# Notable Substituent Electronic Effects on the Regioselectivity of an Oxygen-Atom Abstraction in the Reaction of Unsymmetrically Substituted Monocyclic 1,2-Dioxolanes with Triphenylphosphine

Manabu Abe,* Yohko Sumida, and Masatomo Nojima

*Department of Materials Chemistry, Faculty of Engineering, Osaka University, Suita 565, Japan*

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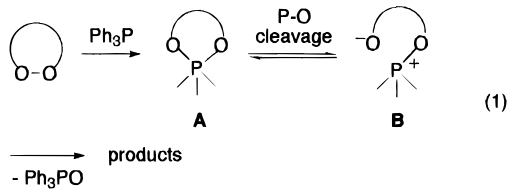
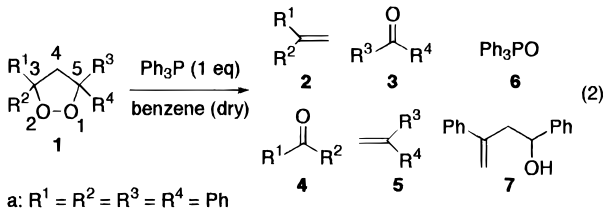
The reactions of triphenylphosphine ($Ph_3P$) with cyclic peroxides, such as ozonides,[1] endoperoxides,[2,3] and dioxetanes,[4,5] have been frequently reported. A reasonable mechanism for the reduction is proposed that the first biphilic insertion of $Ph_3P$ into the peroxide bond generates the phospholane intermediate **A**, which is followed by the subsequent P−O bond scission and the elimination of triphenylphosphine oxide ($Ph_3PO$) via zwitterions **B** to give the corresponding deoxygenated products (eq 1).




(1)

However, the selectivity of which oxygen atom in the peroxy bond is abstracted by $Ph_3P$ has not been firmly established (Figure 1). We now report herein that in the reduction of monocyclic 1,2-dioxolanes **1** with $Ph_3P$, the electronic effect of the substituents attached to the peroxide linkage controls the regioselectivity of the oxygen-atom abstraction.

To understand the mode of the reaction of monocyclic 1,2-dioxolanes with $Ph_3P$, the symmetrically-substituted 3,3,5,5-tetraphenyl-1,2-dioxolane **1a** was selected first (eq 2 and Table 1). Treatment with an equimolar amount




(2)

a: $R^1 = R^2 = R^3 = R^4 = Ph$
b: $R^1 = R^2 = p\text{-}MeOC_6H_4$, $R^3 = R^4 = Ph$
c: $R^1 = R^2 = R^3 = Ph$, $R^4 = H$
d: $R^1 = R^3 = Ph$, $R^2 = CH_3$, $R^4 = H$

of $Ph_3P$ in dry benzene at 60 °C resulted in the formation of the O−O, C−C, and C−O bond cleavage products, diphenylethylene **2a** and benzophenone **3a** together with $Ph_3PO$ **6** (entry 1).[6] Next, the unsymmetrically substituted 3,3-di-*p*-anisyl-5,5-diphenyl 1,2-dioxolane (**1b**) was used for the reduction to see if the electronic effect influences the regioselectivity on the oxygen-atom abstraction (entry 2). Di-*p*-anisylethylene (**2b**) and benzophenone (**3b**) were mainly produced, together with small amounts of di-*p*-anisyl ketone (**4b**) and diphenylethylene (**5b**). This result suggests that the electronic effect of the *p*-anisyl group, which can stabilize the adjacent carbocation center, is an important factor to control the product selectivity, such that the cleavage of the C4−C5 and C3−O2 bonds predominates. The similar electronic effect was also observed for the reactions of trisubstituted dioxolanes **1c**,**d** (entries 3−5). Namely, disubstituted ethylene **2c**,**d** and the corresponding aldehydes **3c**,**d** were preferentially obtained from **1c**,**d**. In other words, of two peroxidic oxygens the sterically more congested one is predominantly abstracted. In the reaction of **1d**, alcohol **7** was also obtained (*vide supra*, Scheme 2). From these results, it is clear that for the unsymmetrically substituted 1,2-dioxolanes **1b**−**d** the oxygen atom (O2) attached to C3 is predominantly abstracted by $Ph_3P$.

