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$FeCl_3$-Catalyzed Alkenylation of Simple Arenes with Aryl-Substituted Alkynes

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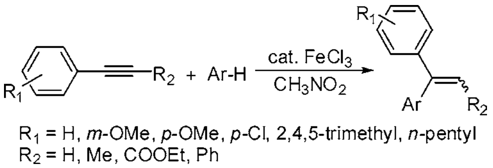
ABSTRACT



An addition of electron-rich arenes to aryl-substituted alkynes to form 1,1-diaryl alkenes is carried out in the presence of $FeCl_3$ as catalyst under mild conditions.

Functionalization of simple arenes plays an important role in the synthesis of pharmaceuticals, agrochemicals, and fine chemicals. A well-known process involving the formation of new C−C bonds from aromatic C−H bonds is the Friedel−Crafts alkylation of various arenes, especially electron-rich arenes with alkyl halides, alcohols, or alkenes.[1] On the other hand, the pioneering work on alkenylation of simple arenes was an oxidative coupling of arenes with alkenes in the presence of palladium complexes and a rhodium-catalyzed addition of aromatic and heteroaromatic compounds to alkynes in the presence of carbon monoxide.[2] Thereafter, a few efficient methods of hydroarylation of alkynes have been developed. In these processes, transition metals as catalysts including rhodium,[3] ruthenium,[4] palladium,[5] platinum,[5] gold,[6] or rare-metals[7] are normally used, and in some systems acids or ionic liquids are necessary.[5a,b,7b] However, since these catalysts are expensive or the turnover numbers of these processes are not very high, their large-scale applications are restricted.

According to our knowledge, there is no example of the alkenylation of arenes with alkynes using inexpensive catalysts through an economical and efficient method.[8] However, iron as an abundant, economical, and environmentally friendly metal shows increasing and promising catalytic abilities in many organic syntheses.[9] In one prominent case, iron has been proven to be a practical alternative catalyst in an arylation of benzyl alcohols and carboxylates, formerly catalyzed by expensive late transition metals.[9b] Herein, we report a convenient $FeCl_3$-catalyzed

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(1) (a) Olah, G. A.; Krishnamurit, R.; Prakash, G. K. S. *Friedel-Crafts Alkylations in Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, UK, 1991. (b) Carey, F.; Sundberg, R. *Advance Organic Chemistry*, 4th ed.; Kluwer Academic/Plenum Publishers: New York, 2000; Part B.

(2) (a) Moritani, I.; Fujiwara, Y. *Tetrahedron Lett.* **1967**, 1119. (b) Jia, C.; Kitamura, T.; Fujiawara, Y. *Acc. Chem. Res.* **2001**, *34*, 633. (c) Hong, P.; Cho, B.-R.; Yamazaki, H. *Chem. Lett.* **1979**, 339. (d) Hong, P.; Cho, B.-R.; Yamazaki, H. *Chem. Lett.* **1980**, 507.

(3) (a) Ritleng, V.; Sirlin, C.; Pfeffer, M. *Chem. Rev.* **2002**, *102*, 1731. (b) Boese, W. T.; Goldman, A. S. *Organometallics* **1991**, *10*, 782.

(4) (a) Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Nature* **1993**, *366*, 529. (b) Merlic, C. A.; Pauly, M. E. *J. Am. Chem. Soc.* **1996**, *118*, 11319. (c) Murakami, M.; Hori, S. *J. Am. Chem. Soc.* **2003**, *125*, 4720.

(5) (a) Jia, C.; Piao, D.; Oyamada, J.; Lu, W.; Kitamura, T.; Fujiwara, Y. *Science* **2000**, *287*, 1992. (b) Jia, C.; Lu, W.; Oyamada, J.; Kitamura, T.; Matsuda, K.; Irie, M.; Fujiwara, Y. *J. Am. Chem. Soc.* **2000**, *122*, 7252. (c) Lu, W.; Jia, C.; Kitamura, T.; Fujiwara, Y. *Org. Lett.* **2000**, *2*, 2927.

