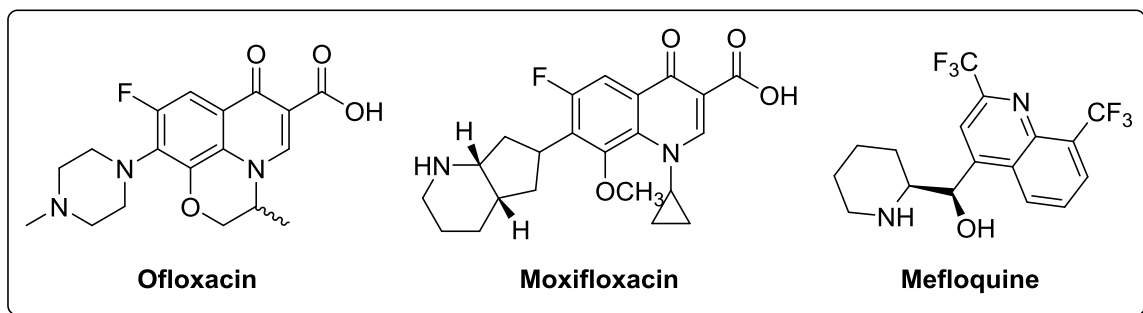
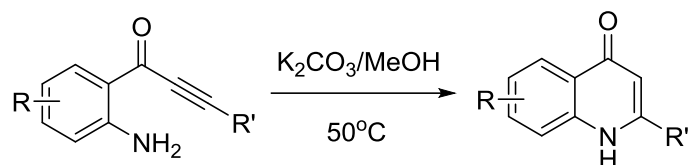


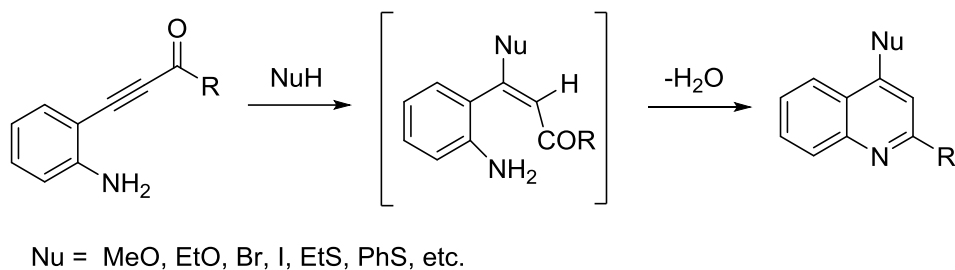
Figure 1: Examples of FDA approved quinoline-containing drugs indicated for the treatment of malaria and tuberculosis.

Quinolines may be prepared *via* cyclization of *ortho*-aminophenyl substituted ynones under basic conditions (Scheme 3).^[17]



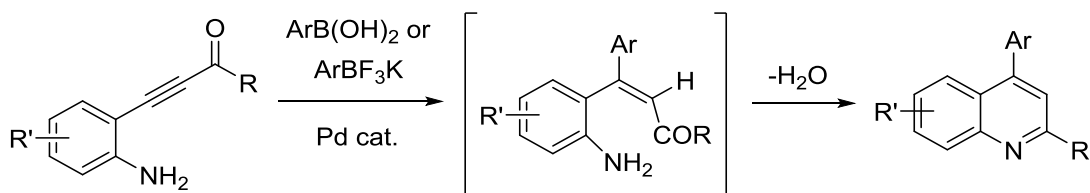
Scheme 3: Cyclization of *o*-aminophenyl ynones under basic conditions

It is possible to obtain functionalized 2,4-disubstituted quinolines from ynone starting materials through tandem nucleophilic addition/annulation reactions (Scheme 4).^[3b]



Scheme 4: Preparation of functionalized 2,4-disubstituted quinolines through tandem nucleophilic addition/annulation reactions.

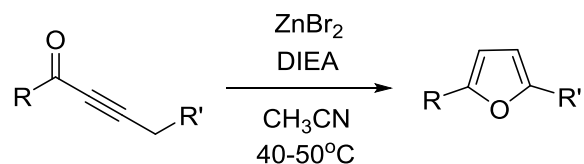
Organoboron derivatives may also be applied towards the preparation of more interesting 2,4-disubstituted quinolines from ynones (Scheme 5).^[3a]



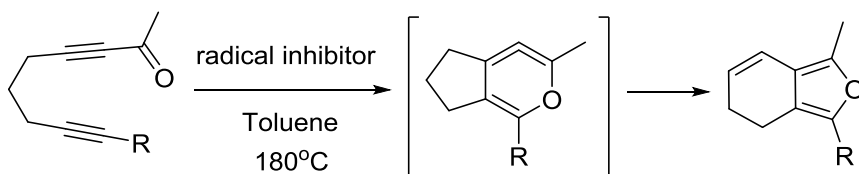
Scheme 5: Preparation of 4-arylsubstituted quinolines with organoboron derivatives.

Furan scaffolds have broad applicability in the production of conjugated polymers with desirable optical and electronic properties for applications such as solar cells, electronics, and biological devices.^[18] 2,5-disubstituted furan derivatives have been synthesized from ynones with a methylene unit adjacent to the triple bond (Scheme 6).^[4b] Polycyclic furans may be formed by heating conjugated ynones in the presence of a radical inhibitor to

promote intramolecular cycloaddition and subsequent rearrangement to a furan (Scheme 7).^[4a]

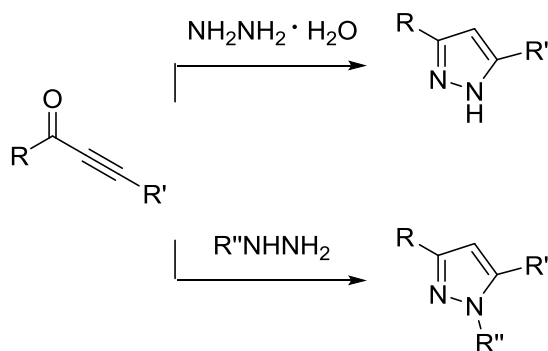


Scheme 6: Zinc promoted ynone cyclization to form 2,5-disubstituted furans.



Scheme 7: Intramolecular [4+2] cyclization of conjugated ynones to form polycyclic furans.

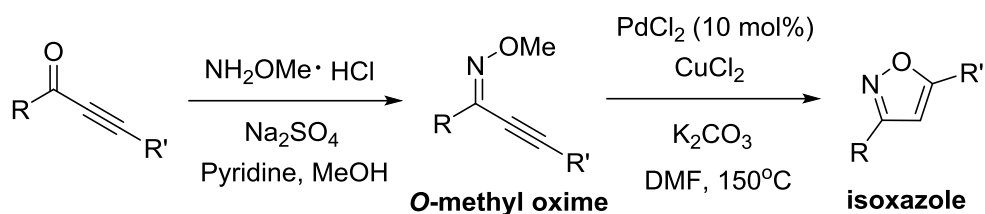
Substituted pyrazole derivatives are known to possess valuable biological activities including antimicrobial,^[19] anti-inflammatory,^[20] and anti-cancer properties.^[21] Straightforward synthesis of pyrazoles from ynone precursors may be achieved by exposing them to hydrazine (Scheme 8).^[5]



Scheme 8: Straightforward preparation of substituted pyrazoles from ynone precursors.

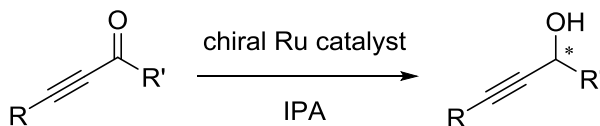
O-methyl oximes are valuable intermediates toward the synthesis of isoxazoles. Substituted isoxazoles have been shown to have a range of bioactivities including anticancer,^[22] analgesic,^[23] anti-inflammatory,^[23] and antinociceptive^[24] characteristics.

O-methyl oximes are readily prepared by stirring an ynone in the presence of methoxylamine hydrochloride, pyridine and sodium or magnesium sulfate.^[6a] 3,5-disubstituted isoxazoles may be prepared by palladium catalyzed cyclization of *O*-methyl oximes (Scheme 9).^[6a] Isoxazoles may be further substituted in the 4-position by performing the cyclization in the presence of an electrophile such as iodine monochloride to form the corresponding 4-iodoisoxazole. Submission of 4-iodoisoxazole to palladium-catalyzed reactions can yield a variety of 3,4,5-trisubstituted isoxazoles.^[6b]



Scheme 9: Conversion of ynones to isoxazoles *via* *O*-methyl oxime intermediates

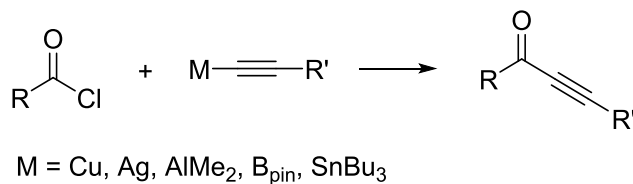
Chiral propargylic alcohols are valuable intermediates for the enantioselective preparation of complex structures of structural and biological interest such as steroids,^[25] alkaloids,^[26] macrolides,^[27] and enediyne antibiotics^[28] to name just a few examples. The selective reduction of ynones to propargylic alcohols with high enantiomeric purity may be achieved by transfer hydrogenation using chiral Ru(II) catalysts and isopropanol as the hydrogen donor (Scheme 10).^[7c] Alternatively, propargylic alcohols may be obtained with high enantiomeric purity through catalytic enantioselective reduction of ynones with a chiral oxazaborolidine and catecholborane.^[7a]



Scheme 10: Asymmetric transfer hydrogenation of ynones

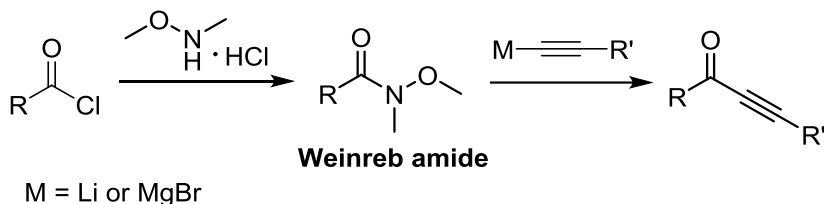
1.2.2 PREPARATION OF YNONES

Given their function as building blocks for a variety of useful organic scaffolds, there are a number of methods in the literature for the preparation of ynones. Ynones are commonly prepared by reacting acyl chlorides with metal^[29] or metalloid^[30] acetylides (Scheme 11).



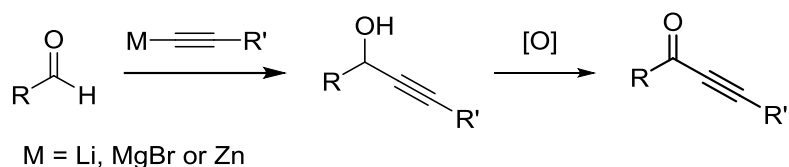
Scheme 11: Preparation of ynones from acyl chlorides and metal or metalloid acetylides.

Alternatively, ynones may be prepared in two-step procedures by converting acyl chlorides to N-methoxy-N-methylamides (known as Weinreb amides) and reacting them with alkynyllithium or Grignard reagents (Scheme 12).^[31]



Scheme 12: Preparation of ynones using Weinreb amides and alkynylmetallic reagents.

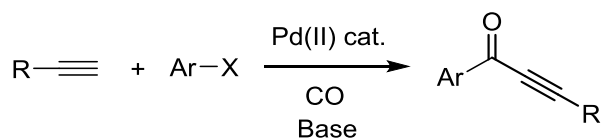
Ynones may also be formed by addition of an alkynylmetallic reagent to an aldehyde, followed by oxidation of the resulting secondary alcohol to the corresponding ketone (Scheme 13).^[32]



Scheme 13: Preparation of ynones by addition of alkynylmetallic reagents to aldehydes followed by oxidation.

The metal acetylides employed in several of the aforementioned methods for ynone preparation are associated with poor functional group tolerance thus limiting their substrate scope and utility. Additionally, multi-step procedures that require purification of reaction intermediates are inconvenient and result in reduced yields.

Transition-metal-catalyzed carbonylative Sonogashira couplings are another more recent method that has emerged for the preparation of ynones (Scheme 14).^[33] Unfortunately, transition metal-catalyzed reactions often require elevated pressures of carbon monoxide and result in formation of unwanted direct coupling byproduct. In addition to these undesirable features, transition metal catalysts are costly and toxic.



Scheme 14: Preparation of ynones by carbonylative Sonogashira coupling of terminal alkynes with aryl halides.

Clearly, given their utility as synthetic building blocks, a more straightforward method for the preparation of ynones is desirable.

1.2.3 PREPARATION OF *O*-ALKYNOYLPHENOLS

O-Alkynoylphenol compounds (Figure 2) are a class of *ortho*-hydroxyaryl substituted ynones that are of particular synthetic interest. A convenient method for the preparation of functionalized *o*-alkynoylphenols is appealing because these compounds are synthetic

intermediates in the preparation of aurone and flavone natural product derivatives.^[34] Many of the aforementioned synthetic methods for the preparation of ynones are poorly suited to the preparation of sterically hindered ynones including *o*-alkynoylphenols. This section details the methods that have been employed for the preparation of *o*-alkynoylphenols including the sterically hindered examples that have been reported.

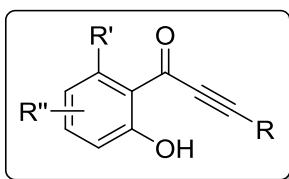
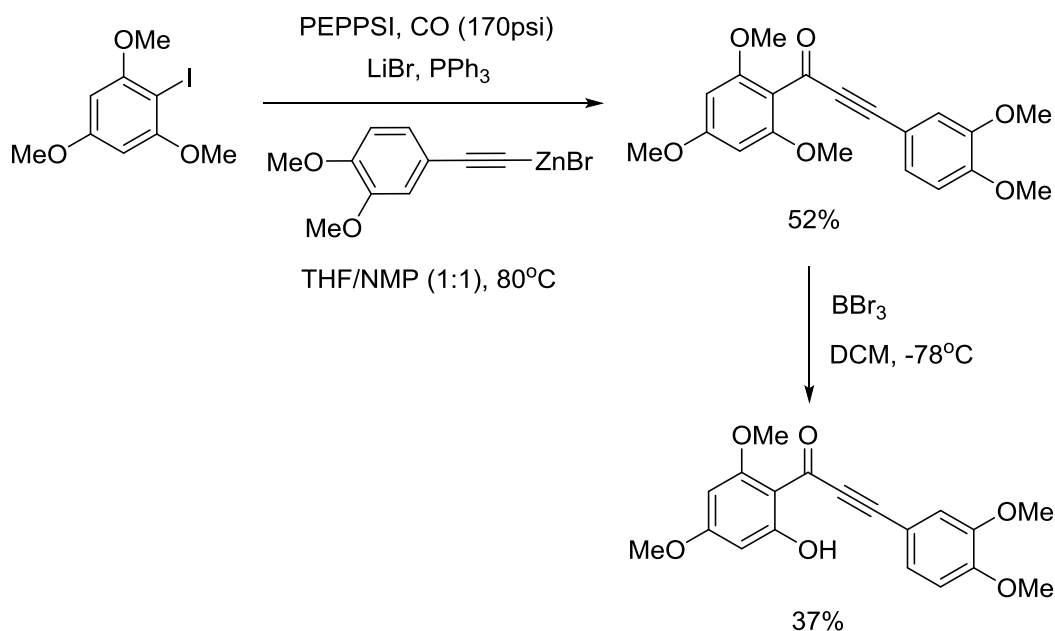


Figure 2: General structure of a sterically hindered *o*-alkynoylphenol

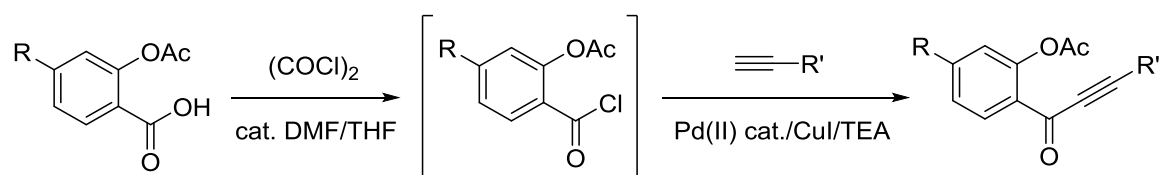


Scheme 15: Preparation of substituted *o*-alkynoylphenol by carbonylative Negishi coupling

Sterically bulky ynones have been prepared by carbonylative cross-coupling of 2,6-dimethyliodobenzene with alkynylboronic esters or alkynylzinc reagents.^[35] Electron-rich 2-iodo-3,5-dimethylanisole proved to be a more challenging substrate, resulting in formation of unwanted direct-coupling byproduct. Recently, carbonylative Negishi

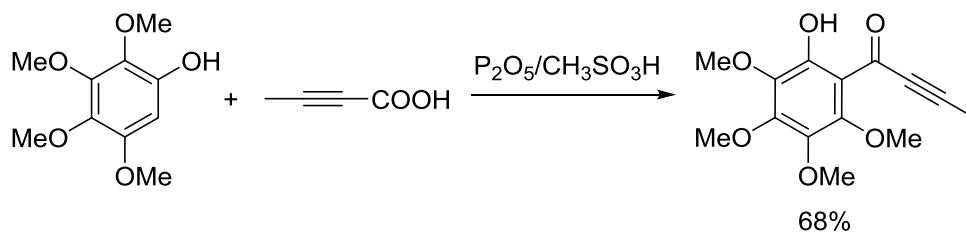
coupling of an alkynylzinc reagent with electron-rich 2,4,6-trimethoxyiodobenzene has been demonstrated in modest yield (Scheme 15).^[36] Selective monodemethylation of *ortho*-hydroxy group is a challenge.

Protected *o*-alkynoylphenol acetates have been prepared *via* Sonogashira coupling of acyl chlorides with terminal alkynes (**Scheme 16**).^[37] No sterically hindered examples have been reported by this method. Due to the limited availability of substituted benzoyl chloride derivatives, it is necessary to prepare the acyl chloride from the corresponding benzoic acid *in situ* using oxalyl chloride.



Scheme 16: Preparation of protected *o*-alkynoylphenol by Sonogashira coupling of acyl chloride with terminal alkyne.

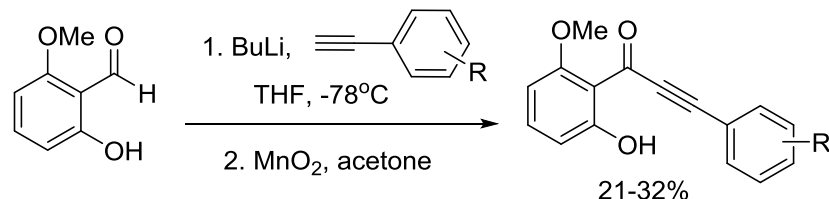
Hindered *o*-alkynoylphenol has been prepared by reacting a substituted phenol and 2-butyneic acid in Eaton's reagent^[38] (10% phosphorus pentoxide in methanesulfonic acid) in 68% yield (Scheme 17).^[39] Unfortunately, this method is very limited since examples of this particular reaction that do not employ a penta-substituted starting material result in a mixture of several products.



Scheme 17: Preparation of sterically bulky *o*-alkynoylphenol using Eaton's reagent.

Di-*ortho* substituted *o*-alkynoylphenol compounds have been prepared by adding a lithium acetylide to an aldehyde and subsequently oxidizing the secondary alcohol to the

corresponding ketone (Scheme 18).^[34f, 34g] Yields of hindered ynones prepared by this method are quite poor and, as previously mentioned, this method is not preferable due to the limited substrate scope of metal acetylides.



Scheme 18: Preparation of sterically bulky *o*-alkynoylphenol by addition of a lithium acetylide to an aldehyde followed by oxidation.

1.3 POTASSIUM ORGANOTRIFLUOROBORATE SALTS

Our laboratory is interested in transition-metal-free reactions of organoboranes. In particular, potassium organotrifluoroborate salts have recently gained momentum as versatile reagents in organic synthesis. Organotrifluoroborate salts are appealing reagents as a result of their straightforward preparation, low toxicity, and inherent stability.^[40] Traditionally, organotrifluoroborate salts have been a convenient alternative to unstable boronic acids for palladium-catalyzed Suzuki-Miyaura coupling.^[41]

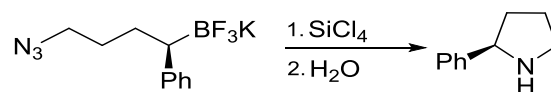
1.3.1 NON-METAL-CATALYZED REACTIONS OF POTASSIUM ORGANOTRIFLUOROBORATE SALTS

Although potassium organotrifluoroborate compounds are well known for their utility in transition metal catalyzed reactions, trifluoroborates have recently emerged as attractive reagents in mild, transition-metal-free reactions.^[42]

1.3.1.1 Lewis acid catalyzed reactions

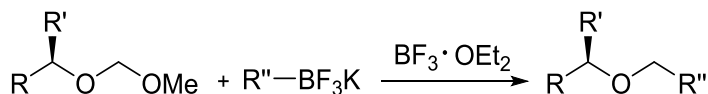
In 2002 Matteson demonstrated the value of organotrifluoroborate salts in non-metal-catalyzed reactions with the preparation of asymmetric secondary amines *via* reaction of

alkyltrifluoroborates with azides (Scheme 19). Here, tetrachlorosilane was used as a defluorinating agent to form a reactive difluoroborane intermediate.^[43]



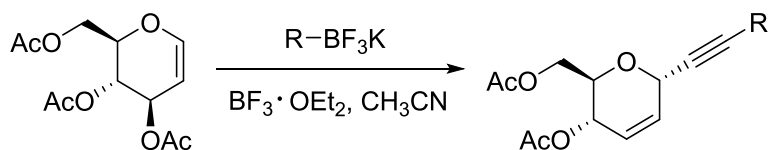
Scheme 19: Lewis acid catalyzed secondary amine preparation from potassium alkyltrifluoroborate and azide.

Bode and coworkers have illustrated a straightforward approach for the preparation of unsymmetrical dialkyl ethers from aryl-, alkenyl, and alkynyltrifluoroborates and mixed acetals (Scheme 20). In this case boron trifluoride diethyletherate was used to strip a fluoride from the salt to form a Lewis acidic organodifluoroborane species.^[44] More recently, the reaction has been improved through the use of a hydroxamate leaving group. This improved the regioselectivity of challenging substrates, reduced the need for a large excess of organotrifluoroborate and Lewis acid, and increased the yield of the ether formation allowing for the use of more challenging electron-withdrawing substrates.^[45]



Scheme 20: Lewis acid catalysed mixed ether formation from potassium organotrifluoroborate and acetal.

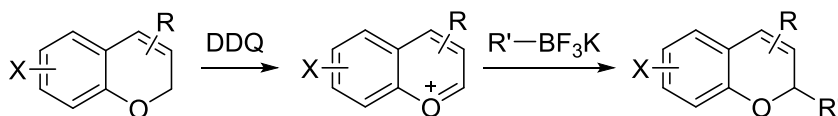
Stefani and coworkers developed a mild and stereoselective method for α -C-glycosidation of D-glucal with a variety of potassium alkynyltrifluoroborates (Scheme 21).^[46] Activation of the alkynyltrifluoroborate with boron trifluoride diethyletherate results in formation of a Lewis acidic difluoroborane species. The difluoroborane intermediate activates acetal protected D-glucal, generating an oxonium cation and a nucleophilic species that attacks from the α -side to regioselectively afford the α -anomer of the alkynyl C-glycoside. Boron trifluoride has also been used to promote the formation of C-glycosides from glycosyl fluorides and alkynyl or alkenyltrifluoroborates with good yields and high diastereoselectivity.^[47]



Scheme 21: Lewis acid catalyzed preparation of α -C-glycosides

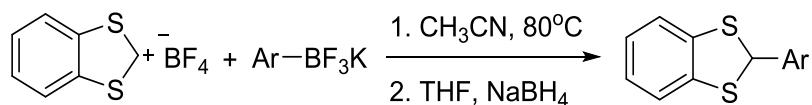
1.3.1.2 Reactions with persistent carbenium ions

DDQ has been demonstrated to promote oxidative carbon-hydrogen cleavage of chromenes to form persistent aromatic oxocarbenium ions. Reaction of these oxocarbenium intermediates with alkynyl, alkenyl, and phenylpotassium trifluoroborates affords the corresponding 2-substituted-2*H*-chromenes (Scheme 22).^[48] In this case the trifluoroborate is acting as a nucleophilic species, attacking the reactive oxocarbenium ion.



Scheme 22: Chromene functionalization *via* nucleophilic attack of potassium organotrifluoroborates on persistent aromatic oxocarbenium ion

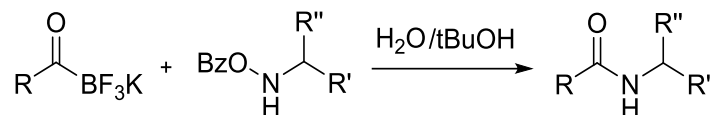
Benzodithiolylum tetrafluoroborate is a commercially available carbenium ionic compound that has been shown to undergo direct reaction with potassium (hetero)aryltrifluoroborates (Scheme 23).^[49]



Scheme 23: Reaction of Benzodithiolylum tetrafluoroborate with potassium aryltrifluoroborate

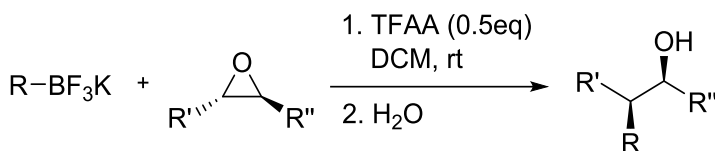
1.3.1.3 Other metal-free reactions of organotrifluoroborates

Acyltrifluoroborates have been used toward the straightforward preparation of amides from *o*-benzoyl hydroxylamines (Scheme 24).^[50] In this case a fluorophile is not required to activate the trifluoroborate species. The mechanism of this particular reaction is unclear, however it likely proceeds *via* a hemiaminal intermediate which forms from attack of the hydroxylamine on the electrophilic carbonyl of the acyltrifluoroborate species.



Scheme 24: Amide formation from Acyltrifluoroborates and hydroxylamines in water.

Regioselective ring-opening of epoxides with potassium organotrifluoroborates has been demonstrated in the presence of trifluoroacetic anhydride (Scheme 25).^[51]



Scheme 25: Trifluoroacetic anhydride promoted stereospecific ring-opening of epoxides with potassium trifluoroborates

1.4 NATURAL PRODUCTS: AURONES AND FLAVONES

Aurones and flavones (Figure 3) are structurally isomeric classes of flavonoid natural products that are recognized as valuable organic scaffolds due to their biological activities.^[52] Aurones are characterized by a 3-benzofuranone scaffold with a benzylidene moiety linked to the 2 position. Flavones are characterized by a 4-benzopyranone scaffold with a benzene ring at the 2 position. Structurally, these functional groups are quite similar, the distinguishing feature being the size of the central oxygen heterocycle.

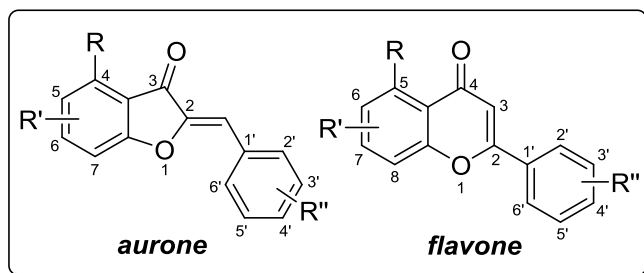


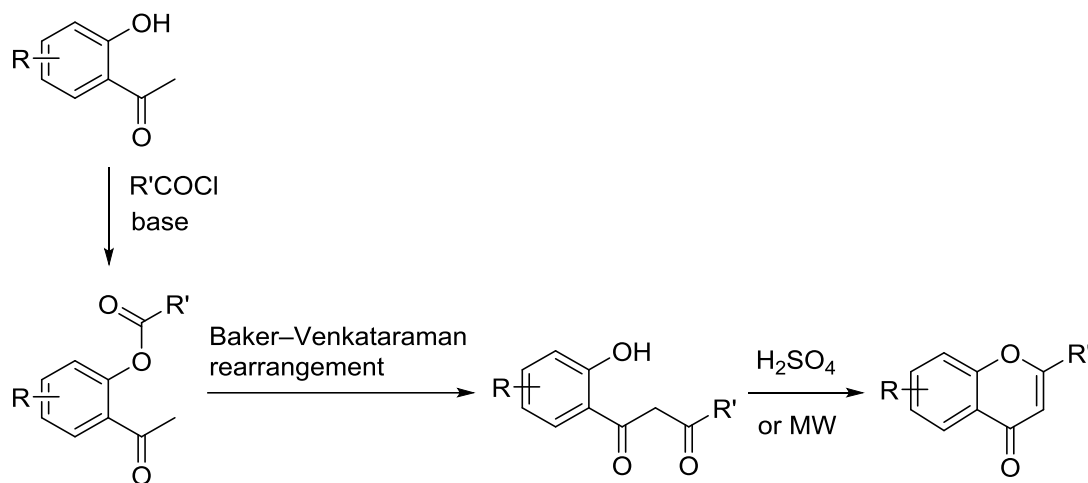
Figure 3: Structures of substituted aurone and flavone scaffolds

There are a wide variety of natural aurone and flavone derivatives as a result of the possibility for functionalization of either aromatic ring. A wide array of hydroxyl and methoxy-substituted flavones can be found in fruits, vegetables, flowers, and barks.^[53] In particular, polymethoxyflavones (PMFs) are an interesting sub-class of flavones due to their biological activities including anti-inflammatory, anti-carcinogenic, and anti-atherogenic properties.^[53a, 54] Furthermore, increased metabolic stability of PMFs has been demonstrated in comparison to unmethylated polyhydroxyflavone analogues.^[55] Potent anti-cancer activity of PMFs has recently been demonstrated.^[56] Aurones are relatively limited in their natural abundance compared to flavones and as a result have been less extensively studied. Also found in some marine organisms, aurones are yellow dyes that contribute to the colouration of many fruits, vegetables, and flowers.^[57] Aurones have been identified as phytoalexins, contributing to the defense mechanisms of plants against infections.^[58] Additionally, functionalized aurones have been demonstrated as functional scaffolds for the modulation of proteins linked to multidrug resistance in cancer chemotherapy.^[59]

1.4.1 SYNTHESIS OF FLAVONES

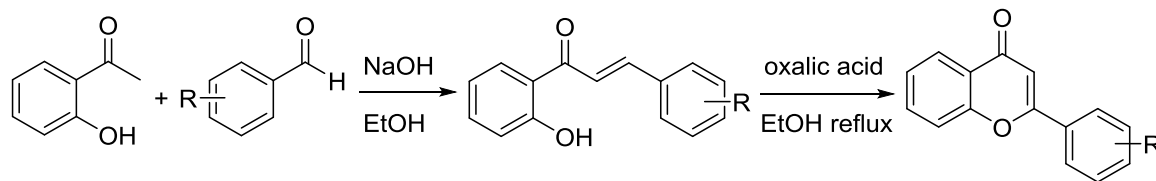
Flavone scaffolds are of particular synthetic interest as a result of the diversity of favourable biological activities that they exhibit. Consequently, a number of methods for the synthesis, transformation, and functionalization of flavones are available.^[60]

Flavones are frequently prepared from β -diketone intermediate prepared using the base-catalyzed Baker-Venkatarman rearrangement of 2-acetoxyacetophenones (Scheme 26).^[61] Harsh conditions such as treatment with concentrated sulfuric acid^[62] or microwave irradiation^[63] are required to promote cyclization of the diketone.



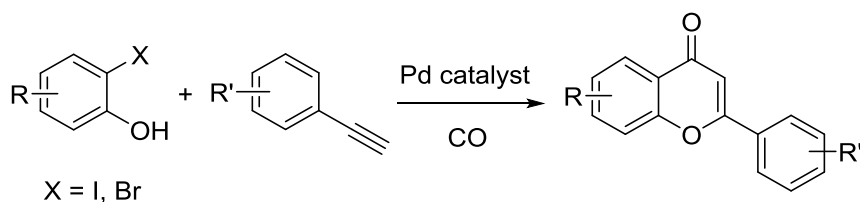
Scheme 26: Flavone synthesis by cyclization of diketone formed by Baker-Venkatarman rearrangement.

An alternative method for the preparation of flavones involves the oxidative cyclization of substituted 2-hydroxy chalcones, which are prepared by an aldol condensation between an aldehyde and a 2-hydroxyacetophenone (**Scheme 27**).^[64]



Scheme 27: Flavone synthesis by oxidative cyclization of 2-hydroxy chalcones.

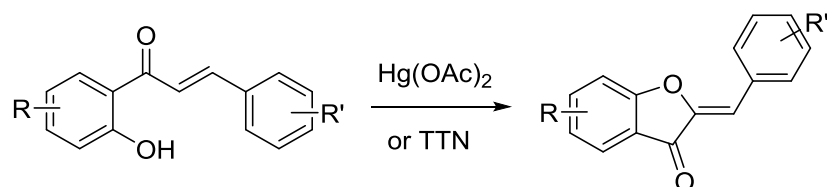
Recently, the preparation of flavones has been achieved by palladium-catalyzed carbonylative Sonogashira coupling of aryl halides with terminal alkynes (Scheme 28).^[65]



Scheme 28: Flavone synthesis by palladium catalyzed carbonylative coupling of terminal alkynes with aryl halides.

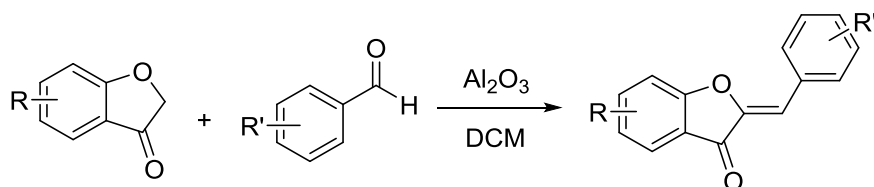
1.4.2 SYNTHESIS OF AURONES

Generally, the synthesis of aurones is achieved by one of two methods: oxidative cyclization of 2'-hydroxychalcones^[66] or aluminum oxide catalyzed condensation of substituted benzaldehydes with benzofuranones.^[67] Oxidative cyclization of 2'-hydroxychalcones may be achieved in the presence of mercury acetate^[66b] or thallium(III) trinitrate (TTN) (Scheme 29).^[66c]



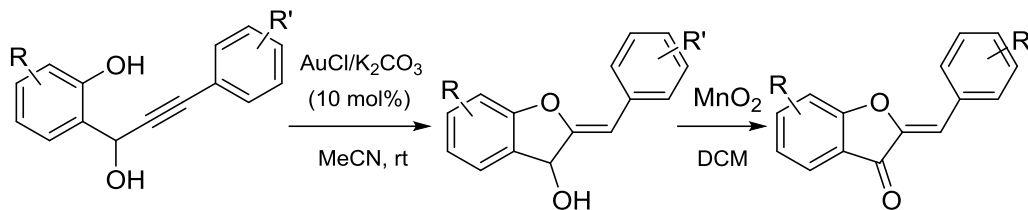
Scheme 29: Oxidative cyclization of 2-hydroxy chalcones to form aurones.

Aluminum oxide catalyzed preparation of aurone scaffolds from benzofuranone and benzaldehydes is straightforward (Scheme 30). This method becomes less trivial if the benzofuranone starting material is not commercially available since the preparation requires multiple steps.^[67a, 67b]



Scheme 30: Aluminum oxide catalyzed aurone synthesis from benzofuranones and benzaldehydes.

Another method for the production of aurones involves the gold(I) catalyzed cyclization of *ortho*-(1-hydroxyprop-2-ynyl)phenols and subsequent oxidation of the secondary alcohol to a ketone (**Scheme 31**).^[68]

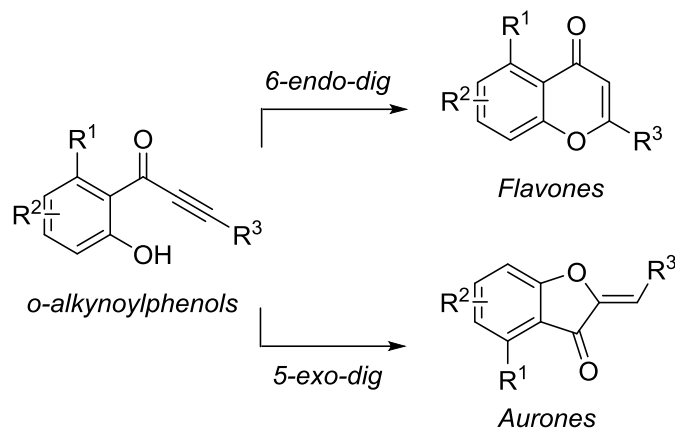


Scheme 31: Aurone synthesis by gold chloride catalyzed cyclization of *ortho*-(1-hydroxyprop-2-ynyl)phenols and subsequent oxidation.

Aurones have also been prepared in good yields by palladium catalyzed carbonylative annulation of terminal alkynes and 2-bromophenols.^[65b] Modification of the ligands employed in the palladium catalyzed reaction makes it possible to favour the formation of aurone products over flavones. In all cases, however, a product mixture was recovered with 3-8% flavone product composition.

1.4.3 CYCLIZATION OF *O*-ALKYNOYLPHENOLS

In addition to the previously discussed methods, both aurone and flavone scaffolds may be obtained *via* cyclization of *o*-alkynoylphenol precursors (Scheme 32). Conventional methods for the preparation of aurones and flavones are associated with disadvantages such as onerous multi-step procedures, harsh reaction conditions, the need for transition metal catalysts, and relatively poor yields. As a result of these deficiencies, the cyclization of *o*-alkynoylphenols is an appealing strategy.



Scheme 32: Cyclization of *o*-alkynoylphenols to form flavone and aurone scaffolds.

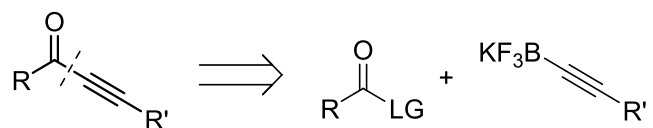
Under basic conditions the 5-*exo* and 6-*endo* ring closure of *o*-alkynoylphenols are competing pathways.^[34a, 34b, 34d] Basic conditions generally favour the 5-*exo* cyclization mode resulting in aurone products, however, this is largely dependent on the nature of the base and the conditions applied. The major product may be influenced by manipulation of the reaction conditions, however accounts in the literature indicate a mixture of both cyclization products.^[34a, 34b, 34d] The 5-*exo* cyclized aurone product is primarily formed by silver (I) ion catalysis, however, trace amounts of the flavone product are also formed.^[34c] Recently, the 5-*exo* cyclization of *o*-alkynoylphenols was also found to be favoured in tributylphosphine-catalyzed reactions.^[34e] Unfortunately, separation of structurally similar aurone and flavone products is not trivial, and therefore methods resulting in a product mixture are not ideal.

Application of the principles of the Morita-Baylis-Hillman reaction makes possible the regioselective 6-*endo* cyclization of *o*-alkynoylphenols.^[69] Exclusive preparation of flavones from *o*-alkynoylphenol precursors may be achieved by 1,4-addition of a nucleophile to the β -carbon of the ynone system. Intramolecular Michael addition and subsequent elimination of the nucleophile results in the 6-*endo* cyclized flavone product.^[34f, 34g, 70] Trifluoromethanesulfonic acid (TfOH) has been successfully employed to promote the exclusive 6-*endo* cyclization of *o*-alkynoylphenols to produce various flavone products using this strategy.^[34f]

1.5 THESIS OBJECTIVE

Section 1.3.1 highlighted the utility of organotrifluoroborate salts as nucleophiles in non-metal-catalyzed reactions. In the presence of a Lewis acid, trifluoroborate salts are converted to a species with nucleophilic character, facilitating an attack towards an electrophilic species.

Our goal was to develop a straightforward, metal-free procedure for the preparation of ynones. Much like traditional methods for ynone synthesis, our retrosynthetic approach was to make a disconnection between the carbonyl and the triple bond of the desired functional group (Scheme 33). In this case, however, we would avoid the use of alkynyl metallic nucleophiles. We hypothesized that, in the presence of a Lewis acid, an alkynyl trifluoroborate salt could react with an electrophilic carbonyl in order to form an ynone functional group.



Scheme 33: Retrosynthetic analysis for the metal-free preparation of ynones

The overall objective of this research is to explore the formation of new carbon-carbon bonds using potassium organotrifluoroborate salt starting materials. Specifically, the goal of this project is to develop and optimize a convenient method for the preparation of functionalized ynones and apply it towards the straightforward synthesis of a variety of aurone and flavone natural product scaffolds.

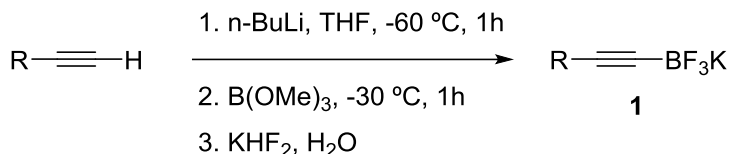
2. EXPERIMENTAL METHODS

2.1 GENERAL EXPERIMENTAL CONSIDERATIONS

Unless otherwise noted, all reagents and materials were obtained from commercial suppliers and used without further purification. Reactions were carried out under air unless otherwise noted. NMR characterization data was obtained at 25 °C on an Oxford AS400 NMR spectrometer as solutions in deuterated solvents (CDCl_3 and DMSO-d_6 obtained from Cambridge Isotope Laboratories, Inc.). ^1H NMR spectra were recorded at 400 MHz and referenced to the residual solvent peak at 7.24 ppm for CDCl_3 and 2.50 ppm for DMSO-d_6 . $^{13}\text{C}\{^1\text{H}\}$ NMR spectra were recorded at 100MHz and referenced to the residual solvent peak at 77.00 ppm for CDCl_3 and 39.51 ppm for DMSO-d_6 . ^{19}F NMR spectra were collected at 400 MHz and referenced to the lock position. ^{11}B NMR spectra were collected at 100 MHz and referenced to $\text{BF}_3\cdot\text{OEt}_2$. FT-IR spectra were recorded on a Nicolet Avatar 370 DTGS spectrometer or a Bruker ALPHA spectrometer and only partial data are provided. High resolution mass spectra (HRMS) were obtained by the University of Michigan, Department of Chemistry. An Agilent Q-TOF mass spectrometer was used for samples analyzed by electrospray (ESI) and atmospheric-pressure chemical ionization (APCI) and a Waters VG 70-250-S magnetic sector mass spectrometer was used for samples analyzed by electron impact ionization (EI). Flash column chromatography on silica gel (60 Å, low acidity, obtained from EMD Chemicals Inc.) was performed using reagent grade solvents unless otherwise specified. Tetrahydrofuran (THF) and triethylamine (TEA) was purified using an Innovative Technology PS-MD-3 solvent purification system.

2.2 PREPARATION OF POTASSIUM ALKYNYLTRIFLUOROBORATES

Potassium alkynyltrifluoroborate salts were prepared from terminal alkynes according to a procedure modified from Stefani and coworkers.^[46]



General Procedure for the preparation of potassium alkynyltrifluoroborate salts: A solution of the indicated terminal alkyne (1.0 equiv.) in dry THF was cooled to -60 °C under argon atmosphere, *n*-BuLi (1.0 equiv.) was added dropwise and the solution was stirred for 1 h at this temperature. Trimethylborate (1.5 equiv.) was added dropwise at -30 °C. The solution was stirred at -30 °C for 1 h and allowed to warm to room temperature for 1 h. A saturated aqueous solution of potassium hydrogen difluoride (6.0 equiv.) was added at -20 °C. The mixture was allowed to stir for 1 h at -20 °C followed by 1 h at room temperature. The solvent was removed, and the resulting solid was placed under vacuum for 2 h. The solid was washed several times with hot acetone which was decanted off and collected. The product was precipitated from acetone with diethyl ether and cooled to 4 °C to complete precipitation. The crystalline solids were collected by suction filtration and dried under vacuum to afford trifluoroborate salts **1a-g** (Figure 4).

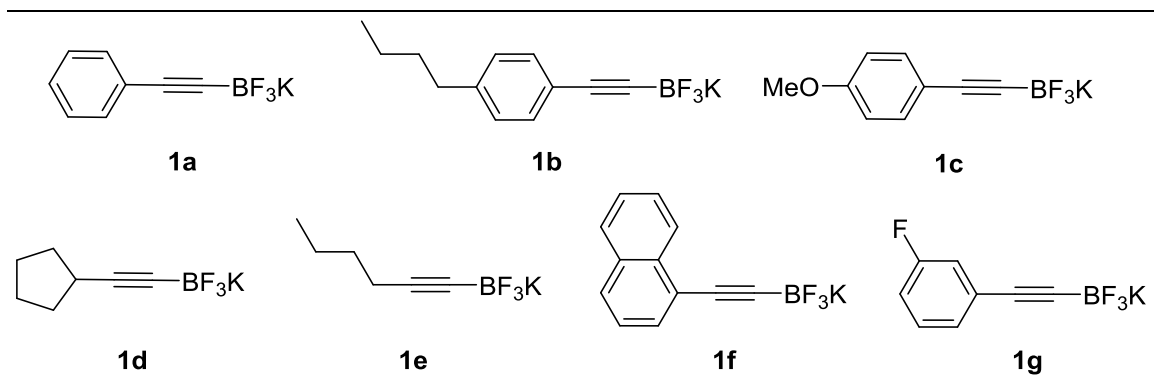
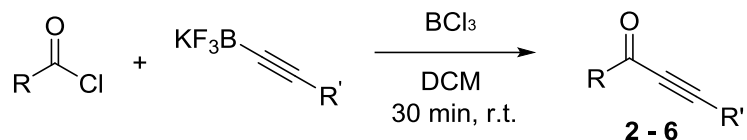


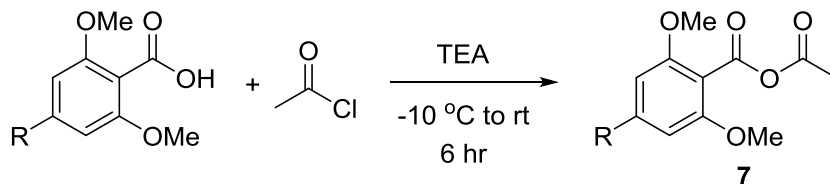
Figure 4: Alkynyltrifluoroborate salts used in this manuscript.

