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$Pd(OAc)_2$ catalyzed homocoupling of arenediazonium salts in ionic liquids: synthesis of symmetrical biaryls

Hemantkumar M. Savanur [a], Rajesh G. Kalkhambkar [a,*], Kenneth K. Laali [b,*]

[a] Department of Chemistry, Karnatak University's Karnatak Science College, Dharwad, Karnatak 580001, India
[b] Department of Chemistry, University of North Florida, 1 UNF Drive, Jacksonville, FL 32224, USA

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ABSTRACT

A facile, high yielding, and simple method for the synthesis of a library of symmetrical biaryls by homocoupling of arenediazonium salts is reported, employing catalytic amounts of $Pd(OAc)_2$ and the readily available imidazolium ionic liquids (ILs), without oxidants, ligands, additives, or volatile solvents. Simple product isolation and recycling/reuse of the IL represent additional advantages of this method.

The biaryl moiety is an important structural motif and building block that is widely present in natural products, pharmaceuticals, advanced materials, conducting polymers and liquid crystals.[1] Consequently, a plethora of synthetic methods for aryl–aryl bond formation have been developed over the years.[1a] Among various metal-mediated protocols for the synthesis of biaryls, the palladium-catalyzed Suzuki coupling utilizing aryl halides, sulfonates, or triflates, and aryl-boronic acids have been widely employed.[1]

The discovery of aryl-diazonium salts as highly efficient coupling partners in Pd-catalyzed reactions,[2] opened up a new chapter in diazonium ion chemistry, and prompted the development of improved methods for arylation via Suzuki–Miyaura,[3–7] Sonogashira,[8–10] and Heck reactions.[11,12]

Imidazolium ILs represent ideal media for metal-mediated coupling reactions with arenediazonium salts because both ArN_2^+ salts and $Pd(OAc)_2$ can be dissolved in the ionic liquid. The method also offers the added advantage to recycle and reuse the IL.

We previously reported on Heck–Matsuda coupling reactions with $[ArN_2][X]$ in IL solvents to synthesize a wide range of olefins,[13] and on the synthesis of novel SF_5-bearing alkenes, alkynes, and biaryls via Heck, Sonogashira, and Suzuki couplings by employing the pentafluorosulfanyl-diazonium salt $[SF_5\text{-}PhN_2][BF_4]$ as coupling partner.[14]

Here we report our study of $Pd(OAc)_2$-catalyzed homocoupling of benzenediazonium terafluoroborates in readily available imidazolium ILs, exploring the scope of the reaction for access to a library of symmetrical biaryls (Scheme 1).

To our knowledge previous studies on the synthesis of symmetrical biaryls via Pd-catalyzed homocoupling of arenediazonium salts have not been extensive,[15] and use of methanol as solvent for this reaction in an earlier study resulted in competing formation of ArH due to hydro-dediazoniation.

Result and discussion

At the onset feasibility studies were performed for metal-catalyzed homocoupling of parent benzenediazonium-BF_4 to form biphenyl in $(bmim)BF_4$ and $(bmim)PF_6$ as solvents, and optimization of the reaction conditions namely type of catalyst, the IL, reaction time, and temperature were carried out (Table 1).

Optimizations were initially performed in $(bmim)PF_6$ with 10 mol % of $PdCl_2$ at 50 °C for 3 h under air, leading to a 36% yield of biphenyl (entry 1), and with a slight improvement in conversion (41%) when the reaction was carried out in $(bmim)BF_4$ at 50 °C for 4 h (entry 2). Poor conversions were noted (TLC monitoring) when $Pd_2(dba)_3$ or $Pd(PPh_3)_4$ were used as catalysts in $(bmim)PF_6$ or in $(bmim)BF_4$ as solvent (entries 3–6; therefore not isolated). Slight improvement was observed by employing Pd-catalysts along with phosphine ligands (entries 7–10), and by using 10% Pd/C (entries 11–12). No significant improvement in the homocoupling yields was achieved in the Pd-I_2 catalyzed reaction (entries 13–14), and

* Corresponding authors. Tel.: +1 904 620 1503; fax: +1 904 620 3535.
E-mail addresses: rgkalkhambkar@gmail.com (R.G. Kalkhambkar), kenneth.laali@UNF.edu (K.K. Laali).

