

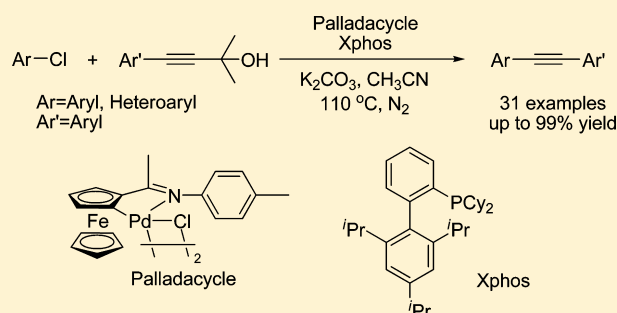
Palladacycle-Catalyzed Deacetonative Sonogashira Coupling of Aryl Propargyl Alcohols with Aryl Chlorides

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Supporting Information

ABSTRACT: An efficient and general protocol for the deacetonative Sonogashira coupling of aryl propargyl alcohols with aryl chlorides is described. The reaction proceeded smoothly with the catalyst system of palladacycle/Xphos. This result represents the first successful deacetonative Sonogashira version for electron-poor, electron-neutral, and even inactive sterically hindered electron-rich aryl chlorides.

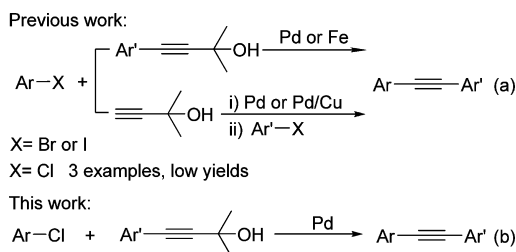


The Sonogashira reaction has been one of the most straightforward and efficient tools for C(sp)–C(sp²) bond-forming reactions, thereby dominating the synthesis of diaryl acetylenes.¹ Significant progress has been achieved in the coupling of commercially available aryl chlorides by Buchwald, Fu, and others.² However, this reaction still suffers from some limitations, especially the problem of poor tolerance to electron-poor terminal alkynes and generation of diynes as byproducts.³ To address these challenges, decarboxylative and deacetonative Sonogashira couplings have emerged as two promising alternatives within recent years.^{4,5} In particular, deacetonative coupling was first reported in 2001 by Chow's group, who described a PdCl₂(PPh₃)₂/CuI-catalyzed tandem catalytic reaction of aryl-2-methyl-3-butyne-2-ol with aryl bromides (Scheme 1a).^{5a} Subsequently, significant progress

acetylenes with low yields.^{5d} Recently, Tsai and co-workers described FeCl₃-catalyzed one-pot Sonogashira–Hagihara coupling of aryl iodides with aryl propargyl alcohols.^{5f} However, the substrate scope in the above-mentioned reports is mainly limited to aryl iodides and bromides, and successful examples for commercially available aryl chlorides remain rare. From the viewpoint of synthetic cost, developing a generally applicable catalytic system for aryl chlorides would be challenging but highly desirable (Scheme 1b).

In recent years, our research group has focused on the catalytic application of a family of versatile palladacyclic catalysts: cyclopalladated ferrocenylimines (Figure 1).⁶ The

Scheme 1. Synthesis of Unsymmetrical Diaryl Acetylenes via Catalytic Deacetonative Sonogashira Coupling



has been achieved by the groups of Kotschy, Shirakawa, Hua, and Tsai (Scheme 1a).^{5b–f} Especially, Hua and co-workers developed the first deacetonative Sonogashira reaction of aryl chlorides using PdCl₂(PCy₃)₂ as the catalyst. This protocol is quite effective for the synthesis of symmetrical diaryl acetylenes but provided only three examples for unsymmetrical diaryl

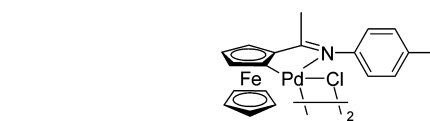


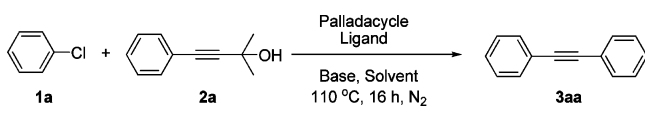
Figure 1. Palladacycle: cyclopalladated ferrocenylimine.

bulky alkylphosphine ligands were developed in Buchwald's group and have been widely applied to the cross-coupling of aryl chlorides.^{2d} Just recently, with the aid of the palladacycle and an alkylphosphine ligand, we realized the first successful decarboxylative Sonogashira reaction of alkynyl carboxylic acids with aryl chlorides in xylene/H₂O.^{6g} To further explore another alternative catalytic version of the traditional Sonogashira reaction, in this work we attempted to fulfill the palladacycle/alkylphosphine-catalyzed deacetonative Sonogashira reaction of aryl propargyl alcohol with aryl chlorides to facilitate the industrial demand.

