DOI: 10.1002/adsc.200800708

A Mild and Efficient Iron-Catalyzed Synthesis of Alkenyl Halides *via* Direct Addition of Benzyl Halides to Arylalkynes

Zhongquan Liu,[a],* Jianguo Wang,[a] Yankai Zhao,[a] and Bo Zhou[a]

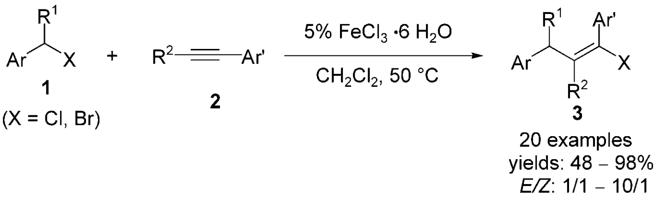
[a] Institute of Organic Chemistry, Gannan Normal University, 341000, Ganzhou, Jiangxi, State Key Laboratory of Applied Organic Chemistry and Department of Chemistry, Lanzhou University, Lanzhou 730000, People's Republic of China
Fax: (+86)-931-862-5657; phone: (+86)-931-891-2280; e-mail: liuzhongquan@yahoo.cn

Received: November 15, 2008; Revised: January 16, 2009; Published online: February 2, 2009

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.200800708.

Abstract: An efficient and mild iron-catalyzed synthesis of alkenyl halides has been developed *via* direct carbon-carbon bond formation by using benzyl halides and arylalkynes.

Keywords: alkenyl halides; C–C bond formation; electrophilic addition; homogeneous catalysis; iron



Scheme 1. Iron-catalyzed addition of benzyl halides to aryl alkynes.

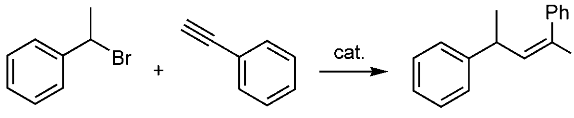
The development of direct C–C bond formation processes that use sustainable, environmentally benign and low-cost catalysts is a critical challenge for organic synthetic chemists. First row transition metals, especially iron, may become the possible alternatives of precious metals such as palladium, rhodium, iridium, and ruthenium. Recently, some efficient iron-catalyzed systems have been explored for carbon-carbon couplings.[1] We wish to report herein an efficient and mild iron-catalyzed synthesis of various substituted alkenyl halides *via* addition of benzyl halides to arylalkynes.

In the past decades, Lewis acid-promoted C–C bond formation reactions by addition of carbenium ions to alkenes have been extensively explored.[2] However, compared with alkenes, the use of alkynes as electron-rich substrates to be attacked by carbenium ions seems limited. In addition, most of these procedures were catalyzed by anhydrous zinc chloride and bromide.[3] The main drawbacks of these systems are the difficulties in handling the moisture-sensitive catalyst as well as the need for anhydrous conditions and long reaction times.[3] Therefore, the development of more efficient and mild catalysts to promote the generation of alkenyl halides by direct addition of various halides to alkynes remains attractive. We have successfully accomplished an efficient and mild synthesis of alkenyl halides *via* addition of benzyl halides to arylalkynes by using 5 mol% of $FeCl_3{\cdot}6H_2O$ as the active catalyst (Scheme 1). To the best of our knowledge, this is the first example of an iron-catalyzed formation of alkenyl halides *via* direct addition of benzyl halides to arylalkynes.

For the initial test reaction, we selected 1-phenylethyl bromide (**1a**) and phenylacetylene (**2a**) as standard substrates to optimize suitable conditions for this addition reaction (Table 1). The desired alkenyl bromide (**3a**) was obtained in 84% yield using 5 mol% of anhydrous $FeCl_3$ at 50 °C in CH_2Cl_2 (Table 1, entry 1). Surprisingly, the isolated yield of the product increased to 97% by using 5 mol% of $FeCl_3{\cdot}6H_2O$ as catalyst (Table 1, entry 2). However, other iron salts and copper salts were inactive to this reaction (Table 1, entries 3–6). A decrease or increase of the catalyst dosage was less efficient than 5 mol% also (Table 1, entries 7 and 8). A low yield of **3a** was isolated at room temperature (Table 1, entry 9). Further investigation of the solvent effect showed that CH_2Cl_2 is a more effective solvent (Table 1, entries 10–18). A 61% isolated yield of **3a** was obtained catalyzed by 5 mol% of $FeCl_3$ in a mixed solvent (CH_3OH/CH_2Cl_2) involving the proton source (Table 1, entry 19).

