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## Phosphorus, Sulfur, and Silicon and the Related Elements

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### An Efficient Synthesis and Antibacterial Screening of Novel Oxazepine $\alpha$ -Aminophosphonates by Ultrasound Approach

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## AN EFFICIENT SYNTHESIS AND ANTIBACTERIAL SCREENING OF NOVEL OXAZEPINE $\alpha$ -AMINOPHOSPHONATES BY ULTRASOUND APPROACH

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*An efficient synthesis of novel  $\alpha$ -aminophosphonates by the reaction of quino[2,3-b][1,5]benzoxazepines with triethyl phosphite in the presence of the easily available, inexpensive, and nontoxic catalyst *p*-toluene sulphonic acid (*p*-TSA). This method affords the  $\alpha$ -aminophosphonates under the influence of ultrasound irradiation in solvent-free conditions, in short reaction times (4–6 min), high yields (80–90%), with improved purity. The synthesized  $\alpha$ -aminophosphonates show antibacterial activity against Gram-positive and Gram-negative bacteria.*

*Supplemental materials are available for this article. Go to the publisher's online edition of Phosphorus, Sulfur, and Silicon and the Related Elements to view the free supplemental file.*

**Keywords**  $\alpha$ -Aminophosphonates; *p*-TSA; quino[2,3-b][1,5]benzoxazepine; solvent-free; triethyl phosphite; ultrasound irradiation

## INTRODUCTION

Phosphorus chemistry ranges over a wide field of science including biochemistry and technology. In the new century, many phosphorus compounds will play a vital role in new high-tech areas such as life science, medical drugs, and nanometer technology.<sup>1</sup> Phosphonates functionalized with amino groups have attracted considerable attention since they are considered as structural analogues of the corresponding  $\alpha$ -amino acids, and their utilities as enzyme inhibitors, antibiotics, pharmacological agents, peptidomimetics, hapten design in antibody generation, and many other applications are well documented.<sup>2</sup> In addition, phosphonates show antibacterial activity with the quinoline nucleus.<sup>3</sup>

Quinoline ring systems represent a major class of heterocycles, as they occur in various natural products, especially in alkaloids.<sup>4</sup> They possess diverse biological and physiological activities such as antimalarial,<sup>5a</sup> anti-inflammatory,<sup>5b</sup> antitumor,<sup>5c</sup> DNA binding

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capacity,<sup>5d</sup> and antibacterial properties.<sup>5e</sup> Recently, quinoline has been employed in the study of bio-organic and bio-organometallic processes.<sup>5f</sup> Seven-membered heterocycles with two heteroatoms in the 1,4-position are known to possess diverse biological activities. In particular, derivatives of benzoxazepine exhibit a broad spectrum of biological properties such as neurotropic and psychotropic,<sup>6a</sup> anti-inflammatory,<sup>6b</sup> anticonvulsive,<sup>6c</sup> antagonistic properties against prostaglandin,<sup>6d</sup> high ceiling diuretics,<sup>6e</sup> and antidepressant activities.<sup>6f</sup> The metal complexes of quino[2,3-b][1,5]benzoxazepines show effective antibacterial and antifungal activities.<sup>7</sup> There are very few reports on the synthesis of quino[2,3-b][1,5]benzoxazepines.<sup>8</sup>

Generally,  $\alpha$ -aminophosphonates are prepared by the nucleophilic addition of phosphite to imine in the presence of a Brønsted acid<sup>9a</sup> or Lewis acids such as  $\text{ZnCl}_2$ ,<sup>9b</sup>  $\text{BF}_3 \cdot \text{Et}_2\text{O}$ ,<sup>9c</sup>  $\text{CdI}_2/\text{benzene}$ ,<sup>9d</sup> and  $\text{CdI}_2/\text{microwave}$ .<sup>9e</sup>  $\alpha$ -Aminophosphonates also have been synthesized by the one-pot reaction of phosphite with imines generated in situ from aldehydes and amines in organic solvents using  $\text{InCl}_3$ ,<sup>10a</sup>  $\text{ZrCl}_4$ ,<sup>10b</sup>  $\text{GaI}_3$ ,<sup>10c</sup>  $\text{BiCl}_3$ ,<sup>10d</sup> and  $\text{SbCl}_3/\text{Al}_2\text{O}_3$ .<sup>10e</sup> In addition, the solvent-free transformation of phosphite to  $\alpha$ -aminophosphonates could be accomplished in the presence of TFA,<sup>11a</sup>  $\text{LiClO}_4$ ,<sup>11b</sup> metal triflates,<sup>11c</sup> and  $\text{Na}_2\text{CaP}_2\text{O}_7$ .<sup>11d</sup> There is only one report for the synthesis of  $\alpha$ -aminophosphonates by ultrasound irradiation.<sup>12</sup>

