Spin-trapping with 2-methyl-2-nitrosopropane: photochemistry of carbonyl-containing compounds. Methyl radical formation from dimethyl sulfoxide

IONEL ROSENTHAL,¹ MAGDI M. MOSSOBA, AND PETER RIESZ

Laboratory of Pathophysiology, National Cancer Institute, National Institutes of Health, Bethesda, MD 20205, U.S.A. Received September 1, 1981

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The photochemical reactions of several carbonyl-containing compounds investigated by spin-trapping with 2-methyl-2nitrosopropane revealed different modes of scission depending on the structure of the initial compound. Thus, in photo-Fries rearrangements, the acyl radical was detected. 1,3-Diphenyl-2-propanone decarbonylated to yield the benzyl radical. Finally, valerophenone yielded the radicals expected by γ -hydrogen abstraction. In a dark reaction, dimethyl sulfoxide reacts with NaOH to generate methyl radicals. The latter result suggests the need for caution in the use of dimethyl sulfoxide with 2-methyl-2nitrosopropane for the detection of hydroxyl radicals.

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Les réactions photochimiques de plusieurs composés contenant un carbonyle, étudiés par captage de spin avec le méthyl-2 nitroso-2 propane, révèlent des modes différents de scission selon la structure du composé de départ. Ainsi dans les réarrangements photochimiques de Fries, on a décelé le radical acyle. La diphényl-1,3 propanone-2 par décarbonylation conduit au radical benzyle. Finalement, la valérophénone donne les radicaux attendus par élimination γ d'hydrogène. A l'abri de la lumière, le diméthylsulfoxyde réagit avec la NaOH en générant des radicaux méthyles. Ce dernier résultat suggère d'utiliser avec précaution le diméthylsulfoxyde avec le méthyl-2 nitroso-2 propane lors de la détection des radicaux hydroxyles.

[Traduit par le journal]

Introduction

The advent of the spin-trapping method in esr spectroscopy (1, 2) has facilitated the identification of the free radicals produced at room temperature in fluid solutions. Consequently, it is feasible to use spin-trapping to provide direct support for conceivable reaction pathways, otherwise indirectly implied, in various chemical processes, or to reveal the basic chemical reactions.

In this note we report the results of studying several chemical reactions by spin-trapping with 2-methyl-2-nitrosopropane (MNP).

Experimental

Spin-trap solutions were prepared by dissolving about 1–1.5 mg of MNP per mL of organic solvent at room temperature in the dark for 20 min. Aqueous solutions of MNP were prepared by stirring 1.5 mg of MNP per mL of H_2O (or D_2O) at room temperature in the dark overnight. MNP, phenyl acetate, phenyl benzoate, acetanilide, 1,3-diphenyl-2-propanone, valerophenone, dibenzoyl peroxide, and hexadecyltrimethylammonium chloride were purchased from Aldrich Chemical Co. 1,8-Diaminooctane was obtained from Sigma Chemical Co. Hydrogen peroxide (30%) was acquired from Fisher Scientific Co. Deuterium oxide (99.8%) was purchased from Bio-Rad Laboratories.

The photolyses were performed *in situ* at room temperature, in aerated solutions, in the standard aqueous quartz cell ($60 \times 10 \times 0.25$ mm) placed in the esr cavity, using a Schoeffel 1000 W high pressure Hg-Xe lamp coupled with a grating monochromator. The irradiation time was about 5 minutes.

A Varian E-9, X-band Spectrometer was used for esr measurements. The magnetic field modulation frequency was 100 kHz.

¹On sabbatical leave from Department of Technology, Agricultural Research Organization, Volcani Center, Bet-Dagan, Israel. The scans were traced with a modulation amplitude equal to, or lower than 0.2 G, and the microwave power level was maintained at 10 mW to avoid saturation. An NMR Gauss Meter was used to calibrate the magnetic field. The hyperfine couplings are accurate to \pm 0.05 G. All esr measurements were carried out at room temperature.

