Oxidation reaction of 1,1'-bis(*o*-substituted phenyl)ferrocenes

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Abstract: The oxidation reactivity of 1,1'-bis(*o*-substituted phenyl)ferrocenes was measured. For acetyl- and methoxycarbonyl derivatives, the accelerating effect found for mono substituted derivatives disappeared. This was accounted for by a proton transfer between the two carbonyl oxygens.

Keywords: Ferrocene derivatives; oxidation reaction; intramolecular interaction.

1. Introduction

air (or oxygen gas) under acid conditions. The oxidation reactivity is reported to be influenced by the electron-donating ability of a substituent.[2,3] The reaction mechanism would be as follows. A proton coordinates to the iron atom of the ferrocene derivative, and a ferrocenonium ion forms. The ferrocenonium ion is converted to a ferrocenium ion by the abstraction of a hydrogen atom by oxygen gas (Scheme 1). The ferrocenium ion formed is stabilized by a delocalization mechanism of the positive charge to the α-position of the substituent accompanying by the change from η^5−cyclopentadienyl ring to η^4−fulvenoid structure.[6]

In our previous paper,[7] the oxidation reaction of mono(substituted phenyl)ferrocenes was discussed. It was clarified that the reactivity of these ferrocenes is influenced by the coordination facility of protons to the iron atom. The coordination facility is governed by both the I-effect and the steric effect of the substituent. The oxidation rate of these (*o*-substituted phenyl)ferrocenes was compared with that of (*p*-substituted phenyl)ferrocenes. For acetyl-, methoxycarbonyl- and methoxy derivatives, the *o*-isomers showed higher reactivity than the corresponding *p*-isomers. However, the *o*-isomers of

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methyl- and hydroxyl derivatives showed lower reactivity. These results were not accounted for by the electron-donating ability of the substituents but by the conformation of the ferrocenes.
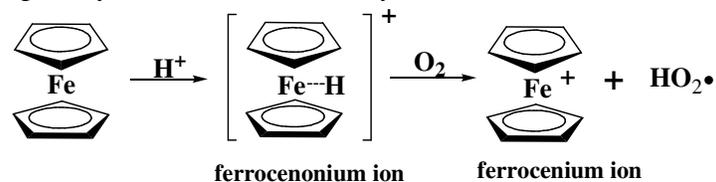
Scheme 1. Oxidation mechanism of ferrocene

In this paper, we found different effects for the oxidation reaction of 1,1'-bis(*o*-substituted phenyl)ferrocenes.

2. Results and Discussion

　　　　Mono(substituted phenyl)ferrocenes can be classified into three groups: (1) chloro derivative which has no specific effect from the *o*-substituent, (2) methyl derivative which shows a suppressing effect, and (3) acetyl-, methoxycarbonyl-, and methoxy derivatives which show an accelerating effect for the oxidation reaction.
　　　　Our results regarding 1,1'-bis(substituted phenyl)ferrocenes are now recorded in Table 1. They are covered in the following discussion.

Table 1. The rate constants of (substituted phenyl)ferrocenes

Entry	X	$k(mono) \times 10^5/s^{-1}$ [a]	$k(bis) \times 10^5/s^{-1}$	$k(bis)/k(mono)$
1	H	2.49	1.24	0.50
2	*p*-Cl	0.98	0.49	0.50
3	*o*-Cl	1.11	0.54	0.48
4	*p*-CH$_3$	3.92	--	--
5	*o*-CH$_3$	2.06	0.68	0.33
6	*p*-OCH$_3$	3.92	--	--
7	*o*-OCH$_3$	7.10	7.97	1.12
8	*p*-COCH$_3$	0.39	--	--
9	*o*-COCH$_3$	1.85	0.22	0.12
10	*p*-COOCH$_3$	0.43	--	--
11	*o*-COOCH$_3$	1.10	0.32	0.29

a　Ref. 7.

2.1. 1,1'-diphenylferrocene and 1,1'-bis(p-chlorophenyl)ferrocene

As mentioned in the previous paper,[7] phenylferrocene is more slowly oxidized than unsubstituted ferrocene. 1,1'-Diphenylferrocene was more difficult to oxidize than monophenylferrocene (Table 1, Entry 1). The order of the reactivity was found to be as follows,

ferrocene > phenylferrocene > 1,1'-diphenylferrocene.
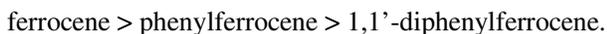
This would be due to the influence of the electron-withdrawing effect of the phenyl group. Here, the reactivity of 1,1'-diphenylferrocene was about 50% of that of phenylferrocene. Namely, k(bis)/k(mono) is 0.50. For the *p*-chloro derivative (Table 1, Entry 2), the same relationship was recognized (k(bis)/k(mono) is 0.50).

