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Preparation of unsymmetrical biaryls via palladium-catalyzed coupling reaction of aryl halides

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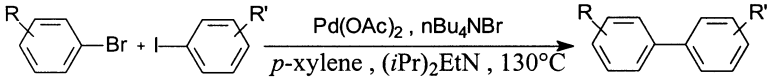
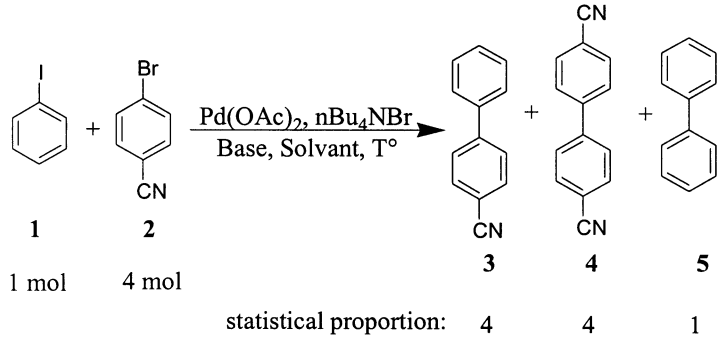
Abstract—The synthesis of unsymmetrical biaryls is achieved using $Pd(OAc)_2$ as the catalyst. A great variety of aryl halides having electron withdrawing and electron donating functional groups in *para*, *meta* and *ortho* positions have been successfully coupled.

The synthesis of unsymmetrical biaryls is of the utmost importance in organic synthesis in view of their numerous potential applications.[1–4] The preparation of unsymmetrical biaryls is generally allowed by the Stille[5] reaction, Suzuki[6] reaction and Grignard cross-coupling reaction.[7] These methods, despite of their efficiency, involve the use of a stoichiometric amount of organometallic intermediate. Otherwise, there are efforts to develop catalytic methods for Stille[8] and Suzuki[9] reactions where catalytic amounts of tin and borane have been used. The Ullmann cross-coupling reaction between two different aryl halides has been already reported.[10] The reaction of nitro-substituted iodobenzoates with an excess of iodonaphthalene was used as a key step for the synthesis of poly-nitrobenzanthrones. But this method needs a stoichiometric amount of copper and high reaction temperature. In order to improve the yields and to avoid the homocoupling reaction, a very slow addition of nitro-substituted iodobenzoates to the bulk of iodonaphthalene was necessary. The yields depend on the position of the nitro substituents, the selectivity of the reaction of iodonaphthalene was considerably lowered in the presence of nitro group at the *meta* position compared to *para* position. Recently, the palladium-catalyzed homocoupling reaction of aryl halides has received much attention.[11–15] We have recently developed the synthesis of symmetrical biaryls and biheterocycles from aryl halides using $Pd(OAc)_2$ as the catalyst (Scheme 1). We have already shown that the palladium acetate in the presence of base is a useful catalytic system



Scheme 1. Cross-coupling of aryl bromide with aryl iodide catalyzed by palladium.



Scheme 2. Cross-coupling of 4-bromobenzonitrile with iodobenzene catalyzed by palladium.

Keywords: aryl halides; biaryls; Ullmann reaction; cross-coupling reaction; pyridines; thiophenes.
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Table 1. Unsymmetrical coupling of 4-bromobenzonitrile with iodobenzene, the effect of the reaction conditions

Entry[a]	Base	Solvent[b,c] (temperature, °C)	Ratio, nBu$_4$NBr[d]/ ArI (mol)	Time (h)	Ratio ArBr/ ArI (mol)	Conv.[e] (%)	Ar–Ar′ yield[f] GC (%)	Ar–Ar yield[g] GC (%)
1	K_2CO_3	DMF/H_2O (110)	1/1	24	2/1	19	17	2
2	(iPr)$_2$EtN	Toluene (105)	1/1	24	2/1	33	27	9
3	(i-Pr)$_2$EtN	Toluene (105)	0.5/1	30	2/1	35	20	15
4	(i-Pr)$_2$EtN	Toluene (105)	2/1	24	2/1	30	22	8
5	(i-Pr)$_2$EtN	Toluene (105)	1/1	46	3/1	96	66	30
6	(i-Pr)$_2$EtN	Toluene (105)	1/1	48	4/1	98	82	16
7	(i-Pr)$_2$EtN	p-Xylene (130)	1/1	24	4/1	100	95 (35)[h]	5

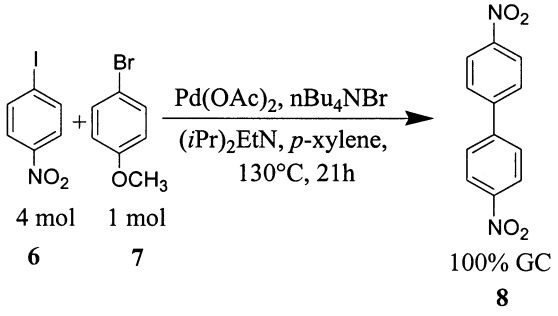
[a] See general procedure.
[b] HPLC grade solvent.
[c] Reactions carried out at 115°C in DMF, 105°C in toluene and 130°C in p-xylene.
[d] Tetrabutylammonium bromide 98% from Lancaster.
[e] Calculated for aryl iodide.
[f] Determined by GC.
[g] The homocoupling product of iodobenzene.
[h] The value in parentheses indicates isolated yield.

for the homocoupling reaction of aryl halides.[16–19] We report herein the effectiveness of $Pd(OAc)_2$ as a catalyst for the direct preparation of unsymmetrical biaryls.[20] Aryl bromides react with aryl iodides to form unsymmetrical biaryls with marked selectivity. The reaction is exemplified by the coupling of aryl, thiophene and pyridine bromides with aryl, naphthalene and phenanthrene iodides.

