958. *Radical-capture Agents in Tetralin. Measurement of Relative Efficiencies and Correlation with Structure.*

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Measurements of the inhibition of the autoxidation of tetralin have been used to determine the relative rates of the radical-capture reaction

$$TO_2\cdot + AH \longrightarrow TO_2H + A\cdot$$

($TO_2\cdot$ = tetralyl peroxide radical: AH = antioxidant)

for a series of simple phenols. Electron-repelling substituents in the phenols increase the rate and electron-attracting ones decrease it. For polyalkylated phenols, the effects of substituents on the logarithm of the rate are additive, except for 2 : 6-substitution. There is a correlation between the energy of the highest occupied molecular orbital in a phenol (as calculated by the non-bonding orbital method) and the rate at which it captures radicals.

Substances containing hydrocarbon chains, *e.g.*, petroleum, rubber, edible fats, Polythene, are commonly preserved from oxidative deterioration by addition of antioxidants. It has been established [1-4] that sometimes these oxidations occur by the mechanism

$$\begin{array}{ll}
(1) & I \longrightarrow X\cdot \\
(2) & X\cdot + RH \longrightarrow R\cdot + XH \\
(3) & R\cdot + O_2 \longrightarrow RO_2\cdot \\
(4) & RO_2\cdot + RH \longrightarrow RO_2H + R\cdot
\end{array}\left.\vphantom{\begin{array}{l}a\\a\end{array}}\right\}\text{chain propagation}$$

$$\begin{array}{ll}
(5) & RO_2\cdot + RO_2\cdot \longrightarrow \text{dead products (termination in absence of antioxidant)} \\
(6) & RO_2\cdot + AH \longrightarrow RO_2H + A\cdot \text{ (termination in presence of antioxidant)}
\end{array}$$

In this system, I is an initiator (present perhaps by chance) which gives radicals X·; RH is the hydrocarbon suffering oxidation, and AH the antioxidant. For AH to be efficient, reaction (6) must be fast and the derived radical A· must be unable to generate

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[1] Bolland and Gee, *Trans. Faraday Soc.*, 1946, **42**, 236.
[2] Bolland and ten Have, *ibid.*, 1947, **43**, 201.
[3] *Idem, ibid.*, 1949, **45**, 93.
[4] Bamford and Dewar, *Proc. Roy. Soc.*, 1949, *A*, **198**, 252.

fresh R· radicals from RH. The way in which these properties vary with the structure of AH is therefore of obvious practical as well as theoretical interest. This paper describes the development of an experimental method for measuring radical-capture efficiency in a model oxidation which can be used to investigate as many as possible of the various types of radical-capture agents.

Bolland and ten Have[2] have carried out this type of measurement for a few inhibitors, using the benzoyl peroxide-catalysed autoxidation of ethyl linoleate as their reference system, and Bamford and Dewar[4] used the effects of three inhibitors in elucidating the kinetics of the oxidation of tetralin. Our present method was developed directly from the methods of these authors : tetralin has been the substrate normally used, but measurements have also been carried out with ethyl linoleate.

The main difficulty encountered was the establishment of an initiator system which could be used with the widest possible variety of antioxidants. Photochemical methods were tried, with anthraquinone and its derivatives as photosensitisers, but failed because many inhibitors give coloured products. The photosensitiser solutions also proved inconveniently unstable. In our hands initiation by benzoyl peroxide proved unsatisfactory, partly because this substance can react directly with many of the phenols which were studied (although Bolland and ten Have were able to use it for a limited number of phenols), and partly because the oxidation rates were sensitive to the state of the surface of the reaction vessel. The final choice was azo*iso*butyronitrile (AZDN) which gives radicals by the reaction

$$\mathrm{CN{\cdot}CMe_2{\cdot}N{:}N{\cdot}CMe_2{\cdot}CN \longrightarrow 2CN{\cdot}CMe_2{\cdot} + N_2}$$

at a rate virtually independent of the environment.[5, 6]

Oxidation Kinetics.—Application of the stationary-state method to steps (1)—(4) and (6) of the above reaction scheme leads to the equation

$$-\mathrm{d}[\mathrm{O_2}]/\mathrm{d}t = R_i(1 + k_4[\mathrm{TH}]/k_6[\mathrm{AH}]) \quad . \quad . \quad . \quad . \quad . \quad \text{(i)}$$

so that a plot of $-\mathrm{d}[\mathrm{O_2}]/\mathrm{d}t$ against $1/[\mathrm{AH}]$ should give a straight line if R_i, the rate of chain-starting, is constant. Fig. 1 shows two cases in which (i) was tested directly; straight lines were obtained, the intercepts being equal within the experimental error.

