EurJOC
European Journal of Organic Chemistry

A Journal of ChemPubSoc Europe

Accepted Article

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To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.201801543

Link to VoR: http://dx.doi.org/10.1002/ejoc.201801543

Supported by ACES Asian Chemical Editorial Society

WILEY-VCH

European Journal of Organic Chemistry 10.1002/ejoc.201801543

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FULL PAPER

Arylzinc Halides by Silver Catalyzed Zinc Insertion to Aryl Iodides

Gianluca Casotti,*[a] Anna Iuliano,[a] and Adriano Carpita†,[a]

Abstract: A catalytic amount of silver acetate efficiently promotes direct insertion of zinc metal into aryl iodides, having different structure, in ethereal solvent. Electron-rich substrates also rapidly undergo oxidative metalation. The arylzinc iodides formed give Negishi coupling products under mild reaction conditions to give biaryls in high yields. Sensitive functional groups like aldehydes and primary amides are well-tolerated.

Introduction

Organozinc halides are useful reagents for organic synthesis, as witnessed by their wide use as nucleophiles in the Negishi coupling, a powerful and versatile reaction for carbon-carbon bond formation.[1]

Direct insertion of zinc metal to organic halides provides the most practical and atom-economical way for preparing these organometallic reagents.

Nevertheless, oxidative metalation often has limited application due to the long reaction times required by many substrates.[2,3]

Aryl iodides are known to be unreactive with normal zinc powder under standard reaction conditions used for other oxidative metalations, such as the Grignard preparation: as a matter of fact, special formulation like Rieke zinc,[4] the use of polar or high-boiling solvents[5–12] or some kind of activation or additives[6,10,13–16] are required. Despite the great importance of these methods, some drawbacks, like pyrophoricity of highly active zinc formulations, affect their use. Furthermore, organozinc halides, normally, must be directly used in the successive reactions in the solvent where they are prepared. Therefore the use of an uncommon medium for organometallic reactions (polar or high-boiling solvents), as well as additives with a potential activity in the successive synthetic steps, might constitute a limitation of these methods, depending on the reactions where they have to be used.[12]

These considerations, together with the request for mild and efficient protocols for the achievement of these organometallic reagents, prompted us to search for different synthetic methods.

Results and Discussion

Herein we report a novel, simple and general procedure for the preparation of arylzinc iodides in ethereal solvents, even starting from electron-rich substrates, in short reaction times.

Inspired by previous works where the zinc-silver couple[17] has been used together with tetramethylethylenediamine (TMEDA) to promote zinc insertion in various substrates,[18–20] we tried a similar approach to obtain arylzinc iodides.

Although there are not specific studies on the role of silver in these couples, it can be assumed to facilitate electron transfer from zinc to the organic halide, probably the rate determining step of the metalation.[5] TMEDA, in this context, is supposed to stabilize the organometallic reagent, providing faster conversion of the halide.[18]

In our first trials zinc-silver couple was formed following a previously reported procedure.[18]

In order to verify the efficiency of the method, we chose substrates that notoriously provide insertion products with long reaction times even by using additives,[13] as the electron-rich 4-iodoanisole (**1a**) and 4-iodotoluene (**1b**), and, for comparison, iodobenzene (**1c**) as well (Table 1, entries 1-3). In all cases, high conversions were achieved within reasonable reaction times, even on scarcely reactive substrates.[2]

Encouraged by these results, 1,2-dimethoxyethane (DME) was used to further shorten the reaction times. Being higher-boiling than THF, DME could be used both at the reflux temperature and at 70 °C, which is close to the THF reflux temperature. The solvent change had practically no effect at 70°C (Table 1, entry 4), while resulted in a dramatic improvement of the reaction rate when it was employed at the reflux temperature (ca. 85°C) (Table 1, entry 5). It is noteworthy that under these conditions, direct insertion on **1a** was completed in just 10 h (Table 1, entry 6).

In order to check if these results could be reproduced, both the preparation of the zinc-silver couple and the oxidative metalation on **1a** were repeated several times.

