



On the Lewis base-promoted alkynylation of electron-deficient fluorobenzenes with trimethylsilylacetylenes



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ABSTRACT

The Lewis base-promoted alkynylation of fluorobenzenes using trimethylsilylacetylenes studying the reactivity as a function of the number of fluoride groups is described. The reaction of 1-(pentafluorophenyl)- and 1-(3,4,5-trifluorophenyl)-2-phenylacetylenes and 1-(4-methoxyphenyl)-2-trimethylsilylacetylene with CsF/18-crown-6 in DMSO gave the alkynylated products in moderate to good yields with high regioselectivity under mild conditions. However, the 3,4-difluorophenyl derivative showed low reactivity.

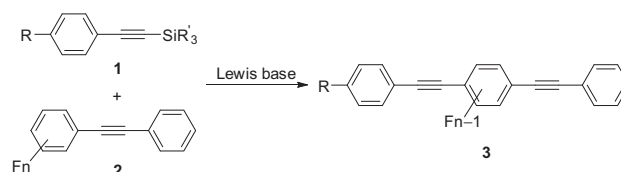
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Transition-metal-catalyzed Sonogashira cross-coupling is one of the most important synthetic protocols for organic compounds and is also applied for the synthesis of conjugated oligo- and polymers.¹ Although this coupling reaction represents a great success, it requires transition-metal catalysts, for example, expensive Pd catalysts and toxic Cu salts. For this reason, alternative pathways to construct C–C bonds under transition-metal-free conditions are highly appealing.² However, few examples of transition-metal-free Sonogashira-type coupling have been reported to date.³ Among them, the nucleophilic aromatic substitution (S_NAr) reaction is one of the alternatives.⁴ For example, activated trimethylsilylacetylene, i.e., nucleophilic pentacoordinate silicate,^{5,6} promoted by Lewis base could be used in the S_NAr reaction. The reaction is simple, but has little precedent.⁷ In addition, the hexafluorobenzene and pentafluorophenyl groups are usually used as the aryl groups in the reaction.

Herein, we report a Lewis base-promoted alkynylation of electron-deficient fluorobenzenes with trimethylsilylacetylenes via highly selective C–F bond cleavage. This strategy enables us to obtain a variety of corresponding fluoroarylated alkynes in moderate to good yields. We also show the reactivity of the fluorobenzenes as a function of the number of fluoride groups. The resulting fluoroarylated alkynes would be fascinating. This is because the structural modification by the replacement of hydrogen by fluorine in organic molecules has usually made an impact

in various applications, ranging from pharmaceutical chemistry to materials science.⁸ The scope of silylacetylenes as a substrate also permits application of the present method to material chemistry. For example, Watson and co-workers⁹ and we¹⁰ reported the polymerization of trimethylsilylacetylene and fluorobenzene with a catalytic amount of fluoride ions to afford poly(*p*-phenylene-neethynylene)s.

Initially, the reaction of 1-(4-methoxyphenyl)-2-(trimethylsilyl)acetylene **1a** and 1-pentafluorophenyl-2-phenylacetylene **2a** with CsF/18-crown-6 (1 equiv) in DMSO was examined (Scheme 1). Table 1 summarizes the results. To our delight, the reaction proceeded at room temperature for 2 h to give 1-(4-methoxyphenyl)-4-phenylethynyltetrafluorobenzene **3a** in 58% isolated yield (entry 1). It is noted that no detectable amount of other ethynyl-substituted products was found under our conditions, indicating that the reaction is highly regioselective. The reaction at 80 °C afforded the coupling product in 73% isolated yield (entry 2). When



Scheme 1. Lewis base-promoted alkynylation of fluorobenzenes **2** with trimethylsilylacetylenes **1**.

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Table 1
Lewis base-promoted alkyne coupling of fluorobenzenes **2** with trimethylsilylacetylenes **1**

Entry	1	2	Lewis base (equiv)/conditions	Product, yield ^{a,b}
1			CsF, 18-crown-6 (1)/rt, 2 h	 3a , 58%
2	1a	2a	CsF, 18-crown-6 (1)/80 °C, 2 h	3a , 73%
3	1a	2a	CsF, 18-crown-6 (0.1)/80 °C, 2 h	3a , 61%
4	1a	2a	CsF, 18-crown-6 (0.05)/80 °C, 2 h	3a , 51%
5	1a	2a	<i>t</i> -BuOK (0.1)/80 °C, 2 h	3a , 73%
6	1a	2a	TBAF (1)/rt, 2 h ^d	3a , 33%
7	1a	2a	TBAF (1)/80 °C, 18 h	3a , 0%
8		2a	CsF, 18-crown-6 (1)/80 °C, 2 h	 3b , 48%
9		2a	CsF, 18-crown-6 (1)/80 °C, 2 h	 3c , 34%
10	1a		CsF, 18-crown-6 (1)/rt, 2 h	 3d , nd ^c (35%)
11	1a	2b	CsF, 18-crown-6 (1)/rt, 4 h	3d , nd ^c (36%)
12	1a	2b	CsF, 18-crown-6 (1)/rt, 6 h	3d , 37%
13	1a	2b	CsF, 18-crown-6 (1)/80 °C, 2 h	3d , 44%
14	1a	2b	CsF, 18-crown-6 (0.1)/80 °C, 2 h	3d , 33%
15	1a	2b	CsF, 18-crown-6 (1) ^e /rt, 2 h	3d , 53%
16	1a	2b	CsF, 18-crown-6 (1) ^e /80 °C, 2 h	3d , 10%
17	1a	2b	<i>t</i> -BuOK (1)/80 °C, 2 h	 3d , 40%/4, 33% (80%)
18	1a	2b	<i>t</i> -BuOK, cryptand[2.2.2] (1)/80 °C, 2 h	3d , 52%/4, 26% (90%)
19	1a	2b	<i>t</i> -BuOK, cryptand[2.2.2] (1) ^e /rt, 2 h	3d , 55%/4, 26%
20	1a	2b	TBAF (1)/80 °C, 2 h	3d , 29% (37%)
21	1b	2b	CsF, 18-crown-6 (1)/80 °C, 2 h	 3e , 37%
22	1c	2b	CsF, 18-crown-6 (1)/80 °C, 2 h	 3f , 32%
23		2b	CsF, 18-crown-6 (1) ^e /rt, 2 h	 5 , 37%
24	1a		CsF, 18-crown-6 (1) ^e /rt, 2 h	 3g-p , 47%
25	1a		CsF, 18-crown-6 (1) ^e /rt, 2 h	 3g-o , 47%
				 3h , 8.6%

^a Isolated yield.

^b The figures in parentheses are conversion of **2b** (%) determined by ¹⁹F NMR using 1-trifluoromethyl-4-methylbenzene as an internal standard.

^c Not determined.

^d THF was used as the solvent.

^e **2** was added to a mixture of **1** and CsF/18-crown-6 in DMSO.

10 or 5 mol % of CsF/18-crown-6 against the substrates was employed, the product was obtained in good yields, 61% or 51%, respectively (entries 3 and 4). This indicates that the fluoride ion could catalyze the coupling reaction. On the other hand, when ter-

minal alkynes were used instead of trimethylsilyl-substituted alkynes, no reaction occurred. Potassium *t*-butoxide (10 mol %) as the base also gave **3a** as a good result (entry 5). The yield was 73%. However, tetrabutylammonium fluoride (TBAF) was less effective

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