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Peroxides as "Switches" of Dialkyl *H*-Phosphonate: Two Mild and Metal-Free Methods for Preparation of 2-Acylbenzothiazoles and Dialkyl Benzothiazol-2-ylphosphonates

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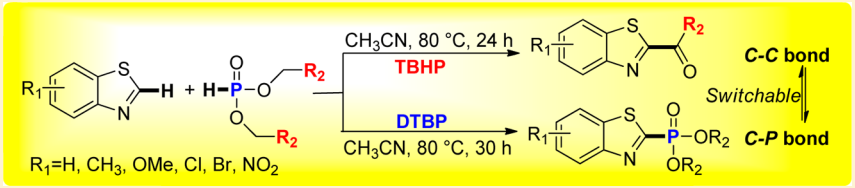
Supporting Information



ABSTRACT: Two mild and metal-free methods for the preparation of two kinds of important benzothiazole derivatives, 2-acylbenzothiazoles and dialkyl benzothiazol-2-ylphosphonates, respectively, were developed. The dialkyl *H*-phosphonate $(RO)_2P(O)H$ exists in equilibrium with its tautomer dialkyl phosphite $(RO)_2POH$. TBHP triggered *α*-carbon-centered phosphite radical formation, whereas DTBP triggered phosphorus-centered phosphonate radical formation. The two types of radicals led respectively to two different reaction processes, the direct C_2-acylation of benzothiazoles and C_2-phosphonation of benzothiazoles.

INTRODUCTION

The importance of phosphorus compounds in organic synthesis,[1−3] materials,[4] and medicinal chemistry[5] has been well documented for years. The dialkyl *H*-phosphonates occupy a major position in organophosphorus chemistry, since they are frequent intermediates in the synthesis of a variety of bioactive products including aminophos-phosphonates, aminophos-phonic acids, P−C phosphonates, hydroxyalkyl phosphonates, amidophosphates, nucleoside *H*-phosphonates, poly(alkylene *H*-phosphonates) and poly(alkylene phosphates), phosphorus-containing polyesters, etc.[6] The property that is most important from the point of view of synthetic applications is the tautomeric equilibrium between their phosphite and phospho-nate forms: the tricoordinated phosphorus(III) form and the tetracoordinated phosphorus(V) form (Figure 1). The strongly polar character of the phosphoryl group of the *H*-phosphonates is responsible to a great extent for the reactivity of this class of compounds. The versatility of these compounds is determined by the presence of two types of reaction centers in their molecule: the phosphorus atom and the *α*-carbon atom of the alkoxy groups.[6g] Herein, we wish to disclose a very new aspect of *H*-phosphonate chemistry, which, due to "flexbility", makes dialkyl phosphites unexpectedly efficient synthetic precursors in preparing two kinds of important benzothiazole derivatives, 2-acylbenzothiazoles and dialkyl benzothiazol-2-ylphosphonates (Figure 1), respectively.

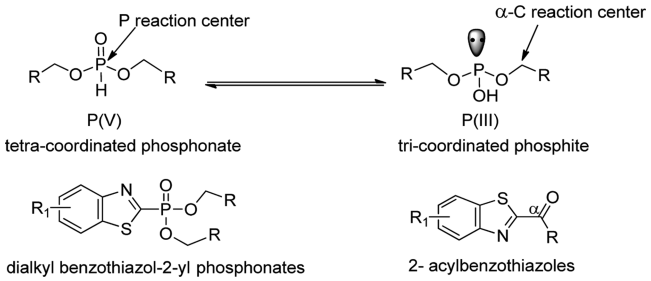


Figure 1. Tautomerization leading to different products.

RESULTS AND DISCUSSION

As it is well-known that the parent compound benzothiazole is not widely used, many of its derivatives are found in commercial products or in nature and exhibit significant biological and pharmacological activities.[7] As derivatives of benzothiazole, 2-acylbenzothiazoles have attracted considerable attention due to their increasing applications in medical

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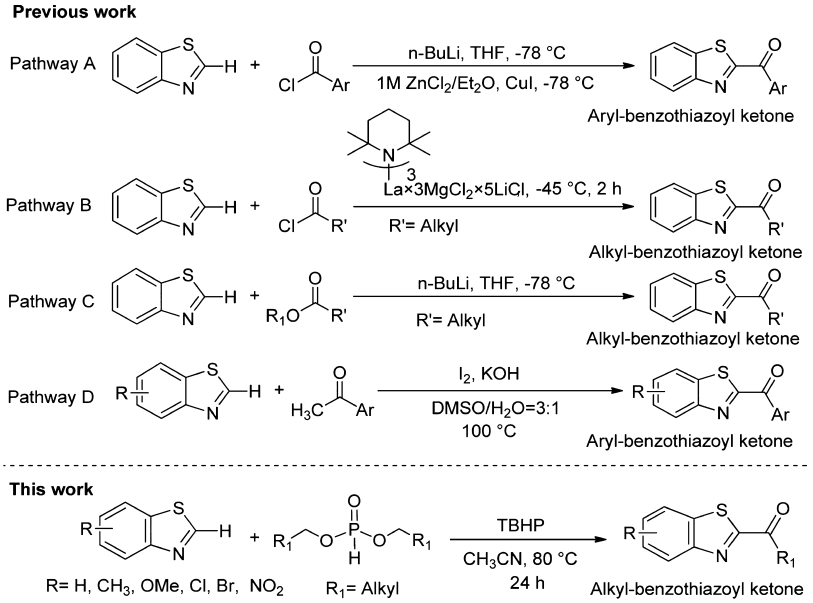
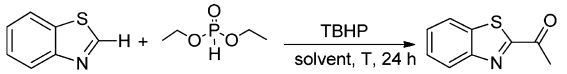
Scheme 1. Comparison of Previous Works with This Work



fields.[8−16] It is especially worth noting that only a few methods aiming to synthesize 2-acylbenzothiazoles with benzothiazoles as starting materials have been developed. However, most previous methods suffer from harsh conditions and metal salts. For example, with both benzothiazoles and acyl chlorides as starting materials, Koskinen et al. (Scheme 1, pathway A) employed *n*-BuLi to activate the C2−H covalent bond of benzothiazole at very low temperature, and meanwhile $ZnCl_2$ and CuI were necessarily employed to form an active metal-containing intermediate in the reaction process.[17,18] Knochel's group carried out their reaction at relatively low temperature (Scheme 1, pathway B) by employing the complicated catalyst $tmp_3{\cdot}La{\cdot}MgCl_2{\cdot}5LiCl$ (tmp = 2,2,6,6-tetramethylpiperid) to activate the C2−H bond.[19] Ablordeppey's group carried out a method in 2012 (Scheme 1, pathway C) using esters instead of unstable acyl chlorides as acylating agents; *n*-BuLi was still needed to activate the C2−H bond at very low temperature, and in addition, only a limited number of esters were tested.[11] Wu's group very recently developed a novel method to synthesize 2-acylbenzothiazoles from benzothiazoles and aryl ketones. However, it is worth noting that only aryl benzothiazoyl ketones, not alkyl benzothiazoyl ketones, were obtained via this method (Scheme 1, pathway D).[20] In contrast, we disclose herein a mild and metal-free approach, through which a large variety of alkyl benzothiazoyl ketones was synthesized (Scheme. 1).

It is well-known that both *tert*-butyl hydroperoxide (TBHP) and di-*tert*-butyl peroxide (DTBP) are commonly used as radical initiators in organic synthesis and polymer chemistry. We initiated this unprecedented study, starting with establishing optimal experimental conditions in the presence of TBHP. The screening results are summarized in Table 1. The influence of temperature on the model reaction was first investigated under solvent-free conditions (Table 1, entries 1−5). No reaction occurred when the reaction temperature was below 40 °C. The yield was increased over the temperature range of 60−80 °C, from 35% to 61%, and then decreased to 54% when the temperature reached 100 °C. The effect of solvents was also investigated (Table 1, entries 6−11). A relatively higher yield of **3a** was obtained when acetonitrile was used as a solvent (83%)

Table 1. Optimization of the Reaction Conditions[a]



1a **2a** **3a**

entry	amt of TBHP (mmol)	amt of **2a** (mmol)	T(°C)	solvent	yield (%)[b]
1	10	5	40		0
2	10	5	60		35
3	10	5	80		61
4	10	5	100		54
5	10	5	120		43
6	10	5	80	DMSO	35
7	10	5	80	DMF	24
8	10	5	80	toluene	28
9	10	5	80	CH_2Cl_2	31
10	10	5	80	acetone	64
11	**10**	**5**	**80**	**CH_3CN**	**83**
12	10	1	80	CH_3CN	33
13	10	3	80	CH_3CN	61
14	10	10	80	CH_3CN	83
15	5	5	80	CH_3CN	68
16	15	5	80	CH_3CN	83
17	10	5	80	CH_3CN	51

[a]Reaction conditions: **1a** (1.0 mmol), **2a** (1.0−10.0 mmol), TBHP (5.0−15.0 mmol), solvent (2.0 mL) for 24 h. [b]Isolated yields.

