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Synthesis and Crystal Structure Study of Diethyl Aryl(benzo[*d*]thiazol-2-ylamino)methyl Phosphonates

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ABSTRACT: *A three-component synthesis of α-aminophosphonate is described from a reaction between aldehydes, 2-aminobenzothiazole, and triethyl phosphite in the presence of $InCl_3$ as a catalyst under solvent-free conditions for the generation of the particular α-aminophosphonates. These products have two potentially biologically active parts, aminophosphonate and benzothiazole. This method offers advantages such as short reaction times, good yields, solvent-free conditions, and easy workup with the green aspects by avoiding toxic catalysts and solvents. The crystal structure of* **4b** *has been determined by X-ray crystallography. This compound crystallizes in the monoclinic space group C2/c with cell parameters $a = 21.9285(5)$ Å, $b = 10.3221(2)$ Å, $c = 18.5979(5)$ Å, $\beta = 108.759(3)^\circ$, $V = 3985.99(18)$ Å^3, $D_{calc} = 1.301$ mg m^{-3}, and $Z = 8$. The final R value is 0.0501 for 3741 reflections.* © 2012 Wiley Periodicals, Inc. Heteroatom Chem. 24:58–65, 2013; View this article online at wileyonlinelibrary.com. DOI 10.1002/hc.21063

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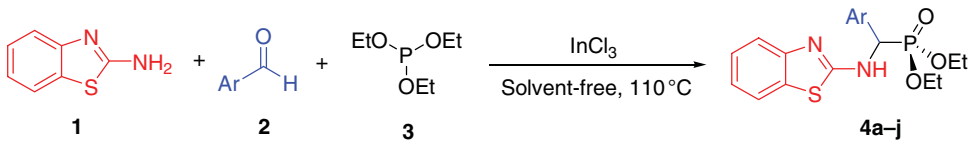
INTRODUCTION

α-Aminophosphonate is a biologically important compound as peptidomimetics, haptens design in antibody generation [1], and also in enzyme inhibitory activity [2]. In addition, α-aminophosphonate derivatives have broad applications such as herbicids, insecticides, fungicides, antibiotics, and pharmacological agents [3]. Among the number of synthetic approaches regarding α-aminophosphonates, one of the most powerful methods is the Kabachnik–Fields reaction in which aldehyde, amine, and di- or trialkyl phosphite are reacted in a one-pot setup [4]. This reaction can be promoted by several acid catalysts such as $NbCl_5$ [5], $ChCl{\cdot}2ZnCl_2$ [6], $InCl_3$ [7], $YbCl_3$ [8], $Ce(OTf)_4$ [9], $Sn(OTf)_2$ [10], $Mg(ClO_4)_2$ [11], $LiClO_4$ [12], $ZrOCl_2{\cdot}8H_2O$ [13], CAN [14], $Yb(PFO)_3$ [15], SmI_2 [16], $TaCl_5$-SiO_2 [17], $SbCl_3/Al_2O$ [18], sulfamic acid [19], oxalic acid [20], and silica sulfuric acid [21]. In recent years, α-aminophosphonates were synthesized containing the benzothiazole moiety, which has antitumor and antimicrobial activity [11,13,22].

Molecules featuring of the benzothiazole structural motif play a key part in a wide variety of chemistry. Their diverse functions range from electron



SCHEME 1 Synthesis of α-aminophosphonates **4a-j** catalyzed by $InCl_3$.

TABLE 1 Optimization of Catalyst on a Model Reaction[a]

Entry	*Catalyst*	*Isolated Yield (%)*
1	–	33
2	*p*-TsOH·H_2O	55
3	$ZrCl_4$	21
4	$ZrOCl_2 \cdot 8H_2O$	57
5	$Zr(NO_3)_4$	41
6	$InCl_3$	65
7	CAN	37

[a]Reaction conditions: 2-Aminobenzothiazole (1.0 mmol), 4-chlorobenzaldehyde (1.0 mmol), and triethyl phosphite (1.0 mmol) with 10 mol% catalyst for 30 min at 100°C under solvent-free conditions.

TABLE 2 Optimization of Reaction Conditions[a]

Entry	*Catalyst (mol%)*	*Temperature (°C)*	*Time (min)*	*Isolated Yield (%)*
1	5	90	30	40
2	10	90	30	56
3	15	90	30	54
4	5	100	30	45
5	10	100	15	67
6	15	100	13	67
7	10	110	11	77
8	15	110	11	70