2.2. 1,1'-bis(o-chlorophenyl)ferrocene

The rate constants of *o*-chloro derivatives are shown in Entry 3 of Table 1.

1,1'-bis(*o*-chlorophenyl)ferrocene was more slowly oxidized than mono(*o*-chlorophenyl)ferrocene. In the preferred conformation of this derivative, the chlorine atom would twist forward in an exo position in analogy to the corresponding monosubstituted derivative.[8] Therefore, a coordination of a catalytic proton to the iron atom would not be influenced by the substituent, but only by the electron-withdrawing effect of chlorine atom. Namely, the oxidation of 1,1'-bis(*o*-chlorophenyl)ferrocene does not show a specific effect due to the *o*-substituent.

The rate constants of mono- and 1,1'-bis(*o*-chlorophenyl)ferrocene were compared. The latter is about 50% of the former (k(bis)/k(mono) is 0.48). This relation is identical with the relation in phenyl- or *p*-chlorophenyl derivatives which have no specific effect due to the substituent. Therefore, if there is no specific effect by a substituent, the rate constants of the disubstituted derivative will be about 50% of these of the mono derivatives.

2.3. 1,1'-bis(o-methylphenyl)ferrocene

The oxidation rate constants of methyl derivatives are shown in Entries 4 and 5 of Table 1.

Mono(*o*-methylphenyl)ferrocene is more difficult to oxidize than the corresponding *p*-isomer.[7] Namely, the electron density of the iron atom decreases due to a CH-d type attractive interaction between the methyl group and the iron atom: The coordination of a proton then becomes difficult, so that the oxidation reactivity becomes lower.

However, the reactivity of 1,1'-bis(*o*-methylphenyl)ferrocene was much smaller than that of the monosubstituted derivative (k(bis)/k(mono) is 0.33). This decrease is not explained by the reason mentioned above. In 1,1'-bis(*o*-methylphenyl)ferrocene, the endo conformation as in the methyl group is preferred, so that the *cis*-like conformer on Cp-Fe-Cp bond rotation is unstable.[8] Therefore, the steric effect around the iron atom would become larger. As a result, two (*o*-methylphenyl) groups would suppress the coordination of a proton to the iron atom. This phenomenon is in contrast with the case of *t*-butylferrocenes, for which the stability of the five antiprismatic conformers is equal,[9] and no steric hindrance by the t-butyl groups is recognized for the oxidation reaction.[10] Namely, the oxidation reactivity of 1,1' –bis(*o*-methylphenyl)ferrocene would be controlled by the steric hindrance of the two methyl groups together with the CH-d type attractive interaction between the methyl group and the iron atom.

2.4. 1,1'-bis[o-acetyl-, (methoxycarbonyl)- and methoxyphenyl]ferrocene

The oxidation reactivity of mono [*o*-acetyl-, (methoxycarbonyl)- and methoxyphenyl]ferrocene was higher than that of the corresponding *p*-isomers. This higher reactivity was interpreted as the result of coordination of a proton to the carbonyl- or ethereal oxygen and formation of a chelate-like ring.[7]

The reactivity of 1,1'-bis(o-methoxyphenyl)ferrocene is higher than that of the corresponding monosubstituted derivative (Table 1, Entry 7). The result indicates that the reaction accelerating effect by the o-methoxy group occurs not only in the monosubstituted derivative but also in the disubstituted derivative.

The rate constants of acetyl- and methoxycarbonyl derivatives are shown in entries 9 and 11 of Table 1. 1,1'-Bis[o-acetyl- and (methoxycarbonyl)phenyl]ferrocene were more slowly oxidized than the corresponding monosubstituted derivatives. The rate constant of these disubstituted derivatives was less than 50% of that of the monosubstituted derivatives. Especially, for 1,1'-bis (o-acetylphenyl)ferrocene, the value of k(bis)/k(mono) is 0.12. These values for disubstituted derivatives indicate that the accelerating effect found for monosubstituted derivatives becomes smaller in the case of a 1,1'-disubstituted derivative.

