

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 H_2O_2 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 $R\dot{N}(O)H$ (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.¹ In connection with experiments performed with some related substances, it was found that 1(2),3-dimethyl-4-nitrosopyrazol-5-ol **1**, dissolved in methanol or dimethyl sulfoxide (DMSO), together with a small amount of H_2O_2 , 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 $R\dot{N}(O)H$ (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 **1** 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 **1**. The monomethyl compound, i.e. 3-methyl-4-nitroso-5-pyrazolone was obtained by Wolff² as a by-product in the reaction between hydrazine sulfate and the isonitroso 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-nitrosopyrazole-5-ol (1). Methylhydrazine (2.9 g) was added over 15 min to a stirred ice-cold solution of methyl 3-oxo-2-oximinobutanoate³ (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 CH_2Cl_2 (3×200 ml). The dried

(Na_2SO_4) extracts were combined and evaporated, to leave a yellow-red solid (2.1 g); m.p. after vacuum sublimation 116–120 °C (decomp). $\lambda_{max}(H_2O)$ 297.5 and 259.0 nm (Shimadzu UV 160). The 1H NMR spectra [$(CD_3)_2SO$] (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 30Q) showed a molecular peak at 141, consistent with the formula $C_5H_7N_3O_2$. Found (Novo Industri AS): C 42.4; H 5.03; N 28.0. Calc. for $C_5H_7N_3O_2$: C 42.6; H 5.04; N 29.8.

1-Methyl-4-nitroso-3,5-diphenylpyrazole was prepared as described by Boyd and Norris:⁴ $\lambda_{max}(CHCl_3)$ 322.0 and 246.0 nm. $(CD_3)_2SO$, CH_3OD and D_2O were obtained from Merck. Other chemicals and solvents were of analytical grade.

Preparation of radicals. The pyrazole derivative **1** was dissolved in CH_3OH , CH_3OD , $(CH_3)_2SO$ (DMSO), $(CD_3)_2SO$, or other solvents tested, to a concentration of between 10 and 20 mmol. 10–15 μ l of 30 % hydrogen peroxide or *tert*-butyl hydroperoxide in H_2O was added to 0.5 ml of a solution of **1**. 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 ($a_N = 13.0$ 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_2O .

Fig. 2 shows the spectrum obtained when **1** was dissolved in CH_3OD . The spectrum is a superposition of the spectrum of Fig. 1 and a 3×3 line spectrum. Similar spectra were obtained with CH_3OH-D_2O (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 $(CD_3)_2SO$. The spectrum consists of six lines of equal

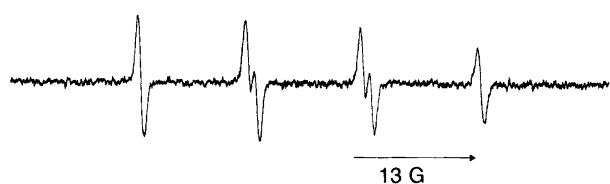


Fig. 1. ESR spectrum of the photochemically generated radicals in a solution of **1** in CH_3OH together with a small amount of H_2O_2 .

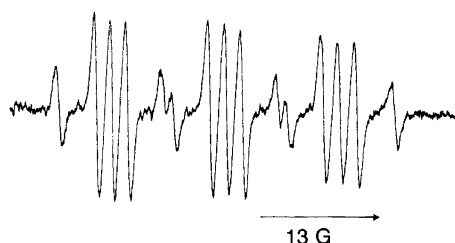


Fig. 2. ESR spectrum of the photochemically generated radicals in a solution of **1** in CH_3OD together with a small amount of H_2O_2 .

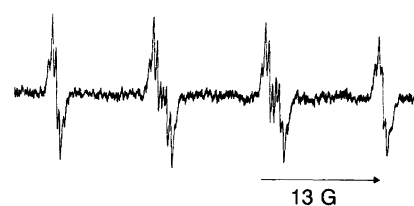


Fig. 3. ESR spectrum of the photochemically generated radicals in a solution of **1** in $(CH_3)_2SO$ together with a small amount of H_2O_2 .

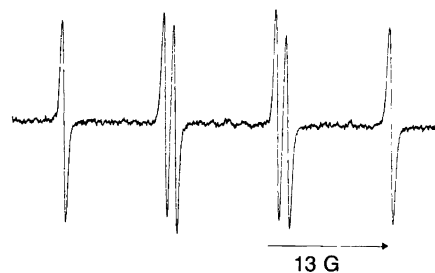


Fig. 4. ESR spectrum of the photochemically generated radicals in a solution of **1** in $(CD_3)_2SO$ together with a small amount of H_2O_2 .

intensity. No traces of the incompletely resolved narrow splittings could be observed.

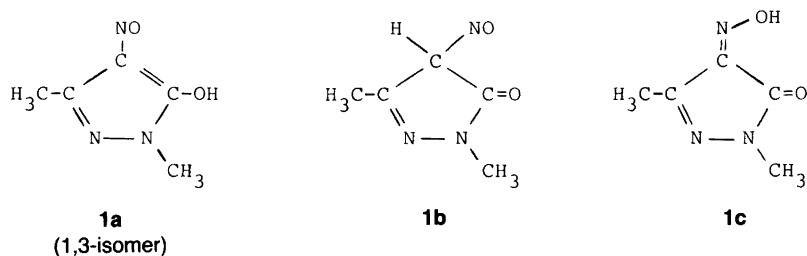
The results indicated that radicals were formed which exhibited hyperfine interactions with one ^{14}N nucleus, one hydrogen atom, exchangeable with deuterium, together with hydrogen atoms of the methyl groups of DMSO in the reaction with this solvent. The coupling constants are given in Table 1.

