

## Alkyl/Aryl Di[3-(4-substitutedphenyl)-2-Thioxo-3,4-Dihydro- 2H-1,3,2λ<sup>5</sup>-Benzoxazaphosphinin-2-yl] Phosphates의 합성 및 항균활성시험

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## Synthesis, Antimicrobial Activity of Alkyl/Aryl Di[3-(4-substitutedphenyl)-2-Thioxo- 3,4-Dihydro-2H-1,3,2λ<sup>5</sup>-Benzoxazaphosphinin-2-yl] Phosphates

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## INTRODUCTION

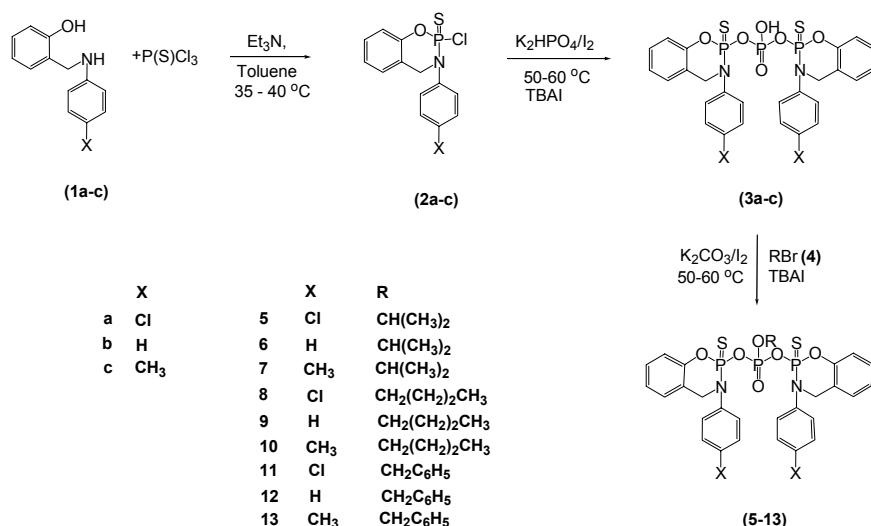
Trisphosphates are chiefly used as additives in a variety of industrial products, such as flame retardants, elastomers, fiberglass resins, surface coatings, sealants and rigid foams.<sup>1,2</sup> Synthesis of high quality flame retardants with low flammability and melt dripping limits is an urgent need now-a-days.<sup>3,4</sup> Phosphorus based fire retardants are known to act in both gas and condensed phases and also concurrently in both phases.<sup>5,6</sup> Phosphatidylinositol 3,4,5-triphosphate is attracting much attention due to its several biological roles<sup>7</sup> in signal transduction,<sup>8</sup> non-capacitative calcium influx,<sup>9</sup> cell regulation etc.<sup>10</sup> Phosphoric acid derivatives play a major role in driving some metabolic processes by energy release that accompanies the cleavage of a phosphate group.<sup>11</sup> Herein, we introduced I<sub>2</sub> as catalyst in addition to TBAI and synthesized triphosphate esters in less time with high yields.

## RESULTS AND DISCUSSION

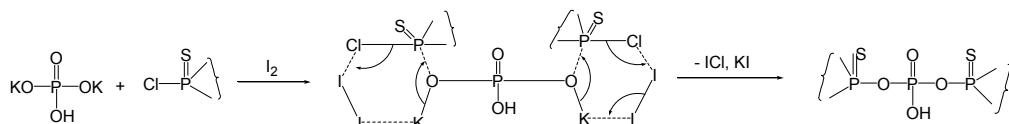
Cyclocondensation of 2-[(4-substituted anilino)methyl] phenol (**1**) with thiophosphoryl chloride in dry toluene in the presence of triethylamine at 10 - 40 °C afforded 2-chloro-3-(4-substitutedphenyl)-3,4-dihydro-2H-1,3,2λ<sup>5</sup>-benzoxa-

zaphosphinin-2-thione (**2**). Reaction of **2** with dipotassium salt of phosphoric acid/I<sub>2</sub> and TBAI<sup>12,13</sup> in dry toluene at 50 - 60 °C gave di[3-(4-substituted-phenyl)-2-thioxo-3,4-dihydro-2H-1,3,2λ<sup>5</sup>-benzoxazaphos-phinin-2-yl]hydrogenphosphate (**3**). Further, reaction of **3** with alkyl/aryl halide (**4**) in the presence of K<sub>2</sub>CO<sub>3</sub>/I<sub>2</sub><sup>14,15</sup> at 50 - 60 °C yielded the title compounds **5-13** (Scheme 1).

