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Copper-free palladium-catalyzed sonogashira-type coupling of aryl halides and 1-aryl-2-(trimethylsilyl)acetylenes

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Abstract—A one-pot procedure for the direct coupling of 1-aryl-2-trimethylsilylacetylenes with aryl halides to give diaryl acetylenes is reported. The procedure does not involve the use of copper(I) iodide. Improvement in reaction yields has been obtained by replacing conventional oil bath heating with the use of microwave dielectric heating.

1. Introduction

The palladium-catalyzed carbon–carbon bond forming reactions developed through the last decades remain of great value to synthetic organic chemists. One such reaction, the Sonogashira coupling,[1–3] involves the preparation of substituted acetylenes by coupling aryl or vinyl halides with terminal acetylenes in the presence of a palladium catalyst and copper(I) iodide as cocatalyst. Although there are examples of Sonogashira-type couplings without the use of a copper cocatalyst,[4–9] its use together with palladium is by far the most common procedure. Furthermore, copper(I) in itself is known to efficiently mediate the homo- and heterocoupling of terminal acetylenes,[10] being an undesirable side-reaction in several applications of the Sonogashira reaction.

Numerous reports describe the coupling of trimethylsilylacetylene with aryl halides in Sonogashira-type reactions. The C(sp)–Si bond is generally not affected by these reaction conditions. The silyl group can, therefore, if desired, subsequently be removed to furnish a structurally modified terminal alkyne.[2,5] The trimethylsilyl group is thereby used as a protective group, and as recently exemplified within solid-phase synthesis, the functionalized terminal alkyne formed by cleaving off the trimethylsilyl functionality with for example tetrabutylammonium fluoride (TBAF) or aqueous alkali can subsequently be subjected to reactions like the Mannich reaction[11] or a second Sonogashira cross-coupling step.[12]

We have studied the direct coupling of trimethylsilylacetylenes to give disubstituted acetylenes in a one-pot procedure which does not require isolation of the terminal alkyne after deprotection.[13] It has been described that this type of palladium-mediated coupling can be accomplished in the presence of equivalent[14] or catalytic[15] amounts of silver ions. In another recent study, describing the copper-palladium cocatalyzed cross-coupling of (arylethynyl)trimethylsilanes and aryl halides or triflates, it was concluded that catalytic amounts of copper are required for such a coupling reaction to take place.[16] Thus, with the omission of copper(I) chloride in the otherwise successful reaction of 4-acetylphenyl trifluoromethanesulfonate with 1-phenyl-2-trimethylsilylacetylene these authors could not detect any formation of the desired coupling product. In contrast to the use of an either catalytic[17,18] or stoichiometric[19] amount of copper, the result of our work presented here is a procedure for the direct coupling of trimethylsilylacetylenes to give 1,2-diaryl acetylenes in a palladium-catalyzed reaction without the use of a copper cocatalyst and furthermore with a reduction in the reaction time from several hours[16] to only minutes by means of microwave heating. Regarding the use of microwaves,[19–27] it has recently been reported that aryl trimethylsilylacetylenes can be prepared efficiently from trimethylsilylacetylene and an aryl halide using standard Sonogashira coupling conditions and microwave irradiation with much reduced reaction times.[28] Thus, as recently exemplified in a one-pot procedure,[16] combining the introduction of the trimethylsilylethynyl functionality and subsequent coupling with an aryl halide represents a useful tool for the preparation of diarylacetylenes. An example of this class of compounds which has been of great interest to us is the neuroactive compound 2-methyl-6-(phenylethynyl)pyridine (MPEP, **4**, Table 2), found to be a

Keywords: Microwaves; Sonogashira-type coupling; 1-Aryl-2-trimethylsilylacetylenes; Diaryl acetylenes.
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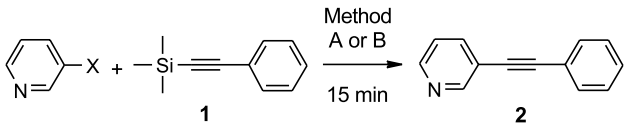
Table 1. Reaction conditions for coupling of 1-phenyl-2-(trimethylsilyl)acetylene (**1**) and 3-halopyridines



