was added to a solution of $[Os(OEP)]_2$ (14 mg, 0.009 mmol) in 7 mL of benzene. The reaction mixture was stirred overnight. The purple solid was collected and purified as for **2** (11 mg, 76%): NMR (CD_2Cl_2) H_{meso} 8.49 (br s), CH_2 6.45 (br s), 5.15 (br s), CH_3 1.73 (br s) ppm; UV-vis (CH_2Cl_2) λ_{max} (log ϵ) 328 (4.71), 358 (4.83) (Soret), 488 (3.93) nm. Anal. Calcd for $C_{72}H_{88}F_6N_8POs_2$: C, 54.36; H, 5.57; N, 7.04. Found: C, 54.88; H, 5.47; N, 6.69.

Bis((octaethylporphyrinato)osmium(III,III)) Hexafluorophosphate (11). A suspension of $[FeCp_2](PF_6)$ (6 mg, 0.018 mmol) in 600 μL of THF was added to a solution of $[Os(OEP)]_2$ (12 mg, 0.008 mmol) in 7 mL of benzene. Precipitation occurred immediately. The resulting brown solid was collected and purified as for **2** (14 mg, 97%): NMR CD_2Cl_2) H_{meso} 10.01 (s), CH_2 4.49 (m), 4.32 (m), CH_3 1.66 (7.5 Hz, t) ppm; UV-vis (CH_2Cl_2) λ_{max} (log ϵ) 331 (4.81), 364 (4.75), 448 (sh), 481 (3.97) nm. No satisfactory elemental analysis was obtained for $C_{72}H_{88}F_{12}N_8P_2Os_2$.

Bis((octaethylporphyrinato)osmium(II,III)) Hexachloroantimonate (6). A freshly prepared solution of TBPAH (6.4 mg, 0.007 mmol) in 900 μL of THF was added to a solution of $[Os(OEP)]_2$ (12 mg, 0.008 mmol) in 10 mL of benzene. The solution was stirred overnight. The purple solid was collected and purified as for **2** (10 mg, 72%): NMR (CD_2Cl_2) H_{meso} 8.47 (br s), CH_2 6.36 (br s), 5.09 (br s), CH_3 1.73 (br s) ppm; UV-vis (CH_2Cl_2) λ_{max} (log ϵ) 358 (4.58) (Soret), 3.92 (4.45), 500 (3.83), 5.96 (3.67) nm. Anal. Calcd for $C_{72}H_{88}Cl_6N_8SbOs_2$: C, 48.57; H, 4.98; N, 6.29. Found: C, 47.81; H, 4.71; N, 6.14.

Bis((octaethylporphyrinato)osmium(III,III)) Hexachloroantimonate (12). A freshly prepared solution of TBPAH (25 mg, 0.031 mmol) in 1.5 mL of THF was added to a solution of $[Os(OEP)]_2$ (21 mg, 0.014 mmol) in 10 mL of benzene. Precipitation occurred immediately, and the resulting brown solid was collected and purified as for **2** (29 mg, 94%): NMR (CD_2Cl_2) H_{meso} 9.78 (s), CH_2 4.48 (m), 4.29 (m), CH_3 1.72 (7.5 Hz, t) ppm; UV-vis (CH_2Cl_2) λ_{max} (log ϵ) 334 (sh), 355 (5.05) (Soret), 482 (sh), 537 (sh) nm. Anal. Calcd for $C_{72}H_{88}Cl_{12}N_8Sb_2Os_2$: C, 40.89; H, 4.19; N, 5.30. Found: C, 40.93; H, 4.07; N, 5.33.

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Registry No. 1, 101494-43-3; **2**, 101494-44-4; **3**, 101494-45-5; **4**, 101494-47-7; **5**, 101494-48-8; **6**, 101494-49-9; **7**, 101695-28-7; **8**, 101695-29-8; **9**, 101695-30-1; **10**, 101695-25-4; **11**, 101695-26-5; **12**, 101695-27-6; TBPAH, 40927-19-3; $[Ru(OEP)]_2$, 54762-43-5; $[FeCp_2](PF_6)$, 11077-24-0; $[Os(OEP)]_2$, 89184-09-8; $[Os(OEP)]_2^-$, 101652-23-7; $[Ru(OEP)]_2^-$, 101652-27-1; $[Os(OEP)]_2^{2-}$, 101652-22-6; $[Ru(OEP)]_2^{2-}$, 101652-26-0; $[Os(OEP)]_2^{3+}$, 101652-25-9; $[Ru(OEP)]_2^{3+}$, 101652-29-3; $[Os(OEP)]_2^{4+}$, 101652-24-8; $[Ru(OEP)]_2^{4+}$, 101652-28-2; $AgBF_4$, 14104-20-2; Os, 7440-04-2; Ru, 7440-18-8.

Oxygenase Model Reactions. 1. Intra- and Extradiol Oxygenations of 3,5-Di-*tert*-butylcatechol Catalyzed by (Bipyridine)(pyridine)iron(III) Complex

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Abstract: 3,5-Di-*tert*-butylcatechol (**1**) is oxygenated by (bipyridine)(pyridine)iron(III) complex with insertion of molecular oxygen to give intra- and extradiol oxygenation products. Isolation and reactivity of intermediate compounds have clarified that the intradiol oxygenation proceeds via a cyclic intermediate **4** to give a lactone **3** and the extradiol oxygenation via an acylic intermediate **12** to form a lactone **5**. It has been shown that **12** gives thermally **10** and **6**. Products **7–9** are also formed. The stepwise insertion of oxygen rather than the one-step process via dioxetane intermediates has been clearly demonstrated by the $^{18}O_2$ tracer studies, especially by the insertion of one and two ^{18}O atoms to **4** and **3**, respectively. Oxygenation mechanism involving the formation of a 1:1 catechol–iron complex, the oxygen attack on the catecholate ligand to form a catecholate ligand with a peroxide substituent, and oxygen insertion by the migration of the acyl group to the peroxide oxygen have been proposed. Formation of a 1:1 complex between **1** and iron(III) has been demonstrated by measurements of optical spectra. Reactivities of tris(3,5-di-*tert*-butylcatecholato)- and tris(3,5-di-*tert*-butylsemiquinonato)iron(III) complexes with oxygen and superoxide ion have supported the above mechanism.

Oxygenase, which plays important roles in the metabolitic sequences of various oganic substrates, has been studied extensively in recent years. Aside from works on monooxygenase and its model catalysts which function the epoxidation, hydroxylation, etc.,[1] there are many results on dioxygenase, which functions the cleavage of aromatic and indole rings, dihydroxylation, etc. Since the discovery of incorporation of an O_2 molecule into muconic acid in the oxygenation of catechol catalyzed by pyrocatechase,[2] activation of molecular oxygen by coordination to iron in the iron–enzymes has widely attracted attention, but experimental evidences for the coordination of oxygen to iron have not been obtained.[3] On the mechanism of oxygenation of catechols, the proposal of the one-step oxygenation via a dioxetane intermediate[2] seems to be superseded by that of the stepwise oxygenation via

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Table I. Effects of Mono- and Multidentate Ligands on the Oxygenation of **1**[a]

ligand[b]			rate,[c]	yield,[d] %								
monodentate	multidentate	solv	$cm^3\ min^{-1}$	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
py	bipy	THF	0.63		52	20	1	9		3	2	9
py	bipy	CH_3CN	0.80		73	11		5		3	1	7
py	bipy	dioxane	1.17		59	14	1	9	1	3	2	9
py	bipy	DMF	0.32		53	21[e]		5		7	tr[f]	8
py	bipy	Me_2SO	[g]	17	53	8		2	1	10	tr	9
2-Me-py	bipy	THF	0.53	6	60	2	9	2	2	4		4
3-Me-py	bipy	THF	1.15	3	49	16		8		4	1	7
4-Me-py	bipy	THF	1.17		55	18		10		4	1	7
2,6-Me_2-py	bipy	THF	0.03[h]	7	65	2	11	4		3	1	3
3,5-Me_2-py	bipy	THF	0.07	3	66	10		4		5	1	4
quinoline	bipy	THF	0.07	5	55	8	11	4	2	4		7
isoquinoline	bipy	THF	0.89	1	42	14		11		3	1	9
4-CN-py	bipy	THF		94	5							
imidazole	bipy	THF	0.12	1	59	5				11		
py	phen	THF	0.30	10	47	18	2	4	3	3		7
py	tripy	THF	0.64	12	59	11		4	2	2		6
py	oxine	THF	0.34	2	67	9		4	2	2		6
py	salic	THF	1.71	2	59	12		6	2	2		12
py		THF	1.88		64	12		6		2	2	9

[a] **1** (2 mmol), $FeCl_3$ (0.25 mmol), monodentate ligand (22.4 mmol), multidentate ligand (0.25 mmol) except for 2,2'-bipyridine and salicylaldoxime (0.75 mmol) in 20 cm^3 of solution, 25 °C, 1 atm O_2. [b] py, bipy, phen, tripy, and salic denote pyridine, 2,2'-bipyridine, 1,10-phenanthroline, α,α',α''-tripyridyl, and salicylaldoxime, respectively. [c] Initial rate of oxygen uptake. [d] Mol % based on **1** after the 24-h reaction except for the cases of 2,6- and 3,5-Me_2-py and quinoline (after 48-h reaction). [e] Including 11% of DMF adduct of **3**. [f] Trace. [g] Induction period was observed. [h] Oxygen uptake in the initial 20 min was more rapid (0.18 $cm^3\ min^{-1}$), but it changed to the constant slow oxygen uptake.

a seven-membered lactone intermediate,[4] and the formation of this type of intermediate was shown by the formation of 2-pyrone-6-carboxylic acid[5,6] and 2-hydroxy-*cis,cis*-muconic acid[6] and by the ^{18}O-labeling studies in the cleavage of pyrogallol.[5,6] Apart from the enzymatic studies to elucidate reaction mechanisms and structures of catechol dioxygenases,[3,7-9] various kinds of biomimetic approaches have been carried out in recent years. These involve structural studies on catecholate complexes to elucidate the coordination mode of catecholate and other ligands,[10] mechanistic studies to elucidate the active oxygen species and the steps of activation of catechol and oxygen, and catalytic studies to realize the oxygenations in the similar way to enzyme, e.g., reactivities of singlet oxygen,[11] superoxide ion,[12] peracid,[13-15] oxygen in alkaline solution,[16,17] and oxygen in the presence of metal complexes.[18-23] Reactivity of copper complexes was first noticed as models for dioxygenase, but it has been demonstrated later on that the mechanism of oxygen incorporation is essentially different from that of the iron–enzymes.[18] From the viewpoint of the model for enzyme, we thought it important to find iron complexes, which catalyze oxygenation of catechols in the analogous mechanism to that of the enzyme. We first found the oxygenation of 3,5-di-*tert*-butylcatechol (**1**) by iron complex prepared by mixing in situ $FeCl_2{\cdot}4H_2O$, bipyridine, and pyridine in tetrahydrofuran and obtained 3,5-di-*tert*-butyl-5-(carboxymethyl)-2-furanone (**3**) as oxygenated product.[19a] We used the Fe(II) salt at that time since the oxygen activation by coordination to Fe(II) seemed to be essential for oxygenation, but later we have found that the reaction proceeds in the similar way by using $FeCl_3$,[19b] suggesting an Fe(III) complex as an active species. We have also found that the complex catalyzes both intra- and extradiol oxygenations.[19b] Since it is known that pyrocatechase catalyzes both types of oxygenations in the cases of substituted catechol such as methyl- or methoxycatechol,[24] the reactivity of the iron complex is more analogous to that of enzyme than the iron complexes which catalyze only the intradiol oxygenation of **1**.[22] We report here the details of the oxygenation of **1** by the (bipyridine)(pyridine)iron(III) complex including the evidences for product formation steps and oxygen insertion based on the detection and/or isolation of intermediate compounds and $^{18}O_2$ labeling studies. Recent results on the structure of pyrocatechase and protocatecuate-2,3-dioxygenase have suggested that iron(III) is coordinated by two tyrosine and two histidine residues.[8,9b,10b] Compared with the coordination by oxygen (tyrosine) and nitrogen (histidine),

