Spin Trapping of Radicals Formed in the Photochemical Reactions Involving Hydrogen Peroxide, Methanol or Dimethyl Sulfoxide Using 1(2),3-Dimethyl-4-nitrosopyrazol-5-ol. Evidence for Charge Transfer between Nitroxide Radicals and Dimethyl Sulfoxide

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1(2),3-Dimethyl-4-nitrosopyrazol-5-ol dissolved in methanol or dimethyl sulfoxide (DMSO) together with a small amount of H₂O₂ gives rise to nitroxide radicals when irradiated by UV light. The radicals can be detected only as long as the samples are irradiated. The ESR spectra indicated that a hydrogen atom had been trapped, and that the radical had the structure RN(OH) (R = the pyrazole ring system). A number of additional narrow hyperfine splittings observed in the ESR spectra obtained in DMSO indicated charge transfer between the radicals and DMSO molecules.

1-Methyl-4-nitroso-3,5-diphenylpyrazole and sodium 3-(4-nitroso-3,5-diphenyl-1-pyrazolyl)propane-1-sulfonate were introduced as effective spin traps by Kaur and Perkins. In connection with experiments performed with some related substances, it was found that 1(2),3-dimethyl-4-nitrosopyrazol-5-ol I, dissolved in methanol or dimethyl sulfoxide (DMSO), together with a small amount of H₂O₂, gave rise to nitroxide radicals when irradiated by UV light. The radicals could be detected only as long as the samples were irradiated. The ESR spectra indicated that a hydrogen atom had been trapped, and that the radical had the structure RN(OH) (R = the pyrazole ring system). A number of additional narrow hyperfine splittings observed in the ESR spectra, obtained in DMSO, indicated charge transfer between the radicals and DMSO molecules.

Compound I was prepared from methylhydrazine and methyl 3-oxo-2-oximinobutanoate, a reaction in which the methyl group of the ester was split off to give the 5-hydroxy derivative I. The monomethyl compound, i.e. 3-methyl-4-nitroso-5-pyrazolone was obtained by Wolff as a by-product in the reaction between hydrazine sulfate and the iso-nitroso derivative of ethyl acetoacetate, leading to the analogous splitting off of the ethyl group of the ester.

Materials and methods

1(2),3-Dimethyl-4-nitrosopyrazol-5-ol (I). Methylhydrazine (2.9 g) was added over 15 min to a stirred ice-cold solution of methyl 3-oxo-2-oximinobutanoate (4.5 g) in 50 ml of ethanol, and stirring and cooling were continued for 1 h. The mixture was poured into 1 M HCl (400 ml) and the product was extracted with CH₂Cl₂ (3 × 200 ml). The dried (Na₂SO₄) extracts were combined and evaporated, to leave a yellow-red solid (2.1 g); m.p. after vacuum sublimation 116–120°C (decomp). λₘₚ(H₂O) 297.5 and 259.0 nm (Shimadzu UV 1600). The ¹H NMR spectra ([(CD₃)₂]SO) (Varian XL-400) showed two sets of sharp peaks (methyl protons): one set at 2.055 and 3.155 ppm, the other at 2.228 and 3.170 ppm (30°C). The ratio of the intensities of the two sets (high field/low field) was 1.0 at 30°C, but decreased to 0.55 at 45°C. In addition to these peaks, the spectra exhibited an incompletely resolved doublet absorption at about 14.2 ppm at 30°C that merged into a single peak at 45°C (OH protons). Mass spectroscopy (MAT LAB 300) showed a molecular peak at 141, consistent with the formula C₆H₆N₂O₂. Found (Novo Industri AS): C 42.4; H 5.03; N 28.0. Calc. for C₆H₆N₂O₂: C 42.6; H 5.04; N 29.8.

1-Methyl-4-nitroso-3,5-diphenylpyrazole was prepared as described by Boyd and Norris. λₘₚ(CHCl₃) 322.0 and 246.0 nm. (CD₃)₂SO, CH₃OD and D₂O were obtained from Merck. Other chemicals and solvents were of analytical grade.