1. Study of reaction conditions

The coupling reaction of iodobenzene **1** with 4-bromobenzonitrile **2** was examined in order to optimize the reaction conditions (Scheme 2).

The influence of various parameters on substrate conversion and product selectivity was studied. Table 1 gives the reaction conditions and results for the cross-coupling reaction of 4-bromobenzonitrile **2** with iodobenzene **1** catalyzed by palladium. In previous work, we found that the diisopropylethylamine is more efficient and selective than K_2CO_3 as a base for the coupling reaction (entries 1 and 2, Table 1). Tetrabutylammonium bromide also influences the reaction. It probably plays a role not only as phase transfer agent but also in regeneration of zerovalent palladium catalyst.[21] When the amount of the quaternary ammonium decreases (entry 3, Table 1), a loss of selectivity towards the unsymmetrical product is observed. The selectivity also falls down when an excess of quaternary ammonium is used (entry 4, Table 1). It can be seen that the yield of the unsymmetrical compound remarkably increases when the amount of 4-bromobenzonitrile **2** increases (entries 5 and 6, Table 1), and that the homocoupling of iodobenzene **1** becomes less competitive. The unsymmetrical coupling is predominant at higher temperature (entry 7, Table 1). In all cases, the homocoupling product from 4-bromobenzonitrile was observed in low yields.

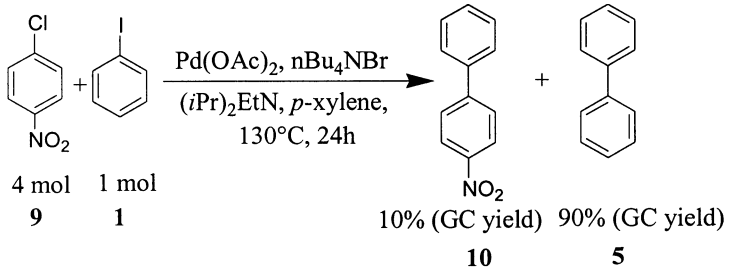


Scheme 3. Coupling of 4-nitroiodobenzene with 4-methoxybromobenzene catalyzed by palladium.

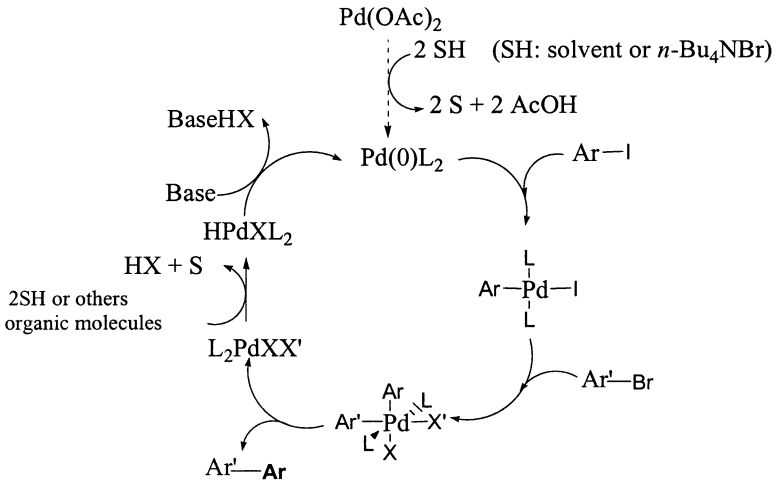
Finally, it is important to note that the selectivity obtained for unsymmetrical products is much higher than the selectivity expected if only statistical coupling occurs. Therefore, the mechanism of this reaction should induce a preference for the reaction of the unactivated iodoaryl and the activated bromoaryl.

2. Substituent effect

The reaction works with aryl bromides having electron withdrawing group and aryl iodides having electron donating



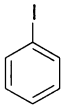
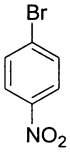
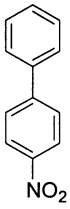
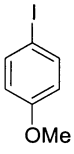
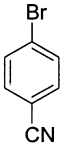
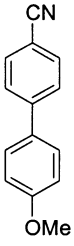
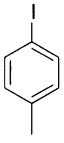
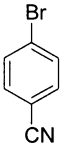
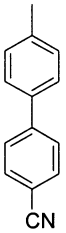
Scheme 4. Cross-coupling of 4-nitrochlorobenzene with 4-iodobenzene catalyzed by palladium.



Scheme 5. Postulated mechanism.

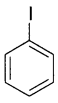
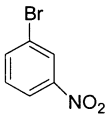
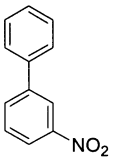
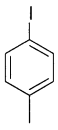
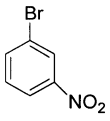
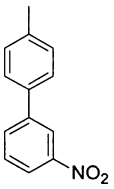
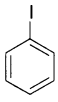
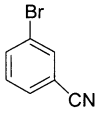
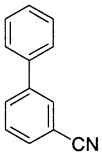
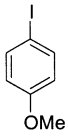
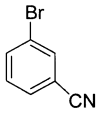
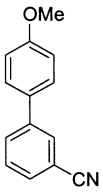
groups. The electron withdrawing groups accelerate the oxidative addition of aryl halides onto palladium. The coupling reaction does not occur with aryl iodides having an electron-withdrawing group. The oxidative addition of 4-nitroiodobenzene **6** onto palladium is fast and leads to a symmetrical product. In contrast, the oxidative addition of 4-methoxybromobenzene **7** onto palladium does not occur under our reaction conditions (Scheme 3).

Table 2. Unsymmetrical coupling of aryl iodides and *para*-aryl bromides catalyzed by palladium

Entry	Ar-I	Ar-Br	Time (h)	Product	Ref[a]	Chemical yield[b] Ar-Ar′	Homocoupling yield[c] GC (%)
1			**24**	 **10**	27	**79 (32)**	**21**
2			**24**	 **11**	28	**79 (19)**	**14**
3			**24**	 **12**	4	**78 (53)**	**18**

[a] All products have been characterized and are in agreement with published data.
[b] The value in parentheses indicates isolated yield.
[c] The homocoupling product of aryl iodide.