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We began the reaction conditions optimization with the reaction of chlorobenzene (**1a**) and 4-phenyl-2-methyl-3-butyne-2-ol (**2a**) in DMF using Xphos as the ligand, and a relatively low but promising isolated yield of 48% was observed (Table 1, entry 1). Next, other solvents (e.g., DMA, DMSO,

Table 1. Screening for Optimal Conditions^a



entry	ligand	solvent	base	yield (%)
1	Xphos	DMF	K ₂ CO ₃	48
2	Xphos	DMA	K ₂ CO ₃	67
3	Xphos	DMSO	K ₂ CO ₃	60
4	Xphos	dioxane	K ₂ CO ₃	46
5	Xphos	toluene	K ₂ CO ₃	39
6	Xphos	CH ₃ CN	K ₂ CO ₃	96
7	Xphos	CH ₃ CN	K ₃ PO ₄	76
8	Xphos	CH ₃ CN	KOH	<5
9	Xphos	CH ₃ CN	KF	<5
10	Xphos	CH ₃ CN	KOAc	<5
11	Xphos	CH ₃ CN	NaOH	<5
12	Xphos	CH ₃ CN	Na ₂ CO ₃	<5
13	PPh ₃	CH ₃ CN	K ₂ CO ₃	<5
14	Davephos	CH ₃ CN	K ₂ CO ₃	<5
15	Dppf	CH ₃ CN	K ₂ CO ₃	<5
16 ^b	Xphos	CH ₃ CN	K ₂ CO ₃	25
17 ^c	Xphos	CH ₃ CN	K ₂ CO ₃	20
18 ^d	Xphos	CH ₃ CN	K ₂ CO ₃	32
19 ^e	Xphos	CH ₃ CN	K ₂ CO ₃	<5
20 ^f	Xphos	CH ₃ CN	K ₂ CO ₃	28
21 ^g	Xphos	CH ₃ CN	K ₂ CO ₃	<5
22 ^h	Xphos	CH ₃ CN	K ₂ CO ₃	<5

^aReaction conditions: **1a** (0.4 mmol), **2a** (0.5 mmol), palladacycle (1 mol %), ligand (4 mol %), and base (1.0 mmol) in solvent (2.0 mL) at 110 °C (oil bath temperature) under a nitrogen atmosphere for 16 h.

^bUnder air. ^cAt 90 °C (oil bath temperature). ^dPdCl₂ (2 mol %) was used instead of the palladacycle. ^ePd(OAc)₂ (2 mol %) was used instead of the palladacycle. ^fPd₂(dba)₃ (1 mol %) was used instead of the palladacycle. ^gNiCl₂ (5 mol %)/Xphos (10 mol %) was used instead of the palladacycle. ^hCuI (5 mol %)/Xphos (10 mol %) was used instead of the palladacycle.

dioxane, toluene, and CH₃CN) were evaluated, and to our surprise, CH₃CN gave up to 96% yield (Table 1, entries 1–6). Some other bases (e.g., KOH, KF, KOAc, NaOH, and Na₂CO₃) were also employed, and only K₃PO₄ could lead to a moderate yield of 76% (Table 1, entries 7–12). Subsequently, different ligands such as PPh₃, 2-dicyclohexylphosphino-2'-(*N,N*-dimethylamino)biphenyl (Davephos), and 1,1'-bis-(diphenylphosphino)ferrocene (dppf) were also screened, and unfortunately, no products were observed (Table 1, entries 13–15). Performing reaction under air in place of nitrogen or at a lower oil bath temperature of 90 °C resulted in lower yields (Table 1, entries 16 and 17), which indicated that both the nitrogen atmosphere and the temperature play key roles in this reaction. Finally, some commercially available transition-metal sources such as PdCl₂, Pd(OAc)₂, Pd₂(dba)₃, NiCl₂, and CuI were also checked and did not display better catalytic activity (Table 1, entries 18–22).

With the optimized reaction conditions in hand, we then examined the substrate scope of aryl chlorides (Table 2).

Generally, electronic and *ortho*-steric effects had no significant influence on this coupling, and the reactions could tolerate various functional groups such as MeO, NO₂, MeOOC, CN, and CF₃, leading to the desired products in good to excellent yields. Aryl chlorides bearing one *ortho*-sterically hindered group could be coupled with 4-phenyl-2-methyl-3-butyne-2-ol, leading to excellent isolated yields (Table 2, **3ea**, **3fa**, **3ia**, and **3oa**). Notably, even the more sterically hindered 2-chloro-*m*-xylene gave a 99% isolated yield (Table 2, **3ga**). Moreover, the reactions of some heteroaryl chlorides also smoothly generated the desired products in excellent yields (Table 2, **3sa**, **3ta**, **3ua**, and **3va**).

Subsequently, experiments were directed at establishing the scope of aryl propargyl alcohols (Table 3). The results indicated that electronic and steric effects have no obvious influence. Notably, sterically hindered aryl propargyl alcohols possessing one or two *ortho*-sterically hindered groups could be efficiently converted into the corresponding products in moderate yields of 76%, 42%, and 58% (Table 3, **3hd**, **3he**, and **3hi**, respectively). In addition, electron-withdrawing groups on the aryl ring did not hamper the coupling significantly, and the corresponding products were also obtained in yields of 78% and 75% (Table 3, **3hh** and **3hj**, respectively).

