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# Oxygenation of Aromatic and Aliphatic Hydrocarbons by a New Reagent System, $Fe(CH_3CN)_6^{2+}$–$H_2O_2$–$Ac_2O$: An Effective Model Reagent for Mono-oxygenase

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Reactions of aromatic and aliphatic hydrocarbons with a new reagent system, $Fe(CH_3CN)_6^{2+}$–$H_2O_2$–$Ac_2O$ in $CH_3CN$, gave oxygenation products with fairly high reaction efficiency (Tables I and II) compared to known reagent systems used as enzyme models for mono-oxygenases. Investigations of the mechanism of these reactions indicated the involvement of either complex C, $Fe^{IV}(OH)(OAc)^{2+}$, or complex D, $Fe^{IV}(OAc)_2^{2+}$, depending on the organic substrate.

**Keywords**——oxygenation; aromatic hydrocarbon; aliphatic hydrocarbon; hexakisacetonitrile iron(II) perchlorate; hydrogen peroxide; enzyme model; mono-oxygenase

Much attention has been focussed on oxygenation of aromatic and aliphatic compounds by mono-oxygenases and model systems. Recently, the presence of effector molecules has been noted for cytochrome P-450 dependent mono-oxygenase.[1] A number of model reagent systems are based on activation of various di-oxygen species catalyzed by transition metals, and in particular, iron has been recognized as an important metal for activation of oxygen moieties. Several kinds of reagent systems catalyzed by iron ions or complexes have been developed which can be classified into four categories, namely: (a) reagent systems involving reductive activation of $O_2$ (*e.g.* Udenfriend's system, *etc.*);[2] (b) reagent systems involving reductive activation of $H_2O_2$ (*e.g.*, Fenton's reagent, Hamilton's system, *etc.*);[3] (c) reagent systems involving reductive activation of $RCO_3H$ (*e.g.*, the reagent systems of $Fe^{II}$ or $Fe^{III}$ complexes with peracids, *etc.*);[1,4] and (d) reagent systems involving activation of single oxygen donors (*e.g.*, the reagent system of $Fe^{III}$–tetraphenylporphinatoiron(III) chloride–PhIO, Groves' system, *etc.*).[5] Among these reagents, recent interest has been centered on the reagent system $Fe(ClO_4)_2$–$H_2O_2$–AN (AN: acetonitrile) or $Fe(ClO_4)_2$–peracid–AN, because these reagents are simple and have non-aqueous media. These reagent systems can also be classified into two categories, namely, water-containing[3b,c] and anhydrous[3d] systems, in which these two types of reagents show different reaction behaviors.

In the previous paper,[6] we reported that the iron(III) AN complex, $Fe(AN)_6(ClO_4)_3$, and related solvates can be prepared conveniently by simple addition of $Ac_2O$ to a solution of $Fe(ClO_4)_3 \cdot 6H_2O$ in the appropriate solvent, and we showed that the iron(III) AN complex has the highest formal redox potential ($E^0 = 1.73$ V *vs.* saturated calomel electrode (SCE)) among these solvates. The iron(II) AN complex, $Fe(AN)_6(ClO_4)_2$, can also be prepared easily from $Fe(ClO_4)_2 \cdot 6H_2O$ in the same manner. We report herein that reactions of aromatic and aliphatic hydrocarbons with a new reagent system, $Fe(AN)_6^{2+}$–$H_2O_2$–$Ac_2O$ in AN, afford oxygenation products with fairly high reaction efficiency compared to previously known reagent systems, and the system provides an effective enzyme model for certain mono-oxygenases, as described below.

TABLE I. Oxidation of Aromatic Compounds

| Substrate | Method[a] | Products (%)[b] | Reaction efficiency (%)[c] |
|---|---|---|---|
| Benzene | A | **1** (50.6), **2** (3.5) | 58 |
| Toluene | A | **3** (56.2; *o*-:*m*-:*p*-=63:5:32)[d] | 56 |
| *p*-Xylene | A | **4** (16.1), **5** (6.9),[d] **6** (3.4), **7** (2.8) | e) |
| Mesitylene | A | **8** (20.5), **9** (34.7), **10** (3.2) | *ca.* 100 |
| Cumene | A | **11** (16.7; *o*-:*m*-:*p*-=44:18:38),[d] **12** (4.3) | e) |
| Phenyl acetate | A | **2** (23) | 46 |
| Anisole | A | **13** (3.2), **14** (34.8) | e) |
| | B | **13** (47.1) | *ca.* 100 |
| Naphthalene | C | **15** (21.8), **16** (16.6), **17** (7.2), **18** (2.0), **19** (14.5) | *ca.* 70 |
| 1-Chloronaphthalene | D | **20** (17), **21** (14.7) | e) |
| Phenanthrene | D | **22** (68), **23** (9.1) | *ca.* 100 |