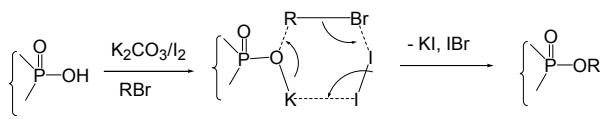
O-phosphorylation of K<sub>2</sub>HPO<sub>4</sub> with cyclic phosphoromonochlorides **2a-c** were found to occur selectively at the two '-OK' groups of K<sub>2</sub>HPO<sub>4</sub> when the reaction was carried out initially at 0 °C and later at 50 - 60 °C in a mixture of toluene:hexane (3:1) in the presence of catalytic amount of TBAI and I<sub>2</sub>. TBAI/I<sub>2</sub> were found to be essential for the completion of the reaction at a faster rate and to form the products **3a-c** in relatively pure state and in high yield. Further O-alkyl/arylation of the free -OH present in **3a-c** was effective reaction with K<sub>2</sub>CO<sub>3</sub> and I<sub>2</sub> followed by alkyl/aryl bromides was in toluene. Basically, I<sub>2</sub> weakens P-Cl and C-Br bonds and helps formation of P-O and C-O bonds respectively (Scheme 2, 3). The merit of the reaction is that it provides scope even for the preparation of *P*-alkyl/arylphosphoric acid bis-esters through the manipulation of the free -OH group by appropriate methodology. Thus, a variety of divergent ligands at P in trisphosphates could be synthesized by this



### Scheme 1



**Scheme 2**



*Scheme 3*

simple procedure. All compounds were purified by re-crystallization from acetone and were characterized by elemental, IR,  $^1\text{H}$ ,  $^{31}\text{P}$  and partly by mass spectral analysis.

Compounds **3a-c**, **5-13** exhibited characteristic IR absorption bands in the regions 1210-1276, 753-775, 1178-1189, 1095-1108, and 935-973 for P=O,<sup>4,16,17</sup> P=S,<sup>4</sup> P(V)-OH,<sup>4</sup> P-O and O-C of P-O-C(<sub>Ar</sub>)<sup>4,18,19</sup> respectively. <sup>1</sup>H NMR spectra of **3a-c**, **5-13** showed multiplets in the range  $\delta$  6.74-7.68 for aromatic protons. Methylene protons in the six-membered chair-like conformation of benzoxazaphosphinine system resonated as two doublets of doublets or multiplets at  $\delta$  4.95-4.90, 4.63-4.46 indicating their non equivalence coupling with phosphorus.<sup>4,20</sup> The other aliphatic protons gave signals in the expected region. <sup>13</sup>C NMR chemical shifts are in good agreement with the assigned structures.<sup>4,21</sup> The <sup>31</sup>P NMR chemical shifts appeared in the range of  $\delta$  58.93-52.54 for P <sub>$\alpha$</sub>  and P <sub>$\gamma$</sub>  and 51.67 to 43.24 for P <sub>$\beta$</sub> . The above data suggest that

the two benzoxazaphosphonine rings are present in the same chemical and magnetic environment.

## ANTIMICROBIAL ACTIVITY

Compounds **3a-c**, **5-13** were screened for their antibacterial activity<sup>22</sup> against gram-positive bacteria such as *staphylococcus aureus*, and gram-negative bacteria such as *Klebsiella Pneumoniae* by the disc-diffusion method in nutrient agar medium at two different concentrations (200, 400 ppm) in DMF (*Table 1*). The solutions were added to each filter disc, and the plates were incubated at 35 °C and examined for zone of bacterial inhibition around each disc after 24 h. Results were compared with the activity of the standard antibiotic penicillin. Antifungal activity was also evaluated against *pellicularia solamnicolor* and *Macrophomina Phaseolina* at two different concentrations<sup>23</sup> (200, 400) using Griseofulvin as reference compound. Fungal cultures were grown on potato dextrose agar at 25 °C and spore suspension was adjusted to 10<sup>5</sup> spore/mL. Compounds **5** and **11** exhibited high antimicrobial and antifungal activity when compared with that of reference compounds.

