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Calcium carbide as a cost-effective starting material for symmetrical diarylethynes via Pd-catalyzed coupling reaction

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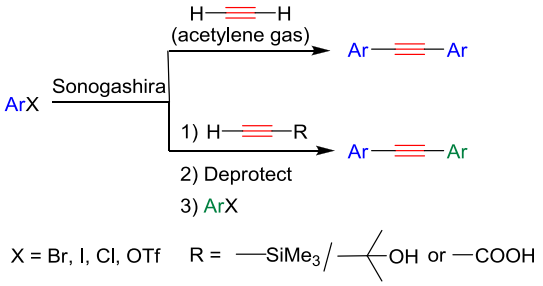
ABSTRACT

A convenient and cost-effective synthetic method for symmetrical diarylethynes from inexpensive calcium carbide and aryl iodide has been developed. The reaction not only proceeds with high yield and selectivity but also tolerates a wide range of functional groups. Application of this reaction has enabled the synthesis of highly functionalized oligo (phenyleneethynylenes) to be accomplished.

1. Introduction

Over the past two decades, Pd-catalyzed cross-coupling reactions, such as Heck, Suzuki, Nigishi, Stille, and Sonogashira reactions have been the most powerful tools for C–C bond construction.[1–7] Among these, the Sonogashira cross-coupling reaction is the most efficient method to connect sp-C to sp^2-C in the synthesis of diarylalkynes and areneethynylene polymers due to the simplicity of the reaction process.[8–18] These compounds have caught much attention recently in the fields of bioactive compounds and functional materials.[19–22] Historically, the Sonogashira reaction utilized terminal acetylene, usually obtained from protected acetylene, as an sp-C source, and later, acetylene gas has also been used (Scheme 1).[8–18,23–25] Acetylene gas is appreciably more economical than the terminal acetylenes for the synthesis of symmetrical diarylethyne that can be accomplished within one step. Due to complicated handling and close attention required for an application of highly flammable acetylene gas, the three-step synthesis of diarylethynes from terminal acetylene is currently a more favorable route. Recently, a number of reports demonstrated the use of inexpensive and readily available calcium carbide, as the acetylene surrogate in the preparation of carbon nanotubes,[26] polyynes,[27] and aryltriazoles.[28] The utilization of calcium carbide for Pd-catalyzed coupling reaction was pioneered by Zhang[29] using aryl bromides for preparation of symmetrical diarylethynes. Even though it was the first report on the use of calcium carbide for the synthesis of diarylalkynes, a non-commercially available amino phosphine ligand and elevated reaction temperature were required to obtain reasonable yields of the desired products. We found that this inspiring work worth further exploring as a general and economical synthetic approach for symmetrical diarylethynes. Herein, we report a convenient synthetic method for symmetrical diarylethynes from calcium carbide and aryl iodides at room temperature using commercially available and inexpensive reagents including the catalyst and base. The reaction also displayed a wide range of functional group compatibility.[1]



Scheme 1. Typical methods for the synthesis of diarlyethynes.

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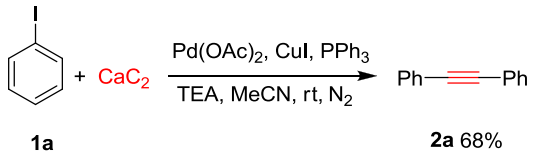
2. Results and discussion

2.1. Initial observation

Our initial attempts involved the treatment of calcium carbide with halobenzene (Br, I) or sulfonate esters (OTs, OTf), in acetonitrile at room temperature in the presence of $Pd(OAc)_2$ (2.5 mol %), triphenylphosphine (PPh_3, 5 mol %), CuI (5 mol %), and triethylamine (TEA). The reaction of bromobenzene or triflate gave no desired product and only a small amount of starting material could be recovered along with unidentified complex mixtures. In the case of the tosylate, only a trace amount of the target compound diphenylethyne was isolated along with an almost quantitative recovery of starting material. It was assumed that aryl iodides would enhance the formation of the desired product under these conditions. To our delight, switching from bromide to iodide analogues, diphenylethyne **2a** was obtained in 68% yield along with recovery of iodobenzene (15%) (Scheme 2).

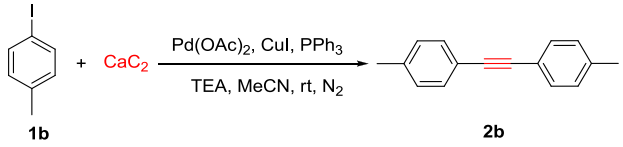


Scheme 2. Initial observation. All reactions were carried out with phenyl derivatives (1 equiv), CaC_2 (3 equiv), $Pd(OAc)_2$ (2.5%), CuI (5%), PPh_3 (5%), and triethylamine (3 equiv) at rt for 10 h.

2.2. Reaction condition screening

Following this initial observation, 4-iodotoluene (**1b**) was selected, due to a clear difference between the methyl group ^1H NMR signal of the starting material **1b** and that of its product **2b**, for reaction optimization, including palladium and copper sources, bases, temperature, and catalyst amount (Table 1). $Pd(OAc)_2$ was found to be the most effective palladium source for this reaction in comparison with bis(triphenylphosphine)-palladium(II) dichloride and palladium tetrakis (entries 1–3). Cleary, CuI is needed in the reaction, and its absence resulted in a lower yield (22%, entry 4).

