2 H, $CH_2CH_2CH_3$), 3.2 (s, 3 H, CH_3), 3.80 (m, 6 H, NCH_2, CH_2OH), 5.10 (br s, 1 H, OH exchangeable); ^{13}C NMR ($CDCl_3$) 11.17 (C_3), 20.32 (C_2), 38.78 (CH_3), 42.53 (C_1) 51.45 (C_1'), 65.42 (C_2'), 156.58 (C=O); MS, *m/e* (relative intensity) 158.0933 (6.42, $M^+ - H_3O^+$, $C_6H_{12}N_3O_2$, 158.0929), 131.0455 (58.04, $C_4H_7N_2O_3$, 131.0457), 102.0556 (100.00, $C_4H_8NO_2$, 102.0556).

Preparation of 2-Hydroxyethyl *N*-Cyclohexylthionocarbamate (19). Cyclohexyl isothiocyanate (6.25 g, 50 mmol) was added dropwise to a stirred suspension of ethylene glycol (3.90 g, 50 mmol) in dry benzene and the reaction mixture was stirred at ambient temperature for 12 h. The solvent was removed in vacuo and the residue was triturated with petroleum ether to afford 8.5 g (84% yield) of 2-hydroxyethyl *N*-cyclohexylthionocarbamate (**19**): mp 55 °C (ether/petroleum ether); IR ($CDCl_3$) 3220 (br, NH, OH), 1665 (C=S), 1525, 1212 cm^{-1}; ^1H NMR ($CDCl_3$) 1.2–2.20 (m, 10 H, CH_2), 3.10 (t, 2 H), 3.75 (br s, 1 H, OH), 3.85 (t, 2 H, OCH_2), 5.75 (br m, 1 H, NH); ^{13}C NMR (acetone-d_6) 24.50 (C_3', C_5'), 25.66 (C_4'), 32.63 (C_1), 33.52 (C_2', C_6'), 38.73 (C_2), 51.33 (C_1'), 166.25 (C=S); MS, *m/e* (relative intensity) 203.0972 (2.06, $C_7H_{17}NO_2S$, 203.0964), 159.0712 (2.60, $C_7H_{13}NOS$, 159.0708), 144.1020 (24.57, $C_7H_{14}NO_2$, 144.1024), 83.0861 (100.00, C_6H_{11}, 83.0860).

3-Methyl-2-oxazolidinone (28). Carbon monoxide was passed slowly into a suspension of selenium (7.8 g, 100 mmol), 2-(methylamino)ethanol (7.5 g, 100 mmol), triethylamine (70 mL), and dimethylformamide (400 mL) for 3 h until the solution became clear. A slow stream of oxygen was passed into this solution to precipitate the selenium. Removal of the precipitated selenium by filtration and solvent in vacuo and then further distillation of the residual oil at reduced pressure gave 8.5 g (85% yield) of N_3-methyl-2-oxazolidinone (**28**): bp 75 °C 0.3 mm (lit.[8] bp 120 °C 1 mm); ^1H NMR ($CDCl_3$) 2.75 (s, 3 H, CH_3), 3.55 (t, 2 H, NCH_2), 4.42 (t, 2 H, OCH_2); ^{13}C NMR ($CDCl_3$) 31.0 (CH_3), 46.87 (C_4), 61.65 (C_5), 158.97 (C_2); MS, *m/e* (relative intensity) 101.0475 (100.0, $C_4H_7NO_2$, 101.0476), 56.0520 (32.53, C_3H_6N, 56.0500).

3-Methyl-2-oxazolidine-2-thione (23). This compound was prepared by following the method of Sakai et al.[9] starting from 2-(methylamino)ethanol (2.25 g, 30 mmol) and tributyltin diethylamide (27.7 g, 60 mmol) and carbon disulfide (4.5 g, 60 mmol) at room temperature. Distillation of the reaction mixture at 120 °C (0.3 mm) [lit.[9] bp 127 °C (0.4 mm)] gave 1.7 g (50% yield) of 3-methyl-2-oxazolidine-2-thione (**23**); ^1H NMR ($CDCl_3$) 3.25 (s, 3 H, CH_3), 3.90 (t, 2 H, NCH_2), 4.52 (t, 2 H, OCH_2; MS, *m/e* (relative intensity) 117.0248 (100.0, C_4H_7NOS, 117.0249).