It is seen from Table 2 that arylalkynes with electron-withdrawing groups such as fluorine gave excellent yields of the desired product (Table 2, entry 1) while arylalkynes bearing electron-donating groups

Table 1. Optimization of the typical reaction conditions.[a]



1a **2a** **3a** (*E/Z*)

Entry	Catalyst [mol%]	Solvent	*T* [°C]	Yield [%][b]
1	$FeCl_3$ (5)	CH_2Cl_2	50	84
2[c]	**$FeCl_3 \cdot 6H_2O$ (5)**	**CH_2Cl_2**	**50**	**97**
3	$Fe_2(SO_4)_3$ (5)	CH_2Cl_2	50	0
4	$FeCl_2$ (5)	CH_2Cl_2	50	0
5	$CuBr_2$ (5)	CH_2Cl_2	50	0
6	CuBr (5)	CH_2Cl_2	50	0
7	$FeCl_3 \cdot 6H_2O$ (1)	CH_2Cl_2	50	82
8	$FeCl_3 \cdot 6H_2O$ (10)	CH_2Cl_2	50	76
9	$FeCl_3 \cdot 6H_2O$ (5)	CH_2Cl_2	r.t.	31
10	$FeCl_3 \cdot 6H_2O$ (5)	DCE	50	53
11	$FeCl_3 \cdot 6H_2O$ (5)	$CHCl_3$	50	35
12	$FeCl_3 \cdot 6H_2O$ (5)	CCl_4	50	0
13	$FeCl_3 \cdot 6H_2O$ (5)	H_2O	50	0
14	$FeCl_3 \cdot 6H_2O$ (5)	CH_3OH	50	0
15	$FeCl_3 \cdot 6H_2O$ (5)	THF	50	0
16	$FeCl_3 \cdot 6H_2O$ (5)	benzene	50	0
17	$FeCl_3 \cdot 6H_2O$ (5)	cyclohexane	50	0
18	$FeCl_3 \cdot 6H_2O$ (5)	CH_3NO_2	50	0
19[d]	$FeCl_3$ (5)	CH_3OH/CH_2Cl_2	50	61

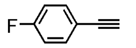
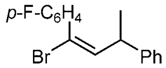
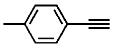
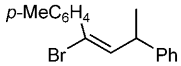
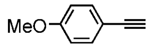
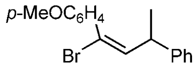
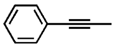
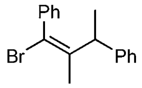
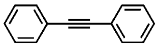
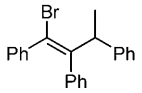
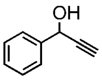
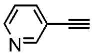
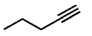
[a] *Reaction conditions:* 1-phenylethyl bromide (0.5 mmol), phenylacetylene (0.6 mmol), 12 h.

[b] Isolated yield of the *E/Z* mixture.

[c] $E/Z = 3:1$ (determined by ^1H NMR).

[d] *Conditions:* **1a** (0.5 mmol), **2a** (0.6 mmol), CH_3OH (0.6 mmol), CH_2Cl_2 (2 mL), 12 h.

Table 2. Addition of different alkynes to 1-phenylethyl bromide **1a**.[a]

Entry	Alkynes	Main product		Yield [%][b] (*E/Z*)
1		**3b**		98 (5:1)
2		**3c**		93 (5:1)
3		**3d**		77 (2:1)
4		**3e**		50 (3:1)
5		**3f**		81 (1:1)
6		–		0
7		–		0
8		–		0

[a] *Reaction conditions:* 1-phenylethyl bromide **1a** (0.5 mmol), alkyne (0.6 mmol), 5 mol% $FeCl_3 \cdot 6H_2O$, CH_2Cl_2, 50 °C, 12 h.

[b] Isolated yield of the *E/Z* mixture; the *E/Z* ratios were determined by ^1H NMR.

gave appreciably lower yields (Table 2, entries 2 and 3). Alkenyl halides can be also generated smoothly using 1,2-substituted ethynes such as 1-phenyl-1-propyne (Table 2, entry 4) and diphenylethyne (Table 2, entry 5). Propargyl alcohols, heteroarylalkynes and alkylalkynes were inactive in this reaction (Table 2, entries 6–8).

Various benzyl halides were investigated as substrates for addition to phenylacetylene under the typical conditions (Table 3). Benzyl chlorides gave moderate yields of the corresponding alkenyl chlorides, electronic and steric effects were not obvious (Table 3, entries 1–8). Benzyl bromides also gave moderate yields of the desired products without distinct inductive and steric effects besides *p*-nitrobenzyl bromide (Table 3, entries 9–14). Diphenylmethyl bromides gave excellent yields of the corresponding product (Table 3, entry 15). However, alkenyl bromide proved to be inactive in this system (Table 3, entry 16).

