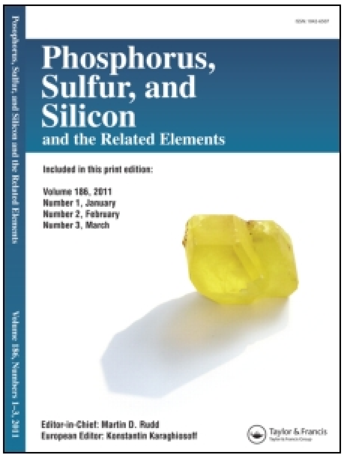

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Synthesis, Spectral, and Antifungal Evaluation of Phosphorylated and Thiophosphorylated Benzothiazole Derivatives

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Synthesis, Spectral, and Antifungal Evaluation of Phosphorylated and Thiophosphorylated Benzothiazole Derivatives

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The phosphorylated and thiophosphorylated benzothiazole derivatives have been synthesized by the reaction of phosphorus oxychloride/phosphorus thiochloride with 2-(2′-aminophenyl)benzothiazole in 1:1, 2:1, 3:1, and 1:2 molar ratios in presence of triethylamine. Plausible structures have been proposed on the basis of elemental analysis IR, ^{1}H NMR, ^{31}P NMR, and mass spectral studies. The fungicidal activity of these derivatives have been evaluated against pathogenic fungi Aspergillus niger *and* Fusarium oxysporium. *The fungicidal data reveals that these compounds are more fungitoxic than the parent 2-(2′-aminophenyl)benzothiazole compound.*

Keywords Phosphorylation; phosphorylated derivatives; 2-(2′-aminophenyl) benzothiazole; fungicidal activity

INTRODUCTION

Organophosphorus compounds being ubiquitous in nature have found multifaced applications. These are being used as pesticides, insecticides, fungicides, and bactericides.[1–3] Various phosphorylated compounds of benzothiazole and amines are also associated with antifungal activities.[4–6]

In continuation of our previous work,[7] we report herein the synthesis, characterization, and antifungal activity of some phosphorylated and thiophosphorylated benzothiazole derivatives.

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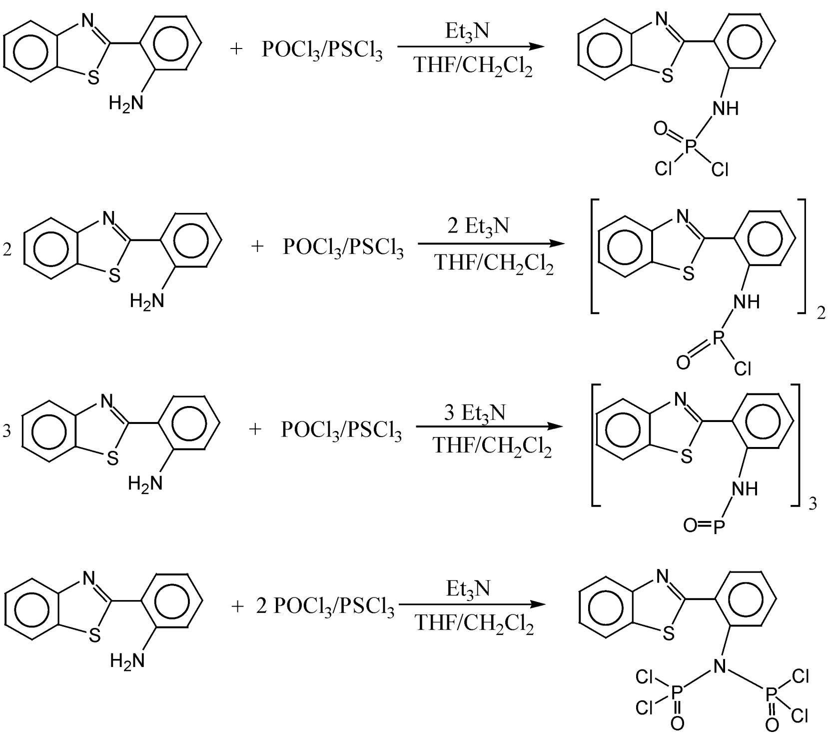

SCHEME 1

RESULT AND DISCUSSION

2-(2′-aminophenyl)benzothiazole were reacted with $POCl_3/PSCl_3$ (1:1, 2:1, 3:1, and 1:2 molar ratio) in the presence of stoichiometric amount of triethylamine in THF/methylene dichloride resulted in the formation of corresponding phosphorylated and thiophosphorylated benzothiazole derivatives (Scheme 1). Physical and analytical details of the compounds are given in Table 1.

