gent grade) was used without further purification. 2,6-Di-t-butyl-p-cresol was purified by repeated recrystallization from ethanol; m.p. 69–70°.

Estimation of Benzoyl Peroxide.—Benzoyl peroxide was assayed by the usual iodometric method.

Inhibition Period and Oxidation Rates.—Absorption of oxygen was followed using the apparatus described earlier.[1] Gas volumes were measured at 70° and 744 mm.

The Effect of Cumyl Hydroperoxide on the Behavior of Oxidation Inhibitors

BY GEORGE S. HAMMOND AND UMA SHANKAR NANDI

The nature of the reversible interaction of peroxy radicals with antioxidants has been further investigated. If $RO_2\cdot$ were to equilibrate with inhibitor in a hydrogen abstraction reaction, one would anticipate that the inhibitory efficiency should be decreased by addition of a hydroperoxide. Since no such effect is observed we infer that reversible formation of a molecular complex gives a better account of the facts.

In an earlier paper[1] we reported that the rate of oxidation of tetralin in the presence of weak antioxidants such as phenol or N-methylaniline follows the kinetic law of eq. 1.

$$\frac{-dO_2}{dt} = \frac{c[RH][Initiator]^{1/2}}{[Inhibitor]^{1/2}} \quad (1)$$

The rate law implies that some reversible interaction occurs between $RO_2\cdot$ and the inhibitors. On the basis of this and other evidence, it was suggested that the antioxidants functioned by virtue of their ability to form charge-transfer complexes with peroxy radicals.

$$RO_2\cdot + In \rightleftarrows [In \rightarrow RO_2\cdot] \quad (2)$$

$$[In \longrightarrow RO_2\cdot] + RO_2\cdot \longrightarrow Products \quad (3)$$
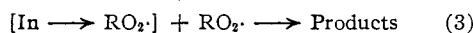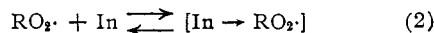
Shortly afterward, Bickel and Kooyman[2] reported a magnificent study of the rates of oxidation of 9,10-dihydroanthracene in the presence of various phenolic antioxidants. They showed that a wide variety of kinetic laws was observed including the one in eq. 1. They also showed that satisfactory fits to all cases could be based upon the supposition that peroxy radicals abstract hydrogen atoms from the phenols in a step that may or may not be reversible, depending on the structure of the phenol and other variables relating to reaction conditions.

$$RO_2\cdot + ArOH \rightleftarrows RO_2H + ArO\cdot \quad (4)$$
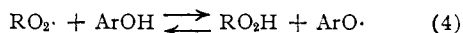
Using this mechanism, which is really that of Bolland and tén Have,[3] to explain the rate law of eq. 1 requires that equilibrium be established in reaction 4 with a small equilibrium constant. A test of this hypothesis is readily available since the formulation requires that addition of hydroperoxide should repress the conversion to $ArO\cdot$, thereby decreasing the potency of the inhibitor.

Results and Discussion

Figure 1 shows the consequences of adding 3.34 × 10⁻² mole per liter of cumyl hydroperoxide to a standard oxidation mixture containing cumene, chlorobenzene, azoisobutyronitrile and phenol at

70°. The fact that the rate of oxygen consumption is slightly lowered by the hydroperoxide is sufficient grounds for elimination of reaction 4 as a reversible step in the mechanism.

Phenol is the most appropriate inhibitor to use in this type of study since the half-order law has been shown to describe the inhibitory action of the compound and because the antioxidant action is weak enough to permit an easily measurable oxidation rate during the induction period. However, experiments have also been done in which cumyl hydroperoxide was added in systems inhibited by N,N'-diphenyl-p-phenylenediamine and p-methoxyphenol, compounds which are more potent antioxidants as judged by the sharpness of inhibition periods. The results are represented in Table I.

TABLE I

EFFECT OF CUMYL HYDROPEROXIDE ON THE INHIBITORY ACTION OF ANTIOXIDANTS IN CUMENE[a,b,c] OXIDATION AT 70°

Antioxidant	Concn. of cumyl hydroperoxide × 10², mole l.⁻¹	$R_0 \times 10^6$ (during induction period), mole l.⁻¹ sec.⁻¹	Induction period, minutes
Phenol	Nil	2.97	30.2
	3.34	2.53	29.8
4-Methoxyphenol	Nil	1.10	29.6
	42.0	0.55	32.2
N,N'-Diphenyl-p-phenylenediamine	Nil	4.40	27.0
	1.67	1.98	26.4
	Nil	4.18	27.1
	3.34	1.98	26.0
	42.0	2.11	30.4

[a] Cumene, 2.39 mole l.⁻¹; total volume of reaction mixture 6 ml. [b] Oxygen pressure, 744 mm. [c] Azoisobutyronitrile, 8.33 × 10⁻² mole l.⁻¹.