*a*) Molar ratio (substrate: $Fe^{2+}$: $H_2O_2$); A=1:0.01:1, B=1:1:1, C=1:0.01:2, D=1:0.03:3. *b*) Isolated yields based on starting materials. *c*) Mole % of $H_2O_2$ consumed for oxidation of substrates (total yields based on $H_2O_2$). *d*) Isomer distributions were determined by GLC analysis on a 3 m 10% Chromosorb W DEGS column (80—100 mesh). *e*) Reaction efficiency could not be estimated because the reaction residue contained products which could not be purified. **1**, phenyl acetate; **2**, 4-acetoxyphenyl acetate; **3**, tolyl acetate; **4**, 2,5-dimethylphenyl acetate; **5**, 2,4-dimethylphenyl acetate; **6**, 4-acetoxy-2,5-dimethylphenyl acetate; **7**, 2,5-dimethyl-1,4-benzoquinone; **8**, 2,4,6-trimethylphenyl acetate; **9**, 3-acetoxy-2,4,6-trimethylphenyl acetate; **10**, 3,5-diacetoxy-2,4,6-trimethylphenyl acetate; **11**, isopropylphenyl acetate; **12**, acetophenone; **13**, 2-methoxyphenyl acetate; **14**, 4-methoxyacetophenone; **15**, 1-acetoxynaphthalene; **16**, 1,4-naphthoquinone; **17**, 2-acetoxy-1,4-naphthoquinone; **18**, 1,5-diacetoxynaphthalene; **19**, 1,4-diacetoxynaphthalene; **20**, 3-chloro-2-hydroxy-1,4-naphthoquinone; **21**, 5-chloro-1,4-naphthoquinone; **22**, 9,10-phenanthraquinone; **23**, 1,4-phenanthraquinone.

## Electrophilic Oxygenation of Aromatic Hydrocarbons

Aromatic hydroxylation by mono-oxygenases is considered to be an electrophilic oxygenation based on isotope effect studies.[7] The isomer distributions in aromatic hydroxylation have been used to establish the presence or absence of hydroxy radical as a reactive species in both chemical and biological processes, and the existence of the National Institute of Health (NIH) shift in aromatic hydroxylation has also been used as a criterion for enzyme models.

Oxidations of aromatic hydrocarbons with our new reagent system gave the results shown in Table I.

It is clear that this reagent has a fairly good reaction efficiency (conversion % based on $H_2O_2$), and the following results are noteworthy: (a) a methyl-NIH shift product **5** and a chlorine-NIH shift product **20** were obtained in the oxidations of *p*-xylene and 1-chloronaphthalene, respectively; (b) no side chain oxidation product was obtained in the reactions of alkylbenzenes except for minor acetophenone formation from cumene; (c) formation of biphenyl or bibenzyl was not detected in the oxidation of benzene or toluene; (d) in the oxidation of toluene, the isomer distribution of the acetoxylated compounds was mainly *o*- and *p*-isomers, and resembles the isomer distributions of the oxygenation products in ionic reactions with $H_2O_2$–HF,[8] $H_2O_2$–$AlCl_3$,[9] $H_2O_2$–superacid,[10] and $CF_3CO_3H$;[11] (e) only *p*-diacetoxybenzene was produced by oxidation of benzene or phenyl acetate, but only the *o*-isomer from anisole; (f) in oxidations of fused aromatic hydrocarbons, formation of quinones (which were not artifacts of hydrolysis during the isolation process) was characteristic; (g) these reactions occurred with a catalytic amount of either iron(II) salt or iron(III) salt.

The results suggest that this reaction for aromatic hydrocarbons may be an ionic electrophilic reaction. The absence of a hydrogen isotope effect ($k_H/k_D=1.07$) supports this

electrophilic mechanism. Such behavior is in marked contrast with that of similar reagent systems, $Fe^{2+}$–$H_2O_2$–AN, where the water-containing systems[3c] give practically the same oxygenation products as aqueous Fenton chemistry[3a] involving ·OH, and the anhydrous system gives no hydroxylation product or $^1O_2$ oxidation products.[3d]

## Oxygenation of Aliphatic Hydrocarbons

Selective insertion of an oxygen atom into an unactivated carbon–hydrogen bond in

TABLE II. Oxidation of Alkanes

| Substrate | Method[a] | Product (%)[b] | | |
|---|---|---|---|---|
| | | Monoacetate | Diacetate | Acetamide |
| Cyclohexane | E | **24** (17.2) | **25** (11.5) | **26** (4.5) |
| Cyclohexyl acetate | F | | **25** (32.8) | **26**[c] |
| Norbornane | G | **27** (21.9) | **28** (16.8) | **29**[c] |
| 2-*exo*-Acetoxynorbornane | F | | **28** (24.1) | **29** (34.1) |

*a*) Molar ratio (substrate: $Fe^{2+}$: $H_2O_2$); E=1:1:1, F=1:1:2, G=1:0.5:2. *b*) Isolated yields based on starting materials. *c*) A small amount.

TABLE III. Isomer Distribution (%) of Cyclohexyl Diacetate in the Oxidation Product[a]

| Substrate | 1,2-*cis* | 1,2-*trans* | 1,3-*trans* | 1,4-*trans* | 1,3- and 1,4-*cis* |
|---|---|---|---|---|---|
| Cyclohexane | 10.8 | 24.4 | 26.4 | 15.9 | 22.5 |
| Cyclohexyl acetate | 3.9 | 5.9 | 44.7 | 11.0 | 34.5 |
| (added $HClO_4$) | 4.5 | 7.2 | 43.4 | 12.0 | 33.0 |
| (added imidazole) | 4.4 | 5.8 | 39.4 | 13.1 | 37.3 |

*a*) Determined by GLC analysis on a 3 m 10% Chromosorb W DEGS column (80—100 mesh).[3b] 1,3-*cis* and 1,4-*cis* isomers could not be distinguished by this method.

