

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Synthesis and Characterization of Some Antifungal O-Alkyl (O-Aryl) Trithiophosphato Derivatives of 1, 3, 2-Dioxaborinanes

Mukesh Chand Gupta, Kiran Sankhala and Alok Chaturvedi*

Synthetic and Surface Science Laboratory, Dept. of Chemistry, Govt. College, Ajmer (Raj.) 305001, India

ABSTRACT

Complexes of the type $(\text{OCH}_2\text{C}(\text{CH}_3)_2\text{CH}_2\text{OB})_2\text{S}_2\text{P}(\text{S})\text{OR}$ (where $\text{R}=\text{Me, Et, Pr}^i, \text{Bu}^i, \text{Ph, CH}_2\text{Ph}$) have been synthesized by the reactions of 2-chloro-1,3,2-dioxaborinanes and potassium salt of O-alkyl (O-aryl) trithiophosphates in 2:1 molar ratio in refluxing benzene. The product formed is white or light yellow coloured monomeric solid, soluble in common organic solvents and exhibit high sensitivity towards atmospheric moisture. These complexes have been characterized by elemental analysis (C, H, S, B), molecular weight measurement, IR and NMR ($^1\text{H}, ^{11}\text{B}, ^{31}\text{P}$) spectral studies. On the basis of above studies it is postulated that boron is in three coordinated state. The newly synthesized complexes show effectiveness against powdery mildew disease at a fixed interval of days.

Keywords: 2-chloro-1,3,2-dioxaborinanes, O-alkyl (O-aryl) trithiophosphates $^1\text{H}, ^{11}\text{B}, ^{31}\text{P}$ spectral studies, antifungal activity.

*Corresponding author



INTRODUCTION

The development of organoboron chemistry during the last two decades indicates that synthesis and applications of organoboranes and borates in organic synthesis continue to be pursued actively and represents a fruitful area [1,2].

The reactivity of boron as an electrophilic centre in a variety of 1,3-dioxo-2-borins has been studied[3]. It has been reported that 1,3,2-dioxaborolanes and borinanes behave in the same way as trialkoxyboranes[4-7]. On the other hand 2-alkoxy-1,3,2-benzodioxaborolanes, -borols, -borinanes and -borines are very reactive and tend to form four coordinated derivatives with a variety of bidentated oximes and β -diketonates[8,9].

Potassium salt of O-alkyl trithiophosphates $[(RO)P(S)(SK)_2]$ show the tendency of isomerization and there exist an equilibrium between $>P=S$ and $>P=O$ which can show interesting chemical bonding modes in metal and organometal derivatives[10-11]. Boron compounds have been extensively studied as soluble additives in lubricating oils, as solid lubricants and as surface coatings [12-15]. Oil soluble organoboron compounds are promising friction modifiers, corrosion inhibitor, antioxidants and effective antiwear additives [16-21].

In continuation to our earlier investigations [22,23] trithiophosphato derivatives of tin, it was considered worthwhile to synthesis O-alkyl trithiophosphato derivative of 1,3,2-dioxaborinane and show their effectiveness against powdery mildew disease at a fixed interval of days.

EXPERIMENTAL

Reagents and Solution

Moisture was carefully excluded throughout the experimental manipulations. Dipotassium salt of O-alkyltrithiophosphate were prepared by the method reported earlier[24]. All the solvents and reagents used during present investigation were of reagent grade and even made anhydrous by standard methods. 2-Isopropoxy-4H-1,3,2-benzodioxaborin was prepared by the method reported earlier in the literature[25] Boron and sulfur were estimated by Thomas's method[25] and Messenger's method[26], respectively.

Apparatus

A Knauer – vapour pressure osmometer in chloroform was used for molecular weight determination. FTIR spectra were recorded on Shimadzu 8201 PC spectrophotometer in the range $4000-400\text{cm}^{-1}$ using CsI cells.