In each case the rate of oxygen absorption was decreased in the presence of the hydroperoxide. As is shown in Fig. 2, addition of hydroperoxide actually increases, by a small amount, the induction period shown by p-methoxyphenol.

The small synergistic effect of the hydroperoxide on the antioxidant action is interesting. There are apparently two kinds of effect. In the presence of phenol there is a very small depression of the rate of oxygen uptake during the induction period. In the presence of p-methoxyphenol and N,N'-diphenyl-
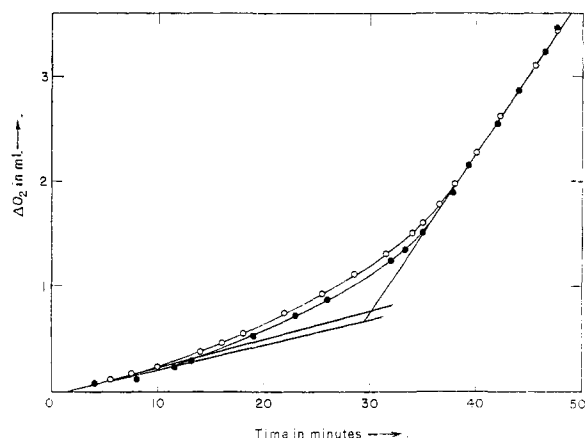
(1) G. S. Hammond, C. E. Boozer, C. E. Hamilton and J. N. Sen, *J. Am. Chem. Soc.*, **77**, 3238 (1955).

(2) A. F. Bickel and E. C. Kooyman, *J. Chem. Soc.*, 2215 (1956).

(3) J. L. Bolland and P. tén Have, *Trans. Faraday Soc.*, **43**, 201 (1947).

Fig. 1.—Effect of cumyl hydroperoxide on phenol-inhibited oxidation of cumene at 70°; cumene, 2.39 moles 1.$^{-1}$; ABN, 8.33 × 10^{-2} mole 1.$^{-1}$; phenol, 3.34 × 10^{-3} mole 1.$^{-1}$; solvent, chlorobenzene in both the runs: O, no cumyl hydroperoxide; ●, 3.34 × 10^{-2} mole 1.$^{-1}$ of cumyl hydroperoxide.
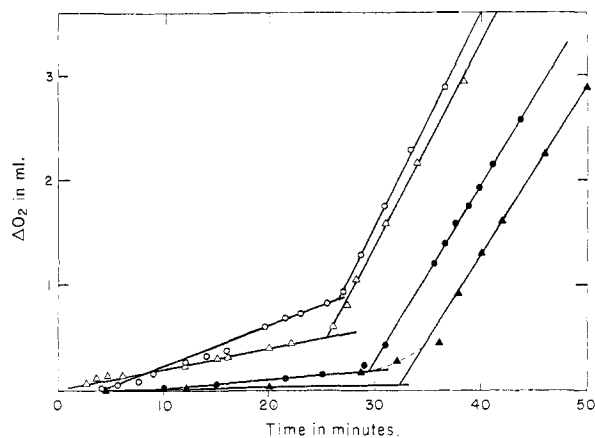

Fig. 2.—Effect of cumyl hydroperoxide (ROOH) on cumene oxidation inhibited by 4-methoxyphenol and N,N'-diphenyl-p-phenylenediamine at 70° in chlorobenzene; cumene, 2.39 moles 1.$^{-1}$; ABN, 8.33 × 10^{-2} mole 1.$^{-1}$; antioxidant, 3.34 × 10^{-3} mole 1.$^{-1}$ in all the runs: ●, 4-methoxyphenol, no ROOH; ▲, 4-methoxyphenol, 0.42 mole 1.$^{-1}$ of ROOH; O, N,N'-diphenyl-p-phenylenediamine, no ROOH; △, N,N'-diphenyl-p-phenylenediamine, 3.34 × 10^{-2} mole 1.$^{-1}$ of ROOH.

p-phenylenediamine the rate of oxidation during the induction period is slightly depressed, and the induction period is nearly the same except that it is slightly extended in the two cases where a very high concentration of the hydroperoxide (0.42 mole 1.$^{-1}$) was used. Depression of the rate of oxidation may be due to oxygen-producing chain transfer reactions between RO$_2$· and RO$_2$H. Extension of the induction period, on the other hand, probably is due to catalysis of ionic decomposition of the hydroperoxide by the antioxidant.[4] Such a reaction would produce phenol, which would extend the inhibition period by virtue of its own inhibitory reactivity. The nature of the curve after the normal induction period resembles that of phenol.

