Selected Paper

# Conversion of Alcohols to Alkyl Aryl Sulfides by a New Type of Oxidation–Reduction Condensation Using Phenyl Diphenylphosphinite

**Kiichi Kuroda,[1] Yuji Maruyama,[2] Yujiro Hayashi,*[1] and Teruaki Mukaiyama*[3]**

[1]Department of Industrial Chemistry, Faculty of Engineering, Tokyo University of Science, Kagurazaka, Shinjuku-ku, Tokyo 162-8601

[2]Department of Applied Chemistry, Faculty of Science, Tokyo University of Science, Kagurazaka, Shinjuku-ku, Tokyo 162-8601

[3]Center for Basic Research, Kitasato University, 6-15-5 (TCI) Toshima, Kita-ku, Tokyo 114-0003

Received August 11, 2008; E-mail: mukaiyam@abeam.ocn.ne.jp

Preparation of alkyl aryl sulfides from alcohols and arenethiols such as 2-sulfanyl-1,3-benzothiazole (BtzSH) is described by a new type of oxidation–reduction condensation using phenyl diphenylphosphinite ($PhOPPh_2$) and benzoquinone derivatives or azide compounds. This reaction proceeds under mild and neutral conditions and is applicable to the thioetherification of various alcohols in which the chiral secondary and tertiary alcohols are converted into the corresponding chiral sulfides with almost complete inversion of configuration.

Preparation of various alkyl aryl sulfides is an important synthetic process in organic chemistry[1] and therefore many trials have been made to develop useful synthetic methods. For example, a nucleophilic substitution of activated alkyl halides or sulfonates with aryl thiolate prepared from aryl thiol in the presence of strong base[2] is a fundamental methodology. Since the synthetic scope of this classical reaction is generally limited due to the harsh conditions (long reaction time and high reaction temperature), alternative methods for alkyl aryl sulfides have recently been studied.[3,4] On the other hand, direct substitution reactions of alcohols by thiolate anion under mild and neutral conditions is considered to be most attractive and efficient. Procedures developed previously by Mitsunobu et al. or Hata et al. based on the concept of "oxidation–reduction condensation"[5] are known to be useful for this transformation: that is, alcohols are converted into the corresponding sulfides or thioesters by treating with weakly acidic sulfur nucleophiles such as arenethiols or thioacetic acids in the presence of triphenylphosphine and diethyl azodicarboxylate (DEAD)[6,7] or with tributylphosphine and diaryl disulfides.[8] In these reaction systems,[9] primary and secondary alcohols are the most suitable substrates, and chiral secondary sulfides and thioesters are formed from chiral secondary alcohols with complete inversion of configuration by an $S_N2$ displacement. However, it is generally known that the sterically hindered tertiary alcohols are not converted to the corresponding tertiary sulfides[10] because the starting alcohols are recovered or undesired olefins are produced exclusively by elimination reactions. Thus, nucleophilic substitution at quaternary carbon centers via $S_N2$ displacement has been a very difficult problem and one of the most challenging topics in current organic synthesis.[11]

It has been reported from our laboratory that the oxidation–reduction condensation[12] of alkyl diphenylphosphinites ($ROPPh_2$), that were prepared from the corresponding alcohols, with various nucleophiles (Nu–H) gave the formal dehydrated condensation products (R–Nu) in the presence of benzoquinone derivatives as oxidants.[13–16] It is noteworthy that the tertiary alcohols are converted into the corresponding *tert*-alkyl products by preparing the intermediates of the alkyl diphenylphosphinites from the corresponding alcohols and chlorodiphenylphosphine in advance. When 2-sulfanyl-1,3-benzothiazole (BtzSH) was employed as a sulfur nucleophile in the presence of 2,6-di-*tert*-butyl-1,4-benzoquinone (DBBQ), chiral *tert*-alkyl diphenylphosphinites were converted into the corresponding chiral *tert*-alkyl sulfides with inversion of configuration.[16] In this reaction, the yields and enantiomeric excesses of the desired Btz sulfides are influenced by the $\alpha$-substituents of alcohols. For example, chiral *tert*-alkyl sulfides are obtained in good yields with complete inversion of configuration when *tert*-alcohols having $\alpha$-ester groups are employed as the starting materials (Scheme 1). The chiral *tert*-alkyl Btz sulfide obtained is converted to the corresponding chiral *tert*-thiol in high yield on treatment with $LiAlH_4$.

In order to improve the synthetic utility of this reaction system ($ROPPh_2$–BQ–BtzSH), it is important to develop a new method for one-pot synthesis of sulfides from alcohols without preparing the intermediate, $ROPPh_2$. Recently, a newer type of oxidation–reduction condensation by using a combination of aryl diphenylphosphinite ($ArOPPh_2$) and benzoquinone derivatives[17] or azide compounds[18] was reported from our laboratory, which was then applied to the direct synthesis of sulfides from alcohols and 2-sulfanyl-1,3-benzothiazole (BtzSH) as a sulfur nucleophile. In this paper, we would like to report on these condensation reactions to further examine the scope and limitation.

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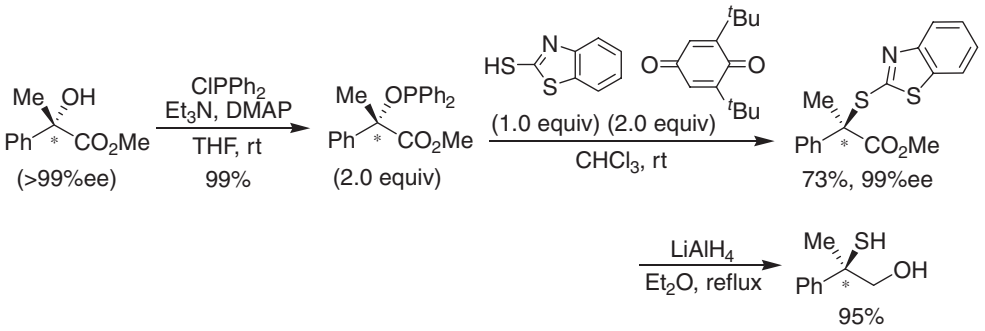
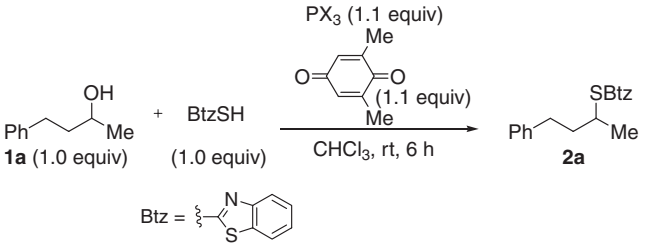



**Scheme 1.**

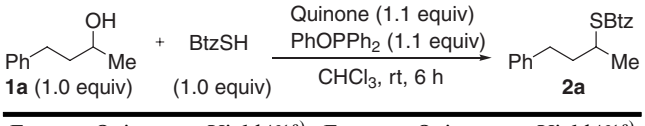
**Table 1.** Screening of Phosphorus(III) Compound

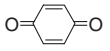
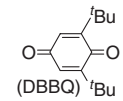
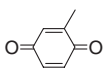
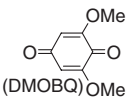
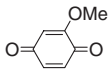
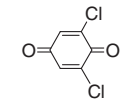
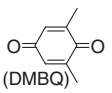
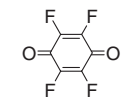



| Entry | $PX_3$ | Yield /%[a)] | Entry | $PX_3$ | | Yield /%[a)] |
|---|---|---|---|---|---|---|
| 1 | $PPh_3$ | N.D. | 5 | $Ph_2PCl$ | | 8 |
| 2 | $PBu_3$ | N.D. | 6 | R<br>OPPh2 | R = H | 64 |
| 3 | $P(OPh)_3$ | N.D. | 7 | | R = Cl | 54 |
| 4 | $PhP(OPh)_2$ | 21 | 8 | | R = OMe | 58 |

a) Isolated yield.

**Table 2.** Screening of Quinone Derivatives




| Entry | Quinone | Yield/%[a)] | Entry | Quinone | Yield/%[a)] |
|---|---|---|---|---|---|
| 1 |  | 33 | 5 |  (DBBQ) | 61[b)] |
| 2 |  | 46 | 6 |  (DMOBQ) | 73 |
| 3 |  | 23 | 7 |  | 3 |
| 4 |  (DMBQ) | 64 | 8 |  | 3 |

a) Isolated yield. b) Determined by $^1$H NMR analysis.

## Results and Discussion

**Preparation of Alkyl Aryl Sulfides from Alcohols and 2-Sulfanyl 1,3-Benzothiazole (BtzSH) by Oxidation–Reduction Condensation Using Phenyl Diphenylphosphinite and Benzoquinone Derivatives.** Initially effects of phosphorus(III) compounds were examined in order to find a suitable reductant by taking condensation reaction of 4-phenylbutan-2-ol (**1a**) and 2-sulfanyl-1,3-benzothiazole (BtzSH) in the presence of 2,6-dimethyl-1,4-benzoquinone (DMBQ) as a model (Table 1). The desired sulfide **2a** was not obtained when $PPh_3$, $PBu_3$, and $P(OPh)_3$ were used (Entries 1–3) while $PhP(OPh)_2$ and $Ph_2PCl$ afforded **2a** in low yields (Entries 4 and 5). In the case of aryl diphenylphosphinites, the yield of **2a** markedly increased (Entries 6–8). As a result of examination of the influence of substituents on the aryl group, it was shown that the phenyl diphenylphosphinite ($PhOPPh_2$) gave the best result (Entry 6).

Next, various 1,4-benzoquinone derivatives were examined to find a suitable oxidant (Table 2). A condensation reaction that used simple 1,4-benzoquinone afforded the desired product **2a** in lower yield compared to that of DMBQ (Entry 1). Introduction of one substituent at the 2-position of 1,4-benzoquinones did not give good results (Entries 2 and 3) while the yield improved if disubstituted 1,4-benzoquinones were used (Entries 4–6). The reaction with 2,6-dimethoxy-1,4-benzoquinone (DMOBQ) afforded **2a** in 73% yield. On the other hand, when electron-withdrawing groups were introduced to benzoquinones, **2a** was obtained in quite low yield (Entries 7 and 8).

