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Regioselective Oxygenations of *S-Trans* Dienes, Silyl Dienol Ethers (SDEs), by Triphenyl Phosphite Ozonide (TPPO) and Its Mechanistic Study

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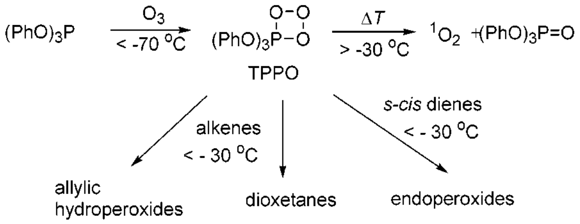
The direct oxygenation of *s-trans* dienes, silyl dienol ethers (SDEs) **2**, by triphenyl phosphite ozonide (TPPO) has been examined in detail. The regioselective oxygenation was found to give hydroperoxide **3**, alcohol **4**, ketone **5**, dimer **6**, and peroxy phosphate **7** with concomitant formation of triphenyl phosphate **8** and diphenyl trimethylsilyl phosphate **10**. The formation of peroxy phosphate **7** was found for the first time in TPPO oxygenation reactions. The low temperature ^{31}P and ^{1}H NMR spectroscopic analyses proved the direct reaction of SDEs with TPPO without generation of singlet oxygen. The formation of the oxygenated products **3**−**7** is reasonably explained by the intervention of the zwitterion **ZI**, which can be formed by the nucleophilic attack of SDE to the central oxygen of the ozonide. The regioselective attack of SDE to the central oxygen of the ozonide was supported by the quantum chemical calculation (B3LYP/6-31G*).

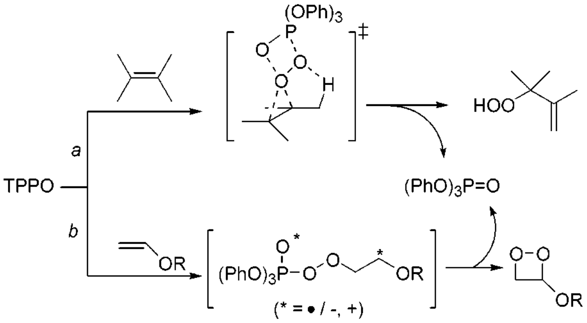
Introduction

Triphenyl phosphite ozonide (TPPO), formed by the addition of ozone to triphenyl phosphite below −70 °C, has attracted considerable attention from its unique structure and reactivity (Scheme 1).[1−3] The decomposition spontaneously occurs at ca. −30 °C to give triphenyl phosphate and singlet oxygen.[3b,d,4] Thus, the ozonide (TPPO) has been well recognized as a chemical source of singlet oxygen ($^1O_2$). Alternatively, the ozonide can also react directly with electron rich alkenes to afford the oxygenated products, which are quite similar to those observed in singlet-oxygen reactions, i.e. allylic hydroperoxides, dioxetanes, and endoperoxides.[5]

Scheme 1. Formation of Triphenyl Phosphite Ozonide (TPPO) and Its Reactivity



Scheme 2. Proposed Mechanism for TPPO Oxygenation of Monoalkenes



The mechanistic studies on the direct oxygenation process have been mainly concentrated on the reaction with monoalkenes, which reveal that the mechanism seems to be largely dependent upon the substrates. For example, the concerted pathway has been proposed for the formation of allylic hydroperoxides in the reaction of alkyl-substituted alkenes (Scheme 2, *a*).[5h] Alternatively, the intermediacy of a diradical or zwitterion has been postulated for dioxetane formations in vinyl ether oxygenations (Scheme 2, route b).[5c,g] Although the formation of endoperoxides has been proposed for an *s-cis* diene,[5i] the TPPO oxygenation of *s-trans* dienes has scarcely been investigated until now.

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(1) For reviews, see; (a) Murray, R. W. In *Singlet Oxygen*; Wasserman, H. H.; Murray, R. W., Eds.; Academic Press: New York, 1979; Chapter 3. (b) Mendenhall, G. D. In *Advances in Oxygenated Processes*; Baumstark, A. L., Ed.; JAI Press: London, 1990; Vol. 2, pp 203−231.

(2) (a) Thompson, Q. E. *J. Am. Chem. Soc.* **1961**, *83*, 845. (b) Murray, R. W.; Kaplan, M. L. *J. Am. Chem. Soc.* **1969**, *91*, 5358. (c) Koch, E. *Tetrahedron* **1970**, *26*, 3503. (d) Razumovski, S. D.; Mendenhall, G. D. *Can. J. Chem.* **1973**, *51*, 1257. (e) Mendenhall, G. D.; Kessick, R. F.; Dobrzdewski, M. J. *J. Photochem.* **1987**, *25*, 227.

(3) For other phosphite ozonides, see (a) El Khatib, F.; Tachon, C.; Caminade, A.-M.; Koenig, M. *Tetrahedron Lett.* **1985**, *26*, 3007. (b) Stephenson, L. M.; McClure, D. E. *J. Am. Chem. Soc.* **1973**, *95*, 3074. (c) Schaap, A. P.; Thayer, A. L.; Faler, G. R.; Goda, K.; Kimura, T. *J. Am. Chem. Soc.* **1974**, *96*, 4025. (d) Schaap, A. P.; Kees, K.; Thayer, A. L. *J. Org. Chem.* **1975**, *40*, 1185.