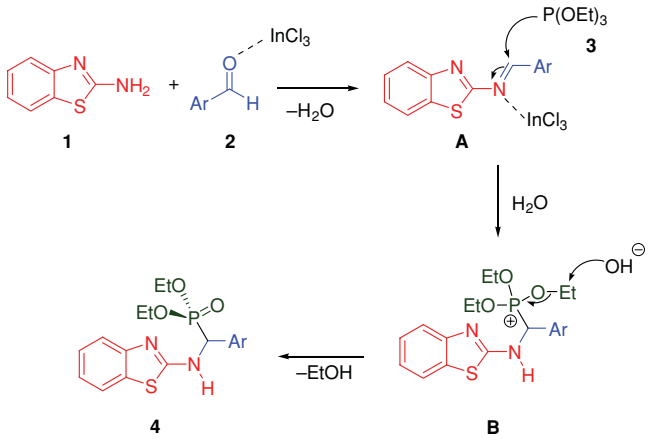
[a]Reaction conditions: 2-Aminobenzothiazole (1.0 mmol), 4-chlorobenzaldehyde (1.0 mmol), triethyl phosphite (1.0 mmol), and $InCl_3$ as a catalyst.

transfer facilitation in the firefly luciferine cycle [23], through antitumor [24] and antidiabetic activity [25] to an Alzheimer disease tracer [26] and an anticancer agent in pharmaceutical chemistry [27]. The 2-aminobenzothiazole nuclei, as a privileged scaffold, are found in many natural products and pharmaceuticals that exhibit remarkable biological activities [28]. In addition, some compounds with this skeleton have application in drugs for the treatment of various diseases [29].

RESULTS AND DISCUSSION

In continuation of our ongoing research [30–36], we investigated the $InCl_3$-catalyzed three-component reaction between 2-aminobenzothiazole and aldehydes in the presence of triethyl phosphite under solvent-free and thermal conditions for the synthesis of different α-aminophosphonates **4a–j** (Scheme 1).

At the outset of experiment, the one-pot, three-component reaction between 2-aminobenzothiazole, 4-chlorobenzaldehyde, and triethyl phosphite was chosen as a pattern to optimize the reaction conditions in the presence of some catalysts such as *p*-TsOH·H_2O, $ZrCl_4$, $ZrOCl_2 \cdot 8H_2O$, $Zr(NO_3)_4$, $InCl_3$, and CAN. In the absence of catalyst, only 33% of product could be obtained when the mixture of the reaction was heated at 100°C for 30 min. This indicated that the catalyst should be necessary for this transformation (Table 1). The effect of amount of catalyst was also investigated along with effects of temperature and time on the



SCHEME 2 Speculative mechanism for the synthesis of α-aminophosphonates **4a–j** catalyzed by $InCl_3$.

yield. Herein, a reaction occurred efficiently to afford the corresponding α-aminophosphonates in 77% yield when 10 mol% $InCl_3$ was used at 110°C under solvent-free conditions (Table 2, entry 7).

A speculative mechanism is presented for the synthesis of compounds **4a–j** in Scheme 2. In the first step, it is believed to involve the formation of activated imine **A** [37]. In the second step, phosphite adds to the C=N bond of the transient imine **A** to afford phosphonium intermediate **B,** which then undergoes the reaction with water generated during formation of imine to give α-amino phosphonates **4** and EtOH.

The chemical structures of all the new compounds (Table 3) were confirmed by IR, ^1H, ^{13}C, and

TABLE 3 Synthesis of α-Aminophosphonates **4a–j**.

Entry	*Ar*	*Product*	*Time (min)*	*Yield (%)*
1	Ph	**4a**	14	77
2	4-MeC_6H_4	**4b**	13	75
3	4-ClC_6H_4	**4c**	11	77
4	3-ClC_6H_4	**4d**	12	76
5	2-ClC_6H_4	**4e**	12	70
6	3-BrC_6H_4	**4f**	10	72
7	3-$MeOC_6H_4$	**4g**	13	71
8	4-HOC_6H_4	**4h**	16	80
9	4-HO-3-$MeOC_6H_3$	**4i**	16	89
10	5-Br-2-HOC_6H_3	**4j**	14	78

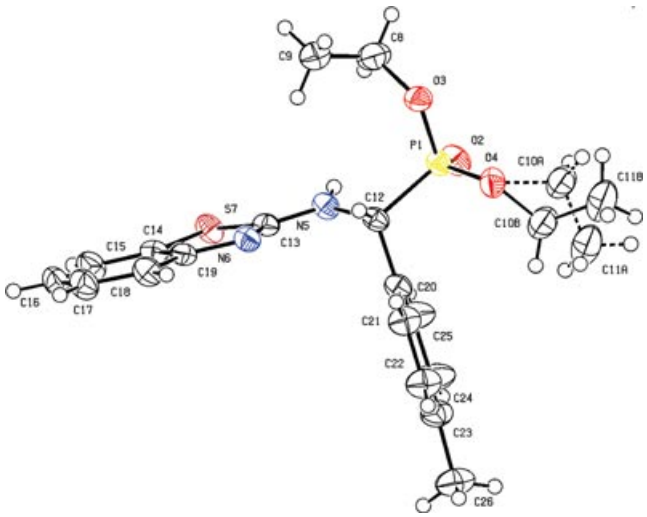


FIGURE 1 ORTEP view of the molecular geometry of compound **4b**. Ellipsoids have been drawn at the 50% probability level.

