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Copper-catalyzed decarboxylative coupling of aryl halides with alkynyl carboxylic acids performed in water

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ABSTRACT

Most alkynes are volatile liquids, which are relatively difficult to use and to transport. In contrast, alkynyl carboxylic acids offer a stable and attractive alternative for the alkynylation reactions. Here, we employed alkynyl carboxylic acids as reaction partners for the alkynylation of aryl halides. Copper-catalyzed decarboxylative coupling, including various challenging aryl bromides with phenylpropiolic acid, was performed in water without using co-solvents with good yields. Our approach provides a low-loading, low-cost, stable and environmentally friendly copper catalyst system for decarboxylative coupling.

1. Introduction

Transition metal-catalyzed cross-coupling reactions are extremely useful in organic synthesis of materials or drugs for modern chemical and medical applications, because they offer a powerful means for the construction of many carbon–carbon bonds.[1] In particular, the Sonogashira reaction of terminal alkynes with aryl and alkenyl halides is an effective approach for the preparation of acetylene derivatives.[2] As a result, enormous effort has been devoted to improve catalytic activity and expand the scope of substrates of this useful reaction, which was first reported by Sonogashira in 1975.[3,4] However, most of the alkynes are volatile liquids, which are relatively difficult to use and transport.[5] Therefore, the use of some other readily available substrates rather than terminal alkynes for the straightforward synthesis of arylalkynes, remains a practical challenge.[5] Recently, alkynyl carboxylic acids were found to represent a promising alternative to terminal alkynes for coupling reactions.[6] In 2008, P. H. Lee and co-workers developed the first example of such decarboxylative coupling in the presence of $Pd_2(dba)_3$ and phosphine-ligands, including dppf and dppb.[6a] In addition, Kim and Lee also found that $Pd_2(dba)_3$ together with PPh_3 or Xantphos could also catalyze the couplings in high yields.[6b] Very recently, Li found that combination of $Pd(OAc)_2$ and Xphos could catalyze decarboxylative coupling reactions of alkynyl carboxylic acids with a wide range of aryl halides.[6c] Furthermore, Song and Lee have prepared the symmetrical and unsymmetrical diarylalkynes from propiolic acid using decarboxylative coupling using $Pd(PPh_3)_2Cl_2$/dppb catalytic system.[6d] However, these protocols were limited to academic use owing to the high cost of palladium complexes. There are two routes to solve the problem of catalyst expense: one method is to reduce the catalytic loading of the palladium catalyst or alternatively, to introduce cheaper catalysts, preferably those with lower toxicity than palladium to facilitate downstream processing. Encouragingly, You and his co-workers recently developed the first example of such decarboxylative coupling in the presence of commercially available CuI and 1,10-phenanthroline (phen), although the catalyst loading is high (10 mol %) and reaction conditions are slightly harsh (130 °C).[6f] Recently, we just reported that $Fe(acac)_3$/CuI showed better catalytic activity with low-loading catalyst,[6g] however, the reaction temperature of this protocol was still high (140 °C). After screening various ligands, we found that copper-catalyzed decarboxylative coupling between aryl halide and alkynyl carboxylic acids could be conducted efficiently in DMSO at 90 °C using PPh_3 as the ligand.[6h] With the further effort, we just found the reaction could be performed in water and good results were obtained. Considering that the current methodology was more useful and practical, herein, we want to disclose all of findings about the copper-catalyzed decarboxylative coupling as a full paper.

Water is considered as the 'green' solvent and has low-cost. It is also safer than the usual solvents, which are often inflammable and

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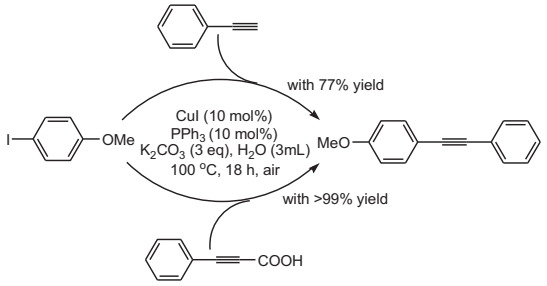
explosive. From an industrial point of view, the use of a two-phase system allows an easy separation of the products from the water-soluble organometallic catalyst by simple phase separation.[7] More importantly, the development of organic reactions in water is helpful to understand the nature of the enzymes-catalyzed reaction performed in the human body. With our increasing interest in various cross-coupling reactions,[8] we describe our efforts on the development of the low-loading, low-cost, stable and environmentally friendly copper catalyst system for such decarboxylative coupling.

2. Results and discussion

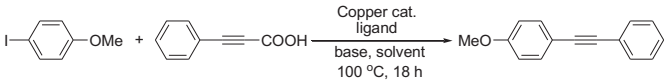
Initially, we chose phenylacetylene as the cross-coupling partner and examined its reaction with 4-iodoanisole in the presence of CuI and PPh_3 in water.[9] The desired product was obtained in moderate yield (77%) as shown in Scheme 1. Considering the poor solubility of the phenylacetylene in water, phenylpropiolic acid was then chosen as the alternative partner. Without any need for further optimization, treatment of 4-iodoanisole with phenylpropiolic acid afforded the corresponding product in quantitative yield.



Scheme 1. Copper-catalyzed alkynylation of 4-iodoanisole in the presence of different alkyne partners.

