

헴에 의한 가역산화 때문에 철(II) 촉매에서 산소에 의한 기질의 산화

Oxidation of a substrate by O₂ in Fe(II) catalysis for the reversible oxidation effected by heme

이용희*, 박봉진**, 서명교***, 이영세

Yong-Hee Lee*, Bong-Jin Park**, Myung-Gyo Suh***, Young-Sei Lee

<요약>

Fe(II)하에서 분자산소에 의한 기질의 산화는 헴에 의해 나타난 가역산화반응에 의해서 대단한 생물학적 흥미가 있다. 적당한 조건하에서 산화되어진 리간드로서 염인 피리딘이나 아마이드, 그리고 두 가지 종류의 Fe(II)-acac나 Fe(II)-sal의 complex와 산화되는 기질의 성질이 비라디칼 조건하에서 안정하다는 것을 알았다.

Key words : heme, substrate, Fe(II), oxidation, nonradical condition

1. Introduction

Most transition metal catalyzed oxidation takes place by radical mechanism¹⁻²⁾. Hanzlik³⁾ reported nonradical reaction by oxidation of tributylphosphine(Bu₃P) to phosphonium oxide (Bu₃PO) at 0°C in acetonitrile solution. We wish to determine that the process conforms to the general reaction mechanism of a dioxygen complex of Fe(II). The O₂ uptake could result from an adventitious presence of a metal ion that would homolytically reduce the solvent and create peroxy radicals. However, such a process was inhibited by a radical suppressor⁴⁾. But a radical suppressor had no effect on the reaction, formation of a dioxygen complex appears to be the most likely alternative. Dioxygen complexes of Fe

(II)-porphyrin and Fe(II) complexes with porphyrin-like ligands⁵⁾ show characteristic absorption bands at low temperature when the complex is stable. Most reactions on O₂ activation involve Fe(II)-porphyrin complexes modeled after heme. Such studies explain the way to block irreversible oxidation of Fe(II) to Fe(III) during the reversible reaction. Oxidation of a substrate by molecular oxygen in the presence of Fe(II) catalysts is of great biological interest in view of the reversible oxidation effected by heme because such a data can not seem to be available that describe in detail autoxidation of a substrate catalyzed by a Fe(II) complex. The various concentrations of Fe(II) in the wide range of solvents were used to investigate the oxidation of excess ligand.

* 동의대학교 기초과학연구소, 理博

** 롯데제과(주), 理碩

*** 동의공업대학 환경정보시스템과, 부교수, 工博

† 상주대학교 응용화학공학부, 부교수, 工博

* Research Institute of Basic Sciences, Dongeui University

** LOTTECONFECTIONERY Co., Ltd.

*** Dept. of Env. & Bio-Eng., Dongeui Institute of Technology

† School of Applied Chem, Eng., Sangju National University

To whom correspondence should be address

2 Experiment

2.1 Theory of Polarography

In a polarographic experiment, an ion is reduced at the dropping mercury electrode (DME) at some specific potential related to the standard reduction potential of the ion.

$$E_{1/2} = E^0 - \frac{0.0591}{n} \log(D_O/D_R)^{1/2}$$

where $E_{1/2}$ represents the half-wave potential, E^0 is the standard reduction potential, D_O and D_R are the diffusion coefficients of the oxidized and reduced forms the ion. Fig. 1 represents polarographic wave due to reduction of Fe(acetylacetonate; acac)₃ to Fe²⁺ state at the DME. The $E_{1/2}$ corresponds to the potential of the midpoint of the wave, and is independent of the concentration of the ion. The diffusion current is the maximum current shown by the diffusion current plateau after correction for the blank base current. The diffusion current is directly proportional to the concentration of ion by ILKOVIC's equation.

$$I_d = 607nD^{1/2}m^{2/3}t^{1/6}C$$

It is thus seen that the current measured at -0.8V represents the diffusion current.

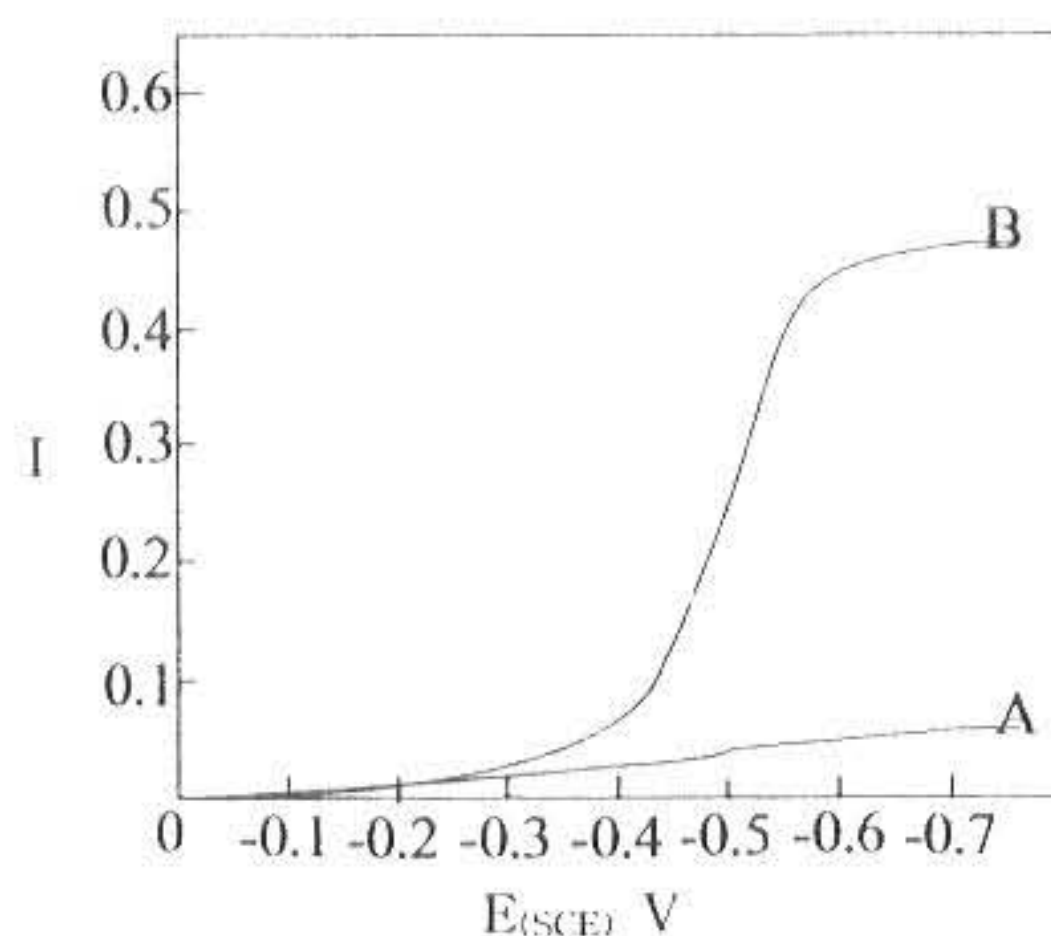


Figure 1. Polarograms of Fe(acac)₃ in DMA. LiClO₄: 7.25×10^{-3} M, DMA: 18ml, Fe(acac)₃: 4.35×10^{-5} M, Total volume of solution: 18ml.

