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Studies on Ferrocene Derivatives. V.[1] Oxidation Reaction of (*o*-Substituted phenyl)ferrocenes

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The oxidation reactivity of (*o*-substituted phenyl)ferrocenes with air was measured in acidic solution. The reactivity of *o*-acetyl, *o*-methoxycarbonyl, and *o*-methoxy derivatives was higher than that of the corresponding *p*-isomers. On the other hand, for *o*-hydroxy and *o*-methyl derivatives, the reactivity was lower than that of *p*-isomers. It was considered that the reactivity of *o*-isomers is influenced by the coordination ability of proton to iron atom. The coordination ability is governed by both the I-effect and steric effect of substituent.

Ferrocene (Fc) is very stable in air, and the oxidation from Fe(II) to Fe(III) is difficult. However, in an acidic solution, Fc is readily oxidized to ferrocenium ion[2] with air.

Investigations on oxidation reaction of substituted ferrocenes with air (or oxygen gas) in acidic solution have been done by several workers.[3,4] It has been reported that the rate of the reaction is influenced by electron-donating ability of a substituent.[3] The reaction mechanism was considered as follows:[4] ferrocenonium ion[2] is formed by coordination of a proton to iron atom of Fc, and is converted continuously to ferrocenium ion with loss of hydrogen atom by attack of oxygen (Eq. 1). That is to say,

$$\mathrm{Fc} \xrightarrow{\mathrm{H}^+} [\mathrm{Fc{-}H}]^+ \xrightarrow{\mathrm{O}_2} \mathrm{Fc}^+, \qquad (1)$$

where the active species on the oxidation reaction is ferrocenonium ion (protonated ferrocene). Therefore, it was considered that the rate of the reaction depends on the values of pK_a of catalytic acid.[5] Ferrocenonium ion was observed in $BF_3 \cdot H_2O$ by means of ^{1}H NMR.[6] However, in trifluoroacetic acid, the species was not found,[6] and the concentration of ferrocenonium ion was quite low.[4] On the other hand, the second step reaction was reported as follows:[4] In ferrocenonium ion, Cp groups are tilted by formation of Fe–H bond, and the metal orbitals are exposed to attack by O_2.[7] The oxidation reaction proceeded via insertion of O_2 into the Fe–H bond, followed by loss of $\dot{H}O_2$ radical.[4]

In our previous papers,[8,9] conformational studies on (*o*-substituted phenyl)ferrocenes were carried out by ^{1}H and ^{13}C NMR. It was clarified that the degree and orientation of the twist of the bond between phenyl (Ph) group and cyclopentadienyl (Cp) group vary with the kind of ortho substituent. In the present work, the oxidation reaction of (*o*-substituted phenyl)ferrocenes with air in acidic solution has been studied. The results were compared with those of the corresponding *p*-isomers. For acetyl, methoxycarbonyl, and methoxy derivatives, the oxidation reactivity of *o*-isomers was higher than that of corresponding *p*-isomers. On the other hand, for hydroxy and methyl derivatives, the reactivity of *o*-isomers was lower than that of *p*-isomers. Namely, no linear relationship was recognized between the oxidation reactivity and electron-donating ability of ortho substituent. Hence, the relation between the reactivity and the conformation is discussed.

Experimental

Preparation of Materials. The preparation and physical properties of (substituted phenyl)ferrocenes were reported in a preceding paper.[8]

Measurements of Oxidation Reactivity. Small three-necked flask fitted with reflux condenser, thermometer, and dropping funnel were employed for oxidation reaction. Air was introduced from the top of the condenser (Fig. 1). (Substituted phenyl)ferrocene (0.3 mmol) and 1,2-dichloroethane (50 ml) were added in the flask. Trichloroacetic acid (57 mmol) was dissolved in 10 ml of 1,2-dichloroethane. This solution was added through the dropping funnel. When all the materials were added, the reaction measurement was started. Reaction temperature was 40.0±0.1 °C, and air was introduced at a rate of 25±1 ml min^{-1}. The reaction mixture was stirred at 500 rpm by a magnetic stirrer with 25 mm length stirring bar. Sampling of reaction mixture was carried out at a regular interval. The sample was added