We continued our investigation using phenylpropiolic acid and 4-iodoanisole as model substrates. First, in order to confirm our promising initial result and to attempt to exclude the influence of metal contaminant, we carried out experiments in new flasks with new stirring bars and new caps. We found that CuI of higher purity (99.999%, from Aldrich) and K_2CO_3 (99.0%, from Alfa) could catalyze this coupling in high yield (>99%) (Table 1, entry 1) (for certificate of analysis, see the Supplementary data). In comparison, traditional Pd species, such as $Pd(OAc)_2/PPh_3$ and $Pd(OAc)_2/CuI/PPh_3$ could not show any catalytic activity in this reaction (Table 1, entries 2 and 3). Lower reaction temperature led to poor result (Table 1, entry 4). Subsequently, various readily available ligands were employed, including other monodentate P-ligands (PCy_3 and $P(OPh)_3$), O,O-ligands (binaphthol (binol)), N,N-ligand (1,10-phenanthroline (phen)) and N,O-ligand (8-hydroxquinoline) (Table 1, entries 5–9). Commercially available PPh_3 afforded the best catalytic results. Control experiments confirmed that CuI alone in the absence of ligand was unable to catalyze the coupling reaction (Table 1, entry 10). With the optimized CuI/PPh_3 catalytic system in hand, we then screened other various catalytic conditions. First, various inorganic and organic bases were tested: K_3PO_4, Cs_2CO_3 and Et_3N as the base also resulted in almost quantitative desired product (Table 1, entries 11–13). However, NaOAc as the base afforded the corresponding product in only 39% yield (Table 1, entry 14). Subsequently, varying amounts of CuI and PPh_3 were investigated (Table 1, entries 15–18). The best ratio of CuI and PPh_3 was 1:2 (Table 1, entry 18). Subsequently, different copper sources were evaluated at low-catalyst loading (2 mol %), including $Cu(acac)_2$, CuBr and Cu powder (Table 1, entries 19–21). The best result was generated from CuI-catalyzed coupling. Finally, longer reaction time (24 h) under argon atmosphere gave exclusively the desired product in almost quantitative yield (Table 1, entry 22). Under the same conditions, the commonly-used solvents, such as NMP, dioxane, toluene, DMF and DMSO, were employed into the reaction (Table 1, entries 23–27) and DMSO afforded the quantitative product (Table 1, entry 27).[6h]

Table 1
Screening catalytic conditions in decarboxylative coupling between 4-iodoanisole and phenylpropiolic acid performed in water[a]

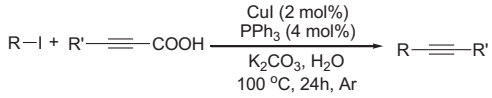


Entry	Cat. (mol %)	Ligand (mol %)	Solvent	Base	Yield[b] (%)
1[c]	CuI (10)	PPh_3 (10)	Water	K_2CO_3	>99
2	$Pd(OAc)_2$ (10)	PPh_3 (10)	Water	K_2CO_3	Trace
3[d]	Pd–Cu (10)	PPh_3 (10)	Water	K_2CO_3	Trace
4[e]	CuI (10)	PPh_3 (10)	Water	K_2CO_3	30
5	CuI (10)	Phen (10)	Water	K_2CO_3	5
6	CuI (10)	Oxine (10)	Water	K_2CO_3	8
7	CuI (10)	Binol (10)	Water	K_2CO_3	Trace
8	CuI (10)	PCy_3 (10)	Water	K_2CO_3	<5
9	CuI (10)	$P(OPh)_3$ (10)	Water	K_2CO_3	<5
10	CuI (10)	—	Water	K_2CO_3	<5
11	CuI (10)	PPh_3 (10)	Water	K_3PO_4	98
12	CuI (10)	PPh_3 (10)	Water	Et_3N	97
13	CuI (10)	PPh_3 (10)	Water	Cs_2CO_3	96
14	CuI (10)	PPh_3 (10)	Water	NaOAc	39
15	CuI (5)	Phen (10)	Water	K_2CO_3	>99
16	CuI (5)	Phen (5)	Water	K_2CO_3	91
17	CuI (2)	PPh_3 (2)	Water	K_2CO_3	83
18	CuI (2)	PPh_3 (4)	Water	K_2CO_3	93
19	$Cu(acac)_2$ (2)	PPh_3 (4)	Water	K_2CO_3	80
20	CuBr (2)	PPh_3 (4)	Water	K_2CO_3	92
21	Cu (2)	PPh_3 (4)	Water	K_2CO_3	90
22[f]	CuI (2)	PPh_3 (4)	Water	K_2CO_3	99
23[f,g]	CuI (2)	PPh_3 (4)	NMP	K_2CO_3	11
24[f,g]	CuI (2)	PPh_3 (4)	DMF	K_2CO_3	97
25[f,g]	CuI (2)	PPh_3 (4)	Dioxane	K_2CO_3	78
26[f,g]	CuI (2)	PPh_3 (4)	Toluene	K_2CO_3	29
27[f,g]	CuI (2)	PPh_3 (4)	DMSO	K_2CO_3	>99

[a] Reaction conditions: 4-iodoanisole (0.3 mmol), phenylpropiolic acid (0.4 mmol), base (0.9 mmol), water (3 mL), 100 °C, 18 h, under air.
[b] Isolated yield (based on 4-iodoanisole).
[c] CuI (99.999%) from Aldrich was employed.
[d] $Pd(OAc)_2$ (10 mol %), CuI (10 mol %).
[e] 80 °C.
[f] 24 h, in Ar.
[g] 90 °C.

