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1-Aryltriazenes in the Suzuki, Heck, and Sonogashira Reactions in Imidazolium-ILs, with [BMIM(SO$_3$H][OTf] or Sc(OTf)$_3$ as Promoter, and Pd(OAc)$_2$ or NiCl$_2$.glyme as Catalyst

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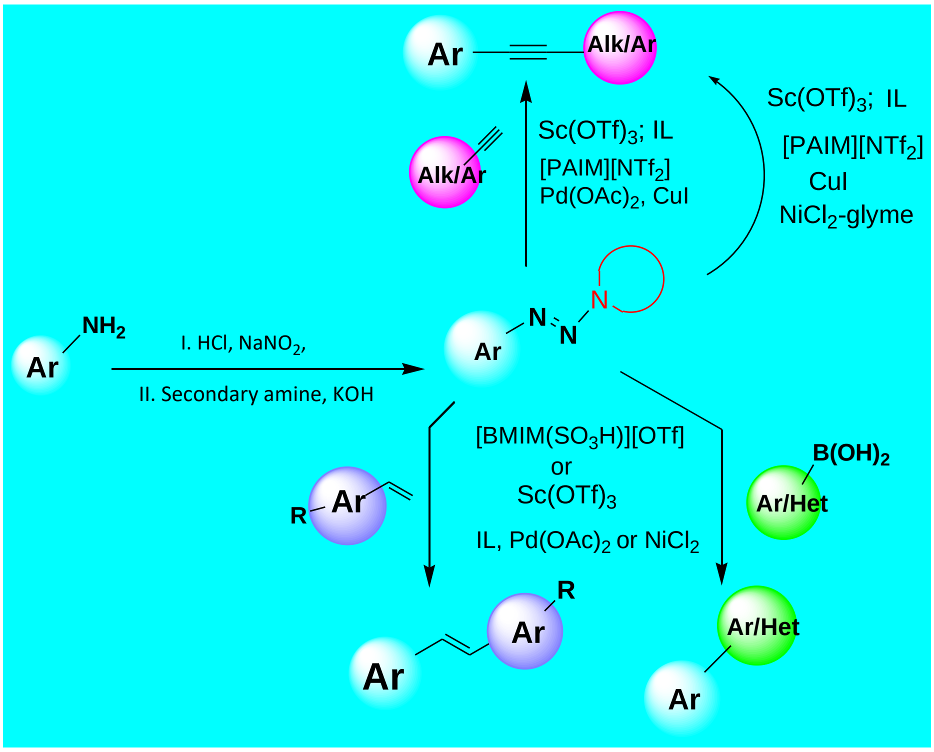
https://www.unf.edu/coas/chemistry/faculty/Kenneth_Laali.aspx



Keywords: 1-aryltriazene; cross-coupling; Pd(OAc)$_2$ or NiCl$_2$.glyme; [BMIM(SO$_3$H)][OTf] or Sc(OTf)$_3$; [PAIM][NTf$_2$]

Key topic: cross-coupling

TOC text: 1-aryl-triazenes as coupling partners in the Suzuki, Heck, and Sonogashira reactions in ionic liquids.

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Abstract

1-Aryltriazenes, the protected and more stable form of aryl-diazonium species, can be conveniently unmasked with Brønsted acidic-IL or Sc(OTf)$_3$ and coupled with a host of aryl/heteroaryl boronic acids, styrenes, and aryl/alkyl acetylenes in the Suzuki, Heck and Sonogashira reactions in one-pot and in respectable isolated yields, by using palladium or nickel catalyst in readily available imidazolium ILs as solvent, under mild conditions. The scope of these reactions are explored, and the potential for recovery/reuse of the IL solvent is also addressed.

