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

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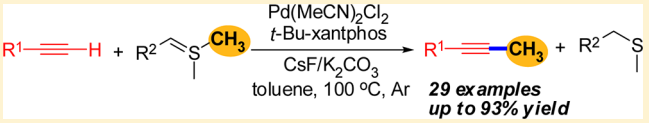
Supporting Information

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

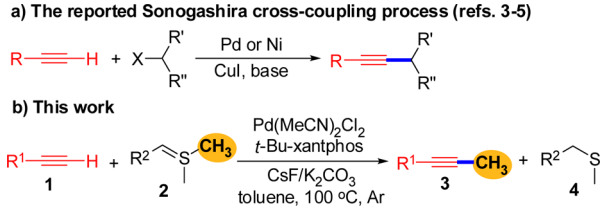


INTRODUCTION

Alkynes, particularly functionalized internal alkynes, are important unsaturated organic compounds that are found in a wide range of natural products, bioactive compounds, and materials and 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 of research.[1−7] In this context, the classical Sonogashira cross-coupling reaction, 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 cocatalyst,[2−5] represents one of the most powerful methods for the synthesis of functionalized internal alkynes. Despite impressive advances in the Sonogashira cross-coupling field, examples of transition-metal-catalyzed Sonogashira cross-couplings of alkyl electrophiles with terminal alkynes are quite rare (Scheme 1a).[3−5] Fu's group first established the Pd/N-heterocyclic carbene catalytic system for the Sonogashira coupling of primary alkyl iodides and bromides.[3] Subsequently, Glorius' group[4] reported another Pd/N-heterocyclic carbene catalytic system, extending the scope to secondary alkyl bromides. Recently, Hu's group showed that a Ni^{II} pincer complex is an efficient catalyst for the Sonogashira coupling with alkyl halides, even primary alkyl chlorides.[5] In these cases, however, a Cu cocatalyst is still necessary to trigger these transformations by the in situ generation of copper acetylides, and phosphine ligands are 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 carbon−carbon bonds. To our knowledge, however, it is reasonable to expect that the use of 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 in which 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 for the selective synthesis of methyl-functionalized internal alkynes via PdCl$_2$(MeCN)$_2$/*t*-Bu-xantphos-catalyzed methylation of alkynyl C(sp)−H bonds with dimethyl sulfonium ylides, wherein the dimethyl sulfonium ylides are used as methyl electrophiles (Scheme 1b).

Scheme 1. Alkylation of Alkynyl C(sp)−H Bonds



RESULTS AND DISCUSSION

We began with our evaluation of 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 afforded only a trace of 1-methoxy-4-(prop-1-ynyl)-benzene (**3aa**) (entry 1). The reported literature suggested that the presence of ligands can improve the Sonogashira coupling reaction with alkyl electrophiles. As expected, a series of ligands

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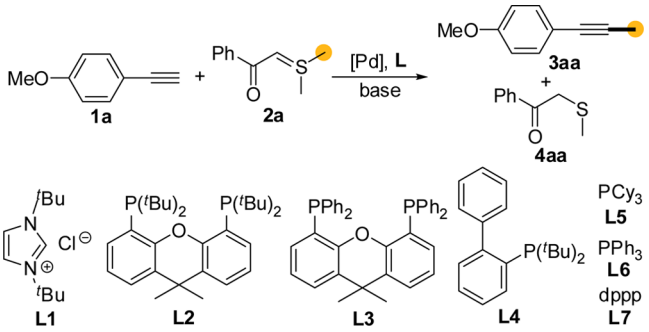
Table 1. Screening for Optimal Conditions[a]



