Journal of the Korean Chemical Society
2010, *Vol. 54, No. 5*
Printed in the Republic of Korea
DOI 10.5012/jkcs.2010.54.5.653

단신

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

K. R. Kishore Kumar Reddy, K. Reddi Mohan Naidu, A. Bala Krishna, P. Hari Krishna†, and C. Suresh Reddy*

Department of Chemistry, Sri Venkateswara University, Tirupati, 517 502, India
†Department of Plant pathology, Sri Venkateswara Agriculture University, Tirupati, 517 502, India
(접수 2009. 3. 10; 수정 2010. 4. 8; 게재확정 2010. 5. 3)

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

K. R. Kishore Kumar Reddy, K. Reddi Mohan Naidu, A. Bala Krishna, P. Hari Krishna†, and C. Suresh Reddy*

Department of Chemistry, Sri Venkateswara University, Tirupati, 517 502, India
†Department of Plant pathology, Sri Venkateswara Agriculture University, Tirupati, 517 502, India
**E-mail: csrsvu@gmail.com*
(Received March 10, 2009; Revised April 8, 2010; Accepted May 3, 2010)

주제어: Benzoxazaphosphinine, Iodine, Tetrabutylammoniumiodide, TrisPhosphates, 항균활성

Keywords: Benzoxazaphosphinine, Iodine, Tetrabutylammoniumiodide, TrisPhosphates, Antimicrobial activity

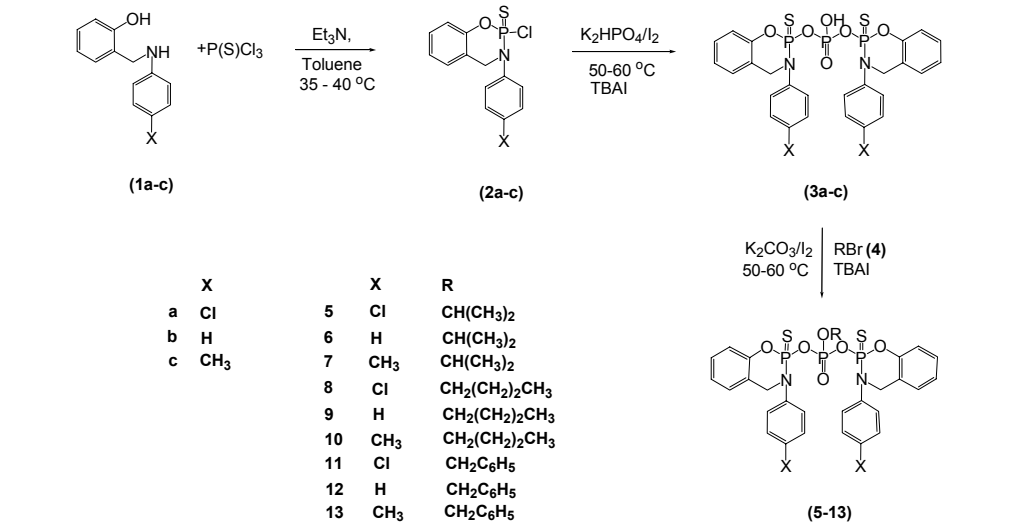
INTRODUCTION

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.[1,2] Synthesis of high quality flame retardants with low flammability and melt dripping limits is an urgent need now-a-days.[3,4] Phosphorus based fire retardants are known to act in both gas and condensed phases and also concurrently in both phases.[5,6] Phosphatidylinositol 3,4,5-triphosphate is attracting much attention due to its several biological roles[7] in signal transduction,[8] non-capacitative calcium influx,[9] cell regulation etc.[10] Phosphoric acid derivatives play a major role in driving some metabolic processes by energy release that accompanies the cleavage of a phosphate group.[11] Herein, we introduced I_2 as catalyst in addition to TBAI and synthesized triphosphate esters in less time with high yields.

