Mechanisms of Antioxidant Action: Reactions of Phosphites with Hydroperoxides

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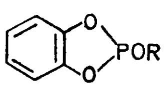
The decomposition of 1-methyl-1-phenylethyl hydroperoxide by 4-methyl-2,6-di-t-butylphenyl *o*-phenylene phosphite (Ic) is a catalytic pseudo-first-order reaction which does not appear to involve free radicals. It is preceded by a faster, second-order reaction between the phosphite and hydroperoxide which corresponds to the conversion of the phosphite to the active catalytic species in a reaction which involves four molecules of hydroperoxide for each molecule of the phosphite. Triphenyl phosphite by contrast reacts in a strictly stoicheiometric reaction with 1-methyl-1-phenylethyl hydroperoxide but other cyclic phosphites, ethylene isopropyl and isopropyl propane-1,3-diyl phosphites (III) and (IV), behave similarly to the *o*-phenylene phosphites but give different first-order rate constants in the catalytic stage of the reaction. The implications of these results for the antioxidant behaviour of cyclic phosphites are discussed.

In an earlier communication [1] evidence was presented to suggest that products derived from cyclic phosphites based on catechol (catechol phosphites) were powerful antioxidants for the oxidation of cumene initiated by 1-methyl-1-phenylethyl hydroperoxide (cumene hydroperoxide). This inhibition was preceded by a reaction between the hydroperoxide and the phosphite in which free radicals were produced, as evidenced by pro-oxidant behaviour. The purpose of the work described in the present study is to examine the chemistry of the hydroperoxide decomposition in detail.

RESULTS AND DISCUSSION

The rates of decomposition of cumene hydroperoxide in nitrogen by three different phosphites (Ia—c) are shown in Figure 1. All are catalysts for the decomposition and show first-order kinetics with respect to hydroperoxide. The apparent first-order rate constants for the three phosphites are listed in Table 1.



(I)

a; R = Pr^i

b; R = Ph

c; R =

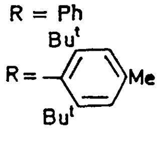


TABLE 1

Apparent first-order rate constants for the decomposition of 0·2M-cumene hydroperoxide in nitrogen at 75 °C by 0·02M-phosphite (I)

Phosphite	k_1/s^{-1}
(Ia)	$8{\cdot}0 \times 10^{-4}$
(Ib)	$2{\cdot}5 \times 10^{-3}$
(Ic)	$6{\cdot}7 \times 10^{-5}$

The phosphite (Ic) decomposed the hydroperoxide in chlorobenzene at the same rate whether oxygen was present in the system or not (see Figure 2) indicating that, for the major part of the decomposition at least, radicals are not involved in the catalytic reaction. Subsequent studies were therefore carried out in the presence of air.

Although apparent first-order kinetics were observed, it was found that the rate constant was dependent on the initial concentration of phosphite (Table 2) indicating a pseudo-first-order reaction of the type (1) where

$$-[\mathrm{CHP}]/\mathrm{d}t = k_2[\mathrm{CHP}]^1 \times [\mathrm{P}]^x \qquad (1)$$

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[1] G. Scott, *Pure and Appl. Chem.*, 1972, **30**, 267.

CHP = cumene hydroperoxide and P = some active peroxide decomposer which is either present in large excess or is a genuine catalyst for the decomposition.

Table 2

Pseudo-first-order rate constants for the decomposition of 0·2M-CHP by phosphite (Ic) in chlorobenzene at 75 °C

[Phosphite]/M	k_1/s^{-1}
0·01	$5·13 \times 10^{-5}$
0·02	$1·08 \times 10^{-4}$
0·03	$1·45 \times 10^{-4}$
0·04	$2·02 \times 10^{-4}$
0·05	$2·39 \times 10^{-4}$

By plotting the log of the pseudo-first-order rate constant against the log of the phosphite concentration a good straight line with a slope of unity was obtained indicating that the reaction is first order with respect to the species P and since this is formed from the phosphite which is present in deficiency, P must be a catalyst for the decomposition of hydroperoxide. Confirmation was obtained for this by the addition of further hydroperoxide at the end of the experiment when it was found (see Figure 3) that the rate of hydroperoxide decomposition was the same (within experimental error) as the original first-order rate but without the initial more rapid reaction. When this procedure was repeated many times over several hours, the same rate was always observed and several hundred-fold excess of hydroperoxide was destroyed. Further confirmation from this hypothesis was that the pseudo-first-order rate constant was essentially independent of the initial hydroperoxide concentration $[CHP]_0$.

