Zinc mediated selective acylation of ferrocene under solvent-free conditions

Vishal H. Purecha, Nitin S. Nandurkar, Bhalchandra M. Bhanage and Jayashree M. Nagarkar*

Department of Chemistry, Institute of Chemical Technology (Autonomous), University of Mumbai, N. Parekh Marg, Matunga, Mumbai – 19, India

A simple, convenient and environmentally-friendly method for selective acylation of ferrocene to monoacylferrocene in the presence of Zn metal under solvent-free conditions is described. The protocol requires mild operating conditions, affording higher yields of desired products both with acyl chloride/carboxylic acid within a short reaction time (15–30 min).

Keywords: ferrocene, acyl chloride, carboxylic acid, zinc, solvent-free conditions

The study of ferrocene and its derivatives has been widespread owing to their enormous application in many fields of chemistry,[1] such as material science,[2] asymmetric catalysis[3] and biologically active compounds.[4] Thus, derivatisation of ferrocene has received considerable interest. Acylation of ferrocene has gained importance as it introduces carbonyl functionality, which can be easily manipulated. Acylferrocenes are important intermediates for the production of varied functional materials such as functional polymers, surfactants, charge transfer complexes, ion sensors, masking agents, coupling agents, chiral and combustion catalysts for propellants.[5-7] For these reasons, during the past decade, the development of more eco-compatible method for acylation of ferrocene has become a fundamental goal of the general green revolution. Several efforts have been made by different research groups to achieve the goal of making the Lewis acid heterogenous for carrying out acylation reactions.

However, up to now only a few works have been devoted for acylation of ferrocene using acyl chlorides/anhydrides in addition with additives like $AlCl_3$,[8] $BF_3.Et_2O$,[9] H_3PO_4,[10] metal triflates,[11] clays[12] and ionic liquids.[13] Acylation using carboxylic acids in presence of PCl_3/Al-anode[14] and triflic anhydride/Al_2O_3[15] has also been reported. However, in spite of their potential utility, the above report requires the use of toxic chemicals like $AlCl_3$, $BF_3.Et_2O$. Also the reaction suffers from disadvantages like longer reaction time, lower substrate compatibility, use of expensive regent and solvent. Therefore the search for milder and environmentally acceptable method for performing the acylation of ferrocene has been the subject of recent focus.

Recently organic reactions promoted by inexpensive and reusable metals or their salts, avoiding harsh reaction conditions have received a considerable attention. Among the inexpensive metals, zinc powder was found to be a highly efficient, reusable and mild additive used for a number of organic transformations.[16-18] Herein we report a simple, convenient and environment-friendly method for selective acylation of ferrocene both with acyl chlorides and carboxlic acids in the presence of Zn metal under solvent-free conditions.

In order to optimise the reaction conditions, the reaction of ferrocene with butyryl chloride in presence of zinc metal was selected as a model reaction. The best result was achieved by carrying out the reaction with (1 : 1 : 1) mole ratios of ferrocene, zinc and butyryl chloride at room temperature. A variety of solvents were screened using the optimised conditions and the results are presented in Table 1. Although dichloromethane and dichloroethane were found to be effective solvents, considering stringent environmental regulations, solvent-free reactions are desired. Therefore, we intended the monoacylation of ferrocene under solvent-free conditions. The activity of the recycled zinc metal was also examined under the present conditions. It exhibited remarkable activity and reusability affording 100%, 94%, 84% conversion of ferrocene after 1–3 runs respectively (Table 1, entry 1). Another interesting behaviour of zinc powder lies in the fact that it can be re-used after simple washing with diethyl ether, thus rendering the process more economical.