Introduction

1-Aryltriazenes Ar-N=N-NR$_2$ are accessible by reaction of secondary amines with the *in-situ* generated ArN$_2^+$,[1] or directly with diazonium salts.[2] Compared to ArN$_2^+$ salts, 1-aryltriazenes have increased stability and longer shelf life, and can be readily purified.[3] Upon treatment with protic or Lewis acids, Ar-N=N-NR$_2$ is transformed back to ArN$_2^+$.[3,4] These attributes imply that Ar-triazenes may be ideal electrophilic partners for cross-coupling reactions as substitutes for ArN$_2^+$ salts. To that end, limited number of studies focusing on the Heck[3]and Suzuki reactions[4,5] have so far been reported employing Pd(0) catalysts along with phosphine ligands[4] or polymer-supported NHC[5], with BF$_3$.Et$_2$O, TFA, or HBF$_4$ as typical promoters[3-5] to "unmask" the triazene. For the Suzuki reaction using BF$_3$.Et$_2$O, it was suggested that formation of an aryltriazenes-BF$_3$ complex promotes trans-metallation, possibly in a concerted fashion.[4] The reactions were performed in a variety of solvents (DME, DMF-H$_2$O, dioxane, DMAC, NMP, toluene, THF, and refluxing MeOH)[3,-5], and the yields varied significantly depending on the solvent.[4]

In continuation of our work on developing synthetic methods in ILs as catalysts and solvents,[6] and our recent studies of metal-mediated cross-coupling reactions,[7] we report here on the utility of 1-aryltriazenes as coupling partners in the Suzuki, Heck, and Sonogashira reactions, by employing Brønsted acidic IL and Sc(OTf)$_3$ as promoters, and the piperidine-appended-IL [PAIM][NTf$_2$] as base for the Sonogashira reaction[7e,7f], without the need for ligand. Considering the ongoing interest in the use of Ni-based catalysts in place of Pd, and the reports of successful application of Ni in the Suzuki reaction,[8-10] we also report on the efficacy of NiCl$_2$.glyme as substitute for Pd(OAc)$_2$ in the present study.

Results and Discussion

At the onset, a small library of 1-aryltriazenes was prepared in good isolated yields by *in-situ* diazotization of aniline and substituted anilines and subsequent reaction with piperidine, pyrrolidine, and morpholine (Table 1). Focusing first on the Suzuki coupling reaction, the Ar-triazenes were reacted with a set of aryl- and heteroaryl-boronic acids employing [BMIM(SO_3H)][OTf] or Sc(OTf)$_3$, as Brønsted and Lewis acid promoters respectively, to unmask the triazenes, with Pd(OAc)$_2$ as catalyst, and employing the readily available [BMIM][BF_4] and [BMIM][PF_6] as solvent, under moderate heating (Table 2, entries 1-11). Selection of [BMIM(SO_3H)][OTf] and Sc(OTf)$_3$ as promoter was based on their demonstrated efficacy as catalyst and promoter in a host of electrophilic and metal-mediated reactions in ILs.[6.7] In the present study they proved almost equally effective, with yields in 96-80% range when fresh IL was used. Lower isolated yields were observed when recycled IL solvent was used to start a new reaction, and a further decrease occurred when recycled IL was used to start a third reaction.

Table 3 (entries 12-17) represents a survey employing NiCl$_2$.glyme instead of Pd(OA$_C$)$_2$, showing that the isolated yields were on average 7-15% lower but still generally acceptable.

Turing our attention to the Heck coupling, the aryl-triazenes were allowed to react with different styrenes and aryl-ethenes, using either [BMIM(SO_3H)][OTf] or Sc(OTf)$_3$ as promoter, and with Pd(OAc)$_2$ as catalyst, in the same IL solvents under moderate heating, and the corresponding Heck coupling products were isolated in 92-74% yields (Table 4, entries 18-25). Lower isolated yields were obtained when recycled ILs were used directly to start a new reaction. When fresh IL was used, [BMIM(SO_3H)][OTf] and Sc(OTf)$_3$ proved equally effective, but precise side by side effectiveness could not be determined due to other variable.

Switching to NiCl$_2$.glyme as catalyst (Table 5, entries 26-30) the Heck coupling products were isolated in 91-78% yields, in a similar range to Pd(OAc)$_2$, with [BMIM(SO_3H)][OTf] and Sc(OTf)$_3$ being equally effective as promoters.

