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A new, efficient, and inexpensive copper(II)/salicylic acid complex catalyzed Sonogashira-type cross-coupling of haloarenes and iodoheteroarenes with terminal alkynes

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ABSTRACT

A new, efficient, and inexpensive $CuCl_2$/salicylic acid catalytic system has been developed to catalyze Sonogashira-type cross-coupling of haloarenes and iodoheteroarenes with terminal alkynes under mild reaction conditions to afford the corresponding coupling products in 18–95% yields. The role of salicylic acid might act as a bidentate O,O-donor ligand to activate the catalytic reactivity of copper chloride in coupling reactions was also briefly discussed.

1. Introduction

Alkynes are useful building blocks in organic synthesis and a basic functional group in many natural products and bioactive compounds.[1] The Sonogashira reaction (palladium complexes in the presence of an amine and a catalytic amount of CuI catalyzed coupling of terminal alkynes with aryl and alkenyl halides) has been known as one of the most powerful and straightforward methods for the construction of C(sp)–C(sp^2) bonds in organic synthesis.[2] This method has been widely used for the synthesis of natural products,[3] biologically active molecules,[4] and some interesting and useful materials.[5] However, the palladium complexes commonly used are considerably expensive and air-sensitive, especially the involvement of a tedious multistep procedure toward the synthesis of various phosphine ligands. These drawbacks have limited their application for large scale reactions.[6]

Recently, much attention has been attracted to the use of copper complexes as the catalysts for the Sonogashira-type cross-coupling of aryl halides with terminal alkynes,[7,8] because copper salts are more economic and the system is relatively simple and mild. Notably, the ligand associated with copper has been found to play an important role in the reaction. For examples, recent studies have shown that a copper catalyst associated with a P-donor ligand [such as PPh_3[8a]], a N- or N,N-donor ligand [such as 1,10-phenanthroline,[8d,e] *N*,*N*-dimethylglycine,[8c] ethylenediamine,[8d] DABCO,[8f] 1,1′-binaphthyl-2,2′-diamine (BINAM)[8g]], an O,O-donor ligand [such as rac-BINOL[8h] and β-diketone[8i]], and a N,O-donor ligand [such as 8-hydroxyquinoline[8j]] are effective catalysts in the Sonogashira reaction. Copper nanoparticles with no Pd, ligand, and co-catalyst also have been demonstrated to catalyze the cross-coupling of alkynes and aryl halides to give the corresponding disubstituted alkynes in good yields.[9] It is believed that the Cu-catalyzed coupling occurs through a Cu^{I}/Cu^{III} mechanistic pathway, as postulated by Miura and co-workers.[8a] Although significant contributions have been made in these methods, they still have some drawbacks, such as the high cost of ligands, in some cases high reaction temperatures (≥140 °C), and/or poor substrate generality. Hence, to find other efficient, more economic, and readily available ligands for copper-catalyzed Sonogashira type coupling reaction with broad variety of the substrates is still desirable.

In recent reports, metal carboxylates have been extensively studied not only due to their interesting electro-conductive, optical, and magnetic properties,[10] but also because the carboxylic group can bind to metal ion in various modes, such as monodentate, bidentate, and bridging.[11] From the coordination chemistry point of view, salicylic acid is a versatile ligand for chelating metal ion, since

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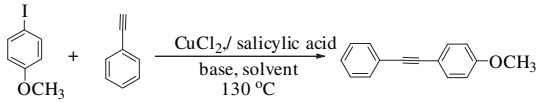
it can offer two hard and strongly basic O-donor centers either from both of carboxylic and hydroxyl group or only from the carboxylic group as a bidentate chelator. Particularly, Cu(II) complexes of salicylic acid are of interest from both structural and biological view points. For example, dinuclear Cu(II) salicylates are biologically interesting owing to their anti-inflammatory activity.[12] It has been reported that $Cu(dps)_2$ [dps=3,5-diisopropylsalicylate] and other Cu(II) salicylates can show superoxide dismutase activity,[13] which may be used in the photodynamic therapy.[14] Moreover, $Cu(dps)_2$ also has been suggested to be an active ingredient in a sunscreen composition.[15] Surprisingly, although Cu(II) complexes of salicylic acid have been demonstrated as an effectively bioactive species, no further reports dealing with these complexes in metal-catalyzed cross-coupling reactions have been presented up to date. To the best of our knowledge, only two related studies have been reported. One is from Buchwald's group, which is an efficient Cu(I)-catalyzed amination of aryl bromides with primary alkylamines by using diethylsalicylamide as the ligand.[16a] The other one is from Fu's group, which also demonstrated an efficient Cu(I)-catalyzed N-arylations of aliphatic amines by using rac-BINOL as the ligand, but no cross-coupling reaction product was obtained in their study while using salicylic acid as the ligand.[16b] In general, the catalyst of Cu(I) species always plays an important role in the copper-catalyzed cross-coupling reactions. Nevertheless, it must be noted that the reaction is catalyzed by Cu(I) species that are either added directly as cuprous salts, or generated by the reduction of Cu(II) salts, or by the in situ oxidation of copper metal to give Cu(I) species. Rothenberg and co-workers have reported that there is no need for a reducing agent as in the case of Cu(II) except reactions being relatively slow and requiring a significant amount of catalyst.[17] It is interesting to note that the two speculated and concomitant mechanisms usually used to interpret experimental results have been proposed.[18] In general, Cu(0) and Cu(I) starting materials and Cu(I), Cu(II), and Cu(III) intermediates can be involved in these coupling processes. In view of this, we are prompted to examine salicylic acid as an efficient and versatile ligand in a variety of Cu (II)-catalyzed cross-coupling reactions. This report will disclose our results in the $CuCl_2$/salicylic acid mixture catalyzed cross-coupling reactions for aryl–alkyne bond formations by using this new protocol.

2. Results and discussion

As a model study, we first chose to study the effect of salicylic acid as a bidentate O,O-donor ligand on the efficiency of the $CuCl_2$-catalyzed cross-coupling reaction of phenylacetylene with iodoanisole and the results are summarized in Table 1. When the reaction was performed with 20 mol % of CuI and 20 mol % of salicylic acid ligand in the presence of Cs_2CO_3 as a base in DMF at 130 °C for 36 h, the expected cross-coupling product of 1-methoxy-4-(phenylethynyl)benzene **3** was afforded in 88% yield with homocoupling reaction product of phenylacetylene in 6% yield (Table 1, entry 5). For a blank test (Table 1, entry 6), a significantly lower 34% yield of the cross-coupling product **3** was obtained with 27% isolated yield of homocoupling product while the same reaction condition was carried out in the absence of the salicylic acid ligand. The result indicates that this bidentate O,O-donor ligand must play an important role on accelerating the rate of the Cu(II)-catalyzed cross-coupling reaction. For further optimization of the reaction conditions, the decreasing yields of the coupling product were observed by decreasing the added amounts of $CuCl_2$ (20, 10, and 5 mol %) and/or salicylic acid/ligand (20, 10, and 5 mol %) (Table 1, entries 1–4). To evaluate the effect of the solvent (Table 1, entries 5, 7–11), results showed that both of DMSO and DMF are effective, but DMF is the best choice. For comparison on the efficiency of the base in this coupling reaction (Table 1, entries 5, 12, 13), Cs_2CO_3 was found to be the most effective although K_3PO_4, K_2CO_3, and *t*-BuOK were also effective. Interestingly, the ratio of $CuCl_2$ and salicylic acid/ligand used in this study is only equal to 1:1 while the 1:2 ratio is usually used in most of other copper-catalyzed cross-coupling reactions by using other bidentate ligands. Notably, this probably indicates that this bidentate O,O-donor ligand might be more effective in stabilizing or solublizing the copper complex.

