

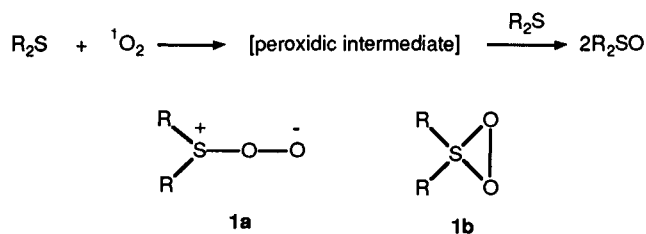
# SINGLET OXYGEN OXIDATION OF ORGANOPHOSPHORUS COMPOUNDS: COOXIDATION OF OLEFIN WITH PHOSPHADIOXIRANE

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The reaction of singlet oxygen with phosphite in the presence of olefin has been investigated. Singlet oxygen oxidation of phosphite caused cooxidation of olefins to the corresponding epoxides in substantial yields. The epoxidation of olefin by the active oxidizing species generated in photosensitized oxygenation of the phosphite is provided, suggesting that the new epoxidizing species is probably the phosphadioxirane intermediate.

**Keywords:** singlet oxygen; organophosphorus compound; phosphadioxirane; photooxidation.

The photooxidation of organic hetero-atom compounds such as organosulfur compounds continues to yield fascinating results.<sup>1,2</sup> In the past more than two decades the reactions of singlet oxygen ( $^1\text{O}_2$ ) with a wide variety of sulfur-containing compounds including sulfides and disulfides have been reported. Since some of the naturally occurring sulfur compounds isolated so far have sulfur-oxygen bonds, these S-oxidation products can play important roles in biochemical reactions.<sup>3</sup> The photooxygenation of sulfides is responsible for the loss of activity of several important enzymes which are damaged in photodynamic action.<sup>4</sup> Much attention has been devoted to the structures and reactivities of initially formed reactive intermediates such as persulfoxide **1a** and thiadioxirane **1b** intermediates in singlet oxygen oxidation of sulfides (Scheme I).<sup>1</sup>

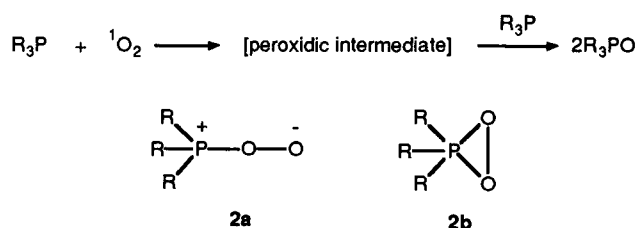


*Scheme I*

Meanwhile, only a few reactions of singlet oxygen with organophosphorus compounds have hitherto been known. It was shown that irradiation of trialkyl phosphite and benzyl diethyl phosphite in dry air or oxygen readily gives the corresponding phosphates in quantitative yield.<sup>5</sup> Triphenyl phosphite was only partially oxidized under the standard conditions of reaction. The process probably involves homolysis of otherwise stable unidentified impurities followed by a radical chain reaction. The photosensitized oxidation of several trialkyl phosphites gave the corresponding phosphates.<sup>6</sup> Foote and coworkers reported that trimethyl phosphite is relatively inert toward singlet oxygen but very efficient in trapping the intermediates in the photooxidation of diethyl sulfide<sup>7</sup> and biadamantylidene.<sup>8</sup>

In relation to photodynamic action, however, cooxidation of olefin by the active oxidizing species generated in the photooxidation of organic hetero-atom compounds is of more interest and importance, since an unsaturated bond is contained in many biologically important compounds such as lipids. We

report here cooxidation of olefin to epoxide in singlet oxygen oxidation of phosphite derivative in the presence of olefin. Phosphadioxirane intermediate is proposed as a new active oxidizing species that oxidizes olefin and sulfide to epoxide and sulfoxide (Scheme II).



