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Reactivity of p-Nitrotoluene and p-Nitrophenylacetic Acid in Alkali Solutions

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p-Nitrotoluene undergoes oxidative condensation in alkali solution in the presence of oxidizing agents to give dibenzyl and stilbene derivatives; other oxidation products also are formed. The kinetic data on the oxygen absorption of p-nitrotoluene and of p-nitrophenylacetic acid indicate that the rate of oxygen absorption is proportional to the concentration of the nitro compound and to the mean ionic activity of alkali or to its square; a linear relation was found between the rate and the partial pressure of oxygen. A reaction mechanism is proposed.

It has long been known that the reactivity of the alkyl group of o- and p-nitrotoluene and their derivatives is enhanced by the action of alkali; for example, o-nitrotoluene gives anthranilic acid,[1] while p-nitrotoluene, under similar conditions, undergoes condensation to an orange-yellow substance $C_{28}H_{20}N_4O_4$.[2] In the latter case, if the reaction is carried out in the presence of air[3] or of an oxidizing agent,[4] p,p'-dinitrobibenzyl and p,p'-dinitrostilbene are formed primarily.

Two mechanisms, both of which seem unlikely, have been proposed for this reaction. Porai-Koshitz[5] assumed that it proceeds by the preliminary oxidation of p-nitrotoluene to the alcohol or aldehyde followed by condensation. Since p,p'-dinitrobibenzyl is converted to p,p'-dinitrostilbene by alkali in the presence of oxygen,[6] this oxidative step appears to be unnecessary; moreover, intermolecular condensation between the aldehyde and methyl groups of mononitro compounds proceeds only with difficulty.[7] Plisov[8] assumed that p-nitrotoluene was deformed to a quinoid form by the action of alkali followed by condensation to a bibenzyl derivative. In a similar way, he accounted for the formation of o,o'-dinitrostilbene from o-nitrobenzyl chloride,[9] but the dehydrochlorination of the chloromethyl group is a more probable explanation of the latter reaction. Furthermore, Plisov's suggestion is not supported experimentally since it is more difficult to prepare bibenzyl or stilbene derivatives from o-nitro compounds than from the p-isomers.[10,11]

Since the product, $C_{28}H_{20}N_4O_4$, obtained by the treatment of p-nitrotoluene with alkali in the absence of air, can be reduced to p,p'-diaminostilbene,[2,3] oxidation must have occurred at the methyl group. On the other hand, since $C_{28}H_{20}N_4O_4$ is equivalent to four molecules of p-nitrotoluene

minus four molecules of water, the nitro group must have been reduced in the course of the reaction. It therefore seems reasonable to assume that the oxidative condensation of the methyl group is related to the oxidizing power of the nitro group.

Recently it has been found that p-nitro-substituted methylene compounds, e.g., o-nitroethylbenzene,[10] p,p'-dinitrodiphenylmethane[10] and p-nitrophenylacetic acid,[12] undergo a similar condensation. To elucidate of this reaction mechanism, we have studied the oxygen absorption of p-nitrotoluene and p-nitrophenylacetic acid in the presence of alkali and the dependence of the rate of absorption upon the concentration of the nitro compound and of alkali and upon the partial pressure of oxygen.

Experimental

Materials.—C.P. grade reagents were used. Methanol, mercury, p-nitrotoluene (m.p. 52°), and nitrobenzene (b.p. 209–211°) were purified. m-Nitrotoluene (b.p. 123° at 33 mm.) was prepared from m-nitro-p-toluidine by the standard method[13a]; p,p'-dinitrodibenzyl (m.p. 180–182°) by Green's procedure[3]; and p-nitrobenzoic acid (m.p. 237°) by oxidation of p-nitrotoluene with potassium dichromate. p-Nitrophenylacetic acid[13b] (m.p. 152°) was obtained from benzyl chloride via benzyl cyanide and p-nitrobenzyl cyanide. The sodium hydroxide and potassium hydroxide contained 4.7 and 14.5% water, respectively.