**Table 1.** Antibacterial and antifungal activity of **3a-c, 5-13**.

Compound	Zone of inhibition							
	Staphylococcus Aureus		Klebsiella Pneumoniae		Pellicularia solamnicolor		Macrophomina Phaseolina	
	200 <sup>a</sup>	400 <sup>a</sup>		200 <sup>a</sup>	400 <sup>a</sup>		200 <sup>a</sup>	400 <sup>a</sup>
3a	17	38	20	43	18	45	23	43
3b	12	35	16	37	15	40	18	40
3c	15	40	18	39	13	38	19	39
5	20	39	22	40	20	41	22	38
6	14	36	20	34	16	39	18	40
7	18	32	21	36	19	37	18	41
8	18	35	22	43	21	46	25	38
9	15	32	21	39	20	39	20	37
10	14	31	19	40	17	37	17	36
11	21	37	19	45	20	43	19	45
12	16	33	16	36	18	40	17	34
13	18	34	17	38	19	39	21	35
penicillin	22	41	24	46				
Griseofulvin					22	44	24	46

<sup>a</sup>Concentrations in ppm.

## EXPERIMENTAL SECTION

Melting points were determined in open capillary tubes on a Mel-Temp apparatus. IR spectra were recorded on perkin elmer 1000 units. The <sup>1</sup>H, <sup>13</sup>C and <sup>31</sup>P NMR spectra were recorded Bruker AMX 400 NMR spectrometers operating at 400 MHz (<sup>1</sup>H), 100.61 MHz (<sup>13</sup>C) and 121.9 MHz (<sup>31</sup>P). Mass spectra were recorded by Fast atom bombardment, Liquid Chromatograph and De Ionized mass spectrometer. All compounds are dissolved in CDCl<sub>3</sub>, DMSO-d<sub>6</sub>, chemical shifts are referenced to TMS (<sup>1</sup>H, <sup>13</sup>C) and 85% H<sub>3</sub>PO<sub>3</sub> (<sup>31</sup>P). Micro analytical data were obtained from Central Drug Research Institute, Lucknow, India.

### General procedure for the Synthesis : (I) Di[3-(4-substitutedphenyl)-2-thioxo-3,4-dihydro-2H-1,3,2λ<sup>5</sup>-benzoxaza-phosphinin-2-yl] hydrogenphosphate (3a-c).

A solution of thiophosphoryl chloride (4.5 mmol) in 10 mL of dry toluene was added drop wise to a stirred solution of [2-(4-chlorophenyl amino) methyl phenol (**1c**) (4 mmol) in 40 mL of dry toluene and triethylamine (8.6 mmol) at 0 °C for a period of 20 min. Later, the temperature was increased to 55 - 60 °C. The progress of the reaction was monitored by TLC analysis. Triethylamine hydrochloride was filtered off. The filtrate was cooled to 0 °C and K<sub>2</sub>HPO<sub>4</sub> (2 mmol), dry hexane (10 mL) and a catalytic amount of I<sub>2</sub> and TBAI were added. The reaction mixture was allowed to warm up to room temperature and stirred for 20 min. It was then stirred for

10 - 12 hrs at 55 - 60 °C. By TLC analysis, it was observed that reaction was completed. The KCl formed in the reaction was filtered off and the filtrate was concentrated under reduced pressure. The residue obtained was washed with water and recrystallized from acetone to yield the desired pure hydrogen phosphate (**3a**). Compounds 3b and 3c were prepared using the same above procedure.

**Di[3-(4-chlorophenyl-2-thioxo-3,4-dihydro-2H-1,3,2λ<sup>5</sup>-benzoxazaphosphinin-2-yl) hydrogen phosphate (3a):** Pale yellow color crystals, mp 81 - 83 °C; yield: 94%; <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 7.07-7.38 (12H, m, Ar-H), 6.86 (4H, d, J = 6.4 Hz, Ar-H), 4.93-4.88 (2H, m, -<sup>4</sup>H<sub>b</sub>), 4.58-4.49 (2H, m, -<sup>4</sup>H<sub>a</sub>), 1.50 (1H, s, β-OH); <sup>31</sup>P NMR (121 MHz, DMSO-d<sub>6</sub>): δ 57.32 (P<sub>α</sub> and P<sub>γ</sub>), 50.17 (P<sub>β</sub>); IR (KBr): v 1210 (P=O), 767 (P=S), 1097(P (V)-OH), 938, 1180 cm<sup>-1</sup> (P-O-C<sub>aromatic</sub>); FAB MS m/z (%): 687 (16) [MH<sup>+</sup>+2], 685 (23) [MH<sup>+</sup>], 641 (40), 639 (62), 613 (38), 581 (100), 560 (42), 518 (57), 462 (80), 443 (51), 396 (18), 360 (26), 321 (23), 311 (38), 277 (35), 240 (19); Anal(%). Calcd. for C<sub>26</sub>H<sub>21</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>6</sub>P<sub>3</sub>S<sub>2</sub>: C, 45.56; H, 3.09. Found: C, 45.52; H, 3.11.

