Synthesis, characterization, and application of [1-methylpyrrolidin-2-one-SO$_3$H]Cl as an efficient catalyst for the preparation of $\alpha$-aminophosphonate and docking simulation of ligand bond complexes of cyclin-dependent kinase 2

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ABSTRACT
A sulfonic acid functionalized ionic liquid was designed, synthesized and successfully used as a Brønsted acid catalyst for the one-pot synthesis of $\alpha$-aminophosphonates containing benzothiazole at room temperature under solvent-free conditions in excellent yields. The advantages of this method are the reusability of the catalyst, high conversion, short reaction time, and simple experimental procedure. A computer modeling and docking simulation of ligand bond complexes of cyclin-dependent kinase 2 are presented. The results indicate that diethyl ((4-(dimethylamino) phenyl) ((6-nitrobenzo[d]thiazol-2-yl) amino)methyl)phosphonate was found to be the best selective inhibitor of cyclin-dependent kinase 2.

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Acidic ionic liquid; solvent-free; reusable catalyst; $\alpha$-aminophosphonates; docking simulation

INTRODUCTION
$\alpha$-Aminophosphonates are considered to be the structural analogs of the corresponding esters of $\alpha$-amino acids and have been reported to exert several pharmacological activities such as their potential usage as anticancer drugs, enzymes inhibitors, haptons of catalytic antibodies, pharmacologic agents, antifungals, insecticides, plant growth regulators, and anti-HIV agents. Several multistep synthetic approaches for the synthesis of $\alpha$-aminophosphonates have been reported in the literature including alkylation of nuclophile Schiff bases, Hofmann rearrangement of substituted phosphonaocetic esters and conversion of 1-hydroxypophonates to the corresponding $\alpha$-aminophosphonates. An alternative synthesis of $\alpha$-aminophosphonates involves the nuclophilic addition of phosphites to imines. However, since many imines are hygroscopic and are not sufficiently stable for isolation, this method has certain limitations. The most simple and straightforward synthetic method for the synthesis of $\alpha$-aminophosphonates is the Kabachnik–Fields reaction which involves a one-pot three-component coupling of an aldehyde, an amine and a phosphite ester. In this regard, numerous protocols for the synthesis of these compounds have been developed using various Lewis and Brønsted acid catalysts such as sulfonic catalyst, molecular iodine, Xanthan sulfuric acid, DTP/SiO$_2$, phenylphosphonic acid, SnCl$_2$, SiO$_2$/AlCl$_3$, InCl$_3$, Mg(ClO$_4$)$_2$, M(OTf)$_3$, CeCl$_3$·7H$_2$O, FeCl$_3$, TiO$_2$, NaHSO$_4$/SiO$_2$, nano-Fe$_3$O$_4$, γ-Fe$_2$O$_3$@SiO$_2$-PA, IRMOF-3-nano, Fe/SWCNTs, ZrOCl$_2$·8H$_2$O, TiCl$_4$, VCl$_3$, and ethyl ammonium nitrate. In recent years, ionic liquids (ILs) have received great attention due to their high thermal stability, broad liquid range, biological activities, such as antiviral, antifungal, and anticancer activities, and as catalysts in organic synthesis and analytical chemistry. Among them, liquid Brønsted acids with useful characteristics of both solid acids and mineral liquid acids, have been designed to replace traditional mineral liquid acids, like sulfuric acid and hydrochloric acid, in chemical procedures.

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Recently, we have introduced a new category of ionic liquids that were successfully employed as catalysts to prepare α-haloketones\textsuperscript{35} aryl iodosides and azides,\textsuperscript{36} 2-aryl-1H-phenanthro[9,10-d]imidazoles,\textsuperscript{37} and α-aminophosphonates.\textsuperscript{38} An important principle of green chemistry is replacing the use of common and hazardous organic solvents needed for chemical transformations using solvent-free protocols.\textsuperscript{39} Solvent-free conditions offer several distinct advantages such as clean reaction profile, enhanced reaction rates, high selectivity and higher yield.

