Efficient Copper(II) Acetate Catalyzed Homo- and Heterocoupling of Terminal Alkynes at Ambient Conditions

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Abstract: Symmetrical 1,3-diynes were obtained in quantitative yields using the copper(II) acetate catalyzed homocoupling of terminal alkynes in the presence of a stoichiometric amount of piperidine at 25 °C under aerobic conditions. We also accomplished facile syntheses of unsymmetric 1,3-diynes by heterocoupling terminal alkynes in very good yields under the reported reaction conditions.

Key words: terminal alkynes, copper(II) acetate, piperidine, homocoupling, heterocoupling, symmetric 1,3-diynes, unsymmetric 1,3-diynes

Many natural products,[1] particularly antifungal agents,[2] contain conjugated polyyne structures.[3] Conjugated diynes are essential and recurring building blocks in industrial intermediates and in electronic and optical materials.[4] In 1869, Glaser observed the historic acetylenic coupling of copper(I) phenylacetylide under aerobic conditions.[5] Eglinton and Galbraith improved the procedure of Glaser under homogeneous conditions using a stoichiometric amount of copper(II) acetate in pyridine.[6] *N*,*N*,*N*′,*N*′-Tetramethylethylenediamine was used as the co-complexing agent in Hay's procedure for the copper(I)-catalyzed homocoupling of terminal alkynes in the presence of oxygen as an oxidant with pyridine as solvent.[7] Sonogashira[8] and Cadiot–Chodkiewicz[9] coupling methods were employed to accomplish the syntheses of 1,4-disubstituted 1,3-diynes. Glaser coupling is also catalyzed by the bimetallic Pd(0)/Cu(I) system, where copper(I) acts as a co-catalyst.[10] Although these bimetallic palladium-catalyzed homocouplings of terminal alkynes are highly efficient, palladium reagents are far more expensive than readily available copper(I) and copper(II) salts. The requirement for oxidants other than oxygen to regenerate the palladium active species is an added disadvantage in these protocols.[10a,c,d,g,j] To circumvent the use of expensive palladium catalysts, several methodologies have emerged in recent years for the oxidative homocoupling of terminal alkynes using copper(I) or copper(II) salts. Li et al. reported the copper(I) iodide/iodine-mediated homocoupling of alkynes at 80 °C in the presence of sodium carbonate.[11] By replacing iodine by *N*-bromosuccinimide, terminal alkynes were converted into 1,3-diynes in the presence of Hünig's base at ambient temperature.[12] At 110 °C, copper(I)-modified zeolites [Cu(I)-USY] proved to be very efficient catalysts for the homocoupling of terminal alkynes.[13] The influence of bases and ligands on the homocoupling of terminal alkynes using copper(I) was recently reported by Beifuss et al.[14] Efficient copper(I)-mediated homocoupling of terminal alkynes requires a stoichiometric amount of DBU together with a catalytic amount of TMEDA and an oxygen atmosphere. All these palladium-free, efficient, and inexpensive copper(I)-mediated homocouplings of terminal alkynes usually occur only in the presence of excess oxidant, a rigid inorganic base,[11] and at high temperatures; they also require the preparation of the catalyst[13] and additives.[12,14] Copper(II) salt catalyzed oxidative coupling has proved to be of great value since its discovery,[6] but it has gained importance only in recent years. Copper(II) chloride promoted homocoupling of terminal alkynes in supercritical carbon dioxide was reported by Jiang et al.[15] This protocol requires special equipment, high carbon dioxide pressures, and elevated temperatures. The homocouplings of alkynyl boronates[16] and alkynyltrifluoroborates[17] were catalyzed by copper(II) acetate at 60 °C. It is, indeed, necessary to activate terminal alkynes into borates/boronates in these methods. Jiang et al. used CuAl-LDH (Layered Double Hydroxide), which was synthesized by co-precipitation of copper and aluminum nitrates, as a catalyst for the oxidative homocoupling of terminal alkynes.[18] This protocol requires an additional step to synthesize the CuAl-LDH reagent. Apart from all these drawbacks most copper-catalyzed homocoupling, suffer from a very low turnover number.[19]

Developing a methodology for the oxidative homocoupling of alkynes using inexpensive copper(II) salts in the presence of base with no further additives, such as co-catalysts, co-oxidants, or oxygen atmosphere, at ambient temperature is highly desirable. Here we report our findings on the effects of various bases on the formation of 1,3-diynes catalyzed by copper(II) salts under aerobic conditions. We further explored the scope of readily available copper(II) acetate in the presence of piperidine for the syntheses of symmetrical 1,3-diynes and unsymmetrical 1,3-diynes.

