The Oxidation of Phenylhydrazones. Part II.*

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The rates of oxidation of various nuclear-substituted benzaldehyde phenylhydrazones with perbenzoic acid have been determined at three temperatures, and the entropies, free energies, and heats of activation have been calculated. A theory is advanced for the mechanism of the reaction.

It has been shown that benzylazoxybenzenes are formed in excellent yields by the oxidation of nuclear-substituted benzaldehyde phenylhydrazones with perbenzoic and perphthalic acid (Part I *; Witkop and Kissman, *J. Amer. Chem. Soc.*, 1953, **75**, 1975) :

$$\text{Ar·CH:N·NHAr}' + \text{Ph·CO}_3\text{H} \longrightarrow \text{Ar·CH}_2\text{·N(O):NAr}' + \text{Ph·CO}_2\text{H}$$

In this paper, the rates of the reaction of perbenzoic acid with substituted benzaldehyde phenylhydrazones have been measured by determining the " active " oxygen remaining after different times.

The solvent was diethyl ether, and measurements were made at three temperatures; only freshly prepared solutions of perbenzoic acid were used, since it was found that the rate increased when samples of perbenzoic acid which had undergone some spontaneous decomposition were used (cf. Friess, *J. Amer. Chem. Soc.*, 1949, **71**, 2571; Doering and Speers, *ibid.*, 1950, **72**, 5515; Badger, Buttery, and Lewis, *J.*, 1953, 2143).

The rates of the reactions studied were unaffected by exposure to daylight, unlike the similar oxidations of aromatic azo-compounds with perbenzoic acid (Badger *et al.*, *loc. cit.*).

EXPERIMENTAL

M.p.s are corrected.

Reagents.—Perbenzoic acid was prepared by Braun's method (*Org. Synth.*, Coll. Vol. I., 1946, p. 431) except that diethyl ether was used to extract the peracid. The minimum purity, estimated by iodometric titration, was 92·0%.

Diethyl ether was purified by Vogel's method (" A Textbook of Practical Organic Chemistry," Longmans, 1950, p. 162).

Benzene was purified by Vogel's method (*op. cit.*, p. 171) and dried over sodium.

Substituted benzaldehyde phenylhydrazones were prepared by condensation of the appropriate benzaldehyde and phenylhydrazine in ethanol, and were crystallised from aqueous ethanol immediately before use. Their m. p.s are given in the following Table. M. p.s in parentheses are those reported in the literature. In benzaldehyde phenylhydrazone the positions in the Ph·NH group are indicated by primed numerals.

No.	1	2	3	4	5	6	7	8
Substituent	3-OMe	4-OMe	3'-OMe	4'-OMe	3-Me	4-Me	3'-Me	4'-Me
M. p.	76° (76°)	122° (120°)	101° (101°)	124° (123°)	88° (87°)	112° (112°)	100° (96°)	126° (125°)

No.	9	10	11	12	13	14	15	16
Substituent	Nil	3-Cl	4-Cl	3'-Cl	4'-Cl	3-NO₂	4-NO₂	3'-NO₂
M. p.	158° (157°)	136° (134°)	129° (127°)	133° (133°)	129° (127°)	122° (120°)	158° (155°)	131° (131°)

Apparatus.—A bath was used whose temperature was controlled within ± 0·05°. Reactions were performed in calibrated standard 50-ml. or (with sparingly soluble phenylhydrazones) 100-ml. flasks.

Method of Estimation.—The phenylhydrazone (*ca.* 3—5 × 10⁻³ mole) was weighed into the reaction vessel, which was placed in the bath until temperature equilibrium was attained. A pre-heated solution of perbenzoic acid (*ca.* 8—10 × 10⁻²M) was added to the mark, and the mixture was vigorously shaken. When the phenylhydrazone dissolved slowly, it was first dissolved in diethyl ether in the flask and then a known volume of a solution of perbenzoic acid was added, together with diethyl ether to make up to the mark. Aliquots (2 ml.) were withdrawn at determined times and added to a mixture of carbon tetrachloride (10 ml.), 0·2N-

* Part I, *J.*, 1953, 2517.

potassium iodide (5 ml.), and 2N-sulphuric acid (5 ml.). The liberated iodine was titrated with 0·04N-sodium thiosulphate (starch). Attempted estimation in the absence of carbon tetrachloride gave unsatisfactory end-points. The perbenzoic acid solution was also estimated immediately before use.

