**Synthetic Methods**

# Dramatic Enhancement of Catalytic Activity in an Ionic Liquid: Highly Practical Friedel–Crafts Alkenylation of Arenes with Alkynes Catalyzed by Metal Triflates**

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The Friedel–Crafts alkylation of aromatic compounds with alkenes is one of the fundamental methods for incorporating carbon skeletons into aromatic systems and, thus, has been extensively studied and is well established.[1] In contrast, the corresponding alkenylation process with alkynes still remains to be solved. One major drawback from the direct Friedel–Crafts alkenylation of arenes is alkyne polymerization, which results in the formation of a variety of undesirable side products.[2] Well-known Lewis acidic metal chlorides, such as $ZrCl_4$ and $AlCl_3$, produce the desired alkenylated products but in extremely low yields (for example, 1 and 6% yields of 1-phenyl-1-(p-xylyl)ethene for the reaction of p-xylene with phenylacetylene at 85 °C, respectively).[3] Recently, a number of catalysts, such as the solid acid zeolite HSZ-360,[4] phenoxymagnesium bromide,[5] and $SnCl_4$/$NBu_3$,[6] were found to be active for the *ortho* selective alkenylation of phenols with a limited range of alkynes (only aryl-substituted terminal alkynes underwent this reaction). It has been also found that $GaCl_3$ can promote the alkenylation of arenes with silylethyne, but excessive amounts of this Lewis acid (3 equiv) are required.[7] Recently, Tsuchimoto et al. made a breakthrough on this important reaction by finding that some metal triflates [$M(OTf)_n$; M = Sc, Zr, In] catalyze the alkenylation of arenes with internal alkynes as well as terminal alkynes through an alkenyl cation intermediate.[3] However, the catalytic activity of these metal triflates is far too low for preparative use. For example, the reaction of benzene and phenylacetylene in the presence of 10 mol% of $Sc(OTf)_3$ at 85 °C requires 186 hours to give 1,1-diphenylethene in 73% yield.[3] Moreover, $Sc(OTf)_3$ was totally inactive for electron-deficient alkynes, such as p-trifluoromethylphenylacetylene and p-chlorophenylacetylene. Therefore, a more efficient and practical catalytic system for Friedel–Crafts alkenylation is still highly desirable. Herein, we report that the use of ionic liquids in Friedel–Crafts alkenylations of aromatic compounds by alkynes catalyzed by metal triflates not only enhanced catalytic activity markedly but also decreased by-product formation, which resulted in higher yields of the monoalkenylated arenes. Moreover, in some cases, reactions that do not usually occur in conventional organic solvents were found to proceed smoothly in ionic liquids.

Room-temperature ionic liquids (RTILs) are now regarded as eco-friendly alternatives to volatile organic solvents in chemical processes.[8] During the course of our extensive efforts on the utilization of RTILs in various catalytic reactions, we found that switching from an organic solvent to an ionic liquid often resulted in significant improvements in catalytic performance (for example, increased reaction rates, improved selectivities, etc.) as well as catalyst recycling.[9] Recently, we found that the $Sc(OTf)_3$-catalyzed Friedel–Crafts alkylation of aromatic compounds with alkenes is dramatically accelerated in the presence of hydrophobic ionic liquids, such as [bmim][$PF_6$] or [bmim][$SbF_6$] (bmim = 1-butyl-3-methylimidazolium).[9a] This result encouraged us to investigate the metal triflate catalyzed Friedel–Crafts alkenylation of aromatics with alkynes in ionic liquids.
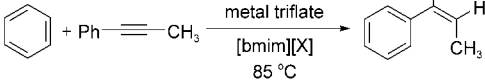


[bmim][X] (X = $PF_6$, $SbF_6$)
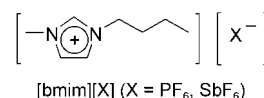
To investigate the effect of ionic liquids on the catalytic activity of metal triflates in Friedel–Crafts alkenylation we first examined the reaction between benzene and 1-phenyl-1-propyne under various conditions (Table 1).