The direct testing of (i) is however tedious, and a quicker method of checking the applicability of the reaction scheme is to consider the variation of rate with time during a single experiment. If we assume that the antioxidant is only used in stopping oxidation chains, then under stationary-state conditions

$$[\mathrm{AH}] = [\mathrm{AH}]_0 - R_i t \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(ii)}$$

where $[\mathrm{AH}]_0$ is the initial concentration. From (i) and (ii)

$$\frac{1}{-\mathrm{d}[\mathrm{O_2}]/\mathrm{d}t - R_i} = \frac{k_6}{k_4[\mathrm{TH}]} \cdot \left\{ \frac{[\mathrm{AH}]_0}{R_i} - t \right\} \quad . \quad . \quad . \quad . \quad . \quad \text{(iii)}$$

If R_i is constant for the period in question, and further if it is negligible compared with $\mathrm{d}[\mathrm{O_2}]/\mathrm{d}t$, then a plot of $1/(-\mathrm{d}[\mathrm{O_2}]/\mathrm{d}t)$ against time should be linear.

As regards the first condition, it is known[5, 6] that approximately 1% of AZDN decomposes in 1 hr. at 50°, so that in these experiments (maximum duration 2 hr.) the amount of initiator could be taken as constant throughout. It is, however, also known[7, 8] that not every radical derived from the decomposition of AZDN starts chains; Bateman and Morris[7] find that the ratio of R_i to the total number of radicals produced in the same time is 0·5 in tetralin at 45°, while in the present work it was found by the same method to be 0·6 at 50°.

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[5] Overberger, O'Shaughnessy, and Shalit, *J. Amer. Chem. Soc.*, 1949, **71**, 2661 (cf. Melville and Cooper, *J.*, 1951, 1994).

[6] Bawn and Mellish, *Trans. Faraday Soc.*, 1951, **47**, 1223.

[7] Bateman and Morris, *Trans. Faraday. Soc.*, 1952, **48**, 1149.

[8] Hammond, Sen, and Boozer, *J. Amer. Chem. Soc.*, 1955, **77**, 3244.

For constancy of R_i it is therefore also necessary that this ratio should be constant under the conditions used and unaffected by the presence of an antioxidant. From the results quoted below it seems clear that this condition is, in fact, fulfilled, and Fig. 4 shows that at constant $[AH]_0$ the initial rate of oxidation varies linearly with [AZDN].

The quantity measured in these experiments was the net absorption of gas by the system, $-dG/dt$, which is of course the resultant of the absorption of oxygen by the tetralin, $-d[O_2]/dt$, the absorption of oxygen by AZDN radicals, and the evolution of nitrogen by decomposing AZDN molecules. If dG'/dt, the sum of the last two terms, and R_i are together negligible compared with the rate of absorption of oxygen by the tetralin, (iii) becomes

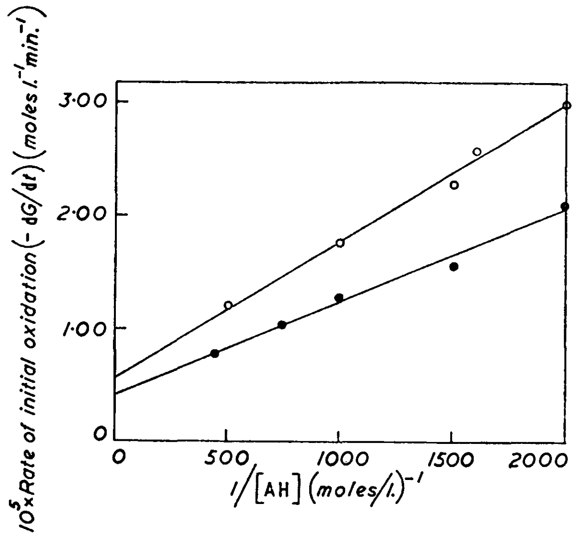


FIG. 1. *Plot of initial rate of oxidation against* 1/[*antioxidant*].