**Di(3-phenyl-2-thioxo-3,4-dihydro-2H-1,3,2λ<sup>5</sup>-benzoxaza-phosphinin-2-yl)hydrogen phosphate (3b):** Colorless crystals, mp 98 - 100 °C; yield: 90%; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.11-7.42 (18H, m, Ar-H), 4.90-4.86 (2H, m, -<sup>4</sup>H<sub>b</sub>), 4.63-4.52 (2H, m, -<sup>4</sup>H<sub>a</sub>), 1.62 (1H, s, β-OH); <sup>31</sup>P NMR (121 MHz, CDCl<sub>3</sub>): δ 56.6 (P<sub>α</sub> and P<sub>γ</sub>), 47.2 (P<sub>β</sub>); IR (KBr): v 1276 (P=O),

754 (P=S), 1108 (P (V)-OH), 937, 1185 cm<sup>-1</sup> (P-O-C<sub>aromatic</sub>); LCMS: *m/z* (%): 617 (100)[MH<sup>+</sup>], 615 (86)[M-H<sup>+</sup>], 513 (41), 513 (75). Anal(%). Calcd. for C<sub>26</sub>H<sub>23</sub>N<sub>2</sub>O<sub>6</sub>P<sub>3</sub>S<sub>2</sub>: C, 50.65; H, 3.76. Found: C, 50.61; H, 3.74.

**Di[3-(4-methylphenyl)-2-thioxo-3,4-dihydro-2H-1,3,2λ<sup>5</sup>-benzoxazaphosphinin-2-yl] hydrogen phosphate (3c):** Pale yellow color crystal, mp 67 - 69 °C; yield: 92%; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>): δ 7.04-7.49 (1H, m, Ar-H), 4.95-4.88 (2H, m, <sup>-4</sup>H<sub>b</sub>), 4.58-4.46 (2H, m, <sup>-4</sup>H<sub>a</sub>), 2.31 (6H, s, 2xAr-CH<sub>3</sub>), 1.76 (1H, s, β-OH); <sup>31</sup>P NMR (161.9 MHz, DMSO-*d*<sub>6</sub>): δ 58.9 (P<sub>α</sub> and P<sub>γ</sub>), 51.6 (P<sub>β</sub>); IR (KBr): v 1254 (P=O), 769 (P=S), 1095 (P(V)-OH), 939, 1180 cm<sup>-1</sup> (P-O-C<sub>aromatic</sub>); Anal (%). Calcd. for C<sub>28</sub>H<sub>27</sub>N<sub>2</sub>O<sub>6</sub>P<sub>3</sub>S<sub>2</sub>: C, 52.17; H, 4.22. Found: C, 52.21; H 4.24.

**General procedure for the synthesis: (II) Substituted di[3-(4-chlorophenyl)-2-thioxo-3,4-dihydro-2H-1,3,2λ<sup>5</sup>-benzoxazaphos-phinin-2-yl] phosphate (5-13).**

The next synthetic route involves addition of potassium carbonate (2 mmol) in dry toluene; the reaction mixture was allowed to warm up to room temperature and stirred for 2 hrs to get the potassium salts of the thiotriphosphates. The solution was then cooled down to 0 °C before addition of the required isopropyl bromide (2.2 mmol) and a catalytic amount of I<sub>2</sub> and TBAI. The stirring was continued for a further 6 - 8 hrs until 50 - 60 °C. The reaction was monitored by TLC analysis.

The solvent was removed under reduced pressure and the residue obtained by washed with water followed by chilled hexane and recrystallized from acetone to yield triphosphate ester.

