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A Convenient Preparation of Functionalized Arylzinc Compounds by the Reaction of Zinc/Silver-Graphite with Aryl Iodides.

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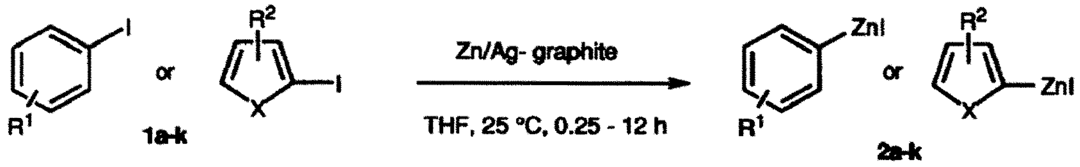
***Summary:** Aryl- and hetero-aryl iodides react under very mild conditions (THF, 25 °C) with a Zn(Ag) couple deposited on graphite leading to the corresponding zinc reagents in excellent yields. In the presence of CuCN·2LiCl or catalytic amounts of Pd(0), these unsaturated zinc species can be acylated, allylated or coupled with iodoalkenes.*

Organozinc compounds are useful organometallic intermediates for organic synthesis.[1] Their high functional group tolerance associated with their excellent reactivity toward electrophiles in the presence of stoichiometric amounts of copper salts, catalytic amounts of titanium[2] or palladium[3] complexes makes them a unique class of nucleophilic reagents. Whereas alkylzinc iodides, allylic and benzylic zinc halides are readily prepared by the direct insertion of zinc dust,[1] the preparation of arylzinc iodides is less straightforward. It requires either the use of polar solvents[4] or the use of highly activated zinc prepared by the lithium napthalenide reduction of zinc chloride in THF .[5] This last method, although providing an extremely reactive zinc requires dry box techniques and the removal of 2 mol-equivalents of naphthalene which complicates the workup procedures. We report herein a new convenient generation of a reactive zinc powder using C_8K and its application for the preparation of a variety of arylzinc halides under mild conditions and in good yields.



R^1 = COPh, CN, COOEt, F, CF_3, OMe; R^2 = CN, COR; X = N, S

> 80 %

The addition of a THF slurry of zinc chloride containing 10 mol % of silver acetate to the graphite intercalation compound C_8K[6](25 °C, 1 h) produces a suspension of activated zinc on graphite[7] which rapidly reacts with various aromatic and heteroaromatic iodides **1a-k** (THF, 25 °C, 0.25 - 12 h) providing the corresponding zinc reagents **2** in over 80% yield as judged by the iodolysis of reaction aliquots (Table 1). The presence of an electron withdrawing-substituent on the aromatic ring or the presence of an heteroatom at the α-position to the carbon-iodine bond considerably facilitates the zinc insertion. Thus the iodides **1d-e**, **1g**, **1i-k** are completely converted into the corresponding zinc reagents within 20 min at 25 °C. Interestingly, the presence of two cyano groups allows zinc insertion into the *carbon-bromine* bond of 2-bromo-4,5-dicyano-1-methylimidazole **1h**,[8] although in this case a reaction time of ca. 24 h is required. The resulting arylzinc halides can be transmetalated with the THF soluble copper salt CuCN·2LiCl (-20 to 0 °C, 5 min)[9] and reacted subsequently with an allylic halide such as ethyl 2-(bromomethyl)acrylate[10] (-60 to -10 °C, 0.5 h; see products **3h**, **3j**, **3m** of Table 1) or acylated by the reaction with an acid chloride (-20 to 0 °C, ca. 10 h; see products **3a-b**, **3d-g**, **3l** of Table 1) in good yields (68 - 93%). A palladium catalyzed reaction with aromatic bromides or alkenyl iodides can be efficiently performed by using bis(benzylideneacetone)palladium(0)[11] (Pd(dba)$_2$; 5 mol %) and triphenylphosphine (20 mol %; 25 °C, ca. 12 h) as a catalyst leading to the desired mixed coupling products **3i**, **3k** and **3n** (Table 1) in 41 - 78% yield.

In summary, activated zinc produced by the reduction of $ZnCl_2$ with C_8K in the presence of AgOAc (10 mol %)[7c] in THF inserts smoothly into aromatic and heteroaromatic iodides producing the corresponding organozinc reagents which react after a transmetalation with CuCN·2LiCl with allylic halides and acid chlorides and in the presence of catalytic amounts of (Pd(dba)$_2$ with alkenyl iodides and aryl bromides leading to a wide range of polyfunctional aromatic molecules. Compared to previous methods, this zinc activation is very convenient and gives efficient insertion reactions under mild conditions. Applications to the preparation of more complex zincated nucleosides and related biologically relevant reagents are currently underway in our laboratories.[12]

Table 1. Preparation of aromatic and heteroaromatic zinc halides **2** by the insertion of activated zinc to the corresponding halides and their copper or palladium- catalyzed reaction with electrophiles leading to the polyfunctional products **3a-n**.

