PRECISION DEUTERATION AND HYDROFUNCTIONALIZATION OF ARYL ALKYNES AND ALKENES

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by

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ABSTRACT
PRECISION DEUTERATION AND HYDROFUNCTIONALIZATION OF
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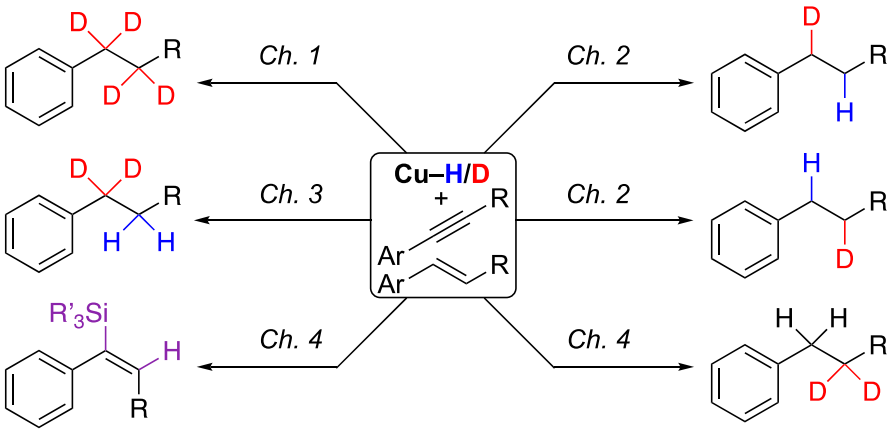
The similar nature of the hydrogen atom to its isotope, deuterium, allows for the simple exchange of hydrogen atoms for deuterium atoms in drug molecules to alter the absorption, distribution, metabolism, and excretion properties. Installing the deuterium functionality into a specific site in the molecule is essential. Selective hydrofunctionalization reactions of alkynes and alkenes using the highly reactive catalytic Cu–H species have been well developed, and synthetic organic chemistry methods to selectively incorporate one or two deuterium atoms into the benzylic site of organic compounds, a key metabolic position, are elusive. A Cu–H catalytic approach offers selectivity and reactivity to undergo a transfer hydrodeuteration of alkynes or alkenes. Initiating the reaction development with a transfer hydrogenation protocol demonstrated high chemoselectivity on a diverse array of aryl alkynes. Expanding this method to a transfer deuteration generated aryl alkane products with up to 5 deuterium atoms, 2 of which were located at the benzylic carbon. Preliminary regioselective results were explored, providing 2 deuterium atoms at the benzylic position and 2 hydrogen atoms at the homobenzylic position (*Chapter 1)*. One deuterium atom was installed exclusively into aryl alkanes from aryl alkenes using a transfer hydrodeuteration reaction, and MRR, molecular rotational resonance spectroscopy, was explored as an analytical tool to detect different isotopic species present in the product mixture, confirming the highest selectivity reported to date (*Chapter 2*). Two deuterium atoms were installed selectively into the benzylic site of aryl alkanes from the transfer hydrodeuteration of aryl alkynes, forming α,α-d_2-alkane products, including complex small molecules. This was based on the electronic stability of the DTB-DPPBz ligand, which was explored both experimentally and computationally (*Chapter 3).* Exchanging the silane source for diphenylsilane and eliminating the alcohol allowed for a regio-, stereo-, and chemoselective hydrosilylation of aryl alkynes to be accomplished on biologically relevant small molecules, as well as 4 drug analogues, to access α-*E*-vinylsilanes. Additionally, this protocol permitted the selective deuterosilylation reaction to access β,β-d_2-alkane products (*Chapter 4)*. Through extensive reaction development, optimization, and mechanistic exploration, highly selective methods of precision deuteration and hydrosilylation were achieved by using a Cu–H catalytic protocol.



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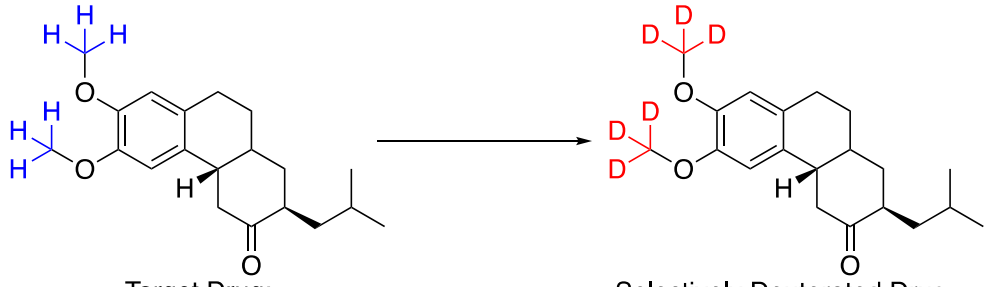
Introduction

Deuterium, ^{2}H or D, is a stable isotope of hydrogen, differing only in the addition of one neutron to the nucleus. Due to the extra neutron, D is slightly heavier than H (2.01 g/mol vs. 1.01 g/mol). Additionally, deuterium-carbon bonds can be up to ten times stronger than hydrogen-carbon bonds.[1] In 1934, Harold Clayton Urey won The Nobel Prize in Chemistry "for his discovery of heavy hydrogen".[2] His discovery was confirmed by distilling liquid hydrogen and observing a hydrogen isotope that was twice as heavy as hydrogen. It was later found that deuterium has a natural abundance of about 0.02% of all of the naturally occurring hydrogen in the ocean.

Deuterated small molecules are thoroughly used in research and medicine because of their similarity to hydrogen-containing small molecules. There are many beneficial applications of deuterated small molecules. From a physical and analytical chemistry standpoint, deuterated small molecules can be used as standards for high-resolution mass spectrometry, containing three-four deuterium atoms.[3] From an organometallic and synthetic organic chemistry perspective, deuterated small molecules can be used to explain and understand reaction mechanisms, and to perform kinetic isotope effect (KIE) measurements.[4, 5] Finally, labeling a metabolically significant site on drug molecules with deuterium helps to alter the drug's absorption, distribution, metabolism, and excretion (ADME) properties.[6-8]

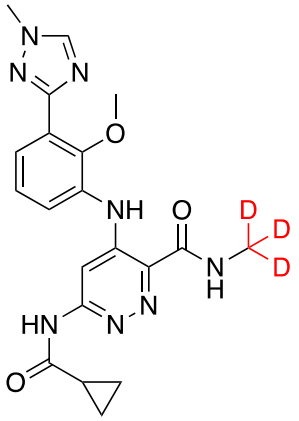
Scheme 1: Tetrabenazine vs Deutetrabenazine



The development of deuterated small molecule drugs is an up-and-coming field of study in the pharmaceutical industry, as seen in 2017 by the first FDA approved deuterated drug, Deutetrabenazine (Scheme 1).[1, 9] The deuterium incorporation provides improved pharmacokinetic properties.

Deutetrabenazine is used to treat chorea associated with Huntington's disease and with the chemical change of exchanging the hydrogen atoms (blue) for deuterium atoms (red), the drug is metabolized slower and has an increased half-life. This allows the deuterated molecule to remain as an active drug in the body for a longer period of time. Since the drug remains active longer, less frequent dosing is needed and therefore a decrease in side effects such as sleepiness, depression, and anxiety, is observed. Clinical trials demonstrated that dosing only twice per day was needed compared to three times per day for Tetrabenazine.[1]

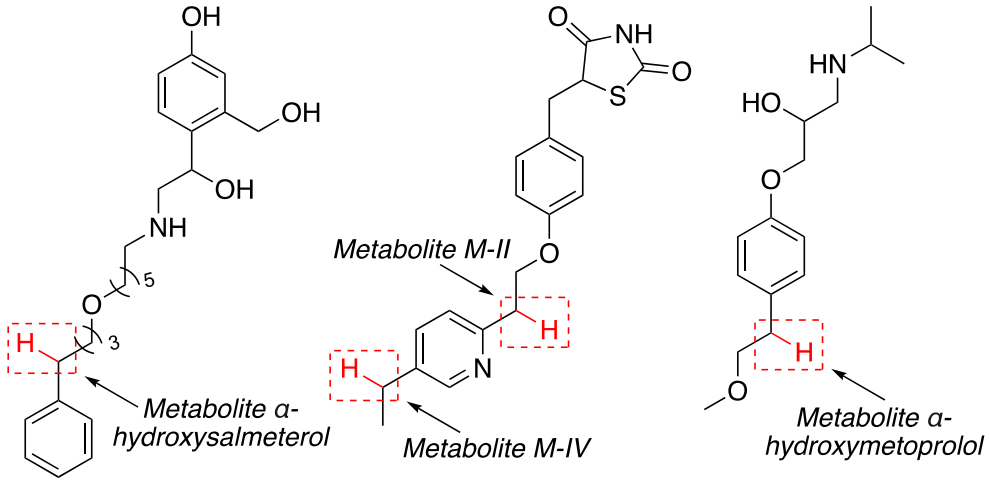
Scheme 2: Deucravacitinib



Selectively Deuterated Drug:
Deucravacitinib

Additionally, in 2022 the FDA approved Deucravacitinib for psoriasis and other autoimmune diseases (Scheme 2).[10] The deuterium incorporation in this molecule can improve drug selectivity.[11] This prevents the formation of non-selective metabolites and ultimately improves this drug's effect on the body.

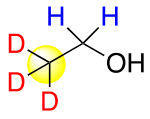
Scheme 3: Drug Molecules Containing Benzylic Metabolites



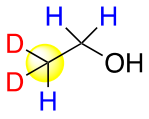
As seen with Deutetrabenazine, the substitution of a deuterium atom for a hydrogen atom in a drug molecule can prolong the half-life of the drug in the body due to a slower rate of metabolism and degradation in the liver. This allows for greater efficacy of the drug molecule, and a decrease of side effects due to less frequent dosing, while retaining the original potency. An important metabolically active site in certain drug molecules is the benzylic site or the α-arene position, as demonstrated in Salmeterol, Pioglitazone, and Metoprolol (Scheme 3).[12-15] Due to the higher bond dissociation energy of a C–D bond than a C–H bond, selective installation of deuterium into the exclusive benzylic site of bioactive molecules and drugs has the potential to improve the drug's metabolic properties, while retaining the original function.[16-18] The challenge lies in the methodology to undergo such a selective transformation. Precision deuteration and hydrofunctionalization of arene containing small molecules at the benzylic site proves to be an underexplored field in organic chemistry.

Scheme 4: Isotopic Impurities Present in Deuterated Compounds

Isotopologues

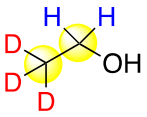


Chemical formula: $C_2H_3D_3O$
Exact mass: 49.0607 g/mol
Molecular Weight: 49.0873 g/mol

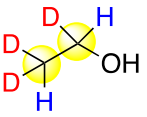


Chemical formula: $C_2H_4D_2O$
Exact mass: 48.0544 g/mol
Molecular Weight: 48.0812 g/mol

Isotopomers



Chemical formula: $C_2H_3D_3O$
Exact mass: 49.0607 g/mol
Molecular Weight: 49.0873 g/mol



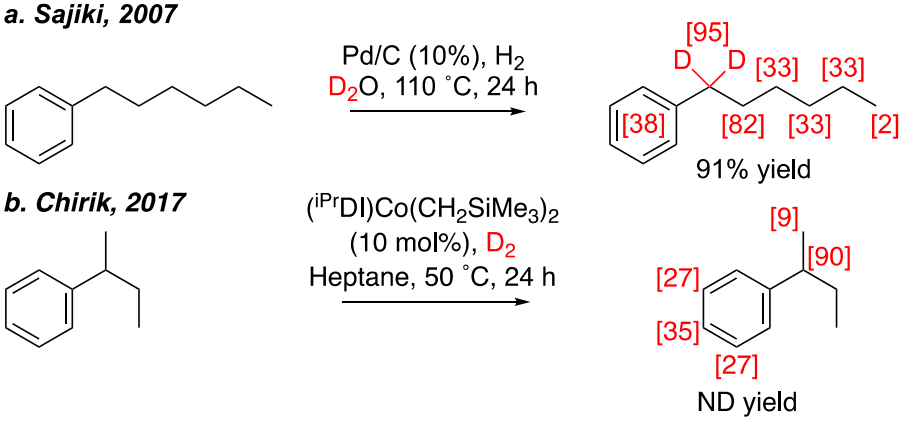
Chemical formula: $C_2H_3D_3O$
Exact mass: 49.0607 g/mol
Molecular Weight: 49.0873 g/mol

Precise and selective deuteration methods are crucial because of the potential for isotopic mixtures to be generated. Isotopic mixtures can contain isotopologues, differing in the number of isotopic substitutions, and isotopomers, differing in the position of each isotopic substitution (Scheme 4).[19] Common spectroscopic techniques have limitations in the characterization of isotopic product mixtures. Mass spectrometry (MS) can only analyze the isotopologue composition because of the difference in mass (g/mol). Nuclear magnetic resonance (NMR) cannot perform the composition analysis when isotopologues and isotopomers share deuterium substitution at the same atom, because the different isotopic species will contribute to the same $^{1}H/^{2}H$ resonances. Additionally, due to the similarity of the physical properties of hydrogen to deuterium, isotopic mixtures of isotopologues and isotopomers are inseparable using common purification techniques.

For the development of highly selective reactions to install deuterium into precise locations, especially if this chemistry is eventually adopted in the synthesis of novel deuterated pharmaceuticals, NMR and MS characterization tools alone are not appropriate. However, molecular rotational resonance (MRR) spectroscopy can determine product ratios in complex isotopic product mixtures.[20, 21] Professor Brooks H. Pate at the University of Virginia, and BrightSpec Inc., have the ability to obtain a unique spectral signature for each isotopic variant in a product mixture using MRR. MRR spectroscopy has exceptionally high spectral resolution to determine the signals for each isotopic variant, even in complex mixtures. The

rotational spectra for each isotopic variant can be predicted using quantum chemistry, so there is no need for reference samples. Although the identification and quantification of isotopologues and isotopomers in isotopic product mixtures are feasible through MRR, selective deuterium incorporation methods are still necessary because of the lack of ease in separating the reaction isotopic products for deuterated-molecule applications.

Scheme 5: Hydrogen Isotope Exchange



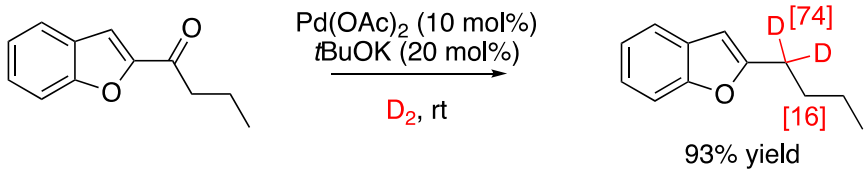
Selective benzylic deuterium incorporation methodology has been explored in the past, but key challenges were faced. Hydrogen isotope exchange reactions (HIE) can be used to promote the exchange of a benzylic hydrogen atom for a deuterium atom.[22, 23] However, these methods lack control in the quantity and precise placement of the deuterium atom. HIE reactions can occur through either heterogeneous or homogeneous catalysis, although heterogenous catalyzed HIE reactions tend to lead to unspecific deuterium incorporation with multiple deuterium atoms in a molecular scaffold.[22, 24-26] This can be seen in Scheme 5a where Sajiki and coworkers report a Pd/C catalyzed heterogeneous HIE reaction.[15, 25] The deuterium incorporation is unselective for the benzylic site, and the transformation requires high temperature and an inert atmosphere. For some substrates, the transformation required a repeat procedure on the resulting mixture from the first run to obtain full deuterium conversion.

Even though homogenous catalyzed HIE reactions tend to be slightly more selective than heterogeneous catalysis, there remains room for improvement. The Chirik group developed a cobalt catalyzed HIE method (Scheme 5b), using expensive and flammable D_2 gas.[26] The reaction demonstrated

over-deuteration on the aryl ring and unselective deuterium incorporation at the benzylic substituted methyl substituent as well. No yields were reported, not determined (ND), and the deuterium incorporation was only characterized by NMR.

Scheme 6: Reductive Deuteration Method

Su, 2020

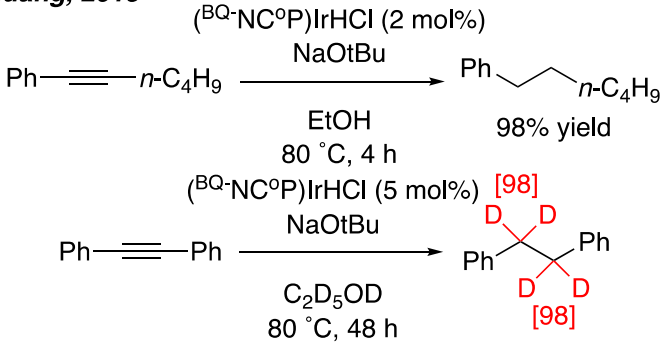


Reductive deuteration, involving the reduction of a carbonyl functionality, is another feasible method for deuterium incorporation at the benzylic site. However, over and/or under deuteration are observed at the benzylic and homobenzylic sites in the example published by Su and coworkers in 2020 (Scheme 6).[27] Therefore, the ultimate goal was to develop a regioselective precision deuteration method, that allowed for high levels of deuterium incorporation at specific sites on arene containing small molecules.

The organic chemistry reaction of the reduction of an alkyne to an alkane is commonly done with a heterogenous catalyst and hydrogen gas.[28] However, the use of H_2 gas presents limitations, such as functional group compatibility and safety hazards.[28] The transfer hydrogenation of alkynes offers the same organic chemistry transformation but is a mild and selective method that obviates the use of flammable hydrogen gas.[29-32] Transfer hydrogenation is defined as the addition of hydrogen to a molecule from a source other than H_2 gas.[33] The hydrogen donors are relatively inexpensive, commercial, and easy to handle. Although transfer hydrogenation has been explored for the reduction of polarized π-functionality, methods for the reduction of alkynes to alkanes using a transfer hydrogenation protocol are scarce.[31] Based on the significance of selectively deuterated small molecules, a transfer hydrogenation method for the reduction of alkynes to alkanes could be adapted to a transfer deuteration method, and ultimately a regioselective transfer hydrodeuteration method. This would allow for one proton and one deuterium atom to be added at specific sites on a molecule in a unique mechanism. The transfer hydrodeuteration reaction of aryl alkynes is extremely novel, as no groups have demonstrated such a transformation to the best of our knowledge.

Scheme 7: Transfer Hydrogenation and Transfer Deuteration of Aryl Alkynes

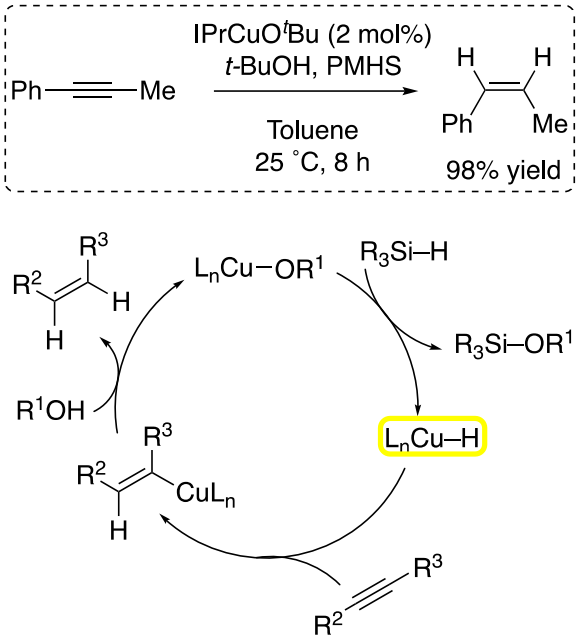
Huang, 2018



In 2018, Huang and coworkers elegantly demonstrate their work exploring the transfer hydrogenation and transfer deuteration of aryl alkynes (Scheme 7).[34] A precious-metal catalyzed transfer hydrogenation of an alkyne (1-phenyl-1-hexyne) to the corresponding alkane (1-phenyl-1-hexane) was one example explored. Other transfer hydrogenation examples were presented, as well as a transfer deuteration example. 1,2-Diphenylethyne underwent transfer deuteration resulting in 98% deuterium incorporation at both sites of the symmetric alkane.

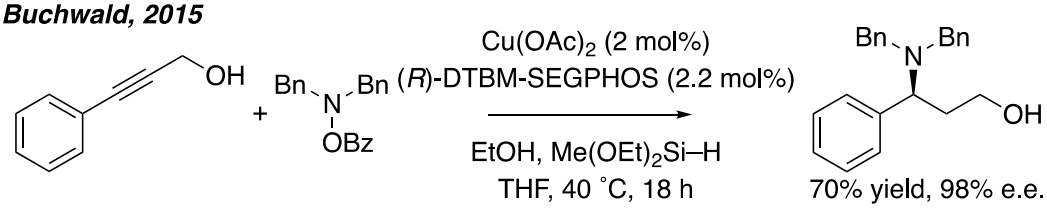
In 2013, Lalic and coworkers published their work using the first-row transition metal, copper, as a base metal that offers low cost and global availability to undergo transfer hydrogenation of alkynes to *cis*-alkenes (Scheme 8).[35] They propose that a catalytic copper species initially reacts with a Si–H source to generate the highly reactive $L_nCu–H$, which will insert across the alkyne (1-phenyl-1-propyne) to form the vinyl-copper species, which then undergoes proto-decupration with an alcohol to generate the corresponding *cis*-alkene. This reaction was optimized to perform a semi-reduction of alkynes to their respective *cis*-alkenes, and no over reduction to alkane was observed.

Scheme 8: Transfer Hydrogenation to *cis*-alkenes
Lalic, 2013

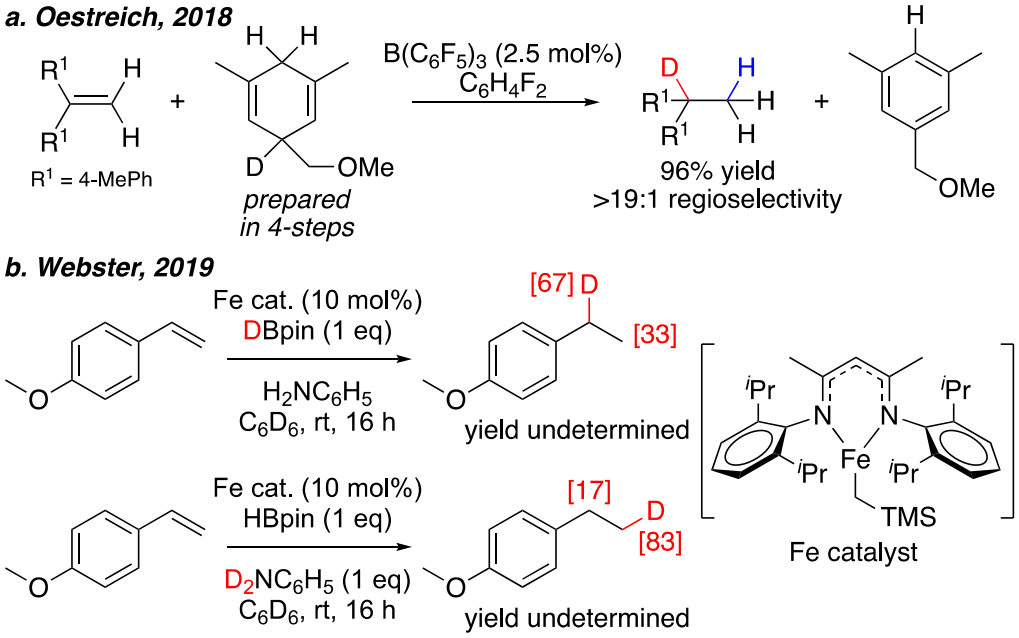


The formation of the highly reactive Cu–H catalytic species has been explored for various hydrofunctionalization reactions of both alkynes and of alkenes.[35-52] The alkyne compounds have the opportunity to undergo hydrofunctionalization twice with diverse functional group combinations, minimizing experimentation, cost, and waste. These reactions require sufficient reactivity and accurate selectivity to control the hydrofunctionalization. A novel, highly selective hydroamination of alkynes using the reactive Cu–H catalytic species was demonstrated by Buchwald and coworkers in 2015 (Scheme 9).[40] With the literature reiterating that a Cu–H catalytically active species can undergo highly selective hydrofunctionalizations of either aryl alkenes or aryl alkynes, a Cu–H catalyzed hydrodeuteration reaction was appealing.

Scheme 9: Hydroamination of Alkynes
Buchwald, 2015

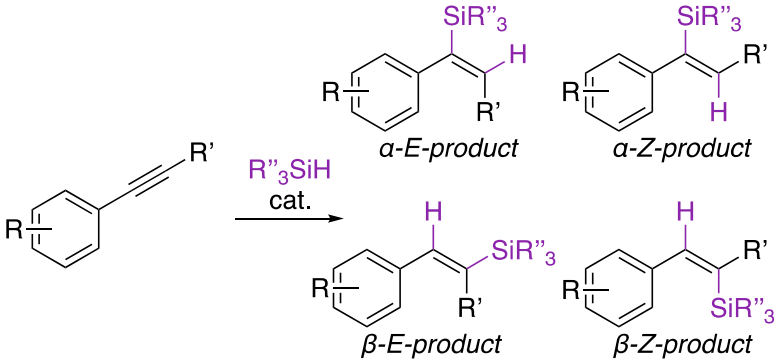


Scheme 10: Transfer Hydrodeuteration Precedent



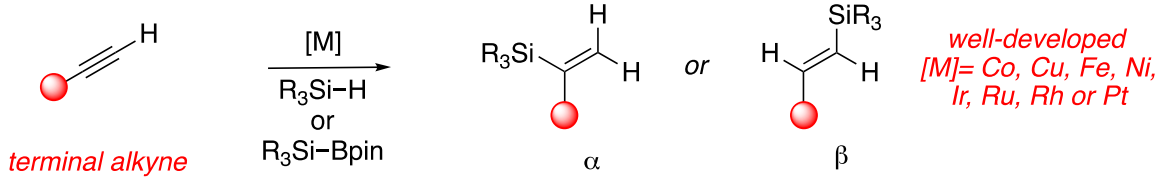
Site-selective transfer hydrodeuterations have been explored previously on aryl alkenes to obtain deuterated alkanes.[53-55] In 2018, Oestreich and coworkers published their work using a boron catalyst and a monodeuterated cyclohexa-1,4-diene to undergo transfer hydrodeuteration selectively, showing >19:1 regioselective results from activated 1,1-diarylalkenes (Scheme 10a).[54] In 2019, Webster and coworkers demonstrated the use of an iron catalyst to undergo the transfer hydrodeuteration of alkenes (Scheme 10b).[55] Using a deuterated BPin source, they observed majority deuteration at the benzylic site. Alternatively, using a deuterated amine, majority deuterium incorporation was observed at the terminal (homobenzylic) position. Using the Fe-catalyzed protocol, moderate reaction selectivity was observed.

Scheme 11: Hydrosilylation Possible Isomeric Products



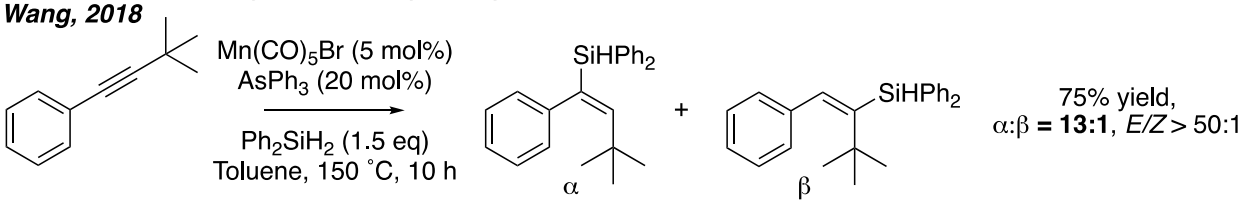
In addition to using deuterium as the functionality in a hydrofunctionalization reaction, silane can be used to undergo a hydrosilylation. In an atom economical hydrosilylation reaction, highly valuable vinylsilane products are accessible and useful in organic synthesis because of their low-toxicity, ease of handling, and stability.[56] Also, they can be used as building blocks in Denmark-Hiyama cross couplings, Fleming-Tamao Oxidations, halogenations, and reduction reactions.[57-59] However, access to a single isomer of a vinylsilane product from the hydrosilylation of alkynes is not straightforward. Isotopic product mixtures are likely to form, containing up to 4 isomers, including the α-*E*-product, α-*Z*-product, β-*E*-product, and β-*Z*-product (Scheme 11). When undergoing hydrosilylation with a terminal alkyne, the key question is in terms of regioselectivity and if the silane will position at the terminal site or the internal site of the alkyne (Scheme 12). Various metal catalyzed methods have been explored, assuring that either regioisomer can be targeted in a specific transformation.[58, 60-74]

Scheme 12: Regioselective catalytic terminal alkyne hydrosilylation



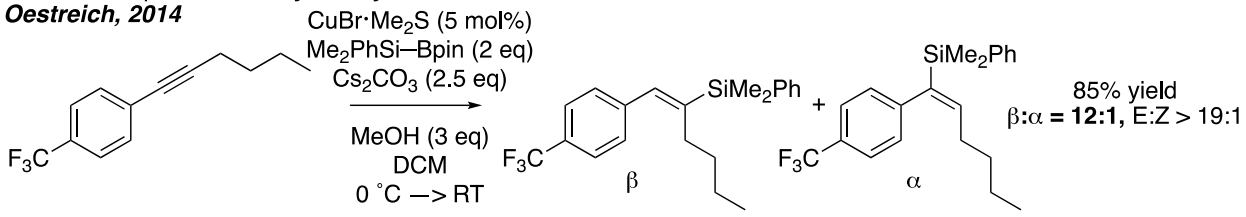
Expanding the substrate class to internal alkynes poses an additional hurdle because the question of stereoselectivity arises. To offset this challenge, symmetrical internal alkynes have been evaluated.[57, 74-81] Additionally, directing groups and steric hindrance have been used to tackle the stereoselectivity question on unsymmetrical internal alkynes.[78, 79, 82-87] Wang and coworkers were able to isolate the *tert*-butyl sterically hindered α-vinylsilane product in 75% yield, with a regioselectivity ratio of 13:1 and a stereoselectivity ratio of >50:1 (Scheme 13).[79]

Scheme 13: Sterically Hindered Hydrosilylation
Wang, 2018



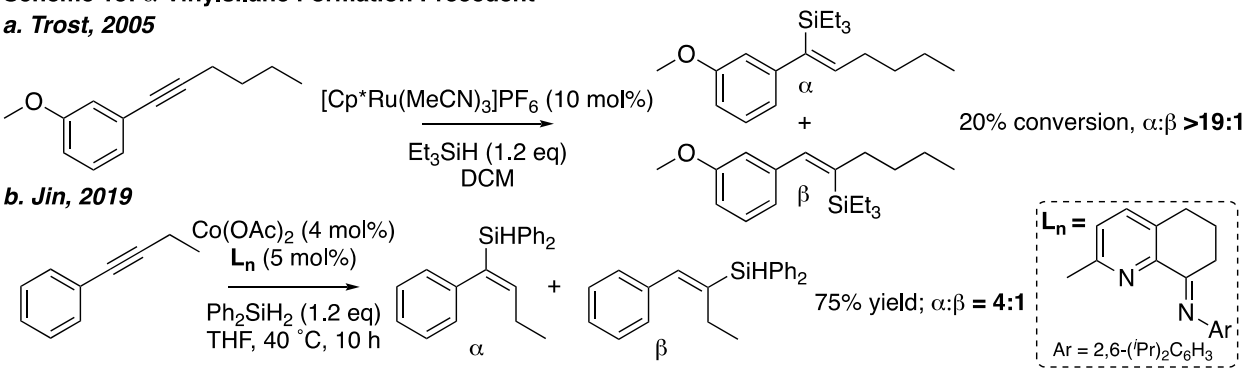
However, a non-directed, highly regio- *and* stereoselective transition metal-catalyzed hydrosilylation method of unsymmetrical internal alkynes is limited. Formation of β–vinylsilane products from unsymmertical internal alkynes is more advanced, as shown in the copper-catalyzed protocol by the Oestreich group in 2014 (Scheme 14).[88-90]

Scheme 14: β-Selective Hydrosilylation
Oestreich, 2014



However, access to the α–vinylsilane products are limited to simple hydrocarbons.[56, 57, 71, 78, 80, 91, 92] Trost and coworkers explored a regio- and stereoselective hydrosilylation of unsymmetrical internal alkynes where they demonstrated a Ru catalyzed hydrosilylation of 1-(1-hexyn-1-yl)-3-methoxybenzene.[77] They obtained only a 20% conversion to product, but observed a >19:1 regioselectivity ratio of both *trans*-addition products, providing predominately the α-Z-vinylsilane product (Scheme 15a). This result shows the promise of an α–vinylsilane forming unsymmetrical internal aryl alkyne hydrosilylation. Other groups have investigated using metals such as Co, like the Jin group in 2019, where they obtained high yields of the α–*E*–vinylsilane hydrocarbon product with a regioselectivity ratio of 4:1 (Scheme 15b).[56] However, the substrate scope is limited to simple hydrocarbon aryl alkynes without heteroatoms or varied functionality.

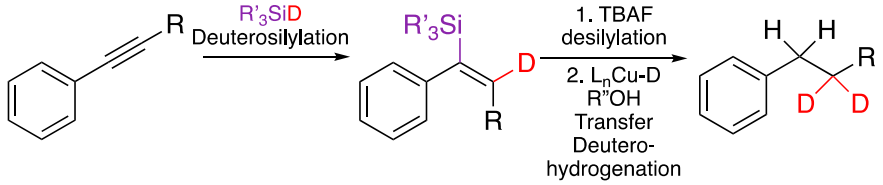
Scheme 15: α-Vinylsilane Formation Precedent
a. Trost, 2005



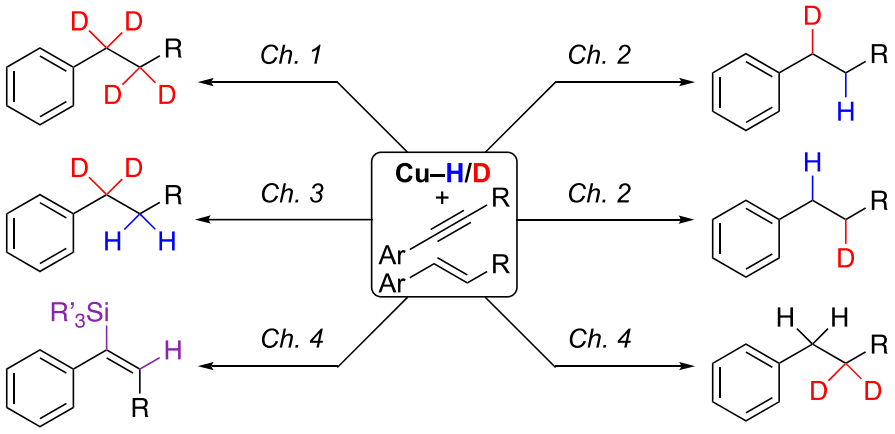
With our expertise in the highly regioselective transfer hydrodeuteration of aryl alkynes, we hypothesized that we could address the challenges associated with the hydrosilylation of unsymmetrical

internal alkynes.[93] We were inspired to investigate a Cu–H catalyzed unsymmetrical internal aryl alkyne hydrosilylation. Additionally, if these α–*E*–vinylsilane species became available, this would provide potential access to β,β-d_2-aryl alkane products through a deuterosilylation, desilylation, and then aryl alkene transfer deuterohydrogenation procedure (Scheme 16).[21]

Scheme 16: Access To β,β-d_2-Aryl Alkane Products



Therefore, by using a Cu–H catalytic system, access to α,α,β,β-d_4 (Chapter 1), α,α-d_2 (Chapter 3), β,β-d_2 (Chapter 4), α-d_1 (Chapter 2), and β-d_1 (Chapter 2) aryl alkanes, and α–*E*–vinylsilanes (Chapter 4), would be achievable.

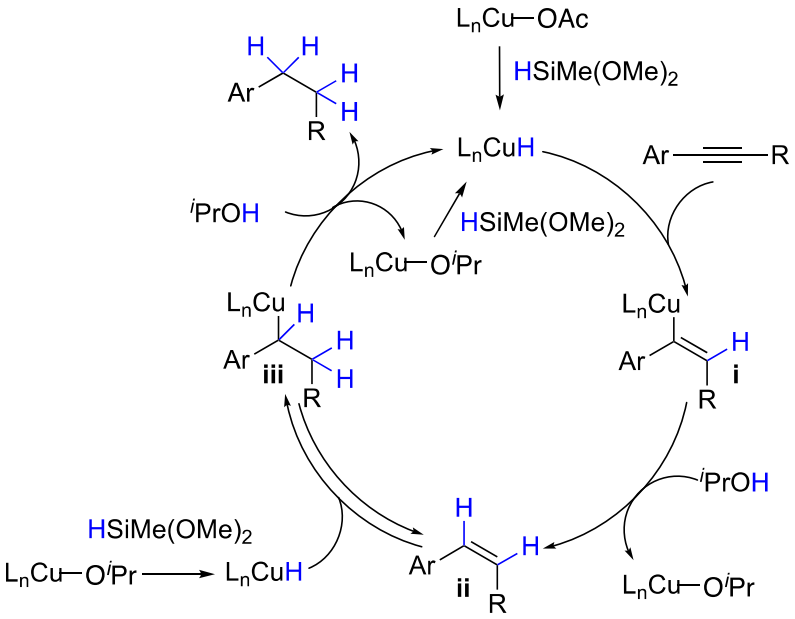


Chapter 1

Copper-Catalyzed Formal Transfer Hydrogenation/Deuteration of Aryl Alkynes

Transfer hydrogenation is defined as the addition of hydrogen to a molecule from a non-H_2 gaseous source.[33] This prevents the use of pressurized or flammable gaseous experimental set ups. The hydrogen donors are readily available, inexpensive, and easy to handle. The Huang and Lalic groups (Scheme 7 and 8) both elegantly show examples of using transfer hydrogenation on alkyne compounds.[34, 35] Huang expands their work to using transfer deuteration to obtain deuterated alkanes. These prior works encouraged us to develop a Cu–H catalyzed chemo- and regioselective method for the transfer hydrogenation, transfer deuteration, and transfer hydrodeuteration of aryl alkynes.

Scheme 17: Proposed Transfer Hydrogenation Mechanism

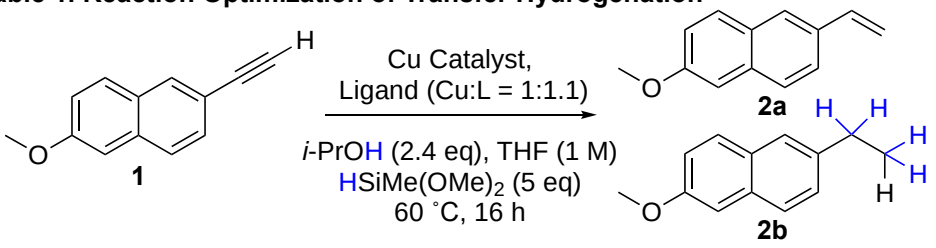


Beginning our studies with exploring a transfer hydrogenation protocol seemed most practical. We hypothesized a reaction mechanism (Scheme 17).[94] The proposed mechanism would initiate by formation of a Cu–H species from the transmetallation of the ligated $Cu(OAc)_2$ and dimethoxy(methyl)silane, the hydride source. The L_nCu–H would then insert across the aryl alkyne substrate to generate the vinyl copper intermediate (Scheme 17, **i**). An alcohol, the proton source, would promote protodecupration to generate the alkene intermediate (Scheme 17, **ii**). The same mechanistic steps would proceed based on the

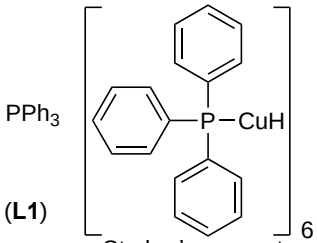
reformation of the reactive $L_nCu–H$ species from $L_nCu–O^iPr$ and excess dimethoxy(methyl)silane. The reformed $L_nCu–H$ would insert across the alkene intermediate to generate the alkyl-copper intermediate (Scheme 17, **iii**), followed by protodecupration with the alcohol to extrude the desired alkane product, and close the catalytic cycle.

Based on this proposed transfer hydrogenation mechanism, we initiated our reaction optimization studies by screening commercial copper sources and phosphine ligands, which are known to promote Cu–H formation when combined with a silane source.[40] A commercially available aryl alkyne, 2-ethynyl-6-methoxynaphthalene, was used for the reaction optimization. Although triphenylphosphine and other achiral and racemic bidentate phosphine ligands were ineffective in the desired transformation (Table 1, entries 1-6), SEGPHOS type ligands showed more promise (Table 1, entries 7-10). Although these ligands were chiral, and the desired synthetic process was an achiral process, the literature precedent demonstrated these ligands to support highly reactive Cu–H catalyzed transformations.[40, 95] The optimal ligand found was DTBM-SEGPHOS (Table 1, entry 8), with no preference for the (*R)* or (*S)*- enantiomer. Decreasing the catalyst loading down to 1 mol% (Table 1, entry 9) and 2 mol % (Table 1, entry 10) resulted in slightly diminished yields of the alkane, although still provided useful yields. Eliminating the catalyst or ligand completely resulted in no reactivity (Table 1, entries 11-12), which demonstrated the necessity for the transition metal catalyst and DTBM-SEGPHOS ligand partnership. Other silane sources were screened in the reaction optimization to further explore the generation of the highly reactive Cu–H from a different silane source other than dimethoxy(methyl)silane, and interestingly both poly(methylhydrosiloxane) and diethoxy(methyl)silane were successful in generating the desired alkane product (Table 1, entries 13-14). Due to the interest of undergoing a transfer deuteration procedure through exchange of the optimal conditions and reagents for deuterated reagents, the practicality of generating dimethoxy(methyl)silane-d_1 from dimethoxy(methyl)silane made it the preferred Si–H source. Also, dimethoxy(methyl)silane had the lowest boiling point of the silane sources that were explored, and therefore it was the easiest to remove by simple evaporation.

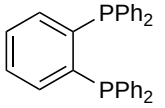
Table 1. Reaction Optimization of Transfer Hydrogenation[a]



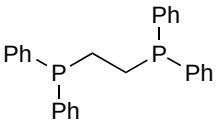
Entry	Cu Catalyst (mol%)[b]	Ligand	Yield of **2a** (%)	Yield of **2b** (%)	RSM **1** (%)
1	$Cu(OAc)_2$ (5)	L1	11	trace[c]	48
2	Stryker's Reagent (5)	N/A	53	trace[c]	6
3	$Cu(OAc)_2$ (5)	L2	5	trace[c]	82
4	$Cu(OAc)_2$ (5)	L3	8	trace[c]	75
5	$Cu(OAc)_2$ (5)	L4	11	trace[c]	72
6	$Cu(OAc)_2$ (5)	L5	12	trace[c]	49
7	$Cu(OAc)_2$ (5)	L6	30	4[d]	45
8	$Cu(OAc)_2$ (5)	L7	0	98[d]	0
9	$Cu(OAc)_2$ (1)	L7	3.5	87[d]	0
10	$Cu(OAc)_2$ (2)	L7	0	91[d]	0
11	N/A	N/A	4	0[c]	86
12	$Cu(OAc)_2$ (2)	N/A	3	0[c]	80
13[e]	$Cu(OAc)_2$ (2)	L7	0	95[d]	0
14[f]	$Cu(OAc)_2$ (2)	L7	0	93[d]	0



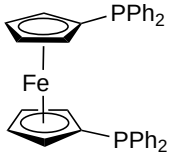
(**L1**) Stryker's reagent



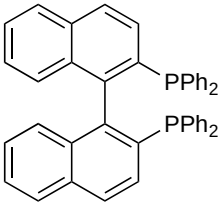
DPPBz (**L2**)



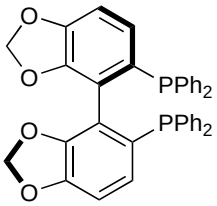
DPPE (**L3**)



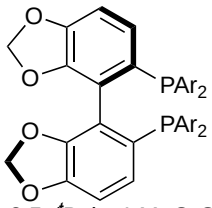
DPPF (**L4**)



rac-BINAP (**L5**)



(*R*)-SEGPHOS (**L6**)



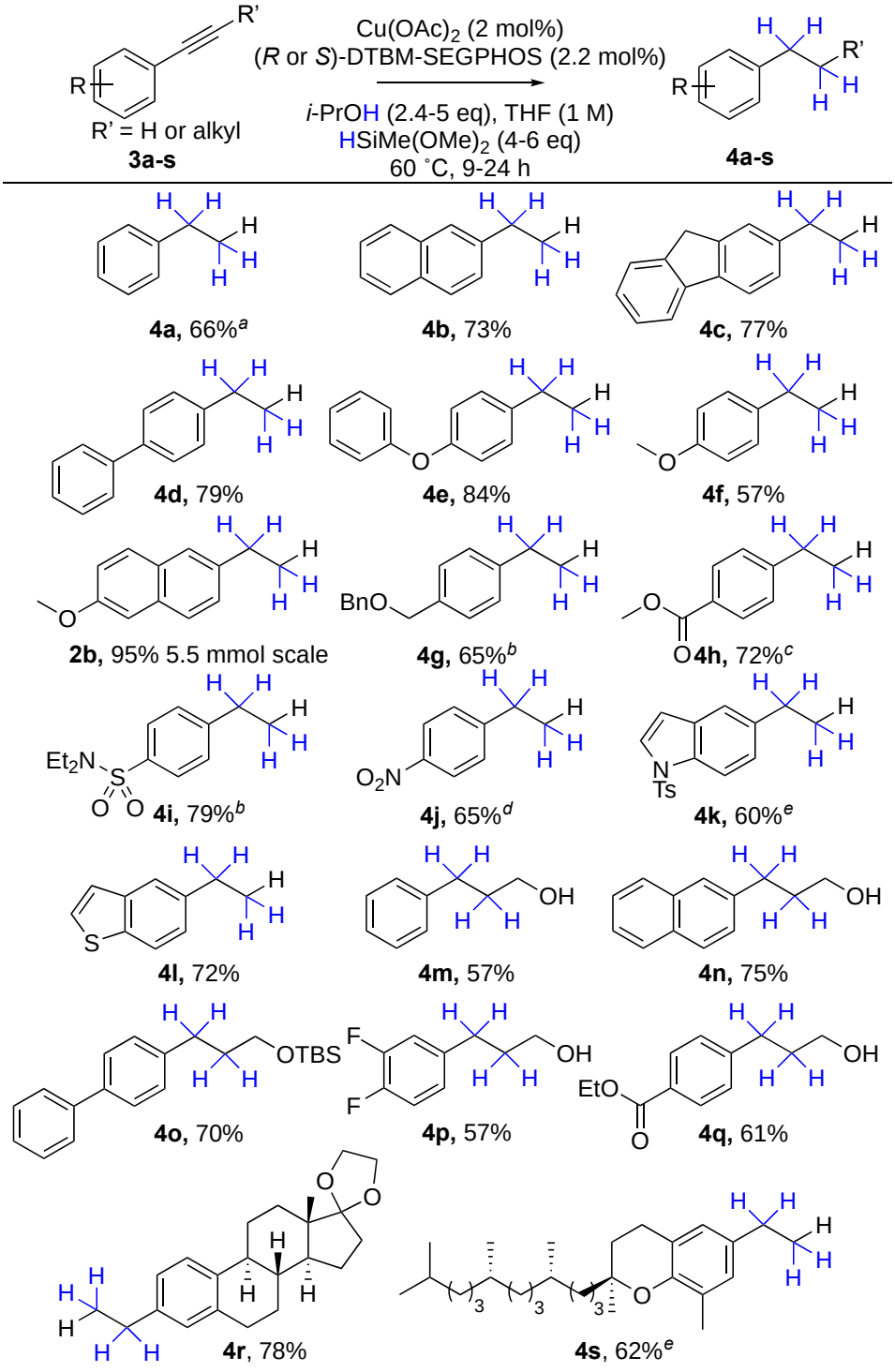
Ar = 3,5-(^{t}Bu)$_2$-4-MeO-C_6H_2
(*R*)-DTBM-SEGPHOS (**L7**)

[a]Reactions were conducted using 0.2 mmol of substrate. [b]$Cu(OAc)_2$ was used in the reactions as a 0.2 M solution in THF. [c]Yield was determined by ^{1}H NMR analysis of the crude reaction mixture, using 1,3,5-trimethylbenzene as an internal standard. [d]Yield determined after purification by flash column chromatography. [e]Poly(methylhydrosiloxane) (5 eq) was used instead of dimethoxy(methyl)silane. [f]Diethoxy(methyl)silane (5 eq) was used instead of dimethoxy(methyl)silane.

With the optimized reaction conditions in hand (Table 1, entry 10), we proceeded to explore the substrate scope of the transfer hydrogenation of aryl alkynes (Scheme 18). Starting with phenyl acetylene, substrate **3a** was reduced to ethyl benzene (Scheme 18, **4a**) in a 66% yield by ^{1}H NMR due to the volatility of the compound. 1,3,5-Trimethylbenzene was used as the internal standard to determine the yield, and neither alkene nor recovered starting material (RSM) were observed in the crude ^{1}H NMR. All new transfer hydrogenation products were characterized by ^{1}H NMR, ^{13}C NMR, HRMS, and IR, but if the compound had been previously reported, like ethyl benzene, the ^{1}H and ^{13}C were compared and confirmed by previously reported spectra. The transfer hydrogenated products of three polyaromatic compounds, 2-ethynyl-naphthalene (**3b)**, 2-ethynyl-*9H*-fluorene (**3c**), and 4-ethynyl-1,1'-biphenyl (**3d)**, were obtained in 73-79% yields when run with the optimized reaction conditions at 60 ˚C. These substrates were isolated by flash column chromatography, and all of the ^{1}H and ^{13}C spectra matched previously reported data. More electron-donating substituted compounds were explored, such as 1-ethyl-4-phenoxybenzene (**4e)**, 1-ethyl-4-methoxybenzene (**4f)**, 2-ethyl-6-methoxynaphthalene (**2b)**, and 1-((benzyloxy)methyl)-4-ethylbenzene (**4g**), ranging from 57-95% in yields. The optimized substrate, **2b,** was run on a gram-scale reaction and the product was isolated in 95% yield. It was observed that substrate **4f** required an increase in equivalents of 2-propanol (up to 5 equivalents) to result in full conversion to the alkane product. This observation was used to promote reactivity of less-reactive substrates throughout the transfer hydrogenation and transfer deuteration protocol. The versatility of the reaction was demonstrated in substrate **4g** by exchanging the 2-propanol proton source for ethanol, only requiring a slight increase in alcohol equivalents (up to 2.6 equivalents) and a slight increase in silane equivalents (up to 6 equivalents) to reach reaction completion. Excitingly, no overreduction of the *o*-benzyl protecting group in this substrate was observed in the crude reaction mixture.[96] 1-((Benzyloxy)methyl)-4-ethylbenzene (**4g**) was fully characterized by ^{1}H NMR, ^{13}C NMR, HRMS, and IR because it was a newly reported product. Electron-withdrawing substrates were also explored, including methyl-4-ethylbenzoate (**4h**), *N*,*N*,-4-triethylbenzenesulfonamide (**4i**), and 4-ethylnitrobenzene (**4j)**. Substrates **4h-4j** were isolated in 65-79% yield, with no overreduction products

seen. A slight change in the temperature of the reaction was required; the methyl ester (**4h)** was run at 40 ˚C and the nitrobenzene (**4j)** was run at room temperature.

Scheme 18: Transfer Hydrogenation Substrate Scope



[a]Yield determined by ^{1}H NMR analysis using 1,3,5-trimethylbenzene as an internal standard. [b]2.4-2.6 eq of EtOH used. [c]Reaction performed at 40 ˚C. [d]Reaction performed at 23 ˚C. [e]5 mol% $Cu(OAc)_2$ and 5.5 mol% DTBM-SEGPHOS used.

Additionally, the sulfonamide substrate (**4i**) demonstrated adaptability of the transfer hydrogenation method because 2.4 equivalents of ethanol was used instead of 2-propanol. These three substrates matched the previously reported ^{1}H NMR and ^{13}C NMR spectra.

Due to the importance of heterocycles in bioactive compounds, nitrogen and sulfur containing heterocycles were explored.[97] Increasing the catalyst loading to 5 mol% $Cu(OAc)_2$ and 5.5 mol% (*S*)-DTBM-SEGPHOS, and increasing to 5 equivalents of 2-propanol, was essential to obtain a 60% yield of 5-ethyl-1-tosyl-1H-indole (**4k**). 5-Ethylbenzo[*b*]thiophene was obtained in 72% yield with the optimal reaction conditions. Both **4k** and **4l** were new products and were fully characterized.

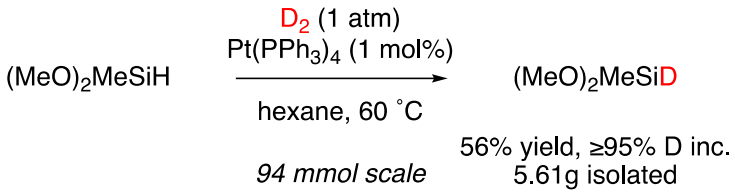
Internal alkynes posed a greater challenge due to the increased steric hindrance of the alkyne. However, with the transfer hydrogenation protocol, 3-phenyl-2-propanol (**4m)** and 2-naphthalenepropanol (**4n)** were successfully obtained in 57% and 75% yield, respectively, using the optimized reaction conditions. Using an even more sterically hindered substrate, containing a *tert*-butyl-dimethyl-silyl ether, a slight increase in 2-propanol to 5 equivalents was needed to obtain the product in 70% yield (Scheme 18, **4o**). Electron-poor internal alkynes containing two fluorine substituents (**4p)** or containing an ethyl-ester para to the alkyne (**4q)** were explored, and the alkane products were generated in 57-61% yield.

Finally, the reactivity of the Cu–H catalytic species towards alkyne-containing complex natural product analogues was explored. The estrone analogue (**4r)** and the δ-tocopherol analogue (**4s)** were isolated in 78% and 62% yields, respectively, when subjected to the transfer hydrogenation conditions. The δ-tocopherol analogue did require an increase in catalyst loading to 5 mol% $Cu(OAc)_2$.

As the ultimate goal of the transfer hydrogenation protocol was to be able to adapt it to a chemoselective transfer deuteration protocol, deuterium sources were explored in exchange for the proton sources. Gratifyingly, deuterated alcohols are commercially available and relatively cheap; however, many deuterated silane sources are not. So, inspired by previously reported work by the Apeloig group, a scalable and reliable method to synthesize dimethoxy(methyl)silane-d_1 from dimethoxy(methyl)silane was developed (Scheme 19).[98] Through an inert atmosphere technique, a catalytic amount of $Pt(PPh_3)_4$ in hexane

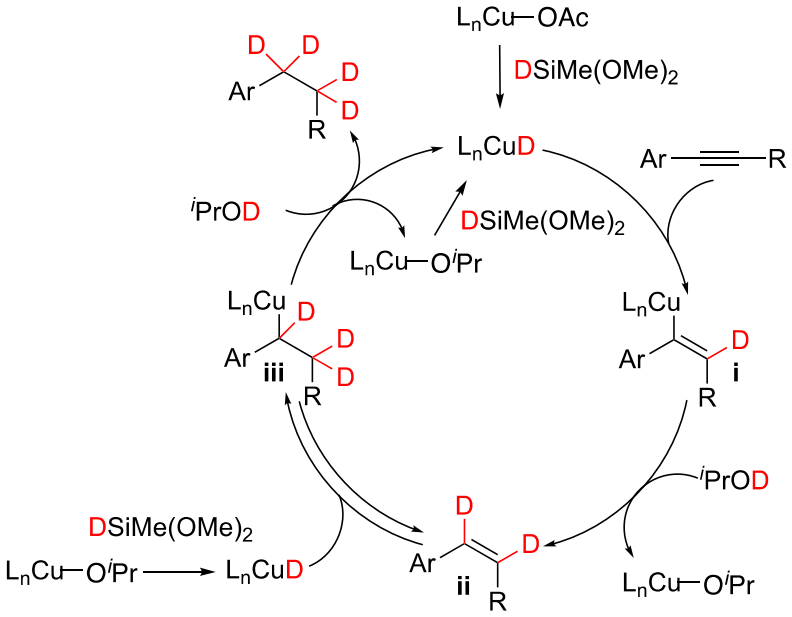
with D_2 gas promoted the exchange of a "H" by a "D" on the silane in dimethoxy(methyl)silane. This method could be done on a 94 mmol scale while retaining the high deuterium incorporation (≥95% D inc.).

Scheme 19: Synthesis of Deuterated Silane



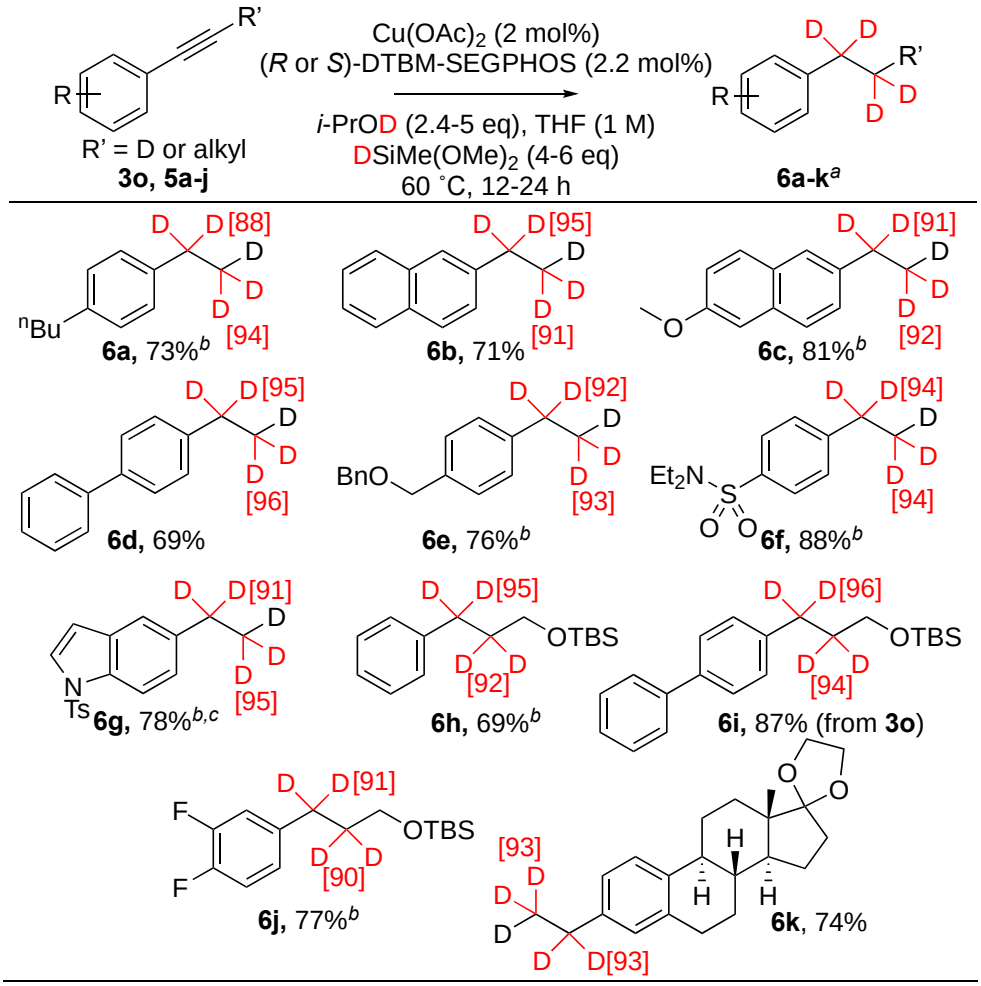
Deuterated small molecules that are used as internal standards for high-resolution mass spectrometry commonly need at least three-four deuterium atoms in the molecule to allow for good separation of peaks in the mass spectrum.[3] By exchanging an acetylenic proton on a terminal alkyne with a deuterium followed by the transfer deuteration method, or by subjecting the transfer deuteration method directly to internal alkynes, small molecules with four-five deuterium atoms were synthesized.[99] The proposed mechanism would proceed in a similar manner to the transfer hydrogenation mechanism. By simply switching the alcohol for a deuterated alcohol and the silane for a deuterated silane source, a transfer deuteration method was feasible (Scheme 20).

Scheme 20: Proposed Transfer Deuteration Mechanism



After the dimethoxy(methyl)silane-d_1 was successfully synthesized, the substrate scope of the transfer deuteration was explored (Scheme 21). Electron neutral and electron rich substrates, 1-butyl-4-(ethyl-d_5)benzene (**6a)**, 2-(ethyl-d_5)naphthalene (**6b**), 2-(ethyl-d_5)-6-methoxynaphthalene (**6c**), 4-(ethyl-d_5)-1,1'-biphenyl (**6d)**, and 1-((benzyloxy)methyl-4-(ethyl-d_5)benzene (**6e**), were chemoselectively reduced from their corresponding d_1-terminal alkynes in 69-81% yield. Substrates **6a, 6c,** and **6e** required 5 equivalents of deuterated alcohol, and substrate **6e** needed an increase to 6 equivalents of dimethoxy(methyl)silane-d_1, but the rest of the optimized reaction conditions stayed consistent. Again, no overreduction of 1-((benzyloxy)methyl-4-(ethyl-d_5)benzene (**6e**) was observed, demonstrating a chemoselective transformation.

Scheme 21: Transfer Deuteration Substrate Scope



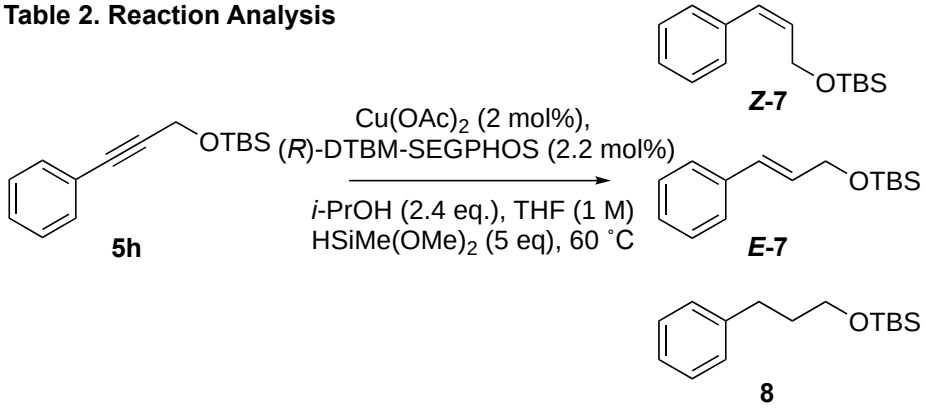
[a]Deuterium incorporation measured by ^{1}H NMR and/or ^{2}H NMR. [b]2-propanol-d_8 used and found to be equally effective as *i*-PrOD. [c]5 mol% $Cu(OAc)_2$ and 5.5 mol% DTBM SEGPHOS used.

All of the transfer deuteration substrates were characterized by ^{1}H NMR, ^{2}H NMR, ^{13}C NMR, IR, and HRMS. ^{2}H NMR was extremely important because the homobenzylic site of some of the substrates showed a ^{1}H NMR shift that overlapped with grease or water, effecting the integration and percent deuterium incorporation calculation. If no overlap with an impurity was observed, the deuterium incorporation was calculated from the integration of the protonated peak in the ^{1}H NMR and confirmed by the ^{2}H NMR. If overlap was observed, ^{2}H NMR was used to determine deuterium incorporation. Only two peaks appeared in the ^{2}H NMR for all compounds, and the ratio of the two peaks was correlated to the calculated deuterium incorporation at the benzylic peak in the ^{1}H NMR. This ratio was then used to confirm/determine the percent deuterium incorporation at both sites. It was seen that throughout the entire transfer deuteration substrate scope, ≥88% deuterium incorporation was observed at both the benzylic and homobenzylic sites.

Expanding the deuterated substrate scope, nitrogen containing substrates were also explored. *N*,*N*-Diethyl-4-(ethyl-d_5)benzenesulfonamide (**6f)** and 5-(ethyl-d_5)-1-tosyl-1*H*-indole (**6g**) were generated under the transfer deuteration protocol, requiring a slight increase in alcohol equivalents. As seen with the transfer hydrogenation method, 5-(ethyl-d_5)-1-tosyl-1H-indole (**6g**) required an increase in catalyst loading (up to 5 mol%). Both substrates were isolated in excellent yields, with greater than 90% deuterium incorporation at each benzylic and homobenzylic site. The internal alkynes that were explored for the transfer deuteration method required a *tert*-butyl-dimethylsilane protecting group on the respective alcohol, generating more steric hindrance on the internal alkyne. Regardless, the transfer deuteration method was successful in generating *tert*-butyldimethyl(3-phenylpropoxy-2,2,3,3-d_4)silane (**6h**), (3-([1,1'-biphenyl]-4-yl)propoxy-2,2,3,3-d_4)(*tert*-butyl)dimethylsilane (**6i**), and *tert*-butyl(3-(3,4-difluorophenyl)propoxy-2,2,3,3-d_4)dimethylsilane (**6j**) in 69-87% yields with greater than 90% deuterium incorporation at each carbon site. Only an increase in alcohol equivalents to 5 equivalents was necessary to obtain the α,α,β,β-d_4-alkanes (benzylic-d_2 and homobenzylic-d_2 alkanes) from their respective internal alkynes. After exchanging the acetylenic proton for a deuterium atom, the estrone-analogue (**6k)** underwent transfer deuteration through the optimized reaction conditions with an increase in deuterated alcohol to 5 equivalents, and the d_5-alkane was isolated in 74% yield with 93% deuterium incorporation at both benzylic and homobenzylic carbons.

The d_5-estrone analogue represents a chemoselective method to generate a highly deuterated biologically relevant organic molecule.

Table 2. Reaction Analysis



Entry	Reaction Time (min)	***Z*-7**[a](%)	***E*-7**[a](%)	**8**[a](%)
1	15	74	0	6
2	30	48	2	25
3	45	40	5	36
4	90	17	7	54
5	180	7	5	61
6	9 h	0	0	79

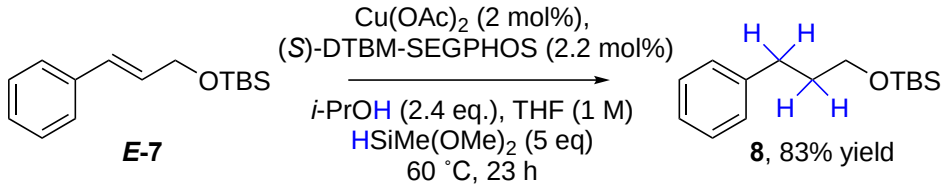
[a]Yields of each product were determined by ^{1}H NMR of the combined products after purification.

To further probe the reaction mechanism of both the transfer hydrogenation and transfer deuteration methods (Scheme 17 and Scheme 20), mechanistic studies were explored. First, a time course analysis was studied because we wanted to observe which reaction intermediates were forming (Table 2). We hypothesized that the proto/deutero-decupration step (from **i** to **ii**) promoted the initial formation of the *cis*-alkene intermediate. The *cis*-alkene would then undergo further reduction by the Cu–H to generate the alkyl-copper intermediate **iii**. This could be a reversible step due to the potential for bond rotation of the C–C single bond in **iii**, followed by β-hydride elimination, to generate the thermodynamically favored *trans*-alkene intermediate. If this hypothesis were correct, there should be both *cis*-alkene and *trans*-alkene present in an incomplete reaction mixture of products. To explore this, the reduction of ((3-(phenyl)prop-2-yn-1-yl)oxy)(*tert*-butyl)dimethylsilane (**5h**) through the transfer hydrogenation method was evaluated over several time periods. Consistent with the hypothesis, *cis*-alkene (***Z*-7)** was present after only 15

minutes of reaction time (Table 2, entry 1), and after 30 minutes the appearance of *trans*-alkene **(*E*-7)** was seen. After 45 and 90 minutes of reaction time, more *trans*-alkene **(*E*-7)** was observed (Table 2, entries 3-4), and after only 9 hours the reaction was complete as only alkane product was observed (Table 2, entry 6). The ratio of these products was determined by ^{1}H NMR, using 1,3,5-trimethylbenzene as an internal standard. This indeed confirms the reversibility hypothesis in the proposed mechanism.

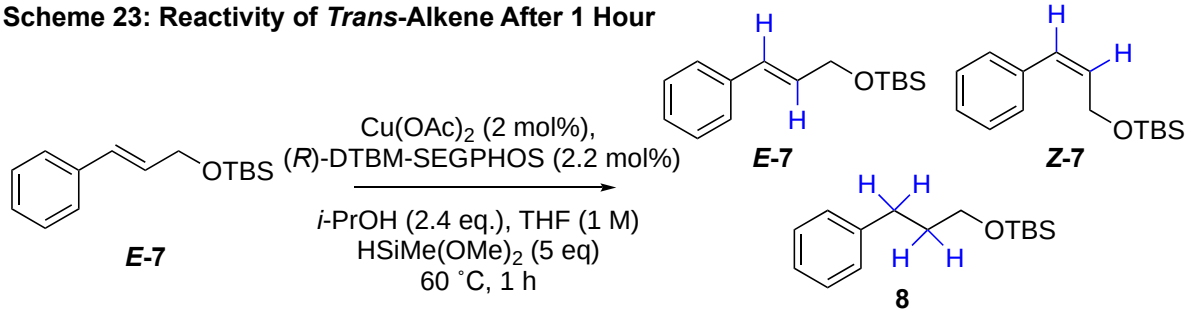
Additionally, *tert*-butyl-dimethyl-silyl protected cinnamyl alcohol (***E*-7**) was subjected to the optimal, standard transfer hydrogenation conditions to confirm the reactivity of the *trans*-alkene (***E*-7**) intermediate (Scheme 22).

Scheme 22: Reactivity of *Trans*-Alkene



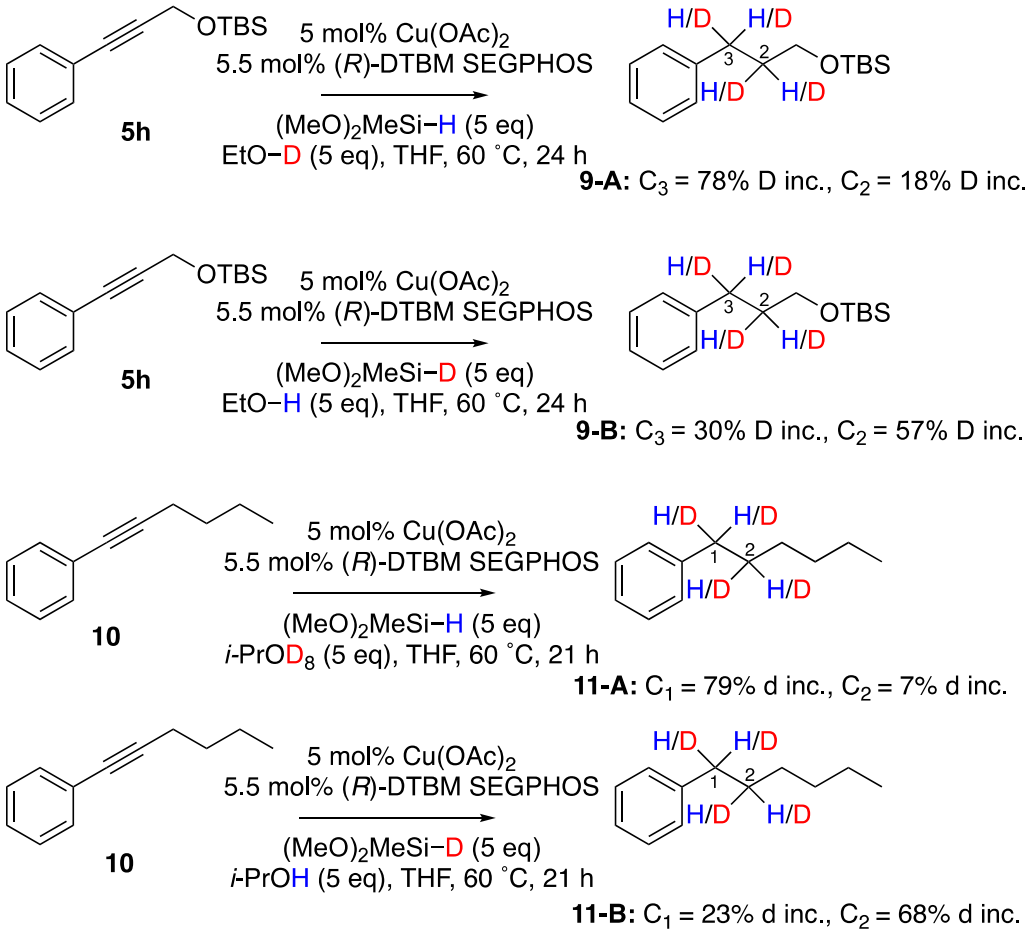
The alkane product was successfully isolated in 83% yield after 23 hours. Another mechanistic experiment was completed by subjecting t*ert*-butyl-dimethyl-silyl protected cinnamyl alcohol (***E*-7**) to the optimal transfer hydrogenation conditions for a reaction time of only 1 hour, and trace amounts of *cis*-alkene (***Z*-7**) were observed in the crude ^{1}H NMR mixture (Scheme 23). These results further confirm the reversibility of the mechanistic step from intermediate **ii** to **iii** as both *cis*-alkene and *trans*-alkene products are observed, and they support that *trans*-alkene **(*E*-7)** is a viable and reactive alkene for the second transfer hydrogenation step in the proposed mechanism.

Scheme 23: Reactivity of *Trans*-Alkene After 1 Hour



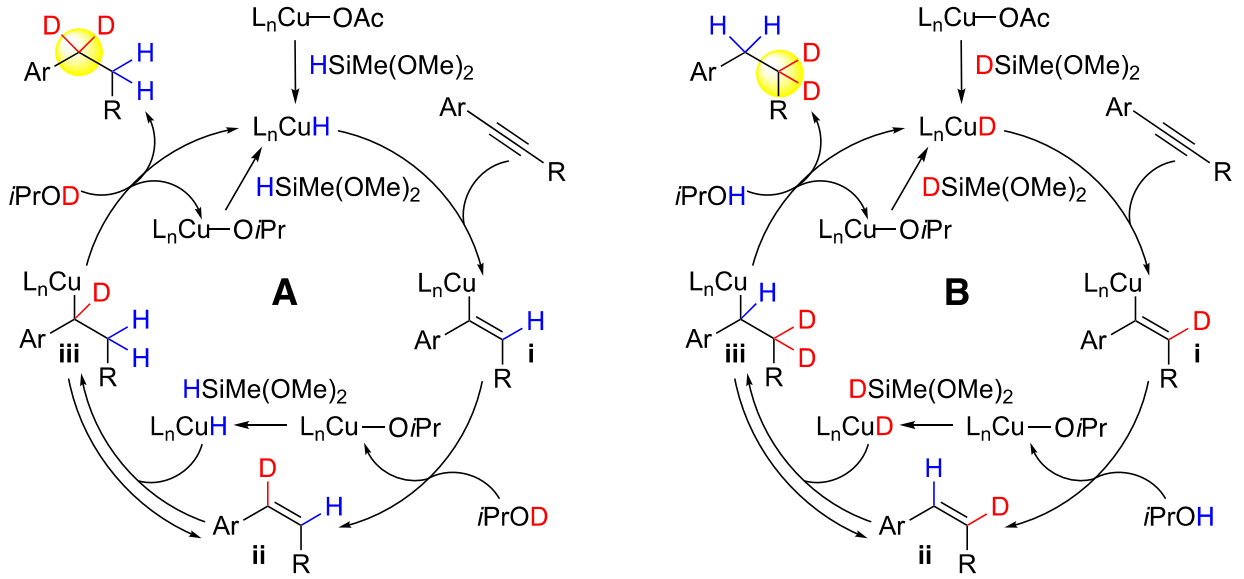
To explore a more regioselective approach of installing deuterium into the benzylic site or homobenzylic site of small molecules, and to further probe the reaction mechanism, a transfer hydrodeuteration protocol of aryl alkynes was investigated. The goal of the transfer hydrodeuteration method was to be able to install two deuterium atoms into the benzylic carbon of the alkane exclusively, while also installing two hydrogen atoms into the homobenzylic carbon of the alkane. The goal of the transfer deuterohydrogenation was the opposite, two hydrogen atoms at the benzylic site and two deuterium atoms at the homobenzylic site. We hypothesized that since there are two proton or deuterium sources in the transfer hydrogenation or deuteration method, if we exchanged one of the proton sources for the respective deuterium source, we could control where the deuterium or proton atom would install, as each occurs at different points in the proposed mechanism.

Scheme 24: Regioselective Transfer Hydrodeuteration Preliminary Results



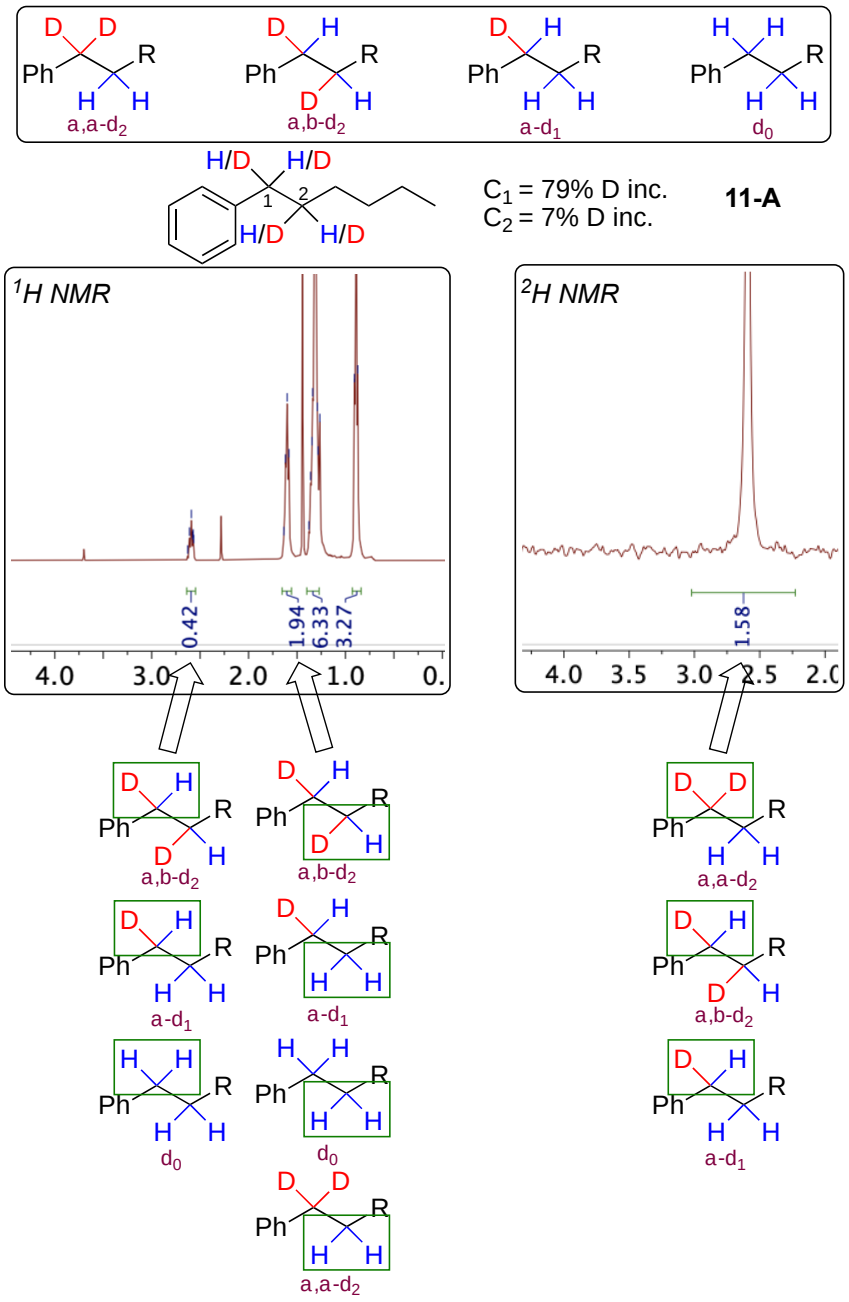
Starting from the transfer hydrogenation reagents, we exchanged the alcohol reagent for deuterated alcohol (ethanol vs. ethanol-OD) and ran the transfer hydrodeuteration reaction on ((3-(phenyl)prop-2-yn-1-yl)oxy)(*tert*-butyl)dimethylsilane (**5h**). Gratifyingly, product **9-A** (Scheme 24, **9-A**) showed 78% deuterium incorporation at carbon 3, the benzylic site, and 18% deuterium incorporation at carbon 2, the homobenzylic site. Targeting the opposite selectivity, ((3-(phenyl)prop-2-yn-1-yl)oxy)(*tert*-butyl)dimethylsilane (**5h**) was subjected to transfer deuterohydrogenation conditions using ethanol and dimethoxy(methyl)silane-d_1. The reaction product demonstrated 30% deuterium incorporation at carbon 3 and 57% deuterium incorporation at carbon 2, benzylic and homobenzylic sites respectively (Scheme 24, **9-B**). In an effort to avoid any regioselectivity bias from the proximal heteroatom functionality to the alkyne, transfer hydrodeuteration reactions were performed on 1-hexyn-1-yl-benzene (**10)**. A slight increase in regioselectivity was observed, as product **11-A** was formed from dimethoxy(methyl)silane and 2-propanol-d_8 with 79% deuterium incorporation at carbon 1, benzylic, and 7% deuterium incorporation at carbon 2, homobenzylic. On the contrary, transfer deuterohydrogenation product **11-B** was formed from dimethoxy(methyl)silane-d_1 and 2-propanol with 23% deuterium incorporation at carbon 1 and 68% deuterium incorporation at carbon 2. Mild to good regioselectivity was observed in all four of the regioselective reactions (Scheme 24), supporting a mildly regioselective Cu–H/Cu–D addition across the alkyne and then the alkene.

Scheme 25: Transfer Hydrodeuteration and Deuterohydrogenation Proposed Mechanisms



The proposed mechanism follows a similar catalytic cycle as the transfer hydrogenation/transfer deuteration mechanisms, but catalytic cycle **A** (Scheme 25) involves the exchange of 2-propanol for 2-propanol-OD resulting in selective deuteration at the benzylic carbon. Catalytic cycle **B** (Scheme 25) involves the exchange of dimethoxy(methyl)silane for dimethoxy(methyl)silane-d_1, forming a Cu–D species, and results in selective deuteration at the homobenzylic carbon (Scheme 25). We refer to the mechanistic pathway **B** as transfer deuterohydrogenation because the deuteration occurs first in the proposed mechanism, followed by protodecupration, allowing the deuterium to end up on the homobenzylic carbon. These preliminary results promoted strong interest in optimizing the regioselective transfer hydrodeuteration method, because the current results, though promising, show mixtures of isotopic species that are both inseparable and indistinguishable. There are likely multiple isotopic species that are contributing to one deuterium incorporation which is determined by ^{1}H and ^{2}H NMR, because all of the isotopic species will share the same ^{1}H and ^{2}H NMR chemical shifts (Scheme 26, **11-A**). The objective is to minimize the formation of these undesired isotopic species in the reaction by optimizing a regioselective process, and then be able to differentiate and quantify the small amount of isotopic species that are formed.

Scheme 26: Possible Isotopic Species Formed in Transfer Hydrodeuteration Contributing To The Same $^{1}H/^{2}H$ NMR Signal



Chapter 2

Copper-Catalyzed Transfer Hydrodeuteration of Aryl Alkenes with Quantitative Isotopomer Purity Analysis by Molecular Rotational Resonance Spectroscopy

In an attempt to further probe the second half of the regioselective transfer hydrodeuteration of aryl alkynes mechanism (involving alkene to alkane), as well as the encouraging isolated yield of the transfer hydrogenation of t*ert*-butyl-dimethyl-silyl protected cinnamyl alcohol (***E*-7)** obtained in Scheme 22, the aryl alkene transfer hydrodeuteration was investigated.[21, 94] A key regioselectivity challenge arises for the hydrocupration step of the transfer hydrodeuteration mechanism, the L_nCu–H could insert into the aryl alkene through pathway **A** or **B** (Scheme 27). Pathway **A** involves copper inserting at the benzylic position, and pathway **B** involves copper inserting at the homobenzylic position. The benzylic-copper intermediate **iii**, resulting from the **A** insertion pathway across the alkene, is a thermodynamically favored intermediate likely stabilized throughout the aryl ring.[38] With the benzylic stabilization of the alkyl-copper intermediate, we imagined that we could undergo the selective transfer hydrodeuteration method of aryl alkenes and install one deuterium atom at the benzylic site and one hydrogen atom at the homobenzylic site if we were to use $(OMe)_2MeSiH$ and ROD, a deuterated alcohol. This proposed mechanism would allow for an expansion of regioselective methodology to install a single deuterium atom selectively into the benzylic site of small molecules.

Scheme 27: Highly Regioselective Aryl Alkene Transfer Hydrodeuteration

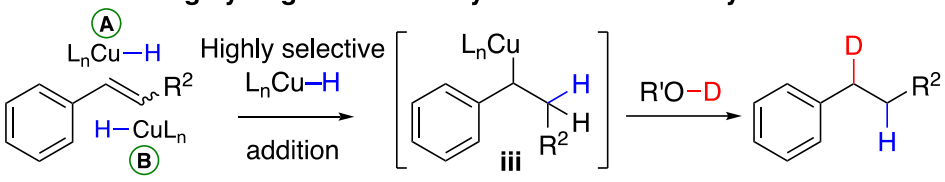
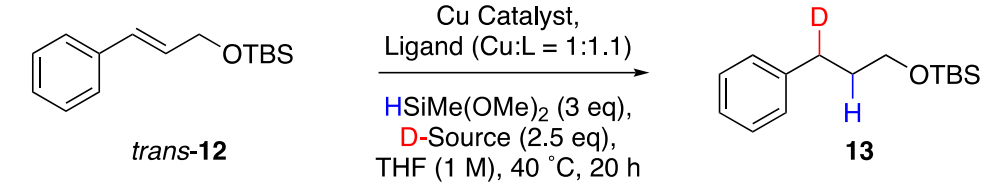
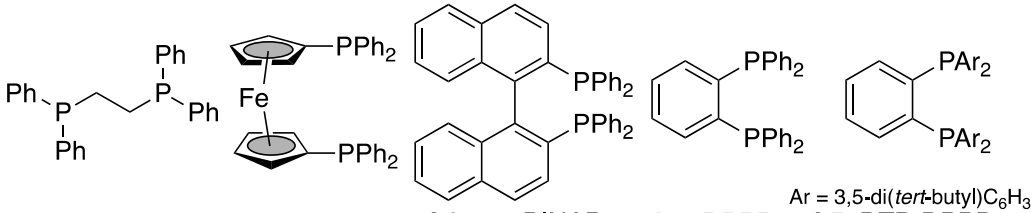


Table 3. Reaction Optimization[a]



trans-**12** **13**

Entry	$Cu(OAc)_2$	Ligand	D-Source	**12** (%)	**13** (%)
1	2 mol%	L1	EtOD	69%[b]	—
2	2 mol%	L2	EtOD	70%[b]	—
3	2 mol%	L3	EtOD	89%[b]	—
4	2 mol%	L4	EtOD	47%[b]	—
5	2 mol%	L5	EtOD	—	85%[c]
6	2 mol%	L5	MeOD	8%[c]	69%[c]
7	2 mol%	L5	D_2O	59%[c]	21%[c]
8	1 mol%	L5	IPA-d_8	—	85%[c]
9	1 mol%	L5	EtOD	—	90%[c]



L1: DPPE **L2:** DPPF **L3:** *rac*-BINAP **L4:** DPPBz **L5**: DTB-DPPBz

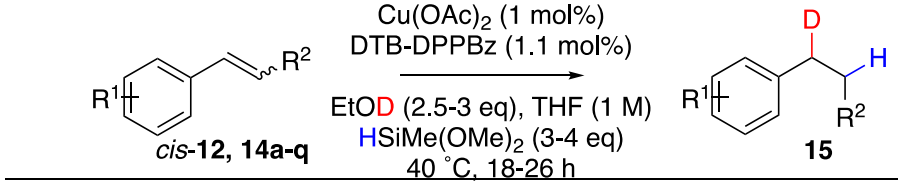
[a]Reactions conducted using 0.2 mmol of substrate. $Cu(OAc)_2$ was used as a 0.2 M solution in THF. [b]Yield was determined by ^1H NMR analysis of the crude reaction mixture, using mesitylene as an internal standard. [c]Denotes isolated product yield.