○ 2-*tert*.-Butyl-4 : 6-dimethylphenol.
● Quinol.

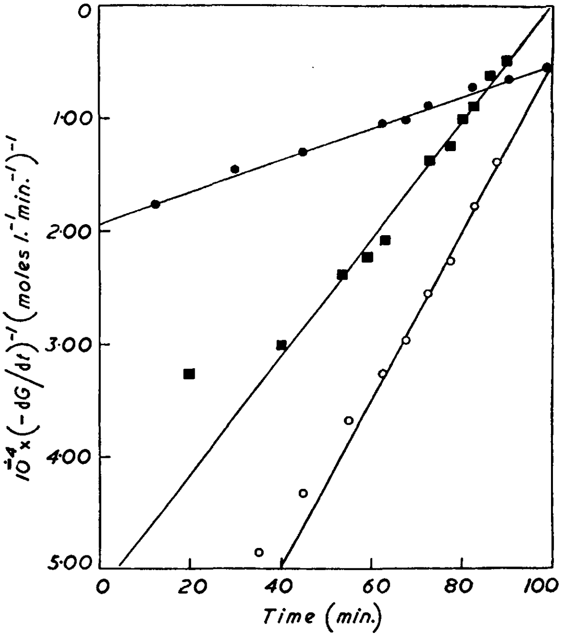


FIG. 2. *Plot of* $(-dG/dt)^{-1}$ *against time* ($[AH]_0$ *constant at* 10^{-3} *mole/l.*).

○ Quinol.
■ 2-*tert*.-Butyl-4 : 6-dimethylphenol.
● 2 : 4-Dimethylphenol.

$$\frac{1}{-dG/dt} = \frac{k_6}{k_4[TH]}\left\{\frac{[AH]_0}{R_i} - t\right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (iv)$$

This equation held satisfactorily in all cases tested, below a particular antioxidant concentration depending on the activity of the antioxidant, *i.e.*, above a certain rate of oxidation. Fig. 2 illustrates this point; it will be seen that with the two better antioxidants the rates of oxidation are at first too low for (iv) to hold (though the earliest deviations are partly due to initial disturbances of the system), but later, when $(R_i + dG'/dt)$ has become negligible compared with $-d[O_2]/dt$, (iv) is closely followed; (iv) also predicts that the intercept of the $1/(-dG/dt)$ against t line should be $[AH]_0/R_i$ times the slope, and Fig. 3, which gives the results of plotting the slopes against the intercepts measured for a series of antioxidants at constant $[AH]_0$, shows that there is in fact a constant proportionality between the two quantities.

FIG. 3. *Plot of slopes against intercepts from the* $(-dG/dt)^{-1}$*–time graphs.*

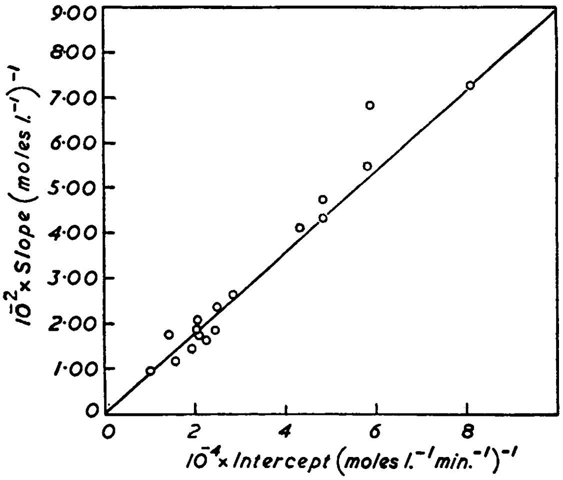
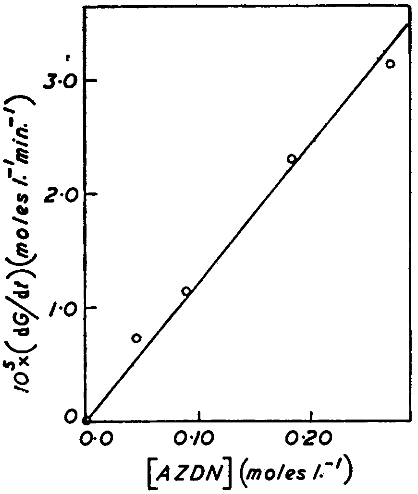


FIG. 4. *Plot of initial rate of oxidation against initiator concentration* ([AH] *constant at* 10^{-3} *mole/l. of* 2-tert.*-butyl-4 : 6-dimethylphenol*).