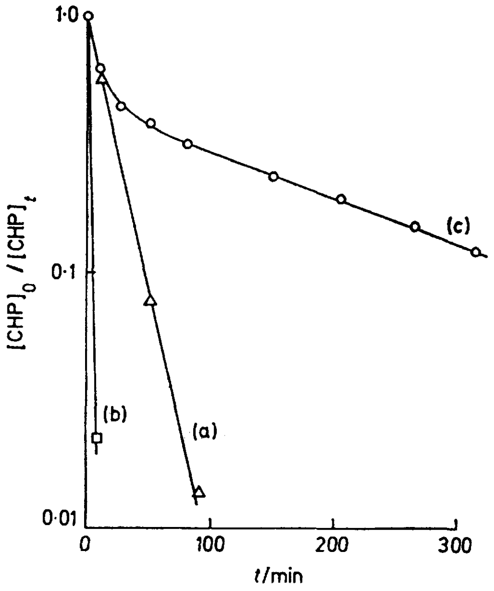


Figure 1 First-order plot for the decomposition of cumene hydroperoxide (0·2M) in cumene by catechol phosphites (0·02M) at 75° under nitrogen: (a), phosphite (Ia); (b), phosphite (Ib); (c), phosphite (Ic)

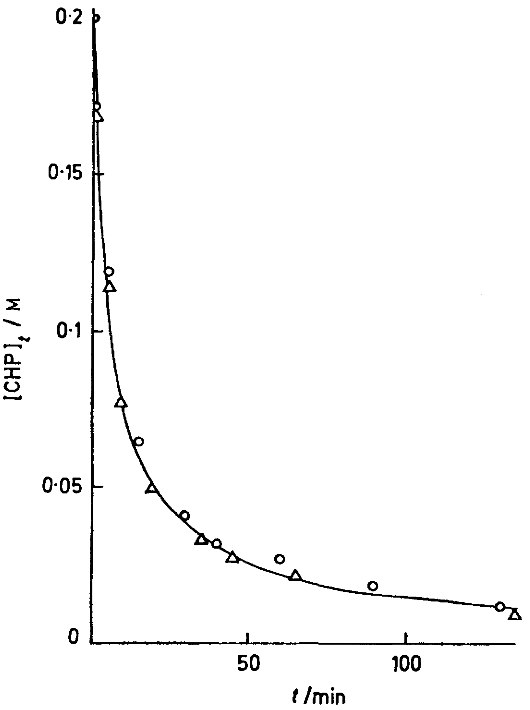


Figure 2 Decomposition of cumene hydroperoxide (0·2M) by phosphite (Ic) (0·02M) in chlorobenzene at 75° in air (○) and in nitrogen (△)

Table 3

Dependence of k_1 on $[CHP]_0$

$[CHP]_0$/M	k_1/s^{-1}
0·1	$1·04 \times 10^{-4}$
0·5	$1·11 \times 10^{-4}$

The behaviour of the acyclic phosphite esters is quite different from that of the catechol phosphites.