The cyclin-dependent kinases (CDKs), a family of proline-directed serine/threonine kinases, play a key role in the regulation of the cell cycle in eukaryotic cells.\textsuperscript{40} In addition to the positive regulatory role of cyclins and CAK, many negative regulatory proteins (CDK inhibitors, CKIs) have been detected. Since deregulation of cyclins and/or alteration or absence of CKIs has been associated with many cancers, there is strong interest in CDK inhibitors that could play an essential role in the discovery of a new family of antitumor agents. The development of computational methods as another tool for predicting the properties of chemical compounds has been subject of intensive studies.

Herein, we report the synthesis of sulfonic acid functionalized 1-methylpyrrolidin-2-one chloride [1-methylpyrrolidin-2-one-SO$_2$H]Cl (AIL) as a new Bronsted acidic ionic liquid from inexpensive and commercially available starting materials (Scheme 1) and its characterization using FT-IR, $^1$H NMR spectroscopy, thermal gravimetric analysis (TGA), and differential thermal gravimetric analysis (DTA). Furthermore, we report herein a highly efficient, cost effective, and much milder one-pot multicomponent protocol for the synthesis of α-aminophosphonate derivatives via the condensation of various aldehydes, 2-aminobenzothiazole derivatives and diethyl phosphite using a homogeneous and recyclable ionic liquid catalyst at room temperature under solvent-free conditions in excellent yields (Scheme 2). In this study, the Auto-Dock 4.0 package was employed for docking synthetic compounds to cyclin-dependent kinase 2 (PDB ID: 1 GIH).\textsuperscript{41} 2-Aminobenzothiazole derivatives were synthesized and their cyclin-dependent kinase 2 inhibitory activities together with the SAR (structure–activity relationships) studies were evaluated.

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\textbf{Scheme 1.} Synthesis of acidic ionic liquid (AIL).
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\textbf{Scheme 2.} Synthesis of α-aminophosphonates by AIL.
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**Results and discussion**

The structure of Bronsted acidic ionic liquid (AIL) was identified by studying its IR, $^1$H NMR, TG, and DTA spectra.

The IR spectrum of AIL showed a broad peak at 2750–3500 cm$^{-1}$ related to OH of the SO$_2$H group. The C=O function was observed at 1695 cm$^{-1}$. Moreover, two bands observed at 1088 and 1282 cm$^{-1}$ correspond to the vibrational modes of the N-SO$_2$ motive.

The $^1$H NMR spectrum of AIL showed one signal at $\delta = 13.10$ for the acidic hydrogen atom of SO$_2$H. The pH value for the AIL was determined using a 0.1 mol L$^{-1}$ solution of AIL, which was titrated with 0.114 mol L$^{-1}$ solution of NaOH. A solution of potassium hydrogen phthalate (KHP) was prepared at concentration 0.100 M and 25.00 mL of KHP solution was used to standardize the NaOH solution. The pH of the solution was measured using a calibrated glass electrode pH meter. The pH value of the AIL is 3.1.

 Thermal gravimetric (TG) and differential thermal gravimetric (DTA) analysis of AIL were studied between 25 and 600°C with a temperature increase rate of 10°C min$^{-1}$ in an argon atmosphere (Figure S2). The TG and DTA values of the catalyst showed two weight losses. The first was observed at 90°C and corresponds to H$_2$O loss, while the second weight loss was observed above 300°C. Therefore, AIL could be applied as catalysts below 300°C.

The application of this AIL was studied in a new one-pot method for the synthesis of α-aminophosphonates in the presence of a catalytic amount of the AIL under solvent-free conditions (Scheme 2).

