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# Catalytic Friedel-Crafts Acylation of Benzene, Chlorobenzene, and Fluorobenzene Using a Novel Catalyst System, Hafnium Triflate and Trifluoromethanesulfonic Acid

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***Abstract:*** *Catalytic Friedel-Crafts acylation of benzene and unactivated benzenes such as chlorobenzene and fluorobenzene has been successfully carried out using hafnium (IV) triflate and trifluoromethanesulfonic acid as catalysts. Both aromatic and aliphatic carboxylic acid chlorides reacted smoothly under the conditions to afford the corresponding aromatic ketones in good yields.* 

Friedel-Crafts alkylation and acylation reactions are fundamental and important processes in organic synthesis as well as in industrial chemistry.[1] While the alkylation reaction proceeds in the presence of a catalytic amount of a Lewis acid such as $AlCl_3$ or $BF_3$, the acylation reaction requires more than stoichiometric amounts of a Lewis acid due to the consumption of the acid by coordination to produced aromatic ketones. In addition, rather drastic reaction conditions, tedious work up procedures, use of large amounts of acids, etc., which may induce environmental pollution, remain as severe problems to overcome especially in large-scale industrial processes. Although some catalysts which complete the acylation by catalytic use have been reported,[2] substrates were limited to activated benzenes or aroyl derivatives in most cases and development of more efficient and powerful catalysts is strongly demanded.[3,4]

We have shown that metal triflates such as lanthanides including scandium and yttrium, zirconium, and hafnium triflates, etc. are excellent Friedel-Crafts catalysts.[5-7] Among them, $Hf(OTf)_4$ gave the best result hitherto.[7] While catalytic acylation of toluene proceeded smoothly, ca. 20% yield of an aromatic ketone was obtained in the acylation of benzene using 10 mol% of $Hf(OTf)_4$ in a nitromethane ($CH_3NO_2$)-lithium perchlorate ($LiClO_4$) system. In the course of our investigations to develop more efficient catalytic Friedel-Crafts acylations, particularly catalytic acylation of benzene and unactivated benzenes such as chlorobenzene and fluorobenzene, we have found a new catalytic system. In this paper, we report the Friedel-Crafts acylation of benzene, chlorobenzene, and fluorobenzene in the presence of catalytic amounts of hafnium (IV) triflate ($Hf(OTf)_4$) and trifluoromethanesulfonic acid (TfOH).

While $Hf(OTf)_4$ was a very effective catalyst not only in Friedel-Crafts acylation but also in Fries rearrangement[8] in a $CH_3NO_2$-$LiClO_4$ system, we examined several reaction conditions, focusing on high concentration conditions as well as generation of activated acylating species under catalytic conditions. After several trials, we found that combination of $Hf(OTf)_4$ and TfOH accelerated the catalytic Friedel-Crafts acylation of benzene dramatically. The effect of the amounts of $Hf(OTf)_4$ and TfOH in the benzoylation and *p*-chlorobenzoylation of benzene is summarized in Table 1. While much lower yields were obtained in the presence of 5 mol% of $Hf(OTf)_4$ or 5 mol% of TfOH, a 77% yield of benzophenone was obtained when

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combining 5 mol% of $Hf(OTf)_4$ and 5 mol% of TfOH. No $LiClO_4$ was used in this case. The yield was slightly improved when 10 mol% each of $Hf(OTf)_4$ and TfOH was used, and *p*-chlorobenzoylation of benzene also proceeded smoothly under these conditions. Further increases of the amounts of the catalysts did not improve the yield.

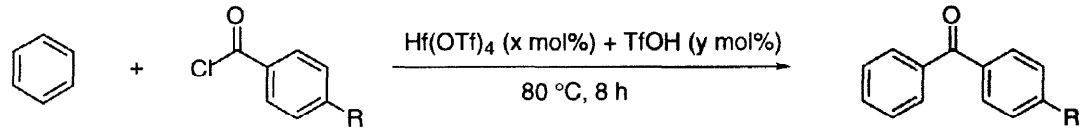



**Table 1.** Effect of the Amounts of $Hf(OTf)_4$ and TfOH[a]

| Ently | R | $Hf(OTf)_4$/x mol% | TfOH/y mol% | Yield/%[b] |
|---|---|---|---|---|
| 1 | H | 5 | 0 | 10 |
| 2 | H | 0 | 5 | 34 |
| 3 | H | 5 | 5 | 77 |
| 4 | H | 10 | 10 | 82 |
| 5 | Cl | 10 | 10 | 78 |
| 6 | Cl | 20 | 10 | 75 |
| 7 | Cl | 20 | 20 | 73 |
| 8 | Cl | 20 | 30 | 54 |

[a]Twenty equiv of benzene were used. [b]Isolated yield.