(6) (a) Reetz, M. T.; Sommer, K. *Eur. J. Org. Chem.* **2003**, 3485. (b) Shi, Z.; He, C. *J. Org. Chem.* **2004**, *69*, 3669. (c) Ne-vado, C.; Echavarren, A. M. *Chem. Eur. J.* **2005**, *11*, 3155.

(7) (a) Tsuchimoto, T.; Maeda, T.; Shirakawa, E.; Kawakami, Y. *Chem. Commun.* **2000**, 1573. (b) Song, C.; Jung, D.; Choung, S.; Roh, E.; Lee, S. *Angew. Chem.* **2004**, *116*, 6309; *Angew. Chem., Int. Ed.* **2004**, *43*, 6183.

(8) Ni(0)-catalyzed alkenylation of heteroarenes. See: Nakao, Y.; Kanyiva, K.; Oda, S.; Hiyama, T. *J. Am. Chem. Soc.* **2006**, *128*, 8146.

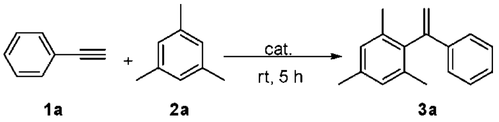
(9) (a) Bolm, C.; Legros, J.; Paih, J.; Zani, L. *Chem. Rev.* **2004**, *104*, 6217. (b) Jovel, I.; Mertins, K.; Kischel, J.; Zapf, A.; Beller, M. *Angew. Chem.* **2005**, *117*, 3981; *Angew. Chem., Int. Ed.* **2005**, *44*, 3913. (c) Kischel, J.; Jovel, I.; Mertins, K.; Zapf, A.; Beller, M. *Org. Lett.* **2006**, *8*, 19. (d) Nakamura, M.; Hirai, A.; Nakamura, E. *J. Am. Chem. Soc.* **2000**, *122*, 978. (e) Komeyama, K.; Morimoto, T.; Takaki, K. *Angew. Chem.* **2006**, *118*, 3004; *Angew. Chem., Int. Ed.* **2006**, *45*, 2938.

10.1021/ol070737u CCC: \$37.00

alkenylation of electron-rich arenes with aryl-substituted alkynes under mild conditions, which is a Friedel−Crafts-type process.

Initially, we tried to seek an effective system for the alkenylation of phenylacetylene **1a** with mesitylene **2a** to produce 1-mesityl-1-phenylethene **3a** (Table 1). After screening a variety of catalysts under the same conditions, we found that the target product was prepared in a good yield just in the case of $FeCl_3$ as the catalyst (Table 1, entry 1). Although the conversions are very high in the presence of $Pd(OAc)_2$ or $PdCl_2$, a number of oligomers or polymers were detected instead of the target product (Table 1, entries 11 and 12). In contrast, almost no alkenylation reaction occurred with other catalysts or without any catalyst.

Table 1. Alkenylation of Mesitylene with Phenylacetylene in the Presence of Various Catalysts[a]

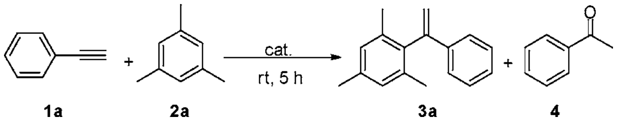


entry	catalyst	time [h]	yield [%]	convn [%]
1	$FeCl_3$	5	86	>99
2	$FeCl_2{\cdot}4H_2O$	5	0	0
3	$Fe(NO_3)_3{\cdot}9H_2O$	24	0	0
4	$BiCl_3$	5	0	0
5	$CuCl_2{\cdot}2H_2O$	24	0	0
6	$ZnCl_2$	24	7	
7	$CoCl_2{\cdot}6H_2O$	24	0	trace
8	$NiCl_2{\cdot}6H_2O$	24	0	trace
9	AgOAc	5	0	0
10[b]	$PtCl_2$	5	0	0
11[b]	$Pd(OAc)_2$	5	0	>99
12[b]	$PdCl_2$	5	0	>99
13[b]	$FeCl_3$	5	35	43
14[c]	HCl	5	0	0
15	none	5	0	0

