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Cu-Catalyzed Fe-Driven C_{sp}–C_{sp} and C_{sp}–C_{sp2} Cross-Coupling: An Access to 1,3-Diynes and 1,3-Enynes

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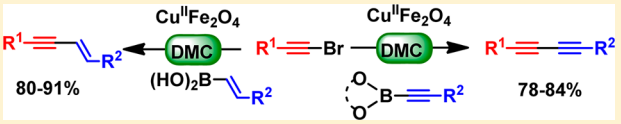
Supporting Information

ABSTRACT: An efficient C_{sp}–C_{sp} cross-coupling of alkynyl bromide and pinacol ester of alkynyl boronic acid catalyzed by $CuFe_2O_4$ nanoparticles has been accomplished in dimethyl carbonate to produce unsymmetric 1,3-diynes. This protocol is also extended for the C_{sp}–C_{sp2} coupling of alkynyl bromide and alkenyl boronic acid to provide conjugated 1,3-enynes. The aliphatic, aromatic, and heteroaromatic alkynes couple with various substituted alkynyl/alkenyl boronates/boronic acids by this procedure to furnish a library of 1,3-diynes and enynes in high yields. The catalyst was easily separated by an external magnet and recycled 10 times.



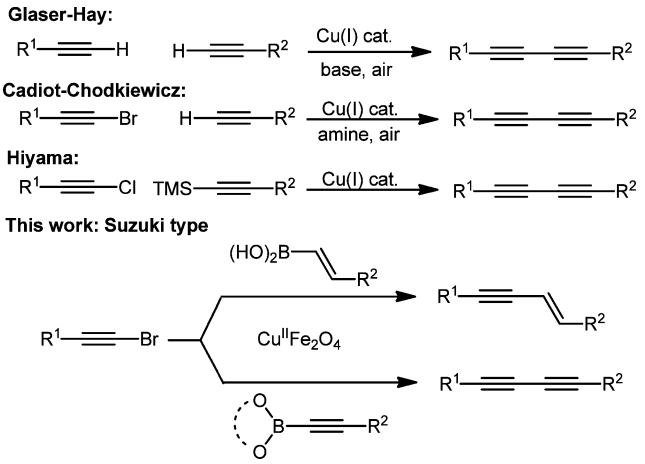
INTRODUCTION

The unsymmetric 1,3-diynes have received considerable attention as these units are important structural motifs in many natural products[1] and molecules of pharmaceutical and material interest.[2] For example, norcapillene,[3] thiarubrine,[4] and falcarindol[5] containing this subunit showed prominent biological activities. Thus, the construction of an unsymmetric 1,3-diyne moiety is of much interest. Although there are many methods for the synthesis of symmetric diynes,[6] those unsymmetric ones still remain a challenge. Cadiot-Chodkiewicz cross-coupling of haloalkyne and terminal alkyne catalyzed by Cu(I) is the most widely used method for the synthesis of unsymmetric diynes.[7] However, this protocol is often associated with low efficiency and poor selectivity. During the past few years, a few other methods involving Pd-catalyzed cross-coupling of 1,3-diynylzincs,[8a] C_{sp}–C_{sp} cross-coupling of alkynyl bromides and terminal alkynes,[8b] nickel-catalyzed cross-coupling of acetylenic sulfones and alkynyl Grignard reagents,[9a] $NiCl_2$/Cu(I)-catalyzed oxidative coupling of two different alkynes,[9b] Cu(I)-catalyzed coupling of alkynyl silanes,[10a] cross-coupling of terminal alkynes with 1-bromoalkynes,[10b] heterocoupling of terminal alkynes,[10c] decarboxylative coupling of alkynyl carboxylates with 1,1-dibromoalkynes,[10d] coupling of propiolic acid with terminal alkynes,[10e] and coupling of terminal alkynes with *cis*-styrenyl bromides[10f] were also reported.

The conjugated 1,3-enynes are also of much importance as they are present in many biologically active naturally occurring and synthetic molecules[11] and are used as important building blocks in organic synthesis.[1] A straightforward approach for the synthesis of 1,3-enynes involves the Pd/Cu-catalyzed Sonogashira coupling of terminal alkyne with vinyl halide.[12] Several other methods based on noble-metal-catalyzed dimerization of terminal alkynes,[13a] coupling of an alkyne and a structurally defined organometallic alkene,[13b] and Suzuki coupling of chloroenynes with boronic acid[13c] were also developed.

In view of the importance of unsymmetric 1,3-diynes and conjugated 1,3-enynes, there is a need for a more efficient and general procedure for the synthesis of both molecules involving less expensive metals and reagents. The $CuFe_2O_4$ nanoparticle is a well-known catalyst for carbon–heteroatom bond formation[14] (C–N, C–O, C–S, C–Se, C–Te), although it is less explored for C–C bond formation. It is also commercially available. Thus, we became interested to find its activity toward C–C bond formation, particularly C_{sp}–C_{sp} coupling, and we report here a novel common protocol for C_{sp}–C_{sp} and C_{sp}–C_{sp2} coupling of alkynyl bromides with pinacol ester of alkynyl boronic acid/alkenyl boronic acid using a magnetically separable $CuFe_2O_4$ nanoparticle catalyst in a green reaction medium, dimethyl carbonate in the presence of a base (Scheme 1), as a part of our continuing efforts to explore nanoparticles for useful reactions.

Scheme 1. Synthesis of Conjugated Diynes and Enynes



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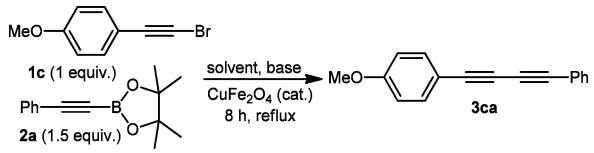
The organo-boronates/boronic acids, used in this reaction are easily accessible and are relatively benign. Morever, they have not been used in this type of coupling previously.