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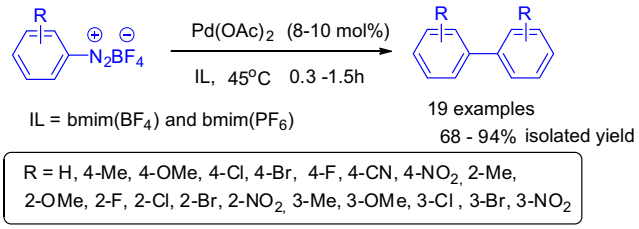
0040-4039/



Scheme 1. Synthesis of symmetrical biaryls by homocoupling of $[ArN_2][BF_4]$ in IL.

by using $Pd(acac)_2$ (entries 15–16). Interestingly, the desired biphenyl was obtained within 1.2 h in 89% yield from the $Pd(OAc)_2$-catalyzed reaction in $(bmim)PF_6$ (entry 17), and in 94% yield when the reaction was carried out at 50 °C in $(bmim)BF_4$ for 1 h (entry 18). Several other metal catalysts were also tested but proved ineffective (entries 19–22).

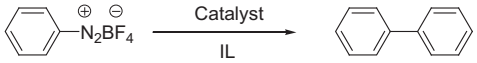
After optimizing the type of catalyst, the catalyst loading was varied to reach optimal conversion (Table 2). Initially the reaction was carried out with 5 mol % of $Pd(OAc)_2$ at room temperature, and the progress of the reaction was monitored by TLC. After 2 h, only 39% yield was reached (entry 1). By increasing the temperature to 45 °C, a 58% yield was achieved after 1 h (entry 2), and 62% yield was obtained at 60 °C (entry 3). By increasing the catalyst loading to 8–10% optimal conversions (88–90%) were reached (entries 4 and 5), and further increase in catalyst loading did not result in notable improvement (entry 6 and 7).

In control experiments using (bmim)Cl, no reaction occurred with 5 mol % catalyst at 60 °C, (Table 2, entry 13), and with 10–15 mol % catalyst only moderate yields (44–48%) could be reached after 3 h (Table 2, entries 14 and 15).

Based on the yield data in Table 2, the prospect of recycling and reuse of the imidazolium IL solvent in these reactions appear reasonable, given the conversions obtained in entries 8 and 9 (for bmim-PF_6), and in 11 and 12 (with bmim-BF_4) in which recycled IL had been employed (see Table 2 and footnotes).

With the optimization data at hand a survey study of the scope of symmetrical biaryl synthesis via the $Pd(OAc)_2$-catalyzed

Table 2
Optimization of catalyst loading[a]

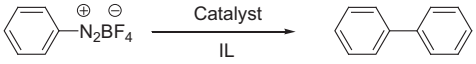


1 1a

Entry	IL	$Pd(OAc)_2$ (mol %)	Time (h)	Temp[b] (°C)	Yield[c] (%)
1	$(bmim)PF_6$	5	2	28	39
2	$(bmim)PF_6$	5	1	45	58
3	$(bmim)PF_6$	5	3	60	62
4	$(bmim)PF_6$	8	0.45	45	88
5	$(bmim)PF_6$	10	1	45	90
6	$(bmim)PF_6$	12	1	45	90
7	$(bmim)PF_6$	15	1.2	50	93
8	$(bmim)PF_6$	8	1	50	86[d]
9	$(bmim)PF_6$	8	1	50	81[e]
10	$(bmim)BF_4$	8	1	45	91
11	$(bmim)BF_4$	8	1	50	87[d]
12	$(bmim)BF_4$	8	1.2	52	79[e]
13	(bmim)Cl	5	1	60	NR
14	(bmim)Cl	10	2	60	44
15	(bmim)Cl	15	3	60	48

NR—no reaction
[a] Reaction carried out using compound **1** (1.0 mmol) and $Pd(OAc)_2$ (5–15 mol %) in 3 mL of the IL solvent.
[b] Oil-bath temperature.
[c] Isolated yield of pure product.
[d] Reaction performed in used IL (2nd cycle).
[e] Reaction performed in used IL (3rd cycle).