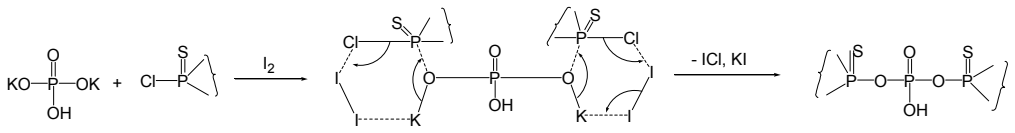
RESULTS AND DISCUSSION

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-2*H*-1,3,2λ^5-benzoxazaphosphinin-2-thione (**2**). Reaction of **2** with dipotassium salt of phosphoric acid/I_2 and TBAI[12,13] in dry toluene at 50 - 60 °C gave di[3-(4-substituted-phenyl)-2-thioxo-3,4-dihydro-2*H*-1,3,2λ^5-benzoxazaphos-phinin-2-yl]hydrogenphosphate (**3**). Further, reaction of **3** with alkyl/aryl halide (**4**) in the presence of K_2CO_3/I_2[14,15] at 50 - 60 °C yielded the title compounds **5-13** (*Scheme* 1).

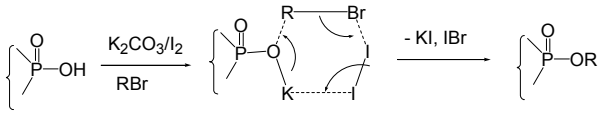
O-phosphorylation of K_2HPO_4 with cyclic phosphoromonochloridates **2a-c** were found to occur selectively at the two '-OK' groups of K_2HPO_4 when the reaction was carried out initially at 0 °C and later at 50 - 60 °C in a mixture of toluene:hexane (3:1) in the presence of catalytic amount of TBAI and I_2. TBAI/I_2 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_2CO_3 and I_2 followed by alkyl/aryl bromides was in toluene. Basically, I_2 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}H, ^{31}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,[4,16,17] P=S,[4] P(V)-OH,[4] P-O and O-C of P-O-C$_{(Ar)}$[4,18,19] respectively. ^{1}H NMR spectra of **3a-c**, **5-13** showed multiplets in the range δ 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 δ 4.95-4.90, 4.63-4.46 indicating their non equivalence coupling with phosphorus.[4,20] The other aliphatic protons gave signals in the expected region. ^{13}C NMR chemical shifts are in good agreement with the assigned structures.[4,21] The ^{31}P NMR chemical shifts appeared in the range of δ 58.93-52.54 for P_{α} and P_{γ} and 51.67 to 43.24 for P_{β}. 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[22] 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 diffferent concentrations[23] (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^{5} 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[a]	400[a]	200[a]	400[a]	200[a]	400[a]	200[a]	400[a]
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

[a]Concentations 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 ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded Bruker AMX 400 NMR spectrometers operating at 400 MHz (^{1}H), 100.61 MHz (^{13}C) and 121.9 MHz (^{31}P). Mass spectra were recorded by Fast atom bombardment, Liquid Chromatograph and De Ionized mass spectrometer. All compounds are dissolved in $CDCl_3$, DMSO-d_6, chemical shifts are referenced to TMS (^{1}H, ^{13}C) and 85% H_3PO_3 (^{31}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-2*H*-1,3,2λ^5-benzoxazaphosphinin-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_2HPO_4 (2 mmol), dry hexane (10 mL) and a catalytic amount of I_2 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 recrystallzed 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-2*H*-1,3,2λ^5-benzoxazaphosphinin-2-yl) hydrogen phosphate (3a): Pale yellow color crystals, mp 81 - 83 °C; yield: 94%; ^{1}H NMR (400 MHz, DMSO-d_6): 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, -^{4}H$_b$), 4.58-4.49 (2H, m, -^{4}H$_a$), 1.50 (1H, s, β-OH); ^{31}P NMR (121 MHz, DMSO-d_6): δ 57.32 (P_α and P_γ), 50.17 (P_β); IR (KBr): ν 1210 (P=O), 767 (P=S), 1097(P (V)-OH), 938, 1180 cm^{-1} (P-O-$C_{aromatic}$); FAB MS$m/z$ (%): 687 (16) [MH^++2], 685 (23) [MH^+], 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 $C_{26}H_{21}Cl_2N_2O_6P_3S_2$: C, 45.56; H, 3.09. Found: C, 45.52; H, 3.11.

Di(3-phenyl-2-thioxo-3,4-dihydro-2*H*-1,3,2λ^5-benzoxazaphosphinin-2-yl)hydrogen phosphate (3b): Colorless crystals, mp 98 - 100 °C; yield: 90%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.11-7.42 (18H, m, Ar-H), 4.90-4.86 (2H, m, -^{4}H$_b$), 4.63-4.52 (2H, m, -^{4}H$_a$), 1.62 (1H, s, β-OH); ^{31}P NMR (121 MHz, $CDCl_3$): δ 56.6 (P_α and P_γ), 47.2 (P_β); IR (KBr): ν 1276 (P=O),

754 (P=S), 1108 (P (V)-OH), 937, 1185 cm^{-1} (P-O-$C_{aromatic}$); LCMS: *m/z* (%): 617 (100)[MH^+], 615 (86)[M-H^+], 513 (41), 513 (75). Anal(%). Calcd. for $C_{26}H_{23}N_2O_6P_3S_2$: C, 50.65; H, 3.76. Found: C, 50.61; H, 3.74.