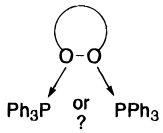
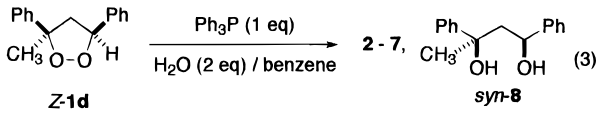
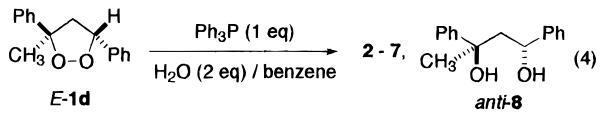



**Figure 1.**

To clarify the intervention of the zwitterionic intermediate, such as **B** in eq 1, the reactions of (*E*)- and (*Z*)-**1d** with $Ph_3P$ were performed in the presence of $H_2O$, respectively (eqs 3, 4 and entries 6, 7).[7] The stereochemistry of **1d** was determined by the NOE measurements (Figure 2). The diol **8** was produced at the expense of the formation of **2**−**5** and **7**. Interestingly, the formation of the diol **8** was stereospecific. The *syn*-**8** was exclusively produced from (*Z*)-**1d**, while *anti*-**8** was the sole product from (*E*)-**1d**. These results strongly support the intervention of the zwitterionic intermediates **10d** and **11d** (Schemes 1, 2). The stereospecific formation of the diols **8** may be rationalized in terms of the nucleophilic attack of water on the cationic P atom (Scheme 1). The $^{18}O$-tracer study using $H_2{}^{18}O$ (5% $^{18}O$) seems to support this. Namely, in the reaction of (*Z*)-**1d** the isolated $Ph_3PO$ (83%) was labeled in 3% $^{18}O$, in contrast to the formation of the nonlabeled diol *syn*-**8** (61%).




(3)




(4)

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(6) The 1,2-dioxolanes **1** used in this study were stable at 60 °C for 10 h.
(7) The similar $H_2O$-trapping experiment of the zwitterionic intermediate was reported by Clennan et al., see ref 2d.

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**Table 1. Reduction of Dioxolanes 1 with $PPh_3$ in Dry Benzene at 60 °C**

| entry | 1[a] | time (h) | additive | products and yields (%)[b] |
|---|---|---|---|---|
| 1 | **1a** | 10 | | **2a** (83), **3a** (88), **6** (92) |
| 2 | **1b** | 10 | | **2b** (68), **3b** (69), **6** (91), **4b** (18), **5b** (14) |
| 3 | **1c** | 8 | | **2c** (48), **3c** (52),[c] **6** (91), **4c** (8), **5c** (11)[c] |
| 4 | *Z*-**1d** | 8 | | **2d** (44),[c] **3d** (48),[c] **6** (89), **7** (20), **4d** (8),[c] **5d** (12)[c] |
| 5 | *E*-**1d** | 8 | | **2d** (42),[c] **3d** (46),[c] **6** (88), **7** (18), **4d** (9),[c] **5d** (11)[c] |
| 6[d] | *Z*-**1d** | 8 | $H_2O$ | **2d** (14),[c] **3d** (16),[c] **6** (88), **7** (5), *syn*-**8** (63), **4d** (2),[c] **5d** (3),[c] |
| 7[d] | *E*-**1d** | 8 | $H_2O$ | **2d** (15),[c] **3d** (17),[c] **6** (89), **7** (3), *anti*-**8** (51), **4d** (3),[c] **5d** (4)[c] |

[a] The used dioxolanes **1** were dried over $P_2O_5$ under reduced pressure due to their hygroscopicities. [b] Isolated yields unless otherwise noted. [c] The yields were determined by GC analyses by using *n*-decane as an internal standard. [d] The reactions were performed in the presence of 2 equiv of $H_2O$.

