Oxidation of Substituted Hydrazines by Superoxide Ion: The Initiation Step for the Autoxidation of 1,2-Diphenylhydrazine

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Abstract: Superoxide ion ($O_2^{-}\cdot$) in aprotic media and in the gas phase reacts with 1,2-disubstituted hydrazines to produce the anion radical of the 1,2-disubstituted azo compound. The latter species, upon exposure to molecular oxygen, is rapidly and cleanly oxidized to the pure azo compound. This combination of reactions represents a superoxide-catalyzed autoxidation; for 10 mM 1,2-diphenylhydrazine and O_2 at 1 atm in dimethyl sulfoxide catalytic turnover numbers in excess of 200 are observed. The reaction cycle parallels the *xanthine oxidase* catalyzed autoxidation of reduced flavin/xanthine, which produces H_2O_2 and fractional quantities of $O_2^{-}\cdot$. Monosubstituted hydrazines (e.g., $PhNHNH_2$) are oxidized by $O_2^{-}\cdot$ with a one-to-two stoichiometry; $PhNHNH_2 + 2O_2^{-}\cdot \rightarrow PhH + N_2 + 2HO_2^{-}$. Mechanisms are proposed for the $O_2^{-}\cdot$/hydrazine oxidation processes and for the $O_2^{-}\cdot$-induced autoxidation of 1,2-disubstituted hydrazines.

The oxidation of substituted hydrazines by superoxide ion ($O_2^{-}\cdot$) has been reported previously—either by a direct chemical observation[1,2] or by inference in biological systems.[3-7] However, the studies were limited to the qualitative indentification of products and to speculation as to the reaction mechanism. The nature of this chemistry is important because of its potential relevance to the hemolytic effects of hydrazines.[3,5] Physiological studies have shown that the reaction of phenylhydrazine with hemoglobin is oxygen dependent, with hydrogen peroxide the major product.[4] This has prompted speculation that oxygen radicals, particularly superoxide ion, are involved in the reaction and may be responsible for the toxicity of substituted hydrazine.[3-7] As part of a detailed investigation of the reaction of $O_2^{-}\cdot$ with activated secondary amines, a series of substituted hydrazines have been studied under carefully controlled conditions in aprotic solvents as well as in the gas phase.

Experimental Section

Equipment. Conventional electrochemical instrumentation, cells, and electrodes were employed for the cyclic-voltammetric and controlled-potential coulometric measurements.[8] A Pine Instruments Co. Model RDE 3 dual potentiostat, Model PIR rotator, and glassy carbon ring–disc electrode were used to make the kinetic measurements.[9]

Product species that contained an aromatic ring were identified by use of an Altex Model 330 isocratic liquid chromatograph with UV detection at 254 nm; the 250-nm × 4.6mm stainless-steel column was packed with 10-μm Merck Lichrosorb RP-2. The more volatile reaction products were separated and identified with a Hewlett Packard Model 5880 GC that was equipped with a 12.5-m glass capillary column and by mass spectrometry. A Vacuum Atmosphere Corp. inert atmosphere glovebox was used for the storage and preparation of solutions of tetramethylammonium superoxide.

Cary Model 17D and 219 spectrophotometers were used for the UV–vis spectrophotometric measurements, and ESR spectra were recorded with a Bruker Model ESR 200 X-band spectrometer. A Nicolet Analytical Instrument FTMS-1000 Fourier transform mass spectrometer with a 3.0 T super-conducting magnet and a 2.54-cm × 2.54-cm × 7.62-cm trapped-ion cell was used for the study of gas-phase ion–molecule reactions.

Chemicals and Reagents. Burdick and Jackson "distilled in glass" UV grade solvents were used as received for most of the experiments. When necessary, acetonitrile was further dried by passing it through a column of Woelm N Super I alumina. Tetraethylammonium perchlorate (TEAP) from G. Frederick Smith Chemical Co. was dried in vacuo and used as the supporting electrolyte (0.1 M TEAP) in the electrochemical experiments. Other reagents and substrates were analytical grade or highest purity available and were used without further purification.

Methods. Controlled-potential electrolytic reduction of O_2 (1 atm) at a platinum-mesh electrode was used to prepare solutions of $O_2^{-}\cdot$. The residual dioxygen was removed by bubbling with argon, and the concentration of $O_2^{-}\cdot$ was determined by anodic linear-sweep voltammetry. To such solutions a quantity of substrate was added, which, on the basis of five or more trials, was sufficient to consume about 80% of the $O_2^{-}\cdot$. The unreacted $O_2^{-}\cdot$ concentration was again measured by anodic voltammetry. These data provided a measure of the stoichiometry for the reaction of $O_2^{-}\cdot$ with substrate.