RESULTS AND DISCUSSION

To standardize the reaction conditions, a series of experiments were performed with variation of reaction parameters such as base, solvent, catalyst loading, and time for a representative $C_{sp}-C_{sp}$ coupling reaction of 1-(2-bromoethynyl)-4-methoxybenzene (**1c**) and pinacol ester of 2-phenylethynylboronic acid (**2a**). The results are summarized in Table 1. As the reaction

Table 1. Standardization of Reaction Conditions[a]



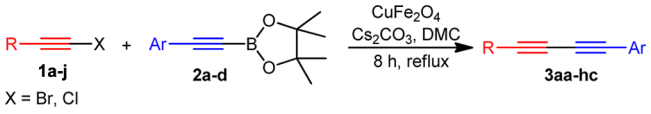
entry	solvent	base	catalyst (mol %)	yield (%)
1	toluene	K_2CO_3	5	
2	xylene	K_2CO_3	5	
3	THF	K_2CO_3	5	
4	dioxane	K_2CO_3	5	14
5	DMF	K_2CO_3	5	23
6	NMP	K_2CO_3	5	38
7	DMSO	K_2CO_3	5	
8	H_2O	K_2CO_3	5	
9	DMC	K_2CO_3	5	41
10	DMC	K_3PO_4	5	58
11	DMC	Cs_2CO_3	5	82
12	DMSO	Cs_2CO_3	5	
13	DMF	Cs_2CO_3	5	42
14	toluene	Cs_2CO_3	5	
15	DMC	Cs_2CO_3	8	77
16[b]	DMC	Cs_2CO_3	3	43
17[b]	DMC	Cs_2CO_3		
18[c]	DMC	Cs_2CO_3	5	80

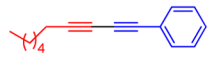
[a]Yields refer to those of purified products characterized by ^1H and ^{13}C NMR spectroscopic data. [b]Required 12 h. [c]In the presence of TEMPO (2 equiv).

did not start at room temperature, these are carried out under reflux. Among various bases, Cs_2CO_3 was found to work better than K_2CO_3 and K_3PO_4 under similar conditions. Dimethyl carbonate (DMC) was found to be the best solvent among THF, dioxane, DMF, NMP, DMSO, and H_2O attempted for this reaction. The amount of catalyst was optimized to 5 mol % (with reapect to **1**). Use of less than that (3 mol %) led to marginal progress. The best yield was obtained using DMC as a solvent and 5 mol % of $CuFe_2O_4$ nanoparticles as catalyst in the presence of Cs_2CO_3 under reflux (100 °C) for 8 h (Table 1, entry 11). Thus, in a typical experimental procedure, a mixture of alkynyl bromide and pinacol ester of 2-arylethynylboronic acid was subjected to reaction under these optimized conditions. Extraction of the reaction mixture with ethyl acetate and standard workup followed by purification provided the pure product. The catalyst $CuFe_2O_4$ was separated easily by a magnetic rod.

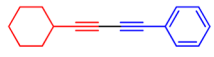
A series of diversely substituted alkynyl bromides underwent reactions with substituted alkynyl boronic esters by this procedure to provide the corresponding unsymmetrical 1,3-diynes. The results are summarized in Table 2. The alkyl,

Table 2. Synthesis of Unsymmetrical 1,3-Diynes[a]

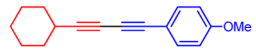




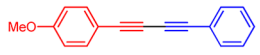
3aa, 81%



3ba, 78%

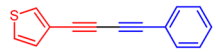


3bb, 82%



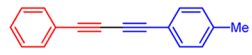
3ca, Br = 82%

Cl = 51 %

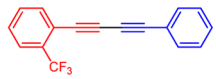


3da, 84%

3gb, 82%

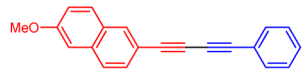


3jc, Br = 80%



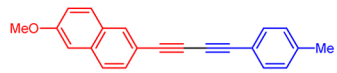
3ea, 81%

Cl = 46 %

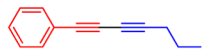


3ha, 85%

3ia, 83 %



3hc, 78%



3jd, 0%[b]

[a]Yields refer to those of purified products characterized by ^1H and ^{13}C NMR spectroscopic data. [b]Reaction was carried out with pentynyl boronate ester.

cycloalkyl, aryl, and heteroaryl-substituted ethynyl bromides participated in this reaction with uniform results (Table 2). However, a small amount (2−5%) of homocoupled products was formed, and these were removed easily during the purification process. A variety of substituents such as −OMe, $-CF_3$, −Me, −*t*-Bu, and −Br on the aryl ring of alkynyl bromide (Table 2) and alkynyl boronic esters are compatible under the reaction conditions. Thus, a series of functionalized aryl alkyl (**3aa**), aryl cycloalkyl (**3ba**, **3bb**), diaryl (**3gb**, **3jc**, **3ea**, **3ha**, **3ia**, **3hc**), and aryl heteroaryl (**3da**) 1,3-diynes were easily obtained by this procedure. However, the reaction of alkyl-substituted alkynyl boronic ester with alkyl/aryl ethynyl bromide did not proceed under the reaction conditions. The coupling of alkynyl boronate occurs selectively with the bromo functionality of the alkynyl bromide **1i** at the acetylenic end, leaving the other one on the aromatic ring unaffected (**3ia**). This chemoselectivity leaves scope for further manipulation on the aryl bromo group.

The reaction of alkynyl bromides and 2-aryl/alkyl ethenyl boronic acids by the same procedure provided the corresponding conjugated 1,3-enynes. The results are reported in Table 3. Significantly, the (*E*)-styrenyl and vinyl boronic acids produced the corresponding (*E*)-1,3-enynes with complete retention of

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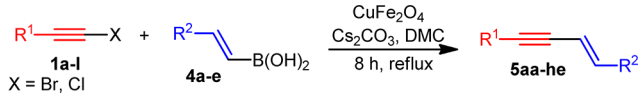
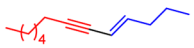
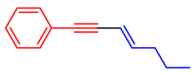
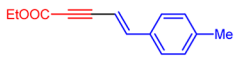
Table 3. Synthesis of Conjugated 1,3-(*E*)-Enynes[a]



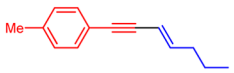

5aa, 88%


5ja, Br = 89%

Cl = 54 %

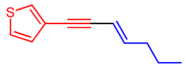


5mb, 86%

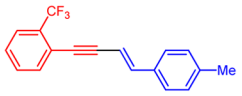


5fa, Br = 91%

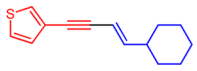
Cl = 62%



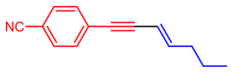
5da, 87%



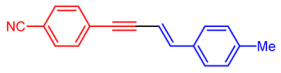
5eb, 80%



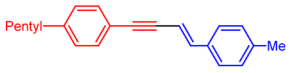
5dc, 81%



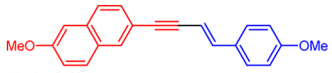
5ka, 85%



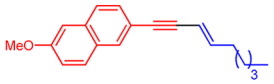
5kb, 82%



5lb, 80%



5hd, 86%

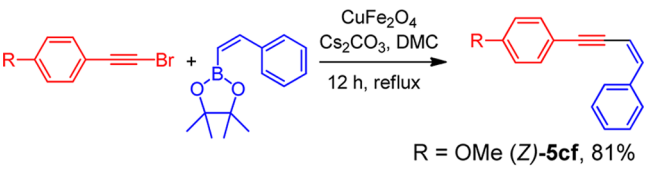


5he, 88%

[a]Yields refer to those of purified products characterized by ^{1}H and ^{13}C NMR spectroscopic data.

stereochemistry. The (*Z*)-styrenyl boronate esters also provided (*Z*)-enyne products with excellent stereospecificity (Scheme 2). The aliphatic ethynyl bromides coupled with vinyl/styrenyl boronic acids without any difficulty (Table 3).