^1H and ^{11}B NMR spectra were recorded in CDCl_3 and ^{31}P NMR spectra were recorded in benzene. NMR spectra were recorded on Bruker DRX 300 spectrophotometer using TMS (for ^1H) $\text{Et}_2\text{O} \cdot \text{BF}_3$ (for ^{11}B) and H_3PO_4 85% (for ^{31}P) as external references.

Synthesis of 2-(O-methyltrithiophosphato) bis- (1,3,2-dioxaborinanes)

A mixture of 2-chloro-1,3,2-dioxaborinanes (0.9125g; 6.16mmol) and potassium-O-methyl trithiophosphate (0.7307g; 3.09mmol) in dry and distilled benzene (~40ml) was refluxed for 4 hours. Potassium chloride was precipitated. It was removed by filtration on removing the solvent under reduced pressure. A colourless semisolid was obtained which was washed 3-4 times with n-hexane and recrystallized it by method of recrystallization [Table -1].

Table 1: Synthetic and analytical data of 2-[O-alkyl (O-aryl) trithiophosphato]bis[1,3,2- dioxaborinanes]

S.No.	Reactants g(mmol)		Product ----g -----%		Analyses (%) Found (Calcd.)			
	C	B	H	S	C	B	H	S
1	$\text{OCH}_2\text{C}(\text{CH}_3)_2\text{CH}_2\text{OBCl}$ 0.9125(6.16)	$\text{K}_2\text{S}_3\text{POMe}$ 0.7307(3.09)	$[\text{OCH}_2\text{C}(\text{CH}_3)_2\text{CH}_2\text{OB}]_2\text{S}_2\text{P}(\text{S})\text{OMe}$ 0.9617	81.1	3408 (37.37)	5.42 (5.74)	5.72 (5.98)	24.82 (25.06)
2	$\text{OCH}_2\text{C}(\text{CH}_3)_2\text{CH}_2\text{OBCl}$ 0.8825(5.96)	$\text{K}_2\text{S}_3\text{POEt}$ 0.7450(2.98)	$[\text{OCH}_2\text{C}(\text{CH}_3)_2\text{CH}_2\text{OB}]_2\text{S}_2\text{P}(\text{S})\text{OEt}$ 0.9739	82.1	36.02 (36.18)	5.29 (5.52)	6.14 (6.28)	23.84 (24.12)
3	$\text{OCH}_2\text{C}(\text{CH}_3)_2\text{CH}_2\text{OBCl}$ 0.8823(5.96)	$\text{K}_2\text{S}_3\text{OPr}^i$ 0.8882(2.98)	$[\text{OCH}_2\text{C}(\text{CH}_3)_2\text{CH}_2\text{OB}]_2\text{S}_2\text{P}(\text{S})\text{OPr}^i$ 1.2337	80.4	37.53 (37.86)	4.20 (4.94)	6.18 (6.55)	20.10 (21.57)
4	$\text{OCH}_2\text{C}(\text{CH}_3)_2\text{CH}_2\text{OBCl}$ 0.8823(5.96)	$\text{K}_2\text{S}_3\text{POBu}^i$ 0.7586(2.87)	$[\text{OCH}_2\text{C}(\text{CH}_3)_2\text{CH}_2\text{OB}]_2\text{S}_2\text{P}(\text{S})\text{OBu}^i$ 0.9625	81.4	39.40 (39.43)	5.02 (5.35)	6.68 (6.80)	23.00 (23.35)
5	$\text{OCH}_2\text{C}(\text{CH}_3)_2\text{CH}_2\text{OBCl}$ 0.8823(5.96)	$\text{K}_2\text{S}_3\text{POPh}$ 0.7555(2.71)	$[\text{OCH}_2\text{C}(\text{CH}_3)_2\text{CH}_2\text{OB}]_2\text{S}_2\text{P}(\text{S})\text{OPh}$ 0.9225	79.8	42.87 (43.04)	4.82 (5.17)	5.38 (5.60)	21.34 (22.58)
6	$\text{OCH}_2\text{C}(\text{CH}_3)_2\text{CH}_2\text{OBCl}$ 0.8618(5.82)	$\text{K}_2\text{S}_3\text{POCH}_2\text{Ph}$ 0.9048(2.90)	$[\text{OCH}_2\text{C}(\text{CH}_3)_2\text{CH}_2\text{OB}]_2\text{S}_2\text{P}(\text{S})\text{OCH}_2\text{Ph}$ 1.2092	85.1	44.12 (44.34)	4.54 (4.78)	5.42 (5.65)	20.58 (25.86)

