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An ESR Study of the Photolysis of *N*-Nitrosodialkylamines

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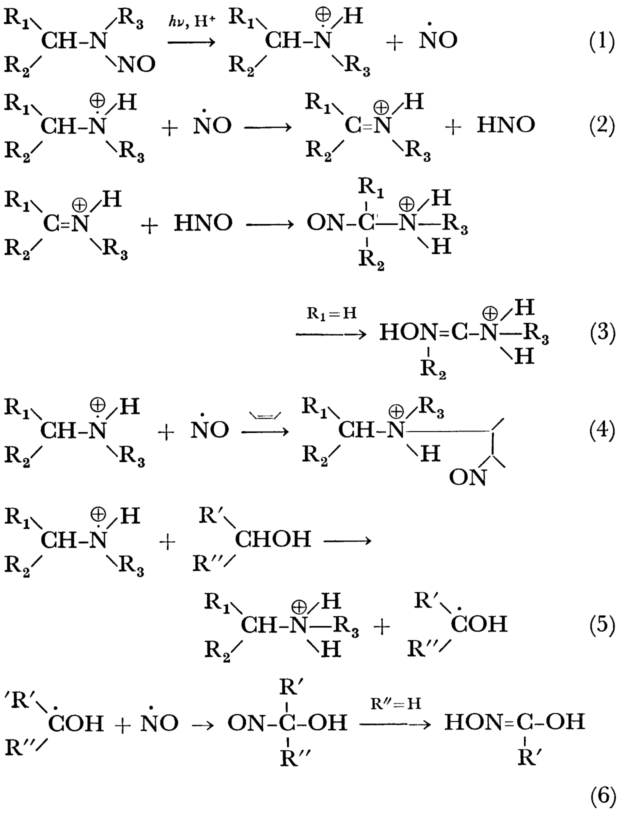
The nitroxide radicals which are formed when acidic, neutral, and alkaline solutions containing *N*-nitrosodialkylamines are photolysed, have been characterized by electron spin resonance spectroscopy. Nitrosamines are found to be photolytically active only in acidic solutions. In neutral and alkaline solutions nitrosamines only participate in secondary reactions involving the alcohol derived radicals. Some possible reaction pathways have been postulated.

As a class of compounds, *N*-nitrosodialkylamines when photolysed in neutral solutions, are effectively stable towards UV irradiation.[1–3] However in dilute acid solutions, nitrosamines undergo a large variety of photoinitiated free radical reactions, many of which are of interest in synthetic organic chemistry.[1–4] The primary photochemical event have been established to be an acid catalysed breaking of the nitrogen-nitrogen bond to produce an aminium radical and nitrogen monoxide. A generalized reaction scheme is given below: (for more detailed information the reader is directed to the review article by Chow[3] and references therin).



$$\mathrm{R_1R_2CH{-}N(R_3){-}NO \xrightarrow{h\nu,\,H^+} R_1R_2CH{-}\overset{\oplus}{N}H{-}R_3 + \dot{N}O} \quad (1)$$

$$\mathrm{R_1R_2CH{-}\overset{\oplus}{N}H{-}R_3 + \dot{N}O \longrightarrow R_1R_2C{=}\overset{\oplus}{N}H{-}R_3 + HNO} \quad (2)$$

$$\mathrm{R_1R_2C{=}\overset{\oplus}{N}H{-}R_3 + HNO \longrightarrow ON{-}CR_1R_2{-}\overset{\oplus}{N}H_2{-}R_3}$$

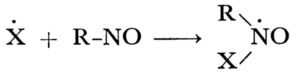
$$\mathrm{\xrightarrow{R_1=H} HON{=}CR_2{-}\overset{\oplus}{N}H_2{-}R_3} \quad (3)$$

$$\mathrm{R_1R_2CH{-}\overset{\oplus}{N}H{-}R_3 + \dot{N}O \rightleftharpoons R_1R_2CH{-}\overset{\oplus}{N}R_3H \cdots ON} \quad (4)$$

$$\mathrm{R_1R_2CH{-}\overset{\oplus}{N}H{-}R_3 + R'R''CHOH \longrightarrow R_1R_2CH{-}\overset{\oplus}{N}H_2{-}R_3 + R'R''\dot{C}OH} \quad (5)$$

$$\mathrm{R'R''\dot{C}OH + \dot{N}O \rightarrow ON{-}CR'R''{-}OH \xrightarrow{R''=H} HON{=}CR'{-}OH} \quad (6)$$