Table 1
$CuCl_2$/salicylic acid-catalyzed Sonogashira-type cross-coupling reaction of 4-iodoanisole with phenylacetylene[a]



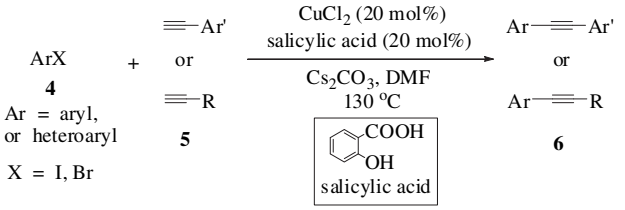
1 **2** **3**

Entry	$CuCl_2$:ligand	Base	Solvent	Yield[b] Product **3**
1	5:5	Cs_2CO_3	DMF	12
2	10:10	Cs_2CO_3	DMF	38
3	10:20	Cs_2CO_3	DMF	60
4	20:10	Cs_2CO_3	DMF	57
5	20:20	Cs_2CO_3	DMF	88
6	20:0	Cs_2CO_3	DMF	34
7	20:20	Cs_2CO_3	$PhCH_3$	6
8	20:20	Cs_2CO_3	CH_3CN	37
9	20:20	Cs_2CO_3	DMSO	60
10	20:20	Cs_2CO_3	Dioxane	24
11	20:20	Cs_2CO_3	MeOH	10
12	20:20	K_3PO_4	DMF	78
13	20:20	K_2CO_3	DMF	56
14	20:20	*t*-BuOK	DMF	40

[a] Reaction conditions: 4-iodoanisole (1.0 mmol), $CuCl_2$ (5, 10, or 20 mol %), salicylic acid(0, 5, 10, or 20 mol %), phenylacetylene (1.2 mmol), and base (2.0 mmol) in solvent (2 mL) at 130 °C for 36 h.
[b] Only isolated yield of cross-coupling product was reported, not including homocoupling product of phenylacetylene.

On the basis of the optimized reaction conditions obtained, we initiated our investigation into the scope of $CuCl_2$/salicylic acid catalyzed Sonogashira-type coupling reactions and the results are summarized in Table 2. By using this new protocol, the coupling reaction of various functionalized aryl and heteroaryl iodides with various substituted terminal alkynes can give the corresponding arylated or heteroarylated alkynes in good to excellent yields. It has been found that iodobenzene containing electron-withdrawing groups, such as acetyl, cyano, nitro, and ester group (Table 2, entries 2–7) reacted with phenylacetylene to afford arylated alkynes in very high isolated yields, while it containing electro-donating groups, such as methoxy, amino, and methyl group often gave lower yields even with a longer reaction time (Table 2, entries 8–13). Interestingly, no significant steric effects were observed in this study, because highly sterically hindered *ortho*-substituted iodobenzene also provided good yields with phenylacetylene and *n*-butyl acetylene (Table 2, entries 9–11, 14, 16, and 18). Substituted phenylacetylenes also reacted with aryl iodides and/or heteroaryl iodide to give corresponding arylated products in good to very good isolated yields even in 24 h (Table 2, entries 21–25). Under our optimized reaction conditions, it has been found that iodoheteroarenes can readily react with terminal alkynes in 24 h to afford the corresponding C-arylated alkynes (Table 2, entries 25–27), but aryl bromides reacted less effectively with terminal alkynes to provide the expected cross coupling products in 24 h or even in extending reaction time to 36 h (Table 2, entries 28–30). As a practical procedure, two scale-up reactions were also testified and the results came out as expected good yields while the longer reaction time (72 h) was needed (Table 2, entries 4 and 8).

Table 2
$CuCl_2$/salicylic acid-catalyzed Sonogashira-type cross-coupling reaction of various aryl halides with terminal alkynes[a]



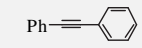
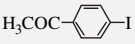
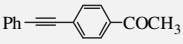
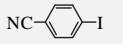
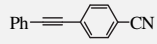
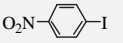
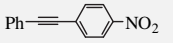
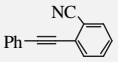
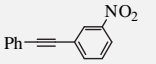
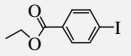
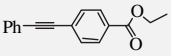
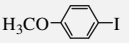
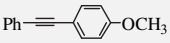
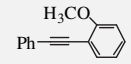
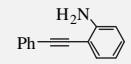
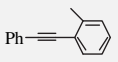
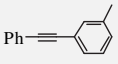
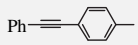
Entry	Aryl hailides	Alkynes	Products	Yield[b]
1				89
2				87
3				95
4				91 86[d]
5				88
6				81
7				84
8				88[c] 82[d]
9				80[c]
10				76[c]
11				87[c]
12				87[c]
13				85[c]
14				90
15				76[c]
16				82[c]
17				85[c]
18				80[c]
19				72[c]
20				83[c]
21				70

Table 2 (*continued*)

Entry	Aryl hailides	Alkynes	Products	Yield[b]
22				92
23				84
24				75
25				73
26				92
27				88
28				30
29				18[c]
30				50

[a] Reaction conditions: aryl halides and/or heteroaryl iodides (1.0 mmol), $CuCl_2$ (20 mol %), salicylic acid (20 mol %), terminal alkynes (1.2 mmol), and Cs_2CO_3 (2.0 mmol) in DMF (2 mL) at 130 °C for 24 h.
[b] Isolated yield.
[c] 36 h.
[d] Scale-up reaction conditions: aryl iodides (10.0 mmol), $CuCl_2$ (20 mol %), salicylic acid (20 mol %), terminal alkynes (12.0 mmol), and Cs_2CO_3 (20.0 mmol) in DMF (20 mL) at 130 °C for 72 h.

Based on the results as shown above, the bidentate O,O-donor ligand of salicylic acid must play an important role on accelerating the rate of the Cu(II)-catalyzed cross-coupling reaction. For further understanding how salicylic acid activated the catalytic reactivity of copper chloride in these coupling reactions, the direct isolation of the $CuCl_2$/salicylic acid complex from the reaction mixture has been tried but was failed.

