Mechanisms of Antioxidant Action: Products of the Reaction between Hydroperoxides and *o*-Phenylene Phosphites

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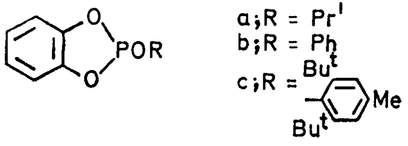
4-Methyl-2,6-di-t-butylphenyl *o*-phenylene phosphite (Ic) reacts with 1-methyl-1-phenylethyl hydroperoxide to give phenol, acetone, and α-methylstyrene as major products with acetophenone and 1-methyl-1-phenylethyl alcohol as minor products. At high ratios of hydroperoxide to phosphite, the former products which are formed by an acid catalysed reaction predominate, although a substantial proportion of the products formed by a radical induced decomposition are present under all conditions. At low hydroperoxide:phosphite ratios the product is almost entirely α-methylstyrene and can be accounted for on the basis of stoicheiometric reduction of 1-methyl-1-phenylethyl hydroperoxide to 1-methyl-1-phenylethyl alcohol. 4-Methyl-2,6-di-t-butylphenyl *o*-phenylene phosphate (IV) and its hydrolysis product the free acid (V) have been identified as products of the reaction. The former is formed both by reaction of the phosphite with hydroperoxide and with alkylperoxyl radicals.

PREVIOUS work has shown [1] that the decomposition of 1-methyl-1-phenylethyl hydroperoxide (cumene hydroperoxide) by phosphites (I) takes place in two stages. The first is a very rapid series of reactions during which the phosphites esters are converted to new chemical species which are powerful catalysts for hydroperoxide decomposition. The first stage appears to consume about four molecules of hydroperoxide for each molecule of phosphite and it involves the formation of free radicals which can initiate autoxidation,[2] and it has also been shown that such a combination can also initiate vinyl polymerisation.[2,3] The purpose of the present work was to study the products formed during the course of the reaction. It has previously been shown that cumene hydroperoxide gives different products depending on the mechanism of its decomposition and that this can be used as a diagnostic test of mechanism.[4] Lewis acid catalysed decomposition gives rise to phenol and acetone in good yield whereas homolytic decomposition, involving the intermediate formation of the aralkoxyl radicals, gives cumyl alcohol or its dehydration product α-methylstyrene and acetophenone depending on the conditions. In the present studies it was not found to be possible to follow the change in product formation during the course of an experiment since the phosphorus-containing catalysts were strongly held on the column support under all conditions and hence catalysed the further decomposition of hydroperoxide during the analysis. The alternative technique was adopted of examining the products of complete decomposition of the hydroperoxide at widely varying initial concentration ratios of hydroperoxide to phosphites.

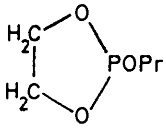


(I)

RESULTS AND DISCUSSION

It was found that when present in molar deficiency all three phosphites (Ia—c) decomposed cumene hydroperoxide to give mainly phenol, acetone, and α-methylstyrene with minor amounts of acetophenone and 1-methyl-1-phenylethyl (α-cumyl) alcohol. No dicumyl peroxide was observed in any of the experiments. At a fixed hydroperoxide concentration (0·02M), the product distribution in chlorobenzene was found to vary considerably with the phosphite concentration. At a molar ratio [CHP] : [Phosphite] of 0·5 the product was found to be entirely α-methylstyrene; no acetone or phenol, the products expected by Lewis acid catalysed decomposition, were formed (see Figure 1). At a molar ratio of 10, the amount of α-methylstyrene formed had reduced to a limiting value of *ca.* 30% and that of phenol approached a limiting value of *ca.* 60%. The same results were obtained irrespective of whether the experiments were carried out in air, vacuum, or nitrogen, reproducibility being better than ±5%.

When the same experiments were carried out in cumene and in nitrobenzene, all in nitrogen, it was found (see Table 1 and Figure 2) that in the more polar solvent, the limiting concentration of α-methylstyrene was much lower (3—5%) and the limiting yields of acetone and phenol were higher.



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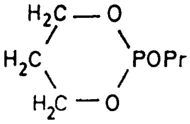

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[1] K. J. Humphris and G. Scott, preceding paper.

