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Structure and Reactivity of Nitroso Oxides

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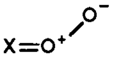
Abstract: The presence of nitroso oxide intermediates has been studied in the photooxidation of phenyl azide. The hydroxylation of benzenes occurred and was accelerated by electron-donating groups. Sulfides were oxidized to sulfoxides, but the oxygenation and deoxygenation of sulfoxides proceeded concurrently; these reactions were facilitated by electron-donating substituents. Trapping of the intermediates by added nitrosobenzenes was most efficient, approaching 80% O transfer. The relative reactivity order (styrenes, PhN=O ≫ Ph_2S > Ph_2SO > PhH), substituent effects, and the stereochemistry of hydroxylation of C-H bonds characterized the electrophilic radical nature of nitroso oxides. An ^{18}O-tracer study revealed that a unimolecular isomerization of nitroso oxides to nitro compounds proceeds competitively with the O transfers. The reactivity of XOO species is discussed on the basis of electronegativity of X.

Structure and reactivity of nitrene intermediates in the thermolysis or photolysis of azides have been thoroughly studied by means of product analysis,[1] matrix isolation techniques,[2] and laser flash spectroscopy.[3,4] Reactions of nitrenes are important in various fields of organic chemistry and are also useful in photoaffinity labeling[5] and as photoresists.[6] The decompositions of azides in the presence of oxygen often result in complex reactions that yield tarry products incorporating oxygen. The interaction of nitrenes with oxygen is sometimes inevitable when the intermediates are to be produced under aerobic conditions as in photolabeling or in photoresists. However, the reaction of nitrene intermediates with oxygen has not been thoroughly clarified. It is known that the photooxidation of arylnitrenes yields the corresponding nitro compounds[7] and that the chain decomposition of azides is effectively inhibited by oxygen.[8] Although an ESR study in low-temperature matrices revealed some structural evidence for intermediate nitroso oxides (**1**, X = RN),[9] little is known about their reactivity.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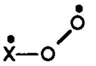
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Table I. Products from the Photolysis of Phenyl Azide under Oxygen[a]

run	substrate	products (%)[b] $PhNO_2$	products (%)[b] others
1	under argon	<1	PhN=NPh (41)
2		34	PhN=O (~4)
3	0.1 M $Ph_2C=O$[c]	31	PhN=O (3)
4	10% benzene	33	PhOH (15)
5	10% toluene	32	cresol (12), PhCHO (5), $PhCH_2OH$ (0.6)
6	10% cyclohexane	41	cyclohexanone (5), cyclohexanol (17)
7	0.1 M Ph_2S	25	Ph_2SO (9)
8	0.1 M Ph_2SO	24	Ph_2SO_2 (13), Ph_2S (5)
9	0.005 M *p*-$ClC_6H_4N=O$	8	*p*-$ClC_6H_4NO_2$ (43)
10	0.01 M *p*-$ClC_6H_4N=O$	3	*p*-$ClC_6H_4NO_2$ (45)

[a] Acetonitrile solutions of 5 mM PhN_3 were irradiated at >350 nm under oxygen, unless otherwise noted, for 4-5 h at ca. 20 °C. Conversions of PhN_3 were 70-90%. [b] Products were determined by GLC and percent yields are based on PhN_3 consumed. The amounts of nitrosobenzene were determined only for runs 1-3. [c] Since the absorbances of 5 mM PhN_3 and 0.1 M $Ph_2C=O$ at 366 nm are 0.043 and >2, respectively, over 98% of light was absorbed by benzophenone.

We became interested in the chemistry of carbonyl oxides (X = R_2C),[10,11] which are known to be intermediates in the reaction of olefins with ozone,[12] of diazo compounds with singlet oxygen or of carbenes with oxygen.[13] The most characteristic reaction of carbonyl oxides is a nucleophilic oxygen transfer, indicating the importance of dipolar structure **1a**.[10a] The related dioxirane species (**2**, X = R_2C),[14] produced from ketones and monoperoxysulfate, are recently revealed to be stable enough to be isolated and to react as typical electrophilic oxidants.[15] These facts indicate that carbonyl oxides and dioxiranes are different species and not interconvertible into one another. For the case of persulfoxides (**1**, X = R_2S), the dipolar structure **1** is of importance,

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[1] (a) Reiser, A.; Wagner, H. M. In *The Chemistry of the Azido Group*; Patai, S., Ed.; Interscience: New York, 1971; p 221. (b) Abramovitch, R. A.; Kyba, E. P. *Ibid.* 1971; p 256. (c) Smith, P. A. S. In *Nitrenes*; Lwowski, W., Ed.; Wiley: New York, 1970. (d) Scriven, E. F. V. In *Reactive Intermediates*; Abramovitch, R. A., Ed.; Plenum Press: New York, 1982; Vol. 2.

[2] (a) Chapman, O. L.; LeRoux, J.-P. *J. Am. Chem. Soc.* **1978**, *100*, 282. (b) Dunkin, I. R.; Thomson, P. C. P. *J. Chem. Soc., Chem. Commun.* **1982**, 1192. (c) Dunkin, I. R.; Donnelly, T.; Lockhart, T. S. *Tetrahedron Lett.* **1985**, *26*, 359. (d) Donnelly, T.; Dunkin, I. R.; Norwood, D. S. D.; Prentice, A.; Shields, C. J.; Thomson, P. C. P. *J. Chem. Soc., Perkin Trans. 2* **1985**, 307.

[3] (a) Schrock, A. K.; Schuster, G. B. *J. Am. Chem. Soc.* **1984**, *106*, 5228. (b) Schrock, A. K.; Schuster, G. B. *Ibid.* **1984**, *106*, 5234. (c) Liang, T.-Y.; Schuster, G. B. *Ibid.* **1986**, *108*, 546. (d) Liang, T.-Y.; Schuster, G. B. *Ibid.* **1987**, *109*, 7803. (e) Shields, C. J.; Chrisope, D. R.; Schuster, G. B.; Dixon, A. J.; Poliakoff, M.; Turner, J. J. *Ibid.* **1987**, *109*, 4723. (f) Sigman, M. E.; Autrey, T.; Schuster, G. B. *Ibid.* **1988**, *110*, 4297.

[4] Leyva, E.; Platz, M. S.; Persy, G.; Wirz, J. *J. Am. Chem. Soc.* **1986**, *108*, 3783.

[5] (a) Knowles, J. R. *Acc. Chem. Res.* **1972**, *5*, 155. (b) Bayley, H.; Knowles, J. R. *Methods Enzymol.* **1977**, *46*, 69.

[6] (a) *Photopolymer*; Technical Association of Photopolymer, Japan, Ed.; CMC: Tokyo, 1977. (b) Tsuda, M.; Oikawa, S.; Yokota, a.; Yabuta, M.; Kanai, W.; Kashiwagi, K.; Hijikata, I.; Nakane, H. *Polym. Eng. Sci.* **1983**, *23*, 993.

[7] (a) Abramovitch, R. A.; Challand, S. R. *J. Chem. Soc., Chem. Commun.* **1972**, 964. (b) Schriven, E. F. In *Reactive Intermediates*; Abramovitch, R. A., Ed.; Plenum: New York, 1982; Vol. 2, p 18.

[8] (a) Lee Go, C.; Waddell, W. H. *J. Org. Chem.* **1983**, *48*, 2897. (b) Waddell, W. H.; Lee Go, C. *J. Am. Chem. Soc.* **1982**, *104*, 5804. (c) Costantino, J. P.; Richter, H. W.; Lee Go, C.; Waddell, W. H. *Ibid.* **1985**, *107*, 1744.

