Organic Heterocyclothiazenes. Part 17.[1] Preparation, Acylation, and Metallation of 1,3,5,2,4-Trithiadiazepine

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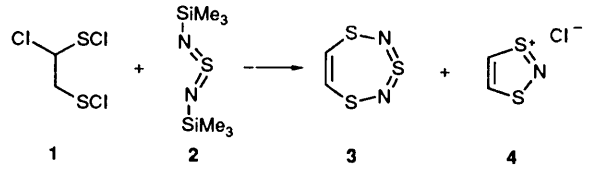
A larger scale preparation, with higher volume efficiency, is described for trithiadiazepine **3**, which can be acylated with acid anhydrides in the presence of trifluoromethanesulphonic acid. 6-Acetyltrithiadiazepine **10** is brominated to **11**, nitrated to **12**, and oxidised to the corresponding glyoxal **16** and carboxylic acid; it forms an oxime and phenylhydrazone sluggishly. Trithiadiazepine is readily mercuriated to give the bis(acetoxymercuri) derivative **20** in high yield and the mono(acetoxymercuri) derivative **19** in low yield. 6-Bromotrithiadiazepine can also be mercuriated, under more vigorous conditions, but 6-nitrotrithiadiazepine is unexpectedly converted into bis(6-nitrotrithiadiazepinyl)mercury **22** (with linear C–Hg–C bonds) which can be cleaved with iodine to give 6-iodo-7-nitrotrithiadiazepine. In contrast with mercuriation, thalliation of the trithiadiazepine **3** with thallium tris(trifluoroacetate) gives only the mono-metallated product **8**, which is readily converted into the corresponding cyano, iodo, and methoxycarbonyl trithiadiazepines.

In earlier Parts of this series we described the synthesis[2] and chemistry[3] of 1,3,5,2,4-trithiadiazepine **3**. We now describe a larger scale preparation of **3** together with more of its chemistry, particularly the formation and reactions of acylated and metallated derivatives.

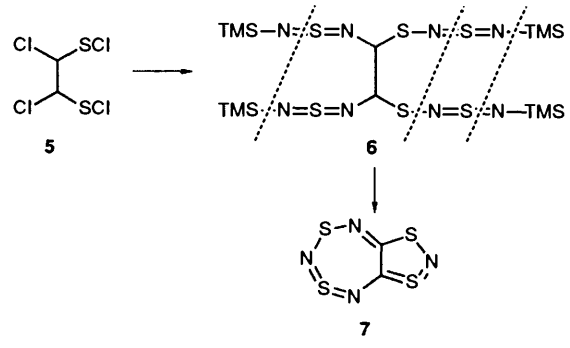
Larger Scale Preparation of 1,3,5,2,4-*Trithiadiazepine* **3**.—Our original preparation involved the slow synchronous delivery of dilute dichloromethane solutions of 1-chloroethane-1,2-bis(sulphenyl chloride) **1** and bis(trimethylsilyl)sulphurdiimide **2** into a stirred volume of dichloromethane at room temperature under nitrogen.[2] The addition was carried out over 48 h using motor-driven syringes, followed by a further period of stirring (48 h); yields of up to 30% could then be obtained. On scaling up this



1 **2** **3** **4**

procedure directly, the volumes of solvent became unacceptable and the use of syringes impractical. However, relatively high dilution conditions were found to be necessary, so experiments were performed in which the reagents were added to the reaction mixture from 1-l dropping funnels. This enabled the reagents to be added already diluted, the total volume of reaction mixture to be reduced, and the high dilution conditions to be maintained. The dropping funnel procedure was then used with increasing concentrations of starting materials, and the results are summarised in Table 1. Overall reaction times were also reduced significantly. A large increase in volume efficiency was achieved, making possible the isolation of nearly 2 g of trithiadiazepine per litre of reaction mixture, at the maximum concentration of starting material used. In our largest scale reaction, trithiadiazepine (9.6 g) was obtained from ethane-1,2-dithio (24.4 g) and bis(trimethylsilyl)sulphurdiimide **2** (53.5 g). The product was recrystallised from light petroleum, and the significant amounts of material remaining in solution were utilised by direct bromination[3] or nitration[3] of the liquors; the 6-bromo and 6-nitro derivatives so formed were readily isolated by chromatography. Direct bromination and nitration of the crude trithiadiazepine was also useful in the preparation of these key intermediates.

This increase of scale made possible the isolation and characterisation of some very minor products which were formed in variable yields, together with the other major product, 1,3,2-dithiazolium chloride **4**[2] (30–40%); these were 6-chlorotrithiadiazepine (< 1%), 6,7-dichlorotrithiadiazepine (< 1%), tetrasulphur tetranitride (< 5%) and 1,3,5,7-tetrathia-2,4,6,8-tetraza-azulene **7**[4] (< 0.5%). The mono and dichloro compounds were probably formed from polychlorinated impurities in the 1-chloroethane-1,2-bis(sulphenyl chloride) **1** starting material. The crude trichloro compound as routinely used in the preparation of the trithiadiazepine **3** was shown to contain 1,2-dichloroethane-1,2-bis(sulphenyl chloride) **5** by mass spectrometry and ^{1}H NMR spectroscopy. This tetra-



5 **6** **7**

chloro compound was formed as a clear yellow oil, which deposited yellow crystals on storage at 4 °C, when ethane-1,2-dithiol was more extensively chlorinated at 10 °C rather than 0 °C; ^{1}H and ^{13}C NMR spectroscopy confirmed its symmetrical structure. When this was treated with bis(trimethylsilyl)sulphurdiimide **2** the reaction was even more complex and gave only a very low yield of the expected 6-chlorotrithiadiazepine (1.4%), together with the same minor products as above, including the tetrathiatetraza-azulene **7**. Although this last product was formed in extremely low yields it was positively identified in the products, but not the starting materials, by direct comparison. Its unexpected formation can be formally rationalised by condensation of the tetrachloro compound **5** with 4 equiv. of bis(trimethylsilyl)sulphurdiimide **2** to give **6** followed by loss of 2 equiv. of bis(trimethylsilyl) amine and 0.5 equiv. of S_4N_4.

