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Palladium-Catalyzed Decarboxylative Coupling Reactions of Propiolic Acid Derivatives and Arylsulfonyl Hydrazide

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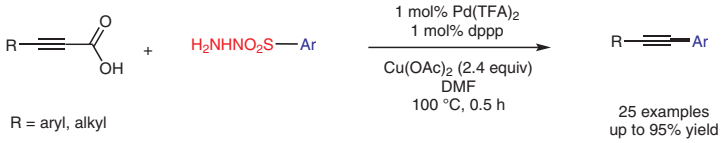

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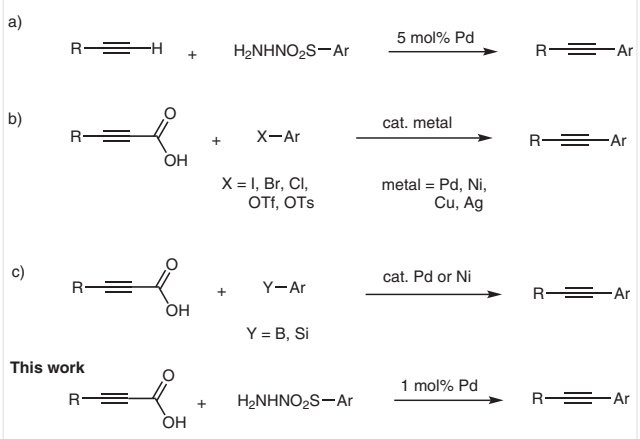
Abstract Arylsulfonyl hydrazides were employed as coupling partners for the decarboxylative coupling reaction of propiolic acid derivatives. When the reaction was conducted using $Pd(TFA)_2$ (1.0 mol%), dppp (1.0 mol%), and $Cu(OAc)_2$ (2.4 equiv) in DMF at 100 °C for 0.5 hour, the desired coupled products were formed in moderate to good yields. The reaction showed good tolerance toward functional groups such as ester, ketone, cyano, nitro, chloro, and bromo groups.

Keywords decarboxylative coupling, propiolic acid, arylsulfonyl hydrazide, palladium, arylalkyne

Palladium-catalyzed cross-coupling reactions are among the most straightforward tools for the construction of carbon–carbon or carbon–heteroatom bonds.[1] Palladium is known to activate a nucleophile or/and an electrophile to be coupled with both of them. Among the wide variety of coupling partners that can serve as an electrophile, organic halides such as iodides, bromides, and chlorides are the most frequently employed. These electrophiles are activated by palladium to produce the corresponding organopalladium complex, which can further react with a nucleophile. This is an oxidative step and is generally known to be a rate-determining step.[2] As an alternative method, oxidative coupling has been developed, in which the coupling partner is substituted with a palladium ligand to provide the organopalladium complex. A number of coupling partners have been developed in this type of reactions.[3]

Sonogashira coupling, an important cross-coupling reaction carried out using a palladium catalyst, is a very useful tool for constructing sp-carbon and sp^2-carbon bonds.[4] Terminal alkynes have been coupled with aryl halides to provide arylalkynes, which are important building blocks in agricultural, pharmaceutical, and materials sciences.[5] In addition, a variety of coupling partners have been developed.

Recently, Dong and Zhou's group employed arylsulfonyl hydrazides in palladium-catalyzed coupling reactions with terminal alkynes for the synthesis of arylalkyne derivatives (Scheme 1, a).[6] They demonstrated that the Sonogashira-type coupling reaction with arylsulfonyl hydrazide is acid- and base-free and shows good tolerance toward the bromide group. However, this reaction requires a high palladium catalyst loading.



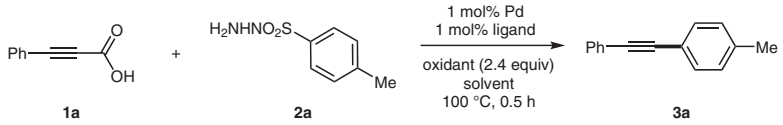
Scheme 1 Synthesis of arylalkynes using coupling reactions

Decarboxylative coupling of alkynoic acids has received much attention as an alternative tool for the synthesis of arylalkynes.[7] The use of an arylalkynoic acid has several advantages such as simple preparation and easy handling.[8] Since our first report in this regard, a variety of coupling partners, including aryl halides, have been developed for the decarboxylative coupling of alkynoic acids (Scheme 1,

b).[9] Recently, we developed oxidative decarboxylative coupling reactions using arylboronic acid and arylsiloxane (Scheme 1, c).[10]

As part of our continuous efforts to develop decarboxylative coupling reactions with arylalkynoic acids, we became interested in using arylsulfonyl hydrazides as coupling partners. Herein we report the decarboxylative coupling reaction of propiolic acid derivatives with arylsulfonyl hydrazides in the presence of a palladium catalyst.