Entry	X	Method[a]	Solvent	Catalyst	T (°C)	Base/transf. cat.[b]	Yield (%)
1	Br	A	DMF	$Pd(OAc)_2$	100	A	32
2	Br	B	DMF	$Pd(OAc)_2$	100	B	53[c]
3	Br	A	DMF	$Pd(OAc)_2$	100	B	61[c]
4	Br	A	DMF	$Pd(OAc)_2/(o\text{–tol})_3P$	100	B	71
5	I	A	*n*-Bu_2O	$Pd(OAc)_2$	100	B	16
6	I	A	H_2O/DMF 1:9	$Pd(OAc)_2$	100	C	64
7	I	A	DMF	$Pd(OAc)_2$	100	D	5
8	I	A	DMA	$Pd(OAc)_2$	100	B	80
9	I	A	DMA	$Pd(OAc)_2/(o\text{–tol})_3P$	100	B	80
10	I		DMF	$Pd(OAc)_2$	rt[d]	B	28
11	I	B	DMF	$Pd(OAc)_2$	100	B	62[c]
12	I	A	DMF	$Pd(OAc)_2$	100	B	74[c]
13	I	A	DMF	$Pd(OAc)_2$	140	B	58
14	I	A	DMF	$Pd(OAc)_2$	180[e]	B	37
15	I	A	DMF	$Pd(PPh_3)_2$	100	B	87
16	I	A	DMF	$Pd(OAc)_2/(o\text{–tol})_3P$	100	B	90

[a] Method A: microwave heating, Method B: conventional heating.
[b] A: NaOAc/Bu_4NBr, B: NaOAc/Bu_4NCl, C: K_2CO_3/Bu_4NCl, D: triethylamine.
[c] Average of two determinations (see footnote[†]).
[d] Reaction time 16 h.
[e] Reaction time 4 min.

highly potent and selective antagonist for the metabotropic glutamate receptor subtype mGlu5.[29,30]

2. Results and discussion

Initially, we studied the coupling of 1-phenyl-2-(trimethylsilyl)acetylene (**1**) with 3-bromo- or 3-iodopyridine to identify the optimal reaction conditions (Table 1). Compound **2** was isolated in a moderate 28% yield (entry 10, Table 1) when the reaction (scale 2.50 mmol) was carried out at room temperature overnight in the presence of 5 mol% palladium acetate together with sodium acetate and tetrabutylammonium chloride. Performing this transformation at elevated temperature applying 15 min of microwave irradiation (Method A), resulted in an initial improvement of the reaction to 74% isolated yield of **2** when starting from 3-iodopyridine (entry 12, Table 1).[†]

We found the reaction to be highly reproducible when using a microwave instrument that allows for control and monitoring of temperature as well as giving efficient stirring. For most of our experiments DMF was used as solvent. With its high polarity it absorbs microwaves well, resulting in very rapid heating. Using typically 50 ml of DMF as solvent and irradiation at 450 W, we achieved a temperature increase from room temperature to 100 °C within less than 30 s.

As can be seen from Figure 1, heating the reaction mixture in a hot oil bath (Method B) results in much slower heating and conversion rates, and the rapid heating when applying microwaves may be the explanation for the higher isolated yields obtained in the cases where comparable experiments were carried out.

