$Ln(OTf)_3$–$LiClO_4$ as reusable catalyst system for Friedel–Crafts acylation†

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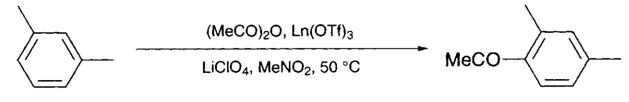
Lithium perchlorate is found to accelerate $Ln(OTf)_3$-catalysed Friedel–Crafts acylation; the catalytic system, $Ln(OTf)_3$–$LiClO_4$, is easily recovered from the reaction mixture by simple extraction and can be reused without decrease in its catalytic activity.

The Friedel–Crafts acylation is a convenient method for the synthesis of aromatic ketones. This reaction is generally performed using aluminum trichloride ($AlCl_3$) as a Lewis acid catalyst. It is a common problem, particularly in industrial processes, that the reaction requires more than a stoichiometric amount of $AlCl_3$, which can not be reused because of its instability in the aqueous workup.[1] In order to solve this problem, several approaches to catalytic Friedel–Crafts acylations have been recently reported.[2]

In previous papers, we reported that a catalytic amount of lanthanide trifluoromethanesulfonate [lanthanide triflate, $Ln(OTf)_3$] promotes Friedel–Crafts acylation, and that the catalyst was easily recovered and reused.[3,4] Lanthanide triflate is stable in water and therefore does not decompose under aqueous work up conditions, unlike conventional Lewis acids. By utilizing these properties, the catalysts have been successfully applied to several synthetic reactions.[5] In the Friedel–Crafts reactions, however, we found that this catalytic system only works with highly electron-donative aromatics because of its low Lewis acidity. For example, while the acylation proceeded with anisole, mesitylene and xylenes, acylation of benzene and toluene did not occur.

In the course of our investigation to enhance the acylation reactivity, we focused on the properties of lithium perchlorate ($LiClO_4$). Lithium perchlorate was reported to form a cationic species when mixed with an acylating agent in the presence of an antimony or hafnium compound.[6,7] If such a cationic species is generated by $LiClO_4$ in the presence of $Ln(OTf)_3$, it is expected that its high reactivity would ensure successful acylation. We also expected that $Ln(OTf)_3$–$LiClO_4$ catalytic system would be easily recovered by the aqueous workup of the reaction mixture, because both $LiClO_4$ and $Ln(OTf)_3$ are soluble and stable in aqueous media. Here we report a study on the novel reusable catalytic system, $Ln(OTf)_3$–$LiClO_4$.

Table 1 Acceleration of acylation by $LiClO_4$[a]



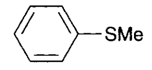
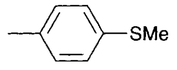
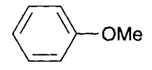
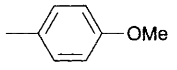
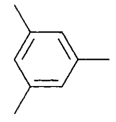
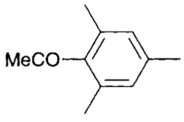
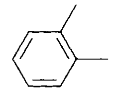
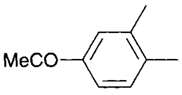
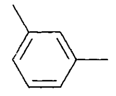
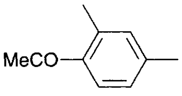
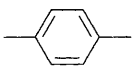
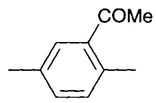
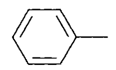
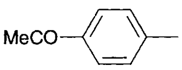
Ln = Sc[b] LiClO₄ (equiv.)	Yield (mol%)[d]	Ln = Yb[c] LiClO₄ (equiv.)	Yield (mol%)[d]
none	12	none	n.d.[e]
0.4	22	0.4	8
0.8	28	0.8	17
1.0	36	1.0	22
2.0	51	2.0	38
4.0	75	4.0	67
6.0	82	6.0	83
8.0	88		
10.0	89		

[a] *Conditions*: *m*-Xylene (5 mmol) acetic anhydride (5 mmol), $Sc(OTf)_3$ (1 mmol), $LiClO_4$, $MeNO_2$ (5 ml) 50 °C. [b] Reaction time 1 h. [c] Reaction time 4 h. [d] Yields were determined by the internal standard method in GLC. [e] Not detected.

Effects of $LiClO_4$ in the reaction of *m*-xylene with acetic anhydride using the $Ln(OTf)_3$-$LiClO_4$ system are summarized in Table 1. $Sc(OTf)_3$ or $Yb(OTf)_3$ were used as representative $Ln(OTf)_3$, and remarkable acceleration of the acylation by $LiClO_4$ was observed. In each case, higher yields of dimethylacetophenone were obtained as the amount of $LiClO_4$ increased. In the absence of $LiClO_4$, $Sc(OTf)_3$-catalysed acylation gave only a 12% yield of the product. On the other hand, when $Sc(OTf)_3$ was combined with 10 equiv. of $LiClO_4$, the yield improved to 89%. In the absence of $Ln(OTf)_3$ [$Sc(OTf)_3$ or

Table 2 $Sc(OTf)_3$–$LiCLO_4$ Catalysed Friedel–Crafts Acylation[a]

$$\text{Ar–H} \xrightarrow[\text{LiClO}_4,\ \text{MeNO}_2,\ 50\,^\circ\text{C},\ 1\ \text{h}]{(\text{MeCO})_2\text{O},\ \text{Sc(OTf)}_3} \text{MeCO–Ar}$$

Entry	Ar–H	LiClO₄ (equiv.)	Product	Yield (%)[b]
1		4		99
2		2		90
3		0.2		83
4		4		55
5		4		69
6		4		19
7[c]		4		47

[a] *Conditions*: As in Table 1, 1 h. [b] Yields were determined by the internal standard method in GLC. [c] Reaction was carried out for 18 h.