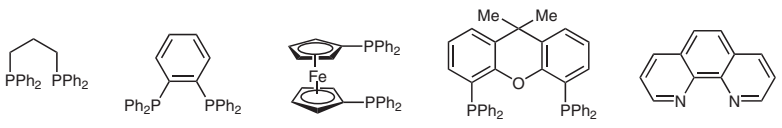
Table 1 Optimization of Decarboxylative Coupling Reaction with **1a** and **2a**[a]



1a **2a** **3a**

Entry	Pd (mol %)	Ligand (mol%)	Oxidant	Solvent	**3a** Yield (%)[b]
1[c]	$Pd(OAc)_2$	dppp	$Cu(OAc)_2·H_2O$	DMF	68
2	$Pd(OAc)_2$	dppp	$Cu(OAc)_2·H_2O$	DMF	65
3	$Pd(OAc)_2$	dppbz	$Cu(OAc)_2·H_2O$	DMF	61
4	$Pd(OAc)_2$	dppf	$Cu(OAc)_2·H_2O$	DMF	58
5	$Pd(OAc)_2$	Xantphos	$Cu(OAc)_2·H_2O$	DMF	59
6	$Pd(OAc)_2$	1,10-Phen	$Cu(OAc)_2·H_2O$	DMF	42
7	$Pd(dba)_2$	dppp	$Cu(OAc)_2·H_2O$	DMF	74
8	$PdCl_2$	dppp	$Cu(OAc)_2·H_2O$	DMF	72
9	$Pd(TFA)_2$	dppp	$Cu(OAc)_2·H_2O$	DMF	90
10	$Pd(TFA)_2$	dppbz	$Cu(OAc)_2·H_2O$	DMF	83
11	$Pd(TFA)_2$	dppf	$Cu(OAc)_2·H_2O$	DMF	72
12	$Pd(TFA)_2$	Xantphos	$Cu(OAc)_2·H_2O$	DMF	87
13	$Pd(TFA)_2$	dppp	$Cu(acac)_2$	DMF	trace
14	$Pd(TFA)_2$	dppp	$Cu(OTf)_2$	DMF	5
15	$Pd(TFA)_2$	dppp	CuO	DMF	19
16	$Pd(TFA)_2$	dppp	CuS	DMF	11
17	$Pd(TFA)_2$	dppp	$CuBr_2$	DMF	trace
18	$Pd(TFA)_2$	dppp	$CuCl_2$	DMF	trace
19	$Pd(TFA)_2$	dppp	$Cu(OAc)_2·H_2O$	DMSO	38
20	$Pd(TFA)_2$	dppp	$Cu(OAc)_2·H_2O$	diglyme	12
21	$Pd(TFA)_2$	dppp	$Cu(OAc)_2·H_2O$	toluene	14
22[d]	$Pd(TFA)_2$	dppp	$Cu(OAc)_2·H_2O$	DMF	70
23[e]	$Pd(TFA)_2$	dppp	$Cu(OAc)_2·H_2O$	DMF	40

Structures of the ligands:

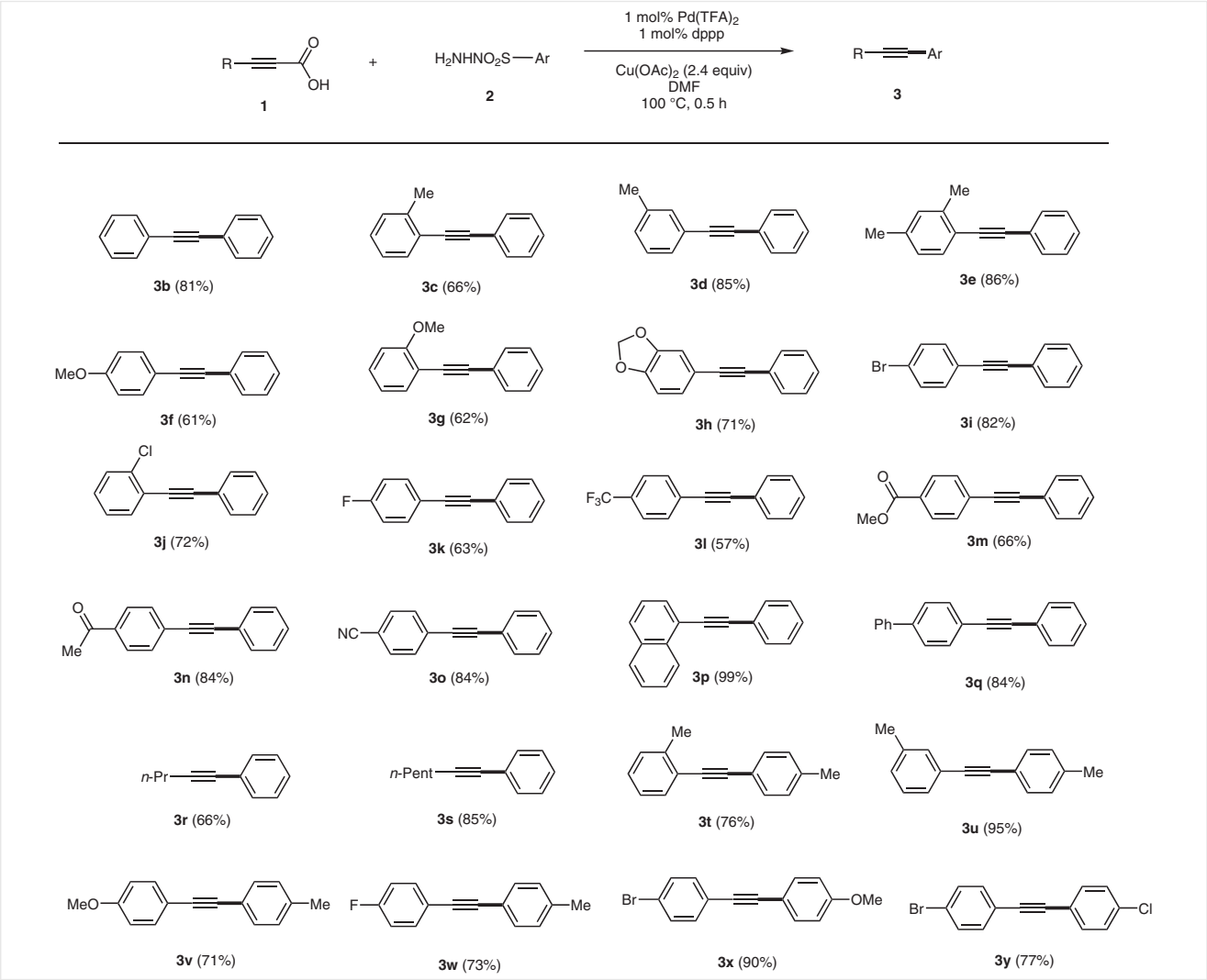


dppp dppbz dppf Xantphos 1,10-Phen

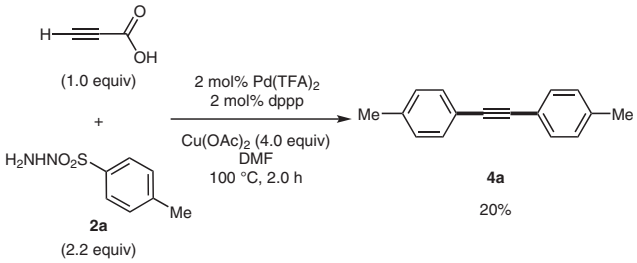
[a] Reaction conditions: **1a** (0.33 mmol), **2a** (0.3 mmol), Pd (0.003 mmol), ligand (0.003 mmol), and oxidant (0.72 mmol) were allowed to react in a solvent (1.0 mL) at 100 °C for 0.5 h.
[b] Yield was determined by gas chromatography with an internal standard.
[c] $Pd(OAc)_2$ (0.015 mmol) and dppp (0.015 mmol) were used.
[d] Reaction temperature: 80 °C; time: 2 h.
[e] Reaction temperature: 50 °C; time: 6 h.

First, phenylpropiolic acid (**1a**) and *p*-tolylsulfonyl hydrazide (**2a**) were chosen as standard substrates for the coupling reaction and allowed to react under various conditions. Under the optimized conditions reported for the coupling of terminal alkynes, the desired product **3a** was formed in 68% yield. Surprisingly, the product yield was 65% when 1.0 mol% of palladium and the ligand was used (Table 1, entry 2). Among the tested ligands, 1,3-bis(diphenylphosphino)propane (dppp) gave the highest yield (entries 2–6). Then, using dppp as the ligand, we tested different palladium sources such as $PdCl_2$, $Pd(TFA)_2$, and $Pd(dba)_2$ (entries 7–9), and found that the combination of $Pd(TFA)_2$ and dppp provided the highest yield of 90% (entry 9). The combination of $Pd(TFA)_2$ and other ligands such as dppbz, dppf, and Xantphos afforded the desired product in good yields, although the yields were lower than those obtained with $Pd(TFA)_2$ and dppp (entries 10–12). A number of oxidants were tested instead of $Cu(OAc)_2$, but they did not give satisfactory results (entries 13–18). The reaction gave much lower yields when carried out in solvents such as DMSO, diglyme, and toluene as compared to that in DMF (entries 19–21). Decreasing the reaction temperature to 80 °C and 50 °C lowered the product yield to 70% and 40%, respectively (entries 22 and 23).

The optimized conditions were as follows: arylpropiolic acid (1.1 equiv), arylsulfonyl hydrazide (1.0 equiv), $Pd(TFA)_2$ (1.0 mol%), dppp (1.0 mol%), and $Cu(OAc)_2{\cdot}H_2O$ (2.4 equiv) were allowed to react in DMF at 100 °C for 0.5 hour. To evaluate the reaction efficiency under these optimized conditions, a variety of substituted arylpropiolic acids were allowed to react with phenylsulfonyl hydrazide. As shown in Scheme 2, phenylpropiolic acid reacted with phenylsulfonyl hydrazide to give the desired product **3b** in 81% yield. Alkyl-substituted arylpropiolic acids afforded the coupled



Scheme 2 Synthesis of arylalkynes. *Reagents and conditions*: **1** (3.3 mmol), **2** (3.0 mmol), $Pd(TFA)_2$ (0.03 mmol), dppb (0.03 mmol), and $Cu(OAc)_2$ (7.2 mmol) were allowed to react in DMF (10 mL) at 100 °C for 0.5 h.



Scheme 3 Synthesis of symmetrical diarylalkyne

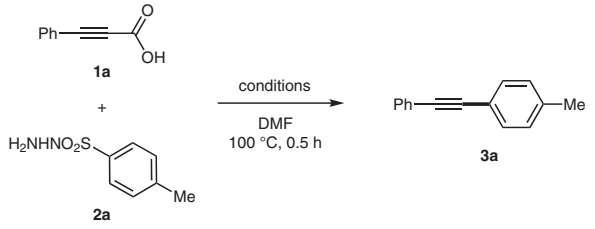
products **3c**, **3d**, and **3e** in 66%, 85%, and 86% yield, respectively. Alkoxide-substituted arylpropiolic acids provided the desired products **3f**, **3g**, and **3h** in 61%, 62%, and 71% yield, respectively. Bromo-, chloro-, fluoro-, and trifluoromethyl-substituted arylpropiolic acids furnished **3i**, **3j**, **3k**, and **3l** in good yields. Arylpropiolic acids bearing ester, ketone, and cyano groups on the phenyl ring coupled with phenylsulfonyl hydrazide to give the corresponding products **3m**, **3n**, and **3o** in good yields. 3-(Naphthalen-1-yl)- and 3-[(1,1′-biphenyl)-4-yl]propiolic acids showed good yields in the formation of **3p** and **3q**. Alkyl-substituted propiolic acids such as hexynoic and octynoic acids provided **3r** and **3s** in 66% and 85% yield, respectively.