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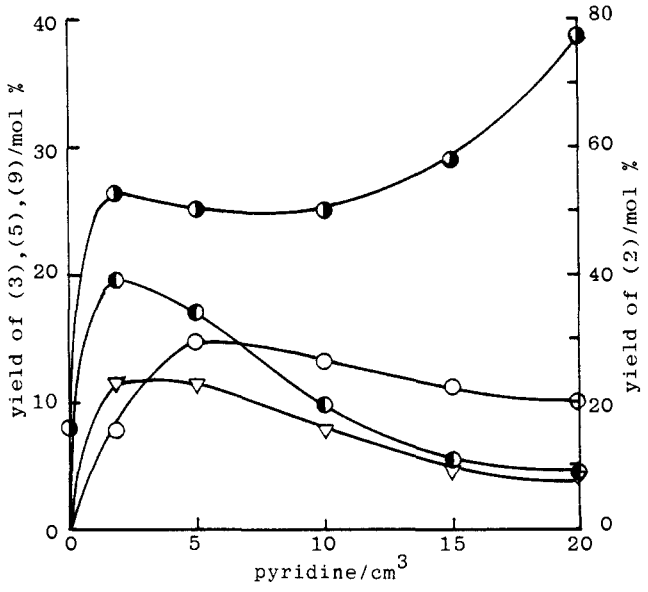
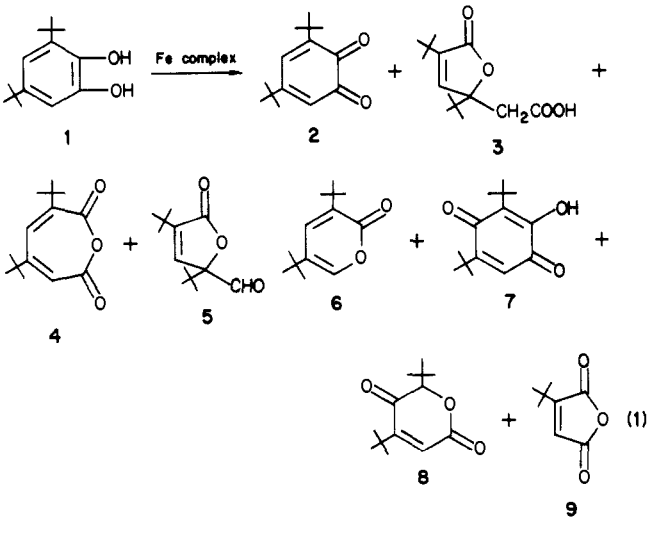


Figure 1. Effect of pyridine on the yields of **2**, **3**, **5**, and **9** after 24 h. Reaction condition is the same as that in Table I except with varying pyridine content (pyridine + THF = 20 cm^3): ◑, **2**; ◐ **3**; ○, **5**; ▽, **9**.

the present complex involves the coordination of ligands only by nitrogen (pyridine, bipyridine). In spite of this difference and the presence of protein in the case of enzyme, oxygenation by the iron complex proceeds basically in the similar way to that of the enzyme.

Results

Products of Oxygenation of 3,5-Di-*tert*-butylcatechol (1) by the (Bipyridine)(pyridine)iron Complex. Oxygenation of **1** was performed at 25 °C in anhydrous tetrahydrofuran (THF) under an atmosphere of oxygen in the presence of $FeCl_3$ or $FeCl_2{\cdot}4H_2O$, bipyridine (bipy), and pyridine (py) ((**1**):Fe:bipy:py, 4:1:3:23). Oxygen uptake was observed in the first 4-h period, but the reaction was performed for 24 h. Products were extracted with dichloromethane by treating the reaction solution with acid to remove iron complexes, bipyridine, and pyridine. As shown in eq 1, products isolated and identified included not only the de-



hydrogenation product, 3,5-di-*tert*-butyl-1,2-benzoquinone (**2**) but also the oxygenation products such as, 3,5-di-*tert*-butyl-5-(carboxymethyl)-2-furanone (**3**), 3,5-di-*tert*-butyl-1-oxacyclohepta-3,5-diene-2,7-dione (**4**), 3,5-di-*tert*-butyl-5-(formyl)-2-furanone (**5**), 3,5-di-*tert*-butyl-2-pyrone (**6**), and 3-*tert*-butylfuran-2,5-dione (**9**). Acid product **3** was isolated by treating the extract with the aqueous $KHCO_3$ solution and others with liquid column chromatography and preparative GLC. Yields of these products were estimated by HPLC and GLC.

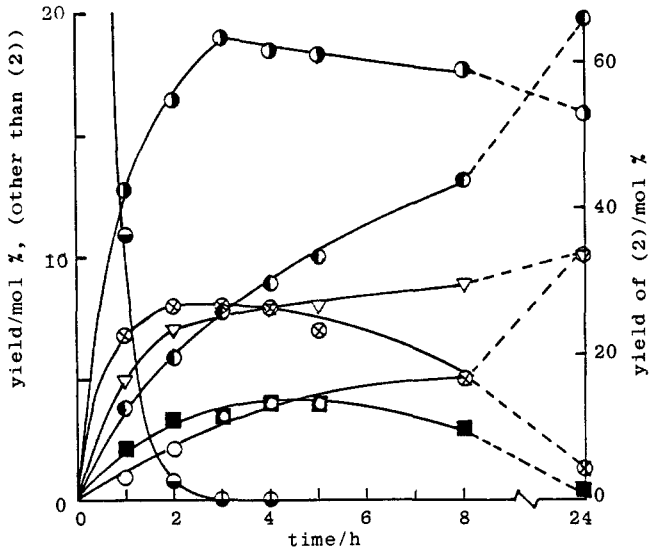


Figure 2. Time-course of the oxygenation of **1** by the (bipyridine)(pyridine)iron(III) complex in THF. Reaction condition is the same as that in Table I, and yields determined by GLC and HPLC are based on **1**: ◒, **1**; ◑, **2**; ◐, **3**; ⊗, **4**; ○, **5**; ■, **6**; ▽, **9**.

Table I shows yields of products in various conditions. Oxygenation to form products other than **2** proceeded in various solvents, but yields of oxygenation products were highest in THF. The yield of the oxygenation products was also high in DMF, but **3** reacted with DMF to give an adduct in the presence of pyridine. As shown in Figure 1, the oxygenation did not proceed in the absence of pyridine indicating that pyridine is essential, but excess amounts of pyridine brought about the increase in the yield of **2**. The initial rate of the oxygen uptake reflected mostly the rate of formation of **2** rather than that of oxygenations. The oxygen uptake was accelerated by using 3- and 4-picolines in place of pyridine but not by using 2-picoline and dimethylpyridines. The cyano group on pyridine inhibited the reaction. This indicates that electron-donating substituents on pyridine are effective in promoting the reaction if the substituents do not hinder sterically the coordination of pyridine. As for the oxygenation, the highest yields of the oxygenation products were obtained when the monodentate ligand was pyridine. Bipyridine and phenanthroline were not essential for oxygenation, but they increased the yields of oxygenation products; however, other multidentate ligands studied were not effective. Oxygenation did not proceed when *N*,*N*′-bis(salicylidene)ethylenediamine (salen) and 1-(2-pyridylazo)-2-naphthol (PAN) were used. This is consistent with the importance of two available adjacent sites on the iron center of the enzyme.[25,26]

Time-Course of the Reaction. The time-course of the reaction was followed by analyzing the reaction products at regular time intervals by HPLC and GLC. As shown in Figure 2, **1** was completely converted, and yields of **2** and **4** became maximum after 3 h. The yield of **6** became maximum after 4 h. The increase in the yields of **3** and **5** and the decrease in the yields of **4** and **6** suggested that **4** and **6** might be the intermediates for **3** and **5**, respectively. Reactions of **4** and **6** in place of **1** were performed independently under the oxygenation conditions to check the above probability. **4** gave **3** stoichiometrically, but **6** did not react. The conversion of **4** to **3** was performed under the conditions: (a) under O_2, (b) under Ar, (c) under O_2 in the presence of a small amount of water, and (d) under O_2 in the presence of an equimolar amount of 2,5-di-*tert*-butylhydroquinone as a proton donor. The rate of conversion was in the order of (d) > (c) > (a) ≃ (b), but the formation of **3** from **1** in the initial stage (Figure 2) was faster than the conversion of **4** to **3**. This suggests the presence of the direct formation of **3** from an intermediate complex, not via **4**.

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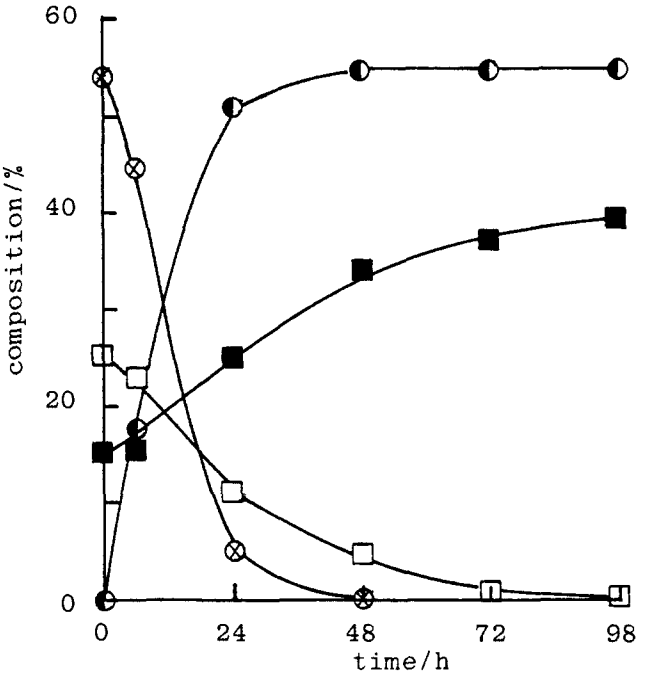
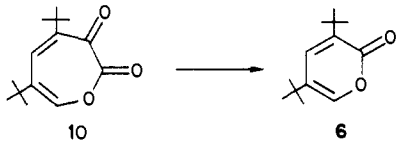


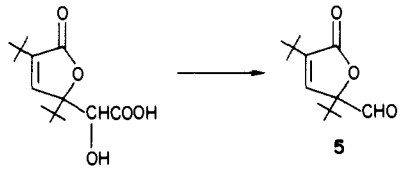
Figure 3. Reaction of the mixture of **4**, **6**, and **10** in the oxygenation condition. Reaction condition: see text. Products were analyzed by GLC and HPLC: ◐, **3**; ⊗, **4**; ■, **6**; □, **10**.

The result that **6** was not an intermediate for **5** suggested the presence of a common intermediate for **5** and **6**. The probability that both compounds are formed directly from a stable intermediate complex was studied. When the product mixture obtained after the reaction for 3 h was allowed to react again with the iron complex, the time-course of the reaction traced the curves in Figure 2, suggesting that both products are formed via an iron-free organic intermediate compound. When the oxygen atmosphere was replaced with argon in the course of the reaction of **1**, the formation of **5** ceased while that of **3** was little affected, indicating that oxygen participates in the conversion of the intermediate into **5** but not into **3**.

If **5** and **6** are extradiol oxygenation products, **10** is expected to be a probable intermediate; but **10** was not isolated from the reaction mixture. A mixture of **4** (54%), **10** (26%), and **6** (15%), which was obtained by the reaction of **2** with *m*-chloroperbenzoic acid, was allowed to react with the iron complex under oxygen. As shown in Figure 3, products were **3** (54%), **6** (39%), and a small amount of unidentified compounds, but **5** was hardly formed. This suggests that **10** might be an intermediate for **6** but not for **5**.



10 **6** (2)



11 **5** (3)

However, the slow conversion of **10** to **6** in Figure 3 is not consistent with the initial rapid formation of **6** in Figure 2. On the other hand, **11**, which was prepared from **1** by the oxygenation under an alkaline aqueous media, was quantitatively converted to **5** under the oxygenation condition. Since **11** was not detected in the product mixture, it seems probable that **5** is formed from the precursor for **11**.

