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Efficient Aerobic Oxidation of Phosphines, Phosphites, and Sulfides by Using Trialkylborane

Kosuke Motoshima, Akinori Sato, Hideki Yorimitsu,* and Koichiro Oshima*

Department of Material Chemistry, Graduate School of Engineering, Kyoto University, Kyoto-daigaku Katsura, Nishikyo-ku, Kyoto 615-8510

Received May 24, 2007; E-mail: yori@orgrxn.mbox.media.kyoto-u.ac.jp

Treatment of phosphines, phosphites, or sulfides with trialkylborane under air afforded the corresponding oxides in good yields.

Trialkylborane can initiate radical reactions in the presence of a small amount of oxygen.[1] Trialkylborane rapidly reacts with molecular oxygen to generate an alkyl radical, which is used as an initiating radical (Eq. 1).[2] On the other hand, the reaction concomitantly yields a dialkylborylperoxy radical. The generation of the peroxy radical suggests that trialkylborane can effectively capture molecular oxygen in solution yielding a strong oxidizing agent. Here, we report efficient aerobic oxidation of some organophosphorus[3] and –sulfur[4] compounds by using trialkylborane as a preoxidant.

$$R_3B \xrightarrow{O_2} R\bullet + R_2BOO\bullet \quad (1)$$

Stirring a solution of triphenylphosphine (**1a**, 1.0 mmol) in THF (5 mL) under air in the presence of triethylborane (0.60 mmol) for 20 min afforded triphenylphosphine oxide (**2a**) quantitatively (Table 1, Entry 1). In the absence of triethylborane, the reaction at reflux as well as at ambient temperature overnight afforded a trace of **2a**. The amount of triethylborane could be reduced to 0.40 mmol, although the reaction was slow (Entries 2 and 3). Tri-*p*-tolylphosphine (**1b**) and tri-*m*-tolylphosphine (**1c**) were converted to the corresponding oxides quantitatively (Entries 4 and 5). However, conversion of tri-*o*-tolylphosphine (**1d**) did not proceed to completion (Entry 6). The methyl groups at the ortho position flatten the C–P–C angles to increase the p character of the lone pair on the phosphorus atom. The increased p character renders **1d** less reactive.[5] When two equimolar amounts of triethylborane were used, the oxidation of **1d** went to completion (Entry 7). Electron-rich tris(*p*-methoxyphenyl)phosphine (**1e**) was readily oxidized, whereas tri-2-furylphosphine (**1f**), which has electron-withdrawing furyl groups,[6] was oxidized more slowly (Entries 8 and 9). Oxidation of bidentate phosphines **1g** and **1h** was facile (Entries 10 and 11). Due to the low solubility of BINAP in THF, a large amount of THF was necessary for the oxidation of BINAP.

Table 1. Aerobic Oxidation of Phosphines and Phosphites with Triethylborane

R_3P **1** (1.0 mmol) —0.60 mmol Et_3B, THF (5 mL), 20 °C, air→ $R_3P{=}O$ **2**

Entry	R	Time/min	Conversion/%[a]
1	Ph (**a**)	20	100 (97)[b]
2[c]	Ph (**a**)	20	89
3[c]	Ph (**a**)	60	99
4	*p*-Me-C_6H_4 (**b**)	20	100
5	*m*-Me-C_6H_4 (**c**)	40	100
6	*o*-Me-C_6H_4 (**d**)	120	42
7[d]	*o*-Me-C_6H_4 (**d**)	330	100
8	*p*-MeO-C_6H_4 (**e**)	20	100
9	2-Furyl (**f**)	120	80
10[e]	(DPPP)[f] (**g**)	20	100
11[e]	(BINAP)[g,h] (**h**)	60	99
12	EtO (**i**)	60	91
13[d]	PhO (**j**)	330	27
14[i]	PhO (**j**)	330	47

a) Based on ^{31}P NMR. b) Isolated yield of **2a**. c) Triethylborane (0.40 mmol) was used. d) Triethylborane (2.0 mmol) was used. e) 0.50 mmol of **1** was used. The products were the corresponding dioxides. f) 1,3-Bis(diphenylphosphino)propane. g) 2,2′-Bis(diphenylphosphino)-1,1′-binaphthyl. h) THF (30 mL) was used to dissolve BINAP. i) Tributylborane (2.0 mmol) was used.

$$Et_3B \xrightarrow{O_2} Et\bullet + Et_2BOO\bullet \longrightarrow Et_2BOOEt$$

$$Et_2BOOEt + Ph_3P \longrightarrow Et_2BOEt + Ph_3P{=}O$$

$$Et_2BOEt \xrightarrow{O_2} Et\bullet + Et(EtO)BOO\bullet \longrightarrow Et(EtO)BOOEt$$

$$Et(EtO)BOOEt + Ph_3P \longrightarrow EtB(OEt)_2 + Ph_3P{=}O$$

$$EtB(OEt)_2 \xrightarrow{O_2} Et\bullet + (EtO)_2BOO\bullet \longrightarrow (EtO)_2BOOEt$$

$$(EtO)_2BOOEt + Ph_3P \longrightarrow B(OEt)_3 + Ph_3P{=}O$$

Scheme 1. Plausible mechanism.

