

of *p*-tolyl *p*-toluenethiolsulfonate, as was reported originally. The composition of the thiolsulfonate mixture was determined by the n.m.r. method outlined above. It was found to consist of 69 mole % *p*-tolyl *p*-toluenethiolsulfonate and 31 mole % *n*-butyl *p*-toluenethiolsulfonate, in reasonable agreement with the 2:1 mole ratio for the two thiolsulfonates required by eq. 1.

Except for a band of moderate intensity at 3000 cm.<sup>-1</sup> the infrared spectrum of the butyl ester is remarkably similar to that of the *p*-tolyl ester. This makes infrared a rather poor way of detecting the butyl ester in the presence of larger amounts of the *p*-tolyl ester, and this, combined with the fact that only *p*-tolyl *p*-toluenethiolsulfonate can be isolated as a crystalline product from such mixtures of the two esters, is presumably the reason the butyl compound was not detected in the earlier work. Fur-

ther, since the yield of *p*-tolyl *p*-toluenethiolsulfonate reported in those studies<sup>2</sup> was based on the total weight of the thiolsulfonate fraction, now known to have been in part *n*-butyl *p*-toluenethiolsulfonate, it was naturally too high.

The n.m.r. spectra of the two esters, on the other hand, differ sufficiently to make it easy to detect and determine quite accurately small amounts of *n*-butyl *p*-toluenethiolsulfonate in the presence of larger amounts of the *p*-tolyl ester.

**Acknowledgment.**—The n.m.r. spectra described in this work were obtained on a Varian A-60 instrument whose purchase was made possible by a National Science Foundation grant to Oregon State University.

[CONTRIBUTION FROM THE CANCER RESEARCH INSTITUTE, NEW ENGLAND DEACONESS HOSPITAL, AND THE DEPARTMENT OF BIOLOGICAL CHEMISTRY, HARVARD MEDICAL SCHOOL, BOSTON, MASS.]

## Studies on the Mechanism of the Elbs Peroxydisulfate Oxidation<sup>1a</sup>

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RECEIVED JUNE 26, 1963

Second-order rate constants have been measured for the reaction of a series of monosubstituted phenols with persulfate. Electron-releasing groups facilitate the reaction while electron-withdrawing groups retard it. Rate constants vary from 0.093 for *o*-nitrophenol to 21 for *p*-methoxyphenol (30°, 1./mole-min.). Enthalpies and entropies of activation have been determined for some of these reactions. The values are in the ranges 12 to 16 kcal./mole ( $\Delta H^\ddagger$ ) and -15 to -30 e.u. ( $\Delta S^\ddagger$ ). A comparison of the rates of reaction of a series of 2,4- and 2,6-disubstituted phenols has shown that steric hindrance about the phenolic group increases the rate. The question of rate-limiting attack at oxygen or at carbon is considered in terms of the Hammett correlations and steric effects. Allyl alcohol, an inhibitor of the reaction of persulfate with 2-propanol, has no effect on the rate of the persulfate-phenol reaction.

### Introduction

A previous investigation<sup>1b</sup> indicated that the rate-limiting step in the Elbs peroxydisulfate oxidation is an electrophilic attack by the persulfate ion on the phenolate ion. There was no evidence for a kinetically significant homolytic or heterolytic initiation step. The evidence was insufficient to draw conclusions as to the nature of the transition state. In particular, the question of whether the primary attack was at carbon or oxygen was undecided. In this paper, we shall consider some electronic and steric demands of the reaction.

### Experimental

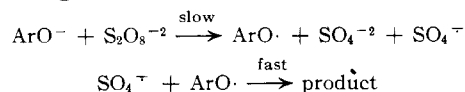
**Materials.**—Phenols were purchased from the Aldrich Chemical Co., Eastman, or Matheson Coleman and Bell and either recrystallized or redistilled before use. Distillation was carried out *in vacuo* (water-pump) under nitrogen. *o*-Cyanophenol was prepared according to the procedure of Bone<sup>2</sup> and recrystallized from benzene; m.p. 94.5 to 95.5°. *p*-Dioxane was purified according to the method of Hess and Frahm<sup>3</sup> as given by Fieser.<sup>4</sup> 2,6-Di-*t*-butylbenzoquinone was synthesized by oxidation of 2,6-di-*t*-butylphenol with trifluoroacetic acid according to the procedure of Chambers, *et al.*,<sup>5</sup> for the dimethylphenol. A 60% yield of crude product was obtained after crystallization from 90% ethanol according to McClure.<sup>6</sup> The quinone was further purified by sublimation (m.p. 66–67°). 2,6-Di-*t*-butylhydroquinone was prepared by catalytic reduction of the quinone<sup>7a</sup> and gave m.p. 117.5 to 118° (lit.<sup>7a</sup> 110° dec.) after two crystallizations from *n*-hexane and one from methylcyclohexane;  $\epsilon_{287}^{25}$  mμ (95% EtOH) 3350. *Anal.* Calcd. for C<sub>14</sub>H<sub>22</sub>O<sub>2</sub>: C, 75.6; H, 10.0. Found: C, 75.7; H, 10.0. Upon adding alkali to an ethanolic solution of the hydroquinone and shaking in air, the quinone,

$\epsilon_{286}^{25}$  mμ (95% EtOH) 17,000 (lit.<sup>7b</sup>  $\epsilon_{286}^{25}$  m 15,400), is rapidly and quantitatively formed.

