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Ligand-Free Sonogashira Coupling Reactions with Heterogeneous Pd/C as the Catalyst

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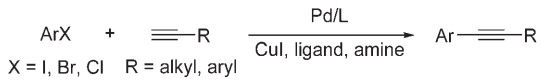
Abstract: A variety of aryl iodides were coupled with aromatic and aliphatic terminal alkynes to give the corresponding 1,2-disubstituted aromatic alkynes in good yields by using only 0.4 mol% of the heterogeneous 10% Pd/C as the catalyst without a ligand, copper salt, or amine in an aqueous medium.

Keywords: alkynes · C–C coupling · environmental chemistry · heterogeneous catalysis · palladium

Introduction

Aryl alkynes are important intermediates as synthons for a wide variety of synthetic target molecules, such as natural products, pharmaceuticals, agrochemicals, functionalized materials, etc.[1] The Sonogashira reaction with homogeneous palladium and a cuprous salt as the cocatalyst system is the most practical and powerful method for the construction of $C(sp^2)$–C(sp) bonds (Scheme 1).[2]



Scheme 1.

The original protocol generally required a homogeneous palladium catalyst, such as $[Pd(PPh_3)_4]$ or $[PdCl_2(PPh_3)_2]$, copper(I) iodide, and an amine (e.g., triethylamine, diethylamine, or diisopropylamine) as a base in organic solvents, such as benzene, toluene, THF, DMF, or dioxane. In recent years, modifications and improvements to the Sonogashira reaction have been repeatedly investigated. The most important improvement was the elimination of copper(I) iodide which could frequently induce a homocoupling reaction of terminal alkynes to diynes in the presence of oxygen (Glaser coupling reaction),[3] although most of such copper-free Sonogashira reactions require a large excess amount of triethylamine or piperidine as the solvent.[4] While the copper- and amine-free Sonogashira reactions have also been reported in the literature, they require stoichiometric amounts of silver(I) oxide together with tetrabutylammonium fluoride or tetrabutylammonium hydroxide as an activator, a specific ligand, etc.[5] Recently, a copper-, ligand-, and amine-free Sonogashira reaction with a homogeneous palladium catalyst has also been developed.[6] The use of the homogeneous palladium catalyst could generally result in a significant amount of residual palladium in the desired product due to the difficulty in separation and recovery of the catalyst from the reaction mixture.

A method for overcoming these drawbacks would involve the use of a heterogeneous palladium catalyst, especially palladium on carbon (Pd/C), which is a widely used charcoal-supported catalyst. Palladium on carbon possesses some potential advantages that include ease of recovery from the reaction mixture by the simple filtration and avoidance of residual palladium in the product. Several procedures for the Pd/C-catalyzed Sonogashira reactions have been reported, although the use of CuI, a phosphine ligand, and an amine is required.[7] In light of recent developments towards greener chemistry, a copper-, ligand-, and amine-free Pd/C-catalyzed Sonogashira coupling reaction under mild and aqueous reaction conditions would be of major interest for both industrial and academic applications. We now report the development of such a Sonogashira coupling reaction with a low Pd/C loading (0.4 mol%) and its application under aerobic conditions by using a wet-type (less pyrophoric) form of Pd/C.

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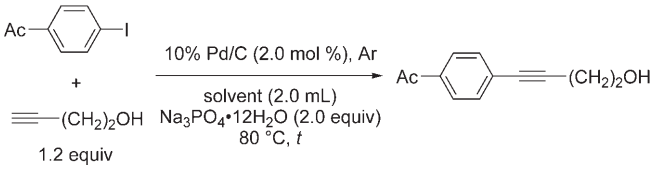
Results and Discussion

Initially, we choose $Na_3PO_4 \cdot 12H_2O$ as an environmentally-friendly inorganic base because its pK_{aH} value is nearly the same as amines universally used for the traditional Sonogashira coupling reaction, such as triethylamine or diethylamine. We then investigated the solvent effect for the 10% Pd/C-catalyzed Sonogashira coupling reaction between 4′-iodoacetophenone and 3-butyn-1-ol. Protic solvents, such as MeOH and 50% *i*PrOH, led to the good formation of the desired 1-[4-(4-hydroxybut-1-ynyl)phenyl]ethanone (Table 1, entries 7 and 9). However, lower yields were obtained in aprotic solvents, such as toluene, dioxane, and DMF, which were commonly used in the conventional Sonogashira protocol by using a homogeneous palladium catalyst, presumably due to the decomposition of the starting terminal alkyne (entries 1–5).[2] 50% *i*PrOH could dissolve $Na_3PO_4 \cdot 12H_2O$ and would work as a type of ligand for the Pd metal to enhance the reactivity.