Apparatus and Procedure.—The apparatus consisted of a 250-ml. shaking vessel, connected by a tube and stopcock to an oxygen-filled buret, and a thermostat maintained at 25 ± 0.1°. A 50-ml. methanolic or aqueous solution of alkali was pipetted into the reaction vessel, the air expelled with a rapid stream of oxygen or with a mixture of O_2 and N_2 of known composition; and the vessel, connected with the gas buret, shaken for a while. Then with the stopcock closed, a solution of the nitro compound[14] was introduced rapidly. The cock was opened, the volume of oxygen in the gas buret was read and the shaking at a rate of 200 strokes per minute begun. The volume of oxygen in the buret was read at appropriate intervals, with the vessel at atmospheric pressure. Typical runs are illustrated in Fig. 1. The initial rates of oxygen absorption were evaluated from the straight line portions of the oxygen absorption curves.

Analysis. (a) p-Nitrotoluene as Reactant.—To the reaction mixture, which had absorbed oxygen for seven hours, was added 235 ml. of water and the precipitate and filtrate were analyzed. The precipitate was washed with methanol to remove the unreacted p-nitrotoluene, and the residue treated with hot benzene, whereby the sparingly soluble

(1) L. Preuss and A. Binz, Z. angew. Chem., 13, 385 (1900).

(2) H. Klinger, Ber., 16, 941 (1883); F. Bender and G. Schultz, ibid., 19, 3234 (1886); O. Fischer and E. Hepp, ibid., 26, 2231 (1893).

(3) A. G. Green, A. H. Davies and R. S. Horsfall, J. Chem. Soc., 91, 2076 (1907).

(4) C. Ris and C. Simon, Ber., 30, 2619 (1897); A. G. Green and A. R. Wahl, ibid., 30, 3097 (1897).

(5) A. E. Porai-Koshitz, Anilinokrasochnaya Prom., 4, 261 (1934); C. A., 29, 139 (1935).

(6) R. Oda and T. Tsuruta, Repts. Chem. Research Inst., Kyoto Univ., 16, 6 (1947); C. A., 46, 950 (1952).

(7) L. Chardonnes and P. Heinrich, Helv. Chim. Acta, 22, 1471 (1939).

(8) A. K. Plisov, Ukrainskii Khem. Zhur., 4, Sci. Pt., 241 (1929); C. A., 24, 1108 (1930).

(9) C. A. Bischoff, Ber., 21, 2071 (1888).

(10) R. Oda and T. Tsuruta, J. Soc. Org. Synth. Chem. Japan, 6, 59, 61 (1948).

(11) A. G. Green and J. Baddiley, J. Chem. Soc., 93, 1724 (1908), reported the self-condensation of 2,4-dinitrotoluene.
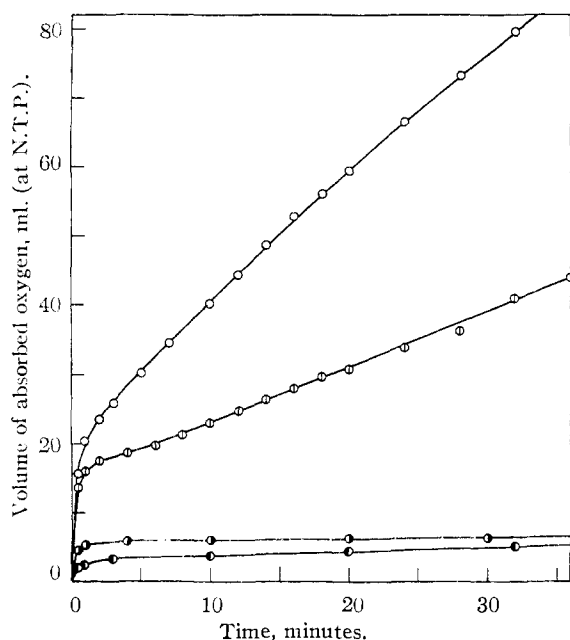
(12) Huang-Minlon, THIS JOURNAL, 70, 2802 (1948).