[9] Brinen, J. B.; Singh, B. *J. Am. Chem. Soc.* **1971**, *93*, 6623.

[10] (a) Sawaki, Y.; Kato, H.; Ogata, Y. *J. Am. Chem. Soc.* **1981**, *103*, 3832. (b) Sawaki, Y.; Ishiguro, K. *Tetrahedron Lett.* **1984**, *25*, 1487. (c) Ishiguro, K.; Hirano, Y.; Sawaki, Y. *J. Org. Chem.* **1988**, *53*, 5397.

[11] (a) Kumar, S.; Murray, R. W. *J. Am. Chem. Soc.* **1984**, *106*, 1040. (b) Mitchell, J. C. *Chem. Soc. Rev.* **1985**, *14*, 399.

[12] (a) Bailey, P. S. *Ozonation in Organic Chemistry*; Academic Press: New York, 1978; Vol. 1; 1982; Vol. 2. (b) Kuczkowski, R. L. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; Vol. 2 p 197.

[13] Highly, D. P.; Murray, R. W. *J. Am. Chem. Soc.* **1974**, *96*, 3330.

[14] Review: (a) Murray, R. W. *Chem. Rev.* **1989**, *89*, 1187. (b) Adam, W.; Curci, R.; Edwards, J. O. *Acc. Chem. Res.* **1989**, *22*, 205.

[15] (a) Edward, J. O.; Pater, R. H.; Curci, R.; Furia, F. D. *Photochem. Photobiol.* **1979**, *30*, 63. (b) Gallopo, A. R.; Edwards, J. O. *J. Org. Chem.* **1981**, *46*, 1684. (c) Murray, R. W.; Jeyaraman, R. *Ibid.* **1985**, *50*, 2847. (d) Cassidei, L.; Fiorentino, M.; Mello, R.; Sciacovelli, O.; Curci, R. *Ibid.* **1987**, *52*, 699.

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Table II. Hydroxylation of Substituted Benzenes (C_6H_5X) during the Photooxidation of Phenyl Azide[a]

substituent X	relative rates[b]	isomer ratios (o:m:p)	partial rate factors		
			o	m	p
MeO	5.98	66:<1:34	12	<0.2	12
Me	2.59	60:15:25	4.7	1.2	3.9
H	1.00		1.0	1.0	1.0
Cl	0.56	51:25:24	0.86	0.42	0.81

[a] For reaction conditions, see footnote *a* in Table I. Product yields were determined by GLC. [b] Relative rates for the hydroxylation were determined from competitive reactions in the presence of 15 volume % of each arene.

their characteristic reaction being nucleophilic O transfer.[16]

In relation to reactions of carbonyl oxides and persulfoxides, we were interested in the reactivity of nitroso oxides (**1**, X = RN).[17] Herein, we summarize our trapping and tracer studies on the reactions of nitroso oxides. In contrast to the cases of carbonyl oxides and persulfoxides, nitroso oxides are shown to behave as electrophilic peroxy radicals and to isomerize easily to the cyclic form **2**, therefore yielding nitro compounds.

Results

Photolysis of Phenyl Azide under Oxygen. Irradiation of 2–10 mM phenyl azide in acetonitrile under argon at >350 nm using a 300-W medium-pressure Hg lamp afforded 30–40% of azobenzene. In the presence of oxygen, the yield of azobenzene decreased to almost zero (<1%) and instead a 30% yield of nitrobenzene together with a small amount (3–5%) of nitrosobenzene was obtained as shown in Table I. The reaction may simply be written as eq 1. The other products from the azide were of nonvolatile tarry materials.[18] The decomposition rate and products were practically the same when benzophenone was added as a triplet sensitizer (run 3). As noted previously,[7a] singlet oxygen is not involved in the photolysis since tetraphenylporphine, an $^1O_2$ sensitizer, retarded the photoreaction significantly; e.g., the photolysis in the presence of 0.1 mM sensitizer was slowed down 4-fold.

$$PhN_3 \xrightarrow{h\nu} PhN \xrightarrow{O_2} PhNOO \twoheadrightarrow PhNO_2 + PhN{=}O \qquad (1)$$

Addition of various substrates in the photooxidation of PhN_3 resulted in oxygen transfers such as the hydroxylation of cyclohexane (run 6) and benzene (run 4 in Table I). While sulfides were oxidized to sulfoxides (run 7), both O transfer and O abstraction from sulfoxides occurred concurrently as shown in run 8 in Table I. Details of this reaction will be described later. The oxygen transfer to nitrosobenzenes to yield nitro compounds was the most efficient; for example, the addition of 0.01 M *p*-chloronitrosobenzene resulted in the formation of *p*-chloronitrobenzene in 45% yield. These facts indicate that an O-transfer ring intermediate is produced at least in ca. 50% yield.

Control experiments showed that these O transfers occur only in the copresence of PhN_3, O_2, and substrate under irradiation. O transfers were not observed with $PhNO_2$ or PhN=O in place of PhN_3. Diphenyl sulfide or sulfoxide did not react with singlet oxygen under the reaction conditions (e.g., 5-h irradiation in the presence of tetraphenylporphine). These facts suggest that the present O transfers proceed clearly via nitroso oxide intermediates, which have been sometimes postulated[3d,7] but never clearly demonstrated. The detailed features on their reactivity are described in the following.

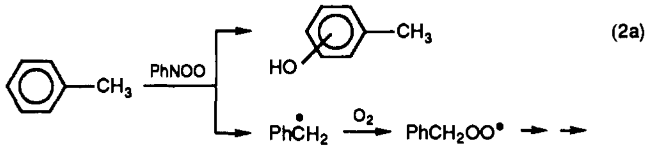
Reaction of Nitroso Oxide Intermediates with Benzenes. The hydroxylation of benzenes proceeded, during the photooxidation of PhN_3, to afford phenols in 10–20% yields as exemplified in runs 4 and 5 in Table I. The relative rates for the hydroxylation of substituted benzenes were determined competitively and are listed in Table II. The hydroxylation rates were much higher for benzenes with electron-donating groups, i.e., the decreasing order of anisole > toluene > benzene > chlorobenzene. In the case of anisole, the hydroxylation took place solely at o,p-positions. In Table II are also listed the derived partial rate factors for the hydroxylation. The Hammett's ρ values calculated for the m- and p-positions are -1.49 vs σ^+ ($r = 0.976$) and -1.96 with σ ($r = 0.898$), r being the correlation coefficient. The correlation with σ^+ was more satisfactory, and the negative ρ value reflects the electrophilic nature of nitroso oxide intermediates.

Table III. Products from Saturated Hydrocarbons in the Photooxidation of Phenyl Azides and Hydrogen Peroxide

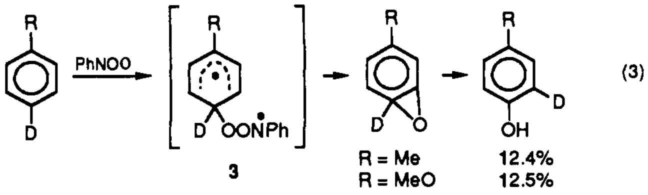
run	conditions	substrate	product (%)[a]	
			$PhNO_2$	alcohols
11	PhN_3/O_2[b]	5% isopentane	42	pentanols (2.7; 1°:2°:3° = 1.0:1.7:6.3)
12	H_2O_2/O_2[c]	5% isopentane		pentanols (1; 1°:2°:3° = 1.0:1.2:6.7)
13	PhN_3/O_2[b]	10% *cis*-decalin[d]	39	9-decalol (11.3; cis:trans = 65:35)
14	PhN_3/O_2[b]	10% *trans*-decalin[d]	53	9-decalol (2.8; cis:trans = 2:98)
15	H_2O_2/O_2[c]	10% *cis*-decalin[d]		9-decalol (15; cis:trans = 31:69)
16	H_2O_2/O_2[c]	10% *trans*-decalin[d]		9-decalol (6; cis:trans = 4:96)

[a] Percent yields based on PhN_3 or H_2O_2 charged. [b] Acetonitrile solutions (5 mM) were irradiated at >350 nm for 8 h, unless noted otherwise. Conversions of PhN_3 were 80–90%. [c] 10 mM H_2O_2 in place of PhN_3, irradiated at >250 nm. [d] To solubilize decalin, 25% CH_2Cl_2 was added.