Table 3. Unsymmetrical coupling of various aryl iodides and *meta*-aryl bromides catalyzed by palladium

Entry	Ar-I	Ar-Br	Time (h)	Product	Ref[a]	Chemical yield[b] Ar-Ar′	Homocoupling yield[c] GC (%)
1			**7**	 **13**	29	**100 (20)**	-
2			**70**	 **14**	30	**83 (10)**	**9**
3			**112**	 **15**	30	**79 (21)**	**21**
4			**112**	 **16**	31	**71 (16)**	**29**

[a] All products have been characterized and are in agreement with published data.
[b] The value in parentheses indicates isolated yield.
[c] The homocoupling product of aryl iodide.

3. Postulated mechanism

The mechanism of the reaction is still unknown and will be the subject of further studies. In the light of our results, some hypotheses could be induced. The $Pd(OAc)_2$/nBu$_4$NBr association leads to an active species Pd(0). The Pd(0) species is probably formed at the start of the reaction, the $Pd(OAc)_2$ is known for its oxidative characteristic.[22] The mechanism involves a fast oxidative addition of aryl iodide onto palladium. We checked the possibility that the second step could be a nucleophilic substitution, especially if substituent effect is taken into account. In order to verify this hypothesis, the coupling reaction of aryl iodide and aryl chloride has been performed. The chloride is a good leaving group for nucleophilic substitution reaction and the presence of an electron-withdrawing group must facilitate this type of reaction. However, under our reaction conditions, chlorinated aromatics reacted very slowly due to the poor reactivity in the oxidative addition step onto palladium. The symmetrical coupling from aryl iodide derivative is predominant (Scheme 4).

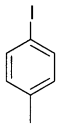
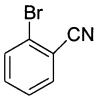
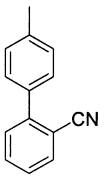
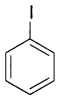
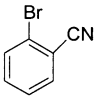
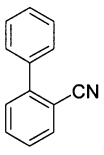
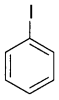
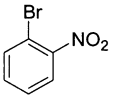
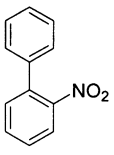
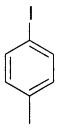
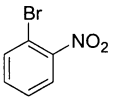
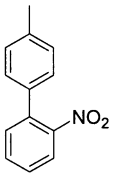
Consequently, the reaction does not involve a nucleophilic substitution. The second step could therefore involve another oxidative addition of aryl bromide forming a Pd(IV) species. This type of palladium complexes has already been characterized.[23–25] A reductive elimination leads to the coupling product. The L_2PdX_2 species is then reduced in HPdX species, and finally the Pd(0) is regenerated in the presence of a base[21] (Scheme 5).

In conclusion, the formation of unsymmetrical biaryls should be due to the difference of reactivity of the two aryl halides towards the oxidative addition onto palladium species but the preference for the unsymmetrical coupling remains unexplained.

4. Unsymmetrical coupling of various aryl iodides with *para* and *meta*-aryl bromides

Unsymmetrical *para* and *meta* substituted biaryls were obtained in good selectivity using $Pd(OAc)_2$ as the catalyst. The *para* 4-nitrobiphenyl was obtained in good selectivity (entry 1, Table 3). The synthesis of 4-cyano-4′-methoxybiphenyl (entry 2, Table 2) and 4-cyano-4′-methylbiphenyl

Table 4. Unsymmetrical coupling of aryl iodides and *ortho*-aryl bromides catalyzed by palladium

Entry	Ar-I	Ar-Br	Time (h)	Product	Ref[a]	Chemical yield[b] Ar-Ar′	Homocoupling yield[c] GC (%)
1			**63**	 **17**	32	**86 (33)**	**14**
2			**43**	 **18**	27	**85 (21)**	**15**
4			**50**	 **19**	33	**100 (12)**	**-**
5			**69**	 **20**	28	**96 (45)**	**4**

[a] All products have been characterized and are in agreement with published data.
[b] The value in parentheses indicates isolated yield.
[c] The homocoupling product of aryl iodide.

(entry 3, Table 1) led to a good selectivity in comparison to the competitive symmetrical Ullmann reaction. The main limitation of such method lies in the purification. Both the excess of the brominated substrate and the symmetrical biphenyl are difficult to separate in small-scale synthesis. On the other hand, few volatile dehalogenation products from aryl iodide were probably formed and were lost during the reaction. Only traces of anisol, nitrobenzene and benzonitrile have been observed.

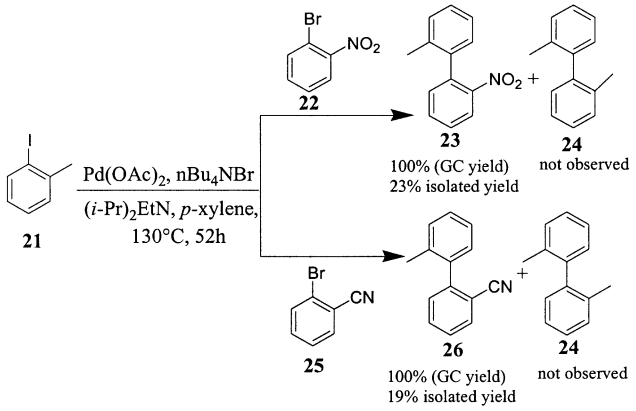
A number of substituted biaryls have been successfully prepared with $Pd(OAc)_2$ catalyzed coupling reaction of aryl iodides and substituted *meta* aryl bromides (Table 3). In the case of 3-bromonitrobenzene (entry 1, Table 2), the homocoupling of aryl iodide is not allowed. The unsymmetrical compound was obtained with an excellent selectivity. The reaction of aryl iodide with 3-bromobenzonitrile also led to unsymmetrical biaryl with good selectivity (entry 3, Table 2). Unsymmetrical biaryls having donor and acceptor groups have been synthesized with marked selectivity (entries 2 and 4, Table 3). This type of compounds have largely been used in the preparation of materials for nonlinear optic.[4]

5. Unsymmetrical coupling of aryl iodides with *ortho*-aryl bromides

The use of *ortho* substituted derivatives obviously introduces a steric hindrance, which have been evaluated by using 2-cyano and 2-nitro bromobenzene.

