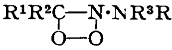
684. *The Autoxidation of Phenylhydrazones. Part I.*

By K. H. Pausacker.

The rate of autoxidation of various phenylhydrazones of aromatic aldehydes has been investigated semi-quantitatively. A structure is advanced for the autoxidation product, and the mechanism of the reaction is discussed.

Busch and Dietz (*Ber.*, 1914, **47**, 3277), in contrast to Baly and Tuck (*J.*, 1906, **89**, 988), found that, when hydrazones, in benzene solution, were shaken with oxygen, approximately one mole of oxygen was absorbed and the empirical formula of the product contained two more atoms of oxygen than that of the original hydrazone. Hydrazone (I) could be autoxidised if (*a*) R^1 and R^3 = aryl, and R^2 and R^4 = H, (*b*) R^1 and R^3 = aryl, R^2 = H, and R^4 = alkyl, (*c*) R^1 and R^2 = alkyl, R^3 = aryl, and R^4 = H, or (*d*) R^1 and R^3 = aryl, R^2 = alkyl, and R^4 = H. On the basis of these results they ascribed the structure (II) to the autoxidation product.

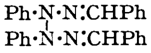
(I.) $\mathrm{R^1R^2C{:}N\cdot NR^3R^4}$



$$\begin{array}{l}\mathrm{R^1R^2C{-}N\cdot NR^3R^4}\\ \quad\mathrm{O{-}O}\end{array}$$

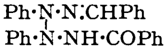
(II.)

Busch and Kunder (*Ber.*, 1916, **49**, 2345) found autoxidation of benzaldehyde phenylhydrazone in ethyl-alcoholic solution containing a small amount of acetic acid to take an entirely different course, giving (III)—(VI), benzophenone phenylhydrazone, β-benzoylphenylhydrazine, benzoic acid, and benzaldehyde.



$$\begin{array}{l}\mathrm{Ph\cdot N\cdot N{:}CHPh}\\ \mathrm{Ph\cdot N\cdot N{:}CHPh}\end{array}$$

(III.)



$$\begin{array}{l}\mathrm{Ph\cdot N\cdot N{:}CHPh}\\ \mathrm{Ph\cdot N\cdot NH\cdot COPh}\end{array}$$

(IV.)

$$\begin{array}{r}\mathrm{Ph\cdot NH\cdot N{:}CPh}\\ \mathrm{Ph\cdot CO\cdot NH\cdot NPh}\end{array}$$

(V.)

$\mathrm{Ph\cdot N{:}N\cdot CHPh_2}$

(VI.)

In the present paper, a study has been made of the effect of substituents on the autoxidation rate of benzaldehyde phenylhydrazone, measured by determining the volume of oxygen absorbed after different times. As a thermostat was not used, the results are only semi-quantitative.

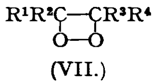
As oxidation rates are, in general, greatly influenced by the presence of impurities (see, for example, Raymond, *J. Chim. physique*, 1931, **28**, 480; Almquist and Branch, *J. Amer. Chem. Soc.*, 1932, **54**, 2293), the rates were measured both for the " pure " substance (known as the " uncatalysed " reaction) and after addition of 0·02 mole of benzoyl peroxide per mole of hydrazone (the " catalysed " reaction). In all cases the reaction was of the first order, *i.e.*, $-\mathrm{d(O_2)}/\mathrm{d}t = k(V_\infty - V_t)$ where V_∞ and V_t are the volumes of oxygen absorbed at infinite time and time t respectively.

Like many autoxidation reactions (Waters, " Chemistry of Free Radicals," Oxford, 1946, pp. 234 *et seq.*), this reaction has been found to display the characteristics of a free-radical reaction. Thus, in light, the uncatalysed reaction ($t_{\frac{1}{2}}$ = 12·9 minutes at 22°) is slower than the catalysed reaction ($t_{\frac{1}{2}}$ = 8·0 minutes at 21°), but both these reactions are slower when performed in the dark (catalysed, $t_{\frac{1}{2}}$ = 24·6 minutes at 15°; uncatalysed, 25·6 minutes at 15°). Moreover, the reaction in light has an induction period when β-naphthol is added, in contrast to both the catalysed and the uncatalysed reaction for which no induction period is observed. Finally, the autoxidation rate varies with the solvent in the order benzene > *cyclo*hexane > methyl alcohol ≃ acetone, which agrees with that demonstrated by Waters (*op. cit.*, p. 16) for a free-radical reaction. In certain solvents (notably carbon tetrachloride), the reaction appears to follow a different course, forming entirely different products, and this variation will be the subject of a separate study.

