Organic Heterocyclothiazenes. Part 13.[1] Rational Synthesis and Chemistry of 1,3,5,2,4-Trithiadiazines

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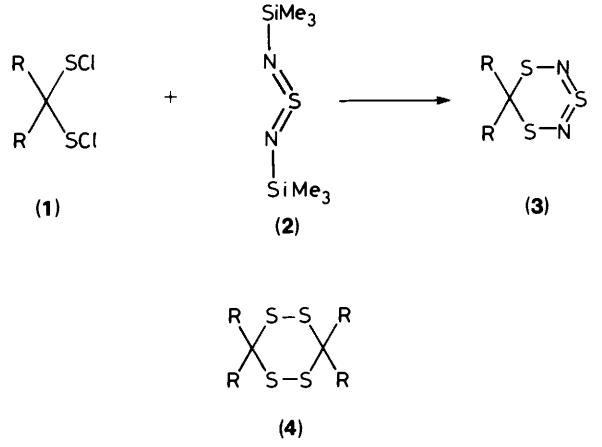
1,3,5,2,4-Trithiadiazines, previously formed from tetrasulphur tetranitride and diazoalkanes, are synthesised from 1,1-bis-sulphenyl chlorides (**1**; R = H, Cl), (**5**), (**11**) and bis(trimethylsilyl)sulphurdiimide (**2**), and this reaction extends to trithiadiazines with functional groups on carbon. Bis-sulphenyl chlorides (**5a–d**) are formed in one step from malonic esters and amides and sulphur dichloride. Pentathiepane (lenthionine) (**14**), prepared from di-iodomethane and disodium disulphide, gives methanebis(sulphenyl chloride) on chlorinolysis and hence, with (**2**), the parent trithiadiazine (**3**; R = H). Similarly the pentathiepane (**16**) is converted into bis-sulphenyl chloride (**11**) and the spirotrithiadiazine (**12**). The sensitivity of the heterocyclic ring towards strongly polar reagents precluded the generation of the trithiadiazine cation (**17**) and anion (**19**), but the radical (**18**) is formed on treatment with benzoyl peroxide and benzoyl t-butyl nitroxide (**22**), resulting in the benzoyloxy and amino-oxy derivatives (**21**) and (**24**). *m*-Chloroperbenzoic acid or nitrogen tetroxide convert trithiadiazine into the *S*-oxide (**25**).

In the preceding Part of this series we described the formation of 1,3,5,2,4-trithiadiazines (**3**) from tetrasulphur tetranitride and diazoalkanes.[1] The yields in these reactions were variable and the scope was limited to the formation of alkyl and aryl substituted trithiadiazines (**3**; R = H, alkyl, aryl). We therefore sought a more rational route to the ring system, and one which was compatible with functional groups on the ring carbon. Of the several disconnections possible, that between the two divalent sulphurs and the adjacent nitrogens appeared most attractive, giving a 1,3-bis-nucleophilic NSN component and a 1,3-bis-electrophilic SCS component. The former could be the well-known bis(trimethylsilyl)sulphurdi-imide (**2**) which we have used for the similar construction of seven-membered trithiadiazepine rings.[2] The latter, such as 1,1-bis-sulphenyl chlorides (**1**), are much less well known, but the corresponding 1,1-dithiols[3] or the cyclic tetrathianes (**4**)[4] might be useful precursors. Dichloromethanebis(sulphenyl chloride) (**1**; R = Cl)[5] and malondianilide-2,2-bis(sulphenyl chloride) (**5a**)[6] have been reported.



6,6-*Dichloro*-1,3,5,2,4-*trithiadiazine* (**3**; R = Cl).—Synthesis of this compound was particularly attractive since the chlorine atoms could be reactive enough to give various substitution products, including derivatives of the 6-oxo compound.

Chlorine is known to add to the thiocarbonyl bond[7] and dichloromethanebis(sulphenyl chloride) has been made in this way by irradiation of carbon disulphide and chlorine at −5 °C; care is required to prevent further chlorine addition. In a modification of the literature method[5] we used an internally illuminated, jacketed (−15 °C to −5 °C) photochemical reactor with a water-cooled high density mercury vapour lamp. By irradiation for no more than 2.5 h we readily obtained workable amounts (1–2 g) of product from 100 cm^3 of carbon disulphide. The reaction of the bis-sulphenyl chloride (**1**; R = Cl) and sulphurdi-imide (**2**) was conducted at room temperature under high dilution conditions to minimise polymerisation; the mixture slowly changed to yellow, orange, and then deep red and evaporation and chromatography gave 6,6-dichlorotrithiadiazine (**3**; R = Cl) (56%) as a distillable red liquid. Its structure was based on analysis and spectroscopy; in the infrared spectrum there were two principal trithiadiazine absorptions (1 087 and 632 cm^{-1}) very similar to those of the parent compound (1 080 and 640 cm^{-1}),[1] and the mass spectrum had an isotopic abundance consistent with the presence of two chlorine atoms. The yield of the trithiadiazine was higher than in the same reaction of sulphurdi-imide (**2**) with the more flexible 1,2-ethanebis(sulphenyl chloride) (22%), and slightly higher than that with benzene-1,2-bis(sulphenyl chloride) (50%). In agreement with this trend, propane-1,3-bis(sulphenyl chloride) gave none of the analogous 8-membered ring product under the same conditions.

A preliminary investigation of the chemistry of the dichlorotrithiadiazine (**3**; R = Cl) was unproductive. Treatment with silver benzoate or silver nitrate in acetonitrile or xylene from −10 °C to 100 °C, with lithium methoxide in methanol at −78 °C, and with butyl-lithium in ether at −78 °C caused extensive decomposition giving chromatographic baseline products only.