Scheme 2. Synthesis of (*Z*)-Enynes[a]



[a]Yields refer to those of purified products characterized by ^{1}H and ^{13}C NMR spectroscopic data.

Similarly, the aryl and heteroaryl-substituted ethynyl bromides reacted with aryl/cycloalkyl ethenyl boronic acids to provide the corresponding products efficiently. A variety of substituents such as $-CO_2Et$, $-CN$, $-OMe$, and $-CF_3$ were compatible in this reaction.

In general, the reactions are very clean and high yielding. The products are obtained in high purity and characterized properly by spectroscopic data. The $C_{sp}-C_{sp}$ and $C_{sp}-C_{sp2}$ cross-coupling reaction using alkynyl chlorides (Table 2 and Table 3) led to relatively low (46–62%) yield of products (**3ca**, **3jc** and **5ja**, **5fa**). The reactions of alkynyl boronates and alkenyl boronic acids provided uniform results in terms of yields and reactivity (Table 2 and Table 3). The $CuFe_2O_4$ nanoparticle catalyst is recycled at least up to 10 times with marginal loss of activity in subsequent runs (Figure 1). After completion of the

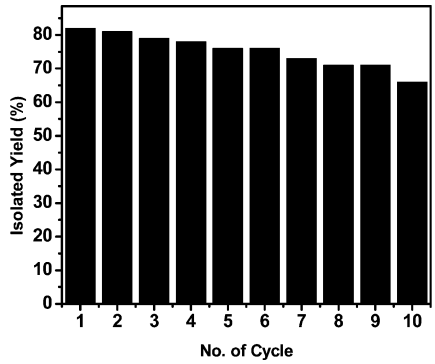


Figure 1. Recyclability of the catalyst.

reaction, the magnetic bar covered with catalyst was collected by a magnetic rod and the bar was successively washed with ethanol and acetone before being used for the next cycle of reaction. After each run, the size of the $CuFe_2O_4$ nanoparticles increased due to agglomerization, although it did not affect the outcome of the reaction significantly. The TEM (transmission electron microscope) (Figure 4) and SEM (scanning electron microscope) (Figure 5) images of the fresh catalyst and the recovered catalyst after the fifth cycle show that the morphology of the catalyst remained unaltered. The XRD patterns (Figure 6) of the catalyst before and after the fifth cycle revealed that the geometry of the metal center also remained the same.

A detailed investigation was undertaken to understand the mechanism of this $CuFe_2O_4$ nanoparticle-catalyzed C–C bond formation through the coupling of alkynyl bromides and boronic acids. To check whether the reaction proceeds through a homogeneous or heterogeneous catalysis pathway, ICP-MS studies at different stages of the reaction were carried out. The fresh catalyst was found to contain 4.180 mmol·g^{-1} of copper and 8.360 mmol·g^{-1} of iron, whereas the recovered catalyst after the fourth cycle contains 4.172 mmol·g^{-1} of copper and 8.354 mmol·g^{-1} of iron. These data indicate marginal leaching of catalyst in the reaction mixture. For the homogeneity test, we have performed an experiment where a reaction of 1-(2-bromoethynyl)-4-methoxybenzene (**1c**) and pinacol ester of 2-phenylethynylboronic acid (**2a**) was stopped at 3 h after 30% conversion (NMR spectroscopy). Then the heterogeneous catalyst was separated, and the reaction was allowed to run. Even after 12 h, no further formation of product was observed (NMR spectroscopy) and also no trace of copper and iron was

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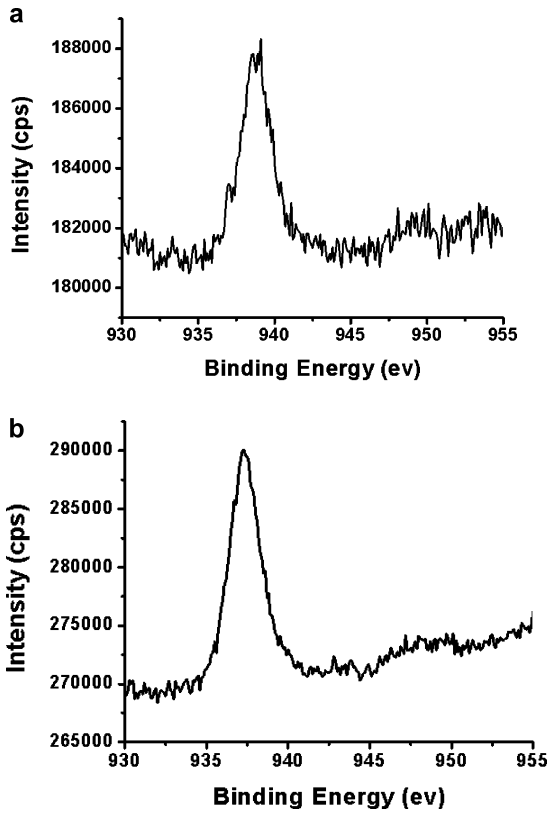

Figure 2. (a) XPS study of the catalyst at intermediate stage. (b) XPS study of the catalyst after completion of the reaction.

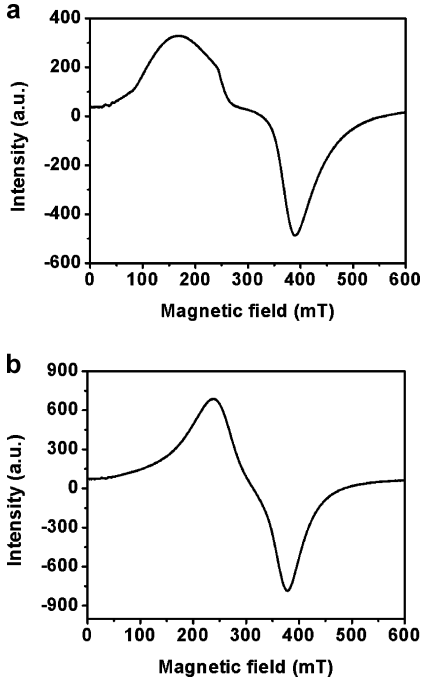

Figure 3. (a) EPR study of the catalyst at intermediate stage of the reaction. (b) EPR study of the catalyst after the completion of the reaction.

identified in the reaction mixture (ICP-MS). Thus, this study clearly established heterogeneous catalysis in this process.