(4) (a) Corey, E. J.; Taylor, W. C. *J. Am. Chem. Soc.* **1964**, *86*, 3880. (b) Murray, R. W.; Kaplan, M. L. *J. Am. Chem. Soc.* **1968**, *90*, 537. (c) Murray, R. W.; Kaplan, M. L. *J. Am. Chem. Soc.* **1968**, *90*, 4161. (d) Wasserman, E.; Murray, R. W.; Kaplan, M. L.; Yager, W. A. *J. Am. Chem. Soc.* **1968**, *90*, 4160.

(5) (a) Howard, J. A.; Mendenhall, G. D. *Can. J. Chem.* **1975**, *53*, 2199. (b) Bartlett, P. D.; Mendenhall, G. D. *J. Am. Chem. Soc.* **1970**, *92*, 210. (c) Schaap, A. P.; Bartlett, P. D. *J. Am. Chem. Soc.* **1970**, *92*, 6055. (d) Sam, T. W.; Sutherland, J. K. *J. Chem. Soc., Chem. Commun.* **1972**, 424. (e) Kopecky, K. R.; van de Sande, J. H. *Can. J. Chem.* **1972**, *50*, 4034. (f) Bestmann, H. J.; Kisielowski, L.; Distler, W. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 298. (g) Bartlett, P. D.; Chu, H.-K. *J. Org. Chem.* **1980**, *45*, 3000. (h) Stephenson, L. M.; Zielinski, M. B. *J. Am. Chem. Soc.* **1982**, *104*, 5819. (i) Iwata, C.; Takemoto, Y.; Nakamura, A.; Imanishi, T. *Tetrahedron Lett.* **1985**, *26*, 3227. (j) Dussault, P. H.; Woller, K. R. *J. Org. Chem.* **1997**, *62*, 1556.

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Table 1. Direct Oxygenation of Silyl Dienol Ethers 2a−e by TPPO[a]

entry	**2**	products and yields (%)[b]					mass balance (%)[c]
		3	**4**	**5**	**6**	**7**	
1	**2a**	**3a** (30)	**4a** (12)	**5a** (trace)	**6a** (20)	−	82
2	**2b**	**3b** (49)	**4b** (10)	**5b** (24)	**6b** (trace)	−	89
3	**2c**	**3c** (60)	**4c** (11)	**5c** (20)	**6c** (trace)	−	91
4[d]	**2c**	**3c** (57)	**4c** (11)	**5c** (9)	**6c** (13)		90
5	**2d**	**3d** (30)	**4d** (13)	**5d** (35)	**6d** (trace)	−	80
6	**2e**	**3e** (42)	**4e** (11)	-	**6e** (trace)	**7e** (19)	82

[a] The oxygenations were performed at −78 °C in CH_2Cl_2 by the slow addition of a precooled solution of SDE **2** to a solution of TPPO (1.5 equiv), unless otherwise noted. [b] Isolated yields (%) after flash column chromatography on silica gel. 1,3-Dioxin-4-ones **1** were recovered; **1a** (18%), **1b** (6%), **1c** (trace), **1d** (2%), **1e** (10%). The isolated yields (%) of triphenyl phosphate **8** were 80−85% on the basis of triphenyl phosphite used in the reactions. Phenol was also obtained ca. 10% isolated yield. [c] The mass balance (%) was determined for SDE **2**, including the recovered **1**. [d] 2 equiv of SDE **2c** was used for the oxygenation by TPPO.

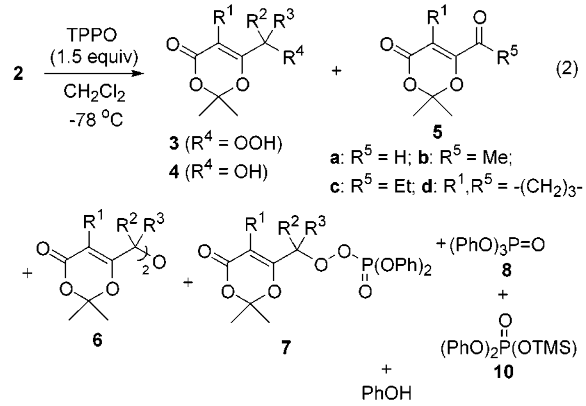
In conjunction with our continuing investigation on the oxygenation of silyl enol ethers[6] and the synthetic approach for functionalized hydroperoxides,[7] we have decided to investigate in detail the TPPO oxygenation of silyl dienol ethers (SDEs) **2a**−**e** derived from the corresponding 1,3-dioxin-4-ones **1a**−**e** (eq 1).[8] The following pertinent questions shall be addressed in the present study: What reaction modes will be operated in the TPPO oxygenation of the *s-trans* dienes? How are the oxygenated products formed, i.e. mechanism?