^{31}P NMR spectroscopy, elemental analysis, and mass spectrometry. The structure of compound **4b** established through single-crystal X-ray analysis (Fig. 1). Compound **4b** exhibited characteristic IR stretching frequencies at 3234 and 1232 cm^{-1} for N—H and P=O, respectively [38]. In the ^{1}H NMR spectrum of **4b**, the P—C—H proton resonated as a doublet of doublet at δ 5.53 with $^2J_{PH}$ = 22.0 Hz and $^3J_{HH}$ = 8.4 Hz due to its coupling with phosphorus and NH [39]. A broad singlet at δ 7.46 corresponds to NH proton (using D_2O exchange). The methylene protons of P—O—CH_2—CH_3 showed a multiplet in the region δ 3.76–4.22, and the methyl protons of P—OCH_2—CH_3 gave two triplets at δ 1.18 and 1.31 with $^3J_{HH}$ = 6.8 Hz [39].

The carbon chemical shifts were observed in the title compounds for P—CH, P—O—$\underline{C}H_2$ (two δ), and P—O—C—$\underline{C}H_3$ (two δ) at δ 55.46, 63.50, 63.65, 16.27, and 16.50, respectively with coupling constants involving 154.9 Hz ($^1J_{CP}$), 7.0 Hz ($^2J_{CP}$), and 6.0 Hz ($^3J_{CP}$), respectively [38, 40, 41]. The ^{31}P NMR signal appeared at δ 20.90 for **4b** [42].

TABLE 4 Hydrogen Bond Geometries of Compound **4b** in the Crystal Packing (Å, deg)

D—H···A	D—H	H···A	D···A	D—H···A
N5—H5···O2	0.86	2.64	3.025 (3)	108
C8—H8A···O2	0.97	2.78	3.164 (3)	104
C9—H9C···N5	0.96	2.83	3.527 (4)	131
C10A—H10A···O2	0.97	2.74	3.142 (7)	106
C10A—H10A···O2	0.97	2.74	3.142 (7)	106
C10B—H10D···O2	0.97	2.47	2.978 (6)	113
C10B—H10D···O2	0.97	2.47	2.978 (6)	113
C12—H12···N6	0.98	2.48	2.810 (3)	99
C25—H25···N5	0.93	2.77	2.984 (4)	94
N5—H5···O2^{i}	0.86	2.17	2.841 (2)	135
C25—H25···O2^{i}	0.93	2.86	3.702 (3)	151
C9—H9A···N6^{ii}	0.96	2.88	3.631 (4)	136
C21—H21···O4^{iii}	0.93	2.80	3.699 (3)	163
C11B—H11E···N6^{iii}	0.96	2.86	3.610 (10)	135
C21—H21···O3^{iii}	0.93	2.66	3.390 (3)	136
C16—H16···O3^{iv}	0.93	2.55	3.359 (3)	145

Symmetry codes: (i) $-x$, $-y$, $-z$; (ii) $-x$, y, $-z-1/2$; (iii) $-x$, $-y+1$, $-z$; (iv) $x-1/2$, $-y+1/2$, $z-1/2$.

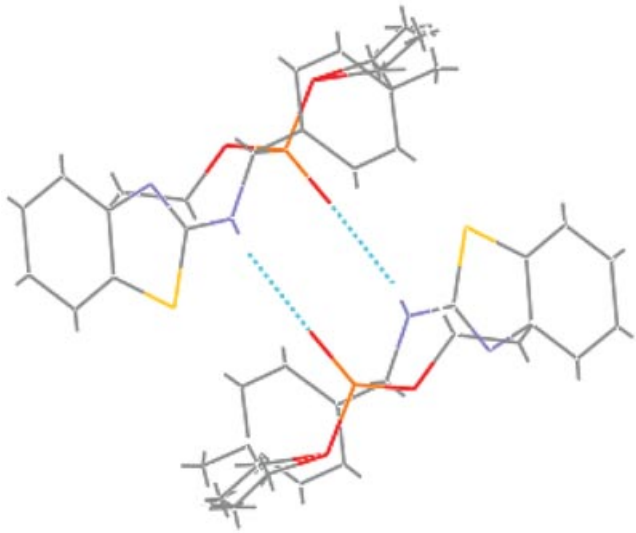


FIGURE 2 A pair of hydrogen bonds in a centrosymmetric dimer of **4b**.

In this compound, there are weak intermolecular —P=O···H—N— hydrogen bond (Table 4) that are effective in the stabilization of the crystal structure. A pair of hydrogen bond can be seen in a centrosymmetric dimer of compound **4b** (Fig. 2).