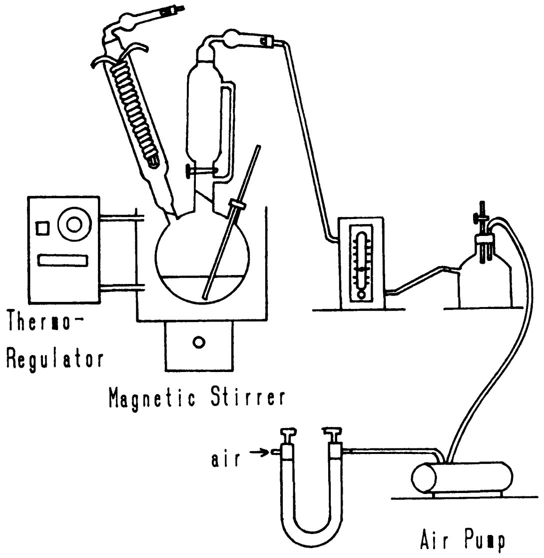


Fig. 1. Apparatus for oxidation reaction.

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 1,2-dichloroethane layer. The amount of unreacted material in the presence of internal standard was determined by HPLC method. As mentioned above, the concentration of ferrocenonium ion in this solution was quite low.[4] Hence, it was considered that only ferrocenium ion was extracted in water. The conversion of the reaction is expressed by Eq. 2.

$$\text{Conversion} = ([\text{Fc}]_0 - [\text{Fc}])/[\text{Fc}]_0, \qquad (2)$$

where [Fc] is the concentration of (substituted phenyl)ferrocene, and $[\text{Fc}]_0$ is the starting concentration. The rate constants were calculated as the pseudo-first order reaction about ferrocene derivatives; because the concentration of trichloroacetic acid was much higher than that of (substituted phenyl)ferrocene.

NMR Spectra. The method of NMR measurement was described in the preceding paper.[8]

IR Spectra. A JASCO IR-G type spectrometer was used. The measurements were done by the paste method (disperse medium: paraffin liquid).

Results and Discussion

Oxidation Reaction of (*p*-Substituted phenyl)ferrocenes. The conversions of the oxidation of (*p*-substituted phenyl)ferrocenes are shown in Fig. 2. The rate constants are presented in Table 1. The order of the reactivity was found as follows:

$$\text{OH} \fallingdotseq \text{OCH}_3 \fallingdotseq \text{CH}_3 > \text{H} > \text{Cl} > \text{COCH}_3 \fallingdotseq \text{COOCH}_3.$$

The order coincides approximately with that of electron-donating ability of para substituents. The relation between the Hammett constants[10] and the rate constants is shown in Fig. 3; a linear relationship was recognized. The reason was considered as follows. The electron density of the iron atom in the ferrocenes increased with an increase in electron-donating ability of para substituent. The coordination of catalytic proton to iron atom seems to be accelerated by higher electron density of iron atom. This order agrees with that of the polarographical oxidation potential value[11] of iron atom in ferrocene derivatives.

Oxidation Reaction of (*o*-Substituted phenyl)ferrocenes. The conversions of the oxidation of (*o*-substituted phenyl)ferrocenes are shown in Fig. 4. The rate constants are presented in Table 1. The order of the reactivity was found as follows:

$$\text{OCH}_3 > \text{CH}_3 \fallingdotseq \text{COCH}_3 > \text{OH} \fallingdotseq \text{Cl} \fallingdotseq \text{COOCH}_3.$$

The relation between the Hammett constants[10] and the rate constants is shown in Fig. 5. However, no linear relationship was recognized contrary to the case of the *p*-isomers.

The differences (Δk) of the rate constants between (*o*-substituted phenyl)ferrocenes and the correspond-

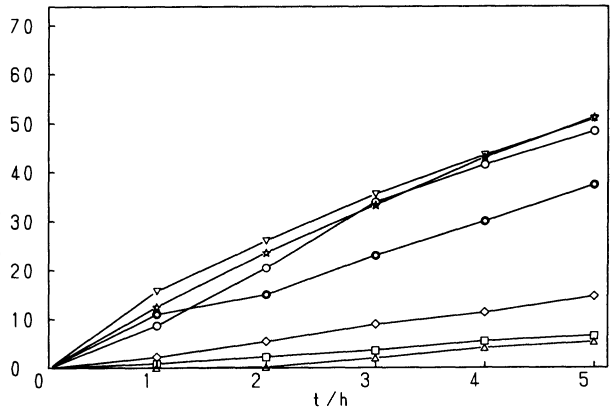


Fig. 2. Conversion of (*p*-substituted phenyl)ferrocenes. ◎: H-, ○: *p*-CH_3-, ◇: *p*-Cl-, □: *p*-CH_3CO-, △: *p*-CH_3COO-, ▽: *p*-OH-, ☆: *p*-CH_3O-.