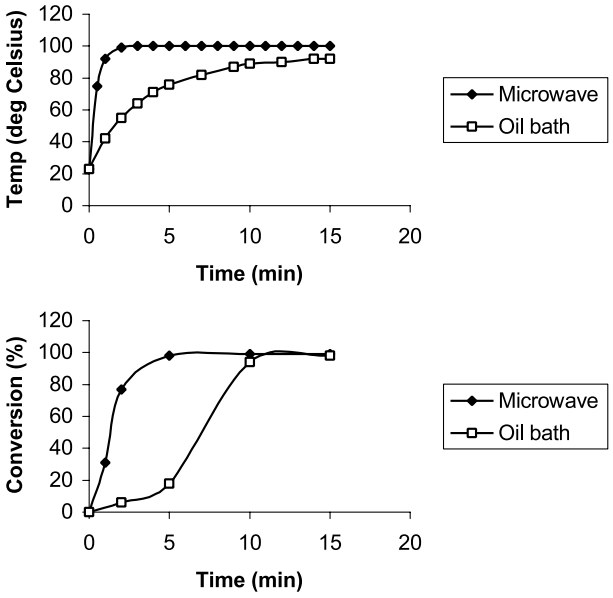


Figure 1. Experiments performed using identical scale (50 ml solvent) and identical reaction flasks and magnetic stirring bars. Upper graph: For MW experiment, a sensor placed in the reaction mixture allows for on-line temperature control and monitoring. For oil bath, values are average of three determinations (maximal deviation two degrees Celsius). Lower graph: Conversion rates (single determination) were calculated from H-NMR spectral data of crude product (desired product/aryl halide).

[†] Isolated yields obtained in the repeated microwave experiments: 75 and 73% from 3-iodopyridine (Table 1, entry 12); 61 and 60% from 3-bromopyridine (Table 1, entry 3). For the oil bath experiments, 60 and 64% were obtained from 3-iodopyridine (Table 1, entry 11) and 50 and 56% from 3-bromopyridine (Table 1, entry 2).

Thus, for the synthesis of **2** an average of 74% yield from two determinations (entry 12, Table 1) was obtained in the former case as compared to 62% for two otherwise identical experiments using a pre-heated oil bath (entry 11, Table 1).[†] A similar tendency was found when starting from 3-bromopyridine (entry 2 and 3, Table 1).[†] To this end, it should be noticed that microwave heating is now generally considered as having only thermal effects although some discussion is still active in the literature regarding a specific 'microwave effect'.

We generally used palladium acetate as pre-catalyst but observed in most cases a significantly improved yield when introducing a phosphine ligand. This could be explained by a stabilizing effect of the phosphine ligand on the reactive palladium species, or by a facilitated reduction of the palladium (II) to a palladium(0) species as previously discussed for example the palladium-catalyzed Heck coupling.[31,32] Using either palladium acetate/tri(*o*-tolyl)-phosphine (entry 16, Table 1) or tetrakis(triphenyl-phosphine)palladium (entry 15, Table 1) very high yields of **2** were obtained. Regarding the base, sodium acetate turned out to be superior to aqueous potassium carbonate and, in particular, triethylamine, for which only poor yield was obtained (entry 7, Table 1).

In order to study the scope of this reaction, a number of aryl halides and heteroaryl halides were subjected to this transformation (Table 2). The yields are highly substrate-dependent, and the coupling product was formed only in cases where the aryl halide was sufficiently activated. As could be expected, iodides afforded better results than the corresponding bromides. For the benzoic acid methyl esters, efficient conversion-rates were obtained for the 3- and 2-substituted derivatives, yielding after 15 min at 100 °C compounds **8** and **9** in 84 and 85% yield, respectively. For comparison, the latter result is identical to what has previously been published in the synthesis of **9** from methyl 2-iodobenzoate applying Cu(I) as cocatalyst and stirring two days at room temperature.[33]

In contrast to the successful reactions using 2- and 3-substituted benzoic acid methyl esters, the corresponding 4-bromosubstituted substrate gave compound **7** in a poor 7% yield from a complex mixture of reaction products. In the reaction of 2-bromo-3-hydroxypyridine, the 3-hydroxy group participates in an intramolecular cyclization and the expected disubstituted acetylenic product was, therefore, not isolated. Instead, the further cyclized 2-phenyl-furo(3,2b)pyrrole **5** was obtained in 33% yield. This result corresponds to what has been reported by Sakamoto et al. for the reaction of 2-iodo-3-hydroxypyridine with phenyl-acetylene.[34]