Table 1
Optimization of reaction condition[a]



Entry	Pd/Cu source	Base	Solvent	Yield[b] (%)
1	$Pd(OAc)_2$/CuI	TEA	MeCN	50
2	$PdCl_2(PPh_3)_2$/CuI	TEA	MeCN	24
3	$Pd(PPh_3)_4$/CuI	TEA	MeCN	24
4	$Pd(OAc)_2$/—	TEA	MeCN	22
5	$Pd(OAc)_2$/CuOAc	TEA	MeCN	50
6	$Pd(OAc)_2$/$(CuOAc)_2$	TEA	MeCN	50
7	$Pd(OAc)_2$/CuI	DIPEA	MeCN	41
8	$Pd(OAc)_2$/CuI	K_2CO_3	THF	0[c]
9	$Pd(OAc)_2$/CuI	K_2CO_3	MeOH	16
10	$Pd(OAc)_2$/CuI	TEA	MeCN	40[d]
11	$Pd(OAc)_2$/CuI	TEA	MeCN	30[e]
12	$Pd(OAc)_2$/CuI	TEA	MeCN	99[f]

[a] Unless otherwise noted, a mixture of 4-iodotoluene (1 equiv), CaC_2 (3 equiv), Pd catalyst (2.5%), PPh_3 (5%), Cu catalyst (5%), and base (3 equiv) was stirred at room temperature for 10 h.
[b] Isolated yield.
[c] 4-Iodotoluene (90%) was recovered.
[d] Heated at 60 °C.
[e] Reaction was carried out under air.
[f] $Pd(OAc)_2$ (5%), 10% CuI, and 10% of PPh_3 were used.

However, alternative copper sources, such as CuOAc and $Cu(OAc)_2$, could be used in this transformation (entries 5 and 6). Base screening indicated that TEA was the most effective base in comparison with others, although diisopropylethylamine gave satisfactory results (entry 7). When the reaction was carried out at 60 °C, 40% of 1,2-di-p-tolylethyne was isolated without the recovery of any starting material (entry 10). Under atmospheric condition, a lower yield of the desired product was isolated (30%, entry 11) in comparison with that under inert nitrogen environment. We were pleased to realize that the reactions went to completion with an increased amount of catalyst. Most interestingly, reaction proceeded smoothly at room temperature (Table 1, entry 12). Thus, the optimized conditions involved treatment of 4-iodotoluene **1b** (1 equiv), CaC_2 (3 equiv), $Pd(OAc)_2$ (5%), PPh_3 (10%), CuI (10%), and triethylamine (3 equiv) in MeCN at room temperature under a nitrogen atmosphere. Under these optimized conditions, the coupling product **2b** was isolated in 99% yield (Table 1, entry 12). It must be noted that under these conditions, complete conversion to **2b** was observed by NMR spectroscopic analysis and TLC. To the best of our knowledge, formation of diarylethynes under these efficient and mild conditions has not been reported in the literature.[12,16–18,25,29–31,38]

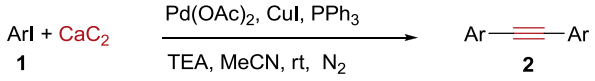
2.3. Substrate scope

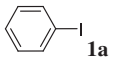
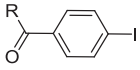
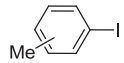
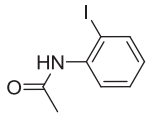
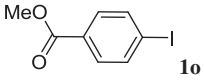
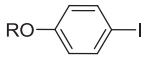
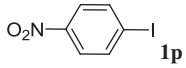
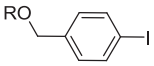
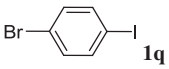
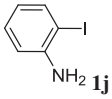
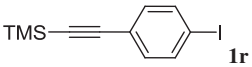
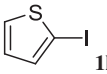
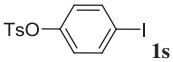
The new method has allowed variety functional groups to be tested. Therefore, a series of aryl iodides either commercially available or prepared according to literature procedures were subjected to the coupling reaction with CaC_2 under the optimized reaction conditions (Table 1, entry 12) and the results were summarized in Table 2. The aryl iodides bearing an electron donating group, such as methyl, naphthyl, and, methoxy (entries 2–4) yielded the desired bisarylacetylenes in good to excellent yields. Notably, the substituent position effect was found to be minimal in our study, as seen in the case of three isomers of iodotoluenes (**1b**, **1c**, and **1d**), providing the coupling products **2b**, **2c**, and **2d** in 99%, 99%, and 96% yields, respectively (entry 2). However, 4-iodobenzyl alcohol (**1i**) and 4-iodo aniline (**1j**) were not suitable for this transformation as they afforded the target compounds, **2i** in only 41% yield, while complex mixtures were obtained in the case of **1j**. These results may be due to the chelation of the palladium catalyst with the high electron density oxygen or nitrogen atoms. The yield was significantly increased when the hydroxyl moiety in 1i was methylated. The product **2h** was isolated in much higher yield. Interestingly, the presence of a sulfur atom had no effect in this reaction, as shown in the coupling reaction of 2-iodothiophene (**1k**). The product **2k** was produced in 99% yield. The substrates bearing electron-withdrawing groups, such as the aldehyde, ketone, amido, ester, and nitro moieties reacted efficiently to obtain the coupled products in good to high yields (entries 8–11). In contrast to previous report, our experiment resulted in good yields of product **2m** and **2p**.[29] This outcome suggests that the rate determining step of this reaction may not be the same as the reactions investigated by Zhang.[29] Moreover, other leaving groups, such as bromo and tosyl as well as trimethylsilyl protecting groups well tolerated the reaction conditions and iodo group were reacted selectively, giving the desired products in excellent yields (entries 12–14). We attributed the wide range of functional group tolerance to the heterogeneous nature of calcium carbide and proper concentration of gradually generated acetylene gas under the reaction condition. These high functional group selectivity and compatibility should expand the scope of this reaction in the synthesis of more complex π-conjugated molecules with further modification at the remaining reactive groups.