(Table 1, entry 11). Other solvents resulted in lower yields of **3a**: i.e. DMSO (35%), DMF (24%), toluene (28%), CH_2Cl_2 (31%), and acetone (64%) (Table 1, entries 6−10). The optimal amount of **2a** and TBHP was also explored (Table 1, entries 11−17). The amount of **2a** and TBHP shown in entry 11 still brought about the most satisfied yield.

The substrate scope of benzothiazoles and dialkyl phosphites under the optimized reaction conditions was then examined (Table 2). All of the dialkyl phosphites reacted well with benzothiazole, giving the resulting 2-acylbenzothiazoles in moderate to good yields from 69% to 83% (**3a**−**f**). It is worth noting that the yield slightly decreased with the length of

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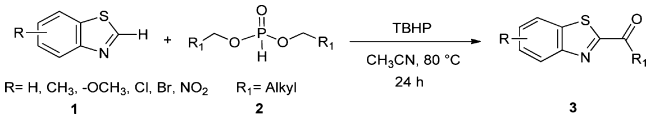
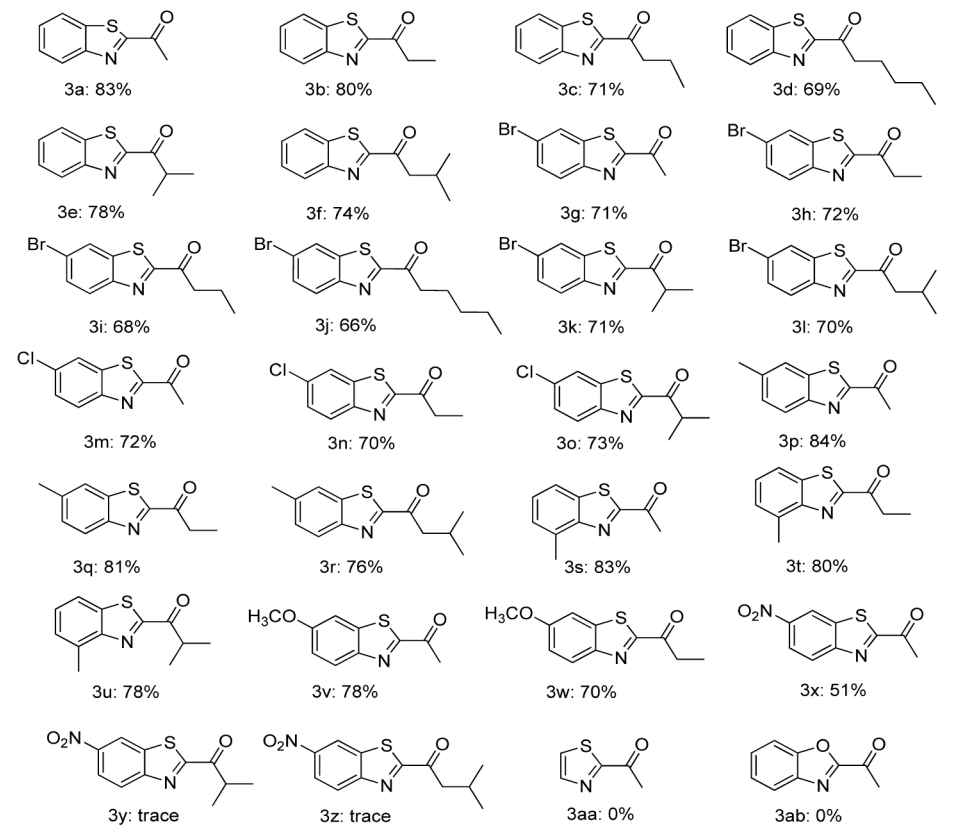
Table 2. Scope of Benzothiazoles and Alkyl Phosphonates[a]





[a]Reaction conditions: **1** (1.0 mmol), **2** (5.0 mmol), TBHP (10.0 mmol) in CH_3CN (2.0 mL) at 80 °C for 24 h. The isolated yields are provided. The scarcely formed **3y,z** were detected by ESI/MS(+). **3aa,ab** were detected by TLC.

the straight carbon chain of the corresponding dialkyl phosphites, from 83% to 69% in the case of **3a**−**d**. In comparison with the straight-chain alkyl phosphites, two branched dialkyl phosphites, diisopropyl and diisobutyl phosphites, slightly enhanced the acylation reactivity, affording **3e**,**f** in 78% and 74% yields, respectively. Furthermore, benzothiazoles bearing electron-donating and electron-withdrawing substituents (CH_3, Br, Cl, OCH_3, and NO_2) were also employed to react with dialkyl phosphites. Benzothiazoles bearing methyl and methoxyl substituents gave higher yields (**3p**−**w**) in comparison with nonsubstituted benzothiazole (**3a**−**f**). Introducing a bromo or chloro group, weakly electron withdrawing groups, on the benzothiazole ring slightly weakened the acylation reactivity, giving the resulting 2-acylbenzothiazoles in moderate to good yields from 66% to 73% (**3g**−**o**). Introducing a nitro group, a very strongly electron withdrawing group, seriously slowed the reaction, affording **3x** in a medium yield (51%) and traces of products **3y,z**. It is worth mentioning that thiazole and benzoxazole did not progress well under the optimized reaction conditions (**3aa**,**ab**). It is concluded that, in most cases, the representative benzothiazoles and dialkyl phosphites reacted smoothly to afford the desired products under the optimal reaction conditions.

A plausible mechanism for the acylation reaction is proposed in pathway I of Scheme 2. Diethyl phosphite has the tautomeric forms phosphonate **2a** and phosphite **3′a**.[21] TBHP initially cleaved into *tert*-butoxy radical as well as hydroxyl radical, which subsequently triggered hydrogen atom abstraction from the 2-position sp^2 C−H of benzothiazole **1a** and the α-position sp^3 C−H bond of tautomer **3′a**, respectively, forming the corresponding radical **1a′**[22] and α-carbon-centered radical **3′a′**. Carbon−carbon bond formation via termination of two radicals afforded the cross-coupling product **3**, which further lost the remaining α-hydrogen of **3**, forming the tertiary radical **4**. The hydroxyl radical then coupled with **4** to form the tetrahedral intermediate **5**, immediately followed by an energetically favorable elimination, leading to the final product **3a** along with ethyl hydrogen phosphonate **6** or **7**. It is especially worth noting that it is the α-carbon-centered radical **3′a′** formed by hydrogen abstraction from the α-position sp^3 C−H bond of tautomer **3′a′** that led the reaction way to the final 2-acylbenzothiazole **3a**. ^{31}P NMR traced the progress of the reactions. The essentially related phosphorus-containing compounds **3′a**, **3**, and **6** or **7**[23] were all well tracked in proper sequence, as shown in Figure 2. This ^{31}P NMR stacks diagram strongly backed the mechanism proposed.

More synthetic experiments were subsequently designed and carried out to deepen the related mechanism studies. In order

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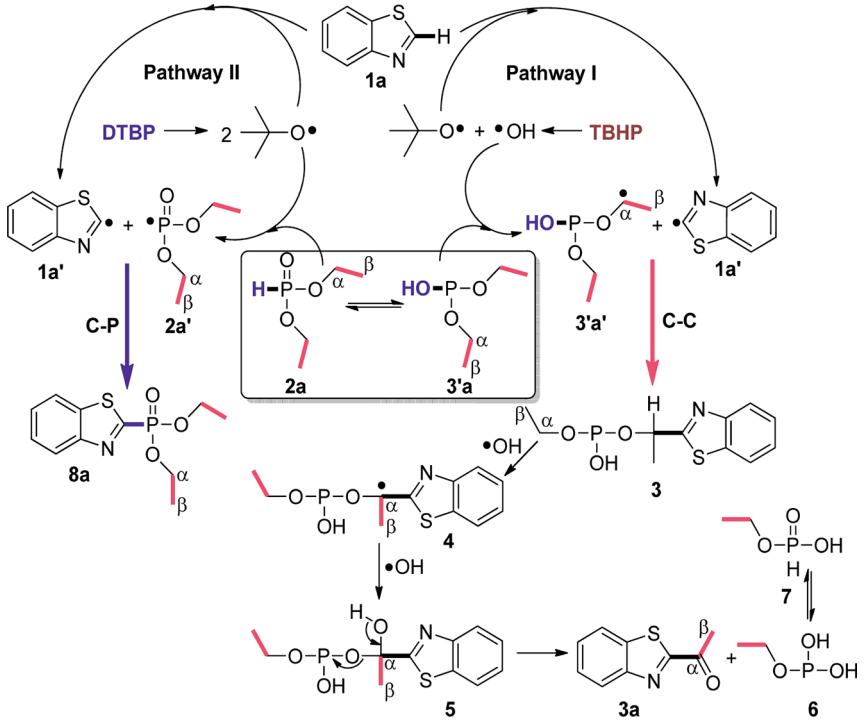
Scheme 2. Proposed Reaction Mechanisms of Benzothiazole with Diethyl Phosphite and TBHP (Pathway I) and with Diethyl Phosphite and DTBP (Pathway II), Respectively