Next, we investigated the use of substituted arylsulfonyl hydrazides in the decarboxylative coupling reactions. *p*-Tolylsulfonyl hydrazide coupled with substituted arylpropiolic acids to give the desired products in good yields. When 3-(4-bromophenyl)propiolic acid was allowed to react with substituted arylsulfonyl hydrazide, the desired products **3x**, and **3y** were formed in good yields. These bromo-substituted products could be employed as starting materials for further coupling reactions.

We then attempted to apply this reaction system for the synthesis of symmetrical diarylalkyne. When *p*-tolysulfonyl hydrazide (2.2 equiv) and propiolic acid (1.0 equiv) were allowed to react under the modified optimal conditions, symmetrical diarylalkyne **4a** was formed in 20% yield, as shown in Scheme 3.

To study the role of palladium, ligand, and $Cu(OAc)_2$ in this coupling reaction, the reaction was conducted in the absence of one of these entities. As shown in Table 2, the desired product was not formed in any of the reactions (Table 2, entries 1–4). These results supported that both palladium and copper are important in this coupling reaction and that copper acts as both the oxidant and the coupling reagent. When using 0.6 equivalent and 1.2 equivalents of $Cu(OAc)_2$, the desired product was formed in 5% and 10% yield, respectively (entries 5 and 6). It was found that 2.4 equivalents of $Cu(OAc)_2$ was required to obtain the desired product in good yields.

Table 2 Role of Palladium and Copper[a]

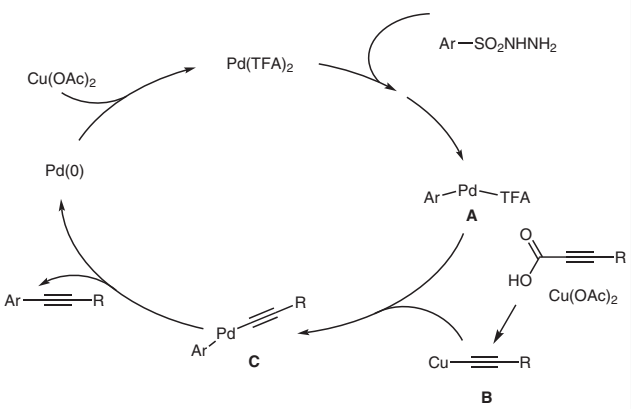


Entry	$Pd(TFA)_2$	dppp	$Cu(OAc)_2·H_2O$	**3a** Yield (%)[b]
1	–	–	–	0
2	1.0 mol%	1.0 mol%	–	0
3	–	–	2.4 equiv	0
4	–	1.0 mol%	2.4 equiv	0
5	1.0 mol%	1.0 mol%	0.6 equiv	5
6	1.0 mol%	1.0 mol%	1.2 equiv	10

[a] Reaction conditions: **1a** (0.3 mmol) and **2a** (0.3 mmol) were reacted at 100 °C for 0.5 h under the described conditions.
[b] Yield was determined by gas chromatography with an internal standard.

Based on a previous report and the experimental results in the present study, we propose a plausible mechanism for this coupling reaction, as shown in Scheme 4. Arylpalladium(II) complex **A** may be formed via the reaction pathway proposed by Dong and Zhou's group. The arylpropiolic acid reacts with $Cu(OAc)_2$ to give alkynylcopper complex **B** through decarboxylation. Complex **B** reacts with the arylpalladium complex to provide arylalkynylpalladium complex **C** via transmetalation, which undergoes reductive elimination to afford the desired coupling product. Finally, Pd(0) is oxidized by $Cu(OAc)_2$ to give the Pd(II) active catalytic species.

In summary, we have developed decarboxylative coupling reactions of propiolic acid derivatives with arylsulfonyl hydrazide using a palladium catalyst. We found that $Cu(OAc)_2$ played the role of a an oxidant and a coupling reagent. As opposed to previous methods in which a terminal alkyne was used as a coupling partner, the present method using propiolic acid derivatives required only 1 mol%



Scheme 4 Proposed mechanism

$Pd(TFA)_2$ and gave good yields in most cases. This methodology showed good tolerance toward functional groups such as ester, ketone, cyano, nitro, bromo, and chloro groups. In addition, the reaction with propiolic acid afforded a symmetrical diarylalkyne.

General Information

All reagents and solvents were purchased and used without further purification. Analytical thin layer chromatography (TLC) was performed on Merck pre-coated silica gel 60 F_{254} plates. The TLC plates were visualized by shortwave (254 nm) or long-wave (360 nm) UV light. Flash chromatography on silica gel (230–400 mesh) was performed. ^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) was recorded in $CDCl_3$ on VARIAN VnmrJ.