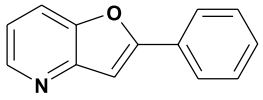


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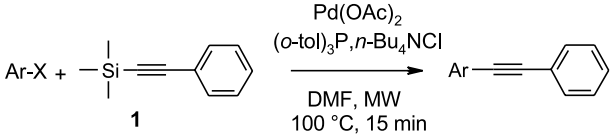
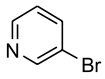
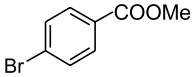
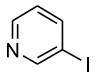
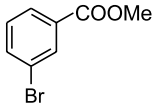
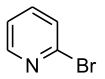
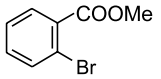
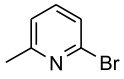
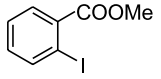
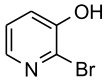
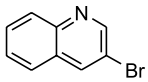
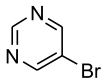
Table 2. Coupling reactions of 1-phenyl-2-trimethylsilyl)acetylene (**1**)



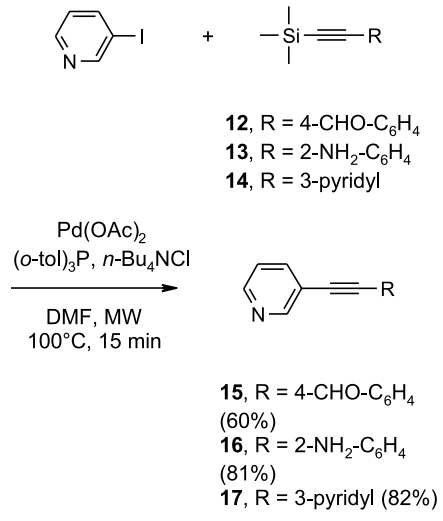
Ar–X	Product, yield (%)[a]	Ar–X	Product, yield (%)[a]
	**2** 71 (61)[b]		**7** (7)
	**2** 90 (74)[b]		**8** 84 (60)
	**3** (39)[c]		**9** 85 (60)
	**4** 50[d] (40)		**9** 85 (70)
	**5** (33)[e]		**10** 44 (37)
	**6** 55 (57)		**11** 84 (60)

[a] Numbers in parentheses are isolated yields obtained without the use of (*o*-tol)$_3$P.
[b] Average of two determinations.
[c] 35% isolated yield obtained with $T=140$ °C.
[d] 2.5 min, 600 W, 120 °C.
[e] From 2-bromo-3-hydroxypyridine further cyclized **5** was obtained.

Furthermore, it should be mentioned that neither phenyl bromide nor phenyl iodide gave the desired product, although trace amounts of diphenylacetylene had apparently been formed in the latter case (TLC). Generally, good results were obtained from heterocyclic aryl halides. The two pyrimidine derivatives **10** and **11** were prepared from their respective bromides. An early study of Sonogashira couplings on iodopyrimidines[35] previously reported the synthesis of **10** in high yield (93%) from 2-iodopyrimidine and phenylacetylene. In contrast, we isolated **10** in 44% yield when starting from the corresponding 2-bromopyrimidine, whereas the more reactive 5-bromopyrimidine gave the novel compound **11** in up to 83% isolated yield. As observed for the pyrimidines, pyridines having the halide positioned meta to the heterocyclic nitrogen atom gave the best results in this reaction (Table 2). It should be noted, that **3** has been reported synthesized from the corresponding heterocyclic triflate using conventional Sonogashira coupling conditions in 68% yield in the presence of copper.[16]

To further broaden the versatility of the reaction we were also interested in introducing functionalized substituents via the alkyne substrate.

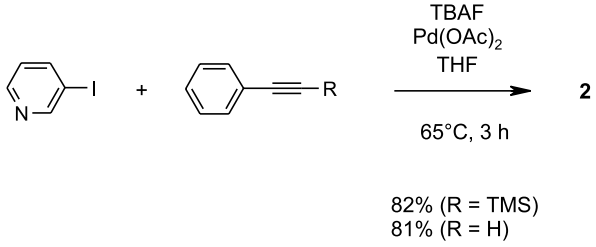
Moreover, using as substrate 4-(trimethylsilylethynyl)-benzaldehyde (**12**) or 2-(trimethylsilylethynyl)aniline (**13**) it was possible to introduce an aldehyde moiety as well as an amino group and obtain the desired coupling products **15** and **16** in 60 and 81% yield, respectively (Scheme 1). Thus, neither of these, respectively, electron-withdrawing and electron-donating functional groups appear to significantly affect the reactivity of the phenylacetylene substrate, suggesting tolerance to a wide range of substituents. Finally, 3,3′-ethynediyl-bis-pyridine (**17**) was synthesized in high yield from **14** whereas an attempt to introduce an aliphatic substituent, using 1-(trimethylsilyl)-1-pentyne, was unsuccessful.



