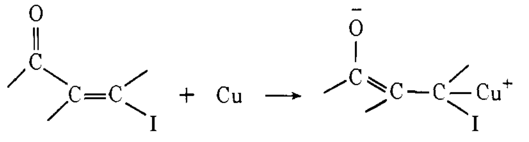
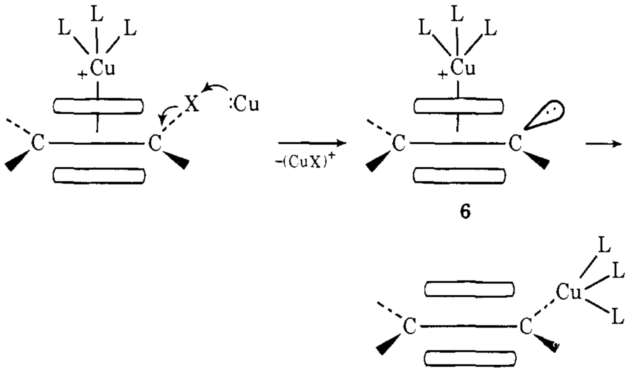
tolysis of an organocopper intermediate,[2] then formation and protolysis of the latter must occur with complete retention of configuration; the alternative hypothesis, that both processes occur with inversion, is unlikely in view of the coupling results. The stereospecific conversion of the iodides to organocoppers renders unlikely not only a radical course[12] for the first stage in the reaction but also a mechanism involving nucleophilic displacement of the iodide by a copper atom,[9] since the resulting intermediate (5) would presumably be capable of rotation about the single bond with consequent loss of stereochemistry.



5

A close similarity exists between the Ullmann coupling and the copper–quinoline decarboxylation.[13] The rates of both reactions are enhanced by most substituents on the benzene ring,[9,14] strong electron-attracting ortho substituents such as the nitro group being most effective.[9,13–15] Both reactions appear to involve organocopper intermediates[2,13–15] and they proceed with a high degree of retention of configuration when applied to vinyl systems.[14] Cuprous ion is the catalyst in the decarboxylation and, although copper metal is usually used in the Ullmann coupling, cuprous oxide has frequently been found effective;[16] when copper is used in the coupling it is strongly activated by washing it with complexing agents, a procedure which is thought to result in a copper surface coated with readily accessible cuprous oxide.[3] Both reactions are strongly promoted by heterocyclic complexing agents such as quinoline and pyridine when used as solvents.[2,14–16] All this suggests that the mechanism previously proposed for the decarboxylation[14] may by suitable modification be applicable to the conversion of the aryl or vinyl halide to an organocopper.



6

L = ligand

The π complexing of a cuprous ion may inductively increase the stability of the σ anion 6 and thereby increase its rate of formation. In the decarboxylation, the carboxylate group (X) can readily eject carbon dioxide, leaving behind the electron pair, whereas halogen, which is very unstable as the cation, must accept a pair of electrons from a copper atom or cuprous ion before it can generate the anion 6.

The synthetic potential of the coupling of vinyl halides is obvious.[17] A further attractive feature of this reaction is the potential utilization of the vinylcopper intermediates in some of the wide variety of carbon–carbon bond forming reactions which have recently been discovered for organocopper compounds.[18] Those vinyl halides which would most readily undergo the copper–halogen exchange are just those (bearing groups such as carbethoxy and nitro) which cannot be converted to organocopper compounds by the standard procedure *via* organolithium or Grignard reagents.

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Chloroperoxidase. IX. The Structure of Compound I[1]

Sir:

The nature of peroxidase and catalase compound I (I), the initial intermediate observed spectrally in the reaction of these heme enzymes with hydrogen peroxide, has been the subject of intense research for many years.[2–15] In this communication, we report ^{18}O studies with chloroperoxidase (CPO) and a peracid substrate which allow us to suggest a definite chemical composition for I.

