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Intradiol Oxygenation of 3,5-Di-t-butylcatechol Catalyzed by Iron(III) Salts[#]

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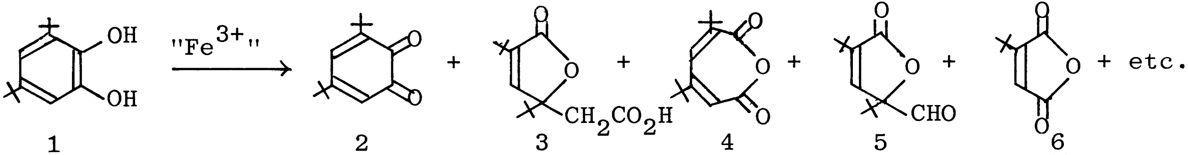
3,5-Di-t-butylcatechol is oxygenated by Fe(III) salts without addition of ligands in THF/water, DMF, or DMF/aqueous borate buffer to give intradiol cleavage products. Intermediate formation of semiquinonatoiron(II) and catecholatoiron(III) complexes is indicated by electronic, Mössbauer, ESR spectroscopy.

Catechol dioxygenase such as pyrocatechase plays an important role in the metabolism of aromatic compounds. In the studies to clarify the mechanisms of the enzymatic oxygenation and to realize the selective oxygenation process catalyzed by model metal complexes, we first found that the oxygenation of 3,5-di-t-butylcatechol 1 is catalyzed by an iron complex such as (bipyridine)(pyridine)iron(III) to give intra- and extradiol oxygenation products (Eq. 1-(i)),[1-3] and that the oxygenation proceeds in the analogous way to that of the enzyme.[3] Some other metal complexes have been reported to catalyze the oxygenation,[4-7] but in the case of metal complexes oxygenation is accompanied by the formation of o-quinone, different from the enzymatic system. In order to improve the selectivity in the model system, it is important to know the role of ligand in the regulation of the selectivity. This work was performed to know whether the addition of ligand is essential for the oxygenation. We report here that the oxygenation is catalyzed only by iron(III) salts in tetrahydrofuran (THF) or N,N-dimethylformamide (DMF) in the presence or absence of water or aqueous borate buffer (pH 8.5) to give a fairly good yield of intradiol oxygenation products (Eq. 1-(ii)).



(1)

"Fe^{3+}":(i)$FeCl_3$, bipyridine, pyridine, THF
(ii)FeX_3, H_2O or aqueous buffer, THF or DMF (X=Cl, NO_3, ClO_4)

The reaction was performed in THF or DMF at 25 °C under 1 atm O_2. Fe(III) salt (0.125 or 1.0 mmol) and 1 (1.0 mmol) were dissolved in 10 cm^3 solvent. The effects of water and aqueous borate buffer (pH 8.5) were studied in THF and DMF, respective-

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[#] This paper is dedicated to the late Professor Ryozo Goto, Kyoto University.

Table 1. Oxygenation of 3,5-Di-t-butylcatechol by Fe(III) Salts in THF[a)]

Fe(III) Salt	Additive cm^3	Products/mol%[b)] 1	2	3	4	5	6
$FeCl_3$	-	79	20	0	trace	-	-
$FeCl_3$	H_2O(0.09)	4	88	1	2	-	6
$FeCl_3$	H_2O(0.9)	0	72	0	12	-	6
$FeCl_3 \cdot 6H_2O$	-	50	43	2	1	-	2
$Fe(NO_3)_3 \cdot 9H_2O$	-	0	61	3	15	-	10
$FeCl_3$	py(0.9)[c)]	0	52	20	1	9	9

a)Fe salt:0.125 mmol, 1:1.0 mmol, THF + additive:10 cm^3, at 25 °C, 1 atm O_2. b)Yield based on 1, after 24 h. c)0.9 cm^3 of pyridine and 0.375 mmol of bipyridine were added.[3)]

ly. Effect of addition of sodium nitrilotriacetate (Na_3NTA) for comparison with the reported results[6)] and dipicolinic acid (DPA) was also studied in DMF. Products were separated from the reaction solution and analyzed quantitatively by GLC and HPLC in the way described previously.[3)] Electronic, Mössbauer, and ESR spectra were measured at room temperature, 110 K, and 77 K, respectively.