As observed by Tsuchimoto et al.,[3] the alkenylation of benzene with 1-phenyl-1-propyne in the presence of 10 mol% of $Sc(OTf)_3$ without an ionic liquid proceeded very slowly with a yield of only 27% after 96 hours (entry 1). Moreover, this long reaction time resulted in increased the formation of undesired side products. On the other hand, when the reaction was carried out in hydrophobic ionic liquids, such as [bmim][$PF_6$] or [bmim][$SbF_6$], the catalytic activity of $Sc(OTf)_3$ was dramatically enhanced: the reaction was completed within 4 hours to afford the desired product (1,1-diphenyl-1-propene) in excellent yields (91 or 90%, respectively; entries 2 and 3).[10,11] Among the various metal triflates investigated for catalytic activity, indium triflate, hafnium triflate, and yttrium triflate in particular were found to exhibit higher activity than scandium triflate, with the reaction completed within 2.5, 1, and 2 hours, respectively (entries 4, 7, and 10). The reactions proceeded smoothly with excellent yields even in the presence of smaller amounts of these metal triflates (5 and 2.5 mol%; entries 5, 6, 8, and 9). Ytterbium triflate and lutetium triflate also exhibited similar catalytic acivities to that of scandium triflate (entries 11 and 12). This

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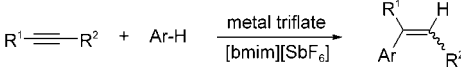Fax: (+82) 2-958-5189
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**Table 1:** Friedel–Crafts alkenylation of benzene by 1-phenyl-1-propyne.[a]



| Entry | Catalyst (equiv) | Ionic liquid | t [h] | Yield [%][b] |
|---|---|---|---|---|
| 1 | Sc(OTf)$_3$ (0.1) | none | 96 | 27 |
| 2 | Sc(OTf)$_3$ (0.1) | [bmim][SbF$_6$] | 4 | 91 |
| 3 | Sc(OTf)$_3$ (0.1) | [bmim][PF$_6$] | 4 | 90 |
| 4 | In(OTf)$_3$ (0.1) | [bmim][SbF$_6$] | 2.5 | 81 |
| 5 | In(OTf)$_3$ (0.05) | [bmim][SbF$_6$] | 6 | 94 |
| 6 | In(OTf)$_3$ (0.025) | [bmim][SbF$_6$] | 24 | 91 |
| 7 | Hf(OTf)$_4$ (0.1) | [bmim][SbF$_6$] | 1 | 90 |
| 8 | Hf(OTf)$_4$ (0.05) | [bmim][SbF$_6$] | 5 | 91 |
| 9 | Hf(OTf)$_4$ (0.025) | [bmim][SbF$_6$] | 9 | 85 |
| 10 | Y(OTf)$_3$ (0.1) | [bmim][SbF$_6$] | 2 | 80 |
| 11 | Yb(OTf)$_3$ (0.1) | [bmim][SbF$_6$] | 4 | 81 |
| 12 | Lu(OTf)$_3$ (0.1) | [bmim][SbF$_6$] | 4 | 94 |

[a] All reactions were carried out at 85 °C using 1-phenyl-1-propyne (1 mmol), benzene (6 mL), and the ionic liquid (1 mL) in the presence of the metal triflate as a catalyst. [b] Yield of isolated product based on 1-phenyl-1-propyne.

**Table 2:** Friedel–Crafts alkenylation of various arenes with various alkynes.[a]



| Entry | R$^1$ | R$^2$ | Arene | Catalyst | t [h] | Yield [%][b] |
|---|---|---|---|---|---|---|
| 1 | Ph | Me | p-xylene | Sc(OTf)$_3$ | 4 | 96[c] |
| 2 | Ph | H | benzene | Sc(OTf)$_3$ | 4 | 68 |
| 3 | Ph | H | p-xylene | Sc(OTf)$_3$ | 4 | 60 |
| 4 | Ph | H | p-xylene | In(OTf)$_3$ | 3 | 80 |
| 5 | Ph | H | p-xylene | Hf(OTf)$_4$ | 3 | 85 |
| 6 | Ph | Ph | benzene | Sc(OTf)$_3$ | 2 | 59 |
| 7[d] | Ph | Ph | benzene | Sc(OTf)$_3$ | 4 | 62 |
| 8 | Ph | Ph | benzene | In(OTf)$_3$ | 2 | 72 |
| 9 | Ph | Ph | benzene | Hf(OTf)$_4$ | 1 | 92 |
| 10 | Ph | Ph | p-xylene | Sc(OTf)$_3$ | 4 | 80[c] |
| 11 | Ph | Ph | toluene | Sc(OTf)$_3$ | 2 | 83[e] |
| 12 | Ph | Ph | chlorobenzene | Sc(OTf)$_3$ | 6 | 44[e] |
| 13 | Ph | Ph | anisole | Sc(OTf)$_3$ | 2 | 73[e] |
| 14 | p-CF$_3$Ph | H | p-xylene | Sc(OTf)$_3$ | 22 | 73 |
| 15 | p-CF$_3$Ph | H | p-xylene | In(OTf)$_3$ | 5 | 78 |
| 16 | p-CF$_3$Ph | H | p-xylene | Hf(OTf)$_4$ | 5 | 58 |
| 17 | p-ClPh | H | p-xylene | Sc(OTf)$_3$ | 12 | 63 |
| 18 | p-ClPh | H | p-xylene | Hf(OTf)$_4$ | 4 | 70 |
| 19 | Ph | CO$_2$Et | benzene | Hf(OTf)$_4$ | 22 | 89 |
| 20 | Ph | CO$_2$Et | p-xylene | Hf(OTf)$_4$ | 10 | 70[c] |

