JOC The Journal of Organic Chemistry

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Palladium-Catalyzed Carbonylative Sonogashira Coupling of Aryl Bromides via *tert*-Butyl Isocyanide Insertion

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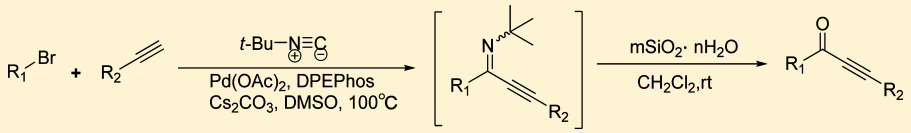
Supporting Information



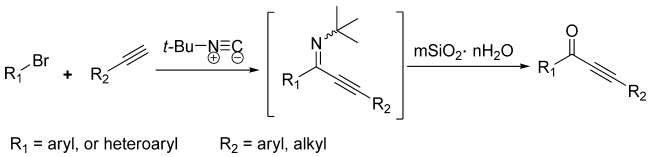
ABSTRACT: A simple and efficient palladium-catalyzed carbonylative Sonogashira coupling via *tert*-butyl isocyanide insertion has been developed, which demonstrates the utility of isocyanides in intermolecular C−C bond construction. This methodology provides a novel pathway for the synthesis of alkynyl imines which can undergo simple silica gel catalyzed hydrolysis to afford alkynones. The approach is tolerant of a wide range of substrates and applicable to library synthesis.

INTRODUCTION

Within the past few decades, isocyanides have emerged as powerful building blocks in modern synthetic organic chemistry, with deep implications in the construction of important medicinal molecules and natural products.[1] Since the pioneering work of Passerini[2] and Ugi,[3] isocyanide insertion reactions have attracted the attention of many chemists. A vast number of articles including two-component reactions[4] and multicomponent reactions (MCRs)[5] have been reported.

On the other hand, owing to the great influence of transition-metal-catalyzed coupling reactions on organic synthesis, carbonylative coupling incorporating carbon monoxide has been well established. Also, crystalline CO-releasing molecules (CORMs) have been investigated to liberate CO for application in carbonylation reactions.[6] Isocyanide, a stable and economic liquid compound which is isoelectronic with carbon monoxide, can be considered to replace carbon monoxide in coupling reactions. So far, a number of transition-metal-catalyzed coupling reactions via the insertion of isocyanides to form C−N[7,8] and C−O[9] bonds have been investigated. For example, Huang and co-workers have reported a palladium-catalyzed cyclization reaction of isocyanides with *o*-halobenzamides.[7g] Very recently, our group developed a simple and facile method for the synthesis of substituted lactones with 1-(2-bromophenyl)ethanones and *tert*-butyl isocyanide, in which isocyanide was easily coupled with an enolic oxygen atom.[9b] Nevertheless, reactions via isocyanide insertion to form C−C bonds have been rarely described. Only recently did the groups of Chatani[4b] and Takemoto[4e] report related reactions with isocyanides. On the basis of these findings, we surmised that it might be possible for the insertion of isocyanides into aryl bromides and terminal alkynes to construct intermolecular C−C bonds to generate alkynones (Scheme 1). Herein, we report a palladium-catalyzed coupling of aryl bromides and terminal alkynes via *tert*-butyl isocyanide insertion, which discloses the utility of isocyanides in intermolecular C−C bond construction. To the best of our knowledge, there have been no reports of carbonylative Sonogashira coupling from isocyanides.

Scheme 1. Strategy to Alkynones via *tert*-Butyl Isocyanide Insertion



Due to the importance of alkynones, they appear in various biologically active molecules[10] and also constitute key intermediates in the synthesis of natural products.[11] The traditional route to prepare alkynones involves the reaction of alkynes with acid chloride.[12] An alternative approach is the palladium-catalyzed carbonylative coupling of alkynes with aryl halides,[13,14] aryl triflates,[15] or aryl amines[16] in the presence of carbon monoxide. However, the drawbacks of high toxicity, harsh reaction conditions, and modest tolerance of functional groups have limited their application. Hence, our methodology may represent a valuable example for the synthesis of alkynones because of the advantage over other methods of simple handling, wide substrate scope, and mild conditions.

