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SYNTHESIS AND FUNGICIDAL ACTIVITY OF SUBSTITUTED DIBENZYL TRISULFIDES

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ABSTRACT. The synthesis and fungicidal activity of substituted dibenzyl trisulfides **1(1a-f)** are reported. The compounds were characterized by elemental analysis, nuclear magnetic resonance (^{1}H NMR and ^{13}C NMR) and mass spectrometric techniques. The results of the biological screening showed high fungicidal activity of the synthesized compounds.

KEY WORDS: Substituted dibenzyl trisulfides, Fungicidal activity

INTRODUCTION

Although there are several excellent methods for the synthesis of disulfides [1-7], only a few are available for trisulfides [3], mainly because of the greater thermal instability of trisulfides [8]. However, dialkyl trisulfides have been synthesized with various degrees of purity by a number of methods, for example, the reaction of sulfur dichloride with thiols (Scheme 1) [9].

$$2RSH + SCl_2 \longrightarrow RSSSR + 2HCl$$

Scheme 1

Akiyama [10] also prepared dialkyl trisulfide by the reduction of sulfur dioxide with thiols. The weakness of his method was that a mixture of products was obtained (Scheme 2).

$$SO_2 + 4RSH \xrightarrow{Et_3N} 2RSSR + S + 2H_2O$$

$$RSSR + S \longrightarrow RSSSR$$

Scheme 2

Also, the reactions of Bunte salts (*i.e.* salts of *S*-alkyl or *S*-aryl hydrogen thiosulfates) with sodium sulfide or sodium mercaptide have been reported to give alkyl or aryl trisulfides [11]. In addition to the desired trisulfides, disulfides and tetrasulfides were reported as being formed as by-products, and the relative proportions of di-, tri- and tetrasulfides were determined by gas-liquid chromatography [12, 13]. Methods for the synthesis of organic trisulfides had been reviewed [4, 5, 12, 14].

Sulfur and its compounds particularly trisulfides continue to have applications in agrochemicals, as shown by large varieties of new sulfur-based crop protection chemicals in development around the world [15-17].

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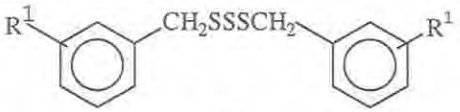
In the present investigation, the synthesis and fungicidal activity of substituted dibenzyl trisulfides (**1**) are reported. The synthesized compounds were characterized by ^{1}H NMR, ^{13}C NMR and mass spectrometric techniques. To our knowledge, no detailed study of the synthesis and fungicidal activity of these compounds have been reported in the literature.

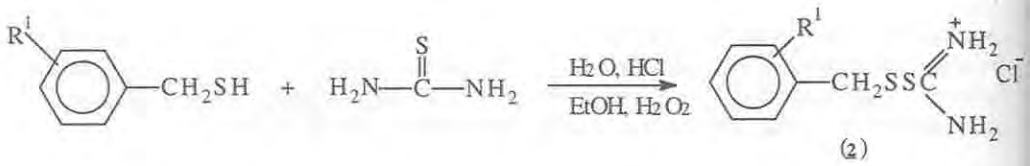


(**1**)

R^1 = H (**1a**), *o*-Me (**1b**), *p*-Me (**1c**), *p*-MeO (**1d**), *o*-Cl (**1e**), *p*-Cl (**1f**)

RESULTS AND DISCUSSION

Due to the limitations [12, 13] of the methods mentioned above for the synthesis of trisulfides, the method used in the present work involved the reaction of an *S*-benzylthioisothiouronium chloride with an amine. Various substituted derivatives of *S*-benzylthioisothiouronium chloride (**2**) were easily prepared in good yield by the method of Sirakawol *et al.* [18]. The reaction proceeds according to Scheme 3 below.