To the best of our knowledge there are no reports in the literature regarding the effects of varying the base on copper(II)-catalyzed alkyne homocouplings. Phenylacetylene (**1a**) was chosen as a test substrate in order to identify the optimal reaction conditions for homocoupling. Oxidative homocoupling of phenylacetylene was carried out using

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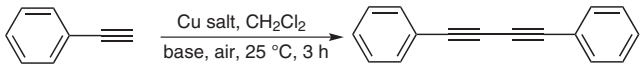
various copper salts (10 mol%) in the presence of base (1 equiv) at room temperature in dichloromethane under air. No oxygen atmosphere, co-oxidants, or additives were utilized. We tested seven copper salts and fifteen different bases and the results are given in Table 1. Initially homocoupling was attempted in the presence of 10 mol% of the copper salt with no addition of base. It is unsurprising that conversion of phenylacetylene (**1a**) into 1,3-diyne **2a** was not observed under these conditions (entry 1). It is clear that no inorganic base (entries 2–6) facilitated oxidative coupling of terminal alkynes under the reaction conditions. This can be attributed to the poor solubility of inorganic bases in dichloromethane. After these disappointing experiments, alkyne coupling was carried out with *N*,*N*,*N*′,*N*′-tetramethylethylenediamine, triethylamine, and diisopropylethylamine (entries 7–9). The presence of these aliphatic tertiary amines did not have any effect on the expected outcome of homocoupling of phenylacetylene (**1a**). In the case of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (entry 7) very low yields of 1,3-diyne **2a** were obtained only when copper(I) iodide, copper(I) chloride, or copper(II) chloride were used as catalysts. When triethylamine was used as the base, copper(II) acetate mediated homocoupling proceeded in 15% yield, but in the case of copper(I) chloride the isolated yield was only 8% (entry 8). Diisopropylethylamine also did not give the expected results for homocoupling (entry 9). The use of bipyridine (entry 10) afforded 1,3-diyne **2a** in moderate yield when copper(I) chloride was the catalyst. Copper(I) chloride and copper(II) acetate mediated oxidative homocoupling afforded 1,3-diynes in good yields in the presence of pyridine (entry 11). No other copper salt was able to catalyze the homocoupling reaction in the presence of pyridine (entry 11). A very good yield of 1,3-diyne **2a** was obtained when DABCO was utilized in the presence of copper(II) acetate (entry 12), however, it did not work very well across the spectrum of copper salts screened except for copper(I) chloride where 75% of homocoupling product was isolated.

In order to identify a base that would effect the transformation of terminal alkynes into 1,3-diynes we expanded our search into secondary amines. It is evident from Table 1 that both pyrrolidine and piperidine are excellent additives for the catalysis of the homocoupling of terminal alkynes in the presence of copper salts (entries 15 and 16). The results clearly indicate that cyclic secondary amines (entries 15 and 16) are superior to acyclic secondary

Table 1 Optimization of the Copper Catalyst and Base for the Homocoupling of Phenylacetylene (**1a**)[a]



