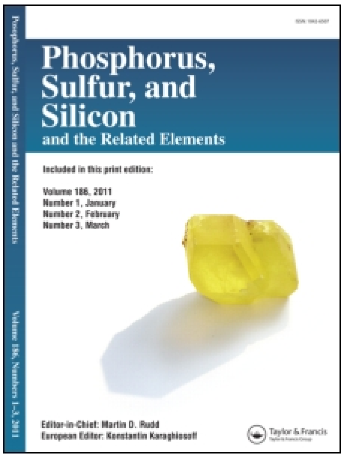

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Synthesis and Biological Activity of a Novel Compound: $(C_6F_5)_2SbPh$

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A novel organoantimony compound "$(C_6F_5)_2SbPh$" was synthesized in high yields by modified method and evaluated for insecticidal and antimicrobial activities. The compound was very effective against polyphagous insect pest of crops Spodoptera litura (Lepidoptera: Noctuidae) and polyphagous mite pest of crops Tetranychus urticae (Tetranychidae: Acari). The LC_{50} value for Spodoptera litura was 0.187 (μg/insect) and 0.385% respectively in topical application and leaf dip methods. The compound also showed very high antifeedant activity against Spodoptera litura (EC_{50}: 0.155%). The LC_{50} value against Tetyranychus urticae was 0.021%. Antibacterial activity of the compound (1%) was also tested against human pathogenic bacteria Klebsiella pneumoniae, Staphylococcus aureus, and Pseudomonas aeruginosa showed inhibition zone of 19.78 ± 0.44, 25.49 ± 0.73, and 19.71 ± 0.74 mm, respectively. The minimum inhibitory concentration (MIC) of the novel organoantimony compound against fungi Aspergillus flavus was 125 μg/mL.

Keywords $(C_6F_5)_2SbPh$; Antimicrobial; *Aspergillus flavus*; insecticidal; *Klebsiella pneumoniae; Pseudomonas aeruginosa; Spodoptera litura; Staphylococcus aureus; Tetranychus urticae*

INTRODUCTION

Organometallic compounds have played an important role in medicines as well as in control of insects and pest for many years. The importance

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Address correspondence to R. Kant, Department of Chemistry, Lucknow University, Lucknow 226007, India. E-mail: drravikant78@gail.com of metal ions lies in the fact that they are essential components for various physicochemical processes occurring in living system.[1]

Among organometallics only organotins compound are exploited for their insecticidal activities, whereas organoantimony compounds are not well studied for insecticidal and pesticidal activities.

The triorganoantimony (III) compounds were generally prepared earlier by using Grignard reaction,[4] but by this reaction, only homopolymers could be made in a very low yield. Triorganoantimony (III) compounds could also be prepared by transmetallation reactions,[5–7] that were also a low yielding reaction. They may also be prepared by the reaction of organolithium compounds and antimony (III) halide in the presence of a donor solvent like THF/ether,[8,9] but due to the flammable nature of organolithium compounds in air and moisture, the reaction is very skilled and difficult. Triorganoantimony (III) compounds could also be prepared by using sodium metal in a high boiling hydrocarbon and halocarbon solvents with antimony (III) halides,[10] but such cases only homotriorgano derivatives could be prepared and the disposal of untreated sodium creates hazards. There is no known suitable method to date for the preparation of mixed triorganoantimony compounds.

In view of the above shortcomings and constraints, there was a need to develop a process, which could yield pure mixed triorganoantimony (III) compound in high yield and employing safer handling. Though some similar compounds have been synthesized, but their use as insecticides, pesticides have been not explored.

In this present communication, we have successfully prepared a mixed fluoro based organoantimony compound in a high yield using a modified one pot Grignard synthesis (*PCT: WO* 2006/067800A-1).[11] Fluoro-based compounds are preferred in synthesis because of their higher water and lipid solubility, which enhances the biological activity. The water and lipid solubility is important for water rich cells and for crossing cell membrane respectively. The compound was assayed for insecticidal and antimicrobial activity, as well.

EXPERIMENTAL

Preparation of Tris (Pentafluorophenyl) Antimony

Pentafluorobromobenzene (12.35 g, 0.05 mol) dissolved in dry ether was added drop wise to Mg (1.2 g, 0.05 mol) turnings at 0°C. The resulting Grignard solution was cooled to -10°C and (3.78 g, 0.01 mol) $SbCl_3$ dissolved in dry ether was slowly added with constant stirring. This mixture was stirred for an additional hour at room temperature and subsequently refluxed for one more hour. The mixture was then cooled to 0°C and treated with ice water containing NH_4Cl followed by the addition of 4 N HCl (1 ml) and stirred to make the solution acidic. The ether layer was separated and dried over Na_2SO_4 and evaporated to give $(C_6F_5)_3Sb$.