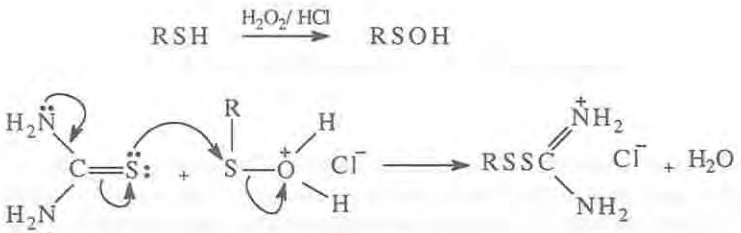


(**2**)

R^1 = H (**2a**), *o*-Me (**2b**), *p*-Me (**2c**), *p*-MeO (**2d**), *o*-Cl (**2e**), *p*-Cl (**2f**)

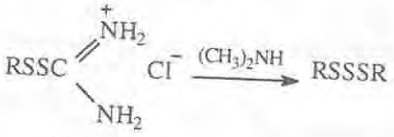
Scheme 3

A mechanism which was proposed [18] involves oxidation of thiol to the corresponding sulfenic acid, and then reaction of the sulfenic acid with thiourea to give the *S*-benzylthioisothiouronium chloride (**2**) (Scheme 4).



Scheme 4

The symmetrical trisulfides (**1**) were prepared [18] by treating the corresponding *S*-benzylthioisothiouronium chloride (**2**) with dimethylamine (DMA) (Scheme 5).

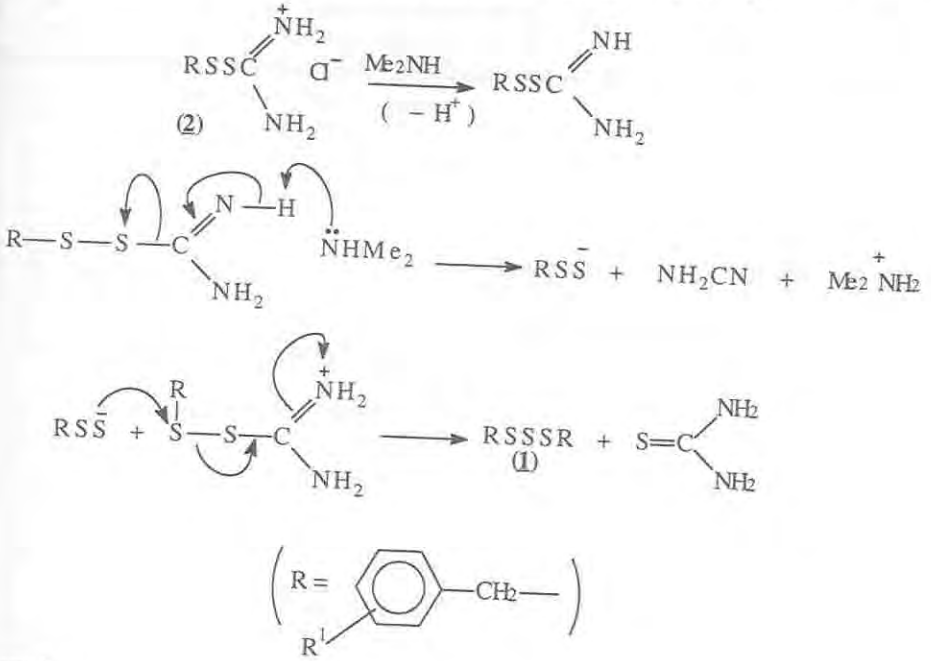


(2) (1)

Scheme 5

On addition of dimethylamine to a solution of the *S*- benzylthioisothiouronium chloride (**2**) in methanol, with rigorous stirring, a solid (**1**) was precipitated out after 20 to 35 minutes.

A mechanism that we proposed for this reaction is depicted in Scheme 6.

