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Hafnium Trifluoromethanesulfonate (Hf(OTf)$_4$) as an Efficient Catalyst in the Fries Rearrangement and Direct Acylation of Phenol and Naphthol Derivatives

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Abstract: Hafnium trifluoromethanesulfonate (hafnium triflate, Hf(OTf)$_4$) was found to be an efficient catalyst in the Fries rearrangement of acyloxy benzene or naphthalene derivatives. The reactions proceeded smoothly in the presence of 5-20 mol% Hf(OTf)$_4$. Regioselective direct acylation of phenol and naphthol derivatives with acid chlorides was also achieved by using Hf(OTf)$_4$ as a catalyst.

Hydroxyarylketones are versatile intermediates in the synthesis of biologically active naphthoquinones,[1] phenols or naphthalenes containing LC polymers, low molecular weight mesogens,[2] etc. Although the Fries rearrangement of acyloxy benzenes or naphthalenes provides useful routes to these compounds, more than a stoichiometric amount of $AlCl_3$ is required because the acid is trapped by the products.[3] On the other hand, an alternative method is direct acylation of phenol and naphthol derivatives using $AlCl_3$[4] or $HClO_4$[5] as a promoter.[6] However, in this case also, requirement of more than stoichiometric amounts of the acids has caused some severe side reactions, and therefore, development of new catalysts which promote the above mentioned reactions catalytically is strongly desired. In this paper, we describe the catalytic Fries rearrangement of acyloxy benzene or naphthalene derivatives and also catalytic direct acylation of phenol and naphthol derivatives with acid chlorides using Hf(OTf)$_4$ as a catalyst.

Recently, we found that the Fries rearrangement of acyloxy naphthalenes proceeded smoothly in the presence of a catalytic amount of scandium trifluoromethanesulfonate (scandium triflate, Sc(OTf)$_3$) to afford the corresponding hydroxynaphthyl ketones in high yields.[7] We then investigated the Fries rearrangement of acyloxy benzene derivatives using Sc(OTf)$_3$. When *m*-tolyl acetate was heated at 100 °C in toluene for 6 h in the presence of 20 mol% Sc(OTf)$_3$, 2-hydroxy-4-methylphenyl methyl ketone was isolated in a 34% yield. In order to improve the yield, several Lewis acids were examined. Quite recently, we synthesized Hf(OTf)$_4$, which has proved to be an efficient catalyst in the Friedel-Crafts acylation and alkylation reactions in lithium perchlorate-nitromethane ($LiClO_4$-$MeNO_2$).[8] It was found that Hf(OTf)$_4$ was also effective in the Fries rearrangement, and that the yield of 2-hydroxy-4-methylphenyl methyl ketone was improved to 64%.[9] Several examples of the Hf(OTf)$_4$-catalyzed Fries rearrangement of acyloxy benzene or naphthalene derivatives are summarized in Table 1.[10] In the reaction of phenyl acetate, the rearrangement occurred sluggishly in toluene at 100 °C, but proceeded in 12 M $LiClO_4$-$MeNO_2$ at 50 °C to give 4-acetyl phenol and 2-acetyl phenol in 52% and 5% yields, respectively. In other cases, complete regioselectivities were obtained and 2-acylated phenol or naphthol derivatives were isolated in good yields. No migration or loss of the *t*-butyl group was observed in the rearrangement of 3-*t*-butylphenyl acetate.[1,11]

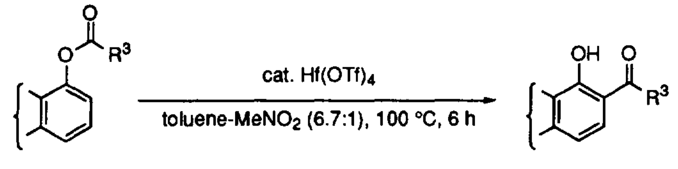
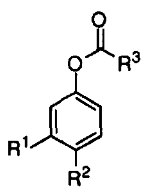
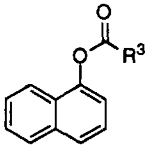


Table 1. The Fries Rearrangement of Acyloxy Benzene or 1-Naphthalene Derivatives Using $Hf(OTf)_4$

Entry		R^1	R^2	R^3	$Hf(OTf)_4$ (mol%)	Yield (%)
1		H	H	CH_3	10	57 [a, b)]
2		OMe	H	CH_3	20	53
3		OMe	H	c-C_6H_{11}	20	72
4		CH_3	H	CH_3	20	64
5		*t*-Bu	H	CH_3	10	60 [a)]
6		H	CH_3	CH_3	20	62 [a, c)]
7		—	—	CH_3	5	76
8		—	—	c-C_6H_{11}	5	82

a) The reaction was carried out in 12 M $LiClO_4$-$MeNO_2$ at 50 °C.
b) Consisting of 2-acylated adduct (5%) and 4-acylated adduct (52%).
c) The reaction was carried out for 14 h.