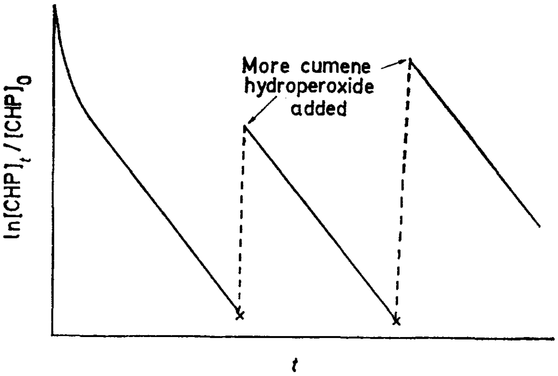


Figure 3 Repeated first-order catalytic decomposition of cumene hydroperoxide in chlorobenzene at 75°

The reaction between cumene hydroperoxide and triphenyl phosphite in chlorobenzene was studied between

75 °C and in all cases a strict stoicheiometry was observed (see Table 4). The reaction was complete even after 1 min at 0 °C.

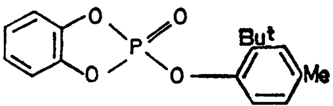
TABLE 4

Stoicheiometry of the reaction between triphenyl phosphite and cumene hydroperoxide

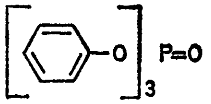
[Phosphite]/M	CHP destroyed/M	Phosphite : CHP stoicheiometry
0·0235	0·025	1 : 1·06
0·0478	0·053	1 : 1·07
0·1003	0·104	1 : 1·03
0·2050	0·200	1 : 1·02

The pseudo-first-order rate constants for the catechol phosphite reaction were measured over a range of temperatures and an Arrhenius plot gave a good straight line from which the activation energy of the catalytic process was calculated as 60·4 ± 1 kJ mol^{-1}. As no information was available on the concentration of the catalytic species [P], the entropy of activation and Arrhenius frequency factor could not be computed.

Extrapolation of the straight line portion of the first-order plot of hydroperoxide destruction to zero time (see Figure 1) gave, over a wide range of concentrations of phosphite (Ic) and hydroperoxide, a constant utilisation of four equivalents of hydroperoxide (±0·4) for the attainment of pseudo-first-order kinetics. This suggests that up to four molecules of hydroperoxide are involved in the formation of the catalytic species. The first product likely to be formed is the phosphate ester and the behaviour of the catechol phosphate (IIa) with triphenyl phosphate (IIb) were compared in the decomposition of cumene hydroperoxide. The first was found to be a powerful catalyst for this reaction whereas the latter was inert. The catalytic activity of (IIa) will be discussed in the following paper,[2] but in accordance with the above stoicheiometry, the phosphate (IIa) is not, in fact, the catalytic species P.

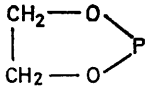


(IIa)

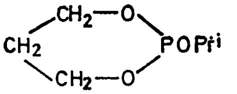


(IIb)

Two other cyclic phosphites were compared with the catechol phosphite (Ic) for peroxide decomposing activity. The five-membered ring compound, ethylene isopropyl phosphite (III), reacted rapidly with cumene hydroperoxide in chlorobenzene at 75 °C, and a slower pseudo-first-order reaction followed. Again the reaction was strongly catalytic and for $[CHP]_0 = 0{\cdot}2$M and $[Phosphite]_0 = 0{\cdot}02$M, k_1 was found to be $5{\cdot}4 \times 10^{-5}$ s^{-1}. The analogous six-membered ring compound (IV) gave similar results with a rather lower decomposition rate.



(III)



(IV)

It is clear then that the catalytic decomposition is general for cyclic phosphites and does not depend on associated aromaticity of the cyclic portion of the molecule.

In view of the apparent pro-oxidant nature of the initial step,[1] this was studied in more detail in stoicheiometric proportion. It was found that the stoicheiometric reaction gives good second-order kinetics (see Figure 4) in chlorobenzene at 20 °C. Somewhat surprisingly, the same kinetics were obtained in the presence and absence of oxygen and in the presence and absence of 4-methyl-2,6-di-t-butylphenol, an efficient antioxidant (see Figure 5). A plot of initial rate *versus* initial phosphine concentration gave a straight line of slope 1·04 (Figure 6) and an analogous series of experiments at constant phosphite concentration gave a straight line of slope 1·02. The overall reaction is therefore (2).

