tetramethylcyclobutane, 19206-11-2; 3-methoxytetramethylcyclobutanone, 19203-26-0; 3-methoxytetramethylcyclobutanone tosylhydrazone, 19203-27-1.

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# Kinetic Studies on the Autoxidation of Phenylhydrazones[1]

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Detailed kinetic studies were carried out on the thermally initiated autoxidation of cyclohexanone phenylhydrazone (CHPH) and cyclopentanone phenylhydrazone (CPPH) to their corresponding phenylazoalkane hydroperoxides. The rate of oxidation was measured over the range of 0–35° in four different solvents, *i.e.*, benzene, *n*-heptane, acetone, and methanol. In all solvents, CHPH was oxidized more rapidly than CPPH, reflecting the sterochemistry of the cyclohexane and cyclopentane ring systems at the carbon–nitrogen linkage during the allylic rearrangement of the intermediate free radical which takes place in the autoxidation process. The rate of oxidation of both CHPH and CPPH is more rapid in nonpolar solvents than in polar solvents. A compensation effect was observed with CPPH; it has oxidized more rapidly in benzene than in acetone, but the observed activation energy was less (11.5 *vs.* 7.3 kcal/mol). These results suggest that solvent–phenylhydrazone interaction is greater than solvent–radical interaction.

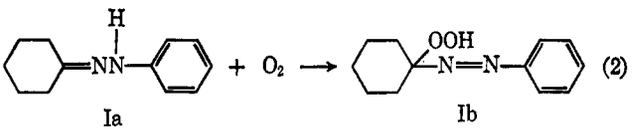
In recent years, studies in these laboratories have been concerned with the oxidation of thiols under a variety of conditions.[2] These studies aroused our interest in an "*in situ*" peroxidation technique for thiols. Phenylhydrazones looked attractive for this purpose since it has been reported that they are readily autoxidized to hydroperoxides.[3–5] A careful examination of the literature disclosed that there is a paucity of data on the mechanism of this reaction. Most studies have been qualitative in nature and have employed either unsubstituted or substituted benzaldehyde phenylhydrazones. Spectroscopic studies have established that the initial oxidation products are unstable phenylazoalkane hydroperoxides.[6–8] In view of this situation, we undertook a detailed study of the kinetics of the thermally initiated autoxidation of both cyclohexanone phenylhydroazone (CHPH) and cyclopentanone phenylhydarzone (CPPH).[9]

## Results

In preliminary experiments the reaction stoichiometry shown below (eq 1) was confirmed by a comparison of

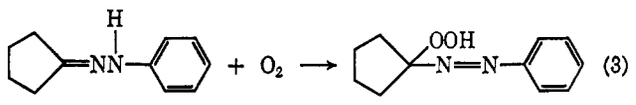
$$PH + O_2 \rightarrow POOH \quad (1)$$

oxygen consumption and phenylhydrazone (PH) disappearance by glpc for a number of runs. Direct evidence for hydroperoxide formation was obtained from the 60-MHz proton spectra of freshly oxidized Ia and IIa in benzene (eq 2 and 3). Both products




(2)

Ia Ib




(3)

IIa IIb

exhibited a diagnostic singlet resonance band at *ca.* $\tau$ 0.1 which is ascribed to the proton of the hydroperoxide group. Similar results were obtained by Bellamy and Guthrie.[6] Accordingly, proton spectroscopy afforded a complementary method for monitoring the formation of hydroperoxide formed from Ia and IIa.

An examination of the rates of oxidation of CPPH and CHPH indicated that the reaction was initially autocatalytic with the rate increasing exponentially with time.[9] As pointed out by Semenov, such initial autoacceleration is typical of many thermal (*i.e.*, noncatalyzed) hydrocarbon oxidations.[10] Initial reaction rates in terms of the moles of PH oxidized per liter per second were obtained from semilogarithmic plots of rate *vs.* time by extrapolating the linear portion of these curves to zero reaction time. The rate of oxidation at "lined-out" conditions was also obtained; however, a comparison of "lined-out" rates and initial rates indicated that both sets of data produced the same directional effects. Initial rates were employed to obtain kinetic parameters because such values can be directly associated with a given phenylhydrazone and oxygen concentration. A study was first made of the effect of phenylhydrazone concentration and oxygen

(1) This work was carried out under U. S. Army Contract No. DA18-035-AMC-330(A) and was monitored by the Chemical Research Laboratory, Edgewood Arsenal, Md.