Yield (0.9617g; 81.1%).

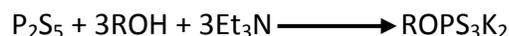
Analysis found % $[\text{OCH}_2\text{C}(\text{CH}_3)_2\text{CH}_2\text{OB}]_2\text{S}_2\text{P}(\text{S})\text{OMe}$ C=34.08, B=5.42, H=5.72, S=24.82

calcd. $[\text{OCH}_2\text{C}(\text{CH}_3)_2\text{CH}_2\text{OB}]_2\text{S}_2\text{P}(\text{S})\text{OMe}$ C=37.37, B=5.74, H=5.98, S=25.06

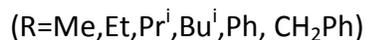
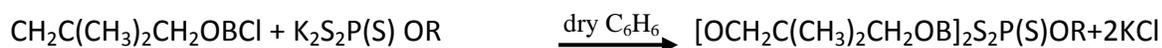
Rest derivatives were synthesized by similar method.

RESULTS AND DISCUSSION

Dipotassium salt of O-alkyl (O-aryl) trithiophosphates have been synthesized by dropwise addition of mixture of triethylamine and appropriate alcohol to a suspension of phosphorus pentasulphide in benzene. A solution of KOH in methanol was then added to a separated upper layer of the above solution.



Reaction of dipotassium salt of O-alkyl (O-aryl) trithiophosphate with 2-chloro-1,3,2-dioxaborinanes in 1:2 molar ratio have been carried out in refluxing dry and distilled benzene.



The products, from the above reactions are obtained as white or light yellow crystalline solids after filtering off the precipitate potassium chloride and removing the solvent in vacuum. The newly formed compounds have been purified by washing them 3-4 times with n-hexane and recrystallized them. These complexes are soluble in common organic solvents like benzene, toluene, chloroform and are readily hydrolysed by atmospheric moisture.

IR spectra

Assignment of some important IR spectral frequencies of 2-[O-alkyl(O-aryl) trithiophosphato] bis-[1,3,2-dioxaborinanes] are listed in Table-2. A medium intensity band is observed in the region 1328-1307 cm^{-1} which is assigned to $\nu B-O$ vibrations. The bands due to $\nu(P)-O-C$ and $\nu P-O-(C)$ vibrations are present in the region 1028-1010 cm^{-1} and 825-812 cm^{-1} , respectively. The absorption band for $\nu(P=S)$ is found in the region 700-682 cm^{-1} . The absorption bands in the region 552-545 cm^{-1} may be attributed to $\nu(P-S)$ vibrations. The appearance of a new medium intensity absorption band in the region 899-890 cm^{-1} is assigned to $\nu B-S$ band suggesting the chelation of trithio ligands with boron atom.

1H NMR spectra

1H NMR spectra of these derivatives have been recorded in $CDCl_3$ and spectral data are listed in Table-3.

In the NMR spectrum of $(OCH_2C(CH_3)_2CH_2OB)_2 S_2P(S)OCH_3$, two singlets are observed at $\delta 1.10$ and $\delta 3.80$ ppm for CH_3 and OCH_2 protons of glycolate moiety, respectively. A doublet is observed at $\delta 3.64$ ppm for OCH_3 protons of ligand moiety.