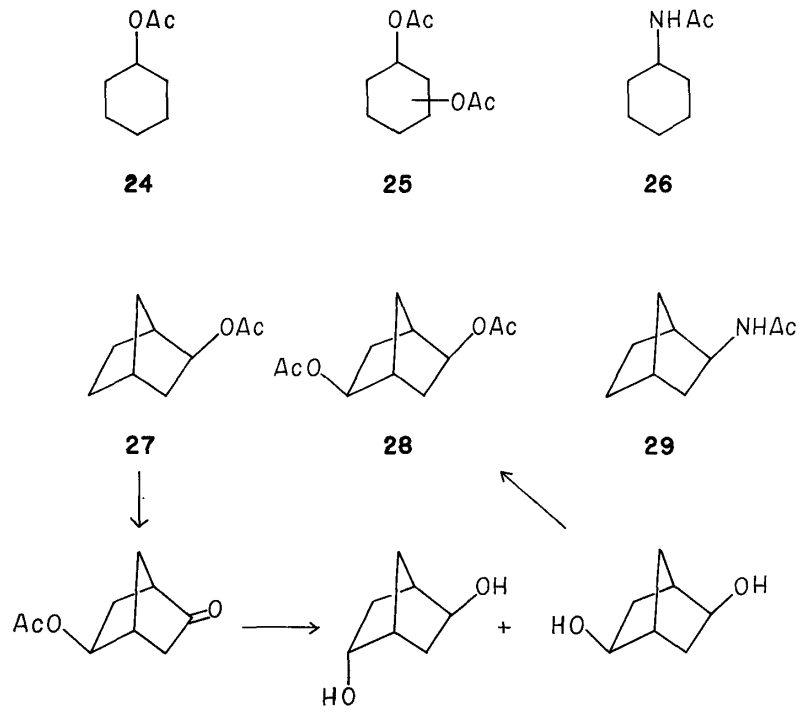


Chart 1

aliphatic compounds by heme-containing cytochrome P-450 dependent mono-oxygenases is involved in the metabolism of a wide variety of compounds. In oxygenation of aliphatic compounds by model systems, interest has been focussed on whether or not the regio- and stereoselective hydroxylations observed in biological systems could be reproduced.

Oxidations of cycloalkanes by the reagent system, $Fe(AN)_6^{2+}$–$H_2O_2$–$Ac_2O$ in AN, afforded the results shown in Table II. The isomer distributions of cyclohexyl diacetate in the oxidations of cyclohexane and cyclohexyl acetate are shown in Table III.

The following features in the oxidation of cycloalkanes seem noteworthy: (a) product yields with this reagent system are fairly high compared with other reported results (a few % yields)[3b,4a]; (b) the 1,3-*trans* isomer of cyclohexyl diacetate was the main product in the oxygenation of cyclohexane or cyclohexyl acetate (the main product is 1,3-*cis* isomer in other reports)[3b,4a]; (c) the diacetate **28** was obtained as a specific oxygenation product from norbornane or *exo*-2-acetoxynorbornane (the structure of **28** was identified by direct comparison with an authentic sample prepared by the known procedure, as shown in Chart 1)[12]; (e) a relatively large amount of iron salts was necessary for oxygenation of aliphatic hydrocarbons as compared with aromatic hydrocarbons.

## Discussion

As described in the experimental section, this reagent system consists of $Fe(ClO_4)_2 \cdot 6H_2O$,[13] 30% $H_2O_2$, organic substrate, and $Ac_2O$ (sufficient to remove water contained in the iron(II) salts and $H_2O_2$ and still to leave 2 mol eq with respect to $H_2O_2$) in AN.[14] Excess $Ac_2O$ not only produces an anhydrous system in this reagent by removal of the aqua ligand of the iron(II) salts to form the iron(II) AN complex, $Fe(AN)_6(ClO_4)_2$, (Eq. i) and by the removal of water in $H_2O_2$, but also forms peracetic acid ($AcO_2H$) by reaction with $H_2O_2$ catalyzed by the iron salts (as a Lewis acid) (Eq. ii). The formation and involvement of $AcO_2H$ in this system can be assumed on the basis that reactions in which $AcO_2H$[15] is used instead of $H_2O_2$ in the presence of one equimolar amount of $Ac_2O$ give the same results.

$$Fe(H_2O)_6^{2+} + 6\ Ac_2O + 6\ AN \longrightarrow Fe(AN)_6^{2+} + 12\ AcOH \quad \text{(i)}$$

$$Ac_2O + H_2O_2 \longrightarrow AcO_2H + AcOH \quad \text{(ii)}$$

As soon as the iron(II) AN complex with $AcO_2H$ forms complex A, $Fe^{II}(AcO_2H)^{2+}$ (Eq. iii), the $AcO_2H$ ligand of complex A may simultaneously undergo homolytic reductive cleavage by one electron back-donation from the iron(II) to give the complex $Fe^{III}(OH)^{2+}$ (Eq. iv) which may transform further to the complex $Fe^{III}(OAc)^{2+}$ by acetylation with $Ac_2O$ (Eq. v) or from the iron(II) AN complex directly (Eq. vi).