Although triethyl phosphite (**1i**) was oxidized smoothly (Entry 12), attempts to oxidize triphenyl phosphite (**1j**) suffered from low conversion even with a larger amount of triethylborane (Entry 13). We assume that triethylborane itself is oxidized competitively to consume active oxidizing species in the solution. Next, we examined the use of tributylborane. Tributylborane would be less sensitive to oxidation than triethylborane, yet still reactive enough to trap molecular oxygen efficiently. This was indeed the case, and the oxidation of **1j** led to improved conversion in the presence of 2.0 equimolar amounts of tributylborane (Entry 14).

A possible mechanism of the oxidation is shown in Scheme 1.[2b] The oxidation of triethylborane would produce Et_2BOOEt (1st Eq.). The peroxide oxidizes triphenylphosphine rapidly (2nd Eq.) to produce **2a** along with Et_2BOEt. Et_2BOEt would be still reactive enough to trap molecular oxygen, which generates Et(EtO)BOOEt (3rd Eq.). This oxidant

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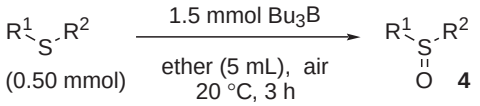
Table 2. Aerobic Oxidation of Sulfides with Tributylborane



Entry	R^1	R^2	**3**	Isolated yield of **4**/%[a]
1	*n*-$C_{12}H_{25}$	*n*-Pr	**3a**	76
2[b]	*n*-$C_{12}H_{25}$	*n*-Pr	**3a**	53
3	*n*-$C_{12}H_{25}$	CH_2=$CHCH_2$	**3b**	63
4	*p*-MeO-C_6H_4	*n*-Pr	**3c**	73
5	Ph	*n*-Bu	**3d**	49
6	Ph	Ph	**3e**	10
7	*sec*-Bu	*sec*-Bu	**3f**	48
8	*tert*-Bu	*tert*-Bu	**3g**	33

a) The rest was the starting material **3**. b) Triethylborane (1.5 mmol) was used.

reacts with **1a** with concomitant formation of $EtB(OEt)_2$ (4th Eq.). A similar oxidation process would proceed with $EtB(OEt)_2$ (5th and 6th Eqs.), although the efficiency of the 5th reaction is low.

Oxidation of sulfides took place with tributylborane (Table 2). Exposure of dodecyl propyl sulfide (**3a**) to air in the presence of 3.0 equimolar amount of tributylborane for 3 h afforded the corresponding sulfoxide **4a** in 76% isolated yield (Entry 1). This result is better than that obtained by using triethylborane (Entry 2). Allyl dodecyl sulfide (**3b**) and an alkyl aryl sulfide **3c** having an electron-rich aryl group were converted smoothly to sulfoxide **4b** and **4c** in good yields (Entries 3 and 4), respectively. However, oxidation of butyl phenyl sulfide (**3d**) was not efficient (Entry 5), and diphenyl sulfide (**3e**) resisted the oxidation (Entry 6). Aerobic oxidation of di-*sec*-butyl sulfide (**3f**) and di-*tert*-butyl sulfide (**3g**) proceeded albeit low yields (Entries 7 and 8). The slower reactions may be attributed to the steric hindrance around the sulfur atoms. In each reaction, only a trace of the corresponding sulfone was detected.

Oxidation of triphenylphosphine proceeded smoothly enough to use a near stoichiometric amount of molecular oxygen. Fine bubbles of air (86 mL, 1.5 equimolar amout of O_2 relative to **1a**, 1 mL min^{-1}) were injected through a sintered glass filter to a solution of **1a** (0.50 mmol) and triethylborane (0.20 mmol) in THF, as shown in Fig. 1, and oxide **2a** was obtained quantitatively. This result implies that triethylborane efficiently captured the molecular oxygen introduced as fine bubbles and that most of the oxygen was used in the oxidation of **1a**. Although isotopically labeled molecular oxygen is usually the oxygen source for labeling experiments,[7] labeled oxygen gas is expensive. Hence, the oxidation using a near stoichiometric amount of oxygen is desirable.

