Palladium-Catalyzed Heck Alkynylation of Benzyl Chlorides

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This article is dedicated to Richard F. Heck in honor of his seminal contributions to organic and organometallic chemistry.

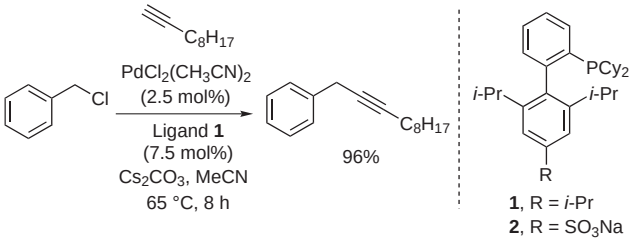
Abstract: An efficient and general protocol for the palladium-catalyzed Heck alkynylation of benzyl chlorides was developed. A catalyst system comprised of $PdCl_2(CH_3CN)_2$ and 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl (XPhos), with Cs_2CO_3 as the base, efficiently couples a wide range of functionalized terminal alkynes and substituted benzyl chlorides at 65 °C. We have also demonstrated that the corresponding aryl allene product can be selected for using an excess amount of base and higher reaction temperatures (80 °C) in a one-pot procedure.

Key words: palladium, alkynes, Heck alkynylation, benzyl chlorides, allene

Over the past 30 years, transition-metal-catalyzed cross-coupling methodology to form carbon–carbon bonds has become a staple of modern synthesis.[1] The preeminent method for the incorporation of an alkynyl moiety in organic compounds is the palladium-catalyzed cross-coupling reaction of terminal alkynes and organic electrophiles.[1,2] The most widely used of these is a cross between the Cu-promoted Castro–Stephens reaction[3] and the Heck alkynylation,[4] known as the Sonogashira reaction.[5] While significant advances in palladium-based systems to catalyze the reaction of aryl halides and terminal alkynes have been made through the development of more sterically hindered/electron-rich phosphine ligands, very few reports for the coupling of alkyl or benzyl halides have been reported.[6] For example, the report of Fu and coworkers that a catalyst system derived from $[PdCl(\pi\text{-allyl})]_2$/CuI and 1,3-bis(1-adamantyl)imidazolium chloride allowed the coupling of unactivated alkyl bromides and iodides and terminal alkynes represents the most general method for coupling these difficult electrophiles.[7]

We had previously disclosed that a catalyst system based on $PdCl_2(CH_3CN)_2$/2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl (XPhos, **1**) provided excellent reactivity in the Heck alkynylation (copper-free Sonogashira coupling) of aryl chlorides/tosylates and terminal alkynes.[8] We were interested in expanding the substrate scope of this catalyst system to include readily available benzyl chlorides as coupling partners. To our knowledge, only one protocol is operative with substoichiometric metal, in which the alkynylation of benzyl bromide is accomplished using palladium and tris(alkynyl)indiums as the transmetallating agent.[2,9] A system using catalytic palladium can also be used with alkynyl zinc reagents to couple simple benzyl bromides.[10] Interestingly, a reported attempt to couple benzyl halides with terminal alkynes using a $PdCl_2(PPh_3)_2$/CuCl catalyst only provides small amounts of the desired benzyl-substituted alkyne. Instead, highly substituted enynes are produced via a tandem Sonogashira–carbopalladation–Sonogashira sequence.[11]

We postulated that the use of an electron-rich bulky ligand (XPhos, **1**) would suppress formation of the proposed Pd-bound benzyl alkynyl species and prevent formation of the enyne product. Indeed, using catalytic $PdCl_2(CH_3CN)_2$/**1** and 2.5 equivalents Cs_2CO_3 as the base in acetonitrile (MeCN), benzyl chloride and 1-decyne were efficiently combined providing the benzyl alkyne in 96% yield (Equation 1). Note that this transformation proceeds in the absence of a copper co-catalyst and without isomerization to the undesired allene. In fact, the addition of 4 mol% CuI inhibited the desired alkynylation while forming multiple side products. Exploration of these initial catalytic conditions revealed that while KOAc provides a faster initial reaction rate than Cs_2CO_3, it also consumes the terminal alkyne leaving significant amounts of unreacted benzyl chloride. The use of most other bases is unproductive, but NaOAc and $K_3PO_4 \cdot H_2O$ do provide 50% conversion to product in the same time frame in which the reaction with Cs_2CO_3 is complete. While the process is water-tolerant, if it is not carried out under an inert atmosphere, the rate is 4–5 times slower. Utilization of $Pd(OAc)_2$ as the precatalyst is just as efficacious as $PdCl_2(CH_3CN)_2$ with either MeCN or THF as the solvent.