Results and discussion

The short-lived radicals generated by uv photolysis which react with MNP to produce stable nitroxide radicals exhibit a primary triplet hyperfine coupling from the ¹⁴N of the nitroxyl group. The primary triplet is split into secondary lines which generally arise from the interaction of the free electron with the magnetic nuclei of the trapped radical. The α , β , and γ positions of the nuclei on the spin adduct are defined with respect to the nitroxyl nitrogen as illustrated below:

$(CH_3)_3CN(\dot{O})C^{\alpha}H_2^{\beta}-C^{\beta}H_2^{\gamma}-$

I. Study of the photo-Fries rearrangement

The photo-Fries rearrangement has attracted intensive attention (3) (eq. [1])



Flash photolyses (4) and CIDNAP studies (5) indicated the homolytic cleavage of the O-acyl

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Substrate	Radical	a N(nitroxyl)			
		СН₃ОН	CH ₃ CN	C ₆ H ₆	Dioxan
Phenyl acetate Phenyl benzoate Acetanilide	CH₃CO· C ₆ H₅CO· CH₃CO·	7.8 8.1 7.8	7.9 8.1 7.9	7.8 8.0 7.8	8.0 8.0 8.0

TABLE 1. Hyperfine coupling constants $a_{N(nitroxyl)}$ (G) of the spin-trapped radicals in the photo-Fries rearrangement at 260 ± 10 nm

bond, as the first step in the rearrangement of aryl esters.

We attempted the direct detection of the free radicals involved in the photo-Fries rearrangements of phenyl acetate, phenyl benzoate, and acetanilide by spin-trapping with MNP. Thus, MNP solutions containing the substrates (50 μ L/mL) in different solvents were irradiated with light of $\lambda = 260 \pm 10$ nm.

In all cases, a spectrum composed of a sharp triplet was recorded, and it was assigned to acyl radicals in view of the characteristically small hyperfine splittings of the nitrogen of the nitroxyl group (6). The results of these experiments are summarized in Table 1. The aromatic radical counterpart of the acyl radical could not be spintrapped. Occasionally, di-*tert*-butylnitroxide radical (DTBN) was also detected and the lines due to DTBN are labelled (S) in the figures. The ¹⁴N hyperfine coupling constants of the nitrogen of the nitroxyl group were 16.03 G (methanol) and 15.15 G (benzene or acetonitrile).

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Parenthetically, we noted that an unusual spin adduct was recorded when the photolysis of phenyl acetate in acetonitrile was induced with light of $\lambda =$ 313 ± 10 nm. This spin adduct (Fig. 1a) could be analyzed in terms of $3 \times 3 \times 3$ lines and was initially attributed tentatively to the hydrogen atom abstraction from acetonitrile (I) ($a_N = 15.3$ G, $a_H =$ 10.9 G (2H), and $a_N = 2.0$ G).

I

Spin adduct I was not reported previously in the literature, acetonitrile being considered to be fairly inert to radical attack.² However, by reaction of acetonitrile with OH[•] generated photochemically from H₂O₂ (100 µL of 30% H₂O₂ per mL of CH₃CN containing MNP (1 mg/mL) irradiated with $\lambda = 260$ nm for 20 s) we successfully generated I and recorded it as a simple triplet of triplets (Fig. 1b) of

 $a_{N(nitroxyl)} = 15.5 \text{ G}$ and $\beta a_{H} = 9.0 \text{ G}$ (2H). Furthermore, the 313 nm photolyses of phenyl acetate in solvents other than CH₃CN, such as benzene, also generated a similar $3 \times 3 \times 3$ line spectrum $(a_{N(nitroxyl)} = 14.8 \text{ G}, \beta a_{H} = 10.9 \text{ G}$ (2H) and $\beta a_{N} = 2.0 \text{ G}$) which under these circumstances can be attributed only to radical II, whose complete structure could not be ascertained from the present data, in which the nitrogen originates from the spin trap.

$$Bu - N - CH_2 - N$$

II. Photodecarbonylation of 1,3-diphenyl-2propanone

1,3-Diphenyl-2-propanone is one of the few noncyclic ketones which loses carbon monoxide nearly quantitatively and with high quantum yield when irradiated (7-10) (eq. [2]).

[2]
$$C_6H_5CH_2CCH_2C_6H_5$$

 \xrightarrow{hv} $C_6H_5CH_2CH_2C_6H_5 + CO$

A free radical mechanism which involves decarbonylation and radical recombination was suggested on the basis of the analyses of the chemical products (7–9) and CIDNAP studies (11). The question of whether the mechanism is concerted, or stepwise, involving the formation of phenylacetyl radical and benzyl radical, has been decided in favor of the latter (10) by experiments of radical recombination of these two radicals with the nitroxide 2,2,6,6-tetramethylpiperidine-1-oxyl.