RESULTS AND DISCUSSION

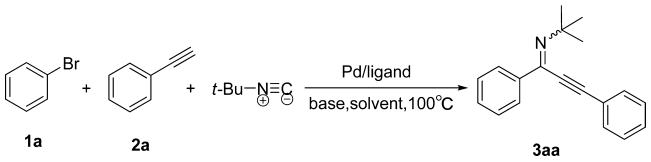
In a pilot experiment, bromobenzene and phenylacetylene were reacted with *tert*-butyl isocyanide in the presence of $Pd(OAc)_2$ and DPEPhos with K_2CO_3 as base. When the reaction was

Received: January 17, 2013
Published: February 25, 2013

   dx.doi.org/10.1021/jo4001096 | *J. Org. Chem.* 2013, 78, 3170−3175

performed in DMF at 100 °C for 2 h, the desired product *N*-(1,3-diphenylprop-2-ynylidene)-2-methylpropan-2-amine (**3aa**) was formed in 52% yield (Table 1, entry 1). Then, the bases for

Table 1. Condition Optimizations[a]



entry	catalyst	ligand	base	solvent	yield[b] (%)
1	$Pd(OAc)_2$	DPEPhos	K_2CO_3	DMF	52
2	$Pd(OAc)_2$	DPEPhos	Cs_2CO_3	DMF	69
3	$Pd(OAc)_2$	DPEPhos	*t*-BuONa	DMF	0
4	$Pd(OAc)_2$	DPEPhos	Cs_2CO_3	DMSO	96
5	$Pd(OAc)_2$	DPEPhos	Cs_2CO_3	dioxane	56
6	$Pd(OAc)_2$	DPEPhos	Cs_2CO_3	toluene	71
7	$Pd(OAc)_2$	Xantphos	Cs_2CO_3	DMSO	75
8	$Pd(OAc)_2$	X-Phos	Cs_2CO_3	DMSO	41
9	$Pd(OAc)_2$	(*R*)-BINAP	Cs_2CO_3	DMSO	84
10	$Pd(OAc)_2$	DPPF	Cs_2CO_3	DMSO	trace
11	$Pd(OAc)_2$	DPPP	Cs_2CO_3	DMSO	0
12	$Pd(OAc)_2$	$BuPAd_2$	Cs_2CO_3	DMSO	87
13	$Pd(OAc)_2$	PCy_3	Cs_2CO_3	DMSO	33
14	$PdCl_2$	DPEPhos	Cs_2CO_3	DMSO	79
15	$Pd_2(dba)_3$	DPEPhos	Cs_2CO_3	DMSO	86

[a]Reaction conditions: all reactions were performed with **1a** (0.5 mmol), **2a** (0.6 mmol), *tert*-butyl isocyanide (0.6 mmol), catalyst (0.015 mmol), ligand (0.03 mmol), and base (1.0 mmol) in 2.0 mL of solvent at 100 °C for 2 h. Abbreviations: DPEPhos = bis[(2-diphenylphosphino)phenyl] ether, Xantphos = 4,5-bis-(diphenylphosphino)-9,9-dimethylxanthene, X-Phos =2-(dicyclohexyl-phosphino)-2′,4′,6′-triisopropylbiphenyl, (*R*)-BINAP = (*R*)-2,2′-bis-(diphenylphosphino)-1,1′-binaphthyl, DPPF = 1,1′-bis(diphenyl-phosphino)ferrocene, DPPP = 1,3-bis(diphenylphosphino)propane. [b]Isolated by neutral alumina chromatography.

the activity of the reaction were examined. To our delight, the yield was improved to 69% when Cs_2CO_3 was used (Table 1, entries 2 and 3). Solvent screening revealed that DMSO appeared to be the best solvent and the yield was significantly increased to 96% (Table 1, entries 4−6). Other commercially available mono- and bidentate ligands were also tested to improve the yield further. However, none of them were found to compete with DPEPhos (Table 1, entries 7−13). In comparison with $Pd(OAc)_2$, other palladium sources such as $PdCl_2$ or $Pd_2(dba)_3$ resulted in diminished yields (Table 1, entries 14 and 15). As for the hydrolysis conditions, a stronger acid led to the addition of a C−C triple bond in comparison to silica gel. Therefore, the optimal reaction conditions were $Pd(OAc)_2$ (3 mol %) and DPEPhos (6 mol %) as the catalyst system, with Cs_2CO_3 (2 equiv) as the base and DMSO as the solvent. Subsequently, silica gel catalyzed hydrolysis of **3aa** afforded alkynone **4aa** in high yield.

With the optimized reaction conditions in hand, we then extended the protocol with a range of commercially available aryl bromides. As illustrated in Table 2, most substrates shown gave clean conversion with no competing formation of Sonogashira products. Both electron-withdrawing as well as electron-donating substituents in the para, meta, and ortho positions were well tolerated and the corresponding 1,3-diarylalkynones were isolated in moderate to excellent yields (Table 2, entries 1−10). To our delight, bromoarenes containing sensitive functional groups such as *p*-Cl and *p*-$COOCH_3$ and strongly electron deficient groups such as *p*-CF_3 and *p*-NO_2 were all coupled smoothly (Table 2, entries 7−10). In addition, disubstituted aryl bromides were also efficiently transformed into the desired products (Table 2, entries 11 and 12). Furthermore, 2-bromonaphthalene, 4-bromobiphenyl, and several heteroaromatic substrates were successfully converted into the corresponding products in good yields (Table 2, entries 13−18). In addition, 1,4-dibromobenzene bearing two bromo substituents could undergo isocyanide insertion twice, thus demonstrating the ultility of the present scaffold (Table 2, entry 19).