**Methods.**—The methods used have been described.<sup>1</sup>

### Results

**Further Evidence on the Lack of Free-Radical Participation.**—A crucial finding in our previous study was the fact that allyl acetate, a sulfate-radical trap, had no detectable effect on the rate of disappearance of persulfate in the reaction with *o*-nitrophenol. This observation effectively eliminated mechanisms depending for their initiation on homolysis of persulfate. A mechanism involving the participation of sulfate radicals in a nonrate-limiting step was nevertheless possible,<sup>7c</sup> *e.g.*



The reaction of *o*-nitrophenol with persulfate in carbonate buffer was, therefore, repeated under the conditions previously described.<sup>1</sup> Allyl acetate had no effect on the rate or extent of product formation as measured by the appearance of Folin-positive material. The participation of sulfate radicals at any stage of the reaction thus seems unlikely.

The use of allyl acetate is, of course, limited by its rate of hydrolysis. Thus, the effect of allyl acetate on the rate of the reaction could be studied conveniently only with highly acidic phenols. It was desirable to generalize the lack of effect of allyl acetate on the disappearance of persulfate from which the kinetic nonparticipation of sulfate free radicals in the initiation step was concluded. Hence, a search was made for an alkali-stable free-radical trap. Allyl pivalate, *N*-allylpivalamide, and *N,N*-diallylpivalamide were found to be insufficiently water soluble. Allyl ethyl ether was found to accelerate the disappearance of persulfate in the presence of 2-propanol. Carr<sup>8</sup> (see also Bartlett and Cotman<sup>9</sup>) had already observed the relatively slow

(1) (a) Presented in part at the 145th National Meeting of the American Chemical Society, New York, N. Y., Sept., 1963, Abstracts, p. 170; (b) E. J. Behrman and P. P. Walker, *J. Am. Chem. Soc.*, **84**, 3454 (1962).

(2) W. A. Bone, *J. Chem. Soc.*, **63**, 1346 (1893).

(3) K. Hess and H. Frahm, *Ber.*, **71**, 2627 (1938).

(4) L. F. Fieser, "Experiments in Organic Chemistry," Third Ed., D. C. Heath and Co., Boston, Mass., 1957, p. 285.

(5) R. D. Chambers, P. Goggin, and W. K. R. Musgrave, *J. Chem. Soc.*, 1804 (1959).

(6) J. D. McClure, *J. Org. Chem.*, **28**, 69 (1963).

(7) (a) K. U. Ingold, *J. Phys. Chem.*, **64**, 1836 (1960); (b) S. J. Metro, *J. Am. Chem. Soc.*, **77**, 2901 (1955); W. K. Wilmarth and A. Haim, in "Free-radical Reaction Mechanisms," J. O. Edwards, Ed., Interscience, New York, N. Y., 1962, p. 204.

(8) E. M. Carr, M.S. Thesis, University of Minnesota, 1952.

(9) P. D. Bartlett and J. D. Cotman, Jr., *J. Am. Chem. Soc.*, **71**, 1419 (1949).

rate of reaction of allyl alcohol with persulfate as compared with the reactions of methanol and ethanol. Carr<sup>8</sup> was unable to detect the polymerization of allyl alcohol, and he considered the main pathway to be oxidation. A free-radical mechanism is probable in either case, however,<sup>8-10</sup> and the allyl alcohol radical, owing to its greater stability relative to methanol, ethanol, or 2-propanol radicals, might well be expected to have a retarding effect on reactions requiring the sulfate free radical. Figure 1 shows clearly the retarding effect of allyl alcohol on the persulfate oxidation of 2-propanol.<sup>11</sup>

Table I shows an approximate half-order dependence on allyl alcohol concentration in agreement with the work of Ball, *et al.*,<sup>10</sup> on 2-propanol.

TABLE I  
THE PERSULFATE OXIDATION OF ALLYL ALCOHOL: ALLYL ALCOHOL DEPENDENCE  
Conditions: 30.0°, 0.039 M S<sub>2</sub>O<sub>8</sub><sup>-2</sup>, 0.95 M KOH

(Allyl alcohol)	k', min. <sup>-1a</sup>	k'/(allyl alcohol) <sup>1/2</sup>
0.147	0.00972	0.0253
.294	.01205	.0223
.588	.0147	.0191
1.470	.0301	.0247

<sup>a</sup> The disappearance of S<sub>2</sub>O<sub>8</sub><sup>-2</sup> followed first-order kinetics after an induction period of variable length which appeared to be dependent on the presence of dissolved oxygen.