Whilst this work was in progress, Boozer, Hammond, and their co-workers [9] brought evidence to show that with antioxidants of " intermediate activity " the simple hydrogen-abstraction reaction (6) is not the chain-termination step in the inhibited oxidation of tetralin and cumene. This led the authors to postulate a two-stage reaction involving first the reversible formation of a molecular complex between $RO_2\cdot$ and AH, followed by reaction of this complex with another peroxide radical giving inactive products. In the case of phenol and diphenylamine the rate of oxidation was shown to be proportional to $\sqrt{R_i}$ and $1/\sqrt{[AH]}$.

In the present paper phenol and compounds 1 and 2 shown in Table 1 were found to be of such low antioxidant activity that the linear relation between $1/(-dG/dt)$ and time [equation (v)] no longer applies. But for all other compounds listed in the Table there is good evidence that the kinetic scheme and underlying assumptions are sound, and one may therefore consider the antioxidant activities so measured.

Relative Antioxidant Efficiencies.—Table 1 gives the relative values of the rate constant k_6 for capture of tetralyl peroxide radicals, determined in the form of the ratio k_6/k_4 at 50°, for a series of simple phenols.

Effect of varying substituents in the para*-position.* The values for compounds 1—8 show that, in the *para*-position, an electron-releasing substituent (alkoxyl, alkyl groups) generally improves the efficiency and an electron-withdrawing substituent impairs it. The values for the very poor antioxidants phenol, *p*-chlorophenol, and *p*-nitrophenol have

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[9] (*a*) Boozer and Hammond, *J. Amer. Chem. Soc.*, 1954, **76**, 3861; (*b*) Boozer, Hammond, *et al.*, *ibid.*, 1955, **77**, 3233; (*c*) *Idem*, *ibid.*, p. 3238.

qualitative rather than quantitative significance, because the rates of oxidation here are becoming close to the "uninhibited" rate, so that termination by reaction (5) cannot be ignored, and because there is some evidence[10] that the phenoxide radicals in these cases may be able to re-start chains.

Effect of polysubstitution by alkyl groups. Polysubstitution by alkyl groups is, as might be expected, more effective than monosubstitution. Moreover, the total effect of the various groups in a di- or tri-substituted compound on the logarithm of k_6 is usually the sum of the effects of the individual groups in the appropriate monosubstituted phenols. This is shown in Fig. 5. Here, values of $\Delta \log k$ have been set up for the 2-, 3-, and 4-methyl, and 2- and 4-*tert.*-butyl groups, and the rates then calculated for the polysubstituted compounds by simply summing the appropriate logarithm increments. As can be seen, agreement between calculated and observed rates is quite good until substituents are inserted in both the 2- and the 6-position. For all such compounds, the observed rates of chain termination are lower than expected, the discrepancy being especially marked in the case of 2 : 6-di- and 2 : 4 : 6-tri-*tert.*-butylphenols. The interpretation of this seems clear: the alkyl groups influence the ease of fission of the O–H bond by the usual mesomeric effect. This is primarily reflected in the activation energy, E_6, and each group makes its own individual contribution to the lowering of E_6, unperturbed by the presence of other groups.

TABLE 1. *Phenols: Effect of substituents on radical-capture efficiency and hydroxyl band frequency.*

