

Brønsted acid-catalyzed reaction of alkynyltrifluoroborates with acetals and ketals

By

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of the requirements for the Degree of**

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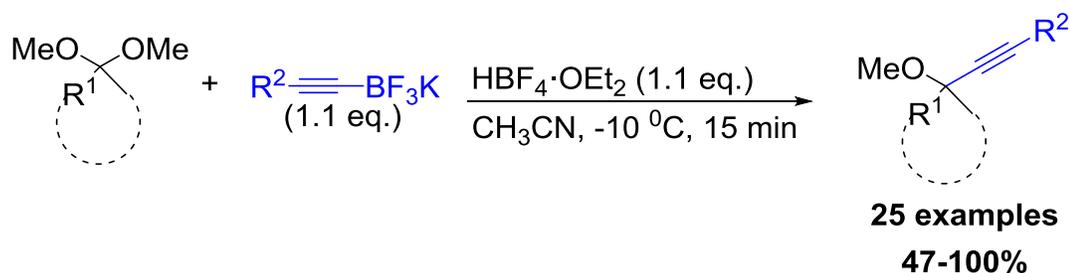
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Abstract

The synthesis of small molecules is crucial in the pharmaceutical industry for producing drugs or biologically active compounds. Developing new methods to synthesize molecules is necessary for the advancement of new pharmaceutical compounds. Specifically, the formation of new carbon-carbon bonds is of great importance in synthetic organic chemistry. Brønsted acid catalysis is a powerful synthetic tool to make many different compounds, however, the current carbon-based nucleophiles are the major limitation of acid-catalyzed reactions. In effort to expand repertoire of Brønsted acid compatible nucleophiles, we present a novel carbon-carbon bond forming methodology between acetals, ketals, and potassium phenylacetylene trifluoroborate salts. In the presence of a Brønsted acid, acetals form oxocarbenium electrophiles, which subsequently react with trifluoroborates to form propargylic ethers. Reaction times of 15 minutes and use of 1.1 equiv. of acid and trifluoroborate make this methodology very atom economical. Excellent functional group tolerance is observed with this protocol including, halogen, nitrile, nitro, acid and carbonyl functionalities. To our knowledge, this is also the first alkynylation procedure compatible with ketal substrates.



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List of Abbreviations

Equiv: equivalents

TMSOTf: trimethylsilyl triflate

$\text{BF}_3 \cdot \text{OEt}_2$: boron trifluoride diethyl etherate

TMS: trimethylsilyl

C-C: carbon-carbon

AlEt_2Cl : diethylaluminum chloride

CH_2Cl_2 : dichloromethane

Et_2O : diethyl ether

DIPEA: N,N-diisopropylethylamine

CH_3CN : acetonitrile

AgOTf: silver (I) triflate

$\text{Au}(\text{PPh}_3)\text{Cl}$: Chloro(triphenylphosphine)gold (I)

DCE: dichloroethane

$\text{HC}(\text{OEt})_3$: triethylorthoformate

AgNTf₂: Silver bis(trifluoromethanesulfonyl)imide

$(t\text{-Bu})_2(o\text{-biphenyl})\text{PAuCl}$: chloro[(1,1'-biphenyl-2-yl)di-tert-butylphosphine]gold(I)

$\text{Cu}(\text{MeCN})_4\text{PF}_6$: tetrakis(acetonitrile)copper(I) hexafluorophosphate

ZnCl_2 : Zinc (II) chloride

SnCl_4 : tin (IV) chloride

SiCl_4 : silicon tetrachloride

H₂O: water

r.t: room temperature

TFAA: trifluoroacetic anyhdride

DDQ: 2,3-dichloro-5,6-dicyano-1,4-benzoquinone

LiClO₄: lithium perchlorate

4 Å MS: 4 Angstrom molecular sieves

C-H: carbon-hydrogen

BCl₃: boron trichloride

n-BuLi: butyl lithium

pK_a: acid dissociation constant

NEt₃: triethylamine

TiCl₄: titanium (IV) chloride

MeOH: methanol

B(OMe)₃: trimethylborate

THF: tetrahydrofuran

KHF₂: potassium hydrogen difluoride

HCl: hydrochloric acid

HF₆Sb·6 H₂O: fluoroantimonic acid hexahydrate

CF₃COOH: trifluoroacetic acid

HBF₄·OEt₂ : tetrafluoroboric acid diethyl etherate

min: minutes

CH₃CH₂CN: propionitrile

Ar_(g): argon gas

MgSO₄: magnesium sulfate

¹H-NMR: proton nuclear magnetic resonance spectroscopy

¹³C-NMR: carbon nuclear magnetic resonance spectroscopy

¹⁹F-NMR: fluorine nuclear magnetic resonance spectroscopy

¹¹B-NMR: boron nuclear magnetic resonance spectroscopy

FT-IR: Fourier transform infrared spectroscopy

HRMS: High resolution mass spectrometry

Chapter 1: Introduction and Literature Review

1.1 Brønsted acid catalysis

The use of a protic acid in the presence of a nucleophile is the fundamental principle of Brønsted acid catalysis. This is in contrast to Lewis acid catalysis, where an electron deficient species will activate a C=X bond (X = O, NR, CR₂), promoting a nucleophilic attack (Figure 1).¹

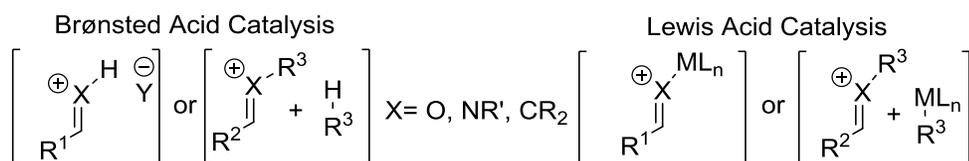


Figure 1. Reaction intermediates of Lewis acid and Brønsted acid catalysis.

Esterification and acetalization reactions are known Brønsted acid catalyzed processes, however, carbon-carbon bond forming reactions using Brønsted acids are not as prevalent compared to Lewis acid catalyzed processes.¹ This growing field encompasses transformations such as the Mannich reaction,²⁻⁴ allylations⁵⁻⁹, aldol reactions^{10,11} and asymmetric syntheses¹, using many different Brønsted acids (Figure 2).¹

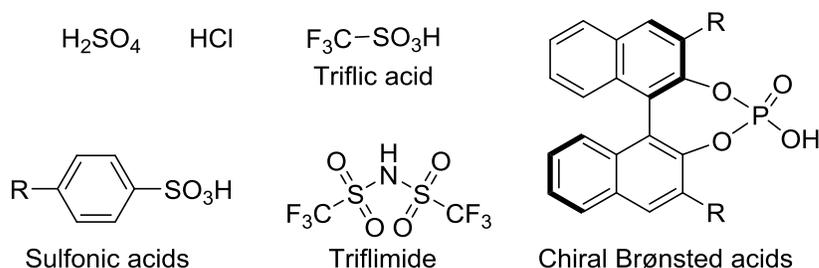


Figure 2. Common Brønsted acid catalysts.

These different carbon-carbon bond forming reactions involve electrophiles such as activated alkenes,¹² aldehydes^{5,6,8} and acetals.⁷ For all of these known reactions, the nucleophile scope is limited to enol derivatives,³ allylating agents^{5-7,9} and heteroatoms¹³ (OH, NHR₂, SH) (Figure 3). To the best of our knowledge, potassium alkynyltrifluoroborate salts have not been used as nucleophiles in a Brønsted acid catalyzed reaction.

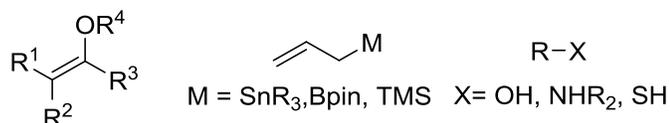
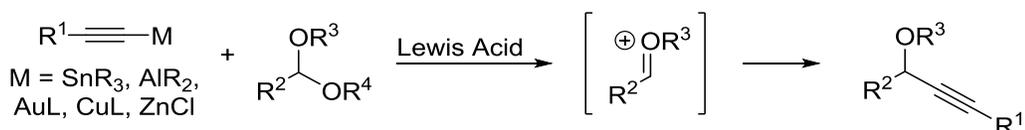


Figure 3. Nucleophile scope of Brønsted acid catalyzed reactions.

1.2 Alkynylation of acetals using alkynylmetal reagents

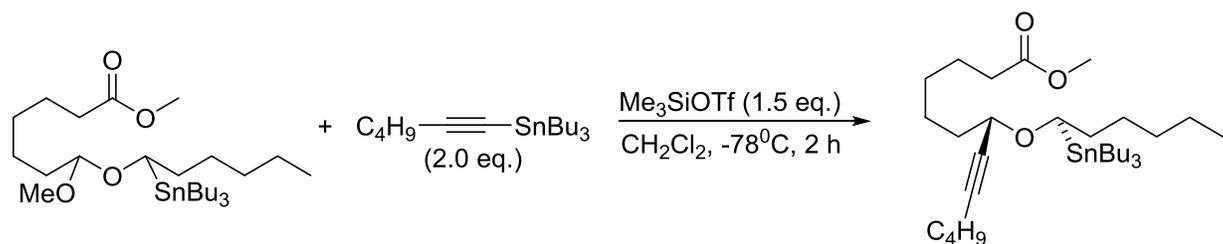
Alkynyl metal nucleophiles including stannanes,^{14,15} alanes,¹⁶⁻¹⁹ gold,^{20,21} copper²² and zinc²³ are all known to react with acetal electrophiles in the presence of Lewis acids to form propargylic ethers. These reactions proceed through the formation of an oxocarbenium intermediate, which is the electrophilic species of the reaction (Scheme 1).



Scheme 1: General mechanism for alkynylation of acetals using alkynylmetal reagents.

1.2.1 Alkynylstanne reactions with acetals

Linderman and coworkers demonstrated that alkynylstannanes react with mixed acetals in the presence of a Lewis acid catalyst.¹⁴ The reaction is also stereoselective when using a stannyl substituted acetal. This method, though high yielding, has substrate tolerance limited to alkyl, phenyl and alkyl ester containing acetals. Tolerance of the ester functional group is only observable when it is in a remote location on the acetal (Scheme 2). The reaction also requires the use of 2.0 equiv. of alkynylzinc reagent and 1.5 equiv. of TMSOTf.

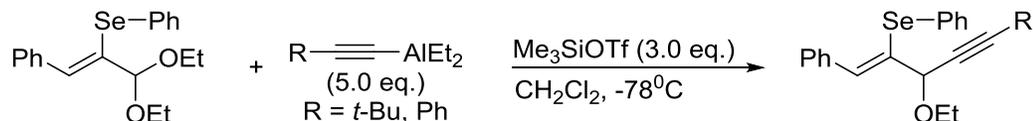


Scheme 2: Alkynylation of mixed acetals with alkynylstannanes

Alkynylstannes have also been shown to react with cyclic acetals in the presence of a TiCl_4 Lewis acid, to form chiral alcohols.¹⁵ This method required the use of 2.0 equiv. of alkynylzinc reagent and 1.6 equiv. of TiCl_4 . Very limited functional group tolerance was observed for this synthesis as well.

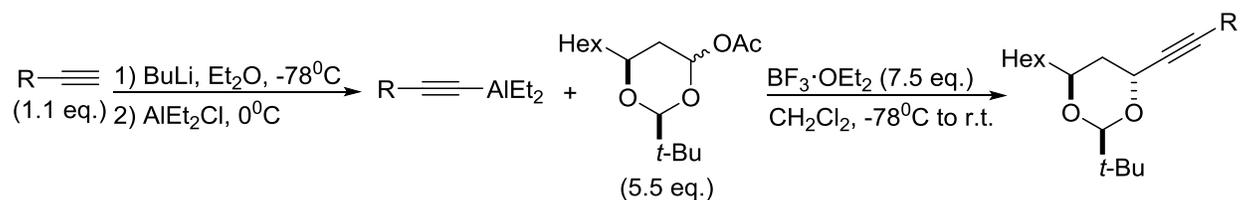
1.2.2 Alkynylalane reactions with acetals

Alkynylalanes react with acetals in the presence of Lewis acids as demonstrated by Yoshimatsu and coworkers. Two examples of alkynylalanes were shown to react with 2-(chalcogeno)prop-2-enal acetals (Scheme 3).¹⁶ This procedure required 3 equiv. of TMSOTf and 5 equiv. of alkynylalane to afford the desired product.



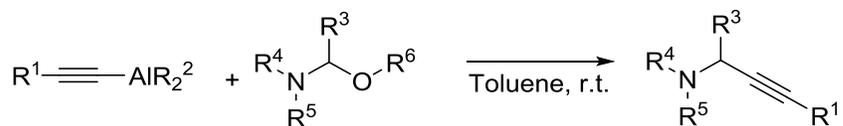
Scheme 3: Alkynylation of acetals with alkynylalanes

Rychnovsky and coworkers demonstrated a variety of alkynylalanes reacting with 4-acetoxy-1,3-dioxanes.¹⁹ With this approach, the alkynylalanes are pre-formed as the limiting reagent using *n*-BuLi, before the addition of 7.5 equiv. of $\text{BF}_3 \cdot \text{OEt}_2$ and 5.5 equiv. of starting material (Scheme 4). This procedure only tolerates TMS-acetylenes and unsubstituted alkynes and requires a large excess of Lewis acid catalyst and starting material, thus it has a low atom economy.



Scheme 4: Alkynylation of 4-acetoxy-1,3-dioxanes with alkynylalanes

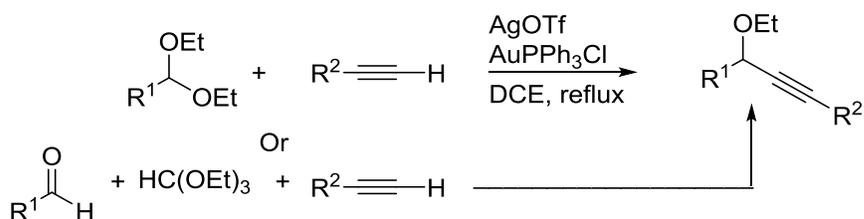
The alkynylation of N,O-acetals have also been reported using alkynylalanes.^{17,18} Though the products of these reactions are amines, the mechanism is similar, proceeding through an iminium ion intermediate (Scheme 5). In both cases, only alkyl and halogen functional groups are tolerated.



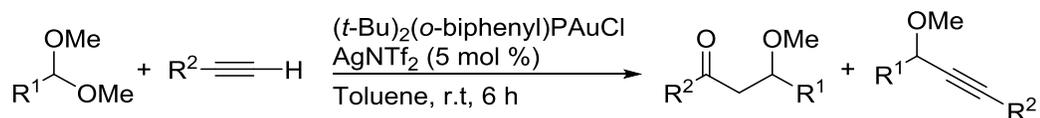
Scheme 5: Alkynylation of N,O-acetals with alkynylalanes.

1.2.3 Gold catalyzed alkynylation reactions with acetals

Two accounts show gold catalysts activating terminal alkynes to react with acetals, forming propargylic ether products. Wang and coworkers demonstrated that gold and silver catalyze the reaction of acetals and aldehydes with alkynes (Scheme 6).²⁰ A method reported by Hu, X. and coworkers results in the formation of a propargylic ether by-product, for a gold catalyzed aldol based reaction (Scheme 7).²¹ Both methods require a loading of 5 mol % gold catalysts for the preparation of these products.



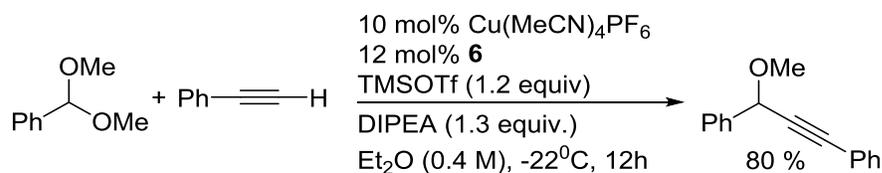
Scheme 6: Gold catalyzed reaction of acetals with terminal alkynes.



Scheme 7: Gold catalyzed aldol based reaction; propargylic ether by-product.

1.2.4 Copper-catalyzed alkynylation of oxocarbenium ions

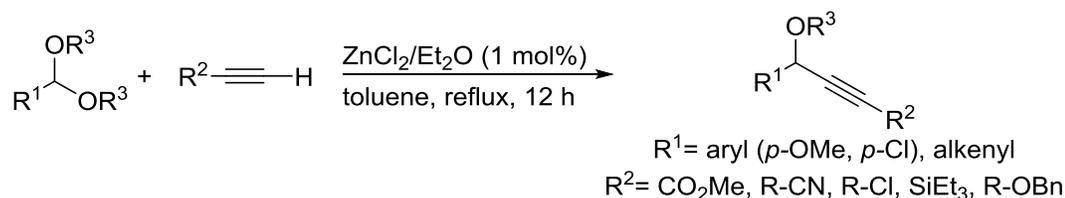
Isochroman acetals are known to react with terminal alkynes in the presence of copper and Lewis acid catalysts as shown by Watson and coworkers.²² The reaction conditions are also effective at alkynylating acyclic acetals (Scheme 8). These conditions although effective, have functional group tolerance limited to halogens, ethers and esters, and require 12 hour reaction times.



Scheme 8: Copper-catalyzed reaction of acetals with terminal alkynes.

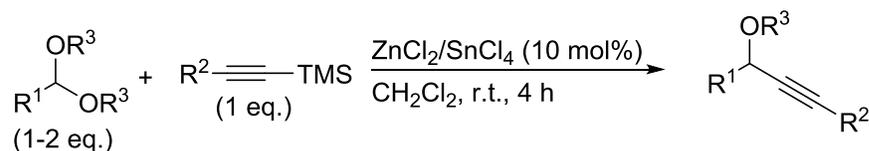
1.2.5 Zinc-catalyzed coupling of alkynes with acetals

Alkynylzinc reagents are also effective coupling partners with acetals.²³ Many different functionalized terminal alkynes were shown to effectively couple with acetals to form propargylic ethers. A diverse substrate scope was observed for the alkyne; while the acetals used were limited to ether or halogen substituents (Scheme 9).



Scheme 9: Scope of propargylic ether synthesis from alkynylzinc reagents and acetals.

A final example, reported by Hayashi and coworkers makes use of a zinc and tin catalyst system for the synthesis propargylic ethers from trimethylsilyl-alkynes and acetals.²⁴ This reaction only tolerated alkyl and aryl acetals and trimethylsilyl-alkynes, often needing excess of acetal (Scheme 10).



Scheme 10: Metal catalyzed reaction of TMS-acetylenes and acetals.

1.2.6 Conclusions of metal-catalyzed alkynylations of acetals

Various literature examples of metal-catalyzed alkynylations of acetals all prove effective at synthesizing propargylic ethers. A common theme of poor functional group tolerance is observed, due to the use of Lewis acid catalysts. In many cases, it is necessary to pre-form unstable starting materials. In addition, the use of expensive metal

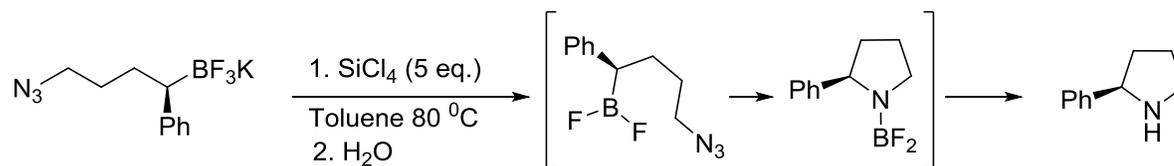
catalysts is sometimes required. Therefore, there is a need for new efficient and more functional group tolerant methodologies for the synthesis of propargylic ethers.

1.3 Lewis acid catalyzed reactions of organotrifluoroborates

Organotrifluoroborate salts have emerged as powerful tools for C-C bond forming reactions in metal-free catalysis.²⁵ Lewis acid catalyzed reactions with trifluoroborates have been reported with azides,²⁶ epoxides,²⁷ glucals,^{28,29} acyl chlorides³⁰ and acetals.^{31,32} Among these examples, the reaction of trifluoroborates with oxocarbenium electrophiles has been reported.^{28,30-32}

1.3.1 Reactions of trifluoroborates with azides

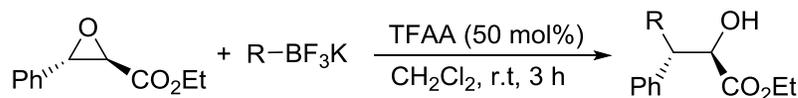
Matteson has reported the asymmetric synthesis of secondary amines from azide containing alkyltrifluoroborates.²⁶ This reaction requires the use of excess Lewis acid to promote the formation of an alkyldifluoroborane intermediate, which reacts with the terminal azide to form secondary amines (Scheme 11).



Scheme 11: Synthesis of secondary amines from azide functionalized alkyltrifluoroborates.

1.3.2 Reactions of trifluoroborates with epoxides

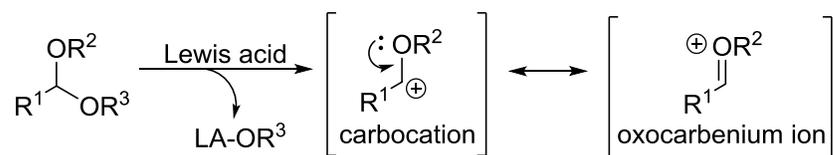
Csáký reported the opening of epoxides with trifluoroborate salts using TFAA as a catalyst (Scheme 12). His work shows alkenyl and aryl trifluoroborates are needed in slight excess for the reaction with epoxides, while requiring only 50 mol% of a Lewis acid catalyst.



Scheme 12: Lewis acid-catalyzed opening of epoxides with trifluoroborates.

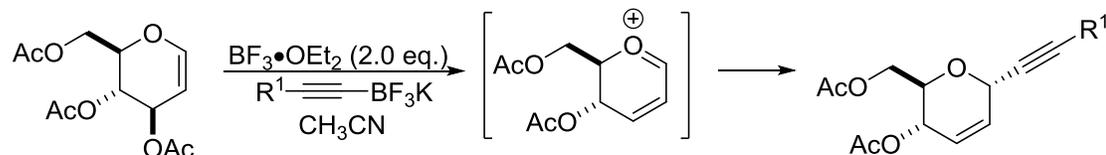
1.3.3 Reactions of trifluoroborates with oxocarbenium ions

Overall, six accounts of Lewis acid catalyzed reactions of trifluoroborate salts with oxocarbenium ions have been reported. Oxocarbenium ions constitute stabilized carbocations making them excellent candidates for C-C bond forming reactions (Scheme 13).



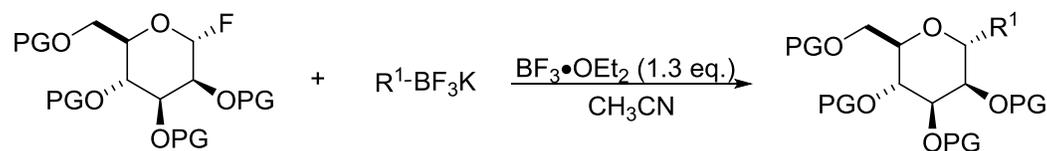
Scheme 13: Lewis acid promoted formation of oxocarbenium ion from acetals.