To check the possibility of a radical process, we performed the coupling reaction of 4 and 1-bromophenyl acetylene in the presence of THF (radical scavenger) and nitro arene (electron acceptor);[15] however, no effect was observed. The presence of TEMPO also did not affect the yield of the reaction (Table 1, entry 18). These results did not suggest the involvement of radicals in this process. Moreover, when the reaction was carried out with both *cis*- and *trans*-styryl or vinyl boronic

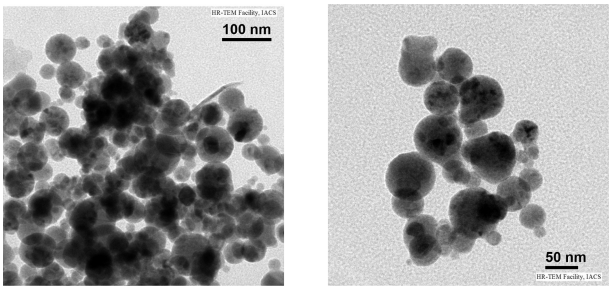

Figure 4. TEM image of the fresh catalyst (left). TEM image of the catalyst after the fifth cycle (right).

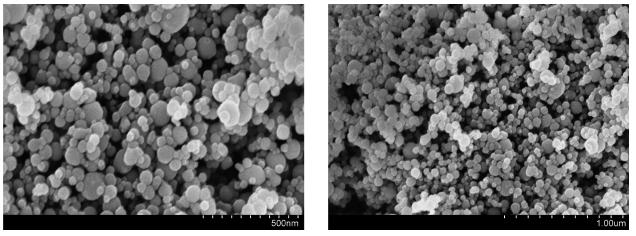

Figure 5. SEM image of the fresh catalyst (left). SEM image of the catalyst after the fifth cycle (right).

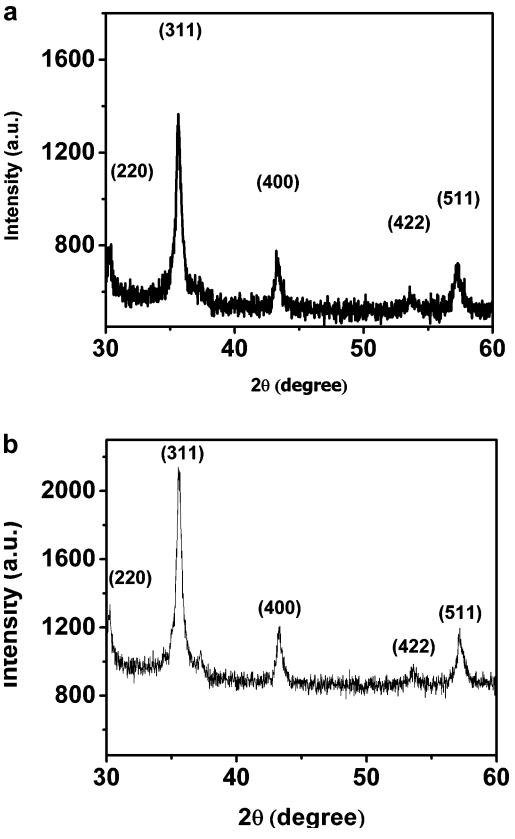

Figure 6. (a) XRD pattern of the fresh catalyst. (b) XRD pattern of the catalyst after 5th cycle.

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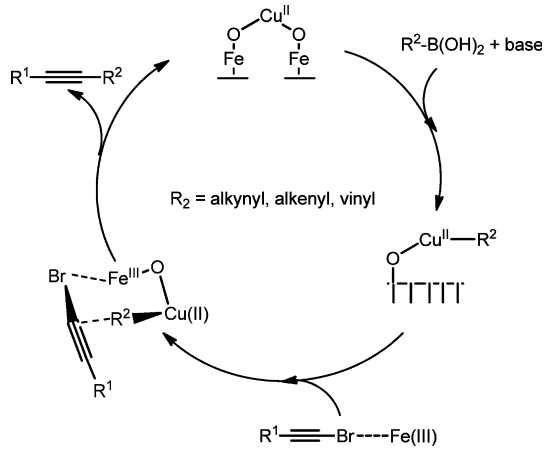
acids/esters, the corresponding products were obtained (Table 3, Scheme 2) with complete retention of configuration. This observation, too, does not support the radical pathway as the involvement of vinyl radicals would provide a mixture of stereoisomers undergoing a rapid inversion of the configuration.[16]

Oxidative addition−reductive elimination mechanism with a catalyst bearing a Cu^{II} and Fe^{III} center is quite unlikely due to the rare occurrence of Cu^{IV} and Fe^{V} species. The XPS spectrum of the catalyst (Figure 2) clearly shows a Cu peak at 936 eV along with a shake up peak at 950 eV at intermediate stages of the reaction after 4 h and completion of the reaction. This clearly indicates +2 oxidation state of copper.[17]

On the other hand, a four-line hyperfine spectrum in EPR (Figure 3) clearly suggests Cu(II) in a tetrahedrally substituted geometry bearing a single electron in the $d_{x^2-y^2}$ orbital.[17] The similar result was obtained at an intermediate stage of the reaction and after completion of the reaction.

Although in both cases we obtained an EPR of Cu(II), the difference in the EPR pattern of the metal center at the intermediate stage may occur due to some coordination with the oxygen center of the solvent. Thus, we propose a Cu^{II}- and Fe^{III}-assisted nucleophilic displacement pathway for this C−C bond forming reaction. We suggest that, initially, the alkynyl/alkenyl moiety comes close to the coordination sphere of tetrahedrally substituted Cu^{II} toward nucleophilic activation in the presence of base (Scheme 3). The Fe^{III} center (a good

Scheme 3. Plausible Mechanism



Lewis acid)[18] activates the C−Br bond and makes the C(sp) center electrophilic. The final product was obtained by copper- and iron-assisted nucleophilic displacement through a six-membered transition state.

In fact, the copper center is engaged in nucleophilic activation where the Fe^{III} center is responsible for electrophilic activation. It was observed that when the reaction was carried out with the CuO nanoparticle, only a trace amount of product was formed. On the other hand, when the reaction was performed in the presence of iron(III) oxide nanoparticles, virtually no reaction was initiated. This observation indicates that iron has a specific role in this reaction.