The effect of the solvent was next examined in the condensation of alcohol **2a** with BtzSH in the presence of $PhOPPh_2$ and DMOBQ (Table 3). Whereas polar solvents such as $Et_2O$, THF, and EtOAc lowered the yield of the desired sulfide **2a** (Entries 1–3), $CH_3CN$ or halogenated solvents gave better yields (Entries 4–6), and toluene was among the best (Entry 7).

After a suitable reductant and an oxidant were chosen, condensation reactions of various alcohols with BtzSH were tried to investigate the scope of this reaction under the optimized conditions (Table 4). Reactions of benzyl alcohol (**1b**), allyl alcohols **1c**, and primary alcohol **1d** having a furan ring proceeded smoothly to afford the corresponding sulfides in high yields (Entries 1–3). Primary alcohols **1e** and **1f** with a ketone group and a *tert*-butyldimethylsilyl group were also converted into the corresponding sulfides in good yields while alcohols **1g** and **1h** bearing indole and a *N-tert*-butoxycarbonyl group retarded the thioetherification under the above conditions (Entries 4–7). Cyclic secondary alcohol **1i** was successfully used in this reaction (Entry 8). Further, the reactions of various

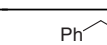
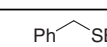
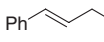
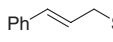
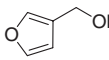
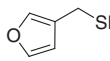
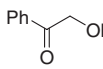
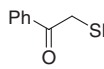
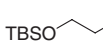
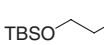
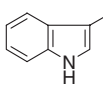
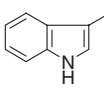
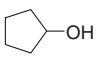
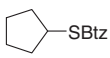
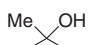
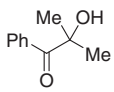
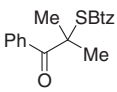
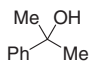
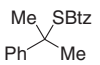
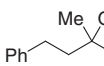
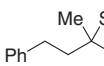
**Table 3.** Effect of Solvent[a)]

| Entry | Solvent | Yield/% |
|---|---|---|
| 1 | $Et_2O$ | 42 |
| 2 | THF | N.D. |
| 3 | EtOAc | 50 |
| 4 | $CH_3CN$ | 64 |
| 5 | $CH_2Cl_2$ | 71 |
| 6 | $CHCl_3$ | 73 |
| 7 | Toluene | 81 (62)[b)] |

a) The reactions were carried out by using **1a** (1.0 equiv), BtzSH (1.0 equiv), $PhOPPh_2$ (1.1 equiv), and DMOBQ (1.1 equiv). b) DMBQ was used instead of DMOBQ.

**Table 4.** Thioetherification of Various Alcohols

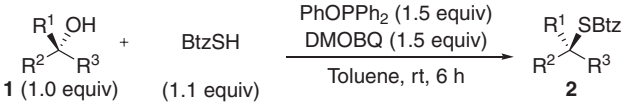
ROH (**1** (1.0 equiv)) + BtzSH (1.1 equiv) —$PhOPPh_2$ (1.5 equiv), DMOBQ (1.5 equiv), Toluene, rt, 6 h→ R−SBtz (**2**)

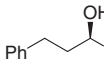
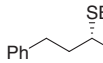
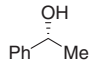
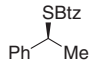
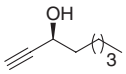
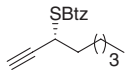
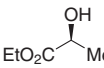
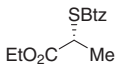
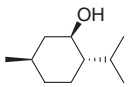
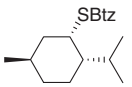
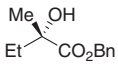
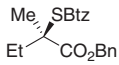
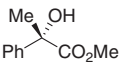
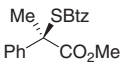
| Entry | ROH | **1** | Product | **2** | Yield/%[a)] |
|---|---|---|---|---|---|
| 1 |  | **1b** |  | **2b** | 97 |
| 2 |  | **1c** |  | **2c** | 98 |
| 3 |  | **1d** |  | **2d** | 90 |
| 4 |  | **1e** |  | **2e** | 81 |
| 5 |  | **1f** |  | **2f** | 78 |
| 6 |  | **1g** |  | **2g** | 69 |
| 7 |  | **1h** |  | **2h** | 49 |
| 8 |  | **1i** |  | **2i** | 89 |
| 9[b)] |  | **1j** |  | **2j** | 87<br>79[c)] |
| 10[b)] |  | **1k** |  | **2k** | 42 |
| 11[b)] |  | **1l** |  | **2l** | 20 |
| 12[b)] |  | **1m** |  | **2m** | <15 |

a) Isolated yeild. b) The reaction was carried out by using BtzSH (2.0 equiv), DMBQ (2.0 equiv), and $PhOPPh_2$ (2.0 equiv) at 40 °C for 24 h. c) DMOBQ was used instead of DMBQ.

tertiary alcohols were next tried (Entries 9–12). Although *tert*-alcohol **1j** having an $\alpha$-ester group was converted into the corresponding sulfide in 79% yield, the yield was improved to 87% when DMBQ was used instead of DMOBQ (Entry 9). *tert*-Alcohol **1k** with an $\alpha$-ketone group gave the desired product in moderate yield but the yield of the desired sulfide markedly decreased when alcohol **1l** bearing an $\alpha$-phenyl group and aliphatic alcohol **1m** were used (Entries 10–12).

**Table 5.** Thioetherification of Various Alcohols



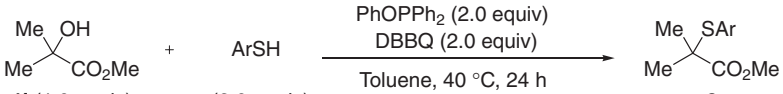

| Entry | ROH | **1** (%ee) | Product | **2** | Yield/%[a)] (%ee[b)]) |
|---|---|---|---|---|---|
| 1 |  | **1a** (>99) |  | **2a** | 99 (>99) |
| 2 |  | **1n** (>99) |  | **2n** | 77 (96) |
| 3 |  | **1o** (98) |  | **2o** | 87 (98) |
| 4 |  | **1p** (>99) |  | **2p** | 85 (98) |
| 5[c)] |  | **1q** |  | **2q** | 62 |
| 6[d),e)] |  | **1r** (>99) |  | **2r** | 55 (>99) |
| 7[d)] |  | **1s** (>99) |  | **2s** | 56 (>99) |

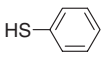
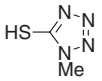
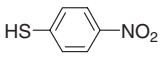
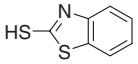
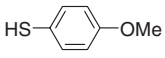
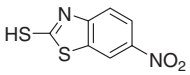
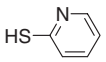
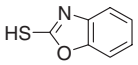
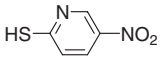
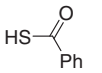
a) Isolated yield. b) Determined by HPLC analysis. c) The reaction was carried out by using BtzSH (2.0 equiv), DMOBQ (3.0 equiv), and $PhOPPh_2$ (3.0 equiv) for 24 h. d) The reaction was carried out by using BtzSH (4.0 equiv), DMBQ (4.0 equiv), and $PhOPPh_2$ (4.0 equiv) for 24 h. e) When DBBQ was used instead of DMBQ, the desired sulfide **2r** was obtained in 52% yield with >99%ee.

Taking the above results into consideration, thioetherification of various chiral alcohols was next tried in order to examine the stereochemistry of this reaction (Table 5). It was shown that the desired sulfides were obtained in good to excellent yields with almost complete inversions of stereochemistry even when acetylene and ethyl ester groups coexisted in the same molecules (Entries 1–4). This suggests that the reaction basically proceeded via $S_N2$ mechanism. Since the reaction of chiral benzylic alcohol **1n** afforded the desired product with slightly lowered optical purity, it is considered that this reaction proceeded partially via $S_N1$ mechanism as the benzylic cation was generated more easily (Entry 2). The thioetherification of sterically-hindered (−)-(*l*)-menthol (**1q**) gave the inverted product in moderate chemical yield without any other accompanying products (Entry 5). Further, more hindered tertiary alcohols were employed as substrates in order to study the potential application of this reaction to the asymmetric construction of quaternary carbon (Entries 6 and 7). The reactions of chiral tertiary alcohol **1r** and chiral benzylic alcohol **1s** bearing $\alpha$-ester groups afforded the corresponding sulfides in moderate yields with complete inversion of configuration.

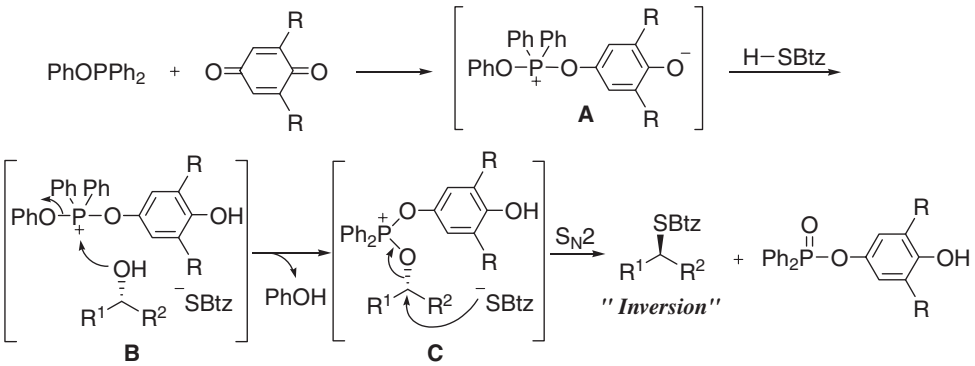
In order to extend the scope of this condensation reaction, reactions of various arenethiols or thiobenzoic acid with tertiary alcohol **1j** were examined (Table 6). When benzenethiol ($pK_a$ 7.76 in $EtOH/H_2O$, 10.3 in DMSO)[19a] was used as a

**Table 6.** Condensation of Tertiary Alcohol **1j** with Various ArSH




| Entry | ArSH | Product **3** | Yield/%[a] | Entry | ArSH | Product **3** | Yield/%[a] |
|---|---|---|---|---|---|---|---|
| 1 |  | **3a** | 83 | 6 |  | **3f** | 68 |
| 2 |  | **3b** | 72 | 7 |  | **2j** | 90 (87)[b] |
| 3 |  | **3c** | 78 | 8 |  | **3g** | 83 |
| 4 |  | **3d** | 67 (N.D.)[b] | 9 |  | **3h** | 82 (80)[b] |
| 5 |  | **3e** | 91 (21)[b] | 10 |  | **3i** | 19 |

a) Isolated yield. b) DMBQ was used instead of DBBQ.