(13) (a) H. Gilman, "Organic Syntheses," Vol. I, 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1948, p. 415; (b) pp. 107, 396 and 406.

(14) In most cases, 1 g. of p-nitro compound was dissolved in 15 ml. of methanol at 25°. With water as solvent, the weighed p-nitrophenylacetic acid was suspended in a few ml. of water and warmed to 50°; the equivalent amount of potassium bicarbonate, in sufficient water to bring the total volume to 20 ml., was added slowly. The resulting clear solution was kept at 25°. The amount of water resulting from the neutralization of 1 g. of p-nitrophenylacetic acid is only 0.1 ml., which is negligible in comparison with the total volume.

Fig. 1.—Oxygen absorption courses of some nitro compounds at 25°: O, 3 g. of p-nitrotoluene; ⊙, 1 g. of p-nitrotoluene; ◑, 3 g. of m-nitrotoluene; ●, 5 g. of nitrobenzene; [KOH] = 4.260 M; temperature, 25°.

stilbene derivative was separated from the bibenzyl. The filtrate was tested for formaldehyde with fuchsin–sulfite solution and for formic acid by the resorcinol test.[15] Formaldehyde was determined iodometrically; the formic acid by acid–base titration.

(b) p-Nitrophenylacetic Acid as Reactant.—The aqueous alkali solution of p-nitrophenylacetic acid, which had been shaken with oxygen for about 30 minutes, was usually clear and reddish-brown in color. However, when the concentration of alkali was relatively high or the temperature of the solution was lowered after the reaction, yellow needles (A) were deposited which were identified as the alkali salt of dinitrodicarboxylic acid. When the mother liquor was warmed to 50° and warm dilute hydrochloric acid added, yellowish-white crystals separated which were washed with water, dried and identified as dinitrodicarboxylic acid; the melting point was not depressed by admixture with an authentic specimen.[13] The resorcinol test applied to the reaction mixture suggested the presence of oxalate which probably was formed by the oxidative degradation of p-nitrophenylacetic acid. However, no p-nitrobenzoic acid was detected by paper chromatography. The methanolic reaction mixtures were examined similarly.

Potentiometric Measurement of the Activity of Alkali.— The apparatus consisted of an ion concentration cell, a cadmium standard cell, a potentiometer and a galvanometer

Hg, HgO | Methanolic | K–Hg or | Methanolic | HgO, Hg
     | alkali(m_1) | Na–Hg | alkali(m_2) |
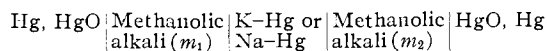
where m_1 and m_2 denote the total concentration of alkali in moles/l. The measurements were made by the standard method.[16]

For a methanolic solution of potassium hydroxide, the observed electromotive force ΔE would be related to the relative mean ionic activity $a_r(m_2)$ at the concentration of alkali m_2 by

$$\Delta E = \frac{2RT}{F} \ln a_r(m_2) + \frac{RT}{F} \ln \frac{p(m_1)}{p(m_2)}$$

or at 25°

$$\Delta E = 0.1183 \log a_r(m_2) + 0.0591 \log (p(m_1)/p(m_2))$$

where $a_r(m_2)$ represents $a(m_2)/a(m_1)$. The second term which

(15) F. Krauss and H. Tampke, *Chem. Ztg.*, **45**, 521 (1921).
(16) H. S. Harned and M. A. Cook, THIS JOURNAL, **59**, 496 (1937).

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is concerned with the vapor pressure p of the solvent was evaluated according to Harned and Cook.[16] The results are presented in Table I.