To the best of our knowledge, the only photochemical ESR investigations of the photolysis of nitrosamines are two communications from this laboratory[5,6] which supported the N–N cleavage as the primary chemical event. As can be seen from the above scheme, any ESR study to characterize the free radical intermediates will be bedevilled by a host of nitroxide radicals formed from the various *C*-nitroso compounds by spin trapping,[7]



$$\dot{\mathrm{X}} + \text{R-NO} \longrightarrow \mathrm{RX\dot{N}O} \quad (7)$$

or by secondary photolysis.[3,7]

Many of these problems can be minimized by photolysing flowing solutions and in this report we will describe the radicals obtained when solutions containing either *N*-nitrosodimethylamine, *N*-nitrosodicyclohexylamine or 1-nitrosopyrollidine were photolysed.

Experimental

The chemicals were purchased from Aldrich (*N*-nitrosodicyclohexylamine, 1-nitrosopyrollidine, acetone oxime, cyclopentanone oxime, maleic acid), K and K (*N*-nitrosodimethylamine), Baker (triethylamine), BDH (propionic acid), McArthur Chemicals (acetic acid). The solvents were obtained from a number of commercial sources. All chemicals were used as supplied except triethylamine which was distilled before use.

The concentrations of the nitrosamines in the solutions were 0.03—0.1 mol dm^{-3} and when di-*t*-butyl peroxide was added, its concentration was 1—2 vol %. All solutions were deoxygenated by purging with gaseous nitrogen. The flowing solutions were photolysed directly in the cavity of a Varian E-3 spectrometer with light from a 1000 W high pressure mercury lamp. The flow rate was varied (0—4 ml min^{-1}) to optimize the spectrum under study. For most samples this flow was 0.5 to ≈1.0 ml/min. The sample temperature in the cavity was regulated by flowing thermostated nitrogen gas by the spectrosil flow tube. The ESR simulations were performed on a Nicolet 1180 computer.

Results

Photolysis of Acidic Solutions. *(a)* N-*Nitrosodimethylamine (NDMA)*: No radicals were detected on photolysis of flowing solutions of NDMA in acetic acid, or 10 vol % acetic acid : benzene, however, if an alcohol was added to this solution an ESR spectrum was observed. In general the spectrum arose from two radicals, one of which, a nitroxide with $a^{\mathrm{N}} \approx$ 1.45 mT, was formed through secondary processes as its intensity increased markedly relative to the second radical on decreasing the flow rate. This secondary radical was not studied in detail. With the other radical (I), the number of interacting nuclei varied depending on the alcohol added. With 2-propanol and 2-butanol, splittings from two nitrogens and two protons were observed from I (see Fig. 1 and Table 1)

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Table 1. The hyperfine coupling constants (mT) for radical I

Solvent	a^H	a^H	a^H	a^N	a^N
10 vol% acetic acid : 2-propanol	0.87	0.83	—	0.29	1.40
8 vol% acetic acid : 30 vol% water : 2-propanol	0.94	0.94	—	0.29	1.39
10 vol% acetic acid : 10 vol% 2-propanol : benzene	0.78	0.78	—	0.38	1.34
4 vol% 2-propanol : acetic acid	0.86	0.86	—	0.34	1.38
10 vol% acetic acid : 2-butanol	0.94	0.77	—	0.31	1.38
10 vol% acetic acid : 1-propanol	0.98	0.66	0.62	0.34	1.34
10 vol% acetic : ethanol	0.91	0.76	0.71	0.31	1.35