The NMR spectra of the product mixture obtained by the reaction for 3 h indicated the presence of an aldehyde other than

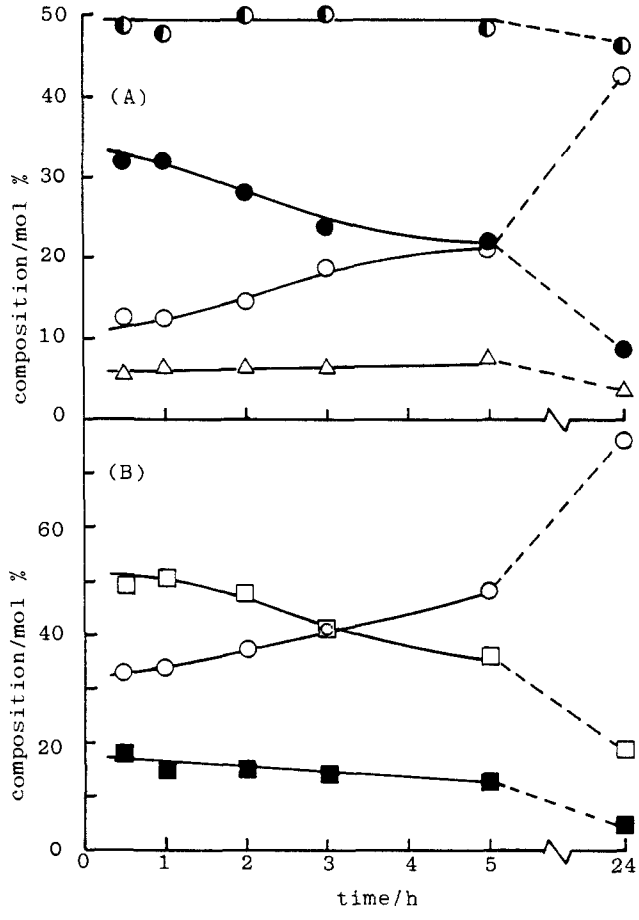
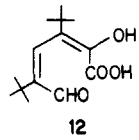
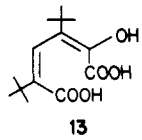


Figure 4. Reaction of the acid mixture under the oxygenation condition. The acid mixture obtained by the reaction of 4.0 mmol of **1** for 3 h was reacted with the iron complex ($FeCl_3$ = 0.50 mmol) in 20 cm^3 THF under oxygen. (A) and (B) show changes of compositions estimated by ^1H NMR and GLC, respectively: ◐, **3**; ○, **5**; ■, **6**; □, **10**; ●, **12**; △, unidentified product.

5. When the product mixture was treated with the $KHCO_3$ solution to separate acid products, the aldehyde product was found in the acid products. The acid product comprised two major and one minor products. One of the major product was **3**, and the other was identified as **12**



12



13

on the NMR and IR spectra although it was not isolated. The structure of the minor product has not been clarified. We have not obtained spectral data sufficient enough to correspond the minor product to **13**, and the results in Figures 4 and 5 do not support that **12** is converted to **5** via the minor product.

When the acid mixture was allowed to react with the iron complex under oxygen, **5** was formed. When products were analyzed by ^1H NMR (Figure 4A), it was shown that compositions of **3** and the minor product were constant but that of **12** decreased accompanied with the increase in that of **5**. When the products were analyzed by GLC (Figure 4B), **6** and **10** were detected in addition to **5**, and the ratio of **5**:**6** + **10** was nearly the same as that of **5**:**12** in Figure 4A. Figure 5 shows the variation of the composition of the acid products in the reaction of **1**. The curves of **3** and **12** are similar to those of **5** and **6** in Figure 2. These results indicated that **12** was converted slowly to **5** in solution and to **10** and **6** thermally in the column of GLC.

Figure 2 shows that the products **2** and **7**–**9** were mostly formed in the initial stage of the reaction. This suggests that these products are formed without formation of stable intermediates, different from the cases of **3** and **5**. The curve of **2** showed a slight

Table II. Mass Analysis of the Lactone **3** Formed under $^{16}O_2$ and $^{18}O_2$[a]

	reactn under $^{16}O_2$			reactn under $^{18}O_2$		
peak[b]	m/z (error)[c]	PC[d]	assgnmnt	m/z (error)	PC	assgnmnt
$P^+ + H$	255.1612 (1.7)	3.2	$C_{14}H_{23}O_4$	259.1712 (3.2)	3.0	$C_{14}H_{23}O_2{}^{18}O_2$
				257.1637 (0.0)	2.2	$C_{14}H_{23}O_3{}^{18}O$
$P^+ - C_4H_7$	199.0932 (−3.7)	16.2	$C_{10}H_{15}O_4$	203.1039 (−1.4)	4.5	$C_{10}H_{15}O_2{}^{18}O_2$
				201.0966 (−4.5)	8.3	$C_{10}H_{15}O_3{}^{18}O$
$P^+ - C_5H_{10}$	184.0175 (−1.9)	11.1	$C_9H_{12}O_4$	188.0792 (−2.7)	9.4	$C_9H_{12}O_2{}^{18}O_2$
				186.0703 (−7.3)	7.6	$C_9H_{12}O_3{}^{18}O$
$P^+ - C_4H_8$	198.0891 (0.0)	100.0	$C_{10}H_{14}O_4$	202.0983 (0.7)	73.2	$C_{10}H_{14}O_2{}^{18}O_2$[e]
				200.0951 (0.0)	85.9	$C_{10}H_{14}O_3{}^{18}O$
$P^+ - C_5H_{11}$	183.0659 (0.2)	100.0	$C_9H_{11}O_4$	187.0734 (−0.7)	69.6	$C_9H_{11}O_2{}^{18}O_2$[e]
				185.0677 (−2.1)	85.7	$C_9H_{11}O_3{}^{18}O$
				183.0624 (−3.2)	2.3	$C_9H_{11}O_4$
$P^+ - C_5H_9O_2$	153.0907 (−0.7)	23.1	$C_9H_{13}O_2$	155.0942 (−1.4)	31.4	$C_9H_{13}O^{18}O$
$P^+ - C_5H_{10}O_2$	152.0837 (0.0)	3.4	$C_9H_{12}O_2$	154.0825 (−5.4)	2.1	$C_9H_{12}O^{18}O$
$P^+ - C_6H_{12}O_2$	138.0652 (−2.5)	2.1	$C_8H_{10}O_2$	140.0690 (−3.1)	6.5	$C_8H_{10}O^{18}O$
$P^+ - C_6H_{13}O_2$	137.0642 (4.0)	7.5	$C_8H_9O_2$	139.0627 (−1.7)	9.9	$C_8H_9O^{18}O$

[a] The lactone **3** obtained after the 24-h reaction under 1 atm $^{16}O_2$ or $^{18}O_2$ (98.75%) was analyzed by mass spectroscopy. [b] P^+:parent ion; $P^+ - R$:fragment ion after loss of R; C_5H_{10}:$C_4H_7 + CH_3$, C_5H_{11}:$C_4H_8 + CH_3$, $C_5H_9O_2$:$C_4H_7 + CO + H_2O$, $C_5H_{10}O_2$:$C_4H_8 + CO + H_2O$, $C_6H_{12}O_2$:$C_4H_7 + CH_3 + CO + H_2O$, $C_6H_{13}O_2$:$C_4H_8 + CH_3 + CO + H_2O$. [c] Errors of mass multiplied by 10^4. [d] Relative peak heights. [e] Peaks of 204.1051 (PC 7.1) and 189.0764 (PC 8.4) were observed. Although either $C_9{}^{13}CH_{14}O_2{}^{18}O_2$ (error, 2.3) and $C_8{}^{13}CH_{11}O_2{}^{18}O_2$ (error, −9.1) or $C_{10}H_{14}O^{18}O_3$ (error, 3.2) and $C_9H_{11}O^{18}O_3$ (error, −2.0) seem to be probable species, the assignment remained obscure. We cannot support the $^{18}O_3$ incorporation in the reaction process without further evidences.

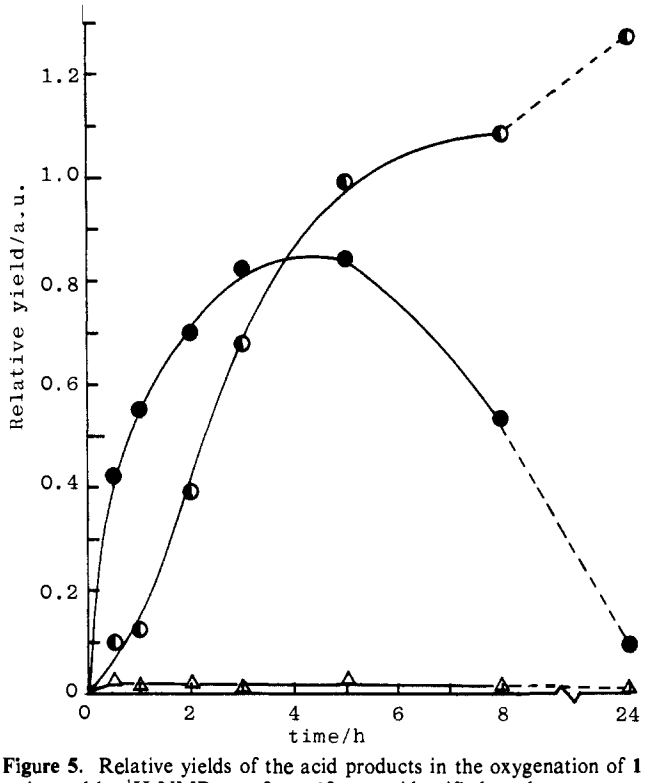


Figure 5. Relative yields of the acid products in the oxygenation of **1** estimated by ^1H NMR: ◐, **3**; ●, **12**; △, unidentified product.

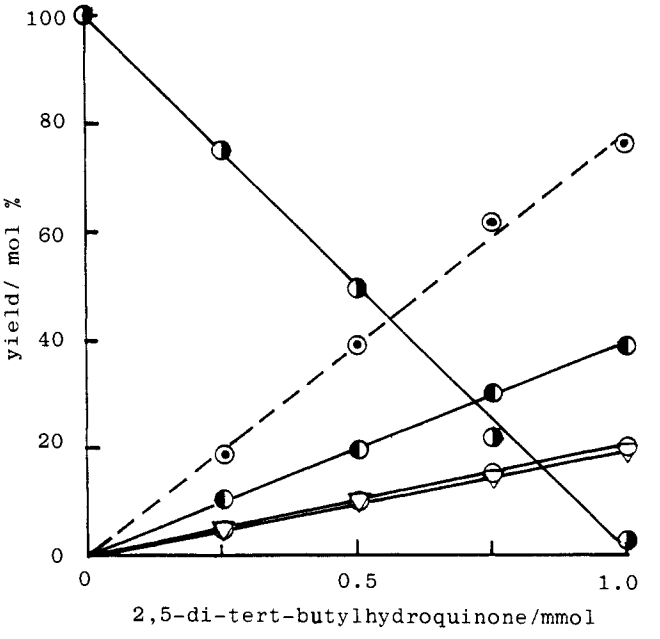


Figure 6. Oxygenation of **2** in the presence of 2,5-di-*tert*-butylhydroquinone. **2**, 0.50 mmol; $FeCl_3$, 0.63 mmol; bipyridine, 0.19 mmol, pyridine, 0.45 cm^3; THF, 4.55 cm^3. Hydroquinone (0.25 mmol) was added at 24-h intervals. Yield is based on **2**: ◑, **2**; ◐, **3**; ○, **5**; ▽, **9**; ⊙, (**3**) + (**5**) + (**9**).

decrease in the yield after 3 h, suggesting the conversion of **2** catalyzed by the iron complex. However, no reaction proceeded when **2** was used as a substrate in place of **1**. We examined the effect of a proton donor. As shown in Figure 6, **2** was oxygenated in the presence of 2,5-di-*tert*-butylhydroquinone to give the same products as those obtained from **1**, indicating that **2** is oxygenated after conversion into **1** in the presence of proton donors. Since the hydroquinone is also oxidized to 1,4-benzoquinone by the iron complex, the highest yield of oxygenation products from **1** was obtained when the hydroquinone was added by portions rather than all at once or before addition of **2**. It seems probable that some proton donors such as a pyridinium ion are formed in the oxygenation of **1**, and conversion of **2** into **1** proceeds to some extent.