Equation 1

Unfortunately, when the conditions in Equation 1 were applied to the coupling of 4-fluorobenzyl chloride and 4-cyano-1-butyne, an inseparable mixture of alkyne and allene products were formed, with the allene predominating. Lowering the stoichiometry of base to 1.5 equivalents gave a 1:2 ratio of alkyne to allene and to 1.1 equivalents

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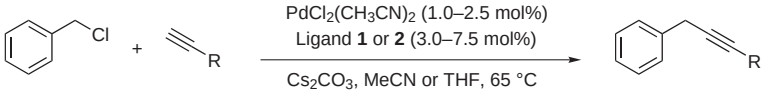
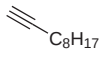
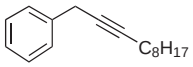
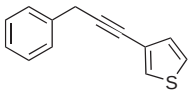
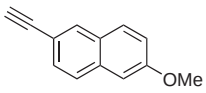
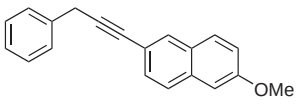
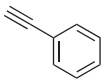
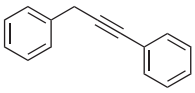
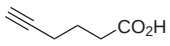
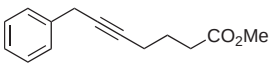
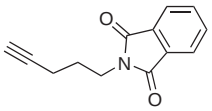
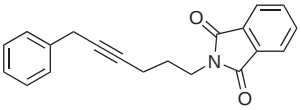
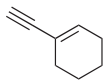
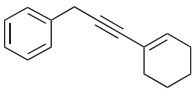
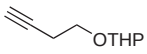
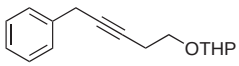
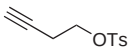
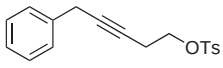
finally provided a majority of the desired alkyne product in a 5:1 ratio. Switching the solvent to THF, toluene, or dioxane is the key to obtaining solely the alkynyl Heck product for this more highly functionalized set of substrates, with the reactions in both THF and dioxane proceeding to completion. If the alkynyl Heck product is not prone to isomerization to the allene, then the original conditions in acetonitrile also cleanly provide the coupled product.

As is illustrated in Table 1, a wide variety of terminal alkynes can be successfully coupled with benzyl chloride using this catalyst system derived from $PdCl_2(CH_3CN)_2$ and XPhos (**1**). Aryl and heteroaryl alkynes are effective coupling partners as shown with 3-ethynylthiophene and 2-ethynyl-6-methoxynaphthalene where, in contrast to the Heck alkynylation of aryl chlorides using this same catalyst system, slow addition of the aryl/heteroaryl alkyne is not necessary (Table 1, entries 2, 3). This may be attributed to the fact that oxidative addition to benzyl chloride occurs much faster than non-productive alkyne polymerization. However, it should be noted that the reaction of 3-ethynylthiophene must be halted after two hours as the alkynyl product begins to isomerize to the allene upon consumption of the benzyl chloride starting material. Interestingly, the water-soluble sodium sulfonate version of XPhos (**2**) in biphasic mixture of H_2O–MeCN is proficient in the coupling of benzyl chloride with both phenylacetylene and the water-soluble terminal alkyne, 5-hexynoic acid, where 94% and 81% of the disubstituted alkynes are obtained, respectively (Table 1, entries 4, 5).[12] Phthalimide-protected 5-aminohexyne is smoothly coupled with benzyl chloride in THF (Table 1, entry 6). Terminal aliphatic alkynes possessing either tetrahydropyran- or tosyl-protected alcohols are well tolerated and provide the corresponding benzyl alkynes in 82% and 95% yield, respectively (Table 1, entries 8, 9).