Results

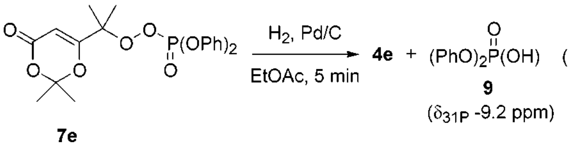
Preparation of Silyl Dienol Ethers. The silyl dienol ethers (SDEs) **2a**−**e** were prepared from the corresponding 1,3-dioxin-4-ones **1a**−**e**[9] by treatment with base (LDA or KHMDS), followed by the addition of trimethylsilyl chloride (eq 1). Since SDEs **2a**−**e** are labile, they should be handled and stored under dry nitrogen atmosphere.

a: R^1, R^2, R^3 = H; **b**: R^1 = H, R^2 = Me or H, R^3 = H or Me;
c: R^1 = H, R^2 = Et or H, R^3 = H or Et; **d**: R^1, R^2 = $-(CH_2)_3-$, R^3 = H;
e: R^1 = H, R^2, R^3 = Me

Product Analyses in the Oxygenation Reactions of SDEs 2a−e with TPPO. The direct oxygenation was performed by the careful addition of a precooled solution of SDE **2** to TPPO (1.5 equiv) prepared freshly from ozone and triphenyl phosphite at −78 °C in dichloromethane (eq 2 and Table 1), unless otherwise stated. After 1 h stirring at −78 °C, the mixture was warmed to room temperature, and the products were carefully analyzed. The evidence for the direct reaction of SDE **2** with TPPO without generation of singlet oxygen at such a temperature (−78 °C) has been provided by the low temperature ^{31}P NMR studies, which are presented later.



The oxygenated products **3**−**7** derived from SDE **2**, triphenyl phosphate **8**, phenol, and 1,3-dioxin-4-one **1** were isolated and fully characterized by the careful spectroscopic analyses. The products and their chemical yields (%) were listed in Table 1, together with their mass balance (%). The regioselective oxygenation (mass balance > 80%) was revealed by the structure of the oxygenated products, in which the 1,3-dioxin-4-one skeleton was remained. The recovery of 1,3-dioxin-4-ones **1a**−**e** (trace~18%) is probably due to the lability of SDEs **2**. The dimeric ether **6a** (20%) was also isolated in the TPPO oxygenation of **1a** ($R^1 = R^2 = R^3 = H$) (entry 1). For the other cases, it was difficult to identify the formation of the dimers **6b**−**e** due to their low yields (entries 2, 3, 5, 6). However, the significant increase of the yield of **6c** (13%) was observed, when the excess amounts of SDE **2c** (2 equiv relative to TPPO) was used for the oxygenation (entry 4). The result is quite informative for the mechanism of the dimerization (vide infra). In the case of the oxygenation of SDE **2e** (R^1 = H, $R^2 = R^3$ = Me), peroxy phosphate **7e** (19%) was obtained together with the oxygenated products **3**−**5** by the quick column chromatography (entry 6). The labile peroxy phosphate **7e** (δ_{31P} −10.8 ppm, relative to 85% H_3PO_4) was fully characterized by the spectroscopic analyses (including elemental analysis). Furthermore, the structure was unequivocally confirmed by the chemical transformation (eq 3) and the synthesis from hydroperoxide **3e** (eq 4). Namely, the peroxide **7e** was quantitatively converted to alcohol **4e** and diphenyl phosphate **9** (δ_{31P} −9.2 ppm) under hydrogenation conditions (H_2, Pd/C, eq 3), and was independently synthesized from the reaction of hydroperoxide **3e** and diphenyl chlorophosphate (eq 4).[10] This is the first example for the isolation of such a peroxide in TPPO oxygenation reactions.



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[6] (a) Einaga, H.; Nojima, M.; Abe, M. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2507. (b) Einaga, H.; Nojima, M.; Abe, M. *Main Group Metal Chem.* **1999**, *22*, 539.

[7] For examples, (a) Tokuyasu, T.; Ito, T.; Masuyama, A.; Nojima, M. *Heterocycles* **2000**, *53*, 1293. (b) Tokuyasu, T.; Masuyama, A.; Nojima, M.; Kim, H.-S.; Wataya, Y. *Tetrahedron Lett.* **2000**, *41*, 3145. (c) Tokuyasu, T.; Masuyama, A.; Nojima, M.; McCullough, K. J. *J. Org. Chem.* **2000**, *65*, 1069.

[8] The reaction of singlet oxygen ($^1O_2$), which was photochemically (>400 nm, tetraphenylporphine (TPP)) generated, with SDE **2e** afforded the relatively complex mixture, including hydroperoxide **3e** (11%) and alcohol **4e** (13%).

[9] Sato, M.; Ogasawara, H.; Komatsu, S.; Kato, T. *Chem. Pharm. Bull.* **1984**, *32*, 3848.

$$\mathbf{3e}\ \xrightarrow[\text{2) (PhO)}_2\text{P(O)Cl}]{\text{1) NaH, 0 °C/THF}}\ \mathbf{7e}\ (57\%) \qquad (4)$$

To clarify the mechanism for the formation of hydroperoxides **3a**−**e** and alcohols **4a**−**e**, the direct NMR (^{1}H and ^{13}C) spectroscopic analyses were performed before subjecting the reaction mixture to the column chromatography on silica gel. Signals corresponding to the silyl peroxy ether of hydroperoxide **3** were not detected. The results suggest that the silyl peroxy ether, if it is formed, is not stable under the reaction conditions to give hydroperoxide **3**. And also, alcohols **4a**−**e** were not detected by the direct NMR analyses. Thus, the silica gel-induced decomposition of hydroperoxide **3a**−**e** was proposed for the alcohol formation. In fact, the pure hydroperoxide **3c**, for example, was converted in part (ca. 15%) to alcohol **4c** by treatment with silica gel. The low temperature (ca. 0 °C) column chromatography on silica gel resulted in increasing the isolated yields of the hydroperoxides, which also supports the silica gel-induced decomposition of the hydroperoxides. For example, the isolated yield of **3b** (56%) was increased with decreasing the yield of alcohol **4b** (4%), compared with entry 2 in Table 1.

