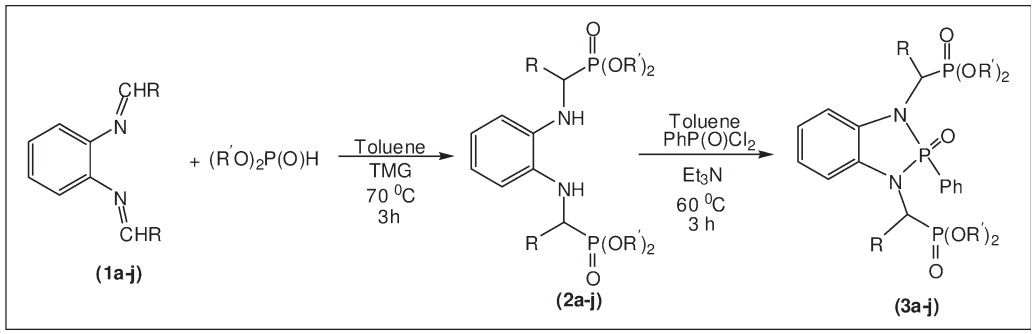
B. Siva Kumar, M. Veera Narayana Reddy, G. Chandra Sekhar Reddy,
N. Bakthavatchala Reddy, and C. Suresh Reddy*

Department of Chemistry, Sri Venkateswara University, Tirupati 517502, Andhra Pradesh, India
*E-mail: csrsvu@gmail.com
Received December 25, 2009
DOI 10.1002/jhet.530
Published online 7 October 2010 in Wiley Online Library (wileyonlinelibrary.com).



Syntheses of novel [{(3-dialkoxy-phosphoryl)-(substituted-phenyl-methyl)-2-oxo-2-phenyl-2,3-dihydro-2λ^5–benzo [1,3,2] diazaphosphol-1-yl}-(substituted-phenyl)-methyl]-phosphonic acid diethyl/dimethyl esters (**3a–j**) were conveniently accomplished by cyclocondensation of [(2-{(dimethoxy-phosphoryl)-phenyl-methyl)-amino}-phenyl amino)-phenyl-methyl]phosphonic acid diethyl/dimethyl esters (**2a–j**) with phenyl phosphonic dichloride in dry toluene in the presence of triethylamine at 40°C. The title compounds were characterized by physicospectral techniques. All the synthesized compounds were found to possess antimicrobial properties.

J. Heterocyclic Chem., **48**, 221 (2011).

INTRODUCTION

Trisphosphates are chiefly used as additives in a variety of industrial products, such as flame retardants, elastomers, fiberglass resins, surface coatings, scalants, 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].

In this research, synthesis of [{(3-dialkoxy-phosphoryl)-(substituted-phenyl-methyl)-2-oxo-2-phenyl-2,3-dihydro-2λ^5–benzo-[1,3,2]-diaza-phosphol-1-yl}-(substituted-phenyl)-methyl]-phosphonic acid diethyl/dimethyl esters (**3a–j**) was accomplished successfully and they exhibited moderate to high antimicrobial activity.