Table 1 Palladium-Catalyzed Coupling of Benzyl Chloride and Terminal Alkynes[a]

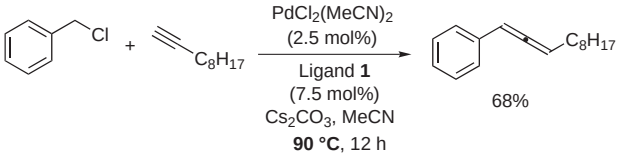


Entry	Alkyne	Product	Time (h)	Yield (%)[b]
1			8	96[c]
2			2	88[c]
3			1.5	96[c]
4			10	94[d]
5			10	81[d,e]
6			17	94
7			1.5	91
8			4	82
9			12	95

[a] *Reaction conditions*: 1.0 equiv benzyl chloride, 1.3–1.5 equiv alkyne, 1.05 equiv Cs_2CO_3, THF (2.5 mL/mmol), $PdCl_2(CH_3CN)_2$ (2.0 mol%), ligand **1** (6.0 mol%), 65 °C.
[b] Yield of isolated product (average of 2 runs).
[c] MeCN was used as the solvent.
[d] Ligand **2** and a H_2O–MeCN solvent system were used.
[e] To ease in purification, the product was converted to the methyl ester using trimethylsilyldiazomethane.

The substrate scope was expanded further by varying the type and position of substituents on the benzyl halide. As shown in Table 2, electron-rich 4-methoxybenzyl chloride and triethylsilyl-protected acetylene react to form the corresponding benzyl alkyne in nearly quantitative yield (Table 2, entry 1). Electron-deficient 3-trifluoromethylbenzyl chloride is combined with 1-ethynylcyclohexene with high fidelity (Table 2, entry 2). Complete selectivity of a benzyl chloride over an aryl chloride is achieved when coupling both 4-chloro and 2-chloro benzyl chloride with terminal alkynes (Table 2, entries 3, 4). The coupling products of 4-fluorobenzyl chloride and either tetrahydropyran-protected propynol or 3-chlorophenylacetylene are also produced in good yields (Table 2, entry 5, 6). While primary benzyl chlorides were suitable coupling partners using this catalyst system, reactions conducted with secondary benzyl chlorides resulted in significant amounts of styrene (presumably formed via β-hydride elimination).[13]

In the initial optimization studies, we found that if we heated the reaction to greater than 65 °C for the simple combination of benzyl chloride and 1-decyne, instead of only forming the desired benzyl alkyne, a significant amount of aryl allene is produced. In fact, heating the reaction at 90 °C for 12 hours with excess Cs_2CO_3 (2.5 equiv) produced aryl allene in a modest 68% yield (Equation 2).

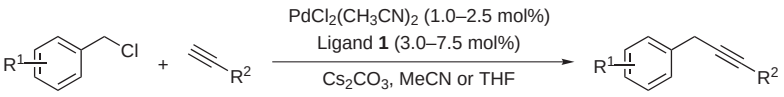


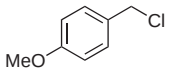
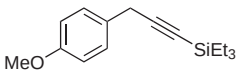
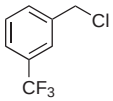
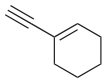
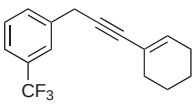
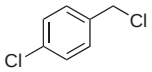
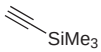
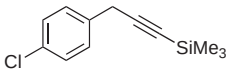
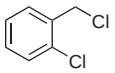
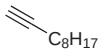
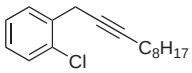
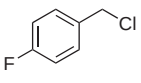
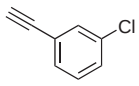
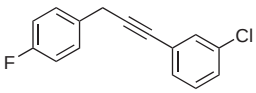
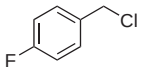
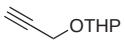
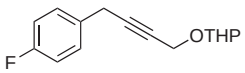
Equation 2

To determine whether the isomerization was mediated by the metal or by the base, we subjected the octyl-benzyl alkyne product from Table 1, entry 1 to 2.5 equivalents Cs_2CO_3 in MeCN at 90 °C for 10 hours. Under these conditions, the product is completely converted to the corresponding aryl allene, confirming the role of the base in this reaction. As is seen in Table 3, by changing the amount of base used, as well as the solvent, and temperature, one can predictably convert benzyl chlorides to either the benzyl alkyne (65 °C, 1.05 equiv Cs_2CO_3) or the aryl allene (>80 °C, 2.50 equiv Cs_2CO_3) in a one-pot protocol. For substrates in which the reaction in MeCN gives a mixture of alkyne and allene even at 65 °C with only 1.05 equivalents of base, switching the solvent to THF provides solely the alkyne product.