In order to optimize the reaction conditions, the reaction of 4-dimethylaminobenzaldehyde (1 mmol), 2-aminobenzothiazole (1 mmol) and diethyl phosphite (1 mmol) was carried out using different quantities of AIL at room temperature. As can be seen in Table 1, maximum yield was

| Entry | Catalyst (mol%) | Temperature (°C) | Time (h) | Isolated yield (%) |
|-------|----------------|-----------------|----------|--------------------|
| 1     | –              | rt              | 24       | 30                 |
| 2     | 1              | rt              | 1        | 45                 |
| 3     | 2              | rt              | 1        | 70                 |
| 4     | 5              | rt              | 1        | 80                 |
| 5     | 10             | rt              | 1        | 96                 |
| 6     | 15             | rt              | 1        | 96                 |
| 7     | 20             | rt              | 1        | 90                 |

Reaction conditions: 2-aminobenzothiazole (1.0 mmol), 4-dimethyl aminobenzaldehyde (1.0 mmol), diethyl phosphate (1.0 mmol), and AIL as a catalyst.

\textbf{Table 1.} Optimization of the reaction conditions for the preparation of α-aminophosphonates 4a.
obtained with 10 mol% of the catalyst under solvent-free conditions (Table 1, entry 5). A low yield (30%) was obtained when the reaction was carried out in the absence of AIL at room temperature under solvent-free conditions for 24 h (Table 1, entry 1).

In order to examine the scope of this process, several aromatic aldehydes and 2-aminobenzothiazole derivatives were allowed to react under, the optimized conditions, and the results are shown in Table 2.

The synthesized compounds (4a-j) gave satisfactory elemental analyses and their molecular structures were confirmed by FTIR and ^1^H, ^1^3C and ^3^1P NMR spectroscopy. The IR spectra showed the expected absorption bands at 2985–3305 and 1225–1326 cm

-1, which were attributed to NH and P = O stretching vibrations, respectively. The ^1^H NMR spectra of 4a, recorded in CDCl

3 solution, exhibited the signal of CHP proton as a doublet at 5.36 ppm, and in the ^1^3C NMR spectrum the corresponding ^1^3C NMR signal appeared as a doublet at 55.6 ppm with \( J_{CP} = 155 \) Hz. The values are typical for proton and carbon atoms from a CHP fragment. The methyl protons from the ethoxy groups give rise to two triplets due to the nonequivalence of these groups. The POCH

3 proton signals appear as three multiplets at about 3.80–4.23 ppm. The NH resonance was observed as a broad signal, which in some derivatives overlapped with other signals.

A plausible mechanism is shown in (Figure S1). The mechanism involves the activation of the carbonyl group of the aldehyde by AIL followed by the nucleophilic addition of the amine to afford the imine by the removal of water. The activated imine further reacts with the dialkyl phosphonate leading to formation of the corresponding \( \alpha \)-aminophosphonates.

The recyclability and recovery of the AIL catalyst was investigated for the synthesis of \( \alpha \)-aminophosphonates by the one-pot three-component condensation of 2-aminobenzothiazole and 4-dimethylaminobenzaldehyde with diethyl phosphite as model substrates at room temperature under solvent-free conditions for 1 h. As shown in (Figure S3), the catalyst could be reused at least 4 times with only a slight reduction in activity.

### Molecular docking

**Materials and methods**

Inhibitor molecules were drawn with Chem Draw 8.0. The geometry was optimized through by Hartree-Fock method with Basic Set 3–21 G. The 1GIH molecular model (from the PDB) was used in the simulated docking studies. Input protein structures were prepared by adding hydrogen atoms and removing non-functional water molecules. The Auto-dock software version 1.5.6 was used for the molecular docking process. The Lamarckian Genetic Algorithm method was used for the global optimum binding position search. The Lamarckian Genetic Algorithm method was used for the global optimum binding position search. The Lamarckian Genetic Algorithm method was used for the global optimum binding position search. The Lamarckian Genetic Algorithm method was used for the global optimum binding position search. The Lamarckian Genetic Algorithm method was used for the global optimum binding position search. The Lamarckian Genetic Algorithm method was used for the global optimum binding position search. The Lamarckian Genetic Algorithm method was used for the global optimum binding position search. The Lamarckian Genetic Algorithm method was used for the global optimum binding position search. The Lamarckian Genetic Algorithm method was used for the global optimum binding position search.

