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INTRA- AND EXTRADIOL OXYGENATIONS OF 3,5-DI-TERT-BUTYLCATECHOL CATALYZED BY BIPYRIDINEPYRIDINEIRON(III) COMPLEX

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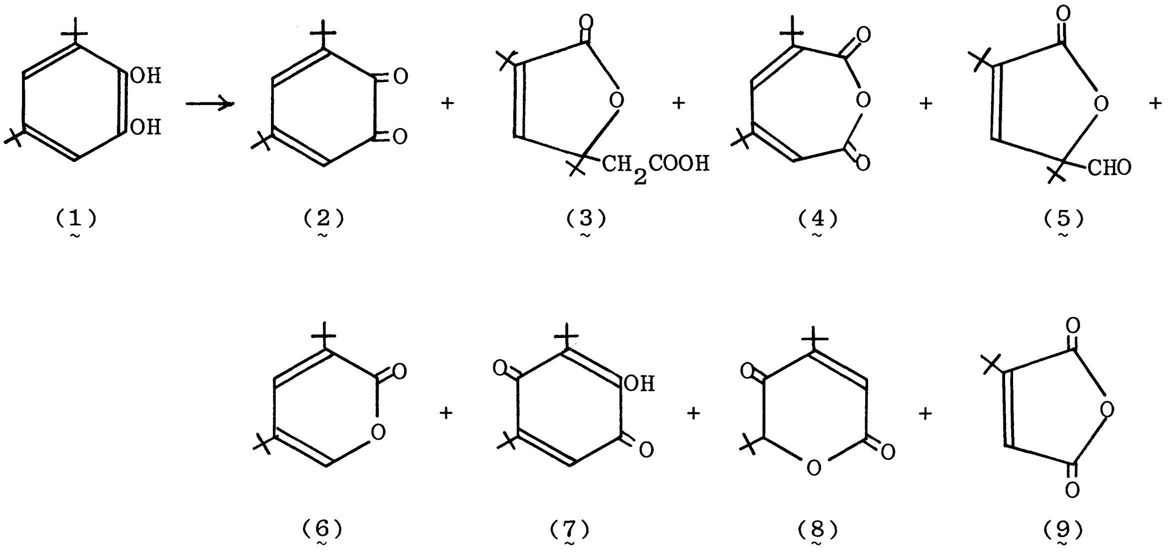
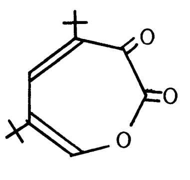
Iron(III) complex coordinated by 2,2'-bipyridine and pyridine catalyzes oxygenation of 3,5-di-t-butylcatechol with molecular oxygen to give intra- and extradiol fission products as well as oxidation to give 3,5-di-t-butyl-1,2-benzoquinone. Structures and reactivities of the products have indicated that the oxygenation proceeds by the Hamilton process rather than the dioxetane process.

Dioxygenase model reaction catalyzed by metal complexes is of current interest in connection with the development of new oxygenation catalysts and the elucidation of the reaction mechanism of oxygenase. Previously,1) we have first reported the oxygenation of 3,5-di-t-butylcatechol (1) catalyzed by an iron(II) complex coordinated by 2,2'-bipyridine (bpy) and pyridine (py), yielding 3,5-di-t-butyl-5-(carboxymethyl)-2-furanone (3) in addition to 3,5-di-t-butyl-1,2-benzoquinone (2). Although we have proposed an intermediate formation of $[Fe(bpy)(1)(py)O_2]^{2+}$, the oxygenation process has not been clear. Recently, oxygenation of (1) was performed by ruthenium complexes, and it was indicated that (3) was formed via 3,5-di-t-butyl-1-oxacyclohepta-3,5-diene-2,7-dione (4) and 4,6-di-t-butyl-2-pyrone (11) via 4,6-di-t-butyl-1-oxacyclohepta-4,6-diene-2,3-dione (12).2) It was also reported that vanadium complexes oxygenated (1) to give (4) and (11).3) These results suggest that the oxygenation proceeds by the Hamilton process4) rather than the dioxetane process.5) However, in connection with dioxygenase such as pyrocatechase and metapyrocatechase which involve non-heme iron, it is important to elucidate the oxygenation process catalyzed by the iron complex. In the previous study, we have used the Fe(II) complex because formation of the $Fe(II)-O_2$ complex seemed essential for the oxygenation. However, if the intradiol oxygenation of (1) by the iron complex to form (3) proceeds in a similar way to the Fe(III) enzymes such as pyrocatechase, it is possible that the oxygenation is catalyzed by an Fe(III) complex. Recently, it has been reported that a mixture of ferric perchlorate and sodium nitrilotriacetate catalyzes oxygenation of (1) to give (3) and its methyl ester.6) We report here that a bipyridinepyridineiron(III) complex catalyzes not only intradiol but also extradiol oxygenation of (1) by the Hamilton process.