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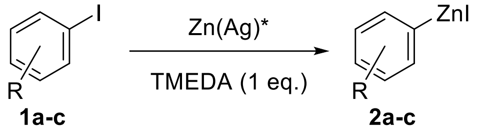
Table 1. Evaluation of Zinc-Silver couple in aryl iodides direct insertion reaction



Entry	Substrate [a]	R	Solvent	Temperature	Particle size	Time	Conversion [b]
1	**1a**	4-MeO	THF	reflux	9.8 µm	23 h	95%
2	**1b**	4-Me	THF	reflux	9.8 µm	19 h	90%
3	**1c**	H	THF	reflux	9.8 µm	10 h	>99%
4	**1c**	H	DME	70°C	9.8 µm	9 h	>99%
5	**1c**	H	DME	reflux	9.8 µm	3 h	>99%
6	**1a**	4-MeO	DME	reflux	9.8 µm	10 h	>99%
7	**1a**	4-MeO	DME	reflux	4 µm	24 h	48%
8	**1a**	4-MeO	DME	reflux	8 µm	10 h	99%

* Zn(Ag) activated with Me_3SiCl. [a] 1M concentration of aryl iodide. [b] GC conversion (determined by analysis on hydrolyzed aliquots).

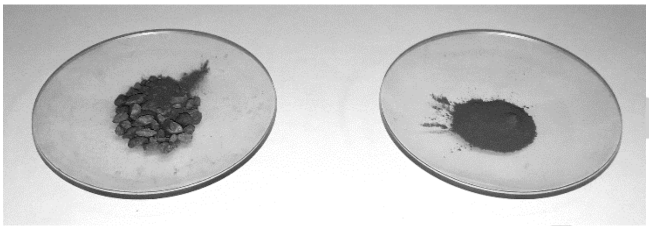
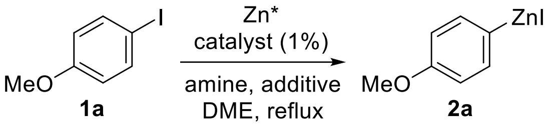


Figure 1. Zn(Ag) made with 4 µm zinc (left) and 9.8 µm (right).

Unfortunately, this procedure seemed to be poorly reproducible.
Further investigations suggested that the success of the method is strictly dependent on the particle size of the zinc. Specifically, zinc dust with particle size of 8-10 µm gave good results (Table 1, entries 6 and 8), while smaller particles provided a less active zinc-silver couple, resulting in poor conversions during the oxidative metalation step (Table 1, entry 7). The low reaction rate is probably due to aggregation of particles during the preparation of the Zn-Ag couple (Figure 1).
Despite these interesting results, the preparation of the zinc-silver couple has to be considered of little interest from a practical outlook, because it requires a long and tedious procedure of preparation and a lot of solvent must be used during the work-up. So, we decided to try a more appealing approach to zinc activation, attempting to form zinc-silver couple directly during the oxidative metalation step, by adding a catalytic amount of silver acetate to the reaction mixture. These results are summarized in Table 2.
This kind of activation, which presumably leads to the formation of a zinc-silver couple "in situ", had an impressive effect with various kind of zinc, leading to complete conversion of **1a** in just 7 h, with zinc powder having particle size ranging from 4 to 63 µm (Table 2, entry 1). Only zinc with particle size of 600 – 800 µm resulted unreactive under these conditions (Table 2, entry 2). Moreover, we have verified that, as previously reported in the literature for other metalation methods, zinc pre-activation with Me_3SiCl is not strictly required (Table 2, entry 3), even if it provides more reproducible results.[12]
To verify if silver acetate was the only salt capable to promote this kind of activation, we decided to try some other silver salts (Table 2, entries 4 and 5). From these trials it emerged that the nitrate is completely unreactive whereas the tosylate has a little effect, even if much less significant with respect to the acetate. Moreover, we have found that copper (II) acetate could not provide the analogous zinc-copper couple "in situ" (Table 2, entry 6). It is remarkable that without silver salts, no reaction occurred in 24 h (Table 2, entry 7). Afterwards, the role of TMEDA as additive was checked, by performing some tests to verify if it could be used in substoichiometric amount.
After 7 h, the time needed to have full conversion of the model substrate with 1 equivalent of TMEDA, the conversion was substantially proportional to the added TMEDA equivalents (Table 2, entries 8 and 9).
It is noteworthy that even without TMEDA, high conversions could be achieved, albeit with long reaction times (Table 2, entry 10).
To find if only TMEDA is capable to accelerate the direct insertion in the presence of silver acetate, the effect of various amounts of other additives was checked. To this aim another bidentate amine, 1,4-diazabicyclo[2.2.2]octane (DABCO) and LiCl, which is known to increase the reaction rate of the metalation,[13] were tried.
The obtained results showed that also DABCO has an accelerating effect, even if smaller than TMEDA (Table 2, entry 13) and LiCl increased the reaction rate with respect to the additives-free conditions (cfr. Table 2, entry 10 vs entry 15). The possibility of a double activation with both TMEDA and LiCl in different amounts (Table 2, entries 11 and 12) was checked as well, but no substantially different results were obtained. Also the