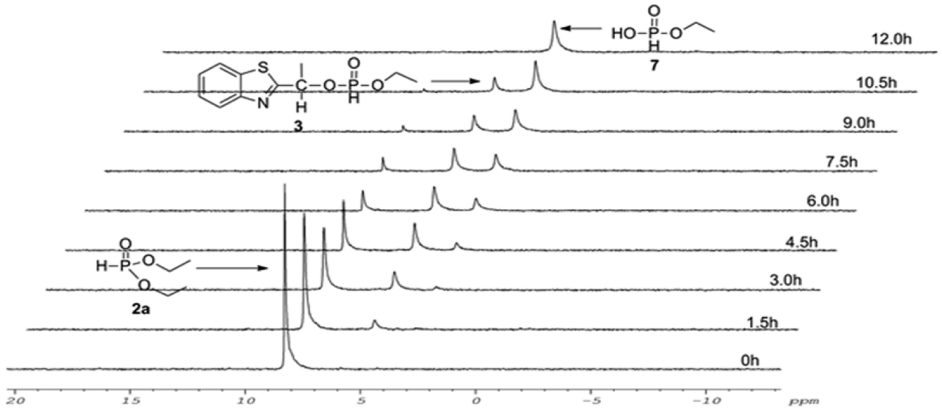


Figure 2. ^{31}P NMR stacks diagram for Scheme 2 (pathway I). Reaction conditions: benzothiazole (**1a**; 1.0 mmol), diethyl phosphite (**2a**; 5.0 mmol), and TBHP (10.0 mmol) under neat condtions at 80 °C for 12 h. The whole process was monitored by ^{31}P NMR every 1.5 h (comp-**2a**, 8.0 ppm; comp-**3**, 5.1 ppm; comp-**7**, 3.3 ppm).

to prove that the carbonyl oxygen of **3a** was from TBHP rather than from water or oxygen in the air, the reaction was carried out under anhydrous conditions and nitrogen protection, using the same amount of TBHP in anhydrous solution (Scheme 3I). Once again, **3a** was effectively obtained. It is especially worth mentioning here that the hydroxyl radical, generated by homolytic cleavage of TBHP, was indispensable for the formation of intermediate **5** on the way to the final 2-acylbenzothiazole **3a**. It is reasonable to believe that hydrogen peroxide (H_2O_2), another hydroxyl radical generator, might also be employed for the synthesis of the α-acylbenzothiazoles, whereas di-*tert*-butyl peroxide (DTBP), generating only *tert*-butoxyl radicals, might otherwise lead to some other products rather than 2-acylbenzothiazoles. The reactions shown in Scheme 3 were carried out to examine the mechanism. Under the optimized reaction conditions, 2-acylbenzothiazole (**3a**) was prepared in 60% yield from diethyl phosphite (**2a**) and benzothiazole (**1a**) using H_2O_2 as radical initiator (Scheme 3II), whereas, as shown in Scheme 3III, treatment of benzothiazole (**1a**) and diethyl phosphite (**2a**) with DTBP resulted accidentally in diethyl benzothiazol-2-ylphosphonate (**8a**) in 70% yield. It is well-known that aryl phospsphonates and their derivatives have found a wide range of applications in medicinal chemistry, catalysis, and organic synthesis.[24] It is notable that the direct phosphonation of benzothiazoles with dialkyl phosphites has been developed very recently by Li's group. However, under argon protection, palladium acetate $Pd(OAc)_2$, a metal salt, was still catalytically required along with a nitrogen-containing ligand for the phosphonation to occur.[25] The relatively simple synthetic method shown in Scheme 3III foreboded a novel, green, and metal-free approach possibly leading to a variety of benzothiazol-2-ylphosphonates.

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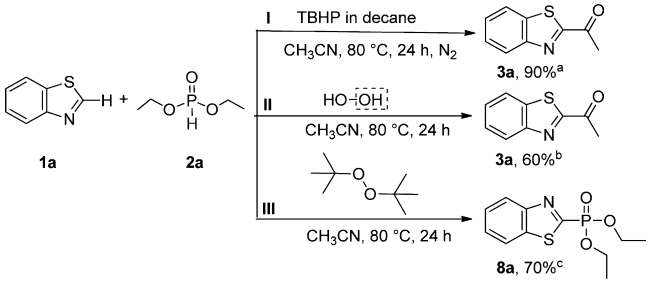
Scheme 3. Proposed Reaction of Benzothiazole and Dialkyl Phosphite with Different Peroxides[a]

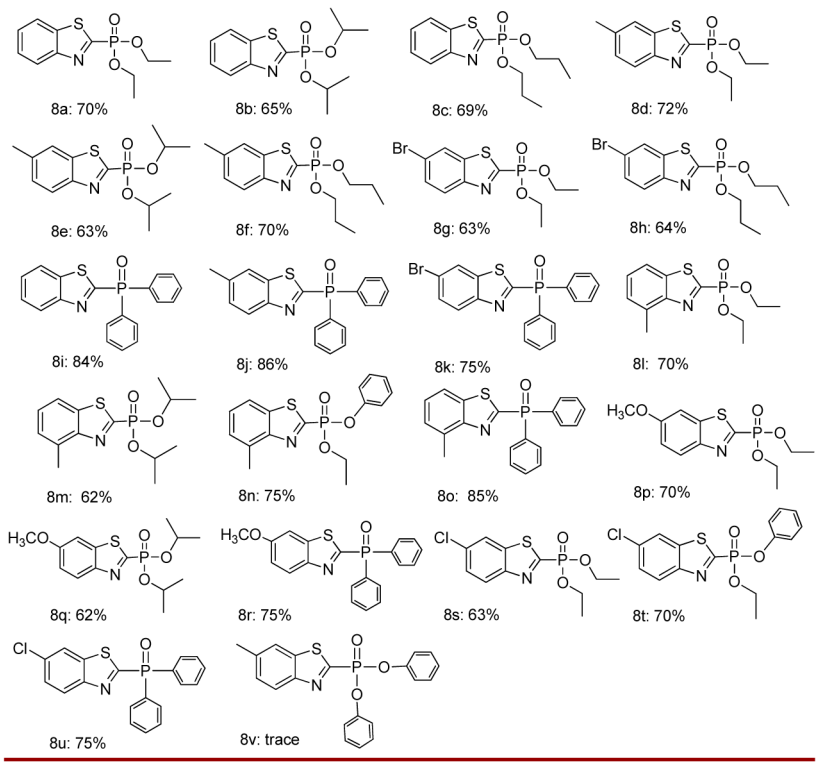


[a]Isolated yields are provided. Reaction conditions: (a) **1a** (1.0 mmol), **2a** (5.0 mmol), TBHP (10.0 mmol, 5−6 M in decane) in anhydrous CH_3CN (2.0 mL) at 80 °C under N_2 protection for 24 h; (b) **1a** (1.0 mmol), **2a** (5.0 mmol), H_2O_2 (10.0 mmol) in CH_3CN (2.0 mL) at 80 °C for 24 h; (c) **1a** (1.0 mmol), **2a** (5.0 mmol), DTBP (10.0 mmol) in CH_3CN (2.0 mL) at 80 °C for 24 h.

Using DTBP as radical initiator, the substrate scope of representative benzothiazoles, including those bearing electron-donating and electron-withdrawing groups (CH_3, Br, Cl, and OCH_3), and dialkyl phosphites was subsequently extended (Table 3). All of the corresponding reactions went smoothly, giving the resulting dialkyl benzothiazol-2-ylphosphonates **8a**−**u** in moderate to good yields from 63% to 85%. A plausible mechanism concerning the novel synthetic method is proposed in Scheme 2, pathway II. It is worth mentioning that Yang's research group has demonstrated that, catalyzed by $AgNO_3$, phosphorus-centered radicals were formed in the process of the carbon phosphorylation reactions of alkenes with diphenylphosphine oxide $Ph_2P(O)H$ or *H*-phosphonates $(RO)_2P(O)$-H.[26] It can be seen here from pathway II that after two *tert*-butoxy radicals were generated from a hemolytic cleavage of DTBP, the *tert*-butoxy radical underwent hydrogen atom abstraction from the P−H bond of tautomer **2a**, rather than a hydrogen atom abstraction from the α-position sp^3 C−H bond of tautomer **3′a** as in the case of pathway I, actually forming the phosphorus-centered radical **2a′**. Meanwhile, the *tert*-butoxy radical underwent hydrogen atom abstraction of the 2-position sp^2 C−H of benzothiazole **1a**, forming **1a′**. Finally, carbon−phosphorus bond formation via termination of two radicals afforded diethyl benzothiazol-2-ylphosphonate (**8a**). Single-crystal X-ray diffraction was successfully conducted to confirm the proposed structures of **3k** and **8i** (Scheme 4).[27]

The two types of radicals, α-carbon-centered phosphite radical **3′a′** and phosphorus-centered phosphonate radical **2a′**, played very different roles in determining in which path the chemical reaction would proceed through. In order to understand the reason the α-carbon-centered phosphite radical **3′a′** was formed in the presence of TBHP or H_2O_2, whereas the phosphorus-centered phosphonate radical **2a′** was formed in the presence of TDBP (Scheme 2), four possible pathways (pathways a−d) have been theoretically investigated using density functional theory (DFT). As shown in Scheme 5, the

Table 3. Scope of Dialkyl Benzothiazol-2-yl Phosphonates[a]



[a]Reaction condition: **1** (1.0 mmol), **2** (5.0 mmol), DTBP (10.0 mmol) in CH_3CN (2.0 mL) at 80 °C for 30 h. Isolated yield provided.