$^{18}O_2$ Tracer Studies. It is very important in the studies of dioxygenase model reactions to make sure that molecular oxygen is incorporated into the substrate and that the mechanism of the incorporation is analogous to that of enzymes. The oxygenation was performed by using $^{18}O_2$ (purity, 98.75%), and the products were analyzed by MS or GC–MS spectroscopy. Fragmentation patterns were compared with those of products obtained by the reaction under the $^{16}O_2$ atmosphere. Some products showed parent peaks, but others exhibited only fragment peaks after loss of CO, CO_2, CH_3, C_4H_8, etc. The numbers and positions of ^{18}O in the molecules were determined by the analyses of the fragment patterns. **4** was found to involve only one atom of ^{18}O in the seven-membered ring oxygen. Table II shows a part of the fragmentation pattern of the product **3** as an example. It indicated clearly that **3** was a mixture of nearly equal amount of the one and two ^{18}O adducts. Considering the fragmentation patterns and relative peak height, the probability of ^{18}O incorporation was calculated to be 100% in the furan ring oxygen and 45% in the carboxyl group. Table III shows a part of the fragmentation pattern of **5**. It was indicated that **5** was also a mixture of the one and two ^{18}O adducts and that ^{18}O was found in the ring (85%) and the carbonyl group (62%) but not in the formyl group. **9** also

Table III. Mass Analysis of the Formyl Lactone **5** Formed under $^{18}O_2$[a]

peak	m/z (error × 10^4)	PC	assgnmnt
$P^+ + H$	229.1594 (2.0)	2.1	$C_{13}H_{21}O^{18}O_2$
	227.1526 (−0.5)	4.2	$C_{13}H_{21}O_2{}^{18}O$
$P^+ - CHO$	199.1468 (0.0)	27.2	$C_{12}H_{19}{}^{18}O_2$
	197.1422 (−0.4)	32.2	$C_{12}H_{19}O^{18}O$
$P^+ - C_4H_8$	172.0880 (0.9)	5.5	$C_9H_{12}O^{18}O_2$
	170.0861 (3.3)	5.4	$C_9H_{12}O_2{}^{18}O$
$P^+ - C_4H_8, CH_3$	157.0665 (2.9)	7.9	$C_8H_9O^{18}O_2$
	155.0596 (0.3)	9.4	$C_8H_9O_2{}^{18}O$
$P^+ - C_4H_8, CO$	144.0907 (−1.4)	2.3	$C_8H_{12}{}^{18}O_2$
	142.0883 (0.4)	7.9	$C_8H_{12}O^{18}O$
	140.0865 (2.9)	4.7	$C_8H_{12}O_2$
$P^+ - C_4H_8, CHO$	143.0869 (2.5)	8.9	$C_8H_{11}{}^{18}O_2$
	141.0847 (4.6)	6.9	$C_8H_{11}O^{18}O$
$P^+ - C_4H_8, CHO, CO$	113.0871 (1.9)	14.9	$C_7H_{11}{}^{18}O$
	111.0773 (−3.6)	2.4	$C_7H_{11}O$

[a] Numbers of the ^{18}O atom incorporated were estimated by calculating $\sum n_i h_i / \sum h_i$ for each group of peaks, where n_i and h_i denote the number of ^{18}O atoms involved in the peak i (n_i = 0, 1, 2) and the peak height, respectively. The number of ^{18}O atoms estimated was the following: 1.45 in the three oxygens of **5** ($P^+ + H$, $P^+ - C_4H_8$, $P^+ - C_4H_8, CH_3$), 1.48 in C=O and O ($P^+ - CHO$, $P^+ - C_4H_8$, CHO), 0.83 in O and CHO ($P^+ - C_4H_8$, CO), and 0.86 in O ($P^+ - C_4H_8$, CHO, CO). The averaged values are 0.85 in O, 0.62 in C=O, and 0 in CHO.

Table IV. Incorporation of $^{18}O_2$ into Products of Oxygenation of **1**[a]

prod.	main peaks for mass anal.	^{18}O contnts in prod.,[b] % M	$M+2$	$M+4$	postn and problty of ^{18}O, %
2	$P^+ - C_4H_8$	100			
3	$P^+ - C_4H_8$		54	46	ring-O (100), COOH (45)
4	$P^+ - C_4H_8$		100		ring-O (100)
5	$P^+ - C_4H_8$		54	46	ring-O (85), 2-CO (62)
6	P^+		100		ring-O (100)
7	P^+		100		4-CO (100)
9	$P^+ - CH_3$			100	ring-O (22), 2-CO (75), 5-CO (98)

[a] The reaction was performed under $^{18}O_2$ (98.75%), and products were analyzed by MS and GC–MS. [b] M, M + 2, and M + 4 denote products including 0, 1, and 2 atoms of ^{18}O in place of ^{16}O.

contained two atoms of ^{18}O in the ring (22%), 2-CO (75%), and 5-CO (98%), indicating that ^{18}O is incorporated into the carbonyl group adjacent to the *tert*-butyl group in the higher probability than the other. The ^{18}O content in the products and position and probability of the ^{18}O incorporation are summarized in Table IV.

Effect of Quenchers. Quenchers were added to the reaction solution to study the probability of formations of free radicals, superoxide ion, or singlet oxygen species. The additions of triphenylmethane to quench free radicals and β-carotene to quench singlet oxygen exhibited no effect on the reaction. When epinephrine, Malachite Green, and tetranitromethane, which are known as quenchers of superoxide ion, were added, epinephrine exhibited no effect, Malachite Green inhibited the reaction, and only **2** was formed by the addition of tetranitromethane. However, **1** was stoichiometrically converted to **2** by tetranitromethane in the absence of the iron complex, indicating that the quenching effect of tetranitromethane did not necessarily support the presence of the superoxide ion.

Formation of a Complex between 1 and Iron(III). It has been proposed that the enzymatic oxygenation of catechol proceeds via a catechol–iron(III) complex. To make sure that the present reaction proceeds also via a complex between **1** and iron(III), optical spectra of the reaction solution were measured. As shown in Figure 7, the complex formed in the presence of pyridine and the absence of bipyridine exhibits two peaks at 550 and 975 nm and that formed in the presence of both pyridine and bipyridine at 782 nm. The spectral change indicates the coordination of bipyridine in the latter. These peaks disappeared after the reaction

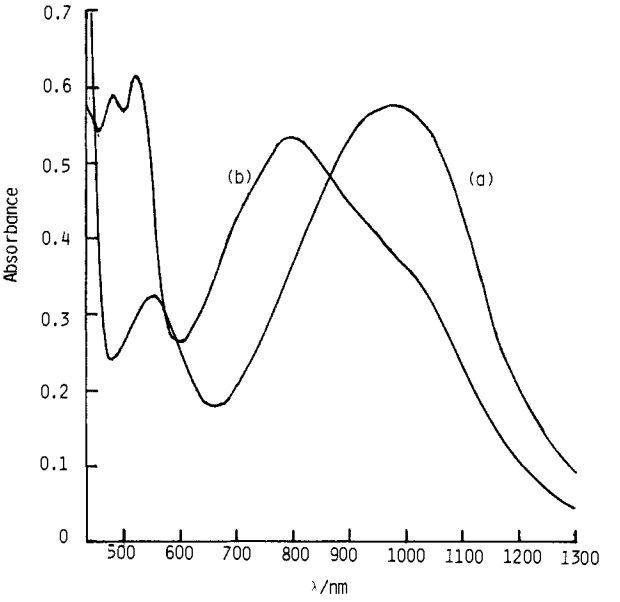


Figure 7. Electronic spectra of catechol–iron complexes. (b) $[FeCl_3]$ = [**1**] = 9.6×10^{-4} mol·dm^{-3}, in THF–pyridine (1:1, v/v); (b) $[FeCl_3]$ = [**1**] = [bipy] = 9.6×10^{-4} mol·dm^{-3}, [py] = 0.54 mol·dm^{-3} in THF. Complexes were prepared under argon atmosphere.

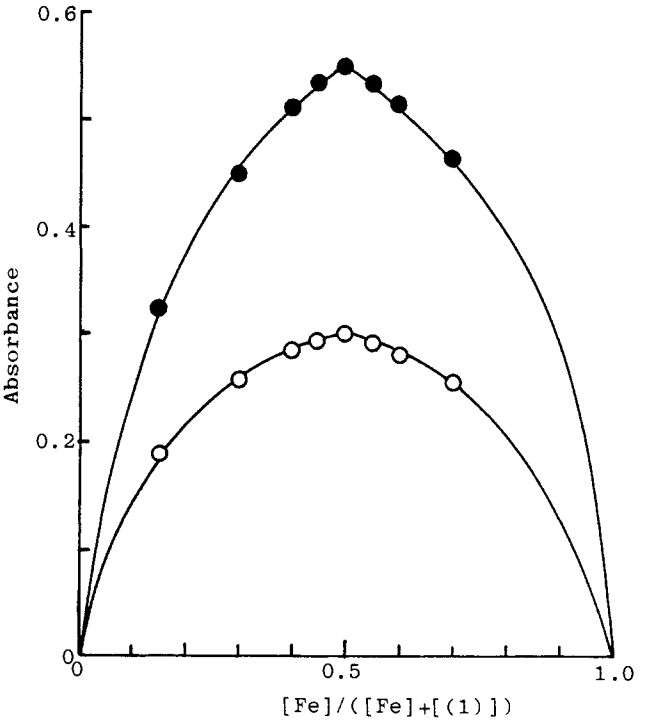


Figure 8. Job's plots at 550 nm (○) and 975 nm (●) [Fe] + [**1**] = 1.9×10^{-3} mol dm^{-3} in THF–pyridine (5:1, v/v) in Ar.

with oxygen but reappeared by the addition of **1**, indicating that the complex is an intermediate in the catalytic process. As shown in Figure 8, the Job's plot of the complex observed in the absence of bipyridine and oxygen indicated clearly the formation of a 1:1 complex between **1** and iron(III). These peaks were not observed when the Fe(II) salt was used in place of the Fe(III) salt in the preparation of the complex in the absence of oxygen but appeared rapidly when oxygen was added to the solution. This indicates that Fe(II) is oxidized to Fe(III) before formation of the complex.