Focusing on the Sonogashira reaction, the 1-aryl-triazenes were allowed to react with representative aryl- and alkyl-ethynes by employing Sc(OTf)$_3$ as promoter, Pd(OAc)$_2$ as catalyst, and the piperidine-appended-imidazolium IL[7e,7f] as basic-IL, along with CuI, in same IL solvents (Table 6, entries 31-39). The corresponding alkynes were isolated in good yields (83-84%) when fresh IL was used, while the yields dropped by approximately 10% after each solvent recycling step.

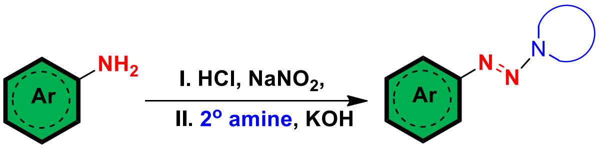
Moving on to $NiCl_2$.glyme as catalyst for this transformation (Table 7, entries 40-45) we found similar isolated yields, and observed similar variations in yields when recycled ILs were used to run a new reaction.

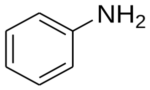
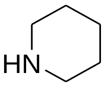
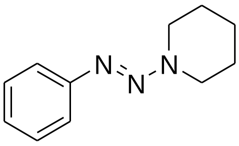
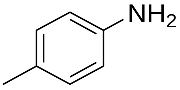
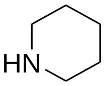
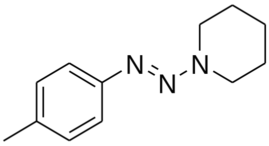
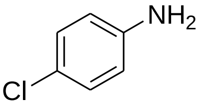
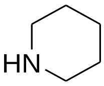
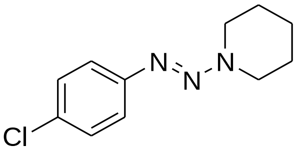
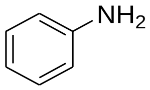
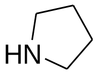
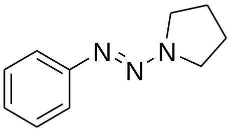
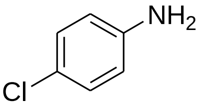
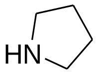
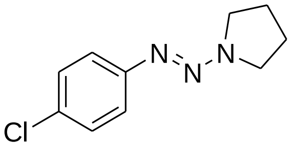
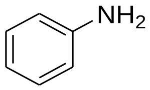
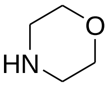
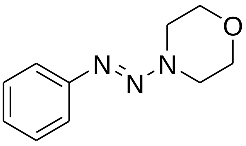
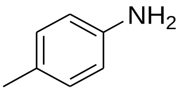
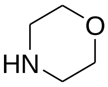
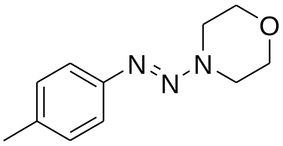
Returning to the recycling/reuse of the IL solvent, for each type of coupling reaction a reference reaction was selected and repeated four consecutive times in [BMIM][PF_6] and in [BMIM][BF_4] solvent. The results presented in graphical format in the SI file (charts 1-3), indicate a fairly consistent trend, and in line with our findings from a previous study,[7f] [BMIM][PF_6] exhibited a somewhat better recovery/reuse profile as compared to [BMIM][BF_4].

Conclusion

In conclusion we have demonstrated the efficacy of 1-aryltriazene as surrogates for aryl-diazonium salts in the Suzuki, Heck, and Sonogashira cross coupling reactions in IL solvents, with the Brønsted-acidic IL [BMIM(SO_3H][OTf] and $Sc(OTf)_3$ serving as efficient promoters for the unmasking of Ar-N=N-NR_2, and [PAIM][NTf_2] serving as basic-IL in the Sonogashira reaction. Reactions were catalyzed with $Pd(OAc)_2$ and with $NiCl_2$.glyme, thus widening the scope of this protocol.