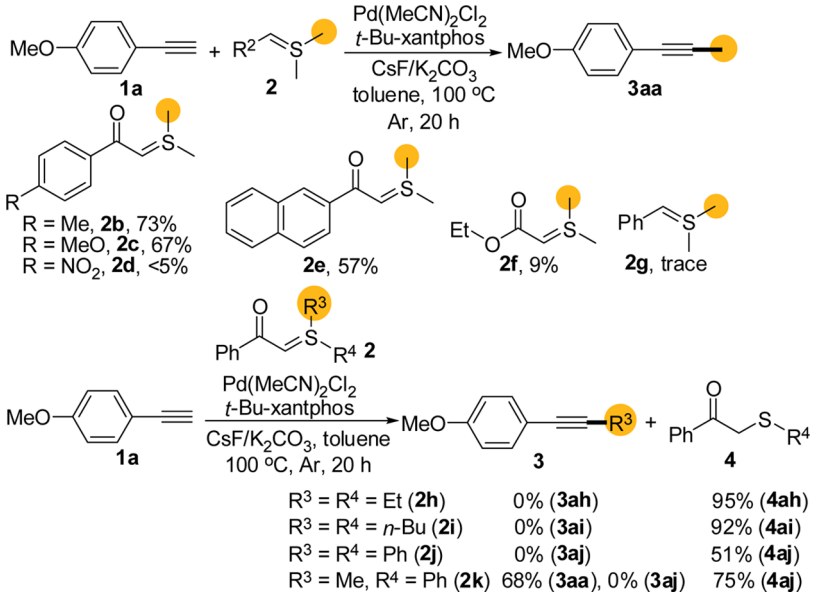
entry	[Pd]	ligand	base (equiv)	T (°C)	yield (%)
1	$PdCl_2(MeCN)_2$	—	^tBuOLi (2)	100	trace
2	$PdCl_2(MeCN)_2$	**L1**	^tBuOLi (2)	100	16
3	$PdCl_2(MeCN)_2$	**L2**	^tBuOLi (2)	100	46
4	$PdCl_2(MeCN)_2$	**L3**	^tBuOLi (2)	100	15
5	$PdCl_2(MeCN)_2$	**L4**	^tBuOLi (2)	100	30
6	$PdCl_2(MeCN)_2$	**L5**	^tBuOLi (2)	100	26
7	$PdCl_2(MeCN)_2$	**L6**	^tBuOLi (2)	100	10
8	$PdCl_2(MeCN)_2$	**L7**	^tBuOLi (2)	100	32
9	$PdCl_2$	**L2**	^tBuOLi (2)	100	40
10	$Pd(OAc)_2$	**L2**	^tBuOLi (2)	100	23
11	$Pd(dba)_2$	**L2**	^tBuOLi (2)	100	35
12	$PdCl_2(MeCN)_2$	**L2**	^tBuONa (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 an argon atmosphere for 20 h. [b]Product **4aa** was isolated in 90% yield.

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 phosphine ligand **L2** was the most efficient (entry 3). In light of these results, 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 the base plays an important role in the reaction (entries 12–18). While both ^tBuONa 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 affects the reaction: product **3aa** was obtained in 65% yield with 2 equiv of CsF (entry 15), and the yield increased to 70% with 1 equiv of 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 of CsF combined with 2 equiv of K_2CO_3 (entry 18). Among the reaction temperatures examined (entries 18–20), it turned out that the reaction at 100 °C gave the best results. It is noteworthy that the reaction cannot take place without the Pd catalyst (entry 21).

As shown in Scheme 2, we next turned our attention to the scope of 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 electron-rich aryl groups were still found to be efficient methylation reagents but gave lower yields than ylide **2a**. However, ylide **2d** with an electron-deficient aryl group was ineffective. Two other sulfonium ylides, dimethyl (2-ethoxy-2-oxoethyl)sulfonium ylide (**2f**) and dimethyl benzylsulfonium ylide (**2g**), were examined, and both were unsuitable methylation reagents. Unfortunately, other ylides, including diethyl (2-oxo-2-phenylethyl)sulfonium ylide (**2h**), di-*n*-butyl (2-oxo-2-phenylethyl)sulfonium ylide (**2i**) and diphenyl (2-oxo-2-phenylethyl)sulfonium ylide (**2j**), could not react with alkyne **1a** under the optimal conditions, although decomposition of the ylides took place. Interestingly, methyl phenyl (2-oxo-2-