Preparation of radicals. The pyrazole derivative I was dissolved in CH₃OH, CH₃OD, (CH₃)₂SO (DMSO), (CD₃)₂SO, or other solvents tested, to a concentration of between 10 and 20 mmol. 10–15 μl of 30% hydrogen peroxide or tert-butyl hydroperoxide in H₂O was added to 0.5 ml of a solution of I. The samples were irradiated with UV light from a mercury lamp (Osram HBO-200) in situ in the ESR cavity when contained in a flat cell.

Electron spin resonance measurements. The ESR spectra were recorded using a Varian E-9 spectrometer at 20°C.
with a microwave power of 1–2 mW and a 100 kHz modulation amplitude of 0.1 to 0.25 G. Hyperfine splitting (hfs) constants were measured by comparison with the splittings of Fremy’s radical ($a_{HH} = 13.0$ G).

**Results and discussion**

Figs. 1–4 show the ESR spectra of the radicals obtained when 1 is dissolved in different solvents together with a small amount of hydrogen peroxide or tert-butyl hydroperoxide. No radicals were observed in reaction mixtures in the absence of a peroxide. Generally, the radicals appeared after an irradiation time of about half a minute. The radicals persisted as long as the samples were irradiated, but disappeared within a few seconds after the UV light had been switched off. Prolonged irradiation (ca. 0.5 h) decreased the radical concentration and impaired the resolution of the spectral components.

Fig. 1 shows the spectrum obtained with 1 dissolved in methanol. The spectrum exhibits six lines of equal intensity. However, the four central components are incompletely resolved. Similar results were obtained with ethanol and 2-propanol. No radicals were observed with tert-butyl alcohol or H$_2$O.

Fig. 2 shows the spectrum obtained when 1 was dissolved in CH$_3$OD. The spectrum is a superposition of the spectrum of Fig. 1 and a 3 x 3 line spectrum. Similar spectra were obtained with CH$_3$OH–D$_2$O (1:1) as the solvent.

Fig. 3 shows the ESR spectrum of 1 dissolved in DMSO. The spectrum consists of four main groups of lines which are further split into a number of incompletely resolved lines, the low- and high-field groups into at least five lines, and the two central groups into eight lines each.

Fig. 4 shows the spectrum observed when 1 was dissolved in (CD$_3$)$_2$SO. The spectrum consists of six lines of equal intensity. No traces of the incompletely resolved narrow splittings could be observed.

The results indicated that radicals were formed which exhibited hyperfine interactions with one $^{14}$N nucleus, one hydrogen atom, exchangeable with deuterium, together with hydrogen atoms of the methyl groups of DMSO in the reaction with this solvent. The coupling constants are given in Table 1.

Possible structures of 1 are as follows: the 1,3- and 2,3-isomers of the enol form 1a, the keto form 1b, and the isonitroso (oxime) form 1c. The NMR spectra of 1 indicated two sets of methyl protons. The relative intensities of the two sets were temperature dependent (see above), indicating an equilibrium between two of the tautomeric forms: very probably between one of the enol isomers 1a and the isonitroso form 1c, since no absorption due to any methine proton was observed, thus precluding the involvement of the keto form b.

The coupling constants indicate that the radicals are nitroxide radicals formed by the addition of primary radicals to the nitroso group of 1a. The large doublet splitting, i.e.

![Photochemically Generated Radicals](image)

**Fig. 3.** ESR spectrum of the photochemically generated radicals in a solution of 1 in (CH$_3$)$_2$SO together with a small amount of H$_2$O$_2$.

**Fig. 4.** ESR spectrum of the photochemically generated radicals in a solution of 1 in (CD$_3$)$_2$SO together with a small amount of H$_2$O$_2$.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>$a_{HH}$</th>
<th>$a_{H}$</th>
<th>$a_0$</th>
<th>$a_{CH_3}$</th>
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<tbody>
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<td>(CH$_3$)$_2$SO</td>
<td>12.0</td>
<td>10.9</td>
<td>0.4</td>
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</tr>
<tr>
<td>(CD$_3$)$_2$SO</td>
<td>12.0</td>
<td>10.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH$_3$OH</td>
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<td>11.7</td>
<td></td>
<td></td>
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<tr>
<td>CH$_3$OD</td>
<td>12.5</td>
<td></td>
<td>1.82</td>
<td></td>
</tr>
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</table>

A complex between the nitroxide radical and methanol is expected to involve hydrogen bonding between the oxygen atom of the nitroxide group and the hydrogen atom of the hydroxy group of a solvent molecule. However, no splittings originating from the hydrogen atom of the hydroxy group could be resolved (Figs. 1 and 2).