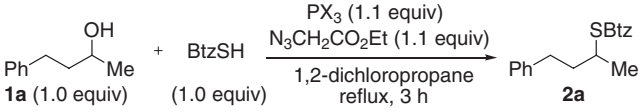


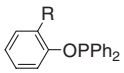

**Scheme 2.**

sulfur nucleophile, the desired sulfide was obtained in good yield (Entry 1). The reactions of **1j** with 4-nitrobenzenethiol ($pK_a$ 5.11 in EtOH/$H_2O$, 5.5 in DMSO)[19a] or 4-methoxybenzenethiol ($pK_a$ 7.99 in EtOH/$H_2O$, 11.2 in DMSO)[19a] proceeded in a similar fashion to afford the corresponding sulfides in good yields (Entries 2 and 3). Thus, the effect of $pK_a$ values of nucleophiles[12,14c,14d,20] was not observed in the case of benzenethiol derivatives. On the other hand, it was shown that the reactivity of 5-nitro-2-sulfanylpyridine was higher than that of 2-sulfanylpyridine whose difference may be attributed to the $pK_a$ values of nucleophiles (Entries 4 and 5). Further, the reactions of various heteroarene thiols were examined (Entries 6–9). It was found then that 1-methyl-1*H*-tetrazole-5-thiol could also be used successfully in this reaction (Entry 6), and 2-sulfanyl-1,3-benzothiazole (BtzSH; $pK_a$ 7.00 in EtOH/$H_2O$)[19b] was the most reactive of the heteroarene derivatives (Entry 7). When thiobenzoic acid ($pK_a$ 5.3 in DMSO)[19c] was used, the yield of the desired product was poor though its acidity was sufficient (Entry 10).

A plausible reaction mechanism is shown in Scheme 2: reaction of phenyl diphenylphosphinite ($PhOPPh_2$) and a benzoquinone derivative[21] such as DMOBQ, DMBQ, or DBBQ gives initially the betain intermediate **A**, and deprotonation of BtzSH by phenoxide anion that follows results in the formation of intermediate **B**. A subsequent nucleophilic attack of alcohol to the positively charged phosphorus atom leads to the formation of an intermediate **C** along with the elimination of phenoxide anion ($PhO^-$). Finally, a nucleophilic attack of thiolate anion ($BtzS^-$) to the carbon atom adjacent to an oxygen atom of alkoxy group via $S_N2$ manner gives the inverted sulfide. The reason why $PhOPPh_2$ among phosphorus compounds gave the best result is considered as follows. Nucleophilicity of a phosphorus compound to benzoquinone derivatives is essential for producing the intermediate **A** in the first step. In fact, DMBQ was consumed when $PBu_3$, $PPh_3$, or $PhOPPh_2$ was used while DMBQ remained when electron-deficient $PhP(OPh)_2$ or $P(OPh)_3$ was used (Table 1). However, the desired product was not obtained in the case of $PBu_3$ or $PPh_3$ without consuming alcohol **1a**. This indicated that alkoxyphosphonium salt **C** as a key intermediate was not formed from phosphonium salt **B** because the attack of alcohol **1a** to the positively charged phosphorus atom was retarded. On the other hand, when $PhOPPh_2$ was used, intermediate **C** was produced from intermediate **B** since phenoxide anion ($PhO^-$)

**Table 7.** Screening of Phosphorus(III) Compounds




| Entry | $PX_3$ | Yield /%[a)] | Entry | $PX_3$ | | Yield /%[a)] |
|---|---|---|---|---|---|---|
| 1 | $PPh_3$ | trace | 5 | $Ph_2PCl$ | | 11 |
| 2 | $PBu_3$ | N.D. | 6 |  | R = H | 69 |
| 3 | $P(OPh)_3$ | 34 | 7 | | R = Cl | 65 |
| 4 | $PhP(OPh)_2$ | 58 | 8 | | R = OMe | 61 |

a) Isolated yield.

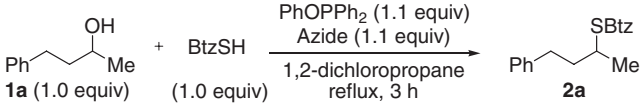
was eliminated by the attack of alcohol **1a** to the positively charged phosphorus atom. When $ClPPh_2$ was used as a reductant, alcohol **1a** was converted into the corresponding chloride by the attack of chloride anion ($Cl^-$) as a leaving group to activated alcohol **1a** while this type side reaction did not proceed in the case of $PhOPPh_2$. Thus, it is proven that $PhOPPh_2$ is a suitable reductant which also contains a good leaving group.

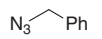
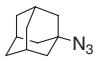
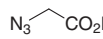
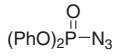
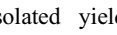
Thus, a new type of oxidation–reduction condensation by the combined use of $PhOPPh_2$ and benzoquinone derivatives was found applicable to the thioetherification of various alcohols. In the case of secondary chiral alcohols, the inverted sulfides were obtained in good to excellent yields under mild and neutral conditions. However, the inverted chiral *tert*-alkyl sulfides were obtained in moderate yield when chiral *tert*-alcohols having $\alpha$-ester groups were employed. In order to improve these yields, our attention was next focused on another type of oxidation–reduction condensation reaction using organic azides as oxidants in place of the above-mentioned benzoquinone derivatives.

**Preparation of Alkyl Aryl Sulfides from Alcohols and 2-Sulfanyl-1,3-benzothiazole (BtzSH) by Oxidation–Reduction Condensation Using Phenyl Diphenylphosphinite and Azide Compounds.** A reaction of organic azides[22] with trivalent phosphorus compounds that affords the corresponding iminophosphoranes (aza-ylides) is known as the Staudinger reaction.[23] Although this iminophosphorane is a versatile intermediate in organic synthesis,[24] there are only few reports[25] on the intermolecular dehydration condensation reactions between alcohols and acidic compounds via this intermediate, iminophosphorane, which are considered to be similar species of an betain intermediate **A** (Scheme 2). Thus, the use of azide compounds[14d,14e] instead of benzoquinone derivatives was tried next in order to determine if this iminophosphorane works as the intermediate in oxidation–reduction condensation.

In order to find the most suitable reductant, effects of phosphorus(III) compounds were first examined by condensation reaction of 4-phenylbutan-2-ol (**1a**) and BtzSH in the presence of ethyl azidoacetate (Table 7). Then, it was shown that the desired sulfide **2a** was not obtained when $PPh_3$ and $PBu_3$ were used (Entries 1 and 2) while it was formed when $P(OPh)_3$, $PhP(OPh)_2$, and $Ph_2PCl$ were used (Entries 3–5). In the case when aryl diphenylphosphinites were employed, the yield of **2a** markedly increased (Entries 6–8) and phenyl diphenylphosphinite ($PhOPPh_2$) was among the best (Entry 6).

**Table 8.** Screening of Azide Compounds




| Entry | Azide | Yield/%[a)] | Entry | Azide | Yield/%[a)] |
|---|---|---|---|---|---|
| 1 |  | 53 | 4 |  | 34 |
| 2 |  | 67 (81)[b)] | 5 |  | N.D. |
| 3 |  | 69 (84)[b)] | 6 | $TMSN_3$ | 7 |

a) Isolated yield. b) Toluene was used instead of 1,2-dichloropropane.

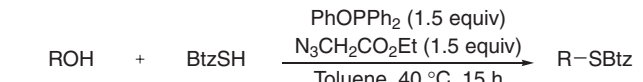
These results were similar to the above reactions of using benzoquinone derivatives.

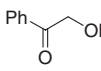
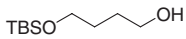
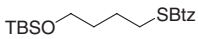
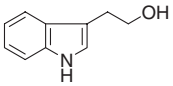
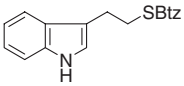
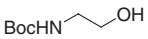
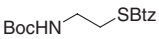
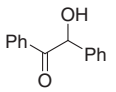
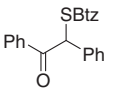
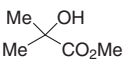
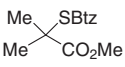
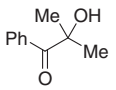
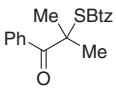
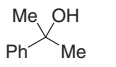
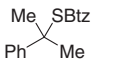
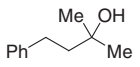
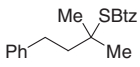
Next, various azide compounds were examined to find a suitable oxidant (Table 8), and a condensation reaction using trimethylsilylmethyl azide afforded the desired product **2a** in moderate yield (Entry 1). The alkyl azides such as benzyl azide and ethyl azidoacetate gave **2a** in good yields (Entries 2 and 3) while 1-azidoadamantane, diphenylphosphoryl azide, or trimethylsilyl azide did not work well (Entries 4–6). In the cases of benzyl azide and ethyl azidoacetate, the yields increased up to 81 and 84%, respectively, by changing solvent from 1,2-dichloropropane to toluene (Entries 2 and 3).

After a suitable reductant and an oxidant were chosen, condensation reactions of various alcohols with BtzSH were tried in order to examine the scope of this reaction under the optimized conditions (Table 9). The reactions of primary and secondary alcohols proceeded smoothly to afford the corresponding sulfides in high yields, indicating that this reaction is tolerant of various functional groups (Entries 1–5). It is noted that the alcohols **1e** and **1t** bearing ketone groups were converted into the corresponding sulfides without any accompanying side reactions (Aza-Wittig type reaction) (Entries 1 and 5). The reaction of tertiary alcohol **1j** with an $\alpha$-ester group afforded the corresponding sulfide also in high yield while yields of *tert*-alcohols **1k** and **1l** bearing an $\alpha$-ketone and an $\alpha$-phenyl groups were moderate (Entries 6–8). In the case of aliphatic substrate **1m**, the yield of the desired sulfide markedly decreased because of elimination reactions that took place to give undesired olefins (Entry 9).