To further explore the scope and generality of this approach, a variety of alkynes were investigated, and the results are summarized in Table 3. Both aromatic and aliphatic alkynes were successfully coupled with *tert*-butyl isocyanide (Table 3, entries 1−6). Electron-rich and electron-poor substituents were well tolerated and led to good yields (Table 3, entries 1−4). But aliphatic alkynes resulted in lower yields of the desired product (Table 3, entries 5 and 6). Note that the intermediate alkynyl imines of *o*-bromotoluene (Table 2, entry 3) and aliphatic alkynes (Table 3, entries 5 and 6) generated the byproducts of C−C triple bond hydration in the hydrolysis step, which led to diminished yields.

A plausible mechanism for this reaction is depicted in Scheme 2. Oxidative addition of **1a** to the Pd(0) catalyst leads to the palladium complex **5**, followed by *tert*-butyl isocyanide insertion to form **6**. With the assistance of Cs_2CO_3, the bromide is exchanged by phenylacetylide, which leads to the generation of **7**. Reductive elimination of **7** gives the intermediate **3aa**, which yields the terminal product **4aa** by silica gel catalyzed hydrolysis.

■ CONCLUSIONS

In summary, we have developed a simple and efficient palladium-catalyzed carbonylative Sonogashira coupling via *tert*-butyl isocyanide insertion, which sets an example of isocyanides as carbonyl sources in catalytic C−C bond construction. This methodology provides a novel pathway for the synthesis of alkynones via $Pd(OAc)_2$/DPEPhos-catalyzed coupling reactions and subsequent silica gel catalyzed hydrolysis. Characterized by wide substrate scope, mild reaction conditions, and good to excellent yields, this protocol may aid the further development of the reactions incorporating isocyanides. Related studies are underway in our laboratory.

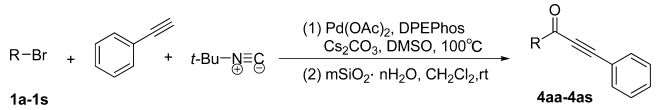
■ EXPERIMENTAL SECTION

General Remarks. Chemicals and reagents were purchased from commercial suppliers and used without special instructions. All anhydrous solvents used in the reactions were dried and freshly distilled. TLC was performed on silica HSGF254 plates. Melting points were determined with a digital melting-point apparatus. ^1H and ^{13}C NMR spectra were obtained from a solution in $CDCl_3$ with TMS as internal standard using a 400/101 MHz ($^1H/^{13}C$) or 300/75 MHz ($^1H/^{13}C$) spectrometer. Chemical shifts (δ) are given in ppm and *J* in Hz. HRMS analyses were carried out on an electrospray ionization (ESI) apparatus using time-of-flight (TOF) mass spectrometry.

General Procedure for the Synthesis of Alkynones. In a 15 mL sealed tube equipped with a magnetic stirring bar were added **1** (0.5 mmol), **2** (0.6 mmol), *tert*-butyl isocyanide (0.6 mmol, 68 μL), $Pd(OAc)_2$ (0.015 mmol, 3 mg), DPEPhos (0.03 mmol, 16 mg), Cs_2CO_3 (1.0 mmol, 326 mg), and anhydrous DMSO (2.0 mL). The tube was purged with argon, and the contents were stirred at 100 °C

dx.doi.org/10.1021/jo4001096 | J. Org. Chem. 2013, 78, 3170−3175

Table 2. Carbonylative Sonogashira Coupling of Various Aryl Bromides with Phenylacetylene via *tert*-Butyl Isocyanide Insertion[a]