Owing to fluctuations in room temperature the rates recorded for the substituted benzaldehyde phenylhydrazones are not strictly comparable. However, indications were obtained that the reaction has not a large activation energy, as the $t_{\frac{1}{2}}$ values did not differ by more than 1 minute with temperature differences of 5°. This agrees with McDowell and Thomas's finding (*J.*, 1949, 2212) that the autoxidation of acetaldehyde has a low activation energy. The rates measured differ widely from the few reported by Busch and Dietz (*loc. cit.*), probably owing to a difference in the efficiency of shaking.

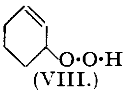
In agreement with Busch and Dietz, it was found that acetophenone phenylhydrazone underwent (catalysed) autoxidation, but at a slower rate ($t_{\frac{1}{2}}$ = 21·3 minutes at 17°) than the unsubstituted compound. Benzaldehyde methylphenylhydrazone appeared not to absorb oxygen at all, although Busch and Dietz state that benzaldehyde benzylphenylhydrazone reacts normally with oxygen; however, it may be noted that the product of this reaction is the only one that they did not analyse, being stated to be too unstable to be isolated.

The formula (II) ascribed by Busch and Dietz to the product of autoxidation is reminiscent of that originally proposed for the autoxidation product (VII) of olefins (Engler, *Ber.*, 1897, **30**, 1669; 1898, **31**, 3046; 1900, **33**, 1090); this was shown to be incorrect by Criegee, Pilz, and Flygare (*ibid.*, 1939, **72**, 1790), who proposed the accepted structure (VIII) for *cyclo*hexyl



$$R^1R^2\underset{|}{C}—\underset{|}{C}R^3R^4 \atop O—O$$

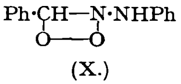
(VII.)



(VIII.)

(IX.) Ph·CH:N·NPh·O·OH

(XI.) Ph·N:N·CHPh·O·OH

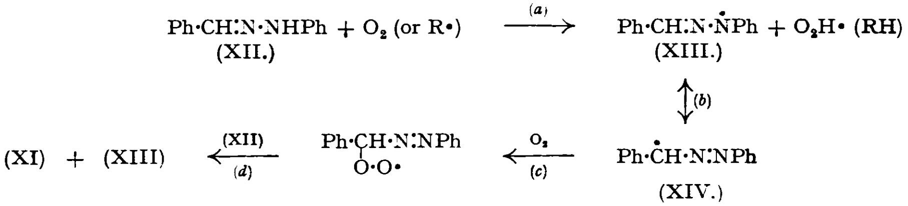


$$Ph·\underset{|}{C}H—\underset{|}{N}·NHPh \atop O——O$$

(X.)

hydroperoxide. By analogy alone, therefore, it may be legitimate to propose the hydroperoxide structure (IX), in place of that (X) favoured by Busch and Dietz for the product formed from benzaldehyde phenylhydrazone. This would be supported by our inability to autoxidise benzaldehyde methylphenylhydrazone. However, a structure such as (IX) appears inherently improbable, and so the structure (XI) is proposed. This is supported by the fact that all the autoxidation products are pale yellow.

Formation of (XI) may proceed as follows :

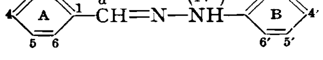


Stages (*a*), (*c*), and (*d*) resemble very closely the corresponding stages in the autoxidation of olefins (Waters, *op. cit.*, p. 241), and stage (*b*) merely indicates resonance between (XIII) and (XIV). Some support for this mechanism is derived from the fact that Busch and Kunder (*loc. cit.*) observed the formation of both (III) and (V) during the autoxidation of (XII) in ethanol. (III) may be formed by dimerisation of (XIII), and (V) by interaction of (XIII) and (XIV) followed by oxidation and rearrangement.