Table 1 Influence of solvent on acylation of ferrocene[a]

Entry	Solvent	Time/h	Conversion/%
1[b]	Without solvent	0.5	100, 94, 84
2	Dichloromethane	4	88
3	Dichloroethane	4	75
4	Chloroform	4	63
5	Carbontetrachloride	4	28
6	Chlorobenzene	4	45
7	Acetonitrile	4	5
8	Ethanol	4	–
9	Toluene	4	–
10	Tetrahydrofuran	4	–

[a]Reaction conditions: ferrocene (1 mmol), butyryl chloride (1 mmol), zinc (1 mmol), solvent (5 ml) at r.t.

[b]Zinc metal recyclablity.

In order to study the generality of the procedure, a series of acyl chlorides having different steric and electronic properties were treated with ferrocene using the optimised conditions and the results are presented in Table 2, Scheme 1. Initially, long chain aliphatic acyl chlorides were treated with ferrocene. They reacted smoothly under the present conditions affording high yields of desired monoacyl products within short reaction times (entries 1–7). Acetyl choride, was also found to acylate ferrocene effectively (entry 8). The protocol was also applicable for the synthesis of aromatic acylferrocenes having both electron withdrawing and donating substituents. It was observed that electron withdrawing substituents like 2-chlorobenzoyl chloride, when reacted with ferrocene, provided 83% yield of desired product within 30 min (entry 11). However, the reaction with 4-chlorobenzoyl chloride was found to be sluggish. Electron donating substituents such as 2-methylbenzoyl chloride also reacted smoothly under the present conditions (entry 14). Thus, the present protocol has the ability to tolerate variations in the acylating agents providing monoacylated products in good to excellent yields.

The scope of this methodology was further extended for acylation of ferrocene by *in situ* generation of the acylating agent from the appropriate carboxylic acid by reaction with thionyl chloride at 80°C under solvent-free conditions, then carrying out the corresponding acylation in presence of zinc metal under the same conditions (Table 3, Scheme 2). Several structurally varied carboxylic acids were transformed smoothly into acyl chlorides and then reacted with ferrocene to provide the monoacylated derivatives of ferrocene in moderate to good

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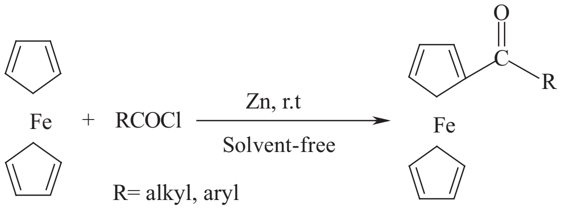
* Correspondent. E-mail: jayashreengarkar@yahoo.co.in; jmn@udct.org

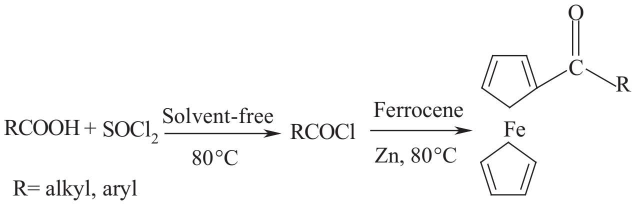
Table 2 Acylation of ferrocene using acyl chlorides[a]

Entry	Acyl chlorides	Acylated product	Time/min	Yield[b]/%
1	n-Butyryl chloride	n-Butyryl ferrocene	30	96
2	Propionyl chloride	Propionyl ferrocene	30	94
3	Acetyl chloride	Acetyl ferrocene	30	75
4	Pivaloyl chloride	Pivaloyl ferrocene	30	92
5	n-Octanoyl chloride	n-Octanoyl ferrocene	30	86
6	Stearoyl chloride	Stearoyl ferrocene	30	72
7	Lauroyl chloride	Lauroyl ferrocene	30	65
8	Phenylacetyl chloride	Phenylacetyl ferrocene	30	58
9[c]	Chloroacetylchloride	Chloroacetylferrocene	15	42
10	Benzoyl chloride	Benzoyl ferrocene	30	88
11	2-Chlorobenzoyl chloride	2-Chlorobenzoyl ferrocene	30	83
12[c]	4-Chlorobenzoyl chloride	4-Chlorobenzoyl ferrocene	15	45
13	Cinnamoyl chloride	Cinnamoyl ferrocene	30	80
14	2-Methylbenzoyl chloride	2-Methylbenzoyl ferrocene	30	73
15	4-Methylbenzoyl chloride	4-Methylbenzoyl ferrocene	30	50

[a]Reaction conditions: ferrocene (1 mmol), acyl chloride (1 mmol), zinc (1 mmol) at r.t. in solvent- free conditions.
[b]Isolated yields based on ferrocene.
[c]At 80°C.