Measurements of the rate of the reaction of superoxide ion with various substrates were made with a rotated glassy carbon ring–disc electrode. The pseudo-first-order rate constants (k_1) were determined by the method that is described in a recent study of $O_2^{-}\cdot/RCCl_3$ reactions[9] and is developed in detail by Albery and Hitchman.[10]

The reaction products from the stoichiometric combination of $O_2^{-}\cdot$ and substrate (at millimolar concentrations) were characterized by GC, HPLC, and mass spectrometry. Solutions of $O_2^{-}\cdot$ were prepared either by controlled-potential electrolysis of O_2 (1 atm) or by dissolution of weighed amounts of tetramethylammonium superoxide $[(Me_4N)O_2]$.[11] The head space for a product solution from the stoichiometric combination of $(Me_4N)O_2$ with a solution of substrate was analyzed by use of a vacuum line to collect a sample for mass spectrometry. Aliquots (10 or 20 mL) of reaction product solutions were assayed for hydrogen peroxide by dilution with 60–80 mL of water that contained 3% KI and 0.1 M HNO_3 and titration with thiosulfate.[12]

The product from the one-to-one combination of 1,2-diphenylhydrazine and $(Me_4N)O_2$ in MeCN was prepared in a glovebox prior to its characterization by UV–vis and ESR spectroscopy. Azobenzene in acetonitrile was reduced in a glovebox by controlled-potential coulometry to produce its anion radical.

Superoxide ion for the gas-phase ion–molecule reactions was produced from O_2 ($P = 4\text{–}5 \times 10^{-7}$ torr) with a 100-ms beam of −5.5-eV electrons. Trapping-plate potentials were −1 to −2 V. The trapped electrons were ejected by the application of a 5.1 MHz radio frequency excitation to one of the trap plates for 1–2 ms. All ions formed by electron impact (except $O_2^{-}\cdot$) were ejected from the cell. A variable delay was used to allow the $O_2^{-}\cdot$ ions to react with the neutral substrate molecules; the anionic products of the reaction were detected by Fourier transform mass spectrometry (FT–MS).[13]

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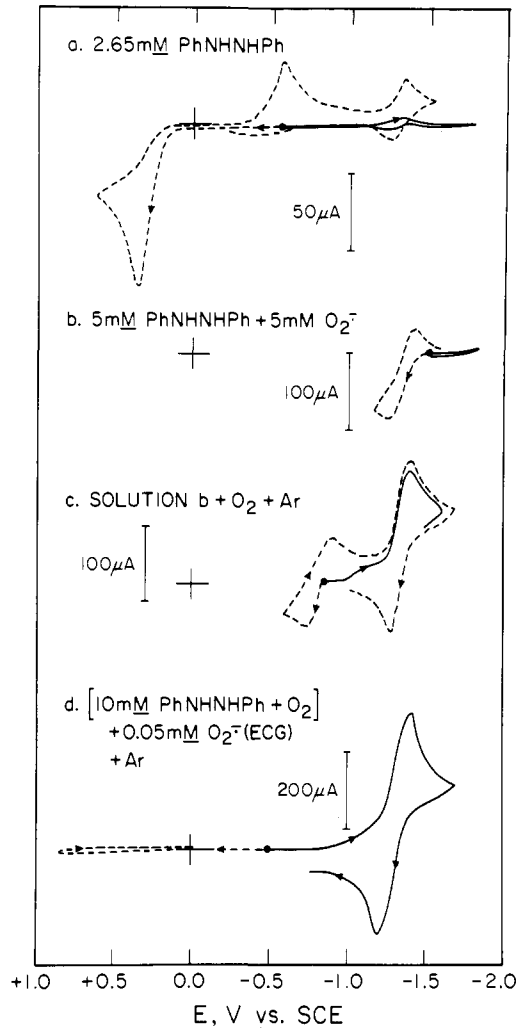

Figure 1. Cyclic voltammograms in dimethyl sulfoxide (0.1 M tetraethylammonium perchlorate) for (a) 1,2-diphenylhydrazine (PhNHNHPh), (b) an equimolar mixture of PhNHNHPh and $O_2^{-}\cdot$ (electrogenerated) in an argon atmosphere, (c) solution b after exposure to O_2 (1 atm) for 3 min followed by a 5-min purge with argon, and (d) 10 mM PhNHNHPh in an O_2 (1 atm)-saturated solution after the in situ electrogeneration of 0.05 mM $O_2^{-}\cdot$ (1 min) followed by a 5-min purge with argon. Measurements were made with a platinum electrode (area, 0.23 cm^2) at a scan rate of 0.1 V s^{-1}.

Hydroxide ion was produced from H_2O molecules ($P = 1-4 \times 10^{-7}$ torr) by a 100-ms beam of −5.5-eV electrons. The substituted hydrazines were introduced via a direct insertion probe to give sample pressures of $0.5-1.0 \times 10^{-7}$ torr.