At higher concentrations of potassium hydroxide, the oxidation of allyl alcohol by persulfate was more rapid. This is only partially an ionic strength effect. No similarly rapid oxidation of methanol was observed in 1.9 M KOH, although the acidities of these two alcohols are comparable.<sup>13</sup> This observation, taken with the effect of pH on the rate of oxidation of allyl alcohol, suggests the participation of the anion radical (Table II).

TABLE II  
THE PERSULFATE OXIDATION OF ALLYL ALCOHOL: pH AND IONIC STRENGTH EFFECTS  
Conditions: 30.0°, 0.039 M S<sub>2</sub>O<sub>8</sub><sup>-2</sup>, 0.588 M allyl alcohol

(KOH)	T <sup>1/2</sup> , min. <sup>a</sup>	(KOH)	T <sup>1/2</sup> , min. <sup>a</sup>
0.178	623	0.570	46 <sup>b</sup>
.535	137	0.950	47
.570	99	1.9	14

<sup>a</sup> The disappearance of S<sub>2</sub>O<sub>8</sub><sup>-2</sup> followed first-order kinetics after an induction period of variable length which appeared to be dependent on the presence of dissolved oxygen. <sup>b</sup> 0.026 M S<sub>2</sub>O<sub>8</sub><sup>-2</sup>, 1.33 M KCl.

The rates of disappearance of persulfate were observed in the presence and absence of allyl alcohol in 0.19 N KOH for the oxidations of *o*-*t*-butylphenol and guaiacol (*o*-methoxyphenol). No differences of rate were noted, although the reaction mixtures following the oxidations, normally very dark with these phenols, were considerably lighter in the presence of allyl alcohol (Table III).

**Structure and Reactivity.**—Table IV lists the second-order rate constants for the oxidations of a number of monosubstituted phenols by persulfate. Some have been determined at two temperatures: for these, the

(10) D. C. Ball, M. M. Crutchfield, and J. O. Edwards, *J. Org. Chem.*, **25**, 1599 (1960).

(11) In terms of the mechanism of Ball, *et al.*,<sup>10</sup> for the reaction in the absence of oxygen, the inhibition can be understood as arising from a lower rate in the *k*<sub>2</sub> and *k*<sub>3</sub> steps in the case of allyl alcohol and an equilibrium between the two alcohol radicals which favors the allyl alcohol radical. This type of inhibition would also satisfactorily explain the observations of Levitt and Levitt<sup>12</sup> on the inhibition of 2-propanol oxidation by 2-butanol without recourse to other mechanisms.

(12) L. S. Levitt and B. W. Levitt, *Can. J. Chem.*, **41**, 209 (1963).

(13) P. Ballinger and F. A. Long, *J. Am. Chem. Soc.*, **82**, 795 (1960).

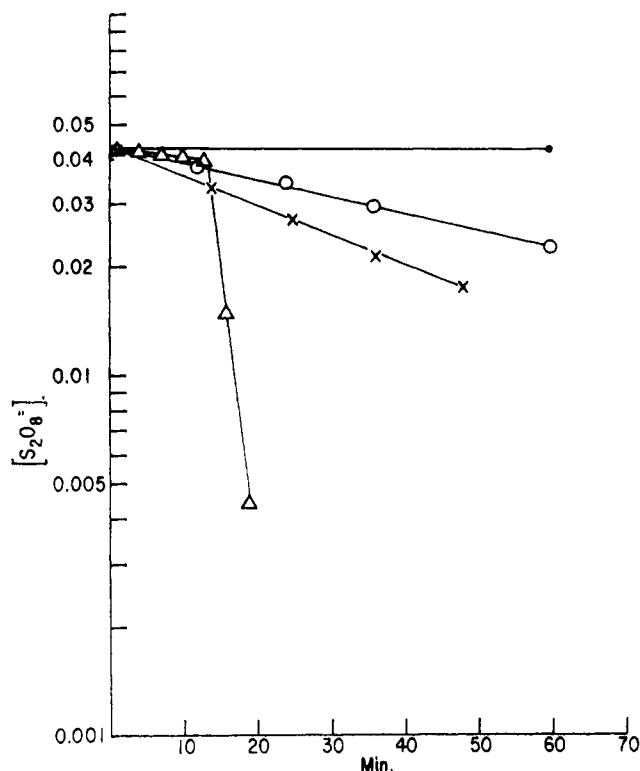


Fig. 1.—The inhibition by allyl alcohol of the persulfate oxidation of 2-propanol; conditions: 60.0°, 0.19 N KOH, 0.044 M S<sub>2</sub>O<sub>8</sub><sup>-2</sup>, final volume 50 ml.: ●—●, no additions; ○—○, 0.5 ml. of allyl alcohol; △—△, 5.0 ml. of 2-propanol; ×—×, 0.5 ml. of allyl alcohol + 5.0 ml. of 2-propanol.

enthalpy and entropy of activation are listed as well. These were calculated from the usual equations.<sup>14</sup> It is quite clear that electron-donating substituents increase the rate of the reaction while electron-withdrawing groups retard it. The correlation of these data with Hammett  $\sigma^+$  constants<sup>15,16</sup> is shown in Fig. 2.