^{31}P and ^{1}H NMR Study for the TPPO Oxygenation of SDEs 2. As mentioned above, the oxygenated products **3**−**7** derived from SDE **2** were well characterized. However, triphenyl phosphate **8** (up to 85% isolated yield), except for peroxy phosphate **7e**, was the only isolable phosphorus product from the oxygenation reactions by using silica gel column chromatography. To clarify the oxygenation mechanism, it is indispensable to identify the structures of the rest phosphorus products. Thus, the direct ^{31}P NMR (160 MHz) spectroscopic analyses were performed for the oxygenation reactions.

First, to confirm the formation of the ozonide TPPO under our NMR work conditions, the ozonolysis of triphenyl phosphite (δ_{31P} +127.2 ppm, relative to 85% H_3PO_4) was performed in a NMR tube at −78 °C in CD_2Cl_2, until the blue color of ozone was detected (see Experimental Section). After the excess amount of ozone was removed by argon bubbling, the mixture was directly analyzed by ^{31}P NMR at −80 °C (Figure 1a). The formation of TPPO (δ_{31P} −62.8 ppm, relative to 85% H_3PO_4; lit. −63 ppm (ref 2a)), signal a1, and small amount of triphenyl phosphate **8** (δ_{31P} −17.3 ppm), signal a2, were clearly observed (Figure 1a).

The formation of triphenyl phosphate **8** has also observed by Mendenhall as a minor product (ca. 15%) in the ozonolysis of triphenyl phosphite.[11] The ozonide was stable at least for 1−2 h at such conditions. After warming the solution to +20 °C (Figure 1b), signal a1 at δ_{31P} −62.8 ppm disappeared to give cleanly the signal of triphenyl phosphate **8** ($\delta_P = -17.3$ ppm) with exhaustion of molecular oxygen. Thus, our experiments well reproduced the reported results.[2]

Next, to verify the direct reaction of SDE **2** with TPPO, a precooled solution of SDE **2e** ($R^1 = R^2 = R^3 =$ Me) in CD_2Cl_2 was carefully added to a solution of TPPO (ca. 1.1 equiv) prepared in a NMR tube at −78 °C (Figure 1c). As shown in Figure 1c, the formation of triphenyl phosphate **8** (signal c2, δ_{31P} −17.2 ppm) and peroxy phosphate **7e** (signal c3, δ_{31P} −10.8 ppm) were clearly observed at −80 °C together with the excess TPPO (signal c1, δ_{31P} −62.8 ppm). The complete consumption of SDE **2e** and the formation of hydroperoxide **3e** and peroxy phosphate **7e** were clearly observed by ^{1}H NMR (400 MHz) spectroscopic analysis at −80 °C. The excess TPPO was intact under the reaction conditions, i.e., in the presence of hydroperoxide **3e**. The results clearly indicate that the reaction of TPPO with hydroperoxide **3e** is much slower than that with SDE **2e** at −78 °C. The low temperature NMR studies unequivocally provided the evidence of the direct reaction of SDE **2** with TPPO without intervention of singlet oxygen.

Finally, to clarify the mechanism for the formation of ketones **5**, the low temperature ^{31}P and ^{1}H NMR studies in CD_2Cl_2 have been also performed for the TPPO (ca. 1.2 equiv) oxygenation of SDE **2d** (R^1, $R^2 = (CH_2)_3$, $R^3 =$ H). As shown in Figures 1d (^{31}P NMR), the direct oxygenation reaction was also observed, since the intensity of the signal of TPPO (δ_{31P} −62.8 ppm, signal d1) decreased at −80 °C after the careful addition of **2d**. The ^{1}H NMR measurement supports the result. Namely, the complete consumption of SDE **2d** and the production of peroxide **3d** and ketone **5d** at −80 °C were clearly observed. Except for signal d2 at δ_{31P} −20.5 ppm, the low temperature ^{31}P NMR spectrum (Figure 1d) was quite similar to that observed in the reaction of SDE **2e** (Figure 1c): the signal of triphenyl phosphate (signal d3) and a signal at δ_{31P} −10.2 ppm (signal d4) were detected. When the mixture was exposed for 2 h at −80 °C, there was no significant change in the spectrum. Thus, all of the phosphorus compounds are stable at least for 2 h at −80 °C. After the reaction mixture was warmed to −40 °C (Figure 1e), the ratio of signals d1 (TPPO) and d3 (triphenyl phosphate **8**) did not change between the temperatures, d1/d3 = 28/72 at −80 °C; d1/d3 = 25/75 at −40 °C, whose result is consistent with the stability of the ozonide below −40 °C. However, the decrease in intensity of signal d4 was concurrent with the increase in intensity of signal d2; d4/d2 = 13/87 at −80 °C, d4/d2 = 3/97 at −40 °C. A similar phenomenon was also observed in the ^{1}H NMR spectra. Namely, a signal (triplet-like) at δ_H 4.85 ppm decreased as the intensity of a signal (triplet) at δ_H 2.55 ppm increased. The latter signal was assigned to ketone **5d** by comparison with the authentic sample. After warming the mixture up to +20 °C, the signals d1 (TPPO) and d4 completely disappeared to give triphenyl phosphate **8** (signal d3) and a phosphorus compound (signal d2) (Figure 1f). Thus, the phosphorus compound (signal d4), which possesses chemical shifts at δ_{31P} −10.2 and δ_H 4.85, should be the precursor of both ketone **5d** and the phosphorus compound (signal d2) that possesses the chemical shift at δ_{31P} −20.5 ppm. The following experiments clarified the structures of signals d2 and d4.