In recent years, solvent-free organic syntheses have offered more advantages as compared to their homogeneous counterparts due to the growing concern for the influence of organic solvent on the environment as well as on the human body, and also concern for economical demands and simplicity in the processes.<sup>13</sup>

Ultrasound irradiation has been established as an important technique in synthetic organic chemistry. It has been used as an efficient heating source for organic reactions. Shorter reaction time is the main advantage of ultrasound-assisted reactions. Simple experimental procedure, very high yields, increased selectivities, and clean reaction of many ultrasound-induced organic transformations offer additional convenience in the field of synthetic organic chemistry.<sup>14</sup>

It is noted that *p*-toluene sulfonic acid (*p*-TSA) has been exploited as a catalyst in organic synthesis.<sup>15</sup> We have investigated the synthesis of  $\alpha$ -aminophosphonates in the presence of *p*-TSA as a catalyst. It was found that *p*-TSA is an effective promoter in the synthesis of  $\alpha$ -hydroxyphosphonates by the reaction of quino[2,3-b][1,5]benzoxazepine with triethyl phosphite.

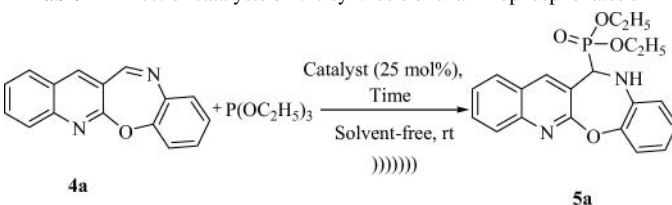
In continuation of our research devoted to the phosphorus chemistry<sup>3,16</sup> and our interest in the development of novel synthetic methodologies,<sup>17</sup> in this article we report a simple, efficient, and rapid method for the synthesis of novel oxazepine  $\alpha$ -aminophosphonates under ultrasonic irradiation.

## RESULTS AND DISCUSSION

Imines **3(a–j)** were prepared from substituted 2-chloroquinoline-3-carbaldehyde **1(a–j)** and 2-hydroxy aniline **2** in absolute ethanol in the presence of a catalytic amount of acetic acid. The product formed at room temperature in excellent yields (95–98%).

Quino[2,3-b][1,5]benzoxazepines **4(a–j)** were synthesized by the cyclization of imines **3(a–j)** under basic conditions ( $\text{DMF}$ ,  $\text{K}_2\text{CO}_3$ ) at  $60^\circ\text{C}$  in 98–100% yields and were confirmed by IR,  $^1\text{H}$  NMR, and mass spectroscopic data and elemental analysis.

The one-pot syntheses of quino[2,3-b][1,5]benzoxazepines **4(a–j)** were also carried out by in situ generation of imine from the condensation of 2-chloroquinolin-3-carbaldehyde

**Table I** Effect of catalysts on the synthesis of  $\alpha$ -aminophosphonates **5a**<sup>a</sup>


Entry	Catalyst	Time (min)	Yield (%) <sup>b</sup>
1	—	90	10
2	FeCl <sub>3</sub>	60	20
3	CaCl <sub>2</sub>	60	35
4	NiCl <sub>2</sub>	60	40
5	CdCl <sub>2</sub>	30	55
6	HgCl <sub>2</sub>	20	60
7	<i>p</i> -TSA	5	90

<sup>a</sup>**4a** (2.5 mmol) was treated with triethyl phosphite (5 mmol) under solvent-free condition.<sup>b</sup>Isolated yields based upon starting aldehyde.