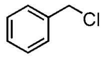
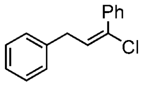
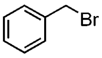
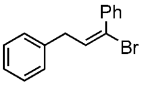
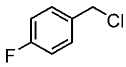
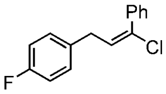
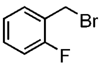
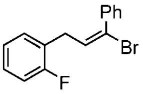
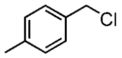
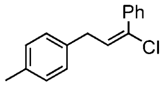
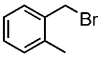
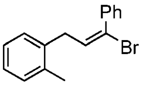
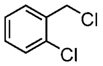
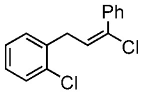
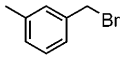
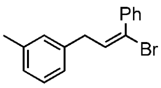
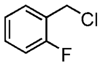
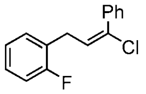
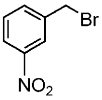
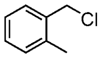
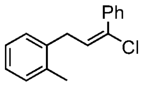
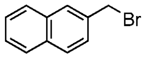
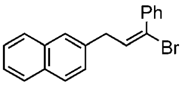
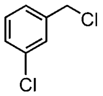
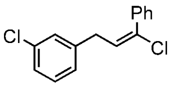
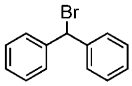
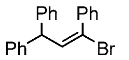
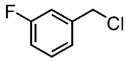
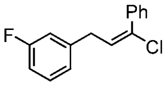
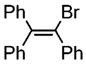
A plausible mechanism for the iron-catalyzed C–C bond formation is depicted in Scheme 2 that is similar to that of the zinc-catalyzed procedure.[4] Benzyl halides are activated by the Lewis acid to form a carbocation intermediate **1**, which attacks the electron-rich arylalkynes to generate a vinyl cation **2**. The *sp*-hybridized vinyl cation can be attacked by an $XFeCl_3$ ion to give the *E*/*Z* mixture of product and the Lewis acid which will be reused as catalyst in the next catalytic cycle.

In conclusion, this work demonstrates an efficient and mild iron-catalyzed synthesis of alkenyl halides *via* direct addition of benzyl halides to arylalkynes. Compared with the traditional system for preparing alkenyl halides by using anhydrous $ZnCl_2$ or $ZnBr_2$ which has long suffered from difficulties in handling the catalyst and moisture sensitive conditions, the present method would provide a better alternative due to its atom efficiency, sustainable catalyst and mild conditions. Extension of this system to other substrates is underway in our laboratory.

Experimental Section

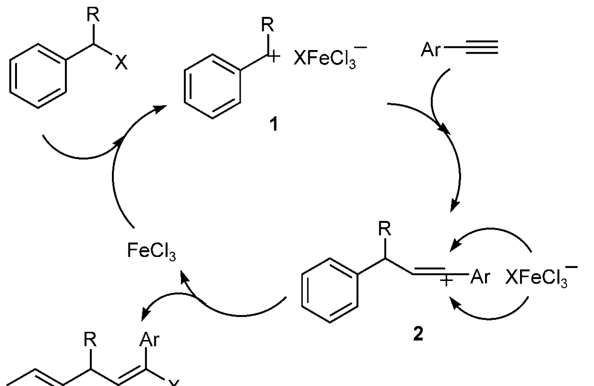
^1H and ^{13}C NMR spectra were recorded on a Varian Mercury Plus-400 spectrometer in $CDCl_3$ with TMS as internal standard. Mass spectra were determined on a Hewlett Packard 5988A spectrometer by direct inlet at 70 eV. GC-MS

Table 3. Addition of different benzyl halides to phenylacetylene.[a]

Entry	Benzyl alcohols	Major product		Yield [%][b] (*E*/*Z*)	Entry	Benzyl alcohols	Major product		Yield [%][b] (*E*/*Z*)
1		**3g**		59 (4:1)	9		**3o**		61 (10:1)
2		**3h**		61 (3:1)	10		**3p**		64 (7:1)
3		**3i**		69 (5:1)	11		**3q**		60 (3:1)
4		**3j**		61 (3:1)	12		**3r**		60 (5:1)
5		**3k**		58 (4:1)	13		–		0
6		**3l**		66 (3:1)	14		**3s**		52 (4:1)
7		**3m**		52 (2:1)	15		**3t**		98 (7:1)
8		**3n**		48 (2:1)	16		–		0

[a] *Reaction conditions:* benzyl halide (0.5 mmol), phenylacetylene (0.6 mmol), 5 mol% $FeCl_3 \cdot 6H_2O$, CH_2Cl_2, 50 °C, 12 h.