Table 1
Catalyst optimization study for the synthesis of symmetrical biphenyl in IL[a]

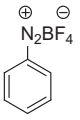
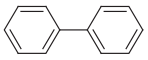
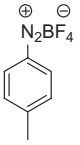
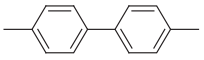
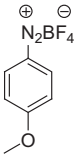
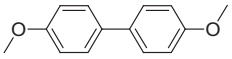
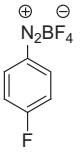
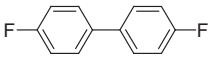
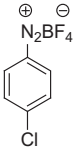
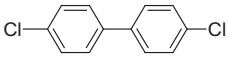
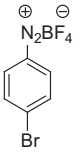
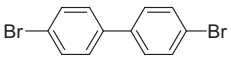
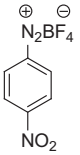
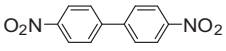
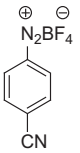
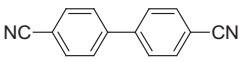
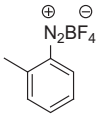
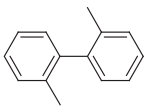
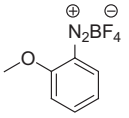
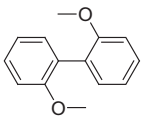
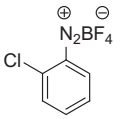
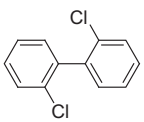
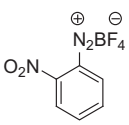
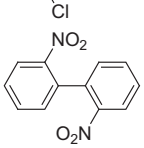


1 1a

Entry	Catalyst[b]	IL	Time (h)	Temp[c] (°C)	Yield[d] (%)
1	$PdCl_2$	$(bmim)PF_6$	3	50	36
2	$PdCl_2$	$(bmim)BF_4$	4	50	41
3	$Pd_2(dba)_3$	$(bmim)PF_6$	4	55	NI
4	$Pd_2(dba)_3$	$(bmim)BF_4$	4	55	NI
5	$Pd(PPh_3)_4$	$(bmim)PF_6$	5	60	NI
6	$Pd(PPh_3)_4$	$(bmim)BF_4$	5	60	NI
7	$PdCl_2(PPh_3)_2$	$(bmim)PF_6$	5	60	40
8	$PdCl_2(PPh_3)_2$	$(bmim)BF_4$	4	58	38
9	$PdCl_2$(dppf)	$(bmim)PF_6$	5	50	38
10	$PdCl_2$(dppf)	$(bmim)BF_4$	4	50	34
11	Pd/C (10%)	$(bmim)PF_6$	4	55	39
12	Pd/C (10%)	$(bmim)BF_4$	4	55	40
13	PdI_2	$(bmim)PF_6$	4	60	NI
14	PdI_2	$(bmim)BF_4$	3	60	NI
15	$Pd(acac)_2$	$(bmim)PF_6$	3.5	60	NI
16	$Pd(acac)_2$	$(bmim)BF_4$	4	60	NI
17	$Pd(OAc)_2$	$(bmim)PF_6$	1.2	45	89
18	$Pd(OAc)_2$	$(bmim)BF_4$	1	50	94
19	$Fe(acac)_3$	$(bmim)PF_6$	5	50	NR
20	$Fe(acac)_3$	$(bmim)BF_4$	5	55	NR
21	$Cu(OAc)_2$	$(bmim)BF_4$	4	60	NR
22	$RhCl(PPh_3)_3$	$(bmim)PF_6$	4	50	NR

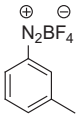
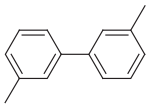
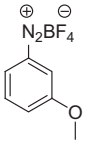
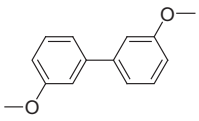
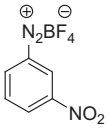
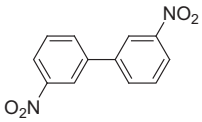
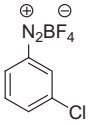
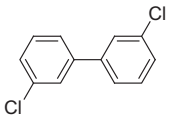
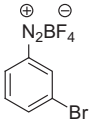
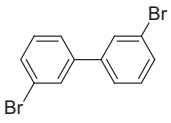
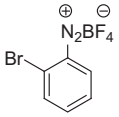
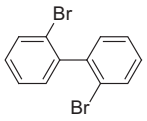
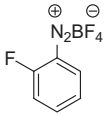
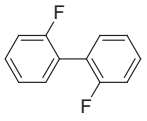
NI—not isolated (low conversion); NR—no reaction.
[a] Reactions were carried out by using compound **1** (1.0 mmol) with catalyst (10 mol %) in 3 mL of the IL solvent.
[b] 10 mol % of catalyst was used.
[c] Oil-bath temperature.
[d] Isolated yield of pure product.