We found that the uv irradiation ($\lambda = 313$ nm) of 1,3-diphenyl-2-propanone ($5 \times 10^{-4} M$) in different solvents at room temperature generated benzyl radical which could be detected as its spin adduct with MNP (III) (Fig. 2). DTNB was found in addition to radical III when dilute solutions of 1,3-diphenyl-2-propanone were photolyzed in

$$tBu - N - CH_2C_6H_5$$
 III
|
O·

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²Y. Y. Wang and L. T. Williams, unpublished results cited in ref. 2, p. 134.

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FIG. 1. The esr spectrum of the spin-trapped radical from (a) 313 nm photolysis of phenyl acetate in CH₃CN in the presence of MNP; (b) 260 nm photolysis of CH₃CN containing MNP and H₂O₂. The lines labelled (S) are due to DTBN.

aqueous solutions in which this ketone is only slightly soluble. The hyperfine coupling constants of radical III are summarized in Table 2.

Since no acyl radicals could be detected in our reaction conditions, we assume that the rate of

decarbonylation of the phenylacetyl radical is much faster than its addition to MNP. The failure to trap the phenyl acetyl radical with MNP has been reported previously in benzene at $40^{\circ}C$ (12).

The recombination of benzyl radicals generated

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FIG. 2. The esr spectrum of the spin-trapped benzyl radical from 313 nm photolysis of 1,3-diphenyl-2-propanone in the presence of MNP in (a) water and (b) benzene. The lines labelled (S) are due to DTBN.

by photodecarbonylation of dibenzyl ketones has been shown to be predetermined in micellar solution (13, 14). We attempted to trap the benzyl radical under these conditions ($5 \times 10^{-2} M$ hexadecyltrimethylammonium chloride in water which is above the critical micelle concentration) at concen-

trations of 1,3-diphenyl-2-propanone $(5 \times 10^{-4} M)$ employed for its detection in other solvents. However, the exclusive paramagnetic species detected was di-*tert*-butylnitroxide ($a_N = 16.6 G$). Since in micellar solution at the concentration ratio employed, the benzyl radical generation is confined to 1490

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the small hydrophobic portion of the micelle with very little diffusion out (13), radical recombination is highly favored, leaving no chance for competitive trapping by MNP. When, however, the same experiment was repeated at a much higher ketone concentration $(5 \times 10^{-3} M)$ so that the ketone is forced into the aqueous phase, the photolysis occurs as in a homogeneous solution and the benzyl spin adduct could be detected.

III. Photolyses of valerophenone

ΩĽ

The photoinduced intramolecular γ -hydrogen abstraction by the triplet state of phenyl alkyl ketones has been well documented (15–17) (eq. [3]).

The irradiation of valerophenone at 313 ± 10 nm in the presence of MNP generated a mixture of two radicals (Fig. 3). The predominant one, which was stable in the dark after initial photogeneration (radical A), showed a triplet of doublets attributed to intramolecular γ -hydrogen abstraction (IV). The

minor signal which could be detected only during uv-irradiation (radical B) could be analyzed in terms of 3×3 lines, and it was attributed to radical (V). The H-atom could be abstracted from acetophenone by photoexcited valerophenone or acetophenone, in an intermolecular reaction subsequent to the cleavage of valerophenone (18). Thus, the identity of radical (V) was confirmed by irradiating solutions of acetophenone in benzene

> TABLE 2. Hyperfine coupling constants (G) of benzyl radical spin adducts obtained by uv photolysis of 1,3-diphenyl-3-propanone at 313 \pm 10 nm

Solvent	a N(nitroxyl)	^β ан
H ₂ O	16.63	10.56
$D_{2}O$	16.63	10.56
Benzene	15.00	7.50
Methanol	15.80	8.50
Acetonitrile	15.23	8.53

and acetonitrile in the presence of MNP. The results are summarized in Table 3.

The photolysis of valerophenone was suggested

v

as a device to probe solute location in micelles (19). When valerophenone (0.01 *M*) was irradiated in an aqueous solution of MNP (1.5 mg/mL) containing hexadecyltrimethyl ammonium chloride (5 × 10⁻² *M*), two overlapping spectra were recorded. Again, the major and the stable one, composed of a triplet of doublets, is explained by the attachment of a —CH— radical to the spin trap ($a_{N(nitroxyl)} =$ 15.56 G, $\beta a_{H} =$ 1.9 G). This radical could originate from the intramolecular γ -hydrogen abstraction in valerophenone or intermolecular H-abstraction from the alkyl chain of the surfactant by valerophenone. The less prominent signal of 3 × 2 lines of equal intensity was light-dependent and was attributed to the H-adduct (VI).



