

Highly selective Friede–Crafts monoacylation of ferrocene catalysed by ytterbium(III) triflate

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In the presence of a catalytic amount of ytterbium(III) triflate [Yb(OTf)₃], ferrocene reacted with anhydrides or acyl chlorides to afford monoacylferrocenes in high yields under moderate conditions. An efficient, simple and environmentally friendly procedure was provided. The catalyst was easily recovered and reused without any loss of activity.

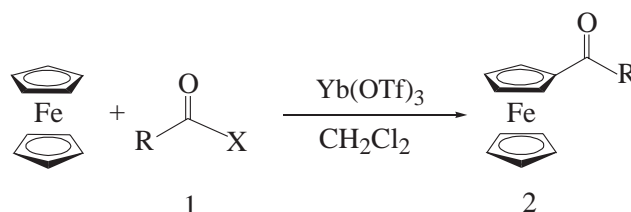
Keywords: ytterbium triflate, ferrocene, acylation, Friede–Crafts

Ferrocene and its derivatives play an important role in many fields of chemistry.¹ The tremendous interest in ferrocene chemistry stems from their increasing use and application in the fields of organic synthesis, material science and catalysis.^{2–5} Acylferrocenes are important derivatives and there are several methods to prepare them. For example, they are obtained from ferrocene with acyl chlorides or anhydrides catalysed by AlCl₃,^{3,6–7} H₃PO₄,^{8–9} BF₃·Et₂O,^{8,10–11} or with carboxylic acid in the presence of PCl₃/Al-anode,^{12–13} or with (CF₃CO)₂O/Al₂O₃.¹⁴ The Friede–Crafts acylation of ferrocene with acyl halide or anhydride catalysed by AlCl₃ has become the classic method among the above catalysts. However, the preparation of diacylferrocene or monoacylferrocene needs control of the reaction conditions in order to avoid side reactions (mono- or di- acylation and oxidation of the iron atom).^{8,15} This is especially true, for conventional Lewis acids, such as AlCl₃, which cannot be recovered and reused because of its instability in the usual aqueous work up. It is desirable from environmental and synthetic points of view that we should find a novel synthetic method to resolve these problems.

Recently, rare earth metal triflate (ytterbium triflate), has been widely used in organic synthesis as an all purpose Lewis acid,^{16–19} especially in the Aldol reaction,²⁰ Mannich-type reaction,²¹ Diels–Alder reaction²² and Friede–Crafts reaction.^{23–26} However, to the best of our knowledge [Yb(OTf)₃]-catalysed Friede–Crafts acylation of ferrocene has not been reported up to date. Judging from these unique properties of [Yb(OTf)₃], we would like to report our work using [Yb(OTf)₃] as the catalyst (Scheme 1).

Results and discussion

[Yb(OTf)₃] as a Lewis acid can catalyse the Friede–Crafts acylations of ferrocene with acyl chlorides or anhydrides in



Scheme 1

dichloromethane at reflux temperature (Scheme 1). The results are summarised in Table 1. From Table 1, we found that the reactions run well with the catalytic amounts of [Yb(OTf)₃], and the products are only monoacylferrocenes. We also wished to synthesize the corresponding diacylferrocenes. Unfortunately by changing the reaction conditions, for instance changing the ratio(ferrocene : acylating agent), solvent, elevated reaction temperatures and prolonged reaction times, we failed to obtain the diacylation products. On the other hand, an extremely prolonged reaction time led to considerable abundance of oxidised ferrocene.

Comparing the yields (Entries 6–9), We see that having an electron-donor in the para position of the aromatic ring gave better results than an electron-withdrawing substituent in the same position. The results also show that acylium ions with electron-withdrawing groups effected electron-transfer rather than acylation, thus giving high yields of the ferricinium cation rather than an acylferrocene in the presence of [Yb(OTf)₃]. In addition, some deactivated acyl chlorides, such as benzenesulfonyl chloride and *p*-toluenesulfonyl chloride are not suitable for this reaction under the described conditions (Entries 12, 13).

Table 1 Acylation of ferrocene in the presence of Yb(OTf)₃^a

Entry	R	X	Reaction time / h	Product	M.p./°C	Yield ^b / %
1	CH ₃	OAC	6	2a	85–87(lit., ¹⁰ 84–86)	96
2	CH ₃	Cl	6	2a	85–87(lit., ¹⁰ 84–86)	91
3	CH ₂ CH ₃	OAC	6	2b	36–38 (lit., ²⁷ 37.5–38)	92
4	CH ₂ CH ₃	Cl	6	2b	36–38 (lit., ²⁷ 37.5–38)	90
5	(CH ₂) ₁₆ CH ₃	Cl	6	2c	62.5–63.5(lit., ²⁸ 63.4–63.7)	91
6	Phenyl	Cl	12	2d	105–107(lit., ²⁹ 108.1–108.3)	79
7	<i>p</i> -CH ₃ Ph	Cl	12	2e	128–130 (lit., ³⁰ 130)	88
8	<i>p</i> -ClPh	Cl	24	2f	118–120(lit., ³¹ 119)	42
9	<i>p</i> -O ₂ NPh	Cl	24	–	–	ND ^c
10	PhCH ₂	Cl	12	2g	128–130(lit., ²⁷ 129–130)	86
11	PhCH=CH	Cl	12	2h	139–141(lit., ¹⁰ 141–142)	89
12	PhSO ₂	Cl	24	–	–	ND ^c
13	<i>p</i> -CH ₃ PhSO ₂	Cl	24	–	–	ND ^c

