

Detection of Oxidized Ferrocenes by LC-MS with Electrospray Ionization Using Picric Acid as the Counter Ion

Yutaka Okada*, Masako Tsuchida

Department of Applied Chemistry, Ritsumeikan University, Kusatsu, Japan

Email: *ygvector@sk.ritsumei.ac.jp

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Abstract

Ferrocene is an organometallic compound that readily undergoes oxidation in atmosphere under acidic conditions. However, because of its diamagnetic nature, ferrocene does not lend itself to structural analysis by nuclear magnetic resonance (NMR) spectroscopy. In this work, the oxidation of ferrocene and several of its derivatives were analyzed by liquid chromatography-mass spectrometry (LC-MS). An electrospray ionization (ESI) source was used, with picrate serving as the counter ion. This method is particularly effective for studying oxidation of ferrocenes because their reactivity toward oxygen under ambient conditions is low.

Keywords

ESI, LC-MS, Ferrocene, Oxidation, Picrate

1. Introduction

Ferrocene (**Figure 1**) is highly stable in air, so oxidation of the central iron atom from Fe (II) to Fe (III) under ambient conditions does not occur readily, but ferrocene oxidizes in air under acidic conditions to form ferrocenium cations [1]. Oxidation of ferrocene derivatives in air under acidic conditions has also been studied by several groups [2] [3]. However, because of their paramagnetic properties, ferrocenium cations are not generally analyzed by NMR, as signals from the nuclei near the diamagnetic center of ferrocene are broadened, which worsens the spectral resolution. In the present study, salts of ferrocene oxidation products and those of several ferrocene derivatives were prepared by addition of picrate. Picrate served as a counter ion for each of the oxidized compounds during LC-MS analysis employing an ESI source.



Figure 1. Structure of ferrocene.

2. Experimental

All reagents were of commercial quality (from Nacalai Tesque, Inc., Japan and Wako Pure Chemical Industries Co., Japan) and were used as received. Solvents were dried and purified using standard techniques.

2.1. Synthesis

The ferrocenes used in the study were synthesized by using previously published methods [4] [5].

2.2. Oxidation Reaction

The oxidation reaction of ferrocene is shown in **Figure 2**.

Each of the ferrocenes (0.3 mmol) was dissolved in 1,2-dichloroethane (25 mL) in a three-neck flask. Trifluoroacetic acid (30 mmol) was dissolved in 1,2-dichloroethane (5 mL) and added to each ferrocene solution via a dropping funnel. The time was recorded as zero ($t = 0$), and each reaction was allowed to proceed for 3 h. A 1 mL aliquot was then withdrawn from each solution, to which 0.3 mmol of picric acid was added prior to LC-MS analysis.

2.3. LC-MS

LC-MS was performed on a Shimadzu QP8000A LCMS system (Shimadzu, Kyoto, Japan). ESI was carried out at a potential of 4.5 kV in positive ion mode and at -3.0 V in negative ion mode. Separation was performed on an ODS column (COSMOSIL/5C18-MS-II ($4.6\Phi \times 150$ mm, $5\ \mu\text{m}$) from Nacalai Tesque, Inc., Japan), using MeOH: H_2O (9:1 v/v) as the mobile phase.

3. Results and Discussion

The mass chromatograms and mass spectra of ferrocenes and ferrocenium picrates are shown in **Figures 3-5**. The retention times of the ferrocenes and the mass spectra showing the ions corresponding to each peak in the chromatogram are summarized in **Table 1**.

3.1. Ferrocene

A peak appeared at 7.2 min in the chromatogram of ferrocene ionized in positive ESI mode. The m/z value for this retention time (R_t) was 186, which corresponded to the molecular ion of the parent compound, ferrocene $[\text{M}]^+$. In addition, a fragment with $m/z = 121$ was detected, which was attributed to the elimination of one cyclopentadiene ligand $[\text{M}-65]$ from ferrocene.