Reaction optimization started with *tert*-butyl-dimethyl-silyl protected cinnamyl alcohol (Table 3, *trans*-**12**).[21] From the previous transfer hydrogenation, deuteration, and hydrodeuteration experiments done, $Cu(OAc)_2$ and dimethoxy(methyl)silane were chosen as the copper catalyst and the silane source. First, ligand screening found that bidentate phosphines such as DPPE, DPPF, *rac*-BINAP, and DPPBz were not able to promote the desired transfer hydrodeuteration transformation (Table 3, entries 1-4). However, switching to the more sterically hindered DTB-DPPBz ligand was successful, and the selectively deuterated aryl alkane was isolated in 85% yield (Table 3, entry 5). Another obvious benefit to using DTB-DPPBz is that it is an achiral ligand being used for an achiral process. In the analysis of different deuterium sources,

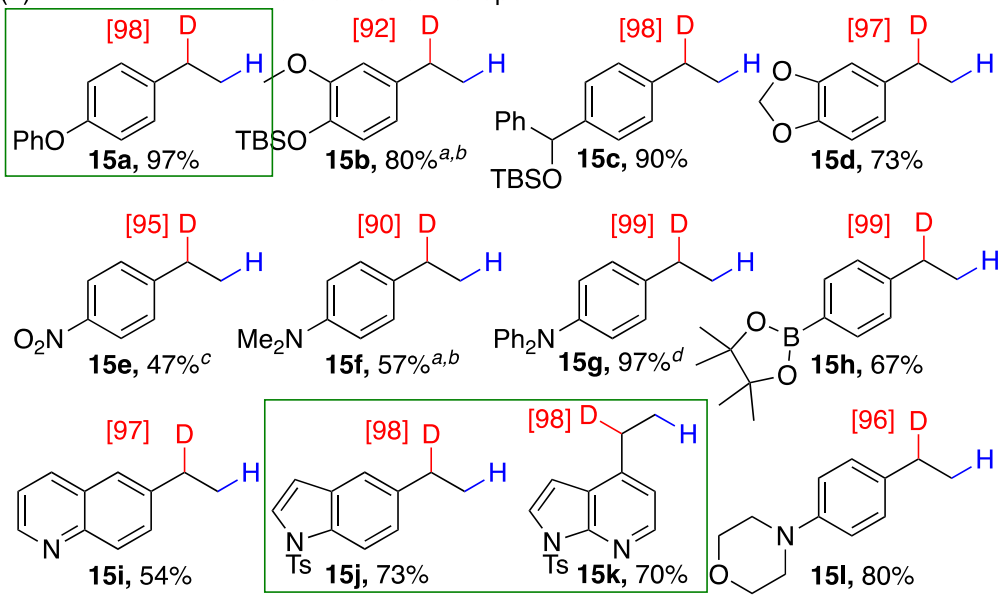
it was seen that MeOD and D_2O were not feasible reagents for this reaction because starting material was still present (Table 3, entry 6-7), but IPA-d_8 showed the same reactivity and selectivity as EtOD (Table 3, entry 8), with a slight decrease in catalyst loading required. Finally, EtOD was used as the deuterium source at 1 mol% catalyst loading, which was deemed to be the optimal reaction condition based on the isolation of the aryl alkane product in 90% yield (Table 3, entry 9). Importantly, the deuterated alkane product was evaluated by ^1H, ^2H, and ^{13}C NMR which showed that one deuterium atom was incorporated exclusively at the benzylic position (>20:1 regioselectivity ratio).

With the optimal reaction conditions of 1 mol% $Cu(OAc)_2$, 1.1 mol% DTB-DPPBz, EtOD, dimethoxy(methyl)silane, and THF at 40 ˚C, the substrate scope was explored. Twenty-seven examples were demonstrated in up to 97% yield, and all were extremely selective with one deuterium atom exclusively incorporated at the benzylic site (Scheme 28). My main contributions to this project included the synthesis of 5 aryl alkene starting materials, the transfer hydrodeuteration of these 5 alkenes, and full characterization of the 5 alkane products shown in green boxes (Scheme 28, **14a/15a, 14j/15j, 14k/15k, 14p/15p, and 14q/15q**).

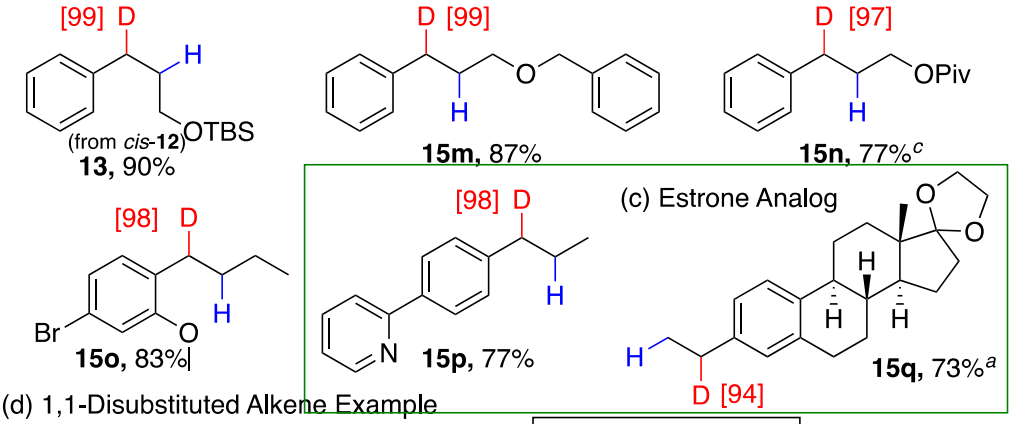
Scheme 28: Aryl Alkene Transfer Hydrodeuteration Substrate Scope



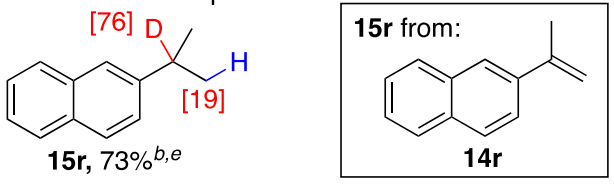
(a) Monosubstituted Alkene Substrate Scope



(b) 1,2-Disubstituted Alkene Substrate Scope



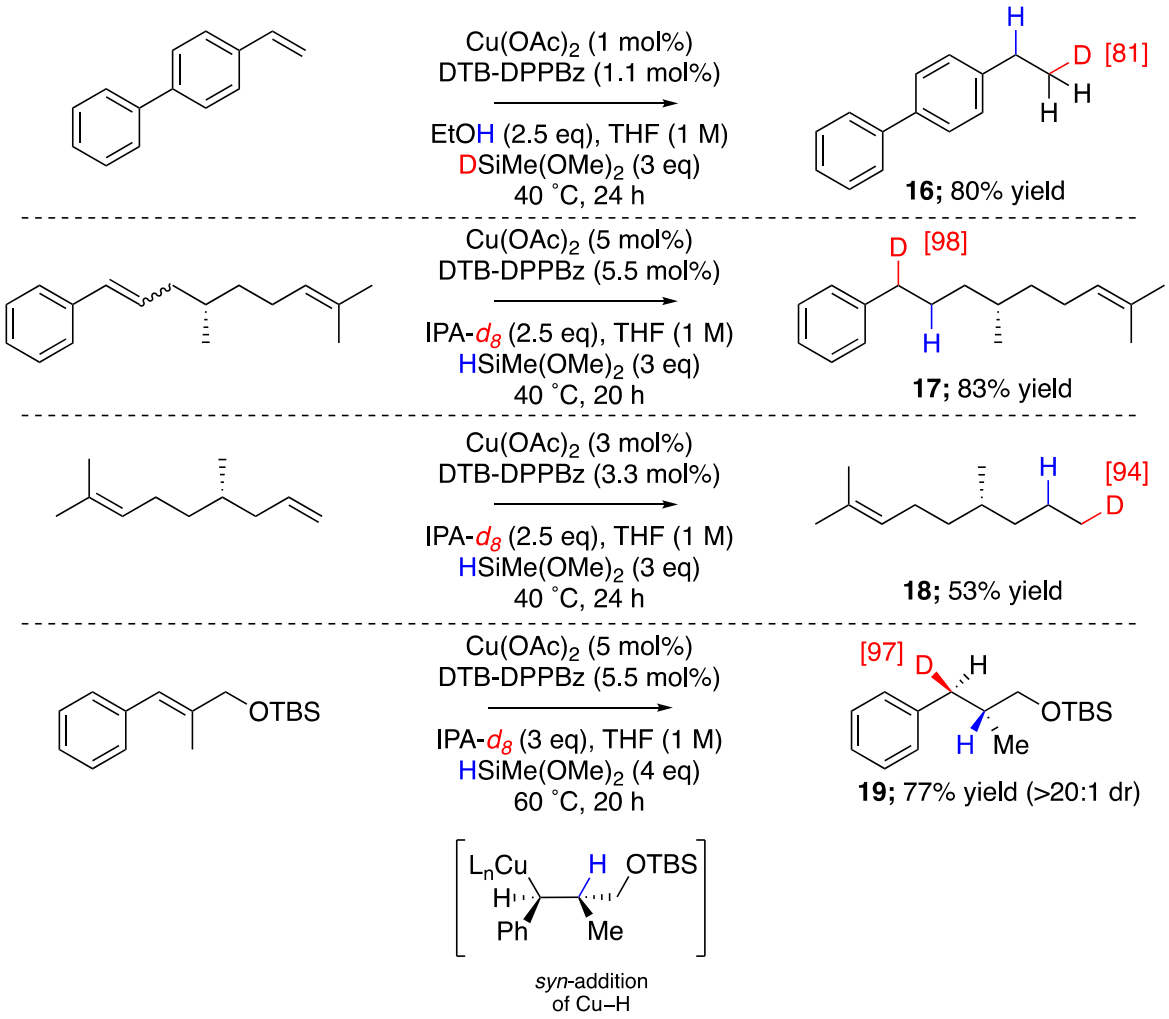
(d) 1,1-Disubstituted Alkene Example



[a]2 mol % $Cu(OAc)_2$ and 2.2 mol % DTB-DPPBz used. [b]IPA-d_8 (3 eq.) used instead of EtOD. [c]Reaction conducted at 5 °C. [d]Polymethylhydrosiloxane (3 eq.) used instead of $HSiMe(OMe)_2$. [e]3 mol% $Cu(OAc)_2$, 3.3 mol% DTB-DPPBZ, and $HSiMe(OMe)_2$ (4 eq.) used at 60 °C.

1-(Ethyl-d_1)-4-phenoxybenzene was isolated in excellent yield and demonstrated that electron-rich monosubstituted alkenyl arenes containing oxygen functionality will undergo selective transfer hydrodeuteration. Due to the prevalence of nitrogen containing heterocycles in bioactive molecules, indole, azaindole, and 4-phenyl-pyridine substituted alkenes were explored. Both 5-(ethyl-d_1)-*N*-tosylindole and 4-(ethyl-d_1)-1-tosyl-1*H*-pyrrolo[2,3-b]pyridine (Scheme 28, **15j and 15k)** were run with the optimized reaction conditions and isolated in 70-73% yield, with 98% deuterium incorporation at the benzylic site. Both ^{1}H and ^{2}H NMR confirm no deuterium incorporation elsewhere on the alkane. 2-(4-(Propyl-d_1)-phenyl)pyridine (Scheme 28, **15p)** demonstrated the feasibility for an internal alkene, 1,2-disubstituted, to undergo regioselective transfer hydrodeuteration efficiently under the optimal conditions. The added steric bulk of the internal alkene did not affect the regioselectivity, as 98% deuterium incorporation was observed by ^{1}H and ^{2}H NMR selectively at the benzylic carbon. Finally, the ability of the transfer hydrodeuteration procedure to occur in a complex small molecule setting was observed. An increase in catalyst loading to only 2 mol% was required to observe the vinyl substituted estrone analogue **15q** undergoing the transfer hydrodeuteration. The alkane product was isolated in high yield, with 94% deuterium incorporation selectively at the benzylic site, with less than 1% deuterium incorporation observed at the homobenzylic site, determined by ^{1}H and ^{2}H NMR.

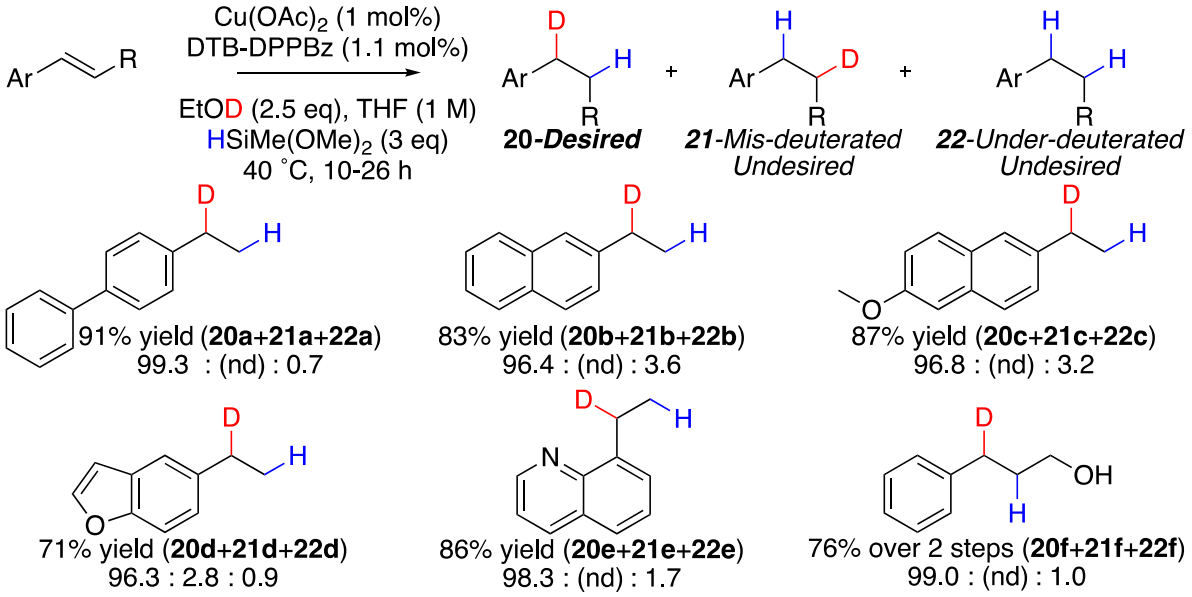
Scheme 29: Reaction Studies



To further explore the alkene transfer hydrodeuteration reaction, chemoselectivity and mechanistic studies were done (Scheme 29). First, the transfer deuterohydrogenation experiment was run, exchanging the dimethoxy(methyl)silane for dimethoxy(methyl)silane-d_1 and the EtOD for EtOH. The β-d_1-ethyl-1,1'-biphenyl product was isolated in 80% yield with 81% deuterium incorporation selectively at the homobenzylic site (Scheme 29), which is likely below the predicted deuterium incorporation due to a low deuterium incorporation in the synthesized dimethoxy(methyl)silane-d_1 or the presence of water in the reaction. The chemoselectivity of the transfer hydrodeuteration was demonstrated by running a substrate that contained both a 1,2-disubstituted styrenyl alkene and a 1,1,2-trisubstituted alkene. No reduction of the 1,1,2-trisubstituted alkene was observed, as only the 1,2-disubstituted styrenyl alkene was reduced with excellent regioselectivity for deuteration at the benzylic site (98% D inc., Scheme 29). Additionally, an

unactivated alkyl diene, containing both a terminal alkene and a 1,1,2-trisubstituted alkene was evaluated post-transfer hydrodeuteration. The 1,1,2-trisubstituted alkene was tolerated, as no reduction of this alkene was observed, and only complete reduction of the terminal alkene was seen. Finally, the Cu–H insertion step across the aryl alkene was evaluated by running the transfer hydrodeuteration of a 1,2,2-trisubstituted styrenyl alkene, and it was concluded that the Cu–H inserted into the aryl alkene with *syn*-addition based on the ^{1}H NMR relationship of the dashed-benzylic proton with the wedged-homobenzylic proton (blue) in a >20:1 dr (Scheme 29). These mechanistic studies provided conclusive evidence that the transfer hydrodeuteration of aryl alkenes proceeds in a completely regioselective and chemoselective manner, installing one deuterium atom at the benzylic site and one proton atom at the homobenzylic site through a *syn*-Cu–H insertion into aryl alkenes.

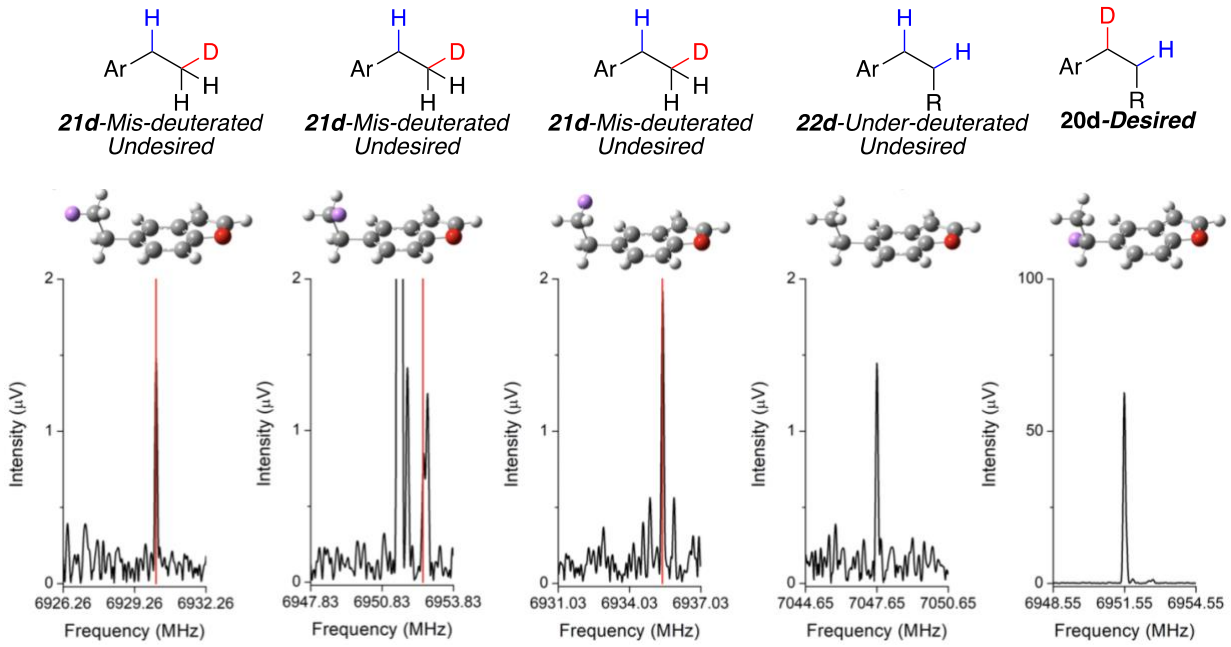
Scheme 30: D_1-Aryl Alkanes Analyzed by MRR



Additionally, six alkenyl arene substrates that underwent transfer hydrodeuteration were analyzed by molecular rotational resonance (MRR) spectroscopy by Professor Brooks H. Pate at the University of Virginia (Scheme 30). MRR is a novel spectroscopic technique that allows for differentiation of isotopomers and isotopologues because each isotopic species has a unique spectral signature.[21] Upon quantification of each isotopic product, ratios of product mixtures can be determined. This was

demonstrated on six substrates: 4-vinyl-1,1'-biphenyl, 2-vinylnaphthalene, 2-methoxy-6-vinylnaphthalene, 5-vinylbenzofuran, 8-vinylquinoline, and 1-*tert*-butyldimethylsilyloxy-3-phenyl-2-propene. All of the deuterated products were isolated in great yields (Scheme 30, 71-91% yield). However, in the transfer hydrodeuteration of aryl alkene reaction there are two additional isotopic species that can be formed. The "desired" product is the benzylic-deuterated alkane product (**20a-f**). The other two isotopic species are the "misdeuterated" reaction product where the deuterium is placed at the homobenzylic site of the alkane (**21a-f**) or the "underdeuterated" reaction product where there is no deuterium incorporation in the alkane product at all (**22a-f**). Isotopic species **22** is expected from hydrogen impurities in the alcohol-OD or trace H_2O in the alkenyl arene substrate, silane, and alcohol-OD. Isotopic species **21** is expected from the Cu–H species inserting in the undesired mechanistic pathway, where the copper will be positioned at the homobenzylic site, and the hydride at the benzylic site. The MRR results of the six deuterated alkane products are demonstrated in Scheme 30, and all products show that the "desired" product is the major isotopic species. The 1,1'-biphenyl, 2-vinylnaphthalene, 2-methoxy-6-naphthalene, 8-quinoline, and 3-phenyl-propanol alkane substrates all show "nd" for isotopic species **21,** meaning that there was no "misdeuterated" products observed in these reaction mixtures at all. The benzofuran substrate was also highly regioselective with the strongest isotopic product being **20d**, the desired product. However, minimal amounts of the "misdeuterated" and "underdeuterated" products were observed in this substrate. Isotopic species **22** "underdeuterated" was very minor for all six compounds, demonstrating regioselectivity ratios up to >140:1 for the "desired" α-d_1-benzylic alkane products.

Scheme 31: MRR of Benzofuran (20d+21d+22d)



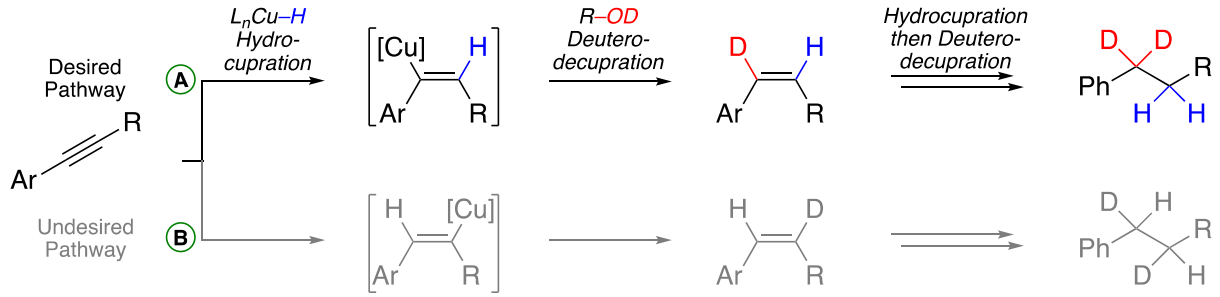
The MRR spectra are run and analyzed by our collaborators at the University of Virginia and BrightSpec Inc. However, to demonstrate how novel this spectroscopic tool is, Scheme 31 shows spectral windows of the three different isotopic species present in the dibenzofuran product mixture. From left to right, the first three spectral windows show a unique frequency associated with each conformational isomer of species **21d,** the "misdeuterated" product. The deuterium can be seen as the pink atom. The fourth window shows the unique frequency of species **22d**, the "underdeuterated" species. Finally, the fifth window shows the unique frequency of the desired α-d_1-alkane product, "desired" **20d**, displaying the largest intensity of all 5 spectral windows. Note that each isotopic species is observed at a different frequency. Using MRR spectroscopy allows for the appropriate confirmation and characterization of isotopic product mixtures of selectively deuterated compounds. The data presented herein demonstrates, confirmed by MRR, the highest regioselectivity ratios for a transfer hydrodeuteration of aryl alkenes protocol reported to date.

Chapter 3

Precision Deuteration Using Cu-Catalyzed Transfer Hydrodeuteration to Access Small Molecules Deuterated at the Benzylic Position

Selectively installing 2 deuterium atoms exclusively into the benzylic site of small molecules and pharmaceutically relevant compounds is elusive. Under transfer hydrodeuteration conditions, the H-donor and the D-donor would operate at distinct points during the reaction mechanism, which would allow for the precise insertion of each atom at a select carbon within the transformation. The preliminary regioselective transfer hydrodeuteration of aryl alkyne results, demonstrated in Chapter 1, showed promise, though further exploration was essential. As confirmed in Chapter 2, the aryl alkene transfer hydrodeuteration is highly regioselective. Therefore, to start in the exploration of the aryl alkyne transfer hydrodeuteration, we addressed the first half of the reaction mechanism (alkyne to alkene).[93, 94] This involves the hydrocupration of the aryl alkyne followed by the deuterodecupration.

Scheme 32: Two Potential Pathways For Aryl Alkyne Hydrocupration

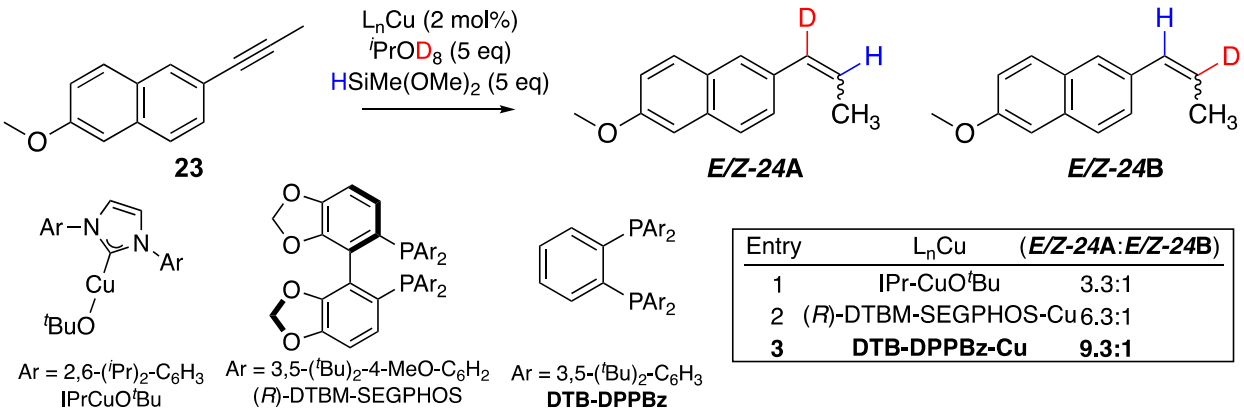


There are two distinct pathways that can occur at the start of the aryl alkyne transfer hydrodeuteration reaction mechanism, and both determine which major product will be formed. First, the desired pathway (Scheme 32, A) involves the hydrocupration step positioning the Cu α-to the arene and the H β-to the arene. This is followed with deuterodecupration to access the α-d_1-alkene. This α-d_1-alkene then undergoes hydrocupration and deuterodecupration in a highly selective manner, as discussed in Chapter 2, which would provide the desired α,α-d_2-alkane with two deuterium atoms selectively positioned at the benzylic site.[21] The undesired pathway (Scheme 32, B) involves hydrocupration positioning the Cu β-to the arene and the H α-to the arene, followed by deuterodecupration to give the β-d_1-alkene. Then,

hydrocupration of the β-d_1-alkene followed by deuterodecupration provides access to the α,β-d_2-alkane, with one deuterium atom at the benzylic site and one deuterium atom at the homobenzylic site, which is undesired.

In an attempt to optimize the reaction for selective formation of the α-d_1-alkene, we underwent ligand optimization and stopped the reaction half-way through, before reaction completion to the alkane, to determine the ratio of the α-d_1-alkene (**E/Z-24A**) to the β-d_1-alkene (**E/Z-24B**) (Scheme 33).

Scheme 33: Ligand Screening on 2-Methoxy-6-(1-propyn-1-yl)naphthalene

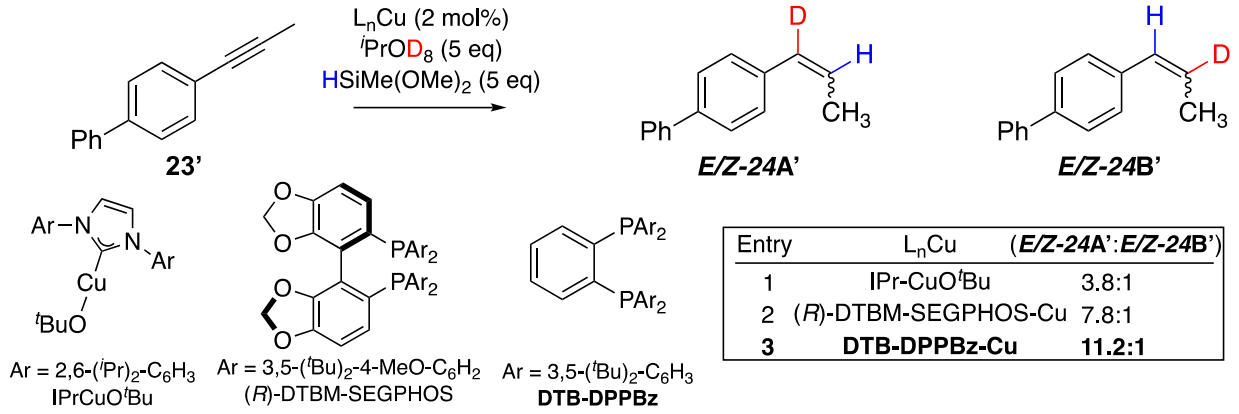


Entry	L_nCu	(*E/Z-24A*:*E/Z-24B*)
1	IPr-CuO^{t}Bu	3.3:1
2	(*R*)-DTBM-SEGPHOS-Cu	6.3:1
3	**DTB-DPPBz-Cu**	**9.3:1**

The ligand optimization transfer hydrodeuteration was run with 2-methoxy-6-(1-propyn-1-yl)naphthalene **23**, $Cu(OAc)_2$, various ligands, $^iPrOD_8$, and $HSiMe(OMe)_2$. Starting with a commonly used NHC-ligand, IPrCuO^{t}Bu, the reaction was run for 5 hours and then analyzed by ^{1}H NMR to observe a 3.3:1 ratio of products **E/Z-24A : E/Z-24B**.[35] Exchanging the ligand for (*R*)-DTBM-SEGPHOS, the reaction was run for 6 hours and analyzed by ^{1}H NMR to observe a 6.3:1 ratio of products **E/Z-24A : E/Z-24B**.[94] This shows that the bisphosphine ligand promoted higher regioselectivity than the NHC-ligand. Finally, DTB-DPPBz was used, and due to the high reactivity of the ligand, the reaction was only run for 27 minutes.[21] Upon analysis by ^{1}H NMR, a 9.3:1 ratio of products **E/Z-24A : E/Z-24B** was observed. This 9.3:1 ratio of products concludes that the α-d_1-alkene (**E/Z-24A**) product is predominately formed in greater than 90%, providing access to alkane products with greater than 90% deuterium incorporation at the benzylic site (Scheme 33). The reason why the ligand screening transfer hydrodeuterations were run for different time periods was due to the different reactivities associated with each ligand. IPrCuO^{t}Bu and (*R*)-DTBM-

SEGPHOS required longer reaction times to observe significant alkene product in the ^{1}H NMR, whereas DTB-DPPBz only required a short period of time due to its higher reactivity.

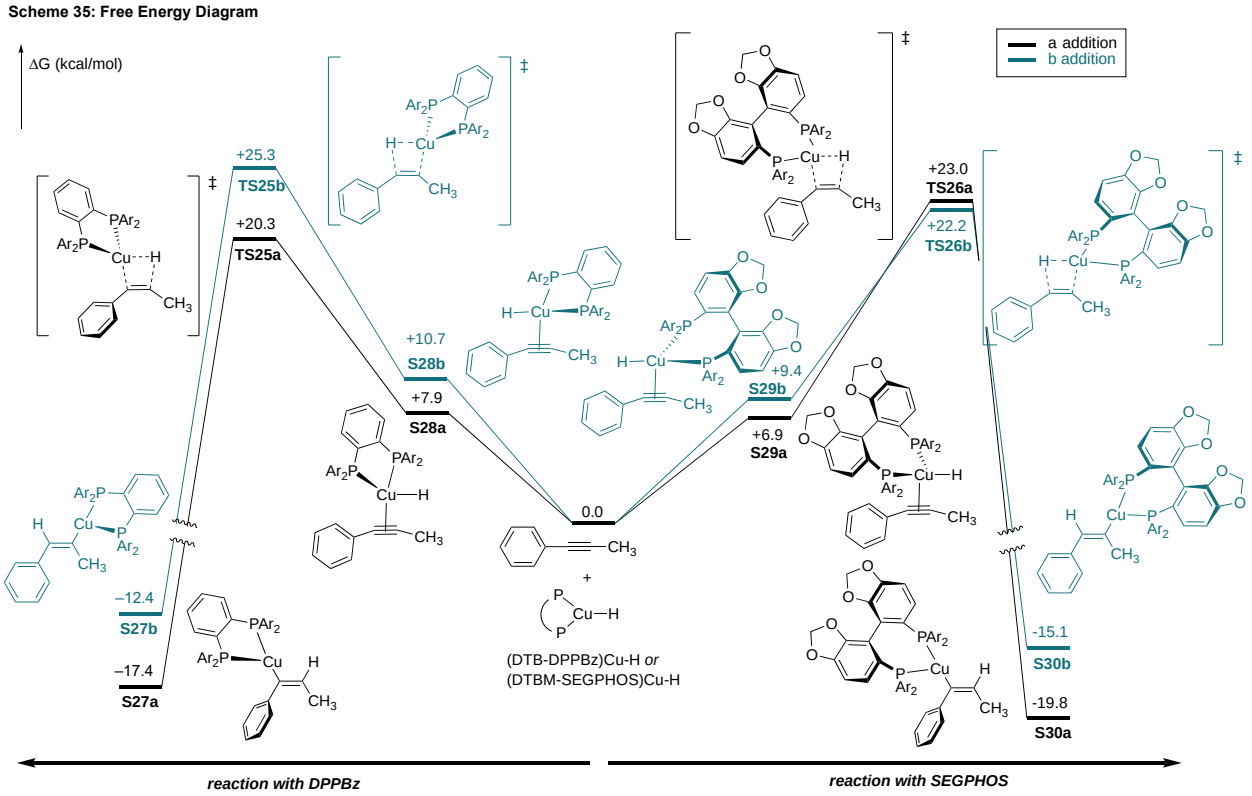
Scheme 34: Ligand Screening on 1,1'-Biphenyl-propyne



Entry	L$_n$Cu	(*E/Z-24A'*:*E/Z-24B'*)
1	IPr-CuO^{t}Bu	3.8:1
2	(*R*)-DTBM-SEGPHOS-Cu	7.8:1
3	**DTB-DPPBz-Cu**	**11.2:1**

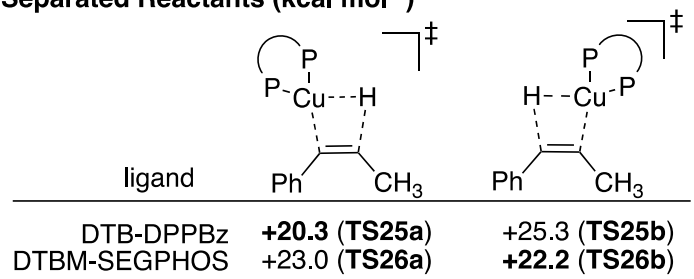
Similar reaction studies and ligand optimization were done on a 1,1'-biphenylpropyne substrate **23'**, and those results showed an even higher 11.2:1 ratio of α-d$_1$-alkene (**E/Z-24A'**) to the β-d$_1$-alkene (**E/Z-24B'**) when using the DTB-DPPBz ligand (Scheme 34). Due to these very promising ligand screening results, we wanted to understand why DTB-DPPBz was preforming so much better.

Scheme 35: Free Energy Diagram



In collaboration with Professor Sharon Neufeldt at Montana State University, we explored the explanation behind DTB-DPPBz promoting such high regioselectivity through DFT studies. A Free Energy Diagram was assembled to show the difference in transition state energies between the DPPBz and SEGPHOS backbone ligands (Scheme 35). From the Free Energy Diagram, it is observed that the energy difference between **TS25a** (Cu-α-to-arene) and **TS25b** (Cu-β-to-arene) is 5 kcal/mol with DPPBz (Scheme 35). However, with SEGPHOS, the energy difference between **TS26a** (Cu-α-to-arene) and **TS26b** (Cu-β-to-arene) is only 0.8 kcal/mol. The greater energy difference associated with DPPBz (5 kcal/mol vs 0.8 kcal/mol) explains why DTB-DPPBz is a more regioselective ligand. These energy differences also show the distinct energetic preference for the formation of **TS25a** (Cu-α-to-arene) using DPPBz in comparison to **TS25b** (Cu-β-to-arene). The smaller energy difference associated with SEGPHOS explains a less regioselective transformation. Also, **TS26b** (Cu-β-to-arene) is slightly favored in its lower transition state energy with the SEGPHOS ligand compared to **TS26a** (Cu-α-to-arene) (Scheme 35 and Scheme 36).

Scheme 36: Transition Structure Energies Relative to Separated Reactants (kcal mol^{-1})



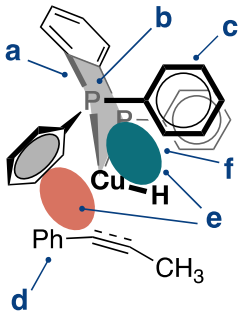
ligand		
DTB-DPPBz	**+20.3** (**TS25a**)	+25.3 (**TS25b**)
DTBM-SEGPHOS	+23.0 (**TS26a**)	**+22.2** (**TS26b**)

The explanation for why DTB-DPPBz is so much more selective of a ligand is due to orbital mixing between the aryl group on the phosphine on the DTB-DPPBz ligand and the Cu catalyst during the transition state (**TS25a**, Scheme 37a). The transition state is in a five-membered cupracycle "envelope" conformation. When the hydride is on the *exo* face of the cupracycle (Scheme 37a), the π* orbitals of the aryl groups on the phosphine ligand can mix with the copper p-type orbital, to lower the energy of the LUMO (lowest unoccupied molecular orbital). This lower energy LUMO promotes electron donation from the alkyne into the copper. In **TS25b**, when the hydride is on the *endo* face of the cupracycle, there is poor orbital overlap between the ligand and the metal (Scheme 37b). When DTBM-SEGPHOS is used, a seven-membered ring

forms in the transition state. This does not allow for the same orbital mixing. With the computational explanation matching the experimental results, a diverse scope of the aryl alkyne transfer hydrodeuteration was evaluated.

Scheme 37: Orbital Mixing Promoting Favored Transition State

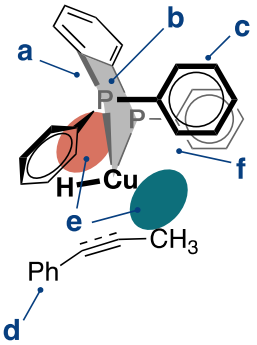
a. Frontier Molecular Orbital Analysis of the (DTB-DPPBz)CuH Fragment When Distorted into the Transition State Geometry for the Favored TS25a[a]



a *endo* face of 5-mem. ring
b *exo* face of 5-mem. ring
c "axial" aryl groups approx. parallel (orbital mixing)
d larger group on alkyne (Ph) points toward endo face (less steric congestion)
e Cu-centered unoccupied MO
f good overlap between aryl and Cu orbitals (orbital mixing)

[a]*Line drawing simplified for clarity (*^{t}*Bu groups not shown, one P-aryl not shown)*

b. Frontier Molecular Orbital Analysis of the (DTB-DPPBz)CuH Fragment When Distorted into the Transition State Geometry for the Disfavored TS25b[a]



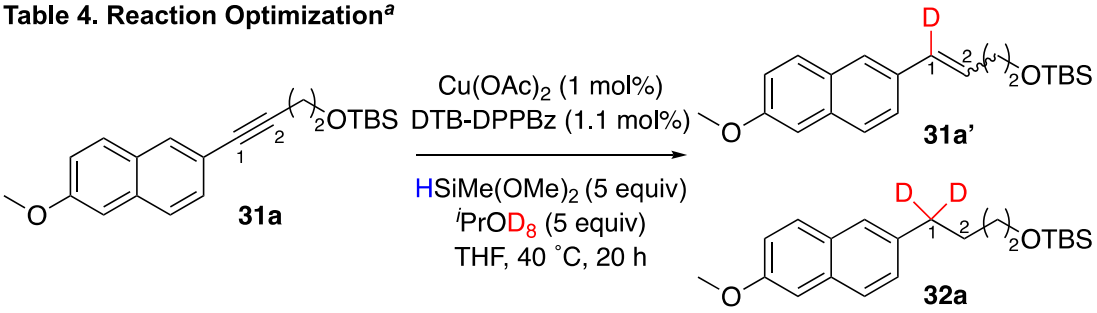
a *endo* face of 5-mem. ring
b *exo* face of 5-mem. ring
c "axial" aryl groups approx. parallel (orbital mixing)
d larger group on alkyne (Ph) points toward endo face (less steric congestion)
e Cu-centered unoccupied MO
f poor overlap between aryl and Cu orbitals (less orbital mixing)

[a]*Line drawing simplified for clarity (*^{t}*Bu groups not shown, one P-aryl not shown)*

Experimental results from the reaction optimization with 2-[4-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-butyn-1-yl]-6-methoxynaphthalene agreed with the computational results and with the ligand screening results (Table 4). When using $Cu(OAc)_2$ (1 mol%), DTB-DPPBz (1.1 mol%), $HSiMe(OMe)_2$ (5 eq), $^iPrOD_8$ (5 eq), THF (1 M), 40 ˚C, for 20 h, the desired transfer hydrodeuteration reaction goes to completion, and the alkane product is isolated in 97% yield with 95% deuterium incorporation (Table 4, entry 1). Deviating from these reaction conditions, besides running the reaction at room temperature (Table 4, entry 2; 95% yield, 95% D inc.), significantly hindered the reaction results (Table 4, entries 3, 6-11). However, PMHS (poly(methylhydrosiloxane) and DEMS

(diethoxymethylsilane) were shown as feasible silane sources to promote the transfer hydrodeuteration, albeit, producing the product in lower isolated yields (Table 4, entry 4-5; 75-89% yield, 94% D inc.). Attempting the reaction with EtOD, MeOD, ^{t}BuOD, or D_2O negatively impacted the product yields (Table 4, entry 6-9). Finally, as seen through the computational studies, DTB-DPPBz is essential for this transformation because when it was eliminated completely, no product was generated (Table 4, entry 10-11).

Table 4. Reaction Optimization[a]



Entry	Deviations	31a (%)	31a' (%)	32a (%)	D inc.[b]
1	none	0	0	97[c]	95
2	rt	0	0	95[c]	95
3[g]	5 °C	0	3.5[c]	84[c]	97
4[g]	PMHS[e]	0	0	75[c]	94
5[g]	DEMS[f]	0	0	89[c]	94
6[g]	EtOD	0[c]	41[c]	39[c]	93
7[g]	MeOD	10[c]	53[c]	12[c]	
8[g]	^{t}BuOD	20[c]	47[c]	14[c]	
9[g]	D_2O	75[d]	15[d]	0[d]	
10[g]	Stryker's Reagent	99[d]	0	0	
11[g]	No ligand	84[d]	0	0	

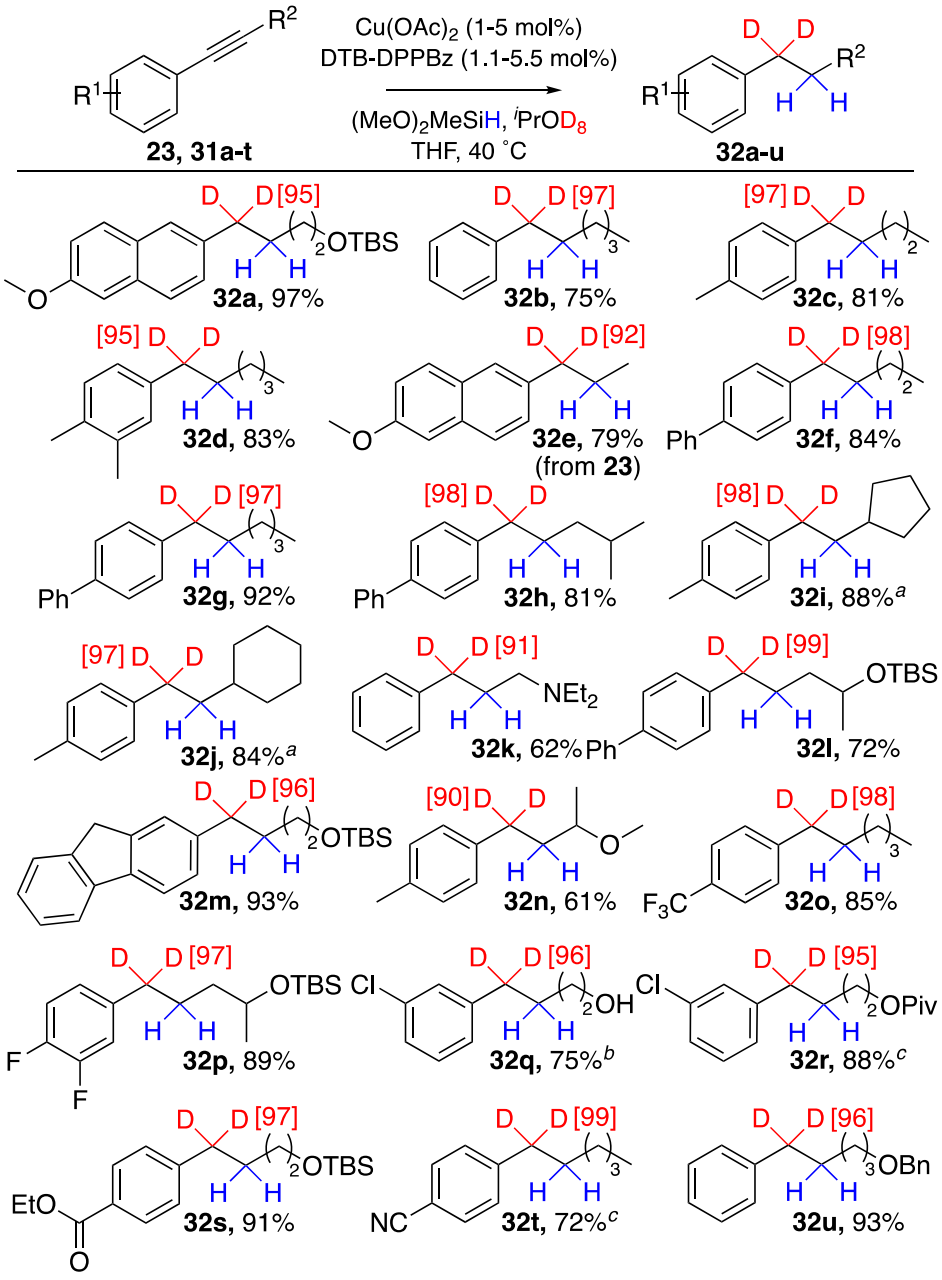
[a]Reactions were conducted using 0.2 mmol of substrate. $Cu(OAc)_2$ was used in the reactions as a 0.2 M solution in THF. [b]Deuterium incorporation at C_1 of alkane **32a** products. [c]Yield was determined after purification by flash column chromatography. [d]Yield was determined by ^{1}H NMR analysis of the crude reaction mixture using 1,3,5-trimethylbenzene as an internal standard. [e]*Poly*(methylhydrosiloxane). [f]Diethoxymethylsilane. [g]2 mol% $Cu(OAc)_2$ and 2.2 mol% DTB-DPPBz were used.

We sought out to explore a wide variety of internal aryl alkyne substrates for this transformation. Synthesizing the starting materials was rather straightforward since a Sonogashira coupling procedure could accomplish the formation of all internal alkynes.[100] All products were characterized by ^{1}H, ^{2}H, ^{13}C NMR,

IR, and HRMS. First, electron rich, methoxynaphthalene **32a and 32e** (Scheme 38, 79% and 97% yield, 92% and 95% D incorporation, respectively), containing substrates were explored and isolated in excellent yields. Note that changing the alkyne substitution from TBS-protected butynol to propyne had a slight effect on the deuterium incorporation. Electron neutral substrates including phenyl, tolyl, xylol, and biphenyl arenes, show consistently high isolated yields and excellent deuterium incorporation (**32b-d, 32f-h;** 75-92% yield, 95-98% D inc.).

A direct comparison of the preliminary regioselective result in Scheme 24 (**11-A,** transfer hydrodeuteration of 1-hexyn-1-yl-benzene: *79% deuterium incorporation at the benzylic site and 7% deuterium incorporation at the homobenzylic site* when using 5 mol% $Cu(OAc)_2$, 5.5 mol% (*R*)-DTBM-SEGPHOS, 5 equivalents of dimethoxy(methyl)silane and 5 equivalents of 2-propanol-d_8 in THF at 60 ˚C) to the optimized reaction conditions in Scheme 38 (**32b,** transfer hydrodeuteration of 1-hexyn-1-yl-benzene after reaction optimization: *97% deuterium incorporation at the benzylic site* when using only 1 mol% $Cu(OAc)_2$, 1.1 mol% DTB-DPPBz, 5 equivalents of dimethoxy(methyl)silane and 5 equivalents of 2-propanol-d_8 in THF at 40 ˚C) confirm the significant improvement in selectivity and reactivity that the DTB-DPPBz ligand offers compared to (*R*)-DTBM-SEGPHOS.

Scheme 38: Aryl Alkyne Substrate Scope

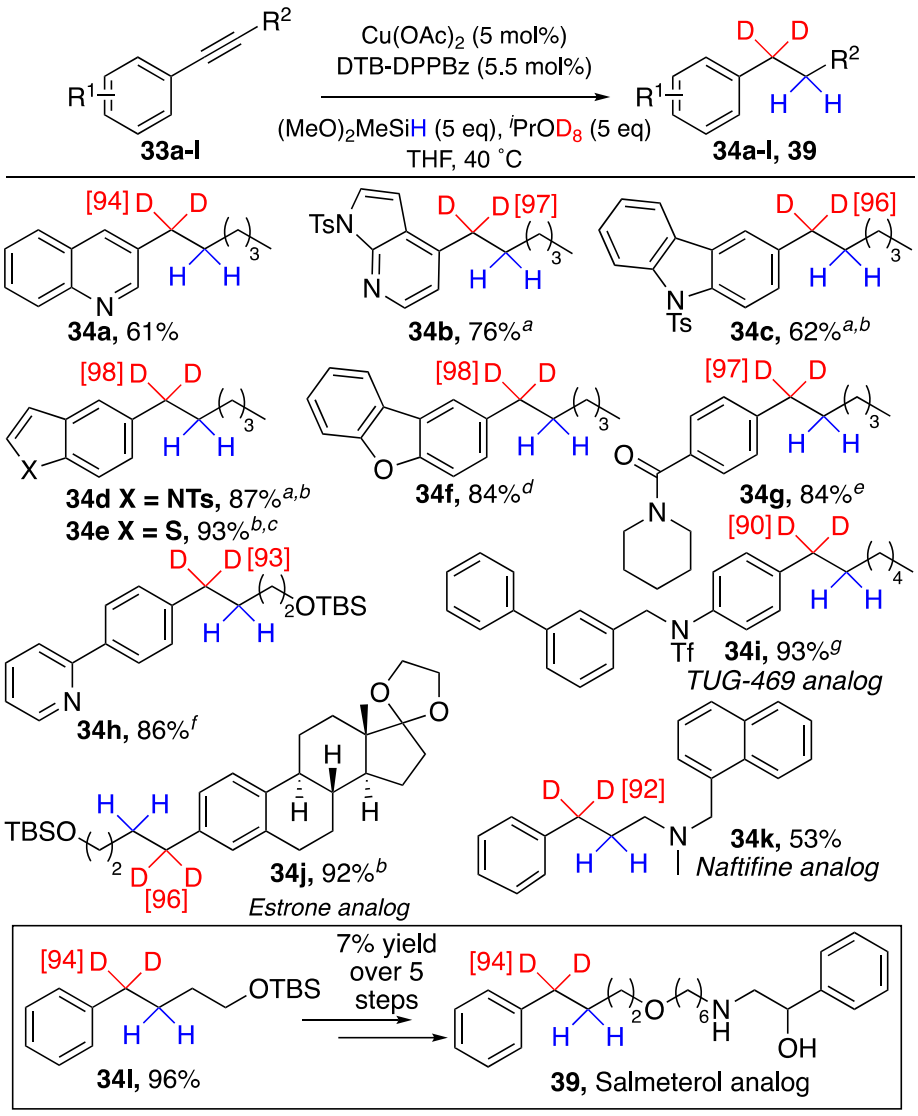


[a]Poly(methylhydrosiloxane) (5 eq.) used. [b]Isolated yield over 2-steps. [c]Reaction performed at 5 °C.

Altering the steric bulk proximal to the alkyne did not modify the deuterium incorporation, as still 97-98% D inc was observed in substrates **32i-j (**84-88% yield**).** Also, poly(methylhydrosiloxane) was a feasible silane source for these examples, and isolation from poly(methylhydrosiloxane) was possible due to the nonpolar nature of the alkane product. Lewis basic nitrogen functionality and oxygen containing

substrates are compatible with the transfer hydrodeuteration (**32k-n;** 61-93% yield, 90-99% D inc.), although alcohols did require simple protecting groups. Halogen containing, as well as sensitive functionality (esters, cyano, and benzyl ethers) were tolerated in this transformation (**32o-u;** 72-93% yield, 95-99% D inc.). In all substrate cases, less than 5% deuterium incorporation was observed at the undesired homobenzylic site, confirmed by ^{1}H and ^{2}H NMR, proving that a highly selective method for deuterium incorporation at the benzylic site has been developed.

Scheme 39: Heterocycle and Complex Molecule Substrate Scope



[a]Reaction performed at 60 ˚C. [b]6 eq of $(MeO)_2MeSiH$ was used. [c]1 mol% $Cu(OAc)_2$ and 1.1 mol% DTB-DPPBz used. [d]2 mol% $Cu(OAc)_2$ and 2.2 mol% DTB-DPPBz used. [e]6 eq of $^iPrOD_8$ used. [f]6.8 mol% $Cu(OAc)_2$, 7.4 mol% DTB-DPPBz, 8.1 eq $(MeO)_2MeSiH$, and 6.8 eq $^iPrOD_8$ used. [g]5.2 mol% $Cu(OAc)_2$, 5.7 mol% DTB-DPPBz, 5.2 eq $(MeO)_2MeSiH$, and 5.2 eq $^iPrOD_8$.

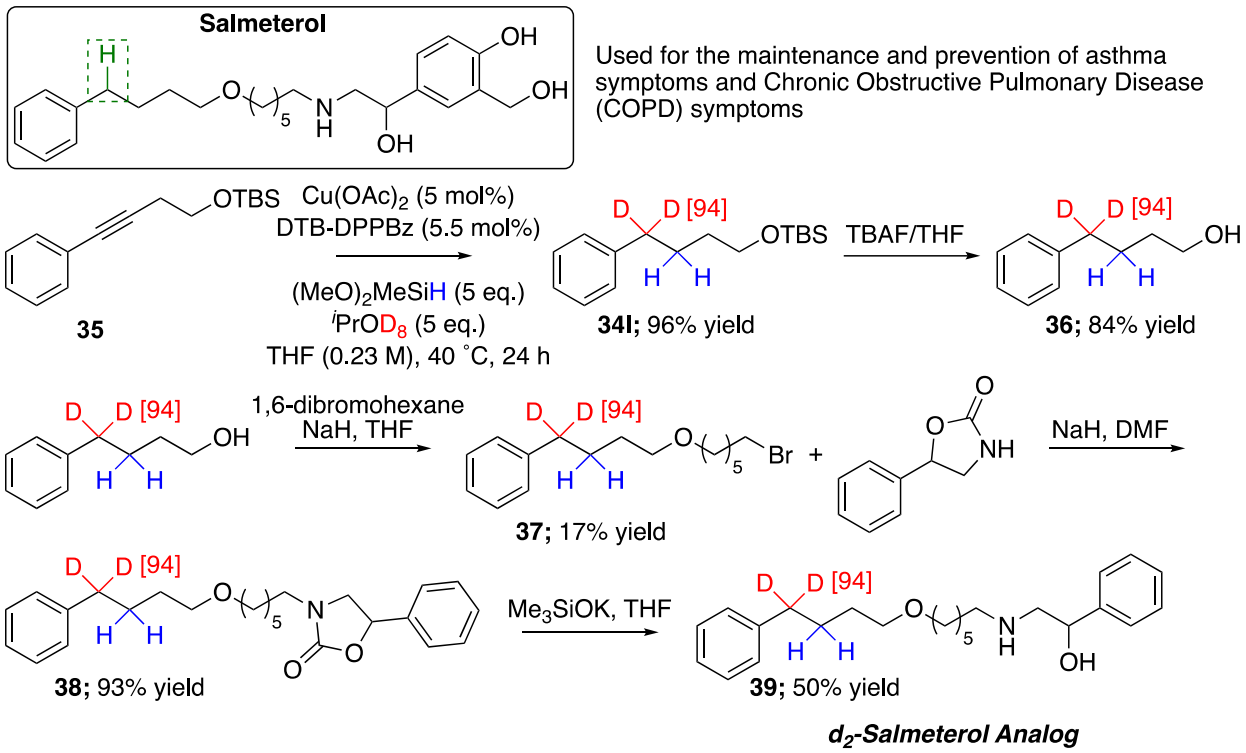
Due to the prevalence of heterocycle containing compounds in bioactive molecules, heterocycle containing aryl alkynes were explored for the transfer hydrodeuteration. Quinoline, tosyl-protected aza-indole, tosyl-protected carbazole, and tosyl-protected indole containing substrates were isolated after successful transfer hydrodeuteration (Scheme 39, **34a-d**; 61-87% yield, 94-98% D inc.). Additionally, the selectively deuterated products of a benzothiophene, dibenzofuran, an amide containing arene, and a

pyridine substituted aryl alkyne were isolated in excellent yields (Scheme 39, **34e-h;** 84-93% yield, 93-98% D inc.). Interestingly, the amide functionality was tolerated in this transformation, as no overreduction product was observed in the crude ^{1}H NMR. However, a ketone containing substrate, 1-(4-(hex-1-yn-1-yl)phenyl)ethan-1-one, was not tolerated and indeed over reduction of the ketone functionality was observed. Unfortunately, debromination was seen with the transfer hydrodeuteration of 4-bromo-1-(hex-1-yn-1-yl)-2-methoxybenzene. Therefore, although a highly diverse substrate scope was demonstrated, substrate limitations included ketones and aryl bromide containing compounds.

Finally, complex molecules and drug analogues were explored. TUG-469 is a FFA1 agonist, and its alkyne derivative was synthesized, followed by subjection to the transfer hydrodeuteration. The desired product was isolated in 93% yield, with 90% deuterium incorporation observed at the benzylic site (Scheme 39, **34i)**. This compound required further reaction optimization, and it was found that using a solvent mixture of THF:1,4-Dioxane (4:1) was essential for this transformation. Also, the reaction concentration was decreased down to 0.23 M, and the reaction was run for 48 hours. Similarly, the estrone analogue was synthesized and then subjected to the Cu-catalyzed reaction, and the product was isolated in 92% yield with 96% deuterium incorporation observed at the benzylic site **(34j)** after running the reaction for 72 hours. A Naftifine analogue, an antifungal drug, was synthesized and then subjected to transfer hydrodeuteration, and it was isolated in 53% yield and 92% D inc (**34k**). Salmeterol is a drug molecule that is used for asthma and Chronic Obstructive Pulmonary Disease symptoms, and a key metabolite of salmeterol is α-hydroxysalmeterol: involving metabolic oxidation at the benzylic site.[12, 101] Therefore, synthesizing a benzylic d_2-salmeterol analogue was intruiging. Using an early-stage functionalization technique, the transfer hydrodeuteration of the TBS-protected 1-phenyl-butynol **35** was run on a 2.00 mmol scale and isolated in 96% yield with 94% deuterium incorporation observed (Scheme 40, **34l**). Following the transfer hydrodeuteration, the product was subjected to silane deprotection using tetrabutylammonium fluoride (TBAF) to generate product **36**, and then the deprotonation of the alcohol with NaH in the presence of 1,6-dibromohexane allowed for the formation of the alkyl-bromide intermediate **37**. Using 5-phenyl-2-oxazolidine with NaH provided the protected d_2-salmeterol analogue **38**, and finally subjection to Me_3SiOK

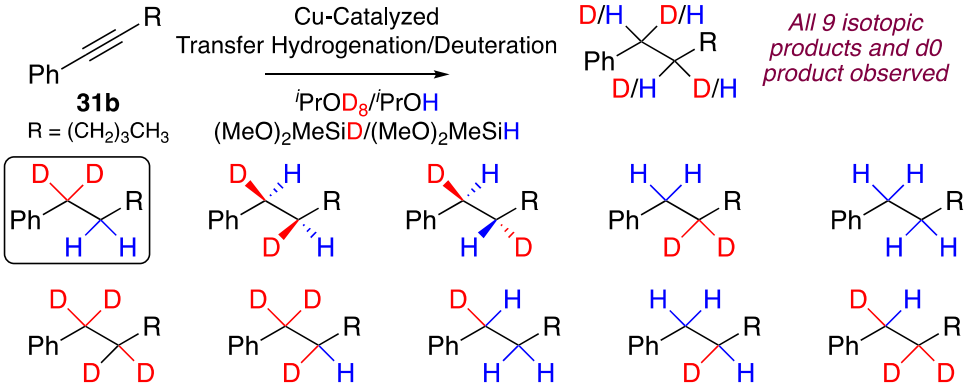
in THF for deprotection allowed for the desired d_2-salmeterol analogue **39** to be generated in 50% yield with 94% deuterium incorporation at the benzylic site. It is important to note that 94% deuterium incorporation was retained throughout all 4 synthetic transformations.

Scheme 40: D_2-Salmeterol Analogue Synthesis



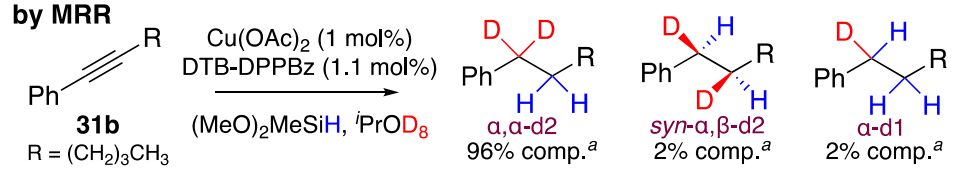
To further confirm the high regioselectivity observed in the transfer hydrodeuteration reaction of aryl alkynes, we reestablished our collaboration with Professor Brooks Pate at the University of Virginia and BrightSpec Inc. to determine the isotopic product ratios in our aryl alkyne reaction product mixture. First, we ran a Cu-catalyzed transfer hydrogenation/transfer deuteration on 1-phenyl-1-hexyne with both deuterated alcohol and silane, and protonated alcohol and silane, in a 1:1 ratio. This would allow for all possible isotopic products, including the d_0 species, to be formed (Scheme 41). A unique spectral signal was detected on MRR for each of these isotopic species.

Scheme 41: Alkyne Reduction to Access All Possible Isotopic Species



This was followed by direct MRR analysis of the standard transfer hydrodeuteration product of 1-phenyl-1-hexyne (Scheme 42, **31b**). Scheme 42 shows that 96% composition of the isolated product was the desired α,α-d_2-alkane (two deuterium positioned at the benzylic site). Only 2% of the *syn*-α,β-d_2-alkane and 2% of the α-d_1-alkane were observed. This allows for confirmation through MRR that the Cu-catalyzed transfer hydrodeuteration of aryl alkynes is indeed a highly regioselective method for the production of diverse bisdeuterated benzylic alkane products (α,α-d_2-alkanes).

Scheme 42: Regioselective Transfer Hydrodeuteration Reaction Measured by MRR

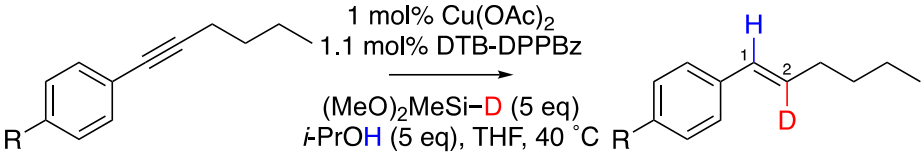


[a]Denotes the average percent composition of isolated product from two runs.

Finally, to address the transfer deuterohydrogenation reaction, we explored the regioselectivity of 2 electron neutral substrates using $Cu(OAc)_2$, DTB-DPPBz as the ligand, dimethoxy(methyl)silane-d_1 (instead of dimethoxy(methyl)silane) and 2-propanol (instead of 2-propanol-d_8) (Scheme 43). We stopped the reaction about halfway through, so we could observe the regioselectivity ratios of the alkene species. We observed a 91% deuterium incorporation at the β-carbon of the β-d_1-alkene (C_2) when subjecting 1-phenyl-1-hexyne **40** to the transfer deuterohydrogenation. Also, we observed a 92% deuterium incorporation at the β-carbon of the β-d_1-alkene (C_2) when subjecting 1,1'-biphenyl-1-hexyne **41** to the

reaction conditions (Scheme 43). These results assure that a highly regioselective transfer deuterohydrogenation of aryl alkynes is also feasible.

Scheme 43: Regioselective Transfer Deuterohydrogenation



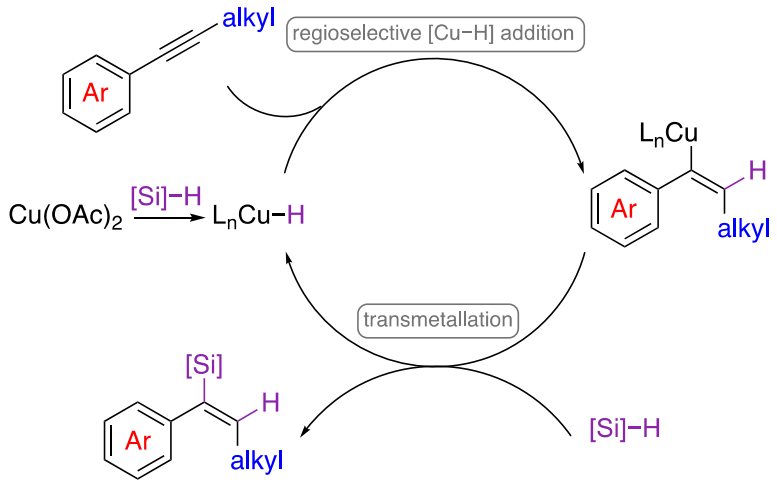
Substrate	%D C_1 Alkene	%D C_2 Alkene
R = H (**40**)	0	91
R = Ph (**41**)	0	92

Chapter 4

Regioselective Cu-Catalyzed Hydrosilylation of Internal Aryl Alkynes

The high regioselectivities of aryl alkene and alkyne transfer hydrodeuterations achieved in Chapter 2 and 3 inspired exploration into other functional groups in the Cu–H catalyzed hydrofunctionalization reaction.[21, 93] To attempt a hydrosilylation, the alcohol was left out of the typical transfer hydrogenation/transfer hydrodeuteration reaction pot. The reaction included an aryl alkyne, $Cu(OAc)_2$, DTB-DPPBz, and Ph_2SiH_2 in benzene reacting at 40 ˚C overnight. There was some reaction observed, even without the presence of the alcohol. The product formed was the vinylsilane species, confirmed by $^{1}H/^{13}C$ NMR and GCMS. Vinylsilane species are known to be readily stable and easy to handle building blocks in organic synthesis, such as in a Denmark-Hiyama cross coupling, a Fleming-Tamao Oxidation, halogenations, and reduction reactions.[57-59] However, a key challenge associated with the formation of vinylsilane products from a hydrosilylation of alkynes protocol is the formation of isomers, both regioisomers and stereoisomers. This isomer formation challenge has been combated by using symmetrical internal alkynes or by taking advantage of directing groups and steric hindrance. However, access to α–*E*–vinylsilane products from unsymmetrical internal aryl alkynes still remains elusive.

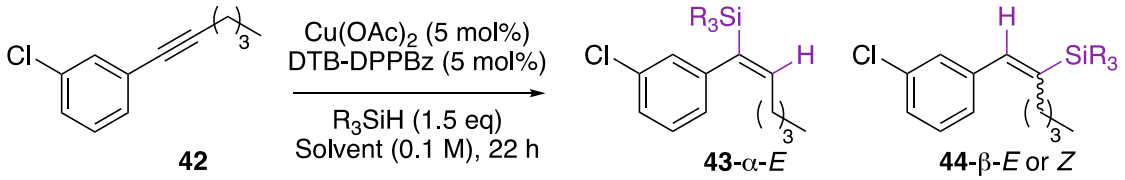
Scheme 44: Proposed Hydrosilylation Catalytic Cycle



We proposed that our expertise in the transfer hydrodeuteration of aryl alkynes would serve beneficial in a regio- and stereoselective hydrosilylation reaction of unsymmetrical internal aryl alkynes.

Ideally, two key mechanistic features in our proposed transfer hydrodeuteration reaction could promote high selectivity in the hydrosilylation. First, the highly regioselective hydrocupration across the alkyne to position copper α-to the arene, followed by the rapid transmetallation of the vinylcuprate with the silane, can allow for highly selective formation of α-*E*-vinylsilane products (Scheme 44).[93] The rapid transmetallation can prevent the formation of multiple isomers. Also, knowing that the Cu–H species inserts *syn* in the transfer hydrodeuteration of aryl alkenes, if the Cu–H also inserts in a *syn*-manner for the transfer hydrodeuteration of alkynes, access to α–*E*–vinylsilane products would be achievable.[21] The proposed reaction mechanism promoted the exploration of the reaction optimization for a highly selective hydrosilylation of unsymmetrical internal aryl alkynes.

Table 5: Hydrosilylation Reaction Optimization



42 **43**-α-*E* **44**-β-*E* or *Z*

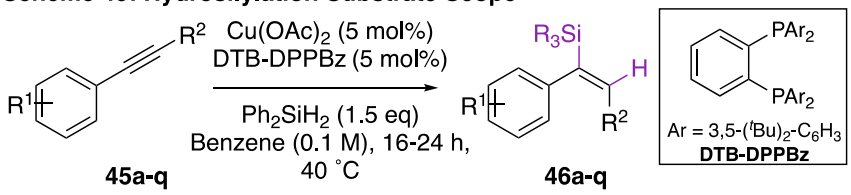
Entry	Solvent	Silane (1.5 eq)	T (˚C)	RSM (**42**)[b]	Yield (**43**)[c]
1[a]	Benzene	Ph_2SiH_2	40	-	73%
2	Benzene	Ph_2SiH_2	40	-	87%
3	Benzene	Ph_3SiH	40	84%	-
4	Benzene	DMMS[d]	40	81%	-
5	Benzene	Ph_2SiH_2	rt	-	84%
6	Benzene	Ph_2SiH_2	5	-	80%
7	Toluene	Ph_2SiH_2	40	-	74%
8	Tetrahydrofuran	Ph_2SiH_2	40	-	82%

Regioselectivity ratios were >20:1 in all cases, indicative of trace (<5%) or no observation of **44** in the crude NMR and purified product. [a]3 mol% $Cu(OAc)_2$ and DTB-DPPBz used. [b]Determined by crude ^1H NMR using mesitylene as an internal standard [c]Isolated yield after purification by flash chromatography. [d]DMMS = dimethoxymethylsilane.

In our prior studies, we discovered that the (DTB-DPPBz)Cu–H catalyst underwent a highly regioselective hydrocupration in internal aryl alkyne substrates due to enhanced orbital mixing interactions between the Cu-metal catalyst and the DTB-DPPBz ligand. We initiated reaction optimization by using a relatively simple substrate, 1-chloro-3-(1-hexyn-1-yl)benzene, with $Cu(OAc)_2$ (3 mol%), DTB-DPPBz (3 mol%), Ph_2SiH_2 (1.5 eq) in benzene (0.1 M total) and ran the reaction for 22 hours at 40 ˚C. The desired

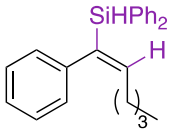
product was obtained in 73% yield with a >20:1 regioselectivity ratio of **43:44** (Table 5, entry 1). Increasing the catalyst loading to 5 mol% provided a higher yield of the α-*E*-vinylsilane product **43** (Table 5, entry 2, 87% yield, >20:1). However, using other silanes such as Ph_3SiH or DMMS ($(OMe)_2MeSiH$) were not feasible in this transformation as only recovered starting material (RSM) was observed (Table 5, entry 3-4). Decreasing the reaction temperature to room temperature or 5 ˚C showed slightly diminished reaction yields and consistently high regioselectivity ratios (Table 5, entry 5-6, 80-84% yield, >20:1). Exchanging the solvent for toluene (Table 5, entry 7, 74% yield, >20:1) or THF (Table 5, entry 8, 82% yield, >20:1), though feasible for the hydrosilylation reaction, resulted in lower product yields with slightly diminished regioselectivity.

Scheme 45: Hydrosilylation Substrate Scope

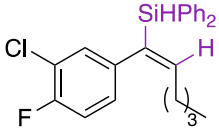


45a-q **46a-q**

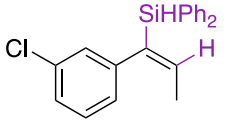
Aryl Alkyne Scope:



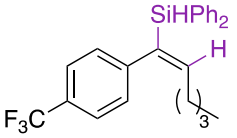
46a, 77% yield (>20:1)[a]



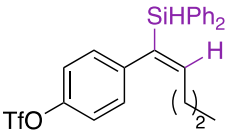
46b, 83% yield (>20:1)



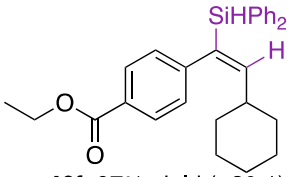
46c, 69% yield (>20:1)[b]



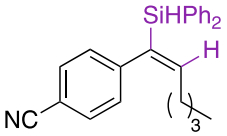
46d, 84% yield (>20:1)



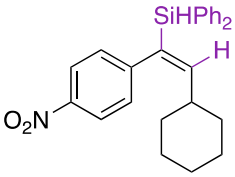
46e, 81% yield (>20:1)



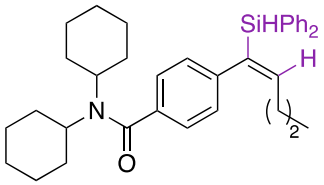
46f, 97% yield (>20:1)



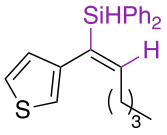
46g, 62% yield (>20:1)



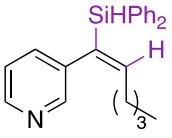
46h, 58% yield (>20:1)[b]



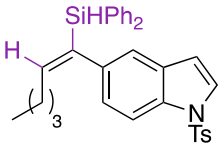
46i, 47% yield (>20:1)



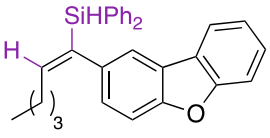
46j, 72% yield (20:1)



46k, 91% yield (>20:1)[c]

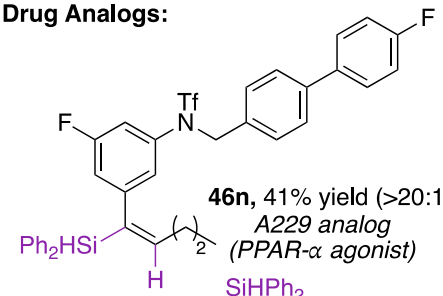


46l, 30% yield (>20:1)

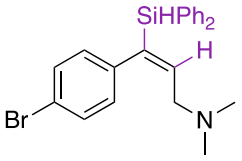


46m, 64% yield (12:1)

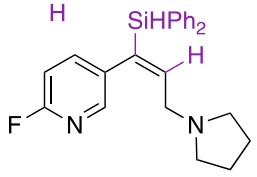
Drug Analogs:



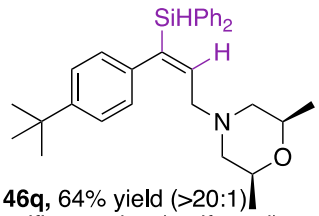
46n, 41% yield (>20:1)
A229 analog
(PPAR-α agonist)



46o, 36% yield (>20:1)
Zimelidine analog
(antidepressant)



46p, 33% yield (>20:1)
Triprolidine analog (antihistamine)



46q, 64% yield (>20:1)
Amorolfine analog (antifungal)

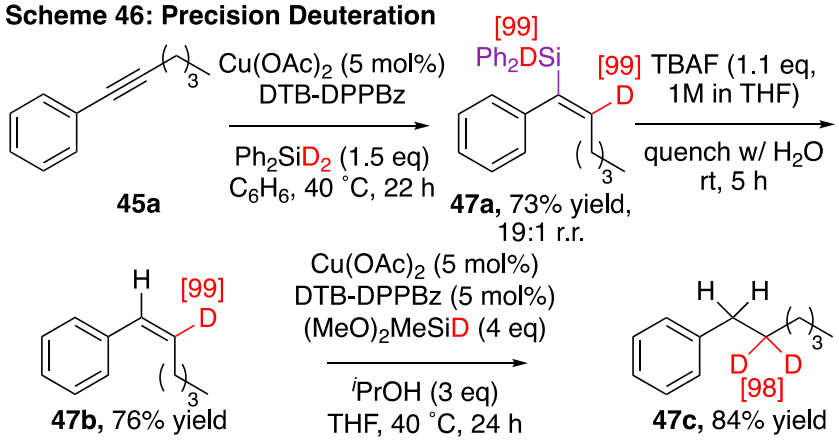
Regioselectivity ratios were determined by ^{1}H NMR after product isolation and denoted in parentheses. [a]Toluene used instead of benzene. [b]Trace (<5%) α-Z product observed. [c]10 mol% Cu(OAc)2/DTB-DPPBz used.

With the optimized reaction conditions in hand (Table 5, entry 2), we performed a regioselective hydrosilylation reaction across aryl alkyne substrates containing functionality relevant to small molecule drugs and biologically relevant compounds (Scheme 45). We also targeted aryl alkyne substrates that had the potential for further modifications, due to the opportunity for vinylsilanes to be used as building blocks. The electron neutral 1-phenyl-hexyne substrate was subjected to the hydrosilylation with toluene instead of benzene, and the α-*E*-vinylsilane product **46a** was isolated in 77% yield with a >20:1 regioselectivity ratio. Halogen substitution on an arene represents an important functional handle for further manipulation. Aryl halide containing substrates allow for cross coupling reactions to be pursued but are also challenging to address in Cu catalysis because of the potential for dehalogenation to occur.[93] Importantly, no dehalogenation was observed in the hydrosilylation of *m*-Cl/*p*-F, *m*-Cl, and *p*-CF_3 containing substrates (Scheme 45, **46b-d,** 69-84% yield, >20:1). A triflate protected phenol, as well as an ethyl ester substituted arene with increased steric bulk on the alkyne, demonstrates the α-*E*-vinylsilane product isolated in high yields (Scheme 45, **46e-f**, 81-97% yield, >20:1). Nitrile, nitro, and amide functionalized aryl alkynes were explored, and although the respective products were isolated in slightly lower yields, the high levels of selectivity were retained (Scheme 45, **46g-i**, 47-62% yield, >20:1). Finally, sulfur, nitrogen, and oxygen containing heterocycles were subjected to the hydrosilylation reaction due to their prevalence in drug molecules, and all were isolated in useful to good yields and demonstrated consistently high regioselectivity ratios (Scheme 45, **46j-m**, 30-91% yield, >20:1 – 12:1). In fact, the dibenzofuran substituted α-*E*-vinylsilane product was the only substrate that showed less than 20:1 regioselectivity.

Drug molecule analogues containing unsymmetrical internal aryl alkynes were synthesized and then subjected to the hydrosilylation reaction. Through a straightforward 3 step synthesis, the alkyne derivative of A229, a PPARα agonist, was synthesized, and then underwent highly regio- and stereoselective hydrosilylation (Scheme 45, **46n,** 41% yield, >20:1).[102] Zimelidine was one of the first SSRI antidepressants on the market and its alkyne derivative was successfully synthesized followed by regio- and stereoselective hydrosilylation (Scheme 45, **46o**, 36% yield, >20:1).[103, 104] A similar synthesis was used

to generate the Triprolidine analogue, an antihistamine, which was then subjected to hydrosilylation (Scheme 45, **46p,** 33% yield, >20:1).[105] Both the Zimelidine and the Triprolidine analogues showed a single regio- and stereoisomer formed throughout the copper catalyzed hydrosilylation. Lastly, an antifungal drug derivative containing a morpholine ring, Amorolfine, underwent hydrosilylation in a highly selective manner to generate only one isomer in a great yield (Scheme 45, **46q,** 64% yield, >20:1).[106]

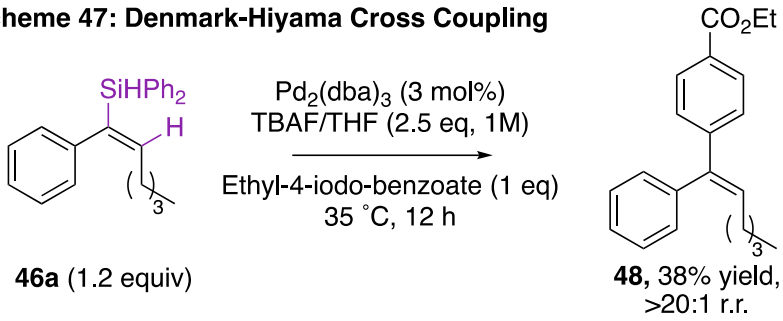
Scheme 46: Precision Deuteration



To demonstrate the broad applicability of these α-*E*-vinylsilane products, we explored small molecule precision deuteration, Denmark-Hiyama cross coupling, Fleming-Tamao oxidation, and silanol and methoxysilane synthesis with the hydrosilylation reaction products. First, subjecting the simple, electron neutral 1-phenyl-1-hexyne substrate to the deuterosilylation reaction conditions with Ph_2SiD_2, rather than Ph_2SiH_2, allowed for the formation of product **47a**, in 73% yield with a 19:1 regioselectivity ratio (Scheme 46). 99% deuterium incorporation was observed at the β-carbon of the alkene as well as on the silane at the α-carbon, determined by both $^1H/^2H$ NMR. This product underwent desilylation with TBAF/THF and was quenched with H_2O to access the β-d_1-phenyl-hexene species (Scheme 46, **47b**, 76% yield, 99% deuterium incorporation).[94] This was followed by transfer deuterohydrogenation, using $Cu(OAc)_2$ (5 mol%), DTB-DPPBz (5.5 mol%), $(MeO)_2MeSiD$ (4 eq), $^{i}PrOH$ (3 eq), THF (0.1 M), and running the reaction at 40 ˚C for 24 h, to access the highly novel β,β-d_2-phenyl-hexane (Scheme 46, **47c,** 84% yield, 98% deuterium incorporation at the homobenzylic site).[21] This species was fully characterized by ^1H, ^2H, ^{13}C-NMR, IR and HRMS, similarly to all other newly reported compounds. To the best of our

knowledge, this is the first example of accessing these types of molecules with such high deuterium incorporation at exclusively the homobenzylic position.

Scheme 47: Denmark-Hiyama Cross Coupling

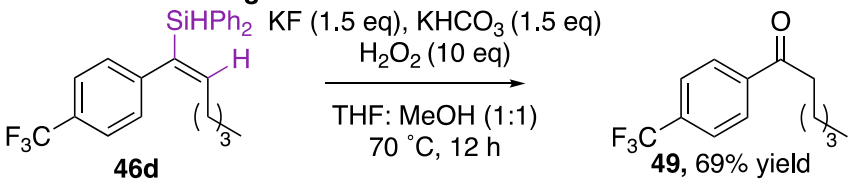


46a (1.2 equiv)

48, 38% yield, >20:1 r.r.

Additionally, we applied the Denmark-Hiyama cross coupling protocol to an electron neutral α-*E*-vinylsilane product and observed 38% isolated yield of the desired product when coupled with ethyl-4-iodobenzoate (Scheme 47, **48**).[57] A >20:1 ratio of isomers was determined by ^{1}H NMR. The low yield of this cross coupling is likely due to the presence of water in the TBAF/THF solution, causing the rapid formation of 1-hexenylbenzene. The Fleming-Tamao oxidation was also explored and shown to be viable with the α-*E*-vinylsilane hydrosilylation reaction products, as a CF_3 substituted α-*E*-vinylsilane underwent oxidation with KF, $KHCO_3$, and H_2O_2 (Scheme 48, **49**, 69% yield) to access the respective benzylic ketone, 1-(4-(trifluoromethyl)phenyl)hexan-1-one in a great yield.[58]

Scheme 48: Fleming-Tamao Oxidation

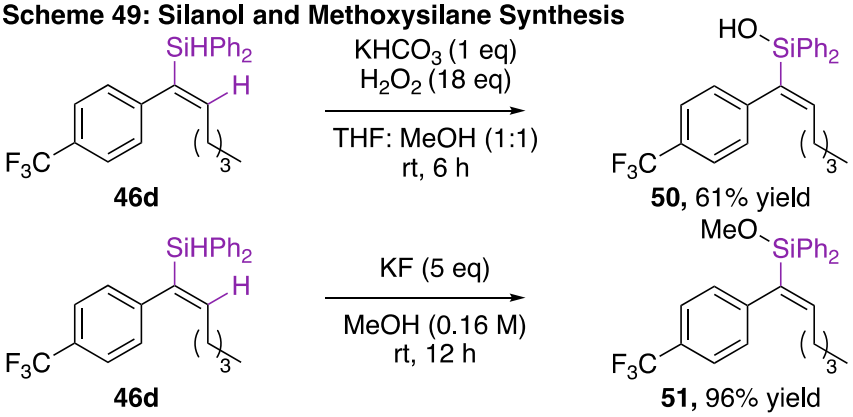


46d

49, 69% yield

Finally, α-*E*-vinylsilane oxidations took place on (*E*)-diphenyl(1-(4-(trifluoromethyl)phenyl)hex-1-en-1-yl)silane **46d** to obtain the desired silanol **50** and methoxysilane **51** products in excellent yields (Scheme 49, **50-51**, 61-96% yield).

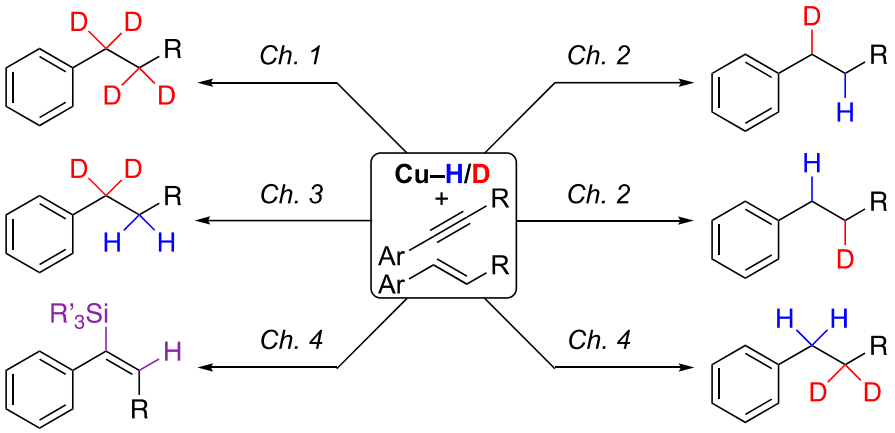
Scheme 49: Silanol and Methoxysilane Synthesis



Conclusion

In conclusion, precision deuteration techniques are elusive, but essential for installing deuterium selectivity into small molecules and drugs. A mild, chemoselective Cu–H catalyzed transfer hydrogenation method was developed with a broad substrate scope and a similar transfer deuteration method was employed, installing up to four deuterium atoms across a diverse set of aryl alkanes, two of which were located at the benzylic site and two at the homobenzylic site (generating α,α,β,β-d_4-aryl alkanes). Through mechanistic studies, it was observed that the proposed mechanism likely goes through both a *cis*- and *trans*-alkene intermediate due to the potential for the hydrocupration of the aryl alkene to be a reversible step. Next, a regioselective approach was taken by exchanging one protonated reagent for one deuterated reagent of the transfer hydrogenation protocol. Mildly regioselective results were observed, but further exploration was required. The second half of the regioselective transfer hydrodeuteration mechanism was initially addressed (aryl alkene to aryl alkane), by investigating the regioselective transfer hydrodeuteration of aryl alkenes to install one deuterium atom at the benzylic site. Through reaction optimization, a highly regioselective protocol was developed, and the high regioselectivity was explored on a wide variety of substrates and confirmed by molecular rotational resonance (MRR) spectroscopy, leading to the formation of α-d_1-aryl alkanes (deuterium at the benzylic site) or β-d_1-aryl alkanes (deuterium at the homobenzylic site). This was followed by the exploration of the first half of the regioselective transfer hydrodeuteration mechanism (aryl alkyne to aryl alkene). Experimental ligand optimization results coincided with DFT conclusions, demonstrating that DTB-DPPBz was the optimal ligand for the regioselective transfer hydrodeuteration of aryl alkynes to obtain a diverse set of deuterated alkanes, with deuterium exclusively positioned at the benzylic site in high quantities, forming α,α-d_2-aryl alkanes. This protocol was demonstrated on diverse substrates including drug molecules and biologically relevant compounds, and the high regioselectivity was confirmed by MRR analysis. Finally, based on the high regioselectivity obtained from the alkyne transfer hydrodeuteration, a regio- and stereoselective hydrosilylation of aryl alkynes was evaluated. Vinylsilanes can be used as building blocks in drug discovery because of their stability and ease

of handling, however obtaining a single regio- and stereoisomer is quite challenging. A hydrosilylation approach, using DTB-DPPBz as the ligand, was explored to access α-*E*-vinylsilane products. A deuterosilylation reaction was feasible on aryl alkynes, followed by desilylation and transfer deuterohydrogenation, to provide access to novel β,β-d_2-aryl alkanes. Future work in this area includes investigating precision deuteration techniques on different substrate classes and positioning deuterium into other metabolically labile locations, such as tertiary sites. Also, future studies include investigating a hydrosilylation of aryl alkynes, followed by a deutero-desilylation, and then a transfer hydrodeuteration to provide unique access to α,α-d_2-aryl alkanes via a hydrosilylation.