***N*$_1$,*N*$_3$-Dipropyl-*N*$_1$-nitrosourea (R = R$_1$ = Propyl).** 1,3-Dipropylurea (2.88 g, 20 mmol) was nitrosated with sodium nitrite (2.80 g, 40 mmol) in formic acid (21 mL) at 0 °C and after the usual workup it afforded 3.09 g (86% yield) of the nitrosourea: mp 31 °C; IR ($CHCl_3$) 3385, 1715, 1530, 1485, 1166, and 1022 cm^{-1}; ^1H NMR ($CDCl_3$) 0.85 (t, 3 H, CH_3, J = 6.5 Hz), 0.95 (t, 3 H, CH_3), 1.50 (m, 2 H, CH_2), 1.62 (m, 2 H CH_2), 3.45 (q, 2 H, CH_2), 8.10 (t, 2 H, CH_2), 7.00 (br m, 1 H, NH exchangeable); MS, *m/e* (relative intensity) 173.1162 (11.64, M^+, $C_7H_{15}N_3O_2$, 173.1164), 88.0639 (100.00, $C_3H_8N_2O$, 88.0637), 86.0608 (18.26, C_4H_8NO, 86.0605); ^{13}C NMR ($CDCl_3$) 11.26 (C_3, C_3'), 20.40 (C_2), 23.00 (C_2'), 41.20 (C_1), 42.48 (C_2'), 153.48 (C=O); ^{13}C NMR (acetone-d_6) 11.49 (C_3, C_3'), 21.05 (C_2), 23.60 (C_2'), 41.49 (C_1), 42.48 (C_1'), 154.23 (C=O).

^{18}O Exchange at the Thiocarbonyl Group of Nitrosothiourea (3). A degassed solution of **3** (0.1 mmol) in a mixture of acetonitrile (0.2 mL) and $H_2{}^{18}O$ (97% enriched 1.5 mL) with 40 mm potassium phosphate buffer, pH 7.1, was allowed to react for 12 h at 25 °C. The reaction mixture was extracted with ether (4 × 10 mL), the extract was dried (Na_2SO_4), and the solvent was removed in vacuo. The residue was analyzed by mass spectrometry. The carbonyl fragment in the corresponding urea which is the major product under these conditions containing the ^{18}O was $CH_3CH_2CH_2NHC{\equiv}{}^{18}O$ 88.0639 (6.35, $C_4H_8N^{18}O$, 88.0630).

Caution. All *N*-nitrosothioureas should be handled with extreme care owing to their potential mutagenicity.

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Registry No. **1**, 79645-01-5; **2**, 79645-03-7; **3**, 84050-92-0; **4**, 84050-94-2; **5**, 84050-93-1; **6**, 79645-04-8; **7**, 84050-96-4; **8**, 79645-05-9; **9**, 84056-92-8; **9a**, 87191-78-4; **10**, 87191-77-3; **14**, 87191-80-8; **15**, 87191-81-9; **15a**, 87191-84-2; **18**, 76310-06-0; **19**, 87191-82-0; **21**, 56242-66-1; **21a**, 87191-85-3; **22**, 13027-13-9; **23**, 30537-18-9; **26**, 87191-86-4; **28**, 19836-78-3; 3-cyclohexyl-1-(2,2-dideuterio-2-hydroxyethyl)thiourea, 77081-32-4; *n*-propyl isothiocyanate, 628-30-8; 2-(methylamino)ethanol, 109-83-1; 3-(2-hydroxyethyl)-3-methyl-1-propylthiourea, 87191-79-5; cyclohexyl isothiocyanate, 1122-82-3; 2-chloroethylamine, 689-98-5; 2-chloroethylamine hydrochloride, 870-24-6; 3-cyclohexyl-1-(2-chloroethyl)thiourea, 87191-83-1; 2-(cyclohexylamino)thiazoline hydrochloride, 80672-59-9; 2-(cyclohexylamino)thiazoline, 56242-66-1; *n*-propyl isocyanate, 627-36-1; 3-(2-hydroxyethyl)-3-methyl-1-propylurea, 87191-87-5; ethylene glycol, 107-21-1; carbon monoxide, 630-08-0; selenium, 7782-49-2; tributyltin diethylamide, 1066-87-1; carbon disulfide, 75-15-0; 1,3-dipropylurea, 623-95-0.

Mechanism of the Fe(III)-Catalyzed Peracetic Acid Oxidation of Catechol. A Biomimetic Reaction for Pyrocatechase[28]

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The Fe(III)-catalyzed peracetic acid (HOOAc) oxidation of catechol to *cis,cis*-muconic acid (MA) is proposed as a model for the action of the Fe(III)-containing dioxygenase pyrocatechase (catechol 1,2-dioxygenase). The yield of MA is a function of the [Fe(III)] reaching a maximum of 75% when the ratio [catechol]/[Fe(III)] is 1000. No appreciable quantity of MA is formed in the absence of Fe(III). Evidence is presented that implicates peracetic acid and hydrogen peroxide as the active oxidants and *o*-benzoquinone as an intermediate in the reaction. Substrate binding to Fe(III) represents an important part of the reaction. The proposed mechanism for the model involves formation of an Fe(III)–catechol complex which is oxidized to an Fe(III)–*o*-benzoquinone species. The Fe(III)–quinone complex then undergoes nucleophilic attack at carbonyl by H_2O_2 to give a peroxide addition product which undergoes intramolecular nucleophilic addition at the adjacent carbonyl to give a dioxetane intermediate. Spontaneous opening of the dioxetane gives MA.