Stefani and coworkers demonstrated the reaction of alkynyltrifluoroborates with D-glucals for the synthesis of α -C-glycosides.²⁸ Various alkynyltrifluoroborates were shown to react with 3,4,6-tri-*O*-Acetyl-D-glucal (Scheme 14). α -Alkynyl-glycosides have multiple applications and can be further transformed into various scaffolds.³³ The use of Lewis acid catalyst BF₃•OEt₂ limits the functional group tolerance to the ester and ether functional groups.



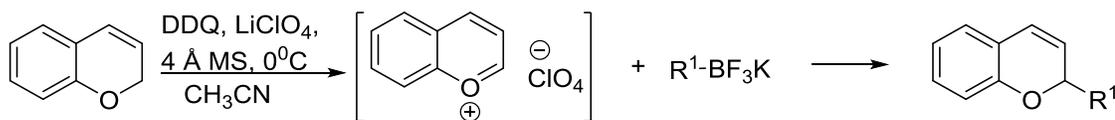
Scheme 14: Synthesis of α -C-glycosides from glucans and trifluoroborates

Liu and coworkers also reported a synthesis of α -C-glycosides from glycosyl fluorides. This reaction was effective at reacting alkynyl and alkenyl trifluoroborate salts with α -F-glycosides bearing a variety of different protecting group (Scheme 15).²⁹



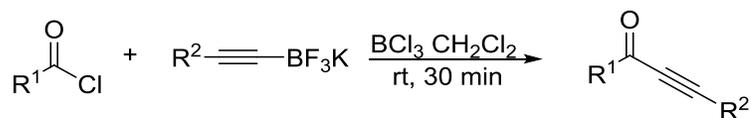
Scheme 15: α -C-glycoside synthesis from organotrifluoroborates and glycosyl fluorides.

Floreancig showed oxocarbenium ions of chromene, which form upon reaction with DDQ, will react with alkynyl, alkenyl and aryl trifluoroborates (Scheme 16).³⁴ This method tolerates various substituted chromene derivatives including, ether, nitrile and silyl functional groups.



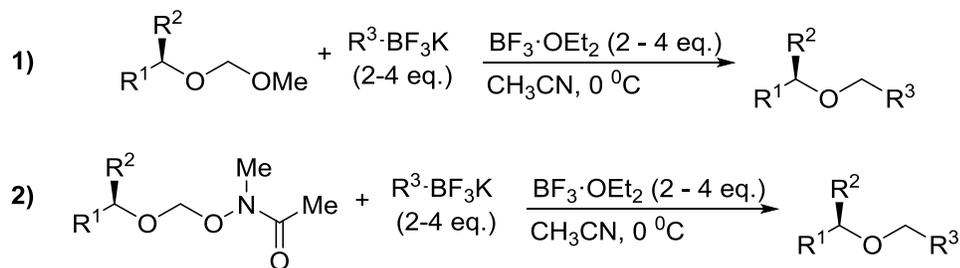
Scheme 16: Reaction of chromene with organotrifluoroborates through oxidative C-H bond cleavage.

Recently, our research group reported a metal free synthesis of ynones from acyl chlorides and alkynyltrifluoroborate salts under very mild conditions.³⁰ *In situ* formation of Lewis acidic dichloroboranes from trifluoroborate salts allows for the oxocarbenium ion to form from the acyl chloride (Scheme 17). These conditions allow for the synthesis of a repertoire of ynones, which have a variety of synthetic applications. This methodology tolerates halogenated and ether functional groups and requires non-forcing reaction conditions.



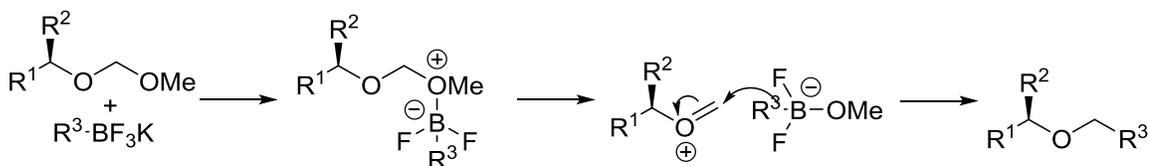
Scheme 17: Metal-free alkylation of acyl chlorides with alkynyltrifluoroborates.

The Lewis acid catalyzed reactions of acetals and trifluoroborates have been explored by Bode using MOM-protected alcohols³¹ and mixed hydroxamic acid derived acetals.³² Both were shown to be effective coupling partners with a variety of trifluoroborate salts (Scheme 18).



Scheme 18: Lewis acid-catalyzed reaction of organotrifluoroborates and acetals.

In both cases, oxocarbenium ions are the electrophilic intermediates that form in the presence of Lewis acids (Scheme 19). Alkynyl, alkenyl, aryl and hetero-aryl trifluoroborate salts react as nucleophiles in these reactions. Though high yielding, these reactions only tolerate esters, ether and halogen functional groups. Another limitation of this method is the need for large excess of reagents. Upwards of 4 equiv. of trifluoroborate and 4 equiv. of $\text{BF}_3\cdot\text{OEt}_2$ are required for the transformation to take place.



Scheme 19: Mechanism of Lewis acid-catalyzed reaction between acetals and $\text{R-BF}_3\text{K}$.

1.4 Literature gaps

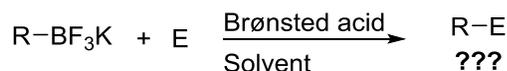
Trifluoroborates are known to react with oxocarbenium ions in the presence of Lewis acid catalysts (Scheme 19). To the best of our knowledge, there are no reports regarding Brønsted acid-catalyzed reaction of trifluoroborates with acetals in the literature. When considering Brønsted acids as catalysts, many potential benefits arise over traditional Lewis acids.

Brønsted acids are shelf stable, less toxic and inexpensive alternatives of Lewis acids.¹ There are also many more commercially available Brønsted acids, which can have a broad range of pKa values and solubility. In addition, Brønsted acids exhibit greater functional group tolerance than their counterparts.

Brønsted acid catalysis currently has a modest repertoire of nucleophiles available, with C-C bond forming reactions limited mainly to enol derivatives, allylating agents and heteroatoms (Figure 3). Expanding the scope of carbon nucleophiles for Brønsted acid catalysis will open doors to new efficient transformations.

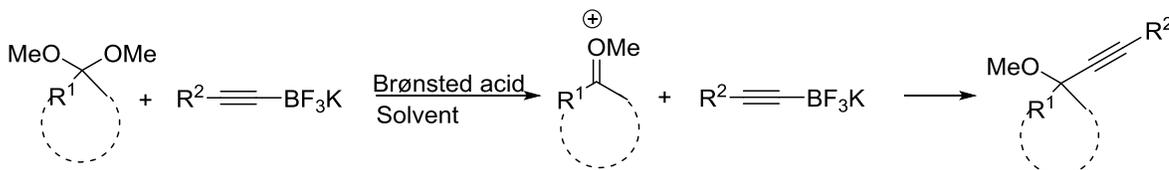
1.5 Research objective

To address these literature gaps, we hypothesized that trifluoroborate salts will act as nucleophiles in the presence of Brønsted acid catalysts (Scheme 20).



Scheme 20: Brønsted acid catalyzed reaction of trifluoroborates with electrophiles.

Our investigation focused on a Brønsted acid-catalyzed reaction between alkynyltrifluoroborate salts and acetals (Scheme 21). Our objective was to develop a novel, efficient methodology for the alkylation of acetals using trifluoroborate salts, which is high yielding, atom economical and tolerates many different functional groups.



Scheme 21: Proposed reaction of alkynyltrifluoroborates with acetals and ketals.

Chapter 2: Development of methodology for the alkylation of acetals and ketals with alkynyltrifluoroborates

2.1 Synthesis of a library of acetals and ketals

Our investigation needed a variety of acetals to use as substrates for the alkylation. Some of these acetals are commercially available. However, the availability and affordability of aldehydes prompted us to use them as starting materials. The acetals were prepared from aldehydes using a modified procedure reported by Porta (Procedure 1, Scheme 29).³⁵ Their report states that using 1 mol % of TiCl₄ catalyst in the presence

of NEt_3 for acetalizations. In our experience, better conversions were achieved when the loading of TiCl_4 was increased to 5 mol %. Various acetals and ketals were synthesized using procedure 1. This method allowed us to synthesize acetals with halogen, nitro, nitrile, ester, ketone and carboxylic acid functional groups on a gram scale (Figure 4).

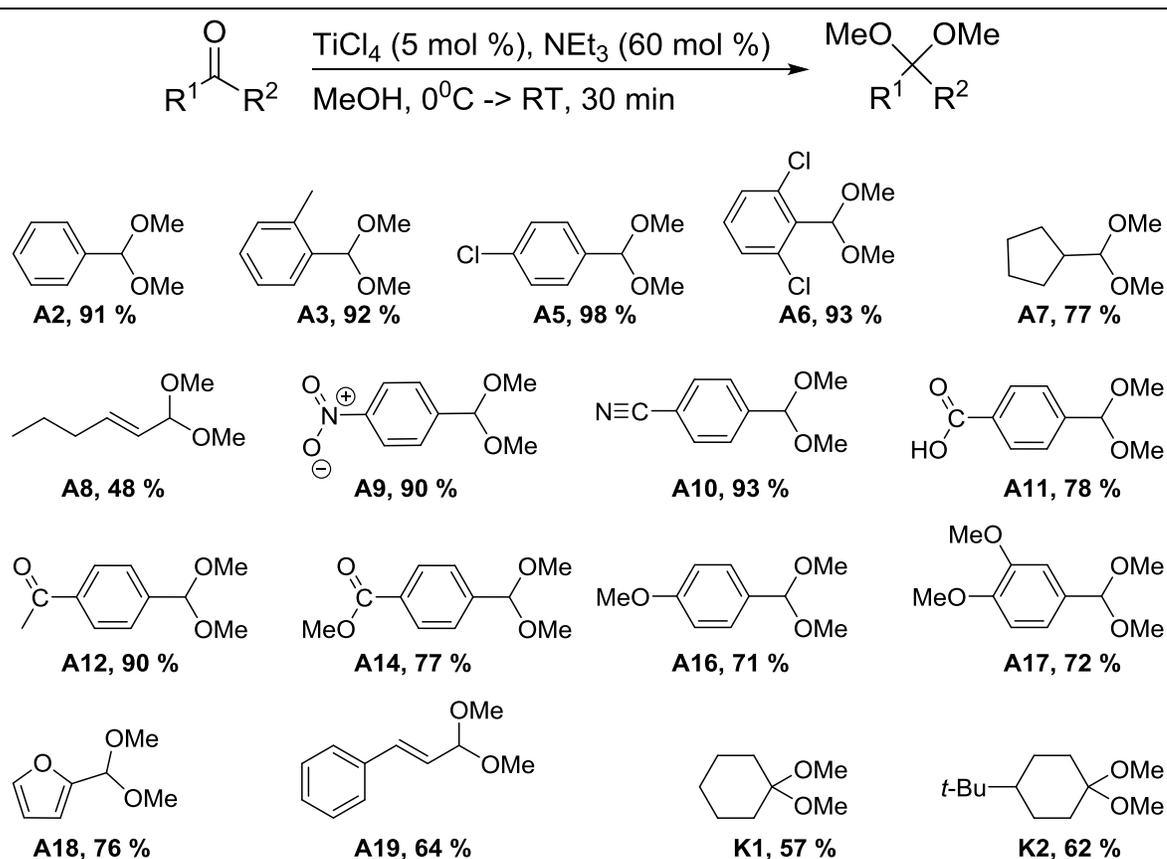


Figure 4: Synthesis of acetals and ketals following procedure 1.

This procedure was very effective at synthesizing a library of acetals, however, some aldehydes were not tolerated (Figure 5). Our available substrate scope was hindered in part due to the limitations of this procedure. **A22** did not react, presumably due to the free 1^o-hydroxyl group present. Nitrogen bearing acetals **A23** and **A24** also did not react under these conditions. We could not do reactions using phenol or aniline derivatives for our methodology.

Ketals **K1** and **K2** were effectively synthesized from cyclohexanone starting materials, however, a number of ketones including acetophenone, benzophenone, cycloheptanone and cyclopentanone did not form desired products. **K8** was not obtained when Cyclopentanone was used as starting material. This is potentially due to the evaporation of the product.

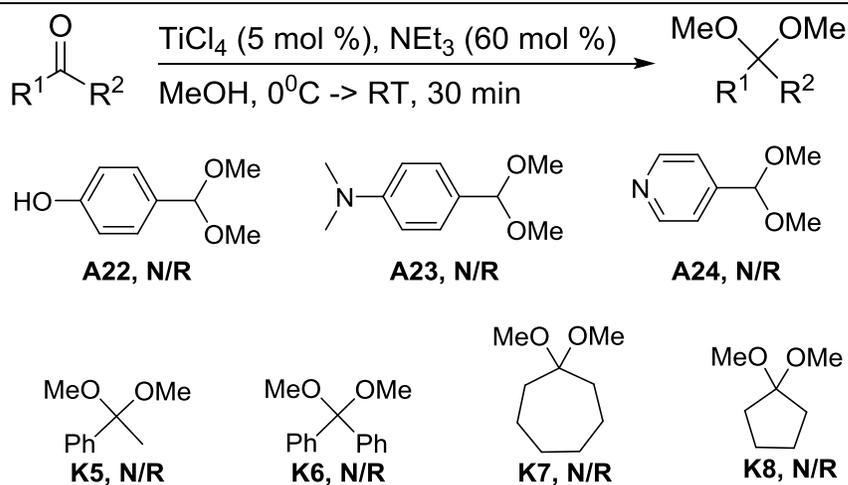


Figure 5: Failed acetalizations and ketalizations

A variety of inexpensive acetal and ketal derivatives were purchased (Figure 6). Aliphatic, halogen, aldehyde, pyridine and alcohol bearing acetals increased the different functional groups we were able to test. **A15** is a cyclic acetal that has some resemblance to a glucals derivative, while **K3** and **K4** were additional acetone and acetophenone derivatives.

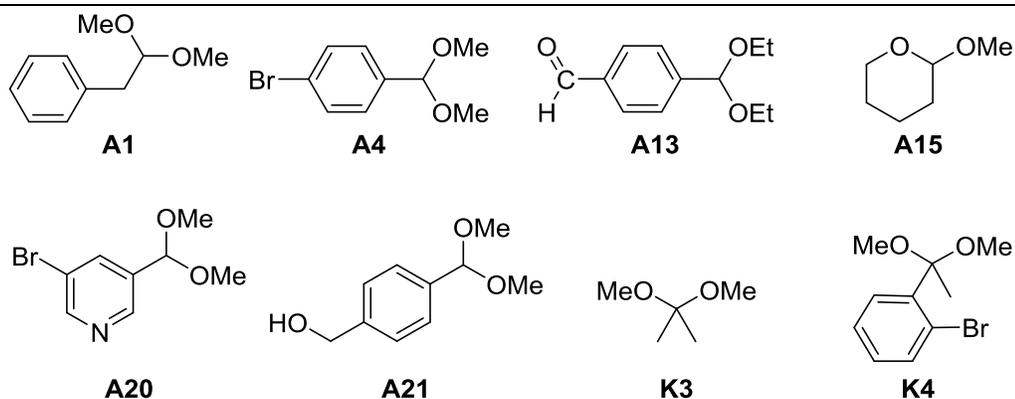


Figure 6. Purchased acetals and ketals.

2.2 Synthesis of various alkynyltrifluoroborate salts

The preparation of alkynyltrifluoroborates was done following procedure 2, reported by Stefani (Scheme 30).²⁸ Trifluoroborates with a variety of functional groups are illustrated in Figure 7. This procedure allowed for gram quantities of trifluoroborates to be synthesized in high purity. Neutral trifluoroborates **S1** to **S3** were obtained in modest to good yields. Electron-rich trifluoroborates **S4** and **S10** were also obtained in modest yields. Electron-deficient trifluoroborates **S5** to **S9** were synthesized in modest to high yields, with **S6** yielding 84 %. Salts **S5** and **S9** bear electron-withdrawing trifluoromethyl groups, which is a functional group seen in a variety of pharmaceutical compounds. Trifluoroborates **S6** and **S7** bear chlorine substituents that can undergo latter metal-catalyzed functionalization. This procedure was effective in synthesizing a variety of different trifluoroborates. Current limitation of this procedure is the use of *n*-Bu-Li, which restricts the different functional groups that can be present on the trifluoroborates.

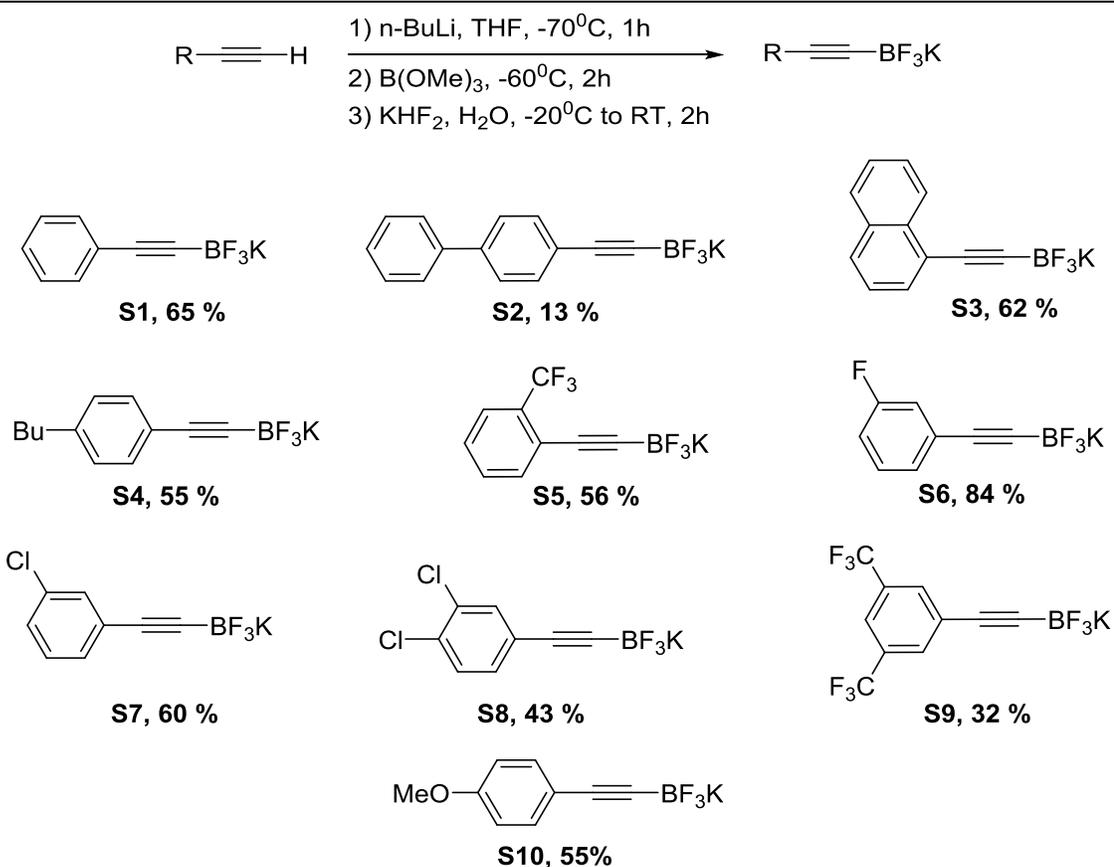


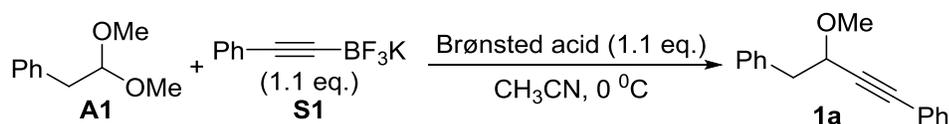
Figure 7. Trifluoroborates synthesized using procedure 2.

2.3 Optimization of reaction between acetals and trifluoroborates.

2.3.1 Brønsted acid catalyst screen

The first challenge we faced was finding a suitable Brønsted acid that would catalyze the reaction between acetals and alkynyltrifluoroborates. We tested a variety of different Brønsted acids using (2,2-dimethoxyethyl)benzene (**A1**) and phenylacetylene trifluoroborate (**S1**) (Table 1). HCl afforded (3-methoxybut-1-yne-1,4-diyl)dibenzene **1a** in a modest 34 % (entry 1), which confirmed our hypothesis that a Brønsted acid can indeed catalyze this reaction. Fluoroantimonic acid gave a similar yield of 36 % for **1a** (entry 2). This superacid did not have a significant increase in the yield of **1a** compared to HCl, which led us to believe that acid strength was not the underlying factor. Fluoroantimonic acid was also in its hydrated form, which ran the risk of degradation of (2,2-dimethoxyethyl)benzene **A1** to its corresponding aldehyde. Trifluoroacetic acid, a commonly employed acid catalyst, produced **1a** in only a 28 % yield. We then utilized $\text{HBF}_4 \cdot \text{OEt}_2$ (entry 4) as a catalyst, which afforded (3-methoxybut-1-yne-1,4-diyl)dibenzene **1a** in a 86 % yield. Further investigation revealed that the reaction was complete in only 10 minutes, yielding 89 % of the desired (3-methoxybut-1-yne-1,4-diyl)dibenzene **1a** (entry 5). This prompted us to use $\text{HBF}_4 \cdot \text{OEt}_2$ as a catalyst, because the reaction proceeds to completion in minutes, using only 1.1 equiv of trifluoroborate and catalyst.

Table 1: Optimization of Brønsted acid catalyst for synthesis of 1a.



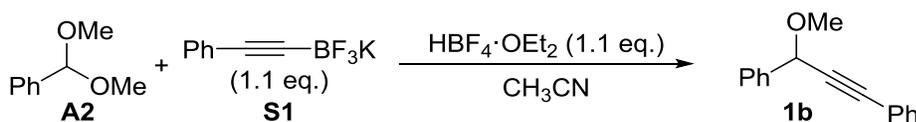
entry	Brønsted acid	Time (mins)	Yield (%)
1	HCl [4M] in dioxane	60	34
2	$\text{HF}_6\text{Sb} \cdot 6\text{ H}_2\text{O}$	60	36
3	CF_3COOH	60	28
4	$\text{HBF}_4 \cdot \text{OEt}_2$	60	86
5	$\text{HBF}_4 \cdot \text{OEt}_2$	10	89

Acetonitrile was used as the solvent with no further optimization. Besides the obvious high yields obtained with acetonitrile, this solvent was shown to be optimal in the work of Bode, J.^{31,32}, as well as by Kayla Fisher for the reaction of trifluoroborates with stabilized carbocations (Bolshan Group, *unpublished results*).

2.3.2 Optimization of reaction temperature for benzylic acetals

Applying the optimized conditions to (dimethoxymethyl)benzene **A2**, significant decrease in yield of (3-methoxyprop-1-yne-1,3-diyl)dibenzene **1b** to 60 % was observed compared to the yield of (3-methoxybut-1-yne-1,4-diyl)dibenzene **1a**, with full consumption of starting material observed (Table 2, entry 1). Decreasing the temperature to -10°C resulted in a drastic increase in yield of (3-methoxyprop-1-yne-1,3-diyl)dibenzene **1b** to 85 % (entry 2). (dimethoxymethyl)benzene **A2** reacted within 10 minutes with only a slight decrease in yield to 83 % at this lower temperature (entry 3).