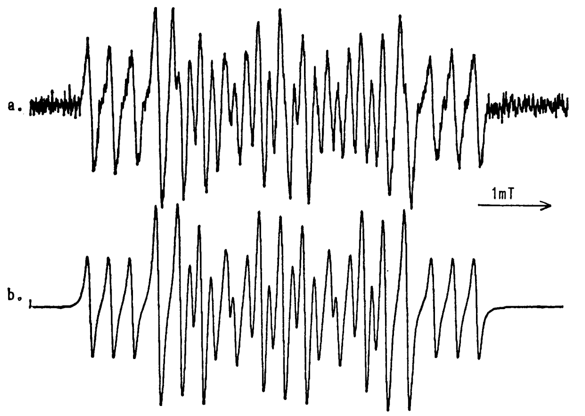


Fig. 1. (a) The ESR spectrum recorded when a NDMA: 8 vol % acetic acid: 30 vol % H_2O: 1% di-*t*-butyl peroxide: 2-propanol solution was photolysed at 22 °C. (b) The simulated ESR spectrum of radical I.

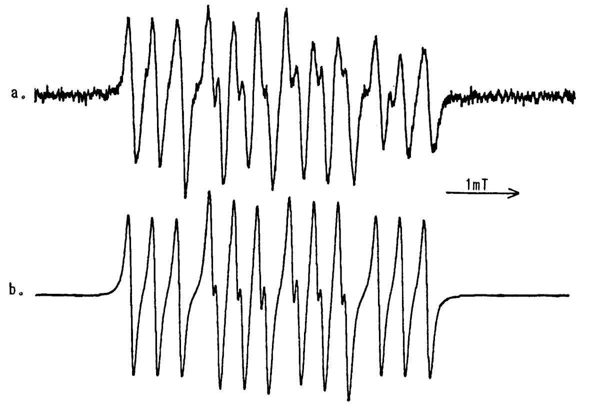


Fig. 2. (a) The ESR spectrum recorded when a NDCHA: 10 vol% acetic acid: ethanol solution was photolysed at 8 °C. (b) The simulated ESR spectrum of radical II.

but when the alcohol was ethanol or 1-propanol, an additional proton splitting was found (Table 1). When di-*t*-butyl peroxide was added to the solution, the spectral intensity of I increased about five fold. Although the hyperfine coupling constants showed little variation with temperature (−30 °C to +35 °C), they did vary slightly with solvent (Table 1). Linewidth effects associated with the coupling of the ***g***- and ***A***-tensors as the radical tumbled slowly could be observed as temperature was lowered in the alcoholic solvents.

For a DMNA:2-propanol solution (with and without di-*t*-butyl peroxide), the same spectrum was observed regardless of whether the acid was acetic or propionic but if maleic acid (0.2 mol dm^{-3}) or concentrated hydrochloric acid (2—10 vol %) was added, no spectrum was observed. Addition of 10 vol % cyclohexene to a DMNA : 10 vol % acetic acid : 2-propanol solution (8 °C) only slightly reduced the yield of I. However, if the flow was stopped, the solution photolysed for a few minutes, and then the spectrum recorded with the light blocked, the spectrum of a persistent nitroxide radical (a^N=1.55 mT, a^H=0.18 mT, linewidth≈0.2 mT) was recorded. In the absence of cyclohexene, no spectrum was observed after this sequence as both I and the other nitroxide decay within seconds.

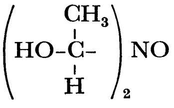
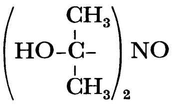
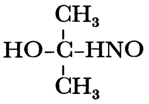
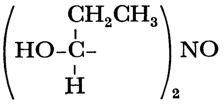
Table 2. The coupling constants (mT) for radical II

Solvent	a^H	a^N	a^N
10 vol% acetic acid : 2-propanol	1.20	0.33	1.11
10 vol% HCl (concd) : 2-propanol	1.21	0.40	1.13
10 vol% acetic acid : ethanol	1.20	0.33	1.10
10 vol% acetic acid : 20 vol% H_2O : 2-propanol	1.25	0.36	1.15
acetic acid	1.22	0.39	1.16

