ESR Studies of Nitroxide Radicals Formed in the Low Temperature Photolysis of N-Nitrosamines

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Various N-nitrosamines were photolyzed in toluene solution in the temperature range -100 °C to -30 °C to yield dialkyl nitroxides. The nitrosamines studied were N-nitrosodimethylamine, N-nitrosodiethylamine, N-nitrosodibutylamine and N-nitrosodicyclohexylamine. Subsequent nitroxide side products were also detected by ESR, and a mechanism for their formation is proposed. Temperature dependent hyperfine couplings of the methylene protons were observed for a few radicals of the type R_1 --CH₂--NO--R₂.

INTRODUCTION

In the photodecomposition of N-nitroso compounds, the primary photochemical process involves N-N bond breakage.¹ Jakubowski and Wan² observed an ESR spectrum at 77 K during the ultraviolet (UV) photolysis of N-nitrosodimethylamine and interpreted this spectrum as being due to the dimethylamino radical. Recently, Flesia et al.³ observed that when Nnitrosoamides were photolyzed in toluene, N-acyl-Nalkyl nitroxide radicals were obtained. We wish to report the observation of ESR spectra of nitroxide radicals generated on irradiation of a series of Nnitrosamines in toluene. In most instances, dialkyl nitroxides and additional secondary radicals were observed and their structures proposed from their respective hyperfine interactions. Since many Nnitrosamines are known carcinogens, the identification of their intermediate photodecomposition products will be extremely helpful in understanding the mechanism leading to the final products and their fate in the environment.

EXPERIMENTAL

Nitrosamines were obtained from Eastman Organic Chemicals, Eastman Kodak Company.

Solutions of 1% to 10% nitrosamines in toluene were photolyzed in the Varian E9 ESR cavity using a high pressure Schoeffel mercury lamp in the temperature range of -30 °C to -100 °C. All solutions were air saturated unless otherwise mentioned. In specific experiments, other solvents such as toluene- d_8 and carbon disulfide were substituted. The ESR spectra were recorded during and after photolysis. The temperature was controlled using a Varian variable temperature accessory.

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RESULTS AND DISCUSSION

N-Nitrosodimethylamine (NNDMA)

An ESR spectrum (Fig. 1(a)) with $g = 2.0052 \pm 0.0003$ was observed during a low temperature (-90 °C) UV irradiation of NNDMA in toluene. A similar, but less intense, spectrum was obtained for nitrogen bubbled



Figure 1. (a) ESR spectrum of NNDMA in toluene upon photolysis (initial short lived radical) at -90 °C; (b) computer simulation of (a).

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Table 1.	Cable 1. ESR hyperfine couplings for $B \to N - O \cdot radicals$									
Radical	Temperature (°C)	A	В	A _N (G)	А _н (G)					
1	-90	-CH3	CH3	15.26	12.4 (6H)					
Α	- 9 0	-CH ₃	CH ₂ Х	13.26	11.9 (3H)					
			-		4.1 (2H)					
В	60	CH₂Y	––CH₂Z	11.2	4.7 (4H)					
с	-30	CH3	CH2-N	<′ 11.3 <″	11.3 (3H)					
				8.2	4.4 (2H)					

solutions. On the basis of the similarity of the hyperfine parameters with those previously published for dimethyl nitroxide,^{4,5} we assign this spectrum as being due to the dimethyl nitroxide radical (1). A computer-simulated spectrum generated using these experimental parameters (see Table 1) is shown in Fig. 1(b). The nitroxide radicals probably arise from the photolytic cleavage of the N—N bond in NNDMA and the subsequent oxidation of the dimethylamino radical by air or nitric oxide.

A similar mechanism was proposed by Flesia *et al.*³ in their study of nitroxide radicals generated by the photolysis of *N*-nitrosoamides. No appreciable alteration of the hyperfine parameters was observed when toluene was replaced by toluene- d_8 or carbon disulfide, indicating that these solvents are not involved in the photolysis of *N*-nitrosamines. After prolonged irradiation at -90 °C, a new ESR spectrum (Fig. 2(a)) with $g = 2.0058 \pm 0.0003$ emerged. The measured hyperfine parameters (see Table 1) indicate an altered structure (A) with substitution of one of the methyl protons.



Again no spectral change was observed using toluene- d_8 as a solvent. A computer simulated spectrum, calculated from the observed splittings for the proposed radical **A**, is presented in Fig. 2(b). Prolonged photolysis at higher temperature, -60 °C, produced a complex ESR spectrum, which on standing in the dark evolved into a spectrum whose major lines correspond to a single radical (Fig. 3). From the observed hyperfine parameters (Table 1), the new nitroxide radical **B**, with $g = 2.0061 \pm 0.0003$, consists



of four equivalent methylene protons, suggesting that substituents Y and Z may be identical. Methylene





Figure 2. (a) ESR spectrum of NNDMA in toluene upon UV photolysis at -90 °C (longer lived radicals after the decay of the initial short lived radical; (b) computer simulation of (a).