$$Fe^{II}(AN)_6^{2+} + AcO_2H \longrightarrow Fe^{II}(AcO_2H)^{2+}\ \text{(complex A)} \quad \text{(iii)}$$

$$Fe^{II}(AcO_2H)^{2+} \longrightarrow Fe^{III}(OH)^{2+} + AcO^{\cdot} \quad \text{(iv)}$$

$$Fe^{III}(OH)^{2+} + Ac_2O \longrightarrow Fe^{III}(OAc)^{2+} + AcOH \quad \text{(v)}$$

$$Fe^{II}(AN)_6^{2+} + AcO^{\cdot} \longrightarrow Fe^{III}(OAc)^{2+} \quad \text{(vi)}$$

Formation of the complex $Fe^{III}(OAc)^{2+}$ can be presumed on the basis of the following evidence in a solution prepared by the addition of 1/2 mol of $AcO_2H$ to $Fe^{II}(AN)_6^{2+}$ (in the absence of substrate): (a) $KMnO_4$ titration of this solution showed that the $Fe^{II}$ complex had already changed to the higher-valent complex (Eq. vii) (Table IV); (b) the rest potential of the solution was *ca.* 1480 mV *vs.* SCE, lower than that of $Fe^{II}(AN)_6^{2+}$ (*ca.* 1550 mV) or $Fe^{III}(AN)_6^{3+}$ (*ca.* 1850 mV) (this suggests that the iron complex in this solution has ligand $^-OAc$ or $^-OH$); (c) the ultraviolet (UV) spectrum of the solution has an absorption maximum

at 346 nm (presumably due to $Fe^{II}(OAc)^{+}$ or $Fe^{III}(OAc)^{2+}$), whereas no absorptions were observed around that region in the simple AN complexes of $Fe^{II}$ and $Fe^{III}$[16]; (d) the solution prepared by mixing $Fe^{III}(AN)_6^{3+}$ with NaOAc (Eq. viii) showed the same behavior as described in (a), (b), and (c). It seems unlikely this solution involves the reaction shown in Eq. ix (two electron back-donation from $Fe^{II}$) because of its low rest potential. In addition, the decarboxylation[4] reaction shown in Eq. x was not observed in this system.

$$Fe^{II}(AN)_6^{2+} + 1/2AcO_2H + 1/2Ac_2O \longrightarrow Fe^{III}(OAc)^{2+} \quad \text{(vii)}$$

$$Fe^{III}(AN)_6^{3+} + NaOAc \longrightarrow Fe^{III}(OAc)^{2+} \quad \text{(viii)}$$

$$Fe^{II}(AcO_2H)^{2+} \longrightarrow Fe^{IV}(OH)(OAc)^{2+} \quad \text{(ix)}$$

$$AcO^{\cdot} \longrightarrow {}^{\cdot}CH_3 + CO_2 \quad \text{(x)}$$

Involvement of a redox system in this reagent can be also presumed in view of the following evidence: (a) the $Al^{III}$ AN complex, $Al(AN)_6(ClO_4)_3$, which was prepared in the same manner as the iron(III) AN complex, did not catalyze such an oxygenation reaction; (b) analysis of $Fe^{II}$ by $KMnO_4$ titration in residual solutions after the reaction with organic substrates showed that the iron complexes always consist of a mixture of $Fe^{II}$ and $Fe^{III}$, as shown in Table IV. Thus, this reaction should involve the transformation of the complex $Fe^{II}(AN)_6^{2+}$ to the complex $Fe^{III}(OAc)^{2+}$ in the initial stage.

Further reaction of the complex $Fe^{III}(OAc)^{2+}$ with $AcO_2H$ may yield complex B, $Fe^{III}(AcO_2H)(OAc)^{2+}$, (Eq. xi). Complex B seems to be stable in the absence of organic substrate and gives diacetyl peroxide on reaction with $Ac_2O$ in almost quantitative yield; this did not participate in the oxygenation (Eq. xv). On the other hand, complex B presumably undergoes homolytic reductive cleavage of AcO–OH bond to give complex C, $Fe^{IV}(OH)(OAc)^{2+}$, in the presence of substrates (Eq. xii). Complex C may be further transformed to complex D, $Fe^{IV}(OAc)_2^{2+}$, by acetylation with $Ac_2O$ (Eq. xiii). Then, complex D oxidizes aromatic hydrocarbons to yield acetoxylates and the iron(II) AN complex, which in turn catalyzes further oxygenation (Eq. xi—xiv and vi). Therefore, organic substrates act as a promoter[17] of this reaction. In the case of substrates which have high oxidation potentials, oxygenation of substrates becomes competitive with the formation of diacetyl peroxide.

