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SPIN TRAPPING OF METHYL RADICALS BY THE ACYL NITROSO COMPOUND PH—C(=O)NO FORMED IN THE PHOTOCHEMICAL REACTION BETWEEN BENZOHYDROXAMIC ACID, DIMETHYL SULFOXIDE AND HYDROGEN PEROXIDE. AN EPR STUDY.

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By the use of EPR spectroscopy, it has been shown that acyl nitroso compounds can act as spin traps for short-lived radicals with the formation of acyl aminoxyl radicals. The reaction was studied for the system benzohydroxamic acid [Ph—C(=O)N(H)] - dimethyl sulfoxide - hydrogen peroxide. The acyl aminoxyl radicals appeared almost immediately when the reaction mixture was irradiated *in situ* in the EPR cavity with UV light. The trapping reaction involved two photochemical reactions, i.e. the oxidation of the hydroxamic acid to the acyl nitroso compound Ph—C(=O)NO, and the formation of methyl radicals from dimethyl sulfoxide. The EPR spectra are superpositions of the spectra of two species of acyl aminoxyl radicals, i.e. the radicals Ph—C(=O)N(O·)H formed by oxidation of the parent benzohydroxamic acid, and the radical Ph—C(=O)N(O·)CH_3, formed by trapping of methyl radicals.

KEY WORDS: Spin trapping, acyl nitroso compounds, acyl aminoxyl radicals.

INTRODUCTION

It has been shown[1] that *tert*-butylhydroxylamine (**1**) gives rise to the radical *t*-BuN(O·)H (**2**) in the reaction with hydrogen peroxide, probably via ·OH radicals which abstract a hydrogen atom from the parent compound. Subsequently, radical **2** is able to participate in a radical-driven Fenton reaction which leads to the formation of the spin trap *t*-BuNO (**3**) and ·OH radicals (eqns 1-3):

$$\underset{\mathbf{1}}{t\text{-BuN(OH)H}} \xrightarrow[-H_2O]{H_2O_2(\cdot OH)} \underset{\mathbf{2}}{t\text{-BuN}(O\cdot)\text{H}} \qquad (1)$$

$$\underset{\mathbf{2}}{t\text{-BuN}(O\cdot)\text{H}} + H_2O_2 \longrightarrow t\text{-BuN(O)H}^+ + \cdot OH + OH^- \qquad (2)$$

$$t\text{-BuN(O)H}^+ \longrightarrow \underset{\mathbf{3}}{t\text{-BuNO}} + H^+ \qquad (3)$$

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In the presence of suitable substrate molecules, the ·OH radicals abstract hydrogen atoms with the formation of short-lived radicals which are trapped by the nitroso compound to give stable aminoxyl radicals, e.g. for ethanol as the substrate, eqns 4-5,

$$CH_3CH_2OH + \cdot OH \longrightarrow CH_3\dot{C}HOH + H_2O \qquad (4)$$

$$CH_3\dot{C}HOH + \underset{\mathbf{3}}{t\text{-BuNO}} \longrightarrow t\text{-BuN(O}\cdot\text{)CH(CH}_3\text{)OH} \qquad (5)$$

In view of these reactions, it was of interest to determine whether analogous reactions could give rise to the the corresponding acyl aminoxyl radicals when the starting material is a hydroxamic acid instead of the hydroxylamine **1**. This means that the spin traps analogous to **3**, i.e. acyl nitroso or oxo nitroso compounds, would have the general structure R—C(=O)NO **5** (R= aryl, alkyl). Such substances (**5**) have been extensively used in a number of synthetic reactions as enophiles or dienophiles (Diels-Alder reactions).[2] However, acyl nitroso compounds (**5**) are unstable and could not be isolated. Therefore, they were produced as transient intermediates in the reaction mixtures by oxidation of the corresponding hydroxamic acids, in many of these reactions, with tetrapropylammonium metaiodate.

By use of the EPR technique, it has now been found that short-lived radicals are trapped by an acyl nitroso compound to give detectable acyl aminoxyl radicals. Since spin trapping with acyl nitroso compounds seems not to have been described so far, the present study was limited to show that such reactions are possible by trapping one single radical species, i.e. methyl radicals, with Ph—C(=O)NO derived from benzohydroxamic acid.