Scheme 1.

We have not investigated the reaction mechanism of this transformation and, as discussed elsewhere,[36] it is not clear whether it takes place via for example, a carbopalladation pathway or via transmetallation between palladium and silicon in analogy with the mechanism recently argued by Itami et al. to explain the palladium-catalyzed coupling of alkenyl silanes with aryl- and vinyl halides in the presence of TBAF.[37]

Fluoride-induced silicon to Pd transmetallation has been invoked in Pd-catalyzed cross-coupling reactions by Hiyama et al.[38] To study this, we carried out a number of experiments in which the coupling of the trimethylsilylacetylene and the aryl halide was carried out in the presence of only TBAF and palladium acetate. Interestingly, **2** could in fact be isolated in good yield from 3-iodopyridine using this procedure (Scheme 2).



Scheme 2.

Despite this result, the same method used on 2- and 5-bromopyrimidine gave low yields of products (8 and 4%, respectively) together with many side-products, and when applied to aldehyde **12**, reaction with 3-iodopyridine gave **15** in 23% isolated yield. Following the addition of TBAF the reaction was in all cases exothermic, and the reaction mixture instantly turned black. In a control experiment, applying an identical procedure, 3-iodopyridine was treated with phenylacetylene (Scheme 2) in the presence of TBAF. This experiment proceeded without the initial development of heat and the reaction mixture did only slowly turn black. Interestingly, the desired product **2** was isolated in similarly high yield (81%) as in the reaction with trimethylsilylacetylene **1**. Thus, on the basis of this control experiment it cannot be concluded whether a transmetallation pathway is operating or if TBAF simply causes desilylation to give phenylacetylene being the actual substrate in the cross-coupling reaction.

In summary, a procedure for diarylacetylene synthesis via the direct coupling of activated aryl- and heteroaryl bromides and iodides with 1-aryl-2-trimethylsilylacetylenes has been developed. It avoids the use of a copper(I) iodide cocatalyst and is carried out by means of microwave heating with short reaction times at elevated temperature.

3. Experimental

3.1. General methods

Reagents and solvents were purchased from commercial sources and used without further purification unless otherwise stated. Melting points were determined in open capillaries and are uncorrected. Microwave irradiation was performed using a MLS-Ethos 1600 instrument or in one case (Table 1, entry 14) by use of a SmithCreator™ instrument. Column chromatography (CC) was performed

using silica gel 60 (0.040–0.063 mm) or prepacked silica gel colums (50 or 70 g). Compounds were visualized on TLC using UV light and $KMnO_4$ spraying reagent. Proton and carbon NMR spectra were recorded on a 400 MHz instrument at 400 and 100 MHz, respectively. Mass spectrometry analyses were obtained using an LC/MSD instrument.

3.1.1. General procedure for the synthesis of 2-(phenylethynyl)arenes. Synthesis of 3-(phenylethynyl)pyridine (2). Method A (microwave heating). 3-Iodopyridine (2.50 mmol, 512 mg), 1-phenyl-2-trimethylsilylacetylene (5.00 mmol, 872 mg), palladium acetate (0.125 mmol, 28.1 mg), Bu_4NCl (2.50 mmol, 695 mg), and sodium acetate (10.0 mmol, 820 mg) in dry DMF (50 ml) were heated under argon in the Ethos 1600 microwave oven for 15 minutes regulating the power (initially 450 W thereafter 40–50 W) in order to keep the temperature constant at 100 °C. After cooling to room temperature, the reaction mixture was added saturated aqueous $NaHCO_3$ and extracted three times with EtOAc. The combined organic phases were dried ($MgSO_4$), filtered, and evaporated to dryness and the residue purified by CC (0–10% EtOAc in hexane) to give **2** as a solid in 75% yield (335 mg); mp 47.8–49.0 °C (lit.[39] mp 50–51 °C). ^{1}H NMR in correspondence with literature;[39] ^{1}H NMR ($CDCl_3$) δ 7.20–7.25 (m, 1H), 7.30–7.36 (m, 3H), 7.51–7.56 (m, 2H), 7.73–7.79 (m, 1H), 8.50–8.55 (m, 1H), 8.75–8.79 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 86.0, 92.7, 120.4, 122.5, 123.0, 128.4, 128.8, 131.7, 138.4, 148.5, 152.2. MS (ES^+) *m/z* 180 ($[M+1]^+$, 100). HRMS: Calcd for $C_{13}H_{10}N$ 180.0813, found 180.0816.

