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ESR Spectra of Nitroxide Radicals derived from N-Methyl, N-Nitroso, p-Toluenesulufonamine

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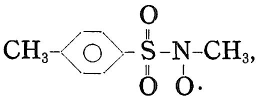
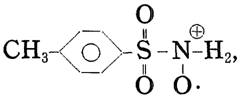
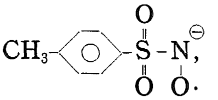
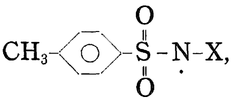
Abstract: Photolysis of toluene solution of N-methyl, N-nitroso, p-toluenesulufonamine gave rise to an amidyl and three nitroxide radicals. These radicals are

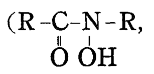
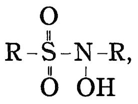
radical (I)  N-methyl, p-toluenesulufonitroxide

radical (II)  p-toluensulufonitroxide cation

radical (III)  p-toluenesulufonitroxide anion,

and radical (IV)  p-toluenesulufo amidyl. These ESR parameters are $g=2.0060$, $A_N=12.3$ G, $A_H=10.35$ G for radical (I), $g=2.0060$, $A_N=11.6$ G, $A_H=6.2$ G, for (II), $g=2.0058$, $A_N=10.2$ G, for (III), and $g=2.0041$, $A_N=29.5$ G, respectively. Radicals (II), (III), and (IV) are presumed to be derived from nitroso p-toluenesulufonamine prepared by oxidation of radical (I). Observation of these radicals may provide many interesting informations on percarciongen such as N-nitrosoamine.

Introduction

Formation of nitroxide radical from N-hydroxylated metabolites is suggested to be a key step in metabolic activation of carcinogenic amines1) and so many ESR studies on nitroxide radicals derived from N-hydroxylated metabolites such as N-hydroxy aminofluorene2) or N-aryl hydroxamic acids3) have been reproted. In previous works4) on structures and stabilities of nitroxide radicals produced in various hydroxamic acids ( $\underset{O}{\overset{\|}{\text{R-C}}}\text{-}\underset{OH}{\overset{|}{N}}\text{-R}$,  $\text{R-}\underset{O}{\overset{O}{S}}\text{-}\underset{OH}{N}\text{-R}$, R,R = aryl, alkyl, hydrogen), many interesting results that carbonyl nitroxide radicals show considerable stability, planarity and reduced A_N values compared with sulfonyl nitroxides, and reaction routes are mainly effected by substituents attached to nitrogen are obtained. Observation of N-nitroso nitroxide radical in oxidation of N-aryl hydroxamic acids may suggest the formation of the nitroso com-

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pounds in metabolic activation of N-aryl hydroxamic acids. Nitroxide anion radical which is found in oxidation of N-methyl sulufohydroxamic acids and benzene sulufohydroxamic acid but in N-methyl hydroxamic acids, was not enough to permit an exact conclusion for an existence of nitroso compound. N-methyl, N-nitroso, p-toluene sulufonamine is therefore preferred in order to explore the possibility of the formation for nitroso compound in oxidation of other hydroxamic acids and for new radical from N-nitroso compounds.

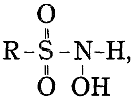
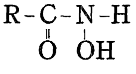
Experimental

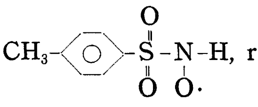
N-methyl, N-nitroso, p-toluenesulufonamine (N-methyl, N-nitroso, p-tosylamine) was purcharsed from Tokyo Kasei and used without further purification. Sample was dissolved in toluene by *ca.* 10^{-1} mol. and bubbled through oxygen gas. 500 W Xe lamp made by WACOM was used as UV source and UV light was directly irradiated on the sample in the ESR cavity. Spectra were recorded by JEOL FE1X at room temperature.

Results and Discussion

Photolysis of N-methyl, N-nitroso, p-toluenesulufonamine for *ca.* 15 min. produced a well resolved spectrum shown in Fig. 1 (a). This triplet quartet spectrum is consisted of the triplet with a relative intensity of 1 : 1 : 1 and the quartet with a relative intensity of 1 : 3 : 3 : 1. The former is attributed to a nitrogen nucleus with a coupling of *ca.* 12 G and the latter is ascribed to three equivalent methyl protons with a spacing of *ca.* 10 G. This spectrum is considered to be attributed to N-methyl, p-toluenesulufo nitroxide radical, radical (I), on the basis of their hyperfine coupling constants and g values shown in Table 1. Hyperfine coupling constants of nitrogen and hydrogen are larger than those of N-methyl carbonyl nitroxide radicals which are planar structure.[4)]

The fact that photolysis of N-methyl, N-nitroso, p-touluenesulufonamine leads to not N-methyl p-toluenesulufo amidyl but N-methyl, p-toluenesulufo nitroxide radical by the cleavage of N-NO bond is very interesting. A striking analogy is found in photolysis of N-nitoroso amides which generate N-acyl, N-alkyl nitroxide radicals. This radical was relatively stable but replaced by one consisting of triplet of triplets under further irradiation.