For the case of toluene and anisole, the side chain oxidation proceeded competitively. For example, toluene afforded, in addition to cresols (12%), PhCHO (5%) and $PhCH_2OH$ (0.6%) as shown in run 5 in Table I. The significant formation of benzaldehyde seems to suggest a side chain oxidation via hydrogen atom abstraction such as eq 2b. Under the same conditions, anisole gave 2.6% PhOH in addition to methoxyphenols (11%). The formation of phenol is similarly explicable by the hydrogen abstraction; e.g., $PhOCH_2^\bullet \rightarrow PhOCH_2OO^\bullet \rightarrow PhOCH_2OH \rightarrow PhOH$. Since bibenzyl was not detected from toluene in a control experiment under argon (i.e., run 5 under Ar), phenylnitrene intermediates are not involved for the side chain oxidation.



A possible involvement of the NIH shift[19] was examined for the hydroxylation of anisole-4-*d* and toluene-4-*d*. GC–MS analysis of the resulting *p*-phenols showed 12% content of deuterium, i.e., 12% of the NIH shift. This suggests that the hydroxylation involves arene oxide intermediates. One likely pathway is eq 3,



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[16] Sawaki, Y.; Ogata, Y. *J. Am. Chem. Soc.* **1981**, *103*, 5947.

[17] Preliminary report: Sawaki, Y.l; Ishikawa, S.; Iwamura, H. *J. Am. Chem. Soc.* **1987**, *109*, 584.

[18] The elemental analysis of the tarry product afforded a C:H:N:O ratio of 5.62:5.01:1.00:2.00, i.e., very close to $(C_6H_5NO_2)_n$, but its IR and NMR spectra showed very broad bands devoid of any characteristic absorptions. The material is probably a polymerized photooxidation product of tetrahydroazepine.

[19] (a) Jerina, D. M.; Daly, J. W. *Science (Washington, D.C.)* **1974**, *185*, 573. (b) Hamilton, G. A. In *Molecular Mechanism of Oxygen Activation*; Hayaishi, O., Ed.; Academic: New York, 1974; p 405.

Table IV. Relative Rates for the Reaction of Nitroso Oxide with Substituted Diphenyl Sulfides and Sulfoxides[a]

substituent in Ar	Ar_2S[b,e]	Ar_2SO[c,e]	
		Ar_2SO_2[f]	Ar_2S
p-MeO	2.2	1.8	d
p-Me	1.4	1.3	1.5
H	1.0	1.0	1.0
p-Cl	0.24	0.40	0.79

[a] Reaction of 5 mM PhN_3 and 50 mM each of substrates irradiated at >350 nm in $MeCN-CH_2Cl_2$ (3:1) for 6 h. [b] Formation of Ar_2SO from Ar_2S. [c] Products were diphenyl sulfoxides by O transfer and sulfides by O abstraction. [d] Not determined. [e] The Hammett ρ value vs σ is −0.93, and r (correlation coefficient) = 0.977. [f] ρ = −0.64, and r = 0.984.

which involves the cyclization of cyclohexadienyl radical **3** to form arene oxides followed by the migration of D. As a related reaction, Murray et al.[11a] have reported an NIH shift of a methyl group in the reaction of carbonyl oxides with polymethylated benzenes.

Reaction with Aliphatic Hydrocarbons. Cyclohexane was converted to cyclohexanol and cyclohexanone (run 6 in Table I). The relative reactivity of C–H bonds was determined from the relative yields of primary, secondary, and tertiary alcohols from isopentane (see Experimental Section for details). From the product ratios in run 11 in Table III, the relative reactivities are 1:7.2:62 for primary, secondary, and tertiary CH, respectively. This ratio is very close to that of 1:5.4:60 for hydroxyl radicals formed in the photolysis of H_2O_2 in MeCN (run 12 in Table III). It is interesting to note that nitroso oxides behave similarly to the typical electrophilic hydroxyl radical.

The stereochemistry of the hydroxylation by nitroso oxides was examined for the case of decalin. While *trans*-decalin afforded *trans*-decalol, *cis*-decalin yielded a mixture of cis and trans alcohols (runs 13 and 14 in Table III). Similar results were obtained with hydroxyl radicals as shown in runs 15 and 16. There results are in sharp contrast to the case of dioxiranes where oxygen atoms are inserted in C–H bonds stereospecifically.[20]

Reaction with Sulfides and Sulfoxides. Sulfides were oxidized by nitroso oxide intermediates to sulfoxides. Relative reactivities were determined by competition methods with substituted diphenyl sulfides as listed in Table IV. The data afforded the ρ value of −0.98 vs σ, indicating an electrophilic nature of the nitroso oxide. In the reaction with sulfoxides, both the oxidation and reduction, i.e., O transfer and O abstraction, occurred concurrently (eq 4).

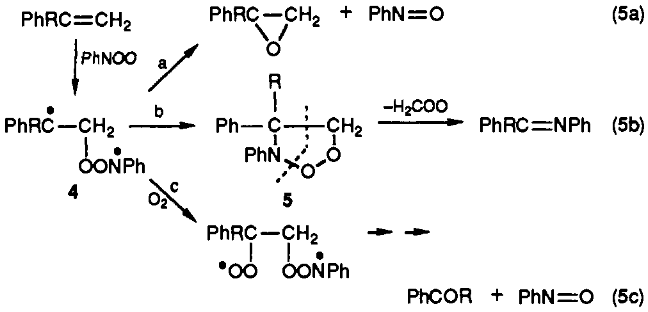
$$Ar_2SO \xrightarrow{PhN_3/O_2/h\nu} Ar_2SO_2 + Ar_2S \qquad (4)$$

The O transfer to sulfoxides resulted with a ρ value of −0.64 vs σ, and the deoxygenation also showed a similar trend of substituent effect; i.e., both reactions are accelerated by electron-donating groups.

Competitive experiments showed that diphenyl sulfide is 5.7 times as reactive as diphenyl sulfoxide. The relative reactivity is in sharp contrast to the case of carbonyl oxides where the relative rate was $Ph_2SO \gg Ph_2S$ and the ρ values for diphenyl sulfoxides were positive.[10,21a,b] While carbonyl oxides showed a nucleophilic attack on sulfoxides, the nitroso oxides react as electrophiles. Another interesting point in the reaction of nitroso oxides is the deoxygenation of sulfoxides. A plausible deoxygenation by nitrene intermediate is not likely since the photolysis in the absence of oxygen resulted in no reaction with sulfoxides, affording azobenzene only. It is then apparent that the deoxygenation proceeds by an intervention of nitroso oxides. Recently, we have reported a deoxygenation of sulfoxides by a carbonyl oxide with a strongly electron attracting CF_3 group.[21c] The present deoxygenation may proceed by a similar pathway, but a conclusion should only be discussed after more detailed experiments including a tracer study are carried out.