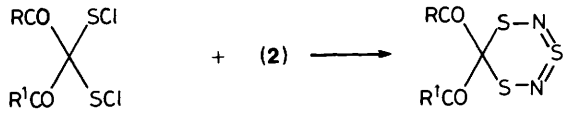
Trithiadiazines from Malonic Acid Derivatives.—We were intrigued by an old report[6] that malondianilide reacted with sulphur dichloride to give the bis-sulphenyl chloride (**5a**), for which the only evidence was elemental analysis. We could find

Table. Trithiadiazines from malonic acid derivatives

$RCOCH_2COR^1 \xrightarrow{\text{Step 1}} (5) \xrightarrow{\text{Step 2}} (6)$

			Step 1		Step 2	
Bis(sulphenyl chloride)	R	R^1	Reaction time	Yield	Trithiadiazine	Yield
(5a)	PhNH	PhNH	3.5 h	34%	(6a)	52%
(5b)	PhNH	EtO	1 h	93% (crude)	(6b)	46%
(5c)	EtO	EtO	36 h	99% (crude)	(6c)	49%
(5d)	MeO	Bu^{t}O	36 h	55% (crude)	(6d)	13%

no further mention of this useful functionalisation of an active methylene group, nor subsequent use of the product (**5a**). Bis-sulphenyl chlorides tend to be moisture sensitive reactive oils which are best prepared an used directly; however (**5a**) was reported to be a crystalline compound, m.p. 164–165 °C, stable on prolonged storage. We therefore repeated the literature reaction; when sulphur dichloride was added to malondianilide in benzene at room temperature there was a vigorous reaction with copious evolution of hydrogen chloride gas. The product, m.p. 166–168 °C, had analytical and spectroscopic properties entirely consistent with the proposed structure (**5a**), although no molecular ion was observed in the mass spectrum. The structure was confirmed by treatment with bis(trimethylsilyl)sulphurdi-imide (**2**) under high dilution conditions to give the highly crystalline, red bis(phenylaminocarbonyl) trithiadiazine (**6a**) (52%), as the only product isolable by chromatography.

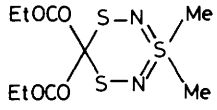


(5) (6)

a; R = R^1 = PhNH
b; R = PhNH. R^1 = EtO
c; R = R^1 = EtO
d; R = MeO. R^1 = Bu^{t}O

This sequence of functionalisation of the methylene group with sulphur dichloride followed by cyclisation proved to be a good general route to trithiadiazines starting from malonamides and malonic esters (Table). The one-step conversion of active methylene groups into 1,1-bis-sulphenyl chlorides is worthy of further investigation; a report that other products were formed from ethyl acetoacetate and diethyl malonate [8] suggests that the reaction may be structurally limited. The low yield of the t-butyl methyl ester (**6d**) possibly results from sensitivity towards acid, though both reactions were carried out with a nitrogen purge to remove hydrogen chloride. As with cyclisation to form 7-membered rings,[2] best results were obtained with slow simultaneous addition of reactants. For example, when bis-(trimethylsilyl)sulphurdi-imide (**2**) was added to the sulphenyl chloride (**5a**) in dichloromethane the yield was halved. But in contrast with cyclisation to 7-membered rings, which usually gave complex reactions,[2] all pure 1,1-bis-sulphenyl chlorides gave the corresponding trithiadiazines in about 50% yield, as the only isolable products.

Having ready access to the trithiadiazine ester (**6b**) we attempted, unsuccessfully, to convert it into the corresponding carboxylic acid with potassium hydroxide, hydrochloric acid, boron tribromide, and trimethylsilyl iodide. There was extensive decomposition of the trithiadiazine ring under all conditions. Dimethyl trithiadiazepine-6,7-dicarboxylate is similarly decomposed by alkali and this was considered to result from ready nucleophilic attack at the formally tetravalent S(3) atom.[9] We therefore sought to prepare trithiadiazines dialkylated on this sulphur, such as (**7**), to see if the ring would now be stable towards base. However, when a variety of bis-sulphenyl chlorides [(**1**; R = Cl), (**5a–c**)] were treated with S,S- dimethylbis(trimethylsilyl)sulphurdi-imide (**8**), none of the corresponding S,S-dimethyltrithiadiazines were obtained. Instead low yields of the S,S-demethylated products (**3**) were isolated as the only characterisable components of complex reaction mixtures, and dimethyl sulphide was detected by smell. In order to confirm the fate of the alkyl groups of the sulphurdi-imide reagent in this reaction, we prepared S,S-dibenzylsulphurdi-imide (**9**) unsubstituted at nitrogen. Reaction of this with the bis-sulphenyl chloride (**5c**) gave the trithiadiazine ester (**6c**), again in low yield (7%), together with a substantial amount of dibenzyl sulphide (51%). Formation of this sulphide possibly occurs *via* oxidation of the sulphurdi-imide (**9**) by the bis-sulphenyl chloride (**5c**) to give S,S-dibenzylthiadiazirine (**10**), followed by rapid extrusion of nitrogen, but these unpromising S,S-dialkylsulphurdi-imide reagents were not investigated further.



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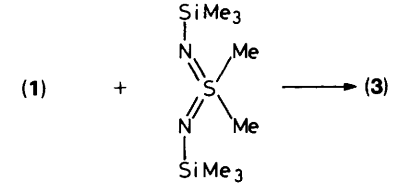

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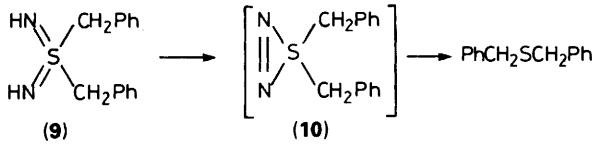
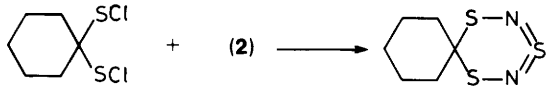


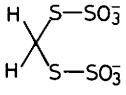
(9) (10)