$$Fe^{III}(OAc)^{2+} + AcO_2H \longrightarrow Fe^{III}(AcO_2H)(OAc)^{2+} \text{ (complex B)} \quad \text{(xi)}$$

$$Fe^{III}(AcO_2H)(OAc)^{2+} \longrightarrow Fe^{IV}(OH)(OAc)^{2+} \text{ (complex C)} + AcO^{\cdot} \quad \text{(xii)}$$

$$Fe^{IV}(OH)(OAc)^{2+} + Ac_2O \longrightarrow Fe^{IV}(OAc)_2^{2+} \text{ (complex D)} + HOAc \quad \text{(xiii)}$$

$$Fe^{IV}(OAc)_2^{2+} + ArH + 6AN \longrightarrow Fe^{II}(AN)_6^{2+} + ArOAc + HOAc \quad \text{(xiv)}$$

$$Fe^{II}(AN)_6^{2+} + AcO^{\cdot} \longrightarrow Fe^{III}(OAc)^{2+} \quad \text{(vi)}$$

TABLE IV. Analysis of Residual $Fe^{II}$ in the Reagent Solution by $KMnO_4$ Titration

| Run | Substrate | Molar ratio before reaction : $Fe(AN)_6^{2+}$ | : $Fe(AN)_6^{3+}$ | : $H_2O_2$ | Mole % after reaction $Fe^{II}$ | $Fe^{III}$ |
|---|---|---|---|---|---|---|
| 1 | Absence | : 1 | : — | : 0.5 | 8.9 | 91.1 |
| 2 | Absence | : 1 | : — | : 2 | 1.5 | 98.5 |
| 3 | Toluene 1 | : 1 | : — | : 2 | 26.5 | 73.5 |
| 4 | Toluene 5 | : 1 | : — | : 10 | 37.1 | 62.9 |
| 5 | Benzene 1 | : — | : 1 | : 2 | 16.6 | 83.4 |
| 6 | Benzene 2 | : 1 | : 1 | : 4 | 20.7 | 79.3 |

$$Fe^{III}(AcO_2H)(OAc)^{2+} + Ac_2O \longrightarrow Fe^{III}(OAc)^{2+} + (AcO)_2 + HOAc \quad (xv)$$

Participation of complex D in the oxygenation is supported by the following evidence. Reactions of benzene with the $Fe(AN)_6^{2+}$ complex and $AcO_2H$[18] in the presence of propionic anhydride[19] and trifluoroacetic anhydride[20] gave phenyl propionate and phenyl acetate, respectively. These results suggest that the reactive species in the former reaction may be mainly $OCOC_2H_5$ in $Fe^{IV}(OAc)(OCOC_2H_5)^{2+}$ (Eq. xvi and xvii) and that in the latter reaction may be $OCOCH_3$ in $Fe^{IV}(OAc)(OCOCF_3)^{2+}$ (Eq. xviii and xix). Therefore, the alternative route involving reaction with complex C (Eq. xx and xxi) may not participate in this reaction.

$$Fe^{IV}(OH)(OAc)^{2+} + (C_2H_5CO)_2O \longrightarrow Fe^{IV}(OCOC_2H_5)(OAc)^{2+} + C_2H_5CO_2H \quad (xvi)$$

$$Fe^{IV}(OCOC_2H_5)(OAc)^{2+} + ArH + 6AN \longrightarrow Fe^{II}(AN)_6^{2+} + ArOCOC_2H_5 + HOAc \quad (xvii)$$

$$Fe^{IV}(OH)(OAc)^{2+} + (CF_3CO)_2O \longrightarrow Fe^{IV}(OCOCF_3)(OAc)^{2+} + CF_3CO_2H \quad (xviii)$$

$$Fe^{IV}(OCOCF_3)(OAc)^{2+} + ArH + 6AN \longrightarrow Fe^{II}(AN)_6^{2+} + ArOAc + CF_3CO_2H \quad (xix)$$

$$Fe^{IV}(OH)(OAc)^{2+} + ArH \longrightarrow Fe^{II}(ArOH)^{2+} + HOAc \quad (xx)$$

$$Fe^{II}(ArOH)^{2+} + Ac_2O + 6AN \longrightarrow Fe^{II}(AN)_6^{2+} + ArOAc + HOAc \quad (xxi)$$

$$Fe^{III}(AcO_2H)(OAc)^{2+} \text{ (complex B)} \longrightarrow Fe^{V}(OH)(OAc)_2^{2+} \quad (xxii)$$

The following questions still remain, namely, (a) is complex D the reactive species in any case? (b) is the cleavage of complex B homolytic? (c) which complexes are responsible for formation of the NIH shift products? (d) though oxygenations of aromatic hydrocarbons are recognized to proceed through ionic electrophilic reaction, does this also apply to oxygenation reactions of aliphatic hydrocarbons? Reactions of aromatic hydrocarbons which are easily oxidized, such as fused aromatic compounds, with an equimolar amount of complex B, prepared according to Eq. xi, in the absence of $Ac_2O$ gave the hydroxylates. These results mean that complex B transforms to complex C in the presence of substrate and the resultant complex C acts as a reactive species to give the hydroxy product (Eq. xii and xx). On the other hand, reactions of complex C with aromatic hydrocarbons which are difficult to oxidize such as benzene afforded only a small amount of oxidation products. The difference of reactivity between complex C and complex D may depend not only on oxidation power but also on turnover numbers, that is, the hydroxy compound formed by oxidation with complex C may block further reaction by forming a strong ligand with iron(II).