Table 1 shows the results in the THF solvent system. The result of the (bipyridine)(pyridine)iron(III) system is also shown for comparison.[3)] The oxygenation was hardly catalyzed by $FeCl_3$ without addition of water, but a small amount of water promoted effectively the reaction to give the intradiol oxygenation product 4 in addition to 2 and 6. The extradiol oxygenation product 5 was not obtained in this system. The reaction with $FeCl_3 \cdot 6H_2O$ was very slow and the yield of 4 was very low, whereas $Fe(NO_3)_3 \cdot 9H_2O$ yielded 4 in the higher yield than $FeCl_3/H_2O$. This suggests that the reaction is affected by the ligand in the salt (Cl, NO_3, etc.). GC-MS analysis of 4 obtained under $^{18}O_2$ in the $FeCl_3/THF/H_2O$ and $Fe(NO_3)_3 \cdot 9H_2O/THF$ systems indicated clearly that one atom of ^{18}O was inserted into 4, similarly to the case of the (bipyridine)(pyridine)iron(III) complex.[3)]

Table 2 shows the results obtained in the DMF system. In DMF, the oxygenation products were obtained without addition of water or ligand, but the yield was higher in DMF/buffer than in DMF. The conversion of 3 to 4 was promoted by the presence of buffer or water. The total yield of 3 + 4, 39%, in DMF/buffer ([Fe]= 0.125 mmol, [1]=1.0 mmol) was very similar to that of 3 + 4 + 5 obtained by (bipyridine)(pyridine)iron(III) complex in THF (Table 1). This result is very different from that by Weller and Weser, who reported the formation of only 2 in the absence of NTA.[6)] In the presence of NTA, the reaction was very slow, reflecting the formation of an intermediate complex so stable as to be isolated.[6,8)] The quinone 2 was formed as a main product and the yield of 3 + 4 was lower than that in the absence of NTA. We could not reproduce the result, 2 (3%) + 3 (84%), which was reported without any experimental details.[6)] We expected that selectivity and activity would be improved by use of DPA in place of NTA since the intermediate might be less stable in the former, but the effect of DPA was not observed. Interestingly, the oxygenation products in DMF were 3 and 4, and 5 or 6 was not formed.

Spectroscopic sutdies were performed to obtain information on the reaction process. Figure 1 shows some electronic spectra of the solutions prepared in argon atmosphere. In THF, a broad band (λ_{max} 690 nm) observed with $FeCl_3$ shifted to λ_{max}

Table 2. Oxygenation of 3,5-Di-t-butylcatechol by Fe(III) Salts in DMF[a)]

Fe(III) Salt	mmol	Additive[b)]	Solvent[c)]	Time d	Product/mol%[d)] 1	2	3	4
$FeCl_3$	1.0	-	DMF	1	0	67	0	13
$FeCl_3\cdot6H_2O$	1.0	-	DMF	1	0	69	0	13
$Fe(ClO_4)_3\cdot6H_2O$	1.0	-	DMF	1	0	56	2	19
$Fe(ClO_4)_3\cdot6H_2O$	0.125	-	DMF	1	2	71	14	9
$Fe(ClO_4)_3\cdot6H_2O$	1.0	-	DMF/buffer	1	0	26	44	6
$Fe(ClO_4)_3\cdot6H_2O$	0.125	-	DMF/buffer	1	3	31	34	5
$Fe(ClO_4)_3\cdot6H_2O$	1.0	NTA	DMF	1	8	41	19	27
$Fe(ClO_4)_3\cdot6H_2O$	0.125	NTA	DMF	1	46	31	7	2
$Fe(ClO_4)_3\cdot6H_2O$	1.0	NTA	DMF/buffer	4	7	49	37	3
$Fe(ClO_4)_3\cdot6H_2O$	0.125	NTA	DMF/buffer	8	16	58	12	2
$Fe(ClO_4)_3\cdot6H_2O$	1.0	DPA	DMF	1	1	44	7	25
$Fe(ClO_4)_3\cdot6H_2O$	1.0	DPA	DMF/buffer	1	3	30	40	8

a)1:1.0 mmol, at 25 °C, 1 atm O_2. b)[Fe]/[additive]=1. c)Solvent:10 cm^3. DMF/buffer =2/1 (v/v). d)Based on 1. e)The yield includes 1-3% of DMF adduct of 3.[3)]