Oxygenation of (1) (2 mmol) was performed in a THF solution at 25°C under an oxygen atmosphere by using an iron complex prepared by mixing in situ $FeCl_3$ (0.25 mmol), 2,2'-bipyridine (0.75 mmol), and pyridine (23 mmol). The reaction solution was washed with 2N HCl and water to remove the iron complex, and extracted with dichloromethane. Products were isolated by liquid column chromatography and preparative GLC, and identified by elemental analysis or GC-MS, IR and ^{1}H and ^{13}C NMR spectroscopy. Products (2)∿(9) were isolated and yields were determined by HPLC (25 cm of Zorbax ODS, eluent: MeOH(83)-pH 3.5 H_2O (17) and GLC (3m of Silicone SE-30, at 180°C).



Yields of products are shown in Table 1. Reactivities of the complexes prepared with $FeCl_3$ and $FeCl_2 \cdot 4H_2O$ were almost identical, suggesting that the real active complex is Fe(III) since Fe(II) is rapidly oxidized to Fe(III) by oxygen. 45 cm^3 (2 mmol) of oxygen was absorbed within 4 h, during which period (1) almost disappeared giving maximum yields of (2), (4), (6)∿(9) and nearly half the maximum yields of (3) and (5). Then, yields of (4) and (6) slowly decreased and those of (3) and (5) increased. Since the reaction of (4) with water gave stoichiometrically (3) as reported previously,$^{2,7)}$ (4) is an intermediate for (3). The product (6) suggests the intermediate formation of (10) in analogy with the formation of (11) from (12). Attempts to isolate (10) have not been successful. Since (6) is stable and was not converted to (5), the decrease in the yield of (6) may suggest that (6) was formed by the thermal decomposition of (10) in the isolation procedure. (5) might be formed directly from (10) after oxidation and decarbonylation, because the slow formation of (5) after 4 h stopped by removal of oxygen and started again by addition of oxygen.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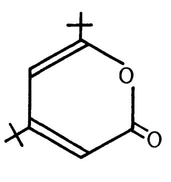
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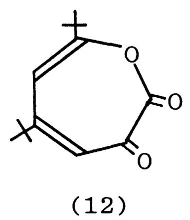
(12)

Table 1. Oxygenation of 3,5-di-t-butylcatechol (**1**) catalyzed by bipyridinepyridineiron(III) complex

Iron chloride$^{a)}$	Time/h	Yields of products/mol %$^{b)}$								
		(**1**)	(**2**)	(**3**)	(**4**)	(**5**)	(**6**)	(**7**)	(**8**)	(**9**)
$FeCl_3$	4	2	61	9	8	4	4	2	1	8
	24	tr	53	20	1	10	tr	3	2	10
$FeCl_2 \cdot 4H_2O$	24	tr	54	17	3	10	tr	3	2	8