Table 1. Effects of solvent on the Sonogashira coupling reaction.



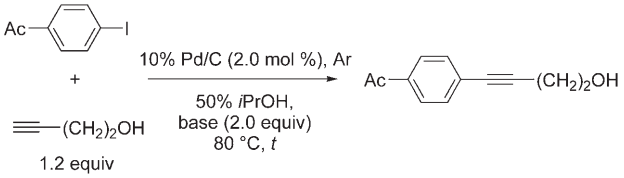
Entry	Solvent	*t* [h]	Yield [%][a]
1	toluene	24	7
2	MeCN	24	19
3	1,4-dioxane	24	22
4	THF	24	24
5	DMF	5	30
6	H_2O	6	34
7	MeOH	0.5	78
8	*i*PrOH	2	48
9	50% *i*PrOH	0.5	79

[a] Isolated yield.

We next optimized the inorganic base, since the reaction never proceeds without base (Table 2, entry 1). The coupling product was obtained in poor yields with relatively weak bases (pK_{aH} = 5-7), such as NaOAc, $NaHPO_4$, $NaHCO_3$, Na_2CO_3, and K_2CO_3 (entries 2–6), although the use of a strong base, $Na_3PO_4 \cdot 12H_2O$ (2 equiv, $pK_{aH} = 12.67$) gave a better result (79% yield, entry 7). It is noteworthy that the decreased use of $Na_3PO_4 \cdot 12H_2O$ from 2.0 to 1.5 equivalents caused a decrease in the reaction efficiency (entry 9).

The temperature of the reaction was also important for the effective progress of the Pd/C-catalyzed Sonogashira coupling reaction (Table 3). Raising the reaction temperature to 80°C significantly shortened the reaction time (entry 3) and afforded a better isolated yield (79%), although a further temperature increase to 100°C rather prolonged the reaction time (entry 4), which means that a temperature-dependent bell-shaped phenomenon of the reaction efficiency was observed.

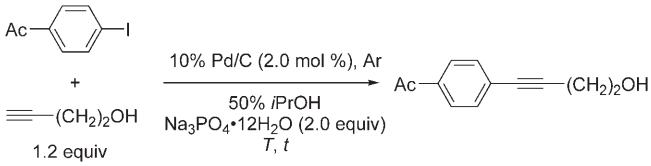
Table 2. Effects of bases on the Sonogashira coupling reaction.



Entry	Base	*t* [h]	Yield [%][a]
1	none	24	0
2	NaOAc	1.5	5
3	$NaHPO_4$	1.5	11
4	$NaHCO_3$	3	20
5	Na_2CO_3	6	19
6	K_2CO_3	6	36
7	$Na_3PO_4 \cdot 12H_2O$	0.5	79
8	$K_3PO_4 \cdot n H_2O$	0.5	66
9[b]	$Na_3PO_4 \cdot 12H_2O$	0.5	68

[a] Isolated yield. [b] 1.5 equivalents of $Na_3PO_4 \cdot 12H_2O$ were used in the reaction.

Table 3. Effects of reaction temperature on the Sonogashira coupling reaction.

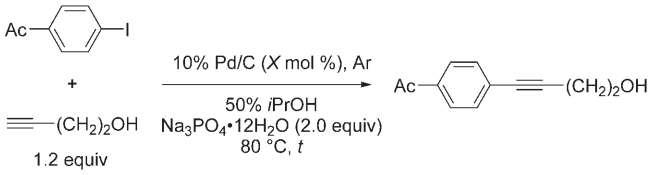


Entry	*T* [°C]	*t* [h]	Yield [%][a]
1	RT	24	34
2	40	6	72
3	80	0.5	79
4	100	3	78

[a] Isolated yield.