Table 3
Scope of the $Pd(OAc)_2$ catalyzed homocoupling of arenediazonium salts in imidazolium-ILs

Entry	Substrate	Product	Time (h)	Ionic liquid	Isolated yield[*] (%)
1			0.45	(bmim)PF_6	88[a]
2			1	(bmim)BF_4	94[a]
3			1	(bmim)PF_6	82[b]
4			0.50	(bmim)PF_6	80[b]
5			0.30	(bmim)BF_4	78[b]
6			1	(bmim)BF_4	75[c]
7			1.2	(bmim)BF_4	90[a]
8			1	(bmim)PF_6	90[a]
9			0.45	(bmim)PF_6	87[b]
10			1	(bmim)PF_6	90[a]
11			1	(bmim)PF_6	71[b]
12			1.5	(bmim)PF_6	68[c]

(*continued on next page*)

Table 3 (*continued*)

Entry	Substrate	Product	Time (h)	Ionic liquid	Isolated yield* (%)
13			1.2	(bmim)BF_4	80[a]
14			1.3	(bmim)BF_4	85[b]
15			1.5	(bmim)BF_4	90[a]
16			1.2	(bmim)PF_6	78[a]
17			1.5	(bmim)PF_6	77[b]
18			1.2	(bmim)PF_6	70[a]
19			2	(bmim)BF_4	84[a]

* Employing 10 mol % $Pd(OAc)_2$.
[a] Fresh IL was used.
[b] 2nd cycle.
[c] 3rd cycle.

homocoupling reaction of arenediazonium salts in (bmim)PF_6 and (bmim)BF_4 as solvent was undertaken and the results are summarized in Table 3.[16,17]

Isolated yields were in 94% to 68% range, depending on the nature and position of the substituents. The relatively low yields observed for the *ortho*-Br (entry 18) and *ortho*-Cl (entry 11) analogs likely stem from steric effect. With the less bulky *ortho*-OMe (entry 10) and *ortho*-methyl (entry 9) the yields were in optimal range. The lowest conversion was observed with the *ortho*-NO_2 (entry 12).

In summary, we have developed a simple, mild, and high yielding method for the synthesis of a symmetrical biaryls by homocoupling of arenediazonium salts in readily available imidazolium ILs, in the presence of catalytic amounts of $Pd(OAc)_2$. Solubility of diazonium salts and Pd-catalyst in imidazolium ILs allows the reactions to be carried out under homogeneous conditions, and the prospect of recycling and reuse of the IL provides an added advantage.

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Supplementary data

Supplementary data (full experimental details, ^1H, ^{13}C NMR, GC–MS, and IR spectra of various biaryls) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2015.12.108.

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16. ***Typical procedure for the synthesis of symmetrical biaryls by homocoupling of arenediazonium salts***. The desired arenediazonium tetrafluoroborate (1 mmol) was introduced at rt into an oven-dried Schlenk tube charged with [bmim][PF_6] or [bmim][BF_4] ionic liquid (~3 mL) under a nitrogen atmosphere. After efficient magnetic stirring (for 10–20 min), $Pd(OAc)_2$ (8–10 mol %) was introduced under nitrogen and the reaction mixture was stirred at 45–60 °C. The progress of the reaction was monitored by TLC until the diazonium salt was fully consumed (this was determined based on disappearance of the reddish-purple color upon treatment with an alkaline solution of H-acid (4-amino-5-hydroxy-2,7-naphthalenedisulfonic acid). The brownish-colored reaction mass was cooled to rt, and the products were extracted with dry diethyl ether (4 times). Removal of solvent under vacuum furnished the crude products which were chromatographed with hexane/ethyl acetate or DCM/MeOH mixtures to afford the pure products which were characterized by GC–MS and NMR. The brown-colored IL was dried overnight under vacuum at 60 °C and reused in the next 2–3 run, after which it was set aside for recovery and recycling as outlined below.
17. ***Procedure for recycling of ionic liquid:*** The combined brown-colored ionic liquids recovered from several set of experiments were dissolved in MeCN, and filtered through celite to remove insoluble black particles. After removal of solvent from the filtrate under vacuum, the recycled IL was dried overnight under vacuum at 60 °C and reused in subsequent runs.