Scheme 1 Acylation of ferrocene using acyl chloride.



Scheme 2 Acylation of ferrocene using carboxylic acid.

yields. Long-chain acyl chlorides and aromatic acyl chlorides were easily converted to their corresponding acyl ferrocenes.

Although the mechanism of the reaction has not been clarified, it seems that coordination of the C=O bond of the acyl chloride to the zinc metal activates the C=O group and enhances the leaving ability of the chloride.

In summary, a novel and highly efficient method for selective acylation of ferrocene both with acyl chlorides and carboxylic acids under solvent-free conditions using zinc metal has been developed. The protocol offers several advantages such as short reaction time, neutral conditions, reusability of zinc metal and simple work up procedure making it an important supplement to the existing methods.

Experimental

All compounds were identified by comparison of their spectral data and physical properties with those of the authentic samples and all yields refer to isolated products. Melting points were determined in a capillary tube and are uncorrected. ^{1}H NMR spectra were recorded on Varian-400 NMR Spectrometer using TMS as an internal standard. FT-IR spectra were recorded on a Perkin-Elmer Paragon 400 spectrometer.

General experimental procedure to synthesise monoacylfrrocene from acyl chloride

A mixture of ferrocene (1 mmol) and zinc powder (1 mmol) was placed in a 25 ml, two-neck, round bottom flask. To it butyryl chloride (1 mmol) was added dropwise at room temperature under an N$_2$ atmosphere. The progress of the reaction was monitored by TLC. After completion of the reaction, to the resulting mixture diethyl ether (15 ml) was added and stirred for 5 min. The resulting solution was filtered to remove the zinc powder. The organic filtrate was washed with an aqueous solution of NaHCO$_3$ (2%), dried over anhydrous Na$_2$SO$_4$ and concentrated under vacuum. The crude product was purified by column chromatography (Silica gel, 60-120 mesh) using petroleum ether as eluent.

General procedure to synthesise monoacylferrocenes from carboxylic acid

Thionyl chloride (1.2 mmol) was added to a two-neck, round bottom flask fitted with a double surface condenser and gas absorption trap. Butyric acid (1 mmol) was added dropwise to it and heated at 80°C for 1.45 h. Then a mixture of ferrocene (1 mmol) and zinc powder (1 mmol) was added. The progress of the reaction was monitored by TLC. After the completion of the reaction, to the resulting mixture diethyl ether (15 ml) was added and stirred for 5 min. The resulting solution was filtered to remove the zinc powder. The organic filtrate was washed with an aqueous solution of NaHCO$_3$ (10%), dried

Table 3 Acylation of ferrocene using carboxylic acid[a]

Entry	Carboxylic acid	Acylated product	Time/h	Yield[b]/%
1	n-Butyric acid	n-Butyryl ferrocene	2	85
2	Propionic acid	Propionyl ferrocene	2	80
3	n-Octanoic acid	n-Octanoyl ferrocene	2	75
4	Phenylacetic acid	Phenylacetyl ferrocene	2	38
5	Stearic acid	Stearoyl ferrocene	2	62
6	Lauric acid	Lauroyl ferrocene	2	57
7	Benzoic acid	Benzoyl chloride	2	76
8	2-Chlorobenzoic acid	2-Chlorobenzoyl ferrocene	2	68
9	Cinnamic acid	Cinnamoyl ferrocene	2	63
10	2-Methylbenzoic acid	2-Methylbenzoyl ferrocene	2	53

[a]Reaction conditions: Carboxylic acid (1 mmol), Thionyl chloride(1.2 mmol), Ferrocene (1 mmol), Zinc (1 mmol) in solvent-free conditions at 80°C.
[b]Isolated yields based on ferrocene.

over anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was purified by column chromatography (Silica gel, 60–120 mesh) using petroleum ether as eluent.