(2) For recent studies, see (a) T. J. Wallace, and A. Schriesheim, *Tetrahedron*, **21**, 2271 (1965); (b) T. J. Wallace, *J. Org. Chem.*, **31**, 3071 (1966); (c) T. J. Wallace, and A. Schriesheim, *J. Appl. Chem.*, **14**, 48 (1967).

(3) M. Busch, and N. Dietz, *Ber.*, **47**, 3281 (1914).

(4) K. H. Pausacker, *J. Chem. Soc.*, 3478 (1950).

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(6) A. J. Bellamy, and R. D. Guthrie, *J. Chem. Soc.*, 2788 (1965).

(7) G. J. Karabatsos, and R. A. Taller, *J. Amer. Chem. Soc.*, **85**, 3627 (1963).

(8) H. C. Yao, and P. Resnick, *J. Org. Chem.*, **30**, 2832 (1965).

(9) For a preliminary account of part of this work, see W. F. Taylor, H. A. Weiss, and T. J. Wallace, *Chem. Ind.* (London), 1226 (1968).

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TABLE I

EFFECT OF PHENYLHYDRAZONE CONCENTRATION AND OXYGEN PARTIAL PRESSURE ON THE INITIAL RATE OF OXIDATION

| Phenylhydrazone | Initial concn, mol/l. | Initial oxygen pressure, Torr | Relative initial rate at 0° in acetone[a] |
|---|---|---|---|
| CHPH | 0.025 | 830 | 0.45 |
| | 0.050 | 830 | 1.00 |
| | 0.100 | 830 | 2.06 |
| | 0.050 | 660 | 0.76 |
| | 0.050 | 830 | 1.00 |
| | 0.050 | 939 | 1.09 |
| CPPH | 0.025 | 830 | 0.47 |
| | 0.05 | 830 | 1.00 |
| | 0.10 | 830 | 1.94 |
| | 0.050 | 660 | 0.80 |
| | 0.050 | 830 | 1.00 |
| | 0.050 | 939 | 1.10 |

[a] Initial rate at given conditions relative to the initial rate at the standard conditions (0.05 mol/l., 830-Torr $O_2$) for the given phenylhydrazone; the relative rate values cannot be used by themselves to compare the oxidation rates of CHPH and CPPH.

partial pressure on the rate of oxidation. This study was made at 0° in acetone. The CHPH and CPPH concentration was varied from 0.025 to 0.100 mol/l. at a fixed oxygen partial pressure of 830 Torr and the oxygen partial pressure was varied from 660 to 939 torr at a fixed PH concentration of 0.050 mol/l. The results of this study are shown in Table I. An examinination of the data indicates that the initial rate is first order in phenylhydrazone and approximately first order in oxygen partial pressure, although the oxygen dependency appears to be decreasing with increasing oxygen

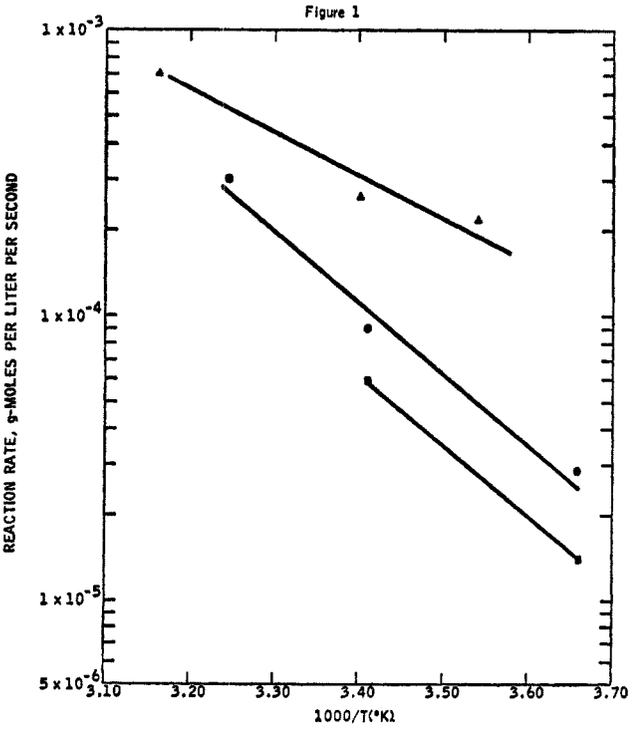



Figure 1.—The temperature dependence of the initial rate of oxidation at an initial concentration of 0.05 mol phenylhydrazone/l. at 830-Torr $O_2$ partial pressure: ▲, cyclohexanone phenylhydrazone in benzene; ●, cyclohexanone phenylhydrazone in acetone; ■, cyclopentanone phenylhydrazone in acetone.