No.	Substituent	k_6/k_4	OH Band frequency (cm.$^{-1}$)	No.	Substituent	k_6/k_4	OH Band frequency (cm.$^{-1}$)
	Single *para*-substituents				Three substituents		
1	p-NO_2	52	3597	22	2 : 4 : 6-Bu^t_3	1430	3642
2	p-CO_2H	52	—	23	2 : 4 : 6-Me_3	3070	3621
3	(H)	83	3610	24	2 : 4-Bu^t, 6-Me	3240	—
4	p-Me	291	3610	25	2 : 6-Bu^t, 4-Me	1990	3643
5	p-Bu^t	464	3614	26	2-Bu^t, 4 : 6-Me_2	3320	3618
6	p-$CH_2Ph{\cdot}O$	1710	3616				
7	p-$Bu^n{\cdot}O$	2330	—		Other compounds		
8	p-OH	5540	3620	27	α-Naphthol	3950	—
				28	β-Naphthol	830	—
	Other single substituents			29	1-Hydroxyphenanthrene	4060	—
9	m-Me	193	—	30	2-Hydroxyphenanthrene	437	—
10	o-Me	522	3612	31	3-Hydroxyphenanthrene	990	—
11	o-Bu^t	787	3609	32	4-Hydroxyphenanthrene	3090	—
	Two substituents						
12	3 : 5-Me_2	545	—				
13	2 : 3-Me_2	591	—				
14	3 : 4-Me_2	697	—				
15	2 : 4-Bu^t_2	1430	3610				
16	2 : 4-Me_2	1310	3616				
17	2-Bu^t, 4-Me	1660	3611				
18	4-Bu^t, 2-Me	1580	—				
19	2 : 6-Bu^t_2	967	3640				
20	2 : 6-Me_2	1110	3621				
21	2-Bu^t, 6-Me	1450	3620				

The mesomeric effect is greatest when the O–H bond lies in the plane of the benzene ring. It is only where two *ortho*-substituents are present that this is unlikely to be the case. When two such groups are present, the conjugation of the p-electrons of the oxygen with the π-electrons of the ring will be impaired, and the electronic effects of the substituents will no longer be so simple. Moreover, it is likely that steric factors will become important, and will cause the rate to fall. The chemical properties of the 2 : 6-dialkylated phenols, as is well known, exhibit this "hindrance."

The Infrared Spectra of Phenolic Antioxidants.—In the discussion in the preceding paragraph, it has been tacitly assumed that the hydrogen atom which is concerned in radical

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[10] Bolland and ten Have, *Discuss. Faraday Soc.*, 1947, **2**, 252.

capture is that attached to the oxygen atom. If this is true, the properties of the O–H bond must be relevant to antioxidant activity, and the most obvious one to investigate is the force constant for stretching, as revealed by the frequency of the appropriate band in the infrared spectrum. These frequencies have been measured, and are recorded in Table 1.

In the series of *para*-monosubstituted compounds (1—8), there is a progressive increase in the O–H stretching frequency (measured in dilute solution in carbon tetrachloride) with increasingly electron-repelling substituents. Although the effect is not large, it is quite definite: the difference between the extreme cases (*p*-nitrophenol and quinol) is 23 wave-numbers, whilst the limits of resolution are 2—3 wave-numbers. There is, therefore, a correlation between the force-constant for O–H stretching and the radical-capture efficiency. Curiously, the direction of this correlation is the reverse of what might have been expected:[11] active radical-capture agents are presumably those for which the resistance to the total rupture of the O–H bond is *least*, and yet it is now found that in these cases the resistance to small displacements (those brought about by infrared quanta) is *greatest*.

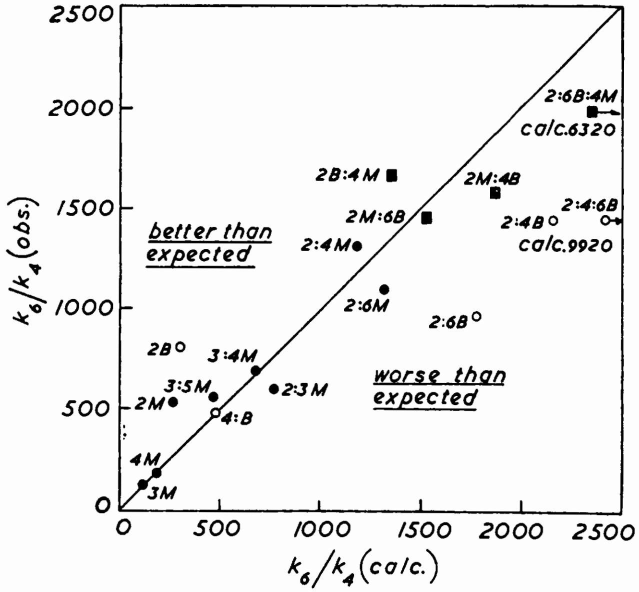

FIG. 5. *Additivity of substituent effects: plot of observed against calculated values of* k_6/k_4.