use of another Lewis acid, instead of LiCl, did not lead to significant effects (Table 2, entry 16).

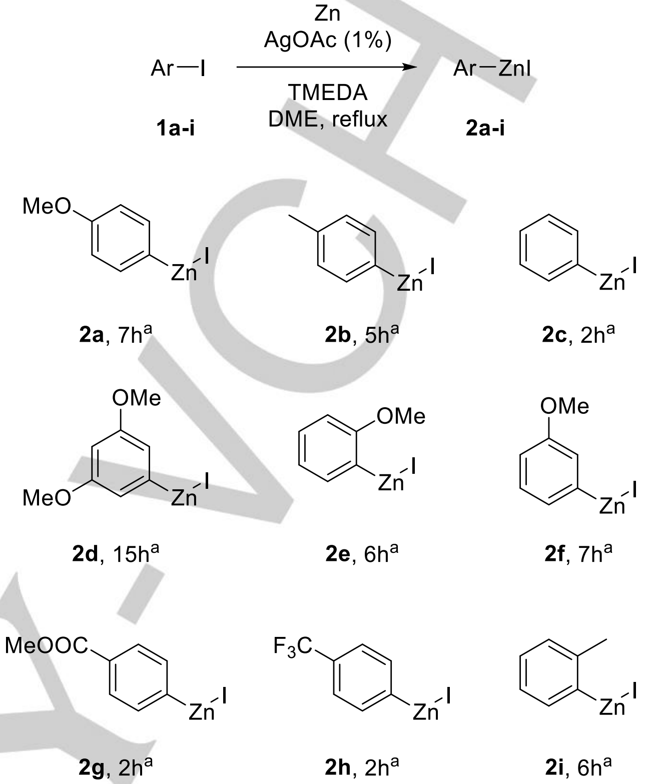
Table 2. Effect of various conditions with zinc-silver “in situ” activation



	Catalyst	Amine (eqs.)	Time	Conv. [a]
1 [b]	AgOAc	TMEDA (1)	7 h	> 99 %
2 [c]	AgOAc	TMEDA (1)	24 h	< 5 %
3 [d]	AgOAc	TMEDA (1)	7 h	> 99 %
4	$AgNO_3$	TMEDA (1)	24 h	< 1 %
5	AgOTs	TMEDA (1)	24 h	20 %
6	$Cu(OAc)_2$	TMEDA (1)	24 h	< 1 %
7		TMEDA (1)	24 h	< 1 %
8	AgOAc	TMEDA (0.2)	7 h	19 %
9	AgOAc	TMEDA (0.1)	7 h	11 %
10	AgOAc		65 h	96 %
11 [e]	AgOAc	TMEDA (1)	7 h [f]	> 99 %
12 [e]	AgOAc	TMEDA (0.2)	7 h	30 %
13	AgOAc	DABCO (1)	15 h	43 %
14	AgOAc	DABCO (0.2)	15 h	21 %
15 [e]	AgOAc		40 h	97 %
16 [g]	AgOAc		15 h	20 %

* Zn activated with Me_3SiCl. [a] GC conversion (determined by analysis on hydrolyzed aliquots). [b] Zn of various particle size: 4, 8, 9.8 and 63 µm. [c] Particle size 600-800 µm. [d] Zn was not activated with Me_3SiCl. [e] 1.5 equivalents of LiCl were added. [f] Time required to provide complete conversion. [e] 1.5 equivalents of $MgBr_2$ were added

Once the best reaction conditions had been found, the procedure was used to obtain arylzinc iodides having different structure (Scheme 1) to test the general applicability of the procedure. As expected, electron-rich aryl iodides underwent oxidative additions in longer times with respect to electron-poor substrates (Scheme 1, compounds **2a** and **2g**).