TABLE III  
THE LACK OF EFFECT OF ALLYL ALCOHOL ON THE PERSULFATE OXIDATION OF *o*-*t*-BUTYLPHENOL AND GUAIACOL  
Conditions: 30.0°, 0.19 N KOH

(Phenol)	(S <sub>2</sub> O <sub>8</sub> <sup>-2</sup> )	(allyl alcohol)	T <sup>1/2</sup> , min.
0.0272 <sup>a</sup>	0.0020	...	3.6
.0272 <sup>a</sup>	.0020	0.367	3.5
.0392 <sup>b</sup>	.00375	...	4.9
.0392 <sup>b</sup>	.00375	0.147	4.9
.0392 <sup>b</sup>	.00313	0.367	5.2

<sup>a</sup> Guaiacol. <sup>b</sup> *o*-*t*-Butylphenol.

The data are plotted in two ways. Figure 2a assumes rate-limiting attack at oxygen while Fig. 2b assumes rate-limiting attack at carbon. For the *m*-substituted phenols, rate-limiting attack at oxygen should give a correlation with  $\sigma_m^+$ , while rate-limiting attack at carbon might be expected to give a poor correlation with  $\sigma_p^+$  due to *ortho* effects. Likewise, for *o*- and *p*-substituted phenols, attack at oxygen would be expected to correlate with  $\sigma_p^+$ , while attack at carbon should give a correlation with the *m*-substituent constants.

The data are displayed, plotted in both ways, in Fig. 2. It is clear that of the two plots, the one which as-

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(15) H. C. Brown in "Steric Effects in Conjugated Systems," ed. by G. W. Gray, Butterworths, London, 1958, p. 100.

(16) L. M. Stock and H. C. Brown, *Advan. Phys. Org. Chem.*, **1**, 35 (1963).