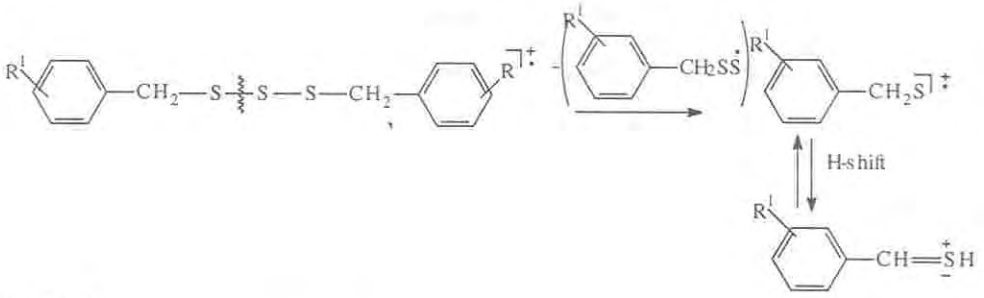


Scheme 6

The analytical and spectral results showed that all the synthesized compounds were pure.

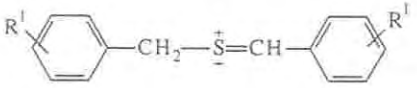
Mass spectrometry. All the synthesized compounds gave relatively weak molecular ions under electron impact (EI) modes except for dibenzyl trisulfide, for which the $(M-1)^+$ peak was observed. The compounds (**1**) (R^1 = H, *o*- or *p*-Me, *p*-MeO, *o*- or *p*-Cl) showed fragment ions at m/z 91, 105, 121 and 125, respectively, which are characteristics of the fragment $R^1C_6H_4CH_2^+$. This ion is formed very readily in the ionization chamber because of the relative ease with which the C–S bond is broken, and in all cases, the base peak is due to this fragment ion. This type of ion is stabilized by delocalization of the benzene ring electrons (Scheme 7). It might also be formulated as the highly stable tropylium ion:

The compounds (**1**) (R^1 = H, *o*- or *p*-Me, *p*-MeO, *o*- or *p*-Cl) also showed fragment ions at 123, 137, 153 and 157, respectively, which are indicative of an ion formed by S–S cleavage [19], possibly with hydrogen transfer [20] to give the more stable sulfonium ion (Scheme 7).



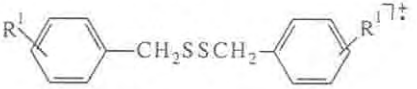
Scheme 7

Peaks at 213, 241, 273 and 281, respectively, for the compounds are assigned to a sulfonium ion:



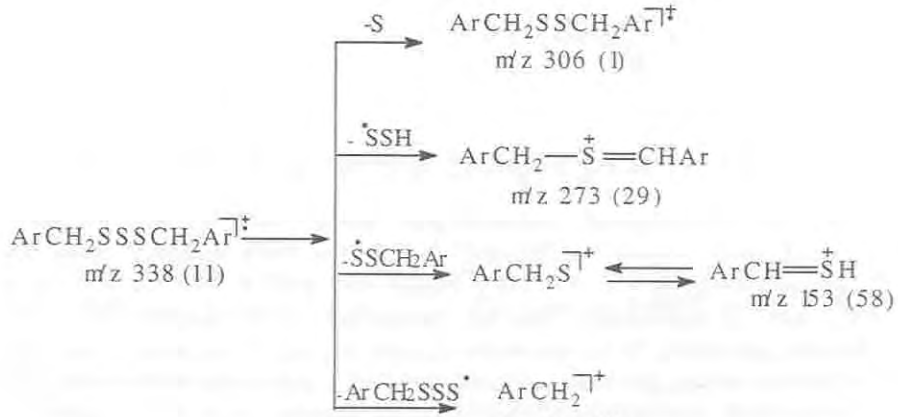
which arises from the loss of S_2H.

Finally, the peaks at 246, 274, 306 and 314, respectively, for the compounds (**1**) are characteristics of .he symmetrical disulfide ion:



which arises from the loss of one sulfur atom from the parent molecular ion.

The fragmentation pattern of di-(*p*-methoxybenzyl) trisulfide (**1d**), as a representative of the various derivatives of the synthesized compound is given in Scheme 8.



