SHORT PAPER

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Efficient aromatic acylation using catalytic ytterbium(III) bis(trifluoromethylsulfonyl)amide activated by lithium perchlorate in nitromethane†

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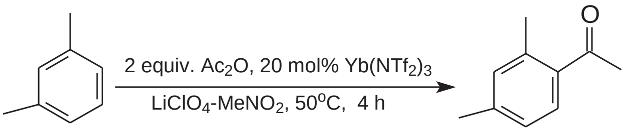
Various aromatic ketones were prepared in good to high yields by acylation using ytterbium bis(trifluoromethylsulfonyl) amide as catalyst in 4M lithium perchlorate in nitromethane.

Keywords: acylation, catalysis, ytterbium(III) bis(trifluoromethylsulfonyl)amide, lithium perchlorate

Friedel–Crafts acylation is a fundamental and important synthetic method for the preparation of aromatic ketones in organic chemistry and Lewis acid catalysts have been employed in the Friedel–Crafts acylation in place of aluminum trichloride.[1,2] Lanthanide triflates, Ln(OTf)$_3$, have been employed by S. Kobayashi *et al.* as excellent Lewis acid catalysts for Friedel–Crafts acylation because they can promote the reaction in catalytic quantities, can be easily recovered from the reaction mixtures and are subsequently reusable.[3,4] It has also been found that lanthanide bis(trifluorosulfonyl)amides, Ln(NTf$_2$)$_3$, are much more effective Lewis acid catalysts for acylation reactions than lanthanide triflates.[5,6] However, the activity for the two kinds of catalyst is essentially limited to the acylation of activated aromatics. To enhance the catalytic power, great efforts have been made with tuning metal and/or counter anions.[7-9] Highly concentrated solutions of lithium perchlorate in various organic solvents have become widely used media for many synthetic transformations which are difficult to carry out under ordinary conditions.[10,11] We report now our results of the remarkably high efficiency of ytterbium bis(trifluoromethylsulfonyl)amide (Yb(NTf$_2$)$_3$) for Friedel–Crafts acylation in lithium perchlorate in nitromethane (LPNM).

The efficiency of Yb(NTf$_2$)$_3$ in the acylation reaction of anisole with acetic anhydride was well demonstrated in a previous report.[5] However, the reaction became sluggish when the substrate was changed to *m*-xylene and benzene. So, the catalytic activities of Yb(NTf$_2$)$_3$ in different concentrations of lithium perchlorate solution in nitromethane were first examined in the acylation of *m*-xylene by acetic anhydride (Table 1). Although Yb(NTf$_2$)$_3$-catalysed acetylation of *m*-xylene gave only a 22% yield of dimethylacetophenone in nitromethane, a remarkable acceleration was found when the reaction was carried out in LPNM. As the concentration of LiClO$_4$ was increased, the yields of the product improved and an 88 % yield was obtained when the reaction was carried out in a 4 M LPNM solution for 4 h. On the other hand, a rate enhancement was also found when the catalyst was substituted by Yb(ClO$_4$)$_3$ in 4 M LPNM but only a 42% yield of acylation product could be achieved under the same experimental conditions. The results, combined with previous reports,[9, 11] clearly show that the type of anionic ligand in the catalyst is also critical to obtaining a high yield in the reaction.

Table 1 Yb(NTf$_2$)$_3$-catalysed acylation of *m*-xylene in LiClO$_4$-MeNO$_2$



Entry	LiClO$_4$-MeNO$_2$	Yield/%[a]
1	0.0M	22
2	0.5M	54
3	1.0M	64
4	2.0M	73
5	4.0M	88

[a]Determined by GC analysis using 1,2,4-trichlorobenzene as an internal standard
[b]84% yield on isolation by column chromatography

Although the acylation was accelerated in the solutions of lithium perchlorate in nitromethane, other lithium salts, such as lithium chloride and lithium bis(trifluoromethylsulfonyl)amide, were not effective. The acceleration of the Friedel–Crafts acylation is reported to be attributed to the formation of a highly active cationic species by lithium perchlorate and acetic anhydride in the presence of the Lewis acid catalyst.[11] Organic reactions involving polar transition states and ionic intermediates are profoundly influenced by the polarity of the medium.[12] The unique character of the current system may be also due to the high polarity of the medium and its ability to stabilise polar transition states.