Reaction with Olefins. Reaction of nitroso oxides with styrenes gave C–C cleavage products, not affording epoxides. For example, an irradiation of 10 mM styrene and 5 mM PhN_3 under oxygen afforded $PhNO_2$ (7%), PhCHO (18%), and PhCH=NPh (6%), yields being based on azide consumed. In a reaction with 0.1 M styrene, the yield of $PhNO_2$ only was reduced to <1%. The photooxidation of 5 mM PhN_3 and 10 mM α-methylstyrene yielded $PhNO_2$ (12%), PhCOMe (9%), and PhMeC=NPh (13%); the epoxidation was inefficient, i.e., ≤1%.

One possible scheme for the formation of these products is outlined in eqs 5a–c. Very low yields of epoxides show that the epoxide-forming cyclization of **4** (path 5a) is not fast. Pathway 5b is one of the major reactions and involves cyclic peroxide **5** via the intramolecular coupling of diradical **4** or its one-step formation from olefin and PhNOO. A control experiment indicated that the imine formation proceeds only in the irradiated mixture of PhN_3, O_2, and olefin. No adduct formation between the azide and olefin was detected under the reaction conditions. Thus, pathway 5b is a likely one at the present time although the intermediacy of carbonyl oxide H_2COO was not ascertained. The C–C cleavage according to eq 5c is similar to a well-known reaction between olefins and peroxy radical ROO•.[22]



The reaction of nitroso oxide with cyclohexene (0.1 M) afforded no volatile product; the yields of cyclohexene oxide, cyclohexenol, or nitrobenzene were very low, i.e., below 1%. The result seems to indicate that nitroso oxide intermediates were effectively trapped by the olefin but the adduct was converted to tarry materials.

Trapping with Nitrosobenzenes. The photooxidation of PhN_3 under O_2 afforded 3–5% of nitrosobenzene in addition to nitrobenzene. As shown in runs 9 and 10 in Table I, the yield of $PhNO_2$ was reduced dramatically by the addition of substituted nitrosobenzene ArN=O, affording in turn high yields of $ArNO_2$. That is, a highly efficient O transfer occurs to ArN=O. This seems to indicate that nitroso oxides behave as efficient radical scavengers since nitroso compounds are well-known spin-trapping agents.[23] Here, the photooxidation of PhN_3 in the presence of 5–10 mM ArN=O was reduced to only 60–70%, owing to light absorption by ArN=O; a control experiment showed that nitrobenzenes were not formed in the photooxidation of ArN=O alone.

The O transfer to nitrosobenzene increased with increasing [ArN=O] and approached a constant value at the higher concentrations. The reciprocal plot of the yield of $ArNO_2$ vs [ArN=O] was linear as shown in Figure 1. From its intercept, the yields of $ArNO_2$ at [ArN=O] = ∞ were calculated to be 77 and 83% for *p*-chloro- and *p*-methylnitrosobenzene, respectively. This means that the nitroso oxide intermediate is produced in ca. 80% yield.

A likely scheme for the O transfer to ArN=O is shown in eq 6a or 6b. If the O transfer proceeds via the cleavage of **6** (path 6a), the resulting nitro compound is solely from ArN=O. Or, if the O transfer is via the cyclic peroxide **7** (path 6b), the product from **7** should be a mixture of $PhNO_2$ and $ArNO_2$. In order to choose pathway 6a or 6b, amounts of nitrobenzenes were determined in the photooxidation of PhN_3 (5 mM) in the presence of

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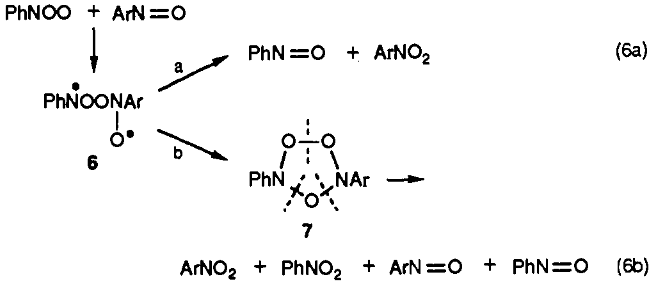
(20) Murray, R. W.; Jeyaraman, R.; Mohan, L. *J. Am. Chem. Soc.* **1986**, *108*, 2470.

(21) (a) Adam, W.; Haas, W.; Sieker, G. *J. Am. Chem. Soc.* **1984**, *106*, 5020. (b) Adam, W.; Lohray, B. B. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 188. (c) Ishiguro, K.; Hirano, Y.; Sawaki, Y. *Tetrahedron Lett.* **1987**, *28*, 6201.

(22) Mayo, F. R. *Acc. Chem. Res.* **1968**, *1*, 193.

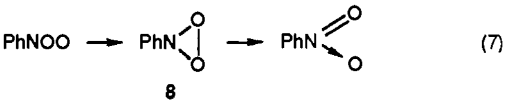
(23) (a) Terabe, S.; Konaka, R. *J. Am. Chem. Soc.* **1969**, *91*, 5655. (b) Janzen, E. G. *Acc. Chem. Res.* **1971**, *4*, 31.



an excess amount (i.e., >0.01 M) of *p*-Cl- or *p*-$MeC_6H_4N{=}O$; the resulting products were solely *p*-Cl- or *p*-$MeC_6H_4NO_2$, $PhNO_2$ being only formed in a trace amount. This result could not be explained on the basis of the symmetrical peroxide **7** of eq 6b. Thus, it is concluded that pathway 6a is likely for the O transfer to ArN=O, affording solely $ArNO_2$.

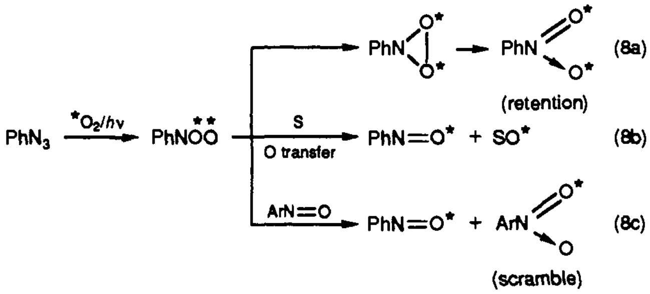
It is interesting to note that the reaction 6a involves the formation of two nonradicals from diradical **6**. A related reaction is the β-scission of alkoxy radicals to yield a ketone an an alkyl radical (i.e., $R^1R^2R^3C{-}O^\bullet \rightarrow R^1R^2C{=}O + R^{3\bullet}$).[24] The present reaction of eq 6a involves a double β-scission of 1,5-diradical **6** and a cleavage of a weak O–O bond. Probably this is the driving force for the facile β-scission of **6** (eq 6a).

^{18}O-Tracer Study for the Formation of Nitrobenzene. An easily conceivable pathway for the formation of nitrobenzene involves an isomerization of the nitroso oxide to a dioxaziridine (**8**) (eq 7). To examine this pathway, a detailed ^{18}O-tracer study with $^{18}O_2$ was carried out and the results are shown in Figure 2 and Table V. Here, retention means that the two oxygen atoms of



$PhNO_2$ are derived from the same molecule of O_2. Scrambling corresponds to a scrambling path in which the two oxygen atoms of $PhNO_2$ originate from two different molecules of O_2. In the absence of additives, the percent retention decreased gradually as shown in Figure 2A. Since the percent retention at low conversion is over 60%, the retention path is predominant at the initial stage. The effect of additives was examined, and the data in Table V show that percent retention in $PhNO_2$ changed with additives from 20 to 80%.

