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Article

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Palladium-Catalyzed Methylation of Alkynyl C(sp)-H Bond with Dimethyl Sulfonium Ylides

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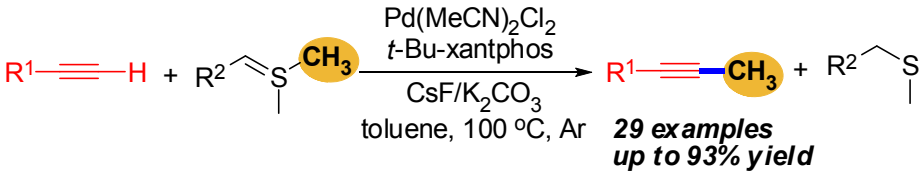
Abstract



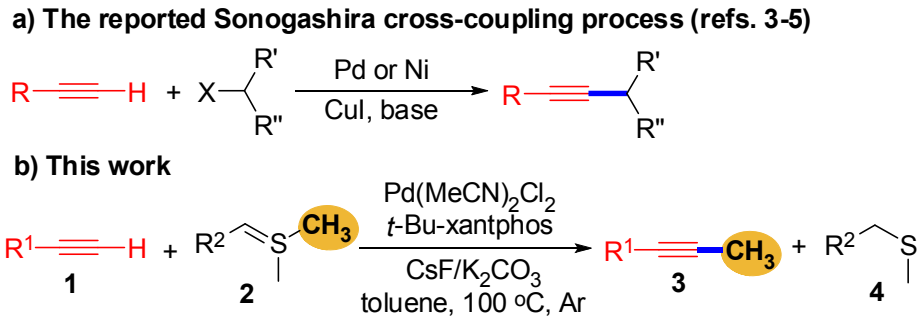
A novel palladium-catalyzed methylation protocol is established for the synthesis of methyl-functionalized internal alkynes. This methylation method is achieved through a C(sp)-C(sp^3) bond formation process and represents a new synthetic application of sulfonium ylides.

Introduction

Alkynes, particularly functionalized internal alkynes, are important unsaturated organic compounds that found in a wide range of natural products, bioactive compounds and materials, as well as are significant as synthetic intermediates in organic synthesis.[1] As a consequence, the development of new chemical methodologies using alkynes as the synthetic targets remains an active area all the while.[1-7] In this content, the classical Sonogashira cross-coupling reaction represents one of the most powerful methods for the functionalized internal alkyne synthesis wherein aryl or vinyl halides and pseudohalides are generally employed to react with terminal alkynes in the presence of a palladium catalyst and a copper co-catalyst.[2-5] Despite impressive advances in the Sonogashira cross-coupling field, examples of transition metal-catalyzed Sonogashira cross-coupling of an alkyl electrophile with a terminal alkyne are quite rare (Scheme 1a).[3-5] Fu group has firstly established the Pd/*N*-heterocyclic carbene catalytic system for the Sonogashira coupling of primary alkyl iodides and bromides.[3] Subsequently, Glorius group[4] has reported another Pd/*N*-heterocyclic carbene catalytic system, extending the scope to secondary alkyl bromides. Recently, Hu group illustrated that the Ni^{II} pincer complex was an efficient catalyst for the Sonogashira coupling with alkyl halides, even primary alkyl chlorides.[5] In these cases, however, Cu co-catalyst was still necessary to trigger these transformations by the in-situ generation of copper acetylides and phosphine ligands were ineffective. Moreover, the synthesis of methyl-functionalized internal alkynes through this C(sp)-C(sp^3) bond formation strategy has not been reported.[3-5] Thus, the development of conceptually novel Cu-free cross-coupling methods involving the use of new alkyl electrophiles and/or new metal catalytic systems for preparing alkyl-substituted internal alkynes is thus particularly important and urgent.[6,7]

Sulfonium ylides are dipolarophiles and widely serve as versatile synthetic blocks in organic synthesis because of their high reactivity and useful functionality.[8] Generally, sulfonium ylides are utilized as nucleophiles to construct the carbon-carbon bonds. To our knowledge, however, it is reasonable to expect that sulfonium ylides as electrophiles for the cross coupling reaction should provide a convenient method for the synthesis of functionalized internal alkynes. More recently, Maulide and co-workers developed a transformation that the C-S linkage of a diphenyl sulfonium ylide was cleaved using

$Pd(OAc)_2$ and silane.[9] Herein, we report a novel, copper-free cross-coupling route to selectively synthesizing methyl-functionalized internal alkynes *via* $PdCl_2(MeCN)_2$/*t*-Bu-xantphos-catalyzed methylation of alkynyl C(sp)-H bond with dimethyl sulfonium ylides, wherein dimethyl sulfonium ylides are used as methyl electrophile (Scheme 1b).