The catalyst use for the present coupling reaction also significantly affected the reaction efficiency (Table 4). The catalyst loading could be lowered to 0.4 mol% without any significant decrease in the isolated yield (entry 5). Further reduction of the catalyst amount would have presumably

Table 4. Effects of catalyst amount on the Sonogashira coupling reaction.



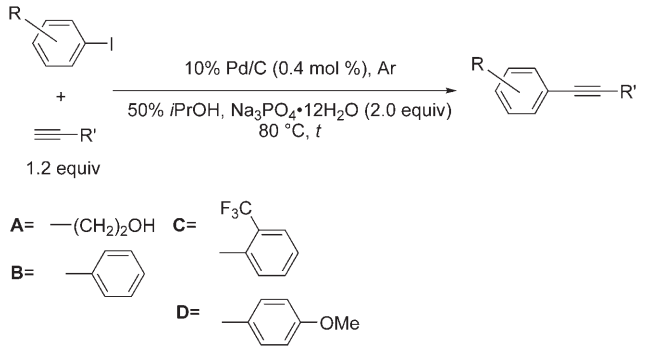
Entry	*X* (loading [mol%])	*t* [h]	Yield [%][a]
1	2	0.5	79
2	1	0.5	79
3	0.8	0.5	82
4	0.6	0.5	80
5	0.4	1	85
6	0.2	1.5	78
7	0.1	10	58

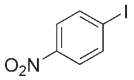
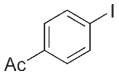
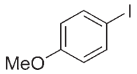
[a] Isolated yield.

caused a significant decrease in the efficiency of some unfavorable reactions, such as homocoupling, oligomerization, and polymerization of the alkynes, rather than the desired Sonogashira coupling reaction (entries 6 and 7).

We next explored the scope and limitations of the substrates under the optimized reaction conditions (10% Pd/C (0.4 mol% Pd) and $Na_3PO_4 \cdot 12H_2O$ (2.0 equiv) in 50% *i*PrOH at 80°C). Iodobenzene and the aryl iodides containing an electron-withdrawing group on the aromatic ring, such as nitro and acetyl functionalities and 3-iodopyridine,[8] a π-deficient heteroaryl iodide, were smoothly coupled with a variety of both aliphatic and aromatic terminal alkynes (Table 5, entries 1–12 and 17–20).[9] While the coupling of 4-iodoanisole containing an electron-donating methoxy group produced relatively lower efficiencies (38–72% yields), the coupling products were smoothly obtained (entries 13–16).

Table 5. Copper-, ligand-, and amine-free Pd/C-catalyzed Sonogashira coupling reactions of various aryl iodides with aliphatic and aromatic terminal alkynes.

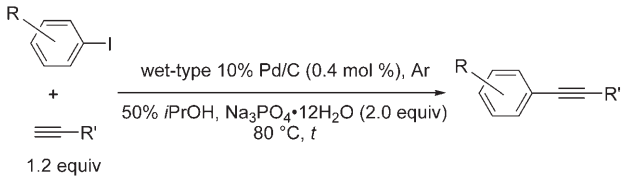


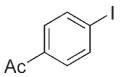
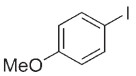
Entry	R	R′	*t* [h]	Yield [%][a]
1		**A**	1	85
2		**B**	0.5	95
3		**C**	0.5	90
4		**D**	1.5	96
5		**A**	1	85
6		**B**	1	93
7		**C**	1	90
8		**D**	0.5	96
9		**A**	0.5	52
10		**B**	0.5	66
11		**C**	0.5	86
12		**D**	0.5	76
13		**A**	0.5	38
14		**B**	0.5	51
15		**C**	0.5	87
16		**D**	0.5	54
17[b]		**A**	0.5	68
18[b]		**B**	3	83
19		**C**	3	96
20		**D**	1	87

[a] Isolated yield. [b] A terminal alkyne (2.0 equiv) was used in the reaction.

