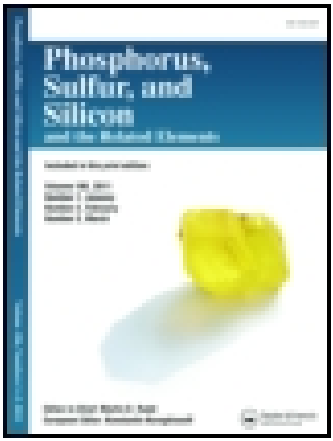

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Synthesis and Biocidal Activity of Organophosphates Derived from Benzothiazole

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Synthesis and Biocidal Activity of Organophosphates Derived from Benzothiazole

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The synthesis, biocidal activity, and spectroscopic data of a new series of S-phosphorylated/thiophosphorylated derivatives of 2-(2′-mercaptophenyl) benzothiazole are reported in this study. Derivatives were prepared by reacting 2-(2′-mercaptophenyl) benzothiazole with phosphorus oxychloride/phosphorus thiochloride in different molar ratios [1:1, 2:1, 3:1]. All of the derivatives were found to be antifungal agents with less toxicity than the standard Dithane M-45.

Keywords Fungicidal activity; **S-**phosphorylated/thiophosphorylated derivatives of 2-(2′-mercaptophenyl) benzothiazole

INTRODUCTION

Heterocyclic compounds are an important group of ligands in organophosphorus chemistry and find a critical role in various fields.[1–3] Organophosphates are biodegradable, short-lived chemical compounds, and their mode of action involves inhibition of acetylcholinesterase (AChE).[4] Organophosphorus compounds have found numerous applications in insecticides, fungicides, herbicides, and pesticides.[5–11] These compounds find considerable use as asymmetric hydrogenating catalysts, medicines, and flame retardants.[12–15] 2-Mercaptobenzoxazole has been found to possess various pharmacological and biological activities.[16] Taking this into consideration, we have synthesized the phosphorylated/thiophosphorylated derivatives of 2-(2′-mercaptophenyl) benzothiazole.

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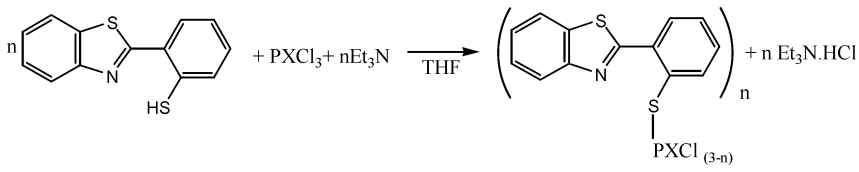

Where n = 1, 2, 3
X = O/S

SCHEME 1

RESULTS AND DISCUSSION

The S-phosphorylated benzothiazole derivatives have been synthesized by the reaction of 2-(2′-mercaptophenyl)benzothiazole with phosphorous oxychloride/phosphorous thiochloride (1:1, 2:1, and 3:1 molar ratio) in the presence of a stoichiometric amount of triethylamine in THF. $(C_{13}H_8NS_2)P(O)Cl_2$ (**1**), $(C_{13}H_8NS_2)P(S)Cl_2$ (**2**), $(C_{13}H_8NS_2)_2P(O)Cl$(**3**), $(C_{13}H_8NS_2)_2P(S)Cl$ (**4**), $(C_{13}H_8NS_2)_3P(O)$ (**5**), and $(C_{13}H_8NS_2)_3P(S)$ (**6**) were synthesized as exhibited in Scheme 1. The physical and analytical data of the compounds are given in Table I.

IR Spectra

In the 2-(2′-mercaptophenyl)benzothiazole ligand, an absorption band is found at 2550 cm^{-1}, which is characteristic of the -SH group. Bands due to ν(S-H) at 2550 cm^{-1} were absent in all the reported phosphorylated and thiophosphorylated benzothiazole derivatives due to the deprotonation of the -SH group, resulting in the formation of P-S-C bonds. In the phosphorylated and thiophosphorylated derivatives of 2-(2′-mercaptophenyl)benzothiazole, characteristic stretching vibrations of ν(P=S), ν(P=O) and ν(P-S-C)[17–18] are found in a range of 654–685, 1240–1255, and 530–575 cm^{-1}, which further confirms the formation of S-phosphorylated/thiophosphorylated benzothiazole. The results of the IR spectra are summarized in Table II.