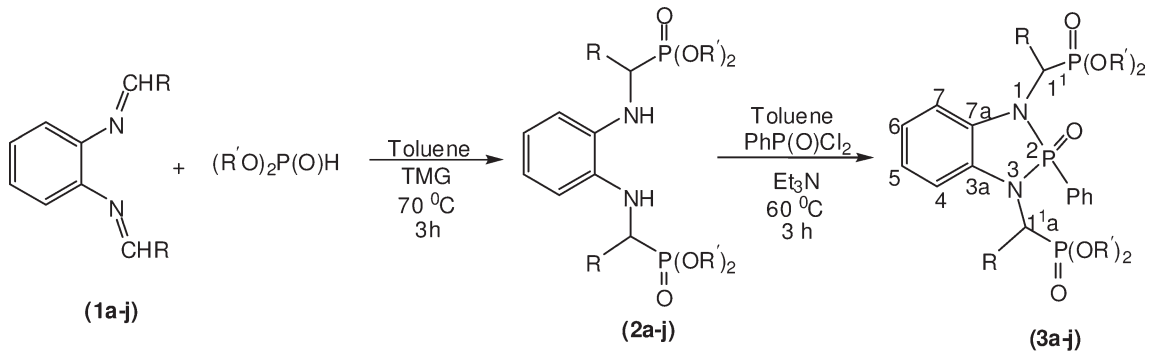
SYNTHESIS AND DISCUSSION

The titled compounds (**3a–j**) were conveniently synthesized by a two-step process. In the first step [(2-{(dimethoxy-phosphoryl)-phenyl-methyl)-amino}-phenyl amino)-phenyl-methyl]-phosphonic acid diethyl/dimethyl esters (**2a–j**) were prepared by reacting the corresponding aldimines (**1a–j**) and dialkylphosphite in the presence of catalytic amount of tetramethyl guanidine (TMG) in dry toluene at reflux condition. Compounds **2a–j** on further cyclocondensation with phenyl phosphonic dichloride in dry toluene in the presence of triethylamine at 40°C (Scheme 1) afforded compounds **3a–j**. Progress of the reaction was monitored by TLC analysis.

The chemical structures of **3a–j** were confirmed by elemental analysis, IR, ^{1}H-, ^{13}C-, ^{31}P-NMR, and mass spectra. Compounds **3a–j** exhibited characteristic IR stretching frequencies in the regions 1259–1272, 1192–1219, and 749–769 cm^{-1} for P=O (phosphonates), P=O (diazaphosphole), and P—C$_{(aliphatic)}$, respectively [12].

The aromatic protons in the compounds **3a–j** gave as multiplet in the region δ 6.1–8.4. The P—C—H protons resonated as doublet [13] in the region δ 4.74–5.83 (d, $^1J_{P-C-H}$ = 10.3–11.8 Hz) due to its coupling with phosphorus. The two methoxy group protons of two dimethyl phosphate moiety in compounds **3a–e** resonated as two distinct doublets in the range of δ 3.43–3.61 (d, $^3J_{P-H}$ = 10.0–11.4 Hz) and δ 3.54–3.67 (d, $^3J_{P-H}$ = 9.3–11.3 Hz) indicating their nonequivalent electronic and

Scheme 1



Compd.	R	R′	Compd.	R	R′
3a	C_6H_5	CH_3	**3f**	C_6H_5	CH_2CH_3
3b	$C_6H_5Cl(4')$	CH_3	**3g**	$C_6H_5Cl(4')$	CH_2CH_3
3c	$C_6H_5NO_2(3')$	CH_3	**3h**	$C_6H_5NO_2(3')$	CH_2CH_3
3d	$C_6H_5Cl(3')$	CH_3	**3i**	$C_6H_5Cl(3')$	CH_2CH_3
3e	$C_6H_4(OCH_3)_2(3'\&4')$	CH_3	**3j**	$C_6H_4(OCH_3)_2(3'\&4')$	CH_2CH_3

magnetic environment [14]. Similarly, the two methyl groups of the two diethyl phosphate moiety in compounds **3f–j** resonated as two distinct triplets in the region δ 1.22–1.31 (t, J = 8.0–8.5 Hz) and δ 1.09–1.16 (t, J = 7.7–8.1 Hz). Their methylene protons directly attached to oxygen showed multiplets in the region 3.61–4.17 ppm due to their coupling with both the phosphorus and adjacent methyl protons [14].

The P—C—H carbon chemical shift signal appeared as a doublet [14] in the range of δ 50.0–54.2 (d, $^1J_{P-C}$ = 163.0–167.42 Hz). The methoxy carbon of dimethylphosphonate group resonated as a singlet at δ 55.03–57.49. Two distinct ^{31}P signals [15] were observed, one at δ 22.13–40.65 (P=O, phosphonates) and the other at δ 0.27–4.03 (P=O, diazaphosphole) for **3a–j**. The mass spectra of compounds **3a**, **3b**, **3f**, and **3j** showed their respective molecular ion peaks in the expected m/z mass values.

EXPERIMENTAL

The melting points were determined in open capillary tubes on a Mel-Temp apparatus and were uncorrected. The IR spectra (ν_{max}, cm^{-1}) were recorded as KBr pellets on Perkin Elmer 1000 unit. The ^1H-, ^{13}C-, and ^{31}P-NMR spectra were recorded on a Varian AMX 400 MHz NMR spectrometer operating at 400 MHz for ^1H, 100.57 MHz for ^{13}C, and 161.7 MHz for ^{31}P. All the compounds were dissolved in $CDCl_3$ or DMSO-d_6, and chemical shifts were referenced to TMS (^1H and ^{13}C) and 85% H_3PO_4 (^{31}P). Microanalyses data were obtained from Central Drug Research Institute, Lucknow, India.