(Ar = *p*-MeO C_6H_4)

Scheme 8

In dibenzyltrisulfide (**1a**), the formation of $(M-1)^+$ peak may be due to the loss of one hydrogen atom from the molecular ion as depicted in Scheme 9 below.

$$PhCH_2SSSCH_2Ph^{\ddagger} \xrightarrow{-H^{\bullet}} \underset{(Ph = C_6H_5)}{PhCHSSSCH_2Ph} \longleftrightarrow \underset{m/z\ 277\ (8)}{PhCH{=}\overset{+}{S}{-}S{-}S{-}CH_2Ph}$$

Scheme 9

Fungicidal screening. Compounds **1, (1a–f)** were tested for fungicidal activity as described in the experimental section. Also tested for fungicidal activity were guazatine/imazalil and phenyl mercury acetate, two well-established fungicides so as to compare their activities with those of synthesized compounds. The fungal organisms against which the compounds were tested are *Fusarium culmorum* (F_1), *Fusarium oxysporium* (F_2) and *Gaeumannomyces graminis* (F_3). Germination of spores was assessed by measuring the diameter of growth of each plate and comparing it with the control. The percentage of inhibition (% I) of growth was calculated by using the following equation.

$$\%\,I = \frac{d_c - d}{d_c} \times 100$$

where d = diameter of growth for the plate treated with chemical and d_c = diameter of growth for the control.

The percentage inhibition (% I) of growth were then ranked as given in Table 1. The results of *in vitro* test are given in Table 2.

Table 1. Ranking of the percentage inhibition (% I) of growth.

Rank	0	1	2	3	4
% I	10	11 – 20	21 – 49	50 – 79	≥ 80

Table 2. *In vitro* test results for $ArCH_2SSSCH_2Ar$ [(**1**); Ar = H (1a), *o*-Me (**1b**), *p*-Me (**1c**), *p*-MeO (**1d**), *o*-Cl (**1e**), *p*-Cl (**1f**)]; guazatine/imazalil and phenyl acetate.

Compound	$^aC_{F_1}$ (ppm)			C_{F_2} (ppm)			C_{F_3} (ppm)		
	10	100	1000	10	100	1000	10	100	1000
1a	3[b]	3	4	2	3	4	1	2	4
1b	3	4	4	2	3	4	2	3	4
1c	2	3	4	2	4	4	1	3	4
1d	2	3	4	1	3	4	2	3	4
1e	3	3	4	2	3	4	1	2	4
1f	1	3	4	2	3	4	2	3	4
Guazatine/imazalil	3	3	4	3	3	4	3	3	4
Phenyl/mercury acetate	3	3	4	2	3	4	2	3	4

[a]Concentration (ppm) of fungal organism. [b]Rank for the percentage inhibition of growth (Table 1).

The compounds tested (**1a–1f**) showed moderately good activity and were able to control the three fungi investigated even at low compound concentration. The activity results obtained for these compounds were comparable with those of guazatine/imazalil and phenyl mercury

acetate, which are the two well established fungicides. The moderately good fungicidal activity of these compounds establishes their potential usefulness as good fungicides.

EXPERIMENTAL

Reagents

Most reagents, for example, all the mercaptans involved in this synthetic work were used without further purification. Diethyl ether was dried over sodium wire.

Analytical methods

Elemental analysis. All the analysis for carbon, hydrogen, nitrogen and sulfur were carried out in the Department of Applied Chemistry, University of North London, using a Carlo Erba 1106 elemental analyzer.

Nuclear magnetic resonance spectroscopy. Routine ^{1}H NMR spectra were obtained using Perkin-Elmer R 12B continuous wave spectrometer at 60 MHz and on a Bruker WP 80 instrument at 80 MHz. Higher field ^{1}H NMR and ^{13}C NMR were recorded on a Bruker AM 250 FT spectrometer at 250.13 MHz and 62.89 MHz, respectively. Chemical shifts for ^{1}H NMR and ^{13}C NMR spectra are given relative to internal standard tetramethylsilane (TMS).

Mass spectrometry. Electron impact (EI) mass spectra were recorded in the Department of Applied Chemistry, University of North London, using a KRATOS "PROFILE" high-resolution mass spectrometer, which is a double-focussing sector field instrument.

