The n.m.r. spectra were measured in dimethyl sulfoxide solution ($\sim$0.8 $M$ in solute) with a Varian model A60 spectrometer, using benzene as an external reference.

The infrared spectra were measured with a Beckman IR-7 spectrometer in $D_2O$ solution, 25-$\mu$ path length, solvent compensated as described in earlier papers.[1,2,11]

The author is indebted to Mr. Joe Frazier and Mr. Robert Bradley for invaluable assistance in measuring the infrared and n.m.r. spectra, respectively.

(11) H. T. Miles, Biochim. Biophys. Acta, 30, 324 (1958).

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## A HYDROXYLATION OF ANISOLE BY HYDROGEN PEROXIDE REQUIRING CATALYTIC AMOUNTS OF FERRIC ION AND CATECHOL[1,2]

*Sir:*

During an investigation of possible models for metal containing enzymes which catalyze oxidation–reduction reactions, we have found that hydrogen peroxide hydroxylates anisole in an aqueous system in the presence of catalytic amounts of ferric ion and catechol. Typical reactant concentrations are given under Fig. 1. The
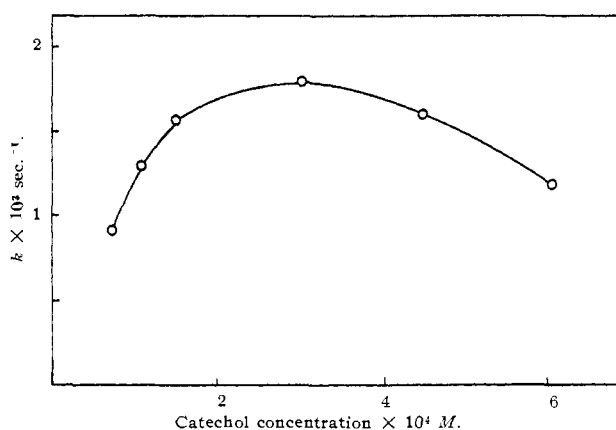


Fig. 1.—The effect of catechol concentration on the rate of reaction of hydrogen peroxide. Initial reactant concentrations: acetate buffer, 0.005 $M$, pH 4.3; $NaClO_4$, 0.15 $M$; $Fe(ClO_4)_3$, 3.94 × $10^{-5}$ $M$; anisole, approximately 0.01 $M$; hydrogen peroxide, 1.75 × $10^{-3}$ $M$; temperature, 25.0°.

hydrogen peroxide (as measured polarographically) reacts according to first-order kinetics and the reaction continues until all the hydrogen peroxide is used up. If either the ferric ion or catechol is omitted, no reaction of hydrogen peroxide occurs. If anisole alone is omitted, approximately 20 to 30% of the hydrogen peroxide reacts and then the reaction stops. The reaction will proceed if either the buffer or sodium perchlorate (necessary for the polarographic assay) is omitted.

The rate of reaction of hydrogen peroxide is directly proportional to the ferric ion concentration at constant catechol concentration. The data in Fig. 1 indicate that at low concentrations of catechol the rate increases with increasing catechol but at high concentrations the rate falls off, the maximum being around 3 × $10^{-4}$ $M$ catechol.

The hydroxylated products observed in this and some other hydroxylation reactions are shown in Table I.

TABLE I

PRODUCTS FROM THE HYDROXYLATION OF ANISOLE BY HYDROGEN PEROXIDE[a]

| Conditions | % Yield of phenols[b] | ortho | meta | para |
|---|---|---|---|---|
| Ferric–catechol system[c] | 55 | 64 | 3 | 33 |
| Ferric–hydroquinone system[d] | 58 | 65 | <5 | 35 |
| Fenton reaction[e] | 20 | 86 | 0 | 14 |
| Udenfriend system[f] | 5 | 88 | 0 | 12 |

[a] Analyzed by gas chromatography. [b] Yield based on initial amount of hydrogen peroxide. [c] Acetate buffer, 0.005 $M$, pH 4.3; $NaClO_4$, 0.15 $M$; anisole, approximately 0.01 $M$; catechol, 15 ×$10^{-5}$ $M$; $Fe(ClO_4)_3$, 7.9 × $10^{-5}$ $M$; $H_2O_2$, 1.75 × $10^{-3}$ $M$. [d] Same as ref. *c* but with hydroquinone, 15 × $10^{-5}$ $M$, instead of catechol. [e] Acetate buffer, $NaClO_4$, anisole, and $H_2O_2$ same as ref. *c* and in addition $Fe(ClO_4)_2$, 2.01 × $10^{-3}$ $M$. [f] Acetate buffer, $NaClO_4$, and anisole same as ref. *c* and in addition: $Fe(ClO_4)_3$, 2.17 × $10^{-3}$ $M$; ethylenediaminetetraacetic acid, 8.0 × $10^{-3}$ $M$; L(+) ascorbic acid, 1.01 × $10^{-2}$ $M$; $H_2O_2$, 1.79 × $10^{-2}$ $M$.