Typical experimental procedure.

General procedure for preparation of (3a).

*[{(3-Dimethoxy-phosphoryl)-(phenyl-methyl)-2-oxo-2-phenyl-2,3-dihydro-2λ⁵-benzo [1,3,2]diazaphosphol-1-yl}-(phenyl)-methyl]-phosphonic acid dimethyl ester (**3a**).* To a stirred solution of *N*,*N*-dibenzylidenebenzene-1,2-diamine (**1a**, 0.005 mol) in dry toluene (25 mL), a solution of dimethylphosphite (0.01 mol) in dry toluene (15 mL) was added dropwise at 0°C in the presence of TMG. After completion of addition, the temperature was raised and kept at room temperature for half an hour and then refluxed at 70°C for 3 h. Progress of the reaction was monitored by TLC analysis. The obtained intermediate [(2-{(dimethoxy-phosphoryl)-phenyl-methyl)-amino}-phenylamino)-phenyl-methyl]-phosphonic acid methyl ester (**2a**) was evaporated in a rotaevaporator. To the concentrated solution of compound **2a** (0.005 mol) in dry toluene in the presence of triethylamine (0.01 mol), a solution of phenyl phosphonic dichloride (0.005 mol) in dry toluene (15 mL) was added slowly at 35°C over a period of half an hour. After addition, the temperature of the reaction mixture was raised and maintained at 60°C for 2 h with stirring. Progress of the reaction was monitored by TLC analysis. The solid triethylamine hydrochloride was filtered and the solvent was removed in a rotaevaporator to get the crude product, and it was purified by column chromatography on 60–120 mesh silica gel using ethylacetate:hexane (3:1) as eluent to obtain pure compound **3a**, 1.70 g (71%), mp 189–191°C. Compounds **3b–j** were synthesized by adopting the above procedure.

Table 1

Antibacterial activity of compounds **3a–j** (μg/mL).

	Zone of inhibition (%)					
	Escherichia coli			*Staphylococcus aureus*		
Compounds	100	50	25	100	50	25
3a	7	5	3	7	3	3
3b	12	9	7	12	8	7
3c	12	8	6	10	7	6
3d	10	8	7	10	7	6
3e	9	6	3	9	6	4
3f	8	6	5	8	6	5
3g	12	9	7	10	7	6
3h	13	7	6	6	6	3
3i	10	7	6	9	6	4
3j	12	8	7	11	7	6
Penicillin[a]	12	8	–	10	7	6

[a] Reference compound.

*[{(3-Dimethoxy-phosphoryl)-(phenyl-methyl)-2-oxo-2-phenyl-2,3-dihydro-2λ^5-benzo [1,3,2]diazaphosphol-1-yl}-(phenyl)-methyl]-phosphonic acid dimethyl ester (**3a**)*. Yield 72%, mp 189–191°C. IR (KBr) cm^{-1}: 1269 (P=O, phosphonate), 1219 (P=O, diazaphosphole), 769 (P—C); ^{1}H-NMR (DMSO-d_6): 6.5–7.5(m,19H), 4.74 (2H, d, J = 11.0 Hz, P—CH), 3.43 (6H, d, J = 10.0 Hz, $POCH_3$) 3.63 (6H, d, J = 11.3 Hz, $POCH_3$); ^{13}C-NMR data: 127.35 (C-3a and C-7a), 113.42 (C-4 and C-7), 117.74 (C-5 and C-6), 50.01 (d, C-1′ and C-1′a, J = 132 Hz), 142.78 (C-2′ and C-2′a), 127.13 (C-3′,C-7′ and C-3′a,C-7′a), 128.39 (C-4′,C-6′ and C-4′a,C-6′a), 126.43 (C-5′ and C-5′a), 135.13 (C-1″), 129.67 (C-2″ and C-6″), 128.62 (C-3″ and C-5″), 131.69 (C-4″), 55.12 ($POCH_3$); ^{31}P-NMR data: δ 24.65 (P=O, phosphonates), 3.00 (P=O, diazaphosphole); FAB-MS m/z: 626 (M^+); Anal. Calcd. for: $C_{30}H_{33}N_2O_7P_3$: C, 57.51; H, 5.31; N, 4.47. Found C, 57.47; H, 5.26; N, 4.41.