Trithiadiazines from Cyclic Polysulphides.—Cyclohexane-1,1-dithiol [10] was treated with chlorine to give the bis-sulphenyl chloride (**11**) which was not isolated but treated directly with bis(trimethylsilyl)sulphurdi-imide (**2**); this produced the spirocyclic trithiadiazine (**12**) as an orange solid, but only in minute yield (1%). We therefore turned our attention to an alternative

source of bis-sulphenyl chlorides: the chlorinolysis of cyclic polysulphides, such as the tetrathianes (**4**). Methanebis(sulphenyl chloride) (**1**; R = H) had been prepared, but not isolated, by chlorinolysis of tetrathiane (**4**; R = H) which in turn had been prepared from the bis-Bunte salt (**13**) with potassium iodide.[11] We repeated this last reaction and obtained, not the tetrathiane, but the pentathiepane (**14**), which is the natural product lenthionine.[12] One synthesis of lenthionine uses the reaction of di-iodomethane and the non-stoicheiometric sodium sulphide, $Na_2S_{2.5}$.[13] In an attempt to prepare tetrathiane (**4**; R = H) analogously, we treated di-iodomethane with disodium disulphide, but again obtained lenthionine; the best medium was a two-phase aqueous dichloromethane mixture at room temperature which gave lenthionine in 18% yield (30% conversion). Presumably the seven membered ring is thermodynamically more stable than the six.



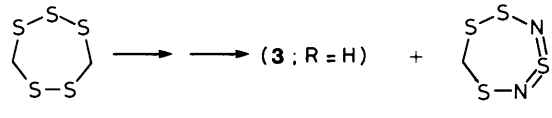
(**11**) (**12**)



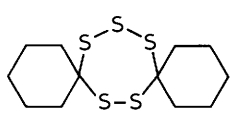
(**13**)

With lenthionine in hand we attempted to prepare the parent trithiadiazine (**3**; R = H) from it. Chlorination in tetrachloromethane at 0 °C, followed by cyclisation with bis(trimethylsilyl)sulphurdi-imide (**2**) gave two products. The first was trithiadiazine (**3**; R = H) (12%) identical with that from tetrasulphur tetranitride and diazomethane[1] and the second was an orange solid which, on the basis of its mass spectrum, was tentatively assigned structure (**15**) (20%); this presumably arose from incomplete sulphur–sulphur bond cleavage by chlorine. Although the formation of trithiadiazine in this way was of interest as its first rational synthesis, it is of little preparative value in view of the low overall yield; the S_4N_4–CH_2N_2 reaction gives 40% yield.[1] But the method may be of use in preparing triathiadiazines unavailable by other routes.

Chlorinolysis of the pentathiepane (**16**),[14] prepared from



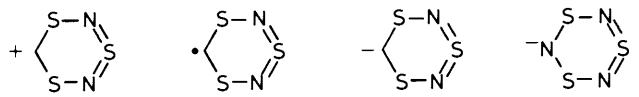
(**14**) (**15**)



(**16**)

cyclohexanone and ammonium disulphide, and treatment with bis(trimethylsilyl)sulphuri-imide (**2**) gave the spiro compound (**12**) in much better yield (22%) than above.

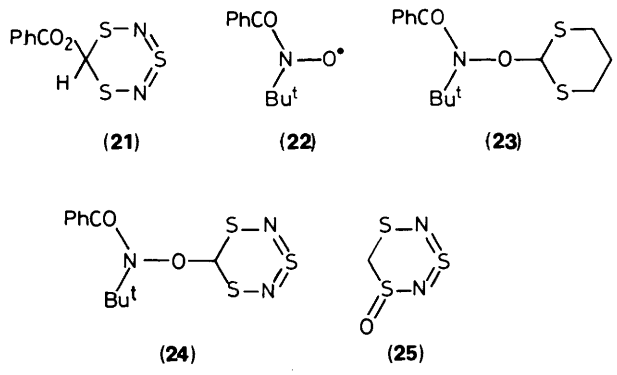
Chemistry of Trithiadiazines.—The 1,3-sulphur atoms of dithiolanes and dithianes confer a wide and interesting range of chemistry on these molecules, and by analogy we hoped to be able to generate the trithiadiazine cation (**17**) radical (**18**), and anion (**19**). If planar and delocalised, the cation would be an antiaromatic 8π, and the anion (**19**) an aromatic 10π electron system. The anion $S_3N_3^-$ (**20**), isoelectronic with (**19**), although delicate, is known and is reported to have a planar delocalised structure consistent with its 10π aromaticity.[15] The cyclic S_3N_3 radical, isoelectronic with (**18**), has also been characterised in the gas phase.[16]



(**17**) (**18**) (**19**) (**20**)

When 6-phenyltrithiadiazine[1] in acetonitrile at room temperature was treated with triphenylmethyl tetrafluoroborate the initially red reaction mixture became green and then yellow over 30 min. No product crystallised and no triphenylmethane was produced (TLC). A similar result was obtained with the parent trithiadiazine, except that the reaction was slower. The reaction mixture was complex, but did not contain triphenylmethane, suggesting that hydride abstraction had not occurred. Accordingly, 6,6-dimethyltrithiadiazine (**3**; R = Me), with no potentially active hydrogen, was treated in the same way and this too gave a similar result. Presumably, decomposition of the ring was being initiated by electrophilic attack on one of the heteroatoms. Generation of the anion (**19**) was no more successful: both sodium hydride and butyl-lithium at −78 °C caused decolourisation and decomposition of trithiadiazine, and no 6-methyltrithiadiazine was obtained when the reaction mixtures were quenched with iodomethane. This sensitivity to bases and nucleophiles is reminiscent of the aromatic trithiadiazepines,[9] but trithiadiazine is more delicate, being slowly decomposed by ethyldi-isopropylamine in methanol at room temperature to give sulphur (70%) as the only elutable product. Trithiadiazines are also less thermally stable than trithiadiazepines and trithiatriazepines, and decompose above 100 °C regardless of their melting point.