1a **2a**

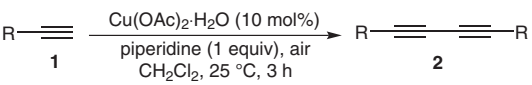
Entry	Base	Isolated yield (%)						
		CuI	CuCl	Cu_2O	$Cu(OAc)_2·H_2O$	$Cu_2SO_4·5\ H_2O$	$CuCl_2·2\ H_2O$	$Cu(OTf)_2$
1	–[b]	–	–	–	–	–	–	–
2	Na_2CO_3	–	trace	–	–	–	–	–
3	K_2CO_3	–	–	–	–	trace	7	trace
4	NaOAc	–	trace	–	–	–	–	trace
5	AgOAc	–	–	trace	–	–	16	–
6	Cs_2CO_3	–	12	trace	–	8	–	–
7	TMEDA	10	9	–	–	–	12	trace
8	Et_3N	–	8	–	15	–	–	trace
9	DIPEA	–	trace	–	16	–	–	trace
10	bipyridine	8	57	trace	30	trace	trace	–
11	pyridine	–	83	–	88	–	–	–
12	DABCO	22	75	8	92	12	11	18
13	*i*-Pr_2NH	15	8	–	10	–	6	trace
14	Et_2NH	93	26	12	38	10	23	21
15	pyrrolidine	71	93	96	91	87	91	92
16	piperidine	91	93	95	97	87	92	98

[a] Reaction conditions: **1a** (1 mmol), Cu salt (10 mol%), base (1 equiv), CH_2Cl_2 (2 mL).
[b] The reaction used copper salts in the absence of base.

amines (entries 13 and 14) and to other bases employed (entries 2–12). It is evident that pyrrolidine or piperidine can be successfully used in combination with copper salts for the efficient dimerization of terminal alkynes at room temperature with no further additives, oxygen atmosphere, or co-oxidants present. Copper(II) acetate and piperidine are readily available and inexpensive. Hence they were chosen for further study to effect the homo- and heterocoupling of various terminal alkynes.

To evaluate the broad substrate scope and to demonstrate the efficiency of the copper(II) acetate/piperidine catalytic protocol for the syntheses of symmetrical 1,3-diynes, a variety of terminal alkynes were subjected to homocoupling using copper(II) acetate monohydrate (10 mol%) and piperidine (1 equiv) at room temperature under aerobic conditions; the results are given in Table 2. Catalytic oxidative homocoupling of phenylacetylenes **1a–c** (entries 1–3) that contain electron-releasing substituents or a chloro group proceeded readily to afford the corresponding 1,3-diyne derivatives **2a–c** up to 97% yield. Conjugated 1,3-diynes **2d**,**e** were obtained from the dimerization of propargylic-derived terminal alcohols **1d**,**e** (entries 4 and 5). Homopropargyl alcohol **1f** afforded diyne **2f** in 84% yield (entry 6). This demonstrates that the hydroxy group does not exert any influence on the progress of dimerization (entries 4–6). Propargyl amine derivatives **1g–i** (entries 7–9) afforded the corresponding diynes **2g–i** under similar reaction conditions. Electron-withdrawing substituents such as the fluoro group (entry 8) or electron-releasing substituents, such as the methoxy group (entries 2 and 9) do not influence the progress of diyne formation. Silyl ethers of propargylic alcohol **1j**,**k** (entries 10 and 11) afforded the corresponding diynes **2j**,**k** in moderate to excellent yields; the volatility of **2j** may be responsible for the moderate yield observed in this dimerization. 1,3-Diyne **2l** was obtained in 75% yield by oxidative homocoupling of aliphatic terminal alkyne, hex-1-yne (**1l**) (entry 12) where as the results of the coupling of alkyl-substituted alkynes were unsatisfactory in the case of copper(I) catalysis.[14] The ester, propargyl benzoate (**1m**), afforded the corresponding diyne **2m** in 71% yield (entry 13). It is obvious that functional groups such as alcohols, halogens, amides, silyl ethers, and esters are stable under these reaction conditions. Mizuno et al. reported effective oxidative alkyne homocoupling with a monomeric dicopper-substituted silicotungstate with a turnover number (TON = amount of **1a** consumed/amount of catalyst) of 468, which is highest amongst copper-catalyzed oxidative homocoupling.[19] In order to determine the TON of our protocol, we performed the homocoupling of phenylacetylene on a 20-mmol scale using 0.2 mol% of copper(II) acetate monohydrate. The TON was found to be 299, the best among simple copper salts to effect the dimerization of terminal alkynes. The strength of our methodology relies on the fact that it uses commercially available and inexpensive copper(II) acetate monohydrate (10 mol%) and piperidine (1 equiv) with no need for any other additives or an oxygen atmosphere. Mild reaction conditions, a simple experimental setup, an easy workup, and high TON are added advantages.