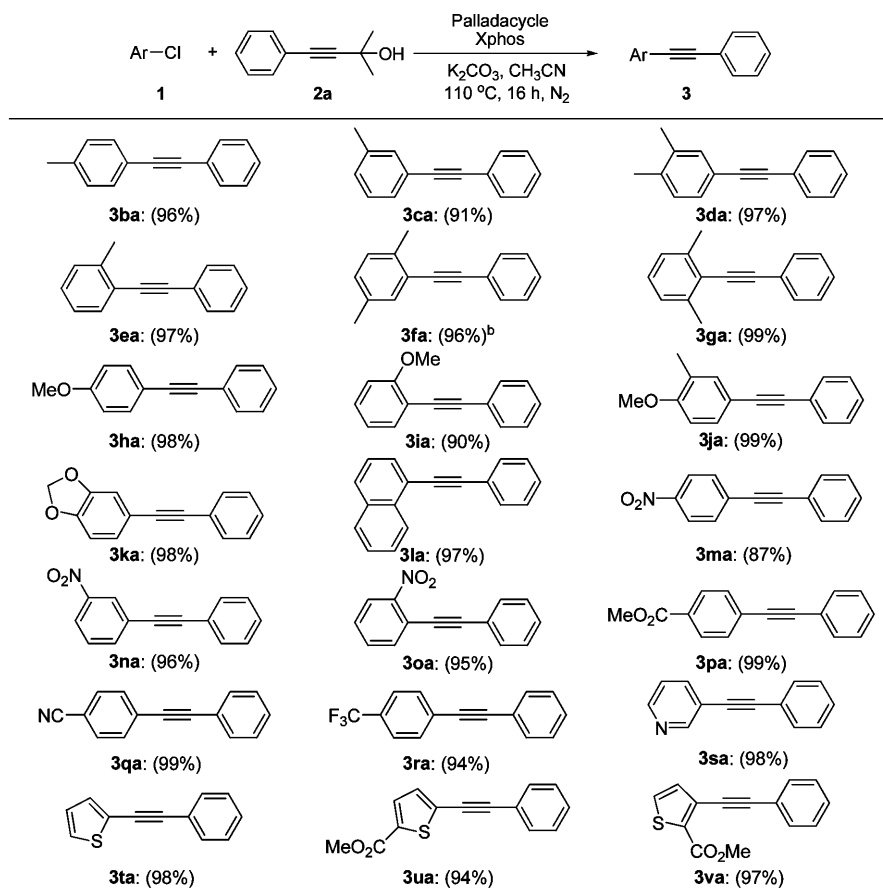
To indicate the advantage of the deacetonative coupling reaction over the traditional Sonogashira coupling, competitive reactions of 4-chloroanisole (**1h**) with 2-methyl-4-(4-nitrophenyl)-3-butyne-2-ol (**2j**) and 1-ethynyl-4-nitrobenzene (**4a**) were finally performed (Scheme 2). The reaction of **2j** generated the product **3hj** in a yield of 75%, while the coupling reaction of **4a** did not occur at all. These results indicate that the deacetonative coupling reaction can tolerate electron-poor alkynes well.

Our previous reports have indicated that the palladacycle just behaves as a reservoir of catalytically active Pd(0) species.^{6d,g} On the basis of these related reports, a possible mechanism is outlined in Scheme 3. Initially, a Pd(0) species is released from the palladacycle to form the catalytically active species Pd(0)L₂ (**I**) with the alkylphosphine ligand. Next, oxidative addition of the aryl chloride (**1**) to Pd(0)L₂ takes place to afford Pd(II) intermediate **II**. Subsequently, the reaction of intermediate **II** with the aryl propargyl alcohol occurs, forming the Pd(II) intermediate **III** via a deacetonative step in the presence of K₂CO₃. Finally, the desired product **3** and active catalyst Pd(0)L₂(**I**) are generated through reductive elimination of intermediate **III** to fulfill the catalytic cycle.

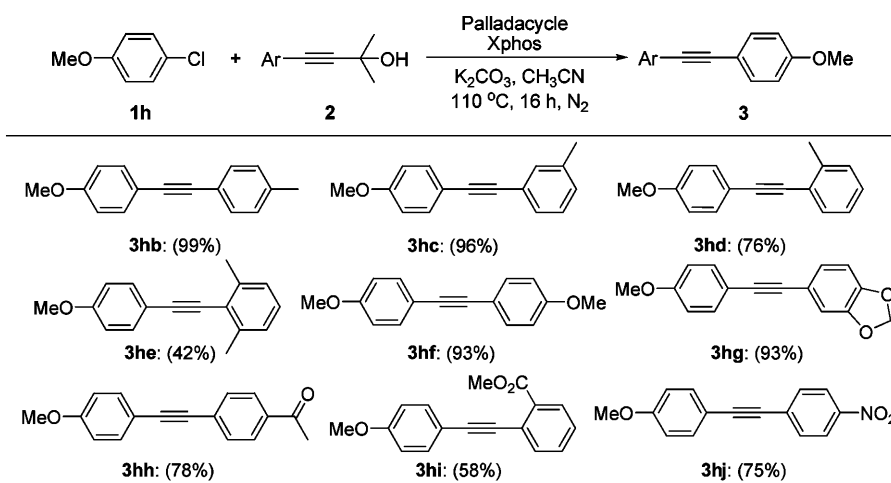
We have developed a general and efficient method for the deacetonative Sonogashira coupling of aryl propargyl alcohols with aryl chlorides using palladacycle/Xphos as the catalyst system, affording symmetrical and unsymmetrical diaryl acetylenes in mostly good to excellent yields. Notably, this deacetonative coupling is applicable to electron-poor, electron-neutral, and even inactive sterically hindered electron-rich aryl chlorides. Moreover, the reaction well tolerates electron-poor alkynes, for which the traditional Sonogashira reaction does not work.

EXPERIMENTAL SECTION

General Methods. ¹H and ¹³C NMR spectra were recorded with CDCl₃ as the solvent and TMS as an internal standard. The palladacyclic catalyst was prepared according to the reported literature procedure.^{6a} The other chemicals were bought from commercial sources and used as received, unless otherwise noted.