TABLE II

EFFECT OF SOLVENT TYPE ON THE RATE OF PHENYLHYDRAZONE OXIDATION

| Solvent | Initial rate, mol/l./sec × 10⁵[a] CHPH | CPPH |
|---|---|---|
| Methanol | 5.5 | 2.6 |
| Acetone | 11.2 | 6.1 |
| n-heptane | 51.0 | 22.5 |
| benzene | 31.8 | 18.9 |

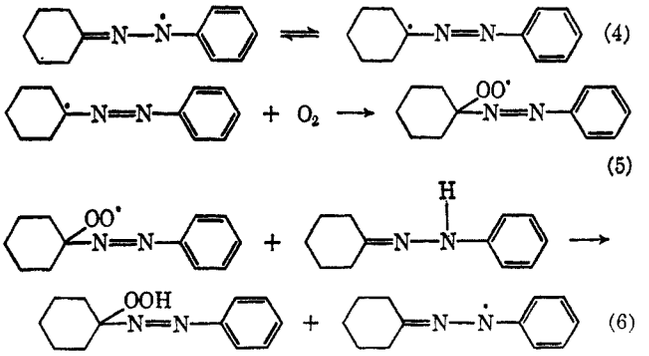
[a] Conditions: 21°, 830-Torr $O_2$ partial pressure, initial phenylhydrazone concentration 0.05 mol/l.

partial pressure, which is typical of many autoxidation reaction processes. The effect of temperature on the initial rate of oxidation was investigated for CHPH and CPPH in acetone and CHPH in benzene at the same PH concentration and oxygen partial pressure. An Arrhenius plot of these initial rates is shown in Figure 1. The temperature dependence of the initial rate of oxidation of CHPH and CPPH in acetone was the same; however, CHPH in benzene exhibited a lower temperature dependence than that observed in acetone. At a given temperature in acetone CHPH was oxidized more rapidly than CPPH. The observed activation energy obtained from the slope of the Arrhenius plots was 11.5 kcal/mol for the oxidation of CHPH and CPPH in acetone and 7.3 kcal/mol for CHPH in benzene.

The effect of solvent type on the initial rate of phenylhydrazone oxidation was investigated at 21° using a phenylhydrazone concentration of 0.05 mol/l. and 830-Torr oxygen partial pressure. Four solvents were employed, *i.e.*, acetone, methanol, *n*-heptane, and benzene. Results are shown in Table II. As shown previously in the acetone solvent system, the initial rate of oxidation of CHPH is faster than that of CPPH in all of the other solvents investigated. Also, the initial rate of oxidation of both CHPH znd CPPH in hydrocarbon media such as heptane and benzene is greater than that observed in the polar solvents (acetone and methanol).

## Discussion

The phenylazoalkane hydroperoxide product (Ib and IIb) observed for the thermal autoxidation of CHPH and CPPH is in agreement with the results obtained by other workers who oxidized various benzaldehyde phenylhydrazones.[4-8] In explaining their results it was assumed that a chain reaction occurred involving radical attack on the N–H bond, followed by allylic shift of the odd electron system as shown in eq 4–6.



As pointed out by Walling,[11] a similar free-radical rearrangement occurs in the autoxidation of tetrahydrocarbazole.

The initial rate of oxidation was much higher in nonpolar solvents than in polar solvents for both CHPH and CPPH. A similar effect of solvent type was observed in semiquantitative studies by Pausacher of the oxidation of benzaldehyde phenylhydrazone[4] and by Bellamy and Guthrie in studies of the oxidation of cyclohexanone phenylhydrazone.[6] In the present work, it can be seen that the solvent affects more than just the rate at a given temperature alone. It exerts an influence on both the rate at a fixed temperature and the activation energy such that a compensation effect results. If one compares the benzene and acetone solvent effects, it can be seen that the highest rate and lowest activation energy occurs in the same solvent. In contrast, as discussed by Huyser,[12] in studies of the effect of solvent on the autoxidation of styrene, cyclohexane, and cumene, the most polar solvents produced the fastest rates of oxidation. Huyzer[12] indicated that complexation of the chain-carrying peroxy radicals by the solvent is probably responsible for the observed solvent effect on rate in these studies. Huyser[13] also discusses the effect of solvent type on a radical-forming reaction. In the decomposition of phenylazotriphenylmethane, the highest rate and lowest activation energy was observed in nonpolar solvents; a compensation effect identical with that observed in the present study. Huyser[13] attributed this effect to the fact that the ground-state azo compound is more strongly solvated by the more polar solvents relative to the nonpolar solvents and that the transition state is not solvated in any of the solvents. These results suggest that the effect of solvent on the present autoxidation reaction system reflects the effect of solvation on the phenylhydrazone itself, rather than on the intermediate phenylazoalkyl peroxy radical.