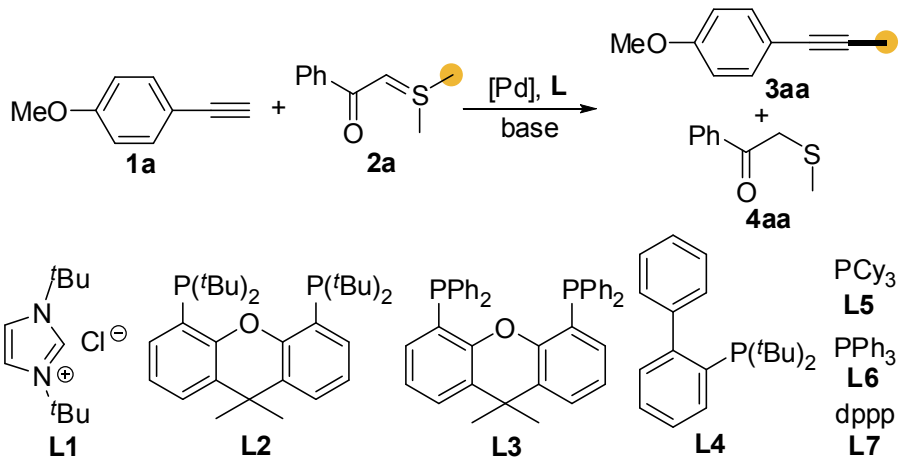
Scheme 1. Alkylation of Alkynyl C(sp)-H Bond.

Results and discussion

We began with our evaluation on the reaction between 1-ethynyl-4-methoxybenzene (**1a**) and dimethyl (2-oxo-2-phenylethyl)sulfonium ylide (**2a**) (Table 1).[10] Unfortunately, treatment of alkyne **1a** with ylide **2a**, $PdCl_2(MeCN)_2$ and ^{t}BuOLi only afforded a trace of 1-methoxy-4-(prop-1-ynyl)benzene (**3aa**) (entry 1). The reported literatures suggested that the presence of ligands can improve the Sonogashira coupling reaction with alkyl electrophiles. As expected, a series of ligands **L1-L7**, including the reported efficient *N*-heterocyclic carbene ligand **L1**[3] and other phosphine ligands **L2-L7**, were found to effect the reaction (entries 2-8), and the phosphine ligand **L2** were the most efficient (entry 3). In light of these, three other Pd catalysts, $PdCl_2$, $Pd(OAc)_2$ and $Pd(dba)_2$ were subsequently tested, and they displayed less catalytic activity (entries 9-11). Extensive screening revealed that bases played an important role in the reaction (entries 12-18). While both ^{t}BuONa and K_2CO_3 suppressed the reaction (entries 12 and 13), both Cs_2CO_3 and CsF favored the reaction (entries 14 and 15). Notably, the amount of base affected the reaction: product **3aa** was obtained in 65% yield at 2 equiv CsF (entry 15),

and increased to 70% yield at 1 equiv CsF (entry 16). We were delighted to discover that the use of mixed bases could increase the yield (entries 17 and 18). For example, the yield of product **3aa** was enhanced to 81% using 1 equiv CsF combined with 2 equiv K_2CO_3 (entry 18). Among the reaction temperature examined, it turned out that the reaction at 100 °C gave the best results (entries 18-20). It is noteworthy that the reaction can not take place without Pd catalysts (entry 21).

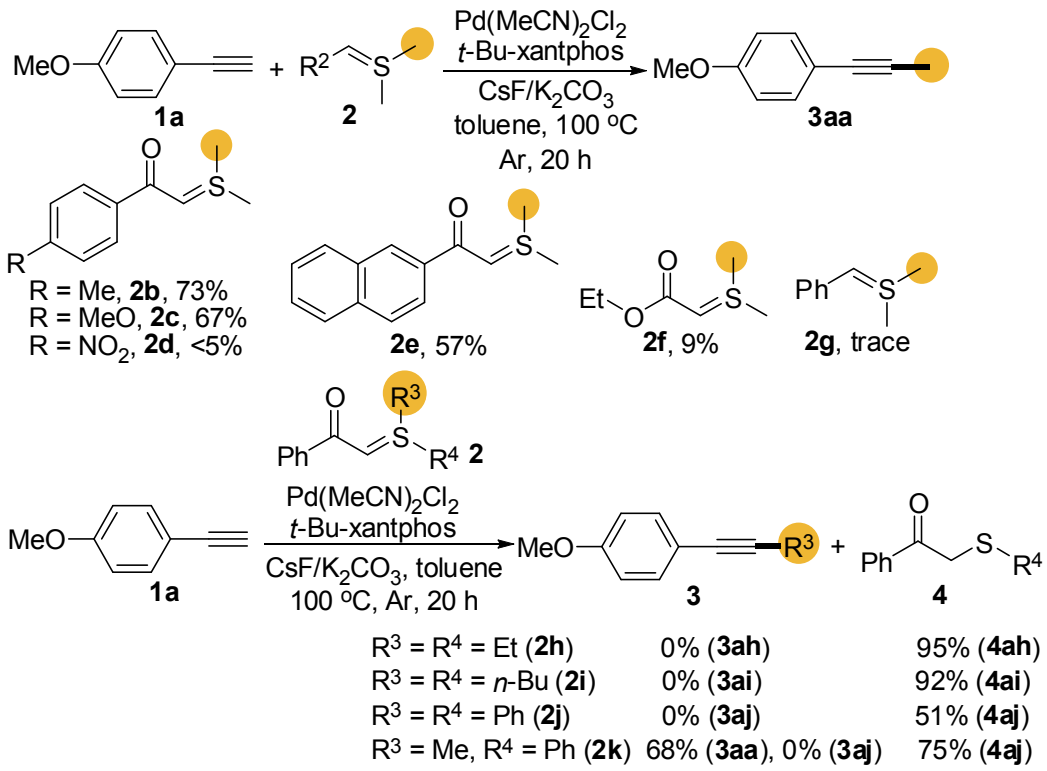
Table 1. Screening Optimal Conditions[a]