IR Spectra

The formation of phosphorylated and thiophosphorylated benzothiazole derivatives was identified by disappearance of ν (NH_2) absorption band at 3400–3300 cm^{-1} present in 2-(2′-amino phenyl)benzothiazole and appearance of absorption band at 2960–2940 cm^{-1} along with 2890–2855 cm^{-1} for N—H stretching of P—NH band.[5] In phosphorylated and thiophosphorylated derivatives of 2-(2′-aminophenyl)benzothiazole, characteristic stretching vibrations

TABLE I Analytical Data of 2-(2′-aminophenyl)benzothiazole and its Phosphorylated and Thiophosphorylated Derivatives

Compounds	Yield (%)	State	Analysis(%) Found (Calcd.)						Mol.Wt. Found (Calcd.)
			C	H	N	S	P	Cl	
$(C_{13}H_9N_2S)P(O)Cl_2$	65	Liquid	45.17 (45.50)	2.58 (2.64)	8.01 (8.16)	9.12 (9.34)	8.76 (9.02)	20.01 (20.66)	340.12 (343.17)
$(C_{13}H_9N_2S)_2P(O)Cl$	59	Liquid	58.10 (58.59)	3.21 (3.40)	10.17 (10.51)	11.84 (12.03)	5.76 (5.81)	6.15 (6.65)	529.23 (533.01)
$(C_{13}H_9N_2S)_3P(S)$	57	Liquid	64.65 (64.76)	3.13 (3.76)	11.58 (11.68)	13.11 (13.30)	4.22 (4.28)	—	714.12 (723.27)
$(C_{13}H_9N_2S)P(S)Cl_2$	58	Liquid	43.39 (43.47)	2.41 (2.52)	7.69 (7.79)	17.21 (17.85)	8.59 (8.62)	18.99 (19.74)	340.23 (359.24)
$(C_{13}H_9N_2S)_2P(S)Cl$	56	Liquid	56.12 (56.87)	3.19 (3.30)	10.03 (10.20)	17.23 (17.52)	5.53 (5.64)	6.39 (6.46)	540.31 (549.08)
$(C_{13}H_9N_2S)_3P(S)$	54	Liquid	62.16 (63.36)	3.43 (3.68)	11.34 (11.42)	17.12 (17.35)	4.01 (4.18)	—	725.35 (739.34)
$(C_{13}H_8N_2S)P(O)(Cl_2)_2$	62	Liquid	33.08 (33.94)	1.69 (1.75)	5.91 (6.09)	6.91 (6.97)	13.37 (13.47)	29.92 (30.83)	458.47 (460.05)

ν(P=S)[1]. ν(P = O)[8] and ν(P-N-C)[5] appears at 900–820 cm^{-1} and 720–655 cm^{-1}, 1255-1230 cm^{-1}, 1050-1040 and 660-650 cm^{-1}, respectively.

^{1}H NMR Spectra

In the ^{1}H NMR spectra of phosphorylated and thiophosphorylated derivatives, the -NH proton signal was observed at δg.6–5.8 ppm as doublet due to 'P' splitting. In ^{x}H NMR spectra of 2-(2′-aminophenyl)benzothiazole NH proton was appeared at δ 5.2 ppm as a singlet. Aromatic protons were observed at δ 6.8–8.6 ppm.

^{31}P NMR Spectral

All the phosphorylated and thiophosphorylated benzothiazole derivatives were characterized by the down field ^{31}P NMR signal at δ 59–71 ppm.[9]

Mass Spectra

Mass spectra was recorded for determining the molecular mass of the phosphorylated compounds. The splitting pattern of the mass spectrum of compound $(C_{13}H_8N_2S)\{P(O)(Cl_2)\}_2$ is represented in Figure 1.