Results

When superoxide ion ($O_2^{-}\cdot$) is added to aprotic solutions of substituted hydrazines, those that contain one or more secondary amine functions are rapidly oxidized. Figure 1 illustrates that cyclic voltammetry provides a convenient means to monitor such reactions and to characterize the redox chemistry of the hydrazine substrates and their oxidation products. The results of such studies for a series of substituted hydrazines are summarized in Table I. The reactant and product stoichiometries have been determined by electrochemically monitored $O_2^{-}\cdot$-substrate titrations and by quantitative characterization of the product solutions by cyclic voltammetry, UV–vis spectroscopy, ESR spectroscopy, gas chromatography, mass spectrometry, and iodide–thiosulfate titrations for H_2O_2/HO_2^{-}.

Because the results of Figure 1 and Table I indicate that hydrazine oxidation of $O_2^{-}\cdot$ occurs via secondary amine hydrogens, the oxidation–reduction potentials for this group of substituted hydrazines as well as for several primary and secondary amines have been evaluated by cyclic voltammetry. The latter group includes redox data for dihydrophenazine[14] and dihydro-3-methyllumiflavin,[15] which are models for reduced flavoproteins.

Table I. Stoichiometries[a] and Kinetics for the Reaction of 0.1–5.0 mM $O_2^{-}\cdot$ with Substituted Hydrazines in Dimethyl Sulfoxide (0.1 M Tetraethylammonium Perchlorate) at 25 °C

substrate (S), 1–10 mM	$O_2^{-}\cdot$ per S	H_2O_2/HO_2^{-} formed per S	primary product	k_1/(S), M^{-1} s^{-1}
PhNHNHPh	1.0 ± 0.1	1.0 ± 0.3	$PhN^{-}\cdot NPh$	>100
MeNHNHMe	1.0 ± 0.1	1.0 ± 0.3	$MeN^{-}\cdot NMe$	>30
$PhNHNH_2$	2.0 ± 0.1	2.0 ± 0.5	PhH, N_2	110 ± 10
$MeNHNH_2$	2.0 ± 0.2	2.0 ± 0.5	CH_4, N_2	16 ± 2
Ph_2NNH_2	NR			<0.01
Me_2NNH_2	NR			<0.01

[a] Reaction stoichiometries determined by incremental titration with substrate of a known amount of $O_2^{-}\cdot$ (~4 mM, electrosynthesized); the residual $O_2^{-}\cdot$ was determined by positive-scan voltammetry.

Table II. Redox Potentials for Substituted Hydrazines and Amines in Acetonitrile (0.1 M TEAP).

substrate	$E_{p,c}$, V vs. SCE	$E_{p,a}$, V vs. SCE: amine	$E_{p,a}$, V vs. SCE: amine anion[a]
	A. Hydrazines		
PhNHNHPh	−1.8	+0.6	−1.1
MeNHNHMe	−2.1	+0.1	−0.8
$PhNHNH_2$	−1.9	+0.4	−0.6
Ph_2NNH_2	−2.3	+0.5	
Me_2NNH_2	>−2.4	+0.3	
	B. Amines		
Ph_2NH	−2.1	+0.9	−0.3
$PhNH_2$	−2.2	+0.9	
indole[b,c]	−1.8	+1.2	0.0
pyrrole[d]	−1.9	+1.3	0.0
imidazole[b,e]	−1.9	+1.0	+0.3
benzimidazole[b,f]	−1.5	+1.9	+0.7
dihydrophenazine[g]		+0.1	−1.1
dihydro-3-methyllumiflavin[h]		−0.1	−0.8

[a] Produced by the stoichiometric addition of tetraethylammonium hydroxide. [b] Deprotonated by $O_2^{-}\cdot$ to form amine anion.

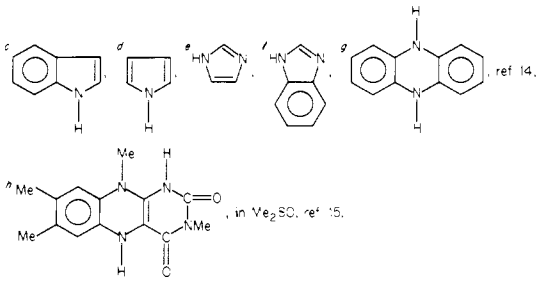

Table II summarizes for this group of substrates (a) their reduction potentials, which provide a relative measure of the acidity for the amine protons (pK_a increases as the peak potential becomes more negative), (b) their oxidation potentials, which provide a measure of the relative ease of a one-electron N–H hydrogen oxidation, and (c) the oxidation potentials for their anions (produced by the stoichiometric addition of OH^{-}), which also provide a measure of the relative ease of a one-electron oxidation. Those substrates without a secondary amine function do not yield anions upon addition of OH^{-}. Likewise, the anions of hydrazines with a second secondary-amine hydrogen (1,2-diphenyl- and 1,2-dimethylhydrazine) are more easily oxidized (to anion radicals) than are the anions of monosubstituted hydrazines (oxidized to neutral radicals). Secondary amines such as indole and imidazole (but not pyrrole or diphenylamine) are deprotonated by superoxide ion in acetonitrile.