2.4. Synthesis of oligo (phenyleneethynylenes)

The success of this Pd-catalyzed reaction turned our attention to the synthesis of oligo-(aryleneethynylenes). Such compounds

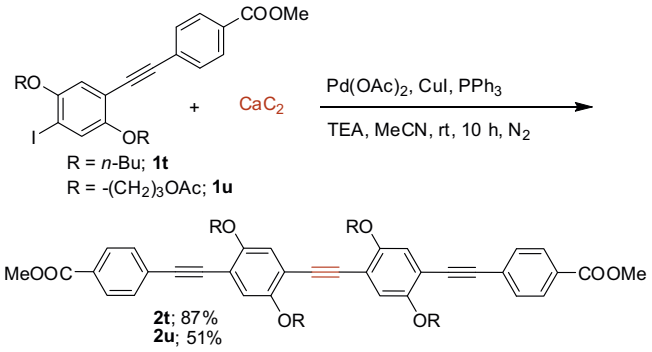
Table 2
Substrate compatibility[a]



Entry	Aryl iodide	Product	Yield[b]	Entry	Aryl iodide	Product	Yield[b]
1	 **1a**	**2a**	96%	8	 R = Me ; **1l** R = H ; **1m**	**2l** **2m**	99% 87%
2	 *p*;**1b**, *m*;**1c**, *o*;**1d**	**2b** **2c** **2d**	99% 99% 96%	9	 **1n**	**2n**	94%
3	 **1e**	**2e**	96%	10	 **1o**	**2o**	74%
4	 R = Me; **1f** R = H ; **1g**	**2f** **2g**	96% 80%[c]	11	 **1p**	**2p**	96%
5	 R = Me; **1h** R = H ; **1i**	**2h** **2i**	99% 41%[c]	12	 **1q**	**2q**	97%
6	 **1j**	**2j**	Complex mixture	13	 **1r**	**2r**	97%
7	 **1k**	**2k**	99%	14	 **1s**	**2s**	99%

[a] General conditions: a mixture of aryl iodides (1 equiv), CaC_2 (3 equiv), $Pd(OAc)_2$ (5%), PPh_3 (10%), CuI (10%), and TEA (3 equiv) was stirred for 12 h, and purified by filtration through a short plug of silica gel.
[b] Isolated yield.
[c] Purified by column chromatography.

attracted considerable interest due to their electronic and photonic properties, which have been applied widely in chemo- and biosensors and electronic devices.[32–36] Compounds **2t** and **2u** bearing three phenyleneethynylene units were prepared from the corresponding iodo-phenyleneethynylenes1t and 1u with calcium carbide under the optimized conditions in 87 and 51% yields, respectively (Scheme 3).



Scheme 3. Synthesis of **2t** and **2u**.

2.5. Effect of water on the reaction

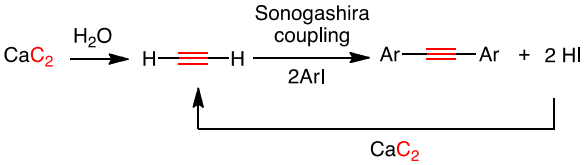
As mentioned above, the reactions were carried out using undried acetonitrile as solvent, we therefore decided to investigate the effect of water on the reaction. The coupling reaction of 4-iodotoluene (**1b**) and calcium carbide were conducted in freshly distilled acetonitrile and the targeted product **2b** was isolated in 52% yield (Table 3, entry 1). Upon the addition of 1.2 or 3.6 equiv of H_2O, the reaction went completely and the coupling product was obtained in quantitative yield (Table 3, entries 2 and 3). On the basis of these data, water is clearly necessary for the reaction. Thus, we hypothesized that the reaction is initiated by the hydrolysis of calcium carbide with H_2O to produce acetylene gas, which is then

Table 3
Effect of water on coupling reaction between 4-iodotoluene and calcium carbide[a]

Entry	H_2O added to freshly distilled CH_3CN (equiv)	Yield of **2b**[b] (%)
1	0	52
2	1.2	99
3	3.6	99

[a] General conditions: a mixture of aryl iodides (1 equiv), CaC_2 (3 equiv), $Pd(OAc)_2$ (5%), PPh_3 (10%), CuI (10%), and TEA (3 equiv) was stirred for 10 h.
[b] Isolated yield.

driven through Sonogashira coupling process to yield the diarylethyne and HI (Scheme 4). The use of freshly distilled acetonitrile gave coupling product in moderate yield (52%) suggesting that H_2O may not be the only proton source for hydrolysis of calcium carbide. In addition, HI can react with calcium carbide to generate more acetylene gas in the coupling reaction.



Scheme 4. Proposed role of H_2O and HI.

3. Conclusion

In conclusion, we have demonstrated an efficient method for synthesizing symmetrical diarylethynes directly from basic chemical feedstock, calcium carbide, via a Pd-catalyzed coupling reaction. The reactions were carried out under mild conditions in undried solvent, and the product can be purified by a simple filtration on a bed of silica gel. Also, inexpensive and commercially available reagents were used in the reaction. Thus, this transformation is proven to be an efficient process for the preparation of symmetrical diarylethynes. Further studies to extend the scope of this reaction toward the synthesis of poly-phenyleneethynelenes and related oligomers are currently under investigation and will be reported in due course.