Although the exact structure of the $CuCl_2$/salicylic acid complex in these coupling reactions is still unknown, some correlated studies have been reported. For example, Chen and co-workers recently have reported a novel neutral mixed-valence Cu(I)Cu(II)Cu(I) linear trinuclear copper metallomacrocycle $[(PPh_3)_2Cu]_2[\mu\text{-}o\text{-}OC_6H_4COO]_2Cu$, which was synthesized by treatment of KOH solution of the salicylic acid with the aqueous solution of $CuSO_4$ resulted in the formation of polynuclear copper complex, and then followed by the reaction of this complex with PPh_3 in acetonitrile.[19] Interestingly, this linear trinuclear copper compound consists of two Cu(I) ions and one Cu(II) ion which are bridged by two salicylate (2^-) ligands, and the external copper(I) atoms are coordinated by four terminal PPh_3. On the other hand, a variety of Cu(II)/salicylate complexes also have been prepared and characterized. Some of the results indicate that both of the carboxylic group and the phenolate oxygen of salicylate ligands participate in the coordination to Cu(II).[20] Notably, it also has been known that the unusual pK_a values of the carboxylic group and phenol of salicylic acid are 3.00 and 12.38, respectively.[21] In the stronger basicity of hydroxide reaction solution, both of carboxylic group and phenol of salicylic acid could be deprotonated completely, but may not be for the case in the weaker basicity of carbonate reaction solution. On the basis of above discussion, although the exact structure of the $CuCl_2$/salicylic acid complex in these coupling reactions is still

unconfirmed, it is probable to expect that salicylic acid might act as a bidentate O,O-donor ligand to activate the catalytic reactivity of copper chloride in this study.

Obviously, some advantages of this new protocol have been observed. For example, salicylic acid, an inexpensive and commercially available bidentate ligand, has not been used effectively in the copper-catalyzed cross-coupling reactions up to date. On the other hand, $CuCl_2$ is less costive and more stable than CuI without increasing the amount of catalyst used in the course of the reaction. Notably, it has also been known that cuprous salt as a catalyst generally performs more effectively than cupric salt in accelerating the rate of cross-coupling reactions, but we have successfully demonstrated that this new $CuCl_2$/salicylic acid catalytic system also performs effectively in the Sonogashira-type coupling reaction.

3. Conclusion

In summary, we have successfully developed a new, efficient, inexpensive, and experimentally simple $CuCl_2$/salicylic acid catalytic system to catalyze Sonogashira-type cross-coupling of haloarenes and iodoheteroarenes with terminal alkynes under mild reaction conditions. Using this new protocol, aryl iodides containing both electron-withdrawing groups and electron-donating groups react effectively with terminal alkynes to provide the corresponding arylated alkynes in high yields, as well as in the case of heteroaryl iodides. Further applications in the synthesis of bioactive molecules by using our new protocol are undergoing the investigation.

4. Experimental section

4.1. General

Dimethylformamide (DMF), dimethylsulfoxide (DMSO), and toluene were freshly distilled over calcium hydride prior to use. All reagents were purchased from Aldrich and other commercial sources, and used without further purification. All reactions were performed in oven-dried glassware under reaction conditions described below. The reactions were monitored by TLC on silica gel 60 F_{254} (Merck, 0.15–0.20 mm), and reaction mixtures were purified by column chromatography using silica gel 60 (Merck, 0.063–0.200 mm). NMR spectra were recorded on a Varian Mercury-400 spectrometer, operating at 400 MHz and 100 MHz for ^1H and ^{13}C, respectively. Proton and carbon spectra were performed by using $CDCl_3$ as solvent and tetramethylsilane (TMS) as the internal standard. Chemical shifts are given on the δ scale (ppm). Coupling constants (J) are given in hertz. Multiplicities are indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), or br (broadened). All coupling constants are expressed in hertz. Mass spectra and high-resolution mass spectra were obtained with a JEOL JMS-SX/SX 102A GC/MS/MS spectrometer. Data are reported as m/z (relative intensity). Infrared spectra were recorded on Hitachi 270-30 or Bruker FTIR (EQUINOX55) spectrophotometer. Melting points were determined on a Fargo melting point apparatus (MP-2D) and are uncorrected.

4.2. General procedure for $CuCl_2$/salicylic acid-catalyzed Sonogashira-type cross-coupling reaction of various aryl halides with terminal alkynes

Cs_2CO_3 (2.0 mmol), $CuCl_2$ (0.2 mmol), and salicylic acid (0.2 mmol) were added to a screw-capped test tube with a septum. The tube was evacuated with heating and back-filled with nitrogen three times. DMF (2 mL), aryl halides (1.0 mmol), and terminal alkynes (1.2 mmol) were added by syringe at room temperature. After the septum of tube was exchanged with a Teflon screw-cap, the reaction mixture was heated at 130 °C for the time as indicated, and then allowed to cool to room temperature. The reaction mixture was directly passed through Celite. After rinsed with further 50 mL of ethyl acetate, the combined filtrate was evaporated by vacuum to yield the crude product. Column chromatography of the residue on silica gel (hexane/EtOAc) afforded the desired product.

4.3. Typical procedure for $CuCl_2$/salicylic acid-catalyzed Sonogashira-type cross-coupling reaction of 4-iodoanisole with phenylacetylene (Table 1)

Typical procedure: Cs_2CO_3 (652 mg, 2.0 mmol), $CuCl_2$ (27.4 mg, 0.2 mmol, 20 mol %), and salicylic acid (27.6 mg, 0.2 mmol, 20 mol %) were added to a screw-capped test tube with a septum. The tube was evacuated with heating and back-filled with nitrogen three times. DMF (2 mL), 4-iodoanisole (234 mg, 1.0 mmol), and phenylacetylene (0.13 mL, 1.2 mmol) were added by syringe at room temperature. After the septum of tube was exchanged with a Teflon screw-cap, the reaction mixture was heated at 130 °C for 36 h, and then allowed to cool to room temperature. The reaction mixture was directly passed through Celite. After rinsed with further 50 mL of ethyl acetate, the combined filtrate was evaporated by vacuum to yield the crude product. The residue was purified by column chromatography on silica gel using ethyl acetate/hexane as eluent to give 1-methoxy-4-(phenylethynyl)benzene **3** (183 mg, 88%) (Table 1, entry 5).

4.4. Spectroscopic and analytical data

*4.4.1. 1-Methoxy-4-(phenylethynyl)benzene (**3**)[22].* White solid: mp 82 °C (lit.[22] 79–81 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 3.83 (3H, s), 6.86 (2H, d, J=8.8 Hz), 7.30–7.37 (3H, m), 7.46–7.52 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.2, 88.0, 89.4, 113.9, 115.3, 123.6, 127.9, 128.3, 131.4, 133.0, 159.6; EIMS m/z (rel int%): 209 (7), 208 (100, [M^+]), 193 (40), 165 (42), 139 (8); IR ν_{max} (cm^{-1}) (KBr): 3039, 2956, 2931, 2859, 2227, 1606, 1508, 1463, 1245.