Since Hayaishi's discovery of the first oxygenase, pyrocatechase (catechol 1,2-dioxygenase), there has been considerable interest in the mechanism of pyrocatechase activity and that of oxygenases in general.[1-9] However, no

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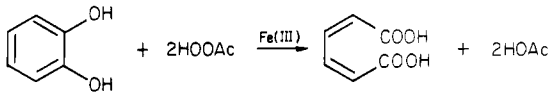
detailed mechanism for the action of pyrocatechase or a model system has been proposed. Pyrocatechase contains 1 mol of nonheme Fe(III) per mol of enzyme and no other cofactors.[10] It is classified as a dioxygenase because it incorporates two atoms of oxygen from molecular oxygen into catechol via intradiol ring cleavage to *cis,cis*-muconic acid.[2]

We propose the Fe(III)-catalyzed peracetic acid oxidation of catechol (1) to *cis,cis*-muconic acid (2, MA)[11] as a



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chemical model for pyrocatechase. Catechol is oxidatively cleaved in an intradiol fashion to MA by HOOAc in the presence of Fe(III), Cu(II), or Mo(VI), with Fe(III) being the most effective catalyst. The yields of MA with Fe(III) are relatively high (about 75%), and MA is not formed in appreciable quantities in the absence of Fe(III), Cu(II), or Mo(VI). Phenol is also oxidized to MA by HOOAc in the presence of catalytic quantities of Fe(III) and Cu(II).[12] This reaction involves hydroxylation of phenol to give a mixture of catechol and *p*-hydroquinone followed by oxidation of catechol to MA. The metal is *not* involved in the hydroxylation process. The yield of MA from phenol was found to be a function of the Fe(III) concentration. Fe(III) was effective at catalyzing the formation of MA in reactions where the ratio [Fe(III)]/[phenol] was as low as 2×10^{-6}.

In this paper, we propose the first detailed mechanism for a pyrocatechase model reaction. The Fe(III)-catalyzed peracetic acid oxidation of catechol provides an excellent model for pyrocatechase since it effectively mimics its activity. The proposed model does exactly what the enzyme does, employing the same substrate and the same metal ion. It is remarkable that Fe(III) alone can accomplish essentially the same transformation as pyrocatechase with the loss of only a small amount of specificity (i.e., the yield is not 100%). These results suggest that Fe(III) plays the pivotal role in pyrocatechase activity and that the protein portion of the enzyme functions primarily to bind the substrate in such a manner to make cleavage 100% regiospecific. The model reaction is extremely rapid, as evidenced by the fact that only trace quantities of Fe(III) are required to effect the transformation of catechol to MA. As far as we are aware, our system represents the only chemical model for pyrocatechase that involves an Fe(III)-catalyzed oxidation of catechol to MA. Other proposed models do not involve Fe(III) catalysis, and some do not involve catechol as the substrate.[13-17] Rogic and Demmin[18] have recently shown that the Cu(II)-induced oxygenolysis of catechol reported earlier by Tsuji and Takayanagi[13] and Rogic and co-workers[16] does *not* involve activation of molecular oxygen or Cu(II) catalysis but rather a direct oxidation by Cu(II) with oxygen functioning to oxidize Cu(I).

Experimental Section

Melting points were determined on a Fisher-Johns apparatus and are uncorrected. UV spectra were obtained on a Varian Model 635 recording spectrophotometer. NMR spectra were recorded on a Perkin-Elmer R12B spectrometer.