2.3 PREPARATION OF YNONES



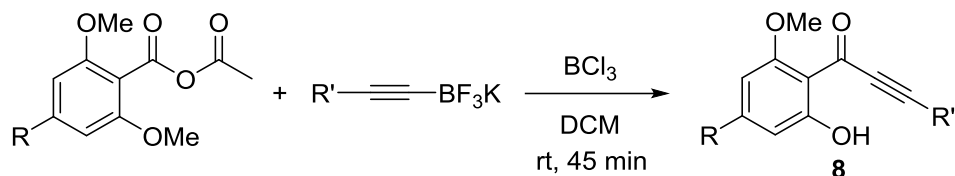
General Procedure for the synthesis of ynones from acyl chlorides and potassium alkynyltrifluoroborate salts: Boron trichloride (1M solution in DCM) was placed in a 2 mL vial containing a stir bar and a 0.2M solution of the indicated potassium alkynyltrifluoroborate salt in anhydrous DCM. The vial was capped, sonicated for 30 s, and stirred for 15 min at room temperature. The indicated acyl chloride was added dropwise to the vial, capped and stirred for 30 min. The reaction was quenched with cold water and extracted into ethyl acetate. The organic layer was washed twice with water and once with brine. The organic layer was dried over MgSO_4 and concentrated. The product was purified by flash column chromatography using hexanes/ethyl acetate and concentrated to afford the ynone products **2a-m** (Figure 5, p 30), **3a-c**, **4a-c**, **5a**, **6a** (Figure 7, p 33).

2.4 PREPARATION OF MIXED ANHYDRIDES



General Procedure for the preparation of mixed anhydrides from carboxylic acids and acetyl chloride: Triethylamine (2.0 equiv.) was added dropwise at ambient temperature to a 0.25M solution of the indicated benzoic acid (1.0 equiv.) in dry THF. The mixture was cooled to $-10\text{ }^\circ\text{C}$ and acetyl chloride (1.1 equiv.) was added dropwise. The mixture was stirred at room temperature for 6 hours, filtered, and evaporated. The crude product was filtered through a pad of silica with ethyl acetate to afford mixed anhydrides **7a** ($\text{R} = \text{OMe}$) and **7b** ($\text{R} = \text{H}$).

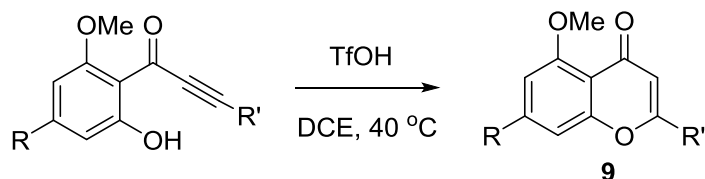
2.5 PREPARATION OF O-ALKYNOYLPHENOLS



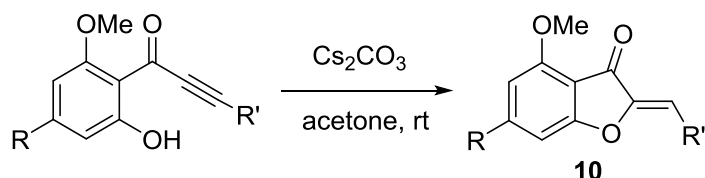
General procedure for the synthesis of *o*-alkynoylphenols from mixed anhydrides and potassium alkynyltrifluoroborate salts: Boron trichloride (1M in DCM, 3.0 equiv.) was added dropwise to the indicated alkynyltrifluoroborate salt (1.5 equiv.) in anhydrous DCM at room temperature under air. The capped reaction was sonicated for 30 s and stirred an additional 20 min. The selected anhydride (1.0 equiv.) was added to the reaction mixture in one lot, capped, and stirred at room temperature for 45 min. The reaction mixture was quenched with cold water and extracted into ethyl acetate. The organic layer was washed twice with water and once with brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography to afford *o*-alkynoylphenol products **8a-f** (Figure 8, p 38).

2.6 CYCLIZATION OF *O*-ALKYNOYLPHENOLS

Flavones were prepared from *o*-alkynoylphenols according to a procedure modified from Doi and coworkers.^[34f]



General Procedure for the 6-*endo* cyclization of *o*-alkynoylphenols: TfOH (5.0 equiv.) was added dropwise to a 0.25M solution of the indicated *o*-alkynoylphenol in 1,2-dichloroethane at 0 °C under argon. The mixture was stirred at 40°C and then quenched with saturated aqueous NaHCO₃ at 0 °C. The organic layer was separated and the aqueous layer extracted twice with ethyl acetate. The combined organic layers were washed with brine, dried over MgSO₄, and filtered. The filtrate was concentrated and the crude product was purified by flash chromatography on silica gel to afford flavone products **9a-e** (Figure 9, p 41).



General Procedure for the 5-*exo* cyclization of *o*-alkynoylphenols: Cs₂CO₃ (3.0 equiv.) was added in one lot to a 0.1M solution of *o*-alkynoylphenol in acetone at ambient temperature under air. After 30 minutes the reaction was quenched with aqueous NH₄Cl. The aqueous layer was extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over MgSO₄, and filtered, and evaporated to afford aurone products **10a-e** (Figure 9, p 41).

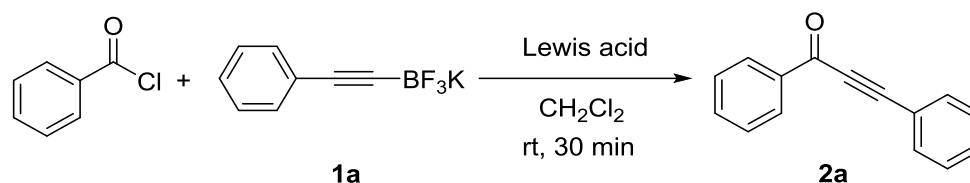
3. PREPARATION OF YNONES FROM ACYL CHLORIDES AND POTASSIUM ALKYNYLTRIFLUOROBORATE SALTS

3.1 OPTIMIZATION OF REACTION CONDITIONS

Initially, we focused on the preparation of ynone **2a** from benzoyl chloride and phenylacetylene trifluoroborate **1a**. In order to find a suitable catalyst, several Lewis acids were screened (Table 1). Silica gel,^[71] silicon tetrachloride,^[41] and boron trifluoride^[44-45] have been reported to convert organotrifluoroborates into organodihaloboranes. Unfortunately, these Lewis acids did not promote the formation of the desired ynone product (Table 1, entries 1-3). Product **2a** was obtained in 24% yield when iron(III) chloride was employed (Table 1, entry 4). Aluminum(III) chloride is known to promote the formation of oxocarbenium ions in Friedel-Crafts acylation reactions.^[72] Indeed, we obtained the desired ynone **2a** in 62% yield in the presence of the aluminum trichloride catalyst under anhydrous conditions (Table 1, entry 5).

Upon running the reaction under non-anhydrous conditions under air a similar was obtained (Table 1, entry 6). When a controlled quantity of water was added to the reaction the yield did not improve (Table 1, entry 7). Once it became apparent that the reaction can tolerate moisture, subsequent reactions (Table 1, entries 8-15) were performed under air in non-dried glassware.

Next, attempts were made to optimize the solvent system. Aprotic solvents including THF, toluene, and dichloroethane as well as polar solvents such as DMSO and acetonitrile were tested with little success (Table 1, entries 8-12). The poor results of the solvent optimization made it apparent that dichloromethane is well suited to this particular reaction.

Table 1: Optimization of Conditions for the Preparation of Ynone 2a^a.

entry	Lewis acid	Lewis acid (equiv)	solvent	yield (%)
1 ^b	SiO ₂	16.5	CH ₂ Cl ₂	0
2	SiCl ₄	1.0	CH ₂ Cl ₂	trace
3	BF ₃ ·OEt ₂	1.0	CH ₂ Cl ₂	trace
4 ^b	FeCl ₃	1.0	CH ₂ Cl ₂	24
5 ^c	AlCl ₃	1.0	CH ₂ Cl ₂	62
6 ^d	AlCl ₃	1.0	CH ₂ Cl ₂	66
7 ^e	AlCl ₃	1.0	CH ₂ Cl ₂	60
8	AlCl ₃	1.0	THF	trace
9	AlCl ₃	1.0	toluene	trace
10	AlCl ₃	2.0	ClCH ₂ CH ₂ Cl	33
11	AlCl ₃	1.0	DMSO	trace
12	AlCl ₃	2.0	acetonitrile	trace
13	AlCl ₃ ·6H ₂ O	1.0	CH ₂ Cl ₂	0
14 ^b	BCl ₃	1.5	CH ₂ Cl ₂	67
15	BBr ₃	1.0	CH ₂ Cl ₂	20

^aReactions were run with 1 equiv benzoyl chloride and 1 equiv potassium phenylacetylenetrifluoroborate **1a**. ^b1.5 equiv **1a**. ^canhydrous conditions. ^dthe reaction was done in non-dried glassware under air.

^eanhydrous conditions + 1 μ L of water.

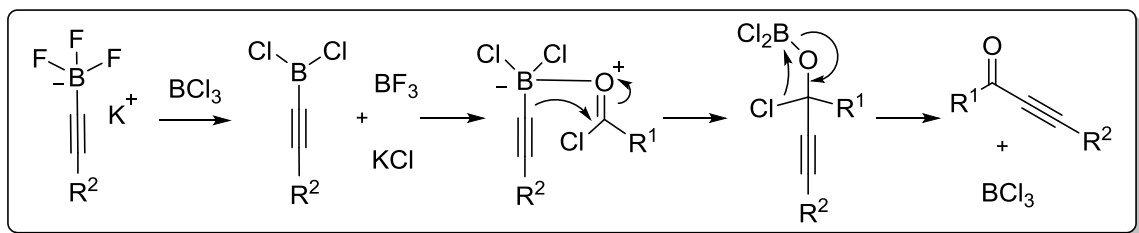
Unfortunately, there were some issues with the reproducibility of the results of the aluminum chloride catalyzed reactions. Exposure to air can result in the formation of aluminum(III) chloride hydrate. We hypothesized that formation of the hydrate on the

surface of the catalyst was inhibiting the reaction. In order to test this hypothesis, commercially available aluminum(III) chloride hexahydrate was tested under the developed reaction conditions. As suspected, the hydrated form of the aluminum trichloride catalyst was inactive and no product formation was observed (Table 1, entry 13).

Therefore, we continued our search for a suitable catalyst. We were pleased to obtain product **2a** in similar yields with better consistency upon employment of a boron trichloride (Table 1, entry 14). Since boron trifluoride and boron trichloride catalysts have been tested, we decided to also try boron tribromide as a catalyst. It catalyzed the formation of product **2a** in a modest 20% yield (Table 1, entry 15).

3.2 PROPOSED MECHANISM

Scheme 34 illustrates the proposed mechanistic pathway for the ynone formation reaction. Interaction of the alkynyltrifluoroborate species with boron trichloride results in the formation of an organodichloroborane species.^[73] The electrophilic organodichloroborane species coordinates with the acyl chloride resulting in the formation of a nucleophilic borate and an activated carbonyl group. A tetrahedral intermediate is formed by transfer of the alkynyl group from the borate to the electrophilic carbonyl.^[74] The desired ynone product is formed upon collapse of the tetrahedral intermediate.



Scheme 34: Proposed mechanistic pathway for the synthesis of ynones

3.3 RESULTS AND DISCUSSION: ACYL CHLORIDE SCOPE

Upon successful optimization of the conditions for the preparation of ynone **2a**, the next step was to explore the scope and functional group tolerance of the acyl chloride starting material.

3.3.1 SUCCESSFUL EXPERIMENTS

In order to test the substrate scope, phenylacetylene trifluoroborate **1a** was submitted to the reaction conditions with a variety of acyl chlorides (Figure 5).

Unsubstituted naphthyl and biphenyl acyl chlorides afforded the expected ynone products in synthetically useful yields (**2b,c**). Reactions with derivatives of benzoyl chloride bearing electron-donating methoxy, methyl, and butyl substituents in the *para*-position as well as the sterically hindered *ortho*-methylbenzoyl chloride proceeded to completion, furnishing the expected products in excellent yields (**2d-g**). Conversely, electron-withdrawing group bearing acyl chlorides proved to be more challenging substrates (**2h,i,m**). Interestingly, the yield of reaction of *ortho*-chlorobenzoyl chloride with **1a** was nearly double compared to that of *para*-chlorobenzoyl chloride (**2h, i**). It is possible that the steric interaction of the *ortho*-substituent forces the carbonyl functional group out of the plane of the aromatic ring, offsetting the electron-withdrawing character of the group. We also had success with non-aromatic acyl chlorides (**1j-m**). Cyclohexyl and cyclopropyl carbonyl chlorides as well as acetyl chloride reacted to form the expected ynones in good yields (**2j-l**). 4-Bromobutyryl chloride reacted to furnish the corresponding ynone in 39% yield (**2m**). This is particularly noteworthy since, to our knowledge, this is the first procedure for the synthesis of ynones that tolerates an alkyl bromide functional group.

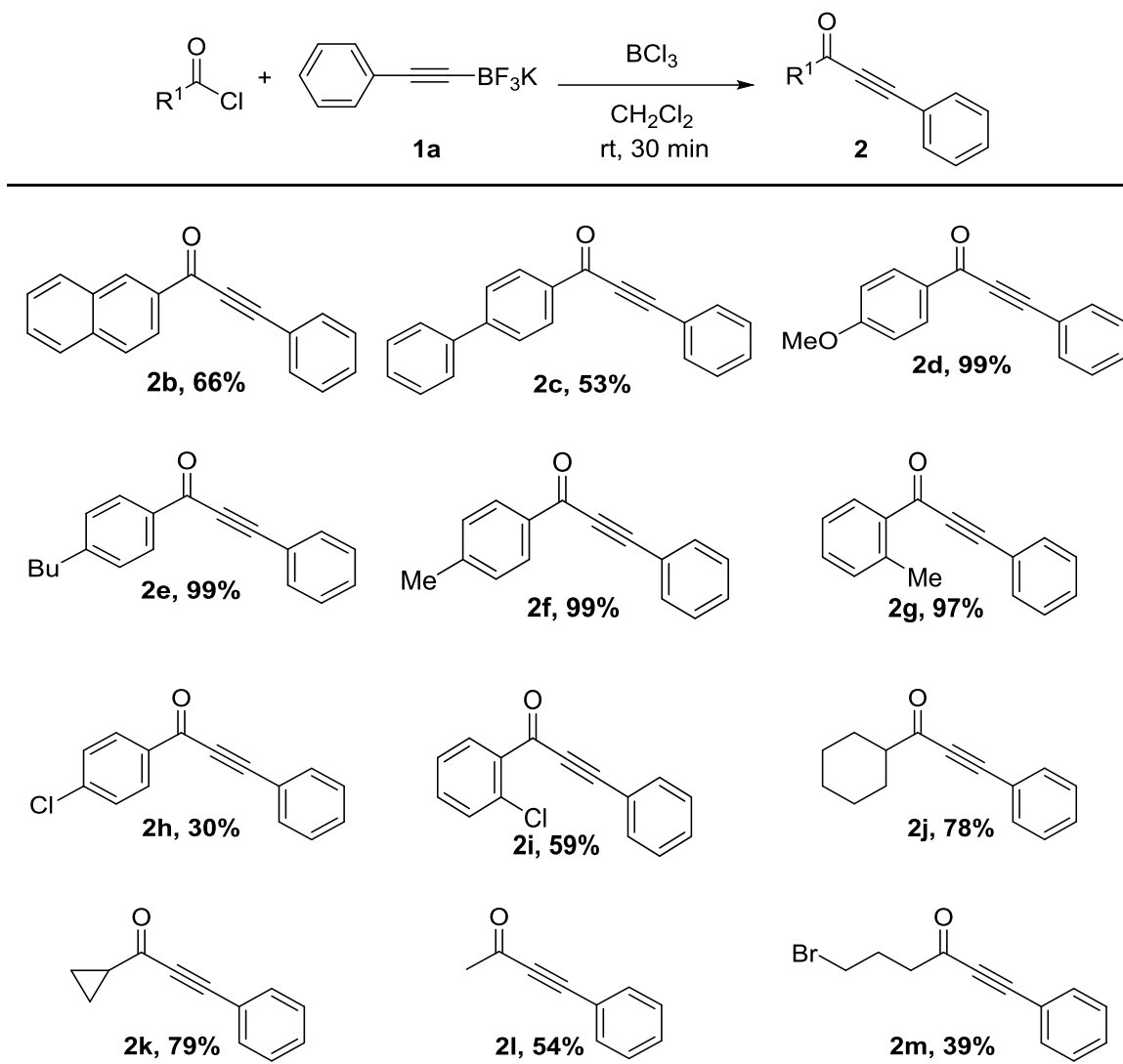


Figure 5: Products obtained by the reaction of phenylacetylene trifluoroborate salt **1a with various acyl chlorides.**

Reactions were run with 1 equiv of acyl chloride, 1.5 equiv potassium phenylacetylenetrifluoroborate **1a**, and 1.5 equiv boron trichloride.

3.3.2 UNSUCCESSFUL EXPERIMENTS

The substrate scope of this methodology allows for the use of aryl and aliphatic acyl chlorides with a variety of functional groups present (Figure 5). However, not all acyl chlorides submitted to the reaction conditions resulted in the clean formation of the desired product (Figure 6).

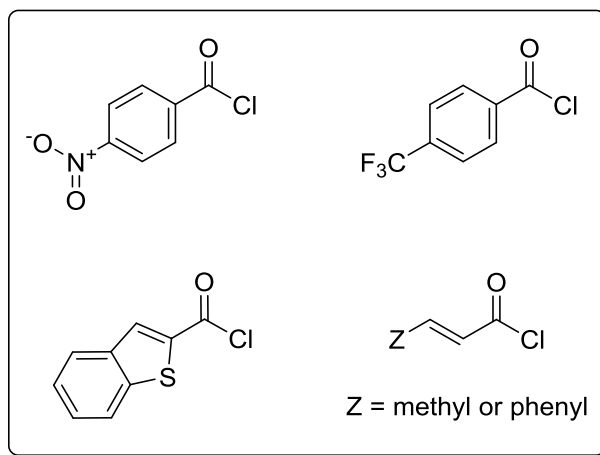


Figure 6: Acyl chlorides that did not result in ynone formation

Benzoyl chloride derivatives bearing strongly electron withdrawing groups such as 4-nitrobenzoyl chloride and 4-trifluoromethylbenzoyl chloride did not result in the formation of ynone products under the optimized conditions. The strongly electron-withdrawing nature of these groups results in an electron deficient carbonyl group that is less likely to act as a Lewis base. The reaction may not proceed since the carbonyl group is not prone to donate a pair of electrons to the organodichloroborane species and therefore the alkynyl group transfer does not take place (Scheme 34).

Acyl chlorides bearing Lewis basic heteroatom functional groups such as benzothiophene-2-carbonyl chloride were also found to be unsuitable for the reaction. In this case, the basic electron pairs on the sulfur group may interfere with the reaction by interacting with the trivalent dichloroborane species.

Alkenyl acyl chlorides such as *trans*-crotonyl chloride and *trans*-cinnamoyl chloride also proved unsuccessful in generating the desired ynones under the developed conditions. Side products may be produced as a result of transfer of the alkynyl group to the β -carbon. Additionally, trivalent boron is known to interact with alkenes, for example in hydroboration reactions.^[75] As a result, the presence of a double bond can result in a complicated mixture of products

3.4 RESULTS AND DISCUSSION: TRIFLUOROBORATE SCOPE

The scope of the methodology was further explored by submitting several other examples of potassium alkynyltrifluoroborate salts to the developed reaction conditions (Figure 7). Derivatives of phenylacetylene trifluoroborate bearing electron-donating butyl- and methoxy- substituents in the *para*- position reacted with aromatic and aliphatic acyl chlorides to form the anticipated ynones in good to excellent yields (**3a-c**, **4a-c**). In most cases, the presence of the electron donating group on the alkynyltrifluoroborate significantly improved the yield of the reaction. For example, the yield of ynone obtained from 4-bromobutyryl chloride increased from 39% when reacted with neutral phenylacetylenetrifluoroborate (**2m**, Figure 5) to 81% when reacted with electron-rich *para*-butyl phenylacetylenetrifluoroborate (**3c**). The yield of ynone obtained from neutral benzoyl chloride increased from 67% for phenylacetylenetrifluoroborate (**2a**, Table 1) to 75% and 87% for electron-rich *para*-methoxy and *para*-butyl phenylacetylenetrifluoroborates, respectively (**3a**, **4a**). Aliphatic alkynyltrifluoroborate salt derivatives were found to be less reactive starting materials. However, modest yields were obtained when electron-rich *para*-methoxybenzoyl chloride was reacted with hexynyl- and cyclopentylethynyl trifluoroborate (**5a**, **6a**).

The appearance of an impurity in the fluorine NMR may account for some of the difficulties encountered with the cyclopentylethynyl and hexynyl trifluoroborate salts. A peak that appears near 148.35ppm, representative of a boron tetrafluoride impurity,^[76] is much more pronounced for these particular salts than the other trifluoroborate salts that had much better reactivity.

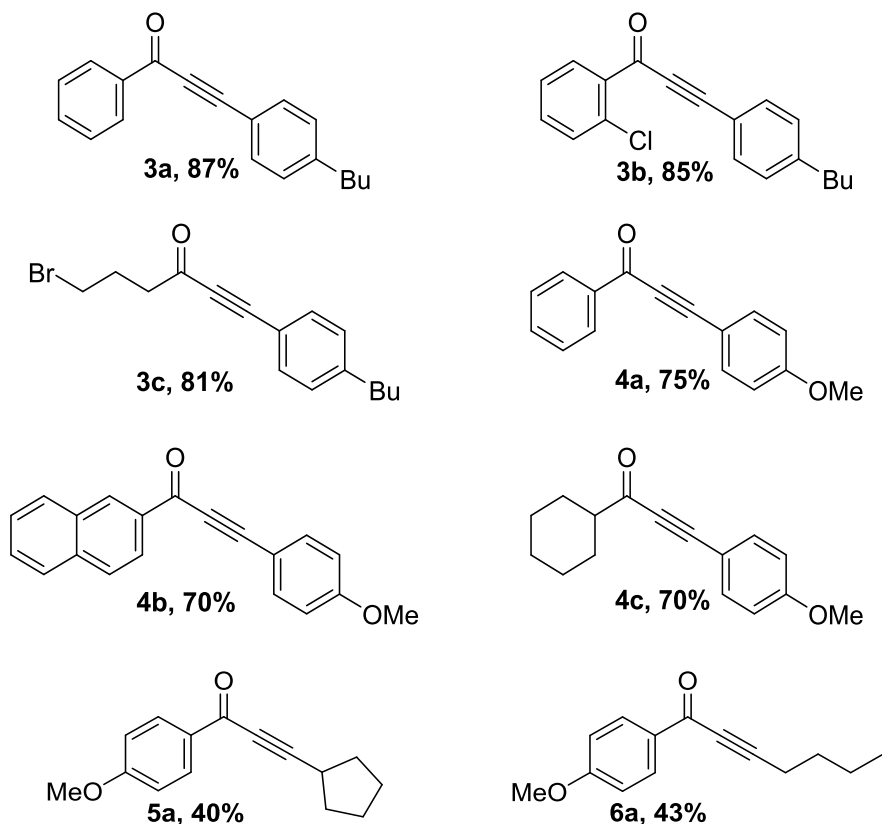
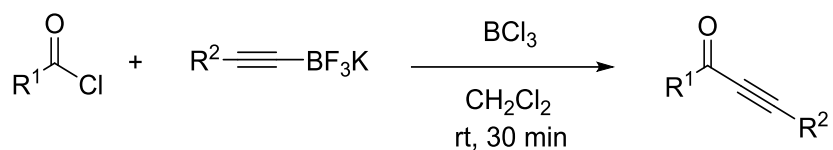


Figure 7: Reactions of various alkynyltrifluoroborates with acyl chlorides.

Reactions were run with 1 equiv of acyl chloride, 2.5 equiv potassium alkynyltrifluoroborate salt and 2.5 equiv boron trichloride.

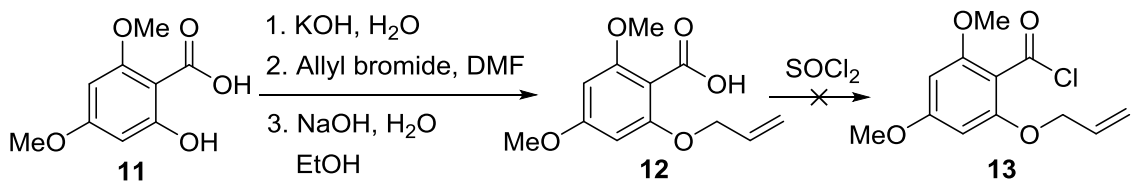
4. PREPARATION OF STERICALLY HINDERED YNONES

Once a procedure has been developed for the preparation of ynone from alkynyltrifluoroborate salts, we began to work towards the preparation of sterically hindered ynone, particularly *o*-alkynoylphenols.

4.1 METHODOLOGY DEVELOPMENT

4.1.1 ATTEMPTS TO PREPARE STERICALLY HINDERED YNONES VIA ACYL CHLORIDE INTERMEDIATE

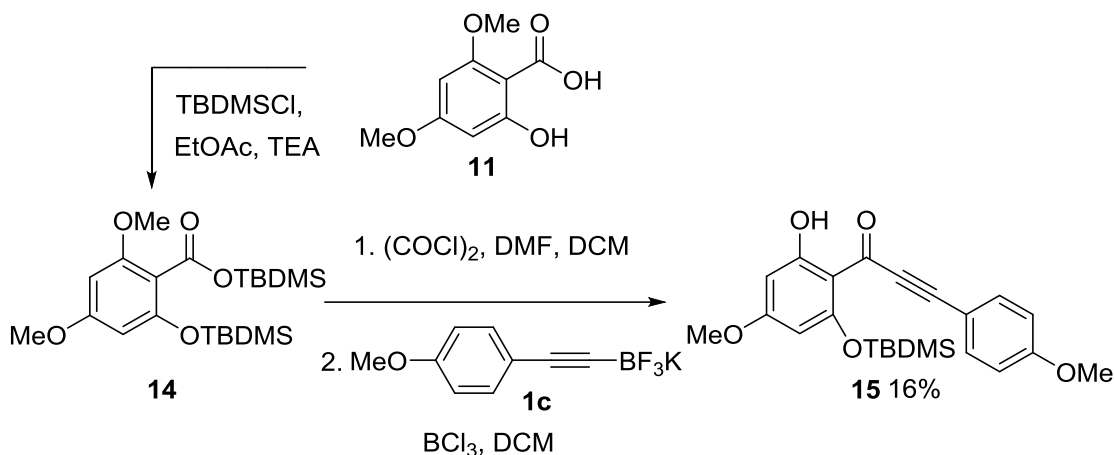
The limited commercial availability of substituted benzoyl chloride derivatives prompted us to explore the use of substituted benzoic acid derivatives as starting materials. Initially, we attempted to convert the sterically hindered *ortho*-hydroxy substituted benzoic acid **11** to an acyl chloride, which could subsequently be submitted to the developed conditions for ynone preparation (Scheme 35). Direct conversion of acid **11** to an acyl chloride using thionyl chloride was not successful. Allyl bromide was used to protect the acid and phenol functional groups. Selective deprotection of the acid group with sodium hydroxide followed by exposure to thionyl chloride was expected to produce protected benzoyl chloride **13**. Once compound **13** is prepared, conversion to the desired ynone is expected to be straightforward. Unfortunately, the conditions required to convert **12** to **13** resulted in some decomposition of the starting material making isolation of clean product a challenge. In addition to the challenges encountered, the number of steps required for this procedure is inconvenient and, therefore, we decided to seek alternative methods.



Scheme 35: Attempted synthesis of benzoyl chloride 3.

Our next strategy was to protect the carboxylic acid starting material using *tert*-butyldimethylsilyl chloride. Protected acid **14** can be directly transformed to an acyl chloride using oxalyl chloride.^[77] The protected acyl chloride was then reacted with *para*-methoxy phenylacetylenetrifluoroborate **1c** under the developed reaction conditions

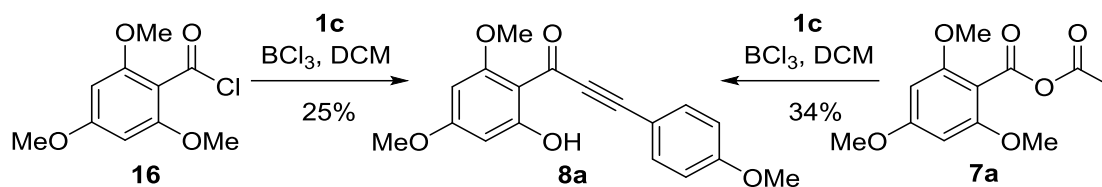
(Scheme 36). Ynone formation did proceed as expected and, additionally, the simultaneous demethylation of the *ortho*-methoxy group was observed. Mono-demethylated ynone product **15** was obtained in 16% yield. The poor yield of this reaction may be attributed to impurities in the acyl chloride intermediate, steric bulk associated with the silyl protecting group, as well as insufficient boron trichloride available to both catalyze the transfer of the alkynyl group of the trifluoroborate^[73-74] and demethylate the *ortho*-methoxy group.^[78]



Scheme 36: Formation of *ortho*-demethylated ynone from *ortho*-hydroxy substituted benzoic acid.

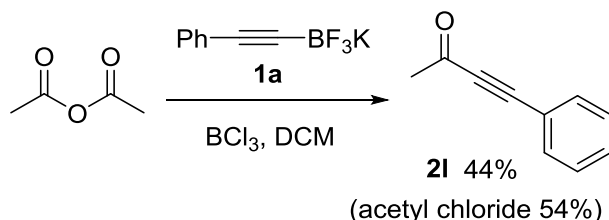
4.1.2 PREPARATION OF YNONES FROM ANHYDRIDES

The observed *ortho*-demethylation under the optimized reaction conditions led us to begin using 2,4,6-trimethoxy substituted starting materials in place of the more costly *ortho*-hydroxy substituted acid. 2,4,6-trimethoxybenzoic acid was converted to acyl chloride **16** using oxalyl chloride. Conversion to **16** was incomplete, however, we proceeded with the next step of the synthesis. The anticipated *ortho*-demethylated ynone **8a** was obtained in 25% yield when **16** was submitted to the boron trichloride catalyzed conditions in the presence of *para*-methoxy phenylacetylenetrifluoroborate **1c** (Scheme 37). Incomplete conversion of the acid starting material to the acyl chloride intermediate may have contributed to the poor yield.



Scheme 37: Preparation of sterically hindered ynone from mixed anhydride and acyl chloride starting materials.

The need for harsh reaction conditions to convert the commercially available carboxylic acid starting material to the desired acyl chloride in addition to challenges with incomplete conversion prompted us to explore alternative starting materials. Anhydrides have similar reactivity to acyl chlorides, and, therefore, we hypothesized that an anhydride substrate might form the desired ynone product under the same conditions. As a proof of concept we submitted acetic anhydride to the optimized reaction conditions in the presence of phenylacetylenetrifluoroborate **1a** (Scheme 38). We were pleased to obtain the expected ynone **2l** in 44% yield, a 10% reduction from the yield obtained for the analogous reaction using acetyl chloride. The slightly reduced yield was expected since anhydrides are less reactive than acyl chlorides.

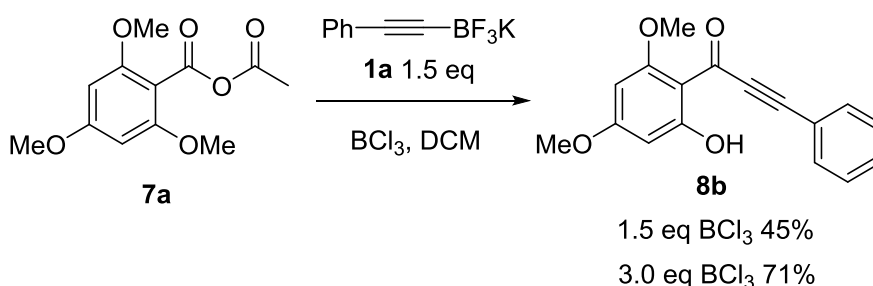


Scheme 38: Ynone preparation from acetic anhydride and phenylacetylene trifluoroborate.

With the knowledge that anhydrides can react with trifluoroborates to form ynones, we set out to prepare mixed anhydride **7a** from 2,4,6-trimethoxybenzoic acid and acetyl chloride in the presence of triethylamine.^[79] Given that electron-donating substituents favour product formation under the developed methodology, we predicted that there would be insignificant formation of the unwanted acetyl ynone side product upon submission of the mixed anhydride to the developed conditions. We were pleased to

obtain *o*-alkynoylphenol **8a** in 34% yield on our first attempt to react the trimethoxy substituted mixed anhydride starting material with *para*-methoxy phenylacetylenetrifluoroborate **1c** (Scheme 37).

A 45% yield of the expected *ortho*-demethylated ynone product was obtained when trimethoxy substituted mixed anhydride **7a** was reacted with 1.5 equivalents of phenylacetylenetrifluoroborate **1a** in the presence of 1.5 equivalents of boron trichloride catalyst (Scheme 39). We hypothesized that boron trichloride now performs the dual function of catalyzing the transfer of the alkynyl group^[73-74] and selective *ortho*-demethylation of a methoxy group.^[78] This led us to increase the number of equivalents of boron trichloride in order to ensure that both product formation and demethylation takes place. Doubling the quantity of boron trichloride catalyst to 3.0 equivalents resulted in a yield increase to 71% for ynone **8b** (Scheme 39).



Scheme 39: Preparation of *ortho*-demethylated ynone from mixed anhydride starting material.

4.2 RESULTS AND DISCUSSION: PREPARATION OF STERICALLY HINDERED *O*-ALKYNOYLPHENOLS

Once the conditions for the straightforward preparation of sterically hindered *o*-alkynoylphenols have been established, we set out to explore the scope of the reaction by preparing several examples from substituted mixed anhydrides and alkynyltrifluoroborate salts (Figure 8). Good yields of the desired *o*-alkynoylphenols were obtained when phenylacetylenetrifluoroborate **1a** was reacted with 2,4,6-trimethoxy and

2,6-dimethoxy substituted mixed anhydrides (**8b-c**). 1-Ethynylnaphthyl trifluoroborate also reacted with 2,6-dimethoxy substituted mixed anhydride under the developed conditions to produce *o*-alkynoylphenol **8e** in good yield. When electron-rich *para*-methoxy phenylacetylenetrifluoroborate **1c** was reacted with the trimethoxy substituted mixed anhydride with the optimized equivalents of catalyst the yield increased from 34% to 49%. It appears that the presence of multiple electron-donating groups can reduce the yield of the reaction. When **1c** was reacted with the dimethoxy substituted mixed anhydride the desired product was obtained in 76% yield (**8d**). Conversely, electron deficient *meta*-fluorophenylacetylene trifluoroborate **1g** furnished a relatively modest yield of *o*-alkynoylphenol product **8f** when reacted with the dimethoxy substituted mixed anhydride.

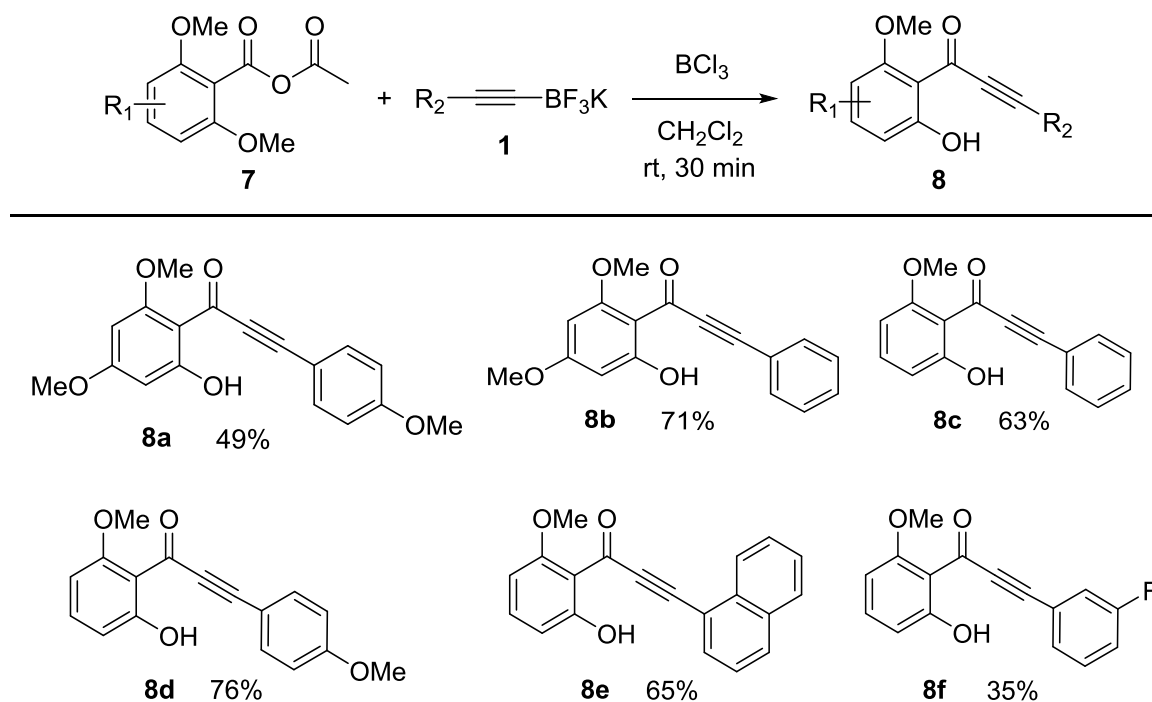


Figure 8: Preparation of sterically hindered *ortho*-demethylated ynones from mixed anhydride starting materials.

Reactions were performed with anhydride **7** (0.1 mmol), alkynyltrifluoroborate **1** (0.15 mmol), and boron trichloride (3.0 equiv.) at room temperature for 45 min under air. Yield of isolated product after purification by silica gel chromatography.

5. CYCLIZATION OF *O*-ALKYNOYLPHENOLS

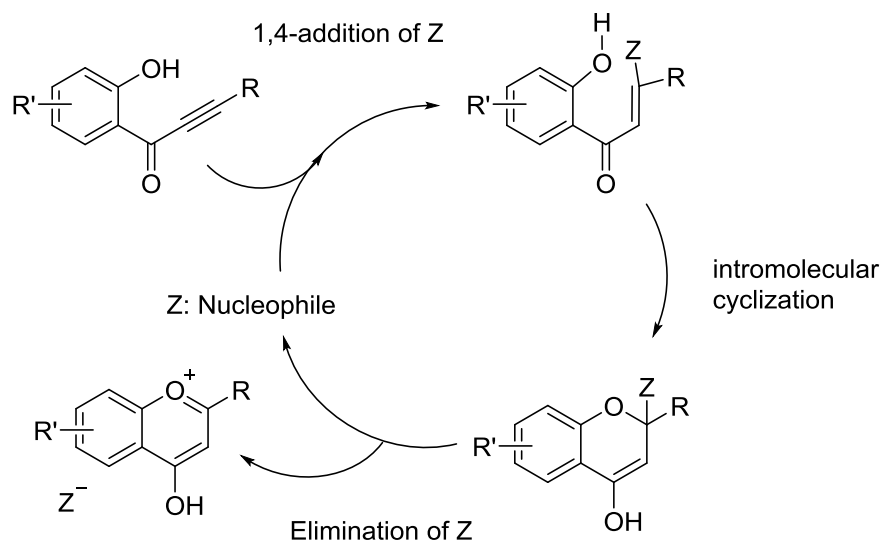
Once a library of *o*-alkynoylphenols was prepared, we set out to cyclize the products under basic and acidic conditions in order to form aurone and flavone scaffolds, respectively.

5.1 BASE PROMOTED 5-*EXO* CYCLIZATION OF *O*-ALKYNOYLPHENOLS

Under basic conditions the 5-*exo* and 6-*endo* cyclization pathways are competing, with formation of the major product depending on the conditions employed.^[34a, 34b, 34d] Initially, when we set out to produce flavones, we attempted to employ cesium carbonate to promote the 6-*endo* cyclization of the *o*-alkynoylphenols.^[36, 80] We observed that rapid 5-*exo* cyclization takes place under these conditions. Aurones **10a-e** were formed in good to excellent yields by stirring the *o*-alkynoylphenol precursors with cesium carbonate in acetone at room temperature (Figure 9).

5.2 ACID PROMOTED 6-*ENDO* CYCLIZATION OF *O*-ALKYNOYLPHENOLS

Regioselective 6-*endo* cyclization of *o*-alkynoylphenols may be achieved by applying the principles of the Morita-Baylis-Hillman reaction.^[69] Intramolecular Michael addition may be promoted *via* 1,4-addition of a nucleophile to the β -carbon in the ynone system. Elimination of the nucleophile yields the 6-*endo* cyclized flavone product (Scheme 40).^[34f, 34g, 70]



Scheme 40: Catalytic cycle for the 6-*endo* cyclization of *o*-alkynoylphenols

5.3 RESULTS AND DISCUSSION: AURONE AND FLAVONE SYNTHESIS

We have employed trifluoromethanesulfonic acid (TfOH) as a catalyst in order to promote the 6-*endo* cyclization of the synthesized *o*-alkynoylphenols.^[34f] This method was successful in promoting the regioselective 6-*endo* cyclization of *o*-alkynoylphenols to produce flavones in moderate to excellent yields (Figure 9, **9a-e**). The presence of an additional electron-rich methoxy- functional group on the phenol ring improved the yield from 76% for **9a** to 97% for **9b**. Conversely, the addition of a methoxy group to aromatic ring adjacent to the triple bond reduced the yields to 51% and 55% for flavones **9c** and **9d**, respectively. Similarly, a modest yield of 32% was obtained for the cyclization of the *o*-alkynoylphenol in the presence of a bulky, electron-rich naphthyl group.

Once 1,4-addition of the TfOH to the *o*-alkynoylphenol has taken place, the phenol oxygen acts as a nucleophile in the intramolecular 6-*endo* cyclization (Scheme 40). The observation that the cyclization is more efficient when electron-rich functional groups are present on the phenol ring is due to the increased nucleophilicity of oxygen. On the other hand, the presence of electron-rich groups on the aryl group originating from the

alkynyltrifluoroborate tend to increase electron density around the electrophilic carbon thereby reducing the efficiency of the reaction.

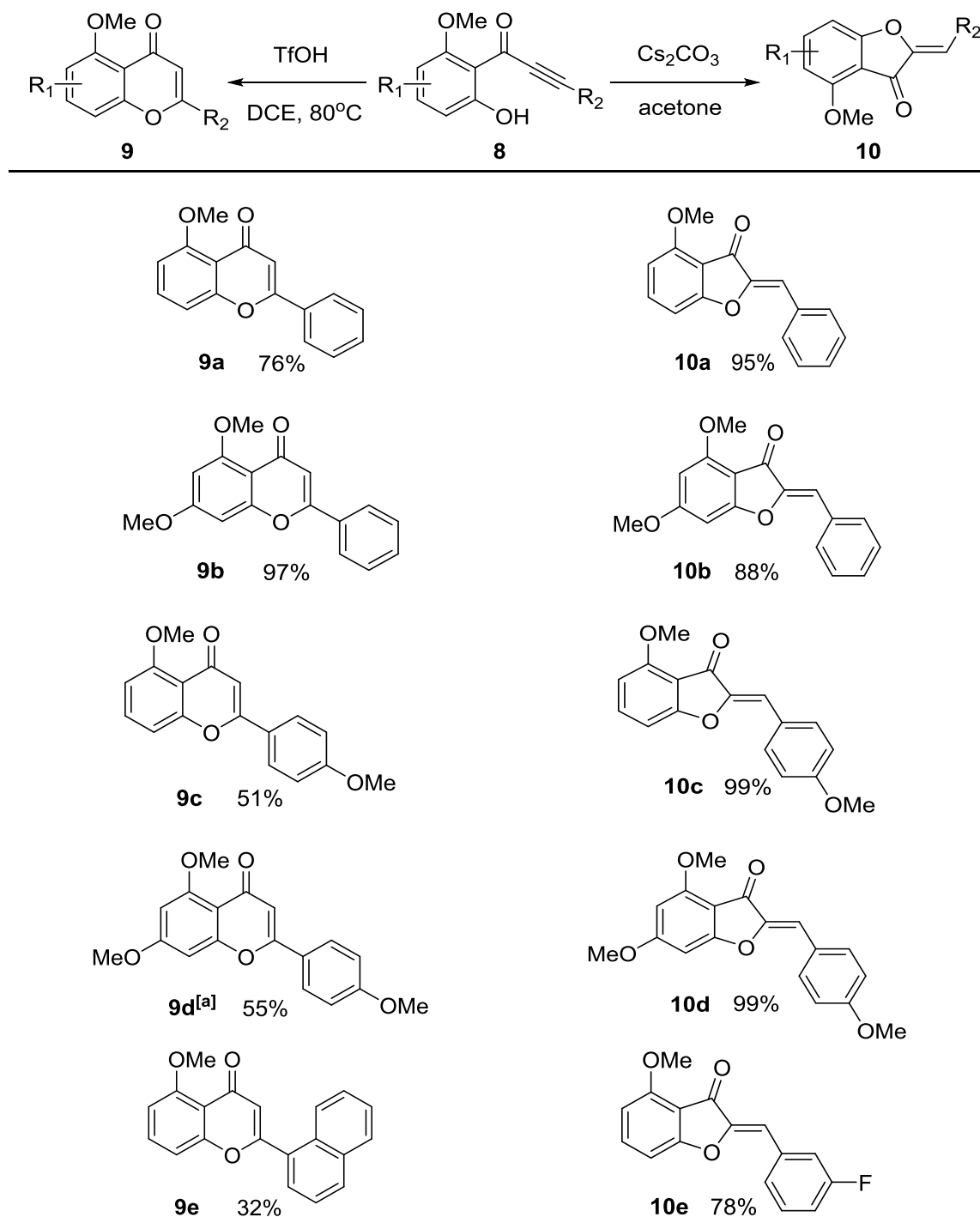


Figure 9: Acid and base promoted ynone cyclization products.