The spectrum shown in Fig. 1 (b) is attributed to result from a nitroxide of new type, showing a triplet due to nitrogen and a triplet due to two equivalent protons, on the basis of their A_N and g values as seen in Table. This ESR pattern is encountered in oxidation of hydroxamic acids with  $\mathrm{R{-}\overset{O}{\underset{O}{S}}{-}\underset{OH}{N}{-}H}$, or  $\mathrm{R{-}\underset{O}{C}{-}\underset{OH}{N}{-}H}$ structure.[4)]

The nitroxide obtained here therefore is attributed to p-toluene sulufo nitroxide cation radical, radical (II). However, such p-toluene sulufo nitroxide as radical found in p-toluenesulufo hydroxamic acid was not observed. It is considered that p-toluenesulufo nitroxide radical, , radical (V), is too unstable to detect although the

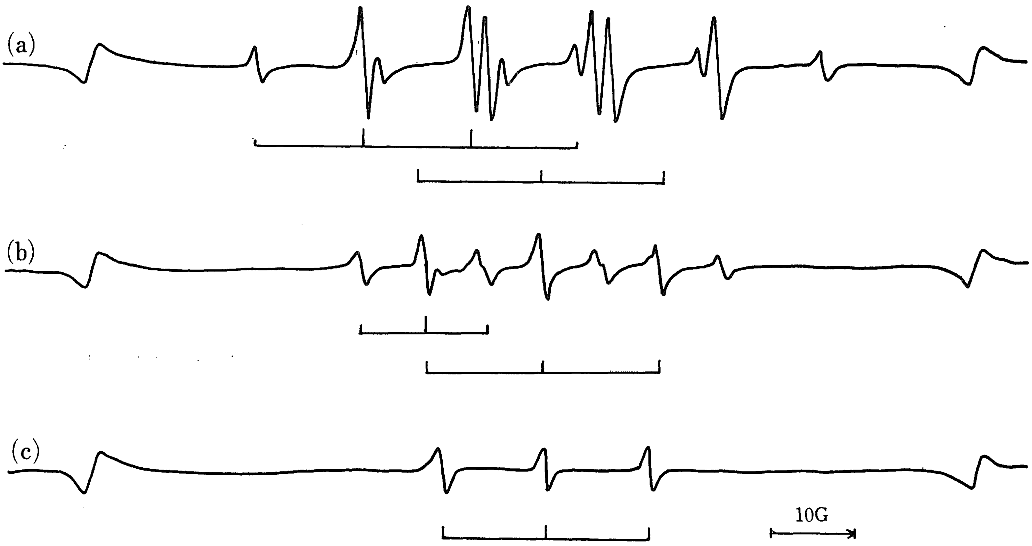
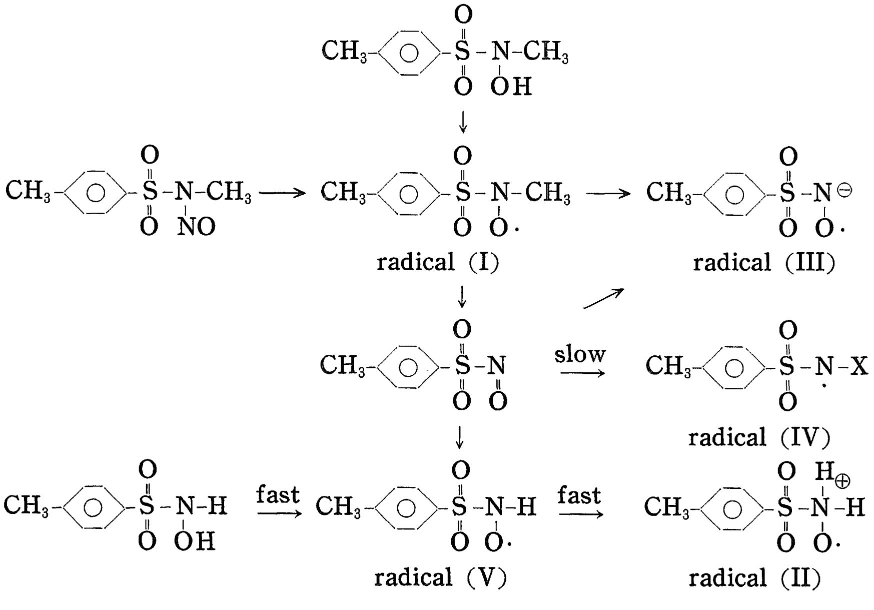


