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Thermodynamically- and kinetically-controlled Friedel–Crafts alkenylation of arenes with alkynes using an acidic fluoroantimonate(V) ionic liquid as catalyst†

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Received (in Cambridge, UK) 16th April 2007, Accepted 11th July 2007
First published as an Advance Article on the web 31st July 2007
DOI: 10.1039/b705719a

By employing superacidic fluoroantimonate ionic liquid (IL), [bmim][Sb_2F_{11}], as catalyst, not only thermodynamically-controlled but also kinetically-controlled Friedel–Crafts alkenylations of arenes with alkynes have been realized for the first time.

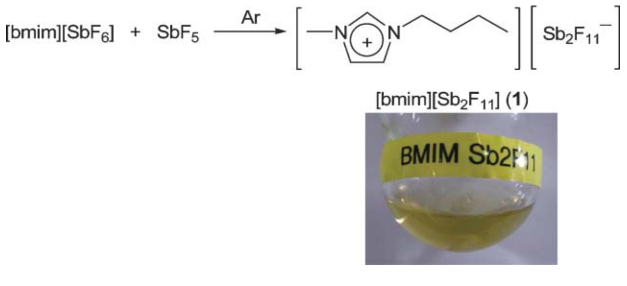
The hydroarylation of alkynes (also known as alkenylation of arenes) catalyzed by transition metal complexes, thereby affording styrene derivatives, has recently received much research attention because this approach is, in principle, simpler than those based on Heck reactions, cross coupling reactions, and olefin cross-metathesis reactions.[1] Depending on the type of interaction between the metal catalyst and the arene or the triple bond, the hydroarylation of alkynes proceeds either *via* σ-aryl–metal species or *via* alkenyl cation intermediates. Using Pd(II), Pt(II) and Au(III) catalysts, σ-aryl–metal species were proposed as intermediates.[2,3] On the other hand, the Friedel–Crafts-type reaction, which proceeds *via* an alkenyl cation intermediate followed by its electrophilic attack on an arene, can be promoted by Lewis acid catalysts.[4,5]

Despite the recent intensive research on this reaction, all catalyst systems reported so far (*e.g.*, Pd(II),[2] Pt(II),[2] Au(III),[3] Sc(III),[4] *etc.*) display narrow substrate scope and low catalytic activity, giving mainly thermodynamically favored isomers. For example, using Pd, Pt or Au catalysts, acceptable yields were obtained usually with highly electron-rich arenes with more than two electron-donating substituents.[2,3] Moreover, internal alkynes showed almost no reactivity with Au catalysts.[3a] The catalytic activity of metal triflates such as $Sc(OTf)_3$ was also very low and thus the reaction of benzene and phenylacetylene in the presence of 10 mol% of $Sc(OTf)_3$ at 85 °C required 186 h.[4] Moreover, $Sc(OTf)_3$ was totally inactive towards electron-deficient alkynes such as *p*-CF_3–phenylacetylene and *p*-Cl–phenylacetylene. Although the substrate scope of metal triflate-catalyzed alkenylation was broadened by employing an ionic liquid (IL),[5] the activity of this catalyst system is not still high enough to conduct the reaction at low temperature, which is desirable to obtain kinetically-controlled products. Therefore, the development of a new and strongly active catalyst system for hydroarylation of alkynes that works even under kinetic conditions (*i.e.*, at low temperatures) is highly desirable.

Herein we report that superacidic fluoroantimonate(V) ionic liquid (IL), [bmim][Sb_2F_{11}] **1** (bmim = 1-butyl-3-methylimidazolium), exhibited the unprecedented high catalytic activity for the Friedel–Crafts alkenylation of a broad scope of arenes with terminal and internal alkynes. Moreover, by employing the superacidic IL **1** as catalyst, not only thermodynamically-controlled but also kinetically-controlled Friedel–Crafts alkenylation of arenes with alkynes has been realized for the first time.

It has been well known that acidic chloroaluminate(III) ILs, *e.g.*, [bmim][Al_2Cl_7], exhibit strong catalytic activities in many organic reactions due to the super Lewis acidity of their anions.[6] Therefore, we envisioned that the anions of the fluoroantimonate ILs, *e.g.*, [bmim][Sb_2F_{11}], would be more powerful Lewis acid sources than chloroaluminate anions. Thus, we prepared a pale-yellow colored superacidic ionic liquid **1**[7] simply by mixing [bmim][SbF_6] with one equivalent of SbF_5 under an argon atmosphere at 0 °C (Scheme 1, for experimental procedure and characterization data, see ESI†) and investigated its catalytic activity for the alkenylation of arenes.