Entry	[Pd]	Ligand	Base (equiv)	T (°C)	Yield (%)
1	$PdCl_2(MeCN)_2$	—	^{t}BuOLi (2)	100	trace
2	$PdCl_2(MeCN)_2$	**L1**	^{t}BuOLi (2)	100	16
3	$PdCl_2(MeCN)_2$	**L2**	^{t}BuOLi (2)	100	46
4	$PdCl_2(MeCN)_2$	**L3**	^{t}BuOLi (2)	100	15
5	$PdCl_2(MeCN)_2$	**L4**	^{t}BuOLi (2)	100	30
6	$PdCl_2(MeCN)_2$	**L5**	^{t}BuOLi (2)	100	26
7	$PdCl_2(MeCN)_2$	**L6**	^{t}BuOLi (2)	100	10
8	$PdCl_2(MeCN)_2$	**L7**	^{t}BuOLi (2)	100	32
9	$PdCl_2$	**L2**	^{t}BuOLi (2)	100	40
10	$Pd(OAc)_2$	**L2**	^{t}BuOLi (2)	100	23
11	$Pd(dba)_2$	**L2**	^{t}BuOLi (2)	100	35
12	$PdCl_2(MeCN)_2$	**L2**	^{t}BuONa (2)	100	42
13	$PdCl_2(MeCN)_2$	**L2**	K_2CO_3 (2)	100	9
14	$PdCl_2(MeCN)_2$	**L2**	Cs_2CO_3 (2)	100	60
15	$PdCl_2(MeCN)_2$	**L2**	CsF (2)	100	65
16	$PdCl_2(MeCN)_2$	**L2**	CsF (1)	100	70
17	$PdCl_2(MeCN)_2$	**L2**	CsF (1)/Cs_2CO_3 (2)	100	76
18[b]	$PdCl_2(MeCN)_2$	**L2**	CsF (1)/K_2CO_3 (2)	100	81
19	$PdCl_2(MeCN)_2$	**L2**	CsF (1)/K_2CO_3 (2)	120	58
20	$PdCl_2(MeCN)_2$	**L2**	CsF (1)/K_2CO_3 (2)	80	66
21	—	**L2**	CsF (1)/K_2CO_3 (2)	100	0

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (1.2 equiv), [Pd] (5 mol %), Ligand (10 mol %), base and toluene (2 mL) at 100 °C under argon atmosphere for 20 h. [b] Product **4aa** was isolated in 90% yield.

As shown in Scheme 2, we next turned our attention to exploit the viable sulfonium ylides for the alkylation reaction in the presence of $PdCl_2(MeCN)_2$, **L2**, CsF and K_2CO_3. The results indicated that the substitution effect had a fundamental influence on the reaction. Ylides **2b**, **2c** and **2e** with an electron-rich aryl groups were still found to be efficient methylation reagents, albeit with lower yields than ylide **2a**. However, ylide **2d** with an electron-deficient aryl groups was ineffective. The other two sulfonium ylides, dimethyl (2-ethoxy-2-oxoethyl)sulfonium ylide (**2f**) and dimethyl benzylsulfonium ylide (**2g**), were examined, and both were unsuitable methylation reagents. Unfortunately, the other ylides, including diethyl (2-oxo-2-phenylethyl)sulfonium ylide (**2ha**), di(*n*-butyl) (2-oxo-2-phenylethyl)sulfonium ylide (**2ia**) and diphenyl (2-oxo-2-phenylethyl)sulfonium ylide (**2ja**), could not react with alkyne **1a** under the optimal conditions, although decomposition of ylides took place. Interestingly, methyl phenyl (2-oxo-2-phenylethyl)sulfonium ylide (**2ka**) selectively gave 1-methoxy-4-(prop-1-ynyl)benzene (**3aa**) alone in 68% yield.