9a-e were prepared with TfOH (5 equiv.) at 80°C. [a] Reaction was performed at 40°C. **10a-e** were prepared with Cs₂CO₃ (3 equiv.) at room temperature.

The cesium carbonate promoted 5-*exo* cyclization of *o*-alkynoylphenols to form aurones was straightforward and resulted in good to excellent yields (Figure 9, **10a-e**). Cyclization of both *o*-alkynoylphenols derived from neutral phenylacetylenetrifluoroborate **1a** yielded the corresponding aurones in very good yields (**10a,b**). *O*-Alkynoylphenols bearing electron-donating methoxy groups on the aromatic ring *alpha*- to the triple bond afforded the corresponding aurones in near quantitative yields (**10c,d**). A slight reduction in yield to 78% was observed when an electron-withdrawing fluorine atom was present (**10e**).

A key piece of evidence supporting the cesium carbonate catalyzed formation of aurones rather than flavones can be found by analyzing the ^{13}C NMR spectra. Flavones exhibit a peak between 176.3 and 178.3 ppm that is representative of the carbonyl carbon. On the other hand the carbonyl carbon on aurone scaffolds appears above 180 ppm.^[81]

Specifically, the cesium carbonate-catalyzed cyclization of *o*-alkynoylphenols results in the formation of the geometric *Z*-isomer. This is made evident by the location of the =CH ^{13}C peak, which differs by about 10 ppm between the two isomers. The =CH ^{13}C peak appears near 111 ppm for the *Z*-isomer and near 121 ppm for the *E*-isomer.^[82] All aurones prepared by this method have a ^{13}C NMR peak appearing between 110 and 112 ppm and do not have any carbons appearing near 121 ppm. Accordingly, it may be concluded that the *Z*-isomer is being formed. The reduced steric interactions between the carbonyl and the aromatic group make the *Z*-isomer more thermodynamically stable.

6. CONCLUSIONS AND FUTURE DIRECTIONS

A novel methodology for the synthesis of functionalized and sterically hindered ynones from potassium alkynyltrifluoroborate salts and acyl chlorides has been developed. Operational simplicity is a key feature of this method. The one-pot reaction proceeds rapidly in the presence of a boron trichloride catalyst and does not require exclusion of air or water. This approach boasts unique functional group tolerance, illustrated by the successful preparation of an ynone bearing an alkyl bromide functional group.

In order to broaden the applicability of this method for the preparation of ynones, it has been expanded to include symmetrical and mixed anhydride starting materials as a substitute for acyl chlorides. Compared to acyl chlorides, a wider variety of functionalized carboxylic acids are commercially available. This opens up many synthetic opportunities given that under basic conditions a desired mixed anhydride may be prepared from a carboxylic acid and an acyl chloride such as acetyl chloride.

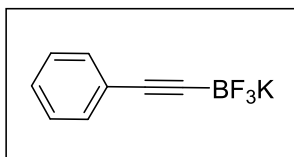
In the presence of the boron trichloride catalyst, a selective *ortho*-demethylation of 2,4,6-trimethoxy and 2,6-dimethoxy substituted mixed anhydrides is observed. As a result, this method lends itself particularly well to the synthesis of *o*-alkynoylphenol compounds. A library of functionalized *o*-alkynoylphenols has been prepared using the developed methodology and further employed toward the production of various natural product scaffolds.

From the *o*-alkynoylphenol products, a series of aurone and flavone derivatives has been prepared. Regioselective 6-*endo* cyclization of *o*-alkynoylphenols was facilitated by trifluoromethanesulfonic acid catalyst. Contrary to reports from the literature, cesium carbonate has been demonstrated to promote the exclusive 5-*exo* cyclization of *o*-alkynoylphenols to for aurone products.

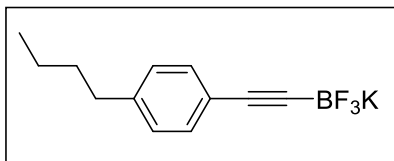
Future directions of this project involve the preparation of more elaborate flavone natural products, for example, through functionalization at carbon 3. Hydroxylation at carbon 3 of flavones to afford flavonols may be achieved using dimethyldioxirane.^[83] Conversion of the hydroxyl group to a triflate, for example, would allow for further functionalization at this location. Alternatively, iodine-mediated cyclization of *o*-alkynoylphenols could be explored for the synthesis 3-iodoflavones.^[84] Preparation of halogenated flavones opens up the possibility for further transformations to furnish interesting functionalized products.

7. APPENDICES

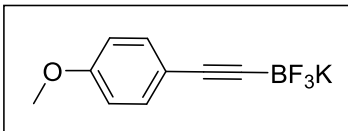
APPENDIX I: COMPOUND CHARACTERIZATION DATA



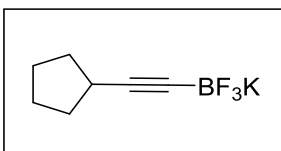
Potassium trifluoro(phenylethynyl)borate (1a): Derived from phenylacetylene (2.45 g, 24.0 mmol, 1.0 equiv.), *n*-BuLi (1.54 g, 24.0 mmol, 1.0 equiv.), B(OMe)₃ (3.74 g, 36.0 mmol, 1.5 equiv.), and aqueous KHF₂ (11.25 g, 144 mmol, 6.0 equiv.) in 50 mL THF. Solubilisation in acetone and precipitation with diethyl ether afforded product **1a** (1.982 g, 40% yield) as a white crystalline solid. ¹H NMR (DMSO) δ 7.27 (m, 4H), 7.24 (m, 1H); ¹³C {¹H} NMR (DMSO) δ 131.0, 128.3, 126.7, 125.5; ¹⁹F NMR (DMSO) δ -131.9 (s, 3F); ¹¹B NMR (DMSO) δ -1.55 (s, 1B); HRMS (ESI/M-) calcd. for C₈H₅BF₃ 169.0442, found 169.0438.



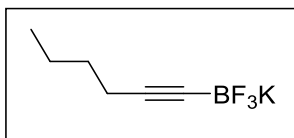
Potassium ((4-butylphenyl)ethynyl)trifluoroborate (1b): Derived from 1-butyl-4-ethynylbenzene (3.00 g, 18.0 mmol, 1.0 equiv.), *n*-BuLi (1.15 g, 18.0 mmol, 1.0 equiv.), B(OMe)₃ (2.81 g, 27.0 mmol, 1.5 equiv.), and aqueous KHF₂ (8.463 g, 108 mmol, 6.0 equiv.) in 50 mL THF. Solubilisation in acetone and precipitation with diethyl ether afforded product **1b** (2.609 g, 55% yield) as a white crystalline solid. ¹H NMR (DMSO) δ 7.19 (dt, *J* = 8.20, 1.5 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 2H), 2.54 (t, *J* = 7.5 Hz, 2H), 1.52 (m, 2H), 1.28 (dq, *J* = 14.80, 7.5 Hz, 2H), 0.88 (t, *J* = 7.23 Hz, 3H); ¹³C {¹H} NMR (DMSO) δ 140.9, 130.8, 128.2, 122.8, 34.6, 32.9, 21.7, 13.8; ¹⁹F NMR (DMSO) δ -131.6 (s, 3F); ¹¹B NMR (DMSO) δ -1.67 (s, 1B); HRMS (ESI/M-) calcd. for C₁₂H₁₃BF₃ 225.1068, found 225.1065.



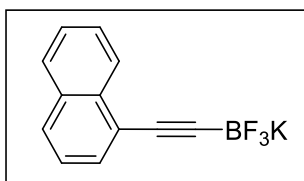
Potassium trifluoro((4-methoxyphenyl)ethynyl)borate (1c): Derived from 4-ethynylanisole (1.00 g, 7.34 mmol, 1.0 equiv.), *n*-BuLi (0.470 g, 7.34 mmol, 1.0 equiv.), B(OMe)₃ (1.14 g, 11.0 mmol, 1.5 equiv.), and aqueous KHF₂ (3.462 g, 44.3 mmol, 6.0 equiv.) in 25 mL THF. Solubilisation in acetone and precipitation with diethyl ether afforded product **1c** (2.609 g, 55% yield) as a white crystalline solid. ¹H NMR (DMSO) δ 7.22 (dt, *J* = 8.99, 2.5 Hz, 2H), 6.84 (dt, *J* = 9.0, 2.0 Hz, 2H), 3.73 (s, 3H); ¹³C {¹H} NMR (DMSO) δ 158.0, 132.2, 117.7, 113.9, 55.0; ¹⁹F NMR (DMSO) δ -131.5 (s, 3F); ¹¹B NMR (DMSO) δ -1.67 (s, 1B); HRMS (ESI/M-) calcd. for C₉H₇OBF₃ 199.0548, found 199.0543.



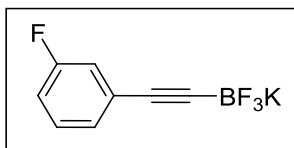
Potassium (cyclopentylethynyl)trifluoroborate (1d): Derived from cyclopentylacetylene (1.10 g, 11.6 mmol, 1.0 equiv.), *n*-BuLi (0.743 g, 11.6 mmol, 1.0 equiv.), B(OMe)₃ (1.79 g, 17.3 mmol, 1.5 equiv.), and aqueous KHF₂ (5.416 g, 69.3 mmol, 6.0 equiv.) in 25 mL THF. Solubilisation in acetone and precipitation with diethyl ether afforded product **1d** (0.5028 g, 22% yield) as a white crystalline solid. ¹H NMR (DMSO) δ 2.40 (t, *J* = 8.0 Hz, 1H), 1.76 (m, 2H), 1.60 (m, 2H), 1.34-1.49 (m, 4H); ¹³C {¹H} NMR (DMSO) δ 33.8, 30.4, 24.4; ¹⁹F NMR (DMSO) δ -131.5 (s, 3F); ¹¹B NMR (DMSO) δ -1.30 (s, 1B); HRMS (ESI/M-) calcd. for C₇H₉BF₃ 161.0755, found 161.0752.



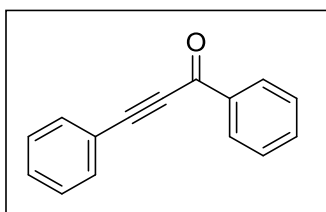
Potassium trifluoro(hex-1-yn-1-yl)borate (1e): Derived from 1-hexyne (2.0 g, 23.6 mmol, 1.0 equiv.), *n*-BuLi (1.51 g, 23.6 mmol, 1.0 equiv.), B(OMe)₃ (3.68 g, 35.4 mmol, 1.5 equiv.), and aqueous KHF₂ (11.06 g, 142 mmol, 6.0 equiv.) in 25 mL THF. Solubilisation in acetone and precipitation with diethyl ether afforded product **1e** (1.659 g, 36% yield) as a white crystalline solid. ¹H NMR (DMSO) δ 1.98 (m, 2H) 1.33 (m, 4H), 0.85 (m, 3H); ¹³C {¹H} NMR (DMSO) δ 31.1, 21.4, 18.5, 13.5; ¹⁹F NMR (DMSO) δ -131.0 (s, 3F); ¹¹B NMR (DMSO) δ -1.30 (s, 1B); HRMS (ESI/M-) calcd. for C₆H₉BF₃ 149.0755, found 149.0749.



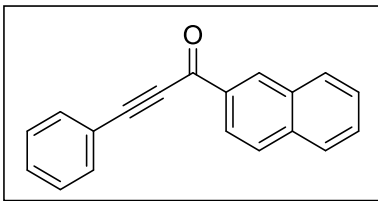
Potassium (1-naphthyl)ethynyltrifluoroborate (1f): Derived from 1-ethynynaphthalene. **1f** was obtained in 62% yield as a pale pink crystalline solid. ¹H NMR (DMSO) δ 8.33 (d, *J* = 8.2 Hz, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.82 (d, *J* = 8.2 Hz, 1H), 7.57 (m, 3H), 7.44 (m, 1H); ¹³C {¹H} NMR (DMSO) δ 132.9, 132.8, 128.9, 128.1, 126.9, 126.3, 126.2, 126.1, 125.5, 123.1; ¹⁹F NMR (DMSO) δ -131.5 (s, 3F); ¹¹B NMR (DMSO) δ -1.56(s, 1B); HRMS (ESI/M-) calcd. for C₁₂H₇BF₃ 219.0598, found 219.0601.



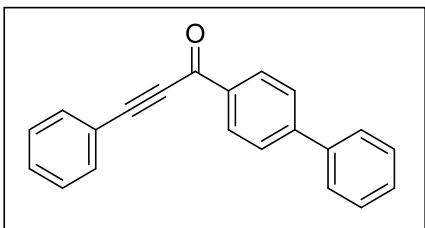
Potassium (3-fluorophenyl)ethynyltrifluoroborate (1g): Derived from 3-fluorophenylacetylene. **1g** was obtained in 84% yield as a white crystalline solid. ^1H NMR (DMSO) δ 7.32 (m, 1H), 7.10 (m, 3H); ^{13}C $\{^1\text{H}\}$ NMR (DMSO) δ 163.0, 160.6, 130.3 (d, J = 9.0 Hz, 1C), 127.3, 117.3 (d, J = 22 Hz, 1C), 114.0 (d, J = 21 Hz, 1C); ^{19}F NMR (DMSO) δ -132.0 (s, 3F), -113.5 (m, 1F); ^{11}B NMR (DMSO) δ -1.82 (s, 1B); HRMS (ESI/M-) calcd. for $\text{C}_8\text{H}_4\text{BF}_3$ 187.0348, found 187.0348.



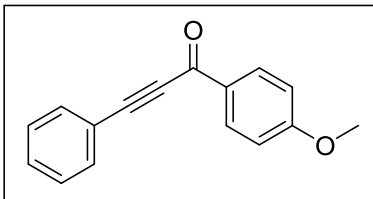
1,3-diphenylprop-2-yn-1-one (2a): Derived from benzoyl chloride (16.9 mg, 0.12 mmol, 1.0 equiv.), potassium trifluoro(phenylethynyl)borate (**1a**) (37.4 mg, 0.18 mmol, 1.5 equiv.) and boron trichloride (21.1 mg, 0.18 mmol, 1.5 equiv.) in 0.6 mL of DCM. Purification by silica gel column chromatography using hexanes/EtOAc (30/1) and pentane wash afforded the product **2a** (16.5 mg, 67% yield) as a yellow oil. IR (film) ν 2200, 1633, 1316, 1290, 762, 688 cm^{-1} ; ^1H NMR (CDCl_3) δ 8.23 (m, 2H), 7.70 (m, 2H), 7.64 (tt, J = 7.5, 2.0 Hz, 1H), 7.47-7.55 (m, 3H), 7.43 (tt, J = 7.5, 1.5 Hz, 2H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3) δ 178.0, 136.9, 134.1, 133.1, 130.8, 129.6, 128.7, 128.6, 120.1, 93.1, 86.9; HRMS (APCI/[M+H] $^+$) calcd. for $\text{C}_{15}\text{H}_{10}\text{O}$ 207.0804, found 207.0795.



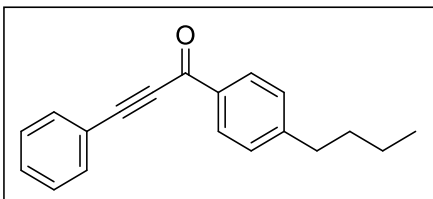
1-(naphthalen-2-yl)-3-phenylprop-2-yn-1-one (2b): Derived from 2-naphthoyl chloride (19.1 mg, 0.10 mmol, 1.0 equiv.), potassium trifluoro(phenylethynyl)borate (**1a**) (31.2 mg, 0.15 mmol, 1.5 equiv.) and boron trichloride (17.6 mg, 0.15 mmol, 1.5 equiv.) in 0.5 mL of DCM. Purification by silica gel column chromatography using hexanes/EtOAc (30/1) and pentane wash afforded the product **2b** (16.8 mg, 66% yield) as a pale yellow solid. IR (film) ν 2206, 1625, 1305, 1125, 759, 688 cm^{-1} ; ^1H NMR (CDCl_3) δ 8.79 (s, 1H), 8.21 (dd, J = 8.5, 1.5 Hz, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.92 (t, J = 9.0 Hz, 2H), 7.74 (m, 2H), 7.60 (tdd, J = 15, 7.0, 1.5 Hz, 2H), 7.51 (tt, J = 7.0, 2.5 Hz, 1H), 7.45 (tt, J = 7.0, 1.5 Hz, 2H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3) δ 177.9, 136.2, 134.4, 133.1, 132.6, 132.4, 130.8, 129.9, 129.0, 128.7, 128.5, 127.9, 126.9, 124.0, 120.2, 93.0, 87.1; HRMS (APCI/[M+H] $^+$) calcd. for $\text{C}_{19}\text{H}_{12}\text{O}$ 257.0961, found 257.0956.



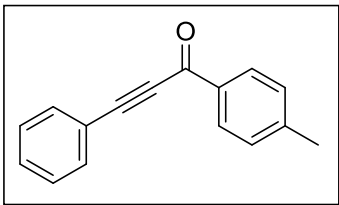
1-([1,1'-biphenyl]-4-yl)-3-phenylprop-2-yn-1-one (2c): Derived from biphenyl-4-carbonyl chloride (43.3 mg, 0.20 mmol, 1.0 equiv.), potassium trifluoro(phenylethynyl)borate (**1a**) (62.4 mg, 0.30 mmol, 1.5 equiv.) and boron trichloride (35.2 mg, 0.30 mmol, 1.5 equiv.) in 1.0 mL of DCM. Purification by silica gel column chromatography using hexanes/EtOAc (25/1) and pentane wash afforded the product **2c** (30.1 mg, 53%) as a yellow solid. IR (film) ν 2202, 1634, 1288, 1214, 1174, 1012, 741, 689 cm^{-1} ; ^1H NMR (CDCl_3) δ 8.29 (m, 2H), 7.71 (m, 4H), 7.65 (m, 2H), 7.48 (m, 3H), 7.42 (t, J = 7.0 Hz, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3) δ 177.5, 146.8, 139.7, 135.7, 133.0, 130.7, 130.1, 129.0, 128.7, 128.4, 127.3, 127.2, 120.1, 93.1, 87.0; HRMS (APCI/[M+H] $^+$) calcd. for $\text{C}_{21}\text{H}_{14}\text{O}$ 283.1117, found 283.1110.



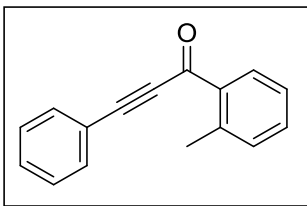
1-(4-methoxyphenyl)-3-phenylprop-2-yn-1-one (2d): Derived from 4-methoxybenzoyl chloride (17.1 mg, 0.10 mmol, 1.0 equiv.), potassium trifluoro(phenylethynyl)borate (**1a**) (31.2 mg, 0.15 mmol, 1.5 equiv.) and boron trichloride (17.6 mg, 0.15 mmol, 1.5 equiv.) in 0.5 mL of DCM. Purification by silica gel column chromatography using hexanes/EtOAc (10/1) afforded the product **2d** (27.7 mg, quantitative yield) as a beige solid. IR (film) ν 2199, 1628, 1601, 1259, 1159, 762, 683 cm^{-1} ; ^1H NMR (CDCl_3) δ 8.20 (dt, J = 9.0, 2.5 Hz, 2H), 7.67 (dt, J = 7.0, 1.5 Hz, 2H), 7.44 (dtt, J = 24, 7.0, 1.5 Hz, 3H), 6.98 (dt, J = 9.0, 2.5 Hz, 2H), 3.89 (s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3) δ 176.6, 164.5, 132.9, 131.9, 130.6, 128.6, 120.3, 113.9, 92.3, 86.9, 55.6; HRMS (ESI/[M+H] $^{+}$) calcd. for $\text{C}_{16}\text{H}_{12}\text{O}_2$ 237.0910, found 237.0910.



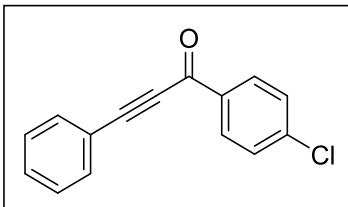
1-(4-butylphenyl)-3-phenylprop-2-yn-1-one (2e): Derived from 4-butylbenzoyl chloride (23.6 mg, 0.12 mmol, 1.0 equiv.), potassium trifluoro(phenylethynyl)borate (**1a**) (37.4 mg, 0.18 mmol, 1.5 equiv.) and boron trichloride (21.1 mg, 0.18 mmol, 1.5 equiv.) in 0.6 mL of DCM. Purification by silica gel column chromatography using hexanes/EtOAc (30/1) afforded the product **2e** (33.5 mg, quantitative yield) as a copper coloured oil. IR (film) ν 2199, 1638, 1605, 1312, 1011, 756, 689 cm^{-1} ; ^1H NMR (CDCl_3) δ 8.14 (d, J = 8.0 Hz, 2H), 7.68 (d, J = 7.5 Hz, 2H), 7.45 (m, 3H), 7.32 (d, J = 8.0 Hz, 2H), 2.70 (t, J = 8.0 Hz, 2H), 1.64 (m, 2H), 1.38 (dq, J = 15, 7.5 Hz, 2H), 0.94 (t, J = 7.5 Hz, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3) δ 178.0, 136.9, 134.1, 133.1, 130.8, 129.6, 128.7, 128.6, 120.1, 93.1, 86.9; HRMS (APCI/[M+H] $^{+}$) calcd. for $\text{C}_{19}\text{H}_{18}\text{O}$ 263.1430, found 263.1421.



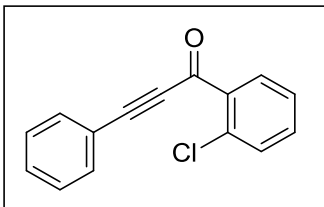
3-phenyl-1-(p-tolyl)prop-2-yn-1-one (2f): Derived from p-toluoyl chloride (15.5 mg, 0.10 mmol, 1.0 equiv.), potassium trifluoro(phenylethynyl)borate (**1a**) (31.2 mg, 0.15 mmol, 1.5 equiv.) and boron trichloride (17.6 mg, 0.15 mmol, 1.5 equiv.) in 0.5 mL of DCM. Purification by silica gel column chromatography using hexanes/EtOAc (25/1) afforded the product **2f** (24.6 mg, quantitative yield) as a light brown solid. IR (film) ν 2202, 1634, 1603, 1286, 1169, 761, 690 cm^{-1} ; ^1H NMR (CDCl_3) δ 8.12 (d, J = 8.5 Hz, 2H), 7.68 (dt, J = 7.0, 1.5 Hz, 2H), 7.45 (dtt, J = 25, 7.0, 1.0 Hz, 3H), 7.31 (d, J = 8.0 Hz, 2H), 2.24 (s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3) δ 145.2, 134.6, 133.0, 130.7, 129.7, 129.3, 128.6, 120.3, 92.6, 87.0, 21.8; HRMS (APCI/[M+H] $^+$) calcd. for $\text{C}_{16}\text{H}_{12}\text{O}$ 221.0961, found 221.0960.



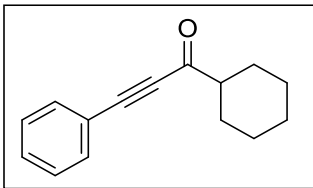
3-phenyl-1-(o-tolyl)prop-2-yn-1-one (2g): Derived from o-toluoyl chloride (15.5 mg, 0.10 mmol, 1.0 equiv.), potassium trifluoro(phenylethynyl)borate (**1a**) (31.2 mg, 0.15 mmol, 1.5 equiv.) and boron trichloride (17.6 mg, 0.15 mmol, 1.5 equiv.) in 0.5 mL of DCM. Purification by silica gel column chromatography using hexanes/EtOAc (20/1) and pentane wash afforded the product **2g** (21.4 mg, 97%) as a yellow oil. IR (film) ν 2361, 2197, 1638, 1307, 1202, 1008, 730, 688 cm^{-1} ; ^1H NMR (CDCl_3) δ 8.30 (dd, J = 7.5, 1.0 Hz, 1H), 7.65 (dt, J = 7.0, 2.0 Hz, 2H), 7.34-7.48 (m, 5H), 7.26 (m, 1H), 2.68 (s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3) δ 179.7, 140.4, 135.7, 133.1, 132.9, 132.8, 132.1, 130.5, 128.6, 125.8, 120.3, 91.8, 88.4, 21.9; HRMS (APCI/[M+H] $^+$) calcd. for $\text{C}_{16}\text{H}_{12}\text{O}$ 221.0961, found 221.0956.



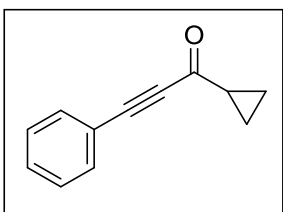
1-(4-chlorophenyl)-3-phenylprop-2-yn-1-one (2h): Derived from p-chlorobenzoyl chloride (17.5 mg, 0.10 mmol, 1.0 equiv.), potassium trifluoro(phenylethynyl)borate (**1a**) (32.0 mg, 0.15 mmol, 1.5 equiv.) and boron trichloride (17.6 mg, 0.15 mmol, 1.5 equiv.) in 0.5 mL of DCM. Purification by silica gel column chromatography using hexanes/EtOAc (20/1) and pentane wash afforded the product **2h** (7.2 mg, 30%) as a pale yellow solid. IR (film) ν 2199, 1651, 1584, 1287, 1008, 751 cm^{-1} ; ^1H NMR (CDCl_3) δ 8.15 (dt, J = 8.5, 2.5 Hz, 2H), 7.68 (dt, J = 7.0, 1.5 Hz, 2H), 7.50 (m, 3H), 7.43 (m, 2H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3) δ 176.7, 140.7, 135.3, 133.1, 131.0, 130.9, 129.0, 128.7, 119.9, 93.6, 86.6; HRMS (EI/ M^+) calcd. for $\text{C}_{15}\text{H}_9\text{ClO}$ 240.0342, found 240.0339.



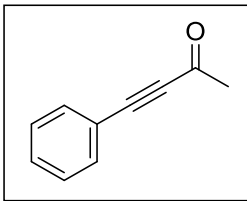
1-(2-chlorophenyl)-3-phenylprop-2-yn-1-one (2i): Derived from o-chlorobenzoyl chloride (17.5 mg, 0.10 mmol, 1.0 equiv.), potassium trifluoro(phenylethynyl)borate (**1a**) (31.2 mg, 0.15 mmol, 1.5 equiv.) and boron trichloride (17.6 mg, 0.15 mmol, 1.5 equiv.) in 0.5 mL of DCM. Purification by silica gel column chromatography using hexanes/EtOAc (20/1) and pentane wash afforded the product **2i** (14.1 mg, 59%) as a yellow oil. IR (film) ν 2359, 2196, 1650, 1303, 1009, 740, 687 cm^{-1} ; ^1H NMR (CDCl_3) δ 8.09 (m, 1H), 7.65 (dt, J = 6.5, 2.0 Hz, 2H), 7.48 (m, 3H), 7.41 (m, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3) δ 176.8, 135.9, 133.6, 133.3, 133.1, 132.5, 131.5, 130.9, 128.7, 126.8, 120.0, 93.9, 88.3; HRMS (EI/ M^+) calcd. for $\text{C}_{15}\text{H}_9\text{ClO}$ 240.0342, found 240.0350.



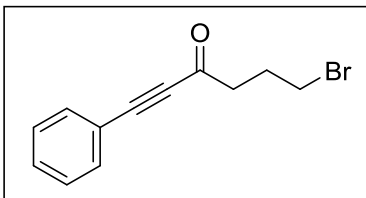
1-cyclohexyl-3-phenylprop-2-yn-1-one (2j): Derived from cyclohexanecarbonyl chloride (14.7 mg, 0.10 mmol, 1.0 equiv.), potassium trifluoro(phenylethynyl)borate (**1a**) (31.2 mg, 0.15 mmol, 1.5 equiv.) and boron trichloride (17.6 mg, 0.15 mmol, 1.5 equiv.) in 0.5 mL of DCM. Purification by silica gel column chromatography using hexanes/EtOAc (25/1) and pentane wash afforded the product **2j** (16.8 mg, 78% yield) as a pale yellow oil. IR (film) ν 2932, 2360, 2199, 1664, 758, 689 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.57 (m, 2H), 7.45 (tt, J = 7.5, 2.5 Hz, 1H), 7.38 (m, 2H), 2.51 (tt, J = 11, 3.5 Hz, 1H), 2.06 (m, 2H), 1.82 (m, 2H), 1.68 (m, 1H), 1.50 (qd, J = 11.98, 3.13 Hz, 2H); 1.22-1.40 (m, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3) δ 191.5, 133.0, 130.5, 128.6, 120.1, 91.3, 87.2, 52.3, 28.3, 25.8, 25.4; HRMS (ESI/[$\text{M}+\text{H}$] $^+$) calcd. for $\text{C}_{15}\text{H}_{16}\text{O}$ 213.1274, found 213.1269.



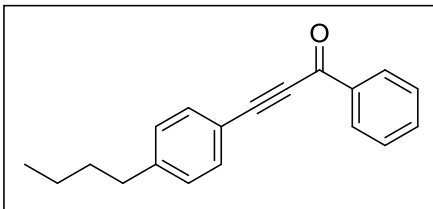
1-cyclopropyl-3-phenylprop-2-yn-1-one (2k): Derived from cyclopropanecarbonyl chloride (20.9 mg, 0.20 mmol, 1.0 equiv.), potassium trifluoro(phenylethynyl)borate (**1a**) (62.4 mg, 0.30 mmol, 1.5 equiv.) and boron trichloride (35.2 mg, 0.30 mmol, 1.5 equiv.) in 1.0 mL of DCM. Purification by silica gel column chromatography using hexanes/EtOAc (30/1) and pentane wash afforded the product **2k** (26.8 mg, 79%) as a yellow oil. IR (film) ν 2362, 2205, 1654, 1108, 798, 688 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.56 (dd, J = 8.0, 1.5 Hz, 2H), 7.45 (t, J = 7.5 Hz, 1H), 7.38 (t, J = 7.0 Hz, 2H), 2.16 (tt, J = 8.0, 4.5 Hz, 1H), 1.33 (m, 2H), 1.09 (m, 2H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3) δ 188.3, 132.9, 130.5, 128.6, 120.0, 90.4, 86.1, 24.5, 11.1; HRMS (ESI/[$\text{M}+\text{H}$] $^+$) calcd. for $\text{C}_{12}\text{H}_{10}\text{O}$ 171.0804, found 171.0799.



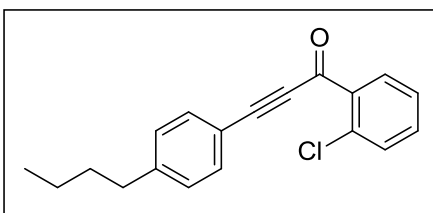
4-phenylbut-3-yn-2-one (2l): Derived from acetyl chloride (15.7 mg, 0.20 mmol, 1.0 equiv.), potassium trifluoro(phenylethynyl)borate (**1a**) (62.4 mg, 0.30 mmol, 1.5 equiv.) and boron trichloride (35.2 mg, 0.30 mmol, 1.5 equiv.) in 1.0 mL of DCM. Purification by silica gel column chromatography using hexanes/EtOAc (30/1) and pentane wash afforded the product **2l** (15.6 mg, 54%) as a brown oil. IR (film) ν 2202, 1672, 1280, 1157, 977, 758, 689 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.57 (dt, J = 7.0, 1.5 Hz, 2H), 7.45 (dt, J = 8.0, 1.5 Hz, 1H), 7.37 (tt, J = 7.0, 2.0, 2H), 2.45 (s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3) δ 184.6, 133.0, 130.7, 128.6, 119.9, 90.3, 88.2, 32.7; HRMS (EI/ M^+) calcd. for $\text{C}_{10}\text{H}_8\text{O}$ 144.0575, found 144.0571.



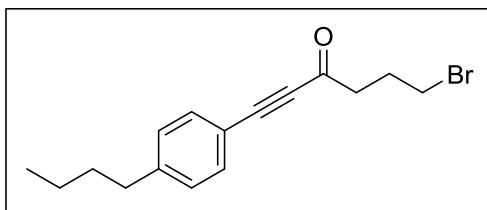
6-bromo-1-phenylhex-1-yn-3-one (2m): Derived from 4-bromobutyryl chloride (18.5 mg, 0.10 mmol, 1.0 equiv.), potassium trifluoro(phenylethynyl)borate (**1a**) (32.0 mg, 0.15 mmol, 1.5 equiv.) and boron trichloride (17.6 mg, 0.15 mmol, 1.5 equiv.) in 0.5 mL of DCM. Purification by silica gel column chromatography using hexanes/EtOAc (15/1) afforded the product **2m** (9.8 mg, 39%) as a yellow oil. IR (film) ν 2201, 1669, 1489, 1283, 1086, 758, 689 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.58 (m, 2H), 7.46 (m, 1H), 7.39 (m, 2H), 3.49 (td, J = 6.5, 1.0 Hz, 2H) 2.89 (td, J = 7.0, 1.0 Hz, 2H) 2.27 (quin, J = 6.0, 2H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3) δ 186.2, 133.1, 130.8, 128.6, 119.7, 91.2, 87.6, 43.5, 32.6, 26.7; HRMS (ESI/ $[\text{M}+\text{H}]^+$) calcd. for $\text{C}_{12}\text{H}_{11}\text{BrO}$ 251.0066, found 251.0054.



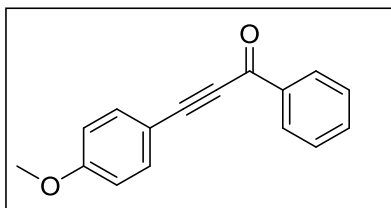
3-(4-butylphenyl)-1-phenylprop-2-yn-1-one (3a): Derived from benzoyl chloride (14.1 mg, 0.10 mmol, 1.0 equiv.), potassium ((4-butylphenyl)ethynyl)trifluoroborate (**1b**) (66.0 mg, 0.25 mmol, 2.5 equiv.) and boron trichloride (29.3 mg, 0.25 mmol, 2.5 equiv.) in 0.5 mL of DCM. Purification by silica gel column chromatography using hexanes/EtOAc (20/1) and pentane wash afforded the product **3a** (22.9 mg, 87%) as a copper coloured oil. IR (film) ν 2196, 1639, 1290, 1212, 1171, 1010, 699 cm^{-1} ; ^1H NMR (CDCl_3) δ 8.23 (dt, J = 8.0, 1.5 Hz, 2H), 7.62 (m, 3H), 7.51 (t, J = 8.0 Hz, 2H), 7.25 (m, 2H), 2.66 (t, J = 8.0 Hz, 2H), 1.62 (m, 2H), 1.37 (dq, J = 15, 7.5 Hz, 2H), 0.94 (t, J = 7.0 Hz, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3) δ 178.0, 146.5, 137.0, 134.0, 133.1, 129.5, 128.8, 128.6, 117.1, 93.9, 86.8, 35.8, 33.2, 22.3, 13.9; HRMS (APCI/[M+H] $^+$) calcd. for $\text{C}_{19}\text{H}_{18}\text{O}$ 263.1430, found 263.1428.



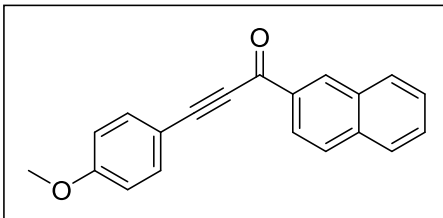
3-(4-butylphenyl)-1-(2-chlorophenyl)prop-2-yn-1-one (3b): Derived from 2-chlorobenzoyl chloride (17.5 mg, 0.10 mmol, 1.0 equiv.), potassium ((4-butylphenyl)ethynyl)trifluoroborate (**1b**) (66.0 mg, 0.25 mmol, 2.5 equiv.) and boron trichloride (29.3 mg, 0.25 mmol, 2.5 equiv.) in 0.5 mL of DCM. Purification by silica gel column chromatography using hexanes/EtOAc (20/1) and pentane wash afforded the product **3b** (25.2 mg, 85%) as a copper coloured oil. IR (film) ν 2360, 2193, 1646, 1302, 1005, 741 cm^{-1} ; ^1H NMR (CDCl_3) δ 8.07 (d, J = 8.5 Hz, 1H), 7.56 (d, J = 8.0 Hz, 2H), 7.48 (m, 2H), 7.40 (m, 1H), 7.22 (d, J = 8.0 Hz, 2H), 2.65 (t, J = 8.0 Hz, 2H), 1.61 (dt, J = 15, 7.5 Hz, 2H), 1.35 (dq, J = 15, 7.0 Hz, 2H), 0.93 (t, J = 7.5 Hz, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3) δ 176.8, 146.7, 136.0, 133.4, 133.2, 133.1, 132.4, 131.5, 128.8, 126.7, 117.1, 94.8, 88.3, 35.8, 33.2, 22.3, 13.9; HRMS (APCI/[M+H] $^+$) calcd. for $\text{C}_{19}\text{H}_{17}\text{ClO}$ 297.1041, found 297.1031.



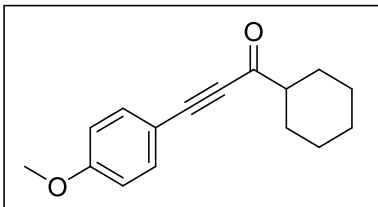
6-bromo-1-(4-butylphenyl)hex-1-yn-3-one (3c): Derived from 4-bromobutyryl chloride (18.5 mg, 0.10 mmol, 1.0 equiv.), potassium ((4-butylphenyl)ethynyl)trifluoroborate (**1b**) (66.0 mg, 0.25 mmol, 2.5 equiv.) and boron trichloride (29.3 mg, 0.25 mmol, 2.5 equiv.) in 0.5 mL of DCM. Purification by silica gel column chromatography using hexanes/EtOAc (20/1) and pentane wash afforded the product **3c** (24.8 mg, 81%) as a tawny brown oil. IR (film) ν 2930, 2360, 2197, 1669, 1085, 833 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.49 (d, J = 8.0 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H), 3.49 (t, J = 6.5 Hz, 2H), 2.88 (t, J = 7.0 Hz, 2H), 2.64 (t, J = 7.0 Hz, 2H), 2.5 (quin, J = 6.5 Hz, 2H), 1.60 (m, 2H), 1.35 (dq, J = 15., 7.5 Hz, 2H), 0.92 (t, J = 7.5 Hz, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3) δ 186.2, 146.6, 133.2, 128.8, 116.8, 92.0, 87.5, 43.5, 35.7, 33.2, 32.6, 26.8, 22.3, 13.9; HRMS (ESI/[M+H] $^+$) calcd. for $\text{C}_{16}\text{H}_{19}\text{BrO}$ 307.0692, found 307.0685.



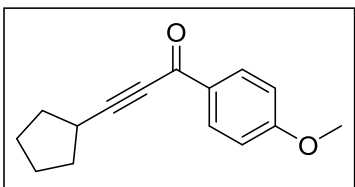
3-(4-methoxyphenyl)-1-phenylprop-2-yn-1-one (4a): Derived from benzoyl chloride (14.1 mg, 0.10 mmol, 1.0 equiv.), potassium trifluoro((4-methoxyphenyl)ethynyl)borate (**1c**) (59.5 mg, 0.25 mmol, 2.5 equiv.) and boron trichloride (29.3 mg, 0.25 mmol, 2.5 equiv.) in 0.5 mL of DCM. Purification by silica gel column chromatography using hexanes/EtOAc (20/1) and pentane wash afforded the product **4a** (17.8 mg, 75%) as a yellow solid. IR (film) ν 2188, 1625, 1599, 1512, 1255, 1211, 1171, 1032, 836, 698 cm^{-1} ; ^1H NMR (CDCl_3) δ 8.22 (d, J = 8.0 Hz, 2H), 7.63 (m, 3H), 7.51 (t, J = 7.0 Hz, 2H), 6.93 (d, J = 8.0 Hz, 2H), 3.86 (s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3) δ 178.0, 161.7, 137.0, 135.1, 133.9, 129.5, 128.5, 114.4, 111.9, 94.3, 86.9, 55.4; HRMS (ESI/[M+H] $^+$) calcd. for $\text{C}_{16}\text{H}_{12}\text{O}_2$ 237.0910, found 237.0907.



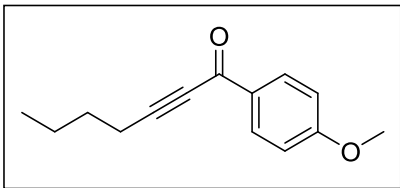
3-(4-methoxyphenyl)-1-(naphthalen-2-yl)prop-2-yn-1-one (4b): Derived from 2-naphthoyl chloride (19.1 mg, 0.10 mmol, 1.0 equiv.), potassium trifluoro((4-methoxyphenyl)ethynyl)borate (**1c**) (34.5 mg, 0.15 mmol, 1.5 equiv.) and boron trichloride (17.6 mg, 0.15 mmol, 1.5 equiv.) in 0.5 mL of DCM. Purification by silica gel column chromatography using hexanes/EtOAc (10/1) and pentane wash afforded the product **4b** (19.9 mg, 70% yield) as a tan solid. IR (film) ν 2192, 1601, 1508, 1257, 159, 1128, 1042, 829, 751 cm^{-1} ; ^1H NMR (CDCl_3) δ 8.77 (s, 1H), 8.21 (dd, J = 8.5, 1.5 Hz, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.91 (t, J = 8.0 Hz, 2H), 7.69 (dt, J = 9.0, 7.62 (td, J = 8.0, 1.0, Hz, 1H), 7.57 (td, J = 8.0, 1.0 Hz, 1H), 6.95 (dt, J = 8.5, 2.5 Hz, 1H), 3.86 (s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3) δ 177.9, 161.7, 136.1, 135.1, 134.6, 132.4, 132.3, 129.8, 128.9, 128.4, 127.9, 126.9, 124.1, 114.4, 112.3, 94.2, 87.0, 55.4; HRMS (ESI/[M+H] $^{+}$) calcd. for $\text{C}_{20}\text{H}_{14}\text{O}_2$ 287.1067, found 287.1066.



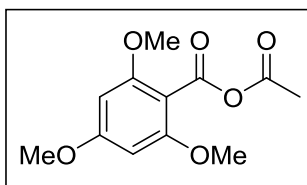
1-cyclohexyl-3-(4-methoxyphenyl)prop-2-yn-1-one (4c): Derived from cyclohexanecarbonyl chloride (14.7 mg, 0.10 mmol, 1.0 equiv.), potassium trifluoro((4-methoxyphenyl)ethynyl)borate **(1c)** (59.5 mg, 0.25 mmol, 2.5 equiv.) and boron trichloride (29.3 mg, 0.25 mmol, 2.5 equiv.) in 0.5 mL of DCM. Purification by silica gel column chromatography using hexanes/EtOAc (15/1) and pentane wash afforded the product **4c** (16.9 mg, 70% yield) as a beige solid. IR (film) ν 2929, 2188, 1650, 1602, 1255, 837 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.53 (dt, $J = 9.0, 2.5$ Hz, 2H), 6.89 (dt, $J = 9.0, 3.0$ Hz, 2H), 3.84 (s, 3H), 2.48 (tt, $J = 12, 2.5$ Hz, 1H), 2.04 (m, 2H), 1.81 (dt, $J = 13, 3.5$ Hz, 2H), 1.67 (m, 1H), 1.49 (m, 2H), 1.29 (m, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3) δ 191.5, 161.5, 135.0, 114.3, 112.0, 92.4, 87.1, 55.4, 52.2, 28.4, 25.8, 25.4; HRMS (ESI/[M+H] $^+$) calcd. for $\text{C}_{16}\text{H}_{18}\text{O}_2$ 243.1380, found 243.1379.



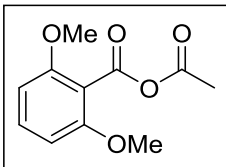
3-cyclopentyl-1-(4-methoxyphenyl)prop-2-yn-1-one (5a): Derived from 4-methoxybenzoyl chloride (34.1 mg, 0.20 mmol, 1.0 equiv.), potassium (cyclopentylethynyl)trifluoroborate **(1d)** (60.0 mg, 0.30 mmol, 1.5 equiv.) and boron trichloride (35.2 mg, 0.30 mmol, 1.5 equiv.) in 1.0 mL of DCM. Purification by silica gel column chromatography using hexanes/EtOAc (10/1) afforded the product **5a** (18.2 mg, 40%) as a pale yellow oil. IR (film) ν 2206, 1629, 1596, 1254, 1169, 1024, 859, 759 cm^{-1} ; ^1H NMR (CDCl_3) δ 8.10 (dt, $J = 9.0, 2.5$ Hz, 2H), 6.94 (dt, $J = 9.0, 2.5$ Hz, 2H), 3.88 (s, 3H), 2.90 (dt, $J = 14, 7.5$ Hz, 1H), 2.05 (m, 2H), 1.81 (m, 4H), 1.64 (m, 2H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3) δ 177.0, 164.1, 131.8, 130.4, 113.7, 100.0, 79.1, 55.5, 33.3, 30.3, 25.2; HRMS (APCI/[M+H] $^+$) calcd. for $\text{C}_{15}\text{H}_{16}\text{O}_2$ 229.1223, found 229.1212.



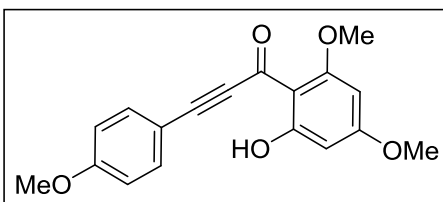
1-(4-methoxyphenyl)hept-2-yn-1-one (6a): Derived from 4-methoxybenzoyl chloride (17.1 mg, 0.10 mmol, 1.0 equiv.), potassium trifluoro(hex-1-yn-1-yl)borate (**1e**) (47.0 mg, 0.25 mmol, 2.5 equiv.) and boron trichloride (29.3 mg, 0.25 mmol, 2.5 equiv.) in 0.5 mL of DCM. Purification by silica gel column chromatography using hexanes/EtOAc (15/1) and pentane wash afforded the product **6a** (9.3 mg, 43%) as a yellow oil. IR (film) ν 2205, 1637, 1596, 1256, 1166, 1029, 845, 758, 687 cm^{-1} ; ^1H NMR (CDCl_3) δ 8.10 (dt, $J = 8.0, 2.5$ Hz, 2H), 6.94 (dt, $J = 8.5, 3.0$ Hz, 2H), 3.88 (s, 3H), 2.49 (t, $J = 7.0$, 2H), 1.66 (quin, $J = 8.0$ Hz, 2H), 1.51 (m, 2H), 0.96 (t, $J = 7.5$, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3) δ 176.9, 164.2, 131.9, 130.4, 113.7, 95.9, 79.6, 55.5, 29.9, 22.1, 18.9, 13.5; HRMS (ESI/[M+H] $^+$) calcd. for $\text{C}_{14}\text{H}_{16}\text{O}_2$ 217.1223, found 217.1213.



