Lanthanide Trifluoromethanesulfonates as Reusable Catalysts: Catalytic Friedel-Crafts Acylation

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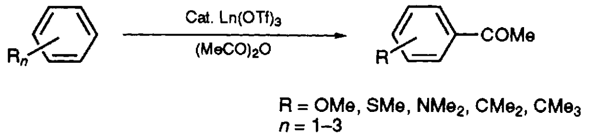
The Friedel-Crafts acylation of substituted benzenes proceeds smoothly by using a catalytic amount of a lanthanide trifluoromethanesulfonate [Ln(OTf)$_3$], which is easily recovered from the reaction mixture and reused without a decrease in catalytic activity.

The Friedel-Crafts acylation is generally achieved using aluminium trichloride ($AlCl_3$) as a Lewis acid catalyst. A common problem, particularly in an industrial process, is that the acylation requires a stoichiometric amount of aluminium trichloride which cannot be reused becasue of its instability in the usual aqueous workup[1].

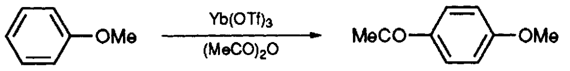
Recently, we found that lanthanide trifluoromethanesulfonates [lanthanide triflates; Ln(OTf)$_3$] worked efficiently as Lewis acids even in aqueous media and that the aldol reaction of silyl enol ethers with aqueous formaldehyde (formalin)[2] or other typical aldehydes,[3] Michael and Diels–Alder reactions[4] proceeded smoothly in the presence of a catalytic amount of the lanthanide compound. It was also demonstrated in these reactions that the catalysts were easily recovered after the reactions were completed and could be reused. Hence, we tried to develop the truly catalytic Friedel-Crafts acylation[5] using lanthanide triflate for the purpose of overcoming the problems caused by the $AlCl_3$-promoted reaction.[6]† Here we report on the acylation reaction of substituted benzenes with acetic anhydride using a catalytic amount of the lanthanide triflate.

A typical experimental procedure is described for the reaction of anisole with acetic anhydride using ytterbium triflate [Yb(OTf)$_3$] as a catalyst; Yb(OTf)$_3$ was prepared from the corresponding oxide (Yb_2O_3) and trifluoromethanesulfonic acid.[7] A mixture of Yb(OTf)$_3$ (620 mg, 1 mmol), anisole (540 µl, 5 mmol) and acetic anhydride (940 µl, 10 mmol) in nitromethane (5 ml) was stirred at 50 °C for 4 h. After dilution with water (10 ml), the reaction mixture was extracted with chloroform (3 × 10 ml). The acylation product, 4-methoxyacetophenone, was dissolved in the chloroform layer and the yield was determined by GLC (70%). The aqueous layer was concentrated to give a crystalline residue, which was finally heated at 190 °C for 4 h *in vacuo* to afford 576.6 mg of white crystals of Yb(OTf)$_3$ (93%). The recovered catalyst was reused in the next acylation reaction.



R = OMe, SMe, NMe$_2$, CMe$_2$, CMe$_3$
n = 1–3

Table 1 Yb(OTf)$_3$ catalysed Friedel-Crafts acylation of anisole[a]



Entry	Yb(OTf)$_3$/ equiv.	MeCO$_2$O/ equiv.	t/h	Solv.	Yield (%)[b]
1	1.0	1.0	24	CS_2	n.d.[c]
2	1.0	1.0	24	$C_2H_4Cl_2$	8
3	1.0	1.0	20	$PhNO_2$	32
4	1.0	excess	3	$(MeCO)_2O$	53
5	0.2	excess	18	$(MeCO)_2O$	48
6	1.0	1.0	24	MeCN	52
7	1.0	1.0	20	$MeNO_2$	78
8	0.2	1.0	48	$MeNO_2$	60
9	0.2	2.0	18	$MeNO_2$	99
10	0.05	2.0	48	$MeNO_2$	79

[a] *Reaction conditions*; anisole 5 mmol, solvent 5 ml, 50 °C. [b] Yields were determined using the internal standard method in GLC. [c] Not detected.

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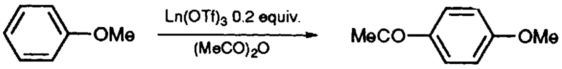
† Fujiwara *et al.*[6] have reported Friedel-Crafts alkylation using 50 mol% of lanthanide trichloride ($LnCl_3$).