Table 2. Deacetonative Sonogashira Coupling of 4-Phenyl-2-methyl-3-butyne-2-ol with Aryl Chlorides^a

^aReaction conditions: aryl chloride (0.4 mmol), 4-phenyl-2-methyl-3-butyne-2-ol (0.5 mmol), palladacycle (1 mol %), Xphos (4 mol %), and K₂CO₃ (1.0 mmol) in CH₃CN (2.0 mL) at 110 °C (oil bath temperature) under a nitrogen atmosphere for 16 h. ^bFor 34 h.

Table 3. Deacetonative Sonogashira Coupling of Aryl Propargyl Alcohols with 4-Chloroanisole^a

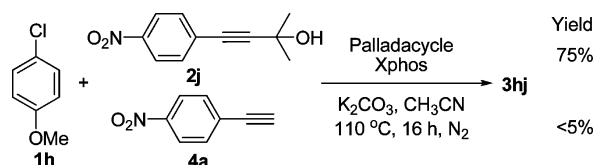
^aReaction conditions: 4-chloroanisole (0.4 mmol), 4-aryl-2-methyl-3-butyne-2-ol (0.5 mmol), palladacycle (1 mol %), Xphos (4 mol %), and K₂CO₃ (1.0 mmol) in CH₃CN (2.0 mL) at 110 °C (oil bath temperature) under a nitrogen atmosphere for 16 h.

Typical Procedure for the Palladacycle-Catalyzed Deacetonative Sonogashira Coupling of 4-Aryl-2-methyl-3-butyne-2-ols with Aryl Chlorides. Aryl chloride (0.4 mmol), 4-aryl-2-methyl-3-butyne-2-ol (0.5 mmol), K₂CO₃ (1.0 mmol), palladacycle (1 mol %), and Xphos (4 mol %) were dissolved in CH₃CN (2 mL) in a 10 mL vial under a nitrogen atmosphere. The reaction was carried out at 110 °C (oil bath temperature) for 16 h. After the reaction was finished, the mixture was filtered through a pad of Celite and extracted with brine

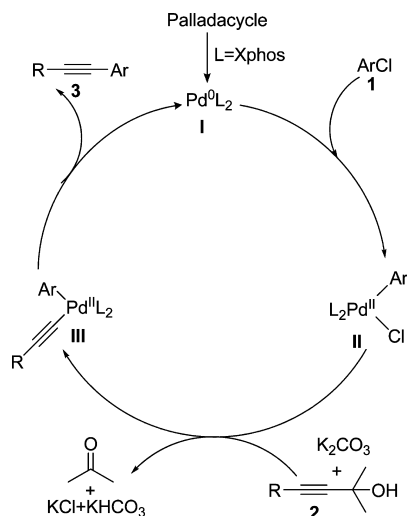
and ethyl acetate three times. The combined organic layers were dried over anhydrous Na₂SO₄ and filtered. After removal of the solvent in vacuum, the residue was purified by flash column chromatography on silica gel (hexane/ethyl acetate) to afford the pure product.

1,2-Diphenylethyne (3aa).⁷ White solid (68 mg, 96%), mp 61–62 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.29–7.37 (m, 6H), 7.50–7.56 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 88.4, 122.2, 127.3, 127.3, 130.6.

Scheme 2. Deacetonative Sonogashira Coupling versus Sonogashira Coupling



Scheme 3. Proposed Mechanism of Palladacycle-Catalyzed Deacetonative Sonogashira Reaction



1-Methyl-4-(phenylethynyl)benzene (3ba).⁷ White solid (74 mg, 96%), mp 69–71 °C; ¹H NMR (400 MHz, CDCl₃) δ 2.36 (s, 3H), 7.15 (d, *J* = 7.6 Hz, 2H), 7.28–7.37 (m, 3H), 7.42 (d, *J* = 7.2 Hz, 2H), 7.48–7.55 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 21.3, 88.5, 89.3, 119.9, 123.2, 127.8, 128.1, 128.9, 131.3, 131.3, 138.1.

3-Phenylethynyltoluene (3ca).^{4c} Colorless oil (70 mg, 91%); ¹H NMR (400 MHz, CDCl₃) δ 2.34 (s, 3H), 7.13 (d, *J* = 7.6 Hz, 1H), 7.23 (t, *J* = 7.6 Hz, 1H), 7.29–7.39 (m, 5H), 7.49–7.55 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 20.2, 88.0, 88.5, 122.0, 122.3, 127.2, 127.2, 127.3, 127.7, 128.2, 130.6, 131.2, 137.0.

1,2-Dimethyl-4-(phenylethynyl)benzene (3da).^{6g} White solid (80 mg, 97%), mp 61–62 °C; ¹H NMR (400 MHz, CDCl₃) δ 2.25 (s, 3H), 2.26 (s, 3H), 7.10 (d, *J* = 7.7 Hz, 1H), 7.27 (d, *J* = 7.2 Hz, 1H), 7.30–7.36 (m, 4H), 7.49–7.54 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 18.6, 18.8, 87.5, 88.7, 119.5, 122.6, 127.0, 127.3, 128.1, 128.7, 130.5, 131.6, 135.7, 136.2.

1-Methyl-2-(phenylethynyl)benzene (3ea).^{6g} Colorless oil (75 mg, 97%); ¹H NMR (400 MHz, CDCl₃) δ 2.54 (s, 3H), 7.14–7.21 (m, 1H), 7.23–7.24 (m, 2H), 7.31–7.38 (m, 3H), 7.49–7.59 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 21.0, 88.6, 93.6, 123.2, 123.8, 125.8, 128.4, 128.5, 128.6, 129.7, 131.7, 132.0, 140.4.