CONCLUSIONS

In conclusion, we have developed a simple and convenient method for the synthesis of α-aminophosphonates through the three-component reaction between 2-aminobenzothiazole, aldehydes,

and triethyl phosphite catalyzed by $InCl_3$ (10 mol%) at 110°C under solvent-free conditions. The advantages of the present method are short reaction times, good yields, solvent-free conditions, and easy workup with the green aspects by avoiding toxic catalysts and solvents.

EXPERIMENTAL

*General Procedure for Synthesis of α-Aminophosphonates (**4a-j**)*

To a mixture of 2-aminobenzothiazole (1.0 mmol), aldehydes (1.0 mmol), and triethyl phosphite (1.0 mmol), $InCl_3$ (10 mol%) was added and stirred at 110°C for appropriate time (Table 3). After completion of the reaction as monitored by TLC, the mixture was cooled to room temperature and the mixture was washed with EtOAc (3 × 3 mL) to afford pure α-aminophosphonates **4a–j**.

*Diethyl Phenyl(benzo[d]thiazol-2-ylamino)methyl Phosphonate (**4a**).* White powder; mp 155–157°C; IR (KBr): ν 3223 (NH), 1249 (P=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ_H 1.16 and 1.31 (2t, $J = 6.8$ Hz, $2CH_3$, 6H), 3.74–4.22 (m, $2CH_2$, 4H), 5.44 (dd, $J_{HP} = 22.0$ Hz, $J_{HH} = 6.4$ Hz, CHP, 1H), 6.58 (brs, NH, 1H), 7.08–7.58 (m, H_{arom}, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 16.26 and 16.52 (2d, $J_{CP} = 6.0$ Hz, $2CH_3$), 55.68 (d, $J_{CP} = 153.9$ Hz, CHP), 63.54 and 63.68 (2d, $J_{CP} = 7.0$ Hz, $2CH_2$), 119.26 (s), 120.67 (s), 121.72 (s), 125.70 (s), 128.18 (d, $J_{CP} = 2.0$ Hz), 128.34 (d, $J_{CP} = 6.0$ Hz), 128.55 (d, $J_{CP} = 1.0$ Hz), 131.20 (s), 135.29 (s), 152.07 (s), 165.96 (d, $J_{CP} = 12.0$ Hz); ^{31}P NMR ($CDCl_3$, 162 MHz): δ_P 20.90; MS (*m/z*) (%): 376 (M^+, 6), 273 (20), 255 (11), 239 (100), 237 (5), 150 (3); Anal. Calcd for $C_{18}H_{21}N_2O_3PS$: C, 57.44; H, 5.62; N, 7.44. Found: C, 57.69; H, 5.67; N, 7.53.

*Diethyl (4-methylphenyl)(benzo[d]thiazol-2-ylamino)methyl Phosphonate (**4b**).* Yellow powder; mp 176–178°C; IR (KBr): ν 3234 (NH), 1232 (P=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ_H 1.18 and 1.31 (2t, $J = 6.8$ Hz, $2CH_3$, 6H), 2.34 (s, CH_3, 3H), 3.76–4.22 (m, $2CH_2$, 4H), 5.53 (dd, $J_{HP} = 22.0$ Hz, $J_{HH} = 8.4$ Hz, CHP, 1H), 7.06–7.56 (m, H_{arom}, 8H), 7.46 (br, NH, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 16.27 and 16.50 (2d, $J_{CP} = 6.0$ Hz, $2CH_3$), 21.22 (s, CH_3), 55.46 (d, $J_{CP} = 154.9$ Hz, CHP), 63.50 and 63.65 (2d, $J_{CP} = 7.0$ Hz, $2CH_2$), 119.28 (s), 120.69 (s), 121.76 (s), 125.74 (s), 128.15 (d, $J_{CP} = 6.0$ Hz), 129.31 (d, $J_{CP} = 2.0$ Hz), 131.10 (s), 132.02 (s), 138.01 (d, $J_{CP} = 3.0$ Hz), 152.02 (s), 165.93 (d, $J_{CP} = 12.0$ Hz); ^{31}P NMR ($CDCl_3$, 162 MHz): δ_P 20.90; MS (*m/z*) (%): 390 (M^+, 33), 281 (21), 254 (67), 253 (100), 252 (8), 251 (14), 150 (5), 105 (5); Anal. Calcd for $C_{19}H_{23}N_2O_3PS$: C, 58.45; H, 5.94; N, 7.17. Found: C, 58.63; H, 6.01; N, 7.23.