(b) N-Nitrosodicyclohexylamine (NDCHA): In contrast to DMNA, when DCHNA was photolysed in acetic acid, 2-propanol containing 10 vol % acetic acid or 10 vol % hydrochloric acid, ethanol containing 10 vol % acetic acid or 0.2 mol dm^{-3} maleic acid, the same radical (II) was always observed. A representative spectrum is shown in Fig. 2 and the coupling constants (for two nitrogens and a proton) are given in Table 2. As with NDMA solutions, a second nitroxide radical spectrum was also observed but its intensity relative to II decreased on increasing the flow rate and it is considered to arise from secondary processes. When di-*t*-butyl peroxide was added to any of the NDCHA solutions studied the intensity of II remained unaltered. Addition of cyclohexene to the solutions did not affect the intensity either.

(c) 1-Nitrosopyrollidine (NP): A limited number of experiments were undertaken with NP. On photolysing a NP:10 vol % acetic acid : 2-propanol solution, radicall III was observed (in addition, a secondary nitroxide was also observed). The coupling constants for III in the solution were a^N=1.36 mT and a^N=a^H=0.28 mT. The intensity of III increased on the addition of di-*t*-butyl peroxide to the solution. When the 2-propanol was replaced by either ethanol or 1-propanol, the spectrum of radical III (which was weak) appeared to have an extra proton coupling(a^H ≈0.58 mT) in

Table 3. Coupling constants (mT) of radicals formed in neutral solutions from NDCHA

Alcohol	a^N	a^N a)	a^H a)	Assignment
Ethanol	1.44	0.07(2)	0.03(6)	 $\left(\mathrm{HO{-}\overset{CH_3}{\underset{H}{C}}{-}}\right)_2\mathrm{NO}$
	1.41	0.51(2)	0.03(2)	?
2-Propanol				
	1.54	—	—	 $\left(\mathrm{HO{-}\overset{CH_3}{\underset{CH_3}{C}}{-}}\right)_2\mathrm{NO}$
	1.32	1.23	—	 $\mathrm{HO{-}\overset{CH_3}{\underset{CH_3}{C}}{-}HNO}$
1-Propanol b)				
	1.40	0.49(2)	—	 $\left(\mathrm{HO{-}\overset{CH_2CH_3}{\underset{H}{C}}{-}}\right)_2\mathrm{NO}$
2-Butanol	1.51	0.27	—	?

a) The number of equivalent nuclei are given in parentheses if different from one. b) Other radicals also present but spectrum too complicated to analysed (see Fig. 4).

addition to the above.

It should be noted that while radicals I, II, and III had half lives of about a second at 10—20 °C, their spectral intensities were not excessively large. When a 10 vol % acetic acid : 2-propanol solution containing either NDMA or NDCHA was photolysed, the respective radicals, I or II, were still observed (although at reduced intensity) when a filter (which blocked light $\lambda < 320$ nm) was inserted in the light beam.

Photolysis of Neutral and Basic Solutions. Photolysis of DCHNA in static alcohol solutions will, after a few minutes, produce strong spectra of nitroxide radicals but if the solutions were flowed no radicals could be detected. However, if di-*t*-butyl peroxide was added to the flowing solutions nitroxide radicals were observed. The effect of adding di-*t*-butyl peroxide was to generate alcohol-derived radicals.

$$t\text{-BuOOtBu} \xrightarrow{h\nu} 2t\text{-Bu}\dot{\text{O}} \tag{8}$$

$$t\text{-Bu}\dot{\text{O}} + \text{R}'\text{R}''\text{CHOH} \longrightarrow t\text{-BuOH} + \text{R}'\text{R}''\dot{\text{C}}\text{OH} \tag{9}$$

The results are summarized for NDCHA in Table 3. The spectra obtained for the alcohols, ethanol and 1-propanol, with NDCHA are shown in Figs. 3 and 4. Only ethanol and 2-propanol were studied for DMNA and, although the spectral intensity was greatly reduced in ethanol, the radicals were the same as in DCHNA.