B = *tert.*-Butyl.
M = Methyl.

Such a state of affairs is of course physically quite possible, but is rather difficult to interpret. For the present, it will not be further discussed.

Correlation of Radical-capture Efficiencies in Different Oxidations.—It is of interest to find out whether variations in the structure of the peroxide radical $RO_2\cdot$ are accompanied by any change in its relative reactivity toward various antioxidants. Table 2 shows a comparison between the present results in tetralin and those of Bolland and ten Have[2] in ethyl linoleate. From this it appears that the efficiencies run parallel and that results are not greatly dependent on the nature of the peroxide radical.

TABLE 2. *Comparison of radical-capture efficiencies in the autoxidation of tetralin and ethyl linoleate.*

	Relative efficiency in	
Compound	tetralin (50°)	ethyl linoleate (45°)
Quinol	1	1
α-Naphthol	0·75	0·56
β-Naphthol	0·15	0·077

Quantum-mechanical Considerations.—If we accept the view that it is the O–H bond

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[11] Cf. Walsh, *Trans. Faraday Soc.*, 1947, **43**, 60.

which participates in the termination reaction, and that variations in antioxidant efficiency are due mainly to changes in the activation energy E_6 of reaction (6), it is possible to consider the effect of structure on antioxidant efficiency, from the quantum-mechanical aspect. If the linear relation between the activation energy and the heat of reaction found in some cases [12] exists here also, then when AH is varied a linear relation may be expected between log k_6 and D_{AH}, the energy of the dissociation of AH into A• and H•, which in turn will depend on the energy U of the most loosely held mobile electron in the compound in question.

The quantity U is very readily evaluated by the non-bonding molecular-orbital method due to Longuet-Higgins [13] and Dewar.[14] If the non-bonding molecular-orbital coefficient $= \alpha$ at that atom in the isoconjugate system which is replaced by oxygen in the hydroxy-compound, the corresponding energy level, in units of β_{cc}, $= \alpha_0^2\delta$ where $\alpha_0 = \delta\beta_{cc}$ and $\beta_{co} = \beta_{cc}$. If it is desired to distinguish between the magnitudes of β_{co} and β_{cc}, writing $\beta_{co} = \gamma\beta_{cc}$, this has the effect of changing the energy level to $\alpha_0^2\delta/\gamma^2[1 - \alpha_0^2(1 - 1/\gamma^2)]$. Since α_0^2 is usually small compared with unity, the parameters enter into the energy expression as a virtually constant factor δ/γ^2 which is irrelevant in a correlation with experimental data. That this method of estimating U is reasonable is demonstrated by carrying out the complete molecular-orbital calculation. Results obtained by Long and Sykes [15] are given in Table 3 and are similar to those of the simplified calculation for the same choice of parameters ($\delta = 2$, $\gamma = 2$).

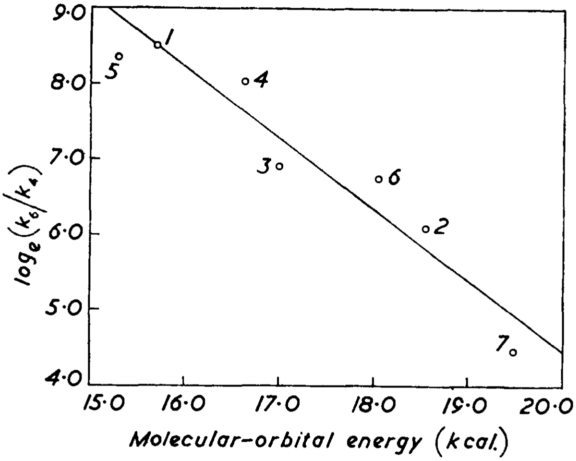

FIG. 6. *Correlation between relative radical capture efficiencies (k_6/k_4) and energies of the highest occupied (non-bonding) molecular orbital.*

(1) 1-Hydroxyphenanthrene.
(2) 2-Hydroxyphenanthrene.
(3) 3-Hydroxyphenanthrene.
(4) 4-Hydroxyphenanthrene.
(5) α-Naphthol.
(6) β-Naphthol.
(7) Phenol.

TABLE 3.