The ^{18}O-tracer data are well-understood by three competitive reactions, a unimolecular isomerization to nitrobenzene (eq 8a) and O transfers to substrate S (eq 8b) and to another ArN=O molecule (eq 8c). The retention path (eq 8a) was ascertained directly by the observed retention of $^*O_2$ in $PhNO_2$. The O transfer to substrate S is apparent in the product study shown in Tables I–IV and by the incorporation of *O in O-transferred products. The following reaction is eq 8c leading to the formation of scrambled nitrobenzenes $ArNO_2$. Since O transfers from nitroso oxide to substrates or solvents produce PhN=O, the combination of eqs 8b and 8c (Ar = Ph) surely leads to the formation of scrambled $PhNO_2$. The observed gradual decrease of the percent retention with increasing conversion (Figure 2A) reflects the increasing intervention of eqs 8b and 8c.



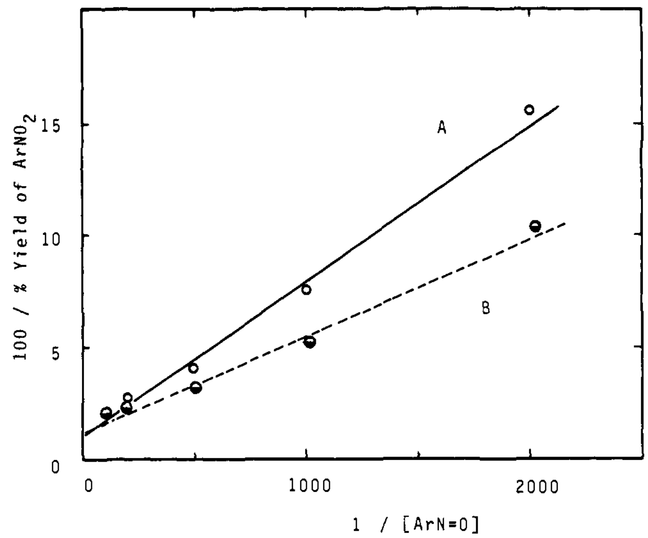
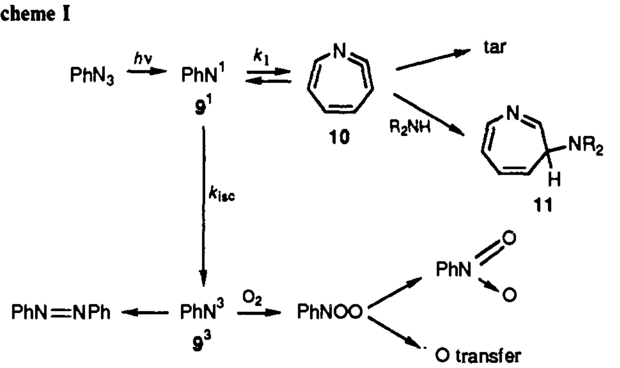


Figure 1. Reciprocal plots for the trapping of nitroso oxide with ArN=O: A, Ar = *p*-MeC_6H_4; B, Ar = *p*-ClC_6H_4.

Scheme I



The addition of another ArN=O to the photooxidation system of PhN_3 afforded additional evidence. When *p*-$ClC_6H_4N{=}O$ (i.e., Ar = *p*-ClC_6H_4) was added (Table V), the major product was scrambled $ArNO_2$ according to eq 8c. Another interesting result here is that although the yield of retained $PhNO_2$ was dramatically reduced (i.e., below 1%), the percent retention increased significantly. The reciprocal plot of 1/[reten] vs 1/[ArN=O] is linear as shown in Figure 2B, and the intercept at [ArN=O] = ∞ shows 96% retention. The linear correlation of Figure 2B indicates that the unimolecular cyclization of nitroso oxide (eq 8a) is competitive with O transfers such as those of eqs 8b and 8c. The decrease of the yield of scrambled $PhNO_2$ in the presence of added ArN=O is well-understood by the fact that the concentration of ArN=O is in large excess relative to that of PhN=O formed as an intermediate (i.e., [ArN=O] $\gg$ [PhN=O]). Similar results were obtained when *p*-$MeC_6H_4N{=}O$ was added.

The decrease of the percent retention in the presence of Ph_2SO (run 23 in Table V) is explicable by O transfer to the sulfoxide to yield Ph_2SO_2 and PhN=O (eq 8b), leading to the extensive scrambling in $PhNO_2$. In this case, the yield of scrambled $PhNO_2$ increases according to eq 8c (Ar = Ph) since another ArN=O is not added. The reaction in the presence of benzophenone, a triplet sensitizer (run 22), resulted in the practically same result as the direct irradiation (run 21).

Discussion

Formation of Nitroso Oxide. In Scheme I are summarized results obtained from recent studies[1-4] involving nitrene intermediates produced in the photolysis of phenyl azide. The photolysis of aromatic azides ArN_3 probably yields singlet (ArN^1) or triplet nitrene (ArN^3), but intermediates usually observed as studied in low-temperature matrices[2] or by laser flash spectroscopy are dehydroazepine **10** produced by ring expansion of ArN^1. Exceptional nitrenes without ring expansion are those with strongly

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[24] (a) Sawaki, Y.; Ogata, Y. *J. Am. Chem. Soc.* **1976**, *98*, 7324. (b) Sawaki, Y.; Ogata, Y. *J. Org. Chem.* **1976**, *41*, 2340.

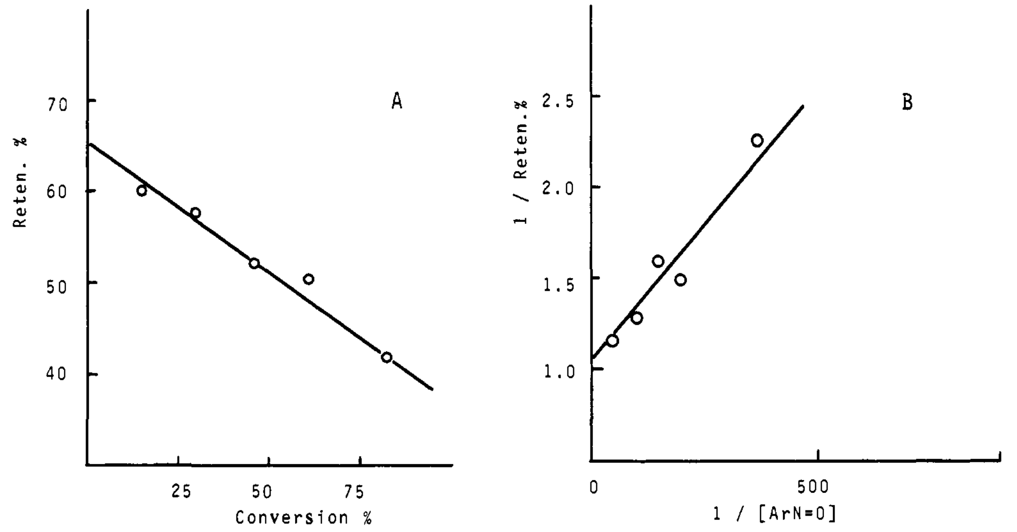


Figure 2. Retention percent of oxygen atoms in $PhNO_2$ from the photolysis of PhN_3 under $^{18}O_2/O_2$. See note *a* in Table V for conditions: A, retention percent vs conversion; B, reciprocal plot of retention percent of $PhNO_2$ vs [*p*-$ClC_6H_4N{=}O$].