Perchlorination of ethane-1,2-dithiol until all ^{1}H NMR

Table 1 Preparation of the trithiadiazepine **3**: effect of increased reagent concentration and reduced addition time on yield and volume efficiency

Starting material concentration (mmol l^{-1} of reaction volume)	Scale (l)	Addition time (h)	Further reaction time (h)	Yield (g)	(%)	Volume efficiency (g l^{-1} of product)
5.0	2.0	48	76	0.3	24	0.18[a]
8.0	5.0	15	9	1.5	25	0.30[b]
16.0	5.0	15	8	3.6	29	0.72[b]
51.8	5.0	10	14	9.6	25	1.92[b]

[a] Reagents added *via* 50 ml motor-driven syringes. [b] Reagents added *via* 1-l dropping funnels.

Table 2 Acylation of trithiadiazepine **3**

$$\mathbf{3} + (RCO_2)O + CF_3SO_3H \longrightarrow 6\text{-RCO-trithiadiazepine}$$

R	Conditions	Yield (%)	Conversion (%)
Me	Ac_2O (solvent), CF_3SO_3H (1.05 equiv.), 22 °C, 90 min	40	71
Et	$(EtCO)_2O$ (solvent), CF_3SO_3H (1.1 equiv.), 22 °C, 30 min	62	66
Ph	$(PhCO)_2O$ (3 equiv.), CF_3SO_3H (1.1 equiv.), CS_2 solvent, 22 °C, 30 min	13	36

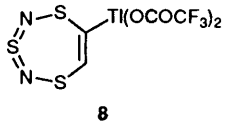
Table 3 Conversion of the trithiadiazepine **3** into the acetyl derivative **10** with varying catalyst concentration and reaction time

CF_3SO_3H (equiv.)	Temp. (°C)	Time (min)	Yield (%)	Conversion (%)
0.2	22	45	56	63
0.5	22	40	38	63
1.1	22	40	52	90
1.5	22	80	55	64
2.0[a]	22	10	31	31
2.0	22	10	45	65
2.0	0 to 22	30	45	81
4.0	0	30	16	63

[a] CF_3SO_3H added undiluted; in all the others this was dissolved in acetic anhydride.

signals had disappeared gave a crude product which reacted with bis(trimethylsilyl)sulphurdiimide **2** to form only polymeric material; neither compound **7** nor any polychlorinated trithiadiazepine products were detected.

Electrophilic Substitution of 1,3,5,2,4-*Trithiadiazepines*.—We have described the bromination and nitration[3] and, in a preliminary communication,[5] the bis(trifluoroacetoxy)thalliation of the trithiadiazepine **3**, and conversion of the thallium intermediate **8** into 6-cyano-, 6-iodo-, and 6-methoxycarbonyltrithiadiazepine; experimental details for these thallium reactions are given in this paper. Previous attempts to acylate



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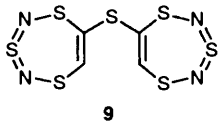

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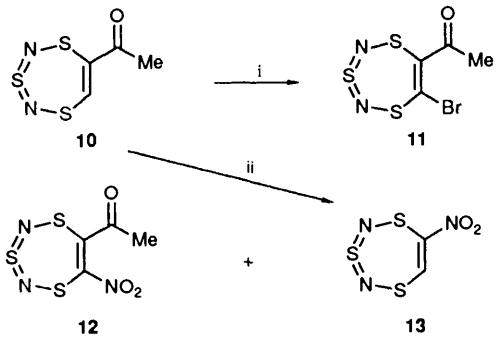
the ring with acid anhydrides or halides and Lewis acids were unsuccessful,[3] but we have now reinvestigated these reactions.

The use of mixed trifluoromethanesulphonic carboxylic anhydrides as highly active acylating agents was demonstrated by Effenberger and Epple.[6] They acylated a range of aromatic substrates using mixed anhydrides, either pre-generated or prepared *in situ* from acyl halides or anhydrides, together with catalytic amounts (1%) of trifluoromethanesulphonic acid. Acylation of the trithiadiazepine **3** was achieved using this approach, though larger amounts of trifluoromethanesulphonic acid were required (up to 2 equiv.), and workable yields were obtained only with acid anhydrides. Addition of undiluted trifluoromethanesulphonic acid to a solution of trithiadiazepine in the acid anhydride gave rapid reactions at 22 °C; carbon disulphide solvent was used with benzoic anhydride. Reaction with acetic, propionic and benzoic anhydrides gave the corresponding 6-acetyl-, propionyl- and benzoyl-trithiadiazepines as stable colourless crystalline solids (see Table 2).

The yields of acyl trithiadiazepines obtained in this way were limited by competing decomposition of starting material to chromatographic baseline products. Optimisation of the acetylation reaction resulted in higher conversions of starting material, but an excess of trifluoromethanesulphonic acid did not result in complete conversion to product, the reactions becoming more complex; nor was any 6,7-diacetyltrithiadiazepine detected. Optimum conditions required addition of a solution of trifluoromethanesulphonic acid in acetic anhydride to a solution of the trithiadiazepine **3** in acetic anhydride at room temperature. The reaction is rapid and essentially complete within 5 min, but running the reaction at reduced temperature does not improve the yield (see Table 3).