*[{(3-Dimethoxy-phosphoryl)-(4-chloro-phenyl-methyl)-2-oxo-2-phenyl-2,3-dihydro-2λ^5-benzo[1,3,2]diazaphosphol-1-yl}-(4-chloro-phenyl)-methyl]-phosphonic acid dimethyl ester (**3b**)*. Yield 70%, mp 197–199°C. IR (KBr) cm^{-1}: 1271 (P=O, phosphonate), 1210 (P=O, diazaphosphole), 753 (P—C); ^{1}H-NMR (DMSO-d_6): 6.8–8.2 (m, 17H, ArH), 5.51 (2H, d, J = 11.3 Hz, PCH), 3.51 (6H, d, J = 10.1 Hz, $POCH_3$) 3.54 (6H, d, J = 9.90 Hz, $POCH_3$); ^{13}C-NMR data: 127.39 (C-3a and C-7a), 113.62 (C-4 and C-7), 118.31 (C-5 and C-6), 50.93 (C-1′ and C-1′a, d, J = 139 Hz), 140.61 (C-2′ and C-2′a), 128.79 (C-3′,C-7′ and C-3′a,C-7′a), 128.97 (C-4′,C-6′ and C-4′a,C-6′a), 130.98 (C-5′ and C-5′a), 134.98 (C-1″), 129.78 (C-2″ and C-6″), 128.69 (C-3″ and C-5″), 131.57 (C-4″), 55.72 ($POCH_3$); ^{31}P-NMR data: δ 40.65 (P=O, phosphonates), 4.03 (P=O, diazaphosphole); FAB-MS m/z: 694 (M^+), 696 (M+2); Anal. Calcd. for: $C_{30}H_{31}N_2O_7P_3Cl_2$: C, 51.81; H, 4.91; N, 4.03. Found C, 51.77; H, 4.85; N, 3.97.

*[{(3-Dimethoxy-phosphoryl)-(3-nitro-phenyl-methyl)-2-oxo-2-phenyl-2,3-dihydro-2λ^5-benzo[1,3,2]diazaphosphol-1-yl}-(3-nitro-phenyl)-methyl]-phosphonic acid dimethyl ester (**3c**)*. Yield 72%, mp 204–206°C. IR (KBr) cm^{-1}: 1264 (P=O, phosphonate), 1205 (P=O, diazaphosphole), 761 (P—C); ^{1}H-NMR (DMSO-d_6): 6.4–7.9 (m, 17H, ArH), 5.67 (2H, d, J = 10.9 Hz, PCH), 3.48 (6H, d, J = 10.3 Hz, $POCH_3$) 3.54 (6H, d, J = 9.30 Hz, $POCH_3$); ^{31}P-NMR data: δ 28.63 (P=O, phosphonates), 2.63 (P=O, diazaphosphole); Anal. Calcd. for: $C_{30}H_{31}N_4O_{11}P_3$: C, 50.29; H, 4.36; N, 7.82. Found C, 50.25; H, 4.30; N, 7.77.

*[{(3-Dimethoxy-phosphoryl)-(3-chloro-phenyl-methyl)-2-oxo-2-phenyl-2,3-dihydro-2λ^5-benzo[1,3,2]diazaphosphol-1-yl}-(3-chloro-phenyl)-methyl]-phosphonic acid dimethyl ester (**3d**)*. Yield 69%, mp 201–203°C. IR (KBr) cm^{-1}: 1272 (P=O, phosphonate), 1192 (P=O, diazaphosphole), 749 (P—C); ^{1}H-NMR (DMSO-d_6): 6.61–7.81 (m, 17H, ArH), 5.75 (2H, d, J = 10.7 Hz, PCH), 3.43 (6H, d, J = 11.4 Hz, $POCH_3$) 3.51 (6H, d, J = 10.3 Hz, $POCH_3$); ^{31}P-NMR data: δ 21.24 (P=O, phosphonates), 0.27 (P=O, diazaphosphole); Anal. Calcd. for: $C_{30}H_{31}N_2O_7P_3Cl_2$: C, 51.81; H, 4.91; N, 4.03. Found C, 51.78; H, 4.88; N, 3.97.