Experimental

Instrumentation and Chemicals. ^{1}H NMR (500 MHz) and ^{13}C NMR (125.7 MHz) spectra were taken on a Varian UNITY INOVA 500 spectrometer and were obtained in $CDCl_3$ with tetramethylsilane as an internal standard. ^{31}P NMR (121.5 MHz) spectra were taken on a Varian GEMINI 300 spectrometer. To determine the conversion of the reaction in Table 1, 0.60 mL of the

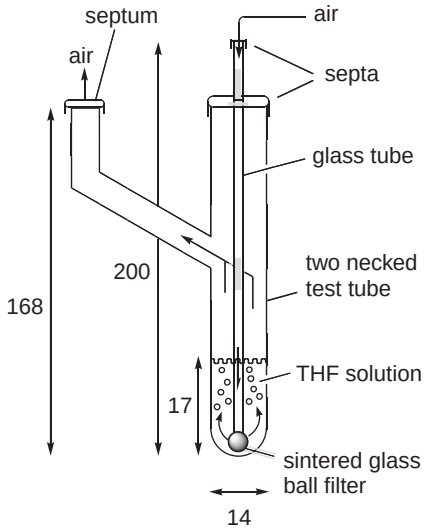


Fig. 1. Two-necked reaction vessel for the oxidation of triphenylphosphine with near stoichiometric molecular oxygen. The numbers refer to lengths in mm.

solution was taken, and the ^{31}P NMR spectra were obtained in THF with 85% H_3PO_4 solution as an external standard and with C_6D_6 in a capillary for locking. The first delay in the ^{31}P NMR measurements was set for 15 s for accurate integrals. IR spectra were obtained on a SHIMADZU FTIR-8200PC spectrometer. Mass spectra were acquired on a JEOL Mstation 700 spectrometer. TLC analyses were performed on commercial glass plates bearing a 0.25-mm layer of Merck Silica gel $60F_{254}$. Silica gel (Wakogel 200 mesh) was used for column chromatography. Elemental analyses were carried out at the Elemental Analysis Center of Kyoto University.

Air was injected into the reaction vessel using a Kinoshita glass ball filter 501G No. 4, with a pore size of 5–10 μm and $\phi = 10$ mm as shown in Fig. 1.

All of the phosphines and phosphites **1** and sulfide **3d**–**3g** were purchased from TCI and Wako Pure Chemicals. Sulfides **3a**–**3c** were quantitatively prepared by the reaction of dodecanethiol or *p*-methoxybenzenethiol with the corresponding alkyl halide in the presence of a base, such as K_2CO_3 and NaOMe.

Oxidation Reaction of Triphenylphosphine (Table 1, Entry 1). Under air, triethylborane (1.0 mol dm^{-3} hexane solution, 0.60 mL, 0.60 mmol) was added to a solution of triphenylphosphine (**1a**, 0.26 g, 1.0 mmol) in THF (5.0 mL). The mixture was stirred for 20 min at ambient temperature. ^{31}P NMR analysis of the solution showed the quantitative formation of triphenylphosphine oxide (**2a**). The solution was concentrated in vacuo. Silica-gel column chromatography (ethyl acetate) afforded analytically pure **2a** as a white solid in 97% yield (0.27 g, 0.97 mmol).

Oxidation Reaction of Dodecyl Propyl Sulfide (Table 2, Entry 1). Under air, tributylborane (1.0 mol dm^{-3} THF solution, 1.5 mL, 1.5 mmol) was added to a solution of dodecyl propyl sulfide (**3a**, 0.12 g, 0.50 mmol) in diethyl ether (5.0 mL). The mixture was stirred for 3 h at ambient temperature. The solution was concentrated in vacuo. Silica-gel column chromatography (hexane/ethyl acetate = 1:2 to hexane/ethyl acetate/methanol = 20:40:3) afforded analytically pure dodecyl propyl sulfoxide (**4a**) as a white solid in 76% yield (0.099 g, 0.38 mmol).

Rapid Oxidation Reaction of Triphenylphosphine with Fine Air Bubble. Under an atmosphere of argon, a solution of 0.13 g

of triphenylphosphine (0.50 mmol) in THF (2.0 mL) was placed in the reaction vessel set as shown in Fig. 1. Triethylborane (1.0 mol dm^{-3} hexane solution, 0.20 mL, 0.20 mmol) was added. Then, 86 mL of air (containing 0.75 mmol of O_2) was added to the solution as fine bubbles (1 mL s^{-1}). After the completion of the bubbling, 0.60 mL of the solution was taken for ^{31}P NMR analysis immediately, which revealed that triphenylphosphine was completely oxidized.