Table 2 Synthesis of Various Conjugated 1,3-Diynes Catalyzed by $Cu(OAc)_2·H_2O$ in the Presence of Piperidine[a]

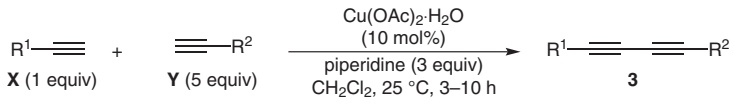


Entry	Alkyne R	1	Time (h)	Product	Yield[b] (%)
1	Ph	**1a**	3	**2a**	97
2	4-$MeOC_6H_4$	**1b**	3	**2b**	88
3	2-ClC_6H_4	**1c**	3	**2c**	94
4	$HOCH_2$	**1d**	3	**2d**	69
5	$HOMe_2C$	**1e**	3	**2e**	88
6	$HOCH_2CH_2$	**1f**	3	**2f**	84
7	$BzNHCH_2$	**1g**	3	**2g**	77
8	2-$FC_6H_4CONHCH_2$	**1h**	3	**2h**	97
9	2-$MeOC_6H_4CONHCH_2$	**1i**	3	**2i**	97
10	$TBDMSOCH_2$	**1j**	3	**2j**	57
11	$TBDPSOCH_2$	**1k**	3	**2k**	92
12	Bu	**1l**	3	**2l**	75
13	$BzOCH_2$	**1m**	3	**2m**	71

[a] Reaction conditions: **1** (1 mmol), $Cu(OAc)_2·H_2O$ (10 mol%), piperidine (1 equiv), CH_2Cl_2, 25 °C.
[b] Isolated and unoptimized yields.

Cadiot–Chodkiewicz and its modified coupling methods are employed in the syntheses of unsymmetric diynes.[20] Palladium-catalyzed heterocouplings of haloalkynes and terminal alkynes are also known for the syntheses of unsymmetrical diynes.[21] Nickel chloride–copper(I) iodide bimetallic catalysis of two different terminal alkynes for the formation of unsymmetric 1,3-diynes was reported by Lei et al.[22] Chen et al. communicated the copper(II) chloride mediated syntheses of heterodiynes in low to moderate yields.[23] Using our protocol, we investigated the cross-coupling of two different alkynes by using an excess of one of the terminal alkyne substrate. Separation of heterocoupling products from homocoupling products would be difficult to achieve if we chose terminal alkynes of similar polarity. Hence we selected one nonpolar and another polar terminal alkyne for heterocoupling reactions. The substrate scope of the synthesis of unsymmetric 1,3-diynes were examined and the results are furnished in Table 3. As shown in Table 3, unsymmetric 1,3-diynes were synthesized in 70–99% yield; these yields are among the best reported yields for the heterocoupling of terminal alkynes. Since we have used one of the alkynes in excess, we also isolate the corresponding homocoupled 1,3-diynes in very good yields. In the presence of air all the reactions pro-

Table 3 Syntheses of Various Conjugated Unsymmetric 1,3-Diynes[a]



Entry	Alkyne **X**		Alkyne **Y**		Product	Time (h)	Yield[b] (%)
	R^1		R^2				
1	Ph	**1a**	$HOCH_2$	**1d**	**3a**	6	75
2	4-$MeOC_6H_4$	**1b**	Ph	**1a**	**3b**	8	79
3	$HOMe_2C$	**1e**	Ph	**1a**	**3c**	3	99
4	$HOCH_2CH_2$	**1f**	Ph	**1a**	**3d**	8	96
5	$BzNHCH_2$	**1g**	Ph	**1a**	**3e**	5	70
6	2-$FC_6H_4CONHCH_2$	**1h**	Ph	**1a**	**3f**	5	90
7	2-$MeOC_6H_4CONHCH_2$	**1i**	Ph	**1a**	**3g**	10	87
8	$BzOCH_2$	**1m**	$HOMe_2C$	**1e**	**3h**	3	90

[a] Reaction conditions: alkyne **X** (1 mmol), alkyne **Y** (5 mmol), $Cu(OAc)_2·H_2O$ (10 mol%), piperidine (3 mmol), CH_2Cl_2, 25 °C, 3–10 h.
[b] Yields are based on amount of **X** used.