Next, thioetherification of various chiral alcohols were tried in order to examine the stereochemistry of this reaction (Table 10). A reaction of chiral secondary alcohol **1a** proceeded smoothly to afford the corresponding sulfide in excellent yield with complete inversion of stereochemistry (Entry 1). Chiral benzylic alcohol **1n** and propargylic alcohol **1o** also gave the desired products in high yields with high enantiomeric excesses (Entries 2 and 3). The thioetherification of sterically hindered (−)-(*l*)-menthol (**1q**) gave the inverted product in high yield without any other accompanying products (Entry 4). Further, more hindered tertiary alcohols bearing $\alpha$-ester groups were employed as substrates in order to study potential application of this reaction to the asymmetric construction of quaternary carbon (Entries 5–7). Then, a reaction of chiral *tert*-alcohol **1r** proceeded smoothly to afford

**Table 9.** Thioetherification of Various Alcohols




| Entry | ROH | 1 | Product | 2 | Yield /%[a] |
|---|---|---|---|---|---|
| 1 |  | **1e** |  | **2e** | 82 |
| 2 |  | **1f** |  | **2f** | 91 |
| 3 |  | **1g** |  | **2g** | 95 |
| 4 |  | **1h** |  | **2h** | 95 |
| 5[b] |  | **1t** |  | **2t** | 94 |
| 6[b,c] |  | **1j** |  | **2j** | 94 |
| 7[b,d] |  | **1k** |  | **2k** | 42 |
| 8[b,d] |  | **1l** |  | **2l** | 53 |
| 9[b,d] |  | **1m** |  | **2m** | 17 |

a) Isolated yield. b) The reaction time was 24 h. c) The reaction was carried out by using BtzSH (2.0 equiv), $PhOPPh_2$ (2.0 equiv), and $N_3CH_2CO_2Et$ (2.0 equiv). d) The reaction was carried out by using BtzSH (4.0 equiv), $PhOPPh_2$ (4.0 equiv), and $N_3CH_2CO_2Et$ (4.0 equiv).

the corresponding sulfide in good yield with complete inversion of stereochemistry (Entry 5). Similarly, chiral benzylic alcohol **1s** gave the desired product in high yield with excellent enantiomeric excess (Entry 6). Also, thioetherification of chiral propargylic alcohol **1u** gave the inverted product in high yield (Entry 7). On the other hand, the reaction of (*R*)-terpinen-4-ol (**1v**) under the above conditions did not proceed and it was recovered, which is probably because its bulky isopropyl group interferes with the attack of **1v** to the positively charged phosphorus atom (Entry 8).

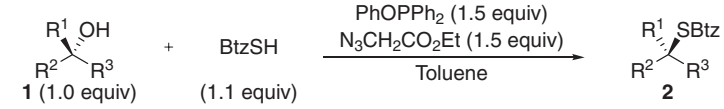
Next, reactions of various arenethiols or thiobenzoic acid with tertiary alcohol **1j** were examined in order to extend the scope of this reaction as well as reactions that used benzoquinone derivatives (see Table 11 and Table 6). When benzenethiol derivatives were used as sulfur nucleophiles, the yields of the products increased in the following order: 4-nitrobenzenethiol ($pK_a$ 5.11 in $EtOH/H_2O$, 5.5 in DMSO) > benzenethiol ($pK_a$ 7.76 in $EtOH/H_2O$, 10.3 in DMSO) > 4-methoxybenzenethiol ($pK_a$ 7.99 in $EtOH/H_2O$, 11.2 in DMSO) (Entries 1–3). These results indicate that the yields of the condensation reactions are influenced by the $pK_a$ values of the nucleophiles. Also, the reactivity of 5-nitro-2-sulfanylpyridine was shown to be higher than that of 2-sulfanylpyridine (Entries 4 and 5). Reactions of various heteroarene thiols were further examined and the corresponding sulfides were obtained in high yields (Entries 6–9). When thiobenzoic acid ($pK_a$ 5.3 in DMSO) was used, the yield of the desired product was poor in spite of sufficient acidity. These results are similar to those that used benzoquinone derivatives except in the case when benzenethiol derivatives were employed as sulfur nucleophiles.

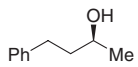
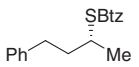
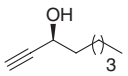
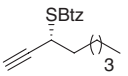
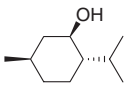
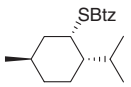
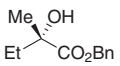
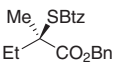
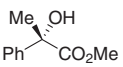
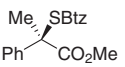
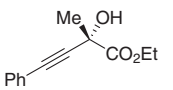
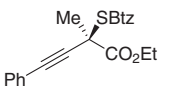
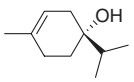
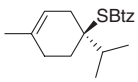
A plausible reaction mechanism is shown in Scheme 3: the Staudinger reaction of phenyl diphenylphosphinite ($PhOPPh_2$) and an azide compound[26] gives initially an iminophosphorane, and deprotonation of BtzSH by the iminophosphorane results in the formation of intermediate **A**. A subsequent nucleophilic attack of alcohol to the positively charged phosphorus atom leads to formation of intermediate **B** and the following nucleophilic attack of thiolate anion ($BtzS^-$) to the carbon atom adjacent to an oxygen atom of alkoxy group in $S_N2$ fashion gives the inverted sulfide. The reason why $PhOPPh_2$ among phosphorus compounds gave the best result is considered as follows. In the first step, most phosphorus compounds gave the corresponding iminophosphoranes quantitatively except for electron-deficient $P(OPh)_3$ (Table 7). In the second step, the basicity of iminophosphorane is essential for formation of intermediate **A**. Since the basicity of iminophosphorane prepared from electron-deficient $PhP(OPh)_2$ or $P(OPh)_3$ is lower than that prepared from $PhOPPh_2$, the reaction rate of formation of intermediate **A** in the case of $PhP(OPh)_2$ or $P(OPh)_3$ is slower than that in the case of $PhOPPh_2$, whose differences affect the yield of the desired product. On the other hand, the desired product was not obtained in the case of $PBu_3$ or $PPh_3$ without consuming alcohol **1a**. This indicated that alkoxyphosphonium salt **B** as a key intermediate was not formed from phosphonium salt **A** as well as in reactions using benzoquinone derivatives. When $ClPPh_2$ was used as a reductant, alcohol **1a** was converted into the corresponding chloride. Thus, it is proven that $PhOPPh_2$ is a suitable reductant which also contains a good leaving group.

Thus, this type of oxidation–reduction condensation by the combined use of $PhOPPh_2$ and azide compounds was successfully applied to the thioetherification of various alcohols including tertiary alcohol. Secondary and tertiary alcohols were converted into the corresponding sulfides in good to excellent yields with almost complete inversion of their configuration under mild and neutral conditions. In most cases, these reactions that used azides as oxidants have advantages over the reactions using benzoquinone derivatives.[27]

Finally, in order to confirm the utility of the above results, condensation of chiral tertiary alcohols **1r** and **1s** with BtzSH were further examined with other oxidation–reduction systems (Table 12). Interestingly, the $PhOPPh_2$–DEAD system afforded the desired sulfides in moderate yields with clean inversion of stereochemistry both using alcohols **1r** and **1s** while the $PPh_3$–DEAD system (Mitsunobu conditions) did not give the desired products. By comparing various oxidation–reduction systems, the yields of products **2r** and **2s** were found to increase in the order of $PhOPPh_2$–$N_3CH_2CO_2Et$ > $PhOPPh_2$–DMBQ > $PhOPPh_2$–DEAD > $PPh_3$–DEAD systems. Since the desired products were not obtained under any oxidation–reduction system when $PPh_3$ was used instead of $PhOPPh_2$, it is proven that $PhOPPh_2$ is a very useful reductant which also contains a good leaving PhO group, a proton acceptor.

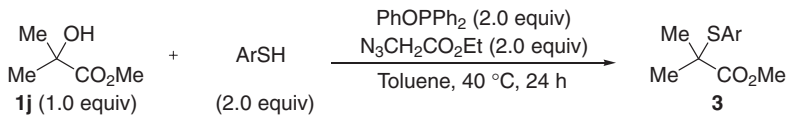
**Table 10.** Thioetherification of Various Chiral Alcohols

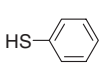
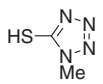
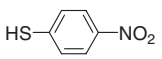
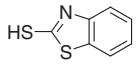
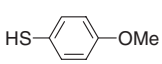
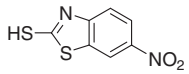
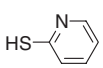
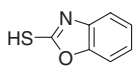
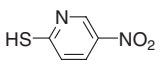



| Entry | ROH | **1** (%ee) | Temp, Time | Product | **2** | Yield/%[a] (%ee)[b] |
|---|---|---|---|---|---|---|
| 1 |  | **1a** (>99) | 40 °C, 24 h |  | **2a** | 99 (>99) |
| 2[c] |  | **1n** (>99) | rt, 12 h |  | **2n** | 83 (97) |
| 3[c] |  | **1o** (98) | rt, 24 h |  | **2o** | 89 (98) |
| 4 |  | **1q** | 80 °C, 6 h |  | **2q** | 85 |
| 5[d] |  | **1r** (>99) | 40 °C, 48 h |  | **2r** | 76 (>99) |
| 6[d] |  | **1s** (>99) | 40 °C, 48 h |  | **2s** | 90 (99) |
| 7[c],[d] |  | **1u** (92) | 27 °C, 48 h |  | **2u** | 87 (92) |
| 8 |  | **1v** | 40 °C, 48 h |  | **2v** | N.R. |

a) Isolated yield. b) Determined by HPLC analysis. c) The solution of $PhOPPh_2$ and ethyl azidoacetate was stirred at 80 °C for 20 min, followed by addition of alcohol and BtzSH at rt. d) The reaction was carried out by using BtzSH (4.0 equiv), $PhOPPh_2$ (4.0 equiv), and ethyl azidoacetate (4.0 equiv).