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Research Methodology and Characterization
Chapter 1

General Information

The following chemicals were purchased from commercial vendors and were used as received: $Cu(OAc)_2$ (99.999% from Alfa Aesar); (*R*)-(-)-4,4'-bis[di(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphino]-3,3'-bi(1,2-methylenedioxybenzene) ((*R)*-DTBM-SEGPHOS) and (*S*)-(+)-4,4'-bis[di(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphino]-3,3'-bi(1,2-methylenedioxybenzene) ((*S)*-DTBM-SEGPHOS) (TCI), dimethoxy(methyl)silane (TCI); 2-propanol-OD (Millipore Sigma); ethanol-OD (Millipore Sigma); 2-propanol-d_8 (Acros Organic); ethanol (Oakwood Chemical); *tert*-butyldimethylsilyl chloride (TBSCl); D_2O (Oakwood Chemical); poly(methylhydrosiloxane) average M_n 1700-3200 (Millipore Sigma); methyltriphenylphosphonium bromide (Oakwood Chemical); Sodium hydride (in oil dispersion) 60% dispersion in mineral oil (Oakwood Chemical); sodium bis(trimethylsilyl)amide 2M in THF (Oakwood Chemical) potassium trifluoro(vinyl)borate (Oakwood Chemical); cesium carbonate (Ambeed Inc.); *n*-butyl lithium (Millipore Sigma).

Anhydrous tetrahydrofuran (THF) was purified by an MBRAUN solvent purification system (MB-SPS). Prior to use, triethylamine (Et_3N) was distilled over CaH_2 and stored over 3Å molecular sieves. Chloroform-*d* ($CDCl_3$) was stored over 3Å molecular sieves. Thin-layer chromatography (TLC) was conducted with Silicycle silica gel 60Å F254 pre-coated plates (0.25 mm) and visualized with UV, Iodine and $KMnO_4$ stains. Flash chromatography was performed using Silia Flash® P60, 40-60 mm (230-400 mesh), purchased from Silicycle. For reactions that required heating (optimization, transfer hydrogenation and deuteration reactions), a PolyBlock for 2 dram vials was used on top of a Heidolph heating/stir plate.

^1H NMR spectra were recorded on a Varian 300 or 400 MHz spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 7.26 ppm). Data reported as: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sxt = sextet, hep = heptet, oct = octet, m = multiplet, br = broad; coupling constant(s) in Hz; integration. ^{13}C NMR spectra were recorded on a Varian 76 MHz or 101 MHz spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 77.16 ppm). ^{19}F NMR spectra were recorded on a Varian 376 MHz spectrometer. ^2H NMR spectra were recorded on a Varian 61 MHz spectrometer. Labeled solvent impurities were calculated out when reporting isolated yields.

High-resolution mass spectra were obtained for all new compounds not previously reported using the resources of the Chemistry Instrument Center (CIC), University at Buffalo, SUNY, Buffalo, NY. Specifically, high resolution accurate mass analysis was conducted using the following instruments: 12T Bruker SolariXR 12 Hybrid FTMS, provided through funding from the National Institutes of Health, NIH S10 RR029517; a Thermo Q-Exactive Focus Orbitrap Liquid Chromatograph Tandem Mass Spectrometer and a Thermo Q-Exactive Orbitrap Gas Chromatograph Tandem Mass Spectrometer, provided through funding from the National Science Foundation, MRI-1919594.

Optimization Studies for Transfer Hydrogenation and Transfer Deuteration of Aryl Alkynes

General procedure A for optimization studies in Table 1:

In a N_2 filled glovebox, ligand, Cu catalyst (Cu:L = 1:1.1), and THF were added to an oven-dried 2-dram vial followed by dropwise addition of dimethoxy(methyl)silane (123 µL, 1 mmol, 5 eq.). A color change from green/blue to orange was observed while stirring for 15 minutes. In a separate oven-dried 1-dram vial was added 2-ethynyl-6-methoxynapthalene (36.4 mg, 0.2 mmol, 1 eq.), THF (0.1 mL), and 2-propanol (37 µL, 0.48 mmol, 2.4 eq.). The solution in the 1-dram vial was added dropwise over 20 seconds to the 2-dram

vial. The total volume of THF was calculated based on having a final reaction concentration of 1M based on the alkyne substrate. The 2-dram vial was capped with a red pressure relief cap, taken out of the glovebox, and stirred for 16 h at 60 °C at which point the reaction was filtered through a 1" silica plug with 20 mL of Et_2O or CH_2Cl_2 followed by an additional 80 mL of the appropriate solvent to elute the crude product into a 200 mL round bottom flask. The solvent was removed by rotary evaporation, and the product was analyzed by ^1H NMR using 1,3,5-trimethylbenzene as an internal standard. Yields for all entries were obtained by isolating the product after flash column chromatography if greater than 5% NMR yield was observed for **2b** in the crude ^1H NMR.

Entry 1. According to the general procedure A for optimization studies, a stirring solution of triphenylphosphine **L1** (5.8 mg, 0.022 mmol, 0.11 eq.), $Cu(OAc)_2$ (50 µL of a 0.2 M solution in THF, 0.01 mmol, 0.05 eq.), and dimethoxy(methyl)silane (123 µL, 1.0 mmol, 5 eq.) in THF (0.05 mL) was prepared, and to this was added a solution of 2-ethynyl-6-methoxynaphthalene (36.4 mg, 0.2 mmol, 1 eq.) and 2-propanol (37 µL, 0.48 mmol, 2.4 eq.) in THF (0.1 mL) dropwise. The reaction stirred for 16 h at 60°C, after which it was filtered through a silica plug with Et_2O (20 mL) and eluted with Et_2O (80 mL). The solvent was removed by rotary evaporation, and the crude product was analyzed by ^1H NMR with 1,3,5-trimethylbenzene as an internal standard, (11% **2a**, trace **2b**, 48% RSM **1**).

Entry 2. According to the general procedure A for optimization studies, a stirring solution of (triphenylphosphine)copper hydride hexamer (Stryker's Reagent) (3.3 mg, 0.0017 mmol, 0.00083 eq.), and dimethoxy(methyl)silane (123 µL, 1.0 mmol, 5 eq.) in THF (0.1 mL) was prepared, and to this was added a solution of 2-ethynyl-6-methoxynaphthalene (36.4 mg, 0.2 mmol, 1 eq.) and 2-propanol (37 µL, 0.48 mmol, 2.4 eq.) in THF (0.1 mL) dropwise. The reaction stirred for 16 h at 60°C, after which it was filtered through a silica plug with Et_2O (20 mL) and eluted with Et_2O (80 mL). The solvent was removed by rotary evaporation, and the crude product was analyzed by ^1H NMR with 1,3,5-trimethylbenzene as an internal standard (53% **2a**, 2.5% **2b**, 6% RSM **1**).

Entry 3. According to the general procedure A for optimization studies, a stirring solution of 1,2-bis(diphenylphosphino)benzene **L2** (4.9 mg, 0.011 mmol, 0.055 eq.), $Cu(OAc)_2$ (50 µL of a 0.2 M solution in THF, 0.01 mmol, 0.05 eq.), and dimethoxy(methyl)silane (123 µL, 1.0 mmol, 5 eq.) in THF (0.05 mL) was prepared, and to this was added a solution of 2-ethynyl-6-methoxynaphthalene (36.4 mg, 0.2 mmol, 1 eq.) and 2-propanol (37 µL, 0.48 mmol, 2.4 eq.) in THF (0.1 mL) dropwise. The reaction stirred for 16 h at 60°C, after which it was filtered through a silica plug with Et_2O (20 mL) and eluted with Et_2O (80 mL). The solvent was removed by rotary evaporation, and the crude product was analyzed by ^1H NMR with 1,3,5-trimethylbenzene as an internal standard (5% **2a**, trace **2b**, 82% RSM **1**).

Entry 4. According to the general procedure A for optimization studies, a stirring solution of 1,2-bis(diphenylphosphino)ethane **L3** (4.4 mg, 0.011 mmol, 0.055 eq.), $Cu(OAc)_2$ (50 µL of a 0.2 M solution in THF, 0.01 mmol, 0.05 eq.), and dimethoxy(methyl)silane (123 µL, 1.0 mmol, 5 eq.) in THF (0.05 mL) was prepared, and to this was added a solution of 2-ethynyl-6-methoxynaphthalene (36.4 mg, 0.2 mmol, 1 eq.) and 2-propanol (37 µL, 0.48 mmol, 2.4 eq.) in THF (0.1 mL) dropwise. The reaction stirred for 16 h at 60°C, after which it was filtered through a silica plug with Et_2O (20 mL) and eluted with Et_2O (80 mL). The solvent was removed by rotary evaporation, and the crude product was analyzed by ^1H NMR with 1,3,5-trimethylbenzene as an internal standard (8% **2a**, trace **2b**, 75% RSM **1**).

Entry 5. According to the general procedure A for optimization studies, a stirring solution of 1,1′-bis(diphenylphosphino)-ferrocene **L4** (6.1 mg, 0.011 mmol, 0.055 eq.), $Cu(OAc)_2$ (50 µL of a 0.2 M solution in THF, 0.01 mmol, 0.05 eq.), and dimethoxy(methyl)silane (123 µL, 1.0 mmol, 5 eq.) in THF (0.05 mL) was prepared, and to this was added a solution of 2-ethynyl-6-methoxynaphthalene (36.4 mg, 0.2 mmol, 1 eq.) and 2-propanol (37 µL, 0.48 mmol, 2.4 eq.) in THF (0.1 mL) dropwise. The reaction

stirred for 16 h at 60°C, after which it was filtered through a silica plug with Et_2O (20 mL) and eluted with Et_2O (80 mL). The solvent was removed by rotary evaporation, and the crude product was analyzed by ^1H NMR with 1,3,5-trimethylbenzene as an internal standard (11% **2a**, trace **2b**, 72% RSM **1**).

Entry 6. According to the general procedure A for optimization studies, a stirring solution of (±)-2,2′-bis(diphenylphosphino)-1,1′-binaphthalene **L5** (6.8 mg, 0.011 mmol, 0.055 eq.), $Cu(OAc)_2$ (50 µL of a 0.2 M solution in THF, 0.01 mmol, 0.05 eq.), and dimethoxy(methyl)silane (123 µL, 1.0 mmol, 5 eq.) in THF (0.05 mL) was prepared, and to this was added a solution of 2-ethynyl-6-methoxynaphthalene (36.4 mg, 0.2 mmol, 1 eq.) and 2-propanol (37 µL, 0.48 mmol, 2.4 eq.) in THF (0.1 mL) dropwise. The reaction stirred for 16 h at 60°C, after which it was filtered through a silica plug with Et_2O (20 mL) and eluted with Et_2O (80 mL). The solvent was removed by rotary evaporation, and the crude product was analyzed by ^1H NMR with 1,3,5-trimethylbenzene as an internal standard (12% **2a**, trace **2b**, 49% RSM **1**).

Entry 7. According to the general procedure A for optimization studies, a stirring solution of (*R*)-(+)-5,5′-bis(diphenylphosphino)-4,4′-bi-1,3-benzodioxole **L6** (6.7 mg, 0.011 mmol, 0.055 eq.), $Cu(OAc)_2$ (50 µL of a 0.2 M solution in THF, 0.01 mmol, 0.05 eq.), and dimethoxy(methyl)silane (123 µL, 1.0 mmol, 5 eq.) in THF (0.05 mL) was prepared, and to this was added a solution of 2-ethynyl-6-methoxynaphthalene (36.4 mg, 0.2 mmol, 1 eq.) and 2-propanol (37 µL, 0.48 mmol, 2.4 eq.) in THF (0.1 mL) dropwise. The reaction stirred for 16 h at 60°C, after which it was filtered through a silica plug with Et_2O (20 mL) and eluted with Et_2O (80 mL). The solvent was removed by rotary evaporation, and the crude product was analyzed by ^1H NMR with 1,3,5-trimethylbenzene as an internal standard. The crude product was dry loaded onto silica gel, and was purified by flash column chromatography using gradient elution (50 mL of hexane, 100 mL of 2% ethyl acetate in hexane, and 50 mL of 5% ethyl acetate in hexane) to yield a white solid (28.8 mg, 30% **2a**, 4% **2b**, 45% RSM **1**).

Entry 8. According to the general procedure A for optimization studies, a stirring solution of (*R*)-(−)-5,5′-bis[di(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphino]-4,4′-bi-1,3-benzodioxole **L7** (13.0 mg, 0.011 mmol, 0.055 eq.), $Cu(OAc)_2$ (50 µL of a 0.2 M solution in THF, 0.01 mmol, 0.05 eq.), and dimethoxy(methyl)silane (123 µL, 1.0 mmol, 5 eq.) in THF (0.05 mL) was prepared, and to this was added a solution of 2-ethynyl-6-methoxynaphthalene (36.4 mg, 0.2 mmol, 1 eq.) and 2-propanol (37 µL, 0.48 mmol, 2.4 eq.) in THF (0.1 mL) dropwise. The reaction stirred for 16 h at 60°C, after which it was filtered through a silica plug with Et_2O (20 mL) and eluted with Et_2O (80 mL). The solvent was removed by rotary evaporation, and the crude product was analyzed by ^1H NMR with 1,3,5-trimethylbenzene as an internal standard. The crude product was dry loaded onto silica gel, and was purified by column chromatography using gradient elution (50 mL of hexanes, 100 mL of 2% ethyl acetate in hexane, and 50 mL of 5% ethyl acetate in hexane) to yield a white solid (36.4 mg, 0.195 mmol, 98% yield).

Entry 9. According to the general procedure A for optimization studies, a stirring solution of (*R*)-(−)-5,5′-bis[di(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphino]-4,4′-bi-1,3-benzodioxole **L7** (2.6 mg, 0.0022 mmol, 0.011 eq.), $Cu(OAc)_2$ (10 µL of a 0.2 M solution in THF, 0.002 mmol, 0.01 eq.), and dimethoxy(methyl)silane (123 µL, 1.0 mmol, 5 eq.) in THF (0.09 mL) was prepared, and to this was added a solution of 2-ethynyl-6-methoxynaphthalene (36.4 mg, 0.2 mmol, 1 eq.) and 2-propanol (37 µL, 0.48 mmol, 2.4 eq.) in THF (0.1 mL) dropwise. The reaction stirred for 16 h at 60°C, after which it was filtered through a silica plug with Et_2O (20 mL) and eluted with Et_2O (80 mL). The solvent was removed by rotary evaporation, and the crude product was analyzed by ^1H NMR with 1,3,5-trimethylbenzene as an internal standard. The crude product was dry loaded onto silica gel, and was purified by column chromatography using gradient elution (50 mL of hexane, 100 mL of 2% ethyl acetate in hexane, and 50 mL of 5% ethyl acetate in hexane) to yield a white solid (33.8 mg, 3.5% **2a**, 87% **2b**).

Entry 10. According to the general procedure A for optimization studies, a stirring solution of (*R*)-(−)-5,5′-bis[di(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphino]-4,4′-bi-1,3-benzodioxole **L7** (5.2 mg, 0.0044 mmol, 0.022 eq.), $Cu(OAc)_2$ (20 µL of a 0.2 M solution in THF, 0.004 mmol, 0.02 eq.), and dimethoxy(methyl)silane (123 µL, 1.0 mmol, 5 eq.) in THF (0.08 mL) was prepared, and to this was added a solution of 2-ethynyl-6-methoxynaphthalene (36.4 mg, 0.2 mmol, 1 eq.) and 2-propanol (37 µL, 0.48 mmol, 2.4 eq.) in THF (0.1 mL) dropwise. The reaction stirred for 16 h at 60°C, after which it was filtered through a silica plug with Et_2O (20 mL) and eluted with Et_2O (80 mL). The solvent was removed by rotary evaporation, and the crude product was analyzed by ^1H NMR with 1,3,5-trimethylbenzene as an internal standard. The crude product was dry loaded onto silica gel, and was purified by column chromatography using gradient elution (50 mL of hexane, 100 mL of 2% ethyl acetate in hexane, and 50 mL of 5% ethyl acetate in hexane) to yield a white solid (33.8 mg, 0.182 mmol, 91% yield).

Entry 11. According to the general procedure A for optimization studies, a stirring solution of dimethoxy(methyl)silane (123 µL, 1.0 mmol, 5 eq.) in THF (0.1 mL) was prepared, and to this was added a solution of 2-ethynyl-6-methoxynaphthalene (36.4 mg, 0.2 mmol, 1 eq.) and 2-propanol (37 µL, 0.48 mmol, 2.4 eq.) in THF (0.1 mL) dropwise. The reaction stirred for 16 h at 60°C, after which it was filtered through a silica plug with Et_2O (20 mL) and eluted with Et_2O (80 mL). The solvent was removed by rotary evaporation, and the crude product was analyzed by ^1H NMR with 1,3,5-trimethylbenzene as an internal standard (4% **2a**, 86% RSM **1**).

Entry 12. According to the general procedure A for optimization studies, a stirring solution of $(Cu(OAc)_2$ (20 µL of a 0.2 M solution in THF, 0.004 mmol, 0.02 eq.) and dimethoxy(methyl)silane (123 µL, 1.0 mmol, 5 eq.) in THF (0.08 mL) was prepared, and to this was added a solution of 2-ethynyl-6-methoxynaphthalene (36.4 mg, 0.2 mmol, 1 eq.) and 2-propanol (37 µL, 0.48 mmol, 2.4 eq.) in THF (0.1 mL) dropwise. The reaction stirred for 16 h at 60°C, after which it was filtered through a silica plug with Et_2O (20 mL) and eluted with Et_2O (80 mL). The solvent was removed by rotary evaporation, and the crude product was analyzed by ^1H NMR with 1,3,5-trimethylbenzene as an internal standard (3% **2a**, 80% RSM **1**).

Entry 13. According to the general procedure A for optimization studies, a stirring solution of (*S*)-(−)-5,5′-bis[di(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphino]-4,4′-bi-1,3-benzodioxole **L7** (5.2 mg, 0.0044 mmol, 0.022 eq.), $Cu(OAc)_2$ (20 µL of a 0.2 M solution in THF, 0.004 mmol, 0.02 eq.), and poly(methylhydrosiloxane) (67 µL, 1.0 mmol, 5 eq.) in THF (0.08 mL) was prepared, and to this was added a solution of 2-ethynyl-6-methoxynaphthalene (36.4 mg, 0.2 mmol, 1 eq.) and 2-propanol (37 µL, 0.48 mmol, 2.4 eq.) in THF (0.1 mL) dropwise. The reaction stirred for 16 h at 60°C, after which it was filtered through a silica plug with Et_2O (20 mL) and eluted with Et_2O (80 mL). The solvent was removed by rotary evaporation, and the crude product was analyzed by ^1H NMR with 1,3,5-trimethylbenzene as an internal standard. The crude product was dry loaded onto silica gel, and was purified by column chromatography using gradient elution (50 mL of hexane, 100 mL of 2% ethyl acetate in hexane, and 50 mL of 5% ethyl acetate in hexane) to yield a white solid (35.4 mg, 0.19 mmol, 95% yield).

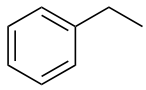
Entry 14. According to the general procedure A for optimization studies, a stirring solution of (*S*)-(−)-5,5′-bis[di(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphino]-4,4′-bi-1,3-benzodioxole **L7** (5.2 mg, 0.0044 mmol, 0.022 eq.), $Cu(OAc)_2$ (20 µL of a 0.2 M solution in THF, 0.004 mmol, 0.02 eq.), and diethoxy(methyl)silane (160 µL, 1.0 mmol, 5 eq.) in THF (0.08 mL) was prepared, and to this was added a solution of 2-ethynyl-6-methoxynaphthalene (36.4 mg, 0.2 mmol, 1 eq.) and 2-propanol (37 µL, 0.48 mmol, 2.4 eq.) in THF (0.1 mL) dropwise. The reaction stirred for 16 h at 60°C, after which it was filtered through a silica plug with Et_2O (20 mL) and eluted with Et_2O (80 mL). The solvent was removed by rotary evaporation, and the crude product was analyzed by ^1H NMR with 1,3,5-trimethylbenzene as an internal standard. The crude product was dry loaded onto silica gel, and was purified by column chromatography using gradient elution (50 mL

of hexane, 100 mL of 2% ethyl acetate in hexane, and 50 mL of 5% ethyl acetate in hexane) to yield a white solid (34.7 mg, 0.186 mmol, 93% yield).

Transfer Hydrogenation Substrate Scope (Scheme 18)

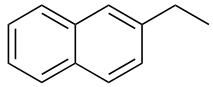
General procedure for transfer hydrogenation (B)
In a N_2 filled glovebox, (*R* or *S*)-DTBM-SEGPHOS (10.4 mg, 0.0088 mmol, 0.022 eq.), $Cu(OAc)_2$ (40 µL of a 0.2 M solution in THF, 0.008 mmol, 0.02 eq.), and THF (0.16 mL) were added to an oven-dried 2-dram vial followed by dropwise addition of dimethoxy(methyl)silane (247 µL, 2 mmol, 5 eq.). A color change from green/blue to orange was observed while stirring for 15 minutes. In a separate oven-dried 1-dram vial was added the alkyne substrate (0.4 mmol, 1 eq.), THF (0.2 mL), and either ethanol or 2-propanol (2.4-5 eq. based on substrate). The solution in the 1-dram vial was added dropwise over 20 seconds to the 2-dram vial. The total volume of THF was calculated based on having a final reaction concentration of 1M based on the alkyne substrate. The 2-dram vial was capped with a red pressure relief cap, taken out of the glovebox, and stirred for 9-24 h at the appropriate temperature at which point the reaction was filtered through a 1" silica plug with 20 mL of Et_2O followed by 80 mL of Et_2O to elute the remaining product into a 200 mL round bottom flask. After removing the Et_2O by rotary evaporation, the crude product was isolated by flash column chromatography.

General purification for alcohol containing substrates after transfer hydrogenation reaction (C)
The crude product was dissolved in THF (1.6 mL) and tetrabutylammonium fluoride (0.8 mL of 1.0 M in THF solution, 2 eq.) was added. The reaction was stirred at room temperature for 1-2 hours until complete by TLC analysis. Upon completion, reaction mixture was diluted with Et_2O (10 mL) and quenched with saturated aqueous NH_4Cl (5 mL). The aqueous layer was extracted with Et_2O (3 x 10 mL) and the combined organic layers were washed with water (10 mL) and brine (10 mL), then dried over anhydrous Na_2SO_4. The mixture was filtered, and the solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography to give the desired product.



Ethyl Benzene [4a]. According to the general transfer hydrogenation procedure B, (*S*)-DTBM-SEGPHOS (10.4 mg, 0.0088 mmol, 0.022 eq.), $Cu(OAc)_2$ (40 µL of a 0.2 M solution in THF, 0.008 mmol, 0.02 eq.), THF (0.16 mL), then dimethoxy(methyl)silane (247 µL, 2 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of ethynylbenzene (40.9 mg, 0.4 mmol, 1 eq.), THF (0.2 mL), and 2-propanol (74 µL, 0.96 mmol, 2.4 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 10 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and 18.5 µL of 1,3,5-trimethylbenzene was used as an internal standard to determine the ^{1}H NMR crude yield (66% crude yield by ^{1}H NMR).

^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.29 (t, *J* = 7.6 Hz, 2H), 7.25 – 7.16 (m, 3H), 2.66 (q, *J* = 7.6 Hz, 2H), 1.27 (t, *J* = 7.6 Hz, 3H).

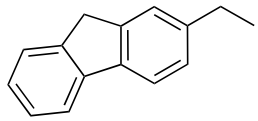


2-Ethylnaphthalene [4b]. According to the general transfer hydrogenation procedure B, (*S*)-DTBM-SEGPHOS (10.4 mg, 0.0088 mmol, 0.022 eq.), $Cu(OAc)_2$ (40 µL of a 0.2 M solution in THF, 0.008 mmol, 0.02 eq.), THF (0.16 mL), then dimethoxy(methyl)silane (247 µL, 2 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of 2-ethynyl-napthalene (60.9 mg, 0.4 mmol, 1 eq.), THF (0.2 mL), and 2-propanol (74 µL, 0.96 mmol, 2.4 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 14 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as

the eluent, the solvent was concentrated, and the crude brown oil was dry loaded onto a silica gel column. Flash chromatography using 350 mL of hexanes as eluent gave the pure product as a clear, colorless oil (45.8 mg, 0.29 mmol, 73% yield). The spectra for the title compound matched previously reported spectra.[1]

^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.86 – 7.76 (m, 3H), 7.65 (s, 1H), 7.51 – 7.39 (m, 2H), 7.38 (d, J = 8.4 Hz, 1H), 2.84 (q, J = 7.6 Hz, 2H), 1.36 (t, J = 7.6 Hz, 3H).

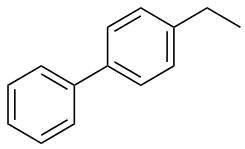
^{13}C NMR: (101 MHz, $CDCl_3$)
δ 141.9, 133.9, 132.1, 127.9, 127.7, 127.6, 127.2, 126.0, 125.7, 125.1, 29.20, 15.7.



2-Ethyl-9*H*-fluorene [4c]. According to the general transfer hydrogenation procedure B, (S)-DTBM-SEGPHOS (10.4 mg, 0.0088 mmol, 0.022 eq.), $Cu(OAc)_2$ (40 µL of a 0.2 M solution in THF, 0.008 mmol, 0.02 eq.), THF (0.16 mL), then dimethoxy(methyl)silane (247 µL, 2 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of 2-ethynyl-*9H*-Fluorene (76.1 mg, 0.4 mmol, 1 eq.), THF (0.2 mL), and 2-propanol (74 µL, 0.96 mmol, 2.4 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 9 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated. The crude brown oil was dry loaded onto a silica gel column. Flash chromatography using 100 mL of hexanes as eluent gave the pure product as a yellow solid (60.0 mg, 0.309 mmol, 77% yield). The spectra for the title compound matched previously reported spectra.[2]

^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.77 (d, J = 7.6, 1H), 7.71 (d, J = 7.8 Hz, 1H), 7.56 – 7.52 (m, 1H), 7.42 – 7.34 (m, 2H), 7.31 – 7.26 (m, 1H), 7.25 – 7.21 (m, 1H), 3.89 (s, 2H), 2.75 (q, J = 7.6 Hz, 2H), 1.31 (t, J = 7.6 Hz, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 143.7, 143.3, 143.3, 141.9, 139.5, 126.8, 126.6, 126.3, 125.1, 124.7, 119.8, 119.7, 37.0, 29.2, 16.1.

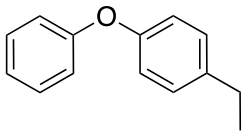


4-Ethyl-1,1'-biphenyl [4d]. According to the general transfer hydrogenation procedure B, (*S*)-DTBM-SEGPHOS (10.4 mg, 0.0088 mmol, 0.022 eq.), $Cu(OAc)_2$ (40 µL of a 0.2 M solution in THF, 0.008 mmol, 0.02 eq.), THF (0.16 mL), then dimethoxy(methyl)silane (247 µL, 2 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of 4-ethynyl-1,1'-Biphenyl (71.3 mg, 0.4 mmol, 1 eq.), THF (0.2 mL), and 2-propanol (74 µL, 0.96 mmol, 2.4 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 9 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and the crude brown oil was dry loaded onto a silica gel column. Flash chromatography using 100 mL of hexanes as eluent gave the pure product as a clear, yellow oil (57.5 mg, 0.316 mmol, 79% yield). The spectra for the title compound matched previously reported spectra.[1]

^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.63 – 7.60 (m, 2H), 7.58 – 7.53 (m, 2H), 7.48 – 7.43 (m, 2H), 7.38 – 7.33 (m, 1H), 7.31 (d, J = 8.1 Hz, 2H), 2.73 (q, J = 7.6 Hz, 2H), 1.32 (t, J = 7.6 Hz, 3H).

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

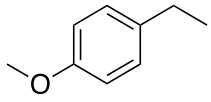
δ 143.5, 141.4, 138.8, 128.8, 128.4, 127.2, 127.2, 127.1, 28.7, 15.7.



1-Ethyl-4-phenoxybenzene [4e]. According to the general transfer hydrogenation procedure B, (S)-DTBM-SEGPHOS (10.4 mg, 0.0088 mmol, 0.022 eq.), $Cu(OAc)_2$ (40 µL of a 0.2 M solution in THF, 0.008 mmol, 0.02 eq.), THF (0.16 mL), then dimethoxy(methyl)silane (247 µL, 2 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of 1-ethynyl-4-phenoxy-benzene (77.7 mg, 0.4 mmol, 1 eq.), THF (0.2 mL), and 2-propanol (74 µL, 0.96 mmol, 2.4 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 9 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and the crude brown oil was dry loaded onto a silica gel column. Flash chromatography using 100 mL of hexanes as eluent gave the pure product as a clear, yellow oil (66.5 mg, 0.335 mmol, 84% yield). The spectra for the title compound matched previously reported spectra.[3]

^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.37 – 7.30 (m, 2H), 7.18 (d, J = 8.5 Hz, 2H), 7.12 – 7.06 (m, 1H), 7.04 – 6.99 (m, 2H), 6.98 –6.94 (m, 2H), 2.66 (q, J = 7.6 Hz, 2H), 1.26 (t, J = 7.6 Hz, 3H).

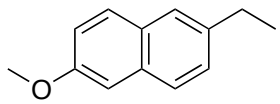
^{13}C NMR: (101 MHz, $CDCl_3$)
δ 157.9, 155.0, 139.4, 129.8, 129.2, 123.0, 119.2, 118.6, 28.3, 15.9.



1-Ethyl-4-methoxybenzene [4f]. According to the general transfer hydrogenation procedure B, (*S*)-DTBM-SEGPHOS (10.4 mg, 0.0088 mmol, 0.022 eq.), $Cu(OAc)_2$ (40 µL of a 0.2 M solution in THF, 0.008 mmol, 0.02 eq.), THF (0.16 mL), then dimethoxy(methyl)silane (247 µL, 2.0 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of 1-ethynyl-4-methoxybenzene (52.9 mg, 0.4 mmol, 1 eq.), THF (0.2 mL), and 2-propanol (153 µL, 2.0 mmol, 5 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 12 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and the crude colorless liquid was dry loaded onto a silica gel column. Flash chromatography using 100 mL of hexanes as eluent gave the pure product as a clear and colorless liquid (30.9 mg, 0.227 mmol, 57% yield). The spectra for the title compound matched previously reported spectra.[4]

^{1}H NMR: (300 MHz, $CDCl_3$)
δ 7.12 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 3.79 (s, 3H), 2.60 (q, *J* = 7.6 Hz, 2H), 1.22 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR: (75 MHz, $CDCl_3$)
δ 157.7, 136.5, 128.9, 113.9, 55.4, 28.1, 16.0.



2-Ethyl-6-methoxynaphthlene [2b]. According to the general transfer hydrogenation procedure B, (*S*)-DTBM-SEGPHOS (142.4 mg, 0.12 mmol, 0.022 eq.), $Cu(OAc)_2$ (0.549 mL of a 0.2 M solution in THF, 0.11 mmol, 0.02 eq.), THF (2.5 mL), then dimethoxy(methyl)silane (3.39 mL, 27.45 mmol, 5 eq.) were

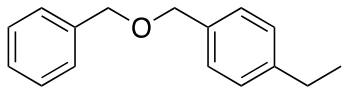
combined in a 20-dram vial followed by addition of a solution of 2-ethynyl-6-methoxynapthalene (1.0 g, 5.49 mmol, 1 eq.), THF (2.5 mL), and 2-propanol (1.01 mL, 13.18 mmol, 2.4 eq.). The 20-dram vial was capped with a red pressure relief cap, and the reaction stirred for 15 h at 60 °C. After silica plug filtration using diethyl ether (200 mL) as the eluent, the solvent was concentrated under vacuum. Purification by flash chromatography using gradient elution (100 mL of hexanes, 200 mL of 5% of ethyl acetate in hexanes, 500 mL of 8% ethyl acetate in hexanes) gave the pure product as a cream colored solid (0.97 g, 5.21 mmol, 95% yield). The spectra for the title compound matched previously reported spectra.[1]

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

δ 7.70 – 7.64 (m, 2H), 7.57 – 7.54 (m, 1H), 7.32 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.15 – 7.09 (m, 2H), 3.91 (s, 3H), 2.78 (q, *J* = 7.6 Hz, 2H), 1.31 (t, *J* = 7.6, 3H).

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

δ 157.2, 139.6, 133.0, 129.3, 129.0, 127.7, 126.8, 125.6, 118.7, 105.8, 55.4, 29.0, 15.8.



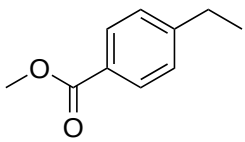
1-((Benzyloxy)methyl)-4-ethylbenzene [4g]. According to the general transfer hydrogenation procedure B, (S)-DTBM-SEGPHOS (10.4 mg, 0.0088 mmol, 0.022 eq.), $Cu(OAc)_2$ (40 µL of a 0.2 M solution in THF, 0.008 mmol, 0.02 eq.), THF (0.16 mL), then dimethoxy(methyl)silane (296 µL, 2.4 mmol, 6 eq.) were combined in a 2-dram vial followed by addition of a solution of 1- ethynyl- 4- [(phenylmethoxy) methyl] - benzene (88.9 mg, 0.4 mmol, 1 eq.), THF (0.2 mL), and ethanol (61 µL, 1.04 mmol, 2.6 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 18 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and the crude brown oil was dry loaded onto a silica gel column. Flash chromatography using gradient elution (75 mL of hexanes, 100 mL of 1% ethyl acetate in hexanes, 100 mL of 2% ethyl acetate in hexanes, 200 mL of 5% ethyl acetate in hexanes) gave the pure product as a clear, yellow oil (58.5 mg, 0.26 mmol, 65% yield).

^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.43 – 7.35 (m, 4H), 7.34 – 7.28 (m, 3H), 7.22 (d, *J* = 7.9 Hz, 2H), 4.57 (d, *J* = 7.6 Hz, 4H), 2.68 (q, *J* = 7.6 Hz, 2H), 1.26 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 143.9, 138.6, 135.6, 128.5, 128.1, 128.0, 127.9, 127.7, 72.2, 72.1, 28.8, 15.8.

ATR-IR (cm^{-1}):
3029, 2964, 2929, 2856, 1718, 1090, 1072.

HRMS: (ESI^+) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{18}NaO$ 249.1250; Found 249.1257.



Methyl 4-ethylbenzoate [4h]. According to the general transfer hydrogenation procedure B, (S)-DTBM-SEGPHOS (10.4 mg, 0.0088 mmol, 0.022 eq.), $Cu(OAc)_2$ (40 µL of a 0.2 M solution in THF, 0.008 mmol, 0.02 eq.), THF (0.16 mL), then dimethoxy(methyl)silane (247 µL, 2 mmol, 5 eq.) were combined in a 2-

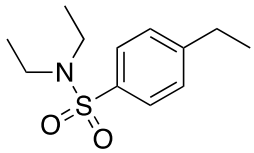
dram vial followed by addition of a solution of methyl 4-ethynylbenzoate (64.1 mg, 0.4 mmol, 1 eq.), THF (0.2 mL), and 2-propanol (74 µL, 0.96 mmol, 2.4 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 22 h at 40 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated under vacuum. Purification by flash chromatography using gradient elution (100 mL of hexanes, 200 mL of 10% of DCM in hexanes, 200 mL of 20% DCM in hexanes, 200 mL of 30% DCM in hexanes) gave the pure product as a clear colorless liquid (47.0 mg, 0.286 mmol, 72% yield). The spectra for the title compound matched previously reported spectra.[5]

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

δ 7.95 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 8.1 Hz, 2H), 3.89 (s, 3H), 2.70 (q, *J* = 7.6 Hz, 2H), 1.25 (t, *J* = 7.6 Hz, 3H).

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

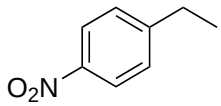
δ 167.3, 149.9, 129.8, 128.0, 127.8, 52.1, 29.1, 15.3.



***N*,*N*,4-Triethylbenzenesulfonamide [4i].** According to the general transfer hydrogenation procedure B, (S)-DTBM-SEGPHOS (10.4 mg, 0.0088 mmol, 0.022 eq.), $Cu(OAc)_2$ (40 µL of a 0.2 M solution in THF, 0.008 mmol, 0.02 eq.), THF (0.16 mL), then dimethoxy(methyl)silane (247 µL, 2 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of *N*,*N*-diethyl-4-ethynyl-benzenesulfonamide (95 mg, 0.4 mmol, 1 eq.), THF (0.2 mL), and ethanol (56 µL, 0.96 mmol, 2.4 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and the crude brown oil was dry loaded onto a silica gel column. Flash chromatography using gradient elution (100 mL of hexanes, 100 mL of 5% ethyl acetate in hexanes, 100 mL of 6% ethyl acetate in hexanes, 200 mL of 8% ethyl acetate in hexanes, 200 mL of 10% ethyl acetate in hexanes, 200 mL of 12% ethyl acetate in hexanes) gave the pure product as a clear, yellow oil (76.4 mg, 0.317 mmol, 79% yield). The spectra for the title compound matched previously reported spectra.[6]

^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.70 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 8.1 Hz, 2H), 3.21 (q, J = 7.2 Hz, 4H), 2.69 (q, J = 7.6 Hz, 2H), 1.24 (t, J = 7.6 Hz, 3H), 1.11 (t, J = 7.2 Hz, 6H).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 149.2, 137.7, 128.5, 127.2, 42.2, 28.8, 15.2, 14.3.



4-Ethylnitrobenzene [4j]. According to the general transfer hydrogenation procedure B, (S)-DTBM-SEGPHOS (10.4 mg, 0.0088 mmol, 0.022 eq.), $Cu(OAc)_2$ (40 µL of a 0.2 M solution in THF, 0.008 mmol, 0.02 eq.), THF (0.16 mL), then dimethoxy(methyl)silane (247 µL, 2 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of methyl-4-ethynylnitrobenzene (58.9 mg, 0.4 mmol, 1 eq.), THF (0.2 mL), and 2-propanol (74 µL, 0.96 mmol, 2.4 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at room temperature. After silica plug filtration using diethyl

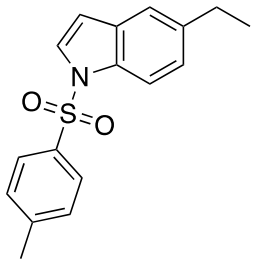
ether (100 mL) as the eluent, the solvent was concentrated, under vacuum. Purification by flash chromatography using gradient elution (100 mL of hexanes, 200 mL of 5% ethyl acetate in hexanes 200 mL of 10% of ethyl acetate in hexanes, 200 mL of 20% ethyl acetate in hexanes) gave the pure product as a clear brown liquid (39.4 mg, 0.26 mmol, 65% yield). The spectra for the title compound matched previously reported spectra.[7]

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

δ 8.13 (d, *J* = 8.7 Hz, 2H), 7.33 (d, *J* = 8.5 Hz, 2H), 2.75 (q, *J* = 7.6 Hz, 2H), 1.27 (t, *J* = 7.6 Hz, 3H).

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

δ 152.2, 146.3, 128.7, 123.7, 29.0, 15.2.



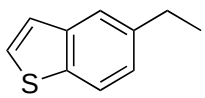
5-Ethyl-1-tosyl-1H-indole [4k]. According to the general transfer hydrogenation procedure B, (S)-DTBM-SEGPHOS (13.0 mg, 0.011 mmol, 0.055 eq.), $Cu(OAc)_2$ (50 µL of a 0.2 M solution in THF, 0.01 mmol, 0.05 eq.), THF (0.05 mL), then dimethoxy(methyl)silane (123 µL, 1.0 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of 5-ethynyl-1-tosyl-1H-indole (59.1 mg, 0.2 mmol, 1 eq.), THF (0.1 mL), and 2-propanol (77 µL, 1.0 mmol, 5 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and the crude brown liquid was dry loaded onto a silica gel column. Flash chromatography using gradient elution (100 mL of 10% ethyl acetate in hexanes, 100 mL of 20% ethyl acetate in hexanes followed by 200 mL of 30% ethyl acetate in hexanes) gave the pure product as a clear and colorless oil (36.1 mg, 0.12 mmol, 60% yield).

^{1}H NMR: (400 MHz, CDC_3)
δ 7.90 (d, *J* = 8.5 Hz, 1H), 7.76 (d, *J* = 8.3 Hz, 2H), 7.53 (d, *J* = 3.6 Hz, 1H), 7.33 (s, 1H), 7.20 (d, *J* = 8.2 Hz, 2H), 7.16 (d, *J* = 8.5 Hz, 1H), 6.59 (d, *J* = 3.6 Hz, 1H), 2.70 (q, *J* = 7.6 Hz, 2H), 2.33 (s, 3H), 1.25 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 144.9, 139.5, 135.5, 133.3, 131.1, 130.0, 126.9, 126.5, 125.1, 120.1, 113.4, 109.1, 28.8, 21.7, 16.1.

ATR-IR (cm^{-1}):
2962, 2926, 2873, 1596, 1367, 1130.

HRMS: (ESI^+) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{17}NNaO_2S$ 322.0872; Found 322.0882.



5-Ethylbenzo[*b*]thiophene [4l]. According to the general transfer hydrogenation procedure B, (S)-DTBM-SEGPHOS (10.4 mg, 0.0088 mmol, 0.022 eq.), $Cu(OAc)_2$ (40 µL of a 0.2 M solution in THF, 0.008 mmol,

0.02 eq.), THF (0.16 mL), then dimethoxy(methyl)silane (247 µL, 2 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of 5-ethynylbenzo[*b*]thiophene (63 mg, 0.4 mmol, 1 eq.), THF (0.2 mL), and 2-propanol (74 µL, 0.96 mmol, 2.4 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 13 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated under vacuum. Purification by flash chromatography using gradient elution (100 mL of hexanes, 200 mL of 5% ethyl acetate in hexanes) gave the pure product as a clear red oil (46.9 mg, 0.289 mmol, 72% yield).

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

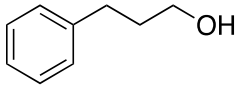
δ 7.82 (d, *J* = 8.1 Hz, 1H), 7.69 – 7.66 (m, 1H), 7.43 (d, *J* = 5.4 Hz, 1H), 7.31 (dd, *J* = 5.4, 0.8 Hz, 1H), 7.24 (dd, *J* = 8.2, 1.7 Hz, 1H), 2.80 (q, *J* = 7.6 Hz, 2H), 1.33 (t, *J* = 7.6 Hz, 3H).

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

δ 140.6, 140.1, 137.3, 126.5, 125.1, 123.8, 122.4, 122.3, 29.0, 16.2.

ATR-IR (cm^{-1}):
2962, 2928, 2868, 1738, 808, 691.

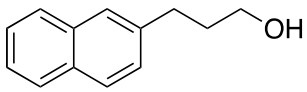
HRMS: (EI^+) *m/z*: $[M]^+$ Calcd for $C_{10}H_{10}S$ 162.0503; Found 162.0496.



3-Phenyl-1-propanol [4m]. According to the general transfer hydrogenation procedure B, (S)-DTBM-SEGPHOS (10.4 mg, 0.0088 mmol, 0.022 eq.), $Cu(OAc)_2$ (40 µL of a 0.2 M solution in THF, 0.008 mmol, 0.02 eq.), THF (0.16 mL), then dimethoxy(methyl)silane (247 µL, 2.0 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of 3-phenyl-2-propyn-1-ol (52.9 mg, 0.4 mmol, 1 eq.), THF (0.2 mL), and 2-propanol (74 µL, 0.96 mmol, 2.4 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 18 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated. The clear crude oil was treated with tetrabutylammonium fluoride following the general procedure C. Flash chromatography using gradient elution (100 mL of hexanes, 100 mL of 5% ethyl acetate in hexanes, 100 mL of 10% ethyl acetate in hexanes, 200 mL of 15% ethyl acetate in hexanes) gave the pure product as a clear and colorless oil (31 mg, 0.227 mmol, 57% yield). The spectra for the title compound matched previously reported spectra.[8]

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.33 – 7.27 (m, 2H), 7.24 – 7.17 (m, 3H), 3.68 (t, *J* = 6.5 Hz, 2H), 2.72 (t, *J* =7.64 Hz, 2H), 1.95 – 1.86 (m, 2H), 1.64 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$)
δ 141.9, 128.5, 128.5, 126.0, 62.4, 34.3, 32.2.

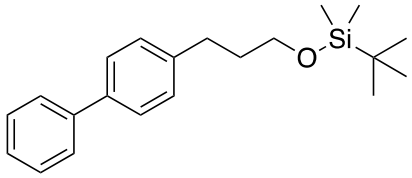


2-Naphthalenepropanol [4n]. According to the general transfer hydrogenation procedure B, (S)-DTBM-SEGPHOS (10.4 mg, 0.0088 mmol, 0.022 eq.), $Cu(OAc)_2$ (40 µL of a 0.2 M solution in THF, 0.008 mmol, 0.02 eq.), THF (0.16 mL), then dimethoxy(methyl)silane (247 µL, 2.0 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of 3-(2-Napthhalenyl)-2-propyn-1-ol (72.8 mg, 0.4 mmol, 1

eq.), THF (0.2 mL), and 2-propanol (74 µL, 0.96 mmol, 2.4 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 18 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated. The clear crude oil was treated with tetrabutylammonium fluoride following the general procedure C. Flash chromatography using gradient elution (100 mL of hexanes, 100 mL of 5% ethyl acetate in hexanes, 200 mL of 10% ethyl acetate in hexanes, 200 mL of 15% ethyl acetate in hexanes) gave the pure product as a white solid (56 mg, 0.30 mmol, 75% yield). The spectra for the title compound matched previously reported spectra.[9]

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.85 – 7.74 (m, 3H), 7.65 (s, 1H), 7.50 – 7.40 (m, 2H), 7.36 (d, *J* = 8.4 Hz, 1H), 3.72 (t, *J* = 6.4 Hz, 2H), 2.89 (t, *J* = 7.6 Hz, 2H), 2.03 – 1.93 (m, 2H), 1.76 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$)
δ 139.4, 133.7, 132.1, 128.1, 127.7, 127.5, 127.4, 126.5, 126.0, 125.3, 62.3, 34.1, 32.3.



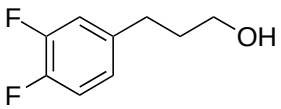
(3-([1,1'-Biphenyl]-4-yl)propoxy)(*tert*-butyl)dimethylsilane [4o]. According to the general transfer hydrogenation procedure B, (S)-DTBM-SEGPHOS (8.0 mg, 0.0068 mmol, 0.022 eq.), $Cu(OAc)_2$ (31 µL of a 0.2 M solution in THF, 0.0628 mmol, 0.02 eq.), THF (0.12 mL), then dimethoxy(methyl)silane (191 µL, 1.55 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of ((3-([1,1'-biphenyl]-4-yl)prop-2-yn-1-yl)oxy)(*tert*-butyl)dimethylsilane (100 mg, 0.31 mmol, 1 eq.), THF (0.15 mL), and 2-propanol (119 µL, 1.55 mmol, 5 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 10 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated. Flash chromatography using gradient elution (100 mL of hexanes, 100 mL of 2% ethyl acetate in hexanes, 100 mL of 5% ethyl acetate in hexanes gave the pure product as a white crystalline solid (71 mg, 0.217 mmol, 70% yield).

^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.59 (d, *J* = 7.2 Hz, 2H), 7.52 (d, *J* = 8.2 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.36 – 7.30 (m, 1H), 7.30 – 7.26 (m, 2H), 3.68 (t, *J* = 6.3 Hz, 2H), 2.76 – 2.70 (m, 2H), 1.95 – 1.83 (m, 2H), 0.93 (s, 9H), 0.08 (s, 6H).

^{13}C NMR: (75 MHz, $CDCl_3$)
δ 141.6, 141.3, 138.8, 129.0, 128.8, 127.2, 127.1, 127.1, 62.5, 34.6, 31.9, 26.1, 18.5, -5.1.

FT-IR (thin film, cm^{-1}):
2930, 2925, 2854, 1250, 1098, 1077.

HRMS: (ESI$^+$) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{30}NaOSi$ 349.1958; Found 349.1968.



3,4-Difluorobenzenepropanol [4p]. According to the general transfer hydrogenation procedure B, (S)-DTBM-SEGPHOS (10.4 mg, 0.0088 mmol, 0.022 eq.), $Cu(OAc)_2$ (40 µL of a 0.2 M solution in THF, 0.008 mmol, 0.02 eq.), THF (0.16 mL), then dimethoxy(methyl)silane (247 µL, 2.0 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of 3,4-difluorobenzenepropynol (67.3 mg, 0.4 mmol, 1

eq.), THF (0.2 mL), and 2-propanol (74 µL, 0.96 mmol, 2.4 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 19 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated. The clear crude oil was treated with tetrabutylammonium fluoride following the general procedure C. Flash chromatography using gradient elution (100 mL of hexanes, 100 mL of 5% ethyl acetate in hexanes, 100 mL of 10% ethyl acetate in hexanes, 200 mL of 15% ethyl acetate in hexanes) gave the pure product as a clear oil (39.0 mg, 0.227 mmol, 57% yield).

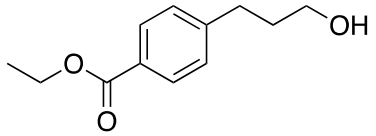
^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.10 – 6.95 (m, 2H), 6.92 – 6.86 (m, 1H), 3.66 (q, *J* = 5.9 Hz, 2H), 2.67 (t, *J* = 7.4, 2H), 1.90 – 1.81 (m, 2H), 1.31 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$)
δ 150.8 (dd, *J* = 144.6, 12.6 Hz), 148.3 (dd, *J* = 142.6, 12.7 Hz), 138.9 (dd, *J* = 5.5, 3.9 Hz), 124.3 (dd, *J* = 6.0, 3.5 Hz), 117.2 (d, *J* = 16.6 Hz), 117.1 (d, *J* = 16.8 Hz), 61.9, 34.1, 31.3.

^{19}F NMR (376 MHz, $CDCl_3$)
δ -138.53, -142.39.

ATR-IR (cm^{-1}):
3319, 2934, 2868, 1717, 1510, 1209, 1116, 1048.

HRMS: (ESI$^+$) *m/z*: $[M+H]^+$ Calcd for $C_9H_{11}OF_2$ 173.0778; Found 173.0780.



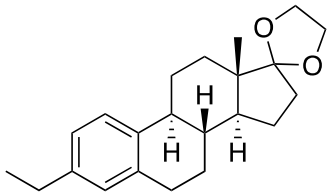
Ethyl-4-(-3-hydroxypropyl)benzoate [4q]. According to the general transfer hydrogenation procedure B, (S)-DTBM-SEGPHOS (10.4 mg, 0.0088 mmol, 0.022 eq.), $Cu(OAc)_2$ (40 µL of a 0.2 M solution in THF, 0.008 mmol, 0.02 eq.), THF (0.16 mL), then dimethoxy(methyl)silane (247 µL, 2.0 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of ethyl-4-(-3-hydroxypropynyl)benzoate (81.8 mg, 0.4 mmol, 1 eq.), THF (0.2 mL), and 2-propanol (73.9 µL, 0.96 mmol, 2.4 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 18 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated. The clear crude oil was treated with tetrabutylammonium fluoride following the general procedure C. Flash chromatography using gradient elution (100 mL of hexanes, 100 mL of 5% ethyl acetate in hexanes, 100 mL of 10% ethyl acetate in hexanes, 200 mL of 15% ethyl acetate in hexanes) gave the pure product as a clear yellow oil (51 mg, 0.244 mmol, 61% yield).

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.95 (d, *J* = 8 Hz, 2H), 7.25 (d, *J* = 7.7 Hz, 2H), 4.35 (q, *J* = 7 Hz, 2H), 3.66 (t, *J* = 6.3 Hz, 2H), 2.76 (t, *J* = 8, 2H), 1.90 (p, 2H), 1.65 (s, 1H), 1.37 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$)
δ 166.8, 147.5, 129.8, 128.5, 128.2, 62.0, 60.9, 33.9, 32.2, 14.4.

ATR-IR (cm^{-1}):
3412, 2986, 2933, 2873, 1713, 1610, 1272, 1102, 1041, 1020.

HRMS: (ESI$^+$) m/z: $[M+Na]^+$ Calcd for $C_{12}H_{16}NaO_3$ 231.0992; Found 231.0999.



(8*R*,9*S*,13*S*,14*S*)-3-Ethyl-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydrospiro[cyclopenta[*a*]phenanthrene-17,2'-[1,3]dioxolane] [4r]. According to the general procedure B, (S)-DTBM-SEGPHOS (5.7 mg, 0.00486 mmol, 0.022 eq.), $Cu(OAc)_2$ (22 µL of a 0.2 M solution in THF, 0.0044 mmol, 0.02 eq.), THF (0.1 mL), then dimethoxy(methyl)silane (136 µL, 1.1 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of (8*R*,9*S*,13*S*,14*S*)-3-(ethynyl)-13-methyl-6,7,8,9,11,12,13,14,15,16 decahydrospiro[cyclopenta[*a*]phenanthrene-17,2'-[1,3]dioxolane] (71.3 mg, 0.22 mmol, 1 eq.), THF (0.1 mL), and 2-propanol (85 µL, 1.1 mmol, 5 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 19 h at 60 °C. After silica plug filtration using dichloromethane as the eluent (100 mL), the solvent was concentrated, and the crude brown oil was dry loaded onto a silica gel column. Flash chromatography using gradient elution (100 mL of hexanes, 100 mL of 3% ethyl acetate in hexanes, 100 mL of 5% ethyl acetate in hexanes, 100 mL of 8% ethyl acetate in hexanes, 200 mL of 9% ethyl acetate in hexanes, 100 mL of 10% ethyl acetate in hexanes) gave the pure product as a clear, yellow oil (56.2 mg, 0.172 mmol, 78% yield).

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

δ 7.25 (d, *J* = 7.9 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 6.95 (s, 1H), 4.02 – 3.86 (m, 4H), 2.94 – 2.80 (m, 2H), 2.60 (q, *J* = 7.6 Hz, 2H), 2.41 – 2.23 (m, 2H), 2.11 – 2.00 (m, 1H), 1.96 – 1.73 (m, 4H), 1.71 – 1.60 (m, 1H), 1.59 – 1.30 (m, 5H), 1.24 (t, *J* = 7.6 Hz, 3H), 0.90 (s, 3H).

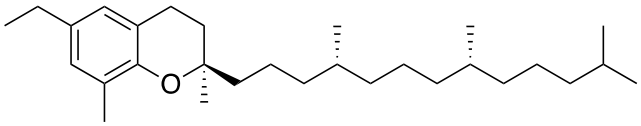
^{13}C NMR (101 MHz, $CDCl_3$)

δ 141.6, 137.8, 136.7, 128.6, 125.5, 125.3, 119.6, 65.4, 64.7, 49.6, 46.3, 44.1, 39.1, 34.4, 30.9, 29.7, 28.4, 27.2, 26.1, 22.5, 15.8, 14.5.

ATR-IR (cm^{-1}):

2965, 2933, 2872, 1735, 1693, 1610, 1103, 1040.

HRMS: (ESI^+) m/z: $[M+H]^+$ Calcd for $C_{22}H_{31}O_2$ 327.2319; Found 327.2329.



(*R*)-6-Ethyl-2,8-dimethyl-2-((4R,8R)-4,8,12-trimethyltridecyl)chromane [4s]. According to the general procedure B, (*S*)-DTBM-SEGPHOS (13 mg, 0.011 mmol, 0.055 eq.), $Cu(OAc)_2$ (50 µL of a 0.2 M solution in THF, 0.01 mmol, 0.05 eq.), THF (0.05 mL), then dimethoxy(methyl)silane (99 µL, 0.8 mmol, 4 eq.) were combined in a 2-dram vial followed by addition of a solution of (R)-6-ethynyl-2,8-dimethyl-2-((4R,8R)-4,8,12-trimethyltridecyl)chromane (82.1 mg, 0.2 mmol, 1 eq.), THF (0.1 mL), and 2-propanol (77 µL, 1.0 mmol, 5 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 16 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and the crude colorless liquid was dry loaded onto a silica gel column. Flash chromatography using gradient elution (100 mL of hexanes followed by 200 mL of 2% ethyl acetate in hexanes) gave the pure product as a clear and colorless liquid (51.2 mg, 0.124 mmol, 62% yield).

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

δ 6.80 (s, 1H), 6.73 (s, 1H), 2.80 – 2.66 (m, 2H), 2.53 (q, *J* = 7.6 Hz, 2H), 2.15 (s, 3H), 1.87 – 1.68 (m, 2H), 1.62 – 1.47 (m, 3H), 1.46 – 1.01 (m, 24H), 0.92 – 0.81 (m, 12H).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 150.2, 134.5, 128.0, 126.1, 126.0, 120.3, 75.9, 40.4, 39.5, 37.6, 37.6, 37.4, 33.0, 32.9, 31.5, 28.1, 28.1, 25.0, 24.6, 24.5, 22.9, 22.8, 22.5, 21.2, 19.9, 19.8, 16.2, 16.1.

ATR-IR (cm^{-1}):
2957, 2924, 2854, 1733, 1598, 1220, 1151.

HRMS: (ESI^+) m/z: $[M+H]^+$ Calcd for $C_{29}H_{51}O$ 415.3934; Found 415.3946.

Transfer Deuteration Reaction Scope

Procedure for the synthesis of dimethoxy(methyl)silane-*d* (Scheme 19)

The procedure was adapted from a previously reported method.[10] To an oven-dried 500 mL Schlenk flask equipped with a Teflon stir bar in a N_2 filled glovebox was added the $Pt(PPh_3)_4$ (1.17 g, 0.941 mmol, 0.01 eq.), dimethoxy(methyl)silane (11.6 mL, 94.1 mmol, 1 eq.), and 5.0 mL of degassed anhydrous hexanes. The Schlenk flask was sealed with a rubber septa and removed from the glovebox, connected to a manifold line, and cooled to -78 ˚C. A single freeze-pump-thaw cycle was performed, and the Schlenk flask was backfilled with D_2 gas from a D_2 purged balloon at room temperature. The flask was sealed with parafilm and heated to 60 °C. After 2 hours, the reaction was cooled to room temperature and then a single freeze-pump-thaw was performed again, backfilling with D_2 gas. The process was repeated 6 times or until the ^{1}H NMR showed ≥95% D incorporation. It is important to maintain a N_2 (g) inert atmosphere while obtaining a minimal quantity of sample for ^{1}H NMR analysis.

The solution was purified through a distillation apparatus; the set up consisted of a flame-dried 25 mL round-bottom receiving flask and a cannula. The 25 mL round-bottom receiving flask was flame-dried, and then filled with N_2. Once the receiving flask reached room temperature, the cannula was inserted, maintaining positive pressure, and tightly sealed with parafilm to prevent condensation from entering. Upon confirmation of positive N_2 flow, the open end of the cannula was inserted into the Schlenk reaction flask. The 25 mL round-bottom receiving flask was cooled to -78 ˚C and closed to the manifold line, and then the Schlenk flask was heated to 80 °C. The heat initiated the distillation of the dimethoxy(methyl)silane-*d* and the hexane through the cannula which were trapped in the cold 25 mL round-bottom receiving flask. Vacuum was also applied to the 25 mL round-bottom receiving flask to promote this process. Once all of the silane and hexane were trapped in the 25 mL round-bottom receiving flask, the flask was removed from the heat and the manifold was closed to vacuum line while the 25 mL round-bottom receiving flask warmed to room temperature. Under positive nitrogen flow, the cannula was removed from the 25 mL round-bottom receiving flask, while keeping it inserted in the Schlenk reaction flask. The 25 mL round-bottom receiving flask was tightly sealed with parafilm, and stored in the -4 ˚C freezer. The final product was in a solution of hexane, and the molarity was calculated by ^{1}H NMR using 1,3,5-trimethylbenzene as an internal standard, and used for the transfer deuteration reactions (5.61 g in a 5.29 M hexane solution, 52.9 mmol, 56% yield).
*Note: it is important to monitor that the end of the cannula does not get clogged by frozen solvent/silane. If this occurs, remove the Schlenk reaction flask from heat and close manifold to vacuum line. Warm the 25 mL round-bottom receiving flask until the solids on the tip of the cannula melt, and then distillation can be resumed.

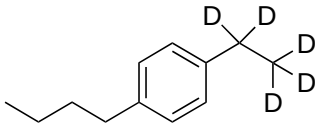
General procedure for transfer deuteration (Scheme 21) (D)

In a N_2 filled glovebox, (*R* or *S*)-DTBM-SEGPHOS (10.4 mg, 0.0088 mmol, 0.022 eq.), $Cu(OAc)_2$ (40 µL of a 0.2 M solution in THF, 0.008 mmol, 0.02 eq.), and THF (0.16 mL) were added to an oven-dried 2-dram vial followed by dropwise addition of dimethoxy(methyl)silane-*d* in hexanes (2 mmol, 5 eq.). A color change from green/blue to orange was observed while stirring for 15 minutes. In a separate 1-dram vial was added the alkyne substrate (0.4 mmol, 1 eq.), THF (0.2 mL), and either 2-propanol-OD or 2-propanol-d_8 (2.4-5 eq. based on substrate). The solution in the 1-dram vial was added dropwise over 20 seconds to the 2-dram vial. The total volume of THF was calculated based on having a final reaction concentration of 1M based on the alkyne substrate. The 2-dram vial was capped with a red pressure relief cap, taken out of the glovebox, and stirred for 9-24 h at 60 °C at which point the reaction was filtered through a 1" silica plug with 20 mL of Et_2O followed by 80 mL of Et_2O to elute the remaining product into a 200 mL round bottom flask. After removing the Et_2O by rotary evaporation, the crude product was isolated by flash chromatography.

Method for calculating deuterium incorporation at each labeled carbon of each substrate:

In the ^{1}H NMR spectra, if both benzylic and homobenzylic peaks were clearly visible and no overlap with other peaks was observed, then the deuterium incorporation was calculated from the integration of the protonated peak. If overlap of other peaks or overlap with an impurity such as water or grease was observed in the homobenzylic region of the ^{1}H NMR spectra, a ^{2}H NMR spectra was obtained. The ratio of the two peaks that appear in the ^{2}H NMR spectra was correlated to the calculated deuterium incorporation at the benzylic peak in the ^{1}H NMR spectra.

*2-propanol-d_8 was used due to a 2-propanol-OD backorder from the supplier during COVID-19.



1-Butyl-4-(ethyl-d_5)benzene [6a]. According to the general procedure D, (*S*)-DTBM-SEGPHOS (5.2 mg, 0.0044 mmol, 0.022 eq.), $Cu(OAc)_2$ (20 µL of a 0.2 M solution in THF, 0.004 mmol, 0.02 eq.), THF (0.08 mL), then dimethoxy(methyl)silane-*d* (0.17 mL of a 5.9 M solution in hexanes, 1.0 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of 1-butyl-4-(ethynyl-*d*)benzene (31.8 mg, 0.2 mmol, 1 eq.), THF (0.1 mL), and 2-propanol-d_8 (77 µL, 1.0 mmol, 5 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 17 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and the crude yellow liquid was dry loaded onto a silica gel column. Flash chromatography using 200 mL of hexanes as eluent gave the pure product as a colorless oil (24.4 mg, 0.146 mmol, 73% yield).

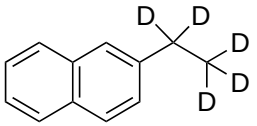
^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.12 (s, 4H), 2.62 – 2.57 (m, 2.24H due to overlap of two benzylic sites), 1.65 –1.55 (m, 2H), 1.43 – 1.31 (m, 2H), 1.19 (br s, integration not determined due to overlap with grease), 0.94 (t, *J* = 7.3 Hz, 3H).

^{2}H NMR: (61 MHz, $CHCl_3$)
δ 2.58 (br s, 1.76D), 1.19 (br s, 2.82D).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 141.4, 140.2, 128.5, 127.8, 35.4, 34.0, 28.3 – 27.2 (m), 22.6, 15.5 – 14.6 (m), 14.1.

ATR-IR (cm^{-1}):
2956, 2927, 2857, 2222, 2079, 1514.

HRMS: (EI$^+$) m/z: [M]$^+$ Calcd for $C_{12}H_{13}D_5$ 168.1722; Found 167.1716.



2-(Ethyl-*d*$_5$)naphthalene [6b]. According to the general procedure D, (*S*)-DTBM-SEGPHOS (10.4 mg, 0.0088 mmol, 0.022 eq.), $Cu(OAc)_2$ (40 µL of a 0.2 M solution in THF, 0.008 mmol, 0.02 eq.), THF (0.16 mL), then dimethoxy(methyl)silane-*d* (0.38 mL of 5.3 M solution in hexanes, 2 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of 2-(ethynyl-*d*)naphthalene (61.2 mg, 0.4 mmol, 1 eq.), THF (0.2 mL), and 2-propanol-OD (74 µL, 0.96 mmol, 2.4 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 21 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and the crude brown oil was dry loaded onto a silica gel column. Flash chromatography using 350 mL of hexanes as eluent gave the pure product as a clear, yellow oil (46.0 mg, 0.285 mmol, 71% yield).

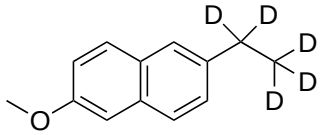
^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.85 – 7.75 (m, 3H), 7.64 (s, 1H), 7.51 – 7.40 (m, 2H), 7.37 (d, *J* = 8.4, 1H), 2.80 (br s, 0.11H), 1.30 (br s, integration not determined due to overlap with grease).

^{2}H NMR: (61 MHz, $CHCl_3$)
δ 2.80 (br s, 1.89D), 1.31 (br s, 2.72D).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 141.9, 133.9, 132.1, 127.9, 127.7, 127.6, 127.2, 126.0, 125.7, 125.1, 29.0 – 27.7 (m), 15.5 – 13.9 (m).

FT-IR (thin film, cm^{-1}):
2961, 2922, 2851, 2221, 1508, 1462.

HRMS: (EI$^+$) *m/z*: [M]$^+$ Calcd for $C_{12}H_7D_5$ 161.1253; Found 161.1247.



2-(Ethyl-*d*$_5$)-6-methoxynaphthalene [6c]. According to the general procedure D, (*R*)-DTBM-SEGPHOS (5.2 mg, 0.0044 mmol, 0.022 eq.), $Cu(OAc)_2$ (20 µL of a 0.2 M solution in THF, 0.004 mmol, 0.02 eq.), THF (0.08 mL), then dimethoxy(methyl)silane-*d* (0.17 mL of a 5.9 M solution in hexanes, 1.0 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of 2-(ethynyl-*d*)-6-methoxynaphthalene (36.6 mg, 0.2 mmol, 1 eq.), THF (0.10 mL), and 2-propanol-*d*$_8$ (77 µL, 1.0 mmol, 5 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 17 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated and the crude colorless solid was dry loaded onto a silica gel column. Flash chromatography using elution (50 mL of hexanes, 200 mL of 2% ethyl acetate in hexanes) gave the pure product as a white solid (31.0 mg, 0.162 mmol, 81% yield).

^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.72 – 7.67 (m, 2H), 7.58 (d, *J* = 0.9 Hz, 1H), 7.34 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.17 – 7.12 (m, 2H), 3.93 (s, 3H), 2.77 (br s, 0.18H), 1.29 (br s, integration not determined due to overlap with grease).

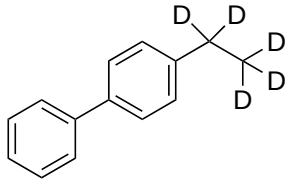
^{2}H NMR: (61 MHz, $CHCl_3$)

δ 2.77 (br s, 1.82D), 1.30 (br s, 2.77D).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 157.2, 139.5, 133.0, 129.3, 129.0, 127.7, 126.8, 125.6, 118.7, 105.7, 55.4, 28.6 – 27.7 (m), 15.2 – 14.5 (m).

ATR-IR (cm^{-1}):
2961, 2938, 2838, 2218, 2062, 1161.

HRMS: (ESI^+) m/z: $[M+H]^+$ Calcd for $C_{13}H_{10}D_5O$ 192.1436; Found 192.1426.



4-(Ethyl-*d*$_5$)-1,1'-biphenyl [6d]. According to the general procedure D, (*S*)-DTBM-SEGPHOS (10.4 mg, 0.0088 mmol, 0.022 eq.), $Cu(OAc)_2$ (40 µL of a 0.2 M solution in THF, 0.008 mmol, 0.02 eq.), THF (0.16 mL), then dimethoxy(methyl)silane-*d* (0.51 mL of 3.9 M solution in hexanes, 2 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of 4-ethynyl-*d*-1,1'-biphenyl (71.6 mg, 0.4 mmol, 1 eq.), THF (0.2 mL), and 2-propanol-OD (74 µL, 0.96 mmol, 2.4 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 13 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and the crude brown oil was dry loaded onto a silica gel column. Flash chromatography using 350 mL of hexanes as eluent gave the pure product as a clear, yellow oil (51.6 mg, 0.276 mmol, 69% yield).

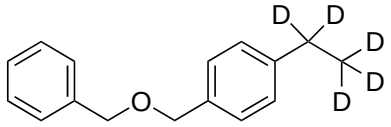
^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.68 – 7.59 (m, 2H), 7.59 – 7.52 (m, 2H), 7.50 – 7.42 (m, 2H), 7.40 – 7.33 (m, 1H), 7.33 – 7.29 (m, 2H), 2.70 (br s, 0.10H), 1.27 (br s, integration not determined due to overlap with grease).

^{2}H NMR: (61 MHz, $CHCl_3$)
δ 2.70 (br s, 1.90D), 1.28 (br s, 2.87D).

^{13}C NMR (75 MHz, $CDCl_3$)
δ 143.5, 141.3, 138.7, 128.8, 128.4, 127.2, 127.2, 127.1, 28.6 – 27.0 (m), 15.7 – 14.1 (m).

ATR-IR (cm^{-1}):
3054, 3028, 2936, 2221, 2067.

HRMS: (EI^+) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_9D_5$ 187.1409; Found 187.1404.



1-((Benzyloxy)methyl)-4-(ethyl-*d*$_5$)benzene [6e]. According to the general procedure D, (*S*)-DTBM-SEGPHOS (5.2 mg, 0.0044 mmol, 0.022 eq.), $Cu(OAc)_2$ (20 µL of a 0.2 M solution in THF, 0.004 mmol, 0.02 eq.), THF (0.08 mL), then dimethoxy(methyl)silane-*d* (0.20 mL of a 5.9 M solution in hexanes, 1.2 mmol, 6 eq.) were combined in a 2-dram vial followed by addition of a solution of 1-((benzyloxy)methyl)-4-(ethynyl-*d*)benzene (45 mg, 0.2 mmol, 1 eq.), THF (0.1 mL), and 2-propanol-d_8 (77 µL, 1.0 mmol, 5 eq.).

The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 18 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and the crude brown oil was dry loaded onto a silica gel column. Flash chromatography using gradient elution (50 mL of hexanes, 100 mL of 3% ethyl acetate in hexanes, 200 mL of 5% ethyl acetate in hexanes) gave the pure product as a colorless oil (35.0 mg, 0.151 mmol, 76% yield).

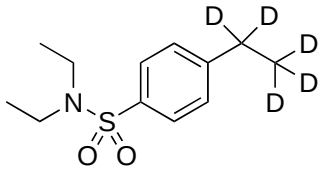
^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.42 – 7.35 (m, 4H), 7.34 – 7.29 (m, 3H), 7.22 (d, *J* = 8.1 Hz, 2H), 4.58 (s, 2H), 4.56 (s, 2H), 2.64 (br s, 0.17H), 1.21 (br s, integration not determined due to overlap with grease).

^{2}H NMR: (61 MHz, $CHCl_3$)
δ 2.64 (br s, 1.83D), 1.22 (br s, 2.78D).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 143.8, 138.5, 135.6, 128.5, 128.1, 128.0, 127.9, 127.7, 72.1, 72.1, 28.4 – 27.3 (m), 15.5 – 14.3 (m).

ATR-IR (cm^{-1}):
3029, 2853, 2222, 2081, 1615, 1090, 1071.

HRMS: (ESI^+/FTICR) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{13}D_5NaO$ 254.1564; Found 254.1570.



***N*,*N*-Diethyl-4-(ethyl-*d*$_5$)benzenesulfonamide [6f].** According to the general procedure D, (*S*)-DTBM-SEGPHOS (10.4 mg, 0.0088 mmol, 0.022 eq.), $Cu(OAc)_2$ (40 µL of a 0.2 M solution in THF, 0.008 mmol, 0.02 eq.), THF (0.16 mL), then dimethoxy(methyl)silane-*d* (0.38 mL of 5.3 M solution in hexanes, 2 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of *N*,*N*-diethyl-4-(ethynyl-*d*)benzenesulfonamide (95 mg, 0.4 mmol, 1 eq.), THF (0.2 mL), and 2-propanol-*d*$_8$ (153 µL, 2.0 mmol, 5 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and the crude brown oil was dry loaded onto a silica gel column. Flash chromatography using gradient elution (100 mL of hexanes,100 mL 4% ethyl acetate in hexane, 300 mL of 8% ethyl acetate in hexanes) gave the pure product as a clear, yellow oil (86.1 mg, 0.35 mmol, 88% yield).

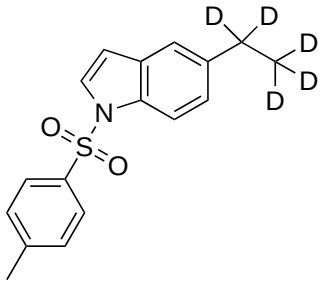
^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.68 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.2 Hz, 2H), 3.19 (q, *J* = 7.2 Hz, 4H), 2.63 (br s, 0.12H), 1.16 (br s, integration not determined due to overlap with grease), 1.09 (t, *J* = 7.2 Hz, 6H).

^{2}H NMR: (61 MHz, $CHCl_3$)
δ 2.63 (br s, 1.88D), 1.17 (br s, 2.83D).

^{13}C NMR (101 MHz, $CDCl_3$)
δ 149.0, 137.6, 128.4, 127.1, 42.1, 32.3 – 31.6 (m), 28.5 – 27.4 (m), 14.2.

ATR-IR (cm^{-1}):
2976, 2936, 2870, 2225, 2079, 1332, 1150.

HRMS: (ESI^+/FTICR) m/z: $[M+Na]^+$ Calcd for $C_{12}H_{14}D_5NNaO_2S$ 269.1343; Found 269.1351.



5-(Ethyl-*d*$_5$)-1-tosyl-1H-indole [6g]. According to the general procedure D, (*S*)-DTBM-SEGPHOS (13.0 mg, 0.011 mmol, 0.055 eq.), $Cu(OAc)_2$ (50 µL of a 0.2 M solution in THF, 0.01 mmol, 0.05 eq.), THF (0.05 mL), then dimethoxy(methyl)silane-*d* (0.17 mL of a 5.9 M solution in hexanes, 1.0 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of 5-(ethynyl-*d*)-1-tosyl-1H-indole (59.3 mg, 0.2 mmol, 1 eq.), THF (0.1 mL), and 2-propanol-d_8 (77 µL, 1.0 mmol, 5 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and the crude brown liquid was dry loaded onto a silica gel column. Flash chromatography using gradient elution (100 mL of hexanes, 100 mL of 5% ethyl acetate in hexanes, 200 mL of 10% ethyl acetate in hexanes) gave the pure product as a colorless oil (47.7 mg, 0.156 mmol, 78% yield).

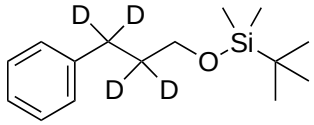
^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.90 (d, *J* = 8.5 Hz, 1H), 7.76 (d, *J* = 8.3 Hz, 2H), 7.53 (d, *J* = 3.6 Hz, 1H), 7.33 (d, *J* = 1.4 Hz, 1H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.16 (dd, *J* = 8.5, 1.4 Hz, 1H), 6.60 (d, *J* = 3.6 Hz, 1H), 2.66 (br s, 0.18H), 2.32 (s, 3H), 1.20 (br s, integration not determined due to overlap with grease).

^{2}H NMR: (61 MHz, $CHCl_3$)
δ 2.66 (br s, 1.82D), 1.21 (br s, 2.84D).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 144.9, 139.4, 135.4, 133.3, 131.1, 129.9, 126.9, 126.5, 125.1, 120.1, 113.4, 109.1, 28.5 – 27.4 (m), 21.7, 15.9 – 14.6 (m).

ATR-IR (cm^{-1}):
3038, 2922, 2221, 2081, 1367, 1130.

HRMS: (ESI^+/FTICR) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{12}D_5NNaO_2S$ 327.1186; Found 327.1195.



***tert*-Butyldimethyl(3-phenylpropoxy-2,2,3,3-*d*$_4$)silane [6h].** According to the general procedure D, (*R*)-DTBM-SEGPHOS (7.8 mg, 0.0066 mmol, 0.022 eq.), $Cu(OAc)_2$ (30 µL of a 0.2 M solution in THF, 0.006 mmol, 0.02 eq.), THF (0.12 mL), then dimethoxy(methyl)silane-*d* (0.28 mL, 1.5 mmol, 5.3 M solution in hexanes, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of ((3-(phenyl)prop-2-yn-1-yl)oxy)(*tert*-butyl)dimethylsilane (73.8 mg, 0.3 mmol, 1 eq.), THF (0.15 mL), and 2-propanol-d_8 (115 µL, 1.5 mmol, 5.0 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 19 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and the crude brown oil was dry loaded onto a silica gel column. Flash chromatography using

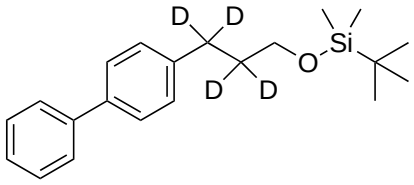
gradient elution (100 mL of hexanes) gave the pure product as a clear and colorless oil (53.0 mg, 0.208 mmol, 69% yield).

^{1}H NMR (300 MHz, $CDCl_3$)
δ 7.38 – 7.26 (m, 2H), 7.22 – 7.19 (m, 3H), 3.65 (s, 2H), 2.67 (br s, 0.11H), 1.83 (br s, 0.16H), 0.94 (s, 9H), 0.08 (s, 6H).

^{13}C NMR (75 MHz, $CDCl_3$)
δ 142.3, 128.6, 128.4, 125.8, 62.4, 34.5 – 33.1 (m), 32.2 – 30.7 (m), 26.1, 18.5, -5.1.

ATR-IR (cm^{-1}):
2928, 2894, 2856, 2211, 2116, 1085.

HRMS: (ESI^+) m/z: $[M+H]^+$ Calcd for $C_{15}H_{23}D_4OSi$ 255.2082; Found 255.2072.



(3-([1,1'-Biphenyl]-4-yl)propoxy-2,2,3,3-*d*$_4$)(*tert*-butyl)dimethylsilane [6i]. According to the general procedure D, (*S*)-DTBM-SEGPHOS (8 mg, 0.0068 mmol, 0.022 eq.), $Cu(OAc)_2$ (31 µL of a 0.2 M solution in THF, 0.0062 mmol, 0.02 eq.), THF (0.13 mL), then dimethoxy(methyl)silane-*d* (0.29 mL, 1.55 mmol, 5.3M solution in hexanes, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of ((3-([1,1'-biphenyl]-4-yl)prop-2-yn-1-yl)oxy)(*tert*-butyl)dimethylsilane (100 mg, 0.31 mmol, 1 eq.), THF (0.15 mL), and 2-propanol-OD (119 µL, 1.55 mmol, 5 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated. Flash chromatography using gradient elution (100 mL of hexanes, 100 mL of 2% ethyl acetate in hexanes, 100 mL of 5% ethyl acetate in hexanes gave the pure product as a white crystalline solid (89 mg, 0.27 mmol, 87% yield).

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

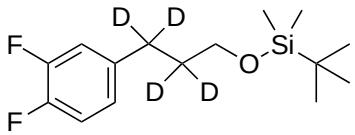
δ 7.64 – 7.59 (m, 2H), 7.55 (d, *J* = 8.2 Hz, 2H), 7.46 (t, *J* = 8.4 Hz, 2H), 7.38 – 7.32 (m, 1H), 7.32 – 7.27 (m, 2H), 3.69 (s, 2H), 2.73 (br s, 0.08 H), 1.88 (t, *J* = 6.6 Hz, 0.13 H), 0.96 (d, *J* = 2.6 Hz, 9H), 0.11 (d, *J* = 1.3 Hz, 6H).

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

δ 141.5, 141.3, 138.8, 129.0, 128.8, 127.2, 127.1, 127.1, 62.4, 34.3 – 33.2 (m), 31.5 – 30.7 (m), 26.1, 18.5, -5.1.

ATR-IR (cm^{-1}):
2953, 2926, 2854, 2203, 2115, 1251, 1110, 1065.

HRMS: (ESI^+/FTICR) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{26}D_4NaOSi$ 353.2209; Found 353.2219.



tert-Butyl(3-(3,4-difluorophenyl)propoxy-2,2,3,3-*d*$_4$)dimethylsilane [6j]. According to the general procedure D, (*S*)-DTBM-SEGPHOS (5.2 mg, 0.0044 mmol, 0.022 eq.), $Cu(OAc)_2$ (20 µL of a 0.2 M solution in THF, 0.004 mmol, 0.02 eq.), THF (0.08 mL), then dimethoxy(methyl)silane-*d* (0.14 mL of a 5.9 M solution in hexanes, 0.8 mmol, 4 eq.) were combined in a 2-dram vial followed by addition of a solution of 1-((benzyloxy)methyl)-4-(ethynyl-*d*)benzene (56.5 mg, 0.2 mmol, 1 eq.), THF (0.1 mL), and 2-propanol-d_8 (77 µL, 1.0 mmol, 5 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and the crude colorless oil was dry loaded onto a silica gel column. Flash chromatography using gradient elution (100 mL of hexanes followed by 200 mL of 1% ethyl acetate in hexanes) gave the pure product as a clear and colorless oil (44.6 mg, 0.154 mmol, 77% yield).

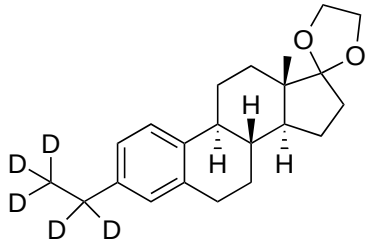
^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.08 – 6.95 (m, 2H), 6.90 – 6.85 (m, 1H), 3.60 (s, 2H), 2.61 (br s, 0.19H), 1.76 (br s, 0.20H), 0.91 (s, 9H), 0.05 (s, 6H).

^{13}C NMR: (75 MHz, $CDCl_3$)
δ 150.3 (dd, *J* = 247.1, 12.6 Hz), 148.8 (dd, *J* = 245.1, 12.6 Hz), 139.3 (dd, *J* = 4.3 Hz), 124.3 (dd, *J* = 5.7, 3.5 Hz), 117.3 (d, *J* = 16.6 Hz), 117.0 (d, *J* = 16.9 Hz), 61.9, 34.2 – 32.8 (m), 31.3 – 30.1 (m), 26.1, 18.5, -5.2.

^{19}F NMR: (376 MHz, $CDCl_3$)
δ -138.80, -142.71.

ATR-IR (cm^{-1}):
2955, 2929, 2857, 2211, 2119, 1607, 1518, 1254, 1087.

HRMS: (ESI^+) m/z: $[M+H]^+$ Calcd for $C_{15}H_{21}D_4F_2OSi$ 291.1894; Found 291.1881.



(*8R,9S,13S,14S*)-3-(Ethyl-*d*$_5$)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydrospiro[cyclopenta[a]phenanthrene-17,2'-[1,3]dioxolane] [6k]. According to the general procedure D, (*R*)-DTBM-SEGPHOS (5.2 mg, 0.0044 mmol, 0.022 eq.), $Cu(OAc)_2$ (20 µL of a 0.2 M solution in THF, 0.004 mmol, 0.02 eq.), THF (0.08 mL), then dimethoxy(methyl)silane-*d* (0.19 mL of 5.3 M solution in hexanes, 1 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of (8*R*,9*S*,13*S*,14*S*)-3-(ethynyl-*d*)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydrospiro[cyclopenta[*a*]phenanthrene-17,2'-[1,3]dioxolane] (64.6 mg, 0.2 mmol, 1 eq.), THF (0.1 mL), and 2-propanol-OD (77 µL, 1.0 mmol, 5 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 38 h at 60 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and the crude brown oil was dry loaded onto a silica gel column. Flash chromatography using gradient elution (100 mL of hexanes,100 mL of 3% ethyl acetate in hexane, 100 mL of 5% ethyl acetate in hexanes, 100 mL of 8% ethyl acetate in hexanes, 200 mL of 9% ethyl acetate in hexanes, 100 mL of 10% ethyl acetate in hexanes) gave the pure product as a clear, yellow oil (48.7 mg, 0.147 mmol, 74% yield).

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

δ 7.25 (d, *J* = 8.0 1H), 7.01 (d, *J* = 8.0, 1H), 6.95 (s, 1H), 4.08 – 3.83 (m, 4H), 2.92 – 2.83 (m, 2H), 2.58 (br s, 0.15H), 2.41 – 2.24 (m, 2H), 2.11 – 2.00 (m, 1H), 1.96 – 1.74 (m, 4H), 1.71 – 1.61 (m, 1H), 1.60 – 1.30 (m, 5H), 1.20 (br s, 0.20H), 0.90 (s, 3H).

^{2}H NMR: (61 MHz, $CHCl_3$)
δ 2.58 (br s, 1.85D), 1.21 (br s, 2.80D).

^{13}C NMR (101 MHz, $CDCl_3$)
δ 141.5, 137.8, 136.7, 128.6, 125.5, 125.3, 119.6, 65.4, 64.7, 49.6, 46.3, 44.1, 39.1, 34.4, 30.9, 29.7, 28.1 – 27.4 (m), 27.2, 26.1, 22.5, 15.5 – 14.2 (m), 14.5.

ATR-IR (cm^{-1}):
2966, 2936, 2872, 2221, 2075, 1700, 1610, 1103, 1042.

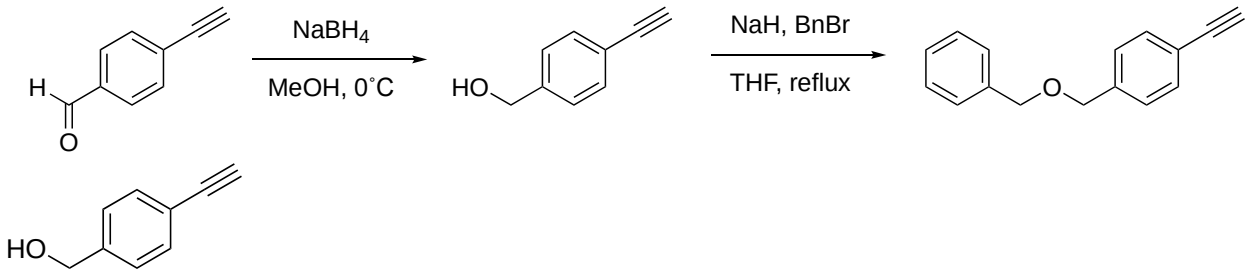
HRMS: (ESI^+) m/z: $[M + Na]^+$ Calcd for $C_{22}H_{25}D_5NaO_2$ 354.2452; Found 354.2462.

Synthesis of Alkyne Substrates

General TBS protection of internal alkynes (E)
To a flame-dried round bottom flask was added the alcohol substrate (2.5 mmol, 1 eq.), dry DCM (7.5 mL) followed by imidazole (340 mg, 5.0 mmol, 2 eq.) and *tert*-butyldimethylsilyl chloride (414 mg, 2.75 mmol, 1.1 eq.). The reaction was stirred at room temperature overnight. Upon completion, the reaction mixture was quenched with water (20 mL) and extracted with diethyl ether (2 x 15 mL). The combined organic layers were washed with brine (15 mL) and dried over anhydrous Na_2SO_4. The mixture was filtered, and the solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography to give the desired TBS protected alcohol.