Table 2: Optimization of temperature for benzylic acetals.



entry	Temperature (°C)	Time (mins)	Yield (%)
1	0	60	60
2	-10	60	85
3	-10	10	83

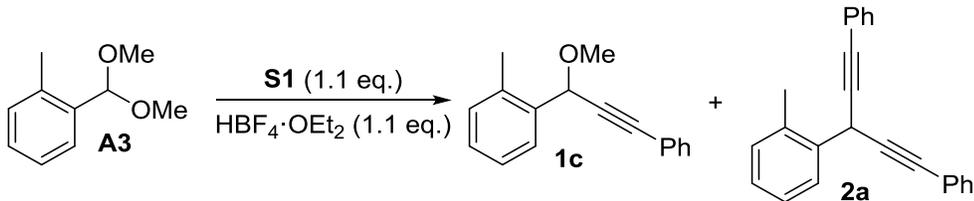
2.3.3 Optimization of benzylic acetals bearing electron donating functional groups

When we used electron rich acetal (Dimethoxymethyl)-2-methylbenzene **A3** under the optimized reaction conditions, a competing dialkynylated product (3-(o-tolyl)penta-1,4-diyne-1,5-diyl)dibenzene **2a** was formed (Table 3, entry 1). The undesired by-product appeared due to the ability of the electron-donating group to stabilize a carbocation. With (dimethoxymethyl)benzene **A2**, decreasing the temperature was effective to suppress the formation of the undesired product. Therefore, this approach was implemented for

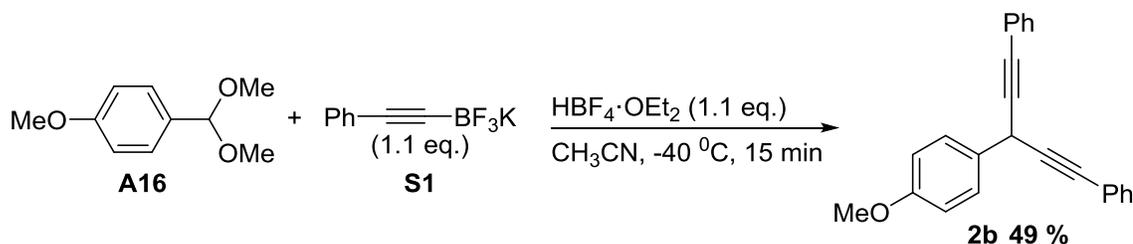
(Dimethoxymethyl)-2-methylbenzene **A3**. A decrease of the reaction temperature to -30°C resulted in a 66 % yield of (1-methoxy-3-phenylprop-2-yn-1-yl)-2-methylbenzene **1c**, and effectively eliminated the formation of (3-(*o*-tolyl)penta-1,4-diyne-1,5-diyl)dibenzene **2a** (entry 2). Further decrease to -40°C had a slight increase in yield of **1c** to 70% (entry 3). Decreasing the reaction time to 15 minutes at -40°C decreased the yield of **1c** to 62 %. Decreasing the temperature of the system was no longer possible due to the fact that acetonitrile solidifies at -48°C. Upon using propionitrile as a solvent, the yields of (1-methoxy-3-phenylprop-2-yn-1-yl)-2-methylbenzene **1c** rose dramatically, while maintaining the temperature at -40°C. A 90 % yield of (1-methoxy-3-phenylprop-2-yn-1-yl)-2-methylbenzene **1c** was obtained after 15 minutes (entry 5), and a 98 % yield was seen after 60 minutes (entry 6). Initially, propionitrile was used due to its low melting point of -93°C. The increase in yield at -40°C might be a consequence of the decreased solubility of trifluoroborates in propionitrile.

While these conditions were effective for weak electron-donating groups, the dialkynylation was still the only observed product for *para*-methoxy substituted **A16** (Scheme 22).

Table 3: Optimization of temperature for electron rich benzylic acetals.



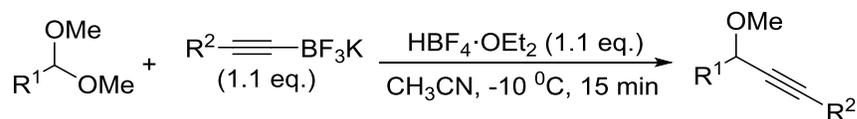
entry	Temp (°C)	Time (mins)	Solvent	Yield 1c (%)	Yield 2a (%)
1	-10	60	CH ₃ CN	trace	21
2	-30	60	CH ₃ CN	66	0
3	-40	60	CH ₃ CN	70	0
4	-40	15	CH ₃ CN	62	0
5	-40	15	CH ₃ CH ₂ CN	90	0
6	-40	60	CH ₃ CH ₂ CN	96	0



Scheme 22: Reactions of acetals bearing strong electron-donating groups

After completing the optimization of reaction conditions, we were ready to explore a variety of substrates to see what was tolerated by this new methodology. The experiments will be conducted using 1.0 equiv of acetal, 1.1 equiv. of trifluoroborate and 1.1 equiv. of $\text{HBF}_4 \cdot \text{OEt}_2$ unless otherwise stated (Scheme 23). The desired -10°C reaction temperature was achieved using a salt ice bath.

2.4 Scope of Brønsted acid-catalyzed alkylation of acetals



Scheme 23: Optimized conditions for reactions of alkynyltrifluoroborates and acetals.

2.4.1 Reaction of various acetals with phenylacetylene trifluoroborate (**S1**)

We further explored the acetal substrate scope with phenylacetylenetrifluoroborate salt **S1** using the optimized reaction conditions (Figure 8). Bromo and chloro substituted acetals **A4** and **A5** gave products 1-bromo-4-(1-methoxy-3-phenylprop-2-yn-1-yl)benzene (**1d**) and 1-chloro-4-(1-methoxy-3-phenylprop-2-yn-1-yl)benzene (**1e**) in high yields of 89 % and 80 % respectively. These halogenated products can be further functionalized *via* transition metal catalysis. 1,3-dichloro-2-(1-methoxy-3-phenylprop-2-yn-1-yl)benzene (**1f**) yielded 64 % of the expected product and showed that sterically hindered 1,3-dichloro-2-(dimethoxymethyl)benzene (**A6**) still reacts well. Electron-withdrawing halogen functional groups are well tolerated using this methodology.

Additional alkyl and alkenyl acetals were reacted. (3-cyclopentyl-3-methoxyprop-1-yn-1-yl)benzene (**1g**) derived from cyclopentyl carboxaldehyde dimethyl acetal **A7** was obtained in a 96 % yield, which showed a similar reactivity to (2,2-

dimethoxyethyl)benzene (**A1**). Alkenyl acetal **A8** yielded (E)-(3-methoxyoct-4-en-1-yn-1-yl)benzene (**1h**) in a modest 49 %. The lower yield of **1h** could be a result of a potential conjugate addition to the alkene, resulting in an undesired by-product.

Electron-withdrawing nitro and nitrile groups present on acetals **A9** and **A10** resulted in higher yields compared to (2,2-dimethoxymethyl)benzene (**A2**). (1-methoxy-3-phenylprop-2-yn-1-yl)-4-nitrobenzene (**1i**) containing a nitro group, was obtained in a quantitative yield. Nitrile containing acetals afforded 4-(1-methoxy-3-phenylprop-2-yn-1-yl)benzotrile (**1j**) in an excellent 94 % yield. Notably the nitrile group did not act as a competing electrophilic site. 4-(dimethoxymethyl)benzoic acid (**A11**) is an acetal bearing a free carboxylic acid. 4-(1-methoxy-3-phenylprop-2-yn-1-yl)benzoic acid (**1k**) was obtained in a modest 39 % yield under the optimized conditions (Table 4, entry1). Albeit modest, this was encouraging because free acids usually require protection before reacting. After a minor optimization, 4-(1-methoxy-3-phenylprop-2-yn-1-yl)benzoic acid (**1k**) was obtained in a 73 % yield with an increase loading of **S1** and $\text{HBF}_4 \cdot \text{OEt}_2$ to 2.0 and 1.5 equiv. respectively. Though an increase of reagents is necessary for **1k**, the success of a free carboxylic acid is unprecedented.

In general this methodology tolerated a wide range of substituents, however, some substrates were not tolerated. Furfural dimethyl acetal **A18** did not afford **1l** under the optimized conditions and cinnamyl aldehyde dimethyl acetal **A19** did not form **1m**. Both reactions of **A18** and **A19** resulted in the generation of an unidentified mixture of by-products. 1-dimethoxymethyl-3,4-methoxybenzene **A17** did not form **1n**, which was expected due to the presence of two electron-donating methoxy groups. Product **1o** was not formed from 3-bromo-5-(dimethoxymethyl)pyridine **A20** using the optimized conditions, nor when 2 equiv. of $\text{HBF}_4 \cdot \text{OEt}_2$ was used. 2 equiv. of $\text{HBF}_4 \cdot \text{OEt}_2$ was to ensure acid was still present in solution upon protonation of pyridine.

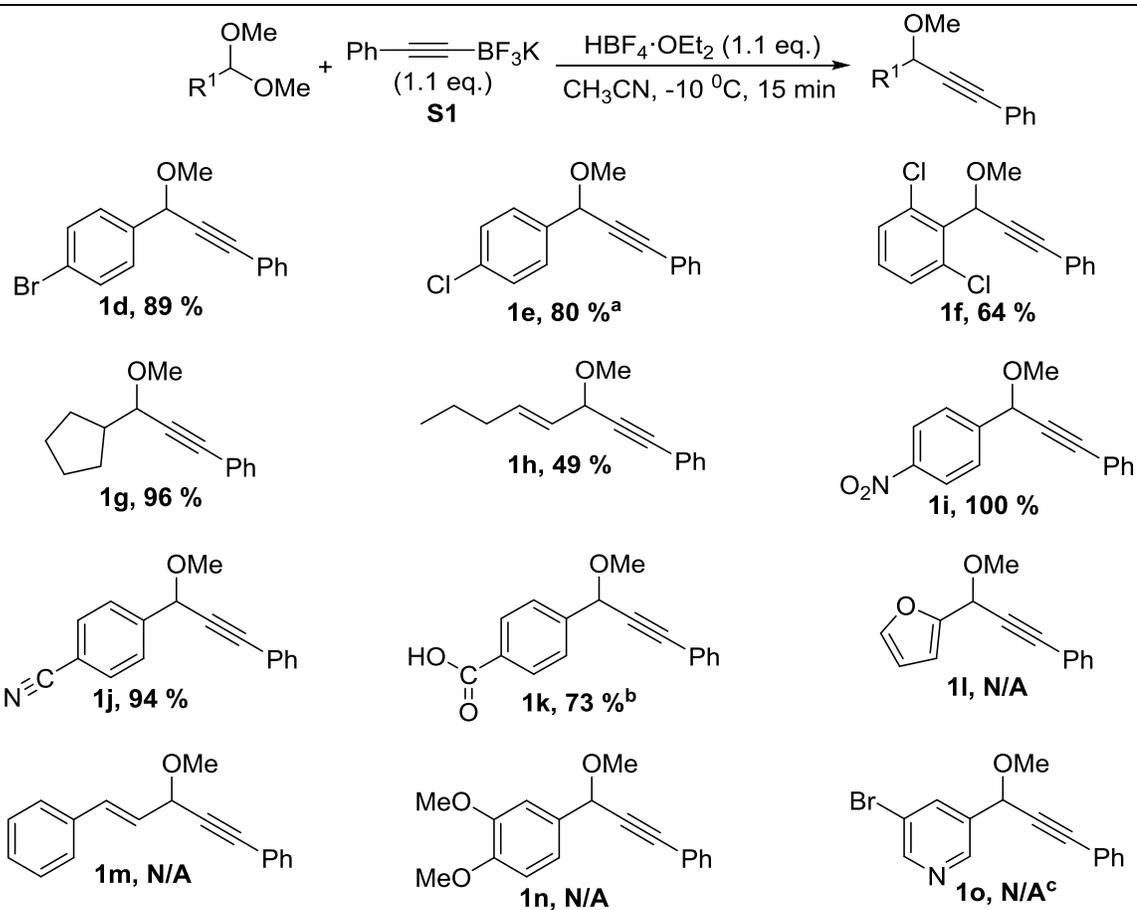
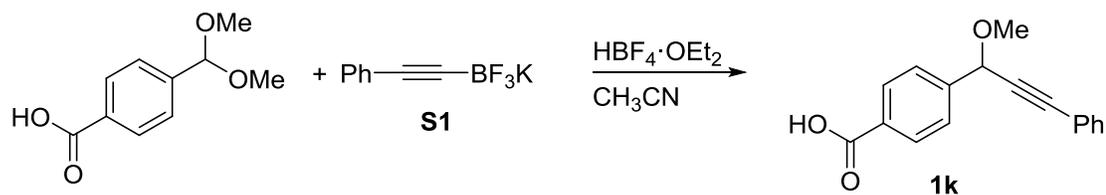


Figure 8. Acetal scope following procedure 3.

^aReaction run for 70 minutes. ^bReaction with 2.0 equiv **S1**, 1.5 equiv HBF₄·OEt₂ and reacted for 80 mins. ^cUsed 2.0 equiv of HBF₄·OEt₂. Isolated yields after chromatography.

Table 4: Optimization of conditions for acetals bearing a free carboxylic acid.

entry	Temp ($^{\circ}\text{C}$)	Time (min)	Acid: S1 (equiv.)	Yield (%)
1	-10	15	1.1:1.1	39 %
2	-10	60	1.5:1.5	26 %
3	-10	80	1.5:2.0	73 %
4	-10	80	2.0:1.5	49 %
5	RT	80	1.5:2.0	62 %
6	-10	80	1.1:2.0	35 %

2.4.2 Reactions of various acetals with alkynyltrifluoroborates

Neutral, electron-rich and electron-poor alkynyltrifluoroborates were then reacted with a variety of different acetals (Figure 9). 4-(3-([1,1'-biphenyl]-4-yl)-1-methoxyprop-2-yn-1-yl)benzotrile (**3a**), derived from (4-dimethoxymethyl)benzotrile (**A10**) and biphenylacetylenetrifluoroborate (**S2**), was obtained in a 75 % yield. This was lower than the yield of 94% obtained for 4-(1-methoxy-3-phenylprop-2-yn-1-yl)benzotrile (**1j**), which was derived from **A10** and phenylacetylenetrifluoroborate (**S1**). Biphenylacetylenetrifluoroborate (**S2**) yielded less than phenylacetylenetrifluoroborate (**S1**) due to the electron donating phenyl ring present on the biphenylacetylenetrifluoroborate (**S2**). This electron donating group could promote protodeborynation, which is a potential explanation for the decrease in yield. (4-dimethoxymethyl)nitrobenzene (**A9**) and naphthylethynyltrifluoroborate (**S3**) yielded 80 % for 1-(3-methoxy-3-(4-nitrophenyl)prop-1-yn-1-yl)naphthalene (**4a**). This was also lower than the quantitative yield of (1-methoxy-3-phenylprop-2-yn-1-yl)-4-nitrobenzene (**1i**) derived from **A9** and phenylacetylenetrifluoroborate (**S1**), which could also be attributed to protodeborynation. 1-(4-(1-methoxy-3-(naphthalen-1-yl)prop-2-yn-1-yl)phenyl)ethan-1-one (**4b**) was obtained in a 79 % from 1-(4-(dimethoxymethyl)phenyl)ethan-1-one (**A12**) and naphthylethynyltrifluoroborate (**S3**),

which has a free ketone present. A comparable reactivity is observed between **A9** and **S3**, which yield 80% for **4a**. Though decreases in yield were observed, all of these neutral trifluoroborate salts still reacted efficiently with different acetals.

1-butyl-4-(3-(4-chlorophenyl)-3-methoxyprop-1-yn-1-yl)benzene (**5a**) was obtained in an excellent yield of 86 % from (4-dimethoxymethyl)chlorobenzene **A5** and 4-butylphenylacetylenetrifluoroborate **S4**. This yield was 6% higher than the yield of product **1e**, derived from **A5** and phenylacetylenetrifluoroborate (**S1**); revealing that electron-rich trifluoroborates are more reactive towards acetals. Temperature of -40⁰C was also required for this reaction due to the increased reactivity.

Electron-deficient trifluoroborates were used in the latter examples. (4-dimethoxymethyl)bromobenzene **A4** and 2-trifluoromethylphenylacetylenetrifluoroborate **S5** yielded 71 % of 1-(3-(4-bromophenyl)-3-methoxyprop-1-yn-1-yl)-2-(trifluoromethyl)benzene (**6a**), which was a significant decrease compared to the reaction of **A4** and phenylacetylenetrifluoroborate (**S1**) to form 1-bromo-4-(1-methoxy-3-phenylprop-2-yn-1-yl)benzene (**1d**). This decrease showed that electron-deficient trifluoroborates are less reactive than neutral trifluoroborates. A similar trend was observed for 1-(3-cyclopentyl-3-methoxyprop-1-yn-1-yl)-3-fluorobenzene (**7a**), which yielded 81 % from cyclopentane carboxaldehyde dimethyl acetal (**A7**) and 3-fluorophenylacetylenetrifluoroborate (**S6**), a decrease of 15 % compared to the yield of product **1g**, which used cyclopentane carboxaldehyde dimethyl acetal **A7** and phenylacetylenetrifluoroborate **S1**. 4-(3-(3-chlorophenyl)-1-methoxyprop-2-yn-1-yl)benzotrile (**8c**) was synthesized in an excellent 86 % yield from (4-dimethoxymethyl)benzotrile (**A10**) and 3-chlorophenylacetylenetrifluoroborate (**S7**). The yield of **8c** was slightly lower when compared to the yield of 94 % for product **1j**, derived from (4-dimethoxymethyl)benzotrile **A10** and phenylacetylenetrifluoroborate **S1**, which followed the trend of decreasing reactivity for electron-deficient trifluoroborates.

Products **4b**, **8a** and **8b** all bear carbonyl functional groups, with the highest yield of 88 % observed for Methyl 4-(3-(3-chlorophenyl)-1-methoxyprop-2-yn-1-yl)benzoate (**8b**), prepared from 4-(dimethoxymethyl)methyl benzoate (**A14**) and 3-

chlorophenylacetylenetrifluoroborate (**S7**). 4-(3-(3-chlorophenyl)-1-ethoxyprop-2-yn-1-yl)Benzaldehyde (**8a**) was afforded in a 62 % yield from 4-(diethoxymethyl)benzaldehyde **A13** and 3-chlorophenylacetylenetrifluoroborate **S7** in the presence of an unprotected aldehyde. Ketones were also compatible as seen with 1-(4-(1-methoxy-3-(naphthalen-1-yl)prop-2-yn-1-yl)phenyl)ethan-1-one (**4b**) derived from 1-(4-(dimethoxymethyl)phenyl)ethan-1-one **A12** and naphthylethynyltrifluoroborate **S3**. Ester-bearing acetals appeared to be more reactive than acetals bearing aldehydes. All of these functional groups are rarely tolerated by known methods due to their electrophilicity. This tolerance eliminates the need for further protection/deprotection that usually accompanies chemical transformations in the presence of these functionalities.

Some trifluoroborate salts were not effective coupling partners for this methodology. (4-dimethoxymethyl)bromobenzene **A4** yield **1d** in an 89 % yield. However, when using *para*-methoxyphenylacetylenetrifluoroborate **S10**, a 20% yield was obtained for 1-bromo-4-(1-methoxy-3-(4-methoxyphenyl)prop-2-yn-1-yl)benzene (**9a**). Though a decrease yield of 1-(3-(4-bromophenyl)-3-methoxyprop-1-yn-1-yl)-2-(trifluoromethyl)benzene (**6a**) to 71 % was observed when using **A4** and 2-trifluoromethylphenylacetylenetrifluoroborate (**S5**), it was not nearly as drastic as using trifluoroborates with strong electron-donating groups present. (4-dimethoxymethyl)nitrobenzene **A9** afforded **1i** in quantitative yields, but when using 3,5-ditrifluoromethylphenylacetylenetrifluoroborate (**S9**), a 29% yield of product 1-(3-methoxy-3-(4-nitrophenyl)prop-1-yn-1-yl)-3,5-bis(trifluoromethyl)benzene (**10a**) was obtained. The presence of two strong electron-withdrawing groups on the trifluoroborate greatly diminished product yields. Product **11a** was not obtained from 3-fluorophenylacetylenetrifluoroborate **S6** and acetal **A21**, bearing a primary alcohol. We suspect it could be due to the presence of a primary alcohol, which is also a nucleophile.

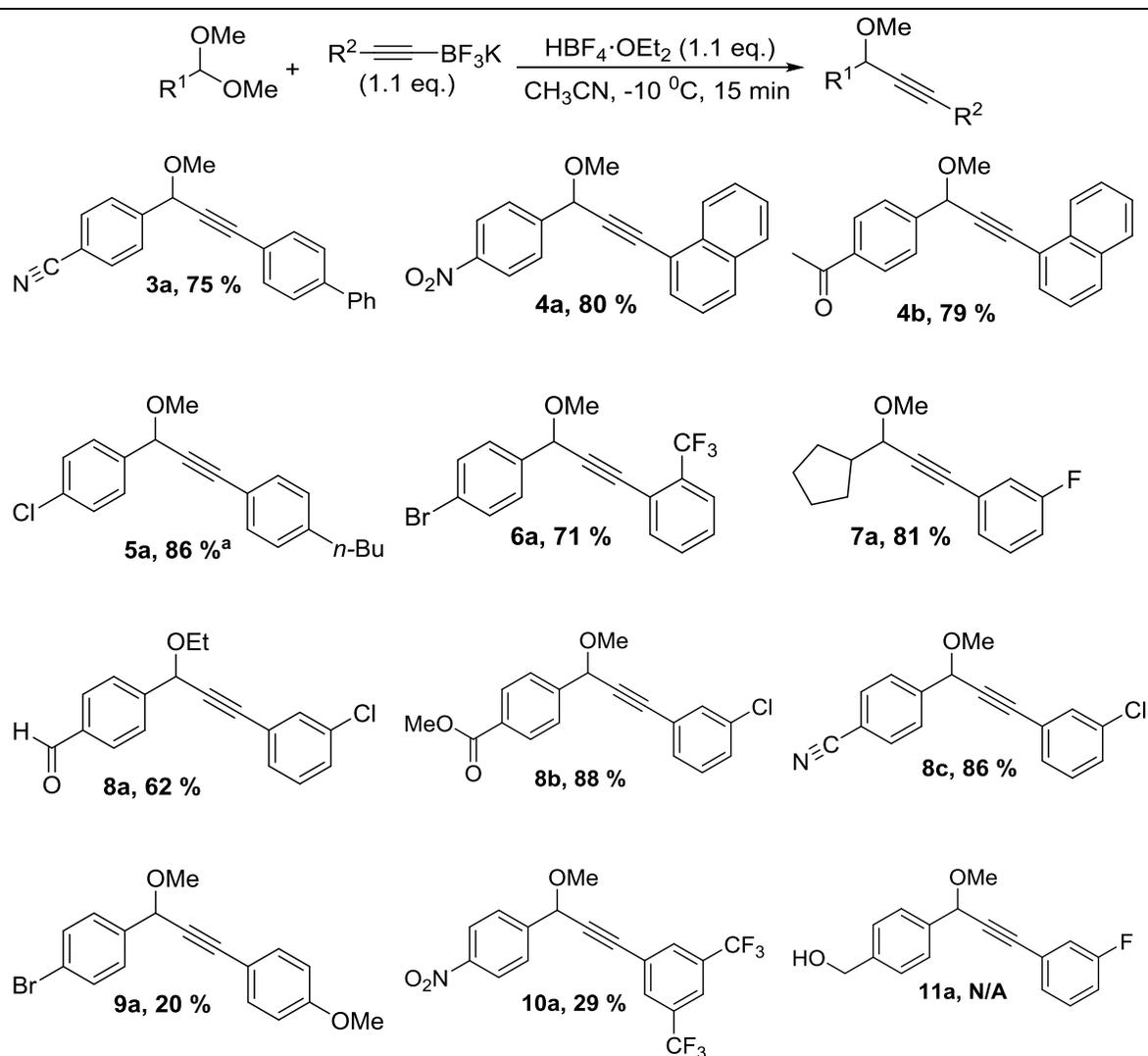
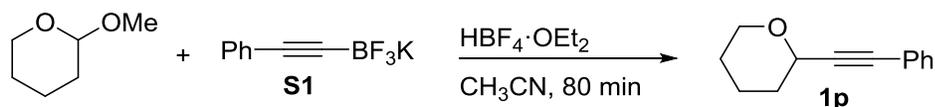


Figure 9. Scope of alkynyltrifluoroborate salts for procedure 3

2.4.3 Application to 2-methoxytetrahydropyran

We then applied our methodology to a cyclic acetal 2-methoxytetrahydropyran, which yielded 30 % for 2-phenylacetylenetetrahydropyran (**1p**) leading to a minor optimization (Table 5). Increasing the equivalents of both acid and **S1** to 1.5 equiv. resulted in an excellent 89 % yield (entry 2). A room temperature reaction with these equivalents resulted in a decrease of **1p**, to 73 %.