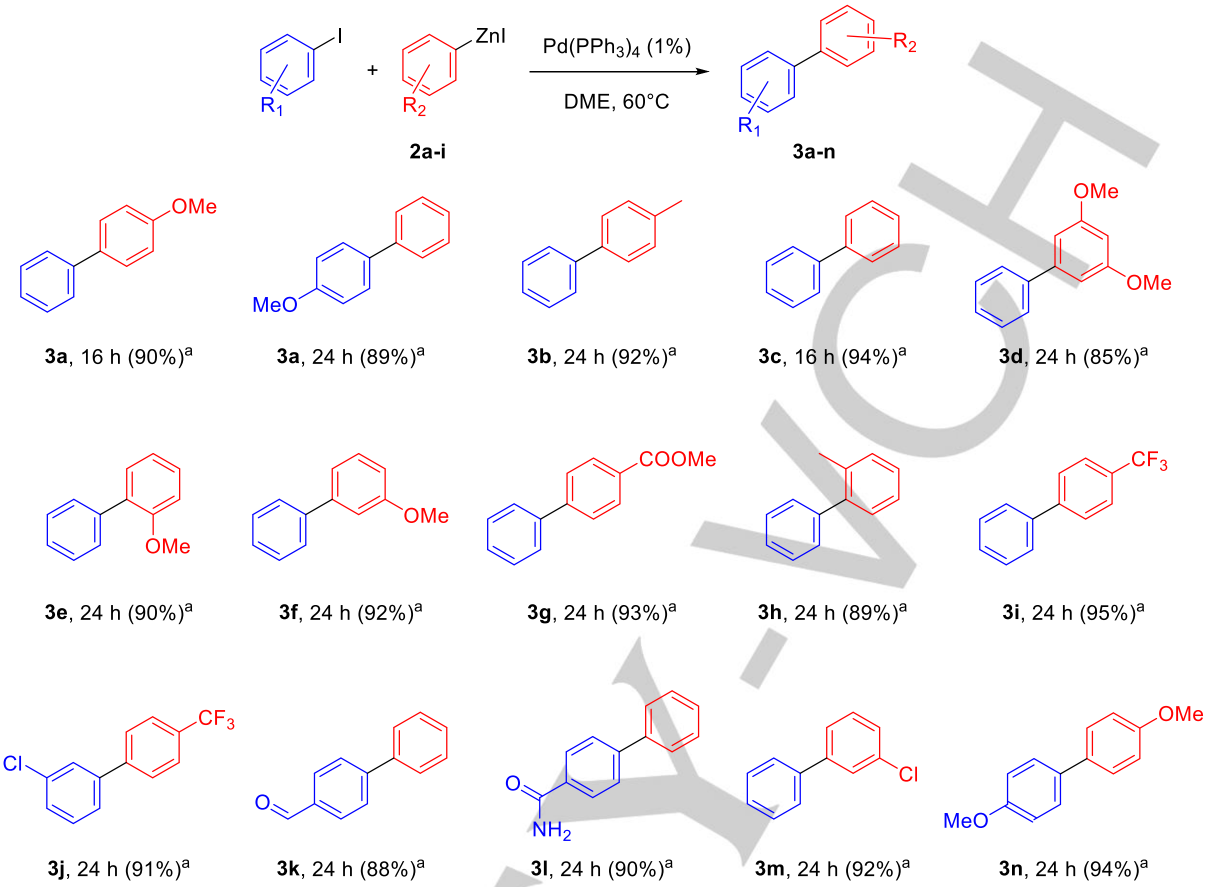


[a] Time required for complete conversion (determined by analysis on hydrolyzed aliquots)

Scheme 1. Preparation of various arylzinc iodides.