3.1.2. Method B (conventional heating). These experiments (Table 1) were carried out exactly identical to the above described (method A), except that the reaction mixture was put in a preheated (100 °C) oil bath for 15 min, cooled to room temperature, and worked up as described for method A.

3.1.3. Method C (Synthesis of 2 using tetrabutylammonium fluoride (TBAF) in THF). 3-Iodopyridine (2.87 mmol, 588 mg), 1-phenyl-2-trimethylsilylacetylene (4.30 mmol, 750 mg), and palladium acetate (0.14 mmol, 32.2 mg) in dry THF (3 ml) was dropwise added in a 1 M solution of TBAF in THF (4.30 mmol) and stirred under argon 3 h at 65 °C. After cooling to rt, the reaction mixture was added saturated aqueous $NaHCO_3$ and extracted three times with EtOAc. The combined organic phases were dried ($MgSO_4$), filtered, and evaporated to dryness. Compound **2** was isolated as a dark solid in 82% yield (423 mg) by flash chromatography (0–10% EtOAc in hexane). Compound characterization (^{1}H NMR and MS) showed that the isolated product was identical to **2** as described above for method A.

3.1.4. 2-(Phenylethynyl)pyridine (3). Method A. Oil, 173 mg (39%). ^{1}H and ^{13}C NMR in correspondence with literature;[40,41] ^{1}H NMR ($CDCl_3$) δ 7.18–7.22 (m, 1H), 7.32–7.36 (m, 3H), 7.48–7.52 (m, 1H), 7.57–7.65 (m, 3H), 8.58–8.62 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 88.6, 89.2, 122.2, 122.7, 127.1, 128.4, 129.0, 132.0, 136.2, 143.4, 150.0. MS (ES^+) *m/z* 180 ($[M+1]^+$, 100).

3.1.5. 2-Methyl-6-(phenylethynyl)pyridine (4). Method A (2.5 min oven setting 600 W, internal temperature 120 °C, 2-bromo-6-methylpyridine (2.9 mmol, 0.50 g), 1-phenyl-2-trimethylsilylacetylene (8.9 mmol, 1.50 g), palladium acetate (0.14 mmol, 32.0 mg), Bu_4NCl (2.9 mmol, 810 mg), and sodium acetate (11.6 mmol, 951 mg) in dry DMF (50 ml)). Isolated as the 1,5-naphthalenedisulfonate salt (crystallized from MeOH—EtOH-Et_2O), 380 mg (47%); mp 296–297 °C. Spectra from corresponding free base: ^{1}H NMR in correspondence with literature;[42] ^{1}H NMR ($CDCl_3$) δ 2.57 (s, 3H), 7.05–7.10 (m, 1H), 7.31–7.36 (m, 4H), 7.51–7.62 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 24.7, 88.9, 89.0, 122.4, 122.6, 124.4, 128.3, 128.5, 128.8, 132.0, 136.4, 142.7, 158.9. MS (ES^+) *m/z* 194 ($[M+1]^+$, 100). Anal. Calcd for $C_{38}H_{30}N_2O_6S_2 \cdot 0.5\ H_2O$: C, 66.75; H, 4.57; N, 4.10; O, 15.20; S, 9.38. Found: C, 66.55; H, 4.53; N, 4.08; O, 15.23; S, 9.32.

