Friedel–Crafts alkenylation of arenes using alkynes catalysed by metal trifluoromethanesulfonates

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Metal trifluoromethanesulfonates [M(OTf)$_n$; M = Sc, Zr, In] catalyse the Friedel–Crafts alkenylation of arenes using alkynes, including internal alkynes, to give, through an alkenyl cation intermediate, 1,1-diarylalkenes in high to excellent yields.

Friedel–Crafts alkylation reactions have been extensively studied and have established a prominent historical position in organic synthesis including industrial applications.[1] In contrast, little has been known about the corresponding Friedel–Crafts alkenylation reaction with either an alkenyl halide or an alkyne. With an alkenyl halide, a substituent such as a phenylthio[2] or an aryl[3] group that stabilizes an alkenyl cation intermediate is required to attain a good yield. The reaction using an alkyne, where a C–H bond of the arene adds to the triple bond of an alkyne, is environmentally friendly without being accompanied by formation of by-products like hydrogen halide. However, the reaction often brings about the polymerization of alkynes and results in the formation of undesired side products.[1b,4] Zeolite HSZ-360 as a heterogeneous acid was found to be efficient especially for *ortho*-selective monoalkenylation of phenol, but only phenylethyne had been examined as a substrate.[5] Recently, alkenylation of arenes with trimethylsilylethyne promoted by an excess amount of GaCl$_3$ was also reported.[6] To the best of our knowledge, the Friedel–Crafts alkenylation reaction with internal alkynes has yet to be explored. We found that metal triflates [M(OTf)$_n$; M = Sc, Zr, In] are effective catalysts for the Friedel–Crafts alkenylation reaction with internal alkynes as well as terminal ones.[7]

The reaction of phenylethyne (**1a**) (0.5 mmol) with *p*-xylene (**2a**) (8.0 ml) at 85 °C for 19 h in the presence of 10 mol% of In(OTf)$_3$ proceeded smoothly to give the corresponding alkenylation product, 1-phenyl-1-(*p*-xylyl)ethene (**3a**), in 80% yield (Scheme 1). Although the reaction using Sc(OTf)$_3$[8] or Zr(OTf)$_4$ required a longer reaction time, **3a** was obtained in 92 or 53% yield, respectively. On the other hand, metal chlorides such as ZrCl$_4$ and AlCl$_3$ gave **3a** only in low yields.
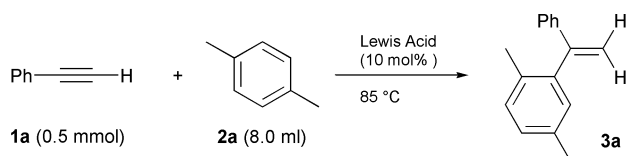
In(OTf)$_3$	Sc(OTf)$_3$[a]	Zr(OTf)$_4$	ZrCl$_4$	AlCl$_3$
80% (19 h)	92% (96 h)	53% (39 h)	1% (100 h)	6% (100 h)

[a] 0.1 ml of MeNO$_2$ was used as an additive.

Scheme 1

These results prompted us to survey the scope of the reaction. The results are summarized in Scheme 2 and Table 1. Arenes except for *p*-dimethoxybenzene were used not only as the substrates but also as solvents. Phenylethyne was successfully reacted with benzene in the presence of Sc(OTf)$_3$ to afford 1,1-diphenylethene in 73% yield (entry 2). A phenylethyne

bearing an electron-donating group (–OMe) at the *para* position was also reacted with *p*-xylene using Sc(OTf)$_3$ to give **3** in 62% yield (entry 3). Although Sc(OTf)$_3$ was totally inactive for more electron-deficient alkynes than phenylethyne, In(OTf)$_3$ was effective for the reaction of phenylethyne having a *p*-Cl or *p*-CF$_3$ group and the products were obtained in high yields (entries 4 and 5). Internal alkynes can obviously participate in this protocol. 1-Phenylprop-1-yne satisfactorily reacted with benzene, toluene, *p*-xylene or anisole using In(OTf)$_3$ to produce the corresponding products (entries 6–11). Zr(OTf)$_4$ was especially effective for the reaction of *p*-dimethoxybenzene to furnish **3** in
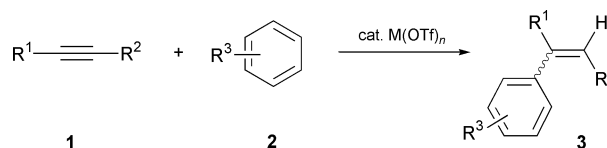
Scheme 2