*Scheme II*

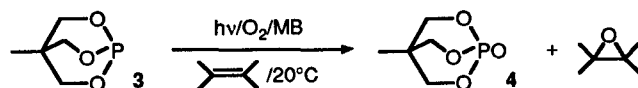
We have examined on the reactive peroxidic intermediates in the reaction of phosphites with singlet oxygen. Phosphites such as dimethyl, diethyl and even diphenyl phosphite are easily oxidized with singlet oxygen.<sup>6</sup> Preliminary trapping study with diphenyl sulfide and diphenyl sulfoxide revealed that added substrates very poorly compete with the phosphite toward the same intermediates, indicative of high reactivity of phosphite itself toward the peroxidic intermediates. Accordingly, the molecule that may serve as a diagnostic test for peroxidic intermediates is clearly desirable for mechanistic studies of the singlet oxygen oxidation of organophosphorus compounds. The candidate is bicyclic phosphite. The particular advantage of bicyclic phosphite is its low reactivity toward electrophile, due to the stereoelectronic effect.<sup>9</sup> The relative reactivity of 1-methyl-4-phospha-3,5,8-trioxabicyclo[2.2.2]octane (**3**) and triethylphosphite with 3-benzylidene-2,4-pentanedione is the ratio 1: 250.<sup>9</sup>

In a typical experiment, a dichloromethane solution of **1** ( $1.0 \times 10^{-1}\text{M}$ ) was photooxygenated at  $20^\circ\text{C}$  with methylene blue (MB,  $2.8 \times 10^{-3}\text{M}$ ) as sensitizer under an oxygen flow, affording the corresponding phosphate (**4**). The resulting mixture was subjected to analytical GLC and GC-Mass. If the photooxygenation is carried out under nitrogen or in the absence of a sensitizer or light, no reaction occurs. The oxygenation is inhibited by dabco, a known singlet oxygen quencher.<sup>10</sup> The control experiments make it probable that singlet oxygen is the primary oxygenating species. When the photooxygenation was carried out in the presence of excess norbornene (20 equiv), the epoxide was produced in 11% yield

based on **1** consumed, together with the phosphate (38%) and **1** (60%) (Table I, run 2). Photoepoxidation of norbornene did not take place at all in the absence of **1**. Meanwhile, in methanol a trace of the epoxide was obtained under the same conditions (Table I, run 3). Yields were determined by GLC, and the reaction conditions are not optimized. Addition of a radical trap (triphenylmethane) does not have any influence on epoxidation. The results are summarized in Table I. The GLC reaction profiles for the photooxygenation of **1** in methylene chloride are presented in Figure 1A and B.

Since less nucleophilic olefins such as stilbene and styrene were scarcely oxidized, the active oxidizing reagent in the epoxidation reaction seems to have an electrophilic nature. Thianthrene 5-oxide was used as a useful chemical monitor for clarifying the electrophilic character of the oxygen-transfer agent.<sup>11</sup> The peroxidic intermediate derived from the singlet oxygen oxidation of **1** gave an essentially electrophilic attack ( $X_{Nu} = 0.40$ ) (Table II, run 8). In the singlet oxygen oxidation of diethyl sulfide, the persulfoxide intermediate (**1a**) acts as a nucleophilic oxidant (Table II, run 2).<sup>12</sup>

Table I. Cooxidation Norbornene in the Photooxidation of Phosphite 3.



run	reaction condns <sup>a</sup>	olefin amt(equiv)	<b>3</b> <sup>a</sup> conv.(%)	epoxide yields(%) <sup>b</sup>
1	CH <sub>2</sub> Cl <sub>2</sub> /12h	-	57	-
2	CH <sub>2</sub> Cl <sub>2</sub> /6h	norbornene 20	62	11
3	CH <sub>2</sub> Cl <sub>2</sub> /6h	norbornene 20	44	1>

