



# Selective monoacylation of ferrocene

## An eco-friendly procedure on the solid phase of alumina

Brindaban C. Ranu,\* Umasish Jana and Adinath Majee

Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Calcutta-700 032, India

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### Summary

A simple, efficient and environment-friendly procedure has been developed for acylation of ferrocene with direct use of carboxylic acid in the presence of trifluoroacetic anhydride on the solid phase of alumina. A wide range of structurally varied carboxylic acids have been found to provide selectively the monoacylated products in high yields.

### Introduction

Ferrocene and its derivatives have been the subject of current interest because of their potential uses as chiral ligands in organic synthesis<sup>1</sup> and as important materials in various fields.<sup>2</sup> Thus, derivatization of ferrocene has received special attention.<sup>3</sup> Acylation of ferrocene is a very important reaction as it introduces a carbonyl functionality which is highly manipulable. Although a number of methods are available in the literature<sup>4</sup> for acylation of ferrocenes they have serious disadvantages of producing a mixture of products containing mono- and di-acylated derivatives together with unreacted starting material which requires separation at a subsequent stage. More seriously, the use of toxic chemicals like  $\text{AlCl}_3$ ,  $\text{BF}_3$ ,  $\text{PCl}_3$  and acid chlorides entails environment pollution. Thus, an efficient and eco-friendly procedure for this important transformation is needed. Recently, we have introduced a simple procedure for regioselective acylation of aromatic ethers with carboxylic acids on the solid phase of alumina in the presence of trifluoroacetic anhydride<sup>5</sup> and we have discovered that this procedure also works very well for acylation of ferrocene.

### Results and discussion

In a typical general procedure, a mixture of carboxylic acid and trifluoroacetic anhydride was added to ferrocene adsorbed on the surface of activated acidic alumina and mixed uniformly with shaking. The mixture was kept at room temperature with occasional shaking for a certain period of time until the reaction was complete. The product was isolated by simple extraction of the solid mass by ether followed by usual workup.

Several structurally varied carboxylic acids were used in this acylation reaction to provide the corresponding monoacylated ferrocenes in excellent yields. The results are summarised in Table 1. The reactions with aromatic acids are rather slow and conversions are not complete even after 8 hours. However, no side product is isolated in these reactions; only the unreacted ferrocene and carboxylic acids were recovered. In general, all the

reactions are very clean and monoacylated products are obtained as the sole isolable compounds. Presumably, alumina acts here as a Lewis acid in effecting the Friedel–Crafts acylation of ferrocene with the mixed anhydride of the carboxylic acid and trifluoroacetic anhydride.

### Conclusion

This method on the solid surface of alumina provides a very convenient and efficient procedure for acylation of ferrocene. The notable advantages of this methodology are direct use of carboxylic acids, mild conditions (room temperature), operational simplicity, generality, excellent selectivity (only monoacylation occurs), high yields (85–98%) and no environmental pollution, and thus it offers significant improvements over other procedures involving Friedel–Crafts acylation of ferrocenes.<sup>4</sup> We believe this will find significant applications in the synthesis of ferrocene derivatives.

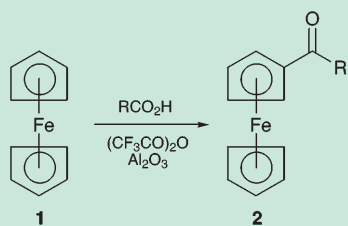
### Representative experimental procedure

A solution of ferrocene (186 mg, 1 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (2 ml) was adsorbed on the surface of activated (heated at 150 °C for 3 h under reduced pressure and then cooled under nitrogen) alu-

### Green Context

Functionalised ferrocenes are currently of great interest due to their potential as planar-chiral ligands for, e.g., hydrogenation catalysts. One of the most important methods of functionalisation of these materials is Friedel–Crafts acylation, a process which typically uses substantial quantities of strong Lewis acids such as aluminium chloride. The development of alternative, green procedures is therefore of interest. The use of alumina and trifluoroacetic anhydride as an activating system for carboxylic acids has been shown to allow the highly selective monoacylation of ferrocene. It is thought that the reaction proceeds *via* a mixed carboxylic/trifluoroacetic anhydride. Yields are excellent in most cases, in others the unreacted carboxylic acid can be easily recovered. Work up procedures are simple and convenient on a small scale, but would need further optimisation to provide a genuinely green overall process. *DJM*

**Table 1** Acylation of ferrocene with carboxylic acid/ TFAA on the surface of alumina



Entry	RCO <sub>2</sub> H, R =	Time/h	Yield of 2 (%) <sup>a</sup>
1	CH <sub>3</sub>	0.5	98
2	CH <sub>3</sub> CH <sub>2</sub>	0.5	90
3	PhCH <sub>2</sub>	1.5	96
4	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>6</sub>	1.0	93
5	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>16</sub>	1.0	94
6	CH <sub>3</sub> CH(NO <sub>2</sub> )(CH <sub>2</sub> ) <sub>2</sub>	1.0	85
7	PhS(CH <sub>2</sub> ) <sub>3</sub>	1.5	88
8	(CH <sub>3</sub> ) <sub>2</sub> CH	0.5	95
9	(Ph) <sub>2</sub> CH	1.5	93
10	PhSCH <sub>2</sub> CH(CH <sub>3</sub> )	1.5	89
11	C <sub>6</sub> H <sub>11</sub>	1.0	92
12	Ph	8.0	55 <sup>b</sup>
13	<i>p</i> -OMe-Ph	8.0	58 <sup>b</sup>

<sup>a</sup> Yields refer to pure isolated products, fully characterized by spectral and analytical data. <sup>b</sup> The rest is recovered starting material.

mina (acidic, 3 g) and then the solvent was evaporated off completely under vacuum. To this was added a mixture of acetic acid (120 mg, 2 mmol<sup>6</sup>) and trifluoroacetic anhydride (525 mg, 2.5 mmol<sup>6</sup>) with shaking. The mixture was then kept at room temperature with occasional shaking under a moisture guard for a certain period of time as required to complete the reaction. [In all the reactions, a colour developed (usually pink, but in a few cases green and blue) and darkened with progress of reaction.] The solid mass was then eluted with Et<sub>2</sub>O, and the ether extract was then washed with an aqueous solution of sodium hydrogen carbonate and brine and dried over anhydrous sodium sulfate. Evaporation of solvent furnished practically pure (by <sup>1</sup>H NMR) monoacetyl ferrocene (223.5 mg, 98%). This was further purified by filtering it through a short column of silica gel to afford the analytically pure product, mp 85–86 °C. The other acylated products are also obtained following the same procedure and identified by spectral (IR, <sup>1</sup>H and <sup>13</sup>C NMR) and analytical data.

The unreacted carboxylic acids (Table 1, entries 12, 13) were recovered from the hydrogen carbonate extract by acidification and extraction with ether. However, trifluoroacetic acid, possibly being too water soluble and not being a high boiling liquid (bp 72 °C), was not isolated in this work-up process.

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- With 1 equivalent of carboxylic acid and 1 equivalent of trifluoroacetic anhydride the reaction is considerably slow and the conversion is also not complete even after 12 h. However, use of 2 equivalents of carboxylic acid and 2.5 equivalents of TFAA accelerated the reaction to a great extent producing only the monoacylated product. But, interestingly, use of 4 equivalents of carboxylic acid and 8 equivalents of TFAA leads to diacylation quantitatively (2 examples) although the condition is yet to be generalised.

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