With optimized conditions now in hand, we explored the scope of this process with respect to a wide array of aryl halides as summarized in Table 2. It can be seen that whether the reactions were performed in DMSO or water, high yields of desired products were obtained. Only several entries showed the obvious difference. Generally, high yields were obtained with substrates, regardless of the positions of aryl substituent (Table 2, entries 1–3). It is noteworthy that the ester group was sensitive in water and lower yield was obtained comparing with the yield in DMSO (40% vs 99%, Table 2, entry 4). In addition, for the aryl iodides with electron-deficient or electron-rich substituents, the desired products were acquired with good to excellent yields (Table 2, entries 5–13). It is of particular relevance that the reaction conditions were compatible with the presence of different functional groups, such as ketone, amino and nitro groups (Table 2, entries 5, 12, 13), which may then be subject to further synthetic transformations. When 2-butynoic acid was used as the substrate, the desired product was obtained in 23% yield using water as solvent and 86% yield was got using DMSO as the solvent (Table 2, entry 14). In comparison, 2-octynoic acid as the alkyne partner gave excellent results (Table 2, entries 15–19). We were pleased to discover that the substituted phenylpropiolic acids

Table 2
Scope of copper-catalyzed decarboxylative coupling of various aryl iodides and alkynoic acids performed in water or DMSO[a]



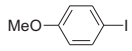
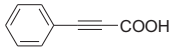
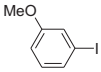
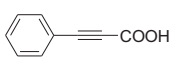
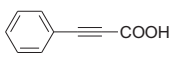
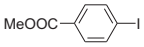
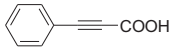
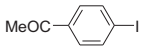
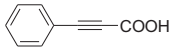
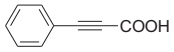
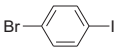
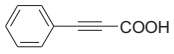
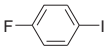
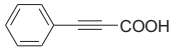
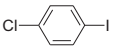
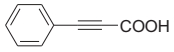
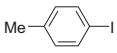
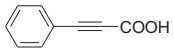
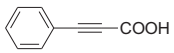
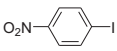
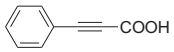
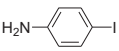
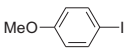
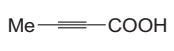
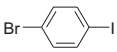
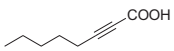
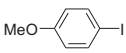
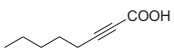
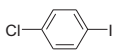
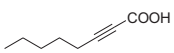
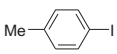
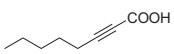
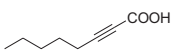
Entry	RI	R′C≡CCOOH	Yield[b] (%)	Yield[c] (%)
1			99	99
2			99	97
3			82	97
4			99	40
5			98	87
6			97	99
7			98	86
8			97	72
9			99	92
10			99	99
11			99	75
12			92	99
13			95	97
14			86	23
15			94	92
16			99	99
17			88	94
18			95	95
19			95	89
20			93	91
21			98	96
22			98	94

Table 2 (*continued*)

Entry	RI	R′C≡CCOOH	Yield[b] (%)	Yield[c] (%)
23			96	99
24			95	91
25			93	89
26			85	NR

[a] Reaction conditions: aryl iodide (0.3 mmol), alkynoic acid (0.4 mmol), CuI (2 mol %), PPh_3 (4 mol %), K_2CO_3 (0.9 mmol), solvent (3 mL), 100 °C, 24 h, under Ar. Isolated yield based on aryl iodide (average of two runs).
[b] DMSO as the solvent.
[c] Water as the solvent.

could couple with aryl iodides to afford the desired products also in high yields (Table 2, entries 20–25). The coupling between 2-phenylethyl iodide and phenylpropiolic acid in water was failure, although the coupling in DMSO afforded the desired product in 85% yield (Table 2, entry 26).

In order to extend the application of our methodology, the coupling of 1,3-diiodobenzene and phenylpropiolic acid was carried out using a lower-loading of catalyst (4 mol % CuI). Almost quantitative desired product was obtained as shown in Scheme 2.

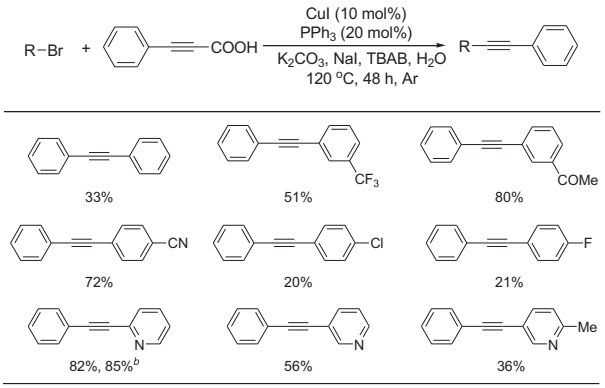
Scheme 2. Coupling of 1,3-diiodobenzene and phenylpropiolic acid using CuI (4 mol %) and PPh_3 (8 mol %).

We then addressed the possibility of using more challenging substrates. After screening different additives, TBAB (tetrabutyl ammonium bromide) as the phase transfer catalyst (PTC) was the shown as the most effective. Furthermore, addition of 2 equiv of NaI could result in markedly higher yields, which is possibly due to the aryl bromides being converted into their corresponding iodides in situ by Br/I exchange during the catalytic reaction.[10] These reactions were carried out in sealed tube at slightly higher temperature (120 °C) and higher catalyst loading. As presented in Table 3, treatment of aryl bromides with phenylpropiolic acid afforded the products in moderate to good yields (up to 82%). For the same substrate, 85% yield of the desired product was obtained when the reaction was performed in DMSO.