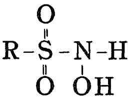
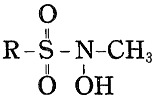
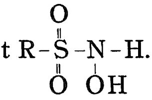
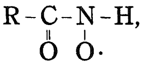
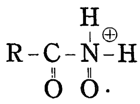
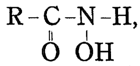
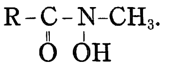
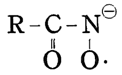
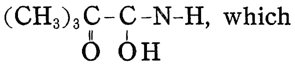
Fig. 1 ESR Spectra of nitroxide radicals derived from UV–irradiated N–methyl, N–nitroso, p–toluenesulufonamine.

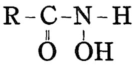
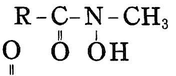
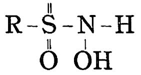
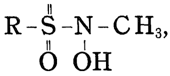
radical is essential for the formation of p-toluenesulufo nitroxide cation radical. Since the formation of nitroso compounds from nitroxide are also found in oxidation of N-aryl nitroxide,[4,5] it is reasonable to assume that such radical (II) and (V) are resulted from not p-toluenesulufo hydroxamic acid as impurties contaminated in N-methyl, N-nitroso, p-toluenesulufonamine, but nitroso compound created in oxidation of N-methyl, N-nitroso, p-toluenesulufonamine. Although the mechanism for the formation of radical (V) is not clear, this radical is presumably produced by an addition of hydrogen to nitroso compound. The reaction scheme for the formation of radical (II) and (V) can be visualized as below.



By further irradiation, a weak triplet with a relative intensity of 1:1:1 and a coupling constant of *ca.* 10 G was seen by overlapping with the spectrum due to radical (II). Although no hyperfine due to other nucleus than nitrogen is observed in this triplet as seen from Fig. 1 (c), this radical is interpreted to a nitroxide radical on the basis of their g and A_N values. This ESR pattern was also found in oxidation of N-methyl toluene sulufo hydroxamic acid, or benzene sulufo hydroxamic acid. This radical may therefore be a p-tosyl nitroxide anion, radical (III), derived from nitroso compound.

After the spectrum due to the radical (III) was disappeared, a new triplet with a coupling constant of 29.5 G is found. This radical is assumed to be an amidyl radical[6] since nitrogen hyperfine coupling is remarkably large and g value is very small for the nitroxide radicals. This amidyl radical is also considered to be created by the reaction with other molecule although the structure of the amidyl radical is not proved.

In photolysis of N-methyl, N-nitroso, p-toluenesulufonamine, the clavage of N-NO bond first was occured, following by the formed N-methyl, p-toluenesulufo nitroxide radical changed into nitroso compound as in oxidation of N-aryl hydroxamic acids.[4,5] Radical (II), and (III) created under further photolysis might be resulted from not radical (I) but nitroso compound. According to previous works,[4] redical (II) was also found in oxidation of sulufohydroxamic acids,  $\mathrm{R-\overset{O}{\underset{O}{S}}-\underset{OH}{N}-H}$ type and thus radical (III) was observed in not only N-methyl, sulufohydroxamic acids  $\mathrm{R-\overset{O}{\underset{O}{S}}-\underset{OH}{N}-CH_3}$ but  $\mathrm{R-\overset{O}{\underset{O}{S}}-\underset{OH}{N}-H}$. On the other hand,  $\mathrm{R-\underset{O}{C}-\underset{O\cdot}{N}-H}$, or/and  $\mathrm{R-\underset{O}{C}-\overset{H}{\underset{O\cdot}{N^{\oplus}}}-H}$ radical were found in many hydroxamic acids  $\mathrm{R-\underset{O}{C}-\underset{OH}{N}-H}$, but not detected in N-mehtyl hydroxamic acids  $\mathrm{R-\underset{O}{C}-\underset{OH}{N}-CH_3}$. Furthermore,  $\mathrm{R-\underset{O}{C}-\underset{O\cdot}{N^{\ominus}}}$ radical is found only in valeric hydroxamic acid,  $\mathrm{(CH_3)_3C-\underset{O}{C}-\underset{OH}{N}-H}$, which is a nonplanar molecule because of possessing a bulky substituent.