Results.—Reactions were followed to at least 50% completion, and were found to follow pure second-order kinetics. The rate constants were calculated by standard methods and were found to obey the Arrhenius equation.

The reaction of *m*-nitrobenzaldehyde phenylhydrazone with perbenzoic acid at 25° is given as a typical example in Table I.

TABLE 1.

Initial phenylhydrazone concn. = 0·07430M (8·08 ml. of 0·03764N-$Na_2S_2O_3$).
Initial perbenzoic acid concn. = 0·0864M (9·39 ml. of 0·03764N-$Na_2S_2O_3$).
First perbenzoic acid estimation = 9·10 ml.
Equivalent phenylhydrazone concn. = 7·79 ml.

Time (min.)	4·8	10·8	18·0	23·3	33·3	40·0	44·3	53·0	77·0	110·0
Titre (ml.)	8·86	8·60	8·28	8·10	7·74	7·53	7·35	7·10	6·67	5·74
$10^3 k_2$ (mole^{-1} l. sec.$^{-1}$)	1·299	1·250	1·257	1·239	1·240	1·238	1·210	1·261	1·252	1·250

Mean : $k_2 = 1·25 \times 10^{-3}$ mole^{-1} l. sec.$^{-1}$.

Results obtained at different temperatures are (averages in parentheses) :

Temp.	15·00°	20·30°	25·00°
$10^3 k_2$ (mole^{-1} l. sec.$^{-1}$)	0·661, 0·675	0·920, 1·00	1·25, 1·25
	(0·668)	(0·960)	(1·25)

The bimolecular constants obey the Arrhenius equation, as shown by the following data (the calculated values are given by $k = 5·72 \times 10^4 e^{-10,450/RT}$) :

Temp.		15·00°	20·30°	25·00°
$10^3 k_2$ { obs.		0·668	0·960	1·25
{ calc.		0·664	0·947	1·257

The results obtained with the various benzaldehyde phenylhydrazones are summarised in Table 2, duplicates being shown :

TABLE 2. *Perbenzoic acid oxidation of substituted benzaldehyde phenylhydrazones.**
(a) *Reactions in diethyl ether.*

No.	15°	20°	25°	$\log_{10} A$	$\Delta H\ddagger$	$\Delta F\ddagger$	$-\Delta S\ddagger$	X	Y	Z
		$10^3 k$ †								
1	6·16, 6·16, 6·28	8·06, 7·87	10·0, 10·1	4·02	7·6	20·2	43·1	−0·2	0·2	−0·4
2	23·1, 23·6	28·9, 30·9	33·8, 36·1	3·80	6·6	19·4	43·7	−1·2	−0·1	−1·1
3	3·38, 3·42	9·25, 9·54	11·79, 12·00	4·02	7·5	20·1	43·1	−0·3	0·2	−0·5
4	40·4, 40·5	49·8, 49·6	60·4, 60·8	3·84	6·3	19·1	43·7	−1·5	−0·2	−1·3
5	3·90, 3·85	4·90, 5·08	6·30, 6·41	3·96	7·8	20·4₅	43·7	0·0	0·15	−0·15
6	6·01, 6·05	7·60, 7·74	9·74, 9·80	4·01	7·6	20·2	43·1	−0·2	0·2	−0·4
7	4·28, 4·22	5·52, 5·55	7·04, 7·00	4·00	7·8	20·4	43·1	0·0	0·2	−0·2
8	6·99, 6·81	8·70, 8·80	11·2, 11·0	3·98	7·5	20·1	43·1	−0·3	0·2	−0·5
9	3·16, 3·10	3·94, 4·09	5·05, 5·20 *a*	3·87	7·8	20·6	43·7	0	0	0
10	1·43, 1·46	1·82, 1·92	2·43, 2·45	4·13	8·6	21·0	42·9	0·8	0·4	0·4
11	2·49, 2·49 *b*	3·05, 3·07 *c*	3·53, 3·61	4·06	8·3	20·8	42·9	0·5	0·3	0·2
12	0·506, 0·513	0·667, 0·683	0·896, 0·917	4·15	9·2	21·6	42·5	1·4	0·4	1·0
13	1·54, 1·55 *b*	1·72, 1·73	2·25, 2·24 *d*	4·11	8·6	21·1	42·9	0·8	0·3	0·5
14	0·661, 0·675	0·920, 1·00	1·25, 1·25	4·76	9·8₅	21·4	39·6	2·0₅	1·2	0·8
15	0·298, 0·318	0·431, 0·455	0·582, 0·610	5·80	11·7	21·9	35·0	3·9	2·6	1·3
16	0·295, 0·297 *b*	0·339, 0·337	0·463, 0·469	4·82	10·5	22·0	39·3	2·7	1·3	1·4

