Communication

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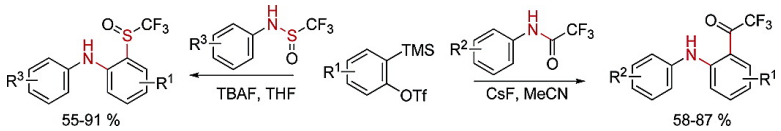
J. Am. Chem. Soc., **2005**, 127 (38), 13112-13113• DOI: 10.1021/ja054079p • Publication Date (Web): 01 September 2005



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Intermolecular C−N Addition of Amides and S−N Addition of Sulfinamides to Arynes

Zhijian Liu and Richard C. Larock*

Department of Chemistry, Iowa State University, Ames, Iowa 50011

Received June 20, 2005; E-mail: larock@iastate.edu

The addition of H−X bonds (X = N, O, and S) to arynes to construct a new carbon−heteroatom bond is well-known.[1] Recently, the Pd-catalyzed insertion of arynes into Si−Si,[2] Sn−Sn,[3] and C−Sn[4] bonds has been reported. While there are examples of the transition-metal-free insertion of arynes into C−C,[5] S−S,[6] and Te−Te[7] bonds, there is only one example of the transition-metal-free insertion of an aryne into a polarized heteroatom-containing bond, namely, the C−N σ-bond of urea.[8] Herein, we report a novel, transition-metal-free, intermolecular C−N addition of amides and S−N addition of sulfinamides to arynes under very mild reaction conditions.

During our work on the *N*-arylation of amines and sulfonamides,[1b] we allowed *N*-phenyltrifluoroacetamide to react with 1.5 equiv of 2-(trimethylsilyl)phenyl triflate (**1a**) and 3.0 equiv of CsF for 20 h. The interesting C−N insertion product 2,2,2-trifluoro-1-[2-(phenylamino)phenyl]ethanone was isolated in a 78% yield. and only a trace of the *N*-arylated product was detected. After optimization, we observed that as little as 1.2 equiv of the silylaryl triflate **1a** and 2 equiv of CsF afforded the insertion product in a 77% yield after only 4 h (Scheme 1).

A variety of functionally substituted *N*-aryltrifluoroacetamides undergoes this chemistry and affords good yields of the insertion products (Table 1). Substrates with both electron-donating and electron-withdrawing groups afford good yields. Even the sterically hindered substrate shown in entry 5 affords the corresponding insertion product in a 69% yield. Besides the simple benzyne precursor **1a**, the 3-MeO-substituted silylaryl triflate **1b** also afforded excellent yields of a single regioisomer (entries 6 and 7). In a similar manner, the substituted aryne precursors **1c** and **1d** also gave good to excellent yields of the corresponding insertion products (entries 8 and 9). Because the reaction does not involve a transition metal, halides are readily tolerated under our reaction conditions. This insertion reaction is not limited to trifluoroacetamides; 2-chloro-2,2-difluoro-*p*-methylacetanilide reacts with the aryne precursor **1b** to afford a good yield of the desired product (entry 10). When aryne precursor **1e** was employed, two isomers were obtained in a 1:1.1 ratio (entry 11). However, acetanilides bearing less electron-withdrawing halogens, such as *N*-phenyltrichloroacetamide, failed to undergo insertion. Interestingly, when *N*,*N*′-1,4-phenylenebis(2,2,2-trifluoroacetamide) was employed, we obtained only the double insertion product in moderate yield (entry 12). When simple β-lactams, such as 2-azetidinone and 2-pyrrolidone or 3,3-difluoro-4-phenyl-2-azetidinone, were employed, no insertion products were detected.

