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Arenediazonium salts immobilized in imidazolium ionic liquids as electrophilic partners in the Pd(OAc)$_2$-catalyzed Matsuda–Heck arylation

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A B S T R A C T

The utility of arenediazonium salts immobilized in imidazolium-ILs [BMIMPF$_6$ and BMIMBF$_4$] for facile, high yielding, synthesis of olefins via the Pd(OAc)$_2$-catalyzed Matsuda–Heck arylation reaction has been demonstrated. The reaction can also be performed as a two-step process in the IL starting from ArNH$_2$, by sequential in-situ diazotization–arylation. Simple product isolation and the recycling/re-use of the IL are additional advantages of this one-pot method.

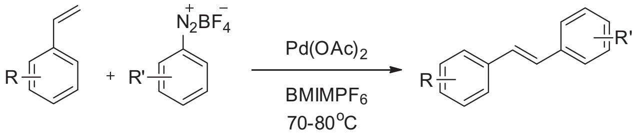
In comparison to aryl halides and oxygen-based electrophiles that are widely used in Pd-catalyzed cross coupling reaction, the utility of diazonium salts as electrophilic partners has not been as widely exploited. Seminal early studies of ArN_2^+ with transition metals by Matsuda and coworkers[1a–e] attracted attention and led to further investigations aimed at improving and expanding the earlier work. The progress in the field was reviewed in 2006 by Roglans et al.[2] More recent studies in this area include: the use of diazonium tosylates, prepared via resin-NO$_2$/TsOH, for Heck arylation of styrene with Pd(OAc)$_2$/EtOH,[3] stereoselective method for the preparation of β,β-disubstituted acrylates using MeCN or alcohol solvents with or without a base,[4] the intramolecular version of Heck–Matsuda reaction applied to the synthesis of benzofuran and indoles,[5a] Heck arylation of enol ethers with arenediazonium salts as a new approach to the synthesis of flavanoids,[5b] and Heck–Matsuda arylation of 2-aza and 2-oxo-substituted acrylates.[5c]

A limited number of studies have explored the use of ILs in the Heck reaction but these employ aryl halides. They include the use of phosphonium ILs,[6a–c] imidazolium ILs along with ultrasound,[7] and application of an ester functionalized imidazolium IL.[8a] In a brief study, Kabalka et al reported styrene dimerization promoted by diazonium salt in imidazolium IL.[8b]

In continuation of our studies on electrophilic and onium ion chemistry in ionic liquids,[9a–j] and building on our earlier studies focusing on diazonium ion chemistry in ILs,[10] we report here a facile Matsuda–Heck process with $ArN_2^+BF_4^-$ salts as electrophilic partners in [BMIM][BF$_4$] and [BMIM][PF$_6$] as solvent, with catalytic amounts (10–20 mol %) of Pd(OAc)$_2$ without an external base, under mild conditions in high yields with high stereoselectivity (when applicable). The reactions were conveniently carried out in a one-pot process with easy product isolation and recycling and re-use of the IL. A variety of styrenes, as well as methyl crotonate and ethyl cinnamate were employed as representative olefins for this study. The product characterization data are gathered in the accompanying supplementary file (for experimental procedures see Ref. [11]).

The arylation reactions with styrenes (Fig. 1) were performed in [BMIM][PF$_6$] as solvent. The isolated yields of corresponding *trans*-stilbenes were in the 82–76% range (see Table 1).

It is possible to perform this reaction starting from the anilines in a two step/one pot diazotization–arylation protocol (Fig. 2, Table 1). The use of a nitrosonium salt for in situ diazotization is convenient because NOX salt can be immobilized in imidazolium



Where R = H, 4-CH$_3$, 4-F
R' = H, 4-CH$_3$, 4-OCH$_3$, 4-Cl, 4-Br, 4-F

Figure 1.