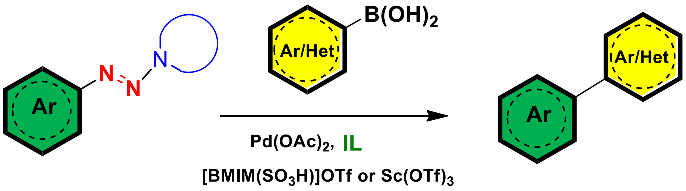
Table 1. Synthesis of 1-aryl-triazenes

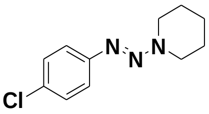
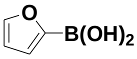
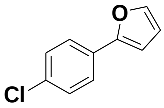
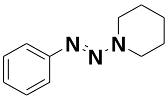
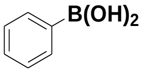
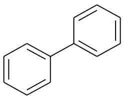
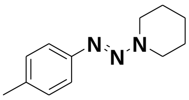
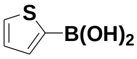
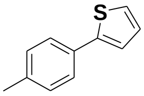
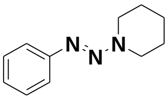
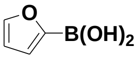
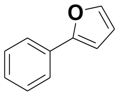
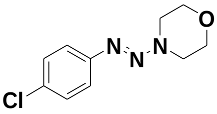
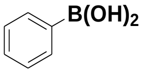
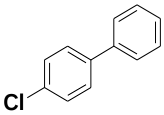
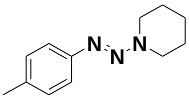
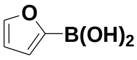
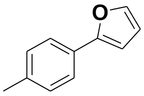
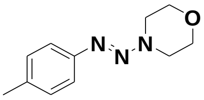
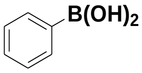
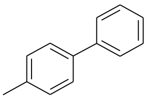
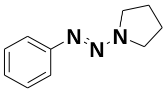
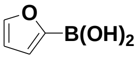
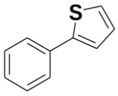
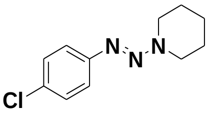
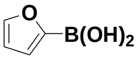
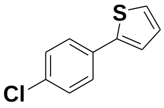
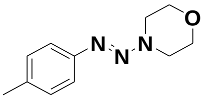
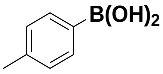
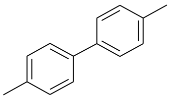
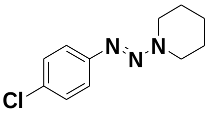
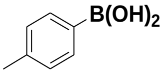
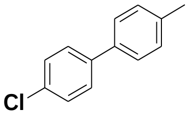


Entry	Ar-NH2	2° amine	Product	Yield* (%)
1				88
2				81
3				79
4				79
6				88
7				77
8				80

*Isolated yields of pure products

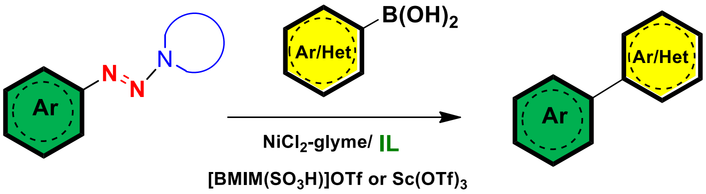
Table 2. Aryl-triazenes as coupling partners in the Suzuki reaction in IL solvents, with $Pd(OAc)_2$ as catalyst, and Brønsted-acidic IL or $Sc(OTf)_3$ as promoter