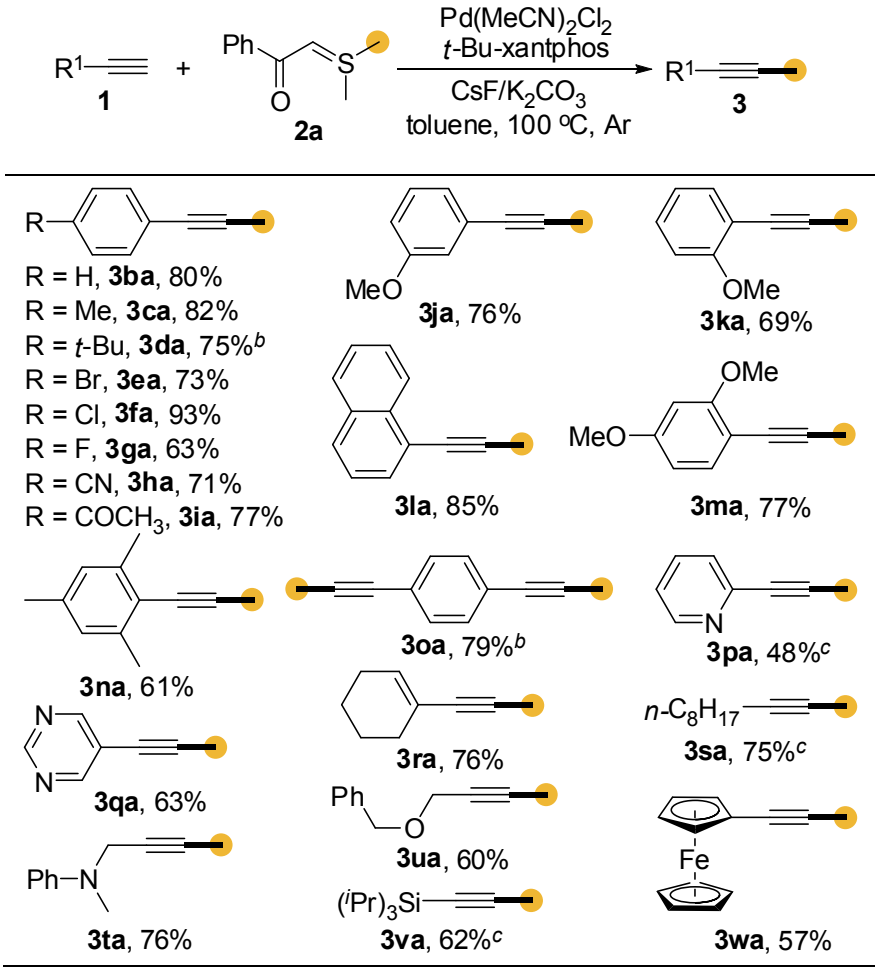


Scheme 2. Scope of Sulfonium Ylides (**2**).

With the optimal reaction conditions in hand, we set out to examine the scope of this new methylation protocol (Table 2). Gratifyingly, this methylation protocol was general to a wide range of terminal alkynes. Initially, a variety of arylalkynes **1b-1q** were employed to react with dimethyl (2-oxo-2-phenylethyl)sulfonium ylide (**2a**) in the presence of $PdCl_2(MeCN)_2$, **L2**, CsF and K_2CO_3 (Products **3ba-qa**). The results showed that several substituents, such as Me, *t*-Bu, Br, Cl, F, CN, $COCH_3$ or MeO, on the aryl ring were well-tolerated, and the order of the reactivity was *para>meta>ortho* (Products **3ba-na**). Phenylacetylene (**1b**), for example, was successfully treated with ylide **2a**, providing the expected alkyne **3ba** in 80% yield. Me- or even bulky *t*-Bu-substituted aryl alkynes **2c** and **2d** were also viable for the methylation reaction (Products **3ca** and **3da**). Importantly, substituents, Br, Cl and F, on the aryl ring were compatible with the optimal conditions, thereby easily facilitating additional modifications at the halogenated positions (Products **3ea-ga**). Using electron-deficient aryl alkynes, good yields were still achieved (Products **3ha** and **3ia**). While 3-MeO- or 2,4-diMeO-substituted aryl alkynes offered the corresponding products **3ja** and **3ma** in 76% and 77% yields, respectively, 2-MeO-substituted aryl

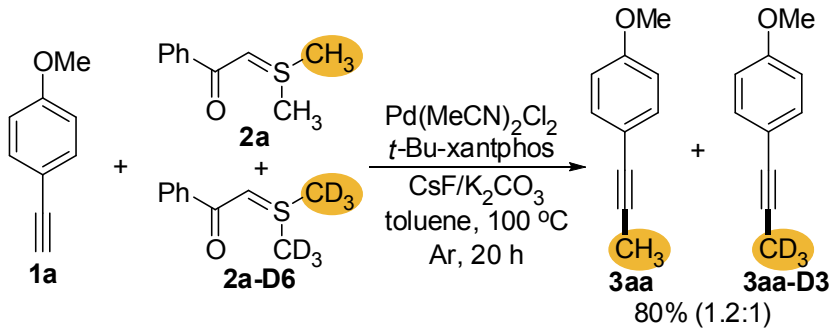
alkyne resulted in product **3ka** in 69% yield. We were pleased to find that the optimal conditions could be applied to access 1-(prop-1-ynyl)naphthalene (**3la**) and bulky 1,3,5-trimethyl-2-(prop-1-ynyl)benzene (**3na**). Interestingly, 1,4-diethynylbenzene **1o** successfully underwent double methylation reactions, providing a dimethylation product, 1,4-di(prop-1-ynyl)benzene (**3oa**), in good yield. Using heteroaryl alkynes **1p** and **1q**, moderate yields were still achieved (Products **3pa** and **3qa**). Extensive screening revealed that both vinyl alkyne **1r** and aliphatic alkyne **1s** were viable to react with ylide **2a** leading to the corresponding products **3ra** and **3sa** in high yields. Notably, oxygen-, nitrogen-, silicon- and iron-functionalized alkynes **1t-1w** were consistent with the optimal conditions, which made this methodology more useful in organic synthesis (Products **3ta-wa**).