[b] Isolated yield of the *E*/*Z* mixture; the *E*/*Z* ratios were determined by ^1H NMR.



Scheme 2. A plausible mechanism for the iron-catalyzed addition of benzyl halides to aryl alkynes.

were determined using a Finnigan Trace 2000 GC/MS system. All products were identified by GC-MS, ^1H and ^{13}C NMR, MS and/or comparison with authentic samples. Chemicals and solvents were purchased from commercial sources.

Typical Procedure

1-Phenylethyl bromide (0.5 mmol, 92.5 mg) was added to a mixture of phenylacetylene (0.6 mmol, 61.2 mg) and $FeCl_3 \cdot 6H_2O$ (0.025 mmol, 6.8 mg) in 2 mL of CH_2Cl_2, then the system was heated at 50 °C for 12 h. The solvent was removed under reduced pressure and column chromatographic separation gave the *E*/*Z* mixture of the product **3a**; yield: 139.2 mg (97%).

References

[1] For recent reviews of iron-catalyzed transformations, see: a) C. Bolm, J. Legros, J. Le Paih, L. Zani, *Chem. Rev.* **2004**, *104*, 6217; b) H. Shinokubo, K. Oshima, *Eur. J. Org. Chem.* **2004**, 2081; c) A. Fürstner, R. Martin, *Chem. Lett.* **2005**, *34*, 624; d) S. Enthaler, K. Junge, M. Beller, *Angew. Chem.* **2008**, *120*, 3363; *Angew. Chem. Int. Ed.* **2008**, *47*, 3317; e) B. D. Sherry, A. Fürstner, *Acc. Chem. Res.* **2008**, DOI: 10.1021/ar800039x; f) A. Correa, O. G. Mancheño, C. Bolm, *Chem. Soc. Rev.* **2008**, *37*, 1108. For selected recent examples of C–C bond formation catalyzed by iron, see: g) F. Minisci, E. Vismara, F. Fontana, *J. Org. Chem.* **1989**, *54*, 5224; h) A. Fürstner, A. Leitner, *Angew. Chem.* **2002**, *114*, 632; *Angew. Chem. Int. Ed.* **2002**, *41*, 609; i) M. Nakamura, K. Matsuo, S.

Ito, E. Nakamura, *J. Am. Chem. Soc.* **2004**, *126*, 3686; j) R. Martin, A. Fürstner, *Angew. Chem.* **2004**, *116*, 4045; *Angew. Chem. Int. Ed.* **2004**, *43*, 3955; k) I. Iovel, K. Mertins, J. Kischel, A. Zapf, M. Beller, *Angew. Chem.* **2005**, *117*, 3981; *Angew. Chem. Int. Ed.* **2005**, *44*, 3913; l) B. Plietker, *Angew. Chem.* **2006**, *118*, 1497; *Angew. Chem. Int. Ed.* **2006**, *45*, 1469; m) Z. Lu, G. Chai, S. Ma, *J. Am. Chem. Soc.* **2007**, *129*, 14546; n) G. Cahiez, V. Habiak, C. Duplais, A. Moyeux, *Angew. Chem.* **2007**, *119*, 4442; *Angew. Chem. Int. Ed.* **2007**, *46*, 4364; o) U. Jana, S. Biswas, S. Maiti, *Tetrahedron Lett.* **2007**, *48*, 4065; p) Z. Li, L. Cao, C.-J. Li, *Angew. Chem.* **2007**, *119*, 6625; *Angew. Chem. Int. Ed.* **2007**, *46*, 6505; q) J. Kischel, K. Mertins, D. Michalik, A. Zapf, M. Beller, *Adv. Synth. Catal.* **2007**, *349*, 865; r) B. Wang, S. Xiang, Z. Sun, B. Guan, P. Hu, K. Zhao, Z. Shi, *Tetrahedron Lett.* **2008**, *49*, 4310; s) C. M. R. Volla, P. Vogel, *Angew. Chem.* **2008**, *120*, 1325; *Angew. Chem. Int. Ed.* **2008**, *47*, 1305.

[2] H. Mayr, *Angew. Chem.* **1990**, *102*, 1415; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 1371.

[3] a) F. Marcuzzi, G. Melloni, *Gazz. Chim. Ital.* **1975**, *105*, 495; b) F. Marcuzzi, G. Melloni, *J. Am. Chem. Soc.* **1976**, *98*, 3295; c) H. Mayr, J. L. Gonzalez, K. Lüdtke, *Chem. Ber.* **1994**, *127*, 525.

[4] R. Maroni, G. Melloni, G. Modena, *J. Chem. Soc. Perkin Trans. 1* **1973**, 2491.