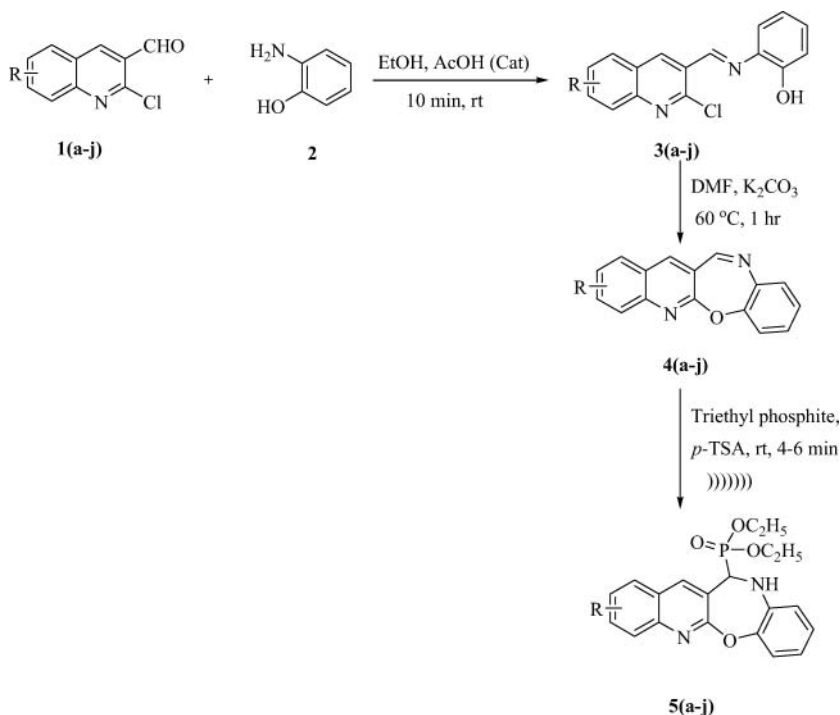
and 2-hydroxy aniline followed by the cyclization under basic conditions. But the cyclization of pure imine **3(a–j)** afforded quino[2,3-*b*][1,5]benzoxazepine in higher yields (overall yield 97–99%) than that arising from the one-pot procedure (86–90%).

In a search for an efficient catalyst and the best experimental reaction conditions, the reaction of quino[2,3-*b*][1,5]benzoxazepines **4a** with triethyl phosphite under the influence of ultrasonic irradiation has been considered as a standard model reaction. All the reactions were carried out at room temperature under solvent-free conditions. When the reaction was carried out in the absence of catalyst, the product formed in very low yield (10%) after prolonged reaction time (Table I, entry 1). In the next step, we have screened different catalysts for the model reaction, such as FeCl<sub>3</sub>, CaCl<sub>2</sub>, CdCl<sub>2</sub>, HgCl<sub>2</sub>, and *p*-TSA. By the use of FeCl<sub>3</sub>, CaCl<sub>2</sub>, and NiCl<sub>2</sub>, as catalysts the product formed in poor yields 20–40% (Table I, entries 2–4), whereas when using CdCl<sub>2</sub> and HgCl<sub>2</sub>, the product was formed in moderate yields 55–60% (Table I, entries 5 and 6). The best result was obtained using 25 mol% of *p*-TSA at room temperature under solvent-free conditions. The product was obtained within 5 min in 90% yield (Table I, entry 7).

To determine the appropriate concentration of the catalyst *p*-TSA, we investigated the model reaction at different concentrations of catalyst: 5, 10, 15, 20, and 25 mol%. The product formed in 72, 77, 85, 90, and 90% yields respectively. This indicates that 20 mol% of *p*-TSA is sufficient for the best result by considering the reaction time and yield of product (Table II, entry 4).