The choice between the structures (IX) and (XI), which are considered most probable for the autoxidation product, has been difficult to make, and definite proof is still lacking. (XI) is preferred for the following reasons : (*a*) it resembles the known hydroperoxides formed by the attack of oxygen on the carbon atom α to a double bond; (*b*) as already mentioned, the colour suggests that a chromophore is present which does not occur in the original hydrazone; (*c*) Busch and Dietz (*loc. cit.*) found that the autoxidation product, like hydroperoxides, could be determined iodometrically and thereby reduced to β-benzoylphenylhydrazine, possibly proceeding by the mechanism :

$$\text{HO·O·CHPh·N:NPh} \xrightarrow{\text{2HI}} \text{HO·CHPh·N:NPh} \longrightarrow \text{HO·CPh:N·NHPh} \longrightarrow \text{Ph·CO·NH·NHPh}$$

Rates of oxidation of various substituted benzaldehyde phenylhydrazones (XV) are given in the table.



(XV.)

As the reaction is apparently susceptible to catalysis, the following discussion will deal principally with the catalysed reaction as traces of impurities can radically alter the " uncatalysed " reaction.

It is seen that all the compounds substituted in ring A were autoxidised more slowly than the parent compound, but it may be noted that all the *meta*-substituted compounds reacted more rapidly that the corresponding *para*-compounds. In comparison, the presence of electron-donors in ring B increased the autoxidation rate (a slight divergence being noted with the 3-methyl compound) and electron-acceptors decreased it. In fact, it is found that the latter rates (catalysed and uncatalysed) may be inter-related by means of Hammett's equation (Hammett, " Physical Organic Chemistry," McGraw-Hill, 1940, p. 186). The agreement is best with the uncatalysed rates. Ordinarily it is considered that Hammett's equation cannot be used with free-radical reactions. However, it has been found (Barron, *J. Biol. Chem.*, 1932, **97**, 287) that the rate of autoxidation of certain leuco-dyes with widely different nuclei, which is most probably a free-radical reaction, is linearly related to the oxidation potential of the dyestuff. Thus this reaction is in accord with Hammett's generalised formulation of his equation.

Substituent	Catalysed		Uncatalysed	
	$t_{\frac{1}{2}}$ (min.)	Temp.	$t_{\frac{1}{2}}$ (min.)	Temp.
3-Me	15·6	17°	13·5	16°
4-Me	17·1	19	20·4	19
3-OMe	17·3	17	16·5	17
4-OMe	20·7	20	31·4	21
3-Cl	26·5	18	37·1	18
4-Cl	32·9	18	35·3	19
3-NO_2	35·9	19	39·2	17
4-NO_2	111·8	18	*ca.* 250	20

Substituent	Catalysed		Uncatalysed	
	$t_{\frac{1}{2}}$ (min.)	Temp.	$t_{\frac{1}{2}}$ (min.)	Temp.
4′-OMe	1·3	19°	4·7	20°
4′-Me	2·9	21	4·8	21
Unsubst.	8·0	21	12·9	22
3′-Me	8·5	19	14·7	19
3′-OMe	13·3	18	27·9	18
4′-Cl	14·9	17	28·7	18
3′-Cl	56·1	17	53·5	17
4′-NO_2	Too slow to measure			
α-Me	21·8	17	41·6	17
N′-Me	Too slow to measure			

Unsubstituted.

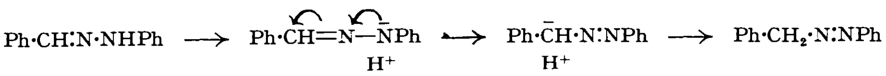
12 Mole % of quinol added : $t_{\frac{1}{2}}$ = 14·2 mins. (20°).
8 Mole % of β-naphthol added : $t_{\frac{1}{2}}$ = 16·4 mins. (21°) (induction period = 4 mins.).
Methyl alcohol as solvent : 73 mins. required to absorb 10 ml. of O_2.
Acetone as solvent : 70 mins. required to absorb 10 ml. of O_2.
*cyclo*Hexane as solvent : 15·2 mins. required to absorb 10 ml. of O_2.
Benzene as solvent : 3·0 mins. required to absorb 10 ml. of O_2.

It is not apparent at first why substituents have different effects depending on the ring to which they are attached, but this may possibly be explained as follows. The rate-determining step may be postulated to be the removal of a hydrogen atom (XII ⟶ XIII).* If this is the case, then the rate of the reaction will be dependent on the energy difference between the starting material (XII) and the radical formed (XIII ⟷ XIV). In the formation of the radical, the resonance energy of the conjugation between ring A and the –CH:N– is largely lost, but this loss will be greater with all compounds substituted in ring A, and particularly with those *para*-substituted, than with the parent molecule. Thus all compounds substituted in ring A will react less readily than the unsubstituted molecule, as has been found.