Table 2. Scope of Alkynes[a]



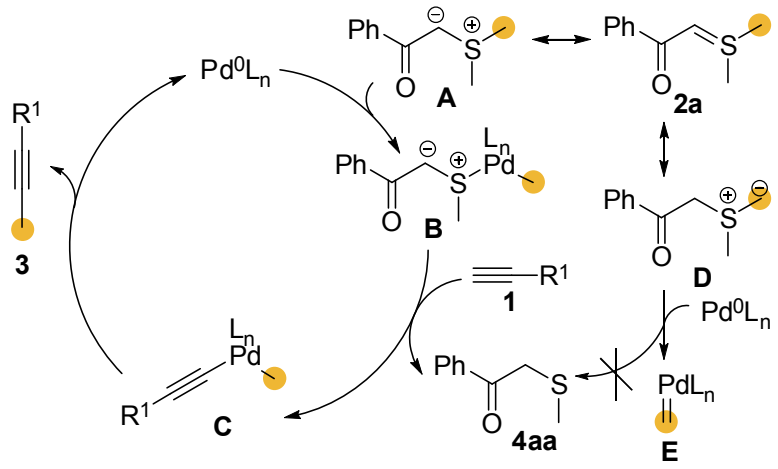
[a] Reaction conditions: **1** (0.5 mmol), **2a** (1.2 equiv), $PdCl_2(MeCN)_2$ (5 mol %), ^{t}Bu-xantphos (10 mol %), CsF (1 equiv), K_2CO_3 (2 equiv) and toluene (2 mL) at 100 ^oC under argon atmosphere for 20 h. [b] **2a** (2.4 equiv). [c] For 48 h.

An intermolecular deuterium-labeled experiment was carried out to understand the mechanism (Scheme 3). The results demonstrated that the ratio of **3aa** and **3aa-D3** was 1.2:1, suggesting that the methyl group is really from dimethyl sulfonium ylide, and the cleavage of the S-CH_3 bond is superior to the cleavage of the S-CD_3.



Scheme 3. Control Experiments.

Consequently, possible mechanisms as outlined in Scheme 4 were proposed on the present results.[2-5,8,9] Initially, oxidative addition of the active Pd^0L_n species to the S-CH_3 bond takes place to yield intermediate **B**. Subsequently, intermediate **B** undergoes the reaction with alkyne **1** to afford intermediate **C** and 2-(methylthio)-1-phenylethanone **4aa**. Finally, reductive elimination of intermediate **C** affords the desired methyl-functionalized internal alkyne **3** and the active Pd^0L_n species. Notably, another possible mechanism including Pd carbene intermediate **E** can be ruled out according to the deuterium-labeled experiment (Scheme 3).



Scheme 4. Possible mechanisms.

Conclusions

In summary, we have illustrated a conceptually novel Cu-free cross-coupling route to methyl-functionalized internal alkynes through a C(sp)-C(sp^3) bond formation process. This new methylation method has a high alkyne compatibility and represents the first example of preparing alkyl-substituted internal alkynes via the cross-coupling of terminal alkynes using sulfonium ylides as alkyl electrophiles.

Experimental Section

General Considerations:

The ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ solvent on a NMR spectrometer using TMS as internal standard. LRMS was performed on a GC-MS instrument and HRMS was measured on an electrospray ionization (ESI) apparatus using time-of-flight (TOF) mass spectrometry. Melting points are uncorrected.

Preparation of Terminal Alkynes:

Alkynes **1a-1c**, **1g-1i**, **1r**, **1s**, **1v** and **1w** were purchased from commercial sources and were used as received. Alkynes **1t**[11], **1u**[12] and the other terminal alkynes **1d-1f** and **1j-1q**[13] were prepared according to literature procedures.

Preparation of Sulfur Ylides:

Sulfide ylides **2a**-**2g** were prepared according to the known procedures.[14] **2a-D** was prepared by the reaction of dimethyl-d_6 sulfide[15] with 2-bromo-1-phenylethanone.[14]

Typical Experimental Procedure for the Pd-Catalyzed Methylation Reaction:

To a Schlenk tube were added alkyne **1** (0.5 mmol) and sulfonium ylide **2** (1.2 mmol), $PdCl_2(MeCN)_2$ (5 mol %), ^{t}Bu-xantphos (**L1**, 10 mol %), CsF (1 equiv), K_2CO_3 (2 equiv) and toluene (2 mL). Then the tube was charged with argon, and was stirred at 100 ^{o}C (oil bath temperature) for the indicated time until complete consumption of starting material as monitored by TLC and GC-MS analysis. After the reaction was finished, the reaction mixture was washed with brine. The aqueous phase was re-extracted with ethyl acetate. The combined organic extracts were dried over Na_2SO_4, concentrated in vacuum, and the resulting residue was purified by silica gel column chromatography (only hexane) to afford the desired product **3**.