First, to assign signal d2, diphenyl trimethylsilyl phosphate **10** was prepared from diphenyl phosphate **9**, according to the reported method (eq 5),[12] and measured by ^{31}P NMR spectroscopy. The ^{31}P NMR spectrum of **10** (δ_{31P} −20.5 ppm) was completely consistent with signal

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(10) Synthesis of alkylperoxy phosphates, see: Sosnovsky, G.; Zaret, E. H. *J. Org. Chem.* **1969**, *34*, 968.

(11) Mendenhall, G. D.; Priddy, D. B. *J. Org. Chem.* **1999**, *64*, 5783.

(12) (a) Chojnwski, J.; Cypryk, M.; Michalski, J.; Wozniak, L. *J. Organomet. Chem.* **1985**, *288*, 275. (b) Chojnwski, J.; Cypryk, M.; Michalski, J.; Wozniak, L. *Phosphorus Chem.* **1981**, 522.

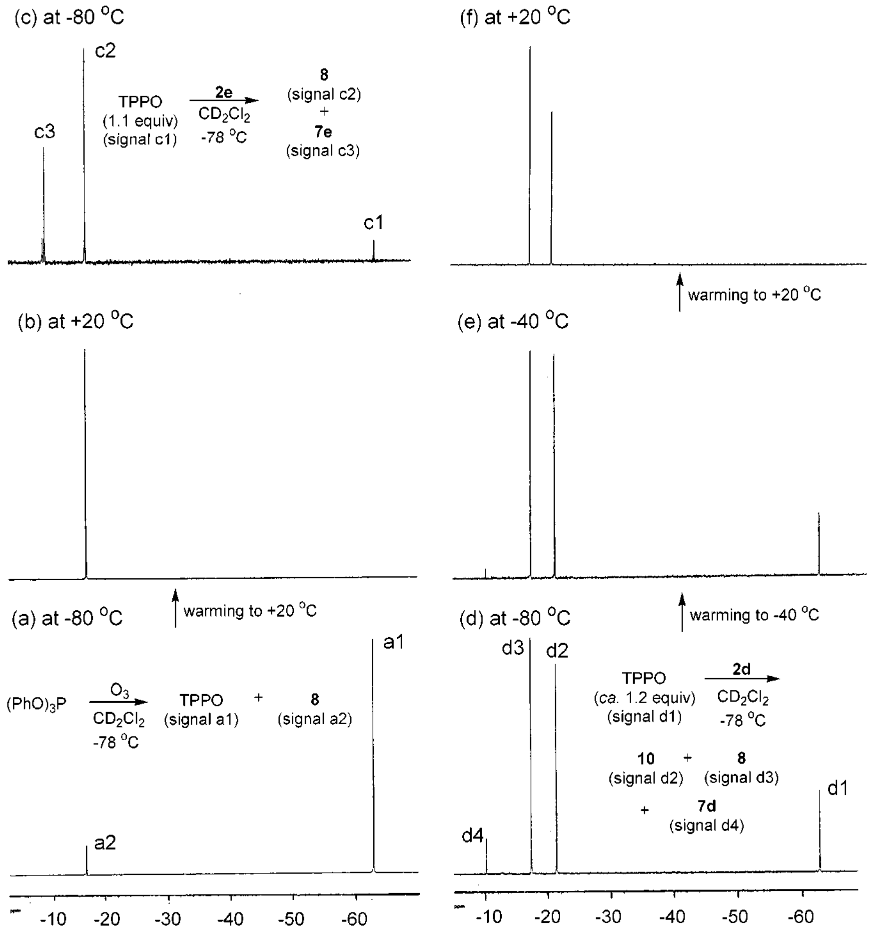
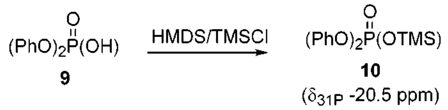


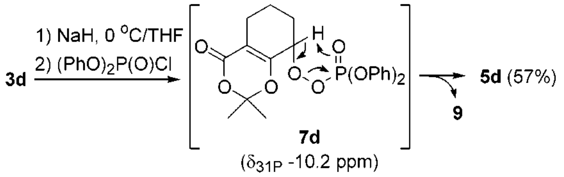
Figure 1. ^{31}P NMR (160 MHz) spectra: (a) The spectrum was measured after ozonolysis of triphenyl phosphite at −78 °C, TPPO (signal a1, δ_{31P} −62.8 ppm) and triphenyl phosphate **8** (signal a2, δ_{31P} −17.3 ppm) at −80 °C. (b) The spectrum was measured after warming the sample up to +20 °C. (c) The spectrum was measured ca.. 30 min later at −80 °C, after mixing SDE **2e** and TPPO (ca. 1.1 equiv) at −78 °C. (d) The spectrum was measure ca. 30 min later at −80 °C, after addition of SDE **2d** to TPPO (ca. 1.2 equiv) at −78 °C. (e) The spectrum was measured after warming the sample up to −40 °C. (f) The spectrum was measured after the sample was warmed to +20 °C.

d2 observed in our NMR work. Thus, the signal d2 was assigned to the phosphate **10**.