Use of wet-type (low pyrophoric) Pd/C: Dry-type Pd/C is extensively used in laboratory-scale reactions because of its ease of handling and storage. However, it is problematic for large-scale reactions, such as industrial processes, due to its pyrophobic nature under dry and atmospheric conditions. To avoid ignition, it is necessary to replace the air (oxygen) in the reaction vessel with an inert gas, such as argon or nitrogen, before carrying out the reaction, although this has not yet been perfected. Therefore, the use of the wet-type Pd/C (including ca. 50 wt% water) would make the reaction very safe and practical for an industrial scale process. Application of the wet-type Pd/C in the present Sonogashira coupling reaction gave totally comparable results with that of the dry-type Pd/C (Table 6, entries 1–8 versus Table 5, entries 5–8 and 13–16). As a result, the highly efficient Sonogashira coupling reaction with the wet-type Pd/C was established.

Table 6. Application of wet-type Pd/C in Sonogashira coupling reactions.



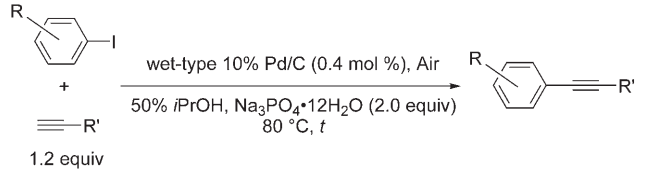
Entry	R	R′	*t* [h]	Yield [%][a]
1		**A**	0.5	81
2		**B**	0.5	90
3		**C**	0.5	91
4		**D**	0.5	87
5		**A**	0.5	50
6		**B**	0.5	56
7		**C**	0.5	81
8		**D**	0.5	52

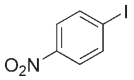
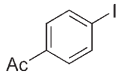
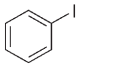
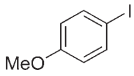
[a] Isolated yield.

Sonogashira coupling reaction with wet-type Pd/C under aerobic conditions: As described above, the present Sonogashira coupling reaction proceeds in aqueous media by using the wet-type Pd/C. The reaction conditions are very safe and there seems little chance for ignition. If the reaction is safely carried out under atmospheric conditions, we could avoid the tedious replacement of air with an inert gas in the reaction vessel. As shown in Table 7, iodobenzene and 4-iodoanisole as well as the 4-nitro- and 4-acetylaryl iodides were smoothly coupled with aromatic and aliphatic terminal alkynes catalyzed by the wet-type Pd/C under atmospheric conditions in 65–95% yields.

Reuse of Pd/C: The reusability of Pd/C (Table 8) has great advantages towards cost reduction and decreasing environmental pollution. The reuse test of Pd/C was examined in the coupling reaction between 4′-iodoacetophenone and 3-butyn-1-ol. The 10% Pd/C could be reused until the second run without significant loss of catalyst efficiency. However, the reaction time was extended and the yield was signifi-

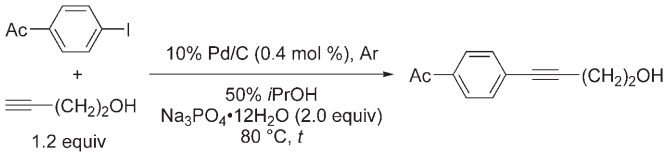
Table 7. Sonogashira coupling reactions with wet-type Pd/C in air.



Entry	R	R′	*t* [h]	Yield [%][a]
1		**B**	1	95
2		**A**	0.5	80
3		**D**	2	65
4		**C**	1	76

[a] Isolated yield.

Table 8. Investigation into the reuse of Pd/C.



Entry	Run	*t* [h]	Yield [%][a]
1	1	3	82
2	2	3	85
3	3	24	25

[a] Isolated yield.

cantly dropped in the third run due to a presumable deactivation of the catalyst.[10] Fresh Pd/C should be used in the present reaction system.

Conclusions

We have developed a copper-, ligand-, and amine-free Pd/C-catalyzed Sonogashira coupling reaction in aqueous media. Various aryl iodides and a heteroaryl iodide underwent the coupling reaction with aliphatic and aromatic alkynes to afford the corresponding aryl and heteroaryl alkynes in moderate to excellent yields. Furthermore, we demonstrated that the wet-type Pd/C-catalyzed Sonogashira coupling reaction efficiently proceeded under argon and aerobic conditions. Our developed protocol will provide a facile, efficient, safe, and environmentally friendly process for the Sonogashira coupling reaction and could be used in industrial applications.