Nitroxide radicals of the type $R'R\text{N}(O)H$ ($R' = \text{alkyl}$) are unstable. A number of such radicals have been produced in flow systems by the oxidation of N-alkyl hydroxylamines, and by the photoreduction of alkyl nitroso compounds by thiophenol. In these reactions, as in those described here, a steady state is established upon UV irradiation between formation and decay, which gives rise to radical concentrations high enough to be detected by ESR spectroscopy.

With a somewhat higher concentration of hydrogen peroxide, other radical species can be trapped by I. Thus, the radical $\text{CH}_3\text{CHOCH}_2\text{H}_2$ formed by the abstraction of a hydrogen atom from diethyl ether by photochemically generated $<\text{OH}$ radicals, was trapped by I. The spin adduct was relatively stable and could be recorded in the dark after UV irradiation ($a_{\text{H}} = 13.3 \text{ G}$, $a_{\text{CH}_3} = 6.0 \text{ G doublet}$).

Some experiments were performed with the spin trap 1-methyl-4-nitroso-3,5-diphenylpyrazole dissolved in DMSO together with a small amount of $\text{H}_2\text{O}_2$. Irradiation of the samples in situ with UV light gave rise to a high yield of nitroxide radicals. The ESR spectra exhibited a $3 \times 4$ line system indicating the trapping of $-\text{CH}_3$ radicals ($a_{\text{H}} = 12.7 \text{ G}$, $a_{\text{CH}_3} = 11.7 \text{ G quartet}$). No trace of radicals of the type shown in Figs. 3 and 4 was present.

The incompletely resolved doublet absorption at about 14.2 ppm in the NMR spectrum of I indicates the presence of two hydroxy protons characterized by strong intramolecular hydrogen bonding as would apply to both Ia and Ic. The intramolecular hydrogen bonding is expected to give rise to six-membered ring arrangements in Ia and Ic involving the NO or $=\text{N-OH}$ groups in position 4, together with the OH or oxo groups in position 5. It is suggested that the different trapping reactions of I and the 3,5-diphenyl derivative of pyrazole are connected, in some way, with the intramolecular hydrogen bonding and ring arrangement in Ia. It is also possible that the different spin-trapping reactions of I and the 3,5-diphenyl derivative may be connected with different absorption spectra (see above) and different excitation behavior of the two compounds.

Compound I is present, in part, as the isonitroso (oxime)
form 1e. Thus, oxidation of 1 dissolved in H₂O with ammonium hexanitratocerate(IV) gave rise to the corresponding iminoyl radical in high yield. A single radical species was present that exhibited a 3 × 3 line spectrum. In addition to the splitting due to interaction with the nitrogen atom of the iminoyl group: aₙ = 31.2 G, the spectrum showed hfs from one of the nitrogen atoms of the pyrazole ring: a₀ = 1.83 G. A six-membered ring arrangement in 1e due to intramolecular hydrogen bonding seems to preclude the formation of more than one single geometric isomer of the iminoyl radicals; this is consistent with the observed spectrum. The iminoyl radicals decayed rather rapidly, but were stable enough to be recorded in the static system used.

Evidently, 1 constitutes a system consisting of both nitroso and isonitroso (oxime) tautomers, a fact that may explain the yellow–red colour of 1 which contrasts with the blue–green colour generally observed for nitroso compounds in the monomeric state.

Acknowledgements. The author is indebted to Dr. R. E. Carter and Dr. M. J. Perkins for valuable discussions, to Dr. J. Deinum for UV–visible spectra, to Mr. P.-Å. Jovall for NMR spectra and to Mr. W. Pimlott for mass spectra. This work was supported by grants from Adlerbergska Forskningsfonden.

References

Received July 6, 1988.