Fig. 1 shows that the ferric acac complex yields a well defined polarographic wave. The solubilities of O₂ in various solvents are

different. Because of its non polar character, dioxygen is much more soluble in organic solvents than in H₂O (Table 1).

Table 1. Voltammetric reduction of 2.1mM O₂ in the presence of a 10- to 30- fold excess (relative to O₂ concentration) of metal cations in Me₂SO(0.1M TEAP)^a at a Pt electrode(0.02V^{s-1})

metal ^b	E _{p.c'} V vs. SCE	n(e/O ₂)
	-0.80	1
Li ⁺	-0.79	1
Zn ²⁺	-0.67	2
Cd ²⁺	-0.67	2
Fe ²⁺	-0.52	2
Mn ²⁺	-0.61	4
Co ²⁺	-0.66	4

^aTetraethylammonium perchlorate.

^bAdded as the hexahydrated perchlorate salts.

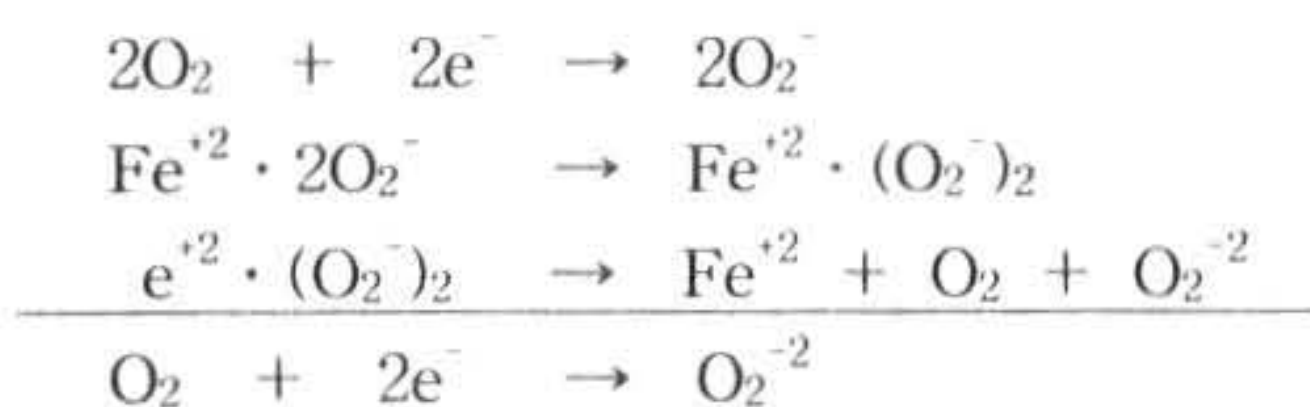
2.2 Method

The solvents employed were acetone, acetonitrile, ethanol, DMF, DMA(*N,N'*-dimethylacetamide), and water. Reagent grade, anhydrous solvents of the highest quality were used, and both DMF and DMA were redistilled before use. The solvents were further checked to be free of peroxide. The other chemicals were also of reagent grade quality and were used, as freshly obtained, without further purification. Fe(ClO₄)₂ · 6H₂O(99+%) was obtained from Johnson Mathey and Fe(ClO₄)₃ · 17.4%H₂O was procured from Alpha Catalog Chemicals. Both iron compounds were checked colorimetrically for their purity before use. A PARC Model 364 polarographic analyzer were used to monitor the concentration of dissolved O₂ in the solutions, which was in the ppm range. Air was employed as a source of oxygen in place of the pure gas because of the spontaneous loss of oxygen from an oxygen-saturated solution exposed to the atmosphere. Also the higher concentration of O₂ resulting from such a treatment produced irreproducible maxima in the polarographic current, which was absent when air was employed instead.

2.3 Reduction of O₂ at the DMF



Effects of cations[6-7], according to the following reaction in the presence of Fe⁺² ion took place at a platinum electrode.



This was also verified in H₂O medium at the dropping mercury electrode. However, when Fe⁺² is complexed with acac, normal 1e⁻ reduction reaction is observed, as shown in Fig. 2.