The molecular ion peak appears at 458.2 thus confirming the formation of compound $(C_{13}H_8N_2S)\{P(O)(Cl_2)\}_2$. This peak after removal of four chlorine radicals in the subsequent steps generates the ion at m/z 423.6, m/z 389.1, m/z 353.6, and m/z 318.2, respectively. It may further lose the ions at m/z 303.24 and m/z 287.2, respectively. Further fragmentation involve removal of two phosphorus radicals in subsequent steps and formation of peaks at m/z 255.3 and m/z 224.2, respectively. After removal of nitrogen radical a peak appears at m/z 211.5, which splits off a phenyl moiety producing an ion at m/z 133.3 in the mass spectrum. Splitting of benzothiazolyl moiety leads to peak at m/z 327. Further fragmentation involves removal of phenyl radical and formation of peak at m/z 249. Relative abundance of these ions are represented in Table V.

Antifungal Activity

Results of the fungicidal screening of the synthesized phosphorylated and thiophosphorylated benzothiazole derivatives against *Aspergillus niger* and *Fusarium oxysporium* are summarized in Table III. The

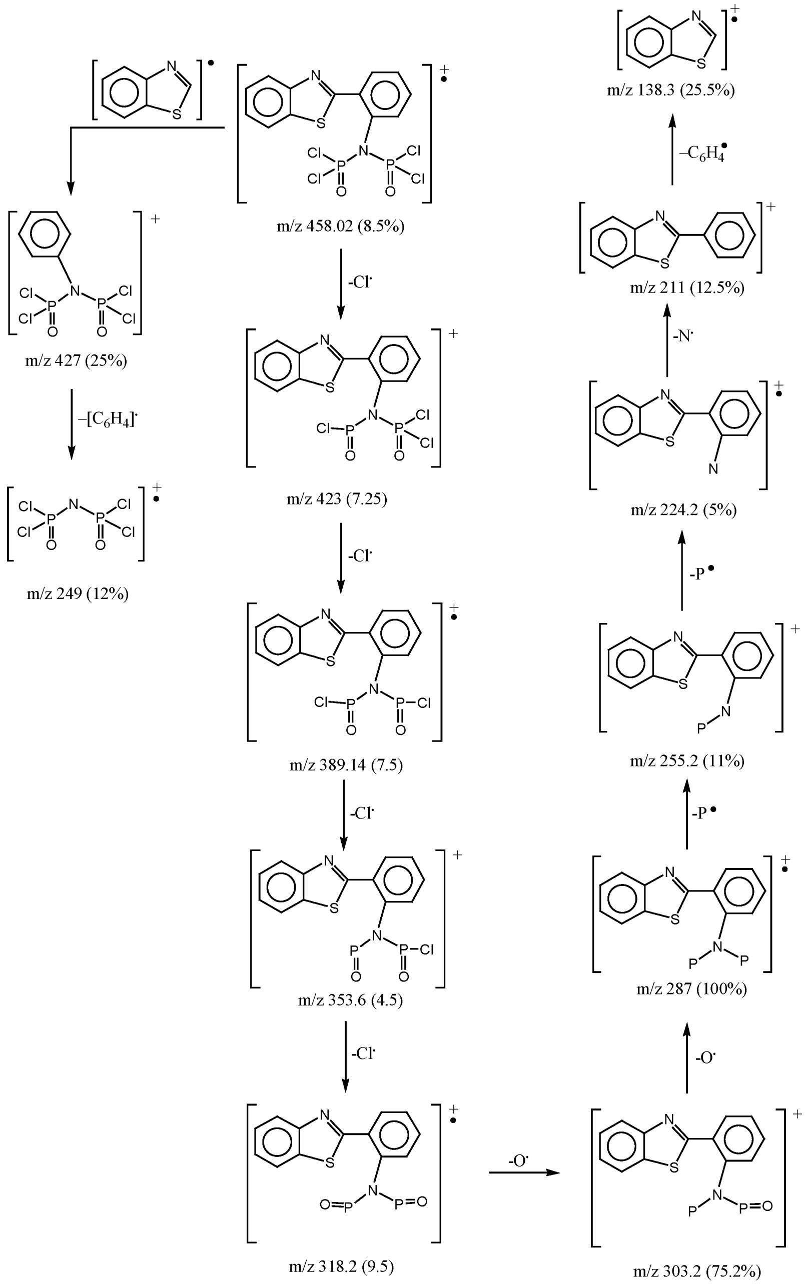

FIGURE 1 Suggested Structure of $(C_{13}H_8N_2S)P(O)(Cl_2)_2$ and the Splitting Pattern of its Mass Spectrum.