Di[3-(4-methylphenyl)-2-thioxo-3,4-dihydro-2*H*-1,3,2λ^5-benzoxazaphosphinin-2-yl] hydrogen phosphate (3c): Pale yellow color crystal, mp 67 - 69 °C; yield: 92%; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.04-7.49 (16 H, m, Ar-H), 4.95-4.88 (2H, m, -^{4}H$_b$), 4.58-4.46 (2H,m, -^{4}H$_a$), 2.31 (6H, s, 2xAr-C<u>H</u>$_3$), 1.76 (1H, s, β-O<u>H</u>); ^{31}P NMR (161.9 MHz, DMSO-d_6): δ 58.9 (P_α and P_γ), 51.6 (P_β); IR (KBr): ν1254 (P=O), 769 (P=S), 1095 (P(V)-OH), 939, 1180 cm^{-1} (P-O-$C_{aromatic}$); Anal (%). Calcd. for $C_{28}H_{27}N_2O_6P_3S_2$: 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-2*H*-1,3,2λ^5-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 potasium 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_2 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-2*H*-1,3,2λ^5-benzoxazaphosphinin-2-yl] isopropyl phosphate (5): Pale yellow color crystals, mp 99 - 100 °C; yield: 87%; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.04-7.41 (12H, m, Ar-H), 6.79 (4H, s, Ar-H), 4.91-4.85 (2H, m, -^{4}H$_b$), 4.59-4.47 (2H, m, -^{4}H$_a$), 3.31 (1H, s, -$^{1"}$C<u>H</u><), 1.32 (6H, s, 2 × -$^{2"}$C<u>H</u>$_3$); ^{31}P NMR (121 MHz, DMSO-d_6): δ 56.42 (P_α and P_γ), 49.33 (P_β); IR (KBr): ν 1211 (P=O), 763(P=S), 941, 1183 cm^{-1} (P-O-$C_{aromatic}$); Anal(%). Calcd. for $C_{29}H_{27}Cl_2N_2O_6P_3S_2$: C, 47.88; H, 3.74. Found: C, 47.83; H, 3.79.

Isopropyldi(3-phenyl-2-thioxo-3,4-dihydro-2*H*-1,3,2λ^5-benzoxaza-phosphinin-2-yl) phosphate (6): Pale yellow color crystals mp 78 - 80 °C; Yield: 84% ^{1}H NMR (400 MHz, DMSO-d_6) : δ 7.08-7.44 (18H, m, Ar-H), 4.92 (2H, dd, $J_{(Ha, Hb)}$ = 15.1 Hz, $J_{(P, Hb)}$ = 7.2 Hz, -^{4}H$_B$), 4.58 (2H, dd, $J_{(Ha, Hb)}$ = 15.1 Hz, $J_{(P, Ha)}$ = 26.0 Hz, -^{4}H$_a$), 3.10-3.08 (1H, m, -$^{1"}$CH<), 1.36-1.40 (t, 6H, 2 × -$^{2"}$CH$_3$). ^{31}P NMR (121 MHz, DMSO-d_6): δ 56.10 (P_α and P_γ), 45.48 (P_β); IR (KBr): 1230 (P=O), 756 (P=S), 964, 1188 cm^{-1} (P-O-$C_{aromatic}$); DIMS: *m/z* (%): 658 (38)[M^+], 634 (19), 575 (16), 552 (24), 483 (35), 460 (14), 419 (18), 373 (16), 350 (13), 281 (11), 52 (100); Anal(%). Calcd. for $C_{29}H_{29}N_2O_6P_3S_2$: 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^5-benzoxazaphosphi-nin-2-yl] phosphate (7). Brown color crystals, mp 91 - 93 °C; yield: 85%; ^{1}H NMR(400 MHz, $CDCl_3$) : δ 6.96-7.51 (16H, m, Ar-H), 4.92 (2H, dd, $J_{(Ha,Hb)}$ = 15.2 Hz, $J_{(P, Hb)}$ = 6.8 Hz, -^{4}H$_b$), 4.56 (2H, dd, $J_{(Ha Hb)}$ = 15.2 Hz, $J_{(P, Ha)}$ = 26.0 Hz, -^{4}H$_a$), 3.08 (1H, d, *J* = 6.4 Hz, -$^{1"}$CH<), 2.37 (s, 6H, 2 × -$^{4'}$CH$_3$), 1.32-1.36 (m, 6H, 2 × -$^{2"}$CH$_3$). ^{13}C NMR (100 MHz, $CDCl_3$): 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_3) , 20.51(CH_3); ^{31}P NMR($CDCl_3$) : δ 56.9 (P_α and P_γ), 45.1 (P_β); IR (KBr): ν 1215 (P=O), 768 (P=S), 933, 1178 cm^{-1} (P-O-$C_{aromatic}$); 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 $C_{31}H_{33}N_2O_6P_3S_2$: C, 54.23; H, 4.84. Found: C, 54.21; H, 4.86.