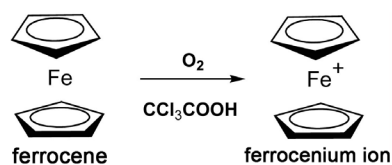


Figure 2. Oxidation reaction of ferrocene to ferrocenium ion.

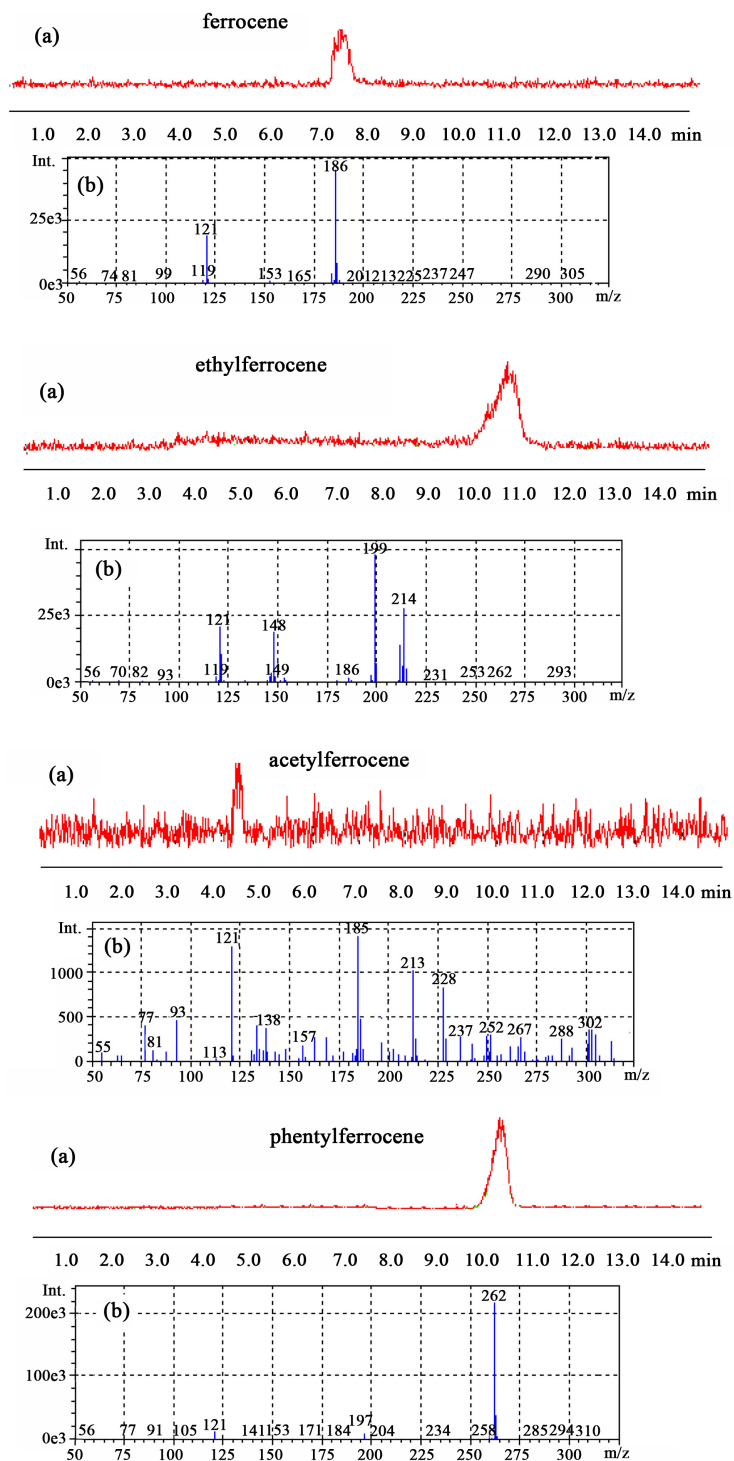


Figure 3. (a) Mass chromatograms and (b) mass spectra of ferrocenes at ESI (+) mode.