Yield: 3.11 g, 30%, M.P.: 74°C

The brownish layer was extracted with $CHCl_3$ and after work up it yielded further $(C_6F_5)_3Sb$.

Preparation of Bis (pentaflorophenyl) Antimony (III) Chloride

Antimony trichloride (2.28 g, 10 mmol) and tris (pentafluorophenyl) antimony (12.45 g, 20 mmol) were heated at 60–70°C in the absence of a solvent for about three hours. Cooling yielded white crystals, which on recrystallization from dichloromethane gave the pure product.

Yield: 11.78 g, 80%

Preparation of Bis (Pentafluorophenyl) Phenyl Antimony (III)

Bromobenzene (31.4 g, 0.2 mol) dissolved in dry ether was added drop wise to Mg (5 g, 0.21 mol) turnings at 0°C. The resulting Grignard solution was cooled to -10°C and bis (pentafluorophenyl) antimony chloride (9.8 g, 0.2 mol) dissolved in dry ether was added to it slowly. This mixture was stirred for an additional hour at room temperature and after completion of the reaction was treated with a saturated NH_4Cl solution.

The ether layer was separated and dried over Na_2SO_4. The solvent was then evaporated from the solution in vacuum and residue recrystallized from ethanol. All operations were undertaken in protective under N_2 atmosphere to avoid moisture.

Yield: 6.39 g, 60%, M.P: 88°C

Insect Cultures

Insect cultures were maintained in the laboratory at a constant temperature of 37 ± 2°C and R.H of 80 ± 10%. *Spodoptera litura* (Lepidoptera: Noctuidae) was maintained in the laboratory on cater leaves (*Recinus communis*) in plastic jars. The jars were covered with wet cloth to maintain moisture of leaves. The full-grown larvae were released in jars containing sterile moist soil for pupation and pupae were left inside soil undisturbed for adult emergence.

The adults emerged were paired (male: female: 1:1). Ten percent sugar solution was provided as food for adults and paper strips were provided in side mating jars for egg laying. The eggs were separated and kept for hatching at 80% R.H in BOD incubator. Culture of spider mites

Tetranychus urticae (Acari: Tetranychidae) was maintained in the laboratory on mulberry leaves (*Morus alba*) on wet cotton in Petri plates.

Insecticidal Activity

The compound was tested for insecticidal and antifeedant activities against *S. litura* and acaricidal activity against spider mites *T. urticae*.

Topical Application

The compound was tested against *S. litura* for toxicity by topical application method.[12] Compound was dissolved in acetone and different concentrations were prepared. Each concentration was separately applied on the dorsal surface of the every fourth instar larvae of *S. litura* (30 larvae were used for each concentration). Larvae treated with acetone alone served as control. The larvae were provided with caster leaf discs as food and mortality was recorded after 48 h of the treatment.

Leaf-Dip Method

Stomach toxicity was tested by leaf dip method.[13] Compound was dissolved in acetone and different concentrations were prepared in water using 0.02% between 20 as an emulsifier. Leaf discs (25 cm^2) were prepared out of caster leaf and were dipped for 30 s in various concentrations of the test compound. Air-dried leaf discs were kept separately in Petri plates. The fourth instar larvae of *S. litura* were release on treated leaves (10 larvae/ replication and three replications were maintained for each concentration). Control consisted of leaf discs dipped in equal amount of acetone in distilled water containing 0.02% between 20. Mortality was recorded after 48 h and mortality data was used for calculation of $LC_{50.}$

Antifeedant Activity

Antifeedant activity of compound was tested against fourth instar larvae of *S. litura* using leaf dip method.[13] Caster leaf discs (25 cm^2) with different concentration of compound as described above are used and each disc was placed in Petri plates separately. Forth instar larvae were released on leaf. Ten leaf discs were used for each concentration and control consisted of leaf discs dipped in equal amount of acetone in distilled water containing 0.02% between 20. Insects were allowed to feed for 48 h. After 48 h, the leaf area left uneaten was measured using leaf area meter. The difference between leaf area provided and leaf area left over was taken as amount of leaf area consumed. Antifeedant activity (%) = (C − T)/(C + T) X100, where C = leaf area consumed in control, T = leaf area consumed in treatment. The data was used for calculation of EC_{50}.