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

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

[4] G. Scott, 'Atmospheric Oxidation and Antioxidants,' Elsevier, Amsterdam, 1965, pp. 192 *et seq.*

Qualitative experiments with other cyclic phosphites (II) and (III) which are known to be catalysts for hydroperoxide decomposition[1] showed that they too gave phenol, acetone, and α-methylstyrene as major products with small traces of acetophenone and α-cumyl alcohol. On the other hand triphenyl phosphite which reacts stoicheiometrically with hydroperoxides[1] gave an almost quantitative yield (97·5 mol %) of α-cumyl alcohol and no other products.

TABLE 1

The effect of solvent on the products of the decomposition of cumene hydroperoxide induced by phosphite (Ic) at 75°; $[\mathrm{CHP}]_0 = 0{\cdot}2\mathrm{M}$

$\frac{[\mathrm{CHP}]}{[\mathrm{Phosphite}]}$	Product (mol %)														
	Phenol			Acetone			α-Methylstyrene †			Acetophenone			α-Cumyl alcohol		
	PhCl	RH	$PhNO_2$	PhCl	RH	$PhNO_2$	PhCl	RH	$PhNO_2$	PhCl	RH	$PhNO_2$	PhCl	RH	$PhNO_2$
0·25		5·0	15·5		9·2	46·0		83·5			*	*		1·8	‡
0·5	0·1	8·0	22·0	1·0	12·0	52·5	100	82·5	26·5	0·25	*	*	*	2·2	‡
1·0	12·0	15·0	31·5	11·5	18·5	45·0	85	70·7	26·0	0·55	0·3	*	*		‡
2·0	35·5			26·2			63·5			1·4			0·4		‡
2·5		34·0	44·5		24·5	59·0		58·0	7·0		0·5	*		1·8	‡
5·0	49	51·2	60·0	48	27·8	69·5	32·8	44·0	4·0	2·0	0·7	*	0·6	2·0	‡
10·0	59	56·6	81·5	50	28·0	74·4	31·0	38·5	3·5	2·45	0·5	*	0·75	2·0	‡

RH = Cumene.

* Trace; not measured. † The yield of α-methylstyrene was subject to some variation which depended on the time the products were allowed to react at 75°. The measurement was made in all cases when the hydroperoxide was just destroyed. ‡ A large unidentified peak with the same retention time as α-cumyl alcohol interfered with the estimation.

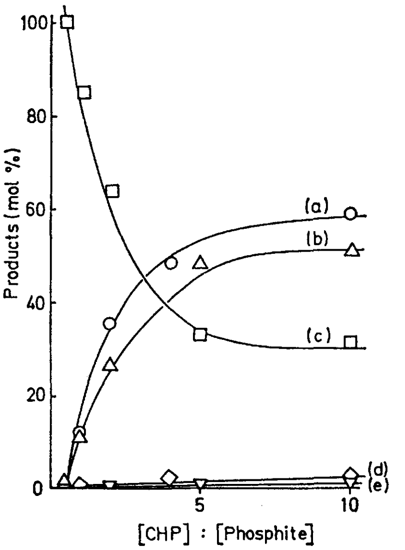


FIGURE 1 Product distribution from the reaction of cumene hydroperoxide ($[\mathrm{CHP}]_0 = 0{\cdot}2\mathrm{M}$) with phosphite (Ic) in chlorobenzene at 75° with varying [CHP] : [Phosphite] ratio: (a), phenol; (b), acetone; (c), α-methylstyrene; (d), acetophenone; (e), α-cumyl alcohol

It seems clear that the course of the reactions of cyclic phosphites can be divided into two consecutive phases. The first, which is identical with the only reaction occurring in the case of the acyclic phosphites is the stoicheiometric oxidation to phosphate with concomittant formation of cumyl alcohol. The formation of α-methylstyrene rather than the parent alcohol indicates the presence of a Lewis acid species capable to catalysing the dehydration of the alcohol in the case of the cyclic phosphites but not in the case of the acyclic phosphites. In the former case the phosphate undergoes further reaction with hydroperoxide to give a catalytic species which appears to have the ability to decompose cumene hydroperoxide contemporaneously in two quite different ways. In the first it acts as a Lewis acid giving phenol and acetone and in the second it promotes the formation of alcohol and hence α-methylstyrene. The latter reaction appears to play a significant role in chlorobenzene at all ratios of hydroperoxide to phosphite (see Figure 1).