Chemical synthesis

*S-Benzylthioisothiouronium chloride (**2a**).* Addition of benzyl mercaptan (12.9 cm^3, 0.11 mol), thiourea (10.05 g, 0.13 mol), concentrated hydrochloric acid (17.5 cm^3) and hydrogen peroxide (14.0 cm^3) gave *S*-benzylthioisothiouronium chloride (19.12 g, 74 %) as a white crystalline solid; (found: C, 40.98; H, 4.83; N, 11.96; S, 27.10%; calc. for $C_8H_{11}ClN_2S_2$: C, 40.91; H, 4.73; N, 11.94; S, 27.27%); m.p. 147–149 °C (lit. [18], m.p. 145–148 °C). Similar procedures were used to prepare the following compounds.

*S-(o-Methylbenzylthio)isothiouronium chloride (**2b**).* Addition of *o*-methylbenzyl mercaptan (10.48 g, 0.076 mol), thiourea (6.82 g, 0.089 mol), concentrated hydrochloric acid (12.06 cm^3) and hydrogen peroxide (9.65 cm^3) gave *S*-(*o*-methylbenzylthio)isothiouronium chloride (14.26 g, 76%) as a white crystalline solid; (found: C, 43.51; H, 5.36; N, 11.36; S, 25.87%; calc. for $C_9H_{12}ClN_2S_2$: C, 43.44; H, 5.28; N, 11.26; S, 25.77%; m.p. 162–163 °C (lit. [18] m.p. 162–163 °C).

*S-(p-Methylbenzylthio)isothiouronium chloride (**2c**).* A mixture of *p*-methylbenzyl mercaptan (10.48 g, 0.076 mol), thiourea (6.82 g, 0.089 mol), hydrochloric acid (12.06 cm^3), water (12.06 cm^3) and ethanol (180 cm^3) was kept at 0–10 °C by means of an ice-salt bath while hydrogen peroxide (9.65 cm^3) was added dropwise with vigorous stirring for a period of 1 h. The stirring was continued for an additional 2 h. Dithioformamidine hydrochloride which was formed was filtered off and the solvent was removed from the filtrate by rotary evaporation to give a solid residue which was then dissolved in a small amount of ethanol. This solution was diluted with ether to give a white solid which was recrystallized from ethanol-ether solvent system, and dried

to give the desired *S*-(*p*-methylbenzylthio)isothiouronium chloride (13.30 g, 71%) as a white crystalline solid; (found: C, 43.54; H, 5.49; N, 11.25; S, 25.80%; calc. for. $C_9H_{13}ClN_2S_2$: C, 43.44; H, 5.28; N, 11.26; S, 25.77%); m.p. 158–159 °C (lit. [18], m.p. 157–159 °C).

S-(p-Methoxybenzylthio)isothiouronium chloride (2d). Addition of *p*-methoxybenzyl mercaptan (10.62 g, 0.069 mol), thiourea (6.17 g, 0.081 mol), concentrated hydrochloric acid (11.0 cm^3) and hydrogen peroxide (9.38 cm^3) gave *S*-(*p*-methoxybenzylthio)isothiouronium chloride (14.29 g, 78%) as a white crystalline solid; (found: C, 40.05; H, 4.65; N, 10.53; S, 24.13%; calc. for $C_9H_{12}ClN_2OS_2$: C, 40.81; H, 4.96; N, 10.58; S, 24.21 %); m.p. 155–156 °C (lit. [18], m.p. 153–155 °C).

S-(o-Chlorobenzylthio)isothiouronium chloride (2e). Addition of *o*-chlorobenzyl mercaptan (9.72 g, 0.06 mol); thiourea (5.53 g, 0.07 mol), concentrated hydrochloric acid (9.54 cm^3) and hydrogen peroxide (7.6 cm^3) gave *S*-(*o*-chlorobenzylthio)isothiouronium chloride (18.53 g, 71%) as a white crystalline solid; (found: C, 35.84; H, 3.61; N, 10.52; S, 23.69%; calc. for $C_8H_{10}Cl_2N_2S_2$: C, 35.67; H, 3.75; N, 10.40; S, 23.81%); m.p. 153–154 °C (lit. [18], m.p. 155–156 °C).