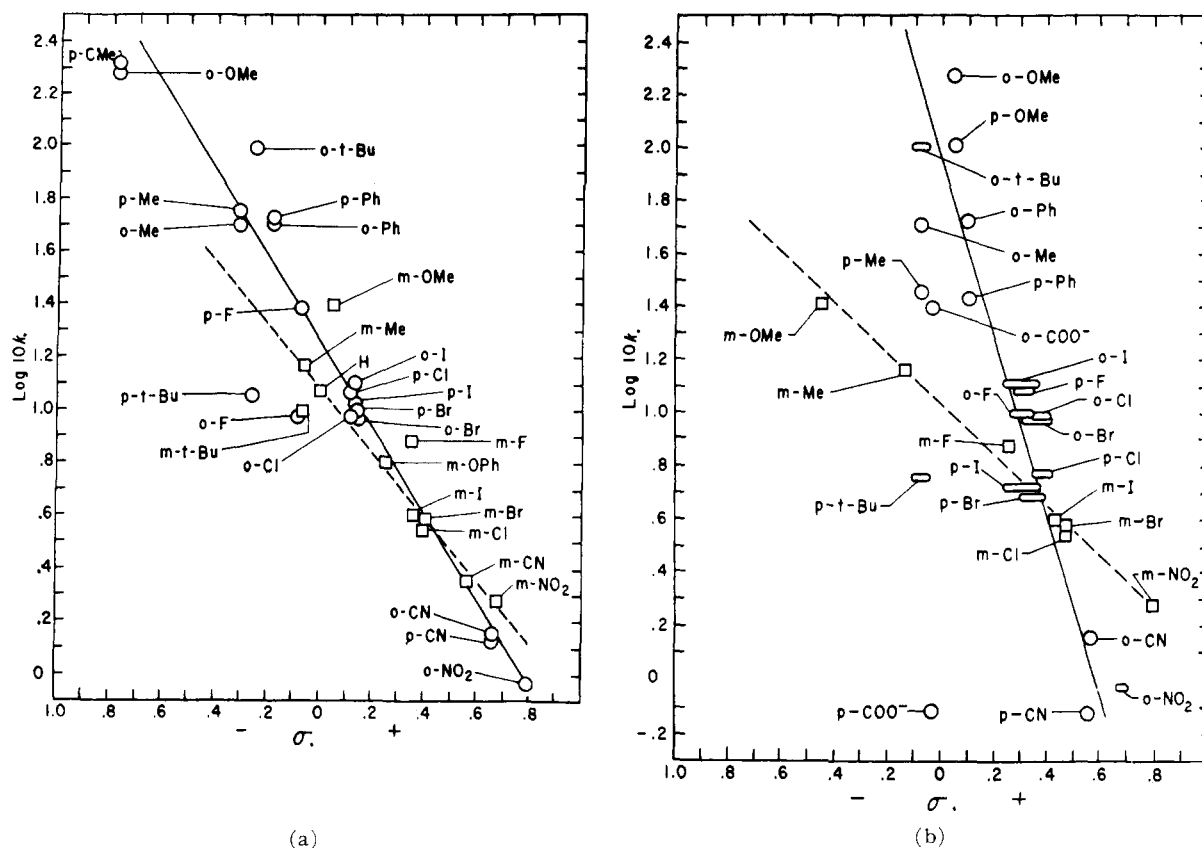


Fig. 2.—In Fig. 2a,  $\sigma_p^+$  values<sup>15,16</sup> have been used for the *p*- and *o*-substituted phenols and  $\sigma_m^+$  values for the *m*-substituted phenols. The use of Miller's  $\sigma^{++}$  values<sup>17</sup> does not seem to result in a significantly better correlation. In Fig. 2b,  $\sigma_m^+$  values have been used for the *o*- and *p*-substituted phenols. For the *p*-substituted phenols, these values are plotted against  $\log 5K$  since two equivalent positions are open for attack;  $\sigma_o$  values calculated from the data of Stock and Brown (ref. 16, pp. 86–87) have been used for the *m*-substituted phenols.

sumes attack at oxygen gives the better over-all correlation (but see Discussion).

**The Reaction with Some 2,4- and 2,6-Disubstituted Phenols.**—In an attempt to clarify the question of oxygen *vs.* carbon attack, the effect of steric hindrance on the rate of the reaction was investigated. To this end, the rates of reaction of a series of 2,4- and 2,6-disubstituted phenols were measured. The results are given in Table V. It is clear that crowding about the phenolic oxygen results in a marked acceleration in the rate of persulfate disappearance.

The rate of oxidation of 0.01 *M* 2,6-di-*t*-butylphenol at 30° by 0.00112 *M* persulfate in 60% dioxane and 0.19 *M* KOH was unaffected by the presence of 0.3 *M* allyl alcohol.

**Analysis of the Products of the Reaction of 2,6-Di-*t*-butylphenol with Persulfate.**—The anomalously rapid rate of oxidation of 2,6-di-*t*-butylphenol necessitated confirmation of the course of the reaction.

The reaction was allowed to proceed to completion (10 half-lives) under nitrogen. The alkaline mixture was then continuously extracted overnight with ether. Examination of the ether extracts by ultraviolet spectroscopy showed only the presence of starting material with less than 1% 3,3',5,5'-tetra-*t*-butyl-4,4'-diphenylquinone.<sup>18</sup> This could reasonably have arisen from traces of oxygen. The aqueous residue had peaks at 250 and 300 *mμ* in alkali and 272 *mμ* in acid. The apparent *pK* was approximately 13, determined spectrophotometrically. The properties of this material are thus consistent with 2,6-di-*t*-butylhydroquinone monosulfate (2,6-di-*t*-butylphenol-4-sulfate).

Acid hydrolysis followed by extraction gave an ether layer with two peaks in the ultraviolet at 287 and 255 *mμ*. The aqueous residue was almost free of ultraviolet-absorbing material. Brief aeration of a portion of the ether solution in ethanolic alkali resulted in a disappearance of the 287 *mμ* peak with intensification of the peak at 255 *mμ*. Authentic 2,6-di-*t*-butylhydroquinone is converted to 2,6-di-*t*-butylbenzoquinone quantitatively under these conditions. Since some of the quinone was always formed during hydrolysis of the hydroquinone sulfate, the calculation of yield was most conveniently made following complete conversion of the hydroquinone to the quinone by the reaction with oxygen under alkaline conditions. The yield of the expected Elbs product (2,6-di-*t*-butylhydroquinone monosulfate) calculated in this way was between 60 and 70% at a phenol-persulfate ratio of 10.

### Discussion

The Elbs peroxydisulfate oxidation is another example of the class of nucleophilic displacements on peroxide oxygen recently reviewed and discussed by Edwards.<sup>19</sup> More recent work includes studies of the oxidation of aromatic amines,<sup>20</sup> of nitrosobenzenes by peroxyacetic acid,<sup>21</sup> and a homologous case of nucleophilic displacement on sulfur.<sup>22</sup>

The salient experimental observations leading to this conclusion are that (a) the kinetics are first order in

(19) J. O. Edwards in "Peroxide Reaction Mechanisms," ed. by J. O. Edwards, Interscience Publishers, Inc., New York, N. Y., 1962, pp. 67–106.

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(21) K. M. Ibne-Rasa, C. G. Lauro, and J. O. Edwards, *ibid.*, **85**, 1163 (1963).