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Table 1
$Pd(OAc)_2$-catalyzed arylation of olefins with arenediazonium salts

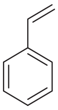
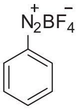
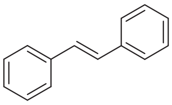
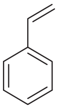
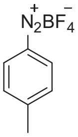
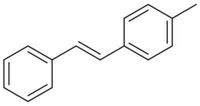
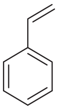
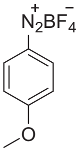
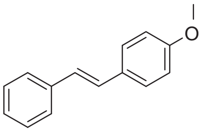
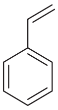
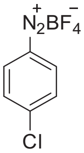
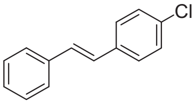
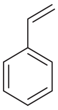
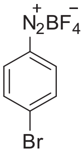
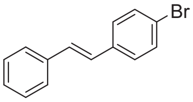
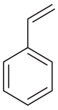
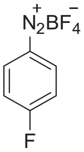
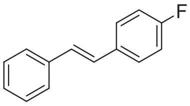
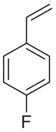
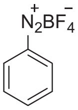
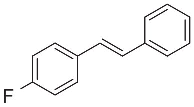
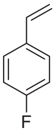
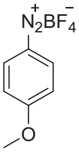
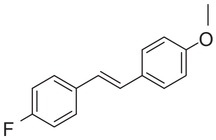
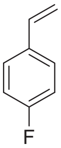
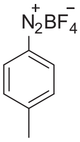
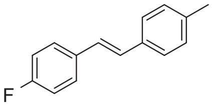
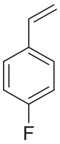
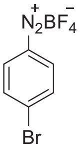
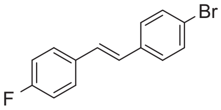
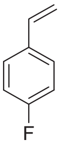
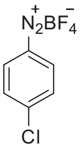
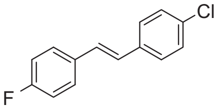
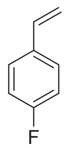
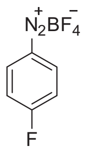
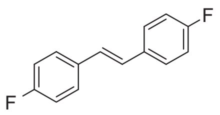
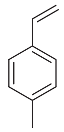
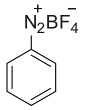
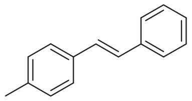
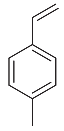
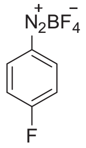
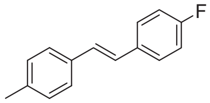
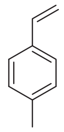
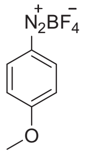
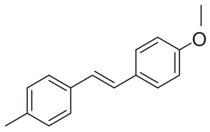
Entry	Alkenes	Diazonium salts	Product	Time (h)	Isolated yield (%)
1				6.5	88, 78[a]
2				5	83, 71[a]
3				7	85
4				8	81
5				8	85
6				8	78
7				8	83
8				6	83
9				6	80
10				5.5	76
11				7.5	77

Table 1 (*continued*)

Entry	Alkenes	Diazonium salts	Product	Time (h)	Isolated yield (%)
12				6.5	78
13				5	82
14				5	80
15				7	82

[a] Reported yield for a one-pot in situ diazotization–arylation.

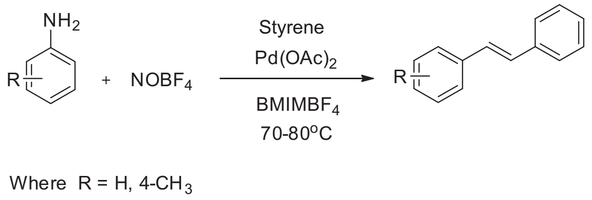


Figure 2.