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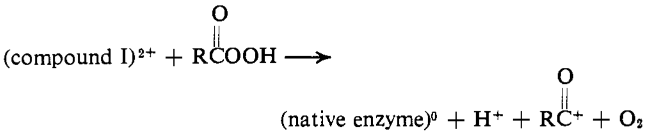
The overall production of oxygen from hydrogen peroxide by peroxidases and catalases is a two-step process involving the reaction of I with a second molecule of hydrogen peroxide.

$$\mathrm{H_2O_2} + \text{peroxidase} \longrightarrow \text{compound I (I)}$$
$$\text{compound I (I)} + \mathrm{H_2O_2} \longrightarrow \mathrm{O_2} + \text{peroxidase}$$

Peroxidases will also react with alkyl hydrogen peroxides and peracids to form I.[15,16] However, CPO is uniquely capable of catalyzing the second step with O_2 evolution using these substrates.[17]

Proposed structures for I range from a classical enzyme–substrate complex[4] to an oxidized heme and/or protein with no incorporation of peroxide.[9] The latter structural hypothesis predicts that the reaction of I with peracids would yield the equivalent of an acyl cation and molecular oxygen with both atoms derived from the same peracid molecule.



$$(\text{compound I})^{2+} + \mathrm{R}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{OOH} \longrightarrow (\text{native enzyme})^{0} + \mathrm{H^+} + \mathrm{R}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}{}^{+} + \mathrm{O_2}$$

Mechanistic schemes where both atoms of an oxygen molecule arise from one substrate molecule (retention mechanism) and those where the atoms are derived from different substrate molecules (scrambling mechanism) predict different isotope distributions from a mixture of ^{18}O doubly labeled and unlabeled substrates.[18] *m*-Chloroperoxybenzoic acid (*m*-CPB) labeled with 6.0% ^{18}O in both peroxy oxygens was prepared by the reaction of *m*-chlorobenzoyl chloride with labeled sodium peroxide.[19] A mixture of labeled and unlabeled peracid was treated with CPO, and the isotope distribution of the product oxygen was analyzed mass spectrometrically (Table I). These results establish a scrambling mechanism for the release of O_2. The oxygen atoms of O_2 are therefore derived from different substrate molecules. A control experiment showed no scrambling of label in a mixture of unlabeled and doubly labeled oxygen using our analytical procedures.

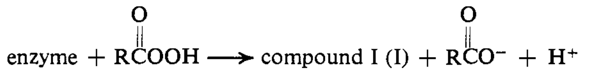
Table I. Mass Spectrometric Analysis[a] of Oxygen Produced by the Reaction of CPO with a Mixture of ^{18}O-Labeled[b] and Unlabeled *m*-CPB

Mole fraction of ^{18}O-labeled peracid added	Mole fraction of ^{18}O–^{18}O in evolved O_2 ($\times 10^4$)	Theoretical mole fraction of ^{18}O–^{18}O: Retention mech ($\times 10^4$)	Theoretical mole fraction of ^{18}O–^{18}O: Scramble mech ($\times 10^4$)
0.22	2.8	8.0	2.2
0.40	7.7	14.6	6.6
0.53	10.9	18.9	11.3

[a] Reference 22. [b] 6.0% ^{18}O in each peroxy oxygen.

When the oxygen evolution reaction was carried out with unlabeled substrate in $H_2{}^{18}O$, no oxygen atoms from water were incorporated into the oxygen (within experimental error of *ca.* 3%). The other product of this reaction, *m*-chlorobenzoic acid (*m*-CB), also showed no incorporation of solvent label above normal background exchange.[20] The only reasonable mechanism which accounts for these observations incorporates at least one oxygen atom from the peracid into I in a manner which does not allow solvent exchange. Subsequent reaction with a second peracid incorporates the oxygen atom, together with one from the second peracid, into molecular oxygen.