4.4.2. 1,2-Diphenylethyne (Table 2, entries 1 and 28)[23]. Colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.42–7.45 (6H, m), 7.65–7.67 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 89.3, 123.2, 128.2, 128.3, 131.5; EIMS m/z (rel int%): 178 (100, [M^+]); HRMS calcd for $C_{14}H_{10}$: 178.0785, found: 178.0788; IR ν_{max} (cm^{-1}) (neat): 3019, 2278, 1642, 1571.

4.4.3. 1-(4-(Phenylethynyl)phenyl)ethanone (Table 2, entry 2)[24]. Yellow solid: mp 95–96 °C (lit.[24] 95–96 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 2.62 (3H, s), 7.37–7.39 (3H, m), 7.54–7.57 (2H, m), 7.62 (2H, d, J=8.4 Hz), 7.95 (2H, d, J=8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.4, 88.5, 92.6, 122.5, 128.0, 128.1, 128.3, 128.7, 131.6, 131.7, 136.1, 197.1; EIMS m/z (rel int%): 220 (80, [M^+]), 205 (100), 176 (41), 151 (16), 117 (16); IR ν_{max} (cm^{-1}) (KBr): 3078, 2920, 2218, 1679, 1602, 1442, 1403.

4.4.4. 4-(Phenylethynyl)benzonitrile (Table 2, entry 3)[25]. White solid: mp 109 °C (lit.[25] 106–108 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.36–7.40 (3H, m), 7.53–7.57 (2H, m), 7.58–7.65 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 87.7, 93.7, 111.5, 118.5, 122.2, 128.2, 128.5, 129.1, 131.7, 132.0, 132.1; EIMS m/z (rel int%): 203 (100, [M^+]), 176 (6), 151 (4); HRMS calcd for $C_{15}H_9N$: 203.0738, found: 203.0741; IR ν_{max} (cm^{-1}) (KBr): 3085, 3021, 2985, 2227, 2216, 1604, 1443.

4.4.5. 1-Nitro-4-(phenylethynyl)benzene (Table 2, entries 4 and 30)[24]. Yellow solid: mp 118–119 °C (lit.[24] 119 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.42 (3H, m), 7.54–7.58 (2H, m), 7.67 (2H, d, J=7.6 Hz), 8.23 (2H, d, J=8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$)

δ 87.5, 94.7, 122.1, 123.6, 128.5, 129.3, 130.2, 131.8, 132.2, 147.0; EIMS *m/z* (rel int%): 223 (100, [M$^+$]), 193 (16), 176 (51), 165 (17), 151 (19); HRMS calcd for $C_{14}H_9NO_2$: 223.0635, found: 223.0637; IR ν_{max} (cm^{-1}) (KBr): 3081, 2217, 1650, 1513.

4.4.6. 2-(Phenylethynyl)benzonitrile (Table 2, entry 5)[26]. Yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.43 (4H, m), 7.56 (1H, t, *J*=8.0 Hz), 7.61–7.64 (3H, m), 7.67 (1H, d, *J*=8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 85.6, 96.0, 115.3, 117.5, 122.0, 127.2, 128.2, 128.4, 129.2, 131.9, 132.1, 132.3, 132.6; EIMS *m/z* (rel int%): 203 (100, [M$^+$]), 202 (28), 191 (17), 176(15); HRMS calcd for $C_{15}H_9N$: 203.0741, found: 203.0747; IR ν_{max} (cm^{-1}) (neat): 3145, 3053, 2987, 2917, 2227, 2165, 1596, 1443.

4.4.7. 1-Nitro-3-(phenylethynyl)benzene (Table 2, entry 6)[27]. Yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.41 (3H, m), 7.50–7.58 (3H, m), 7.81 (1H, d, *J*=7.6 Hz), 8.16 (1H, d, *J*=8.4 Hz), 8.37 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 87.1, 92.2, 122.4, 123.1, 123.7, 125.4, 126.6, 128.7, 129.3, 129.5, 129.6, 132.0, 137.4, 148.4; EIMS *m/z* (rel int%): 223 (100, [M$^+$]), 176 (58), 151 (23); IR ν_{max} (cm^{-1}) (neat): 3038, 2218, 1623, 1538.

4.4.8. Ethyl 4-(phenylethynyl)benzoate (Table 2, entry 7)[28]. Yellow solid: mp 79–80 °C (lit.[28] 83–84 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40 (3H, t, *J*=7.2 Hz), 4.39 (2H, q, *J*=7.6 Hz), 7.37 (3H, t, *J*=2.8 Hz), 7.54 (4H, m), 8.03 (2H, d, *J*=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 61.0, 88.6, 92.2, 122.6, 127.8, 128.3, 128.6, 129.4, 129.7, 131.4, 131.6, 165.9; EIMS *m/z* (rel int%): 250 (91, [M$^+$]), 205 (100), 176 (47), 151 (17); HRMS calcd for $C_{17}H_{14}O_2$: 250.0995, found: 250.0996; IR ν_{max} (cm^{-1}) (KBr): 3059, 2982, 2219, 1710, 1606, 1442, 1278.

*4.4.9. 1-Methoxy-4-(phenylethynyl)benzene (**3**) (Table 2, entries 8, 21, and 29).* The data are same as compound **3** and have been shown in Section 4.4.1.

4.4.10. 1-Methoxy-2-(phenylethynyl)benzene (Table 2, entry 9)[29]. Yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.92 (3H, s), 6.90–6.96 (2H, m), 7.28–7.36 (4H, m), 7.50 (1H, dd, *J*=6.0, 2.4 Hz), 7.55–7.57 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.7, 85.7, 93.3, 110.6, 112.4, 120.4, 123.5, 128.0, 128.2, 129.7, 131.6, 133.4, 159.8; EIMS *m/z* (rel int%): 207 (58), 208 (100, [M$^+$]), 165 (36), 139 (11); IR ν_{max} (cm^{-1}) (neat): 3075, 2956, 2931, 2859, 2216, 1594, 1492, 1463, 1261.

4.4.11. 2-(Phenylethynyl)aniline (Table 2, entry 10)[30]. Yellow solid: mp 91–94 °C (lit.[30] 93–94 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.28 (2H, br s), 6.70–6.74 (2H, m), 7.14 (1H, t, *J*=7.6 Hz), 7.33–7.38 (4H, m), 7.52–7.54 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 86.2, 95.0, 108.2, 114.6, 118.3, 123.6, 128.5, 128.7, 130.0, 131.7, 132.4, 148.1; EIMS *m/z* (rel int%): 193 (100, [M$^+$]), 165 (28), 90 (10); HRMS calcd for $C_{14}H_{11}N$: 193.0908, found: 193.0900; IR ν_{max} (cm^{-1}) (KBr): 3457, 3369, 3059, 2921, 2207, 1569, 1453.