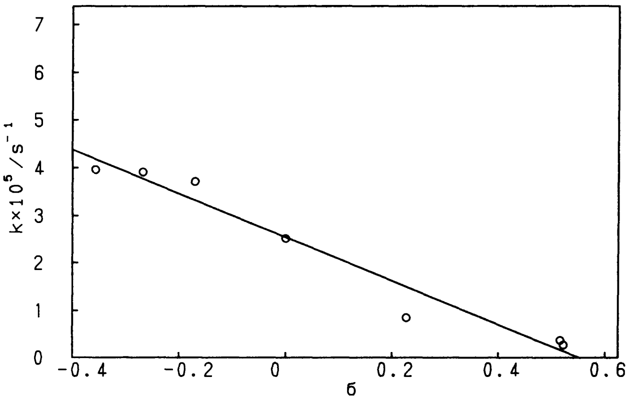


Fig. 3. Relation between Hammett constants and the rate constants of (*p*-substituted phenyl)ferrocenes.

Table 1. The Rate Constants of (Substituted phenyl)ferrocenes

	$k_{(p)}{}^{a)} \times 10^5/\text{s}^{-1}$	$k_{(o)}{}^{a)} \times 10^5/\text{s}^{-1}$	$\Delta k^{b)} \times 10^5/\text{s}^{-1}$
H	2.52	—	—
$COCH_3$	0.38	2.02	1.64
$COOCH_3$	0.28	1.04	0.76
CH_3O	3.92	7.10	3.18
OH	3.97	1.07	−2.90
CH_3	3.72	2.03	−1.69
Cl	0.86	1.04	0.18

a) $k_{(p)}$ and $k_{(o)}$ are the rate constants of *p*- and *o*-isomer, respectively. b) $\Delta k = k_{(o)} - k_{(p)}$.

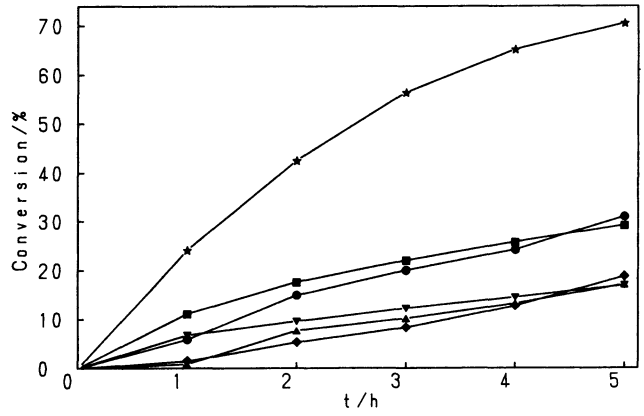


Fig. 4. Conversion of (*o*-substituted phenyl)ferrocenes. ●: *o*-CH_3-, ◆: *o*-Cl-, ■: *o*-CH_3CO-, ▲: *o*-CH_3COO-, ▼: *o*-OH-, ★: *o*-CH_3O-.

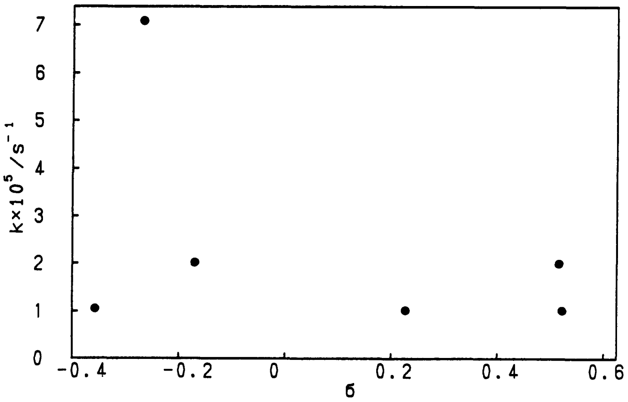


Fig. 5. Relation between Hammett constants and the rate constants of (*o*-substituted phenyl)ferrocenes.

ing *p*-isomers are presented in the right column of Table 1. (Substituted phenyl)ferrocenes can be classified into three groups by the values of Δk. The first group (acetyl, methoxycarbonyl, and methoxy derivatives) has positive values of Δk, and the second group (methyl and hydroxy derivatives) has negative values. In the third group (chloro derivative), the value is very small. The reason will be discussed later.