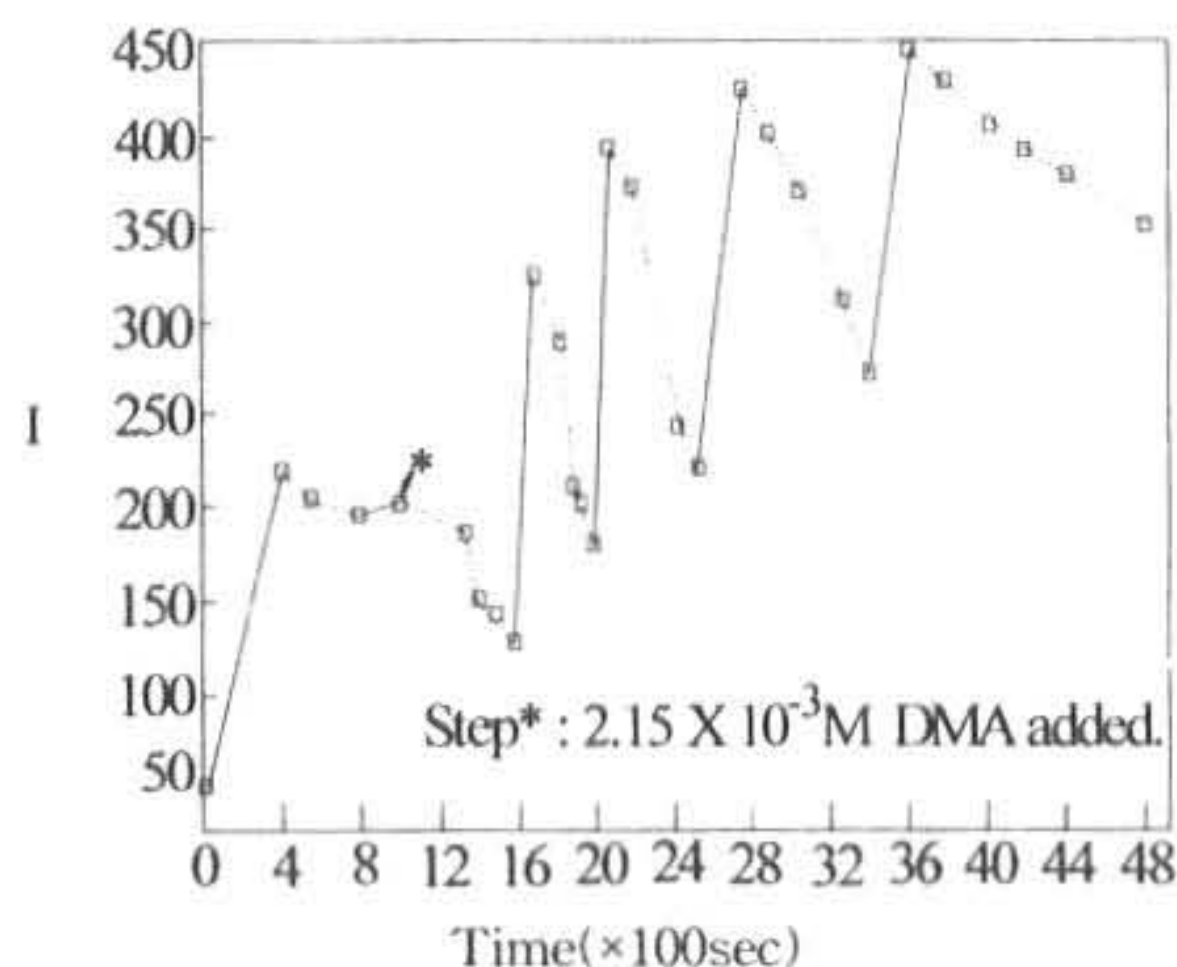


Figure 2. O₂ absorption by polarography in acetone. LiClO₄: 4.70 × 10⁻³ M, Fe(ClO₄)₂ · 6H₂O: 2.70 × 10⁻⁴ M, acetone: 15 ml, acac: 9.74 × 10⁻⁴ M, DMA: 2.15 × 10⁻³ M, Total volume of solution: 18 ml, The ligand(acac)/Fe (II) molar ratio = 3.6 : 1, Solid line: Resaturation with air, Dashed segments: Decay of O₂ current measured at -0.80V(SCE).

2.4 Reduction of Fe⁺² and Fe⁺³ at the DME

Fe⁺² is not reduced within the potential range of the polarograph, either in complexed or uncomplexed form. However, Fe(acac)₃ is reduced to Fe(II) state. Fig. 3 shows the results. Fe(III) produced by the oxidation of Fe(acac)₂ by O₂ behaves essentially in the same way as Fe(acac)₃. Fig. 3 shows the diffusion current of an air-saturated solution of Fe(acac)₃. The diffusion current represents the sum of the diffusion current due to reduction of the dissolved O₂ to O₂⁻ and that of Fe⁺³ to Fe⁺². In monitoring the decay of the dissolved O₂, the change of the diffusion current at -0.6V(SCE)(in H₂O medium) and at -0.8V(in nonaqueous medium) was recorded. The fall of the current with time

can be explained by assuming the rate of removal of the dissolved O₂ by the catalytic reaction to be greater than the rate of formation of Fe⁺³ from oxidation of the Fe (II) complex.

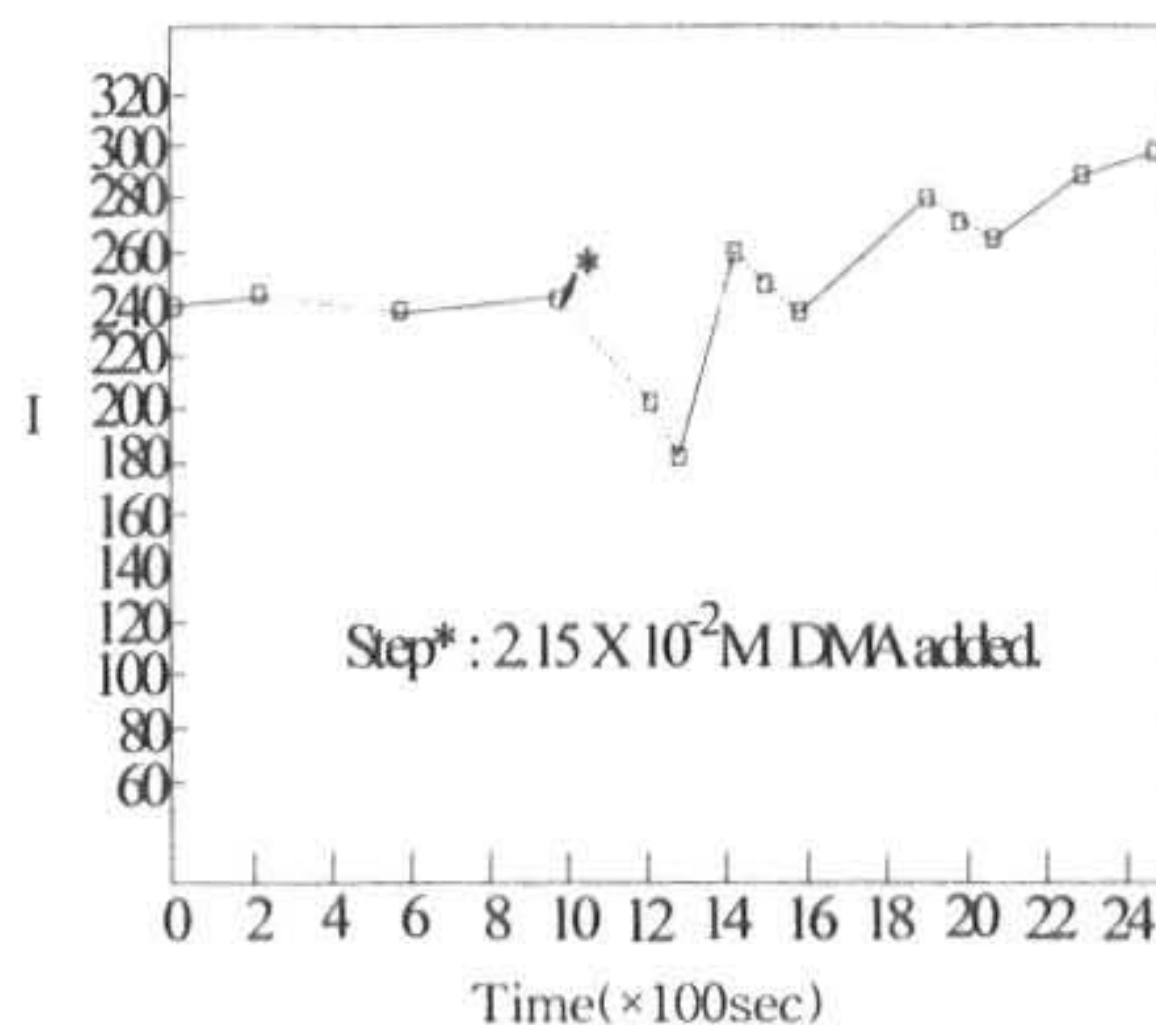


Figure 3. O₂ absorption by polarography in acetone. LiClO₄: 4.70 × 10⁻³ M, Fe(ClO₄)₂ · 6H₂O: 3.58 × 10⁻⁴ M, acetone: 20.0 ml, sal: 4.69 × 10⁻³ M, DMA: 2.15 × 10⁻² M, Total volume of solution: 24 ml, The ligand(sal)/Fe (II) molar ratio = 13.1 : 1, Solid line: Resaturation with air, Dashed segments: Decay of O₂ current measured at -0.80V(SCE).

2.5 Reactions in Water

Fig. 4 shows the O₂ uptake in the presence of 14mg and 41mg of Fe(ClO₄)₂ · 6H₂O mixed with excess acac. Again, no O₂ uptake took place before addition of pyridine.

2.6 Reactions in Acetonitrile

The data show no O₂ uptake by the Fe (II)-acac and Fe(II)-sal complexes until pyridine is added. It is seen that the net fall in the current is revived by the addition of additional pyridine(Fig. 5, 6). Both the Fe (II)-acac and Fe(II)-sal complexes behaved in the same way. This seems to indicate that pyridine is oxidized in the reaction, and, as it is depleted by oxidation, the O₂ uptake slows down and is revived by input of fresh pyridine. The superiority of pyridine over the other solvents, which would also act as Lewis bases, is not well understood. However, similar data are found in literature[8]. In terms of coordinating ability, acetone and the amides may be comparable. However, the Fe(II)-acac complex uptakes O₂ in the amide solvent, but not in acetone, unless pyridine is added.