4.4.12. 1-Methyl-2-(phenylethynyl)benzene (Table 2, entry 11)[8g,29]. Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.52 (3H, s) 7.15–7.26 (3H, m), 7.30–7.39 (3H, m), 7.49–7.55 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 88.3, 93.3, 123.0, 123.5, 125.6, 128.1, 128.2, 128.3, 129.4, 131.4, 131.8, 140.1; EIMS *m/z* (rel int%): 192 (100, [M$^+$]), 189 (37), 165 (24), 139 (4), 115 (11); IR ν_{max} (cm^{-1}) (neat): 2972, 2215, 1642, 1493.

4.4.13. 1-Methyl-3-(phenylethynyl)-benzene (Table 2, entry 12)[31]. Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.25 (3H, s), 7.12 (1H, d, *J*=8.0 Hz), 7.22 (1H, t, *J*=12.0 Hz), 7.34–7.42 (5H, m), 7.51–7.60 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 89.0, 89.6, 123.0, 123.3, 128.1, 128.2, 128.3, 128.6, 129.1, 131.6, 132.1, 137.9; EIMS *m/z* (rel int%): 192 (100, [M$^+$]), 189 (19), 165 (12); IR ν_{max} (cm^{-1}) (neat): 3060, 2206, 1643.

4.4.14. 1-Methyl-4-(phenylethynyl)benzene (Table 2, entry 13)[25]. White solid: mp 72–73 °C (lit.[25] 70–71 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 (3H, s), 7.14 (2H, d, *J*=8.0 Hz), 7.31–7.34 (3H, m), 7.42 (2H, d, *J*=8.0 Hz), 7.50–7.54 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 88.7, 89.5, 120.2, 123.5, 128.0, 128.3, 129.1, 131.4, 131.5, 138.4; EIMS *m/z* (rel int%): 192 (100, [M$^+$]), 189 (15), 165 (10); IR ν_{max} (cm^{-1}) (KBr): 3052, 2963, 2216, 1510, 1441.

4.4.15. 1-Bromo-2-(2-phenylethynyl)benzene (Table 2, entry 14)[32]. Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03–7.10 (1H, m), 7.14–7.19 (1H, m), 7.26–7.31 (3H, m), 7.47–7.57 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 88.0, 93.9, 122.7, 125.2, 125.5, 126.9, 128.3, 128.5, 129.2, 131.5, 132.3, 133.0; EIMS *m/z* (rel int%): 256 (100, [M$^+$]), 202 (51), 176 (74), 151 (28), 88 (25); HRMS calcd for $C_{14}H_9Br$: 255.9900, found: 255.9894; IR ν_{max} (cm^{-1}) (neat): 3059, 2150, 1598, 1464, 842, 752.

4.4.16. 1-Phenylhex-1-yne (Table 2, entry 15)[33]. Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (3H, t, *J*=7.2 Hz), 1.47–1.62 (4H, m), 2.41 (2H, t, *J*=7.2 Hz), 7.24–7.28 (3H, m), 7.39–7.41 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 19.1, 22.0, 30.8, 80.5, 90.4, 124.1, 127.4, 128.1, 131.5; EIMS *m/z* (rel int%): 158 (32, [M$^+$]), 143 (52), 129 (66), 115 (100), 91 (18); HRMS calcd for $C_{12}H_{14}$: 158.1092, found: 158.1094; IR ν_{max} (cm^{-1}) (neat): 3033, 2958, 2232, 1668, 1598.

4.4.17. 1-(1-Hexynyl)-2-methoxybenzene (Table 2, entry 16)[34]. Yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.94 (3H, t, *J*=14.6 Hz), 1.45–1.65 (4H, m), 2.47 (2H, t, *J*=7.2 Hz), 3.87 (3H, s), 6.83–6.89 (2H, m), 7.23 (1H, d, *J*=8.2 Hz), 7.37 (1H, d, *J*=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6, 19.5, 22.0, 30.9, 55.8, 77.0, 94.6, 110.6, 113.3, 120.3, 128.8, 133.6, 159.8; EIMS *m/z* (rel int%): 188 (100, [M$^+$]), 173 (55), 159 (38), 144 (28), 131 (51), 115 (54), 102 (16), 91 (46); IR ν_{max} (cm^{-1}) (neat): 2957, 2932, 2871, 2232, 1777, 1648, 1462.

4.4.18. 1-(1-Hexynyl)-4-methoxybenzene (Table 2, entry 17)[35]. Yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.94 (3H, t, *J*=7.2 Hz), 1.44–1.62 (4H, m), 2.88 (2H, t, *J*=6.8 Hz), 3.80 (3H, s), 6.80 (2H, d, *J*=8.7 Hz), 7.33 (2H, d, *J*=8.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6, 19.0, 22.0, 30.9, 55.2, 80.2, 88.7, 113.7, 116.2, 132.8, 158.9; EIMS *m/z* (rel int%): 188 (80, [M$^+$]), 173 (59), 159 (43), 145 (100), 129 (19), 115 (23), 102 (36), 91 (16); IR ν_{max} (cm^{-1}) (neat): 3040, 2957, 2932, 2871, 2231, 1643, 1607, 1463.

4.4.19. 1-(2-Methylphenyl)hex-1-yne (Table 2, entry 18)[36]. Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.94 (3H, t, *J*=7.2 Hz), 1.46–1.61 (4H, m), 2.44 (3H, s), 2.42 (2H, t, *J*=6.8 Hz), 7.06–7.09 (1H, m), 7.10–7.19 (2H, m), 7.35 (1H, d, *J*=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6, 19.2, 20.7, 22.0, 31.0, 79.4, 94.3, 123.8, 125.4, 127.4, 129.2, 131.7, 139.8; EIMS *m/z* (rel int%): 172 (44, [M$^+$]), 157 (34), 143 (58), 129 (100), 115 (37), 91(13); IR ν_{max} (cm^{-1}) (neat): 3063, 2927, 2231, 1643, 1486.

4.4.20. 1-(3-Methylphenyl)hex-1-yne (Table 2, entry 19)[37]. Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.94 (3H, t, *J*=7.2 Hz), 1.47–1.64 (4H, m), 2.30 (3H, s), 2.40 (2H, t, *J*=6.8 Hz), 7.07–7.10 (1H, m), 7.16–7.26 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6, 19.0, 21.2, 22.0, 30.8, 80.6, 89.9, 123.9, 128.0, 128.3, 128.5, 132.1, 137.7; EIMS *m/z* (rel int%): 172 (41, [M$^+$]), 157 (50), 143 (61), 129 (100), 115 (42), 105 (21), 91 (27); IR ν_{max} (cm^{-1}) (neat): 3038, 2958, 2228, 1648, 1580.