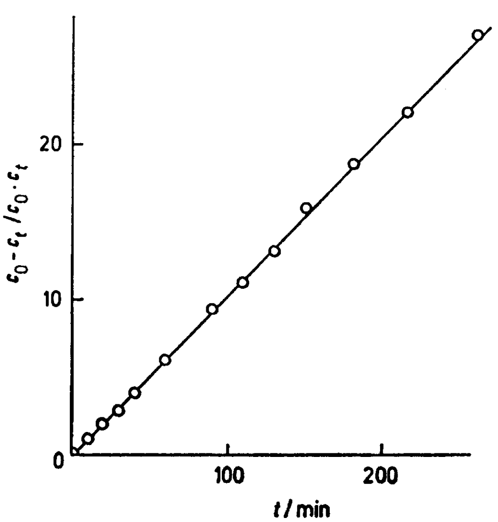


FIGURE 4 Second-order plot for the oxidation of phosphite (Ic) by cumene hydroperoxide (both 0·2M) in chlorobenzene at 20°

$$-d[CHP]/dt = k_2[CHP][Phosphite] \qquad (2)$$

A good Arrhenius plot was obtained by measuring k_2 over a range of temperatures in chlorobenzene from which the activation energy was computed to be 58·9 ± 2 kJ mol^{-1}. $\Delta S^{\ddagger}$ Was found to be −95·3 J mol^{-1} K^{-1} and the frequency factor A was 6×10^7 l mol^{-1} s^{-1}. These data are consistent with a bimolecular polar reaction proceeding by a fairly ordered transition state

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[2] K. J. Humphris and G. Scott, following paper.

and involving the formation of opposite changes,[3] and are qualitatively similar to the same parameters calculated from the results of Rysavy and Slama[4] in a study of the reaction of triphenyl phosphite by t-butyl hydroperoxide. They have reported $E_a = 34$ kJ mol^{-1}. This reaction is, however, faster than the one at present being studied (at 45 °C $k_2 = 3{\cdot}1 \times 10^{-2}$ l mol^{-1} s^{-1}) in accord with the results shown in Figure 1.

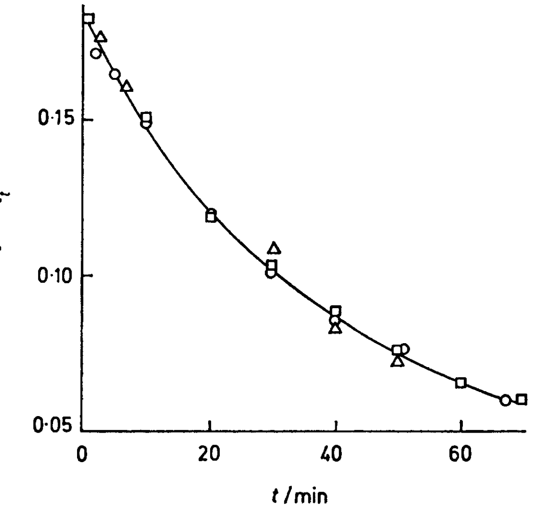


FIGURE 5 Decomposition of cumene hydroperoxide by phosphite (Ic) (both 0·2M) in chlorobenzene at 25° in nitrogen (△), in air (□) and in the presence of 0·05M-4-methyl-2,6-di-t-butylphenol (○)