1-methoxy-4-(prop-1-ynyl)benzene (3aa):[16] 59 mg, 81%; Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.32 (d, J = 8.5 Hz, 2H), 6.81 (d, J = 9.0 Hz, 2H), 3.79 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 159.0, 132.8, 116.2, 113.8, 84.1, 79.4, 55.2, 4.2; LRMS (EI, 70 eV) *m/z* (%): 147 (M^++1, 19), 146 (M^+, 100), 131 (47), 103 (75).

prop-1-ynylbenzene (3ba):[17] 46 mg, 80%; Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.39-7.38 (m, 2H), 7.29-7.25 (m, 3H), 2.04 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 131.5, 128.2, 127.5, 124.0, 85.8, 79.7, 4.3; LRMS (EI, 70 eV) *m/z* (%): 117 (M^++1, 7), 116 (M^+, 77), 115 (100), 89 (12).

1-methyl-4-(prop-1-ynyl)benzene (3ca):[16] 53 mg, 82%; Colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.27 (d, J = 8.0 Hz, 2H), 7.07 (d, J = 8.0 Hz, 2H), 2.32 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 137.4, 131.3, 128.9, 120.9, 84.9, 79.7, 21.3, 4.3; LRMS (EI, 70 eV) *m/z* (%): 131 (M^++1, 13), 130 (M^+, 100), 115 (70), 102 (6).

1-*tert*-butyl-4-(prop-1-ynyl)benzene (3da):[18] 65 mg, 75%; White solid, mp 66.7-67.8 ^{o}C (uncorrected); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.33-7.28 (m, 4H), 2.04 (s, 3H), 1.30 (s, 9H); ^{13}C NMR (125 MHz,

$CDCl_3$) δ: 150.6, 131.2, 125.2, 121.0, 84.9, 79.7, 34.6, 31.2, 4.3; LRMS (EI, 70 eV) *m/z* (%): 173 (M^++1, 5), 172 (M^+, 38), 157 (100), 129 (27).

1-bromo-4-(prop-1-ynyl)benzene (3ea):[16] 71 mg, 73%; Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.40 (d, *J* = 8.5 Hz, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 2.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 132.9, 131.4, 123.0, 121.6, 87.1, 78.7, 4.3; LRMS (EI, 70 eV) *m/z* (%): 194 (M^++1, 4), 193 (M^+, 40), 115 (100), 89 (16).

1-chloro-4-(prop-1-ynyl)benzene (3fa):[19] 70 mg, 93%; Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.30 (d, *J* = 8.5 Hz, 2H), 7.24 (d, *J* = 8.5 Hz, 2H), 2.03 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 133.4, 132.7, 128.5, 122.5, 86.9, 78.7, 4.3; LRMS (EI, 70 eV) *m/z* (%): 152 (M^++2, 20), 150 (M^+, 63), 115 (100), 89 (10).

1-fluoro-4-(prop-1-ynyl)benzene (3ga):[19] 42 mg, 63%; Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.37-7.33 (m, 2H), 6.98-6.94 (m, 2H), 2.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 162.0 (d, *J* = 246.5 Hz), 133.2 (d, *J* = 8.1 Hz), 120.1 (d, *J* = 3.6 Hz), 115.3 (d, *J* = 21.8 Hz), 85.3, 78.6, 4.1; LRMS (EI, 70 eV) *m/z* (%): 135 (M^++1, 3), 134 (M^+, 77), 133 (100), 107 (10).

4-(prop-1-ynyl)benzonitrile (3ha):[16] 50 mg, 71%; Light yellow solid, mp 104.5-105.9 ^{o}C (uncorrected); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.56 (d, *J* = 8.0 Hz, 2H), 7.45 (d, *J* = 8.0 Hz, 2H), 2.08 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 132.0, 131.9, 129.0, 118.6, 110.8, 91.1, 78.6, 4.4; LRMS (EI, 70 eV) *m/z* (%): 142 (M^++1, 10), 141 (M^+, 99), 140 (100), 114 (43).

1-(4-(prop-1-ynyl)phenyl)ethanone (3ia):[20] 61 mg, 77%; White solid, 50.3-51.6 ^{o}C (uncorrected); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.86 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 8.0 Hz, 2H), 2.57 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 197.2, 135.7, 131.5, 129.0, 128.1, 89.6, 79.2, 26.4, 4.3; LRMS (EI, 70 eV) *m/z* (%): 159 (M^++1, 6), 158 (M^+, 55), 143 (100), 115 (71).

1-methoxy-3-(prop-1-ynyl)benzene (3ja):[16] 55 mg, 76%; Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.18 (t, *J* = 8.0 Hz, 1H), 6.98 (d, *J* = 7.5 Hz, 1H), 6.93-6.92 (m, 1H), 6.83-6.81 (m, 1H), 3.78 (s, 3H),

2.04 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 159.3, 129.2, 125.1, 124.0, 116.4, 114.1, 85.7, 79.7, 55.2, 4.2; LRMS (EI, 70 eV) *m/z* (%): 147 (M^++1, 11), 146 (M^+, 100), 131 (13), 115 (36).