In summary, we have developed an efficient procedure for the direct coupling of benzyl chlorides and terminal alkynes using a catalyst comprised of $PdCl_2(CH_3CN)_2$ and ligands **1** or **2**, which provide benzyl alkynes in good to excellent yields. We also found that by using this same catalyst, an excess of base and more forcing reaction conditions, the coupling of benzyl chlorides and terminal

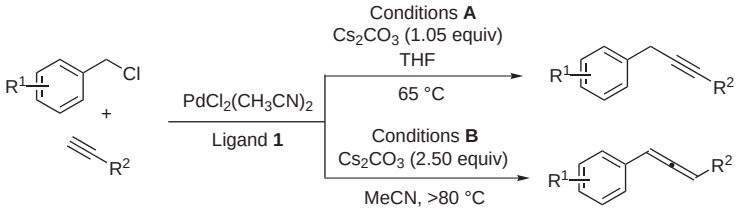
Table 2 Palladium-Catalyzed Coupling of Substituted Benzyl Chlorides and Terminal Alkynes[a]

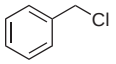
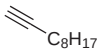
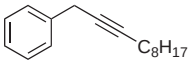
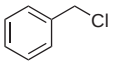
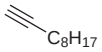
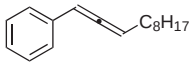
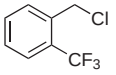
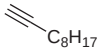
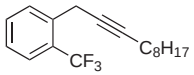
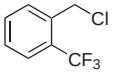
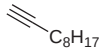
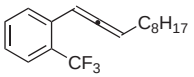
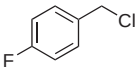
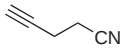
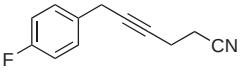
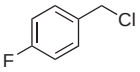
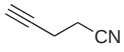
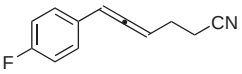


Entry	Benzyl chloride	Alkyne	Product	Time (h)	Yield (%)[b]
1				16	99[c]
2				4	97
3				24	82
4				22	71[c]
5				2	91[c]
6				6	94

[a] *Reaction conditions*: 1.0 equiv benzyl chloride, 1.3–1.5 equiv alkyne, 1.05 equiv Cs_2CO_3, THF (2.5 mL/mmol), $PdCl_2(CH_3CN)_2$ (2.0 mol%), ligand **1** (6.0 mol%), 65 °C.
[b] Yield of isolated product (average of 2 runs).
[c] MeCN used as the solvent.

Table 3 Palladium-Catalyzed Coupling of Benzyl Chlorides with Terminal Alkynes to Form Benzyl Alkynes or Aryl Allenes[a]



Entry	Benzyl chloride	Alkyne	Condition	Product	Time (h)	Yield (%)[b]
1			**A**		8	96
2			**B**		16	68
3			**A**		25	93
4			**B**		12	72
5			**A**		6	91[c]
6			**B**		12	70

[a] Reaction conditions: 1.0 equiv benzyl chloride, 1.3–1.5 equiv alkyne, $PdCl_2(CH_3CN)_2$ (2.0 mol%), ligand **1** (6.0 mol%). Conditions **A**: 1.05 equiv Cs_2CO_3, THF (2.5 mL/mmol), 65 °C, 4–25 h. Conditions **B**: 2.50 equiv Cs_2CO_3, MeCN (2.5 mL/mmol), 80–90 °C, 12 h.
[b] Yield of isolated product (average of 2 runs).
[c] 1,4-Dioxane was used as the solvent.

alkynes produces aryl allenes via a base-catalyzed isomerization of the resultant benzyl alkyne. Further investigation of the scope and potential applications of this methodology are underway in our laboratories.

General Procedure for Heck Alkynylation of Benzyl Chlorides to Form Benzyl Alkynes (Table 1 and Table 2)

A disposable tube equipped with a screw cap, Teflon septum and stir bar was charged with $PdCl_2(CH_3CN)_2$ (5.2 mg, 0.020 mmol, 2 mol%), 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl (28.6 mg, 0.060 mmol, 6 mol%), and Cs_2CO_3 (342 mg, 1.05 mmol). If the benzyl chloride or terminal alkyne was a solid, it was also added at this time. The tube was evacuated and back-filled with argon three times. The solvent/solvents and benzyl chloride (1.00 mmol, liquid) were added. The terminal alkyne (1.30 mmol, liquid) was then added and the solution was heated to the noted temperature until the reaction was complete as judged by GC analysis. After cooling to r.t., the products were extracted from the water layer with Et_2O and dried over $MgSO_4$ or with hexane–EtOAc, filtered through Celite®, and concentrated to dryness. Purification by column chromatography on silica gel provided the benzyl alkyne products (Note: many of these alkynes are unstable upon purification and concentration. It is recommended that they be stored at –20 °C or lower in solution).