TABLE I

RELATIVE MEAN IONIC ACTIVITY (a_r) OF METHANOLIC SOLUTIONS OF ALKALI AT 25°

Potassium hydroxide M	a_r	Sodium hydroxide M	a_r	Sodium methoxide M	a_r
5.263	14.140	5.914	5.843	4.370	8.762
4.510	7.690	5.309	4.132	3.524	2.917
3.241	2.274	4.502	2.709	3.268	2.265
2.450	1.000	2.890	1.000	2.470	1.000
2.048	0.529	1.294	0.217	0.356	0.070
1.024	0.148				

Results and Discussion

Dependence of the Rate of Oxygen Absorption upon the Concentration of the Nitro Compound.— Figure 1 indicates that the rate of oxygen absorption of m-nitrotoluene, nitrobenzene and methanol itself is negligible in comparison with that of p-nitrotoluene. When the velocity of shaking was increased from 200 to 240 strokes per minute, numerous bubbles appeared. Although contact between the two phases was better in the latter case, the rate of oxygen absorption v remained essentially the same. Thus, v is not influenced by the rate of shaking and represents the rate of oxygen decrease in the liquid phase but not the rate of oxygen diffusion into the solution; the solution of p-nitro compound is probably saturated with oxygen during the entire reaction. In some cases, the oxygen absorption was retarded markedly when the velocity of shaking was lowered below a critical point; when shaking was suddenly interrupted, the rate decreased rapidly and the solution became colored.

As the volume of oxygen absorbed by solutions of p-nitrotoluene and p-nitrophenylacetic acid during the initial period of the reaction increases linearly with time and the rates of oxygen absorption evaluated from the slopes of these straight lines are exactly proportional to the initial concentrations of p-nitro compounds, v may be expressed as

$$v = kn$$

where n is the concentration of the p-nitro compound and k is a rate constant which represents the moles of oxygen absorbed per minute by one liter of alkali solution containing one mole of p-nitro compound.[17]

Sometimes the nitro compound absorbed much more oxygen than necessary for self-condensation. Part of the difference was accounted for by the formaldehyde and formic acid in the reaction mixture; presumably they resulted from the oxidation of methanol. The discrepancy in oxygen balance probably is due to the formation of carbon dioxide or of highly viscous resinous substances.[18]

(17) The mean values of k were (4.42 ± 0.12) × 10^{-3} for p-nitrotoluene in 4.260 M methanolic KOH and (5.43 ± 0.06) × 10^{-3} for p-nitrophenylacetic acid in 1.328 M aqueous KOH, respectively.

(18) The oxygen absorbed by 3.027 g. of p-nitrotoluene in a 4.50 M potassium hydroxide solution (reaction time 420 minutes) was 421 ml.; 325.7 ml. of oxygen was accounted for by the dinitrodibenzyl (55.2 ml.), dinitrostilbene (110.4 ml.), formaldehyde (63.0 ml.) and formic acid (97.1 ml.) in the reaction mixture. The theoretical amount of oxygen required for the conversion of 3 g. of p-nitrotoluene to the stilbene derivative is 246 ml. under standard conditions.

Treves[19] in his study of the oxygen absorption of 2-methoxy-4-nitrotoluene also noticed a discrepancy between the yield of the self-condensate and the amount of oxygen theoretically required; it is likely that methanol was oxidized in this case also.

Dependence of the Rate of Oxygen Absorption upon the Mean Ionic Activity of Alkali.—Figures 2[20] and 3 show that p-nitrophenylacetic acid is affected markedly by alkali concentration, but to a lesser extent in aqueous than in methanolic solution. When the alkali concentration was expressed as the ionic activity[21] rather than the analytical value, the rate of oxygen absorption by methanolic solutions was found to be proportional to the square of the mean ionic activity of the alkali

$$v = k' n a_r^2$$

The rate of oxygen absorption by aqueous solutions is proportional to the mean ionic activity

$$v = k'' n a$$

The data supporting these findings are summarized in Table II.