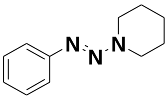
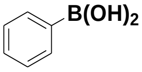
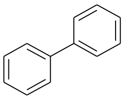
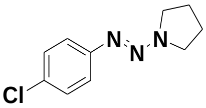
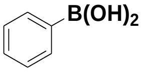
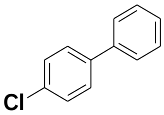
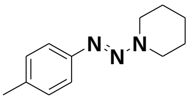
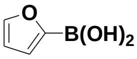
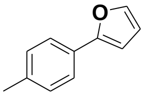
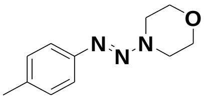
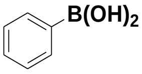
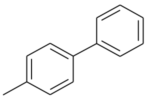
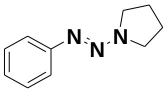
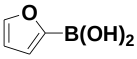
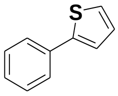
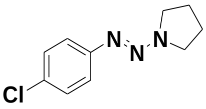
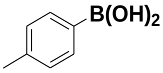
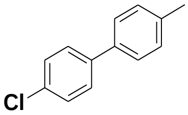


Entry	Ar-Triazene	Ar/Het.Boronic acid	Product[a]	IL	Time[b] (h)	Yield[*] (%)
1				[BMIM]BF_4	6	82[d,f]
2				[BMIM]PF_6	5	96[c,g]
3				[BMIM]BF_4	6	81[d,f]
4				[BMIM]PF_6	6.5	84[c,f]
5				[BMIM]PF_6	6	80[d,g]
6				[BMIM]BF_4	6	89[c,f]
7				[BMIM]BF_4	5.5	82[d,f]
8				[BMIM]BF_4	6.5	73[e,g]
9				[BMIM]BF_4	7	80[c,g]
10				[BMIM]PF_6	5.5	90[c,g]
11				[BMIM]BF_4	6	87[c,f]

[a]Reaction conditions: 1-Ar-triazene (1.2 mmol), Boronic acid (1.0 mmol), Promoter (1.2 mmol), [BMIM][X](7 mL) and $Pd(OAc)_2$ (10 mol %); [b]Oil bath temperature 55-60°C ;[c]Yield employing fresh IL;[d]Yield using recycled IL (2nd cycle); [e]Yield using recycled IL (3rd cycle); [f]$Sc(OTf)_3$; [g][$BMIM(SO_3H)$]OTf; *Isolated yield of pure products.

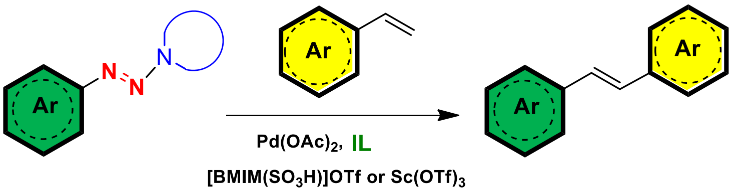
Table 3. Aryl-triazenes as coupling partners in the Suzuki reaction in IL solvents, with $NiCl_2$-glyme as catalyst, and Brønsted-acidic IL or $Sc(OTf)_3$ as promoter

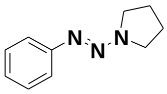
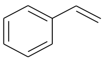
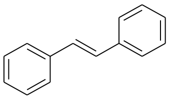
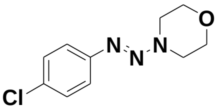
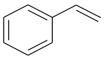
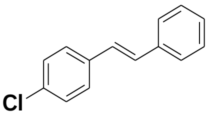
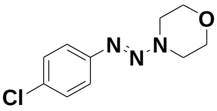
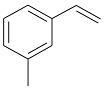
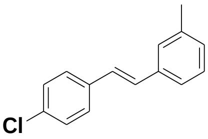
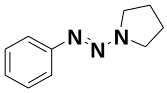
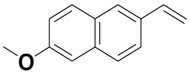
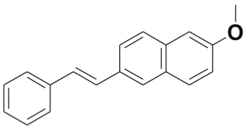
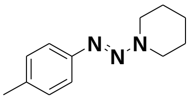
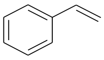
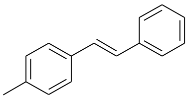
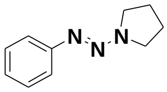
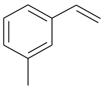
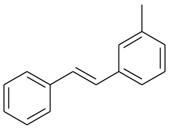
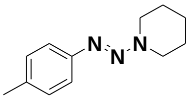
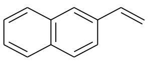
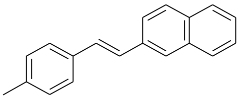
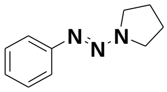
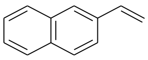
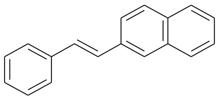