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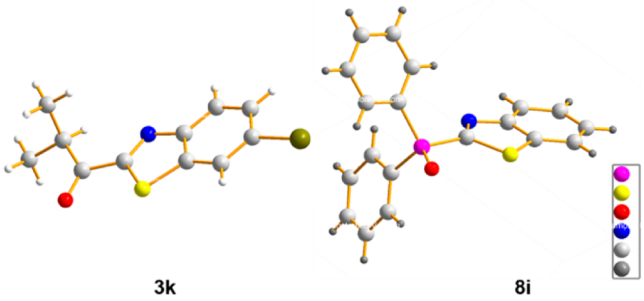
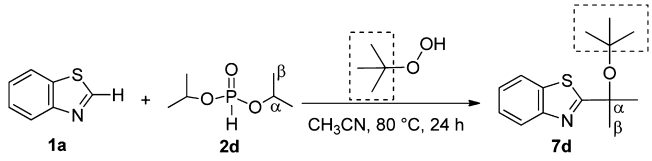
Scheme 4. Single-Crystal X-ray Structures of 3k and 8i



free energy barriers of pathways a–d are 12.58, 15.87, 7.11, and 3.69 kcal/mol, indicating that radical **2a**′ can be generated easily in the absence of the OH radical, and radical **3**′**a**′ can be generated much more easily in the presence of the OH radical, which is in good agreement with our experimental results.

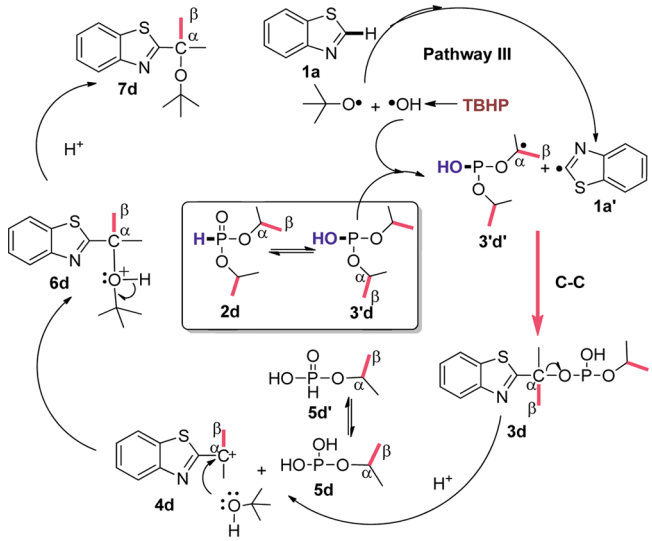
One more synthetic experiment was subsequently designed for further deepening our understanding of the related mechanisms. It is worth emphasizing that it is one secondary α-carbon of diethyl phosphite that finally was transferred into the carbonyl carbon of **3a**, suggesting that only secondary α-carbon containing dialkyl phosphites can possibly be employed for preparation of 2-acylbenzothiazoles. Scheme 6 illustrates what happened to the reaction in the case when diisopropyl phosphite, a tertiary α-carbon containing dialkyl phosphite, was employed. **7d**, a benzothiazole-containing ether, was obtained in that case. A related mechanism is proposed in Scheme 7 (pathway III). Again, TBHP cleaved to *tert*-butoxy radical and hydroxyl radical. Accordingly, α-carbon-centered phosphite radical **3**′**d**′ was generated much more easily in the presence of the OH radical. Again, benzothiazole **1a** underwent hydrogen atom abstraction, forming the radical **1a**′. Carbon–carbon bond formation via termination of the two radicals **1a**′ and **3**′**d**′ afforded the cross-coupling product **3d**. An S_N1 reaction was then followed, which proceeded initially with a heterolytic cleavage of **3d**, forming the monoisopropyl

Scheme 6. C–C Coupling Reaction with Diisopropyl Phosphonate and Benzothiazole[a]



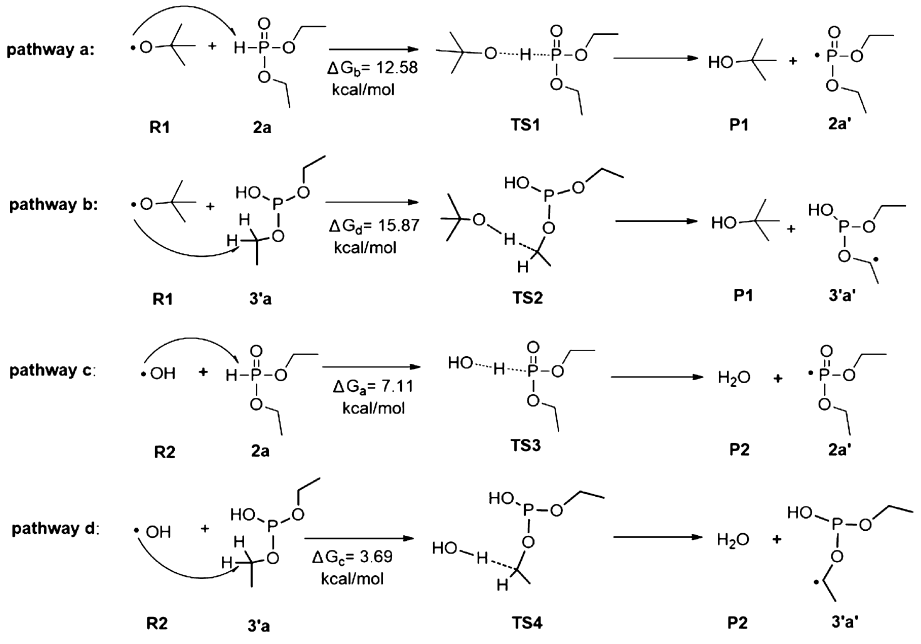
[a]Reaction condition: **1a** (1.0 mmol), **2d** (5.0 mmol), TBHP (10.0 mmol) in CH_3CN (2.0 mL) at 80 °C for 24 h.

Scheme 7. Proposed Reaction Mechanism of Benzothiazole with Diisopropyl Phosphite and TBHP (Pathway III)



phosphite **5d** (**d**′) and the tertiary carbocation **4d**. Acting as a nucleophile, the *tert*-butyl alcohol formed in the reaction subsequently reacted with **4d** to give rise to the protonated ether **6d**, which was subsequently deprotonated to the final product **7d**. The synthetic experiment testified again how

Scheme 5. Four Possible Proton Transfer Pathways and the Corresponding Free Energy Barriers



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TBHP regioselectively affected the formation of the radical intermediates.

CONCLUSION

In conclusion, two mild and metal-free methods, for the preparation of two kinds of important benzothiazole derivatives, 2-acylbenzothiazoles and dialkyl benzothiazol-2-ylphosphonates, were respectively developed. The TBHP triggered carbon-centered phosphite radical formation, whereas DTBP triggered phosphorus-centered phosphonate radical formation. The two types of radicals played very different roles in determining in which path the chemical reaction would proceed through. The direct C2-acylation of benzothiazoles was realized by the reaction of benzothiazoles with secondary α-carbon containing dialkyl phosphites in the presence of TBHP, whereas the direct C2-phosphonation of benzothiazoles was realized by the reaction of benzothiazoles with dialkyl phosphites, in the presence of DTBP. The work disclosed a very new aspect of *H*-phosphonate chemistry, which, due to "flexibility", makes *H*-dialkyl phosphonates unexpectedly efficient synthetic precursors in the preparation of the two types of very important benzothiazole derivatives.

EXPERIMENTAL SECTION

General Information. All commercial reagents and solvents were used without further purification. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ with tetramethylsilane (TMS) as the internal standard, and ^{31}P NMR spectra were obtained in $CDCl_3$ with H_3PO_4 as the internal standard. High-resolution mass spectra (HRMS) were obtained on a Q-TOF mass spectrometer. Column chromatography was carried out with columns of silica gel (200−300 mesh).

Experimental Procedures for the Synthesis of 2-Acylbenzothiazoles (3a−3ab). A mixture of benzothiazole (135.0 mg, 1.0 mmol), phosphonate (5.0 mmol), and TBHP (10.0 mmol) in CH_3CN (2.0 mL) was stirred at 80 °C for 24 h. The reaction mixture was quenched with water (5.0 mL) and extracted with ethyl acetate (3 × 5.0 mL). The combined organic layers were washed with brine (15.0 mL) and dried over anhydrous $MgSO_4$. After filtration, the solvent was evaporated in vacuo. The crude product was purified by silica gel chromatography (petroleum ether/ethyl acetate 20/1) to give the desired product.

*1-(Benzo[d]thiazol-2-yl)ethanone (**3a**):* white solid (0.147 g, 83% yield); mp 107−110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.83 (s, 3H), 7.53 (td, J = 7.6, 1.3 Hz, 1H), 7.58 (td, J = 8.0, 1.3 Hz, 1H), 7.98 (d, J = 8.0 Hz, 1H), 8.18 (d, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.2, 122.5, 125.5, 127.0, 127.7, 137.5, 153.6, 166.5, 193.2; HRMS (ESI) calcd for C_9H_7NOS [M + H]$^+$, 178.0321, found 178.0320.