2-Undecynylbenzene (Table 1, Entry 1; Table 3, Entry 1; Equation 1)[14]

The title compound was obtained as a clear oil (220 mg, 96%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (d, *J* = 7.2 Hz, 2 H), 7.28 (t, *J* = 7.2 Hz, 2 H), 7.17 (t, *J* = 6.8 Hz, 1 H), 3.56 (br t, *J* = 2.4 Hz, 2 H), 2.20 (tt, *J* = 4.8, 2.4 Hz, 2 H), 1.52 (m, 2 H), 1.28–1.42 (m, 10 H), 0.88 (t, *J* = 6.4 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.8, 128.5, 128.0, 126.5, 82.9, 77.7, 32.0, 29.5, 29.4, 29.2, 29.1, 25.3, 22.9, 19.0, 14.3.

3-(3-Phenyl-1-propynyl)thiophene (Table 1, Entry 2)

The title compound was obtained as a brown oil (174 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 (m, 3 H), 7.36 (t, *J* = 7.5 Hz, 2 H), 7.26 (m, 2 H), 7.14 (dd, *J* = 5.0, 1.0 Hz, 1 H), 3.83 (s, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.9, 130.2, 128.8, 128.25, 128.16, 126.9, 125.3, 122.8, 87.3, 77.9. IR (neat): 3107, 3029, 1601, 1521, 1493, 1453, 1357, 1178, 1076, 859, 780, 695, 626 cm^{-1}.

2-Methoxy-6-(3-phenyl-1-propynyl)naphthalene (Table 1, Entry 3)

The title compound was obtained as a white solid (261 mg, 96%, mp: 101–102 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (s, 1 H), 7.71 (t, *J* = 8.1 Hz, 2 H), 7.52 (m, 3 H), 7.41 (m, 2 H), 7.32 (m, 1 H), 7.19 (dd, *J* = 8.9, 2.5 Hz, 1 H), 7.14 (d, *J* = 2.5 Hz, 1 H), 3.95 (s, 3 H), 3.93 (s, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.2, 137.0, 134.0, 131.2, 129.4, 129.3, 128.7, 128.6, 128.1, 126.9, 126.8, 119.4, 118.7, 105.8, 87.3, 83.3, 55.4, 26.0. IR (neat): 3060, 3029, 2938, 1625, 1599, 1493, 1241, 1162, 1027, 896, 857, 818, 697 cm^{-1}.

1,3-Diphenyl-1-propyne (Table 1, Entry 4)[10]
The title compound was obtained as a clear oil (92 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.46 (m, 4 H), 7.33 (t, *J* = 7.2 Hz, 2 H), 7.22–7.30 (m, 4 H), 3.82 (s, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.9, 131.8, 128.7, 128.4, 128.2, 128.0, 126.8, 123.8, 87.7, 82.8, 25.9.

7-Phenyl-5-heptynoic Acid Methyl Ester (Table 1, Entry 5)[15]
The title compound was obtained as a clear oil (108 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.19–7.36 (m, 5 H), 3.66 (s, 3 H), 3.56 (t, *J* = 2.4 Hz, 2 H), 2.45 (t, *J* = 7.2 Hz, 2 H), 2.29 (tt, *J* = 6.8, 2.4 Hz, 2 H), 1.85 (p, *J* = 7.2 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.8, 137.5, 128.7, 128.6, 127.9, 126.6, 81.3, 78.7, 51.7, 33.0, 25.2, 24.3, 18.5.

***N*-(3-Phenyl-1-propynyl)pthalimide (Table 1, Entry 6)**
The title compound was obtained as an off-white oil (284 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (m, 2 H), 7.71 (m, 2 H), 7.30 (m, 4 H), 7.22 (m, 1 H), 3.82 (m, 2 H), 3.45 (m, 2 H), 2.26–2.35 (m, 2 H), 1.99 (m, 2 H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.5, 137.3, 134.0, 132.3, 128.5, 127.9, 126.5, 123.3, 81.2, 78.5, 37.5, 27.7, 25.1, 16.9. IR (neat): 3462, 3289, 3059, 3025, 2936, 2190, 1773, 1709, 1614, 1493, 1438, 1396, 1373, 1116, 1027, 887, 722 cm^{-1}.