S-(p-Chlorobenzylthio)isothiouronium chloride (2f). Addition of *p*-chlorobenzyl mercaptan (17.45 g, 0.11 mol), thiourea (10.05 g, 0.13 mol), concentrated hydrochloric acid (17.5 cm^3) and hydrogen peroxide (14.0 cm^3) gave *S*-(*o*-chlorobenzylthio)isothiouronium chloride (19.26 g, 65%) as a white crystalline solid; (found: C, 35.56; H, 3.62; N, 10.56; S, 23.72%; calc. for $C_8H_{10}Cl_2N_2S_2$: C, 35.67; H, 3.75; N, 10.40; S, 23.81%); m.p. 153–154 °C (lit. [18], m.p. 150–152 °C).

Synthesis of substituted dibenzyl trisulfides (1)

Dibenzyl trisulfide (1a). Addition of dimethylamine (4.51 g, 0.040 mol) and benzylthioisothiouronium chloride (5.00 g, 0.020 mol) gave dibenzyl trisulfide (3.34 g, 61%) as needle-like white crystals; (found: C, 60.58; H, 5.14; S, 34.28%; calc. for $C_{14}H_{14}S_3$: C, 60.41; H, 5.08; S, 34.53%); m.p. 50–51 °C; ^{1}H NMR ($CDCl_3$) δ: 4.02 (ArC$\underline{H}_2$S, s, 4H), 7.30 (Ar–$\underline{H}$, m, 10H); ^{13}C NMR ($CDCl_3$) δ: 43.11 (Ar$\underline{C}H_2$S), 127.56 (Ar$\underline{C}$1), 128.60 (Ar$\underline{C}$–3,5), 129.43 (Ar$\underline{C}$–2,6), 136.50 (Ar$\underline{C}$–4); MS: *m/z* (%), 278 (M^+, 8), 277 ([M-1]$^+$, 31), 246 (12), 213 (54), 181 (7), 155 (1), 123(36), 91(100).

Di-(o-methylbenzyl) trisulfide (1b). Addition of dimethylamine (6.77 g, 0.030 mol) and *S*-(*o*-methylbenzylthio)isothiouronium chloride (3.98 g, 0.015 mol) gave di-(*o*-methylbenzyl) trisulfide (2.42 g, 76%) as a flaky white solid; (found: C, 61.96; H, 5.74; S, 31.30%; calc. for $C_{16}H_{18}S_3$: C, 62.69; H, 5.93; S, 31.38%); m.p. 48–49 °C; ^{1}H NMR ($CDCl_3$) δ: 2.38 (C$\underline{H}_3$, s, 6H), 4.00 (ArC$\underline{H}_2$, s, 4H), 7.23 (Ar–$\underline{H}$, m, 8H); ^{13}C NMR ($CDCl_3$) δ: 19.33 ($\underline{C}H_3$), 41.16 (Ar$\underline{C}H_2$S), 126.05 (Ar$\underline{C}$–1), 127.97 (Ar$\underline{C}$–3), 134.02 (Ar$\underline{C}$–5), 130.62 (Ar$\underline{C}$–2), 136.96 (Ar$\underline{C}$–6), 137.52 (Ar$\underline{C}$–4); MS: *m/z* (%): 306 (M^+, 17), 274, (1), 241 (43), 137 (17), 105 (100).