When a NDCHA : ethanol solution (with or without di-*t*-butyl peroxide) has 10 vol % triethylamine added, only the diethyl nitroxide radical was observed ($a^N = 1.58$ mT, $a^H = 1.08$ mT (4 protons)). Photolysis of a blank solution containing no NDCHA produced no detectable radicals. If the base pyridine was added to a NDCHA : ethanol solution, no radicals were detected on photolysis, whereas on addition of di-*t*-butyl peroxide, the spectrum was the same as when the pyridine was absent.

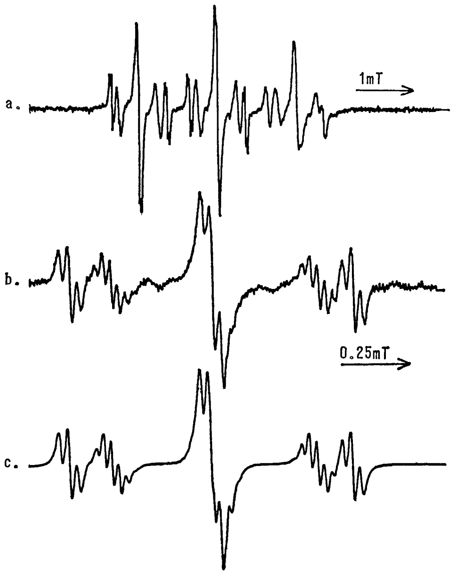


Fig. 3. (a) The ESR spectrum recorded when a NDCHA: ethanol solution containing di-*t*-butyl peroxide was photolysed at −10 °C. (b) The centre portion of the spectrum expanded. (c) The simulated ESR spectrum of (b) using the coupling constants in Table 3.

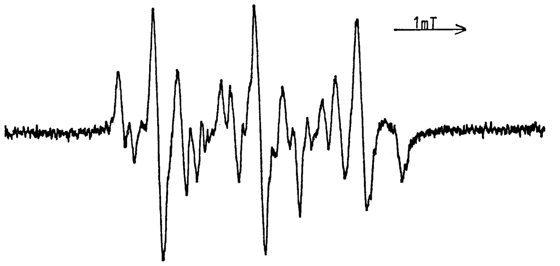


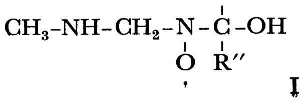
Fig. 4. The ESR spectrum recorded when a NDCHA: 1-propanol solution containing di-*t*-butyl peroxide was photolysed at 10 °C.

Photolysis of Acetone Oxime (AO) and Cyclopentanone Oxime (CPO). As oximes are generated in the photolysis of nitrosamines (Reaction 3), alcohol (2-propanol or ethanol) solutions containing di-*t*-butyl peroxide and AO or CPO were photolysed to see if the oximes would act as spin traps for the alcohol derived radicals (Reaction 9). Only the alcohol radical was observed on photolysis.

If AO or CPO were photolysed in a 25 vol % 2-propanol (or ethanol): acetic acid solution, a nitroxide radical $a^N = a^H = 1.40$ mT was observed. When di-*t*-butyl peroxide was added to the solution, the alcohol derived radical was also observed. Obviously the oximes do not act as efficient spin trapping agents for those alcohol derived radicals.

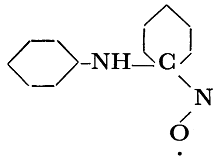
Discussion

Identification of the Radicals. The likely structures for radicals I, II and III, are given below:

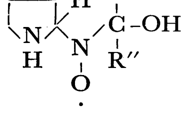


$$\mathrm{CH_3{-}NH{-}CH_2{-}\underset{\dot{O}}{N}{-}\overset{R'}{\underset{R''}{C}}{-}OH}$$