Table 5: Optimization of cyclic acetal substrates.

Entry	Acid : S1 (equiv.)	Temp ($^{\circ}\text{C}$)	Yield (%)
1	1.1:1.1	-10	30 %
2	1.5:1.5	-10	89 %
3	1.5:1.5	RT	73 %

2.4.4 Reaction of acetals with alkenyltrifluoroborates

When applying this methodology to alkenyltrifluoroborates, the over-reactivity observed for (2-methyl)dimethoxymethylbenzene **A3** and (4-dimethoxymethyl)anisole **A16** was seen again (Figure 10). (4-dimethoxymethyl)bromobenzene **A4** was overalkenylated using *trans*-styryltrifluoroborate, forming product **12a** in a 32 % yield. Alkenyltrifluoroborates are generally less reactive than alkynyltrifluoroborates, but the formation of an allylic/benzylic carbocation after the addition of the first styryl group is very favourable. This promoted the addition of a second equivalent of nucleophile and resulted in solely dialkenylated products. Attempting to control this dialkenylation using the optimized conditions from Table 3 and (4-dimethoxymethyl)nitrobenzene **A9** was unsuccessful. Product **13a** was still obtained, showing sole dialkenylation, even at these low temperatures. A conversion of 35% was determined based on the recovery of starting material.

We then applied the optimized conditions for 2-methoxytetrahydropyran to react with *trans*-styryltrifluoroborate. To our delight we found that (E)-2-styryltetrahydro-2H-pyran (**1q**) was formed in a 51% yield (Scheme 24). Though only modest yielding, it was excellent to see our method working for an alkenyltrifluoroborate example.

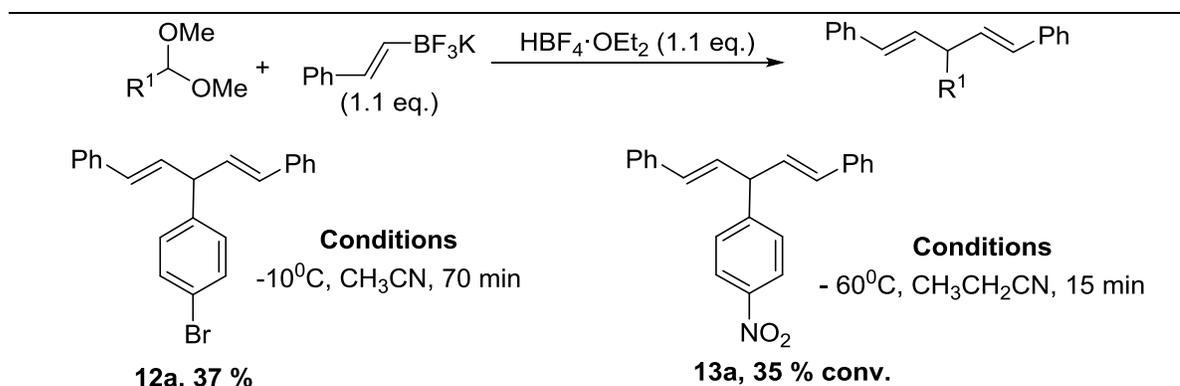
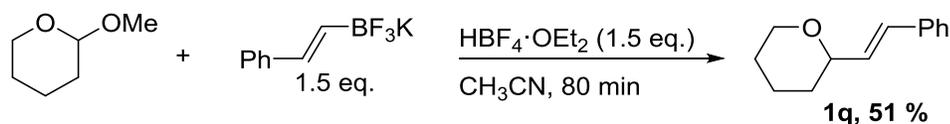


Figure 10: reactions of alkenyltrifluoroborates and acetals



Scheme 24: Reaction of 2-methoxytetrahydropyran with styryltrifluoroborate.

2.4.5 Conclusion of reactions between acetal and trifluoroborate

This methodology has a superior functional group tolerance compared to traditional alkynylmetal reagents or Lewis acid catalysis. Halogen functional groups on both acetals and trifluoroborates promoted the formation of the desired products and resulted in high yields. Electron-withdrawing nitro and nitrile acetals reacted in excellent yields.

Various carbon oxidation states were tolerated, including aldehydes, ketones, esters and free carboxylic acids. Aldehydes and ketones are both competing electrophiles that may react to form undesired byproducts in alternative methods. Higher yields were observed for more oxidized carbonyl-functional groups, when comparing of the results for products **4b**, **8a** and **8b**. To our knowledge, this is also the first report of a free carboxylic acid being tolerated by a procedure for the alkenylation of acetals. This eliminates the need for protection/deprotection steps that are usually mandatory for these functional groups.

The current nucleophile scope of this methodology is mainly limited to alkenyltrifluoroborates, with one alkenyltrifluoroborate example. This is due to the reactivity of the products after the first step. Alkenyltrifluoroborates gave over-alkenylated products even when using electron withdrawn acetals. Though this is not the

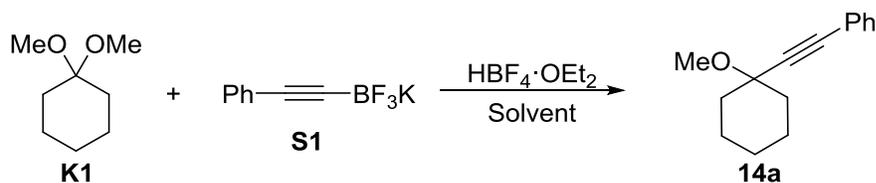
desired product, these 3⁰-carbon centers could have other potential applications as well. 2-methoxytetrahydropyran did afford (E)-2-styryltetrahydro-2H-pyran (**1q**) when reacted with *trans*-styryltrifluoroborate.

2.5 Alkynylation of ketals using alkynyltrifluoroborates

With the great success of these reactions, specifically with 2-phenylacetylenetetrahydropyran **1p**, we wanted to expand the scope of this methodology even further to include ketals. To the best of our knowledge, there has yet to be a method that allows for the alkynylation of ketals in literature. This would allow for the synthesis of 3⁰- propargylic ethers and greatly expand the utility of this methodology.

2.5.1 Optimization of conditions for the alkynylation of ketals

We first applied the conditions optimized for acetals to 1,1-dimethoxycyclohexane (**K1**). This resulted in a modest 30 % yield of the desired product ((1-methoxycyclohexyl)ethynyl)benzene (**14a**) (Table 6, entry1). Increasing the equivalents of HBF₄·OEt₂ and **S1** to 1.5 equiv. respectively resulted in an increase in yield to 48 % (entry 2). Further increase to 2.0 equiv of HBF₄·OEt₂ and **S1** saw a drop in yield to 33 % (entry 3). Therefore, further reactions were done using 1.5 equiv. of HBF₄·OEt₂ and **S1**. Entry 4 showed that decreasing the reaction time to 15 minutes resulted in an increase in yield to 50 %. Changing the solvent to propionitrile showed a marginal increase in yield to 52 % (entry 5). Decreasing the reaction temperature to -40⁰C showed a slight increase in yield of **14a** to 53 % (entry 6). As a result, further reactions were run for 15 min at -40⁰C in propionitrile.

Table 6: Optimization of conditions for alkylation of ketals.

entry	Temp (⁰ C)	Solvent	HBF ₄ ·OEt ₂ : S1 (equiv.)	Time (min)	Yield 14a (%)
1	-10	CH ₃ CN	1.1 : 1.1	70	30
2	-10	CH ₃ CN	1.5 : 1.5	70	48
3	-10	CH ₃ CN	2.0 : 2.0	70	33
4	-10	CH ₃ CN	1.5 : 1.5	15	50
5	-10	CH ₃ CH ₂ CN	1.5 : 1.5	15	52
6	-40	CH ₃ CH ₂ CN	1.5 : 1.5	15	53

2.5.2 Reactions of various alkynyltrifluoroborates with ketals

Different trifluoroborate salts were screened with ketals (Figure 11). 1-chloro-3-((1-methoxycyclohexyl)ethynyl)benzene (**14b**) formed in a 51 % yield from 1,1-dimethoxycyclohexane (**K1**) and 3-chlorophenylacetylenetrifluoroborate (**S7**). This yield is comparable to the 53 % yield of ((1-methoxycyclohexyl)ethynyl)benzene (**14a**), using **K1** and phenylacetylenetrifluoroborate (**S1**). The reaction of 4-*t*-butyl-1,1-dimethoxycyclohexane (**K2**) and **S1** showed a slight increase in yield of ((4-(*tert*-butyl)-1-methoxycyclohexyl)ethynyl)benzene (**15a**) to 59 % compared to product **14a**. Using bulky naphthylacetylenetrifluoroborate **S3** with **K2** resulted in a lower 47 % yield of 1-((4-(*tert*-butyl)-1-methoxycyclohexyl)ethynyl)naphthalene (**15b**). 3-fluorophenylacetylenetrifluoroborate (**S6**) afforded 1-((4-(*tert*-butyl)-1-methoxycyclohexyl)ethynyl)-3-fluorobenzene (**15c**) from **K2** in a 62 % yield, which was comparable to the yield of **15a**. No product formation was observed for the reactions between **K3** and **S1** or between **K4** and **S1** as seen in entries **16a** and **17a** respectively. 2'-bromoacetophenone dimethyl ketal **K4** is a sterically ketal, which could have prevented the reaction with the nucleophile.

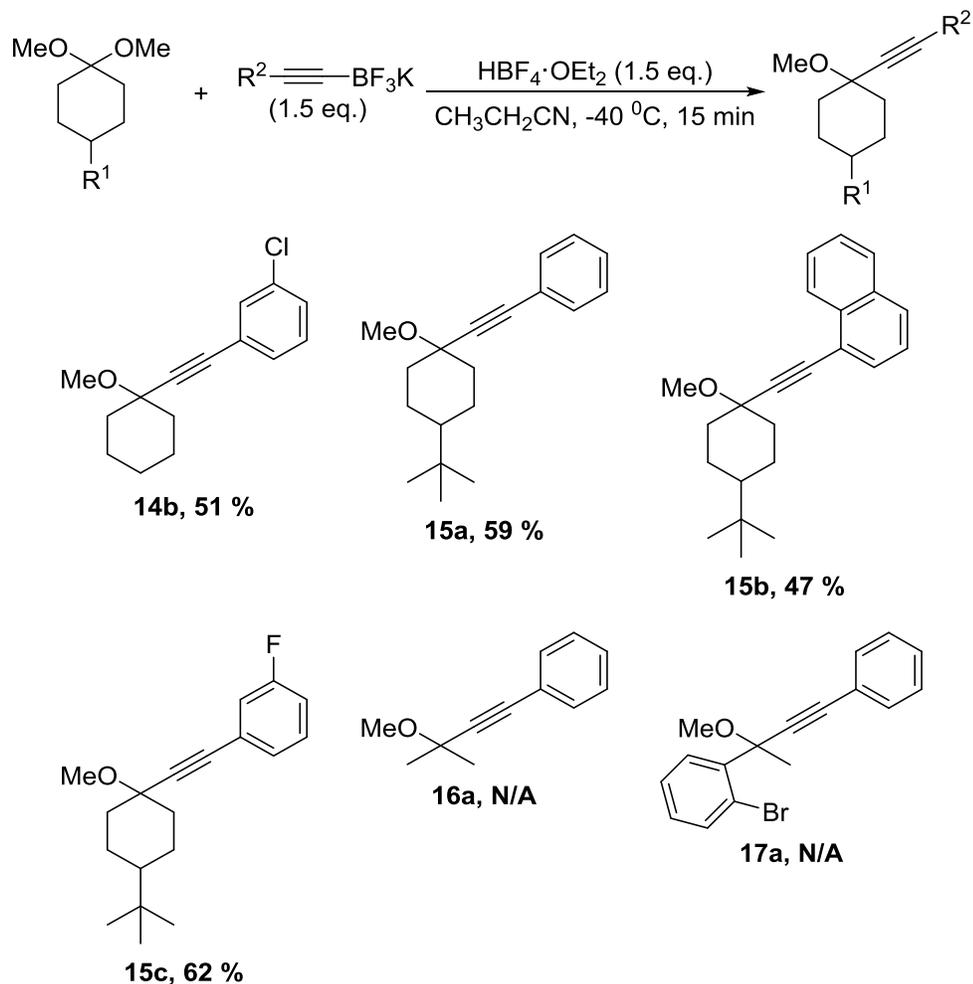


Figure 11. Reactions of various trifluoroborates with ketals.

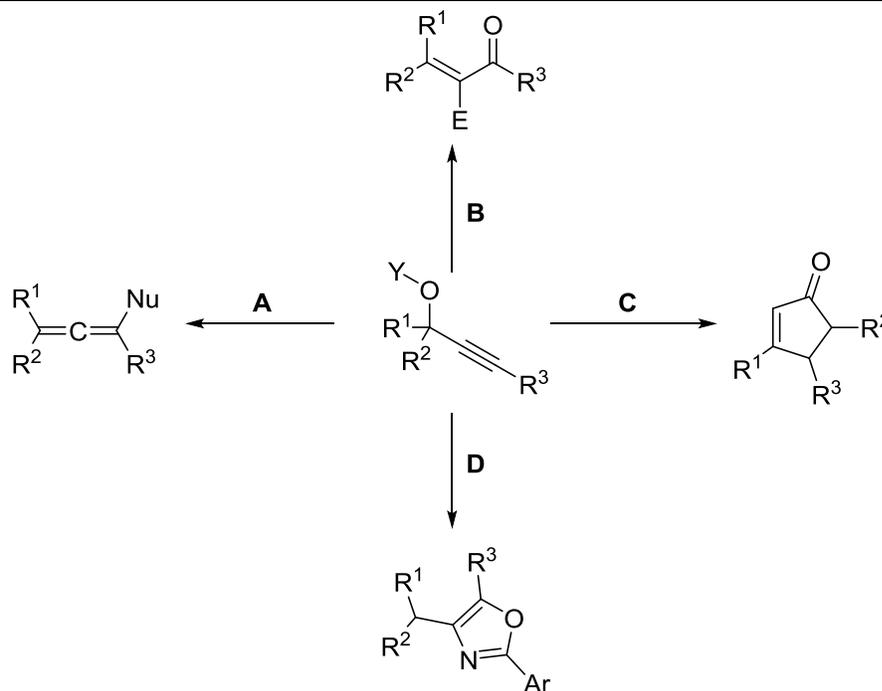
2.5.3 Conclusions on alkylation of ketals

The reactions of ketals with alkynyltrifluoroborates require more catalyst and trifluoroborate to achieve synthetically useful yields. Though yields are modest, to our knowledge this is the first report of a ketal alkylation of any kind. These tertiary propargylic ethers products can be further transformed into allenes, which are very useful synthetic building blocks.³⁶

2.6 Applications of products

Propargylic ethers can be transformed into a variety of different compounds (Scheme 25). The transformation of propargylic ethers into allenes is known, and proceeds through a β -alkoxide elimination (Step A, Scheme 25).³⁶ Transformation **B** shows the formation of β -unsaturated ketones, which proceeds through a Meyer-Schuster

rearrangement. Other applications include cyclizations, and reactions with external nucleophiles.

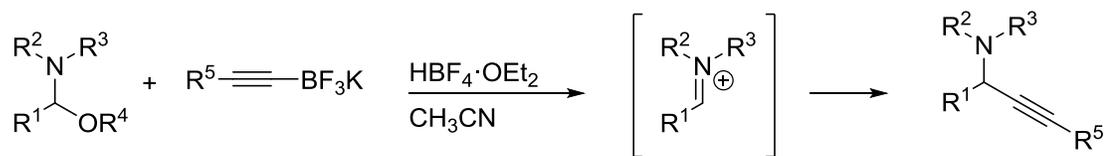


Scheme 25: Applications of propargylic ethers

2.7 Future work

2.7.1 Reaction of trifluoroborates with N,O-acetals for the synthesis of amines

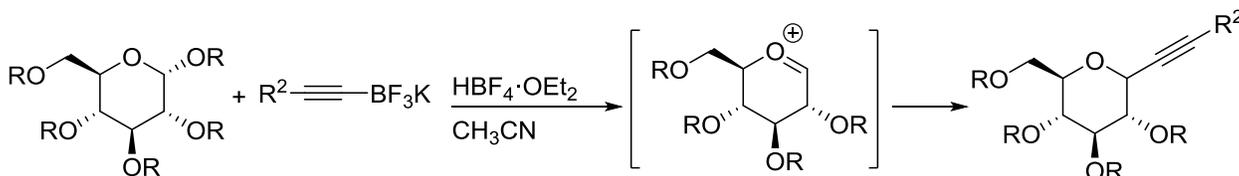
A Brønsted acid reaction of N,O-acetals and trifluoroborates is a potential method for the synthesis of functionalized alkynylamines. N,O-acetals are prepared from aldehydes³⁷ and application of our Brønsted acid catalyzed methodology will proceed through an iminium ion intermediate (Scheme 26).



Scheme 26: Synthesis of propargylic amines from N,O-acetals

2.7.2 Reactions of trifluoroborates with glycosides

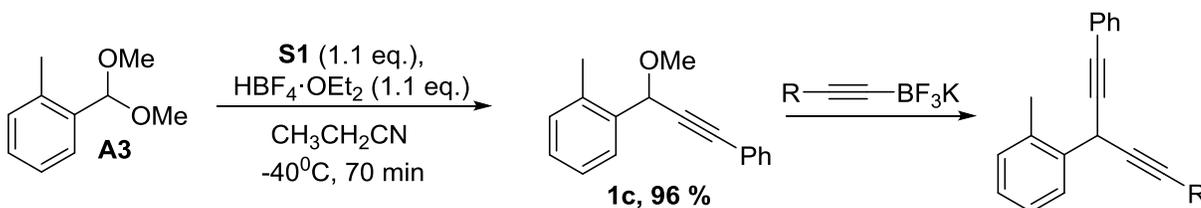
This methodology could be applied to the synthesis of C-glycosides (Scheme 26). Sugar acetylenes are useful building blocks for the synthesis of natural products.³³ With the success of 2-phenylacetylenetetrahydropyran **1p**, our method should transition smoothly to the synthesis of sugar acetylenes.



Scheme 27: Synthesis of sugar acetylenes

2.7.3 Single-pot dialkynylation

The formation of by-product **2a** also gives an opportunity to explore the dialkynylation of acetals using two different trifluoroborate salts. Optimized conditions for (2-methyl)dimethoxymethylbenzene **A3** can afford product **1c** in high yields, which can be subsequently reacted with another equivalent of trifluoroborate (scheme 27). This can be potentially done with ease in one pot synthesis; with addition of trifluoroborate and warming of the reaction mixture.



Scheme 28: Single-pot controlled dialkynylation to form tertiary-carbon centers

2.8 General Conclusions

We have successfully developed a Brønsted acid catalyzed methodology for the synthesis of secondary and tertiary propargylic ethers using acetals/ ketals and trifluoroborates. This method tolerates various functional groups including halogens, nitro, nitrile,

aldehyde, ketone, ester and carboxylic acid bearing acetals (Figure 8, Figure 9). This substrate scope is far superior than current methods using Lewis acid catalysts. To our knowledge, this is the first Brønsted acid catalyzed methodology using alkynyltrifluoroborate salts as well as the first account of alkylation of ketals.

Acetals react rapidly and atom economically to synthesized functionalized propargylic ethers, using very mild reaction conditions. A dialkynylated by-product was observed when electron-rich acetals were employed. This by-product can be suppressed in some instances using lower temperatures, as well using propionitrile as a solvent (Table 3).

Ketals react less efficiently than acetals. The reaction with ketals needed an excess of 1.5 equiv. of both $\text{HBF}_4 \cdot \text{OEt}_2$ and trifluoroborate respectively (Figure 11). Though yields are modest, the only method to synthesized tertiary propargylic ethers involves alkynyl lithium and aldehyde reagents.³⁶ The developed methodology will facilitate access of tertiary propargylic ethers.

Propargylic ethers are useful synthetic intermediates. They can be converted into allenes, enones and other compounds (Scheme 25). This work may be applied to the synthesis of sugar alkynes and C-glycoside derivatives (Scheme 27). Finally, the synthesis of amines from N,O-acetals is also another attractive future direction (Scheme 26).

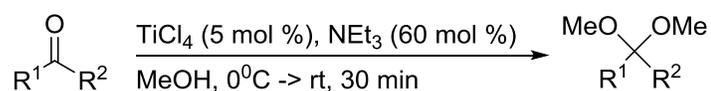
Chapter 3: Experimental Procedures

3.1 General Information

All reactions were carried out in oven dried 5 mL vials under $\text{Ar}_{(\text{g})}$ unless otherwise noted. THF and triethylamine were obtained from a solvent purification system. Anhydrous acetonitrile and methanol were purchased from Sigma-Aldrich and were used without further manipulation. Other commercially available reagents were used as received. Deuterated solvents CDCl_3 and d_6 -DMSO were purchased from Cambridge Isotope Laboratories, Inc. and used for NMR characterization. NMR spectra were collected at 25°C on an Oxford AS400 NMR. ^1H -NMR and ^{19}F -NMR spectra were collected at 400 MHz and 376 MHz respectively while ^{13}C -NMR and ^{11}B -NMR were collected at 100

MHz and 128 MHz respectively. All chemical shifts are expressed in ppm values. ^{11}B -NMR, ^{13}C -NMR and ^{19}F -NMR are all $\{^1\text{H}\}$ -decoupled. High resolution mass spectra (HRMS) were obtained by the University of Michigan, Department of Chemistry using atmospheric-pressure chemical ionization (APCI) and Waters VG 70-250-S magnetic sector mass spectrometer was used for samples analyzed by electron impact ionization (EI). An Agilent Q-TOF mass spectrometer was used for ESI analysis. FT-IR spectra were recorded on a Nicolet Avatar 370 DTGS spectrometer and partial data is provided. Automated flash chromatography was done using the Biotage IsoleraTM or Grace Reveleris[®] X2 flash chromatography systems. Manual Flash chromatography was done using silica gel (60 Å, low acidity silica, from EMD Chemicals Inc.) was performed using reagent grade solvents.

