these limits (1) the binding between MeATP and EG is at least as strong as that between free ATP and EG and (2) all reactions which can be classified as complex ion formation occur at least as fast for Ca^{++} as Mg^{++}. Both these assumptions are very reasonable and do not impose a severe limitation on the results which can be summarized as

For Mg^{++}: $6 \times 10^3\ M^{-1} \geqslant k_3/k_{-3} \geqslant 1.1 \times 10^3\ M^{-1}$; $k_4/k_{-4} \leqslant 5$; $k'_{-4}/k_4' \leqslant 5 \times 10^2\ M^{-1}$; $k_3 \geqslant 3.3 \times 10^6\ M^{-1}$ sec.$^{-1}$; $k_{-3} \geqslant 550$ sec.$^{-1}$; $k_4 \geqslant 3 \times 10^3$ sec.$^{-1}$; $k_{-4} \geqslant 6 \times 10^2$ sec.$^{-1}$; $k_4' \geqslant 3 \times 10^3$ sec.$^{-1}$; $k_{-4}' \geqslant 2 \times 10^5\ M^{-1}$ sec.$^{-1}$

For Ca^{++}: $5 \times 10^3\ M^{-1} \geqslant k_3/k_{-3} \geqslant 1.1 \times 10^3\ M^{-1}$; $k_4k'_4/k_{-4}k'_{-4} \geqslant 4 \times 10^{-3}\ M$; $k_{\pm 3}$ and $k'_{\pm 4}$ same as for Mg^{++}; $k_4 \approx 17$ sec.$^{-1}$

It is obvious that the more complex mechanism only serves to strengthen the conclusions reached earlier concerning the role of the metal ion in the hexokinase system. It should be mentioned that the inequalities presented above are probably equalities within a factor of 2 or 3 in the case of Mg^{++}. Work is now in progress to try and detect the proposed intermediates in a more direct manner.

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[CONTRIBUTION FROM THE CALIFORNIA RESEARCH CORPORATION, RICHMOND, CALIF.]

Inhibition of Cumene Oxidation by Tetralin Hydroperoxide

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Tetralin hydroperoxide is found to retard the rate of catalyzed oxidation of cumene at 57°. The retardation is explained in terms of tetralylperoxy radical formation by peroxidic hydrogen abstraction by cumylperoxy radicals and the more rapid termination reactions occurring between tetralylperoxy radicals with themselves and with cumylperoxy radicais than that between cumylperoxy radicals. The data yield a rate constant of 12 liters/mole sec. for the reaction $RO_2\cdot + TO_2H \rightarrow RO_2H + TO_2\cdot$. Possible reasons for the lack of a kinetic isotope effect, observed for this reaction, are discussed.

Russell[1] found that cumene solutions containing moderate concentrations of tetralin oxidize appreciably slower than either pure hydrocarbon alone. This behavior he showed to be due to the much faster termination reactions of tetralylperoxy radicals with themselves and with cumylperoxy radicals than that between cumylperoxy radicals alone.

If the hydrogen exchange reaction between cumylperoxy radicals and tetralin hydroperoxide proceeds with sufficient speed, it would be anticipated that tetralin hydroperoxide would retard the oxidation rate of cumene. We have observed that such an effect exists and find that as little as $10^{-3}\ M$ tetralin hydroperoxide significantly retards the oxidation rate of $4\ M$ cumene solutions initiated with $4 \times 10^{-3}\ M$ azo-bis-isobutyronitrile (ABN) at 57°. Figure 1 shows the oxidation rate plotted as a function of tetralin hydroperoxide concentration.