CHPH was oxidized more rapidly than CPPH in all solvents studied. This effect reflects the stereochemistry of the cyclohexane and cyclopentane ring systems.[14] In both the CHPH and CPPH systems, autoxidation produces a free radical which rearranges and changes the hybridization at the carbon–nitrogen linkage from $sp^2$ (planar) to $sp^3$ (tetrahedral). In the cyclopentane system, $sp^2$ hybridzation at the carbon–nitrogen linkage is favored over $sp^3$, since it reduces the amount of nonbonded interaction and internal strain in the five-membered ring. By contrast to the cyclopentane system, in the cyclohexane system, nonbonded interaction and internal ring strain are decreased when hybridization at the carbon–nitrogen linkage changes from $sp^2$ to $sp^3$.

(11) C. Walling, "Free Radicals in Solution," John Wiley & Sons, Inc., New York, N. Y., 1957, p 416.

(12) E. S. Huyser, in "Advances In Free Radical Chemistry," Vol. I, Academic Press, 1965, p 119 ff.

(13) Reference 12, p 129 ff.

(14) For a specific discussion, see (a) H. D. Orloff, *Chem. Rev.*, **54**, 347 (1954); (b) V. Prelog, *J. Chem. Soc.*, 420 (1950).

## Experimental

**Reagents.**—Cyclohexanone phenylhydrazone and cyclopentanone phenylhydrazone were prepared by conventional methods in a nitrogen drybox and recrystallized twice from degassed ethanol–water solutions. Melting points were in agreement with published values. The phenylhydrazones were stored under nitrogen prior to use. Stock solutions of the phenylhydrazones were prepared in the nitrogen drybox from degassed spectroquality and chromatoquality grade solvents and were used immediately after preparation.

**Oxidation Apparatus and Procedure.**—The oxidation system consisted of a reaction vessel connected to a Hg manometer. The reaction vessel was a 500-ml round-bottomed flask equipped with a paddle stirrer, thermometer, and serum cap. Oxygen uptake was monitored by use of the Hg manometer. A 100-ml round-bottomed flask was used in series to serve as a ballast flask. A stopcock manifold allowed the introduction of oxygen and vacuum. In a typical run, the solvent was placed in the reaction flask, evacuated, and flushed with oxygen three times. Oxygen was added to the desired pressure. A stock solution (0.5 *M*) of the phenylhydrazone in the same solvent was prepared in a nitrogen drybox. An aliquot was withdrawn and transferred to the reaction flask to give a 0.05 *M* phenylhydrazone solution. Oxygen consumption was measured by the Hg manometer. The reaction vessel was surrounded by a constant-temperature bath. Stirring rates were maintained well above those for diffusion controlled conditions. The reaction mixture was sampled by inserting a Hamilton microliter syringe through the serum cap and withdrawing liquid with the syringe. This was immediately analyzed by glpc.

**Analytical Instruments and Procedures.**—Phenylhydrazone disappearance was followed by glpc using an F & M Model 609 chromatograph equipped with a recorder and a 2-ft 10% silicone rubber on Chromosorb P column, operated at 125° using helium as the carrier gas. N-Hexadecane was used as an internal standard. Peak areas were corrected by relative response factors.

**Nmr Analyses.**—Samples for nmr studies were prepared as concentrated solutions in a $N_2$ drybox using degassed benzene. The phenylhydrazones were oxidized by bubbling oxygen through the solutions and analyzed immediately. Spectra were recorded on a Varian A-60 spectrometer at ambient temperature. Tetramethylsilane was used as an internal standard.

**Registry No.**—CHPH, 946-82-7; CPPH, 1132-58-7.

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