Decarboxylative Coupling Reaction of Propiolic Acid Derivatives and Arylsulfonyl Hydrazide; General Procedure

A 5 mL vial equipped with a magnetic stir bar was charged with arylsulfonyl hydrazide **2** (3.0 mmol, 1.0 equiv), arylpropiolic acid **1** (3.3 mmol, 1.1 equiv), $Pd(TFA)_2$ (10.5 mg, 0.03 mmol, 1 mol%), dppp (12 mg, 0.03 mmol, 1 mol%), $Cu(OAC)_2{\cdot}H_2O$ (1437.5 mg, 7.2 mmol, 2.4 equiv), and DMF (10 mL). The reaction mixture was heated at 100 °C for 0.5 h, then cooled to r.t., and quenched with H_2O. The crude product was extracted with EtOAc, and the combined organic layers were dried (anhyd $MgSO_4$), and concentrated under vacuum. The desired product was isolated by silica gel column chromatography using hexane/EtOAc as the eluent.

1-Methyl-4-(phenylethynyl)benzene (3a)[9d]

3-Phenylpropiolic acid (**1a**; 482.3 mg, 3.3 mmol) and 4-methylbenzenesulfonyl hydrazide (**2a**; 558.7 mg, 3.0 mmol) afforded **3a** (519.1 mg, 2.7 mmol, 90%); white solid; mp 54–56 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.53–7.51 (m, 2 H), 7.44–7.42 (m, 2 H), 7.36–7.31 (m, 3 H), 7.17–7.15 (m, 3 H), 2.37 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 138.4, 131.5, 131.5, 129.1, 128.3, 128.1, 123.5, 120.2, 89.5, 88.7, 21.5.

MS (EI): m/z = 192 (M^+).

1,2-Diphenylethyne (3b)[10c]

3-Phenylpropiolic acid (**1a**; 482.3 mg, 3.3 mmol) and benzenesulfonyl hydrazide (**2b**; 516.6 mg, 3.0 mmol) afforded **3b** (433.1 mg, 2.43 mmol, 81%); white solid; mp 59–61 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55–7.53 (m, 4 H), 7.37–7.33 (m, 6 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 131.6, 128.3, 128.2, 123.2, 89.3.

MS (EI): m/z = 178 (M^+).

1-Methyl-2-(phenylethynyl)benzene (3c)[9d]

3-(*o*-Tolyl)propiolic acid (**1b**; 528.6 mg, 3.3 mmol) and **2b** (516.6 mg, 3.0 mmol) afforded **3c** (380.7 mg, 1.98 mmol, 66%); colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55–7.52 (m, 2 H), 7.50 (d, J = 7.2 Hz, 1 H), 7.36–7.31 (m, 3 H), 7.23–7.22 (m, 2 H), 7.18–7.15 (m, 1 H), 2.52 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 140.2, 131.9, 131.5, 129.5, 128.4, 128.2, 125.6, 123.6, 123.0, 93.4, 88.4, 20.8.

MS (EI): m/z = 192 (M^+).

1-Methyl-3-(phenylethynyl)benzene (3d)[10c]

3-(*m*-Tolyl)propiolic acid (**1c**; 528.6 mg, 3.3 mmol) and **2b** (516.6 mg, 3.0 mmol) afforded **3d** (490.3 mg, 2.55 mmol, 85%); colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.53–7.51 (m, 2 H), 7.34–7.32 (m, 5 H), 7.23 (t, J = 7.6 Hz, 1 H), 7.14 (d, J = 7.6 Hz, 1 H), 2.35 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 138.0, 132.2, 131.6, 129.2, 128.7, 128.4, 128.3, 128.2, 123.4, 123.1, 89.6, 89.1, 21.3

MS (EI): m/z = 192 (M^+).

2,4-Dimethyl-1-(phenylethynyl)benzene (3e)[10c]

3-(2,4-Dimethylphenyl)propiolic acid (**1d**; 574.9 mg, 3.3 mmol) and **2b** (516.6 mg, 3.0 mmol) afforded **3e** (532.2 mg, 2.58 mmol, 86%); pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.53–7.51 (m, 2 H), 7.39 (d, J = 7.8 Hz, 1 H), 7.35–7.30 (m, 3 H), 7.04 (s, 1 H), 6.97 (d, J = 7.8 Hz, 1 H), 2.48 (s, 3 H), 2.32 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 140.0, 138.4, 131.8, 131.5, 130.4, 128.4, 128.0, 126.4, 123.8, 120.0, 92.7, 88.6, 21.5, 20.7.

MS (EI): m/z = 206 (M^+).

1-Methoxy-4-(phenylethynyl)benzene (3f)[10c]

3-(4-Methoxyphenyl)propiolic acid (**1e**; 581.4 mg, 3.3 mmol) and **2b** (516.6 mg, 3.0 mmol) afforded **3f** (381.1 mg, 1.83 mmol, 61%); light yellow solid; mp 151–153 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.51 (dt, J = 8.3, 2.2 Hz, 2 H), 7.49–7.46 (m, 2 H), 7.35–7.30 (m, 3 H), 6.89–6.86 (m, 2 H), 3.82 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 159.6, 133.1, 131.5, 128.3, 127.9, 123.6, 115.4, 114.0, 89.4, 88.1, 55.3.

MS (EI): m/z = 208 (M^+).

1-Methoxy-2-(phenylethynyl)benzene (3g)[10c]

3-(2-Methoxyphenyl)propiolic acid (**1f**; 581.4 mg, 3.3 mmol) and **2b** (516.6 mg, 3.0 mmol) afforded **3g** (387.4 mg, 1.86 mmol, 62%); pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.57–7.55 (m, 2 H), 7.50 (dd, J = 7.6, 1.7 Hz, 1 H), 7.35–7.28 (m, 4 H), 6.93 (t, J = 7.5 Hz, 1 H), 6.89 (d, J = 8.4 Hz, 1 H), 3.90 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 159.9, 133.6, 131.7, 129.8, 128.3, 128.1, 123.6, 120.5, 112.4, 110.7, 93.5, 85.8, 55.9.