*1-(Benzo[d]thiazol-2-yl)propan-1-one (**3b**):* white solid (0.152 g, 80% yield); mp 63−65 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (t, J = 7.3 Hz, 3H), 3.30 (q, J = 7.3 Hz, 2H), 7.52 (t, J = 7.4 Hz, 1H), 7.57 (t, J = 7.2 Hz, 1H), 7.97 (d, J = 7.8 Hz, 1H), 8.17 (d, J = 8.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.89, 32.1, 122.5, 125.3, 126.9, 127.6, 137.2, 153.6, 166.4, 196.0; HRMS (ESI) calcd for $C_{10}H_9NOS$ [M + H]$^+$, 192.0478, found 192.0484.

*1-(Benzo[d]thiazol-2-yl)butan-1-one (**3c**):* yellow solid (0.146 g, 71% yield); mp 43−45 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06 (t, J = 7.4 Hz, 3H), 1.85(m, 2H), 3.27 (t, J = 7.4 Hz, 2H), 7.53 (t, J = 7.2 Hz, 1H), 7.58 (t, J = 7.2 Hz, 1H), 7.98 (d, J = 8.0 Hz, 1H), 8.18 (d, J = 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 17.5, 40.5, 122.5, 125.4, 127.0, 127.6, 137.2, 153.6, 166.6, 195.5; HRMS (ESI) calcd for $C_{11}H_{11}NOS$ [M + H]$^+$, 206.0634, found 206.0641.

*1-(Benzo[d]thiazol-2-yl)hexan-1-one (**3d**):* white solid (0.161 g, 69% yield); mp 50−53 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, J = 6.8 Hz, 3H), 1.39(m, 2H), 1.40(m, 2H), 1.81 (m, 2H), 3.26 (t, J = 7.4 Hz, 2H), 7.51 (t, J = 7.2 Hz, 1H), 7.56 (t, J = 7.8 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 8.18 (d, J = 8.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.5, 31.4, 23.7, 38.6, 122.4, 125.4, 126.9, 127.6, 137.3, 153.6, 166.6, 195.6; HRMS (ESI) calcd for $C_{13}H_{15}NOS$ [M + H]$^+$, 234.0947, found 234.0954.

*1-(Benzo[d]thiazol-2-yl)-2-methylpropan-1-one (**3e**):* yellow liquid (0.160 g, 78% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (d, J = 6.9 Hz, 6H), 3.98 (m, 1H), 7.52 (t, J = 7.5 Hz, 1H), 7.57 (t, J = 7.2 Hz, 1H), 7.97 (d, J = 7.9 Hz, 1H), 8.18(d, J = 8.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.7, 36.3, 122.4, 125.4, 126.9, 127.6, 137.3, 153.6, 166.0, 199.2; HRMS (ESI) calcd for $C_{11}H_{11}NOS$ [M + H]$^+$, 206.0634, found 206.0639.

*1-(Benzo[d]thiazol-2-yl)-3-methylbutan-1-one (**3f**):* yellow liquid (0.162 g, 74% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.05 (d, J = 6.7 Hz, 6H), 2.40 (m, 1H), 3.15 (d, J = 7.0 Hz, 2H), 7.50 (t, J = 7.8 Hz, 1H), 7.56 (t, J = 7.4 Hz, 1H), 7.96 (d, J = 7.9 Hz, 1H), 8.18 (d, J = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.7, 25.1, 47.2, 122.4, 125.4, 126.9, 127.6, 137.3, 153.6, 166.9, 195.2; HRMS (ESI) calcd for $C_{12}H_{13}NOS$ [M + H]$^+$, 220.0791, found 220.0798.

*1-(6-Bromobenzo[d]thiazol-2-yl)ethanone (**3g**):* white solid (0.182 g, 71% yield); mp 150−153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.81 (s, 3H), 7.66 (dd, J = 8.8 Hz, 1H), 8.01 (d, J = 8.8 Hz, 1H), 8.10 (d, J = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 121.9, 125.0, 126.5, 130.7, 138.9, 152.3, 166.9, 192.8; HRMS (ESI) calcd for C_9H_6BrNOS [M + H]$^+$, 255.9426, found 255.9426.

*1-(6-Bromobenzo[d]thiazol-2-yl)propan-1-one (**3h**):* yellow solid (0.195 g, 72% yield); mp 104−106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (t, J = 7.2 Hz, 3H), 3.27(q, J = 7.3 Hz, 2H), 7.65 (d, J = 8.7 Hz, 1H, 5-H), 8.00 (d, J = 8.7 Hz, 1H), 8.10 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.8, 32.1, 121.8, 125.0, 126.4, 130.6, 138.7, 152.4, 166.7, 195.6; HRMS (ESI) calcd for $C_{10}H_8BrNOS$ [M + H]$^+$, 269.9583, found 269.9585.

*1-(6-Bromobenzo[d]thiazol-2-yl)butan-1-one (**3i**):* yellow solid (0.193 g, 68% yield); mp 97−101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.05 (t, J = 7.4 Hz, 3H), 1.84 (m, 2H), 3.23 (t, J = 7.3 Hz, 2H), 7.66 (dd, J = 8.8, 2.0 Hz, 1H), 8.02 (d, J = 8.8 Hz, 1H), 8.12 (d, J = 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 17.5, 40.5, 121.8, 125.0, 126.4, 130.7, 138.8, 152.4, 167.0, 195.2; HRMS (ESI) calcd for $C_{11}H_{10}BrNOS$ [M + H]$^+$, 283.9739, found 283.9744.

*1-(6-Bromobenzo[d]thiazol-2-yl)hexan-1-one (**3j**):* white solid (0.206 g, 66% yield); mp 89−91 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, J = 7.2 Hz, 3H), 1.39 (m, 4H), 1.81 (m, 2H), 3.24 (t, J = 7.5 Hz, 2H), 7.67 (dd, J = 8.8, 1.9 Hz, 1H, 5-H), 8.06 (d, J = 8.8 Hz, 1H, 4-H), 8.12 (d, J = 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.4, 23.6, 31.3, 38.6, 121.8, 125.0, 126.5, 130.7, 138.8, 152.4, 167.1, 195.4; HRMS (ESI) calcd for $C_{13}H_{14}BrNOS$ [M + Na]$^+$, 333.9872, found 333.9876.

*1-(6-Bromobenzo[d]thiazol-2-yl)-2-methylpropan-1-one (**3k**):* white solid (0.202 g, 71% yield); mp 73−76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (d, J = 6.9 Hz, 6H), 3.93 (m, 1H), 7.64 (d, J = 8.8 Hz, 1H), 8.00 (d, J = 8.8 Hz, 1H), 8.09 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.6, 36.4, 121.8, 124.9, 126.4, 130.6, 138.9, 152.4, 166.5, 198.8; HRMS (ESI) calcd for $C_{11}H_{10}BrNOS$ [M + H]$^+$, 283.9739, found 283.9745.

*1-(6-Bromobenzo[d]thiazol-2-yl)-3-methylbutan-1-one (**3l**):* white solid (0.209 g, 70% yield); mp 71−73 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.04 (d, J = 6.7 Hz, 3H), 2.39 (m, 1H), 3.12 (d, J = 6.9 Hz, 2H), 7.64 (d, J = 8.8 Hz, 1H), 8.00 (d, J = 8.8 Hz, 1H), 8.09 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.6, 25.0, 47.2, 121.8, 125.0, 126.4, 130.6, 138.8, 152.4, 167.3, 194.9; HRMS (ESI) calcd for $C_{12}H_{12}BrNOS$ [M + H]$^+$, 297.9896, found 297.9900.

*1-(6-Chlorobenzo[d]thiazol-2-yl)ethanone (**3m**):* white solid (0.152 g, 72% yield); mp 150−151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.82 (s, 3H), 7.53 (dd, J = 2.0 Hz, J = 8.8 Hz, 1H), 7.94 (d, J = 2.0 Hz, 1H), 8.10 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 122.0, 126.2, 128.1, 134.0, 138.5, 152.0, 166.9, 192.8; HRMS (ESI) calcd for C_9H_6ClNOS [M + H]$^+$, 211.9931, found 211.9930.

*1-(6-Chlorobenzo[d]thiazol-2-yl)propan-1-one (**3n**):* yellow solid (0.160 g, 70% yield); mp 120−121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (t, J = 7.2 Hz, 14.4 Hz, 3H), 3.27 (q, J = 6.8 Hz, 14.0 Hz, 2H), 7.53 (d, J = 8.8 Hz, 1H), 8.08 (d, J = 8.8 Hz, 1H), 8.10 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.8, 32.1, 122.0, 126.1, 128.0, 133.9, 138.3,

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152.1, 166.8, 195.7; HRMS (ESI) calcd for $C_{10}H_8ClNOS$ $[M + H]^+$, 226.0088, found 226.0087.