*Diethyl (4-chlorophenyl)(benzo[d]thiazol-2-ylamino)methyl Phosphonate (**4c**).* White powder; mp 195–198°C; IR (KBr): ν 3230 (NH), 1230 (P=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ_H 1.17 and 1.24 (2t, $J = 6.8$ Hz, $2CH_3$, 6H), 3.93–4.19 (m, $2CH_2$, 4H), 5.79 (d, $J_{HP} = 21.6$ Hz, CHP, 1H), 7.06–7.67 (m, H_{arom}, 8H), 8.19 (brs, NH, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 16.31 and 16.53 (2d, $J_{CP} = 5.0$ Hz, $2CH_3$), 54.92 (d, $J_{CP} = 156.0$ Hz, CHP), 63.72 (d, $J_{CP} = 7.0$ Hz, $2CH_2$), 119.33 (s), 120.69 (s), 121.72 (s), 125.78 (s), 128.72 (s), 129.67 (d, $J_{CP} = 6.0$ Hz), 131.16 (s), 134.03 (s), 151.92 (s), 165.68 (d, $J_{CP} = 12.0$ Hz); ^{31}P NMR ($CDCl_3$, 162 MHz): δ_P 20.35; MS (*m/z*) (%): 412 ($M^+ + 2$, 18), 410 (M^+, 48), 275 (100), 273 (83), 255 (16), 237 (26), 135 (10); Anal. Calcd for $C_{18}H_{20}ClN_2O_3PS$: C, 52.62; H, 4.91; N, 6.82. Found: C, 52.81; H, 4.90; N, 6.88

*Diethyl (3-chlorophenyl)(benzo[d]thiazol-2-ylamino)methyl Phosphonate (**4d**).* White powder; mp 153–156°C; IR (KBr): ν 3224 (NH), 1237 (P=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ_H 1.20 and 1.32 (2t, $J = 7.2$ Hz, $2CH_3$, 6H), 3.82–4.31 (m, $2CH_2$, 4H), 6.00 (dd, $J_{HP} = 22.4$ Hz, $J_{HH} = 6.8$ Hz, CHP, 1H), 7.09–7.61 (m, H_{arom}, 8H), 7.23 (br, NH, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 16.27 and 16.50 (2d, $J_{CP} = 5.0$ Hz, $2CH_3$), 55.08 (d, $J_{CP} = 154.9$ Hz, CHP), 63.79 and 63.82 (2d, $J_{CP} = 4.0$ Hz, $2CH_2$), 119.35 (s), 120.70 (s), 121.87 (s), 125.75 (s), 126.48 (d, $J_{CP} = 6.0$ Hz), 128.34 (s), 128.38 (d, $J_{CP} = 6.0$ Hz), 129.79 (d, $J_{CP} = 2.0$ Hz), 131.24 (s), 134.44 (d, $J_{CP} = 2.0$ Hz), 151.93 (s), 165.67 (d, $J_{CP} = 12.0$ Hz); ^{31}P NMR ($CDCl_3$, 162 MHz): δ_P 20.31; MS (*m/z*) (%): 412 ($M^+ + 2$, 3), 410 (M^+, 8), 275 (44), 273 (100); Anal. Calcd for $C_{18}H_{20}ClN_2O_3PS$: C, 52.62; H, 4.91; N, 6.82. Found: C, 52.78; H, 4.99; N, 6.90.

*Diethyl (2-chlorophenyl)(benzo[d]thiazol-2-ylamino)methyl Phosphonate (**4e**).* White powder; mp 193–195°C; IR (KBr): ν 3219 (NH), 1247 (P=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ_H 1.14 and 1.36 (2t, $J = 7.2$ Hz, $2CH_3$, 6H), 3.72–4.31 (m, $2CH_2$, 4H), 6.00 (dd, $J_{HP} = 22.8$ Hz, $J_{HH} = 6.8$ Hz, CHP, 1H), 7.07–7.73 (m, H_{arom}, NH, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 16.18 and 16.50 (2d, $J_{CP} = 6.0$ Hz, $2CH_3$), 52.46 (d, $J_{CP} = 155.9$ Hz, CHP), 63.74 and 63.87 (2d, $J_{CP} = 7.0$ Hz, $2CH_2$), 119.57 (s), 120.71 (s), 121.84 (s), 125.77 (s), 127.24 (d, $J_{CP} = 3.0$ Hz), 129.28 (d, $J_{CP} = 4.0$ Hz), 129.36 (d, $J_{CP} = 5.0$ Hz), 129.56 (d, $J_{CP} = 2.0$ Hz), 131.26 (s), 133.65 (s), 134.32 (d, $J_{CP} = 7.0$ Hz), 152.12 (s), 165.81 (d,

$J_{CP} = 13.0$ Hz); ^{31}P NMR ($CDCl_3$, 162 MHz): δ_P 20.21; MS (*m/z*) (%): 412 ($M^+ + 2$, 7), 410 (M^+, 19), 275 (85), 273 (100), 237 (25), 84 (19); Anal. Calcd for $C_{18}H_{20}ClN_2O_3PS$: C, 52.62; H, 4.91; N, 6.82. Found: C, 52.77; H, 4.96; N, 6.85.