Various substituted 2-chloro-quinoline-carbaldehydes having different substituents such as CH<sub>3</sub>, OCH<sub>3</sub>, OC<sub>2</sub>H<sub>5</sub>, F, and Cl were used for the synthesis of oxazepine  $\alpha$ -aminophosphonates. The reaction was compatible with all the substituents, and no competitive nucleophilic methyl/ethyl ether cleavage was observed for the substrate having OCH<sub>3</sub> or OC<sub>2</sub>H<sub>5</sub> groups.

With these optimized reaction conditions, we have synthesized  $\alpha$ -aminophosphonates (**5a–j**) by reacting quino[2,3-*b*][1,5]benzoxazepines (**4a–j**) with triethyl phosphite in the presence of *p*-TSA (Scheme 1). All the reactions were carried out under the influence of



Scheme 1

ultrasonic irradiation in solvent-free conditions at room temperature. The products formed within 4–6 min in 80–90% yield (Table III). The identities of the products were confirmed by IR,  $^1\text{H}$  NMR, mass spectroscopic data, and elemental analysis.

We have also carried out the identical reactions by conventional methods. In comparison with ultrasonic method, the product was obtained in longer reaction time and lower yields (Table III).

All novel synthesized  $\alpha$ -aminophosphonates were screened for antibacterial activities against Gram-positive *Bacillus subtilis* and *Staphylococci aureus* and Gram-negative *Escherichia coli* and *Salmonella aboney* bacteria. The compounds tested were compared against the standard (streptomycin) by measuring the diameter of the zone of inhibition. Almost all the compounds tested exhibited moderate activity against Gram-positive

**Table II** Effect of concentrations of *p*-TSA for synthesis of  $\alpha$ -aminophosphonates<sup>a</sup> **5**

Entry	<i>p</i> -TSA (mol%)	Time (min)	Yield (%) <sup>b</sup>
1	5	15	72
2	10	12	77
3	15	10	85
4	20	5	90
5	25	5	90

<sup>a</sup>**4a** (2.5 mmol) was treated with triethyl phosphite (5 mmol) under solvent-free conditions.

<sup>b</sup>Isolated yields based upon starting aldehyde.

**Table III** Synthesis of oxazepine  $\alpha$ -aminophosphonates<sup>a</sup> (**5a–j**)

Entry	R <sup>b</sup>	Conventional Method		Ultrasonic Method		Mp (°C)
		Time (min)	Yield (%) <sup>c</sup>	Time (min)	Yield (%) <sup>c</sup>	
<b>5a</b>	H	30	80	5	90	192–194
<b>5b</b>	6-CH <sub>3</sub>	30	76	6	84	153–155
<b>5c</b>	7-CH <sub>3</sub>	30	73	6	81	113–115
<b>5d</b>	8-CH <sub>3</sub>	25	73	5	80	133–135
<b>5e</b>	6-OCH <sub>3</sub>	25	75	6	89	119–121
<b>5f</b>	7-OCH <sub>3</sub>	30	74	5	85	120–122
<b>5g</b>	6-OC <sub>2</sub> H <sub>5</sub>	25	72	4	82	150–152
<b>5h</b>	6-F	25	76	4	85	180–182
<b>5i</b>	7-F	30	72	5	86	134–136
<b>5j</b>	6-Cl	25	76	4	88	144–146

<sup>a</sup>**4a–j** (2.5 mmol) treated with triethyl phosphite (5 mmol) and *p*-TSA (20 mol%) under solvent-free condition.

<sup>b</sup>The numbering is considered upon starting quinoline aldehyde.

<sup>c</sup>Isolated yields based upon **4a–j**.

bacteria, and a few compounds were found to be active against the Gram-negative bacteria used in this study (see Table IV in the Supplemental Materials online).

## ANTIBACTERIAL ACTIVITY

All the compounds were screened for antibacterial activities against Gram-positive *Bacillus subtilis* and *Staphylococci aureus* (ATCC 6538) and Gram-negative *Escherichia coli* (ATCC 8739) and *Salmonella aboney* (NCTC 6017) bacteria using streptomycin (strept.) as a standard. Petri dishes and necessary glassware were sterilized in a hot air oven (190°C, 45 min). Details are provided in the Supplemental Materials (see Supplemental Materials online).