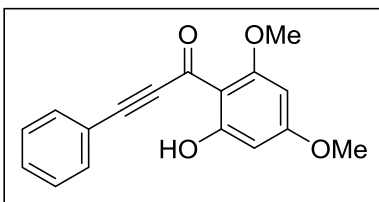
Acetic 2,4,6-trimethoxybenzoic anhydride (7a): Derived from 2,4,6-trimethoxybenzoic acid and acetyl chloride. **7a** was obtained in 66% yield as a tan, crystalline solid. IR (film) ν 1734, 1690, 1597, 1251, 1127, 804, 633 cm^{-1} ; ^1H NMR (400MHz, CDCl_3) δ 6.10(s, 2H), 3.84(s, 3H), 3.84(s, 6H), 2.26(s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100MHz) δ 166.7, 164.0, 160.5, 160.4, 103.4, 90.6, 56.1, 55.5, 22.0. HRMS (ESI/[M+Na] $^+$) calcd. for $\text{C}_{12}\text{H}_{14}\text{O}_6\text{Na}$ 277.0683, found 277.0679.



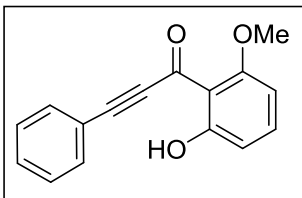
Acetic 2,6-dimethoxybenzoic anhydride (7b): Derived from 2,6-dimethoxybenzoic acid and acetyl chloride. **7b** was obtained in 79% yield as a pale yellow, crystalline solid. IR (film) ν 1755, 1588, 1475, 1257, 1108, 981 cm^{-1} ; ^1H NMR (400MHz, CDCl_3) δ 7.35 (t, J = 8.2 Hz, 1H), 6.58 (d, J = 8.2 Hz), 3.85 (s, 6H), 2.30 (s, 3H). HRMS (ESI/[M+Na] $^+$) calcd. for $\text{C}_{11}\text{H}_{12}\text{O}_5\text{Na}$ 247.0577, found 247.0578.



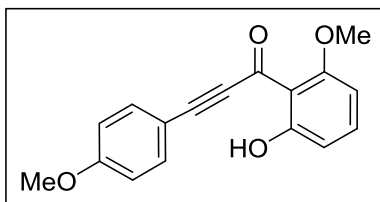
1-(2-hydroxy-4,6-dimethoxyphenyl)-3-(4-methoxyphenyl)prop-2-yn-1-one (8a): Prepared from trifluoroborate **1c** and anhydride **7a**. Ynone **8a** was eluted from the column with hexanes-EtOAc (1:4) and obtained in 49% yield as a brown, crystalline solid. IR (film) ν 2922, 2851, 2190, 1603, 1548, 1249, 1216, 829, 797 cm^{-1} ; ^1H NMR (400MHz, CDCl_3) δ 13.68 (s, 1H), 7.59 (dt, J = 9.0, 2.3 Hz, 2H), 6.93 (dt, J = 9.0, 2.0 Hz, 2H), 6.08 (d, J = 2.3 Hz, 1H), 5.96 (d, J = 2.3 Hz, 1H), 3.94 (s, 3H), 3.87 (s, 3H), 3.85 (s, 3H); ^{13}C { ^1H } NMR (CDCl_3) δ 177.6, 168.2, 167.1, 162.6, 161.5, 135.0, 114.4, 113.0, 110.0, 96.1, 93.5, 91.0, 89.7, 55.8, 55.7, 55.4. HRMS (ESI/[M+H] $^+$) calcd. for $\text{C}_{18}\text{H}_{17}\text{O}_5$ 313.1071, found 313.1072.



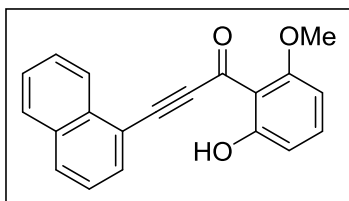
1-(2-hydroxy-4,6-dimethoxyphenyl)-3-phenylprop-2-yn-1-one (8b): Prepared from trifluoroborate **1a** and anhydride **7a**. Ynone **8b** was eluted from the column with hexanes-EtOAc (1:4) and obtained in 71% yield as a yellow solid. IR (film) ν 2991, 2851, 2205, 1614, 1573, 1345, 1293, 1220, 1152, 832, 803, 690, 611 cm^{-1} ; ^1H NMR (400MHz, CDCl_3) δ 13.58 (s, 1H), 7.64 (dt, $J = 7.0, 1.6$ Hz, 2H), 7.43 (m, 3H), 6.09 (d, $J = 2.3$ Hz, 1H), 5.96 (d, $J = 2.3$ Hz, 1H), 3.94 (s, 3H), 3.86 (s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100MHz) δ 177.6, 168.3, 167.4, 162.7, 132.9, 130.4, 128.59, 121.2, 107.1, 94.8, 93.5, 91.1, 89.7, 55.8, 55.7. HRMS (ESI/[M+H] $^+$) calcd. for $\text{C}_{17}\text{H}_{15}\text{O}_4$ 283.0965, found 283.0968.



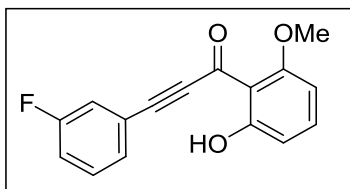
1-(2-hydroxy-6-methoxyphenyl)-3-phenylprop-2-yn-1-one (8c): Prepared from trifluoroborate **1a** and anhydride **7b**. Ynone **8c** was eluted from the column with hexanes-EtOAc (1:7) and obtained in 63% yield as a yellow solid. This compound has been reported in the literature.^[34g] IR (film) ν 2922, 2852, 2197, 1616, 1580, 1454, 1359, 1239, 1087, 800, 744, 683 cm^{-1} ; ^1H NMR (400MHz, CDCl_3) δ 12.81 (s, 1H), 7.65 (dt, $J = 6.6, 1.6$ Hz, 2H), 7.44 (m, 3H), 6.59 (dd, $J = 8.4, 1.0$ Hz, 1H), 6.43 (d, $J = 8.2$ Hz, 1H), 3.98 (s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100MHz) δ 179.6, 165.2, 161.4, 137.5, 133.1, 130.7, 128.7, 120.9, 112.1, 110.5, 101.5, 95.4, 90.0, 55.9.



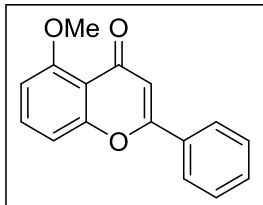
1-(2-hydroxy-6-methoxyphenyl)-3-(4-methoxyphenyl)prop-2-yn-1-one (8d): Prepared from trifluoroborate **1b** and anhydride **7b**. Ynone **8d** was eluted from the column with hexanes-EtOAc (1:5) and obtained in 76% yield as a yellow solid. IR (film) ν 2932, 2838, 2184, 1601, 1553, 1447, 1365, 1239, 1163, 1083, 1029, 822 cm^{-1} ; ^1H NMR (400MHz, CDCl_3) δ 12.91 (s, 1H), 7.61 (dt, J = 9.0, 2.3 Hz, 2H), 7.40 (t, J = 8.2 Hz, 1H), 6.94 (dt, J = 8.6, 2.7 Hz, 2H), 6.59 (dd, J = 8.6, 0.8 Hz, 1H), 6.43 (dd, J = 8.2, 0.8 Hz, 1H), 3.99 (s, 3H), 3.87 (s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100MHz) δ 179.5, 165.2, 161.7, 161.3, 137.2, 135.3, 114.4, 112.7, 112.07, 110.6, 101.4, 96.9, 90.2, 55.9, 55.5. HRMS (ESI/[M+H] $^{+}$) calcd. for $\text{C}_{17}\text{H}_{15}\text{O}_4$ 283.0965, found 283.0968.



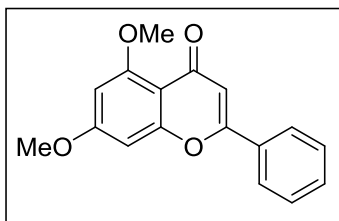
1-(2-hydroxy-6-methoxyphenyl)-3-(naphthalen-1-yl)prop-2-yn-1-one (8e): Prepared from trifluoroborate **1f** and anhydride **7b**. Ynone **8e** was eluted from the column with hexanes-EtOAc (1:15) and obtained in 65% yield as a yellow solid. IR (film) ν 2921, 2852, 2175, 1619, 1586, 1543, 1454, 1357, 1243, 1222, 1088, 797, 771, 685, 628 cm^{-1} ; ^1H NMR (400MHz, CDCl_3) δ 12.89 (s, 1H), 8.51 (d, J = 7.8 Hz, 1H), 7.99 (d, J = 8.2 Hz, 1H), 7.92 (m, 2H), 7.65 (m, 1H), 7.59 (m, 1H), 7.53 (m, 1H), 7.44 (t, J = 8.4 Hz, 1H), 4.00 (s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100MHz) δ 179.5, 165.3, 161.4, 137.5, 133.8, 133.1, 131.3, 128.5, 127.5, 126.9, 126.0, 125.3, 118.5, 112.1, 110.7, 101.5, 94.8, 93.9, 55.9. HRMS (ESI/[M+H] $^{+}$) calcd. for $\text{C}_{20}\text{H}_{15}\text{O}_3$ 303.1016, found 303.1017.



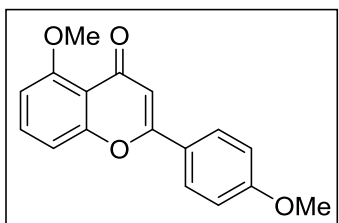
3-(3-fluorophenyl)-1-(2-hydroxy-6-methoxyphenyl)prop-2-yn-1-one (8f): Prepared from trifluoroborate **1g** and anhydride **7b**. Ynone **8f** was eluted from the column with hexanes-EtOAc (1:15) and obtained in 35% yield as a yellow solid. IR (film) ν 2923, 2841, 2200, 1617, 1575, 1544, 1457, 1360, 1224, 1091, 1027, 747, 674 cm^{-1} ; ^1H NMR (400MHz, CDCl_3) δ 12.71 (s, 1H), 7.42 (m, 3H), 7.32 (m, 1H), 7.19 (m, 1H), 6.60 (d, $J = 9.4$, 1H), 6.43 (d, $J = 9.4$, 1H), 3.97 (s, 1H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100MHz) δ 179.3, 165.2, 163.5, 161.4, 137.7, 130.3 (d, $J = 9.0$ Hz, 1C), 128.9, 122.8, 122.7, 119.6 (d, $J = 22$ Hz, 1C), 118.0 (d, $J = 22$ Hz, 1C), 110.6, 101.5, 93.3, 90.2, 55.9. HRMS (ESI/[M+H] $^+$) calcd. for $\text{C}_{16}\text{H}_{12}\text{FO}_3$ 271.0765, found 271.0767.



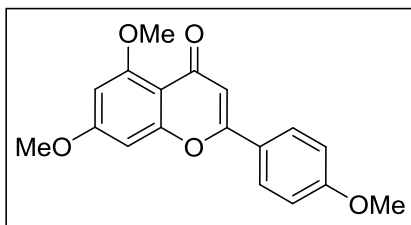
5-methoxyflavone/5-methoxy-2-phenyl-4H-chromen-4-one (9a): Derived from *o*-alkynoylphenol **8c**. Flavone **9a** was eluted from the column with methanol-DCM (1:24) and obtained in 76% yield as a pale yellow solid. This compound has been reported in the literature. ^[34g] IR (film) ν 2921, 2852, 1644, 1598, 1475, 1379, 1261, 1095, 743 cm^{-1} ; ^1H NMR (400MHz, CDCl_3) δ 7.90 (m, 2H), 7.58 (t, $J = 8.2$ Hz, 1H), 7.52 (m, 3H), 7.15 (dd, $J = 8.4$, 1.0 Hz, 1H), 6.84 (d, $J = 7.8$ Hz, 1H), 6.75 (s, 1H), 4.01 (s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100MHz) δ 178.3, 161.1, 159.8, 158.31, 133.7, 131.5, 131.3, 128.94, 126.1, 114.62, 110.2, 109.1, 106.4, 56.5.



5,7-dimethoxyflavone/5,7-dimethoxy-2-phenyl-4H-chromen-4-one (9b): Derived from *o*-alkynoylphenol **8b**. Flavone **9b** was eluted from the column with methanol-DCM (1:19) and obtained in 97% yield as a pale yellow solid. This compound has been reported in the literature.^[85] IR (film) ν 2922, 2851, 1646, 1604, 1347, 1160, 1120, 819, 723 cm^{-1} ; ^1H NMR (400MHz, CDCl_3) δ 7.89 (m, 2H), 7.51 (m, 3H) 6.69(s, 1H), 6.59(d, J = 2.3Hz, 1H), 6.39(d, J = 2.3Hz, 1H), 3.97 (s, 3H), 3.92 (s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100MHz) δ 177.6, 164.0, 160.9, 160.6, 159.9, 131.6, 131.2, 128.9, 125.9, 109.3, 109.1, 96.2, 92.8, 56.4, 55.7.

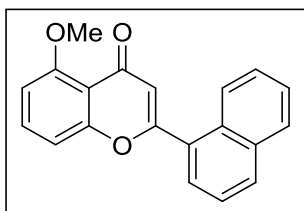


4',5-dimethoxyflavone/5-methoxy-2-(4-methoxyphenyl)-4H-chromen-4-one (9c): Derived from *o*-alkynoylphenol **8d**. Flavone **9c** was eluted from the column with methanol-DCM (1:24) and obtained in 51% yield as a tan solid. This compound has been reported in the literature.^[86] IR (film) ν 2922, 2843, 1645, 1599, 1473, 1258, 1093, 826, 610 cm^{-1} ; ^1H NMR (400MHz, CDCl_3) δ 7.85 (dt, J = 9.0, 2.3 Hz, 2H), 7.56 (t, J = 8.4 Hz, 1H), 7.13 (dd, J = 8.2, 0.8 Hz, 1H), 7.01 (dt, J = 9.0, 2.3 Hz, 2H), 6.83 (d, J = 8.2 Hz, 1H), 6.67(s, 1H), 4.00 (s, 3H), 3.89 (s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100MHz) δ 178.4, 162.2, 161.2, 159.8, 158.3, 133.5, 127.8, 123.7, 114.5, 114.4, 110.1, 107.7, 106.4, 56.5, 55.5.

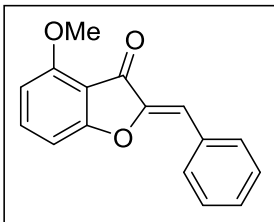


4',5,7-trimethoxyflavone/5,7-dimethoxy-2-(4-methoxyphenyl)-4H-chromen-4-one (9d):

Derived from *o*-alkynoylphenol **8a**. Flavone **9d** was eluted from the column with methanol-DCM (1:24) and obtained in 55% yield as a light brown solid. This compound has been reported in the literature.^[85] IR (film) ν 2924, 2839, 1635, 1598, 1342, 1246, 1157, 1110, 828 cm^{-1} ; ^1H NMR (400MHz, CDCl_3) δ 7.82 (dt, J = 9.0, 2.0 Hz, 2H), 7.00 (dt, J = 9.0, 2.7 Hz, 2H) 6.60(s, 1H), 6.56(d, J = 2.3Hz, 1H), 6.38(d, J = 2.3Hz, 1H), 3.96 (s, 3H), 3.92 (s, 3H), 3.88 (s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100MHz) δ 177.7, 163.9, 162.1, 160.9, 160.8, 159.8, 127.6, 123.8, 114.3, 109.2, 107.6, 96.1, 92.8, 56.4, 55.7, 55.5.

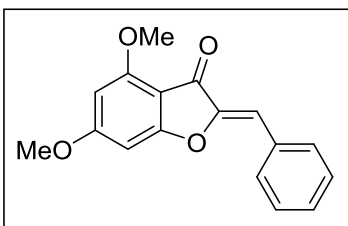


5-methoxy-2-(naphthalen-1-yl)-4H-chromen-4-one (9e): Derived from *o*-alkynoylphenol **8e**. Flavone **9e** was eluted from the column with methanol-DCM (1:20) and obtained in 32% yield as a dark brown oil. IR (film) ν 2925, 2840, 1639, 1602, 1472, 1371, 1080, 725 cm^{-1} ; ^1H NMR (400MHz, CDCl_3) δ 8.16 (m, 1H), 8.02 (d, J = 8.2 Hz, 1H), 7.77 (dd, J = 7.0, 1.2 Hz, 1H), 7.59 (m, 4H), 7.10 (m, 1H), 6.89 (d, 1H), 6.61 (s, 1H), 4.05 (s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100MHz) δ 178.1, 163.1, 160.0, 158.8, 133.8, 133.7, 131.4, 130.4, 128.7, 127.9, 127.3, 126.5, 125.0, 124.9, 114.7, 114.6, 110.3, 110.0, 106.6, 56.6. HRMS (ESI/[M+H]⁺) calcd. for $\text{C}_{20}\text{H}_{15}\text{O}_3$ 303.1016, found 303.1018.



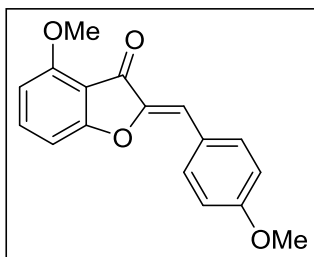
(Z)-4-methoxyaurone/(Z)-2-benzylidene-4-methoxybenzofuran-3(2H)-one (10a):

Derived from *o*-alkynoylphenol **8c**. Aurone **10a** was obtained in 95% yield as a yellow, crystalline solid. IR (film) ν 2924, 2845, 1704, 1654, 1594, 1491, 1250, 1072, 796, 751, 686 cm^{-1} ; ^1H NMR (400MHz, CDCl_3) δ 7.91 (m, 2H), 7.58(t, J = 8.2 Hz, 1H), 7.46 (tt, J = 7.3, 1.2 Hz, 2H), 7.39 (tt, J = 7.4, 1.2 Hz, 1H), 6.90 (d, J = 8.2 Hz, 1H), 6.85 (s, 1H), 6.63 (d, J = 8.6 Hz, 1H), 4.02(s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100MHz) δ 182.4, 167.1, 158.6, 146.9, 138.4, 132.5, 131.3, 129.6, 128.8, 111.9, 110.9, 105.2, 104.8, 56.3. HRMS (ESI/[M+H] $^+$) calcd. for $\text{C}_{16}\text{H}_{13}\text{O}_3$ 253.0859, found 253.0859.

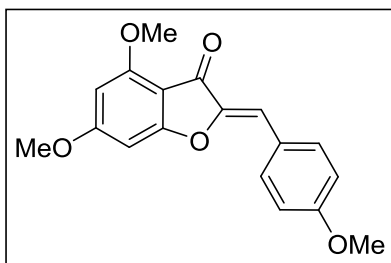


(Z)-4,6-dimethoxyaurone/(Z)-2-benzylidene-4,6-dimethoxybenzofuran-3(2H)-one

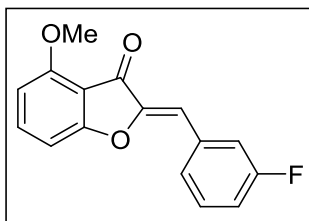
(10b): Derived from *o*-alkynoylphenol **8b**. Aurone **10b** was obtained in 88% yield as a yellow, crystalline solid. This compound has been reported in the literature.^[87] IR (film) ν 2922, 2844, 1693, 1583, 1206, 1150, 1090, 809, 691 cm^{-1} ; ^1H NMR (400MHz, CDCl_3) δ 7.87 (d, J = 7.0 Hz, 2H), 7.44(t, J = 7.4 Hz, 2H), 7.38 (m, 1H), 6.77 (s, 1H), 6.40 (d, J = 1.6 Hz, 1H), 6.14 (d, J = 1.6 Hz, 1H), 3.96(s, 3H), 3.92 (s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100MHz) δ 180.7, 169.1, 169.0, 159.4, 147.9, 132.6, 131.1, 129.3, 128.8, 110.7, 105.2, 94.0, 89.2, 56.2, 56.1.



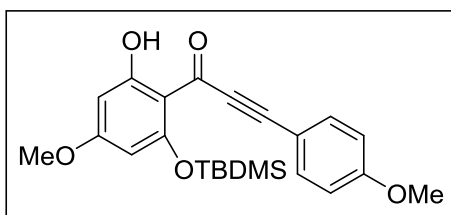
(Z)-4',4-dimethoxyaurone/(Z)-4-methoxy-2-(4-methoxybenzylidene)benzofuran-3(2H)-one (10c): Derived from *o*-alkynoylphenol **8d**. Aurone **10c** was obtained in 99% yield as an orange, crystalline solid. IR (film) ν 2922, 2851, 1697, 1651, 1592, 1494, 1246, 1070, 825, 793, 759 cm^{-1} ; ^1H NMR (400MHz, CDCl_3) δ 7.87 (dt, J = 8.6, 2.3 Hz, 2H), 7.56(t, J = 8.2 Hz, 1H), 6.98 (dt, J = 9.0, 3.1 Hz, 2H), 6.88 (d, J = 8.2 Hz, 1H), 6.83 (s, 1H), 6.61 (d, J = 8.2 Hz, 1H), 4.01 (s, 3H), 3.87 (s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100MHz) δ 182.2, 166.8, 160.8, 158.5, 145.8, 138.0, 133.1, 125.2, 114.4, 112.2, 111.1, 104.9, 104.7, 56.2, 55.3. HRMS (ESI/[M+H] $^+$) calcd. for $\text{C}_{17}\text{H}_{15}\text{O}_4$ 283.0965, found 283.0965.



(Z)-4',4,6-trimethoxyaurone/(Z)-4,6-dimethoxy-2-(4-methoxybenzylidene)benzofuran-3(2H)-one (10d): Derived from *o*-alkynoylphenol **8a**. Aurone **10d** was obtained in 99% yield as a dark yellow, crystalline solid. This compound has been reported in the literature.^[88] IR (film) ν 2922, 2849, 1688, 1588, 1507, 1246, 1206, 1150, 1086, 818 cm^{-1} ; ^1H NMR (400MHz, CDCl_3) δ 7.84 (dt, J = 9.0, 2.3 Hz, 2H), 6.97 (dt, J = 9.0, 2.3 Hz, 2H), 6.77 (s, 1H), 6.40 (d, J = 2.0 Hz, 1H), 6.15 (d, J = 2.0 Hz, 1H), 3.97(s, 3H), 3.93 (s, 3H), 3.87 (s, 3H); ^1H NMR (400MHz, CDCl_3) δ 7.87 (d, J = 7.0 Hz, 2H), 7.44(t, J = 7.4 Hz, 2H), 7.38 (m, 1H), 6.77 (s, 1H), 6.40 (d, J = 1.6 Hz, 1H), 6.14 (d, J = 1.6 Hz, 1H), 3.96(s, 3H), 3.92 (s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100MHz) δ 180.64, 168.7, 160.6, 159.4, 146.8, 132.9, 125.3, 114.3, 111.0, 93.9, 89.2, 56.2, 56.1, 55.4.

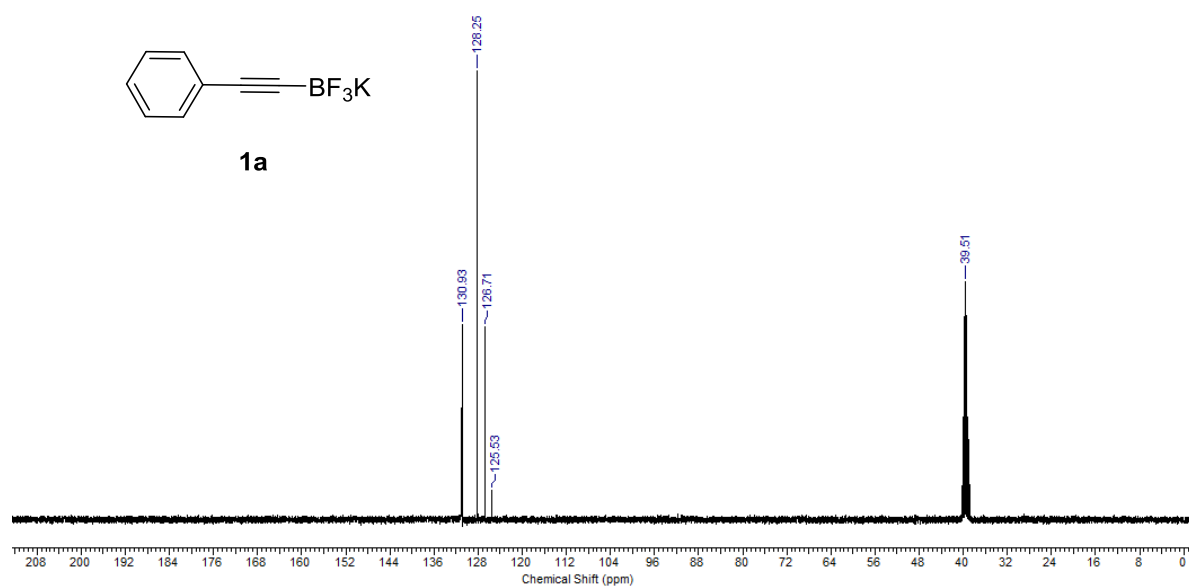
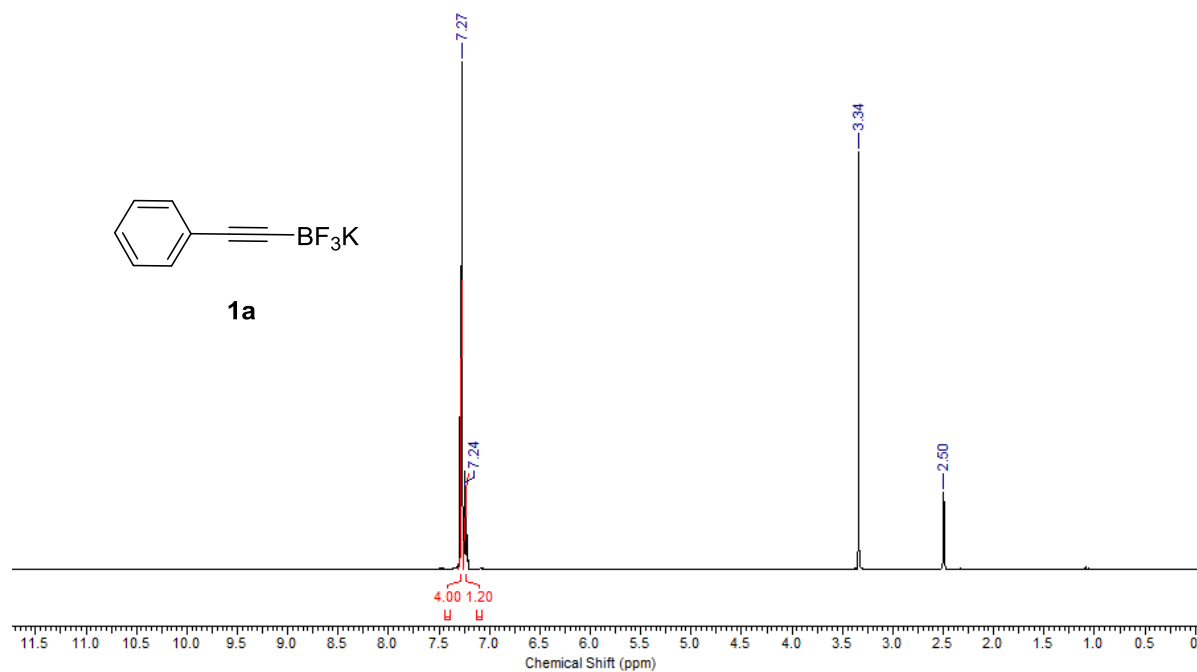


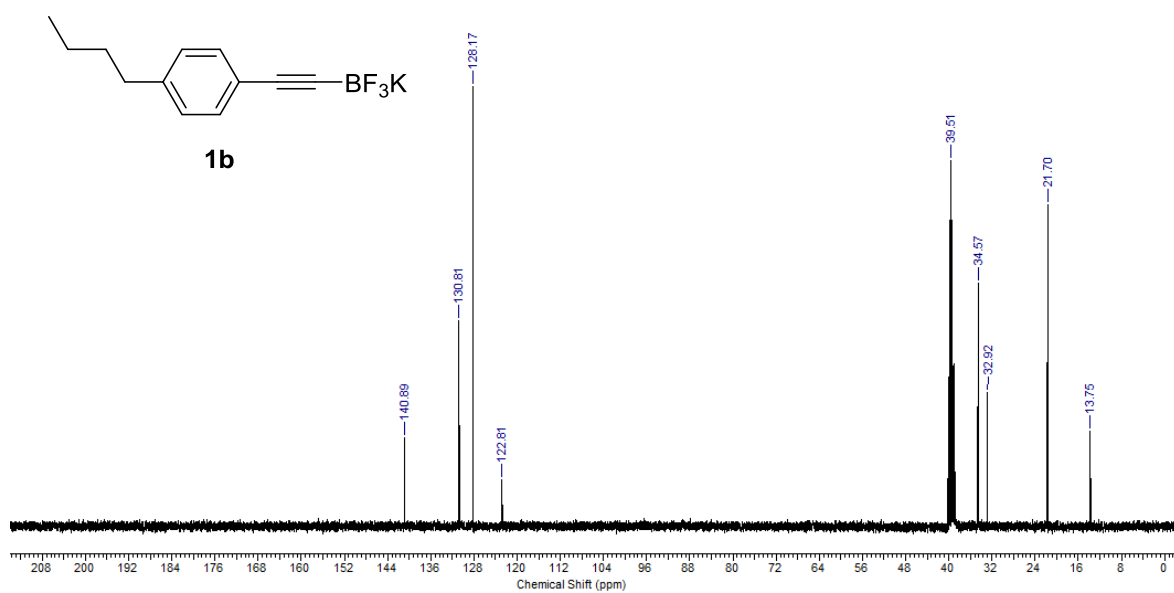
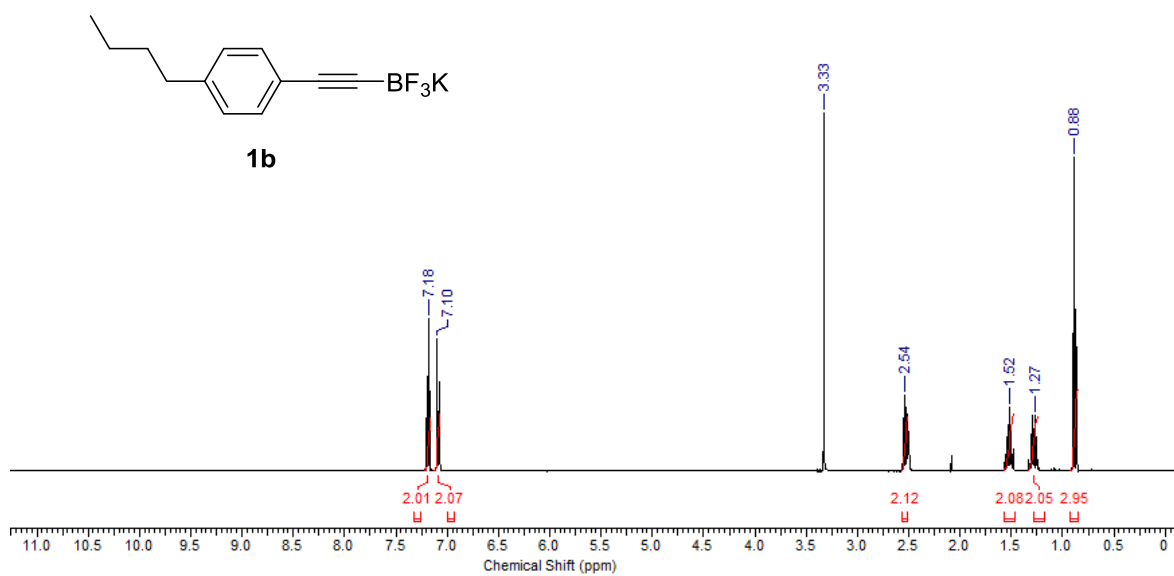
(Z)- 3'-fluoro-4-methoxyaurone/(Z)-2-(3-fluorobenzylidene)-4-methoxybenzofuran-3(2H)-one (10e): Derived from *o*-alkynoylphenol **8f**. **10e** was obtained in 78% yield as a yellow, crystalline solid. IR (film) ν 2918, 2846, 1704, 1651, 1600, 1493, 1442, 1243, 1074, 794, 753, 679 cm^{-1} ; ^1H NMR (400MHz, CDCl_3) δ 7.71 (m, 1H), 7.60 (m, 2H), 7.41 (m, 1H), 7.09 (m, 1H), 6.91 (d, $J = 8.2$ Hz, 1H), 6.79 (s, 1H), 6.65 (d, $J = 8.2$ Hz, 1H), 4.02 (s, 3H); ^{13}C { ^1H } NMR (CDCl_3 , 100MHz) δ 182.3, 167.1, 164.1, 161.6, 158.6, 147.4, 138.7, 134.5, 130.2 (d, $J = 8.0$ Hz, 1C), 127.2, 117.4 (d, $J = 22.0$ Hz, 1C), 116.5 (d, $J = 21.0$ Hz, 1C), 110.3, 105.4, 104.8, 56.3. HRMS (ESI/[M+H] $^+$) calcd. for $\text{C}_{16}\text{H}_{11}\text{O}_3$ 271.0765, found 271.0766.

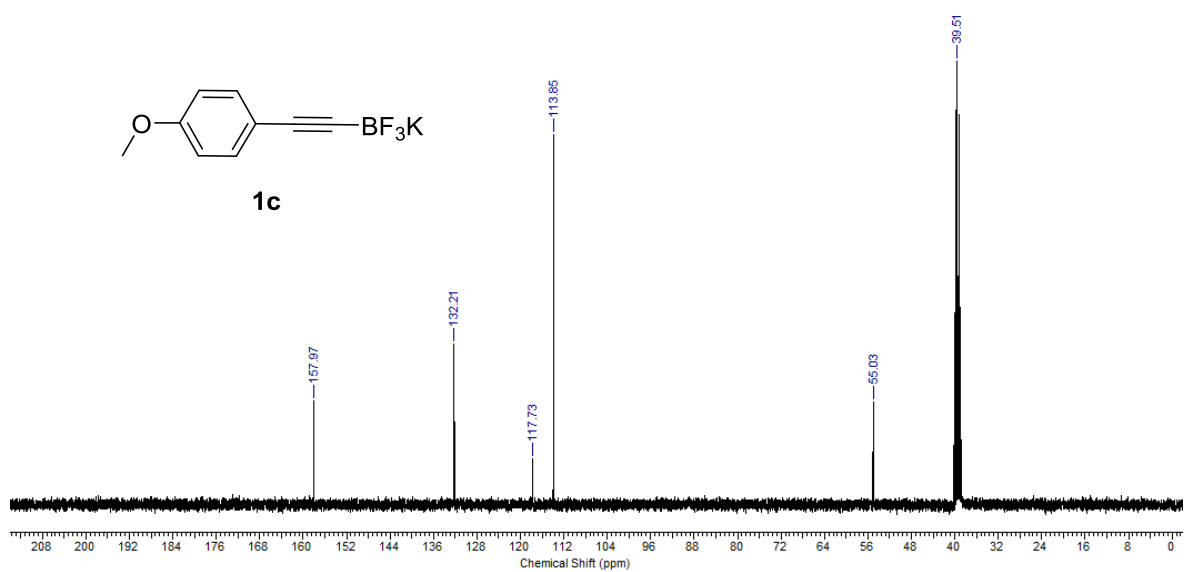
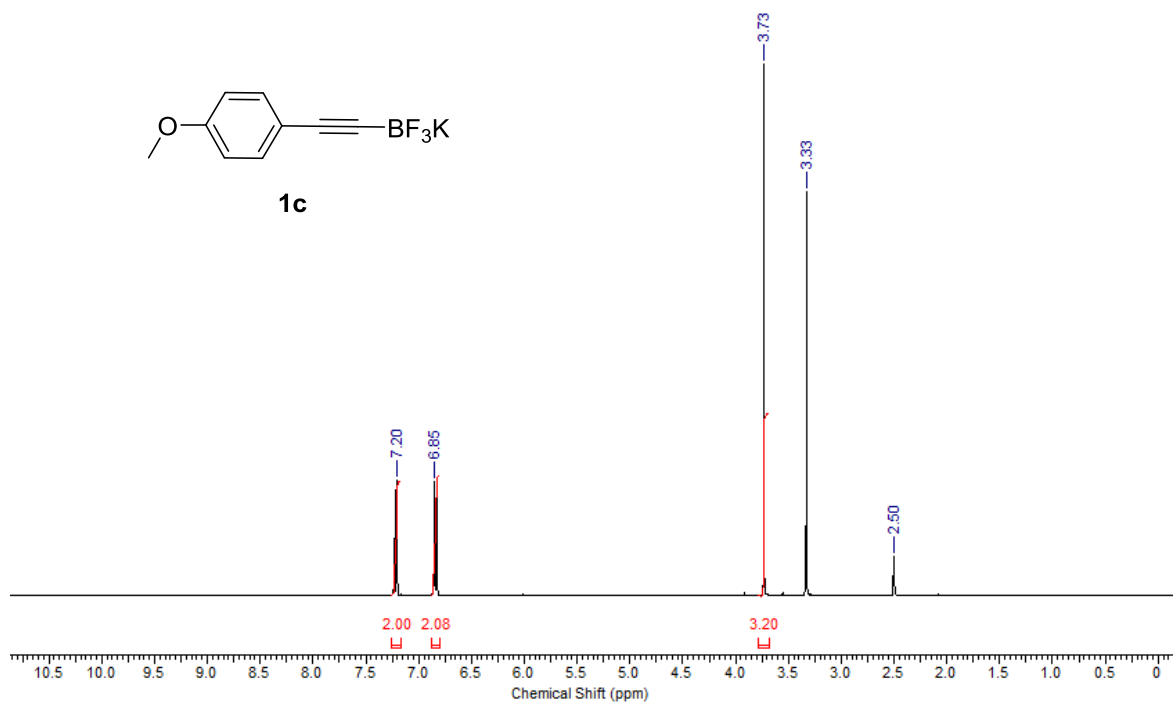


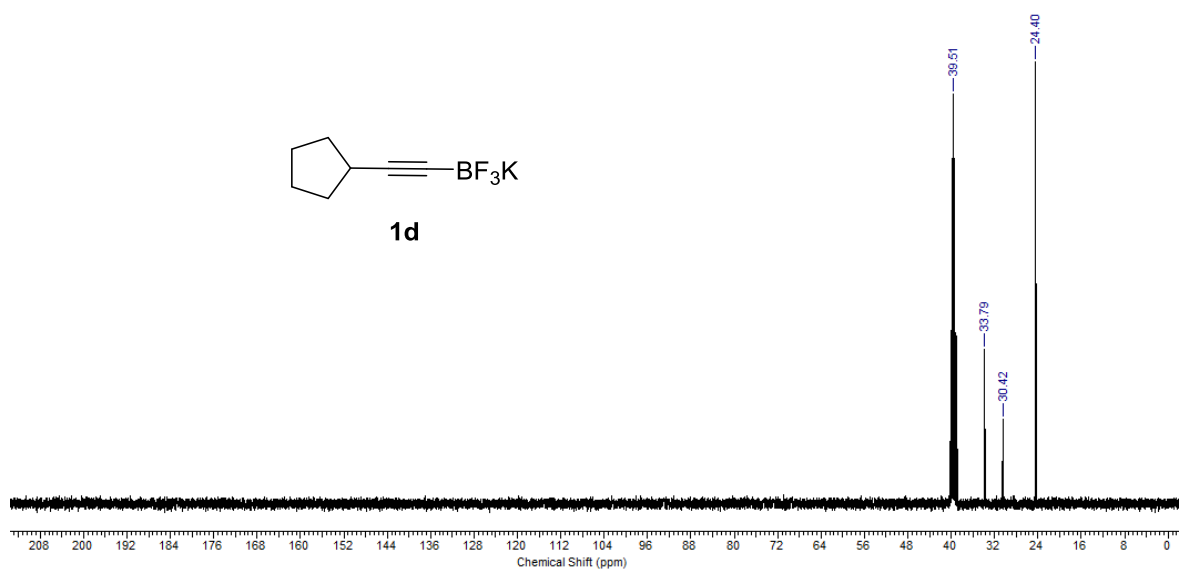
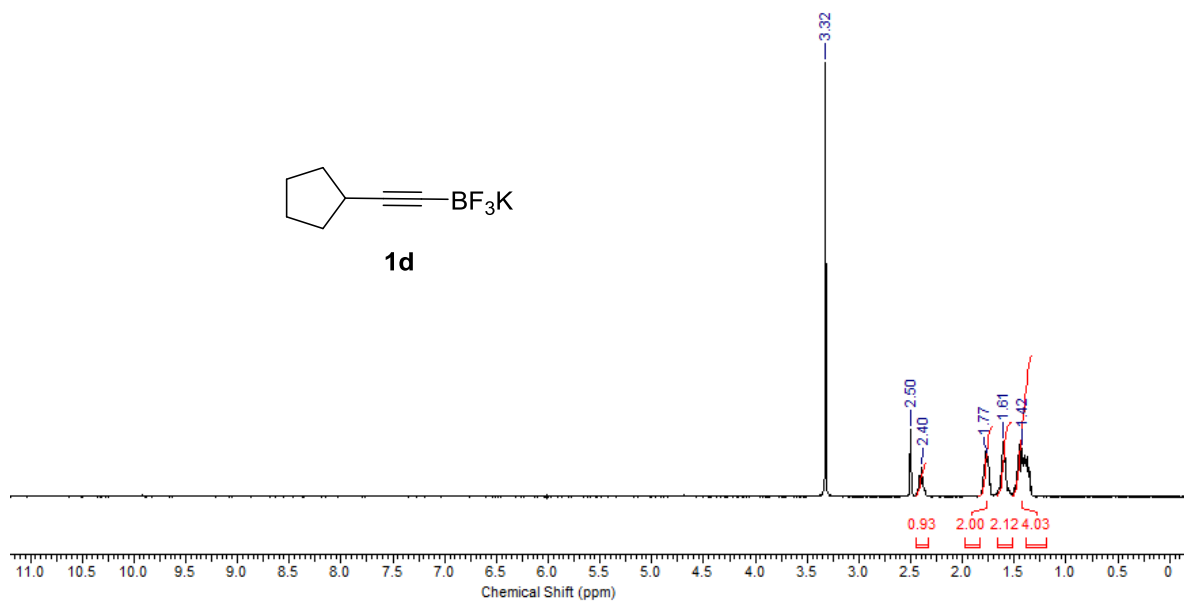
1-(2-((tert-butyldimethylsilyl)oxy)-6-hydroxy-4-methoxyphenyl)-3-(4-methoxyphenyl)prop-2-yn-1-one (15): **15** was obtained in 16% yield as a yellow solid. ^1H NMR (400MHz, CDCl_3) δ 13.01 (s, 1H), 7.54 (d, $J = 8.6$ Hz, 2H), 6.90 (d, $J = 8.6$ Hz, 2H), 6.03 (dd, $J = 60.0, 4.0$ Hz, 2H), 3.85 (s, 3H), 3.82 (s, 3H), 0.96 (s, 6H), 0.26 (s, 9H); ^{13}C { ^1H } NMR (CDCl_3 , 100MHz) δ 178.6, 167.0, 166.5, 161.1, 159.4, 134.4, 114.2, 113.1, 109.8, 99.0, 96.6, 94.4, 89.9, 55.5, 55.4, 29.7, 26.2, 19.1, -3.45.