[a] Conditions: phenylacetlyene **1a** (1.0 mmol), mesitylene **2a** (3.0 mmol), cat. (0.1 mmol, 10 mol %), CH_3NO_2 (0.5 mL), rt; GC analysis. [b] Conditions: cat. (0.05 mmol, 5 mol %). [c] Conditions: cat. (0.30 mmol, 30 mol %).

Moreover, the effect of solvents on this addition reaction was also studied (Table 2). Compared with other solvents, nitromethane (CH_3NO_2) could improve the $FeCl_3$-catalyzed alkenylation efficiently (Table 2, entries 1−8). In addition, the amount of CH_3NO_2 also dramatically influenced this reaction (Table 2, entries 10−13). These adducts were obtained in poor yields (21−33%) in either a small or a large amount of CH_3NO_2 (Table 2, entries 10 and 13). Interestingly, a good yield (86%) of **3a** was detected by GC when 0.5 mL of CH_3NO_2 was used in the presence of 0.1 mmol of $FeCl_3$ in this reaction (Table 2, entry 1). At the same time, acetophenone **4**, a byproduct in 11% yield, was also observed, which might be from the reaction of **1a** with a trace of water in solution. However, when 0.5 mmol of water was added into the reaction, the amount of byproduct did not increase apparently (Table 2, entry 9). This may suggest that this alkenylation can proceed very well without any special treatment of substrates and solvents.

Table 2. Effect of Solvents in $FeCl_3$-Catalyzed Alkenylation of Mesitylene with Phenylacetylene[a]



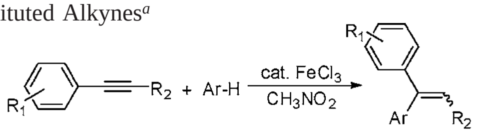
			yield [%]		
entry	**2a** [mmol]	solvent [mL]	3a	4	convn [%]
1	3.0	CH_3NO_2	86	11	>99
2	3.0	CH_2Cl_2	23	5	36
3	3.0	CH_2ClCH_2Cl	30	10	60
4	3.0	$PhNO_2$	41	9	75
5	3.0	CH_3CN	3		
6	3.0	CH_3COOH	6		
7	3.0	CH_3OH	0		
8	3.0	none	10		
9[b]	3.0	CH_3NO_2	85	9	94
10	3.0	CH_3NO_2 (0.05)	33	7	58
11	3.0	CH_3NO_2 (0.25)	72	8	>99
12	3.0	CH_3NO_2 (1.0)	74	16	>99
13	3.0	CH_3NO_2 (2.0)	21	7	29
14	1.0	CH_3NO_2	71	14	>99
15	6.0	CH_3NO_2	85	14	>99

[a] Conditions: phenylacetlyene **1a** (1.0 mmol), mesitylene **2a** (3.0 mmol), $FeCl_3$ (0.1 mmol, 10 mol %), solvent (0.5 mL), rt, 5 h; GC analysis. [b] H_2O (0.5 mmol) was added.