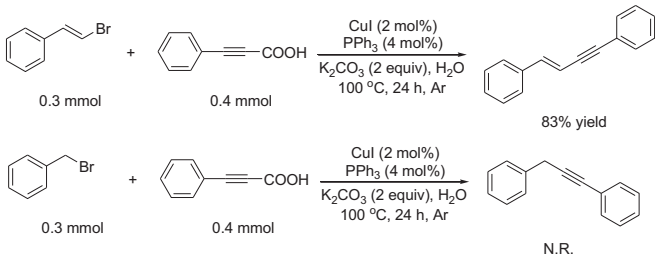
Furthermore, this methodology could be applied to the coupling between phenylpropiolic acid and vinyl bromide to prepare 1,3-enyne with 83% yield, as shown in Scheme 3. In contrast, we were unable to obtain the corresponding product when we chose benzyl bromide as the cross-coupling partner. However, many biologically active molecules contain a 1,3-enyne substructure,[11] and, therefore, this approach provides a novel way of synthesizing useful compounds. Noteworthy is that the double bond geometry of the vinyl halide was retained with our protocol.

A proposed working mechanism as outlined in Fig. 1 was formulated on the basis of the mechanism reported earlier.[9a,12] First, it seems reasonable to propose copper(I) complex (**A**) as a catalytic species with a P-ligand of PPh_3 coordinated to the metal. The reaction between (**A**) and alkynoic acid affords an intermediate (**B**), which undergo decarboxylation to produce the alkynyl copper

Table 3
Scope of copper-catalyzed decarboxylative coupling of various aryl bromides and phenylpropiolic acid performed in water[a]



[a] Reaction conditions: Aryl bromide (0.3 mmol), phenylpropiolic acid (0.4 mmol), CuI (10 mol%), PPh_3 (20 mol%), K_2CO_3 (0.9 mmol), NaI (0.6 mmol), TBAB (0.3 mmol), H_2O (3 mL), 120 °C, 48 h, under Ar. Isolated yield based on aryl bromide (average of two runs). [b] DMSO as the solvent.



Scheme 3. Coupling of (*E*)-β-bromostyrene or benzyl bromide and phenylpropiolic acid using CuI (2 mol %) and PPh_3 (4 mol %).

intermediate (**C**). Addition of aryl halide (**D**), followed by a reductive elimination, gives the coupling product, regenerating copper(I) complex (**A**).

3. Conclusions

In summary, highly effective copper-catalyzed decarboxylative couplings between various aryl halides and alkynoic acids were performed in water. Generally, the desired products were obtained in good to excellent yields. It is noteworthy that this protocol is palladium-free, co-solvent-free and low-catalyst loading, which represents a practical and low-cost way to prepare arylalkynes. Thus, it is potentially useful in synthesis of some biologically active molecules. Further investigations in this direction are in progress.

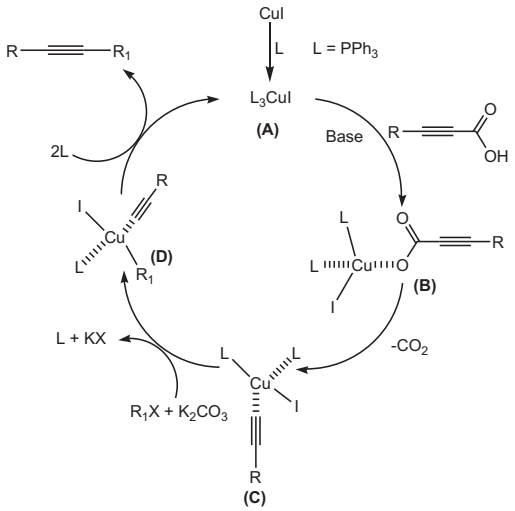


Fig. 1. Possible working mechanism.

4. Experiment

4.1. General information

All reactions were carried out under an argon atmosphere condition. Solvents including NMP, DMF, DMSO, dioxane and toluene were dried and degassed by standard methods, and all aryl halides and bases were purchased from Aldrich, Alfa and TCI. All other commercial reagents and solvents were used without purification. Column chromatography was performed using silica gel (300–400 mesh). Analytical thin-layer chromatography was performed using glass plates pre-coated with 200–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). NMR spectra were measured in $CDCl_3$ on a Varian Inova-400 NMR spectrometer (400 MHz) with TMS as an internal reference.

4.2. General procedure for copper-catalyzed decarboxylative coupling of various aryl halides and alkynoic acids performed in water using PPh_3 as the ligand

Aryl halide (0.5 mmol), alkynoic acid (0.6 mmol), CuI (2 mol %), PPh_3 (4 mol %) and K_2CO_3 (1.0 mmol) were added to a screw-capped test tube. The tube was then evacuated and backfilled with argon (3 cycles). H_2O (3 mL) was added by syringe at room temperature. The tube was again evacuated and backfilled with argon (3 cycles). The mixture was heated to 100 °C and stirred for 24 h. After cooling to room temperature, the mixture was diluted with water, and the combined aqueous phases were extracted three times with ethyl acetate. The organic layers were combined, dried over Na_2SO_4 and concentrated to yield the crude product, which was further purified by silica gel chromatography, using petroleum ether and ethyl acetate as eluent to provide the desired product.

4.2.1. 1-(2-(4-Methoxyphenyl)ethynyl)benzene. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.52–7.50 (m, 2H, ArH), 7.47 (d, J=8.8 Hz, 2H, ArH), 7.36–7.32 (m, 3H, ArH), 6.88 (d, J=8.8 Hz, 2H, ArH), 3.83 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.2 (C), 134.7 (CH), 133.1 (CH), 130.0 (CH), 129.6 (C), 125.2 (CH), 117.0 (C), 115.6 (CH), 91.0 (C), 89.7 (C), 56.9 (OCH_3); HRMS (ESI$^+$): calcd for $[C_{15}H_{12}O]^+$ requires m/z 208.0888, found 208.0896.