Butyl di[3-(4-chlorophenyl)-2-thioxo-3,4-dihydro-2*H*-1,3,2λ^5-benzoxazaphosphinin-2-yl] phosphate (8). Yellow color crystals, mp 140 - 145 °C; yield: 91%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.06 (12H, m, Ar-H), 6.74 (4H, s, Ar-H), 4.95 (2H, dd, $J_{(Ha, Hb)}$ = 14.8 Hz, $J_{(P, Hb)}$ = 7.4 Hz, -^{4}H$_b$), 4.54 (2H, dd, $J_{(Ha, Hb)}$ = 14.8 Hz, $J_{(P, Ha)}$ = 25.3 Hz, -^{4}H$_a$), 4.17-4.19 (2H, br, CH_2) 1.30 (2H, br, CH_2), 1.19 (2H, br, CH_2), 0.82 (3H, br, CH_3); ^{31}P NMR (121 MHz, $CDCl_3$): δ 57.0 (P_α and P_γ), 45.2 (P_β); IR (KBr): ν 1221 (P=O), 755 (P=S), 931, 1186 cm^{-1} (P-O-$C_{aromatic}$). DIMS: *m/z* (%): 740 (100) (M^+), 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 $C_{30}H_{29}Cl_2N_2O_6P_3S_2$: C, 48.59; H, 3.94. Found: C, 48.55; H, 3.97.

Butyl di(3-phenyl-2-thioxo-3,4-dihydro-2*H*-1,3,2λ^5-benzoxazaphosphinin-2-yl) phos-phate (9). Brown color crystals, mp 120 - 122 °C; yield: 89(%); ^{1}H NMR(400 MHz, $CDCl_3$): δ 7.10-7.43 (18H, m, Ar-H), 4.95 (2H, dd, $J_{(Ha,Hb)}$ = 7.6 Hz, $J_{(P, Hb)}$ = 15.2, -^{4}H$_B$), 4.57 (2H, dd, $J_{(Ha Hb)}$ = 15.2, $J_{(P, Ha)}$ = 25.6, -^{4}H$_a$), 4.24-4.28 (2H, m, -$^{1"}$C<u>H</u>$_2$) 1.34-1.38 (m, 2H, -$^{2"}$C<u>H</u>$_2$), 0.95-0.99 (2H, m, -$^{3"}$CH$_2$), 0.84-0.88 (3H, m, -$^{4"}$CH$_3$);

^{31}P NMR(121 MHz, $CDCl_3$): δ 57.1 (P_α and P_γ), 44.7 (P_β); IR (KBr): ν 1232 (P=O), 757 (P=S), 973, 1180 cm^{-1} (P-O-$C_{aromatic}$); DIMS: *m/z* (%): 671 (76) (M^+-H), 625 (69), 566 (60), 520 (70), 497 (82), 474 (77), 429 (83),376 (100), 350 (68), 295 (75), 268 (81); Anal(%). Calcd. $C_{30}H_{31}N_2O_6P_3S_2$: C, 53.57; H, 4.65. Found: C 53.59, H 4.67.