*[{(3-Dimethoxy-phosphoryl)-(3,4-dimethoxy-phenyl-methyl)-2-oxo-2-phenyl-2,3-dihydro-2λ^5-benzo[1,3,2]diazaphosphol-1-yl}-(3,4-dimethoxy-phenyl)-methyl]-phosphonic acid dimethyl ester (**3e**)*. Yield 67%, mp 207–209°C. IR (KBr) cm^{-1}: 1272 (P=O, phosphonate), 1192 (P=O, diazaphosphole), 749 (P—C); ^{1}H-NMR (DMSO-d_6): 6.2–7.9 (m, 29H, ArH), 5.49 (2H, d, J = 11.0 Hz, PCH), 3.61 (6H, d, J = 10.4 Hz, $POCH_3$) 3.67 (6H, d, J = 10.5 Hz, $POCH_3$), 3.71 (s, 12H, OCH_3); ^{31}P-NMR data: δ 26.12 (P=O, phosphonates), 1.32 (P=O, diazaphosphole); Anal. Calcd. for: $C_{34}H_{41}N_2O_{11}P_3$: C, 54.70; H, 5. 54; N, 3.75. Found C, 54.65; H, 5.50; N, 3.70.

*[{(3-Diethoxy-phosphoryl)-(phenyl-methyl)-2-oxo-2-phenyl-2,3-dihydro-2λ^5-benzo [1,3,2]diazaphosphol-1-yl}-(phenyl)-methyl]-phosphonic acid diethyl ester (**3f**)*. Yield 71%, mp 183–185°C. IR (KBr) cm^{-1}: 1259 (P=O, phosphonate), 1207 (P=O, diazaphosphole), 760 (P—C); ^{1}H-NMR (DMSO-d_6): 6.10–7.70 (m, 19H, ArH), 5.47–5.62 (2H, d, J = 10.3 Hz, PCH), 3.62–4.08 (m, 8H, $POCH_2CH_3$), 1.31 (6H, t, J = 8.3 Hz, $POCH_2CH_3$) 1.16 (6H, t, J = 8.1 Hz, $POCH_2CH_3$); ^{13}C-NMR data: 126.30 (C-3a and C-7a), 115.20 (C-4 and C-7), 117.74 (C-5 and C-6), 49.01 (C-1′ and C-1′a, d, J = 132 Hz), 146.78 (C-2′ and C-2′a), 125.19 (C-3′,C-7′ and C-3′a,C-7′a), 128.01 (C-4′,6′ and C-4′a,C-6′a), 124.43 (C-5′ and C-5′a), 133.13 (C-1″), 128.60 (C-2″ and C-6″), 127.69 (C-3″ and

Table 2

Antifungal activity of compounds **3a–j** (μg/mL).

	Zone of inhibition (%)					
	Aspergillus niger			*Helminthosporium oryzae*		
Compounds	100	50	25	100	50	25
3a	8	5	4	9	7	4
3b	14	8	6	13	10	7
3c	12	7	6	12	10	7
3d	8	5	3	10	8	5
3e	10	6	5	10	6	5
3f	10	6	5	11	7	6
3g	13	7	5	9	5	3
3h	13	7	7	12	10	7
3i	9	8	7	10	8	7
3j	12	7	6	12	9	6
Griseofulvin[a]	12	7	–	12	9	–

[a] Reference compound.

Table 3

Minimum inhibitory concentration of compounds **3a–j** (μg/mL).

Bacteria	3a	3b	3c	3d	3e	3f	3g	3h	3i	3j
Escherichia coli	600	380	380	540	580	630	390	300	550	400
Staphylococcus aureus	550	400	310	300	410	500	300	620	410	340

C-5″), 132.61 (C-4″), 63.5 (d, $^2J_{POC}$ = 7.3 Hz, P—O*C*H$_2$—CH$_3$), 15.3 (d, $^3J_{POCC}$ = 6.1 Hz, P—OCH$_2$—*C*H$_3$); ^{31}P-NMR data: δ 31.49 (P=O, phosphonates), 1.91 (P=O, diazaphosphole); Anal. Calcd. for: $C_{34}H_{41}N_2O_{17}P_3$: C, 59.82; H, 6.05; N, 4.10. Found C, 59.78; H, 6.00; N, 4.05.