Acaricidal Activity

Acaricidal activity was tested against spider mites *Tetranychus urticae* using leaf dip method.[13] Different concentrations of the compound were prepared in water using 0.02% between 20 as emulsifier. Leaf discs of mulberry (5 cm^2 dia.) were dipped in different concentrations for 30 seconds, air-dried, and placed over wet cotton in a Petriplates. Adult female mites were released on treated leaf discs and mortality was recorded after 48 h of treatment. Mites released on leaf discs treated with water containing 0.02% between 20 served as control. Mortality data was used for the calculation of LC_{50}.

Antimicrobial Activity

Antibacterial Activity

Antibacterial activity was tested against three pathogenic strains of bacteria S*taphylococcus aureus* (MTCC: 96)*, Klebsiella pneumoniae* (MTCC: 109)*, Pseudomonas aeruginosa* (MTCC: 741) by disc diffusion method.[14] Compound was dissolved in acetone and 1% solution was made in 10% DMSO. Solution was applied (5 μl/disc) on 5 mm filter paper disc (Whatman No. 1) separately and air-dried. A 60 μl suspension of bacteria (10^6 CFU/ml) was spread on nutrient agar plates. The discs impregnated toxicant was placed on the inoculated media and incubated at 37°C for 24 h. The zone of inhibition was measured using digital Vernier caliper. The activity of compound was compared with known antibiotic ampicillin.

Antifungal Activity

Antifungal activity was tested against *Aspergillus flavus* (MTCC: 2798) by tube dilution technique[15] for determination of minimum inhibitory concentration (MIC). Serial dilutions of compound were prepared in 0.5 ml of liquid media. Each tube contains a different concentration of the compound was inoculated with fixed amount of the organism being tested. After incubation, tubes were observed for visible growth. The tube completely inhibiting the growth of organism in the presence of the smallest concentration of the compound is expressed as the Minimum Inhibitory Concentration.

RESULTS AND DISCUSSION

IR Spectra

The IR spectra of $(C_6F_5)_2PhSb$ was recorded in the range 4000–4200 cm^{-1} and the absorption characteristic of C-F and C-H stretching along with mass sensitive vibrational modes of diagnostics value have been identified (Table III). The values are in close proximity with those reported for $(C_6F_5)_3Sb$ and $(C_6H_5)_3Sb$. The characteristic Sb-C stretching frequency occur at 445 cm^{-1}(Sb-C_6F_5) and 460 cm^{-1}(Sb-Ph) corresponding to 'Y' vibrational mode. ν_{sym} (Sb-C) corresponding to 't' mode appear at 279 and 268 cm^{-1} assignable to Sb-C_6F_5 and Sb-Ph stretching mode respectively. These assignments have been made based on approximate normal coordinate analysis carried out on R_3Sb compounds assuming the "R" groups to be single atom.

Raman Spectra

It may be noted that based on Raman spectra tertiary stibine has been reported to possess expected trigonal pyramidal C_{3v} symmetry in structure. Assuming organic group R and $R^{/}$ to be single atoms triarylstibines could have C_{3v} symmetry showing the expected pyramidal structure along with the lone pair presumably occupying the 4th coordination position round the antimony.

UV Spectra

The UV spectra of $(C_6F_5)_2(C_6H_5)Sb$ exhibit an intense absorption at 252 mμ suggesting that the interaction of non bonded electrons of antimony atom with π orbital of the aromatic ring.

^{19}F NMR Spectra

^{19}F NMR spectra of the compound were recorded in $CDCl_3$ using CF_3COOH as reference at δ 5.26 MHz. The characteristic signals of $F_{2,6}$, $F_{3,5}$, and F_4 were observed at -120.34 ppm, -160.36 ppm, and -142.30 ppm respectively. The peak of F_4 was easily recognized due to its half intensity compared to $F_{2,6}$ and $F_{3,5}$ peaks. F_4 signals appear as triplet of triplet due to spin- spin coupling.

^{1}H NMR Spectra

^{1}H NMR spectra showed a multiplet due to aromatic protons in the range δ 7.20–7.90 ppm. The value corresponds to that shown by triphenyl stibines.