Entry	Ar-Triazene	Ar/Het. Boronic acid	Product[a]	IL	Time[b] (h)	Yield[*] (%)
12				[BMIM]BF_4	6	82[c,g]
13				[BMIM]PF_6	7	78[d,g]
14				[BMIM]BF_4	7	79[c,f]
15				[BMIM]BF_4	6.5	71[d,f]
16				[BMIM]BF_4	6.5	68[e,g]
17				[BMIM]PF_6	7	80[c,f]

[a]Reaction conditions: 1-Ar-triazene (1.2 mmol), Boronic acid **(**1.0 mmol), Promoter (1.2 mmol), [BMIM][X](7 mL) and $NiCl_2$.glyme(10 mol %); [b]Oil bath temperature 55-60 °C; [c]Yield employing fresh IL; [d]Yield using recycled IL (2nd cycle);[e]Yield using recycled IL (3rd cycle); [f]$Sc(OTf)_3$; [g][Bmim(SO_3H)]OTf; *Isolated yield of pure products.

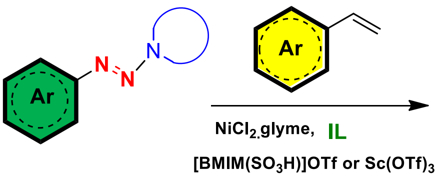
Table 4. Aryl-triazenes as coupling partners in the Heck reaction in IL solvents, with $Pd(OAc)_2$ as catalyst, and Brønsted-acidic IL or $Sc(OTf)_3$ as promoter

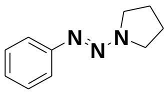
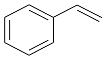
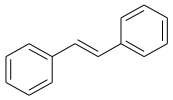
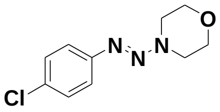
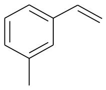
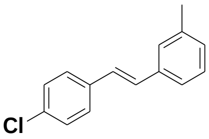
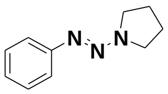
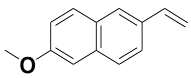
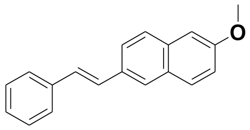
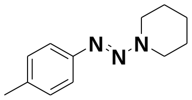
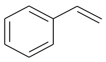
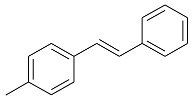
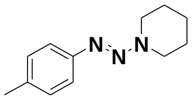
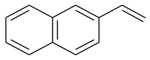
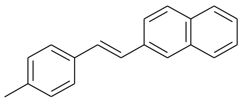


Entry	Ar-Triazene	Arylethenes	Product	IL	Time (h)	Yield* (%)
18				[BMIM]BF_4	2	74^{e,g}
19				[BMIM]BF_4	2.5	82^{c,f}
20				[BMIM]PF_6	2	78^{d,g}
21				[BMIM]BF_4	2.5	65^{e,f}
22				[BMIM]PF_6	2.5	92^{c,f}
23				[BMIM]PF_6	3	86^{c,g}
24				[BMIM]PF_6	3.5	77^{d,f}
25				[BMIM]BF_4	3.5	74^{d,g}

[a]Reaction conditions: 1-Ar-triazene (1.2 mmol), arylethene (1.0 mmol), Promoter (1.2 mmol), [BMIM][X](7 mL) and $Pd(OAc)_2$(10 mol %); [b]Oil bath temperature 70°C; [c]Yield employing fresh IL; [d]Yield using recycled IL (2nd cycle); [e]Yield using recycled IL (3rd cycle); [f]$Sc(OTf)_3$; [g][$BMIM(SO_3H)$]OTf; *Isolated yield of pure products.