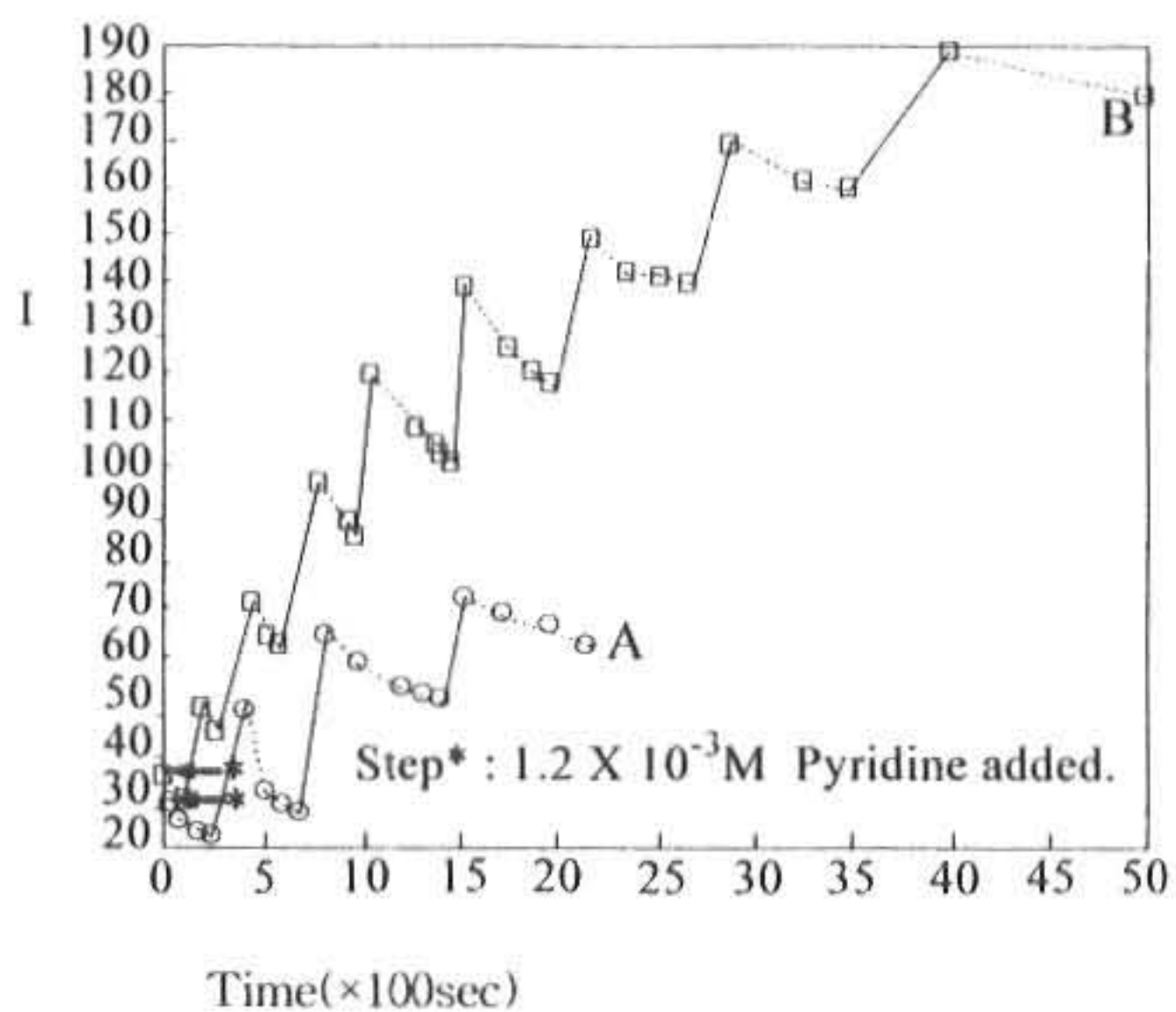


Figure 4. O₂ absorption by polarography in aqueous medium. (A) LiClO₄: 4.70×10⁻³M, Fe(ClO₄)₂·6H₂O: 3.9×10⁻⁵M, acac: 9.7×10⁻⁴M, pyridine: 1.2×10⁻³M added after addition of acac, pure H₂O: 9ml, gelatine: 0.01%, total volume of solution: 12ml, the ligand (acac)/Fe(II) molar ratio: 24.9:1, solid line: resaturation with air, dashed segments: decay of O₂ current measured at -0.65V(SCE). (B) LiClO₄: 4.70×10⁻³M, Fe(ClO₄)₂·6H₂O: 1.1×10⁻⁴M, acac:1.5×10⁻³M, pyridine: 1.2×10⁻³M, pure H₂O: 9ml, gelatine: 0.01%, total volume of solution: 12ml, the ligand (acac)/Fe(II) molar ratio: 13.6:1, solid line: resaturation with air, dashed segments: decay of O₂ current measured at -0.65V(SCE).