**Di[3-(4-chlorophenyl)-2-thioxo-3,4-dihydro-2H-1,3,2λ<sup>5</sup>-benzoxazaphosphinin-2-yl] isopropyl phosphate (5):** Pale yellow color crystals, mp 99 - 100 °C; yield: 87%; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>): δ 7.04-7.41 (12H, m, Ar-H), 6.79 (4H, s, Ar-H), 4.91-4.85 (2H, m, <sup>-4</sup>H<sub>b</sub>), 4.59-4.47 (2H, m, <sup>-4</sup>H<sub>a</sub>), 3.31 (1H, s, <sup>-1</sup>CH<), 1.32 (6H, s, 2 × <sup>-2</sup>CH<sub>3</sub>); <sup>31</sup>P NMR (121 MHz, DMSO-*d*<sub>6</sub>): δ 56.42 (P<sub>α</sub> and P<sub>γ</sub>), 49.33 (P<sub>β</sub>); IR (KBr): v 1211 (P=O), 763 (P=S), 941, 1183 cm<sup>-1</sup> (P-O-C<sub>aromatic</sub>); Anal(%). Calcd. for C<sub>29</sub>H<sub>27</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>6</sub>P<sub>3</sub>S<sub>2</sub>: C, 47.88; H, 3.74. Found: C, 47.83; H, 3.79.

**Isopropyldi(3-phenyl-2-thioxo-3,4-dihydro-2H-1,3,2λ<sup>5</sup>-benzoxaza-phosphinin-2-yl) phosphate (6):** Pale yellow color crystals mp 78 - 80 °C; Yield: 84% <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>): δ 7.08-7.44 (18H, m, Ar-H), 4.92 (2H, dd, *J*<sub>(Ha, Hb)</sub> = 15.1 Hz, *J*<sub>(P, Hb)</sub> = 7.2 Hz, <sup>-4</sup>H<sub>B</sub>), 4.58 (2H, dd, *J*<sub>(Ha, Hb)</sub> = 15.1 Hz, *J*<sub>(P, Ha)</sub> = 26.0 Hz, <sup>-4</sup>H<sub>a</sub>), 3.10-3.08 (1H, m,

- <sup>1</sup>CH<), 1.36-1.40 (t, 6H, 2 × <sup>-2</sup>CH<sub>3</sub>). <sup>31</sup>P NMR (121 MHz, DMSO-*d*<sub>6</sub>): δ 56.10 (P<sub>α</sub> and P<sub>γ</sub>), 45.48 (P<sub>β</sub>); IR (KBr): 1230 (P=O), 756 (P=S), 964, 1188 cm<sup>-1</sup> (P-O-C<sub>aromatic</sub>); DIMS: *m/z* (%): 658 (38)[M<sup>+</sup>], 634 (19), 575 (16), 552 (24), 483 (35), 460 (14), 419 (18), 373 (16), 350 (13), 281 (11), 52 (100); Anal(%). Calcd. for C<sub>29</sub>H<sub>29</sub>N<sub>2</sub>O<sub>6</sub>P<sub>3</sub>S<sub>2</sub>: C, 52.89; H, 4.44. Found: C 52.84, H 4.46.

**Isopropyl di[3-(4-methylphenyl)-2-thioxo-3,4-dihydro-2H-1,3,2λ<sup>5</sup>-benzoxazaphosphi-nin-2-yl] phosphate (7).** Brown color crystals, mp 91 - 93 °C; yield: 85%; <sup>1</sup>H NMR(400 MHz, CDCl<sub>3</sub>): δ 6.96-7.51 (16H, m, Ar-H), 4.92 (2H, dd, *J*<sub>(Ha, Hb)</sub> = 15.2 Hz, *J*<sub>(P, Hb)</sub> = 6.8 Hz, <sup>-4</sup>H<sub>b</sub>), 4.56 (2H, dd, *J*<sub>(Ha Hb)</sub> = 15.2 Hz, *J*<sub>(P, Ha)</sub> = 26.0 Hz, <sup>-4</sup>H<sub>a</sub>), 3.08 (1H, d, *J* = 6.4 Hz, - <sup>1</sup>CH<), 2.37 (s, 6H, 2 × <sup>-4</sup>CH<sub>3</sub>), 1.32-1.36 (m, 6H, 2 × <sup>-2</sup>CH<sub>3</sub> ). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 149.30, 149.17 (C-9), 139.10 (C-1'), 137.96 (C-4'), 130.22 (C-7), 129.67, 129.32 (C-5), 127.35, 127.08 (C-3', C-5'), 126.95 (C-8), 124.95 (C-10), 121.50 (C-6), 119.19, 119.10 (C-2', C-6'), 54.00 (C-4), 46.06 (> CH), 21.19 (Ar-CH<sub>3</sub>), 20.51(CH<sub>3</sub>); <sup>31</sup>P NMR(CDCl<sub>3</sub>) : δ 56.9 (P<sub>α</sub> and P<sub>γ</sub>), 45.1 (P<sub>β</sub>); IR (KBr): v 1215 (P=O), 768 (P=S), 933, 1178 cm<sup>-1</sup> (P-O-C<sub>aromatic</sub>); DI MS: *m/z* (%): 708(24) (M+ Na), 662(33), 612(57), 591(19), 524(54), 501(61), 456(38), 410(52), 364(100); Anal(%). Calcd. for C<sub>31</sub>H<sub>33</sub>N<sub>2</sub>O<sub>6</sub>P<sub>3</sub>S<sub>2</sub>: C, 54.23; H, 4.84. Found: C, 54.21; H, 4.86.