1,2-Diphenylhydrazine is oxidized at +0.45 V vs. SCE by an overall two-electron process to give azobenzene (Figure 1a). When the positive scan is reversed, reduction peaks at −0.55 V (due to the two protons from the oxidation of PhNHNHPh) and at −1.4 V (due to azobenzene)[16] are observed; the latter produces the anion radical of azobenzene [equivalent to the product of the $O_2^{-}\cdot$ PhNHNHPh reaction (Figure 1b)].

1,2-Diphenylhydrazine. As shown by Figure 1 and Table I, a 1:1 combination of 1,2-diphenylhydrazine and $O_2^{-}\cdot$ yields a product that has the electrochemical characteristics of the anion radical of azobenzene. The UV–vis spectrum (Figure 2) and the ESR

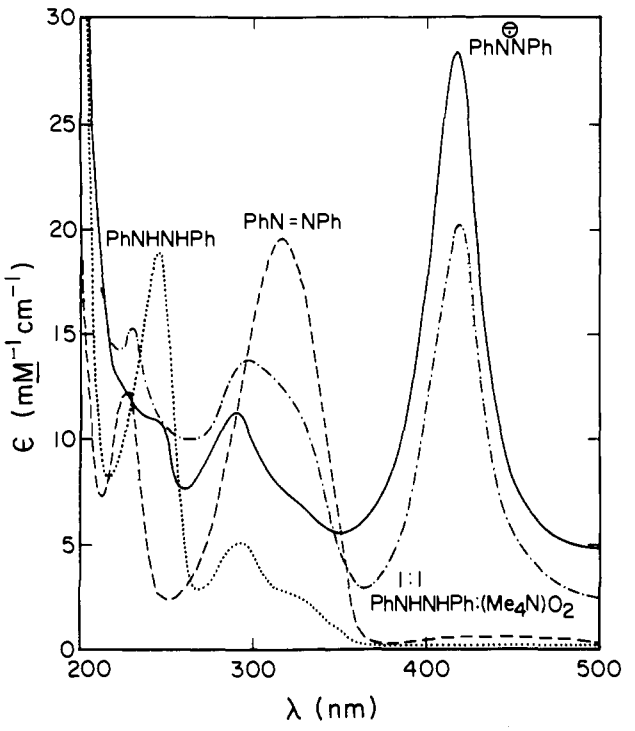

Figure 2. UV–vis absorption spectra in MeCN for 5 mM 1,2-diphenylhydrazine (PhNHNHPh), 5 mM azobenzene (PhN=NPh), 5 mM PhN⁻·NPh (from the one-electron controlled-potential electrolytic reduction of 5 mM PhN=NPh), and the product solution from the 1:1 combination of PhNHNHPh and $(Me_4N)O_2$ (each 5 mM before reaction). The latter spectrum is normalized with respect to ϵ on the assumption that a single 5 mM product species is formed.

spectrum (Figure 3) for the product species are identical with those for the anion radical of azobenzene (produced by the coulometric one-electron reduction of azobenzene).

The rates of reactions for $O_2^{-}\cdot$ with 1,2-diphenylhydrazine and the other substituted hydrazines have been determined by the rotated ring–disc technique (O_2 is reduced at the disc to $O_2^{-}\cdot$, which reacts with substrate, and the unreacted $O_2^{-}\cdot$ is oxidized at the ring electrode),[9,10] and the normalized pseudo-first-order rate constants are tabulated in Table I. Because the anion radical products from the $O_2^{-}\cdot$/1,2-disubstituted hydrazine process react with the residual O_2 in the reaction cell to give $O_2^{-}\cdot$ (see below), the observed rate constants represent lower limits.

When dioxygen is introduced into the reaction vessel after the one-to-one combination of $O_2^{-}\cdot$ and PhNHNHPh, the anion radical (PhN⁻·NPh) reacts rapidly and stoichiometrically to give azobenzene (PhN=NPh) and $O_2^{-}\cdot$ (Figure 1c).[17] Although 100% of the original PhNHNHPh is converted to PhN=NPh (>95% trans), only 40% of the $O_2^{-}\cdot$ from O_2 reduction is recovered (anodic peak, Figure 1c). This loss is due to trace water and H_2O_2 in the media, which induces the disproportionation of $O_2^{-}\cdot$.[18]

Addition of small quantities of $O_2^{-}\cdot$ (0.1–1.0 mM KO_2 in Me_2SO, 0.1–1.0 mM $(Me_4N)O_2$ in MeCN or DMF, or electrogenerated $O_2^{-}\cdot$ in Me_2SO or DMF) to 10 mM PhNHNHPh in O_2-saturated solutions results in the complete oxidation of the PhNHNHPh to azobenzene. When the $O_2^{-}\cdot$ is generated in situ by electrolysis, turnover numbers greater than 200 have been obtained for the oxidation of PhNHNHPh in Me_2SO (Figure 1d) and DMF. Similar results are obtained for $O_2^{-}\cdot$-induced autoxidation of 1,2-dimethylhydrazine.