Table 1 Metal triflate-catalysed Friedel–Crafts alkenylation with alkynes[a]

Entry	R^1—≡—R^2	Ar–H (ml)	Lewis Acid	Time/h	Yield (%)[b]
1	Ph—≡—H	*p*-Xylene (8)	Sc(OTf)$_3$	96	92[c]
2	Ph—≡—H	PhH (10)	Sc(OTf)$_3$	186	73[c]
3	*p*-MeOC$_6$H$_4$—≡—H	*p*-Xylene (8)	Sc(OTf)$_3$	10	62
4[d]	*p*-ClC$_6$H$_4$—≡—H	*p*-Xylene (8)	In(OTf)$_3$	15	73
5[d]	*p*-CF$_3$C$_6$H$_4$—≡—H	*p*-Xylene (8)	In(OTf)$_3$	50	82
6	Ph—≡—Me	PhH (4)	In(OTf)$_3$	16	63
7	Ph—≡—Me	PhMe (4)	In(OTf)$_3$	16	73[e]
8	Ph—≡—Me	*p*-Xylene (4)	In(OTf)$_3$	20	80[f]
9	Ph—≡—Me	*p*-Xylene (4)	Zr(OTf)$_4$	40	68[f]
10	Ph—≡—Me	*p*-Xylene (4)	Sc(OTf)$_3$	152	72[f]
11	Ph—≡—Me	PhOMe (4)	In(OTf)$_3$	5	72[e]
12	Ph—≡—Me	*p*-(MeO)$_2$C$_6$H$_4$[g]	Zr(OTf)$_4$	2	70[f]
13	Ph—≡—Me	PhBr (4)	In(OTf)$_3$	63	33[e]
14	Ph—≡—Me	PhCl (4)	In(OTf)$_3$	112	28[e]
15	Ph—≡—Ph	*p*-Xylene (4)	In(OTf)$_3$	70	79[f]

[a] The reaction was carried out at 85 °C using an alkyne (0.5 mmol) and an arene (4–10 ml) in the presence of 10 mol% of a Lewis acid. Nitromethane (0.1 ml) was used as an additive in entries 1, 2, 3 and 10. [b] Isolated yield based on alkyne. [c] GC yield. [d] The reaction was carried out at 130 °C. [e] The reaction gave a mixture of 6 isomers which consist of *o*-, *m*- and *p*-regioisomers including the corresponding *cis/trans* isomers determined by GC–MS. The isomer ratios are as follows; 30:4:3:2:31:30 (entry 7); 3.0:34.4:0.1:0.3:32.0:30.2 (entry 11); 2:29:1:1:32:35 (entry 13); 2:31:1:1:22:43 (entry 14). [f] Isomer ratios of stereoisomers were determined by GC as follows; 91:9 (entry 8); 91:9 (entry 9); 91:9 (entry 10); 90:10 (entry 12); 93:7 (entry 15). [g] The reaction was carried out with *p*-dimethoxybenzene (2.5 mmol) in chlorobenzene (4 ml) as a solvent.
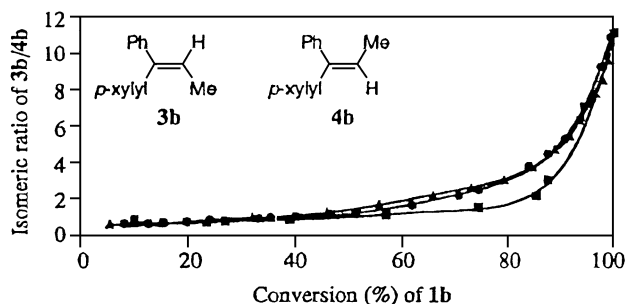
Fig. 1 Plots of isomeric ratio of **3b**:**4b** *versus* conversion (%) of **1b** for In(OTf)$_3$ (-●-), Zr(OTf)$_4$ (-■-), and Sc(OTf)$_3$ (-▲-).