CONCLUSION

In conclusion, we have developed an efficient and general protocol for $C_{sp}-C_{sp}$ and $C_{sp}-C_{sp2}$ cross-coupling of alkynyl bromides and alkynyl boronates/alkenyl boronic acids using a magnetically separable $CuFe_2O_4$ nanoparticle catalyst leading to the synthesis of unsymmetric 1,3-diynes and conjugated 1,3-enynes, respectively. The high yield of products, simple operation, and excellent stereospecificity, recyclability of the catalyst, and use of environment-friendly dimethyl carbonate as reaction medium make this procedure more attractive to existing ones. We are not aware of any $C_{sp}-C_{sp}$ and $C_{sp}-C_{sp2}$ cross-coupling involving alkynyl bromides and alkynyl/alkenyl boronates/boronic acids with such a broad substrate scope. We believe this will find useful applications in organic synthesis.

EXPERIMENTAL SECTION

General. HRMS analysis was performed in a Qtof mass analyzer using ESI ionization method. Elemental analysis was done at our Institute using an autoanalyzer. $CuFe_2O_4$ nanoparticles, vinyl boronic acid, and unsubstituted alkynyl boronates were obtained from commercial sources and were used as such.

General Procedure for 1-Alkynyldioxaborolanes (2): Preparation of 2-(2-(4-Methoxyphenyl)ethynyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2b).[19a] To a solution of 1-ethynyl-4-methoxybenzene (1.56 mL, 12 mmol) in THF (30 mL) was added *n*-BuLi (7.5 mL, 1.6 M hexane solution, 12 mmol) dropwise at −78 °C under argon. The reaction mixture was stirred for 1 h at −78 °C. The resulting mixture was then added to a solution of 4,4,5,5-tetramethyl-2-(1-methylethoxy)-1,3,2-dioxaborolane (2.04 mL, 10 mmol) in THF (30 mL) at −78 °C. After being stirred for 2 h at −78 °C, the reaction mixture was quenched with 1.0 M HCl/Et_2O (12.6 mL, 12.6 mmol), and the mixture was allowed to reach room temperature with additional stirring for 1 h. After filtration and evaporation of solvent, the crude product was purified by short path distillation to afford **2b** (1.51 g, 68%) as a colorless liquid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.31 (s, 12H), 3.78 (s, 3H), 6.83 (m, 2H), 7.45 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 24.7, 55.1, 84.3, 102.2, 113.8, 113.9, 134.0, 160.3; HRMS calculated for $C_{15}H_{20}BO_3$ $[M + H]^+$ 259.1500, found 259.1493.

4,4,5,5-Tetramethyl-2-(2-*p*-tolylethynyl)-1,3,2-dioxaborolane (2c):[19b] White viscous liquid (1.63 g, 73%); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.34 (s, 12H), 2.33 (s, 3H), 7.11 (d, J = 7.9 Hz, 2H), 7.40 (d, J = 8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.6, 24.7, 84.3, 102.2, 118.98, 129.0, 132.1, 132.5, 139.7; HRMS calculated for $C_{15}H_{19}BO_2$ $[M + H]^+$ 243.1600, found 243.1591.

General Experimental Procedure for the Synthesis of Unsymmetrical 1,3-Diyne and Conjugated 1,3-Enyne. Representative Procedure for the Coupling of 1-(2-Bromoethynyl)-4-methoxybenzene (1c) with Pinacol Ester of 2-Phenylethynylboronic acid (2a). A mixture (suspension) of 1-(2-bromoethynyl)-4-methoxybenzene (**1c**) (211 mg, 1.0 mmol), pinacol ester of 2-phenylethynylboronic acid (**2a**) (342 mg, 1.5 mmol), Cs_2CO_3 (651 mg, 2 mmol), and $CuFe_2O_4$ (12 mg, 5 mol %) in DMC (5 mL) was stirred at 100 °C (oil bath temperature) for 8 h (TLC) under argon. The reaction mixture was allowed to cool and extracted with ethyl acetate (3 × 20 mL). The organic extract was washed with brine, dried over anhydrous Na_2SO_4, and evaporated to leave the crude product which was purified by column chromatography over silica gel with hexane/diethyl ether (96:4) as eluent to furnish pure 1-methoxy-4-(4-phenylbuta-1,3-diynyl)benzene (**3ca**) as a white solid (190 mg, 82%): mp 96−98 °C; IR (KBr) 3062, 3006, 2968, 1917, 1618, 1494, 1481, 1382, 1265, 1222, 1164, 1031, 896, 858 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.82 (s, 3H), 6.86 (d, J = 8.5 Hz, 2H), 7.32−7.38 (m, 3H), 7.48 (d, J = 9.0 Hz, 2H), 7.53 (d, J = 7.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 55.4, 72.9, 74.3, 81.2, 82.0, 113.8, 114.3 (2C), 122.1, 128.5 (2C), 129.0, 132.5 (2C), 134.2 (2C), 160.4. These spectroscopic data are consistent with those reported.[10d]

This procedure was followed for all of the reactions listed in Table 2 and Table 3. Although the representative procedure is based on mmol scale reaction, it has been scaled up to gram quantities with reproducible results. A few of these products (**3aa**,[20a] **3ba**,[10d] **3ca**,[10d] **3da**,[20b] **3jc**,[10d] **3gb**,[10b] **3ia**,[10d] **5aa**,[20c] **5ja**,[20d] **5cf**,[20e] **5ff**[20f]) are known compounds, and their spectroscopic data are in agreement with those

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previously reported. The products which are not reported earlier were characterized by their IR, ^{1}H NMR, and ^{13}C NMR spectroscopic data and elemental analysis or HRMS data. All these data are provided below.

1-(Deca-1,3-diynyl)benzene (3aa, Table 2):[20a] Colorless viscous liquid (136 mg, 81%); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, J = 5.4 Hz, 3H), 1.25−1.43 (m, 6H), 1.52−1.62 (m, 2H), 2.35 (t, J = 7.0 Hz, 2H), 7.26−7.33 (m, 3H), 7.45−7.48 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 19.7, 22.6, 28.4, 28.7, 31.4, 65.2, 74.6, 74.8, 85.0, 122.3, 128.3 (2C), 128.7, 132.5 (2C).

1-(4-Cyclohexylbuta-1,3-diynyl)benzene (3ba, Table 2):[10d] White solid (162 mg, 78%); mp 95−98 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.33 (t, J = 9.0 Hz, 2H), 1.50−1.57 (m, 4H), 1.72−1.76 (m, 2H), 1.83−1.85 (m, 2H), 2.53−2.56 (m, 1H), 7.28−7.38 (m, 3H), 7.47 (d, J = 7.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 24.9, 25.8, 29.9, 32.3, 61.1, 74.5, 75.5, 88.7, 122.3, 128.5 (2C), 128.9 (2C), 132.6 (2C).