Spectroscopic data of acylferrocenes

Butyryl ferrocene (Table 1, entry 1): Orange-red solid; m.p. 36–38°C; IR (KBr): v_{max}/cm^{-1} 3140, 2928, 1668, 1455, 1255; ^{1}H NMR (400 MHz; $CDCl_3$) δ = 4.77 (2H, t), 4.48 (2H, t), 4.18 (5H, s), 3.11(1H, heptet).

Acetyl ferrocene (Table 1, entry 3): Orange crystalline solid; m.p. 81–83°C; IR (KBr): v_{max}/cm^{-1} 3116, 2925, 1645, 1456, 1281; ^{1}H NMR (400 MHz; $CDCl_3$) δ = 4.77 (2H, t), 4.50 (2H, t), 4.20 (5H, s), 2.39 (3H, s).

Propionyl ferrocene: Deep orange-red crystals; m.p. 36–38°C; IR (KBr): v_{max}/cm^{-1} 3095, 2960, 1665, 1450, 1276; ^{1}H NMR (400 MHz; $CDCl_3$) δ = 4.75 (2H, t, J = 2 Hz), 4.46 (2H, t, J = 2 Hz), 4.20 (5H, s), 2.59 (3H, s).

Pivaloyl ferrocene: Yellow-orange crystals; m.p. 91–93°C C; IR (KBr): v_{max}/cm^{-1} 3156, 29508, 1675, 1467, 1276; ^{1}H NMR (400 MHz; $CDCl_3$) δ = 4.82 (2H, t, J = 2 Hz), 4.16 (5H, s), 1.34 (9H, s, t-Bu).

Benzoyl ferrocene: Red crystalline solid; m.p. 106–107°C; IR (KBr): v_{max}/cm^{-1} 3100, 2930, 1640, 1452, 1290; ^{1}H NMR: (400 MHz; $CDCl_3$) δ = 7.88 (2H, m), 7.48 (3H, m), 4.90 (2H, t, J = 2 Hz), 4.58 (2H, t, J = 2 Hz), 4.19 (5H, s).

Cinnamoyl ferrocene: Orange-red solid; m.p. 137–139°C; IR (KBr): v_{max}/cm^{-1} 2930, 1652, 1597, 1454, 1106; ^{1}H NMR (400 MHz; $CDCl_3$) δ = 7.79 (1H, d, J = 15 Hz), 7.65 (5H, m), 7.12 (1H, d, J = 15 Hz), 4.90 (2H, s), 4.58 (2H, s), 4.21 (5 h, s).

2-Chlorobenzoyl ferrocene: Red crystalline solid; m.p. 97–99°C; IR (KBr): v_{max}/cm^{-1} 3098, 1652, 1590, 1477; ^{1}H NMR (400 MHz; $CDCl_3$) δ = 7.51–7.32 (4H, m), 4.73 (2H, t, J = 2 Hz), 4.58 (2H, t, J = 2 Hz), 4.26 (5H, s).

4-Methylbenzoyl ferrocene: Orange-red crystals; m.p. 127–128°C; IR (KBr): v_{max}/cm^{-1} 3095, 2928, 1642, 1564, 1470; ^{1}H NMR (400 MHz; $CDCl_3$) δ = 7.79–7.81 (2H, d, J = 8 Hz), 7.72–7.29 (2H, d, J = 8 Hz), 4.88 (2H, t, J = 2 Hz), 4.53 (2H, t, J = 2 Hz),4.22 (5H, s), 2.41(3H,s).

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