MS (EI): *m*/*z* = 208 (M^+).

5-(Phenylethynyl)benzo[*d*][1,3]dioxole (3h)[10c]

3-(Benzo[*d*][1,3]dioxol-5-yl)propiolic acid (**1g**; 627.5 mg, 3.3 mmol) and **2b** (516.6 mg, 3.0 mmol) afforded **3h** (473.4 mg, 2.13 mmol, 71%); white solid; mp 105–108 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.52–7.50 (m, 2 H), 7.34–7.33 (m, 3 H), 7.07 (dd, *J* = 8.0, 1.6 Hz, 1 H), 6.99–6.98 (m, 1 H), 6.80–6.79 (m, 1 H), 6.00 (s, 2 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 147.9, 147.4, 131.5, 128.3, 128.1, 126.3, 123.3, 116.5, 111.5, 108.5, 101.3, 89.3, 87.8.

MS (EI): *m*/*z* = 222 (M^+).

1-Bromo-4-(phenylethynyl)benzene (3i)[11]

3-(4-Bromophenyl)propiolic acid (**1h**; 742.6 mg, 3.3 mmol) and **2b** (516.6 mg, 3.0 mmol) afforded **3i** (632.5 mg, 2.46 mmol, 82%); white solid; mp 82–83 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.53–7.51 (m, 2 H), 7.49–7.47 (m, 2 H), 7.40–7.38 (m, 2 H), 7.37–7.34 (m, 2 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 133.8, 133.0, 131.8, 131.6, 131.6, 128.5, 128.4, 122.9, 122.4, 122.2, 90.5, 88.3.

MS (EI): *m*/*z* = 256 (M^+).

1-Chloro-2-(phenylethynyl)benzene (3j)[12]

3-(4-Bromophenyl)propiolic acid (**1i**; 596.0 mg, 3.3 mmol) and **2b** (516.6 mg, 3.0 mmol) afforded **3j** (459.4 mg, 2.16 mmol, 72%); colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55–7.53 (m, 3 H), 7.42 (dt, *J* = 7.2, 1.5 Hz, 1 H), 7.38–7.36 (m, 3 H), 7.32–7.29 (m, 2 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 134.2, 132.5, 131.7, 131.4, 129.7, 129.6, 128.6, 128.5, 128.4, 128.4, 128.4, 125.0, 122.7, 90.5, 87.9.

MS (EI): *m*/*z* = 212 (M^+).

1-Fluoro-4-(phenylethynyl)benzene (3k)[10c]

3-(4-Fluorophenyl)propiolic acid (**1j**; 541.6 mg, 3.3 mmol) and **2b** (516.6 mg, 3.0 mmol) afforded **3k** (370.9 mg, 1.89 mmol, 63%); off-white solid; mp 91–94 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.53–7.50 (m, 4 H), 7.36–7.33 (m, 3 H), 7.07–7.02 (m, 2 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 162.5 (d, $J_{C,F}$ = 250 Hz), 133.5 (d, $J_{C,F}$ = 8.5 Hz), 131.5, 128.4, 128.3, 123.1, 119.4 (d, $J_{C,F}$ = 3.5 Hz), 115.6 (d, $J_{C,F}$ = 22.1 Hz), 89.0, 88.3.

MS (EI): *m*/*z* = 196 (M^+).

1-(Phenylethynyl)-4-(trifluoromethyl)benzene (3l)[10c]

3-[4-(Trifluoromethyl)phenyl]propiolic acid (**1k;** 707.7 mg, 3.3 mmol) and **2b** (516.6 mg, 3.0 mmol) afforded **3l** (421.1 mg, 1.71 mmol, 57%); white solid; mp 87–88 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.62 (q, *J* = 8.5 Hz, 4 H), 7.56–7.54 (m, 2 H), 7.39–7.36 (m, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 132.5, 131.8, 131.7, 129.9 (q, $J_{C,F}$ = 33.4 Hz), 128.8, 128.2, 126.0 (q, $J_{C,F}$ = 266.9 Hz), 125.3 (q, $J_{C,F}$ = 3.8 Hz), 122.5, 91.7, 88.0.

MS (EI): *m*/*z* = 246 (M^+).

Methyl 4-(Phenylethynyl)benzoate (3m)[10c]

3-[4-(Methoxycarbonyl)phenyl]propiolic acid (**1l**; 673.8 mg, 3.3 mmol) and **2b** (516.6 mg, 3.0 mmol) afforded **3m** (467.8 mg, 1.98 mmol, 66%); light yellow solid; mp 121–122 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 8.2 Hz, 2 H), 7.59 (d, *J* = 8.7 Hz, 2 H), 7.56–7.54 (m, 2 H), 7.38–7.36 (m, 3 H), 3.93 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 166.6, 131.7, 131.5, 129.5, 129.4, 128.8, 128.4, 128.0, 122.7, 92.3, 88.7, 52.3.

MS (EI): *m*/*z* = 236 (M^+).