Since strong repression of inhibitory action by hydroperoxide, predicted by eq. 4, was not observed, we believe that reversible hydrogen abstraction cannot be a key step in the inhibition mechanism. Since the kinetics of oxidation in the presence of phenol seem to demand some sort of reversible interaction between the inhibitor and peroxy radicals, we are again reduced to being able to conceive of no mechanism other than molecular-complex formation, which fits the facts as we see them. The mechanism has been supported recently by Harle and Thomas,[5] who followed the concentration of radicals in an inhibited oxidation by use of electron paramagnetic resonance. They found that the rise and fall of the radical concentration could be fitted much better by equations based upon reversible complex formation than by those based upon irreversible hydrogen abstraction from the inhibitor. Since the present study seems to dispose of reversible hydrogen abstraction, no variant of eq. 4 is tenable.

One of the strong arguments in favor of the molecular-complex mechanism was the absence of a kinetic-isotope effect on the inhibitory action of N-methylaniline and diphenylamine. Since the first report, other studies of the effect of isotopic sub-

(4) C. Walling and R. B. Hodgdon, J. Am. Chem. Soc., 80, 228 (1958).

(5) O. L. Harle and J. R. Thomas, ibid., 79, 2973 (1957).

stitution of phenols and aromatic amines have appeared. These include another case of no measurable effect by Pederson,[6] a report by Ingold and Puddington[7] of a small isotope effect, and reports by Shelton and co-workers[8,9] of a variety of effects ranging from normal to inverse isotope effects and including cases where no effect was detectable. It was our original bias that the molecular-complex hypothesis does not predict that there will be no isotope effect but accommodates the fact more easily than does irreversible hydrogen abstraction. Ingold[7] has shown that the occurrence of a small isotope effect can be rationalized within the framework of the molecular-complex hypothesis, and Shelton[9] has shown that some of the anomalies associated with inhibition of uninitiated oxidation may be associated with initiation by attack of oxygen on the antioxidant. Since the isotope effect in reversible hydrogen transfer, eq. 4, should be small and might be either positive or negative, the demonstration that such equilibration does not occur is required to fortify the association of small isotope effects with reaction 3.[10]

Walling has pointed out[11] that the implication of our hypothesis is that reaction 3 must be enormously faster than the normal chain-terminating reactions involving two RO$_2$·. This conclusion arises from the fact that the kinetics demand that

(6) C. J. Pederson, Ind. Eng. Chem., 48, 188 (1956).

(7) K. U. Ingold and I. E. Puddington, ibid., 51, 1319 (1959).

(8) J. R. Shelton and E. T. McDonel, J. Polymer Sci., 32, 75 (1958).

(9) J. R. Shelton, E. T. McDonel and J. C. Crano, ibid., 42, 289 (1960).

(10) Shelton[9] has suggested that the failure to observe an isotope effect in our original experiments might have been due to loss of deuterium by exchange with traces of water. This reasonable possibility had occurred to us also, and several years ago Dr. Shih-Kung Liu repeated the experiments using reaction mixtures to which excess deuterium oxide was added to maintain the diphenylamine in a highly deuterated condition. The results were identical to those reported earlier.[1]

(11) C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, p. 436.

most of the termination reaction involves a very small fraction of the total RO₂· bound in the form of a complex. We agree that this is a puzzling fact and can only point to the fact that the rate constants for termination by interaction between two RO₂· are small enough[12] to permit entertainment of the view that some bimolecular reactions, such as reaction 3, *may* be faster by several orders of magnitude. Finally, we should like to mention that our confidence in the molecular-complex hypothesis has been considerably fortified by the elegant demonstrations by Russell[13] and by Walling and Mayahi[14] that chlorine atoms are extensively complexed in aromatic solvents with consequent modification of their chemical reactivity. Russell has observed similar but smaller effects on the reactivity of *t*-butoxy radicals.[15] Since both the polarizability and electron affinity of peroxy radicals must be higher than those of alkoxy radicals, we would expect peroxy radicals to be intermediate between alkoxy radicals and chlorine atoms in their aptitude for formation of charge-transfer complexes with electron-rich aromatic systems. Since the radical-complex mechanism is only established for aromatic

solvents it is possible that variations in the inhibition mechanism may occur in other solvents.[16]

Acknowledgment.—We gratefully acknowledge support of this work by a grant from the Petroleum Research Fund of the American Chemical Society.