^{1}H NMR Spectra

The ^{1}H NMR spectrum of 2-(2′-mercaptophenyl) benzothiazole shows a SH proton signal at ~3.60 ppm. In the phosphorylated/thiophosphorylated derivatives of substituted benzothiazole, the signal for the -SH proton is absent due to the removal of H by Cl of $POCl_3$/$PSCl_3$. The signals for the aromatic protons were found in the expected range of 6.4–7.4 ppm.[19]

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

Compounds	Yield (%)	State	Analysis (%) Found (Calcd.) C	H	N	P	S	Cl	Mol. wt. Found (Cal.)
(1) $(C_{13}H_8NS_2)P(O)Cl_2$	63	Liquid	43.16 (43.35)	2.14 (2.24)	3.82 (3.89)	8.49 (8.60)	17.69 (17.80)	19.62 (19.68)	357.33 (360.21)
(2) $(C_{13}H_8NS_2)P(S)Cl_2$	59	Liquid	41.12 (41.50)	2.11 (2.14)	3.64 (3.72)	8.14 (8.23)	25.49 (25.56)	18.70 (18.84)	374.11 (376.27)
(3) $(C_{13}H_8NS_2)_2P(O)Cl$	56	Liquid	54.23 (55.07)	2.70 (2.84)	4.87 (4.94)	5.37 (5.46)	22.53 (22.61)	6.16 (6.25)	561.67 (567.09)
(4) $(C_{13}H_8NS_2)_2P(S)Cl$	58	Liquid	53.12 (53.55)	2.69 (2.76)	4.61 (4.80)	5.23 (5.31)	27.35 (27.48)	5.92 (6.08)	578.31 (583.15)
(5) $(C_{13}H_8NS_2)_3P(O)$	62	Viscous liquid	59.81 (60.52)	2.98 (3.12)	5.39 (5.43)	3.89 (4.00)	24.72 (24.85)	—	769.24 (773.97)
(6) $(C_{13}H_8NS_2)_3P(S)$	54	Viscous liquid	59.01 (59.29)	2.96 (3.06)	5.21 (5.32)	3.84 (3.92)	28.29 (28.41)	—	787.89 (790.03)

TABLE II Assignment of Main IR Bands (cm^{-1}) of Phosphorylated and Thiophosphorylated Derivatives of 2-(2′-Mercaptophenyl) benzothiazole

	Compound	IR Bands (cm^{-1})			
		ν(P—S—C)	ν(P═O)	ν(P═S)	ν(P—Cl)
(1)	$(C_{13}H_8NS_2)P(O)Cl_2$	575	1255	—	584 (asym) 540 (sym)
(2)	$(C_{13}H_8NS_2)P(S)Cl_2$	555	—	685	554 (asym) 500 (sym)
(3)	$(C_{13}H_8NS_2)_2P(O)Cl$	565	1248	—	490
(4)	$(C_{13}H_8NS_2)_2P(S)Cl$	536	—	660	480
(5)	$(C_{13}H_8NS_2)_3P(O)$	560	1240	—	—
(6)	$(C_{13}H_8NS_2)_3P(S)$	530	—	654	—

^{31}P NMR Spectra

The phosphorylated and thiophosphorylated benzothiazole derivatives were characterized by the ^{31}P NMR signals obtained in the range of 58.4–68.3 ppm.[20] The results of the NMR spectra are summarized in Table III.

Antifungal Activity

The products have been screened for fungicidal properties against two fungi, namely *Aspergillus niger* and *Fusarium oxysporium* at concentrations 50, 100, and 200 ppm. Radial growth method was used to check an activity against fungi. The results of fungicidal screening of the phosphorylated/thiophosphorylated derivatives with standard Dithane M-45 are furnished in Table IV.

All the derivatives exhibited high toxicity towards both the fungi even at low concentrations. The inference drawn from the table reveals

TABLE III ^{1}H NMR and ^{31}P NMR Spectral Data of Phosphorylated and Thiophosporylated Derivatives of 2-(2′-Mercaptophenyl) benzothiazole

	Compounds	^{31}P NMR (δ ppm)	^{1}H NMR (δ ppm)
(1)	$(C_{13}H_8NS_2)P(O)Cl_2$	58.4	6.88–7.2 (m, 8H, Ar-**H**)
(2)	$(C_{13}H_8NS_2)P(S)Cl_2$	61.7	6.4–7.0 (m, 8H, Ar-**H**)
(3)	$(C_{13}H_8NS_2)_2P(O)Cl$	62.5	7.0–7.2 (m, 16H, Ar-**H**)
(4)	$(C_{13}H_8NS_2)_2P(S)Cl$	64.5	6.6–6.9 (m, 24H, Ar-**H**)
(5)	$(C_{13}H_8NS_2)_3P(O)$	65.2	7.0–7.4 (m, 24H, Ar-**H**)
(6)	$(C_{13}H_8NS_2)_3P(S)$	68.3	6.8–7.2(m, 24H, Ar-**H**)