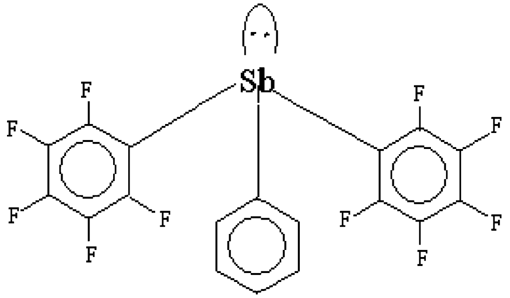
TABLE I Insecticidal and Acaricidal Activity of $(C_6F_5)_2$Sb Ph

Method	Activity	LC_{50}/ EC_{50} 48 h (%)	Fiducial limits	Slope ± S.E	Chi-square
Spodoptera litura					
Topical application	Toxicity	0.187 (μg/insect)	0.13–0.25	2.12 ± 0.38	7.06
Leaf dip	Toxicity	0.385%	0.24–0.58	1.96 ± 0.53	3.76
Leaf dip	Antifeedant	0.155%	0.13–0.18	2.24 ± 0.18	12.17
Tetranychus urticae					
Leaf dip	Toxicity	0.021	0.01–0.03	1.47 ± 0.19	5.14

Mass Spectra

Mass spectra of $(C_6F_5)_2$ SbPh showed the dominance of $(C_6F_5)M^+$ apart from $(C_6F_5)_2$ M^+ by loss of phenyl group, spectra also showed the formation of SbF_2^+, SbF^+ and Sb^+. Similar fragmentations have been reported for $(C_6F_5)_3Sb$.

For the above discussion by the spectral analysis, it is clear that the formula of the compound should be as follows

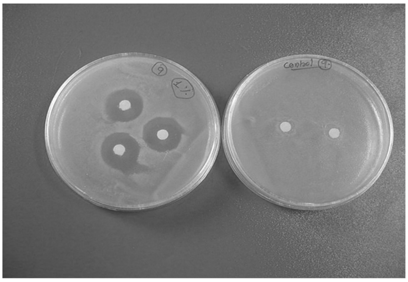


Bioassays

Bioassay (Assay for biological activity, i.e.; Biological activities such as insecticidal, antifeedant, antimicrobial, etc.,) conducted against insect pest of crops S. *litura*, for toxicity and antifeedant activity and against mite pest *T. urtica*e for toxicity. The LC_{50}(Lethal Concentration required for causing 50% mortality) and EC_{50} (Effective Concentration required for causing 50% reduction in feeding) are calculated.

Insecticidal and Acaricidal Activities

The compound was tested for toxicity against *S. litura* by both topical application and leaf dip methods. The $LC_{50}$was found to be



A: treated with $(C_6F_5)_2SbPh$; B: Control

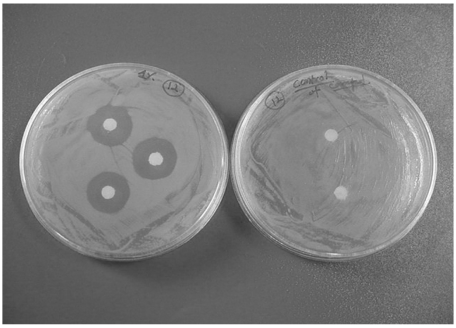
FIGURE 1 Inhibition of Strain *Klebsiella pneumoniae* (MTCC:109) by compound.

0.187 (μg/insect) and 0.385%, respectively, for topical application and leaf dip methods. The compound also showed very high antifeedant activity against *S. litura* (EC_{50}: 0.155%). The Acaricidal activity was tested against *T. urticae*, and the LC_{50} value was found to be 0.021% (Table I). The compound "$(C_6F_5)_2SbPh$" showed potential insecticidal and antifeedant activities. Organometallics are well known for the insect repellent activities. Among Organometallics organotins are the best exploited for antifeedant activities. Triphenyltin acetate was the one of the earliest organotin that was used as an antifeedant against foliage feeding insects.[16]

The presence of fluorine in the compounds may also contribute to the insecticidal and antifeedant activities. Fluorine compounds are being used as insecticide since 1890. They are principally stomach poison

A: treated with $(C_6F_5)_2SbPh$; B: Control

FIGURE 2 Inhibition of Strain *Staphylococcus aeureus* (MTCC:96) by compound.



A: treated with $(C_6F_5)_2SbPh$; B: Control

FIGURE 3 Inhibition of strain *Pseudomonas aeruginosa* (MTCC:741) by compound.

and to a limited extent contact poison. Their insecticidal properties are related to the fluorine content and solubility in the digestive juices of the insect. Fluorides destroy gut epithelium of insects. However, this is not regarded as immediate cause of death.[17]

The compound also showed very good contact toxicity against the *S. litura* suggesting penetration through insect cuticle. The compounds may be acting on insect nervous system similar to that of DDT (dichlorodiphenyltrichloroethane), wherein compounds blocks the axonal membrane of nervous system.