Though one-electron and two-electron reductive cleavage of $AcO_2H$ are possible in these redox reactions as shown by Eq. xii and xxii, the two-electron mechanism could be ruled out by the fact that $Fe^{II}$ always coexists in the reactions with substrates, as shown in Table IV. To investigate the species responsible (either complex C or D) for the NIH shift product formation, the following experiments were carried out. Oxidations of 1-chloronaphthalene by complex C gave the quinone **20** and **21**, respectively. On the other hand, oxidation of *p*-xylene with complex C afforded the phenols in low yields, but the NIH shift product was not detected. Therefore, we could not determine whether the reactions affording the NIH shift product proceed through either complex C or D (by hydroxylation or acetoxylation), or whether they start at the *ipso* or *ortho* position.

Oxygenation reactions of aliphatic compounds in this reagent system can be considered to proceed by a stepwise radical mechanism[11,21] because oxidation of cyclohexane by this reagent in the presence of $CBrCl_3$ afforded 12% cyclohexyl acetate along with 5% bromocyclohexane.

Thus, oxygenation of aromatic and aliphatic hydrocarbons in this new reagent system may occur as shown in Chart 2, where $Ac_2O$ acts as a promoter or effector. Evidently, either

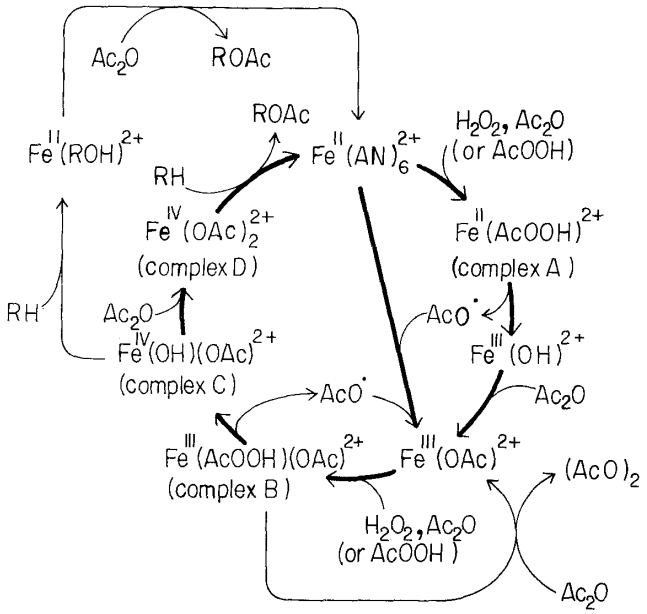


Chart 2

complexes of iron(II) or iron(III) can be used for such reactions, but the iron(III) complex has a considerable limitation because of its high redox potential, resulting in side reactions.[22]

Further applications of this reagent system to organic synthesis are in progress.

## Experimental

All melting points are uncorrected. Infrared (IR) spectra were recorded with a Hitachi 215 or 285 spectrophotometer, proton nuclear magnetic resonance ($^1$H-NMR) spectra with a Hitachi R 600, Varian T-60 or JEOL JNM-FX 100 spectrometer with TMS as an internal standard ($CDCl_3$ soln.) and mass spectra (MS) with a JEOL JMS-D 300 spectrometer. UV and visible spectra were measured on a Hitachi 220A spectrometer. Thin-layer and column chromatographies were performed on Merck Kieselgel 60 F-254 and Mallinckrodt silica gel (100 mesh), respectively. Gas chromatographic analyses were performed on a Hitachi 163 analyzer with an FI detector. Rest potentials were taken on a Toa Denpa HM-20E potentiometer or a Hokuto Denko HA-501 potentiostat.

Analyses of ferrous ion were done by permanganate titration according to the standard procedure.

**General Procedure for Oxidation of Aromatic Compounds (Method A)**——A solution of 30% $H_2O_2$ (1.1 ml, 10 mmol) in AN (2 ml) was added dropwise to a solution of $Fe(ClO_4)_2 \cdot 6H_2O$ (36.2 mg, 0.1 mmol), $Ac_2O$ (8 ml) and an aromatic compound (10 mmol) in AN (40 ml) with vigorous stirring at *ca.* 30 °C for 3 min. The reaction mixture was poured into ice-water and extracted with ether–dichloromethane (5 : 1, 2 × 50 ml). The combined organic layer was washed with brine, $Na_2S_2O_3$ or $Na_2SO_3$ aq., and sat. $NaHCO_3$, and then dried on $Na_2SO_4$ and evaporated. The residue was subjected to silica gel column chromatography using dichloromethane–hexane (1 : 1) as an eluent. Isomeric mixtures which could not be isolated by column chromatography were analyzed by gas chromatography and the retention times were compared with those of authentic samples.

**Oxidation of *p*-Xylene by Method A**——Oxidation of *p*-xylene according to the general procedure gave an isomeric mixture of 2,5-dimethylphenyl acetate (**4**), and 2,4-dimethylphenyl acetate (**5**) (a methyl-NIH shift product) in 23% yield as a colorless oil, 4-acetoxy-2,5-dimethylphenyl acetate (**6**) in 3.4% yield as colorless crystals, mp 134—136 °C, 2,5-dimethyl-1,4-benzoquinone (**7**) in 2.8% yield as pale yellow needles, mp 117—118 °C (ethanol), and a small amount of unidentifiable products. Identification and quantitative analysis of the isomers **4** and **5** were done by comparison of the retention times and peak intensities (half-width method) in gas chromatography on a 3 m, 10% Chromosorb W DEGS (80—100 mesh) column at 120—140 °C (1 °C/min) with those of standard samples.