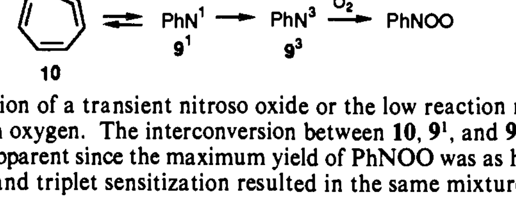
Table V. ^{18}O-Tracer Study on the Formation of Nitrobenzene in the Photolysis of Phenyl Azide under $^{18}O_2/O_2$[a]

		product (%)			formation of $PhNO_2$[c]	
run	additive	$PhNO_2$	others	mass data of $PhNO_2$[b] (M:(M + 2):(M + 4))	reten:scramb	$PhNO_2$ with retention (%)[d]
calcd						
	retention			100:0.6:8.4	100:0	
	scramble			100:16.8:0.7	0:100	
obsd						
17		24		100:11.1:3.7	37:63	8.9
18	6 mM ArN=O[e]	3	$ArNO_2$ (28)	100:6.4:4.8	63:37[f]	1.9
19	10 mM ArN=O[e]	<1	$ArNO_2$ (27)	100:4.2:6.9	78:22[f]	<1
20	20 mM ArN=O[e]	<1	$ArNO_2$ (39)	100:3.5:7.3	83:17[f]	<1
21[g]		23		100:16.8:7.5	44:56	10.1
22[g]	0.1 M $Ph_2C{=}O$	23		100:11.5:5.4	45:55	10.4
23[g]	0.1 M Ph_2SO	24	Ph_2SO_2 (22)	100:22.1:4.8	22:78	5.3

[a] Irradiation (8 h) of 5 mM PhN_3 at 350 nm in MeCN under oxygen ($^{32}O_2$:$^{34}O_2$:$^{36}O_2$ = 100:0.6:8.4). Conversions of PhN_3 were 72–96%, and product yields are based on PhN_3 consumed. [b] Mass spectral data on $PhNO_2$; M = 123. [c] Scramble means that the two oxygen atoms in $PhNO_2$ are derived from two different oxygen molecules. Retention means the formation of $PhNO_2$ from one molecule of oxygen. [d] Percent yields of $PhNO_2$ with retention based on PhN_3 consumed. [e] ArN=O is *p*-$ClC_6H_4N{=}O$. [f] The value for $PhNO_2$. [g] Irradiation (4 h) of 5 mM PhN_3 under oxygen ($^{32}O_2$:$^{34}O_2$:$^{36}O_2$ = 100:0.7:14.3). Calculated M:(M + 2):(M + 4) ratios are 100:0.7:14.3 and 100:28.6:2.0 for retention and scrambling, respectively. Conversions of PhN_3 were 65–88%.

electron attracting groups.[2b,3d] The usual observation of dehydroazepine (e.g., **10**) only seems to reflect its higher concentration together with higher absorbance of **10** compared to that of **9**. An elegant chemical trapping study by Platz et al.[4] on the temperature effect has shown that the ring expansion of $\mathbf{9}^1$ (i.e., k_1 in Scheme I) is much faster than the intersystem crossing to $\mathbf{9}^3$ (i.e., k_{isc}) at ambient temperature.

A laser flash study by Schuster et al.[3d] showed that the observed transient spectra of nitrene intermediates (**9** and/or **10**) were not altered by the addition of oxygen. This means the reaction of **9** or **10** with oxygen is not fast and the nitroso oxide intermediate, if formed, is of low absorbance. However, the present study reveals that the trapping of PhNOO by ArN=O in the PhN_3 photooxidation is as high as 80% yield. This fact suggests that the major reaction proceeds clearly by way of eq 9 in spite of the lack of



(9)

observation of a transient nitroso oxide or the low reaction rate of **9** with oxygen. The interconversion between **10**, $\mathbf{9}^1$, and $\mathbf{9}^3$ as eq 9 is apparent since the maximum yield of PhNOO was as high as 80% and triplet sensitization resulted in the same mixture of products as with direct irradiation. The relatively lower yields (e.g., 20–30%) of $PhNO_2$ for the photooxidation of PhN_3 alone may be due to a reaction of **10** with oxygen or with PhNOO. This is in line with the observed elementary ratio of C:H:N:O = 6:5:1:2 for tarry materials obtained.[18]

O Transfers by Nitroso Oxide Intermediates. The characteristic features of O transfers by nitroso oxide intermediates are summarized in the following. (1) Substituted benzenes are hydroxylated electrophilically (i.e., $\rho = -1.49$ vs σ^+) accompanying the NIH shift. (2) Relative hydroxylation rates of saturated hydrocarbons are in the order of tertiary > secondary > primary close to those of hydroxyl radical. *cis*-Decalin affords mixtures of *cis*- and *trans*-decalol. (3) Olefins are not epoxidized. (4) Sulfides and sulfoxides are oxidized electrophilically. (5) Two pathways, retention and scrambling, are operating for the formation of nitrobenzene. (6) The relative reactivity of substrates is in the order $PhN{=}O \gg Ph_2S > Ph_2SO > PhH$.

The important point here is to discuss the structure of the O-transferring intermediates nitroso oxide PhNOO or dioxaziridine **8**. A diagnostic method is the comparison with the chemistry of dioxiranes.[14] Characteristic points in the reactivity of dioxiranes are (a) the electrophilic O transfer to sulfoxides,[25] (b) the stereoselective O insertion to C–H bonds,[20] and (c) the efficient epoxidation of olefins.[14] The last two reactions are completely different from the present O transfers. That is, the present hydroxylation of C–H bonds is not stereoselective and is similar to that of the hydroxyl radical (item 2). The reactivity toward olefins

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(25) Murray, R. W.; Jeyaraman, R.; Pillay, M. K. *J. Org. Chem.* **1987**, *52*, 746.

Table VI. Polar Effect on Oxygen Atom Transfer by Peroxy Species

peroxy species	substrate[a]	ρ value[b]	Ph_2S/Ph_2SO[c]	ref
$PhCO_3H$	Ar_2S	−1.06	86	10a
R_2CO_2[d]	ArSOMe	−0.76		25
$PhCO_3^-$	Ar_2SO	0.71	0	26
$R_2C{=}O^+O^-$	Ar_2SO	0.26	0.06	10a
$R_2S{=}O^+O^-$	Ar_2SO	0.25	0.13	14
perepoxide	ArSOMe	0.52	0.04	27
PhNOO	Ar_2SO	−0.64	5.7	this work
PhNOO	Ar_2S	−0.98		this work
O_3	Ar_2SO	−1.17	13	28

[a] Ar = XC_6H_4. [b] Hammett's ρ value vs σ. [c] Relative reactivity by competitive trapping. [d] Dioxiranes.

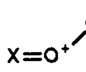
is quite different from that of dioxiranes (e.g., compare items c and 3). This consideration leads to the conclusion that the O-transfer intermediate is not cyclic peroxide **8** but a nitroso oxide.

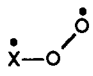
The reactivity of substrates with nitroso oxides is in the order of styrene, PhN=O ≫ Ph_2S > Ph_2SO > PhH. The high reactivity of the nitroso oxide with olefins and nitrosobenzene seems to reflect the radical nature of nitroso oxides. This is clearly supported by the fact that the relative reactivity of C–H bonds is quite similar to that of electrophilic hydroxyl radical. The electrophilicity of nitroso oxides is also reflected in above-mentioned items 1, 2, 4, and 6. Thus, nitroso oxides may be characterized as electrophilic peroxy radicals.

The types of oxygen transfer by several peroxy species are compared in Table VI. Peracids[10a] and their anions[26] are listed as typical electrophilic and nucleophilic reagents, respectively. Dioxiranes[25] oxidize sulfoxides electrophilically. Carbonyl oxides,[10a] persulfoxides,[16] and perepoxides[27] all have nucleophilic reactivity, as shown by the order $Ph_2SO \gg Ph_2S$ and the positive ρ values for sulfoxides. In contrast, nitroso oxides react electrophilically, the order being $Ph_2S \gg Ph_2SO$. The ρ values and the relative reactivities are very close to those of ozone,[28] as listed at the bottom of Table VI. From these data, it is shown that XOO species react as a nucleophilic 1,3-dipole for the case of X = C and S and as an electrophilic diradical when X = N.