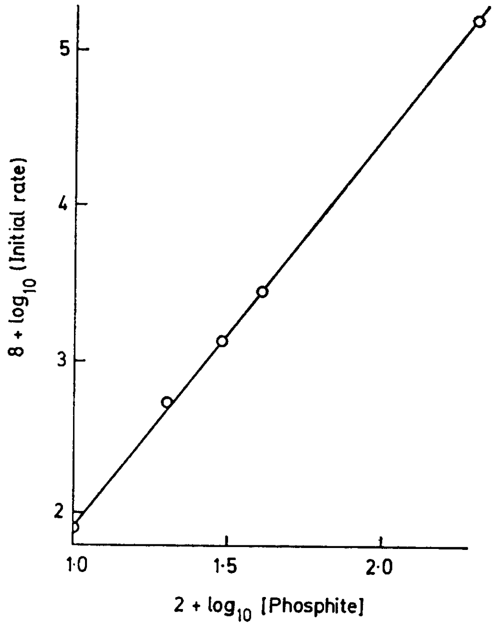
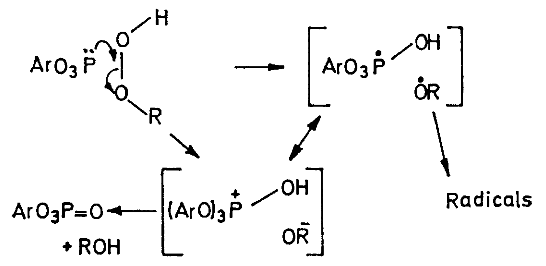


FIGURE 6 Initial rate–initial concentration plot for the reaction of cumene hydroperoxide (0·2M) with phosphite (Ic) in chlorobenzene at 75°

A mechanism consistent with the results is similar to that postulated by Pobedemskii and Buchachenko[5] to explain the formation of free radicals. This involves a nucleophilic redox reaction with the hydroxy-oxygen atom as the rate-determining step, accounting for the low energy of activation.



Since radicals are not involved in the rate-determining step, the absence of interference by radical scavengers is explained. However, radicals can escape from the cage leading to initiation of both oxidation and polymerisation. The latter will be dealt with in a later communication.[6] The nature of the solvent has a very pronounced effect not only on the rate of the catalytic hydroperoxide breakdown (see Table 5) confirming that this is essentially an ionic reaction, but also upon the ratio of the products formed by the two alternative modes of breakdown of the solvent cage. This will be discussed in a subsequent paper.

TABLE 5

Effect of solvent on the catalytic pseudo-first-order decomposition of cumene hydroperoxide by 0·02M-catechol phosphite at 75 °C

Solvent	Dielectric constant	k_1/s^{-1}
Cumene	1·9	$6{\cdot}7 \times 10^{-5}$
Chlorobenzene	4·9	$1{\cdot}08 \times 10^{-4}$
Nitrobenzene	26·9	$1{\cdot}9 \times 10^{-3}$

EXPERIMENTAL

Hydroperoxide concentrations were estimated by the iodimetric method of Mair and Graupner.[7]

A simple reaction vessel was used for the kinetic studies which allowed the reactants to be placed in separate arms until they were equilibrated at the reaction temperature and then mixed. Samples were withdrawn through a septum and two ground glass sockets enabled the reaction mixture to be degassed when required.

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[3] K. J. Laidler, 'Chemical Kinetics,' McGraw-Hill, New York, 1965, p. 237.

[4] D. L. Rysavy and S. Slama, *Chem. průmsyl*, 1968, **18(1)**, 20, (*Chem. Abs.*, 1968, **68**, 96,472h).

[5] D. G. Pobedimskii and A. L. Buchuchenko, *Bull. Akad. Sci. U.S.S.R., Div. Chem. Sci.*, 1968, 1125.

[6] K. J. Humphris and G. Scott, to be published.

[7] R. T. Mair and A. J. Graupner, *Analyt. Chem.*, 1964, **36**, 194.

The reaction of iodine with phosphites, particularly catechol-phosphites, has been reported.[8] It was found however that in the concentration range at which the kinetic experiments were performed, the error involved if all the phosphite reacted with iodine was within the experimental error of the procedure, and for the less reactive catechol-phosphite (Ic), considerably higher concentrations than those used experimentally had little effect.

Thermostatic control was up to 50 (water) ±0·02 °C, 50—120 (Resella oil) ±0·05 °C, and 120—150 (silicone oil) ±0·5 °C. For reactions over long periods, or in an inert atmosphere, or where volatile products were expected, sealed Carius tubes were used.