FIG. 3. The esr spectrum of the spin-trapped radical from photolysis of valerophenone in the presence of MNP at 313 nm.



FIG. 4. The esr spectrum of the spin-trapped (a) CH_3 -radical and (b) CD_3 -radical, generated in the dark reactions between dimethyl sulfoxide and NaOH in the presence of MNP. The lines labelled (S) are due to DTBN.

$$\begin{array}{c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & H \end{array} = 14.0 \text{ G} \end{array}$$
 VI

The formation of the H-adduct can be easily explained by the reaction of an unstable phenylbutylhydroxyl radical with MNP (20–23) (eq. [4]).

IV. On the generation of methyl radical from dimethyl sulfoxide

The photochemically generated OH-radicals react

with dimethyl sulfoxide to generate methyl radicals which are trapped by MNP to yield a very persistent and characteristic spin adduct (24). This reaction has been used in biological systems to detect OH radicals (25).

We found, however, that dimethyl sulfoxide can OH

$$[4] \quad C_6H_5C(CH_2)_3CH_3 + tBu - N = 0$$

$$\rightarrow C_{6}H_{5}C(CH_{2})_{3}CH_{3} + tBu-N-\dot{O}$$

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		Radical IV	Radical V	
Solvent	a _{N(nitroxyl)}	β _{a_H}	a _{N(nitroxyl)}	β _{<i>a</i>_H}
Neat	14.63	1.75 (H)		
Benzene	14.75	1.65 (H)	14.25	7.75 (2H)
Methanol	15.38	1.75 (H) + unidentified radical		
Acetonitrile	15.00	1.73 (H)	14.50	8.06 (2H)

TABLE 3. Hyperfine coupling constants (G) of spin-trapped radicals generated by uv photolysis of valerophenone at 313 ± 10 nm

generate the MNP-methyl spin adduct under reaction conditions which do not involve hydroxyl radical, such as the chemical reaction with a base. Thus, after mixing in the dark, at ambient temperature, a solution of MNP in dimethyl sulfoxide (1.5 mg/mL) with a solution of NaOH in water (2%) in the ratio 1:1, the CH₃ spin adduct can be easily detected $(a_{N(nitroxyl)} = 16.4 \text{ G}, \beta a_{H} = 12.5 \text{ G} (3\text{H})).$ When the reaction is performed in dimethyl sulfoxide- d_6 , the corresponding CD₃-adduct is recorded $(a_{N(nitroxyl)} = 15.9 \text{ G}, \beta a_D = 1.9 \text{ G} (3D))$ (Fig. 4). Since the reaction proceeds relatively slowly at room temperature, a continuous increase in the intensity of the spin adduct can be observed with time. A possible reaction mechanism is depicted in eq. [5].

$$\begin{bmatrix} 5 \end{bmatrix} \quad OH^{-} + CH_{3}SCH_{3} \iff \begin{bmatrix} O^{-} \\ H_{3}SCH_{3} \\ OH \end{bmatrix}$$

$$\xrightarrow{[Oxidation]} \begin{bmatrix} O^{\cdot} \\ CH_{3}SCH_{3} \\ OH \end{bmatrix} \rightarrow \dot{C}H_{3} + CH_{3} - S - OH$$

This suggested mechanism is supported by the observation that dimethyl sulfoxide undergoes oxygen exchange with NaOH (26).

Accidentally, we also detected the methyl spin adduct in an entirely anhydrous medium. Thus, in the course of an investigation of free radicals derived from polyamines (27) it was found that when a dimethyl sulfoxide solution of MNP (1.5 mg/mL) and dibenzoyl peroxide (5 mg/mL) was saturated with 1,8-diaminooctane in the dark, at room temperature, the methyl spin adduct spectrum was exclusively observed. Control experiments indicated that all of these components were necessary for the formation of the methyl adduct. The mechanism of this particular process is unknown at the present time.

We feel that these observations should serve as a cautionary mark for the nondiscriminatory conclusion that the detection of methyl spin adduct from

dimethyl sulfoxide is an indisputable proof for hydroxyl radical generation in complex chemical systems.

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