Using $Pd(OAc)_2$ as the catalyst, the coupling reaction has enjoyed considerable success in the synthesis of several *ortho* substituted unsymmetrical biaryls (Table 4). The coupling reaction of 2-bromobenzonitrile with 4-iodotoluene (entry 1, Table 4) led to unsymmetrical biaryls with good selectivity. In the case of 2-bromonitrobenzene (entries 3 and 4, Table 4), the homocoupling reaction of aryl iodide is nearly nil. The unsymmetrical biaryls, 2-nitrobiphenyl and 2-nitro-4′-methylbiphenyl were synthesized with excellent selectivity.

As previously described in the case of symmetrical coupling reactions, the palladium catalytic system appears to be only weakly sensitive to steric constraints. The cross-coupling reaction of *ortho* substituted aryl iodides and *ortho* substituted aryl bromides has also been successfully



Scheme 6. Cross-coupling of 2-iodotoluene with 2-bromonitrobenzene and 2-bromobenzonitrile, respectively.

accomplished with excellent selectivity (Scheme 6). The synthesis of 2-nitro-2′-methylbiphenyl[34] and 2-cyano-2′-methylbiphenyl[35] were carried out in spite of steric and electronic effects. The homocoupling reaction of 2-iodotoluene was not observed.

6. Unsymmetrical coupling of naphthalene iodide with *para* and *meta*-aryl bromides

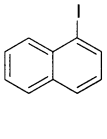
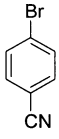
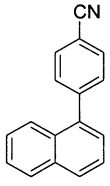
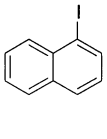
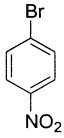
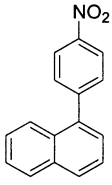
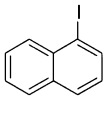
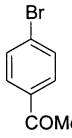
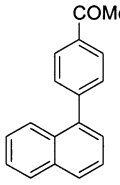
The 1-iodonaphthalene was tested in the cross-coupling reaction and gave the unsymmetrical product. The coupling reaction of 1-iodonaphthalene with 4-bromobenzonitrile led to 1-(4-cyanophenyl)naphthalene (entry 1, Table 5). In the case of 4-bromonitrobenzene and 4-bromoacetophenone, only the unsymmetrical cross-coupling is observed. Even in this case, very little amount of naphthalene was observed. This indicated that the reduction reaction of the iodinated reagent is not the major limitation for the cross-coupling reaction.

The cross-coupling reaction of *meta* substituted aryl bromides with 1-iodonaphthalene was also carried out in good selectivity (Table 6). In the case of 3-bromonitrobenzene (entry 1, Table 6), there is no homocoupling reaction of 1-iodonaphthalene, but the maximum yield obtained was 84% (GC yield) after 120 h.

7. Unsymmetrical coupling of naphthalene iodide and *ortho*-aryl bromides

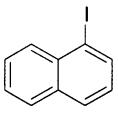
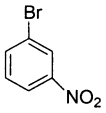
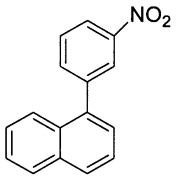
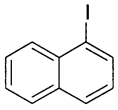
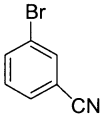
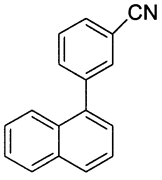
We have also evaluated the efficiency of $Pd(OAc)_2$ as the catalyst of the unsymmetrical coupling reaction in *ortho* position. The coupling reaction of 1-iodonaphthalene with 2-iodobenzonitrile and 2-bromonitrobenzene (Scheme 7) leads to a clear selectivity for the unsymmetrical product,[39,40] but the conversion remains low. These results show the steric limitation of this method.

Table 5. Unsymmetrical coupling of iodonaphthalene and *para*-aryl bromides catalyzed by palladium

Entry	Ar-I	Ar-Br	Time (h)	Product	Ref[a]	Chemical yield[b] Ar-Ar′	Homocoupling yield[c] GC (%)
1			**24**	 **27**	36	**87 (20)**	**13**
2			**24**	 **28**	37	**100 (35)**	-
3			**24**	 **29**	36	**100 (22)**	-

[a] All products have been characterized and are in agreement with published data.
[b] The value in parentheses indicates isolated yield.
[c] The homocoupling product of aryl iodide.

Table 6. Unsymmetrical coupling of iodonaphthalene and *meta*-aryl bromides catalyzed by palladium

Entry	Ar-I	Ar-Br	Time (h)	Product	Ref[a]	Chemical yield[b] Ar-Ar′	Homocoupling yield[c] GC (%)
1			**120**	 **30**	37	**84 (19)**	**-**
2			**28**	 **31**	38	**84 (12)**	**16**

[a] All products have been characterized and are in agreement with published data.
[b] The value in parentheses indicates isolated yield.
[c] The homocoupling product of aryl iodide.