However, it is noteworthy that also highly electron-rich iodides provided the corresponding arylzinc halides in acceptable reaction times (Scheme 1, compound **2d**).

To prove the potential of the organozinc halides thus obtained we decided to test their reactivity in Negishi cross-coupling reactions under mild conditions (Scheme 2). In all these examples high yields have been achieved in reasonable reaction times, either with electron-rich or electron-poor donors. Even sensitive functional groups like aldehydes and primary amides are well-tolerated.



[a] Isolated yield after flash chromatography

Scheme 2. Negishi cross-coupling.

Conclusions

In conclusion, we have shown that a catalytic amount of silver acetate activates normal zinc powder of different particle size, allowing oxidative metalation of various aryl iodides, even electron-rich, under straightforward conditions and short reaction times. The effect of several additives and their synergies has been verified. Arylzinc iodides obtained with the protocol described have been used in Negishi cross-coupling reactions with aryl iodides bearing various functional groups to give the corresponding biaryls in high yields.

Experimental Section

General Information

All reactions were performed in flame dried glassware under argon atmosphere. Solutions and liquids were transferred with hypodermic syringes. Ethereal solvents were refluxed over sodium-potassium alloy / benzophenone and distilled before the use. Liquid tertiary amines were refluxed over calcium hydride and distilled before the use. All other liquid reagents were distilled and dried over molecular sieves. Lithium chloride, magnesium bromide and zinc were flame dried under high vacuum before the use. $Pd(PPh_3)_4$ was freshly prepared according to the literature procedure.[21] All other solid reagents were dried under high vacuum before the use. GLC analyses were performed on a Varian CP-3800 GC instrument with a Split/Splitless injector a FID detector and a Varian CP-8400 Autosampler, equipped with an Agilent HP5 FSOT column (30 m x 0.25 mm i.d. x 0.25 µm). GLC/MS analyses were performed using an Agilent 6890 Network GC system equipped with an Agilent HP5-MS FSOT column (30 m x 0.25 mm i.d. x 0.25 µm) interfaced with an Agilent 5973 Network Mass Selective Detector. ^1H and ^{13}C NMR spectra were recorded on a Bruker DRX 400 MHz spectrometer. Purifications were performed by flash chromatography on silica-gel (40-63 µm, Sigma-Aldrich) employing ethyl acetate – hexane mixtures as eluents.

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Zinc was purchased from Sigma-Aldrich: powders of 4, 8 and 9.8 µm (Aldrich, product number 209988), lot numbers, respectively: SHBG9711V, SHBG1827V and SHBF7346V; zinc of 63 µm (EMD Millipore, product number 1.08774.1000) lot number K48461974645, zinc of 600-800 µm (Aldrich, product number 243469) lot number MKBZ3503V.

General procedure for the preparation of ArZnX by direct insertion

In a typical procedure, zinc powder (490 mg, 7.5 mmol) was flame dried under high vacuum (10^{-2} mbar) and cooled under argon atmosphere in a round-bottomed flask equipped with reflux condenser and magnetic stirrer; silver acetate (8.4 mg, 0.05 mmol) was then added under argon and the mixture dried again under high vacuum; the flask was refilled with argon and anhydrous DME (5 mL) and chlorotrimethylsilane (15 µL, 0.075 mmol) were added. The mixture was stirred and heated at the reflux for 5 minutes. After cooling, anhydrous TMEDA (750 µL, 5 mmol) and the aromatic iodide (5 mmol) were added.

The mixture was heated at the reflux and stirred for the time needed for each substrate (see Scheme 1), then was cooled, settled down and the supernatant was used in the following coupling reaction. To verify full conversion, an aliquot of the supernatant solution was quenched with NH_4Cl and extracted with Et_2O and another aliquot was iodolyzed and extracted with Et_2O, both the samples were analysed by GLC.

General procedure for the Negishi cross-coupling reactions

In a typical procedure, $Pd(PPh_3)_4$ (38 mg, 0.033 mmol) was dried under high vacuum (10^{-2} mbar) in a round-bottomed flask equipped with magnetic stirrer; the flask was refilled with argon and the aromatic iodide (3.3 mmol) and the organozinc halide solution (5 mL) were added. The mixture was heated at 60 °C and stirred for the time needed for each substrate (see Scheme 2) before being quenched with NH_4Cl and extracted with Et_2O (3 x 10 mL). Flash chromatography purification on silica gel with hexane or hexane / ethyl acetate mixtures afforded the pure compounds.