However we were more successful with radical reactions where strongly polar reagents could be avoided. Treatment of trithiadiazine (**3**: R = H) with one equivalent of benzoyl peroxide in boiling benzene gave a more polar, red compound for which analytical and spectroscopic evidence showed the 6-benzoyloxy structure (**21**) (27%), the first trithiadiazine with a ring oxygen substitutent. However, similar reactions with di-t-butyl peroxide, t-butyl peroxyacetate, di-t-butyl peroxyoxalate, and t-butyl peroxybenzoate gave either no reaction or decomposition of the trithiadiazine ring. We then sought a less reactive, longer lived radical to maximise the possibility of coupled products, and so prepared benzoyl t-butyl nitroxide (**22**),[17] which readily gives radical substitution α to sulphur in tetrahydrothiophene.[18] In a model reaction with 1,3-dithiane the expected product (**23**) was formed in 95% yield. When the parent trithiadiazine was treated similarly [(**22**)(2 equiv.), boiling benzene, 16 h] the analogous product (**24**) (55%) was obtained as bright red needles. As expected the reaction with the nitroxide (**22**) was slower than with benzoyl peroxide reflecting the lower reactivity of the nitroxide, but it was higher yielding presumably because of the much higher concentration of the coupling radical. No dimer of the trithiadiazine radical (**18**) was observed in any of these reactions, suggesting that it is not substantially stabilised by delocalisation. Interestingly, when the 1:1 adduct (**24**) was treated with another two equivalents of nitroxide (**22**) in boiling benzene the disubstituted product was



(21) (22) (23)

(24) (25)

not observed, possibly indicating a marked conformational effect on the ease of hydrogen abstraction.

The parent trithiadiazine (**3**; R = H) was inert towards iodomethane, but was rapidly decomposed by ultraviolet irradiation and by triphenylphosphine, to give triphenylphosphine sulphide (67%) as the only elutable product. With *m*-chloroperbenzoic acid (1 equiv.) in dichloromethane the red colour faded rapidly and the yellow, highly crystalline mono-*S*-oxide (**25**), m.p. 96–97 °C, (50%) was formed. The same oxide was produced (43%), and more easily purified, with dinitrogen tetroxide in dichloromethane at 0 °C. Structure (**25**), in which the divalent rather than tetravalent sulphur has been oxidised, was based on strong infrared absorption at 1 075 cm^{-1} (N=S=N intact) and the pair of geminally coupled proton signals at δ 2.72 and 5.33 in the ^1H NMR spectrum (unsymmetrical methylene). The structure was confirmed by *X*-ray diffraction which also showed the S–O bond to be equatorial.[19]

Experimental

Light petroleum refers to the fraction b.p. 40–60 °C.

Dichloromethanebis(sulphenyl chloride) (**1**; R = Cl).—Dichloromethanebis(sulphenyl chloride) was prepared by modification of the literature method.[5] Carbon disulphide (100 cm^3) was placed in a water cooled photochemical reactor fitted with a high pressure mercury vapour lamp. The apparatus was immersed in a cooling bath at −20 to −5 °C. Dry chlorine gas was passed into the solution through a glass frit. The mixture was illuminated for 2 h 30 min (longer reaction times led to the formation of trichloromethanesulphenyl chloride). The reaction mixture was carefully evaporated on a steam bath, the oily residue was fractionally distilled at 25 °C under high vacuum to give firstly mixtures containing sulphur dichloride, trichloromethanesulphenyl chloride and dichloromethanebis(sulphenyl chloride) (2.29 g) distilled at 0.5 mmHg pressure, and secondly dichloromethanebis(sulphenyl chloride) (1.58 g) distilled at 0.02 mmHg; ν_{max}(film) 12.1, 12.8, 12.4, and 13.7 μm identical with the literature values.[5]

6,6-*Dichloro*-1,3,5,2,4-*trithiadiazine* (**3**; R = Cl).—Bis(trimethylsilyl)sulphurdi-imide (**2**) (0.37 g, 1.69 mmol) was dissolved in dichloromethane (50 cm^3). Dichloromethanebis(sulphenyl chloride) (**1**; R = Cl) (0.35 g, 1.69 mmol) was similarly dissolved in dichloromethane (50 cm^3). These solutions were added dropwise simultaneously to stirred dichloromethane (250 cm^3) at room temperature over 4 h. The mixture became red and the solution was stirred for 1 h after the addition was complete. The reaction mixture was evaporated under reduced pressure and chromatographed (light petroleum) to give 6,6-*dichloro*-1,3$\lambda^4\delta^2$,5,2,4-*trithiadiazine* as a deep-red volatile oil (0.197 g, 56%). Analytically pure material was obtained by chromatography as above and triple distillation (kugelrohr) at 70–80 °C and 5–10 mmHg (Found: N, 13.6; Cl, 34.0. $CCl_2N_2S_3$ requires N, 13.5; Cl, 34.2%); λ_{max}(cyclohexane) 292 (log ε 3.40) and 489 nm (2.97); ν_{max}(film) 1 081, 972, 810, 738, 717, and 630 cm^{-1}; *m/z* (4.6 eV, 110 °C) 206 (M^+, 49%), 171 (3), 162 (24), 160 (31), 114 (4), 92 (40), 79 (100), and 46 (93).