TABLE II

DEPENDENCE OF THE RATE OF OXYGEN ABSORPTION UPON THE CONCENTRATION OF ALKALI

Reactant	Alkali	Solvent	No. of detmn.	k/a_r^2
p-Nitrotoluene	KOH	CH₃OH	33	$(1.21 \pm 0.022) \times 10^{-4}$
p-Nitro-phenyl-acetic acid	KOH	CH₃OH	13	$(1.49 \pm .020) \times 10^{-2}$
	NaOH	CH₃OH	12	$(2.26 \pm .027) \times 10^{-2}$
	NaOCH₃	CH₃OH	14	$(0.72 \pm .020) \times 10^{-2}$
	KOH	H₂O	17	$(0.50 \pm .006) \times 10^{-2a}$
	NaOH	H₂O	5	$(0.55 \pm .011) \times 10^{-2a}$

^{a} Values for k/a.

Correlation of the Rate of Oxygen Absorption with the Partial Pressure of Oxygen.—The data pertaining to the correlation between the rate of oxygen absorption and the volume percentage[22] of oxygen in the N_2–O_2 gas mixture, are summarized in Table III.

For a given alkali activity, the rate constant of oxygen absorption k is proportional to the volume percentage of oxygen. Therefore, if the other variables are constant, v may be expressed by

$$v = v_0 + u[O_2]$$

where the constants v_0 and u are both dependent upon the concentrations of p-nitrotoluene and alkali. This relationship holds for both methanolic and aqueous solutions of p-nitrophenylacetic acid, as the values for v_0/n and u/n show.

Reaction Mechanism.—From the results obtained, the following rate expression is possible

$$v = (k_1 + k_2[O_2]) n a^m \qquad (1)$$

where a is the mean ionic activity, m is 1 with water as solvent or 2 with methanol as solvent, and k_1 and k_2 are constants.

(19) G. R. Treves, THIS JOURNAL, 70, 875 (1948).

(20) A similar curve was obtained when the oxygen absorption of methanolic solution of p-nitrotoluene was plotted against the concentration of potassium hydroxide.

(21) The activity values for aqueous solutions of alkali are given in the literature: ref. 19 and H. S. Harned and J. C. Hecker, THIS JOURNAL, 55, 4838 (1933). The values for methanolic solutions were determined as described above.

(22) Since the vapor pressure of methanol is constant under the experimental conditions, the partial pressure of oxygen can be expressed as the product of the oxygen content of the gas mixture and a constant.
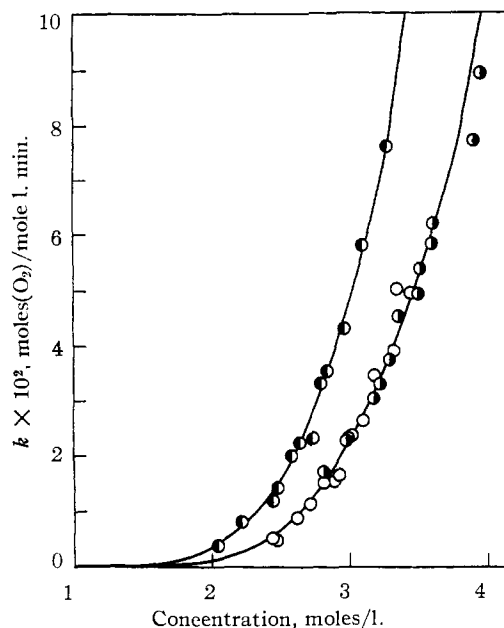