*1-(6-Chlorobenzo[d]thiazol-2-yl)-2-methylpropan-1-one (**3o**):* yellow liquid (0.175 g, 73% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 1.33 (d, J = 7.2 Hz, 6H), 3.96 (m, 1H), 7.55 (dd, J = 2.0 Hz, 8.8 Hz, 1H), 7.97 (d, J = 2.0 Hz, 1H), 8.1 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.6, 36.4, 122.0, 126.2, 127.9, 133.9, 138.4, 152.2, 166.5, 198.9; HRMS (ESI) calcd for $C_{11}H_{10}ClNOS$ $[M + H]^+$, 240.0244, found 240.0232.

*1-(6-Methylbenzo[d]thiazol-2-yl)ethanone (**3p**):* white solid (0.161 g, 84% yield); mp 88−90 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 2.52 (s, 3H), 2.81 (s, 3H), 7.38 (dd, J = 8.5, 1.2 Hz, 1H), 7.74 (s, 1H), 8.05 (d, J = 8.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.8, 26.1, 120.0, 124.9, 129.0, 137.7, 138.4, 151.7, 165.5, 193.2; HRMS (ESI) calcd for $C_{10}H_9NOS$ $[M + H]^+$, 192.0478, found 192.0484.

*1-(6-Methylbenzo[d]thiazol-2-yl)propan-1-one (**3q**):* yellow solid (0.166 g, 81% yield); mp 76−78 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 1.29 (t, J = 7.3 Hz, 3H), 2.52 (s, 3H), 3.29 (q, J = 7.3 Hz, 2H), 7.38 (dd, J = 8.5, 1.2 Hz, 1H), 7.75 (s, 1H), 8.04 (d, J = 8.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.9, 21.8, 32.0, 120.0, 124.8, 129.0, 137.4, 138.2, 151.7, 165.4, 196.0; HRMS (ESI) calcd for $C_{11}H_{11}NOS$ $[M + H]^+$, 206.0634, found 206.0643.

*3-Methyl-1-(6-methylbenzo[d]thiazol-2-yl)butan-1-one (**3r**):* yellow solid (0.177 g, 76% yield); mp 48−50 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 1.04 (d, J = 6.7 Hz, 6H), 2.40 (m, 1H), 2.52 (s, 3H), 3.14(d, J = 7.0 Hz, 2H), 7.38 (dd, J = 8.2, 1H), 7.75 (s, 1H), 8.05 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.8, 22.7, 25.1, 47.1, 122.0, 124.9, 128.8, 137.6, 138.2, 151.8, 160.0, 195.3; HRMS (ESI) calcd for $C_{13}H_{15}NOS$ $[M + H]^+$, 234.0947, found 234.0947.

*1-(4-Methylbenzo[d]thiazol-2-yl)ethanone (**3s**):* white solid (0.159 g, 83% yield); mp 66−70 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 2.80 (s, 3H, -CH_3), 2.83 (s, 3H), 7.36 (d, J = 7.2 Hz, 1H), 7.41 (t, J = 8.0 Hz, 15.2 Hz, 1H), 7.79 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.2 (-CH_3), 26.1, 119.8, 127.2, 127.7, 135.8, 137.5, 153.2, 165.1, 193.5; HRMS (ESI) calcd for $C_{10}H_9NOS$ $[M + H]^+$, 192.0478, found 192.0478.

*1-(4-Methylbenzo[d]thiazol-2-yl)propan-1-one (**3t**):* white solid (0.164 g, 80% yield); mp 65−68 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 1.30 (t, J = 7.2 Hz, J = 14.4 Hz, 3H,), 2.80 (s, 3H, -CH_3), 3.32 (q, J = 7.2 Hz, 14.4 Hz, 2H), 7.36 (d, J = 7.2 Hz, 1H), 7.41 (t, J = 7.6 Hz, 15.2 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.0, 18.2 (-CH_3), 32.0, 119.7, 127.1, 127.6, 135.7, 137.3, 153.2, 165.0, 196.3; HRMS (ESI) calcd for $C_{11}H_{11}NOS$ $[M + H]^+$, 206.0634, found 206.0633.

*1-(4-Methylbenzo[d]thiazol-2-yl)-2-methylpropan-1-one (**3u**):* yellow liquid (0.171 g, 78% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 1.34 (d, J = 6.8 Hz, 6H), 2.80 (s, 3H, -CH_3), 4.0 (m, 1H), 7.35 (d, J = 7.2 Hz, 1H), 7.40 (t, J = 7.6 Hz, 15.2 Hz, 1H), 7.79 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.2 (-CH_3), 18.8, 36.3, 119.7, 127.1, 127.5, 135.7, 137.4, 153.2, 164.7, 199.4; HRMS (ESI) calcd for $C_{12}H_{13}NOS$ $[M + H]^+$, 220.0791, found 220.0790.

*1-(6-Methoxybenzo[d]thiazol-2-yl)ethanone (**3v**):* white solid (0.162 g, 78% yield); mp 138−140 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 2.81 (s, 3H), 3.93 (s, 3H, −OCH_3), 7.20 (dd, J = 2.4 Hz, 8.8 Hz, 1H), 7.94 (d, J = 2.8 Hz, 1H), 8.10 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 55.9 (-OCH_3), 103.6, 117.7, 126.1, 139.5, 148.1, 159.8, 164.0, 193.0; HRMS (ESI) calcd for $C_{10}H_9NO_2S$ $[M + H]^+$, 208.0427, found 208.0429.

*1-(6-Methoxybenzo[d]thiazol-2-yl)propan-1-one (**3w**):* yellow solid (0.155 g, 70% yield); mp 118−120 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 1.30 (t, J = 7.2 Hz, 14.4 Hz, 3H), 3.28 (q, J = 7.2 Hz, 14.4 Hz, 2H), 3.93 (s, 3H, -OCH_3), 7.20 (dd, J = 2.4 Hz, 9.2 Hz, 1H), 7.40 (d, J = 2.4 Hz, 1H), 8.0 (d, J = 9.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.0, 31.9, 55.8 (-OCH_3), 103.7, 117.6, 126.0, 139.2, 148.1, 159.7, 163.9, 195.8; HRMS (ESI) calcd for $C_{11}H_{11}NO_2S$ $[M + H]^+$, 222.0583, found 222.0585.

*1-(6-Nitrobenzo[d]thiazol-2-yl)ethanone (**3x**):* yellow solid (0.133 g, 51% yield); mp 191−192 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 2.86 (s, 3H), 8.31 (d, J = 9.1 Hz, 1H), 8.42 (dd, J = 9.1, 2.2 Hz, 1H), 8.93 (d, J = 2.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.2, 119.1, 122.1, 126.0, 137.5, 146.6, 156.9, 171.4, 192.4; HRMS (ESI) calcd for $C_9H_6N_2O_3S$ $[M + H]^+$, 223.0172, found 223.0175.

Experimental Procedure for the Direct Phosphonation of Benzothiazoles with Dialkyl Phosphites (8a−u). A mixture of benzothiazole (135.0 mg, 1.0 mmol), phosphonate (5.0 mmol), and DTBP (10.0 mmol) in CH_3CN (2.0 mL) was stirred at 80 °C for 30 h. The reaction mixture was quenched with water (5.0 mL) and extracted with ethyl acetate (3 × 5.0 mL). The combined organic layers were washed with brine (15.0 mL) and dried over anhydrous $MgSO_4$. After filtration, the solvent was evaporated in vacuo. The crude product was purified by silica gel chromatography (petroleum ether/ethyl acetate 10/1) to give the desired product.

*Diethyl benzo[d]thiazol-2-ylphosphonate (**8a**):* light yellow oil (0.190 g, 70% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 1.32 (t, J = 7.2 Hz, 6H), 4.19−4.34 (m, 4H), 7.42−7.52 (m, 2H), 7.93 (d, J = 8.0 Hz, 1H), 8.16 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.2 (d, J = 6.0 Hz), 64.0 (d, J = 6.0 Hz), 121.9 (d, J = 1.0 Hz), 124.9, 126.8, 127.0, 136.3 (d, J = 2.0 Hz), 154.6 (d, J = 29 Hz)), 161.2 (d, J = 237.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 3.97 (s); HRMS (ESI) calcd for $C_{11}H_{14}NO_3PS$ $[M + H]^+$, 272.0505, found 272.0510; $[M + Na]^+$, 294.0324, found 294.0330;

*Diisopropyl benzo[d]thiazol-2-ylphosphonate (**8b**):* light yellow oil (0.195 g, 65% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 1,36−1.26 (dd, J = 6.0 Hz, 34.0 Hz, 12H), 4.89−4.81 (m, 2H), 7.50−7.40 (m, 2H), 7.92 (d, J = 7.6 Hz, 1H), 8.16 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.7, 73.1 (d, J = 6.0 Hz), 121.8 (d, J = 1.0 Hz), 124.8, 126.7, 126.8, 136.3 (d, J = 1.0 Hz), 154.6 (d, J = 28.0 Hz), 162.5 (d, J = 237.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 1.87 (s); HRMS (ESI) calcd for $C_{13}H_{18}NO_3PS$ $[M + Na]^+$, 322.0637, found 322.0641.