3.2 Acetal and ketal synthesis

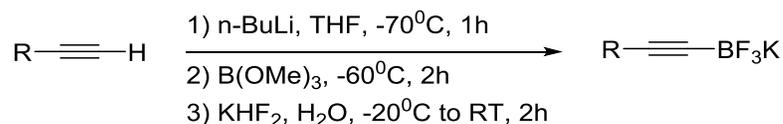


Scheme 29: Synthesis of acetals and ketals.

3.2.1 General procedure for acetal and ketal synthesis (Procedure 1)

A solution of aldehyde or ketone (5.0 mmol, 1 equiv.) in 10.0 mL of anhydrous methanol in a 20 mL vial was cooled to 0°C under $\text{Ar}_{(\text{g})}$. TiCl_4 (1.0 M in CH_2Cl_2 , 250 μL , 5.0 mol %) was slowly added to the solution at 0°C . The solution was allowed to warm to room temperature and stirred for 15 mins. Triethylamine (415 μL , 60.0 mol %) was then added to solution and stirring was continued for 15 mins. The bulk reaction was suspended into diether ether (75 mL) and was washed with water (5 x 15 mL), dried over MgSO_4 and evaporated under reduced pressure. No further purification was undertaken. Characterization data of acetals and ketals are included in the Appendix.

3.3 Synthesis of alkynyltrifluoroborates

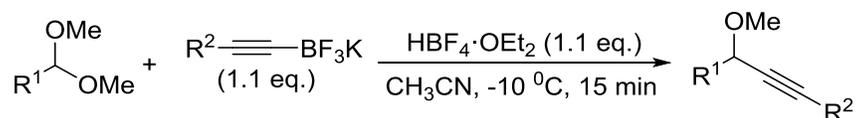


Scheme 30: Synthesis of potassium alkynyltrifluoroborate salts.

3.3.1 General procedure for the synthesis of alkynyltrifluoroborates (Procedure 2)

A solution of terminal alkyne (1.0 equiv.) in dry THF was cooled to -70°C under $\text{Ar}_{(\text{g})}$ atmosphere. *n*-BuLi (1.0 equiv.) was added dropwise to the solution. The reaction was stirred for 1 h at -70°C . Trimethylborate (1.5 equiv.) was added dropwise at -60°C then stirred at this temperature for 2 h. The solution was warmed to -20°C and then a saturated $\text{KHF}_2(\text{aq.})$ solution (6 equiv.) was added. The solution was allowed to warm-up to room temperature with vigorous stirring over 2 h. The solvent was removed under reduced pressure at 50°C , and the resulting solid was placed under vacuum for 12 h to remove residual water. The solid was washed with hot acetone (4 x 10 mL), which was collected and concentrated to a volume of ~5 mL. The product was precipitated with diethyl ether (30 mL) and collected via vacuum filtration. The crystalline trifluoroborate salt was washed with ether (10 mL) then dried under vacuum.

3.4 General Procedure for the reaction of acetals and alkynyltrifluoroborates

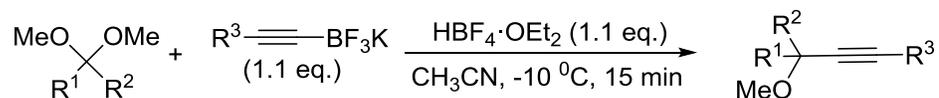


Scheme 31: Alkynylation of acetals using alkynyltrifluoroborates

3.4.1 alkynylation of acetals with trifluoroborates (procedure 3)

All reactions were carried out in an oven dried 5 mL vial purged with $\text{Ar}_{(\text{g})}$ with a micro stir bar (3 x 10mm). First, the indicated potassium trifluoroborate salt (1.1 equiv.) was added to the vial followed by acetonitrile (1.0 mL). The acetal (1.0 equiv.) was then added to the solution, and the solution was stirred at -10°C for two minutes. $\text{HBF}_4\cdot\text{OEt}_2$ (1.1 equiv.) was added to the stirring solution at -10°C , and the solution was stirred for 15 minutes at -10°C . The reaction mixture was quenched with ethyl acetate. The crude product was extracted using 25 mL of ethyl acetate. The organic layer was washed with water (2 x 10 mL) and brine (1 x 10 mL). The organic layer was dried over MgSO_4 , concentrated under vacuum. The product was purified by flash column chromatography using a hexane/diethyl ether mobile phase.

3.5 General Procedure for the reaction of ketals and alkynyltrifluoroborates



Scheme 32: Alkynylation of ketals using alkynyltrifluoroborates

3.5.1 alkynylation of ketals with trifluoroborates (procedure 4)

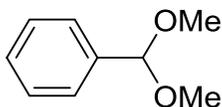
All reactions were carried out in an oven dried 5 mL vial purged with Ar_(g) with a micro stir bar (3 x 10mm). First, the indicated potassium trifluoroborate salt (1.5 equiv.) was added to the vial followed by acetonitrile (1.0 mL). The acetal (1.0 equiv.) was then added to the solution, and the solution was stirred at -10⁰C for two minutes. HBF₄·OEt₂ (1.5 equiv.) was added to the stirring solution at -10⁰C, and the solution was stirred for 15 minutes at -10⁰C. The reaction mixture was quenched with ethyl acetate. The crude product was extracted using 25 mL of ethyl acetate. The organic layer was washed with water (2 x 10 mL) and brine (1 x 10 mL). The organic layer was dried over MgSO₄, concentrated under vacuum. The product was purified by flash column chromatography using a hexane/diethyl ether mobile phase.

References

- (1) Akiyama, T. *Chem. Rev.* **2007**, *107*, 5744.
- (2) Akiyama, T.; Takaya, J.; Kagoshima, H. *Synlett* **1999**, *344*, 1045.
- (3) Akiyama, T.; Itoh, J.; Yokota, K.; Fuchibe, K. *Angew. Chem. Int. Edit.* **2004**, *43*, 1566.
- (4) Takaya, J.; Kagoshima, H.; Akiyama, T. *Org. Lett.* **2000**, *2*, 1577.
- (5) Yanagisawa, A.; Inoue, H.; Morodome, M.; Yamamoto, H. *J. Am. Chem. Soc.* **1993**, *115*, 10356.
- (6) Loh, T.-P.; Xu, J. *Tetrahedron Lett.* **1999**, *40*, 2431.
- (7) Kampen, D.; List, B. *Synlett* **2006**, 2589.
- (8) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207.
- (9) Yu, S. H.; Ferguson, M. J.; McDonald, R.; Hall, D. G. *J. Am. Chem. Soc.* **2005**, *127*, 12808.
- (10) Cossy, J.; Lutz, F.; Alauze, V.; Meyer, C. *Synlett* **2002**, 45.
- (11) Boxer, M. B.; Yamamoto, H. *J. Am. Chem. Soc.* **2006**, *128*, 48.
- (12) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063.
- (13) Wabnitz, T. C.; Spencer, J. B. *Org. Lett.* **2003**, *5*, 2141.
- (14) Linderman, R. J.; Chen, S. *Tetrahedron Lett.* **1996**, *37*, 3819.
- (15) Granja, J. R.; Castedo, L.; Mourino, A. *J. Org. Chem.* **1993**, *58*, 124.
- (16) Yoshimatsu, M.; Gotoh, S.; Ikeda, K.; Komori, M. *J. Org. Chem.* **1998**, *63*, 6619.
- (17) Feuvrie, C.; Blanchet, J.; Bonin, M.; Micouin, L. *Org. Lett.* **2004**, *6*, 2333.
- (18) Korbad, B. L.; Lee, S. H. *Eur. J. Org. Chem.* **2014**, *2014*, 5089.
- (19) Powell, N. A.; Rychnovsky, S. D. *Tetrahedron Lett.* **1998**, *39*, 3103.
- (20) Li, C.; Mo, F.; Li, W.; Wang, J. *Tetrahedron Lett.* **2009**, *50*, 6053.
- (21) Zhang, M.; Wang, Y.; Yang, Y.; Hu, X. *Adv. Syn. Catal.* **2012**, *354*, 981.
- (22) Maity, P.; Srinivas, H. D.; Watson, M. P. *J. Am. Chem. Soc.* **2011**, *133*, 17142.
- (23) Suzuki, I.; Yasuda, M.; Baba, A. *Chem. Commun.* **2013**, *49*, 11620.
- (24) Hayashi, M.; Inubushi, A.; Mukaiyama, T. *B. Chem. Soc. JPN.* **1988**, *61*, 4037.
- (25) Roscales, S.; Csáký, A. *Chem. Soc. Rev.* **2014**, *43*, 8215.
- (26) Matteson, D. S.; Kim, G. Y. *Org. Lett.* **2002**, *4*, 2153.
- (27) Roscales, S.; Csáký, A. G. *Chem. Commun.* **2014**, *50*, 454.
- (28) Vieira, A. S.; Fiorante, P. F.; Ludtke, D. S.; Stefani, H. A. *et Al. Org. Lett.* **2008**, *10*, 5215.
- (29) Zeng, J.; Vedachalam, S.; Xiang, S.; Liu, X.-W. *Org. Lett.* **2010**, *13*, 42.
- (30) Taylor, C.; Bolshan, Y. *Org. Lett.* **2013**, *16*, 488.
- (31) Mitchell, T. A.; Bode, J. W. *J. Am. Chem. Soc.* **2009**, *131*, 18057.
- (32) Vo, C.-V. T.; Mitchell, T. A.; Bode, J. W. *J. Am. Chem. Soc.* **2011**, *133*, 14082.
- (33) Isobe, M.; Nishizawa, R.; Hosokawa, S.; Nishikawa, T. *Chem. Commun.* **1998**, 2665.
- (34) Clausen, D. J.; Floreancig, P. E. *J. Org. Chem.* **2012**, *77*, 6574.
- (35) Clerici, A.; Pastori, N.; Porta, O. *Tetrahedron* **1998**, *54*, 15679.
- (36) Zhang, H.; Fu, X.; Chen, J.; Wang, E.; Liu, Y.; Li, Y. *J. Org. Chem.* **2009**, *74*, 9351.
- (37) Dumas, A. M.; Bode, J. W. *Org. Lett.* **2012**, *14*, 2138.

Appendix

Synthesis of (Dimethoxymethyl)benzene (A2)

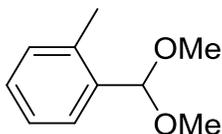


Benzaldehyde (508 μL , 5.0 mmol), TiCl_4 ([1.0 M] in CH_2Cl_2 , 250 μL , 5.0 mol %) and triethylamine (415 μL , 60.0 mol %) in 10.0 mL of methanol following **procedure 1**, afforded **A2** (0.7075 g, 91%) as a clear colourless oil.

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz): δ 7.48-7.45 (m, 2H), 7.40-7.33 (m, 3H), 5.41 (s, 1H), 3.34 (s, 6H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz): δ 138.02, 128.37, 128.12, 126.62, 103.11, 52.61

Synthesis of (Dimethoxymethyl)-2-methylbenzene (A3)

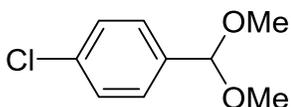


2-methylbenzaldehyde (596 μL , 5.0 mmol), TiCl_4 ([1.0 M] in CH_2Cl_2 , 250 μL , 5.0 mol %) and triethylamine (415 μL , 60.0 mol %) in 10.0 mL of methanol following **procedure 1**, afforded **A3** (0.7703 g, 92%) as a clear red oil.

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz): δ 7.55-7.53 (m, 1H), 7.24-7.15 (m, 3H), 5.46 (s, 1H), 3.33 (s, 6H), 2.38 (s, 3H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz): δ 136.23, 135.64, 130.50, 128.34, 126.51, 125.39, 101.78, 53.00, 18.85

Synthesis of 1-chloro-4-(Dimethoxymethyl)benzene (A5)

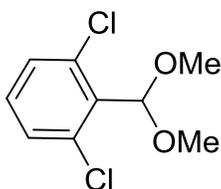


4-chlorobenzaldehyde (725 μL , 5.0 mmol), TiCl_4 ([1.0 M] in CH_2Cl_2 , 250 μL , 5.0 mol %) and triethylamine (415 μL , 60.0 mol %) in 10.0 mL of methanol following **procedure 1**, afforded **A5** (0.9159 g, 98%) as a clear yellow oil.

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz): δ 7.40-7.37 (m, 2H), 7.35-7.32 (m, 2H), 5.37 (s, 1H), 3.31 (s, 6H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz): δ 136.62, 134.23, 128.35, 128.15, 102.27, 52.54

Synthesis of 2,6-dichloro-4-(Dimethoxymethyl)benzene (**A6**)

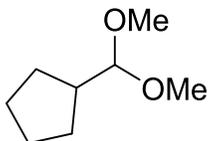


2,6-dichlorobenzaldehyde (884 μL , 5.0 mmol), TiCl_4 ([1.0 M] in CH_2Cl_2 , 250 μL , 5.0 mol %) and triethylamine (415 μL , 60.0 mol %) in 10.0 mL of methanol following **procedure 1**, afforded **A6** (1.032 g, 93%) as a clear yellow oil.

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz): δ 7.30 (d, $J = 8.2$ Hz 2H), 7.16 (dd, $J = 8.6, 7.4$ Hz, 1H), 5.85 (s, 1H), 3.48 (s, 6H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz): δ 134.99, 132.74, 129.91, 129.33, 103.97, 55.95

Synthesis of (Dimethoxymethyl)cyclopentane (**A7**)

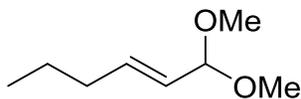


Cyclopentanecarboxaldehyde (551 μL , 5.0 mmol), TiCl_4 ([1.0 M] in CH_2Cl_2 , 250 μL , 5.0 mol %) and triethylamine (415 μL , 60.0 mol %) in 10.0 mL of methanol following **procedure 1**, afforded **A7** (0.5440 g, 77%) as a clear yellow oil.

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz): δ 4.08 (d, $J = 8.2$ Hz, 1H), 3.31 (s, 6H), 2.19 (m, 1H), 1.73-1.66 (m, 2H), 1.60-1.49 (m, 4H), 1.37-1.31 (m, 2H)

¹³C-NMR: (CDCl₃, 100 MHz): δ 108.30, 52.83, 41.67, 28.18, 25.63

Synthesis of (E)-1,1-dimethoxyhex-2-ene (A8)

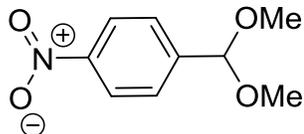


2-hexenal (592 μL, 5.0 mmol), TiCl₄ ([1.0 M] in CH₂Cl₂, 250 μL, 5.0 mol %) and triethylamine (415 μL, 60.0 mol %) in 10.0 mL of methanol following **procedure 1**, afforded **A8** (0.3450 g, 48%) as a clear yellow oil.

¹H-NMR: (CDCl₃, 400 MHz): δ 5.86-5.79 (m, 1H), 5.44 (ddt, *J* = 15.6, 5.5, (2x1.6) Hz, 1H), 4.71 (d, *J* = 5.1 Hz, 1H), 3.31 (s, 6H), 2.09-2.03 (m, 2H), 1.48-1.38 (m, 2H), 0.90 (t, *J* = 7.4 Hz, 3H)

¹³C-NMR: (CDCl₃, 100 MHz): δ 135.55, 126.51, 103.45, 52.61, 31.14, 22.00, 13.63

Synthesis of (Dimethoxymethyl)-4-nitrobenzene (A9)

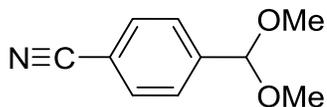


4-Nitrobenzaldehyde (0.7632 g, 5.0 mmol), TiCl₄ ([1.0 M] in CH₂Cl₂, 250 μL, 5.0 mol %) and triethylamine (415 μL, 60.0 mol %) in 10.0 mL of methanol following **procedure 1**, afforded **A9** (0.8824 g, 90%) as a clear yellow oil.

¹H-NMR: (CDCl₃, 400 MHz): δ 8.21 (d, *J* = 8.6 Hz, 2H), 7.63 (d, *J* = 8.6 Hz, 2H), 5.46 (s, 1H), 3.33 (s, 6H)

¹³C-NMR: (CDCl₃, 100 MHz): δ 147.99, 145.07, 127.80, 123.40, 101.55, 52.69

Synthesis of 4-(dimethoxymethyl)benzonitrile (A10)

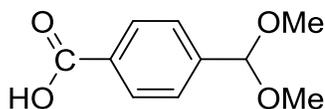


4-Formylbenzotrile (0.6900 g, 5.0 mmol), TiCl₄ ([1.0 M] in CH₂Cl₂, 250 μL, 5.0 mol %) and triethylamine (415 μL, 60.0 mol %) in 10.0 mL of methanol following **procedure 1**, afforded **A10** (0.8397 g, 94%) as a clear yellow oil.

¹H-NMR: (CDCl₃, 400 MHz): δ 7.64-7.62 (m, 2H), 7.55-7.53 (m, 2H), 5.39 (s, 1H), 3.29 (s, 6H)

¹³C-NMR: (CDCl₃, 100 MHz): δ 143.20, 132.02, 127.55, 118.63, 112.25, 101.72, 52.67

Synthesis of 4-(dimethoxymethyl)benzoic acid (**A11**)

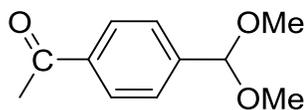


4-Formylbenzoic acid (0.7739 g, 5.0 mmol), TiCl₄ ([1.0 M] in CH₂Cl₂, 250 μL, 5.0 mol %) and triethylamine (415 μL, 60.0 mol %) in 10.0 mL of methanol following **procedure 1**, using ethyl acetate as the organic phase for extraction, which afforded **A11** (0.7620 g, 78%) as a white crystalline solid.

¹H-NMR: (CDCl₃, 400 MHz): δ 8.13 (d, *J* = 8.2 Hz, 2H), 7.58 (d, *J* = 8.2 Hz, 2H), 5.47 (s, 1H), 3.34 (s, 6H)

¹³C-NMR: (CDCl₃, 100 MHz): δ 171.80, 143.85, 130.16, 129.34, 126.93, 102.25, 52.67

Synthesis of 1-(4-(dimethoxymethyl)phenyl)ethan-1-one (**A12**)

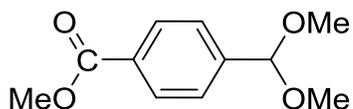


4-Acetylbenzaldehyde (0.7637 g, 5.0 mmol), TiCl₄ ([1.0 M] in CH₂Cl₂, 250 μL, 5.0 mol %) and triethylamine (415 μL, 60.0 mol %) in 10.0 mL of methanol following **procedure 1**, using ethyl acetate as the organic phase for extraction, which afforded **A12** (0.8714 g, 90%) as a clear yellow oil.

¹H-NMR: (CDCl₃, 400 MHz): δ 7.94 (d, *J* = 8.6 Hz, 2H), 7.53 (d, *J* = 8.2 Hz, 2H), 5.42 (s, 1H), 3.31 (s, 6H), 2.58 (s, 3H)

¹³C-NMR: (CDCl₃, 100 MHz): δ 197.76, 143.07, 137.10, 128.22, 126.97, 102.28, 52.66, 26.64

Synthesis of Methyl 4-(dimethoxymethyl)benzoate (A14)

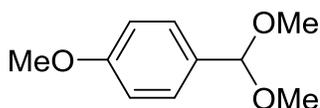


Methyl(4-formylbenzoate) (0.8291 g, 5.0 mmol), TiCl₄ ([1.0 M] in CH₂Cl₂, 250 μL, 5.0 mol %) and triethylamine (415 μL, 60.0 mol %) in 10.0 mL of methanol following **procedure 1**, which afforded **A14** (0.8110 g, 77%) as a clear yellow oil.

¹H-NMR: (CDCl₃, 400 MHz): δ 8.01 (d, *J* = 8.6 Hz, 2H), 7.49 (dd, *J* = 8.6, 0.8 Hz, 2H), 5.40 (s, 1H), 3.88 (s, 3H), 3.29 (s, 6H)

¹³C-NMR: (CDCl₃, 100 MHz): δ 166.74, 142.91, 130.15, 129.45, 126.74, 102.27, 52.56, 52.02

Synthesis of 1-dimethoxymethyl-4-methoxybenzene (A16)

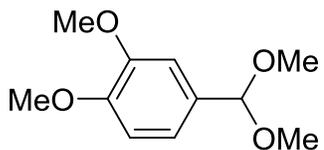


4-Methoxybenzaldehyde (0.6808 g, 5.0 mmol), TiCl₄ ([1.0 M] in CH₂Cl₂, 250 μL, 5.0 mol %) and triethylamine (415 μL, 60.0 mol %) in 10.0 mL of methanol following **procedure 1**, which afforded **A16** (0.6469 g, 71%) as a clear yellow oil.

¹H-NMR: (CDCl₃, 400 MHz): δ 7.35 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 5.35 (s, 1H), 3.80 (s, 3H), 3.31 (s, 6H)

¹³C-NMR: (CDCl₃, 100 MHz): δ 130.36, 127.90, 114.29, 113.51, 103.04, 55.22, 52.56

Synthesis of 1-dimethoxymethyl-3,4-methoxybenzene (A17)

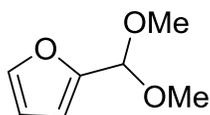


3,4-dimethoxybenzaldehyde (0.8309 g, 5.0 mmol), TiCl_4 ([1.0 M] in CH_2Cl_2 , 250 μL , 5.0 mol %) and triethylamine (415 μL , 60.0 mol %) in 10.0 mL of methanol following **procedure 1**, which afforded **A17** (0.7641 g, 72%) as a clear yellow oil.

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz): δ 6.98-6.96 (m, 2H), 6.84 (d, $J = 8.60$, 1H), 5.31 (s, 1H), 3.88 (s, 3 H), 3.86 (s, 3 H), 3.31 (s, 6H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz): δ 149.04, 148.87, 130.78, 119.17, 110.56, 109.46, 103.19, 56.14, 55.86, 52.72

Synthesis of 2-(dimethoxymethyl)furan (A18)

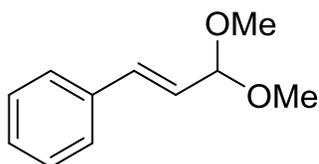


Furan-2-carboxaldehyde (0.4805 g, 5.0 mmol), TiCl_4 ([1.0 M] in CH_2Cl_2 , 250 μL , 5.0 mol %) and triethylamine (415 μL , 60.0 mol %) in 10.0 mL of methanol following **procedure 1**, which afforded **A18** (0.5402 g, 76%) as a clear colourless oil.