**Table 2. \( \alpha \)-Aminophosphonate derivatives synthesized using AIL.**

| Entry | R\(^1\) | R\(^2\) | Time (h) | Yield (%) |
|-------|---------|---------|----------|-----------|
| 4a    | H       | 4-NMe\(_2\) | 1        | 96        |
| 4b    | H       | 4-NEt\(_2\) | 1.5      | 92        |
| 4c    | 6-CH\(_3\) | 4-NMe\(_2\) | 2        | 94        |
| 4d    | 6-CH\(_3\) | 4-NEt\(_2\) | 1.5      | 90        |
| 4e    | 6-OC\(_2\) | 4-NMe\(_2\) | 2        | 95        |
| 4f    | 6-OC\(_2\) | 4-NEt\(_2\) | 1        | 88        |
| 4g    | 6-OCH\(_3\) | 4-NMe\(_2\) | 1.5      | 90        |
| 4h    | 6-OCH\(_3\) | 4-NEt\(_2\) | 2        | 92        |
| 4i    | 6-NO\(_2\) | 4-NMe\(_2\) | 2.5      | 85        |
| 4j    | 6-NO\(_2\) | 4-NEt\(_2\) | 1        | 90        |
Bonding affinity of the designed molecular structures (inhibitors 1–10) was studied. Docked conformers of those were generated in Auto-Dock Tools (ADT) software. In docking process, flexible side chain of the active site pocket residues was allowed to be rotatable (THERE1 in cyclin-dependent kinase 2).

The phosphonic acid moiety is considered to bind to the affected protein more strongly than the corresponding carboxylic acid because of its diatomic character. Some polyphosphates containing R-aminomethylene fragments are now industrially used in enormous quantities as antiscaling and anticorrosive agents.\(^{48}\)

The analysis of the number of hydrogen bonds between inhibitors and CDK2 shows that the CDK2–triallyused enormous quantities as antiscaling and anticorrosive agents.\(^{48}\)

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Further inhibition experiments can confirm this prediction.

### Conclusions

In summary, we have designed and synthesized an AIL and have characterized it by FT-IR, \(^1\)H NMR, TGA, and DTA. We have successfully employed it as a catalyst for the one-pot synthesis of \(\alpha\)-aminophosphonates containing benzothiazole moiety in excellent yields. The application of this AIL is studied in a new one-pot method for the synthesis of \(\alpha\)-aminophosphonate derivatives under solvent-free conditions. The advantages offered by this protocol include reusability of the catalyst, high conversion, short reaction time, and simple experimental procedure. A computer modeling and docking simulation of ligand bond complexes of cyclin-dependent kinase 2 indicate that 4i has the most selective inhibitor of cyclin-dependent kinase 2, because it shows the lowest docked energy.

### Experimental

### Materials and instrumentation

All reagents were purchased from Merck and used without further purification. The melting points of the products were determined with an Electrothermal Type 9100 melting point apparatus. The Fourier transform Infrared (FT-IR) spectra were recorded with an Avatar 370 FT-IR Thermal Nicolet spectrometer. The mass spectra were recorded with a 5973 Network Mass Selective Detector. The \(^1\)H, \(^13\)C, and \(^31\)P NMR spectra were recorded with a Bruker DRX-400 spectrometer at 400, 100.65, and 165 MHz, respectively, using DMSO-\(d_6\) or CDCl\(_3\) as deuterated solvents. Chemical shifts are reported in ppm downfield from TMS as internal standard; coupling constants \(J\) are given in Hz.