(12) C. Walling, ref. 11, p. 422.

(13) G. A. Russell, *J. Am. Chem. Soc.*, **80**, 4987 (1958).

(14) C. Walling and M. F. Mayahi, *ibid.*, **81**, 1485 (1959).

(15) G. A. Russell, *J. Org. Chem.*, **24**, 300 (1959).

(16) C. E. Boozer, G. S. Hammond, C. E. Hamilton and C. Peterson, *J. Am. Chem. Soc.*, **77**, 3380 (1955).

(17) C. E. Boozer, G. S. Hammond, C. E. Hamilton and J. N. Sen, *ibid.*, **77**, 3233 (1955).

The Kinetics of the Base-catalyzed Deuterium Exchange of 2,2-Dihalo-1,1,1-trifluoroethanes[1]

BY JACK HINE, ROBERT WIESBOECK AND ROBERT G. GHIRARDELLI

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The base-catalyzed deuterium exchange of CF₃CDCl₂, CF₃CDBrCl, CF₃CDBr₂ and CF₃CDI₂ was found to proceed with negligible interference from base-consuming side reactions. Kinetics of the exchange were studied in water and methanol and the following reactivity sequence noted: CF₃CDBr₂ > CF₃CDI₂ ∼ CF₃CDBrCl > CF₃CDCl₂. By studies on CF₃CHCl₂ and CF₃CHBrCl in heavy water the deuterium kinetic isotope effects were estimated to be 1.26 and 1.41, respectively. The trifluoromethyl substituent appears to be equal to or superior to the fluoro substituent at facilitating carbanion formation.

Introduction

Previous articles on the kinetics of the base-catalyzed deuterium exchange of haloforms have shown that α-halogen substituents facilitate carbanion formation in the order I ∼ Br > Cl > F.[2] This order, being almost exactly the reverse of the relative electronegativities of the halogens, did not agree with some of the existing explanations of the activity of the hydrogen atoms of haloforms. A knowledge of the effect of more distantly situated halogen substituents on ease of carbanion formation would be useful in several ways. For example, one of the strongest points of evidence that the dehydrohalogenations of most saturated organic halides (and many other elimination reactions) are concerted E2 reactions that do not involve intermediate carbanions is the fact that many such reactions are much faster than seems plausible for

carbanion formation.[3] The most obvious loophole in this argument is our ignorance of the effect of β-halogen substituents on ease of carbanion formation.

Fluorobenzene has been found to form carbanions at its *ortho* position quite rapidly in the presence of potassium amide in liquid ammonia but the rate at which the other monohalobenzenes do so is unknown and may also be quite fast.[4] The interpretation of the semi-quantitative experiments of Miller and Lee on the deuterium exchange of the dihaloethylenes[5] is complicated by the simultaneous changing of both an α- and a β-substituent. However, if it is assumed that the α-halogen substituents on these unsaturated compounds have the same relative effect that has been observed with the haloforms, then it follows that

(1) Part X in the series "The Effect of Halogen Atoms on the Reactivity of Other Halogen Atoms in the Same Molecule"; for part IX see J. Hine and R. J. Rosscup, *J. Am. Chem. Soc.*, **82**, 6115 (1960).

(2) J. Hine, N. W. Burske, M. Hine and P. B. Langford, *ibid.*, **79**, 1406 (1957).

(3) J. Hine, "Physical Organic Chemistry," McGraw–Hill Book Co., Inc., New York, N. Y., 1956, p. 169.

(4) G. A. Hall, R. Piccolini and J. D. Roberts, *J. Am. Chem. Soc.*, **77**, 4540 (1955); J. D. Roberts, D. A. Semenow, H. E. Simmons, Jr., and L. A. Carlsmith, *ibid.*, **78**, 601 (1956).

(5) S. I. Miller and W. G. Lee, *ibid.*, **81**, 6313 (1959).