1-(4-Cyclohexylbuta-1,3-diynyl)-4-methoxybenzene (3bb, Table 2): Dirty white solid (195 mg, 82%); mp 92−94 °C; IR (KBr) 2929, 2854, 2138, 1602, 1566, 1508, 1442, 1282, 1249, 1172, 1031, 831 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.32−1.34 (m, 2H), 1.49−1.56 (m, 4H), 1.70−1.75 (m, 2H), 1.79−1.85 (m, 2H), 2.49−2.57 (m,1H), 3.80 (s, 3H), 6.81 (d, J = 7.5 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.8 (2C), 25.9, 29.9, 32.3 (2C), 55.4, 65.3, 73.2, 75.6, 88.0, 114.2 (2C), 114.3, 134.1(2C), 160.0. Anal. Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.63; H, 7.59.

3-(4-Phenylbuta-1,3-diynyl)thiophene (3da, Table 2):[20b] White solid (174 mg, 84%); mp 86−87 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.19 (d, J = 6.0 Hz, 1H), 7.29−7.40 (m, 4H), 7.53 (d, J = 8.5 Hz, 2H), 7.60 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 73.7, 74.1, 81.5, 81.7, 121.1, 122.0, 125.7, 128.6 (2C), 129.3, 130.3 (2C), 131.4, 132.6.

1-(4-(4-*tert*-Butylphenyl)buta-1,3-diynyl)-4-methoxybenzene (3gb, Table 2):[10b] White solid (236 mg, 82%); mp 81−84 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.32 (s, 9H), 3.82 (s, 3H), 6.86 (d, J = 8.5 Hz, 2H), 7.36 (d, J = 8.5 Hz, 2H), 7.46−7.48 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 31.2 (3C), 35.0, 55.4, 73.1, 73.7, 81.5, 81.6, 114.0, 114.3 (2C), 119.0, 125.6 (2C), 132.3 (2C), 134.2 (2C), 152.6, 160.4.

1-(4-*p*-Tolylbuta-1,3-diynyl)benzene (3jc, Table 2):[10d] White solid (173 mg, 80%); mp 117−118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H), 7.15 (d, J = 8.0 Hz, 2H), 7.33−7.38 (m, 3H), 7.42−7.45 (m, 2H), 7.53−7.55 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.7, 73.5, 74.2, 81.4, 82.0, 118.9, 122.0, 128.5 (2C), 129.2 (2C), 129.4 (2C), 132.5 (2C), 132.6 (2C).

1-(4-(2-(Trifluoromethyl)phenyl)buta-1,3-diynyl)benzene (3ea,Table 2): Dirty white solid (218 mg, 81%); mp 84−85 °C; IR (KBr) 3029, 2210, 1598, 1569, 1487, 1448, 1317, 1261, 1163, 1110, 1031, 812 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.33−7.37 (m, 4H), 7.51−7.56 (m, 3H), 7.67 (d, J = 8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 73.7, 74.0, 81.7, 83.6, 121.6, 121.7, 123.2 (q, J_{C-F} = 273.4 Hz, 1C), 126.2 (q, J_{C-F} = 9.8 Hz, 1C), 128.6 (2C), 128.9, 129.3, 129.6, 131.6, 132.4 (2C), 132.7, 135.1. Anal. Calcd for $C_{17}H_9F_3$: C, 75.55; H, 3.36. Found: C, 75.50; H, 3.31.

2-Methoxy-6-(4-phenylbuta-1,3-diynyl)naphthalene (3ha, Table 2): White solid (239 mg, 85%); mp 89−91 °C; IR (KBr) 3026, 2918, 2130, 1923, 1587, 1512, 1446, 1102, 1074, 812 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.95 (s, 3H), 7.11 (s, 1H), 7.15−7.19 (m, 1H), 7.34−7.36 (m, 3H), 7.49−7.56 (m, 3H), 7.66−7.72 (m, 2H), 7.99 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 56.4, 73.7, 74.3, 81.6, 82.1, 106.3, 116.9, 117.8, 119.4, 126.8, 129.3 (2C), 129.4, 129.6, 131.5, 132.6 (2C), 132.9, 134.8, 140.5, 158.4; HRMS calcd for $C_{21}H_{14}O$ [M + H]$^+$ 283.1116, found 283.1123.

1-(4-(4-Bromophenyl)buta-1,3-diynyl)benzene (3ia, Table 2):[10d] White solid (233 mg, 83%); mp 91−93 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.37−7.42 (m, 5H), 7.50 (d, J = 7.5 Hz, 2H), 7.56 (d, J = 7.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 73.8, 74.0, 75.2, 81.7, 121.9, 128.5 (2C), 128.7, 129.3 (2C), 131.7, 131.9, 132.6 (2C), 133.9 (2C).

2-Methoxy-6-(4-*p*-tolylbuta-1,3-diynyl)naphthalene (3hc, Table 2): White solid (231 mg, 78%); mp 92−95 °C; IR (KBr) 3062, 3006, 2968, 1917, 1618, 1595, 1481, 1382, 1265, 1222, 1164, 1031, 896 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.37 (s, 3H), 3.93 (s, 3H), 7.10 (s, 1H), 7.14−7.18 (m, 3H), 7.44 (d, J = 8.0 Hz, 2H), 7.50 (d, J = 8.5 Hz, 1H), 7.66−7.71 (m, 2H), 7.98 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.8, 55.5, 74.1, 74.2, 81.9, 82.0, 106.1, 117.1, 117.4, 118.7, 119.8, 127.1, 129.3 (2C), 129.4, 129.6, 132.6 (2C), 132.9, 134.8, 140.2, 158.9; HRMS calcd for $C_{22}H_{16}O$ [M + H]$^+$ 297.1271, found 297.1279.

(*E*)-Tridec-4-en-6-yne (5aa, Table 2):[20c] Yellowish viscous liquid (156 mg, 88%); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.91 (t, J = 7.5 Hz, 6H), 1.24−1.35 (m, 4H), 1.36−1.43 (m, 4H), 1.48−1.58 (m, 2H), 2.03−2.07 (m, 2H), 2.26−2.30 (m, 2H), 5.45 (d, J = 16.0 Hz, 1H), 6.00−6.06 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.6, 14.0, 19.3, 22.0, 22.5, 28.6, 28.8, 31.4, 35.0, 79.2, 88.7, 110.0, 143.0.