Di-(p-methylbenzyl) trisulfide (1c). Addition of dimethylamine (6.77 g, 0.060 mol) and *S*-(*p*-methylbenzylthio)isothiouronium chloride (7.46 g, 0.030 mol) gave di-(*p*-methylbenzyl) trisulfide (4.35 g, 72%) as needle-like white crystals; (found: C, 61.90; H, 6.17; S, 31.16%; calc. for $C_{16}H_{18}S_3$: C, 62.10; H, 5.93; S, 31.38 %); m.p. 54–55 °C; ^{1}H NMR ($CDCl_3$) δ: 2.32 (C$\underline{H}_3$, s, 6H), 4.01 (ArC$\underline{H}_2$S, s, 4H),7.27 (Ar–$\underline{H}$, m, 8H); ^{13}C NMR ($CDCl_3$) δ: 21.17 ($\underline{C}H_3$), 42.89

(ArCH$_2$S), 129.32 (ArC–1), 128.83 (ArC–3,5), 133.37 (ArC–2,6),137.32 (ArC–4); MS: *m/z* (%), 306 (M$^+$, 2), 274 (1), 241 (12),137 (5), 105 (100).

Di-(p-methoxybenzyl) trisulfide (1d). A solution of dimethylamine (6.77 g, 0.060 mol) was added to a stirred solution of *S*-(*p*-methoxybenzylthio)isothiouronium chloride (7.92 g, 0.030 mol) in methanol (37.5 cm^3). After 35 minutes of the addition, a white solid separated out and the stirring was continued for an additional 2 h. The solid that formed was filtered off, washed with several portions of methanol and recrystallised twice from ethanol to give di-(*p*-methoxybenzyl) trisulfide (7.50 g, 74 %) as needle-like white crystals; (found: C, 56.80; H, 5.33; S, 29.20%; calc. for $C_{16}H_{18}O_2S_3$: C, 56.77; H, 5.37; S, 28.40 %); m.p. 172–173 °C; ^{1}H NMR ($CDCl_3$) δ: 3.78 (CH$_3$O, s, 6H), 4.06 (ArCH$_2$S, s, 4H), 7.20 (Ar–H, m, 8H); ^{13}C NMR ($CDCl_3$) δ: 42.61 (ArCH$_2$S), 55.24 (CH$_3$O), 113.51 (ArC–1), 128.43 (ArC–3,5), 130.58 (ArC–2,6), 159.06 (ArC–4); MS: *m/z* (%), 338 (M$^+$, 11), 306 (1), 273 (29), 153 (58), 138 (4), 121 (41), 109 (8).

Di-(o-chlorobenzyl) trisulfide (1e). Addition of dimethylamine (6.77g, 0.060 mol) and *S*-(*o*-chlorolbenzylthio)isothiouronium chloride (8.08 g, 0.030 mol) gave di-(*o*-chlorobenzyl) trisulfide (7.65 g, 74%) as needle-like white crystals; (found: C, 48.26; H, 3.39; S, 27.50%; calc. for $C_{14}H_{12}Cl_2S_3$: C, 48.41; H, 3.49; S, 27.68 %); m.p. 75–76 °C; ^{1}H NMR ($CDCl_3$) δ: 4.14 (ArCH$_2$S, s, 4H), 7.35 (Ar–H, m, 8H); ^{13}C NMR ($CDCl_3$) δ: 40.48 (ArCH$_2$S), 126.75 (ArC–1), 129.05 (ArC–3), 129.78 (ArC–5), 131.70 (ArC–2), 134.25 (ArC–6), 134.28 (ArC–4); MS: *m/z* (%), 347 (M$^+$, 9), 314 (1), 281 (12), 157 (7), 125 (100).

Di-(p-chlorobenzyl) trisulfide (1f). Addition of dimethylamine (6.77 g, 0.060 mol) and *S*-(*p*-chlorolbenzylthio)isothiouronium chloride (8.08 g, 0.030 mol) gave di-(*p*-chlorobenzyl) trisulfide (7.79 g, 75%) as a white flaky solid; (found: C, 48.51; H, 3.51; S, 27.68%; calc. for $C_{14}H_{12}Cl_2S_3$: C, 48.41; H, 3.49; S, 27.68 %); m.p. 81–82 °C; ^{1}H NMR ($CDCl_3$) δ: 3.97 (ArCH$_2$S, s, 4H), 7.27 (Ar–H, m, 8H); ^{13}C NMR ($CDCl_3$) δ: 42.25 (ArCH$_2$S), 128.76 (ArC–1), 130.73 (ArC–3,5), 133.49 (ArC–2,6), 134.96 (ArC–4); MS: *m/z* (%), 347 (M$^+$, 4), 314 (1), 281 (13),157 (11), 125 (100).