Only one additional piece of information is necessary to arrive at a structural hypothesis for I. Schonbaum,[21] using horseradish peroxidase and aromatic peracids, has observed release of the parent carboxylic acid concomitant with the formation of I. Based on the stoichiometric reaction between enzyme and substrate and the quantitative recovery of acid even in the absence of enzyme turnover[22] (Table II), we similarly conclude that *m*-CB is released as a coproduct with the formation of CPO I. The stoichiometry of the reaction of CPO with *m*-CPB was determined by titration studies using a stopped-flow spectrophotometer. The reaction product was shown to be *m*-CB when the substrate concentration was less than, equal to, or greater than the enzyme concentration (Table II).



$$\text{enzyme} + \mathrm{R}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{OOH} \longrightarrow \text{compound I (I)} + \mathrm{R}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{O^-} + \mathrm{H^+}$$

Table II. Stoichiometry of CPO and *m*-CPB[a]

Enzyme	Substrate	Compound I	Acid formed
8.0[b]	7.7		7.7
8.0[b]	4.0		4.0
0.21[b]	790		790
0.413[c]	0.0	0.0	
0.413[c]	0.080	0.017	
0.413[c]	0.378	0.321	
0.413[c]	0.775	0.400	

[a] All values are expressed in nanomoles. [b] Enzyme and product were separated by Sephadex G-25 gel filtration. Acid recovery (±10%) was determined by absorbance at 205 nm (ϵ 4.3 × 10^4). [c] I was determined spectrophotometrically (400 nm, ϵ 3 × 10^4) and CPO by rate assay.[22]

From the above experiments we deduce the salient structural features of I. The ^{18}O double label results require that at least one peroxy oxygen atom of the *m*-CPB be incorporated into the intermediate. The release of the acid product from the enzyme without turnover indicates that the acyl moiety of the substrate is not retained in I. Since no solvent label is incorporated into either *m*-CB or I, both must be formed in a step involving O–O bond cleavage rather than C–O bond cleavage. Thus, it can be concluded that *exactly one oxygen from the peroxy acid is incorporated into compound I.*

Numerous analogies point to the probable location of the single oxygen atom of I as a ligand to the heme iron. Magnetic susceptibility[14] and Mossbauer spectroscopy[7] studies of this class of enzymes, as well as

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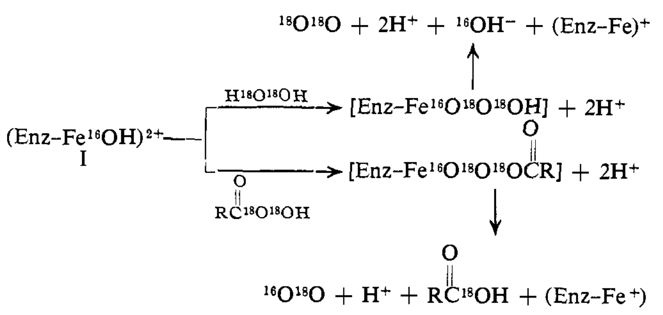
model studies,[12,13] suggest that the two-electron oxidation leading to I involves oxidation of iron(III) to iron(IV) and the porphyrin ring system to a π cation radical. The combination of these elements presents a nearly complete structure for the active center of I of the peroxidases and catalases.

In accord with previous results[18] with catalase we find that the CPO–H_2O_2 reaction proceeds by a nonscrambling mechanism.[23] This is compatible with the spectral evidence for the identity of I formed from H_2O_2 and *m*-CPB, if an additional mechanism, here illustrated schematically, is operative for the oxidation of H_2O_2 by I.



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[23] L. P. Hager and coworkers, unpublished results.