¹¹B NMR spectra

¹¹B NMR spectra of the newly synthesized compounds have been recorded in CDCl₃, It shows a sharp singlet at δ18.42 to δ19.16ppm and provide a convincing evidence for the chelation of boron to sulphur as well as purity of these derivatives and suggests three coordinated nature of boron atom [Table - 4].

Table 2: IR spectral data of 2-[O-alkyl(O-aryl) trithiophosphato] bis-[1,3,2-dioxaborinanes]

S.No.	Compound	ν(B-O)	ν(P)-O-C	νP O-(C)	ν(B-S)	ν(P=S)	ν(P-S)
1	[OCH ₂ C(CH ₃) ₂ CH ₂ OB] ₂ S ₂ P(S)OMe	1307s	1010s	820s	893m	700s	545s
2	[OCH ₂ C(CH ₃) ₂ CH ₂ OB] ₂ S ₂ P(S)OEt	1309s	1012s	816s	899m	698s	546s
3	[OCH ₂ C(CH ₃) ₂ CH ₂ OB] ₂ S ₂ P(S)OPr ⁱ	1310s	1016s	812ms	895m	682s	548s
4	[OCH ₂ C(CH ₃) ₂ CH ₂ OB] ₂ S ₂ P(S)OBu ⁱ	1315m	1020s	818m	898s	690s	552s
5	[OCH ₂ C(CH ₃) ₂ CH ₂ OB] ₂ S ₂ P(S)OPh	1324m	1028s	825m	890m	695m	550m
6	[OCH ₂ C(CH ₃) ₂ CH ₂ OB] ₂ S ₂ P(S)OCH ₂ Ph	1328m	1026s	821m	894m	698m	552m

Table 3: ¹H NMR spectral data of 2-[O-Alkyl(O-aryl) trithiophosphato]bis[1,3,2-dioxaborinanes]

S.No.	Compound	Chemical Shift (δppm)
1	[<u>OCH₂C(CH₃)₂CH₂OB</u>] ₂ S ₂ P(S)OMe	1.10s, 12H(CH ₃); 3.80s, 8H(OCH ₂); 3.64d, 3H(OCH ₃).
2	[OCH ₂ C(CH ₃) ₂ CH ₂ OB] ₂ S ₂ P(S)OEt	1.12,s,12H(CH ₃),0.96,t,3H(CH ₃), 3.47,s,8H(OCH ₂), 2.47,q,2H(CH ₂)
3	[<u>OCH₂C(CH₃)₂CH₂OB</u>] ₂ S ₂ P(S)OPr ⁱ	0.80d,6H(CH ₃); 1.12s,12H(CH ₃); 3.74s,8H(OCH ₂);4.724.88m, 1H(OCH)
4	[<u>OCH₂C(CH₃)₂CH₂OB</u>] ₂ S ₂ P(S)OBu ⁱ	0.85d,6H(CH ₃);1.10s,12H(CH ₃);2.10m,1H(CH);3.64s,8H(CH ₃); 3.72-3.86,m(OCH ₂).
5	[<u>OCH₂C(CH₃)₂CH₂OB</u>] ₂ S ₂ P(S)OPh	1.10s,12H(CH ₃); 3.80s, 8H(CH ₃);6.90-7.30m, 5H(C ₆ H ₅)
6	[<u>OCH₂C(CH₃)₂CH₂OB</u>] ₂ S ₂ P(S)OCH ₂ Ph	1.05,s,12H(CH ₃);3.86s8H(OCH ₂);3.46,s,2H(OCH ₂)7.32- 7.85,m,54(C ₆ H ₅)

Table 4: ³¹P NMR spectral data of 2-[Oalkyl(O-aryl) trithiophosphato] bis-[1,3,2-dioxaborinanes]