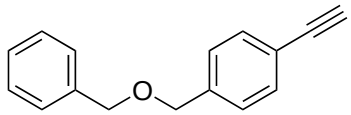
General Sonogashira Coupling for the synthesis of internal alkynes[11] (F)
To a flame-dried round bottom flask under N_2 was added triethylamine (15 mL), which was degassed for 10 minutes. The aryl halide (3.0 mmol, 1 eq.), $Pd(PPh_3)_2Cl_2$ (42 mg, 0.06 mmol, 0.02 eq.) and CuI (23 mg, 0.12 mmol, 0.04 eq.) were then sequentially added at room temperature. The mixture was stirred for 10 minutes followed by the addition of propargyl alcohol (3.3 mmol, 1.1 eq.). After 16 h of stirring at room temperature, the reaction was quenched with water (10 mL) and extracted with ethyl acetate (3 x 15 mL). The organic layers were washed with water (4 x 10 mL) and then dried over anhydrous Na_2SO_4. The mixture was filtered, and the solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography to give the desired aryl substituted propargyl alcohol.

General Aryl Finkelstein procedure[12] (G)
In a N_2 filled glovebox, a 25 mL dry Schlenk tube was charged with CuI (46.1 mg, 0.242 mmol, 0.05 eq.), aryl bromide compound (4.83 mmol, 1 eq.), and NaI (1.45g, 9.66 mmol, 2 eq.), followed by addition of trans-*N,N'*-dimethyl-1,2-cyclohexane diamine (0.076 mL, 0.483 mmol, 0.1 eq.) and anhydrous dioxane (4.83 mL). The Schlenk tube was equipped with a cold finger condenser, sealed and removed from the glovebox. The reaction was stirred at reflux in an oil bath under N_2 for 24 hours. Upon completion, the reaction was cooled to room temperature and was quenched with ammonia aqueous solution (prepared by diluting 0.5 mL of 0.5 M NH_3/dioxane solution in 40 mL of water). The aqueous layer was then extracted with CH_2Cl_2 (3 x 15 mL). The combined organic layers were washed with water (1 x 20 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The crude product was purified by column chromatography to give the desired aryl iodide.



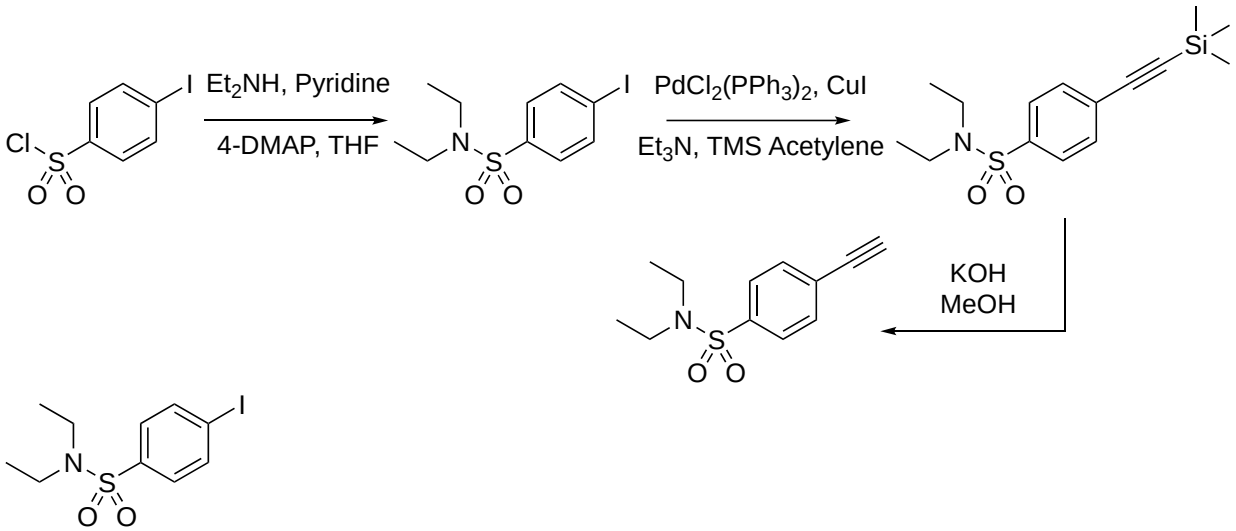
4-Ethynylbenzyl alcohol
To a flame dried 500 mL round bottom flask equipped with a Teflon stir bar was added 4-ethynylbenzaldehyde (3.94 g, 30.3 mmol, 1 eq.), $NaBH_4$ (2.29 g, 60.6 mmol, 2 eq.), and anhydrous methanol (235 mL). Reaction was stirred in ice bath until completion, monitored by TLC. Upon completion, the reaction was quenched with saturated $NaHCO_3$ aqueous solution and extracted with CH_2Cl_2 (4 x 100 mL). The combined organic layers were washed with water, dried over Na_2SO_4, and concentrated under vacuum. Excess solvent was removed by vacuum, and pure product was afforded as a yellow solid (3.38 g, 25.6 mmol, 85% yield). The spectra for the title compound matched previously reported spectra.[13]

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.49 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 4.70 (s, 2H), 3.07 (s, 1H), 1.75 (s, 1H).



1-((Benzyloxy)methyl)-4-ethynylbenzene [3g]
The benzyl protection was performed using a procedure adapted from the literature [14], a flame dried 300 mL round bottom flask was equipped with a Teflon stir bar and to this was added 4-ethynylbenzyl alcohol (1.0 g, 7.57 mmol, 1 eq.), THF (7.8 mL), and NaH (60% dispersion in mineral oil) (0.303 g, 7.57 mmol, 1 eq.). Reaction was heated to reflux in an oil bath for 30 minutes, then cooled to room temperature. Benzyl bromide (0.89 mL, 7.5 mmol, 0.99 eq.) was added, and reaction was heated to reflux for 48 hours. Reaction was monitored by TLC and when reaction reached completion, reaction was cooled to room temperature followed by addition of water (10 mL). Solvent was removed by rotary evaporation, and 3M KOH was added into the round bottom flask until pH = 12 was reached. The crude reaction mixture was transferred to a separatory funnel with DCM and extracted with DCM (3 x 10 mL). The combined organic layers were washed with brine (2 x 10 mL), dried over anhydrous Na_2SO_4, and concentrated under vacuum. Crude product was dry loaded onto a column, and the pure product was purified by flash column chromatography with elution gradient (100 mL of hexanes, 200 mL of 10% ethyl acetate in hexanes, 400 mL of 25% ethyl acetate in hexanes), the title compound was afforded as a colorless oil (1.15 g, 5.17 mmol, 68% yield). The spectra for the title compound matched previously reported spectra.[15]

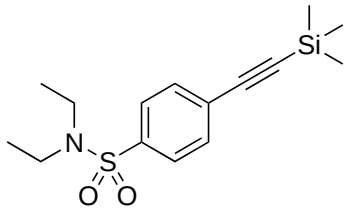
^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.49 (d, *J* = 8.1 Hz, 2H), 7.39 – 7.28 (m, 7H), 4.56 (s, 2H), 4.55 (s, 2H), 3.07 (s, 1H).



***N,N*-Diethyl-4-iodobenzenesulfonamide**
To a flame-dried round bottom flask was added pyridine (11 mL) and 4-iodo-benzenesulfonylchloride (2.0 g, 6.6 mmol, 1 eq.), followed by addition of diethyl amine (0.75 mL, 7.27 mmol, 1.1 eq.) in THF (4 mL). The reaction flask was cooled over an ice bath and was added 4-DMAP (4-dimethylaminopyridine) (6.5 mg, 0.053 mmol, 0.008 eq.). The reaction was then warmed to room temperature and stirred for 48 hours. Reaction was monitored by TLC and upon completion, the mixture was poured into water (30 mL). The resulting precipitate was collected by vacuum filtration and rinsed with water (2 x 10 mL). The solid was dissolved in ethyl acetate (15 mL) and washed with 5% HCl (3 x 10 mL), water (2 x 10 mL), and brine (10 mL). The ethyl acetate solution was dried over anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was dry loaded onto a column, and the pure product was eluted out through flash column

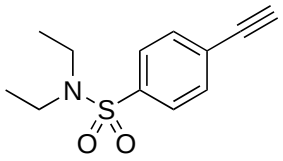
chromatography (200 mL of hexanes, 300 mL of 5% ethyl acetate in hexanes, 300 mL of 10% ethyl acetate in hexanes, 300 mL of 15% ethyl acetate in hexanes, and 300 mL of 20% ethyl acetate in hexanes) to afford the pure product (1.40 g, 4.14 mmol, 63% yield). The spectra for the title compound matched previously reported spectra.[16]

^{1}H NMR (300 MHz, $CDCl_3$)
δ 7.74 (d, *J* = 8.6 Hz, 2H), 7.41 (d, *J* = 8.6 Hz, 2H), 3.10 (q, *J* = 7.2 Hz, 4H), 0.99 (t, *J* = 7.2 Hz, 6H).



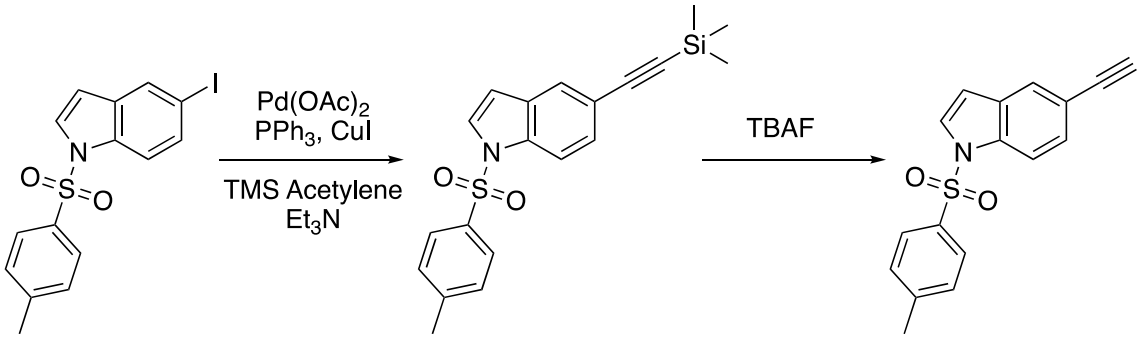
***N*,*N*-Diethyl-4-trimethylsilylethynylbenzenesulfonamide**
Under N_2 atomosphere, to a stirred solution of *N*,*N*-diethyl-4-iodo-benzenesulfonamide (1.40 g, 4.14 mmol, 1 eq.) in degassed triethylamine (7 mL) was added $Pd(PPh_3)_2Cl_2$ (58 mg, 0.083 mmol, 0.02 eq.) and CuI (39 mg, 0.21 mmol, 0.05 eq.) at room temperature. The mixture was then stirred for 10 minutes followed by the addition of trimethylsilyl acetylene (0.86 mL, 6.21 mmol, 1.5 eq.). Reaction was stirred at 60 ˚C in an oil bath overnight, and upon completion, was quenched with water (10 mL) and extracted with diethyl ether (3 x 15 mL). The combined organic layers were washed with 1 M HCl (100 mL) and water (4 x 10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The crude product was purified by flash column chromatography (100 mL of hexanes, 200 mL of 5% ethyl acetate in hexanes, 300 mL of 10% ethyl acetate in hexanes, 200 mL of 20% ethyl acetate in hexanes) to afford the pure orange solid product. Quantitative yield was assumed, and product was taken immediately to the TMS-deprotection step.

^{1}H NMR (300 MHz, $CDCl_3$)
δ 7.72 (d, *J* = 8.5 Hz, 2H), 7.54 (d, *J* = 8.5 Hz, 2H), 3.21 (q, *J* = 7.2 Hz, 4H), 1.09 (t, *J* = 7.2 Hz, 6H), 0.24 (s, 9H).



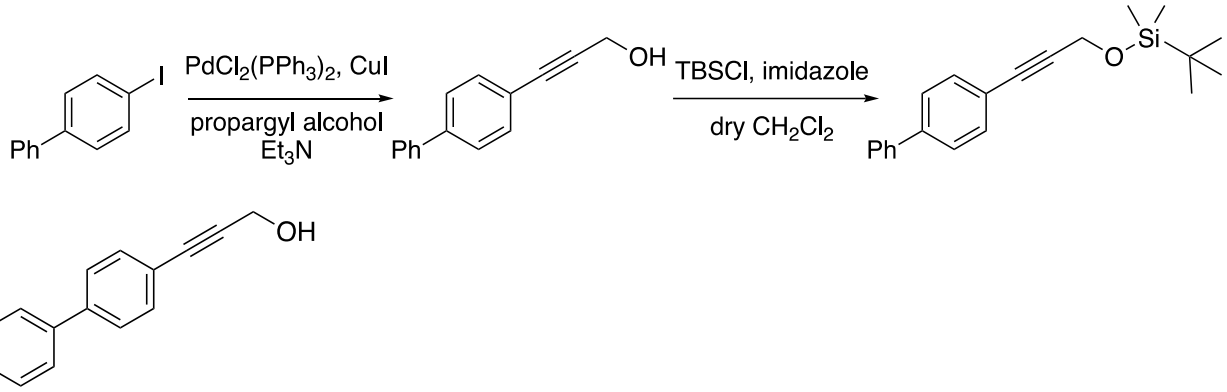
***N*,*N*-Diethyl-4-ethynylbenzenesulfonamide [3i].**
The mixture of the TMS-protected sulfonamide (1.28 g, 4.14 mmol, 1 eq.), KOH (4.55 mL of 1 M aqueous solution, 4.55 mmol, 1.1 eq.), and MeOH (26 mL) were stirred at room temperature for 14 hours. The reaction progress was monitored by TLC. Upon completion, the reaction mixture was diluted with water (10 mL) and extracted with Et_2O (3 x 15 mL). The combined organic layers were washed with 1 M HCl (20 mL), water (20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4, and filtered. The solvent was then removed by rotary evaporation. The crude product was dry loaded onto a column, and purified by flash column chromatography (100 mL of hexanes, 200 mL of 5% ethyl acetate in hexanes, 800 mL of 10% ethyl acetate in hexanes, 200 mL of 20% ethyl acetate in hexanes) to afford the pure orange solid product (703 mg, 2.96 mmol, 72% yield). The spectra for the title compound matched previously reported spectra.[17]

^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.57 (d, *J* = 8.2 Hz, 2H), 3.27 – 3.17 (m, 5H), 1.10 (t, *J* = 7.2 6H).



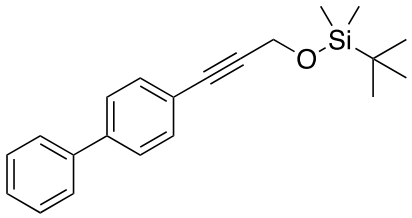
5-Ethynyl-1-tosyl-1*H*-indole [3k]. Following a previously reported method, from 5-iodo-1-tosyl-1*H*-indole (0.863 g, 2.17 mmol), the title compound was obtained as a yellow solid (0.492 g, 1.67 mmol, 77% yield). The spectra for the title compound matched previously reported spectra.[18]

^{1}H NMR: (300 MHz, $CDCl_3$)
δ 7.96 (d, *J* = 8.6 Hz, 1H), 7.75 (d, *J* = 8.3 Hz, 2H), 7.67 (d, *J* = 1.4 Hz, 1H), 7.59 (d, *J* = 3.7 Hz, 1H), 7.44 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.19 (d, *J* = 8.3 Hz, 2H), 6.61 (d, *J* = 3.7, 1H), 3.05 (s, 1H), 2.29 (s, 3H).



((3-([1,1'-Biphenyl]-4-yl)prop-2-yn-1-yl)). Synthesized according to the general procedure F from 4-iodo-1,1'-biphenyl (1.00 g, 3.57 mmol), the title compound was obtained as a light yellow solid (633 mg, 3.04 mmol, 85%). The spectra for the title compound matched previously reported spectra.[19]

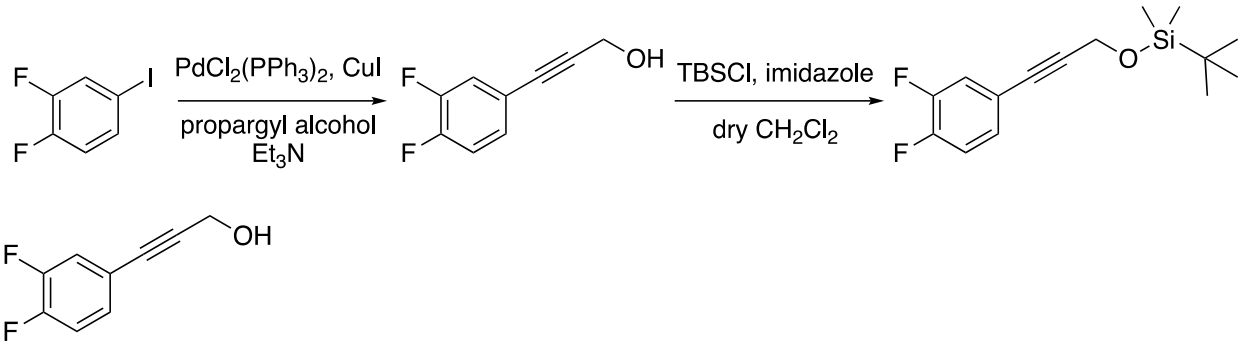
^{1}H NMR (300 MHz, $CDCl_3$)
δ 7.63 – 7.48 (m, 6H), 7.45 (t, 2H), 7.40 – 7.32 (m, 1H), 4.53 (d, *J* = 6.2, 2H), 1.66 (t, *J* = 6.1 Hz, 1H).



((3-([1,1'-Biphenyl]-4-yl)prop-2-yn-1-yl)oxy)(*tert*-butyl)dimethylsilane [3o]. Following the general procedure E, the alcohol substrate (500 mg, 2.4 mmol, 1 eq.) in dry DCM (7.5 mL) followed by imidazole (327 mg, 4.8 mmol, 2 eq.) and *tert*-butyldimethylsilyl chloride (398 mg, 2.64 mmol, 1.1 eq.). Purified with flash column chromatography using gradient elution (100 mL of hexanes, 100 mL of 3% ethyl acetate in hexanes, 300 mL of 5% of ethyl acetate in hexanes), the title compound was obtained as a light yellow solid (633 mg, 1.96 mmol, 82% yield). The spectra for the title compound matched previously reported spectra.[20]

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.61 – 7.56 (m, 2H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 1H), 4.57 (s, 2H), 0.95 (s, 9H), 0.19 (s, 6H).

^{13}C NMR (75 MHz, $CDCl_3$)
δ 141.1, 140.4, 132.1, 128.9, 127.7, 127.1, 127.0, 122.0, 88.7, 84.8, 52.4, 26.0, 18.5, -4.9.



3-(3,4-Difluorophenyl)-2-propyn-1-ol [3p]. Following the general procedure F, $Pd(PPh_3)_2Cl_2$ (117 mg, 0.167 mmol, 0.02 eq.) and CuI (63 mg, 0.33 mmol, 0.04 eq.) were sequentially added to a solution of 1,2-difluoro-4-iodobenzene (2.0 g, 8.34 mmol, 1 eq.) in degassed triethylamine (42 mL) under nitrogen at room temperature. To the reaction mixture was added propargyl alcohol (0.53 mL, 9.17 mmol, 1.1 eq.). The reaction mixture was stirred for 22 hr. Crude product was purified with flash chromatography using gradient elution (100 mL of hexanes, 100 mL of 5% ethyl acetate in hexanes, 100 mL of 10% of ethyl acetate in hexanes, 400 mL of 15% of ethyl acetate in hexanes), **3u** was obtained as a clear dark yellow oil (0.959 g, 5.70 mmol, 68.4% yield).

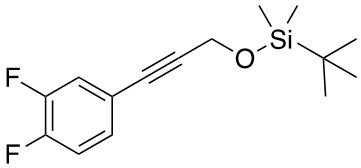
^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.25 – 7.18 (m, 1H), 7.17 – 7.12 (m, 1H), 7.11 – 7.03 (m, 1H), 4.47 (s, 2H), 2.34 (br s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$)
δ 152.1 (dd, *J* = 58.5, 12.8 Hz), 148.7 (dd, *J* = 55.8, 12.7 Hz), 128.5 (dd, *J* = 6.5, 3.6 Hz), 119.5 (dd, *J* = 7.6, 4.2 Hz), 121.1 – 116.9 (m), 87.9, 83.7, 51.5.

^{19}F NMR (376 MHz, $CDCl_3$)
δ -135.60, -137.11.

ATR-IR (cm^{-1}): 3321, 2927, 2866, 2232, 1734, 1512, 1216, 1167.

HRMS: (EI^+) *m/z*: $[M]^+$ Calcd for $C_9H_6OF_2$ 168.0400; Found 168.0380.



***tert*-Butyl((3-(3,4-difluorophenyl)prop-2-yn-1-yl)oxy)dimethylsilane [5j]**. According to the general procedure E, from alcohol **3u** (0.330g, 1.96 mmol) the title compound was obtained as a clear and colorless oil (0.47 g, 1.66 mmol, 85% yield).

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

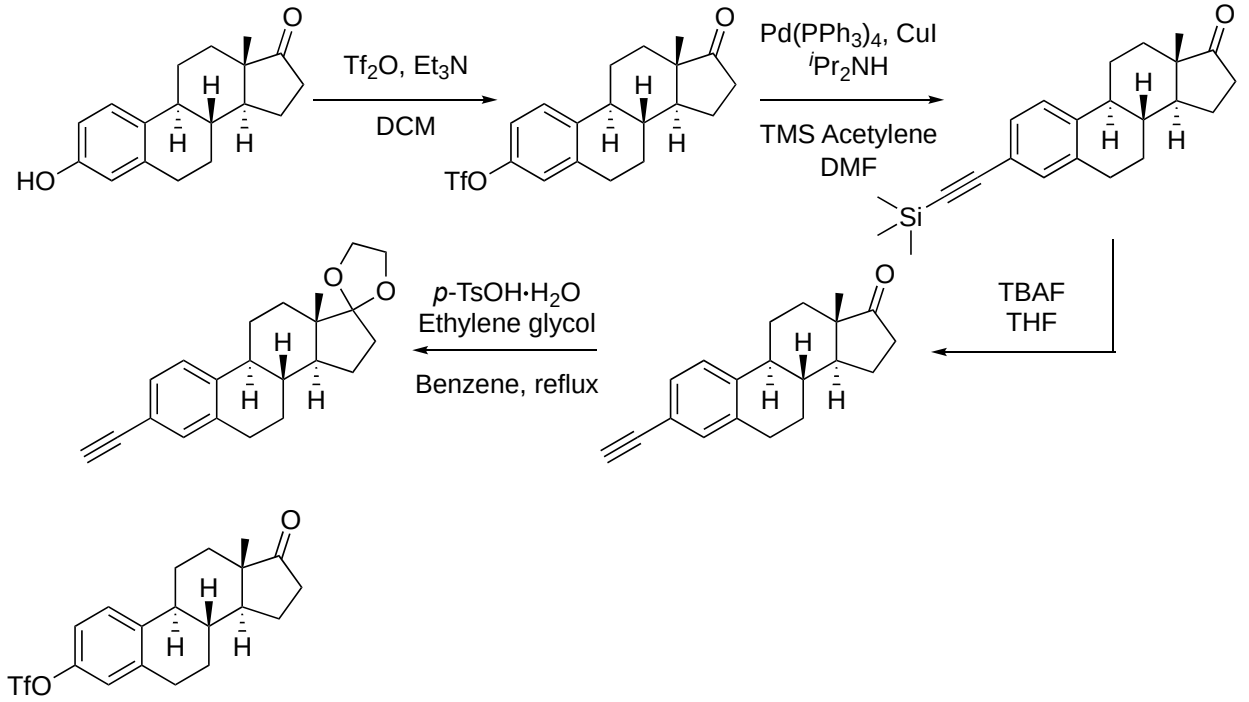
δ 7.26 – 7.03 (m, 3H), 4.51 (s, 2H), 0.94 (s, 9H), 0.16 (s, 6H).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 150.7 (dd, *J* = 251.3, 12.5 Hz), 150.1 (dd, *J* = 249.1, 13.1 Hz), 128.3 (dd, *J* = 5.8, 3.9 Hz), 120.7 (d, *J* = 18.4 Hz), 120.0 (dd, *J* = 7.4, 4.3 Hz), 117.5 (d, *J* = 17.8 Hz), 88.7, 82.8, 52.2, 26.0, 18.5, -5.0.

^{19}F NMR: (376 MHz, $CDCl_3$)
δ -136.07, -137.28.

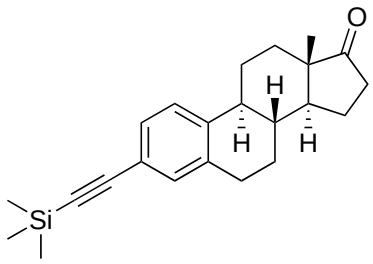
ATR-IR (cm^{-1}): 2954, 2856, 2215, 1513, 1251, 1217, 1080.

HRMS: (ESI^+) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{20}F_2NaOSi$ 305.1144; Found 305.1147.



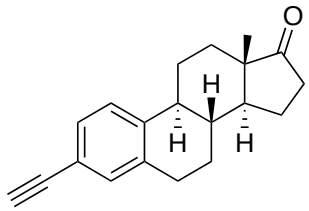
(8*R*,9*S*,13*S*,14*S*)-13-Methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl trifluoromethanesulfonate. In a 100 mL flame dried round bottom flask equipped with a Teflon stir bar was added estrone (1 g, 3.7 mmol, 1 eq.), Et_3N (1.03 mL, 7.4 mmol, 2 eq.), and DCM (18 mL), and was stirred in an ice bath for 15 minutes. Triflic anhydride (0.685 mL, 4.07 mmol, 4 eq.) was added dropwise, and a brown color persisted in the reaction flask. The reaction was stirred at room temperature for 8 hours and progress was monitored by TLC. Upon completion the reaction was quenched with saturated aqueous $NaHCO_3$ (10 mL). The aqueous layer was extracted with DCM (3 x 20 mL), the combined organic layers were washed with brine (20 mL), dried over Na_2SO_4 and concentrated under vacuum. The crude product was dry loaded onto a column, and purified by flash column chromatography (100 mL of hexanes, 100 mL of 5% ethyl acetate in hexanes, 100 mL of 7% ethyl acetate in hexanes, 100 mL of 10% ethyl acetate in hexanes, 300 mL of 12% ethyl acetate in hexanes, 300 mL of 15% ethyl acetate in hexanes, and 300 mL of 17% ethyl acetate in hexanes) to afford the pure, white solid product (1.36 g, 3.38 mmol, 91% yield). The spectra for the title compound matched previously reported spectra.[21]

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.34 (d, 1H), 7.07 – 6.97 (m, 2H), 2.99 – 2.88 (m, 2H), 2.52 (dd, *J* = 18.8, 8.7 Hz, 1H), 2.46 – 2.36 (m, 1H), 2.35 – 2.27 (m, 1H), 2.23 – 1.94 (m, 4H), 1.72 – 1.40 (m, 6H), 0.92 (s, 3H).



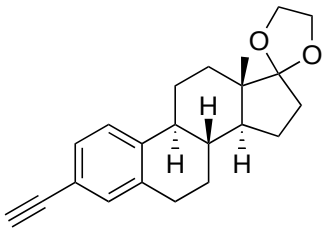
(8*R*,9*S*,13*S*,14*S*)-13-Methyl-3-((trimethylsilyl)ethynyl)-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one. In a 100 mL oven dried Schlenk tube equipped with a Teflon stir bar was added (8*R*,9*S*,13*S*,14*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl trifluoromethanesulfonate (1 g, 2.49 mmol, 1 eq.), DMF (30 mL), $Pd(PPh_3)_4$ (287 mg, 0.249 mmol, 0.1 eq.), CuI (47 mg, 0.249 mmol, 0.1 eq.), and $^{i}Pr_2NH$ (1.05 mL, 7.46 mmol, 3 eq.). The reaction mixture was degassed with N_2 for 20 minutes, followed by addition of trimethylsilyl acetylene (0.414 mL, 2.99 mmol, 1.2 eq.). Using a cold finger condenser, the reaction was heated to reflux in an oil bath for 24 hours. The reaction progress was monitored by TLC. Upon completion, reaction was diluted with Et_2O, washed with brine (3 x 10 mL), dried over Na_2SO_4, and concentrated under vacuum. The crude product was dry loaded onto a column, and purified by flash column chromatography (200 mL of hexanes, 100 mL of 2% ethyl acetate in hexanes, 300 mL 4% ethyl acetate in hexanes, 600 mL of 6% ethyl acetate in hexanes, 500 mL of 7% ethyl acetate in hexanes, and 600 mL of 8% ethyl acetate in hexanes) to afford the pure white solid product (474 mg, 1.35 mmol, 54% yield). The spectra for the title compound matched previously reported spectra.[22]

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.25 – 7.18 (m, 3H), 2.92 – 2.83 (m, 2H), 2.51 (dd, *J* = 18.8, 8.7 Hz, 1H), 2.45 – 2.35 (m, 1H), 2.34 – 2.24 (m, 1H), 2.21 – 1.91 (m, 4H), 1.70 – 1.36 (m, 6H), 0.91 (s, 3H), 0.24 (s, 9H).



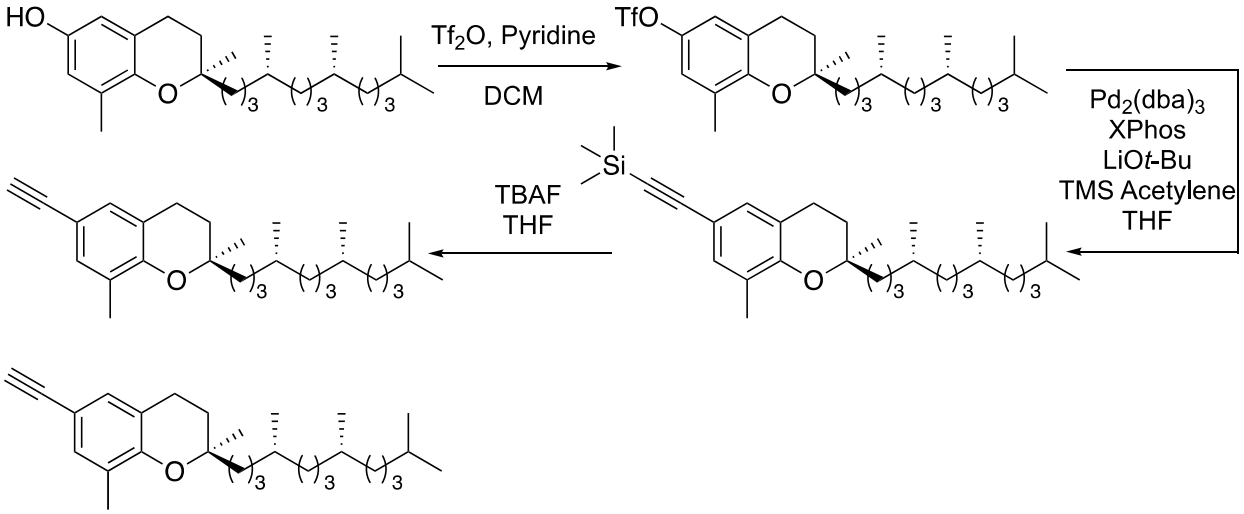
(8*R*,9*S*,13*S*,14*S*)-3-Ethynyl-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one. In a round bottom flask, (8*R*,9*S*,13*S*,14*S*)-13-methyl-3-((trimethylsilyl)ethynyl)-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one (514 mg, 1.47 mmol, 1 eq.), TBAF (1.62 mL of 1 M TBAF in THF, 1.1 eq.) and THF (6.6 mL) were combined and stirred for 5 hours, reaction progress was monitored by TLC. Upon completion, the reaction was quenched with distilled water (20 mL), extracted with DCM (3 x 10 mL), dried over Na_2SO_4, and concentrated under vacuum. The crude product was dry loaded onto a column, and purified by flash column chromatography (100 mL of hexanes, 100 mL of 2% ethyl acetate in hexanes, 100 mL 4% ethyl acetate in hexanes, 300 mL of 6% ethyl acetate in hexanes, and 600 mL of 8% ethyl acetate in hexanes) to afford the white solid product (310 mg, 1.11 mmol, 76% yield). The spectra for the title compound matched previously reported spectra.[22]

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.30 – 7.19 (m, 3H), 3.02 (s, 1H), 2.94 – 2.85 (m, 2H), 2.51 (dd, *J* = 18.8, 8.7 Hz, 1H), 2.45 – 2.37 (m, 1H), 2.36 – 2.25 (m, 1H), 2.21 – 1.92 (m, 4H), 1.69 – 1.38 (m, 6H), 0.91 (s, 3H).



(8*R*,9*S*,13*S*,14*S*)-3-Ethynyl-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydrospiro[cyclopenta[*a*]phenanthrene-17,2'-[1,3]dioxolane] [3r] To a 100 mL round bottom flask equipped with a Teflon stir bar was added (8*R*,9*S*,13*S*,14*S*)-3-ethynyl-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one (307 mg, 1.1 mmol, 1 eq.), *p*-TsOH•H_2O (19 mg, 0.10 mmol, 0.091 eq.), ethylene glycol (1.23 mL, 22 mmol, 20 eq.), and benzene (8 mL). The reaction flask was fitted with a condenser equipped with a Dean Stark trap for the removal of water, and heated to reflux in an oil bath. Progress was monitored by TLC, and upon completion, reaction was poured into 10 mL of water, and extracted with DCM (3 x 10 mL). The combined organic layers were washed with water (10 mL), brine (10 mL), and dried over Na_2SO_4. Solvent was removed by rotary evaporation, and the crude product was dry loaded onto a column, and purified by flash column chromatography (80 mL of hexanes, 100 mL of 3% ethyl acetate in hexanes, 100 mL of 5% ethyl acetate in hexanes, 100 mL of 6% ethyl acetate in hexanes, 100 mL of 8% ethyl acetate in hexanes, and 500 mL of 9% ethyl acetate in hexanes) to afford the white solid product (148 mg, 0.459 mmol, 42% yield). The spectra for the title compound matched previously reported spectra.[18]

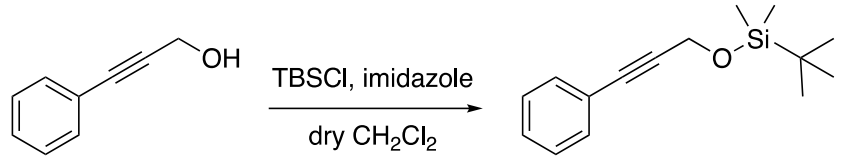
^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.28 – 7.21 (m, 3H), 4.01 – 3.84 (m, 4H), 3.00 (s, 1H), 2.87 – 2.80 (m, 2H), 2.37 – 2.22 (m, 2H), 2.08 – 1.98 (m, 1H), 1.96 – 1.71 (m, 4H), 1.69 – 1.59 (m, 1H), 1.59 – 1.28 (m, 5H), 0.88 (s, 3H).



(*R*)-6-Ethynyl-2,8-dimethyl-2-((*4R,8R*)-4,8,12-trimethyltridecyl)chromane [3s]. Following a previously reported method, from (*R*)-2,8-dimethyl-2-((*4R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl trifluoromethanesulfonate (1.07 g, 2.00 mmol), the title compound was obtained as a pale yellow oil (0.41 g, 1.00 mmol, 50% yield). The spectra for the title compound matched previously reported spectra.[18]

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

δ 7.17 – 7.06 (m, 2H), 2.94 (s, 1H), 2.79 – 2.67 (m, 2H), 2.16 (s, 3H), 1.90 – 1.70 (m, 2H), 1.67 – 1.04 (m, 24H), 0.97 – 0.81 (m, 12H).



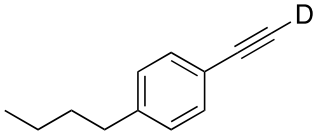
((3-(Phenyl)prop-2-yn-1-yl)oxy)(*tert*-butyl)dimethylsilane [5h]. The compound was synthesized according to the general procedure E. 3-phenylprop-2-yn-1-ol (2.0 g, 15.1 mmol, 1 eq.) and dry DCM (45 mL) were added to a flame dried 200 mL round bottom flask equipped with a Teflon stir bar, followed by imidazole (1.87 g, 30.2 mmol, 2 eq.) and *tert*-butyldimethylsilyl chloride (2.50 g, 16.6 mmol, 1.1 eq.). The reaction was allowed to stir at room temperature overnight. The mixture was then transferred to a separatory funnel and extracted with diethyl ether (2 x 30 mL). The combined organic layers were washed with brine (15 mL) and dried over anhydrous Na_2SO_4. The mixture was filtered, and the solvent was removed by rotary evaporation. The crude oil was purified by flash chromatography (250 mL of hexanes, 200 mL of 2% ethyl acetate in hexanes) to afford a clear oil (3.6 g, 14.6 mmol, 97%). The spectra for the title compound matched previously reported spectra.[23]

^{1}H NMR (300 MHz, $CDCl_3$)
δ 7.50 – 7.36 (m, 2H), 7.35 – 7.27 (m, 3H), 4.55 (s, 2H), 0.95 (s, 9H), 0.18 (s, 6H).

Synthesis of D-alkyne Substrates

General Procedure for Preparation of D-alkynes (H)

Following a previously reported procedure for the terminal deuteration of alkynes[24], a flame dried round bottom flask equipped with a Teflon stir bar was purged with N_2 and to this was added, aryl alkyne (1 eq.), anhydrous K_2CO_3 (1.5 eq.), and anhydrous CH_3CN sequentially. After stirring for 30 minutes, D_2O (50 eq.) was added to the round bottom flask and the reaction was stirred at room temperature for 12 – 48 hours. Reaction progress was followed by ^{1}H NMR. Upon completion, the mixture was extracted with dichloromethane or diethyl ether. The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The products were used in the next step without further purification.



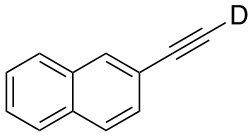
1-Butyl-4-(ethynyl-*d*)benzene [5a]. Following the general procedure H, in a N_2 filled glovebox, 1-butyl-4-ethynylbenzene (0.63 g, 4.0 mmol, 1 eq.), anhydrous K_2CO_3 (0.83 g, 6.0 mmol, 1.5 eq.) and anhydrous CH_3CN (12.0 mL) were stirred for 30 min. D_2O (3.61 mL, 200 mmol, 50 eq.) was added to the reaction, and the mixture was stirred for 36 h at room temperature under nitrogen atmosphere. Upon completion, the reaction was extracted with diethyl ether (3 x 10 mL). The combined extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum to afford the title compound as a light yellow liquid (0.52 g, 3.27 mmol, 82% yield).

^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.44 (d, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 3.05 (br s, 0.07H), 2.63 (t, *J* = 7.5 Hz, 2H), 1.67 – 1.55 (m, 2H), 1.44 – 1.30 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 144.0, 132.1, 128.5, 119.3, 83.5 (t, *J* = 7.6 Hz, 1C), 76.8 –75.9 (multiplet overlapping with $CDCl_3$ signal, 1C), 35.7, 33.5, 22.4, 14.1.

ATR-IR (cm^{-1}): 3296, 3081, 3028, 2957, 2929, 2871, 2859, 2584, 1910, 1508, 1466, 821.

HRMS: (EI^+) *m/z*: $[M]^+$ Calcd for $C_{12}H_{13}D$ 159.1200; Found 159.1153.



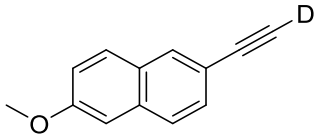
2-(Ethynyl-*d*)naphthalene [5b]. Following the general procedure H, in a N_2 filled glovebox, 2-ethynyl-napthalene (200 mg, 1.31 mmol, 1 eq.), K_2CO_3 (272 mg, 1.97 mmol, 1.5 eq.), and CH_3CN (2.0 mL) were added to a flame dried 200 mL round bottom flask equipped with a Teflon stir bar. After stirring for 30 minutes, deuterium oxide (1.18 mL, 66.5 mmol, 50 eq.) was added to round bottom flask. After stirring at room temperature for 12 h, the reaction was quenched with distilled water (10 mL), and extracted with dichloromethane (3 x 10 mL). The organic layers were combined, dried over anhydrous Na_2SO_4 and concentrated to afford the white solid (200 mg, 1.31 mmol, >99% yield).

^{1}H NMR: (400 MHz, $CDCl_3$)
δ 8.04 (s, 1H), 7.87 – 7.76 (m, 3H), 7.57 – 7.47 (m, 3H), 3.15 (br s, 0.09H).

^{13}C NMR: (75 MHz, $CDCl_3$)
δ 133.2, 132.9, 132.4, 128.7, 128.2, 127.9 (+ 1 overlapping signal), 127.0, 126.7, 119.5, 83.7 (t, *J* = 7.3 Hz, 1C), 77.9 –77.3 (multiplet overlapping with $CDCl_3$ signal, 1C).

ATR-IR (cm^{-1}): 3276, 3049, 2922, 2572, 1971, 1593.

HRMS: (EI^+) *m/z*: $[M]^+$ Calcd for $C_{12}H_7D$ 153.0700; Found 153.0680.



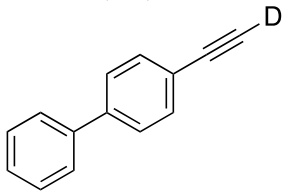
2-(Ethynyl-*d*)-6-methoxynaphthalene [5c]. Following the general procedure H, in a N_2 filled glovebox, 2-ethynyl-6-methoxynaphthalene, (0.18 g, 0.99 mmol, 1 eq.) anhydrous K_2CO_3 (0.205 g, 1.49 mmol, 1.5 eq.) and anhydrous CH_3CN (3.0 mL) were stirred for 30 min. D_2O (0.90 mL, 50 mmol, 50 eq.) was added to the reaction. The reaction mixture was stirred for 36 h at room temperature under nitrogen atmosphere. Upon completion, the reaction was extracted with diethyl ether (3 x 5 mL). The combined extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum to afford the title compound as a light yellow solid (0.18 g, 0.98 mmol, 99% yield).

^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.96 (s, 1H), 7.69 (t, *J* = 8.8 Hz, 2H), 7.50 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.17 (dd, *J* = 8.9, 2.3 Hz, 1H), 7.10 (d, *J* = 2.2 Hz, 1H), 3.92 (s, 3H), 3.13 (br s, 0.06H).

^{13}C NMR: (75 MHz, $CDCl_3$)
δ 158.6, 134.5, 132.2, 129.5, 129.3, 128.4, 127.0, 119.6, 117.0, 105.9, 83.9 (t, *J* = 7.2 Hz, 1C), 77.0 – 76.2 (multiplet overlapping with $CDCl_3$ signal, 1C), 55.5.

ATR-IR (cm^{-1}): 3257, 3059, 3002, 2967, 2938, 2903, 2841, 2564, 1225, 1028.

HRMS: (EI$^+$) *m/z*: [M]$^+$ Calcd for $C_{13}H_9DO$ 183.0800; Found 183.0788.



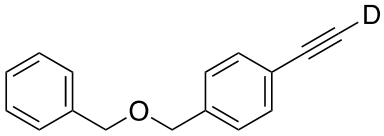
4-(Ethynyl-*d*)-1,1'-biphenyl [5d]. Following the general procedure H, in a N_2 filled glovebox, 4-ethynyl-1,1'-biphenyl (200 mg, 1.12 mmol, 1 eq.), K_2CO_3 (0.698 g, 5.05 mmol, 4.5 eq.), and CH_3CN (1.5 mL) were combined. After stirring for 30 minutes, D_2O (75 µL, 4.14 mmol, 3.7 eq.) was added to round bottom flask and the reaction was stirred at room temperature for 12 h. The reaction was quenched with distilled water, and extracted with dichloromethane (3 x 10 mL). The organic layers were combined and dried over anhydrous Na_2SO_4 then concentrated. The reaction was repeated three times to allow for full deuterium incorporation. The title compound was afforded as an orange solid product (200 mg, 1.12 mmol, >99% yield).

^{1}H NMR (300 MHz, $CDCl_3$)
δ 7.65 – 7.52 (m, 6H), 7.50 – 7.41 (m, 2H), 7.41 – 7.32 (m, 1H), 3.14 (br s, 0.09H).

^{13}C NMR (75 MHz, $CDCl_3$)
δ 141.7, 140.4, 132.7, 129.0, 127.9, 127.2, 127.1, 121.1, 83.2 (t, *J* = 6.9 Hz, 1C), 78.3 – 77.3 (multiplet overlapping with $CDCl_3$ signal, 1C).

ATR-IR (cm^{-1}): 3272, 3056, 3028, 2922, 2851, 2572.

HRMS: (EI$^+$) *m/z*: [M]$^+$ Calcd for $C_{14}H_9D$ 179.0800; Found 179.0837.



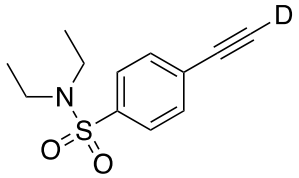
1-((Benzyloxy)methyl)-4-(ethynyl-*d*)benzene [5e]. Following the general procedure H, in a N_2 filled glovebox, 1-((benzyloxy)methyl)-4-ethynylbenzene (1.11 g, 4.99 mmol, 1 eq.), anhydrous K_2CO_3 (1.04 g, 7.49 mmol, 1.5 eq.) in anhydrous CH_3CN (15.0 mL) were stirred for 30 min. D_2O (4.51 mL, 250 mmol, 50 eq.) was added to the reaction. The reaction mixture was stirred for 36 h at room temperature under nitrogen atmosphere. Upon completion, the reaction was extracted with diethyl ether (3 x 15 mL). The combined extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum to afford the title compound as a white solid (1.05 g, 4.70 mmol, 94% yield).

^{1}H NMR: (300 MHz, $CDCl_3$)
δ 7.55 (d, *J* = 8.4 Hz, 2H), 7.48 – 7.33 (m, 7H), 4.61 (s, 2H), 4.60 (s, 2H), 3.13 (s, 0.00H).

^{13}C NMR: (75 MHz, $CDCl_3$)
δ 139.2, 138.1, 132.2, 128.5, 127.8, 127.8, 127.6, 121.3, 83.2 (t, *J* = 7.1 Hz, 1C), 77.4 – 76.6 (multiplet overlapping with $CDCl_3$ signal), 72.3, 71.6.

ATR-IR (cm^{-1}): 3287, 3087, 3063, 3031, 2925, 2856, 2580, 1702, 1087, 1070

HRMS: (ESI$^+$) m/z: [M+Na]$^+$ Calcd for $C_{16}H_{13}DNaO$ 246.1000; Found 246.1002.



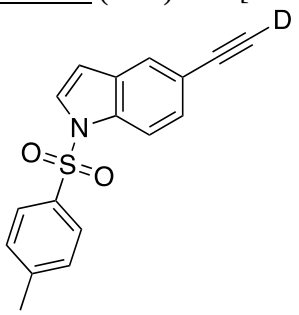
***N*,*N*-Diethyl-4-(ethynyl-*d*)benzenesulfonamide [5f].** Following the general procedure H, in a N_2 filled glovebox, *N*,*N*-diethyl-4-(ethynyl)-benzenesulfonamide (500 mg, 2.11 mmol, 1 eq.), K_2CO_3 (0.437 g, 3.16 mmol, 1.5 eq.), and CH_3CN (3.24 mL) were added to a 200 mL flame dried round bottom flask equipped with a Teflon stirbar. After stirring for 30 minutes, D_2O (1.91 mL, 106 mmol, 50 eq.) was added to the reaction and stirred at room temperature for 12 h. The reaction was quenched with distilled water (10 mL), and extracted with dichloromethane (3 x 10 mL). The organic layers were combined and dried over anhydrous Na_2SO_4, then concentrated to afford the product as a yellow solid (470 mg, 1.97 mmol, 93% yield).

^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.75 (d, *J* = 8.5 Hz, 2H), 7.58 (d, *J* = 8.5 Hz, 2H), 3.22 (q, *J* = 7.1 Hz, 4.1H), 1.11 (t, *J* = 7.2 Hz, 6H).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 140.5, 132.7, 127.0, 126.4, 81.8 (t, *J* = 7.1 Hz, 1C), 80.6 (t, *J* = 19.7 Hz, 1C), 42.1, 14.2.

ATR-IR (cm^{-1}): 3253, 2977, 2923, 2565, 1963, 1331, 1154.

HRMS: (ESI$^+$) m/z: $[M+Na]^+$ Calcd for $C_{12}H_{14}DNNaO_2S$ 261.0778; Found 261.0781.



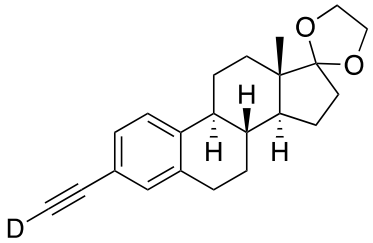
5-(Ethynyl-*d*)-1-tosyl-1H-indole [5g]. Following the general procedure H, in a N_2 filled glovebox, 5-(ethynyl)-1-tosyl-1H-indole (0.40 g, 1.35 mmol, 1 eq.), anhydrous K_2CO_3 (0.280 g, 2.03 mmol, 1.5 eq.) in anhydrous CH_3CN (4.0 mL) were stirred for 30 min. D_2O (1.22 mL, 67.5 mmol, 50 eq.) was added to the reaction. The reaction mixture was stirred for 36 h at room temperature under nitrogen atmosphere. Upon completion, the reaction was extracted with ethyl acetate (3 x 10 mL). The combined extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum to afford the title compound as a white solid (0.38 g, 1.28 mmol, 95% yield).

^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.97 (d, *J* = 8.6 Hz, 1H), 7.75 (d, *J* = 8.3 Hz, 2H), 7.67 (d, *J* = 1.6 Hz, 1H), 7.59 (d, *J* = 3.7 Hz, 1H), 7.45 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.18 (d, *J* = 8.3 Hz, 2H), 6.61 (d, *J* = 3.7 Hz, 1H), 3.07 (br s, 0.05H), 2.27 (s, 3H).

^{13}C NMR: (75 MHz, $CDCl_3$)
δ 145.3, 134.9, 134.5, 130.6, 130.0, 128.4, 127.4, 126.8, 125.5, 117.1, 113.5, 108.8, 83.4 (t, *J* = 5.5 Hz, 1C), 76.4 (t, *J* = 38.4 Hz, 1C), 21.5.

ATR-IR (cm^{-1}): 3117, 2920, 2573, 1370, 1116.

HRMS: (ESI$^+$) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{12}DNNaO_2S$ 319.0622; Found 319.0626.



(8*R*,9*S*,13*S*,14*S*)-3-(Ethynyl-*d*)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydrospiro[cyclopenta[*a*]phenanthrene-17,2'-[1,3]dioxolane] [5j]. Following the general procedure H, in a N_2 filled glovebox, (8*R*,9*S*,13*S*,14*S*)-3-(ethynyl)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydrospiro[cyclopenta[*a*]phenanthrene-17,2'-[1,3]dioxolane (213 mg, 0.661 mmol, 1 eq.), K_2CO_3 (0.137 g, 0.991 mmol, 1.5 eq.), and CH_3CN (2 mL) were added to a flame dried 300 mL round bottom flask equipped with a Teflon stir bar. After stirring for 30 minutes, D_2O (0.597 mL, 33.1 mmol, 50 eq.) was added to round bottom flask. After stirring at room temperature for 24 h, reaction was quenched with distilled water, and extracted with dichloromethane (3 x 10 mL). The organic layers were combined and dried over Na_2SO_4, then concentrated to afford a white solid (215 mg, 0.665 mmol, >99% yield).

^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.25 – 7.22 (m, 2H), 7.22 – 7.19 (m, 1H), 3.99 – 3.81 (m, 4H), 2.99 (br s, 0.07H), 2.88 – 2.79 (m, 2H), 2.36 – 2.21 (m, 2H), 2.07 – 1.97 (m, 1H), 1.95 – 1.70 (m, 4H), 1.69 – 1.59 (m, 1H), 1.59 – 1.24 (m, 5H), 0.87 (s, 3H).

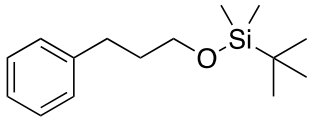
^{13}C NMR: (101 MHz, $CDCl_3$)
δ 141.6, 137.0, 132.6, 129.3, 125.5, 119.4, 119.2, 83.6 (br s), 76.6 –75.3 (multiplet overlapping with $CDCl_3$ signal, 1C), 65.3, 64.7, 49.5, 46.2, 44.2, 38.7, 34.3, 30.7, 29.3, 26.8, 25.9, 22.4, 14.4.

ATR-IR (cm^{-1}):
2978, 2939, 2875, 2587, 2249, 1735, 1620, 1590, 1179, 1044.

HRMS: (ESI$^+$) m/z: $[M + H]^+$ Calcd for $C_{22}H_{26}DO_2$ 324.2068; Found 324.2075.

Mechanistic Studies
General Procedure for Time Reaction Analysis (Table 2: Reaction Analysis)

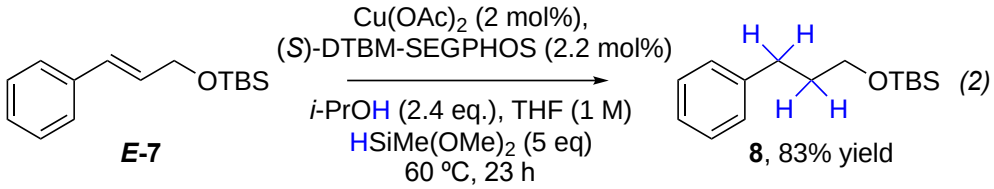
In a N_2 filled glovebox, (*R*)-DTBM-SEGPHOS (5.2 mg, 0.0044mmol, 0.022 eq.), $Cu(OAc)_2$ (20 µL of a 0.2 M solution in THF, 0.004 mmol, 0.02 eq.), and THF (0.08 mL) were added to an oven-dried 2-dram vial followed by dropwise addition of dimethoxy(methyl)silane (123 µL, 1 mmol, 5 eq.). A color change from green/blue to orange was observed while stirring for 15 minutes. In a separate oven-dried 1-dram vial was added the ((3-(phenyl)prop-2-yn-1-yl)oxy)(*tert*-butyl)dimethylsilane (49 mg, 0.2 mmol, 1 eq.), THF (0.1 mL), and 2-propanol (37 µL, 0.48 mmol, 2.4 eq.). The solution in the 1-dram vial was added dropwise over 20 seconds to the 2-dram vial. The total volume of THF was calculated based on having a final reaction concentration of 1M based on the alkyne substrate. The 2-dram vial was capped with a red pressure relief cap, taken out of the glovebox, and stirred at 60 ˚C for the designated time. The reaction mixture was then filtered through a 1" silica plug with 20 mL of Et_2O followed by 80 mL of Et_2O to elute the remaining product into a 200 mL round bottom flask. After removing the Et_2O by rotary evaporation, the crude product was isolated by flash column chromatography using gradient elution (100 mL of hexanes followed by 200 mL of 5% ethyl acetate in hexanes) to give *tert*-butyldimethyl(3-phenylpropoxy)silane as a clear, colorless oil. The spectra for the title compound matched previously reported spectra.[25]



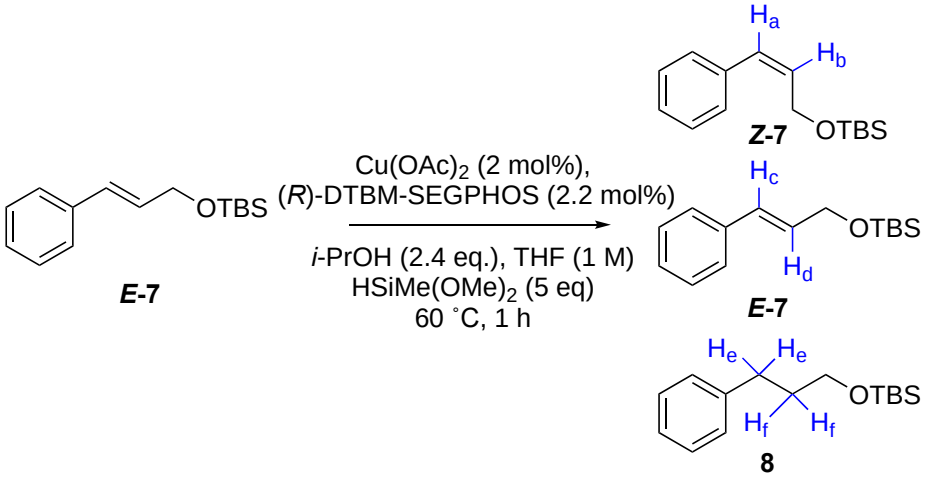
***tert*-Butyldimethyl(3-phenylpropoxy)silane (8)**

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.33 – 7.25 (m, 2H), 7.23 – 7.16 (m, 3H), 3.65 (t, *J* = 6.3 Hz, 2H), 2.69 (t, *J* = 7.9 Hz, 2H), 1.90 – 1.80 (m, 2H), 0.93 (s, 9H), 0.07 (s, 6H).

^{13}C NMR (101 MHz, CDCl3)
δ 142.4, 128.6, 128.4, 125.8, 62.5, 34.6, 32.2, 26.1, 18.5, -5.1



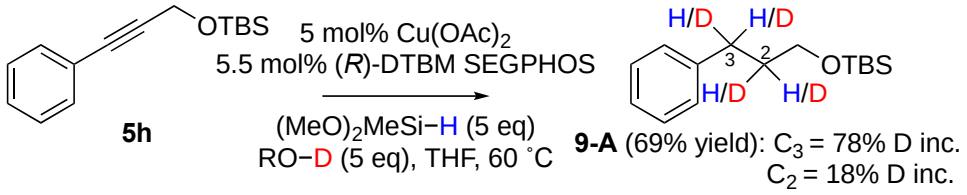
***tert*-Butyldimethyl(3-phenylpropoxy)silane (Scheme 21)**
In a N_2 filled glovebox, (*S*)-DTBM-SEGPHOS (7.8 mg, 0.0066mmol, 0.022 eq.), $Cu(OAc)_2$ (30 µL of a 0.2 M solution in THF, 0.006 mmol, 0.02 eq.), and THF (0.12 mL) were added to an oven-dried 2-dram vial followed by dropwise addition of dimethoxy(methyl)silane (185 µL, 1.5 mmol, 5 eq.). A color change from green/blue to orange was observed while stirring for 15 minutes. In a separate oven-dried 1-dram vial was added the ***E*-7** (74.5 mg, 0.3 mmol, 1 eq.), THF (0.15 mL), and 2-propanol (55 µL, 0.72 mmol, 2.4 eq.). The solution in the 1-dram vial was added dropwise over 20 seconds to the 2-dram vial. The total volume of THF was calculated based on having a final reaction concentration of 1M based on the alkyne substrate. The 2-dram vial was capped with a red pressure relief cap, taken out of the glovebox, and stirred at 60 °C for 23 h. The reaction mixture was then filtered through a 1" silica plug with 20 mL of Et_2O followed by 80 mL of Et_2O to elute the remaining product into a 200 mL round bottom flask. After removing the Et_2O by rotary evaporation, the crude product was isolated by flash column chromatography using gradient elution (100 mL of hexanes followed by 100 mL of 2% ethyl acetate in hexanes) to give *tert*-butyldimethyl(3-phenylpropoxy)silane as a clear, colorless oil (62 mg, 0.248 mmol, 83% yield). The spectra for the title compound matched previously reported spectra.[25]



***tert*-Butyldimethyl(3-phenylpropoxy)silane (Scheme 23)**
In a N_2 filled glovebox, (*S*)-DTBM-SEGPHOS (7.8 mg, 0.0066mmol, 0.022 eq.), $Cu(OAc)_2$ (30 µL of a 0.2 M solution in THF, 0.006 mmol, 0.02 eq.), and THF (0.12 mL) were added to an oven-dried 2-dram

vial followed by dropwise addition of dimethoxy(methyl)silane (185 µL, 1.5 mmol, 5 eq.). A color change from green/blue to orange was observed while stirring for 15 minutes. In a separate oven-dried 1-dram vial was added the ***E*-7** (74.5 mg, 0.3 mmol, 1 eq.), THF (0.15 mL), and 2-propanol (55 µL, 0.72 mmol, 2.4 eq.). The solution in the 1-dram vial was added dropwise over 20 seconds to the 2-dram vial. The total volume of THF was calculated based on having a final reaction concentration of 1M based on the alkyne substrate. The 2-dram vial was capped with a red pressure relief cap, taken out of the glovebox, and stirred at 60 °C for 1 h. The reaction mixture was then filtered through a 1" silica plug with 20 mL of Et_2O followed by 80 mL of Et_2O to elute the remaining product into a 200 mL round bottom flask. After removing the Et_2O by rotary evaporation, the crude product was isolated by flash column chromatography using gradient elution (100 mL of hexanes followed by 100 mL of 2% ethyl acetate in hexanes) to give *tert*-butyldimethyl(3-phenylpropoxy)silane as a clear, colorless oil (61 mg combination of all products, 42% alkane **8**, 39% ***E*-7**, trace ***Z*-7**).

Regioselective Transfer Hydrodeuteration Experiments (Scheme 24):



***Tert*-butyldimethyl(3-phenylpropoxy)silane-d_2 [9-A].**

In a N_2 filled glovebox, (*R*)-DTBM-SEGPHOS (13 mg, 0.011mmol, 0.055 eq.), $Cu(OAc)_2$ (50 µL of a 0.2 M solution in THF, 0.01 mmol, 0.05 eq.), and THF (0.05 mL) were added to an oven-dried 2-dram vial followed by dropwise addition of dimethoxy(methyl)silane (123 µL, 1 mmol, 5 eq.). A color change from green/blue to orange was observed while stirring for 15 minutes. In a separate oven-dried 1-dram vial was added the ((3-(phenyl)prop-2-yn-1-yl)oxy)(*tert*-butyl)dimethylsilane (49 mg, 0.2 mmol, 1 eq.), THF (0.10 mL), and ethanol-OD (58 µL, 1 mmol, 5 eq.). The solution in the 1-dram vial was added dropwise over 20 seconds to the 2-dram vial. The 2-dram vial was capped with a red pressure relief cap, taken out of the glovebox, and stirred at 60 °C for 24 h. The reaction mixture was then filtered through a 1" silica plug with 20 mL of Et_2O followed by 80 mL of Et_2O to elute the remaining product into a 200 mL round bottom flask. After removing the Et_2O by rotary evaporation, the crude product was isolated by flash column chromatography using gradient elution (100 mL of hexanes followed by 100 mL of 2% ethyl acetate in hexanes) to give *tert*-butyldimethyl(3-phenylpropoxy)silane-d_2 as a clear, colorless oil (34.9 mg, 0.138 mmol, 69% yield).

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

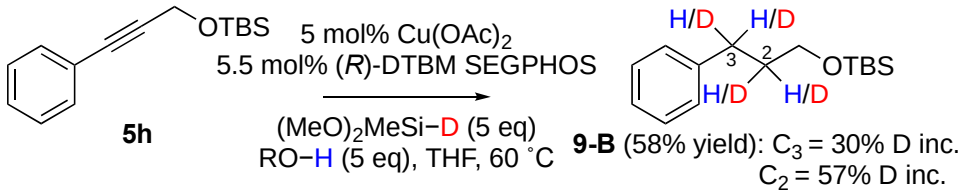
δ 7.31 – 7.26 (m, 2H), 7.21 – 7.17 (m, 3H), 3.66 – 3.63 (m, 2H), 2.69 – 2.65 (m, 0.44H), 1.87-1.82 (m, 1.65H), 0.92 (s, 9H), 0.06 (s, 6H).

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

δ 142.3, 128.6, 128.4, 125.8, 62.5, 34.5– 34.0 (m), 32.3 – 31.2 (m), 26.1, 18.5, -5.1.

ATR-IR (cm^{-1}): 3084, 3062, 3026, 2953, 2928, 2894, 2856, 2132, 1091.

HRMS: (ESI^+) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{24}D_2NaOSi$ 275.1771; Found 275.1773.



5h **9-B** (58% yield): C_3 = 30% D inc. C_2 = 57% D inc.

***Tert*-butyldimethyl(3-phenylpropoxy)silane-*d*$_2$ [9-B].**

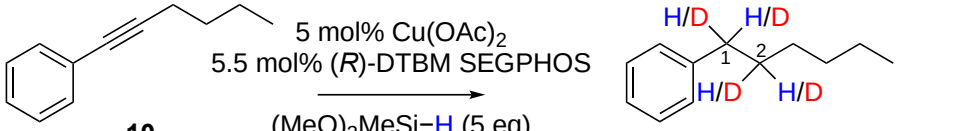
In a N_2 filled glovebox, (*R*)-DTBM-SEGPHOS (13 mg, 0.011 mmol, 0.055 eq.), $Cu(OAc)_2$ (50 µL of a 0.2 M solution in THF, 0.01 mmol, 0.05 eq.), and THF (0.05 mL) were added to an oven-dried 2-dram vial followed by dropwise addition of dimethoxy(methyl)silane-*d* (0.14 mL, 1 mmol, 7.1 M solution in hexanes, 5 eq.). A color change from green/blue to orange was observed while stirring for 15 minutes. In a separate oven-dried 1-dram vial was added the ((3-(phenyl)prop-2-yn-1-yl)oxy)(*tert*-butyl)dimethylsilane (49 mg, 0.2 mmol, 1 eq.), THF (0.1 mL), and ethanol (58 µL, 1 mmol, 5 eq.). The solution in the 1-dram vial was added dropwise over 20 seconds to the 2-dram vial. The 2-dram vial was capped with a red pressure relief cap, taken out of the glovebox, and stirred at 60 °C for 24 h. The reaction mixture was then filtered through a 1" silica plug with 20 mL of Et_2O followed by 80 mL of Et_2O to elute the remaining product into a 200 mL round bottom flask. After removing the Et_2O by rotary evaporation, the crude product was isolated by flash column chromatography using gradient elution (100 mL of hexanes followed by 100 mL of 2% ethyl acetate in hexanes) to give *tert*-butyldimethyl(3-phenylpropoxy)silane-*d*$_2$ as a clear, colorless oil (40.5 mg, 58% alkane, 23% alkene).

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

δ 7.42 – 7.14 (m, 7.2H, overlap with alkene aromatic protons), 6.61 (d, *J* = 14.1 Hz, 0.12H), 6.50 (s, 0.14H), 6.35 – 6.23 (m, 0.11H), 5.89 – 5.78 (m, 0.10H), 4.50 – 4.41 (m, 0.4H), 4.40 – 4.33 (m, 0.38H), 3.73 – 3.55 (m, 2H), 2.75 – 2.55 (m, 1.4H), 1.92 – 1.74 (m, 0.87H), 0.96 (s, 1.79H), 0.92 (s, 10.5H), 0.13 (s, 1.24H), 0.06 (s, 6.76H).

ATR-IR (cm^{-1}): 3085, 3062, 3027, 2954, 2928, 2895, 2856, 2153, 1087.

HRMS: (EI^+) *m/z*: $[M-H]^+$ Calcd for $C_{15}H_{24}D_2OSi$ 251.1830; Found 251.1795.



10 **11-A** (85% yield): C_1 = 79% D inc. C_2 = 7% D inc.

Hexylbenzene-*d*$_2$ [11-A].

In a N_2 filled glovebox, (*R*)-DTBM-SEGPHOS (13 mg, 0.011 mmol, 0.055 eq.), $Cu(OAc)_2$ (50 µL of a 0.2 M solution in THF, 0.01 mmol, 0.05 eq.), and THF (0.05 mL) were added to an oven-dried 2-dram vial followed by dropwise addition of dimethoxy(methyl)silane (123 µL, 1 mmol, 5 eq.). A color change from green/blue to orange was observed while stirring for 15 minutes. In a separate oven-dried 1-dram vial was added the 1-hexyn-1-yl-benzene (31.7 mg, 0.2 mmol, 1 eq.), THF (0.1 mL), and 2-propanol-*d*$_8$ (77 µL, 1 mmol, 5 eq.). The solution in the 1-dram vial was added dropwise over 20 seconds to the 2-dram vial. The 2-dram vial was capped with a red pressure relief cap, taken out of the glovebox, and stirred at 60 °C for 21 h. The reaction mixture was then filtered through a 1" silica plug with 20 mL of Et_2O followed by 80 mL of Et_2O to elute the remaining product into a 200 mL round bottom flask. After removing the Et_2O by rotary evaporation, the crude product was isolated by flash column chromatography using gradient elution (200 mL of hexanes) to give hexylbenzene-*d*$_2$ as a clear, colorless oil (28 mg, 0.17 mmol, 85% yield).

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

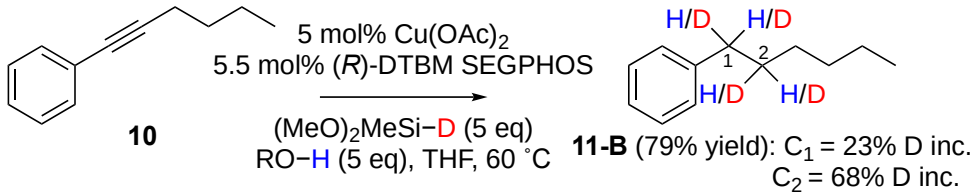
δ 7.32 – 7.24 (m, 2H), 7.22 – 7.13 (m, 3H), 2.64 – 2.55 (m, 0.42H), 1.66 – 1.54 (m, 1.94H, overlaps with H_2O), 1.40 – 1.21 (m, 6H, overlaps with grease), 0.89 (t, *J* = 6.7 Hz, 3H).

^{2}H NMR: (61 MHz, $CHCl_3$)
δ 2.59 (br s, 1.58D), 1.62 (br s, 0.13D).

^{13}C NMR (101 MHz, $CDCl_3$)
δ 143.1, 128.5, 128.4, 125.7, 36.4 – 35.3 (m), 31.9, 31.8 – 30.9 (m), 29.2, 22.8, 14.2.

ATR-IR (cm^{-1}): 3084, 3061, 3025, 2956, 2923, 2855, 2191, 1074.

HRMS: (EI^+) *m/z*: $[M]^+$ Calcd for $C_{12}H_{16}D_2$ 164.1500; Found 164.1528.



Hexylbenzene-*d*$_2$ [11-B].
In a N_2 filled glovebox, (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 0.055 eq.), $Cu(OAc)_2$ (100 µL of a 0.2 M solution in THF, 0.02 mmol, 0.05 eq.), and THF (0.15 mL) were added to an oven-dried 2-dram vial followed by dropwise addition of dimethoxy(methyl)silane-*d* (288 µL, 2 mmol, 7.1 M solution in hexanes, 5 eq). A color change from green/blue to orange was observed while stirring for 15 minutes. In a separate oven-dried 1-dram vial was added the 1-hexyn-1-yl-benzene (63 mg, 0.4 mmol, 1 eq.), THF (0.15 mL), and 2-propanol (153 µL, 2 mmol, 5 eq.). The solution in the 1-dram vial was added dropwise over 20 seconds to the 2-dram vial. The 2-dram vial was capped with a red pressure relief cap, taken out of the glovebox, and stirred at 60 °C for 21 h. The reaction mixture was then filtered through a 1" silica plug with 20 mL of Et_2O followed by 80 mL of Et_2O to elute the remaining product into a 200 mL round bottom flask. After removing the Et_2O by rotary evaporation, the crude product was isolated by flash column chromatography using gradient elution (200 mL of hexanes) to give hexylbenzene-*d*$_2$ as a clear, colorless oil (52.0 mg, 0.317 mmol, 79% yield).

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.33 – 7.27 (m, 2H), 7.24 – 7.17 (m, 3H), 2.66 – 2.58 (m, 1.54H), 1.69 – 1.56 (m, 0.76H, overlaps with H_2O), 1.42 – 1.24 (m, 6H, overlaps with grease), 0.92 (t, *J* = 6.8 Hz, 3H).

^{2}H NMR: (61 MHz, $CHCl_3$)
δ 2.61 (br s, 0.46D), 1.60 (br s, 1.34D).

^{13}C NMR (101 MHz, $CDCl_3$)
δ 143.1, 128.5, 128.4, 125.7, 36.2-35.3 (m), 31.9, 31.7 – 30.9 (m), 29.1, 22.8, 14.3.

ATR-IR (cm^{-1}): 3085, 3063, 3026, 2956, 2921, 2871, 2855, 2361, 2150, 1077.

HRMS: (EI^+) *m/z*: $[M]^+$ Calcd for $C_{12}H_{16}D_2$ 164.1500; Found 164.1528.

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Chapter 2

General Information

The following chemicals were purchased from commercial vendors and were used as received: $Cu(OAc)_2$ (99.999% from Alfa Aesar); 1,2-Bis[bis[3,5-di(*t*-butyl)phenyl]phosphino]benzene (DTB-DPPBz) (Wako Pure Chemical Industries), dimethoxy(methyl)silane (TCI); ethanol-OD (Millipore Sigma); 2-propanol-d_8 (Millipore Sigma); poly(methylhydrosiloxane) average M_n 1700-3200 (Millipore Sigma); *tert*-butyldimethylsilyl chloride (TBSCl) (Oakwood Chemical); methyltriphenylphosphonium bromide (Oakwood Chemical); Sodium hydride (in oil dispersion) 60% dispersion in mineral oil (Oakwood Chemical); sodium bis(trimethylsilyl)amide 2M in THF (Oakwood Chemical) potassium trifluoro(vinyl)borate (Oakwood Chemical); cesium carbonate (Ambeed Inc.); *n*-butyl lithium (Millipore Sigma).

Anhydrous tetrahydrofuran (THF) was purified by an MBRAUN solvent purification system (MB-SPS). Chloroform-*d* ($CDCl_3$) was stored over 3Å molecular sieves. Thin-layer chromatography (TLC) was conducted with Silicycle silica gel 60Å F254 pre-coated plates (0.25 mm) and visualized with UV and a $KMnO_4$ stain. Flash chromatography was performed using SiliaFlash® P60, 40-60 mm (230-400 mesh), purchased from Silicycle. For reactions that required heating (optimization, transfer hydrodeuteration), a PolyBlock for 2-dram vials was used on top of a Heidolph heating/stir plate.

^{1}H NMR spectra were recorded on a Varian 300 or 400 MHz spectrometer and are reported in ppm using deuterated solvent as an internal standard ($CDCl_3$ at 7.26 ppm). Data reported as: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sxt = sextet, m = multiplet, br = broad; coupling constant(s) in Hz; integration. ^{13}C NMR spectra were recorded on a Varian 76 MHz or 101 MHz spectrometer and are reported in ppm using deuterated solvent as an internal standard ($CDCl_3$ at 77.16 ppm). ^{2}H NMR spectra were recorded on a Varian 61 MHz spectrometer. ^{11}B NMR spectra were recorded on a Varian 128 MHz spectrometer.

High-resolution mass spectra were obtained for all new compounds not previously reported using the resources of the Chemistry Instrument Center (CIC), University at Buffalo, SUNY, Buffalo, NY. Specifically, high resolution accurate mass analysis was conducted using the following instruments: 12T Bruker SolariXR 12 Hybrid FTMS with Imaging MALDI and Nano-LC, provided through funding from the National Institutes of Health, NIH S10 RR029517; a Thermo Q-Exactive Focus Orbitrap Liquid Chromatograph Tandem Mass Spectrometer and a Thermo Q-Exactive Orbitrap Gas Chromatograph Tandem Mass Spectrometer, provided through funding from the National Science Foundation, MRI-1919594.

Optimization Studies (Table 3)

General procedure A for optimization studies

In a N_2 filled glovebox, ligand, Cu catalyst (Cu:L = 1:1.1), and THF were added to an oven-dried 2-dram vial followed by dropwise addition of R_3Si-H (0.60 mmol, 3 eq.). A color change from green/blue to yellow was observed while stirring for 15 minutes. In a separate oven-dried 1-dram vial was added (*E*)-1-*tert*-butyldimethylsilyloxy-3-phenyl-2-propene (50 mg, 0.20 mmol, 1eq.), THF (0.100 mL), and D-Source (0.50 mmol, 2.5 eq.). The solution in the 1-dram vial was added dropwise over 20 seconds to the 2-dram vial. The total volume of THF was calculated based on having a final reaction concentration of 1M based on the alkene substrate. The 2-dram vial was capped with a red pressure relief cap, taken out of the glovebox, and stirred for 20 h at 40°C at which point the reaction was filtered through a 1" silica plug with 100 mL of diethyl ether into a 200 mL round bottom flask. The solvent was removed by rotary evaporation, and the product was analyzed by ^{1}H NMR using 1,3,5-trimethylbenzene as an internal standard. Yields for all entries were obtained by isolating the product after flash column chromatography if greater than 5% NMR yield was observed for **2** in the crude ^{1}H NMR.

Entry 1. According to general procedure A for the optimization studies, a stirring solution of 1,2-Bis(diphenylphosphino)ethane **L1** (1.8 mg, 0.0044 mmol, 0.022 eq), $Cu(OAc)_2$ (20 µL of a 0.2 M solution in THF, 0.004 mmol, 0.02 eq.), and dimethoxy(methyl)silane (74 µL, 0.60 mmol, 3eq.) in THF (0.08 mL) was prepared, and to this was added dropwise a solution of (*E*)-1-*tert*-butyldimethylsilyloxy-3-phenyl-2-propene (50 mg, 0.20 mmol, 1 eq.) and ethanol-OD (29 µL, 0.50 mmol, 2.5 eq.) in THF (100 µL). The reaction stirred for 20 h at 40 ˚C, after which it was filtered through a silica plug with diethyl ether (20 mL) and eluted with an additional (80 mL) of diethyl ether. The solvent was removed by rotary evaporation, and the crude product was analyzed by ^{1}H NMR with 1,3,5-trimethylbenzene as an internal standard (**12**, 69% yield by ^{1}H NMR).

Entry 2. According to general procedure A for optimization studies, a stirring solution of 1,1'-Bis(diphenylphosphino)ferrocene **L2** (2.4 mg, 0.0044 mmol, 0.022 eq.), $Cu(OAc)_2$ (20 µL of a 0.2 M solution in THF, 0.004 mmol, 0.02 eq.), and dimethoxy(methyl)silane (74 µL, 0.60 mmol, 3 eq.) in THF (0.080 mL) was prepared, and to this was added dropwise a solution of (*E*)-1-*tert*-butyldimethylsilyloxy-3-phenyl-2-propene (50 mg, 0.20 mmol, 1 eq.) and ethanol-OD (29 µL, 0.50 mmol, 2.5 eq.) in THF (0.10 mL). The reaction stirred for 20 h at 40 °C, after which it was filtered through a silica plug with diethyl ether (20 mL) and eluted with an additional (80 mL) of diethyl ether. The solvent was removed by rotary evaporation, and the crude product was analyzed by ^{1}H NMR with 1,3,5-trimethylbenzene as an internal standard, (**12**, 70% yield by ^{1}H NMR).

Entry 3. According to general procedure A for the optimization studies, a stirring solution of (±)-2,2'-Bis(diphenylphosphino)-1,1'-binaphthalene **L3** (2.9 mg, 0.0044 mmol, 0.022 eq), $Cu(OAc)_2$ (20 µL of a 0.2 M solution in THF, 0.004 mmol, 0.02 eq.), and dimethoxy(methyl)silane (74 µL, 0.6 mmol, 3eq.) in THF (0.08 mL) was prepared, and to this was added dropwise a solution of (*E*)-1-*tert*-butyldimethylsilyloxy-3-phenyl-2-propene (50 mg, 0.2 mmol, 1 eq.) and ethanol-OD (29 µL, 0.5 mmol, 2.5 eq.) in THF (0.10 mL). The reaction stirred for 20 h at 40 ˚C, after which it was filtered through a silica plug with diethyl ether (20 mL) and eluted with an additional (80 mL) of diethyl ether. The solvent was removed by rotary evaporation, and the crude product was analyzed by ^{1}H NMR with 1,3,5-trimethylbenzene as an internal standard (**12**, 89% yield by ^{1}H NMR).

Entry 4. According to general procedure A for the optimization studies, a stirring solution of 1,2-Bis(diphenylphosphino)benzene **L4** (2.0 mg, 0.0044 mmol, 0.022 eq), $Cu(OAc)_2$ (20 µL of a 0.2 M solution in THF, 0.004 mmol, 0.02 eq.), and dimethoxy(methyl)silane (74 µL, 0.6 mmol, 3eq.) in THF (0.08 mL) was prepared, and to this was added dropwise a solution of (*E*)-1-*tert*-butyldimethylsilyloxy-3-

phenyl-2-propene (50 mg, 0.2 mmol, 1 eq.) and ethanol-OD (29 µL, 0.5 mmol, 2.5 eq.) in THF (0.10 mL). The reaction stirred for 20 h at 40 ˚C, after which it was filtered through a silica plug with diethyl ether (20 mL) and eluted with an additional (80 mL) of diethyl ether. The solvent was removed by rotary evaporation, and the crude product was analyzed by ^{1}H NMR with 1,3,5-trimethylbenzene as an internal standard (**12**, 47% yield by ^{1}H NMR).

Entry 5. According to general procedure A for optimization studies, a stirring solution of 1,2-Bis[bis[3,5-di(*t*-butyl)phenyl]phosphino]benzene **L5** (3.9 mg, 0.0044 mmol, 0.022 eq.), $Cu(OAc)_2$ (20 µL of a 0.2 M solution in THF, 0.004 mmol, 0.02 eq.), and dimethoxy(methyl)silane (74 µL, 0.60 mmol, 3 eq.) in THF (0.08 mL) was prepared, and to this was added dropwise a solution of (*E*)-1-*tert*-butyldimethylsilyloxy-3-phenyl-2-propene (50 mg, 0.20 mmol, 1 eq.) and ethanol-OD (29 µL, 0.50 mmol, 2.5 eq.) in THF (0.100 mL). The reaction stirred for 20 h at 40 °C, after which it was filtered through a silica plug with diethyl ether (20 mL) and eluted with an additional (80 mL) of diethyl ether. The solvent was removed by rotary evaporation, and the crude product was analyzed by ^{1}H NMR with 1,3,5-trimethylbenzene as an internal standard. The crude product was dry loaded onto silica gel, and purified by flash column chromatography using gradient elution (100 mL of 100% hexanes, 100 mL of 2% ethyl acetate in hexanes) to yield a clear colorless oil (**13**, 43 mg, 0.17 mmol, 85% yield).

Entry 6. According to general procedure A for optimization studies, a stirring solution of 1,2-Bis[bis[3,5-di(*t*-butyl)phenyl]phosphino]benzene **L5** (3.9 mg, 0.0044 mmol, 0.022 eq.), $Cu(OAc)_2$ (20 µL of a 0.2 M solution in THF, 0.004 mmol, 0.02 eq.), and dimethoxy(methyl)silane (74 µL, 0.60 mmol, 3 eq.) in THF (0.08 mL) was prepared, and to this was added dropwise a solution of (*E*)-1-*tert*-butyldimethylsilyloxy-3-phenyl-2-propene (50 mg, 0.20 mmol, 1 eq.) and methanol-OD (20 µL, 0.50 mmol, 2.5 eq.) in THF (0.10 mL). The reaction stirred for 20 h at 40 °C, after which it was filtered through a silica plug with diethyl ether (20 mL) and eluted with an additional (80 mL) of diethyl ether. The solvent was removed by rotary evaporation, and the crude product was analyzed by ^{1}H NMR with 1,3,5-trimethylbenzene as an internal standard. The crude product was dry loaded onto silica gel, and was purified by flash column chromatography using gradient elution (100 mL of 100% hexanes, 100 mL of 2% ethyl acetate in hexanes) to yield a clear colorless oil (**12** and **13** isolated as an inseparable mixture, 39 mg (**12**, 8% yield; **13**, 69% yield).

Entry 7. According to general procedure A for optimization studies, a stirring solution of 1,2-Bis[bis[3,5-di(*t*-butyl)phenyl]phosphino]benzene **L5** (3.9 mg, 0.0044 mmol, 0.022 eq.), $Cu(OAc)_2$ (20 µL of a 0.2 M solution in THF, 0.004 mmol, 0.02 eq.), and dimethoxy(methyl)silane (74 µL, 0.60 mmol, 3 eq.) in THF (0.08 mL) was prepared, and to this was added dropwise a solution of (*E*)-1-*tert*-butyldimethylsilyloxy-3-phenyl-2-propene (50 mg, 0.20 mmol, 1 eq.) and D_2O (9 µL, 0.50 mmol, 2.5 eq.) in THF (0.10 mL). The reaction stirred for 20 h at 40 °C, after which it was filtered through a silica plug with diethyl ether (20 mL) and eluted with an additional (80 mL) of diethyl ether. The solvent was removed by rotary evaporation, and the crude product was analyzed by ^{1}H NMR with 1,3,5-trimethylbenzene as an internal standard. The crude product was dry loaded onto silica gel, and was purified by flash column chromatography using gradient elution (100 mL of 100% hexanes, 100 mL of 2% ethyl acetate in hexanes) to yield a clear colorless oil (**1** and **2** isolated as an inseparable mixture, 40 mg (**12**, 59% yield; **13,** 21% yield).

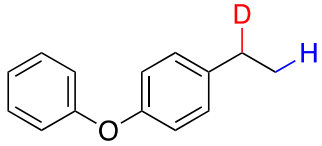
Entry 8. According to general procedure A for optimization studies, a stirring solution of 1,2-Bis[bis[3,5-di(*t*-butyl)phenyl]phosphino]benzene **L5** (3.9 mg, 0.0044 mmol, 0.011 eq.), $Cu(OAc)_2$ (20 µL of a 0.2 M solution in THF, 0.004 mmol, 0.01 eq.), and dimethoxy(methyl)silane (74 µL, 0.60 mmol, 3 eq.) in THF (0.08 mL) was prepared, and to this was added dropwise a solution of (*E*)-1-*tert*-butyldimethylsilyloxy-3-phenyl-2-propene (50 mg, 0.20 mmol, 1 eq.) and 2-propanol-d_8 (38 µL, 0.50 mmol, 2.5 eq.) in THF (0.10 mL). The reaction stirred for 20 h at 40 °C, after which it was filtered through a silica plug with diethyl

ether (20 mL) and eluted with an additional (80 mL) of diethyl ether. The solvent was removed by rotary evaporation, and the crude product was analyzed by ^{1}H NMR with 1,3,5-trimethylbenzene as an internal standard. The crude product was dry loaded onto silica gel, and was purified by flash column chromatography using gradient elution (100 mL of 100% hexanes, 100 mL of 2% ethyl acetate in hexanes) to yield a clear colorless oil (**13**, 42 mg, 0.17 mmol, 85% yield).

Entry 9. According to general procedure A for optimization studies, a stirring solution of 1,2-Bis[bis[3,5-di(*t*-butyl)phenyl]phosphino]benzene **L5** (2.0 mg, 0.0022 mmol, 0.011 eq.), $Cu(OAc)_2$ (10 µL of a 0.2 M solution in THF, 0.002 mmol, 0.01 eq.), and dimethoxy(methyl)silane (74 µL, 0.60 mmol, 3 eq.) in THF (0.09 mL) was prepared, and to this was added dropwise a solution of (*E*)-1-*tert*-butyldimethylsilyloxy-3-phenyl-2-propene (50 mg, 0.20 mmol, 1 eq.) and ethanol-OD (29 µL, 0.50 mmol, 2.5 eq.) in THF (0.10 mL). The reaction stirred for 20 h at 40 °C, after which it was filtered through a silica plug with diethyl ether (20 mL) and eluted with an additional (80 mL) of diethyl ether. The solvent was removed by rotary evaporation, and the crude product was analyzed by ^{1}H NMR with 1,3,5-trimethylbenzene as an internal standard. The crude product was dry loaded onto silica gel, and purified by flash column chromatography using gradient elution (100 mL of 100% hexanes, 100 mL of 2% ethyl acetate in hexanes) to yield a clear colorless oil (**13**, 46 mg, 0.18 mmol, 90% yield).

Transfer Hydrodeuteration of Aryl Alkenes Substrate Scope (Scheme 28, Green Boxes; my contributions)

General procedure for Transfer Hydrodeuteration (K)
In a N_2 filled glovebox, DTB-DPPBz (3.0 mg, 0.0033 mmol, 0.011eq.), $Cu(OAc)_2$ (15 µL of a 0.2 M solution in THF, 0.003 mmol, 0.01 eq.), and THF (0.135 mL) were added to an oven-dried 2-dram vial followed by dropwise addition of dimethoxy(methyl)silane (111 µL, 0.90 mmol, 3 eq.) or poly(methylhydrosiloxane) (60 µL, 0.90 mmol, 3 eq based on Si-H). A color change from green/blue to yellow was observed while stirring for 15 minutes. In a separate oven-dried 1-dram vial was added the alkene substrate (0.30 mmol, 1 eq.), THF (0.150 mL), and ethanol-OD/2-propanol-d_8 (2.5 eq based on substrate). The solution in the 1-dram vial was added dropwise over 20 seconds to the 2-dram vial. The total volume of THF was calculated based on having a final reaction concentration of 1M based on the alkene substrate. The 2-dram vial was capped with a red pressure relief cap, taken out of the glovebox, and stirred for 9-24 h at the appropriate temperature at which point the reaction was filtered through a 1" silica plug with 20 mL of diethyl ether followed by 80 mL of diethyl ether to elute the remaining product into a 200 mL round bottom flask. After removing the diethyl ether by rotary evaporation, the crude product was isolated by flash column chromatography.