4.4.21. 1-(4-Methylphenyl)hex-1-yne (Table 2, entry 20)[38]. Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.94 (3H, t, *J*=7.2 Hz), 1.44–1.60 (4H, m), 2.32 (3H, s), 2.38 (2H, t, *J*=6.8 Hz), 7.07 (2H, d, *J*=8.4 Hz),

7.27 (2H, d, J=8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 19.1, 21.4, 22.0, 30.9, 80.5, 89.5, 121.0, 128.9, 131.4, 137.3; EIMS m/z (rel int%): 172 (32, [M^+]), 157 (53), 143 (46), 129 (100), 115 (30), 91(17); IR ν_{max} (cm^{-1}) (neat): 3028, 2958, 2230, 1649, 1509.

4.4.22. 2-[(4-Methylphenyl)-ethynyl]anisole (Table 2, entry 22)[8g]. Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (3H, s), 3.92 (3H, s), 6.93 (2H, dd, J=7.6, 7.6 Hz), 7.14 (2H, d, J=8.0 Hz), 7.30 (1H, t, J=8.0 Hz), 7.44–7.50 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 55.7, 85.0, 93.5, 110.5, 112.5, 120.4, 128.9, 129.5, 131.4, 133.4, 138.1, 159.7; EIMS m/z (rel int%): 222 (100, [M^+]), 207 (27), 178 (46), 131 (26), 89 (12); HRMS calcd for $C_{16}H_{14}O$: 222.1039, found: 222.1042; IR ν_{max} (cm^{-1}) (neat): 3029, 2959, 2917, 2834, 2250.

4.4.23. 1-(2-(4-Methoxyphenyl)ethynyl)-4-methylbenzene (Table 2, entry 23)[39]. White solid: mp 118–121 °C (lit.[39] 125–126 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (3H, s), 3.83(3H, s), 6.87 (2H, d, J=8.0 Hz), 7.14 (2H, d, J=8.0 Hz), 7.40 (2H, d, J=8.0 Hz), 7.46 (2H, d, J=8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 55.3, 88.2, 88.6, 114.0, 115.6, 120.5, 129.1, 131.3, 133.0, 138.0, 159.5; EIMS m/z (rel int%): 222 (100, [M^+]), 207 (65), 178 (23); IR ν_{max} (cm^{-1}) (KBr): 2967, 2817, 2190, 1643, 1510, 1452, 1246.

4.4.24. 2-[(4-Nitrophenyl)ethynyl]anisole (Table 2, entry 24)[40]. Yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.93 (3H, s), 6.92–6.99 (2H, m), 7.34 (1H, t, J=8.4 Hz), 7.50 (1H, d, J=8.0 Hz), 7.67 (2H, d, J=8.8 Hz), 8.19 (2H, d, J=8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.0, 91.4, 91.5, 110.8, 111.3, 120.6, 123.5, 130.6, 130.8, 132.2, 133.7, 147.0, 160.2; EIMS m/z (rel int%): 253 (100, [M^+]), 206 (30), 178 (32), 163 (31), 131 (26); IR ν_{max} (cm^{-1}) (neat): 3104, 3071, 2965, 2837, 2183, 1591, 1511, 1460, 1380.

4.4.25. 2-(4-Methoxyphenyl)ethynylthiophene (Table 2, entry 25)[41]. White solid: mp 53–54 °C (lit.[41] 53–54 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.80 (3H, s), 6.86 (2H, d, J=8.8 Hz), 6.98 (1H, t, J=4.8 Hz), 7.24–7.26 (2H, m), 7.45 (2H, d, J=9.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.2, 81.2, 93.0, 114.0, 115.0, 123.7, 126.8, 127.0, 132.4, 132.9, 159.7; EIMS m/z (rel int%): 214 (100, [M^+]), 199 (85), 171 (37), 127 (15); HRMS calcd for $C_{13}H_{10}OS$: 214.0444, found: 214.0435; IR ν_{max} (cm^{-1}) (KBr): 3206, 2910, 2205, 1604, 1463.

4.4.26. 2-(Phenylethynyl)pyridine (Table 2, entry 26)[42]. Yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09–7.13 (1H, m), 7.22–7.28(3H, m), 7.42 (1H, d, J=7.6 Hz) 7.55–7.57 (3H, m), 8.52 (1H, d, J=5.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 88.5, 89.0, 122.0, 122.6, 126.9, 128.2, 128.8, 131.8, 135.9, 143.2, 149.8; EIMS m/z (rel int%): 179 (100, [M^+]), 178 (32), 151 (11), 126 (9); HRMS calcd for $C_{13}H_9N$: 179.0739, found: 179.0743; IR ν_{max} (cm^{-1}) (neat): 3079, 2222, 1633, 1491, 989.

4.4.27. 3-(Phenylethynyl)pyridine (Table 2, entry 27)[29]. Yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.30 (1H, m), 7.36–7.38 (3H, m), 7.54–7.56 (2H, m), 7.80 (1H, td, J=8.0, 2.4 Hz), 8.55 (1H, dd, J=6.4 Hz), 8.77 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 85.8, 92.5, 120.3, 122.4, 122.9, 128.3, 128.7, 131.6, 138.3, 148.4, 152.1; EIMS m/z (rel int%): 179 (100, [M^+]), 151 (11), 126 (14); HRMS calcd for $C_{13}H_9N$: 179.0742, found: 179.0749; IR ν_{max} (cm^{-1}) (neat): 3056, 2220, 1491, 1410.

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Supplementary data

Copies of ^{1}H and ^{13}C NMR spectra of all compounds in Tables 1 and 2 and some experimental details. Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2010.07.072.