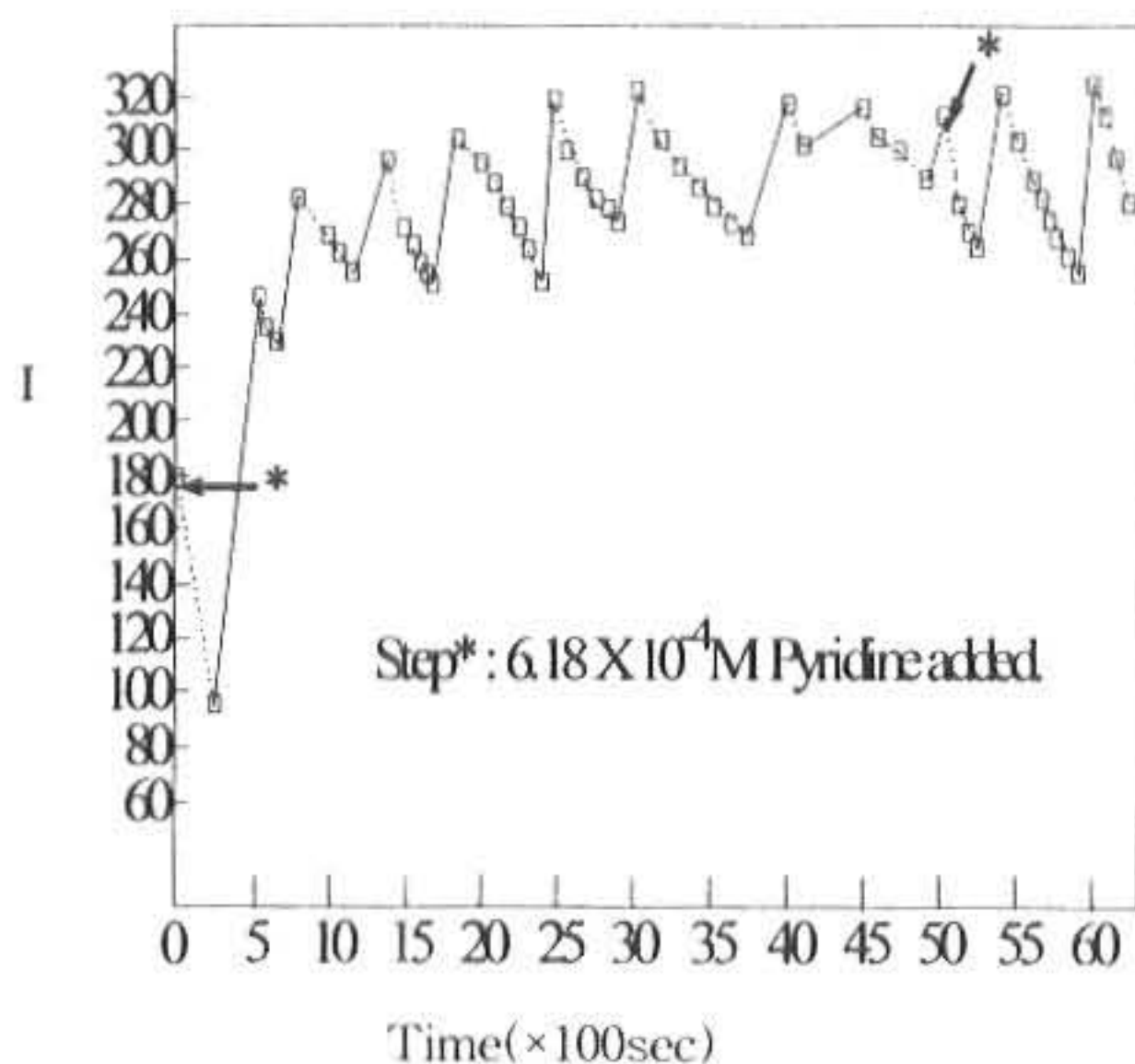


Figure 5. Revival of O₂ uptake by addition of pyridine in CH₃CN. LiClO₄: 4.70×10⁻³M, Fe(ClO₄)₂·6H₂O: 3.86×10⁻⁴M, CH₃CN: 8.0ml, acac: 3.89×10⁻⁴M, pyridine: 6.18×10⁻⁴M, total volume of solution: 10ml, the ligand (acac)/Fe(II) molar ratio = 1:1, solid line: resaturation with air, dashed segments: decay of O₂ current measured at -0.80V(SCE).

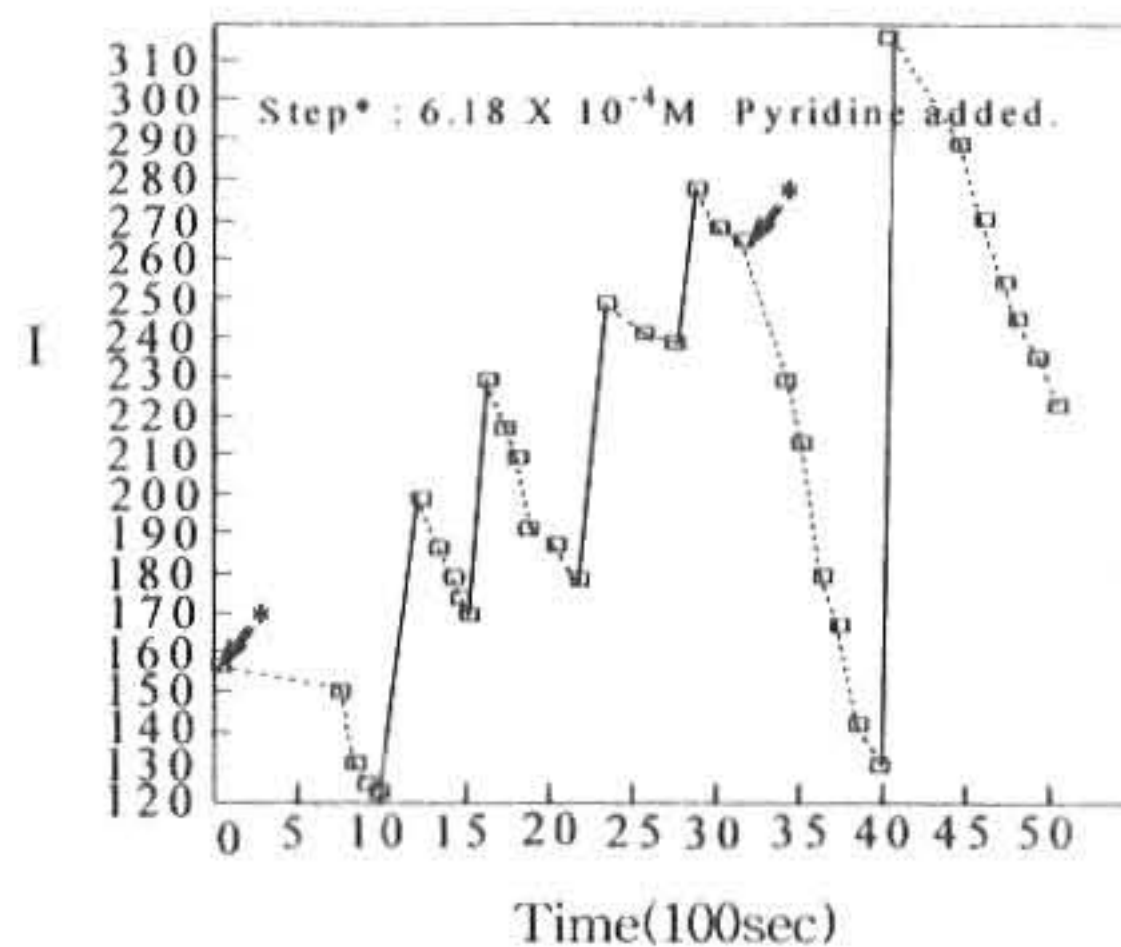


Figure 6. Revival of O₂ uptake by addition of pyridine in CH₃CN. LiClO₄: 4.70×10⁻³M, Fe(ClO₄)₂·6H₂O: 5.70×10⁻⁴M, CH₃CN: 8.0ml, sal: 6.69×10⁻⁴M, pyridine: 6.18×10⁻⁴M, total volume of solution: 10ml, the ligand (sal)/Fe(II) molar ratio = 1.2:1, solid line: resaturation with air, dashed segments: decay of O₂ current measured at -0.80V(SCE).