a)Iron chlorides used for preparation of iron complex. b)HPLC ((**1**)∿(**3**)) and GLC ((**4**)∿(**9**)) yields, based on added (**1**). Biphenyl was used as an internal reference. Followings are NMR data of (**4**)∿(**9**) observed in $CDCl_3$. Resonances are singlets unless otherwise noted. (**4**) ^1H NMR 1.16 (9H), 1.28 (9H), 6.14 (d, 1H), 6.45 (d, 1H); ^{13}C NMR 28.7 (q), 28.2 (q), 36.5, 36.8, 115.7 (d, J_{CH}=167 Hz), 124.1 (d, J_{CH}=157 Hz), 148.4, 159.2, 160.5, 162.0. (**5**) ^1H NMR 1.05 (9H), 1.25 (9H), 6.90 (1H), 9.60 (1H); ^{13}C NMR 24.8)q), 28.1 (q), 32.2, 38.5, 94.5, 141.3 (d, J_{CH}=175 Hz), 146.1, 170.5, 197.3 (d, J_{CH}=185 Hz). (**6**) ^1H NMR 1.20 (9H), 1.32 (9H), 7.04 (d, 1H), 7.14 (d, 1H); ^{13}C NMR 28.4 (q), 29.5 (q), 31.9, 34.8, 127.3, 136.2, 136.3 (d, J_{CH}=156 Hz), 143.8 (d, J_{CH}=197 Hz), 160.9. (**7**) ^1H NMR 1.28 (9H), 1.37 (9H), 6.50 (1H), 7.18 (1H); ^{13}C NMR 29.6 (q), 30.2 (q), 35.5, 36.2, 125.0 (d, J_{CH}=168 Hz), 129.1, 148.8, 162.3, 184.4, 189.2. (**8**) ^1H NMR 1.01 (9H), 1.26 (9H), 4.40 (1H), 6.65 (1H); ^{13}C NMR 26.1 (q), 28.4 (q), 35.3, 37.5, 90.8 (d, J_{CH}=154 Hz), 128.9 (d, J_{CH}=169 Hz), 159.3, 161.9, 193.4. (**9**) ^1H NMR 1.32 (9H), 6.52 (1H); ^{13}C NMR 28.9 (q), 33.4, 126.9 (d, J_{CH}=183.8 Hz), 161.5, 163.5, 164.0.

Formations of (**3**) via (**4**) and (**5**) via (**10**) indicate that intra- and extradiol oxygenations by the Fe(III) complex proceed by the Hamilton process rather than the dioxetane process, similarly to the reactions by ruthenium and vanadium complexes. However, it is noteworthy that the iron complex catalyzes 1,2- and 1,6-bond fissions in contrast to the 1,2- and 2,3-bond fissions catalyzed by ruthenium and vanadium complexes. Reasons for the specific reactivity of the iron complex is not clear at present. Structures of products (**7**)∿(**9**) suggest the intermediate formation of an oxygen adduct at the 4-position of the catechol aromatic ring, and the products may be formed without via intermediates such as (**4**) and (**10**).

Although the present experiments gave no direct information on the structures of active and intermediate complexes, the facts that products are very different from those obtained by the base catalyzed autoxidation of (**1**)$^{8)}$ and that quinone (**2**) is not oxygenated by the iron complex, different from the ruthenium complex,$^{2)}$ suggest the importance of the activation of catechol by coordination to iron. (**1**) may coordinate to iron probably as a monodentate catecholate complex since it has been reported that a chelated catecholate complex is not reactive with oxygen.$^{9)}$ Since (**1**) has two hydroxyl groups, two types of coordination are possible. Supposed that the reaction proceeds via peroxide intermediates imilar to that proposed for the oxygenation by the iron enzyme,$^{10)}$ formations of three types of products, i.e.

{(3), (4)}, {(5), (6)}, and {(7)∿(9)}, seem to be explained by the intermediates formed by addition of dioxygen to the 2-, 6- and 4-positions, respectivity, of the catechlolate ligand coordinated by the 2-hydroxyl group after deprotonation probably by pyridine. However, the possibility that the three types of the oxygenation products are formed by addition of dioxygen to the 1-position of the catecholate ligand coordinated by the 1-hydroxyl group can not be excluded. Further studies are necessary for the discussion on the reaction mechanism.

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