ceeded smoothly. Excess propargyl alcohol (**1d**) (5 mmol) reacted with phenylacetylene (**1a**) to afford unsymmetric 1,3-diyne **3a** in 75% yield (entry 1). Phenylacetylene (**1a**) was successfully cross-coupled with various terminal alkynes in good to excellent yields (entries 2–7). Propargylic alcohols and various functional groups such as amido, methoxy, and fluoro were tolerated well (entries 2–7) under the reaction conditions. Excess 2-methylbut-3-yn-2-ol (**1e**) was reacted with propargyl benzoate (**1m**) to afford heterodimer 1,3-diyne **3h** in 90% yield (entry 8).

Heterocoupling of terminal alkynes using our method does not need a bimetallic catalysis, such as nickel(II) chloride hexahydrate;[22] it also does not suffer from poor yields as in the case of copper(II) chloride.[23] Our mild reaction conditions tolerate a wide range of functional groups such as amide, ester, and alcohol. Electron-withdrawing as well as electron-releasing groups in phenylacetylenes did not influence progress of the reaction to form heterodiynes. In summary the heterocoupling of terminal alkynes can be achieved using our synthetic protocol in good to excellent yields.

In summary, we have developed a copper(II) acetate monohydrate catalyzed aerobic oxidative dimerization that efficiently promoted the homo- and heterocoupling of terminal alkynes under mild conditions in the presence of piperidine. Coupling reactions proceeded with very good yields without any other additives, such as a co-catalyst or an oxygen atmosphere. The products were isolated using a simple workup procedure. All reagents are readily available and inexpensive. The reaction condition is suitable for various substrates bearing electron-donating and -withdrawing groups.

CH_2Cl_2, petroleum ether (PE), and EtOAc were purified prior to use by distillation. Reagents obtained from Aldrich, Fluka, Alfa Aesar, and Merck were used directly. ^1H and ^{13}C NMR data were recorded with a Bruker Avance AV500 (500 MHz and 125.7 MHz) spectrometer with TMS as internal standard. HRMS were measured under the condition of electrospray ionization (ESI) accurate masses were reported for the molecular ion ($[M]^+$, $[M + 1]^+$, $[M + 23]^+$). IR spectra were recorded on an FT-IR instrument. Column chromatography was carried out using 230–400 mesh silica gel (Merck) in PE and EtOAc. TLC was performed on commercially available precoated aluminum-backed plates (0.25 mm silica gel with fluorescent indicator UV 254). Visualization was achieved by either UV or phosphomolybdic acid. For known compounds the physical (e.g., melting points) and spectroscopic data were compared with those in the literature.

Symmetric 1,3-Diynes 2 under Atmospheric Air; General Procedure

A mixture of alkyne **1** (1 mmol), piperidine (1 mmol), and $Cu(OAc)_2·H_2O$ (10 mol%) in CH_2Cl_2 (2 mL) was stirred in open atmospheric air at 25 °C (TLC monitoring) for 3 h, the mixture was concentrated in vacuo and the residue was purified by column chromatography (silica gel, PE–EtOAc) to afford **2**.

N,*N*′-(Hexa-2,4-diyne-1,6-diyl)bis(2-fluorobenzamide) (2h)

Mp 168–170 °C; R_f = 0.7 (hexanes–EtOAc, 1:1).

IR (neat): 3268, 2358, 2021, 1650, 1534, 1301, 1227, 748, 679 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.11 (td, *J* = 7.9, 1.8 Hz, 2 H), 7.51–7.47 (m, 2 H), 7.27 (td, *J* = 7.8, 1.0 Hz, 2 H), 7.13 (m, 2 H), 6.92 (br s, 2 H), 4.36 (d, *J* = 4.4 Hz, 4 H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 162.8, 161.6, 159.7, 133.7, 132.2, 124.9, 116.0, 74.0, 67.7, 30.2.

HRMS (EI): *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{15}F_2N_2O_2$: 353.1102; found: 353.1100.

