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A New Combined Oxidizing Reagent System, $Fe(CH_3CN)_6^{3+}$–IO_4^-: Oxidation of Paraffin Hydrocarbons

Eiichi Kotani, Shigeki Kobayashi, Yoko Ishii,
and Seisho Tobinaga*

*Showa College of Pharmaceutical Sciences, Tsurumaki,
Setagaya-ku, Tokyo 154, Japan*

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Combined oxidizing reagent systems of $Fe(AN)_6(ClO_4)_3$ (AN = acetonitrile) with halogen oxyacids were investigated. In particular, reactions of paraffin hydrocarbons with a combined reagent system of $Fe(AN)_6^{3+}$–IO_4^- were explored because of the high reactivity of this system in the oxidation of adamantane (Table I). Oxidations of bornane, norbornane, cyclohexane, and *n*-hexane gave the corresponding acetamides and acetates (Table II). These results show that the title reagent system can efficiently oxidize organic substrates which have onset potentials of anodic current of *ca.* 2.7 V *vs.* saturated calomel electrode.

Keywords——oxidation; paraffin hydrocarbon; combined reagent system; hexakisacetonitrile iron(III) perchlorate; halogen oxyacid; sodium periodate

Direct oxidation of paraffin hydrocarbons in a specific way under mild conditions is a challenging problem which is of industrial importance and of scientific interest in relation to enzymatic oxidations by cytochrome P-450 dependent mono-oxygenase[1)] or nonheme iron protein oxidases in nature.[2)] Currently, there are several types of methods available, namely, (a) by activation of molecular oxygen with metal complexes in the presence of reducing agents, mimicking mono-oxygenase enzyme systems,[3)] (b) by activation of either metals or oxidants by forming complexes between metal complexes and oxidants, modifying the cytochrome P-450 by-pass route,[4)] (c) by activation of a C–H bond of hydrocarbons by forming organometallic compounds,[5)] *etc.*

We recently reported a convenient preparation of hexakisacetonitrile iron(III) perchlorate, $Fe(AN)_6(ClO_4)_3$ (AN = acetonitrile), and its reactivity as an oxidizing reagent for *prim*- and *sec*-alkylbenzenes.[6)] The results showed that the iron(III) complex has the ability to oxidize organic compounds which have onset potentials of anodic current (E_a) of up to *ca.* 2.0 V *vs.* saturated calomel electrode (SCE) to give the corresponding acetates and amides. Further efforts have been made to prepare oxidizing reagent systems based on $Fe(AN)_6(ClO_4)_3$, and we found that the combined reagent system of the iron(III) complex with certain halogen oxyacids can oxidize paraffin hydrocarbons which have E_a of over *ca.* 2.7 V *vs.* SCE. In particular, oxidations of alkanes by the reagent system of the iron complex with $NaIO_4$ gave the oxidation products in fairly good yields.

This work was initiated because of the finding that when various salts of halogen oxyacids were added to a solution of iron(III) complex in AN (containing a small amount of AcOH), $NaIO_4$, $NaBrO_3$, $NaClO_3$, $NaClO_2$, $Ca(ClO)_2$, and PhIO dissolved in the solution, but $NaIO_3$ and $NaClO_4$ did not. These properties resemble those of cytochrome P-450 with halogen oxyacids reported by Gustafsson *et al.*[7)] Further investigations on the reactions of adamantane with the above combined reagent systems gave the following results (Table I).

Among the oxidations of adamantane by several combined systems, the best result was

Table I. Oxidation of Adamantane[a]