*[{(3-Diethoxy-phosphoryl)-(4-chloro-phenyl-methyl)-2-oxo-2-phenyl-2,3-dihydro-2λ^5-benzo[1,3,2]diazaphosphol-1-yl}-(4-chloro-phenyl)-methyl]-phosphonic acid diethyl ester (**3g**).* Yield 68%, mp 195–197°C. IR (KBr) cm^{-1}: 1261 (P=O, phosphonate), 1201 (P=O, diazaphosphole), 757 (P—C); ^{1}H-NMR (DMSO-d_6): 66.6–8.4 (m, 17H, ArH), 5.58 (2H, d, J = 11.5 Hz, PCH), 3.61–4.04 (m, 8H, POC*H*$_2$CH$_3$), 1.25 (6H, t, J = 8.0 Hz, POCH$_2$C*H*$_3$), 1.09 (6H, t, J = 7.9 Hz, POCH$_2$C*H*$_3$); ^{31}P-NMR data: δ 29.82 (P=O, phosphonates), 2.47 (P=O, diazaphosphole); Anal. Calcd. for: $C_{34}H_{39}N_2O_7P_3Cl_2$: C, 54.34; H, 5.23; N, 3.73. Found C, 54.30; H, 5.20; N, 3.69.

*[{(3-Diethoxy-phosphoryl)-(3-nitro-phenyl-methyl)-2-oxo-2-phenyl-2,3-dihydro-2λ^5-benzo[1,3,2]diazaphosphol-1-yl}-(3-nitro-phenyl)-methyl]-phosphonic acid diethyl ester (**3h**).* Yield 69%, mp 227–229°C. IR (KBr) cm^{-1}: 1271 (P=O, phosphonate), 1211 (P=O, diazaphosphole), 762 (P—C); ^{1}H-NMR (DMSO-d_6): 6.1–8.3 (m, 17H, ArH), 5.24 (2H, d, J = 10.8 Hz, PCH), 3.73–4.17 (m, 8H, POC*H*$_2$CH$_3$), 1.22 (6H, t, J = 8.5 Hz, POCH$_2$C*H*$_3$), 1.12 (6H, t, J = 7.8 Hz, POCH$_2$C*H*$_3$); ^{31}P-NMR data: δ 22.13 (P=O, phosphonate), 3.12 (P=O, diazaphosphole); Anal. Calcd. for: $C_{34}H_{39}N_4O_{11}P_3$: C, 53.85; H, 5.09; N, 7.25. Found C, 52.80; H, 5.03; N, 7.20.

*[{(3-Diethoxy-phosphoryl)-(3-chloro-phenyl-methyl)-2-oxo-2-phenyl-2,3-dihydro-2λ^5-benzo[1,3,2]diazaphosphol-1-yl}-(3-chloro-phenyl)-methyl]-phosphonic acid diethyl ester (**3i**).* Yield 65%, mp 220–222°C. IR (KBr) cm^{-1}: 1267 (P=O, phosphonate), 1197 (P=O, diazaphosphole), 759 (P—C); ^{1}H-NMR (DMSO-d_6): 6.8–8.5 (m, 17H, ArH), 5.31 (2H, d, J = 11.4 Hz, PCH), 3.72–4.11 (m, 8H, POC*H*$_2$CH$_3$), 1.28 (6H, t, J = 8.1 Hz, POCH$_2$C*H*$_3$), 1.11 (6H, t, J = 7.7 Hz, POCH$_2$C*H*$_3$); ^{31}P-NMR data: δ 24.12 (P=O, phosphonates), 2.11 (P=O, diazaphosphole); Anal. Calcd. for: $C_{34}H_{39}N_2O_7P_3Cl_2$. Found C, 54.34; H, 5.23; N, 3.73 C, 54.28; H, 5.19; N, 3.70.