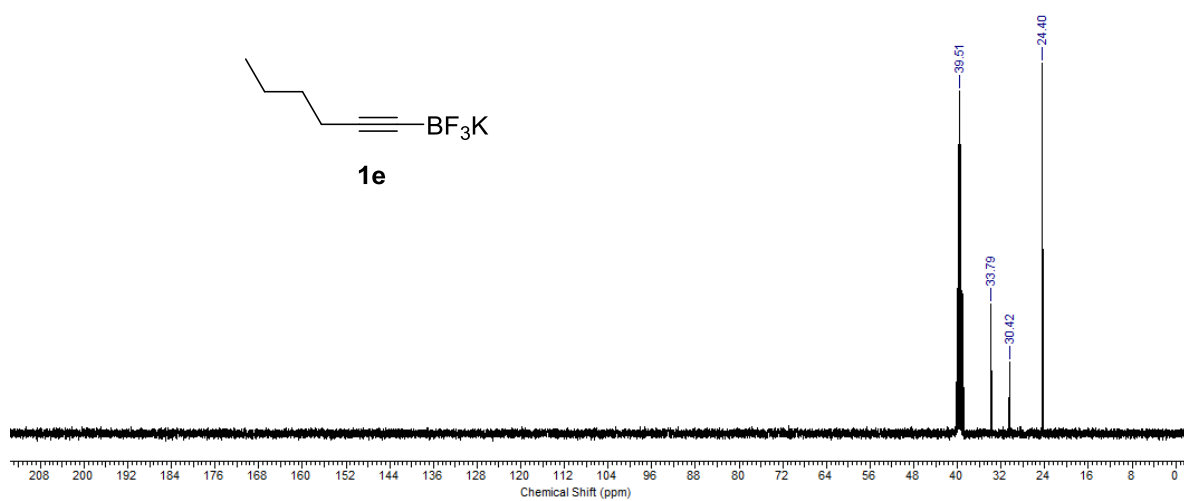
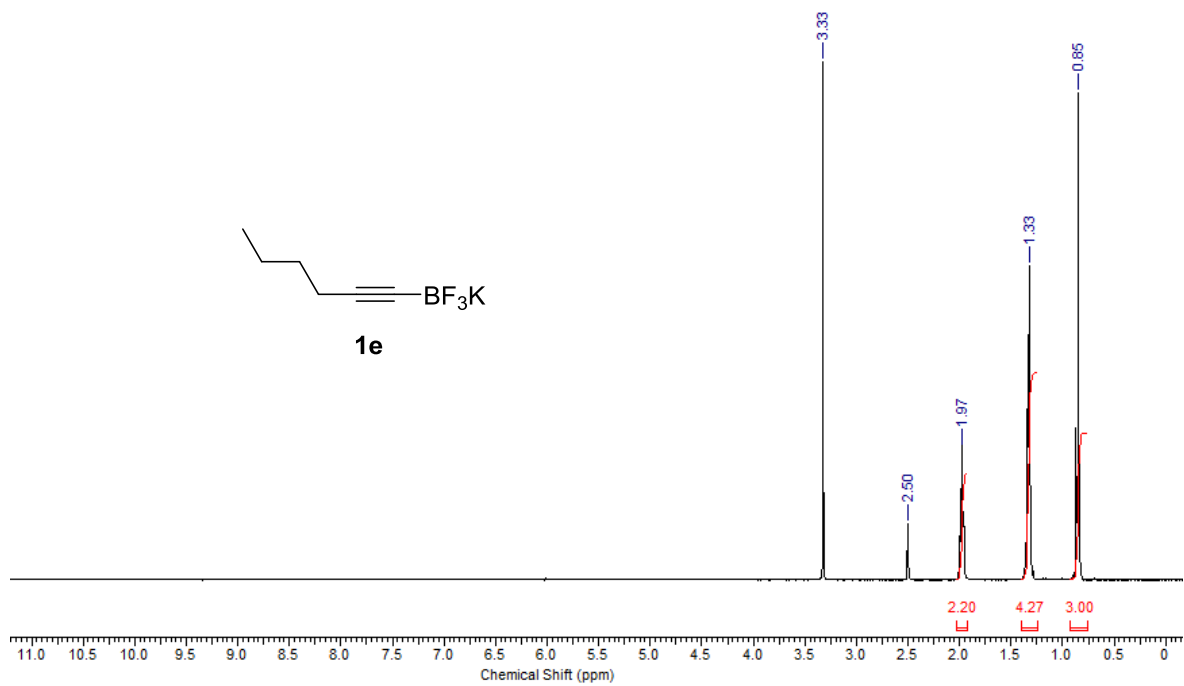
APPENDIX II: NMR SPECTRA FOR SYNTHESIZED COMPOUNDS

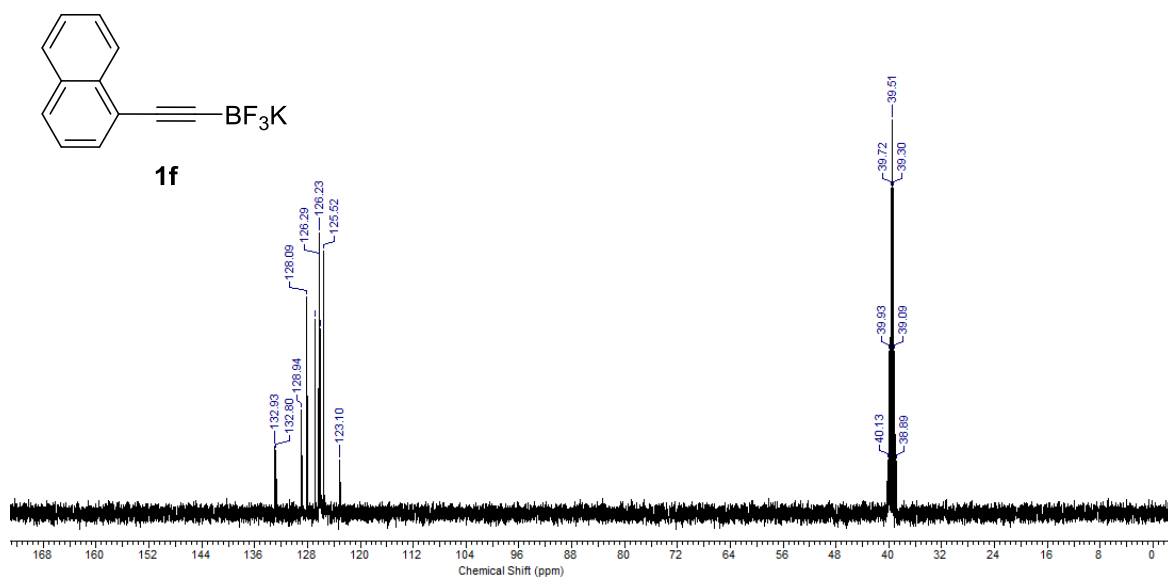
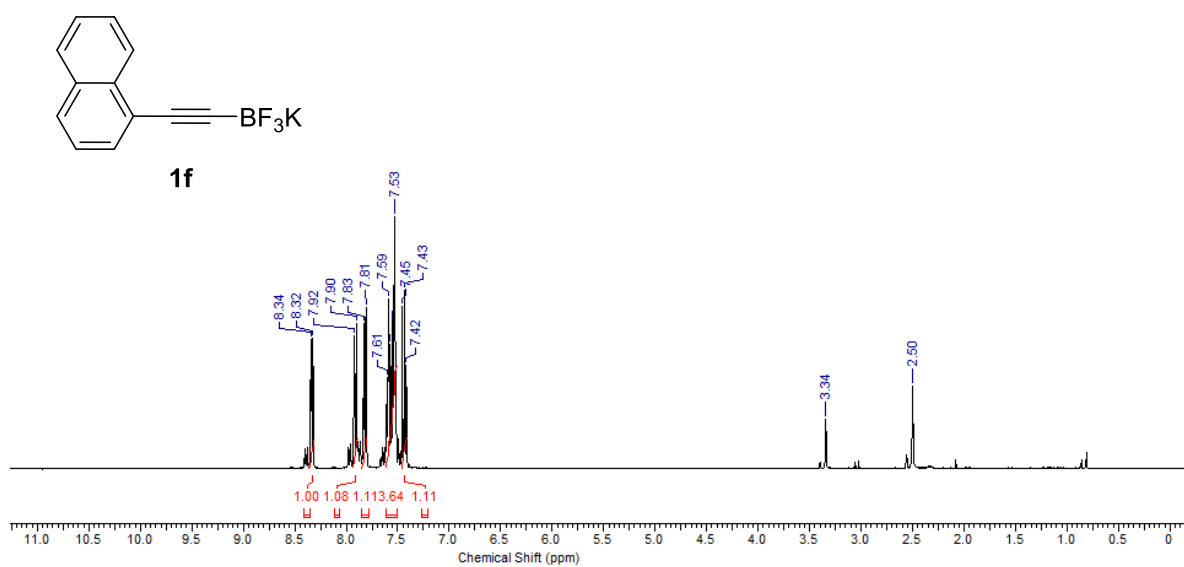


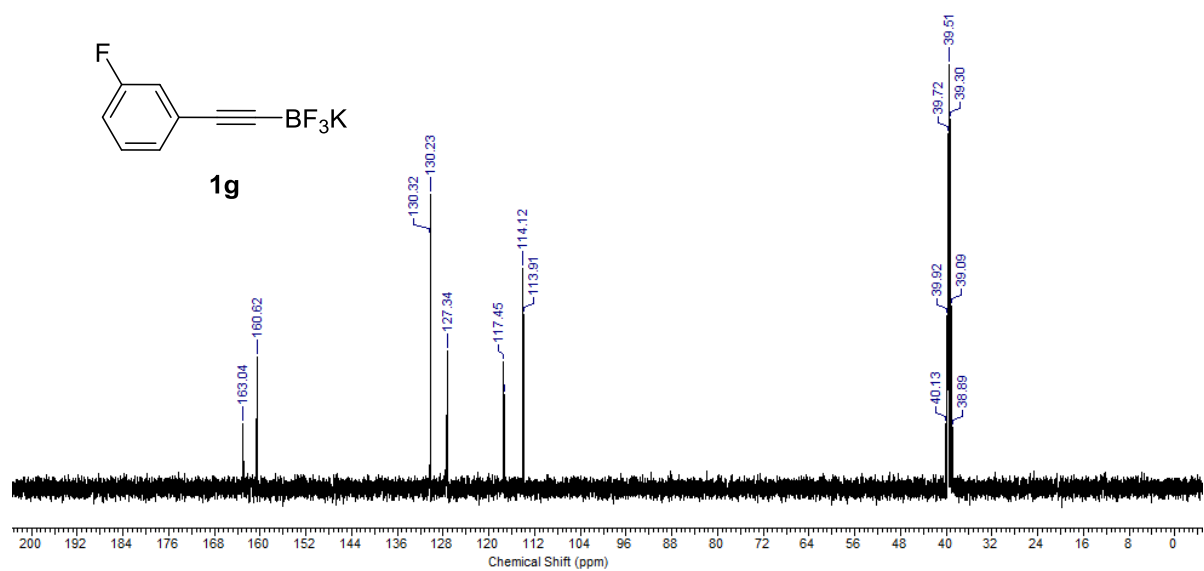
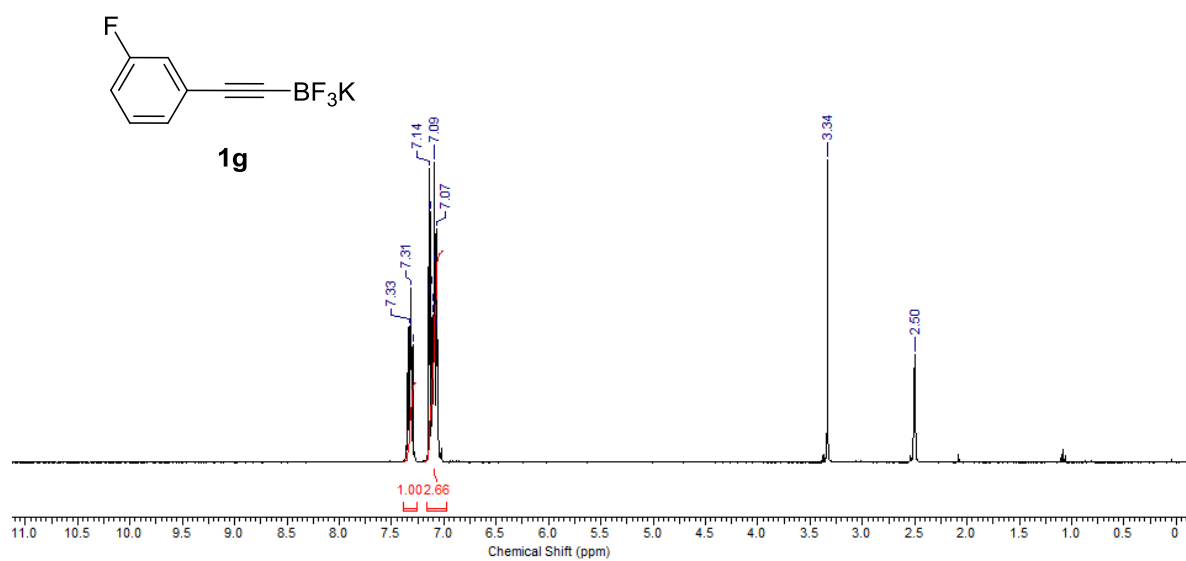


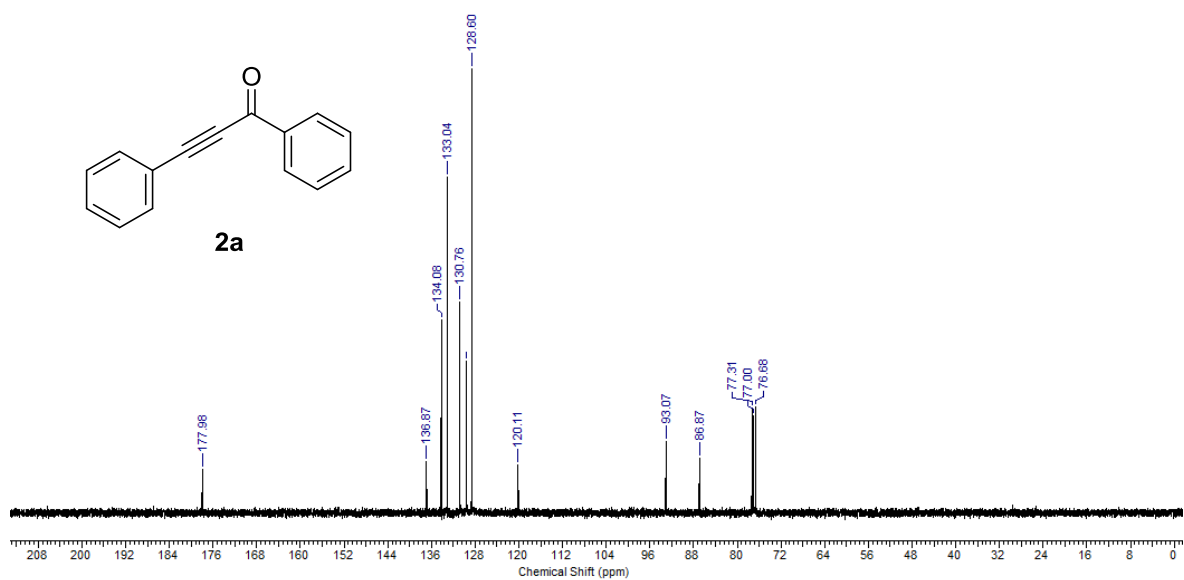
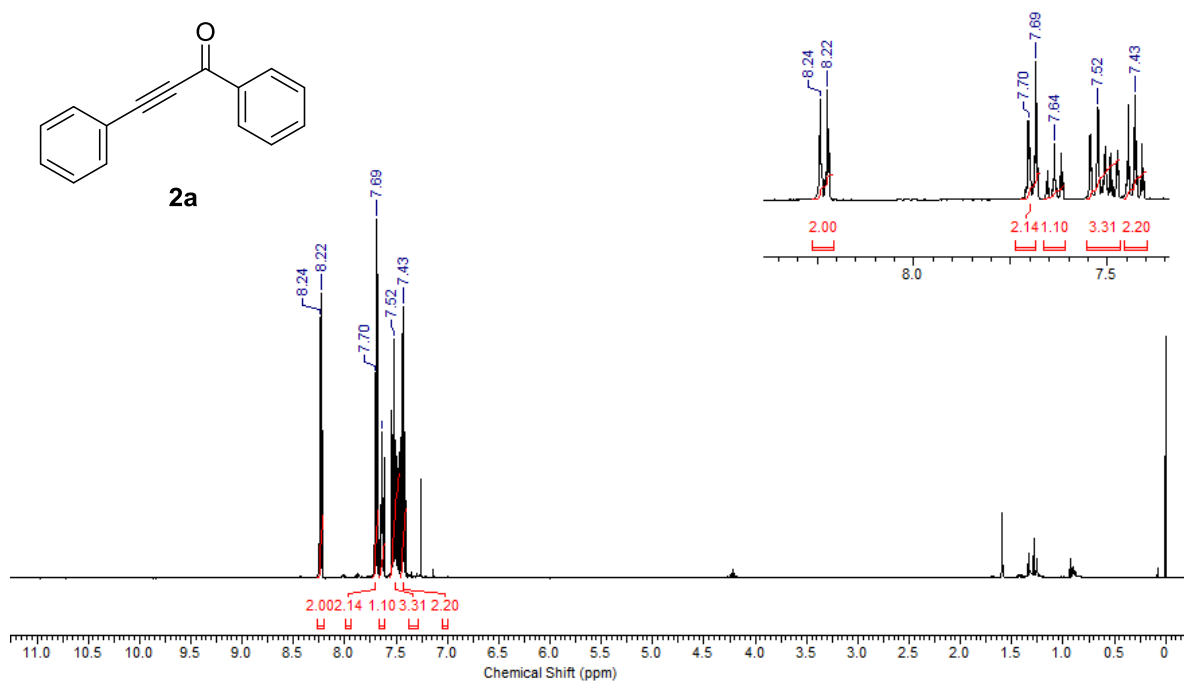


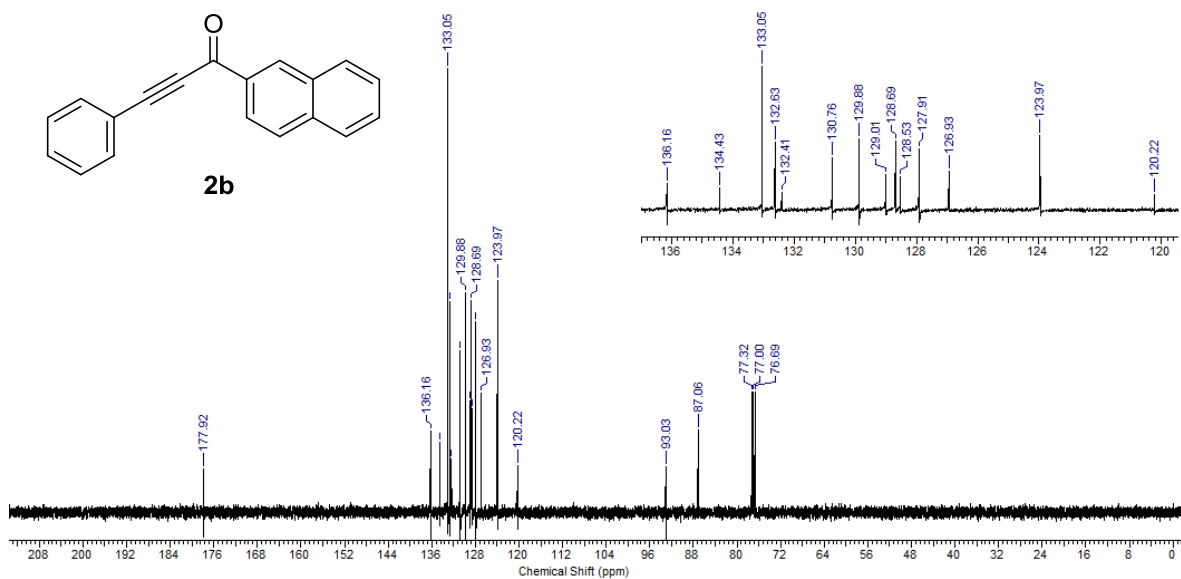
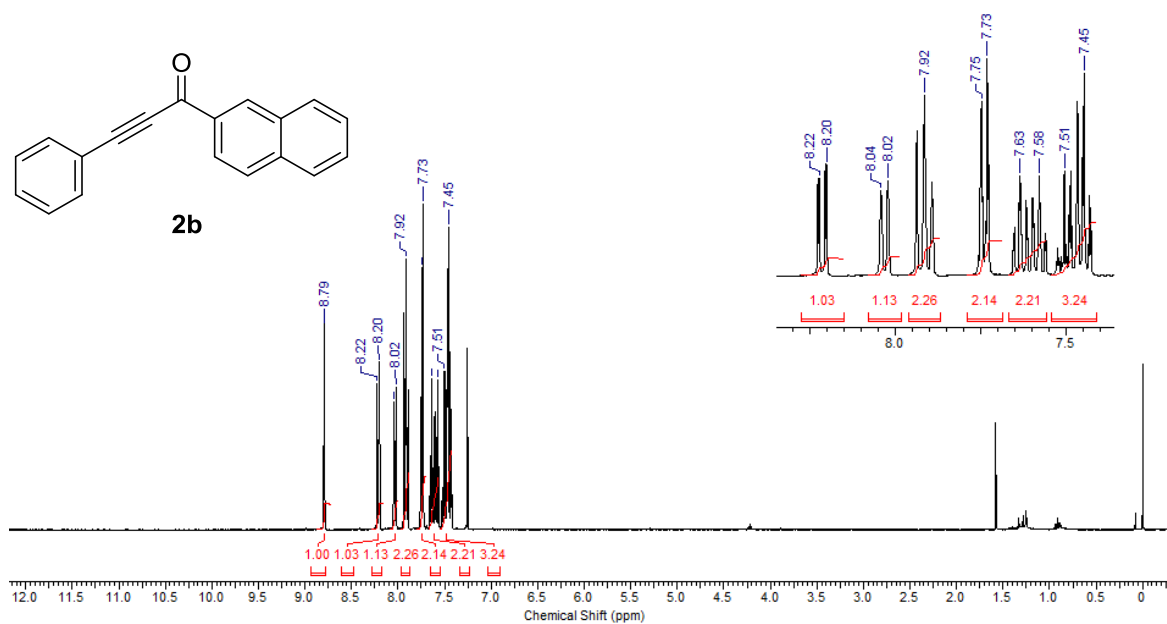


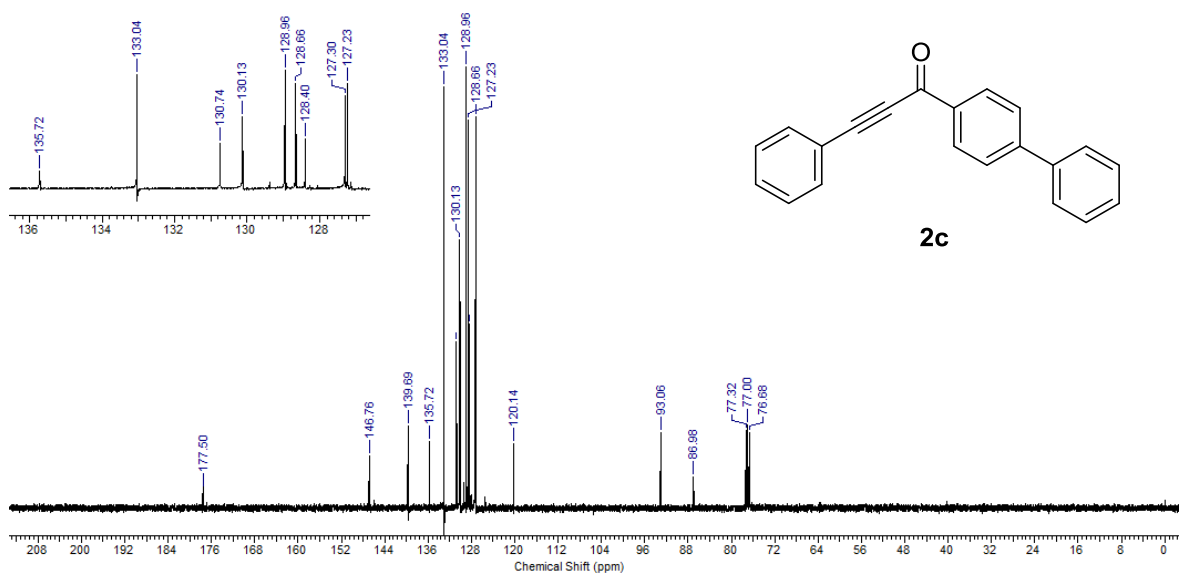
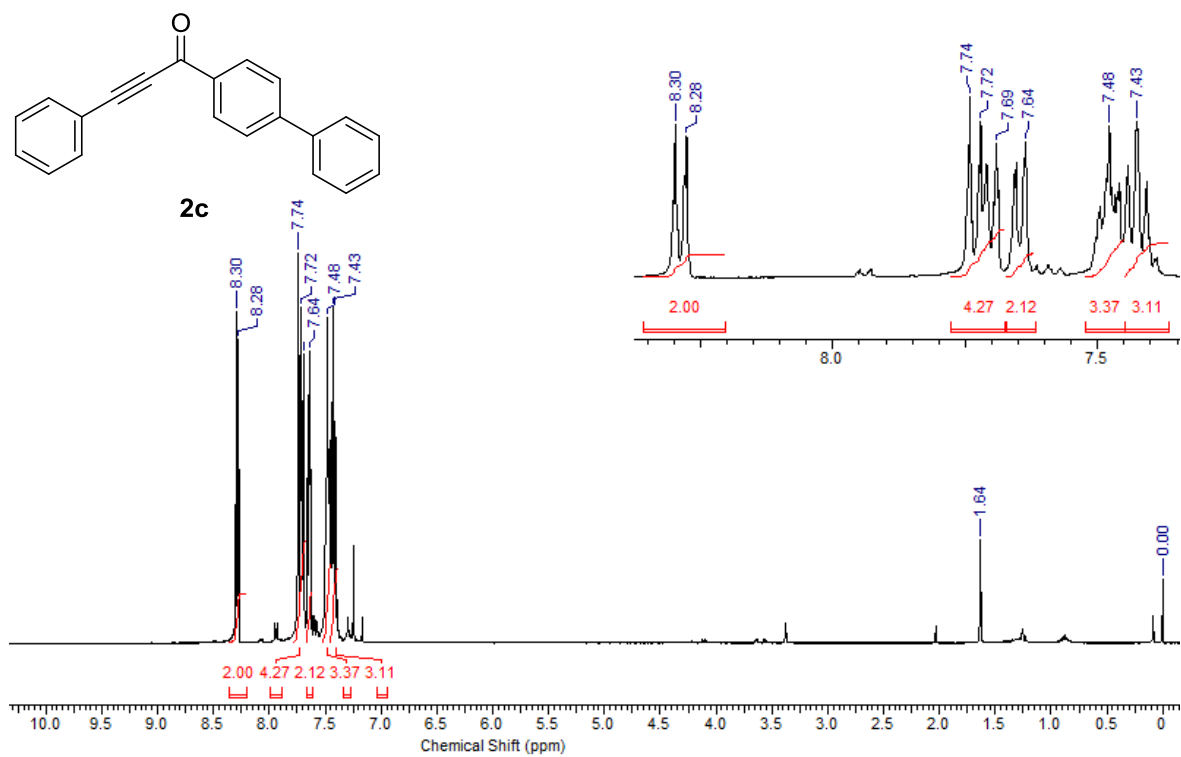


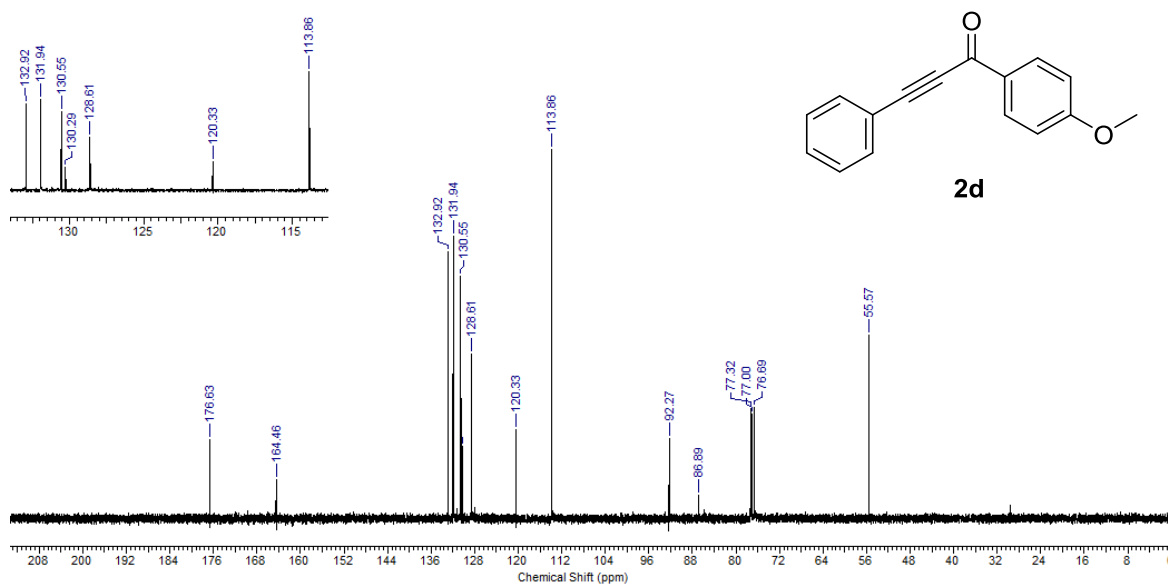
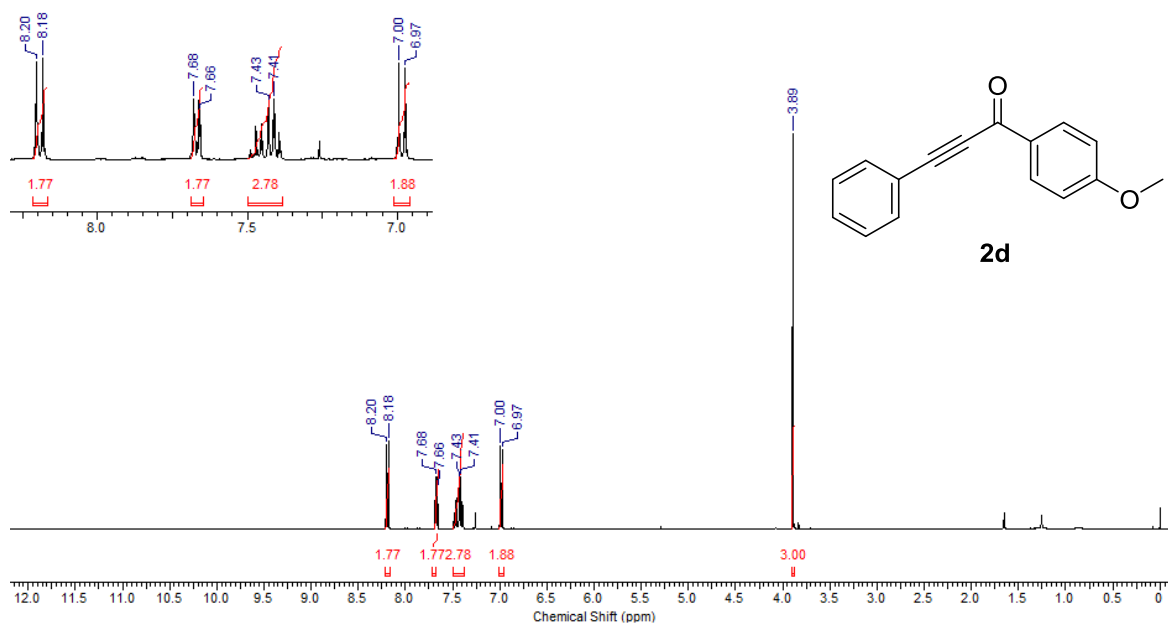


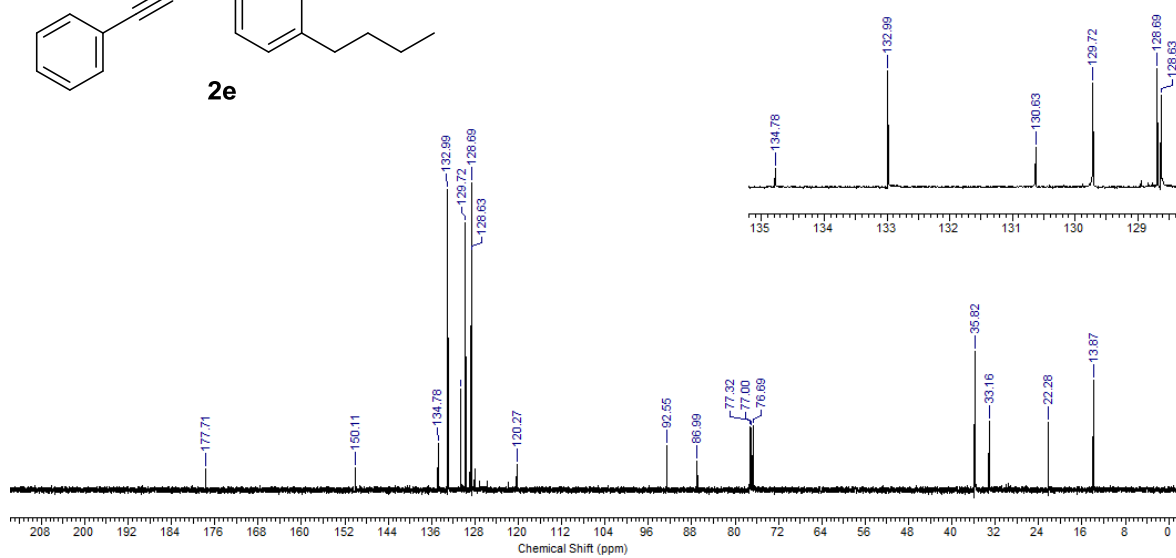
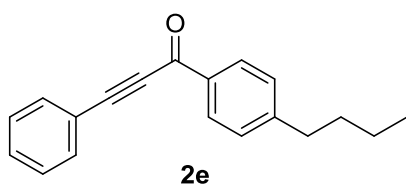
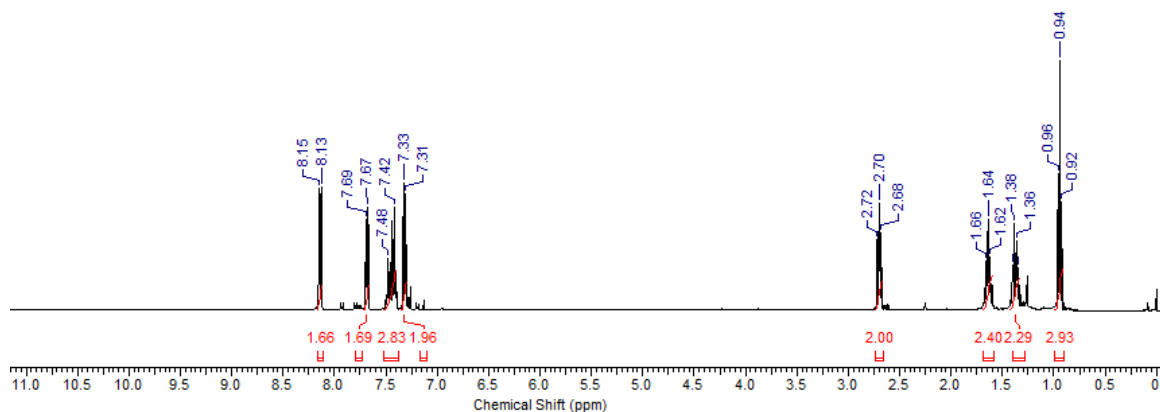
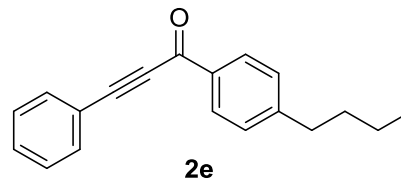
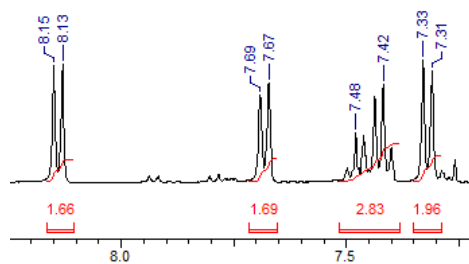


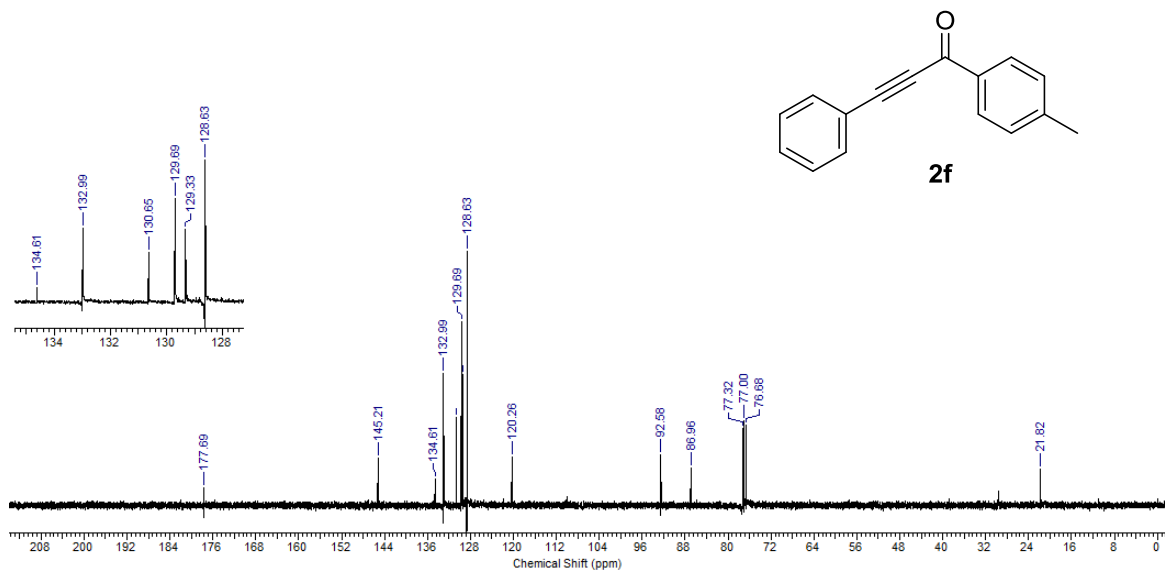
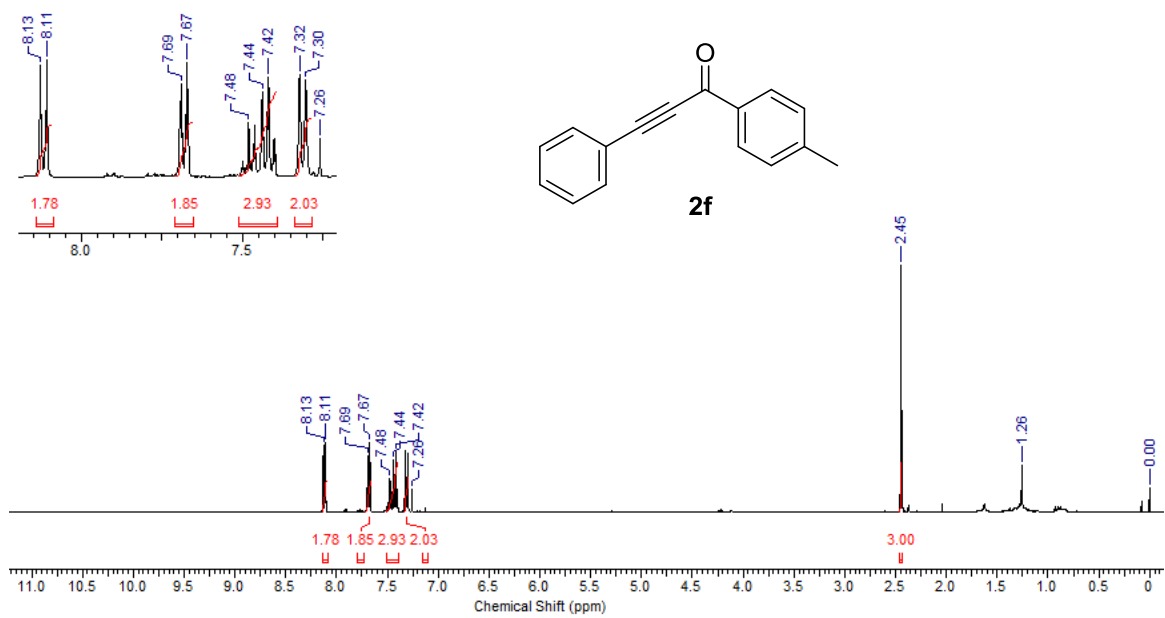


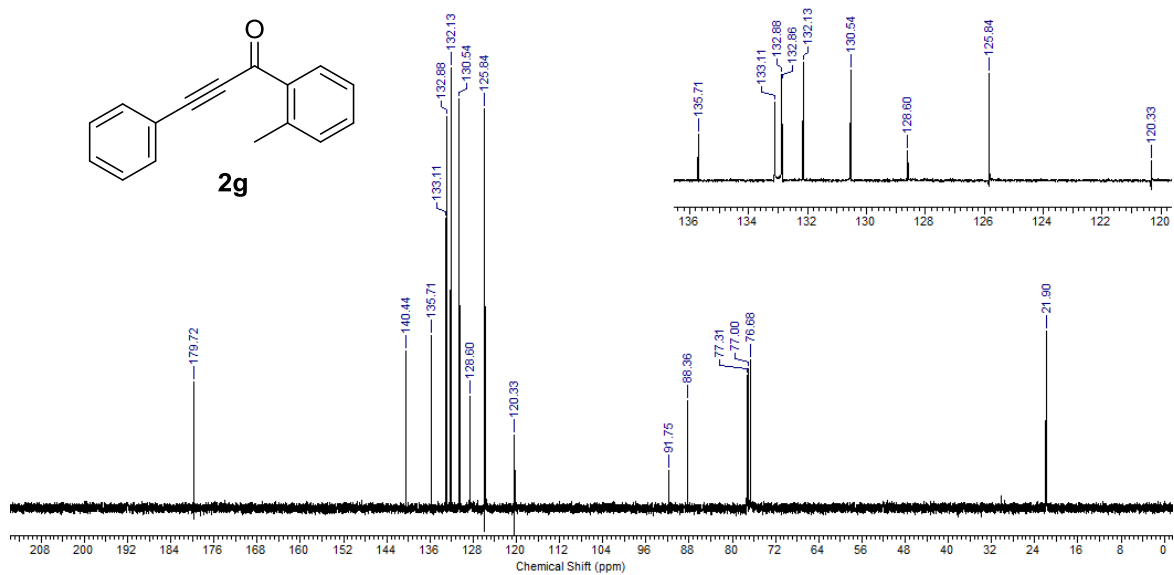
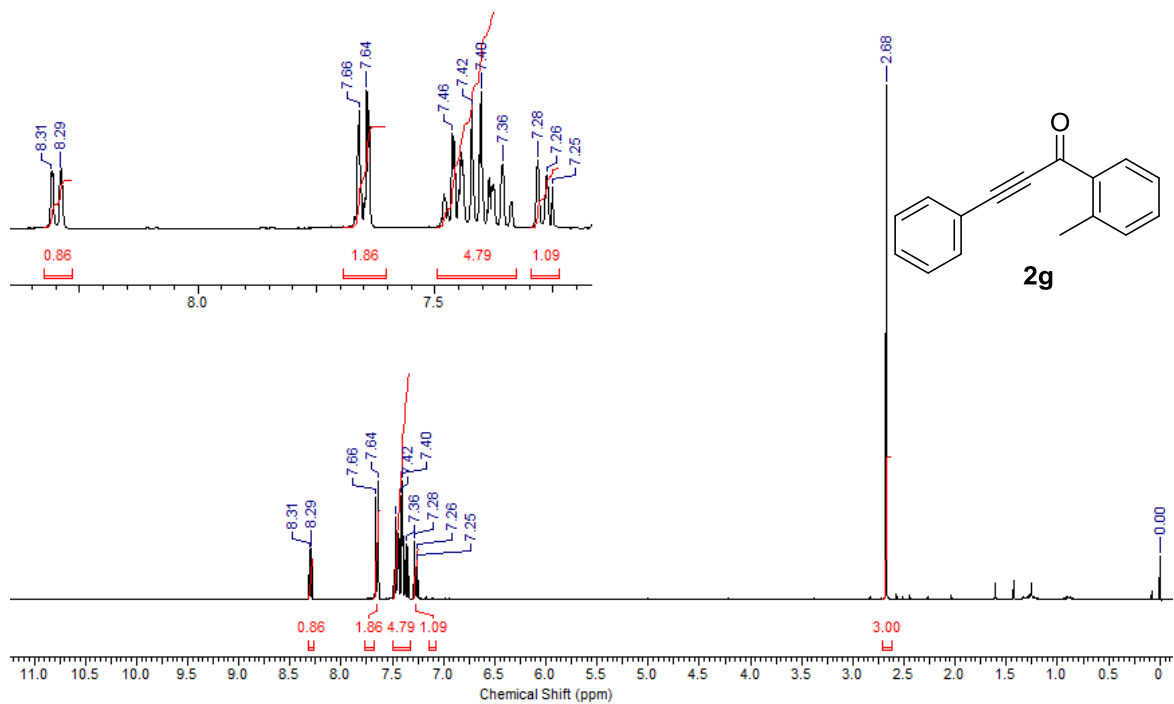


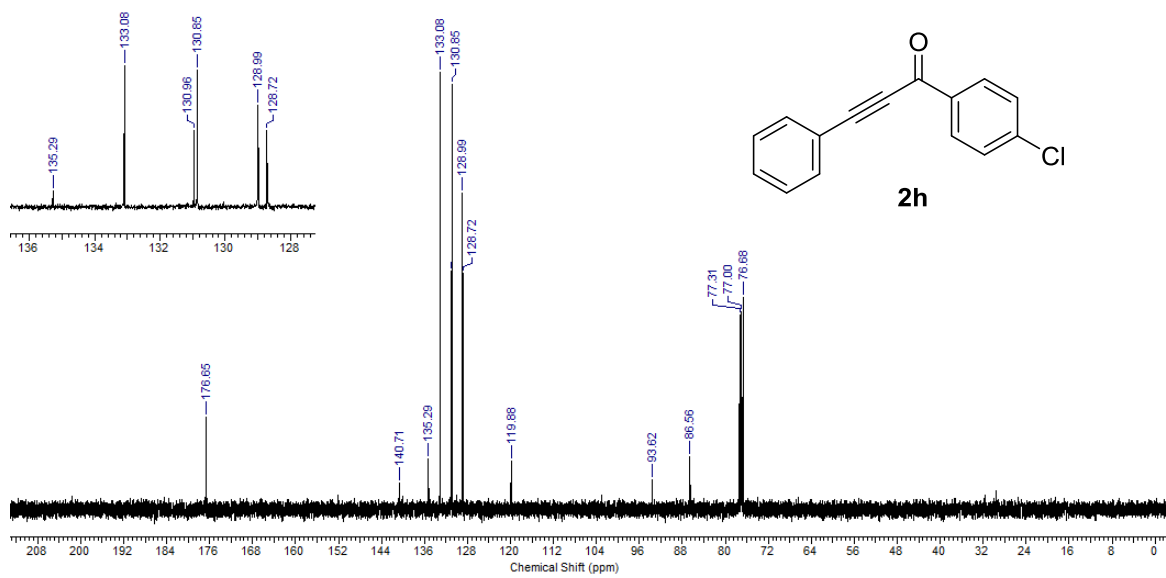
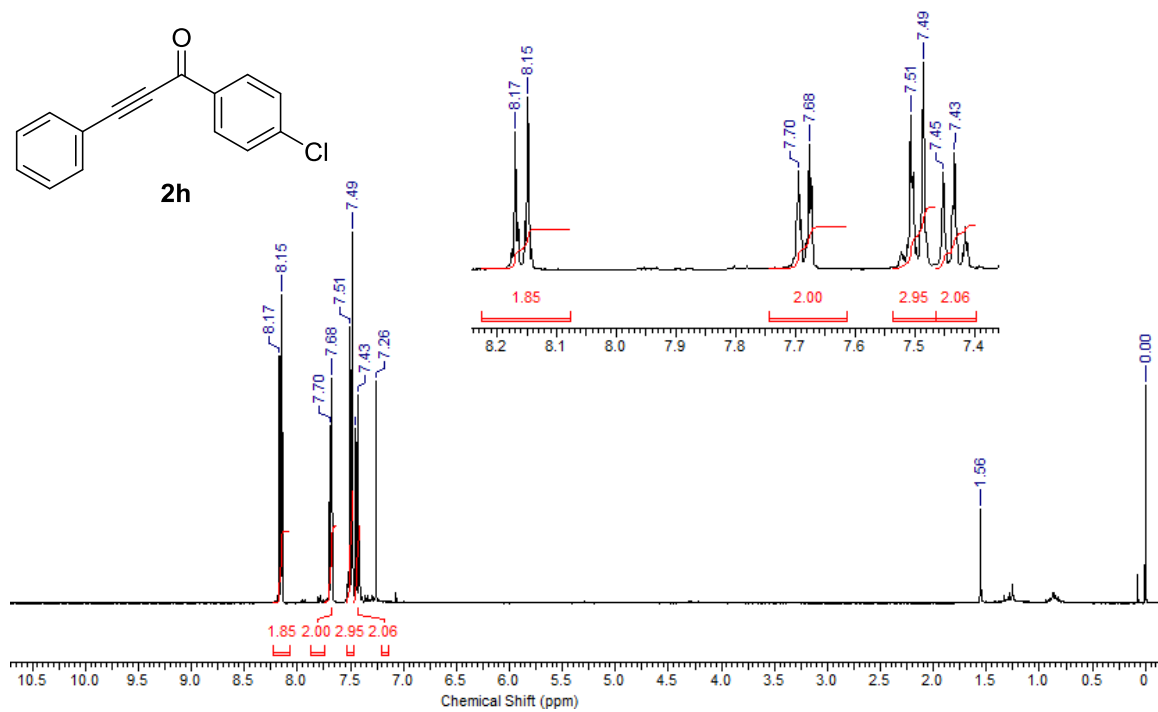