Materials. The acetic acid was Matheson Scientific, ACS reagent. The peractic acid was obtained from FMC as a 40 wt % solution. Catechol was supplied by Fisher (certified). Veratrole, 9,10-phenanthrenequinone, and diphenic acid were obtained from Aldrich. *m*-Chloroperoxybenzoic acid was supplied by MCB. The ferric acetate (purified powder basic) was obtained from City Chemical Corporation. The cupric acetate monohydrate (reagent grade) was supplied by MCB and was found to contain 0.0007 wt % Fe as determined by atomic absorption analysis. With the exceptions of W(VI), Ti(IV), Al(III), and Mo(VI), all metals employed in reactions were obtained as reagent grade acetate salts and were used as received. The sources of the other metal ions were as follows: Al(III), $Al(OH)_3$; Ti(IV), TiO_2; W(VI), $Na_2WO_4 \cdot 2H_2O$; Mo(VI), $NaMoO_4 \cdot 2H_2O$. The $Na_2WO_4 \cdot 2H_2O$ contained 0.11 wt % Fe as determined by atomic absorption and hence catalyzed the formation of MA. The sodium molybdate (ACS reagent) was supplied by Spectrum Chemical and was found to contain less than 1 ppm Fe as determined by atomic absorption analysis. The hydrogen peroxide was ACS reagent from Spectrum. The acetic anhydride was ACS reagent from Eastman.

General Procedure for Metal-Catalyzed Peracetic Acid Oxidations of Catechol. With the exception of varying the kind and quantity of metal, the same procedure was followed for all catechol oxidations. The following Fe(III)-catalyzed reaction illustrates the general procedure.

To a magnetically stirred solution of 5.0 mL of HOAc, 15.0 mL of 40% HOOAc (6.90 g, 0.0908 mol of HOOAc), and 0.0032 g (0.000168 mol) of ferric acetate at 25 °C in a 50-mL Erlenmeyer flask was slowly added, at a rate of approximately 1 drop/min from a micrometer addition funnel, 10.0 mL of an HOAc solution containing 3.07 g (0.0279 mol) of catechol. MA began to precipitate from solution after about 1 h. The catechol addition was complete in 5 h. The reaction mixture was stirred an additional hour and then cooled in an ice-water bath. The white product was isolated by filtration, yielding 2.91 g (73%) of MA. The product was characterized as previously described.[12]

Fe(III)-Catalyzed Peracetic Acid Oxidations of Catechol with Added Ethylenediaminetetraacetic Acid (EDTA) or Water. The same general procedure described above was used except that varying amounts of EDTA (disodium salt, Mallinckrodt, Analytical reagent) or water were added to the initial solution of Fe(III), HOOAc, and HOAc. In experiments with added water, the total volume was kept constant by removal of a corresponding amount of acetic acid.

Fe(III)-Catalyzed Hydrogen Peroxide Oxidations of Catechol. The same general procedure was employed except that 30% H_2O_2 was used in place of peracetic acid. The reaction mixture became very dark (essentially black) after 24 h and *no*

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MA precipitated from solution.

When one drop of concentrated H_2SO_4 was added to the Fe(III)/HOAc/H_2O_2 mixture and it was allowed to stand for 24 h before the reaction was initiated by catechol addition, a 27% yield of MA was obtained.

Attempted Fe(III)-Catalyzed *m*-Chloroperoxybenzoic Acid Oxidation of Catechol. To a magnetically stirred solution of 0.0061 g (0.0000319 mol) of ferric acetate and 4.24 g (0.0245 mol) of *m*-chloroperoxybenzoic acid, dissolved in a mixture of 10 mL of chloroform and 5 mL of HOAc, was added dropwise, over a period of 1 h, 0.136 g (0.00123 mol) catechol dissolved in 10 mL chloroform. The reaction mixture was stirred at room temperature for 48 h after which a saturated aqueous Na_2SO_3 solution was added dropwise to the reaction mixture until all peroxides were reduced, as indicated by KI–starch test paper. The organic layer was washed with water, dried with $MgSO_4$, and concentrated to 2.7 g of solid, mp 145–155 °C, which was determined by UV analysis to be primarily *m*-chlorobenzoic acid containing small amounts of catechol. *No* MA was found to be present.

Attempted Fe(III)-Catalyzed Oxidation of Catechol with Hydrogen Peroxide Free Peracetic Acid. The general procedure was followed except that hydrogen peroxide free peractic acid was employed as the oxidant. It was freshly prepared before each use by adding 30% H_2O_2 dropwise to a slight excess of acetic anhydride. Standard methods of analysis indicated that no hydrogen peroxide was present in these freshly prepared solutions.[22] Oxidations of catechol with this reagent gave intensely black solutions containing no MA.

Attempted Fe(III)-Catalyzed Peracetic Acid Oxidation of Veratrole (1,2-Dimethoxybenzene). The procedure was the same as that for catechol oxidations. The ratio [veratrole]/[Fe(III)] was 900. A 91% yield of unreacted veratrole was obtained. NMR and UV spectra were identical to those of authentic veratrole samples and further indicated the absence of *cis,cis*-muconic acid and derivatives.