I

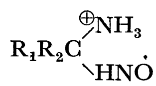


II



III

R′ and R″ are the substituents on the alcohol (see Reaction 9). The secondary amine nitrogen may also be protonated in these acidic solutions. The large nitrogen coupling constants (1.1—1.4 mT) observed for all radicals are consistent with nitroxide radicals.[7–14)] For radicals I and III, the observation of an extra proton splitting (≈0.6 mT) when ethanol or 1-propanol was present is indicative of spin trapping of the alcohol radical[7,8)] whereas for II, the a^{H}—a^{N}_{NO} is characteristic of a –NHO fragment.[12)] From the magnitude of the smaller nitrogen coupling constant (≈0.3 mT) in all three radicals, it is possible to assign this nitrogen as being directly bonded to the nitroxide nitrogen[9–11)] or to a carbon adjacent to this nitrogen.[11,12)] However since proton splittings consistent with a CH_2 fragment (a^{H}≈0.8 mT) in I and CH (a^{H}≈0.3 mT) in III were always present and, together with the close similarity between the coupling constants for I, II, and III and those observed for radicals of the form[12)]



$$R_1R_2C\begin{matrix}\overset{\oplus}{N}H_3\\ H\dot{N}O\end{matrix}$$

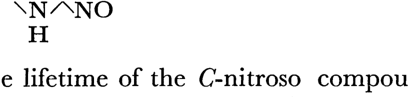
all suggest our assignment for I, II, and III are correct.

All the nitroxide radicals observed when neutral solutions containing di-*t*-butyl peroxide and NDCHA (or NDMA) were photolysed had a^{N}_{NO}≈1.3 to 1.6 mT. This indicates that the radicals are not alkoxy-substituted nitroxides (a ≈2.8 mT)[7,8)] formed from *t*-BuO. Some tentative assignments are given in Table 3. In ethanol solutions, where the linewidths were small enough to resolve splittings of about 0.03 mT (Fig. 3), only one of the two radicals could be assigned. The small splittings in both radicals are consistent with protons bound to a *β*-carbon.[13–14)]

Possible Reaction Pathways. As I, II, and III were relatively long lived ($t_{1/2}$≈second) and their steady state concentrations were relatively low, this implies that these radicals are formed by minor pathways. Although I, II, and III are structurally similar it is obvious that II is formed from a mechanism different to I and III as alcohol derived radicals (Reaction 9 and/or 5) are involved in the generation of I and III but not II.

Since the alcohol-derived radicals appear not to be trapped by oximes, it is likely that they are trapped by the *C*-nitroso intermediate[7,8)] formed in Reaction 3 to generate I and III

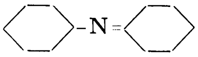
$$CH_3\text{-}\overset{\oplus}{N}H_2\text{-}CH_2\text{-}NO + R'R''\dot{C}OH \longrightarrow I \qquad (10a)$$



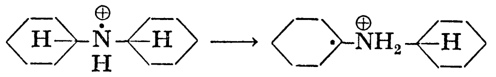
$$+ R'R''\dot{C}OH \longrightarrow III \qquad (10b)$$

The lifetime of the *C*-nitroso compound before it isomerizes to the oxime should be sufficiently long for Eq. 10 to occur as *C*-nitrosomethane and -ethane *etc.* can be isolated and characterized.[15)] The increase in yield of I and III on addition of di-*t*-butyl peroxide reflects the additional formation of alcohol radicals through Eq. 9 over the original reaction (Eq. 5).

While II is formed through an alternative mechanism to I and III, the photoproducts from NDCHA are also different from *N*-nitrosodi-*n*-alkylamines and *N*-nitrosocyclicamines (*e.g.* 1-nitrosopiperidine) in that no oxime can be formed (although the *C*-nitroso intermediate might be). The principal product for NDCHA is the imine