Butyl di[3-(4-methylphenyl)-2-thioxo-3,4-dihydro-2*H*-1,3,2λ^5-benzox-azaphosphinin-2-yl]phosphate (10). Color less crystals, mp 113 - 115 ^{o}C; yield: 85(%); ^{1}H NMR(400 MHz, $CDCl_3$): δ 7.09-7.43 (16H, m, Ar-H), 4.94 (2H, dd, $J_{(Ha, Hb)}$ =15.1 Hz, $J_{(P, Hb)}$ = 7.6 Hz, -^{4}H$_B$) 4.59 (2H, dd, $J_{(Ha, Hb)}$ = 15.1 Hz, $J_{(P, Ha)}$ = 25.3 Hz, -^{4}H$_a$), 4.30-4.33 (2H, t, -$^{1"}$CH$_2$), 2.41 (s, 6H, 2 × -$^{4'}$CH$_3$), 1.25 (2H, m, -$^{2"}$CH$_2$), 0.72-1.08 (5H, m, -$^{3"}$CH$_2$, -$^{4"}$CH$_3$); ^{13}C NMR($CDCl_3$): 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"); ^{31}P NMR ($CDCl_3$): δ 57.3 (P_α and P_γ), 43.6 (P_β); IR (KBr): ν 1216 (P=O), 775 (P=S), 935, 1183 cm^{-1} (P-O-$C_{aromatic}$); Anal(%). Calcd. for $C_{32}H_{35}N_2O_6P_3S_2$: C, 54.85, H, 5.03. Found: C, 54.80, H, 5.09.

Benzyl di[3-(4-chlorophenyl)-2-thioxo-3,4-dihydro-2*H*-1,3,2λ^5-benzox-azaphosphinin-2-yl] phosphate (11). Yellow color crystals, mp 110 - 112 ^{o}C; yield: 93(%); ^{1}H NMR (CDCl): δ 6.72-6.74 (4H, t, Ar-H), 7.08-7.56 (17H, m, Ar-H), 4.94 (2H, dd, $J_{(Ha, Hb)}$ = 14.8 Hz, $J_{(P, Hb)}$ = 7.4 Hz, -^{4}H$_b$), 4.57 (2H, dd, $J_{(Ha, Hb)}$ = 14.8 Hz, $J_{(P, Ha)}$ = 24.8 Hz, -^{4}H$_a$), 3.14 (2H, s, P-O-CH$_2$). ^{31}P NMR ($CDCl_3$): δ 54.5 (P_α and P_γ), 43.2 (P_β); IR (KBr): ν 1217 (P=O), 753 (P=S), 960, 1179 cm^{-1} (P-O-$C_{aromatic}$); DIMS: *m/z* (%) 773 (56) $[M-H]^+$, 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 $C_{33}H_{27}Cl_2N_2O_6P_3S_2$: C, 51.11; H, 3.51. Found: C, 51.08, H, 3.55.

Benzyl di(3-phenyl-2-thioxo-3,4-dihydro-2*H*-1,3,2λ^5-benzoxazaphos-phinin-2-yl)phos-phate (12). Brown color crystals, mp 97 - 99 ^{o}C; yield: 87(%); ^{1}H NMR(400 MHz, CDCl): δ 7.01-7.68 (23H, m, Ar-H), 4.92 (2H, dd, $J_{(Ha, Hb)}$ = 6.8 Hz, $J_{(P, Hb)}$ = 14.8 -^{4}H$_b$), 4.55 (2H, dd, $J_{(Ha, Hb)}$ = 14.8, $J_{(P, Ha)}$ = 24.8 -^{4}H$_a$), 3.10 (2H, s, P-O-CH$_2$); ^{13}C NMR(100 MHz, $CDCl_3$): 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 (^{Ar}-C); ^{31}P NMR(121 MHz, $CDCl_3$): δ 52.6 (P_α and P_γ), 44.5 (P_β). IR (KBr): 1221 (P=O), 758 (P=S), 966, 1183 cm^{-1} (P-O-$C_{aromatic}$); Anal(%). Calcd. for $C_{33}H_{29}N_2O_6P_3S_2$: C, 56.09; H, 4.14. Found: C 56.06, H 4.18.

Benzyl di[3-(4-methylphenyl)-2-thioxo-3,4-dihydro-2*H*-1,3,2λ^5-benzo-xazaphosphinin-2-yl] phosphate (13). Color less crystals, mp 105 - 107 ^{o}C. yield: 84%; ^{1}H NMR(400 MHz, $CDCl_3$): δ 6.99-7.65 (23H, m, Ar-H), 4.93 (2H, dd, $J_{(Ha,Hb)}$ = 7.6 Hz, $J_{(P, Hb)}$ = 15.1, -^{4}H$_b$), 4.56 (2H, dd, $J_{(Ha Hb)}$ 15.1, $J_{(P, Ha)}$ = 24.4 -^{4}H$_a$), 3.10 (s, 2H, P-O-CH$_2$), 2.38 (s, 6H, 2 × -$^{4'}$CH$_3$); ^{31}P NMR(121 MHz, $CDCl_3$): δ 53.1 (P_α and P_γ), 43.8 (P_β); IR (KBr): ν 1243 (P=O), 761 (P=S), 972, 1188 cm^{-1} (P-O-$C_{aromatic}$); Anal(%). Calcd. for $C_{35}H_{33}N_2O_6P_3S_2$: 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.