### Synthesis of [1-methylpyrrolidin-2-one-SO\(_3\)H]Cl ionic liquid

A 100-mL round-bottom flask was charged with 1-methylpyrrolidin-2-one (10 mmol, 0.99 g) in dry CH\(_2\)Cl\(_2\) (50 mL), and then chlorosulfonic acid (10 mmol, 1.15 g) was dropped into the mixture under stirring for 30 min at room temperature. Afterwards the reaction mixture was stirred for 1 h and the CH\(_2\)Cl\(_2\) was decanted. The residue was washed with dry CH\(_2\)Cl\(_2\) (3 \times 20 mL) and dried under vacuum to give [1-methylpyrrolidin-2-one-SO\(_3\)H]Cl as a viscous colorless oil. IR (Nujol): \(\nu = 750, 880, 1060, 1173, 1494, 1695, 2550–3550\) cm\(^{-1}\); \(^1\)H NMR (DMSO-\(d_6\), TMS, 500 MHz): \(\delta = 1.83–1.89\) (m, 2H, CH\(_2\)), 2.17 (t, \(J = 4.8\) Hz, 2H, CH\(_2\)), 2.67 (s, 3H, NCH\(_3\)), 3.29 (t, \(J = 3.2\) Hz, 2H, CH\(_2\)), 13.10 (br, 1H, SO\(_3\)H). Elemental analysis for C\(_3\)H\(_9\)ClNO\(_3\)S: Calcd.: C, 27.85; H, 4.67; N, 6.50; S, 14.87; Found: C, 27.60; H, 4.65; N, 6.15; S, 14.10%.

### Preparation of \(\alpha\)-Aminophosphonates 4a–4j: General procedure

The corresponding aldehyde (1.0 mmol), 2-aminobenzothiazole (1.0 mmol), diethyl phosphate (1.0 mmol), and AIL (10 mol%) were mixed together and stirred at room temperature for appropriate time (Table 2). After the completion of the reaction as monitored by TLC, the mixture was washed with CH\(_2\)Cl\(_2\) (3 \times 3 mL). The combined extracts were filtered and the solvent was removed under reduced pressure to afford the residue.

### Diethyl ([Benz[d]thiazol-2-ylamino](4-(dimethylamino)phenyl)methyl)phosphonate (4a)

White solid; Yield: 96%; m.p.: 179–180\(^\circ\)C.\(^{49}\)

### Diethyl ([Benz[d]thiazol-2-ylamino](4-(diethylamino)phenyl)methyl)phosphonate (4b)

Yellow solid; Yield: 92%; m.p.: 190–192\(^\circ\)C. IR (\(v_{max}\) cm\(^{-1}\)): 3224, 1233 (P–O), 1205 (P–OEt); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta = 1.14\) (t, \(J = 7.2\) Hz, 6H, NCH\(_2\)CH\(_3\)), 1.17 (t, \(J = 7.2\) Hz, 3H, POCH\(_2\)CH\(_3\)), 1.29 (t, \(J = 7.6\) Hz, 3H, POCH\(_2\)CH\(_3\)), 3.32 (q, \(J = 6.8\) Hz, 4H, NCH\(_2\)CH\(_3\)), 3.77–3.84 (m, 1H, POCH\(_2\)CH\(_3\)), 3.99–4.05 (m, 1H, POCH\(_2\)CH\(_3\)), 5.29 (d, \(J_{PC} = 22.0\) Hz, 1H, CHP), 6.66 (d, \(J = 8.8\) Hz, 2H, arom-H), 6.75 (br, 1H, NH), 7.07 (t, \(J = 8.4\) Hz, 1H, arom-H), 7.28 (t, \(J = 8.4\) Hz, 1H, arom-H), 7.39 (dd, \(J = 7.2, 2.0\) Hz, 2H, arom-H). \(^13\)C NMR (CDCl\(_3\), 100 MHz): \(\delta = 12.6\) (NCH\(_2\)CH\(_3\)), 16.3 (d, \(J_{PC} = 5.2\) Hz, POCH\(_2\)CH\(_3\)), 16.4 (d, \(J_{PC} = 5.8\) Hz, POCH\(_2\)CH\(_3\)), 43.0 (NCH\(_2\)CH\(_3\)), 55.6 (d, \(J_{PC} = 154.3\) Hz, CHP), 63.3 (d, \(J_{PC} = 6.8\) Hz, POCH\(_2\)CH\(_3\)), 63.4 (d, \(J_{PC} = 6.8\) Hz, POCH\(_2\)CH\(_3\)), 113.2 (C1, C3), 118.7 (C22), 120.9 (C25), 121.1 (C23), 124.2 (C24), 128.5 (C5), 129.7 (C4, C6), 137.5 (C19), 149.4 (C2), 165.2 (C18), 166.1 (C21); \(^31\)P NMR (162.5 MHz, CDCl\(_3\)): \(\delta = 21.4\), MS (EI) \(m/z\): 447 [M\(^+\)]; Elemental analysis for C\(_{32}\)H\(_{39}\)N\(_3\)O\(_9\)PS: Calcd. C, 59.04; H, 6.54; N, 9.05; S, 6.58%.
Diethyl (4-(Dimethylamino)phenyl)((6-methoxybenzo[d]thiazol-2-yl)amino)methyl)phosphonate (4f)