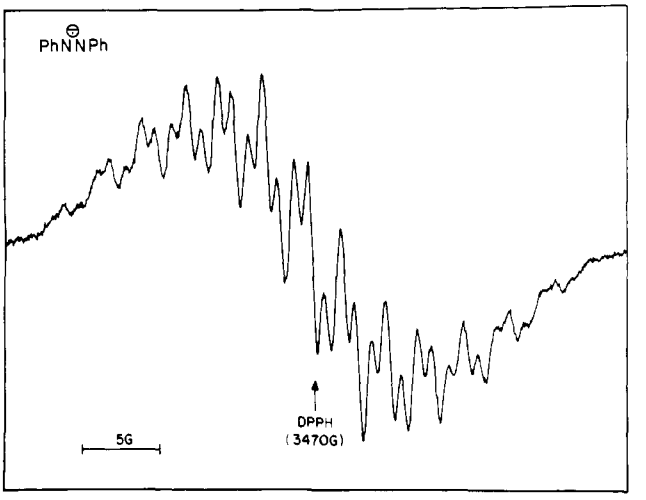

Figure 3. ESR spectrum at 77 K for the product species (10 mM) from the 1:1 combination of PhNHNHPh with $O_2^{-}\cdot$ $[(Me_4N)O_2]$ in MeCN. This spectrum is identical with that for the product (PhN⁻·NPH) from the one-electron controlled-potential electrolytic reduction of 10 mM PhN=NPh.

The addition of small amounts of tetraethylammonium hydroxide (0.5 mM) to an oxygen-saturated (~8 mM) solution of PhNHNHPh (5 mM) in acetonitrile also induces its rapid autoxidation. The process yields one azobenzene and one H_2O_2 per PhNHNHPh.

Phenylhydrazine. Superoxide ion reacts with phenylhydrazine (and other monosubstituted hydrazines) via a two-to-one stoichiometry in O_2-free aprotic solvents to give benzene (methane from methylhydrazine), nitrogen, and two peroxide ions as products (Table I). The stoichiometry of two $O_2^{-}\cdot$ per monosubstituted hydrazine is reproducible and independent of which reagent is in excess. With the $O_2^{-}\cdot$/phenylhydrazine reaction, benzene is the major product and there is no detectable aniline or phenol, but a small amount (<5%) of biphenyl is produced. Analysis of the headspace of the reaction cell confirms that the only volatile nitrogen-containing product is dinitrogen and that O_2 is not produced in the reaction. Spin-trapping experiments with DMPO indicate that some phenyl radical is produced as an intermediate.

If the reaction $O_2^{-}\cdot$ with monosubstituted hydrazines is carried out in the presence of O_2 at 1 atm, then the 2:1 stoichiometry changes to 0.3-to-0.8 $O_2^{-}\cdot$ per hydrazine.

The 1,1-disubstituted hydrazines do not react with superoxide ion within the lifetime of our experiments (10–15 min).

Gas-Phase Ion–Molecule Reactions. Figure 4 illustrates that both $O_2^{-}\cdot$ and ^{-}OH react rapidly with 1,2-diphenylhydrazine in the gas phase (P, $\sim 1 \times 10^{-7}$ torr) to give the anion radical of azobenzene (PhN⁻·NPh, m/e^{-} 182) and its anion (PhN⁻NHPh, m/e^{-} 183), respectively. When $O_2^{-}\cdot$ is ejected from the experiment, the 182 peak disappears. In contrast to the exponential decay that is observed for the OH^{-} peak with time (Figure 4b), the ion current for $O_2^{-}\cdot$ decays to a steady-state concentration. Apparently, the PhN⁻·NPh product reacts with residual O_2 to give $O_2^{-}\cdot$ and azobenzene in a process that is analogous to the $O_2^{-}\cdot$-induced autoxidation in MeCN solutions (Figure 1d). The $O_2^{-}\cdot$/PhNHNHPh process does not produce any other detectable anionic products.

The appearance of a peak at m/e^{-} 92 from the ^{-}OH/PhNHNHPh reaction indicates that the ^{-}OH ion is not completely thermalized after formation from H_2O. Hence, it is able to cause some N–N bond breakage in the PhN⁻NHPh anion after the collisional energy transfer that accompanies proton abstraction. When ^{-}OH is ejected from the experiment, both peaks (183 and 92) disappear.

The combination of $O_2^{-}\cdot$ and phenylhydrazine ($PhNHNH_2$) in the gas phase ($P = \sim 1 \times 10^{-7}$ torr) yields anions with m/e^{-} values of 106 (PhN⁻·NH), 107 (PhN⁻NH_2), and 77 (Ph^{-}). Al-

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(15) Sawyer, D. T.; Komai, R. Y.; McCreery, R. L. *Experientia, Suppl.* **1971**, *18*, 563.
(16) Sadler, J. L.; Bard, A. J. *J. Am. Chem. Soc.* **1968**, *90*, 1979.
(17) The UV–vis (Figure 2) and ESR (Figure 3) spectra from the 1:1 combination of PhNHNHPh and $O_2^{-}\cdot$ are identical with those for the one-electron reduction of azobenzene by controlled-potential electrolysis. Similar results are observed for the $O_2^{-}\cdot$/1,2-dimethylhydrazine system.
(18) Sawyer, D. T.; Valentine, J. S.; *Acc. Chem. Res.* **1981**, *14*, 393.

though $PhNNNH_2$ that is produced by simple H-atom transfer cannot be detected, the absence of a product peak at m/e^- 33 (HO_2^-) indicates that this is an unfavored process. Ejection of $O_2^{-}\cdot$ from the experiment causes the 106 and 77 peaks to disappear and the 107 peak to lose 70% of its intensity. Ejection of the m/e^- ion during the experiment causes a substantial decrease in the intensity for the m/e^- 77 ion.