Run	Molar ratio of $M(AN)_6^{3+}$, oxidant, and adamantane (Ad)	Yield of product (mol%)[b]	
		1	**2**
1	$Fe(AN)_6^{3+}$: $NaIO_4$: Ad = 1.8 : 1.2 : 1	96	4
2	$Fe(AN)_6^{3+}$: $NaIO_4$: Ad = 1 : 1 : 1	73	0
3	$Fe(AN)_6^{3+}$: $NaIO_4$: Ad = 3 : 2 : 1	73	27
4	$Fe(AN)_6^{3+}$: $NaIO_4$: Ad = 0.1 : 1.2 : 1	9	0
5	$Fe(AN)_6^{3+}$: H_5IO_6 : Ad = 1.8 : 1.2 : 1	97	3
6	$Fe(AN)_6^{3+}$: $NaBrO_3$: Ad = 1.8 : 1.2 : 1	83	7.2
7	$Fe(AN)_6^{3+}$: $NaClO_3$: Ad = 1.8 : 1.2 : 1	26	0
8	$Fe(AN)_6^{3+}$: $NaClO_2$: Ad = 1.8 : 1.2 : 1	11	0
9	$Fe(AN)_6^{3+}$: $Ca(OCl)_2$: Ad = 1.8 : 1.2 : 1	21	4[c]
10	$Fe(AN)_6^{3+}$: PhIO : Ad = 1.8 : 1.2 : 1	4	0
11	$Al(AN)_6^{3+}$: H_5IO_6 : Ad = 1.8 : 1.2 : 1	0	0
12	$Al(AN)_6^{3+}$: $NaBrO_3$: Ad = 1.8 : 1.2 : 1	75	3.6

a) All reactions were carried out at 20—25 °C for 10 min. *b*) Isolated yield based on adamantane. Starting material was recovered, in addition to **1** and **2**. *c*) In addition, 1- and 2-chloroadamantane were isolated in 28% total yield.

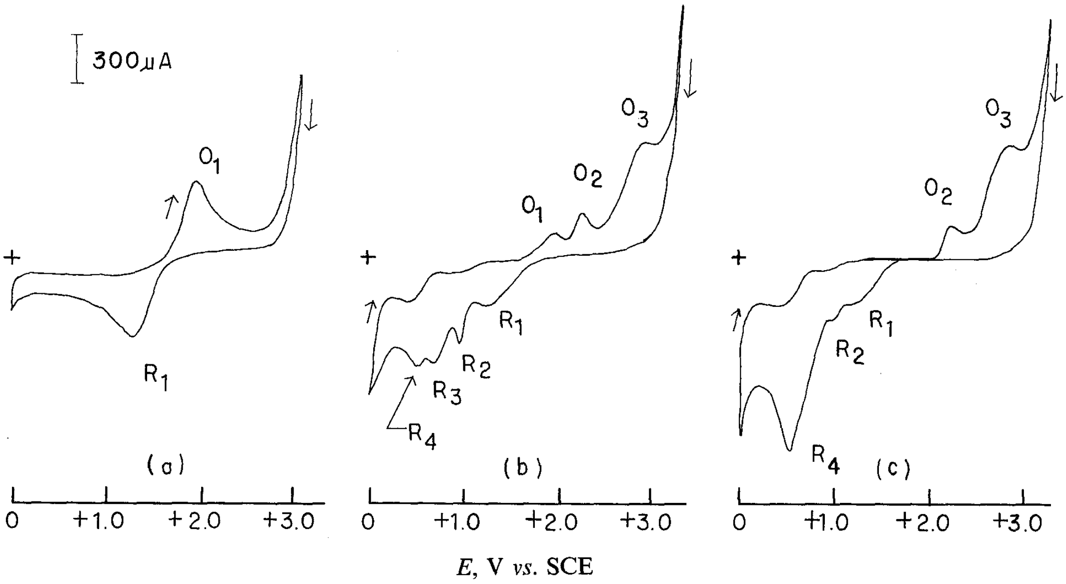

Fig. 1. Cyclic Voltammograms of (a) a Solution of $Fe(AN)_6(ClO_4)_3$ (0.1 mmol) in 10 ml of AN, (b) after Addition of $NaIO_4$ ($0.1 \times 2/3$ mmol) to (a), and (c) after Addition of $NaIO_4$ (0.1 mmol) to (a)

Supporting electrolyte, 0.1 M Et_4NClO_4; working electrode, platinum disk; sweep rate, 200 mV s^{-1}.

obtained in the reagent system of the iron(III) AN complex with $NaIO_4$ in the ratio of $Fe(AN)_6^{3+}:IO_4^-:$adamantane$=1.8:1.2:1$ as shown in Table I. In oxidation with the title reagent system, excess oxidizing reagent caused a decrease of **1** and increase of **2** in the products (Table I, run 3). Further, oxidation of **1** by the same reagent system gave **2** in 80% yield. Thus, our investigation was focussed on reactions of paraffin hydrocarbons in a combined reagent system, $Fe(AN)_6(ClO_4)_3$ and $NaIO_4$, because of its noteworthy reactivity among the combinations tested.