S.No.	Compound	Chemical Shift (δppm)	
		¹¹ B	³¹ P
1	[OCH ₂ C(CH ₃) ₂ CH ₂ OB] ₂ S ₂ P(S)OMe	19.16	94.38
2	[OCH ₂ C(CH ₃) ₂ CH ₂ OB] ₂ S ₂ P(S)OEt	19.06	90.56
3	[OCH ₂ C(CH ₃) ₂ CH ₂ OB] ₂ S ₂ P(S)OPr ⁱ	19.12	82.45
4	[OCH ₂ C(CH ₃) ₂ CH ₂ OB] ₂ S ₂ P(S)OBu ⁱ	18.82	86.14
5	[OCH ₂ C(CH ₃) ₂ CH ₂ OB] ₂ S ₂ P(S)OPh	18.42	86.14
6	[OCH ₂ C(CH ₃) ₂ CH ₂ OB] ₂ S ₂ P(S)OCH ₂ Ph	18.68	88.24

Table 5: Effect of newly synthesized complexes on powdery mildew disease of roses caused by *Sphaerotheca pannosa* var. *rosae* pathogens on different concentrations

Conc.(%)	Percent Disease Intensity (PDI)				
	During I Spray	After 7 th Day During II spray	After 15 Days	After 21 Day During III spray	After 28 Days
0.5000	100	86	72	53	29
0.2500	100	80	71	51	24
0.1250	100	66	56	43	19
0.0625	100	61	54	45	18
0.0312	100	58	46	37	14
0.0156	100	53	43	37	13
0.0078	100	44	38	27	12

³¹P NMR spectra

³¹P NMR spectra of these derivatives have been scanned in CHCl₃ and the spectral data are summarized in [Table-4].

The ³¹P NMR spectra of 2-[O-alkyl (O-aryl) trithiophato] bis-[1,3,2-dioxaborinanes) show only one resonance signal for each complex in the region δ82.45-94.38ppm. The chemical shift values are shifted to downfield (δ11-22ppm) as compared to parent trithiophosphates (³¹P=δ71.21-72.55ppm).

Antifungal studies

It is observed that when O-alkyltrithiophosphates derivatives of 1,3,2-dioxaborinanes are applied in the form of dilute solution to various concentrations, they show their effectiveness against powdery mildew disease at a fixed interval of days. Antifungal activity of newly synthesized complexes has been carried out with the powdery mildew of roses. Percent disease intensity (PDI) was recorded by modifying the coyier rating scale[27] and it (PDI) was calculate using following formula –

$$PDI = \frac{\text{Sum of all rating} \times 100}{\text{Total number of observations} \times \text{Maximum class rating}}$$

All these compounds indicates their potency against *Sphaerotheca pannosa* var. *rosae* at different concentrations (Table – 5). The rose plants were severely infected by powdery mildew disease, when the first foiler spracy was carried out. Remarkable results were observed after seventh day of first spray. The intensity of powdery mildew disease decreases. Second spray was done after seventh day of first spray. After 15 day and after 21st day of first spray observation were again made. The 21st day resulted in a very small change in PDI values in comparison to previous spray.

CONCLUSION

On the basis of above IR and NMR (^1H , ^{11}B , ^{31}P) studies following structure may be proposed for the newly synthesized complexes.

Boron is in tricoordinated state (Fig. 1). Derivatives show antifungal activity against powdery mildew disease.

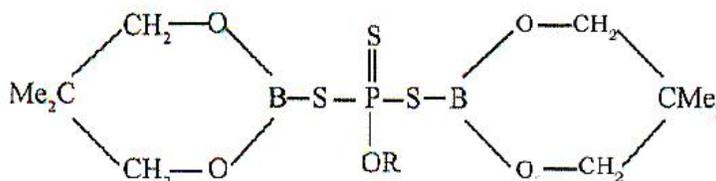


Fig 1: (R=Me,Et,Prⁱ,Buⁱ,Ph,CH₂Ph)

ACKNOWLEDGEMENT

Authors Mukesh Chand Gupta and Kiran Sankhala (S.R.F) are thankful to C.S.I.R. New Delhi for financial assistance and also thankful to S.A.I.F. (C.D.R.I.), Luknow for spectral analysis.