4. Experimental section

4.1. General information

Unless otherwise indicated, all starting materials were obtained from commercial suppliers, and were used without further purification. All solvents were used directly without drying. Calcium carbide was grinded before use. Analytical thin-layer chromatography (TLC) was performed on Kieselgel F_{254} precoated plastic TLC plates from EM Science. Visualization was performed with a 254 nm ultraviolet lamp. Silica gel column chromatography was carried out with silica gel (60, 230–400 mesh) from ICN Silitech. The ^{1}H and ^{13}C NMR spectra were recorded on a Varian or Bruker (400 MHz for ^{1}H and 100 MHz for ^{13}C) in $CDCl_3$, $(CD_3)_2SO$ or $(CD_3)_2CO$. ^{1}H and ^{13}C NMR chemical shifts were referenced to $CDCl_3$ (δ 7.26 for ^{1}H, δ 77.00 for ^{13}C), $(CD_3)_2SO$ (δ 39.43 for ^{13}C) or $(CD_3)_2CO$ (δ 2.09 for ^{1}H, δ 30.60 for ^{13}C). Coupling constants (J) are reported in Hertz (Hz). Splitting patterns are designated as s (singlet), d (doublet), t (triple), q (quartet), br s (broad singlet), m (multiplet).

4.2. General procedure for Pd-catalyzed coupling reaction of calcium carbide with aryl iodides

A 100 mL round bottom flask with a magnetic stir bar was charged with copper iodide (0.1 equiv), palladium acetate (0.05 equiv), and triphenylphosphine (0.1 equiv) in acetonitrile. The solution was degassed with nitrogen for 20 min. Then, triethylamine (3 equiv), aryl iodides (1 equiv), and calcium carbide (3 equiv) were added. The mixture was stirred at room temperature overnight under nitrogen atmosphere. The reaction mixture was then filtrated through a short plug of silica gel and washed with hexane. The filtrate was evaporated under vacuum to give the desired compound.

*4.2.1. 1,2-Diphenylethyne (**2a**)*[16,29,37]. Synthesized according to general procedure from iodobenzene (200 mg, 0.98 mmol), calcium carbide (188.5 mg, 2.94 mmol), copper iodide (18.67 mg, 0.098 mmol), palladium(II)acetate (11.0 mg, 0.049 mmol), triphenylphosphine (25.7 mg, 0.098 mmol), and triethylamine (297.6 mg, 2.94 mmol) to afford 83.9 mg (0.47 mmol, 96%) of **2a** as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.63–7.56 (4H, m), 7.43–7.35 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 131.6, 128.3, 128.2, 123.2, 89.4; IR (neat, cm^{-1}) 3065, 3027.

*4.2.2. 1,2-Di-p-tolylethyne (**2b**)*[16,29]. Synthesized according to general procedure from 4-iodotoluene (200 mg, 0.917 mmol), calcium carbide (176.4 mg, 2.75 mmol), copper iodide (17.52 mg, 0.092 mmol), palladium(II)acetate (10.3 mg, 0.046 mol), triphenylphosphine (24.0 mg, 0.092 mmol), and triethylamine (278.4 mg, 2.752 mmol) to afford 94.2 mg (0.456 mmol, 99%) of **2b** as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.42 (4H, d, J=7.8 Hz), 7.15 (4H, d, J=7.8 Hz), 2.37 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.1, 131.4, 129.1, 120.4, 88.9, 21.5; IR (neat, cm^{-1}) 3018, 2917, 2843.

*4.2.3. 1,2-Di-m-tolylethyne (**2c**)*[16]. Synthesized according to general procedure from 3-iodotoluene (200 mg, 0.917 mmol), calcium carbide (176.4 mg, 2.75 mmol), copper iodide (17.52 mg, 0.092 mmol), palladium(II)acetate (10.3 mg, 0.046 mmol), triphenylphosphine (24.0 mg, 0.092 mmol), and triethylamine (278.4 mg, 2.752 mmol) to afford 93.7 mg (0.454 mmol, 99%) of **2c** as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.36–7.33 (4H, m), 7.23 (2H, d, J=7.6 Hz), 7.15 (2H, d, J=7.6 Hz), 2.36 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.0, 132.2, 129.1, 128.7, 128.2, 123.2, 89.2, 21.3; IR (neat, cm^{-1}) 3050, 2917.

*4.2.4. 1,2-Di-o-tolylethyne (**2d**)*[16]. Synthesized according to general procedure from 2-iodotoluene (200 mg, 0.917 mmol), calcium carbide (176.4 mg, 2.75 mmol), copper iodide (17.52 mg, 0.092 mmol), palladium(II)acetate (10.3 mg, 0.046 mmol), triphenylphosphine (24.0 mg, 0.092 mmol), and triethylamine (278.4 mg, 2.752 mmol) to afford 91.2 mg (0.442 mmol, 97%) of **2d** as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.54–7.52 (2H, m), 7.27–7.19 (6H, m), 2.55 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.0, 131.9, 129.5, 128.2, 125.6, 123.3, 92.3, 21.0; IR (neat, cm^{-1})3056, 3009.