Malondianilide-2,2-bis(sulphenyl chloride) (**5a**).—This was prepared by a modification of the literature method.[6] Malondianilide (1 g, 3.9 mmol) was suspended in benzene (10 cm^3). Sulphur dichloride (2 g, 19.4 mmol) was added and evolution of hydrogen chloride occurred immediately and the mixture formed a thick paste. Benzene (3 cm^3) was added and the mixture was heated at reflux for 3 h 30 min. The cooled mixture was filtered and the solid was recrystallized from benzene to give malondianilide-2,2-bis(sulphenyl chloride) (**5a**) (0.52 g, 34%) as pale yellow needles, m.p. 166–168 °C (lit.,[6] 164–165 °C) (Found: C, 46.6; H, 3.0; Cl, 18.0; N, 7.1; S, 16.7. Calc. for $C_{15}H_{12}Cl_2N_2O_2S_2$: C, 46.5; H, 3.1; Cl, 18.3; N, 7.2; S, 16.55%); ν_{max}(Nujol) 3 285 (NH), 1 647 (C)), 1 598, 1 537, 1 510, 1 446, 1 235, and 742 cm^{-1}; δ_H[60 MHz; $(CD_3)_2CO$] 7.1–7.9 (10 H, m br), and 10.5 (2 H, s br).

Ethyl 2,2-Bis(chlorothio)-3-oxo-3-(phenylamino)propanoate (**5b**).—Sulphur dichloride (5.8 g, 56.6 mmol) was added to a solution of ethyl 3-oxo-3-(phenylamino)propanoate (2.34 g, 11.5 mmol) in benzene (23 cm^3); immediate reaction occurred with evolution of hydrogen chloride. The mixture was stirred at room temperature for 1 h and then heated at reflux for 1 h. A small portion of the reaction mixture was removed and evaporated; analysis by ^1H NMR showed the methylene peaks at δ 3.2 to be absent. The mixture was evaporated under nitrogen and final traces of solvent and sulphur dichloride were removed under high vacuum to give *ethyl 2,2-bis(chlorothio)-oxo-3-(phenylamino)propanoate* (**5b**) as a viscous yellow oil (3.8 g, 97%); δ_H(60 MHz; $CDCl_3$) 1.3 (3 H, t), 4.3 (2 H, q), 7.1–7.8 (5 H, m), and 8.8 (1 H, s, br); *m/z* (70 eV, 130 °C), 339 (M^+, 0.1%), 303 (0.7), 271 (4), and 78 (100).

Diethyl 2,2-Bis(chlorothio)propane-1,3-dioate (**5c**).—Diethyl malonate (2.4 g, 15 mmol) and sulphur dichloride (9.27 g, 90 mmol) were mixed in benzene (20 cm^3). The mixture was heated at reflux for 36 h and then evaporated to dryness and final traces of benzene and sulphur dichloride were removed under high vacuum to give *diethyl 2,2-bis(chlorothio)propane-1,3-dioate* (**5c**) (4.37 g, 99%) as a viscous yellow oil; ν_{max}($CHCl_3$) 2 985, 1 736, 1 269, 1 028, and 521 cm^{-1}; δ_H(60 MHz; $CDCl_3$) 1.3 (6 H, t), and 4.4 (4 H, q); *m/z* (70 eV, 100 °C), 292 (M^+, 0.3%), 260 (4), 84 (48), and 29 (100).

t-Butyl Methyl 2,2-Bis(chlorothio)propane-1,3-dioate (**5d**).—t-Butyl methyl propane-1,3-dioate (1 g, 5.7 mmol) and sulphur dichloride (1.2 g, 11.6 mmol) were mixed in benzene (20 cm^3) the mixture was purged with nitrogen and maintained at reflux for 36 h. Analysis by ^1H NMR as previously described showed the absence of the methylene peak at δ 3.0. The mixture was evaporated to dryness and distilled under high vacuum (5×10^{-4} mmHg, 70–90 °C) to give *t-butyl methyl 2,2-bis(chlorothio)propane-1,3-dioate* (**5d**) (0.97 g, 55%) as a viscous yellow oil; δ_H(60 MHz; $CDCl_3$) 1.5 (9 H, s), and 3.9 (3 H, s); *m/z* (70 eV, 110 °C) 306, (M^+, 0.2%), 259 (1.4), 227 (3), and 57 (100).

6,6-*Bis(phenylaminocarbonyl)*-1,3,5,2,4-*trithiadiazine* (**6a**).—Malonanilide-2,2-bis(sulphenyl chloride) (**5a**) (0.13 g, 0.33 mmol) was dissolved in 1,4-dioxane (50 cm^3). Bis(trimethylsilyl)-sulphurdi-imide (**2**) (0.07 g, 0.34 mmol) was dissolved in dichloromethane (50 cm^3). The two solutions were added simultaneously dropwise over 30 min to dichloromethane (200

cm^3) stirred at room temperature. During the course of the addition the reaction mixture became yellow and then orange. The solution was stirred overnight at room temperature. The reaction mixture was evaporated and the red residue was chromatographed (dichloromethane) to give 6,6-*bis*(*phenylaminocarbonyl*)-1,3$\lambda^4\delta^2$,5,2,4-*trithiadiazine* (0.064 g, 52%) as red needles, m.p. 126–128 °C (from light petroleum–dichloromethane) (Found: C, 47.8; H, 3.1; N, 14.7. $C_{15}H_{12}N_4O_2S_3$ requires C, 47.85; H, 3.2; N, 14.9%); λ_{max}(EtOH) 253 (log ε 4.41) and 444 nm (3.18); ν_{max}($CHCl_3$) 3 370, 3 270, 1 695, 1 662, 1 600, 1 521, 1 500, 1 443, 1 315, 1 080, and 635 cm^{-1}; δ_H(250 MHz; $CDCl_3$) 7.14 (2 H, m), 7.38 (4 H, m), 7.54 (4 H, m), and 9.25 (2 H, s, br).