[a] All reactions were carried out with an alkyne (1 mmol), an arene (6 mL), and [bmim][SbF$_6$] (1 mL) in the presence of the metal triflate catalyst (10 mol %) at 85 °C. [b] Yield of isolated product based on the alkyne. [c] cis/trans ratios were determined by $^1$H NMR spectroscopy as follow: 96/4 (entry 1), 88/12 (entry 10), and 87/13 (entry 20). [d] Reaction was carried out with the recovered ionic liquid phase from entry 6 without further addition of Sc(OTf)$_3$. [e] The reaction gave an inseparable mixture of four isomers of ortho and para regioisomers, including the corresponding cis/trans isomers. The isomer ratios determined by GC-MS analysis are as follows; 2/33/32/32 (entry 11); 2/35/31/32 (entry 12); 8/18/34/40 (entry 13).

significant rate acceleration may be ascribed to the stabilization of the unstable vinyl cationic intermediate in a highly polar ionic liquid, in which the polar vinyl cation may gain a longer lifetime. The catalytic activities of other metal triflates were also investigated, for example (yields are given in parentheses), Ag(OTf) (4 %), Cu(OTf)$_2$ (27 %), Mg(OTf)$_2$ (21 %), Zn(OTf)$_2$ (2 %), Sn(OTf)$_2$ (69 %), La(OTf)$_3$ (62 %), Pr(OTf)$_3$ (19 %), Nd(OTf)$_3$ (37 %), Sm(OTf)$_3$ (15 %), Eu(OTf)$_3$ (16 %), Gd(OTf)$_3$ (23 %), Tb(OTf)$_3$ (34 %), Dy(OTf)$_3$ (28 %), Ho(OTf)$_3$ (30 %), Er(OTf)$_3$ (40 %), and Tm(OTf)$_3$ (22 %). However, their catalytic activities were much lower than those of Sc(OTf)$_3$, In(OTf)$_3$, Hf(OTf)$_4$, Y(OTf)$_3$, Yb(OTf)$_3$, and Lu(OTf)$_3$.

To study the scope of this reaction a series of Friedel–Crafts alkenylations of arenes with various types of alkynes were carried out in [bmim][SbF$_6$] (Table 2). In all cases, the reactions proceeded successfully within a few hours to afford the corresponding alkenylated products in good to excellent yields. In particular, Sc(OTf)$_3$, In(OTf)$_3$, and Hf(OTf)$_4$ effectively catalyzed the alkenylation of the electron-deficient alkynes, such as p-tifluoromethylphenylacetylene and p-chlorophenylacetylene, which were totally inactive without the presence of an ionic liquid (entries 14–18).[3] Similarly, the reaction of arenes with ethyl phenylpropiolate in the presence of Hf(OTf)$_4$ proceeded smoothly in [bmim][SbF$_6$] (entries 19 and 20), whereas without [bmim][SbF$_6$] a conversion of only <5 % was observed. It should also be noted that the ionic liquid phase containing the metal triflate could be readily recovered by simple decantation of the organic layer (the upper phase) after reaction. The recovered ionic liquid phase containing the metal triflate was reused without further addition of metal triflate. However, a decrease in catalytic activity over successive reactions was observed and, thus, the reaction time became longer upon reuse (compare entries 6 and 7 in Table 2).

Finally, our protocol has been further extended to intramolecular Friedel–Crafts alkenylations. The intramolecular reaction of aryl phenyl propiolates catalyzed by Hf(OTf)$_4$ (10 mol %) in a mixture of [bmim][SbF$_6$] and methylcyclohexane at 85 °C for 9–10 hours resulted in the formation of the 4-phenylcoumarins in moderate yields (Scheme 1). Surprisingly, the reaction of aryl-2-butynoates also was successfully performed to afford the corresponding coumarin in an excellent yield (89 %; Scheme 1). The smaller stabilizing influence of the alkyl group on the vinyl cation intermediate
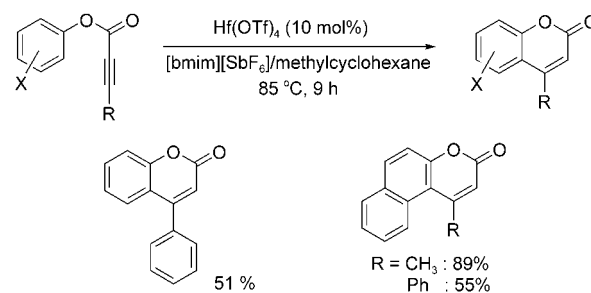