Reaction of Catechol–Iron(III) Complexes with O_2 and $O_2^{-\cdot}$. With the view of obtaining information on reactivity of a catecholate ligand, $Fe(DTBSQ)_3$, $K_3[Fe(DTBC)_3]$, and $K[Fe(DTBC)(bipy)(OH)_2]\cdot C_2H_5OH$ were synthesized where DTBC and DTBSQ denote 3,5-di-*tert*-butylcatecholate and semiquinonate ligands, respectively, and reactions with oxygen and superoxide

Table V. Reaction of Catechol-Iron(III) Complexes with Oxygen and Superoxide Ion[a]

iron complex	O spec,[c] mmol		solv[d]	yield,[e] mol % 1	2	3	14[f]
$Fe(DTBSQ)_3$	O_2		py/THF	34	60	1	
	$O_2^{-\cdot}$	0.15	py/THF	3	1	92	2
$K_3[Fe(DTBC)_3]$	O_2		py/THF		43	38	7
	O_2		THF	2	58	29	8
	$O_2^{-\cdot}$	0.15	py/THF	18	4	32	4
$K[Fe(DTBC)(bipy)(OH)_2]$[b]	O_2		py/THF	6	64	26	
	$O_2^{-\cdot}$	0.15	py/THF	38	29	31	2

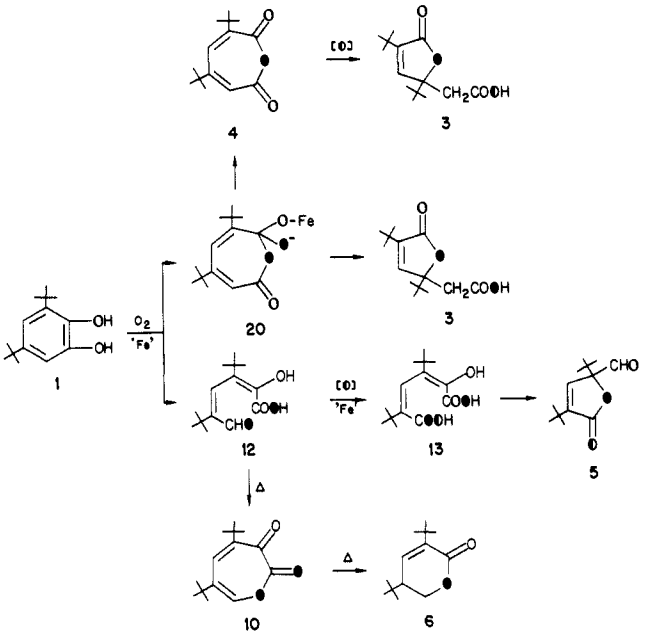
[a] Iron complex (0.05 mmol), 25 °C. [b] $K[Fe(DTBC)(bipy)(OH)_2]\cdot C_2H_5OH$. [c] Superoxide anion was generated from KO_2/18-crown-6 under Ar. [d] Total volume of solvent was 1.25 cm^3. Py/THF denotes a mixture of pyridine and THF (3:2, v/v). [e] Yield after 24 h, based on the catecholate ligand of the iron complex. [f] 3,5-Di-*tert*-butyl-5-hydroxy-2-furanone.

ion were studied. As shown in Table V $Fe(DTBSQ)_3$ yielded quinone **2** under oxygen, and oxygenation hardly occurred. **1** might be formed by the decomposition of the complex by acid in the product extraction step. On the other hand, the complex reacted with the superoxide ion to give the intradiol oxygenation product **3** selectively and in a good yield. The catecholate complex, $K_3[Fe(DTBC)_3]$, reacted with oxygen in the presence or absence of pyridine to give **2** and **3**. **3** was also formed by the reaction of $K_3[Fe(DTBC)_3]$ with superoxide ion, but yield of **2** was low probably due to the further oxidation. The reactivity of $K[Fe(DTBC)(bipy)(OH)_2]$ with oxygen was similar to the tris-catecholate complex. Suppose that **1** was formed by the decomposition of the complex in the product isolation process, the greater yield of **1** in the reaction with superoxide ion than with oxygen indicates the greater reactivity of the catecholate ligand with oxygen than superoxide ion.

Discussion

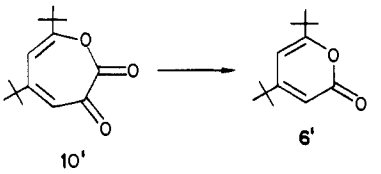
Product analysis and the time-course of the reaction in Figure 2 have indicated clearly that the (bipyridine)(pyridine)iron(III) complex prepared by mixing in situ $FeCl_3$, bipyridine, and pyridine in anhydrous THF catalyzes the oxygenation of the catechol **1** to give both intra- and extradiol oxygenation products. Isolation of muconic acid anhydride **4** from the reaction mixture, its conversion to lactone **3**, and the correlative variations of curves corresponding to **3** and **4** in Figure 2 indicated that the intradiol oxygenation of **1** proceeds by the stepwise oxygen insertion via the monooxygenated intermediate **4** rather than the one-step insertion of an oxygen molecule via a dioxetane intermediate. The formation of **3** or **4** from **1** has been shown in the oxygenation of **1** by other metal complexes,[20,21] but the stepwise conversion of **1** to **3** via **4** in the reaction solution has first been observed here. As shown in Tables II–IV, the $^{18}O_2$ tracer experiments have indicated clearly that one ^{18}O atom is incorporated into a ring oxygen of **4** as in the case of the Fe(NTA) complex[25] and two ^{18}O atoms into **3**. In the latter case, one ^{18}O atom was found as a ring oxygen and the other as a carboxylate oxygen in a 45% probability. In the intradiol oxygenation of catechol by enzyme under $^{18}O_2$, the *cis,cis*-muconic acid was 98–99% doubly labeled, with one ^{18}O incorporation into each carboxylate.[2,6,26,27] The low probability of the ^{18}O incorporation into carboxylate in the present case suggests the presence of the ^{16}O source. It seems probable that H_2O is a contaminant in the solution in spite of the effort to perform the reaction in the anhydrous condition. The formation of **4** with one ^{18}O into the seven-membered ring oxygen indicates the presence of the intermolecular reaction between **4** and $H_2{}^{18}O$ from $^{18}O_2$ and H_2O from contaminant. However, the more rapid initial formation of **3** from **1** than that expected from the reaction of **4** with water suggests the presence of the process of the intramolecular addition of the remaining ^{18}O from $^{18}O_2$ to form the doubly-labeled product **3** via e.g., **20** in Scheme I, similarly to the process proposed for the $^{18}O_2$ incorporation by the Fe(III) center coordinated by H_2O or OH^- in the enzyme.[28,29] The observation

Scheme I



of the incorporation of two ^{18}O atoms into the oxygenation product is the first example in the model system and indicates that the oxygenation by the iron complex proceeds in the analogous way to dioxygenase, i.e., by the stepwise oxygenation mechanism proposed by Hamilton.[4]

We have isolated formyl lactone **5** and pyrone **6** which involve 13 carbon atoms after the loss of one carbon from **1**. The formation of these products by the extradiol oxygenation was demonstrated by elucidation of the reaction path. The extradiol oxygenation of **1** by metal complexes has been proposed on the isolation of **6'** in the reactions catalyzed by ruthenium[20] and



(4)

vanadium[21a,b] complexes. **10'** has been assumed as an intermediate for the formation of **6'**.[20] It is interesting to know that **6** was isolated instead of **6'** in the present iron system. The reason why the direction of the oxygen insertion is different between iron and other complexes is not clear at the present but may be related to the coordination mode of **1** to metals.

We first supposed the conversion of **6** to **5** on the basis of the correlative curves in Figure 2, but it was readily demonstrated that this was not the case. Probability of formation of **10** as an intermediate for both compounds was studied. **10** was converted to **6** but not to **5** (Figure 3). The facts that the conversion from **10** to **6** is very slow compared with the initial rapid formation of

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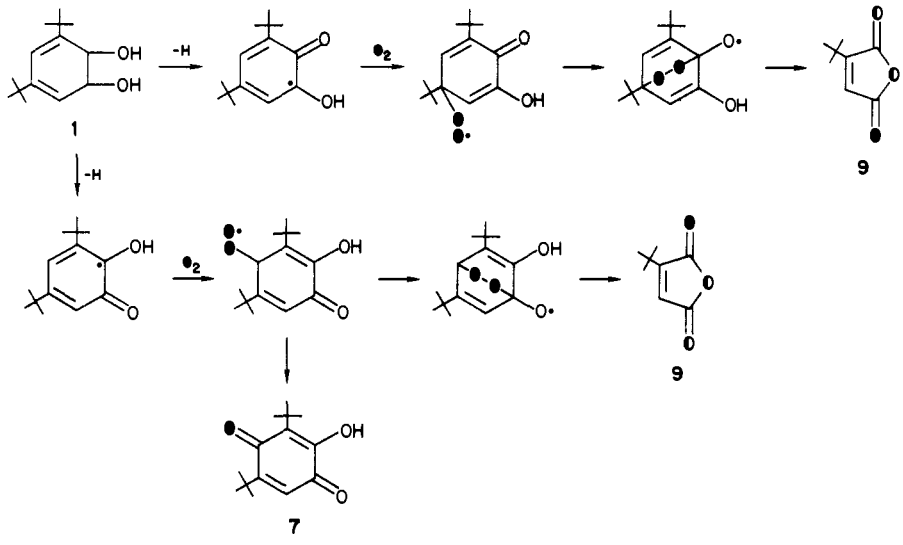
Scheme II



6 in Figure 2 and that **10** is not detected as a product in the reaction of **1** have suggested that **10** is not formed as an intermediate.

On the other hand, we have detected an acylic intermediate **12** by ^{1}H and ^{13}C NMR. The results in Figures 4 and 5 clearly indicated the following: (a) yield of **12** becomes maximum after 4 h, indicating that **12** is an intermediate compound; (b) the formation curve of **12** resembles that of **6** in Figure 2; (c) **12** is converted to **5** under the oxygenation condition; (d) **12** is converted to **6** not under the oxygenation condition but thermally in a column of GLC. The thermal conversion seems to proceed in the way **12** → **10** → **6**. Since **5** was formed stoichiometrically from **11**, it is very probable that **5** is formed from **12** which is a precursor for **11**.

In the oxygenation of catechols by enzymes, formation of acyclic products such as *cis,cis*-muconic acid is well-known, but such acylic products have not been detected in the model reactions of substituted catechol.[12] This is due to the easy lactonization of these acyclic products.[30] Although **12** was not isolated, the NMR data and the reactivities of **12** first indicated the intermediate formation of an acyclic product. It is reasonable to assume that **12** is oxygenated to **13** before lactonization, which may proceed by the attack of carboxylate (6-COO^-) to the olefinic carbon (3-C) as proposed in the oxygenation of **2** by superoxide ion.[12] This is supported by the facts that the conversion of **12** to **5** requires the presence of oxygen and that ^{18}O is incorporated not into the formyl group of **5** but into the carbonyl group (64%). We have detected a minor acid product in addition to **12**, but data are not enough to correspond it to **13**. The intra- and extradiol oxygenations of **1** by the iron complex discussed above are summarized in Scheme I.

Mechanisms of the bond fissions in the formation of **7–9** are rather complicated and have not been clarified, but initial rapid formations of **7–9** suggest that the oxygenation mechanisms are very different from those of **3–6**. The ^{18}O atom content in the three oxygens of **9**, i.e., 97% in ring-O + 2-CO and 98% in 5-CO, serves as a useful information for elucidation of the mechanism. The structure of **9** and the ^{18}O distribution suggest the transannular cleavage of the aromatic ring. In the three possible cleavages, i.e., 1,4-, 2,5-, and 3,6-fissions, incorporation of two ^{18}O atoms is expected by 1,4- and 2,5-fissions and three ^{18}O atoms by 3,6-fission, but the latter is not consistent with the experimental result. The incorporation of one ^{18}O in 4-CO (between the two *tert*-butyl groups) of **7** suggests the formation of the oxygen adduct at the 4-position, and this is consistent with the result that a carbonyl compound is formed from an oxygen adduct having an α-proton.[31] However, in the case of 1,4-fission, the nearly 100% incorporation of ^{18}O into 2-CO and less than 100% in 5-CO is expected, but the result showed the opposite orientation. This suggests the probability of the presence of the 2,5-fission as shown in Scheme II. Little information has been obtained regarding the route of formation of **8**.