These results might show that nitroxide radicals resulted from hydroxamic acids  $\mathrm{R-\underset{O}{C}-\underset{OH}{N}-H}$ or  $\mathrm{R-\underset{O}{C}-\underset{OH}{N}-CH_3}$ type were stable but nitroxide produced in sulufo hydroxamic acids  $\mathrm{R-\overset{O}{\underset{O}{S}}-\underset{OH}{N}-H}$ or  $\mathrm{R-\overset{O}{\underset{O}{S}}-\underset{OH}{N}-CH_3}$, or N-methyl, N-nitroso sulufonamine instantly changed into nitroso compound. Thus nitroso compound created here produced many radicals (II)-(V), although radical (V) is not detected here. These results that nitroso compounds were unstable to react with other molecule to produce many radicals may suggest behaviors of such compounds as N-methyl, N-nitroso sulufonamine *in vivo.*

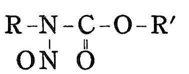
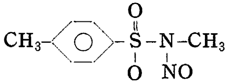
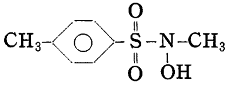
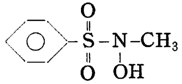
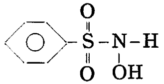
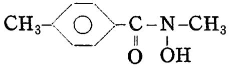
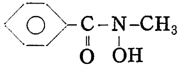
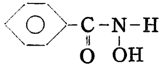
Observation of nitroxide or amidyl radical derived in photolysis of N-methyl, N-nitroso, p-toluenesulufonamine provide many interest informations on precarcinogen such as nitroso compounds. Further studies on radicals derived from N-nitroso compound such as N-nitroso urethane  $\mathrm{R-\underset{ON}{N}-\underset{O}{C}-O-R'}$ are necessary for researching nitroso compounds as precarcinogen.

Table 1 ESR Parameters of nitroxide radicals derived from UV-irradiated hydroxamic acids.

radicals	$R-\overset{O}{\underset{O}{S}}-\underset{O\cdot}{N}-CH_3$			$R-\overset{O}{\underset{O}{S}}-\underset{O\cdot}{N}-H$			$R-\overset{O}{\underset{O}{S}}-\underset{O\cdot}{\overset{H^{\oplus}}{N}}-H$			$R-\overset{O}{\underset{O}{S}}-\underset{O\cdot}{N^{\ominus}}$	
compounds	g value	A_N(G)	A_N(G)	g value	A_N(G)	A_N(G)	g value	A_N(G)	A_N(G)	g value	A_N(G)
	2.0060	12.3	10.4				2.0060	11.6	6.2	2.0058	10.2
	2.0060	12.1	10.5							2.0062	10.6
	2.0060	11.9	10.5							2.0062	10.8
$CH_3-\overset{O}{\underset{O}{S}}-\underset{OH}{N}-CH_3$	2.0062	10.3	10.9							2.0065	11.3
				2.0064	9.1	8.18	2.0063	10.5	2.9	2.0059	10.3
	$R-\underset{O}{C}-\underset{O\cdot}{N}-CH_3$			$R-\underset{O}{C}-\underset{O\cdot}{N}-H$			$R-\underset{O}{C}-\underset{O\cdot}{\overset{H^{\oplus}}{N}}-H$			$R-\underset{O}{C}-\underset{O\cdot}{N^{\ominus}}$	
	2.0067	7.7	8.3								
	2.0068	7.5	8.4								
$CH_3-\underset{O}{C}-\underset{OH}{N}-CH_3$	2.0065	7.4	8.5								
				2.0070	6.14	10.4	2.0069	7.3	5.5		
$CH_3-\underset{O}{C}-\underset{OH}{N}-H$				2.0067	6.08	10.6					
$(CH_3)_3C-\underset{O}{C}-\underset{OH}{N}-H$				2.0064	7.3	8.5	2.0066	7.8	3.2	2.0066	8.1

References

1) J. A. Miller, C. S. Wyatt, E. C. Miller, and H. A. Hartmao, Cancer Res., **21,** 1465 (1961).
2) H. Bartsch, Mtraut, and E. hecker, Biochim. Biophys. Acta, **237.** 556 (1971).
3) A. R. Forrester, M. M. Ogilvy, and R. H Thomason, J. Chem. Soc., (C), 1981, **1970**.
4) Unpublished data. These data will be reported in J. Chem. Phys.
5) J. I. G. Cadogan, R. M. Paton, and C. Thomson, J. Chem. Soc., (B), 583, **1971**.