750 nm (a shoulder at 900 nm) with a great increase in the intensity by addition of water. The intensity was in the order of $Fe(NO_3)_3\cdot9H_2O$>>$FeCl_3/H_2O$>>$FeCl_3\cdot6H_2O$ which is consistent with the order of the reactivity in Table 1. In DMF, the spectrum with $FeCl_3$ was very similar to that in THF/H_2O. When $Fe(ClO_4)_3\cdot6H_2O$ was used, the intensity at ≈900 nm increased relatively. The intensity was greater in DMF/buffer than in DMF, in accordance with the reactivity. The addition of NTA and DPA shifted ${}_{max}$ to 580 and 700 nm, respectively, indicating coordination of the additive as a ligand. These bands disappeared after the reaction with O_2, indicating the intermediate formation of catechol-iron complex.

Figure 2 shows Mössbauer spectra of the complex prepared with $^{57}FeCl_3$. In argon, formation of a high-spin Fe(II) complex (IS 0.73, ΔE 3.46 mm s^{-1}) was observed in addition to high- and low-spin Fe(II) complexes. When O_2 was added, the Fe(II) complex disappeared and the intensity of high-spin Fe(III) (IS 0.60, ΔE 0.85 mm s^{-1}) increased, with slight increase in low-spin Fe(III) (IS 0.27, ΔE 1.17 mm s^{-1}). This process was followed by electronic spectra. The formation of the high-spin Fe(III) complex was

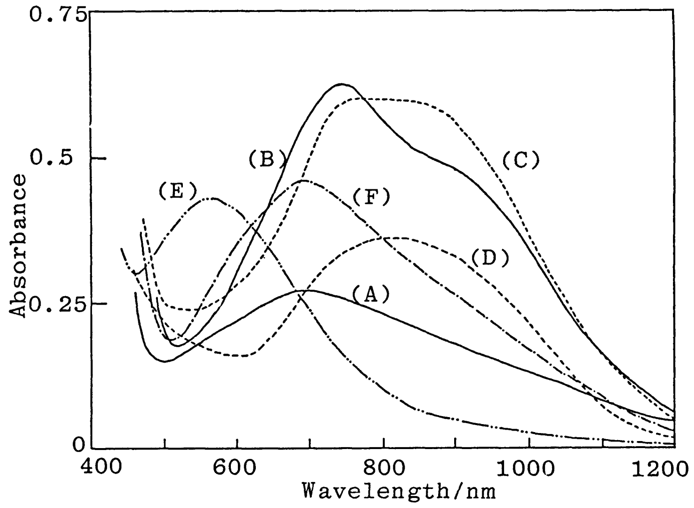


Fig. 1. Electronic spectra of the solutions prepared in Ar.

(A), (B):$FeCl_3$, (C)-(F):$Fe(ClO_4)_3\cdot6H_2O$; (A)in THF, [Fe]=5×10^{-2} M; (B)in THF/H_2O (10/1) (v/v), [Fe]=5×10^{-2} M; (C)in DMF, [Fe] =5×10^{-2} M; (D)in DMF/buffer, [Fe]=1×10^{-2} M; (E)in DMF/buffer, [Fe]=[NTA]=7.4×10^{-2} M; (F)in DMF/buffer, [Fe]=[DPA]=7.4×10^{-2} M
Light path length:1 mm; [1]/[Fe]=1

detected also by ESR (g value:3.8, 4.2, 5.1, 8.5).

As observed in the pyridineiron(III) system,9) the high-spin Fe(II) and Fe(III) species well correspond to semiquinonatoiron(II) and catehcolatoiron(III) complexes. The former, which may exhibit a characteristic band near at 900-1000 nm3,9) and is very reactive with oxygen, may be converted to oxygenated products as well as to quinone. The latter which may exhibit a band at 500-800 nm, seems to be stable against oxygen. As observed with the low reactivity of the NTA complex which forms a very stable catecholate complex, the equilibrium between the semiquinonatoiron(II) and chatecholatoiron(III) must be an important step in determination of the reactivity. It seems probable that oxygen activation by coordination to iron is involved in the oxygenation process (Eq. 2), which has been proposed based on the detection of the semiquinonatoiron(II) species in the pyridineiron(III) system.9) In the absence of the strong coordination ligand, solvents may coordinate to iron to stabilize the complex and be effective for the formation of an isolated iron species, e.g. $(FeCl_3)_n \rightarrow nFeCl_3$. Water or DMF may play a role as proton acceptor or transfer reagent, which is important for the formation of an intermediate complex or products. Anionic ligand such as Cl may be bound to iron in the oxygenation process,[10] but ClO_4 may be separate from iron. This should be clarified in the further studies.