Figure 3. ESR spectrum of NNDMA in toluene upon UV photolysis at -60 °C for an extended period (>15 min).

proton hyperfine couplings in nitroxide radicals with alkyl or aryl substituents usually range between 7 and 11G;⁶ in radicals **A** and **B** the splittings are much reduced. We therefore suspect that groups which are not carbon-centered may be involved in the X, Y, or Z substituents in radicals **A** and **B**. The following scheme involving the well documented nitrone formation from alkyl nitroxides⁷ is invoked to explain the results.



The nitroxide **2A** on subsequent nitrone formation could react with dimethyl nitroxide to give radical **3B**.



Radical **3B** is formed only after prolonged irradiation. Although the nitrone formation does not require light, prolonged irradiation is necessary to build up the dimethyl nitroxide concentration in order to form a sufficient amount of nitrone to obtain an observable quantity of the product.

Another new spectrum with $g = 2.0061 \pm 0.0003$ was observed when NNDMA was photolyzed at -30 °C and followed over a range of temperatures (-30 °C to -100 °C), and is consistent with the following proposed structure.



At temperatures below -30 °C the methylene proton splittings showed a line width alternation effect (Fig. 4 (a and b)). Due to steric hindrance, nitroxides of the type R₁--CH₂-NO--R₂ possess two symmetrically related conformers.⁶ This phenomenon is divided into a fast exchange limit with two approximately equivalent protons, a slow exchange limit with two unequal hyperfine splittings and an intermediate region with line width alternation. All three regions have been observed for radicals in the temperature range of -30 °C to -100 °C (Table 2). Lagercrantz and Setaka⁸ further postulated that, for nitroxides with nonequivalent β -methylene protons which possess a chiral center β to the nitrogen atom, two unsymmetrical conformers can exist for each of the above conformers. Under these circumstances the two methylene protons give rise to an 8-line spectrum at the slow exchange limit due to the superposition of these two conformers; the lines coalesce into a 4-line spectrum



Figure 4. ESR spectrum of NNDMA in toluene, photolyzed at -30 °C and observed at (a) -30 °C; (b) -90 °C (hyperfine analysis shown in lower part. See Table 2 for hyperfine coupling constants).

Table 2.	Tempers	ture-depen	dent methy	lene
	proton	hyperfine	splittings	for
	radiaala			

CH ₃ N—O· X—CH ₂						
Temperature (°C)	A _H (G)					
-30	4.15 (2H)					
70	4.7 (1H), 3.5 (1H)					
-80	5.1 (1H), 3.1 (1H)					
-90	5.1 (1H), 3.1 (1H)					
-100	5.2 (1H), 3.0 (1H)					

at the fast exchange limit. Consequently, the substituents X' and X" of radical C are probably identical. Another possible structure for radical C, by analogy to the N-nitrosodiethylamine case (see the following section), is radical 4C.



N-Nitrosodiethylamine (NNDEA)

Photolysis of NNDEA at -100 °C resulted in the spectrum shown in Fig. 5, with $g = 2.0060 \pm 0.0003$, which can be attributed to the hyperfine interactions of one nitrogen and four equivalent protons (5). The



Figure 5. ESR spectrum of NNDEA in toluene during photolysis at -100 °C.

hyperfine parameters are listed in Table 3 and are identical to the previously published results. Radical 5 was also generated by the peroxide oxidation of diethylamine. After radical 5 decayed, a more stable radical appeared and the ESR spectrum (Fig. 6) was observed

at -90 °C. The hyperfine couplings (Table 3) indicated the presence of three non-equivalent protons (13G, 7.2G and 3.5G) and two non-equivalent nitrogen nuclei (11.8G and 8.1G). A computer-simulated spectrum is shown in Fig. 6(b). The first line in Fig. 6(a) when expanded, shows further splittings with seven



Figure 6. (a) ESR spectrum at -90 °C of photolyzed NNDEA after the decay of the initial radical; (b) computer simulation of (a).

						A
Table 3.	ESR	hyperfine	coupling	constants	for	NO· radicals
						B

Initial	Irradiation temperature	Observed temperature								
compound	(°C)	(°C)	Α	В	A _{N1} (G)	A _{N2} (G)	A _H (G)	A _H (G)	A _H (G)	A _H (G)
NNDEA	100	-100	CH3-CH2-	CH ₃ CH ₂	15		10.2 (4H)			
NNDEA	-80	9 0	CH ₃ CH ₂	CH ₃ —CH	11.8	8.10	13.0 (1H)	7.2 (1H)	3.5 (1H)	0.2 (6H)
				¹⁴N≔O						
NNDEA	-80	- 9 0	CH₃CH₂	CH₃—CH I	11.8	11.4	13.0 (1H)	7.2 (1H)	3.5 (1H)	0.2 (6H)
				¹⁵ N—O						
NNDEA	-100	9 0	CH3-		13.7		15.2 (2H)			
			CH₃-	_CH						
NNDPA	-100	-60	CH ₃ CH ₂ CH ₂	CH₃CH₂ CH 	11.8	8.2	11.5 (1H)	6.7 (1H)	3.0 (1H)	0.2 (4H)
		70	•	Ń—C) 11.8	8.2	11.7	6.2 (1H)	3.0 (1H)	0.2 (4H)
		-80			11.8	8.4	11.7	6.1 (1H)	3.0 (1H)	0.2 (4H)
		-90			11.8	8.4	11.7	5.7 (1H)	3.0 (1H)	0.2 (4H)
		-100			11.8	8.6	11.9	5.6 (1H)	2.9 (1H)	0.2 (4H)
NNDBA	90	-80	CH ₃ (CH ₂) ₃	CH ₃ (CH ₂) ₂ CH	11.8	8.6	11.6 (1H)	6.1 (1H)	2.7 (1H)	0.2 (4H)
			I	Ń—0)					
NNDCA	- 80	8 0			13.2		6.1 (2H)			