1-(ethyl-1-*d*)-4-phenoxybenzene [15a]. According to the general procedure K, DTB-DPPBz (3.0 mg, 0.0033 mmol, 0.011eq.), $Cu(OAc)_2$ (15 µL of a 0.2 M solution in THF, 0.003 mmol, 0.01 eq.), and THF (0.135 mL) then dimethoxy(methyl)silane (111 µL, 0.90 mmol, 3 eq.) were combined in a 2-dram vial followed by addition of a solution of 1-Ethenyl-4-phenoxybenzene (59 mg, 0.30 mmol, 1 eq.), THF (0.150 mL), and ethanol-OD (44 µL, 0.75 mmol, 2.5 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 18 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Flash column chromatography (300 mL of 100% hexanes) to give the pure product as a clear colorless oil (57 mg, 0.29 mmol, 97% yield).

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

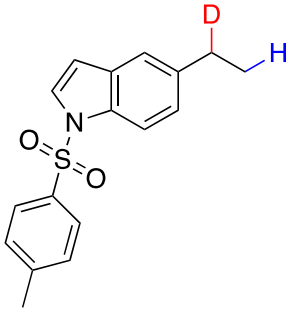
δ 7.34 (t, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.4 Hz, 2H), 7.09 (t, *J* = 7.3 Hz, 1H), 7.02 (d, *J* = 8.2 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 2H), 2.70 – 2.59 (m, 1.02 H), 1.26 (d, *J* = 7.5 Hz, 3H).

^{2}H NMR: (61 MHz, $CHCl_3$):
δ 2.64 (s, 0.98D), 1.26 (s, 0.01D).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 157.89, 155.02, 139.40, 129.78, 129.16, 122.95, 119.21, 118.56, 27.95 (t, *J* = 19.5 Hz), 15.81.

ATR-IR (cm^{-1}):
3030, 2962, 2927, 2873, 2136, 1230, 1165.

HRMS: (EI^+) *m/z*: $[M]^+$ Calcd for $C_{14}H_{13}DO$ 199.1107; Found 199.1100.



5-(ethyl-1-*d*)-*N*-tosylindole [15j]. According to the general procedure K, DTB-DPPBz (3.0 mg, 0.0033 mmol, 0.011eq.), $Cu(OAc)_2$ (15 µL of a 0.2 M solution in THF, 0.003 mmol, 0.01 eq.), and THF (0.135 mL), then dimethoxy(methyl)silane (111 µL, 0.90 mmol, 3 eq) were combined in a 2-dram vial followed by addition of a solution of 5-vinyl-*N*-tosylindole (89 mg, 0.3 mmol, 1 eq.), THF (0.150 mL), and ethanol-OD (44 µL, 0.75 mmol, 2.5 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 23 h at 40 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and the crude oil was dry loaded onto a silica gel column. Flash column chromatography using gradient elution (100 mL 100% hexanes, 100 mL 3% ethyl acetate in hexanes, and 100 mL 6% ethyl acetate in hexanes) to give the pure product as a purple oil (66 mg, 0.22 mmol, 73% yield).

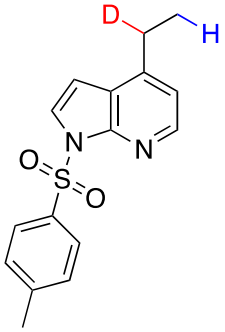
^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.91 (d, *J* = 8.5 Hz, 1H), 7.77 (d, *J* = 8.2 Hz, 2H), 7.53 (d, *J* = 3.7 Hz, 1H), 7.34 (d, *J* = 1.8 Hz, 1H), 7.23 – 7.14 (m, 3H), 6.60 (d, *J* = 3.6 Hz, 1H), 2.75 – 2.63 (m, 1.02H), 2.32 (s, 3H), 1.24 (d, *J* = 7.6 Hz, 3H).

^{2}H NMR: (61 MHz, $CHCl_3$)
δ 2.70 (s, 0.98D).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 144.89, 139.47, 135.47, 133.31, 131.10, 129.93, 126.89, 126.48, 125.07, 120.10, 113.39, 109.06, 28.47 (t, *J* = 19.5 Hz), 21.63, 16.02.

ATR-IR (cm^{-1}):
3142, 3113, 2963, 2929, 2873, 2360, 1590, 1366, 1170

HRMS: (EI^+) m/z: $[M]^+$ Calcd for $C_{17}H_{16}DNO_2S$ 300.1000; Found 300.1035.



4-(ethyl-1-*d*)-1-tosyl-1*H*-pyrrolo[2,3-*b*]pyridine [15k]. According to the general procedure K, DTB-DPPBz (3.0 mg, 0.0033 mmol, 0.011eq.), $Cu(OAc)_2$ (15 µL of a 0.2 M solution in THF, 0.003 mmol, 0.01 eq.), and THF (0.135 mL), then dimethoxy(methyl)silane (111 µL, 0.90 mmol, 3 eq) were combined in a 2-dram vial followed by addition of a solution of 1-tosyl-4-vinyl-1*H*-pyrrolo[2,3-*b*]pyridine (90 mg, 0.30 mmol, 1 eq.), THF (0.150 mL), and ethanol-OD (44 µL, 0.75 mmol, 2.5 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 23 h at 40 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and the crude oil was dry loaded onto a silica gel column. Flash column chromatography using gradient elution (50 mL 100% hexanes, 100 mL 10% ethyl acetate in hexanes, and 100 mL 15% ethyl acetate in hexanes) to give the pure product as a yellow solid (63 mg, 0.21 mmol, 70% yield).

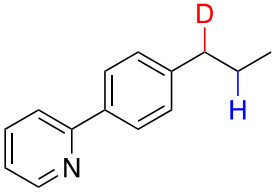
^{1}H NMR: (400 MHz, $CDCl_3$)
δ 8.33 (d, *J* = 5.0 Hz, 1H), 8.06 (d, *J* = 8.5 Hz, 2H), 7.68 (d, *J* = 4.1 Hz, 1H), 7.24 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 5.1 Hz, 1H), 6.61 (d, *J* = 4.1 Hz, 1H), 2.86 – 2.74 (m, 1.02H), 2.34 (s, 3H), 1.26 (d, *J* = 7.5 Hz, 3H).

^{2}H NMR: (61 MHz, $CHCl_3$)
δ 2.82 (s, 0.98D).

^{13}C NMR: (75 MHz, $CDCl_3$)
δ 147.28, 146.73, 145.25, 145.10, 135.63, 129.68, 128.08, 125.60, 122.21, 117.88, 103.66, 25.44 (t, *J* = 19.6 Hz), 21.70, 13.97.

ATR-IR (cm^{-1}):
3151, 3117, 2964, 2929, 2879, 2323, 1592, 1367, 1145.

HRMS: (ESI^+) m/z: $[M+H]^+$ Calcd for $C_{16}H_{16}DN_2O_2S$ 302.1080; Found 302.1065.



2-(4-(propyl-1-*d*)phenyl)pyridine [15p]. According to the general procedure K, DTB-DPPBz (3.0 mg, 0.0033 mmol, 0.011 eq.), $Cu(OAc)_2$ (15 µL of a 0.2 M solution in THF, 0.003 mmol, 0.01 eq.), and THF (0.135 mL) then dimethoxy(methyl)silane (111 µL, 0.90 mmol, 3 eq.) were combined in a 2-dram vial followed by addition of a solution of (*E*/*Z*)-2-(4-(prop-1-en-1- yl)phenyl)pyridine (59 mg, 0.30 mmol, 1 eq.), THF (0.150 mL), and ethanol-OD (44 µL, 0.75 mmol, 2.5 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 22 h at 40 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and the crude oil was dry loaded onto a silica gel column. Flash column chromatography using gradient elution (100 mL of 100% HPLC hexanes, 300 mL

3% ethyl acetate in HPLC hexanes, and 100 mL 5% ethyl acetate in HPLC hexanes) to give the pure product as a yellow oil (45 mg, 0.23 mmol, 77% yield).

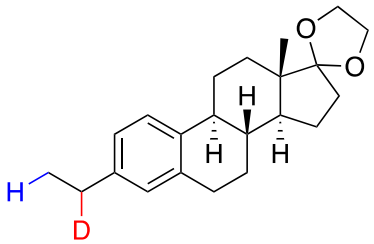
^{1}H NMR: (400 MHz, $CDCl_3$)
δ 8.68 (d, *J* = 4.1 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 2H), 7.77 – 7.68 (m, 2H), 7.29 (d, *J* = 7.8 Hz, 2H), 7.24 – 7.16 (m, 1H), 2.68 – 2.58 (m, 1.02H), 1.68 (p, *J* = 7.4 Hz, 2H), 0.97 (t, *J* = 7.4 Hz, 3H).

^{2}H NMR: (61 MHz, $CHCl_3$)
δ 2.63 (s, 0.98D).

^{13}C NMR: (75 MHz, $CDCl_3$)
δ 157.65, 149.72, 143.82, 137.00, 136.75, 129.01, 126.88, 121.88, 120.38, 37.90 (s, peak represents dihydrogen at the benzylic carbon), 37.52 (t, *J* = 19.3 Hz), 24.51, 13.90.

ATR-IR (cm^{-1}):
3050, 3008, 2958, 2928, 2870, 2359, 1296.

HRMS: (ESI^+) m/z: $[M+H]^+$ Calcd for $C_{14}H_{15}DN$ 199.1380; Found 199.1338.



(8*R*,9*S*,13*S*,14*S*)-3-(ethyl-1-*d*)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydrospiro[cyclopenta[*a*]phenanthrene-17,2'-[1,3]dioxolane] [15q]. Following the general procedure K, in a N_2 filled glovebox, DTB-DPPBz (6.0 mg, 0.0066 mmol, 0.022 eq.), $Cu(OAc)_2$ (30 µL of a 0.2 M solution in THF, 0.006 mmol, 0.02 eq.), and THF (0.120 mL) then dimethoxy(methyl)silane (111 µL, 0.90 mmol, 3 eq.) were combined in a 2-dram vial followed by addition of a solution of 8*R*,9*S*,13*S*,14*S*)-13-methyl-3- vinyl-6,7,8,9,11,12,13,14,15,16- decahydrospiro[cyclopenta[*a*]phenanthrene -17,2'-[1,3]dioxolane] (97 mg, 0.30 mmol, 1 eq.), THF (0.150 mL), and ethanol-OD (44 µL, 0.75 mmol, 2.5 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 26 h at 40 °C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and the crude oil was dry loaded onto a silica gel column. Flash column chromatography using gradient elution (100 mL 100% HPLC hexanes, 100 mL 5% ethyl acetate in HPLC hexanes, and 100 mL 9% ethyl acetate in HPLC hexanes) to give the pure product as a viscous yellow oil (72 mg, 0.22 mmol, 73% yield).

^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.25 (d, *J* = 8.5 Hz, 1H), 7.02 (d, *J* = 8.0 Hz, 1H), 6.95 (s, 1H), 4.04 – 3.86 (m, 4H), 2.97 – 2.81 (m, 2H), 2.65 – 2.54 (m, 1.06H), 2.41 – 2.24 (m, 2H), 2.11 – 2.01 (m, 1H), 1.98 – 1.74 (m, 4H), 1.73 – 1.61 (m, 1H), 1.61 – 1.33 (m, 5H), 1.24 (d, *J* = 7.6 Hz, 3H), 0.90 (s, 3H).

^{2}H NMR: (61 MHz, $CHCl_3$)
δ 2.60 (s, 0.94D), 1.25 (s, 0.02D).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 141.51, 137.77, 136.72, 128.59, 125.46, 125.28, 119.56, 65.38, 64.71, 49.58, 46.28, 44.09, 39.06, 34.35, 30.89, 29.70, 28.08 (t, *J* = 19.6 Hz), 27.16, 26.09, 22.49, 15.69, 14.45.

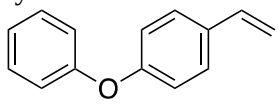
ATR-IR (cm^{-1}):
2933, 2872, 1739, 1614, 1104, 1044.

HRMS: (EI^+) *m/z*: $[M]^+$ Calcd for $C_{22}H_{29}DO_2$ 327.2309; Found 327.2303.

Synthesis of Alkene Starting Materials

General Wittig procedure (L)
Adapted from a previously reported procedure[1], to a flame-dried round bottom flask under N_2 atmosphere containing a Teflon stirbar was added dry THF (15 mL, 0.25M) and alkyltriphenylphosphonium bromide (4.03 mmol, 1.1 eq.). The round bottom flask was cooled to 0 ˚C and sodium hydride or sodium bis(trimethylsilyl)amide 2M in THF (4.03 mmol, 1.1 eq) was added slowly. The mixture stirred for 15 minutes at 0 ˚C. The aldehyde substrate (3.67 mmol, 1 eq.) was added in portions and the reaction stirred at room temperature for 18 hr. Upon completion, the reaction was placed in an ice bath, and quenched with water (20 mL) and extracted with ether (3 x 15 mL). The combined organic layers were washed with brine (20 mL) and then dried over anhydrous Na_2SO_4. The mixture was filtered, and the solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography to give the desired vinyl arene product.

General Suzuki-Miyaura Coupling procedure (M):
Adapted from a previously reported procedure[2], to a flame-dried round bottom flask was added a Teflon stir bar, THF/H_2O (7 mL, 9:1) and the solution was degassed for 15 minutes using N_2. In an oven-dried 25 mL pressure vessel under N_2 was added potassium trifluoro(vinyl)borate (477 mg, 3.56 mmol, 1 eq.), cesium carbonate (1.74g, 5.34 mmol, 1.5 eq.), $PdCl_2(PPh_3)_2$ (50 mg, 0.071 mmol, 0.02 eq.), and the halogen substrate (3.56 mmol, 1 eq.). The THF/H_2O solution was added to the 25 mL pressure vessel and kept under a nitrogen atmosphere while the reaction was stirred in an oil bath at 85 ˚C for 16-18 hr. Upon completion, the reaction mixture was cooled to room temperature, quenched with H_2O, and extracted with dichloromethane (3 x 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4. The mixture was filtered, and the solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography to give the desired vinyl arene product.



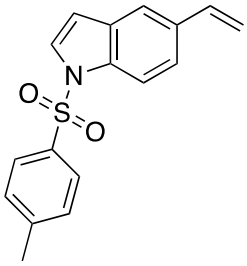
1-ethenyl-4-phenoxybenzene [14a]. 14a was prepared according to general procedure L, using dry THF (5 mL), methyltriphenylphosphonium bromide (1.01 g, 2.83mmol, 1.12 eq.), sodium bis(trimethylsilyl)amide 2M in THF (1.41 mL, 2.82 mmol, 1.12 eq.) and 4-Phenoxybenzaldehyde (500 mg, 2.52 mmol, 1 eq.). The crude product was purified by flash column chromatography (400 mL of 100% hexanes) to obtain the product as a clear colorless oil (483 mg, 2.46 mmol, 98% yield).

^{1}H NMR: (300 MHz, $CDCl_3$)
δ 7.53 – 7.37 (m, 4H), 7.20 (t, *J* = 7.1 Hz, 1H), 7.15-7.04 (m, 4H), 6.79 (dd, *J* = 17.6 Hz, 1H), 5.77 (d, *J* = 17.5 Hz, 1H), 5.29 (d, *J* = 10.9 Hz, 1H).

^{13}C NMR: (75 MHz, $CDCl_3$)
δ 157.20, 157.05, 136.10, 132.89, 129.85, 127.68, 123.42, 119.00, 118.93, 112.93.

ATR-IR (cm^{-1}):
3064, 3040, 3008, 2981, 1230, 1165.

HRMS: (EI^+) *m/z*: $[M]^+$ Calcd for $C_{14}H_{12}O$ 196.0888; Found 196.0881.



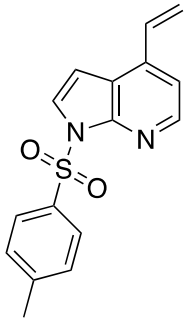
5-Vinyl-*N*-tosylindole [14j]. 14j was prepared following general procedure M, using THF/H_2O (9:1) (7 mL) solution, potassium trifluoro(vinyl)borate (477 mg, 3.56 mmol, 1 eq.), cesium carbonate (1.740g, 5.34 mmol, 1.5 eq.), the 5-bromo-1-tosylindole (1.25 g, 3.56 mmol, 1 eq.), and $PdCl_2(PPh_3)_2$ (50 mg, 0.071 mmol, 0.02 eq.). The crude product was purified by flash column chromatography using gradient elution (100 mL 100% hexanes, 200 mL 5% ethyl acetate in hexanes, and 200 mL 10% ethyl acetate in hexanes) to provide the title compound as a yellow solid (518 mg, 1.74 mmol, 49% yield).

^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.93 (d, *J* = 8.6 Hz, 1H), 7.75 (d, *J* = 8.2 Hz, 2H), 7.55 – 7.49 (m, 2H), 7.40 (d, *J* = 8.6 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 2H), 6.76 (dd, *J* = 17.6, 10.9 Hz, 1H), 6.63 (d, *J* = 3.6 Hz, 1H), 5.73 (d, *J* = 17.5 Hz, 1H), 5.21 (d, *J* = 10.9 Hz, 1H), 2.33 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 145.11, 136.86, 135.33, 134.60, 133.26, 131.22, 130.01, 127.00, 126.91, 122.92, 119.38, 113.68, 113.32, 109.35, 21.69.

ATR-IR (cm^{-1}):
3141, 3118, 2980, 2920, 2851, 1594, 1367, 1169.

HRMS: (EI^+) *m/z*: $[M]^+$ Calcd for $C_{17}H_{15}NO_2S$ 297.0823; Found 297.0816.



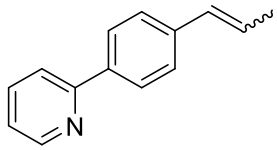
1-tosyl-4-vinyl-1*H*-pyrrolo[2,3-*b*]pyridine [14k]. 14k was prepared following general procedure M, using THF/H_2O (9:1) (5 mL) solution, potassium trifluoro(vinyl)borate (336 mg, 2.51 mmol, 1 eq.), cesium carbonate (1.23 g, 3.77 mmol, 1.5 eq.), 4-bromo-1-tosyl-1*H*-pyrrolo[2,3-*b*]pyridine (882 mg, 2.51 mmol, 1 eq.), and $PdCl_2(PPh_3)_2$ (35 mg, 0.050 mmol, 0.02 eq.). The crude product was purified by flash column chromatography using gradient elution (100 mL 100% hexanes, 200 mL 2% ethyl acetate in hexanes, 200 mL 4% ethyl acetate in hexanes, 200 mL 6% ethyl acetate in hexanes, and 200 mL 8% ethyl acetate in hexanes) to provide the title product as a yellow solid (406 mg, 1.36 mmol, 54% yield).

^{1}H NMR: (400 MHz, $CDCl_3$)
δ 8.38 (d, *J* = 5.1 Hz, 1H), 8.06 (d, *J* = 8.3 Hz, 2H), 7.74 (d, *J* = 4.1 Hz, 1H), 7.26 (d, *J* = 8.1 Hz, 2H), 7.22 (d, *J* = 5.1 Hz, 1H), 6.93 (dd, *J* = 17.7, 11.0 Hz, 1H), 6.75 (d, *J* = 4.1 Hz, 1H), 6.02 (d, *J* = 17.6, 0.9 Hz, 1H), 5.59 (dd, *J* = 11.1, 0.8 Hz, 1H), 2.36 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 147.99, 145.23, 145.00, 138.58, 135.39, 132.33, 129.67, 128.05, 126.44, 120.70, 120.23, 114.96, 103.74, 21.66.

ATR-IR (cm^{-1}):
3152, 3115, 2975, 2924, 1590, 1364, 1149

HRMS: (ESI^+) m/z: $[M+H]^+$ Calcd for $C_{16}H_{15}N_2O_2S$ 299.0880; Found 299.0848.



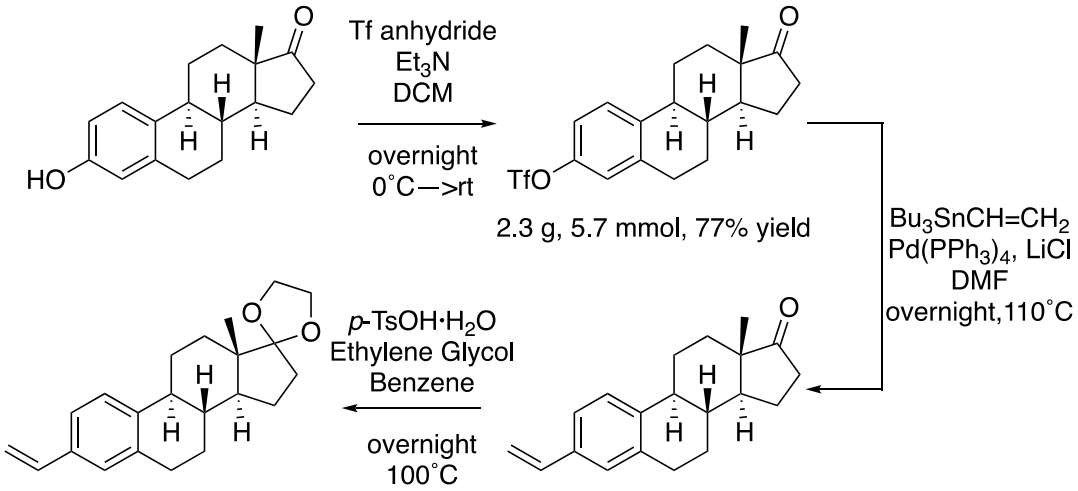
(*E*/*Z*)-2-(4-(prop-1-en-1- yl)phenyl)pyridine [14p]. 14p was prepared according to general procedure L, using dry THF (30 mL), ethyltriphenylphosphonium bromide (4.56 g, 12.3 mmol, 1.5 eq.), *n*-butyl lithium (10.4 mL calculated based off 1.18 M solution, 12.3 mmol, 1.5 eq.) and 4-Pyridin-2-yl-benzaldehyde (1.5 g, 8.19 mmol, 1 eq.) The crude product was purified by flash chromatography using gradient elution (100 mL of 100% hexanes, 200 mL of 5% ethyl acetate in hexanes, 200 mL of 7.5% ethyl acetate in hexanes, and 200 mL of 10% ethyl acetate in hexanes) to yield the pure product as a yellow solid which is a mixture of *E*/*Z* isomers (74 mg, 3.8 mmol, 46% yield).

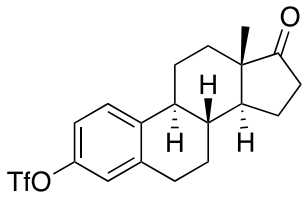
^{1}H NMR: (400 MHz, $CDCl_3$) mixture of *E*/*Z* isomers
δ 8.72-8.66 (m, 0.96H), 8.06 – 7.96 (m, 0.46H), 7.96 – 7.92 (m, 1.54H), 7.77 – 7.69 (m, 2.15H), 7.48 – 7.39 (m, 2.11H), 7.24 – 7.17 (m, 1.08H), 6.51 – 6.40 (m, 1H), 6.33 (dq, *J* = 15.8, 6.5 Hz, 0.8H), 5.85 (dq, *J* = 11.6, 7.2 Hz, 0.2H), 1.95 (dd, *J* = 7.2, 1.8 Hz, 0.62H), 1.91 (dd, *J* = 6.5, 1.5 Hz, 2.4H).

^{13}C NMR: (101 MHz, $CDCl_3$) mixture of *E*/*Z* isomers
δ 157.26, 157.23, 149.79, 149.75, 138.69, 138.44, 137.75, 137.46, 136.84, 136.81, 130.70, 129.54, 129.36, 127.68, 127.09, 126.72, 126.70, 126.30, 122.10, 122.02, 120.49, 120.37, 18.75, 14.94.

ATR-IR (cm^{-1}):
3050, 3004, 2929, 2909, 2851, 1265.

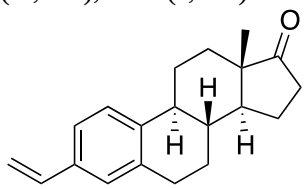
HRMS: (ESI^+) m/z: $[M+H]^+$ Calcd for $C_{14}H_{14}N$ 196.108; Found 196.1120.





3-(Trifluoromethanesulfonyl)estrone was synthesized following a previously reported procedure[3], using estrone (2.0 g, 7.4 mmol, 1 eq.), Et_3N (2.05 mL, 14.8 mmol, 2 eq.), dichloromethane (37 mL, 0.2 M solution), and triflic anhydride (1.37 mL, 8.14 mmol, 1.1 eq.). The crude product was purified by flash column chromatography using gradient elution (100 mL of 100% hexanes, 100 mL of 5% ethyl acetate in hexanes, 100 mL of 10% ethyl acetate in hexanes, and 300 mL 1of 5% ethyl acetate in hexanes) to yield a white solid (2.3 g, 5.7 mmol, 77% yield). The NMR data were consistent with previously reported spectra.[3]

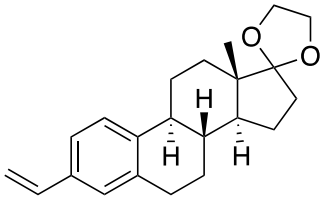
^{1}H NMR: (300 MHz, $CDCl_3$)
δ 7.34 (d, *J* = 8.6 Hz, 1H), 7.04 (dd, *J* = 8.6, 2.9 Hz, 1H), 6.99 (d, *J* = 2.8 Hz, 1H), 3.02 – 2.87 (m, 2H), 2.52 (dd, *J* = 18.3, 8.5 Hz, 1H), 2.45 – 2.36 (m, 1H), 2.36 – 2.23 (m, 1H), 2.23 – 1.92 (m, 4H), 1.78 – 1.37 (m, 6H), 0.92 (s, 3H).



3-Vinyl-estrone was synthesized following a previously reported procedure,[4] using 3-(Trifluoromethanesulfonyl)estrone (600 mg, 1.49 mmol, 1 eq.), vinyltributylstannane (436 µL, 1.49 mmol, 1 eq.), $Pd(PPh_3)_4$ (35 mg, 0.03 mmol, 0.02 eq), LiCl (316 mg, 7.45 mmol, 5 eq.), and DMF (23 mL, 0.067M solution). The crude product was purified by flash column chromatography using gradient elution (500 mL of 100% hexanes, 200 mL of 5% ethyl acetate in hexanes, and 300 mL of 8% ethyl acetate in hexanes) to yield 313 mg of a white solid containing an alkyl tin byproduct impurity. The NMR data was consistent with previously reported spectra.[4] The impurity was carried through to the next reaction step and removed after isolation of **21q**.

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

δ 7.27 (d, *J* = 8.1 Hz, 1H), 7.23 (d, *J* = 8.3 Hz, 1H), 7.16 (s, 1H), 6.68 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.72 (d, *J* = 17.6 Hz, 1H), 5.21 (d, *J* = 10.8 Hz, 1H), 2.97 – 2.89 (m, 2H), 2.52 (dd, J = 18.8, 9.0 Hz, 1H), 2.47 – 2.39 (m, 1H), 2.35 – 2.25 (m, 1H), 2.22 – 1.94 (m, 4H), 1.80 – 1.22 (m, 9H, includes an alkyl impurity likely form an inseparable tin byproduct), 0.93 (s, 3H).



(8*R*,9*S*,13*S*,14*S*)-13-methyl-3-vinyl-6,7,8,9,11,12,13,14,15,16-decahydrospiro[cyclopenta[*a*]phenanthrene -17,2'-[1,3]dioxolane] [14q]. To a flame-dried 25 mL round bottom flask equipped with a Teflon stir bar, was added *p*-TsOH •H_2O (19 mg, 0.102 mmol, 0.091 eq.), 3-vinyl-estrone (313 mg, 1.12 mmol, 1 eq.), ethylene glycol (1.3 mL, 22.4 mmol, 20 eq.), and benzene (8 mL, 0.144 M solution). A Dean Stark trap fitted with a condenser was connected to the 25 mL round bottom flask was heated to 100 ˚C and stirred open to air until deemed complete by TLC analysis. Upon reaction completion, the reaction was poured into 20 mL of water and extracted with dichloromethane (3 x 10 mL). The combined organic layers were washed with brine (3 x 10 mL) and dried over anhydrous Na_2SO_4. The reaction was dry loaded onto silica gel and purified by flash column chromatography using gradient elution (800 mL of 100% hexanes, 200 mL of 5% ethyl acetate in hexanes, 300 mL of 8% ethyl acetate in hexanes) to provide the title product as a yellow oil (287 mg, 0.885 mmol, 59% yield over 2 steps).

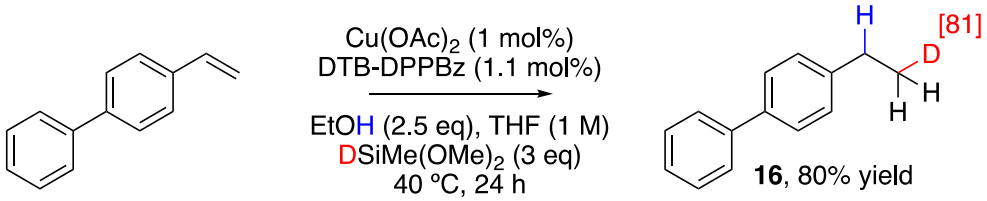
^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.26 (d, 1H), 7.20 (d, *J* = 8.1, 1.9 Hz, 1H), 7.13 (s, 1H), 6.67 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.70 (d, *J* = 17.6 Hz, 1H), 5.18 (d, *J* = 10.8 Hz, 1H), 4.01 – 3.85 (m, 4H), 2.91 – 2.83 (m, 2H), 2.41 – 2.23 (m, 2H), 2.09 – 1.98 (m, 1H), 1.95 – 1.72 (m, 4H), 1.71 – 1.60 (m, 1H), 1.60 – 1.28 (m, 5H), 0.89 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 140.39, 136.99, 136.80, 135.07, 126.97, 125.69, 123.55, 119.54, 113.09, 65.41, 64.73, 49.58, 46.26, 44.26, 38.96, 34.36, 30.86, 29.66, 27.07, 26.07, 22.50, 14.46.

ATR-IR (cm^{-1}):
3083, 2971, 2936, 2870, 1740, 1630, 1103, 1044.

HRMS: (EI^+) *m/z:* $[M]^+$ Calcd for $C_{22}H_{28}O_2$ 324.2089; Found 324.2082.

Reaction Studies (Scheme 29)



4-(ethyl-2-*d*)-biphenyl [16]. According to the general procedure B, DTB-DPPBz (2.0 mg, 0.0022 mmol, 0.011 eq.), $Cu(OAc)_2$ (10 µL of a 0.2 M solution in THF, 0.002 mmol, 0.01 eq.), THF (0.09 mL), then dimethoxy(methyl)silane-*d* (113 µL of a 5.29 M solution in hexanes, 0.60 mmol, 3 eq.) were combined in a 2-dram vial followed by addition of a solution of 4-Vinylbiphenyl (36 mg, 0.20 mmol, 1 eq.), THF

(0.10 mL), ethanol (29 µL, 0.50 mmol, 2.5 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 40°C. After silica plug filtration using diethyl ether (100 mL) as the eluent, the solvent was concentrated, and the crude oil was dry loaded onto a silica gel column. Flash column chromatography (150 mL of 100% HPLC hexanes) gave the pure product as a white crystalline solid (30 mg, 0.16 mmol, 80% yield).

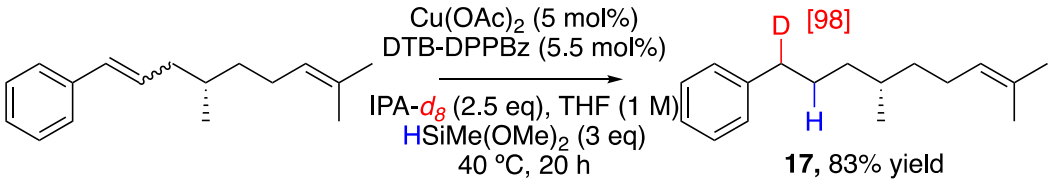
^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.62 (d, *J* = 7.6 Hz, 2H), 7.55 (d, *J* = 7.8 Hz, 2H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.31 (d, *J* = 7.8 Hz, 2H), 2.72 (t, *J* = 7.6 Hz, 2H), 1.34 – 1.25 (m, 2.19H).

^{2}H NMR: (61 MHz, $CHCl_3$)
δ 1.29 (s, 0.81 D)

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 143.52, 141.32, 138.73, 128.84, 128.42, 127.21, 127.15, 127.10, 28.57, 15.45 (t, *J* = 19.5 Hz).

ATR-IR (cm^{-1}):
3054, 3029, 2930, 2850, 2176.

HRMS: (EI^+) *m/z*: $[M]^+$ Calcd for $C_{14}H_{13}D$ 183.1158; Found 183.1151.



(*S*)-(4,8-dimethylnon-7-en-1-yl-1-*d*)benzene [17]. According to the general procedure B, DTB-DPPBz (14.8 mg, 0.0165 mmol, 0.055 eq.), $Cu(OAc)_2$ (75 µL of a 0.2 M solution in THF, 0.015 mmol, 0.05 eq.), THF (0.075 mL), then dimethoxy(methyl)silane (111 µL, 0.90 mmol, 3 eq) were combined in a 2-dram vial followed by addition of a solution of (*E/Z*)-(*S*)-(4,8-dimethylnona-1,7-dien-1-yl)benzene (68 mg, 0.30 mmol, 1 eq.), THF (0.150 mL), 2-propanol-d_8 (57 µL, 0.75 mmol, 2.5 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Flash column chromatography (100 mL of 100% HPLC hexanes) gave the pure product as a clear colorless oil (57 mg, 0.25 mmol, 83% yield).

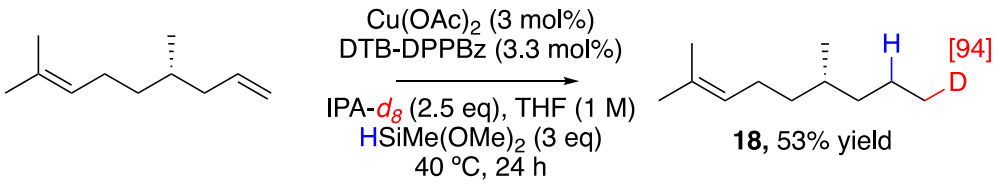
^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.34 – 7.28 (m, 2H), 7.24 – 7.18 (m, 3H), 5.14 (t, J = 7.1 Hz, 1H), 2.66 – 2.55 (m, 1H), 2.10 – 1.91 (m, 2H), 1.73 (s, 3H), 1.64 (s, 3H), 1.70 – 1.57 (m, 2H) 1.54 – 1.43 (m, 1H), 1.43 – 1.32 (m, 2H), 1.27 – 1.14 (m, 2H), 0.91 (d, *J* = 6.6 Hz, 3H).

^{2}H NMR (61 MHz, $CDCl_3$)
δ 2.60 (s, 0.99D).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 143.04, 131.15, 128.52, 128.37, 125.71, 125.15, 37.20, 36.77, 36.09 (t, *J* = 19.6 Hz), 32.45, 29.09, 25.87, 25.70, 19.70, 17.77.

ATR-IR (cm^{-1}): 3084, 2962, 2923, 2855, 2151, 1800, 1604, 740.

HRMS: (EI$^+$) *m/z*: [M]$^+$ Calcd for $C_{17}H_{25}D$, 231.2100; Found 231.2091.



(-)-2,6-Dimethyl-2-nonene [12]. According to the general procedure B, DTB-DPPBz (11.6 mg, 0.013 mmol, 0.033 eq.), $Cu(OAc)_2$ (60 µL of a 0.2 M solution in THF, 0.012 mmol, 0.03 eq.), THF (0.140 mL), then dimethoxy(methyl)silane (148 µL, 1.2 mmol, 3 eq) were combined in a 2-dram vial followed by addition of a solution of (*S*)-4,8-Dimethylnona-1,7-diene (61 mg, 0.40 mmol, 1 eq.), THF (0.200 mL), 2-propanol-d_8 (57 µL, 1.0 mmol, 2.5 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Flash column chromatography (200 mL of 100% HPLC hexanes) gave the pure product as a clear colorless oil (32 mg, 0.21 mmol, 53% yield).

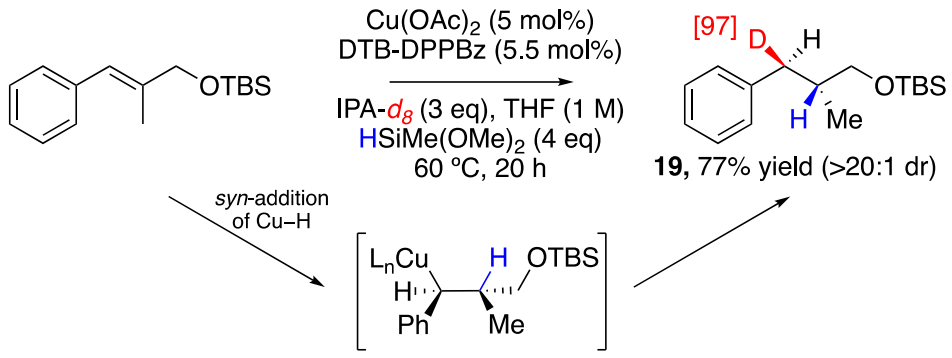
^{1}H NMR (400 MHz, $CDCl_3$)
δ 5.10 (t, *J* = 7.3 Hz, 1H), 2.08 – 1.85 (m, 2H), 1.69 (s, 3H), 1.61 (s, 3H), 1.47 – 1.24 (m, 5H), 1.18 – 1.04 (m, 2H), 0.89 – 0.83 (m, 5.06H).

^{2}H NMR (61 MHz, $CHCl_3$)
δ 0.87 (s, 0.94D).

^{13}C NMR (101 MHz, $CDCl_3$)
δ 131.10, 125.25, 39.43, 37.31, 32.31, 25.89, 25.73, 20.18, 19.70, 17.77, 14.26 (t, *J* = 19.2 Hz).

ATR-IR (cm^{-1}):
2957, 2923, 2851, 2363, 1462, 1376.

HRMS: EI$^+$) *m/z*: [M]$^+$ Calcd for $C_{11}H_{21}D$, 155.1784; Found 155.1778.



***tert*-butyldimethyl(2-methyl-3-phenylpropoxy-3-*d*)silane [19]:** According to the general procedure B, DTB-DPPBz (14.8 mg, 0.0165 mmol, 0.055 eq.), $Cu(OAc)_2$ (75 µL of a 0.2 M solution in THF, 0.015 mmol, 0.05 eq.), THF (0.075 mL), then dimethoxy(methyl)silane (148 µL, 1.20 mmol, 4 eq.) were combined in a 2-dram vial followed by addition of a solution of (*E*)-*tert*-butyldimethyl((2-methyl-3-phenylallyl)oxy)silane (79 mg, 0.30 mmol, 1 eq.), THF (0.150 mL), 2-propanol-d_8 (69 µL, 0.9 mmol, 3 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 60°C.

Upon completion, the crude product mixture was dry loaded onto a silica gel column. Flash chromatography using gradient elution (200 mL of 100% HPLC hexanes, 100 mL 1% ethyl acetate in HPLC hexanes) gave the pure product as a clear colorless oil (62 mg, 0.23 mmol, 77% yield).[4,5]

^{1}H NMR (400 MHz, CDCl3)
δ 7.29 (t, *J* = 7.4 Hz, 2H), 7.24 – 7.15 (m, 3H), 3.46 (d, *J* = 5.9 Hz, 2H), 2.87 – 2.78 (m, 0.03H), 2.32 (d, *J* = 8.4 Hz, 1H), 1.90 (hept, *J* = 6.1 Hz, 1H), 0.94 (s, 9H), 0.88 (d, *J* = 6.7 Hz, 2H), 0.07 (s, 6H).
*We attribute the signal at 2.87-2.78ppm that integrates to 0.03 to the d_0 impurity, which is consistent with the measurements in scheme 3.

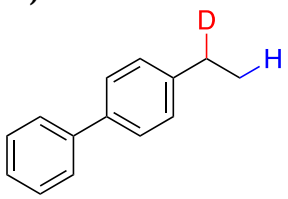
^{2}H NMR (61 MHz, CHCl3)
δ 2.83 (s, 0.97D).

^{13}C NMR (101 MHz, $CDCl_3$)
δ 141.29, 129.36, 128.24, 125.79, 67.62, 39.35 (t, *J* = 19.5 Hz), 38.00, 26.11, 18.49, 16.56, -5.20 (d, *J* = 3.1 Hz).

ATR-IR (cm^{-1}):
3026, 2954, 2928, 2157, 1802, 1605, 1087.

HRMS: (EI^+) *m/z*: $[M]^+$ Calcd for $C_{12}H_{18}DOSi$ 208.1300; Found 208.1260.
The major ion peak represents the parent molecule after loss of the *t*-Bu cation.

Transfer Hydrodeuteration Substrate Scope Analyzed by Molecular Rotational Resonance (Scheme 30)



4-(ethyl-1-*d*)-biphenyl [20a]. According to the general procedure B but on a 2.17x scale, DTB-DPPBz (6.4 mg, 0.00715 mmol, 0.011 eq.), $Cu(OAc)_2$ (33 µL of a 0.2 M solution in THF, 0.0065 mmol, 0.01 eq.), THF (0.297 mL), then poly(methylhydrosiloxane) (130 µL, 1.95 mmol, 3 eq. based on Si-H)[1] were combined in a 2-dram vial followed by addition of a solution of 4-Vinylbiphenyl (117 mg, 0.65 mmol, 1 eq.), THF (0.320 mL), ethanol-OD (95 µL, 1.63 mmol, 2.5 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 26 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Flash column chromatography (200 mL of 100% HPLC hexanes) gave the pure product as a white crystalline solid (109 mg, 0.59 mmol, 91% isolated yield of isotopic product mixture). *Product was analyzed by the Broadband instrument.

^{1}H NMR: (300 MHz, $CDCl_3$)
δ 7.60 (d, *J* = 7.4 Hz, 2H), 7.54 (d, *J* = 7.9 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 2H), 7.36 – 7.30 (m, 1H), 7.27 (d, *J* = 7.9 Hz, 2H), 2.79 – 2.56 (m, 1H), 1.28 (d, *J* = 7.5 Hz, 3H).

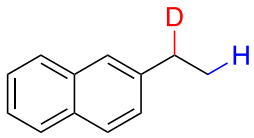
^{2}H NMR: (61 MHz, $CHCl_3$)
δ 2.68 (s, 1D).

^{13}C NMR: (75 MHz, $CDCl_3$)

δ 143.40, 141.29, 138.72, 128.82, 128.47, 127.18, 127.10, 127.07, 28.29 (t, *J* = 19.5 Hz), 15.64.

ATR-IR (cm^{-1}):
3054, 3028, 2962, 2930, 2873, 2135.

HRMS: (EI^+) *m/z*: $[M]^+$ Calcd for $C_{14}H_{13}D$ 183.1200; Found 183.1152.



2-(ethyl-1-*d*)-naphthalene [20b]. According to the general procedure B but on a 2.17x scale, DTB-DPPBz (6.4 mg, 0.00715 mmol, 0.011 eq.), $Cu(OAc)_2$ (33 µL of a 0.2 M solution in THF, 0.0065 mmol, 0.01 eq.), THF (0.297 mL), then poly(methylhydrosiloxane) (173 µL, 2.60 mmol, 4 eq. based on Si-H)[1] were combined in a 2-dram vial followed by addition of a solution of 2-Vinylnaphthalene (100 mg, 0.65 mmol, 1 eq.), THF (0.320 mL), ethanol-OD (95 µL, 1.63 mmol, 2.5 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 9.5 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Flash column chromatography (200 mL of 100% HPLC hexanes) gave the pure product as a clear colorless oil (85 mg, 0.54 mmol, 83% isolated yield of isotopic product mixture). *Product was analyzed by the Broadband instrument.

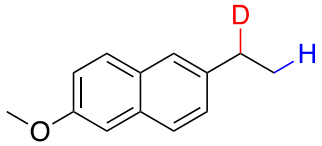
^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.88 – 7.76 (m, 3H), 7.65 (s, 1H), 7.50 – 7.40 (m, 2H), 7.37 (d, *J* = 8.5 Hz, 1H), 2.88 – 2.77 (m, 1.01H), 1.34 (d, *J* = 7.6 Hz, 3H).

^{2}H NMR: (61 MHz, $CHCl_3$)
δ 2.82 (s, 0.99D).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 141.88, 133.82, 132.06, 127.93, 127.73, 127.55, 127.22, 125.96, 125.68, 125.14, 28.84 (t, *J* = 19.3 Hz), 15.61.

ATR-IR (cm^{-1}):
3049, 2962, 2930, 2872, 2166, 1506, 1454.

HRMS: (EI^+) *m/z*: $[M]^+$ Calcd for $C_{12}H_{11}D$ 157.1000; Found 157.0995.



2-(ethyl-1-*d*)-6-methoxynaphthalene [20c]. According to the general procedure B, DTB-DPPBz (3.0 mg, 0.0033 mmol, 0.011 eq.), $Cu(OAc)_2$ (15 µL of a 0.2 M solution in THF, 0.003 mmol, 0.01 eq.), THF (0.135 mL), then dimethoxy(methyl)silane (111 µL, 0.90 mmol, 3 eq) were combined in a 2-dram vial followed by addition of a solution of 2-Ethenyl-6-methoxynaphthalene (55 mg, 0.30 mmol, 1 eq.), THF (0.150 mL), ethanol-OD (44 µL, 0.75 mmol, 2.5 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 17 h at 40°C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Flash column chromatography using gradient elution (100 mL of 100% HPLC hexanes, 100 mL of 1% ethyl acetate in HPLC hexanes) gave the pure product as a white solid (48 mg, 0.26 mmol, 87% isolated yield of isotopic product mixture).

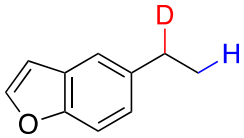
^{1}H NMR: (300 MHz, $CDCl_3$)
δ 7.70 (dd, *J* = 8.0, 2.2 Hz, 2H), 7.58 (s, 1H), 7.34 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.18 – 7.10 (m, 2H), 3.93 (s, 3H), 2.85 – 2.72 (m, 1.04H), 1.33 (d, *J* = 7.9 Hz, 3H).

^{2}H NMR: (61 MHz, $CHCl_3$)
δ 2.78 (s, 0.96 D)

^{13}C NMR: (75 MHz, $CDCl_3$) δ 157.21, 139.55, 133.02, 129.30, 129.03, 127.68, 126.82, 125.56, 118.72, 105.79, 55.41, 28.62 (t, *J* = 19.2 Hz), 15.69.

ATR-IR (cm^{-1}):
2980, 2958, 2926, 2908,2889,2868, 2280,1160.

HRMS: (EI^+) *m/z*: $[M]^+$ Calcd for $C_{13}H_{13}DO$ 187.1107; Found 187.1101.



5-(ethyl-1-*d*)-benzofuran [20d]. According to the general procedure B but on a 2.33x scale, DTB-DPPBz (7.0 mg, 0.0077 mmol, 0.011 eq.), $Cu(OAc)_2$ (35 μL of a 0.2 M solution in THF, 0.007 mmol, 0.01 eq.), THF (0.315 mL), then dimethoxy(methyl)silane (259 μL, 2.10 mmol, 3 eq.) were combined in a 2-dram vial followed by addition of a solution of 5-Vinylbenzofuran (101 mg, 0.70 mmol, 1 eq.), THF (0.350 mL), ethanol-OD (102 μL, 1.75 mmol, 2.5 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 25.5 h at 40°C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Flash column chromatography (150 mL of 100% HPLC hexanes) gave the pure product as a clear colorless oil (73 mg, 0.50 mmol, 71% isolated yield of isotopic product mixture). * Product was analyzed by the Broadband instrument.

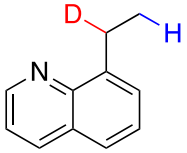
^{1}H NMR: (400 MHz, CDCl3)
δ 7.63 – 7.59 (m, 1H), 7.48 – 7.41 (m, 2H), 7.16 (d, *J* = 8.6 Hz, 1H), 6.75 – 6.72 (m, 1H), 2.80 – 2.68 (m, 1.05H), 1.30 (d, *J* = 7.6, 3H).

^{2}H NMR: (61 MHz, CHCl3)
δ 2.75 (s, 0.95D), 1.30 (s, 0.03D)

^{13}C NMR: (75 MHz, $CDCl_3$)
δ 153.62, 145.16, 138.89, 127.61, 124.61, 119.89, 111.11, 106.53, 28.61 (t, *J* = 19.5 Hz), 16.40.

ATR-IR (cm^{-1}):
3022, 2959, 2923, 2853, 2170, 1258.

HRMS: (EI^+) *m/z*: $[M]^+$ Calcd for $C_{10}H_9DO$ 147.0800; Found 147.0789.



8-(ethyl-1-*d*)-quinoline [20e]. According to the general procedure B but on a 2.17x scale, DTB-DPPBz (12.8 mg, 0.0143 mmol, 0.022 eq.), $Cu(OAc)_2$ (65 µL of a 0.2 M solution in THF, 0.013 mmol, 0.02 eq.), THF (0.260 mL), then dimethoxy(methyl)silane (241 µL, 1.95 mmol, 3 eq.) were combined in a 2-dram vial followed by addition of a solution of 8-Vinylquinoline (101 mg, 0.65 mmol, 1 eq.), THF (0.325 mL), ethanol-OD (95 µL, 1.63 mmol, 2.5 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 25 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a neutral alumina brock column. Flash column chromatography using gradient elution (300 mL of 100% HPLC hexanes, 100 mL of 2% ethyl acetate in HPLC hexanes) gave the pure product as a yellow oil (89 mg, 0.56 mmol, 86% isolated yield of isotopic product mixture).

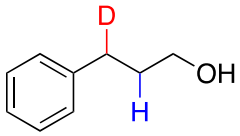
^{1}H NMR: (400 MHz, $CDCl_3$)
δ 8.95 (d, *J* = 4.0 Hz, 1H), 8.17-8.10 (m, 1H), 7.66 (d, *J* = 8.1 Hz, 1H), 7.58 (d, *J* = 7.0 Hz, 1H), 7.48 (t, J = 7.5 Hz, 1H), 7.42 – 7.36 (m, 1H), 3.36 – 3.25 (m, 1.02H), 1.39 (d, J = 7.5 Hz, 3H).

^{2}H NMR: (61 MHz, $CHCl_3$)
δ 3.33 (s, 0.98D).

^{13}C NMR: (101 MHz, $CDCl_3$)
δ 149.37, 146.87, 143.01, 136.50, 128.50, 128.05, 126.55, 125.94, 120.92, 24.40 (t, *J* = 19.4 Hz), 15.10.

ATR-IR (cm^{-1}):
3039, 3002, 2962, 2930, 2870, 2185, 1364.

HRMS: (ESI^+) *m/z*: $[M+H]^+$ Calcd for $C_{11}H_{11}DN$ 159.1080; Found 159.1026.



3-phenyl-(propan-3-*d*)-1-ol [20f]. According to the general procedure B but on a 4.07x scale, DTB-DPPBz (12.0 mg, 0.0134 mmol, 0.011 eq.), $Cu(OAc)_2$ (61 µL of a 0.2 M solution in THF, 0.0122 mmol, 0.01 eq.), THF (0.549 mL), then dimethoxy(methyl)silane (451 µL, 3.66 mmol, 3 eq.) were combined in a 2-dram vial followed by addition of a solution of 1-*tert*-butyldimethylsilyloxy-3-phenyl-2-propene (303 mg, 1.22 mmol, 1 eq.), THF (0.610 mL), ethanol-OD (178 µL, 3.05 mmol, 2.5 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 23 h at 40 °C. After silica plug filtration using diethyl ether (200 mL) as the eluent, the solvent was concentrated, and the crude oil was treated with tetrabutylammonium fluoride (2.44 mL, 2 eq.) and THF (5 mL) for 23 h. Upon completion, reaction mixture was quenched with saturated aqueous NH_4Cl (5 mL) and water (10mL). The aqueous layer was extracted with diethyl ether (3 x 10 mL) and the combined organic layers were washed with water (10 mL) and brine (10 mL), then dried over anhydrous Na_2SO_4. The mixture was filtered, and the solvent was removed by rotary evaporation. Flash column chromatography using gradient elution (100 mL of 100% HPLC hexanes, 100mL of 5% ethyl acetate in HPLC hexanes, 100mL of 10% ethyl acetate in HPLC hexanes, 300mL of 15% ethyl acetate in HPLC hexanes) gave the pure product as a clear colorless oil (127mg, 0.93 mmol, 76% isolated yield over 2 steps of isotopic product mixture).

^{1}H NMR: (400 MHz, $CDCl_3$)
δ 7.33 – 7.27 (m, 2H), 7.24 – 7.17 (m, 3H), 3.68 (td, *J* = 6.5, 1.1 Hz, 2H), 2.75 – 2.65 (m, 1H), 1.90 (q, *J* = 6.7 Hz, 2H), 1.56 (br s, 1H).

^{2}H NMR: (61 MHz, $CHCl_3$)
δ 2.70 (s, 1D).

^{13}C NMR: (75 MHz, $CDCl_3$)
δ 141.90, 128.55, 128.52, 125.99, 62.37, 34.26, 31.84 (t, *J* = 19.5 Hz).

ATR-IR (cm^{-1}):
3325, 3060, 3025, 2934, 2873, 2153, 1054.

HRMS: (EI^+) *m/z*: $[M]^+$ Calcd for $C_9H_{11}DO$ 137.1000; Found 137.0945.

References (Research Methodology and Characterization Chapter 2):

1. Hsu, M. C.; Junia, A. J.; Haight, A. R.; Zhang, W., Synthesis of Erythromycin Derivatives via the Olefin Cross-Metathesis Reaction. *J. Org. Chem.* **2004,** *69*, 3907-3911.

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3. Furuya, T.; Strom, A. E.; Ritter, T., Silver-Mediated Fluorination of Functionalized Aryl Stannanes. *J. Am. Chem. Soc.* **2009,** *131*, 1662-1663.

4. Skoda-Földes, R.; Kollár, L.; Marinelli, F.; Arcadi, A., Direct and carbonylative vinylation of steroidal triflates in the presence of homogeneous palladium catalysts. *Steroids* **1994,** *59*, 691-695.

Chapter 3

General Information
The following chemicals were purchased from commercial vendors and were used as received: $Cu(OAc)_2$ (99.999% from Alfa Aesar); 1,2-Bis[bis[3,5-di(t-butyl)phenyl]phosphino]benzene (DTB-DPPBz) (Wako Pure Chemical Industries), dimethoxy(methyl)silane (TCI); 2-propanol-OD (Millipore Sigma); 2-propanol-d_8 (Acros Organic); 2-propanol (Alfa Aesar); *tert*-butyldimethylsilyl chloride (TBSCl); D_2O (Oakwood Chemical). Anhydrous tetrahydrofuran (THF) was purified by an MBRAUN solvent purification system (MB-SPS). Prior to use, triethylamine (Et_3N) was distilled over CaH_2 and stored over 3Å molecular sieves. Chloroform-d ($CDCl_3$) was stored over 3Å molecular sieves.

Thin-layer chromatography (TLC) was conducted with Silicycle silica gel 60Å F254 pre-coated plates (0.25 mm) and visualized with UV, Iodine and $KMnO_4$ stains. Flash chromatography was performed using Silia Flash® P60, 40-60 μm (230-400 mesh), purchased from Silicycle. For reactions that required heating (optimization, transfer hydrodeuteration reactions), a PolyBlock for 2 dram vials was used on top of a Heidolph heating/stir plate.

^{1}H NMR spectra were recorded on a Varian 300 or 400 MHz spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 7.26 ppm). Data reported as: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sxt = sextet, hep = heptet, m = multiplet, br = broad; coupling constant(s) in Hz; integration. ^{13}C NMR spectra were recorded on a Varian 76 MHz or 101 MHz spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 77.16 ppm). ^{19}F NMR spectra were recorded on a Varian 376 MHz spectrometer. ^{2}H NMR spectra were recorded on a Varian 61 MHz spectrometer. Labeled solvent impurities were calculated out when reporting isolated yields.

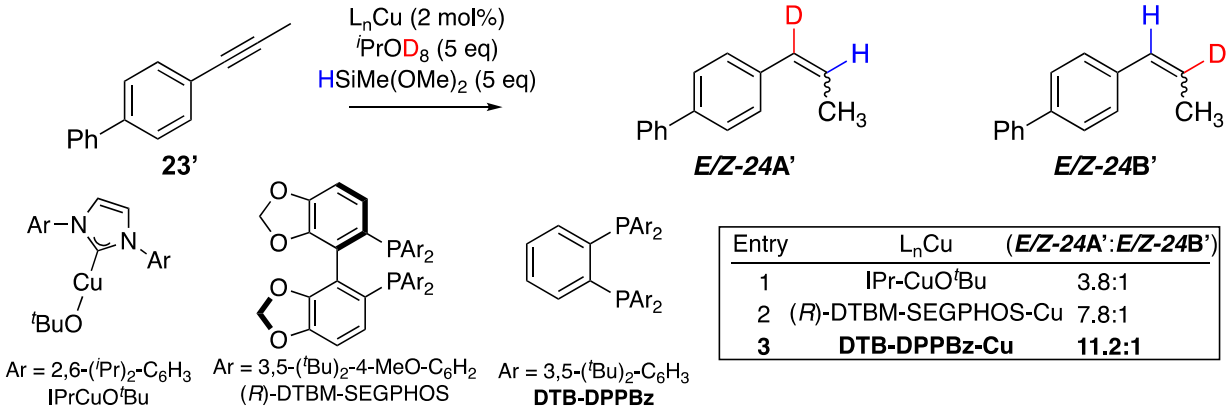
This work was completed using the resources of the Chemistry Instrument Center (CIC), University at Buffalo, SUNY, Buffalo, NY, che-ic@buffalo.edu for sample inquiries. This work utilized a Bruker SolariXR FT-ICRMS that was purchased with funding from National Institutes of Health grant, S10 RR029517. Also, this work utilized a Thermo Scientific Q-Exactive Orbitrap Gas Chromatography/Tandem Mass Spectrometer that was purchased with funding from a National Science Foundation grant, CHE-1919594.

Regioselectivity Studies

General Procedure A for Regioselectivity Studies in Scheme 33 and Scheme 34:

In a N_2 filled glovebox, Cu. cat (0.00400 mmol, 0.0200 eq.) and THF (0.0800 mL) were added to an oven-dried 2-dram vial followed by dropwise addition of dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.). A color change from green/blue to yellow was observed while stirring for 15 minutes. In a separate oven-dried 1-dram vial was added the alkyne substrate **23** or **23'** (0.200 mmol, 1.00 eq.), THF (0.100 mL), and 2-propanol-*d8* (76.6 µL, 1.00 mmol, 5.00 eq.). The solution in the 1-dram vial was added dropwise over 20 seconds to the 2-dram vial. The total volume of THF was calculated based on having a final reaction concentration of 1M based on the alkyne substrate. The 2-dram vial was capped with a red pressure relief cap, taken out of the glovebox, and stirred for the respective time at 40 °C, at which point the reaction was filtered through a 1" silica plug with 50 mL of Et_2O followed by 50 mL of Et_2O to elute the remaining product into a 200 mL round bottom flask. After removing the solvent by rotary evaporation, the crude product was dry loaded onto silica gel and purified by flash column chromatography (100 mL of 100% hexanes and 200 mL 3% ethyl acetate in hexanes for product ***E/Z*-24A and *E/Z*-24B,** 300 mL of 100% hexanes for product ***E/Z*-24A' and *E/Z*-24B'**) and the ratio of products to products was determined by ^{1}H NMR analysis of the alkene region of the isolated product mixture. For clarity, only the signals in the alkene region is reported for each entry. Ratios in Scheme S1 were assigned by direct comparison to a synthesized standard of the *E/Z* compound.

Scheme 34: Ligand Screening on 1,1'-Biphenyl-propyne



Entry	L_nCu	(*E/Z*-24A':*E/Z*-24B')
1	IPr-CuO^{t}Bu	3.8:1
2	(*R*)-DTBM-SEGPHOS-Cu	7.8:1
3	**DTB-DPPBz-Cu**	**11.2:1**

Entry 1. IPr-CuO^{t}Bu was pre-formed by addition of IPrCuCl (100 mg, 0.205 mmol, 1.00 eq), NaO^{t}Bu (19.7 mg, 0.205 mmol, 1.00 eq), and THF (1.03 mL, 0.200 M solution) to an oven-dried 20 mL vial. This was stirred at room temperature for 20 minutes. Then, according to the general procedure A, IPrCuO^{t}Bu (20.0 µL of a 0.200 M solution in THF, 0.00400 mmol, 0.0200 eq), THF (0.080 mL), and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 4-(prop-1-yn-1-yl)-1,1'-biphenyl **23'** (38.4 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and 2-propanol-*d8* (76.6 µL, 1.00 mmol, 5.00 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 3 h at 40 °C. Upon completion and crude ^{1}H NMR analysis, the crude product was dry loaded onto silica gel and isolated by flash column chromatography (300 mL of 100% hexanes) to give a white solid containing a mixture of products (***E/Z*-24A'** : ***E/Z*-24B'**, 3.8:1).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 6.53-6.47 (m, 1H), 5.85 (q, *J* = 7.3 Hz, 3.78H)

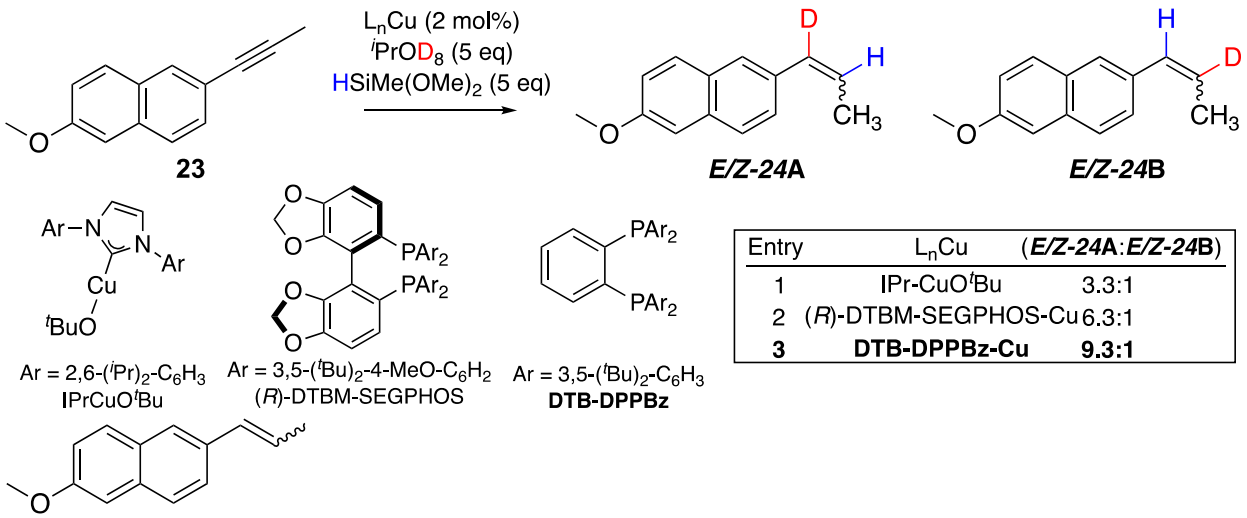
Entry 2. According to the general procedure A, (*R*)-DTBM-SEGPHOS (5.20 mg, 0.00440 mmol, 0.0220 eq), $Cu(OAc)_2$ (20.0 µL of a 0.200 M solution in THF, 0.00400 mmol, 0.0200 eq), THF (0.0800 mL), and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 4-(prop-1-yn-1-yl)-1,1'-biphenyl **23'** (38.4 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and 2-propanol-*d8* (76.6 µL, 1.00 mmol, 5.00 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 3.5 h at 40 °C. Upon completion and crude ^{1}H NMR analysis, the crude product was dry loaded onto silica gel and isolated by flash column chromatography (300 mL of 100% hexanes) to give a clear oil containing a mixture of products (***E/Z*-24A'** : ***E/Z*-24B'**, 7.8:1).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 6.52-6.48 (m, 1H), 6.34-6.28 (m, 0.20H), 5.85 (q, *J* = 7.4 Hz, 7.69H).

Entry 3. According to the general procedure A, DTB-DPPBz (4.00 mg, 0.00440 mmol, 0.0220 eq), $Cu(OAc)_2$ (20.0 µL of a 0.200 M solution in THF, 0.00400 mmol, 0.0200 eq), THF (0.0800 mL), and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 4-(prop-1-yn-1-yl)-1,1'-biphenyl **23'** (38.4 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and 2-propanol-*d8* (76.6 µL, 1.00 mmol, 5.00 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 15 minutes at 40 °C. Upon completion and crude ^{1}H NMR analysis, the crude product was dry loaded onto silica gel and isolated by flash column chromatography (300 mL of 100% hexanes) to give a clear oil containing a mixture of products (***E/Z*-24A'** : ***E/Z*-24B'**, 11.2:1).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 6.52-6.46 (m, 1H), 6.34-6.26 (m, 0.09H), 5.85 (q, *J* = 7.4 Hz, 11.14H).

Scheme 33: Ligand Screening on 2-Methoxy-6-(1-propyn-1-yl)naphthalene



Entry	L_nCu	(*E/Z*-24A:*E/Z*-24B)
1	IPr-CuO^{t}Bu	3.3:1
2	(*R*)-DTBM-SEGPHOS-Cu	6.3:1
3	**DTB-DPPBz-Cu**	**9.3:1**

(*E/Z*)-2-methoxy-6-(prop-1-en-1-yl)naphthalene [*E/Z*-24A and *E/Z*-24B]. Synthesized from a previously reported procedure[1], ethyltriphenylphosphoniumbromide (2.39 g, 6.44 mmol, 1.20 eq), NaH (60% dispersion in mineral oil, 0.969 g, 24.2 mmol, 4.51 eq), 6-methoxy-2-naphthalenecarboxaldehyde (1.00 g, 5.37 mmol, 1.00 eq), and THF (27.0 mL, 0.200 M) were combined to form the desired product as a cream colored solid (0.906 g, 4.57 mmol, 85% yield). This product was used as a reference standard for ^{1}H NMR analysis of the isolated product mixtures from entries 1-3 in Scheme S1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 –7.62 (m, 2.91H), 7.60 (s, 0.21H), 7.54 (dd, *J* = 8.5, 1.8 Hz, 0.20H), 7.43 (dd, *J* = 8.5, 1.8 Hz, 0.78H), 7.19 – 7.06 (m, 2.17H), 6.62 – 6.55 (m, 0.44H), 6.55 – 6.48 (m,

0.36H), 6.38 – 6.24 (m, 0.20H), 5.90 – 5.78 (m, 0.83H), 3.93 (s, 2.52H), 3.92 (s, 0.56H), 1.99 (dd, *J* = 7.2, 1.9 Hz, 2.27H), 1.94 (dd, *J* = 6.7, 1.7 Hz, 0.62H).

Entry 1. IPr-CuO^{t}Bu was pre-formed by addition of IPrCuCl (100 mg, 0.205 mmol, 1.00 eq), NaO^{t}Bu (19.7 mg, 0.205 mmol, 1.00 eq), and THF (1.03 mL, 0.200 M solution) to an oven-dried 20 mL vial. This was stirred at room temperature for 20 minutes. Then, according to the general procedure A, IPrCuO^{t}Bu (20.0 µL of a 0.200 M solution in THF, 0.00400 mmol, 0.0200 eq), THF (0.080 mL), and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 6-methoxy-2-(1-propynyl)naphthalene **23** (39.3 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and 2-propanol-*d8* (76.6 µL, 1.00 mmol, 5.00 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 5 h at 40 °C. Upon completion and crude ^{1}H NMR analysis, the crude product was dry loaded onto silica gel and isolated by flash column chromatography (100 mL of 100% hexanes and 200 mL of 3% ethyl acetate in hexanes) to give a white solid containing a mixture of products (***E/Z*-24A** : ***E/Z*-24B**, 3.3:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.61-6.47 (m, 1H), 6.39-6.22 (m, 0.24H), 5.83 (q, *J* = 7.2 Hz, 3.05H)

Entry 2. According to the general procedure A, (*R*)-DTBM-SEGPHOS (5.20 mg, 0.00440 mmol, 0.0220 eq), $Cu(OAc)_2$ (20.0 µL of a 0.200 M solution in THF, 0.00400 mmol, 0.0200 eq), THF (0.0800 mL), and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 6-methoxy-2-(1-propynyl)naphthalene **23** (39.3 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and 2-propanol-*d8* (76.6 µL, 1.00 mmol, 5.00 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 6 h at 40 °C. Upon completion and crude ^{1}H NMR analysis, the crude product was dry loaded onto silica gel and isolated by flash column chromatography (100 mL of 100% hexanes and 200 mL of 3% ethyl acetate in hexanes) to give a white solid containing a mixture of products (***E/Z*-24A** : ***E/Z*-24B**, 6.3:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.59-6.51 (m, 1H), 6.36-6.28 (m, 0.35H), 5.84 (q, *J* = 7.3 Hz 5.9H).

Entry 3. According to the general procedure A, DTB-DPPBz (4.00 mg, 0.00440 mmol, 0.0220 eq), $Cu(OAc)_2$ (20.0 µL of a 0.200 M solution in THF, 0.00400 mmol, 0.0200 eq), THF (0.0800 mL), and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 6-methoxy-2-(1-propynyl)naphthalene **23** (39.3 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and 2-propanol-*d8* (76.6 µL, 1.00 mmol, 5.00 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 27 minutes at 40 °C. Upon completion and crude ^{1}H NMR analysis, the crude product was dry loaded onto silica gel and isolated by flash column chromatography (100 mL of 100% hexanes and 200 mL of 3% ethyl acetate in hexanes) to give a white solid containing a mixture of products (***E/Z*-24A** : ***E/Z*-24B**, 9.3:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.59-6.54 (m, 1H), 6.38-6.25 (m, 0.28H), 5.85 (q, *J* = 7.3 Hz, 9H).

Optimization Studies

General Procedure B for Optimization Studies in Table 4:

In a N_2 filled glovebox, ligand, Cu catalyst (Cu:L = 1:1.1), and THF were added to an oven-dried 2-dram vial followed by dropwise addition of R_3Si-H (1.00 mmol, 5.00 eq.). A color change from green/blue to orange was observed while stirring for 15 minutes. In a separate oven-dried 1-dram vial was added *tert*-butyl((4-(6-methoxynaphthalen-2-yl)but-3-yn-1-yl)oxy)dimethylsilane **4a** (68.1 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and the alcohol-OD (1.00 mmol, 5.00 eq.). The solution in the 1-dram vial was added dropwise over 20 seconds to the 2-dram vial. The total volume of THF was calculated based on having a final reaction concentration of 1M based on the alkyne substrate. The 2-dram vial was capped with a red pressure relief cap, taken out of the glovebox, and stirred for 20 h at the respective temperature

at which point the reaction was filtered through a 1" silica gel plug with 50 mL of Et_2O followed by an additional 50 mL of Et_2O to elute the crude product into a 200 mL round bottom flask. The solvent was removed by rotary evaporation, and the product was analyzed by ^{1}H NMR using 1,3,5-trimethylbenzene as an internal standard. If greater than 5% ^{1}H NMR yield was observed for **5a** in the crude ^{1}H NMR, yields were obtained by isolating the product by flash column chromatography.

Entry 1. According to the general procedure B, DTB-DPPBz (2.00 mg, 0.00220 mmol, 0.0110 eq), $Cu(OAc)_2$ (10.0 µL of a 0.200 M solution in THF, 0.00200 mmol, 0.0100 eq), THF (0.0900 mL), and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of *tert*-butyl((4-(6-methoxynaphthalen-2-yl)but-3-yn-1-yl)oxy)dimethylsilane **31a** (68.1 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and 2-propanol-d_8 (76.6 µL, 1.00 mmol, 5.00 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 40 °C. Upon completion and crude ^{1}H NMR analysis, the crude product was dry loaded onto silica gel and isolated by flash column chromatography (100 mL of 100% hexanes, 200 mL of 2% ethyl acetate in hexanes) to give the pure product as an orange solid (**32a,** 67.4 mg, 0.194 mmol, 97% yield).

Entry 2. According to the general procedure B, DTB-DPPBz (2.00 mg, 0.00220 mmol, 0.0110 eq), $Cu(OAc)_2$ (10.0 µL of a 0.200 M solution in THF, 0.00200 mmol, 0.0100 eq), THF (0.0900 mL), and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of *tert*-butyl((4-(6-methoxynaphthalen-2-yl)but-3-yn-1-yl)oxy)dimethylsilane **31a** (68.1 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and 2-propanol-d_8 (76.6 µL, 1.00 mmol, 5.00 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at room temperature. Upon completion and crude ^{1}H NMR analysis, the crude product was dry loaded onto silica gel and isolated by flash column chromatography (100 mL of 100% hexanes, 200 mL of 2% ethyl acetate in hexanes) to give the pure product as an orange solid (**32a,** 65.7 mg, 0.190 mmol, 95% yield).

Entry 3. According to the general procedure B, DTB-DPPBz (4.00 mg, 0.00440 mmol, 0.0220 eq), $Cu(OAc)_2$ (20.0 µL of a 0.200 M solution in THF, 0.00400 mmol, 0.0200 eq), THF (0.0800 mL), and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of *tert*-butyl((4-(6-methoxynaphthalen-2-yl)but-3-yn-1-yl)oxy)dimethylsilane **31a** (68.1 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and 2-propanol-d_8 (76.6 µL, 1.00 mmol, 5.00 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 5 °C. Upon completion and crude ^{1}H NMR analysis, the crude product was dry loaded onto silica gel and isolated by flash column chromatography (100 mL of 100% hexanes, 200 mL of 2% ethyl acetate in hexanes) to give the pure product as an orange solid (**31a'** and **32a** isolated as an inseparable mixture, 60.7 mg (**31a'**, 3.5% yield; **32a**, 84% yield).

Entry 4. According to the general procedure B, DTB-DPPBz (4.00 mg, 0.00440 mmol, 0.0220 eq), $Cu(OAc)_2$ (20.0 µL of a 0.200 M solution in THF, 0.00400 mmol, 0.0200 eq), THF (0.0800 mL), and poly(methylhydrosiloxane) (66.7 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of *tert*-butyl((4-(6-methoxynaphthalen-2-yl)but-3-yn-1-yl)oxy)dimethylsilane **31a** (68.1 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and 2-propanol-d_8 (76.6 µL, 1.00 mmol, 5.00 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 40 °C. Upon completion and crude ^{1}H NMR analysis, the crude product was dry loaded onto silica gel and isolated by flash column chromatography (100 mL of 100% hexanes, 200 mL of 2% ethyl acetate in hexanes) to give the pure product as an orange solid (**32a,** 51.6 mg, 0.149 mmol, 75% yield).

Entry 5. According to the general procedure B, DTB-DPPBz (4.00 mg, 0.00440 mmol, 0.0220 eq), $Cu(OAc)_2$ (20.0 µL of a 0.200 M solution in THF, 0.00400 mmol, 0.0200 eq), THF (0.0800 mL), and diethoxy(methyl)silane (160 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of *tert*-butyl((4-(6-methoxynaphthalen-2-yl)but-3-yn-1-yl)oxy)dimethylsilane **31a** (68.1 mg,

0.200 mmol, 1.00 eq.), THF (0.100 mL), and 2-propanol-d_8 (76.6 µL, 1.00 mmol, 5.00 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 40 °C. Upon completion and crude ^{1}H NMR analysis, the crude product was dry loaded onto silica gel and isolated by flash column chromatography (100 mL of 100% hexanes, 200 mL of 2% ethyl acetate in hexanes) to give the pure product as an orange solid (**32a,** 61.7 mg, 0.178 mmol, 89% yield).

Entry 6. According to the general procedure B, DTB-DPPBz (4.00 mg, 0.00440 mmol, 0.0220 eq), $Cu(OAc)_2$ (20.0 µL of a 0.200 M solution in THF, 0.00400 mmol, 0.0200 eq), THF (0.0800 mL), and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of *tert*-butyl((4-(6-methoxynaphthalen-2-yl)but-3-yn-1-yl)oxy)dimethylsilane **31a** (68.1 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and ethanol-OD (58.4 µL, 1.00 mmol, 5.00 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 40 °C. Upon completion and crude ^{1}H NMR analysis, the crude product was dry loaded onto silica gel and isolated by flash column chromatography (100 mL of 100% hexanes, 200 mL of 2% ethyl acetate in hexanes) to give the pure product as an orange solid (**31a'** and **32a** isolated as an inseparable mixture, 55.4 mg (**31a'**, 41% yield; **32a,** 39% yield)).

Entry 7. According to the general procedure B, DTB-DPPBz (4.00 mg, 0.00440 mmol, 0.0220 eq), $Cu(OAc)_2$ (20.0 µL of a 0.200 M solution in THF, 0.00400 mmol, 0.0200 eq), THF (0.0800 mL), and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of *tert*-butyl((4-(6-methoxynaphthalen-2-yl)but-3-yn-1-yl)oxy)dimethylsilane **31a** (68.1 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and methanol-OD (40.7 µL, 1.00 mmol, 5.00 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 40 °C. Upon completion and crude ^{1}H NMR analysis, the crude product was dry loaded onto silica gel and isolated by flash column chromatography (100 mL of 100% hexanes, 200 mL of 2% ethyl acetate in hexanes) to give the pure product as an orange solid (**31a, 31a',** and **32a** isolated as an inseparable mixture, 51.2 mg (**31a,** 10%; **31a'**, 53% yield; **32a,** 12% yield)).

Entry 8. According to the general procedure B, DTB-DPPBz (4.00 mg, 0.00440 mmol, 0.0220 eq), $Cu(OAc)_2$ (20.0 µL of a 0.200 M solution in THF, 0.00400 mmol, 0.0200 eq), THF (0.0800 mL), and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of *tert*-butyl((4-(6-methoxynaphthalen-2-yl)but-3-yn-1-yl)oxy)dimethylsilane **31a** (68.1 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and *tert*-butanol-OD (95.6 µL, 1.00 mmol, 5.00 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 40 °C. Upon completion and crude ^{1}H NMR analysis, the crude product was dry loaded onto silica gel and isolated by flash column chromatography (100 mL of 100% hexanes, 200 mL of 2% ethyl acetate in hexanes) to give the pure product as an orange solid (**31a, 31a',** and **32a** isolated as an inseparable mixture, 55.5 mg (**31a,** 20%; **31a'**, 47% yield; **32a,** 14% yield)).

Entry 9. According to the general procedure B, DTB-DPPBz (4.00 mg, 0.00440 mmol, 0.0220 eq), $Cu(OAc)_2$ (20.0 µL of a 0.200 M solution in THF, 0.00400 mmol, 0.0200 eq), THF (0.0800 mL), and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of *tert*-butyl((4-(6-methoxynaphthalen-2-yl)but-3-yn-1-yl)oxy)dimethylsilane **31a** (68.1 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and D_2O (18.0 µL, 1.00 mmol, 5.00 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 40 °C. Upon completion, the crude ^{1}H NMR was analyzed using 1,3,5-trimethylbenzene as an internal standard. (**31a,** 75% yield by ^{1}H NMR; **31a'**, 15% yield by ^{1}H NMR).

Entry 10. According to the general procedure B, (triphenylphosphine)copper hydride hexamer (Stryker's reagent) (1.31 mg, 0.00066 mmol, 0.00330 eq), THF (0.100 mL), and dimethoxy(methyl)silane

(123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of *tert*-butyl((4-(6-methoxynaphthalen-2-yl)but-3-yn-1-yl)oxy)dimethylsilane **31a** (68.1 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and 2-propanol-d_8 (76.6 µL, 1.00 mmol, 5.00 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 40 °C. Upon completion, the crude ^{1}H NMR was analyzed using 1,3,5-trimethylbenzene as an internal standard. (**31a,** 99% yield by ^{1}H NMR).

Entry 11. According to the general procedure B, $Cu(OAc)_2$ (20.0 µL of a 0.200 M solution in THF, 0.00400 mmol, 0.0200 eq), THF (0.0800 mL), and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of *tert*-butyl((4-(6-methoxynaphthalen-2-yl)but-3-yn-1-yl)oxy)dimethylsilane **31a** (68.1 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and 2-propanol-d_8 (76.6 µL, 1.00 mmol, 5.00 eq.). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 40 °C. Upon completion, the crude ^{1}H NMR was analyzed using 1,3,5-trimethylbenzene as an internal standard. (**31a,** 84% yield by ^{1}H NMR).

Transfer Hydrodeuteration Reaction Substrate Scope

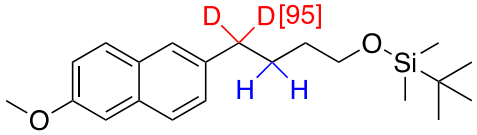
General Procedure C for Transfer Hydrodeuteration Reactions in Scheme 38 and Scheme 39:

In a N_2 filled glovebox, DTB-DPPBz (0.0110 eq.), $Cu(OAc)_2$ (0.200 M solution in THF, 0.0100 eq.), and THF were added to an oven-dried 2-dram vial followed by dropwise addition of dimethoxy(methyl)silane (185 µL, 1.50 mmol, 5.00 eq.) or poly(methylhydrosiloxane) (100 µL, 1.50 mmol, 5.00 eq based on Si-H). A color change from green/blue to yellow was observed while stirring for 15 minutes. In a separate oven-dried 1-dram vial was added the alkyne substrate **23, 31a-t, 33a-l** (0.300 mmol, 1.00 eq.), THF (0.150 mL), and 2-propanol-d_8 (115 µL, 1.50 mmol, 5.00 eq.). The solution in the 1-dram vial was added dropwise over 20 seconds to the 2-dram vial. The total volume of THF was calculated based on having a final reaction concentration of 1M based on the alkyne substrate. The 2-dram vial was capped with a red pressure relief cap, taken out of the glovebox, and stirred for the respective time at the appropriate temperature, at which point the reaction was filtered through a 1" silica plug with 50 mL of Et_2O or CH_2Cl_2 followed by 50 mL of Et_2O or CH_2Cl_2 to elute the remaining product into a 200 mL round bottom flask. After removing the solvent by rotary evaporation, the crude product was isolated by flash column chromatography.

Method for calculating deuterium incorporation at each labeled carbon of each substrate:

The ratio of the two peaks that appear in the ^{2}H NMR spectra was correlated to the calculated deuterium incorporation at the benzylic peak in the ^{1}H NMR spectra.

Scheme 38. Aryl Alkyne Transfer Hydrodeuteration Substrate Scope



D_2-*Tert*-butyl-(4-(6-methoxy-2-naphthalene)-3-butan-1-oxy)-dimethylsilane [32a]. According to the general procedure C, DTB-DPPBz (2.00 mg, 0.00220 mmol, 0.0110 eq.), $Cu(OAc)_2$ (10.0 µL of a 0.200 M solution in THF, 0.00200 mmol, 0.0100 eq.), THF (0.0900 mL) and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of *tert*-butyl-(4-(6-methoxy-2-naphthalenyl)-3-butyn-1-oxy)-dimethylsilane **31a** (68.1 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and 2-propanol-OD (76.6 µL, 1.00 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 40 °C. Upon completion and crude ^{1}H NMR analysis, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column

chromatography (100 mL of 100% hexanes, 200 mL of 2% ethyl acetate in hexanes) gives the pure product as a colorless oil (63.0 mg, 0.182 mmol, 91% yield).

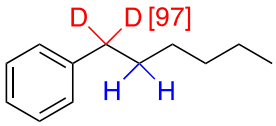
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.75-7.66 (m, 2H), 7.57 (s, 1H), 7.37 – 7.30 (m, 1H), 7.19 – 7.10 (m, 2H), 3.93 (s, 3H), 3.67 (t, *J* = 6.3 Hz, 2H), 2.80 – 2.72 (m, 0.11H), 1.82 – 1.72 (m, 1.89H), 1.62 (p, *J* = 6.5 Hz, 2H), 0.93 (s, 9H), 0.08 (s, 6H).

^{2}H NMR (61 MHz, Chloroform-*d*) δ 2.76 (s, 1.89D), 1.77 (s, 0.10D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 157.19, 137.86, 133.04, 129.22, 129.01, 127.98, 126.78, 126.34, 118.71, 105.73, 63.20, 55.38, 35.02 (p, *J* = 19.5 Hz), 32.52, 27.61, 26.13, 18.51, -5.13.

IR: 3007, 2926, 2852, 2179, 1603, 1502, 1183.

HRMS: (ESI^{+}) m/z: [M+Na]$^{+}$ Calcd for $C_{21}H_{30}D_2NaO_2Si$ 369.2197; Found 369.2189.



D$_2$-Hexyl-benzene [32b]. According to the general procedure C, DTB-DPPBz (3.00 mg, 0.00330 mmol, 0.0110 eq.), Cu(OAc)$_2$ (15.0 µL of a 0.200 M solution in THF, 0.00300 mmol, 0.0100 eq.), THF (0.135 mL) and dimethoxy(methyl)silane (185 µL, 1.50 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 1-hexyn-1-yl-benzene **31b** (47.5 mg, 0.300 mmol, 1.00 eq.), THF (0.150 mL), and 2-propanol-d$_8$ (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 23 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (250 mL of 100% hexanes) gives the pure product as a clear colorless oil (37.0 mg, 0.225 mmol, 75% yield).

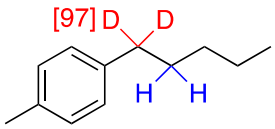
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.24 (m, 2H), 7.23 – 7.14 (m, 3H), 2.64 – 2.56 (m, 0.07H), 1.67 – 1.57 (m, 1.95H), 1.42 – 1.29 (m, 6H), 0.95 – 0.86 (m, 3H).

^{2}H NMR (61 MHz, Chloroform) δ 2.61 (s, 1.93D), 1.63 (s, 0.02D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 143.05, 128.54, 128.36, 125.69, 35.40 (p, *J* = 19.2 Hz), 31.90, 31.49, 29.12, 22.77, 14.25.

IR: 3025, 2956, 2923, 2855, 2199, 1606, 1510, 696.

HRMS: (EI^{+}) m/z: [M]$^{+}$ Calcd for $C_{12}H_{16}D_2$ 164.1534; Found 164.1527.



1-Methyl-4-(pentyl-1,1-*d*$_2$)benzene [32c]. According to the general procedure C, DTB-DPPBz (3.00 mg, 0.00330 mmol, 0.0110 eq.), Cu(OAc)$_2$ (15.0 µL of a 0.200 M solution in THF, 0.00300 mmol, 0.0100 eq.), THF (0.135 mL) and dimethoxy(methyl)silane (185 µL, 1.50 mmol, 5 eq.) were combined in a 2-dram vial followed by addition of a solution of 1-methyl-4-(pent-1-yn-yl)benzene **31c** (47.5 mg, 0.300 mmol, 1.00 eq.), THF (0.150 mL), and 2-propanol-d$_8$ (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with

a red pressure relief cap, and the reaction stirred for 22 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (100 mL of 100% hexanes) gives the pure product as a clear colorless oil (39.7 mg, 0.242 mmol, 81% yield).

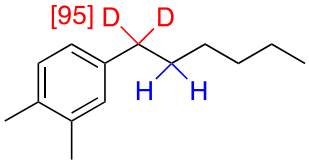
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.13 - 7.06 (m, 4H), 2.58 – 2.52 (m, 0.07H), 2.33 (s, 3H), 1.65 – 1.56 (m, 1.92H), 1.42 – 1.25 (m, 4H), 0.90 (t, *J* = 7.1 Hz, 3H).

^{2}H NMR (61 MHz, Chloroform) δ 2.56 (s, 1.93D), 1.61 (s, 0.04D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 139.95, 135.07, 129.05, 128.41, 34.90 (p, *J* = 19.3 Hz), 31.63, 31.34, 22.73, 21.14, 14.19.

IR: 3019, 2956, 2922, 2858, 2190, 1515, 1466, 1116.

HRMS: (EI^{+}) *m/z*: [M]$^{+}$ Calcd for $C_{12}H_{16}D_2$ 164.1534; Found 164.1527.



D_2-4-hexyl-1,2-dimethyl-benzene [32d]. According to the general procedure C, DTB-DPPBz (15.0 mg, 0.0165 mmol, 0.0550 eq.), $Cu(OAc)_2$ (75.0 µL of a 0.200 M solution in THF, 0.0150 mmol, 0.0500 eq.), THF (0.0750 mL) and dimethoxy(methyl)silane (185 µL, 1.50 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 4-(1-hexyn-1-yl)-1,2-dimethyl-benzene **31d** (55.9 mg, 0.300 mmol, 1.00 eq.), THF (0.150 mL), and 2-propanol-d_8 (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 23 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (300 mL of 100% hexanes) gives the pure product as a colorless oil (48.0 mg, 0.250 mmol, 83% yield).