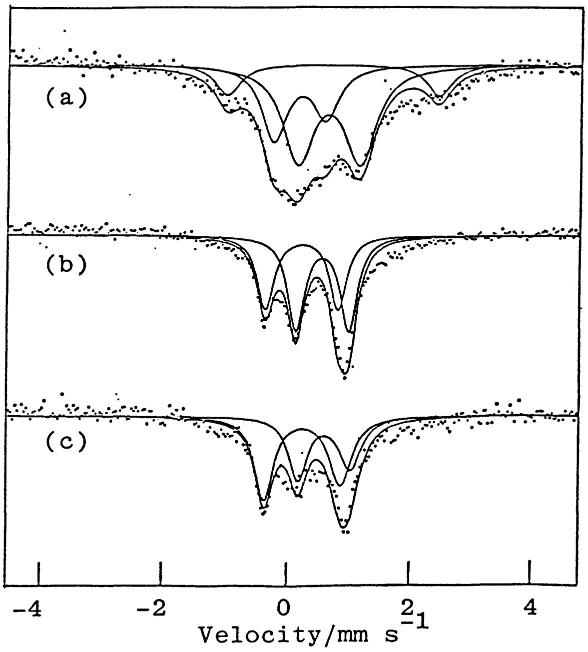
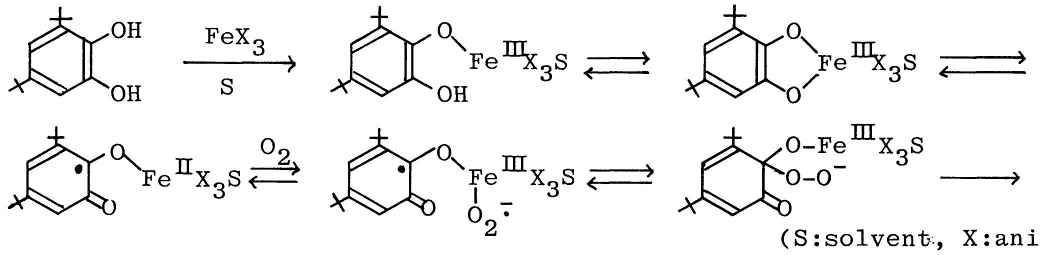


Fig. 2. Mössbauer spectra of the DMF solution prepared with $^{57}FeCl_3$ and **1**.

(a):in Ar. (b):3 h in O_2. (c):24 h in O_2. [**1**]=[^{57}Fe]=5.6×10^{-2} M, observed at 110 K.



(2)

(S:solvent, X:anionic ligand)

References

1)T.Funabiki, H.Sakamoto, S.Yoshida, and K.Tarama, J.Chem.Soc.,Chem.Commun., 1979, 754.
2)T.Funabiki, A.Mizoguchi, T.Sugimoto, and S.Yoshida, Chem.Lett., 1983, 917.
3)T.Funabiki, A.Mizoguchi, T.Sugimoto, S.Tada, M.Tsuji, H.Sakamoto, and S. Yoshida, J.Am.Chem.Soc., 108, 2921 (1986).
4)Y.Tatsuno, M.Tatsuda, and S.Otsuka, J.Chem.Soc.,Chem.Commun., 1982, 1100.
5)M.Matsumoto and K.Kuroda, J.Am.Chem.Soc., 104, 1433 (1982).
6)M.G.Weller and U.Weser, J.Am.Chem.Soc., 104, 3752 (1982).
7)Y.Nishida, H.Shimo, and S.Kida, J.Chem.Soc.,Chem.Commun., 1984, 1611.
8)L.S.White, P.V.Nilsson, L.H.Pignolet, and L.Que,Jr., J.Am.Chem.Soc., 106, 8312 (1984).
9)T.Funabiki, S.Tada, T.Yoshioka, and S.Yoshida, J.Chem.Soc.,Chem.Commun., 1986, 1699.
10)S.Ito and M.Matsumoto, J.Org.Chem., 48, 1133 (1983).

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