*4.2.5. 1,2-Di(naphthalen-1-yl)ethyne (**2e**)*[16,38]. Synthesized according to general procedure from 1-iodonaphthalene (200 mg, 0.787 mmol), calcium carbide (151.4 mg, 2.36 mmol), copper iodide (15.0 mg, 0.079 mmol), palladium(II)acetate (8.8 mg, 0.039 mmol), triphenylphosphine (20.6 mg, 0.079 mmol), and triethylamine (278.5 mg, 2.752 mmol) to afford 104.5 mg (0.376 mmol, 97%) of **2e** as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.62 (2H, d, J=8.0 Hz), 7.92 (6H, m), 7.68 (2H, t, J=7.6 Hz), 7.59 (2H, t, J=7.4 Hz), 7.54 (2H, t, J=7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.2, 130.6, 128.9, 128.4126.9, 126.5, 126.3, 125.3, 121.0, 92.4; IR (neat, cm^{-1}) 3056, 3009.

*4.2.6. 1,2-Bis(4-methoxyphenyl)ethyne (**2f**)*[16,29]. Synthesized according to general procedure from 4-iodoanisole (200 mg, 0.855 mmol), calcium carbide (164.4 mg, 2.56 mmol), copper iodide (16.3 mg, 0.086 mmol), palladium(II)acetate (9.6 mg, 0.043 mmol), triphenylphosphine (22.4 mg, 0.086 mmol), and triethylamine (278.3 mg, 2.56 mmol) to afford 98.1 mg (0.412 mmol, 97%) of **2f** as a white solid: ^{1}H NMR (400 MHz, CDCl3): δ ppm 7.45 (4H, d, J=8.8 Hz), 6.87 (4H, d, J=8.8 Hz), 3.83 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.4, 132.9, 115.7, 114.0, 87.9, 55.3; IR (neat, cm^{-1})3000, 2968, 2832.

*4.2.7. 4,4′-(Ethyne-1,2-diyl)diphenol (**2g**)*[38]. Synthesized according to general procedure from 4-iodophenol (200 mg, 0.91 mmol), calcium carbide (174.8 mg, 2.73 mmol), copper iodide (17.3 mg,

0.091 mmol), palladium(II)acetate (10.2 mg, 0.045 mmol), triphenylphosphine (23.0 mg, 0.091 mmol), and triethylamine (275.9 mg, 2.73 mmol) to afford 76.4 mg (0.364 mmol, 81%) of **2g** as a brown solid: ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ ppm 8.76 (2H, s), 7.31 (4H, d, J=8.4 Hz), 6.81 (4H, d, J=8.4 Hz); ^{13}C NMR (100 MHz, $(CD_3)_2CO$): δ 159.4, 134.6, 117.4, 116.5, 89.4.

*4.2.8. 1,2-Bis(4-(methoxymethyl)phenyl)ethyne (**2h**)*[39]. Synthesized according to general procedure from 1-iodo-4-(methoxymethyl) benzene (200 mg, 0.86 mmol), calcium carbide (165.0 mg, 2.57 mmol), copper iodide (16.4 mg, 0.086 mmol), palladium(II) acetate (9.6 mg, 0.043 mmol), triphenylphosphine (22.5 mg, 0.086 mmol), and triethylamine (260.6 mg, 2.57 mmol) to afford 101.1 mg (0.428 mmol, 99%) of **2h** as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.52 (4H, d, J=7.7 Hz), 7.32 (4H, d, J=7.7 Hz), 4.47 (4H, s), 3.40 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.4, 132.5, 131.6, 127.5, 122.4, 89.2, 74.2, 58.1; IR (neat, cm^{-1}) 3003, 2923, 2864.

*4.2.9. (4,4′-(Ethyne-1,2-diyl)bis(4,1-phenylene))dimethanol (**2i**)*[38]. Synthesized according to general procedure from (4-iodophenyl)methanol (200 mg, 0.855 mmol), calcium carbide (164.4 mg, 2.56 mmol), copper iodide (16.3 mg, 0.086 mmol), palladium(II)acetate (9.6 mg, 0.043 mmol), triphenylphosphine (22.4 mg, 0.086 mmol), and triethylamine (259.5 mg, 2.56 mmol) and purified by flash chromatography to afford 41.6 mg (0.175 mmol, 41%) of **2i** as a brown solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.53 (4H, d, J=8.4 Hz), 7.35 (4H, d, J=8.4 Hz), 4.72 (4H, s), 3.41 (1H, s); ^{13}C NMR (100 MHz, $(CD_3)_2SO$): δ 143.4, 132.6, 131.5, 127.1, 127.1, 120.9, 89.4, 62.9.

*4.2.10. 1,2-Di(thiophen-2-yl)ethyne (**2k**)*[16]. Synthesized according to general procedure from 2-iodothiophene (200 mg, 0.952 mmol), calcium carbide (183 mg, 2.86 mmol), copper iodide (18.2 mg, 0.095 mmol), palladium(II)acetate (10.7 mg, 0.048 mmol), triphenylphosphine (25.0 mg, 0.095 mmol), and triethylamine (289.1 mg, 2.86 mmol) to afford 89.6 mg (0.472 mmol, 99%) of **2k** as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.33–7.26 (4H, m), 7.05–6.99 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 132.1, 127.6, 127.1, 122.9, 86.2; IR (neat, cm^{-1})3101, 3080.