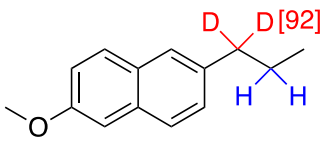
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.07 (d, *J* = 7.6 Hz, 1H), 6.98 (s, 1H), 6.94 (dd, *J* = 7.6, 1.9 Hz, 1H), 2.57 – 2.51 (m, 0.10H), 2.27 (s, 3H), 2.25 (s, 3H), 1.65 – 1.55 (m, 1.96H), 1.41 – 1.29 (m, 6H), 0.96 – 0.86 (t, *J* = 6.6 Hz, 3H).

^{2}H NMR (61 MHz, Chloroform) δ 2.47 (s, 1.90D), 1.53 (s, 0.06D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 140.51, 136.40, 133.72, 129.92, 129.62, 125.85, 35.32 - 34.47 (m), 31.93, 31.70, 29.21, 22.78, 19.91, 19.45, 14.27.

IR: 3030, 2956, 2922, 2856, 2198, 1620, 1504, 1453, 806.

HRMS: (EI^{+}) m/z: [M]$^{+}$ Calcd for $C_{14}H_{20}D_2$ 192.1847; Found 192.1842.



D_2-2-methoxy-6-propyl-naphthalene [32e]. According to the general procedure C, DTB-DPPBz (4.00 mg, 0.00440 mmol, 0.0220 eq.), $Cu(OAc)_2$ (20.0 µL of a 0.200 M solution in THF, 0.00400 mmol, 0.0200

eq.), THF (0.0800 mL) and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 2-methoxy-6-(1-propyn-1-yl)-naphthalene **23** (39.3 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and 2-propanol-d_8 (77.0 µL, 1.00 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 21 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (100 mL of 100% hexanes and 200 mL 3% ethyl acetate in hexanes) gives the pure product as a clear orange solid (32.0 mg, 0.158 mmol, 79% yield).

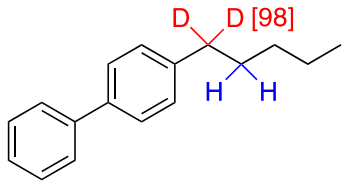
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 4.2 Hz, 1H), 7.67 (d, *J* = 3.4 Hz, 1H), 7.55 (s, 1H), 7.31 (d, *J* = 8.3, 1H), 7.19 – 7.08 (m, 2H), 3.92 (s, 3H), 2.75 – 2.66 (m, 0.16H), 1.72 (q, *J* = 7.3 Hz, 1.81H), 0.98 (t, *J* = 7.4 Hz, 3H).

^{2}H NMR (61 MHz, Chloroform) δ 2.71 (s, 1.84D), 1.72 (s, 0.09D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 157.18, 137.94, 133.03, 129.22, 129.02, 128.08, 126.71, 126.39, 118.70, 105.76, 55.41, 37.36 (p, *J* = 20.2), 24.53, 13.95.

IR: 2961, 2925, 2874, 2190, 1602, 1462, 1029.

HRMS: (EI$^+$) m/z: [M]$^+$ Calcd for $C_{14}H_{14}D_2O$ 202.1327; Found 202.1320.



D_2-4-pentyl-1,1'-biphenyl [32f]. According to the general procedure C, DTB-DPPBz (3.00 mg, 0.00330 mmol, 0.0110 eq.), $Cu(OAc)_2$ (15.0 µL of a 0.200 M solution in THF, 0.00300 mmol, 0.0100 eq.), THF (0.135 mL) and dimethoxy(methyl)silane (185 µL, 1.50 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 4-(1-pentyn-1-yl)-1,1'-biphenyl **31f** (66.1 mg, 0.300 mmol, 1.00 eq.), THF (0.150 mL), and 2-propanol-d_8 (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 18 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (300 mL of 100% hexanes) gives the pure product as a colorless oil (57.0 mg, 0.252 mmol, 84% yield).

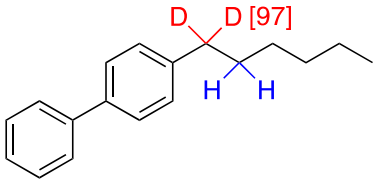
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 (d, *J* = 7.2, 2H), 7.55 (d, *J* = 7.9 Hz, 2H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 2H), 2.70 – 2.61 (m, 0.05H), 1.75 – 1.60 (m, 1.95H), 1.46 – 1.34 (m, 4H), 0.95 (t, *J* = 6.5 Hz, 3H).

^{2}H NMR (61 MHz, Chloroform) δ 2.66 (s, 1.95H), 1.68 (s, 0.03H).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 142.18, 141.34, 138.68, 128.95, 128.83, 127.14, 127.13, 127.09, 34.99 (p, *J* = 19.6 Hz), 31.66, 31.19, 22.73, 14.20.

IR: 3027, 2955, 2922, 2200, 1601, 1520, 1486, 757.

HRMS: (EI$^+$) m/z: [M]$^+$ Calcd for $C_{17}H_{18}D_2$ 226.1691; Found 226.1684.



4-(hexyl-1,1-*d*$_2$)-1,1'-biphenyl [32g]. According to the general procedure C, DTB-DPPBz (3.00 mg, 0.00330 mmol, 0.0110 eq.), $Cu(OAc)_2$ (15.0 µL of a 0.200 M solution in THF, 0.00300 mmol, 0.0100 eq.), THF (0.135 mL) and dimethoxy(methyl)silane (185 µL, 1.50 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 4-(1-hexyn-1-yl)-1,1'-biphenyl **31g** (70.3 mg, 0.300 mmol, 1.00 eq.), THF (0.150 mL), and 2-propanol-d_8 (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (200 mL of 100% hexanes) gives the pure product as a clear crystalline solid (66.4 mg, 0.276 mmol, 92% yield).

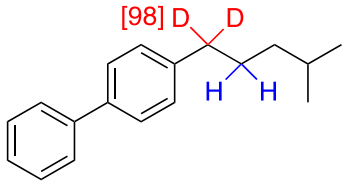
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (d, *J* = 8.0 Hz, 2H), 7.53 (d, *J* = 7.8 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.34 (t, *J* = 7.2 Hz, 1H), 7.27 (d, *J* = 7.4 Hz, 2H), 2.68 – 2.61 (m, 0.06H), 1.65 (t, *J* = 7.1 Hz, 1.93H), 1.44 – 1.29 (m, 6H), 0.91 (t, *J* = 6.3 Hz, 3H).

^{2}H NMR (61 MHz, Chloroform) δ 2.63 (s, 1.94D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 142.16, 141.33, 138.67, 128.94, 128.83, 127.12 (2 overlapping carbon signals), 127.07, 35.02 (p, *J* = 19.1 Hz), 31.92, 31.48, 29.17, 22.79, 14.28.

IR: 2955, 2917, 2855, 2169, 1599, 1521, 1485, 1118.

HRMS: (EI$^+$) *m/z*: $[M]^+$ Calcd for $C_{18}H_{20}D_2$ 240.1847; Found 240.1841.



D$_2$-4-(4-methylpentyl)-1,1'-biphenyl [32h]. According to the general procedure C, DTB-DPPBz (13.0 mg, 0.0141 mmol, 0.0550 eq.), $Cu(OAc)_2$ (64.0 µL of a 0.200 M solution in THF, 0.0128 mmol, 0.0500 eq.), THF (0.0920 mL) and dimethoxy(methyl)silane (158 µL, 1.28 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 4-(4-methyl-1-pentyn-1-yl)-1,1'-biphenyl **31h** (60.0 mg, 0.256 mmol, 1.00 eq.), THF (0.100 mL), and 2-propanol-d_8 (98.0 µL, 1.28 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 22 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (300 mL of 100% hexanes) gives the pure product as a clear colorless oil (50.0 mg, 0.208 mmol, 81% yield).

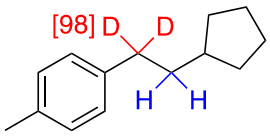
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 8.0 Hz, 2H), 7.54 (d, *J* = 7.9 Hz, 2H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.34 (t, *J* = 7.2 Hz, 1H), 7.28 (d, *J* = 7.8 Hz, 2H), 2.68 – 2.58 (m, 0.05H), 1.71 – 1.55 (m, 2.94H), 1.28 (q, *J* = 7.4 Hz, 2H), 0.91 (d, *J* = 6.7 Hz, 6H).

^{2}H NMR (61 MHz, Chloroform) δ 2.64 (s, 1.95D), 1.67 (s, 0.03D).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 142.19, 141.32, 138.68, 128.94, 128.84, 127.14, 127.13, 127.09, 38.79, 35.27 (p, J = 19.2), 29.38, 28.08, 22.76.

IR: 3027, 2953, 2925, 2199, 1601, 1520, 1485, 756.

HRMS: (EI$^+$) m/z: [M]$^+$ Calcd for $C_{18}H_{20}D_2$ 240.1847; Found 240.1840.



1-(2-cyclopentylethyl-1,1-*d*$_2$)-4-methylbenzene [32i]. According to the general procedure C, DTB-DPPBz (3.00 mg, 0.00330 mmol, 0.0110 eq.), Cu(OAc)$_2$ (15.0 µL of a 0.200 M solution in THF, 0.00300 mmol, 0.0100 eq.), THF (0.135 mL) and poly(methylhydrosiloxane) (100 µL, 1.50 mmol, 5.00 eq based on Si-H) were combined in a 2-dram vial followed by addition of a solution of 1-(cyclopentylethynyl)-4-methylbenzene **31i** (55.3 mg, 0.300 mmol, 1.00 eq.), THF (0.150 mL), and 2-propanol-d$_8$ (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (200 mL of 100% hexanes) gives the pure product as a clear colorless oil (50.4 mg, 0.265 mmol, 88% yield).

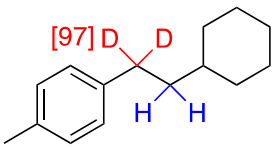
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.09 (s, 4H), 2.60 – 2.53 (m, 0.04H), 2.33 (s, 3H), 1.84 – 1.73 (m, 3H), 1.66 –1.43 (m, 6H), 1.20 – 1.07 (m, 2H).

^{2}H NMR (61 MHz, Chloroform) δ 2.57 (s, 1.96D), 1.62 (s, 0.03D)

^{13}C NMR (75 MHz, Chloroform-*d*) δ 140.05, 135.02, 129.06, 128.36, 39.74, 38.28, 34.08 (p, *J* = 19.2 Hz), 32.81, 25.39, 21.13.

IR: 3010, 2958, 2921, 2225, 1510, 1066, 814.

HRMS: (EI$^+$) *m/z*: [M]$^+$ Calcd for $C_{14}H_{18}D_2$ 190.1691; Found 190.1684.



1-(2-cyclohexylethyl-1,1-*d*$_2$)-4-methylbenzene [32j]. According to the general procedure C, DTB-DPPBz (3.00 mg, 0.00330 mmol, 0.0110 eq.), Cu(OAc)$_2$ (15.0 µL of a 0.200 M solution in THF, 0.00300 mmol, 0.0100 eq.), THF (0.135 mL) and poly(methylhydrosiloxane) (100 µL, 1.50 mmol, 5.00 eq based on Si-H) were combined in a 2-dram vial followed by addition of a solution of 1-(2-cyclohexylethynyl)-4-methylbenzene **31j** (59.5 mg, 0.300 mmol, 1.00 eq.), THF (0.150 mL), and 2-propanol-d$_8$ (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (150 mL of 100% hexanes) gives the pure product as a clear colorless oil (51.6 mg, 0.253 mmol, 84% yield).

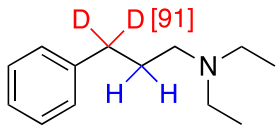
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.09 (s, 4H), 2.61 – 2.53 (m, 0.06H), 2.33 (s, 3H), 1.83 – 1.61 (m, 5H), 1.48 (d, *J* = 6.7 Hz, 1.98H), 1.31 – 1.16 (m, 4H), 0.94 (q, *J* = 11.8 Hz, 2H).

^{2}H NMR (61 MHz, Chloroform) δ 2.56 (s, 1.94D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 140.23, 135.00, 129.07, 128.35, 39.57, 37.40, 33.48, 32.19 (p, *J* = 19.6 Hz), 26.87, 26.50, 21.13.

IR: 3018, 2919, 2849, 2196, 1515, 1447, 1116, 787.

HRMS: (EI^{+}) *m/z*: [M]$^{+}$ Calcd for $C_{15}H_{20}D_2$ 204.1847; Found 204.1841.



D$_2$-*N*,*N*-diethyl-benzenepropanamine [32k]. According to the general procedure C, DTB-DPPBz (6.00 mg, 0.00660 mmol, 0.0220 eq.), Cu(OAc)$_2$ (30.0 µL of a 0.200 M solution in THF, 0.00600 mmol, 0.0200 eq.), THF (0.120 mL) and dimethoxy(methyl)silane (185 µL, 1.50 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of *N*,*N*-diethyl-3-phenyl-2-propyn-1-amine **31k** (56.2 mg, 0.300 mmol, 1.00 eq.), THF (0.150 mL), and 2-propanol-d$_8$ (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a neutral Brockmann Grade II alumina column. Purification using neutral Brockmann Grade II alumina flash column chromatography (100 mL of 100% hexanes, 100 mL of 2% ethyl acetate in hexanes, and 200 mL 3% ethyl acetate in hexanes) gives the pure product as a clear colorless oil (36.0 mg, 0.186 mmol, 62% yield).

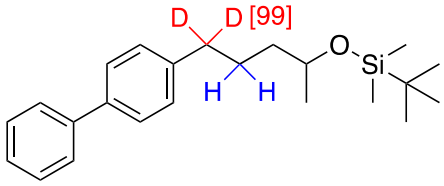
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 – 7.23 (m, 2H), 7.23 – 7.13 (m, 3H), 2.64-2.57 (m, 0.18H), 2.57 – 2.42 (m, 6H), 1.77 (t, *J* = 7.7 Hz, 1.89H), 1.01 (t, *J* = 7.2 Hz, 6H).

^{2}H NMR (61 MHz, Chloroform) δ 2.59 (s, 1.82D), 1.77 (s, 0.11D).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 142.51, 128.48, 128.40, 125.80, 52.55, 46.99, 34.28 – 32.54 (m), 28.72, 11.84.

IR: 3025, 2967, 2931, 2797, 2204, 1605, 1496, 1201, 697.

HRMS: (EI^{+}) m/z: [M]$^{+}$ Calcd for $C_{13}H_{19}D_2N$ 193.1800; Found 193.1793.



((5-([1,1'-biphenyl]-4-yl)(5,5-^{2}H$_2$)pentan-2-yl)oxy)(*tert*-butyl)dimethylsilane [32l]. According to the general procedure C, DTB-DPPBz (6.00 mg, 0.00660 mmol, 0.0220 eq.), Cu(OAc)$_2$ (30.0 µL of a 0.200 M solution in THF, 0.00600 mmol, 0.0200 eq.), THF (0.120 mL) and dimethoxy(methyl)silane (185 µL, 1.50 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of ((5-([1,1'-biphenyl]-4-yl)pent-4-yn-2-yl)oxy)(*tert*-butyl)dimethylsilane **31l** (105 mg, 0.300 mmol, 1.00 eq.), THF (0.150 mL), and 2-propanol-d$_8$ (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 21 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (100

mL of 100% hexanes and 150 mL of 1% ethyl acetate in hexanes) gives the pure product as a colorless oil (76.5 mg, 0.215 mmol, 72% yield).

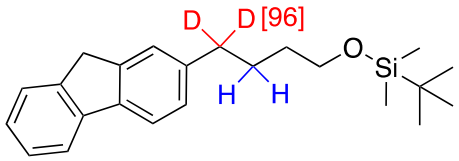
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.68 – 7.61 (m, 2H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 7.3 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 2H), 3.89 (sext, *J* = 6.1 Hz, 1H), 2.72 – 2.64 (m, 0.03H), 1.86 – 1.64 (m, 2H), 1.63 – 1.45 (m, 2H) 1.20 (d, *J* = 6.1 Hz, 3H), 0.96 (s, 9H), 0.12 (s, 6H).

^{2}H NMR (61 MHz, Chloroform) δ 2.69 (s, 1.97D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 141.83, 141.29, 138.71, 128.91, 128.81, 127.12, 127.10, 127.06, 68.58, 39.35, 34.95 (p, *J* = 19.0 Hz), 27.37, 26.06, 23.97, 18.28, -4.23, -4.54.

IR: 3027, 2955, 2856, 2192, 1487, 1253, 1142, 1036, 1003, 831, 756.

HRMS: (ESI^{+}) m/z: [M+Na]$^{+}$ Calcd for $C_{23}H_{32}D_2NaOSi$ 379.2404; Found 379.2397.



(4-(9*H*-fluoren-3-yl)butoxy-4,4-*d*$_2$)(*tert*-butyl)dimethylsilane [32m]. According to the general procedure C, DTB-DPPBz (6.00 mg, 0.00660 mmol, 0.0220 eq.), $Cu(OAc)_2$ (30.0 µL of a 0.200 M solution in THF, 0.00600 mmol, 0.0200 eq.), THF (0.120 mL), and dimethoxy(methyl)silane (185 µL, 1.50 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of ((4-(9*H*-fluoren-3-yl)but-3-yn-1-yl)oxy)(*tert*-butyl)dimethylsilane **31m** (105 mg, 0.300 mmol, 1.00 eq.), THF (0.150 mL), and 2-propanol-d_8 (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (100 mL of 100% hexanes, and 100 mL of 2.5% ethyl acetate in hexanes) gives the pure product as a yellow solid (99.0 mg, 0.279 mmol, 93% yield).

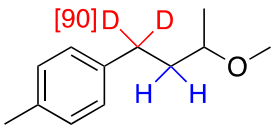
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 (d, *J* = 7.7 Hz, 1H), 7.72 (d, *J* = 7.7 Hz, 1H), 7.55 (d, *J* = 7.3 Hz, 1H), 7.45 – 7.35 (m, 2H), 7.34 – 7.26 (m, 1H), 7.22 (d, *J* = 7.6 Hz, 1H), 3.89 (s, 2H), 3.69 (t, *J* = 6.1, 5.4 Hz, 2H), 2.75 - 2.68 (m, 0.09H), 1.78 – 1.70 (m, 2H), 1.68 – 1.58 (m, 2H), 0.95 (s, 9H), 0.15 – 0.05 (m, 6H).

^{2}H NMR (61 MHz, Chloroform) δ 2.86 (s, 1.91D), 1.35 (s, 0.05D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 143.56, 143.24, 141.91, 141.50, 139.52, 127.14, 126.76, 126.33, 125.19, 125.07, 119.73, 119.68, 63.20, 36.92, 35.24 (p, J = 19.2 Hz), 32.54, 27.92, 26.13, 18.51, -5.11.

IR: 3025, 2926, 2855, 2197, 1640, 1464, 1087, 832.

HRMS: (EI^{+}) m/z: [M]$^{+}$ Calcd for $C_{23}H_{30}D_2OSi$ 354.2348; Found 354.2340.



D_2- 1-(3-methoxybutyl)-4-methylbenzene [32n]. According to the general procedure C, DTB-DPPBz (9.00 mg, 0.00990 mmol, 0.0330 eq.), $Cu(OAc)_2$ (45.0 µL of a 0.200 M solution in THF, 0.00300 mmol, 0.0300 eq.), THF (0.105 mL) and dimethoxy(methyl)silane (222 µL, 1.80 mmol, 6.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 1-(3-methoxybut-1-yn-1-yl)-4-methylbenzene **31n** (52.3 mg, 0.300 mmol, 1 eq.), THF (0.150 mL), and 2-propanol-d_8 (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 23 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (150 mL of 0.5% ethyl acetate in hexanes and 100 mL of 1% ethyl acetate in hexanes) gives the pure product as a colorless oil (33.0 mg, 0.183 mmol, 61% yield).

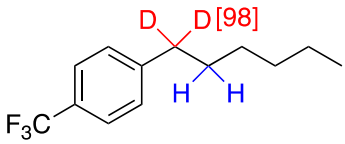
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.14 – 7.09 (m, 4H), 3.38 – 3.28 (m, 4H), 2.70 – 2.59 (m, 0.20H), 2.34 (s, 3H), 1.84 (dd, *J* = 13.6, 7.1 Hz, 1H), 1.69 (dd, *J* = 13.3, 4.2 Hz, 1H), 1.19 (d, *J* = 6.1 Hz, 3H).

^{2}H NMR (61 MHz, Chloroform) δ 2.78 – 2.41 (m, 1.80D), 1.81 (s, 0.06D), 1.65 (s, 0.08D).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 139.31, 135.21, 129.13, 128.41, 76.04, 56.05, 38.27, 30.65 (p, J=19.2 Hz), 21.11, 19.10.

IR: 3018, 2970, 2926, 2818, 2117, 1515, 1148, 1089

HRMS: (ESI$^+$) m/z: $[M+Na]^+$ Calcd for $C_{12}H_{16}D_2NaO$ 203.1383; Found 203.1375.



1-(hexyl-1,1-*d*$_2$)-4-(trifluoromethyl)benzene [32o]. According to the general procedure C, DTB-DPPBz (3.00 mg, 0.00330 mmol, 0.0110 eq.), $Cu(OAc)_2$ (15.0 µL of a 0.200 M solution in THF, 0.00300 mmol, 0.0100 eq.), THF (0.135 mL) and dimethoxy(methyl)silane (185 µL, 1.50 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 1-(1-hexyn-1-yl)-4-(trifluoromethyl)benzene **31o** (68.0 mg, 0.300 mmol, 1.00 eq.), THF (0.150 mL), and 2-propanol-d_8 (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 23 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (150 mL of 100% hexanes) gives the pure product as a clear colorless oil (59.4 mg, 0.256 mmol, 85% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.53 (d, *J* = 7.8 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 2.68 – 2.60 (m, 0.04H), 1.67 – 1.57 (m, 2H), 1.41 – 1.24 (m, 6H), 0.90 (t, *J* = 6.6 Hz, 3H).

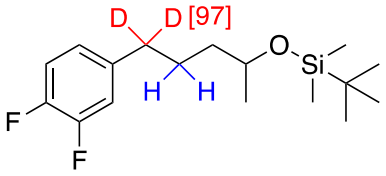
^{2}H NMR (61 MHz, Chloroform) δ 2.65 (s, 1.96D).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 147.14, 128.82, 128.13 (q, *J* = 32.2 Hz), 125.29 (q, *J* = 3.8 Hz), 124.42 (q, *J* = 272.2 Hz), 35.23 (p, *J* = 19.2 Hz), 31.84, 31.20, 29.01, 22.75, 14.21.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.28 (s, 3F).

IR: 3020, 2958, 2927, 2859, 2197, 1621, 1581, 1467, 1323, 1066.

HRMS: (EI$^+$) *m/z*: $[M]^+$ Calcd for $C_{13}H_{15}D_2F_3$ 232.1408; Found 232.1403.



***tert*-butyl((5-(3,4-difluorophenyl)pentan-2-yl-5,5-d_2)oxy)dimethylsilane [32p].** According to the general procedure C, DTB-DPPBz (3.00 mg, 0.00330 mmol, 0.0110 eq.), $Cu(OAc)_2$ (15.0 µL of a 0.200 M solution in THF, 0.00300 mmol, 0.0100 eq.), THF (0.135 mL) and dimethoxy(methyl)silane (185 µL, 1.50 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of *tert*-butyl((5-(3,4-difluorophenyl)pent-4-yn-2-yl)oxy)dimethylsilane **31p** (93.1 mg, 0.300 mmol, 1.00 eq.), THF (0.150 mL), and 2-propanol-d_8 (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (100 mL of 100% hexanes, 100 mL of 3% ethyl acetate in hexanes) gives the pure product as a yellow oil (84.7 mg, 0.268 mmol, 89% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.04 (q, *J* = 8.4 Hz, 1H), 6.99 – 6.91 (m, 1H), 6.89 – 6.82 (m, 1H), 3.79 (sxt, *J* = 5.6 Hz, 1H), 2.58 – 2.50 (m, 0.06H), 1.73 – 1.62 (m, 1H), 1.61 – 1.49 (m, 1H), 1.50 – 1.31 (m, 2H), 1.11 (d, *J* = 6.1 Hz, 3H), 0.88 (s, 9H), 0.03 (s, 6H).

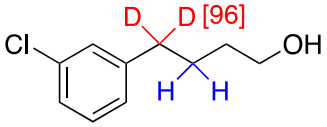
^{2}H NMR (61 MHz, Chloroform) δ 2.54 (s, 1.94D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 151.27 (dd, *J* = 247.3, 12.6 Hz), 148.77 (dd, *J* = 245.5, 12.7 Hz), 139.79 – 139.52 (m), 124.20 (dd, *J* = 6.0, 3.4 Hz), 117.03 (dd, *J* = 16.7, 11.2 Hz) (over-lap of two carbon signals), 68.45, 39.07, 35.33 – 33.67 (m), 27.19, 26.02, 23.94, 18.26, -4.24, -4.59.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -138.71 – -138.91 (m, 1F), -142.67 – -142.84 (m, 1F).

IR: 2955, 2929, 2857, 2237, 1604, 1516, 1255, 1099.

HRMS: (EI$^+$) *m/z*: [M-H] Calcd for $C_{17}H_{25}D_2F_2OSi$ 315.1940 Found 315.1920.



4-(3-chlorophenyl)butan-4,4-d_2-1-ol [32q]. According to the general procedure C, DTB-DPPBz (3.00 mg, 0.00330 mmol, 0.011eq.), $Cu(OAc)_2$ (15.0 µL of a 0.200 M solution in THF, 0.00300 mmol, 0.0100 eq.), THF (0.135 mL) and dimethoxy(methyl)silane (185 µL, 1.50 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of *tert*-butyl((4-(3-chlorophenyl)but-3-yn-1-yl)oxy)dimethylsilane **31q** (88.5 mg, 0.300 mmol, 1 eq.), THF (0.150 mL), and 2-propanol-d_8 (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 19 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (50 mL of 100% hexanes, 100 mL of 3% ethyl acetate in hexanes) gives *tert*-butyl(4-(3-chlorophenyl)butoxy-4,4-d_2)dimethylsilane as a clear colorless oil (86.3 mg, 0.287 mmol, 96% yield). The product was dissolved in THF (1.60 mL) and tetrabutylammonium fluoride (0.600 mL of 1.00 M in THF solution, 0.600 mmol, 2.00 eq.) was added. The reaction was stirred at room temperature for 1-2 hours until complete by TLC analysis. Upon completion, reaction mixture was diluted with Et_2O (10 mL) and quenched with saturated aqueous NH_4Cl (5 mL). The aqueous layer was extracted with Et_2O (3 x 10 mL) and the combined organic layers were

washed with water (10 mL) and brine (10 mL), then dried over anhydrous Na_2SO_4. The mixture was filtered, and the solvent was removed by rotary evaporation. Purification using silica gel flash chromatography (100 mL of hexanes, 100 mL of 10% ethyl acetate in hexanes, 150 mL of 15% ethyl acetate in hexanes) gives the pure product as a clear oil (42.0 mg, 0.225 mmol, 75% yield).

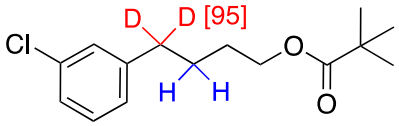
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 – 7.13 (m, 3H), 7.05 (d, *J* = 7.2 Hz, 1H), 3.65 (t, *J* = 6.4 Hz, 2H), 2.63 – 2.55 (m, 0.08H), 1.73 – 1.63 (m, 2H), 1.63 – 1.54 (m, 3H, hydrogen on alcohol is present under peak).

^{2}H NMR (61 MHz, Chloroform) δ 2.59 (s, 1.92D), 1.67 (s, 0.03D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 144.41, 134.14, 129.65, 128.62, 126.72, 126.05, 62.73, 34.67 (p, *J* = 19.5 Hz), 32.20, 27.26.

IR: 3333, 3061, 2932, 2862, 2203, 1598, 1569, 1473, 1055.

HRMS: (EI$^+$) *m/z*: [M]$^+$ Calcd for $C_{10}H_{11}D_2ClO$ 186.0780; Found 186.0773.



4-(3-chlorophenyl)butyl-4,4-*d*$_2$ pivalate [32r]. According to the general procedure C, DTB-DPPBz (3.00 mg, 0.00330 mmol, 0.0110 eq.), $Cu(OAc)_2$ (15.0 µL of a 0.200 M solution in THF, 0.00300 mmol, 0.0100 eq.), THF (0.135 mL), and dimethoxy(methyl)silane (185 µL, 1.50 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 4-(3-chlorophenyl)but-3-yn-1-yl pivalate **31r** (79.4 mg, 0.300 mmol, 1.00 eq.), THF (0.150 mL), and 2-propanol-d_8 (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 21 h at 5 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (100 mL of 100% hexanes, 100 mL of 2.5% ethyl acetate in hexanes, and 100 mL of 5% ethyl acetate in hexanes) gives the pure product as a yellow oil (71.1 mg, 0.263 mmol, 88% yield).

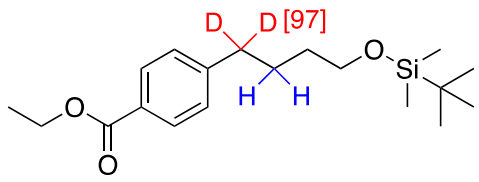
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.24 – 7.12 (m, 3H), 7.08 – 7.00 (m, 1H), 4.07 (t, *J* = 6.0 Hz, 2H), 2.62 - 2.56 (m, 0.10H), 1.75 – 1.60 (m, 4H), 1.19 (s, 9H).

^{2}H NMR (61 MHz, Chloroform) δ 2.60 (s, 1.89D), 1.66 (s, 0.09D).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.70, 144.18, 134.24, 129.72, 128.61, 126.69, 126.17, 64.11, 38.87, 35.08 – 33.93 (m), 28.22, 27.44, 27.34.

IR: 3050, 2958, 2870, 2201, 1725, 1598, 1570, 1479, 1283, 1151.

HRMS: (EI$^+$) m/z: [M]$^+$ Calcd for $C_{15}H_{19}D_2O_2Cl$ 270.1356; Found 270.1350.



Ethyl 4-(4-((*tert*-butyldimethylsilyl)oxy)butyl-1,1-d_2)benzoate [32s]. According to the general procedure C, DTB-DPPBz (3.00 mg, 0.00330 mmol, 0.0110 eq.), $Cu(OAc)_2$ (15.0 µL of a 0.200 M solution in THF, 0.00300 mmol, 0.0100 eq.), THF (0.135 mL) and dimethoxy(methyl)silane (185 µL, 1.50 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of ethyl 4-(4-((*tert*-butyldimethylsilyl)oxy)but-1-yn-1-yl)benzoate **31s** (99.8 mg, 0.300 mmol, 1.00 eq.), THF (0.150 mL), and 2-propanol-d_8 (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 21 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (100 mL of 100% hexanes, 100 mL of 3% ethyl acetate in hexanes) gives the pure product as a clear colorless oil (92.2 mg, 0.274 mmol, 91% yield).

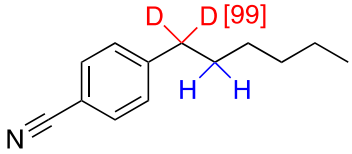
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.95 (d, *J* = 8.2 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.62 (t, *J* = 6.3 Hz, 2H), 2.71 – 2.62 (m, 0.07H), 1.73 – 1.63 (m, 2H), 1.59 – 1.50 (m, 2H), 1.38 (t, *J* = 7.1 Hz, 3H), 0.89 (s, 9H), 0.04 (s, 6H).

^{2}H NMR (61 MHz, Chloroform) δ 2.66 (s, 1.93D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 166.84, 148.15, 129.74, 128.51, 128.19, 63.00, 60.86, 35.11 (p, *J* = 18.5 Hz), 32.40, 27.37, 26.09, 18.48, 14.49, -5.16.

IR: 3030, 2953, 2929, 2857, 2114, 1717, 1612, 1572, 1272, 1177, 1098.

HRMS: (ESI$^+$) *m/z*: $[M+Na]^+$ Calcd for $C_{19}H_{30}D_2NaO_3Si$ 361.2146; Found 361.2138.



4-(hexyl-1,1-d_2)benzonitrile [32t]. According to the general procedure C, DTB-DPPBz (2.00 mg, 0.00220 mmol, 0.0110 eq.), $Cu(OAc)_2$ (10.0 µL of a 0.200 M solution in THF, 0.00200 mmol, 0.0100 eq.), THF (0.0900 mL) and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 4-(hex-1-yn-1-yl)benzonitrile **31t** (36.7 mg, 0.200 mmol, 1 eq.), THF (0.100 mL), and 2-propanol-d_8 (77.0 µL, 1.00 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 5 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (100 mL of 100% hexanes, 100 mL of 1% ethyl acetate in hexanes, 100 mL of 2% ethyl acetate in hexanes, 100 mL of 4% ethyl acetate in hexanes) gives the pure product as a yellow oil (27.4 mg, 0.145 mmol, 72% yield).

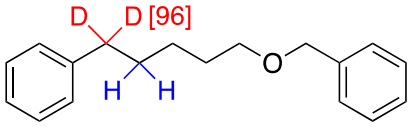
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56 (d, *J* = 7.9 Hz, 2H), 7.26 (d, *J* = 7.4 Hz, 2H), 2.67 – 2.60 (m, 0.03H), 1.59 (t, *J* = 6.9 Hz, 2H), 1.37 – 1.22 (m, 6H), 0.92 – 0.83 (m, 3H).

^{2}H NMR (61 MHz, Chloroform) δ 2.63 (s, 1.97D).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 148.66, 132.19, 129.28, 119.33, 109.54, 36.04 - 34.98 (m), 31.71, 30.91, 28.89, 22.65, 14.16.

IR: 2956, 2925, 2856, 2227, 2080, 1610, 1504, 808.

HRMS: (EI$^+$) m/z: $[M]^+$ Calcd for $C_{13}H_{15}D_2N$ 189.1487; Found 189.1480.



(5-(benzyloxy)pentyl-1,1-d_2)benzene [32u]. According to the general procedure C, DTB-DPPBz (6.00 mg, 0.00660 mmol, 0.0220 eq.), $Cu(OAc)_2$ (30.0 µL of a 0.200 M solution in THF, 0.0600 mmol, 0.0200 eq.), THF (0.120 mL) and dimethoxy(methyl)silane (185 µL, 1.50 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of (5-(benzyloxy)pent-1-yn-1-yl)benzene **31u** (75.0 mg, 0.300 mmol, 1 eq.), THF (0.150 mL), and 2-propanol-d_8 (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (50 mL of 100% hexanes, 100 mL of 2% ethyl acetate in hexanes, 100 mL of 5% ethyl acetate in hexanes) gives the pure product as a yellow oil (71.4 mg, 0.278 mmol, 93% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.34 (m, 4H), 7.31 (t, *J* = 7.3 Hz, 3H), 7.25 – 7.17 (m, 3H), 4.53 (s, 2H), 3.50 (t, *J* = 6.6 Hz, 2H), 2.68 – 2.58 (m, 0.09H), 1.75 – 1.57 (m, 4H), 1.51 – 1.40 (m, 2H).

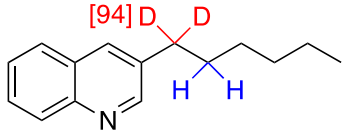
^{2}H NMR (61 MHz, Chloroform) δ 2.63 (s, 1.91D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 142.72, 138.79, 128.51, 128.46, 128.36, 127.74, 127.60, 125.74, 72.99, 70.45, 35.28 (p, *J* = 19.4 Hz), 31.31, 29.76, 25.95.

IR: 3025, 2929, 2855, 2188, 1604, 1495, 1098, 731.

HRMS: (ESI$^+$) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{20}D_2NaO$ 279.1696; Found 279.1688.

Scheme 39. Heterocycle and Complex Small Molecule Scope



D_2-3-hexyl-quinoline [34a]. According to the general procedure C, DTB-DPPBz (9.80 mg, 0.0110 mmol, 0.0550 eq.), $Cu(OAc)_2$ (50.0 µL of a 0.200 M solution in THF, 0.0100 mmol, 0.0500 eq.), THF (0.0500 mL) and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 3-(1-hexyn-1-yl)-quinoline **33a** (41.9 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and 2-propanol-d_8 (77.0 µL, 1.00 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 22 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a neutral alumina brock column. Purification using neutral alumina brock flash column chromatography (100 mL of 100% hexanes and 200 mL of 1% ethyl acetate in hexanes) gives the pure product as a colorless oil (26.0 mg, 0.121 mmol, 61% yield).

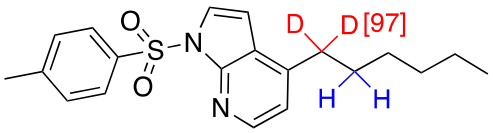
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.78 (d, *J* = 2.3 Hz, 1H), 8.07 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 2.2 Hz, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.65 (t, *J* = 7.3 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 2.82 – 2.71 (m, 0.13H), 1.75 – 1.64 (m, 1.96H), 1.46 – 1.20 (m, 6H), 0.96 – 0.81 (m, 3H).

^{2}H NMR (61 MHz, Chloroform) δ 2.77 (s, 1.87D), 1.70 (s, 0.02D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 152.31, 146.94, 135.46, 134.19, 129.32, 128.58, 128.34, 127.43, 126.61, 33.31 – 31.93 (m), 31.79, 31.09, 28.95, 22.72, 14.21.

IR: 3025, 2923, 2856, 2091, 1569, 1492, 785.

HRMS: (EI$^+$) m/z: [M]$^+$ Calcd for $C_{15}H_{17}D_2N$ 215.1643; Found 215.1638.



D$_2$-4-(hexane)-1-tosyl-1*H*-pyrrolo[2,3-*b*] [34b]. According to the general procedure C, DTB-DPPBz (9.80 mg, 0.0110 mmol, 0.0550 eq.), Cu(OAc)$_2$ (50.0 µL of a 0.200 M solution in THF, 0.0100 mmol, 0.0500 eq.), THF (0.0500 mL) and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 1-tosyl-4-hexyn-yl-1*H*-pyrrolo[2,3-*b*]pyridine **33b** (71.0 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and 2-propanol-d$_8$ (77.0 µL, 1.00 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 25 h at 60 °C. Upon completion, the crude product mixture was dry loaded onto a neutral alumina brock column. Purification using neutral alumina brock flash column chromatography (100 mL of 100% hexanes, 100 mL 3% ethyl acetate in hexanes, 200 mL 5% ethyl acetate in hexanes) gives the pure product as a colorless oil (54.0 mg, 0.151 mmol, 76% yield).

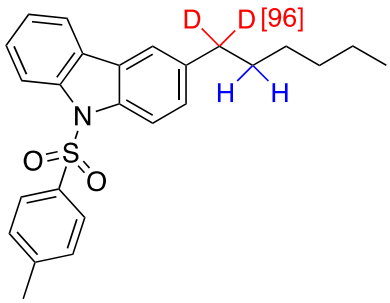
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.30 (d, *J* = 4.9 Hz, 1H), 8.06 (d, *J* = 8.0 Hz, 2H), 7.67 (d, *J* = 4.0 Hz, 1H), 7.32 – 7.19 (m, 2H), 6.96 (d, *J* = 4.9 Hz, 1H), 6.60 (d, *J* = 4.0 Hz, 1H), 2.80 – 2.70 (m, 0.06H), 2.34 (s, 3H), 1.69 – 1.54 (m, 2H), 1.37 – 1.20 (m, 6H), 0.91 – 0.78 (m, 3H).

^{2}H NMR (61 MHz, Chloroform) δ 2.75 (s, 1.94D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 147.16, 145.76, 145.13, 144.96, 135.64, 129.70, 128.12, 125.63, 122.58, 118.67, 103.79, 32.47 - 30.73 (m), 31.67, 29.79, 29.12, 22.61, 21.71, 14.13.

IR: 3100, 2923, 2856, 2110, 1594, 1517, 1367, 1176.

HRMS: (EI$^+$) m/z: [M]$^+$ Calcd for $C_{20}H_{22}D_2N_2O_2S$ 358.1684; Found 358.1679.



3-(1,1-D)hexyl-9-((4-methylphenyl)sulfonyl)-9*H*-carbazole [34c]. According to the general procedure C, DTB-DPPBz (15.0 mg, 0.0170 mmol, 0.0550 eq.), Cu(OAc)$_2$ (75.0 µL of a 0.200 M solution in THF, 0.0150 mmol, 0.0500 eq.), THF (0.0750 mL) and dimethoxy(methyl)silane (222 µL, 1.80 mmol, 6.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 3-(hex-1-yn-1-yl)-9-((4-methylphenyl)sulfonyl)-9*H*-carbazole **33c** (121 mg, 0.30 mmol, 1.00 eq.), THF (0.150 mL), and 2-propanol-d$_8$ (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 60 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (50 mL of 100% hexanes, 100 mL 2% ethyl acetate in hexanes, and 100 mL of 4% ethyl acetate in hexanes) gives the pure product as a colorless oil (75.9 mg, 0.186 mmol, 62% yield).

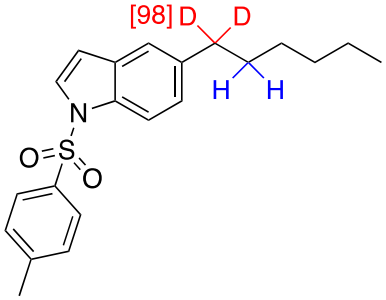
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.32 (d, *J* = 8.2 Hz, 1H), 8.23 (d, *J* = 8.6 Hz, 1H), 7.88 (d, *J* = 7.7 Hz, 1H), 7.73 – 7.66 (m, 3H), 7.47 (t, *J* = 7.8 Hz, 1H), 7.40 – 7.28 (m, 2H), 7.07 (d, *J* = 8.6 Hz, 2H), 2.75-2.69 (m, 0.08H), 2.24 (s, 3H), 1.66 (t, *J* = 7.3 Hz, 2H), 1.44 – 1.25 (m, 6H), 0.94 – 0.86 (m, 3H).

^{2}H NMR (61 MHz, Chloroform) δ 2.72 (s, 1.92D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 144.82, 138.85, 138.74, 136.76, 135.13, 129.71, 128.13, 127.27, 126.64, 126.60, 126.57, 123.88, 120.00, 119.48, 115.28, 114.98, 35.18 (p, *J* = 19.4 Hz), 31.86, 31.76, 29.07, 22.73, 21.58, 14.23.

IR: 2921, 2848, 2119, 1597, 1443, 1187, 1172, 1089, 974.

HRMS: (ESI^{+}) m/z: [M+Na]$^{+}$ Calcd for $C_{25}H_{25}D_2NNaO_2S$ 430.1788; Found 430.1780.



5-(1,1-^{2}H$_2$)hexyl-1-((4-methylphenyl)sulfonyl)-1*H*-indole [34d]. According to the general procedure C, DTB-DPPBz (15.0 mg, 0.0170 mmol, 0.0550 eq.), $Cu(OAc)_2$ (75.0 µL of a 0.200 M solution in THF, 0.0150 mmol, 0.0500 eq.), THF (0.0750 mL) and dimethoxy(methyl)silane (222 µL, 1.80 mmol, 6.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 5-(hex-1-yn-1-yl)-1-((4-methylphenyl)sulfonyl)-1*H*-indole **33d** (105 mg, 0.300 mmol, 1.00 eq.), THF (0.150 mL), and 2-propanol-d_8 (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 21 h at 60 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (50 mL of 100% hexanes, 100 mL 2% ethyl acetate in hexanes, and 100 mL of 4% ethyl acetate in hexanes) gives the pure product as a colorless oil (93.7 mg, 0.262 mmol, 87% yield).

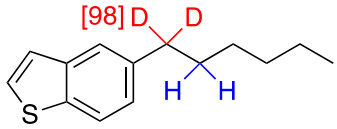
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.89 (d, *J* = 8.5 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.52 (d, *J* = 3.6 Hz, 1H), 7.31 (d, *J* = 1.0 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.14 (dd, *J* = 8.5, 1.4 Hz, 1H), 6.59 (d, *J* = 3.6 Hz, 1H), 2.67 – 2.59 (m, 0.05H), 2.33 (s, 3H), 1.68 – 1.51 (m, 2H), 1.39 – 1.23 (m, 6H), 0.93 – 0.84 (m, 3H).

^{2}H NMR (61 MHz, Chloroform) δ 2.64 (s, 1.95D), 1.61 (s, 0.02D).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 144.87, 138.12, 135.52, 133.33, 131.04, 129.91, 126.90, 126.43, 125.51, 120.68, 113.30, 109.04, 35.17 (p, *J* = 19.3 Hz), 31.84, 31.80, 29.05, 22.71, 21.62, 14.20.

IR: 3029, 2923, 2854, 2116, 1597, 1369, 1174, 1128, 1091, 995, 752, 670.

HRMS: (EI^{+}) m/z: [M]$^{+}$ Calcd for $C_{21}H_{23}D_2NO_2S$ 357.1732; Found 357.1723.



5-(hexyl-1,1-*d*$_2$)benzo[*b*]thiophene [34e]. According to the general procedure C, DTB-DPPBz (3.00 mg, 0.00330 mmol, 0.0110 eq.), $Cu(OAc)_2$ (15.0 µL of a 0.200 M solution in THF, 0.00300 mmol, 0.0100 eq.), THF (0.135 mL) and dimethoxy(methyl)silane (222 µL, 1.80 mmol, 6.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 5-(hex-1-yn-1-yl)benzo[*b*]thiophene **33e** (64.3 mg, 0.300 mmol, 1.00 eq.), THF (0.150 mL), and 2-propanol-d_8 (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 23 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (150 mL of 100% hexanes) gives the pure product as a clear colorless oil (61.5 mg, 0.279 mmol, 93% yield).

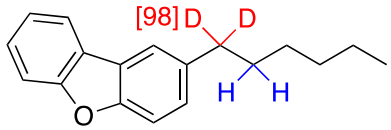
^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.79 (d, *J* = 8.2 Hz, 1H), 7.64 (s, 1H), 7.42 (d, *J* = 5.4 Hz, 1H), 7.29 (d, *J* = 5.4 Hz, 1H), 7.20 (d, *J* = 8.2 Hz, 1H), 2.77 – 2.68 (m, 0.05H), 1.75 – 1.61 (m, 2H), 1.43 – 1.25 (m, 6H), 1.02 – 0.84 (m, 3H).

^{2}H NMR (61 MHz, Chloroform) δ 2.71 (s, 1.95D).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 140.03, 139.11, 137.24, 126.41, 125.54, 123.74, 123.06, 122.22, 35.29 (p, *J* = 19.2 Hz), 31.92, 31.81, 29.08, 22.77, 14.26.

IR: 3100, 2954, 2922, 2854, 2192, 1605, 1550, 1435, 1088.

HRMS: (EI$^+$) m/z: $[M]^+$ Calcd for $C_{14}H_{16}D_2S$ 220.1255; Found 220.1249.



2-(1,1-$^2H_2$)hexyldibenzo[*b*,*d*]furan [34f]. According to the general procedure C, DTB-DPPBz (6.00 mg, 0.00660 mmol, 0.0220 eq.), $Cu(OAc)_2$ (30.0 µL of a 0.200 M solution in THF, 0.00600 mmol, 0.0200 eq.), THF (0.120 mL) and dimethoxy(methyl)silane (185 µL, 1.50 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 2-(hex-1-yn-1-yl)dibenzo[*b*,*d*]furan **33f** (74.5 mg, 0.300 mmol, 1.00 eq.), THF (0.150 mL), and 2-propanol-d_8 (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 22 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (100 mL of 1% ethyl acetate in hexanes and 100 mL of 2% ethyl acetate in hexanes) gives the pure product as a colorless oil (63.8 mg, 0.251 mmol, 84% yield).

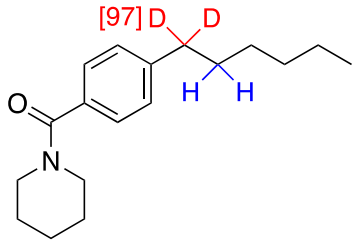
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.96 (d, *J* = 7.7 Hz, 1H), 7.78 (d, *J* = 1.7 Hz, 1H), 7.59 (d, *J* = 8.2 Hz, 1H), 7.54 – 7.42 (m, 2H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.30 (dd, *J* = 8.4, 1.8 Hz, 1H), 2.81-2.74 (m, 0.05H), 1.72 (t, *J* = 6.9 Hz, 2H), 1.47-1.31 (m, 6H), 0.98 – 0.89 (m, 3H).

^{2}H NMR (61 MHz, Chloroform) δ 2.77 (s, 1.95D), 1.72 (s, 0.02D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 156.59, 154.78, 137.51, 127.78, 126.99, 124.46, 124.24, 122.61, 120.65, 120.10, 111.73, 111.27, 35.29 (p, *J* = 19.0 Hz), 32.09, 31.92, 29.07, 22.78, 14.26.

IR: 3050, 2955, 2924, 2855, 2200, 1479, 1449, 1195.

HRMS: (EI$^+$) m/z: [M]$^+$ Calcd for $C_{18}H_{18}D_2O$ 254.1640; Found 254.1635.



(4-(hexyl-1,1-*d*$_2$)phenyl)(piperidin-1-yl)methanone [34g]. According to the general procedure C, DTB-DPPBz (9.85 mg, 0.0110 mmol, 0.0550 eq.), $Cu(OAc)_2$ (50.0 µL of a 0.200 M solution in THF, 0.0100 mmol, 0.0500 eq.), THF (0.950 mL) and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of (4-(hex-1-yn-1-yl)phenyl)(piperidin-1-yl)methanone **33g** (53.9 mg, 0.200 mmol, 1.00 eq.), THF (1.00 mL), and 2-propanol-d_8 (91.9 µL, 1.20 mmol, 6.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (50 mL of 100% hexanes, 200 mL of 25% ethyl acetate in hexanes) gives the pure product as a clear colorless oil (46.0 mg, 0.167 mmol, 84% yield).

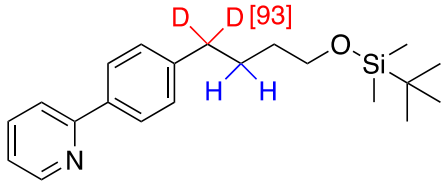
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.30 (d, *J* = 7.9 Hz, 2H), 7.18 (d, *J* = 7.8 Hz, 2H), 3.69 (br s, 2H), 3.37 (br s, 2H), 2.64 – 2.55 (m, 0.07H), 1.77 – 1.44 (m, 8H), 1.37 – 1.25 (m, 6H), 0.88 (t, *J* = 7.0 Hz, 3H).

^{2}H NMR (61 MHz, Chloroform) δ 2.58 (s, 1.93D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 170.62, 144.43, 133.77, 128.40, 126.95, 48.86, 43.22, 35.12 (p, *J* = 19.3 Hz), 31.76, 31.18, 28.91, 26.57, 25.81, 24.70, 22.64, 14.15.

IR: 2923, 2854, 1630, 1564, 1272.

HRMS: (ESI$^+$) m/z: [M+H]$^+$ Calcd for $C_{18}H_{26}D_2NO$ 276.2298; Found 276.2301.



2-(4-(4-((*tert*-butyldimethylsilyl)oxy)butyl-1,1-*d*$_2$)phenyl)pyridine [34h]. According to the general procedure C, DTB-DPPBz (15.0 mg, 0.0165 mmol, 0.0740 eq.), $Cu(OAc)_2$ (75.0 µL of a 0.200 M solution in THF, 0.0150 mmol, 0.0680 eq.), THF (0.750 mL), and dimethoxy(methyl)silane (222 µL, 1.80 mmol, 8.10 eq.) were combined in a 2-dram vial followed by addition of a solution of 2-(4-(4-((*tert*-butyldimethylsilyl)oxy)but-1-yn-1-yl)phenyl)pyridine **33h** (75.0 mg, 0.222 mmol, 1.00 eq.), THF (0.150 mL), and 2-propanol-d_8 (0.115 mL, 1.50 mmol, 6.80 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 21 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a neutral alumina brock column. Purification using neutral alumina brock flash column chromatography (150 mL of 100% hexanes, and 100 mL of 2.5% ethyl acetate in hexanes) gives the pure product as a yellow solid (65.3 mg, 0.190 mmol, 86% yield).

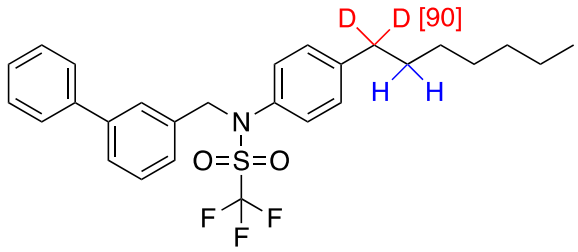
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.68 (d, *J* = 4.9 Hz, 1H), 7.90 (d, *J* = 8.2 Hz, 2H), 7.79 – 7.68 (m, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.23-7.18 (m, 1H), 3.64 (t, *J* = 6.4 Hz, 2H), 2.69-2.63 (m, 0.14H), 1.74 – 1.65 (m, 2H), 1.63 – 1.53 (m, 2H), 0.89 (s, 9H), 0.05 (s, 6H).

^{2}H NMR (61 MHz, Chloroform) δ 2.66 (s, 1.86D), 1.70 (s, 0.04D)

^{13}C NMR (75 MHz, Chloroform-*d*) δ 157.59, 149.66, 143.78, 136.95, 136.85, 128.97, 126.95, 121.93, 120.44, 63.12, 35.55 – 34.17 (m), 32.47, 27.55, 26.11, 18.50, -5.14.

IR: 3020, 2927, 2212, 1600, 1588, 1465, 1253, 1093, 832.

HRMS: (ESI^{+}) m/z: [M+H]$^{+}$ Calcd for $C_{21}H_{30}D_2NOSi$ 344.2380; Found 344.2369.



***N*-([1,1'-biphenyl]-3-ylmethyl)-1,1,1-trifluoro-*N*-(4-(heptyl-1,1-d_2)phenyl)methanesulfonamide [34i].**
According to general procedure C, DTB-DPPBz (9.85 mg, 0.0110 mmol, 0.0567 eq.), $Cu(OAc)_2$ (50.0 µL of a 0.200 M solution in THF, 0.0100 mmol, 0.0515 eq.), THF (0.0500 mL) and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.15 eq.) were combined in a 1-dram vial. In a separate 2-dram vial equipped with a Teflon stir bar was added *N*-([1,1'-biphenyl]-3-ylmethyl)-1,1,1-trifluoro-*N*-(4-(hept-1-yn-1-yl)phenyl)methanesulfonamide **33i** (94.3 mg, 0.194 mmol, 1.00 eq), 3Å molecular sieve powder (20.0 mg), THF (0.600 mL), and 2-propanol-d_8 (77.0 µL, 1.01 mmol, 5.21 eq). The catalyst solution in the 1-dram vial was transferred by 1,4-dioxane (174 µL) to the 2-dram vial. The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 48 h at 40 °C. Upon completion, the crude product mixture was wet loaded onto a silica gel column. Purification using silica gel flash column chromatography (100 mL of 10% ethyl acetate in hexane) gave the desired product. The desired product was then purified by flash C18-reverse phase column chromatography (stationary: C_{18} 60 silica, elution: 150 mL of 100% methanol) to give the pure compound as a colorless oil (89.0 mg, 0.181 mmol, 93%)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.63 – 7.33 (m, 8H), 7.30 – 7.08 (m, 5H), 5.01 (s, 2H), 2.64 – 2.57 (m, 0.20H), 1.69 – 1.56 (m, 2H), 1.44 – 1.26 (m, 8H), 1.04 – 0.86 (m, 3H).

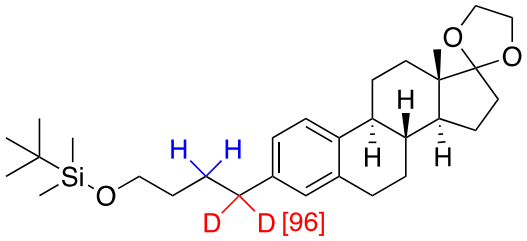
^{2}H NMR (61 MHz, Chloroform) δ 2.61 (s, 1.80D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 144.45, 144.42, 141.60, 140.59, 135.04, 134.12, 129.47, 129.31, 129.19, 128.92, 127.98, 127.65, 127.33, 127.17, 120.70 (q, *J* = 323 Hz), 57.55, 35.75 – 34.80 (m), 31.88, 31.12, 29.33, 29.23, 22.77, 14.21.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -73.59 (s, 3F).

IR: 3061, 3033, 2956, 2927, 2856, 2196, 1394, 1194

HRMS: (ESI^{+}) m/z: [M+Na]$^{+}$ Calcd for $C_{27}H_{28}D_2F_3NO_2SNa$ 514.1972; Found 514.1963.



***tert*-butyldimethyl(4-((8*R*,9*S*,13*S*,14*S*)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydrospiro[cyclopenta[*a*]phenanthrene-17,2'-[1,3]dioxolan]-3-yl)butoxy-4,4-d_2)silane [34j].** According to the general procedure C, DTB-DPPBz (9.85 mg, 0.0110 mmol, 0.0550 eq.), $Cu(OAc)_2$ (50.0 µL of a 0.200 M solution in THF, 0.0100 mmol, 0.0500 eq.), THF (0.0500 mL) and dimethoxy(methyl)silane (148 µL, 1.20 mmol, 6.00 eq.) were combined in a 2-dram vial followed by addition of a solution of *tert*-butyldimethyl((4-((8*R*,9*S*,13*S*,14*S*)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydrospiro[cyclopenta[*a*]phenanthrene-17,2'-[1,3]dioxolan]-3-yl)but-3-yn-1-yl)oxy)silane **33j** (96.2 mg, 0.200 mmol, 1.00 eq.), THF (0.100 mL), and 2-propanol-d_8 (77.0 µL, 1.00 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 72 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (50 mL of 100% hexanes, 100 mL of 2% ethyl acetate in hexanes, 100 mL of 3% ethyl acetate in hexanes) gives the pure product as a yellow oil (89.2 mg, 0.183 mmol, 92% yield).

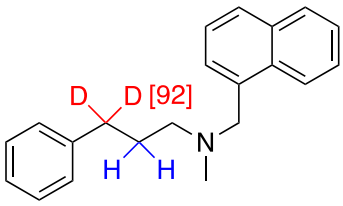
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.22 (d, *J* = 8.0 Hz, 1H), 6.97 (d, *J* = 8.8 Hz, 1H), 6.91 (s, 1H), 4.02 – 3.85 (m, 4H), 3.63 (t, *J* = 6.2 Hz, 2H), 2.90 – 2.80 (m, 2H), 2.59 – 2.51 (m, 0.08H), 2.41 – 2.21 (m, 2H), 2.11 – 1.97 (m, 1H), 1.96 – 1.71 (m, 4H), 1.71 – 1.20 (m, 10H), 0.90 (s, 9H), 0.89 (s, 3H), 0.06 (s, 6H).

^{2}H NMR (61 MHz, Chloroform) δ 2.54 (s, 1.92D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 139.88, 137.82, 136.65, 129.12, 125.80, 125.38, 119.59, 77.16, 65.39, 64.72, 63.20, 49.61, 46.30, 44.10, 39.07, 35.16 – 33.96 (m), 34.37, 32.66, 30.91, 29.69, 27.63, 27.17, 26.13, 22.50, 18.51, 14.46, -5.12.

IR: 2927, 2857, 2241, 1650, 1500, 1100, 1045, 833

HRMS: (ESI$^+$) m/z: $[M+Na]^+$ Calcd for $C_{30}H_{46}D_2NaO_3Si$ 509.3398; Found 509.3395.



***N*-methyl-*N*-(naphthalen-1-ylmethyl)-3-phenylpropan-1-amine-3,3-d_2 [34k].** According to general procedure C, DTB-DPPBz (9.85 mg, 0.0110 mmol, 0.0550 eq.), $Cu(OAc)_2$ (50.0 µL of a 0.200 M solution in THF, 0.0100 mmol, 0.0500 eq.), THF (0.0500 mL) and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq) were combined in a 2-dram vial followed by the addition of a solution of *N*-methyl-*N*-(naphthalen-1-ylmethyl)-3-phenylprop-2-yn-1-amine **33k** (57.1 mg, 0.200 mmol, 1.00 eq), THF (0.720 mL), and 2-propanol-d_8 (77.0 µL, 1.00 mmol, 5.00 eq.). The total volume of THF was calculated based on having a final reaction concentration of 0.24 M based on the alkyne substrate. The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 40 °C. Upon completion, the crude product mixture was filtered through a short silica gel plug and eluted with 25 mL DCM. The solvent was removed by rotary evaporation to afford the crude product. The crude product was dry loaded onto a silica gel

column. Two purifications using silica gel flash column chromatography (first purification: 100 mL of 10% ethyl acetate in hexane with 1% triethyl amine; second purification: 100 mL 5% ethyl acetate in hexane, 100 mL 10% acetone in hexane, 100 mL 15% acetone in hexane), gave the desired compound as a pale-yellow oil (31.0 mg, 0.106 mmol, 53%).

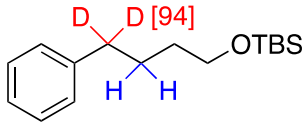
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.32 (d, *J* = 7.8 Hz, 1H), 7.85 (d, *J* = 8.2 Hz, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.56 – 7.44 (m, 2H), 7.44 – 7.37 (m, 2H), 7.26 – 7.22 (m, 2H), 7.17 (d, *J* = 7.1 Hz, 1H), 7.13 (d, *J* = 7.4 Hz, 2H), 3.89 (s, 2H), 2.63 – 2.58 (m, 0.16H), 2.51 (t, *J* = 6.9 Hz, 2H), 2.22 (s, 3H), 1.88 (t, *J* = 6.5 Hz, 1.84H).

^{2}H NMR (61 MHz, Chloroform) δ 2.61 (s, 1.84D), 1.90 (s, 0.08D).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 142.49, 135.17, 133.98, 132.66, 128.54, 128.50, 128.37, 127.94, 127.50, 125.86, 125.76, 125.68, 125.24, 124.87, 61.04, 57.49, 42.38, 33.58 – 32.38 (m), 29.13.

IR: 3057, 3023, 2936, 2838, 2789, 2199, 1146

HRMS: (EI^{+}) m/z: [M]$^{+}$ Calcd for $C_{21}H_{21}D_2N$ 291.1956; Found 291.1950.



***Tert*-butyldimethyl(4-phenylbutoxy-4,4-d_2)silane [34l].** According to the general procedure C, DTB-DPPBz (98.5 mg, 0.110 mmol, 0.0550 eq.), $Cu(OAc)_2$ (500 µL of a 0.200 M solution in THF, 0.100 mmol, 0.0500 eq.), THF (4.10 mL) and dimethoxy(methyl)silane (1.23 mL, 10.0 mmol, 5.00 eq.) were combined in a 100 mL oven-dried round bottom flask equipped with a Teflon stir bar, followed by addition of a solution of *tert*-butyldimethyl((4-phenylbut-3-yn-1-yl)oxy)silane **35** (521 mg, 2.00 mmol, 1.00 eq.), THF (4.10 mL), and 2-propanol-d_8 (0.766 mL, 10.0 mmol, 5.00 eq). The total volume of THF was calculated based on having a final reaction concentration of 0.23 M based on the alkyne substrate. The 100 mL round bottom flask was capped with a Teflon septa, and the reaction stirred for 24 h at 40 °C under a N_2 filled balloon. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (200 mL of 100% hexanes, 600 mL of 3% ethyl acetate in hexanes) gave the desired product as a clear, colorless oil (511 mg, 1.92 mmol, 96% yield).

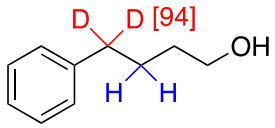
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.28 (m, 2H), 7.24 – 7.18 (m, 3H), 3.67 (t, *J* = 6.3 Hz, 2H), 2.68 – 2.61 (m, 0.13H), 1.74 – 1.67 (m, 1.87H), 1.65 – 1.55 (m, 2H), 0.94 (s, 9H), 0.09 (s, 6H).

^{2}H NMR (61 MHz, Chloroform) δ 2.65 (s, 1.87D), 1.71 (s, 0.06D).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 142.69, 128.53, 128.38, 125.77, 63.15, 35.19 (p, *J* = 19.1 Hz), 32.53, 27.65, 26.13, 18.50, -5.13.

IR: 3020, 2985, 2950, 2925, 2890, 2110, 1100

HRMS: (EI^{+}) m/z: [M-C_4H_9]$^{+}$ Calcd for $C_{12}H_{17}D_2OSi$ 209.1331; Found 209.1323. The major ion peak represents the parent molecule after loss of the *t*-Bu cation.



4-Phenylbutan-4,4-d_2-1-ol [36]. *Tert*-butyldimethyl(4-phenylbutoxy-4,4-d_2)silane **7l** (451 mg, 1.69 mmol, 1.00 eq.) was dissolved in THF (17 mL) and tetrabutylammonium fluoride (3.38 mL of a 1.00 M in THF solution, 3.38 mmol, 2.00 eq.) was added to the reaction mixture. The reaction was stirred at room temperature overnight. Upon completion, the reaction mixture was quenched with saturated aqueous NH_4Cl (20 mL) and evaporated to remove the THF. The aqueous layer was extracted with ethyl acetate (3 x 20 mL) and the combined organic layers were washed with brine (10 mL) then dried over anhydrous Na_2SO_4. The mixture was filtered, and the solvent was removed by rotary evaporation. Purification using silica gel flash column chromatography (100 mL of hexanes, 100 mL of 10% ethyl acetate in hexanes, 500 mL of 15% ethyl acetate in hexanes) gave the pure product as a clear oil (217 mg, 1.43 mmol, 85% yield).

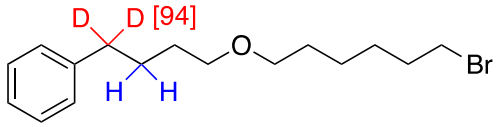
^{1}H NMR (400 MHz, Chloroform-*d* δ 7.34 – 7.27 (m, 2H), 7.24 – 7.17 (m, 3H), 3.64 (t, *J* = 6.4 Hz, 2H), 2.69 – 2.59 (m, 0.13H), 2.31 – 2.07 (m, 1H), 1.73 – 1.66 (m, 1.87H), 1.65 – 1.58 (m, 2H).

^{2}H NMR (61 MHz, Chloroform) δ 2.64 (s, 1.87D), 1.71 (s, 0.06D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 142.35, 128.47, 128.36, 125.81, 62.73, 35.10 (p, *J* = 19.3 Hz), 32.28, 27.47.

IR: 3327, 3060, 3024, 2931, 2862, 2197, 1604, 1495

HRMS: (EI$^+$) m/z: $[M]^+$ Calcd for $C_{10}H_{12}D_2O$ 152.1170; Found 152.1164.



(4-((6-Bromohexyl)oxy)butyl-1,1-d_2)benzene [37]. According to a previously reported procedure[1], to an oven dried 50 mL Schlenk tube equipped with a Teflon stir bar was added 4-Phenylbutan-4,4-d_2-1-ol (148 mg, 0.972 mmol, 1.00 eq.) dissolved in THF (10 mL). This was cooled to 0 °C for 10 minutes followed by addition of NaH (60% dispersion in mineral oil, 78.0 mg, 1.94 mmol, 2.00 eq.). This was stirred at 0 °C for 10 minutes followed by dropwise addition of 1,6-dibromohexane (237 mg, 0.972 mmol, 1.00 eq.). The reaction was equipped with a cold finger condenser and heated in a silicon oil bath to 75 °C overnight. Upon completion, the reaction was quenched with DI water (10 mL) and extracted with ethyl acetate (3 X 20 mL). The combined organic layers were washed with brine (1 X 20 mL), and dried over anhydrous Na_2SO_4. The mixture was filtered, dry loaded on to silica gel, and purified twice by flash column chromatography (first purification: 200 mL 100% hexane, 200 mL 0.5% ethyl acetate in hexane, 200 mL 1.5% ethyl acetate in hexane, 400 mL 3% ethyl acetate in hexane, 200 mL 20% ethyl acetate in hexane; second purification: 100 mL 100% hexanes, 100 mL 0.5% diethyl ether in hexanes, 300 mL 1% diethyl ether in hexanes) to give the desired product as a clear oil (53.0 mg, 0.168 mmol, 17% yield).

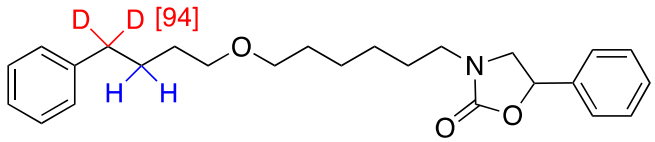
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.25 (m, 2H), 7.21 – 7.16 (m, 3H), 3.47 – 3.35 (m, 6H), 2.66 – 2.58 (m, 0.13H), 1.87 (p, *J* = 6.9 Hz, 2H), 1.73 – 1.53 (m, 6H), 1.51 – 1.33 (m, 4H).

^{2}H NMR (61 MHz, Chloroform) δ 2.63 (s, 1.87D).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 142.54, 128.52, 128.37, 125.79, 70.86, 70.83, 35.11 (p, *J* = 19.6 Hz), 33.99, 32.86, 29.69, 29.47, 28.12, 28.04, 25.55.

IR: 3073, 2990, 2887, 2811, 2224, 1020, 673

HRMS: (ESI^{+}) m/z: [M+H]$^{+}$ Calcd for $C_{16}H_{24}D_2OBr$ 315.1294; Found 315.1284.



5-Phenyl-3-(6-(4-phenylbutoxy-4,4-d_2)hexyl)oxazolidin-2-one [38]. According to a previously reported procedure[2], to an oven dried 25 mL round bottom flask equipped with a Teflon stir bar was added a solution of NaH (60% dispersion in mineral oil, 5.15 mg, 0.129 mmol, 1.11 eq) in DMF (0.300 mL). Under N_2, the mixture was cooled to 0 °C for 10 minutes and then a solution of **5-phenyloxazolidin-2-one** (18.9 mg, 0.116 mmol, 1.00 eq) in DMF (0.600 mL) was added dropwise and stirred at 0 °C for 10 minutes. A solution of (4-((6-Bromohexyl)oxy)butyl-1,1-d_2)benzene (56.4 mg, 0.179 mmol, 1.54 eq) in DMF (0.300 mL) was then added dropwise and the reaction stirred at 0 °C for 1 h and then at room temperature for 3 h. Upon reaction completion, the mixture was re-cooled to 0 °C and quenched with 2 M HCl (4 mL) dropwise. The organic phase was extracted with ethyl acetate (1 X 20 mL) and then the organic phase was washed with brine (1 X 20 mL) and dried over anhydrous Na_2SO_4. The mixture was filtered, dry loaded onto silica gel, and purified by flash column chromatography (100 mL of 100% hexane, 100 mL of 10% ethyl acetate in hexanes, 100 mL of 20% ethyl acetate in hexanes, 100 mL 30% ethyl acetate in hexanes, 100 mL 50% ethyl acetate in hexanes) to give the desired product as a clear oil (43.0 mg, 0.108 mmol, 93% yield).

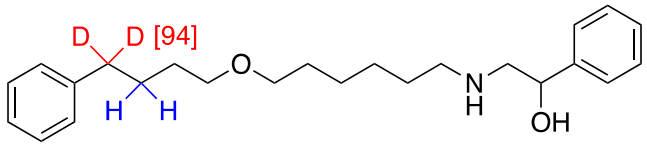
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 – 7.32 (m, 5H), 7.30 – 7.24 (m, 2H), 7.21 – 7.13 (m, 3H), 5.47 (t, *J* = 8.1 Hz, 1H), 3.89 (t, *J* = 8.7 Hz, 1H), 3.44 – 3.35 (m, 5H), 3.35 – 3.21 (m, 2H), 2.66 – 2.57 (m, 0.13H), 1.73 – 1.48 (m, 8H), 1.43 – 1.28 (m, 4H).

^{2}H NMR (61 MHz, Chloroform) δ 2.61 (s, 1.87D), 1.66 (s, 0.04D)

^{13}C NMR (75 MHz, Chloroform-*d*) δ 157.98, 142.52, 138.99, 128.98, 128.84, 128.49, 128.33, 125.75, 125.57, 74.37, 70.82, 70.79, 52.23, 44.22, 35.08 (p, *J* = 20.1 Hz), 29.71, 29.44, 28.02, 27.41, 26.56, 25.95.

IR: 3061, 3014, 2934, 2860, 2196, 1744, 1216, 1111

HRMS: (ESI^{+}) m/z: [M+H]$^{+}$ Calcd for $C_{25}H_{32}D_2NO_3$ 398.2666; Found 398.2661.



1-Phenyl-2-((6-(4-phenylbutoxy-4,4-d_2)hexyl)amino)ethan-1-ol [39]. According to a previously reported procedure[2], to an oven dried 50 mL Schlenk tube equipped with a Teflon stir bar was added 5-Phenyl-3-(6-(4-phenylbutoxy-4,4-d_2)hexyl)oxazolidin-2-one (36.3 mg, 0.0913 mmol, 1.00 eq) and THF (0.850 mL). This was stirred under N_2 for 10 minutes followed by addition of $KOSiMe_3$ (21.7 mg, 0.169 mmol, 1.85 eq.). The reaction was equipped with a cold finger condenser and heated to 75 °C for 6 h and the reaction progress was monitored by TLC. Upon reaction completion, the reaction was cooled to room temperature and quenched with DI water (5 mL). The organic phase was extracted with ethyl acetate (3 X 10 mL) and then the combined organic layers were washed with brine (1 X 10 mL) and then dried over Na_2SO_4. This was filtered and then concentrated by rotary evaporation to give the desired product as a yellow solid (18.6 mg, 0.0500 mmol, 55% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.31 (m, 4H), 7.30 – 7.24 (m, 3H, peak overlaps with residual $CHCl_3$ peak), 7.20 – 7.14 (m, 3H), 4.81 (d, *J* = 6.1 Hz, 1H), 3.93 (s, 2H), 3.39 (dt, *J* = 13.4, 6.5 Hz, 4H), 3.00 – 2.58 (m, 4.13H), 1.71 – 1.52 (m, 8H), 1.36 – 1.30 (m, 4H).

^{2}H NMR (61 MHz, Chloroform) δ 2.61 (s, 1.87D).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 142.58, 142.46, 128.54 (2 carbons overlapping), 128.39, 127.68, 125.93, 125.81, 71.27, 70.94, 70.87, 56.91, 49.30, 35.14 (p, *J* = 19.9 Hz), 29.86, 29.81, 29.51, 28.07, 27.14, 26.19.

IR: 3297, 3083, 3060, 3025, 2927, 2853, 2796, 2191, 1557, 1119

HRMS: (ESI$^+$) m/z: $[M+H]^+$ Calcd for $C_{24}H_{34}D_2NO_2$ 372.2873; Found 372.2862.

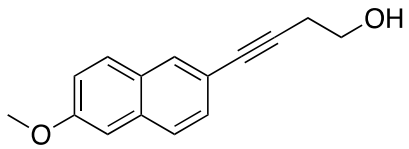
Synthesis of Alkyne Starting Materials

General Sonogashira Coupling Procedure for the Synthesis of Internal Alkynes[3] (D)

To a flame-dried round bottom flask or Schlenk tube under N_2 was added triethylamine (15.0 mL, 0.200 M), which was degassed for 15 minutes. The aryl halide (3.00 mmol, 1.00 eq.), $Pd(PPh_3)_2Cl_2$ (42.0 mg, 0.06 mmol, 0.02 eq.) and CuI (23.0 mg, 0.120 mmol, 0.0400 eq.) were then sequentially added at room temperature. The mixture was stirred for 10 minutes followed by the addition of the alkyne reagent (3.30 mmol, 1.10 eq.). After 16 h of stirring at either room temperature or reflux, the reaction was cooled to room temperature, quenched with water (10 mL) and extracted with ethyl acetate (3 x 15 mL). The organic layers were washed with brine (3 x 10 mL) and then dried over anhydrous Na_2SO_4. The mixture was filtered, and the solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography to give the desired aryl substituted alkyne.

General TBS protection of alcohol containing substrates[3] (E)

To a flame-dried round bottom flask under a N_2 atmosphere with a Teflon stirbar, was added the alcohol substrate (1.86 mmol, 1.00 eq.), dry dichloromethane (5.00 mL) followed by imidazole (253 mg, 3.72 mmol, 2.00 eq.) and *tert*-butyldimethylsilyl chloride (307 mg, 2.04 mmol, 1.10 eq.). The reaction was stirred at room temperature overnight. Upon completion, the reaction mixture was quenched with water (20 mL) and extracted with diethyl ether (2 x 15 mL). The combined organic layers were washed with brine (15 mL) and dried over anhydrous Na_2SO_4. The mixture was filtered, and the solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography to give the desired TBS protected alcohol.



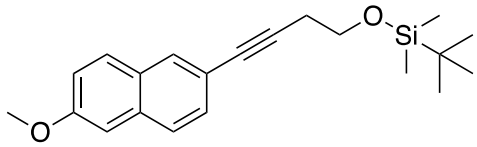
4-(6-Methoxy-2-naphthalenyl)-3-butyn-1-ol. Following general procedure D, triethylamine (38.0 mL), 2-iodo-6-methyoxynaphthalene (2.14 g, 7.55 mmol, 1.00 eq.), $Pd(PPh_3)_2Cl_2$ (106 mg, 0.151 mmol, 0.0200 eq.) and CuI (72.0 mg, 0.378 mmol, 0.0500 eq.) were added to a flame dried round bottom flask, and was stirred for 15 minutes under N_2 at room temperature. 3-Butyn-1-ol (0.629 mL, 8.31 mmol, 1.10 eq.) was then added in one portion, the reaction was equipped with a cold finger condenser, and the reaction was heated to 60°C and stirred under N_2 overnight. Post-reaction work up, the crude product was purified by flash column chromatography (500 mL 10% ethyl acetate in hexanes and 1500 mL 20% ethyl acetate in hexanes) to give the pure product as a white solid (1.34 g, 5.92 mmol, 78% yield).

^{1}H NMR (400 MHz, Chloroform-*d*)
δ 7.86 (s, 1H), 7.66 (t, *J* = 8.5 Hz, 2H), 7.46 – 7.41 (m, 1H), 7.14 (dd, *J* = 8.9, 2.4 Hz, 1H), 7.11 – 7.07 (m, 1H), 3.91 (s, 3H), 3.85 (t, *J* = 8.5 Hz, 2H), 2.74 (t, *J* = 6.2 Hz, 2H) 1.95 (br s, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.15, 133.91, 131.20, 129.18, 129.17, 128.43, 126.74, 119.34, 118.19, 105.72, 85.85, 82.94, 61.24, 55.33, 23.94.

IR: 3244, 3066, 3002, 2958, 2936, 2882, 2831, 1593, 1238, 1030.

HRMS: (ESI$^+$) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{15}O_2$ 227.1074 Found 227.1069.



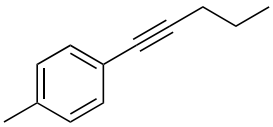
***Tert*-butyl-(4-(6-methoxy-2-naphthalenyl)-3-butyn-1-oxy)-dimethylsilane [31a].** Following a previously reported procedure[3], 4-(6-methoxy-2-naphthalenyl)-3-butyn-1-ol (1.34 g, 5.92 mmol, 1.00 eq.), dry DCM (18.0 mL), imidazole (804 mg, 11.8 mmol, 2.00 eq.), and *tert*-butyldimethylsilyl chloride (981 mg, 6.51 mmol, 1.10 eq.) were combined in a flame-dried round bottom flask. Post-reaction work up, the crude product was purified by flash column chromatography (500 mL 1.5% ethyl acetate in hexanes, 500 mL 3% ethyl acetate in hexanes) to give the pure product as a white solid (1.92 g, 5.64 mmol, 95% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.84 (s, 1H), 7.66 (t, *J* = 9.5 Hz, 2H), 7.46 – 7.39 (m, 1H), 7.17 – 7.11 (m, 1H), 7.11 – 7.07 (m, 1H) 3.91 (s, 3H), 3.86 (t, *J* = 7.1 Hz, 2H), 2.68 (t, *J* = 7.1 Hz, 2H), 0.94 (s, 9H), 0.13 (s, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.18, 133.91, 131.14, 129.37, 129.30, 128.62, 126.79, 119.37, 118.83, 105.85, 86.83, 82.11, 62.20, 55.45, 26.07, 24.07, 18.53, -5.07.

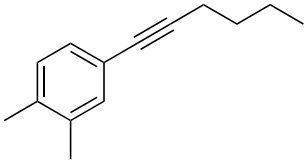
IR: 3025, 2954, 2933, 2914, 2861, 1603, 1203, 1248, 1099.

HRMS: (ESI$^+$) *m/z*: $[M+Na]^+$ Calcd for $C_{21}H_{28}NaO_2Si$ 363.1759 Found 363.1751.



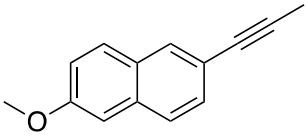
1-Methyl-4-(pent-1-yn-yl)benzene [31c]. Following general procedure D, triethylamine (12.0 mL), 4-iodotoluene (500 mg, 2.29 mmol, 1.00 eq), $Pd(PPh_3)_2Cl_2$ (32.1 mg, 0.0458 mmol, 0.0200 eq.), CuI (17.4 mg, 0.0916 mmol, 0.0400 eq.) were added to a 100 mL flame dried round bottom flask, and was stirred for 15 minutes under N_2 at room temperature. 1-pentyne (0.248 mL, 2.52 mmol, 1.10 eq.) was then added in one portion, the reaction was stirred at room temperature under N_2 overnight. Post-reaction work up, the crude product was purified by flash column chromatography (500 mL of 100% hexanes) to give the pure product as a clear colorless oil (289 mg, 1.83 mmol, 80% yield). The NMR data was consistent with previously reported spectra.[4]

^{1}H NMR (400 MHz, Chloroform-*d*)
δ 7.29 (d, *J* = 7.7 Hz, 2H), 7.08 (d, *J* = 7.7 Hz, 2H), 2.38 (t, *J* = 7.0 Hz, 2H), 2.33 (s, 3H), 1.63 (sxt, *J* = 7.3 Hz, 2H), 1.04 (t, *J* = 7.4 Hz, 3H).



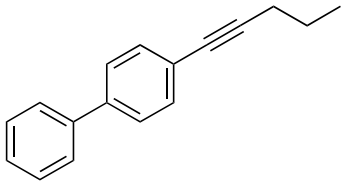
4-(1-hexyn-1-yl)-1,2-dimethyl-benzene [31d]. Following general procedure D, triethylamine (25.0 mL), 4-iodo-1,2-dimethyl-benzene (0.614 mL, 4.31 mmol, 1.00 eq), $Pd(PPh_3)_2Cl_2$ (60.5 mg, 0.0862 mmol, 0.0200 eq.), CuI (32.8 mg, 0.172 mmol, 0.0400 eq.) were added to a 100 mL flame dried round bottom flask, and was stirred for 15 minutes under N_2 at room temperature. 1-Hexyne (0.544 mL, 4.74 mmol, 1.10 eq.) was then added in one portion, the reaction was equipped with a cold finger condenser, and the reaction was heated to 100°C and stirred under N_2 overnight. Post-reaction work up, the crude product was purified by flash column chromatography (500 mL of 100% hexanes) to give the pure product as a red oil (484 mg, 2.60 mmol, 60% yield). The NMR data was consistent with previously reported spectra.[5]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.19 (s, 1H), 7.13 (d, *J* = 7.8 Hz, 1H), 7.04 (d, *J* = 7.7 Hz, 1H), 2.40 (t, *J* = 7.0 Hz, 2H), 2.24 (s, 3H), 2.22 (s, 3H), 1.65 – 1.54 (m, 2H), 1.54 – 1.44 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H).



2-methoxy-6-(1-propyn-1-yl)-naphthalene [23]. Adapted from a previously reported procedure[6], triethylamine (5.00 mL), 2-iodo-6-methoxy-naphthalene (500 mg, 1.76 mmol, 1.00 eq), $Pd(PPh_3)_2Cl_2$ (24.7 mg, 0.0352 mmol, 0.0200 eq.), CuI (13.4 mg, 0.0704 mmol, 0.0400 eq.) were added to a 100 mL flame dried round bottom flask, and was stirred for 15 minutes under N_2 at 50°C. 1-Propyne in THF (1.94 mL of a 1M solution, 1.94 mmol, 1.10 eq.) was then added in one portion and the reaction stirred under N_2 overnight. Post-reaction work up, the crude product was purified by flash column chromatography (100 mL of 100% hexanes, 400 mL of 2% ethyl acetate in hexanes) to give the pure product as a light yellow solid (221 mg, 1.13 mmol, 64% yield). The NMR data was consistent with previously reported spectra.[7]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 (s, 1H), 7.65 (t, *J* = 9.5 Hz, 2H), 7.41 (d, *J* = 8.6 Hz, 1H), 7.17 – 7.06 (m, 2H), 3.92 (s, 3H), 2.09 (s, 3H).



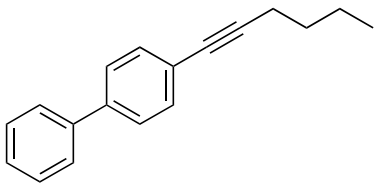
4-(1-Pentyn-1-yl)-1,1'-biphenyl [31f]. Following general procedure D, triethylamine (18.0 mL), 4-iodo-1,1'-biphenyl (1.00 g, 3.57 mmol, 1.00 eq), $Pd(PPh_3)_2Cl_2$ (50.1 mg, 0.0714 mmol, 0.0200 eq.), CuI (27.2 mg, 0.143 mmol, 0.0400 eq.) were added to a 100 mL flame dried round bottom flask, and was stirred for 15 minutes under N_2 at room temperature. 1-Pentyne (0.387 mL, 3.93 mmol, 1.10 eq.) was then added in one portion, the reaction was equipped with a cold finger condenser, and the reaction was heated to 100°C and stirred under N_2 overnight. Post-reaction work up, the crude product was purified by flash column chromatography (500 mL of 100% hexanes) to give the pure product as a yellow oil (649 mg, 2.95 mmol, 83% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (d, *J* = 7.2 Hz, 2H), 7.56 – 7.51 (m, 2H), 7.51 – 7.42 (m, 4H), 7.36 (t, *J* = 7.4 Hz, 1H), 2.43 (t, *J* = 7.1 Hz, 2H), 1.67 (sxt, *J* = 7.2 Hz, 2H), 1.08 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 140.60, 140.29, 132.07, 128.91, 127.55, 127.07, 126.98, 123.18, 91.10, 80.72, 22.37, 21.60, 13.70.

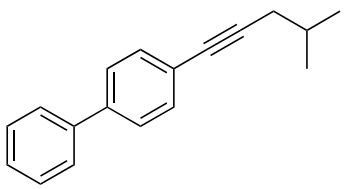
IR: 3045, 2957, 2867, 1690, 1580, 1482, 1005, 839.

HRMS: (EI^+) m/z: $[M]^+$ Calcd for $C_{17}H_{16}$ 220.1252; Found 220.1247.



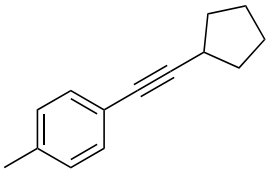
4-(1-hexyn-1-yl)-1,2-dimethyl-benzene [31g]. Following general procedure D, triethylamine (18.0 mL), 4-iodo-1,1'-biphenyl (1.00 g, 3.57 mmol, 1.00 eq), $Pd(PPh_3)_2Cl_2$ (50.1 mg, 0.0714 mmol, 0.0200 eq.), CuI (27.2 mg, 0.143 mmol, 0.0400 eq.) were added to a 100 mL flame dried round bottom flask, and was stirred for 15 minutes under N_2 at room temperature. 1-Hexyne (0.451 mL, 3.93 mmol, 1.10 eq.) was then added in one portion, the reaction was stirred at room temperature under N_2 overnight. Post-reaction work up, the crude product was purified by flash column chromatography (500 mL of 100% hexanes) to give the pure product as a yellow-orange oil (737 mg, 3.15 mmol, 88% yield). The NMR data was consistent with previously reported spectra.[8]

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 7.1 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.50 - 7.41 (m, 4H), 7.35 (t, *J* = 7.4 Hz, 1H), 2.45 (t, *J* = 7.0 Hz, 2H), 1.67 – 1.57 (m, 2H), 1.56 – 1.45 (m, 2H), 0.97 (t, *J* = 7.2 Hz, 3H).