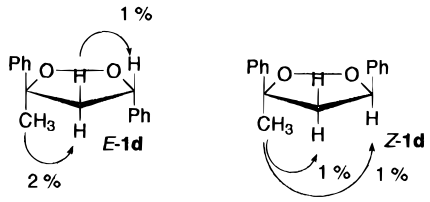



**Figure 2.**

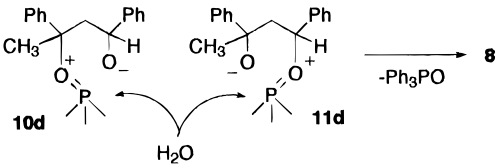
The mechanism for the regioselective oxygen-atom abstraction from **1b**−**d** is summarized in Scheme 2. Biphilic insertion of $Ph_3P$ into the peroxy bond occurs first to generate the labile phospholane intermediate **9**. Subsequent P−O bond scission leads to the zwitterionic intermediates **10** and **11** which may be in equilibrium with **9**. Then, the ionic cleavages of the C−C and C−O bonds occur to give the observed products. As mentioned in the experimental results, it is clear that the electronic effects are important factor to determine the product distributions. The selective formation of **2** and **3** can be explained by the relative rates in the rate-determining step from the zwitterionic intermediates **10**,**11** to the final products. Namely, the rates for the formation of **2**,**3** from **10** may be faster than that for the formation of **4**,**5**, since the transition states for the formation of **2**,**3** from **10** should be more stabilized by the electron-donating substituents at C3, compared with the transition states for the formation of **4**,**5**.[8] The regioselective formation of the unsaturated alcohol would be rationalized by the intramolecular 1,5-$H^+$ shift in the intermediate **10d**.

## Experimental Section

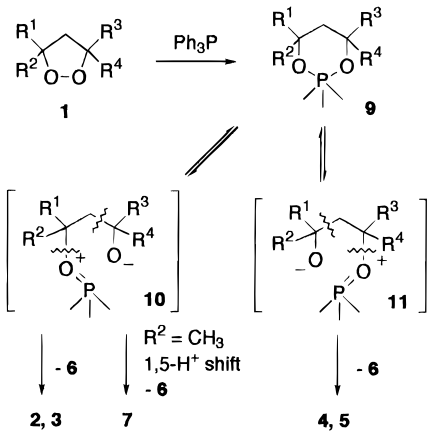
**General.** $^1H$ and $^{13}C$ NMR spectra were recorded on JEOL JNM-EX-270 spectrometer at 270 MHz and 67.8 MHz, respectively. $^1H$ NMR chemical shifts were reported in ppm ($\delta$) using residual $CHCl_3$ ($\delta$ 7.26) in $CDCl_3$. $^{13}C$ NMR chemical shifts were reported in ppm ($\delta$) relative to the internal standard $CDCl_3$ ($\delta$ 77.00). IR spectra were recorded on a Hitachi 260-30 spectrophotometer. Mass spectrometric data were obtained by using a JEOL JNS-BX 303-HF mass spectrometer. GC analyses were performed with a Shimadzu GC-9A utilizing a flame ionization detector on SE-30 capillary column. Flush column chromatography was performed using silica gel (Wakogel C-300) as absorbent. Benzene was dried and distilled from sodium benzophenone ketyl prior to use.

(8) For your information, the heat of formation of **10d** was 0.6 kcal/mol lower than that of **11d**, calculated by PM3 method.[9]

**Scheme 1**




**Scheme 2**




**Syntheses of 1,2-Dioxolanes 1a−d.** Preparation of 1,2-dioxolanes **1a,c,d** were reported previously.[11] The dioxolane **1b** was prepared from 1,1-di-*p*-anisyl-2,2-diphenylcyclopropane by using the electron-transfer photooxygenation reported by Gollnick et al.[12] These hygroscopic dioxolanes **1a**−**d** were dried over $P_2O_5$ under reduced pressure, prior to use. Spectroscopic data for (*E*)- and (*Z*)-**1d** are as follows:

**3,5-Diphenyl-3-methyl-1,2-dioxolane ((*E*)-1d):** $^1H$ NMR $\delta$ 1.71 (s, 3 H), 2.76 (dd, $J$ = 7.8 and 12.2 Hz, 1 H), 3.35 (dd, $J$ = 7.3 and 12.2 Hz, 1 H), 5.19 (dd, $J$ = 7.3 and 7.8 Hz, 1 H), 7.22−7.51 (m, 10 H). (*Z*)-**1d**: $^1H$ NMR $\delta$ 1.72 (s, 3 H), 2.94 (dd, $J$ = 7.8 and 12.2 Hz, 1 H), 3.16 (dd, $J$ = 7.8 and 12.2 Hz, 1 H), 5.44 (dd, $J$ = 7.8 and 7.8 Hz, 1 H), 7.20−7.54 (m, 10 H).