1,4-Dimethyl-2-(phenylethynyl)benzene (3fa).^{6g} Light-yellow solid (79 mg, 96%), mp 77–79 °C; ¹H NMR (400 MHz, CDCl₃) δ 2.31 (s, 3H), 2.47 (s, 3H), 7.04 (d, *J* = 7.7 Hz, 1H), 7.11 (d, *J* = 7.8 Hz, 1H), 7.30–7.37 (m, 4H), 7.50–7.55 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 20.2, 20.8, 88.6, 93.0, 122.8, 123.7, 128.1, 128.4, 129.2, 129.4, 131.5, 132.3, 135.1, 137.1.

1,3-Dimethyl-2-(phenylethynyl)benzene (3ga).^{6g} Colorless oil (82 mg, 99%); ¹H NMR (400 MHz, CDCl₃) δ 2.50 (s, 6H), 7.02–7.14 (m, 3H), 7.29–7.36 (m, 3H), 7.51–7.55 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 20.9, 87.0, 97.7, 122.8, 123.7, 126.5, 127.6, 127.9, 128.2, 131.2, 140.1.

1-Methoxy-4-(phenylethynyl)benzene (3ha).⁸ Light-yellow solid (82 mg, 98%), mp 55–56 °C; ¹H NMR (400 MHz, CDCl₃) δ 3.82 (s, 3H), 6.85–6.90 (m, 2H), 7.29–7.36 (m, 3H), 7.45–7.53 (m, 4H); ¹³C

NMR (100 MHz, CDCl₃) δ 54.3, 87.1, 88.4, 113.0, 114.4, 122.6, 126.9, 127.3, 130.4, 132.0, 158.6.

1-Methoxy-2-(phenylethynyl)benzene (3ia).^{4b} Colorless oil (75 mg, 90%); ¹H NMR (400 MHz, CDCl₃) δ 3.89 (s, 3H), 6.86–6.95 (m, 2H), 7.26–7.35 (m, 4H), 7.49 (dd, *J* = 1.7, 7.5 Hz, 1H), 7.53–7.58 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 55.9, 85.8, 93.5, 110.8, 112.5, 120.5, 123.6, 128.1, 128.3, 129.8, 131.7, 133.6, 156.0.

1-Methoxy-2-methyl-4-(phenylethynyl)benzene (3ja).⁸ Light-yellow solid (88 mg, 99%), mp 84–86 °C; ¹H NMR (400 MHz, CDCl₃) δ 2.20 (s, 3H), 3.83 (s, 3H), 6.77 (d, *J* = 8.4 Hz, 1H), 7.28–7.39 (m, 5H), 7.47–7.52 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 14.9, 54.1, 86.6, 88.5, 108.6, 113.6, 122.5, 125.6, 126.6, 127.1, 129.4, 130.2, 132.6, 156.7.

5-Phenylethynylbenzo[1,3]dioxole (3ka).⁹ White solid (87 mg, 98%), mp 98–100 °C; ¹H NMR (400 MHz, CDCl₃) δ 5.97 (s, 2H), 6.78 (d, *J* = 7.6 Hz, 1H), 6.98 (d, *J* = 1.2 Hz, 1H), 7.06 (dd, *J* = 1.2, 8.2 Hz, 1H), 7.29–7.36 (m, 3H), 7.47–7.52 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 87.5, 89.1, 101.1, 108.3, 111.3, 116.3, 123.1, 126.0, 127.8, 128.1, 131.2, 147.2, 147.7.

1-(Phenylethynyl)naphthalene (3la).^{4c} Colorless oil (89 mg, 97%); ¹H NMR (400 MHz, CDCl₃) δ 7.33–7.40 (m, 3H), 7.41–7.46 (m, 1H), 7.48–7.54 (m, 1H), 7.55–7.61 (m, 1H), 7.64 (dd, *J* = 1.6, 7.7 Hz, 2H), 7.75 (d, *J* = 6.8 Hz, 1H), 7.83 (t, *J* = 9.3 Hz, 2H), 8.45 (d, *J* = 8.3 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 86.5, 93.3, 119.9, 122.4, 124.3, 125.2, 125.4, 125.8, 127.3, 127.4, 127.4, 127.8, 129.4, 130.7, 132.2, 132.3.

1-Nitro-4-(phenylethynyl)benzene (3ma).¹⁰ Light-yellow solid (78 mg, 87%), mp 110–114 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.36–7.41 (m, 3H), 7.53–7.57 (m, 2H), 7.62–7.69 (m, 2H), 8.21 (d, *J* = 8.7 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 86.5, 93.7, 121.1, 122.6, 127.5, 128.3, 129.3, 130.8, 131.3, 146.0.

1-Nitro-3-(phenylethynyl)benzene (3na).^{6g} Light-yellow solid (86 mg, 96%), mp 68–69 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.36–7.40 (m, 3H), 7.52–7.58 (m, 3H), 7.80–7.84 (m, 1H), 8.15–8.19 (m, 1H), 8.37 (t, *J* = 1.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 86.8, 91.9, 122.1, 122.8, 125.1, 126.3, 128.5, 129.0, 129.3, 131.7, 137.2, 148.1.

1-Nitro-2-(phenylethynyl)benzene (3oa).¹¹ Colorless oil (85 mg, 95%); ¹H NMR (400 MHz, CDCl₃) δ 7.33–7.38 (m, 3H), 7.40–7.46 (m, 1H), 7.53–7.61 (m, 3H), 7.68 (dd, *J* = 1.2, 7.8 Hz, 1H), 8.04 (dd, *J* = 0.7, 8.3 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 84.8, 97.1, 118.7, 122.4, 124.7, 128.5, 128.6, 129.3, 132.0, 132.8, 134.6, 149.6.