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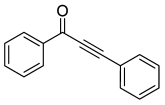
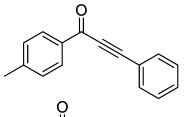
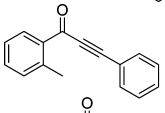
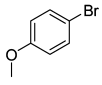
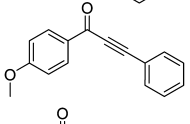
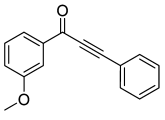
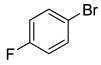
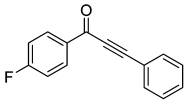
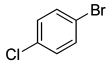
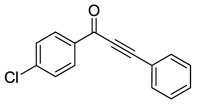
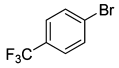
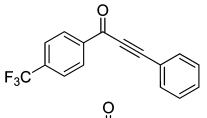
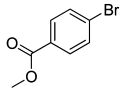
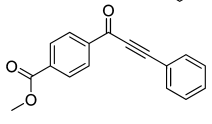
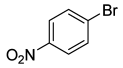
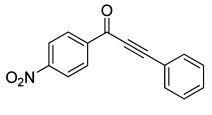
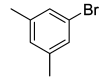
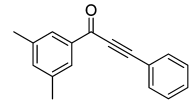
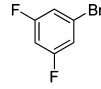
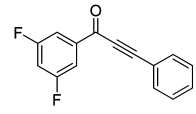
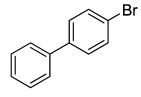
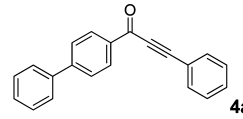
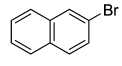
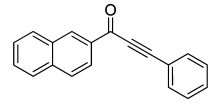
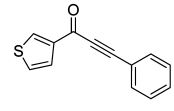
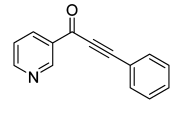
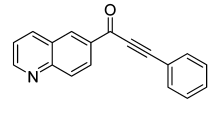
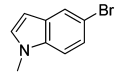
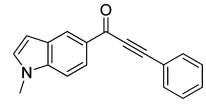
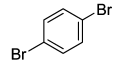
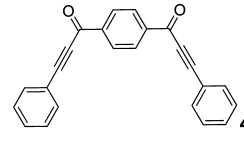
1			94
2			77
3			33
4			79
5			70
6			97
7			69
8			90
9			72
10			55
11			74
12			93
13			76
14			72
15			67
16			61[b]
17			84[b]
18			72[b]
19			42

[a]All reactions were performed under argon on a 0.5 mmol scale, using aryl bromides (0.5 mmol), phenylacetylene (0.6 mmol), *tert*-butyl isocyanide (0.6 mmol), $Pd(OAc)_2$ (0.015 mmol), DPEPhos (0.03 mmol), and Cs_2CO_3 (1.0 mmol) in DMSO (2.0 mL) at 100 °C for 2 h, followed by stirring in methylene dichloride with silica gel at room temperature overnight. [b]Stirring with silica gel for 48 h.

for 2 h. After completion of the reaction as indicated by TLC, the mixture was filtered through neutral aluminum oxide and the solvent was removed under vacuum. Then, the residue was stirred with silica gel in methylene dichloride at room temperature overnight. The resulting mixture was filtered and concentrated, and then the crude product was purified by column chromatography on silica gel using petroleum ether/EtOAc as eluent to provide the pure target product.

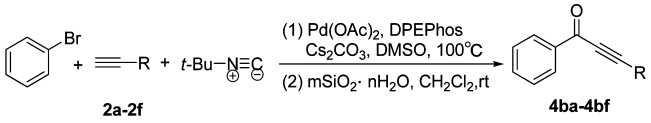
N-(1,3-Diphenylprop-2-ynylidene)-2-methylpropan-2-amine (***3aa***). White solid (125 mg, 96%); mp 59−61 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14−8.03 (m, 2H), 7.60 (dd, J = 7.4, 2.1 Hz, 2H), 7.47−7.38 (m, 6H), 1.56 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 147.0, 139.4, 131.6, 130.0, 129.6, 128.6, 128.1, 127.2, 121.9, 98.9, 84.0, 56.9, 29.5. IR (KBr): ν 2965, 2201, 1599, 1591, 1569, 1488, 1445, 1358, 1313, 1283, 1202, 1017, 758, 692, 670 cm^{-1}. HRMS (ESI): m/z calcd for $C_{19}H_{19}N$ $[M + H]^+$, 262.1596; found, 262.1591.

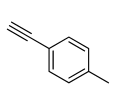
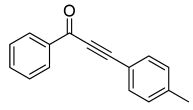
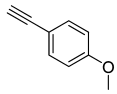
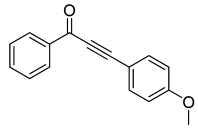
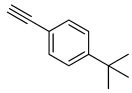
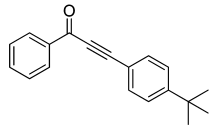
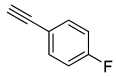
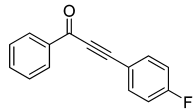
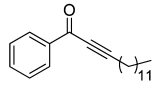
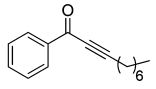
1,3-Diphenylprop-2-yn-1-one (***4aa***).[14] Yellow oil (97 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 7.8 Hz, 2H), 7.71−7.66 (m, 2H), 7.62 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.6 Hz, 2H), 7.47 (d, J = 7.4 Hz, 1H), 7.41 (t, J = 7.4 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.9, 136.7, 134.0, 133.0, 130.7, 129.5, 128.6, 128.5, 120.0, 93.0, 86.8. LRMS (ESI): m/z calcd for $C_{15}H_{10}O$ $[M + H]^+$, 207.1; found, 207.1.