Fig. 2.—Plot of the rate constant of oxygen absorption by a methanolic solution of p-nitrophenylacetic acid against the molar concentration of alkali: O, sodium methoxide; ◐, sodium hydroxide; ◑, potassium hydroxide.
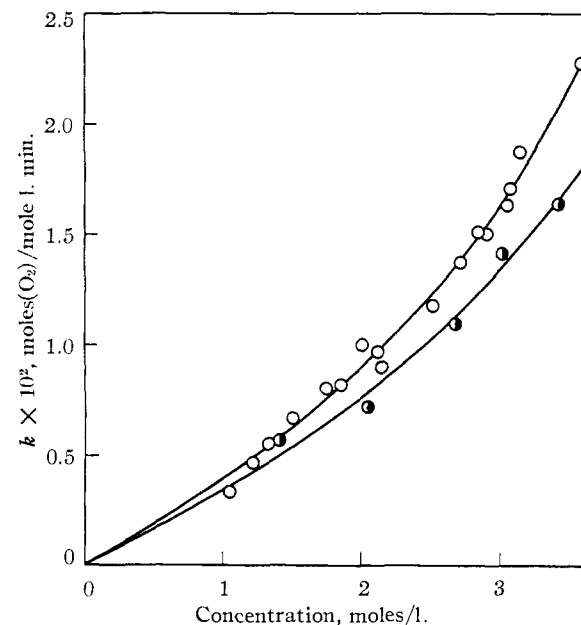

Fig. 3.—Plot of the rate constant of oxygen absorption by p-nitrophenylacetic acid in water against the molar concentration of alkali: O, potassium hydroxide; ◐, sodium hydroxide.

The rate expression consists of two terms; one is independent of the concentration of oxygen and the other is of the first order with respect to it. If we assume the extreme case where the partial pressure of oxygen is zero, then the velocity of oxygen decrease, v_0, is expressed by

$$v_0 = k_1 n a^m \qquad (2)$$

The validity of equation 2 is shown by the fact that the plot of the values for a, given in Table III for p-
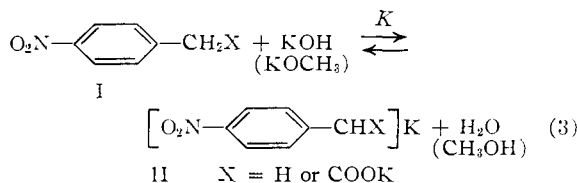
TABLE III

CORRELATION OF THE RATE OF OXYGEN ABSORPTION WITH THE VOLUME PERCENTAGE OF OXYGEN IN GAS MIXTURE

KOH, M	a	O_2, vol. %	$k = v/n$	v_0/n	u/n
_p_-Nitrotoluene with methanol as solvent					
3.535	3.14	100	1.15×10^{-3}		
		70.0	0.96		
		49.7	.77		
		22.8	.56	0.40×10^{-3}	0.765×10^{-5}
		21.0	.58		
		10.5	.42		
		8.5	.49		
		3.9	.43		
_p_-Nitrophenylacetic acid with methanol as solvent					
2.732	1.33	100	2.30×10^{-2}		
		49.7	1.53		
		22.8	0.92	0.46×10^{-2}	19.0×10^{-5}
		21.0	.84		
		8.5	.59		
		3.9	.48		
_p_-Nitrophenylacetic acid with water as solvent					
1.221	0.95	100	0.47×10^{-2}	0.15×10^{-2}	3.16×10^{-5}
		21.0	.22		
1.502	1.22	100	.67	.22	4.43
		21.0	.32		
1.748	1.49	100	.80	.28	5.20
		21.0	.39		
2.724	2.78	100	1.37	.50	8.75
		21.0	0.68		
3.152	3.52	100	1.87		
		62.5	1.44		
		21.0	0.88	.61	12.80
		4.2	.69		
		3.5	.61		

nitrophenylacetic acid in water, against the corresponding values for v_0/n is a straight line; $v_0/na = (0.18 \pm 0.004) \times 10^{-2}$.