Experimental Section

Materials: All reagents and solvents were obtained from commercial suppliers and were used without further purification. Dry-type 10% Pd/C (K-type) and wet-type 10% Pd/C (K-type, 200 g (Pd/C)/454 g) were supplied by the N. E. Chemcat Corporation (Tokyo, Japan). TLC was performed on precoated silica gel 60 F_{254} plates (Merck). The ^{1}H NMR and ^{13}C NMR spectra were recorded on either a JEOL JNM AL-400 or JEOL JNM EX-400 spectrometer, and $CDCl_3$ was used as the solvent. Low and high-resolution mass spectra were taken by using a JEOL JMS-SX 102A spectrometer.

General procedure for Pd/C-catalyzed copper-, ligand-, and amine-free Sonogashira coupling reactions under an argon atmosphere (Table 5): Under an argon atmosphere, a 15 mL test tube was charged with an aryl iodide (0.5 mmol), terminal alkyne (0.6 mmol), dry-type 10% Pd/C (2.1 mg, 0.002 mmol), Na_3PO_4•12H_2O (380 mg, 1.00 mmol), *i*PrOH (1 mL), and H_2O (1 mL). The reaction mixture was placed on the Chemistation personal organic synthesizer (EYELA, Tokyo), heated at 80°C, and stirred for a specific time. The mixture was diluted with EtOAc (10 mL) and H_2O (10 mL), and then filtered by using a membrane filter (Millipore, Millex-LH, 0.45 μm). The organic phase was separated and the water layer was extracted with EtOAc (2×10 mL). The combined organic layers were washed with brine (20 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was removed by vacuum evaporation. The residue was purified by silica-gel column chromatography with *n*-hexane/EtOAc as the eluent.

General procedure for wet-type Pd/C-catalyzed copper-, ligand-, and amine-free Sonogashira coupling reactions in air (Table 7): In air, a 15 mL test tube was charged with the aryl iodide (0.5 mmol), terminal alkyne (0.6 mmol), wet-type 10% Pd/C (4.8 mg, 0.002 mmol), Na_3PO_4•12H_2O (380 mg, 1.00 mmol), *i*PrOH (1 mL), and H_2O (1 mL). The reaction mixture was placed on the Chemistation personal organic synthesizer (EYELA, Tokyo), heated at 80°C, and stirred for a specific time. The mixture was diluted with EtOAc (10 mL) and H_2O (10 mL), and then filtered by using a membrane filter (Millipore, Millex-LH, 0.45 μm). The organic phase was separated and the water layer was extracted with EtOAc (2×10 mL). The combined organic layers were washed with brine (20 mL) and dried with anhydrous Na_2SO_4. After filtration, the solvent was removed by vacuum evaporation. The residue was purified by silica-gel column chromatography by using *n*-hexane/EtOAc as the eluent.

4-(4-Nitrophenyl)but-3-yn-1-ol (Table 5, entry 1): Yellow solid; m.p. 76–78; ^{1}H NMR: δ=8.16 (d, J=8.6 Hz, 2H), 7.54 (d, J=8.6 Hz, 2H), 3.86 (td, J=6.1, 6.1 Hz, 2H), 2.74 (t, J=6.1 Hz, 2H), 1.77 ppm (t, J=6.1 Hz, 1H); ^{13}C NMR: δ=146.9, 132.4, 130.4, 123.5, 92.6, 80.8, 60.9, 23.9 ppm; MS (EI): *m*/*z*: 191 (80) [M^+], 161 (100), 144 (25), 115 (62); HRMS (EI): calcd for $C_{10}H_9NO_3$: 191.05825 [M^+]; found: 191.05748; elemental analysis calcd (%) for $C_{10}H_9NO_3$: C 62.82, H 4.74, N 7.33; found: C 62.61, H 4.69, N 7.28.