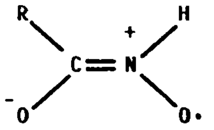
EXPERIMENTAL PROCEDURES

The EPR spectra were recorded at 20°C using a Varian E-9 EPR spectrometer with a microwave power of 1-5 mW and a 100 kHz modulation amplitude of 0.01 to 0.05 mT. The samples were contained in a flat aqueous solution cell. Hyperfine splitting constants were measured by comparison with the splittings of Fremy's radical (a_N = 1.3 mT; 1 Gauss equals 0.10 mT). The samples were irradiated with UV light from a mercury lamp (Osram HBO-200) *in situ* in the EPR cavity. The chemicals used were obtained from Aldrich and Fluka AG. The spectral simulations were performed by use of a modification of a computer program constructed by Oehler and Janzen.[3]

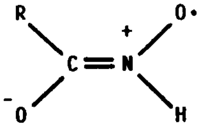
RESULTS AND DISCUSSION

In the experiments to be described, benzohydroxamic acid Ph—C(=O)—N(H)OH (**6**) was used as the parent compound, which was transformed to the spin trap Ph—C(=O)NO (**8**). By analogy with eqn 1, Ph—C(=O)—N(H)OH is at first expected to be oxidized to the radical Ph—C(=O)N(O·)H (**7**) before being converted to the spin trap **8**.

Acyl aminoxyl radicals of the type R—C(=O)N(O·)H (R= alkyl, aryl) exhibit relatively small nitrogen coupling constants a_N, i.e. between 0.5 and 0.8 mT, and hydrogen coupling constant a_H about 1 mT.[4] The small nitrogen coupling constants are believed to be connected with the delocalization of spin density from the nitrogen to the oxygen atoms by admixture of the amide structures **9a** and **9b**

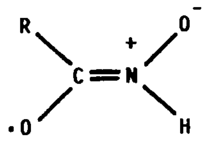


9a (O, O cis)



9b (O, O trans)

and also by the structure **9c**.



9c

The geometric isomers **9a** and **9b** will, in some systems, give rise to a superposition of two six-line EPR spectra.[4] Since any acyl aminoxyl radicals formed by trapping of short-lived radicals in the reaction with an acyl nitroso compound (**5**) are expected to contribute to further superpositions on the two six-line spectra, it is essential that spectral splittings from the acyl aminoxyl radicals formed by trapping are clearly separated, at least in part, from those analogous to **9a** and **9b**, to make a complete interpretation possible.

In view of these considerations, the trapping of methyl radicals produced in the photochemical reaction between dimethyl sulfoxide (DMSO) and hydrogen peroxide should be suitable, since the splittings due to the interaction of the unpaired electron with the hydrogen nuclei of a trapped methyl radical are expected to be rather large and therefore, in part, to be located outside the spectral range of the radicals analogous to **9a** and **9b**. As a comparison, the coupling constants of the aminoxyl radicals formed in the trapping of methyl radicals derived from DMSO with a conventional alkyl nitroso compound are: $a_N = 1.59$ mT; $a_H = 1.36$ mT 5 (quartet).[5] A further reason for the use of methyl radicals derived from DMSO is their high yield in this reaction.

Figure 1a shows the EPR spectrum of the radicals formed by UV irradiation *in situ* in the EPR cavity of a reaction mixture consisting of 55 mg of benzohydroxamic acid dissolved in 400 μl of DMSO corresponding to a concentration of about 1 M, and 30 μl of H_2O_2 (30% in H_2O) giving a concentration of about 0.6 M. The radicals appeared almost immediately after the irradiation had started and persisted for many hours of irradiation. In the dark the radicals disappeared almost immediately. The spectrum is an overlap of three different spectra:

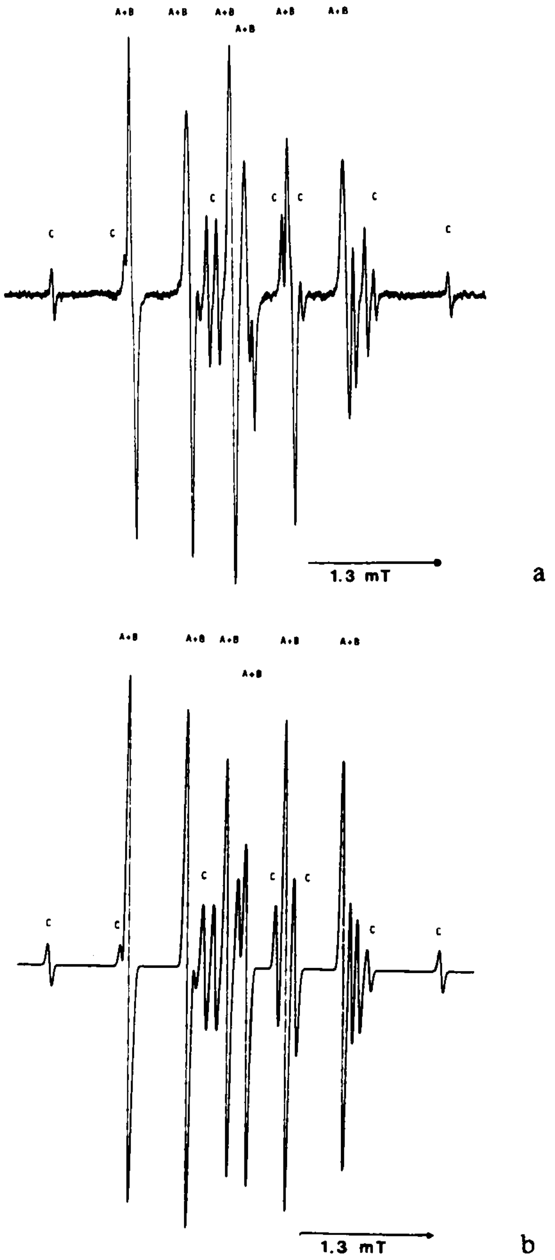


FIGURE 1 *a* shows the EPR spectrum of the acyl aminoxyl radicals formed in the photochemical reaction between benzohydroxamic acid Ph—C(=O)N(OH)H (1 M) and H_2O_2 (0.6 M) dissolved in dimethyl sulfoxide. The spectrum is a superposition of: *A* and *B*. The spectrum of Ph—C(=O)N(O·)H. Six-line spectra. *C*. The spectrum of Ph—C(=O)N(O·)CH_3 formed by trapping of $CH_3^{\cdot}$ radicals by Ph—C(=O)NO. 3 × 4 line pattern. Due to the overlaps, not all of the lines of *C* are marked. *b*. Computer simulation of the experimental spectrum *a*. The fit was obtained with the following parameters:
A. $a_N = 0.57$ mT; $a_H = 0.95$ mT; $g = 2.0074$. Rel. intensity = 1.0
B. $a_N = 0.55$ mT; $a_H = 1.06$ mT; $g = 2.0071$. Rel. intensity = 0.4
C. $a_N = 0.70$ mT; $a_H = 0.80$ mT; $g = 2.0068$. Rel. intensity = 0.3
The line width was set to 0.040 mT for each of the three spectra.

A and *B*: There are two six-line spectra incompletely separated except for the high-field lines. Each spectrum indicated an interaction with one ^{14}N and one hydrogen nucleus. The coupling constants were obtained by spectral simulation and are given in Figure 1b. The radical species that give rise to these patterns are considered to be $\mathrm{Ph{-}C({=}O)N(O\cdot)H}$, or the corresponding amide forms (cf. **9a** and **9b**).

C. 3 × 4 line system. This pattern indicated an interaction with one ^{14}N nucleus and three equivalent hydrogen nuclei. The coupling constants are: $a_N = 0.70$ mT; $a_H = 0.80$ mT (quartet 1:3:3:1) (spectral simulation). These findings are consistent with an acyl aminoxyl radical formed by trapping methyl radicals in the reaction with $\mathrm{Ph{-}C({=}O)NO}$ (**8**). Consequently, the structure of the radical is $\mathrm{Ph{-}C({=}O)N(O\cdot)CH_3}$. This statement was further supported by the results obtained when the reaction was performed with DMSO-d_6 (shown in Figure 2a). The 3 × 4 line pattern of Figuere 1a is replaced by 3 × 7 line pattern, the result of an interaction with one ^{14}N nucleus and three equivalent deuterium nuclei ($I = 1$). Of the 21 lines about 11 are free from overlaps from the spectrum of the radicals described in *A* and *B*. The coupling constants are: $a_N = 0.70$ mT; $a_D = 0.123$ mT. With the ratio of the coupling constants a_H/a_D equal to 6.514, the results are consistent with those obtained with DMSO (Figure 1a), i.e. $0.123 \times 6.514 = 0.80$ mT.

Identical spectral pattern (Figures 1a and 2a) with almost the same proportions between the components *A*, *B* and *C* were obtained when the samples were irradiated again after being kept in the dark for several days in the EPR cuvette. In all these experiments, the six-line pattern (*A* and *B*) was the dominant one. The radical $\mathrm{Ph{-}C({=}O)N(O\cdot)CH_3}$ has previously been obtained by oxidation of the hydroxamic acid $\mathrm{Ph{-}C({=}O)N(CH_3)OH}$ in a flow system with ceric sulfate in dilute sulfuric acid ($a_N = 0.77$ mT; $a_H = 0.88$ mT (q).[6]