*Diethyl (3-bromophenyl)(benzo[d]thiazol-2-ylamino)methyl Phosphonate (***4f***).* White powder; mp 159–162°C; IR (KBr): ν 3227 (NH), 1235 (P=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.21 and 1.32 (2t, $J = 6.8$ Hz, $2CH_3$, 6H), 3.86–4.31 (m, $2CH_2$, 4H), 5.55 (dd, $J_{HP} = 22.0$ Hz, $J_{HH} = 6.4$ Hz, CHP, 1H), 7.02–7.75 (m, H_{arom}, 8H), 7.18 (br, NH, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 16.30 and 16.53 (2d, $J_{CP} = 6.0$ Hz, $2CH_3$), 54.94 (d, $J_{CP} = 154.9$ Hz, CHP), 63.83 and 63.90 (2d, $J_{CP} = 4.0$ Hz, $2CH_2$), 119.30 (s), 120.68 (s), 121.81 (s), 122.60 (d, $J_{CP} = 3.0$ Hz) 125.71 (s), 126.98 (d, $J_{CP} = 5.0$ Hz), 130.07 (d, $J_{CP} = 1.0$ Hz), 131.21 (d, $J_{CP} = 2.0$ Hz), 131.21 (s), 131.27 (s), 131.31 (d, $J_{CP} = 2.0$ Hz) 137.96 (s), 151.94 (s), 165.75 (d, $J_{CP} = 14.0$ Hz); ^{31}P NMR ($CDCl_3$, 162 MHz): δ_P 20.38; MS (*m/z*) (%): 456 ($M^+ + 2$, 7), 454 (M^+, 7), 319 (100), 317 (96), 238 (3); Anal. Calcd for $C_{18}H_{20}BrN_2O_3PS$: C, 47.48; H, 4.43; N, 6.15. Found: C, 47.70.; H, 4.51; N, 6.19.

*Diethyl (3-methoxyphenyl)(benzo[d]thiazol-2-ylamino)methyl Phosphonate (***4g***).* Yellow powder; mp 138–140°C; IR (KBr): ν 3231 (NH), 1257 (P=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.18 and 1.31 (2t, $J = 7.2$ Hz, $2CH_3$, 6H), 3.78 (s, OCH_3, 3H), 3.80–4.30 (m, $2CH_2$, 4H), 5.54 (dd, $J_{HP} = 22.0$ Hz, $J_{HH} = 4.00$ Hz, CHP, 1H), 6.84–7.56 (m, H_{arom}, 8H), 7.44 (br, NH, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 16.27 and 16.49 (2d, $J_{CP} = 6.0$ Hz, $2CH_3$), 55.23 (s, OCH_3), 55.82 (d, $J_{CP} = 153.9$ Hz, CHP), 63.55 and 63.71 (2d, $J_{CP} = 7.0$ Hz, $2CH_2$), 113.82 (d, $J_{CP} = 2.0$ Hz), 119.32 (s), 120.54 (d, $J_{CP} = 6.0$ Hz), 120.70 (s), 121.80 (s), 125.75 (s), 129.56 (d, $J_{CP} = 2.0$ Hz), 131.14 (s), 136.64 (s), 152.03 (s), 159.72 (d, $J_{CP} = 2.0$ Hz) 165.93 (d, $J_{CP} = 13.0$ Hz); ^{31}P NMR ($CDCl_3$, 162 MHz): δ_P 20.71; MS (*m/z*) (%): 406 (M^+, 7), 269 (100), 255 (19), 150 (16), 135 (8); Anal. Calcd for $C_{19}H_{23}N_2O_4PS$: C, 56.15; H, 5.70; N, 6.89. Found: C, 56.25; H, 5.79; N, 6.86.

*Diethyl (4-hydroxyphenyl)(benzo[d]thiazol-2-ylamino)methyl Phosphonate (***4h***).* White powder; mp 215–218°C; IR (KBr): ν 3209 (NH), 3431–3147 (br, OH), 1228 (P=O) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 1.07 and 1.14 (2t, $J = 7.2$ Hz, $2CH_3$, 6H), 3.86–4.05 (m, $2CH_2$, 4H), 5.53 (d, $J_{HP} = 20.8$ Hz, CHP, 1H), 6.75–7.68 (m, H_{arom}, 8H), 8.97 and 9.55 (2br, OH, NH, 2H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ_C 16.56 and 16.73 (2d, $J_{CP} = 6.0$ Hz, $2CH_3$), 54.20 (d, $J_{CP} = 156.0$ Hz, CHP), 62.84 and 63.01 (2d, $J_{CP} = 6.0$ Hz, $2CH_2$), 115.39 (s), 118.75 (s), 121.48 (s), 121.78 (s), 126.04 (s), 129.83 (d, $J_{CP} = 6.0$ Hz), 131.20 (s), 152.06 (s), 157.34 (s) 165.80 (d, $J_{CP} = 10.0$ Hz); ^{31}P NMR (DMSO-d_6): δ_P 21.37; MS (*m/z*) (%): 392 (M+, 4), 283 (9), 273 (19), 255 (100), 150 (8), 135 (10), 83 (11), 65 (11); Anal. Calcd for $C_{18}H_{21}N_2O_4PS$: C, 55.09; H, 5.39; N, 7.14. Found: C, 55.31; H, 5.47; N, 7.19.