Utilizing the mechanism

$$\begin{array}{ll}
ABN \xrightarrow{O_2} AO_2\cdot & k_1 \\
AO_2\cdot + RH \xrightarrow{O_2} AO_2H + RO_2\cdot & k_2 \\
AO_2\cdot + TO_2H \longrightarrow AO_2H + TO_2\cdot & k_3 \\
RO_2\cdot + RH \xrightarrow{O_2} RO_2H + RO_2\cdot & k_4 \\
RO_2\cdot + TO_2H \longrightarrow RO_2H + TO_2\cdot & k_5 \\
TO_2\cdot + RH \xrightarrow{O_2} TO_2H + RO_2\cdot & k_6 \\
TO_2\cdot + TO_2\cdot \longrightarrow \text{inactive products} & k_7 \\
TO_2\cdot + RO_2\cdot \longrightarrow \text{inactive products} & k_8 \\
RO_2\cdot + RO_2\cdot \longrightarrow \text{inactive products} & k_9
\end{array}$$

where RH is cumene and TO_2H is tetralin hydroperoxide, the conventional steady state approximation yields the rate equation

$$\frac{-d[O_2]}{dt} = k_1[ABN] + k_2[RH]\left\{\frac{k_1[ABN]}{k_2[RH] + k_5[TO_2H]}\right\} + k_2[RH]\left[\frac{k_1[ABN]}{\frac{k_5^2k_7[TO_2H]^2}{k_2^2[RH]^2} + \frac{k_5k_8[TO_2H]}{k_2[RH]} + k_9}\right]^{1/2}\left[1 + \frac{k_5[TO_2H]}{k_2[RH]}\right] \quad (1)$$

It is assumed that $k_2 = k_4 = k_6$ and $k_3 = k_5$.

Using values of $k_7 = 2.3 \times 10^7$ liters/mole sec. and $k_9 = 3 \times 10^4$ liters/mole sec. as determined by Melville and Richards[2] and $k_8 = 10^7$ liters/mole sec. as determined by Russell,[1] the value of the rate constant for the exchange reaction k_5 is 12 liters/mole sec. The value of k_1[ABN] was determined by use of diphenylnitric oxide as a radical trap (3.08×10^{-8} mole/liter sec. for $4 \times 10^{-3}M$ ABN). This value is in good agreement with that determined by Hammond, *et al.*[3] The best literature value[2] of k_2 (0.45 liter/mole sec.) gives a calculated oxidation rate of cumene without tetralin hydroperoxide about 45% lower than observed. Consequently, k_2 was adjusted to 0.64 liter/mole sec. to bring experiment and expectation into agreement. Using these values the solid line in Fig. 1 is calculated in accordance with eq. 1.

Additional experiments were done with the following results: (1) Cumene hydroperoxide at concentrations up to $5 \times 10^{-2}M$ had no influence upon the oxidation rate with or without added tetralin hydroperoxide. (2) The addition of tetralin up to $0.03\ M$ had no influence upon the rate, demonstrating that abstraction of "normal" tetralin hydrogens is not involved. (3) There is no measurable kinetic isotope effect observable when TO_2D (65%) is used in place of TO_2H. These experiments were run at

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(1) G. A. Russell, *J. Am. Chem. Soc.*, **77**, 4583 (1955).

(2) H. W. Melville and S. Richards, *J. Chem. Soc.*, 944 (1954).

(3) G. S. Hammond, J. N. Sen and C. E. Boozer, *J. Am. Chem. Soc.*, **77**, 3244 (1955).

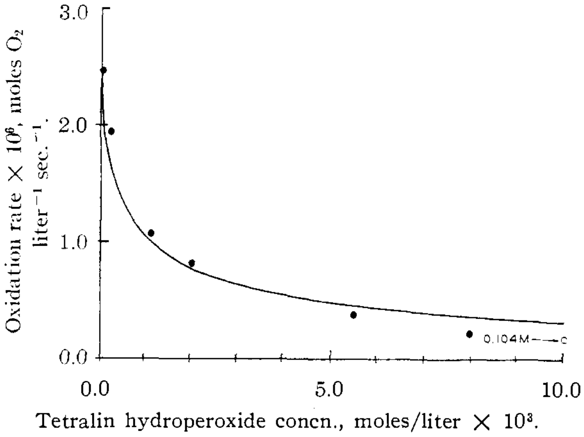

Fig. 1.—Oxidation rate of 4 *M* cumene *vs.* concentration of tetralin hydroperoxide: 4×10^{-3} *M* ABN, 57°, 1 atm. O_2, chlorobenzene diluent.

hydroperoxide concentrations of 10^{-3} *M* and 5×10^{-3} *M*.