3.1.6. 2-phenyl-furo[3,2-b]pyridine (5). Method A (2-bromo-3-hydroxypyridine (5.75 mmol, 1.00 g), 1-phenyl-2-trimethylsilylacetylene (11.5 mmol, 1.98 g), palladium acetate (0.28 mmol, 64.0 mg), Bu_4NCl (5.75 mmol, 1.6 g), and sodium acetate (23.0 mmol, 1.9 g) in dry DMF (50 ml). Reaction temperature 140 °C, 15 min). Solid, 376 mg (33%), mp 91–93 °C (lit.[34] mp 88–89 °C). ^{1}H NMR in correspondence with literature;[34,43] ^{1}H NMR ($CDCl_3$) 7.05–7.49 (m, 5H), 7.72–7.92 (m, 3H), 8.50–8.53 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 102.2, 118.0, 118.9, 125.4, 129.0, 129.7, 129.8, 146.2, 148.1, 149.2, 159.8. MS (EI^+) *m/z* 195 (M^+, 100). Anal. Calcd for $C_{13}H_9NO$: C, 79.98; H, 4.65; N, 7.17; O, 8.20. Found: C, 79.93; H, 4.82; N, 7.16; O, 8.10.

3.1.7. 3-(Phenylethynyl)quinoline (6). Method A (using in addition 10 mol % tri(*o*-tolyl)phosphine). Solid, 316 mg (55%), mp 67–70 °C. ^{1}H NMR ($CDCl_3$) δ 7.20–7.71 (m, 8H), 8.05–8.10 (m, 1H), 8.20 (s, 1H), 8.95 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 86.6, 92.6, 117.4, 122.6, 127.1, 127.2, 127.5, 128.4, 128.8, 129.3, 130.0, 131.7, 138.2, 146.7, 152.0. MS (ES^+) *m/z* 230 ($[M+1]^+$, 100). HRMS: Calcd for $C_{17}H_{12}N$ 230.0970, found 230.0970.

3.1.8. Methyl 4-(phenylethynyl)benzoate (7). Method A. Oil, 40 mg (7%). ^{1}H NMR in correspondence with literature;[44] ^{1}H NMR ($CDCl_3$) δ 3.92 (s, 3H), 7.20–7.60 (m, 7H), 7.98–8.02 (m, 2H). MS (EI^+) *m/z* 236 (M^+, 100).

3.1.9. Methyl 3-(phenylethynyl)benzoate (8). Method A (using in addition 10 mol % tri(*o*-tolyl)phosphine). Solid, 498 mg (84%), mp 77.0–78.2 °C (lit.[45] mp 77–79 °C). ^{1}H NMR in correspondence with literature;[46] ^{1}H NMR ($CDCl_3$) 3.93 (s, 3H), 7.34–7.46 (m, 4H), 7.52–7.57 (m, 2H), 7.68–7.72 (m, 1H), 7.97–8.02 (m, 1H), 8.19–8.23 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 52.3, 88.3, 90.3, 122.9, 123.8, 128.4, 128.5, 128.6, 129.2, 130.5, 131.7, 132.8, 135.7, 166.5. MS (EI^+) *m/z* 236 (M^+, 100).

3.1.10. Methyl 2-(phenylethynyl)benzoate (9). Method A (from methyl 2-iodobenzoate, using in addition 10 mol % tri(*o*-tolyl)phosphine). Oil, 505 mg (85%). ^{1}H NMR in correspondence with literature;[47,48] ^{1}H NMR ($CDCl_3$) 3.95 (s, 3H), 7.31–7.65 (m, 8H), 7.92–7.98 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 52.2, 88.2, 94.3, 123.3, 123.7, 127.9, 128.4, 128.5, 130.5, 131.3, 131.7, 131.9, 134.0, 166.7. MS (ES^+) *m/z* 259 ($[M+Na]^+$, 100).