Yellow solid; Yield: 88%; m.p.: 179–181°C. IR (νmax, cm⁻¹): 3231 (NH), 1224 (P=O), 1057 (P=OEt); ¹H NMR (CDCl₃, TMS, 400 MHz): δ = 1.12–1.16 (m, 9H, NCH₂CH₃, Ar-OCH₂CH₃), 1.16 (t, J = 7.6 Hz, 3H, POCH₂CH₃), 16.4 (d, Jₚₚ = 5.7 Hz, POCH₂CH₃), 42.3 (d, Jₚₚ = 5.7 Hz, POCH₂CH₃), 44.2 (NCH₂CH₃), 55.6 (d, Jₚₚ = 155.4 Hz, CHP), 63.2 (d, Jₚₚ = 7.1 Hz, POCH₂CH₃), 63.4 (d, Jₚₚ = 6.8 Hz, POCH₂CH₃), 64.1 (Ar-OCH₂CH₃), 106.0 (C25), 111.6 (C1, C3), 114.1 (C23), 119.6 (C22), 120.7 (C6, C4), 129.2 (d, Jₚₚ = 4.4 Hz, C5), 132.0 (C19), 146.2 (C18), 147.7 (C2), 154.5 (C24), 164.4 (d, Jₚₚ = 12.4 Hz, C21); ³¹P (CDCl₃, 162.5 MHz): δ = 22.4; MS (EI) m/z: 491 [M⁺]; Elemental analysis for C₃₂H₃₃N₅O₇PS: Calcld. C, 58.64; H, 6.97; N, 8.55; S, 6.52; Found: C, 59.24; H, 6.92; N, 8.35; S, 6.40%.

Diethyl (4-(Dimethylamino)phenyl)((6-methoxybenzo[d]thiazol-2-yl)amino)methyl)phosphonate (4g)