References and notes

1. (a) Viehe, H. G. *Chemistry of Acetylene*; Marcel Dekker: New York, NY, 1969; p 597; (b) Bohlmann, F.; Burkhart, F. T.; Zero, C. *Naturally Occurring Acetylenes*; Academic: New York, NY, 1973; (c) Trahanovsky, W. S. *Oxidation in Organic Chemistry*; Academic: New York, NY, 1973; Vol. 5-B; (d) Hansen, L.; Boll, P. M. *Phytochemistry* **1986**, *25*, 285; (e) Kim, Y. S.; Jin, S. H.; Kim, S. L.; Hahn, D. R. *Arch. Pharm. Res.* **1989**, *12*, 207; (f) Matsunaga, H.; Katano, M.; Yamamoto, H.; Fujito, H.; Mori, M.; Tukata, K. *Chem. Pharm. Bull.* **1990**, *38*, 3480; (g) Hudlicky, M. *Oxidation in Organic Chemistry; ACS Monograph 186*; American Chemical Society: Washington, DC, 1990; p 58; (h) Sonogashira, K. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, UK, 1991; Vol. 3; p 551; (i) Alonso, F.; Beletskaya, I. P.; Yus, M. *Chem. Rev.* **2004**, *104*, 3079.
2. (a) Sonogashira, K. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 3, Chapter 2; (b) Sonogashira, K. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, 1998; Chapter 5; (c) Brandsma, L.; Vasilevsky, S. F.; Verkruijsse, H. D. *Application of Transition Metal Catalysts in Organic Synthesis*; Springer: Berlin, 1998; Chapter 10; (d) Sonogashira, K. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E.-i., Meijere, A., Eds.; Wiley-VCH: New York, NY, 2002; (e) Hundertmark, T.; Littke, A. F.; Buchwald, S. L.; Fu, G. C. *Org. Lett.* **2000**, *2*, 1729; (f) Erdelyi, M.; Gogoll, A. *J. Org. Chem.* **2001**, *66*, 4165; (g) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457; (h) Negishi, E. *Handbook of Organopalladium Chemistry for Organic Synthesis*; Wiley-Interscience: New York, NY, 2002; (i) Yong, B. S.; Nolan, S. P. *Chemtracts: Org. Chem.* **2003**, 205; (j) de Meijere, A.; Diederich, F. *Metal-Catalyzed Cross-Coupling Reactions*; Wiley-VCH: Weinheim, 2004.
3. (a) Paterson, I.; Davies, R. D. M.; Marquez, R. *Angew. Chem., Int. Ed.* **2001**, *40*, 603; (b) Nicolaou, K. C.; Dai, W.-M. *Angew. Chem., Int. Ed.* **1991**, *30*, 1387.
4. (a) Cosford, N. D. P.; Tehrani, L.; Roppe, J.; Schweiger, E.; Smith, N. D.; Anderson, J.; Bristow, L.; Brodkin, J.; Jiang, X.; McDonald, I.; Rao, S.; Washburn, M.; Varney, M. A. *J. Med. Chem.* **2003**, *46*, 204; (b) Kort, M.; Correa, V.; Valentijin, A. R. P. M.; Marel, G. A.; Potter, B. V. L.; Taylor, C. W.; Boom, J. H. *J. Med. Chem.* **2000**, *43*, 3295.
5. (a) Nalwa, H. S.; Miyata, S. *Nonlinear Optics of Organic Molecules and Polymers*; CRC: Boca Raton, FL, 1997; (b) Wegner, G.; Müllen, K. *Electronic Materials the Oligomer Approach*; Wiley-VCH: Weinheim, 1998; (c) Li, J.; Ambroise, A.; Yang, S. I.; Diers, J. R.; Seth, J.; Wack, C. R.; Bocian, D. F.; Holten, D.; Lindsey, J. S. *J. Am. Chem. Soc.* **1999**, *121*, 8927; (d) Onitsuka, K.; Fujimoto, M.; Ohshiro, N.; Takahashi, S. *Angew. Chem., Int. Ed.* **1999**, *38*, 689; (e) Brunsveld, L.; Meijer, E. W.; Prince, R. B.; Moore, J. S. *J. Am. Chem. Soc.* **2001**, *123*, 7978; (f) Wong, K.-T.; Hsu, C. C. *Org. Lett.* **2001**, *3*, 173; (g) Mongin, O.; Porres, L.; Moreaux, L.; Merta, J.; Blanchard-Desce, M. *Org. Lett.* **2002**, *4*, 719; (h) Höger, S.; Rosselli, S.; Ramminger, A.-D.; Enkelmann, V. *Org. Lett.* **2002**, *4*, 4269.
6. For reviews, see: (a) Diederich, F.; Stang, P. J. *Metal-Catalyzed Cross-Coupling Reactions*; Wiley-VCH: Weinheim, Germany, 1998; (b) Miyaura, N. *Cross-Coupling Reaction*; Springer: Berlin, 2002; (c) de Meijere, A.; Diederich, F. *Metal-Catalyzed Cross-Coupling Reactions*; Wiley-VCH: Weinheim, Germany, 2004; (d) Doucei, H.; Hierso, J.-C. *Angew. Chem., Int. Ed.* **2007**, *46*, 834; (e) Chinchilla, R.; Nájera, C. *Chem. Rev.* **2007**, *107*, 874.
7. For special reviews on copper-catalyzed cross-couplings, see: (a) Siemsen, P.; Livingston, R. C.; Diederich, F. *Angew. Chem., Int. Ed.* **2000**, *39*, 2632; (b) Hassan, J.; Sevignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359; (c) Ley, S. V.; Thomas, A. W. *Angew. Chem., Int. Ed.* **2003**, *42*, 5400; (d) Beletskaya, I. P.; Cheprakov, A. V. *Coord. Chem. Rev.* **2004**, *248*, 2337.
8. For papers on the Sonogashira cross-coupling reaction catalyzed by a catalytic amount of copper, see: (a) Okuro, K.; Furuune, M.; Enna, M.; Miura, M.; Nomura, M. *J. Org. Chem.* **1993**, *58*, 4716; (b) Gujadhur, R. K.; Bates, C. G.; Venkataraman, D. *Org. Lett.* **2001**, *3*, 4315; (c) Ma, D.; Liu, F. *Chem. Commun.* **2004**, 1934; (d) Wang, Y. F.; Deng, W.; Liu, L.; Guo, Q. X. *Chin. Chem. Lett.* **2005**, *16*, 1197; (e) Saejueng, P.; Bates, C. G.; Venkataraman, D. *Synthesis* **2005**, 1706; (f) Li, J.-H.; Li, J.-L.; Wang, D.-P.; Pi, S.-F.; Xie, Y.-X.; Zhang, M.-B.; Hu, X.-C. *J. Org. Chem.* **2007**, *72*, 2053; (g) Thakur, K. G.; Jaseer, E. A.; Naidu, A. B.; Sekar, G. *Tetrahedron Lett.* **2009**, *50*, 2865; (h) Mao, J.; Guo, J.; Ji, S. *J. Mol. Catal. A* **2008**, *284*, 85; (i) Monnier, F.; Turtaut, F.; Duroure, L.; Taillefer, M. *Org. Lett.* **2008**, *10*, 3203; (j) Wu, M.; Mao, J.; Guo, J.; Ji, S. *Eur. J. Org. Chem.* **2008**, 4050.
9. Thathagar, M. B.; Beckers, J.; Rothenberg, G. *Green Chem.* **2004**, *6*, 215.
10. (a) Lehn, J. M. *Supramolecular Chemistry, Concepts and Perspectives*; VCH: Weinheim, 1995; (b) Eddaoudi, M.; Moler, D. B.; Li, H.; Chen, B.; Reineke, T. M.; O'Keeffe, M.; Yaghi, O. M. *Acc. Chem. Res.* **2001**, *34*, 319; (c) Maury, O.; Bozec, H. L. *Acc. Chem. Res.* **2005**, *38*, 691; (d) Deacon, G. B.; Phillips, R. J. *Coord. Chem. Rev.* **1980**, *33*, 227.
11. (a) Rao, C. N. R.; Natarajan, S.; Vaidhyanathan, R. *Angew. Chem., Int. Ed.* **2004**, *43*, 1466; (b) Prabusankar, G.; Murugavel, R. *Organometallics* **2004**, *23*, 5644; (c) Murugavel, R.; Banerjee, S. *Inorg. Chem. Commun.* **2003**, *6*, 810; (d) Murugavel, R.; Krishnamurthy, D.; Sathiyendiran, M. *J. Chem. Soc., Dalton Trans.* **2002**, 34; (e) Murugavel, R.; Baheti, K.; Anantharaman, G. *Inorg. Chem.* **2001**, *40*, 6870; (f)