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TABLE IV  
SECOND-ORDER RATE CONSTANTS, ENTHALPIES, AND ENTROPIES  
OF ACTIVATION FOR MONOSUBSTITUTED PHENOLS

Phenol	$k$ , l./mole-min.		$\Delta H^\ddagger$ , kcal./mole	$\Delta S^\ddagger$ , cal./deg.-mole
	10°	30°		
<i>o</i> -NO <sub>2</sub>	0.0153 ± 0.0001	0.0926 ± 0.0006	14.7	-23
<i>p</i> -CN		.140		
<i>o</i> -CN		.142 ± 0.007		
<i>p</i> -Carboxy		.155 ± .005		
<i>m</i> -NO <sub>2</sub>	0.0413 ± 0.0005	.1895 ± .0000	12.4	-29
<i>m</i> -CN		.225 ± .003		
<i>o</i> -CHO		.320 ± .000		
<i>m</i> -Carboxy		.327 ± .009		
<i>m</i> -Cl	0.0824	.350 ± .004	11.7	-30
<i>o</i> -CONH <sub>2</sub>		.368		
<i>m</i> -Br	0.0818	.383	12.6	-27
<i>m</i> -I		.398		
<i>m</i> -CHO		.44 ± 0.04		
<i>m</i> -Phenoxy		.631		
<i>m</i> -F	0.1103	.752 ± 0.003	15.8	-15
<i>o</i> -Br	.174 ± 0.001	.932	13.7	-22
<i>o</i> -Cl	.150 ± 0.005	.962	15.2	-17
<i>o</i> -F		.966 ± 0.002		
<i>p</i> -Br	0.160 ± 0.005	.970 ± .04	14.4	-19
<i>m</i> - <i>t</i> -Butyl	0.148 ± 0.004	.977 ± .002	15.5	-16
<i>p</i> -I		1.05 ± .00		
<i>p</i> - <i>t</i> -Butyl	0.222 ± 0.015	1.124 ± .04	13.2	-23
Phenol	.180 ± .007	1.16 ± .00	15.3	-16
<i>p</i> -Cl	.184 ± .000	1.17 ± .04	15.1	-17
<i>o</i> -I		1.27 ± .04		
<i>m</i> -Methyl	0.304	1.44 ± .06	12.7	-24
<i>p</i> -F		2.42 ± .01		
<i>o</i> -Carboxy	0.224 (1°)	2.45 ± .1	13	-22
<i>m</i> -Methoxy		2.55 ± .1		
<i>o</i> -Methyl	0.825	5.05	14.8	-14.5
<i>o</i> -Phenyl	1.085	5.33 ± 0.00	12.9	-21
<i>p</i> -Phenyl	0.909	5.37 ± .01	14.5	-15.5
<i>p</i> -Methyl	0.856	5.62 ± .05	15.4	-12
<i>o</i> - <i>t</i> -Butyl	1.575	9.81 ± .3	15.0	-12.5
<i>o</i> -Methoxy	3.56 ± 0.01	19.0 ± .3	13.6	-16
<i>p</i> -Methoxy		20.6 ± 1.0		
2-Hydroxypyridine	See ref. 1	0.081	15.7	-20
3-Hydroxypyridine		.143		
4-Hydroxypyridine		.0026		

General reaction conditions: phenol-persulfate ratio = 10, 1.7 *M* KOH.

TABLE V  
SECOND-ORDER RATE CONSTANTS FOR THE REACTION OF SOME  
2,4- AND 2,6-DISUBSTITUTED PHENOLS WITH PERSULFATE

Sub- stituent	$k$ , l./mole-min.		$k_{2,6}/k_{2,4}$
	2,4-Isomer	2,6-Isomer	
Cl <sup>a</sup>	0.985 ± 0.005	0.780 ± 0.01	0.792
Br <sup>a</sup>	0.747 ± .012	0.740 ± 0.014	0.990
CH <sub>3</sub> <sup>a</sup>	12.04 ± .03	18.6 ± 1.0	1.54
<i>t</i> -Butyl <sup>a</sup>	5.4	...	...
<i>t</i> -Butyl <sup>c</sup>	0.765 ± 0.02	31 ± 0.5 <sup>d</sup>	40.5

<sup>a</sup> 1.7 *N* KOH, H<sub>2</sub>O, 30°. <sup>b</sup> 2,6-Di-*t*-butylphenol is not appreciably soluble in aqueous 1.7 *N* KOH. <sup>c</sup> 0.85 *N* KOH, 40% *p*-dioxane (by volume), 30°. <sup>d</sup> Under nitrogen.

both persulfate and phenolate ions; (b) radical inhibitors affect neither the rate of consumption of persulfate nor the rate of appearance of product; (c) electron-donating substituents on the phenol increase the rate of the reaction, while electron-withdrawing groups retard it; (d) the activation parameters (Table IV) correspond to those reviewed by Edwards.<sup>19</sup>

With these facts in mind, there are still at least two general reaction schemes possible in view of the ambident nature of the nucleophile.<sup>23</sup> These schemes are shown in Fig. 3.