In the above discussion we have revealed the structures of intermediate compounds for the intra- and extradiol oxygenations of **1**. Since iron is not essential for the transformation of the intermediates to the final products, it is important to reveal the process of formation of the intermediates from **1**. In the first step of oxygenation of catechol, there are three possibilities: (i) reaction of molecular oxygen with the catechol activated by coordination to iron, (ii) reaction of catechol with the oxygen activated by coordination to iron, and (iii) reaction between coordinated catechol and oxygen. There is no support for (ii) although the prior coordination of oxygen has been proposed for the extradiol oxygenation by metapyrocatechase,[32] and many spectral evidences support the formation of the catechol iron complex. (iii) was first proposed in the field of biochemistry and is believed to be the most probable, but no convincing evidence for the coordination of oxygen has been obtained. As shown in Figures 7 and 8, we have obtained the spectral evidence for the rapid formation of a 1:1 complex between catechol (**1**) and iron(III) which reacts with oxygen. Since the reaction forms not only oxygenation products but also dehydrogenation products, the complex does not unequivocally correspond to the intermediate for the oxygenation reaction, but it seems reasonable to assume that oxygenation proceeds by the reaction of a 1:1 complex with oxygen. Spectroscopic studies on the formation of active complexes and structures of intermediate complexes will be reported in detail elsewhere.[33]

When catechol coordinates to Fe(III) in the presence of a deprotonation reagent such as pyridine, three types of a catechol–iron complex are probable, i.e., chelated catecholate–Fe(III), monodentated catecholate–Fe(III), and semiquinonate–Fe(II) complexes. Oxygen may react with one of these intermediates to form a monodentated catecholate ligand with a peroxide substituent. The chelated catecholate complex if formed may be most stable and react with oxygen after cleavage of an Fe–O bond.[22b,25] The probable complexes of the peroxide adduct are **15–17** in Scheme III. **15**, in which catechol coordinates to iron(III) with the 1-OH group, is converted to both intra- and extradiol oxygenation products via **18** and **19** by the Baeyer–Villiger[4] or Criegee rearrangement.[25] It is not easy to choose one of these two re-

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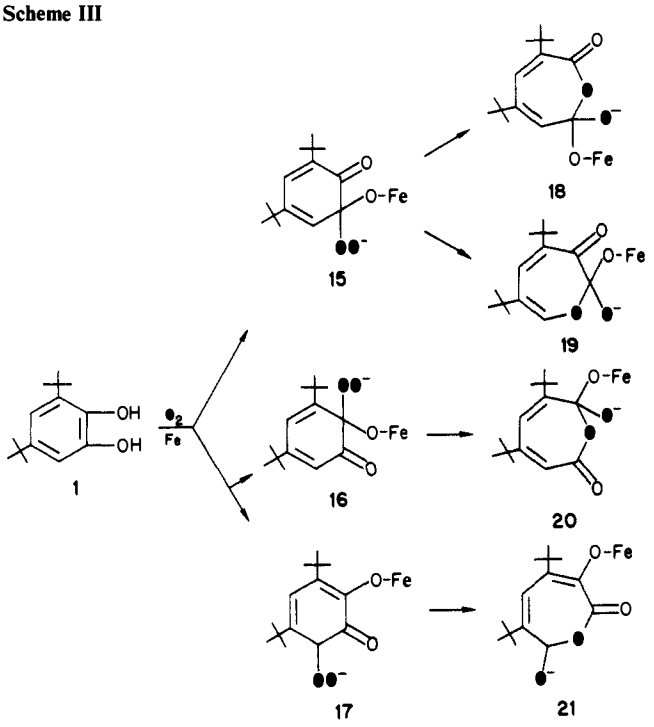
Scheme III



arrangements as a more probable oxidation process in the present system, but this process seems to be generally preferred on the reason that the steric repulsion between the *tert*-butyl group and ligands may be smaller.[11,14,15,21] The greater yield of products of the intradiol oxygenation than the extradiol (ca. 2:1) may be explained by the more facile migration of the acyl group than the vinyl group in the oxidation.

On the other hand, intra- and extradiol oxygenations can be explained by the processes via **16** and **17**, in which catechol coordinates to iron with the 2-OH group. These complexes are converted to **20** and **21** by the acyl migration. Previously,[19b] we have proposed this process because the steric hindrance seemed not to be essential, and the application of the same migration for both reactions seemed to be more reasonable than that of the different types of migration. Recently, the formation of **16** has been proposed on the basis of the different lengths of the two O–Fe bonds of the coordinated 3,5-di-*tert*-butylcatechol as a chelated ligand in the nitrilotriacetato–iron complex: 1.979 Å for O(1)–Fe and 1.887 Å for O(2)–Fe,[25] supporting that the formation of **16** cannot be excluded on the steric reason. The $^{18}O_2$ tracer study has clarified that one ^{18}O atom is incorporated into muconic acid anhydride **4** as a ring oxygen and that two ^{18}O atoms are incorporated into the formyl lactone **5** as ring and carbonyl oxygens. The latter requires that the singly labeled formyl group in **12**, which can be formed from either **15** or **17**, is oxidized to the doubly-labeled carboxyl group. The incorporation of 1.47 atoms of ^{18}O (Table IV) indicates the contamination of ^{16}O in the oxidation step. The isolation of **4** with one ^{18}O suggests the fairly rapid cleavage of C–O^- bond in **18** or **20** by the interaction between O^- and Fe(III). In the case of extradiol oxygenation, we have not isolated **10**, even though similar interaction between O^- of C–O^- and Fe(III) is expected in **18–20**. This suggests that the intermediate **21**, in which the distance between O^- and Fe(III) is longer than in **20**, is more probable. In this case, the ratio of the intra- to extradiol oxygenation may be related to the difference of stability or of facility of the acyl migration between **16** and **17**.

As mentioned above, we have supposed the formation of peroxide complexes such as **16** and **17**, but it is not easy to obtain direct evidences for the species. Participation of the free active oxygen species such as singlet oxygen and superoxide ion was studied by addition of quenchers. Formation of singlet oxygen is not probable, but quencher was not effective in clarifying the participation of superoxide ion. Reactivity of superoxide ion formed from KO_2 was also studied, but the result did not bring about clear-cut result. However, structures of products were different from those obtained by the oxygenation of the catechol **1** or the quinone **2** with $O_2^{-\bullet}$,[12] suggesting that the mechanism of oxygenation with molecular oxygen is different from the oxygenation with superoxide ion.

On the other hand, results in Table V give interesting information on the reactivity of the coordinated catechol. The selective formation of **3** from the semiquinone complex, $Fe(DTBSQ)_3$, by the reaction with superoxide ion but not with oxygen supports the intermediate formation of the peroxide species by the electron transfer from $O_2^{-\bullet}$ to semiquinone ligand. The formation of **2** in the reaction with O_2 is explained by disproportionation without participation of oxygen, since **2** was formed from the complex in the absence of oxygen. **3** is formed from the catecholate complexes, $[Fe(DTBC)_3]^{3-}$ and $[Fe(DTBC)(bipy)(OH)_2]^-$, by reaction with O_2. This also supports the probability of the peroxide species formed by electron transfer from the catecholate ligand to oxygen. It has been reported that catecholate–iron complexes such as $[Fe(DTBC)(salen)]^-$ react neither with O_2 nor $O_2^{-\bullet}$,[10a] but $[Fe(NTA)(DTBC)]^{2-}$ reacts with O_2.[22,25] These results indicate that the stability of the DTBC ligand depends greatly on the other ligands. As shown in Table V, the catecholate complexes react with $O_2^{-\bullet}$ to give **3**, although reactivities are not high. In this case, the formation of the peroxide species requires the reduction of Fe(III) to Fe(II). The reaction of the catecholate ligand with O_2 or $O_2^{-\bullet}$ was studied with the manganese complex, $[Mn(DTBC)_3]$. There are two arguments: one claims the formation of semiquinone complexes, $[Mn(DTBC)_2(DTBSQ)(O_2^{-\bullet})]^{2-}$[34,35] and $[Mn(DTBC)_2(DTBSQ)(O_2^{-\bullet})]^{3-}$,[36] and the other claims reaction of the catecholate ligand with oxygen to give either free or bound semiquinone.[37] It is not easy to compare the reactivity of the catecholate ligand with oxygen species between iron and manganese complexes, but it seems probable that the formation of the peroxide species proceeds without formation of the free $O_2^{-\bullet}$ species.

On the basis of these results, we propose Scheme IV which explains most reasonably the intra- and extradiol oxygenations of **1** by the iron complex. The present data are not enough to discuss further in detail the process of the formation of the peroxide species. It has been reported that the Fe(III) state is retained throughout the oxygenation by enzyme,[26] but the transient formation of a semiquinonate–Fe(II) from a chelated catecholate–Fe(III) is probable. The mesomeric structures of the semiquinonate ligand of the semiquinonate–Fe(II) complex are convenient to explain the peroxide adducts at the 2-, 4-, and 6-aromatic carbons, which are shown in Schemes II and III, and the formation of quinone **2**. Preliminary results of Mössbauer spectroscopy indicated the formation of high-spin Fe(II) and Fe(III) complexes in the reaction solutions, and we will discuss elsewhere the structures of the catechol–iron complexes and roles of these complexes in the oxygenation.[33]

The formation of a catecholate–iron complex requires the deprotonation of catechol (**1**). The fact that pyridine is essential for the oxygenations as shown in Figure 1 is consistent with the observation that pyridine functions as a deprotonation reagent. This is also supported by the result that 4-cyanopyridine (pK_a = 1.86) is not effective for oxygenation. However, the role of pyridine as a coordination ligand is also important as seen from the result that pyridines of high pK_a values, e.g., dimethylpyridines, increase the yield of **2** rather than **3**. This is explained by the promotion of the replacement of the catecholate ligand by pyridine forming a Fe(II) complex and 3,5-di-*tert*-butylsemiquinone which is converted to **2**. Steric effects of the substituents also suggest the importance of the coordination of pyridine. Thus, pyridines

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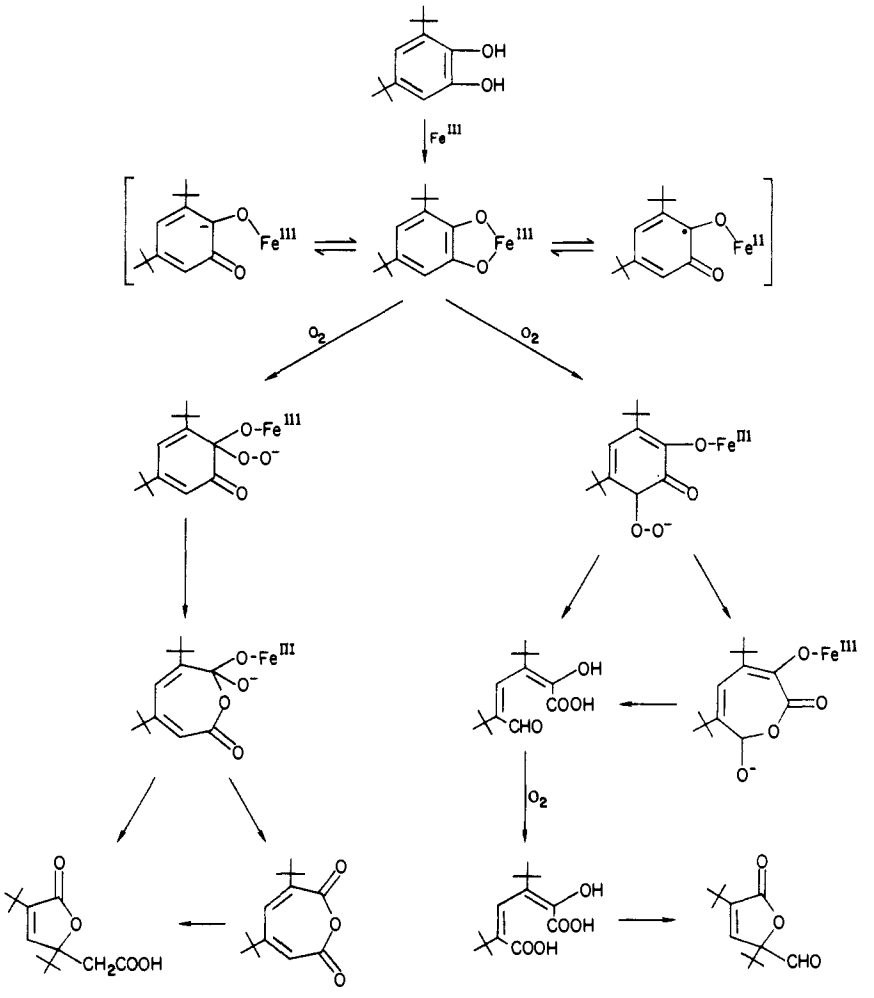
Scheme IV



of moderate pK_a values (pK_a = 4–6), e.g., pyridine and methylpyridine, are effective both for deprotonation and stabilization of the catecholate complex.