1-methoxy-2-(prop-1-ynyl)benzene (3ka):[16] 50 mg, 69%; Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.38-7.36 (m, 1H), 7.24-7.21 (m, 1H), 6.89-6.83 (m, 2H), 3.86 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 159.8, 133.5, 128.8, 120.3, 113.0, 110.4, 89.9, 75.8, 55.7, 4.6; LRMS (EI, 70 eV) *m/z* (%): 147 (M^++1, 11), 146 (M^+, 100), 131 (66), 115 (30).

1-(prop-1-ynyl)naphthalene (3la):[16] 71 mg, 85%; Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.35 (d, *J* = 8.5 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 8.5 Hz, 1H), 7.61(d, *J* = 7.0 Hz, 1H), 7.55-7.52 (m, 1H), 7.50-7.47(m, 1H), 7.38 (t, *J* = 8.0 Hz, 1H), 2.19 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 133.5, 133.2, 129.9, 128.1, 127.9, 126.4, 126.3, 126.2, 125.2, 121.7, 90.8, 77.7, 4.6; LRMS (EI, 70 eV) *m/z* (%): 167 (M^++1, 12), 166 (M^+, 88), 165 (100), 139 (7).

2,4-dimethoxy-1-(prop-1-ynyl)benzene (3ma):[21] 68 mg, 77%; Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.30-7.27 (m, 1H), 6.43-6.41 (m, 2H), 3.86 (s, 3H), 3.80 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 160.9, 160.5, 134.2, 105.6, 104.6, 98.3, 88.2, 75.5, 55.8, 55.3, 4.7; LRMS (EI, 70 eV) *m/z* (%): 177 (M^++1, 12), 176 (M^+, 100), 161 (28), 133 (19).

1,3,5-trimethyl-2-(prop-1-ynyl)benzene (3na):[22] 48 mg, 61%; Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.83 (s, 2H), 2.37 (s, 6H), 2.25 (s, 3H), 2.12 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 139.9, 136.6, 127.6, 127.4, 120.7, 93.0, 21.2, 20.9, 4.5; LRMS (EI, 70 eV) *m/z* (%): 159 (M^++1, 14), 158 (M^+, 100), 143 (63), 128 (73).

1,4-di(prop-1-ynyl)benzene (3oa):[23] 61 mg, 79%; White solid, 104.3-105.5 ^{o}C (uncorrected); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.37 (s, 4H), 2.12 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 131.3, 123.2, 87.3, 79.5, 4.3; LRMS (EI, 70 eV) *m/z* (%): 155 (M^++1, 13), 154 (M^+, 100), 139 (8), 115 (19).

2-(prop-1-ynyl)pyridine (3pa):[24] 28 mg, 48%; Light yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.54 (d, *J* = 4.5 Hz, 1H), 7.62-7.59 (m, 1H), 7.36 (d, *J* = 7.5 Hz, 1H), 7.19-7.17 (m, 1H), 2.08 (s, 3H); ^{13}C NMR

(125 MHz, $CDCl_3$) δ: 149.8, 143.9, 136.0, 126.6, 122.3, 86.6, 79.6, 4.3; LRMS (EI, 70 eV) *m/z* (%): 118 (M^++1, 10), 117 (M^+, 100), 89 (54), 78 (11).

5-(prop-1-ynyl)pyrimidine (3qa): 37 mg, 63%; Light yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.12 (s, 1H), 8.75 (s, 2H), 7.36 (d, *J* = 7.5 Hz, 1H), 7.19-7.17 (m, 1H), 2.08 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 158.7, 156.2, 120.5, 93.7, 73.2, 4.5; LRMS (EI, 70 eV) *m/z* (%): 119 (M^++1, 9), 118 (M^+, 100), 91 (39), 64 (80); HRMS *m/z* (ESI) calcd for $C_7H_7N_2$ $(M+H)^+$ 119.0609, found 119.0606.

1-(prop-1-ynyl)cyclohex-1-ene (3ra):[25] 46 mg, 76%; Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.99 (t, *J* = 4.0 Hz, 1H), 2.10-2.06 (m, 4H), 1.92 (s, 3H), 1.64-1.54 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 133.0, 120.9, 82.5, 81.4, 29.4, 25.4, 22.3, 21.5, 4.0; LRMS (EI, 70 eV) *m/z* (%): 121 (M^++1, 9), 120 (M^+, 90), 105 (100), 91 (95).

undec-2-yne (3sa):[7f] 57 mg, 75%; Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.13-2.09 (m, 2H), 1.77 (t, *J* = 3.0 Hz, 3H), 1.50-1.44 (m, 2H), 1.39-1.28 (m, 10H), 0.88 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 79.4, 75.2, 31.9, 29.2 (2C), 29.1, 28.9, 22.7, 18.7, 14.0, 3.4; LRMS (EI, 70 eV) *m/z* (%): 152 (M^+, 0.22), 109 (29), 95 (100), 81 (80), 67 (91).