TABLE IV Fungitoxic Screening Data of Organophosphorus Derivatives of 2-(2′-Mercaptophenyl)benzothiazole

		Percent mycelial inhibition					
		Aspergillus niger compounds (ppm)			*Fusarium oxysporium* compounds (ppm)		
	Compound	50	100	200	50	100	200
(1)	$(C_{13}H_8NS_2)P(O)Cl_2$	22.1	43.3	70.6	25.3	52.4	68.4
(2)	$(C_{13}H_8NS_2)P(S)Cl_2$	31.4	58.9	74.3	38.1	58.7	74.6
(3)	$(C_{13}H_8NS_2)_2P(O)Cl$	30.2	59.1	78.2	39.3	55.3	76.4
(4)	$(C_{13}H_8NS_2)_2P(S)Cl$	38.6	62.3	86.9	45.1	63.2	82.3
(5)	$(C_{13}H_8NS_2)_3P(O)$	78.3	85.6	92.4	73.1	83.2	88.1
(6)	$(C_{13}H_8NS_2)_3P(S)$	81.4	89.3	94.0	84.1	92.4	96.2
	Dithane M-45	87.0	92.0	100.0	76.0	94.0	100.0

that the activity of derivatives increases with an increase in concentration. Derivatives having a P=S bond resulted in higher toxicity than derivatives having P=O bond, with the same substituents attached to the phosphorus. $(C_{13}H_8NS_2)_3P(S)$ was found to be most toxic. Although the toxicity of all the newly synthesized derivatives was quite high, it was less than the standard Dithane M-45. The results show that the phosphorylated and thiophosphorylated derivatives are more effective fungicidal inhibitors than their parent benzothiazole counterparts, and it also reveals that the results are comparable to standard fungicide Dithane M-45. It is evident from the literature that organophosphorus compounds are less harmful as they get easily hydrolyzed in aqueous media and also on oxidation, organophosphorus fungicides result in less toxic products. Moreover, organophosphates are biodegradable, short-lived chemical compounds, so they do not get concentrated as they move up the food chain.

EXPERIMENTAL

Solvents were distilled and dried by standard procedures before use. Melting points were determined by the capillary method and are uncorrected. NMR data were recorded on FT NMR spectrometer JEOL FX-90Q using $CDCl_3$ as solvent. IR spectra were recorded on a Shimadzu 8400 S FT-IR spectrometer as KBr discs. ^{31}P NMR spectra were recorded on a JEOL AL 300 MHz FTNMR spectrometer. The ligand 2-(2′-mercaptophenyl)benzothiazole was synthesized according to the reported method.[21]

Synthesis of $(C_{13}H_8NS_2)P(O)Cl_2/(C_{13}H_8NS_2)P(S)Cl_2$

In the fast stirring solution of 2-(2′-mercaptophenyl)benzothiazole (0.001 mol) in dry THF (30 mL) and Et_3N (0.001 mol) in dry THF (20 mL), a solution of $POCl_3/PSCl_3$ (0.001 mol) in dry THF was added dropwise at 0°C. The reaction was brought to room temperature, and stirring was continued for 20–22 hours. Then it was cooled, and the adduct (Et_3N.HCl) that formed during the reaction was filtered through a closed sintered funnel. The filtrate was then concentrated and recrystallized.

Synthesis of $(C_{13}H_8NS_2)_2P(O)Cl/(C_{13}H_8NS_2)_2P(S)Cl$

In the fast stirring solution of 2-(2′-mercaptophenyl)benzothiazole (0.002 mol) in dry THF (30 mL) and Et_3N (0.002 mol) in dry THF (20 mL), the solution of $POCl_3/PSCl_3$ (0.001 mol) in dry THF (30 mL) was added dropwise at 0°C. Then a reaction was carried out in a manner similar as described above.

Synthesis of $(C_{13}H_8NS_2)_3P(O)/(C_{13}H_8NS_2)_3P(S)$

In the fast stirring solution of 2-(2′-mercaptophenyl)benzothiazole (0.003 mol) in dry THF (30 mL) and Et_3N (0.003 mol) in dry THF (20 mL), a solution of $POCl_3/PSCl_3$ (0.001 mol) in dry THF (30 mL) was added dropwise at 0°C. Then a reaction was carried out in a manner similar as described above.

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