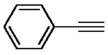
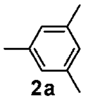
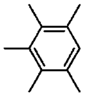
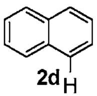
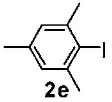
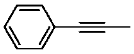
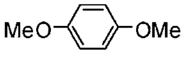
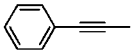
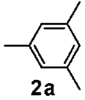
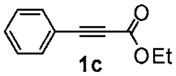
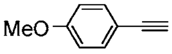
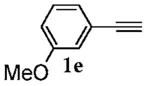
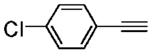
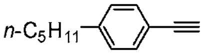
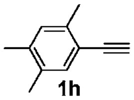
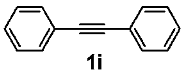
Meanwhile, a moderate excess of **2a** could enhance the selectivity of this alkenylation of arene under the same conditions. And, if the ratio of **2a** to **1a** was larger than 3, the selectivity of this reaction would not be improved further (Table 2, entries 1, 14, and 15).

On the basis of the optimization of the reaction conditions, the scope of this $FeCl_3$-catalyzed alkenylation of simple arenes with various alkynes was explored. For arenes, both mesitylene **2a** and pentamethylbenzene **2b** could react with **1a** to give the corresponding adducts respectively in good yields after a short time (Table 3, entries 1 and 2). In the case of *p*-xylene **2c**, heating was needed to accelerate the reaction rate and to increase the yield (Table 3, entry 3). However, for benzene **2g**, not only heating but also a stable internal alkyne, diphenyl acetylene **1i**, were necessary to give the adduct in a poor yield of only 11% (Table 3, entry 15). In contrast, diphenyl acetylene **1i** could be hydroarylated by **2a** to give its product in an isolated yield of 51% at 80 °C (Table 3, entry 14). A more electron-rich arene, 1,4-dimethoxybenzene **2f**, reacted with another internal alkyne **1b** very easily and a quantitive yield of product **3f** was detected by GC (Table 3, entry 6). Moreover, the desired products **3e** in an isolated yield of 41% were obtained from the addition of iodomesitylene **2e** to **1a** and these iodo-substituted groups of phenyl rings were not affected during the reaction (Table 3, entry 5). Overall, electron-rich arenes are still more active ones in these alkenylations. On the other

Table 3. FeCl$_3$-Catalyzed Alkenylation of Various Arenes with Aryl-Substituted Alkynes[a]



1a-i + **2a-g** → **3a-o**

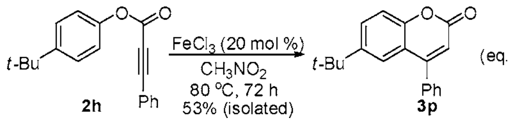
entry	alkyne	arene	time [h]	yield [%][b] Z/E
1	 **1a**	 **2a**	5	**3a** 78 (86)
2	**1a**	 **2b**	5	**3b** 79 (87)
3[c]	**1a**	 **2c**	5	**3c** 80 (93)
4[d]	**1a**	 **2d**	5	**3d** (52)
5[e]	**1a**	 **2e**	12	**3e** 41
6[c]	 **1b**	 **2f**	5	**3f** (>99) 85/15[h]
7[c]	 **1b**	 **2a**	5	**3g** 68 86/14
8[f]	 **1c**	**2a**	38	**3h** 42 94/6
9	 **1d**	**2a**	5	**3i** 87 (>99)
10	 **1e**	**2a**	5	**3j** 62
11	 **1f**	**2a**	6	**3k** 69 (77)
12	 **1g**	**2a**	6	**3l** (68)
13	 **1h**	**2a**	6	**3m** 86 (95)
14[g]	 **1i**	**2a**	20	**3n** 51 40/60[h]
15[f,i]	**1i**	 **2g**	17	**3o** 11

[a] Conditions: alkyne (1.0 mmol), arene (3.0 mmol), FeCl$_3$ (0.1 mmol, 10 mol %), CH$_3$NO$_2$ (0.5 mL), rt; GC analysis. [b] Isolated yield (GC yield in parentheses) based on the alkyne. Z/E ratios were determined by ^{1}H NMR spectroscopy. [c] 60 °C. [d] CH$_3$NO$_2$ (1.0 mL). [e] 40 °C. [f] Conditions: 80 °C, FeCl$_3$ (0.2 mmol, 20 mol %). [g] Conditions: 80 °C, conversion: 68%. [h] Double bond structure was not identified. [i] Conversion: 36%.

hand, all adducts are 1,1-diaryl alkenes, which shows an excellent regioselectivity of this addition reaction.