3-Phenyl-1-p-tolylprop-2-yn-1-one (***4ab***).[17] Yellowish solid (85 mg, 77%); mp 63−65 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (d, J = 8.0 Hz, 2H), 7.68 (d, J = 7.2 Hz, 2H), 7.50−7.38 (m, 3H), 7.31 (d, J = 7.9 Hz, 2H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.7, 145.2, 134.6, 133.0, 130.6, 129.7, 129.3, 128.6, 120.2, 92.6, 86.9, 21.8. LRMS (ESI): m/z calcd for $C_{16}H_{12}O$ $[M + H]^+$, 221.1; found, 221.1.

dx.doi.org/10.1021/jo4001096 | J. Org. Chem. 2013, 78, 3170−3175

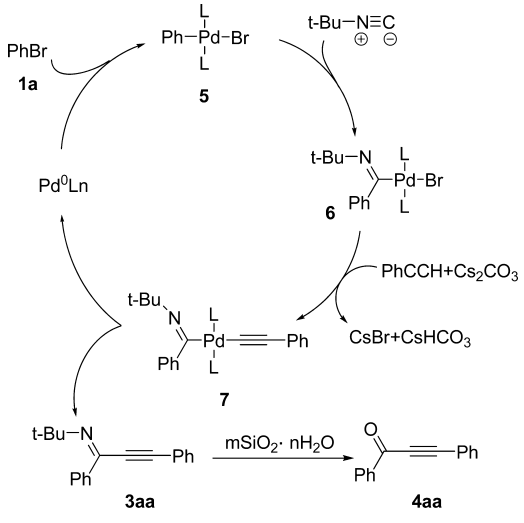
Table 3. Carbonylative Sonogashira Coupling of Bromobenzene with Various Alkynes via *tert*-Butyl Isocyanide Insertion[a]



entry	substrate	product	yield (%)
1	 2a	 4ba	95
2	 2b	 4bb	92
3	 2c	 4bc	88
4	 2d	 4bd	93
5	 2e	 4be	42
6	 2f	 4bf	30

[a]All reactions were performed under argon on a 0.5 mmol scale, using bromobenzene (0.5 mmol), alkynes (0.6 mmol), *tert*-butyl isocyanide (0.6 mmol), $Pd(OAc)_2$ (0.015 mmol), DPEPhos (0.03 mmol), and Cs_2CO_3 (1.0 mmol) in DMSO (2.0 mL) at 100 °C for 2 h, followed by stirring in methylene dichloride with silica gel at room temperature overnight.

Scheme 2. Plausible Mechanism for the Synthesis of 4aa



3-Phenyl-1-o-tolylprop-2-yn-1-one (**4ac**).[17] Yellow oil (36 mg, 33%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31 (d, J = 7.5 Hz, 1H), 7.65 (d, J = 7.0 Hz, 2H), 7.50–7.33 (m, 5H), 7.28 (d, J = 7.2 Hz, 1H), 2.68 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 179.7, 140.5, 135.6, 133.2, 132.9, 132.1, 130.6, 128.6, 125.8, 120.3, 91.8, 88.3, 22.0. LRMS (ESI): m/z calcd for $C_{16}H_{12}O$ $[M + H]^+$, 221.1; found, 221.1.

1-(4-Methoxyphenyl)-3-phenylprop-2-yn-1-one (**4ad**).[14] White solid (93 mg, 79%); mp 91–93 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (d, J = 8.6 Hz, 2H), 7.67 (d, J = 7.3 Hz, 2H), 7.49–7.37 (m, 3H), 6.98 (d, J = 8.6 Hz, 2H), 3.89 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 176.6, 164.4, 132.9, 131.9, 130.5, 130.2, 128.6, 120.3, 113.8, 92.3, 86.9, 55.6. LRMS (ESI): m/z calcd for $C_{16}H_{12}O_2$ $[M + H]^+$, 237.1; found, 237.1.

1-(3-Methoxyphenyl)-3-phenylprop-2-yn-1-one (**4ae**).[12c] Yellow oil (83 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, J = 7.5 Hz, 1H), 7.72–7.65 (m, 3H), 7.51–7.38 (m, 4H), 7.20–7.15 (m, 1H), 3.87 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.7, 159.7, 138.1, 133.0, 130.8, 129.6, 128.6, 122.8, 120.9, 120.0, 112.7, 92.9, 86.9, 55.4. LRMS (ESI): m/z calcd for $C_{16}H_{12}O_2$ $[M + H]^+$, 237.1; found, 237.1.

1-(4-Fluorophenyl)-3-phenylprop-2-yn-1-one (**4af**).[14] Yellowish solid (109 mg, 97%); mp 47–49 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (dd, J = 8.1, 5.7 Hz, 2H), 7.68 (d, J = 7.4 Hz, 2H), 7.53–7.39 (m, 3H), 7.19 (t, J = 8.4 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 176.3, 167.7, 165.1, 133.3, 133.0, 132.2, 132.1, 130.9, 128.7, 119.9, 115.9, 115.7, 93.3, 86.5. LRMS (ESI): m/z calcd for $C_{15}H_9FO$ $[M + H]^+$, 225.1; found, 225.1.