8. Unsymmetrical coupling of aryl iodides and thiophene bromides

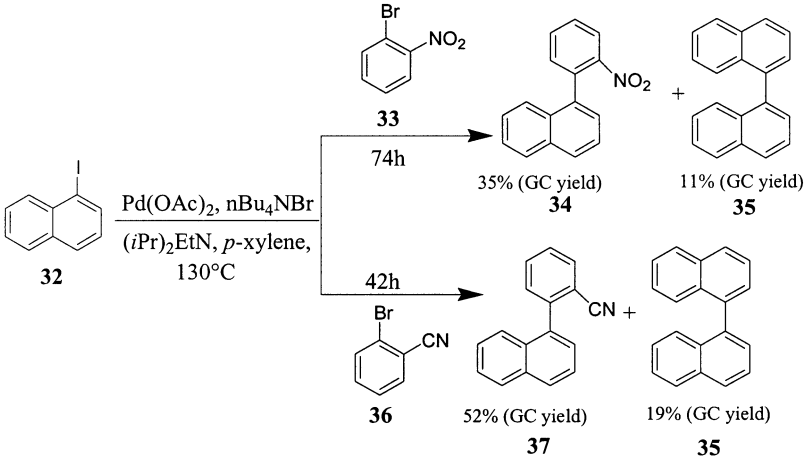
We have already shown the direct arylation of activated thiophenes by iodoaryls using a Heck type reaction with a mixture of $Pd(OAc)_2$ and phase transfer agent as the catalytic system.[41–43] We describe here the synthesis of unsymmetrical heterobiaryls possessing one thiophene moiety and one carbocyclic moiety (Table 7). Initially, the synthesis of 2-phenyl-5-acetylthiophene (entry 1, Table 7) was carried out using 4 mol of 2-bromo-5-acetylthiophene (ArI/2-bromo-5-acetylthiophene: 1/4). The reaction did not go to completion (60% GC yield). Performing the reaction using 2 mol of 2-bromo-5-acetylthiophene increased the selectivity toward the unsymmetrical coupling product (entry 2, Table 7). The cross-coupling reaction of 2-bromo-5-aldehydethiophene with iodobenzene led to the unsymmetrical product in good selectivity (entry 3, Table 7). The homocoupling of iodobenzene is not observed in this case. The last method appears to present several advantages in the case of thiophene derivatives over the aryl halide cross-coupling.

9. The synthesis of 2-phenylpyridine

Among the several reaction conditions examined for the synthesis of 2-phenylpyridine,[45] the best result was obtained using diisopropylethylamine as base in *p*-xylene at 130°C (Scheme 8), but the conversion remains low, which might be due to the poisoning of the Pd catalyst by nitrogen-containing reactants. We are currently investigating such reactions in more detail.

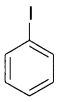
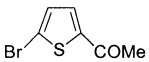
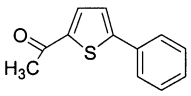
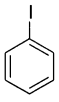
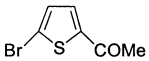
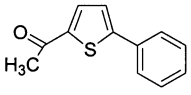
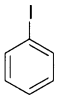
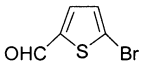
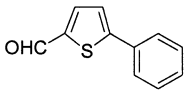
10. Conclusion

We have developed a catalytic synthesis of unsymmetrically

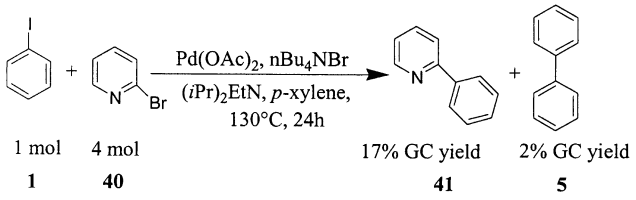


Scheme 7. Unsymmetrical coupling of iodonaphthalene and *ortho*-aryl bromides catalyzed by palladium.

Table 7. Unsymmetrical coupling of aryl iodide and thiophene bromides catalyzed by palladium

Entry	Ar-I	Ar-Br	Time (h)	Product	Ref[a]	Chemical yield[b] Ar-Ar′	Homocoupling yield[c] GC (%)
1			100	 **38**	44	**60 (16)**	-
2			118	 **38**	44	**92 (16)**	-
3			103	 **39**	44	**88 (15)**	-

[a] All products have been characterized and are in agreement with published data.
[b] The value in parentheses indicates isolated yield.
[c] The homocoupling product of aryl iodide.



Scheme 8. The cross-coupling reaction of iodobenzene with 2-bromopyridine catalyzed by palladium.

substituted biaryls using $Pd(OAc)_2$ as catalyst. The coupling reaction is compatible with various groups such as methoxy, cyano, and nitro. This method allows the formation of unsymmetrical biaryls from aryl, naphthalene iodides with or without electron donating groups with aryl, thiophene bromides with electron withdrawing groups. This procedure is efficient even with substituents in *ortho* position. The unsymmetrical biaryl yields considerably depend on the nature of substituents. The cross-coupling reaction does not occur in the presence of an electron-withdrawing group on the aryl iodide. This method suffers from several drawbacks. First of all, the use of excess of one of the reagents (generally the brominated aryl). This induces difficulties in separation, which decrease the isolated yield, at least in small-scale synthesis. On the other hand, results described in this paper offer new insight on the mechanism of aryl cross-coupling.

11. Experimental

11.1. General procedure

A mixture of diisopropylethylamine (8 mmol), palladium acetate (0.4 mmol), tetra-*n*-butylammonium bromide (8 mmol), aryl iodide (8 mmol) and aryl bromide (32 mmol) in *p*-xylene (5 ml) was stirred under nitrogen atmosphere. The mixture was maintained at 130°C for a period of time indicated in the tables. After cooling to room temperature, water and ether were added. The organic phase was washed with water and dried over $MgSO_4$. The solvent was evaporated under vacuum. The mixture was distilled under reduced pressure to eliminate unreacted aryl bromide, then the unsymmetrical product was purified either by thin layer chromatography or through a silica gel column.