Fe(III)-Catalyzed Peracetic Acid Oxidation of 9,10-Phenanthrenequinone. To a magnetically stirred solution containing 0.0066 g (0.000034 mol) of ferric acetate, 5 mL of HOAc, and 15 mL of 40% HOOAc (0.0908 mol HOOAc) was added, dropwise over 30 min, a solution of 1.01 g (0.00485 mol) of 9,10-phenanthrenequinone dissolved in 45 mL of chloroform. The reaction mixture was stirred at room temperature for 48 h, after which it was treated with saturated, aqueous Na_2SO_3 until there was no color change in KI–starch test paper. After separation, the aqueous layer was extracted with ether and then chloroform. The combined organic phases were washed with water, dried with $MgSO_4$, filtered, and concentrated to 0.73 g of solid, mp 227–233 °C. A UV spectrum was identical to that of an authentic sample of diphenic acid (mmp 225–232 °C). The yield was 62%.

A 51% yield of diphenic acid was obtained in a reaction carried out in the absence of Fe(III).

Fe(III)-Catalyzed Hydrogen Peroxide Oxidation of 9,10-Phenanthrenequinone. To a magnetically stirred solution containing 0.0063 g (0.0000329 mol) of ferric acetate, 5 mL of HOAc, and 10 mL of 30% H_2O_2 (3.3 g, 0.097 mol) was added dropwise, over a period of 45 min, a solution of 1.04 g (0.00499 mol) of 9,10-phenanthrenequinone dissolved in 25 mL of chloroform. The resulting two-phase system was vigorously stirred for 48 h at room temperature, after which it was treated with saturated, aqueous Na_2SO_3 until there was no color change in KI–starch test paper. The aqueous layer was extracted with ether, and the combined organic layers were washed with water, dried with $MgSO_4$, filtered, and concentrated to 0.91 g (75%) of diphenic acid, mp 230–233 °C (characterized as described in the previous procedure).

A 59% yield of diphenic acid was obtained in a reaction carried out in the absence of Fe(III).

Attempted Fe(III)-Catalyzed Oxidation of 9,10-Phenanthrenequinone with *m*-Chloroperoxybenzoic Acid. To a magnetically stirred solution of 0.0058 g (0.000030 mol) of ferric acetate and 4.77 g (0.0277 mol) of *m*-chloroperoxybenzoic acid, dissolved in a mixture of 10 mL of HOAc and 10 mL of chloroform, was added dropwise a solution of 0.235 g (0.00113 mol) of 9,10-phenanthrenequinone dissolved in 40 mL of chloroform. The reaction mixture was stirred at room temperature for 48 h. Workup as described above gave 4 g of white solid, mp 155–158 °C, which was determined to be *m*-chlorobenzoic acid. UV analysis of the reaction mixture indicated the absence of diphenic acid.

Table I. Metal Catalysts for HOOAc Oxidation of Catechol

metal	log K_s[a]	reduction potentials[b] $M^{n+} + xe^- \rightarrow M^{n-x}$, E°, V
Fe(III)	21[c]	$Fe^{3+} \rightarrow Fe^{2+}$, +0.77
Ti(IV)	19	$Ti^{4+} \rightarrow Ti$, −0.86
Al(III)	17	$Al^{3+} \rightarrow Al$, −1.66
Cu(II)	14	$Cu^{2+} \rightarrow Cu^{+}$, +0.15
Zn(II)	10	$Zn^{2+} \rightarrow Zn$, −0.76
Ni(II)	9	$Ni^{2+} \rightarrow Ni$, −0.25
Co(II)	8	$Co^{2+} \rightarrow Co$, −0.28
Mn(II)	8	$Mn^{2+} \rightarrow Mn$, −1.18
Fe(II)	6	$Fe^{2+} \rightarrow Fe$, −0.44
W(VI)	6	$W^{6+} \rightarrow W$, −0.09
Mo(VI)	5	$Mo^{6+} \rightarrow Mo^{5+}$, +0.4
V(O)	*d*	$V^{2+} \rightarrow V$, −1.2
Ag(I)	*d*	$Ag^{+} \rightarrow Ag$, +0.80
Na(I)	*d*	$Na^{+} \rightarrow Na$, −2.71
Hg(II)	*d*	$2\,Hg^{2+} \rightarrow Hg_2^{2+}$, +0.92
Cr(III)	*d*	$Cr^{3+} \rightarrow Cr^{2+}$, −0.41
Ru(III)	*d*	$Ru^{3+} \rightarrow Ru$, −0.1

[a] From ref 25 unless otherwise indicated. K_s is the stability constant for the catechol complex, ML^{n-2}. [b] Reference 26. [c] Reference 27. [d] Not reported; expected to be small.