We first examined the reactions of *p*-xylene with the challenging, electron-deficient alkynes such as *p*-Cl– and *p*-CF_3–phenylacetylene using 5 mol% of **1** at 90 °C. The results are summarized in Table 1, together with the reported data obtained with other catalyst systems. As shown in Table 1, the fluoroantimonate IL **1** showed surprisingly high catalytic activity and, thus, the reactions (entries 5 and 9) proceeded within 30 min, which is significantly faster than those using the other catalyst systems. Other reported catalyst systems such as $AuCl_3$–$AgSbF_6$[3a] (entry 1) and $Sc(OTf)_3$[4] (entries 2 and 6) were shown to be nearly inactive. Notably, the superacidic chloroaluminate(III) IL, [bmim][Al_2Cl_7] also showed no catalytic activity with the electron-deficient alkynes (entries 4 and 8). Although the same reactions using $Sc(OTf)_3$–[bmim][SbF_6] afforded the desired adducts in satisfactory yields, much longer reaction times were required (12 and 22 h, entries 3 and 7, respectively).[5a]



Scheme 1 Preparation of fluoroantimonate IL **1**.

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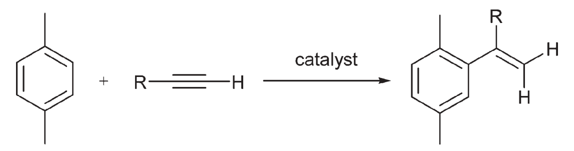
† Electronic supplementary information (ESI) available: Experimental procedure and characterization data for all compounds. See DOI: 10.1039/b705719a

Table 1 Activities of various catalytic systems for Friedel–Crafts alkenylation of *p*-xylene with electron-deficient terminal alkynes



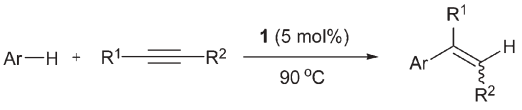
Entry	R	Catalyst	Time	Yield (%)[a] (TOF/h)
1[b]	*p*-ClPh	$AuCl_3$–$AgSbF_6$	4 h	28 (4.6)
2[c]	*p*-ClPh	$Sc(OTf)_3$	15 h	NR (0)
3[d]	*p*-ClPh	$Sc(OTf)_3$–[bmim][SbF_6]	12 h	63 (0.5)
4[e]	*p*-ClPh	[bmim][Al_2Cl_7]	1 h	NR (0)
5[f]	*p*-ClPh	**1**	10 min	71 (85.2)
6[c]	*p*-CF_3Ph	$Sc(OTf)_3$	15 h	NR (0)
7[d]	*p*-CF_3Ph	$Sc(OTf)_3$–[bmim][SbF_6]	22 h	73 (0.3)
8[e]	*p*-CF_3Ph	[bmim][Al_2Cl_7]	1 h	NR (0)
9[f]	*p*-CF_3Ph	**1**	30 min	90 (36)

[a] Isolated yields based on alkyne. [b] From ref. 3*a* (using 1.5 mol% catalyst): GC yield (not isolated). [c] From ref. 4 (using 10 mol% catalyst). [d] From ref. 5*a* (using 10 mol% catalyst). [e] The reaction was carried out at 90 °C using alkyne (1 mmol) and arene (6 mL) in the presence of [bmim][Al_2Cl_7] (5 mol%). [f] The reaction was carried out at 90 °C using alkyne (1 mmol) and arene (6 mL) in the presence of **1** (5 mol%), NR = no reaction.