1-[2-(4-Nitrophenyl)ethynyl]benzene (Table 5, entry 2): ^{1}H NMR: δ=8.23 (d, J=8.8 Hz, 2H), 7.67 (d, J=8.8 Hz, 2H), 7.57–7.55 (m, 2H), 7.40–7.38 ppm (m, 3H); MS (EI): *m*/*z*: 223 (100) [M^+], 193 (30), 176 (45), 151 (20); the ^{1}H NMR spectrum was identical to that reported in the literature.[11]

1-Nitro-4-{2-[2-(trifluoromethyl)phenyl]ethynyl}benzene (Table 5, entry 3): Pale-yellow solid; m.p. 94–96; ^{1}H NMR: δ=8.24 (dd, J=7.7, 1.2 Hz, 2H), 7.74–7.68 (m, 4H), 7.57 (t, J=7.4 Hz, 1H), 7.49 ppm (t, J=7.4 Hz, 1H); ^{13}C NMR: δ=147.4, 134.0, 132.4, 132.1, 131.6, 129.6, 129.0, 126.1 (q, $^3J_{CF}$=5.2 Hz), 123.7, 123.4 (q, $^1J_{CF}$=273.6 Hz), 120.4 (q, $^2J_{CF}$=2.2 Hz), 92.7, 90.3 ppm; MS (EI): *m*/*z*: 291 (100) [M^+], 261 (20), 245 (20), 225 (20); HRMS (EI): calcd for $C_{15}H_8F_3NO_2$: 291.05071 [M^+]; found: 291.05020; elemental analysis calcd (%) for $C_{15}H_8F_3NO_2$•1/8H_2O: C 61.39, H 2.83, N 4.77; found: C 61.74, H 3.16;, N 4.87.

1-[2-(4-Methoxyphenyl)ethynyl]-4-nitrobenzene (Table 5, entry 4): ^{1}H NMR: δ=8.20 (d, J=9.0 Hz, 2H), 7.63 (d, J=9.0 Hz, 2H), 7.50 (d, J=8.8 Hz, 2H), 6.91 (d, J=8.8 Hz, 2H), 3.85 ppm (s, 3H); MS (EI): *m*/*z*:

253 (100) [M^+], 233 (15), 207 (15), 163 (20); the ^{1}H NMR spectrum was identical to that reported in the literature.[12]

1-[4-(4-Hydroxybut-1-ynyl)phenyl]ethanone (Table 5, entry 5): ^{1}H NMR: δ=7.89 (d, J=8.5 Hz, 2H), 7.49 (d, J=8.5 Hz, 2H), 3.84 (td, J=6.3, 6.3 Hz, 2H), 2.73 (t, J=6.3 Hz, 2H), 2.60 (s, 3H), 1.78 ppm (t, J=6.3 Hz, 1H); MS (EI): m/z: 188 (90) [M^+], 173 (100), 143 (48), 115 (30); the ^{1}H NMR spectrum was identical to that reported in the literature.[13]

1-[4-(2-Phenylethynyl)phenyl]ethanone (Table 5, entry 6): ^{1}H NMR: δ= 7.94 (d, J=8.3 Hz, 2H), 7.61 (d, J=8.3 Hz, 2H), 7.57–7.54 (m, 2H), 7.38–7.36 (m, 3H), 2.62 ppm (s, 3H); MS (EI): m/z: 220 [M^+] (70), 205 (100), 176 (35), 151 (15); the ^{1}H NMR spectrum was identical to that reported in the literature.[11]

1-{4-[2-(2-Trifluoromethylphenyl)ethynyl]phenyl}ethanone (Table 5, entry 7): Pale-yellow solid; m.p. 82–84; ^{1}H NMR: δ=8.24 (dd, J=8.6, 1.6 Hz, 2H), 7.72–7.68 (m, 2H), 7.63 (dd, J=8.6, 1.6 Hz, 1H), 7.55 (t, J= 7.7 Hz, 1H), 7.46 (t, J=7.7 Hz, 1H), 2.62 ppm (s, 3H); ^{13}C NMR: δ= 197.4, 136.9, 134.1, 132.3, 132.0, 131.7, 128.7, 128.5, 127.7, 126.2 (q, $^3J_{CF}$= 5.0 Hz), 123.8 (q, $^1J_{CF}$=273.4 Hz), 121.1 (q, $^2J_{CF}$=2.2 Hz), 94.1, 88.6, 26.7 ppm; MS (EI): m/z: 288 (55) [M^+], 273 (100), 245 (20), 225 (20); HRMS (EI): calcd for $C_{17}H_{11}OF_3$: 288.07621 [M^+]; found: 288.07505; elemental analysis calcd (%) for $C_{17}H_{11}OF_3$: C 70.83, H 3.85; found: C 70.95, H 3.89.