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.

Table 1. Coupling constants in G of the radicals observed in different solvents.

Solvent	a_N	a_H	a_D	a_{HCH_3}
$(CH_3)_2SO$	12.0	10.9		0.4
$(CD_3)_2SO$	12.0	10.9		
CH_3OH	12.5	11.7		
CH_3OD	12.5		1.82	



$a_H = 10.9$ – 11.7 G, is consistent with the trapping of a hydrogen atom bound directly to the nitrogen atom of the nitroxide group. Consequently, the radicals have the structure $R\dot{N}(O)H$ or $R\dot{N}(O)D$ where R is the pyrazole ring system. The reaction mechanism is believed to involve homolytic abstraction of a hydrogen atom from H_2O_2 or *tert*-butyl hydroperoxide by the excited state of **1a** since no radicals are observed in the absence of peroxide. It is less probable that $\cdot OH$ radicals derived from the peroxide are trapped (cf. Ref. 5). It seems more probable that one of the enol isomers (**1a**) constitutes the actual radical trap since no hfs could be observed originating from the hydrogen atom in position 4 of **1b**.

The ESR spectra observed with $(CH_3)_2SO$ and $(CD_3)_2SO$ (Figs. 3 and 4) show interactions of the unpaired electron with the hydrogen atoms of the methyl groups of this solvent, in addition to the interactions with one ^{14}N nucleus and one hydrogen atom. Evidently, the radical structures $R\dot{N}(O)H$ and $R\dot{N}(O)D$ are not consistent with the trapping of radicals such as $\cdot CH_3$ or $\cdot S(O)CH_3$ derived from DMSO.^{6,7}

The polarity of the medium and bonding of hydrogen-donating solvent molecules to the nitroxide group are known to influence the a_N value of nitroxide radicals.^{8,9} Calculations have shown that the electronic structure of both the radicals and the ligands change which leads to the appearance of non-zero spin density on the atoms of the ligands.^{10,11} Consequently, it is very probable that the narrow hyperfine splittings obtained with the aprotic polar solvent DMSO originate from a non-zero spin density on DMSO molecules bound to the nitroxide radicals in a donor-acceptor complex, mediated by the oxygen atom of the nitroxide group and the sulphur atom of DMSO [$(CH_3)_3S^+O^- \leftrightarrow (CH_3)_2S=O^{12}$]. It is suggested that the charge transfer between the nitroxide radical and DMSO is stimulated, at least in part, by the UV irradiation of the samples. The delocalization of non-zero spin density to the complexed DMSO is expected to stabilize the radical state. No hfs of the type concerned here seems to have been reported so far in reactions with DMSO. Evidently, the association of DMSO with the radicals is rather firm since the hfs are not blurred by any fast exchange of bound DMSO molecules. No radicals of the actual type were obtained in reactions of **1** when dissolved in other aprotic polar solvents such as acetone or hexamethylphosphoric triamide.

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 $R^1\dot{N}(O)H$ ($R^1 = \text{alkyl}$) are unstable. A number of such radicals have been produced in flow systems by the oxidation of N-alkyl hydroxylamines,¹³ and by the photoreduction of alkyl nitroso compounds by thiophenol.¹⁴ 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 **1**. Thus, the radical $CH_3\dot{C}HOCH_2H_5$ formed by the abstraction of a hydrogen atom from diethyl ether by photochemically generated $\cdot OH$ radicals, was trapped by **1**. The spin adduct was relatively stable and could be recorded in the dark after UV irradiation ($a_N = 13.3$ G, $a_H = 6.0$ G doublet).

Some experiments were performed with the spin trap 1-methyl-4-nitroso-3,5-diphenylpyrazole¹ dissolved in DMSO together with a small amount of H_2O_2 . Irradiation of the samples *in situ* with UV light gave rise to a high yield of nitroxide radicals. The ESR spectra exhibited a 3×4 line system indicating the trapping of $\cdot CH_3$ radicals^{1,6} ($a_N = 12.7$ G, $a_H = 11.7$ 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 **1** indicates the presence of two hydroxy protons characterized by strong intramolecular hydrogen bonding as would apply to both **1a** and **1c**. The intramolecular hydrogen bonding is expected to give rise to six-membered ring arrangements in **1a** and **1c** involving the NO or =N-OH groups in position 4, together with the OH or oxo groups in position 5. It is suggested that the very different trapping reactions of **1** and the 3,5-diphenyl derivative of pyrazole are connected, in some way, with the intramolecular hydrogen bonding and ring arrangement in **1a**. It is also possible that the different spin-trapping reactions of **1** and the 3,5-diphenyl derivative may be connected with different absorption spectra (see above) and different excitation behavior of the two compounds.

Compound **1** is present, in part, as the isonitroso (oxime)

form **1c**. Thus, oxidation of **1** dissolved in H₂O with ammonium hexanitratocerate(IV) gave rise to the corresponding iminoxyl 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 iminoxyl group: $a_N = 31.2$ G, the spectrum showed hfs from one of the nitrogen atoms of the pyrazole ring: $a_N = 1.83$ G. A six-membered ring arrangement in **1c** due to intramolecular hydrogen bonding seems to preclude the formation of more than one single geometric isomer of the iminoxyl radicals; this is consistent with the observed spectrum. The iminoxyl 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.

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