On the steady-state assumption, the two cases are kinetically indistinguishable. Nor, on the assumption of oxygen attack, can these kinetic studies distinguish between inter- or intramolecular sulfate transfer. The evidence in this study which bears on the question of oxygen or carbon attack is of three kinds. There is

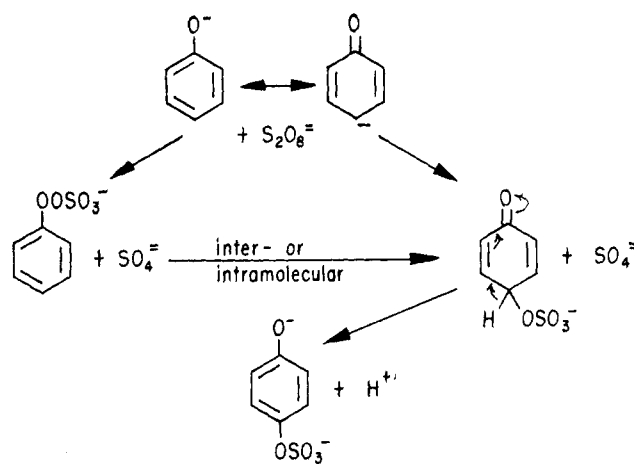


Figure 3.

first of all the correlation (or lack of correlation) of the rate data with the Hammett  $\sigma^+$  constants. If rate-limiting attack is uniformly at oxygen, then *o*- and *p*-substituted phenols should correlate with  $\sigma_p^+$  (although the *o*-series should give considerable scatter) and the *m*-substituted phenols with  $\sigma_m^+$ . On the other hand, uniform rate-limiting attack at carbon should lead to a correlation of the *o*- and *p*-substituted phenols with  $\sigma_m^+$ , while the *m*-substituted phenols should show a relatively scattered correlation with  $\sigma_p^+$ . But it should be noted that, on this latter assumption, one might expect a correlation within each isomer group, but not among the groups, since the persulfate ion attacks an unhindered *p*-position in the case of the *o*-substituted phenols, a position *ortho* to the hydroxyl in the case of the *p*-substituted phenols, and a position *ortho* to a variable R-group in the case of the *m*-substituted phenols.

Of the two plots shown in Fig. 2, it is clear that Fig. 2a gives the better over-all correlation (consistent with attack at oxygen), while Fig. 2b gives a line of clearly different slope for the *m*-substituted phenols (consistent with attack at carbon). Hence, the evidence from the Hammett plots is not of great value in distinguishing between these two possibilities.

It is perhaps relevant to point out that the dinegative persulfate ion is not a typical electrophilic reagent, and hence the transition state, whatever it may be, arising from the interaction of the persulfate ion and the phenolate ion, cannot be the electron-deficient state usually pictured for electrophilic aromatic substitution. The use of  $\sigma^+$  values may therefore be open to question.

The Hammett correlation (linear free-energy relationships in general) appears to apply to reaction series in which either the entropies of activation for the series are constant or in which the variation in entropy of activation is linearly related to changes in the enthalpy of activation.<sup>24-27</sup>

It is clear from an examination of Table IV that this reaction is not isoentropic, even allowing for an error in the  $\Delta S^\ddagger$  determinations of 3 to 4 e.u. (see ref. 27 for a discussion of the probable errors in this determination). A correlation of the log  $K$  values with  $\sigma^+$  is then to be expected only if  $\Delta S^\ddagger$  varies linearly with  $\Delta H^\ddagger$ . A plot of  $\Delta H^\ddagger$  vs.  $\Delta S^\ddagger$  shows some scatter, but a line of slope 291°K. can be discerned. It might be noted in this connection, however, that great caution must be exercised in the interpretation of enthalpy-entropy

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relationships, as Leffler<sup>25</sup> emphasized in his original discussion. Useful criteria for this relationship have been suggested by Petersen, Markgraf, and Ross.<sup>28</sup> They have shown that the error in  $\Delta S^\ddagger$  ( $\sigma$ ) is directly proportional to the error in  $\Delta H^\ddagger$  ( $\delta$ ) and that under conditions where sufficient errors in the rate determinations exist, a plot of  $\Delta H^\ddagger$  vs.  $\Delta S^\ddagger$  will be a straight line with a slope  $2TT'/3T' - T$  (or  $2TT'/T' + T$ <sup>29</sup>), where  $T$  and  $T'$  are the two temperatures ( $^\circ\text{K.}$ ) at which the rate determinations were made. For the temperatures used in this study,  $2TT'/3T' - T = 274^\circ\text{K.}$  and  $2TT'/T' + T = 293^\circ\text{K.}$ , both close to the observed value of  $291^\circ\text{K.}$

Application of the error criteria of Petersen, *et al.*,<sup>28</sup> gives a value for  $2\delta$  ( $\alpha = 0.1$ ) of 3.4 kcal./mole; the experimental range of  $\Delta H^\ddagger$  is 4.1 kcal./mole.