We then examined $Hf(OTf)_4$-catalyzed direct acylations of phenol and naphthol derivatives.[12] *m*-Methoxyphenol was treated with acetyl chloride in the presence of 20 mol% $Hf(OTf)_4$ in toluene-nitromethane (6.7:1) at 100 °C for 6 h, to afford the corresponding ketone in an 84% yield. It is noted that this yield is much higher than that of the Fries rearrangement of *m*-methoxyphenyl acetate. Several examples of direct acylation reactions of phenol or naphthol derivatives with acyl chlorides are shown in Table 2.[13] In every case, the reaction proceeded smoothly using a catalytic amount of $Hf(OTf)_4$ to afford the corresponding hydroxyaryl ketones in good to high yields. In particular, 1-naphthol reacted smoothly to give the acylated adduct in higher yields in the presence of a smaller amount of the catalyst.

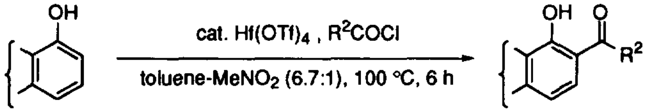
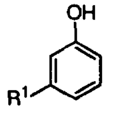
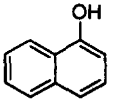


Table 2. 2-Acylation Reactions of Phenols and 1-Naphthols Using Hf(OTf)$_4$

Entry		R^1	R^2	Hf(OTf)$_4$ (mol%)	Yield (%)
1		H	CH$_3$	10	64$^{a, b)}$
2		OMe	CH$_3$	20	84
3		OMe	c-C$_6$H$_{11}$	20	78
4		CH$_3$	CH$_3$	20	53
5		t-Bu	CH$_3$	10	76$^{a)}$
6		—	CH$_3$	5	90
7		—	c-C$_6$H$_{11}$	5	97

a) The reaction was carried out in 12 M LiClO$_4$-MeNO$_2$.
b) Consisting of 2-acylated adduct (3%) and 4-acylated adduct (61%).

The yields of the direct acylation were higher than those of the Fries rearrangement in most cases. By-products of the Fries rearrangement were deacylated phenol or naphthol derivatives (10-30%). Although the precise reaction mechanism is not yet clear at this stage, it is suggested that both a direct acylating pathway and formation of esters followed by the Fries rearrangement are included in the reactions of phenol or naphthol derivatives with acid chlorides.

In summary, Hf(OTf)$_4$ is an efficient catalyst in both the Fries rearrangement of acyloxy benzene or naphthalene derivatives and the direct acylation reactions of phenol and naphthol derivatives with acid chlorides. It is noted that Hf(OTf)$_4$ is not trapped by the free hydroxy groups of the phenol or naphthol derivatives or the carbonyl oxygens of the products, and effectively catalyzes the reactions. Further investigations to develop other synthetic reactions using Hf(OTf)$_4$ are now in progress.

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(6) *o*-Acylation of phenols via phenol salts under basic conditions has been reported. Sartori G.; Bigi. F. *J. Org. Chem.* **1990**, *55*, 4371, and references cited therein.

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(9) In general, the yields were found to be higher using $Hf(OTf)_4$ than $Sc(OTf)_3$. For example, in the Fries rearrangement of phenol, 57% and 16% yields were obtained by using $Hf(OTf)_4$ and $Sc(OTf)_3$, respectively.

(10) A typical experimental procedure is described for the Fries rearrangement of *m*-tolyl acetate: To $Hf(OTf)_4$ (0.1 mmol, 20 mol%) was added *m*-tolyl acetate (0.5 mmol) in toluene (1.0 ml) and nitromethane (0.15 ml) at room temperature. The mixture was stirred for 6 h at 100 °C and then cooled to room temperature. Water was added to quench the reaction and dichloromethane was added. After separation of the organic layer, the aqueous layer was extracted with dichloromethane and the combined organic layer was dried (Na_2SO_4). The solvents were removed under reduced pressure and the crude product was chromatographed on silica gel to afford 2-hydroxy-4-methylphenyl methyl ketone in a 64% yield.

(11) For example, (a) Chatterjea, J. N.; Gupta, S. N. P.; Mehrotra, V. N. *J. Indian Chem. Soc.* **1965**, *42*, 205. (b) Martin, R.; Betoux, J. M.; Coton, G. *Bull. Soc. Chim. Fr.* **1972**, 4319, and references cited therein.

(12) $Sc(OTf)_3$ is also effective in the direct acylation. Kobayashi, S.; Moriwaki, M.; Hachiya, I. *Synlett* **1995**, 1153. Full details including comparison of catalysts will be reported in due course.

(13) A typical experimental procedure is described for the 2-acylation reaction of *m*-methoxyphenol: To $Hf(OTf)_4$ (0.1 mmol, 20 mol%) was added a mixture of *m*-methoxyphenol (0.5 mmol) and acetyl chloride (0.55 mmol) in toluene (1.0 ml) and nitromethane (0.15 ml) at room temperature. The mixture was stirred for 6 h at 100 °C and then cooled to room temperature. Water was added to quench the reaction and dichloromethane was added. After separation of the organic layer, the aqueous layer was extracted with dichloromethane and the combined organic layer was dried (Na_2SO_4). The solvents were removed under reduced pressure and the crude product was chromatographed on silica gel to afford 2-hydroxy-4-methoxylphenyl methyl ketone in an 84% yield.

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