## CONCLUSION

In conclusion, *p*-TSA is an efficient catalyst for the synthesis of novel oxazepine  $\alpha$ -aminophosphonates by the reaction of quino[2,3-*b*][1,5]benzoxazepines (**4a–j**) with triethyl phosphite using an ultrasonic approach. The synthesized  $\alpha$ -aminophosphonates show moderate antibacterial activity against Gram-positive and Gram-negative bacteria. The remarkable advantages offered by this method are solvent-free reaction condition, short reaction time, ease of product isolation, and high yields.

## EXPERIMENTAL

All melting points were determined in open capillaries in a paraffin bath and are uncorrected. A Bandelin Sonorex (35 kHz) ultrasonic bath was used for ultrasonic irradiation. <sup>1</sup>H NMR spectra were recorded on Mercury Plus Varian in DMSO or CDCl<sub>3</sub> at 400 MHz using TMS as an internal standard. IR spectra were recorded on a Perkin-Elmer FTIR using KBr discs. Mass spectra were recorded on Micromass Quattro II using electrospray ionization technique, showing (*m*+1) peak as a base peak. The elemental analysis was

carried out on Flash EA-1112, 50/60 Hz, 1400-VA CHNS analyzer. The progress of the reactions was monitored by TLC.

### Typical Experimental Procedure: 2-((2-Chloroquinolin-3-yl)methyleneamino) phenol (3a-j)

To the stirred solution of 2-chloroquinoline-3-carbaldehyde (2.5 mmol) in absolute ethanol (10 mL), 2-hydroxy aniline (3 mmol) and 4 to 5 drops of acetic acid were added at room temperature. The progress of the reaction was monitored using TLC in solvent system hexane:ethyl acetate (8:2). After completion of the reaction, it was poured onto crushed ice and separated out as a yellow colored solid product.

### Quinolino[3,2-b]benzodiazepine (4a-j)

A mixture of 2-((2-chloroquinolin-3-yl)methyleneamino) phenol (2.5 mmol) and  $K_2CO_3$  (3 mmol) in DMF (10 mL) was stirred at 60°C in an oil bath for 1 h. The progress of the reaction was monitored using TLC in solvent system hexane:ethyl acetate (8:2). After the completion of the reaction, it was poured onto crushed ice and separated out as a solid product. The crude product was recrystallized from ethyl acetate.

### One-Pot Syntheses of Quinolino[3,2-b]benzodiazepine (4a-j)

A solution of 2-chloroquinoline-3-carbaldehyde (2.5 mmol), 2-hydroxyaniline (3 mmol) in absolute ethanol (10 mL), and 4 to 5 drops of acetic acid was stirred at room temperature for 10 min. The solvent was distilled out on rota-evaporator under reduced pressure. To the yellow homogeneous residue DMF (10 mL) and  $K_2CO_3$  (5 mmol), the content was added and stirred at 60°C in an oil bath for 2 h. After completion of the reaction, as monitored by TLC, the reaction mass was poured onto crushed ice and the solid product was separated out. The crude product was recrystallized from ethyl acetate.

### $\alpha$ -Aminophosphonates (5a-j)

**Conventional method.** A mixture of quino[2,3-b][1,5]benzoxazepine (2.5 mmol), triethyl phosphite (5 mmol), and *p*-TSA (20 mol%) was stirred at room temperature for 25–30 min (Table III). The progress of the reaction was monitored using TLC and using hexane:ethyl acetate (7:3). After completion of the reaction, the reaction mass was poured onto crushed ice. The yellow colored solid was separated out, and the crude material was recrystallized from ethanol.

**Ultrasonic irradiation.** A mixture of quino[2,3-b][1,5]benzoxazepine (2.5 mmol), triethyl phosphite (5 mmol), and *p*-TSA (20 mol%) was irradiated under ultrasonic waves at room temperature for 4–6 min (Table III). After completion of the reaction, as monitored by TLC, the reaction mass was poured onto crushed ice. The yellow colored solid was separated out, and the crude material was recrystallized from ethanol.