Results and Discussion

Catalysts. We have carried out the catechol oxidation in the presence of the metals listed in Table I. Only Fe(III), Mo(VI), and Cu(II) are effective catalysts in the reaction, giving yields of MA as high as 75%, 40%, and 37%, respectively. The other metals listed give little or no MA product.[19] It appears there are two criteria that must be met for a metal to serve as an effective catalyst in this reaction. (1) The metal must bind catechol strongly, i.e., the stability constant for the metal–catechol complex must be large. (2) The metal must be easily reduced. Table I lists the metals we have used in our studies and gives their respective reduction potentials and stability constants for catechol complexes. As is evident from the data, Fe(III), Mo(VI), and Cu(II) fit the stated criteria best, with Fe(III) being the most effective catalyst. Although Al(III) and Ti(IV) form very stable catechol complexes, they do not possess the desired redox chemistry, and, hence, do not serve as catalysts for the reaction.

EDTA and water were found to inhibit the formation of MA in Fe(III)-catalyzed reactions. As the ratio [EDTA]/[Fe(III)] was increased, the yield of MA dropped, eventually becoming 6% at a ratio of 100:1. EDTA binds Fe(III) strongly,[20] thus competing with the substrate (catechol) for available Fe(III) resulting in a lower yield of MA.

Added water also lowers the yield of MA in Fe(III)-catalyzed oxidations of catechol, presumably because it ties up the Fe(III) through complex ion formation. We obtained a 74% yield of MA in 4 M water (no added water),[21] a 64% yield in 13 M water, and a 51% yield in 31 M water. No MA was formed in aqueous solvent.

(19) Trace Quantities of MA are probably formed in all oxidations; however, in the absence of Fe(III), Cu(II), or Mo(VI) the yield is estimated to be less than 1%.

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(21) 40% peracetic acid contains 13.3% water which translates into 4 M for reactions carried out without "added" water.

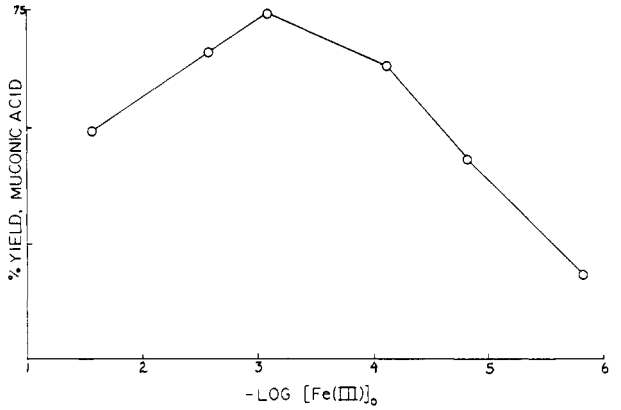


Figure 1. Yield of muconic acid vs. -log [Fe(III)]$_0$ ([catechol]$_0$ = 0.93 M).

The use of tris(2,2′-bipyridyl)iron(III) sulfate, a substitution-inert complex, in place of iron(III) acetate lowers the yield of MA from 64% to 28%.

The above results give strong evidence for the Fe(III) binding of substrate and/or intermediates during the course of the reaction.

The yield of MA is a function of the Fe(III) concentration as shown in Figure 1 and decreases at both high and low [Fe(III)], reaching a maximum of 75% at 8.4×10^{-4} M. The decreased yield at high [Fe(III)] is due to a competing reaction that does not yield MA—the direct oxidation of catechol by Fe(III) presumably to *o*-quinone and polymerized byproducts. This was confirmed by an experiment in which HOAc solutions of catechol and Fe(III) (molar ratio 50:1) were mixed in the absence of HOOAc, giving, in minutes, a black solution containing black particulate matter.

Active Oxidant. Peracetic acid and hydrogen peroxide are required for MA formation in the Fe(III)-catalyzed oxidation of catechol. If either is absent, *no* MA is formed. The 40% peracetic acid used in our experiments is actually an equilibrium mixture consisting of approximately 41% HOOAc, 39% HOAc, 13% H_2O, and 5% H_2O_2 (by wt).[22] It is prepared by the supplier (FMC Corp.) by reacting 90% H_2O_2 with glacial acetic acid in the presence of small quantities of sulfuric acid.

When the oxidation of catechol was attempted with 30% hydrogen peroxide *no* MA was formed. Although a solution of hydrogen peroxide and glacial acetic acid (the solvent) was ineffective in oxidizing catechol to MA, if a trace of strong acid (H_2SO_4) was added to the peroxide–acetic acid mixture and it was allowed to stand for several hours before the reaction was initiated, a 27% yield of MA was obtained. The strong acid and waiting period allowed significant equilibrium quantities of peracetic acid to accumulate. These results clearly support the idea that peracetic acid is required in the oxidation of catechol to MA.