Methyl 4-(phenylethynyl)benzoate (3pa).^{4b} Light-yellow solid (94 mg, 99%), mp 114–116 °C; ¹H NMR (400 MHz, CDCl₃) δ 3.93 (s, 3H), 7.37 (t, *J* = 3.2 Hz, 3H), 7.52–7.57 (m, 2H), 7.59 (d, *J* = 8.3 Hz, 2H), 8.02 (d, *J* = 8.3 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 52.0, 88.4, 92.1, 122.4, 127.8, 128.2, 128.5, 129.2, 129.3, 131.3, 131.5, 166.3.

4-(Phenylethynyl)benzonitrile (3qa).^{4c} Yellow solid (80 mg, 99%), mp 105–106 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.36–7.41 (m, 3H), 7.52–7.57 (m, 2H), 7.58–7.66 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 86.7, 92.8, 110.4, 117.5, 121.2, 127.2, 127.5, 128.1, 130.8, 131.0, 131.1.

1-(2-Phenylethynyl)-4-(trifluoromethyl)benzene (3ra).¹² White solid (93 mg, 94%), mp 103–105 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.34–7.41 (m, 3H), 7.52–7.57 (m, 2H), 7.58–7.66 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 86.9, 90.7, 121.5, 122.9 (q, *J* = 270.0 Hz), 124.3 (q, *J* = 3.8 Hz), 126.1, 127.4, 127.8, 128.9 (q, *J* = 34.0 Hz), 130.7, 130.8.

3-(Phenylethynyl)pyridine (3sa).^{4b} Colorless oil (70 mg, 98%); ¹H NMR (400 MHz, CDCl₃) δ 7.25–7.31 (m, 1H), 7.34–7.40 (m, 3H), 7.52–7.58 (m, 2H), 7.81 (d, *J* = 7.9 Hz, 1H), 8.55 (d, *J* = 4.7 Hz, 1H), 8.77 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 84.7, 91.4, 119.3, 121.3, 121.9, 127.3, 127.6, 130.5, 137.2, 147.4, 151.1.

2-(Phenylethynyl)thiophene (3ta).⁷ Colorless oil (72 mg, 98%); ¹H NMR (400 MHz, CDCl₃) δ 6.98–7.02 (m, 1H), 7.25–7.29 (m, 2H), 7.31–7.36 (m, 3H), 7.48–7.54 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 81.6, 92.0, 121.9, 122.2, 126.1, 126.2, 127.3, 127.4, 130.4, 130.9.

Methyl 5-(phenylethynyl)thiophene-2-carboxylate (3ua).¹³ Yellow solid (91 mg, 94%), mp 70–72 °C; ¹H NMR (CDCl₃) δ 3.89 (s, 3H), 7.28 (d, *J* = 3.8 Hz, 1H), 7.34–7.38 (m, 3H), 7.49–7.56 (m,

2H), 7.68 (d, $J = 3.8$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 52.3, 82.0, 95.7, 122.2, 128.5, 129.1, 130.1, 131.6, 132.2, 133.3, 133.8, 162.0.

Methyl 3-(Phenylethynyl)thiophene-2-carboxylate (3va).¹⁴ Colorless oil (94 mg, 97%); ^1H NMR (400 MHz, CDCl_3) δ 3.92 (s, 3H), 7.19 (d, $J = 6.3$ Hz, 1H), 7.32–7.37 (m, 3H), 7.44 (d, $J = 5.1$ Hz, 1H), 7.55–7.61 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 52.2, 84.0, 95.4, 123.0, 127.5, 128.4, 128.8, 130.5, 131.9, 132.1, 133.4, 161.9.

1-Methoxy-4-(4-tolylethynyl)benzene (3hb).¹⁰ Light-yellow solid (88 mg, 99%), mp 119–122 °C; ^1H NMR (400 MHz, CDCl_3) δ 2.36 (s, 3H), 3.82 (s, 3H), 6.87 (d, $J = 8.4$ Hz, 2H), 7.14 (d, $J = 7.6$ Hz, 2H), 7.40 (d, $J = 8.0$ Hz, 2H), 7.46 (d, $J = 8.0$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 20.5, 54.3, 87.2, 87.6, 113.0, 114.6, 119.5, 128.1, 130.3, 132.0, 137.0, 158.5.

1-((4-Methoxyphenyl)ethynyl)-3-methylbenzene (3hc).^{5c} Yellow solid (85 mg, 96%), mp 43–45 °C; ^1H NMR (400 MHz, CDCl_3) δ 2.33 (s, 3H), 3.79 (s, 3H), 6.83–6.88 (m, 2H), 7.11 (d, $J = 7.6$ Hz, 1H), 7.21 (t, $J = 7.6$ Hz, 1H), 7.29–7.35 (m, 2H), 7.43–7.48 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 21.0, 55.0, 88.0, 88.8, 113.8, 115.2, 123.2, 128.0, 128.3, 128.6, 131.8, 132.8, 137.7, 159.3.

1-((4-Methoxyphenyl)ethynyl)-2-methylbenzene (3hd).^{6g} Light-yellow solid (68 mg, 76%), mp 74–75 °C; ^1H NMR (400 MHz, CDCl_3) δ 2.50 (s, 3H), 3.80 (s, 3H), 6.87 (d, $J = 8.8$ Hz, 2H), 7.12–7.23 (m, 3H), 7.44–7.50 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 20.5, 55.1, 86.8, 93.1, 113.8, 115.4, 123.1, 125.3, 127.8, 129.2, 131.4, 132.7, 139.7, 159.3.