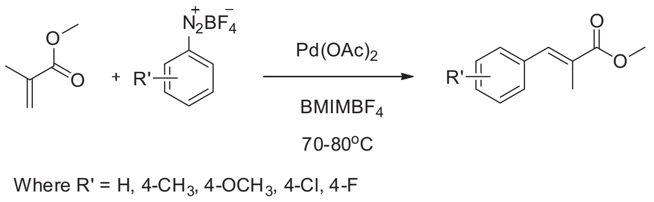


Figure 4.

ILs.[10b,12] In the two representative cases studied, isolated yields for the two-step process were slightly lower (see Table 1).

The arylation reactions with ethyl cinnamate (Fig. 2 and Table 2) and methyl crotonate (Fig. 3 and Table 3) were carried out in [BMIM][BF_4] as solvent.

In a 2009 report, Pastre and Correia[4] studied the Heck arylation of *p*-methoxybenzenediazonium tetrafluoroborate with methyl cinnamate in various solvents (MeCN, MeOH, EtOH, *i*PrOH, and 1,2-propanediol) under reflux or at rt, employing $Pd(OAc)_2$ and $Pd_2(dba)_3$ as catalyst. Variable *E*/*Z* ratios (from 98:2 to 60:40) were obtained depending on the conditions. In the present study in the IL, with R′ = H, 4-Me, 4-Cl, 4-Br, and 4-F (see Fig. 3) the reactions were highly *E* selective (verified by NOED and NOESY measurements; see Supplementary data), and NMR analysis of the products showed only traces of another isomer (~2%). With *p*-OMe (as was also observed in Ref. 4) notable amounts of the *Z* isomer were present (in our case the *E*/*Z* ratio was 60:40 by ^{1}H NMR). With methyl crotonate, in the studied examples (see Fig. 4) only the *E* isomers were observed by NMR. In this regard, observation of a four-bond Me/H coupling (~1.5 Hz) in the alkene products is noteworthy (see Supplementary data, also including corroboratory NOE and NOESY data).

In summary, the ionic liquid version of Mastuda–Heck arylation reported here offers a number of advantages over the existing procedures. High yields and selectivity can be achieved in a simple procedure by using catalytic amounts of $Pd(OAc)_2$, without the need to employ MeCN or ROH solvents and without an added base.

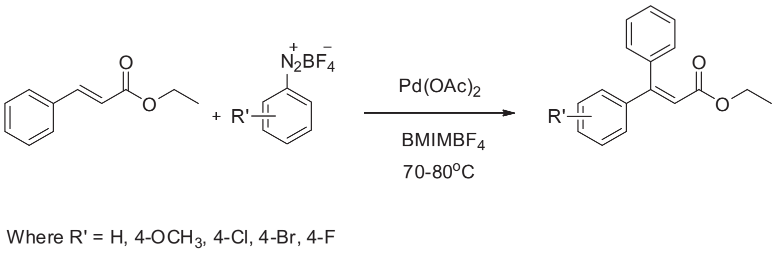
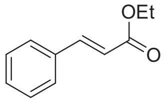
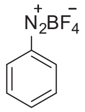
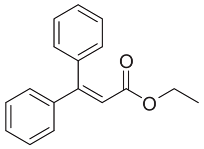
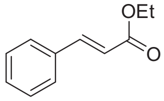
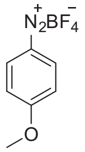
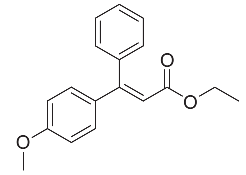
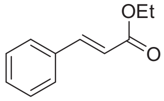
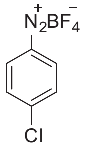
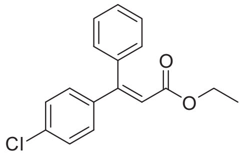
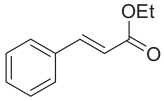
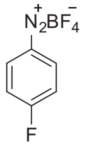
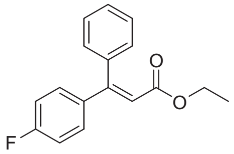
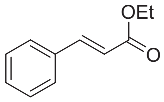
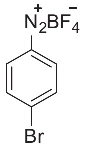
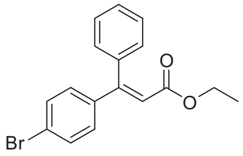