1-[4-(Phenylethynyl)phenyl]ethanone (3n)[10b]

3-(4-Acetylphenyl)propiolic acid (**1m**; 620.1 mg, 3.3 mmol) and **2b** (516.6 mg, 3.0 mmol) afforded **3n** (555.1 mg, 2.52 mmol, 84%); light yellow solid; mp 124–125 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 8.7 Hz, 2 H), 7.61 (d, *J* = 8.7 Hz, 2 H), 7.56–7.54 (m, 2 H), 7.38–7.36 (m, 3 H), 2.62 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 197.4, 136.2, 131.7, 131.7, 128.8, 128.5, 128.3, 128.2, 122.6, 92.7, 88.6, 26.7.

MS (EI): *m*/*z* = 220 (M^+).

4-(Phenylethynyl)benzonitrile (3o)[10c]

3-(4-Cyanophenyl)propiolic acid (**1n**; 564.8 mg, 3.3 mmol) and **2b** (516.6 mg, 3.0 mmol) afforded **3o** (512.2 mg, 2.52 mmol, 84%); light yellow solid; mp 109–111 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.65–7.60 (m, 4 H), 7.56–7.54 (m, 2 H), 7.39–7.38 (m, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 132.0, 132.0, 131.8, 129.1, 129.0, 128.2, 122.2, 118.6, 111.5, 93.8, 87.7, 30.0.

MS (EI): *m*/*z* = 203 (M^+).

1-(Phenylethynyl)naphthalene (3p)[10c]

3-(Naphthalen-1-yl)propiolic acid (**1o**; 647.5 mg, 3.3 mmol) and **2b** (516.6 mg, 3.0 mmol) afforded **3p** (678.0 mg, 2.97 mmol, 99%); pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.46–8.44 (m, 1 H), 7.84–7.79 (m, 2 H), 7.76–7.74 (m, 1 H), 7.65–7.63 (m, 2 H), 7.60–7.56 (m, 1 H), 7.52–7.49 (m, 1 H), 7.44–7.41 (m, 1 H), 7.38–7.32 (m, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 133.3, 133.2, 131.8, 130.5, 128.9, 128.5, 128.5, 128.4, 126.9, 126.5, 125.4, 123.5, 121.0, 94.4, 87.6.

MS (EI): *m*/*z* = 228 (M^+).

4-(Phenylethynyl)-1,1′-biphenyl (3q)[13]

3-([1,1′-Biphenyl]-4-yl)propiolic acid (**1p**; 733.4 mg, 3.3 mmol) and **2b** (516.6 mg, 3.0 mmol) afforded **3q** (641.0 mg, 2.52 mmol, 84%); white solid; mp 156–158 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.64–7.56 (m, 8 H), 7.47 (t, *J* = 7.6 Hz, 2 H), 7.40–7.35 (m, 4 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 141.0, 140.3, 132.0, 131.6, 128.9, 128.4, 128.3, 127.6, 127.0 (2C), 123.3, 122.2, 90.1, 89.3.

MS (EI): *m*/*z* = 254 (M^+).

Pent-1-yn-1-ylbenzene (3r)[14]

Hex-2-ynoic acid (**1q**; 370.0 mg, 3.3 mmol) and **2b** (516.6 mg, 3.0 mmol) afforded **3r** (285.5 mg, 1.98 mmol, 66%); pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40–7.38 (m, 2 H), 7.27–7.21 (m, 3 H), 2.37 (t, *J* = 7.1 Hz, 2 H), 1.65–1.58 (m, 2 H), 1.04 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 131.5, 128.1, 127.4, 124.0, 90.2, 80.7, 22.2, 21.3, 13.5.

MS (EI): *m*/*z* = 144 (M^+).

Hept-1-yn-1-ylbenzene (3s)[15]

Oct-2-ynoic acid (**1r**; 462.6 mg, 3.3 mmol) and **2b** (516.6 mg, 3.0 mmol) afforded **3s** (439.3 mg, 2.55 mmol, 85%); colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40–7.38 (m, 2 H), 7.29–7.25 (m, 3 H), 2.40 (t, *J* = 7.2 Hz, 2 H), 1.66–1.56 (m, 2 H), 1.47–1.40 (m, 1 H), 1.39–1.33 (m, 2 H), 0.92 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 131.5, 128.2, 127.5, 124.1, 90.5, 80.5, 31.2, 28.5, 22.2, 19.4, 14.0.

MS (EI): *m*/*z* = 172 (M^+).

1-Methyl-2-(*p*-tolylethynyl)benzene (3t)[6]

3-(*o*-Tolyl)propiolic acid (**1b**; 528.6 mg, 3.3 mmol) and 4-methylbenzenesulfonyl hydrazide (**2c**; 558.7 mg, 3.0 mmol) afforded **3t** (470.3 mg, 2.28 mmol, 76%); white solid; mp 47–49 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.54 (d, *J* = 7.4 Hz, 1 H), 7.49–7.48 (m, 2 H), 7.27–7.26 (m, 2 H), 7.21–7.19 (m, 3 H), 2.56 (s, 3 H), 2.41 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 140.1, 138.1, 131.8, 131.4, 129.5, 129.2, 128.2, 125.6, 123.2, 120.5, 93.6, 87.7, 21.6, 20.1.

MS (EI): *m*/*z* = 206 (M^+).