Structure and Reactivity of Nitroso Oxides. Few experimental verifications of the structure of nitroso oxides exist. Direct observation was successful only in matrices at low temperature; the photolysis of aromatic azides and aeration yielded yellow intermediates that were converted to nitrobenzenes by further irradiation.[9] This observation is quite interesting since in low-temperature matrices carbonyl oxides have recently been shown to isomerize photochemically to dioxiranes.[29] Singh et al.[9] noted that ESR spectra of ArNOO were not observed except for the case of *p*-diazidobenzene. The lack of observation of an ESR spectrum is now understandable since nitroso oxides are calculated to have a singlet ground state,[30] just as carbonyl oxides do.

As mentioned above, the O-transfer intermediates at ambient temperature are characterized as electrophilic peroxy radicals. Then, how is the observed radical nature of nitroso oxides to be understood? The answer is that even when an XOO species has a singlet ground state, it may have a diradical nature. In fact, the contribution of radical structure for XOO species has been estimated by VB method[31] and from the energy difference between RHF and UHF calculations.[32] Percent contributions of radical structure **1b** are, for example, 43, 55, and 59% for H_2COO, HNOO, and OOO, respectively.[31] The radical nature increases in the order H_2COO < HNOO < OOO, which is the same order of electronegativity of X; i.e., C < N < O. It seems to be quite natural that the contribution of diradical **1b** becomes predominant as the electronegativity of X approaches that of the oxygen atom.


1a


1b

Finally, some discussion is noted on the cyclization of **1** to form **2**. MO calculations on carbonyl oxides have all suggested that dioxirane (**2**, X = H_2C) is more stable than carbonyl oxides (**1**, X = H_2C), the energy differences being 30–40 kcal/mol.[33] However, there is no evidence that cyclization to the more stable dioxirane proceeds smoothly in solution.[10c] This is due to a high activation energy for the isomerization to dioxirane.[31c] On the other hand, the cyclic form (**2**, X = O) of ozone is calculated to be less stable than the open bent structure (**1**, X = O) by 20–40 kcal/mol.[34] For the case of nitroso oxide (X = HN), UHF calculations predict the cyclic form as much less stable;[30,35] that is, the isomerization of nitroso oxide (**1**, X = HN) to dioxaziridine (**2**, X = HN) would not be facile. The present experimental results, however, indicate a facile cyclization of the nitroso oxide eventually leading to nitro compounds. The importance of the diradical nature present in the nitroso oxide seems to be due to the decreased double bond order of the N–O bond, resulting in the reduction of activation energy for the cyclization. This is in line with a prediction that the activation energy for the cyclization of carbonyl oxide is considerably lowered for the oxide F_2COO with strongly electron attracting group.[36] No observation of O transfers from cyclized dioxirane (**8**) indicates the facile conversion of **8** to nitro compounds. We have no experimental evidence to answer whether **8** is an intermediate or a transition state.[37] The present data is consistent with either interpretation.

In conclusion, it is shown that nitroso oxide PhNOO is produced effectively in the photooxidation of phenyl azide. Trapping experiments revealed that the oxide reacts as an electrophilic peroxy radical. The radical nature of XOO species increases in the order of C < N < O, reflecting the increase in their electronegativity. The ^{18}O-tracer study revealed that the cyclization of nitroso oxides is facile and competitive with intermolecular O transfers.

Experimental Section

GC–MS spectra were recorded with a JEOL D300 mass spectrometer and ^1H NMR spectra with a Hitachi R24B NMR spectrometer. GLC analyses were performed with a Yanagimoto G180 gas chromatograph with 1- or 2-m columns: PEG 20M, 20% on Chromosorb WAW; KG02 on Uniport HP; Carbowax, 2% on Chromosorb WAW; Gaskuropack 54.

Materials. Phenyl azide was prepared[38] and purified by distillation. Toluene-4-*d* and anisole-4-*d* were prepared by adding D_2O to the Grignard reagent from *p*-bromotoluene and *p*-bromoanisole;[39] deuterium contents were 94.1 and 92.6%, respectively, determined by GC–MS analysis. $^{18}O_2$ (99% pure) gas from CEA was diluted with natural O_2 gas. Other reagents were of commercial sources and of guaranteed grade.

Typical Procedure of the Photooxidation. A 3-mL acetonitrile solution of 5 mM phenyl azide in a 20-mL Pyrex test tube was purged with oxygen and irradiated with a 300-W medium-pressure Hg lamp through a 5% $NaNO_3$ filter solution (i.e., >350 nm) for 4 h at ca. 20 °C. The conversion of PhN_3 was determined by GLC (PEG 20M) to be 80–90%. Products were analyzed by GLC and identified by GC–MS in comparison to authentic samples; PEG 20M and KG02 columns at 60–250 °C.

The relative reactivities of various substrates was determined competitively by adding two substrates in the photooxidation of PhN_3. For concentrations, see notes in Tables II and IV. After the irradiation under oxygen, the yields of products were determined by GLC and the resulting

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(26) Curci, R.; Modena, G. *Gazz. Chim. Ital.* **1964**, *94*, 1257.

(27) Schaap, A. P.; Rechter, S. G.; Faler, G. R.; Villasenor, S. R. *J. Am. Chem. Soc.* **1983**, *105*, 1691.

(28) Ishikawa, S.; Sawaki, Y. Unpublished results.

(29) (a) Chapman, O. L.; Hess, T. C. *J. Am. Chem. Soc.* **1984**, *106*, 1842. (b) Sander, W. W. *Angew. Chem., Int. Ed. Engl.* **1985**, *25*, 988. (c) Sander, W. W. *J. Org. Chem.* **1988**, *53*, 121.

(30) (a) Yamaguchi, K.; Yabushita, S.; Fueno, T. *J. Chem. Phys.* **1979**, *71*, 2321. (b) Houk, K. N.; Yamaguchi, K. Reference 12b, p 407.

(31) Hiberty, P. C.; Leforestier, C. *J. Am. Chem. Soc.* **1978**, *100*, 2012.

(32) Kahn, S. D.; Hehre, W. J.; Pople, J. A. *J. Am. Chem. Soc.* **1987**, *109*, 1871.

(33) (a) Harding, L. B.; Goddard, W. A., III. *J. Am. Chem. Soc.* **1978**, *100*, 7180. (b) Cremer, D. *Ibid.* **1979**, *101*, 7199. (c) Hull, L. A. *J. Org. Chem.* **1978**, *43*, 2780.

(34) Cremer, D. In *The Chemistry of Peroxides*; Patai, S., Ed.; Interscience: New York, 1983; p 33.

(35) Yamaguchi, K. Private communication.

(36) Rahman, M.; McKee, M. L.; Shevlin, P. B.; Sztyrbicka, R. *J. Am. Chem. Soc.* **1988**, *110*, 4002.

(37) We are thankful to a reviewer for the consideration on this point.

(38) Lindsay, R. O.; Allen, G. F. H. In *Organic Syntheses*; Wiley: New York, 1955; Collect. Vol. III, p 710.

(39) Gold, V.; Satchell, D. P. N. *J. Chem. Soc.* **1956**, 2743.

relative yields correspond to the relative reactivity since excess amounts of substrates were added.