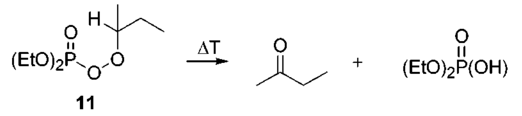


$$\underset{\mathbf{9}}{(PhO)_2\overset{O}{\overset{\|}{P}}(OH)} \xrightarrow{\text{HMDS/TMSCl}} \underset{\substack{\mathbf{10}\\(\delta_{31P}\ -20.5\ \text{ppm})}}{(PhO)_2\overset{O}{\overset{\|}{P}}(OTMS)} \quad (5)$$

Although it was rather difficult to assign the structures of signal d4, the signal was reasonably proposed to be peroxy phosphate **7d** by comparison of its ^{31}P chemical shift (δ_{31P} −10.2 ppm) with that of the isolable **7e** (δ_{31P} −10.8 ppm), and also by the reaction depicted in eq 6.



(6)



(7)

When peroxy phosphate **7d** was independently prepared from the reaction of hydroperoxide **3d** with diphenyl chlorophosphate according to the method for the preparation of peroxy phosphates **7e**, the formation of ketone **5d** (57%) and diphenyl phosphate **9** was observed (eq 6). Krysov et al. reported the similar reactivity of an alkylperoxy phosphate (eq 7).[13] Namely, the thermal decomposition of diethyl *sec*-butylperoxy phosphate **11** has been found to give 2-butanone and diethyl phosphite, as shown in eq 7. The results indicate that peroxy phosphate **7d** is one of the precursors of ketone **5d**.

As mentioned above, the ketone **5d** has been already formed at −80 °C, a temterature at which the peroxy phosphate **7d** was stable. The results clearly suggest that another pathway for the formation of ketone **5d** without intervention of the peroxide **7d** must exist in the direct oxygenation reaction (see, path c in Scheme 3).

Discussion

Mechanism. We have performed for the first time the detailed study on the direct oxygenation of *s-trans* dienes, SDEs **2**, by TPPO. On the basis of the experimental results, the mechanism is reasonably proposed as shown in Scheme 3.

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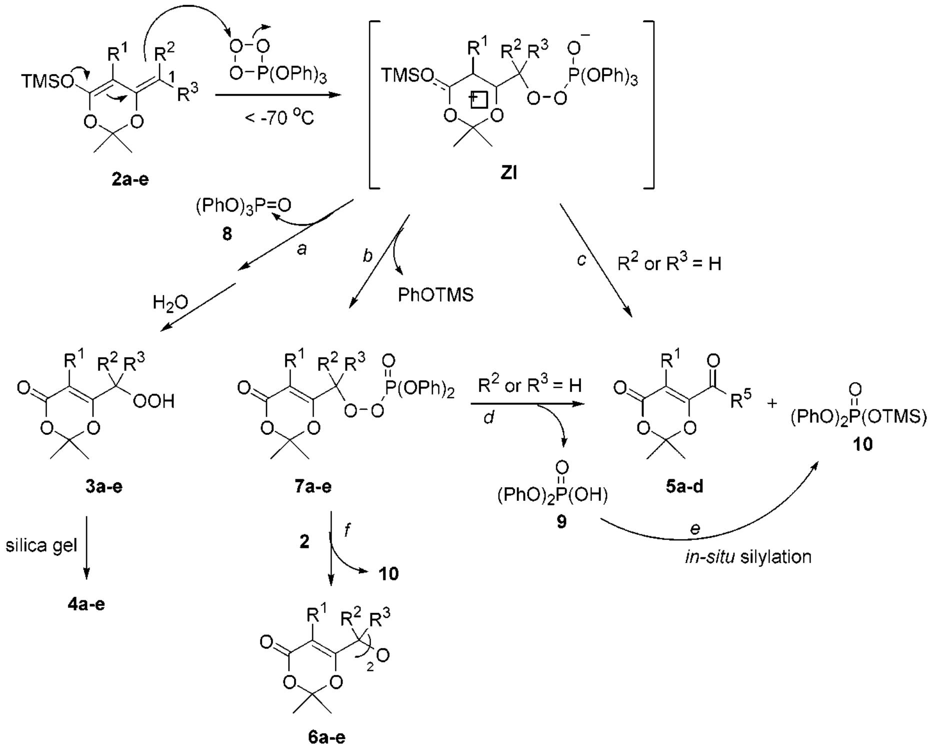
[13] Krysov, V. V.; Maslennikov, V. P.; Sergeeva, V. P. *J. Gen. Chem. USSR* **1973**, 1641.

Scheme 3. Proposed Mechanism for the Direct TPPO Oxygenation of SDEs 2



As judged by the nucleophilic character of SDEs **2** and the electrophilic profile[14] of the peroxide linkage, the nucleophilic attack of the C1 carbon of SDE **2** to the central oxygen of the ozonide TPPO has been proposed to be the initial step of the direct reaction, generating the zwitterion **ZI**. The selective addition on the central oxygen can be supported by the electrostatic charge calculation[15] at B3LYP/6-31G* level of theory,[16,17] which was performed for trimethyl phosphite ozonide as a model (Figure 2).