Table 5. Aryl-triazenes as coupling partners in the Heck reaction in IL solvents, with $NiCl_2$-glyme as catalyst and Brønsted-acidic IL or $Sc(OTf)_3$ as promoter

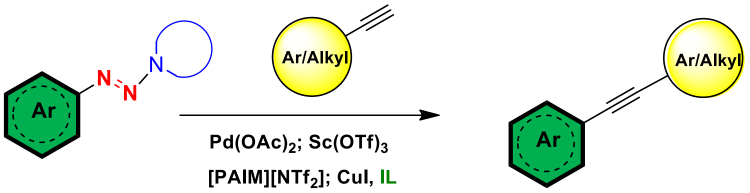


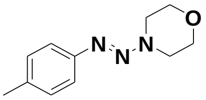
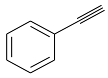
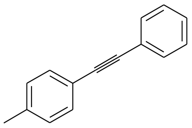
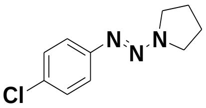
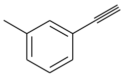
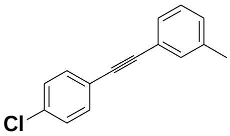
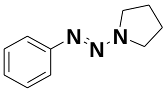
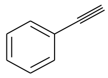
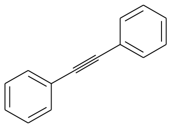
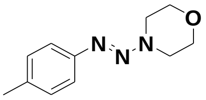
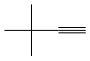
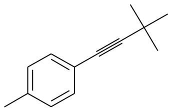
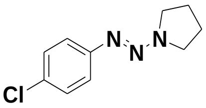
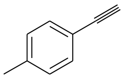
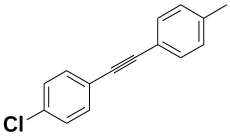
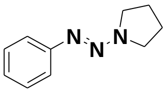
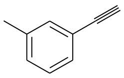
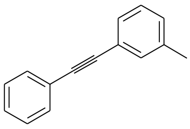
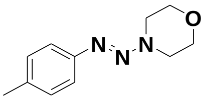
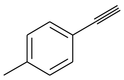
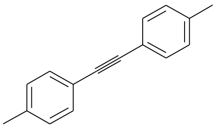
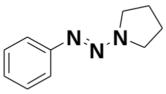
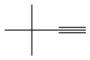
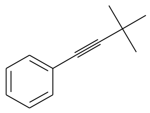
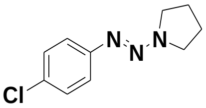
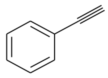
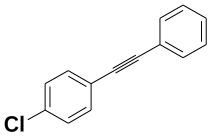
Entry	Ar-Triazene	Arylethene	Product	IL	Time (h)	Yield* (%)
26				$[BMIM]PF_6$	3.5	78[d,f]
27				$[BMIM]BF_4$	4	91[c,e]
28				$[BMIM]PF_6$	4.5	81[d,f]
29				$[BMIM]PF_6$	3,5	87[c,e]
30				$[BMIM]BF_4$	4	87[c,e]

[a]Reaction conditions: Ar-triazene (1.2 mmol), arylethene (1.0 mmol), promoter (1.2 mmol), [BMIM][X](7 mL) and $NiCl_2$.glyme(10 mol %); [b]Oil bath temperature 70 °C; [c]Yield employing fresh IL; [d]Yield using recycled IL (2nd cycle); [e]$Sc(OTf)_3$; [f]$[BMIM(SO_3H)]OTf$; *Isolated yield of pure products

10.1002/ejoc.201901070

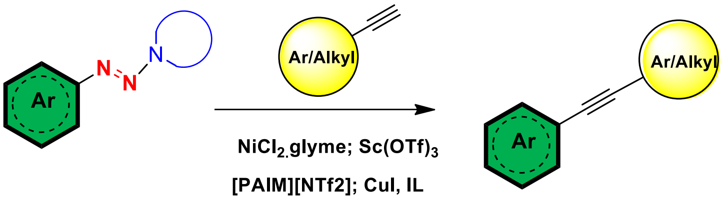
Table 6. Aryl-triazenes as coupling partners in the Sonogashira reaction in IL solvents, $Pd(OAc)_2$ as catalyst, $Sc(OTf)_3$ as promoter, and $[PAIM][NTf_2]$ as base