2-((4-Methoxyphenyl)ethynyl)-1,3-dimethylbenzene (3he).¹⁵ Yellow solid (41 mg, 42%), mp 70–71 °C; ^1H NMR (400 MHz, CDCl_3) δ 2.43 (s, 6H), 3.76 (s, 3H), 6.81 (d, $J = 8.7$ Hz, 2H), 6.94–7.08 (m, 3H), 7.40 (d, $J = 8.7$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 21.2, 55.4, 85.8, 97.8, 114.0, 116.0, 123.3, 126.7, 127.4, 132.8, 140.0, 159.5.

1,2-Bis(4-methoxyphenyl)ethyne (3hf).⁷ Light-yellow solid (89 mg, 93%), mp 143–145 °C; ^1H NMR (400 MHz, CDCl_3) δ 3.82 (s, 6H), 6.84–6.89 (m, 4H), 7.42–7.47 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 54.3, 86.9, 112.9, 114.7, 131.9, 158.4.

5-((4-Methoxyphenyl)ethynyl)benzo[1,3]dioxole (3hg).⁹ Yellow solid (94 mg, 93%), mp 123–125 °C; ^1H NMR (400 MHz, CDCl_3) δ 3.81 (s, 3H), 5.97 (s, 2H), 6.77 (d, $J = 8.0$ Hz, 1H), 6.86 (d, $J = 8.4$ Hz, 2H), 6.96 (d, $J = 0.9$ Hz, 1H), 7.00–7.05 (m, 1H), 7.44 (d, $J = 8.8$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 55.0, 87.5, 87.7, 101.0, 108.2, 111.2, 113.7, 115.2, 116.6, 125.8, 132.7, 147.2, 147.4, 159.2.

1-(4-((4-Methoxyphenyl)ethynyl)phenyl)ethanone (3hh).¹⁶ White solid (78 mg, 78%), mp 125–128 °C; ^1H NMR (400 MHz, CDCl_3) δ 2.61 (s, 3H), 3.84 (s, 3H), 6.90 (d, $J = 8.4$ Hz, 2H), 7.49 (d, $J = 8.8$ Hz, 2H), 7.58 (d, $J = 8.0$ Hz, 2H), 7.93 (d, $J = 8.0$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 26.4, 55.1, 87.3, 92.7, 113.9, 114.4, 128.0, 128.4, 131.2, 133.0, 135.6, 159.8, 197.1.

Methyl 2-((4-Methoxyphenyl)ethynyl)benzoate (3hi).¹⁷ Colorless oil (62 mg, 58%); ^1H NMR (CDCl_3 , 400 MHz) δ 3.76 (s, 3H), 3.89 (s, 3H), 6.82 (d, $J = 8.8$ Hz, 2H), 7.24–7.32 (m, 1H), 7.35–7.49 (m, 3H), 7.55 (d, $J = 7.5$ Hz, 1H), 7.89 (d, $J = 7.2$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 52.2, 55.3, 87.1, 94.6, 114.0, 115.4, 124.1, 127.5, 130.5, 131.6, 131.7, 133.3, 133.8, 159.9, 166.8.

1-Methoxy-4-((4-nitrophenyl)ethynyl)benzene (3hj).¹⁰ Yellow solid (76 mg, 75%), mp 110–111 °C; ^1H NMR (400 MHz, CDCl_3) δ 3.85 (s, 3H), 6.91 (d, $J = 8.8$ Hz, 2H), 7.50 (d, $J = 8.8$ Hz, 2H), 7.63 (d, $J = 8.4$ Hz, 2H), 8.20 (d, $J = 8.8$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 28.7, 54.3, 85.6, 94.1, 113.2, 122.6, 129.7, 131.0, 132.4, 145.7, 159.4.

■ ASSOCIATED CONTENT

Supporting Information

Copies of NMR spectra for all of the compounds. 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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■ REFERENCES