Ethyl 6-(*Phenylaminocarbonyl*)-1,3,5,2,4-*trithiadiazine*-6-*carboxylate* (**6b**).—Ethyl 2,2-(bis(chlorothio)-3-oxo-3-(phenylamino)propanoate (**5b**) (0.81 g, 2,4 mmol) was dissolved in dichloromethane (50 cm^3). Bis(trimethylsilyl)sulphurdi-imide (**2**) (0.99 g, 4.8 mmol) was similarly dissolved in dichloromethane 50 cm^3). These solutions were added dropwise simultaneously to dichloromethane (250 cm^3) stirred at room temperature over 1 h. The reaction mixture changed from yellow to red as the addition proceeded. The mixture was stirred at room temperature overnight and then evaporated under reduced pressure. Chromatography (light petroleum–dichloromethane) gave *ethyl* 6-(*phenylaminicarbonyl*)-1,3$\lambda^4\delta^2$,5,2,4-*trithiadiazine*-6-*carboxylate* (0.36 g, 46%) as orange needles, m.p. 101–102 °C (from light petroleum–dichloromethane) (Found: C, 40.0; H, 3.3; N, 12.6; S, 29.4. $C_{11}H_{11}N_3O_3S_3$ requires C, 40.1; H, 3.4; N, 12.75; S, 29.2%); λ_{max}(EtOH) 440 nm (log ε 3.17); ν_{max}(CCl_4) 3 400, 3 050, 3 020, 2 990, 1 720, 1 695, 1 600, 1 523, 1 495, 1 445, 1 390, 1 350, 1 232, 1 212, 1 300, 1 230, 1 085 (NSN), 1 045, 690, 645, and 635 cm^{-1}; δ_H(270 MHz; $CDCl_3$; TMS) 1.35 (3 H, t, *J* 5.6 Hz), 4.35 (2 H, q, *J* 5.6 Hz), 7.2 (1 H, m), 7.39 (2 H, m), 7.55 (2 H, m), and 8.50 (1 H, s, br); δ_C(69 MHz; $CDCl_3$) 13.89, 49.30, 64.36, 120.58, 125.81, 129.24, 136.23, 159.97, and 165.58. *m/z* (70 eV, 110 °C) 329 (M^+, 15%), 220 (3), 210 (16), 164 (16), and 119 (100).

Diethyl 1,3,5,2,4-*Trithiadiazine*-6,6-*dicarboxylate* (**6c**).—(i) Dichloromethane (50 cm^3) was added to diethyl 2,2-bis(chlorothio)propane-1,3-dioate (**5c**) (4.37 g, 14.9 mmol). Bis(trimethylsilyl)sulphurdi-imide (**2**) (3.6 g, 17.4 mmol) was dissolved in dichloromethane (50 cm^3). These solutions were added dropwise and simultaneously to dichloromethane (250 cm^3), stirred at room temperature, over 45 min. During the addition the mixture became yellow and then orange. The solution was stirred at room temperature overnight, and then evaporated under reduced pressure. Chromatography (light petroleum–dichloromethane) gave diethyl 1,3$\lambda^4\delta^2$,5,2,4-trithiadiazine-6,6-dicarboxylate (2.25 g, 49%) identical with authentic material.[1]

(ii) Diethyl 2,2-bis(chlorothio)propane-1,3-dioate (**5c**) (0.544 g, 1.85 mmol) was dissolved in dichloromethane (50 cm^3). A solution *S,S*-dimethyl-*N,N'*-bis(trimethylsilyl)sulphuri-imide (**8**) (0.44 g, 1.8 mmol) in dichloromethane (50 cm^3) was also prepared. These solutions were added simultaneously dropwise to dichloromethane (250 cm^3), stirred at room temperature, over 1 h 30 min. The mixture was evaporated to a small volume and chromatographed (light petroleum–dichloromethane) to give diethyl 1,3$\lambda^4\delta^2$,5,2,4-trithiadiazine-6,6-dicarboxylate (0.05 g, 10%) identical with authentic material.

(iii) A solution of *S,S*-dibenzylsulphurdi-imide (**9**) (0.47 g, 1.9 mmol) and triethylamine (0.39 g, 3.9 mmol) in dichloromethane (50 cm^3) was prepared. A solution of diethyl 2,2-bis(chlorothio)propan-1,3-dioate (**5c**) in dichloromethane (50 cm^3) was similarly prepared. These solutions were added dropwise simultaneously to dichloromethane (250 cm^3) at room temperature over 1 h. The mixture was evaporated under reduced pressure and chromatography (light petroleum–dichloromethane) gave dibenzyl sulphide (0.208 g, 51%) and diethyl 1,3$\lambda^4\delta^2$,5,2,4-trithiadiazine-6,6-dicarboxylate (35 mg, 6.5%), both identical with authentic material.

t-Butyl Methyl 1,3,5,2,4-*Trithiadiazine*-6,6-*dicarboxylate* (**6d**).—t-Butyl methyl 2,2-bis(chlorothio)propane-1,3-dioate (**5d**) (0.5142 g, 1.67 mmol) was dissolved in dichloromethane (50 cm^3). Bis(trimethylsilyl)sulphurdi-imide (**2**) (0.345 g, 1.67 mmol) was similarly dissolved in dichloromethane (50 cm^3). These solutions were added dropwise and simultaneously to dichloromethane (250 cm^3), purged with nitrogen and stirred at room temperature, over 1 h. The mixture became yellow and then orange on stirring overnight. The mixture was evaporated and chromatography (light petroleum–dichloromethane) gave *t-butyl methyl* 1,3$\lambda^4\delta^2$,5,2,4-*trithiadiazine*-6,6-*dicarboxylate* (66 mg, 13.4%) as an orange oil which slowly crystallized on prolonged storage at 4 °C, m.p. 53–56 °C (Found: M^+, 295.9966. $C_8H_{12}N_2O_4S_3$ requires 295.9959); λ_{max}(EtOH) 288 (log ε 3.95) and 428 nm (3.53); ν_{max}($CHCl_3$) 2 982, 1 770vs, 1 746vs, 1 372, 1 262vs, 1 230vs, 1 150vs, and 1 091 (NSN) cm^{-1}; δ_H(250 MHz; $CDCl_3$) 1.5 (9 H, s), and 3.85 (3 H, s); *m/z* (70 eV, 160 °C), 296 (M^+, 10%), 240 (16), 196 (4), 150 (11), 78 (8), and 57 (100)'