**Table 11.** Condensation of Tertiary Alcohol **1j** with Various ArSH

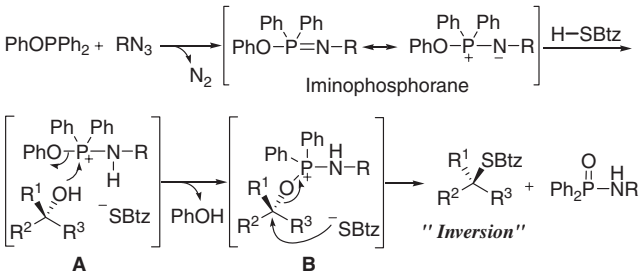



| Entry | ArSH | Product **3** | Yield/%[a] | Entry | ArSH | Product **3** | Yield/%[a] |
|---|---|---|---|---|---|---|---|
| 1 |  | **3a** | 44 | 6 |  | **3f** | 83 |
| 2 |  | **3b** | 85 | 7 |  | **2j** | 94 |
| 3 |  | **3c** | 19 | 8 |  | **3g** | 91 |
| 4 |  | **3d** | 72 | 9 |  | **3h** | 89 |
| 5 |  | **3e** | 97 | 10 |  | **3i** | 34 |

a) Isolated yield.

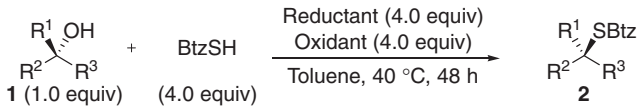
## Conclusion

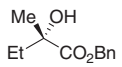
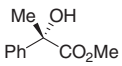
A new type of oxidation–reduction condensation by the combined use of $PhOPPh_2$ with azide compounds or benzoquinone derivatives was established. This reaction system was applied to the thioetherification of various alcohols including tertiary alcohol, and it was shown that the reaction using azides as oxidants is advantageous over that using benzoquinone derivatives in most cases. It is noted that chiral *sec*- or *tert*-alkyl sulfides were formed from the corresponding chiral alcohols




**Scheme 3.**

**Table 12.** Reaction of Tertialy Alcohols with BtzSH




| ROH | 1 | Oxidation–Reduction system (Yield/% (%ee)) | | | |
|---|---|---|---|---|---|
| | | $PPh_3$ DEAD | $PhOPPh_2$ DEAD | $PhOPPh_2$ DMBQ | $PhOPPh_2$ $N_3CH_2CO_2Et$ |
|  | **1r** | trace | 43 (>99) | 55 (>99)[a)] | 76 (>99) |
|  | **1s** | N.D. | 53 (>99) | 56 (>99)[a)] | 90 (99) |

a) The reaction was carried out at rt for 24 h.

with almost complete inversion of configuration under mild and neutral conditions. Since the chiral *tert*-alkyl Btz sulfide obtained was converted to the corresponding chiral *tert*-thiol in high yield on treatment with $LiAlH_4$, a concise method for the chiral thiols from the corresponding alcohols was established. This is the first example of the stereospecific syntheses of inverted chiral *tert*-thiol derivatives formed directly from chiral *tert*-alcohols by an $S_N2$ displacement.

## Experimental

**General.** All melting points were determined on a Yanagimoto micro melting point apparatus (Yanaco MP-S3) and remain uncorrected. Infrared (IR) spectra were recorded on a Sens*IR* Technologies Travel*IR* portable FT-IR spectrometer. $^1$H NMR spectra were recorded on a JEOL JNM-EX270L (270 MHz) spectrometer; chemical shifts ($\delta$) are reported in parts per million relative to tetramethylsilane. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. $^{13}$C NMR spectra were recorded on a EX270L (68 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in parts per million relative to tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$; $\delta$ 77.0). Carbon–$^{31}$P coupling constants are reported when possible. High-resolution mass spectral analysis (HRMS) was carried out on a Bruker-Daltonics micrOTOF focus instrument. The optical rotations were measured with a JASCO P-1020 polarimeter. High-performance liquid chromatography (HPLC) was carried out using a Hitachi LC-Organizer, L-4000UV Detecter, L-6200 Intelligent Pump, and D-2500 Chromato-Integrator. Analytical TLC was performed on Merck preparative TLC plates (silica gel 60 GF254, 0.25 mm). Preparative thin-layer chromatography (PTLC) was carried out on silica gel Wakogel B-5F. All reactions were carried out under an argon atmosphere in dried glassware, unless otherwise noted. Dry solvents (1,2-dichloropropane) were prepared by distillation over appropriate drying agents. Dehydrated solvents (Toluene, THF, $Et_2O$, $CHCl_3$, $CH_2Cl_2$, and EtOAc) were purchased from KANTO KAGAKU. Dehydrated solvents ($CH_3CN$) were purchased from KOKUSAN KAGAKU. Arenethiols, alcohols, $PPh_3$, $PBu_3$, $P(OPh)_3$, $ClPPh_2$, $Et_3N$, DMAP, benzoquinone derivatives, $TMSCH_2N_3$, DPPA, $TMSN_3$, and DEAD were purchased from Tokyo Kasei Kogyo (TCI) unless otherwise noted. $N_3CH_2CO_2Et$ and $BnN_3$ were purchased from Wako. (*S*)-4-Phenylbutan-2-ol, 4-(*tert*-butyldimethylsilyl)oxy-1-butanol, and 1-azidoadamantane were purchased from Aldrich.

**Procedure for the Preparation of Chiral Tertiary Alchohols.** (*S*)-Benzyl 2-hydroxy-2-methylbutyrate (Table 5, Entry 6) and (*S*)-methyl $\alpha$-phenyllactate (Table 5, Entry 7) were prepared following a literature procedure.[16a] Ethyl (*S*)-2-hydroxyl-2-methyl-4-phenyl-3-butynoate (Table 10, Entry 7) was prepared from ethyl pyruvate and phenylacetylene according to Jiang's procedure for the preparation of the R enantiomer.[28]

**General Procedure for the Preparation of Aryl Diphenylphosphinite ($ArOPPh_2$).** A typical procedure for the preparation of aryl diphenylphosphinites is described for phenyl diphenylphosphinite ($PhOPPh_2$). To a stirred solution of phenol (1.88 g, 20 mmol) and DMAP (489 mg, 4 mmol) in dry THF (50 mL) were added $Et_3N$ (3.33 mL, 24 mmol) followed by $ClPPh_2$ (4.04 mL, 22 mmol) under argon atmosphere. After stirring at rt for 2 h, the resulting white slurry was concentrated by a rotary evaporator. After dilution of the residue with hexane/ethyl acetate (v/v = 9/1, ca. 160 mL, HPLC grade), the mixture was filtered through a pad of alumina (activated, 300 mesh; purchased from Wako Pure Chemical Industries, Ltd.) and Celite. The filtrate was concentrated under reduced pressure to give phenyl diphenylphosphinite (5.40 g, 97%), which is pure enough without further purification. $PhOPPh_2$ was similarly synthesized in the absence of DMAP.

**Phenyl Diphenylphosphinite ($PhOPPh_2$):** Colorless oil; IR (neat, cm$^{-1}$): 1488, 1212, 863, 741, 721, 688; $^1$H NMR (270 MHz, $CDCl_3$): $\delta$ 7.64–7.47 (m, 4H), 7.40–6.90 (m, 11H); $^{13}$C NMR (68 MHz, $CDCl_3$): $\delta$ 157.1 (d, $J$ = 10.1 Hz), 140.7 (d, $J$ = 16.8 Hz), 130.4 (d, $J$ = 22.4 Hz), 129.6, 129.4, 128.4 (d, $J$ = 7.3 Hz), 122.4, 118.7 (d, $J$ = 10.6 Hz); HRMS (ESI) Calcd for $C_{18}H_{16}OP$: $[M + H]^+$ 279.0939. Found: 279.0920.

**2-Chlorophenyl Diphenylphosphinite ($2\text{-}ClC_6H_4OPPh_2$):** Colorless oil; IR (neat, cm$^{-1}$): 1475, 1232, 870, 736, 692, 673; $^1$H NMR (270 MHz, $CDCl_3$): $\delta$ 7.73–7.60 (m, 4H), 7.46–7.32 (m, 7H), 7.22–7.06 (m, 2H), 6.97–6.88 (m, 1H); $^{13}$C NMR (68 MHz, $CDCl_3$): $\delta$ 152.8 (d, $J$ = 10.1 Hz), 140.4 (d, $J$ = 17.9 Hz), 130.4 (d, $J$ = 22.9 Hz), 130.2, 129.8, 128.4 (d, $J$ = 7.3 Hz), 127.5, 125.1 (d, $J$ = 2.8 Hz), 123.1, 119.2 (d, $J$ = 17.3 Hz); HRMS (ESI) Calcd for $C_{18}H_{14}OPClNa$: $[M + Na]^+$ 335.0369. Found: 335.0363.

**2-Methoxyphenyl Diphenylphosphinite ($2\text{-}MeOC_6H_4OPPh_2$):** Colorless oil; IR (neat, cm$^{-1}$): 1498, 1254, 870, 739, 693; $^1$H NMR (270 MHz, $CDCl_3$): $\delta$ 7.70–7.57 (m, 4H), 7.44–7.30 (m, 6H), 7.07–6.76 (m, 4H), 3.79 (s, 3H); $^{13}$C NMR (68 MHz, $CDCl_3$): $\delta$ 151.0 (d, $J$ = 3.4 Hz), 141.5 (d, $J$ = 17.9 Hz), 130.5 (d, $J$ = 22.4 Hz), 129.4, 129.1, 128.2 (d, $J$ = 6.7 Hz), 123.4 (d, $J$ = 1.7 Hz), 120.7, 120.2 (d, $J$ = 11.7 Hz), 112.5, 55.9; HRMS (ESI) Calcd for $C_{19}H_{18}O_2P$: $[M + H]^+$ 309.1044. Found: 309.1054.

**Diphenyl Phenylphosphonite ($PhP(OPh)_2$).** To a stirred solution of phenol (3.76 g, 40 mmol) and DMAP (489 mg, 4 mmol) in dry THF (60 mL) were added $Et_3N$ (6.13 mL, 44 mmol) followed by $Cl_2PPh$ (2.71 mL, 20 mmol) under argon atmosphere. After stirring at rt for 4 h, the resulting white slurry was concentrated by a rotary evaporator. After dilution of the residue

with hexane/ethyl acetate (v/v = 9/1, ca. 200 mL, HPLC grade), the mixture was filtered through a pad of alumina (activated, 300 mesh; purchased from Wako Pure Chemical Industries, Ltd.) and Celite. The filtrate was concentrated under reduced pressure to give diphenyl phenylphosphonite (4.88 g, 83%). Colorless oil; IR (neat, $cm^{-1}$): 1484, 1217, 1191, 855, 760, 749, 720, 687; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 7.85–7.74 (m, 2H), 7.51–7.42 (m, 3H), 7.30–7.18 (m, 4H), 7.13–7.00 (s, 6H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 155.0 (d, $J = 5.6$ Hz), 139.8 (d, $J = 14.5$ Hz), 130.9, 129.6 (d, $J = 23.5$ Hz), 129.5, 128.3 (d, $J = 6.1$ Hz), 123.5 (d, $J = 1.1$ Hz), 119.9 (d, $J = 8.4$ Hz); HRMS (ESI) Calcd for $C_{18}H_{15}O_2PNa$: $[M + Na]^+$ 317.0707. Found: 317.0734.