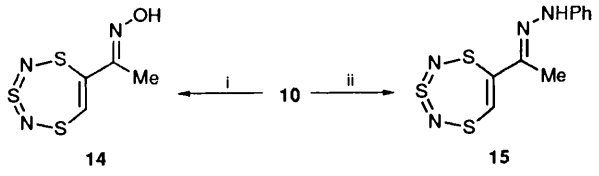
Treatment of the trithiadiazepine **3** with trifluoroacetic anhydride alone did not give 6-trifluoroacetyltrithiadiazepine, even at reflux. Attempts to catalyse this reaction with trifluoromethanesulphonic acid resulted in extensive decomposition, with isolation of the heteroaryl sulphide **9** as the major product; the thioether sulphur atom in **9** was presumably derived from decomposition of the heterocyclic ring. The powerful trifluoroacetylating agent, trifluoroacetic trifluoromethanesulphonic anhydride (trifluoroacetyl triflate)[7] in carbon disulphide decomposed the trithiadiazepine **3** at room temperature.

6-Acetyltrithiadiazepine **10** underwent bromination and nitration with *N*-bromosuccinimide and nitronium tetrafluoroborate respectively (Scheme 1). Yields were lower than for corresponding reactions of the parent trithiadiazepine **3**,[3] and some decomposition of the starting material was observed. Bromination to give **11** was sluggish at room temperature, confirming that the ring was somewhat deactivated; higher reaction temperatures caused more decomposition. Nitration gave the expected 6-acetyl-7-nitrotrithiadiazepine **12**, together with 6-nitrotrithiadiazepine **13**, presumably through *ipso* nitration and deacetylation. This indicates that the substituted



Scheme 1 *Reagents and conditions:* i, NBS, MeCN, 22 °C, 6 days; ii, NO_2BF_4, MeCN, −20 to 0 °C, 5 min

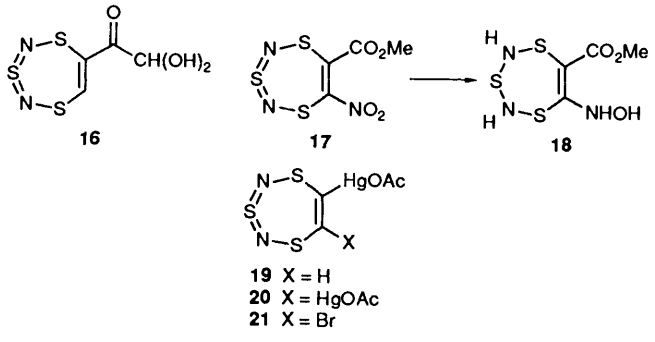
ring carbon of acetyltrithiadiazepine is still relatively electron rich, despite bearing an electron-withdrawing substituent. This property is also reflected in the diminished reactivity of the carbonyl group towards nucleophiles. Oxime and phenylhydrazone formation from 6-acetyltrithiadiazepine **10** (Scheme 2) were sluggish and accompanied by decomposition of the



Scheme 2 *Reagents and conditions:* i, NH_2OH HCl, pyridine, EtOH, reflux, 24 h; ii, $PhNHNH_2$, EtOH–AcOH, reflux, 40 min

starting material. The oxime **14** and phenylhydrazone **15** are stable crystalline solids, but the latter decomposes slowly in solution, possibly because of the sensitivity of the heterocyclic ring to the basic hydrazone function. X-Ray structural analysis of the oxime **14** shows the expected *trans* relationship between the ring and the hydroxy group; the oxime is dimeric in the crystalline state, with hydrogen bonding between one oxime nitrogen and another oxime hydroxy group.[8] Attempted Beckmann rearrangement on the oxime **14** and Baeyer–Villiger reaction on the ketone **10** were unsuccessful.

The methyl group of 6-acetyltrithiadiazepine **10** was oxidised with selenium dioxide in aqueous dioxane to give trithiadiazepinyl glyoxal monohydrate **16** as a crystalline hygroscopic solid. ^1H NMR and IR spectroscopy suggest that **16** exists largely as the hydrate; the ^1H NMR spectrum in [$^2H_6$]-DMSO showed a triplet δ 5.71 and a doublet at δ 7.15 corresponding to the proton on the terminal carbon and the hydroxy protons respectively; the ring proton resonates at δ 9.48. After exchange



with D_2O, only singlets at δ 5.71 and 9.48 were observed. Baeyer–Villiger oxidation of **10** with MCPBA presumably gave the mixed anhydride which was hydrolysed *in situ* to give the previously unknown 1,3,5,2,4-trithiadiazepine-6-carboxylic acid in low yield. The acid is a colourless crystalline solid, m.p. 240–242 °C, with a ^1H NMR signal for the ring proton at δ 8.80; it shows hydroxy and carbonyl absorptions in its IR spectrum at 3375 and 1674 cm^{-1}. On nitration with nitronium tetrafluoroborate the 6-carboxylic acid gave 6-nitro and 6,7-dinitro-trithiadiazepine, rather than the desired nitro acid, by *ipso* nitration and decarboxylation. However, methyl 7-nitrotrithiadiazepine-6-carboxylate **17** was formed (57%) by similar nitration of the 6-methoxycarbonyl derivative. The nitro ester **17** could not be hydrolysed to the nitro acid, and attempted reduction of the nitro group under a range of standard conditions resulted in decomposition of the starting material. Reduction of **17** with tin(II) chloride dihydrate in ethanol,[9] however, gave methyl 2,4-dihydro-7-hydroxylaminotrithiadiazepine-6-carboxylate **18** as a waxy solid (72%). The mass spectrum of **18** showed peaks for NS, NHS, CO_2Me, N_2H_2S, S_2, and NS_2 in addition to the loss of some of these fragments from the molecular ion at *m/z* 241; the IR spectrum showed absorption for NH and OH (3587, 3330 cm^{-1}) and C = O (1736 cm^{-1}). Other reductions of the sulphurdimide unit will be described in a later Part.