CONCLUSIONS

The results indicate that short-lived radicals, i.e. methyl radicals, can be trapped by transient acyl nitroso compounds such as $\mathrm{Ph{-}C({=}O)NO}$ (**8**), formed by oxidation of the corresponding hydroxamic acid, to give acyl aminoxyl radicals which are stable during UV irradiation. However, it is not clear whether the radical $\mathrm{Ph{-}C({=}O)N(O\cdot)H}$ (**7**) (*A* and *B*) constitutes a direct precursor of the acyl nitroso compound as participant in a reaction analogous to eqns 1-3, i.e. a reductive cleavage of H_2O_2, or the parent hydroxamic acid is directly oxidized to the acyl nitroso compound. Irrespective of this problem, it is considered that the radical $\mathrm{Ph{-}C({=}O)N(O\cdot)H}$ (*A* and *B)* is formed by an one-electron transfer from a photochemically excited state of the parent benzohydroxamic acid to H_2O_2 or DMSO, followed by a loss of a proton, eqn 6,

$$\underset{\mathbf{6}}{\mathrm{Ph{-}C({=}O)N(OH)H}} \xrightarrow{h\nu} [\mathrm{Ph{-}C({=}O)N(OH)H}]^{*} \xrightarrow[-H^{+}]{-e^{-}} \longrightarrow \underset{\mathbf{7}}{\mathrm{Ph{-}C({=}O)N(O\cdot)H}} \qquad (6)$$

Thus, the trapping reaction that leads to the acyl aminoxyl radicals (*C*) involves two photochemical reactions, the oxidation of the hydroxamic acid to the acyl nitroso compound, and the formation of methyl radicals from DMSO in the reaction with

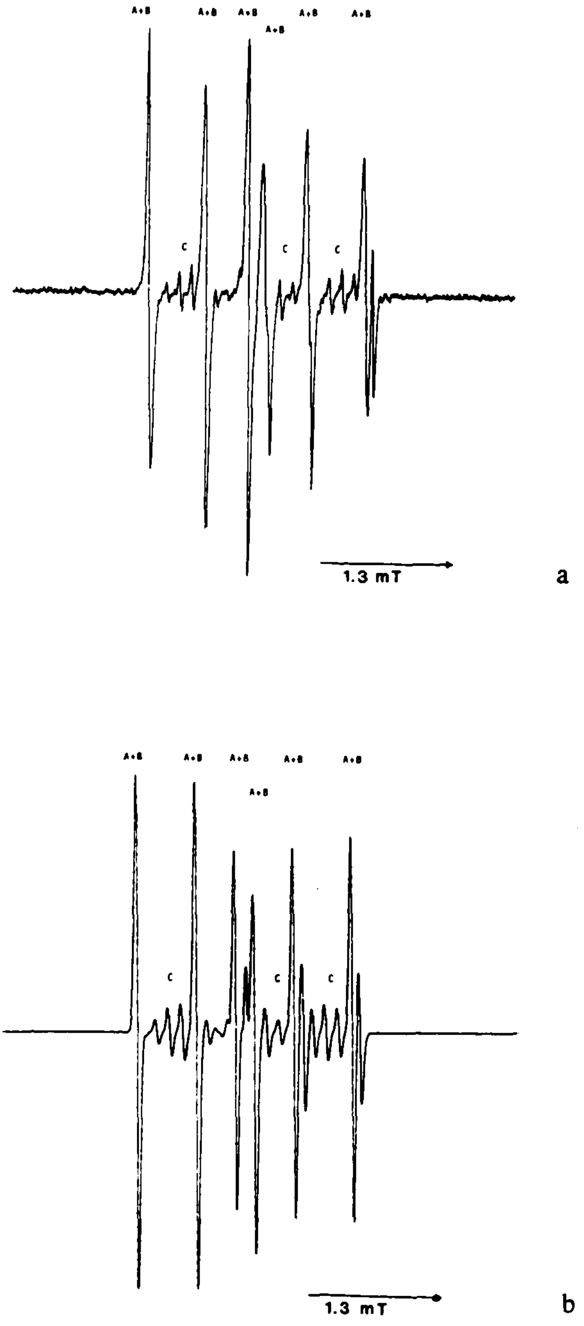


FIGURE 2 *a* shows the spectrum obtained with deuterated dimethyl sulfoxide (DMSO-d_6). *b*. Computer simulation of the experimental spectrum of *a*. For *A* and *B* the same parameters were used as for Figure 1b. *C*. $a_N = 0.70$ mT; $a_D = 0.80/6.514 = 0.123$ mT; $g = 2.0068$. Rel. intensity = 0.15. The line width was set to 0.040 mT for each of the three spectra.

H_2O_2. The intensity proportion between the dominant radical species, i.e. *A* and *B*, and *C*, seems to be the result of different kinetic equilibria of their formation and decay.

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