**Oxidation of 1-Chloronaphthalene by Method D**——A solution of 30% $H_2O_2$ (3.3 ml, 30 mmol) in AN (6 ml) was added dropwise with stirring to a solution of $Fe(ClO_4)_2 \cdot 6H_2O$ (108.6 mg, 0.3 mmol), $Ac_2O$ (24 ml) and 1-chloronaphthalene (1.63 g, 10 mmol) in AN (80 ml) at room temperature for 10 min at *ca.* 30 °C. The reaction mixture was poured into ice-water and extracted with ether–methylene chloride (5 : 1). The organic layer was washed with brine, $Na_2S_2O_3$ aq., and sat. $NaHCO_3$, and then dried and concentrated. The $NaHCO_3$ layer yielded 354 mg (17%) of 3-chloro-2-hydroxy-1,4-naphthoquinone (**20**) (a chlorine–NIH shift product),[20] mp 222—224 °C (ethanol–ether) as orange-yellow crystals after usual treatment. Silica gel column chromatography of the organic residue gave 283 mg

(14.7%) of 5-chloro-1,4-naphthoquinone (**21**), mp 152—153 °C (ethanol), as yellow crystals, and products which could not be purified, as well as 63 mg (4%) of starting material.

**Oxidation of Benzene by $Fe(AN)_6(ClO_4)_2$ with $AcO_2H$ in the Presence of $Ac_2O$**——Peracetic acid [which was prepared by adding 30% $H_2O_2$ (1.1 ml, 10 mmol) to $Ac_2O$ (5 ml) with stirring at 40 °C and allowing the mixture to stand overnight at room temperature] was added dropwise with stirring to a solution of $Fe(ClO_4)_2 \cdot 6H_2O$ (36.2 mg, 0.1 mmol), $Ac_2O$ (3 ml) and benzene (780 mg, 10 mmol) in AN (40 ml) for 3 min at *ca.* 30 °C. The reaction mixture was worked up according to the general procedure to afford almost the same result as that obtained by method A.

**Oxidation of Benzene by $Fe(AN)_6(ClO_4)_2$ with $AcO_2H$ in the Presence of $(CF_3CO)_2O$**——A 25% $AcO_2H$ solution (1.5 ml, 5 mmol) was added dropwise with vigorous stirring to a solution of $Fe(ClO_4)_2 \cdot 6H_2O$ (18.1 mg, 0.05 mmol), $(CF_3CO)_2O$ (5 ml) and benzene (400 mg, 5 mmol) in AN (25 ml) at *ca.* 30 °C for 5 min. The reaction mixture was worked up according to the general procedure to give 453 mg (66.6%) of phenyl acetate and 45 mg (4.6%) of 4-acetoxyphenyl acetate.

**Oxidation of Benzene by $Fe(AN)_6(ClO_4)_2$ with $AcO_2H$ in the Presence of $(CH_3CH_2CO)_2O$**——A 25% $AcO_2H$ solution (2 ml, 6.6 mmol) was added to a solution of $Fe(ClO_4)_2 \cdot 6H_2O$ (36.2 mg, 0.1 mmol), $(CH_3CH_2CO)_2O$ (10 ml) and benzene (550 mg, *ca.* 7 mmol) in AN (50 ml). The reaction mixture was worked up according to the general procedure to yield 25 mg (2.7%) of phenyl acetate and 423 mg (42%) of phenyl propionate.

**Isotope Effect for Oxidation of Benzene**——A solution of 30% $H_2O_2$ (4.4 ml, 40 mmol) in AN (10 ml) was added dropwise with stirring to a solution of $Fe(ClO_4)_2 \cdot 6H_2O$ (1.45 g, 4 mmol), $Ac_2O$ (30 ml), benzene (835 mg, 10.9 mmol), and hexadeuterobenzene (913 mg, 10.8 mmol) in AN (80 ml) at *ca.* 30 °C for 5 min. The reaction mixture was worked up in accordance with the general procedure. A mixture of phenyl acetate and deuterophenyl acetate was obtained by silica gel column chromatography of the reaction residue. The ratio $C_6H_5OAc : C_6D_5OAc$ was found by $^1$H-NMR measurement to be 1.07.

**Oxidation of Benzene by Complex C**——A 25% $AcO_2H$ solution (0.9 ml, 3 mmol) was added dropwise with stirring to a solution of $Fe(ClO_4)_3 \cdot 9H_2O$ (516 mg, 1 mmol) and $Ac_2O$ (0.9 ml) in AN (10 ml) at *ca.* 20 °C for a few min. The resultant orange solution was added dropwise with stirring to a solution of benzene (240 mg, *ca.* 3 mmol) in AN (5 ml) at 30 °C for a few min. The reaction mixture was worked up according to the general procedure to give only 16 mg (5.7%) of phenol.