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz): δ 7.40 (dd, $J = 2.0, 0.8$ Hz, 1H), 6.42-6.41 (m, 1H), 6.36 (dd, $J = 3.3, 1.8$ Hz, 1H), 5.34 (s, 1H), 3.35 (s, 6H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz): δ 150.86, 142.45, 109.99, 108.41, 97.96, 52.82

Synthesis of (E)-(3,3-dimethoxyprop-1-en-1-yl)benzene (A19)

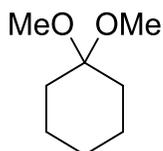


Cinnamylaldehyde (0.6608 g, 5.0 mmol), TiCl₄ ([1.0 M] in CH₂Cl₂, 250 μL, 5.0 mol %) and triethylamine (415 μL, 60.0 mol %) in 10.0 mL of methanol following **procedure 1**, which afforded **A19** (0.6060 g, 64%) as a clear colourless oil.

¹H-NMR: (CDCl₃, 400 MHz): δ 7.44-7.41 (m, 2H), 7.35-7.32 (m, 2H), 7.29-7.27 (m, 1H), 6.74 (d, *J* = 16.4 Hz, 1H), 6.17 (dd, *J* = 16.0, 5.1 Hz, 1H), 4.97 (dd, *J* = 4.9, 1.0 Hz, 1H), 3.39 (s, 6H)

¹³C-NMR: (CDCl₃, 100 MHz): δ 136.11, 133.57, 128.59, 128.11, 126.74, 125.73, 102.91, 52.71

Synthesis of 1,1-dimethoxycyclohexane (**K1**)



Cyclohexanone (491 μL, 5.0 mmol), TiCl₄ ([1.0 M] in CH₂Cl₂, 250 μL, 5.0 mol %) and triethylamine (415 μL, 60.0 mol %) in 10.0 mL of methanol following **procedure 1**, which afforded **K1** (0.4075 g, 57%) as a clear yellow oil.

¹H-NMR: (CDCl₃, 400 MHz): δ 3.12 (s, 6H), 1.59-1.56 (m, 4H), 1.44 (dt, *J* = 11.6, 5.2 Hz, 4H), 1.37-1.34 (m, 2H)

¹³C-NMR: (CDCl₃, 100 MHz): δ 99.87, 47.21, 32.63, 25.55, 22.77

Synthesis of 4-(*t*-butyl)-1,1-dimethoxycyclohexane (**K2**)

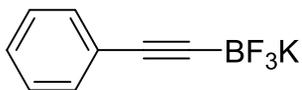


Cyclohexanone (771.3 mg, 5.0 mmol), TiCl₄ ([1.0 M] in CH₂Cl₂, 250 μL, 5.0 mol %) and triethylamine (415 μL, 60.0 mol %) in 10.0 mL of methanol following **procedure 1**, which afforded **K2** (0.6221 g, 62%) as a clear colourless oil.

¹H-NMR: (CDCl₃, 400 MHz): δ 3.18 (s, 3H), 3.13 (s, 3H), 2.06-2.02 (m, 2H), 1.64-1.60 (m, 2H), 1.26-1.22 (m, 2H), 1.16-1.12 (m, 2H), 1.03-0.97 (m, 1H), 0.84 (s, 9H)

¹³C-NMR: (CDCl₃, 100 MHz): δ 99.85, 47.58, 47.33, 32.76, 32.25, 27.63, 23.60

Synthesis of Potassium trifluoro(phenylethynyl)borate (S1):



Phenylacetylene (1.04 g, 10.0 mmol, 1.0 equiv.) was added to 32 mL of dry THF and then cooled to -80⁰C. *n*-BuLi (4.0 mL, [2.5 M in hexane], 10.0 mmol, 1.0 equiv) was added dropwise and the solution was stirred for 1 h at this temperature. B(OMe)₃ (1.56 g, 15.0 mmol, 1.5 equiv) was added dropwise at -80⁰C and then stirred for 2 h at this temperature. Aqueous KHF₂ (4.69 g, 60.0 mmol, 6 equiv.) was added at -20⁰C then stirred vigorously for 2 h, where it was allowed to warm to room temperature. The solvent was removed under reduced pressure at 50⁰C, and the resulting solid was placed under vacuum overnight to remove remaining water. The solid was washed with hot acetone (4 x 10 mL), which was collected and concentrated to a volume of ~5 mL. The product was precipitated with diethyl ether (30 mL) and collected by suction filtration. The crystalline trifluoroborate salt was washed with ether (10 mL) then placed under vacuum to remove remaining diethyl ether. **S1** (1.343 g, 65 %) was obtained as a crystalline white solid.

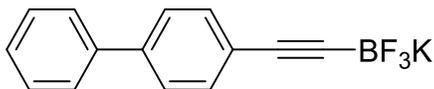
¹H-NMR: (D₆-DMSO, 400 MHz): δ 7.28-7.26 (m, 4H), 7.24-7.21 (m, 1H)

¹³C-NMR: (D₆-DMSO, 100 MHz): δ 130.92, 128.24, 126.69, 125.52 (*sp* carbons are not observed)

¹⁹F-NMR: (D₆-DMSO): δ -131.71 (s, 3F)

¹¹B-NMR: (D₆-DMSO): δ -1.55 (s, 1B)

Synthesis of Potassium trifluoro((4-biphenyl)ethynyl)borate (S2)



4-ethynylbiphenyl (1.00 g, 5.44 mmol, 1.0 equiv.), *n*-BuLi (2.18 mL, [2.5 M in hexane], 5.44 mmol, 1.0 equiv.), B(OMe)₃ (0.85 g, 8.16 mmol, 1.5 equiv.) and aqueous KHF₂ (2.54 g, 32.7 mmol, 6.0 equiv.) in 17.0 mL of THF following **Procedure 2**, afforded **S2** (0.201 g, 13 %) as an off white solid.

¹H-NMR: (D₆-DMSO, 400 MHz): δ 7.64 (d, *J* = 7 Hz, 2H), 7.58 (d, *J* = 8.6 Hz, 2H), 7.44 (t, *J* = 7.6, 2H), 7.37-7.32 (m, 3H)

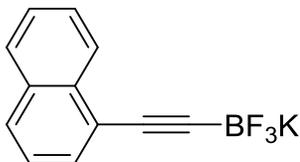
¹³C-NMR: (D₆-DMSO, 100 MHz): δ 139.52, 138.28, 131.51, 128.94, 127.46, 126.48, 126.45, 124.66 (*sp* carbons are not observed)

¹⁹F-NMR: (D₆-DMSO): δ -131.70 (s, 3F)

¹¹B-NMR: (D₆-DMSO): δ -1.22 (s, 1B)

HRMS (ESI/M⁻): C₁₄H₉BF₃: calculated: 245.0755, found: 245.0757

Synthesis of Potassium trifluoro((4-naphthyl)ethynyl)borate (S3)



1-ethynyl-naphthalene (0.880 g, 5.44 mmol, 1.0 equiv.), *n*-BuLi (2.18 mL, [2.5 M in hexane], 5.44 mmol, 1.0 equiv.), B(OMe)₃ (0.85 g, 8.16 mmol, 1.5 equiv.) and aqueous KHF₂ (2.54 g, 32.7 mmol, 6.0 equiv.) in 17.0 mL of THF following **Procedure 2**, afforded **S3** (0.8762 g, 62 %) as a slightly pink solid.

¹H-NMR: (D₆-DMSO, 400 MHz): δ 8.32 (d, *J* = 8.2 Hz, 1H), 7.89 (d, *J* = 7.8 Hz, 1H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.57-7.50 (m, 3H), 7.42 (t, *J* = 15.2 Hz, 1H)

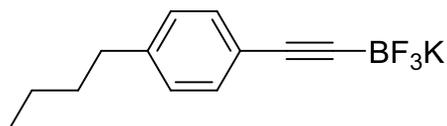
¹³C-NMR: (D₆-DMSO, 100 MHz): δ 132.93, 132.80, 128.95, 128.09, 126.88, 126.29, 126.23, 126.13, 125.52, 123.10 (*sp* carbons are not observed)

¹⁹F-NMR: (D₆-DMSO): δ -131.46 (s, 3F)

¹¹B-NMR: (D₆-DMSO): δ -1.56 (s, 1B)

HRMS (ESI/M-): C₁₂H₇BF₃: calculated: 219.0598, found: 219.0601

Synthesis of Potassium trifluoro((4-butylphenyl)ethynyl)borate (S4)



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 (8.46 g, 108 mmol, 6.0 equiv.) in 50.0 mL of THF following **Procedure 2**, afforded **S4** (2.609 g, 55 %) as a white crystalline solid.

¹H-NMR: (D₆-DMSO, 400 MHz): δ 7.19 (d, *J* = 8.20 Hz, 2H), 7.09 (d, *J* = 7.8 Hz, 2H), 2.54 (t, *J* = 7.5 Hz, 2H), 1.54-1.48 (m, 2H), 1.30-1.22 (m, 2H), 0.88 (t, *J* = 7.23 Hz, 3H)

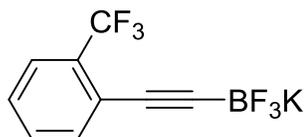
¹³C-NMR: (D₆-DMSO, 100 MHz): δ 140.9, 130.8, 128.2, 122.8, 34.6, 32.9, 21.7, 13.8 (*sp* carbons are not observed)

¹⁹F-NMR: (D₆-DMSO): δ -131.6 (s, 3F)

¹¹B-NMR: (D₆-DMSO): δ -1.67 (s, 1B)

HRMS (ESI/M-): C₁₂H₇BF₃: calculated: 225.1068, found: 225.1065

Synthesis of Potassium trifluoro(((2-trifluoromethyl)phenyl)ethynyl)borate (S5)



1-Ethynyl-2-trifluoromethylbenzene (1.00 g, 5.70 mmol, 1.0 equiv.), *n*-BuLi (2.28 mL, [2.5 M in hexane], 5.70 mmol, 1.0 equiv.), B(OMe)₃ (0.90 g, 8.55 mmol, 1.5 equiv.) and aqueous KHF₂ (2.67 g, 34.2 mmol, 6.0 equiv.) in 17.0 mL of THF following **Procedure 2**, afforded **S5** (0.8790 g, 56 %) as a crystalline white solid.

¹H-NMR: (D₆-DMSO, 400 MHz): δ 7.65 (d, *J* = 9.2 Hz, 1H), 7.54 (m, 2H), 7.41 (t, *J* = 16.3 Hz, 1H)

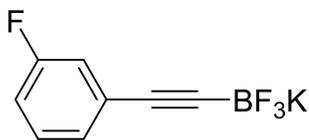
¹³C-NMR: (D₆-DMSO, 100 MHz): δ 134.08, 132.03, 129.37 (q, *J* = 88.95 Hz), 126.85, 125.46 (q, *J* = 16.65 Hz), 125.08 (q, *J* = 546.73 Hz) (*sp* carbons are not observed)

¹⁹F-NMR: (D₆-DMSO): δ -60.85 (s, 3F), -132.09 (s, 3F)

¹¹B-NMR: (D₆-DMSO): δ -1.61 (s, 1B)

HRMS (ESI/M-): C₉H₄BF₆: calculated: 237.0316, found: 237.0318

Synthesis of Potassium trifluoro((3-fluorophenyl)ethynyl)borate (**S6**)



1-Ethynyl-3-fluoro-benzene (0.667 g, 5.44 mmol, 1.0 equiv.), *n*-BuLi (2.18 mL, [2.5 M in hexane], 5.44 mmol, 1.0 equiv.), B(OMe)₃ (0.85 g, 8.16 mmol, 1.5 equiv.) and aqueous KHF₂ (2.54 g, 32.6 mmol, 6.0 equiv.) in 17.0 mL of THF following **Procedure 2**, afforded **S6** (1.0380 g, 84 %) as a crystalline white solid.

¹H-NMR: (D₆-DMSO, 400 MHz): δ 7.35-7.30 (m, 1H), 7.14-7.07 (m, 3H)

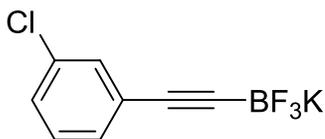
¹³C-NMR: (D₆-DMSO, 100 MHz): δ 163.04, 160.62, 130.28 (d, *J* = 9.2 Hz), 127.32 (d, *J* = 3.1 Hz), 117.38 (d, *J* = 22 Hz), 114.01 (d, *J* = 22 Hz) (*sp* carbons are not observed)

¹⁹F-NMR: (D₆-DMSO): δ -113.49 (s, 1F), -131.97 (s, 3F)

¹¹B-NMR: (D₆-DMSO): δ -1.56 (s, 1B)

HRMS (ESI/M-): C₈H₄BF₄: calculated: 187.0348, found: 187.0348

Synthesis of Potassium trifluoro((3-chlorophenyl)ethynyl)borate (S7)



1-Chloro-3-ethynyl-benzene (0.44 g, 3.25 mmol, 1.0 equiv.), *t*-BuLi (0.21 g, 3.25 mmol, 1.0 equiv.), B(OMe)₃ (0.51 g, 4.87 mmol, 1.5 equiv.) and aqueous KHF₂ (1.52 g, 19.5 mmol, 6.0 equiv.) in 10.0 mL of THF afforded product S4 (0.4597 g, 59 % yield) as a white crystalline solid.

¹H-NMR: (D₆-DMSO, 400 MHz): δ 7.30-7.28 (m, 3H), 7.26-7.22 (m, 1H)

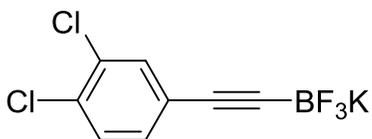
¹³C-NMR: (D₆-DMSO, 100 MHz): δ 132.84, 130.30, 130.14, 129.70, 127.42, 126.90 (*sp* carbons are not observed)

¹⁹F-NMR: (D₆-DMSO): δ -131.98 (s, 3F)

¹¹B-NMR: (D₆-DMSO): δ -1.58 (s, 1B)

HRMS (ESI/M⁻): C₈H₄BClF₃: calculated: 203.0052, found: 203.0054

Synthesis of Potassium trifluoro((3,4-dichlorophenyl)ethynyl)borate (S8)



1,2-dichloro-4-ethynyl-benzene (0.9212 g, 5.19 mmol, 1.0 equiv.), *n*-BuLi (2.08 mL, [2.5 M in hexane], 5.19 mmol, 1.0 equiv.), B(OMe)₃ (0.81 g, 8.50 mmol, 1.5 equiv.) and aqueous KHF₂ (2.66 g, 21.3 mmol, 6.0 equiv.) in 17.0 mL of THF following **Procedure 2**, afforded **S8** (0.6175 g, 43 %) as a crystalline white solid.

¹H-NMR: (D₆-DMSO, 400 MHz): δ 7.52-7.49 (m, 2H), 7.26 (dd, *J* = 8.2, 2.0 Hz, 1H)

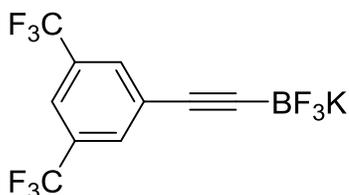
¹³C-NMR: (D₆-DMSO, 100 MHz): δ 132.84, 131.67, 131.42, 130.97, 130.90, 126.44, 109.99 (*sp* carbons are not observed)

¹⁹F-NMR: (D₆-DMSO): δ -131.12 (s, 3F)

¹¹B-NMR: (D₆-DMSO): δ -1.70 (s, 1B)

HRMS (ESI/M-): C₈H₃BCl₂F₃: calculated: 236.9662, found: 236.9664

Synthesis of Potassium trifluoro ((3,5-bis(trifluoromethyl)phenyl)ethynyl)borate (S9)



3,5-Bis(trifluoromethyl)phenylacetylene (0.961 g, 4.03 mmol, 1.0 equiv.), *n*-BuLi (1.61 mL, [2.5 M in hexane], 3.5 mmol, 1.0 equiv.), B(OMe)₃ (0.63 g, 6.05 mmol, 1.5 equiv.) and aqueous KHF₂ (1.90 g, 21.3 mmol, 6.0 equiv.) in 12.2 mL of THF following **Procedure 2**, afforded **S9** (0.4444 g, 32 %) as a crystalline white solid.

¹H-NMR: (D₆-DMSO, 400 MHz): δ 7.92-7.90 (m, 3H)

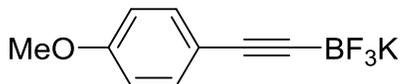
¹³C-NMR: (D₆-DMSO, 100 MHz): δ 131.75, 131.47, 131.14, 130.81, 130.49, 128.33, 127.53, 124.82, 122.10, 120.50 (m), 119.39 (*sp* carbons are not observed)

¹⁹F-NMR: (D₆-DMSO): δ -61.63 (s, 6F), -132.41 (s, 3F)

¹¹B-NMR: (D₆-DMSO): δ -0.57, -1.75 (s, 1B)

HRMS (ESI/M-): C₁₀H₃BF₉: calculated: 305.0190, found: 305.0193

Synthesis of Potassium trifluoro ((4-methoxy)phenyl)ethynyl)borate (S10)



4-ethynylanisole (1.00 g, 7.34 mmol, 1.0 equiv.), *n*-BuLi (0.470 g, [2.5 M in hexane], 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 25.0 mL of THF following **Procedure 2**, afforded **S10** (2.609 g, 55 %) as a crystalline white solid.

¹H-NMR: (D₆-DMSO, 400 MHz): δ 7.22 (dt, *J* = 9.0, 2.5, 2H), 6.84 (dt, *J* = 9.0, 2.0, Hz, 2H), 3.73 (s, 3H)

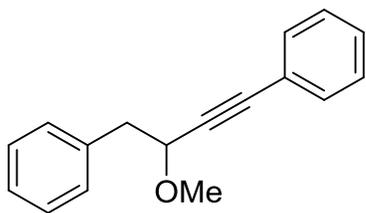
¹³C-NMR: (D₆-DMSO, 100 MHz): δ 158.0, 132.2, 117.7, 113.9, 55.0 (*sp* carbons are not observed)

¹⁹F-NMR: (D₆-DMSO): δ -131.5 (s, 3F)

¹¹B-NMR: (D₆-DMSO): δ -1.67 (s, 1B)

HRMS (ESI/M-): C₉H₇OBF₃: calculated: 199.0548, found: 199.0543

(3-methoxybut-1-yne-1,4-diyl)dibenzene (1a)



Derived from (2,2-dimethoxyethyl)benzene (**A1**) (16.6 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro(phenylethynyl)borate (**S1**) (22.9 mg, 0.11 mmol, 1.1 equiv.) and HBF₄·OEt₂ (15.1 μL, 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile at 0^oC, following **Procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (19:1) afforded product **1a** (20.9 mg, 89% yield) as a yellow oil.

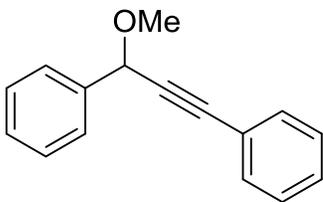
FT-IR: ν 2925.90, 1489.56, 1338.29, 1096.67, 753.66, 689.58 cm⁻¹

¹H-NMR: (CDCl₃, 400 MHz) δ 7.43-7.40 (m, 2H), 7.35-7.30 (m, 7H), 7.28-7.26 (m, 1H), 4.38 (t, *J* = 6.6 Hz, 1H), 3.49 (s, 3H), 3.18-3.06 (m, 2H)

¹³C-NMR: (CDCl₃, 100 MHz) δ 137.28, 131.67, 129.69, 128.33, 128.24, 128.19, 126.61, 122.70, 87.55, 86.75, 72.72, 56.63, 42.22

HRMS: C₁₇H₁₆O: calculated: 236.1201, found: 236.1204

(3-methoxyprop-1-yne-1,3-diyl)dibenzene (1b)



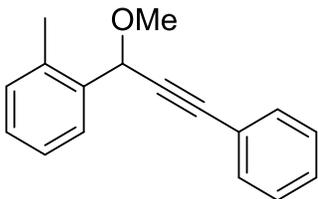
Derived from (dimethoxymethyl)benzene (**A2**) (15.2 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro(phenylethynyl)borate (**S1**) (22.9 mg, 0.11 mmol, 1.1 equiv.) and HBF₄·OEt₂ (15.1 μL, 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile following **Procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (9:1) afforded product **1b** (18.5 mg, 83% yield) as a yellow oil.

FT-IR: ν 2926.86, 1489.37, 1330.13, 1072.31, 745.45, 689.33 cm⁻¹

¹H-NMR: (CDCl₃, 400 MHz) δ 7.61-7.58 (m, 2H), 7.51-7.49 (m, 2H), 7.43-7.37 (m, 3H), 7.36-7.32 (m, 3H), 5.33 (s, 1H), 3.51 (s, 3H)

¹³C-NMR: (CDCl₃, 100 MHz) δ 138.53, 131.79, 128.51, 128.44, 128.28, 127.50, 122.55, 87.74, 86.65, 73.50, 55.93 (only 11 peaks observed)

(1-methoxy-3-phenylprop-2-yn-1-yl)-2-methylbenzene (1c)



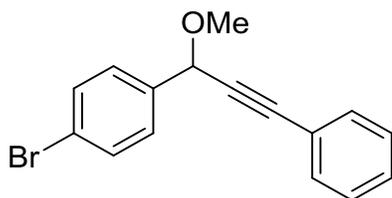
Derived from (Dimethoxymethyl)-2-methylbenzene (**A3**) (16.6 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro(phenylethynyl)borate (**S1**) (22.9 mg, 0.11 mmol, 1.1 equiv.) and HBF₄·OEt₂ (15.1 μL, 0.11 mmol, 1.1 equiv.) in 1.0 mL of propionitrile at -40⁰C for 1 h, following **Procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (19:1) afforded product **1c** (22.7 mg, 96% yield) as a red oil.

FT-IR: ν 2959.24, 1488.84, 1076.27, 753.27, 740.85, 689.73 cm^{-1}

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz) δ 7.70-7.68 (m, 1H), 7.51-7.49 (m, 2H), 7.34-7.32 (m, 3H), 7.27-7.22 (m, 3H), 5.44 (s, 1H), 3.53 (s, 3H), 2.49 (s, 3H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz) δ 136.45, 136.38, 131.76, 130.71, 128.45, 128.27, 127.67, 126.01, 122.67, 87.56, 86.52, 71.57, 56.15, 19.01 (only 14 peaks observed)

1-bromo-4-(1-methoxy-3-phenylprop-2-yn-1-yl)benzene (1d)



Derived from 1-bromo-4-(Dimethoxymethyl)benzene (**A4**) (23.6 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro(phenylethynyl)borate (**S1**) (22.9 mg, 0.11 mmol, 1.1 equiv.) and $\text{HBF}_4 \cdot \text{OEt}_2$ (15.1 μL , 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile, following **Procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (12:1) afforded product **1d** (26.7 mg, 89% yield) as a yellow oil.

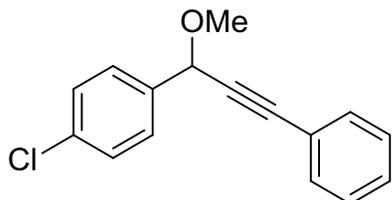
FT-IR: ν 2927.39, 1487.40, 1069.62, 1011.56, 754.66, 689.79 cm^{-1}

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz) δ 7.54-7.45 (m, 6H), 7.34-7.32 (m, 3H), 5.28 (s, 1H), 3.50 (s, 3H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz) δ 137.65, 131.78, 131.62, 129.12, 128.68, 128.32, 122.45, 122.28, 88.05, 86.04, 72.78, 55.97

HRMS: $\text{C}_{16}\text{H}_{13}\text{BrO}$: calculated: 300.0150, found: 300.0151

1-chloro-4-(1-methoxy-3-phenylprop-2-yn-1-yl)benzene (1e)



Derived from 1-bromo-4-(Dimethoxymethyl)benzene (**A5**) (23.6 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro(phenylethynyl)borate (**S1**) (22.9 mg, 0.11 mmol, 1.1 equiv.) and $\text{HBF}_4 \cdot \text{OEt}_2$ (15.1 μL , 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile, which was stirred for 70 min, following **Procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (12:1) afforded product **1e** (20.5 mg, 80% yield) as a yellow oil.