The rest potential of the reagent system ($Fe(AN)_6^{3+}:IO_4^-=3:2$) showed a high value over 2 V *vs.* SCE, suggesting that this combined reagent system has very strong oxidizing power. The change of the cyclic voltammograms (CV) on step-by-step addition of periodate

TABLE II. Oxidation of Paraffin Hydrocarbons by $Fe(AN)_6^{3+}$–IO_4^- [a)]

	Oxidation potential E_a, V *vs.* SCE[b)]	Product (yield, mol%)[c)]
Bornane	2.5	**3** (46); **4** (7)
Norbornane	2.6	**5** (60)
Cyclohexane	2.65	**6a** (32); **6b** (11)
n-Hexane	2.7[d)]	**7a** (21); **8a** (12) **7b** (2); **8b** (2)

a) Reactions were carried out at 20—25 °C for 1 h with a ratio of $Fe(AN)_6(ClO_4)_3 : NaIO_4$: substrate = 3 : 2 : 1. *b*) Onset potentials of anodic current (E_a) were measured on a Pt electrode at 25 °C in 1 mM solutions of the substrates in dry AN containing 0.1 M Et_4NClO_4. The voltage scan rate was $100\,mV\,s^{-1}$. *c*) Isolated yield. *d*) The supporting electrolyte Et_4NClO_4 is oxidized at 2.7 V.