1-Methyl-3-(*p*-tolylethynyl)benzene (3u)[6]

3-(*m*-Tolyl)propiolic acid (**1c**; 528.6 mg, 3.3 mmol) and **2c** (558.7 mg, 3.0 mmol) afforded **3u** (587.9 mg, 2.85 mmol, 95%); white solid; mp 71–72 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.44 (d, *J* = 7.9 Hz, 2 H), 7.38–7.34 (m, 2 H), 7.25 (t, *J* = 7.6 Hz, 1 H), 7.18–7.14 (m, 3 H), 2.39 (s, 3 H), 2.37 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 138.3, 138.0, 132.1, 131.5, 129.1, 129.0, 128.6, 128.2, 123.2, 120.3, 89.2, 88.9, 21.5, 21.3.

MS (EI): *m*/*z* = 206 (M^+).

1-Methoxy-4-(*p*-tolylethynyl)benzene (3v)[10c]

3-(4-Methoxyphenyl)propiolic acid (**1e**; 581.4 mg, 3.3 mmol) and **2c** (558.7 mg, 3.0 mmol) afforded **3v** (473.5 mg, 2.13 mmol, 71%); light yellow solid; mp 126–128 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.46 (d, *J* = 8.9 Hz, 2 H), 7.40 (d, *J* = 8.0 Hz, 2 H), 7.14 (dd, *J* = 7.9, 0.6 Hz, 2 H), 6.87 (d, *J* = 8.9 Hz, 2 H), 3.82 (s, 3 H), 2.36 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 159.4, 138.0, 133.0, 131.3, 129.0, 120.4 116.0, 114.0, 86.6, 88.2, 55.3, 21.5.

MS (EI): *m*/*z* = 222 (M^+).

1-Fluoro-4-(*p*-tolylethynyl)benzene (3w)[6]

3-(4-Fluorophenyl)propiolic acid (**1j**; 541.6 mg, 3.3 mmol) and **2c** (558.7 mg, 3.0 mmol) afforded **3w** (460.4 mg, 2.19 mmol, 73%); white solid; mp 90–91 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.49–7.46 (m, 2 H), 7.40 (d, *J* = 8.1 Hz, 2 H), 7.12 (dd, *J* = 8.4, 0.6 Hz, 2 H), 7.00 (t, *J* = 8.8 Hz, 2 H), 2.33 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 162.4 (d, $J_{C,F}$ = 249.8 Hz), 138.5, 133.4 (d, $J_{C,F}$ = 8.8 Hz), 131.5, 129.2, 120.0, 119.6 (d, $J_{C,F}$ = 3.8 Hz), 115.6 (d, $J_{C,F}$ = 21.4 Hz), 89.3, 87.7.

MS (EI): *m*/*z* = 210 (M^+).

1-Bromo-4-[(4-methoxyphenyl)ethynyl]benzene (3x)[13]

3-(4-Bromophenyl)propiolic acid (**1h**; 742.6 mg, 3.3 mmol) and 4-methoxybenzenesulfonyl hydrazide (**2d**; 606.7 mg, 3.0 mmol) afforded **3x** (775.3 mg, 2.70 mmol, 90%); white solid; mp 153–155 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.47–7.45 (m, 4 H), 7.36 (d, *J* = 8.7 Hz, 2 H), 6.87 (d, *J* = 8.9 Hz, 2 H), 3.82 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 159.7, 133.0, 132.8, 131.5, 122.5, 122.0, 115.0, 114.0, 90.5, 87.0, 55.3.

MS (EI): *m*/*z* = 286 (M^+).

1-Bromo-4-[(4-chlorophenyl)ethynyl]benzene (3y)[6]

3-(4-Bromophenyl)propiolic acid (**1h**; 742.6 mg, 3.3 mmol) and 4-chlorobenzenesulfonyl hydrazide (**2e**; 620.0 mg, 3.0 mmol) afforded **3y** (673.5 mg, 2.31 mmol, 77%); white solid; mp 176–179 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.49 (d, *J* = 8.6 Hz, 2 H), 7.45 (d, *J* = 8.7 Hz, 2 H), 7.38 (d, *J* = 8.6 Hz, 2 H), 7.33 (d, *J* = 8.7 Hz, 2 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 134.5. 133.0. 132.8. 131.7. 128.8. 122.7. 121.9. 121.4. 89.3. 89.2.

MS (EI): *m*/*z* = 290 (M^+).

1,2-Di-(*p*-tolyl)ethyne (4a)[9c]

A 5 mL vial equipped with a magnetic stir bar was charged with 4-methylbenzenesulfonyl hydrazide (**2a**; 1.352 g, 7.26 mmol), propiolic acid (231.6 mg, 3.3 mmol), $Pd(TFA)_2$ (21.9 mg, 0.066 mmol, 2 mol%), dppp (27.2 mg, 0.066 mmol, 2 mol%), $Cu(OAc)_2{\cdot}H_2O$ (2635.4 mg, 13.2 mmol, 4.0 equiv), and DMF (10 mL). The reaction mixture was heated at 100 °C for 2 h, then cooled to r.t., and quenched with H_2O. The crude product was extracted with EtOAc, and the combined organic layers were dried (anhyd $MgSO_4$) and concentrated under vacuum. The desired product **4a** (136.1 mg, 0.66 mmol, 20%) was isolated by silica gel column chromatography using hexane/EtOAc as the eluent; white solid; mp 139–140 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42–7.40 (m, 4 H), 7.13 (dd, *J* = 8.14, 0.6 Hz, 4 H), 2.34 (s, 6 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 138.1, 131.4, 129.0, 120.3, 88.8, 21.5.

MS (EI): *m*/*z* = 206 (M^+).

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Supporting Information

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