The effect of the amount of Yb(NTf$_2$)$_3$ on the acylation of *m*-xylene is summarised in Table 2. The results showed that the best result, 98% yield, was achieved by using 10 mol% Yb(NTf$_2$)$_3$ for 9 h. Interestingly, the high efficiency of the system was demonstrated by the 92% yield of the product even using only 1 mol% of Yb(NTf$_2$)$_3$ (Entry 1). We can see that under same experimental conditions, satisfactory product yields could be obtained when the acylation reactions were carried out for only 1 h.

Table 2 The acylation of m-xylene catalysed by ytterbium complexes at different concentrations in 4M LiClO$_4$-MeNO$_2$ [a]

Entry	Yb(NTf$_2$)$_3$/mol%	Yield/%[b]	Turnover
1	1	92(53)	92
2	5	95(79)	19
3	10	98(84)	10
4	20	96(73)	5

[a]Reaction time 9 h, other conditions were same as Table 1.
[b]Determined by GC analysis using 1,2,4-trichlorobenzene as an internal standard.
Figures in parentheses represent the results obtained in 1h.

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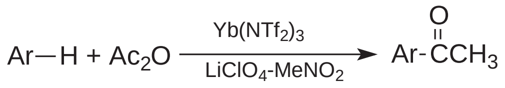
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 3 $Yb(NTf_2)_3$-catalysed acylation of structurally diverse benzenes with acetic anhydride in 4M $LiClO_4$-$MeNO_2$



$$\mathrm{Ar{-}H + Ac_2O \xrightarrow[LiClO_4\text{-}MeNO_2]{Yb(NTf_2)_3} Ar\text{-}\overset{\displaystyle O}{\overset{\|}{C}}CH_3}$$

Entry	Ar-H	$Yb(NTf_2)_3$ /equiv.	Ac_2O /equiv.	Conditions	Yield/%[a]
1	*p*-xylene	0.2	2.0	50°C, 24 h	74
2	Toluene	0.2	2.0	50°C, 24 h	82
3	*iso*-butylbenzene	0.2	2.0	50°C, 48 h	83
4	Benzene	0.2	2.0	50°C, 24 h	trace

[a] Determined by GC analysis using 1,2,4-trichlorobenzene as an internal standard.

Several examples of the Friedel–Crafts acylation reaction are shown in Table 3. Although the acylation of benzene gave only a trace amount of the desired aromatic ketone, the acylation of toluene afforded 82% 4-methylacetophenone. The acetylation of *p*-xylene, and isobutyl benzene also gave the corresponding acetylated product in an excellent yield (Entries 1, 3). Each reaction gave only a single product, no other isomers were detected by GC.

The ytterbium(III) bis(trifluoromethylsulfonyl)amide, $Yb(NTf_2)_3$, was prepared from the reaction of the sulfonamide, $HNTf_2$, with Yb_2O_3 in water.[13] A typical experimental procedure is described for the acylation reaction of *m*-xylene and acetic anhydride catalysed by $Yb(NTf_2)_3$ in 4M $LiClO_4$ in nitromethane: To a solution of $LiClO_4$ (2130 mg, 20 mmol) in nitromethane (5 ml), $Yb(NTf_2)_3$ (1013 mg, 1 mmol), *m*-xylene (610 µl, 5 mmol) and acetic anhydride (940 µl, 10 mmol) were successively added. The reaction mixture was stirred for 1 h at 50°C and then quenched with water, the reaction mixture was then extracted with chloroform. The acylation product, 2,4-dimethylacetophenone, was dissolved in the chloroform layer and the yield was determined by GC analysis by using 1,2,4-trichlorobenzene as an internal standard. The standard samples of all products were commercially available from Aldrich or prepared according to the procedures in the literature[14] and their purity was checked by the FT-IR, ^1H NMR, and GC analysis.

In summary, this paper demonstrates that ytterbium(III) bis(trifluoromethylsulfonyl)amide is an efficient Lewis acid catalyst for the Friedel–Crafts acylation of *m*-xylene when the reaction is carried out in high concentrated lithium perchlorate in nitromethane. Acylation reactions of aromatics such as *p*-xylene, toluene and isobutyl benzene also proceed smoothly in the novel catalytic system.

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