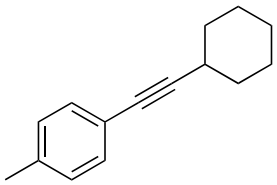
4-(4-methyl-1-pentyn-1-yl)-1,1'-biphenyl [31h]. Following general procedure D, triethylamine (10.0 mL), 4-iodo-1,1'-biphenyl (500 mg, 1.79 mmol, 1.00 eq), $Pd(PPh_3)_2Cl_2$ (25.1 mg, 0.0358 mmol, 0.0200 eq.), CuI (13.6 mg, 0.0716 mmol, 0.0400 eq.) were added to a 100 mL flame dried round bottom flask, and was stirred for 15 minutes under N_2 at room temperature. 4-methyl-1-pentyne (0.232 mL, 1.97 mmol, 1.10 eq.) was then added in one portion and the reaction stirred under N_2 overnight. Post-reaction work up, the crude product was purified by flash column chromatography (500 mL of 100% hexanes) to give the pure product as an orange oil (223 mg, 0.952 mmol, 53% yield). The NMR data was consistent with previously reported spectra.[8]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 7.4 Hz, 2H), 7.53 (d, *J* = 8.2 Hz, 2H), 7.50 – 7.40 (m, 4H), 7.35 (t, *J* = 7.6 Hz, 1H), 2.33 (d, *J* = 6.7 Hz, 2H), 1.93 (hep, *J* = 6.8 Hz, 1H), 1.06 (d, *J* = 6.7 Hz, 6H).



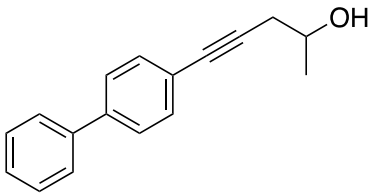
1-(cyclopentylethynyl)-4-methylbenzene [31i]. Following general procedure D, triethylamine (10.0 mL), 4-iodotoluene (1.22 g, 5.58 mmol, 1.05 eq), $Pd(PPh_3)_2Cl_2$ (37.3 mg, 0.0531 mmol, 0.0100 eq.), CuI (50.7 mg, 0.266 mmol, 0.0500 eq.) were added to a 100 mL flame dried round bottom flask, and was stirred for 15 minutes under N_2 at room temperature. Cyclopentylacetylene (0.616 mL, 5.31 mmol, 1.00 eq.) was then added in one portion, the reaction was refluxed at 60 ˚C N_2 overnight. Post-reaction work up, the crude product was purified by flash column chromatography (400 mL of 100% hexanes) to give the pure product as a clear colorless oil (867 mg, 4.70 mmol, 89% yield). The NMR data was consistent with previously reported spectra.[9]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 (d, *J* = 8.3 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 2.81 (p, *J* = 7.5 Hz, 1H), 2.33 (s, 3H), 2.05 – 1.93 (m, 2H), 1.84 – 1.55 (m, 6H).



1-(cyclohexylethynyl)-4-methylbenzene [31j]. Following general procedure D, triethylamine (15.0 mL, 0.500 M), 4-iodotoluene (1.69 g, 7.77 mmol, 1.05 eq), $Pd(PPh_3)_2Cl_2$ (52.0 mg, 0.0740 mmol, 0.0100 eq.), CuI (70.5 mg, 0.370 mmol, 0.0500 eq.) were added to a 100 mL flame dried round bottom flask, and was stirred for 15 minutes under N_2 at room temperature. Cyclohexylacetylene (0.968 mL, 7.40 mmol, 1.00 eq.) was then added in one portion, the reaction was refluxed at 60 ˚C N_2 overnight. Post-reaction work up, the crude product was purified by flash column chromatography (400 mL of 100% hexanes) to give the pure product as a clear colorless oil (1.41 g, 7.11 mmol, 96% yield). The NMR data was consistent with previously reported spectra.[9]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 (d, *J* = 8.0 Hz, 2H), 7.08 (d, *J* = 7.8 Hz, 2H), 2.62 – 2.53 (m, 1H), 2.33 (s, 3H), 1.93 – 1.84 (m, 2H), 1.81 – 1.70 (m, 2H), 1.60 – 1.47 (m, 3H), 1.42 – 1.28 (m, 3H).



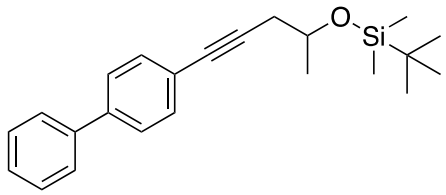
5-([1,1'-biphenyl]-4-yl)pent-4-yn-2-ol. Following general procedure D, triethylamine (9.00 mL), 4-iodo-1,1'-biphenyl (500 mg, 1.79 mmol, 1.00 eq.), $Pd(PPh_3)_2Cl_2$ (25.1 mg, 0.0358 mmol, 0.0200 eq.), CuI (17.0 mg, 0.0895 mmol, 0.0500 eq.) were added to a 25 mL flame dried Schlenk tube, and was stirred for 15 minutes under N_2. 4-pentyn-2-ol (0.186 mL, 1.97 mmol, 1.10 eq.) was then added in one portion, and the reaction stirred under N_2 at room temperature overnight. Post-reaction work up, the crude product was purified by flash column chromatography (500 mL of 10% ethyl acetate in hexanes, 250 mL of 20% ethyl acetate in hexanes) to give the pure product as a white solid (347 mg, 1.47 mmol, 82% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 – 7.42 (m, 8H), 7.36 (t, *J* = 7.5 Hz, 1H), 4.07 (sxt, *J* = 6.2 Hz, 1H), 2.70 – 2.53 (m, 2H), 1.88 (br s, 1H), 1.35 (d, *J* = 6.3 Hz, 3H).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 140.84, 140.51, 132.21, 128.98, 127.72, 127.14, 127.10, 122.39, 86.92, 83.08, 66.72, 30.26, 22.58.

IR: 3306, 3029, 2978, 2932, 2212, 1447, 1093, 1073.

HRMS: (EI$^+$) m/z: $[M]^+$ Calcd for $C_{17}H_{16}O$ 236.1201; Found 236.1195.



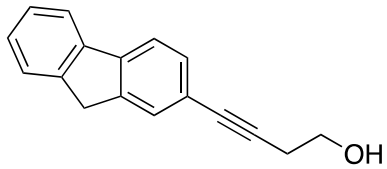
((5-([1,1'-biphenyl]-4-yl)pent-4-yn-2-yl)oxy)(*tert*-butyl)dimethylsilane [31l]. Following general procedure E, 5-([1,1'-biphenyl]-4-yl)pent-4-yn-2-ol (283 mg, 1.20 mmol, 1.00 eq.), dry DCM (6.00 mL), imidazole (163 mg, 2.40 mmol, 2.00 eq.), and *tert*-butyldimethylsilyl chloride (199 mg, 1.32 mmol, 1.10 eq.) were combined in a flame-dried round bottom flask. Post-reaction work up, the crude product was purified by flash column chromatography (100 mL 100% hexanes, 150 mL 1% ethyl acetate in hexanes) to give the pure product as a colorless solid (354 mg, 1.01 mmol, 84% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.64 – 7.43 (m, 8H), 7.37 (t, *J* = 7.3 Hz, 1H), 4.11 (sxt, *J* = 6.1 Hz, 1H), 2.68 – 2.49 (m, 2H), 1.35 (d, *J* = 6.0 Hz, 3H), 0.97 (s, 9H), 0.17 (s, 3H), 0.15 (s, 3H).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 140.60, 140.45, 132.08, 128.94, 127.61, 127.10, 127.01, 122.99, 88.63, 81.85, 68.03, 30.61, 25.99, 23.75, 18.29, -4.49, -4.51.

IR: 2927, 2855, 1470, 1387, 1248, 1187, 1096, 840, 771.

HRMS: (ESI$^+$) m/z: $[M+Na]^+$ Calcd for $C_{23}H_{30}NaOSi$ 373.1966; Found 373.1958.



4-(9*H*-fluoren-2-yl)but-3-yn-1-ol

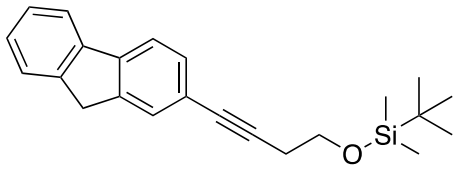
Following general procedure D, to a flame-dried round bottom flask under N_2 was added triethylamine (8.50 mL). The aryl iodide (0.500 g, 1.71 mmol, 1.00 eq.), $Pd(PPh_3)_2Cl_2$ (24.0 mg, 0.0342 mmol, 0.0200 eq.) and CuI (13.0 mg, 0.0684 mmol, 0.0400 eq.) were then sequentially added at room temperature. The mixture was stirred for 10 minutes followed by the addition of 3-butyn-1-ol (0.142 mL, 1.88 mmol, 1.10 eq.) and the reaction stirred under N_2 at room temperature overnight. Post-reaction work up, the crude product was purified by flash column chromatography (200 mL of hexanes, 200 mL of 5% ethyl acetate in hexanes, 200 mL of 10% ethyl acetate in hexanes, 500 mL of 15% ethyl acetate in hexanes) to give the pure product as an off-white solid (288 mg, 1.23 mmol, 72% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.77 (d, *J* = 7.5 Hz, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.60 (s, 1H), 7.54 (d, *J* = 7.4 Hz, 1H), 7.44 (d, *J* = 7.9 Hz, 1H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.31 (t, *J* = 7.1 Hz, 1H), 3.88 (s, 2H), 3.84 (t, *J* = 6.2 Hz, 2H), 2.73 (dd, *J* = 6.8, 5.4 Hz, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 143.61, 143.27, 141.69, 141.22, 130.63, 128.39, 127.20, 127.02, 125.21, 121.45, 120.26, 119.84, 86.30, 83.30, 61.37, 36.84, 24.08.

IR: 3292, 3095, 2931, 2220, 1635, 1419, 1035, 835.

HRMS: (ESI$^+$) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{14}NaO$ 257.0945; Found 257.0936.



((4-(9*H*-fluoren-3-yl)but-3-yn-1-yl)oxy)(*tert*-butyl)dimethylsilane [31m].

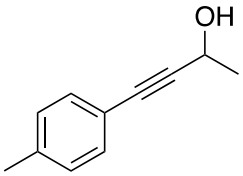
Following general procedure E, to a flame-dried round bottom flask was added 4-(9*H*-fluoren-2-yl)but-3-yn-1-ol (288 mg, 1.23 mmol, 1.00 eq.), dry DCM (2.46 mL) followed by imidazole (167 mg, 2.46 mmol, 2.00 eq.) and *tert*-butyldimethylsilyl chloride (204 mg, 1.35 mmol, 1.10 eq.). The reaction was stirred at room temperature overnight. Post-reaction work up, the crude product was purified by flash column chromatography (200 mL of hexanes, 400 mL of 2.5% ethyl acetate in hexanes) to give the pure product as an off-white solid (418 mg, 1.20 mmol, 98% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 7.5 Hz, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.58 (s, 1H), 7.54 (d, *J* = 7.4 Hz, 1H), 7.43 (d, *J* = 8.1 Hz, 1H), 7.38 (t, *J* = 7.3 Hz, 1H), 7.31 (t, *J* = 8.1, 7.4 Hz, 1H), 3.92 – 3.83 (m, 4H), 2.67 (t, *J* = 7.1 Hz, 2H), 0.94 (s, 9H), 0.13 (s, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 143.59, 143.21, 141.41, 141.31, 130.54, 128.28, 127.08, 126.98, 125.17, 121.96, 120.19, 119.78, 87.17, 82.32, 62.19, 36.84, 26.07, 24.07, 18.53, -5.07.

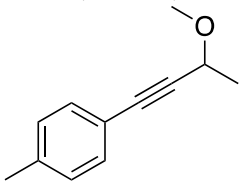
IR: 3050, 2953, 2205, 1590, 1420, 1250, 1093, 832, 731.

HRMS: (ESI$^+$) m/z: $[M+Na]^+$ Calcd for $C_{23}H_{28}NaOSi$ 371.1809; Found 371.1804.



4-(4-methylphenyl)but-3-yn-2-ol. Following general procedure D, triethylamine (23.0 mL), 4-methyl-1-iodobenzene (1.00 g, 4.59 mmol, 1.00 eq.), $Pd(PPh_3)_2Cl_2$ (64.4 mg, 0.0918 mmol, 0.0200 eq.), CuI (44.7 mg, 0.230 mmol, 0.0500 eq.) were added to a 100 mL flame dried round bottom flask, and was stirred for 15 minutes under N_2. 3-Butyn-2-ol (0.396 mL, 5.05 mmol, 1.10 eq.) was then added in one portion and the reaction stirred at room temperature under N_2 overnight. Post-reaction work up, the crude product was purified by flash column chromatography (500 mL of 5% ethyl acetate in hexanes, 800 mL of 20% ethyl acetate in hexanes) to give the pure product as a pale yellow solid (609 mg, 3.80 mmol, 83% yield). The spectra were consistent with the previously reported data.[10]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 (d, *J* = 8.1 Hz, 2H), 7.08 (d, *J* = 8.2 Hz, 2H), 4.78 (q, *J* = 6.6, Hz, 1H), 3.35 (br s, 1H), 2.33 (s, 3H), 1.57 (d, *J* = 6.7 Hz, 3H)



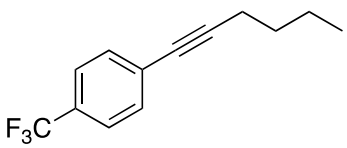
1-(3-methoxybut-1-yn-1-yl)-4-methylbenzene [31n]. To a flame dried 25 mL round bottom flask equipped with a magnetic stir bar was added 4-(4-methylphenyl)but-3-yn-2-ol (230 mg, 1.44 mmol, 1.00 eq.) and THF (5.00 mL). The solution was cooled to 0°C, and to this, NaH (60% dispersion in mineral oil, 69.2 mg, 1.73 mmol, 1.20 eq.) was added and stirred for 10 minutes before methyl iodide (0.269 mL, 4.32 mmol, 3.00 eq.) was added dropwise. Reaction progress was monitored by TLC. After 4 hours, reaction was quenched with water (5 mL) and diluted with 10 mL dichloromethane. The aqueous layer was extracted with dichloromethane (2 x 10 mL), and the combined organic fractions were washed with water (3 x 10 mL) and brine (1 x 10 mL), dried over Na_2SO_4, and the crude oil was purified by flash column chromatography (50 mL 100% hexanes, 100 mL 1% ethyl acetate in hexanes, 100 mL 1.5% ethyl acetate in hexanes) to give the pure product as a clear oil (217 mg, 1.25 mmol, 87% yield).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.34 (d, *J* = 8.1 Hz, 2H), 7.11 (d, *J* = 7.8 Hz, 2H), 4.30 (q, *J* = 6.6 Hz, 1H), 3.47 (s, 3H), 2.35 (s, 3H), 1.52 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 138.53, 131.74, 129.14, 119.77, 88.19, 85.35, 67.48, 56.47, 22.21, 21.59.

IR: 3029, 2986, 2934, 2819, 1509, 1114, 1098.

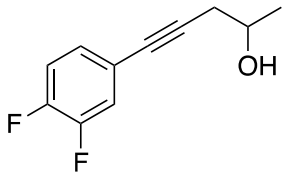
HRMS: (ESI$^+$) m/z: $[M+Na]^+$ Calcd for $C_{12}H_{14}NaO$ 197.0945 Found 197.0937.



1-(1-Hexyn-1-yl)-4-(trifluoromethyl)benzene [31o]. Following general procedure D, triethylamine (9.00 mL), 4-iodobenzotrifluoride (500 mg, 1.84 mmol, 1.00 eq), $Pd(PPh_3)_2Cl_2$ (25.8 mg, 0.0368 mmol, 0.0200 eq.), CuI (14.2 mg, 0.0748 mmol, 0.0400 eq.) were added to a 100 mL flame dried round bottom flask, and

was stirred for 15 minutes under N_2 at room temperature. 1-Hexyne (0.232 mL, 2.02 mmol, 1.10 eq.) was then added in one portion, the reaction was stirred at room temperature under N_2 overnight. Post-reaction work up, the crude product was purified by flash column chromatography (500 mL of 100% hexanes) to give the pure product as a clear colorless oil (228 mg, 1.01 mmol, 55% yield). The NMR data was consistent with previously reported spectra.[11]

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.56 – 7.42 (m, 4H), 2.43 (t, *J* = 6.9 Hz, 2H), 1.66 – 1.39 (m, 4H), 0.96 (t, *J* = 7.2 Hz, 3H).



5-(3,4-difluorophenyl)pent-4-yn-2-ol. Following general procedure D, triethylamine (10.0 mL), 1,2-difluoro-4-iodobenzene (500 mg, 2.08 mmol, 1.00 eq), $Pd(PPh_3)_2Cl_2$ (29.2 mg, 0.0416 mmol, 0.0200 eq.), CuI (19.8 mg, 0.104 mmol, 0.0500 eq.) were added to a 100 mL flame dried round bottom flask, and was stirred for 15 minutes under N_2 at room temperature. 4-Pentyn-2-ol (0.216 mL, 2.29 mmol, 1.10 eq.) was then added in one portion, the reaction was stirred at room temperature under N_2 overnight. Post-reaction work up, the crude product was purified by flash column chromatography (400 mL of 10% ethyl acetate in hexanes, 300 mL of 20% ethyl acetate in hexanes) to give the pure product as a brown oil (320 mg, 1.63 mmol, 78% yield).

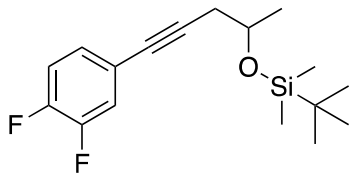
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.21 (ddd, *J* = 10.9, 7.6, 2.0 Hz, 1H), 7.16 – 7.11 (m, 1H), 7.10 – 7.03 (m, 1H), 4.05 (h, *J* = 6.3, 5.2 Hz, 1H), 2.65 – 2.47 (m, 2H), 2.03 (s, 1H), 1.32 (d, *J* = 6.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 150.44 (dd, *J* = 250.6, 12.3 Hz), 150.02 (dd, *J* = 249.0, 12.7 Hz), 128.35 (dd, *J* = 6.3, 3.6 Hz), 120.71 (d, *J* = 18.3 Hz), 120.36 (dd, *J* = 7.8 Hz), 117.47 (dd, *J* = 17.6, 1.2 Hz), 87.06 (d, *J* = 1.7 Hz), 81.60 – 80.99 (m), 66.60, 29.96, 22.62.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -136.41 – -137.01 (m, 1F), -137.45 (ddd, *J* = 21.4, 10.8, 7.9 Hz, 1F).

IR: 3464, 3076, 2980, 2930, 1719, 1610, 1084, 771.

HRMS: (EI$^+$) m/z: $[M]^+$ Calcd for $C_{11}H_{10}OF_2$ 196.0700; Found 196.0693.



***tert*-butyl((5-(3,4-difluorophenyl)pent-4-yn-2-yl)oxy)dimethylsilane [31p].** Following general procedure E, 5-(3,4-difluorophenyl)pent-4-yn-2-ol (0.295 g, 1.50 mmol, 1.00 eq.), dry DCM (5.00 mL), imidazole (204 mg, 3.00 mmol, 2.00 eq.), and *tert*-butyldimethylsilyl chloride (249 mg, 1.65 mmol, 1.10 eq.) were combined in a flame-dried round bottom flask. Post-reaction work up, the crude product was purified by flash column chromatography (200 mL of 2% ethyl acetate in hexanes) to give the pure product as a light yellow oil (364 mg, 1.17 mmol, 78% yield).

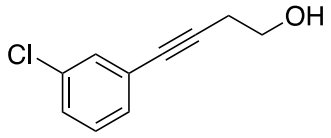
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.18 (ddd, *J* = 11.0, 7.6, 1.8 Hz, 1H), 7.14 – 7.01 (m, 2H), 4.03 (h, *J* = 6.2 Hz, 1H), 2.59 – 2.40 (m, 2H), 1.27 (d, *J* = 6.1 Hz, 3H), 0.90 (d, *J* = 1.1 Hz, 9H), 0.09 (s, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 150.27 (dd, *J* = 245.6, 8.0 Hz), 149.87 (dd, *J* = 246.8, 11.5 Hz), 128.17 (dd, *J* = 6.2, 3.5 Hz), 120.89 (dd, *J* = 7.8, 4.2 Hz), 120.68 – 120.43 (m), 117.51 – 117.26 (m), 88.65 (d, *J* = 1.7 Hz), 80.25 – 79.84 (m), 67.79, 30.39, 25.95, 23.73, 18.27, -4.49, -4.59.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -137.08 – -137.30 (m, 1F), -137.66 (ddd, *J* = 21.5, 10.8, 7.7 Hz, 1F).

IR: 2963, 2930, 2858, 2888, 1597, 1514, 1258, 1170, 1098.

HRMS: (ESI^{+}) m/z: [M+Na]$^{+}$ Calcd for $C_{17}H_{24}F_2NaOSi$ 333.1464; Found 333.1457.



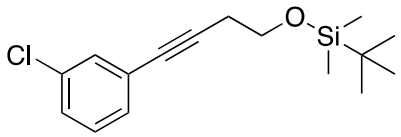
4-(3-chlorophenyl)but-3-yn-1-ol. Following general procedure D, triethylamine (10.5 mL), 3-Chloroiodobenzene (501 mg, 2.10 mmol, 1.00 eq), $Pd(PPh_3)_2Cl_2$ (29.5 mg, 0.0420 mmol, 0.0200 eq.), CuI (16.0 mg, 0.0840 mmol, 0.0400 eq.) were added to a 100 mL flame dried round bottom flask, and was stirred for 15 minutes under N_2 at room temperature. 3-Butyn-1-ol (0.175 mL, 2.31 mmol, 1.10 eq.) was then added in one portion, the reaction was stirred at room temperature under N_2 overnight. Post-reaction work up, the crude product was purified by flash column chromatography (100 mL of 100% hexanes, 100 mL of 10% ethyl acetate n hexanes, 1000 mL of 15% ethyl acetate in hexanes) to give the pure product as a brown oil (365 mg, 2.02 mmol, 96% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 (s, 1H), 7.32 – 7.18 (m, 3H), 3.82 (t, *J* = 6.3 Hz, 2H), 2.69 (t, *J* = 6.3 Hz, 2H), 1.97 – 1.80 (m, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 134.18, 131.72, 129.92, 129.60, 128.37, 125.18, 87.98, 81.23, 61.18, 23.89.

IR: 3348, 3061, 2949, 2884, 1721, 1592, 1038.

HRMS: (EI^{+}) m/z: [M]$^{+}$ Calcd for $C_{10}H_9OCl$ 180.0342; Found 180.0335.



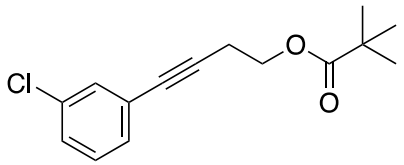
***tert*-butyl((4-(3-chlorophenyl)but-3-yn-1-yl)oxy)dimethylsilane [31q].** Following general procedure E, 4-(3-chlorophenyl)but-3-yn-1-ol (365 mg, 2.02 mmol, 1.00 eq.), dry dichloromethane (6.00 mL), imidazole (270 mg, 3.96 mmol, 2.00 eq.) and *tert*-butyldimethylsilyl chloride (329 mg, 2.18 mmol, 1.10 eq.) were added to a 100 mL flame dried round bottom flask. The crude product was purified by flash column chromatography (100 mL of 100% HPLC hexanes, 600 mL of 2% ethyl acetate in HPLC hexanes) to yield the title compound as a clear colorless oil (516 mg, 1.75 mmol, 87% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 (s, 1H), 7.29 – 7.17 (m, 3H), 3.81 (t, *J* = 7.0 Hz, 2H), 2.62 (t, *J* = 7.1 Hz, 2H), 0.92 (s, 9H), 0.10 (s, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 134.12, 131.63, 129.83, 129.53, 128.08, 125.66, 88.85, 80.43, 61.90, 26.03, 23.94, 18.49, -5.11.

IR: 3075, 2928, 2856, 1593, 1560, 1472, 1251, 1094.

HRMS: (ESI$^+$) m/z: [M+Na]$^+$ Calcd for $C_{16}H_{23}ClNaOSi$ 317.1107; Found 317.1099.



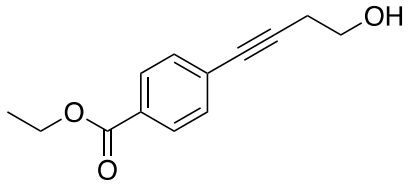
4-(3-chlorophenyl)but-3-yn-1-yl pivalate [31r]. To an oven-dried round bottom flask, under N_2, equipped with a stir bar, was added 4-(3-chlorophenyl)but-3-yn-1-ol (757 mg, 4.19 mmol, 1.00 eq) and DCM (8.38 mL). The solution was cooled to 0 °C and Et_3N (0.818 mL, 5.87 mmol, 1.40 eq) was added, followed by 4-dimethylaminopyridine (51.2 mg, 0.419 mmol, 0.100 eq). Then, pivaloyl chloride (0.671 mL, 5.45 mmol, 1.30 eq) was added dropwise. The reaction was allowed to stir for 18 h at room temperature. Upon completion, the reaction was quenched with $NaHCO_3$ (10 mL). Then extracted with DCM (20 mL). The organic layer was then washed with 0.1 M HCl (10 mL) and brine (10 mL). The organic layer was then dried over Na_2SO_4. Solvent was removed by rotary evaporation, and the crude product was dry loaded onto a column, and purified by flash column chromatography (200 mL of hexanes, 200 mL of 2.5% ethyl acetate in hexanes, 200 mL of 3% ethyl acetate in hexanes, 200 mL of 5% ethyl acetate in hexanes, 200 mL of 7.5% ethyl acetate in hexanes, and 200 mL of 10% ethyl acetate in hexanes). The title compound was afforded as a yellow oil (674 mg, 2.55 mmol, 61% yield).

^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.40 – 7.35 (m, 1H), 7.32 – 7.18 (m, 3H), 4.24 (t, *J* = 6.7 Hz, 2H), 2.74 (t, *J* = 6.7 Hz, 2H), 1.22 (s, 9H).

^{13}C NMR (Chloroform-*d*): 190.45, 134.19, 131.64, 129.88, 129.60, 128.33, 125.29, 87.21, 80.72, 62.06, 38.93, 27.31, 20.05.

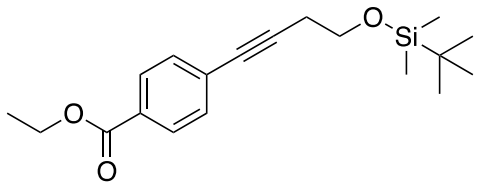
IR: 3080, 2971, 1727, 1593, 1561, 1476, 1281, 1143.

HRMS: (ESI$^+$) m/z: [M+Na]$^+$ Calcd for $C_{15}H_{17}ClNaO_2$ 287.0817; Found 287.0809.



Ethyl 4-(4-hydroxybut-1-yn-1-yl)benzoate. Following general procedure D, triethylamine (18.0 mL), ethyl 4-iodobenzoate (1.00 g, 3.62 mmol, 1.00 eq), $Pd(PPh_3)_2Cl_2$ (50.8 mg, 0.0724 mmol, 0.0200 eq.), CuI (27.6 mg, 0.145 mmol, 0.0400 eq.) were added to a 100 mL flame dried round bottom flask, and was stirred for 15 minutes under N_2 at room temperature. 3-Butyn-1-ol (0.301 mL, 3.98 mmol, 1.10 eq.) was then added in one portion, the reaction was stirred at room temperature under N_2 overnight. Post-reaction work up, the crude product was purified by flash column chromatography (100 mL of 100% hexanes, 100 mL of 10% ethyl acetate in hexanes, 100 mL of 20% ethyl acetate in hexanes, 100 mL of 25% ethyl acetate in hexanes, 350 mL of 30% ethyl acetate in hexanes) to give the pure product as a brown oil (707 mg, 3.24 mmol, 90% yield). The NMR data was consistent with previously reported spectra.[12]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.94 (d, *J* = 8.2 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 3.81 (t, *J* = 6.3 Hz, 2H), 2.69 (t, *J* = 6.4 Hz, 2H), 1.37 (t, *J* = 7.2 Hz, 3H). Hydrogen on alcohol not detected.



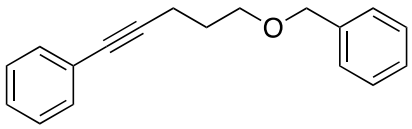
Ethyl 4-(4-((*tert*-butyldimethylsilyl)oxy)but-1-yn-1-yl)benzoate [31s]. According to the general procedure E, ethyl 4-(4-hydroxybut-1-yn-1-yl)benzoate (406 mg, 1.86 mmol, 1.00 eq.), dry dichloromethane (6.20 mL), imidazole (253 mg, 3.72 mmol, 2.00 eq.) and *tert*-butyldimethylsilyl chloride (309 mg, 2.05 mmol, 1.10 eq.) were combined. The crude product was purified by flash column chromatography (100 mL of 100% HPLC hexanes, 350 mL of 3% ethyl acetate in HPLC hexanes) to yield the title compound as a clear colorless oil (615 mg, 1.85 mmol, 99% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.96 (d, *J* = 8.3 Hz, 2H), 7.44 (d, *J* = 8.1 Hz, 2H), 4.37 (q, *J* = 7.2 Hz, 2H), 3.83 (t, *J* = 7.0 Hz, 2H), 2.65 (t, *J* = 7.0 Hz, 2H), 1.39 (t, *J* = 7.2 Hz, 3H), 0.91 (s, 9H), 0.10 (s, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.30, 131.59, 129.51, 128.59 (2 overlapping carbon signals), 90.79, 81.22, 61.87, 61.19, 26.03, 24.07, 18.50, 14.46, -5.11.

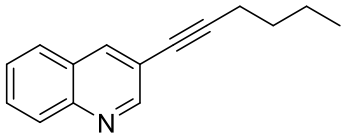
IR: 2928, 2856, 1717, 1606, 1472, 1269, 1094.

HRMS: (ESI$^+$) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{28}NaO_3Si$ 355.1708; Found 355.1700.



(5-(benzyloxy)pent-1-yn-1-yl)benzene [31u]. Following a previously reported procedure[13], 5-phenyl-4-pentyn-1-ol (800 mg, 4.99 mmol, 1.00 eq), sodium hydride (200 mg, 4.99 mmol, 1.00 eq), benzyl bromide (0.593 mL, 4.99 mmol, 1.00 eq), THF (5.14 mL) were combined to form the desired product as a yellow oil (746 mg, 2.98 mmol, 60% yield). The NMR data was consistent with previously reported spectra.[14]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.32 (m, 6H), 7.32 – 7.25 (m, 4H), 4.55 (s, 2H), 3.64 (t, *J* = 6.2 Hz, 2H), 2.55 (t, *J* = 7.0 Hz, 2H), 1.92 (p, *J* = 6.6 Hz, 2H).



3-(1-hexyn-1-yl)-quinoline [33a]. Following general procedure D, triethylamine (24.0 mL), 3-bromo-quinoline (999 mg, 4.80 mmol, 1.00 eq), $Pd(PPh_3)_2Cl_2$ (67.4 mg, 0.096 mmol, 0.0200 eq.), CuI (36.6 mg, 0.192 mmol, 0.0400 eq.) were added to a 100 mL flame dried round bottom flask, and was stirred for 15 minutes under N_2 at room temperature. 1-Hexyne (0.606 mL, 5.28 mmol, 1.10 eq.) was then added in one portion, the reaction was equipped with a cold finger condenser, and the reaction was heated to 100°C and stirred under N_2 overnight. Post-reaction work up, the crude product was purified by flash column chromatography (500 mL of 100% hexanes, 300 mL of 6% ethyl acetate in hexanes, 500 mL of 8% ethyl

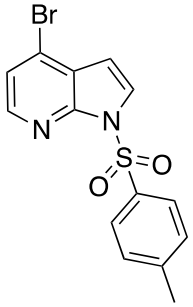
acetate in hexanes, 300 mL of 10% ethyl acetate in hexanes) to give the pure product as a red oil (934 mg, 4.46 mmol, 93% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.87 (d, *J* = 2.1 Hz, 1H), 8.15 (d, *J* = 2.1 Hz, 1H), 8.06 (d, *J* = 8.5 Hz, 1H), 7.74 (d, *J* = 8.2 Hz, 1H), 7.71 – 7.64 (m, 1H), 7.57 – 7.49 (m, 1H), 2.48 (t, *J* = 7.1 Hz, 2H), 1.70 – 1.58 (m, 2H), 1.58 – 1.45 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 152.43, 146.46, 137.78, 129.49, 129.26, 127.33, 127.27, 126.98, 118.20, 94.00, 77.92, 30.63, 22.02, 19.19, 13.61.

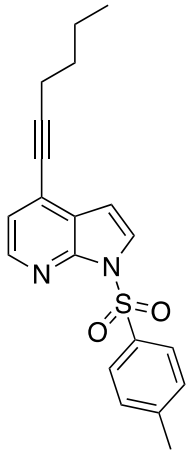
IR: 3075, 2956, 2931, 1596, 1566, 1344, 749.

HRMS: (ESI$^+$) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{15}NNa$ 232.1104; Found 232.1097.



4-Bromo-1-tosyl-1H-pyrrolo[2,3-*b*]pyridine. Following a previously reported procedure[15], 3-bromo-1*H*-pyrrolo[2,3-b]pyridine (1.00 g, 5.10 mmol, 1.00 eq), THF (36.0 mL), NaH (60% dispersion in mineral oil, 245 mg, 6.12 mmol, 1.20 eq.), and *p*-toluenesulfonyl chloride (1.26 g, 6.63 mmol, 1.30 eq) were reacted and purified by column chromatography (100 mL 100% hexanes, 200 mL 5% ethyl acetate in hexanes, 800 mL 10% ethyl acetate in hexanes) to afford the title compound as a white solid (1.50 g, 4.27 mmol, 84% yield). The spectra matched previously reported data.[15]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.24 (d, *J* = 5.2 Hz, 1H), 8.10 (d, *J* = 8.4 Hz, 2H), 7.81 (d, *J* = 4.0 Hz, 1H), 7.32 (d, *J* = 5.2 Hz, 1H), 7.29 – 7.19 (m, 2H), 6.61 (d, *J* = 4.0 Hz, 1H), 2.31 (s, 3H).



1-Tosyl-4-hexyn-yl-1*H*-pyrrolo[2,3-*b*]pyridine [33b]. Following general procedure D, triethylamine (7.00 mL), 4-Bromo-1-tosyl-1H-pyrrolo[2,3-*b*]pyridine (500 mg, 1.42 mmol, 1.00 eq), $Pd(PPh_3)_2Cl_2$ (20.0 mg, 0.0284 mmol, 0.0200 eq.), CuI (10.8 mg, 0.0568 mmol, 0.0400 eq.) were added to a 100 mL flame dried round bottom flask, and was stirred for 15 minutes under N_2 at room temperature. 1-Hexyne (0.179 mL, 1.56 mmol, 1.100 eq.) was then added in one portion, the reaction was equipped with a cold finger

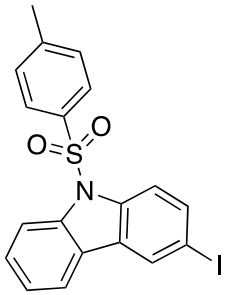
condenser, and the reaction stirred at 100°C under N_2 overnight. Post-reaction work up, the crude product was purified by flash column chromatography (100 mL of 100% hexanes, 100 mL of 2% ethyl acetate in hexanes, 300 mL of 5% ethyl acetate in hexanes, and 300 mL of 10% ethyl acetate in hexanes) to give the pure product as an dark oil (395 mg, 1.12 mmol, 79% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.32 (d, *J* = 5.1 Hz, 1H), 8.03 (d, *J* = 8.3 Hz, 2H), 7.71 (d, *J* = 4.0 Hz, 1H), 7.29 – 7.19 (m, 2H), 7.12 (d, *J* = 5.1 Hz, 1H), 6.69 (d, *J* = 4.0 Hz, 1H), 2.48 (t, *J* = 7.0 Hz, 2H), 2.36 (s, 3H), 1.67 – 1.56 (m, 2H), 1.56 – 1.42 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 147.24, 145.29, 144.68, 135.39, 129.71, 128.04, 126.46, 125.60, 124.15, 121.06, 104.92, 99.05, 76.59, 30.57, 22.06, 21.69, 19.41, 13.67.

IR: 3098, 2931, 2871, 1583, 1513, 1261, 1145.

HRMS: (ESI$^+$) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{20}N_2NaO_2S$ 375.1145; Found 375.1138.



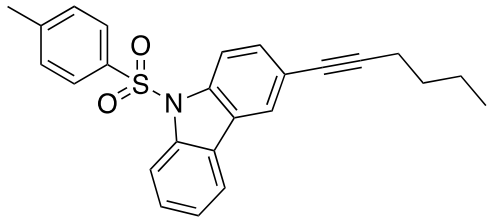
3-iodo-9-((4-methylphenyl)sulfonyl)-9*H*-carbazole. To a flame dried 100 mL round bottom flask equipped with a magnetic stir bar was added 3-iodo-9*H*-carbazole (2.00 g, 6.82 mmol, 1.00 eq.) and THF (50.0 mL). The solution was cooled to 0°C, and to this, NaH (60% dispersion in mineral oil, 355 mg, 8.87 mmol, 1.30 eq.) was added and stirred for 10 minutes before *p*-toluenesulfonyl chloride (1.94 g, 10.2 mmol, 1.50 eq.) was added and left to stir overnight. Reaction was quenched with water (50 mL) and diluted with 50 mL ethyl acetate. The organic layer was washed with water (3 x 30 mL) and brine (1 x 20 mL), dried over Na_2SO_4, and the crude solid was purified by flash column chromatography (500 mL 5% ethyl acetate in hexanes, 1000 mL 10% ethyl acetate in hexanes), to give the product as a white solid (2.60 g, 5.81 mmol, 85% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.31 (d, *J* = 8.5 Hz, 1H), 8.21 (d, *J* = 1.8 Hz, 1H), 8.10 (d, *J* = 8.8 Hz, 1H), 7.84 (d, *J* = 7.7 Hz, 1H), 7.75 (dd, *J* = 8.8, 1.8 Hz, 1H), 7.67 (d, *J* = 8.5 Hz, 2H), 7.55 – 7.48 (m, 1H), 7.40 – 7.34 (m, 1H), 7.11 (d, *J* = 8.0 Hz, 2H), 2.27 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 145.31, 138.54, 137.91, 135.94, 134.80, 129.91, 129.12, 128.81, 128.24, 126.60, 125.08, 124.32, 120.28, 117.13, 115.29, 87.89, 21.67.

IR: 3059, 2922, 2788, 1594, 1434, 1364, 1202, 1166, 1156, 1011, 1088, 984

HRMS: (ESI$^+$) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{14}INNaO_2S$ 469.9690; Found 469.9686.



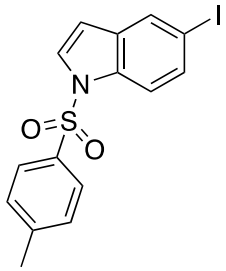
3-(hex-1-yn-1-yl)-9-((4-methylphenyl)sulfonyl)-9*H*-carbazole [33c]. Following general procedure D, triethylamine (5.50 mL), 3-iodo-9-((4-methylphenyl)sulfonyl)-9*H*-carbazole (500 mg, 1.12 mmol, 1.00 eq.), $Pd(PPh_3)_2Cl_2$ (15.7 mg, 0.0224 mmol, 0.0200 eq.), CuI (10.7 mg, 0.0560 mmol, 0.0500 eq.) were added to a 25 mL flame dried Schlenk tube, and was stirred for 15 minutes under N_2. 1-Hexyne (0.141 mL, 1.23 mmol, 1.10 eq.) was then added in one portion, and the reaction stirred at room temperature under N_2 overnight. The crude product was purified by flash column chromatography (1000 mL of 10% ethyl acetate in hexanes, followed by trituration with *n*-pentane to afford the product as a tan solid (0.370 g, 0.922 mmol, 82% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.31 (d, *J* = 8.3 Hz, 1H), 8.25 (d, *J* = 8.7 Hz, 1H), 7.93 (s, 1H), 7.86 (d, *J* = 7.7 Hz, 1H), 7.67 (d, *J* = 8.3 Hz, 2H), 7.55 – 7.46 (m, 2H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 8.3 Hz, 2H), 2.45 (t, *J* = 7.0 Hz, 2H), 2.25 (s, 3H), 1.67 – 1.57 (m, 2H), 1.56 – 1.45 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 145.13, 138.84, 137.57, 134.88, 130.94, 129.81, 127.80, 126.58 (2 overlapping carbon signals), 126.03, 124.19, 123.23, 120.21, 119.87, 115.33, 115.17, 90.39, 80.39, 31.00, 22.19, 21.63, 19.26, 13.81.

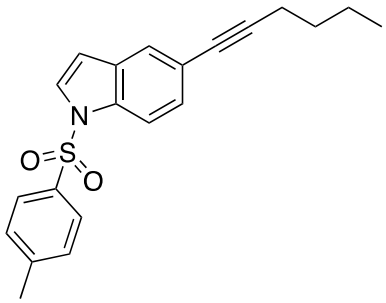
IR: 2923, 2854, 1597, 1443, 1307, 1187, 1173, 1132, 1019, 969

HRMS: (ESI$^+$) m/z: $[M+Na]^+$ Calcd for $C_{25}H_{23}NNaO_2S$ 424.1349 Found 424.1342.



5-(iodo)-1-((4-methylphenyl)sulfonyl)-1*H*-indole. To a flame dried 100 mL round bottom flask equipped with a magnetic stir bar was added 5-iodo-1*H*-indole (2.00 g, 8.23 mmol, 1.00 eq.) and THF (60.0 mL). The solution was cooled to 0°C, and to this, NaH (60% dispersion in mineral oil, 428 mg, 10.7 mmol, 1.30 eq.,) was added and stirred for 10 minutes before *p*-toluenesulfonyl chloride (2.34 g, 12.3 mmol, 1.50 eq.) was added and left to stir overnight. Reaction was quenched with water (50 mL) and diluted with 50 mL ethyl acetate. The organic layer was washed with water (3 x 40 mL) and brine (1 x 30 mL), dried over Na_2SO_4, and the crude solid was purified by flash column chromatography (500 mL 5% ethyl acetate in hexanes, 500 mL 10% ethyl acetate in hexanes, 500 mL 20% ethyl acetate in hexanes), to give the product as a brown solid (2.10 g, 5.29 mmol, 64% yield). The spectra were consistent with previously reported data.[16]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.88 – 7.86 (m, 1H), 7.78 – 7.70 (m, 3H), 7.57 (dd, *J* = 8.8, 1.8 Hz, 1H), 7.54 – 7.50 (m, 1H), 7.25 – 7.20 (m, 2H), 6.59 – 6.56 (m, 1H), 2.35 (s, 3H).



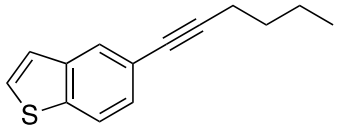
5-(hex-1-yn-1-yl)-1-((4-methylphenyl)sulfonyl)-1*H*-indole [33d]. Following general procedure D, triethylamine (7.00 mL), 5-(iodo)-1-((4-methylphenyl)sulfonyl)-1*H*-indole (500 mg, 1.26 mmol, 1.00 eq.), $Pd(PPh_3)_2Cl_2$ (17.7 mg, 0.0252 mmol, 0.0200 eq.), CuI (12.0 mg, 0.0630 mmol, 0.0500 eq.) were added to a 25 mL flame dried Schlenk tube, and was stirred for 15 minutes under N_2. 1-Hexyne (0.160 mL, 1.39 mmol, 1.10 eq.) was then added in one portion and the reaction stirred at room temperature under N_2 overnight. The crude product was purified by flash column chromatography (50 mL 100% hexanes, 100 mL 4% ethyl acetate in hexanes, 100 mL 8% ethyl acetate in hexanes, 100 mL 10% ethyl acetate in hexanes) to give the pure product as an orange oil (427 mg, 1.21 mmol, 96% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.89 (d, *J* = 8.6 Hz, 1H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.58 – 7.51 (m, 2H), 7.33 (d, *J* = 8.7 Hz, 1H), 7.20 (d, *J* = 8.1 Hz, 2H), 6.59 (d, *J* = 3.6 Hz, 1H), 2.40 (t, *J* = 7.0 Hz, 2H), 2.33 (s, 3H), 1.63 – 1.53 (m, 2H), 1.47 (h, *J* = 7.0 Hz, 2H), 0.94 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 145.19, 135.21, 134.02, 130.84, 130.01, 128.22, 127.17, 126.88, 124.68, 119.28, 113.54, 109.02, 89.64, 80.59, 31.00, 22.13, 21.68, 19.21, 13.78.

IR: 3143, 2955, 2930, 2860, 1596, 1455, 1370, 1286, 1234, 1173, 1158, 1124, 993, 811, 666.

HRMS (ESI^+) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{21}NNaO_2S$ 374.1193; Found 374.1185.



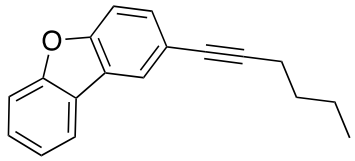
5-(hex-1-yn-1-yl)benzo[*b*]thiophene [33e]. Following general procedure D, triethylamine (10.0 mL), 5-iodo-1-benzothiophene (530 mg, 2.04 mmol, 1.00 eq), $Pd(PPh_3)_2Cl_2$ (28.6 mg, 0.0408 mmol, 0.0200 eq.), CuI (15.5 mg, 0.0816 mmol, 0.0400 eq.) were added to a 100 mL flame dried round bottom flask, and was stirred for 15 minutes under N_2 at room temperature. 1-Hexyne (0.257 mL, 2.24 mmol, 1.10 eq.) was then added in one portion, the reaction was stirred at room temperature under N_2 overnight. Post-reaction work up, the crude product was purified by flash column chromatography (850 mL of 100% hexanes) to give the pure product as a brown oil (345 mg, 1.61 mmol, 79% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.89 – 7.87 (m, 1H), 7.78 (d, *J* = 8.1 Hz, 1H), 7.44 (d, *J* = 5.5 Hz, 1H), 7.37 (d, *J* = 8.3 Hz, 1H), 7.28 (d, *J* = 5.5 Hz, 1H), 2.45 (t, *J* = 7.0 Hz, 2H), 1.67 – 1.58 (m, 2H), 1.58 – 1.46 (m, 2H), 0.98 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 139.65, 138.97, 127.60, 127.19, 126.83, 123.73, 122.36, 120.13, 89.99, 80.79, 31.02, 22.18, 19.29, 13.82.

IR: 3075, 2955, 2929, 2859, 1597, 1539, 1436.

HRMS: (EI^+) m/z: $[M]^+$ Calcd for $C_{14}H_{14}S$ 214.0816; Found 214.0808.



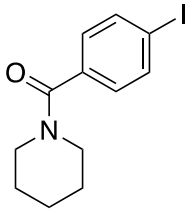
2-(hex-1-yn-1-yl)dibenzo[*b*,*d*]furan [33f]. Following general procedure D, triethylamine (8.00 mL), 2-iododibenzo[*b*,*d*]furan (500 mg, 1.70 mmol, 1.00 eq.), $Pd(PPh_3)_2Cl_2$ (23.9 mg, 0.0340 mmol, 0.0200 eq.), CuI (16.2 mg, 0.0850 mmol, 0.0500 eq.) were added to a 25 mL flame dried Schlenk tube, and was stirred for 15 minutes under N_2. 1-Hexyne (0.215 mL, 1.87 mmol, 1.10 eq.) was then added in one portion, and the reaction stirred at room temperature under N_2 overnight. The crude product was purified by flash column chromatography (250 mL of 1% ethyl acetate in hexanes, 250 mL of 2% ethyl acetate in hexanes) to give the pure product as a yellow oil (300 mg, 1.21 mmol, 71% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.00 (s, 1H), 7.92 (d, *J* = 7.7 Hz, 1H), 7.56 (d, *J* = 8.3 Hz, 1H), 7.53 – 7.42 (m, 3H), 7.35 (t, *J* = 7.5 Hz, 1H), 2.46 (t, *J* = 7.0 Hz, 2H), 1.70 – 1.58 (m, 2H), 1.58 – 1.45 (m, 2H), 0.98 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 156.67, 155.50, 130.90, 127.58, 124.43, 124.02, 123.88, 123.05, 120.88, 118.76, 111.88, 111.71, 89.48, 80.58, 31.07, 22.22, 19.27, 13.84.

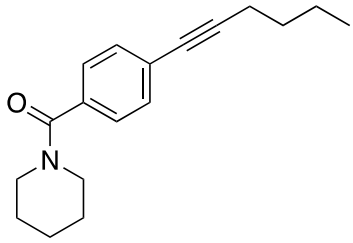
IR: 2957, 2929, 2871, 2858, 1590, 1448, 1474, 1192, 1178, 1116, 815.

HRMS: (EI$^+$) m/z: $[M]^+$ Calcd for $C_{18}H_{16}O$ 248.1201; Found 248.1196.



(4-iodophenyl)(piperidin-1-yl)methanone. In an oven-dried 20 mL vial with pressure relief cap equipped with a Teflon stir bar was added piperidine (0.948 mL, 9.60 mmol, 1.60 eq). 4-Iodobenzoyl chloride (3.00 mL of a 2 M solution in THF, 6.00 mmol, 1.00 eq) was added dropwise. The reaction was stirred at room temperature overnight. Upon reaction completion, monitored by TLC, the reaction mixture was transferred to a 125 mL separatory funnel containing 50 mL of dichloromethane. The organic layer was washed with 1 M HCl (50 mL), 1 M KOH (50 mL x 2), brine (20 mL), and then dried over anhydrous Na_2SO_4. The mixture was filtered and the solvent was removed by rotary evaporation to afford the crude product. The crude product was purified by recrystallization using boiling hexanes, adding ethyl acetate dropwise until no solid remained. After filtration, the pure product was obtained as an orange crystal (657 mg, 2.08 mmol, 35% yield). The spectra were consistent with previously reported data.[17]

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.74 (d, *J* = 8.1 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 3.69 (br s, 2H), 3.32 (br s, 2H), 1.76 – 1.60 (m, 4H), 1.58 – 1.43 (m, 2H).



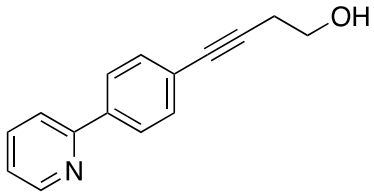
(4-(Hex-1-yn-1-yl)phenyl)(piperidin-1-yl)methanone [33g]. In an oven-dried 20 mL vial with pressure relief cap equipped with a Teflon stir bar was added (4-iodophenyl)(piperidin-1-yl)methanone (600 mg, 1.90 mmol, 1.00 eq), $Pd(PPh_3)_2Cl_2$ (13.3 mg, 0.0190 mmol, 0.01 eq), CuI (7.24 mg, 0.0380 mmol, 0.0200 eq), THF (2.50 mL), and triethylamine (0.800 mL). The mixture was degassed with N_2 for 10 mins. Then, 1-hexyne (0.240 mL, 2.09 mmol, 1.10 eq) was added dropwise. The reaction mixture was stirred under nitrogen at 75 ˚C overnight. Upon reaction completion, monitored by TLC, the reaction mixture was transferred with diethyl ether (50 mL) to a separatory funnel and washed with saturated NH_4Cl (45 mL). The aqueous layer was extracted with diethyl ether (50 mL x 2), and then the combined organic layers were washed with brine (100 mL) and dried over anhydrous Na_2SO_4. The mixture was filtered and the solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography (500 mL of 35% ethyl acetate in hexanes) to give the pure product as a thick brown oil (488 mg, 1.81 mmol, 95%).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.40 (d, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 7.9 Hz, 2H), 3.68 (br s, 2H), 3.31 (br s, 2H), 2.41 (t, *J* = 6.9 Hz, 2H), 1.73 – 1.40 (m, 10H), 0.94 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 169.92, 135.39, 131.60, 126.91, 125.43, 92.03, 80.11, 48.83, 43.26, 30.82, 26.63, 25.71, 24.67, 22.11, 19.22, 13.74.

IR: 2932, 2856, 1628, 1606, 1275.

HRMS: (ESI$^+$) m/z: $[M+H]^+$ Calcd for $C_{18}H_{24}NO$ 270.1860; Found 270.1858.



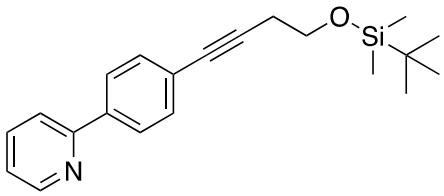
4-(4-(Pyridin-2-yl)phenyl)but-3-yn-1-ol. Following general procedure D, triethylamine (22.0 mL), 2-(4-iodophenyl)pyridine (1.20 g, 4.27 mmol, 1.00 eq.), $Pd(PPh_3)_2Cl_2$ (59.9 mg, 0.0854 mmol, 0.0200 eq.) and CuI (32.6 mg, 0.171 mmol, 0.0400 eq.) were added to a 100 mL flame dried round bottom flask at room temperature and this was stirred for 15 minutes. 3-Butyn-1-ol (0.356 mL, 4.70 mmol, 1.10 eq.) was then added in one portion and the reaction was stirred at room temperature overnight. Post-reaction work up, the crude product was purified by flash column chromatography (200 mL of hexanes, 200 mL of 5% ethyl acetate in hexanes, 200 mL of 10% ethyl acetate in hexanes, 200 mL of 15% ethyl acetate in hexanes, 200 mL of 17% ethyl acetate in hexanes, 200 mL of 30% ethyl acetate in hexanes, 200 mL of 40% ethyl acetate in hexanes, 500 mL of 50% ethyl acetate in hexanes) to give the pure product as a red oil (318 mg, 1.42 mmol, 33% yield).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.67 (d, *J* = 5.2 Hz, 1H), 7.92 (d, *J* = 8.4 Hz, 2H), 7.78 – 7.61 (m, 2H), 7.50 (d, *J* = 8.3 Hz, 2H), 7.25 – 7.14 (m, 1H), 3.81 (t, *J* = 5.8 Hz, 2H), 2.69 (t, *J* = 6.4 Hz, 2H), 2.56 (br s, 1H).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 156.71, 149.81, 138.77, 136.97, 131.56, 126.82, 124.12, 122.44, 120.70, 88.00, 82.34, 61.21, 24.03.

IR: 3262, 3081, 3039, 2952, 2932, 2901, 2853, 1590, 1470, 1289, 1052, 784.

HRMS: (ESI$^+$) m/z: [M+Na]$^+$ Calcd for $C_{15}H_{13}NNaO$ 246.0897; Found 246.0888.



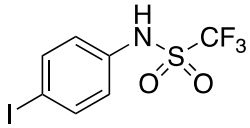
2-(4-(4-((*tert*-butyldimethylsilyl)oxy)but-1-yn-1-yl)phenyl)pyridine [33h]. Following general procedure E, to a flame-dried round bottom flask was added 4-(4-(pyridin-2-yl)phenyl)but-3-yn-1-ol (318 mg, 1.42 mmol, 1.00 eq.), dry DCM (2.85 mL) followed by imidazole (193 mg, 2.84 mmol, 2 .00 eq.) and *tert*-butyldimethylsilyl chloride (235 mg, 1.56 mmol, 1.10 eq.). The reaction was stirred at room temperature overnight and post-reaction work up, the crude product was purified by flash column chromatography (200 mL of hexanes, 500 mL of 5% ethyl acetate in hexanes) to give the pure product as a yellow oil (218 mg, 0.646 mmol, 45% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.66 (d, *J* = 4.8 Hz, 1H), 7.92 (d, *J* = 8.5 Hz, 2H), 7.72 – 7.62 (m, 2H), 7.49 (d, *J* = 8.5 Hz, 2H), 7.19 – 7.14 (m, 1H), 3.83 (t, *J* = 7.0 Hz, 2H), 2.65 (t, *J* = 7.0 Hz, 2H), 0.92 (s, 9H), 0.10 (s, 6H).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 156.64, 149.73, 138.49, 136.78, 132.01, 126.69, 124.48, 121.52, 120.46, 88.70, 81.55, 61.96, 25.97, 23.99, 18.41, -5.17.

IR: 2955, 2925, 2859, 1586, 1467, 1247, 1092, 775.

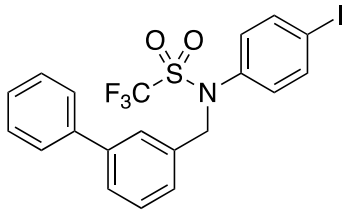
HRMS: (ESI$^+$) m/z: [M+Na]$^+$ Calcd for $C_{21}H_{27}NNaOSi$ 360.1762; Found 360.1753.



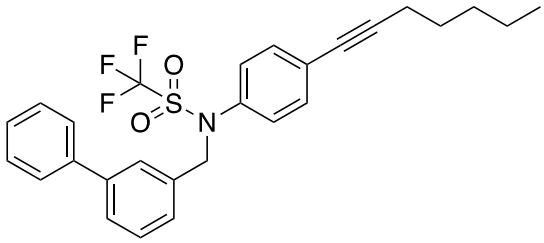
1,1,1-trifluoro-*N*-(4-iodophenyl)methanesulfonamide

In a 100 mL flame dried round bottom flask equipped with a Teflon stir bar was added 4-iodoaniline (1.10 g, 5.02 mmol, 1.00 eq), Et_3N (1.05 mL, 7.53 mmol, 1.50 eq), and DCM (10.0 mL). The reaction mixture was cooled to 0 °C and stirred for 5 minutes. Trifluoromethanesulfonic anhydride (0.99 mL, 6.02 mmol, 1.20 eq) was then added dropwise to the reaction mixture. The reaction mixture was stirred at room temperature under nitrogen overnight. Upon reaction completion, monitored by TLC, the reaction was quenched with brine (15 mL), extracted with DCM (3 x 30 mL), and the combined organic layers were dried over anhydrous Na_2SO_4. The mixture was filtered and the solvent was removed by rotary evaporation. The crude product was wet loaded onto a silica gel column and purified by silica gel flash column chromatography (1000 mL of 50% DCM in hexane) to give the desired compound as a white crystal (697 mg, 1.99 mmol, 40% yield). Spectra matches previously reported data.[18]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.87 (d, *J* = 8.8 Hz, 2H), 7.12 (d, *J* = 8.5 Hz, 2H).



***N*-([1,1'-biphenyl]-3-ylmethyl)-1,1,1-trifluoro-*N*-(4-iodophenyl)methanesulfonamide.**
In an oven-dried 20 mL vial equipped with a Teflon stir bar and a pressure relief cap was added 1,1,1-trifluoro-*N*-(4-iodophenyl)methanesulfonamide (527 mg, 1.50 mmol, 1.00 eq), 3-(bromomethyl)-1,1'-biphenyl (445 mg, 1.80 mmol, 1.20 eq), K_2CO_3 (249 mg, 1.80 mmol, 1.20 eq), and DMF (2.70 mL). The reaction was heated to 65 °C in an oil bath under nitrogen overnight. Upon reaction completion, the reaction mixture was cooled to room temperature and diluted with DI water (15 mL), extracted with ethyl acetate (3 x 30 mL), and the combined organic layers were washed with DI water (30 mL) and brine (50 mL) and then dried over anhydrous Na_2SO_4. The mixture was filtered, and the solvent was removed by rotary evaporation. The crude product was afforded as a pink oil and taken forward without further characterization (681 mg, 1.32 mmol, 88% yield).



***N*-([1,1'-biphenyl]-3-ylmethyl)-1,1,1-trifluoro-*N*-(4-(hept-1-yn-1-yl)phenyl)methanesulfonamide**
[33i]. Following general procedure D, triethylamine (6.50 mL), *N*-([1,1'-biphenyl]-3-ylmethyl)-1,1,1-trifluoro-*N*-(4-iodophenyl)methanesulfonamide (673 mg, 1.30 mmol, 1.00 eq), $Pd(PPh_3)_2Cl_2$ (18.2 mg, 0.0260 mmol, 0.0200 eq), and CuI (9.90 mg, 0.0520 mmol, 0.0400 eq) were added to an oven dried 20 mL vial equipped with a teflon stir bar and a pressure relief cap at room temperature, and this was stirred and heated to 40 °C for 15 minutes. 1-Heptyne (163 µL, 1.24 mmol, 0.954 eq) was then added dropwise and the reaction mixture was stirred at 40 °C overnight. Upon reaction completion, monitored by TLC, the crude product was purified by silica gel flash column chromatography (250 mL of 5% ethyl acetate in hexane and 250 mL of 10% ethyl acetate in hexane). The collected product was then purified again by flash C18-reverse phase column chromatography (stationary: C_{18} silica, elution: 150 mL of 100% methanol) to give the desired compound as a colorless oil (484 mg, 0.997 mmol, 77% yield).

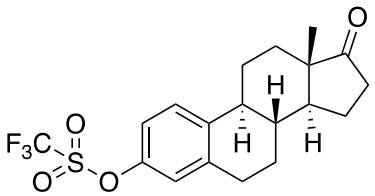
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.52 – 7.44 (m, 3H), 7.44 – 7.35 (m, 3H), 7.36 – 7.28 (m, 4H), 7.16 – 7.08 (m, 3H), 4.93 (s, 2H), 2.36 (t, *J* = 7.1 Hz, 2H), 1.58 (p, *J* = 7.0 Hz, 2H), 1.46 – 1.27 (m, 4H), 0.91 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 141.73, 140.43, 135.49, 134.69, 132.61, 129.28, 129.22, 128.93, 127.86, 127.73, 127.67, 127.41, 127.14, 125.50, 120.60 (q, *J* = 324.0 Hz), 92.89, 79.46, 57.28, 31.16, 28.36, 22.29, 19.41, 14.05.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -73.55.

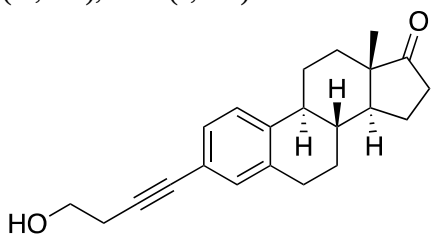
IR: 3061, 3036, 2957, 2933, 2860, 1394, 1195, 1145

HRMS: (ESI$^+$) m/z: $[M+H]^+$ Calcd for $C_{27}H_{27}F_3NO_2S$ 486.1716; Found 486.1708.



(8*R*,9*S*,13*S*,14*S*)-13-Methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl trifluoromethanesulfonate. Synthesized according to a previously reported procedure[3] to afford the pure white solid product (1.30 g, 3.23 mmol, 88% yield). The spectra for the title compound matched the previously reported spectra.[3]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 (d, *J* = 8.7 Hz, 1H), 7.08 – 6.96 (m, 2H), 3.00 – 2.89 (m, 2H), 2.52 (dd, *J* = 27.7, 8.6 Hz, 1H), 2.46 – 2.37 (m, 1H), 2.37 – 2.23 (m, 1H), 2.23 – 1.94 (m, 4H), 1.71 – 1.40 (m, 6H), 0.92 (s, 3H).



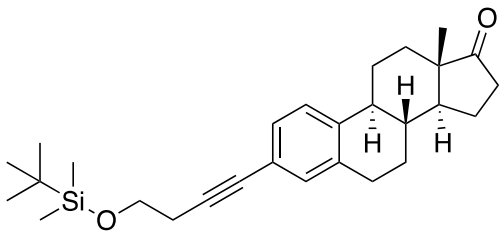
(8*R*,9*S*,13*S*,14*S*)-3-(4-hydroxybut-1-yn-1-yl)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one. In a 100 mL oven dried round bottom flask equipped with a Teflon stir bar was added (8*R*,9*S*,13*S*,14*S*)-13-Methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl trifluoromethanesulfonate (1.40 g, 3.47 mmol, 1.00 eq.), DMF (42.0 mL), $Pd(PPh_3)_4$ (401 mg, 0.347 mmol, 0.100 eq.), CuI (66.1 mg, 0.347 mmol, 0.100 eq.), and $^iPr_2NH$ (1.47 mL, 10.4 mmol, 3.00 eq.). The reaction mixture was degassed with N_2 for 20 minutes, followed by addition of 3-butyn-1-ol (0.315 mL, 4.16 mmol, 1.20 eq.). Using a condenser, the reaction was heated to reflux in an oil bath for 19 hours. The reaction progress was monitored by TLC. Upon completion, reaction was diluted with Et_2O, washed with brine (3 x 10 mL), dried over Na_2SO_4, and concentrated under vacuum. The crude product was dry loaded onto a column, and purified by flash column chromatography (200 mL of hexanes, 200 mL of 5% ethyl acetate in hexanes, 200 mL 10% ethyl acetate in hexanes, 200 mL of 12% ethyl acetate in hexanes, 200 mL of 15% ethyl acetate in hexanes, 200 mL of 17% ethyl acetate in hexanes, 200 mL of 25% ethyl acetate in hexanes, and 600 mL of 50% ethyl acetate in hexanes) to afford as a yellow solid (742 mg, 2.30 mmol, 66% yield).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.28 (s, 1H), 7.25 – 7.17 (m, 2H), 3.83 (q, *J* = 6.3 Hz, 2H), 2.94 – 2.85 (m, 2H), 2.71 (t, *J* = 6.2 Hz, 2H), 2.53 (dd, *J* = 18.3, 8.4 Hz, 1H), 2.48 – 2.38 (m, 1H), 2.38 – 2.26 (m, 1H), 2.24 – 1.93 (m, 4H), 1.84 (t, *J* = 6.4 Hz, 1H), 1.73 – 1.37 (m, 6H), 0.93 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 220.98, 140.02, 136.66, 132.29, 129.09, 125.46, 120.73, 85.66, 82.66, 61.34, 50.61, 48.09, 44.54, 38.10, 35.98, 31.67, 29.21, 26.47, 25.71, 24.01, 21.71, 13.97.

IR: 2952, 2927, 2856, 1737, 1595, 1469, 1248, 1098, 774.

HRMS: (ESI$^+$) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{26}NaO_2$ 345.1833; Found 345.1824.



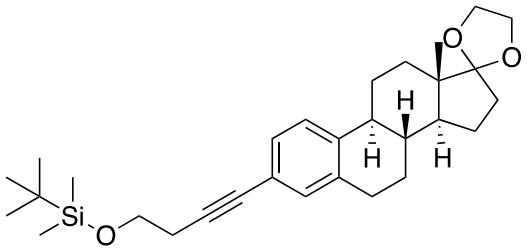
(8*R*,9*S*,13*S*,14*S*)-3-(4-((*tert*-butyldimethylsilyl)oxy)but-1-yn-1-yl)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one. To a flame-dried round bottom flask was added (8*R*,9*S*,13*S*,14*S*)-3-(4-hydroxybut-1-yn-1-yl)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one (742 mg, 2.30 mmol, 1.00 eq.), dry DCM (4.60 mL) followed by imidazole (313 mg, 4.60 mmol, 2.00 eq.) and *tert*-butyldimethylsilyl chloride (381 mg, 2.53 mmol, 1.10 eq.). The reaction was stirred at room temperature overnight. Upon completion, the reaction mixture was quenched with water (20 mL) and extracted with diethyl ether (2 x 15 mL). The combined organic layers were washed with brine (15 mL) and dried over anhydrous Na_2SO_4. The mixture was filtered, and the solvent was removed by rotary evaporation. Crude product was dry loaded onto a column, and the pure product was purified by flash column chromatography (200 mL of hexanes, 200 mL of 2% ethyl acetate in hexanes, and 400 mL of 4% ethyl acetate in hexanes), the title compound was afforded as a white solid (596 mg, 1.36 mmol, 59% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 – 7.12 (m, 3H), 3.80 (t, *J* = 7.1 Hz, 2H), 2.90 – 2.82 (m, 2H), 2.61 (t, *J* = 7.1 Hz, 2H), 2.51 (dd, *J* = 18.8, 8.7 Hz, 1H), 2.44 – 2.34 (m, 1H), 2.33 – 2.23 (m, 1H), 2.21 – 1.92 (m, 4H), 1.69 – 1.34 (m, 6H), 0.93 – 0.89 (m, 12H), 0.10 (s, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 220.91, 139.67, 136.54, 132.19, 129.03, 125.38, 121.24, 86.53, 81.63, 62.18, 50.64, 48.09, 44.55, 38.13, 35.98, 31.70, 29.23, 26.51, 26.06, 25.72, 24.00, 21.72, 18.51, 13.97, -5.08.

IR: 2952, 2361, 1737, 1595, 1469, 1248, 1098, 774.

HRMS: (ESI$^+$) m/z: $[M+Na]^+$ Calcd for $C_{28}H_{40}NaO_2Si$ 459.2698; Found 459.2696.



***tert*-butyldimethyl((4-((8*R*,9*S*,13*S*,14*S*)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydrospiro[cyclopenta[*a*]phenanthrene-17,2'-[1,3]dioxolan]-3-yl)but-3-yn-1-yl)oxy)silane [33j].** To a 100 mL round bottom flask equipped with a Teflon stir bar was added (8*R*,9*S*,13*S*,14*S*)-3-(4-((*tert*-butyldimethylsilyl)oxy)but-1-yn-1-yl)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one (596 mg, 1.36 mmol, 1.00 eq.), *p*-TsOH•H_2O (23.6 mg, 0.124 mmol, 0.0910 eq.), ethylene glycol (1.52 mL, 27.2 mmol, 20.0 eq.), and benzene (9.00 mL). The reaction flask was fitted with a condenser equipped with a Dean Stark trap for the removal of water, and heated to reflux in an oil bath. Progress was monitored by TLC, and upon completion, reaction was poured into 10 mL of water, and extracted with DCM (3 x 10 mL). The combined organic layers were washed with water (10 mL), brine (10 mL), and dried over Na_2SO_4. Solvent was removed by rotary evaporation, and the crude product was dry loaded onto a column, and purified by flash column chromatography (200 mL of

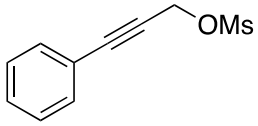
hexanes, 200 mL of 1% ethyl acetate in hexanes, 200 mL of 2% ethyl acetate in hexanes, and 500 mL of 3% ethyl acetate in hexanes) to give the pure product as a white solid (451 mg, 0.938 mmol, 69% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 – 7.10 (m, 3H), 4.00 – 3.86 (m, 4H), 3.80 (t, *J* = 7.1 Hz, 2H), 2.85 – 2.75 (m, 2H), 2.61 (t, *J* = 7.1 Hz, 2H), 2.36 – 2.19 (m, 2H), 2.08 – 1.97 (m, 1H), 1.94 – 1.71 (m, 4H), 1.68 – 1.23 (m, 6H), 0.91 (s, 9H), 0.88 (s, 3H), 0.09 (s, 6H).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 140.43, 136.84, 132.16, 128.84, 125.39, 120.92, 119.53, 86.26, 81.78, 65.41, 64.74, 62.22, 49.60, 46.25, 44.23, 38.82, 34.36, 30.84, 29.37, 26.96, 26.07, 25.95, 24.01, 22.50, 18.52, 14.46, -5.08.

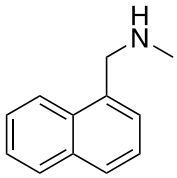
IR: 2980, 2883, 1600, 1469, 1383, 1087, 836.

HRMS: (ESI^{+}) m/z: $[M+Na]^{+}$ Calcd for $C_{30}H_{44}NaO_3Si$ 503.2960; Found 503.2960.



3-Phenylprop-2-yn-1-yl methanesulfonate

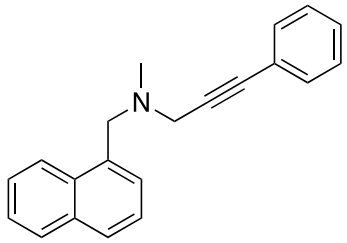
Following a previously reported procedure[19], in an oven-dried 50 mL round bottom flask equipped with a Teflon stir bar was added 3-phenylprop-2-yn-1-ol (502 mg, 3.80 mmol, 1.00 eq), Et_3N (0.800 mL, 5.70 mmol, 1.50 eq), and THF (15.0 mL). The reaction mixture was cooled to 0 °C and stirred for 10 min. Methanesulfonyl chloride (0.353 mL, 4.56 mmol, 1.20 eq) was then added dropwise to the reaction mixture. The reaction mixture was stirred at room temperature under nitrogen for 30 mins. Upon reaction completion, monitored by TLC, the reaction mixture was quenched with brine (20 mL), extracted with ethyl acetate (3 x 30 mL), and the combined organic layers were washed with 2 M HCl (50 mL), DI water (50 mL), saturated $NaHCO_3$ solution (50 mL), and brine (50 mL). The organic layers were dried over Na_2SO_4. The mixture was filtered, and the solvent was removed by rotary evaporation. The crude product was taken forward without further purification.



***N*-methyl-1-(naphthalen-1-yl)methanamine**

According to a previously reported procedure[20], in an oven-dried 50 mL round bottom flask equipped with a Teflon stir bar was added 1-naphthaldehyde (2.34 g, 15.0 mmol, 1.00 eq) and MeOH (30 mL). The methylamine solution (7.5 mL of a 2 M in THF solution, 15.0 mmol, 1.00 eq) was then added dropwise over 3 h via a syringe. After the addition of methylamine was complete, $NaBH_4$ (284 mg, 7.50 mmol, 0.500 eq) was added to reaction mixture and the reaction mixture was heated to 40°C overnight. Upon reaction completion, the solvent was removed by rotary evaporation to afford the crude product which was purified by flash column chromatography (1000 mL of 25% MeOH in DCM) to give the desired compound as a yellow oil (1.64 g, 9.58 mmol, 64%). Spectra matched previously reported data.[21]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.13 (d, *J* = 8.3 Hz, 1H), 7.87 (d, *J* = 8.1 Hz, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.57 – 7.40 (m, 4H), 4.21 (s, 2H), 2.56 (s, 3H), 1.55 (s, 1H).



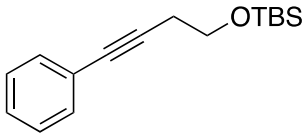
***N*-methyl-*N*-(naphthalen-1-ylmethyl)-3-phenylprop-2-yn-1-amine [33k].**
In an oven-dried 20 mL vial equipped with a Teflon stir bar and a pressure relief cap was added Cs_2CO_3 (4.07 g, 12.5 mmol, 5.00 eq), *N*-methyl-1-(naphthalen-1-yl)methanamine (428 mg, 2.50 mmol, 1.00 eq) in acetonitrile (3.80 mL), and 3-phenylprop-2-yn-1-yl methanesulfonate (553 mg, 2.63 mmol, 1.05 eq) in acetonitrile (3.80 mL). The reaction mixture was stirred at 70°C overnight and upon reaction completion, monitored by TLC, the reaction mixture was diluted with DI water (15 mL), extracted with ethyl acetate (3 x 15 mL), and the combined organic layers were washed with brine (50 ml) and dried over anhydrous Na_2SO_4. The mixture was filtered and the solvent was removed by rotary evaporation. The crude product was dry loaded onto a silica gel column and the product was purified by silica gel flash column chromatography (200 mL of 5% ethyl acetate in hexane, 200 mL of 10% ethyl acetate in hexane, 200 mL of 15% ethyl acetate in hexane) to give the desired compound as an orange oil (444 mg, 1.55 mmol, 62%).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.37 (d, *J* = 8.1 Hz, 1H), 7.86 (dd, *J* = 17.6, 7.8 Hz, 2H), 7.62 – 7.31 (m, 9H), 4.10 (s, 2H), 3.59 (s, 2H), 2.50 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 134.41, 134.01, 132.73, 131.87, 128.55, 128.45, 128.32, 128.17, 127.86, 126.14, 125.76, 125.27, 124.78, 123.48, 86.05, 84.68, 58.36, 46.00, 42.34.

IR: 3044, 2939, 2835, 2791, 1597, 1122.

HRMS: (ESI$^+$) m/z: $[M+H]^+$ Calcd for $C_{21}H_{20}N$ 286.1597; Found 286.1585.



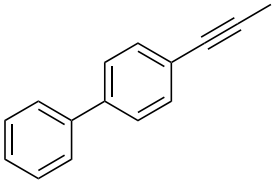
***Tert*-butyldimethyl((4-phenylbut-3-yn-1-yl)oxy)silane [35].** According to the general procedure E, 4-phenylbut-3-yn-1-ol (1.27 g, 8.68 mmol, 1.00 eq.), dry dichloromethane (18.0 mL), imidazole (1.18 g, 17.36 mmol, 2.00 eq.) and *tert*-butyldimethylsilyl chloride (1.44 g, 9.55 mmol, 1.10 eq.) were combined. The crude product was purified by flash column chromatography (200 mL of 100% hexanes, 800 mL of 3% ethyl acetate in hexanes) to yield the desired compound as a clear colorless oil (1.68 g, 6.45 mmol, 74% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.39 (m, 2H), 7.32 – 7.27 (m, 3H), 3.85 (t, *J* = 7.1 Hz, 2H), 2.65 (t, *J* = 7.1 Hz, 2H), 0.95 (s, 9H), 0.13 (s, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 131.70, 128.31, 127.77, 123.91, 87.30, 81.69, 62.09, 26.04, 23.97, 18.49, -5.11.

IR: 3081, 2954, 2928, 2856, 1100

HRMS: (ESI$^+$) m/z: $[M+H]^+$ Calcd for $C_{16}H_{25}OSi$ 261.1676; Found 261.1669.

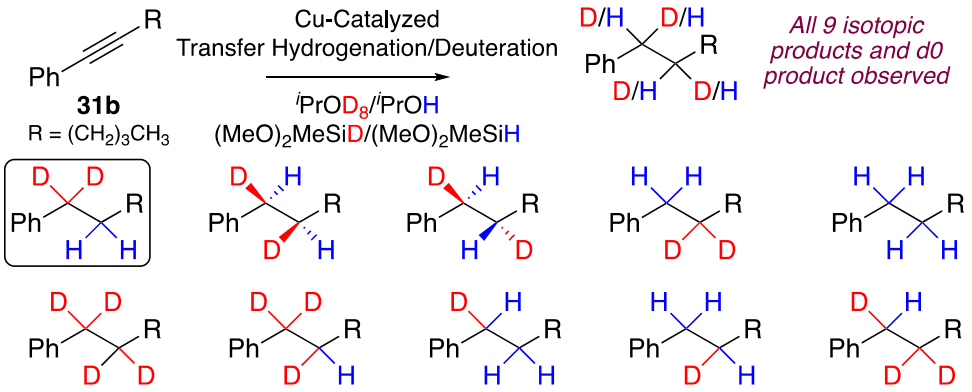


4-(Prop-1-yn-1-yl)-1,1'-biphenyl **[23']**. Adapted from a previously reported procedure[6], triethylamine (11.00 mL), 4-iodo-1,1'-biphenyl (1.00 g, 3.57 mmol, 1.00 eq), $Pd(PPh_3)_2Cl_2$ (50.0 mg, 0.0714 mmol, 0.0200 eq.), CuI (27.0 mg, 0.143 mmol, 0.0400 eq.) were added to a 100 mL flame dried round bottom flask, and was stirred for 15 minutes under N_2 at 50°C. 1-Propyne in THF (3.93 mL of a 1M solution, 3.93 mmol, 1.10 eq.) was then added in one portion and the reaction stirred under N_2 overnight. Post-reaction work up, the crude product was purified by flash column chromatography (800 mL of 100% hexanes) to give the pure product as a light yellow solid (643 mg, 3.34 mmol, 94% yield). The NMR data was consistent with previously reported spectra.[22]

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.63 – 7.56 (m, 2H), 7.56 – 7.50 (m, 2H), 7.50 – 7.40 (m, 4H), 7.39 – 7.30 (m, 1H), 2.08 (s, 3H).

Analysis by Molecular Rotational Resonance

Scheme 41: Alkyne Reduction to Access All Possible Isotopic Species

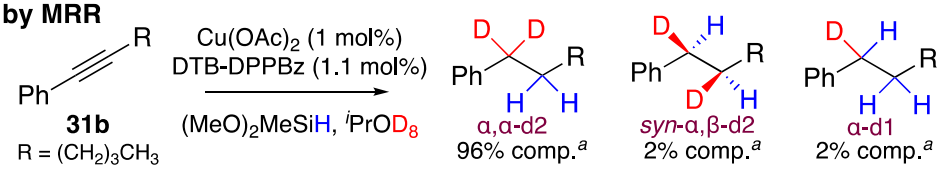


In a N_2 filled glovebox, DTB-DPPBz (62.2 mg, 0.0695 mmol, 0.0220 eq.), $Cu(OAc)_2$ (316 µL of a 0.200 M solution in THF, 0.0632 mmol, 0.0200 eq.), and THF (1.42 mL) were added to a flame-dried 100 mL round bottom flask followed by dropwise addition of dimethoxy(methyl)silane (974 µL, 7.90 mmol, 2.50 eq.) and dimethoxy(methyl)silane-*d* (1.47 mL of a 5.36 M solution in hexanes, 7.90 mmol, 2.50 eq.). A color change from green/blue to brown was observed while stirring for 15 minutes. In a separate oven-dried 2- dram vial was added 1-phenyl-1-hexyne (500 mg, 3.16 mmol, 1.00 eq.), THF (1.42 mL), 2-propanol (605 µL, 7.90 mmol, 2.50 eq), and 2-propanol-d_8 (605 µL, 7.90 mmol, 2.50 eq). The solution in the 2-dram vial was added dropwise over 20 seconds to the 100 mL round bottom flask. The total volume of THF was calculated based on having a final reaction concentration of 1M based on the alkene substrate. The 100 mL round bottom flask was capped with a septum, taken out of the glovebox, and a balloon filled with N_2 was inserted through the septum as the reaction stirred for 24 h at 40°C. Upon completion, the crude product mixture was dry loaded onto a silica gel column and purified by flash column chromatography using 100% hexanes to give the product as a clear oil (437 mg, 2.66 mmol, 84% yield). Since the product contains a mixture of d_0, d_1 and d_2 isotopologues and isotopomers, isolated yields were calculated based on an average deuterium incorporation of two deuterium.

^{1}H NMR (400 MHz, Chloroform-*d*): 7.32 – 7.27 (m, 2H), 7.24 – 7.17 (m, 3H), 2.66 – 2.57 (m, 0.92H), 1.68 – 1.54 (m, 1.24H), 1.41 – 1.27 (m, 6H), 0.95 – 0.87 (m, 3H).

^{2}H NMR (61 MHz, Chloroform) δ 2.63 (s, 1.08D), 1.65 (s, 0.85D).

Scheme 42: Regioselective Transfer Hydrodeuteration Reaction Measured by MRR



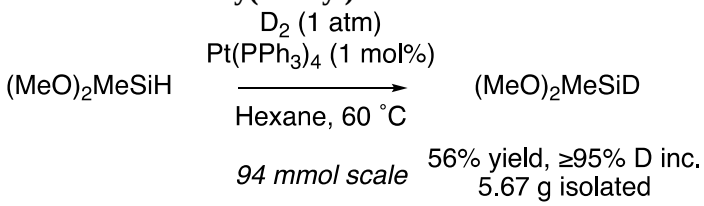
[a]Denotes the average percent composition of isolated product from two runs.

D_2-Hexyl-benzene [32b-MRR]. According to the general procedure C, DTB-DPPBz (4.00 mg, 0.00440 mmol, 0.0110 eq.), $Cu(OAc)_2$ (20.0 µL of a 0.200 M solution in THF, 0.00400 mmol, 0.0100 eq.), THF (0.180 mL) and dimethoxy(methyl)silane (247 µL, 2.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 1-hexyn-1-yl-benzene **31b** (63.3 mg, 0.400 mmol, 1.00 eq.), THF (0.200 mL), and 2-propanol-d_8 (153 µL, 2.00 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 23 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (250 mL of 100% hexanes) gives the pure product as a clear colorless oil (52.0 mg, 0.317 mmol, 79% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.27 (m, 2H), 7.25 – 7.16 (m, 3H), 2.66 – 2.57 (m, 0.04H), 1.69 – 1.57 (m, 2H), 1.41 – 1.26 (m, 6H), 0.98 – 0.85 (m, 3H).

^{2}H NMR (61 MHz, Chloroform) δ 2.62 (s, 1.96D), 1.65 (s, 0.02D).

Procedure for the Synthesis of dimethoxy(methyl)silane-*d*

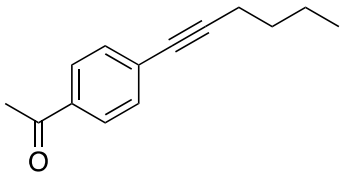


The procedure was adapted from a previously reported method.[23] To an oven-dried 500 mL Schlenk flask equipped with a Teflon stir bar in a N_2 filled glovebox was added the $Pt(PPh_3)_4$ (1.17 g, 0.941 mmol, 0.0100 eq.), dimethoxy(methyl)silane (11.6 mL, 94.1 mmol, 1.00 eq.), and 5.00 mL of degassed anhydrous hexanes. The Schlenk flask was sealed with a rubber septa and removed from the glovebox, connected to a manifold line, and cooled to -78 ˚C. A single freeze-pump-thaw cycle was performed, and the Schlenk flask was backfilled with D_2 gas from a D_2 purged balloon at room temperature. The flask was sealed with parafilm and heated to 60 °C. After 2 hours, the reaction was cooled to room temperature and then a single freeze-pump-thaw was performed again, backfilling with D_2 gas. The process was repeated 6 times or until the ^{1}H NMR showed ≥95% D incorporation. It is important to maintain a N_2 (g) inert atmosphere while obtaining a minimal quantity of sample for ^{1}H NMR analysis. The solution was purified through a distillation apparatus; the set up consisted of a flame-dried 25 mL round-bottom receiving flask and a cannula. The 25 mL round-bottom receiving flask was flame-dried, and then filled with N_2. Once the receiving flask reached room temperature, the cannula was inserted, maintaining positive pressure, and tightly sealed with parafilm to prevent condensation from entering. Upon confirmation of positive N_2 flow, the open end of the cannula was inserted into the Schlenk reaction flask. The 25 mL round-bottom receiving flask was cooled to -78 ˚C and closed to the manifold line, and then

the Schlenk flask was heated to 80 °C. The heat initiated the distillation of the dimethoxy(methyl)silane-d and the hexane through the cannula which were trapped in the cold 25 mL round-bottom receiving flask. Vacuum was also applied to the 25 mL round-bottom receiving flask to promote this process. Once all of the silane and hexane were trapped in the 25 mL round-bottom receiving flask, the flask was removed from the heat and the manifold was closed to vacuum line while the 25 mL round-bottom receiving flask warmed to room temperature. Under positive nitrogen flow, the cannula was removed from the 25 mL round-bottom receiving flask, while keeping it inserted in the Schlenk reaction flask. The 25 mL round-bottom receiving flask was tightly sealed with Parafilm, and stored in the -4 ˚C freezer. The final product was in a solution of hexane, and the molarity was calculated by ^{1}H NMR using 1,3,5-trimethylbenzene as an internal standard, and used for the transfer deuteration reactions (5.67 g in a 5.29 M hexane solution, 52.9 mmol, 56% yield).

*Note: it is important to monitor that the end of the cannula does not get clogged by frozen solvent/silane. If this occurs, remove the Schlenk reaction flask from heat and close manifold to vacuum line. Warm the 25 mL round-bottom receiving flask until the solids on the tip of the cannula melt, and then distillation can be resumed.

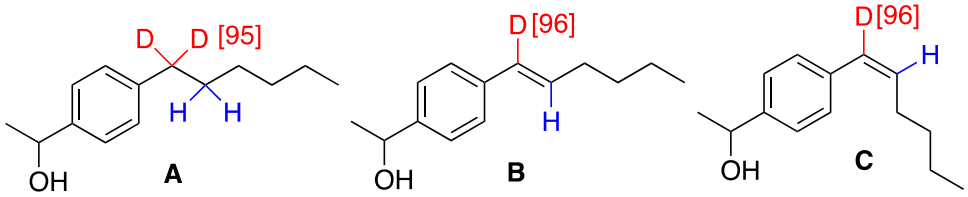
Substrate Limitations



1-(4-(Hex-1-yn-1-yl)phenyl)ethan-1-one. In an flame dried 100mL round bottom flask equipped with a Teflon stir bar was added $Pd(PPh_3)_4$ (578 mg, 0.500 mmol, 0.0500 eq), CuI (191 mg, 1.00 mmol, 0.100 eq), 1-(4-bromophenyl)ethan-1-one (2.00 g, 10.0 mmol, 1.00 eq), THF (5.00 mL) and Et_3N (4.00 mL). The mixture was degassed for 10 min, then 1-hexyne (1.37 mL, 12.0 mmol, 1.20 eq) was added dropwise. The reaction mixture was stirred at 100 ˚C under nitrogen overnight. Upon completion (judged by TLC), the reaction mixture was diluted with 20 mL Et_2O and washed with 40 mL sat. NH_4Cl (aq). The aqueous layer was extracted with Et_2O (2 X 40 mL). The combined organic layers were washed with 100 mL brine and dried over anhydrous $MgSO_4$. The mixture was filtered and the solvent was removed by rotary evaporation. The crude product was purified by silica gel flash column chromatography (200 mL 100% hexanes, 200 mL 5% ethyl acetate in hexanes, 400 mL 20% ethyl acetate in hexanes) and the title compound was afforded as a dark brown oil (1.90 g, 9.70 mmol, 97% yield). The spectra matched previously reported data.[24]

^{1}H NMR (400 MHz, cdcl$_3$) δ 7.82 (d, *J* = 8.0 Hz, 2H), 7.41 (d, *J* = 8.0 Hz, 2H), 2.53 (s, 3H), 2.39 (t, *J* = 7.1 Hz, 2H), 1.63 – 1.37 (m, 4H), 0.92 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, cdcl$_3$) δ 197.28, 135.62, 131.63, 129.16, 128.16, 94.37, 80.12, 30.64, 26.54, 22.04, 19.23, 13.64.