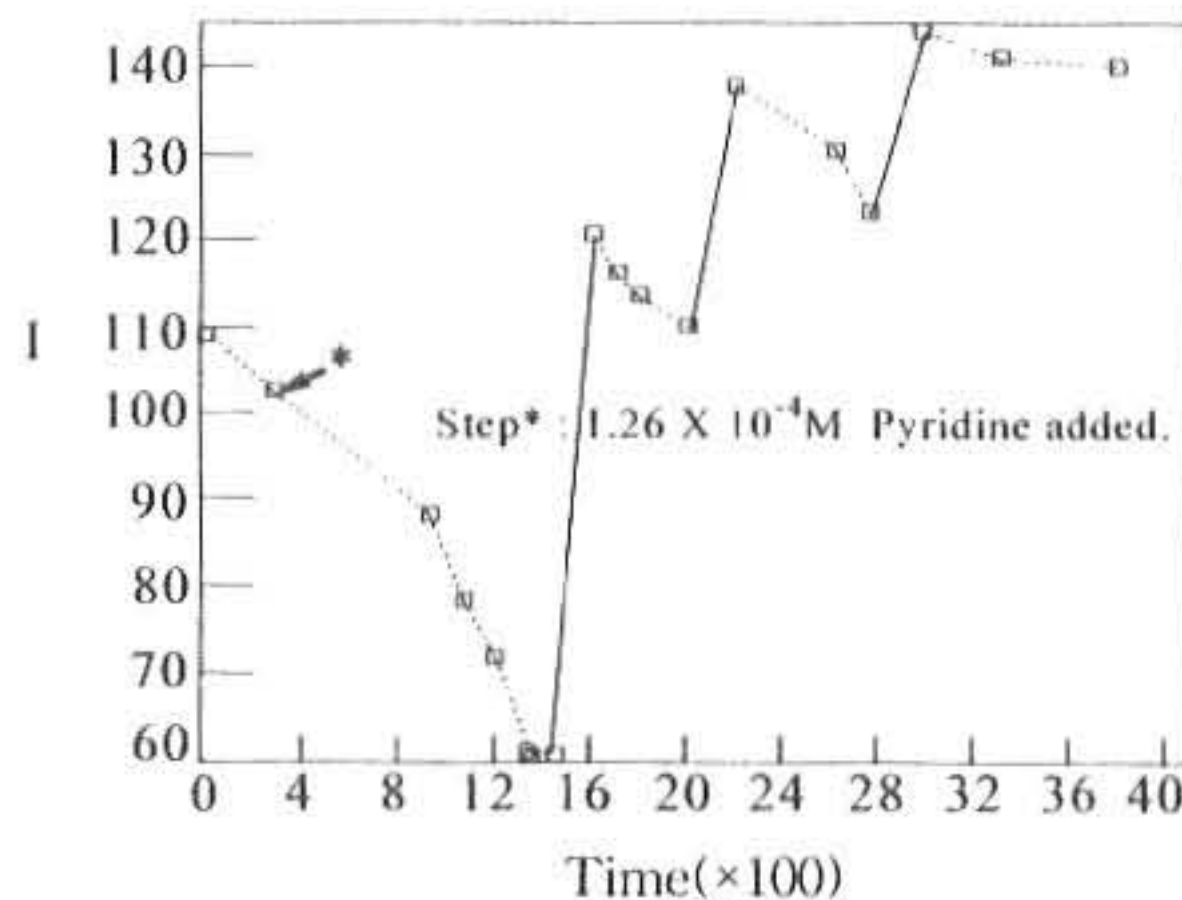


Figure 7. O₂ absorption by polarography in ethanol. LiClO₄:4.70×10⁻³M, Fe(ClO₄)₂·6H₂O: 7.34×10⁻⁵M, ethanol: 10ml, acac: 4.99×10⁻⁴M, pyridine: 1.26×10⁻⁴M, total volume of solution: 13ml, the ligand (acac)/Fe(II) molar ratio = 6.8:1, solid line: resaturation with air, dashed segments: decay of O₂ current measured at -0.80V(SCE).

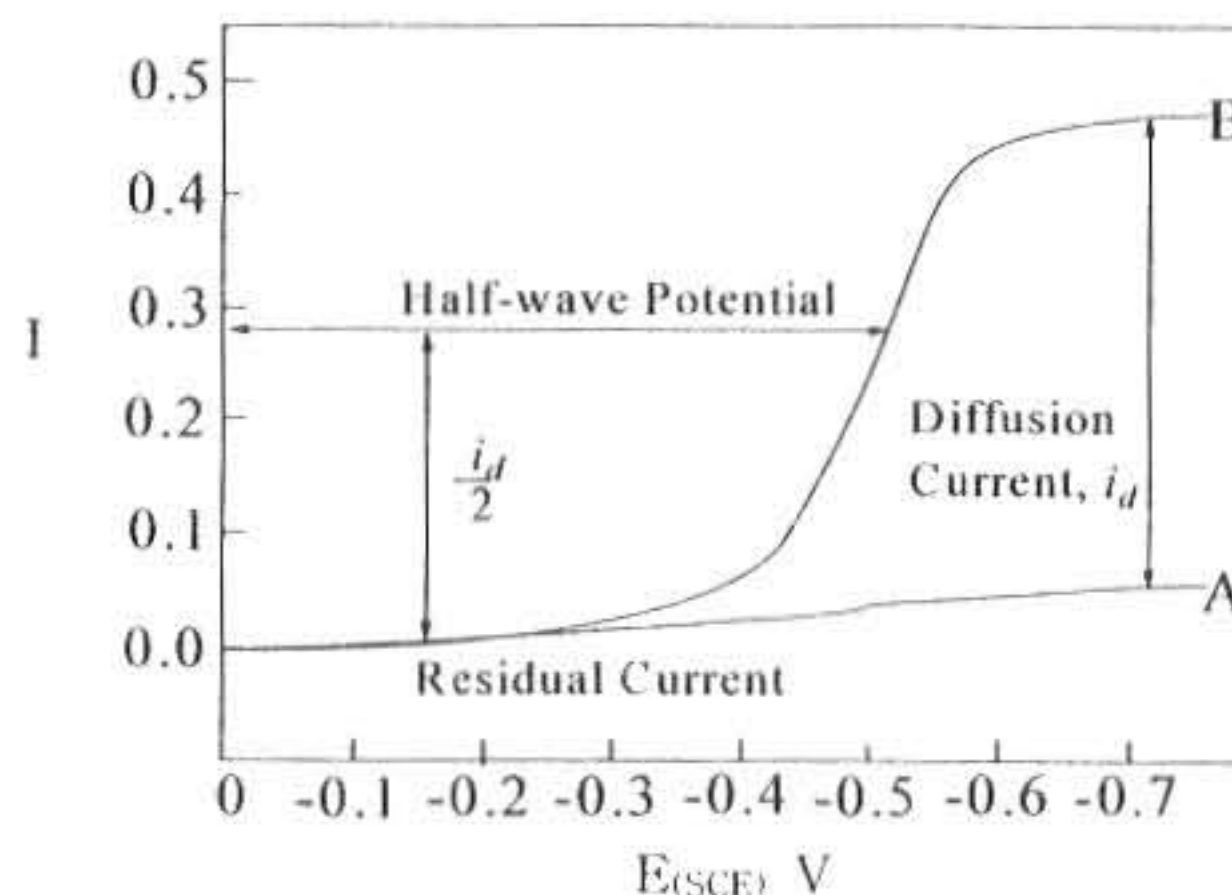


Figure 8. A well-defined polarographic wave of Fe(acac)₃. curve(A): nitrogenated blank; 7.25×10⁻³M LiNO₃ in 18ml DMA, curve(B): added 4.50×10⁻⁵M(acac)₃ in (A), total volume of solution: 18ml.

2.7 Reactions in Acetone

In this solvent, data are presented to show no catalytic activity, addition of a small quantity of DMA led to O₂ uptake (Fig. 7, 8). Pyridine is expected to behave in the same way as the amide. Both the Fe(II)-acac and Fe(II)-salicylaldehyde(sal) complexes (Fig. 7, 8) behave similarly, although the effect is much more pronounced with the acac complex.