**Oxidation of 1-Chloronaphthalene by Complex C**——A solution of complex C [prepared from 25% $AcO_2H$ (2.7 ml, 9 mmol), $Fe(ClO_4)_2 \cdot 6H_2O$ (1.086 g, 3 mmol) and $Ac_2O$ (1.8 ml) in AN (30 ml)] was added dropwise with stirring to a solution of 1-chloronaphthalene (490 mg, 3 mmol) in AN (20 ml) at 30 °C for a few min. The reaction mixture was worked up in the same manner as described above for the oxidation of 1-chloronaphthalene by method D, yielding 26 mg of 3-chloro-2-hydroxy-1,4-naphthoquinone (**20**) from the $NaHCO_3$ soluble portion, and 131 mg (22.7%) of 5-chloro-1,4-naphthoquinone (**21**) and 240 mg of **20** from the neutral organic layer portion (the total yield of chlorine-NIH shift product **20** was 42.5%) along with 65 mg (13.3%) of the starting material.

**General Procedure for Oxidation of Aliphatic Compounds (Method E)**——A solution of 30% $H_2O_2$ (3.3 ml, 30 mmol) in AN (10 ml) was added dropwise with stirring to a solution of $Fe(ClO_4)_2 \cdot 6H_2O$ (10.86 g, 30 mmol), $Ac_2O$ (42 ml) and an aliphatic compound (30 mmol) in AN (200 ml) at 30 °C for a few min. The reaction mixture was worked up in the same manner as described in the general procedure for oxidation of aromatic compounds.

**Oxidation of Bicyclo[2.2.1]heptane by Method G**——A solution of 30% $H_2O_2$ (6.6 ml, 60 mmol) in AN (10 ml) was added to a solution of $Fe(ClO_4)_2 \cdot 6H_2O$ (5.43 g, 15 mmol), $Ac_2O$ (48 ml), and norbornane (2.88 g, 30 mmol) in AN (150 ml), and the mixture was worked up according to the general procedure. Chromatographic purification gave 1.01 g (22%) of 2-*exo*-acetoxybicyclo[2.2.1]heptane (**27**), 535 mg (16.8%) of 2-*exo*,5-*exo*-diacetoxybicyclo[2.2.1]-heptane (**28**), and a small amount of 2-*exo*-acetamidobicyclo[2.2.1]heptane (**29**).

2-*exo*,5-*exo*-Diacetoxylbicyclo[2.2.1]heptane (**28**): Colorless oil. IR (neat) $cm^{-1}$: 1725 and 1240. NMR ($CDCl_3$) $\delta$: 1.45—1.67 (m, 6H, C(3)-2H, C(6)-2H, and C(7)-2H), 2.02 (s, 6H, 2 × OCOMe), 2.34—2.39 (m, 2H, fine coupling, C(1)-H and C(4)-H), 4.56 (m, 2H, fine coupling, C(2)-*endo*-H and C(5)-*endo*-H). MS *m/e*: Calcd for $C_{11}H_{16}O_4$ ($M^+$): 212.1049. Found: 212.1064.

**Oxidation of Cyclohexane in the Presence of Bromotrichloromethane**——A solution of 30% $H_2O_2$ (0.55 ml, 5 mmol) in AN (5 ml) was added dropwise with stirring under a nitrogen atmosphere in the dark to a solution of $Fe(ClO_4)_2 \cdot 6H_2O$ (1.81 g, 5 mmol), $Ac_2O$ (10 ml), cyclohexane (420 mg, 5 mmol) and $BrCCl_3$ (2 g, *ca.* 10 mmol) in AN (50 ml). The reaction mixture was worked up according to the general procedure, and the residue was subjected to column chromatography to give 40 mg (5%) of bromocyclohexane, 85 mg (12%) of cyclohexyl acetate and trace amounts of cyclohexyl diacetates.

## References and Notes

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13) Ferrous tetrafluoroborate instead of perchlorate gave similar results. Ferric perchlorate also gave similar results, with some limitations. On the other hand, iron(III) complexes such as $Fe(DMF)_6(ClO_4)_3$, $Fe(bpy)_3(ClO_4)_3$, $Fe(acac)_3$, *etc.*, where the ligands are difficult to replace, did not catalyze the oxygenation reaction. Perchlorates of other metal ions such as $Cu^{2+}$, $Mn^{2+}$, $Ni^{2+}$, $Co^{2+}$, $Al^{3+}$, *etc.* were not effective.

14) Among iron(II) solvates other than AN, nitromethane and acetone acted as catalysts for the oxygenation in the presence of $Ac_2O$ in the corresponding solvents, but the solvates of $Ac_2O$, AcOEt, and other solvents which have larger donicity than water did not act as catalysts.

15) $CF_3CO_3H$ or *m*-chloroperbenzoic acid instead of $AcO_2H$ did not afford any oxygenation products.

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18) Oxygenation did not proceed upon addition of $H_2O_2$ instead of $AcO_2H$ in these anhydride-containing solutions. This may be because of the difficulty of forming perpropionic acid under these conditions, and the inactivity of $Fe^{IV}(OCOCF_3)_2^{2+}$ for oxygenation.

19) Other products such as 4-acetoxyphenyl acetate were not produced even in trace amounts.

20) Phenol or phenyl trifluoroacetate was not detected.

21) Reactions in this reagent system were not affected by $O_2$ or air.

22) Side reaction can be prevented by the addition of NaOAc to a solution of $Fe(AN)_6(ClO_4)_3$, decreasing the redox potential of the iron complex.