*[{(3-Diethoxy-phosphoryl)-(3,4-dimethoxy-phenyl-methyl)-2-oxo-2-phenyl-2,3-dihydro-2λ^5-benzo[1,3,2]diazaphosphol-1-yl}-(3,4-dimethoxy-phenyl)-methyl]-phosphonic acid diethyl ester (**3j**).* Yield 70%, mp 215–217°C. IR (KBr) cm^{-1}: 1269 (P=O, phosphonate), 1203 (P=O, diazaphosphole), 749 (P—C); ^{1}H-NMR (DMSO-d_6): 6.2–8.2 (m, 29H, ArH), 5.48 (2H, d, J = 11.8 Hz, PCH), 3.69–4.08 (m, 8H, POC*H*$_2$CH$_3$), 1.26 (6H, t, J = 8.4 Hz, POCH$_2$C*H*$_3$) 1.14 (6H, t, J = 8.1 Hz, POCH$_2$C*H*$_3$), 3.73 (s, 12H,(OCH$_3$); ^{13}C-NMR data: 126.51 (C-3̂ and C-7a), 113.92 (C-4 and C-7), 116.13 (C-5 and C-6), 51.13 (C-1′ and C-1′a, d, J = 133 Hz), 134.72 (C-2′ and C-2′a), 113.22 (C-3′ and C-3′a), 146.20 (C-4′ and C-4′a), 144.12 (C-5′ and C-5′a), 114.96 (C-6′ and C-6′a), 118.02 (C-7′ and C-7′a), 134.02 (C-1″), 128.09 (C-2″ and C-6″), 127.71 (C-3″ and C-5″), 131.90 (C-4″), 55.13 (OCH$_3$) 62.5 (d, $^2J_{POC}$ = 7.5 Hz, P—O*C*H$_2$—CH$_3$), 16.3 (d, $^3J_{POCC}$ = 6.9 Hz, P—OCH$_2$—*C*H$_3$); ^{31}P-NMR data: δ 25.32 (P=O, phosphonate), 1.02 (P=O, diazaphosphole); Anal. Calcd. for: $C_{38}H_{49}N_2O_{11}P_3$: C, 56.86; H, 6.15; N, 3.49. Found C, 56.80; H, 6.10; N, 3.44.

Antimicrobial activity. Antimicrobial activity of **3a–j** was tested against the growth of *Staphylococcus aureus* (ATCC 25923) (Gram +ve) and *Escherichia coli* (ATCC 25922) (Gram −ve) by disc diffusion method at various concentrations (100, 50, and 25 ppm; Table 1) [16]. All the compounds showed moderate activity against both the bacteria. The highlight is that the five compounds, **3b**, **3c**, **3g**, **3h**, and **3j** were more effective than even the standard penicillin.

They were also screened for antifungal activity against *Aspergillus niger* (ATCC 16404) and *Helminthosporium oryzae* (ATCC 11000) species along with the standard fungicide Griseofulvin (Table 2) by the disc diffusion method at three different concentrations (100, 50, and 25 ppm). It is gratifying to observe that majority of the compounds (**3a–j**) exhibited higher antifungal activity when compared with that of Griseofulvin. Significant result is that **3b**, **3c**, **3g**, **3h**, and **3j** exhibited higher activity than the standard Griseofulvin against both the fungi. Thus new group of compounds with very high antimicrobial/fungicidal activity than the presently used commercial bactericides/fungicides have been discovered.

Determination of minimum inhibitory concentration. Minimum inhibitory concentration was determined for the compounds **3a–j** (Table 3) that showed total growth inhibition using the protocol described below. The compound concentration of 50–700 μg/mL in steps of 25 μg/mL was evaluated. Specifically 0.1 mL of standardized inoculum (1–2 × 10^7 CFU/mL) was added to each test tube. Two controls (DMSO with bacteria and antibiotics with bacteria) were maintained for each test sample. The tubes were incubated aerobically at 37°C for 18–24 h [17].

Acknowledgments. The authors thank CSIR, Human Resources Development Group, Government of India, New Delhi, for providing financial assistance (01/2347/09/EMR-II).

REFERENCES AND NOTES

[1] Weil, E. D. In Handbook of Organophosphorus Chemistry; Engel, R., Ed.; Marcel Dekker: New York, 1992; p 683.

[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. In Fire Retardancy of Polymeric Materials; Grand, A., Wilkie, C.A., Eds.; Marcel Dekker: New York, 2000; p 147.

[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, R371.

[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. EP472077, 1992.

[12] Ordonez, M.; Rojas-Cabrera, H.; Cativiela, C. Tetrahydron 2009, 65, 17.

[13] Kiran, Y.B.; Reddy, C. D.; Gunasekar, D.; Reddy, C. S.; Leon A.; Barbosa, L. C. A. Eur J Med Chem 2008, 43, 885.

[14] Narayana Reddy, M. V.; Siva Kumar, B.; Balakrishna, A.; Reddy, C. S.; Nayak, S. K.; Reddy, C. D. ARKIVOC 2007, xv, 246.

[15] Reddy, M. V. N.; Krishna, A. B.; Anil Kumar, M.; Reddy, G. C. S.; Reddy, C. S.; Krishna, T. M. Chem Pharm Bull 2009, 57, 1391.

[16] Mangte, D. V.; Deshmukh, S. P.; Bhokare, D. D.; Arti Deshpande, A. Indian J Pharm 2007, 69, 295.

[17] Omer, E. Biologia 2006, 61, 275.