^aThe reaction were carried out in the presence of 1 equiv. of ferrocene, 0.1 equiv. of Yb(OTf)₃ and 1.1 equiv. of acyl chloride or anhydride.

^bYields based on ferrocene.

^cNot detected.

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In order to examine the activity of aliphatic compounds, we also have synthesised several monoacylferrocenes (**2b–c**, **2g–h**) as described above. From the experimental results, we found that aliphatic acylferrocenes are synthesised easier than aromatic acylferrocenes. Considering that $[\text{Yb}(\text{OTf})_3]$ can promote the Friede–Crafts acylation²⁶ and compounds **2g** and **2h** have an aromatic ring, our interest was if these acylferrocenes containing an aromatic ring have a similar activity or not. When the reaction was complete, two equivalents of acylating agent were added subsequently into the mixture (Entries 10, 11). Unfortunately, no desired products were detected in our experiment. We postulated that the possible reason was the activity of aromatic ring is much weaker than the ferrocene ring.

In addition, we have investigated the recycle problem of $[\text{Yb}(\text{OTf})_3]$ using acetic anhydride as the acylating agent. It was found that the reaction proceeded smoothly to completion in around 6 h, with both yield and catalyst recovery of around 95%.

In conclusion, the method in the presence of $[\text{Yb}(\text{OTf})_3]$ provided an efficient and convenient procedure for synthesis of monoacylferrocenes. Compared to conventional Lewis acids, the notable advantages of the present work are mild conditions, simple operation, generality, excellent selectivity, low environmental pollution and excellent yields.

Experimental

All reagents are commercial available. Dichloromethane was dried over P_2O_5 just before use; cinnamoyl chloride was synthesised by a literature procedure;³² $[\text{Yb}(\text{OTf})_3]$ was prepared from ytterbium oxide with trifluoromethanesulfonic acid in water according to the literature.³³ All reactions were performed under an atmosphere of dry dinitrogen. Melting points were recorded on Digital Melting Point Apparatus WRS-1B and are uncorrected. ^1H NMR spectra were recorded on a Varian-400 MHz instrument using CDCl_3 as the solvent and chemical shifts were expressed in ppm using TMS as an internal standard. IR measurements were carried out with a Nicolet Aviator-370 instrument. Mass spectra were measured with a Thermo Finnigan LCQ-Advantage (ESI). All spectra data of the acylated products were identical to authentic samples.

Representative experimental procedure

A solution of ferrocene 2 mmol (0.372 g) in dichloromethane 15 ml was stirred under an anhydrous N_2 atmosphere in a three necked round bottom bottle. Then, acetic anhydride (2.2 mmol in 10 ml of dichloromethane) and $[\text{Yb}(\text{OTf})_3]$ (0.2 mmol, 0.124 g) was added subsequently. The mixture was refluxed for 6 hours and turned dark violet. The resulting mixture was diluted with dichloromethane (15 ml) and treated with water (10 ml). The aqueous layer was extracted with CH_2Cl_2 (15 \times 3 ml). $[\text{Yb}(\text{OTf})_3]$ can be recovered from the aqueous layer by removing the water according to the literature procedure.³⁴ The combined organic layers were washed with saturated aqueous (NaHCO_3) solution 10 ml, dried over MgSO_4 and concentrated in a vacuum. The residue was purified by preparative TLC (cyclohexane: petroleum ether: ethyl acetate = 3:3:1) and afforded monoacetyl ferrocene (0.438 g, 96%). Spectral data of **2a** are as follows.

Acetyl ferrocene 2a: Orange crystalline solid m.p. 85–87°C (lit.,¹⁰ 84–86°C); IR (KBr) V/cm^{-1} : 3114, 3096–3077, 2924, 1661, 1456, 1358, 1280, 1115, 1005, 893; ^1H NMR: δ (ppm) 4.78(t, 2H, $J=1.8$ Hz), 4.51(t, 2H, $J=1.8$ Hz), 4.21(s, 5H), 2.40(s, 3H); m/z (ESI): 229.0($\text{M}+\text{H}^+$).

We are grateful to the National Natural Science Foundation of China (No. 20276072), National Basic Research Program (No. 2003CB114400) and National Natural Science Foundation of Zhejiang Province (No. 2002095) for financial support.

Received 11 April 2004; accepted 29 June 2004
Paper 04/2436

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