Table 2 Effect of various lanthanide triflates [$Ln(OTf)_3$][a]

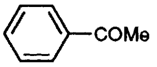
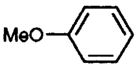
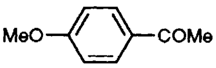
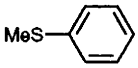
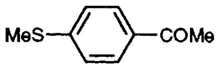
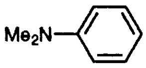
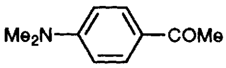
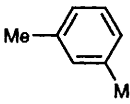
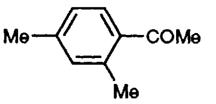


$Ln(OTf)_3$	Yield (%)[b]	$Ln(OTf)_3$	Yield (%)[b]
$La(OTf)_3$	41	$Dy(OTf)_3$	85
$Pr(OTf)_3$	87	$Ho(OTf)_3$	79
$Nd(OTf)_3$	79	$Er(OTf)_3$	78
$Sm(OTf)_3$	80	$Tm(OTf)_3$	84
$Eu(OTf)_3$	78	$Yb(OTf)_3$	99
$Gd(OTf)_3$	78	$Lu(OTf)_3$	81

[a] *Reaction conditions*; anisole 5 mmol, $(MeCO)_2CO$ 10 mmol, $MeNO_2$ 5 ml, 50 °C, 18 h. [b] Yields were determined using the internal standard method in GLC.

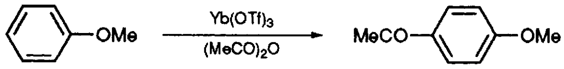
Table 3 Lanthanide triflate catalysed Friedel-Crafts acylation[a]

$$\text{Ar–H} + (MeCO)_2O \xrightarrow{Yb(OTf)_3\ 0.2\ \text{equiv.}} \text{Ar–COMe}$$

Ar–H	Products	*t* / h	Yield (%)
		18	n.d.[b]
		18	99[c]
		42	83[c]
		18	76[d]
		18	25[c]

[a] *Reaction conditions*: Ar-H 5 mmol, $(MeCO)_2O$ 10 mmol, $MeNO_2$ 5 ml, 50 °C, 18 h. [b] Not detected. [c] Yields were determined using the internal standard method in GLC. [d] Isolated yield.

Table 4 Recycling of $Yb(OTf)_3$ in acetylation of anisole[a]



No. of times used	Conv. (%)	Yield (%)[b]	Recovery of catalyst[c]
1	72	70	93
2	71	69	90
3	73	71	92

[a] *Reaction conditions*: anisole 1.0 equiv., $(MeCO)_2O$ 2 equiv., $MeNO_2$, 50 °C, 4 h. [b] Yields were determined using the internal standard method in GLC. [c] Recovery of catalyst was determined by the ratio of the isolated amount of crystal from aqueous layer based on initial amount of $Yb(OTf)_3$.

Optimization of the conditions in the reaction of anisole with acetic anhydride is shown in Table 1. When acetic anhydride, acetonitrile or nitromethane was used as a solvent (entries 4–10), homogeneous acylation reaction readily proceeded and nitromethane gave the highest yield of the desired product (entries 7–10). On the other hand, in carbon disulfide, dichloromethane, or nitrobenzene (entries 1–3), the reaction mixture was heterogeneous and the yield of acylation product was very poor. It should be noted that a quantitative acylation product was obtained by using a catalytic amount of $Yb(OTf)_3$ (0.2 equiv., entry 9). Even when 0.05 equiv. of the catalyst was employed, the acylation product was obtained in 79% yield (entry 10).

Effects of the various lanthanide triflates as catalysts in the acetylation reaction of anisole are shown in Table 2. Each lanthanide triflate was effective for the acetylation of anisole, however, the activities of $La(OTf)_3$ were relatively low.

Several substituted benzenes were subjected to $Yb(OTf)_3$ catalysed acetylation and the results are summarized in Table 3. Though the acylation of benzene did not occur, introduction of methylthio or dimethylamino group brought about high yields of the acetylation products. The presence of a methyl group was also effective and *m*-xylene was acetylated to the dimethylacetophenone in moderate yield.

Finally, the catalytic activities of the recovered catalyst were examined. As shown in Table 4, the yields of 4-methoxyacetophenone in the second and third uses of the catalyst were almost same as that in the first use. Furthermore, almost 90% of ytterbium triflate was easily recovered from aqueous layer by simple extraction (see typical procedure).

In summary, the efficient Friedel-Crafts actylation was realized by using a catalytic amount of lanthanide triflate. Although the yields are not yet optimized in some cases, this novel lanthanide catalysed reaction has characteristic properties and advantages over the $AlCl_3$-promoted reaction.[6]

Further investigation to apply lanthanide triflates as catalysts to other related synthetic reactions for aromatic compounds such as Friedel-Crafts alkylation, Gattermann-Koch reaction and the Fries rearrangement is now in progress.

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