1-{4-[2-(4-Methoxyphenyl)ethynyl]phenyl}ethanone (Table 5, entry 8): ^{1}H NMR: δ=7.93 (d, J=8.8 Hz, 2H), 7.58 (d, J=8.8 Hz, 2H), 7.49 (d, J=9.0 Hz, 2H), 6.89 (d, J=9.0 Hz, 2H), 3.84 (s, 3H), 2.61 ppm (s, 3H); MS (EI): m/z: 250 (100) [M^+], 207 (15), 163 (20); the ^{1}H NMR spectrum was identical to that reported in the literature.[11]

4-Phenyl-but-3-yn-1-ol (Table 5, entry 9): ^{1}H NMR: δ=7.42–7.40 (m, 2H), 7.30–7.28 (m, 2H), 3.81 (td, J=6.1, 6.1 Hz, 2H), 2.69 (t, J=6.1 Hz, 2H), 1.85 ppm (t, J=6.1 Hz, 1H); MS (EI): m/z: 146 (50) [M^+], 128 (10), 115 (100); the ^{1}H NMR spectrum was identical to that reported in the literature.[14]

Diphenylacetylene (Table 5, entry 10): ^{1}H NMR: δ=7.54–7.50 (m, 4H), 7.36–7.32 ppm (m, 6H); MS (EI): m/z: 178 (100) [M^+], 173 (100); the ^{1}H NMR spectrum was identical to that reported in the literature.[11]

1-{2-[2-(Trifluoromethyl)phenyl]ethynyl}benzene (Table 5, entry 11): ^{1}H NMR: δ=7.64 (d, J=7.7 Hz, 1H), 7.62 (d, J=7.7 Hz, 1H), 7.55–7.53 (m, 2H), 7.46 (t, J=7.7 Hz, 1H), 7.37–7.32 ppm (m, 4H); MS (EI): m/z: 246 (100) [M^+], 225 (15); the ^{1}H NMR spectrum was identical to that reported in the literature.[15]

1-[2-(4-Methoxyphenyl)ethynyl]benzene (Table 5, entries 12 and 14): ^{1}H NMR: δ=7.52–7.46 (m, 4H), 7.34–7.32 (m, 3H), 6.88 (d, J=9.1 Hz, 2H), 3.83 ppm (s, 3H); MS (EI): m/z: 208 (100) [M^+], 165 (30); the ^{1}H NMR spectrum was identical to that reported in the literature.[11]

4-(4-Methoxyphenyl)but-3-yn-1-ol (Table 5, entry 13): ^{1}H NMR: δ=7.34 (d, J=8.8 Hz, 2H), 6.81 (d, J=8.8 Hz, 2H), 3.79 (s, 3H), 3.79 (t, J= 6.3 Hz, 2H), 2.66 (t, J=6.3 Hz, 2H), 2.02 ppm (brs, 1H); ^{13}C NMR: δ= 159.3, 133.0, 115.4, 113.8, 84.7, 82.2, 61.2, 55.2, 23.8 ppm; MS (EI): m/z: 176 (55) [M^+], 145 (100); HRMS (EI): calcd for $C_{11}H_{12}O_2$: 176.08373 [M^+]; found: 176.08334.

1-[2-(4-Methoxyphenyl)ethynyl](trifluoromethyl)benzene (Table 5, entry 15): Yellow solid; m.p. 68–72; ^{1}H NMR: δ=7.64–7.59 (m, 2H), 7.55–7.53 (m, 2H), 7.48–7.42 (m, 1H), 7.32 (t, J=7.7 Hz, 1H), 6.85 (d, J=8.2 Hz, 2H), 3.77 ppm (s, 3H); ^{13}C NMR: δ=159.8, 133.1, 132.9, 131.8, 131.5, 131.3, 131.0, 130.7, 130.4, 129.3, 127.8, 127.2, 126.4, 126.3, 125.5 (q, $^3J_{CF}$=5.2 Hz), 123.4 (q, $^1J_{CF}$=273.4 Hz), 121.6 (q, $^2J_{CF}$=2.2 Hz), 114.5, 113.9, 113.7, 94.9, 84.0, 54.9 ppm; MS (EI): m/z: 276 (100) [M^+], 233 (20); HRMS (EI): calcd for $C_{16}H_{11}OF_3$: 276.07621 [M^+]; found: 276.07696; elemental analysis calcd (%) for $C_{16}H_{11}OF_3$: C 69.56, H 4.01; found: C 69.30, H 4.07.