Biological screening experiments

In vitro screening of compounds. After a couple of trials that involved cultivation of the fungi *Fusarium culmorum, Fusarium oxysporum* and *Gaeumannomyces graminis* in different nutrients, it was found that the most suitable was saboround dextrose agar (SDA). Therefore, these fungi were cultivated in this nutrient for all the screening experiments.

A solution of the chemical to be tested (1000 ppm) in SDA medium was prepared by dissolving 0.2 g in acetone (20 cm^3), followed by the addition of distilled water (80 cm^3) at 60 °C. This mixture was then added to sterilize SDA solution containing agar (13 g) in water (100 cm^3). (Sterilization of the SDA solution had been previously carried out by placing it in an autoclave at 121 °C and leaving it at this temperature for 15 min). Addition of 20 cm^3 of the 1000 ppm solution to a solution containing SDA (13 g) in water (180 cm^3) gave a 100 ppm solution. Similarly, a 10 ppm solution was prepared by adding 20 cm^3 of the 100 ppm solution to a solution containing SDA (13 g) in water (200 cm^3). Also, solutions containing (a) guazatine/imazalil and (b) phenyl mercury acetate at various concentrations of active ingredients (1000 ppm, 100 ppm and 10 ppm) were prepared as standard.

The solutions were poured in petri dishes and allowed to cool. Each plate was then inoculated with a 5 mm agar plug containing actively growing fungus. All plates were kept inside a sterilized incubator, maintained at 25 °C. The growth diameter of the fungal spore was measured every three days until there was complete growth on the control dish, *i.e.* until all the surface of the plate was covered with fungal spore (approximate diameter, 86 cm^3).

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REFERENCES

1. Zeise, W.C. *J. Prakt. Chem.* **1834**, 1, 257.
2. Muspratt, S. *J. Chem. Soc.* **1851**, 3, 18.
3. Field, L. *Organic Chemistry of Sulfur,* Oea, S. (Ed.), Plenum: London; **1977**; p 303.
4. Kharasch, N. *Organic Sulfur Compounds* **1961**, 1, 25.
5. Cavallini, C. *Enzymologia* **1960**, 22, 161.
6. Ayodele, E.T.; Olajire, A.A.; Adebisi, J.A.; Oladoye, S.O. *Bull. Chem. Soc. Ethiop.* **1999**, 13, 135.
7. Ayodele, E.T.; Olajire, A.A. *Bull. Chem. Soc. Ethiop.* **1999**, 13, 57.
8. Reiu, E.E. *J. Am. Chem. Soc.* **1967**, 89, 2364.
9. Baroni, A.; Levi, G.R. *Atti Accad. Lincei* **1929**, 9, 772.
10. Akiyama, F. *J. Chem. Soc. Perkin Trans.* **1978**, 9, 1046.
11. Milligan, B.; Saville, B.; Swan, J.M. *J. Chem. Soc.* **1963**, 3608.
12. Bernhard, J. *Ber.* **1950**, 83, 578.
13. Böhme, H.; Clement, M. *Liebigs Ann. Chem.* **1952**, 576, 61.
14. Haitinger, L. *Monatsh.* **1883**, 4, 165.
15. Horpkins, W.L. *Ag. Chem. New Product Review* **1990**, 8.
16. Anon, E. *Agrichem. Age* **1989**, 33, 20.
17. Young, D.E., *U.S. Pat.* **1984**, 4, 476, 113.
18. Sirakawa, K.; Aki, O.; Tsujikawa, T.; Tsuda, T. *Chem. Pharm. Bull.* **1970**, 18, 235.
19. Sample, S.; Djerassi, C. *J. Am. Chem. Soc.* **1966**, 88, 1937.
20. Mclarfferty, F.W. *J. Am. Chem. Soc.* **1957**, 29, 1782.