Light white solid; Yield: 90%; m.p.: 170–172°C. IR (νmax, cm⁻¹): 3225 (NH), 1225 (P=O), 1054 (P=OEt); ¹H NMR (CDCl₃, TMS, 400 MHz): δ = 1.21 (t, J = 6.8 Hz, 3H, POCH₂CH₃), 1.40 (t, J = 6.8 Hz, 3H, POCH₂CH₃), 2.93 (s, 6H, N(CH₃)₂), 3.75–3.82 (m, 1H, POCH₂CH₃), 3.96–4.05 (m, 1H, POCH₂CH₃), 3.81 (s, 3H, Ar-OCH₃), 3.96–4.04 (m, 1H, POCH₂CH₃), 4.12–4.24 (m, 2H, POCH₂CH₃), 5.35 (d, Jₚₚ = 21.6 Hz, 1H, CHP), 6.43 (d, J = 8.8 Hz, 2H, arom-H), 6.71 (d, J = 8.4 Hz, 1H, arom-H), 7.32 (s, 1H, arom-H), 7.43 (d, J = 8.4 Hz, 2H, arom-H), 7.46 (d, J = 7.02 Hz, 1H, arom-H); ¹³C NMR (CDCl₃, TMS, 100 MHz): δ = 14.9 (Ar-OCH₂CH₃), 16.3 (d, Jₚₚ = 5.5 Hz, POCH₂CH₃), 16.5 (d, Jₚₚ = 5.7 Hz, POCH₂CH₃), 40.4 (N(CH₃)₂), 55.5 (d, Jₚₚ = 155.2 Hz, CHP), 63.3 (d, Jₚₚ = 7.0 Hz, POCH₂CH₃), 63.4 (d, Jₚₚ = 6.8 Hz, POCH₂CH₃), 64.1 (Ar-OCH₂CH₃), 105.9 (C25), 112.3 (d, Jₚₚ = 1.1 Hz, C5), 114.0 (C1, C3), 119.5 (C23), 121.2 (C22), 129.0 (d, Jₚₚ = 6.0 Hz, C6, C4), 132.0 (C19), 146.2 (C18), 150.4 (C2), 154.4 (C24), 164.5 (d, Jₚₚ = 13.2 Hz, C21); ³¹P (CDCl₃, TMS, 162.5 MHz): δ = 21.5; MS (EI) m/z: 463 [M⁺]; Elemental analysis for C₃₂H₃₃N₅O₇PS: Calcld. C, 57.01; H, 6.52; N, 9.07; S, 6.92; Found: C, 56.80; H, 6.12; N, 8.49; S, 6.74%.
**Diethyl ((4-Diethylamino)phenyl)((6-nitrobenzo[d]thiazol-2-yl)amino)methylphosphonate (4i)**

Yellow solid; Yield: 85%; m.p.: 186–188°C. IR (ν_max, cm⁻¹): 3229 (NH), 1230 (P=O), 1054 (P=OEt); ¹H NMR (CDCl₃, TMS, 400 MHz): δ = 1.27 (t, J = 7.2 Hz, 3H, POCH₃CH₂), 1.40 (t, J = 7.2 Hz, 3H, POCH₃CH₂), 2.91 (s, 6H, N(CH₃)₂), 3.73–380 (m, 1H, POCH₂CH₃), 3.96–4.06 (m, 1H, POCH₂CH₃), 4.09–4.22 (m, 2H, POCH₂CH₃), 5.29 (d, J_H/N = 22.0 Hz, 1H, CH₃), 6.69 (d, J = 8.4 Hz, 2H, arom-H), 6.81 (d, J = 8.8 Hz, 1H, arom-H), 7.09 (d, J = 2.1 Hz, 1H, arom-H), 7.27 (s, 1H, arom-H), 7.42 (d, J = 8.4 Hz, 2H, arom-H); ¹³C NMR (CDCl₃, TMS, 100 MHz): δ = 16.5 (d, J_PC = 5.6 Hz, POCH₂CH₃), 16.4 (d, J_PC = 5.6 Hz, POCH₂CH₃), 40.6 (N(CH₃)₂), 55.7 (d, J_PC = 153.1 Hz, CH₃), 63.3 (d, J_PC = 6.9 Hz, POCH₂CH₃), 63.4 (d, J_PC = 6.9 Hz, POCH₂CH₃), 104.8 (C25), 113.5 (C1, C3), 115.3 (C23), 120.5 (C22), 123.1 (C23), 130.1 (d, J_PC = 6.2, C5), 133.1 (C6, C4), 145.3 (C19), 149.9 (d, J_PC = 11.1 Hz, C21), 155.6 (C2), 163.5 (C24); ³¹P (CDCl₃, 162.5 MHz): δ = 21.5; MS (EI) m/z: 464 [M⁺]; Elemental analysis for C₂₃H₂₃N₄O₄P: Calcld. C, 51.72; H, 5.43; N, 12.06; S, 6.90; Found: C, 51.42; H, 5.34; N, 11.75; S, 6.28%.

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