*Dipropyl benzo[d]thiazol-2-ylphosphonate (**8c**):* light yellow oil (0.207 g, 69% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 0.97 (t, J = 7.2 Hz, 6H), 1.82−1.73 (m, 4H), 4.29−4.16 (m, 4H), 7.60−7.51 (m, 2H), 7.93 (d, J = 8.0 Hz, 1H), 8.16 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.9, 23.7 (d, J = 7.0 Hz), 69.5 (d, J = 6.0 Hz), 121.9 (d, J = 1.0 Hz), 124.9, 126.9, 127.0, 136.4, 154.5 (d, J = 29.0 Hz), 161.1 (d, J = 237.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 4.14 (s); HRMS (ESI) calcd for $C_{13}H_{18}NO_3PS$ $[M + H]^+$, 300.0818, found 300.0819.

*Diethyl 6-methylbenzo[d]thiazol-2-ylphosphonate (**8d**):* light yellow oil (0.205 g, 72% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 1.39−1.35 (t, J = 7.2 Hz, 6H), 2.49 (s, 3H), 4.33−4.26 (m, 4H), 7.36−7.34 (d, J = 8.0 Hz, 1H), 7.75 (s, 1H), 8.10 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.2 (d, J = 6.0 Hz), 21.6, 64.0 (d, J = 6.0 Hz), 121.4, 124.3, 127.8, 128.6, 137.5 (d, J = 83.0 Hz), 152.8 (d, J = 28.0 Hz), 160.0 (d, J = 238.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 4.27 (s); HRMS (ESI) calcd for $C_{12}H_{16}NO_3PS$ $[M + H]^+$, 286.0661, found 286.0661.

*Diisopropyl 6-methylbenzo[d]thiazol-2-ylphosphonate (**8e**):* light yellow oil (0.197 g, 63% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 1.44−1.34 (dd, J = 6.0 Hz, 35.6 Hz, 12H), 2.54 (s, 3H), 4.95−4.90 (m, 2H), 7.40−7.38 (d, J = 8.0 Hz, 1H), 7.80 (d, 1H), 8.13−8.11 (d, J = 8.0 Hz, 1H, 4-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 24.1−23.7 (dd, J = 5.0 Hz, 28 Hz), 73.2−73.1 (d, J = 6.0 Hz), 121.4, 121.5, 124.4, 128.6, 137.4 (d, J = 58.0 Hz), 153.0 (d, J = 29 Hz), 161.3 (d, J = 239.0 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ 2.27 (s); HRMS (ESI) calcd for $C_{14}H_{20}NO_3PS$ $[M + H]^+$, 314.0974, found 314.0976.

*Dipropyl 6-methylbenzo[d]thiazol-2-ylphosphonate (**8f**):* light yellow oil (0.219 g, 70% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 1.00−0.97 (t, J = 7.2 Hz, 6H), 1.83−1.74 (m, 4H), 4.29−4.16 (m, 4H), 7.42−7.40 (d, J = 8.4 Hz, 1H), 7.81 (s, 1H), 8.15−8.13 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.9, 21.7, 23.7 (d, J = 6.0 Hz), 69.4 (d, J = 6.0 Hz), 121.4, 124.4, 128.6, 136.7, 137.5, 152.6 (d, J = 28 Hz), 159.8 (d, J = 238.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 4.46 (s); HRMS (ESI) calcd for $C_{14}H_{20}NO_3PS$ $[M + H]^+$, 314.0974, found 314.0978.

*Diethyl 6-bromobenzo[d]thiazol-2-ylphosphonate (**8g**):* yellow oil (0.221 g, 63% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 1.39 (t, J = 7.2 Hz, 6H), 4.40−4.25 (m, 4H), 7.67−7.65 (q, 1H), 8.07 (d, J = 8.8 Hz, 1H), 8.14 (d, J = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.3 (d, J = 6.0 Hz), 64.2 (d, J = 5.0 Hz), 121.2, 124.5 (d, J = 1.0 Hz),

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125.9, 130.6, 138.0, 153.4 (d, J = 28 Hz), 161.9 (d, J = 237.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 3.34 (s); HRMS (ESI) calcd for $C_{11}H_{13}BrNO_3PS$ $[M + H]^+$, 349.9610, found 349.9608;

*Dipropyl 6-bromobenzo[d]thiazol-2-ylphosphonate (**8h**):* yellow oil (0.242 g, 64% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.97 (t, J = 7.2 Hz, 6H), 1.82−1.73 (m, 4H), 4.30−4.16 (m, 4H), 7.70−7.67 (dd, J = 1.6 Hz, 8.4 Hz, 1H), 8.09 (d, J = 8.8 Hz, 1H), 8.16 (d, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.9, 23.7 (d, J = 6.0 Hz), 69.6 (d, J = 6.0 Hz), 121.1, 124.5 (d, J = 2.0 Hz), 125.9, 130.5, 137.9 (d, J = 1.0 Hz), 153.3 (d, J = 28 Hz), 161.9 (d, J = 237.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 3.37 (s); HRMS (ESI) calcd for $C_{13}H_{17}BrNO_3PS$ $[M + H]^+$, 377.9923, found 377.9925; $[M + Na]^+$, 399.9742, found 399.9746.

*Diphenyl benzo[d]thiazol-2-ylphosphonate (**8i**):* white solid (0.282 g, 84% yield); mp 162−164 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47−7.39 (m, 8H), 7.48−7.50 (m, 5H), 7.51 (d, J = 2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 122.1, 124.7 126.7 (d, J = 4.0 Hz), 128.7 (d, J = 13.0 Hz), 130.5, 131.6, 131.9 (d, J = 10.0 Hz), 132.6 (d, J = 3.0 Hz), 136.7, 155.4 (d, J = 22 Hz), 167.4 (d, J = 126.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 19.80 (s); HRMS (ESI) calcd for $C_{19}H_{14}NOPS$ $[M + H]^+$, 336.0606, found 336.0611; $[M + Na]^+$, 358.0426, found 358.0430.

*Diphenyl 6-methylbenzo[d]thiazol-2-ylphosphonate (**8j**):* yellow solid (0.300 g, 86% yield); mp 122−124 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.51 (s, 3H, -CH_3), 7.37−7.35 (dd, J = 1.2 Hz, 8.4 Hz, 1H), 7.51−7.47 (m, 4H), 7.51−7.59 (m, 2H), 7.80 (s, 1H), 7.98−7.93 (m, 4H), 8.05 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6 (-CH_3), 121.6, 124.1, 128.5, 128.7 (d, J = 13.0 Hz), 130.5, 131.6, 131.9 (d, J = 10.0 Hz), 132.6 (d, J = 3.0 Hz,) 137.1 (d. J = 14.0 Hz), 153.4 (d, J = 22.0 Hz), 165.8 (d, J = 127.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 20.01 (s); HRMS (ESI) calcd for $C_{20}H_{16}NOPS$ $[M + H]^+$, 350.0763, found 350.0768; $[M + Na]^+$, 372.0582, found 372.0582

*Diphenyl 6-bromobenzo[d]thiazol-2-ylphosphonate (**8k**):* yellow solid (0.331 g, 75% yield); mp 126−128 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47−7.39 (m, 7H), 7.48−7.50 (m, 5H), 7.51 (d, J = 2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 120.8, 124.6, 125.7, 128.8 (d, J = 13.0 Hz), 130.1 (d, J = 18.0 Hz), 131.2 (s), 131.8 (d, J = 10.0 Hz), 132.8 (d, J = 3.0 Hz), 138.4, 155.4 (d, J = 22 Hz), 167.4 (d, J = 124.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 19.74 (s); HRMS (ESI) calcd for $C_{19}H_{13}BrNOPS$ $[M + H]^+$, 413.9712, found 413.9712

*Diethyl 4-methylbenzo[d]thiazol-2-ylphosphonate (**8l**):* light yellow oil (0.200 g, 70% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40−1.43 (t, J = 7.2 Hz, 14.0 Hz, 6H), 2.82 (s, 3H), 4.29−4.40 (m, 4H), 7.35−7.37 (d, J = 6.8 Hz, 1H), 7.40−7.44 (t, J = 7.6 Hz, 15.2 Hz 1H), 7.81−7.83 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.2 (d, J = 6.0 Hz) 18.4, 64.1 (d, J = 6.0 Hz), 119.0, 119.3, 126.9, 127.0, 135.1 (d, J = 121.0 Hz), 154.3 (d, J = 28.0 Hz), 158.6 (d, J = 239.0 Hz, 2-C); ^{31}P NMR (162 MHz, $CDCl_3$) δ 3.38 (s); HRMS (ESI) calcd for $C_{12}H_{16}NO_3PS$ $[M + H]^+$, 286.0661, found 286.0662.

*Diisopropyl 4-methylbenzo[d]thiazol-2-ylphosphonate (**8m**):* light yellow oil (0.194 g, 62% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46−1.38 (dd, J = 6.0 Hz, 23.6 Hz, 12H), 2.83 (s, 3H), 4.99−4.91 (m, 2H), 7.35−7.37 (d, J = 7.2 Hz, 1H), 7.43−7.39 (t, J = 8.0 Hz, 15.2 Hz 1H), 7.84−7.82 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.4, 24.1−23.7 (dd, J = 5.0 Hz, 31.0 Hz), 73.1 (d, J = 6.0 Hz), 119.0, 119.2, 126.8, 127.0, 135.1 (d, J = 132.0 Hz), 154.3 (d, J = 28.0 Hz), 158.6 (d, J = 239.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 2.31 (s); HRMS (ESI) calcd for $C_{14}H_{20}NO_3PS$ $[M + H]^+$, 314.0974, found 314.0976.