1-(4-Chlorophenyl)-3-phenylprop-2-yn-1-one (**4ag**).[12c] Yellow solid (83 mg, 69%); mp 96–98 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (d, J = 8.3 Hz, 2H), 7.68 (d, J = 7.3 Hz, 2H), 7.48 (d, J = 8.1 Hz, 3H), 7.42 (t, J = 7.4 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 176.6, 140.6, 135.2, 133.1, 130.9, 130.8, 128.9, 128.7, 119.8, 93.6, 86.5. LRMS (ESI): m/z calcd for $C_{15}H_9ClO$ $[M + H]^+$, 241.0; found, 241.0.

3-Phenyl-1-(4-(trifluoromethyl)phenyl)prop-2-yn-1-one (**4ah**).[17] White solid (123 mg, 90%); mp 64–66 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33 (d, J = 7.9 Hz, 2H), 7.79 (d, J = 7.9 Hz, 2H), 7.70 (d, J = 7.4 Hz, 2H), 7.55–7.49 (m, 1H), 7.45 (t, J = 7.3 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.7, 139.3, 135.3, 134.9, 133.2, 131.2, 129.8, 128.8, 125.7, 125.6, 125.3, 119.6, 94.4, 86.5. LRMS (ESI): m/z calcd for $C_{16}H_9F_3O$ $[M + H]^+$, 275.1; found, 275.1.

Methyl 4-(3-phenylpropioloyl)benzoate (**4ai**).[17] White solid (95 mg, 72%); mp 95–97 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (d, J = 8.2 Hz, 2H), 8.16 (d, J = 8.2 Hz, 2H), 7.68 (d, J = 7.3 Hz, 2H), 7.52–7.39 (m, 3H), 3.95 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.1, 166.0, 139.8, 134.6, 133.1, 131.0, 129.7, 129.3, 128.7, 119.7, 94.1, 86.7, 52.5. LRMS (ESI): m/z calcd for $C_{17}H_{12}O_3$ $[M + H]^+$, 265.1; found, 265.1.

1-(4-Nitrophenyl)-3-phenylprop-2-yn-1-one (**4aj**).[12c] Yellow solid (69 mg, 55%); mp 151–153 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (s, 4H), 7.71 (d, J = 7.3 Hz, 2H), 7.58–7.50 (m, 1H), 7.46 (t, J = 7.4 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 175.9, 150.8, 140.9, 133.3, 131.4, 130.4, 128.8, 123.8, 119.3, 95.4, 86.5. LRMS (ESI): m/z calcd for $C_{15}H_9NO_3$ $[M + H]^+$, 252.1; found, 252.1.

1-(3,5-Dimethylphenyl)-3-phenylprop-2-yn-1-one (**4ak**). Yellowish oil (87 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (s, 2H), 7.69 (d, J = 7.3 Hz, 2H), 7.52–7.39 (m, 3H), 7.26 (s, 1H), 2.41 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 178.4, 138.3, 136.9, 135.9, 133.0, 130.6, 128.6, 127.3, 120.2, 92.6, 87.1, 21.2. IR (KBr): ν 2208, 1638, 1605, 1490, 1315, 1170, 1159, 1070, 760, 744, 688 cm^{-1}. HRMS (ESI): m/z calcd for $C_{17}H_{14}O$ $[M + H]^+$, 235.1123; found, 235.1118.

1-(3,5-Difluorophenyl)-3-phenylprop-2-yn-1-one (**4al**). Yellowish solid (112 mg, 93%); mp 79–81 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76–7.65 (m, 4H), 7.51 (t, J = 7.3 Hz, 1H), 7.43 (t, J = 7.5 Hz, 2H), 7.07 (t, J = 8.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 175.1, 164.2, 164.1, 161.7, 161.6, 139.7, 139.6, 139.6, 133.2, 131.3, 128.8, 119.4, 112.4, 112.3, 112.2, 112.1, 109.5, 109.3, 109.0, 94.4, 86.1. IR (KBr): ν 2205, 1642, 1591, 1439, 1321, 1151, 1123, 984, 858, 760, 739, 688 cm^{-1}. HRMS (ESI): m/z calcd for $C_{15}H_8F_2O$ $[M + Na]^+$, 265.0441; found, 265.0440.

1-(Biphenyl-4-yl)-3-phenylprop-2-yn-1-one (**4am**). Yellow solid (107 mg, 76%); mp 133–135 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ

dx.doi.org/10.1021/jo4001096 | J. Org. Chem. 2013, 78, 3170–3175

8.31 (d, J = 7.8 Hz, 2H), 7.78−7.69 (m, 4H), 7.66 (d, J = 7.2 Hz, 2H), 7.46 (dd, J = 17.3, 10.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.5, 146.7, 139.6, 135.6, 133.0, 130.7, 130.1, 128.9, 128.6, 128.4, 127.3, 127.2, 120.1, 93.1, 86.9. IR (KBr): ν 2203, 1635, 1603, 1486, 1311, 1287, 1213, 1172, 1033, 1010, 995, 846, 764, 739, 689 cm^{-1}. HRMS (ESI): m/z calcd for $C_{21}H_{14}O$ [M + Na]$^+$, 305.0942; found, 305.0946.