### Spectral Data of Principal Compounds

**4a:** IR (KBr,  $cm^{-1}$ ): 1615 (C=C), 1207 (C–O–C).  $^1H$  NMR ( $CDCl_3$ , 400 MHz,  $\delta$  ppm): 8.56 (s, 1H, Ar–CH), 8.22 (s, 1H, Ar–CH), 7.99 (d, 1H,  $J = 8.52$  Hz, Ar–CH),

7.84 (d, 1H,  $J = 8.12$  Hz, Ar-CH), 7.75 (td, 1H,  $J = 7.04, 1.4$  Hz, Ar-CH), 7.53 (td, 1H,  $J = 6.04, 1$  Hz, Ar-CH), 7.43 (dd, 2H,  $J = 6.32, 1.6$  Hz, Ar-CH), 7.28 (m, 2H, Ar-CH). ES-MS:  $m/z$  247. Elemental analysis:  $C_{16}H_{10}N_2O$  Calc.: C: 78.03%, H: 4.09%, N: 11.38%; Found: C: 78.08%, H: 4.14%, N: 11.43%.

**5:** IR (KBr,  $cm^{-1}$ ): 3280 (N-H), 1615 (C=C), 1248 (P=O), 1040 (P-O-C).  $^1H$  NMR ( $CDCl_3$ , 400 MHz,  $\delta$  ppm): 8.20 (d, 1H,  $J = 1.92$  Hz, Ar-CH), 7.98 (d, 1H,  $J = 8.44$  Hz, Ar-CH), 7.77 (d, 1H,  $J = 8.08$  Hz, Ar-CH), 7.70 (t, 1H,  $J = 7.28$  Hz, Ar-CH), 7.48 (td, 1H,  $J = 7.08, 0.92$  Hz, Ar-CH), 7.39 (dd, 1H,  $J = 6.6, 1.4$  Hz, Ar-CH), 6.98 (td, 1H,  $J = 6.16, 1.4$  Hz, Ar-CH), 6.87 (m, 2H, Ar-CH), 5.0 (dd, 1H,  $J = 13.56, 5.6$  Hz, P-CH), 4.5 (d, 1H,  $J = 5.6$  Hz, NH), 4.0 (m, 3H, O-CH<sub>2</sub>), 3.8 (m, 1H, O-CH), 1.2 (t, 6H,  $J = 5.72$  Hz, CH<sub>3</sub>). ES-MS:  $m/z$  385. Elemental analysis:  $C_{20}H_{21}N_2O_4P$  Calc.: C: 62.50%, H: 5.51%, N: 7.29%; Found: C: 63.00%, H: 5.93%, N: 7.36%.

**5d:** IR (KBr,  $cm^{-1}$ ): 3270 (N-H), 1609 (C=C), 1251 (P=O), 1020 (P-O-C).  $^1H$  NMR ( $DMSO-d_6$ , 400 MHz,  $\delta$  ppm): 8.42 (s, 1H, Ar-CH), 7.74 (d, 1H,  $J = 8$  Hz, Ar-CH), 7.58 (d, 1H,  $J = 7.2$  Hz, Ar-CH), 7.42 (t, 1H,  $J = 8.0, 7.2$  Hz, Ar-CH), 7.12 (d, 1H,  $J = 8.4$  Hz, Ar-CH), 6.85 (m, 2H, Ar-CH), 6.66 (m, 2H, Ar-CH), 5.0 (dd, 1H,  $J = 13.6, 6.4$  Hz, P-CH), 3.90 (m, 3H, O-CH<sub>2</sub>), 3.80 (m, 1H, O-CH), 2.62 (s, 3H, Ar-CH<sub>3</sub>), 1.07 (t, 6H,  $J = 7.2$  Hz, CH<sub>3</sub>). ES-MS:  $m/z$  399. Elemental analysis:  $C_{21}H_{23}N_2O_4P$  Calc.: C: 63.31%, H: 5.82%, N: 7.03%; Found: C: 63.77%, H: 5.89%, N: 7.06%.