*Diethyl (4-hydroxy-3-methoxyphenyl)(benzo[d]thiazol-2-ylamino)methyl Phosphonate (***4i***).* White powder; mp 206–208°C; IR (KBr): ν 3206 (NH), 3425–3160 (br, OH), 1246 (P=O) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 1.08 and 1.14 (2t, $J = 7.2$ Hz, $2CH_3$, 6H), 3.78 (s, OCH_3, 3H), 3.86–4.06 (m, $2CH_2$, 4H), 5.62 (d, $J_{HP} = 20.8$ Hz, CHP, 1H), 6.75–7.69 (m, H_{arom}, 7H), 8.97 and 9.10 (2br, OH, NH, 2H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ_C 16.58 and 16.74 (2d, $J_{CP} = 5.0$ Hz, $2CH_3$), 54.47 (d, $J_{CP} = 155.0$ Hz, CHP), 56.14 (s, OCH_3), 62.86 and 63.02 (2d, $J_{CP} = 7.0$ Hz, $2CH_2$), 112.84 (d, $J_{CP} = 5.0$ Hz), 115.46 (s), 118.74 (s), 121.30 (d, $J_{CP} = 6.0$ Hz), 121.49 (s), 121.80 (s), 126.07 (s), 126.72 (s), 131.17 (s), 146.56 (s), 147.72 (s), 152.07 (s), 165.78 (d, $J_{CP} = 8.0$ Hz); ^{31}P NMR (DMSO-d_6 162 MHz): δ_P 21.25; MS (*m/z*) (%): 422 (M^+, 5), 317 (12), 285 (100), 273 (7), 178 (8), 150 (89), 123 (10), 96 (8); Anal. Calcd for $C_{19}H_{23}N_2O_5PS$: C, 54.02; H, 5.49; N, 6.63. Found: 54.33; H, 5.44; N, 6.70.

*Diethyl (5-bromo-2-hydroxyphenyl)(benzo[d]thiazol-2-ylamino)methyl Phosphonate (***4j***).* White powder; mp 193–195°C; IR (KBr): ν 3220 (NH), 3420–3154 (br, OH), 1238 (P=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.23 and 1.34 (2t, $J = 7.2$ Hz, $2CH_3$, 6H), 4.02–4.31 (m, $2CH_2$, 4H), 5.62 (d, $J_{HP} = 24.0$ Hz, CHP, 1H), 6.58 (br, NH, 1H), 6.90–7.86 (m, H_{arom}, NH, 8H), 10.67 (br, OH, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 16.20 and 16.51 (2d, $J_{CP} = 6.0$ Hz, $2CH_3$), 49.84 (d, $J_{CP} = 162.0$ Hz, CHP), 64.10 and 64.17 (2d, $J_{CP} = 4.0$ Hz, $2CH_2$), 112.73 (s), 118.88 (s), 121.09 (s), 121.56 (s), 125.54 (s), 126.24 (s), 130.46 (s), 131.66 (d, $J_{CP} = 5.0$ Hz), 133.07 (s), 149.81 (s), 155.12 (d, $J_{CP} = 10.0$ Hz), 167.14 (d, $J_{CP} = 14.0$ Hz); ^{31}P NMR ($CDCl_3$, 162 MHz): δ_P 20.90; MS (*m/z*) (%): 472 ($M^+ + 2$, 16), 470 (M^+,16), 426 (25), 397 (8), 335 (100), 333 (99), 317 (14), 150 (13), 135 (26); Anal. Calcd for $C_{18}H_{20}BrN_2O_4PS$: C, 45.87; H, 4.28; N, 5.94. Found: C, 46.11; H, 4.34; N, 6.03.

TABLE 5 Crystal Data and Structure Refinement for Compound **4b**

Empirical formula	$C_{19}H_{23}N_2O_3PS$
Formula weight	390.42
Temperature	120(2)
Crystal system	Monoclinic
Space group	*C2/c*
Unit cell dimensions	$a = 21.9285(5)$ Å $b = 10.3221(2)$ Å $c = 18.5979(5)$ Å $\beta = 108.759(3)$
Volume	3985.99(18) Å^3
Z	8
Density (calculated)	1.301 mg m^{-3}
Absorption coefficient	2.375
Crystal size	0.04 × 0.11 × 0.33 mm^3
θ range for data collection	2.3–35.25°
Index ranges	$-24 \le h \le 26$, $-8 \le k \le 12$, $-22 \le l \le 21$
Reflections collected	8067
Independent reflections	3741 [R(int) = 0.03]
Goodness-of-fit on F2	1.069
Data/restraints/parameters	3741/4/244
Final R indices [I>2σ(I)]	$R1 = 0.0501$ $wR2 = 0.1205$
R indices (all data)	$R1 = 0.0606$ $wR2 = 0.1290$
CCDC number	888011