Pyridine may work also as a proton transfer reagent in a similar manner to the imidazole group in the histidine residue of an enzyme. This was suggested by the slow reaction of quinone **2** as shown in Figure 2. The role of pyridinium ion as a proton transfer reagent is also proposed in the reduction of 1,4-benzoquinone by an iron porphyrin complex.[38] Participation of the proton transfer was clearly indicated by the result that **2** is catalytically oxygenated in the presence of a proton transfer reagent such as 2,6-di-*tert*-butylhydroquinone as shown in Figure 6.

Bidentate ligands such as bipyridine and phenanthroline also contribute to stabilize the catecholate–iron complex for the reaction with oxygen. As shown in Figure 7, the shift of the maximum peak of the catecholate complex by addition of bipyridine to a pyridine complex indicates clearly the formation of a complex coordinated by bipyridine and catechol. The stability of the catecholate complex may be affected by the solvent, and the promotion of formation of **2** in the solvents of high dielectric constant seems to be related to the instability of $Fe(DTBSQ)_3$ in those solvents.[39]

In conclusion, we have clarified the reaction routes of intra- and extradiol oxygenations of 3,5-di-*tert*-butylcatechol by a (bipyridine)(pyridine)iron(III) complex. The reaction proceeds by the formation of a catecholate complex, reaction with oxygen to form peroxide intermediates, and incorporation of oxygen accompanying the ring opening. Yields of the oxygenation products depend on the conditions which affect the stability of the intermediate complexes. The catecholate ligand should be activated by the electron transfer from other ligands but stable enough against elimination as 3,5-di-*tert*-butyl-1,2-benzoquinone. Bipyridine and pyridine are the most favorable of the ligands studied in this work.

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Experimental Section

Materials. $FeCl_2 \cdot xH_2O$ (x = ca. 4, Kanto Chemical), $FeCl_3$ (Merk), KO_2 (Morton Thiokol), and 18-crown-6 (Nakarai Chemical) were used without further purification. 3,5-Di-*tert*-butylcatechol (**1**) (Aldrich) was recrystallized 3 times from pentane solution. Tetrahydrofuran, pyridine, and other solvents were dried and distilled before use. 2,2′-Bipyridine, 1,10-phenanthroline, and other ligands were commercially supplied and used without further purification.

Oxygenation Procedure of 3,5-Di-*tert*-butylcatechol (1). **1** (0.445 g, 2.00 mmol) and bipyridine (0.117 g, 0.75 mmol) were placed in a 50-cm^3 three-necked flask, which was connected to a gas buret. After the flask was purged with oxygen, pyridine (1.8 cm^3, 23 mmol), and $FeCl_3$ (0.041 g, 0.25 mmol) dissolved portions of 18.2 cm^3 of THF were added, and the solution were stirred magnetically at 25 °C. The progress of the reaction was followed by the HPLC and GLC analyses of the products. Thus, 1 cm^3 of the reaction solution was diluted with 2 cm^3 of dichloromethane, washed with 4 cm^3 of 2 N HCl and 6 cm^3 of water, and concentrated in vacuo. The residue was dissolved in 1 cm^3 of dichloromethane and analyzed by GLC (Shimadzu GC-4CM; column: 3 m Silicone SE-30, 10% on Uniport B (60–80 mesh); at 180 °C; naphthalene as an internal reference). Dichloromethane was evacuated, 1 cm^3 of methanol was added, and the methanol solution was analyzed by HPLC (Shimadzu LC-3A; column: 4.6 mm × 25 cm of Zorbax ODS; UV detector (215 nm); methanol/pH 3.5 water (83/17, v/v); biphenyl as an internal reference). Data were analyzed by Shimadzu Chromatopac E1A and C-R1B.

Isolation of Products. Products were isolated from the reaction mixtures after 3- or 24-h reactions. The dichloromethane extract, which was washed with 2 N HCl and water, successively, was shaken with the aqueous solution of saturated potassium bicarbonate to separate acid products. The aqueous layer was acidified, extracted with dichloromethane, and evaporated in vacuo. The dichloromethane layer after

separation of acid products was dried and concentrated in vacuo. The residue was distilled at 70 °C at 0.2 mmHg with a Kugelrohr apparatus (Buchi's Glass Tube Oven GKR-50) or chromatographed on silica gel. **2**, **3**, **5**, **8**, and **9** were isolated from the solution after the 24-h reaction, and **4**, **6**, and **7** were isolated after the 3-h reaction. **2**, **3**, and **5** were purified by recrystallization from pentane, **4**, **6**, **7**, and **8** by the preparative GLC, and **9** by sublimation. Structures of these products were determined by elemental analysis, GC–MS, IR, and ^1H and ^{13}C NMR spectroscopy.

3,5-Di-*tert*-butyl-5-(carboxymethyl)-2-furanone (3): mp 132–133 °C (lit.[10] mp 133–134 °C); IR (KBr) ν_{CO} 1748, 1721, $\nu_{C=C}$ 1639 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (s, 9 H), 1.23 (s, 9 H), 2.81 (d, J = 14.3 Hz, 1 H), 2.95 (d, J = 14.3 Hz, 1 H), 6.94 (s, 1 H), 9.50 (s); ^{13}C NMR ($CDCl_3$) δ 25.3 (q, J_{CH} = 127 Hz), 28.0 (q, J_{CH} = 127 Hz), 31.6 (s), 37.4 (t, J_{CH} = 131 Hz), 37.8 (s), 88.1 (s), 143.9 (s), 145.5 (d, J_{CH} = 171 Hz), 171.2 (s), 175.4 (s). Anal. Calcd for $C_{14}H_{22}O_4$: C, 66.12; H, 8.72; O, 25.16. Found: C, 66.10; H, 8.92; O, 24.98.

3,5-Di-*tert*-butyl-1-oxacyclohepta-3,5-diene-2,7-dione (4): mp 95–96 °C (lit.[40] mp 93–94 °C); IR (KBr) ν_{CO} 1780, 1730, $\nu_{C=C}$ 1630, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.16 (s, 9 H), 1.28 (s, 9 H), 6.14 (d, J = 1.5 Hz), 6.45 (d, J = 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 28.7 (q, J_{CH} = 127 Hz), 29.1 (q, J_{CH} = 127 Hz), 36.6 (s), 36.8 (s), 115.7 (dd, J_{CH} = 167 Hz, J_{CCH} = 6 Hz), 124.1 (dd, J_{CH} = 157 Hz, J_{CCH} = 11 Hz), 148.3 (s), 159.2 (s), 160.5 (s), 162.0 (s). Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53; O, 20.31. Found: C, 71.04; H, 8.54; O, 20.42.

3,5-Di-*tert*-butyl-5-(formyl)-2-furanone (5): mp 80–81.5 °C; IR (KBr) ν_{CO} 1756, 1744, 1725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05 (s, 9 H), 1.25 (s, 9 H), 6.90 (s, 1 H), 9.60 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 24.8 (q, J_{CH} = 127 Hz), 28.1 (q, J_{CH} = 127 Hz), 32.2 (s), 38.5 (s), 94.5 (s), 141.3 (d, J_{CH} = 175 Hz), 146.1 (s), 170.5 (s), 197.3 (d, J_{CH} = 185 Hz). Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99; O, 21.47. Found: C, 69.34; H, 8.99; O, 21.40.

3,5-Di-*tert*-butyl-2-pyrone (6): GC–MS data found for $C_{13}H_{20}O_2$, m/e 208.1505; IR (KBr) ν_{CO} 1710, $\nu_{C=C}$ 1635, 1560 cm^{-1}; ^1H NMR (CCl_4) δ 1.20 (s, 9 H), 1.32 (s, 9 H), 7.04 (d, 1 H), 7.14 (d, 1 H); ^{13}C NMR ($CDCl_3$) δ 28.4 (q, J_{CH} = 127 Hz), 29.5 (q, J_{CH} = 127 Hz), 31.9 (s), 34.8 (s), 127.3 (s), 136.2 (s), 136.3 (d, J_{CH} = 156 Hz), 143.8 (d, J_{CH} = 197 Hz), 160.9 (s).

3,5-Di-*tert*-butyl-2-hydroxy-1,4-benzoquinone (7):[41] IR (neat) ν_{OH} 3340, ν_{CO} 1660, 1640, $\nu_{C=C}$ 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (s, 9 H), 1.37 (s, 9 H), 6.50 (s, 1 H), 7.18 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 29.6 (q, J_{CH} = 127 Hz), 30.2 (q, J_{CH} = 127 Hz), 35.5 (s), 36.2 (s), 125.0 (d, J_{CH} = 168 Hz), 129.1 (s), 148.8 (s), 162.3 (s), 184.4 (s), 189.2 (s). Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53; O, 20.31. Found: C, 70.92; H, 8.70; O, 20.38.

2,5-Di-*tert*-butyl-2*H*-pyran-3,6-dione (8): IR (KBr) ν_{CO} 1725, 1690, $\nu_{C=C}$ 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.01 (s, 9 H), 1.26 (s, 9 H), 4.40 (s, 1 H), 6.65 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 26.1 (q, J_{CH} = 128 Hz), 28.4 (q, J_{CH} = 128 Hz), 35.3 (s), 37.5 (s), 90.8 (d, J_{CH} = 154 Hz), 128.9 (d, J_{CH} = 169 Hz), 159.3 (s), 161.9 (s), 193.4 (s). Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99; O, 21.40. Found: C, 69.22; H, 9.05; O, 21.73.

3-*tert*-Butylfuran-2,5-dione (9): mp 65 °C; IR (KBr) ν_{CO} 1835, 1765, $\nu_{C=C}$ 1615 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (s, 9 H), 6.52 (s, 1 H); ^{13}C NMR ($CDCl_3$) 28.0 (q, J_{CH} = 128 Hz), 33.4 (s), 126.9 (d, J_{CH} = 139 Hz), 161.5 (s), 163.5 (s), 164.0 (s). Anal. Calcd for $C_8H_{10}O_3$: C, 62.33; H, 6.54; O, 31.13. Found: C, 62.15; H, 6.54; O, 30.89.

Synthesis and Reaction of 4,6-Di-*tert*-butyl-1-oxacyclohepta-4,6-diene-2,3-dione (10). Quinone **2** (0.22 g, 1.0 mmol) was dissolved in 3 cm^3 of THF at 0 °C in Ar. *m*-Chloroperbenzoic acid (0.33 g, 1.5 mmol) was added by portions to give a pale yellow solution. The solution was filtered at −78 °C to separate *m*-chlorobenzoic acid. The residue obtained after evaporation of THF was a mixture of **4**, **6**, and **10** (NMR analysis). The composition estimated by HPLC and GLC was 54%, 15%, and 26%, respectively. **10**: ^1H NMR ($CDCl_3$) δ 1.15 (s, 9 H), 1.26 (s, 9 H), 6.44 (d, 1 H), 6.45 (d, 1 H); ^{13}C NMR ($CDCl_3$) δ 29.1 (q), 29.3 (q), 34.7 (s), 36.4 (s), 131.0 (d), 133.7 (d, J_{CH} 166 Hz), 149.6 (s), 163.5 (s), 169.9 (s), 189.8 (s). The mixture was dissolved in 3 cm^3 of THF, and 1.5 cm^3 of the solution was added to the 3.0 cm^3 of THF solution containing $FeCl_3$ (8 mg, 0.05 mmol), bipyridine (23 mg, 0.15 mmol), and pyridine (0.36 cm^3) under O_2 or Ar. The time-course of the reaction was followed in the same way as that described above. The reactivity under O_2 and Ar was very similar, and a mixture of **3** and **6** was obtained. Although **6** was formed thermally from **10** in the column of GLC, the curves in Figure 3 reflect the changes occurring in the solution.