Hydroquinone gives a reaction similar to that catalyzed by catechol but both these systems give an isomer distribution of products which is different from that observed in the Fenton reaction[3] or in a system involving ascorbic acid, originally studied by Udenfriend and co-workers[4] and more recently by others.[5] The Fenton reaction, in which stoichiometric amounts of $Fe^{++}$ and $H_2O_2$ are used, apparently involves the hydroxyl radical as the hydroxylating agent,[3] and the similarity of products in the Udenfriend system indicates that the same hydroxylating species is involved.[6] Presumably a different hydroxylating agent is involved in the catechol and hydroquinone systems since higher yields of products are obtained and the isomer distribution is different. Also, ascorbic acid is present in stoichiometric amounts in the Udenfriend system, whereas the catechol and hydroquinone systems are catalytic; at least seven to ten molecules of methoxyphenol are formed for each initial molecule of catechol or hydroquinone.

We have not been able to rationalize the kinetics of the reaction in terms of a free radical chain mechanism. The products indicate that a free hydroxyl radical is not the hydroxylating species and suggest that the hydroxylating species is electrophilic. A mechanism consistent with our data is shown in Chart 1.

CHART 1
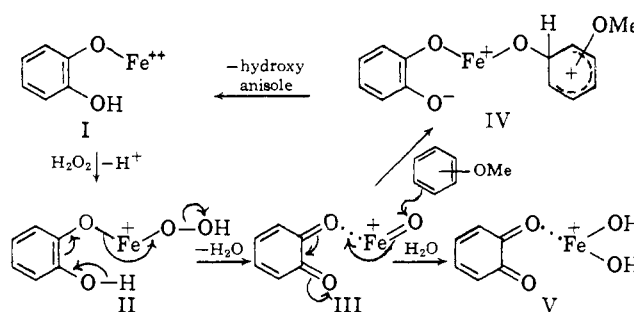


The kinetic dependence on catechol concentration suggests that a complex such as I is involved; at high catechol concentrations more than one molecule can complex with ferric ion and these complexes must be inactive since the rate decreases. The kinetic effect of hydrogen peroxide concentration is consistent with the formation of a complex such as II. A possible hy-

(3) For a recent review with references see: G. H. Williams, "Homolytic Aromatic Substitution," Pergamon Press, New York, N. Y., 1960, p. 110 ff.

(4) S. Udenfriend, C. T. Clark, J. Axelrod and B. B. Brodie, J. Biol. Chem., 208, 731 (1954).

(5) (a) R. O. C. Norman and G. K. Radda, Proc. Chem. Soc., 138 (1962); (b) R. R. Grinstead, J. Am. Chem. Soc., 82, 3472 (1960); (c) R. Breslow and L. N. Lukens, J. Biol. Chem., 235, 292 (1960).

(6) This conclusion and similar results have been reported previously by Norman and Radda, ref. 5a.

droxylating species can be envisaged if II loses a molecule of water to give III. Several resonance structures of III can be written.
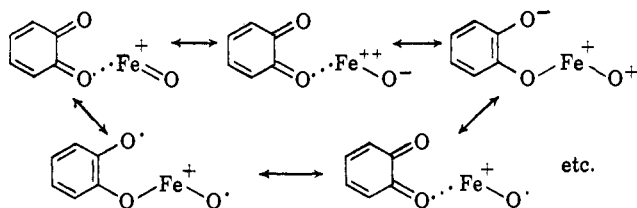


Electrophilic attack of intermediate III on anisole would give IV, which on migration of a proton and dissociation of the hydroxy anisole would give I, thus completing the cycle. According to this mechanism the catechol is oxidized in the conversion of II to III and reduced in the hydroxylation step, III to IV; hydroquinone would be expected to react similarly. With no anisole present, hydroxylation of catechol and reaction of III with water to give V could account for the uptake of 20 to 30% of the $H_2O_2$. Also, we observe that the less reactive chlorobenzene is not hydroxylated in this system; presumably III is removed (to give V) before it hydroxylates chlorobenzene.[7]

The function of the metal ion in the proposed scheme is to transfer electrons from the catechol to the hydrogen peroxide and then in the hydroxylation step back to the catechol. In effect, the metal ion extends the conjugation and allows an electronic link between two or more molecules. Presumably it can do this by the overlap of its d electron orbitals with the p orbitals of the ligands. The application of this type of mechanism to several other metal ion catalyzed reactions, including some enzymatic oxidation–reduction reactions, has been discussed[1] and will be the subject of future publications from this Laboratory.

(7) In Chart 1, the hydroxylation is depicted as an electrophilic substitution; however, III could presumably act as a free radical reagent as well. In the present case, the isomer distribution of products suggests an electrophilic attack rather than radical.

(8) Participant in the National Science Foundation undergraduate research program, summer, 1961.

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## THE STRUCTURE OF THE CUPROUS CHLORIDE–CYCLOÖCTADIENE-1,5 COMPLEX[1]

*Sir:*

As part of a program concerned with metal–olefin pi-complexes, a structural investigation of these compounds has been initiated. We wish to report here our findings on the cuprous chloride–cycloöctadiene-1,5 complex (I). Previous studies of cuprous chloride complexes with unsaturates have provided either erroneous[2] or inconclusive[3] results. To the best of our knowledge this report represents the first successful elucidation of such a complex structure.