**Reduction of 1,2-Dioxolane 1 with $Ph_3P$. A General Procedure**. A reaction flask (50 mL) was flushed with dry argon. A mixture of **1** (1 mmol) and $Ph_3P$ (1 mmol) was heated in dry benzene (10 mL) at 60 °C. After the reaction was finished, the crude mixture of products was subjected to the GC analyses by using *n*-decane as an internal standard. Then, the solvent was removed under reduced pressure. The residue was subjected to a flush column chromatographic separation on silica gel [elution with a mixture of ethyl acetate−hexane (5:95−30:70)]. Products and yields are listed in Table 1. The isolated **7** was identified by the comparison of the NMR spectrum with that of the reported authentic sample.[13]

**1,3-Diphenyl-3-buten-1-ol (7):** $^1H$ NMR $\delta$ 2.12 (s, 1 H), 2.84 (dd, $J$ = 8.9 and 14.2 Hz, 1 H), 2.99 (dd, $J$ = 4.3 and 14.2 Hz, 1 H), 4.71 (dd, $J$ = 4.3 and 8.9 Hz, 1 H), 5.15 (s, 1 H), 5.40 (s, 1 H), 7.20-7.65 (m, 10 H).

**Reduction of (*E*)- and (*Z*)-1d with $Ph_3P$ in the Presence of $H_2O$.** A reaction mixture of (*E*)-**1d** or (*Z*)-**1d** (1 mmol) and $Ph_3P$ (1 mmol) in dry benzene (10 mL) was heated in the presence of $H_2O$ (2 mmol) at 60 °C, respectively. After the reaction was finished, the products were analyzed by GC as shown above. The reaction mixture was subjected to a flush column chromatographic separation on silica gel [elution with a mixture of ethyl acetate−hexane (5:95−30:70)]. The isolated

(9) Molecular orbital calculations by the PM3 method[10] were performed with the MOPAC program (ver 6.0) using Iris Indigo R4000 computer. The structural output was recorded by using the MOLGRAPH program (ver 2.8) by Daikin Industries, Ltd.

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*anti*- or *syn*-**8** were identified by the comparison of the NMR spectra with those of the reported authentic samples.[14]

**2,4-Diphenylbutane-2,4-diol (*anti*-8):** $^1$H NMR $\delta$ 1.51 (s, 3 H), 2.12 (dd, $J$ = 2.7 and 14.9 Hz, 1 H), 2.81 (dd, $J$ = 10.3 and 14.9 Hz, 1 H), 4.36 (s, 1 H), 4.36 (s, 1 H), 4.46 (dd, $J$ = 2.7 and 10.3 Hz, 1 H), 7.18−7.54 (m, 10 H). ***syn*-8:** $^1$H NMR $\delta$ 1.80 (s, 3 H), 1.97 (dd, $J$ = 2.4 and 14.9 Hz, 1 H), 2.18 (dd, $J$ = 10.8 and 14.9 Hz, 1 H), 3.44 (s, 1 H), 4.41 (s, 1 H), 5.18 (dd, $J$ = 2.4 and 10.8 Hz, 1 H), 7.20−7.53 (m, 10 H).

**$^{18}$O-Tracer Study.** A $^{18}$O-tracer study was performed in the same conditions depicted above except for using $H_2{}^{18}O$ (5% labeled). The contents of $^{18}$O atom in the products were determined by the comparison of the mass spectroscopic data of the products with those of the authentic samples by the reported method.[15] Mass spectroscopic data for labeled $Ph_3PO$ and natural $Ph_3PO$ are as follows:

**Labeled $Ph_3PO$**: EIMS *m*/*z* (relative intensity) 278 ($M^+$, 52), 279 (M+1, 18), 280 (M+2, 5). **Natural $Ph_3PO$**: EIMS *m*/*z* (relative intensity) 278 ($M^+$, 53), 279 (M + 1, 10), 280 (M + 2, 1).

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