With the exception of the kinetic isotope effect, the results are in excellent accord with the proposed exchange mechanism. The lack of influence of 5×10^{-2} *M* cumene hydroperoxide in the presence of 10^{-3} *M* tetralin hydroperoxide is in accord with the appropriate modification of eq. 1 which predicts only a 5% increase in oxidation rate for these conditions. This calculation assumes that the rate constant for hydrogen abstraction from cumene hydroperoxide by tetralylperoxy radicals is the same as that for cumylperoxy radicals reacting with tetralin hydroperoxide.

The value of the exchange rate constant, k_5, is about the same as that for hydrogen abstraction from tetralin by tetralylperoxy radicals[4] correcting for the number of abstractable hydrogens. The relative ease of hydrogen abstraction from the hydroperoxide most likely arises from the stabilization energy of the peroxy radical due to its three-electron bond.

Just as one is able to conduct the oxidation of cumene, propagated, and terminated by tetralylperoxy radicals, it should in principal be possible to conduct the oxidation of tetralin propagated and terminated by cumylperoxy radicals. Calculation by the appropriate variant of eq. 1 indicates that the oxidation rate of a 1 *M* tetralin solution would only be doubled by cumene hydroperoxide present at a concentration of 2 *M*, however. In the limit of high cumene hydroperoxide concentrations and low tetralin concentrations, the oxidation rate of tetralin should be accelerated about 28-fold.

The absence of a kinetic isotope effect is puzzling since it would seem that the reaction would involve a linear transition state in which the hydrogen is equally strongly bonded to the two reactants. This is the ideal condition for obtaining the maximum theoretical kinetic isotope effect.[5] The explanation may lie in the possibility that under our conditions the hydroperoxide exists as a cyclic dimer thus destroying the linear transition state. Such an occurrence would not invalidate our kinetic arguments as long as the hydroperoxide exists as dimer under all conditions studied.

An alternative explanation might be that the rapidly terminating radical is produced by abstraction of hydrogen other than the peroxidic hydrogen. The negligible effect of small concentrations of tetralin upon the rate of cumene oxidation excludes the possibility that "normal" tetralin hydrogens are being abstracted, as mentioned previously. Conceivably the hydrogen of the peroxidized carbon is activated and easily removed. The resulting peroxy radical could be the rapidly terminating species responsible for the inhibiting effect of the hydroperoxide. Two facts argue against this possibility. First, the resulting peroxy radical, being tertiary, would be expected to terminate slowly rather than rapidly. Second, we have examined the oxidation rate of tetralin hydroperoxide itself and find that it oxidizes less rapidly than tetralin. Consequently, we believe that the inhibiting effect of tetralin hydroperoxide involves abstraction of the peroxidic hydrogen.

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Experimental

Oxidation Rates.—Oxygen uptake rates where measured in a stirred reactor using a sensitive gasometer. The reactor and gas reservoir were immersed in a carefully regulated water bath at 57.0°.

Materials.—The cumene used was an Eastman Kodak Co. product passed through an alumina column. The tetralin hydroperoxide was purified by recrystallization from hexane. The cumene hydroperoxide was purified *via* its sodium salt. Azo-bis-isobutyronitrile was an Eastman Kodak Co. product purified by recrystallization from methanol.

Determination of k_1 [ABN].—The radical yield from ABN under our conditions was determined by using diphenylnitric oxide as a radical counter. The results will be presented in full in a forthcoming publication.

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(4) C. H. Bamford and M. J. S. Dewar, *Proc. Roy. Soc.* (*London*), **A198**, 252 (1949).

(5) F. H. Westheimer, *Chem. Revs.*, **61**, 265 (1961).