**General Procedure for Condensation of Alcohols with BtzSH by Using $PhOPPh_2$ and Benzoquinone Derivatives.** A typical procedure for the preparation of alkyl aryl sulfides is described for sulfide **2a**. To a solution of $PhOPPh_2$ (125.2 mg, 0.45 mmol) and (*S*)-4-phenylbutan-2-ol (**1a**) (45.1 mg, 0.30 mmol) in dry toluene (1.50 mL) were added BtzSH (55.2 mg, 0.33 mmol) followed by DMOBQ (75.7 mg, 0.45 mmol) at rt under argon atmosphere. The reaction mixture was stirred for 6 h and the crude product was purified by preparative TLC to afford the corresponding sulfide **2a** (89.2 mg, 99%).

**General Procedure for Condensation of Alcohols with BtzSH by Using $PhOPPh_2$ and Azide Compounds.** A typical procedure for the preparation of alkyl aryl sulfides is described for sulfide **2s**. To a solution of $PhOPPh_2$ (222.6 mg, 0.80 mmol) and chiral alcohol **1s** (35.8 mg, 0.199 mmol) in dry toluene (0.60 mL) were added BtzSH (133.8 mg, 0.80 mmol) followed by ethyl azidoacetate (103.3 mg, 0.80 mmol) at rt under argon atmosphere. The reaction mixture was stirred at 40 °C for 48 h and the crude product was purified by preparative TLC to afford the corresponding sulfide **2s** (58.9 mg, 90%).

**(*R*)-2-(1-Methyl-3-phenylpropylsulfanyl)-1,3-benzothiazole (2a):** Colorless oil; >99% ee; The ee value was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H column, hexane/*i*-PrOH = 250/1, flow rate = 1.0 mL $min^{-1}$): $t_R = 15.0$ (*S*), 26.2 min (*R*); $[\alpha]_D^{38} = +43.0$ (*c* 0.79, $CHCl_3$); IR (neat, $cm^{-1}$): 1454, 1425, 989, 752, 726, 697; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 7.87 (d, $J = 8.1$ Hz, 1H), 7.72 (d, $J = 7.9$ Hz, 1H), 7.42–7.14 (m, 7H), 4.02–3.95 (m, 1H), 2.81 (d, $J = 8.1$ Hz, 2H), 2.19–1.93 (m, 2H), 1.54 (d, $J = 6.9$ Hz, 3H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 166.0, 153.2, 141.1, 135.1, 128.3, 125.9 (×2), 124.1, 121.4, 120.8, 43.9, 38.5, 33.2, 21.6; HRMS (ESI) Calcd for $C_{17}H_{17}NS_2Na$: $[M + Na]^+$ 322.0700. Found: 320.0699.

**2-(Benzylsulfanyl)-1,3-benzothiazole (2b):** Colorless oil; IR (neat, $cm^{-1}$): 1454, 1425, 992, 753, 724, 696, 668; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 7.88 (d, $J = 8.1$ Hz, 1H), 7.70 (d, $J = 7.9$ Hz, 1H), 7.50–7.19 (m, 7H), 4.58 (s, 2H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 166.2, 152.9, 136.0, 135.1, 129.0, 128.5, 127.6, 125.9, 124.1, 121.4, 120.8, 37.7; HRMS (ESI) Calcd for $C_{14}H_{11}NS_2Na$: $[M + Na]^+$ 280.0231. Found: 280.0225.

**2-[(*E*)-3-Phenyl-2-propenylsulfanyl]-1,3-benzothiazole (2c):** White solid; mp 61–63 °C; IR (neat, $cm^{-1}$): 1453, 1422, 993, 967, 748, 726, 703, 689; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 7.88 (d, $J = 8.2$ Hz, 1H), 7.72 (d, $J = 7.9$ Hz, 1H), 7.43–7.15 (m, 7H), 6.67 (d, $J = 15.7$ Hz, 1H), 6.35 (dt, $J = 15.7$, 7.3 Hz, 1H), 4.14 (d, $J = 7.3$ Hz, 2H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 165.9, 152.9, 136.1, 135.1, 134.1, 128.4, 127.7, 126.3, 125.9, 124.1, 123.3, 121.4, 120.8, 36.0; HRMS (ESI) Calcd for $C_{16}H_{13}NS_2Na$: $[M + Na]^+$ 306.0387. Found: 306.0385.

**2-(3-Furylmethylsulfanyl)-1,3-benzothiazole (2d):** Pale yellow oil; IR (neat, $cm^{-1}$): 1456, 1425, 1018, 993, 872, 753, 724, 705, 664; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 7.88 (d, $J = 8.1$ Hz, 1H), 7.73 (d, $J = 7.9$ Hz, 1H), 7.50–7.23 (m, 4H), 6.45 (s, 1H), 4.42 (s, 2H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 165.9, 152.9, 143.2, 140.9, 135.1, 125.9, 124.2, 121.4, 120.9, 120.1, 110.8, 27.9; HRMS (ESI) Calcd for $C_{12}H_9NOS_2Na$: $[M + Na]^+$ 270.0023. Found: 270.0023.

**2-(Phenacylsulfanyl)-1,3-benzothiazole (2e):** Yellow solid; mp 110–111 °C; IR (neat, $cm^{-1}$): 1678, 1426, 1288, 1191, 995, 750, 688; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 8.05 (d, $J = 7.3$ Hz, 2H), 7.82–7.23 (m, 7H), 4.95 (s, 2H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 192.7, 165.0, 152.7, 135.3, 133.7, 128.6, 128.4, 125.9, 124.3, 121.3, 120.9, 41.0; HRMS (ESI) Calcd for $C_{15}H_{11}NOS_2Na$: $[M + Na]^+$ 308.0180. Found: 308.0166.

**2-[4-(*tert*-Butyldimethylsilyloxy)butylsulfanyl]-1,3-benzothiazole (2f):** Colorless oil; IR (neat, $cm^{-1}$): 1460, 1427, 1099, 993, 835, 774, 754, 724, 706; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 7.85 (d, $J = 8.1$ Hz, 1H), 7.74 (d, $J = 7.9$ Hz, 1H), 7.43–7.37 (m, 1H), 7.31–7.25 (m, 1H), 3.66 (t, $J = 6.1$ Hz, 2H), 3.38 (d, $J = 7.3$ Hz, 2H), 1.96–1.85 (m, 2H), 1.75–1.65 (m, 2H), 0.88 (s, 9H), 0.05 (s, 6H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 167.0, 153.1, 135.0, 125.8, 124.0, 121.3, 120.8, 62.4, 33.5, 31.8, 26.0, 25.9, 18.4, −5.2; HRMS (ESI) Calcd for $C_{17}H_{27}NOS_2SiNa$: $[M + Na]^+$ 376.1201. Found: 376.1211.

**2-[2-(Indol-2-yl)ethylsulfanyl]-1,3-benzothiazole (2g):** Yellow solid; mp 134–136 °C; IR (neat, $cm^{-1}$): 3226, 1739, 1455, 1423, 1220, 1004, 758, 739, 726, 668; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 8.07 (br, 1H), 7.89 (d, $J = 7.9$ Hz, 1H), 7.75–7.72 (m, 2H), 7.50–7.00 (m, 6H), 3.66 (t, $J = 7.3$ Hz, 2H), 3.29 (t, $J = 7.3$ Hz, 2H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 166.9, 153.2, 136.1, 135.1, 127.0, 125.9, 124.0, 122.1, 122.0, 121.3, 120.9, 119.4, 118.8, 114.0, 111.1, 34.2, 25.6; HRMS (ESI) Calcd for $C_{17}H_{14}N_2S_2Na$: $[M + Na]^+$ 333.0496. Found: 333.0503.

***tert*-Butyl [2-(1,3-Benzothiazol-2-ylsulfanyl)ethyl]carbamate (2h):** White needles; mp 103–105 °C; IR (neat, $cm^{-1}$): 3372, 1682, 1524, 1453, 1424, 1265, 1251, 1240, 1167, 1140, 1002, 751, 723; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 7.84 (d, $J = 8.1$ Hz, 1H), 7.73 (d, $J = 7.7$ Hz, 1H), 7.44–4.24 (m, 2H), 5.34 (br, 1H), 3.62–3.42 (m, 4H), 1.43 (s, 9H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 166.0, 155.6, 152.9, 135.2, 125.9, 124.2, 121.4, 120.8, 79.4, 40.5, 33.6, 28.4; HRMS (ESI) Calcd for $C_{14}H_{18}N_2O_2S_2Na$: $[M + H]^+$ 333.0707. Found: 333.0705.

**2-(Cyclopentylsulfanyl)-1,3-benzothiazole (2i):** Colorless oil; IR (neat, $cm^{-1}$): 1454, 1424, 989, 753, 724; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 7.87 (d, $J = 8.1$ Hz, 1H), 7.74 (d, $J = 7.9$ Hz, 1H), 7.43–7.24 (m, 2H), 4.16–4.06 (m, 1H), 2.37–2.18 (m, 2H), 1.90–1.58 (m, 6H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 167.3, 153.2, 135.0, 125.8, 123.9, 121.4, 120.7, 46.6, 33.8, 24.9; HRMS (ESI) Calcd for $C_{12}H_{13}NS_2Na$: $[M + Na]^+$ 258.0387. Found: 258.0374.