*4.2.11. 1,1′-(4,4′-(Ethyne-1,2-diyl)bis(4,1-phenylene))diethanone (**2l**)*[16,40]. Synthesized according to general procedure from 1-(4-iodophenyl)ethanone (200 mg, 0.813 mmol), calcium carbide (156.3 mg, 2.44 mmol), copper iodide (11.6 mg, 0.081 mmol), palladium(II)acetate (9.1 mg, 0.041 mmol), triphenylphosphine (23.3 mg, 0.081 mmol), and triethylamine (246.8 mg, 2.44 mmol) to afford 105 mg (0.400 mmol, 99%) of **2l** as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.96 (4H, d, J=8.3 Hz), 7.63 (4H, d, J=8.3 Hz), 2.62 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.2, 136.6, 131.9, 128.3, 127.5, 91.6, 26.6.

*4.2.12. 4,4′-(Ethyne-1,2-diyl)dibenzaldehyde (**2m**)*[29]. Synthesized according to general procedure from 4-iodobenzaldehyde (200 mg, 0.858 mmol), calcium carbide (165.1 mg, 2.57 mmol), copper iodide (16.4 mg, 0.086 mmol), palladium(II)acetate (9.6 mg, 0.043 mmol), triphenylphosphine (22.5 mg, 0.086 mmol), and triethylamine (261.4 mg, 2.57 mmol) to afford 87.7 mg (0.372 mmol, 87%) of **2m** as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 10.04 (1H, s), 7.90 (2H, d, J=8.4 Hz), 7.71 (2H, d, J=8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.3, 135.9, 132.3, 129.6, 128.7, 92.1; IR (neat, cm^{-1})3080, 1687.

*4.2.13. N,N′-(4,4′-(Ethyne-1,2-diyl)bis(4,1-phenylene))diacetamide (**2n**).* Synthesized according to general procedure from *N*-(2-iodophenyl)acetamide (200 mg, 0.766 mmol), calcium carbide (147.3 mg, 2.36 mmol), copper iodide (14.6 mg, 0.077 mmol), palladium(II)acetate (8.6 mg, 0.034 mmol), triphenylphosphine (20.1 mg, 0.077 mmol), and triethylamine (232.6 mg, 2.36 mmol) to afford 105.7 mg (0.362 mmol, 94%) of **2n** as a brown solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.31 (2H, d, J=8.2 Hz), 7.90 (2H, s), 7.50 (2H, d, J=7.5 Hz), 7.41 (2H, t, J=7.9 Hz), 7.13 (2H, t, J=7.5 Hz), 2.25 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.5, 139.0, 132.0, 130.4, 123.9, 120.5, 91.1, 24.8; IR (neat, cm^{-1})3293, 2959, 2920, 1729; HRMS (ESI) calcd for $C_{18}H_{16}N_2O_2Na$, 315.1104; found, 315.1107.

*4.2.14. Dimethyl 4,4′-(ethyne-1,2-diyl)dibenzoate (**2o**)*[16]. Synthesized according to general procedure from 4-iodobenzoate (200 mg, 0.76 mmol), calcium carbide (146.8 mg, 2.29 mmol), copper iodide (14.5 mg, 0.076 mmol), palladium(II)acetate (8.6 mg, 0.038 mmol), triphenylphosphine (20.0 mg, 0.076 mmol), and triethylamine (230.9 mg, 2.29 mmol) to afford 83.2 mg (0.278 mmol, 74%) of **2o** as a brown solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.03 (4H, d, J=8.2 Hz), 7.60 (4H, d, J=8.2 Hz), 3.93 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 131.6, 130.0, 129.6, 127.4, 91.4, 52.3; IR (neat, cm^{-1})3012, 2959, 1711.

*4.2.15. 1,2-Bis(4-nitrophenyl)ethyne (**2p**)*[41]. Synthesized according to general procedure from 4-iodonitrobenzene (200 mg, 0.80 mmol), calcium carbide (154.5 mg, 2.41 mmol), copper iodide (15.3 mg, 0.080 mmol), palladium(II)acetate (9.0 mg, 0.040 mmol), triphenylphosphine (21.0 mg, 0.080 mmol), and triethylamine (243.8 mg, 2.4 mmol) to afford 102.7 mg (0.400 mmol, 95%) of **2p** as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.26 (4H, d, J=8.7 Hz), 7.72 (4H, d, J=8.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.7, 132.6, 128.9, 127.7, 92.0; IR (neat, cm^{-1})3104, 3071, 2926, 1593.

*4.2.16. 1,2-Bis(4-bromophenyl)ethyne (**2q**)*[16]. Synthesized according to general procedure from 1-bromo-4-iodobenzene (200 mg, 0.71 mmol), calcium carbide (136 mg, 2.12 mmol), copper iodide (13.5 mg, 0.071 mmol), palladium(II)acetate (7.9 mg, 0.035 mmol), triphenylphosphine (18.5 mg, 0.071 mmol), and triethylamine (214.6 mg, 2.12 mmol) to afford 115.3 mg (0.34 mmol, 97%) of **2q** as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.49 (4H, d, J=8.5 Hz), 7.38 (4H, d, J=8.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.0, 131.7, 122.8, 121.8, 89.4; IR (neat, cm^{-1})3074, 3071, 2926, 1593.

*4.2.17. 1,2-Bis(4-((trimethylsilyl)ethynyl)phenyl)ethyne (**2r**)*[42]. Synthesized according to general procedure from ((4-iodophenyl)ethynyl)trimethylsilane (200 mg, 0.667 mmol), calcium carbide (128.2 mg, 2.00 mmol), copper iodide (12.7 mg, 0.067 mmol), palladium(II)acetate (7.5 mg, 0.033 mmol), triphenylphosphine (17.5 mg, 0.067 mmol), and triethylamine (202.4 mg, 2.00 mmol) to afford 118.8 mg (0.321 mmol, 96.6%) of **2r** as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.46 (4H, s), 7.44 (4H, s), 0.26 (18H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 131.9, 131.4, 123.0, 104.5, 96.5, 91.0, −0.1.