1,3,5,2,4-*Trithiadiazaspiro*[5.5]*undecane* (**12**).—(i) Cyclohexane-1,1-dithiol (1 g, 6.7 mmol) was dissolved in tetrachloromethane (11 cm^3) and stirred at room temperature. A solution of sulphuryl chloride (2.01 g, 15 mmol) in tetrachloromethane (10 cm^3) was added dropwise over 10 min. The reaction mixture was placed in a dropping funnel and diluted with dichloromethane (50 cm^3). A solution of bis(trimethylsilyl)-sulphurdi-imide (**2**) (1.39 g, 6.7 mmol) in dichloromethane (50 cm^3) was prepared. The solutions were added simultaneously dropwise to dichloromethane (250 cm^3) stirred at room temperature over 1 h. The mixture was stirred at room temperature overnight. Chromatography (light petroleum) followed by preparative thin layer chromatography (silica; light petroleum) gave 1,3$\lambda^4\delta^2$,5,2,4-trithiadiazaspiro[5.5]-undecane (10 mg, 1%) identical with that described in the next experiment.

(ii) To a solution of 4,4,7,7-bis(pentamethylene)-1,2,3,5,6-pentathiepane (**16**)[14] (100 mg, 0.31 mmol) in tetrachloromethane (6 cm^3) stirred at −5 °C was added a solution of chlorine in tetrachloromethane (0.60 cm^3, 1.0 mmol). The mixture was stirred at −5 °C for 30 min. Thin layer chromatography showed no remaining pentathiepane (**16**). The yellow solution was placed under water pump vacuum (protected by a calcium chloride guard tube) to remove any remaining chlorine. The reaction mixture was transferred to a dropping funnel and diluted with dichloromethane (50 cm^3). Bis(trimethylsilyl)sulphurdi-imide (**2**) (0.127 g, 0.61 mmol) was dissolved in dichloromethane (50 cm^3). The solutions thus prepared were added dropwise, simultaneously to dichloromethane (250 cm^3), stirred at room temperature, over 2 h. The reaction mixture slowly changed to yellow and then orange during the addition. The mixture was stirred at room temperature overnight and then evaporated to dryness. Chromatography (light petroleum) gave firstly 1,3$\lambda^4\delta^2$,5,2,4-*trithiadiazaspiro*[5.5]*undecane* (27.7 mg, 22%) as orange solid, m.p. 43–46 °C (Found: M^+, 206.0011. $C_6H_{10}N_2S_3$ requires 206.0006); λ_{max}(cyclohexane) 413 nm (log ε 3.28); ν_{max}(CCl_4) 2 931vs, 2 855s, 1 445vs, and 1 093vs (NSN) cm^{-1}; δ_H(250 MHz; $CDCl_3$) 1.0–2.5 (br); *m/z* (70 eV, 100 °C) 206 (M^+, 49%), 160 (14), 114 (77), and 81 (100), and secondly an unidentified orange oil (3.8 mg).

1,2,3,5,6-*Pentathiepane*(*Lenthionine*) (**14**).—A solution of di-

sodium disulphide (2.8 g, 25.5 mmol) in water (100 cm^3) was added to a solution of di-iodomethane (6.81 g, 25.5 mmol) in dichloromethane (100 cm^3). The two phase mixture was stirred vigorously at room temperature for 5 days. The bright yellow aqueous layer slowly became colourless. The organic phase was separated and dried over Na_2SO_4. Chromatography (light petroleum) gave firstly di-iodomethane (2.6 g, 38%), and secondly 1,2,3,5,6-pentathiepane (0.44 g, 18%), m.p. 60–61 °C (lit.,[13] 61 °C).

1,3,5,2,4-*Trithiadiazine* (**3**; R = H) *from* 1,2,3,5,6-*Pentathiepane* (**14**).—1,2,3,5,6-Pentathiepane (**14**) (0.097 g, 0.52 mmol) was dissolved in tetrachloromethane (20 cm^3) with warming. The solution was then cooled to 0 °C. A solution of chlorine in tetrachloromethane (1.1 cm^3; 1.63 mol dm^{-3}) was added, and the mixture was stirred at 0 °C for 1 h. The yellow solution was placed under water pump vacuum (protected by a calcium chloride guard tube) to remove any unchanged chlorine. The reaction mixture was diluted with dichloromethane (30 cm^3) then transferred to a stoppered dropping funnel fitted with a cooling jacket at 0 °C. The methanebis(sulphenyl chloride) (**1**; R = H) solution so prepared was used without further purification. A solution of bis(trimethylsilyl)sulphurdi-imide (**2**) (0.212 g, 1.0 mmol) in dichloromethane (50 cm^3) was prepared. Both solutions were added simultaneously, dropwise to dichloromethane (250 cm^3) stirred at room temperature over 2 h. The mixture slowly became orange. After addition was complete the mixture was stirred at room temperature for 45 min. The solution was evaporated and chromatography (light petroleum) gave 1,3$\lambda^4\delta^2$,5,2,4-trithiadiazine (17.8 mg, 12%) identical with authentic material,[1] and an orange solid (18 mg, 20%), *m/z* 170 (M^+) tentatively assigned structure (**15**).