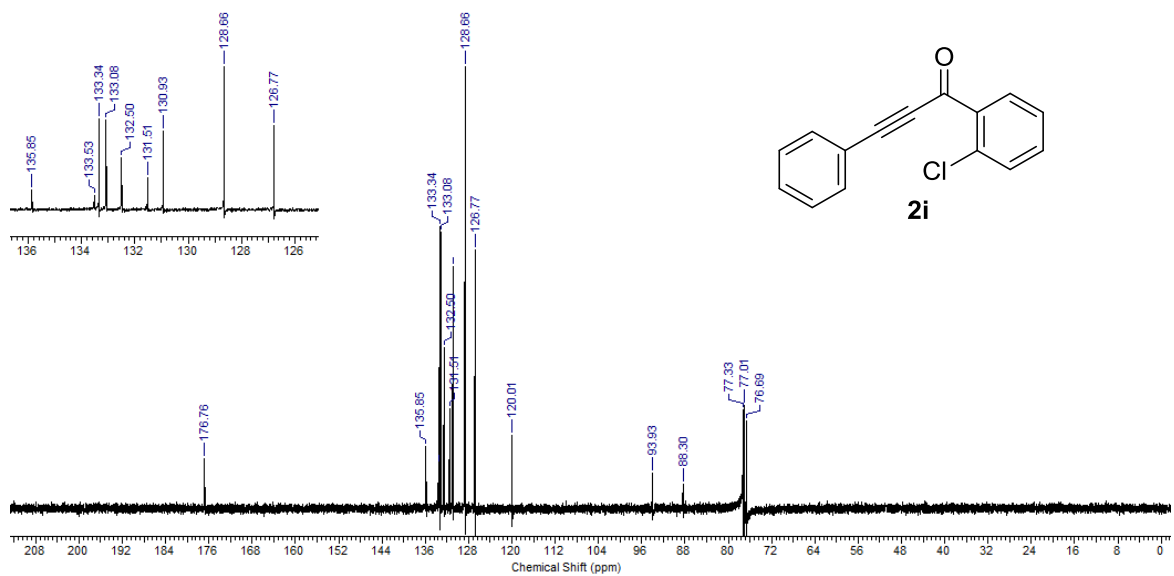
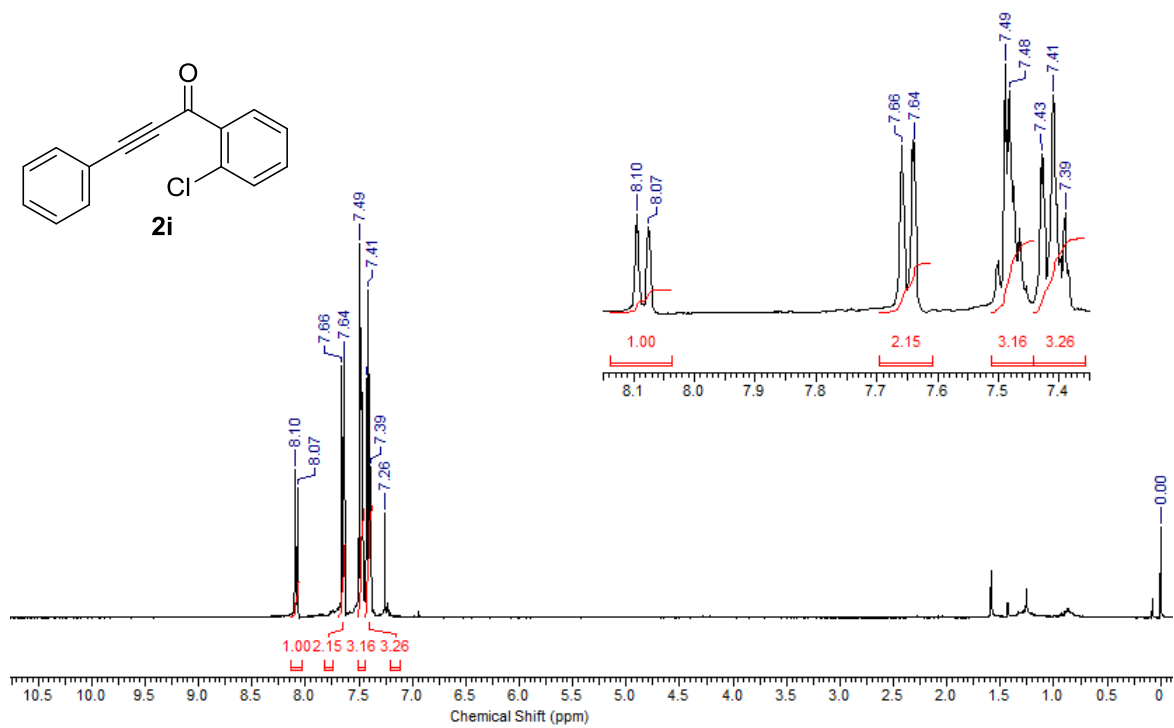


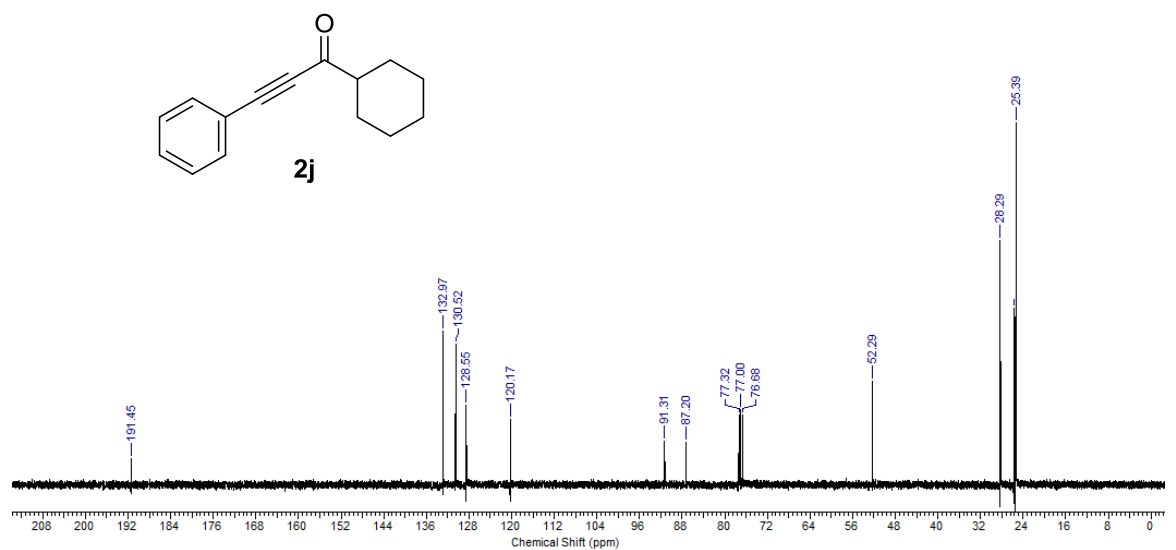
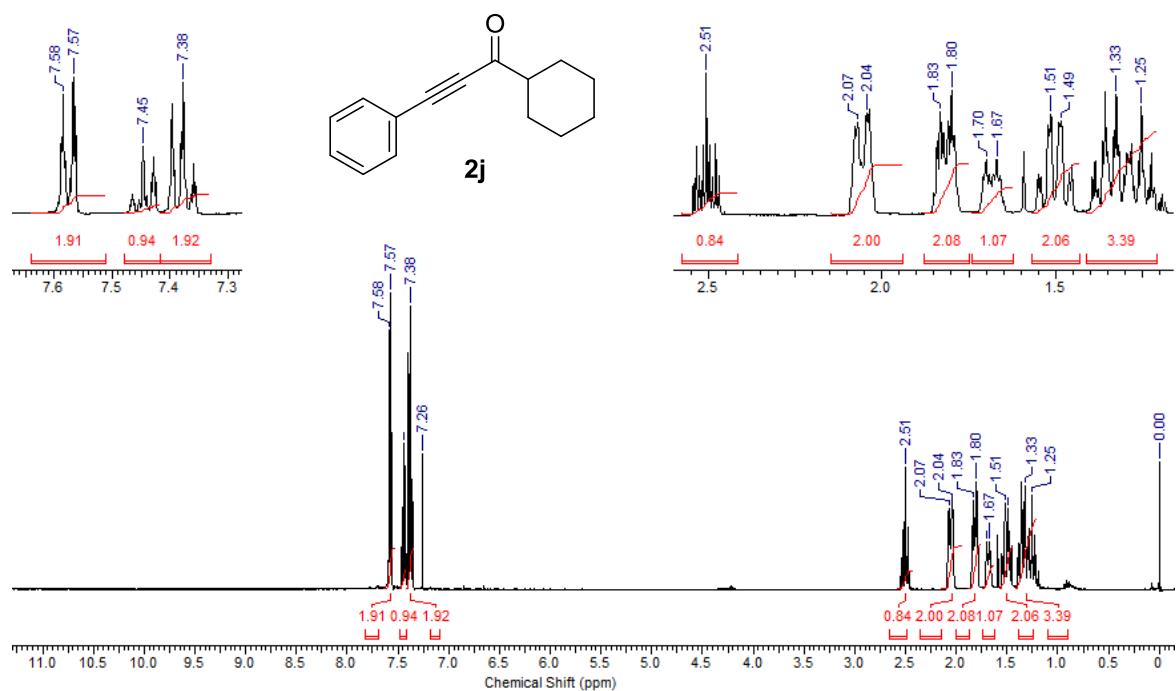


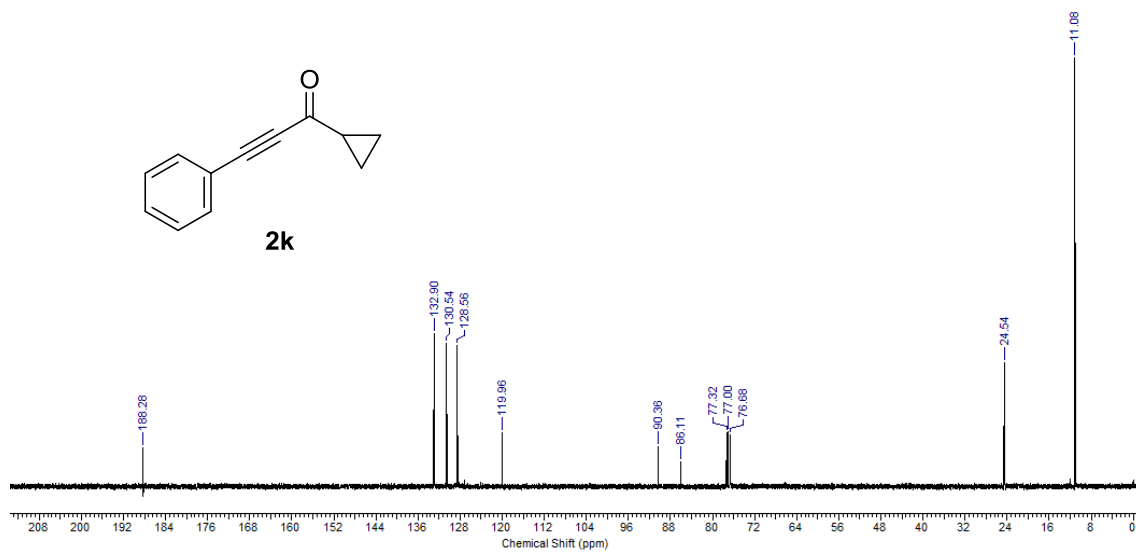
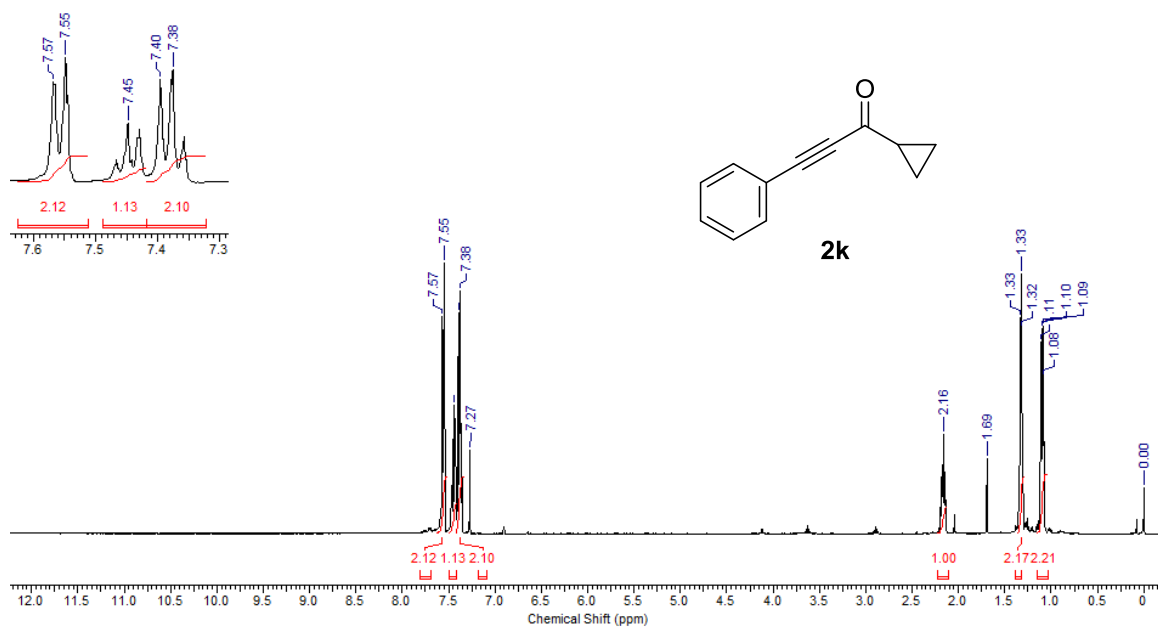


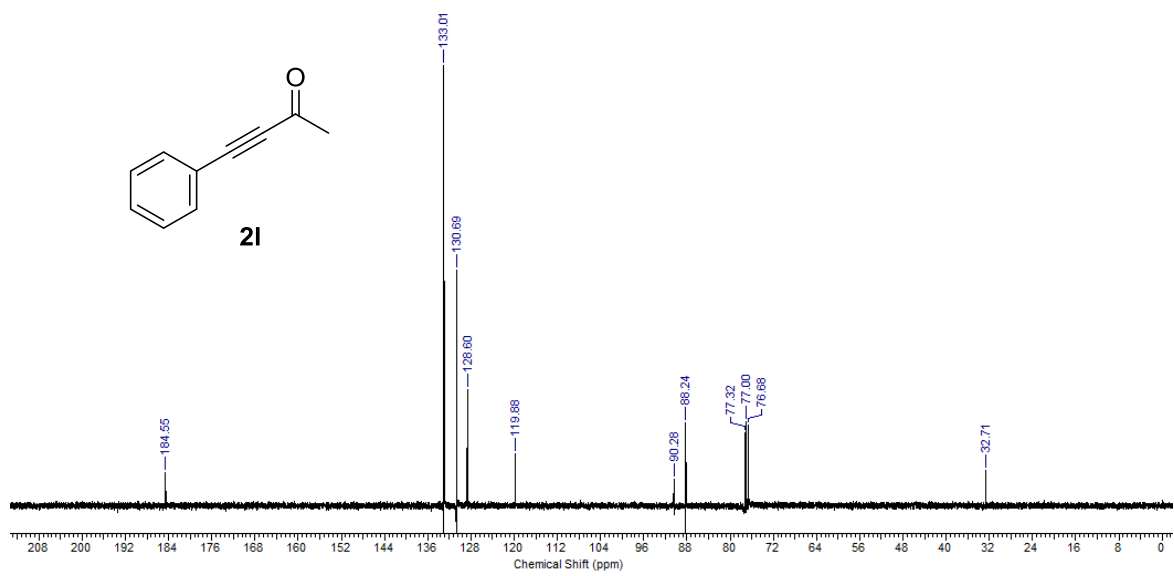
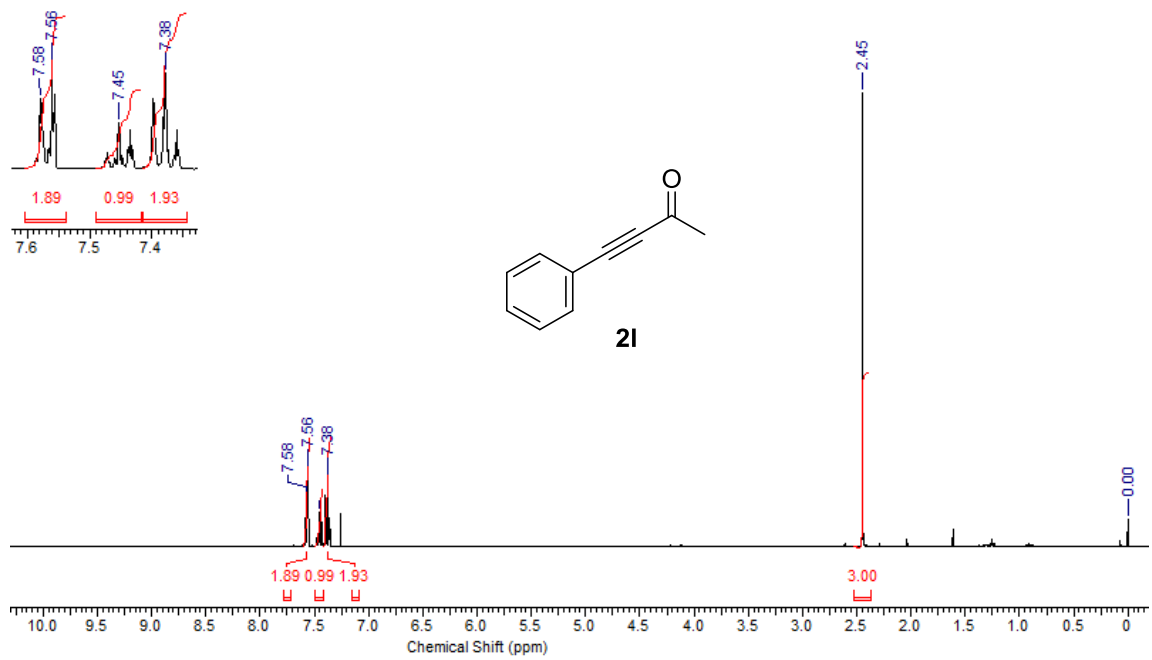


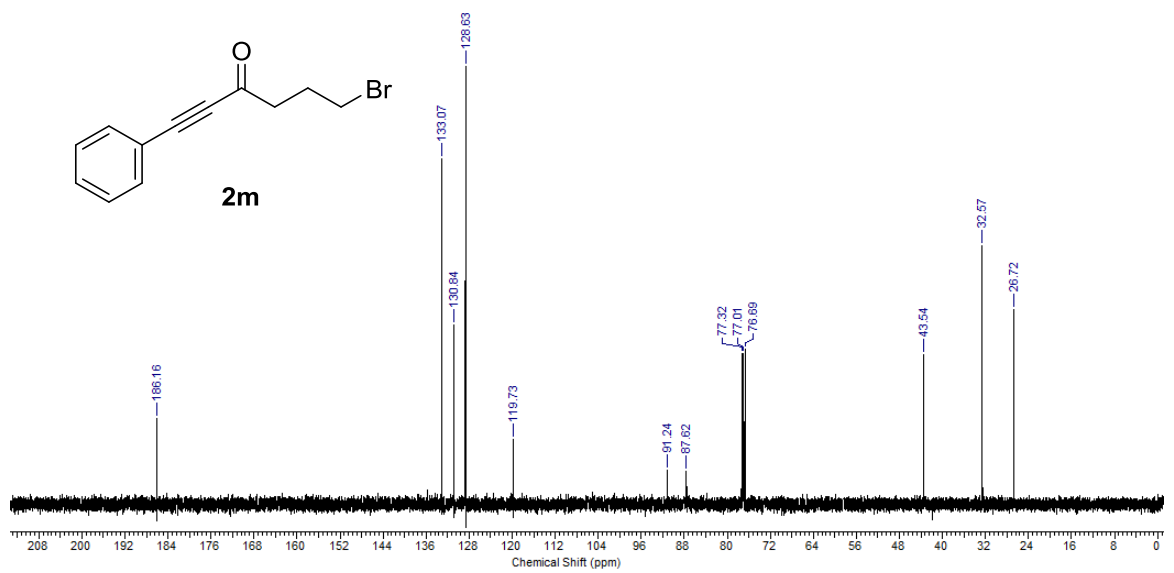
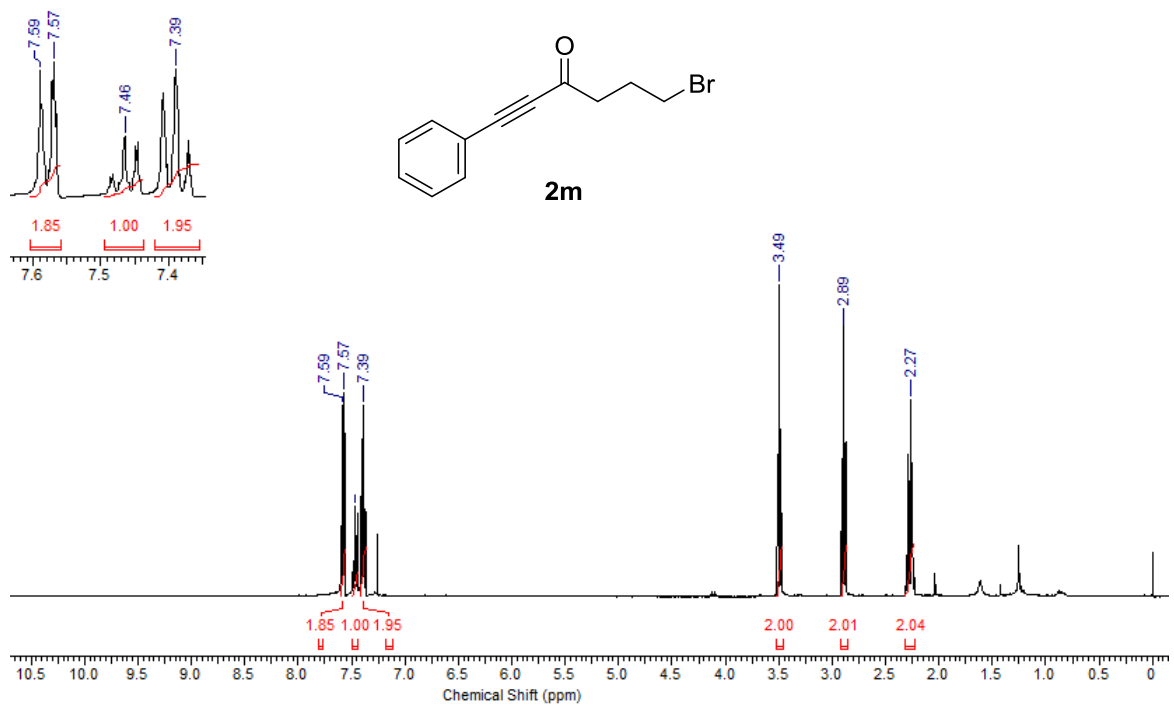


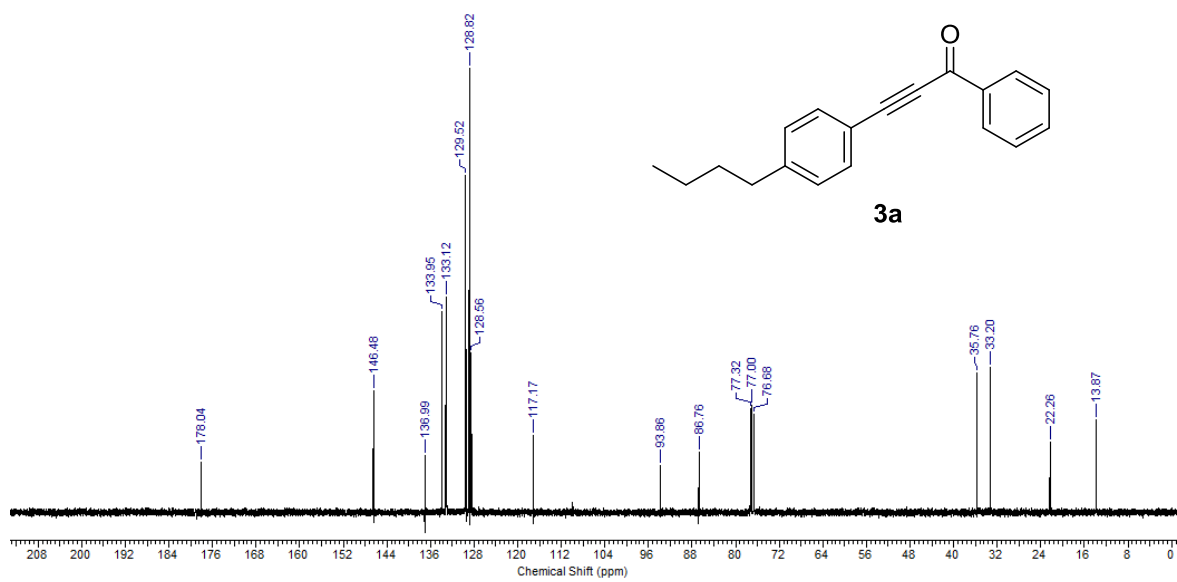
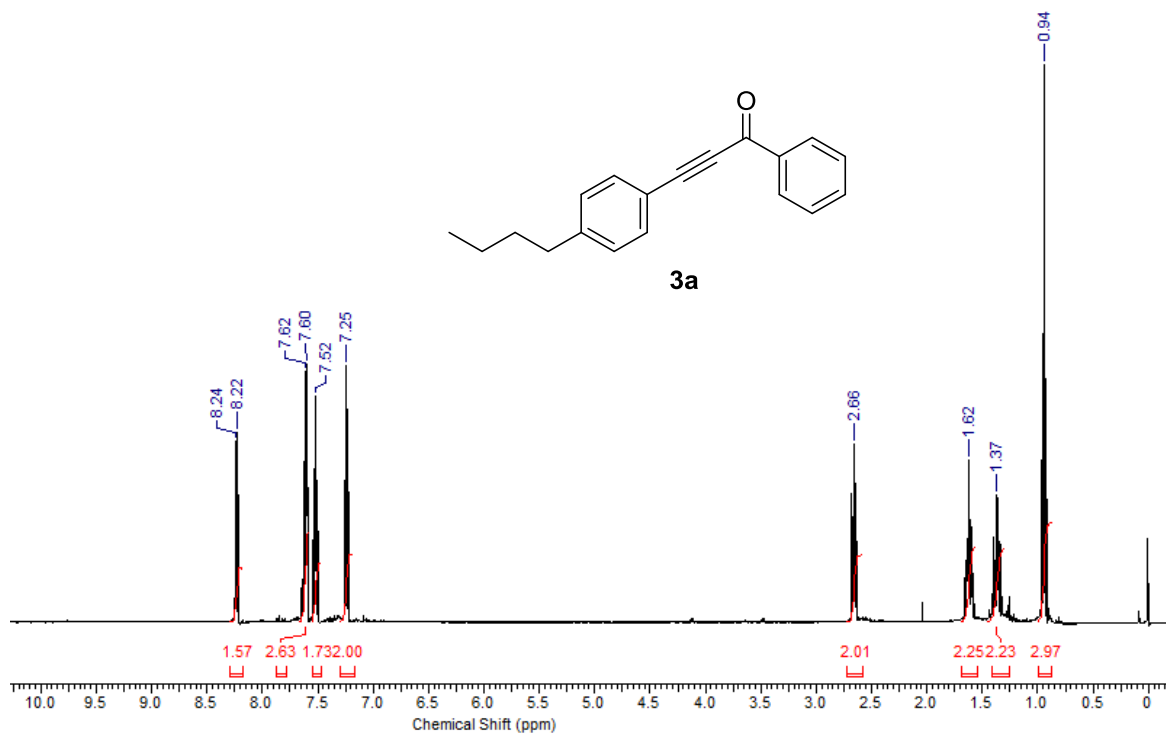


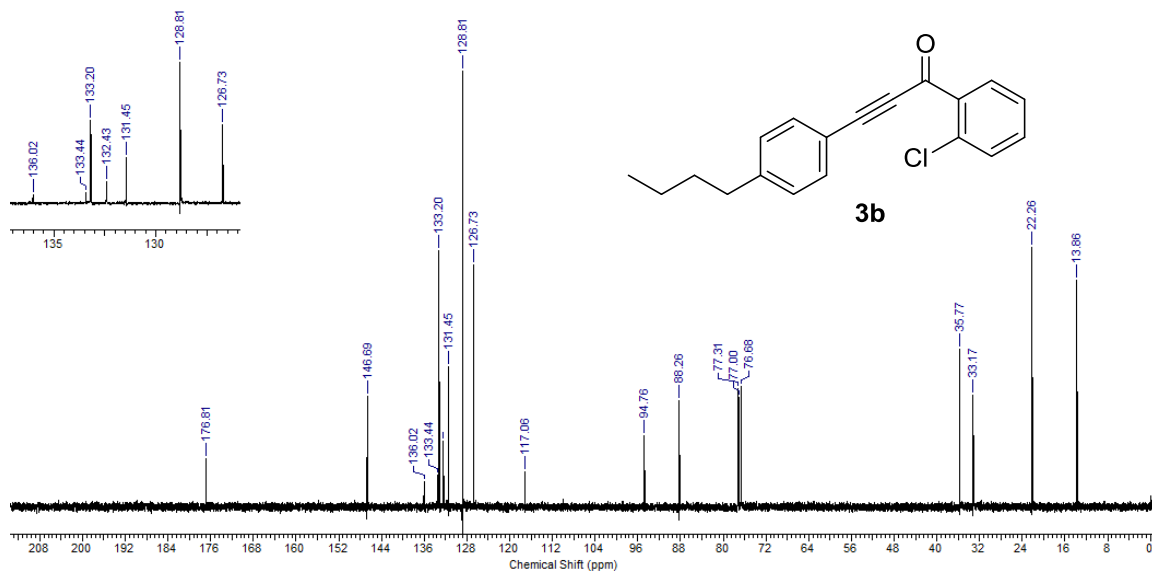
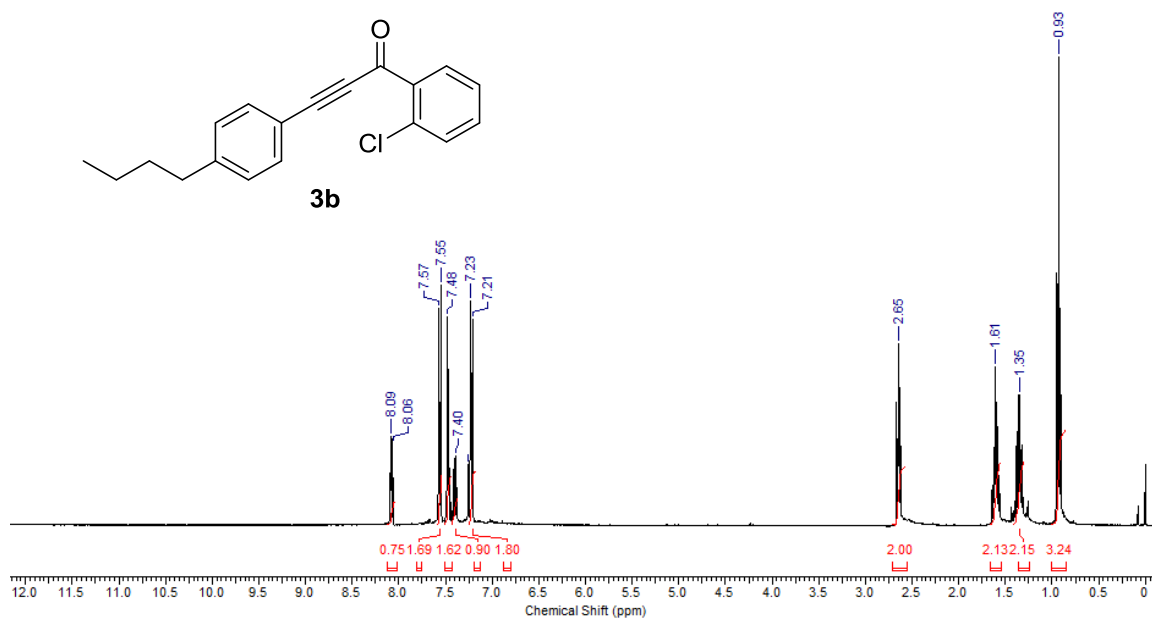
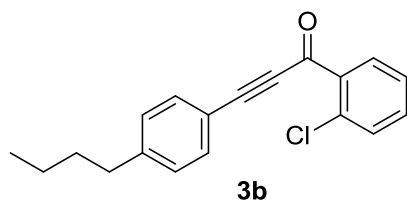


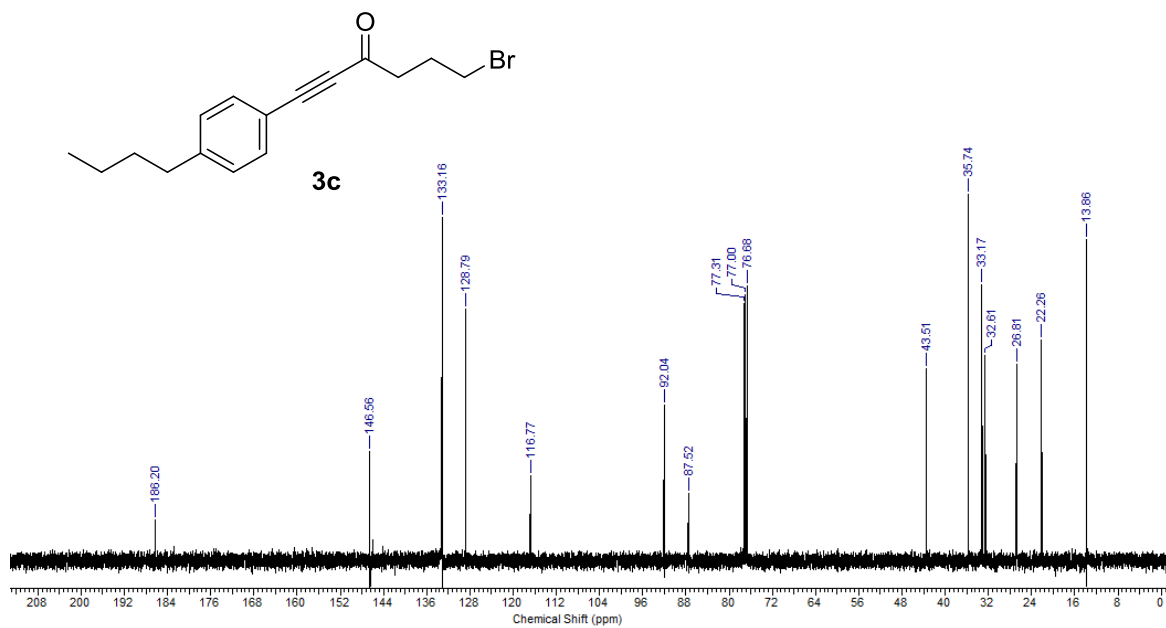
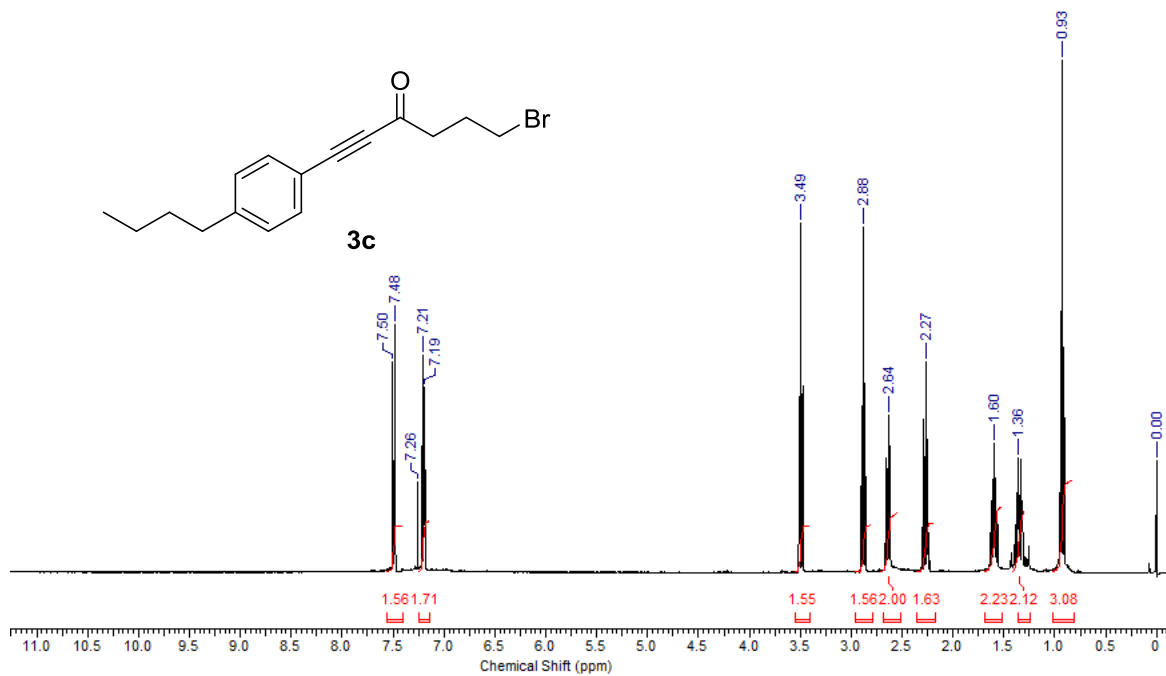


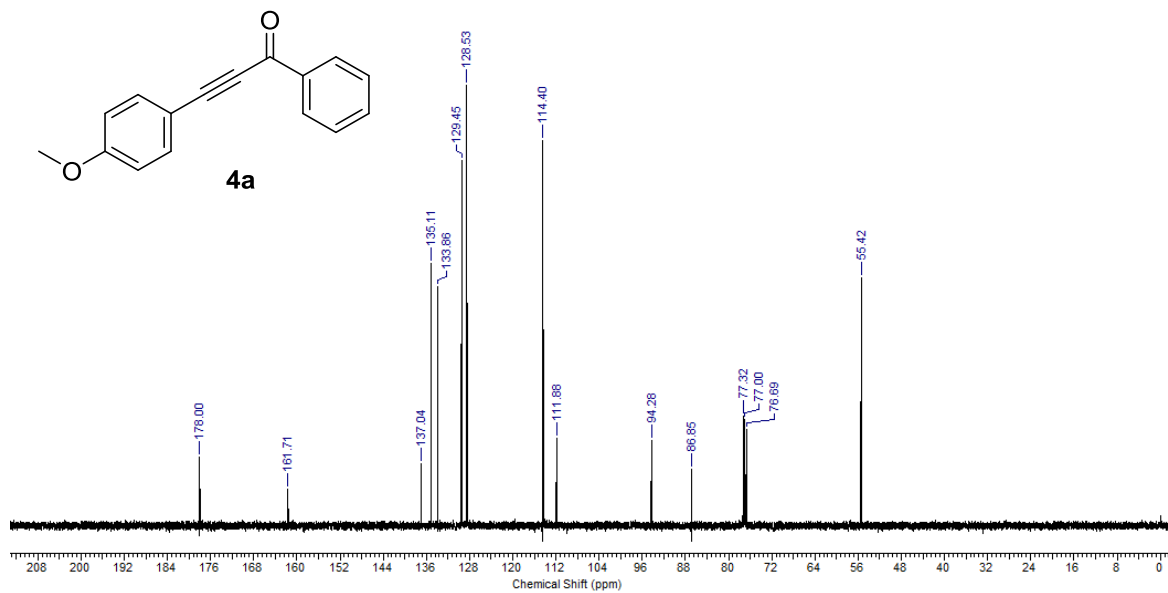
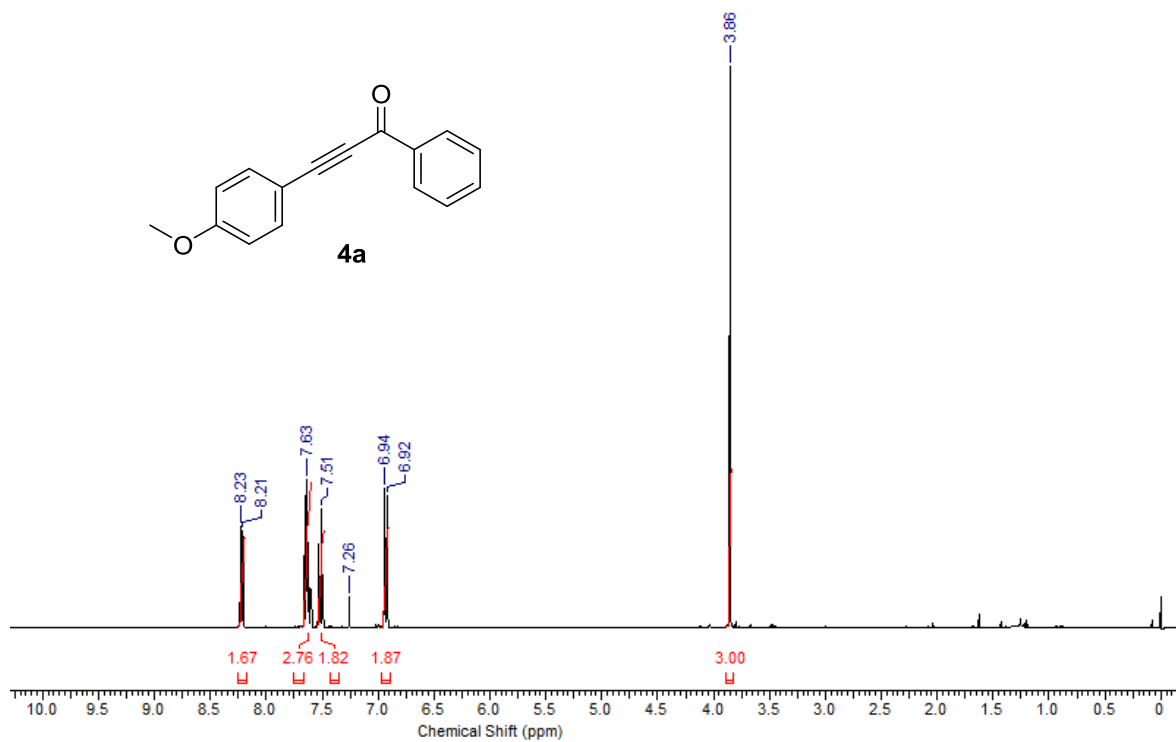