equally spaced lines approximately 0.2G apart, indicating the presence of six equivalent protons.

In order to determine the origin of the second nitrogen splitting, ¹⁵N-labeled NNDEA ($\mathbf{6}$) was synthesized⁹. Photolysis of $\mathbf{6}$ yielded the spectrum with

$$CH_3 - CH_2$$

 $CH_3 - CH_2$
 $H_3 - CH_2$
(6)

 $g = 2.0067 \pm 0.0003$ shown in Fig. 7(a). The hyperfine couplings are the same as in the ¹⁴N case for all the nuclei except for one of the nitrogen atoms, which is



Figure 7. (a) ESR spectrum at -90 °C of photolyzed ¹⁵N— NNDEA in toluene where —NO group is replaced by NO after the decay of the initial unstable radical; (b) computer simulation of (a).

approximately 1.4 times larger than the ^{14}N —NNDEA coupling. These results suggest the structure **7** for this radical.





Figure 8. ESR spectrum at -90 °C of NNDEA in toluene after extended photolysis at -100 C.

Extended irradiation at -100 °C gave a simple ESR spectrum (Fig. 8) with two equivalent protons. The relatively large proton splitting (15.2G) (Table 3) led us to suspect the possibility of a 3-membered ring nitroxide (8), which has not been observed previously.



Relatively large β -proton couplings have been observed in substituted 4-membered ring nitroxides.⁶ We are currently working on the synthesis of various substituted *N*-nitrosoaziridines in order to identify radical **8** conclusively.

N-Nitrosodipropylamine (NNDPA)

Unlike NNDEA and NNDMA, the dipropyl nitroxide radical (9) was not observed upon UV irradiation of

$$CH_3 - CH_2 - CH_2$$

 $CH_3 - CH_2 - CH_2$
 O

NNDPA in toluene, but instead, the ESR spectrum of another radical. By analogy to NNDEA, the formation of radical **10** is proposed after nitric oxide addition to the nitrone formed by the disproportionation of radical **9**. The hyperfine coupling constants for radical **10**



are listed in Table 3. As expected, the methylene protons of radical **10** also exhibited line width alternation effects. The temperature dependent proton hyperfine coupling constants are listed in Table 3.

N-Nitrosodibutylamine (NNDBA)

The initial radical expected from NNDBA (dibutyl nitroxide), was not observed under UV irradiation at -90 °C. Instead, a spectrum which is almost identical to that of radical **10** was observed. The hyperfine coupling constants are shown in Table 3 and are consistent with the proposed radical **11**.

$$CH_3 - CH_2 - CH_2 - CH_2 - CH_2$$

$$CH_3 - CH_2 - CH_2 - CH$$

$$N = O$$
11

N-Nitrosodicyclohexylamine (NNDCHA)

A very simple ESR spectrum was observed when NNDCHA was irradiated, attributable to one nitrogen and two equivalent protons; the spectrum is probably due to the formation of the dicyclohexyl nitroxide radical (12). The β proton coupling constant (6.1G) is



smaller than that for dialkyl nitroxides, possibly due to changes in the dihedral angles caused by the steric hindrance from the bulky cyclohexyl rings.

CONCLUSIONS

Photolysis of the N-nitrosamines resulted in N-N bond cleavage. The dialkylamino radicals thus formed were oxidized to their respective dialkyl nitroxides, and were observed for dimethyl, diethyl and dicyclohexyl nitrosamines. Observation of these dialkyl nitroxides is in agreement with the work of Chow¹⁰ who had previously isolated dibutylamine, a photolytic by-product of NNDMA. The dialkyl nitroxides then underwent rearrangement to yield nitrones, which acted as internal spin-traps and gave a variety of other nitroxides. As expected, the nitroxides containing methylene groups exhibited line width alternation effects. The synthesis of ¹⁵N-labeled NNDEA helped considerably in the interpretation of the spectrum of one of the radicals from NNDEA which conclusively showed the presence of a second nitrogen. A similar scheme was proposed by Chow¹⁰ after the detection of N-n-butylbutyramidoxime and N-cyclohexylformamidoxime from the photolysis of NNDBA and Nnitroso-N-methylcyclohexylamine, respectively.

The tentative assignment of the final radical product in the case of NNDEA as a 3-membered ring nitroxide needs further scrutiny and is being pursued.

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