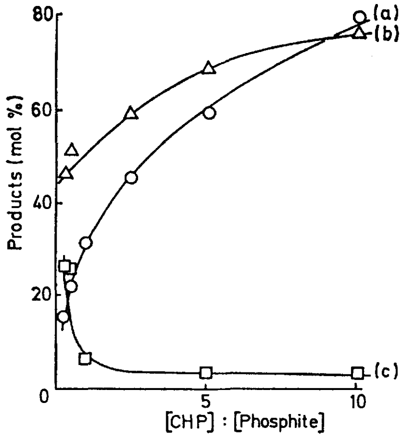


FIGURE 2 Product distribution from the reaction of cumene hydroperoxide ($[\mathrm{CHP}]_0 = 0{\cdot}2\mathrm{M}$) with phosphite (Ic) in nitrobenzene at 75° with varying [CHP] : [Phosphite] ratio: (a), phenol; (b), acetone; (c), α-methylstyrene

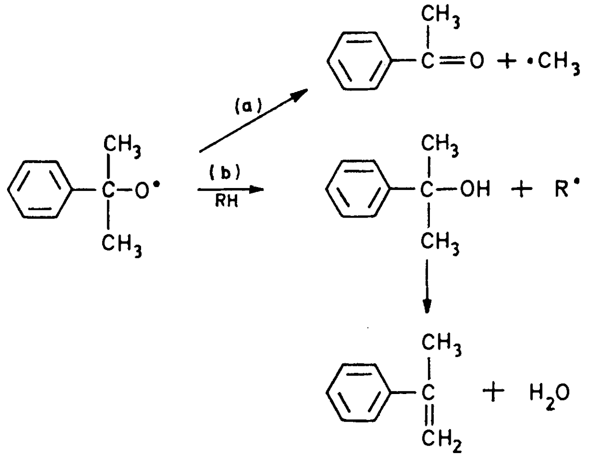
When the phosphite was reacted with a four-fold excess of hydroperoxide (which it was shown earlier is enough to convert it to catalytic species[1]) and was then allowed to decompose a further four-fold excess of hydroperoxide, the amount of α-methylstyrene produced was reduced but not to zero. In the second stage 17 mol % of α-methyl styrene was still produced (see Table 2).

TABLE 2

Principal products formed from the decomposition of cumene hydroperoxide by phosphite (Ic) and by its oxidation products in chlorobenzene at 75°

	Products (mol %)		
Reaction	Phenol	Acetone	α-Methylstyrene
1. CHP (0·2M) + Phosphite (0·2M)	49	42	37
2. Reaction products of above +CHP (0·2M)	58	46	27
Products formed in reaction 2	67	50	17

When cumene was used as solvent rather more α-methylstyrene and cumyl alcohol were formed (see Table 1). Also less acetophenone was formed than in chlorobenzene. These facts are consistent with a contribution from the competitive hydrogen abstraction from the solvent (Scheme).



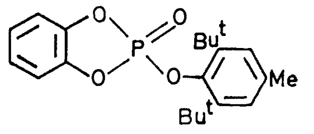
SCHEME

It was found that all the cyclic phosphites had the ability to catalytically dehydrate α-cumyl alcohol to α-methylstyrene. A kinetic study in chlorobenzene at 75° showed that in the case of the phosphite (Ic) good second-order kinetics were obtained ($k_2 = 2{\cdot}1 \times 10^{-3}$ l mol^{-1} s^{-1}) by monitoring the formation of α-methylstyrene. The reaction was not catalysed by hydroperoxide. This contrasted with the behaviour of triphenyl phosphite which did not catalyse the decomposition of α-cumyl alcohol after many hours at 75°. Lewis acid catalysed dehydrations of tertiary alcohols are well known[5] and it seems likely that the same Lewis acid species is responsible for the dehydration of alcohol and the catalytic decomposition of cumene hydroperoxide to phenol and acetone.

It is difficult to see how α-cumyl alcohol and α-methylstyrene can be formed in the amounts reported here other than by a radical induced decomposition of hydroperoxide. The alternative base catalysed reaction reported by Kharasch and his co-workers[6] seems unlikely in the presence of a Lewis acid. It has been reported previously[7] that in the case of the dithiocarbamate salts which are also powerful peroxide decomposing antioxidants very high yields of phenol and acetone were formed in benzene with little or none of the homolytically derived products. A similar situation is found in the present work in the case of nitrobenzene at hydroperoxide : phosphite ratios above 5. That is, if the stoicheiometry of catalyst formation is 4 : 1, the major reaction occurring in this case is Lewis acid decomposition.