Murugavel, R.; Karambelkar, V. V.; Anantharaman, G.; Walawalkar, M. G. *Inorg. Chem.* **2000**, *39*, 1381.
12. (a) Sorenson, J. R. J.; Hangarter, W. *Inflammation* **1977**, *2*, 217; (b) Lemoine, P.; Viossat, B.; Morgant, G.; Greenaway, F. T.; Tomas, A.; Dung, N.-H.; Sorenson, J. R. J. *J. Inorg. Biochem.* **2002**, *89*, 18; (c) Garland, M. T.; Le Marouille, J. Y.; Spondine, E. *Acta Crystallogr., Sect. C* **1985**, *41*, 855.
13. (a) O' Young, C.-L.; Lippard, S. J. *J. Am. Chem. Soc.* **1980**, *102*, 4920; (b) Sorenson, J. R. J. *J. Med. Chem.* **1984**, *27*, 1747.
14. Athar, M.; Elmets, C. A.; Zaim, M. T.; Jenifer, J. R.; Bickers, D. R.; Mukhtar, H. *Proc. SPI Int. Soc. Opt. Eng.* **1988**, *847*, 193.
15. Smith, W.P.; Marenus, K.D.; Pelle, E. Eur. Patent Appl., 1989, EP 321929 (CAN 113:11936).
16. (a) Kwong, F. Y.; Buckwald, S. L. *Org. Lett.* **2003**, *5*, 793; (b) Jiang, D.; Fu, H.; Jiang, Y.; Zhao, Y. *J. Org. Chem.* **2007**, *72*, 672.
17. Pachon, L. D.; van Maarseveen, J. H.; Rothenberg, G. *Adv. Synth. Catal.* **2005**, *347*, 811.
18. (a) Corbet, J. P.; Mignani, G. *Chem. Rev.* **2006**, *106*, 2651; (b) Litvac, V.; Shein, S. *Zh. Org. Khim.* **1975**, *11*, 92; (c) Paine, A. *J. Am. Chem. Soc.* **1987**, *109*, 1496.
19. Yuan, W. G.; Chen, Y. J.; Chen, J. H. *Inorg. Chem. Commun.* **2009**, *12*, 1197.
20. (a) Kunkely, H.; Vogler, A. *Inorg. Chim. Acta* **2004**, *357*, 888; (b) Longguan, Z.; Kitagawa, S.; Kondo, M.; Miyasaka, H. *Chem. Lett.* **2000**, 536; (c) Geraghty, M.; Sheridan, V.; McCann, M.; Devereux, M.; McKee, V. *Polyhedron* **1999**, *18*, 2931.
21. Dean, J. A. *Lange's Handbook of Chemistry*, 11th ed.; McGraw-Hill: New York, NY, 1973; pp 5–15.
22. Novak, Z.; Nemes, P.; Kotschy, A. *Org. Lett.* **2004**, *6*, 4917.
23. Soheili, A.; Albaneze-Walker, J.; Murry, J. A.; Dormer, P. G.; Hughes, D. L. *Org. Lett.* **2003**, *5*, 4191.
24. Gholap, A. R.; Venkatesan, K.; Pasricha, R.; Daniel, T.; Lahoti, R. J.; Srinivasan, K. V. *J. Org. Chem.* **2005**, *70*, 4869.
25. Sotiriou-Leventis, C.; Wang, X.; Mulik, S.; Thangavel, A.; Leventis, N. *Synth. Commun.* **2008**, *38*, 2285.
26. Rubin, M.; Trofimov, A.; Gevorgyan, V. *J. Am. Chem. Soc.* **2005**, *127*, 10243.
27. Chow, H. F.; Wan, C. W.; Low, K. H.; Yeung, Y. Y. *J. Org. Chem.* **2001**, *66*, 1910.
28. (a) Urgaonkar, S.; Verkade, J. G. *J. Org. Chem.* **2004**, *69*, 5752; (b) Kochi, J.; Hammond, G. S. *J. Am. Chem. Soc.* **1953**, *75*, 3452.
29. Huang, H.; Liu, H.; Jiang, H.; Chen, K. *J. Org. Chem.* **2008**, *73*, 9061.
30. Yasuhara, A.; Kasano, A.; Sakamoto, T. *J. Org. Chem.* **1999**, *64*, 2301.
31. Carril, M.; Correa, A.; Bolm, C. *Angew. Chem., Int. Ed.* **2008**, *47*, 4862.
32. Kamikawa, T.; Hayashi, T. *J. Org. Chem.* **1998**, *63*, 8922.
33. Crisp, G. T.; Turner, P. D.; Stephens, K. A. *J. Organomet. Chem.* **1998**, *570*, 219.
34. Furster, A.; Mathes, C. *Org. Lett.* **2001**, *3*, 221.
35. Cheng, J.; Sum, Y.; Wang, F.; Guo, M.; Xu, J. H.; Pan, Y.; Zhang, Z. *J. Org. Chem.* **2004**, *69*, 5428.
36. Hill, L. L.; Smith, J. M.; Brown, W. S.; Moore, L. R.; Guevera, P.; Pair, E. S.; Porter, J.; Chou, J.; Wolterman, C. J.; Craciun, R.; Dixon, D. A.; Shaughnessy, K. H. *Tetrahedron* **2008**, *64*, 6920.
37. Roesch, K. R.; Larock, R. C. *J. Org. Chem.* **2001**, *66*, 412.
38. Katritzky, A. R.; Wang, J.; Karodia, N.; Li, J. *J. Org. Chem.* **1997**, *62*, 4142.
39. Mao, J.; Xie, G.; Wu, M.; Guo, J.; Ji, S. *Adv. Synth. Catal.* **2008**, *350*, 2477.
40. Yue, D.; Yao, T.; Larock, R. C. *J. Org. Chem.* **2005**, *70*, 10292.
41. Csekei, M.; Novak, Z.; Kotschy, A. *Tetrahedron* **2008**, *64*, 975.
42. Saleh, S.; Picquet, M.; Meunier, P.; Hierso, J. C. *Tetrahedron* **2009**, *65*, 7146.