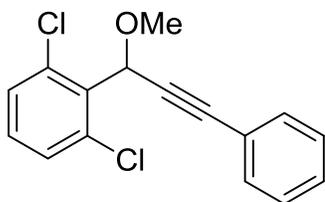
FT-IR: ν 2927.48, 1488.38, 1079.94, 821.85, 754.23, 689.57 cm^{-1}

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz) δ 7.53-7.48 (m, 4H), 7.38-7.32 (m, 5H), 5.29 (s, 1H), 3.50 (s, 3H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz) δ 137.12, 134.26, 131.78, 128.81, 128.66, 128.32, 122.29, 88.03, 86.11, 72.75, 55.96 (only 11 peaks observed)

HRMS: $\text{C}_{16}\text{H}_{13}\text{ClO}$: calculated: 256.0655, found: 256.0653

1,3-dichloro-2-(1-methoxy-3-phenylprop-2-yn-1-yl)benzene (**1f**)



Derived from 1,3-dichloro-2-(dimethoxymethyl)benzene (**A6**) (22.1 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro(phenylethynyl)borate (**S1**) (22.9 mg, 0.11 mmol, 1.1 equiv.) and $\text{HBF}_4 \cdot \text{OEt}_2$ (15.1 μL , 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile, following **Procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (14:1) afforded product **1f** (18.7 mg, 64% yield) as a clear, colourless oil.

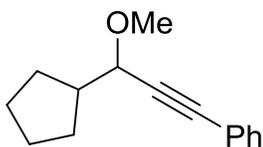
FT-IR: ν 2926.27, 1434.70, 1094.01, 1080.70, 753.71, 720.14, 689.14 cm^{-1}

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz) δ 7.48-7.46 (m, 2H), 7.36-7.34 (m, 2H), 7.32-7.29 (m, 3H), 7.20 (dd, $J = 8.6, 7.5$ Hz, 1H), 6.06 (s, 1H), 3.50 (s, 3H)

¹³C-NMR: (CDCl₃, 100 MHz) δ 135.69, 133.34, 131.87, 129.86, 129.24, 128.54, 128.21, 122.55, 87.10, 84.94, 69.35, 56.82

HRMS: C₁₆H₁₂Cl₂O: calculated: 290.0265, found: 290.0262

(3-cyclopentyl-3-methoxyprop-1-yn-1-yl)benzene (1g)



Derived from (dimethoxymethyl)cyclopentane (**A7**) (14.4 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro(phenylethynyl)borate (**S1**) (22.9 mg, 0.11 mmol, 1.1 equiv.) and HBF₄·OEt₂ (15.1 μL, 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile, following **Procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (19:1) afforded product **1g** (20.6 mg, 96% yield) as a yellow oil.

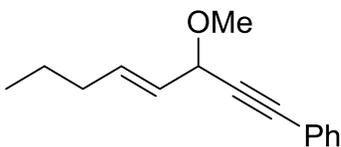
FT-IR: ν 2950.82, 2866.71, 1489.25, 1443.8, 1086.07, 754.20, 689.47 cm⁻¹

¹H-NMR: (CDCl₃, 400 MHz) δ 7.46-7.44 (m, 2H), 7.37-7.26 (m, 3H), 4.04 (d, *J* = 7.0 Hz, 1H), 3.48 (s, 3H), 2.37-2.24 (m, 1H), 1.89-1.74 (m, 2H), 1.68-1.65 (m, 2H), 1.61-1.48 (m, 4H)

¹³C-NMR: (CDCl₃, 100 MHz) δ 131.72, 128.22, 128.17, 122.97, 87.71, 85.86, 75.97, 56.72, 44.42, 29.17, 28.67, 25.77, 25.68

HRMS: C₁₅H₁₈O: calculated: 214.1358, found: 214.1356

(E)-(3-methoxyoct-4-en-1-yn-1-yl)benzene (1h)



Derived from (E)-1,1-dimethoxyhex-2-ene (**A8**) (14.4 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro(phenylethynyl)borate (**S1**) (22.9 mg, 0.11 mmol, 1.1 equiv.) and HBF₄·OEt₂ (15.1 μL, 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile, following

Procedure 3. Purification by silica gel chromatography using hexanes/diethyl ether (19:1) afforded product **1h** (10.4 mg, 49% yield) as a clear, colourless oil.

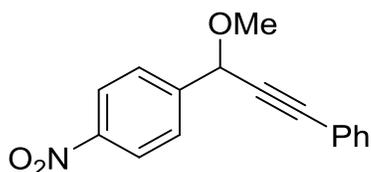
FT-IR: ν 2958.27, 2928.96, 2871.12, 1489.84, 1124.27, 1093.82, 956.31, 755.06, 689.78 cm^{-1}

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz) δ 7.45-7.43 (m, 2H), 7.33-7.30 (m, 3H), 6.07 (dd, $J = 16$, 7.4 Hz, 1H), 5.87 (d, $J = 16$ Hz, 1H), 3.63 (q, $J = 6.9$ Hz, 1H), 3.31 (s, 3H), 1.63-1.55 (m, 1H), 1.52-1.47 (m, 1H), 1.43-1.37 (m, 2H), 0.93 (t, $J = 7.0$ Hz, 3H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz) δ 144.00, 131.49, 128.28, 128.18, 123.21, 111.58, 89.76, 87.30, 81.71, 56.57, 37.44, 18.47, 13.98

HRMS: $\text{C}_{15}\text{H}_{18}\text{O}$: calculated: 214.1358, found: 214.1364

(1-methoxy-3-phenylprop-2-yn-1-yl)-4-nitrobenzene (1i)



Derived from (dimethoxymethyl)-4-nitrobenzene (**A9**) (19.7 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro(phenylethynyl)borate (**S1**) (22.9 mg, 0.11 mmol, 1.1 equiv.) and $\text{HBF}_4 \cdot \text{OEt}_2$ (15.1 μL , 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile, following **Procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (6.5:1) afforded product **1i** (26.8 mg, 100% yield) as a yellow solid.

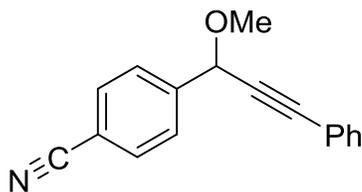
FT-IR: ν 2929.61, 1518.74, 1345.93, 1078.02, 877.93, 755.19, 727.39, 689.4 cm^{-1}

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz) δ 8.25(d, $J = 8.6$ Hz, 2H), 7.76 (d, $J = 8.6$ Hz, 2H), 7.51-7.47 (m, 2H), 7.37-7.31 (m, 3H), 5.40 (s, 1H), 3.56 (s, 3H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz) δ 147.86, 145.69, 131.81, 128.95, 128.40, 128.06, 123.73, 121.89, 88.79, 85.21, 72.42, 56.38

HRMS: $\text{C}_{16}\text{H}_{13}\text{NO}_3$: calculated: 267.0895, found: 267.0892

4-(1-methoxy-3-phenylprop-2-yn-1-yl)benzotrile (1j)



Derived from 4-(dimethoxymethyl)benzotrile (**A10**) (17.7 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro(phenylethynyl)borate (**S1**) (22.9 mg, 0.11 mmol, 1.1 equiv.) and $\text{HBF}_4 \cdot \text{OEt}_2$ (15.1 μL , 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile, following **Procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (4:1) afforded product **1j** (23.1 mg, 94% yield) as a clear, yellow oil.

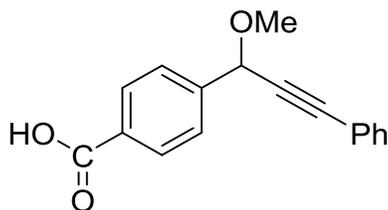
FT-IR: ν 2930.59, 2227.96, 1488.98, 1077.21, 755.31, 699.80, 565.52 cm^{-1}

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz) δ 7.69 (s, 4H), 7.49-7.47 (m, 2H), 7.36-7.32 (m, 3H), 5.35 (s, 1H), 3.54 (s, 3H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz) δ 143.78, 132.35, 131.80, 128.92, 128.38, 127.94, 121.95, 118.63, 112.21, 88.67, 85.28, 72.65, 56.31

HRMS: $\text{C}_{17}\text{H}_{13}\text{NO}$: calculated: 247.0997, found: 247.0996

4-(1-methoxy-3-phenylprop-2-yn-1-yl)benzoic acid (1k)



Derived from 4-(dimethoxymethyl)benzoic acid (**A11**) (19.6 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro(phenylethynyl)borate (**S1**) (41.6 mg, 0.20 mmol, 2.0 equiv.) and $\text{HBF}_4 \cdot \text{OEt}_2$ (20.5 μL , 0.15 mmol, 1.5 equiv.) in 1.0 mL of acetonitrile, which was stirred for 80 min, following **Procedure 3**. Purification by silica gel chromatography using CH_2Cl_2 /methanol (gradient: 100:0 to 9:1) afforded product **1k** (19.4 mg, 73% yield) as a yellow solid.

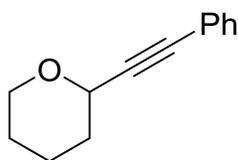
FT-IR: ν 2922.65, 2889.72, 1684.10, 1286.50, 1077.90, 755.16, 731.44, 550.82 cm^{-1}

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz) δ 8.16 (d, $J = 8.2$ Hz, 2H), 7.70 (d, $J = 8.2$ Hz, 2H), 7.51-7.49 (m, 2H), 7.35-7.33 (m, 3H), 5.39 (s, 1H), 3.54 (s, 3H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz) δ 144.40, 131.82, 130.49, 128.75, 128.34, 127.41, 122.20, 88.35, 85.81, 72.94, 56.15 (Only 12 peaks observed)

HRMS: $[\text{M-H}]$ - $\text{C}_{17}\text{H}_{13}\text{O}_3$: calculated: 265.0870, found: 265.0872

2-(phenylethynyl)tetrahydro-2H-pyran (**1p**)

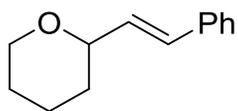


Derived from (2-methoxy)tetrahydropyran (**A15**) (11.6 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro(phenylethynyl)borate (**S1**) (31.2 mg, 0.15 mmol, 1.5 equiv.) and $\text{HBF}_4 \cdot \text{OEt}_2$ (20.6 μL , 0.15 mmol, 1.5 equiv.) in 1.0 mL of acetonitrile, which was stirred for 70 min, following **Procedure 3**. Purification by silica gel chromatography using hexane/diethyl ether (19:1) afforded product **1p** (16.6 mg, 89% yield) as a clear colourless oil.

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz) δ 7.47-7.43 (m, 2H), 7.31-7.28 (m, 3H), 4.51 (dd, $J = 7.6$, 2.9 Hz, 1H), 4.07-4.03 (m, 1H), 3.61-3.56 (m, 1H), 1.96-1.90 (m, 2H), 1.83-1.76 (m, 1H), 1.65-1.56 (m, 4H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz) δ 131.74, 128.25, 128.18, 122.75, 88.11, 85.18, 67.44, 66.62, 32.18, 25.68, 21.81

(E)-2-styryltetrahydro-2H-pyran (**1q**)

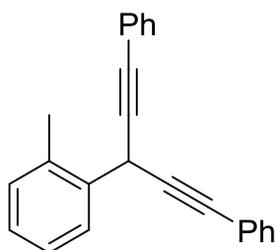


Derived from (2-methoxy)tetrahydropyran (**A15**) (11.6 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro(phenylethenyl)borate (31.5 mg, 0.15 mmol, 1.5 equiv.) and $\text{HBF}_4 \cdot \text{OEt}_2$ (20.6 μL , 0.15 mmol, 1.5 equiv.) in 1.0 mL of acetonitrile, which was stirred for 80 min, following **Procedure 3**. Purification by silica gel chromatography using hexane/diethyl ether (19:1) afforded product **1q** (9.6 mg, 51% yield) as a clear colourless oil.

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz) δ 7.39-7.37 (m, 2H), 7.32-7.19 (m, 3H), 6.61-6.57 (m, 1H), 6.21 (dd, $J = 16, 5.9$ Hz, 1H), 4.09-4.05 (m, 1H), 4.00-3.96 (m, 1H), 3.58-3.52 (m, 1H), 1.92-1.89 (m, 1H), 1.77-1.73 (m, 1H), 1.66-1.49 (m, 4H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz) δ 137.02, 130.64, 129.73, 128.46, 127.40, 126.39, 78.02, 68.42, 32.23, 25.87, 23.44

(3-(*o*-tolyl)penta-1,4-diyne-1,5-diyl)dibenzene (2a)

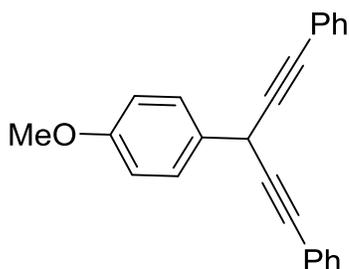


Derived from (dimethoxymethyl)-2-methylbenzene (**A3**) (16.6 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro(phenylethynyl)borate (**S1**) (22.9 mg, 0.11 mmol, 1.1 equiv.) and $\text{HBF}_4 \cdot \text{OEt}_2$ (15.1 μL , 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile for 70 mins following **Procedure 3**. Purification by silica gel chromatography using Hexane/diethyl ether (9:1) afforded product **2a** (6.4 mg, 21% yield) as a clear yellow oil.

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz) δ 7.48-7.36 (m, 4H), 7.32-7.28 (m, 10H), 5.23 (s, 1H), 2.57 (s, 3H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz) δ 136.11, 135.87, 131.76, 130.79, 128.18, 128.16, 127.70, 127.64, 126.46, 123.03, 86.29, 82.42, 28.21, 19.34

(3-(4-methoxyphenyl)penta-1,4-diyne-1,5-diyl)dibenzene (2b)

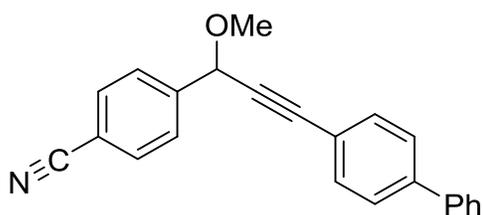


Derived from 1-dimethoxymethyl-4-methoxybenzene (**A16**) (18.2 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro(phenylethynyl)borate (**S1**) (22.9 mg, 0.11 mmol, 1.1 equiv.) and $\text{HBF}_4 \cdot \text{OEt}_2$ (15.1 μL , 0.11 mmol, 1.1 equiv.) in 1.0 mL of propionitrile at -40°C for 15 min, following **Procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (19:1) afforded product **2b** (15.8 mg, 49% yield) as a clear colourless oil.

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz) δ 7.60 (d, $J = 8.2$ Hz, 2H), 7.50-7.48 (m, 4H), 7.32-7.31 (m, 5H), 6.94 (d, $J = 8.6$ Hz, 3H), 5.17 (s, 1H), 3.83 (s, 3H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz) δ 159.00, 131.79, 128.37, 128.19, 123.02, 114.10, 86.91, 82.58, 55.35, 29.33

4-(3-([1,1'-biphenyl]-4-yl)-1-methoxyprop-2-yn-1-yl)benzotrile (3a)



Derived from 4-(dimethoxymethyl)benzotrile (**A10**) (17.7 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro((4-biphenyl)ethynyl)borate (**S2**) (31.3 mg, 0.11 mmol, 1.1 equiv.) and $\text{HBF}_4 \cdot \text{OEt}_2$ (15.1 μL , 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile, following **Procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (9:1) afforded product **3a** (24.2 mg, 75% yield) as a white solid.

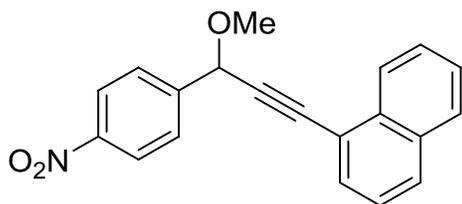
FT-IR: ν 2925.59, 2226.74, 1282.95, 1073.92, 842.24, 818.01, 763.73, 553.85 cm^{-1}

¹H-NMR: (CDCl₃, 400 MHz) δ 7.73-7.69 (m, 4H), 7.60-7.56 (m, 6H), 7.48-7.44 (m, 2H), 7.40-7.36 (m, 1H), 5.38 (s, 1H), 3.56 (s, 3H)

¹³C-NMR: (CDCl₃, 100 MHz) δ 143.79, 141.71, 140.11, 132.38, 132.25, 128.90, 127.96, 127.81, 127.03, 120.79, 118.65, 112.23, 109.99, 88.57, 85.94, 72.72, 56.35

HRMS: C₂₃H₁₇NO: calculated: 323.1310, found: 323.1313

1-(3-methoxy-3-(4-nitrophenyl)prop-1-yn-1-yl)naphthalene (4a)



Derived from (dimethoxymethyl)-4-nitrobenzene (**A9**) (19.7 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro((4-naphthyl)ethynyl)borate (**S3**) (28.4 mg, 0.11 mmol, 1.1 equiv.) and HBF₄·OEt₂ (15.1 μL, 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile, following **Procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (gradient: 100:0 → 3:1) afforded product **4a** (25.4 mg, 80% yield) as a yellow oil.

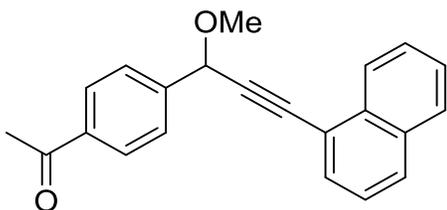
FT-IR: ν 2989.32, 1518.03, 1344.35, 1096.21, 1075.71, 798.60, 771.46, 743.12, 704.59 cm⁻¹

¹H-NMR: (CDCl₃, 400 MHz) δ 8.30-8.26 (m, 3H), 7.88-7.82 (m, 4H), 7.74 (dd, *J* = 7.0, 1.2 Hz, 1H), 7.58-7.54 (m, 2H), 7.45 (dd, *J* = 8.2, 7.0 Hz, 1H), 5.56 (s, 1H), 3.65 (s, 3H)

¹³C-NMR: (CDCl₃, 100 MHz) δ 147.91, 145.78, 133.24, 133.14, 131.01, 129.48, 128.43, 128.12, 127.07, 126.56, 125.75, 125.14, 123.81, 119.51, 90.07, 86.98, 72.68, 56.52

HRMS: C₂₀H₁₅NO₃: calculated: 317.1052, found: 317.1054

1-(4-(1-methoxy-3-(naphthalen-1-yl)prop-2-yn-1-yl)phenyl)ethan-1-one (4b)



Derived from 1-(4-(dimethoxymethyl)phenyl)ethan-1-one (**A12**) (19.4 mg, 0.10 mmol, 1.0 equiv.), potassium trifluoro((4-naphthyl)ethynyl)borate (**S3**) (28.4 mg, 0.11 mmol, 1.1 equiv.) and $\text{HBF}_4 \cdot \text{OEt}_2$ (15.1 μL , 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile, following **procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (3:1) afforded product **4b** (24.7 mg, 79% yield) as a viscous, yellow oil.

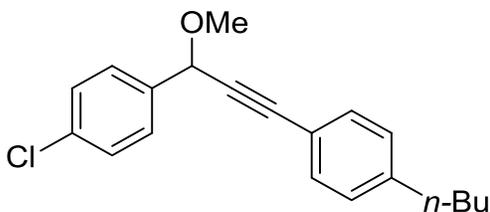
FT-IR: ν 2947.13, 1681.09, 1263.82, 1096.45, 1075.60, 955.19, 798.61, 771.70, 594.33 cm^{-1}

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz) δ 8.30 (dd, $J = 8.2, 0.8$ Hz, 1H), 8.02 (dd, $J = 8.2, 2.0$ Hz, 2H), δ 7.86 (dd, $J = 7.0, 1.2$ Hz, 2H), 7.77 (d, $J = 8.2$ Hz, 2H), 7.73 (dd, $J = 7.0, 1.2$ Hz, 1H), 7.57-7.52 (m, 2H), 7.44 (dd, $J = 8.2, 7.0$ Hz, 1H), 5.53 (s, 1H), 3.62 (s, 3H), 2.63 (s, 3H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz) δ 197.69, 143.74, 137.11, 133.29, 133.13, 130.89, 129.25, 128.66, 128.36, 127.55, 126.98, 126.49, 125.91, 125.14, 119.85, 90.79, 86.46, 73.19, 56.30, 26.71

HRMS: $\text{C}_{18}\text{H}_{20}\text{O}_2$ calculated: 314.1307, found: 314.1304

1-butyl-4-(3-(4-chlorophenyl)-3-methoxyprop-1-yn-1-yl)benzene (5a)



Derived from 1-chloro-4-(dimethoxymethyl)benzene (**A5**) (18.7 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro((4-butylphenyl)ethynyl)borate (**S4**) (29.1 mg, 0.11 mmol, 1.1 equiv.) and $\text{HBF}_4 \cdot \text{OEt}_2$ (15.1 μL , 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile, at -40°C , following **procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (9:1) afforded product **5a** (26.9 mg, 86% yield) as a yellow oil.

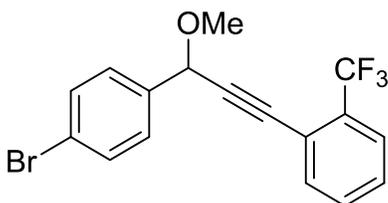
FT-IR: ν 2955.79, 2928.27, 2857.90, 1508.76, 1489.27, 1085.67, 1015.36, 819.60, 532.01 cm^{-1}

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz) δ 7.52 (d, $J = 8.2$ Hz, 2H), 7.39-7.35 (m, 4H), 7.14 (d, $J = 8.6$ Hz, 2H), 5.29 (s, 1H), 3.49 (s, 3H), 2.61 (t, $J = 7.8$ Hz, 2H), 1.61-1.57 (m, 2H), 1.35 (dq, $J = 14.9, 7.4$ Hz, 2H), 0.93 (t, $J = 7.4$, 3H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz) δ 143.86, 137.26, 134.19, 131.70, 128.83, 128.63, 128.44, 119.40, 88.29, 85.38, 72.77, 55.89, 35.57, 33.36, 22.27, 13.90

HRMS: $\text{C}_{20}\text{H}_{21}\text{ClO}$: calculated: 312.1281, found: 312.1281

1-(3-(4-bromophenyl)-3-methoxyprop-1-yn-1-yl)-2-(trifluoromethyl)benzene (**6a**)



Derived from 1-bromo-4-(dimethoxymethyl)benzene (**A4**) (23.6 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro(((2-trifluoromethyl)phenyl)ethynyl)borate (**S5**) (29.1 mg, 0.11 mmol, 1.1 equiv.) and $\text{HBF}_4 \cdot \text{OEt}_2$ (15.1 μL , 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile, following **Procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (gradient: 100:0 \rightarrow 2:1) afforded product **6a** (26.2 mg, 71% yield) as a viscous, yellow oil.