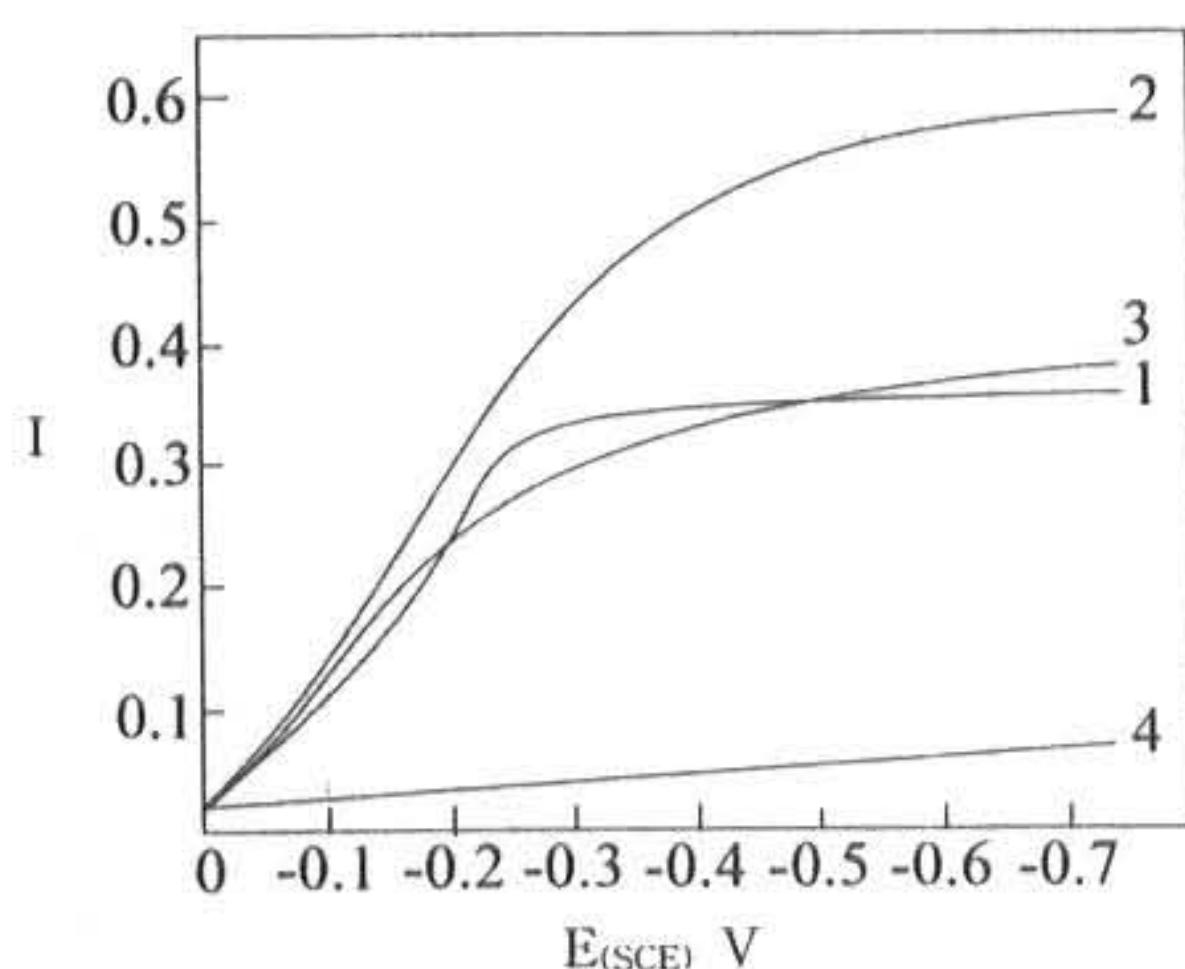


Figure 9. reduction of O₂ in the presence of Fe(II) and Fe(acac)₂. curve(1): blank (air-saturated); 4.70 × 10⁻³ M LiClO₄, 0.01% gelatine, 8ml H₂O, curve(2): added 4.7 × 10⁻⁵ M Fe(ClO₄)₂ · 6H₂O, curve(3): 4.7 × 10⁻⁵ M Fe(acac)₂ · air (4.7 × 10⁻⁴ M acac added), curve(4): nitrogenated solution of curve(3), total volume of solution: 10ml.

2.8 Reactions in Ethanol

Fig. 9 shows the O₂ uptake in ethanol in the presence of pyridine. No oxygen uptake takes place in the absence of pyridine. The trend is similar to that seen with the other solvents.

3 Result and Discussion

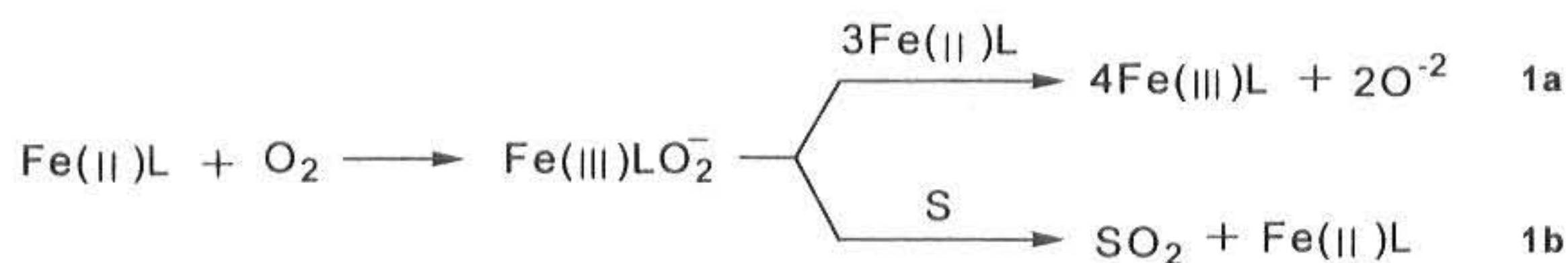
We were not able to detect such a bond in an oxygen-saturated solution of Fe(acac)₂ in DMF at a temperature substantially less than zero. This may be due to a basic difference in the nature of our ligand (oxygen-coordinating) from the other systems. On the other hand, it might indicate a different structure of the O₂ complex. The O₂ uptake was followed polarographically, as explained in the experimental section. The diffusion currents measured at -0.8V or -0.6V represent the sum of the

diffusion currents due to reduction of O₂ and Fe⁺³, and thus the change of diffusion current with time did not directly reflect the rate of O₂ uptake by the reaction, but the resultant of the two effects; relative rates of depletion of O₂ by the catalytic reaction and the rate of formation of Fe⁺³ by the concurrent oxidation of Fe(II). Based on our assumption of formation of an O₂ complex as the initial step, we propose the following scheme 1. The scheme 1 is based on the reactions of Fe(II)-porphyrin oxygen complex given in the literature [8-9].

Based on scheme 1. if the steps 1a and 1b took place at the same rate, the net current must increase with time. However, we find a net fall of current with time, which can only be explained by assuming 1b to be more than three times faster than 1a. We have attempted to determine the effect of concentrations of the Fe(II)L complex on the net current.

