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Facile Synthesis of *N*-Alkyl-*N*′-arylimidazolium Salts via Addition of Imidazoles to Arynes

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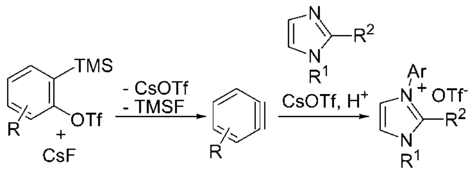
ABSTRACT



A novel synthetic approach to *N*-alkyl-*N*′-arylimidazolium salts has been developed on the basis of addition of imidazoles to arynes. A variety of *N*-alkyl-*N*′-arylimidazolium salts can be synthesized straightforwardly in modest to good yields. Furthermore, utility of the resulting imidazolium salts has been demonstrated by the palladium-catalyzed Suzuki–Miyaura coupling of aryl chlorides.

Since the benzyne molecule was proposed and supported by Wittig in 1942,[1] the chemistry of this reactive intermediate and its derivatives (i.e., arynes) has been recognized as a potential tool in organic synthesis.[2] Arynes undergo a variety of reactions such as electrophilic coupling, cycloaddition, and ene reaction. Among these, the reaction with heterocyclic compounds offers a unique straightforward way to synthesize a wide variety of aromatic ring-containing heterocycles.[2g] Although various nitrogen-containing heterocyclic compounds such as azirines,[3] pyrroles,[4] oxazoles,[5] and pyridines[6] are known to react with arynes, there is no precedent for the reaction of N-substituted imidazoles, to the best of our knowledge.[7] Herein we report that *N*-alkylimidazoles **1** readily add to arynes to provide in one step diverse *N*-alkyl-*N*′-arylimidazolium salts, which are difficult to obtain by conventional methods.[8] The resulting imidazolium salts have been utilized as precursors of unsymmetrical N-heterocyclic carbene[9,10] ligands in the Suzuki−Miyaura coupling[11,12] reaction.

We first carried out the reaction of benzyne generated in situ by treatment of 2-(trimethylsilyl)phenyl triflate (**2a**)[13]

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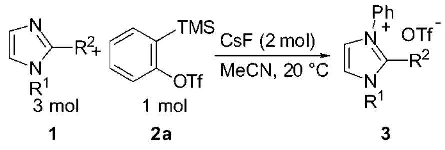
Scheme 1



with cesium fluoride (Scheme 1 and Table 1). When a mixture of **2a** and CsF was allowed to react with 1-(methoxymethyl)imidazole (**1a**) in acetonitrile at 20 °C for 14 h, 1-methoxymethyl-3-phenylimidazolium triflate (**3a**) was obtained in 59% yield (entry 1).[14] The present method could be applied to the reactions of other imidazoles. Thus, primary alkyl group-substituted imidazoles **1b**−**d** reacted smoothly with benzyne to give the corresponding imidazolium salts in moderate yields (entries 2−4). Imidazoles bearing a secondary (**1e**) or tertiary alkyl group (**1f**) also participated in the reaction and afforded the products in 55 and 53% yields, respectively (entries 5 and 6). Furthermore, addition of 1,2-dimethylimidazole (**1g**) to benzyne took place effectively, indicating that a substituent in the 2-position of the imidazole is compatible with the reaction (entry 7). 1-Methyl-2-phenylimidazole (**1h**) afforded **3h** in 33% yield, although longer reaction time was required (entry 8). In contrast, such N-arylated imidazoles as 1-phenylimidazole did not lead to product formation.

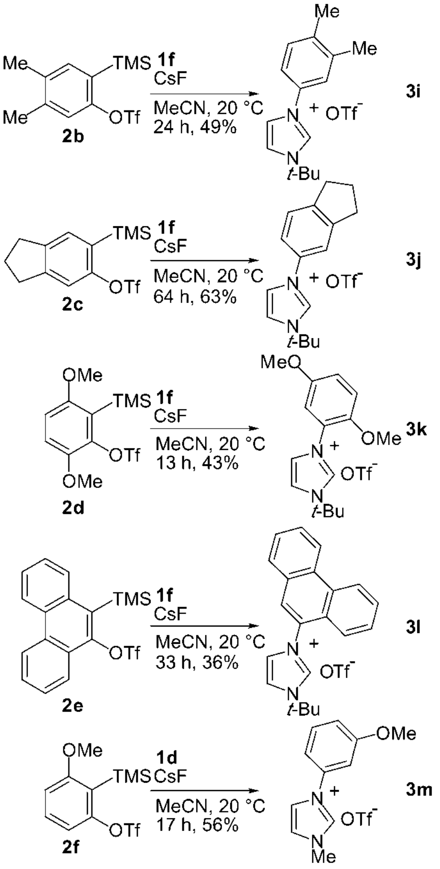
Table 1. Addition of Imidazoles to Benzyne[a]