**Scheme 1.** Synthesis of 4-phenylcoumarins by intramolecular Friedel–Crafts alkenylations.

resulted in the alkyl-substituted alkynes usually undergoing self-oligomerization rather than the desired alkenylation reaction. Intramolecular alkenylation allowed us to synthesize 2(1*H*)-quinolinones from the corresponding aryl amides of phenylpropiolic acid in good yields (Scheme 2).
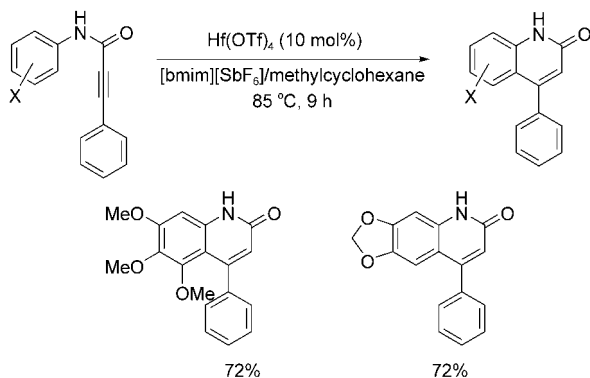


**Scheme 2.** Synthesis of 2(1*H*)-quinolinones by intramolecular Friedel–Crafts alkenylations.

In conclusion, we have found that the employment of hydrophobic ionic liquids dramatically enhanced the catalytic activities of metal triflates in Friedel–Crafts alkenylations, and thus allowed the development of a simple and highly efficient method for coupling aromatic compounds with various alkyl- and aryl-substituted alkynes. In some cases, reactions that were not possible in conventional organic solvents also proceeded smoothly in the presence of ionic liquids. To our knowledge, the described protocol could be the most efficient preparative Friedel–Crafts alkenylation method published to date for the synthesis of a range of alkenylated arenes,[12] such as styrenes, *cis*-aryl-α,β-unsaturated carbonyl compounds, coumarines, and 2(1*H*)-quinolinones. Studies into the origin of the effects of ionic liquids on catalytic activity are in progress.

### Experimental Section

Typical procedure for intermolecular Friedel–Crafts alkenylations in an ionic liquid: 1-Phenyl-1-propyne (178.2 mg, 1 mmol) was added to a mixture of Sc(OTf)$_3$ (49.2 mg, 0.1 mmol), benzene (6 mL), and [bmim][SbF$_6$] (1 mL) under a nitrogen atmosphere. Two phases formed and the mixture was heated to reflux for 4 h. After completion of the reaction, the reaction mixture was cooled to room temperature. The organic layer (upper phase) was separated by extraction with benzene to leave the ionic liquid phase containing the catalyst, which could be reused. All the volatile organic compounds were then removed under reduced pressure and the residue was purified by flash column chromatography on silica gel (hexane) to give 177 mg (91%) of pure 1,1-diphenyl-1-propene as a pale yellow solid.

Typical procedure for intramolecular Friedel–Crafts alkenylations in an ionic liquid: A mixture of Hf(OTf)$_4$ (77.4 mg, 0.1 mmol), phenyl 3-phenylpropiolate (222.1 mg, 1 mmol), methylcyclohexane (6 mL), and [bmim][SbF$_6$] (1 mL) was heated to reflux for 9 h under a nitrogen atmosphere. The reaction mixture was then cooled to room temperature. All the volatile organic compounds were then removed under reduced pressure and the residue was purified by flash column chromatography on silica gel (hexane/diethyl ether) to give 113 mg (51%) of pure 4-phenylcoumarin as a pale yellow solid.

[1] For reviews of Friedel–Crafts alkylation reactions, see: a) *Friedel–Crafts and Related Reactions, Vol. II*, part 1 (Ed.: G. A. Olah), Wiley-Interscience, New York, **1964**; b) *Friedel–Crafts Alkylation Chemistry. A Centry of Discovery* (Eds.: R. M Roberts, A. A. Khalaf), Marcel Dekker, New York, **1984**; c) G. A. Olah, R. Krishnamurit, G. K. S. Prakash, in *Friedel–Crafts Alkylations in Comprehensive Organic Synthesis* (Eds.: B. M. Trost, I. Fleming), Pergamon, Oxford, **1991**.