The data indicate that with higher concentrations of Fe(II)L (large amounts of Fe(II) and ligand used), the fall in current is not observed initially. This is in agreement with the proposed scheme 1. We also wanted to confirm that Fe⁺³ species produced by the oxidation of Fe(II)L were all reducible within the given potential range (at -0.6V in H₂O; 0.8V in nonaqueous solvents).

This was confirmed by comparing the diffusion current of solutions containing Fe(acac)₂(Fe(ClO₄)₂ · 6H₂O + excess acac in water), after oxidation for several hours ensuring complete oxidation. These diffusion currents were about the same, showing that the Fe(III)L species obtained from oxidation of Fe(II)L with oxygen were fully reducible the given range of potential as Fe(acac)₃ produced from mixing Fe(ClO₄)₃ · 6H₂O with excess amounts of acac. Experiments were also performed to confirm that the diffusion current due to reduction of dissolved O₂ in air-saturated solution of Fe(acac)₃ or Fe(acac)₂ was equal to that in the absence of these complexes, and in the presence of LiClO₄ as a supporting electrolyte (Fig. 10)¹⁰. The effect of Fe⁺² on the reduction of O₂ at the DME was studied and found to be in general accord with the data in literature (Table 2).



scheme 1.

The results in acetone (Fig. 7, 8) seem to be different from in the other solvents, and this needs to be further studied. We wish to determine the nature of the substrate being oxidized. Since the O₂ uptake takes place in all the solvents studied so far, it is reasonable to assume that the solvent is not being oxidized. Thus we conclude that the ligands are being oxidized. Since there are two kinds of ligands associated with Fe(II)-acac or Fe(II)-sal, and the base as a ligand, pyridine (Fig. 4, 5, 6, 9) or amide (DMA; Fig. 7, 8)), it has to be resolved whether either one of them or both are oxidized under appropriate conditions. The work done by Hanzlik on the oxidation of tributylphosphine would support similar oxidation of pyridine to pyridinium oxide.

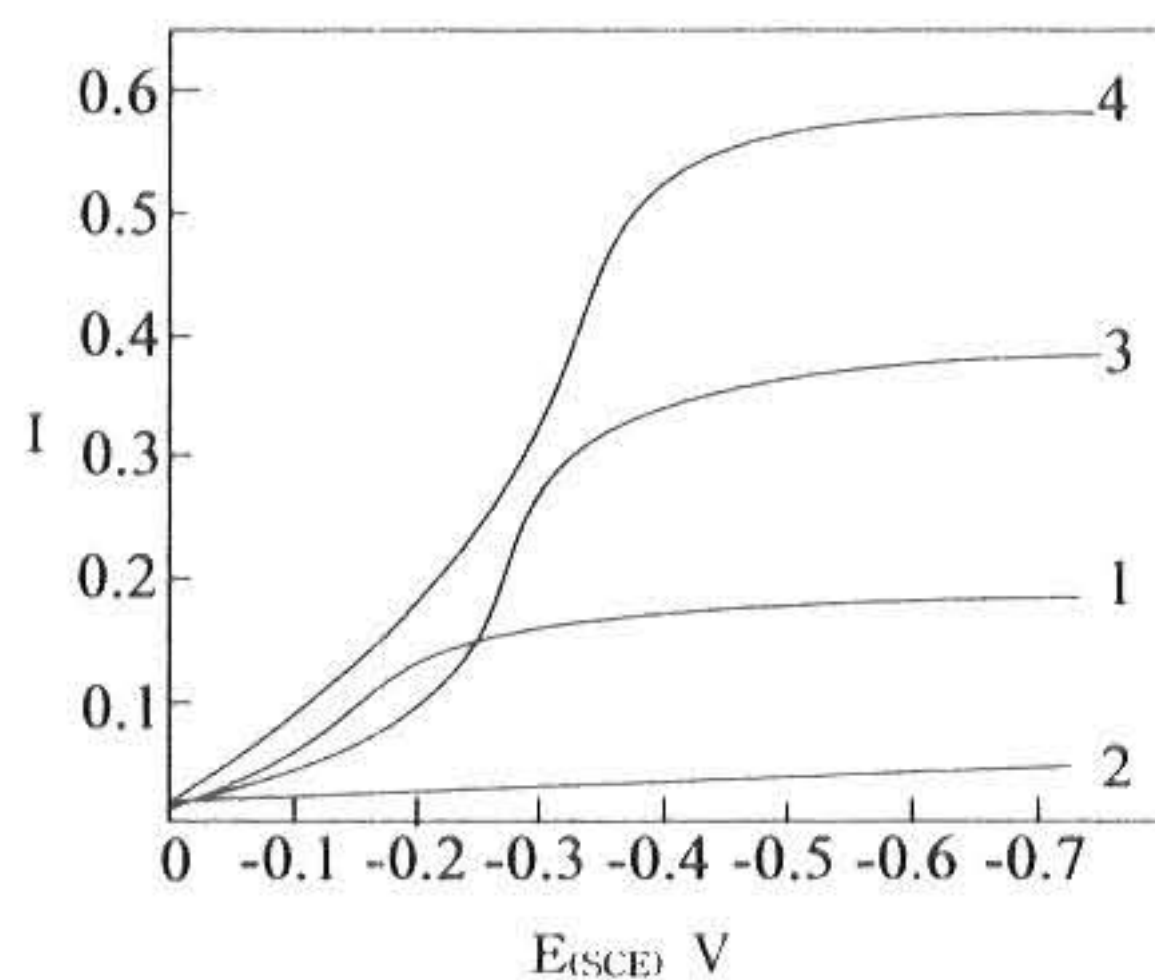


Figure 10. reduction of O₂ in the presence of Fe(acac)₃. curve(1): blank (air-saturated); 4.70 × 10⁻³ M LiClO₄, 0.01% gelatine, 8 ml H₂O, 9.7 × 10⁻⁴ acac, 1.2 × 10⁻³ M pyridine, curve(2): nitrogenation of solution, curve(3): added 4.96 × 10⁻⁵ M Fe(ClO₄)₃ · 6H₂O under N₂, curve(4): air-saturated solution,

4 Conclusion

We have noted a dependence on the O₂ uptake on the amount of pyridine added (Fig. 4, 5, 6, 9), which would support such an assumption.

Table 2. Solubilities of O₂(1atm) in various solvents.

Solvent	[O ₂] 1atm, mM
H ₂ O	1.0
DMF	4.8
MeCN	8.1

However, there is a basic difference between Fe(acac)₂ and Co(acac)₂ as the catalyst, in view of the fact that the oxidant in the latter case appear to be the Co(III) peroxy dimer, which is a stable species. On the other hand, the corresponding Fe(III) peroxy dimer is unstable and the oxidant may be more likely to be the superoxo complex Fe(III) · L · O₂⁻.

In the amide solvent, in analogy with the oxidation of pyridine, one would expect the amide to be oxidized. However, the amides are stable solvents under nonradical conditions; and, thus, oxidation of the β-diketone may be a more likely alternative. This remains to be resolved. We determined the nature of the substrate being oxidized in the two kinds of ligands in Fe(II)-acac or Fe(II)-sal, pyridine or amide being base as a ligand were oxidized under appropriate conditions because these are stable under nonradical condition.

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