Antimicrobial Activity

Compound was tested for antibacterial activity of at 1% concentration against human pathogenic bacteria *K. pneumoniae, S. aureus* and *P. aeruginosa* showed zone of inhibition of 19.78 ± 0.44, 25.49 ± 0.73 and

TABLE II Antimicrobial Activity of $(C_6F_5)_2SbPh$

		Inhibition Zone (mm: 24h)	
S.N	Microorganism (MTCC: NO)	$(C_6F_5)_2Sb(C_6H_5)$ (1%)	Ampicillin (1%)
1	*Klebsiella* pneumoniae (MTCC:109). Fig1	19.78 ± 0.44	18.78 ± 0 .3
2	*Staphylococcus auerus* (MTCC: 96). Fig2	25.49 ± 0.73	No inhibition
3	*Pseudomonas aeruginosa* (MTCC:741). Fig3	19.71 ± 0.74	41.52 ± 0.47

TABLE III IR Assignment (cm^{-1}) of the X-Sensitive Modes for Ph–Sb and F_5C_6Sb in $(C_6F_5)_2SbPh$

Group	q-Mode	r-Mode	y-Mode	t-Mode	x-Mode	μ–Mode
C_6H_5	1065s	651w	457ww	276ww	216	—
C_6F_5	969ws	614w	446w	283w	—	—

19.71 ± 0.74 mm respectively (Figures 1–3 and Table II). The activity when compared with known antibiotic ampicillin. The compound was found more effective than ampicillin in inhibiting *K. Pneumoniae* and *S. aureus* and less effective compared to ampicillin against *P. aeruginosa.* The compound showed minimum inhibitory concentration (MIC) against fungi *Aspergillus flavus* at 125 μg/ mL. Since the compound containing fluorine might form complexes with metaloenzymes, particularly those which are responsible in basic physiology such as cytochrome oxidase. The may also react with peptidoglycan layer of bacterial cell wall and damage it causing death of bacterial cell.

CONCLUSION

The compound $(C_6F_5)_2SbPh$ has shown promising insecticidal, antibacterial and antifungal activities. It has high potential for use in plant protection for control of both insect pests as well as plant diseases, if the compound is suitably formulate for use in the plant protection. However, detailed toxicological investigations are needed to determine the toxic effects of the compound against higher mammals. The detailed studies are also needed on the mode of action of compound and the toxicity to other insect species and microorganisms.

REFERENCES

[1] M. Nath, S. Pokharia, G. Ing, X. Song, and A. Kumar, *Eur. J. Med. Chem.*, 272 (2004).
[2] J. M. Bernes and L. Magos, *Organometal. Chem. Rev.*, **3,** 137 (1968).
[3] H. G. Langer, U.S. Patent, 3,442,922 (1969).
[4] G. O. Doak and L. D. Freedman, *Organometallic Compounds of Arsenic, Antimony and Bismuth* (Wiley Interscience, New York 1970), p. 361.
[5] A. L. Rheingold and P. Choudhary, *J. Organomet. Chem.*, **128,** 155 (1977).
[6] P. Jutzi and M. Kuhm, *Chem. Ber.*, **107,** 1228 (1974).
[7] S. N. Bhattacharya and P. Raj, *Ind. J. Chem.*, **15A,** 799, (1977).
[8] L. I. Zakhark and O. Yu. Okhlobyslin, *Dokl. Akad. Nauk. SSSR.* **116,** 236 (1957).
[9] F. B. Makein and W. A.Waters, *J. Chem. Soc.*, 843, (1983).
[10] A. Michaelis and A. Reisea, *Ann. Chem.*, 3116 (1955).

[11] K. Chandrashekar, H. M. Behl, V. Kumar, O. P. Sidhu, P. Pushpangadan, Ch. V. Rao, R. Kant, S. K. Shukla, K. Singhal, A. Ranjan, A. K. Saxena, and P. Raj, *PCT: WO* 2006/067800A-1.

[12] S. D. Deshmukh and M. N. Borle, *Ind. J. Entomol.*, **37**(1), 11 (1976).

[13] V. G. Dethie, L. B. Browne, and C. N. Smith, *J. Econ. Entomol.*, **53,** 134 (1960).

[14] R. S. Verma and S. A. Imam, *Ind. J. Microbiol.*, **13,** 45 (1973).

[15] J. G. Horshfall, *Bot. Rev.*, **5,** 357 (1945).

[16] K. P. Srivastava, Ed. In Textbook of Applied Entomology (Kalyani Publishers, New Delhi, (1996), Vol. 1, Chap., 17, pp. 321.

[17] K. P. Srivastava, Ed. In Textbook of Applied Entomology (Kalyani Publishers, New Delhi, (1996), Vol. 1, Chap., 11, pp. 321.