[2] O. W. Cook, V. J. Chaber, *J. Am. Chem. Soc.* **1921**, *43*, 334; J. S. Reichert, J. A. Nieuwland, *J. Am. Chem. Soc.* **1923**, *45*, 3090; J. A. Reilly, J. A. Nieuwland, *J. Am. Chem. Soc.* **1928**, *50*, 2564.

[3] T. Tsuchimoto, T. Maeda, E. Shirakawa, Y. Kawakami, *Chem. Commun.* **2000**, 1573.

[4] G. Sartori, F. Bigi, A. Pastorio, C. Porta, A. Arienti, R. Maggi, N. Moretti, G. Gnappi, *Tetrahedron Lett.* **1995**, *36*, 9177.

[5] G. Casiraghi, G. Casnati, G. Puglia, G. Sartori, G. Terenghi, *Synthesis* **1977**, 122.

[6] M. Yamaguchi, Y. Kido, A. Hayashi, M. Hirama, *Angew. Chem.* **1997**, *109*, 1370; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1313; Y. Kido, S. Yoshimura, M. Yamaguchi, T. Uchimaru, *Bull. Chem. Soc. Jpn.* **1999**, *72*, 1445.

[7] M. Yamaguch, A. Hayashi, M. Hirama, *J. Am. Chem. Soc.* **1995**, *117*, 1151.

[8] For recent reviews on ionic liquids, see: a) C. E. Song, *Chem. Commun.* **2004**, 1033; b) R. Sheldon, *Chem. Commun.* **2001**, 2399; c) P. Wasserscheid, W. Kein, *Angew. Chem.* **2000**, *112*, 3926; *Angew. Chem. Int. Ed.* **2000**, *39*, 3772; d) T. Welton, *Chem. Rev.* **1999**, *99*, 2071.

[9] Our recent examples: a) C. E. Song, W. H. Shim, E. J. Roh, J. H. Choi, *Chem. Commun.* **2000**, 1695; b) C. E. Song, E. J. Roh, *Chem. Commun.* **2000**, 837; c) C. E. Song, W. H. Shim, E. J. Roh, S.-g. Lee, J. H. Choi, *Chem. Commun.* **2001**, 1122; d) S.-g. Lee, J. W. Park, J. Kang, J. K. Lee, *Chem. Commun.* **2001**, 1698; e) D. W. Kim, C. E. Song, D. Y. Chi, *J. Am. Chem. Soc.* **2002**, *124*, 10278; f) S.-g. Lee, J. W. Park, *Bull. Korean Chem. Soc.* **2002**, *23*, 1367; g) D. W. Kim, C. E. Song, D. Y. Chi, *J. Org. Chem.* **2003**, *68*, 4281; h) E. J. Kim, S. Y. Ko, C. E. Song, *Helv. Chim. Acta* **2003**, *86*, 894; i) S.-g. Lee, Y. J. Zhang, P. Z. Yu, H. Yoon, C. E. Song, J. H. Choi, J. Hong, *Chem. Commun.* **2003**, 2624; j) S.-g. Lee, J. W. Park, *J. Mol. Catal. A* **2003**, *194*, 49.

[10] In sharp contrast to these results, only very small amounts of the alkenylated product was obtained (<2% yield) in the hydrophilic ionic liquids, [bmim][BF$_4$] or [bmim][OTf].

[11] Recently, Rogers and co-workers reported the instability of the ionic liquids' counterion PF$_6$ towards moisture, which resulted in hydrolysis and the formation of HF (R. P. Swatloski, J. D. Holbrey, R. D. Rogers, *Green Chem.* **2003**, *5*, 361). Therefore, to examine the possible catalytic effect of HF on this reaction, we also carried out the reaction only in [bmim][SbF$_6$] or in a mixture of [bmim][SbF$_6$] and water (1:1, v/v) without any metal triflate catalyst. However, the reaction did not occur at all.

[12] A new synthetic route to alkenylated arenes involving Pd- and Pt-catalyzed addition of arenes to alkynes in the presence of trifluoroacetic acid was recently reported: a) C. Jia, D. Piao, J. Oyamada, W. Lu, T. Kitamura, Y. Fujiwara, *Science* **2000**, *287*, 1992; b) C. Jia, W. Lu, J. Oyamada, T. Kitamura, K. Matsuda, M. Irie, Y. Fujiwara, *J. Am. Chem. Soc.* **2000**, *122*, 7252.