TABLE II Assignment of Main IR Bands (cm^{-1}) of Phosphorylated and Thiophosphorylated Benzothiazole Derivatives

Compounds	v (P—NH)	v (P=S)	v (P—Cl)	v(P-Cl) (P—Cl)	v (P—N—Cl)
$(C_{13}H_9N_2S)P(O)Cl_2$	2940 2855	—	515 (sym) 600 (asym)	1230	1040 (I) 650 (II)
$(C_{13}H_9N_2S)_2P(O)Cl$	2945 2860	—	520 (sym) 600 (asym)	1245	1045 (I) 660 (II)
$(C_{13}H_9N_2S)_3P(S)$	2950 2890	—	—	1255	1055 (I) 650 (II)
$(C_{13}H_9N_2S)P(S)Cl_2$	2955 2880	820 655	520 (sym) 610 (asym)	—	1045 (I) 650 (II)
$(C_{13}H_9N_2S)_2P(S)Cl$	2955 2870	855 695	530 (sym) 610 (asym)	—	1055 (I) 655 (II)
$(C_{13}H_9N_2S)_3P(S)$	2960 2890	895 720	—	—	1060 (I) 655 (II)
$(C_{13}H_8N_2S)\{P(O)(Cl_2)\}_2$	—	—	515 (sym) 600 (asym)	1250	1050 (I) 660 (II)

antifungal activity of phosphorylated and thiophosphorylated derivatives were found to be greater than that of the corresponding starting material. These compounds were compared with commercial fungicides dithane M-45.

Among phosphorylated and thiophosphorylated derivatives $(C_{13}H_9N_2S)_3P(S)$ showed stronger fungitoxic activity against both fungi which is in accordance to the literature.[7]

TABLE III Fungitoxic Screening Data of Organophosphorus Derivatives Containing 2-Substituted Benzothiazoles

	Percent mycelial inhibition					
	Aspergillus niger compound dose (ppm)			*Fusarium oxysporium* compounddose (ppm)		
Compounds	50	100	200	50	100	200
$(C_{13}H_9N_2S)P(O)Cl_2$	15.5	58.1	76.3	18.7	47.3	63.7
$(C_{13}H_9N_2S)_2P(O)Cl$	36.7	61.6	76.1	39.3	54.4	74.6
$(C_{13}H_9N_2S)_3P(S)$	45.3	68.4	86.3	48.5	65.9	78.2
$(C_{13}H_9N_2S)P(S)Cl_2$	21.2	61.5	78.2	37.3	57.7	69.1
$(C_{13}H_9N_2S)_2P(S)Cl$	51.2	73.7	81.6	45.8	74.2	76.3
$(C_{13}H_9N_2S)_3P(S)$	69.3	81.8	92.7	69.1	88.5	94.5
$(C_{13}H_8N_2S)\{P(O)(Cl_2)\}_2$	43.4	65.4	79.2	47.1	64.7	76.5
Dithane M-45	75	90	100	73	92	100

TABLE IV ^{1}H NMR and ^{31}P NMR Spectral data of Phosphorylated and Thiophosphorylated Derivatives

