

Catalytic Direct C-Acylation of Phenol and Naphthol Derivatives Using Carboxylic Acids as Acylating Reagents

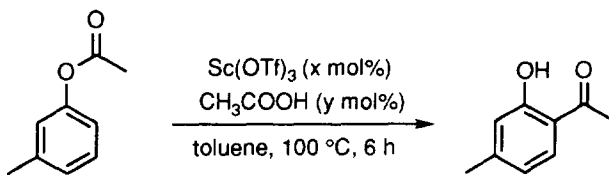
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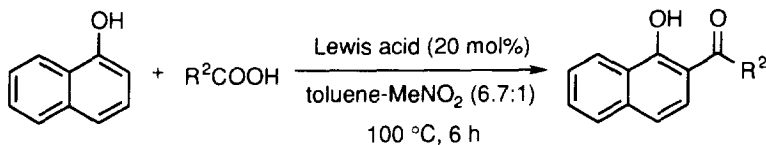
Abstract: Direct regioselective C-acylation of phenol and naphthol derivatives was carried out by using carboxylic acids as acylating reagents. The reactions proceeded smoothly in the presence of a catalytic amount of $\text{Hf}(\text{OTf})_4$ to afford the corresponding aromatic ketones in good yields. Copyright © 1996 Elsevier Science Ltd

Acylation of aromatic compounds is a well-known but still challenging topic in organic synthesis. For example, Friedel-Crafts acylation is one of the most popular reactions for the synthesis of aromatic ketones,¹ and direct C-acylation of phenol and naphthol derivatives also provides useful synthetic methods for the preparation of 2-hydroxyphenyl or 2-hydroxynaphthyl ketone derivatives.²⁻⁴ While these reactions have been carried out by using more than a stoichiometric amount of AlCl_3 , treatment of the aluminum residue has sometimes induced environmental problems, and the drastic reaction conditions have caused some severe side reactions. On the other hand, acid chlorides or acid anhydrides are commonly used as acylating reagents in these reactions. These reagents are usually prepared from carboxylic acids, and therefore, it would be desirable if the acylations could be carried out by using carboxylic acids as acylating reagents.^{5,6} In this paper, we describe the direct C-acylation of phenols and naphthol derivatives catalyzed by hafnium trifluoromethanesulfonate (hafnium triflate, $\text{Hf}(\text{OTf})_4$) using carboxylic acids as acylating reagents.

Recently, we reported efficient Fries rearrangements of acyloxybenzenes and naphthalenes,⁷ and also direct C-acylation reactions of phenol and naphthol derivatives with acid chlorides using $\text{Sc}(\text{OTf})_3$ ⁸ or $\text{Hf}(\text{OTf})_4$ ⁹ as a catalyst. Through developing these reactions, it was found that a catalytic amount of carboxylic acid accelerated the Fries rearrangement. Namely, in the presence of $\text{Sc}(\text{OTf})_3$ (20 mol%), *m*-tolyl acetate (**1**) rearranged in toluene (100 °C for 6 h) to afford 2-hydroxy-4-methylphenyl methyl ketone (**2**) in a 34% yield. This yield was improved to 60% when acetic acid (10 or 20 mol%) was added (see Table 1). We thought these results might be explained by assuming that acetic acid worked as an acylating reagent. We then combined *m*-cresol with acetic acid in the presence of $\text{Sc}(\text{OTf})_3$ (20 mol%). After 6 h in toluene at 100 °C, **2** was obtained in a 5% yield. We then searched for a more efficient catalyst in this reaction. Quite recently, we