*1-(Naphthalen-2-yl)-3-phenylprop-2-yn-1-one (**4an**).*[18] Yellow solid (92 mg, 72%); mp 81−83 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.78 (s, 1H), 8.20 (d, J = 8.5 Hz, 1H), 8.02 (d, J = 7.9 Hz, 1H), 7.90 (t, J = 8.9 Hz, 2H), 7.73 (d, J = 7.4 Hz, 2H), 7.59 (dt, J = 14.7, 7.0 Hz, 2H), 7.54−7.42 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.9, 136.1, 134.3, 133.0, 132.6, 132.3, 130.7, 129.8, 129.0, 128.7, 128.5, 127.9, 126.9, 123.9, 120.1, 93.0, 87.0. LRMS (ESI): m/z calcd for $C_{19}H_{12}O$ [M + H]$^+$, 257.1; found, 257.1.

*3-Phenyl-1-(thiophen-3-yl)prop-2-yn-1-one (**4ao**).*[18] Yellow oil (71 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 (d, J = 1.2 Hz, 1H), 7.69−7.62 (m, 3H), 7.51−7.45 (m, 1H), 7.41 (t, J = 7.3 Hz, 2H), 7.35 (dd, J = 4.4, 2.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.3, 142.9, 135.4, 132.9, 130.7, 128.6, 126.8, 126.7, 120.0, 91.3, 87.3. LRMS (ESI): m/z calcd for $C_{13}H_8OS$ [M + H]$^+$, 213.0; found, 213.0.

*3-Phenyl-1-(pyridin-3-yl)prop-2-yn-1-one (**4ap**).*[17] White solid (63 mg, 61%); mp 60−62 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.47 (s, 1H), 8.86 (s, 1H), 8.45 (d, J = 7.8 Hz, 1H), 7.71 (d, J = 7.4 Hz, 2H), 7.56−7.42 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.4, 154.1, 151.4, 136.3, 133.3, 132.2, 131.3, 128.8, 123.6, 119.5, 94.8, 86.3. LRMS (ESI): m/z calcd for $C_{14}H_9NO$ [M + H]$^+$, 208.1; found, 208.1.

*3-Phenyl-1-(quinolin-6-yl)prop-2-yn-1-one (**4aq**).* Yellow solid (108 mg, 84%); mp 120−122 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.03 (d, J = 2.1 Hz, 1H), 8.74 (s, 1H), 8.45 (d, J = 8.6 Hz, 1H), 8.33 (d, J = 8.1 Hz, 1H), 8.19 (d, J = 8.8 Hz, 1H), 7.72 (d, J = 7.3 Hz, 2H), 7.53−7.41 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.1, 153.0, 150.5, 137.7, 134.6, 133.1, 132.0, 130.9, 130.1, 128.7, 127.9, 127.4, 122.1, 119.9, 93.7, 86.8. IR (KBr): ν 2203, 1627, 1324, 1294, 1165, 1117, 910, 848, 803, 781, 760, 725, 688 cm^{-1}. HRMS (ESI): m/z calcd for $C_{18}H_{11}NO$ [M + H]$^+$, 258.0919; found, 258.0923.

*1-(1-Methyl-1H-indol-5-yl)-3-phenylprop-2-yn-1-one (**4ar**).* Crimson solid (93 mg, 72%); mp 102−104 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.60 (s, 1H), 8.10 (d, J = 8.5 Hz, 1H), 7.71 (d, J = 7.0 Hz, 2H), 7.50−7.39 (m, 3H), 7.35 (d, J = 8.6 Hz, 1H), 7.13 (d, J = 1.9 Hz, 1H), 6.66 (d, J = 1.6 Hz, 1H), 3.80 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 178.2, 139.7, 132.8, 130.7, 130.3, 129.3, 128.5, 127.9, 125.4, 122.4, 120.5, 109.2, 103.3, 91.6, 87.4, 33.0. IR (KBr): ν 2203, 1619, 1601, 1313, 1272, 1242, 1158, 1143, 1097, 995, 760, 744, 689 cm^{-1}. HRMS (ESI): m/z calcd for $C_{18}H_{13}NO$ [M + Na]$^+$, 282.0895; found, 282.0883.

*1,1′-(1, 4-Phenylene)bis(3-phenylprop-2-yn-1-one) (**4as**).*[12c] Yellowish solid (70 mg, 42%); mp 188−190 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.35 (s, 4H), 7.71 (d, J = 7.2 Hz, 4H), 7.55−7.49 (m, 2H), 7.45 (t, J = 7.2 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.0, 140.4, 133.2, 131.2, 129.6, 128.8, 119.6, 94.5, 86.8. LRMS (ESI): m/z calcd for $C_{24}H_{14}O_2$ [M + H]$^+$, 335.1; found, 335.1.