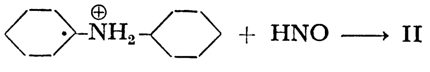


formed *via* Reaction 2, whereas oximes are principal products for the other two classes of nitrosamines.[1,2)] The isotopic labelling experiments of Axenrod and Milne[16)] have demonstrated that the reactants in Eq. 2 are not necessarily those formed in the original photochemical cage in Eq. 1. Hence the aminyl radical and NO must have a reasonable lifetime in solution (although they were not detected). It is not unreasonable to suggest that some of the dicyclohexylaminyl radicals might rearrange to a carbon centre radical



(11)

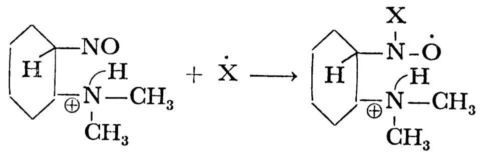
which then could react with HNO formed in Reaction 2.



(12)

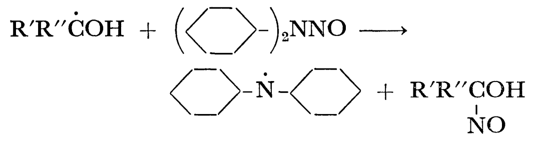
Circumstantial evidence supporting this mechanism is the observation of II but not I when hydrochloric acid was used instead of acetic acid in the photolyses. In NDMA solution, the presence of the stronger acid may increase the rate of nitroso-oxime isomerization and hence minimize the spin trapping reaction (Eq. 10). In the mechanism proposed above for II, there is no equivalent step to be interfered with by the hydrochloric acid.

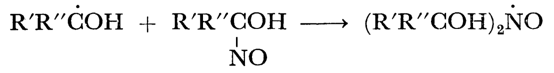
The absence of I when maleic acid was present is evidence for the facile photoaddition of NDMA to double bonds[17)] Eq. 4 whereas with NDCHA, which does not undergo photoaddition[18)], radical II was still observed. Apparently photoaddition of NDMA to cyclohexene is not as efficient as to maleic acid since I was still observed with 10 vol % cyclohexene present. However some photoaddition did occur as evidenced by the persistent nitroxide radical (a^{N}_{NO}=1.55 mT, a^{H}=0.18 mT) observed after a static solution was photolysed. This radical is consistent with what would be expected from spin trapping by the photoaddition product in an acetic acid: 2-propanol solution.



(13)

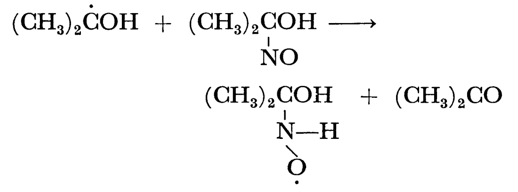
Although positive identification was not possible of all the nitroxide radicals generated when neutral alcohol and alkaline solutions of DCHNA containing di-*t*-butyl peroxide were photolysed, these experiments do indicate that nitrosamines are susceptible to reaction with alcohol radicals. The absence of a nitrogen splitting extra to that of the nitroxide nitrogen suggests the pathway, in part, might be Reactions 8 and 9 followed by


(14)


(15)

$$\mathrm{R'R''\dot{C}OH} + \mathrm{R'R''\underset{NO}{C}OH} \longrightarrow \mathrm{(R'R''COH)_2\dot{N}O} \qquad (15)$$

The *C*-nitroso compound formed in Eq. 14 can then act as a radical trap to form the nitroxide radicals observed in Eq. 15. When the alcohol is 2-propanol apparently a minor reaction is


(16)

$$\mathrm{(CH_3)_2\dot{C}OH} + \mathrm{(CH_3)_2\underset{NO}{C}OH} \longrightarrow \mathrm{(CH_3)_2\underset{\underset{\dot{O}}{N-H}}{C}OH} + \mathrm{(CH_3)_2CO} \qquad (16)$$

Reaction 14 may not occur in acid solutions due to protonation of NDCHA.[3] Furthermore, we have no explanation for the results observed when triethylamine was present. However, these results in neutral and alkaline solution support the product analyses[1-4] which conclude that nitrosamines are photolytically active only in acid solutions. In neutral solutions they are only involved in secondary reactions initiated photochemically.

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