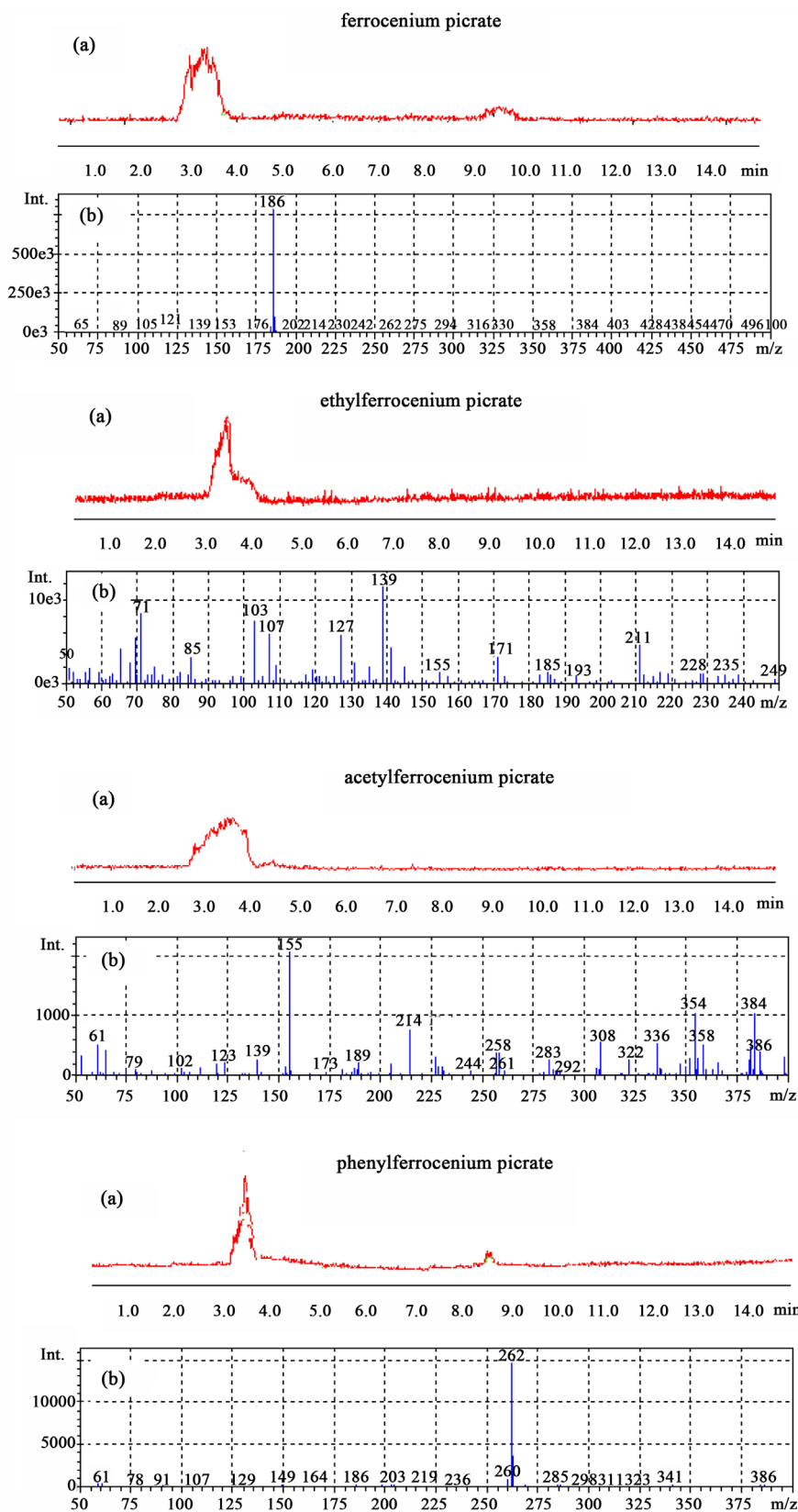


Figure 4. (a) Mass chromatograms and (b) mass spectra of ferrocenium picrates at ESI (+) mode.