11.1.1. Preparation of 4-cyanobiphenyl[26] 3. According to the procedure described above; yield: 35%; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 7.56 (m, 1H2, 1H3, 1H5, 1H6); 7.2–7.5 (m, 1H2′, 1H3′, 1H4′, 1H5′, 1H6′); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 140.9 (C1); 136.6 (C1′); 132.5 (C5, C3); 127.4 (C6′, C2′, C4′); 128.1 (C6, C2); 129 (C5′, C3′); 116.5 (C7); 111.4 (C4); MS, *m*/*z* (%): 175 (100) [M^+]; 180 (100) [M+1]; 164 (22); 152 (100); 140 (56); 126 (80); 113 (51); 102 (32).

11.1.2. Preparation of 4-nitrobiphenyl[27] 10. According to the procedure described above; yield: 32%; mp 114°C; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 8.35 (d, 1H5, 1H3, J= 8.9 Hz); 7.75 (m, 1H6, 1H2); 7.63 (m, 1H6′, 1H2′); 7.49 (m, 1H3′, 1H4′, 1H5′); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 147.5 (C4); 147 (C1); 138.7 (C1′); 129.1 (C3′, C5′); 128.8 (C2, C6); 127.7 (C2′, C6′); 127.3 (C4′); 124 (C3, C5); MS, *m*/*z* (%): 199 (100) [M^+]; 200 (8) [M+1]; 152 (85); 151 (30); 169 (28); 141 (20); 76 (15).

11.1.3. Preparation of 4′-methoxy-4-cyanobiphenyl[28] 11. According to the procedure described above; yield: 19%; mp 104°C; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 7.67–7.74 (m, 1H2, 1H3, 1H5, 1H6); 7.54 (d, 1H6′, 1H2′, J=9 Hz); 7.0 (d, 1H3′, 1H5′, J=9 Hz); 3.87 (s, 3H7′); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 160.2 (C4′); 145 (C1); 132.4 (C5, C3); 131.4 (C1′); 128.2 (C6′, C2′); 127 (C6, C2);

118.9 (C7); 114.5 (C5′, C3′); 110 (C4); 55.3 (C7′); MS, *m/z* (%): 209 (100) [M$^+$]; 210 (10) [M+1]; 194 (35); 166 (37); 140 (22).

11.1.4. Preparation of 4′-methyl-4-cyanobiphenyl[4] 12. According to the procedure described above; yield: 52%; mp 110–111°C; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 7.73 (d, 1H3, 1H5, J=8.2 Hz); 7.66 (d, 1H6, 1H2, J=8.2 Hz); 7.50 (d, 1H2′, 1H6′, J=8 Hz); 7.32 (d, 1H3′, 1H5′, J=8 Hz); 2.41 (s, 3H7′); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 145.6 (C1); 40.5 (C4); 138.8 (C4′); 136.3 (C1′); 132.6 (C5, C3); 129.9 (C5′, C3′); 127.5 (C6, C2); 127.1 (C6′, C2′); 111.9 (C7); 21.2 (C7′); MS, *m/z* (%): 193 (100) [M$^+$]; 192 (40); 140 (4); 165 (28); 91 (10); 82 (6); 75 (3).

11.1.5. Preparation of 3-nitrobiphenyl[29] 13. According to the procedure described above; yield: 20%; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 8.47 (t, 1H2, J=2 Hz); 7.94 (m, 1H4, 1H5); 7.64 (m, 1H6, 1H2′, 1H6′); 7.51 (m, 1H4′, 1H5′, 1H3′); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 148.9 (C3); 137.5 (C1); 136.6 (C1′); 133.5 (C6); 129.9 (C5); 129 (C5′, C3′); 127.4 (C6′, C2′, C4′); 122.5 (C2, C4); MS, *m/z* (%): 199 (80) [M$^+$]; 152 (100); 153 (52); 76 (15); 141 (12); 51 (6).

11.1.6. Preparation of 3-nitro-4′-methyl-biphenyl[30] 14. According to the procedure described above; yield: 10%; mp 76–77°C; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 7.80 (dd, 1H2, J=8, 2.5 Hz); 7.57 (td, 1H4, J=8, 2.5, 2.5 Hz); 7.41 (m, 1H5, 1H6); 7.19 (m, 1H2′, 1H3′, 1H6′, 1H5′); 2.37 (s, 3H7′); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 142.8 (C3); 138.6 (C1′); 136.17 (C4′); 135.8 (C1); 134.8 (C6); 130.7 (C5); 129.9 (C3′); 129.6 (C5′); 127 (C6′, C2′); 121.7 (C2, C4); 21 (C7′). MS, *m/z* (%): 213 (82) [M$^+$]; 214 (100) [M+1]; 152 (65); 139 (15); 63 (12).

11.1.7. Preparation of 3-cyanobiphenyl[30] 15. According to the procedure described above; yield: 21%; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 7.58–7.48 (m, 1H2, 1H4, 1H5, 1H6); 7.33–7.45 (m, 1H2′, 1H3′, 1H4′, 1H5′, 1H6′); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 138.9 (C1); 136.1 (C1′); 130.7 (C6); 129.6 (C5′, C3′); 129.1 (C5); 128.4 (C2, C4); 127.1 (C4′, C6′, C2′), 116 (C7); 113 (C3); MS, *m/z* (%): 179 (100) [M$^+$]; 180 (27); 152 (16); 76 (25); 63 (10); 51 (7).

11.1.8. Preparation of 3-cyano-4′-methoxybiphenyl[31] 16. According to the procedure described above; yield: 16%. ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 7.7 (m, 1H2, 1H4, 1H5, 1H6); 7.5 (m, 1H2′, 1H6′); 7.0 (m, 1H5′, 1H3′); 3.87 (s, 3H7′); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 160 (C4′); 142 (C1); 131.3 (C1′); 130.2 (C6); 130 (C5); 129.6 (C2, C4); 128.2 (C6′, C2′); 119 (C7); 114 (C5′, C3′); 112.9 (C3); 56 (C7′). MS, *m/z* (%): 209 (100) [M$^+$]; 210 (15) [M+1]; 194 (42); 166 (62); 140 (38); 113 (8); 63 (6).