For alkynes, various terminal aryl-substituted alkynes were favorable to react with **2a** to give adducts in moderate or excellent yields (Table 3, entries 9−13). These different terminal aryl-substituted alkynes could not influence the efficiency of the addition reaction seriously. However, in the alkenylations of **2a**, an internal alkyne, 1-phenylpropyne **1b** compared with phenylacetylene **1a**, its product yield decreased a little and Z/E isomers were formed (Table 3, entries 1 and 7). Further, another internal alkyne with an electron-poor substituted group, ethyl 3-phenylpropiolate **1c**, became an inactive one in the same reaction even at high temperature in a long reaction time (Table 3, entry 8). One reason is attributed to the electron insufficiency of the triple bond besides the steric hindrance.

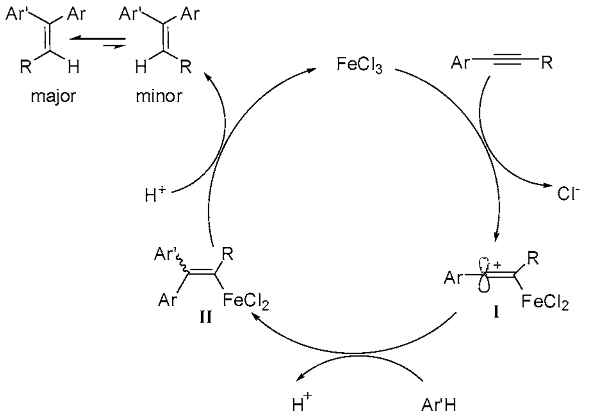
Moreover, an intramolecular alkenylation of arene in the presence of FeCl$_3$ was tested. One example is the cyclization of 4′-*tert*-butylphenyl phenylpropiolate **2h** catalyzed by FeCl$_3$ to form 4-phenyl-6-*tert*-butylcoumarin **3p** in a moderate yield of 53%, which indicates that the intramolecular version of this alkenylation is also feasible (eq 1).



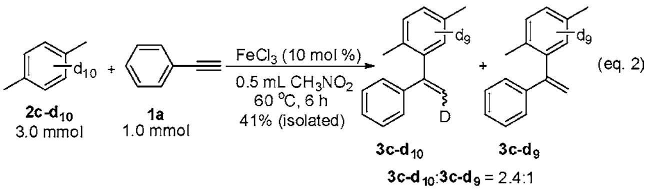
2h **3p**

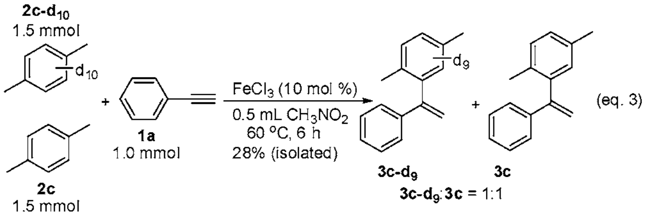
A proposed mechanism of this alkenylation of electron-rich arenes with aryl-substituted alkynes is shown in Scheme 1. It is thought to be a Friedel−Crafts-type process,[6a,7a] which is different from some of other hydroarylations via aromatic C−H activation.[5c,8] The first step is the formation of a more stable aryl-substituted alkenyl cation **I** by the FeCl$_3$ as Lewis acid attacking an aryl-substituted alkyne. Subsequently, an electrophilic aromatic substitution occurs between the alkenyl cation **I** and an arene to produce an intermediate **II** in excellent regioselectivity. Finally, after the protonation and isomerization of the intermediate **II**,[7a] the target adduct 1,1-

Scheme 1. Possible Mechanism of FeCl$_3$-Catalyzed Alkenylation of Arenes with Aryl-Substituted Alkynes



diaryl alkene is prepared and the iron catalyst cycle is complete as well. However, the result of an isotope exchange indicates that the vinyl protons are not only from arenes at the protonation step of this reaction since the formation of **3c**-*d*$_9$ is observed (eq 2). Furthermore, no deuterated product was found in the reacton of **2c** with **1a** in CD_3NO_2; this may suggest that CH_3NO_2 does not provide protons in this reaction.