*4-methoxy-1,1'-biphenyl (**3a**)*

Purification by flash chromatography (SiO_2, hexane / ethyl acetate 98:2) afforded the product as a white solid: by using iodobenzene (**1c**) as acceptor and 4-methoxyphenylzinc iodide (**2a**) as donor 549 mg (2.98 mmol, 90%) were obtained, by using 4-iodoanisole (**1a**) as acceptor and phenylzinc iodide (**2c**) as donor 543 mg (2.95 mmol 89%) were obtained.

The NMR data agree with the literature.[22]

^{1}H NMR (401 MHz, $CDCl_3$) δ 7.57 (t, J = 8.5 Hz, 4H), 7.44 (t, J = 7.6 Hz, 2H), 7.32 (t, J = 7.3 Hz, 1H), 7.00 (d, J = 8.7 Hz, 2H), 3.87 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 141.0, 133.9, 128.9, 128.3, 126.9, 126.8, 114.3, 55.5.

*4-methyl-1,1'-biphenyl (**3b**)*

Purification by flash chromatography (SiO_2, hexane) afforded the product as a white solid: by using iodobenzene (**1c**) as acceptor and 4-methylphenylzinc iodide (**2b**) as donor 511 mg (3.04 mmol, 92%) were obtained.

The NMR data agree with the literature.[22]

^{1}H NMR (401 MHz, $CDCl_3$) δ 7.69 (d, J = 7.4 Hz, 2H), 7.61 (d, J = 8.1 Hz, 2H), 7.53 (t, J = 7.6 Hz, 2H), 7.43 (t, J = 7.4 Hz, 1H), 7.35 (d, J = 7.9 Hz, 2H), 2.50 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.3, 138.5, 137.1, 129.6, 128.9, 128.8, 127.1, 127.1, 21.2.

*1,1'-biphenyl (**3c**)*

Purification by flash chromatography (SiO_2, hexane) afforded the product as a white solid: by using iodobenzene (**1c**) as acceptor and phenylzinc iodide (**2c**) as donor 479 mg (3.11 mmol, 94%) were obtained.

The NMR data agree with the literature.[22]

^{1}H NMR (401 MHz, $CDCl_3$) δ 7.64 (d, J = 7.5 Hz, 4H), 7.48 (t, J = 7.5 Hz, 4H), 7.39 (t, J = 7.3 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.4, 128.9, 127.4, 127.3.

*3,5-dimethoxy-1,1'-biphenyl (**3d**)*

Purification by flash chromatography (SiO_2, hexane / ethyl acetate 96:4) afforded the product as a white solid: by using iodobenzene (**1c**) as acceptor and 3,5-dimethoxyphenylzinc iodide (**2d**) as donor 600 mg (2.80 mmol, 85%) were obtained.

The NMR data agree with the literature.[23]

^{1}H NMR (401 MHz, $CDCl_3$) δ 7.60 (d, J = 7.4 Hz, 2H), 7.45 (t, J = 7.5 Hz, 2H), 7.37 (t, J = 7.3 Hz, 1H), 6.76 (d, J = 2.2 Hz, 2H), 6.49 (t, J = 2.2 Hz, 1H), 3.86 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2, 143.6, 141.3, 128.8, 127.7, 127.3, 105.6, 99.4, 55.5.

*2-methoxy-1,1'-biphenyl (**3e**)*

Purification by flash chromatography (SiO_2, hexane / ethyl acetate 98:2) afforded the product as a white solid: by using iodobenzene (**1c**) as acceptor and 2-methoxyphenylzinc iodide (**2e**) as donor 545 mg (2.96 mmol, 90%) were obtained.

The NMR data agree with the literature.[22]

^{1}H NMR (401 MHz, $CDCl_3$) δ 7.55 (d, J = 7.6 Hz, 2H), 7.43 (t, J = 7.5 Hz, 2H), 7.34 (t, J = 6.5 Hz, 3H), 7.09 – 6.96 (m, 2H), 3.83 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.6, 138.7, 131.0, 130.9, 129.7, 128.7, 128.1, 127.0, 121.0, 111.4, 55.7.