1-((*E*)-Hept-3-en-1-ynyl)benzene (5ja, Table 3):[20d] Yellow liquid (151 mg, 89%); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.84−0.87 (m, 3H), 1.35−1.42 (m, 2H), 2.04−2.08 (m, 2H), 5.62 (d, J = 16.0 Hz, 1H), 6.14−6.20 (m, 1H), 7.20−7.23 (m, 3H), 7.33−7.35 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.8, 22.1, 35.4, 88.0, 88.5, 109.8, 123.8, 128.4, 127.9 (2C), 131.5 (2C), 145.1.

(*E*)-Ethyl-5-*p*-tolylpent-4-en-2-ynoate (5mb, Table 3): Yellow liquid (184 mg, 86%); IR (neat) 3444, 2981, 2923, 2204, 1728, 1705, 1604, 1514, 1367, 1276, 1253, 1097, 1020 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.34 (t, J = 7.5 Hz, 3H), 2.36 (s, 3H), 4.25−4.29 (q, J = 7.5 Hz, 2H), 6.14 (d, J = 16.0 Hz, 1H), 7.16 (d, J = 7.5 Hz, 2H), 7.22 (d, J = 16.0 Hz, 1H), 7.31 (d, J = 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.2, 21.5, 62.0, 82.3. 86.4, 103.6, 127.0 (2C), 129.7 (2C), 132.5, 140.5, 147.8, 154.2; HRMS calcd for $C_{14}H_{14}O_2$ [M + H]$^+$ 215.1069, found 215.1072.

1-((*E*)-Hept-3-en-1-ynyl)-4-methylbenzene (5fa, Table 3): Yellow liquid (167 mg, 91%); IR (neat) 3448, 3028, 2960, 2929, 2871, 2187, 1716, 1660, 1604, 1508, 1458, 1178 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.94 (t, J = 7.5 Hz, 3H), 1.44−1.50 (m, 2H), 2.12−2.17 (m, 2H), 2.34 (s, 3H), 5.70 (d, J = 16.0 Hz, 1H), 6.20−6.26 (m, 2H), 7.11 (t, J = 8.0 Hz, 2H), 7.32 (t, J = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.7, 21.5, 22.1, 35.4, 87.8, 88.1, 109.9, 120.7, 129.1 (2C), 131.4 (2C), 138.0, 144.6. Anal. Calcd for $C_{14}H_{16}$: C, 91.25; H, 8.75. Found: C, 91.27; H, 8.72.

3-((*E*)-Hept-3-en-1-ynyl)thiophene (5da, Table 3): Dark gray liquid (153 mg, 87%); IR (neat) 3107, 2958, 2930, 2871, 2198, 1654, 1519, 1456, 1355, 1184, 954 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.94 (t, J = 7.0 Hz, 3H), 1.42−1.50 (m, 2H), 2.12−2.16 (m, 2H), 5.68 (d, J = 16.0 Hz, 1H), 6.20−6.26 (m, 1H), 7.11 (d, J = 5.0 Hz, 1H), 7.24−7.26 (m, 1H), 7.40 (d, J = 3.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.7, 22.1, 35.4, 83.0, 88.0, 109.7, 122.7, 125.3, 128.1, 129.9, 144.9; HRMS calcd for $C_{11}H_{12}S$ [M + H]$^+$ 177.0731, found 177.0738.

1-(Trifluoromethyl)-2-((*E*)-4-*p*-tolylbut-3-en-1-ynyl)benzene (5eb, Table 3): Colorless liquid (229 mg, 80%); IR (neat) 3028, 2956, 2198, 1598, 1569, 1488, 1448, 1317, 1263, 1182, 1164, 1118, 952 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.38 (s, 3H), 6.38 (d, J = 16.0 Hz, 1H), 7.09 (d, J = 16.0 Hz, 1H), 7.18 (d, J = 8.0 Hz, 2H), 7.35−7.41 (m, 3H), 7.50 (t, J = 7.5 Hz, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.4, 87.3, 94.9, 106.7, 122.0, 123.4 (q, J_{C-F} = 271.2 Hz, 1C), 125.9 (q, J_{C-F} = 5.0 Hz, 1C), 126.0, 126.6 (2C), 127.8, 129.6 (2C), 131.5, 133.5, 133.8, 139.2, 142.7. Anal. Calcd for $C_{18}H_{13}F_3$: C, 75.51; H, 4.58. Found: C, 75.47; H, 4.61.

3-((*E*)-4-Cyclohexylbut-3-en-1-ynyl)thiophene (5dc, Table 3): Light gray liquid (175 mg, 81%); IR (neat) 3107, 3016, 2923, 2850, 2198, 1660, 1519, 1448, 1353, 1184 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.09−1.22 (m, 3H), 1.25−1.33 (m, 2H), 1.66 (d, J = 12.5 Hz, 1H), 1.75 (d, J = 11.0 Hz, 4H), 2.05−2.11 (m, 1H), 5.63 (d, J = 16.0 Hz, 1H), 6.17−6.22 (dd, J_1 = 16.0 Hz, J_2 = 16.0 Hz, 1H), 7.10 (d, J = 5.0 Hz, 1H), 7.24−7.26 (m, 1H), 7.39 (d, J = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 25.9, 26.1 (2C), 32.4 (2C), 41.5, 83.3, 88.1, 107.2, 122.8, 125.3, 128.0, 129.9, 150.5. Anal. Calcd for $C_{14}H_{16}S$: C, 77.72; H, 7.45. Found: C, 77.74; H, 7.41.

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4-((*E*)-Hept-3-en-1-ynyl)benzonitrile (5ka, Table 3): Colorless liquid (166 mg, 85%); IR (neat) 2960, 2929, 2227, 2200, 1600, 1498, 1406, 1269, 1176 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.95 (t, J = 15.0 Hz, 3H), 1.44−1.51 (m, 2H), 2.15−2.19 (m, 2H), 5.71 (d, J = 16.0 Hz, 1H), 6.30−6.36 (m, 1H), 7.48 (d, J = 8.0 Hz, 2H), 7.60 (d, J = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.7, 21.9, 35.4, 86.5, 93.1, 109.2, 111.1, 118.7, 128.8, 131.9 (2C), 132.0 (2C), 147.2. Anal. Calcd for $C_{14}H_{13}N$: C, 86.12; H, 6.71; N, 7.17. Found: C, 86.15; H, 6.69; N, 7.16.