70% yield, whereas In(OTf)$_3$ did not catalyse the reaction (entry 12). Treatment of halobenzenes, which can be used as a solvent in the Friedel–Crafts alkylation, with 1-phenylprop-1-yne gave the products in somewhat lower yields (entries 13 and 14). Arenes attacked these alkynes exclusively at the carbon having the aryl group. The reaction of 1,2-diphenylethyne with *p*-xylene using In(OTf)$_3$ as a catalyst also gave **3** in 79% yield (entry 15). In all cases, the triarylalkane that would be produced by the reaction of **3** and **4** with an arene was not observed.

Dependence of the isomer ratio between alkenylated products **3b** and **4b** on the conversion of 1-phenylprop-1-yne (**1b**) in the reaction with *p*-xylene is illustrated in Fig. 1.[9] Fig. 1 indicates that (1) both stereoisomers **3b** and **4b** already exist in almost a 1:1 ratio at the early stage of the reaction, and (2) there is a drastic change of the isomer ratio at the late stage of the reaction.

Two routes (path A and path B) are possible for this alkenylation reaction (Scheme 3). In path A, the attack of an arene to initially formed zwitterionic intermediate **5** from both X and Y sites affords a mixture of **7** and **8**, which are transformed by protonation to **3** and **4**, respectively. As regards path B, the activation of an alkyne by a metal triflate and the attack of an arene to the alkyne proceeds through a concerted mechanism. Therefore, an arene attacks **1b** stereoselectively from the side opposite to the metal triflate to furnish **7** and subsequent protonation of **7** gives **3** as the sole stereoisomer. The existence of both **3b** and **4b** at the early stage of the reaction
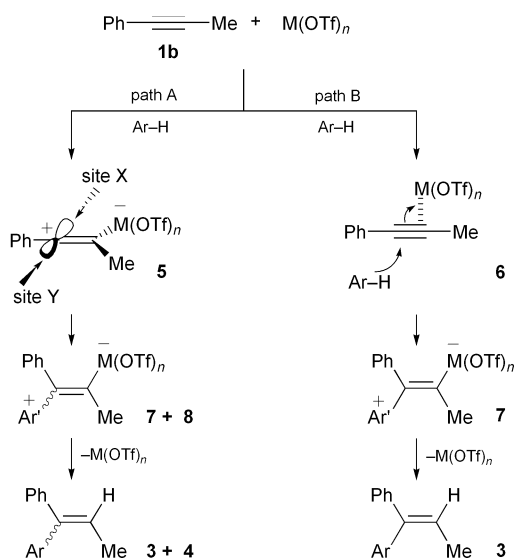
Scheme 3
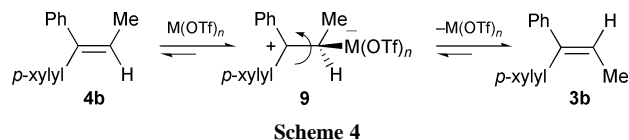
Scheme 4

strongly suggests that path A works in the reaction. The predominance of **3b** at the end of the reaction should be due to an equilibrium between **3b** and **4b** under the reaction conditions (Scheme 4). Thus, formation of alkyl cation **9** by the reaction of **4b** with a metal triflate and subsequent bond rotation followed by elimination of the metal triflate would induce the isomerization from **4b** to thermodynamically favored **3b**. Prolonged reaction time (100 h) showed no further change in the isomer ratio.

The drastic change in the isomer ratio around the point over 80% conversion of **1b**, *i.e.*, almost consumption of **1b**, may show that metal triflates prefer an alkyne rather than an alkene for complexation under the reaction conditions. Actually, in the absence of **1b**, the isomerization catalysed by 10 mol% of In(OTf)$_3$ in *p*-xylene at 85 °C was completed within 20 min to give a 91:9 ratio of **3b** and **4b** from a mixture of **3b** and **4b** in a ratio of 45:55. Such salient character of metal triflates should be ideal for the Friedel–Crafts alkenylation with alkynes to reduce the possibility of side reactions through alkyl cation **9**.

In summary, we disclose here the preliminary results on the use of some metal triflates as efficient catalysts for the Friedel–Crafts alkenylation of arenes with alkynes including internal ones. Further investigation on the reaction of alkynes with nucleophiles other than arenes is currently in progress.

Notes and references

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