Compounds	^{31}P NMR ($CDCl_3$)	^{1}HNMR(δ ppm) (Ar—H)	^{1}HNMR(δ ppm) (P—NH)
$(C_{13}H_9N_2S)P(O)Cl_2$	68.2	6.8–7.9	5.6
$(C_{13}H_9N_2S)_2P(O)Cl$	63.5	7.7–8.4	5.7
$(C_{13}H_9N_2S)_3P(S)$	59.7	7.9–8.6	5.8
$(C_{13}H_9N_2S)P(S)Cl_2$	70.6	7.5–8.0	5.7
$(C_{13}H_9N_2S)_2P(S)Cl$	65.8	8.6–8.0	5.8
$(C_{13}H_9N_2S)_3P(S)$	61.3	7.7–8.2	5.8
$(C_{13}H_8N_2S)\{P(O)(Cl_2)\}_2$	66.4	7.8–8.5	5.7

EXPERIMENTAL

All the commercial reagents and solvents were dried and distilled by common methods before use. $POCl_3/PSCl_3$ were purchased from Fluka.

Melting points were determined by capillary method and are uncorrected. All operations involving phosphorus compounds were carried out in dry equipment under nitrogen atmosphere. IR spectra were recorded on a Perkin-Elmer 577 grating spectrometer in KBr discs in the region 4000–200 cm^{-1}. NMR spectra were recorded on JEOL FX-90Q spectrophotometer using $CDCl_3$ as solvent. Nitrogen was estimated by Kjeldahl's method. Phosphorus was estimated as ammonium phosphomolybdate. Chlorine was estimated volumetrically by Volhard's method.

Synthesis of Ligand

The ligand 2-(2′-aminophenyl)benzothiazole was synthesized on the basis of previously reported method.[10]

Synthesis of $(C_{13}H_9N_2S)P(O)Cl_2/(C_{13}H_9N_2S)P(S)Cl_2$

In a fast stirring solution of 2-(2′-aminophenyl)benzothiazole (0.001 mol) and Et_3N (0.001 mol) in dry THF/CH_2Cl_2, solution of $POCl_3/PSCl_3$

TABLE V Mass Spectral Data of $(C_{13}H_8N_2S)P(O)(Cl_2)_2$ (Relative Abundance is Given in Parent Theses)

Compound	m/z %
$(C_{13}H_8N_2S)\{P(O)(Cl_2)\}_2$	458.2 (8.5%), 423.1 (7.5%), 389.6 (7.5%), 353.6(4.5%), 327 (25%), 318.2 (9.5%), 303.2 (75%), 287 (100%), 255.3 (11%), 249(12%), 224.2 (5%),211.5 (12.5%), 133.3 (25.5%)

(0.001 mol) in dry THF was added dropwise. Reaction mixture was then filtered through closed sintered funnel in another round bottom flask and then refluxed under nitrogen atmosphere for 14–15 h. Then it was cooled and filtered through closed sintered funnel. Filtrate was then concentrated to 1/4 of its volume and kept for crystallization in vaccum for 2 days. It was recrystallized from dry ethanol.

Synthesis of $(C_{13}H_9N_2S)_2P(O)Cl$/ $(C_{13}H_9N_2S)_2P(S)Cl$

In a fast stirring solution of 2-(2′-aminophenyl)benzothiazole (0.002 mole) and Et_3N (0.002 mol) in dry THF/CH_2Cl_2, solution of $POCl_3$/$PSCl_3$ (0.001 mol) in dry THF was added dropwise. Then the reaction was carried out in a manner similar to described above. Product was filtered, concentrated, and recrystallized from dry ethanol.

Synthesis of $(C_{13}H_9N_2S)_3P(O)$/$(C_{13}H_9N_2S)_3P(S)$

In a fast stirring solution of 2-(2′-aminophenyl)benzothiazole (0.003 mol) and Et_3N (0.003 mol) in dry THF/CH_2Cl_2, solution of $POCl_3$ (0.001 mol) in dry THF was added dropwise by dropping funnel. Then the reaction was carried out in a similar manner as described above. Product was recrystallized from dry ethanol.

Synthesis of $(C_{13}H_8N_2S)\{P(O)(Cl_2)\}_2$

In a fast stirring solution of 2-(2′-aminophenyl)benzothiazole (0.001 mol) and Et_3N (0.001 mole) in dry THF/CH_2Cl_2, solution of $POCl_3$ (0.002 mol) in dry THF was added dropwise by dropping funnel. Then the reaction was carried out in a similar manner as described above. Product was recrystallized from dry ethanol.

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