*1-Phenyl-3-p-tolylprop-2-yn-1-one (**4ba**).*[14] White solid (105 mg, 95%); mp 50−52 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (d, J = 7.6 Hz, 2H), 7.65−7.56 (m, 3H), 7.52 (t, J = 7.5 Hz, 2H), 7.23 (d, J = 7.8 Hz, 2H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 178.0, 141.5, 136.9, 134.0, 133.1, 129.5, 129.5, 128.6, 116.9, 93.8, 86.7, 21.8. LRMS (ESI): m/z calcd for $C_{16}H_{12}O$ [M + H]$^+$, 221.1; found, 221.1.

*3-(4-Methoxyphenyl)-1-phenylprop-2-yn-1-one (**4bb**).*[14] White solid (108 mg, 92%); mp 68−70 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (d, J = 7.5 Hz, 2H), 7.67−7.59 (m, 3H), 7.51 (t, J = 7.5 Hz, 2H), 6.93 (d, J = 8.5 Hz, 2H), 3.85 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 178.0, 161.7, 137.0, 135.1, 133.9, 129.4, 128.5, 114.4, 111.8, 94.3, 86.8, 55.4. LRMS (ESI): m/z calcd for $C_{16}H_{12}O_2$ [M + H]$^+$, 237.1; found, 237.1.

*3-(4-tert-Butylphenyl)-1-phenylprop-2-yn-1-one (**4bc**).*[14] Yellow oil (115 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (d, J = 7.6 Hz, 2H), 7.63 (t, J = 7.6 Hz, 3H), 7.52 (t, J = 7.5 Hz, 2H), 7.45 (d, J = 8.1 Hz, 2H), 1.34 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 178.0, 154.5, 136.9, 134.0, 133.0, 129.5, 128.5, 125.7, 116.9, 93.8, 86.7, 35.0, 31.0. LRMS (ESI): m/z calcd for $C_{19}H_{18}O$ [M + H]$^+$, 263.1; found, 263.1.

*3-(4-Fluorophenyl)-1-phenylprop-2-yn-1-one (**4bd**).*[19] White solid (104 mg, 93%); mp 73−75 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (d, J = 7.5 Hz, 1H), 8.19 (d, J = 7.5 Hz, 1H), 7.74−7.46 (m, 5H), 7.18−7.05 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.7, 165.1, 162.6, 136.6, 135.3, 135.2, 134.1, 129.4, 128.5, 116.2, 116.1, 116.0, 91.9, 86.7. LRMS (ESI): m/z calcd for $C_{15}H_9FO$ [M + H]$^+$, 225.1; found, 225.1.

*1-Phenylpentadec-2-yn-1-one (**4be**).* Yellow oil (62 mg, 42%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, J = 7.6 Hz, 2H), 7.60 (t, J = 7.3 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 2.50 (t, J = 7.1 Hz, 2H), 1.73−1.63 (m, 2H), 1.51−1.43 (m, 2H), 1.36−1.22 (m, 16H), 0.88 (t, J = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 178.2, 136.8, 133.8, 129.5, 128.4, 96.9, 79.6, 31.9, 29.6, 29.4, 29.3, 29.0, 28.9, 27.8, 22.7, 19.2, 14.1. IR (KBr): ν 2925, 2853, 2236, 2202, 1647, 1450, 1313, 1264, 799, 702 cm^{-1}. HRMS (ESI): m/z calcd for $C_{21}H_{30}O$ [M + Na]$^+$, 321.2194; found, 321.2184.

*1-Phenyldec-2-yn-1-one (**4bf**).* Yellow oil (34 mg, 30%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, J = 7.8 Hz, 2H), 7.60 (t, J = 7.3 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 2.50 (t, J = 7.1 Hz, 2H), 1.73−1.63 (m, 2H), 1.52−1.43 (m, 2H), 1.39−1.24 (m, 6H), 0.90(t, J = 6.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 178.2, 136.9, 133.8, 129.5, 128.4, 96.9, 79.6, 31.6, 28.9, 28.7, 27.8, 22.6, 19.2, 14.1. IR (KBr): ν 2928, 2855, 2235, 2202, 1646, 1451, 1313, 1264, 800, 703 cm^{-1}. HRMS (ESI): m/z calcd for $C_{16}H_{20}O$ [M + Na]$^+$, 251.1412; found, 251.1403.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Figures giving ^{1}H and ^{13}C NMR spectra. 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.

■ ACKNOWLEDGMENTS

We gratefully acknowledge financial support by the PAPD (A Project Funded by the Priority Academic Program Development of Jiangsu Higher Education Institutions) and NSFC (National Nature Science Foundation of China, No. 21172162).

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