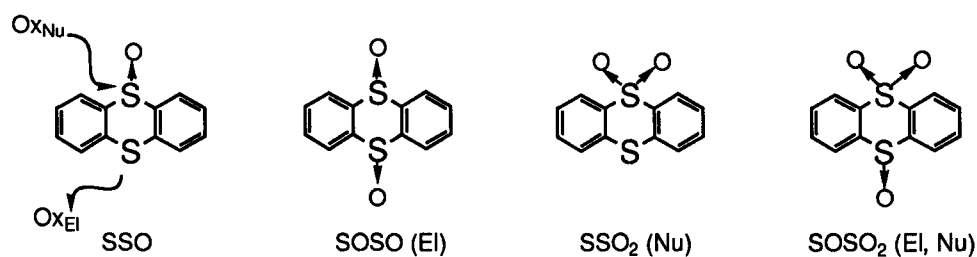
<sup>a</sup>In each case phosphate **4** was obtained.

<sup>b</sup>Yields are based on **3** consumed.

Table II. Nucleophilic Character ( $X_{Nu}$ ) of Oxygen-Transfer Agents Derived with Thianthrene 5-Oxide

oxygen-transfer reactions	total yields, %	abs yields, $\mu\text{M}^a$			$X_{Nu}^b$
		SSO <sub>2</sub> , $n_{Nu}$	SOSO, $n_{EI}$	SOSO <sub>2</sub> , $n_{Nu}, n_{EI}$	
1. KO <sub>2</sub> ; 18-crown-6; C <sub>6</sub> H <sub>6</sub> ; 20°C <sup>c</sup>	0.50	4.71			1.00
2. Et <sub>2</sub> S; <sup>1</sup> O <sub>2</sub> ; CH <sub>2</sub> Cl <sub>2</sub> ; 20°C <sup>d</sup>	5.31	46.0			1.00
3. t-BuOOK; 18-crown-6; C <sub>6</sub> H <sub>6</sub> ; 20°C <sup>c</sup>	3.65	14.4	0.39		0.97
4. Ph <sub>2</sub> C=N <sub>2</sub> ; <sup>1</sup> O <sub>2</sub> ; CH <sub>2</sub> Cl <sub>2</sub> ; 0°C <sup>c</sup>	7.76	33.0	0.39	4.24	0.89
5. Et <sub>2</sub> S; <sup>1</sup> O <sub>2</sub> ; Fe(TPPF) Cl; CH <sub>2</sub> Cl <sub>2</sub> ; 20°C <sup>d</sup>	5.26	33.2	78.2	trace	0.68
6. Me <sub>2</sub> C-O; KSO <sub>3</sub> H; 18-crown-6; CH <sub>2</sub> Cl <sub>2</sub> /H <sub>2</sub> O; 0°C <sup>c</sup>	10.1	75.5	19.3	33.3	0.67
7. PhIO; CH <sub>2</sub> Cl <sub>2</sub> ; 20°C <sup>d</sup>	10.2	47.8	20.7	20.9	0.62
8. (MeO) <sub>3</sub> P; <sup>1</sup> O <sub>2</sub> ; CH <sub>2</sub> Cl <sub>2</sub> ; 20°C	1.5	0.34	0.85	0.62	0.40
9. m-CPBA; CH <sub>2</sub> Cl <sub>2</sub> ; 20°C <sup>c</sup>	27.0	22.4	42.7	2.48	0.36
10. PhIO; Fe(TPPF)Cl; CH <sub>2</sub> Cl <sub>2</sub> ; 20°C <sup>d</sup>	15.6	29.6	78.2	29.0	0.35
11. H <sub>2</sub> O <sub>2</sub> ; 1 N HCl; Et <sub>2</sub> O; 20°C <sup>c</sup>	3.27	0.65	15.0	0.30	0.06