*3-methoxy-1,1'-biphenyl (**3f**)*

Purification by flash chromatography (SiO_2, hexane / ethyl acetate 98:2) afforded the product as a white solid: by using iodobenzene (**1c**) as acceptor and 3-methoxyphenylzinc iodide (**2f**) as donor 559 mg (3.03 mmol, 92%) were obtained.

The NMR data agree with the literature.[22]

^{1}H NMR (401 MHz, $CDCl_3$) δ 7.63 (d, J = 7.5 Hz, 2H), 7.47 (t, J = 7.6 Hz, 2H), 7.39 (dt, J = 7.9, 4.3 Hz, 2H), 7.22 (d, J = 7.7 Hz, 1H), 7.17 (s, 1H), 6.94 (dd, J = 8.2, 2.1 Hz, 1H), 3.89 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.1, 142.9, 141.2, 129.9, 128.9, 127.5, 127.3, 119.8, 113.0, 112.8, 55.4.

*methyl [1,1'-biphenyl]-4-carboxylate (**3g**)*

Purification by flash chromatography (SiO_2, hexane / ethyl acetate 98:2) afforded the product as a white solid: by using iodobenzene (**1c**) as acceptor and (4-

(methoxycarbonyl)phenyl)zinc iodide (**2g**) as donor 649 mg (3.09 mmol, 93%) were obtained.
The NMR data agree with the literature.[22]
^{1}H NMR (401 MHz, $CDCl_3$) δ 8.12 (d, J = 8.4 Hz, 2H), 7.65 (m, J = 14.9, 7.8 Hz, 4H), 7.47 (t, J = 7.4 Hz, 2H), 7.40 (t, J = 7.3 Hz, 1H), 3.95 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 145.8, 140.1, 130.2, 129.0, 128.3, 127.4, 127.2, 52.2.

*2-methyl-1,1'-biphenyl (**3h**)*
Purification by flash chromatography (SiO_2, hexane) afforded the product as a white solid: by using iodobenzene (**1c**) as acceptor and 2-methylphenylzinc iodide (**2i**) as donor 494 mg (2.94 mmol, 89%) were obtained.
The NMR data agree with the literature.[22]
^{1}H NMR (401 MHz, $CDCl_3$) δ 7.54 – 7.42 (m, 2H), 7.43 – 7.34 (m, 3H), 7.36 – 7.23 (m, 4H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.10, 142.07, 135.46, 130.43, 129.92, 129.32, 128.19, 127.37, 126.88, 125.89, 20.60.

*4-(trifluoromethyl)-1,1'-biphenyl (**3i**)*
Purification by flash chromatography (SiO_2, hexane / ethyl acetate 99:1) afforded the product as a white solid: by using iodobenzene (**1c**) as acceptor and 4-(trifluoromethyl)phenylzinc iodide (**2h**) as donor 695 mg (3.13 mmol, 95%) were obtained.
The NMR data agree with the literature.[22]
^{1}H NMR (401 MHz, $CDCl_3$) δ 7.71 (s, 4H), 7.62 (d, 2H), 7.49 (t, 2H), 7.45 – 7.40 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.88, 139.91, 129.13, 128.33, 127.56, 127.42, 125.85 (q, $J_{C\text{-}F}$ = 3.7 Hz).

*3-chloro-4'-(trifluoromethyl)-1,1'-biphenyl (**3j**)*
Purification by flash chromatography (SiO_2, hexane / ethyl acetate 99:1) afforded the product as a white solid: by using 1-chloro-3-iodobenzene (**1j**) as acceptor and 4-(trifluoromethyl)phenylzinc iodide (**2h**) as donor 770 mg (3.00 mmol, 91%) were obtained.
The NMR data agree with the literature.[24]
^{1}H NMR (401 MHz, $CDCl_3$) δ 7.78 – 7.63 (m, 4H), 7.59 (s, 1H), 7.52 – 7.33 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.41, 141.68, 135.08, 130.36, 128.35, 127.55, 125.99 (q, $J_{C\text{-}F}$ = 3.7 Hz), 125.56.