* $\Delta H_0\ddagger$, $\Delta F_0\ddagger$ (in kcal.), and $\Delta S_0\ddagger$ (in cal. deg.$^{-1}$) are the heat of activation, the free energy of activation, and the entropy of activation, respectively, for the unsubstituted benzaldehyde phenylhydrazone. $X = \Delta H\ddagger - \Delta H_0\ddagger$; $Y = T(\Delta S\ddagger - \Delta S_0\ddagger)$; $Z = \Delta F\ddagger - \Delta F_0\ddagger$; all in kcal. $\Delta F\ddagger$ and $\Delta S\ddagger$ for the various compounds are calculated from the rates at 25°. A is the frequency factor.
a When an equimol. mixture of benzoic and perbenzoic acid was used, $10^3 k$ was 6·26, 6·43. *b* Both values at 18°. *c* Both values at 22°. *d* At 28°, 2·66. † Mole^{-1} l. sec.$^{-1}$.

(b) *Reaction in benzene.* Only the unsubstituted benzaldehyde phenylhydrazone was investigated. The reaction was of second order and the rates of reaction followed the Arrhenius equation. Summarised results are :
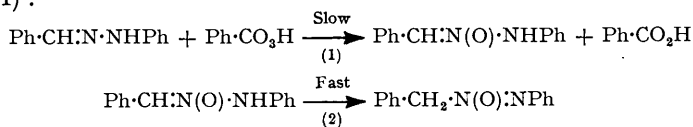
Temp.	20°	25°	35°
$10^3 k$	18·2, 19·2	23·6, 22·8	35·8, 34·8

$k = 5·25 \times 10^3 e^{-7,310/RT}$ mole^{-1} l. sec.$^{-1}$.
$\Delta F\ddagger = 19·7$ kcal., $\Delta S\ddagger = -44·5$ cal. deg.$^{-1}$.
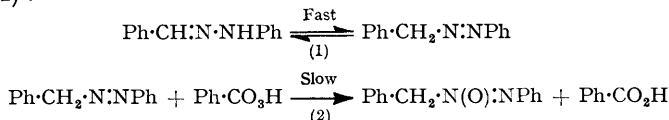
DISCUSSION

Two mechanisms can be postulated which satisfy the observed second-order kinetics :

Mechanism (I) :

$$Ph \cdot CH \colon N \cdot NHPh + Ph \cdot CO_3H \xrightarrow[\text{(1)}]{\text{Slow}} Ph \cdot CH \colon N(O) \cdot NHPh + Ph \cdot CO_2H$$

$$Ph \cdot CH \colon N(O) \cdot NHPh \xrightarrow[\text{(2)}]{\text{Fast}} Ph \cdot CH_2 \cdot N(O) \colon NPh$$

Mechanism (II) :

$$Ph \cdot CH \colon N \cdot NHPh \underset{\text{(1)}}{\overset{\text{Fast}}{\rightleftharpoons}} Ph \cdot CH_2 \cdot N \colon NPh$$

$$Ph \cdot CH_2 \cdot N \colon NPh + Ph \cdot CO_3H \xrightarrow[\text{(2)}]{\text{Slow}} Ph \cdot CH_2 \cdot N(O) \colon NPh + Ph \cdot CO_2H$$

Step (2) of mechanism (I) is analogous to the reversion of an *aci*-nitro-compound to the stable isomer. The intermediate of mechanism (II) has been isolated by several workers (Thiele, *Annalen*, 1910, **376**, 267; Gallagher, *Bull. Soc. chim.*, 1921, **29**, 683; Uemura and Inamura, *Bull. Chem. Soc. Japan*, 1935, **10**, 169) but no quantitative studies of its equilibrium with benzaldehyde phenylhydrazone have been made. The slow step (2) of mechanism (II) involves the oxidation of an azo-compound to the corresponding azoxy-compound by perbenzoic acid, which is known to occur readily with both aliphatic and aromatic azo-compounds (cf. Langley, Lythgoe, and Rayner, *J.*, 1952, 4191; Swern, *Chem. Reviews*, 1949, **45**, 1).