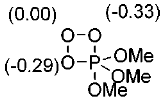
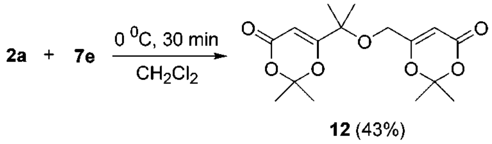


Figure 2. Charge distribution of trimethyl phosphite ozonide, calculated by B3LYP/6-31G*.

The central oxygen atom O2 (0.00) of the ozonide moiety has been calculated to be the most positively charged oxygen relative to the other oxygen atoms, O1 (−0.33) and O2 (−0.29).

In the case of SDE **2e** (R^1 = H, R^2 = R^3 = Me), the mechanism for the formation of the observed products can be concluded as follows; The eliminations of the peroxide moiety (path a) and the phenoxy group (path b) from zwitterion **ZI** competitively occur to give hydroperoxide **3e** and peroxy phosphate **7e**. When the proton exists at C1 position, i.e. **2a**−**d**, the two additional routes (paths c and d) should be considered for the product formations. As observed in the low-temperature NMR analyses (Figure 1), the direct pathway for the formation of ketone **5** and diphenyl trimethylsilyl phosphate **10** from zwitterion **ZI** would be involved. As can be easily imagined from the structure of **ZI**, the successive proton abstraction and elimination is proposed for the concomitant production of ketone **5** and the phosphate **10** (path c). Another reaction pathway (path d) for the formation of **5** has been already mentioned in eq 6, in which diphenyl phosphate **9** was concomitantly formed. A question quickly arose: Why was the diphenyl phosphate **9** (δ_{31P} −9.2 ppm) not observed in the ^{31}P NMR spectra (Figure 1)? To understand the chemical phenomenon, a small portion, ca. 0.1 equiv, of diphenyl phosphate **9** was added to the reaction mixture after the TPPO oxygenation of **2d** was completed. Interestingly, the signal of **9** (δ_{31P} −9.2 ppm) was not observed by ^{31}P NMR analysis, and an increase in intensity of **10** was observed. Thus, although the reagent for the silylation of **9** is not clear, the in-situ silylation (path e) of **9** to **10** is proposed, which would be analogous to the reaction mentioned in eq 5.

The difficult task still remains: How are the dimeric ethers **6** formed? The following experiment gave important information. As shown in eq 8, the analogous ether



12 (43%) (8)

12 (43%) was obtained in the reaction of peroxy phosphate **7e** with SDE **2a**. Thus, the nucleophilic attack of SDE **2** to the peroxide linkage of **7** is proposed for the ether production (path f). The mechanism is also sup-

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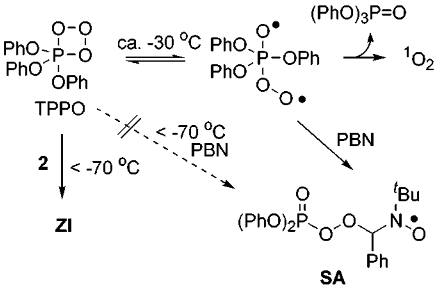
[14] (a) *Organic Peroxide*; Ando, W. T., Ed.; Wiley: New York, 1992. (b) Workentin, M. S.; Donkers, R. L. *J. Am. Chem. Soc.* **1998**, *120*, 2664. (c) Abe, M.; Inakazu, T.; Munakata, J.; Nojima, M. *J. Am. Chem. Soc.* **1999**, *121*, 6556.

[15] (a) Chirlian, L. E.; Francl, M. M. *J. Comput. Chem.* **1987**, *8*, 894. (b) Breneman, C. M.; Wiberg, K. B. *J. Comput. Chem.* **1990**, *11*, 361.

[16] The calculation was performed within TITAN.; Wavefunction, Inc., Schrödinger, Inc., 1999.

[17] (a) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785. (b) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098. (c) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.

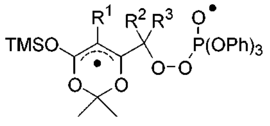
Scheme 4. Generation of Singlet Oxygen from the Diradical Form of TPPO and PBN Radical Trapping



ported by the result mentioned in Table 1, entry 4: the use of the excess amounts of the SDE **2c** increased the formation of the dimeric ether **6c** (trace to 13%) with a decrease of ketone **5c** (20% to 9%). Thus, the competitive formation of ether **6** (path f) and ketone **5** (path e) has been strongly proposed. The reason for the low yields of **6b**−**e** (R^2 or/and R^3 = alkyl) can be rationalized by the steric interaction, which would suppress the S_N2-type of displacement. The retardation by the steric effect has also been observed in a similar S_N2 reaction between 1,2-dioxetanes and nucleophiles, reported by Adam et al.[18]

As mentioned above, the intervention of zwitterion **ZI** can reasonably rationalize the major course of the oxygenation reactions. In this section, we would like to discuss the possibility of other intermediates.

As described in the Introduction, the diradical intermediate is often proposed for the direct reaction of monoalkenes with TPPO. Our experimental results would be also explained by the analogous intermediate, **DR**.