[Acetyl-, (Methoxycarbonyl)-, and Methoxyphenyl]-ferrocene: In [acetyl-, (methoxycarbonyl)-, and methoxyphenyl]ferrocene, the values of Δk were positive (Table 1). That is to say, the oxidation reactivity of the *o*-isomer was higher than that of the corresponding *p*-isomer (Fig. 6). In particular, the reactivity of (*o*-methoxyphenyl)ferrocene was highest in all the derivatives measured in this study. The reason will be discussed below.

As mentioned in the preceding paper,[8] the bond between Ph group and Cp group of (*o*-substituted phenyl)ferrocene is twisted. The twist is mainly produced by a steric repulsion between ortho substituent and α-proton of Cp group. It was considered that the degree of the twist in acetyl and methoxycarbonyl derivative is almost equal.[8] On the other hand, the reactivity of acetyl derivative in *o*-isomer is higher than that of methoxycarbonyl derivative (Fig. 6). Therefore, it appears that the difference in this reactivity is not influenced by the I-effect which reflects on the twist of the bond between Ph group and Cp group, but depends on a different reason.

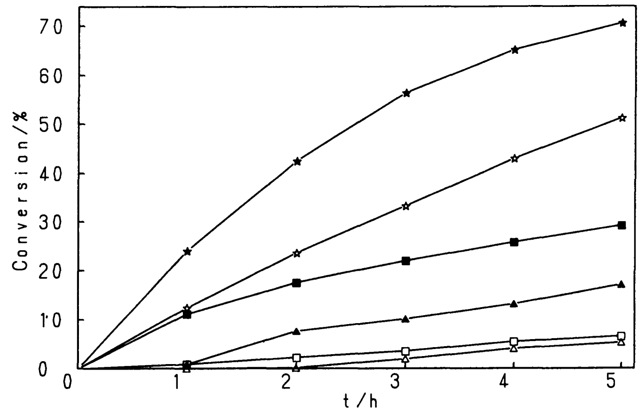
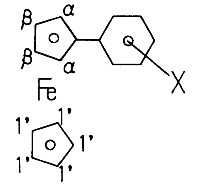


Fig. 6. Conversion of [methoxy-, acetyl-, and (methoxycarbonyl)phenyl]ferrocenes. ☆: *p*-CH_3O-, ★: *o*-CH_3O-, □: *p*-CH_3CO-, ■: *o*-CH_3CO-, △: *p*-CH_3COO-, ▲: *o*-CH_3COO-.

Table 2. The Values of $\Delta\delta$[a] of (Substituted phenyl)ferrocenes

	$H_{1'}$[b]	H_α[b]	H_β[b]	CH_3
p-CH_3CO	0.00	0.02	0.02	0.06
o-CH_3CO	0.01	0.01	0.02	0.06
p-CH_3COO	0.00	0.00	0.01	0.03
o-CH_3COO	0.02	0.01	0.02	0.04
p-CH_3O	0.02	0.02	0.03	0.02
o-CH_3O	0.03	0.05	0.06	0.02
p-CH_3	0.02	0.03	0.02	0.00
o-CH_3	0.01	0.02	0.01	0.00

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.



Proton chemical shift values of [acetyl- and (methoxycarbonyl)phenyl]ferrocene are shown in Table 2; the value of $\Delta\delta$ is defined as the difference between δ' and δ: δ' is the chemical shift value measured in the presence of equimolar trichloroacetic acid, and δ is the value at normal conditions. The value of $\Delta\delta$ was positive in all the protons of these derivatives. The values of $\Delta\delta$ of methyl groups in all the derivatives were larger than those of Cp groups. In Table 3, IR spectral data of (substituted phenyl)ferrocene are given. The values ν' measured in the presence of

Table 3. The Values of $\Delta\nu$ of [Acetyl- and (Methoxycarbonyl)phenyl]ferrocenes

	$\nu^{a)}/\mathrm{cm}^{-1}$	$\nu'^{a)}/\mathrm{cm}^{-1}$	$\Delta\nu^{b)}/\mathrm{cm}^{-1}$
p-$COCH_3$	1666	1624	42
o-$COCH_3$	1680	1632	48
p-$COOCH_3$	1701	1686	15
o-$COOCH_3$	1710	1689	21

a) ν' is carbonyl streching frequency in the presence of trichloroacetic acid (ferrocene derivative: trichloroacetic acid=1 : 10) and ν is the value at normal conditions. b) $\Delta\nu=\nu-\nu'$.