After examining the C−N addition of amides to arynes, we focused on trifluoromethanesulfinamides,[9] which can be readily prepared from the corresponding anilines and trifluoromethanesulfinate salts.[10] Because the highly electrophilic nature of the sulfur atom is enhanced by the CF_3 moiety, we expected that these sulfinamides should also undergo S−N addition to arynes. Indeed, when we allowed *N*-phenyltrifluoromethanesulfinamide to react with triflate **1a** under our standard reaction conditions, the product of S−N addition was obtained in a 40% yield. By using *n*-Bu_4NF

Scheme 1

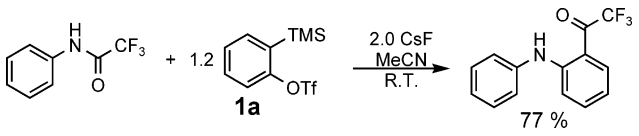
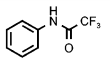
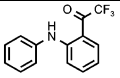
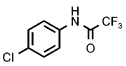
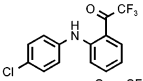
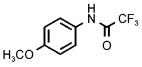
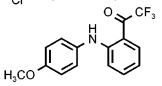
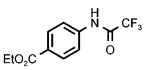
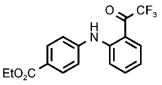
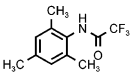
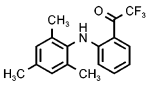
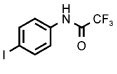
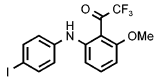
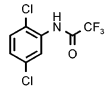
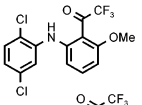
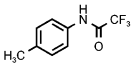
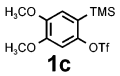
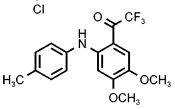
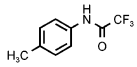
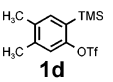
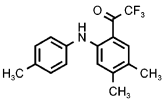
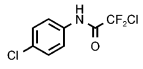
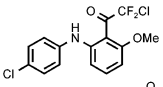
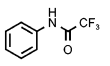
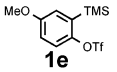
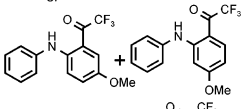
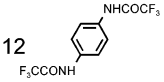
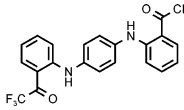


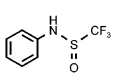
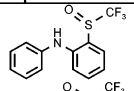
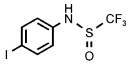
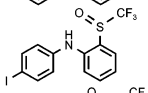
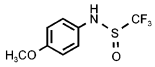
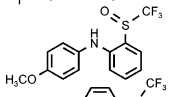
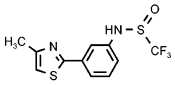
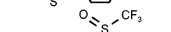
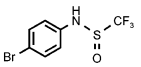
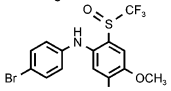
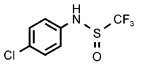
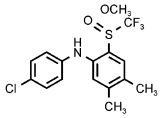
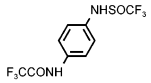
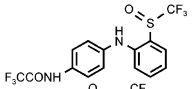
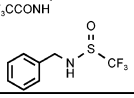
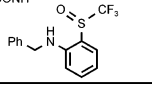
Table 1. C−N Addition of Amides to Arynes[a]

entry	amide	aryne	product	% yield[b]
1		 **1a**		77
2		**1a**		86
3		**1a**		78
4		**1a**		60
5		**1a**		69
6		 **1b**		88
7		**1b**		87[c]
8		 **1c**		70
9		 **1d**		58
10		**1b**		66
11		 **1e**		73 (1:1.1)
12		**1a**		48[d]

[a] Reaction conditions: 0.5 mmol of amide, 1.2 equiv of aryne precursor, and 2.0 equiv of CsF in 5.0 mL of MeCN at room temperature for 4 h. [b] Isolated yield. [c] X-ray crystallography data for this compound are available in the Supporting Information. [d] Employed with 2.4 equiv of **1a** and 4.0 equiv of CsF.

10.1021/ja054079p CCC: $30.25

Table 2. S−N Addition of Sulfinamides to Arynes[a]

entry	sulfimide	aryne	product	% yield[b]
1		**1a**		80
2		**1a**		81
3		**1a**		91
4		**1a**		75
5		**1c**		72
6		**1d**		55
7		**1a**		58[c,d]
8		**1a**		41

[a] Reaction conditions: 0.5 mmol of sulfinamide, 1.5 equiv of aryne precursor, and 1.8 equiv of TBAF in 5.0 mL of THF at room temperature for 30 min. [b] Isolated yield. [c] Employed with 1.0 equiv of **1a**. [d] The reaction is messy when CsF was employed as the base in MeCN.