A recent paper of Brown<sup>29</sup> has argued for a much broader application of the linear enthalpy-entropy relationship than that put forward by Leffler.<sup>25</sup> Brown recognized the arguments of Petersen, *et al.*, but, nevertheless, used many examples in which the experimental temperatures are close to the  $\Delta H^\ddagger$  vs.  $\Delta S^\ddagger$  slope and are thus open to serious question on the criteria of Petersen, *et al.* It appears justified to conclude with Petersen, Markgraf, and Ross that for many reaction series, including this one, it is probable that the linear relationship between  $\Delta H^\ddagger$  and  $\Delta S^\ddagger$  is no more than the result of the direct proportionality of the errors involved in the determination of these two quantities.

Two points should be mentioned which must contribute, at least, to nonsystematic variations in  $\Delta S^\ddagger$  and  $\Delta H^\ddagger$  and hence to scatter in the Hammett plots. The first of these is that since isomer distributions were not determined, partial rate factors have not been used. Two isomers are possible for the *o*-substituted phenols and three for the *m*-substituted phenols, although in this latter case the isomer resulting from substitution of the sulfate group *para* to the existing substituent has not been detected.<sup>30</sup> Substitution *meta* to the phenolic group has never been found. When the reaction is carried out using an equimolar concentration of reactants, the *o/p* ratio for the *o*- and *m*-substituted phenols is generally of the order of 1/10.<sup>30,31</sup> This ratio, however, would be expected to be even smaller under the conditions we have used (a tenfold excess of phenol).

The second and perhaps more important point concerns the ambident nature of the phenolate ion. Presumably, the relative nucleophilicity of carbon and oxygen in the different phenols studied is not constant.<sup>28</sup> Thus, there may well be a varying contribution from attack at oxygen or at carbon as a function of the structure of the phenol. This possibility would certainly be expected to influence both  $\Delta H^\ddagger$  and  $\Delta S^\ddagger$ .

Another type of evidence bearing on the question of oxygen *vs.* carbon attack concerns the relative magnitudes of  $\Delta S^\ddagger$ . On the assumption of oxygen attack, one might expect a relatively low  $\Delta S^\ddagger$  for the *ortho* series, whereas for the assumption of carbon attack one might expect a relatively low  $\Delta S^\ddagger$  for the *meta* series. Table IV shows a generally relatively low entropy term for the *meta* series, and no marked entropy differences between *o*- and *p*-pairs.

The final type of evidence concerns the behavior of the 2,4- and 2,6-disubstituted phenols. In contrast to the observations of Walling and Hodgdon<sup>32</sup> on the reaction between phenols and benzoyl peroxide, the Elbs peroxydisulfate oxidation appears not to be subject to steric hindrance about the phenolic hydroxyl. On the contrary, the behavior of this system recalls the reaction of oxygen and phenols studied by Gersmann and Bickel.<sup>33</sup> These authors investigated the attack of oxygen on various substituted phenols in alkaline solution. The rate of reaction in this system is fast only for those phenols with severe steric hindrance about the phenolic group. They concluded that a rapid rate of reaction was, in fact, correlated with the degree of solvation of the oxyanion, steric hindrance leading to an increased contribution of the carbanion.

An entirely analogous effect has been observed by Cohen and Jones<sup>34</sup> in their study of the alkaline hydrolysis of substituted benzamides and benzonitriles. Here, since attack on the amide or nitrile is by a nucleophile, the effect is in the opposite direction: the hydrolysis of 3,5-di-*t*-butyl-4-hydroxybenzamide, for example, is anomalously slow. Again, this effect can be attributed to increased contributions of the carbanion form to the resonance hybrid.

The same effect appears to be operating in the reaction of persulfate with 2,6-di-*t*-butylphenol. The ratio of 40.5 given for the di-*t*-butylphenols is a minimum value. Gersmann and Bickel<sup>33a</sup> gave the *pK* for 2,6-di-*t*-butylphenol in 90% ethanol as  $13.6 \pm 0.2$ . The *pK* for the 2,4-isomer can be estimated at about 12.7 in 90% ethanol from the data of Coggeshall and Glessner.<sup>35</sup> Thus, although the 2,4-isomer was more completely ionized under the reaction conditions, the 2,6-isomer was nevertheless much more rapidly attacked by persulfate. The results are clearly incompatible with attack at oxygen in this case.

**Acknowledgments.**—This investigation was supported by United States Public Health Service Grant A567 and by United States Atomic Energy Commission Contract AT(30-1)-901 with the New England Deaconess Hospital. I would like to thank Dr. B. M. Pitt for many stimulating discussions and Messrs. R. Lynch and C. Moore for their patient help with the majority of the experiments.

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