The reaction of ^-OH with $PhNHNH_2$ yields an m/e^- 107 ion (PhN^-NH_2) as the major product plus small amounts of m/e^- 92 and 93 ions. Experiments with methylhydrazine, 1,1-dimethylhydrazine, and 1,1-diphenylhydrazine indicate that they do not react to a significant extent with either $O_2^{-}\cdot$ or ^-OH in the gas phase.

Discussion and Conclusions

The results that are summarized in Table I and Figures 1 and 3 confirm that $O_2^{-}\cdot$ oxidizes 1,2-diphenylhydrazine to the anion radical of azobenzene ($PhN^{-}\cdot NPh$)

$$PhNHNHPh + O_2^{-}\cdot \xrightarrow{k_{bi} > 100\ M^{-1}\ s^{-1}} PhN^{-}\cdot\text{–}NPh + H_2O_2 \quad (1)$$

The results of Figure 2 indicate that the product species from a stoichiometric combination of PhNHNHPh and $O_2^{-}\cdot$ (and in the absence of excess base) undergo partial proton transfer and disproportionation

$$PhN^{-}\cdot NPh + H_2O_2 \rightleftarrows PhN\dot{N}HPh + HO_2^- \rightarrow (1/2)PhN{=}NPh + (1/2)PhNHNHPh \quad (2)$$

The facility of the $O_2^{-}\cdot$/PhNHNHPh reaction, the absence of byproducts or intermediates in both the condensed-phase and gas-phase experiments, and the unit stoichiometric coefficients for reactants and products are consistent with a primary process that involves the concerted transfer from PhNHNHPh to $O_2^{-}\cdot$ of a proton and a hydrogen atom. In particular, the absence of any other ions in the gas-phase experiment (Figure 4) requires either a concerted H^+–$H\cdot$ transfer or a rapid two-step sequence within the reaction complex with zero leakage of intermediates. Such a concerted mechanism has been proposed for the oxidation of ascorbic acid by $O_2^{-}\cdot$.[19] From a consideration of the necessary energetics, the $O_2^{-}\cdot$ species needs to become protonated (in a concerted or sequential process) to become an effective hydrogen-atom (1,2-disubstituted hydrazines) or one-electron oxidant (mono-substituted hydrazines). The gas-phase data indicate that ^-OH is an effective base for proton removal from PhNHNHPh.

When dioxygen is introduced into the reaction vessel after the one-to-one combination of $O_2^{-}\cdot$ and PhNHNHPh, the anion radical product ($PhN^{-}\cdot$–NPh) reacts rapidly and stoichiometrically to give azobenzene (PhN=NPh) and $O_2^{-}\cdot$ (eq 3, Figure 1c).

$$PhN^{-}\cdot\text{–}NPh + O_2 \xrightarrow{\text{fast}} PhN{=}NPh + O_2^{-}\cdot \quad (3)$$

Because the redox potentials for $PhN^{-}\cdot$–NPh and O_2 are –1.3 V vs. SCE (Figure 1) and –0.75 V,[18] respectively, this represents a favored (exothermic) one-electron transfer reaction. Combination of eq 1 and eq 3 yields the overall stoichiometric process (eq 4), one in which there is no net consumption of superoxide ion.

$$PhNHNHPh + O_2 \xrightarrow{O_2^{-}\cdot} PhN{=}NPh + H_2O_2 \quad (4)$$

The reaction of eq 4 indicates that the overall process is equivalent to a superoxide ion-catalyzed autoxidation. Experimental proof for this proposition is provided by the results from the addition of catalytic quantities of $O_2^{-}\cdot$ to PhNHNHPh in O_2-saturated solutions [turnover numbers from 25 to 200 (Figure 1d)].

1,2-Dimethylhydrazine also exhibits one-to-one reaction stoichiometry with $O_2^{-}\cdot$ (equivalent to the process of eq 1) and is catalytically autoxidized to azomethane (eq 5).[17]

$$CH_3NHNHCH_3 + O_2 \xrightarrow{O_2^{-}\cdot} CH_3N{=}NCH_3 + H_2O_2 \quad (5)$$

The hydroxide ion induced autoxidation of PhNHNHPh that is noted in the Results section appears to be initiated by abstraction of a proton

$$PhNHNHPh + OH^- \rightarrow PhN^{-}NHPh \quad (6)$$

In turn, the hydrazine anion reacts with the dissolved O_2 to give HO_2^-

$$PhN^{-}NHPh + O_2 \rightarrow PhN{=}NPh + HO_2^- \quad (7)$$

which, in the presence of another OH^-, undergoes a partial conproportionation with O_2

$$HO_2^- + O_2 \xrightleftharpoons{OH^-} 2\,O_2^{-}\cdot + H_2O \quad (8)$$

The resultant $O_2^{-}\cdot$ induces the further autoxidation of PhNHNHPh via reactions 1 and 3.