3.1.11. 2-(Phenylethynyl)pyrimidine (10). Method A (using in addition 10 mol % tri(*o*-tolyl)phosphine). Solid, 197 mg (44%), mp 84–86 °C (lit.[35] mp 84–85 °C). ^{1}H NMR ($CDCl_3$) δ 7.15–7.22 (m, 1H), 7.32–7.40 (m, 3H), 7.62–7.69 (m, 2H), 8.71–8.76 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 77.5, 87.9, 119.7, 121.2, 128.7, 129.7, 132.5, 153.2, 157.3. MS (ES^+) *m/z* 181 ($[M+1]^+$, 100). HRMS: Calcd for $C_{12}H_9N_2$ 181.0766, found 181.0766.

3.1.12. 5-(Phenylethynyl)pyrimidine (11). Method A (using in addition 10 mol % tri(*o*-tolyl)phosphine). Solid, 375 mg (83%), mp 51.5–53.5 °C. ^{1}H NMR ($CDCl_3$) δ 7.35–7.42 (m, 3H), 7.53–7.58 (m, 2H), 8.85 (s, 2H), 9.14 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 82.3, 96.3, 119.9, 121.8, 128.6, 129.4, 131.8, 156.7, 158.6. MS (EI^+) *m/z* 180 (M^+, 100). Anal. Calcd for $C_{12}H_8N_2$: C, 79.98; H, 4.47; N, 15.54. Found: C, 79.83; H, 4.55; N, 15.30.

3.1.13. 4-(3-Pyridylethynyl)benzaldehyde (15). Method A (using in addition 10 mol % tri(*o*-tolyl)phosphine). Solid, 309 mg (60%); a sample was recrystallized (EtOAc/hexane) for mp and elemental analysis; mp 98.5–99.3 °C. ^{1}H NMR ($CDCl_3$) δ 7.29–7.35 (m, 1H), 7.68–7.73 (m, 2H), 7.82–7.93 (m, 3H), 8.57–8.63 (m, 1H), 8.78–8.83 (m, 1H), 10.03 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 89.7, 91.6, 119.7, 123.1, 128.7, 129.6, 132.2, 135.8, 138.6, 149.2, 152.4, 191.3. MS (ES^+) *m/z* 208 ($[M+1]^+$, 100). Anal. Calcd for $C_{14}H_9NO$: C, 81.14; H, 4.38; N, 6.76. Found: C, 80.81; H, 4.52; N, 6.89.

3.1.14. 2-(3-Pyridylethynyl)aniline (16). Method A (using in addition 10 mol % tri(*o*-tolyl)phosphine). Solid, 394 mg (81%); a sample was recrystallized (EtOAc) for mp and elemental analysis; mp 113.5–115.0 °C (lit.[49] mp 104–106 °C). ^{1}H NMR and ^{13}C NMR in correspondence with literature;[49] ^{1}H NMR ($CDCl_3$) δ 4.32 (br s, 2H), 6.70–6.77 (m, 2H), 7.13–7.20 (m, 1H), 7.24–7.31 (m, 1H), 7.35–7.41 (m, 1H), 7.76–7.82 (m, 1H), 8.50–8.55 (m, 1H), 8.74 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 89.4, 91.2, 107.0, 114.5, 118.0, 120.5, 123.1, 130.3, 132.3, 138.2, 148.0, 148.5, 152.0. MS (ES^+) *m/z* 195 ($[M+1]^+$, 100). Anal. Calcd for $C_{13}H_{10}N_2 \cdot 0.05$ EtOAc: C, 79.81; H, 5.28; N, 14.10. Found: C, 79.86; H, 5.32; N, 14.45.

3.1.15. 3,3′-Ethynediyl-bis-pyridine (17). Method A (using in addition 10 mol % tri(*o*-tolyl)phosphine). Solid, 369 mg (82%); mp 53–56 °C (lit.[50] mp 60–62 °C). ^{1}H NMR ($CDCl_3$) δ 7.26–7.32 (m, 2H), 7.80–7.86 (m, 2H), 8.55–8.60 (m, 2H), 8.78 (s, 2H). ^{13}C NMR ($CDCl_3$) δ 89.2, 119.8, 123.1, 138.5, 149.1, 152.3. MS (ES^+) *m/z* 181 ($[M+1]^+$, 100).

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