Samples of I were prepared according to the following procedures.

(Ia) Cuprous chloride (2 g.) was dissolved in 50 ml. of 0.18 N hydrochloric acid, and the solution was added to 5 g. of cycloöctadiene-1,5 (COD). The reaction mixture was shaken for 10 min., and the precipitate was separated by filtration. The complex was washed with water and pentane and was dried under vacuum over calcium chloride for 24 hr. (*Anal.* Calcd. for

(1) Presented in part at the American Crystallographic Association Meeting, Villanova, Pennsylvania, June, 1962.

(2) J. Österlöf, *Acta Chem. Scand.*, **4**, 374 (1950).

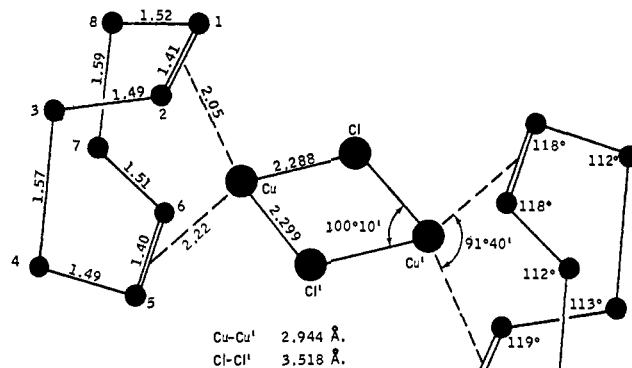(3) F. L. Carter and E. W. Hughes, *Acta Cryst.*, **10**, 801 (1957).



Fig. 1.—Relevant bond angles and distances for the $Cu_2Cl_2$-(cycloöctadiene-1,5)$_2$ complex.

$C_8H_{12}CuCl$: C, 46.38; H, 5.84; Cu, 30.67. Found: C, 44.08; H, 5.88; Cu, 31.48.)

(Ib) Cupric chloride dihydrate (2.5 g.) was dissolved in 15 ml. of 95% ethyl alcohol, and 3 g. of COD was added. Sulfur dioxide was passed into the reaction mixture for 10 min.[4] The precipitated complex was removed by filtration, washed three times with ethanol and vacuum dried over calcium chloride for 24 hr. (*Anal.* Found: C, 45.25; H, 5.88; Cu, 30.58.)

(Ic) A sample of freshly prepared complex Ia was recrystallized from 50 ml. of ethyl acetate. (*Anal.* Found: C, 46.35; H, 6.07; Cu, 30.70.)

Complexes Ib and Ic were obtained as well defined crystals; complex Ia separated as a fine powder. The heat of dissociation of the complex was determined as being 23.5 kcal./mole,[5] which is in accord with the observed high stability of the complex.

X-ray diffraction studies of single crystals of complex Ic showed it to be triclinic, space group P Ī, with the unit cell dimensions $a = 9.028$ ($\pm 0.003$ Å.), $b = 9.020$ ($\pm 0.003$ Å.), $c = 6.387$ ($\pm 0.005$ Å.), $\alpha = 124.4°$, $\beta = 95.7°$, $\gamma = 104.9°$. The observed density is between 1.60 and 1.65 g./cm.$^3$ indicating the presence of two formula units ($C_8H_{12}CuCl$) per unit cell (calcd. density = 1.633 g./cm.$^3$).

Reflection data were obtained using a single crystal orienter with an XRD-5 G.E. diffractometer. The integrated intensities were recorded for filtered Cu K-$\alpha$ radiation ($\lambda = 1.5418$ Å.) using the equatorial plane diffraction method with the specimen and counter rotating in a ratio of 1:2. Lorentz-polarization and absorption corrections were applied to the data. Patterson vector maps of three projections yielded the positions of the copper and chlorine atoms, and a calculation of a series of Fourier and difference-Fourier syntheses[6] determined the locations of the carbon atoms. Refinement of the three dimensional data[7] for approximately 600 reflections yielded a discrepancy factor of 0.13.

The complex is centro-symmetrical and consists of two formula units joined through chlorine–chlorine bridging with the copper and the chlorine atoms forming a rhombus. The copper atoms are quasi-tetrahedrally bonded to two chlorine atoms and the two double bonds of a COD molecule (Fig. 1). The COD molecule

(4) Private communication, H. Haight and J. R. Doyle, Chemistry Department, State University of Iowa, Iowa City, Iowa.

(5) Private communication from Dr. R. B. Long, Esso Research and Engineering Company, Linden, New Jersey.

(6) W. G. Sly, D. P. Shoemaker and J. H. van den Hende, Two- and Three-Dimensional Crystallographic Fourier Summation Program for the IBM 7090 Computer, IBM SHARE Library, No. 1344.

(7) J. H. van den Hende, Crystallographic Structure Factors and Least Squares Refinement Program for the IBM 7090 Computer, IBM SHARE Library, No. 1240.