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The Oxidation of Phenols by Potassium Disulfonate Nitroxyl

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The oxidation of phenols is one of the most stimulating subjects in the chemical and biochemical fields. When potassium disulfonate nitroxyl (Fremy's salt; $\cdot ON(SO_3K)_2$)[1] is used as an oxidizing agent, phenols are oxidized to produce benzoquinones in high yields. Teuber and his co-workers[2] have investigated the reaction through product analysis, but no details on the reaction mechanism have been published. The reaction is characteristic in that benzoquinones (*i.e.*, *o*-benzoquinones and *p*-benzoquinones) are produced exclusively, accompanied by no coupling products, and the yields are relatively high. Moreover, whereas *p*-benzoquinones are selectively produced when the para position of phenols is not occupied by any substituents, *o*-benzoquinones are the sole products in high yields when the para position is substituted.

Because of our interest in this high selective oxidation of phenols by Fremy's salt, we attempted to elucidate the reaction mechanism.

Results and Discussion

We will now investigate the relative reactivity of phenols to Fremy's salt. The substrates examined here are phenols with no substituents at the position para to their hydroxyl group, such as phenol, 2-methylphenol, 3-methylphenol, 2,5-dimethylphenol, 2,6-dimethylphenol, 2-*t*-butylphenol, 2,6-di-*t*-butylphenol, 2-chlorophenol, and 2-nitrophenol.

The course of the reaction and the subsequent spectrophotometric determination of *p*-benzoquinones produced are depicted in Fig. 1. The amount of *p*-benzoquinones produced 10 min after the beginning of the reaction is determined as a measure of the relative rates of the oxidation of phenols (Table 1).

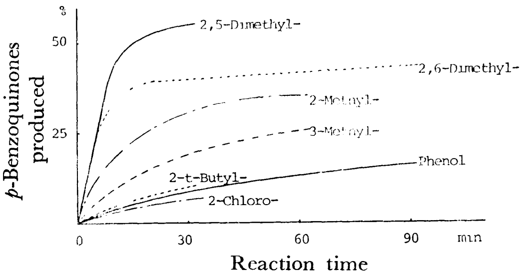

Fig. 1. Relative oxidation rates of phenols.

TABLE 1. RELATIVE REACTIVITIES OF PHENOLS AND THEIR NMR CHEMICAL SHIFT OF HYDROXYL PROTONS

Phenols	*p*-Benzoquinones	Yields after 10 min (%)	Chemical shift of OH[a] (ppm)
Phenol	*p*-Benzoquinone	4	4.31
2-Methyl-	2-Methyl-	19	4.33
3-Methyl-	2-Methyl-	9	4.21
2,5-Dimethyl-	2,5-Dimethyl-	44	4.22
2,6-Dimethyl-	2,6-Dimethyl-	35	4.30
2-*t*-Butyl-	2-*t*-Butyl-	5	4.47
2,6-Di-*t*-butyl-	no reaction		4.96
2-Chloro-	2-Chloro-	3	5.38
2-Nitro-	no reaction		10.57

a) The values are measured in infinite dilution with CCl_4.

From these results, it can be deduced that the rate of this reaction is enhanced by electron-donating substituents and that it is depressed with strong electron-withdrawing substituents, such as the nitro group. 2-Nitrophenol, for instance, is not oxidized and is recovered quantitatively after being treated with Fremy's salt for 30 min. When the reaction rates of monomethylphenols are compared with those of di-

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[1] D. J. Cram and R. A. Reeves, *J. Amer. Chem. Soc.*, **80**, 3099 (1958).

[2] a) H. J. Teuber and G. A. Jellinek, *Chem. Ber.*, **85**, 95 (1952). b) H. J. Teuber and W. Rau, *ibid.*, **86**, 1036 (1953).

methylphenols, dimethylphenols such as 2,5-dimethylphenol and 2,6-dimethylphenol are found to be more reactive than monomethylphenols. According to Teuber and Rau,[2b)] 2-chlorophenol could not be oxidized to 2-chloro-*p*-benzoquinone by Fremy's salt. However, in this work, 2-chlorophenol is found to be oxidized to the corresponding *p*-benzoquinone, although the reaction rate is considerably slow, because of the electron-withdrawing nature of the chlorine atom.

Although the reaction rate of 2-*t*-butylphenol is nearly the same as that of non-substituted phenol, 2,6-di-*t*-butylphenol is not oxidized under the same conditions. That is; the reaction rate of phenols with the *t*-butyl group at the *o*-position is rather slower than would be expected only from the above-mentioned electronic effects. The observed effect of the *t*-butyl group may be explained as the steric hindrance to the attack of the reagent on the hydroxyl group in phenols.

The molar ratio of phenols to Fremy's salt varies from 0.4 to 4.0. Within this range, the reaction rate is changed linearly with the molar ratio. The reaction between phenols and Fremy's salt can thus be described as follows:

$$\text{Rate} = k[\text{Phenols}][\text{Fremy's salt}]$$

$$k = 2.01\times10^{-2}\ l/\text{mol}\cdot\text{sec for 2,6-dimethylphenol at } 0^\circ\text{C}$$

On the other hand, the decay of Fremy's salt in the reaction system was followed by using ESR spectroscopy, as is shown in Fig. 2. The peak height of the ESR absorption signal is proportional to the concentration of Fremy's salt, because the ESR absorption signal of Fremy's salt has the same half-height width at every stage of the reaction. Thus, in view of the decay rate of the peak height of the ESR absorption signal, Fremy's salt in the reaction system decreases in first order to time. This result is also in good agreement with the rate equation presented above.