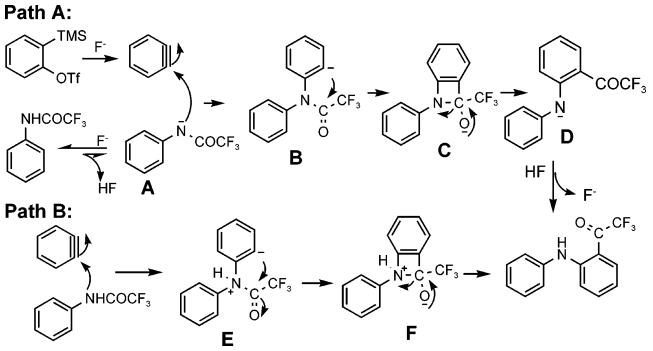
(TBAF) as the fluoride source, instead of CsF, and THF as the solvent, we were able to obtain the desired insertion product in an 80% yield in 30 min at room temperature (Table 2, entry 1).

The scope of this chemistry has been examined (Table 2). All trifluoromethanesulfinamides work well with our standard aryne precursors to afford the corresponding S−N insertion products in high yields. Again, substrates with electron-donating or electron-withdrawing groups afford high yields (entries 2 and 3). An interesting thiazole derivative also afforded a high yield of aryne insertion product (entry 4). Once again, these sulfinamides react with the aryne precursors **1c** and **1d** to produce the corresponding insertion products in good yields (entries 5 and 6). More interestingly, the reaction of a substrate bearing both a trifluoroacetamide and a trifluoromethanesulfinamide group afforded only the S−N insertion product in a good yield, leaving the trifluoroacetamide group untouched (entry 7). An *N*-alkyl sulfinamide has also been shown to undergo this insertion chemistry, although the yield is a little lower (entry 8).

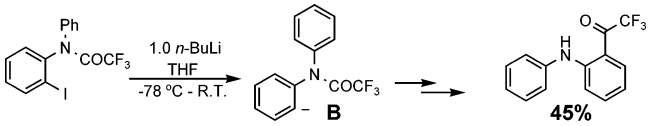
As part of our mechanistic studies, we allowed *N*-phenylacetamide, *N*-phenyltrichloroacetamide, *N*-phenyltrichloromethanesulfinamide, and *N*-methyl-*N*-phenyltrifluoroacetamide to react with the benzyne precursor **1a** and CsF. No insertion products were detected in any of these reactions, even when adding an additional base, such as DBU. The presence of the CF_3 moiety is clearly critical to the success of this insertion chemistry, presumably because this strong electron-withdrawing group increases the acidity of the amide and also increases the electrophilicity of the carbonyl carbon of the amide and the sulfinyl sulfur atom of the sulfinamide.

On the basis of our results, we propose the reaction mechanism shown in Path A (Scheme 2), although we cannot rule out Path B. Fluoride anion can both react with silylaryl triflate **1a** to generate benzyne and also act as a base to abstract the hydrogen on the amide nitrogen to afford anion **A**, which can attack the benzyne to

Scheme 2



Scheme 3



produce intermediate **B**. Intermediate **B** can then undergo intramolecular nucleophilic attack on the carbonyl carbon (or sulfinyl group) to generate the unstable four-membered ring intermediate **C**, which readily undergoes ring opening and protonation to afford the final C−N insertion product.

To obtain further evidence to support our mechanism, we allowed *N*-(2-iodophenyl)-*N*-phenyltrifluoroacetamide to react with *n*-BuLi at a low temperature to generate intermediate **B**. Subsequent rearrangement should afford the anticipated ketone. Indeed, we obtained the desired ketone in a 45% yield (Scheme 3).

In summary, we have developed an efficient, mild, transition-metal-free method for the intermolecular C−N addition of amides and S−N addition of sulfinamides to arynes. Insertion products, such as those produced herein, should prove useful in the preparation of Efavirenz derivatives[11] and for the molecular recognition of anions.[12] A variety of functional groups are compatible with the reaction conditions. Further studies on the reaction mechanism and the scope of this process are in progress.

Acknowledgment. We gratefully acknowledge the National Science Foundation for support of this research.

Supporting Information Available: Detailed experimental procedure, and X-ray diffraction and characterization data for all previously unknown products. This material is available free of charge via the Internet at http://pubs.acs.org.

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JA054079P