1,2-Bis(4-methoxyphenyl)ethyne (Table 5, entry 16): ^{1}H NMR: δ=7.44 (d, J=8.5 Hz, 4H), 6.86 (d, J=8.5 Hz, 4H), 3.82 ppm (s, 3H); MS (EI): m/z: 238 (100) [M^+], 223 (55), 195 (10), 152 (10); the ^{1}H NMR spectrum was identical to that reported in the literature.[16]

4-(Pyridin-3-yl)but-3-yn-1-ol (Table 5, entry 17): ^{1}H NMR: δ=8.53 (s, 1H), 8.37 (dd, J=4.8, 1.7 Hz, 1H), 7.60 (dd, J=6.2, 1.7 Hz, 1H), 7.15–7.11 (m, 1H), 4.15 (brs, 1H), 3.76 (dd, J=6.3, 2.6 Hz, 2H), 2.63 ppm (dd, J=6.3, 2.9 Hz, 2H); MS (EI): m/z: 147 (80) [M^+], 117 (100); the ^{1}H NMR spectrum was identical to that reported in the literature.[17]

3-(2-Phenylethynyl)pyridine (Table 5, entry 18): ^{1}H NMR: δ=8.53 (s, 1H), 8.37 (dd, J=4.8, 1.7 Hz, 1H), 7.60 (dd, J=6.2, 1.7 Hz, 1H), 7.15–7.11 (m, 1H), 4.15 (brs, 1H), 3.76 (dd, J=6.3, 2.6 Hz, 2H), 2.63 ppm (dd, J=6.3, 2.9 Hz, 2H); MS (EI): m/z; 147 (80) [M^+], 117 (100); the ^{1}H NMR spectrum was identical to that reported in the literature.[11]

3-{2-[2-(Trifluoromethyl)phenyl]ethynyl}pyridine (Table 5, entry 19): Yellow oil; ^{1}H NMR: δ=8.78 (d, J=1.6 Hz, 1H), 8.58 (dd, J=5.0, 1.6 Hz, 1H), 7.84–7.81 (m, 1H), 7.70 (d, J=7.6 Hz, 1H), 7.68 (d, J= 7.6 Hz, 1H), 7.53 (t, J=7.6 Hz, 1H), 7.45 (t, J=7.6 Hz, 1H), 7.32–7.28 ppm (m, 1H); ^{13}C NMR: δ=152.2, 149.0, 138.5, 133.7, 131.8, 131.5, 128.5, 125.9 (q, $^3J_{CF}$=4.9 Hz), 123.5 (q, $^1J_{CF}$=273.6 Hz), 123.0, 120.7, 119.9, 91.3, 88.5 ppm; MS (EI): m/z: 247 (100) [M^+], 226 (215); HRMS (EI): calcd for $C_{14}H_8NF_3$: 247.06088 [M^+]; found: 247.06069; elemental analysis calcd (%) for $C_{15}H_8F_3NO_2 \cdot 1/8\,H_2O$: C 61.39, H 2.83, N 4.77; found: C 61.74, H 3.16, N 4.87.

3-[2-(4-Methoxyphenyl)ethynyl]pyridine (Table 5, entry 20): ^{1}H NMR: δ=8.74 (d, J=1.7 Hz, 1H), 8.52 (dd, J=5.1, 1.7 Hz, 1H), 7.77 (dt, J= 7.7, 1.9, 1.9 Hz, 1H), 7.48 (d, J=8.7 Hz, 2H), 7.28–7.25 (m, 1H), 6.89 (d, J=8.7 Hz, 2H), 3.84 ppm (s, 3H); MS (EI): m/z: 209 [M^+], 100), 194 (40), 166 (25); the ^{1}H NMR spectrum was identical to that reported in the literature.[11]

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