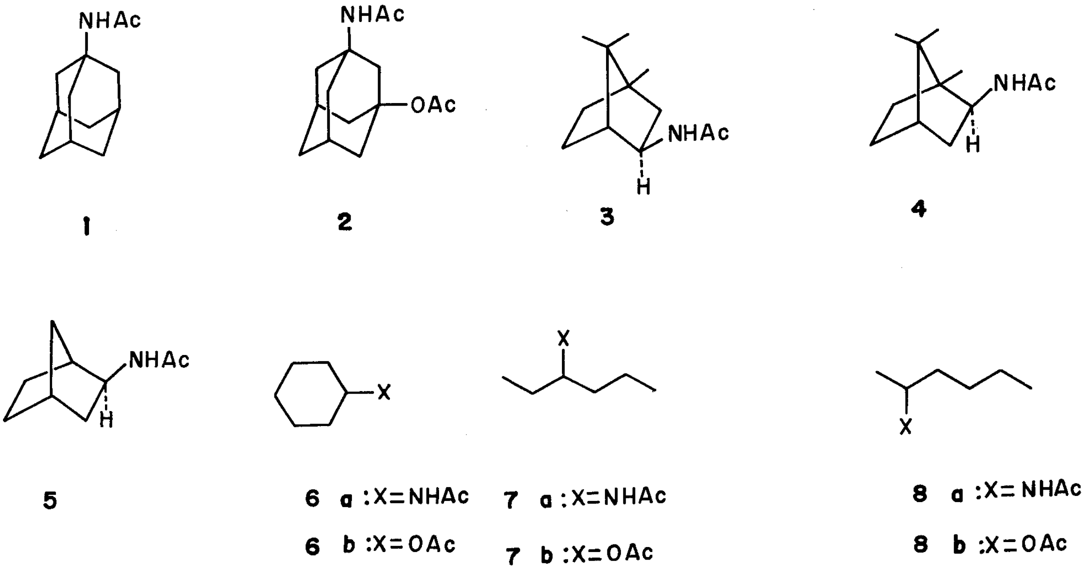

Chart 1

to a solution of $Fe(AN)_6(ClO_4)_3$ in AN is shown in Fig. 1. The reversible redox pair R_1 and O_1, depending on $Fe(AN)_6^{3+} + e^- \rightleftarrows Fe(AN)_6^{2+}$, disappeared on addition of periodate and new peaks R_2, R_3, R_4, O_2, and O_3 appeared. Finally, addition of 3 mol eq of periodate gave rise to a precipitate of $Fe(IO_4)_3$. This CV change suggests that bond formation occurs between Fe^{3+} and IO_4^-. On the other hand, it is known that the bond between Fe^{3+} and IO_4^- in $Fe(IO_4)_3$ is covalent, but the bond between Fe^{3+} and IO_3^- in $Fe(IO_3)_3$ is ionic.[8)] As described above, $NaIO_3$ and the iron(III) AN complex do not form a homogeneous solution and have no oxidation activity. Further, $Al(AN)_6(ClO_4)_3$, prepared in the same manner as the iron(III) AN complex, did not form a complex with periodate and had no ability to oxidize organic substrates, even though Al^{3+} complex has similar Lewis acid character to the Fe^{3+} complex.[9)] Therefore, it may be suggested that there is a close relationship between the bond character in these combined reagent systems and the oxidizing ability.

Oxidations of other alkanes which have high oxidation potentials, namely, bornane, norbornane, cyclohexane, and hexane, by the title reagent system were explored, and the results are shown in Table II.

Among these oxidation products, the structure of **3**, mp 134—135 °C, was identified by comparison with a synthetic sample prepared by an alternative route, namely, by the Ritter reaction[10)] of (±)-*epi*-isoborneol, which was prepared by reduction of (±)-epicamphor[11)] with $LiAlH_4$. The structure of **4**, mp 141—142 °C, was identified by comparison with a synthetic sample synthesized from isoborneol or camphene by the Ritter reaction. The other compounds were also identified by comparison with authentic samples.

It is of interest to compare oxidation products formed in this system with those formed by cyctochrome P-450 dependent mono-oxygenase or iron tetraphenylporphyrin chloride.[12] In this case, reactions may proceed *via* carbonium ion intermediates by two-electron oxidation followed by nucleophilic participation of AN or AcOH to yield the amides or acetates. The sites of oxidation coincide well with the positions of largest frontier electron density of hydrogens of the substrates.[13] The attacking sites of nucleophiles are also compatible with the fact that the lobes of LUMO of the carbonium ions at C_2 and C_3 in bornane and norbornane are larger at the *exo*-site than at the *endo*-site.[14]

Further applications of this reagent system to organic synthesis and investigations of the reactivities of other reagent systems are in progress.

Experimental

All melting points are uncorrected. Infrared (IR) spectra were recorded with a Hitachi 285 spectrophotometer, proton nuclear magnetic resonance (^1H-NMR) spectra with a JEOL JNM-FX 100 spectrometer with TMS as an internal standard ($CDCl_3$ soln.) and high-resolution mass spectra (HRMS) with a JEOL JMS-D 300 spectrometer. CV and rest potentials were taken on a Hokuto Denko HA-501 potentiostat. Column chromatography and thin layer chromatography (TLC) were done with Mallinckrodt silica gel (100 mesh) and Merck Kieselgel 60 F-254 (0.25 mm thick), respectively. Gas chromatographic analyses were performed on an SE-30 column in a Hitachi 163 apparatus with a flame ionization detector.

General Procedure for Oxidation of Alkanes——Acetic anhydride (26 ml, 9 × 30 mmol) was added dropwise to a solution of $Fe(ClO_4)_3 \cdot 9H_2O$ (15.5 g, 30 mmol) and alkane (10 mmol) in AN (200 ml) with stirring under ice-water cooling. To the resulting pale yellow solution, well fined sodium periodate (4.28 g, 20 mmol) was added in one portion, and the mixture was stirred vigorously at 20—25 °C for 1 h (10 min for the oxidation of adamantane). The reaction mixture was poured into dilute HCl and extracted with chloroform (3 × 50 ml). The combined organic layer was washed with aqueous solutions of $Na_2S_2O_3$, $NaHCO_3$, and brine, dried on anhydrous Na_2SO_4, and then concentrated. The residue was purified by silica gel chromatography.

Oxidation of Adamantane——Oxidation of adamantane was carried out according to the general procedure. Column chromatography of the reaction residue using chloroform as an eluent gave **1** and **2** in yields of 73% and 27%, respectively. The results under other reaction conditions are given in Table I. The acetamide **1** was identified by comparison with an authentic sample.