4-((*E*)-4-*p*-Tolylbut-3-en-1-ynyl)benzonitrile (5kb, Table 3): White solid (199 mg, 82%); mp 88−90 °C ; IR (KBr) 3085, 3024, 2225, 2190, 1595, 1496, 1406, 1176, 1105, 970 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.37 (s, 3H), 6.32 (d, J = 16.0 Hz, 1H), 7.10 (d, J = 16.0 Hz, 1H), 7.17 (d, J = 7.5 Hz, 2H), 7.33 (d, J = 7.5 Hz, 2H), 7.52 (d, J = 8.0 Hz, 2H), 7.60 (d, J = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.5, 89.8, 93.9, 106.2, 111.3, 118.7, 126.6 (2C), 128.7, 129.7 (2C), 132.0, 132.1 (2C), 133.3, 139.5, 143.3 (2C); HRMS calcd for $C_{18}H_{13}N$ $[M + H]^+$ 244.1123, found 244.1126.

1-Methyl-4-((*E*)-4-(4-pentylphenyl)but-1-en-3-ynyl)benzene (5lb, Table 3): Yellow liquid (231 mg, 80%); IR (neat) 3024, 2950, 2854, 2192, 1905, 1606, 1506, 1456, 1409, 1373, 1116, 954 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.93 (t, J = 6.5 Hz, 3H), 1.34−1.38 (m, 4H), 1.64 (t, J = 7.5 Hz, 2H), 2.38 (s, 3 H), 2.63 (t, J = 7.5 Hz, 2H), 6.36 (d, J = 16.0 Hz, 1H), 7.03 (d, J = 16.0 Hz, 1H), 7.16−7.18 (m, 4H),7.34 (d, J = 8.0 Hz, 2H), 7.42 (d, J = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.1, 21.4, 22.6, 31.0, 31.6, 36.0, 88.6, 91.8, 107.4, 120.8, 126.3 (2C), 128.6 (2C), 129.6 (2C), 131.5 (2C), 133.8, 138.7, 141.0, 143.4. Anal. Calcd for $C_{22}H_{24}$: C, 91.61; H, 8.39. Found: C, 91.58; H, 8.37.

2-Methoxy-6-((*E*)-4-(4-methoxyphenyl)but-3-en-1-ynyl)-naphthalene (5hd, Table 3): Yellow solid (274 mg, 86%); mp 96−98 °C; IR (KBr) 2962, 2852, 2098, 1724, 1593, 1506, 1458, 1386, 1251, 1166, 1024, 960 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 3.82 (s, 3H), 3.92 (s, 3H), 6.29 (d, J = 16.5 Hz, 1H), 6.88 (d, J = 9.0 Hz, 2H), 7.02 (d, J = 16.5 Hz, 1H), 7.10 (s, 1H), 7.15 (d, J = 9.0 Hz, 1H), 7.38 (d, J = 8.5 Hz, 2H), 7.48 (d, J = 8.5 Hz, 1H), 7.68 (t, J = 10.0 Hz, 2H), 7.91 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 55.5 (2C), 89.1, 91.8, 106.0, 114.3 (2C), 118,7, 119.5, 125.1, 126.9, 127.8 (2C), 128.7, 129.1, 129.5, 131.1, 134.1, 135.4, 140.7, 158.4, 160.2; HRMS calcd for $C_{22}H_{18}O_2$ $[M + H]^+$ 315.1381, found 315.1385.

1-Methoxy-4-((*E*)-non-3-en-1-ynyl)benzene (5he, Table 3): Yellow liquid (245 mg, 88%); IR (neat) 3018, 2947, 2861, 2194, 1908, 1612, 1521, 1422, 1401, 1384, 1128 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.89 (m, 3H), 1.30−1.36 (m, 4H), 1.41−1.58 (m, 2H) 2.16−2.20 (m, 2H), 3.92 (s, 3H), 5.73 (d, J = 16.0 Hz, 1H), 6.24−6.30 (m, 1H), 7.09 (s, 1H), 7.13 (d, J = 7.0 Hz, 1H) 7.44 (d, J = 8.5 Hz, 1H), 7.64−7.68 (m, 2H), 7.86 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.2, 22.7, 28.9, 31.8, 33.4, 55.5, 88.2, 88.5, 106.0, 109.8, 118.7, 119.4, 126.9, 128.7, 129.2, 129.4, 131.1, 134.1, 145.2, 158.3. Anal. Calcd for $C_{20}H_{22}O$: C, 86.29; H, 7.97. Found: C, 86.31; H, 7.95.

1-((*Z*)-4-(4-Methoxyphenyl)but-1-en-3-ynyl)benzene (5cf, Scheme 2):[20e] Light yellow liquid (189 mg, 81%); ^1H NMR ($CDCl_3$, 500 MHz) δ 3.74 (s, 3H), 5.83 (d, J = 12.0 Hz, 1H), 6.57 (d, J = 12.0 Hz, 1H), 6.80 (d, J = 7.8 Hz, 2H), 7.28−7.36 (m, 5H), 7.84 (d, J = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 55.4, 87.3, 96.2, 107.8 (2C), 114.3, 115.8, 126.3, 128.4 (2C), 128.8 (2C), 133.1, 137.9, 159.9.

1-((*Z*)-4-*p*-Tolylbut-1-en-3-ynyl)benzene (5ff, Scheme 2):[20f] Light yellow liquid (161 mg, 74%); ^1H NMR ($CDCl_3$, 500 MHz) δ 2.37 (s, 3H), 5.92 (d, J = 12.0 Hz, 1H), 6.68 (d, J = 12.0 Hz, 1H), 7.16 (d, J = 8.0 Hz, 2H), 7.37−7.43 (m, 5H), 7.93 (d, J = 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.7, 87.8, 96.3, 107.7, 120.6, 128.4 (2C), 128.6, 128.9 (2C), 129.3 (2C), 131.5 (2C), 136.8, 138.4, 141.0.

Procedure for the Experiment To Test the Homogeneity of the Catalyst in the Coupling Reaction. A mixture (suspension) of 1-(2-bromoethynyl)-4-methoxybenzene (**1c**) (211 mg, 1.0 mmol), pinacol ester of 2-phenylethynylboronic acid (**2a**) (342 mg, 1.5 mmol), Cs_2CO_3 (651 mg, 2 mmol), and $CuFe_2O_4$ (12 mg, 5 mol %) in DMC (5 mL) was stirred at 100 °C (oil bath temperature) for 3 h under argon and allowed to cool to room temperature. The catalyst was separated out, and an aliquot (1 mL) was then withdrawn from the supernatant reaction mixture. After evaporation of solvent from the aliquot, the residue was checked by ^1H NMR, which showed 30% conversion of product with respect to **1c**. The remaining reaction mixture without catalyst was stirred at 100 °C for 12 h. Similarly, an aliquot (1 mL) was withdrawn and checked by ^1H NMR, which showed the same 30% conversion without any further progress.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^1H NMR and ^{13}C NMR spectra for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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