4.2.2. 1,2-Diphenylethyne. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59–7.48 (m, 4H, ArH), 7.39–7.29 (m, 6H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 133.3 (CH), 130.0 (CH), 129.9 (CH), 124.9 (C), 91.0 (C); HRMS (ESI$^+$): calcd for $[C_{14}H_{10}]^+$ requires m/z 178.0783, found 178.0791.

4.2.3. 1-Methyl-4-(2-phenylethynyl)benzene. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.54–7.52 (m, 2H, ArH), 7.43 (d, J=8.0 Hz, 2H, ArH), 7.37–7.33 (m, 3H, ArH), 7.16 (d, J=8.0 Hz, 2H, ArH), 2.37 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.0 (C), 133.2 (CH), 133.1 (CH), 130.8 (CH), 130.0 (CH), 129.7 (CH), 125.1 (C), 121.8 (C), 91.2 (C), 90.4 (C), 23.2 (CH_3); HRMS (ESI$^+$): calcd for $[C_{15}H_{12}]^+$ requires m/z 192.0939, found 192.0926.

4.2.4. 1-Chloro-4-(2-phenylethynyl)benzene. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.53 (t, J=7.6 Hz, 2H, ArH), 7.46 (d, J=8.4 Hz, 2H, ArH), 7.36–7.34 (m, 4H, ArH), 7.32 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 135.9 (C), 134.5 (CH), 133.3 (CH), 130.3 (CH), 130.1 (CH),

130.0 (CH), 124.6 (C), 123.4 (C), 91.9 (C), 89.9 (C); HRMS (ESI^+): calcd for $[C_{14}H_9Cl]^+$ requires *m*/*z* 212.0393, found 212.0396.

4.2.5. 1-Methoxy-3-(2-phenylethynyl)benzene. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.55–7.52 (m, 2H, ArH), 7.37–7.34 (m, 3H, ArH), 7.27–7.23 (m, 1H, ArH), 7.13 (d, *J*=7.6 Hz, 2H, ArH), 7.06 (s, 1H, ArH), 6.91–9.88 (m, 1H, ArH), 2.82 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.0 (C), 133.3 (CH), 131.1 (CH), 130.0 (CH), 130.0 (CH), 125.9 (CH), 125.8 (C), 124.8 (CH), 117.9 (C), 116.6 (CH), 90.9 (C), 90.8 (C), 56.9 (OCH_3); HRMS (ESI^+): calcd for $[C_{15}H_{12}O]^+$ requires *m*/*z* 208.0888, found 208.0884.

4.2.6. 1-Fluoro-4-(2-phenylethynyl)benzene. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.53–7.50 (m, 4H, ArH), 7.36–7.34 (m, 3H, ArH), 7.05 (t, *J*=8.6 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.4 (d, *J*=249.5 Hz, C), 135.2 (d, *J*=8.3 Hz, CH), 133.2 (CH), 130.0 (d, *J*=3.7 Hz, CH), 124.7 (C), 121.0 (d, *J*=3.4 Hz, CH), 117.4 (C), 117.2 (C), 90.7 (C), 89.2 (C); HRMS (ESI^+): calcd for $[C_{14}H_9F]^+$ requires *m*/*z* 196.0688, found 196.0690.

4.2.7. 1-(2-Phenylethynyl)naphthalene. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.45 (d, *J*=8.0 Hz, 1H, ArH), 7.88–7.76 (m, 3H, ArH), 7.67–7.59 (m, 3H, ArH), 7.56–7.54 (m, 2H, ArH), 7.48–7.39 (m, 3H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 134.9 (C), 134.8 (C), 133.3 (C), 132.0 (CH), 130.4 (CH), 130.1 (CH), 130.1 (CH), 130.0 (CH), 128.5 (CH), 128.1 (CH), 127.9 (CH), 127.0 (CH), 125.0 (CH), 122.5 (C), 95.9 (C), 89.2 (C); HRMS (ESI^+): calcd for $[C_{18}H_{12}]^+$ requires *m*/*z* 228.0939, found 228.0938.

4.2.8. 1-Bromo-4-(2-phenylethynyl)benzene. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.52–7.47 (m, 4H, ArH), 7.40–7.35 (m, 5H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 137.7 (C), 134.6 (CH), 133.2 (CH), 130.1 (CH), 130.0 (CH), 124.5 (CH), 124.1 (C), 123.8 (C), 92.1 (C), 89.9 (C); HRMS (ESI^+): calcd for $[C_{14}H_9Br]^+$ requires *m*/*z* 255.9888, found 255.9886.

4.2.9. 1-(2-(2-Methoxyphenyl)ethynyl)benzene. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.67–7.64 (m, 2H, ArH), 7.59 (d, *J*=7.6 Hz, 1H, ArH), 7.42–7.39 (m, 4H, ArH), 7.04–6.97 (m, 2H, ArH), 3.99 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.5 (C), 135.2 (CH), 133.3 (CH), 131.4 (CH), 129.9 (CH), 129.8 (CH), 125.2 (CH), 122.1 (C), 114.0 (C), 112.3 (CH), 95.1 (C), 87.4 (C), 57.5 (OCH_3); HRMS (ESI^+): calcd for $[C_{15}H_{12}O]^+$ requires *m*/*z* 208.1000, found 208.1000.

4.2.10. 1,3-Bis(2-phenylethynyl)benzene. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.39–7.32 (m, 7H, ArH), 7.49 (d, *J*=7.6 Hz, 2H, ArH), 7.54 (t, *J*=3.6 Hz, 4H, ArH), 7.72 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 136.2 (CH), 133.3 (CH), 132.9 (CH), 130.1 (CH), 130.1 (CH), 130.1 (CH), 125.2 (C), 124.6 (C), 91.6 (C), 90.2 (C); HRMS (ESI^+): calcd for $[C_{22}H_{14}]^+$ requires *m*/*z* 278.1096, found 278.1096.