The ring proton of acetyl-, propionyl-, and benzoyl-trithiadiazepines resonate in the region δ 8.40–8.70, compared with δ 7.76 for the parent ring, reflecting the influence of the electron-withdrawing group. These compounds show strong carbonyl absorptions in the IR region 1650–1690 cm^{-1}, and the bromo **11** and nitro **12** derivatives absorb at 1713 and 1720 cm^{-1} respectively; the ring sulphurdiimide absorption is always close to 1160 cm^{-1}. Mass spectra of these acyl compounds show a molecular ion, with peaks for NS, NS_2, and N_2S_3; peaks for the acyl fragment and for loss for this fragment are also observed. The UV spectra of these compounds show the characteristic trithiadiazepine π–π^* absorption at *ca.* 335 nm (364 nm for the 6-acetyl-7-nitro derivative **12**).

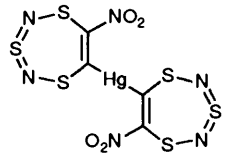
Mercuriation of Trithiadiazepine **3** *and Related Reactions.*—Mercuriation of trithiadiazepine was investigated as a means of isolating stable aryl metal derivatives and functionalising the heterocyclic ring [as with the non-isolable thallium bis(trifluoroacetate) **8**], particularly with respect to disubstituted trithiadiazepines.

Treatment of **3** with 2 equiv. of mercury(II) acetate in acetic acid gave 6,7-bis(acetoxymercuri)trithiadiazepine **20** in high yield (89%). When 0.2 equiv. of the mercuriating agent was used, **20** was again the major product (75%), with fractional crystallisation being needed to isolate the mono-mercuriated product **19** (11%). Thiophene and furan show a similar tendency towards polymercuriation.[10] This very ready disubstitution complements the exclusive mono-metallation of **3** observed with thallium(III) tris(trifluoroacetate).[5] These hetarylmercurials are thermally stable, highly crystalline solids (m.p. > 200 °C) giving good elemental analyses.

6-Bromotrithiadiazepine was mercuriated similarly to give **21** (44%) but more vigorous conditions (refluxing THF + acetic acid, 18 h) were required for this less reactive substrate, which could not be thalliated under any conditions. 6-Nitrotrithiadiazepine was similarly resistant to the most vigorous thalliation conditions, but attempted mercuriation gave an unexpected product, the symmetrical bis(7-nitrotrithiadiazepin-6-yl)mercury **22** (49%), again using more vigorous conditions (refluxing acetic acid, 72 h). This is a yellow crystalline high-melting solid, and its structure was confirmed by X-ray diffraction[8] on material crystallised from DMSO and ethanol. The C–Hg–C bonds are linear, as in bis(2-thienyl)-mercury.[11] Formation of the bisarylmercury **22** may have resulted from the formation of an internal mercury complex by the nitro group; this could weaken the mercury–oxygen bond in the first-formed acetoxymercuri derivative or displace acetate completely to give the cyclic intermediate **23** which could be

Table 4 Treatment of 6-acetoxymercuri-7-bromotrithiadiazepine **21** with copper(II) thiocyanate (5 equiv.)

Conditions	Trithiadiazepine isolated (%)			
	6-SCN	6,7-$(SCN)_2$	6-Br-7-SCN	6-Br
Benzene, reflux, 72 h	15	21	21	0
Toluene, reflux, 60 h	32	0	42	20
Xylene, reflux, 15 h	47	Trace	24	16



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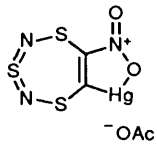

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an effective mercuriating agent for another mole of substrate. Attempted plumbiation with lead tetra-acetate and lead tetrakis(trifluoroacetate) led only to decomposition of the trithiadiazepine **3**.

Bis(7-nitrotrithiadiazepin-6-yl)mercury **22** was cleanly and rapidly demercuriated with iodine in THF at room temperature to give 6-iodo-7-nitrotrithiadiazepine. This is a useful preparation of a key intermediate since the corresponding bromo nitro compound is available only in very low yield from the nitration of 6-bromotrithiadiazepine and not at all from the bromination of 6-nitrotrithiadiazepine.[4] An alternative route to the 6-iodo-7-nitro compound was investigated following a literature method for the synthesis of nitroaryl iodides by nitration of arylthallium derivatives.[12] Nitration of trithiadiazepinylthallium bis(trifluoroacetate) **8** with acetyl nitrate, followed by *in situ* iodination, gave 6-iodo-7-nitrotrithiadiazepine together with 6-nitro- and 6,7-dinitro-trithiadiazepine, and the yield was much lower than in the mercuriation method.

The reaction of bis(acetoxymercuri)trithiadiazepine **20** with thiocyanogen, prepared from silver thiocyanate and bromine, did not result in the expected formation[13] of the bis(thiocyanato)trithiadiazepine. However, reaction of either bis(acetoxymercuri)trithiadiazepine **20** or, better, 6-acetoxymercuri-7-bromotrithiadiazepine **21** with copper(II) thiocyanate in refluxing hydrocarbon solvents gave a mixture of 6-thiocyanatotrithiadiazepine, 6,7-bis(thiocyanato)trithiadiazepine, 6-bromo-7-thiocyanatotrithiadiazepine and 6-bromotrithiadiazepine (see Table 4).

Experimental

For general points see earlier Parts of this series.