Monosubstituted Hydrazines. The overall reaction stoichiometry and products from the combination of $O_2^{-}\cdot$ and phenylhydrazine ($PhNHNH_2$) in Me_2SO are represented by eq 9 (Table I).

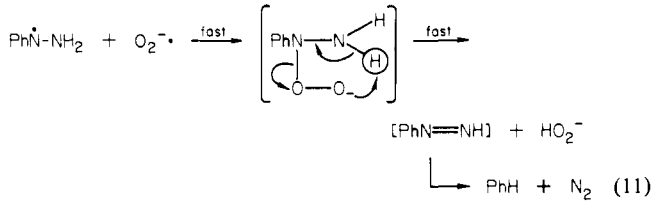
$$PhNHNH_2 + 2O_2^{-}\cdot \rightarrow PhH + N_2 + 2HO_2^- \quad (9)$$

Because half of the $PhNHNH_2$ remains unreacted from a 1:1 $O_2^{-}\cdot$/$PhNHNH_2$ combination, the primary step must be rate limiting and followed by a rapid step that consumes a second $O_2^{-}\cdot$. Second-order kinetics are observed by the rotated ring–disk voltammetric experiment,[9] and molecular oxygen is not detected during the course of the process or as a product.

A reasonable reaction sequence that is consistent with the experimental results has H-atom abstraction by $O_2^{-}\cdot$ as the primary rate-limiting step (eq 10), followed by rapid coupling of the radical

$$PhNHNH_2 + O_2^{-}\cdot \rightarrow PhN\dot{N}H_2 + HO_2^- \quad (10)$$

product with a second $O_2^{-}\cdot$ and degradation to the final products (eq 11).[14] Attempts to detect phenyldiazene (PhN=NH) as an



(11)

intermediate were unsuccessful, although it is a moderately stable species.[20] The limited yield of biphenyl (<5%), the trace amounts of trapped phenyl radical, and the absence of oxygenated phenyl products are consistent with the reaction sequence of eq 10 and 11, and with the reaction intermediate of eq 11. The reaction of $O_2^{-}\cdot$ with methylhydrazine is analogous to that for phenylhydrazine with methane the major product (k_{bi} = 16 M^{-1} s^{-1}). The slower rate is consistent with the enhanced stabilization of radical intermediates by aromatic substituents.

Unsymmetrical disubstituted hydrazines (1,1-diphenylhydrazine and 1,1-dimethylhydrazine) do not exhibit a detectable reaction with $O_2^{-}\cdot$ in the gas phase nor in Me_2SO within approximately 10 min. This is consistent with the hypothesis that only those substituted hydrazines with a secondary amine function react with $O_2^{-}\cdot$ by hydrogen-atom transfer. Although there is a report[2] that 1,1-diphenylhydrazine reacts with superoxide to produce *N*-nitrosodiphenylamine, such a product is more consistent with a peroxide reaction (a likely possibility for the reaction conditions).

Previous work[1] has demonstrated that $O_2^{-}\cdot$ oxidizes dihydrophenazine and dihydro-3-methyllumiflavin. Although this earlier study was conducted in the presence of oxygen, the primary process must be analogous to that for PhNHNHPh (eq 1) to give the anion

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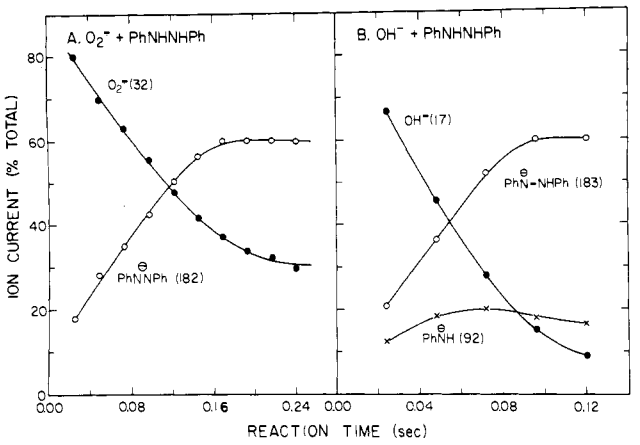

Figure 4. Time-resolved mass spectral intensities for the anions that result from the gas-phase reaction of 1,2-diphenylhydrazine with (A) $O_2^{\cdot-}$ and (B) ^-OH.