Meanwhile, the kinetic isotope effect experiments of **2c**/**2c**-*d*$_{10}$ with **1a** have also confirmed the proposed mechanism further (eq 3). The k_H/k_D (ca. 1.0)[10] calculated is consistent with an intermolecular electrophilic aromatic substitution, which does not usually exhibit a primary kinetic isotope effect.[11] Furthermore, to eliminate the possible effect of concentration fluctuation, **1a** was used to react with **2c**-*d*$_{10}$ and **2c** respectively in the presence of 3 mol % of $FeCl_3$ at room temperature and the reaction processes were monitored by GC analysis. On the basis of the initial rates of these two separate reactions (Figure 1), a similar k_H/k_D (ca. 0.98) is obtained to support the possible mechanism.

In addition, since neither loss of the aromatic hydrogen of **2a** nor D−H exchange between **2c**-*d*$_{10}$ and CH_3NO_2/H_2O were observed by ^1H NMR in the presence of $FeCl_3$ under reaction conditions, this alkenylation may not involve an aromatic C−H activation.

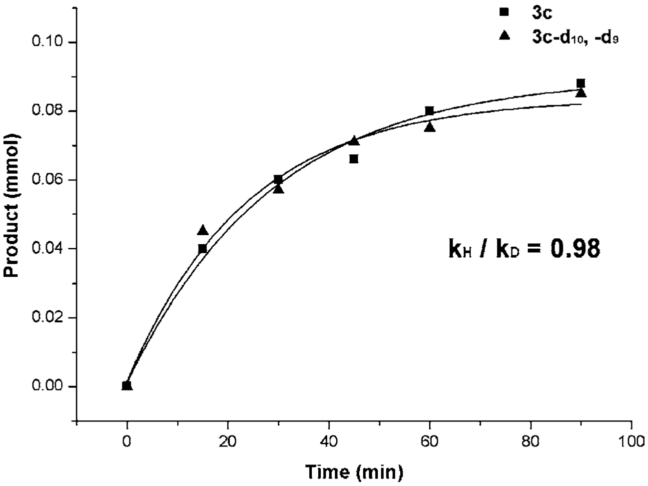


Figure 1. The time dependence of the amount of products in two separate reactions of xylene-*d*$_{10}$ (**3c**-*d*$_{10}$, 3 mmol) or xylene (**3c**, 3 mmol) with phenylacetylene (**1a**, 1 mmol) in the presence of 3 mol % of $FeCl_3$ at room temperature.

In conclusion, we have developed a novel system on the alkenylation of electron-rich arenes with aryl-substituted alkynes under mild conditions. This $FeCl_3$-catalyzed method reported here has common benefits in other iron-catalyzed reactions, which are convenient, economic, and envirometally friendly. In addition, since this reaction is runing at room temperature or low heating temperature without adding acids or special reagents, its large-scale application is also possible. Extending the scope of this inter- and intramolecular alkenylation of arenes with alkynes through a Friedel−Crafts-type process is ongoing.

Acknowledgment. We thank the National Natural Science Foundation of China (20572069) and the Scientific Research Foundation for the Returned Overseas Chinese Scholars, State Education Ministry for financial support.

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

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[10] The value of k_H/k_D was calculated only by the amounts of arene protons.

[11] Tunge, J. A.; Forsee, L. N. *Organometallics* **2005**, *24*, 6440.