Materials.—The purification of solvents has been described previously.

o-*Phenylene Phosphorochloridite.*—This was prepared by the method of Crofts,[9] in 60% yield based on catechol, b.p. 91—92° at 18 mmHg, n_D^{20} 1·5710 (lit.,[9] 91° at 18 mmHg, n_D^{20} 1·5724).

Isopropyl o-*Phenylene Phosphite.*—This was prepared from the phosphorochloridite and propan-2-ol by the method of Crofts,[9] yield 56%, b.p. 76° at 3 mmHg, n_D^{18} 1·5060 (lit.,[10] 73—74° at 3 mmHg, n_D^{17} 1·472) (Found: C, 54·1; H, 5·5; P, 15·1. Calc. for $C_9H_{11}O_3P$: C, 54·5; H, 5·5; P, 15·65%).

Phenyl o-*Phenylene Phosphite.*—This was prepared similarly using phenol, b.p. 155° at 12 mmHg (lit.,[11] 150° at 12 mmHg), n_D^{20} 1·5790 (Found: C, 61·9; H, 3·7; P, 12·7. Calc. for $C_{12}H_9O_3P$: C, 62·0; H, 3·8; P, 13·3%).

4-*Methyl*-2,6-*di*-*t*-*butylphenyl* o-*Phenylene Phosphite.*—This was prepared by a modification of Kirpichnikov's method.[12] *o*-Phenylene phosphorochloridite (43 g, 0·25 mol) in dry benzene (50 ml) was added dropwise with stirring to a mixture of triethylamine (25 g, 0·25 mol) and 4-methyl-2,6-di-t-butylphenol (55 g, 0·25 mol) in benzene (200 ml) and cooled to 0°. After refluxing for 3 h, the precipitate was filtered and the product was distilled at 203—204° and 5 mmHg to give a solid (75%) which on crystallisation from absolute ethanol had m.p. 104—105° (lit.,[12] 86—89°) (Found: C, 69·9; H, 7·7; P, 7·2. Calc. for $C_{21}H_{27}O_3P$: C, 70·2; H, 7·8; P, 8·6%) The ^1H n.m.r. spectrum was consistent with the suggested structure and mass spectrum gave a parent peak, at *m*/*e* 358 (Found: M^+, 358·169775. Calc. for $C_{21}H_{27}O_3P$: *M*, 358·170984).

All three catechol phosphites showed a strong i.r. absorption at 1230—1240 cm^{-1} assigned to the P–O–C stretching mode.[13]

Ethylene Phosphorochloridite.—This was prepared by the method of Lucas *et al.*[14] in 66%, b.p. 45—47° at 15 mmHg (lit.,[14] 46·5° at 15 mmHg).

Propane-1,3-*diyl Phosphorochloridite.*—This was prepared similarly in 60% yield, b.p. 66—67° at 15 mmHg, n_D^{22} 1·4885 (lit.,[14] 66° at 15 mmHg, n_D^{25} 1·4884).

Ethylene Isopropyl Phosphite.—Propan-2-ol (24 g, 0·4 mol) in light petroleum (50 ml) was added slowly with stirring below 5° to a mixture of ethylene phosphorochloridite (50 g, 0·4 mol) and pyridine (48 g, 0·6 mol) in light petroleum (250 ml). The product was distilled after filtration of the amine hydrochloride, b.p. 67—69° at 25 mmHg, and after refractionation had b.p. 50° at 10 mmHg, n_D^{20} 1·4365 (lit.,[14] 69° at 25 mmHg, n_D^{25} 1·437) (Found: C, 39·7; H, 7·5; P, 19·1. Calc. for $C_5H_{11}O_3P$: C, 40·0; H, 7·3; P, 20·7%).

Isopropyl Propane-1,3-*diyl Phosphite.*—This was prepared similarly, b.p. 52° at 5 mmHg, n_D^{23} 1·4415 (Found: C, 43·2; H, 7·95; P, 17·35. $C_6H_{13}O_3P$ requires C, 43·9; H, 7·95; P, 18·9%).

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