**Butyl di[3-(4-chlorophenyl)-2-thioxo-3,4-dihydro-2H-1,3,2λ<sup>5</sup>-benzoxazaphosphinin-2-yl] phosphate (8).** Yellow color crystals, mp 140 - 145 °C; yield: 91%; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.42-7.06 (12H, m, Ar-H), 6.74 (4H, s, Ar-H), 4.95 (2H, dd, *J*<sub>(Ha, Hb)</sub> = 14.8 Hz, *J*<sub>(P, Hb)</sub> = 7.4 Hz, <sup>-4</sup>H<sub>b</sub>), 4.54 (2H, dd, *J*<sub>(Ha, Hb)</sub> = 14.8 Hz, *J*<sub>(P, Ha)</sub> = 25.3 Hz, <sup>-4</sup>H<sub>a</sub>), 4.17-4.19 (2H, br, CH<sub>2</sub>) 1.30 (2H, br, CH<sub>2</sub>), 1.19 (2H, br, CH<sub>2</sub>), 0.82 (3H, br, CH<sub>3</sub>); <sup>31</sup>P NMR (121 MHz, CDCl<sub>3</sub>): δ 57.0 (P<sub>α</sub> and P<sub>γ</sub>), 45.2 (P<sub>β</sub>); IR (KBr): v 1221 (P=O), 755 (P=S), 931, 1186 cm<sup>-1</sup> (P-O-C<sub>aromatic</sub>). DIMS: *m/z* (%): 740 (100) (M<sup>+</sup>), 612 (65), 633 (61), 574 (44), 528 (29), 505 (43), 450 (28), 437 (24), 391 (61), 349 (82), 299 (20), 277 (14), 211 (12), 165 (29). Anal(%). Calcd. for C<sub>30</sub>H<sub>29</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>6</sub>P<sub>3</sub>S<sub>2</sub>: C, 48.59; H, 3.94. Found: C, 48.55; H, 3.97.

**Butyl di(3-phenyl-2-thioxo-3,4-dihydro-2H-1,3,2λ<sup>5</sup>-benzoxazaphosphinin-2-yl) phos-phate (9).** Brown color crystals, mp 120 - 122 °C; yield: 89(%); <sup>1</sup>H NMR(400 MHz, CDCl<sub>3</sub>): δ 7.10-7.43 (18H, m, Ar-H), 4.95 (2H, dd, *J*<sub>(Ha, Hb)</sub> = 7.6 Hz, *J*<sub>(P, Hb)</sub> = 15.2, <sup>-4</sup>H<sub>B</sub>), 4.57 (2H, dd, *J*<sub>(Ha Hb)</sub> = 15.2, *J*<sub>(P, Ha)</sub> = 25.6, <sup>-4</sup>H<sub>a</sub>), 4.24-4.28 (2H, m, <sup>-1</sup>CH<sub>2</sub>) 1.34-1.38 (m, 2H, <sup>-2</sup>CH<sub>2</sub>), 0.95-0.99 (2H, m, <sup>-3</sup>CH<sub>2</sub>), 0.84-0.88 (3H, m, <sup>-4</sup>CH<sub>3</sub>);