CRYSTAL STRUCTURE ANALYSIS

The single crystals were grown from a CH_2Cl_2/*n*-hexane solution. The X-ray diffraction measurements of **4b** were made on an Oxford Diffraction Xcalibur Gemini R CCD single crystal diffractometer 120K (Cu Kα radiation, graphite monochromator, $\lambda = 1.54180$ Å). The structure of title compound was solved by SIR2004 [43] and refined by full matrix least squares on F2 (SHELXL-97) [44]. Absorption correction, data collection, cell refinement, and data reduction have been carried out using CrysAlisPro [45], PARST97 [46] for the geometrical calculations, ORTEP-3 for windows [47] and Mercury [48] for molecular graphics, and WinGX (publication material) [49].

CRYSTALLOGRAPHIC DATA

CCDC 888011 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Center. Copies of the data can be obtained, free of qcharge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223–336033, e-mail: deposit@ccdc.cam.ac.uk), or via www.ccdc.cam.ac.uk/data_request/cif

Crystallography

Compound **4b** was synthesized from the reaction between 2-aminobenzothiazole, benzaldehyde, triethyl

TABLE 6 Selected Bond Lengths, Bond Angles, and Torsion Angles for Compound **4b**

Bond Lengths	*(Å)*	*Bond Angles*	*(°)*	*Torsion Angles*	*(°)*
P1–O2	1.4718(17)	C13–S7–C14	88.26(10)	C14–S7–C13–N5	–178.4(2)
P1 –O3	1.5712(19)	C13–N6—C19	109.92(19)	C14–S7–C13–N6	0.7(2)
P1–O4	1.5625(17)	S7–C13–N6	116.65(17)	O2–P1–O3–C8	47.0(2)
P1–C12	1.823(2)	C12–N5—C13	118.15(18)	O4–P1–O3–C8	172.9(2)
O3–C8	1.442(4)	P1–C12–C20	112.63(17)	C12–P1–O3–C8	–78.5(2(
C8–C9	1.493(5)	O2–P1–O3	115.03(10)	O2–P1–O4–C10B	–28.1(3)
O4–C10B	1.450(6)	P1–O3–C8	123.82(17)	O3–P1-O4–C10B	–152.9(3)
C10B–C11B	1.427(10)	O3–C8–C9	108.8(3)	O3–P1–O4–C10B	–152.9(3
O4–C10A	1.477(7)	O2–P1–O4	116.61(10)	O2-P1–C12-N5	–48.75(18)
C10A–C11A	1.448(11)	P1–O4–C10B	118.4(3)	O2–P1–C12–C20	76.37(17)
N5–C12	1.461(3)	P1–O4–C10A	127.2(3)	O3–P1–C12–N5	78.35(16)
N5 -C13	1.360(3)	O4–C10B–C11B	109.5(5)	O3–P1–C12–C20	–156.53(14)
S7–C13	1.766(2)	O4–C10A–C11A	110.9(6)	O4–P1–C12–N5	–176.02(14
S7–C14	1.747(2)	O2–P1–C12	112.37(10)	O4–P1–C12–C20	–50.90(17
N6–C13	1.295(3)	O3–P1–O4	100.22(9)	P1–O3–C8–C9	111.1(3)
N6–C19	1.392(3)	O3–P1–C12	106.91(10)	P1–O4–C10B–C11B	137.7(5)
C12–C20	1.512(3)	O4–P1–C12	104.39(10)	C13–N5–C12–P1	–157.40(17)
		P1–O4–C10A	127.2(3)	C13–N5–C12–C20	78.0(3)
		P1–C12–N5	106.67(15)	C12–N5–C13–S7	–163.39(17)
		N5–C12—C20	113.48(19)	C12–N5–C13–N6	17.6(3)
		S7–C13–N5	119.05(16)	C19–N6 -C13–S7	–1.1(3)
		N5–C13—N6	124.3(2)	C19–N6–C13–N5	178.0(2)
		S7–C14–C19	109.23(17)	C13–N6–C19 -C14	0.9(3)
		S7 -C14 -C15	128.95(19)	C13–N6–C19–C18	–179.4(2)
				P1–C12–C20–C21	106.7(2
				P1–C12–C20–C25	–74.0(3)

phosphite, and $InCl_3$ as a catalyst. The molecular structure of compound **4b**, showing the atom numbering scheme is presented in Fig. 1.

Crystallographic data and the refinement procedures are given in Table 5, and selected bond lengths, bond angles, and torsion angles of **4b** are listed in Table 6. As can be seen, there is good agreement between the crystallographic and theoretical data.

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