Following these encouraging results, we carried out a series of alkenylations of various electron-rich and electron-poor arenes (benzene, *p*-xylene, mesitylene, pentamethylbenzene, *p*-chlorotoluene and chlorobenzene) with various terminal and internal alkynes using 5 mol% of **1** at 90 °C to survey the scope of our protocol. As shown from the results in Table 2, all reactions with aryl-substituted terminal alkynes were completed within a few to 30 min, affording the corresponding alkenylated products in good to excellent yields with perfect regioselectivity in favor of the Markovnikov-type 1,1-product (entries 1–4 and 7–9). The perfect regiochemistry can be attributed to the conjugative stabilizing effect of the α-aryl group on the vinyl cation intermediate. The reactions of arenes with a terminal alkyne conjugated to an electron-withdrawing group (–COMe), 3-butyn-2-one, also proceeded very fast in regio- and stereoselective manner, giving thermodynamically favored β-aryl-substituted *trans*-alkene, (*E*)-4-aryl 3-buten-2-ones, nearly as sole products (entries 10 and 13). Moreover, all reactions of internal alkynes with arenes also proceeded smoothly with high regio- and stereoselectivity, even with electron-poor arenes (*e.g.*, *p*-chlorotoluene, chlorobenzene), affording the corresponding adducts with very high (*Z*)-selectivity[8] (*Z* : *E*-ratio = up to 99 : 1) (entries 5–6, 11–12 and 14–15). Previously, our group[5] and Tsuchimoto's group[4] observed that the composition of stereoisomers at the initial stage of the reaction gradually changed over time *via* Lewis acid-catalyzed isomerization, yielding thermodynamically-favored isomer as the major product at the end of the reaction. In fact, most reactions in Table 2 were completed within 10 min to afford the products, albeit with lower (*Z*)/(*E*)-ratios. Thus, the reaction times were prolonged to obtain higher (*Z*)/(*E*)-ratios. For example, the reaction of mesitylene with 1-phenyl-1-propyne at 90 °C was completed in 5 min to give a mixture of (*Z*)- and (*E*)-1-mesityl-1-phenyl-1-propene in 70 : 30 ratio. The (*Z*) : (*E*) ratio of 99 : 1 was obtained from the same reaction mixture when the reaction time was prolonged to 30 min (entry 11).

Having an extremely active catalyst **1** in hand, finally we investigated the possibility of obtaining the kinetically-controlled stereoisomer. For this goal, the reactions were carried out using

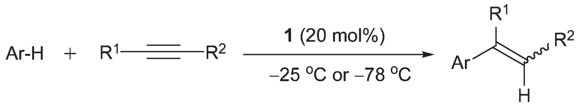
Table 2 Friedel–Crafts alkenylation of arenes with various alkynes catalyzed by the superacidic fluoroantimonate IL **1**[a]



Entry	Ar–H	R^1	R^2	Time	Yield (%)[b]	*E* : *Z*-ratio[c]
1	Benzene	Ph	H	5 min	57	—
2	Benzene	*p*-ClPh	H	20 min	68	—
3	Benzene	*p*-CF_3Ph	H	30 min	53	—
4	*p*-Xylene	Ph	H	5 min	74	—
5	*p*-Xylene	Ph	Me	30 min	89	7 : 93
6	*p*-Xylene	Ph	Ph	30 min	89	9 : 91
7	Mesitylene	Ph	H	5 min	79	—
8	Mesitylene	*p*-ClPh	H	5 min	84	—
9	Mesitylene	*p*-CF_3Ph	H	5 min	90	—
10	Mesitylene	H	COMe	30 min	88	98 : 2
11	Mesitylene	Ph	Me	30 min	81	1 : 99
12	Mesitylene	Ph	Ph	2 h	87	2 : 98
13[d]	Pentamethylbenzene	H	COMe	30 min	65	94 : 6
14[e]	*p*-Chlorotoluene	Ph	Me	30 min	28 (*o*)	7 : 93
					30 (*m*)	10 : 90
15[f]	Chlorobenzene	Ph	Me	30 min	35 (*o*)	17 : 83
					31 (*p*)	1 : 1[9]

[a] Unless otherwise indicated all reactions were carried out using alkyne (1 mmol), and arene (6 mL) in the presence of **1** (5 mol%) as catalyst at 90 °C. [b] Isolated yield based on the alkyne. [c] *E* : *Z* ratios were determined by GC/MS and NMR spectroscopy, and *E*/*Z* configurations of products were established on the basis of differential NOE experiments (see ESI). [d] 1 Equivalent of solid arene based on alkyne (1 mmol) and 4 mL of 1,2-dichloroethane as a co-solvent were used. [e] The reaction gave the mixture of *ortho*- and *meta*-regioisomers to the methyl group of *p*-chlorotoluene, including the corresponding (*E*)/(*Z*) isomers. [f] The reaction gave the mixture of *ortho*- and *para*-regioisomers, including the corresponding (*E*)/(*Z*) isomers.