- (1) For selected reviews, see: (a) Sonogashira, K. *J. Organomet. Chem.* **2002**, 653, 46. (b) Negishi, E.; Anastasia, L. *Chem. Rev.* **2003**, 103, 1979. (c) Tykwinski, R. R. *Angew. Chem., Int. Ed.* **2003**, 42, 1566. (d) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem., Int. Ed.* **2005**, 44, 4442. (e) Chinchilla, R.; Nájera, C. *Chem. Rev.* **2007**, 107, 874. (f) Doucet, H.; Hierso, J.-C. *Angew. Chem., Int. Ed.* **2007**, 46, 834. (g) Plenio, H. *Angew. Chem., Int. Ed.* **2008**, 47, 6954. (h) Chinchilla, R.; Nájera, C. *Chem. Soc. Rev.* **2011**, 40, 5084.
- (2) For representative papers on the palladium-catalyzed Sonogashira reaction of aryl chlorides, see: (a) Eberhard, M. R.; Wang, Z.; Jensen, C. M. *Chem. Commun.* **2002**, 818. (b) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, 41, 4176. (c) Choudary, B. M.; Madhi, S.; Chowdari, N. S.; Kantam, M. L.; Sreedhar, B. *J. Am. Chem. Soc.* **2002**, 124, 14127. (d) Gelman, D.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2003**, 42, 5993. (e) Kollhofer, A.; Pullmann, T.; Plenio, H. *Angew. Chem., Int. Ed.* **2003**, 42, 1056. (f) Komáromi, A.; Novák, Z. *Chem. Commun.* **2008**, 4968. (g) Anderson, K. W.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2005**, 44, 6173.
- (3) (a) Park, J.; Park, E.; Kim, A.; Park, S.-A.; Lee, Y.; Chi, K. W.; Jung, Y. H.; Kim, I. S. *J. Org. Chem.* **2011**, 76, 2214. (b) Kim, Y.; Park, A.; Park, K.; Lee, S. *Tetrahedron Lett.* **2011**, 52, 1766.
- (4) For representative papers on decarboxylative coupling, see: (a) Moon, J.; Jeong, M.; Nam, H.; Ju, J.; Moon, J. H.; Jung, H. M.; Lee, S. *Org. Lett.* **2008**, 10, 945. (b) Moon, J.; Jang, M.; Lee, S. *J. Org. Chem.* **2009**, 74, 1403. (c) Kim, H.; Lee, P. H. *Adv. Synth. Catal.* **2009**, 351, 2827. (d) Zhao, D.-B.; Gao, C.; Su, X.-Y.; He, Y.-Q.; You, J.-S.; Xue, Y. *Chem. Commun.* **2010**, 46, 9049. (e) Li, T.-Y.; Qu, X.-M.; Zhu, Y.; Sun, P.; Yang, H.-L.; Shan, Y.-Q.; Zhang, H.-X.; Liu, D.-F.; Zhang, X.; Mao, J.-C. *Adv. Synth. Catal.* **2011**, 353, 2731. (f) Reddy, P. V.; Srinivas, P.; Annapurna, M.; Bhargava, S.; Wagler, J.; Mirzadeh, N.; Kantam, M. L. *Adv. Synth. Catal.* **2013**, 355, 705.
- (5) For deacetonative Sonogashira coupling, see: (a) Chow, H.-F.; Wan, C.-W.; Low, K.-H.; Yeung, Y.-Y. *J. Org. Chem.* **2001**, 66, 1910. (b) Novák, Z.; Nemes, P.; Kotschy, A. *Org. Lett.* **2004**, 6, 4917. (c) Shirakawa, E.; Kitabata, T.; Otsuka, H.; Tsuchimoto, T. *Tetrahedron* **2005**, 61, 9878. (d) Yi, C. Y.; Hua, R. M.; Zeng, H. X.; Huang, Q. F. *Adv. Synth. Catal.* **2007**, 349, 1738. (e) Csékei, M.; Novák, Z.; Kotschy, A. *Tetrahedron* **2008**, 64, 975. (f) Hung, T.-T.; Huang, C.-M.; Tsai, F.-Y. *ChemCatChem* **2012**, 4, 540.
- (6) (a) Huo, S.-Q.; Wu, Y.-J.; Du, C.-X.; Zhu, Y.; Yuan, H.-Z.; Mao, X.-A. *J. Organomet. Chem.* **1994**, 483, 139. (b) Yang, F.; Cui, X.-L.; Li, Y.-N.; Zhang, J.-L.; Ren, G.-R.; Wu, Y.-J. *Tetrahedron* **2007**, 63, 1963. (c) Yang, F.; Wu, Y.-J. *Eur. J. Org. Chem.* **2007**, 3476. (d) Ren, G.-R.; Cui, X.-L.; Yang, E.-B.; Yang, F.; Wu, Y.-J. *Tetrahedron* **2010**, 66, 4022. (e) Xu, K.; Yang, F.; Zhang, G.-D.; Wu, Y.-J. *Green Chem.* **2013**, 15, 1055. (f) Xu, K.; Hu, H.; Yang, F.; Wu, Y.-J. *Eur. J. Org. Chem.* **2013**, 319. (g) Li, X.; Yang, F.; Wu, Y.-J. *J. Org. Chem.* **2013**, 78, 4543.
- (7) Park, K.; Bae, G.; Moon, J.; Choe, J.; Song, K. H.; Lee, S. *J. Org. Chem.* **2010**, 75, 6244.
- (8) Wan, S.; Wang, S. R.; Lu, W. J. *J. Org. Chem.* **2006**, 71, 4349.
- (9) Castagnolo, D.; Botta, M. *Eur. J. Org. Chem.* **2010**, 3224.
- (10) Rao, M. L. N.; Jadhav, D. N.; Dasgupta, P. *Org. Lett.* **2010**, 12, 2048.
- (11) Yamane, Y.; Liu, X. H.; Hamasaki, A.; Ishida, T.; Haruta, M.; Yokoyama, T.; Tokunaga, M. *Org. Lett.* **2009**, 11, 5162.
- (12) Truong, T.; Daugulis, O. *Org. Lett.* **2011**, 13, 4172.
- (13) D'Auria, M.; Piancatelli, G.; Ferri, T. *J. Org. Chem.* **1990**, 55, 4019.

- (14) Iaroshenko, V. O.; Ali, S.; Babar, T. M.; Abbasi, M. S. A.; Sosnovskikh, V. Y.; Villinger, A.; Tolmachev, A.; Langer, P. *Tetrahedron* **2013**, *69*, 3167.
- (15) Maji, M. S.; Murarka, S.; Studer, A. *Org. Lett.* **2010**, *12*, 3878.
- (16) Liang, B.; Dai, M. J.; Chen, J. H.; Yang, Z. *J. Org. Chem.* **2005**, *70*, 391.
- (17) Shi, Y. L.; Roth, K. E.; Ramgren, S. D.; Blum, S. A. *J. Am. Chem. Soc.* **2009**, *131*, 18022.