**Table 1.** Effect of CH_3COOH as an Additive

Sc(OTf)_3 /mol%	CH_3COOH /mol%	Yield (%)
20	0	34
20	10	60
20	20	60
0	20	0

**Table 2.** Effects of Lewis Acids

Lewis acid	Yield (%)
AlCl_3	0
$\text{BF}_3 \cdot \text{OEt}_2$	0
TiCl_4	trace
SnCl_4	trace
Sc(OTf)_3	54
TiCl(OTf)_3	13
Zr(OTf)_4	31
Hf(OTf)_4	81
(TiOH)	(44)

first synthesized Hf(OTf)_4 and found that it was quite effective in catalytic Friedel-Crafts acylation and alkylation.¹⁰ Hf(OTf)_4 was used instead of Sc(OTf)_3 in the reaction of *m*-cresol with acetic acid, and it was found that the yield improved to 55%.¹¹ The efficiency of Hf(OTf)_4 is obvious from Table 2. While an 81% yield of 1-hydroxy-2-acetonaphthone was obtained using Hf(OTf)_4 ,¹² none or only a trace amount of the adduct was produced using typical Lewis acids such as AlCl_3 , $\text{BF}_3 \cdot \text{OEt}_2$, TiCl_4 , or SnCl_4 . Other examples of

Hf(OTf)₄-catalyzed direct C-acylation using carboxylic acids are summarized in Table 3. Although phenol reacted sluggishly in toluene-nitromethane (6.7:1) at 100 °C, the acylation proceeded smoothly in 12 M LiClO₄-MeNO₂¹⁰ to afford the 4-acylated adduct in a good yield. It is known that in phenol derivatives having a *t*-butyl group, migration of the *t*-butyl group occurs under some Lewis acidic conditions.¹³ No migration took place in the present reaction, and the acylation of 3-*t*-butylphenol proceeded in 12 M LiClO₄-MeNO₂ to afford 2-hydroxy-4-*t*-butylphenyl methyl ketone in a good yield. Cyclohexanecarboxylic acid (entry 5) and propionic acid (entry 7) were also employed as acylating reagents. In the reactions of naphthol derivatives, higher yields were obtained.

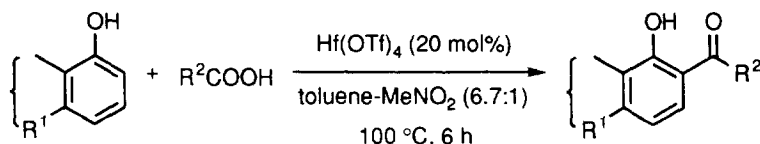


Table 3. Hf(OTf)₄-Catalyzed Direct Acylation of Phenol and Naphthol Derivatives Using a Carboxylic Acid as an Acylating Reagent

Entry	R ¹	R ²	Yield (%)	
1		H	Me	63 ^{a,b)}
2		Me	Me	55
3		^t Bu	Me	66 ^{a)}
4	OMe	Me	65	
5	OMe	<i>c</i> -C ₆ H ₁₁	72	
6		—	Me	81
7		—	Et	80

a) The reaction was carried out in 12M LiClO₄-MeNO₂ at 50°C.

b) Only the 4-acylated adduct was obtained.

A typical experimental procedure is described for the reaction of 1-naphthol with acetic acid: To Hf(OTf)₄ (0.1 mmol, 20 mol%) was added 1-naphthol (0.5 mmol) and acetic acid (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 was 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 layers were dried (Na₂SO₄). The solvents were removed under reduced pressure and the crude product was chromatographed on silica gel to afford 1-hydroxy-2-acetonaphthone (81% yield).

Thus, direct C-acylation reactions of phenol or naphthol derivatives with carboxylic acids have been achieved by using $\text{Hf}(\text{OTf})_4$ as a catalyst. Further investigations to clarify the reaction mechanism as well as to develop other reactions using carboxylic acids as acylating reagents are now in progress.

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- (11) Toluene-nitromethane (6.7:1) was used as a solvent. $\text{Hf}(\text{OTf})_4$ was dissolved in this media.
- (12) When 10 mol% of $\text{Hf}(\text{OTf})_4$ was used, 1-hydroxy-2-acetonaphthone was obtained in a 71% yield. On the other hand, 1-hydroxy-2-acetonaphthone (39%) and 1-acetoxynaphthalene (11%) along with the starting material (42%) were isolated when 5 mol% of $\text{Hf}(\text{OTf})_4$ was used.
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