4.2.11. 1-Nitro-4-(2-phenylethynyl)benzene. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.24 (d, *J*=8.8 Hz, 2H, ArH), 7.69 (d, *J*=7.6 Hz, 2H, ArH), 7.60–7.57 (m, 2H, ArH), 7.42–7.41 (m, 3H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 148.6 (C), 133.9 (CH), 133.5 (CH), 131.9 (CH), 130.9 (CH), 130.2 (CH), 125.3 (C), 123.7 (C), 96.3 (C), 89.2 (C); HRMS (ESI^+): calcd for $[C_{14}H_9NO_2]^+$ requires *m*/*z* 223.0633, found 223.0635.

4.2.12. 1-Chloro-4-(hept-1-ynyl)benzene. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.39 (d, *J*=8.4 Hz, 2H, ArH), 7.32 (d, *J*=8.4 Hz, 2H, ArH), 2.47–2.44 (m, 2H), 1.71–1.63 (m, 2H), 1.51–1.40 (m, 4H), 1.00–0.97 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 134.4 (C), 131.5 (CH), 130.1 (CH), 121.7 (C), 93.2 (C), 81.1 (C), 32.8 (CH_2), 30.0 (CH_2), 23.9 (CH_2), 21.0 (CH_2), 15.6 (CH_3); HRMS (ESI^+): calcd for $[C_{13}H_{15}Cl]^+$ requires *m*/*z* 206.0862, found 206.0864.

4.2.13. 1-Bromo-4-(hept-1-ynyl)benzene. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.41 (d, *J*=8.0 Hz, 2H, ArH), 7.26 (d, *J*=7.6 Hz, 2H, ArH), 2.39 (t, *J*=7.2 Hz, 2H), 1.58–1.65 (m, 2H), 1.33–1.47 (m, 4H), 0.94 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 133.3 (C), 131.6 (CH), 123.3 (CH), 121.8 (C), 92.0 (C), 79.8 (C), 31.4 (CH_2), 28.6 (CH_2), 22.5 (CH_2), 19.7 (CH_2), 14.3 (CH_3); HRMS (ESI^+): calcd for $[C_{13}H_{15}Br]^+$ requires *m*/*z* 250.0357, found 250.0357.

4.2.14. 1-(Hept-1-ynyl)-4-methoxybenzene. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.33–7.35 (m, 2H), 6.81–6.83 (m, 2H), 3.80 (s, 3H), 2.39 (t, *J*=7.2 Hz, 2H), 1.57–1.64 (m, 2H), 1.43–1.46 (m, 2H), 1.34–1.40 (m, 2H), 0.93 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 137.7 (CH), 134.4 (CH), 117.9 (CH), 115.4 (CH), 90.4 (C), 81.8 (C), 56.8 (CH_3), 32.8 (CH_2), 30.2 (CH_2), 23.9 (CH_2), 21.0 (CH_2), 15.7 (CH_3); HRMS (ESI^+): calcd for $[C_{14}H_{18}O]^+$ requires *m*/*z* 202.1358, found 202.1360.

4.2.15. 1-(Hept-1-ynyl)-4-methylbenzene. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.28 (d, *J*=8.0 Hz, 2H), 7.07 (d, *J*=8.0 Hz, 2H), 2.38 (t, *J*=7.2 Hz, 2H), 2.32 (s, 3H), 1.56–1.63 (m, 2H), 1.32–1.46 (m, 4H), 0.92 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 137.6 (C), 131.6 (C), 129.2 (CH), 121.2 (CH), 89.9 (C), 80.8 (C), 31.4 (CH_2), 28.8 (CH_2), 22.5 (CH_2), 21.7 (CH_2), 19.7 (CH_3), 14.3 (CH_3); HRMS (ESI^+): calcd for $[C_{14}H_{18}]^+$ requires *m*/*z* 186.1409, found 186.1409.

4.2.16. 1-(Hept-1-ynyl)benzene. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.41–7.43 (m, 2H), 7.29–7.30 (m, 3H), 2.43 (t, *J*=7.2 Hz, 2H), 1.60–1.67 (m, 2H), 1.37–1.48 (m, 4H), 0.95 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 133.2 (CH), 129.8 (CH), 129.1 (CH), 125.7 (CH), 92.1 (C), 82.2 (C), 32.8 (CH_2), 30.1 (CH_2), 23.9 (CH_2), 21.0 (CH_2), 15.7 (CH_3); HRMS (ESI^+): calcd for $[C_{13}H_{16}]^+$ requires *m*/*z* 172.1252, found 172.1250.

4.2.17. 1-(Trifluoromethyl)-3-(2-phenylethynyl)benzene. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.80 (s, 1H, ArH), 7.70 (d, *J*=7.6 Hz, 2H, ArH), 7.59–7.54 (m, 3H, ArH), 7.48 (t, *J*=8.0 Hz, 1H, ArH), 7.37 (t, *J*=3.2 Hz, 3H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 136.2 (C), 134.1 (CH), 133.3 (CH), 130.4 (q, *J*=186 Hz), 130.1 (C), 130.0 (C), 129.9 (CH), 126.7 (CH), 126.4 (q, *J*=44 Hz), 125.9 (CH), 124.2 (CH), 92.5 (C), 89.4 (C); HRMS (ESI^+): calcd for $[C_{15}H_9F]^+$ requires *m*/*z* 246.0656, found 246.0653.