Attempts to identify the catalytic species were only partially successful due to the complexity of the products which included not only phosphorus residues but also high molecular weight products derived from the polymerisation of α-methylstyrene.

Mass spectroscopic examination of the residue showed the presence of phosphate (IV) by peak matching of the parent ion (*m/e* 374). Subsequently compound (IV) was synthesised by oxidation of the corresponding phosphite with t-butyl hydroperoxide in chlorobenzene at 75°. Oxygen in the presence of azobisisobutyronitrile was also shown to oxidise the phosphite (Ic) to the corresponding phosphate. A solution containing 0·1M-phosphite and 0·01M-azobisisobutyronitrile in chlorobenzene was thermostatted under oxygen at 75° until the azo-compound had decomposed (20 h). The concentration of the phosphate was found to be 0·0065M by mass spectrometry, (*i.e.* a 30% yield based on theoretical alkylperoxyl radical available). This is a result of the non-terminating displacement involving scission of the O–O bond.[8]



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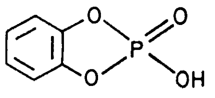

(V)

The phosphate (V) was found to be present as a product from the reaction of cumene hydroperoxide with both phosphite (Ic) and phosphate (IV) by mass spectrometry (*M*, 171·992544). Small quantities of

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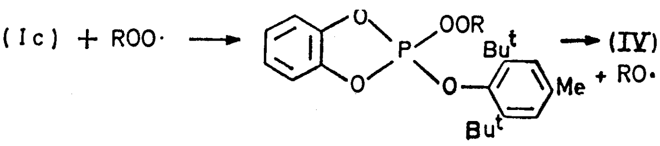
[5] H. Knozinger, 'The Chemistry of the Hydroxyl Group,' ed. S. Patai, Interscience, New York, 1971, vol. 2, p. 642.

[6] M. S. Kharasch, A. Fono, and W. Nudenberg, *J. Org. Chem.*, 1951, **16**, 113.

[7] J. D. Holdsworth, G. Scott, and D. Williams, *J. Chem. Soc.*, 1964, 4692.

[8] C. Walling and R. Rabinowitz, *J. Amer. Chem. Soc.*, 1959, **81**, 1243.

4-methyl-2,6-di-t-butylphenol corresponding to this were also found at high hydroperoxide : phosphite ratios.



The behaviour of these derived products as peroxide decomposing antioxidants will be discussed in a later publication.

EXPERIMENTAL

All samples were analysed on a Pye ' Series 104 ' chromatograph using a flame ionisation detector. All glass columns (5 ft) were packed with 10% polyethylene glycol adipate on Celite, and were pre-heated for 48 h at 190°. All service gases were purified by passage through molecular sieves (Union Carbide type 13X), and nitrogen was used throughout as carrier gas. Output from the amplifier was fed to a millivolt recorder. In the quantitative work internal standards were used to eliminate the difficulties and inaccuracies inherent in measuring small volumes precisely. The determination of cumene hydroperoxide decomposition products was carried out for convenience at two temperatures. The characteristics of the internal standard are shown in Table 3. Solutions containing a fixed concentration of standard and varying concentrations of product were chromatographed. Two injections were made for each concentration. Calibration curves obtained by plotting the peak ratio (product : standard) against concentration gave excellent straight lines. In all cases the mixture of internal standards was added to the mixture after completion of the reaction and with quenching to ensure no reaction occurred with the standards.

TABLE 3

G.l.c. characteristics of standards and products formed from the decomposition of cumene hydroperoxide

Product	Retention distance (cm)	Internal standard	Retention distance	Temp. (°C)
Phenol	8·3	*p*-Cresol	11·1	140
Acetophenone	6·6			
α-Cumyl alcohol	3·6			
Acetone	0·9	Dioxan	2·3	65
α-Methylstyrene	10·7			

Quantitative Mass Spectrometry.—This technique was used to estimate the phosphate (IV) using the integrated ion-current method due to Jenkins and Majer.[9] The peak at *m/e* 374 (the parent ion) was selected and the area under the ion-current curve obtained by controlled evaporation of the sample was measured by cutting out the recorded trace and weighing. The calibration plot for ' peak weight ' against concentration gave a good straight line.