<sup>a</sup>Represents amount of conversion of thianthrene 5-oxide into SSO<sub>2</sub>, SOSO, and SOSO<sub>2</sub> products determined by GLC on a fused silica capillary column, using diphenyl sulfone as internal standard. <sup>b</sup>Mole fraction of amount of nucleophilic attack, i.e.,  $n_{Nu}/(n_{Nu} + n_{EI})$ ; SOSO<sub>2</sub> represents double oxygen-transfer product either via the sequence SSO  $\xrightarrow{OX_{EI}}$  SOSO  $\xrightarrow{OX_{Nu}}$  SOSO<sub>2</sub> or SSO  $\xrightarrow{OX_{Nu}}$  SOSO<sub>2</sub>  $\xrightarrow{OX_{EI}}$  SOSO<sub>2</sub>, so that the yield of SOSO<sub>2</sub> is equally added to  $n_{Nu}$  and to  $n_{EI}$ . <sup>c</sup>Reference 11a. <sup>d</sup>Reference 12.



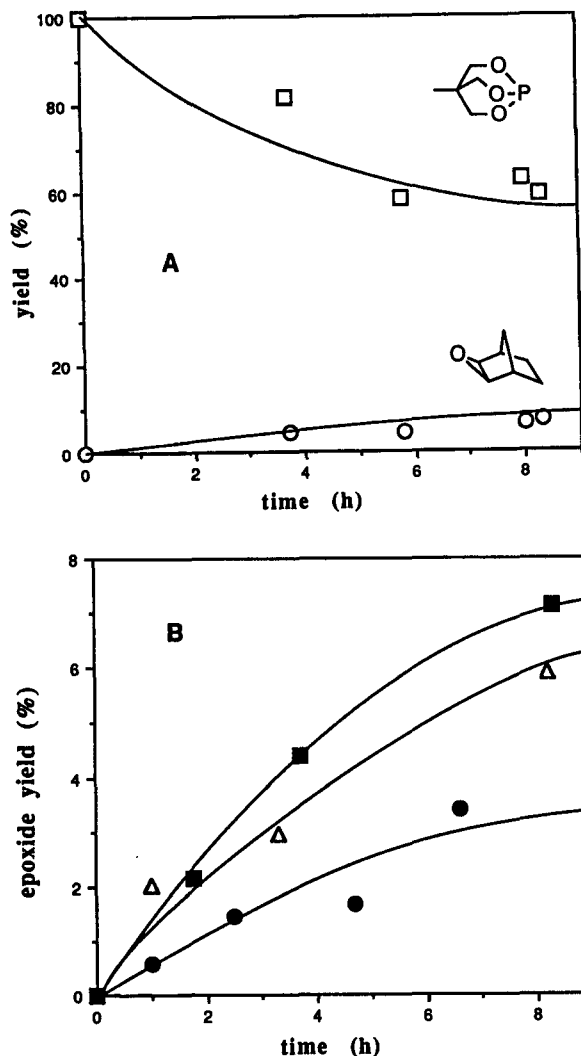


Figure 1. Photooxidation of 3 in methylene chloride in the presence of norbornene. A.  $[3] = 1.0 \times 10^{-1} \text{ M}$ ;  $[\text{norbornene}] = 2.0 \text{ M}$ . B.  $\blacksquare$ ,  $[3] = 2.5 \times 10^{-2} \text{ M}$ ;  $[\text{norbornene}] = 2.0 \text{ M}$ .  $\Delta$ ,  $[3] = 5.0 \times 10^{-2} \text{ M}$ ;  $[\text{norbornene}] = 2.0 \text{ M}$ .  $\bullet$ ,  $[3] = 1.0 \times 10^{-1} \text{ M}$ ;  $[\text{norbornene}] = 2.0 \text{ M}$ .

On the basis of these observations, the primary peroxidic intermediate 2 is likely to transfer an oxygen atom electrophilically to olefin and sulfide to afford epoxide and sulfoxide (Scheme II). We therefore may conclude that the labile intermediate formed in singlet oxygen oxidation of phosphite is a phosphadioxirane and that structure 2b best represents this molecule. It is noteworthy that this is a first example for efficient epoxidation of olefins by the active oxidizing species generated in the photooxygenation of organophosphorus compounds.

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