Since the entropy of activation is approximately constant for all the compounds investigated (excepting the nitro-substituted compounds), either the free energies or the heats of activation may be used to interpret the effects of substituents. Although there is not a very large change in the free energies and heats of activation, electron-donating substituents decrease these quantities, whereas electron-accepting substituents increase them. The qualitative effects of substituents are therefore in agreement with the established nature of per-acids as electrophilic reagents (Swern, *loc. cit.*; *J. Amer. Chem. Soc.*, 1947, **69**, 1692; Derbyshire and Waters, *Nature*, 1950, **165**, 401). The effect of substituents is more apparent when the rates of the various substituted compounds (10^3k at 25°) are listed : 4'-OMe (60·6) > 4-OMe (35·5) > 3'-OMe (11·9) > 4'-Me (11·1) > 3-OMe (10·1) > 4-Me (9·8) > 3'-Me (7·0) > 3-Me (6·35) > H (5·1) > 4-Cl (3·6) > 3-Cl (2·4) > 4'-Cl (2·25) > 3-NO$_2$ (1·25) > 3'-Cl (0·91) > 4-NO$_2$ (0·60) > 3'-NO$_2$ (0·47). The 4'-NO$_2$-substituted compound reacted too slowly for measurements to be made. In all cases, the effects of substituents in the Ph·NH ring are more marked than in the Ph·CH ring.

This evidence lends strong support to mechanism (II), in which the former ring is conjugated with the reactive centre, whereas in mechanism (I) this applies to the other ring. Thus the effects of substituents in the Ph·NH ring will be more marked if mechanism (II) is correct. Substituents in the other ring would, of course, exert the same type of overall effect but as it is separated from the reactive centre by a methylene group and is thus not conjugated with the point of attack the effects would be smaller.

The effects of substituents in this reaction are noticeably different from their effects on the autoxidation of benzaldehyde phenylhydrazone (Pausacker, *J.*, 1950, 3478). In the latter case it was found that all substituents in the Ph·CH ring lowered the rate of reaction, whereas the rates of compounds substituted in the Ph·NH ring obeyed Hammett's equation. This is due to the free-radical nature of the autoxidation reaction.

The low values of the frequency factor (10^4—10^6) for the per-acid oxidations lend further support to mechanism (II). It has been shown (cf. Moelwyn-Hughes, " Kinetics of Reactions in Solution," Oxford Univ. Press, 1947, p. 235) that " slow " (*i.e.*, $A < 10^{12}$—10^{13}) reactions may be caused by the fact that an added substance may exist in equilibrium with a very small proportion of another compound which is the actual reacting entity. According to mechanism (II), if the logical assumption is made that the azo-compound has a small equilibrium concentration compared with the hydrazone, then the " slow " nature of the reaction is satisfactorily explained.

With regard to the actual mode of action of perbenzoic acid, it has been assumed (Witkop and Kissman, *loc. cit.*) that attack by a hydroxyl cation is involved, by analogy with the mechanism previously proposed (cf. Swern, " Organic Reactions," Wiley, 1953, Vol. VII, p. 386) for the reaction of olefins with per-acids. Our results show that the entropy of activation of the perbenzoic acid oxidation of benzaldehyde phenylhydrazone is virtually identical in benzene and in diethyl ether. The energy of activation is actually less (and the rate is greater) in benzene solution. If the reaction is ionic this would not be expected, as the more polar diethyl ether would be expected to increase the rate and decrease the activation energy. An alternative mechanism for olefin oxidation has been suggested by Swern (*op. cit.*) but this cannot be applied to our reaction, as once again it is ionic.

We therefore regard perbenzoic acid as acting as an electrophilic, molecular (not ionic) reagent in this particular reaction, *i.e.* :
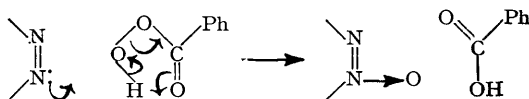
The acid-catalysis noted may be due to protonation of the carbonyl oxygen atom, which facilitates the envisaged electronic shifts. These concepts may profitably be extended to explain the mode of epoxidation of olefins.

The mechanism proposed for the mode of attack of the perbenzoic acid agrees very closely with that recently formulated by Overberger and Cummins (*J. Amer. Chem. Soc.,* 1953, **75**, 4250) for the reaction of perbenzoic acids with 4 : 4'-dichlorobenzyl sulphide.

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