The NIH Shift. The NIH shift values were determined for phenols from toluene-4-*d* and anisole-4-*d*. An acetonitrile solution containing 5 mM PhN_3 and 25% toluene-4-*d* or anisole-4-*d* was irradiated for 4 h under oxygen at ca. 20 °C. D contents in *p*-cresol and *p*-methoxyphenol were determined by GC-MS analysis with use of PEG 20M columns. The method and calculation have been described previously.[40]

Hydroxylation of Isopentane. A 3-mL acetonitrile solution containing 5 mM PhN_3 and 5% isopentane was irradiated for 8 h at ≥350 nm under oxygen at ca. 20 °C. The conversion of PhN_3 was 76%, and the yield of nitrobenzene was 42%. The alcohols obtained were 2-methyl-2-butanol (1.9%), 3-methyl-2-butanol (0.5%), and 2- and 3-methyl-1-butanol (0.3%) as determined by GLC with use of Gaskuropack 54. When the yields were divided by the numbers of hydrogens available, the relative reactivity was 1:7.2:62 for primary, secondary, and tertiary CH, respectively.

The hydroxylation of isopentane with hydroxy radical was carried out similarly by irradiating an acetonitrile solution of 0.15 M H_2O_2 and 5‰ isopentane for 8 h at >250 nm under oxygen. Product alcohols were determined similarly and listed in Table III. The relative yields of primary, secondary, and tertiary alcohols were practically the same when the concentration of H_2O_2 was 0.05 or 0.025 M.

Hydroxylation of Decalin. A 3-mL solution of 5 mM PhN_3 and 10% *cis*-decalin in $MeCN–CH_2Cl_2$ (3:1) was irradiated at ≥350 nm for 8 h under oxygen. Dichloromethane was added to solubilize decalin. The resulting alcohols were analyzed by GLC (PEG 20M, 1 m); the yields of *cis*- and *trans*-9-decalol were 7.4 and 3.1%, respectively, in comparison to authentic samples. A similar reaction with *trans*-decalin afforded *trans*-9-decalol (5.6%) and only a trace amount of cis alcohol. The hydroxylation of 10 mM H_2O_2 in place of PhN_3 was carried out similarly, and the results are listed in Table III.

^{18}O-Tracer Study. A 1-mL solution of 5 mM PhN_3 in MeCN was placed in a 20-mL Pyrex test tube with a septum rubber cap. After the solution was purged with argon, oxygen gas $^{18}O_2/O_2$ ($^{32}O_2$:$^{34}O_2$:$^{36}O_2$ = 100:0.6:8.4) was introduced into the test tube through a syringe by exhausting the argon gas with use of another syringe. Irradiations and product analyses were carried out as described above. The ^{18}O contents in $PhNO_2$ were determined by GC–MS. The averaged values after 3–5 determinations are listed in Table V.

Acknowledgment. This work was supported in part by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture of Japan. We acknowledge Mr. Masaaki Kondo for his technical assistance.

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(40) Kurata, T.; Watanabe, Y.; Katoh, M.; Sawaki, Y. *J. Am. Chem. Soc.* **1988**, *110*, 7472.

Thermal Cis–Trans Rearrangement of Semirigid Polyenes as a Model for the Anticarcinogen β-Carotene: An *all-trans*-Pentaene and an *all-trans*-Heptaene

W. von E. Doering* and Toshikazu Kitagawa

Contribution from the Department of Chemistry, Harvard University,
Cambridge, Massachusetts 02138-2902. *Received November 23, 1990*

Abstract: To assess the possible role of a 15,15′ 90°-twisted, singlet diradical in the anticarcinogenicity of β-carotene, activation parameters for the thermal, cis–trans interconversion of *all-trans-β*-carotene (**1**) and 15,15′-*cis-β*-carotene (**2**), polyenes of order 11, are needed. Indirect achievement of this goal is initiated here by determining activation parameters for cis–trans rearrangement in a set of semirigid, *all-trans*-polyenes of order 3, 5, and 7 (9 to follow). These data also provide a test of theoretical calculations of stabilization energies of polyenyl radicals. For the coherent series, $\mathbf{3}_{1,1,1}$, $\mathbf{5}_{2,1,2}$, and $\mathbf{7}_{3,1,3}$, these activation parameters ($\Delta H^{\ddagger}$ (kcal/mol), $\Delta S^{\ddagger}$ (cal/mol·K)) are found: 38.9, –6.0; 32.1, –4.4; 27.5, –4.4. The trend is a diminishing return as the order is increased. "Stabilization energies", defined as extra stabilization associated with delocalization of the odd electron and derived with allyl as the reference point (SE_1 = 13.5 kcal/mol), are pentadienyl, SE_2 = 16.9 kcal/mol, and heptatrienyl, SE_3 = 19.2 kcal/mol. Heptaene **7** rearranges in a range, 64–104 °C, that is close enough to 37 °C to forewarn of thermal lability of β-carotene in cell membranes.

Enthalpies of stabilization of polyenyl radicals are fundamental (a) to an experimental, quantitative test of theoretical calculations of their magnitude and (b) to an assessment of thermally induced, configurational interconvertibility in polyenes generally and β-carotenes specifically. In this work, a kinetic study of thermal, cis–trans isomerization about the central double bond in systematically designed *all-trans*-polyenes of order 3, 5, and 7 ("order" specifies the number of double bonds) is undertaken in pursuit of these goals.

β-Carotene as Anticarcinogen

An exciting development in cancer prevention has been the recognition of several anticarcinogenic constituents in the human diet.[1,2] Among these, the common, all-trans stereoisomer of β-carotene (**1**) has gained laboratory and epidemiological support and is currently the subject of long-term, randomized trials.[3] The works of Santamaria and co-workers[4] and of Levenson et al.[5] are particularly noteworthy and provide reference to an extensive literature.

One mechanistic hypothesis parallels that established by Foote, Chang, and Denny[6] for the protection **1** gives to plants against chemically devastating, singlet dioxygen.[7] Its function is reconversion of singlet dioxygen to triplet dioxygen by a quenching process that owes its effectiveness to a perfect match between the energetic splittings of singlet and triplet *all-trans-β*-carotene (**1**) and singlet and triplet dioxygen (both 22 kcal/mol).

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(1) Ames, B. N. *Science* **1983**, *221*, 1256–1264.

(2) Willett, W. C.; MacMahon, B. *New England J. Med.* **1984**, *310*, 633–638; 697–703. (b) Stryker, W. S.; Kaplan, L. A.; Stein, E. A.; Stampfer, M. J.; Sober, A.; Willett, W. C. *Am. J. Epidemiol.* **1988**, *127*, 283–296.

(3) (a) Hennekens, C. H. *Am. J. Epidemiol.* **1983**, *118*, 453–454. (b) Ziegler, R. G. *J. Nutr.* **1989**, *119*, 116–122.

(4) Bianchi, A.; Santagati, G.; Andreoni, L.; Bermond, P.; Santamaria, L. *Med. Biol. Environ.* **1982**, *10*, 25–31.

(5) Levenson, S. M.; Rettura, G.; Seifter, E. In *Vitamin A, β-Carotene, Neoplasia, Therapy*; Academic Press: New York, 1983; Chapter 11, pp 169–203.

(6) Foote, C. S.; Chang, Y. C.; Denny, R. W. *J. Am. Chem. Soc.* **1970**, *92*, 5218–5219.

(7) (a) Farmilo, A.; Wilkinson, F. *Photochem. Photobiol.* **1973**, *18*, 447–450. (b) Wilkinson, F.; Ho, W.-T. *Spectrosc. Lett.* **1978**, *11*, 455–463. (c) Rodgers, M. A. J.; Bates, A. L. *Photochem. Photobiol.* **1980**, *31*, 533–537.

0002-7863/91/1513-4288$02.50/0