Scheme 2. Scope of Sulfonium Ylides 2



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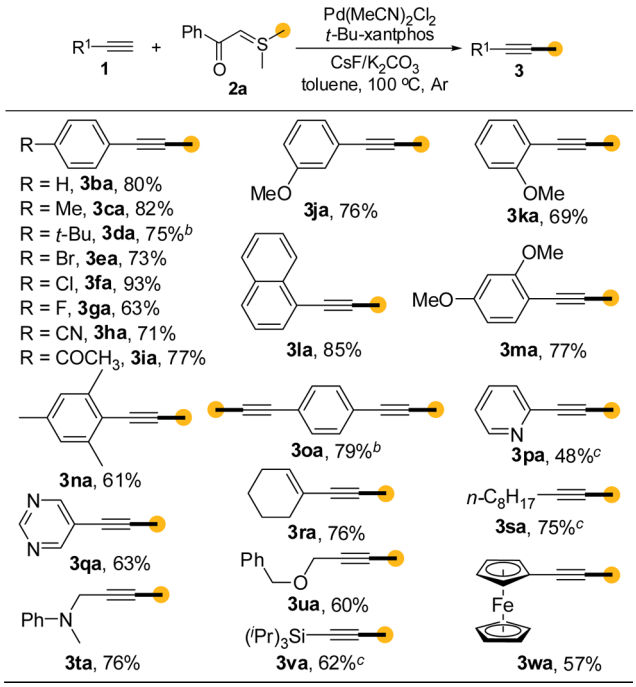
phenylethyl)sulfonium ylide (**2k**) selectively gave 1-methoxy-4-(prop-1-ynyl)benzene (**3aa**) alone in 68% yield.

With the optimal reaction conditions in hand, we set out to examine the scope of this new methylation protocol (Table 2).

Table 2. Scope of Alkynes[a]

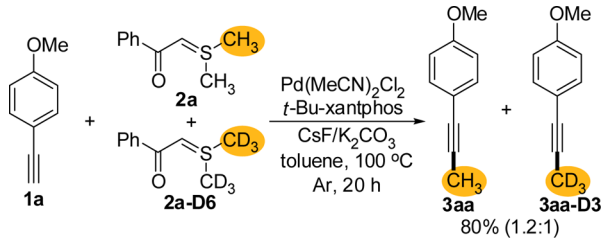


[a]Reaction conditions: **1** (0.5 mmol), **2a** (1.2 equiv), $PdCl_2(MeCN)_2$ (5 mol %), *t*-Bu-xantphos (10 mol %), CsF (1 equiv), K_2CO_3 (2 equiv), and toluene (2 mL) at 100 °C under an argon atmosphere for 20 h. [b]**2a** (2.4 equiv). [c]For 48 h.

Gratifyingly, this methylation protocol was general for a wide range of terminal alkynes. Initially, a variety of aryl alkynes **1b**–**q** 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 on the aryl ring, such as Me, *t*-Bu, Br, Cl, F, CN, $COCH_3$, and MeO, 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- (**2c**) or even bulky *t*-Bu-substituted (**2d**) aryl alkynes were also viable for the methylation reaction (products **3ca** and **3da**). Importantly, Br, Cl, and F substituents on the aryl ring were compatible with the optimal conditions, thereby easily facilitating additional modifications at the halogenated positions (products **3ea**–**ga**). When electron-deficient aryl alkynes were used, good yields were still achieved (products **3ha** and **3ia**). While 3-MeO- or 2,4-di-MeO-substituted aryl alkynes offered the corresponding products **3ja** and **3ma** in 76% and 77% yield, respectively, the 2-MeO-substituted aryl alkyne afforded 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 two methylation reactions, providing the dimethylation product 1,4-bis(prop-1-ynyl)benzene (**3oa**) in good yield. With 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**, giving the corresponding products **3ra** and **3sa** in high yields. Notably, oxygen-, nitrogen-, silicon-, and iron-functionalized alkynes **1t**–**w** were consistent with the optimal conditions (products **3ta**–**wa**), making this methodology more useful in organic synthesis.