**Methyl 2-[(1,3-Benzothiazol-2-yl)sulfanyl]-2-methylpropionate (2j):** Spectral data were consistent with these of the literature.[16a] Colorless oil; IR (neat, $cm^{-1}$): 1731, 1457, 1427, 1264, 1153, 1122, 986, 756, 727; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 7.93 (d, $J = 7.9$ Hz, 1H), 7.77 (d, $J = 7.9$ Hz, 1H), 7.46–7.26 (m, 2H), 3.75 (s, 3H), 1.74 (s, 6H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 173.6, 161.7, 153.2, 136.3, 126.0, 124.9, 122.5, 120.9, 53.9, 52.9, 26.4.

**2-[(1,3-Benzothiazol-2-yl)sulfanyl]-2-methylpropiophenone (2k):** Spectral data are consistent with those of the literature.[16a] Pale yellow oil; IR (neat, $cm^{-1}$): 1677, 1456, 1426, 1254, 989, 973, 756, 725, 705, 692, 661; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 8.09 (d, $J = 7.9$ Hz, 2H), 7.88 (d, $J = 7.9$ Hz, 1H), 7.70 (d, $J = 7.9$ Hz, 1H), 7.53–7.23 (m, 5H), 1.86 (s, 6H); $^{13}C$ NMR (68 MHz, $CDCl_3$):

$\delta$ 200.3, 161.2, 153.0, 136.6, 136.2, 131.6, 128.9, 127.8, 126.0, 124.8, 122.4, 120.8, 58.1, 27.4.

**2-[(1-Methyl-1-phenylethyl)sulfanyl]-1,3-benzothiazole (2l):** Spectral data are consistent with those of the literature.[16a] Colorless oil; IR (neat, $cm^{-1}$): 1452, 1424, 978, 755, 727, 695, 671; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 7.94 (d, $J = 8.1$ Hz, 1H), 7.71–7.57 (m, 3H), 7.45–7.23 (m, 5H), 1.96 (s, 6H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 163.3, 152.8, 144.8, 136.4, 128.3, 127.2, 126.7, 125.8, 124.7, 122.5, 120.7, 54.8, 30.4.

**2-[(1,1-Dimethyl-3-phenylpropyl)sulfanyl]-1,3-benzothiazole (2m):** Spectral data are consistent with those of the literature.[16a] Colorless oil; IR (neat, $cm^{-1}$): 1453, 1425, 978, 754, 726, 697, 671; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 7.97 (d, $J = 7.9$ Hz, 1H), 7.79 (d, $J = 7.7$ Hz, 1H), 7.50–7.10 (m, 7H), 2.91–2.75 (m, 2H), 2.23–2.07 (m, 2H), 1.61 (s, 6H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 163.0, 153.7, 142.0, 136.3, 128.4, 128.3, 125.9, 125.7, 124.8, 122.5, 120.8, 54.3, 44.5, 31.6, 29.1.

**(*S*)-2-(1-Phenylethylsulfanyl)-1,3-benzothiazole (2n):** Colorless oil; 97% ee; the ee value was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H column, hexane/*i*-PrOH = 250/1, flow rate = 1.0 mL $min^{-1}$): $t_R = 11.9$ (*S*), 34.6 min (*R*); $[\alpha]_D^{38} = -337.6$ (*c* 0.71, $CHCl_3$); IR (neat, $cm^{-1}$): 1454, 1424, 989, 754, 725, 695, 658; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 7.89 (d, $J = 8.1$ Hz, 1H), 7.70 (d, $J = 7.6$ Hz, 1H), 7.49–7.21 (m, 7H), 5.15 (q, $J = 7.1$ Hz, 1H), 1.84 (d, $J = 7.1$ Hz, 3H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 165.6, 153.0, 141.6, 135.2, 128.5, 127.6, 127.2, 125.8, 124.2, 121.5, 120.8, 47.5, 22.7; HRMS (ESI) Calcd for $C_{15}H_{13}NS_2Na$: $[M + Na]^+$ 294.0387. Found: 294.0390.

**(*R*)-2-(1-Ethynylhexylsulfanyl)-1,3-benzothiazole (2o):** Colorless oil; 98% ee; the ee value was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H column, hexane/*i*-PrOH = 250/1, flow rate = 1.0 mL $min^{-1}$): $t_R = 11.7$ (*S*), 22.4 min (*R*); $[\alpha]_D^{15} = +166.5$ (*c* 1.02, $CHCl_3$); IR (neat, $cm^{-1}$): 3298, 2927, 1458, 1426, 991, 754, 725; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 7.90 (d, $J = 7.9$ Hz, 1H), 7.76 (d, $J = 7.9$ Hz, 1H), 7.46–7.24 (m, 2H), 4.73–4.67 (m, 1H), 2.40 (d, $J = 2.3$ Hz, 1H), 2.07–1.86 (m, 2H), 1.69–1.53 (m, 2H), 1.43–1.25 (m, 4H), 0.97–0.82 (m, 3H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 164.2, 152.9, 135.4, 125.9, 124.4, 121.8, 120.9, 82.3, 72.7, 38.0, 35.2, 31.1, 26.6, 22.5, 14.1; HRMS (ESI) Calcd for $C_{15}H_{17}NS_2Na$: $[M + Na]^+$ 298.0700. Found: 298.0696.

**(*R*)-Ethyl 2-[(1,3-Benzothiazol-2-yl)sulfanyl]propionate (2p):** Colorless oil; 98% ee; the ee value was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H column, hexane/*i*-PrOH = 150/1, flow rate = 1.0 mL $min^{-1}$): $t_R = 11.4$ (*S*), 28.8 min (*R*); $[\alpha]_D^{33} = +130.0$ (*c* 1.50, $CHCl_3$); IR (neat, $cm^{-1}$): 1730, 1457, 1426, 1309, 1238, 1158, 1072, 1017, 990, 754, 725; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 7.86 (d, $J = 8.1$ Hz, 1H), 7.74 (d, $J = 7.7$ Hz, 1H), 7.49–7.24 (m, 2H), 4.68 (q, $J = 7.3$ Hz, 1H), 4.32–4.10 (m, 2H), 1.71 (d, $J = 7.3$ Hz, 3H), 1.25 (t, $J = 7.1$ Hz, 3H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 171.4, 164.0, 152.8, 135.3, 125.9, 124.3, 121.6, 120.9, 61.8, 45.1, 18.0, 14.1; HRMS (ESI) Calcd for $C_{12}H_{13}NO_2S_2Na$: $[M + Na]^+$ 290.0285. Found: 290.0277.

**(1*S*,2*S*,5*R*)-2-[(2-Isopropyl-5-methylcyclohexyl)sulfanyl]-1,3-benzothiazole (2q):** Colorless oil; $[\alpha]_D^{38} = +93.9$ (*c* 0.93, $CHCl_3$); IR (neat, $cm^{-1}$): 1455, 1426, 987, 753, 725, 700; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 7.85 (d, $J = 8.1$ Hz, 1H), 7.71 (d, $J = 7.4$ Hz, 1H), 7.41–7.05 (m, 1H), 7.28–7.22 (m, 1H), 4.56 (br, 1H), 2.28–2.17 (m, 1H), 1.97–1.55 (m, 4H), 1.48–1.35 (m, 1H), 1.33–1.19 (m, 1H), 0.84 (m, 11H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 167.3, 153.3, 135.1, 125.8, 123.9, 121.3, 120.7, 50.7, 48.6, 41.5, 35.2, 30.7, 27.7, 27.0, 22.1, 21.1, 20.9; HRMS (ESI) Calcd for $C_{17}H_{24}NS_2$: $[M + H]^+$ 306.1315. Found: 306.1346.

**(*R*)-Benzyl 2-[(1,3-Benzothiazol-2-yl)sulfanyl]-2-methylbutyrate (2r):** Spectral data are consistent with those of the literature.[16a] Colorless oil; >99% ee; the ee value was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H column, hexane/*i*-PrOH = 700/1, flow rate = 1.0 mL $min^{-1}$): $t_R = 67.4$ (*S*), 74.6 min (R); $[\alpha]_D^{38} = +15.0$ (*c* 1.25, $CHCl_3$); IR (neat, $cm^{-1}$): 1728, 1454, 1427, 1228, 1144, 1121, 987, 754, 727, 696, 676; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 7.85 (d, $J = 7.9$ Hz, 1H), 7.74 (d, $J = 7.7$ Hz, 1H), 7.44–7.18 (m, 7H), 5.17 (m, 2H), 2.24–1.95 (m, 2H), 1.76 (s, 3H), 1.01 (t, $J = 7.4$ Hz, 3H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 172.4, 161.7, 153.2, 136.3, 135.4, 128.3, 127.9, 125.9, 124.8, 122.5, 120.8, 67.4, 59.0, 31.8, 23.1, 9.3.

**(*R*)-Methyl 2-[(1,3-Benzothiazol-2-yl)sulfanyl]-2-phenylpropionate (2s):** Spectral data are consistent with those of the literature.[16a] Colorless solid; mp 45–47; 99% ee; The ee value was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H column, hexane/*i*-PrOH = 700/1, flow rate = 1.0 mL $min^{-1}$): $t_R = 68.1$ (*S*), 75.3 min (*R*); $[\alpha]_D^{27} = -88.4$ (*c* 1.05, $CHCl_3$); IR (neat, $cm^{-1}$): 1730, 1453, 1427, 1237, 984, 755, 726, 694; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 7.92 (d, $J = 8.2$ Hz, 1H), 7.73 (d, $J = 7.9$ Hz, 1H), 7.63–7.55 (m, 2H), 7.47–7.27 (m, 5H), 3.79 (s, 3H), 2.24 (s, 3H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 172.0, 162.5, 152.9, 138.7, 136.1, 128.7, 128.4, 126.8, 125.9, 124.8, 122.4, 120.9, 61.6, 53.4, 25.8.

**2-[(1,3-Benzothiazol-2-yl)sulfanyl]-1,2-diphenylethanone (2t):** Yellow solid; mp 105–107 °C; IR (neat, $cm^{-1}$): 1692, 1426, 1197, 998, 748, 740, 725, 690, 680; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 8.05 (d, $J = 7.3$ Hz, 2H), 7.75–7.15 (m, 12H), 6.95 (s, 1H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 194.0, 164.7, 152.6, 135.4 (×2), 134.5, 133.2, 129.0, 128.9, 128.5, 125.7, 124.2, 121.3, 120.9, 58.2; HRMS (ESI) Calcd for $C_{21}H_{15}NOS_2Na$: $[M + Na]^+$ 384.0493. Found: 384.0487.