***N*-(but-2-ynyl)-*N*-methylaniline (3ta):** 60 mg, 76%; Light yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.27-7.23 (m, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 6.78 (t, *J* = 7.5 Hz, 1H), 3.98-3.97 (m, 2H), 2.94 (s, 3H), 1.76 (t, *J* = 2.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 149.3, 129.0, 117.8, 114.0, 79.6, 74.5, 42.6, 38.5, 3.5; LRMS (EI, 70 eV) *m/z* (%): 160 (M^++1, 12), 159 (M^+, 100), 144 (30), 104 (18); HRMS *m/z* (ESI) calcd for $C_{11}H_{14}N$ $(M+H)^+$ 160.1126, found 160.1122.

((but-2-ynyloxy)methyl)benzene (3ua):[26] 48 mg, 60%; Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.36-7.33 (m, 4H), 7.29-7.26 (m, 1H), 4.57 (s, 2H), 4.13-4.12 (m, 2H), 1.86 (t, *J* = 2.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 137.5, 128.3, 128.0, 127.7, 82.6, 75.0, 71.4, 57.6, 3.5; LRMS (EI, 70 eV) *m/z* (%): 160 (M^++1, 3), 159 (M^+, 18), 145 (22), 105 (85), 91 (100).

triisopropyl(prop-1-ynyl)silane (3va):[27] 61 mg, 62%; Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.91 (s, 3H), 1.08-1.05 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 104.3, 79.4, 18.6, 11.3, 4.8; LRMS (EI, 70 eV) *m/z* (%): 197 (M^++1, 2), 196 (M^+, 8), 153 (100), 125 (48), 97 (80).

prop-1-ynylferrocene (3wa): 64 mg, 57%; Brown solid, mp 89.7-91.2 ^{o}C (uncorrected); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.34 (t, *J* = 2.0 Hz, 2H), 4.19 (s, 5H), 4.12 (t, *J* = 2.0 Hz, 2H), 1.93 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 81.7, 77.3, 71.0, 69.7, 68.0, 66.5, 4.4; LRMS (EI, 70 eV) *m/z* (%): 225 (M^++1, 2), 224 (M^+, 17), 223 (100), 157 (24), 120 (18); HRMS *m/z* (ESI) calcd for $C_{13}H_{13}Fe$ $(M+H)^+$ 225.0367, found 225.0361.

2-(methylthio)-1-phenylethanone (4aa):[28] 75 mg, 90%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.98-7.97 (m, 2H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 2H), 3.76 (s, 2H), 2.13 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 193.9, 135.1, 133.2, 128.6, 128.5, 38.9, 15.7; LRMS (EI, 70 eV) *m/z* (%): 167 (M^++1, 3), 166 (M^+, 28), 120 (7), 105 (100).

2-(ethylthio)-1-phenylethanone (4ah):[29] 86 mg, 95%; Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.90 (d, *J* = 7.6 Hz, 2H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 2H), 3.72 (s, 2H), 2.54-2.48 (m, 2H), 1.18 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.5, 135.1, 133.2, 128.7, 128.6, 36.7, 26.2, 14.1; LRMS (EI, 70 eV) *m/z* (%): 181 (M^++1, 6), 180 (M^+, 44), 120 (87), 105 (100).

2-(butylthio)-1-phenylethanone (4ai):[30] 96 mg, 92%; Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.90 (d, *J* = 8.0 Hz, 2H), 7.49 (t, *J* = 7..2 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 2H), 3.70 (s, 2H), 2.48 (t, *J* = 7.6 Hz, 2H), 1.53-1.46 (m, 2H), 1.35-1.26 (m, 2H), 0.82 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.5, 135.2, 133.2, 128.7, 128.6, 37.0, 32.0, 30.9, 21.8, 13.6; LRMS (EI, 70 eV) *m/z* (%): 209 (M^++1, 2), 208 (M^+, 13), 120 (42), 105 (100).

1-phenyl-2-(phenylthio)ethanone (4aj):[31] 86 mg, 75%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.94-7.92 (m, 2H), 7.58-7.55 (m, 1H), 7.46-7.43 (m, 2H), 7.39-7.37 (m, 2H), 7.28-7.24 (m, 2H), 7.23-7.19 (m, 1H), 4.27 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 194.0, 135.3, 134.7, 133.4, 130.4, 129.0, 128.6, 127.0, 41.1; LRMS (EI, 70 eV) *m/z* (%): 229 (M^++1, 3), 228 (M^+, 20), 123 (7), 105 (100).

2a-D6: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.79-7.77 (m, 2H), 7.35-7.33 (m, 3H), 4.34 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 183.0, 140.8, 129.4, 127.8, 126.2, 50.8 (the deuterated carbon).

3aa and 3aa-D3: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.33-7.30 (m, 2H), 6.82-6.79 (m, 2H), 3.78 (s, 3H), 2.02 (s, 1.6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 159.0, 132.8, 116.2, 113.8, 84.1, 84.0, 79.4 (2C), 55.2, 4.2.

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Supporting Information Available: (1) Copies of spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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