11.1.9. Preparation of 2-cyano-4′-methylbiphenyl[32] 17. According to the procedure described above; yield: 33%; mp 48–49°C; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 7.40–7.20 (m, 1H3, 1H4, 1H5, 1H6, 1H2′, 1H3′, 1H5′, 1H6′); 2.26 (s, 3H7′); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 145.2 (C1′); 138.7 (C4′); 135.3 (C1); 133.6 (C5); 132.5 (C3); 130 (C5′); 129.4 (C3′); 128.6 (C4, C6); 127.2 (C6′, C2′); 118.9 (C7); 111.1 (C2); 21.4 (C7′); MS, *m/z* (%): 193 (100) [M$^+$]; 192 (15); 165 (10); 82 (7); 51 (6).

11.1.10. Preparation of 2-cyanobiphenyl[27] 18. According to the procedure described above; yield: 21%; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 7.78 (ddd, 1H5, J=7.7, 1.2, 0.5 Hz); 7.66 (dd, 1H6, J=7.6, 1.4 Hz); 7.59 (d, 1H2′, 1H6′, J=7.1 Hz); 7.53 (ddd, 1H5′, J=7.7, 1.4, 0.5 Hz); 7.50 (m, 1H3′, 1H4′, 1H5′); 7.45 (dd, 1H4, J=7.5, 5.1 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 145.4 (C1′); 138.1 (C1); 133.7 (C5); 132.8 (C3, C5′); 128.6 (C3′); 128.6 (C6′, C2′, C4′); 127.5 (C4, C6); 118.7 (C7); 112.2 (C2); MS, *m/z* (%): 179 (100) [M$^+$]; 178 (27) [M+1]; 177 (15); 152 (17); 151 (16); 76 (15).

11.1.11. Preparation of 2-nitrobiphenyl[33] 19. According to the procedure described above; yield: 12%; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 7.48 (dd, 1H3, J=1.1, 8.1 Hz); 7.62–7.58 (m, 1H4); 7.48–7.45 (m, 1H5); 7.43 (dd, 1H6, J=1.4, 7.5 Hz); 7.41–7.39 (m, 1H2′, 1H3′, 1H6′, 1H5′); 7.32–7.29 (m, 1H4′); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 147.3 (C2); 137.4 (C1′); 136.4 (C5); 130 (C1); 128.7 (C5′); 128.3 (C3′); 128.2 (C4); 128.1 (C6); 127.9 (C6′, C2′, C4′); 124.1 (C3); MS, *m/z* (%): 199 (18) [M$^+$]; 182 (45); 171 (60); 152 (100); 143 (32); 127 (20); 115 (92); 102 (11).

11.1.12. Preparation of 2-nitro-4′-methylbiphenyl[28] 20. According to the procedure described above; yield: 45%; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 7.80 (dd, 1H3, J=8, 2.5 Hz); 7.57 (dd, 1H4, J=8, 2.5 Hz); 7.41 (m, 1H5, 1H6); 7.19 (m, 1H2′, 1H3′, 1H5′, 1H6′); 2.3 (s, 3H7′); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 147.3 (C2); 136.6 (C4′); 133.6 (C1′); 135.1 (C5); 131.7 (C1); 129.7 (C5′, C3′); 128.3 (C4, C6); 127.3 (C2′, C6′); 124.1 (C3); 20.9 (C7′); MS, *m/z* (%): 213 (42) [M$^+$]; 196 (48); 165 (100); 152 (82); 129 (72); 115 (95); 77 (68); 63 (75); 51 (72).

11.1.13. Preparation of 2-cyano-6′-methylbiphenyl[25] 23. According to the procedure described above; yield: 19%; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 7.79–7.6 (m, 1H3, 1H4, 1H5, 1H6); 7.50–7.23 (m, 1H2′, 1H3′, 1H4′, 1H5′); 2.31 (s, 3H7′); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 145.9 (C1); 138.1 (C1′); 135.7 (C6′); 132.8 (C5); 132.4 (C3); 129.4 (C5′); 128.7 (C4, C6); 127.5 (C2′, C4′); 125.9 (C3′); 118.1 (C7); 112.9 (C2); 18.8 (C7′); MS, *m/z* (%): 193 (100) [M$^+$]; 165 (65); 166 (22); 152 (4); 139 (5); 115 (4).

11.1.14. Preparation of 2-nitro-6′-methylbiphenyl[34] 26. According to the procedure described above; yield: 23%; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 7.95 (dd, 1H5, J=8.0, 8.0 Hz); 7.67–7.47 (m, 1H3, 1H4); 7.35–7.08 (m, 1H5′, 1H4′, 1H3′, 1H2′, 1H6); 2.10 (s, 3H7′); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 147.3 (C2); 137.3 (C1′); 136.6 (C6′); 135.1 (C5); 131.7 (C1); 129.7 (C5′); 128.3 (C4, C6); 127.3 (C4′, C2′); 126 (C3′); 124.1 (C3); 14.3 (C7′); MS, *m/z* (%): 213 (13) [M$^+$]; 196 (50); 183 (55); 165 (100); 152 (30); 115 (25); 82 (16); 51 (8).

11.1.15. Preparation of 1-(4-cyanophenyl)-naphthalene[36] 27. According to the procedure described above, yield: 20%; mp 76–77°C; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm):

7.97–7.4 (m, 11H); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 145.7 (C1′); 138.2 (C1); 133.8 (C10); 132.1 (C5′, C3′); 131 (C9); 128.8 (C2′, C6′); 128.5 (C5, C8); 126.6 (C4); 126 (C3); 125.3 (C6, C7); 125.2 (C2); 116.5 (C7′); 111.22 (C4′); MS, *m/z* (%): 225 (100) [M^+]; 230 (17) [M+1]; 201 (16); 111 (22); 97 (40); 83 (47); 71 (60); 57 (60); 43 (40).