(3-Cyclo-1-hexenyl-2-propynyl)benzene (Table 1, Entry 7)[10]
The title compound was obtained as a light-yellow oil (179 mg, 91%). This compound decomposes significantly when concentrated and stored at –20 °C for 8 d (only trace decomposition of the same sample stored in $CDCl_3$ was observed). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.31 (m, 4 H), 7.26 (t, *J* = 7.1 Hz, 1 H), 6.10 (m, 1 H), 3.74 (s, 2 H), 2.16 (m, 2 H), 2.10 (m, 2 H), 1.67–1.58 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.4, 134.0, 128.6, 128.1, 126.6, 121.0, 84.7, 29.7, 25.8, 25.7, 22.6, 21.8.

2-(5-Phenyl-3-pentynyloxy)tetrahydropyran (Table 1, Entry 8)
The title compound was obtained as a pale-yellow oil (299 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.30 (m, 4 H), 7.25 (m, 1 H), 4.67 (t, *J* = 3.5 Hz, 1 H), 3.87 (m, 2 H), 3.61–3.48 (m, 3 H), 2.55 (tt, *J* = 7.1, 2.4 Hz, 2 H), 1.83 (m, 1 H), 1.72 (m, 2 H), 1.62–1.51 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.5, 128.6, 128.0, 126.6, 98.9, 79.5, 78.9, 66.2, 62.3, 30.8, 25.6, 25.3, 20.5, 19.6. IR (neat): 3291, 3063, 3030, 2943, 2874, 2237, 2207, 1734, 1704, 1454, 1353, 1263, 1201, 1137, 1121, 1072, 1034, 980, 699 cm^{-1}.

Toluene-4-sulfonic Acid 5-Phenyl-3-pentynyl Ester (Table 1, Entry 9)
The title compound was obtained as a yellow oil (299 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.3 Hz, 2 H), 7.31 (m, 6 H), 7.25 (m, 1 H), 4.13, (t, *J* = 7.0 Hz, 2 H), 3.53 (s, 2 H), 2.61 (tt, *J* = 7.0, 2.3 Hz, 2 H), 2.44 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 136.8, 133.0, 128.6, 128.0, 127.9, 126.7, 80.4, 76.5, 68.2, 25.1, 21.7, 19.9. IR (neat): 3061, 3030, 2958, 2919, 2236, 2201, 1700, 1598, 1495, 1454, 1361, 1176, 1097, 987, 902, 816, 770, 725, 664 cm^{-1}.

Triethyl[3-(4-methoxyphenyl)-1-propynyl]silane (Table 2, Entry 1)
The title compound was obtained as a clear oil (259 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 (d, *J* = 8.4 Hz, 2 H), 6.90 (d, *J* = 8.4 Hz, 2 H), 3.84 (s, 3 H), 3.67 (s, 2 H), 1.06 (t, *J* = 8.0 Hz, 9 H), 0.68 (q, *J* = 8.0 Hz, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.4, 128.9, 128.7, 113.9, 105.9, 83.9, 55.4, 25.5, 7.7, 4.7. IR (neat): 2955, 2911, 2874, 2174, 1612, 1586, 1512, 1462, 1417, 1333, 1302, 1247, 1175, 1039, 1020, 815, 807, 726 cm^{-1}.

1-(3-Cyclohex-1-enylprop-2-ynyl)-3-trifluoromethylbenzene (Table 2, Entry 2)
The title compound was obtained as a clear oil (256 mg, 97%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (s, 1 H), 7.44–7.29 (m, 3 H), 5.98 (m, 1 H), 3.64 (s, 2 H), 2.05–1.96 (m, 4 H), 1.55–1.43 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.4, 134.6, 131.5, 129.1, 124.9 (q, *J* = 3.9 Hz), 123.6 (q, *J* = 3.9 Hz), 120.8, 85.4, 83.5, 29.6, 25.8, 25.7, 22.5, 21.7. IR (neat): 3067, 3024, 2939, 2862, 2212, 2185, 1708, 1676, 1653, 1616, 1450, 1327, 1257, 1124, 1070, 918, 795, 702, 660 cm^{-1}.