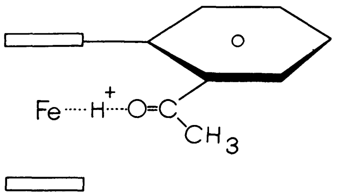


Fig. 7. Oxidation reaction of (*o*-acetylphenyl)ferrocene.

trichloroacetic acid were lower than the values ν measured at normal conditions. From these data, it was considered that coordination of proton occurs not only to iron atom but also to carbonyl oxygen. Hence, higher reactivity values of *o*-isomers are interpreted as follows: (i) Coordination of proton occurs to carbonyl oxygen at first. (ii) The proton was transferred to iron atom by formation of a chelate-like ring (Fig. 7). However, in *p*-isomer, the chelate-like ring is impossible to form.

If the oxidation reactions of [*o*-acetyl- and *o*-(methoxycarbonyl)phenyl]ferrocene are promoted by the chelating effect as shown in Fig. 7, the reactivity will be influenced by proton-coordinating ability or basicity of carbonyl oxygen. The basicity was examined by means of ^{1}H NMR.[12] The results indicate that basicity of acetyl group is higher than that of methoxycarbonyl group. Higher basicity of acetyl group was also shown by the IR spectral data in Table 3. (The values of $\Delta\nu$ of acetyl derivatives were larger than those of methoxycarbonyl derivatives.) Therefore, it was expected that the oxidation reactivity of (*o*-acetylphenyl)ferrocene is higher than that of methoxycarbonyl derivative. The experimental results agreed with this assumption. Namely, the difference in the reactivity between [*o*-acetyl- and *o*-(methoxycarbonyl)phenyl]ferrocene can be explained by the chelating effect as shown in Fig. 7.

The unusually high reactivity of (*o*-methoxyphenyl)ferrocene was considered by analogy. The values of $\Delta\delta$ of methyl groups in methoxy derivatives were positive (Table 2), whereas those in methyl derivatives were zero. Therefore, the oxidation reaction of this methoxy derivative seems to be promoted by the chelating effect as shown in Fig. 8. That is to say, coordination of catalytic proton occurs at ethereal oxygen at first, and the proton transfer to iron atom follows by forming a chelate-like ring. Both the chelating effect of oxygen and the large I-effect of methoxyl group are presumed to raise the oxidation reactivity of (*o*-methoxyphenyl)ferrocene.

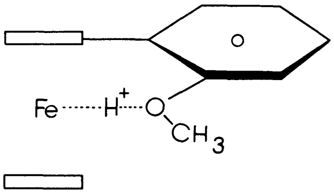


Fig. 8. Oxidation reaction of (*o*-methoxyphenyl)ferrocene.

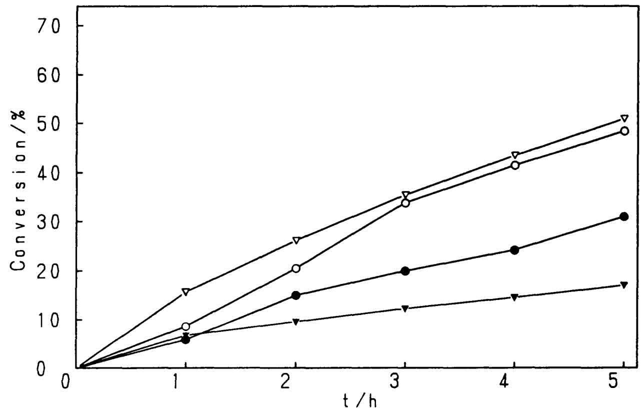


Fig. 9. Conversion of (hydroxy- and methylphenyl)ferrocenes.

▽: *p*-OH-, ▼: *o*-OH-, ○: *p*-CH_3-, ●: *o*-CH_3-.

(Hydroxy- and Methylphenyl)ferrocene: In (hydroxy- and methylphenyl)ferrocene, the values of Δk were negative (Table 1), showing that the oxidation reactivity of the *o*-isomer is lower than that of the corresponding *p*-isomer (Fig. 9). The reason will be discussed below.

