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LETTERS

Direct Homocoupling of Aryl Halides Catalyzed by Palladium

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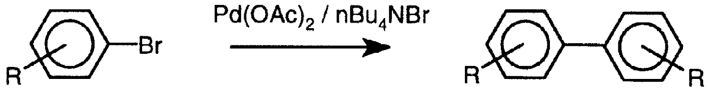
Abstract: Symmetrical functionnalized biaryls are obtained in good yield via homocoupling of aryl halides, bromo or iodo ones, using the combination of $Pd(OAc)_2$ and nBu_4NBr as catalyst system. © 1998 Published by Elsevier Science Ltd. All rights reserved.

The most usual way to prepare symmetrical biaryls is the Ullmann synthesis[1] which consists in the condensation of two molecules of aryl halides in the presence of copper. The main drawback of this method is the requirement of equimolar amounts of copper. More recently, the preparation of biaryls by Pd(0)-catalyzed cross-coupling of aryl halides with arylstannanes[2], arylboronic acids[3] and arylzinc[4] derivatives has been used. These methodologies are efficient but they require stoichiometric amounts of the organometallic intermediate. Other methods based on either a Ni(0)/Zn[5] coupling or a Pd/formiate[6] coupling have been developped for the synthesis of bipyridines but such methodologies require over-stoichiometric amounts of metal and/or give rise to only moderate yield. Recently, we showed the efficiency of $Pd(OAc)_2$ / nBu_4NBr mixture as a catalyst precursor for the direct arylation of activated thiophenes by iodoaryls[7]. However, symmetrical biphenyls resulting from a competitive reaction may also be produced. Thus, we investigate now the ability of the $Pd(OAc)_2$ / nBu_4NBr mixture to catalyze an Ullmann like cross-coupling of various aryl halides (Scheme 1, Table 1).



Scheme 1 : Cross-coupling of aryl halides catalyzed by Palladium

In every case, the solvent is dimethylformamide. It can include isopropanol in order to accelerate the regeneration of Pd(0) (methods A or C) and / or water (methods A or B) if the substrate is not really sensitive to C-Br bond reduction[8] or hydrolysis (nitrile). In that way, the homocoupling reaction can be effective with iodo- or bromoaryls substituted by various groups such as cyano, nitro, aldehyde, methoxy or halogen (Cl, F). Bipyridines have also been successfully synthetised by this method (entries 7 and 8). In all cases good to excellent isolated yields are obtained after a reaction time of a few hours to two days.

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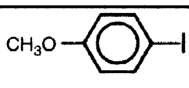
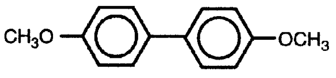
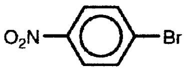
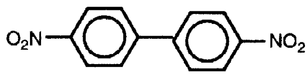
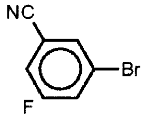
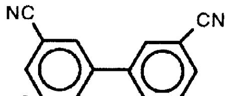
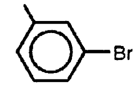
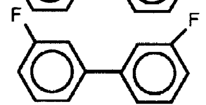
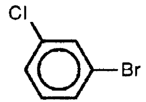
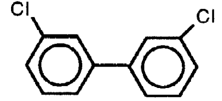
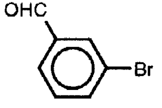
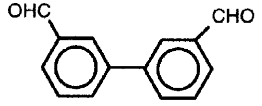
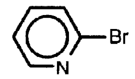
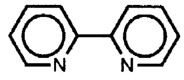
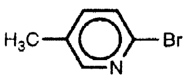
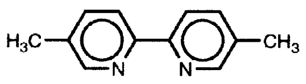
Table 1 : Cross-coupling of various aryl halides catalyzed by palladium

Entry	Substrate **1**	Reaction^a conditions	Time (hours)	Product **2**	Ref^b	Yield (%)^c
1		A	8		9	81
2		A	7		10	85
3		C	23		11	(64)57
4		A	30		13	86
5		B	32		12	(83)42
6		D	50		13	(67)60
7		A	45		5	(100)92
8		A	45		14	(100)95

a) All coupling reactions were carried out at 115°C with 8.10^{-3} mole (1 equiv.) of aryl halide and a $Pd(OAc)_2$ / nBu_4NBr (0.05/0.5) mixture. Method A: solvent DMF/H_2O (0.9 mL/0.35 mL), isopropanol (1.25 mL) and K_2CO_3 (1 equiv.). Method B: solvent DMF/H_2O (0.9 mL/0.35 mL) and K_2CO_3 (1 equiv.). Method C: solvent DMF (0.9 mL), isopropanol (1.25 mL) and NEt_3 (3 equiv.). Method D: solvent DMF (0.9 mL) and NEt_3 (1 equiv.).

b) All products **2** have been fully characterized and comparisons with already published data are in agreement.

c) Isolated yield based on amount of **1** used. The value in parentheses indicates GLC yield.

In summary, we have found that the association of palladium acetate and tetra-n-butylammonium bromide is a powerful and convenient catalyst for Ullmann type reactions. This method allows the preparation of functionalized biphenyls or bipyridines directly from the corresponding halide with catalytic amounts of a metal derivative.

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