[3-(4-Chlorophenyl)prop-1-ynyl]trimethylsilane (Table 2, Entry 3)
The title compound was obtained as clear oil (183 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 (m, 4 H), 3.63 (s, 2 H), 0.20 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.0, 132.6, 129.4, 128.8, 103.8, 87.6, 25.8, 0.3. IR (neat): 3041, 3031, 2960, 2899, 2361, 2340, 1492, 1417, 1250, 1091, 1030, 1017, 844, 797, 760, 644 cm^{-1}.

1-Chloro-2-undec-2-ynylbenzene (Table 2, Entry 4)
The title compound was obtained as a light-yellow oil (259 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 7.6 Hz, 1 H), 7.37 (dd, *J* = 1.6, 8.0 Hz, 1 H), 7.30 (td, *J* = 1.6, 5.6 Hz, 1 H), 7.21 (td, *J* = 2.0, 6.0 Hz, 1 H), 3.71 (t, *J* = 2.4 Hz, 2 H), 2.30 (tt, *J* = 2.4, 4.8 Hz, 2 H), 1.52 (q, *J* = 2.4 Hz, 2 H), 1.51–1.35 (m, 10 H), 0.95 (t, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.4, 133.6, 129.7, 129.2, 127.9, 126.9, 83.9, 76.2, 32.1, 29.5, 29.4, 29.2, 29.1, 23.5, 22.9, 19.0, 14.3. IR (neat): 2955, 2927, 2855, 1705, 1593, 1573, 1468, 1444, 1322, 1050, 1038, 748 cm^{-1}.

1-(*m*-Chlorophenyl)-3-(*p*-fluorobenzyl)-1-propyne (Table 2, Entry 5)
The title compound was obtained as a yellow oil (221 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.49 (m, 1 H), 7.24–7.41 (m, 5 H), 7.06–7.10 (m, 2 H), 3.83 (s, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9 (163.2, 160.7, d, *J* = 244.4 Hz), 134.3, 132.2 (132.20, 132.16, d, *J* = 3.2 Hz), 131.7, 129.9, 129.6 (129.67, 129.61, d, *J* = 5.1 Hz), 129.5, 128.4, 125.4, 115.5 (115.69, 115.48, d, *J* = 21.4 Hz), 88.9, 81.7, 25.1. IR (neat): 3069, 2893, 2226, 2205, 1700, 1593, 1561, 1509, 1475, 1418, 1225, 1158, 1095, 1016, 882, 818, 785, 682 cm^{-1}.

2-[4-(4-Fluorophenyl)-2-butynyloxy]tetrahydropyran (Table 2, Entry 6)
The title compound was obtained as a clear oil (233 mg, 94%) and decomposes quickly upon concentration. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (m, 2 H), 6.99 (m, 2 H), 4.83 (t, *J* = 3.3 Hz, 1 H), 4.31 (qt, *J* = 15.0, 2.2 Hz, 2 H), 3.85 (m, 1 H), 3.61 (s, 2 H), 3.53 (m, 1 H), 1.88–1.50 (m, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.8 (163.0, 160.6, d, *J* = 244.4 Hz), 132.3 (132.30, 132.27, d, *J* = 3.2 Hz), 129.5 (129.50, 129.43, d, *J* = 7.8 Hz), 115.5, 115.3, 96.9, 83.9, 78.4, 62.1, 54.7, 30.4, 25.5, 24.6, 19.2. IR (neat): 3070, 3043, 2944, 2871, 2854, 2359, 2340, 1604, 1509, 1454, 1223, 1132, 1117, 1025, 905, 816 cm^{-1}.

1-Trifluoromethyl-2-undec-2-ynylbenzene (Table 3, Entry 3)
The title compound was obtained as a clear oil (270 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 7.8 Hz, 1 H), 7.62 (d, *J* = 7.8 Hz, 1 H), 7.54 (t, *J* = 7.6 Hz, 1 H), 7.34 (t, *J* = 7.6 Hz, 1 H), 3.80 (s, 2 H), 2.25 (tt, *J* = 7.1, 2.4 Hz, 2 H), 1.54 (m, 2 H), 1.41 (m, 2 H), 1.30, (m, 10 H), 0.89 (t, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.2, 132.2, 130.3, 126.7, 125.9 (q, *J* = 5.7 Hz), 84.2, 76.3, 32.1, 29.5, 29.4, 29.1, 22.9, 22.33 (q, *J* = 3.2 Hz). IR (neat): 3074, 2929, 2855, 2361, 2334, 1710, 1457, 1315, 1158, 1124, 1060, 1037, 768 cm^{-1}.