Displacing methyl group of (methoxyphenyl)ferrocene by hydrogen atom gives (hydroxyphenyl)ferrocene. The reactivity of two *o*-isomers, however, was strikingly different. Particular reactivity of methoxy derivative was mentioned above. The oxidation reactivity of (*o*-hydroxyphenyl)ferrocene was lowest in all the *o*-isomers examined in this study. The reason was considered in view of conformation of (*o*-hydroxyphenyl)ferrocene as follows. In this derivative, the degree of twist of the bond between Ph group and Cp group is distinctly large in spite of small size of hydroxyl group.[8] Furthermore, the endo conformation as in hydroxyl group is preferred than exo one. The driving force was suggested[8] to be an OH-d type hydrogen bond between hydroxyl group and d-electron of iron atom (Fig. 10). Therefore, it was considered that the electron density of iron atom in

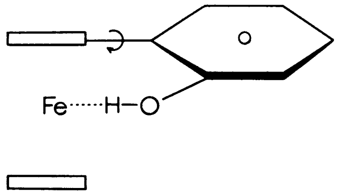


Fig. 10. Conformation of (*o*-hydroxyphenyl)ferrocene.

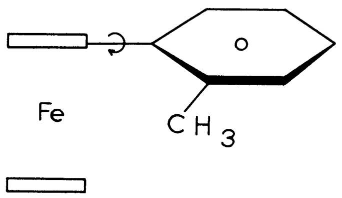


Fig. 11. Conformation of (*o*-methylphenyl)ferrocene.

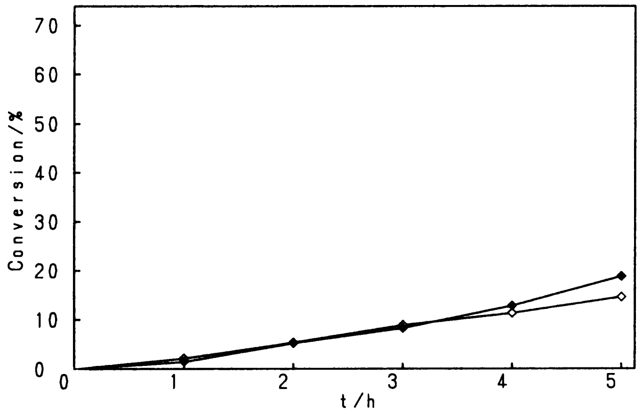


Fig. 12. Conversion of (chlorophenyl)ferrocene.
◇: *p*-Cl-, ◆: *o*-Cl-.

(*o*-hydroxyphenyl)ferrocene decreased strikingly by this hydrogen bond. Consequently, the oxidation reactivity of (*o*-hydroxyphenyl)ferrocene was remarkably low.

In (*o*-methylphenyl)ferrocene as well as hydroxy derivative, the endo conformation as in methyl group is preferred (Fig. 11).⁸⁾ The driving force to prefer the endo conformation is considered to be a CH-d type attractive interaction between methyl proton and d-electron of iron atom.⁸⁾ It is expected that the electron density of iron atom in (*o*-methylphenyl)ferrocene decreased slightly by this interaction. The CH-d type interaction will be weaker than the OH-d type hydrogen bond. Hence it seems that the electron density of iron atom in (*o*-methylphenyl)ferrocene is higher than that in (*o*-hydroxyphenyl)ferrocene. Consequently, the oxidation reactivity of methyl derivative was higher than that of hydroxy derivative.

(Chlorophenyl)ferrocene: In (chlorophenyl)ferrocene, the value of Δk was very small (Table 1), suggesting that no considerable difference exists in the reactivity between the *o*- and *p*-isomer (Fig. 12).

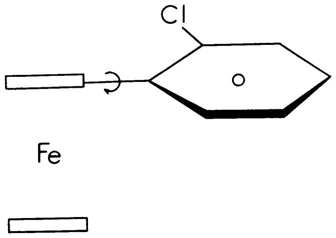


Fig. 13. Conformation of (*o*-chlorophenyl)ferrocene.

As mentioned in the previous paper,⁸⁾ the conformation of (*o*-chlorophenyl)ferrocene is considered as follows. The degree of twist of the bond between Ph group and Cp group is almost equal to that of (*o*-methylphenyl)ferrocene. However, in chloro derivative, the exo conformation (chlorine atom exists in exo position) is preferred (Fig. 13). The driving force to keep the exo conformation is considered to be an electronic repulsion between chlorine atom and d-electron of iron atom.⁸⁾ Therefore, it seems that the electron density of iron atom in chloro derivative does not decrease contrary to the case of methyl derivative. Consequently, the oxidation reactivity of (*o*-chlorophenyl)ferrocene was almost equal to that of *p*-isomer.

Conclusion

The reactivity of (substituted phenyl)ferrocene is influenced by the coordination ability of proton to iron atom. The coordination ability is governed by both the I-effect and the steric effect of the substituent.

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