In addition, in the starting material, ring B is conjugated with the lone pair of electrons on the nitrogen atom, the resonance energy of any compound being greater than the unsubstituted compound when electron-acceptors are present in the ring and less when electron-donors are present. Thus the presence of electron-acceptors in ring B will increase the energy difference between the starting material and the radical, thus causing a decrease in rate, whereas the reverse will be true with electron-donors. This reasoning also serves to explain why Hammett's equation is applicable in this series.

Another possibility should perhaps not be neglected. The hydrazone may first rearrange to an azo-compound, which is then autoxidised in the usual manner :

Apart from the fact that this is a reversal of the normal change (Taylor and Baker, " Sidgwick's Organic Chemistry of Nitrogen," Oxford, 1942, p. 432), it would be expected that the rearrangement would occur as follows :



$$\mathrm{Ph{\cdot}CH{:}N{\cdot}NHPh} \longrightarrow \underset{\mathrm{H^+}}{\mathrm{Ph{\cdot}CH{=}N{-}\bar{N}Ph}} \longleftrightarrow \underset{\mathrm{H^+}}{\mathrm{Ph{\cdot}\bar{C}H{\cdot}N{:}NPh}} \longrightarrow \mathrm{Ph{\cdot}CH_2{\cdot}N{:}NPh}$$

and this change would be favoured by electron-acceptors in ring B, which is certainly not in accord with the autoxidation rates observed.

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* The discussion of the effects of substitution on reaction rate is based on a suggestion by a Referee.

It may be noted that Grammaticakis (*Bull. Soc. chim.*, 1947, **14**, 438) has postulated, on the basis of spectroscopic evidence, that the equilibrium Ar·CR:N·NHPh $\rightleftharpoons$ Ar·CHR·N:NPh exists for phenylhydrazones. As he makes no mention of excluding oxygen from his systems, it is possible that the indications of the presence of an azo-compound are due to the presence of a hydroperoxide such as (XI). This is supported by his statement: " En effet, cette phenylhydrazone [*cyclo*hexanone phenylhydrazone] fraîchement préparée et à l'état solide est incoloré, ce qui indique l'absence de la forme azoïque; mais mise en solution, elle se colore en jaune, par suite de son isomérisation, la vitesse et l'intensité de la coloration dépendant des conditions expérimentales (nature du solvent, etc.)."

EXPERIMENTAL.

Preparation of Phenylhydrazones.—The appropriate phenylhydrazine and benzaldehyde were dissolved in ethyl alcohol, and the product which separated on storage was recrystallised from ethyl alcohol. The m. p.s agreed with those reported in the literature. *Benzaldehyde* m-*methoxyphenylhydrazone*, m. p. 101° (Found: N, 12·3. $C_{14}H_{14}ON_2$ requires N, 12·4%), appears to be new.

Autoxidations.—The phenylhydrazone ($2·08 \times 10^{-3}$ mole) was dissolved in sodium-dried sulphur-free benzene (40 ml.) in a 100-ml. distillation flask. The apparatus was twice evacuated (to *ca.* 60 mm.) and filled with oxygen from a cylinder. The flask was attached to a " Microid " shaker operating at 850 revs./min. Higher rates of shaking did not increase the autoxidation rate. The absorption of oxygen was measured by a gas-burette (to $\pm 0·1$ ml.), containing mercury, the pressure being maintained atmospheric. Between 42 and 50 ml. of oxygen were absorbed (calc.: 46 ml. at N.T.P.). Benzoyl peroxide (10 mg.) was also added in the catalysed experiments. For reactions in the " dark," the flask was sprayed with black enamel.

The $t_{\frac{1}{2}}$ values were obtained as follows. Plotting $\log_{10} (V_\infty - V_t)$ against t disclosed a linear relationship, showing that the reaction is of the first order. When $\log_{10} 2$ is divided by the negative of the slope of the graph, the product is $t_{\frac{1}{2}}$. The slopes of the graphs were obtained by the method of least squares. The values quoted are the mean of two or more experiments and are, in general, accurate to ±1 minute.

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