Table 3 Kinetically-controlled Friedel–Crafts alkenylation of arenes with internal alkynes catalyzed by the superacidic fluoroantimonate IL **1**[a]



Entry	Ar–H	R^1	R^2	Temperature/°C	Time/min	Yield (%)[b]	*E* : *Z*- ratio[c]
1	*p*-Xylene	Ph	Ph	−25	10	47[11]	93 : 7
2	Mesitylene	Ph	Me	−78	15	72	86 : 14
3	Mesitylene	Ph	Ph	−25	15	76	94 : 6
4	Pentamethylbenzene	Ph	Me	−78	5	48[11]	95 : 5
5	Pentamethylbenzene	Ph	Ph	−25	5	87	91 : 9

[a] For detailed experimental conditions, see ESI. [b] Isolated yield based on the alkyne. [c] *E* : *Z* ratios were determined by GC/MS and NMR spectroscopy, and the *E*/*Z* configurations of products were established on the basis of differential NOE experiments (see ESI).

20 mol%[10] of catalyst at low temperatures. Quite surprisingly, the reactions proceeded very fast even at −78 °C, affording the desired kinetically favored product as a major isomer in good yields (Table 3). For example, the reaction of mesitylene with 1,2-diphenylacetylene at −25 °C afforded the adduct with an *E* : *Z* ratio of 94 : 6 (entry 3), whereas the *E* : *Z* ratio of product at 90 °C was 2 : 98 (entry 12 in Table 2). Although a substoichiometric amount (20 mol%)[10] of **1** is still needed, to our knowledge, this is the first example for not only thermodynamically-controlled but also kinetically-controlled Friedel–Crafts alkenylation of arenes with alkynes.

In conclusion, by employing superacidic fluoroantimonate(V) IL **1** as catalyst, not only thermodynamically-controlled but also kinetically-controlled Friedel–Crafts alkenylation of arenes with alkynes has been realized for the first time. The fluoroantimonate IL **1** showed unprecedented high catalytic activity, and thus, by using 5 mol% of **1** most reactions were completed within 30 min at 90 °C, affording the thermodynamically-controlled isomers as the main products. More surprisingly, the catalytic activity of acidic fluoroantimonate IL was shown to be strong enough to conduct the reactions even at −78 °C, and thus, by using 20 mol% of catalyst, the desired kinetic isomers could be obtained as the main products. Studies on the applications of superacidic fluoroantimonate(V) IL **1** to other catalytic organic reactions are currently underway in our laboratory.

This work was supported by grants KRF-2005-005-J11901 (MOEHRD), R01-2006-000-10426-0 (KOSEF), and R11-2005-008-00000-0 (SRC program of MOST/KOSEF).

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7 In the case of chloroaluminate IL, ^{27}Al NMR spectral studies showed the predominance of $Al_2Cl_7^-$ anion in the mixure of [bmim]Cl and $AlCl_3$ in 1 : 2 molar ratio (*i.e.*, 1 : 1 mixture of [bmim][$AlCl_4$] and $AlCl_3$), see: S. J. Nara, J. R. Harjani and M. M. Salunkhe, *J. Org. Chem.*, 2001, **66**, 8616–8620. Similar to this, FAB-MS analysis of **1** clearly showed the existence of $Sb_2F_{11}^-$ anion as the main acidic component (see ESI†).

8 In their previous study,[2] Fujiwara *et al.* assigned the (*Z*)-isomers of trisubstituted alkenes obtained in their work as the kinetic products. However, our MP2/6-31G* calculation results[5b] of both stereoisomers clearly indicate that the (*Z*)-isomers obtained in this study are thermodynamically favored products. In addition, Tsuchimoto *et al.*'s[4] and our experimental data[5] signify that the (*Z*)-isomers are thermodynamically-controlled products rather than kinetically-controlled ones.

9 The non-stereoselectivity of *para*-isomers may be due to the similar energy levels of *E*/*Z*-isomers.

10 Using 5 mol% of **1** at low temperature, the prolonged reaction times were needed to complete the reaction, which resulted in lower (*E*)/(*Z*)-ratios, due to Lewis acid-catalyzed isomerization.

11 Yields could be improved with prolonged reaction time. However, lower (*E*)/(*Z*)-ratios were observed due to Lewis acid-catalyzed isomerization.