DR

However, Pryor's ESR studies[19] in the reaction of TPPO with a spin trap, e.g., α-phenyl-*N*-*tert*-butylnitron (PBN), diminish the possibility (Scheme 4). Namely, the spin trap reaction was only observed at around −30 °C to give the spin adduct **SA**, where singlet oxygen is starting to generate from the diradical form of the ozonide (Scheme 4). The adduct **SA** was not observed below −70 °C. The results clearly suggest that the reaction between PBN and TPPO does not occur below −70 °C. As mentioned in our NMR study, the reaction between SDE and TPPO was smoothly occurred to give the products at −78 °C. Thus, the intervention of diradical **DR** would be excluded, since the content of the diradical form of TPPO should be very small.

Conclusion

In the present study, we have uncovered the regioselective oxygenation of *s-trans* dienes, silyl dienol ethers SDEs, by using TPPO as an oxygen source. The detailed mechanistic study revealed that nucleophilic attack of SDE to the central oxygen of the ozonide, without intervention of singlet oxygen ($^1O_2$), initiates the direct oxygenation reactions.

Experimental Section

Preparation of Silyl Dienol Ethers 1a−e. General Procedure. To a solution of LDA or KHMDS (31.5 mmol) in THF (60 cm^3) was slowly added a solution of the corresponding 1,3-dioxin-4-ones **1**[9] (30 mmol) in THF (10 cm^3) at −78 °C under argon atmosphere. After stirring for 10 min, a solution of TMSCl (30 mmol) in THF (10 cm^3) was added dropwise to the mixture. The reaction mixture was allowed to warm to room temperature (ca. 20 °C). After stirring for 1 h, the solvent was removed under reduced pressure (30 °C/ca. 100 mmHg). The distillation under reduced pressure gave the desired silyl dienol ether **2** in 50−80% isolated yields, of which derivatives **2a**[20] and **2b**[21] are known compound. The spectroscopic data of the new compounds **2c**−**e** were listed in Supporting Information.

General Procedure for the TPPO Oxygenation of Silyl Dienol Ethers 2. Into a solution of triphenyl phosphite (1.5 mmol), which is freshly distilled prior to use, in CH_2Cl_2 (10 cm^3) was bubbled a stream of O_3/O_2 until the blue color of O_3 was detected at −78 °C. After removal of the excess O_3 by bubbling argon, a precooled solution (−78 °C) of silyl dienol ether **2** (1 mmol) in CH_2Cl_2 (10 cm^3) was added slowly under argon atmosphere. The reaction mixture was stirred for 1 h at −78 °C and then warmed to room temperature. After the solvent was removed under reduced pressure (30 °C/100 mmHg), the mixture was subjected to silica gel column chromatography by elution with a mixture of *n*-hexane (*n*-hex) and ethyl acetate (EtOAc). The isolated products **3**−**7** were characterized by their spectroscopic analyses, of which compounds **4a**,**b**,[22] **4c**,[23] and **5b**,**c**[24] are known. The chemical yields (%) are shown in Table 1. The spectroscopic data for the other new compounds **3**−**7** are listed in Supporting Information.

General Procedure for Low-Temperature NMR Analysis. To a solution of triphenyl phosphite (0.1 mmol), which is freshly distilled prior to use, in CD_2Cl_2 (0.8 cm^3), was bubbled a stream of O_3/O_2 through a cold trap (−78 °C) until the blue color of O_3 was detected at −78 °C. After removal of the excess O_3 by bubbling argon through the cold trap, a precooled solution (−78 °C) of silyl dienol ether **2** (0.09 mmol) in CD_2Cl_2 (0.2 cm^3) was added slowly under argon atmosphere. The reaction mixture was then directly analyzed by ^1H and ^{31}P NMR spectroscopy at −80 °C. The results are shown in Figure 1.

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Supporting Information Available: The listed spectroscopic data for new compounds **2**−**7** and **12** prepared in this study. This material is available free of charge via the Internet at http://pubs.acs.org.

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[18] (a) Adam, W.; Heil, M.; Voerckel, V. *J. Org. Chem.* **1992**, *57*, 2680. (b) Adam, W.; Heil, M. *J. Am. Chem. Soc.* **1992**, *114*, 5591. (c) Adam, W.; Blancafort, L. *J. Am. Chem. Soc.* **1996**, *118*, 4778.

[19] Pryor, W. A.; Govindan, C. K. *J. Org. Chem.* **1981**, *46*, 679.

[20] Grunwell, J. R.; Karipides, A.; Wigal, C. T.; Heinzman, S. W.; Parlow, J.; Surso, J. A.; Clayton, L.; Fleitz, F. J.; Daffner, M.; Stevens, J. E. *J. Org. Chem.* **1991**, *56*, 91.

[21] Sato, M.; Sunami, S.; Sugita, Y.; Kaneko, C. *Heterocycles* **1995**, *41*, 1435.

[22] Sato, M.; Sakaki, J.; Takayama, K.; Kobayashi, S.; Suzuki, M.; Kaneko, C. *Chem. Pharm. Bull.* **1990**, *38*, 94.

[23] Sakaki, J.; Suzuki, M.; Kobayashi, S.; Sato, M.; Kaneko, C. *Chem. Lett.* **1990**, 901.

[24] Sakaki, J.; Sugita, Y.; Sata, M.; Kaneko, C. *Tetrahedron* **1991**, *47*, 6197.