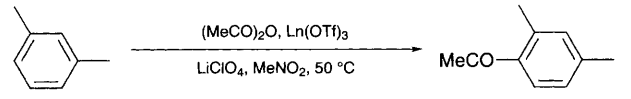
$Yb(OTf)_3$], $LiClO_4$ was not soluble in the reaction mixture and no acylation product was obtained. However, the addition of $Ln(OTf)_3$ [$Sc(OTf)_3$ or $Yb(OTf)_3$] to a suspension of $LiClO_4$, acetic anhydride and *m*-xylene in nitromethane changed the suspension to a dark-red homogeneous solution, and the reaction began to proceed. These results suggest that a highly active cationic species of acylating agent is formed by acetic anhydride and $LiClO_4$ in the presence of $Ln(OTf)_3$.

Several substituted benzenes were subjected to the $Sc(OTf)_3$–$LiClO_4$ catalysed acetylation and the results are summarized in Table 2. In every reaction, the acylation reaction gave a single acetylated product and formation of other isomers was not detected by GLC. It should be noted that toluene was acetylated by the $Sc(OTf)_3$–$LiClO_4$ system and 47% of 4-methylacetophenone was obtained (entry 7), although acetylation of toluene without $LiClO_4$ did not occur. The acetylation of thioanisole and anisole gave the corresponding acetylated product in an excellent yield (entries 1 and 2). Mesitylene and xylenes were acetylated to the 2,4,6-trimethylacetophenone and dimethylacetophenones, respectively, in moderate yields (entries 3–6).

Finally, catalytic activities of the recovered catalysts [$Sc(OTf)_3$ and $LiClO_4$] were examined. As shown in Table 3, the yields of dimethylacetophenone in the 2nd and 3rd uses of the catalyst were almost same as that in the 1st use. In every case, almost 90% of the mixture of $Sc(OTf)_3$ and $LiClO_4$ was easily recovered from reaction mixture by simple extraction.‡

In summary, Friedel–Crafts acylation using the novel reusable catalytic system $Ln(OTf)_3$–$LiClO_4$ has been achieved.

Table 3 Reuse of $Sc(OTf)_3$ and $LiClO_4$[a]



Number of Use	Yield (%)[b]	Recovery of $Sc(OTf)_3$ and $LiClO_4$[c]
1	61	96
2	55	94
3	53	94

[a] *Conditions*: *m*-Xylene (1 equiv.) acetic anhydride (1 equiv.), $Sc(OTf)_3$ (0.2 equiv.), $LiClO_4$ (4 equiv.), $MeNO_2$ (5 ml), 50 °C, 1 h. [b] Yields were determined by the internal standard method in GLC. [c] Recovery of $Sc(OTf)_3$ and $LiClO_4$ was determined by the ratio of the isolated amount of crystals of $Sc(OTf)_3$ and $LiClO_4$ from aqueous layer based on initial amount of $Sc(OTf)_3$ and $LiClO_4$.

Although the yields are not yet optimized for all examples, the acylation catalysed by this novel system has characteristic properties and advantages over the $AlCl_3$-promoted reaction.

Footnotes

† We have already applied for a Japanese patent for the $Ln(OTf)_3$–$LiClO_4$ catalytic system for Friedel–Crafts reactions. Application No. 94-18661, February 15, 1994.

‡ *Typical experimental procedure* for the reaction of *m*-xylene with acetic anhydride using $Sc(OTf)_3$–$LiClO_4$ as a catalytic system: ($Sc(OTf)_3$ was prepared from the corresponding oxide (Sc_2O_3) and trifluoromethanesulfonic acid.[3,4,8] Acetic anhydride (470 μl, 5 mmol) was added to a suspension of $Sc(OTf)_3$ (490 mg, 1 mmol), *m*-xylene (610 μl, 5 mmol) and $LiClO_4$ (2130 mg, 20 mmol) in nitromethane (5 ml), and the mixture was stirred at 50 °C for 1 h. Addition of acetic anhydride changed the suspension to a dark-red homogeneous solution. After dilution with water (10 ml), the reaction mixture was extracted with chloroform (3 × 10 ml). The acylation product, 2,4-dimethylacetophenone, was dissolved in the chloroform layer and the yield was determined by GLC (61%). The aqueous layer was concentrated to give a crystalline residue, which was finally heated at 190 °C for 4 h *in vacuo* to afford a mixture of $LiClO_4$ and $Sc(OTf)_3$ (2510 mg). The recovered catalyst was reused in the next acylation reaction.

References

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