Acknowledgments. The authors thanks to Prof. C. D. Reddy, Dept. of Chemistry, S. V. University, Tirupati for helpful discussions and for BRNS (DAE), Mumbai for providing financial assistance.

REFERENCES

1. Weil, E. D. *Handbook of Organophosphorus Chemistry.* Engel R., ed.; Marcel Dekker Inc.: New York, 1992, Chap. 14.
2. Levchik S.; Weil, E. D. *Polym. Int.* 2005, *54*, 11.
3. Du, X. H.; Wang, Y. Z.; Chen X. T.; Tang, X. D. *Polym. Degrad. Stab*, **2005**, *88*, 52.
4. Kiran, Y. B.; Reddy, C. D.; Gunasekar, D.; Raju, C. N.; Barbosa, L. C. A.; Marney D. C. O.; Russell. L. J. *J. Fire Sci.* **2007**, *25*, 193.
5. Green, J. Phosphorus-Containing Flame Retardants, In: Grand, A.; Wilkie, C. A., ed.; *Fire Retardancy of Polymeric Materials*, Marcel Dekker, Inc; New York, 2000.
6. Levchik, S. V.; Camino, G.; Luda, M. P.; Costa, L.; Muller, G.; Costes B.; Henry Y. *Polym. Adv. Technol.* **1996**, *7*, 823.
7. Hinchliffe, K. A. *Curr. Biol*., **2001**, *11*, 371.
8. Rameh, L. E.; Cantley, L. C. *J. Biol. Chem.*, **1999**, 274, 8347.
9. Tseng, P. H.; Lin, H. P.; Hu, H.; Wang, C.; Zhu, M. X.; Chen, C. S. *Biochemistry.* **2004**, 43, 11701.
10. Hemmings, B. A. *Science.* **1997**, 277, 534.
11. Haebich, D.; Hansen, J.; Paessens, A. *Eur. Pat. Appl*. **1992**, EP472077.
12. Dusan, Z. M.; Vida, D. J.; Slobodan, D. P. *J. Serb. Chem. Soc.*, **2004**, *69*, 85.
13. Ruxer, F. D. L.; Oliver, J. T.; Alford, J. M.; Salvatore, R. N.

Tetrahedron Lett, **2004,** *45,* 401.
14. Mori, N; Togo, H. *Tetrahedron,* **2005**, *61*, 5915.
15. Pranjal, Konwar, D. *Org. Biomol. Chem.* **2005**, *3*, 3473.
16. Kiran, Y. B.; Reddy, P. V. G.; Reddy, C. D.; Gunasekar, D.; Reddy, N. P. E. *J. Agric. Food Chem*. **2007**, *55*, 6933.
17. Kumar, B. S.; Sankar, A. U. R.; Reddy, C. S.; Nayak, S. K.; Raju, C. N. *Arkivoc*, **2007**, (*xiii*), 155.
18. Nyquist, R. A. *Infrared Spectra of Organo-Phosphorus Compounds: New Correlations. Appl. Spectrosc*. **1957**, *11*, 161.
19. Thomas, L. *Spectrochim. Acta.* 1964, *20*, 489.
20. Kumar, B. S.; Sankar, A. U. R.; Reddy, G. C. S.; Reddy, M. V. N.; Reddy, C. D.; Reddy, C. S. *Arkivoc*, **2008**, (xii), 109.
21. Silverstein, R. M.; and Webster, F. X.; (**1998**). *Spectrometric Identification of Organic Compounds*, 6th edn, John Willey & Sons, New York.
22. Cruickshank, R. *Medicinal Microbiology, a Guide to Diagnosis and Control of Reaction*; 11th ed., E. and S Livingstone: Edinburgh and London, U. K. **1986**, p 888.
23. Benson, H. J.; *Microbiological Applications*, 5th ed.; Brown, W. C.: Dubuque, IA, **1990**, p 134.