<sup>31</sup>P NMR(121 MHz, CDCl<sub>3</sub>): δ 57.1 (P<sub>a</sub> and P<sub>γ</sub>), 44.7 (P<sub>b</sub>); IR (KBr): ν 1232 (P=O), 757 (P=S), 973, 1180 cm<sup>-1</sup> (P-O-C<sub>aromatic</sub>); DIMS: m/z (%): 671 (76) (M<sup>+</sup>-H), 625 (69), 566 (60), 520 (70), 497 (82), 474 (77), 429 (83), 376 (100), 350 (68), 295 (75), 268 (81); Anal(%). Calcd. C<sub>30</sub>H<sub>31</sub>N<sub>2</sub>O<sub>6</sub>P<sub>3</sub>S<sub>2</sub>: C, 53.57; H, 4.65. Found: C 53.59, H 4.67.

**Butyl di[3-(4-methylphenyl)-2-thioxo-3,4-dihydro-2H-1,3,2λ<sup>5</sup>-benzoxazaphosphinin-2-yl]phosphate (10).** Color less crystals, mp 113 - 115 °C; yield: 85(%); <sup>1</sup>H NMR(400 MHz, CDCl<sub>3</sub>): δ 7.09-7.43 (16H, m, Ar-H), 4.94 (2H, dd, J<sub>(Ha,Hb)</sub>=15.1 Hz, J<sub>(P,Hb)</sub>=7.6 Hz, -<sup>4</sup>H<sub>b</sub>) 4.59 (2H, dd, J<sub>(Ha,Hb)</sub>=15.1 Hz, J<sub>(P,Ha)</sub>=25.3 Hz, -<sup>4</sup>H<sub>a</sub>), 4.30-4.33 (2H, t, -<sup>1</sup>CH<sub>2</sub>), 2.41 (s, 6H, 2 × -<sup>4</sup>CH<sub>3</sub>), 1.25 (2H, m, -<sup>2</sup>CH<sub>2</sub>), 0.72-1.08 (5H, m, -<sup>3</sup>CH<sub>2</sub>, -<sup>4</sup>CH<sub>3</sub>); <sup>13</sup>C NMR(CDCl<sub>3</sub>): 149.24, 149.13 (C-9), 141.710 (C-1'), 129.45 (C-4'), 129.26 (C-7), 127.83 (C-5), 127.19, 126.79 (C-3' and C-5'), 125.49 (C-8), 124.86 (C-10), 121.40 (C-6), 119.12, 119.04 (C-2', C-6'), 53.81, (C-4), 65.02 (C-1"), 29.61 (C-2"), 20.12 (C-3"), 16.48 (C-4"); <sup>31</sup>P NMR (CDCl<sub>3</sub>): δ 57.3 (P<sub>a</sub> and P<sub>γ</sub>), 43.6 (P<sub>b</sub>); IR (KBr): ν 1216 (P=O), 775 (P=S), 935, 1183 cm<sup>-1</sup> (P-O-C<sub>aromatic</sub>); Anal(%). Calcd. for C<sub>32</sub>H<sub>35</sub>N<sub>2</sub>O<sub>6</sub>P<sub>3</sub>S<sub>2</sub>: C, 54.85, H, 5.03. Found: C, 54.80, H, 5.09.

**Benzyl di[3-(4-chlorophenyl)-2-thioxo-3,4-dihydro-2H-1,3,2λ<sup>5</sup>-benzoxazaphosphinin-2-yl] phosphate (11).** Yellow color crystals, mp 110 - 112 °C; yield: 93(%); <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 6.72-6.74 (4H, t, Ar-H), 7.08-7.56 (17H, m, Ar-H), 4.94 (2H, dd, J<sub>(Ha,Hb)</sub>=14.8 Hz, J<sub>(P,Hb)</sub>=7.4 Hz, -<sup>4</sup>H<sub>b</sub>), 4.57 (2H, dd, J<sub>(Ha,Hb)</sub>=14.8 Hz, J<sub>(P,Ha)</sub>=24.8 Hz, -<sup>4</sup>H<sub>a</sub>), 3.14 (2H, s, P-O-CH<sub>2</sub>). <sup>31</sup>P NMR (CDCl<sub>3</sub>): δ 54.5 (P<sub>a</sub> and P<sub>γ</sub>), 43.2 (P<sub>b</sub>); IR (KBr): ν 1217 (P=O), 753 (P=S), 960, 1179 cm<sup>-1</sup> (P-O-C<sub>aromatic</sub>); DIMS: m/z (%): 773 (56) [M-H]<sup>+</sup>, 727 (68), 717 (47), 671 (44), 602 (63), 501 (54), 464 (60), 396 (36), 341 (61), 249 (77), 226 (76), 180 (79), 144 (78), 98 (74); Anal(%). Calcd. for C<sub>33</sub>H<sub>27</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>6</sub>P<sub>3</sub>S<sub>2</sub>: C, 51.11; H, 3.51. Found: C, 51.08, H, 3.55.