6-(4-Fluorophenyl)-hex-4-ynenitrile (Table 3, Entry 5)
The title compound was obtained as a clear oil (170 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30 (m, 2 H), 7.01 (m, 2 H), 3.57 (m, 2 H), 2.60 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.8 (163.0, 160.5, d, *J* = 244.4 Hz), 132.4 (132.39, 132.36, d, *J* = 3.1 Hz), 129.4 (129.45, 129.37, d, *J* = 8.0 Hz), 118.7, 115.5, 115.3, 80.8, 78.3, 24.3, 17.2, 16.3. IR (neat): 3075, 2928, 2854, 2248, 2208, 1722, 1648, 1599, 1508, 1424, 1269, 1225, 1157, 853 cm^{-1}.

General Procedure for Heck Alkynylation of Benzyl Chlorides To Form Benzyl Allenes (Table 3)
A disposable tube with a screw cap, Teflon septum and stir bar was charged with $PdCl_2(CH_3CN)_2$ (5.2 mg, 0.02 mmol, 2.0 mol%), 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl (**1**, 28.6 mg, 0.06 mmol, 6.0 mol%) and Cs_2CO_3 (2.5 equiv). The tube was evacuated and back-filled with argon three times. The benzyl chloride (1.00 mmol) and solvent was added and the reaction mixture was allowed to stir at r.t. for 3 min. The terminal alkyne (1.30 mmol) was added all at once and the solution was heated to the noted temperature until the reaction was complete as judged by GC analysis. After cooling to r.t., the products were extracted from the water layer with Et_2O or EtOAc, dried over $MgSO_4$, filtered through Celite® and concentrated to dryness and purified by column chromatography on silica gel.

Undeca-1,2-dienylbenzene (Table 3, Entry 2/Equation 2)[16]
The title compound was obtained as a clear oil (130 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25–7.32 (m, 4 H), 7.14–7.19 (m, 1 H), 6.11 (m, 1 H), 5.55 (q, *J* = 3.2 Hz, 1 H), 2.11 (qd, *J* = 3.2, 7.2 Hz, 2 H), 1.25–1.51 (m, 15 H), 0.87 (t, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 205.3, 135.4, 128.7, 126.79, 126.77, 95.3, 94.7, 32.0, 29.6, 29.5, 29.4, 29.3, 28.9, 22.9, 14.3.

1-Trifluoromethyl-2-undeca-1,2-dienylbenzene (Table 3, Entry 4)
The title compound was obtained as a clear oil (214 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.52 (t, *J* = 8.0 Hz, 2 H), 7.36 (t, *J* = 7.6 Hz, 1 H), 7.15 (t, *J* = 7.6 Hz, 1 H), 6.41 (m, 1 H), 5.52 (q, *J* = 6.8 Hz, 1 H), 2.06 (qd, *J* = 2.8, 7.6 Hz, 2 H), 1.39 (m, 2 H), 1.10–1.28 (m, 10 H), 0.79 (m, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 206.7, 134.1, 131.8, 128.7, 126.7 (q, *J* = 30.1 Hz), 126.5, 126.0 (q, *J* = 26.7 Hz), 123.3, 120.6, 32.1, 29.6, 29.5, 29.4, 29.3, 28.7, 22.9, 14.3. IR (neat): 2927, 2856, 1950, 1605, 1579, 1493, 1455, 1316, 1159, 1124, 1035, 763 cm^{-1}.

6-(4-Fluorophenyl)hexa-4,5-dienenitrile (Table 3, Entry 6)
The title compound was obtained as a yellow oil (130 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.17 (q, *J* = 5.6 Hz, 2 H), 6.90 (t, *J* = 8.4 Hz, 2 H), 6.17 (m, 1 H), 5.54 (q, *J* = 6.0 Hz, 1 H), 2.32–3.47 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.9, 162.1 (163.3, 160.9, d, *J* = 246.4 Hz), 129.6 (129.77, 129.73, d, *J* = 4.0 Hz), 128.4 (128.45, 128.38, d, *J* = 7.0 Hz), 119.3, 115.6 (115.8, 115.5, d, *J* = 21.9 Hz), 96.2, 92.4, 24.7, 16.6. IR (neat): 2927, 2246, 1951, 1603, 1507, 1224, 1156, 879, 838 cm^{-1}.

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