*[1,1'-biphenyl]-4-carbaldehyde (**3k**)*
Purification by flash chromatography (SiO_2, hexane / ethyl acetate 90:10) afforded the product as a white solid: by using 4-iodobenzaldehyde (**1k**) as acceptor and phenylzinc iodide (**2c**) as donor 528 mg (2.90 mmol, 88%) were obtained.
The NMR data agree with the literature.[25]
^{1}H NMR (401 MHz, $CDCl_3$) δ 10.06 (s, 1H), 7.95 (d, *J* = 8.2 Hz, 2H), 7.75 (d, *J* = 8.2 Hz, 2H), 7.64 (d, *J* = 7.4 Hz, 2H), 7.46 (dt, *J* = 25.7, 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.98, 147.25, 139.78, 135.28, 130.35, 129.11, 128.57, 127.76, 127.45.

*[1,1'-biphenyl]-4-carboxamide (**3l**)*
The crude was quenched with HCl (1M). Purification by flash chromatography (SiO_2, hexane / ethyl acetate 20:80) afforded the product as a white solid: by using 4-iodobenzamide (**1l**) as acceptor and phenylzinc iodide (**2c**) as donor 585 mg (2.97 mmol, 90%) were obtained.
The NMR data agree with the literature.[26]
^{1}H NMR (401 MHz, DMSO-d_6) δ 8.05 (s, 1H), 7.99 (d, *J* = 8.4 Hz, 2H), 7.79 – 7.70 (m, 4H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.45 – 7.36 (m, 2H). ^{13}C NMR (101 MHz, DMSO) δ 167.58, 142.76, 139.23, 133.10, 129.02, 128.18, 128.01, 126.87, 126.45.

*3-chloro-1,1'-biphenyl (**3m**)*
Purification by flash chromatography (SiO_2, hexane) afforded the product as a white solid: by using 1-chloro-3-iodobenzene (**1j**) as acceptor and phenylzinc iodide (**2c**) as donor 577 mg (3.06 mmol, 92%) were obtained.
The NMR data agree with the literature.[24]
^{1}H NMR (401 MHz, $CDCl_3$) δ 7.62 – 7.54 (m, 3H), 7.51 – 7.42 (m, 3H), 7.43 – 7.30 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.21, 139.95, 134.78, 130.11, 129.03, 127.99, 127.43, 127.39, 127.25, 125.43.

*4,4'-dimethoxy-1,1'-biphenyl (**3n**)*
Purification by flash chromatography (SiO_2, hexane / ethyl acetate 98:2) afforded the product as a white solid: by using 4-iodoanisole (**1a**) as acceptor and 4-methoxyphenylzinc iodide (**2a**) as donor 670 mg (3.13 mmol, 94%) were obtained.
The NMR data agree with the literature.[27]
^{1}H NMR (401 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.7 Hz, 4H), 6.98 (d, *J* = 8.7 Hz, 4H), 3.86 (s, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.82, 133.59, 127.84, 114.29, 55.46.

Acknowledgements

This work was supported by the University of Pisa.

Keywords: metalation • zinc • synthetic methods • C-C coupling • biaryls

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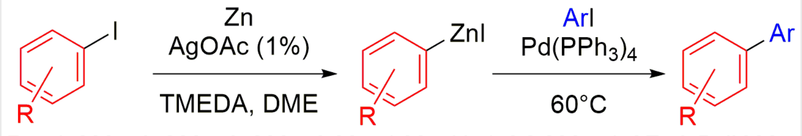

R = 4-OMe, 2-OMe, 3-OMe, 2-Me, 4-Me, H, 4-COOMe, 4-CF_3 3,5-diOMe

A catalytic amount of silver acetate efficiently promotes direct insertion of zinc metal into aryl iodides, having different structure, in ethereal solvent. Electron-rich substrates also rapidly undergo oxidative metalation. The arylzinc iodides formed give Negishi coupling products under mild reaction conditions.

Organozinc halides preparation

Gianluca Casotti, Anna Iuliano, Adriano Carpita*

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Arylzinc Halides by Silver Catalyzed Zinc Insertion to Aryl Iodides