**(*R*)-Ethyl 2-[(1,3-Benzothiazol-2-yl)sulfanyl]-2-methyl-4-phenylbut-3-ynoate (2u):** Yellow oil; 92% ee; the ee value was determined by chiral HPLC analysis (DAICEL CHIRALPAK AS-H column, hexane/*i*-PrOH = 1000/1, flow rate = 0.5 mL $min^{-1}$): $t_R = 46.1$ (*S*), 51.1 min (*R*); $[\alpha]_D^{37} = +132.0$ (*c* 1.02, $CHCl_3$); IR (neat, $cm^{-1}$): 1735, 1230, 1097, 989, 754, 727, 689, 676; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 7.99 (d, $J = 8.1$ Hz, 1H), 7.81 (d, $J = 7.9$ Hz, 1H), 7.50–7.21 (m, 7H), 4.27 (q, $J = 7.1$ Hz, 2H), 2.08 (s, 3H), 1.23 (t, $J = 7.1$ Hz, 3H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 168.7, 160.5, 152.9, 137.0, 131.6, 128.6, 128.0, 126.1, 125.2, 122.9, 121.9, 121.0, 87.2, 86.3, 62.9, 51.1, 26.5, 13.9; HRMS (ESI) Calcd for $C_{20}H_{17}NO_2S_2Na$: $[M + Na]^+$ 390.0598. Found: 390.0593.

**Methyl 2-Methyl-2-(phenylsulfanyl)propionate (3a):** Pale yellow oil; IR (neat, $cm^{-1}$): 1727, 1264, 1151, 1121, 751, 693; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 7.52–7.26 (m, 5H), 3.66 (s, 3H), 1.49 (s, 6H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 174.1, 136.5, 131.1, 129.2, 128.4, 52.1, 51.0, 25.8; HRMS (ESI) Calcd for $C_{11}H_{14}O_2SNa$: $[M + Na]^+$ 233.0612. Found: 233.0603.

**Methyl 2-Methyl-2-[(4-nitrophenyl)sulfanyl]propionate (3b):** Spectral data are consistent with those of the literature.[16a] Pale yellow oil; IR (neat, $cm^{-1}$): 1727, 1516, 1341, 1266, 1152, 1121, 852; $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 8.16 (d, $J = 8.7$ Hz, 2H), 7.57 (d, $J = 8.7$ Hz, 2H), 3.72 (s, 3H), 1.56 (s, 6H); $^{13}C$ NMR (68 MHz, $CDCl_3$): $\delta$ 173.7, 147.6, 140.9, 135.2, 123.4, 52.6, 51.6, 26.1.

**Methyl 2-Methyl-2-[(4-methoxyphenyl)sulfanyl]propionate (3c):** Pale yellow oil; IR (neat, $cm^{-1}$): 1726, 1492, 1285, 1265,

1245, 1173, 1151, 1120, 1028, 828; $^1$H NMR (270 MHz, $CDCl_3$): $\delta$ 7.37 (d, $J = 8.6$ Hz, 2H), 6.84 (d, $J = 8.6$ Hz, 2H), 3.80 (s, 3H), 3.66 (s, 3H), 1.46 (s, 6H); $^{13}$C NMR (68 MHz, $CDCl_3$): $\delta$ 174.2, 160.6, 138.3, 122.1, 114.1, 55.3, 52.1, 51.0, 25.7; HRMS (ESI) Calcd for $C_{12}H_{16}O_3SNa$: $[M + Na]^+$ 263.0718. Found: 263.0712.

**Methyl 2-Methyl-2-[(pyridin-2-yl)sulfanyl]propionate (3d):** Pale yellow oil; IR (neat, cm$^{-1}$): 1728, 1415, 1262, 1152, 1136, 1118, 758, 724; $^1$H NMR (270 MHz, $CDCl_3$): $\delta$ 8.38 (d, $J = 4.3$ Hz, 1H), 7.49 (td, $J = 7.7$, 1.6 Hz, 1H), 7.18 (d, $J = 7.9$ Hz, 1H), 7.04–6.96 (m, 1H), 3.69 (s, 3H), 1.66 (s, 6H); $^{13}$C NMR (68 MHz, $CDCl_3$): $\delta$ 175.0, 157.0, 149.2, 135.9, 123.6, 120.1, 52.6, 50.6, 26.4; HRMS (ESI) Calcd for $C_{10}H_{13}NO_2SNa$: $[M + Na]^+$ 234.0565. Found: 234.0564.

**Methyl 2-Methyl-2-[(5-nitropyridin-2-yl)sulfanyl]propionate (3e):** Spectral data are consistent with those of the literature.[16a] Pale yellow oil; IR (neat, cm$^{-1}$): 1731, 1585, 1566, 1511, 1338, 1264, 1145, 1123, 1098, 854, 750; $^1$H NMR (270 MHz, $CDCl_3$): $\delta$ 9.17 (d, $J = 2.3$ Hz, 1H), 8.24 (dd, $J = 8.8$, 2.6 Hz, 1H), 7.27 (d, $J = 8.9$ Hz, 1H), 3.71 (s, 3H), 1.73 (s, 6H); $^{13}$C NMR (68 MHz, $CDCl_3$): $\delta$ 174.1, 166.2, 144.5, 141.0, 130.4, 121.3, 52.9, 51.7, 26.2.

**Methyl 2-Methyl-2-[(1-methyl-1*H*-tetrazol-5-yl)sulfanyl]-propionate (3f):** Pale yellow oil; IR (neat, cm$^{-1}$): 1730, 1268, 1156, 1121; $^1$H NMR (270 MHz, $CDCl_3$): $\delta$ 4.02 (s, 3H), 3.71 (s, 3H), 1.74 (s, 6H); $^{13}$C NMR (68 MHz, $CDCl_3$): $\delta$ 172.7, 150.5, 54.4, 53.2, 34.0, 26.6; HRMS (ESI) Calcd for $C_7H_{12}N_4O_2SNa$: $[M + Na]^+$ 239.0579. Found: 239.0570.

**Methyl 2-Methyl-2-[(6-nitro-1,3-benzothiazol-2-yl)sulfanyl]-propionate (3g):** Yellow solid; mp 114–115 °C; IR (neat, cm$^{-1}$): 1723, 1433, 1328, 1266, 1122, 1043, 1005, 836, 747; $^1$H NMR (270 MHz, $CDCl_3$): $\delta$ 8.69 (d, $J = 2.1$ Hz, 1H), 8.29 (dd, $J = 8.8$, 2.2 Hz, 1H), 7.92 (d, $J = 9.1$ Hz, 1H), 3.77 (s, 3H), 1.82 (s, 6H); $^{13}$C NMR (68 MHz, $CDCl_3$): $\delta$ 173.2, 170.2, 156.7, 144.2, 135.8, 121.7, 121.6, 117.3, 54.7, 53.1, 26.4; HRMS (ESI) Calcd for $C_{12}H_{12}N_2O_4S_2Na$: $[M + Na]^+$ 335.0136. Found: 335.0130.

**Methyl 2-[(1,3-Benzoxazol-2-yl)sulfanyl]-2-methylpropionate (3h):** Spectral data are consistent with those of the literature.[16a] Pale yellow oil; IR (neat, cm$^{-1}$): 1735, 1503, 1452, 1267, 1237, 1156, 1118, 1091, 743; $^1$H NMR (270 MHz, $CDCl_3$): $\delta$ 7.69–7.60 (m, 1H), 7.50–7.41 (m, 1H), 7.35–7.23 (m, 2H), 3.75 (s, 3H), 1.80 (s, 6H); $^{13}$C NMR (68 MHz, $CDCl_3$): $\delta$ 173.3, 161.3, 151.4, 141.7, 124.4, 124.2, 119.1, 110.0, 53.1, 53.0, 26.6.

**Methyl 2-(Benzoylsulfanyl)-2-methylpropionate (3i):** Colorless oil; IR (neat, cm$^{-1}$): 1735, 1660, 1261, 1208, 1156, 1126, 908, 688; $^1$H NMR (270 MHz, $CDCl_3$): $\delta$ 7.90 (d, $J = 7.4$ Hz, 2H), 7.56 (t, $J = 7.2$ Hz, 1H), 7.43 (t, $J = 7.6$ Hz, 2H), 3.76 (s, 3H), 1.69 (s, 6H); $^{13}$C NMR (68 MHz, $CDCl_3$): $\delta$ 190.9, 174.3, 136.5, 133.4, 128.5, 127.1, 53.0, 51.1, 26.2; HRMS (ESI) Calcd for $C_{12}H_{14}O_3SNa$: $[M + Na]^+$ 261.0561. Found: 261.0559.

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22 For a review of organic azides, see: S. Bräse, C. Gil, K. Knepper, V. Zimmermann, *Angew. Chem., Int. Ed.* **2005**, *44*, 5188.

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26 The effect of azide compounds as oxidants is considered as follows. When 1-azidoadamantane was used, intermediate **A** was not converted into intermediate **B** because the bulky substituent retarded the attack of alcohol **1a** to the positively charged phosphorus atom. On the other hand, intermediate **A** was not formed in the case of DPPA with electron-withdrawing groups because the basicity of an iminophosphorane is very low. In the case of $TMSN_3$, since the Staudinger reaction rate with $PhOPPh_2$ was very slow, an iminophosphorane was not formed efficiently. Thus, it is proven that alkyl azides such as ethyl azidoacetate or benzyl azide are a suitable oxidant.

27 The yield of the desired sulfide obtained by using an azide was lower than that using a benzoquinone derivative only when a sulfur nucleophile having a high $pK_a$ value such as benzenethiol or 4-methoxybenzenethiol was used. This indicates that the basicity of iminophosphorane is lower than that of phenoxide anion of intermediate **A** (Scheme 2). On the other hand, reaction of BtzSH with tertiary alcohol **1r** gave the desired sulfide along with undesired olefins. Since the yield of the desired product obtained by using an azide is higher than that using a benzoquinone derivative, the reaction using an azide might suppress undesired side reactions such as competitive E2 elimination caused by the iminophosphorane while the reaction using a benzoquinone derivative might promote E2 elimination caused by the phenoxide anion. Thus, the reaction using an azide proceeds under milder conditions to afford the desired product in higher yield.

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