4.2.18. 2-(2-Phenylethynyl)pyridine. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.78 (s, 1H), 8.55 (d, *J*=4.8 Hz, 1H, ArH), 7.83–7.81 (m, 1H, ArH), 7.58–7.54 (m, 2H, ArH), 7.38–7.37 (m, 3H, ArH), 7.31–7.28 (m, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 151.4 (CH), 144.8 (C), 138.0 (CH), 133.7 (CH), 130.7 (CH), 130.0 (CH), 128.8 (CH), 124.4 (CH), 123.8 (C), 91.2 (C), 90.0 (C); HRMS (ESI^+): calcd for $[C_{13}H_9N]^+$ requires *m*/*z* 179.0735, found 179.0731.

4.2.19. 3-(2-Phenylethynyl)pyridine. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.78 (s, 1H), 8.55 (d, *J*=4.0 Hz, 1H, ArH), 7.83–7.80 (m, 1H, ArH), 7.57–7.55 (m, 2H, ArH), 7.38–7.37 (m, 3H, ArH), 7.30–7.28 (m, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.4 (CH), 148.7 (C), 138.7 (CH), 132.0 (CH), 129.0 (CH), 128.7 (CH), 123.3 (CH), 122.7 (CH), 120.7 (C), 92.9 (C), 86.1 (C); HRMS (ESI^+): calcd for $[C_{13}H_9N]^+$ requires *m*/*z* 179.0735, found 179.0735.

4.2.20. 2-Methyl-5-(2-phenylethynyl)pyridine. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.66 (s, 1H), 7.70 (m, *J*=8.0 Hz, 1H, ArH), 7.55–7.53 (m, 2H, ArH), 7.37–7.35 (m, 3H, ArH), 7.16–7.14 (m, 1H, ArH), 2.58 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 157.9 (CH), 151.8 (C), 138.9 (CH), 131.8 (CH), 128.8 (CH), 128.6 (CH), 123.0 (CH), 117.6 (C), 92.1 (C), 86.4 (C), 24.7 (CH_3); HRMS (ESI^+): calcd for $[C_{13}H_9N]^+$ requires *m*/*z* 193.0891, found 193.0891.

4.2.21. 4-(2-Phenylethynyl)benzonitrile. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.55–7.53 (m, 4H, ArH), 7.39–7.33 (m, 5H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 133.7 (C), 133.6 (CH), 130.8 (CH), 130.1 (CH), 129.8 (CH), 123.8 (CH), 120.2 (C), 113.1 (C), 95.4 (C), 89.4 (C); HRMS (ESI^+): calcd for $[C_{15}H_9N]^+$ requires *m*/*z* 203.0735, found 203.0738.

4.2.22. 1-(3-(2-Phenylethynyl)phenyl)ethanone. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.17 (s, 1H, ArH), 7.97 (d, *J*=8.0 Hz, 1H, ArH), 7.77 (d, 4H,

J=8.0 Hz, 1H, ArH), 7.63–7.61 (m, 2H, ArH), 7.53–7.51 (m, 1H, ArH), 7.43–7.41 (m, 3H, ArH), 2.68 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 199.0 (C), 138.8 (C), 137.4 (CH), 133.3 (CH), 133.2 (CH), 130.4 (CH), 130.3 (CH), 130.1 (CH), 129.5 (C), 125.5 (C), 124.4 (CH), 92.0 (C), 90.0 (C), 28.3 (CH_3); HRMS (ESI^+): calcd for $[C_{16}H_{12}O]^+$ requires m/z 220.0888, found 220.0887.

4.2.23. 1-Methoxy-4-(prop-1-ynyl)benzene. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.39 (d, J=8.0 Hz, 2H, ArH), 6.88 (d, J=8.0 Hz, 2H, ArH), 3.86 (s, 3H, OCH_3), 2.10 (s, CH_3, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 159.2 (C), 133.0 (C), 116.4 (CH), 114.0 (CH), 84.4 (C), 79.7 (C), 55.5 (OCH_3), 31.2 (CH_3); HRMS (ESI^+): calcd for $[C_{10}H_{10}O]^+$ requires m/z 146.0732, found 146.0734.

4.2.24. 1-Fluoro-4-(2-(4-methoxyphenyl)ethynyl)benzene. ^1H NMR (400 MHz, $CDCl_3$) δ: 6.89 (d, J=8.8 Hz, 2H, ArH), 7.02–7.06 (m, 2H, ArH), 7.46–7.51 (m, 4H, ArH), 3.84 (s, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 164.2 (d, J=247.5 Hz, C), 159.9 (CH), 133.5 (d, J=7.5 Hz, CH), 133.2 (CH), 119.9 (C), 115.9 (d, J=22.5 Hz, CH), 115.4 (C), 114.2 (C), 89.2 (C), 87.2 (C), 55.5 (OCH_3); HRMS (ESI^+): calcd for $[C_{15}H_{11}FO]^+$ requires m/z 226.0794, found 226.0794.

4.2.25. 4-(2-Phenylethynyl)benzenamine. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.54 (d, J=6.4 Hz, 2H, ArH), 7.38–7.32 (m, 5H, ArH), 7.64 (d, J=6.4 Hz, 2H, ArH), 3.77 (s, 2H, NH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 139.5 (C), 134.6 (CH), 133.0 (CH), 130.0 (CH), 129.4 (CH), 119.0 (CH), 116.4 (C), 114.1 (C), 91.9 (C), 89.0 (C); HRMS (ESI^+): calcd for $[C_{14}H_{11}N]^+$ requires m/z 193.0891, found 193.0892.