**5e:** IR (KBr,  $cm^{-1}$ ): 3273 (N-H), 1610 (C=C), 1249 (P=O), 1020 (P-O-C).  $^1H$  NMR ( $DMSO-d_6$ , 400 MHz,  $\delta$  ppm): 8.33 (s, 1H, Ar-CH), 7.76 (d, 1H,  $J = 8.8$  Hz, Ar-CH), 7.38 (d, 1H,  $J = 8.4$  Hz, Ar-CH), 7.30 (s, 1H, Ar-CH), 7.07 (d, 1H,  $J = 6.4$  Hz, Ar-CH), 6.80 (m, 2H, Ar-CH), 6.63 (m, 2H, Ar-CH), 4.9 (dd, 1H,  $J = 12.4, 5.2$  Hz, P-CH), 3.94 (m, 3H, O-CH<sub>2</sub>), 3.90 (m, 1H, O-CH), 3.80 (s, 3H, Ar-OCH<sub>3</sub>), 1.10 (t, 6H,  $J = 7.2$  Hz, CH<sub>3</sub>). ES-MS:  $m/z$  415. Elemental analysis:  $C_{21}H_{23}N_2O_5P$  Calc.: C: 60.87%, H: 5.59%, N: 6.76%; Found: C: 60.95%, H: 5.64%, N: 6.81%.

**(5g)** IR (KBr,  $cm^{-1}$ ): 3275 (N-H), 1606 (C=C), 1273 (P=O), 1041 (P-O-C).  $^1H$  NMR ( $DMSO-d_6$ , 400 MHz,  $\delta$  ppm): 8.31 (d, 1H,  $J = 1.2$  Hz, Ar-CH), 7.75 (d, 1H,  $J = 9.2$  Hz, Ar-CH), 7.35 (dd, 1H,  $J = 6.8, 2.4$  Hz, Ar-CH), 7.29 (d, 1H,  $J = 2.4$  Hz, Ar-CH), 7.07 (d, 1H,  $J = 8.0$  Hz, Ar-CH), 6.86 (t, 1H,  $J = 8.0, 7.2$  Hz, Ar-CH), 6.79 (d, 1H,  $J = 6.8$  Hz, Ar-CH), 6.62 (m, 2H, Ar-CH), 4.94 (dd, 1H,  $J = 12.4, 6.4$  Hz, P-CH), 4.13 (qua, 2H,  $J = 6.8$  Hz, O-CH<sub>2</sub>), 3.94 (m, 3H, O-CH<sub>2</sub>), 3.84 (m, 1H, O-CH), 1.37 (t, 3H,  $J = 6.8$  Hz, CH<sub>3</sub>), 1.09 (t, 6H,  $J = 7.2$  Hz, CH<sub>3</sub>). ES-MS:  $m/z$  429. Elemental analysis:  $C_{22}H_{25}N_2O_5P$  Calc.: C: 61.68%, H: 5.88%, N: 6.54%; Found: C: 61.72%, H: 5.94%, N: 6.60%.

**5j:** IR (KBr,  $cm^{-1}$ ): 3278 (N-H), 1607 (C=C), 1273 (P=O), 1045 (P-O-C).  $^1H$  NMR ( $DMSO-d_6$ , 400 MHz,  $\delta$  ppm): 8.43 (s, 1H, Ar-CH), 8.06 (d, 1H,  $J = 1.2$  Hz, Ar-CH), 7.87 (d, 1H,  $J = 8.8$  Hz, Ar-CH), 7.73 (dd, 1H,  $J = 7.2, 1.6$  Hz, Ar-CH), 7.09 (d, 1H,  $J = 8.0$  Hz, Ar-CH), 6.86 (m, 2H, Ar-CH), 6.66 (m, 2H, Ar-CH), 5.0 (dd, 1H,  $J = 13.6, 6.4$  Hz, 5P-CH), 3.94 (m, 3H, O-CH<sub>2</sub>), 3.82 (m, 1H, O-CH), 1.10 (t, 6H,  $J = 7.2$  Hz, CH<sub>3</sub>). ES-MS:  $m/z$  419. Elemental analysis:  $C_{20}H_{20}N_2O_4ClP$  Calc.: C: 57.36%, H: 4.81%, N: 6.69%; Found: C: 57.39%, H: 4.87%, N: 6.74%.

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