entry	R^1	R^2		time (h)	yield (%)[b]	product
1	CH_2OMe	H	(**1a**)	14	59 (67)	**3a**
2	CH_2Ph	H	(**1b**)	17	52	**3b**
3	*n*-Bu	H	(**1c**)	11	45	**3c**
4	Me	H	(**1d**)	18	44 (53)	**3d**
5	*i*-Pr	H	(**1e**)	11	55	**3e**
6	*t*-Bu	H	(**1f**)	19	53	**3f**
7	Me	Me	(**1g**)	15	56 (60)	**3g**
8	Me	Ph	(**1h**)	47	33	**3h**

[a] Reaction was carried out in acetonitrile (0.75 mL) at 20 °C using imidazole (0.90 mmol), **2a** (0.30 mmol), and CsF (0.60 mmol). [b] Isolated yields are based on **2a**. ^{1}H NMR yields determined using trichloroethylene as an internal standard are given in parentheses.

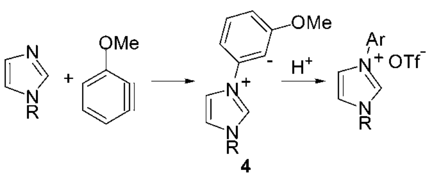
Substituted benzynes could also participate in the present reaction to give the imidazolium salts possessing an aryl moiety other than a phenyl group (Scheme 2). Thus, treatment of 4,5-disubstituted benzyne precursors **2b** and **2c** with **1f** provided respective products **3i** and **3j** in moderate yields. Sterically crowded arynes such as 3,6-dimethoxybenzyne (from **2d**) and 9,10-phenanthryne (from **2e**) underwent the reaction with **1f** as well and afforded the corresponding products. It is worth noting that perfect regioselectivity was observed in the reaction of 3-methoxybenzyne (from **2f**), from which **3m** was produced as the sole product in 56% yield.

Scheme 2



Although details of the reaction pathway remain unclear at present, the fact that arynes are susceptible to addition of nucleophilic heteroatoms may enable us to consider a plausible mechanism, as depicted in Scheme 3.[2f,15] Initially, a nucleophilic nitrogen atom of an imidazole adds to an aryne to give the zwitterion **4**. Subsequent abstraction of a proton from the surroundings produces the final product. The exclusive formation of **3m** in the reaction of 3-methoxybenzyne can be rationally explained by steric and/or electronic effects, both of which favor nucleophilic attack at the meta position of the methoxy group.[2f]

Scheme 3



Finally, utility of the novel imidazolium salts is demonstrated by the palladium-catalyzed Suzuki−Miyaura coupling

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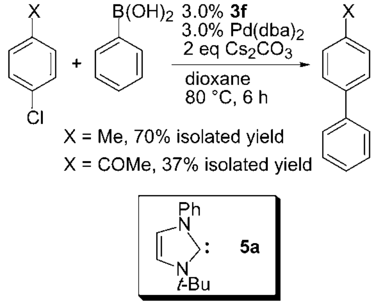
Scheme 4



reaction. As shown in Scheme 4, 4-chlorotoluene or 4-chloroacetophenone underwent the cross-coupling with phenylboronic acid in the presence of Cs_2CO_3, 3.0 mol % of Pd(dba)$_2$, and **3f** (the precursor of N-heterocyclic carbene **5a**), although the cross-coupling required a longer time to be completed compared with previously reported N-heterocyclic carbene ligands.[12a,d]

In conclusion, a general and convenient approach to *N*-alkyl-*N*′-arylimidazolium salts has been developed on the basis of the novel reaction of arynes with imidazoles. Furthermore, a palladium complex coordinated by the N-heterocyclic carbene derived from *N*-*tert*-butyl-*N*′-phenylimidazolium salt allowed Suzuki−Miyaura coupling of aryl chlorides. Further studies on the application of *N*-alkyl-*N*′-arylimidazolium salts for the Suzuki−Miyaura coupling as well as other transition metal-catalyzed reactions are in progress.

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Supporting Information Available: Experimental procedures and characterization of products. This material is available free of charge via the Internet at http://pubs.acs.org.

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