N,*N*′-(Hexa-2,4-diyne-1,6-diyl)bis(2-methoxybenzamide) (2i)

Mp 133–135 °C; R_f = 0.7 (hexanes–EtOAc, 1:1).

IR (neat): 3376, 2928, 2850, 2358, 1716, 1642, 1519, 1292, 1167, 1018, 752 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.20 (dd, *J* = 7.8, 1.8 Hz, 2 H), 8.07 (br s, 2 H), 7.45 (td, *J* = 7.8, 1.8 Hz, 2 H), 7.07 (t, *J* = 7.8 Hz, 2 H), 6.97 (d, *J* = 8.3 Hz, 2 H), 4.34 (d, *J* = 5.1 Hz, 4 H), 3.98 (s, 6 H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 164.9, 157.5, 133.2, 132.4, 121.3, 120.6, 111.3, 74.6, 67.3, 56.0, 29.9.

HRMS (EI): *m*/*z* $[M + H]^+$ calcd for $C_{22}H_{21}N_2O_4$: 377.1501; found: 377.1494.

Unsymmetric 1,3-Diynes 3 under Atmospheric Air; General Procedure

A mixture of alkyne **X** (1 mmol), alkyne **Y** (5 mmol), piperidine (3 mmol), and $Cu(OAc)_2·H_2O$ (10 mol%) in CH_2Cl_2 (5 mL) was stirred in open atmospheric air at 25 °C (TLC monitoring) for 3–10 h. The mixture was concentrated in vacuo and the residue was purified by column chromatography (silica gel, PE–EtOAc) to afford **3**.

***N*-(5-Phenylpenta-2,4-diynyl)benzamide (3e)**

Mp 106–108 °C; R_f = 0.2 (hexanes–EtOAc, 9:1).

IR (neat): 3353, 3067, 2978, 2244, 1763, 1634, 1435, 1044, 755, 689 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.25 (br s, 1 H), 8.04–7.89 (m, 2 H), 7.5–7.30 (m, 8 H), 4.36 (d, *J* = 5.1 Hz, 2 H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 167.0, 133.7, 132.3, 131.4, 129.5, 129.1, 128.3, 128.2, 127.3, 79.7, 76.7, 73.6, 67.1, 30.0.

HRMS (EI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{14}NO$: 260.1075; found: 260.1070.

2-Fluoro-*N*-(5-phenylpenta-2,4-diynyl)benzamide (3f)

Mp 86–88 °C; R_f = 0.1 (hexanes–EtOAc, 9:1).

IR (neat): 3460, 3053, 2971, 2843, 2544, 2213, 2148, 1719, 1660, 1527, 1295, 1030, 752 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.12 (td, *J* = 7.9, 1.9 Hz, 1 H), 7.49–7.47 (m, 3 H), 7.36–7.26 (m, 4 H), 7.16–7.11 (m, 1 H), 6.98 (br s, 1 H), 4.45 (dd, *J* = 5.2, 1.2 Hz, 2 H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 162.9, 160.6, 133.7, 132.4, 130.1, 129.3, 128.4, 124.9, 121.3, 120.1, 116.0, 78.0, 77.3, 73.3, 68.2, 30.5.

HRMS (EI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{13}FNO$: 278.0981; found: 278.0985.

2-Methoxy-*N*-(5-phenylpenta-2,4-diynyl)benzamide (3g)

Mp 120–122 °C; R_f = 0.1 (hexanes–EtOAc, 9:1).

IR (neat): 3384, 3055, 2978, 2936, 2244, 1893, 1649, 1526, 1245, 1025, 753 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.20 (dd, *J* = 7.8, 1.8 Hz, 1 H), 8.10 (br s, 1 H), 7.47–7.43 (m, 3 H), 7.35–7.27 (m, 3 H), 7.06 (t, *J* = 7.6 Hz, 1 H), 6.96 (d, *J* = 8.1 Hz, 1 H), 4.42 (d, *J* = 5.2 Hz, 2 H), 3.97 (s, 3 H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 164.9, 157.5, 133.2, 132.5, 132.4, 129.2, 128.3, 121,4, 121.3, 120.6, 111.3, 79.0, 77.0, 73.5, 67.6, 56.0, 30.2.

HRMS (EI): *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{16}NO_2$: 290.1181; found: 290.1173.