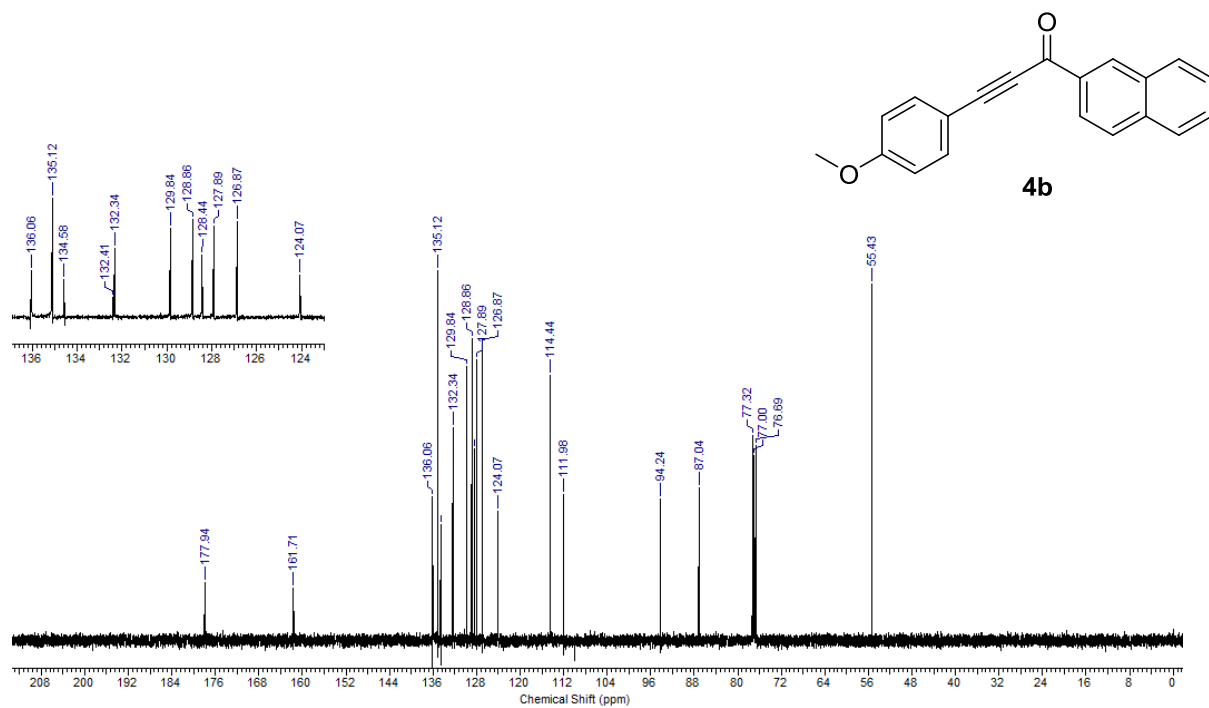
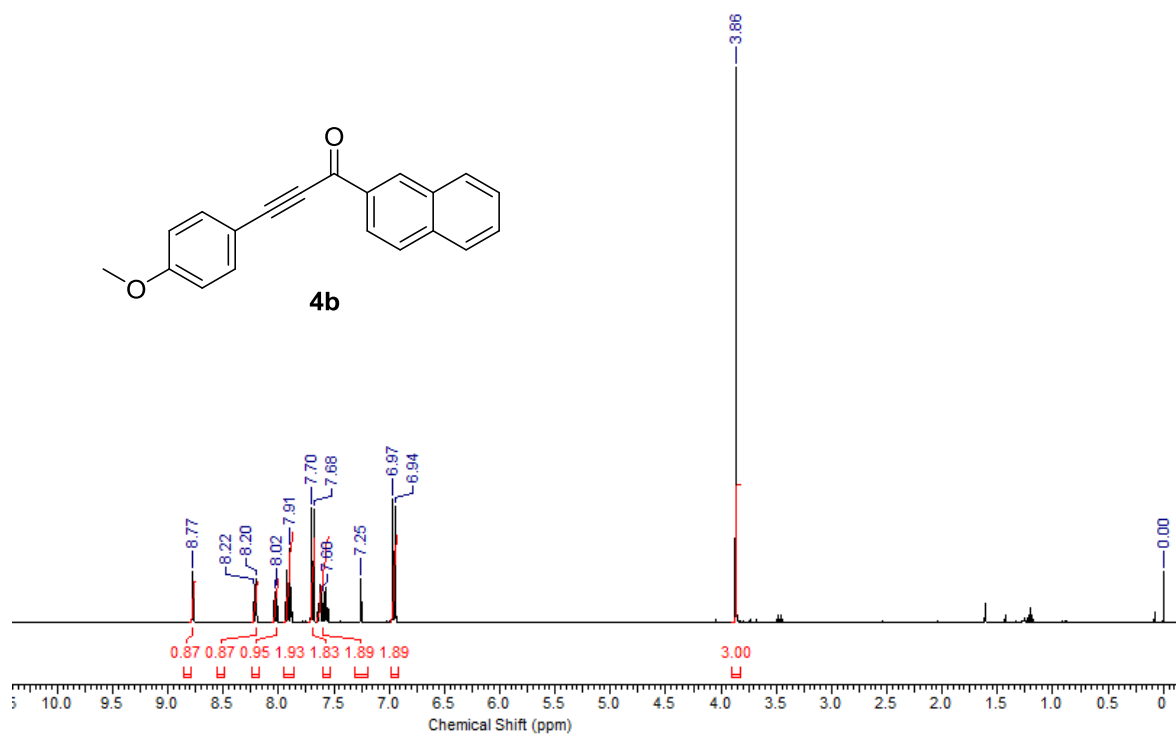


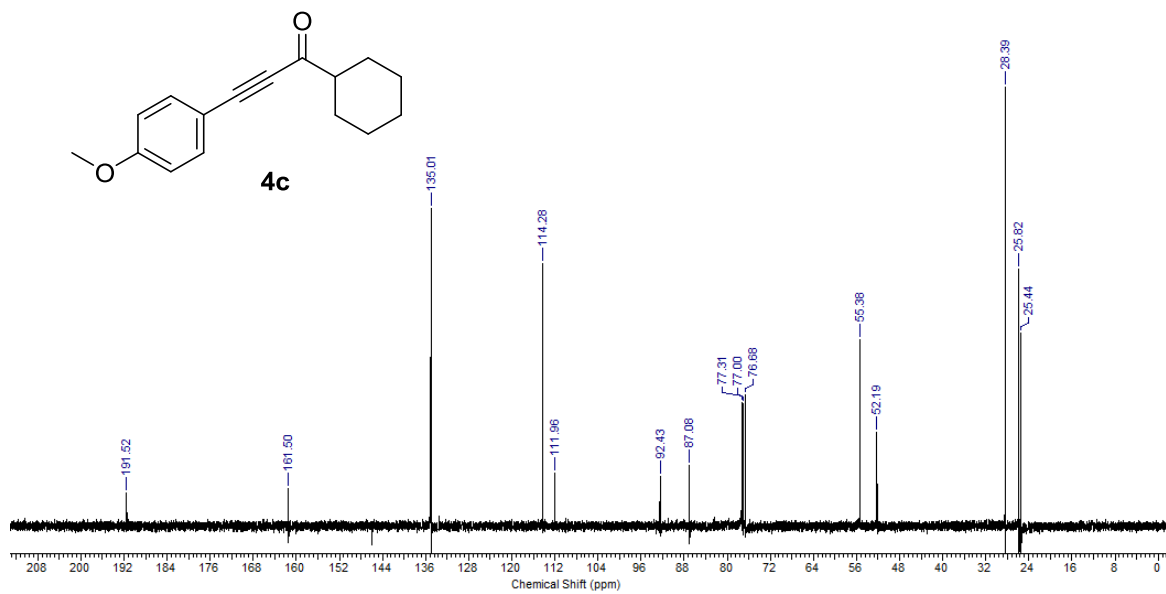
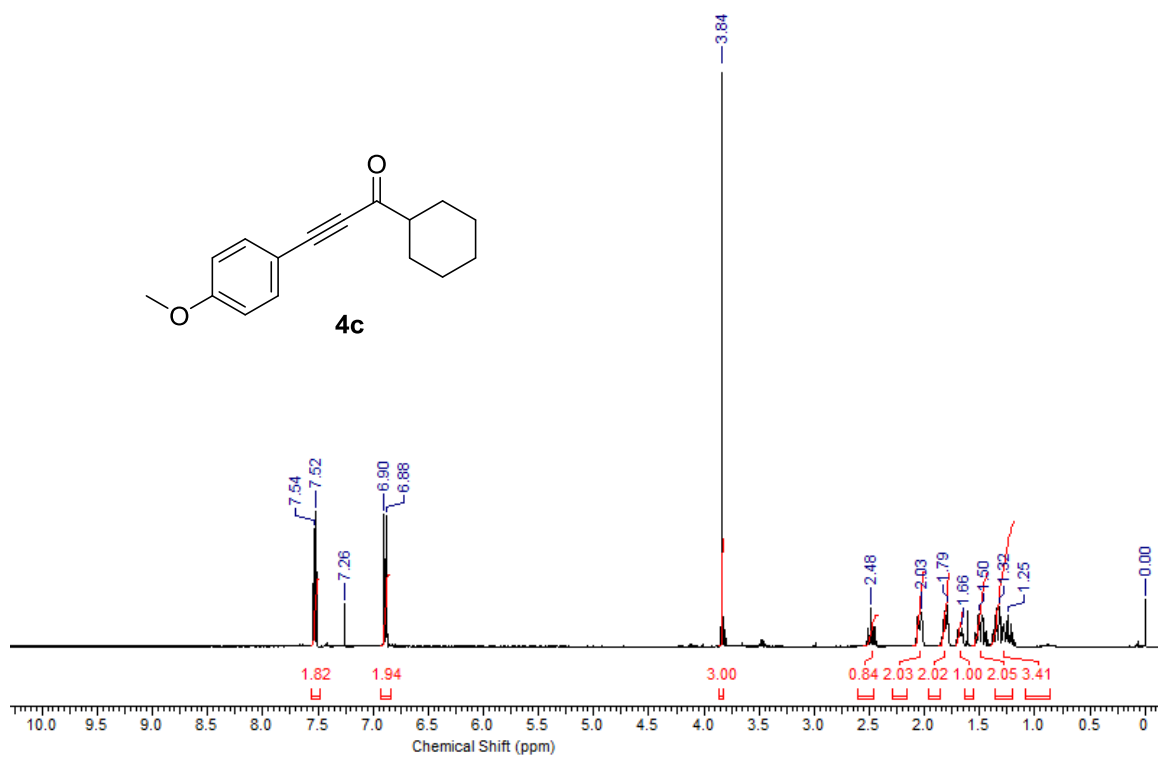


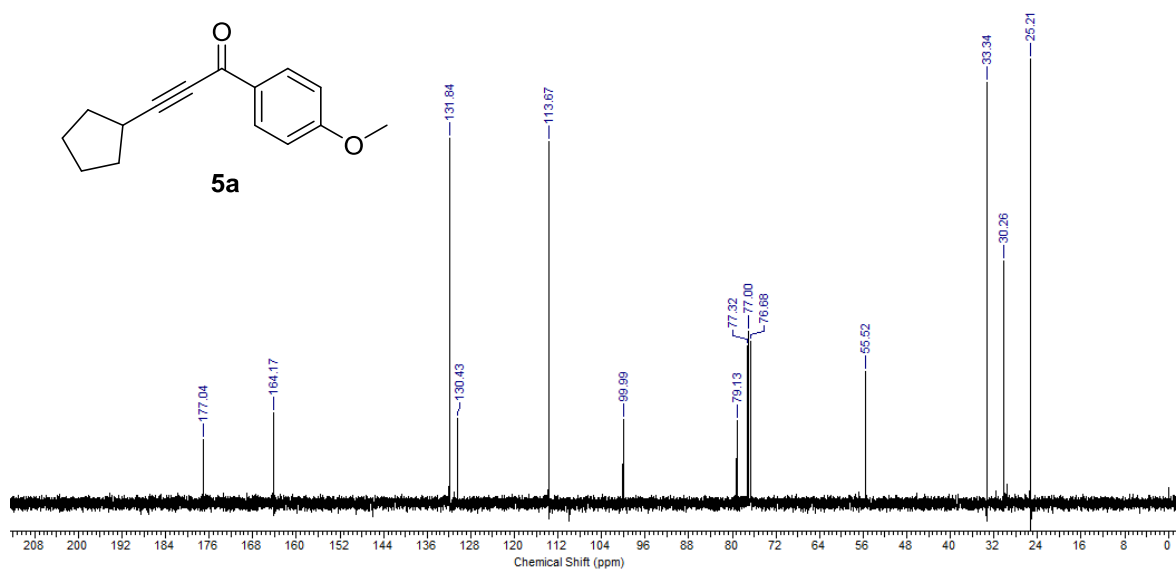
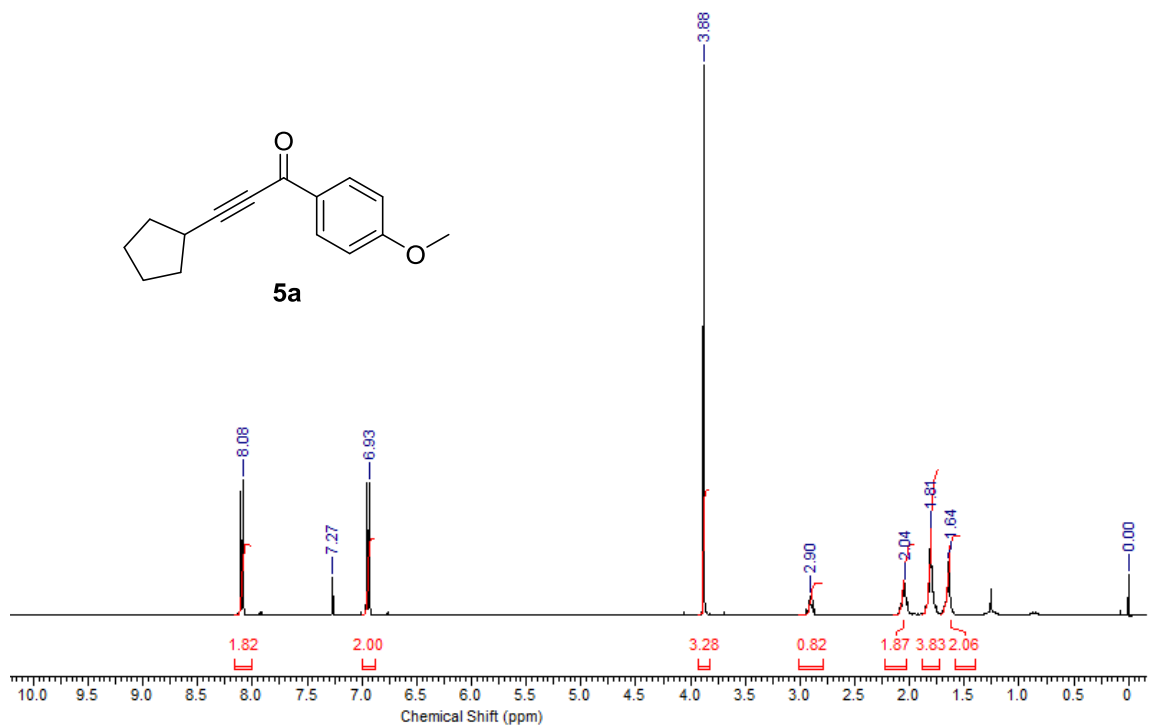


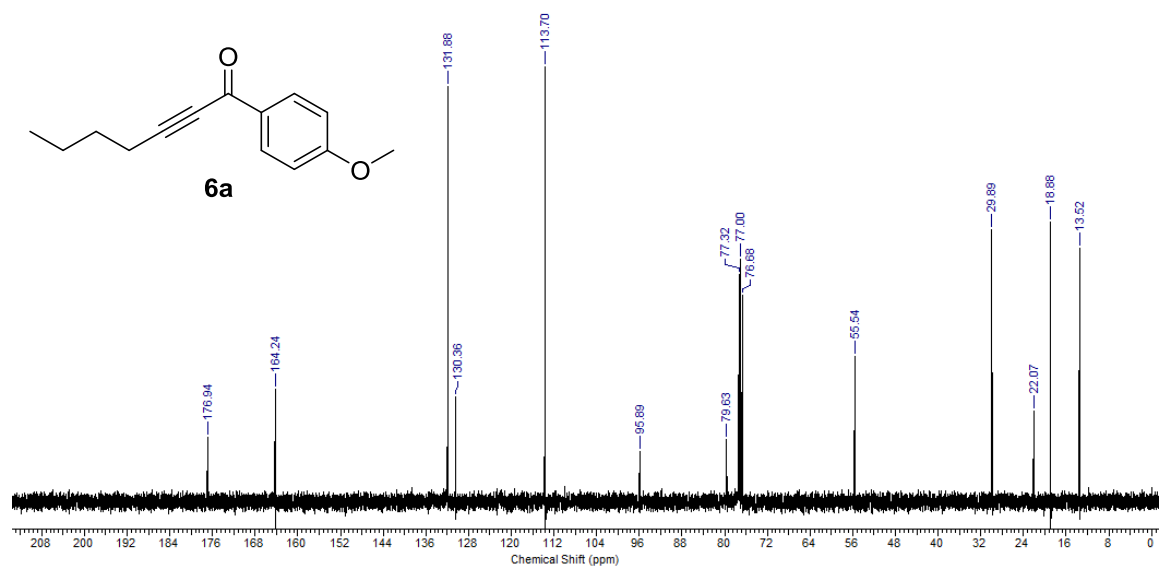
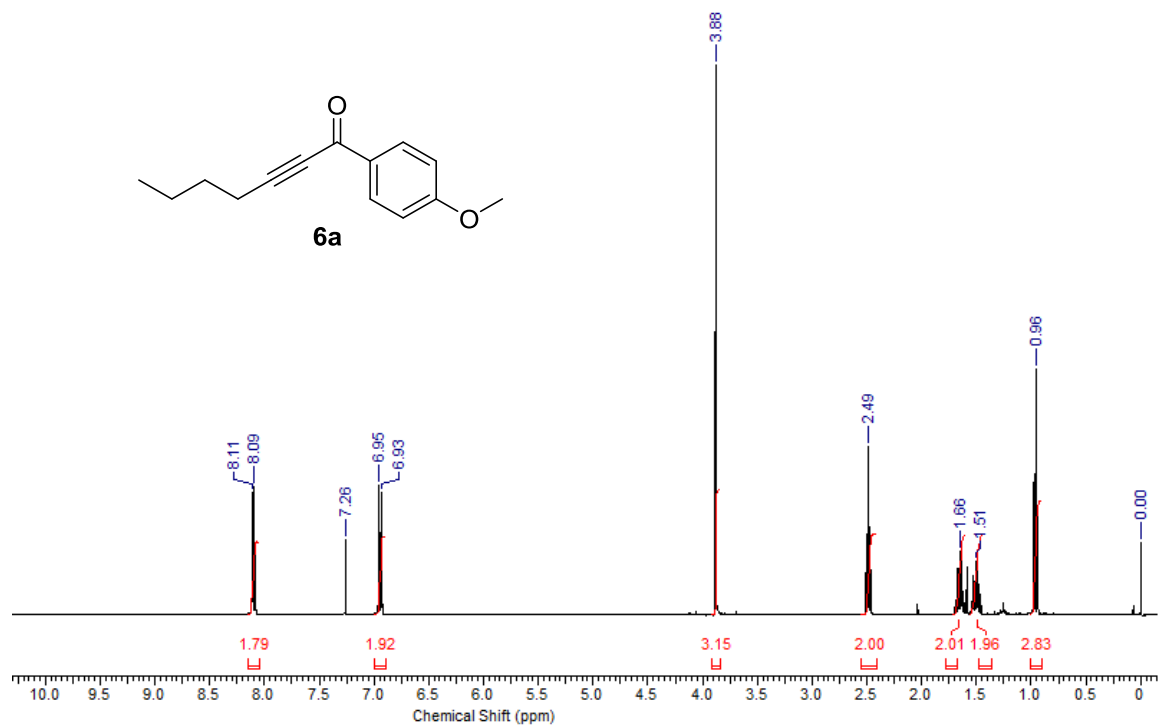


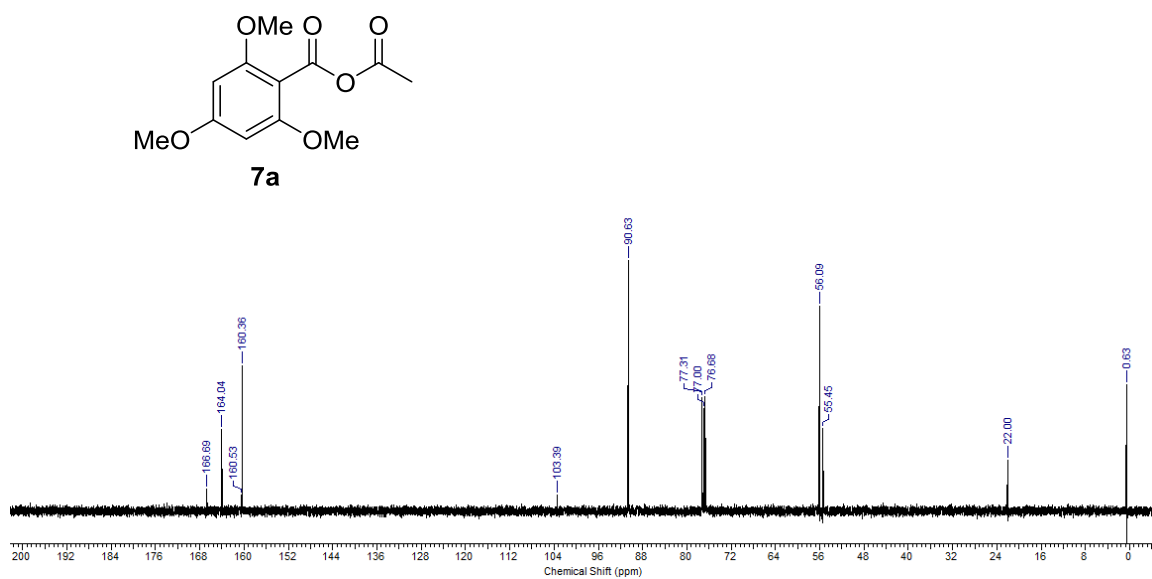
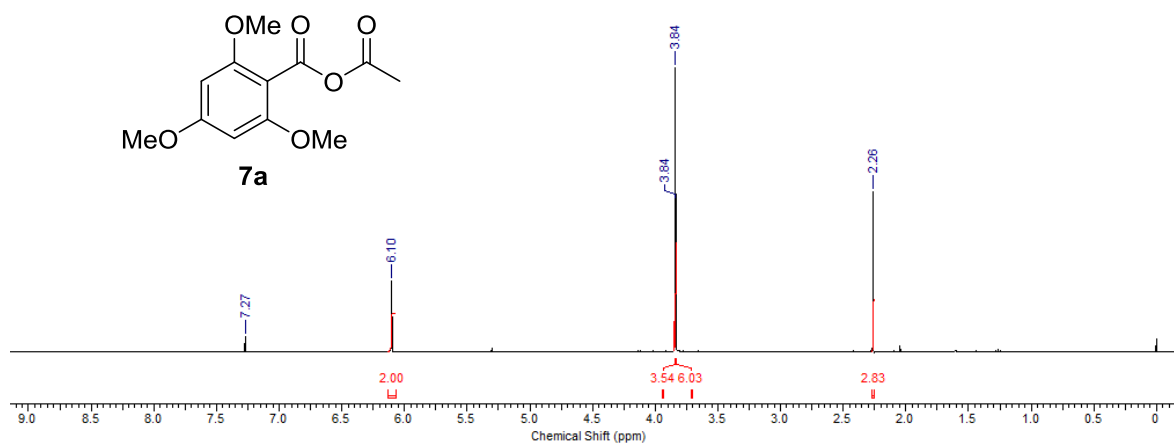


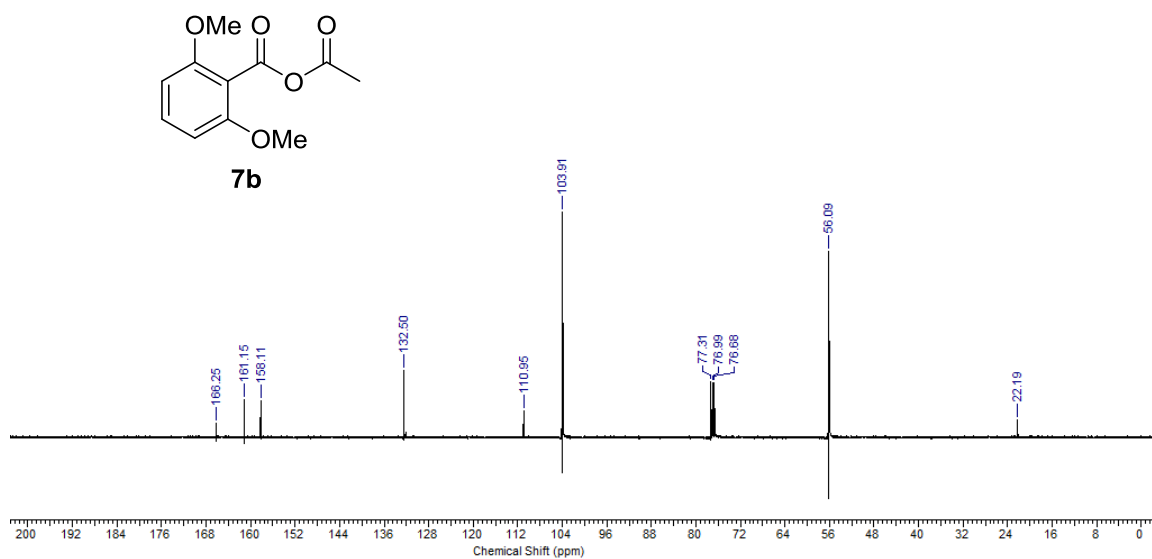
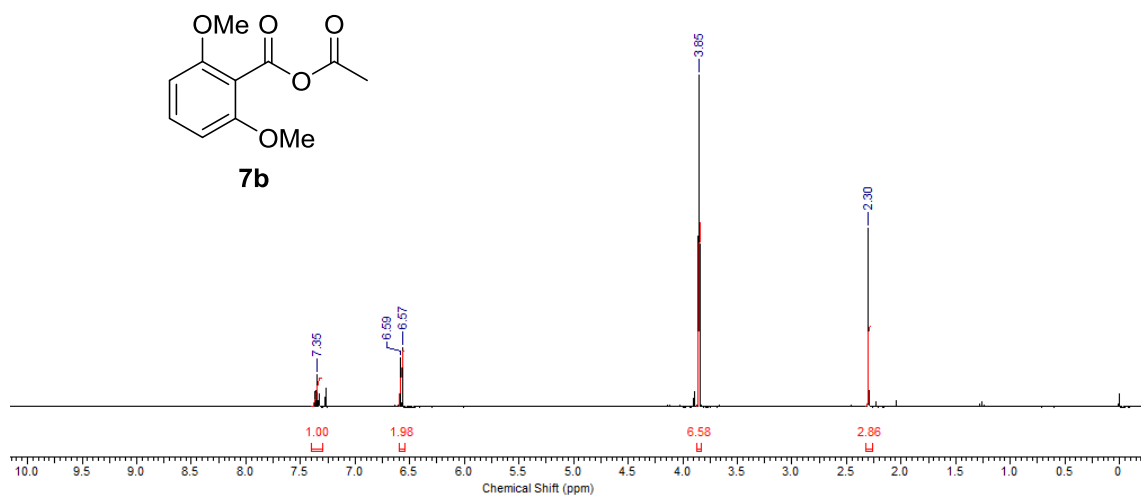


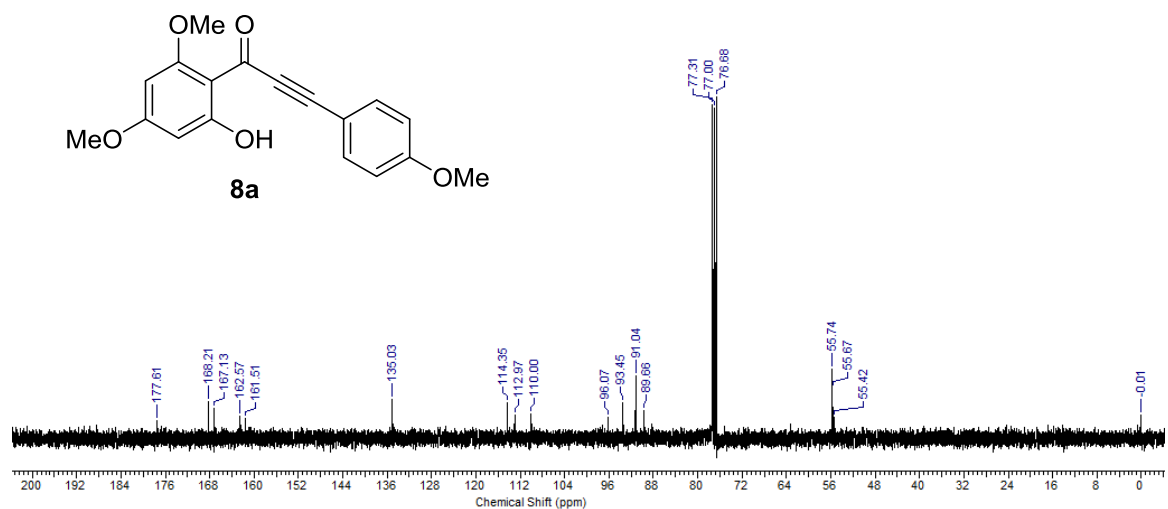
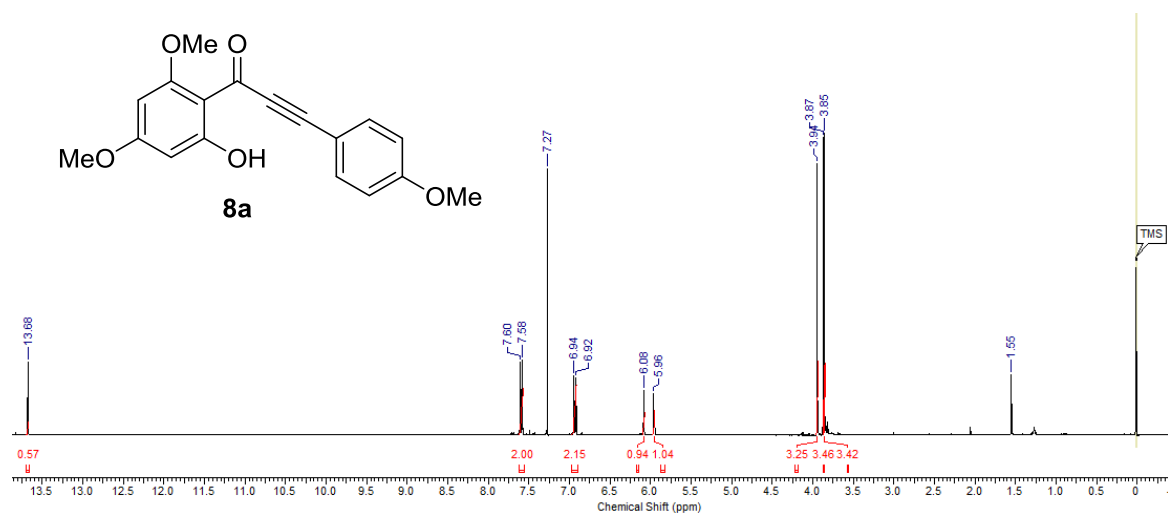


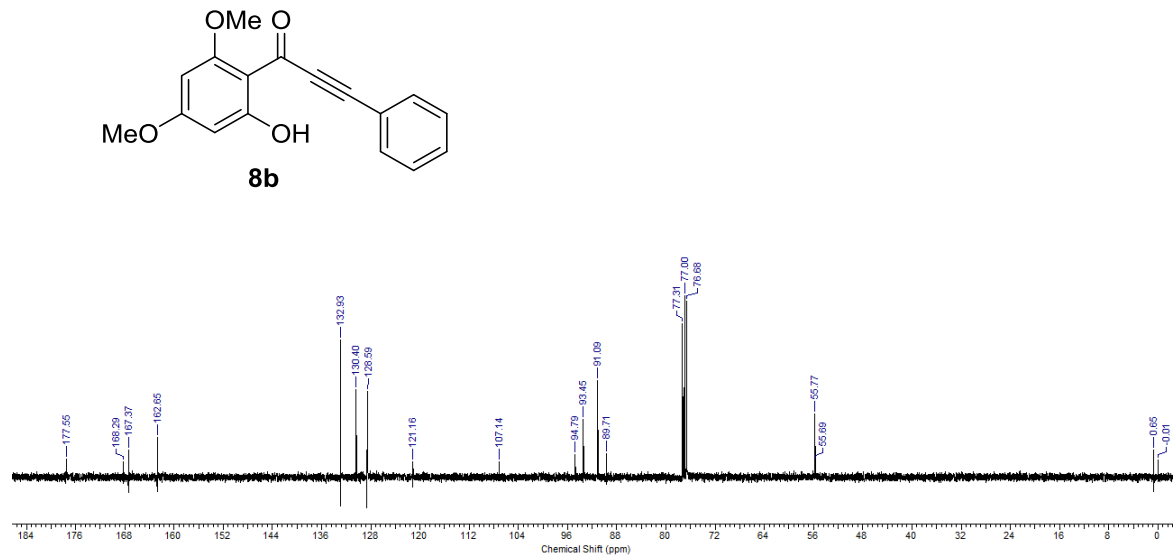
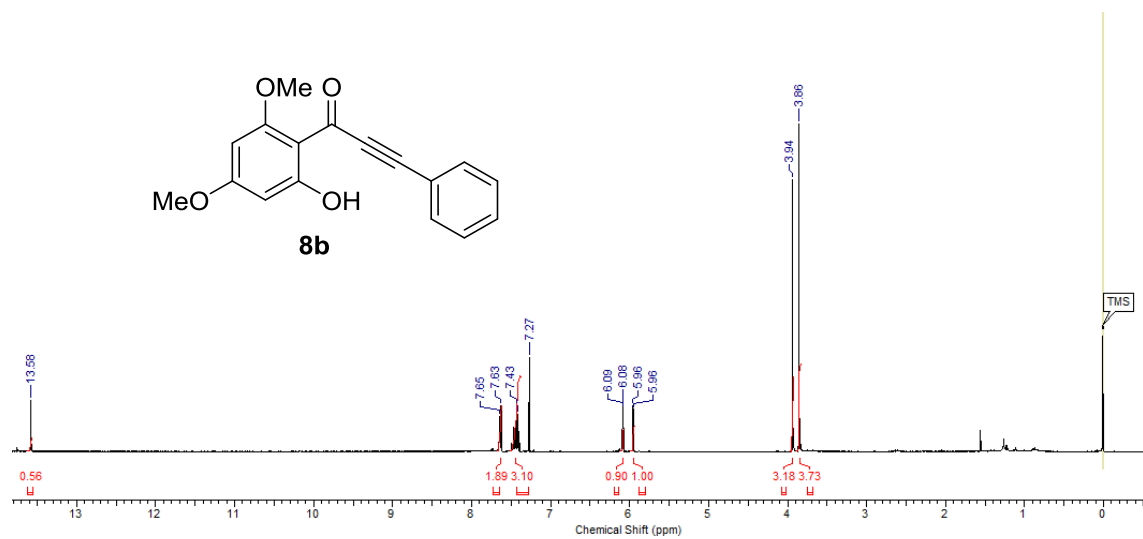


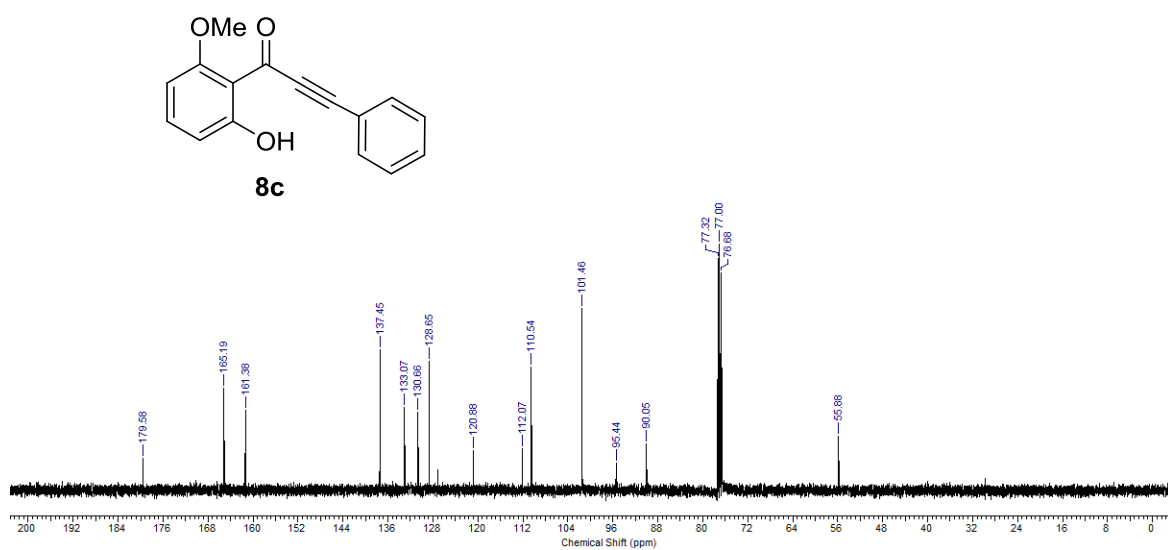
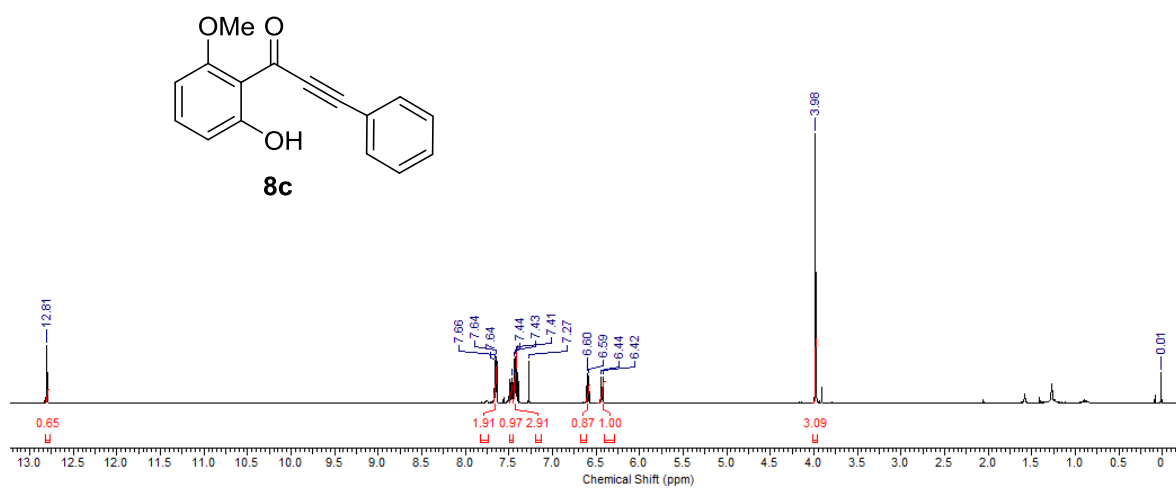


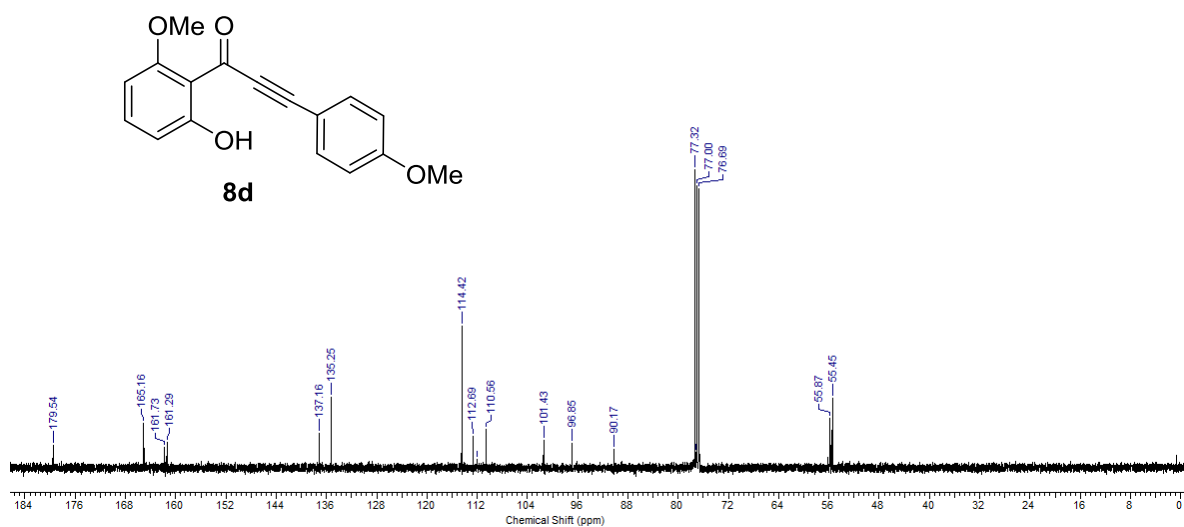
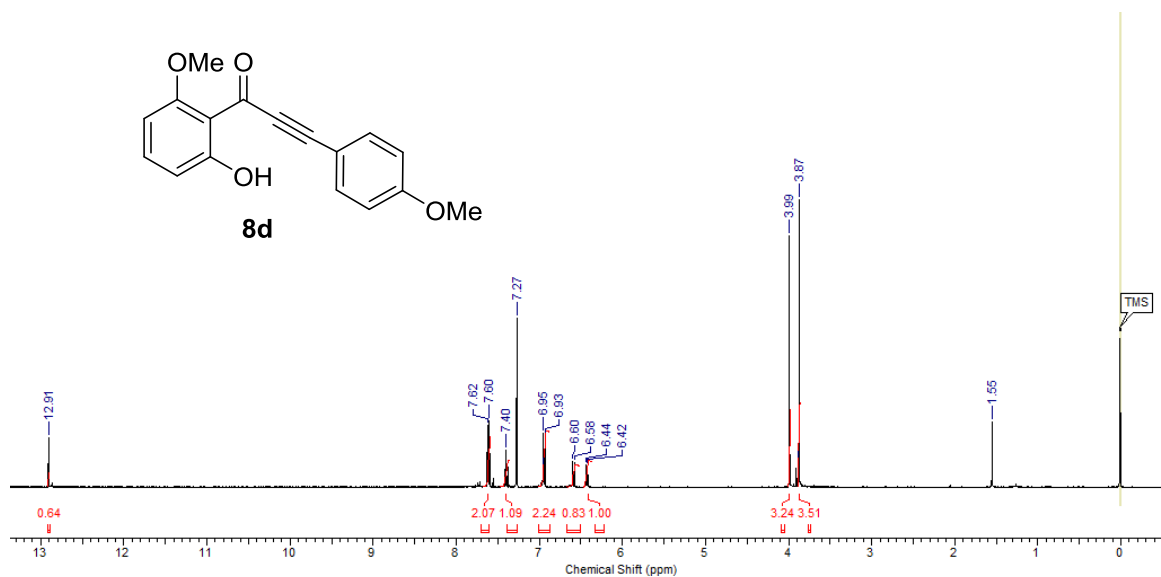


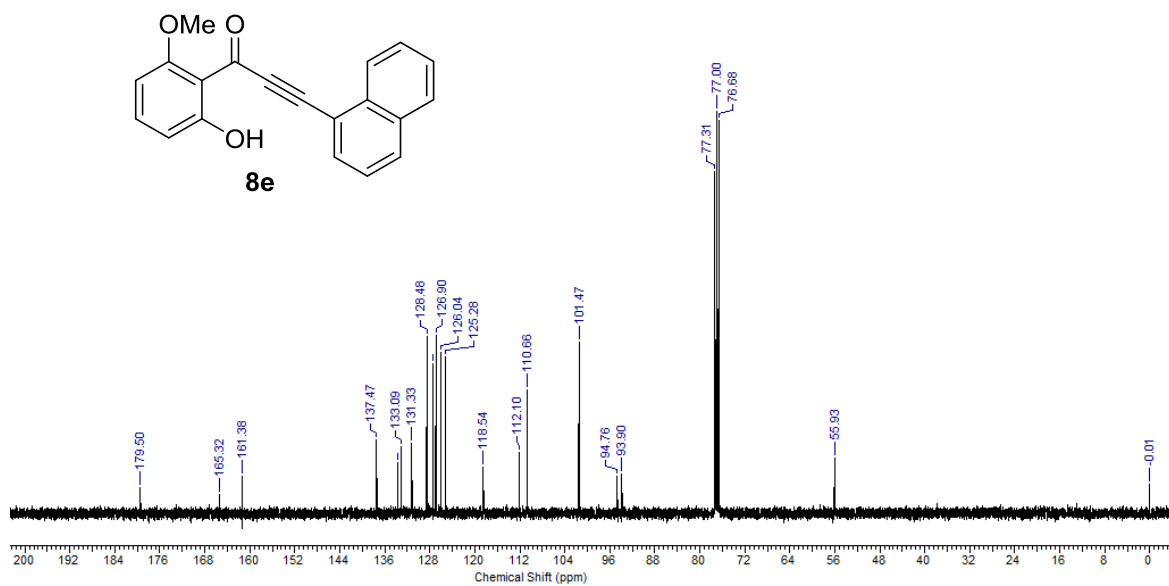
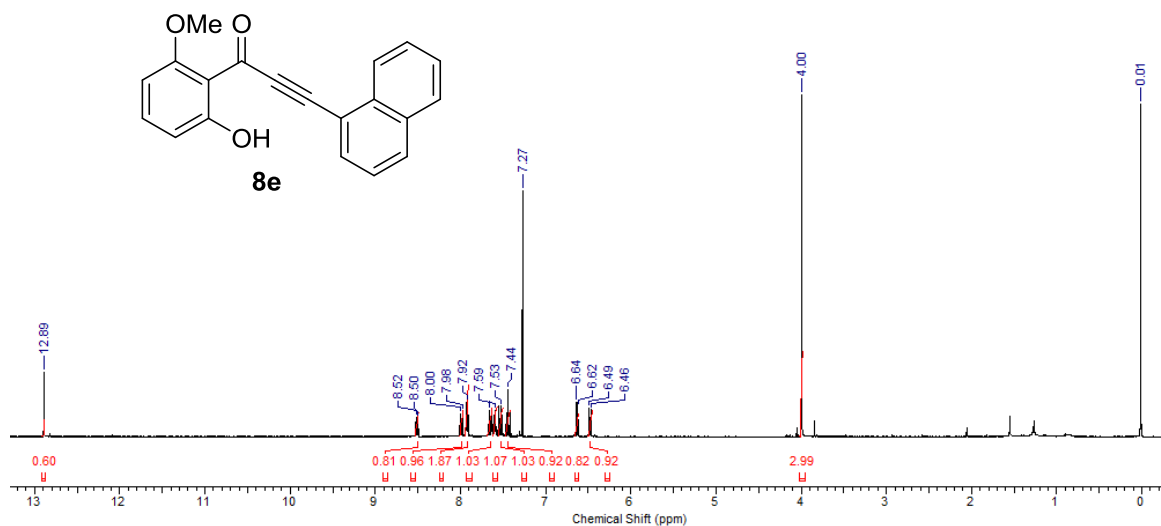