REFERENCES

- [1] Singh OP, Chaturvedi A, Saxena DB, Mehrotra RK, Srivastava G. *Monatshafte fur Chemie* 1994; 125: 607.
- [2] Chaturvedi A, Nagar PN, Srivastava G. *Phosphorus, Sulfur and Silicon* 1994; 90: 219.
- [3] Achran GEMc, Shore SG. *Inorg Chem* 1966; 5: 2044.
- [4] Mehrotra SK, Srivastava G, Mehrotra RC. *Synth React Inorg Met Org-Chem* 1974; 4: 27.
- [5] Bhardwaj PN, Srivastava G. *J Indian Chem Soc* 1982; 59: 300.
- [6] Nagar PN, Srivastava G, Mehrotra RC. *Synth React Inorg Met-Org Chem* 1982; 12: 749.
- [7] Singh OP, Mehrotra RK, Srivastava G. *Synth React Inorg Met Org Chem* 1991; 21: 717.
- [8] Kothiwal AS, Singh A, Rai AK, Mehrotra RC. *Ind J Chem* 1985; 24: 828.
- [9] Singh YP, Rupani P, Singh A, Rai AK, Rogers RD, Atwood JL. *Inorg Chem* 1985; 25: 3076.
- [10] Chaturvedi A, Sharma CS, Nagar PN. *Phosphorus sulfur and Silicon* 2003; 178: 1923.
- [11] Chordia L, Chaturvedi A. *Phosphorus Sulfur and Silicon* 2007; 182: 2821.
- [12] Kimuva Y, Wakabayashi T, Okada K, Wada T, Nishikawa H. *Wear* 1999; 232: 199.
- [13] Lovell M, Higgs CF, Deshmukh P, Mobley AJ. *Pro Teeh* 2006; 177: 87.
- [14] Klepper CC, Williams JM, Truhan JJJ, Qu J, Riestev L, Hazelton RC, Moshchella JJ, Blau PJ, Anderson JP, Popooia OO, Keitz MD. *Thin Solid films* 2008; 516: 3070.
- [15] Wu JH, Phillips BS, Jiang W, Sanders JH, Zabinsk JS, Malshe AP. *Wear* 2006; 261: 592.
- [16] Baldwin BA. *Wear* 1977; 45: 345.
- [17] Hu ZS, Yie Y, Wang LG, Chen GX, Dong GX. *Tribol Lett* 2000; 8: 45.
- [18] Liu W, Jin Z, Xue Q. *Lubricat Sci* 1994; 7: 49.



- [19] Herdan JM. *Lubricat Sci* 2000; 2: 265.
- [20] W Liu, Q Xue, X Zhang, H Wang, C Huang, *Tribol Trans* 1992; 48: 475-479.
- [21] Shen G, Zheng Z, Wan Y, Xu X, Cao L, Yue Q, Sun T, Liu A. *Wear* 2000; 246: 55.
- [22] Chordia L, Chaturvedi A. *Main group Met Chem* 2008; 31(6): 319.
- [23] Chordia L, Chaturvedi A. *J Chin Chem Soc* 2009; 56: 636.
- [24] Kotavich B P, Zemlyanskii N I, Mvzavev I V, Volosin M P. *Zn Obsch Khim* 1968; 38(6): 1282.
- [25] Bhardwaj PN, Srivastava G. *Bull Chem Soc Japan* 1978; 51: 524.
- [26] Vogel AI, *A Textbook of Qualitative Inorganic Analysis*, ELBS, IV Edition 1973.
- [27] Sobti AK, Mathur AK, Siradhana BS. *India Phytopathol* 1992; 45: 200.