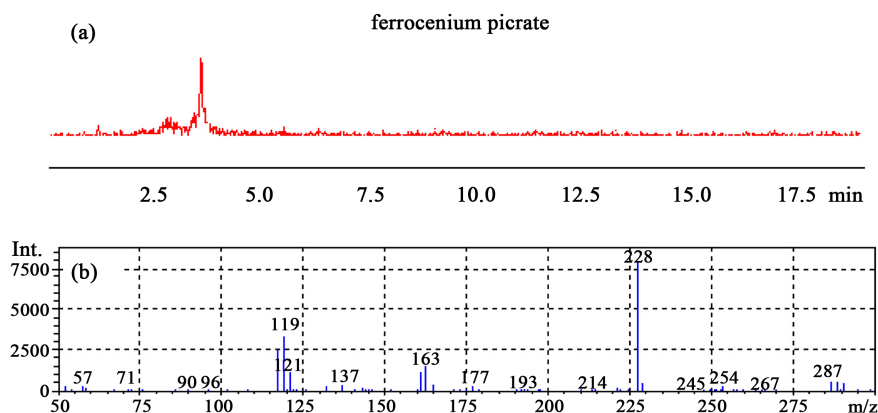


Figure 5. (a) Mass chromatogram and (b) mass spectrum of ferrocene at ESI (–) mode.

Table 1. LC-MS data of the studied compounds.

Compound	Mode	R _t (min)	m/z (relative abundance, %)
ferrocene	(+)	7.2	186 (100); 121 (46)
ferrocenium picrate	(+)	3.5	186
ferrocenium picrate	(–)	3.5	228
ethylferrocene	(+)	10.6	214 (53); 199 (100); 148 (31); 121 (38)
ethylferrocenium picrate	(+)	3.5	214 (40); 155 (100)
ethylferrocenium picrate	(–)	3.5	228
acetylferrocene	(+)	4.4	228 (61); 213 (71); 185 (100); 121 (86)
acetylferrocenium picrate	(+)	3.5	228 (4); 211 (29); 139 (100)
acetylferrocenium picrate	(–)	3.5	228
phenylferrocene	(+)	10.6	262
phenylferrocenium picrate	(+)	3.5	262
phenylferrocenium picrate	(–)	3.5	228
(<i>p</i> -methylphenyl)ferrocene	(+)	14.1	276
(<i>p</i> -methylphenyl) ferrocenium picrate	(+)	3.5	276
(<i>p</i> -methylphenyl) ferrocenium picrate	(–)	3.5	228
(<i>p</i> -hydroxyphenyl)ferrocene	(+)	5.3	278
(<i>p</i> -hydroxyphenyl) ferrocenium picrate	(+)	3.5	278
(<i>p</i> -hydroxyphenyl) ferrocenium picrate	(–)	3.5	228
(<i>p</i> -methoxyphenyl)ferrocene	(+)	8.4	292
(<i>p</i> -methoxyphenyl) ferrocenium picrate	(+)	3.5	292
(<i>p</i> -methoxyphenyl) ferrocenium picrate	(–)	3.5	228
(<i>p</i> -chlorophenyl)ferrocene	(+)	13.2	296 (100); 298 (33)
(<i>p</i> -chlorophenyl) ferrocenium picrate	(+)	3.5	296 (100); 298 (33)
(<i>p</i> -chlorophenyl) ferrocenium picrate	(–)	3.5	228
(<i>p</i> -acetylphenyl)ferrocene	(+)	7.1	304
(<i>p</i> -acetylphenyl) ferrocenium picrate	(+)	3.5	304
(<i>p</i> -acetylphenyl) ferrocenium picrate	(–)	3.5	228

In the chromatogram of oxidized ferrocene, peaks were observed at 3.5 and 7.2 min, the latter being attributed to unoxidized ferrocene (m/z 186). In the ESI (+) mass spectrum at R_t = 3.5 min, only the molecular ion of ferrocene was detected. The only peak visible in the ESI (–) mass spectrum also eluted at 3.5 min. The m/z ratio for this peak was 228, which corresponded to the picrate anion. We therefore concluded that the peak eluting at 3.5 min was ferrocenium picrate.