Modified Synthesis of 1,3,5,2,4-*Trithiadiazepine* **3**.—Ethane-1,2-dithiol (21.7 ml, 0.259 mol) was dissolved in dry tetrachloromethane (360 ml) and treated with chlorine gas at 5–10 °C until ^{1}H NMR assay of the neat reaction mixture showed maximum conversion into 1-chloroethane-1,2-bis(sulphenyl chloride) **1** and no residual starting material nor ethane-1,2-bis(sulphenyl chloride). Solvent was then removed from the reaction mixture on a rotary evaporator and the resulting oil diluted with dry dichloromethane, to make the volume of solution up to 1000 ml. Bis(trimethylsilyl)sulphurdiimide **2** (53.53 g, 0.259 mol) was then dissolved in dichloromethane, the volume of solution being made up to 1000 ml. The solutions of bis(trimethylsilyl)sulphurdiimide and 1-chloroethane-1,2-bis(sulphenyl chloride) were added synchronously into a vigorously stirred volume of dichloromethane (3000 ml) from two 1-l dropping funnels at 22 °C. The addition rate was maintained at 1–2 drops min^{-1}, with a total addition time of 10 h. After addition was complete the reaction mixture, a beige suspension, was stirred for a further 14 h at 22 °C. The suspension was then filtered directly into a rotary evaporator using an upturned sintered glass funnel and plasticiser-free tubing, and the solids were washed with dichloromethane to give crude 1,3,2-dithiazolium chloride **4** (16.9 g, 43%) as a beige powder. Solvent was removed from the filtrate and washings on the rotary evaporator, the temperature being maintained <35 °C in order to reduce losses due to the volatility of the product. The residue was adsorbed onto silica (50 g) and extracted with light petroleum (2000 ml) at 22 °C in a sinter funnel. The light petroleum extract, an orange solution, was evaporated and the residue adsorbed onto silica and separated using flash chromatography on silica. Elution with light petroleum gave 1,3,5,2,4-trithiadiazepine **3** as a yellow–orange solid. This material was recrystallised from light petroleum to give **3** (9.58 g, 25%) as pale yellow plates, m.p. 56–57 °C (from light petroleum), identical with an authentic sample.[2] Other experiments are summarised in Table 1.

1-*Chloroethane*-1,2-*bis*(*sulphenyl chloride*) **1**.—Ethane-1,2-dithiol (20 ml, 0.238 mol) was dissolved in dry tetrachloromethane (220 ml) and treated with chlorine gas at 0–10 °C until ^{1}H NMR assay of the neat reaction mixture showed maximum conversion into **1** and no residual starting material nor ethane-1,2-bis(sulphenyl chloride). Solvent was removed from the reaction mixture on a rotary evaporator to give a red foul-smelling oil (31 ml, 31.9 g). From this oil was taken an aliquot (8.0 ml, 8.24 g) which was distilled at 70–75 °C (0.04 mmHg) using a Kugelrohr apparatus. The title compound **1** (6.14 g, 74% recovery from distillation) was obtained as a red *oil* (Found: C, 12.6; H, 1.4. $C_2H_3Cl_3S_2$ requires C, 12.2; H, 1.5%); ν_{max}(film)/cm^{-1} 2965, 2923, 1393, 1238, 1184, 1132, 1026, 877, 753, 707, 631 and 520; δ_H(60 MHz; CCl_4) 3.76 (1 H, d), 3.86 (1 H, d) and 5.52 (1 H, t); *m/z* (170 °C) 196 (M^+, 9%), 163 (4), 162 (5), 160 (8), 158 (9), 129 (11), 128 (8), 126 (9), 115 (7), 99 (7), 96 (9), 94 (14), 93 (8), 90 (16), 81 (8), 79 (9), 64 (30), 58 (10), 45 (29), 38 (33) and 36 (100).

1,2-*Dichloroethane*-1,2-*bis*(*sulphenyl chloride*) **5**.—Ethane-1,2-dithiol (10 ml, 0.12 mol) was dissolved in dry tetrachloromethane (110 ml) and treated with chlorine gas at 0–10 °C for 2 h until ^{1}H NMR analysis of the neat reaction mixture showed the disappearance of 1-chloroethane-1,2-bis(sulphenyl chloride) signals and the appearance of a singlet at δ 5.78. Solvent was removed from the reaction mixture using a rotary evaporator and the resulting orange oil was set aside at 4 °C overnight. Orange crystals formed in the oil and were separated by decantation of the liquors. The crystals were then washed with cold dichloromethane and dried *in vacuo* to give 1,2-dichloroethane-1,2-bis(sulphenyl chloride) **5** as an orange–yellow solid, melting below room temperature (Found: C, 11.6; H, 1.6. $C_2H_2Cl_4S_2$ requires C, 10.35; H, 0.9%); ν_{max}(film)/cm^{-1} 2961, 2924, 1708, 1399, 1352, 1223, 1175, 1150, 1010, 884, 728, 673, 585 and 525; δ_H(60 MHz; $CDCl_3$) 5.78 (2 H, s); δ_C(62.9 MHz; $CDCl_3$) 72.4; *m/z* (120 °C) 230 (M^+, 20%), 197 (7), 196 (5), 195 (6), 194 (5), 167 (5), 165 (14), 163 (15), 162 (12), 160 (39), 158 (46), 130 (15), 129 (8), 128 (23), 127 (11), 123 (10), 117 (22), 115 (30), 81 (20), 79 (52), 64 (26), 38 (32) and 36 (100).

6-*Acetyl*-1,3,5,2,4-*trithiadiazepine* **10**.—(a) *Addition of undiluted* CF_3SO_3H. Trithiadiazepine **3** (200 mg, 1.30 mmol) was dissolved in acetic anhydride (1 ml) and trifluoromethanesul-

phonic acid (0.12 ml, 1.36 mmol, 1.05 equiv.) added rapidly at 22 °C. The reaction mixture became dark and was stirred at 22 °C for 90 min. The reaction mixture was then diluted with diethyl ether (10 ml) and the ethereal solution treated with saturated aqueous sodium hydrogen carbonate until no further effervescence was observed. The aqueous layer was separated and extracted with diethyl ether (20 ml). The combined organic layers were washed with water (10 ml), dried ($MgSO_4$) and evaporated to give an oil which was adsorbed onto silica and separated using flash chromatography on silica. Elution with diethyl ether (5–20%) in light petroleum gave recovered starting material (89.3 mg, 44%) and then the *title compound* **10** (100.5 mg, 40% yield, 71% conversion) as crystals, m.p. 108–109 °C (from light petroleum) (Found: C, 25.1; H, 2.1; N, 14.5. $C_4H_4N_2OS_3$ requires C, 25.0; H, 2.1; N, 14.6%); λ_{max}(EtOH)/nm 268 (log ε 4.44), and 332 (3.81); $\nu_{max}(CCl_4)/cm^{-1}$ 2981, 1693, 1667, 1504, 1486, 1422, 1359, 1293, 1266, 1217, 1195, 1167, 1004, 949 and 888; δ_H(250 MHz; $CDCl_3$) 2.70 (3 H, s), and 8.70 (1 H, s); δ_C(62.9 MHz; $CDCl_3$) 26.9, 133.5, 145.9 and 191.7; *m/z* (170 °C) 192 (M^+, 58%), 150 (2), 146 (3), 124 (3), 104 (30), 88 (6), 78 (22), 46 (19), 45 (13) and 43 (100).