Oxygenation of 3,5-Di-*tert*-butylcatechol (1) in the Presence of Quenchers. Oxygenation of **1** (0.223 g, 1.00 mmol) by the complex prepared by mixing $FeCl_3$ (0.021 g, 0.13 mmol), bipyridine (0.058 g, 0.38 mmol), and pyridine (0.9 cm^3, 11 mmol) was performed in THF (0.9 cm^3) for 24 h under 1 atm O_2 at 25 °C, in the presence of the quencher (1.00 mmol). In the cases of triphenylmethane (0.244 g) and β-carotene (0.537 g), yields and compositions of products were similar to the case without quenchers. When Malachite Green (0.927 g) was added, 15% of **1** was converted, and only **2** (14%) was formed. When tetranitromethane (0.12 cm^3) was added, **1** was converted completely to form only **2**. However, **1** was converted to **2** only by tetranitromethane in the absence of the iron complex.

Detection of the Acyclic Intermediate 12. (a) Oxygenation of **1** (4.0 mmol) by the iron complex ($FeCl_3$ = 0.5 mmol) was stopped after 3 h, and acid products were obtained by extraction with the $KHCO_3$ solution. ^1H and ^{13}C NMR of the product mixture indicated the formation of **3**, **12**, and another minor product. ***cis*,*cis*-3,5-Di-*tert*-butyl-2-hydroxymuconic semialdehyde (12)**: IR (neat) ν_{OH} ca. 3300 (br), ν_{CO} 1729, 1670, 1644, $\nu_{C=C}$ 1584, 1520, 735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.09 (s, 9 H), 1.16 (s, 9 H), 5.90 (s, 1 H), 9.85 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 25.3 (q, J_{CH} = 127 Hz), 29.9 (q, J_{CH} = 127 Hz), 30.0 (s), 37.0 (s), 100.0 (s), 124.2 (d, J_{CH} = 170.6 Hz), 106.7 (s), 163.0 (s), 174.3 (s), 204.4 (d, J_{CH} = 180.9 Hz). **Minor product**: ^1H NMR ($CDCl_3$) δ 1.31 (s, 9 H), 1.35 (s, 9 H), 6.10 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 28.8 (q), 29.6 (q), 31.3 (s), 33.1 (s), 106.1 (d, J_{CH} = 174 Hz), 122.5 (s), 142.3 (s), 146.1 (s), 152.4 (s), 166.9 (s). (b) The product mixture obtained in (a) was added to the 20 cm^3 THF solution of the iron(III) complex ($FeCl_3$ = 0.25 mmol) under oxygen. The time-course of the reaction was followed by analyzing the products obtained from 3 cm^3 of the reaction solution by ^1H NMR (Figure 4a) and GLC (Figure 4b). The product mixture from each aliquot of the solution was dissolved in 0.3 cm^3 of $CDCl_3$ for ^1H NMR measurement, and relative concentrations of products were estimated by comparing the peak intensity of olefinic proton. (c) The time-course of the formation of the acid products in the reaction of **1** (2.0 mmol) catalyzed by the iron complex (0.25 mmol) in 20 cm^3 of THF was followed by the ^1H NMR measurement of the extract from 3 cm^3 of aliquot of the solution after treatment with the $KHCO_3$ solution at scheduled intervals. Figure 5 shows the change of the intensities of olefinic protons of **3**, **12**, and an unidentified minor product, which are normalized by the peak intensity of $CHCl_3$ in $CDCl_3$.

$^{18}O_2$ Study of Oxygenation of 1. **1** (0.045 g, 0.20 mmol) and bipyridine (0.012 g, 0.075 mmol) were placed in a 10-cm^3 flask which was connected to a vacuum line system attached with a 200 cm^3 cylinder of $^{18}O_2$ (98.75%, CEA). After evacuation of the flask, $^{18}O_2$ and 2 cm^3 of THF solution containing $FeCl_3$ (3.3 mg, 0.021 mmol) and pyridine (0.15 cm^3) were admitted into the flask. The soltuion was stirred magnetically at 25 °C, and Ar was used to maintain 1 atmospheric pressure. After 3 or 24 h, the reaction was stopped by addition of degassed 2 N HCl. Product **3** was separated by the treatment with the $KHCO_3$ solution and analyzed by mass spectroscopy. Other products were separated by GLC and analyzed by GC–MS spectroscopy. Analysis was performed by using Hitachi M-80 (IP = 70 eV; column: 1 m OV1; 105 °C).

Synthesis and Reaction of Fe(DTBSQ)$_3$ (DTBSQ: Semiquinone form of 3,5-Di-*tert*-butyl-1,2-benzoquinone (2)). The complex was prepared by the method of Hendrickson[42] from **2** (1.00 g, 2.54 mmol), anisol (16 cm^3), and $Fe(CO)_5$ (0.2 cm^3, 1.5 mmol; 96% purity, Strem). The reaction of the complex (0.036 g, 0.050 mmol) with oxygen was performed in THF (0.5 cm^3) in the presence of pyridine (0.75 cm^3) for 24 h at 25 °C, and products were extracted in the same way as described above. Products detected were **1** 24%, **2** 60%, and **3** 1%. The reaction with $O_2^{-\cdot}$ was started by addition of pyridine (0.75 cm^3), the THF solution (0.5 cm^3) of KO_2 (0.011 g, 0.15 mmol), and 18-crown-6 (0.040 g, 0.15 mmol) to the complex (0.036 g) in Ar. Products after 24 h were **1** 3%, **2** 1%, **3** 92%, and **14** 2%. Anal. Calcd for $C_{42}H_{60}O_6Fe$: C, 70.48; H, 8.39. Found: C, 70.27; H, 8.54.

Synthesis and Reaction of K$_3$[Fe(DTBC)$_3$] (DTBC: Catecholate Form of 3,5-Di-*tert*-butylcatechol (1)). The degassed 8-cm^3 aqueous solution of $FeCl_3$ (0.162 g, 1.00 mmol) was added dropwise under Ar to the degassed 50% aqueous ethanol solution (15 cm^3) containing **1** (0.667 g, 3.00 mmol) and KOH (0.40 g, 6.0 mmol). Dark violet powder precipitated immediately, and the solution was refluxed for 3 h in Ar. The precipitates were filtered, washed with 50% aqueous ethanol in Ar, and dried under vacuum at 70 °C for 3 h.[43] Reactions of the complex (0.042 g, 0.05 mmol) with O_2 or $O_2^{-\cdot}$ were performed in the same conditions as the reactions of Fe(DTBSQ)$_3$. In the reaction with O_2, **2** 43%, **3** 38%, and **14** 7% were formed. In the reaction with $O_2^{-\cdot}$ 32% of **3** was formed, but the yield of **3** (4%) and the total yield of products were low indicating

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the further conversion of products. Anal. Calcd for $C_{42}H_{60}O_6FeK_3$: C, 60.48; H, 7.25. Found: C, 60.59; H, 7.53.

Synthesis and Reaction of K[Fe(DTBC)(bipy)(OH)$_2$]·C$_2$H$_5$OH. The degassed aqueous solution of $FeCl_3$ (8 cm^3, 0.324 g, 2.00 mmol) was added dropwise to 10 cm^3 of the degassed 50% aqueous ethanol solution containing **1** (0.445 g, 2.00 mmol), bipyridine (0.312 g, 2.00 mmol), and KOH (0.56 g, 10 mmol) and stirred at room temperature for 0.5 h. Dark violet precipitates which were formed were filtered under Ar, washed thoroughly with degassed water, and dried for 3 h at 60 °C under vacuum. The absence of Cl was shown by the elemental analysis. Although the elemental analysis was slightly above acceptable limits, the content of the DTBC ligand was estimated from the total yield of **1** and **2** formed by the decomposition of the complex with 2 N HCl and indicated the ratio of Fe:DTBC = 1:1. Reactions of the complex (0.030 g, 0.05 mmol) with O_2 and $O_2^{-\bullet}$ were performed under the same conditions as the above two cases except the addition of KO_2 (0.004 g, 0.05 mmol) and 18-crown-6 (0.012 g, 0.05 mmol). Product analysis was worked up as described above. Anal. Calcd for $C_{28}H_{42}N_2O_6FeK$: C, 56.62; H, 6.58; N, 5.08; Fe, 10.12. Found: C, 57.49; H, 6.54; N, 4.62; Fe, 10.45 (the Fe content was estimated by the EDTA titration at pH 1.8 after decomposition of the complex).

Oxygenation of 3,5-Di-*tert*-butyl-1,2-benzoquinone (2) in the Presence of 2,5-Di-*tert*-butyl-1,4-hydroquinone. Oxygenation of **2** (0.110 g, 0.500 mmol) was started in the presence of $FeCl_3$ (0.010 g, 0.063 mmol), bipyridine (0.029 g, 0.188 mmol), pyridine (0.45 cm^3, 6.2 mmol), and hydroquinone (0.056 g, 0.25 mmol) in THF (4.5 cm^3) at 25 °C under 1 atm O_2. After 24, 48, 72, and 96 h, 0.25 mmol of the hydroquinone was added. **2** was almost completely converted to give **3** 38%, **5** 20%, and **9** 18%. When the hydroquinone (1.00 mmol) was added all at once in the initial stage, yields of products after 24 h were 25%, 14%, and 18%, respectively, and 27% of **2** was not converted.

Measurements of Optical Spectra. Solutions of the complex (Fe = 10^{-3} - 10^{-1} mol dm^{-3}, the ratio of Fe:**1**:bipy:py was variable) were prepared in THF in an argon atmosphere at 25 °C. The reaction of the complex with oxygen was followed by measuring spectra at half an hour intervals after the atmosphere was replaced with oxygen. Spectra were recorded at room temperature on Shimadzu UV-260 and Hitachi EPS-3T instruments.

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Synthesis and Chemistry of Tetracyclo[8.2.2.2^{2,5}.2^{6,9}]-1,5,9-octadecatriene

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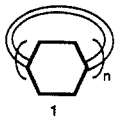
Abstract: The title compound, triene **3**, was prepared by titanium-induced cyclization of the appropriate diketone precursor, and its structure was confirmed by single-crystal X-ray crystallography. Photoelectron spectroscopy indicated that little interaction was present between double bond orbitals across the ring. Electrophilic additions took place to triene **3**, not with the normal anti stereochemistry but with deep-seated skeletal rearrangement leading to formation of hexacyclic products. Epoxidation and cyclopropanation took place normally, however. The trisepoxide prepared from triene **3** proved to be extraordinarily stable to acid treatment because of the absence of any feasible reaction pathway. The monoepoxide prepared from **3** rearranged on treatment with aqueous acid to yield a hexacyclic diol. Attempted dehydrogenation of **3** also led to formation of a rearranged hexacyclic product.

Imagine a group of compounds made of *n* six-membered rings joined by double bonds at their C1 and C4 positions to form a large overall ring as in **1**. The simplest such compound, tricyclo[4.2.2.2^{2,5}]-1,5-dodecadiene (**2**), was recently reported by Wiberg,[1] but more complex members of the group had not been prepared until our recent preliminary communication on the subject.[2]



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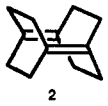
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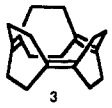
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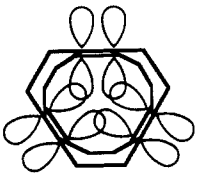
We felt that the second member of the group, tetracyclo[8.2.2.2^{2,5}.2^{6,9}]-1,5,9-octadecatriene (**3**), might prove to be a particularly interesting compound because of its rigid structure and the unusual orientation of its three double bonds. It is possible, for example, that the double bond orbitals in **3** might exhibit a through-space interaction by ppσ overlap, leading to six-electron delocalization and consequent trishomoaromaticity,[3] as indicated in structure **4**. It is also possible that **3** might show interesting chemical reactivity because of its rigidity. For example, molecular models indicate that the interior cavity of **3** is too small to allow approach of a reagent to the inside face of the double bonds. Thus, any electrophilic-addition chemistry of **3** must occur with syn stereochemistry from the outside face of the molecule. But syn addition to one of the double bonds, as in **5**, leads to introduction of a large amount of strain according to models. Unusual chemical consequences might therefore ensue.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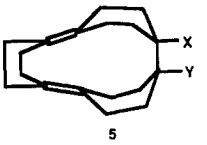

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