4.2.26. Methyl 4-(2-phenylethynyl)benzoate. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.03 (d, J=8.0 Hz, 2H, ArH), 7.59 (d, J=8.0 Hz, 2H, ArH), 7.57–7.54 (m, 2H, ArH), 7.38–7.36 (m, 3H, ArH), 3.92 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.2 (C), 133.4 (CH), 133.1 (CH), 131.1 (CH), 130.4 (CH), 130.1 (CH), 129.9 (CH), 129.6 (C), 124.3 (C), 94.0 (C), 90.3 (C), 53.9 (CH_3); HRMS (ESI^+): calcd for $[C_{16}H_{12}O_2]^+$ requires m/z 236.0837, found 236.0837.

4.2.27. 1-(4-(2-Phenylethynyl)phenyl)ethanone. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.95 (d, J=8.0 Hz, 2H, ArH), 7.62 (d, J=8.0 Hz, 2H, ArH), 7.57–7.56 (m, 2H, ArH), 7.38 (s, 3H, ArH), 2.62 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 199.0 (C), 137.7 (C), 133.4 (CH), 133.3 (CH), 130.5 (CH), 130.1 (CH), 129.9 (CH), 129.8 (C), 124.2 (C), 94.3 (C), 90.2 (C), 28.3 (CH_3); HRMS (ESI^+): calcd for $[C_{16}H_{12}O]^+$ requires m/z 220.0888, found 220.0887.

4.2.28. 1-Methoxy-4-(2-p-tolylethynyl)benzene. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.47–7.39 (m, 4H, ArH), 7.14 (d, J=6.0 Hz, 2H, ArH), 6.87 (d, J=6.0 Hz, 2H, ArH), 3.83 (s, 3H, OCH_3), 2.36 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 159.7 (C), 138.2 (C), 133.2 (CH), 131.2 (CH), 129.5 (CH), 120.7 (CH), 115.8 (C), 114.2 (C), 88.9 (C), 88.4 (C), 55.5 (OCH_3), 21.7 (CH_3); HRMS (ESI^+): calcd for $[C_{16}H_{14}O]^+$ requires m/z 222.1045, found 222.1042.

4.2.29. 1-(2-(3-Methoxyphenyl)ethynyl)-4-methylbenzene. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.42 (d, J=6.0 Hz, 2H, ArH), 7.25–7.20 (m, 1H, ArH), 7.14 (d, J=6.0 Hz, 2H, ArH), 7.10 (s, 1H, ArH), 7.05 (s, 1H, ArH), 6.87 (d, J=9.0 Hz, 1H, ArH), 3.79 (s, 3H, OCH_3), 2.35 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 159.6 (C), 138.7 (C), 131.8 (CH), 129.6 (CH), 129.4 (CH), 124.7 (CH), 120.4 (CH), 116.5 (C), 115.0 (C), 89.7 (C), 88.9 (C), 55.5 (OCH_3), 21.8 (CH_3); HRMS (ESI^+): calcd for $[C_{16}H_{14}O]^+$ requires m/z 222.1045, found 222.1046.

4.2.30. 1-(2-(2-Methoxyphenyl)ethynyl)-4-methylbenzene. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.50 (s, 1H, ArH), 7.45 (d, J=6.0 Hz, 2H, ArH), 7.31–7.24 (m, 1H, ArH), 7.13 (d, J=6.0 Hz, 2H, ArH), 6.95–6.87 (m, 2H, ArH), 3.90 (s, 3H, OCH_3), 2.35 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 160.0 (C), 138.4 (C), 133.7 (CH), 131.8 (CH), 129.8 (CH), 129.2 (CH), 120.7 (CH), 112.9 (C), 110.9 (C), 93.9 (C), 85.2 (C), 56.0 (OCH_3), 21.7 (CH_3); HRMS (ESI^+): calcd for $[C_{16}H_{14}O]^+$ requires m/z 222.1045, found 222.1046.

4.2.31. 1-Fluoro-4-(2-(3-methoxyphenyl)ethynyl)benzene. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.52 (d, J=6.0 Hz, 2H, ArH), 7.26 (d, J=6.0 Hz, 2H, ArH), 7.13–7.01 (m, 3H, ArH), 6.91–6.88 (m, 1H, ArH), 3.81 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 159.6 (C), 133.8 (C), 133.7 (d, J=300 Hz, C), 131.0 (CH), 130.1 (CH), 124.4 (CH), 123.2 (C), 116.6 (d, J=45 Hz, CH), 115.7 (d, J=37.5 Hz, CH), 114.0 (C), 89.2 (C), 88.4 (C), 55.5 (OCH_3); HRMS (ESI^+): calcd for $[C_{15}H_{11}FO]^+$ requires m/z 226.0794, found 226.0796.

4.2.32. (E)-1,4-Diphenylbut-1-en-3-yne. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.49–7.46 (m, 2H, ArH), 7.42 (d, J=7.2 Hz, 2H), 7.36–7.29 (m, 6H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 141.7 (CH), 136.8 (C), 132.0 (CH), 129.2 (CH), 129.0 (CH), 128.8 (CH), 128.7 (CH), 126.8 (CH), 123.8 (C), 108.6 (CH), 92.2 (C), 89.4 (C); HRMS (ESI^+): calcd for $[C_{16}H_{12}]^+$ requires m/z 204.0939, found 204.0939.

4.2.33. 1,2-Bis(4-methoxyphenyl)ethyne. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.15 (d, J=9.0 Hz, 4H, ArH), 6.86 (d, J=9.0 Hz, 4H, ArH), 3.81 (s, 6H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 159.6 (C), 133.1 (C), 115.9 (CH), 114.2 (CH), 88.2 (C), 55.5 (OCH_3); HRMS (ESI^+): calcd for $[C_{16}H_{14}O_2]^+$ requires m/z 238.0994, found 238.0990.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tet.2012.06.003.

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