(b) *Addition of* CF_3SO_3H *in solution; optimised preparative procedure.* Trifluoromethanesulphonic acid (227.6 mg, 1.52 mmol, 1.5 equiv.) was dissolved in acetic anhydride (1 ml) and this solution was added to a solution of trithiadiazepine (151.7 mg, 1.01 mmol) in acetic anhydride (1 ml) at 22 °C. The mixture was stirred at 22 °C for 80 min, diluted with diethyl ether (50 ml) and then treated with saturated aqueous sodium hydrogen carbonate until no further effervescence was observed. The aqueous layer was separated and extracted with diethyl ether (50 ml). The combined organic layers were washed with water (10 ml), dried ($MgSO_4$) and evaporated to give an oil. This oil was adsorbed onto silica and separated using flash chromatography on silica. Elution with diethyl ether (30%) in light petroleum gave recovered starting material **3** (21.8 mg, 14%) and then 6-acetyl-1,3,5,2,4-trithiadiazepine **10** (107.1 mg, 55% yield, 64% conversion), identical with that described previously. Related experiments are summarised in Tables 2 and 3.

6-*Propionyl*-1,3,5,2,4-*trithiadiazepine*.—Trithiadiazepine **3** (200 mg, 1.33 mmol) was dissolved in propionic anhydride (1 ml) and trifluoromethanesulphonic acid (0.13 ml, 1.47 mmol, 1.1 equiv) added to the solution at 22 °C. The solution darkened and an exotherm was observed. After 5 min, solids began to form in the reaction mixture which was stirred for 30 min at 22 °C. The reaction mixture was then diluted with diethyl ether (50 ml) and the ethereal solution treated with saturated aqueous sodium hydrogen carbonate until no further effervescence was observed. The aqueous layer was separated and extracted with diethyl ether (2 × 50 ml). The combined organic layers were washed with water (50 ml), dried ($MgSO_4$) and evaporated to give an oily solid which was adsorbed onto silica and separated using flash chromatography on silica. Elution with diethyl ether (0–10%) in light petroleum gave recovered starting material **3** (13.1 mg, 7%) and then crude 6-propionyl-1,3$\lambda^4\delta^2$,5,2,4-trithiadiazepine (273.3 mg). This was recrystallised from dichloromethane–light petroleum to give the *product* as plates (169.3 mg, 62% yield, 66% conversion), m.p. 98.5–99 °C (from light petroleum) (Found: C, 29.3; H, 2.7; N, 13.6. $C_5H_6N_2OS_3$ requires C, 29.11; H, 2.9; N, 13.6%); λ_{max}(EtOH)/nm 271 (log ε 4.36), and 333 (3.73); $\nu_{max}(CCl_4)/cm^{-1}$ 2984, 2942, 2906, 2880, 1693, 1667, 1503, 1484, 1460, 1410, 1381, 1344, 1265, 1163, 1131, 1057, 1014, 992 and 852; δ_H(90 MHz; $CDCl_3$) 1.25 (3 H, t, Me), 3.05 (2 H, q, CH_2) and 8.70 (1 H, s); *m/z* (140 °C) 206 (M^+, 24%), 177 (21), 160 (3), 150 (4), 124 (4), 104 (38), 88 (7), 78 (25), 57 (100), 46 (24) and 45 (16).

6-*Benzoyl*-1,3,5,2,4-*trithiadiazepine*.—Trithiadiazepine **3** (200 mg, 1.33 mmol) and benzoic anhydride (904 mg, 4.00 mmol, 3 equiv.) were dissolved in carbon disulphide (1 ml) and trifluoromethanesulphonic acid (0.13 ml, 1.47 mmol, 1.1 equiv.) was added to the solution at 22 °C. The reaction mixture became dark and an exotherm was observed. After being stirred for 30 min at 22 °C, the reaction mixture was diluted with diethyl ether (50 ml) and treated with saturated aqueous sodium hydrogen carbonate until no further effervescence was observed. The aqueous layer was separated and extracted with diethyl ether (2 × 50 ml). The combined organic layers were washed with water (50 ml), dried ($MgSO_4$) and evaporated to give an oil which was adsorbed onto silica and separated using flash chromatography on silica. Elution with diethyl ether (5–10%) in light petroleum gave recovered starting material **3** (128.5 mg, 64%) and then crude 6-benzoyl-1,3$\lambda^4\delta^2$,5,2,4-trithiadiazepine (121.7 mg). This was recrystallised from dichloromethane–light petroleum to give the *product* (43.4 mg, 13% yield, 36% onversion) as needles, m.p. 93–94 °C (from light petroleum) (Found: C, 42.7; H, 2.3; N, 10.9. $C_9H_6N_2OS_3$ requires C, 42.5; H, 2.4; N, 11.0%); λ_{max}(EtOH)/nm 218 (log ε 3.98), 260 (4.06), 284 (4.29) and 334 (3.80); $\nu_{max}(CCl_4)/cm^{-1}$ 3067, 2929, 1651, 1598, 1579, 1499, 1448, 1318, 1293, 1246, 1179, 1167, 1082, 1069, 1051, 1025, 910, 849 and 823; δ_H(90 MHz; $CDCl_3$) 7.35–7.86 (5 H, m) and 8.40 (1 H, s); *m/z* (130 °C) 254 (M^+, 38%), 105 (100), 78 (6), 77 (47), 51 (16) and 46 (6).