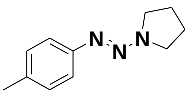
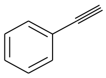
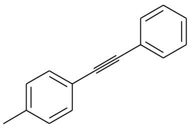
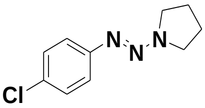
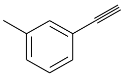
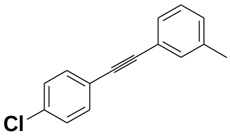
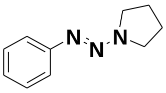
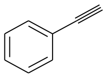
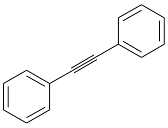
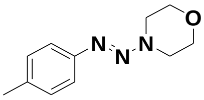
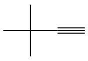
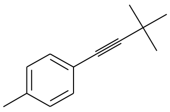
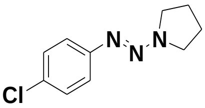
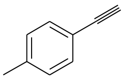
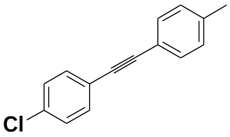
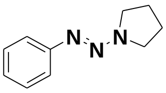
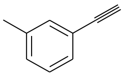
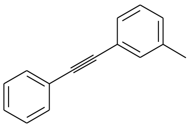


Entry	Ar-triazene	Ar/Alkyl acetylene	Product	IL	Time (h)	Yield* (%)
31				$[BMIM]BF_4$	3	84[c]
32				$[BMIM]BF_4$	3.5	78[d]
33				$[BMIM]PF_6$	3	83[c]
34				$[BMIM]BF_4$	3.5	76[d]
35				$[BMIM]PF_6$	4	63[e]
36				$[BMIM]BF_4$	3	66[e]
37				$[BMIM]PF_6$	3.5	78[d]
38				$[BMIM]PF_6$	3	71[d]
39				$[BMIM]PF_6$	3.5	67[e]

[a]Reaction conditions: Ar-triazene (1.2 mmol), alkyne (1.0 mmol), $[PAIM][NTf_2]$ (3-4 mmol); $Sc(OTf)_3$ (1.2 mmol), [BMIM][X] (7 mL), $Pd(OAc)_2$ (10 mol%) and CuI (10 mol %); [b]Oil bath temperature 50-60°C; [c]Yield employing fresh IL; [d]Yield using recycled IL (2nd cycle); [e]Yield using recycled IL (3rd cycle);*Isolated yield of pure products.

Table 7. Aryl-triazenes as coupling partners in the Sonogashira reaction in IL solvents, with $NiCl_2$-glyme as catalyst, $Sc(OTf)_3$ as promoter, and $[PAIM][NTf_2]$ as base



Entry	Ar-Triazene	Ar/Alkyl acetylene	Product	IL	Time (h)	Yield* (%)
40				$[BMIM]BF_4$	4	81^{c}
41				$[BMIM]PF_6$	5	75^{d}
42				$[BMIM]BF_4$	4	80^{c}
43				$[BMIM]BF_4$	5.5	76^{d}
44				$[BMIM]PF_6$	5.5	70^{d}
45				$[BMIM]PF_6$	5	75^{d}

^{a}Reaction conditions: Ar-triazene (1.2 mmol), alkyne (1.0 mmol), $[PAIM][NTf_2]$ (3-4 mmol); $Sc(OTf)_3$ (1.2 mmol),; [BMIM][X] (7 mL), $NiCl_2$-glyme (10 mol%) and CuI (10 mol %); ^{b}Oil bath temperature 50-60°C; ^{c}Yield employing fresh IL; ^{d}Yield using recycled IL (2nd cycle); ^{e}Yield using recycled IL (3rd cycle);*Isolated yield of pure products

Acknowledgements

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Supporting information

Synthetic procedures, analytical data for isolated compounds, ILrecycling feasibility studies, and NMR spectra data

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