6-Hydroxy-6-methylhepta-2,4-diynyl Benzoate (3h)

R_f = 0.1 (hexanes–EtOAc, 9:1).

IR (neat): 3461, 3322, 3063, 2983, 2935, 2211, 1721, 1602, 1444, 1262, 1101, 956, 832, 711 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.06–8.04 (m, 2 H), 7.59–7.56 (m, 1 H), 7.45 (t, *J* = 7.1 Hz, 2 H), 4.98 (s, 2 H), 1.53 (s, 6 H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 165.7, 133.4, 129.8, 129.2, 128.4, 84.0, 73.5, 70.6, 66.2, 65.5, 52.8, 30.9.

HRMS (EI): *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{14}O_3Na$: 265.0841; found: 265.0848.

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References

(1) (a) Holmes, A. B.; Jennings-White, C. L. D.; Kendrick, D. A. *J. Chem. Soc., Chem. Commun.* **1983**, 415. (b) Nicolaou, K. C.; Zipkin, R. E.; Dolle, R. E.; Harris, B. D. *J. Am. Chem. Soc.* **1984**, *106*, 3548. (c) Crombie, L.; Hobbs, A. J. W.; Horsham, M. A.; Blade, R. J. *Tetrahedron Lett.* **1987**, *28*, 4875. (d) Holmes, A. B.; Tabor, A. B.; Baker, R. *J. Chem. Soc., Perkin Trans. 1* **1991**, 3307. (e) Hoye, T. R.; Hanson, P. R. *Tetrahedron Lett.* **1993**, *34*, 5043. (f) Shi Shun, A. L. K.; Tykwinski, R. R. *Angew. Chem. Int. Ed.* **2006**, *45*, 1034.

(2) Stütz, A. *Angew. Chem. Int. Ed.* **1987**, *26*, 320.

(3) (a) Bohlmann, F.; Burkhardt, T.; Zdero, C. *Naturally Occurring Acetylenes*; Academic Press: London, **1973**. (b) Hansen, L.; Boll, P. M. *Phytochemistry* **1986**, *25*, 285. (c) Matsunaga, H.; Katano, M.; Yamamoto, H.; Fujito, H.; Mori, M.; Takata, K. *Chem. Pharm. Bull.* **1990**, *38*, 3480. (d) Shi Shun, A. L. K.; Tykwinski, R. R. *Angew. Chem. Int. Ed.* **2006**, *45*, 1034.

(4) (a) *Acetylene Chemistry: Chemistry, Biology and Material Science*; Diederich, F.; Stang, P.; Tykwinski, R. R., Eds.; Wiley-VCH: Weinheim, **2005**. (b) *Carbon-Rich Compounds: From Molecules to Materials*; Haley, M. M.; Tykwinski, R. R., Eds.; Wiley-VCH: Weinheim, **2006**.

(5) (a) Glaser, C. *Ber. Dtsch. Chem. Ges.* **1869**, *2*, 422. (b) Glaser, C. *Ann. Chem. Pharm.* **1870**, *154*, 137.

(6) Eglinton, G.; Galbraith, A. R. *Chem. Ind. (London)* **1956**, 737.

(7) (a) Hay, A. S. *J. Org. Chem.* **1960**, *25*, 1275. (b) Hay, A. S. *J. Org. Chem.* **1962**, *27*, 3320.

(8) (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16*, 4467. (b) Sonogashira, K. *Coupling Reactions between sp Carbon Centers,* In *Comprehensive Organic Synthesis*, Vol. 3; Trost, B. M.; Fleming, I., Eds.; Pergamon: Oxford, **1990**, 521.

(9) Cadiot, P.; Chodkiewicz, W. *Chemistry of Acetylenes*; Viehe, H. G., Ed.; Marcel Dekker: New York, **1969**, 597.