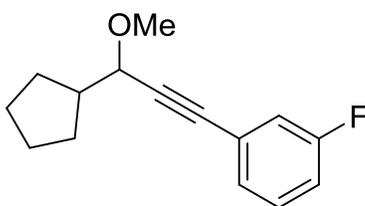
FT-IR: ν 2947.36, 1725.08, 1589.90, 1312.98, 1274.84, 1167.85, 1127.42, 1109.46, 1068.63, 133.26, 101.93, 759.11 cm^{-1}

¹H-NMR: (CDCl₃, 400 MHz) δ 7.66 (dddt, *J* = 21, 7.6, 1.4, 0.6 Hz, 2H), 7.54-7.42 (m, 6H), 5.33 (s, 1H), 3.51 (s, 3H)

¹³C-NMR: (CDCl₃, 100 MHz) δ 137.15, 134.20, 131.83, 131.63, 131.53, 131.43 (d, *J* = 1.5 Hz), 129.13, 128.47, 125.86 (q, *J* = 5.4 Hz), 122.54, 122.09, 120.53 (d, *J* = 1.5 Hz), 109.99, 91.81, 83.90, 72.67, 55.90

HRMS: C₁₇H₁₂BrF₃O: calculated: 368.0024, found: 368.0036

1-(3-cyclopentyl-3-methoxyprop-1-yn-1-yl)-3-fluorobenzene (7a)



Derived from (dimethoxymethyl)cyclopentane (**A7**) (14.4 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro((3-fluorophenyl)ethynyl)borate (**S6**) (24.9 mg, 0.11 mmol, 1.1 equiv.) and HBF₄·OEt₂ (15.1 μL, 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile, following **procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (19:1) afforded product **7a** (18.9 mg, 81% yield) as a clear, colourless oil.

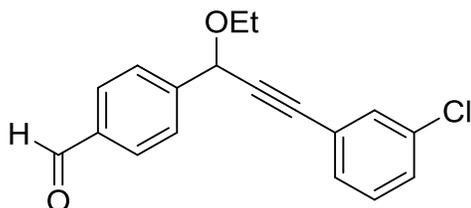
FT-IR: ν 2952.03, 2846.42, 1609.3, 1579.88, 1486.23, 1169.74, 1149.34, 1096.27, 870.03, 782.35, 681.05 cm⁻¹

¹H-NMR: (CDCl₃, 400 MHz) δ 7.29-7.19 (m, 2H), 7.13 (ddd, *J* = 9.4, 2.5, 1.4 Hz, 1H), 7.02 (tdd, *J* = 8.4, 2.7, 1.2 Hz, 1H), 4.02 (d, *J* = 7.0 Hz, 1H), 3.47 (s, 3H), 2.35-2.25 (m, 1H), 1.85-1.81 (m, 2H), 1.69-1.61 (m, 2H), 1.59-1.55 (m, 2H), 1.53-1.47 (m, 2H)

¹³C-NMR: (CDCl₃, 100 MHz) δ 162.31 (d, *J* = 246 Hz), 129.80 (d, *J* = 9.2 Hz), 127.59 (d, *J* = 3.7 Hz), 124.73, 118.52 (d, *J* = 22 Hz), 115.53 (d, *J* = 22 Hz), 88.81, 84.64 (d, *J* = 3.1 Hz), 75.88, 56.79, 44.34, 29.14, 28.66, 25.74, 25.66

HRMS: C₁₅H₁₇FO: calculated: 232.1263, found: 232.1259

4-(3-(3-chlorophenyl)-1-ethoxyprop-2-yn-1-yl)Benzaldehyde (**8a**)



Derived from 4-(diethoxymethyl)benzaldehyde (**A13**) (21.5 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro((3-chlorophenyl)ethynyl)borate (**S7**) (26.7 mg, 0.11 mmol, 1.1 equiv.) and $\text{HBF}_4 \cdot \text{OEt}_2$ (15.1 μL , 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile, following **procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (19:1) afforded product **8a** (18.3 mg, 62% yield) as a clear, colourless oil.

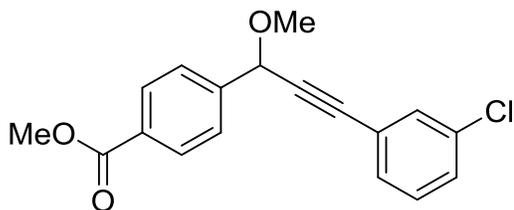
FT-IR: ν 2957.35, 2831.47, 1699.59, 1607.59, 1303.53, 1206.16, 1075.46, 839.69, 811.77, 782.41, 680.53 cm^{-1}

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz) δ 10.04 (s, 1H), 7.91 (d, $J = 8.2$ Hz, 2H), 7.74 (d, $J = 8.2$ Hz, 2H), 7.46 (t, $J = 1.8$ Hz, 1H), 7.36-7.30 (m, 2H), 7.27-7.23 (m, 1H), 3.85 (dq, $J = 9.0$, 7.0 Hz, 1H), 3.64 (dq, $J = 9.0$, 7.0 Hz, 1H), 1.31 (t, $J = 7.0$ Hz, 3H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz) δ 191.79, 145.27, 136.31, 134.19, 131.67, 130.00, 129.91, 129.56, 129.02, 127.79, 123.91, 87.62, 86.45, 71.24, 64.52, 15.14

HRMS: $\text{C}_{18}\text{H}_{15}\text{ClO}_2$; calculated: 298.0761, found: 298.0752

Methyl 4-(3-(3-chlorophenyl)-1-methoxyprop-2-yn-1-yl)benzoate (**8b**)



Derived from methyl 4-(dimethoxymethyl)benzoate (**A14**) (21.0 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro((3-chlorophenyl)ethynyl)borate (**S7**) (26.7 mg, 0.11 mmol, 1.1 equiv.) and $\text{HBF}_4 \cdot \text{OEt}_2$ (15.1 μL , 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile,

following **procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (6.5:1) afforded product **8b** (27.7 mg, 88% yield) as a crystalline, white solid.

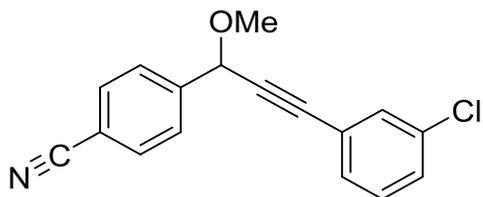
FT-IR: ν 2944.14, 2887.21, 1726.03, 1436.73, 1273.87, 1186.08, 1085.76, 999.45, 783.19, 748.84, 705.60, 675.13 cm^{-1}

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz) δ 8.07 (d, $J = 8.2$ Hz, 2H), 7.63 (d, $J = 8.2$ Hz, 2H), 7.47 (t, $J = 1.8$ Hz, 1H), 7.37-7.30 (m, 2H), 7.27-7.25 (m, 1H), 5.34 (s, 1H), 3.92 (s, 3H), 3.51 (s, 3H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz) δ 166.70, 145.27, 143.13, 134.19, 131.67, 130.25, 129.91, 129.88, 129.57, 129.01, 127.23, 123.92, 87.26, 72.77, 56.25, 52.15

HRMS: $\text{C}_{18}\text{H}_{15}\text{ClO}_3$; calculated: 314.0710, found: 314.0706

4-(3-(3-chlorophenyl)-1-methoxyprop-2-yn-1-yl)benzotrile (**8c**)



Derived from 4-(dimethoxymethyl)benzotrile (**A10**) (17.7 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro((3-chlorophenyl)ethynyl)borate (**S7**) (26.7 mg, 0.11 mmol, 1.1 equiv.) and $\text{HBF}_4 \cdot \text{OEt}_2$ (15.1 μL , 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile, following **Procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (gradient: 100:0 to 3:1) afforded product **8c** (24.2 mg, 86% yield) as a crystalline, white solid.

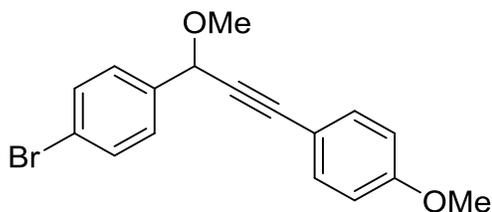
FT-IR: ν 2976.57, 2899.41, 2229.05, 1407.17, 1078.07, 1010.04, 872.89, 785.70, 676.98 cm^{-1}

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz) δ 7.71-7.66 (m, 4H), 7.46 (t, $J = 1.8$ Hz, 1H), 7.37-7.33 (m, 2H), 7.28-7.24 (m, 1H), 5.33 (s, 1H), 3.53 (s, 3H)

¹³C-NMR: (CDCl₃, 100 MHz) δ 143.46, 134.25, 132.40, 131.67, 129.91, 129.63, 129.21, 127.86, 123.62, 118.57, 112.33, 87.12, 86.58, 72.56, 56.44

HRMS: C₁₇H₁₂ClNO: calculated: 281.0607, found: 281.0602

1-bromo-4-(1-methoxy-3-(4-methoxyphenyl)prop-2-yn-1-yl)benzene (9a)

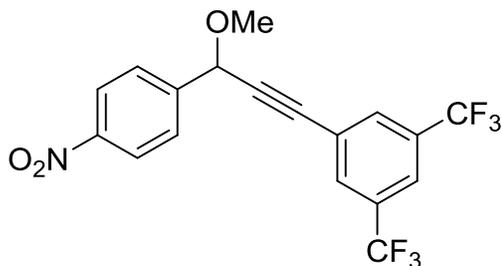


Derived from 1-bromo-4-(Dimethoxymethyl)benzene (**A4**) (23.6 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro((4-methoxyphenyl)ethynyl)borate (**S10**) (26.2 mg, 0.11 mmol, 1.1 equiv.) and HBF₄·OEt₂ (15.1 μL, 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile for 70 min, following **Procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (9:1) afforded product **9a** (6.6 mg, 20% yield) as a yellow oil.

¹H-NMR: (CDCl₃, 400 MHz) δ 7.53-7.51 (m, 2H), 7.46-7.40 (m, 4H), 6.86-6.83 (m, 2H), 5.25 (s, 1H), 3.82 (s, 3H), 3.48 (s, 3H)

¹³C-NMR: (CDCl₃, 100 MHz) δ 137.85, 133.26, 131.58, 129.12, 122.35, 114.34, 113.94, 91.35, 84.64, 72.85, 55.29, 10.35

1-(3-methoxy-3-(4-nitrophenyl)prop-1-yn-1-yl)-3,5-bis(trifluoromethyl)benzene (10a)

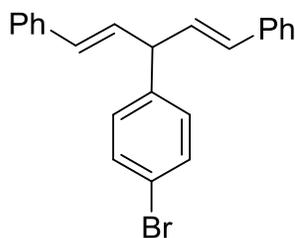


Derived from (dimethoxymethyl)-4-nitrobenzene (**A9**) (19.7 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro((3,5-bis(trifluoromethyl)phenyl)ethynyl)borate (**S9**) (37.8 mg, 0.11 mmol, 1.1 equiv.) and $\text{HBF}_4 \cdot \text{OEt}_2$ (15.1 μL , 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile for 70 min, following **Procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (3:1) afforded product **10a** (11.7 mg, 29% yield) as a yellow liquid.

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz) δ 8.29-8.27 (m, 2H), 7.90-7.85 (m, 3H), 7.74-7.42 (m, 2H), 5.39 (s, 1H), 3.57 (s, 3H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz) δ 148.05, 144.78, 132.12 (q, $J = 34$ Hz), 131.79-131.67 (m), 131.61, 127.90, 124.15 (d, $J = 6.9$ Hz), 123.92, 86.99, 85.37, 72.27, 56.79

((1E,4E)-3-(4-bromophenyl)penta-1,4-diene-1,5-diyl)dibenzene (12a)

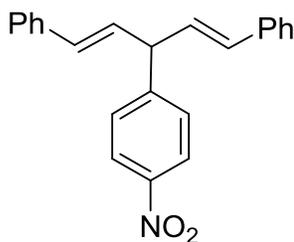


Derived from 1-bromo-4-(dimethoxymethyl)benzene (**A4**) (23.6 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro(trans-styryl)borate (23.1 mg, 0.11 mmol, 1.1 equiv.) and $\text{HBF}_4 \cdot \text{OEt}_2$ (15.1 μL , 0.11 mmol, 1.1 equiv.) in 1.0 mL of acetonitrile for 70 min, following **Procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (19:1) afforded product **12a** (14.0 mg, 37% yield) as a yellow oil.

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz) δ 7.49-7.19 (m, 15H), 6.52-6.40 (m, 4H), 4.39-4.35 (m, 1H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz) δ 142.48, 141.74, 137.05, 136.23, 132.76, 131.69, 131.60, 131.24, 131.13, 130.97, 129.91, 129.65, 128.69, 128.57, 128.54, 128.09, 127.82, 127.48, 127.39, 126.74, 126.29, 126.28, 121.00, 51.63, 50.98

((1E,4E)-3-(4-nitrophenyl)penta-1,4-diene-1,5-diyl)dibenzene (13a)

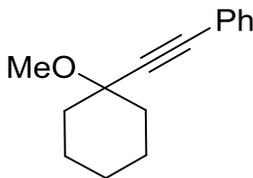


Derived from (dimethoxymethyl)-4-nitrobenzene (**A9**) (19.7 mg, 0.10 mmol, 1.0 equiv) Potassium trifluoro(trans-styryl)borate (23.1 mg, 0.11 mmol, 1.1 equiv.) and HBF₄·OEt₂ (15.1 μL, 0.11 mmol, 1.1 equiv.) in 1.0 mL of propionitrile at -60 °C, following **Procedure 3**. Purification by silica gel chromatography using hexanes/diethyl ether (14:1) afforded product **13a** (9.5 mg, 35 % conversion). 36 % of **A9** Starting material was also recovered as well as 26 % aldehyde.

¹H-NMR: (CDCl₃, 400 MHz) δ 8.18-8.16 (m, 2H), 7.53-7.50 (m, 2H), 7.40-7.23 (m, 10H), 6.72-6.68 (m, 1H), 6.53-6.44 (m, 3H), 4.44 (t, *J* = 5.9 Hz, 1H)

¹³C-NMR: (CDCl₃, 100 MHz) δ 146.76, 143.75, 141.84, 137.07, 136.96, 131.46, 130.78, 129.96, 128.93, 128.83, 128.59, 128.08, 127.5, 128.98, 127.57, 126.98, 126.77, 126.30, 123.98, 123.92, 51.78

((1-methoxycyclohexyl)ethynyl)benzene (14a)



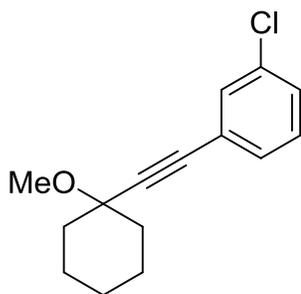
Derived from 1,1-dimethoxycyclohexane (**K1**) (14.4 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro(phenylethynyl)borate (**S1**) (31.2 mg, 0.15 mmol, 1.5 equiv.) and HBF₄·OEt₂ (20.6 μL, 0.15 mmol, 1.5 equiv.) in 1.0 mL of propionitrile, following **Procedure 4**. Purification by silica gel chromatography using hexanes/diethyl ether (gradient: 100:0 → 9:1) afforded product **14a** (11.2 mg, 53% yield) as a clear, colourless oil.

FT-IR: ν 2932.83, 2856.64, 1489.61, 1443.89, 1092.20, 925.33, 754.99, 690.32 cm^{-1}

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz) δ 7.46-7.43 (m, 2H), 7.32-7.29 (m, 3H), 3.44 (s, 3H), 2.02-1.99 (m, 2H), 1.73-1.54 (m, 7H), 1.34-1.32 (m, 1H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz) δ 131.69, 128.21, 128.09, 123.05, 90.31, 86.12, 74.35, 50.79, 36.83, 25.51, 22.90

1-chloro-3-((1-methoxycyclohexyl)ethynyl)benzene (14b)



Derived from 1,1-dimethoxycyclohexane (**K1**) (14.4 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro((3-chlorophenyl)ethynyl)borate (**S7**) (36.4 mg, 0.15 mmol, 1.5 equiv.) and $\text{HBF}_4 \cdot \text{OEt}_2$ (20.6 μL , 0.15 mmol, 1.5 equiv.) in 1.0 mL of propionitrile, following **Procedure 4**. Purification by silica gel chromatography using hexanes/diethyl ether (gradient: 100:0 \rightarrow 9:1) afforded product **14b** (12.6 mg, 51% yield) as a clear, colourless oil.

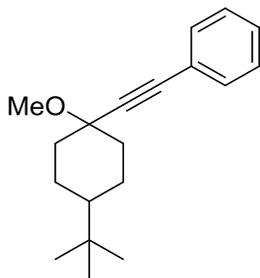
FT-IR: ν 2932.77, 2856.81, 1592.90, 1473.79, 1446.85, 1092.37, 925.40, 781.85, 704.05, 681.08 cm^{-1}

$^1\text{H-NMR}$: (CDCl_3 , 400 MHz) δ 7.43 (t, $J = 1.6$ Hz, 1H), 7.33-7.21 (m, 3H), 3.42 (s, 3H), 2.00-1.96 (m, 2H), 1.74-1.53 (m, 7H), 1.35-1.32 (m, 1H)

$^{13}\text{C-NMR}$: (CDCl_3 , 100 MHz) δ 134.05, 131.58, 129.80, 129.44, 128.39, 124.72, 91.71, 84.72, 74.29, 50.84, 36.70, 25.44, 22.85

HRMS: $\text{C}_{15}\text{H}_{17}\text{ClO}$: calculated: 248.0968, found: 248.0971

((4-(tert-butyl)-1-methoxycyclohexyl)ethynyl)benzene (15a)



Derived from 4-(*t*-butyl)-1,1-dimethoxycyclohexane (**K2**) (20.0 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro(phenylethynyl)borate (**S1**) (31.2 mg, 0.15 mmol, 1.5 equiv.) and HBF₄·OEt₂ (20.6 μL, 0.15 mmol, 1.5 equiv.) in 1.0 mL of propionitrile, following **Procedure 4**. Purification by silica gel chromatography using hexanes/diethyl ether (gradient: 100:0 → 9:1) afforded product **15a** (15.9 mg, 59% yield) as a clear, colourless oil.

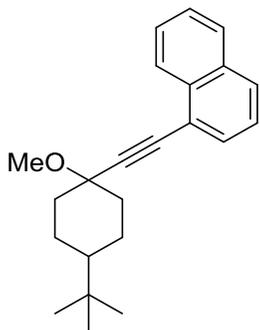
FT-IR: ν 2940.89, 2867.46, 1491.20, 1365.28, 1081.75, 1065.16, 903.68, 754.68, 690.14 cm⁻¹

¹H-NMR: (CDCl₃, 400 MHz) δ 7.44-7.41 (m, 2H), 7.31-7.28 (m, 3H), 3.38 (s, 3H), 2.27-2.22 (m, 2H), 1.68-1.54 (m, 4H), 1.37-1.26 (m, 2H), 1.08-1.01 (m, 1H), 0.87 (s, 9H)

¹³C-NMR: (CDCl₃, 100 MHz) δ 131.68, 128.18, 128.02, 123.05, 91.78, 84.00, 71.68, 50.80, 47.24, 36.19, 32.44, 27.54, 21.80

HRMS: C₁₉H₂₆O: calculated: 270.1984, found: 270.1986

1-((4-(tert-butyl)-1-methoxycyclohexyl)ethynyl)naphthalene (15b)



Derived from 4-(*t*-butyl)-1,1-dimethoxycyclohexane (**K2**) (20.0 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro((4-naphthyl)ethynyl)borate (**S3**) (38.7 mg, 0.15 mmol, 1.5 equiv.) and HBF₄·OEt₂ (20.6 μL, 0.15 mmol, 1.5 equiv.) in 1.0 mL of propionitrile, following **Procedure 4**. Purification by silica gel chromatography using hexanes/diethyl ether (gradient: 100:0 → 9:1) afforded product **15b** (15.1 mg, 47% yield) as a clear, colourless oil.

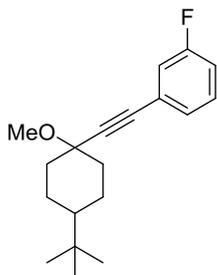
FT-IR: ν 2940.29, 2866.54, 1393.99, 1364.82, 1129.70, 1075.75, 797.19, 771.03 cm⁻¹

¹H-NMR: (CDCl₃, 400 MHz) δ 8.31 (dd, J = 8.2, 0.8 Hz, 1H), 7.85-7.80 (m, 2H), 7.67 (dd, J = 7.0, 1.2 Hz, 1H), 7.59-7.50 (m, 2H), 7.41 (dd, J = 8.2, 7.4 Hz, 1H), 3.48 (s, 3H), 2.40-2.35 (m, 2H), 1.81-1.74 (td, J = 13.7, 3.9 Hz, 2H), 1.64-1.60 (m, 2H), δ 1.44-1.36 (m, 2H), 1.14-1.10 (m, 1H), 0.90 (s, 9H)

¹³C-NMR: (CDCl₃, 100 MHz) δ 133.34, 133.15, 130.36, 128.53, 128.24, 126.68, 126.30, 126.10, 125.15, 120.66, 96.90, 82.04, 72.03, 51.03, 47.29, 36.43, 32.48, 27.56, 21.87

HRMS: C₂₃H₂₈O: calculated: 320.2140, found: 320.2142

1-((4-(*tert*-butyl)-1-methoxycyclohexyl)ethynyl)-3-fluorobenzene (**15c**)



Derived from 4-(*t*-butyl)-1,1-dimethoxycyclohexane (**K2**) (20.0 mg, 0.10 mmol, 1.0 equiv.), Potassium trifluoro((3-fluorophenyl)ethynyl)borate (**S6**) (33.9 mg, 0.15 mmol, 1.5 equiv.) and HBF₄·OEt₂ (20.6 μL, 0.15 mmol, 1.5 equiv.) in 1.0 mL of propionitrile, following **Procedure 4**. Purification by silica gel chromatography using hexanes/diethyl ether (gradient: 100:0 → 9:1) afforded product **15c** (17.9 mg, 62% yield) as a white solid.

FT-IR: ν 2931.81, 1259.22, 1072.43, 1014.69, 862.87, 797.72, 775.11 cm⁻¹

¹H-NMR: (CDCl₃, 400 MHz) δ 7.27-7.19 (m, 2H), 7.13-7.10 (ddd, *J* = 9.6, 2.5, 1.2 Hz, 1H), 7.03-6.98 (m, 1H), 3.37 (s, 3H), 2.25-2.21 (m, 2H), 1.66-1.54 (m, 4H), 1.36-1.26 (m, 2H), 1.08-1.00 (m, 1H), 0.87 (s, 9H)

¹³C-NMR: (CDCl₃, 100 MHz) δ 129.74 (d, *J* = 9.2 Hz), 127.55 (d, *J* = 3.1 Hz), 124.85, 118.60, 118.38, 115.38 (d, *J* = 21 Hz), 92.81, 82.81, 71.65, 50.86, 47.19, 36.08, 32.44, 27.51, 21.74

HRMS: C₁₉H₂₅FO: calculated: 288.1889, found: 288.1891