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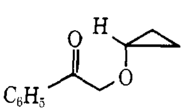
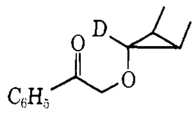
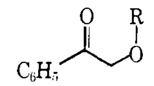
Photochemistry of α-Cyclopropoxyacetophenones. An Unexpected Internally Sensitized Cis–Trans Isomerization[1]

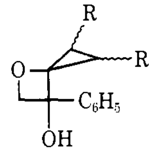
Sir:

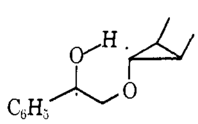
The Norrish type II reactions of butyrophenone and related aryl ketones represent one of the most thoroughly studied and best understood classes of photoreactions.[2] We have undertaken a program to explore the synthetic prospects for these reactions.[3] For example, it seemed possible that suitably substituted α-cyclopropoxyacetophenones might provide a useful route to substituted cyclopropanones, a family of relatively inaccessible but interesting molecules.[4] Indeed, irradiation of benzene solutions of Ia with 313-nm light produces acetophenone and cyclopropanone,[5,6] albeit in low yield, in addition to cyclization product IIIa. However, under identical conditions of excitation, Id (cis-exo) did not produce detectable amounts of dimethylcyclopropanone or significant quantities of acetophenone. The principal reactions of Id (cis-exo) were found to be cyclization and isomerization of the cyclopropane ring (Scheme I) to give, respectively, IIIb and Ib (trans).[7] The occurrence of isomerization products represented a rather unexpected and novel course of reaction and demanded closer mechanistic scrutiny. Our study produced evidence that the standard mechanisms for type II processes[2] are inadequate for proper understanding of the data.


Ia

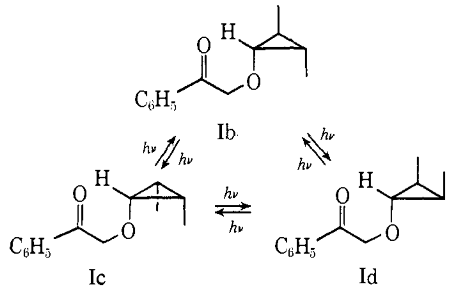

Ie


IIa, R = CH_3
IIb, R = CD_3


IIIa, R = H
IIIb, R = CH_3


IV

Scheme I



Ic

Id

Table I summarizes quantum yield and kinetic data for the photoreactions of Ia–e in benzene. The ketones IIa–b are included for comparison. The salient features of the data are (1) the tremendous drop in reaction efficiency as one proceeds from IIa to Ia (a factor of 13) and then from Ia to Id (a factor of 5); (2) the increase in $1/\tau$ between Ia and Id (cis-exo); (3) the sizable effect of γ deuteration on $1/\tau$ and Φ for Id

Table I. Quantum Yield and Kinetic Data[f]

Compd	$k_q\tau$	$\tau^{-1\,a}$ $(\times 10^{-8})$	Φ
Ia	21	2.4	0.077,[b] 0.018[c]
Ib	2.3	22	0.0060,[b] 0.0030[d]
Ic	0.65	77	0.023,[b] 0.0011,[d] 0.0067[e]
Id	4.4	11	0.015,[b] 0.0043[e]
Ie	10.7	4.7	0.025,[b] 0.0078[e]
IIa	1.6	31	0.99,[b] 0.42[c]
IIb	8.9	5.6	

[a] Assuming $k_q = 5 \times 10^9\ M^{-1}\ sec^{-1}$ in benzene at 25°. [b] Disappearance of ketone. [c] Type II cleavage. [d] Appearance of Id (cis-exo). [e] Appearance of Ib (trans). [f] Plots of product formation *vs.* time were linear out to 15% conversion. Stern–Volmer quenching was confined to this range.

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[6] We have repeated Lewis' work as a control and have obtained independent agreement with his reported quantum yields and quenching constants within his experimental error. Formation of cyclopropanone was monitored by ir and nmr upon partial photolysis of Ia at −60° in methylene chloride solution.

[7] Upon extended irradiation, the photolysis mixture consists of 70% isomeric oxetanols and 5% acetophenone. No detectable olefinic products were formed.