An intermolecular deuterium-labeled experiment was carried out to understand the mechanism (Scheme 3). The results

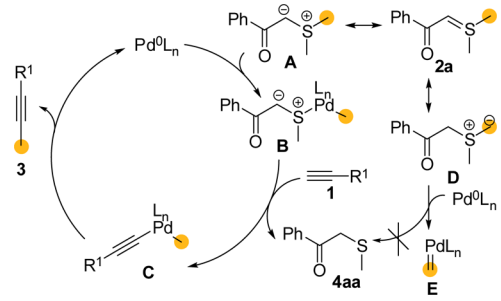
Scheme 3. Control Experiments



demonstrated that the ratio of **3aa** and **3aa-D3** was 1.2:1, suggesting that the methyl group is really from the dimethyl sulfonium ylide and that the cleavage of the S–CH_3 bond is superior to the cleavage of the S–CD_3 bond.

Consequently, a possible mechanism for the present results is proposed,[2−5,8,9] as outlined in Scheme 4. Initially, oxidative

Scheme 4. Possible Mechanism



addition of the active Pd^0L_n species to the S–CH_3 bond takes place to yield intermediate **B**. Subsequently, intermediate **B** reacts 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 on the basis of the deuterium-labeling experiment (Scheme 3).

CONCLUSIONS

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 the preparation of alkyl-substituted internal alkynes via the cross-coupling of terminal alkynes using sulfonium ylides as alkyl electrophiles.

EXPERIMENTAL SECTION

General Considerations. The ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ solvent on a NMR spectrometer using TMS as an internal standard. LRMS was performed on a GC-MS instrument and

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

Preparation of Sulfonium Ylides. Sulfonium ylides **2a−g** were prepared according to the known procedures.[14] **2a-D6** 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). The tube was then charged with argon, and the mixture was stirred at 100 °C (oil bath temperature) for the indicated time until consumption of the starting material was complete 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 and 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] Yield: 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] Yield: 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] Yield: 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] Yield: 65 mg, 75%. White solid, mp 66.7−67.8 °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] Yield: 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] Yield: 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] Yield: 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] Yield: 50 mg, 71%. Light-yellow solid, mp 104.5−105.9 °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] Yield: 61 mg, 77%. White solid, mp 50.3−51.6 °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] Yield: 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] Yield: 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] Yield: 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] Yield: 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] Yield: 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-Bis(prop-1-ynyl)benzene (***3oa***).[23] Yield: 61 mg, 79%. White solid, 104.3−105.5 °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] Yield: 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***). Yield: 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 (ESI) m/z: calcd for $C_7H_7N_2$ (M + H)$^+$ 119.0609, found 119.0606.

1-(Prop-1-ynyl)cyclohex-1-ene (***3ra***).[25] Yield: 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] Yield: 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***). Yield: 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 (ESI) m/z: calcd for $C_{11}H_{14}N$ $(M + H)^+$ 160.1126, found 160.1122.

((But-2-ynyloxy)methyl)benzene (**3ua**).[26] Yield: 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] Yield: 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**). Yield: 64 mg, 57%. Brown solid, mp 89.7−91.2 °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 (ESI) m/z: calcd for $C_{13}H_{13}Fe$ $(M + H)^+$ 225.0367, found 225.0361.

2-(Methylthio)-1-phenylethanone (**4aa**).[28] Yield: 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] Yield: 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] Yield: 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] Yield: 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.

■ ASSOCIATED CONTENT

Supporting Information

Copies of spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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