3.2. Ethylferrocene

Structure of ethylferrocene is illustrated in **Figure 6**. A peak was observed at 10.6 min in the chromatogram of ethylferrocene. The molecular ion (m/z 214) peak and a fragment (m/z 199) peak were detected in the ESI (+) mass spectrum at this R_t , indicating that fragmentation occurred through the elimination of a methyl group [$M-CH_3$].

The only peaks detected in the ESI (+) and ESI (–) mass spectra of this compound following oxidation appeared at R_t = 3.5 min. This indicated that all of the ethylferrocene was oxidized, which was due to the high reactivity of ethylferrocene during oxidation. Only the molecular ion (m/z 214) was observed at 3.5 min in the ESI (+) mass spectrum, while in the ESI (–) mass spectrum, only the picrate anion (m/z 228) was detected.

3.3. Acetylferrocene

A peak was observed at 4.4 min in the ESI (+) chromatogram of acetylferrocene. The m/z ratio observed in the mass spectrum at this R_t was 228, which corresponded to the molecular weight of acetylferrocene (**Figure 7**).

Following the oxidation reaction, a peak was observed at 3.5 min in the ESI (–) chromatogram. The ion appearing in the mass spectrum at this R_t (m/z 228) was attributed to picrate anion. A peak attributed to the molecular ion of acetylferrocene (m/z 228) was observed at around 3.5 min in the ESI (+) chromatogram. However, the signal was quite weak. This was probably because the electron-withdrawing acetyl group facilitated fragmentation of the oxidized acetylferrocenium ion.

3.4. Phenylferrocenes

Phenylferrocenes used in this study are illustrated in **Figure 8**. A peak was observed at 10.6 min in the ESI (+) chromatogram of phenylferrocene. A signal at m/z = 262 was detected in the mass spectrum, which corresponded to the phenylferrocene molecular ion. A fragment ion at m/z = 121 was also observed, which was consistent with elimination of one phenyl group and a cyclopentadiene ring from the parent compound.

After oxidation of phenylferrocene, a single peak eluting at 3.5 min was observed in both the ESI (+) and ESI (–) chromatograms, which was attributed to the phenylferrocenium ion.

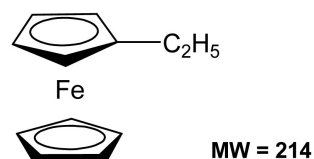


Figure 6. Structure of ethylferrocene.

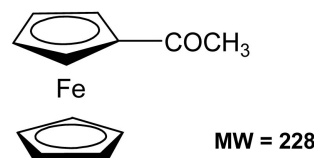


Figure 7. Structure of acetylferrocene.

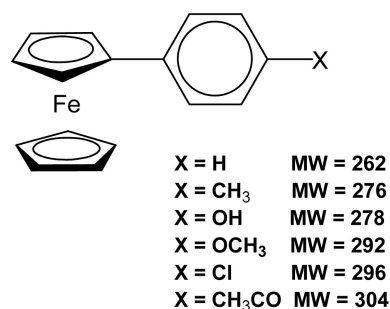


Figure 8. Structure of phenylferrocenes.

(*p*-substituted phenyl) ferrocenium ion was detected in the ESI mass spectra of (*p*-substituted phenyl) ferrocene following the oxidation reaction, indicating that oxidation of this compound proceeded similarly to that of (unsubstituted phenyl) ferrocene.

4. Conclusion

LC-MS in ESI mode, with picrate as a counterion, was an effective means of investigating the oxidation reactions of ferrocene and several of its derivatives. Oxidized ferrocenes were detected by ESI in positive mode, while the picrate counterion was observed in the ESI (–) mass spectra. LC-MS with electrospray ionization is thus a powerful tool for the analysis of ferrocene derivatives that do not oxidize readily, such as acetylferrocene.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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