We then examined other substrates (Table 2). It was very exciting to find that unactivated benzenes such as chlorobenzene and fluorobenzene reacted smoothly in the presence of 10 mol% each of $Hf(OTf)_4$ and TfOH, to afford the corresponding aromatic ketones in high yields. In all cases, the reactions proceeded very cleanly (checked by TLC) and no side reaction products were observed. In addition, it is noted that aliphatic carboxylic acid chloride worked well under these catalytic conditions.

A typical experimental procedure is described for the benzoylation of fluorobenzene. $Hf(OTf)_4$ (0.1 mmol), TfOH (0.1 mmol), benzoyl chloride (1.0 mmol), and fluorobenzene (20.0 mmol) were combined, and the mixture was stirred at 100 °C for 15 h. Saturated aqueous sodium hydrogen carbonate was added to quench the reaction. After a usual work up, the crude product was purified by column chromatography on silica gel to give 4-fluorobenzophenone (83%). Other regioisomers were not produced.

Finally, the assumed catalytic cycle is shown in Scheme 1. A key acylating reagent is proposed to be acyl triflate **1**,[9] which reacts even with unactivated benzenes to afford the corresponding aromatic ketones accompanied by regeneration of TfOH. $Hf(OTf)_4$ is assumed to catalyze both generation of **1** and successive acylation.

In summary, catalytic Friedel-Crafts acylation has been successfully carried out using a new catalyst system, $Hf(OTf)_4$ and TfOH. Benzene, toluene, and even unactivated benzenes such as chlorobenzene and fluorobenzene reacted smoothly under the conditions to afford the corresponding aromatic ketones in good

yields. According to the catalytic cycle shown in Scheme 1, a higher turnover is expected, and this report may open the door to solve the long-term Friedel-Crafts acylation problem.

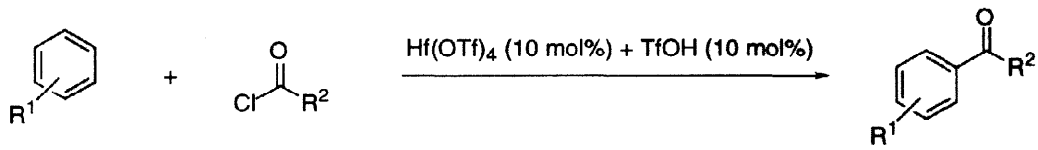
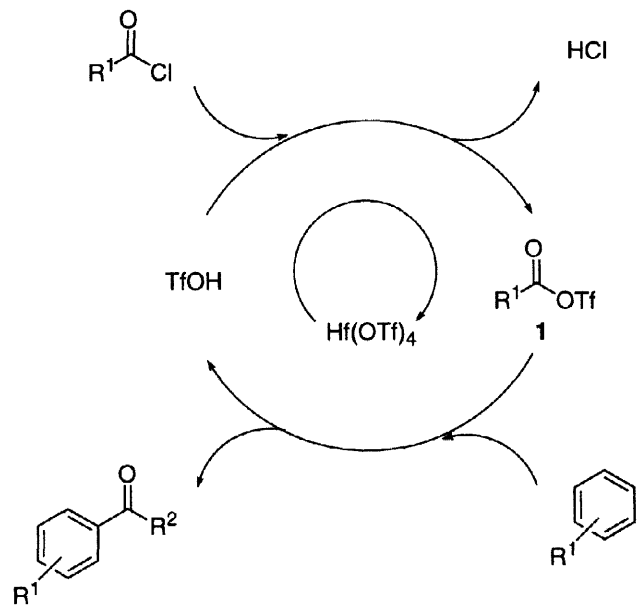



**Table 2.** Catalytic Friedel-Crafts Acylation[a]

| Ently | $R^1$ | $R^2$ | Temp/°C | Time/h | Yield/%[b] |
|---|---|---|---|---|---|
| 1 | H | Ph | 80 | 8 | 82 (77)[c] |
| 2 | H | *p*-ClPh | 80 | 8 | 78 |
| 3 | Cl | Ph | 120 | 15 | 72[d] |
| 4 | Cl | *p*-ClPh | 120 | 15 | 82[e] |
| 5 | F | Ph | 100 | 15 | 83[e] |
| 6 | H | $C_5H_{11}$ | 80 | 8 | 60[e,f] |
| 7 | H | $(CH_3)_2CHCH_2$ | 80 | 6 | 69[e,f] |
| 8 | Me | Ph | 100 | 8 | 82[g] |
| 9 | Me | *p*-ClPh | 100 | 8 | 80[h] |

[a]Twenty equiv of aromatics were used. [b]Isolated yield. [c]$Hf(OTf)_4$ (5 mol%) and TfOH (5 mol%) were used. [d]*Ortho/para* = 7/93. [e]*Ortho/para* = <1/>99. [f]$Hf(OTf)_4$ (20 mol%) and TfOH (30 mol%) were used. [g]*Ortho/para* = 15/85. [h]*Ortho/para* = 8/92.




**Scheme 1.** Assumed Catalytic Cycle

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