6-*Benzoyloxy*-1,3,5,2,4-*trithiadiazine* (**21**).—To a solution of 1,3$\lambda^4\delta^2$,5,2,4-trithiadiazine (**3**; R = H) (27 mg, 0.2 mmol) in benzene (3 cm^3) was added dibenzoyl peroxide (52 mg, 0.21 mmol). The mixture was immersed in an oil bath preheated to 110 °C. Reflux was maintained for 30 min. The mixture was cooled to room temperature and chromatographed (light petroleum–dichloromethane) to give 6-*benzoyloxy*-1,3$\lambda^4\delta^2$,5,2,4-*trithiadiazine* (13.7 mg, 27%) as orange needles, m.p. 85–87 °C (from light petroleum–dichloromethane) (Found: C, 37.5; H, 2.2; N, 10.6. $C_8H_6N_2O_2S_3$ requires C, 37.2; H, 2.3; N, 10.8%); λ_{max}(cyclohexane) 232 (log ε 4.09), 277 (3.58), 283 (3.57), and 458 nm (3.08); ν_{max}($CHCl_3$) 1 736vs (CO), 1 317, 1 283, 1 080 (NSN), and 1 060vs cm^{-1}; δ_H(250 MHz; $CDCl_3$) 7.0 (1 H, s), 7.55 (3 H, m), and 8.15 (2 H, m); *m/z* (70 eV, 180 °C) 258 (M^+, 5.4%), 212 (1), 184 (5), 137 (0.3), 122 (3), 105 (100), and 77 (28) as the only product.

N-*Benzoyl*-N-*t-butyl*-O-(1,3-*dithian*-2-*yl*)*hydroxylamine* (**23**).—1,3-Dithiane (60 mg, 0.5 mmol) was dissolved in a solution of benzoyl t-butyl nitroxide (**22**) (1 mmol) in benzene (2 cm^3). The mixture was heated at reflux for 1 h 30 min during which time the green colour, of the radical had completely faded. Thin layer chromatography (dichloromethane) showed benzoyl t-butyl hydroxylamine and a less polar compound to be the only products. The mixture was cooled to room temperature and diluted with ether (20 cm^3). The solution was washed with sodium hydroxide solution (20% w/v, 2 × 10 cm^3) to remove the *N*-benzoyl-*N*-t-butylhydroxylamine. The ethereal solution was washed with water (2 × 30 cm^3), dried over magnesium sulphate and evaporated to dryness to give N-*benzoyl*-N-*t-butyl*-O-(1,3-*dithian*-2-*yl*)*hydroxylamine* (0.147 g, 95%), m.p. 136–137 °C [light petroleum (b.p. 60–80 °C)–dichloromethane] as colourless needles (Found: C, 57.8; H, 6.9; N, 4.5. $C_{15}H_{21}NO_2S_2$ requires C, 57.8; H, 6.8; N, 4.5%); δ_H(250 MHz; $CDCl_3$) 1.5 (9 H, s), 1.8–2.2 (6 H, br), 5.42 (1 H, s), 7.35 (3 H, m), and 7.7 (2 H, m).

N-*Benzoyl*-N-*t-butyl*-O-(1,3,5,2,4-*trithiadazin*-6-*yl*)*hydroxylamine* (**24**).—To a solution of 1,3$\lambda^4\delta^2$,5,2,4-trithiadiazine (**3**; R = H) (34 mg, 0.25 mmol) in benzene (2 cm^3) was added a solution of benzoyl t-butyl nitroxide (**22**) (0.13 mol dm^{-3}, 3.4 cm^3, 0.44 mmol). The mixture was heated at reflux for 14 h. A further portion of the nitroxide (1.7 cm^3, 0.22 mmol) was added and reflux continued for 2 h after which time the reaction was complete. The mixture was evaporated and chromatographed (light petroleum–dichloromethane) to give N-*benzoyl*-N-*t-butyl*-O-(1,3,5,2,4-*trithiadiazin*-6-*yl*)*hydroxylamine* (45 mg, 55%) as bright red needles, m.p. 105–107.5 °C (from light petroleum–dichloromethane) (Found: C, 43.95; H, 4.5; N, 12.7. $C_{12}H_{15}N_3O_2S_3$ requires C, 43.7; H, 4.6; N, 12.75%); λ_{max}(cyclohexane) 222 log ε 4.20, 275 (3.79), and 459 nm (3.27); ν_{max}($CHCl_3$) 2 979, 1 765, 1 652, 1 600, 1 366, 1 227, 1 194, and 1 088 (NSN) cm^{-1}; δ_H(250 MHz; $CDCl_3$) 1.55 (9 H, s), 5.68 (1 H, s), 7.45 (3 H, m), and 7.68 (2 H, m); *m/z* (70 eV, 150 °C) 329 (M^+, 1%), 283 (1), 227 (0.5), 193 (0.4), 177 (4), 162 (2), 148 (5), 137 (2), 120 (4), 105 (100), and 77 (24).

1,3,5,2,4-*Trithiadiazine* 1-*Oxide* (**25**).—To a stirred solution of 1,3$\lambda^4\delta^2$,5,2,4-trithiadiazine (50 mg, 0.36 mmol) in dichloromethane (20 cm^3) cooled to 0 °C was added a solution of dinitrogen tetroxide in dichloromethane (20%, v/v; 11 μl, 0.34 mmol). The mixture changed from deep red to yellow as the reaction proceeded. Stirring was continued at 0 °C for 70 min. The reaction mixture was evaporated under reduced pressure and chromatographed (light petroleum–dichloromethane) to give 1$\lambda^4\delta^3$,3$\lambda^4\delta^2$,5,2,4-*trithiadiazine* 1-*oxide* (23.7 mg, 43%) as yellow plates, m.p. 96–97 °C (from light petroleum–dichloromethane) (Found: M^+, 153.9322. $CH_2N_2OS_3$ requires 153.9329); λ_{max}(EtOH) 206 (log ε 3.94) and 368 nm (3.54); ν_{max}($CHCl_3$) 1 140, 1 110, 1 075 (NSN), and 965 cm^{-1}; δ_H(250 MHz; $CDCl_3$) 2.72 (1 H, d, *J* 11.6 Hz), and 5.33 (1 H, d, *J* 11.6 Hz); *m/z* (70 eV, 120 °C), 154 (M^+, 7%), 108 (4), 78 (97), and 46 (100).

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