(10) (a) Rossi, R.; Carpita, A.; Bigelli, C. *Tetrahedron Lett.* **1985**, *26*, 523. (b) Vlassa, M.; Ciocan-Tarta, I.; Mārgineanu, F.; Oprean, I. *Tetrahedron* **1996**, *52*, 1337. (c) Liu, Q.; Burton, D. J. *Tetrahedron Lett.* **1997**, *38*, 4371. (d) Lei, A.; Srivastava, M.; Zhang, X. *J. Org. Chem.* **2002**, *67*, 1969. (e) Fairlamb, I. J. S.; Bäuerlein, P. S. B.; Marrison, L. R.; Dickinson, J. M. *Chem. Commun.* **2003**, 632. (f) Batsanov, A. S.; Collings, J. C.; Fairlamb, I. J. S.; Holland, J. P.; Howard, J. A. K.; Lin, Z.; Marder, T. B.; Parsons, A. C.; Ward, R. M.; Zhu, J. *J. Org. Chem.* **2005**, *70*, 703. (g) Li, J. H.; Liang, Y.; Zhang, X. D. *Tetrahedron* **2005**, *61*, 1903. (h) Li, J. H.; Liang, Y.; Xie, Y. X. *J. Org. Chem.* **2005**, *70*, 4393. (i) Shi, M.; Qian, H. X. *Appl. Organomet. Chem.* **2006**, *20*, 771. (j) Yan, J.; Wu, J.; Jin, H. *J. Organomet. Chem.* **2007**, *692*, 3636.

(11) Li, D.; Yin, K.; Li, J.; Jia, X. *Tetrahedron Lett.* **2008**, *49*, 5918.
(12) Li, L.; Wang, J.; Zhang, G.; Liu, Q. *Tetrahedron Lett.* **2009**, *50*, 4033.
(13) Kuhn, P.; Alix, A.; Kumarraja, M.; Louis, B.; Pale, P.; Sommer, J. *Eur. J. Org. Chem.* **2009**, 423.
(14) Adimurthy, S.; Malakar, C. C.; Beifuss, U. *J. Org. Chem.* **2009**, *74*, 5648.
(15) (a) Li, J.; Jiang, H. *Chem. Commun.* **1999**, 2369. (b) Jiang, H. F.; Tang, J. Y.; Wang, A. Z.; Deng, G. H.; Yang, S. R. *Synthesis* **2006**, 1155.
(16) Nishihara, Y.; Okamoto, M.; Inoue, Y.; Miyazaki, M.; Miyasaka, M.; Takagi, K. *Tetrahedron Lett.* **2005**, *46*, 8661.
(17) Paxião, M. W.; Weber, M.; Braga, A. L.; De Azeredo, J. B.; Deobald, A. B.; Stefani, H. A. *Tetrahedron Lett.* **2008**, *49*, 2366.
(18) Zhu, B. C.; Jiang, X. Z. *Appl. Organomet. Chem.* **2007**, *21*, 345.
(19) Kamata, K.; Yamaguchi, S.; Kotani, M.; Yamaguchi, K.; Mizuno, N. *Angew. Chem. Int. Ed.* **2008**, *47*, 2407.
(20) (a) Alami, M.; Ferri, F. *Tetrahedron Lett.* **1996**, *37*, 2763. (b) Nishihara, Y.; Ikegashira, K.; Mori, A.; Hiyama, T. *Tetrahedron Lett.* **1998**, *39*, 4075. (c) Montierth, J. M.; DeMario, D. R.; Kurth, M. J.; Schore, N. E. *Tetrahedron* **1998**, *54*, 11741. (d) Kim, S.; Kim, S.; Lee, T.; Ko, H.; Kim, D. *Org. Lett.* **2004**, *6*, 3601.
(21) (a) Miyaura, N.; Yamada, K.; Suzuki, A. *Tetrahedron Lett.* **1979**, *20*, 3437. (b) Wityak, J.; Chan, J. B. *Synth. Commun.* **1991**, *21*, 977. (c) Amatore, C.; Blart, E.; Genet, J. P.; Jutand, A.; Lemaire-Audoire, S.; Savignac, M. *J. Org. Chem.* **1995**, *60*, 6829.
(22) Yin, W.; He, C.; Chen, M.; Zhang, H.; Lei, A. *Org. Lett.* **2009**, *11*, 709.
(23) Wang, D.; Li, J.; Li, N.; Gao, T.; Hou, S.; Chen, B. *Green Chem.* **2010**, *12*, 45.