When hydrogen peroxide free peracetic acid was used as the oxidant, *no* MA was formed. In addition, *m*-chloroperoxybenzoic acid was ineffective in oxidizing catechol to MA. These results, taken in conjunction with those above, clearly indicate that *both* peracetic acid and hydrogen peroxide are required for the Fe(III)-catalyzed oxidation of catechol to MA.

The oxidation of a stable *o*-quinone analogue, 9,10-phenanthrenequinone, was studied to obtain evidence for the possible intermediacy of *o*-benzoquinone in the oxidation of catechol to MA. A study of the direct, controlled oxidation of *o*-benzoquinone was not possible because of its instability. 9,10-Phenanthrenequinone (**3**) was oxidized

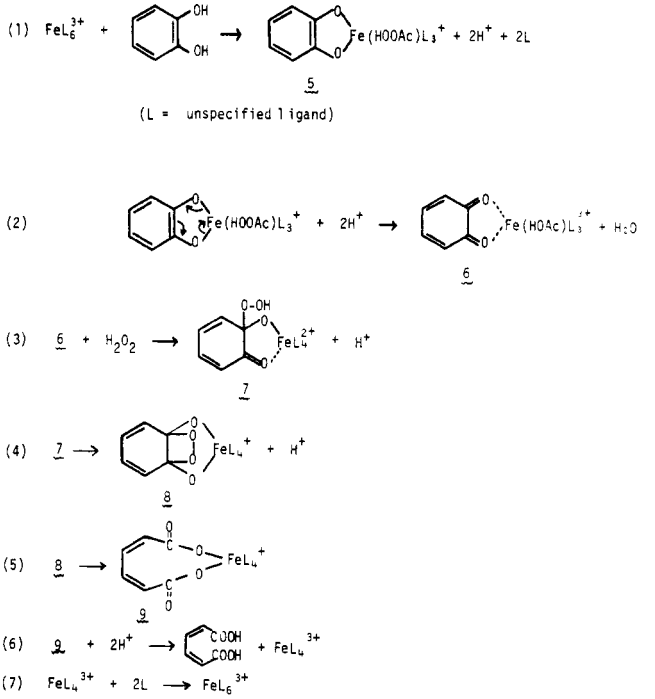
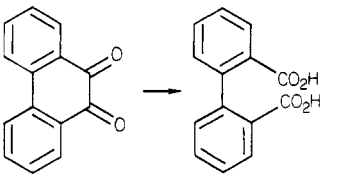


Figure 2. Proposed mechanism for Fe(III)-catalyzed peracetic acid oxidation of catechol.



3 4

to diphenic acid (**4**), an analogue of MA, under the same conditions employed for catechol oxidations.

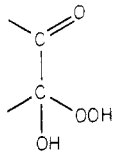
A 62% yield of **4** was obtained in an Fe(III)-catalyzed peracetic acid oxidation, whereas a reaction carried out with *no* Fe(III) gave a 51% yield of **4**. The quinone **3** was oxidized to the acid **4** in 75% yield employing 30% H_2O_2 as the oxidant and Fe(III) as catalyst. When the H_2O_2 oxidation was carried out in the absence of Fe(III), a lower yield of 50% **4** was obtained. The use of a *pure* peracid, *m*-chloroperoxybenzoic acid, as oxidant with Fe(III) as catalyst gave *no* diphenic acid. These results give strong evidence for the intermediacy of *o*-benzoquinone in the catechol oxidation and for H_2O_2 as the active oxidant in the conversion of ortho quinone to dicarboxylic acid. Thus, it appears that HOOAc is the active oxidant for conversion of ortho diol to ortho quinone, but plays no part in the oxidation of the quinone to dicarboxylic acid.

Further evidence for *o*-benzoquinone as an intermediate in the oxidation of catechol was obtained from the attempted and unsuccessful oxidation of veratrole (*o*-dimethoxybenzene) to MA or its dimethyl ester. Veratrole cannot be oxidized to ortho quinone because of the O–CH_3 bond, and thus the aromatic ring is not cleaved to give dimethyl *cis,cis*-muconate.