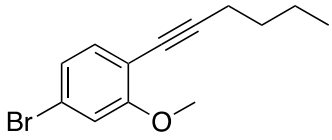
1-(4-(Hexyl-1,1-*d*$_2$)phenyl)ethan-1-ol [A, B, C]. According to the general procedure C, DTB-DPPBz (3.00 mg, 0.00330 mmol, 0.011 eq.), $Cu(OAc)_2$ (15.0 µL of a 0.200 M solution in THF, 0.00300 mmol, 0.0100 eq.), THF (0.135 mL) and dimethoxy(methyl)silane (185 µL, 1.50 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 1-(4-(hex-1-yn-1-yl)phenyl)ethan-1-one (60.1 mg, 0.300 mmol, 1 eq.), THF (0.150 mL), and 2-propanol-d_8 (115 µL, 1.50 mmol, 5.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 19 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (100 mL of 100% hexanes, 100 mL of 3% ethyl acetate in hexanes, 100 mL of 5% ethyl acetate in hexanes) gives an isolated product mixture as a clear colorless oil (95.0 mg, 0.273 mmol, 91% yield). We anticipated that any ketone reduction byproducts would exist as the corresponding silyl ether product and proceeded to perform a subsequent silyl deprotection to achieve alcohol products. Accordingly, the isolated product mixture was dissolved in THF (1.46 mL) and tetrabutylammonium fluoride (0.550 mL of 1.00 M in THF solution, 0.550 mmol, 2.00 eq.) was added. The reaction was stirred at room temperature overnight. Upon completion, the reaction mixture was diluted with Et_2O (10 mL) and quenched with saturated aqueous NH_4Cl (5 mL). The aqueous layer was extracted with Et_2O (3 x 10 mL) and the combined organic layers were washed with water (10 mL) and brine (10 mL), then dried over anhydrous Na_2SO_4. The mixture was filtered, and the solvent was removed by rotary evaporation.

Purification using silica gel flash chromatography (100 mL of hexanes, 100 mL of 10% ethyl acetate in hexanes, 150 mL of 15% ethyl acetate in hexanes) gives the product mixture as a clear oil which was analyzed using 1,3,5-trimethylbenzene as an internal standard (**A, B, C** 60% yield by ^{1}H NMR). Based on ^{1}H NMR analysis, the ketone underwent full reduction (see labeled peaks in the reported spectra below).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.27 (m, 1.52 H), 7.13 (d, *J* = 7.8 Hz, 0.6H), 6.83 (s, 1H, mesitylene internal standard), 6.42 (s, 0.01 H), 6.25 (t, *J* = 6.8, 0.16H), 5.69 (t, J = 7.3 Hz, 0.04 H), 4.89 (q, *J* = 6.5 Hz, 0.53H), 2. 64 – 2.56 (m, 0.06H), 2.31 (s, 3H, mesitylene internal standard), 2.24 (q, *J* = 7.1 Hz, 0.24H), 1.93 (s, 0.7H), 1.67 – 1.55 (m, 0.86H), 1.54 – 1.23 (m, 5.95H), 0.99 – 0.87 (m, 2.2H).

^{2}H NMR (61 MHz, Chloroform-*d*) δ 6.44 (s, 0.72 D), 2.60 (s, 1.94 D), 1.62 (s, 0.11 D).

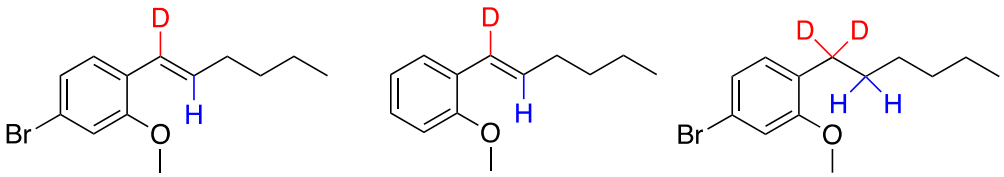
^{13}C NMR (101 MHz, Chloroform-*d*) δ 144.39, 144.00, 143.14, 142.32, 137.84 (mesitylene internal standard), 137.34, 131.22 (d, *J* = 5.6 Hz), 129.00, 128.62, 127.02 (mesitylene internal standard), 126.09, 125.68, 125.47, 125.32, 70.37 (3 representative peaks for the 3 products formed), 36.75, 35.64 – 34.39 (m), 32.81, 32.29, 32.07, 31.87, 31.65, 31.56, 31.48, 29.85, 29.51, 29.10, 28.52, 25.15, 25.12, 22.75, 22.57, 22.40, 21.32 (mesitylene internal standard), 14.24, 14.09.



4-Bromo-1-(hex-1-yn-1-yl)-2-methoxybenzene. In a flame dried 100 mL round bottom flask equipped with a Teflon stir bar was added $Pd(PPh_3)_2Cl_2$ (35.0 mg, 0.0500 mmol, 0.0100 eq), CuI (19.0 mg, 0.100 mmol, 0.0200 eq), 4-bromo-1-iodo-2-methoxybenzene (1.56 g, 5.00 mmol, 1.00 eq), THF (6.50 mL) and Et_3N (2.00 mL). The mixture was degassed for 10 min, and then 1-hexyne (0.630 mL, 5.50 mmol, 1.10 eq) was added dropwise. The reaction mixture was stirred at 75 ˚C under nitrogen overnight. Upon completion (judged by TLC), the reaction mixture was diluted with 50 mL Et_2O and washed with 20 mL sat. NH_4Cl (aq.). The aqueous layer was extracted with Et_2O (2 X 50 mL). The combined organic layers were washed with 100 mL brine and dried over anhydrous $MgSO_4$. The mixture was filtered and the solvent was removed by rotary evaporation. The crude product was purified by silica gel flash column chromatography (200 mL 100% hexanes, 450 mL 10% diethyl ether in hexanes) and the title compound was afforded as a red oil (1.30 g, 4.95 mmol, 99% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 – 7.17 (m, 1H), 7.07 – 6.94 (m, 2H), 3.86 (s, 2H), 2.45 (t, *J* = 7.0 Hz, 2H), 1.67 – 1.39 (m, 4H), 0.94 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $cdcl_3$) δ 160.41, 134.53, 123.67, 122.21, 114.37 (d, *J* = 5.5 Hz), 112.48, 95.95, 75.86, 56.19 (*J* = 6.7 Hz), 30.93, 22.16, 19.61, 13.79.



A **B** **C**

4-Bromo-1-(hexyl-1,1-*d*$_2$)-2-methoxybenzene [A, B, C]. According to the general procedure C, DTB-DPPBz (9.85 mg, 0.0110 mmol, 0.0550 eq.), $Cu(OAc)_2$ (50.0 µL of a 0.200 M solution in THF, 0.0100 mmol, 0.0500 eq.), THF (0.950 mL) and dimethoxy(methyl)silane (123 µL, 1.00 mmol, 5.00 eq.) were combined in a 2-dram vial followed by addition of a solution of 4-Bromo-1-(hex-1-yn-1-yl)-2-

methoxybenzene [9] (53.4 mg, 0.200 mmol, 1.00 eq.), THF (1.00 mL), and 2-propanol-d_8 (91.9 µL, 1.20 mmol, 6.00 eq). The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 20 h at 40 °C. Upon completion, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (600 mL of 100% petroleum ether) gives the product mixture, including trace debromination product which matches previously reported spectra[25], as a clear colorless oil (30 mg of product mixture).

^{1}H NMR (400 MHz, cdcl$_3$) δ 7.22 – 6.80 (m, 3.39H), 6.40 (s, 0.02H), 5.74 (t, *J* = 7.3 Hz, 1H), 3.82 (s, 3H), 2.21 (q, *J* = 7.3 Hz, 2H), 1.46 – 1.27 (m, 5H), 0.88 (t, *J* = 7.1 Hz, 3.41H).

^{2}H NMR (61 MHz, Chloroform-*d*) δ 6.4 (s, 0.98 D), 2.54 (s, 0.08 D).

^{13}C NMR (101 MHz, cdcl$_3$) δ 157.73, 157.56 (debromination product), 151.64, 140.29, 135.87, 133.87 (debromination product), 133.73, 131.08, 129.84 (debromination product), 128.37(debromination product), 126.84 (debromination product), 125.60, 123.13, 122.89, 122.65, 121.04, 120.40 (debromination product), 114.65, 114.07, 110.30 (debromination product), 55.77, 55.35 (debromination product), 34.34, 32.13, 31.92 (debromination product), 30.44, 29.84 (debromination product), 29.38, 28.53, 22.79 (debromination product), 22.54, 21.32, 14.24 (debromination product), 14.09.

References (Research Methodology and Characterization Chapter 3)

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Chapter 4

General Information

The following chemicals were purchased from commercial vendors and were used as received: $Cu(OAc)_2$ (99.999% from Alfa Aesar); dimethoxy(methyl)silane (TCI); Diphenylsilane (Ambeed); diphenyl(silane-d_2) (Sigma Aldrich); tertbutyldimethylsilyl chloride (TBSCl). Anhydrous benzene was purified by an MBRAUN solvent purification system (MB-SPS). Prior to use, triethylamine (Et_3N) was distilled over CaH_2 and stored over 3Å molecular sieves. Chloroform-*d* ($CDCl_3$) was stored over 3Å molecular sieves. 1,2-Bis[bis[3,5-di(t-butyl)phenyl]phosphino]benzene (DTB-DPPBz) was synthesized according to a previously reported procedure.[1]

Thin-layer chromatography (TLC) was conducted with Silicycle silica gel 60Å F254 pre-coated plates (0.25 mm) and visualized with UV, Iodine and $KMnO_4$ stains. Flash chromatography was performed using Silia Flash® P60, 40-60 µm (230-400 mesh), purchased from Silicycle. For reactions that required heating (optimization, hydrosilylation, vinyl silane transformation reactions, and synthesis of alkyne starting materials), a PolyBlock for 2 dram vials or 100 mL round bottom flasks was used on top of a Heidolph heating/stir plate.

^1H NMR spectra were recorded on a Varian 400 or 600 MHz spectrometer and are reported in ppm using residual $CHCl_3$ as an internal standard (7.26 ppm). Data reported as: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sxt = sextet, m = multiplet, br = broad; coupling constant(s) in Hz; integration. ^{13}C NMR spectra were recorded on a Varian 76 MHz or 101 MHz spectrometer and are reported in ppm using residual $CHCl_3$ as an internal standard (77.16 ppm). ^{19}F NMR spectra were recorded on a Varian 376 MHz spectrometer. ^2H NMR spectra were recorded on a Varian 61 MHz spectrometer. Labeled solvent impurities were calculated out when reporting isolated yields.

Optimization Studies

General Procedure A for Optimization Studies in Table 5:

In an N_2 filled glovebox, 1-chloro-3-(1-hexyn-1-yl)benzene **[42]** (57.8 mg, 0.300 mmol, 1.00 eq) was added to an oven-dried 2-dram vial followed by addition of a solution of $Cu(OAc)_2$ and DTB-DPPBz (0.075 M solution in solvent, $Cu(OAc)_2$:DTB-DPPBz = 1:1.01, 0.015 mmol, 0.050 eq). Diphenylsilane (83.8 µL, 0.450 mmol, 1.50 eq) was added dropwise to the 2-dram vial followed by the addition of benzene (2.80 mL, 0.100 M total reaction concentration). The 2-dram vial was capped with a red pressure relief cap, taken out of the glovebox, and stirred for 22 hours at the respective temperature, at which point the reaction was filtered through a 1" silica plug with 50 mL of CH_2Cl_2 followed by 50 mL of CH_2Cl_2 to elute the remaining product into a 200 mL round bottom flask. After removing the solvent by rotary evaporation, the product was analyzed by ^1H NMR using 1,3,5-trimethylbenzene as an internal standard. If greater than 5% ^1H NMR yield was observed for **43** in the crude ^1H NMR, yields were obtained by isolating the product by flash column chromatography.

The isomeric ratio of products was determined by ^1H NMR by adding the integrations of all of the isomers' allylic protons together, and then dividing each isomeric allylic proton integration by the sum to get a ratio of products. The black arrow in each ^1H NMR spectra indicates the allylic protons of the minor regioisomer.

Entry 1. According to the general procedure A, 1-chloro-3-(1-hexyn-1-yl)benzene (57.8 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/DTB-DPPBz solution (0.075 M solution in benzene, 120 µL, 0.009 mmol, 0.030 eq), Ph_2SiH_2 (83.8 µL, 0.450 mmol, 1.50 eq), and benzene (2.88 mL, 0.100 M total concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction was stirred for 22 h at 40 ˚C. Upon completion and crude ^1H NMR analysis, the

crude product was dry loaded onto silica gel and isolated by flash column chromatography (300 mL of 100% hexanes) to give the pure product as a clear oil (82.3 mg, 0.218 mmol, 73% yield, >20:1).

Entry 2. According to the general procedure A, 1-chloro-3-(1-hexyn-1-yl)benzene (57.8 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/DTB-DPPBz solution (0.075 M solution in benzene, 200 µL, 0.015 mmol, 0.050 eq), Ph_2SiH_2 (83.8 µL, 0.450 mmol, 1.50 eq), and benzene (2.80 mL, 0.100 M total concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction was stirred for 22 h at 40 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product was dry loaded onto silica gel and isolated by flash column chromatography (300 mL of 100% hexanes) to give the pure product as a clear oil (98.5 mg, 0.261 mmol, 87% yield, >20:1).

Entry 3. According to the general procedure A, 1-chloro-3-(1-hexyn-1-yl)benzene (57.8 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/DTB-DPPBz solution (0.075 M solution in benzene, 200 µL, 0.015 mmol, 0.050 eq), Ph_3SiH (117.2 mg, 0.450 mmol, 1.50 eq), and benzene (2.80 mL, 0.100 M total concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction was stirred for 22 h at 40 ˚C. Upon completion, the crude ^{1}H NMR was analyzed using 1,3,5-trimethylbenzene as an internal standard (84% RSM **42** observed by crude ^{1}H NMR using 1,3,5-trimethylbenzene as an internal standard).

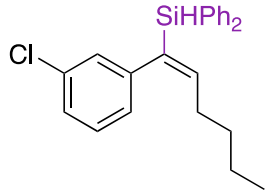
Entry 4. According to the general procedure A, 1-chloro-3-(1-hexyn-1-yl)benzene (57.8 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/DTB-DPPBz solution (0.075 M solution in benzene, 200 µL, 0.015 mmol, 0.050 eq), DMMS (55.5 µL, 0.450 mmol, 1.50 eq), and benzene (2.80 mL, 0.100 M total concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction was stirred for 22 h at 40 ˚C. Upon completion, the crude ^{1}H NMR was analyzed using 1,3,5-trimethylbenzene as an internal standard (81% RSM **42** and trace product observed by crude ^{1}H NMR using 1,3,5-trimethylbenzene as an internal standard).

Entry 5. According to the general procedure A, 1-chloro-3-(1-hexyn-1-yl)benzene (57.8 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/DTB-DPPBz solution (0.075 M solution in benzene, 200 µL, 0.015 mmol, 0.050 eq), Ph_2SiH_2 (83.8 µL, 0.450 mmol, 1.50 eq), and benzene (2.80 mL, 0.100 M total concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction was stirred for 22 h at room temperature. Upon completion and crude ^{1}H NMR analysis, the crude product was dry loaded onto silica gel and isolated by flash column chromatography (300 mL of 100% hexanes) to give the pure product as a clear oil (95.0 mg, 0.252 mmol, 84% yield, >20:1).

Entry 6. According to the general procedure A, 1-chloro-3-(1-hexyn-1-yl)benzene (57.8 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/DTB-DPPBz solution (0.075 M solution in benzene, 200 µL, 0.015 mmol, 0.050 eq), Ph_2SiH_2 (83.8 µL, 0.450 mmol, 1.50 eq), and benzene (2.80 mL, 0.100 M total concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction was stirred for 22 h at 5 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product was dry loaded onto silica gel and isolated by flash column chromatography (300 mL of 100% hexanes) to give the pure product as a clear oil (90.0 mg, 0.239 mmol, 80% yield, >20:1).

Entry 7. According to the general procedure A, 1-chloro-3-(1-hexyn-1-yl)benzene (57.8 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/DTB-DPPBz solution (0.075 M solution in toluene, 200 µL, 0.015 mmol, 0.050 eq), Ph_2SiH_2 (83.8 µL, 0.450 mmol, 1.50 eq), and toluene (2.80 mL, 0.10 M total concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction was stirred for 22 h at 40 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product was dry loaded onto silica gel and isolated by flash column chromatography (300 mL of 100% hexanes) to give the pure product as a clear oil (84.0 mg, 0.223 mmol, 74% yield; 96:4, >20:1).

Entry 8. According to the general procedure A, 1-chloro-3-(1-hexyn-1-yl)benzene (57.8 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/DTB-DPPBz solution (0.075 M solution in THF, 200 µL, 0.015 mmol, 0.050 eq), Ph_2SiH_2 (83.8.0 µL, 0.450 mmol, 1.50 eq), and THF (2.80 mL, 0.10 M total concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction was stirred for 22 h at 40 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product was dry loaded onto silica gel and isolated by flash column chromatography (300 mL of 100% hexanes) to give the pure product as a clear oil (93.0 mg, 0.247 mmol, 82% yield, >20:1).



(*E*)-(1-(3-chlorophenyl)hex-1-en-1-yl)diphenylsilane [43].
^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.56 (d, *J* = 7.1 Hz, 4H), 7.47 – 7.36 (m, 6H), 7.20 – 7.13 (m, 2H), 7.03 (s, 1H), 6.90 (d, *J* = 6.5 Hz, 1H), 6.26 (t, *J* = 7.2 Hz, 1H), 5.23 (s, 1H), 2.13 (q, *J* = 7.3 Hz, 2H), 1.39 (p, *J* = 7.5 Hz, 2H), 1.35 – 1.26 (m, 2H) (overlaps with grease), 0.87 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 148.96, 143.45, 136.92, 135.85, 133.95, 133.21, 129.89, 129.42, 128.46, 128.12, 126.72, 126.06, 31.60, 30.16, 22.45, 14.04.

IR: 3068, 2955, 2925, 2856, 1588, 1559, 1107, 798.

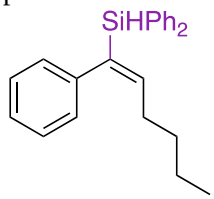
HRMS: (ESI$^+$) m/z: $[M+Na]^+$ Calculated for $C_{24}H_{25}SiClNa$ 399.1312; Found 399.1335

Hydrosilylation Reaction Substrate Scope

General Procedure B for Hydrosilylation Reactions:

In a N_2 filled glovebox, the alkyne substrate (0.300 mmol, 1.00 eq) was added to an oven-dried 2-dram vial followed by addition of a solution of $Cu(OAc)_2$ and DTB-DPPBz (0.075 M solution in benzene, $Cu(OAc)_2$:DTB-DPPBz = 1:1.01, 0.009 – 0.015 mmol, 0.030 - 0.050 eq). Ph_2SiH_2 (83.8 µL, 0.450 mmol, 1.50 eq) was added dropwise over 1 minute to the 2-dram vial followed by addition of benzene (2.80 mL, 0.100 M total reaction concentration). The 2-dram vial was capped with a red pressure relief cap, taken out of the glovebox, and stirred for the respective time at 40 ˚C, at which point the reaction was filtered through a 1" silica plug with 50 mL of Et_2O or CH_2Cl_2 followed by 50 mL of Et_2O or CH_2Cl_2 to elute the remaining product into a 200 mL round bottom flask. After removing the solvent by rotary evaporation, the crude product was isolated by flash column chromatography.

The isomeric ratio of products was determined by ^{1}H NMR, specifically by adding the integrations of all of the isomers' allylic protons together, and then dividing each isomeric allylic proton integration by the sum to get a ratio of products. Respective isomer identified in ^{1}H NMR spectra by black arrow pointing to allylic protons.



(*E*)-diphenyl(1-phenylhex-1-en-1-yl)silane. [46a] According to the general procedure B, 1-phenyl-1-hexyne (47.5 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/DTB-DPPBz solution (0.075 M solution in toluene, 200

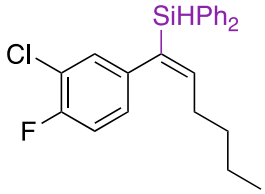
µL, 0.015 mmol, 0.050 eq), Ph_2SiH_2 (83.8 µL, 0.450 mmol, 1.50 eq), and toluene (2.80 mL, 0.100 M total concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction was stirred for 22 h at 40 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product was dry loaded onto silica gel and isolated by flash column chromatography (300 mL of 100% hexanes) to give the pure product as a yellow oil (79.2 mg, 0.231 mmol, 77% yield, >20:1).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.57 (d, *J* = 7.1 Hz, 4H), 7.45 – 7.40 (m, 2H), 7.40 – 7.36 (m, 4H), 7.29 – 7.23 (m, 2H), 7.18 (t, *J* = 7.4 Hz, 1H), 7.04 (d, *J* = 7.4 Hz, 2H), 6.25 (t, *J* = 7.1 Hz, 1H), 5.24 (s, 1H), 2.16 (q, *J* = 7.3 Hz, 2H), 1.39 (p, *J* = 7.5 Hz, 2H), 1.34 – 1.26 (m, 2H) (overlaps with grease), 0.87 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 148.21, 141.51, 137.89, 135.90, 133.76, 129.70, 128.51, 128.15, 128.02, 125.89, 31.75, 30.12, 22.48, 14.07.

IR: 3068, 3050, 3016, 2999, 2955, 2924, 2871, 2857, 1595, 1465.

HRMS: (ESI+) m/z: $[M+H]^+$ Calculated for $C_{24}H_{27}Si$ 343.1882; Found 343.1857.



(*E*)-(1-(3-chloro-4-fluorophenyl)hex-1-en-1-yl)diphenylsilane. [46b] According to the general procedure B, 2-chloro-1-fluoro-4-(hex-1-yn-1-yl)benzene (63.0 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/ DTB-DPPBz solution (0.075 M solution in benzene, 200 µL, 0.015 mmol, 0.050 eq), Ph_2SiH_2 (83.8 µL, 0.450 mmol, 1.50 eq), and benzene (2.80 mL, 0.100 M total reaction concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 40 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (300 mL of 100% hexanes) gives the pure product as a white oil (98.7 mg, 0.250 mmol, 83% yield, >20:1).

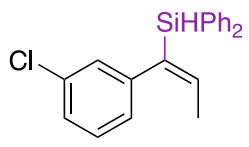
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56 (d, *J* = 7.3 Hz, 4H), 7.49 – 7.36 (m, 6H), 7.07 – 6.98 (m, 2H), 6.88 – 6.81 (m, 1H), 6.27 (t, *J* = 7.1 Hz, 1H), 5.22 (s, 1H), 2.12 (q, *J* = 7.2 Hz, 2H), 1.43 – 1.34 (m, 2H), 1.33 – 1.24 (m, 2H), 0.88 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.55 (d, *J* = 247.2 Hz), 149.34 (d, *J* = 0.8 Hz), 138.50 (d, *J* = 4.1 Hz), 136.16, 135.81, 132.98, 130.36, 129.98, 128.24, 128.18, 120.54 (d, *J* = 17.6 Hz), 116.29 (d, *J* = 20.9 Hz), 31.54, 30.13, 22.45, 14.02.

^{19}F NMR (564 MHz, Chloroform-*d*) δ -119.54.

IR: 3068, 2956, 2925, 2871, 2121, 1492, 1465.

HRMS: (ESI +) m/z: [M+H]+ Calculated for $C_{24}H_{25}FSiCl$ 395.1398; Found 395.1398.



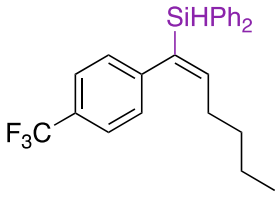
(*E*)-(1-(3-chlorophenyl)prop-1-en-1-yl)diphenylsilane. [46c] According to the general procedure B, 1-chloro-3-(prop-1-yn-1-yl)benzene (45.0 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/ DTB-DPPBz solution (0.075 M solution in benzene, 200 μL, 0.015 mmol, 0.050 eq), Ph_2SiH_2 (83.8 μL, 0.450 mmol, 1.50 eq), and benzene (2.80 mL, 0.100 M total reaction concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 40 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (300 mL of 100% hexanes) gives the pure product as a white oil (69.5 mg, 0.208 mmol, 69% yield, >20:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 (d, *J* = 6.9 Hz, 4H), 7.49 – 7.35 (m, 6H), 7.20 – 7.15 (m, 2H), 7.06 (s, 1H), 6.95 – 6.91 (m, 1H), 6.35 (q, *J* = 6.6 Hz, 1H), 5.24 (s, 1H), 1.76 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 143.15, 143.03, 138.19, 135.85, 134.02, 133.15, 129.91, 129.51, 128.51, 128.12, 126.76, 126.13, 16.52.

IR: 3751, 3067, 2119,1602, 1470, 1109.

HRMS: (ESI +) m/z: [M+Na]+ Calculated for $C_{21}H_{19}SiClNa$ 357.0843; Found 357.0930.



(*E*)-diphenyl(1-(4-(trifluoromethyl)phenyl)hex-1-en-1-yl)silane. [46d] According to the general procedure B, 1-(hex-1-yn-1-yl)-4-(trifluoromethyl)benzene (67.8 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/DTB-DPPBz solution (0.075 M solution in benzene, 200 ul, 0.015 mmol, 0.050 eq), Ph_2SiH_2 (83.8 μL, 0.450 mmol, 1.50 eq), and benzene (2.80 mL, 0.100 M total reaction concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 40 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (300 mL of 100% hexanes) gives the pure product as a yellowish oil (103 mg, 0.251 mmol, 84% yield, >20:1).

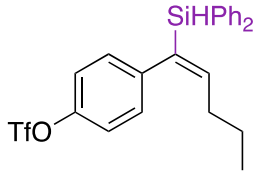
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (d, *J* = 6.8 Hz, 4H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.50 – 7.39 (m, 6H), 7.16 (d, *J* = 7.9 Hz, 2H), 6.35 (t, *J* = 7.2 Hz, 1H), 5.28 (s, 1H), 2.15 (q, *J* = 7.3 Hz, 2H), 1.43 (p, *J* = 6.7 Hz, 2H), 1.32 (sxt, *J* = 7.0 Hz, 2H), 0.90 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 149.12, 145.62, 145.61, 137.28, 135.86, 133.06, 129.99, 128.78, 128.18, 125.18 (q, *J* = 3.6 Hz), 124.54 (q, *J* = 175.9 Hz), 31.60, 30.23, 22.47, 14.03.

^{19}F NMR (564 MHz, Chloroform-*d*) δ -62.22.

IR: 3069, 2957, 2872, 2122, 1428, 1320.

HRMS: (ESI$^+$) m/z: $[M+Na]^+$ Calculated for $C_{25}H_{25}F_3SiNa$ 433.1576; Found 433.1595.



(*E*)-4-(1-(diphenylsilyl)pent-1-en-1-yl)phenyl trifluoromethanesulfonate. [46e] According to the general procedure B, 4-(pent-1-yn-1-yl)phenyl trifluoromethanesulfonate (87.7 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/ DTB-DPPBz solution (0.075 M solution in benzene, 200 μL, 0.015 mmol, 0.050 eq), Ph_2SiH_2 (83.8 μL, 0.450 mmol, 1.50 eq), and benzene (2.80 mL, 0.100 M total reaction concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 40 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (300 mL of 100% hexanes) gives the pure product as a white oil (116 mg, 0.243 mmol, 81% yield, >20:1).

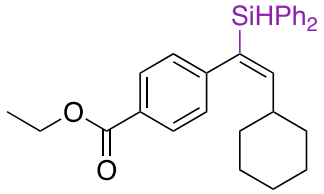
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.53 (d, *J* = 7.4 Hz, 4H), 7.47 – 7.34 (m, 6H), 7.16 (d, *J* = 8.3 Hz, 2H), 7.05 (d, *J* = 8.3 Hz, 2H), 6.30 (t, *J* = 7.1 Hz, 1H), 5.22 (s, 1H), 2.09 (q, *J* = 7.3 Hz, 2H), 1.43 (sxt, *J* = 7.3 Hz, 2H), 0.89 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 149.01, 147.87, 142.14, 136.89, 135.80, 132.94, 130.18, 130.00, 128.18, 121.05, 118.89 (q, *J* = 321.1 Hz), 32.42, 22.58, 13.89.

^{19}F NMR (564 MHz, Chloroform-*d*) δ -72.89.

IR: 3069, 2960, 2124,1496, 1422, 1207, 1177.

HRMS: (ESI +) m/z: [M+H]+ Calculated for $C_{24}H_{24}O_3F_3SiS$ 477.1167; Found 477.1149.



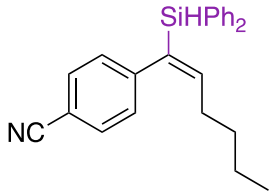
Ethyl (*E*)-4-(2-cyclohexyl-1-(diphenylsilyl)vinyl)benzoate. [46f] According to the general procedure B, ethyl 4-(cyclohexylethynyl)benzoate (72.7 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/ DTB-DPPBz solution (0.075 M solution in benzene, 200 μL, 0.015 mmol, 0.050 eq), Ph_2SiH_2 (83.8 μL ul, 0.450 mmol, 1.50 eq), and benzene (2.80 mL, 0.100 M total reaction concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 40 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (200 mL of 100% hexanes, 400 mL of 2% ethyl acetate in hexanes) gives the pure product as a clear oil (129 mg, 0.292 mmol, 97% yield, >20:1).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.99 (d, *J* = 7.9 Hz, 2H), 7.57 (d, *J* = 7.3 Hz, 4H), 7.46 – 7.41 (m, 2H), 7.41 – 7.37 (m, 4H), 7.11 (d, *J* = 7.9 Hz, 2H), 6.16 (d, *J* = 9.6 Hz, 1H), 5.26 (s, 1H), 4.40 (q, *J* = 6.8 Hz, 2H), 2.29 – 2.20 (m, 1H), 1.74 – 1.58 (m, 5H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.25 – 1.11 (m, 5H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.66, 153.89, 146.94, 135.74, 135.38, 133.08, 129.80, 129.45, 128.30, 128.02, 127.99, 60.80, 39.01, 32.75, 25.85, 25.43, 14.41.

IR: 3068, 2980, 2923, 2849, 1716, 1605, 1269, 1020

HRMS: (ESI$^+$) m/z: $[M+H]^+$ Calculated for $C_{29}H_{33}O_2Si$ 441.2250; Found 441.2268.



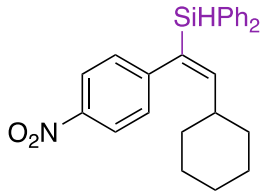
(*E*)-4-(1-(diphenylsilyl)hex-1-en-1-yl)benzonitrile. [46g] According to the general procedure B, 4-(hex-1-yn-1-yl)benzonitrile (55.0 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/ DTB-DPPBz solution (0.075 M solution in benzene, 200 μL, 0.015 mmol, 0.050 eq), Ph_2SiH_2 (83.8 μL, 0.450 mmol, 1.50 eq), and benzene (2.80 mL, 0.100 M total reaction concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 40 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (100 mL of 100% hexanes, 100 mL of 5% dichloromethane in hexanes, 100 mL of 10% dichloromethane in hexanes) gives the pure product as a white solid (85.7 mg, 0.187 mmol, 62% yield, >20:1).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.56 – 7.49 (m, 6H), 7.46 – 7.41 (m, 2H), 7.41 – 7.34 (m, 4H), 7.08 (d, *J* = 7.9 Hz, 2H), 6.29 (t, *J* = 7.2 Hz, 1H), 5.20 (s, 1H), 2.07 (q, *J* = 7.4 Hz, 2H), 1.37 (p, *J* = 7.4 Hz, 2H), 1.26 (sxt, *J* = 7.2 Hz, 2H), 0.84 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 149.23, 147.03, 137.17, 135.74, 132.63, 132.01, 130.05, 129.18, 128.19, 119.23, 109.65, 31.45, 30.24, 22.40, 13.96.

IR: 3068, 2955, 2871, 2354, 2124, 1602, 1428.

HRMS: (ESI+) m/z: [M+H]+ Calculated for $C_{25}H_{26}NSi$ 368.1834; Found 368.1830.



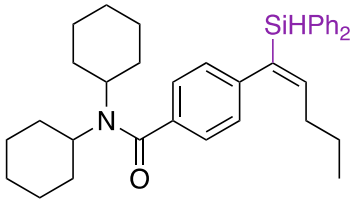
(*E*)-(2-cyclohexyl-1-(4-nitrophenyl)vinyl)diphenylsilane. [46h] According to the general procedure B, 1-(cyclohexylethynyl)-4-nitrobenzene (68.8 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/ DTB-DPPBz solution (0.075 M solution in benzene, 200 μL, 0.015 mmol, 0.050 eq), Ph_2SiH_2 (83.8 μL, 0.450 mmol, 1.50 eq), and benzene (2.80 mL, 0.100 M total reaction concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 22 h at 40 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (100 mL of 100% hexanes, 100 mL of 10% dichloromethane in hexanes, 200 mL of 20% dichloromethane in hexanes) gives the pure product as a clear oil (72.0 mg, 0.174 mmol, 58% yield, >20:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 8.3 Hz, 2H), 7.52 (d, *J* = 7.1 Hz, 4H), 7.47 – 7.34 (m, 6H), 7.11 (d, *J* = 8.3 Hz, 2H), 6.15 (d, *J* = 9.8 Hz, 1H), 5.20 (s, 1H), 2.17 – 2.07 (m, 1H), 1.71 – 1.57 (m, 5H) (overlap with water), 1.24 – 1.06 (m, 5H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.61, 149.51, 146.18, 135.74, 134.73, 132.51, 130.10, 129.10, 128.22, 123.56, 39.31, 32.70, 25.81, 25.41.

IR: 3068, 2923, 2849, 1590, 1514, 1428.

HRMS: (ESI$^+$) m/z: [M+H]$^+$ Calculated for $C_{26}H_{28}NO_2Si$ 414.1889; Found 414.1885.



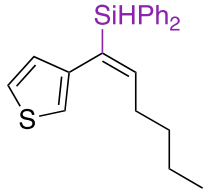
(*E*)-*N*,*N*-dicyclohexyl-4-(1-(diphenylsilyl)pent-1-en-1-yl)benzamide. [46i] According to the general procedure B, *N*,*N*-dicyclohexyl-4-(pent-1-yn-1-yl)benzamide (106 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/ DTB-DPPBz solution (0.075 M solution in benzene, 200 μL, 0.015 mmol, 0.050 eq), Ph_2SiH_2 (83.8 μL, 0.450 mmol, 1.50 eq), and benzene (2.80 mL, 0.100 M total reaction concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 28 h at 40 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (first column: 100 mL of 100% hexanes, 100 mL of 2% ethyl acetate in hexanes, 200 mL of 5% ethyl acetate in hexanes; second column: 100 mL of 100% hexanes, 100 mL of 10% dichloromethane in hexanes, 100 mL of 20% dichloromethane in hexanes, 100 mL of 30% dichloromethane in hexanes, 100 mL of 40% dichloromethane in hexanes, 100 mL of 50% dichloromethane in hexanes) gives the pure product as a white solid (75.0 mg, 0.140 mmol, 47% yield, >20:1). Rotamers are observed in both the ^{1}H and ^{13}C NMR spectra.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.51 (d, *J* = 7.0 Hz, 4H), 7.44 – 7.27 (m, 6H), 7.15 (d, *J* = 7.7 Hz, 2H), 6.97 (d, *J* = 7.6 Hz, 2H), 6.24 (t, *J* = 7.1 Hz, 1H), 5.21 (s, 1H), 3.41 – 2.82 (m, 2H), 2.83 – 2.30 (m, 2H), 2.07 (q, *J* = 7.3 Hz, 2H), 1.90 – 1.28 (m, 16H), 1.18 - 0.88 (m, 4H), 0.83 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.61, 148.30, 141.89, 137.72, 136.42, 135.78, 133.43, 129.70, 128.41, 127.97, 125.45, 59.82, 56.26, 32.36, 31.35, 30.27, 26.61, 25.97, 25.33, 22.65, 13.92.

IR: 3068, 3049, 2957, 2927, 2853, 1628, 1452, 993

HRMS: (ESI$^+$) m/z: [M+H]$^+$ Calculated for $C_{36}H_{46}NOSi$ 536.3348; Found 536.3333.



(*E*)-diphenyl(1-(thiophen-3-yl)hex-1-en-1-yl)silane. [46j] According to the general procedure B, 3-(hex-1-yn-1-yl)thiophene (49.3 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/ DTB-DPPBz solution (0.075 M solution in benzene, 200 μL, 0.015 mmol, 0.050 eq), Ph_2SiH_2 (83.8 μL, 0.450 mmol, 1.50 eq), and benzene (2.80 mL, 0.100 M total reaction concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 40 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product mixture was dry loaded onto a silica gel column.

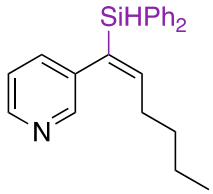
Purification using silica gel flash column chromatography (200 mL of 100% hexanes then 200 mL 2% ethyl acetate in hexanes) gives the pure product as a yellow oil (75.1 mg, 0.215 mmol, 72% yield, 20:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 7.0 Hz, 4H), 7.48 – 7.38 (m, 6H), 7.25 (s, 1H), 6.90 – 6.84 (m, 2H), 6.29 (t, *J* = 7.0 Hz, 1H), 5.28 (s, 1H), 2.30 (q, *J* = 7.2 Hz, 2H), 1.49 – 1.40 (m, 2H), 1.40 – 1.32 (m, 2H), 0.92 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 149.00, 141.06, 135.84, 133.75, 132.06, 129.76, 128.68, 128.06, 124.76, 121.22, 31.76, 30.53, 22.53, 14.08.

IR: 3069, 2957, 2872, 2122,1428, 1320.

HRMS: (ESI^{+}) m/z: [M+H]$^{+}$ Calculated for $C_{22}H_{25}SSi$ 349.1446; Found 349.1449.



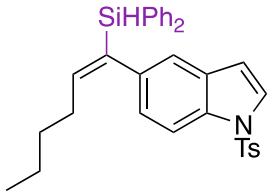
(*E*)-3-(1-(diphenylsilyl)hex-1-en-1-yl)pyridine. [46k] According to the general procedure B, 3-(hex-1-yn-1-yl)-pyridine (31.9 mg, 0.200 mmol, 1.00 eq), $Cu(OAc)_2$/ DTB-DPPBz solution (0.075 M solution in benzene, 267 µl, 0.020 mmol, 0.100 eq), Ph_2SiH_2 (55.9 µl, 0.300 mmol, 1.50 eq), and benzene (1.73 mL, 0.100 M total reaction concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 40 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (50 mL of 100% hexanes, 100 mL of 1% acetone in hexanes, 100 mL of 1.5% acetone in hexanes, 100 mL of 2% acetone in hexanes, 100 mL of 2.5% acetone in hexanes, 100 mL of 3% acetone in hexanes, 100 mL of 3.5% acetone in hexanes, 100 mL of 4% acetone in hexanes) gives the pure product as a white oil (62.2 mg, 0.181 mmol, 91% yield, >20:1).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.42 (br s, 1H), 8.31 (br s, 1H), 7.52 (d, *J* = 7.1 Hz, 4H), 7.44 – 7.31 (m, 6H), 7.25 (d, *J* = 7.1 Hz, 1H) (overlaps with $CDCl_3$), 7.15 (s, 1H), 6.32 (t, *J* = 7.3 Hz, 1H), 5.20 (s, 1H), 2.09 (q, *J* = 7.5 Hz, 2H), 1.36 (p, *J* = 7.7 Hz, 2H), 1.25 (sxt, *J* = 7.6 Hz, 2H), 0.82 (t, *J* = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 150.05, 149.24, 147.15, 137.23, 135.87, 135.81, 134.42, 132.81, 129.99, 128.19, 123.31, 31.57, 30.22, 22.44, 13.99.

IR: 3068, 3049, 3021, 2999, 2956, 2925, 2871, 2856, 1601, 1472, 1429.

HRMS: (ESI^{+}) m/z: [M+H]$^{+}$ Calculated for $C_{23}H_{26}NSi$ 344.1834; Found 344.1850.



(*E*)-5-(1-(diphenylsilyl)hex-1-en-1-yl)-1-tosyl-1*H*-indole. [46l] According to the general procedure B, 5-(hex-1-yn-1-yl)-1-tosyl-1*H*-indole (70.3 mg, 0.200 mmol, 1.00 eq), $Cu(OAc)_2$/ DTB-DPPBz solution (0.075 M solution in benzene, 133 µl, 0.010 mmol, 0.050 eq), Ph_2SiH_2 (55.9 µl, 0.300 mmol, 1.50 eq), and

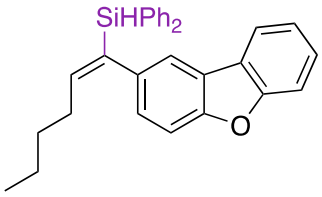
benzene (1.87 mL, 0.100 M total reaction concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 40 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (50 mL of 100% hexanes, 100 mL of 1% acetone in hexanes, 100 mL of 1.5% acetone in hexanes, 100 mL of 2% acetone in hexanes, 100 mL of 2.5% acetone in hexanes, 100 mL of 3% acetone in hexanes, 100 mL of 3.5% acetone in hexanes, 100 mL of 4% acetone in hexanes) gives the pure product as a white oil (32.2 mg, 0.060 mmol, 30% yield, >20:1).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.85 (d, *J* = 8.5 Hz, 1H), 7.76 (d, *J* = 8.2 Hz, 2H), 7.52 – 7.47 (m, 5H), 7.41 – 7.36 (m, 2H), 7.35 – 7.30 (m, 4H), 7.22 (d, *J* = 7.9 Hz, 2H), 7.14 (s, 1H), 6.99 – 6.94 (m, 1H), 6.54 (d, *J* = 3.4 Hz, 1H), 6.22 (t, *J* = 7.0 Hz, 1H), 5.19 (s, 1H), 2.35 (s, 3H), 2.09 (q, *J* = 7.1 Hz, 2H), 1.33 (p, *J* = 7.5 Hz, 2H), 1.24 (sxt, *J* = 7.2 Hz, 2H), 0.79 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 148.54, 144.91, 137.56, 136.68, 135.86, 135.53, 133.74, 133.36, 130.82, 129.94, 129.69, 128.00, 126.96, 126.40, 125.59, 120.87, 113.17, 109.26, 31.69, 30.08, 22.43, 21.68, 14.02.

IR: 3141, 3111, 3067, 3049, 2998, 2955, 2925, 2856, 1597, 1454, 1372, 1130.

HRMS: (ESI$^+$) m/z: [M+H]$^+$ Calculated for $C_{33}H_{34}NO_2SiS$ 536.2079; Found 536.2100.



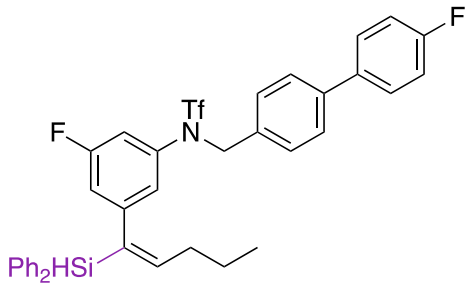
(*E*)-(1-(dibenzo[*b*,*d*]furan-2-yl)hex-1-en-1-yl)diphenylsilane. [46m] According to the general procedure B, 2-(hex-1-yn-1-yl)dibenzo[*b*,*d*]furan (74.5 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/ DTB-DPPBz solution (0.075 M solution in benzene, 200 μL, 0.015 mmol, 0.050 eq), Ph_2SiH_2 (83.8 μL, 0.450 mmol, 1.50 eq), and benzene (2.80 mL, 0.100 M total reaction concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 40 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (first column: 600 mL of 100% hexanes, 300 mL of 1% ethyl acetate in hexanes; second column: 100 mL of hexanes, 300 mL of 10% dichloromethane in hexanes) gives the pure product as a yellowish oil (80.9 mg, 0.190 mmol, 64% yield, 12:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.83 (d, *J* = 7.6 Hz, 1H), 7.60 – 7.54 (m, 6H), 7.47 – 7.41 (m, 4H), 7.40 – 7.37 (m, 4H), 7.35 – 7.29 (m, 1H), 7.11 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.34 (t, *J* = 7.1 Hz, 1H), 5.30 (s, 1H), 2.18 (q, *J* = 7.3 Hz, 2H), 1.40 (p, *J* = 7.0 Hz, 2H), 1.29 (sxt, *J* = 7.0 Hz, 2H), 0.85 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.52, 154.81, 148.61, 137.80, 136.04, 135.92, 133.70, 129.78, 128.08, 127.92, 127.11, 124.44, 124.16, 122.66, 120.71, 120.27, 111.74, 111.28, 31.73, 30.14, 22.49, 14.07.

IR: 3067, 3048, 2998, 2954, 2924, 2870, 2855, 1588, 1473, 1194.

HRMS: (ESI$^+$) m/z: [M+H]$^+$ Calculated for $C_{30}H_{29}OSi$ 433.1987; Found 433.1959.



(*E*)-*N*-(3-(1-(diphenylsilyl)pent-1-en-1-yl)-5-fluorophenyl)-1,1,1-trifluoro-*N*-((4'-fluoro-[1,1'-biphenyl]-4-yl)methyl)methanesulfonamide. [46n] According to the general procedure B, 1,1,1-trifluoro-*N*-(3-fluoro-5-(pent-1-yn-1-yl)phenyl)-*N*-((4'-fluoro-[1,1'-biphenyl]-4-yl)methyl)methanesulfonamide (40.2 mg, 0.082 mmol, 1.00 eq), $Cu(OAc)_2$/ DTB-DPPBz solution (0.075 M solution in benzene, 54.0 μL, 0.004 mmol, 0.050 eq), Ph_2SiH_2 (23.0 μL, 0.122 mmol, 1.50 eq), and benzene (750 μL, 0.100 M total reaction concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 40 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (100 mL of 100% hexanes, 400 mL of 2% ethyl acetate in hexanes) gives the pure product as a colorless oil (23.0 mg, 0.034, 41% yield, >20:1).

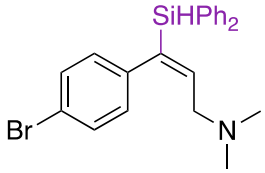
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50 – 7.30 (m, 14H), 7.17 – 7.01 (m, 4H), 6.71 – 6.58 (m, 3H), 6.21 (t, *J* = 7.2 Hz, 1H), 5.13 (s, 1H), 4.75 (br s, 2H), 1.93 (q, *J* = 7.3 Hz, 2H), 1.38 – 1.28 (m, 2H), 0.78 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 163.75 (d, *J* = 48.3 Hz), 161.28 (d, *J* = 50.6 Hz), 149.52, 144.83 (d, *J* = 8.6 Hz), 140.54, 137.36 (d, *J* = 10.7 Hz), 136.18 (d, *J* = 64.9 Hz), 136.47, 135.76, 132.88, 132.60, 130.13, 129.51, 128.76 (d, *J* = 8.1 Hz), 128.26, 127.34, 124.80 (d, *J* = 2.8 Hz), 120.51 (q, *J* = 324 Hz), 116.40 (d, *J* = 21.0 Hz), 115.86 (d, *J* = 21.5 Hz), 114.64 (d, *J* = 23.3 Hz), 56.88, 32.26, 22.42, 13.78.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -73.55, -110.85, -115.17.

IR: 3070, 2959, 2930, 2872, 1653, 1606, 1586, 1499, 1457, 1225, 1189, 1142.

HRMS: (ESI$^+$) m/z: $[M+H]^+$ Calculated for $C_{37}H_{33}F_5NO_2SSi$ 678.1921; Found 678.1913.



(*E*)-3-(4-bromophenyl)-3-(diphenylsilyl)-*N*,*N*-dimethylprop-2-en-1-amine. [46o] According to the general procedure B, 3-(4-bromophenyl)-*N*,*N*-dimethylprop-2-yn-1-amine (71.4 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/ DTB-DPPBz solution (0.075 M solution in benzene, 200 μL, 0.015 mmol, 0.050 eq), Ph_2SiH_2 (83.8 μL, 0.450 mmol, 1.50 eq), and benzene (2.80 mL, 0.100 M total reaction concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 23 h at 40 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (100 mL of 100% hexanes, 100 mL of 10% ethyl acetate in hexanes, 100 mL of 20% ethyl acetate in hexanes, 100 mL of 30% ethyl acetate in hexanes, 100 mL of 40% ethyl acetate in hexanes, 200

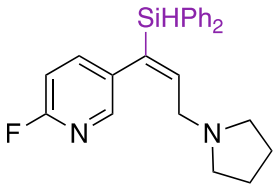
mL of 50% ethyl acetate in hexanes) gives the pure product as a yellow oil (45.0 mg, 0.107 mmol, 36% yield, >20:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.52 (d, *J* = 7.2 Hz, 4H), 7.44 – 7.31 (m, 8H), 6.83 (d, *J* = 8.3 Hz, 2H), 6.30 (t, *J* = 6.3 Hz, 1H), 5.19 (s, 1H), 2.96 (d, *J* = 6.3 Hz, 2H), 2.18 (s, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 144.80, 140.31, 139.87, 135.80, 132.60, 131.40, 130.02, 129.88, 128.20, 120.25, 58.50, 45.41.

IR: 3068, 2941, 2817, 2769, 1675, 1588, 1264, 1009, 799.

HRMS: (ESI^{+}) m/z: [M+H]$^{+}$ Calculated for $C_{23}H_{25}NSiBr$ 422.0939; Found 422.0958.



(*E*)-5-(1-(diphenylsilyl)-3-(pyrrolidin-1-yl)prop-1-en-1-yl)-2-fluoropyridine. [46p] According to the general procedure B, 2-fluoro-5-(3-(pyrrolidin-1-yl)prop-1-yn-1-yl)pyridine (61.3 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/ DTB-DPPBz solution (0.075 M solution in benzene, 200 μL, 0.015 mmol, 0.050 eq), Ph_2SiH_2 (83.8 μL, 0.450 mmol, 1.50 eq), and benzene (2.80 mL, 0.100 M total reaction concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 40 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (100 mL of 100% dichloromethane, 100 mL of 2% methanol in dichloromethane, 300 mL of 3% methanol in dichloromethane, 100 mL of 6% methanol in dichloromethane) gives the pure product as a yellow oil (38.0 mg, 0.098 mmol, 33% yield, >20:1).

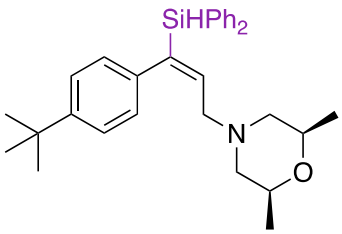
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.81 (s, 1H), 7.51 (d, *J* = 7.1 Hz, 4H), 7.45 – 7.28 (m, 7H), 6.78 (dd, *J* = 8.4, 2.9 Hz, 1H), 6.48 (t, *J* = 6.3 Hz, 1H), 5.19 (s, 1H), 3.16 (d, *J* = 6.3 Hz, 2H), 2.56 – 2.41 (m, 4H), 1.84 – 1.71 (m, 4H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.35 (d, *J* = 238 Hz), 146.46 (d, *J* = 14.3 Hz), 140.82 (d, *J* = 7.7 Hz), 135.77, 135.07, 134.26 (d, *J* = 4.6 Hz), 131.88, 130.26, 128.34, 128.03, 109.12 (d, *J* = 37.3 Hz), 54.96, 54.15, 23.54.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -71.30.

IR: 3068, 2961, 2923, 1585, 1478, 1249, 1115.

HRMS: (ESI^{+}) m/z: [M+H]$^{+}$ Calculated for $C_{24}H_{26}FN_2Si$ 389.1849; Found 389.1827.



(2*S*,6*R*)-4-((*E*)-3-(4-(*tert*-butyl)phenyl)-3-(diphenylsilyl)allyl)-2,6-dimethylmorpholine. [46q] According to the general procedure B, (2*S*,6*R*)-4-(3-(4-(*tert*-butyl)phenyl)prop-2-yn-1-yl)-2,6-dimethylmorpholine (85.6 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/ DTB-DPPBz solution (0.075 M solution in benzene, 200 μL, 0.015 mmol, 0.050 eq), Ph_2SiH_2 (83.8 μL, 0.450 mmol, 1.50 eq), and benzene (2.80 mL, 0.100 M total reaction concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 27 h at 40 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (100 mL of 100% hexanes, 100 mL of 5% ethyl acetate in hexanes, 100 mL of 10% ethyl acetate in hexanes, 200 mL of 12% ethyl acetate in hexanes) gives the pure product as a yellow oil (90.4 mg, 0.192, 64% yield, >20:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.52 (d, *J* = 7.6 Hz, 4H), 7.43 – 7.31 (m, 6H), 7.25 (d, *J* = 7.8 Hz, 2H), 6.91 (d, *J* = 8.0 Hz, 2H), 6.28 (t, *J* = 6.1 Hz, 1H), 5.22 (s, 1H), 3.70 – 3.59 (m, 2H), 3.09 (d, *J* = 6.2 Hz, 2H), 2.69 (d, *J* = 11.2 Hz, 2H), 1.65 (t, *J* = 10.7 Hz, 2H), 1.30 (s, 9H), 1.14 (d, *J* = 6.3 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 149.05, 143.31, 141.47, 137.68, 135.89, 133.38, 129.81, 128.04, 127.78, 125.11, 71.73, 59.48, 57.54, 34.53, 31.47, 19.31.

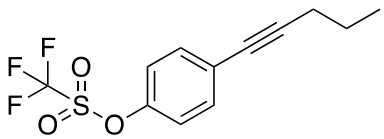
IR: 2966, 2932, 2901, 2867, 2810, 2771, 1143, 1083.

HRMS: (ESI$^+$) m/z: $[M+H]^+$ Calculated for $C_{31}H_{40}NOSi$ 470.2879; Found 470.2856.

Synthesis of New Alkyne Starting Materials

General Sonogashira Coupling Procedure (C) for the Synthesis of Internal Alkynes[2]

To a flame-dried round bottom flask or Schlenk tube under N_2 was added distilled triethylamine (15.0 mL, 0.200 M), which was degassed for 15 minutes. The aryl halide (3.00 mmol, 1.00 eq.), $Pd(PPh_3)_2Cl_2$ (42.0 mg, 0.060 mmol, 0.020 eq.) and CuI (23.0 mg, 0.120 mmol, 0.040 eq.) were then sequentially added at room temperature. The mixture was stirred for 10 minutes followed by the addition of the alkyne reagent (3.30 mmol, 1.10 eq.). After 16 h of stirring at either room temperature or reflux, the reaction was cooled to room temperature, quenched with water (10 mL) and extracted with ethyl acetate (3 x 15 mL). The organic layers were washed with brine (3 x 10 mL) and then dried over anhydrous Na_2SO_4. The mixture was filtered, and the solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography to give the desired aryl substituted alkyne.



4-(pent-1-yn-1-yl)phenyl trifluoromethanesulfonate. [45e] Following a previously reported procedure[3], 4-(1-pentyn-1-yl)phenol (345 mg, 2.16 mmol, 1.00 eq), Et_3N (0.600 mL, 4.31 mmol, 2.00 eq), and DCM (11.0 mL, 0.200 M) were combined followed by dropwise addition of triflic anhydride (1.42 mL, 8.62 mmol, 4.00 eq) at 0 ˚C. Upon reaction completion, the reaction was worked up and then purified by flash

column chromatography (500 mL of 100% hexanes) to afford the pure product as a yellow oil (417 mg, 1.43 mmol, 66% yield).

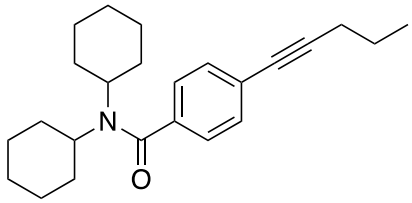
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 (d, *J* = 8.6 Hz, 2H), 7.19 (d, *J* = 8.7 Hz, 2H), 2.39 (t, *J* = 7.0 Hz, 2H), 1.63 (sxt, *J* = 7.2 Hz, 2H), 1.05 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 148.58, 133.46, 124.99, 121.42, 118.86 (q, *J* = 320.9 Hz), 92.70, 79.11, 22.16, 21.47, 13.66.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -72.82.

IR: 2967, 2936, 2876, 1499, 1424, 1206, 1136

HRMS: (ESI^{+}) m/z: [M+H]$^{+}$ Calculated for $C_{12}H_{12}O_3F_3S$ 293.0459; Found 293.0462.



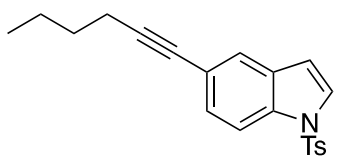
***N*,*N*-dicyclohexyl-4-(pent-1-yn-1-yl)benzamide. [45i]** Following general procedure C, triethylamine (18.0 mL, 0.200 M), THF (5.00 mL, 0.760 M), *N*,*N*-dicyclohexyl-4-iodobenzamide (1.50 g, 3.65 mmol, 1.00 eq), $Pd(PPh_3)_2Cl_2$ (51.3 mg, 0.073 mmol, 0.020 eq), and CuI (27.8 mg, 0.146 mmol, 0.040 eq) were added to an oven-dried 100 mL round bottom flask equipped with a Teflon stir bar at room temperature, and this was stirred for 15 minutes. 1-Pentyne (0.430 mL, 4.38 mmol, 1.20 eq) was then added dropwise and the reaction mixture was equipped with a condenser, stirred, and heated to 75 ˚C overnight. Upon reaction completion, the brown crude product was purified by silica gel flash column chromatography (first column: 100 mL of 100% hexanes, 100 mL of 5% ethyl acetate in hexanes, 200 mL of 10% ethyl acetate in hexanes; second column: 100 mL of 100% hexanes, 100 mL of 10% dichloromethane in hexanes, 100 mL of 20% dichloromethane in hexanes, 100 mL of 30% dichloromethane in hexanes, 100 mL of 40% dichloromethane in hexanes, 100 mL of 50% dichloromethane in hexanes) The product was obtained as a white solid (527 mg, 1.50 mmol, 41% yield). Rotamers are observed in the NMR spectra.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 (d, *J* = 8.3 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 3.44 – 2.86 (m, 2H), 2.78 – 2.43 (m, 2H), 2.39 (t, *J* = 7.0 Hz, 2H), 1.95 – 0.90 (m, 23H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.44, 137.72, 131.28, 125.25, 124.21, 91.04, 80.07, 59.46, 55.87, 30.96, 29.96, 26.19, 25.60, 25.00, 21.92, 21.15, 13.30.

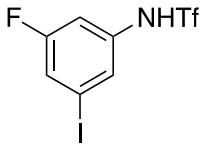
IR: 2950, 2931, 2855, 1623, 1436, 993

HRMS: (ESI^{+}) m/z: [M+H]$^{+}$ Calculated for $C_{24}H_{34}NO$ 352.2640; Found 352.2644.



5-(hex-1-yn-1-yl)-1-tosyl-1*H*-indole. [45l] Following a previously reported procedure[2], the desired product was synthesized, and the spectra matched the previously reported data.[2]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.91 (d, *J* = 8.6 Hz, 1H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.59 – 7.53 (m, 2H), 7.35 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.19 (d, *J* = 8.1 Hz, 2H), 6.59 (dd, *J* = 3.6, 0.9 Hz, 1H), 2.41 (t, *J* = 7.0 Hz, 2H), 2.30 (s, 3H), 1.59 (p, *J* = 6.9 Hz, 2H), 1.48 (sxt, *J* = 7.0 Hz, 2H), 0.95 (t, *J* = 7.2 Hz, 3H).



1,1,1-trifluoro-*N*-(3-fluoro-5-iodophenyl)methanesulfonamide. In a 100 mL oven-dried round bottom flask equipped with a Teflon stir bar was added 3-fluoro-5-iodoaniline (786 mg, 3.32 mmol, 1.00 eq), Et_3N (0.700 mL, 4.98 mmol, 1.50 eq), and DCM (6.60 mL, 0.500 M). The reaction mixture was cooled to 0 ˚C and stirred for 10 minutes. Trifluoromethanesulfonic anhydride (0.700 mL, 3.98 mmol, 1.20 eq) was then added dropwise to the reaction mixture with a 15-minute residence time. The reaction mixture was stirred at room temperature under an N_2 atmosphere overnight. Upon reaction completion, monitored by TLC, the reaction was quenched with brine (15 mL), extracted with DCM (3 x 30 mL), and the combined organic layers were dried over anhydrous Na_2SO_4. The mixture was filtered and the solvent was removed by rotary evaporation. The crude product was dry loaded onto a silica gel column and purified by silica gel flash column chromatography to give the desired compound as a dark brown oil (582 mg, 1.58 mmol, 48% yield).

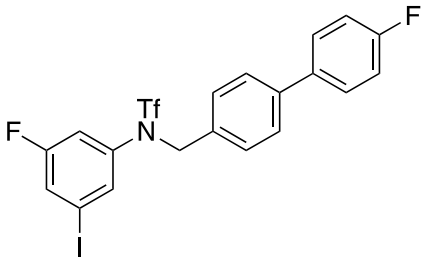
^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.40 – 7.35 (m, 2H), 7.07 (d, *J* = 2.1 Hz, 1H), 4.54 – 3.54 (m, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.49 (d, *J* = 254.1 Hz), 136.07 (d, *J* = 10.6 Hz), 127.27 (d, *J* = 3.6 Hz), 124.08 (d, *J* = 23.4 Hz), 119.66 (q, *J* = 322.4 Hz), 110.04 (d, *J* = 25.5 Hz), 93.76 (d, *J* = 9.4 Hz).

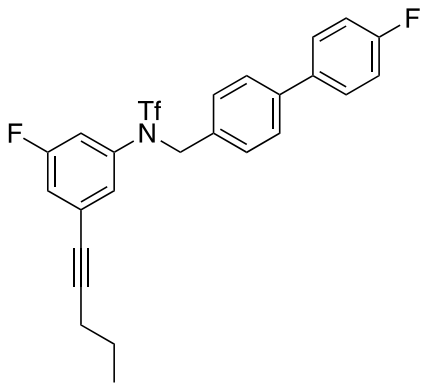
^{19}F NMR (376 MHz, Chloroform-*d*) δ -75.39, -108.01.

IR: 3093, 2921, 2850, 1587, 1415, 1359, 1195, 1132, 916.

HRMS: (ESI$^+$) m/z: $[M+Na]^+$ Calculated for $C_7H_4F_4INO_2SNa$ 391.8842; Found 391.8814.



1,1,1-trifluoro-*N*-(3-fluoro-5-iodophenyl)-*N*-((4'-fluoro-[1,1'-biphenyl]-4-yl)methyl)methanesulfonamide. In an oven-dried 2 mL vial equipped with a Teflon stir bar and a pressure relief cap was added 1,1,1-trifluoro-*N*-(3-fluoro-5-iodophenyl)methanesulfonamide. (309 mg, 0.840 mmol, 1.00 eq), 4-(Bromomethyl)-4'-fluoro-1,1'-biphenyl (265 mg, 1.00 mmol, 1.20 eq), K_2CO_3 (138 mg, 1.00 mmol, 1.20 eq), and DMF (1.40 mL, 0.600 M). The reaction mixture was heated at 65 ˚C in an oil bath under N_2 atmosphere overnight. Upon reaction completion, the orange-brownish mixture was cooled to room temperature and diluted with DI water (10 mL), followed by extraction with ethyl acetate (3 x 20 mL). The combined organic layers were washed with DI water (4 x 20 mL), brine (30 mL), and then dried over anhydrous Na_2SO_4. The mixture was filtered, and the solvent was evaporated by rotary evaporation. The crude product was afforded as an orange-brownish solid and taken forward without further characterization (424 mg, 0.766 mmol, 91%).



1,1,1-trifluoro-*N*-(3-fluoro-5-(pent-1-yn-1-yl)phenyl)-*N*-((4'-fluoro-[1,1'-biphenyl]-4-yl)methyl)methanesulfonamide. [45n] Following general procedure C, triethylamine (2.50 mL, 0.200 M), 1,1,1-trifluoro-*N*-(3-fluoro-5-iodophenyl)-*N*-((4'-fluoro-[1,1'-biphenyl]-4-yl)methyl)methanesulfonamide (270 mg, 0.490 mmol, 1.00 eq), $Pd(PPh_3)_2Cl_2$ (6.90 mg, 0.010 mmol, 0.0200 eq), and CuI (4.70 mg, 0.025 mmol, 0.050 eq) were added to an oven-dried 4 mL vial equipped with a Teflon stir bar and a pressure relief cap at room temperature, and this was stirred and heated to 35 ˚C for 15 minutes. 1-Pentyne (50.0 µL, 0.500 mmol, 1.02 eq) was then added dropwise and the reaction mixture was stirred at 40 ˚C for 24 h. Upon reaction completion, the brown crude product was purified by silica gel flash column chromatography (100 mL of 100% hexane, 100 mL of 1% ethyl acetate in hexane and 200 mL of 2% ethyl acetate in hexane). The product was obtained as a yellow solid (111 mg, 0.224 mmol, 46%).

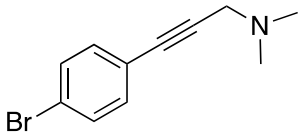
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 – 7.44 (m, 4H), 7.27 – 7.21 (m, 2H), 7.15 – 7.09 (m, 2H), 7.08 – 7.03 (m, 2H), 6.81 (dt, *J* = 9.0, 2.3 Hz, 1H), 4.92 (br s, 2H), 2.36 (t, *J* = 7.0 Hz, 2H), 1.61 (sxt, *J* = 7.2 Hz, 2H), 1.02 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 163.72 (d, *J* = 60.7 Hz), 161.25 (d, *J* = 63.0 Hz), 140.78, 137.85 (d, *J* = 10.8 Hz), 136.49 (d, *J* = 3.3 Hz), 132.81, 129.53, 128.81 (d, *J* = 8.1 Hz), 128.07 (d, *J* = 3.0 Hz), 127.51, 127.09 (d, *J* = 10.9 Hz), 120.52 (q, *J* = 323 Hz), 119.60 (d, *J* = 22.4 Hz), 116.62 (d, *J* = 23.3 Hz), 115.87 (d, *J* = 21.5 Hz), 93.65, 78.63 (d, *J* = 3.7 Hz), 57.04, 22.02, 21.45, 13.68.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -73.50, -110.67, -115.14.

IR: 3032, 2964, 2935, 2875, 1610, 1586, 1499, 1388, 1246, 1221, 1191, 1140.

HRMS: (ESI$^+$) m/z: $[M+H]^+$ Calculated for $C_{25}H_{21}SF_5NO_2$ 494.1213; Found 494.1203.



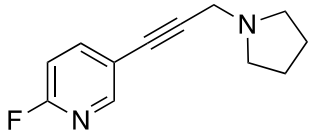
3-(4-bromophenyl)-*N*,*N*-dimethylprop-2-yn-1-amine. [45o] Following general procedure C, triethylamine (9.0 mL, 0.2 M), 4-bromo-iodobenzene (500 mg, 1.77 mmol, 1.00 eq), $Pd(PPh_3)_2Cl_2$ (24.8 mg, 0.035 mmol, 0.020 eq), and CuI (13.5 mg, 0.071 mmol, 0.040 eq) were added to an oven-dried 100 mL round bottom flask equipped with a Teflon stir bar at room temperature, and this was stirred for 15 minutes. 3-Dimethylamino-1-propyne (0.210 mL, 1.95 mmol, 1.10 eq) was then added dropwise and the reaction mixture was stirred at room temperature overnight. Upon reaction completion, the brown crude product was purified by silica gel flash column chromatography (100 mL of 100% hexane, 100 mL of 5% ethyl acetate in hexane and 100 mL of 15% ethyl acetate in hexane, 300 mL of 20% ethyl acetate in hexanes, 200 mL of 100% ethyl acetate). The product was obtained as a yellow oil (338 mg, 1.42 mmol, 80% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 (d, *J* = 8.6 Hz, 2H), 7.29 (d, *J* = 8.5 Hz, 2H), 3.44 (s, 2H), 2.35 (s, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 133.11, 131.46, 122.17, 122.14, 85.94, 84.17, 48.54, 44.27.

IR: 2970, 2939, 2858, 2821, 2772, 1484, 1262, 1032.

HRMS: (ESI^{+}) m/z: $[M+H]^{+}$ Calculated for $C_{11}H_{13}NBr$ 238.0231; Found 238.0249.



2-fluoro-5-(3-(pyrrolidin-1-yl)prop-1-yn-1-yl)pyridine. [45p] Following general procedure C, triethylamine (9.00 mL, 0.200 M), 2-fluoro-5-iodopyridine (370 mg, 1.67 mmol, 1.00 eq), $Pd(PPh_3)_2Cl_2$ (24.8 mg, 0.035 mmol, 0.0200 eq), and CuI (13.5 mg, 0.071 mmol, 0.040 eq) were added to an oven-dried 100 mL round bottom flask equipped with a Teflon stir bar at room temperature, and this was stirred for 15 minutes. 1-(2-Propynyl)pyrrolidine (0.210 mL, 1.84 mmol, 1.10 eq) was then added dropwise and the reaction mixture was stirred at room temperature overnight. Upon reaction completion, the brown crude product was purified by silica gel flash column chromatography (100 mL of 100% dichloromethane, 200 mL of 1% methanol in dichloromethane, 200 mL of 2% methanol in dichloromethane, 600 mL of 5% methanol in dichloromethane, 200 mL of 6% methanol in dichloromethane). The product was obtained as a light yellow oil (181 mg, 0.890 mmol, 53% yield).

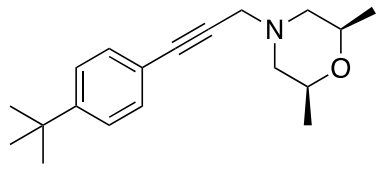
^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.28 (s, 1H), 7.82 – 7.77 (m, 1H), 6.89 – 6.85 (m, 1H), 3.62 (s, 2H), 2.72 – 2.65 (m, 4H), 1.88 – 1.81 (m, 4H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.58 (d, *J* = 241.8 Hz), 150.75 (d, *J* = 15.2 Hz), 143.90 (d, *J* = 8.3 Hz), 118.30 (d, *J* = 4.8 Hz), 109.39 (d, *J* = 38.1 Hz), 88.95, 79.87, 53.01, 43.96, 23.90.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -66.25.

IR: 2963, 2920, 2793, 1590, 1481, 1253, 1122.

HRMS: (ESI^{+}) m/z: $[M+H]^{+}$ Calculated for $C_{12}H_{14}N_2F$ 205.1141; Found 205.1142.



(2*S*,6*R*)-4-(3-(4-(*tert*-butyl)phenyl)prop-2-yn-1-yl)-2,6-dimethylmorpholine. [45q] Following general procedure C, in an oven-dried 100 mL round bottom flask equipped with a Teflon stir bar was added THF (3.16 mL, 0.760 M) and triethylamine (12.0 mL, 0.200 M) which was degassed with N_2 for 20 minutes. 4-Tert-butyl-iodobenzene (617 mg, 2.40 mmol, 1.00 eq), $Pd(PPh_3)_2Cl_2$ (33.7 mg, 0.048 mmol, 0.020 eq), and CuI (18.3 mg, 0.096 mmol, 0.040 eq) were added to the reaction mixture and stirred for 5 minutes, followed by dropwise addition of *rel*-(2*R*,6*S*)-2,6-Dimethyl-4-(2-propyn-1-yl)morpholine (ACI) (400 mg, 2.61 mmol, 1.10 eq). The reaction mixture was stirred under nitrogen at 100 ˚C overnight equipped with condenser. Upon reaction completion, monitored by TLC, the reaction mixture was quenched with DI water (50 mL) and extracted with ethyl acetate (20 mL x 3). The combined organic layers were washed with brine

(100 mL) and dried over anhydrous Na_2SO_4. The mixture was filtered and the solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography (200 mL of 100% hexanes, 200 mL of 5% ethyl acetate in hexanes, 200 mL of 10% ethyl acetate in hexanes, 500 mL of 15% ethyl acetate in hexanes, 200 mL of 20% ethyl acetate in hexanes) to give the pure product as a thick brown oil (368 mg, 1.29 mmol, 54% yield).

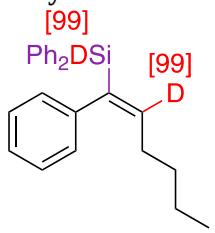
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 3.78 – 3.68 (m, 2H), 3.48 (s, 2H), 2.80 (d, *J* = 10.3 Hz, 2H), 2.02 (t, *J* = 10.7 Hz, 2H), 1.30 (s, 9H), 1.19 (d, *J* = 6.3 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 151.50, 131.58, 125.37, 120.09, 85.61, 83.50, 71.81, 58.33, 47.80, 34.85, 31.29, 19.31.

IR: 2966, 2932, 2902, 2867, 2810, 2771, 1141, 1083.

HRMS: (ESI$^+$) m/z: $[M+H]^+$ Calculated for $C_{19}H_{28}NO$ 286.2171; Found 286.2160.

Vinylsilane Product Derivatization



(*E*)-diphenyl(1-(phenylhex-1-en-1-yl-2-*d*)silane-*d*. [47a] According to the general procedure B, 1-phenyl-1-hexyne (47.5 mg, 0.300 mmol, 1.00 eq), $Cu(OAc)_2$/ DTB-DPPBz solution (0.075 M solution in benzene, 200 μL, 0.015 mmol, 0.050 eq), Ph_2SiD_2 (83.8 μL, 0.450 mmol, 1.50 eq), and benzene (2.80 mL, 0.100 M total reaction concentration) were combined in a 2-dram vial equipped with a Teflon stir bar. The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 22 h at 40 ˚C. Upon completion and crude ^{1}H NMR analysis, the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (200 mL of 100% hexanes then 200 mL 2% ethyl acetate in hexanes) gives the pure product as a clear oil (76.1 mg, 0.220 mmol, 73% yield, 19:1).

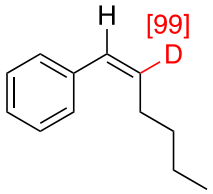
^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.61 (d, J = 7.1 Hz, 4H), 7.48 – 7.39 (m, 6H), 7.29 (t, J = 7.5 Hz, 2H), 7.21 (t, J = 7.4 Hz, 1H), 7.08 (d, J = 7.5 Hz, 2H), 6.30 (t, *J* = 7.1 Hz, 0H), 5.29 (s, 0H), 2.19 (t, J = 7.4 Hz, 2H), 1.43 (p, J = 7.3 Hz, 2H), 1.37 – 1.30 (m, 2H), 0.90 (t, J = 7.3 Hz, 3H).

^{2}H NMR (61 MHz, Chloroform) δ 6.27 (s, 0.99 D), 5.26 (s, 1.00 D).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 147.81 (t, *J* = 23.0 Hz), 141.48, 137.70, 135.89, 133.73, 129.70, 128.51, 128.15, 128.01, 125.89, 31.72, 30.00, 22.49, 14.07.

IR: 3068, 2955, 2924, 2120, 1465, 1113.

HRMS: (ESI$^+$) m/z: $[M+H]^+$ Calculated for $C_{24}H_{25}D_2Si$ 345.2007; Found 345.1996.



(*Z*)-(Hex-1-en-1-yl-2-*d*)benzene. [47b] In 20 mL red pressure-relief cap vial (*E*)-diphenyl(1-phenylhex-1-en-1-yl-2-*d*)silane-*d* (81.5 mg, 0.240 mmol, 1.00 eq) and TBAF (264 µL of 1.00 M TBAF in THF, 0.260 mmol, 1.10 eq) were combined under N_2 and stirred for 5 hours at room temperature. The reaction was quenched with deionized water (15 mL), extracted with DCM (3 x 10 mL), dried over Na_2SO_4, and concentrated under vacuum. The crude product was dry loaded onto a silica column and purified by column chromatography (200 mL of hexanes 100%), to obtain the desired product as a white oil (30.0 mg, 0.183 mmol, 76% yield).

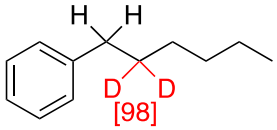
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.27 (m, 4H), 7.22 (t, *J* = 7.1 Hz, 1H), 6.41 (s, 1H), 5.70- 5.60 (m, 0.01H), 2.34 (t, *J* = 7.4 Hz, 2H), 1.49 – 1.40 (m, 2H), 1.40 – 1.31 (m, 2H), 0.90 (t, *J* = 7.2 Hz, 3H).

^{2}H NMR (61 MHz, Chloroform) δ 5.71 (0.99 D).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 137.97, 133.01 (t, *J* = 23.1 Hz), 128.89, 128.68, 128.23, 126.53, 32.28, 28.39, 22.58, 14.13.

IR: 2956, 2923, 2871, 2358, 1492, 697.

HRMS: (ESI$^+$) m/z: $[M+H_2O]^+$ Calculated for $C_{12}H_{17}DO$ 179.1421; Found 179.1425.



(Hexyl-2,2-*d*$_2$)benzene. [47c] DTB-DPPBz (8.00 mg, 0.009 mmol, 0.050 eq), $Cu(OAc)_2$ (45.0 µL of a 0.200 M solution in THF, 0.009 mmol, 0.050 eq.), THF (0.855 mL) and dimethoxy(methyl)silane-*d* (90.0 µL, 0.720 mmol, 4.00 eq) were combined in a 2-dram vial and stirred for 15 mins, followed by slow addition of a solution of (*Z*)-(Hex-1-en-1-yl-2-*d*)benzene (29.5 mg, 0.180 mmol, 1.00 eq), THF (0.900 mL), and 2-propanol (41.0 µL, 0.540 mmol, 3.00 eq) over 10 mins. The 2-dram vial was capped with a red pressure relief cap, and the reaction stirred for 24 h at 40 ˚C. Upon completion, the reaction was quenched over a silica plug with dichloromethane, then the crude product mixture was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (200 mL of 100% hexanes) gives the pure product as a clear colorless oil (25.1 mg, 0.15 mmol, 84% yield).

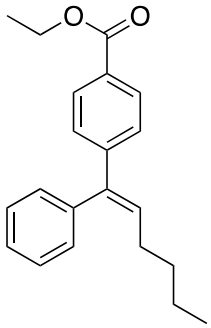
^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.35 – 7.29 (m, 2H), 7.25 – 7.19 (m, 3H), 2.63 (s, 2H), 1.66 – 1.59 (m, 0.05H), 1.42 – 1.28 (m, 6H), 0.93 (t, *J* = 6.2 Hz, 3H).

^{2}H NMR (61 MHz, Chloroform) δ 1.65 (1.96 D).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 143.11, 128.54, 128.36, 125.68, 35.98, 31.86, 30.84 (p, *J* = 19.3 Hz), 28.99, 22.79, 14.26.

IR: 697, 1453, 2853, 2922, 2956

HRMS: (ESI$^+$) m/z: $[M+H]^+$ Calculated for $C_{12}H_{17}D_2$ 165.1612; Found 165.1637.



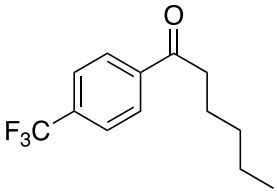
Ethyl (*E*)-4-(1-phenylhex-1-en-1-yl)benzoate. [48] According to a previously reported procedure,[4] to an oven dried 20 mL vial equipped with a Teflon stir bar and (*E*)-diphenyl(1-phenylhex-1-en-1-yl)silane (81.0 mg, 0.237 mmol, 1.21 eq) was added TBAF (0.500 mL, 1.00 M in THF, 2.55 eq). This was stirred at 35 ˚C for 10 minutes, followed by the addition of $Pd_2(dba)_2$ (5.40 mg, 0.006 mmol, 0.030 eq) and ethyl-4-iodobenzoate (33.0 μL, 0.196 mmol, 1.00 eq). The reaction mixture was stirred at 35 ˚C overnight under N_2. Upon reaction completion, the reaction was cooled to room temperature and the crude reaction mixture was filtered through a 1" silica plug with 200 mL of ethyl acetate. The crude product was purified by flash column chromatography (first column: 100 mL of 100% hexanes, 100 mL of 2% ethyl acetate in hexanes, 100 mL of 3% ethyl acetate in hexanes, 100 mL of 4% ethyl acetate in hexanes, 100 mL of 5% ethyl acetate in hexanes; second column: 100 mL of 100% hexanes, 100 mL of 10% dichloromethane in hexane, 100 mL of 20% dichloromethane in hexane, 100 mL of 30% dichloromethane in hexane, 100 mL of 40% dichloromethane in hexane, 100 mL of 50% dichloromethane in hexane) to give the desired product as a yellow oil (23.0 mg, 0.075 mmol, 38% yield, >20:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.93 (d, *J* = 8.0 Hz, 2H), 7.42 – 7.30 (m, 3H), 7.30 – 7.23 (m, 2H), 7.16 (d, *J* = 7.3 Hz, 2H), 6.20 (t, *J* = 7.5 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 2.14 (q, *J* = 7.4 Hz, 2H), 1.49 – 1.27 (m, 7H), 0.86 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.70, 147.40, 140.94, 139.76, 132.59, 130.03, 129.52, 128.75, 128.40, 127.23, 127.14, 60.94, 32.13, 29.75, 22.51, 14.49, 14.09.

IR: 3057, 2957, 2926, 2872, 2857, 1714, 1606, 1507, 1269, 1100, 849.

HRMS: (ESI$^+$) m/z: $[M+H]^+$ Calculated for $C_{21}H_{25}O_2$ 309.1854; Found 309.1864.



1-(4-(trifluoromethyl)phenyl)hexan-1-one. [49] An oven-dried 250 mL Schlenk flask equipped with a Teflon stir bar was charged with (*E*)-diphenyl(1-(4-(trifluoromethyl)phenyl)hex-1-en-1-yl)silane (91.7 mg, 0.220 mmol, 1.00 eq), KF (19.2 mg, 0.330 mmol, 1.50 eq), $KHCO_3$ (33.2 mg, 0.330 mmol, 1.50 eq), THF (6.00 mL), and MeOH (6.00 mL) under N_2 atmosphere. A 50% H_2O_2 (150 mg, 2.20 mmol, 10.0 eq) was added to the flask. The resulting colorless mixture was refluxed at 70 ˚C for 12 h under N_2 atmosphere. Upon reaction completion, the reaction mixture was quenched with 15 mL saturated $Na_2S_2O_3$, extracted with ethyl acetate (3 x 15 mL), and the combined organic layers were washed with brine (30 mL x 2) and dried over anhydrous Na_2SO_4. The solvent was removed by rotary evaporation. The crude product was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography (100 mL of

100% hexanes, 100 mL of 10% dichloromethane in hexane, 300 mL of 20% dichloromethane in hexane) gives the desired product as a white solid (37.1 mg, 0.150 mmol, 69% yield).

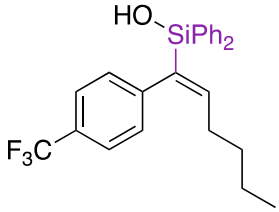
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.05 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 2H), 2.98 (t, *J* = 7.4 Hz, 2H), 1.74 (p, *J* = 7.3 Hz, 2H), 1.41 – 1.32 (m, 4H), 0.90 (t, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 199.64, 139.85, 134.34 (q, *J* = 32.6 Hz), 128.50, 125.79 (q, *J* = 3.8 Hz), 123.77 (q, *J* = 272.5 Hz), 39.02, 31.58, 23.95, 22.65, 14.07.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.12.

IR: 2961, 2931, 2881, 2862, 1680, 1576, 1437, 1324, 850.

HRMS: (ESI^{+}) m/z: [M+H]$^{+}$ Calculated for $C_{13}H_{16}F_3O$ 245.1153; Found 245.1140.



(*E*)-diphenyl(1-(4-(trifluoromethyl)phenyl)hex-1-en-1-yl)silanol. [50] Following a previously reported procedure,[5] to an oven-dried 2-dram vial equipped with a Teflon stir bar was added (*E*)-diphenyl(1-(4-(trifluoromethyl)phenyl)hex-1-en-1-yl)silane (20.0 mg, 0.049 mmol, 1.00 eq), THF (0.300 mL) and MeOH (0.300 mL) under N_2 atmosphere. To the resulting solution was added $KHCO_3$ (5.00 mg, 0.049 mmol, 1.00 eq) followed by H_2O_2 (51.7 µl, 0.882 mmol, 18.0 eq of a 50% aqueous solution) under N_2 atmosphere. The mixture was stirred at room temperature overnight. After reaction completion, the solvent was removed by rotary evaporation. The crude product was dry loaded onto a silica gel column. Purification using silica gel flash column chromatography with gradient elution (100 mL of 100% hexanes, 100 mL of 2% ethyl acetate in hexane, 100 mL of 3% ethyl acetate in hexane, 200 mL of 4% ethyl acetate in hexane) gives the desired product as a colorless liquid (12.8 mg, 0.030 mmol, 61% yield).

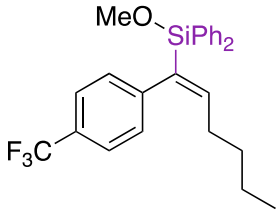
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 (d, *J* = 7.1 Hz, 4H), 7.51 – 7.41 (m, 4H), 7.41 – 7.33 (m, 4H), 7.08 (d, *J* = 7.9 Hz, 2H), 6.27 (t, *J* = 7.2 Hz, 1H), 2.25 (br s, 1H), 2.03 (q, *J* = 7.2 Hz, 2H), 1.38 – 1.28 (m, 2H), 1.28 – 1.17 (m, 2H) (overlaps with grease), 0.81 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 148.66, 144.95, 144.94, 138.93, 135.03, 134.79, 130.28, 128.95, 128.05, 125.17 (q, J = 3.7 Hz), 124.49 (q, *J* = 272 Hz), 31.53, 30.02, 22.48, 14.03.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.32.

IR: 3380, 3070, 3050, 3001, 2957, 2927, 2856, 1614, 1429, 1323.

HRMS: (ESI^{+}) m/z: [M+H]$^{+}$ Calculated for $C_{25}H_{26}F_3OSi$ 427.1705; Found 427.1702.



(*E*)-methoxydiphenyl(1-(4-(trifluoromethyl)phenyl)hex-1-en-1-yl)silane. [51] Following a previously reported procedure,[6] to an oven-dried 2-dram vial equipped with a Teflon stir bar was added (*E*)-diphenyl(1-(4-(trifluoromethyl)phenyl)hex-1-en-1-yl)silane (20.0 mg, 0.049 mmol, 1.00 eq), KF (14.2 mg, 0.245 mmol, 5.00 eq), and MeOH (0.300 mL, 0.16 M total reaction concentration) under N_2 atmosphere. The resulting mixture was stirred at room temperature overnight. After reaction completion, the solvent was removed by rotary evaporation. The crude product mixture was dissolved in 2 mL dichloromethane and then filtered through a 1" silica plug with 100 mL of 2% ethyl acetate in hexanes. The solvent was removed by rotary evaporation to give the desired product as a colorless liquid (20.7 mg, 0.047 mmol, 96% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 (d, *J* = 7.5 Hz, 4H), 7.49 – 7.40 (m, 4H), 7.37 (t, *J* = 7.0 Hz, 4H), 7.06 (d, *J* = 7.9 Hz, 2H), 6.32 (t, *J* = 7.0 Hz, 1H), 3.48 (s, 3H), 2.05 (q, *J* = 7.4 Hz, 2H), 1.35 (p, *J* = 7.2 Hz, 2H), 1.25 (sxt, *J* = 7.2 Hz, 2H), 0.82 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 149.08, 145.22, 145.21, 138.08, 135.46, 133.59, 130.18, 128.98, 128.00, 125.01 (q, *J* = 3.8 Hz), 124.55 (q, *J* = 272 Hz), 52.02, 31.58, 30.01, 22.48, 14.03.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.28.

IR: 3070, 3050, 3001, 2957, 2931, 2858, 2836, 1613, 1467, 1429, 1116.

HRMS: (ESI$^+$) m/z: $[M+H]^+$ Calculated for $C_{26}H_{28}F_3OSi$ 441.1861; Found 441.1880.

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