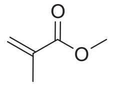
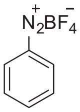
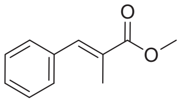
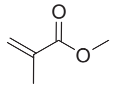
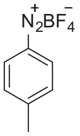
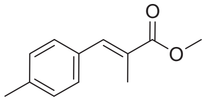
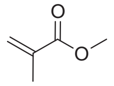
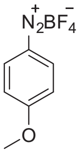
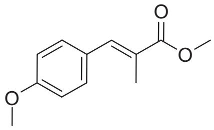
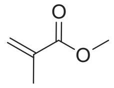
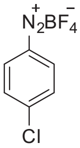
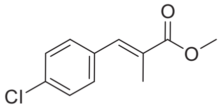
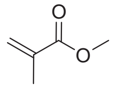
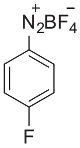
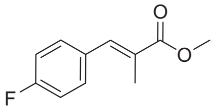
Figure 3.

Table 2
$Pd(OAc)_2$-catalyzed arylation of olefins with arenediazonium salts[a]

Entry	Alkenes	Diazonium salts	Product	Time (h)	Isolated yield (%)
1				11	77
2			 *E/Z* isomer ratio (60:40)[a]	12	76
3				13	75
4				14	89
5				12	83

[a] Determined by ^1H NMR.

Table 3
$Pd(OAc)_2$-catalyzed arylation of olefins with arenediazonium salts

Entry	Alkenes	Diazonium salts	Product	Time (h)	Isolated yield (%)
1				6.5	68
2				7	81
3				5	75
4				8	66
5				4.5	68

Easy product isolation/recovery and reuse of the IL could make this method economically viable for scale-up.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.02.021.

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11. *General procedure*: The desired alkene (1 mmol) and the diazonium salt (2 mmol) were introduced at rt into an oven-dried Schlenk tube charged with [BMIM][PF_6] or [BMIM][BF_4] ionic liquid (~4 mL) under a nitrogen atmosphere. Upon efficient magnetic stirring (for 10–20 min) the diazonium salt was immobilized in the IL, forming a semi-homogenous mixture, which was then charged with $Pd(OAc)_2$ (10–20 mol %) under nitrogen. The reaction mixture was stirred at 70–80 °C under nitrogen and the progress of the reaction was monitored by TLC. The brown-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 mixture (80:20) to afford the pure Heck coupling products which were characterized by GC–MS and NMR. The brown colored IL was dried overnight under vacuum at 50 °C and reused in the next 2–3 run, after which it was set aside for recovery and recycling as outlined below.
    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 50 °C and reused in subsequent runs.
    One-pot in situ diazotization–arylation: A mixture of the aniline (1 mmol), and [NO][BF_4] (1.52 mmol) in [BMIM][BF_4] (3.5 mL) in a Schlenk tube was sonicated at 50 °C for 45 min and then stirred under nitrogen at 60–70 °C for 2 h. The reaction was monitored by TLC for the disappearance of aniline, following which the styrene (0.5 mmol) and $Pd(OAc)_2$ (20–30 mol %) were introduced and stirring was continued at 70–80 °C for 7–8 h. Upon completion, the reaction mass was cooled to rt, the products were extracted in diethyl ether (4 times) and the solvent was removed under vacuum to furnish the crude products which were chromatographed with hexane–ethyl acetate mixture (80:20) to afford pure products which were characterized by GC–MS and NMR (see Table 1, entries 1–2).
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