11.1.16. Preparation of 1-(4-nitrophenyl)-naphthalene[37] **28.** According to the procedure described above; yield: 35%; mp 133°C; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 8.4 (d, 1H5′, 1H3′, *J*=8.5 Hz); 7.59 (d, 1H2′, 1H6′, *J*=8.5 Hz); 7.87 (d, 1H2, *J*=8 Hz); 7.7 (d, 1H3, 1H4, *J*=8.5 Hz); 7.67–7.57 (m, 1H8); 7.57–7.52 (m, 1H7); 7.52–7.49 (m, 1H6); 7.4 (m, 1H5); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 148.4 (C4′); 137.7 (C1); 134.6 (C1′); 133.2 (C10); 131.4 (C9); 129.5 (C7, C6); 129.4 (C6′, C2′); 129.2 (C4); 128.4 (C3); 125.7 (C5, C8); 125.5 (C2); 123.6 (C5′, C3′). MS, *m/z* (%): 249 (100) [M^+]; 202 (100); 189 (10); 152 (8); 101 (27); 88 (15); 75 (6).

11.1.17. Preparation of 1-(4-acetylphenyl)-naphthalene[36] **29.** According to the procedure described above; yield: 22%; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 8.1 (d, 1H3′, 1H5′, *J*=8 Hz); 8.0–7.87 (m, 1H6′, 1H2′, 1H2); 7.8–7.4 (m, 1H3, 1H4, 1H5, 1H6, 1H7, 1H8); 2.56 (s, 3H8′); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 197.8 (C7′); 145.8 (C1′); 136.3 (C4′); 136 (C1); 135.8 (C5′, C3′); 133.8 (C10); 131.2 (C9); 130.3 (C5, C8); 129.2 (C4); 126.4 (C3); 126 (C2); 125.5 (C6′, C2′); 125.3 (C6, C7); 26.6 (C8′); MS, *m/z* (%): 246 (75) [M^+]; 231 (100); 202 (80); 101 (43); 115 (15); 43 (13); 152 (5).

11.1.18. Preparation of 1-(3-nitrophenyl)-naphthalene[37] **30.** According to the procedure described above; yield: 19%; mp 131–132°C; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 8.40–8.26 (m, 1H2′, 1H4′, 1H6′, 1H5′); 8.0–7.47 (m, 1H2, 1H3, 1H4, 1H5, 1H6, 1H7, 1H8); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 148.9 (C3′); 136.4 (C1, C1′); 134.1 (C10); 133.3 (C6′, C9); 129.9 (C5′); 128.2 (C5, C8); 126.8 (C4); 126.4 (C3); 125.8 (C6, C7); 124.9 (C2); 122.3 (C4′); 122.2 (C2′); MS, *m/z* (%): 249 (80) [M^+]; 250 (18) [M+1]; 202 (100); 101 (28); 88 (12); 75 (8).

11.1.19. Preparation of 1-(3-cyanophenyl)-naphthalene[38] **31.** According to the procedure described above; yield: 12%; mp 76–77°C; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 8.04–7.4 (m, 11H); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 137.7 (C1′); 136.1 (C1), 134.5 (C10); 133.5 (C9); 131.1 (C6′); 130.9 (C4′, C2′); 129.2 (C5′); 129 (C4); 127.5 (C8, C5); 127.1 (C3); 126.4 (C6, C7); 125.1 (C2); 116.5 (C7′); 112.6 (C3′); MS, *m/z* (%): 229 (95) [M^+]; 228 (100); 201 (30); 114 (18); 88 (10); 51 (6).

11.1.20. Preparation of 1-(2-nitrophenyl)-naphthalene[39] **34.** According to the procedure described above; GC yield: 35%; MS, *m/z* (%): 249 (100) [M^+]; 232 (47); 220 (33); 202 (97); 204 (77); 189 (30); 165 (25); 101 (41).

11.1.21. Preparation of 1-(2-cyanophenyl)-naphthalene[40] **37.** According to the procedure described above; GC yield: 52%; MS, *m/z* (%): 229 (100) [M^+]; 202 (25); 101 (22); 88 (4); 50 (4).

11.1.22. Preparation of 5-acetyl-2-phenylthiophene[44] **38.** According to the procedure described above; yield: 16%; mp 115°C; MS: ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 7.69–7.64 (m, 1H2′, 1H3′, 1H4′, 1H5′, 1H6′); 7.45 (d, 1H4, *J*=4 Hz); 7.34 (d, 1H3, *J*=4 Hz); 2.57 (s, 3H7); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 190.6 (C6); 152.8 (C2); 143.2 (C5); 133.5 (C1′); 133.4 (C4); 129.1 (C3); 129 (C4′); 126.3 (C3′, C5′); 123.9 (C2′, C6′); 26.6 (C7); MS, *m/z* (%): 202 (60) [M^+]; 187 (100); 115 (78); 89 (10).

11.1.23. Preparation of 2-phenyl-5-carboxaldehydethiophene[44] **39.** According to the procedure described above; yield: 15%; mp 93–93.5°C; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 9.89 (s, 1H6); 7.71 (d, 1H4, *J*=4 Hz); 7.7–7.6 (m, 1H2′, 1H3′, 1H4′, 1H5′, 1H6′); 7.39 (d, 1H3, *J*=4 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 182.8 (C6); 154.3 (C2); 154.5 (C5); 137.4 (C4); 133.9 (C1′); 129.4 (C3′); 129.2 (C5′); 126.4 (C4′); 124.1 (C2′, C6′); 122.7 (C3); MS, *m/z* (%): 188 (100) [M^+]; 187 (95); 115 (80); 89 (15); 51 (10).

11.1.24. Preparation of 2-phenylpyridine[45] **41.** According to the procedure described above; GC yield: 17% MS, *m/z* (%): 155 (100) [M^+]; 156 (10) [M+1]; 152 (8); 128 (20); 127 (60); 115 (8); 102 (15).

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