**Benzyl di(3-phenyl-2-thioxo-3,4-dihydro-2H-1,3,2λ<sup>5</sup>-benzoxazaphos-phinin-2-yl)phos-phate (12).** Brown color crystals, mp 97 - 99 °C; yield: 87(%); <sup>1</sup>H NMR(400 MHz, CDCl<sub>3</sub>): δ 7.01-7.68 (23H, m, Ar-H), 4.92 (2H, dd, J<sub>(Ha,Hb)</sub>=6.8 Hz, J<sub>(P,Hb)</sub>=14.8 -<sup>4</sup>H<sub>b</sub>), 4.55 (2H, dd, J<sub>(Ha,Hb)</sub>=14.8, J<sub>(P,Ha)</sub>=24.8 -<sup>4</sup>H<sub>a</sub>), 3.10 (2H, s, P-O-CH<sub>2</sub>); <sup>13</sup>C NMR(100 MHz, CDCl<sub>3</sub>): 119.67 (C-10), 149.57 (C-9), 120.64 (C-8), 125.79 (C-7), 115.35 (C-6), 123.86 (C-5), 143.35 (C-1'), 116.99, 116.78 (C-2', C-6'), 128..76, 128.48 (C-3' & C-5'), 129.02 (C-4'), 51.52, (C-4), 144.23 (C-1"), 127.48, 127.62 (C-3" & C-5"), 115.35, 114.94 (C-2" & C-6") 124.05 (C-4") 60.32 (<sup>1</sup>R-C); <sup>31</sup>P NMR(121 MHz, CDCl<sub>3</sub>): δ 52.6 (P<sub>a</sub> and P<sub>γ</sub>), 44.5

(P<sub>b</sub>). IR (KBr): 1221 (P=O), 758 (P=S), 966, 1183 cm<sup>-1</sup> (P-O-C<sub>aromatic</sub>); Anal(%). Calcd. for C<sub>33</sub>H<sub>29</sub>N<sub>2</sub>O<sub>6</sub>P<sub>3</sub>S<sub>2</sub>: C, 56.09; H, 4.14. Found: C 56.06, H 4.18.

**Benzyl di[3-(4-methylphenyl)-2-thioxo-3,4-dihydro-2H-1,3,2λ<sup>5</sup>-benzo-xazaphosphinin-2-yl] phosphate (13).** Color less crystals, mp 105 - 107 °C. yield: 84%; <sup>1</sup>H NMR(400 MHz, CDCl<sub>3</sub>): δ 6.99-7.65 (23H, m, Ar-H), 4.93 (2H, dd, J<sub>(Ha,Hb)</sub>=7.6 Hz, J<sub>(P,Hb)</sub>=15.1, -<sup>4</sup>H<sub>b</sub>), 4.56 (2H, dd, J<sub>(Ha,Hb)</sub>=15.1, J<sub>(P,Ha)</sub>=24.4 -<sup>4</sup>H<sub>a</sub>), 3.10 (s, 2H, P-O-CH<sub>2</sub>), 2.38 (s, 6H, 2 × -<sup>4</sup>CH<sub>3</sub>); <sup>31</sup>P NMR(121 MHz, CDCl<sub>3</sub>): δ 53.1 (P<sub>a</sub> and P<sub>γ</sub>), 43.8 (P<sub>b</sub>); IR (KBr): ν 1243 (P=O), 761 (P=S), 972, 1188 cm<sup>-1</sup> (P-O-C<sub>aromatic</sub>); Anal(%). Calcd. for C<sub>35</sub>H<sub>33</sub>N<sub>2</sub>O<sub>6</sub>P<sub>3</sub>S<sub>2</sub>: C, 57.22; H, 4.53. Found: C, 57.24; H, 4.61.

## CONCLUSION

New classes of trisphosphates with significant antimicrobial activity were synthesized by a simple procedure conveniently in good yields under catalyzed conditions which is cost effective and we expect good flame retarding for our synthesized compounds.

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