*4.2.18. 4,4′-(Ethyne-1,2-diyl)bis(4,1-phenylene) bis(4-methylbenzenesulfonate) (**2s**).* Synthesized according to general procedure from 4-iodophenyl 4-methylbenzenesulfonate (200 mg, 0.536 mmol), calcium carbide (103 mg, 1.63 mmol), copper iodide (10.2 mg, 0.05 mmol), palladium(II)acetate (6.0 mg, 0.027 mmol), triphenylphosphine (14.0 mg, 0.05 mmol), and triethylamine (162.2 mg, 1.63 mmol) to afford 137.7 mg (0.266 mmol, 99.4%) of **2s** as a brown solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.70 (4H, d, J=7.5 Hz), 7.41 (4H, d, J=7.7 Hz), 7.32 (4H, d, J=7.5 Hz), 6.97 (4H, d, J=7.7 Hz), 2.45 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.4, 145.6, 132.9, 129.8, 128.5, 122.6, 121.9, 90.0, 21.7; IR (neat, cm^{-1})3039, 2920, 1590; HRMS (ESI) calcd for $C_{28}H_{22}O_6S_2Na$, 541.0750; found, 541.0756.

*4.2.19. Dimethyl 4,4′-(4,4′-(ethyne-1,2-diyl)bis(2,5-dibutoxy-4,1-phenylene))bis(ethyne-2,1-diyl)dibenzoate (**2t**).* Synthesized according

to general procedure from methyl 4-((2,5-dibutoxy-4-iodophenyl) ethynyl)benzoate **1t** (200 mg, 0.407 mmol), calcium carbide (78.3 mg, 1.22 mmol), copper iodide (7.8 mg, 0.041 mmol), palladium(II)acetate (4.6 mg, 0.020 mmol), triphenylphosphine (10.7 mg, 0.041 mmol), and triethylamine (123 mg, 1.22 mmol) and purified by flash chromatography to afford 133.4 mg (0.171 mmol, 87.1%) of **2t** as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.03 (4H, d, J=8.2 Hz), 7.58 (4H, d, J=8.2 Hz), 7.02 (4H, s), 4.05 (8H, dd, J=14.8, 6.6 Hz), 3.93 (6H, s), 1.89–1.78 (8H, m), 1.62–1.53 (9H, m), 1.05–0.95 (12H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 153.8, 153.5, 131.4, 131.4, 129.5, 129.4, 128.2, 117.1, 117.1, 114.9, 113.4, 94.1, 91.7, 89.1, 69.5, 69.3, 52.2, 31.4, 31.4, 19.3, 13.9, 13.9; IR (neat, cm^{-1})2956, 2864, 2205; HRMS (ESI) calcd for $C_{50}H_{54}O_8Na$, 805.3711; found, 805.3713.

*4.2.20. Dimethyl 4,4′-(4,4′-(ethyne-1,2-diyl)bis(2,5-dibutoxy-4,1-phenylene))bis(ethyne-2,1-diyl)dibenzoate (**2u**).* Synthesized according to general procedure from 3,3′-(2-iodo-5-((4-(methoxycarbonyl) phenyl)ethynyl)-1,4-phenylene)bis(oxy)bis(propane-3,1-diyl)diacetate **1u** (100 mg, 0.166 mmol), calcium carbide (32.4 mg, 0.50 mmol), copper iodide (3.2 mg, 0.017 mmol), palladium(II)acetate (1.9 mg, 0.009 mmol), triphenylphosphine (4.4 mg, 0.017 mmol), and triethylamine (50.1 mg, 0.5 mmol) and purified by flash chromatography to afford 17.8 mg (0.019 mmol, 50.8%) of **2u** as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.03 (4H, d, J=8.2 Hz), 7.60 (4H, d, J=8.2 Hz), 7.04 (4H, d, J=6.9 Hz), 4.38–4.31 (8H, m), 4.18–4.11 (8H, m), 3.93 (6H, s), 2.23–2.14 (8H, m), 2.07–2.03 (12H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.0, 170.9, 166.5, 153.6, 153.2, 131.5, 131.5, 129.6, 127.9, 117.2, 117.1, 114.7, 113.7, 94.5, 91.5, 88.5, 66.1, 66.0, 61.3, 61.2, 61.2, 61.1, 52.2, 28.75, 28.7, 20.9, 20.9; IR (neat, cm^{-1}) 3059, 2205, 1702; HRMS (ESI) calcd for $C_{50}H_{54}O_{16}Na$, 981.3304; found, 981.3308.

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Supplementary data

Images of ^{1}H and ^{13}C NMR spectrum of compounds **2a**–**u** are available in the Supplementary data. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2011.08.042. These data include MOL files and InChiKeys of the most important compounds described in this article.