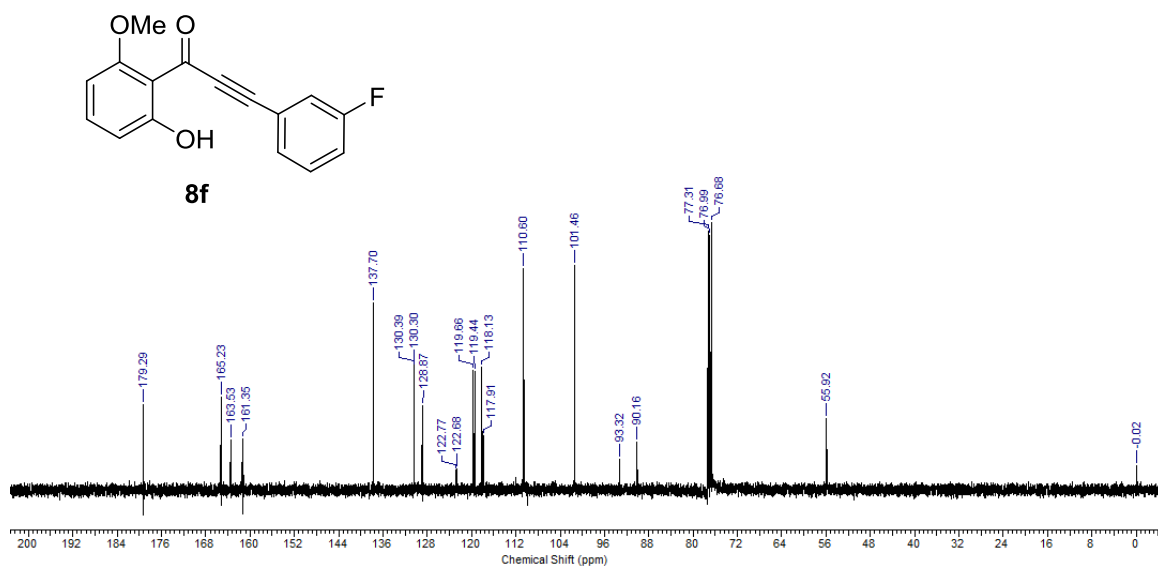
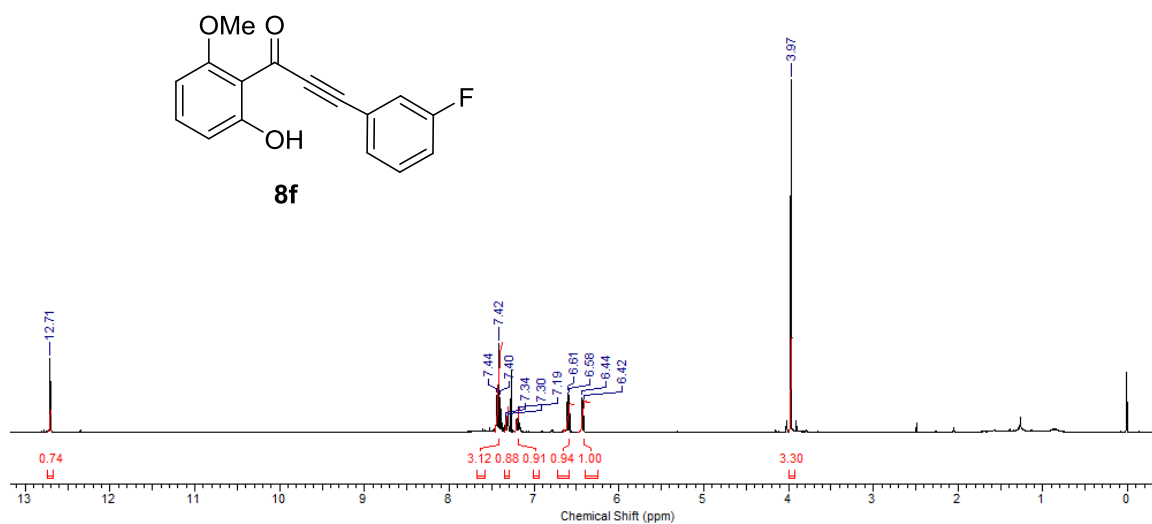


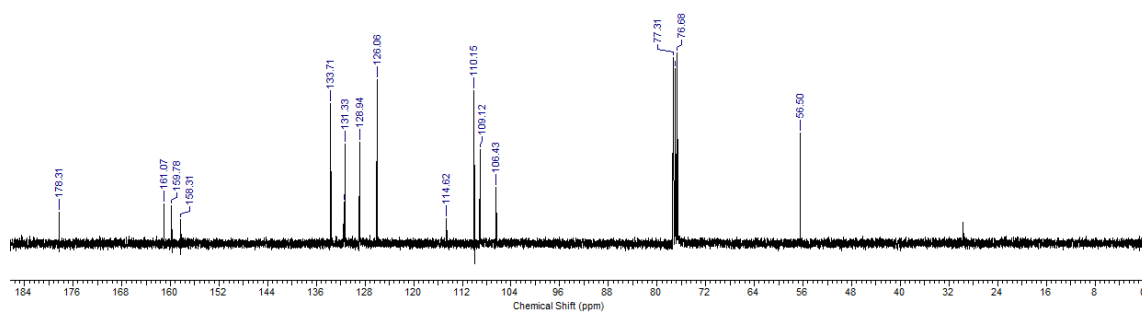
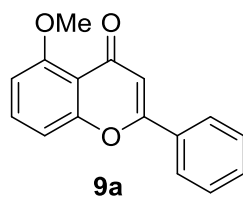
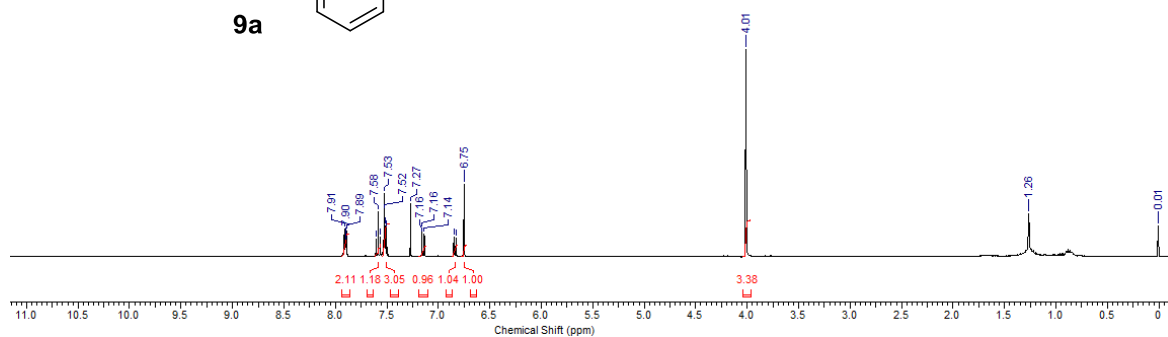
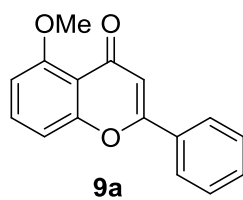


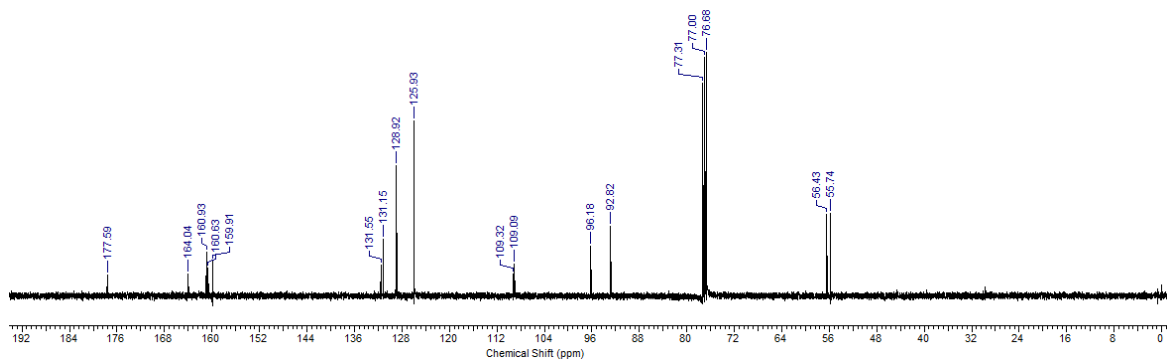
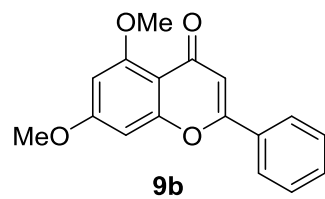
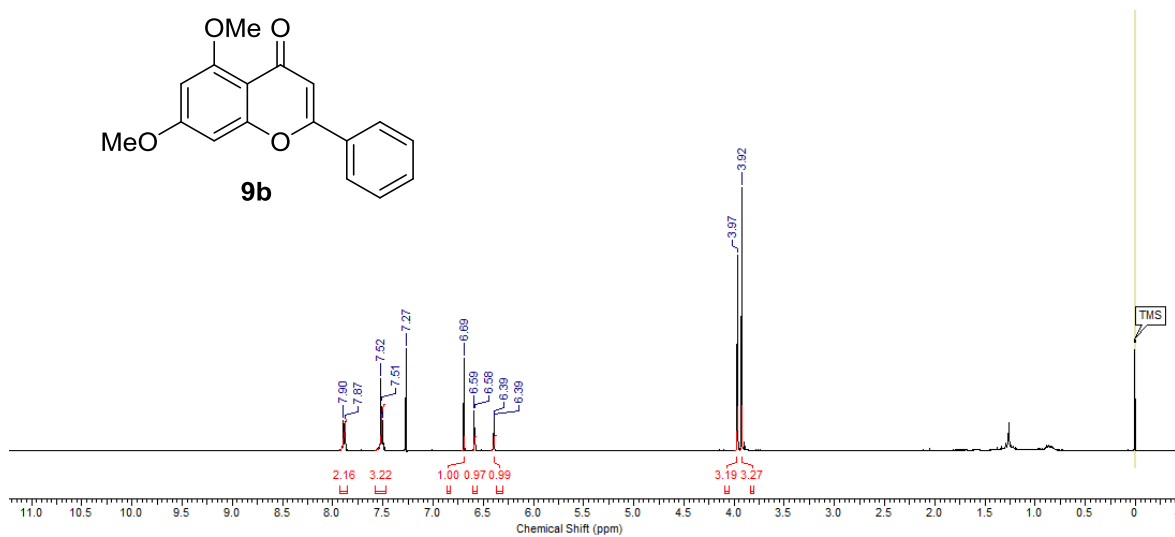
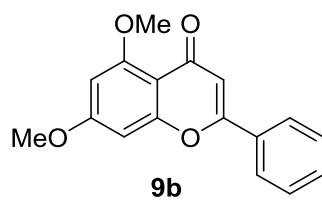


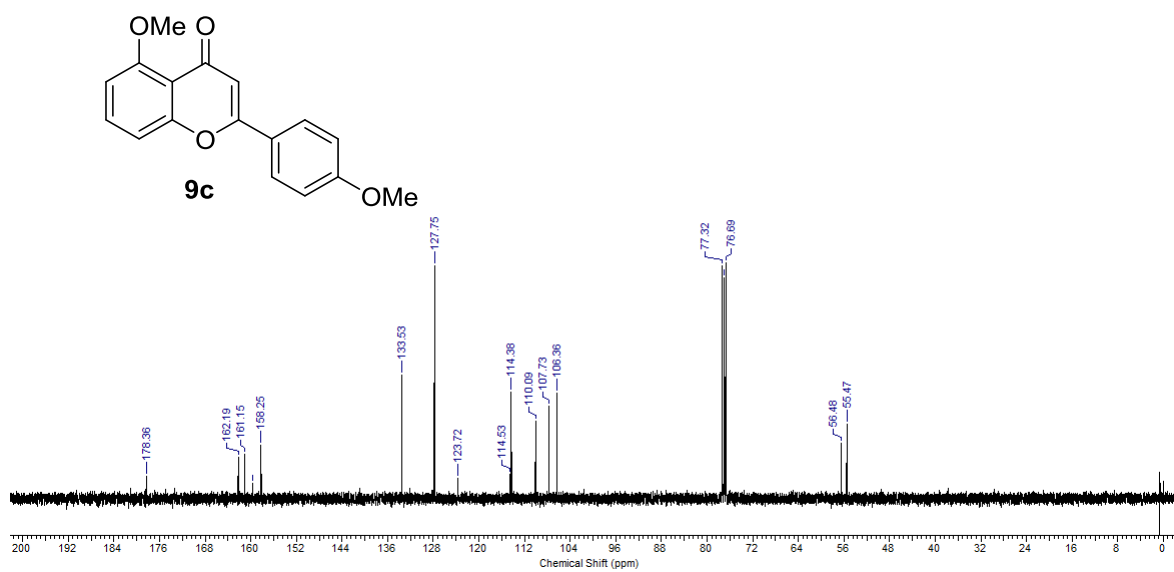
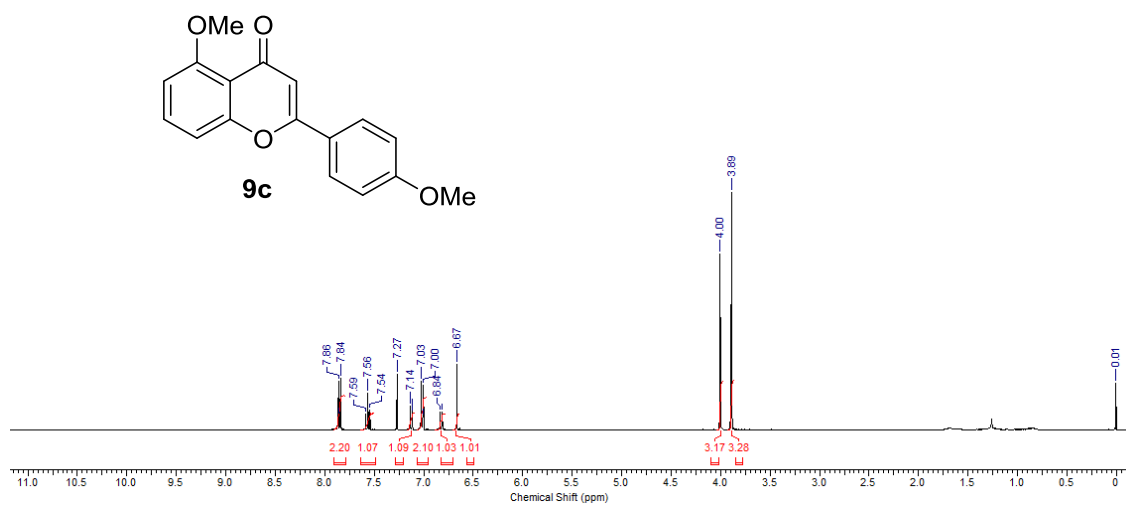


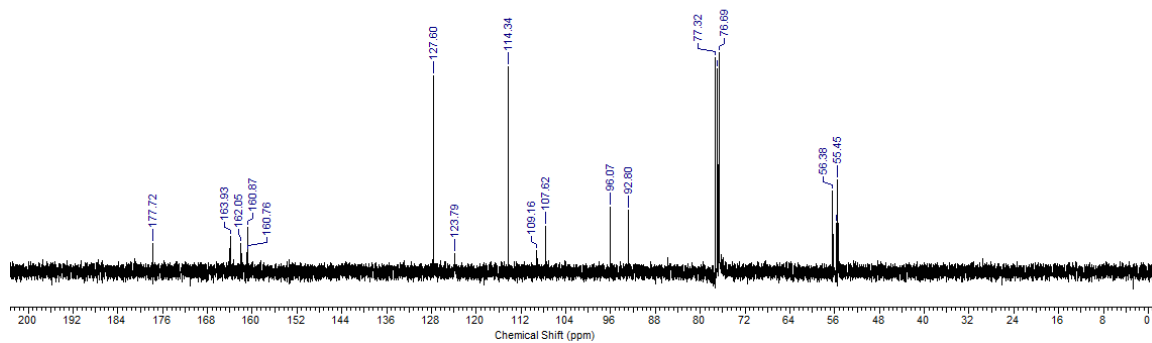
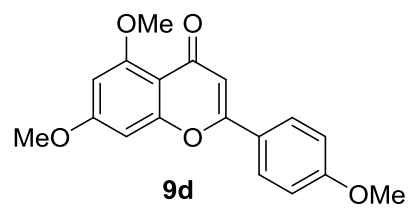
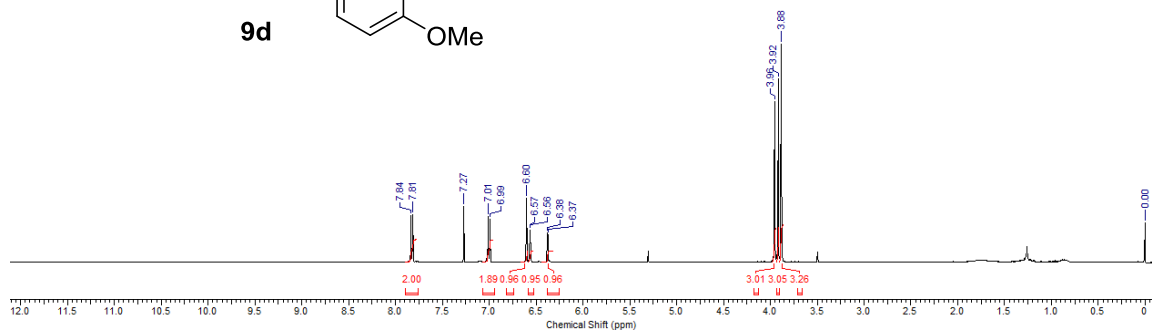
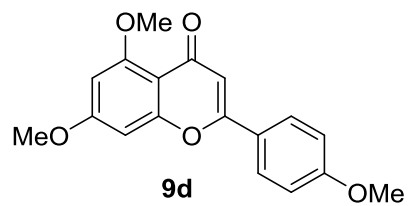


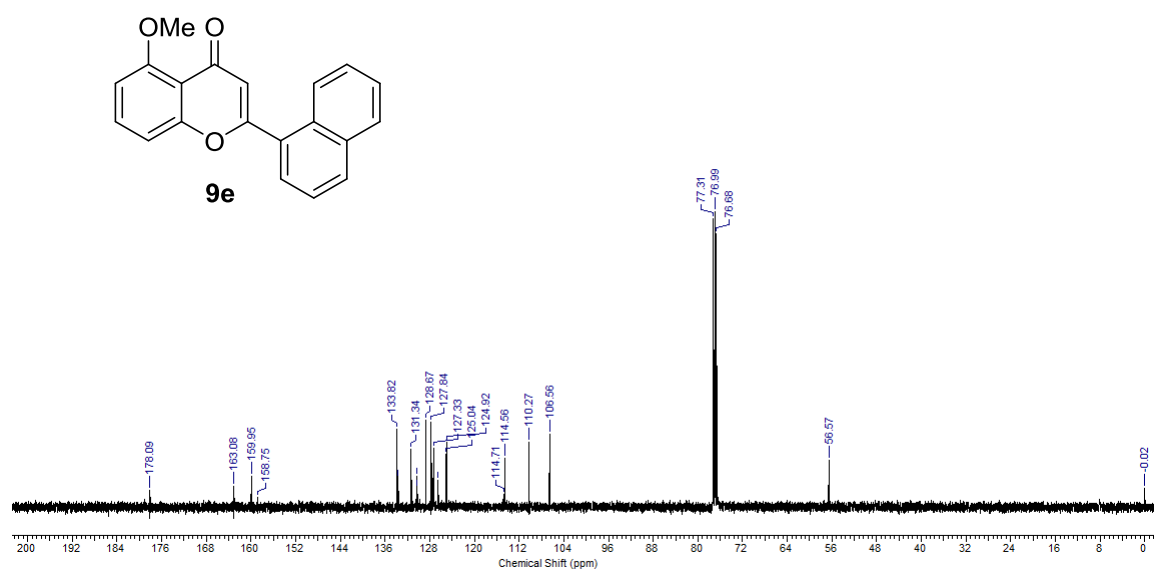
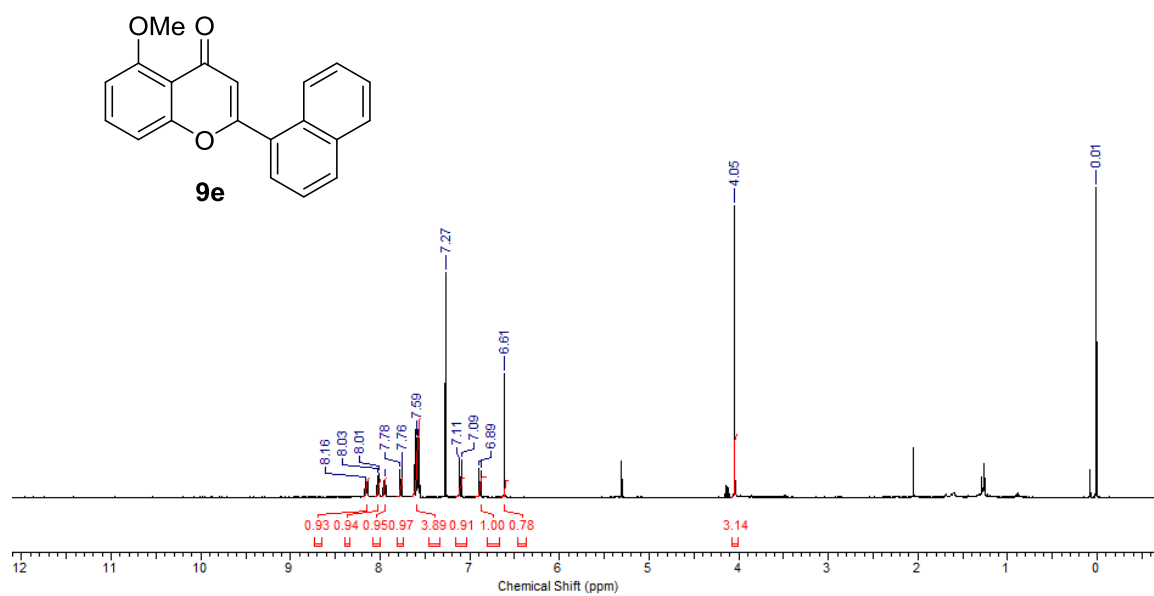


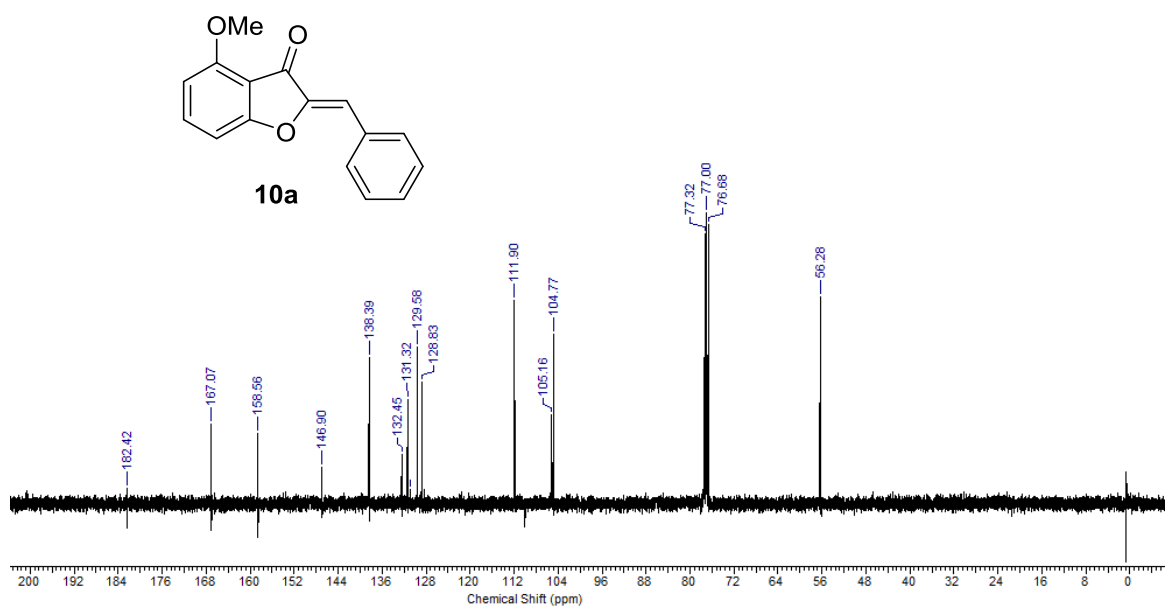
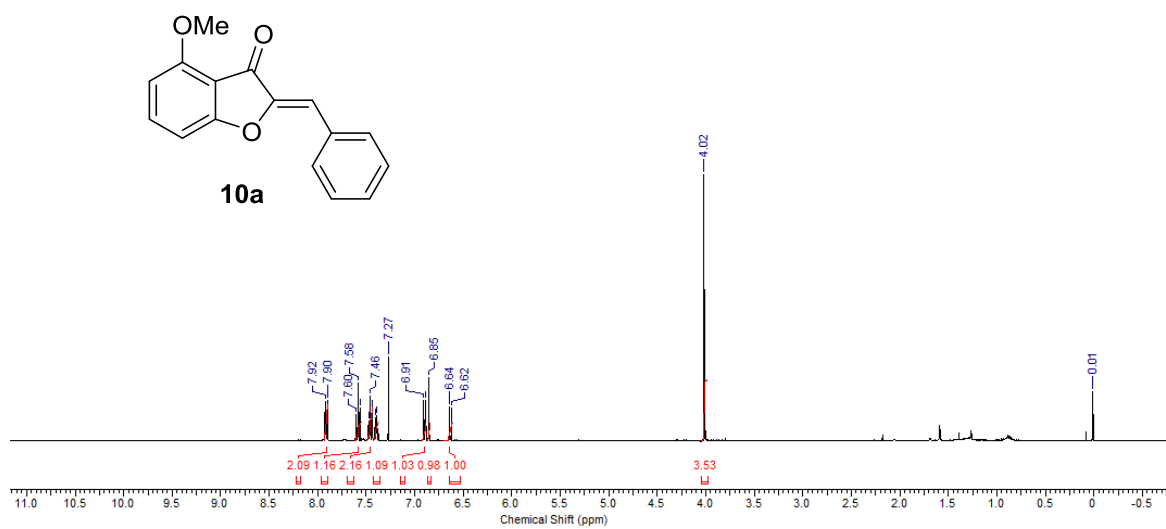


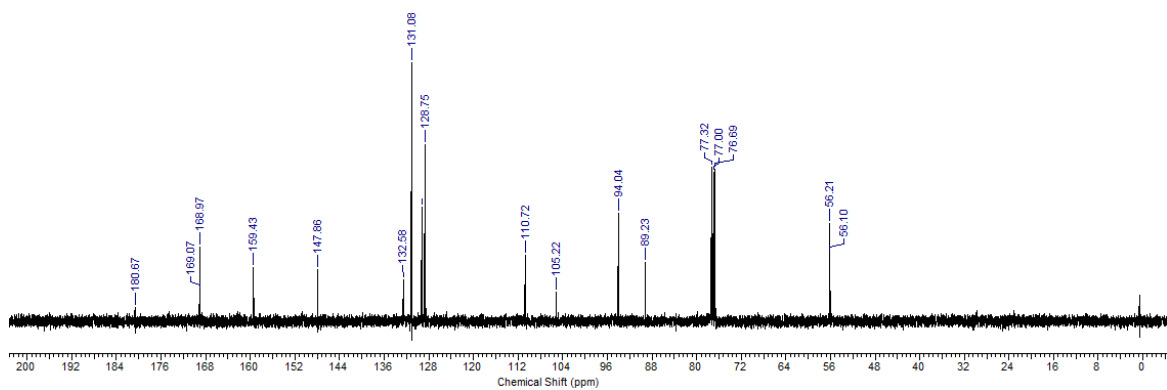
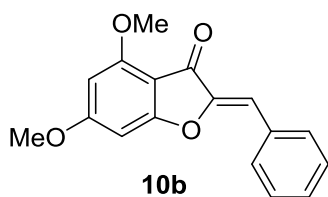
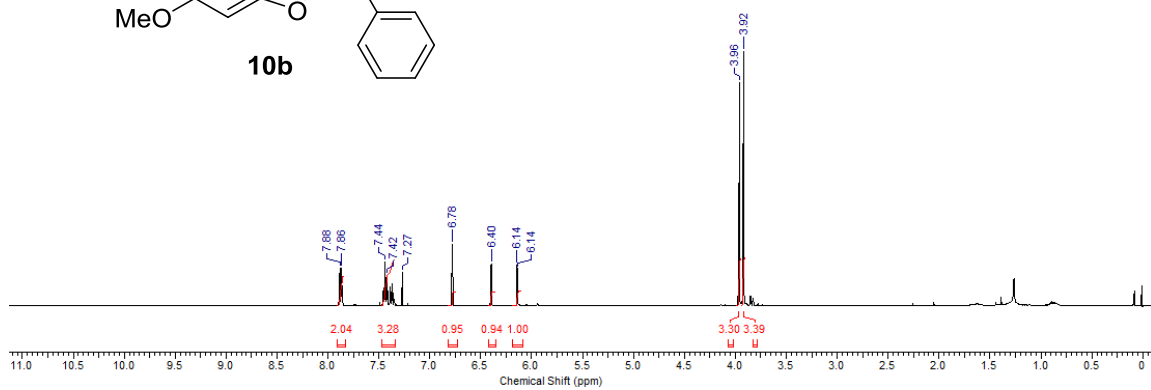
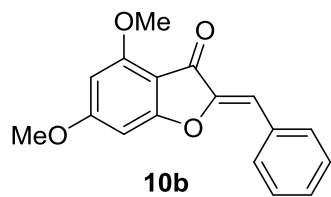


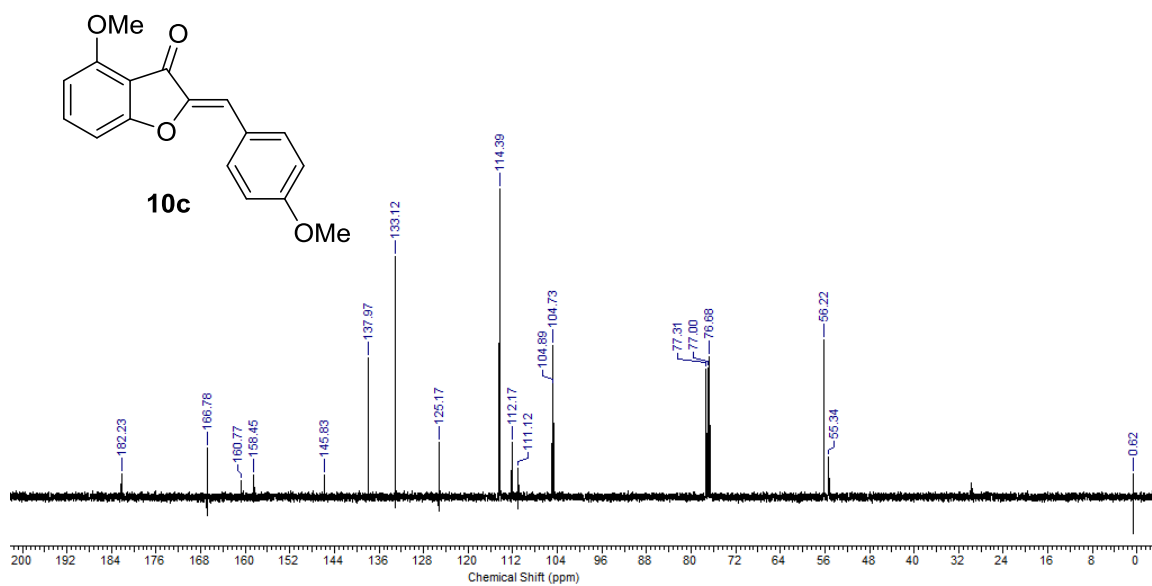
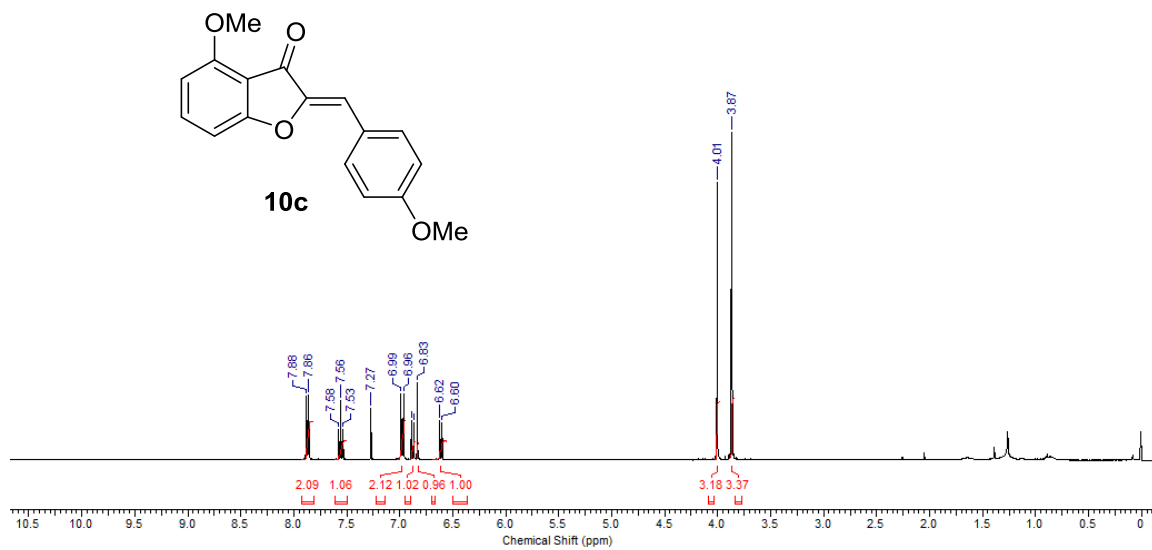


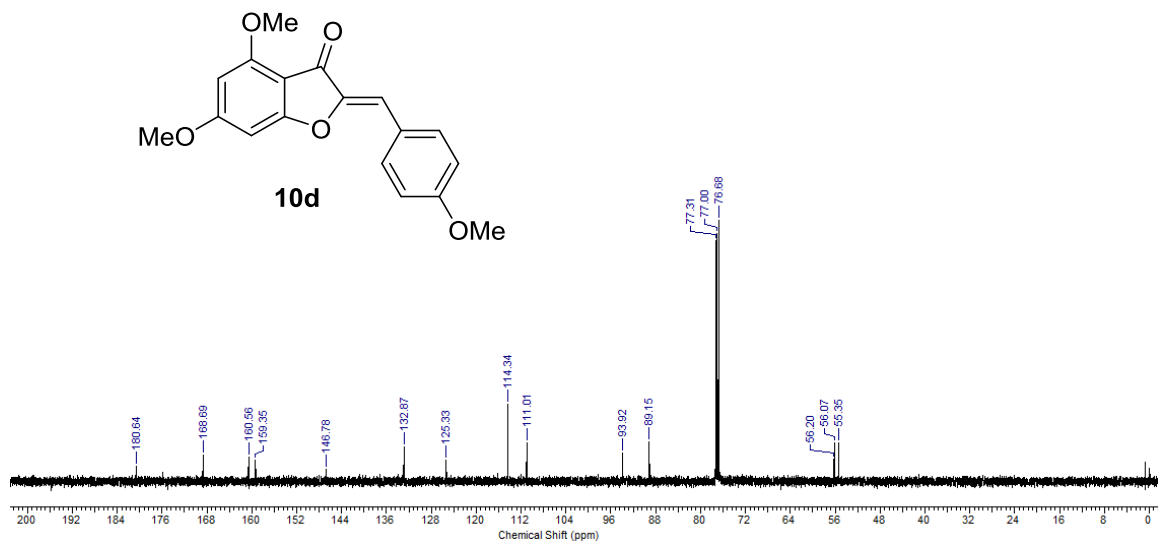
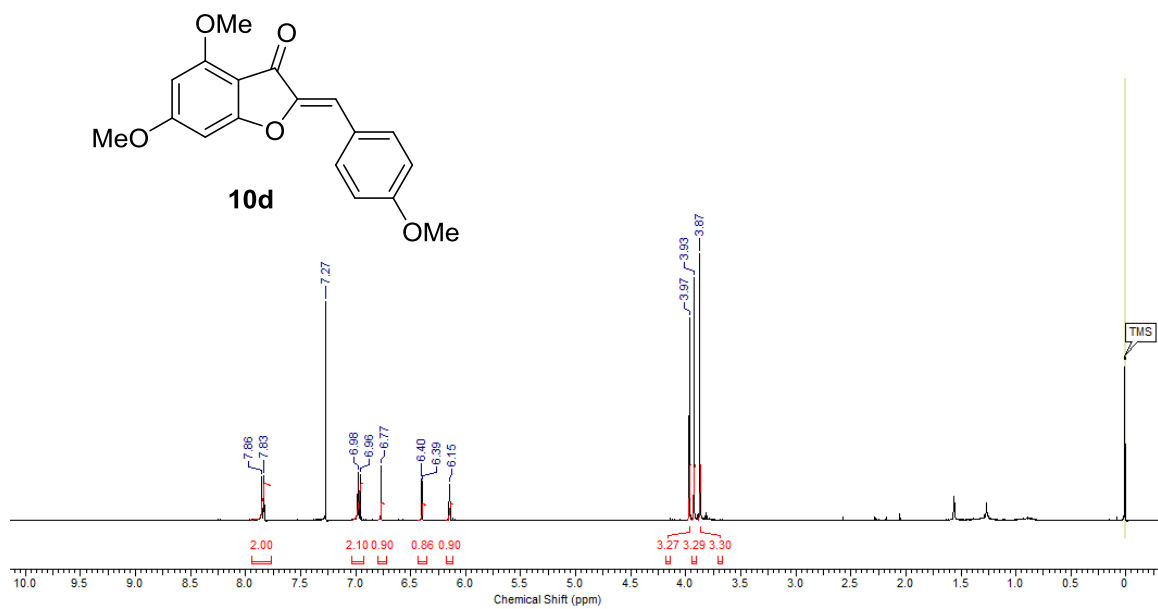


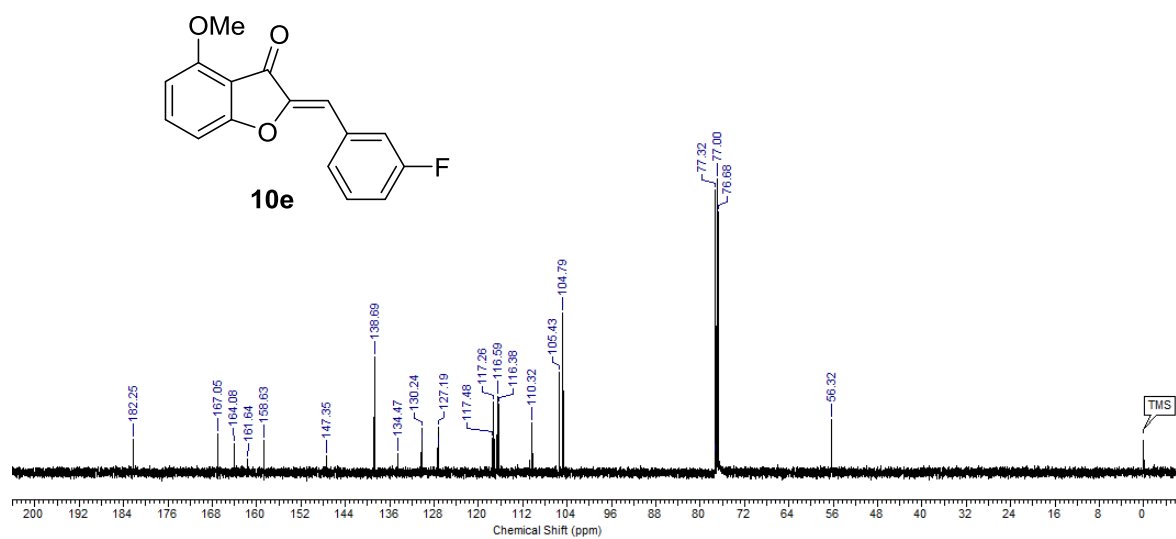
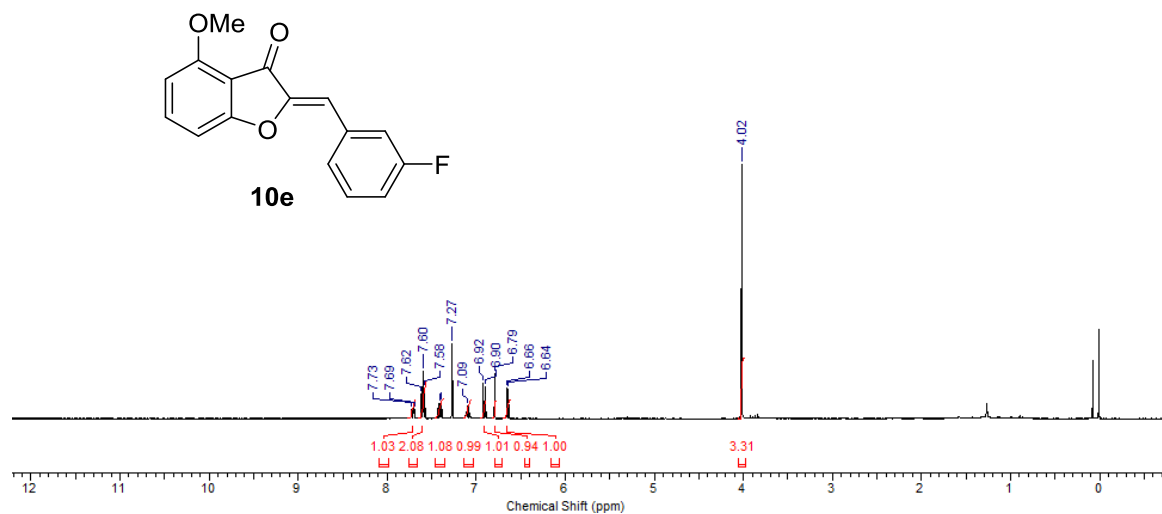


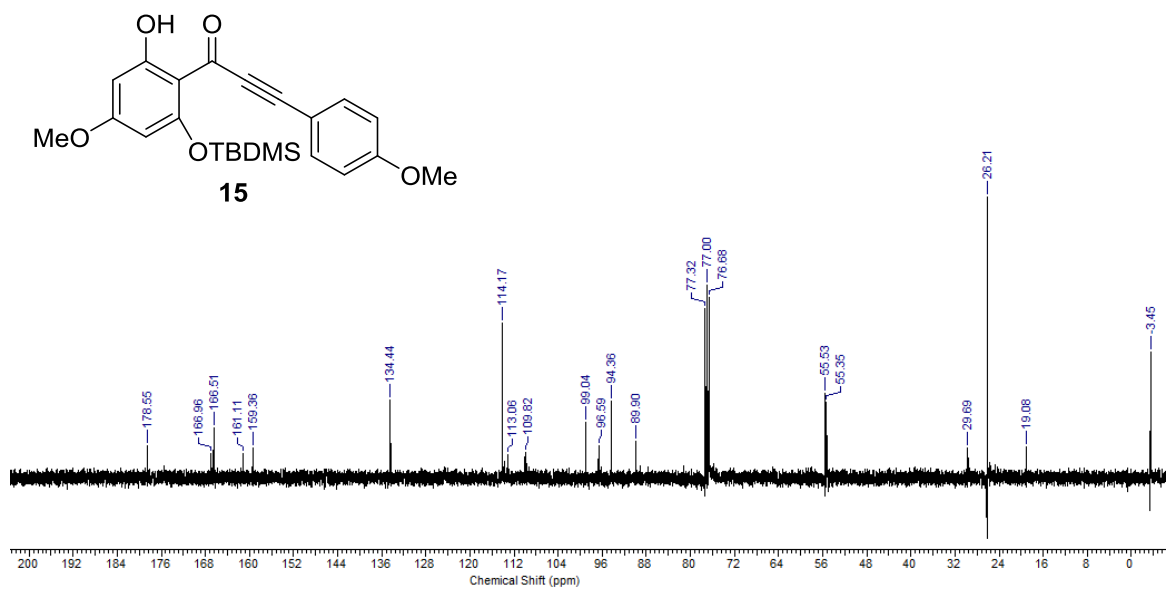
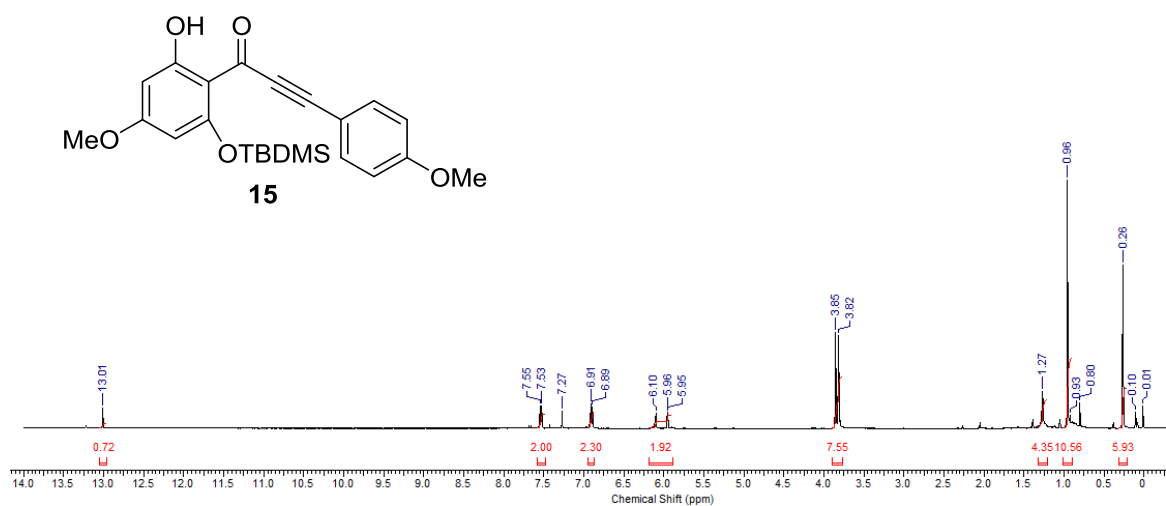












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