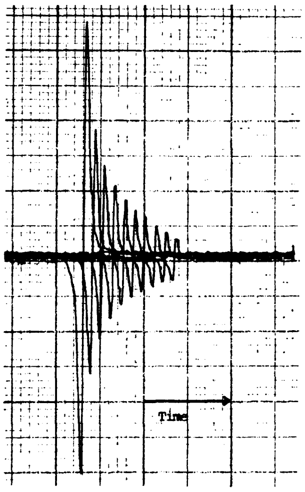


Fig. 2. Decay of Fremy's salt in its reaction with 2,6-dimethylphenol. Time interval; 170 sec

These results indicate that the electrophilic attack of Fremy's salt on phenols is the rate-determining process in this reaction. As a matter of fact, the steric factor of the substituents to the hydroxyl group of phenols should be considered at the same time. Moreover, whether or not the reaction proceeds is well correlated with the NMR chemical shift of the hydroxyl proton and, consequently, with the acidity of phenols. The NMR chemical shifts of the hydroxyl protons are shown in Table 1. Considering from the NMR data, the fact that 2-nitrophenol is not oxidized may be explained by its high acidity.

In the reaction described above, no coupling products were isolated, and the ESR spectra of free phenoxy radicals could not be observed. Thus, no free phenoxy radicals with a fairly long lifetime may exist under those reaction conditions; that is, the phenoxy radicals produced decay too rapidly to establish their existence by ESR spectroscopy. These results also indicate that the rate-determining process may be the stage of the first attack of Fremy's salt on phenols.

The decay of Fremy's salt, as followed by ESR measurements, is considerably fast if the phenols have no substituent on the *o*- and/or *p*-position to their hydroxyl group, such as 2,6-dimethylphenol. In the case of 2,4,6-trimethylphenol, however, the decay of Fremy's salt is rather slow. Although the ESR spectra of free phenoxy radicals could not be observed at any stage of the reaction, the ESR spectra corresponding to Fremy's salt are broadened and the coupling constant due to nitrogen, a_N, becomes slightly smaller than that of free Fremy's salt (Fig. 3). The above-mentioned deformation may be ascribed to a complex formation between Fremy's salt and 2,4,6-trimethylphenol. Considering a_N, some part of the free spin of Fremy's salt may be delocalized onto 2,4,6-trimethylphenol, thus making a labile molecular complex. In the case of phenols with free *o*- and/or *p*-positions, therefore, the formation of such a complex would make the subsequent attack of Fremy's salt easier than the first attack on phenols; this would be the origin of the high selectivity of this reaction.

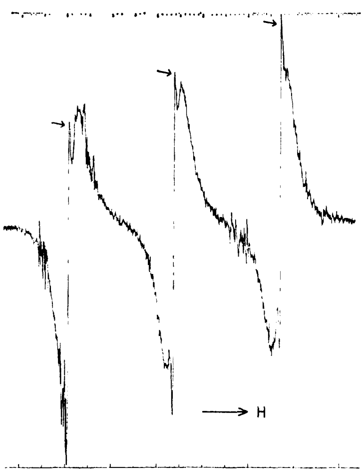


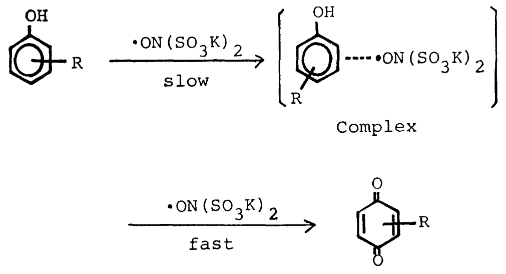
Fig. 3. ESR spectra observed in the reaction of 2,4,6-trimethylphenol with Fremy's salt. Three lines indicated by arrows are due to free Fremy's salt as an external standard.

Considering the above results, the course of the reaction may be described as follows:

TABLE 2. PHYSICAL PROPERTIES OF *p*-BENZOQUINONES

p-Benzoquinones	Mp (°C)	$\lambda^{a)}$ (nm)	ε ($CHCl_3$)	Chemical shift (CCl_4)	
				Substituents (ppm)	Benzene ring (ppm)
p-Benzoquinone	111	437	20.4	—	6.70
2-Methyl-	66	436	28.2	2.05	6.50—6.70
2,5-Dimethyl-	123—124	430	27.0	2.03	6.50—6.60
2,6-Dimethyl-	71	430	42.5	2.04	6.48
2-*t*-Butyl-	53	440	24.0	1.28	6.50—6.65
2-Chloro-	55	415	24.0	—	6.75—6.95

a) The wavelength used for determination for *p*-benzoquinones.



Experimental

2.5×10^{-3} mol of Fremy's salt[1] was dissolved into 50.0 m*l* of water buffered with sodium acetate (pH 8.2), after which the solution was cooled to about 2°C. To the solution, 1.0×10^{-3} mol of phenols dissolved in 2.0 m*l* of ether was then added all at once (0—3°C). After the reaction had stopped, the products were separated by using TLC and were determined spectroscopically. The physical properties of *p*-benzoquinones thus produced are shown in Table 2. An ME-3X-type ESR spectrometer with 100 kHz modulation was used in this experiment.