References and notes

1. King, A. O.; Okukado, N.; Negishi, E. *J. Chem. Soc., Chem. Commun.* **1977**, 683–684.
2. Heck, R. F. *J. Am. Chem. Soc.* **1968**, *90*, 5518–5526.
3. Miyaura, N.; Suzuki, A. *J. Chem. Soc., Chem. Commun.* **1979**, 866–867.
4. Milstein, D.; Stille, J. K. *J. Am. Chem. Soc.* **1978**, *100*, 3636–3638.
5. Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16*, 4467–4470.
6. Nicolaou, K. C.; Bulger, P. G.; Sarla, D. *Angew. Chem., Int. Ed.* **2005**, *44*, 4442–4489.
7. Torborga, C.; Bellera, M. *Adv. Synth. Catal.* **2009**, *351*, 3027–3043.
8. Chinchilla, R.; Najera, C. *Chem. Rev.* **2007**, *107*, 874–922.
9. Eckhardt, M.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 13642–13643.
10. Yasuhara, A.; Kanamori, Y.; Kaneko, M.; Numata, A.; Kondo, Y.; Sakamoto, T. *J. Chem. Soc., Perkin Trans. 1* **1999**, 529–534.
11. Fiandanese, V.; Bottalico, D.; Marchese, G.; Punzi, A. *Tetrahedron* **2008**, *64*, 53–60.
12. Novak, Z.; Nemes, P.; Kotschy, A. *Org. Lett.* **2004**, *6*, 4917–4920.
13. Siemsen, P.; Livingston, R. C.; Diederich, F. *Angew. Chem., Int. Ed.* **2000**, *39*, 2632–2657.
14. Fusano, A.; Fukuyama, T.; Nishitani, S.; Inouye, T.; Ryu, I. *Org. Lett.* **2010**, *12*, 2410–2413.
15. Liu, J.; Lam, J. Y.; Tang, B. Z. *Chem. Rev.* **2009**, *109*, 5799–5867.
16. Mio, M. J.; Kopel, L. C.; Braun, J. B.; Gadzikwa, T. L.; Hull, K. L.; Brisbois, R. G.; Markworth, C. J.; Grieco, P. A. *Org. Lett.* **2002**, *4*, 3199–3202.
17. Liang, Y.; Xie, Y. X.; Li, J. H. *J. Org. Chem.* **2006**, *71*, 379–381.
18. Severin, R.; Reimer, J.; Doye, S. *J. Org. Chem.* **2010**, *75*, 3518–3521.
19. Yamashita, M.; Horiguchi, H.; Hirano, K. *J. Org. Chem.* **2009**, *74*, 7481–7488.
20. Li, C.; Salaven, W.; John, V. *Chem. Commun.* **1997**, 1569–1570.
21. Iyoda, M.; Vorasingha, A.; Kuwatani, Y. *Tetrahedron Lett.* **1998**, *39*, 4701–4704.
22. Bunz, U. *Macromol. Rapid Commun.* **2009**, *30*, 772–805.
23. Li, C.; Li, D.; Costello, C. *Org. Process Res. Dev.* **1997**, *1*, 325–327.
24. Pal, M.; Kundu, N. *J. Chem. Soc., Perkin Trans. 1* **1996**, 449–451.
25. Moon, J.; Jeong, M.; Nam, H.; Ju, J.; Moon, J. H.; Jung, H. M.; Lee, S. *Org. Lett.* **2008**, *10*, 945–948.
26. Pang, L. L.; Bi, J. Q.; Bai, Y. J.; Zhu, H. L.; Qi, Y. Z.; Wang, C. G.; Han, F. D.; Li, S. J. *J. Phys. Chem. C* **2008**, *112*, 12134–12137.
27. Cataldo, F. *Carbon* **2005**, *43*, 2792–2800.
28. Jiang, Y.; Kuang, C.; Yang, Q. *Synlett* **2009**, 3163–3166.
29. Zhang, W.; Wu, H.; Liu, Z.; Zhong, P.; Zhang, L.; Huang, X.; Cheng, J. *Chem. Commun.* **2006**, 4826–4828.
30. Shirakawa, E.; Kitabata, T.; Otsuka, H.; Tsuchimoto, T. *Tetrahedron* **2005**, *61*, 9878–9885.
31. Novak, Z.; Szabo, A.; Repasi, J.; Kotschy, A. *J. Org. Chem.* **2003**, *68*, 3327–3329.
32. Wackerly, J. M.; Moore, J. S. *Macromolecules* **2006**, *39*, 7269–7276.
33. Tour, J. M. *Acc. Chem. Res.* **2000**, *33*, 791–804.
34. Martin, R. E.; Diederich, F. *Angew. Chem., Int. Ed.* **1999**, *38*, 1350–1377.
35. Bunz, U. H. F. *Chem. Rev.* **2000**, *100*, 1605–1644.
36. Weder, C. *Chem. Commun.* **2005**, 5378–5389.
37. Li, J. H.; Zhang, X. D.; Xie, Y. X. *Eur. J. Org. Chem.* **2005**, *20*, 4256–4259.
38. Yum, E. K.; Son, J. W.; Kim, S. K.; Kim, S. N.; Kim, K. M.; Lee, C. W. *Bull. Korean Chem. Soc.* **2010**, *31*, 2097–2099.
39. Rudenko, A. P.; Vasil'ev, A. V. *Russ. J. Org. Chem.* **1995**, *31*, 1360–1379.
40. Chebny, V. J.; Gwengo, C.; Gardinier, J. R.; Rathore, R. *Tetrahedron Lett.* **2008**, *49*, 4869–4872.
41. Ravera, M.; Amato, D.; Guerri, A. *J. Organomet. Chem.* **2005**, *690*, 2376–2380.
42. Simpson, C. D.; Brand, J. D.; Berresheim, A. J.; Przybilla, L.; Joachim Rader, H.; Mullen, K. *Chem.—Eur. J.* **2002**, *8*, 1424–1429.