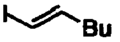
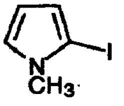
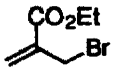
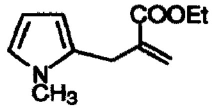
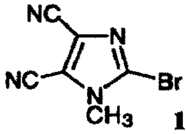
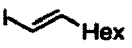
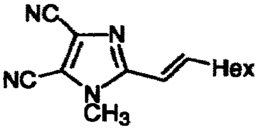
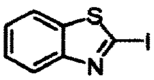
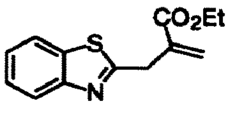
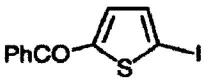
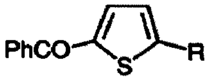
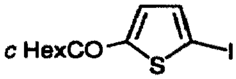
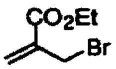
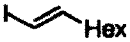
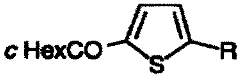
Aromatic halide **1**	Electrophile	Product **3**	Yield(%)[a]
p NC-C_6H_4-I **1a**	benzoyl chloride	*p*NC-C_6H_4-COPh **3a**	89
p EtOOC-C_6H_4-I **1b**	acetyl chloride	*p*EtOOC-C_6H_4-COMe **3b**	68
	 Bu	*E* -*p*EtOOC-C_6H_4-CH=CH-Bu **3c**	81
F_5C_6-I **1c**	benzoyl chloride	F_5C_6-COPh **3d**	89
o CF_3-C_6H_4-I **1d**	benzoyl chloride	*o* CF_3-C_6H_4-COPh **3e**	80

Table 1 (continued)

Aromatic halide 1	Electrophile	Product 3	Yield(%)[a]
o $PhCOC_6H_4$-I **1e**	benzoyl chloride	*o* $PhCOC_6H_4$-COPh **3f**	80
p$MeOC_6H_4$-I **1f**	acetyl chloride	*p*$MeOC_6H_4$-COMe **3g**	80
 **1g**		 **3h**	85
 **1h**		 **3i**	41
 **1i**		 **3j**	81
 **1j**	*p* bromobenzonitrile benzoyl chloride	 **3k** : R = *p* CN-Ph **3l** : R = CO-Ph	74 76
 **1k**	 	 **3m** : $CH_2C(CO_2Et)CH_2$ **3n** : *E* - 1- hexenyl	93 78

[a] All yields refer to isolated yields of analytically pure products showing the expected spectroscopic data (^1H NMR, ^{13}C NMR, IR and MS).

Acknowledgments

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12 *Experimental Procedure.*

A 100 mL three-neck flask equipped with an argon inlet, a glass stopper and a septum cap was charged with graphite (1.65 g, 137 mmol) and heated to 160 °C. Potassium (0.67 g, 17.1 mmol) was added in small pieces under a steady stream of argon with vigorous stirring resulting in the formation of bronze colored C_8K within 15 min as a fine powder. A second three-neck flask was charged with zinc chloride (1.17 g, 8.6 mmol) which was dried at 140 °C for 2 h on high vacuum. After cooling to 25 °C, THF (10 mL) was added affording a solution to which AgOAc (140 mg, 0.85 mmol) was added. The resulting heterogeneous slurry was transferred at 25 °C with a syringe to the previously prepared C_8K while vigourously stirring (alternatively a mixture of $ZnCl_2$ and AgOAc can be added as a solid to a suspension of C_8K in THF). A slighly exothermic reaction occurs. After 1 h stirring 5-benzoyl-2-iodothiophene **1j** (900 mg, 2.9 mmol) was added as a solid. GC analysis of an iodolyzed and hydrolyzed reaction aliquot indicates that a complete insertion has occurred after 15 min reaction time. The excess zinc/silver-graphite was allowed to settle for 1-2 h and the supernatant solution of the zinc reagent **2j** was transferred to a THF (2 mL) solution of CuCN (0.26 g, 3.0 mmol) and LiCl (0.24 g, 5.7 mmol) at -60 °C. The solution was allowed to warm to -10 °C and stirred for 0.5 h before cooling back to -60 °C. Benzoyl chloride (0.30 g, 2.14 mmol, 0.75 equiv.) was added and the reaction mixture was warmed to -10 °C and stirred ca. 14 h at -10 °C and worked up in the usual way. The crude light brown residue was purified by flash chromatography (hexane-ether 10:1, then hexane-chloroform 5:1) affording 470 mg (76% yield) of the analytically pure 2,5-dibenzoylthiophene **3l**.

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