Materials.—The synthesis of the phosphites esters is described in the preceding paper.[1] The purification of the g.l.c. chromatography standards was carried out as follows. AnalaR grade phenol was distilled and a middle cut taken at 179° and 748 mmHg, which cooled to give needles, m.p. 36—40° which were stored in a darkened desiccator. AnalaR grade acetone was used without further purification. Acetophenone was distilled at 199—200° and 748 mmHg, n_D^{22} 1·5313. 4-Methyl-2,6-di-t-butylphenol (from I.C.I., Heavy Organic Chemicals Division) was recrystallised thrice from ethanol–water, yielding off-white crystals, m.p. 34°. 2-Phenylpropan-2-ol (α-cumyl alcohol) was distilled at 93·94° and 13 mmHg, recrystallised thrice from light petroleum, and had m.p. 34°. 2-Phenylpropene (α-methylstyrene) was distilled at 164—166° and 755 mmHg, n_D^{21} 1·5362. AnalaR grade *p*-cresol was used without further purification. All components gave a single peak on g.l.c.

4-Methyl-2,6-di-t-butylphenyl o-*Phenylene Phosphate* (IV).—Unsuccessful attempts were made to synthesise this by reaction of the phosphorochloridate with 4-methyl-2,6-di-t-butylphenol. A complex mixture of products was obtained. Ozonisation was found to give the desired product in low yields. Phosphite (Ic) (10 g, 0·028 mol) in CH_2Cl_2 (30 cm^3) was cooled to $-78°$ and air containing the equivalent of 0·7 g O_3 per hour (60 l mixture h^{-1}) was bubbled through the solution for 2 h. Removal of solvent followed by trituration with methanol gave a solid (15%) which after recrystallisation from ethyl acetate had m.p. 223—225° (Found: C, 67·2; H, 7·3; P, 8·35. Calc. for $C_{21}H_{27}O_4P$: C, 67·3; H, 7·25; P, 8·3%). The i.r. spectrum was closely similar to that of the parent phosphite with an additional strong band at 1310 cm^{-1} assigned to the phosphoryl absorption,[10,11] and the n.m.r. spectrum was consistent with the structure assumed. The mass spectrum showed a parent ion at *m/e* 374 (Found: M^+, 374·162995. Calc. for $C_{21}H_{27}O_4P$: *M*, 374·164134).

Subsequently it was found that the phosphate could be obtained in better yield by oxidation of the phosphite with t-butyl hydroperoxide. Phosphite (Ic) (8 g, 0·025 mol) and of t-butyl hydroperoxide (2 g, 0·025 mol) were thermostatted in chlorobenzene (100 ml) at 75° until no more hydroperoxide remained. Removal of solvent and volatiles by rotary evaporation yielded a brown solid from which the product was obtained in 80% yield by trituration with methanol. The physical constants were identical with those reported above.

Hydrogen o-*Phenylene Phosphate* (V).—This was prepared by heating P_2O_5 (71 g, 0·5 mol) with catechol (137 g, 1·25 mol) for 30 min at 100°.[12] Distillation at 135° and 3 mmHg yielded a viscous syrup which solidified to a glassy solid on standing. The product was refractionated through a Dufton all-glass column at 125—130° and 3 mmHg (lit.,[12] 125° at 3 mmHg). Exposure to the atmosphere resulted in rapid hydrolysis and the i.r. spectrum could not be obtained. The mass spectrum showed a parent peak at *m/e* 172 (Found: M^+, 171·992257. Calc. for $C_6H_5O_4P$: *M*, 171·990853).

Dihydrogen o-*Hydroxyphenyl Phosphate*.—This was pre-

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[9] A. E. Jenkins and J. R. Majer, *Talanta*, 1967, **14**, 777.

[10] L. J. Bellamy, ' Infrared Spectra of Complex Molecules,' Methuen, London, 1958, 2nd edn., p. 323.

[11] D. E. C. Corbridge, ' Topics in Phosphorus Chemistry,' Interscience, New York, 1969, vol. 6, p. 235.

[12] E. Cherbuliez, M. Schwartz, and J. P. Leber, *Helv. Chem. Acta*, 1951, **34**, 841.

pared[12] by dissolving the phosphate (V) in a small amount of water; on removal of the excess by rotary evaporation, a syrup which solidified on cooling was obtained. Crystallisation from benzene–ethyl acetate gave a solid, m.p. 139—141° (lit.,[12] 139°). The i.r. spectrum contained a broad shallow band from 2000—3500 cm^{-1} with maxima at 2700 and 3300 cm^{-1} associated with extensive hydrogen bonding.[10,11]

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