On the basis of the rate law, the following reaction mechanism is postulated. First of all, the _p_-nitro compound is converted to the alkali salt II

$$O_2N-\!\!\!\!\bigcirc\!\!\!\!-CH_2X + KOH \underset{(KOCH_3)}{\overset{K}{\rightleftarrows}}$$

I

$$\left[O_2N-\!\!\!\!\bigcirc\!\!\!\!-CHX\right]K + H_2O \quad (3)$$
$$(CH_3OH)$$

II   X = H or COOK

Alkali participates in this equilibrium in the first or second order with respect to the mean ionic activity a, as shown by

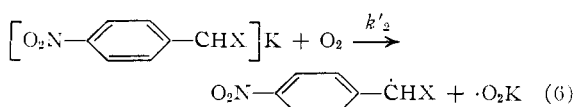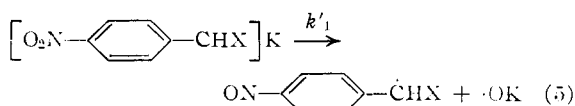$$\frac{[II][H_2O(or\ CH_3OH)]}{[I]a_r{}^m} = K \quad (4)$$

where K is an equilibrium constant. In aqueous solution, ionization of potassium _p_-nitrophenylacetate is probably easier than in methanolic solution. In contrast to the undissociated carboxyl group which is electron withdrawing, the anion COO^- may be expected to be electron donating[23] and con-

(23) T. Alfrey, Jr., C. G. Overberger and S. H. Pinner, THIS JOURNAL, **75**, 4221 (1953), studied the copolymerization of methacrylic acid and with both diethylaminoethyl methacrylate and acrylonitrile; they reported that, in terms of the _Q-e_ scheme, the double bond of methacrylate anion possesses a negative _e_-value, whereas that of un-ionized methacrylic acid possesses a positive one.

sequently to counteract activation of the methylene group by the nitro group.

Accordingly the carboxylate anion should not form a salt of type II; this may be responsible for the different behavior of _p_-nitrophenylacetic acid toward alkali in the two solvents.

As nitro compounds undergo oxidation reactions usually in the presence of alkali, it is possible that they are converted to a reactive form by the alkali. In the reactive state II the nitro group readily loses oxygen, while the hydrogen-releasing ability of the methyl or methylene group is enhanced. Since the oxygen absorption follows the relatively simple rate law 1 in spite of the formation of various oxidation by-products, the rate-determining step seems to consist of the stages

$$\left[O_2N-\!\!\!\!\bigcirc\!\!\!\!-CHX\right]K \xrightarrow{k'_1}$$
$$ON-\!\!\!\!\bigcirc\!\!\!\!-\dot{C}HX + \cdot OK \quad (5)$$

$$\left[O_2N-\!\!\!\!\bigcirc\!\!\!\!-CHX\right]K + O_2 \xrightarrow{k'_2}$$
$$O_2N-\!\!\!\!\bigcirc\!\!\!\!-\dot{C}HX + \cdot O_2K \quad (6)$$

The unstable nitroso group rapidly absorbs oxygen

$$XH\dot{C}C_6H_4-NO + O_2 \longrightarrow XH\dot{C}C_6H_4-NO_2 + O \quad (7)$$
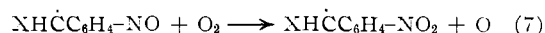
a step which proceeds so rapidly that the rate of oxygen absorption should be determined by reaction 5. The benzyl radicals thus produced combine to give bibenzyl derivatives; stilbene derivatives are formed from bibenzyl by a similar process as stated above. The radicals, $\cdot OK$, $\cdot O_2K$ and O, would act on solvent and reactant with the formation of the various oxidized by-products.

Thus, the observed rate of oxygen absorption v should be expressed as the sum of the rates of reactions 5 and 6

$$v = (k'_1 + k'_2[O_2])[11] \quad (8)$$

The rate expression 1 can be derived from equations 4 and 8 with $k'_1 K/[H_2O(or\ CH_3OH)]$ and $k'_2 K/[H_2O(or\ CH_3OH)]$ as k_1 and k_2, respectively. When the contact of the reacting solution with oxygen is insufficient, the nitroso compound produced by reaction 5 loses its oxygen atom with the eventual formation of an azo or azoxy bonding to which the color of $C_{28}H_{20}N_4O_4$ probably is due. The oxidizing power of the nitro group may be interpreted reasonably by the first term of equation 1.