The basicity of these derivatives was examined by means of ^{1}H-NMR and IR spectroscopy (Tables 2 and 3). From the NMR data, the value of $\Delta\delta$ was positive for all protons. The values of the methyl
groups were larger than that of the cyclopentadienyl groups. Therefore, a proton would coordinate to the carbonyl oxygen of 1,1'-disubstituted derivatives as well as monosubstituted derivatives. From the IR data, it is considered that the order of the basicity of the carbonyl groups is as follows,

o-Ac, p-Ac > di o-Ac, di p-Ac > o-COOMe, p-COOMe > di o-COOMe, di p-COOMe.

Namely, the basicity of the carbonyl group of these disubstituted derivatives is smaller than that of the corresponding monosubstituted derivatives. The decrease of the basicity should be due to the proton transfer between the two carbonyl oxygens.

Table 2. The values of $\Delta\delta^a$ of (substituted phenyl)ferrocenes

X	$H_{1'}$	H_α	H_β	CH_3
p-COCH$_3$ mono	0.00	0.01	0.02	0.06
p-COCH$_3$ bis	--	0.03	0.03	0.04
o-COCH$_3$ mono	0.01	0.01	0.02	0.06
o-COCH$_3$ bis	--	0.03	0.03	0.04
p-COOCH$_3$ mono	0.00	0.00	0.01	0.02
p-COOCH$_3$ bis	--	0.01	0.01	0.01
o-COOCH$_3$ mono	0.01	0.01	0.01	0.02
o-COOCH$_3$ bis	--	0.02	0.02	0.02

[a] $\Delta\delta = \delta' - \delta$, where δ' is proton chemical shift value measured in the presence of equimolar trichloroacetic acid and δ is the value at normal conditions.

**Table 3.** The values of Δν of (substituted phenyl)ferrocenes

X		ν^a/cm,	ν'^a/cm	$\Delta\nu^b$/cm
p-COCH₃	mono	1666	1624	42
p-COCH₃	bis	1666	1632	34
o-COCH₃	mono	1680	1632	48
o-COCH₃	bis	1682	1651	31
p-COOCH3₃	mono	1705	1692	12
p-COOCH₃	bis	1728	1726	2
o-COOCH₃	mono	1715	1699	16
o-COOCH₃	bis	1715	1705	10

[a] ν' is carbonyl streching frequency in the presence of trichloroacetic acid ferrocene derivative :
trichloroaceticacid = 1 : 10) and   is the value at normal conditions.
[b] Δν = ν - ν'

3. Conclusion

The oxidation mechanism would be as follows: (i) Coordination of a proton to one carbonyl oxygen occurs at first. (ii) The proton migrates to another carbonyl oxygen. That is to say, the proton would be transferred between the two carbonyl groups (Fig. 1). This transfer should prevent the formation of a chelate-like ring found in monosubstituted derivatives, so that the accelerating effect found for monosubstituted derivatives should disappear.
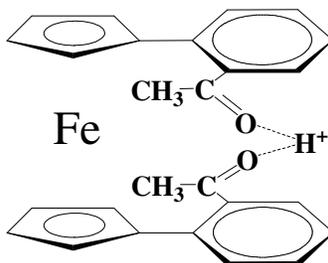
Figure 1. The interaction between proton and carbonyl oxygens of 1,1'-bis(*o*-acetylphenyl)ferrocene.

For methoxy derivatives mentioned above, the accelerating effect remained in the disubstituted derivative. Because one methoxyl group is away from another in the molecule, so that the proton transfer between the two groups should not occur.

4. Experimental

4.1. Syntheses

1,1'-bis(substituted phenyl)ferrocenes were synthesized as mentioned in a previous paper.[11]

4.2. Measurements of oxidation reactivity

The oxidation reaction was preceded by the use of trichloroacetic acid as a catalyst in 1,2-dichloroethane. Sampling of the reaction mixture was carried out at regular intervals. The sample was added to water and vigorously stirred to stop the reaction. Then, the oxidation product (ferrocenium ion) was extracted in water; unreacted material and internal standard (nitrobenzene or 1,3,5-trichlorobenzene) remained in the 1,2-dichloroethane layer. The amount of unreacted material in the presence of internal standard was determined by by HPLC.[7,12] The concentration of ferrocenonium ion in this solution was quite low. Hence, it was considered that only ferrocenium ion was extracted in water. The rate constants were calculated as a pseudo-first order reaction regarding a ferrocene derivative.

4.3. Instrumentation

NMR spectra were measured on a JEOL ALPHA-400 spectrometer with TMS as an internal standard. IR spectra were obtained by a SHIMADZU FTIR-8400 spectrometer.

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