radicals of phenazine ($Phen^{\cdot-}$) and 3-methyllumiflvanin (3-$MeFl^{\cdot-}$). These must in turn react with O_2 to give $O_2^{\cdot-}$ plus phenazine and 3-methyllumiflavin, respectively; the process is analogous to that for the anion radical of azobenzene ($PhN^{\cdot-}NPh$, eq 3). The oxidation potentials ($E_{p,a}$) for $PhN^{\cdot-}NPh$ (Figure 1), $Phen^{\cdot-}$,[13] and 3-$MeFl^{\cdot-}$[13] in Me_2SO are −1.3 V vs. SCE, −1.1 V, and −0.8 V, respectively. Each value is sufficiently negative to reduce O_2 to $O_2^{\cdot-}$ (−0.7 V vs. SCE in Me_2SO).[18] Hence, the $O_2^{\cdot-}$-induced autoxidation of PhNHNHPh (eq 4) also is thermodynamically feasible for dihydrophenazine and dihydro-3-methyllumiflavin. The previous results[1] confirm that the sequence of eq 1 and 3 does occur for these two model substrates of reduced flavoproteins. Such an autoxidation reaction sequence may be relevant to the fractional yield of $O_2^{\cdot-}$ from the flavin-mediated activation of O_2[21] and the autoxidation of xanthine (catalyzed by xanthine oxidase (X.O.), a flavoprotein).[22]

(22) McCord, J. M.; Fridovich, I. *J. Biol. Chem.* **1968**, *243*, 5753.

$$Fl + H_2Sub \xrightarrow{X.O} H_2Fl + Sub \quad (12)$$

$$H_2Fl + Fl \overset{OH^-}{\rightleftharpoons} 2Fl^{\cdot-} + 2H_2O \quad (13)$$

$$Fl^{\cdot-} + O_2 \rightarrow Fl + O_2^{\cdot-} \quad (14)$$

$$H_2Fl + O_2^{\cdot-} \rightarrow Fl^{\cdot-} + H_2O_2 \quad (15)$$

Perhaps the most significant aspect of the superoxide-, hydroxide-, or electron-induced autoxidation of donor molecules (1,2-diphenylhydrazine, dihydrophenazine, dihydro-3-methyllumiflavin, and reduced flavoproteins) is the activation of dioxygen to hydrogen peroxide in biological matrices. Thus, within the normal cytochrome P-450 metabolic cycle, either hydroxide ion or an electron-transfer cofactor acts as an initiator (probably to produce $Fl^{\cdot-}$) and reduced flavoprotein is the donor.[23] In contrast, the introduction of $O_2^{\cdot-}$ or hydrated electrons (from ionizing radiation or a disease state) into a biological matrix that contains donor molecules leads to the uncontrolled formation of hydrogen peroxide. If reduced metal ions are present Fenton chemistry occurs to give hydroxyl radicals, which will initiate lipid peroxidation[24] and rancidification of stored foodstuffs.

On the basis of their redox thermodynamics and reaction chemistry with $O_2^{\cdot-}$ in aprotic media, ascorbic acid[19] and some catechols[25] may be subject to an $O_2^{\cdot-}$-catalyzed autoxidation to dehydroascorbic acid and *o*-quinones, respectively.

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Studies on the Reaction of NO^+ with SCN^- Using Energy-Weighted Maximum Overlap and ab Initio Calculations

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Abstract: The reaction of the nitrosyl cation with the thiocyanate anion is described in terms of the concept of charge- and frontier-controlled reactions. The thiocyanate anion possesses two sites for nitrosation: the sulfur and nitrogen atoms, giving nitrosyl thiocyanate (**1**) and nitrosyl isothiocyanate (**2**), respectively. By use of energy-weighted maximum overlap calculations and polyelectronic perturbation theory the sulfur atom of thiocyanate is found to be the most reactive in nitrosation reactions. Geometrical optimization (GAUSSIAN 80 (STO-3G basis set)) of nitrosyl thiocyanate and nitrosyl isothiocyanate reveals that the former should be 1.06 eV more stable than the latter. The calculated bond lengths and angles of nitrosyl thiocyanate are found to be in good agreement with those found by X-ray crystallographic investigations of a stable *S*-nitroso compound (2-(acetylamino)-2-carboxy-1,1-dimethyl thionitrite (**3**)). The inefficiency of nitrosyl thiocyanate to act as a nitrosation reagent compared with other nitrosation reagents (as e.g., nitrosyl chloride (**4**)) is described by using the LUMO energy, molecular orbital coefficient, atomic net charge, and the concept of charge- and frontier-controlled reactions, and good agreement with experimental results is found. The decomposition of nitrosyl thiocyanate is described by studying the energy difference of the lowest triplet state as a function of the distance between the NO and SCN groups, and indications are found for the formation of NO and SCN radicals. These radicals can be involved in carcinogenesis in humans.

The thiocyanate anion is interesting from different points of view: it shows reactivity at both nitrogen and sulfur depending on the nature of the electrophile used[1] (Figure 1).

Smokers have increased amounts of the thiocyanate anion in

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