Characterization Data of New Compounds. Dodecyl Propyl Sulfide (3a): IR (neat) 721, 1237, 1291, 1377, 1466, 2854, 2925 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (t, $J = 7.0$ Hz, 3H), 0.99 (t, $J = 7.5$ Hz, 3H), 1.20–1.41 (m, 18H), 1.54–1.65 (m, 4H), 2.49 (t, $J = 7.5$ Hz, 2H), 2.50 (t, $J = 7.5$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 13.51, 14.08, 22.66, 22.99, 28.95, 29.25, 29.33, 29.52, 29.59, 29.61, 29.64, 29.74, 31.90, 32.11, 34.20. Found: C, 73.44; H, 12.93%. Calcd for $C_{15}H_{32}S$: C, 73.69; H, 13.19%.

Dodecyl Propyl Sulfoxide (4a): IR (Nujol) 722, 1013, 1088, 1198, 1467, 2849, 2919, 3226 (br) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (t, $J = 7.0$ Hz, 3H), 1.09 (t, $J = 7.5$ Hz, 3H), 1.21–1.52 (m, 18H), 1.70–1.87 (m, 4H), 2.55–2.73 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 13.44, 14.10, 16.29, 22.58, 22.67, 28.88, 29.20, 29.32, 29.35, 29.52, 29.59 (2C), 31.89, 52.50, 54.36. HRMS(FAB) Found: 261.2249. Calcd for $C_{15}H_{33}OS$ $[M + H]^+$: 261.2252.

***p*-Methoxyphenyl Propyl Sulfide (3c):** IR (neat) 825, 1033, 1173, 1180, 1246, 1285, 1463, 1495, 1571, 1593, 2961 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.99 (t, $J = 7.5$ Hz, 3H), 1.60 (tq, $J = 7.5$, 7.5 Hz, 2H), 2.79 (t, $J = 7.5$ Hz, 2H), 3.79 (s, 3H), 6.82–6.86 (m, 2H), 7.32–7.36 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 13.29, 22.65, 37.83, 55.30, 114.45, 126.84, 133.00, 158.72. Found: C, 65.88; H, 7.67%. Calcd for $C_{10}H_{14}OS$: C, 65.89; H, 7.74%.

***p*-Methoxyphenyl Propyl Sulfoxide (4c):** IR (neat) 830, 1025, 1089, 1252, 1496, 1595, 2965, 3480 (br) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04 (t, $J = 7.5$ Hz, 3H), 1.60–1.80 (m, 2H), 2.67–2.77 (m, 1H), 2.78–2.88 (m, 1H), 3.86 (s, 3H), 7.03 (d, $J = 9.0$ Hz, 2H), 7.57 (d, $J = 9.0$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 13.22, 15.97, 55.46, 59.28, 114.68, 125.95, 134.72, 161.87. Found: C, 60.39; H, 7.12%. Calcd for $C_{10}H_{14}O_2S$: C, 60.57; H, 7.12%.

Butyl Phenyl Sulfoxide (4d): IR (neat) 692, 750, 998, 1039, 1089, 1444, 1466, 1478, 2873, 2933, 2959, 3500 (br) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (t, $J = 7.5$ Hz, 3H), 1.36–1.53 (m, 2H), 1.55–1.65 (m, 1H), 1.69–1.79 (m, 1H), 2.74–2.84 (m, 2H), 7.46–7.56 (m, 3H), 7.59–7.65 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 13.64, 21.88, 24.12, 57.08, 124.00, 129.15, 130.86, 144.07. Found: C, 65.70; H, 7.71%. Calcd for $C_{10}H_{14}OS$: C, 65.89; H, 7.74%.

Di-*sec*-butyl Sulfoxide (4f, a Mixture of Three Diastereomers): IR (neat) 959, 1032, 1061, 1382, 1456, 1714, 2877, 2934, 2967, 3451 (br) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00–1.36 (m, 12H), 1.46–2.08 (m, 4H), 2.46–2.71 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 9.65, 10.44, 10.76, 11.28 (2C), 11.62, 12.60, 13.78, 21.21, 22.65, 24.61, 25.55, 52.31, 52.75, 53.22, 53.28. HRMS(FAB) Found: 163.1155. Calcd for $C_8H_{19}OS$: $[M + H]^+$: 163.1157.

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