Bis(1,3,5,2,4-*Trithiadiazepin*-6-*yl*) *Sulphide* **9**.—The trithiadiazepine **3** (30 mg, 0.20 mmol) was suspended in trifluoroacetic anhydride (0.5 ml) at 22 °C. Since no reaction appeared to be taking place at 22 °C, the reaction mixture was refluxed for 5 h. After this, TLC showed that minimal reaction had taken place and starting material remained in suspension. The reaction mixture was allowed to cool to ambient temperature and trifluoromethanesulphonic acid (1 drop) added. The system became brown and was stirred at 22 °C for 1 h. After 1 h, TLC showed that very little starting material remained and the reaction mixture was complex. Trifluoroacetic anhydride was removed on a rotary evaporator and diethyl ether (10 ml) and water (5 ml) were added to the residue. The aqueus layer was separated and extracted with diethyl ether (2 × 10 ml). The combined organic layers were washed with water (5 ml), dried ($MgSO_4$) and evaporated to give a dark oily solid which was adsorbed onto silica and separated using flash chromatography on silica. Elution with diethyl ether (50%) in light petroleum gave recovered starting material (3.8 mg, 13%) and then bis(1,3$\lambda^4\delta^2$,5,2,4-trithiadiazepin-6-yl) sulphide (10.1 mg, 15% yield, 18% conversion) as crystals which were recrystallised from dichloromethane–light petroleum to give the *product* **9**, m.p. 179–180 °C (from light petroleum) (Found: C, 14.7; H, 0.6; N, 16.7. $C_4H_2N_4S_7$ requires C, 14.5; H, 0.6; N, 17.0%); λ_{max}(EtOH)/nm 240 (log ε 4.08), 256 (4.11) and 335 (3.83); $\nu_{max}(CCl_4)/cm^{-1}$ 2928, 2857, 1732, 1589, 1489, 1356, 1157, 999 and 962; δ_H(90 MHz; $CDCl_3$) 8.40 (1 H, s); *m/z* (120 °C) 330 (M^+, 100%), 284 (1), 238 (3), 206 (2), 181 (3), 149 (8), 135 (34), 124 (33), 105 (17), 89 (30), 78 (43), 46 (30) and 45 (39). Further elution gave a number of minor unidentified fluorine-containing products.

6-*Acetyl*-7-*bromo*-1,3,5,2,4-*trithiadiazepine* **11**.—6-Acetyltrithiadiazepine **10** (10 mg, 0.052 mmol) was dissolved in dry acetonitrile (1 ml) and *N*-bromosuccinimide (92.7 mg, 0.52 mmol, 10 equiv.) added in one portion at 22 °C. The reaction mixture was stirred at 22 °C for 6 days with frequent monitoring by TLC. After 6 days the reaction mixture was adsorbed onto silica and separated by flash chromatography on silica. Elution with diethyl ether (10–20%) in light petroleum gave, first, elemental sulphur and then the title compound **11** (1.5 mg, 11%

yield, 13% conversion) as needles. Further elution gave recovered starting material **10** (1.6 mg, 16%). The product **11** was purified by flash chromatography on silica, eluting with diethyl ether (0–20%) in light petroleum to give *needles*, m.p. 70–71 °C (from light petroleum) (Found: C, 18.0; H, 1.0; N, 10.0. $C_4H_3BrN_2OS_3$ requires C, 17.7; H, 1.1; N, 10.3%); λ_{max}(EtOH)/nm 221 (log ε 4.08), 239 (3.97), 283 (3.84) and 337 (3.78); $\nu_{max}(CCl_4)/cm^{-1}$ 2928, 2856, 2361, 1713s, 1469, 1422, 1355, 1166s, 1014, 983 and 848; δ_H(270 MHz; $CDCl_3$) 2.71 (3 H, s); *m/z* (170 °C) 270 (M^+, 19%), 228 (4), 182 (7), 124 (19), 78 (18), 46 (13) and 43 (100).

6-*Acetyl*-7-*nitro*-1,3,5,2,4-*trithiadiazepine* **12**.—Nitronium tetrafluoroborate (299.5 mg, 2.26 mmol, 2 equiv.) was suspended in dry acetonitrile (3 ml) and the suspension cooled to −20 °C. A solution of 6-acetyltrithiadiazepine **10** (216.5 mg, 1.128 mmol) in acetonitrile (10 ml) was added dropwise over 5 min at −20 °C and the brown reaction mixture then allowed to warm to 0 °C. Diethyl ether (50 ml) and water (30 ml) were added at 0 °C and the organic layer separated. The aqueous layer was extracted with ether (50 ml) and the combined ethereal solutions were washed with water (30 ml), dried ($MgSO_4$) and evaporated to give a yellow oil which was adsorbed onto silica and separated by flash chromatography. Elution with diethyl ether (10–20%) in light petroleum gave 6-nitro-1,3,5,2,4-trithiadiazepine **13** (48.8 mg, 22%), identical with an authentic specimen.[3] Further elution gave the title compound **12** (26.7 mg, 27%) as yellow crystals which were recrystallised from dichloromethane–light petroleum to give the *product* as yellow crystals, m.p. 126–127 °C (Found: C, 20.1; H, 1.2; N, 17.6%. $C_4H_3N_3O_3S_3$ requires C, 20.3; H, 1.3; N, 17.7%); λ_{max}(EtOH)/nm 212 (log ε 3.84), 296 (4.16) and 364 (3.55); $\nu_{max}(CCl_4)/cm^{-1}$ 2926, 1720s, 1532, 1482, 1426, 1359, 1318, 1298, 1154, 1054, 1025, 998, 920 and 849; δ_H(90 MHz; $CDCl_3$) 2.64 (3 H, s); *m/z* (120 °C) 237 (M^+, 100%), 195 (3), 149 (5), 78 (13), 46 (12) and 43 (63).