*Ethyl phenyl (4-methylbenzo[d]thiazol-2-yl)phosphonate (**8n**):* yellow liquid (0.250 g, 75% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (t, J = 7.2 Hz, 14.0 Hz, 3H), 2.80 (s, 3H), 4.38−4.28(m, 2H), 7.39−7.31 (m, 2H), 7.52−7.48 (m, 2H), 7.60−7.56 (m, 1H), 7.81−7.79 (d, J = 7.6 Hz, 1H), 8.11−8.01 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.5 (d, J = 6.0 Hz), 18.4, 62.8 (d, J = 6.0 Hz), 119.3, 126.8, 127.0, 128.6 (d, J = 14.0 Hz, 28.0 Hz), 130.1, 132.2 (d, J = 10.0 Hz), 133.0 (d, J = 3.0 Hz), 135.1, 136.7, 154.5 (d, J = 23 Hz), 161.5 (d, J = 168.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 20.38 (s); HRMS (ESI) calcd for $C_{16}H_{16}NO_3PS$ $[M + H]^+$, 334.0661, found 334.0671.

*Diphenyl 6-methylbenzo[d]thiazol-2-ylphosphonate (**8o**):* white solid (0.297 g, 85% yield); mp 205−207 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.80 (s, 3H), 7.40−7.34 (m, 2H), 7.53−7.42 (m, 4H), 7.60−7.57 (m, 2H), 7.85−7.83 (d, J = 7.6 Hz, 1H), 8.05−8.0 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): 18.4, 119.4, 126.6 (d, J = 34.0 Hz), 128.6 (d, J = 13.0 Hz), 130.9, 131.9 (d, J = 7.0 Hz), 132.0, 132.5 (d, J = 3.0 Hz), 134.9, 136.7, 154.9 (d, J = 21 Hz), 164.3 (d, J = 129.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 19.30 (s); HRMS (ESI) calcd for $C_{20}H_{16}NOPS$ $[M + H]^+$, 350.0763, found 350.0776

*Diethyl 6-methoxybenzo[d]thiazol-2-ylphosphonate (**8p**):* light yellow oil (0.211 g, 70% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43−1.40 (t, J = 6.8 Hz, 14.0 Hz, 6H), 3.93 (s, 3H, −OCH_3), 4.39−4.27 (m, 4H), 7.21−7.18 (dd, J = 2.4 Hz, 8.8 Hz, 1H), 7.42−7.43 (d, J = 2.4 Hz, 1H), 8.12−8.14 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.1 (d, J = 7.0 Hz), 55.8 (-OCH_3), 63.5 (d, J = 6.0 Hz), 103.2 (d, J = 1.0 Hz), 117.3, 125.4, 138.2, 149.1 (d, J = 28.0 Hz), 159.2, 157.9 (d, J = 240.0 Hz); ^{31}P NMR (162 MHz, CDCl3) δ 4.37 (s); HRMS (ESI) calcd for $C_{12}H_{16}NO_4PS$ $[M + H]^+$, 302.0610, found 302.0613.

*Diisopropyl 6-methoxybenzo[d]thiazol-2-ylphosphonate (**8q**):* light yellow oil (0.204 g, 62% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44−1.34 (dd, J = 6.4 Hz, 35.2 Hz, 11H), 3.92 (s, 3H, −OCH_3), 4.97−4.85 (m, 2H), 7.20−7.17 (dd, J = 2.4 Hz, 9.2 Hz, 1H), 7.42−7.41 (d, J = 2.4 Hz), 8.13−8.11 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.1−23.7 (dd, J = 5.0 Hz, 27.0 Hz), 55.8(s, -OCH_3), 73.2−73.1 (d, J = 6.0 Hz), 103.3 (d, J = 10.0 Hz), 117.1, 125.4, 138.3, 149.5 (d, J = 29.0 Hz), 159.0, 159.4 (d, J = 240.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 2.20 (s); HRMS (ESI) calcd for $C_{14}H_{20}NO_4PS$ $[M + H]^+$, 330.0923, found 330.0927.

*Diphenyl 6-methoxybenzo[d]thiazol-2-ylphosphonate (**8r**):* light yellow oil (0.274 g, 75% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.80 (s, −OCH_3), 7.11−7.07 (dd, J = 2.8 Hz, 9.2 Hz 1H), 7.35 (d, J = 2.4 Hz, 1H), 7.46−7.42 (m, 4H), 7.53−7.48 (m, 2H), 7.97−7.92 (m, 4H), 8.00 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 103.4, 117.2, 125.2, 128.6 (d, J = 13.0 Hz), 130.5, 131.7, 131.8 (t, J = 6.0 Hz, 16.0 Hz), 132.6 (d, J = 4.0 Hz), 138.6, 150.0 (d, J = 22.0 Hz), 158.9, 162.6 (d, J = 129.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 19.84 (s); HRMS (ESI) calcd for $C_{20}H_{16}NO_2PS$ $[M + H]^+$, 366.0712, found 366.0729.

*Diethyl 6-chlorobenzo[d]thiazol-2-ylphosphonate (**8s**):* yellow liquid (0.193 g, 63% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ1.40−1.44 (t, J = 7.2 Hz, 14.4 Hz, 6H), 4.29−4.41 (m, 4H), 7.54−7.57 (dd, J = 2.0 Hz, 8.8 Hz, 1H), 8.00−8.01 (d, J = 2.0 Hz, 1H), 8.15−8.17 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.3 (t, J = 1.6 Hz, 2.4 Hz), 64.2 (d, J = 6.0 Hz), 121.5, 125.7, 127.9, 133.6, 137.6, 153.3 (d, J = 29.0 Hz), 159.6 (d, J = 239.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 3.37 (s); HRMS (ESI) calcd for $C_{11}H_{13}ClNO_3PS$ $[M + H]^+$, 306.0115, found 306.0118.

*Ethyl phenyl (6-chlorobenzo[d]thiazol-2-ylphosphonate (**8t**):* yellow liquid (0.248 g, 70% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (t, J = 7.2 Hz, 14.0 Hz, 3H), 4.37−4.25 (m, 2H), 7.39−7.31 (m, 2H), 7.54−7.49 (m, 3H), 7.62−7.58 (m, 1H), 7.97 (d, J = 2.0 Hz, 1H), 8.08−8.02 (m, 2H), 8.11−8.10 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.5 (d, J = 7.0 Hz), 62.9 (d, J = 7.0 Hz), 121.6, 125.6, 127.8, 128.1, 128.7 (d, J = 15.0 Hz), 129.5, 132.2 (d, J = 5.0 Hz), 133.3 (t, J = 15.0 Hz, 18.0 Hz), 137.9, 153.6 (d, J = 24.0 Hz), 165.7 (d, J = 165.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 20.31 (s); HRMS (ESI) calcd for $C_{15}H_{13}ClNO_3PS$ $[M + H]^+$, 354.0115, found 354.0128.

*Diphenyl 6-chlorobenzo[d]thiazol-2-ylphosphonate (**8u**):* light yellow solid (0.277 g, 75% yield); mp 112−113 °C; 1H NMR (400 MHz, $CDCl_3$) δ 7.51−7.45 (m, 5H), 7.59−7.54 (m, 2H), 7.99−7.94 (m, 5H), 8.08−8.05 (d, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 121.6, 125.5, 127.7, 128.7 (d, J = 13.0 Hz), 130.2, 131.3, 131.9 (d, J = 5.0 Hz), 132.8 (t, J = 2.0 Hz, 16.0 Hz) δ 138.0, 153.8 (d, J = 21 Hz), 168.3 (d, J = 124.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 19.76 (s); HRMS (ESI) calcd for $C_{19}H_{13}ClNOPS$ $[M + H]^+$, 370.0217, found 370.0229.

*2-(2-(tert-Butoxy)propan-2-yl)benzo[d]thiazole (**7d**).* white oil (0.130 g, 52% yield); ^{1}H NMR (400 MHz, $CDCl_3$): 1.26 (s, 9H), 1.74(s, 6H), 7.35 (t, J = 7.2 Hz, 1H), 7.44 (t, J = 7.7 Hz, 1H), 7.88 (d,

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J = 7.9 Hz, 1H), 8.00 (d, J = 8.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.3, 26.6, 79.8, 82.6, 121.6, 123.0, 124.8, 125.5, 135.8, 152.8, 178.0; HRMS (ESI) calcd for $C_{14}H_{19}NOS$ $[M + H]^+$, 250.1260, found 250.1260.

■ ASSOCIATED CONTENT

Supporting Information

Text, tables, figures, and CIF files giving density functional theory (DFT) data, NMR spectra for all compounds, and crystallographic data for **3k** and **8i**. This material is available free of charge via the Internet at http://pubs.acs.org. Crystallographic data have also been deposited at the Cambridge Crystallographic Data Centre (CCDC) as supplementary publication numbers CCDC 953163 (**3k**) and CCDC 953164 (**8i**).

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Notes

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(27) CCDC 953163 and 953164 contain supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.