3-Acetamido-1-adamantyl Acetate (2)——Colorless crystals, mp 130—131.5 °C (ether–hexane). IR (KBr) cm^{-1}: 3290, 1730, 1640, 1550. ^1H-NMR ($CDCl_3$) δ: 1.50—2.38 (14H, m), 1.88 (3H, s, –NHCOMe), 1.93 (3H, s, –OCOMe), 5.36 (1H, br, –NHCO–). HRMS *m/e*: Calcd for $C_{14}H_{21}NO_3$ (M^+): 251.1522. Found: 251.1522.

Oxidation of (±)-Bornane——Oxidation of (±)-bornane was carried out according to the general procedure. Column chromatography of the reaction residue using chloroform as an eluent gave **4**[15] and **3** in yields of 7% and 46%, respectively.

***N*-(2-*exo*-1,7,7-Trimethylbicyclo[2.2.1]heptyl)acetamide (4)**——Colorless crystals, mp 141—142 °C (chloroform–hexane). IR (KBr) cm^{-1}: 3320, 1650, 1540. ^1H-NMR ($CDCl_3$) δ: 0.84, (6H, s, C(7)-Me), 0.91 (3H, s, C(1)-Me), 1.13—1.83 (7H, m, C(3)-H, C(4)-H, C(5)-H, C(6)-H), 1.96 (3H, s, –NHCOMe), 3.86 (1H, ddd, J=4.4, 8.0, 9.0 Hz, C(2)-*endo*-H), 4.01 (1H, br, –NHCO–). *Anal.* Calcd for $C_{12}H_{21}NO$: C, 73.80; H, 10.84; N, 7.17. Found: C, 73.56; H, 11.07; N, 7.14.

***N*-(3-*exo*-1,7,7-Trimethylbicyclo[2.2.1]heptyl)acetamide (3)**——Colorless crystals, mp 134—135 °C (ether–hexane). IR (KBr) cm^{-1}: 3270, 1635, 1540. ^1H-NMR ($CDCl_3$) δ: 0.84 (3H, s, C(7)-Me), 0.88 (3H, s, C(7)-Me), 0.98 (3H, s, C(1)-Me), 1.93 (3H, s, –NHCOMe), 1.25—1.97 (7H, m, C(2)-H, C(4)-H, C(5)-H, C(6)-H), 3.73 (1H, ddd, J=4.9, 8.0, 9.0 Hz, C(3)-*endo*-H), 5.80 (1H, br, –NHCO–). HRMS *m/e*: Calcd for $C_{12}H_{21}NO$ (M^+): 195.1623. Found: 195.1623. *Anal.* Calcd for $C_{12}H_{21}NO$: C, 73.80; H, 10.84; N, 7.17. Found: C, 73.90; H, 10.79; N, 7.27.

Synthesis of 3 from *epi*-Isoborneol——Conc. H_2SO_4 (0.2 ml) was added dropwise to a solution of *epi*-isoborneol[11] (154 mg) in AN (1.6 ml)–Ac_2O (0.1 ml), and the mixture was heated at 80 °C for 10 min, then worked up in the usual manner to give the amide **3**, mp 134—135 °C (ether–hexane), as colorless crystals in 98.5% yield.

Oxidation of Norbornane——Oxidation of norbornane according to the general procedure gave **5**[16] as a sole product in 60% yield.

(±)-*N*-(2-*exo*-Bicyclo[2.2.1]heptyl)acetamide (5)——Colorless crystals, mp 144—145 °C (chloroform–hexane) (rit. mp 139 °C). IR (KBr) cm^{-1}: 3280, 1640, 1540. ^1H-NMR ($CDCl_3$) δ: 1.22 (1H, d, J=1.5 Hz, C(7)-*anti*-H), 1.1—

1.95 (5H, m, C(5)-2H, C(6)-2H, C(7)-*syn*-H), 1.47 (1H, dd, $J=3.0$, 12.0 Hz, C(3)-*exo*-H), 1.76 (1H, ddd, $J=2.0$, 8.0, 12.0 Hz, C(3)-*endo*-H), 1.94 (3H, s, -NHCOMe), 2.20 (2H, fine coupling, C(1)-H, C(4)-H), 3.68 (1H, dddd, $J=1.5$, 3.0, 8.0, 15.0 Hz, C(2)-*endo*-H), 5.81 (1H, br, -NHCO-). HRMS *m/e*: Calcd for $C_9H_{15}NO$ (M^+): 153.1154. Found: 153.1187.

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