Compound	Energy of highest occupied orbital (units of β) by solution of secular equation	Energy of highest occupied orbital (units of β) from non-bonding molecular-orbital method
Phenol	0·458	0·500
α-Naphthol	0·307	0·340
β-Naphthol	0·381	0·439

Values of U plotted against log k_6/k_4 in Fig. 6 have been determined by using $\delta/\gamma^2 = 2$. As can be seen, the correlation is good. Again, in a recent paper, Hush [16] found that the changes in unsaturation energy in the formation of phenoxide radicals are related to the standard redox potentials of the phenols as measured by Fieser's "critical potential" method.[17]

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[12] Evans and Polanyi, *Trans. Faraday Soc.*, 1935, **31**, 875.
[13] Longuet-Higgins, *J. Chem. Phys.*, 1950, **18**, 265.
[14] Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 3341.
[15] Long and Sykes, *J. Chim. phys.*, 1950, **47**, 361.
[16] Hush, *J.*, 1953, 2375.
[17] Fieser, *J. Amer. Chem. Soc.*, 1930, **52**, 5204.

Further, using the non-bonding molecular-orbital method, he has expressed the change in unsaturation energy in terms of the π-electron densities at the extracyclic oxygen atom and found that these also are related to the redox potentials.

To investigate the effect of substituents from a similar standpoint, we may suppose that they have the effect of changing the electronegativity of the carbon atom to which they are attached. Correspondingly, let the Coulomb integral be changed to $\alpha_c + \delta\beta$; U may then be calculated in terms of δ, and from the observed relationship between U and log k_6/k_4, and the known values of log k_6/k_4 for the particular compound, δ can be calculated. For the alkyl groups most extensively investigated, methyl and *tert.*-butyl, the δ values are respectively $-0{\cdot}55$ and $-0{\cdot}75$. Although not much significance can be attached to the precise numerical values, it is reassuring that the sign of the effect is in accordance with the electron-repelling character of these groups.

The effect of *meta*-substituents, *i.e.*, those attached to unstarred atoms, vanishes to a first approximation. But if we include the inductoelectromeric effect[18] with auxiliary inductive parameter[19] = 1/3, then a *meta*-substituent should produce 2/3 of the destabilisation effect of a substituent in an adjacent starred position. This is evident since the two adjacent starred positions have numerically equal coefficients. Finally, it may be shown that when the electronegative effect of the oxygen is explicitly included in determining the charge distribution in the highest occupied orbital, the charge densities at the *meta*-positions are of the order of 1/5 of those for *ortho*- and *para*-positions. Now this appears insufficient to explain an appreciable direct *meta*-substituent effect on its own account and we must conclude that the inductive effect of the substituent at the adjacent active atoms is the main reason for the existence of activation by *meta*-substitution.

EXPERIMENTAL

Materials.—Tetralin was purified by shaking it with concentrated sulphuric acid to remove hydroperoxide, dried, and refluxed over sodium for a few hours in nitrogen, after which it was distilled through a 35-plate Vigreux column. Before use residual impurities (believed to be traces of metals) were removed by passing small amounts of the distillate through a 2 cm. × 3 cm. column of alumina. The material so obtained showed a negligible rate of oxidation at 50° in the absence of added initiator; b. p. 205°, n_D^{20} 1·5411.

Azo*iso*butyronitrile (AZDN), recrystallised from ether, had m. p. 103°.

Antioxidants were purified by distillation or recrystallisation from suitable solvents.

Method.—The oxidation was carried out in small Warburg-type manometers with dibutyl phthalate as the manometric liquid. The tetralin solutions were contained in 10 c.c. glass cells which were connected to the manometer *via* a standard glass joint and a glass spiral (flexible enough to allow the cell to be efficiently shaken on an eccentric), the whole assembly being immersed in a thermostat normally at 50°. Shaking was always rapid enough to ensure that transfer of oxygen was not rate-controlling. In making up the solutions, initiator was first weighed into the cell, followed by tetralin from a microburette, and a solution of antioxidant in tetralin from a microsyringe to make up the volume to 2·00 ml. This enabled very small quantities of antioxidant (10^{-2}—10^{-4} mole/l.) to be accurately introduced. The movement of the manometer liquid was observed with a cathetometer, and from time to time the level was readjusted by admitting more air or oxygen into the bulb.

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[18] Brown and Dewar, *J.*, 1953, 2406.

[19] Brown, *Quart. Reviews*, 1952, **6**, 63.