Reaction Mechanism. The proposed mechanism for the Fe(III)-catalyzed HOOAc oxidation of catechol to MA is shown in Figure 2. It accounts for all the experimental data and employs only known chemical reactions. Step 1 involves binding of Fe(III) to the substrate to form an Fe(III)–catechol complex (**5**), a step strongly suggested by

(22) "Peracetic Acid 40%", Bulletin No. 4; FMC, Becco Chemical Division: Buffalo, NY.

our EDTA and related results. Step 2 represents the oxidation of bound catechol to bound *o*-benzoquinone (**6**). Electrons are transferred through Fe(III) to a coordinated HOOAc ligand which is reduced to HOAc—a two-electron process. Peracetic acid is the oxidant of choice for this process since we have demonstrated that it is required for the overall conversion of catechol to MA but that it is *not* the active oxidant in the conversion of quinone to acid. The binding of *o*-benzoquinone to Fe(III) helps stablize an otherwise unstable structure, and, further, functions to make the carbonyl more susceptible to nucleophilic attack by H_2O_2 in the following step. Steps 3, 4, and 5 represent oxidative ring opening by H_2O_2. Our results with 9,10-phenanthrenequinone clearly indicate that H_2O_2 oxidizes ortho quinones to dicarboxylic acids. Thus, step 3 involves nucleophilic attack on the carbonyl group of the quinone to give **7**. Evidence for this mode of reaction comes from the work of Patchett and Witkop,[23] who isolated a peroxide adduct of the ortho quinone carbonyl group containing structure **10** in the oxidation of *o*-



10

benzoquinone *dimer* with H_2O_2. This compound results from the addition of H_2O_2 to the carbonyl of the ortho quinone structure in the dimer, and it was observed to readily decompose with C–C bond cleavage to give a dicarboxylic acid, the dimeric analogue of MA.

Step 4 involves intramolecular nucleophilic attack on the adjacent carbonyl to give the dioxetane **8**, which spontaneously decomposes (step 5) to give MA. The postulation of a 1,2-dioxetane intermediate is reasonable in light of our results and well-documented studies on the preparation and decomposition of 1,2-dioxetanes formed in singlet oxygen reactions.[24]

We have presented a resonable mechanism of a biomimetic reaction for the dioxygenase, pyrocatechase. Our studies of the model reaction have provided us with insights to the enzymic process and suggest a peroxide mechanism for pyrocatechase activity.

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Registry No. **1**, 120-80-9; **2**, 1119-72-8; **3**, 84-11-7; **4**, 482-05-3; Fe, 7439-89-6; Mo, 7439-98-7; Cu, 7440-50-8; HOOAc, 79-21-0; pyrocatechase, 9027-16-1.

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(28) Presented in part at the 183rd National Meeting of the American Chemical Society, Las Vegas, NV, April 1982.

Stereochemical Kinetics of the Thermal Stereomutations of 1-Cyano-2-phenyl-1,3-dideuteriocyclopropanes

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A complete kinetic analysis of the stereomutations that interconvert the isomers of 1-cyano-2-phenyl-1,3-dideuteriocyclopropane at 242.1 °C has been attained by following the thermolysis of (+)-(1*S*,2*S*,3*S*)-*r*-1-cyano-*t*-2-phenyl-1,*c*-3-dideuteriocyclopropane and its stereoisomers. The kinetic parameters describing the time evolution of the set of eight isomers are K_{eq}(cis/trans) = 0.40 and rate constants ($\times 10^5$ s) $k_1 = 0.76$, $k_2 = 0.33$, $k_{12} = 0.60$, $k'_{12} = 0.43$; k_{13}, k_{23}, k_3, and k'_3 are all found to be zero. In this system, and in contrast to results obtained for the 1-cyano-2-methyl-1,2,3-trideuteriocyclopropanes and the 2,3-dideuterio-2-(methoxymethyl)spiro[cyclopropane-1,1′-indenes], all stereomutations may be rationalized in terms of C(1)–C(2) bond cleavage.

Thermal interconversions of one to another cyclopropane may follow several alternative paths.[1] In an unsymmetrically disubstituted cyclopropane, for instance, the kinetic situation is defined by four possible isomers and five independent kinetic parameters (Scheme I). A kinetic study for such a system can give no more than these five parameters. In Scheme I, the independent rate constants are given symbolic names (with subscripts *d*, *h*, and *v* for diagonal, horizontal, and vertical; rate constants *k* label reactions of a trans isomer, while *k′* rate constants designate reactions of a cis isomer) and are associated with heavy arrows; the reactions symbolized with light arrows all have rate constants that may be calculated from the four rate constants given, the equilibrium constant K_{eq},

(1) Recent reviews on this topic include: Berson, J. A. In "Rearrangements in Ground and Excited States"; Academic Press: New York, 1980; Vol. 1, Chapter 5. Gajewski, J. J. "Hydrocarbon Thermal Isomerizations"; Academic Press: New York, 1981; pp 28-36. Borden, W. T. In "Reactive Intermediates"; Wiley: New York, 1981; Vol. II, Chapter 5.

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