(E)-6-*Acetyl*-1,3,5,2,4-*trithiadiazepine Oxime* **14**.—6-Acetyl-1,3,5,2,4-trithiadiazepine **10** (20 mg, 0.104 mmol) was dissolved in ethanol (2 ml). Hydroxylamine hydrochloride (14.5 mg, 0.208 mmol, 2 equiv.) and pyridine (0.1 ml) were added at 22 °C and the solution refluxed for 24 h. The reaction mixture was allowed to cool to 22 °C and ether (20 ml) and water (10 ml) were added. The aqueous layer was separated, extracted with ether (20 ml) and the combined ethereal extracts were washed with water (10 ml), dried ($MgSO_4$) and evaporated. The remaining oil was adsorbed onto silica and separated by flash chromatography. Elution with diethyl ether (10–100%) in light petroleum gave the *title compound* **14** (12.4 mg, 58%) as a cream solid which was recrystallised from diethyl ether–light petroleum to give needles, m.p. 169–170 °C (Found: C, 23.1; H, 2.3; N, 20.2. $C_4H_5N_3OS_3$ requires C, 23.2; H, 2.4; N, 20.3%); λ_{max}(EtOH)/nm 263 (log ε 4.41) and 342 (3.95); $\nu_{max}(CCl_4)/cm^{-1}$ 3589, 3233, 2952, 1425, 1369, 1250, 1217, 1156, 1012 and 970; δ_H(90 MHz; [$^2H_6$]-DMSO) 2.30 (3 H, s), 8.42 (1 H, s) and 11.64 (1 H, s); *m/z* (160 °C) 207 (M^+, 100%), 190 (4), 161 (58), 145 (15), 144 (51), 143 (11), 124 (61), 104 (17), 103 (43), 102 (14), 78 (52), 57 (15), 46 (29), 45 (22) and 42 (22).

6-*Acetyl*-1,3,5,2,4-*trithiadiazepine Phenylhydrazone* **15**.—Phenylhydrazine (0.25 ml) was dissolved in a 10% solution of glacial acetic acid in absolute ethanol (2.5 ml) at 22 °C. 6-Acetyl-1,3,5,2,4-trithiadiazepine **10** (20 mg, 0.104 mmol) was dissolved in absolute ethanol (2 ml) and to this solution was added an aliquot of the phenylhydrazine solution (1 ml). After the reaction mixture had been stirred at 22 °C for 30 min, TLC showed the presence of starting material in addition to a complex mixture of minor products. The reaction mixture was then refluxed for 40 min to give a multicomponent mixture from which starting material **10** was absent. After the mixture had been allowed to cool to 22 °C, diethyl ether (10 ml) and water (5 ml) were added and the ether layer was separated. The aqueous layer was extracted with ether (10 ml) and the combined organic layers were washed with water, dried ($MgSO_4$) and evaporated to give a brown oil which was adsorbed onto silica and separated by flash chromatography. Elution with diethyl ether (10–50%) in light petroleum gave the *title compound* **15** (14.2 mg, 48%) as an orange solid, in addition to a number of other minor unidentified components. The product **15** was recrystallised from diethyl ether–light petroleum to give yellow–orange crystals, m.p. 134–136 °C (decomp.) (Found: M^+, 282.0063. $C_{10}H_{10}N_4S_3$ requires *M*, 282.0068); $\nu_{max}(CCl_4)/cm^{-1}$ 3366, 3057, 1603, 1501, 1428, 1371, 1312, 1286, 1264, 1242, 1149, 1075, 1027 and 885; δ_H(90 MHz; $CDCl_3$) 2.74 (3 H, s), 7.28–7.80 (5 H, m) and 8.10 (1 H, s); *m/z* (160 °C) 282 (M^+, 100%), 236 (35), 204 (79), 190 (26), 189 (26), 157 (13), 149 (16), 105 (17), 104 (31), 103 (35), 93 (15), 92 (69), 91 (21), 78 (14), 77 (99), 65 (57), 51 (22), 46 (18) and 45 (15).

1,3,5,2,4-*Trithiadiazepin*-6-*ylglyoxal Hydrate* **16**.—6-Acetyl-1,3,5,2,4-trithiadiazepine **10** (245.0 mg, 1.28 mmol) was dissolved in dioxane (15 ml) and water (1 ml). Selenium dioxide (2.12 g, 19 mmol, 15 equiv.) was added in one portion. The reaction mixture was refluxed for 24 h, allowed to cool to ambient temperature and adsorbed directly onto silica. Flash chromatography on silica, eluting with diethyl ether, gave the *title compound* **16** (177.9 mg, 68%) as a cream solid. Recrystallisation of **16** from diethyl ether–light petroleum gave fine crystals, m.p. 122–125 °C (Found: M^+, 205.9277. $C_4H_2N_2O_2S_3$ requires *M*, 205.9278); λ_{max}(EtOH)/nm 220 (log ε 3.49), 275 (4.11) and 335 (3.59); $\nu_{max}(CCl_4)/cm^{-1}$ 3447, 1726w, 1644s, 1493, 1266, 1164, 1093 and 986; δ_H(90 MHz; [$^2H_6$]-DMSO) 5.71 (1 H, t, *J* 6.6), 7.15 (2 H, d, *J* 6.6) and 9.48 (1 H, s); *m/z* (160 °C) 206 (M^+, 56), 177 (100), 131 (15), 105 (12), 103 (16), 78 (26), 76 (7), 57 (14), 53 (10), 46 (35) and 45 (16).

1,3$\lambda^4\delta^2$,5,2,4-*Trithiadiazepine*-6-*carboxylic Acid*.—Trithiadiazepin-6-ylglyoxal monohydrate **16** (30 mg, 0.146 mmol) was suspended in dichloromethane (5 ml) and technical 3-chloroperbenzoic acid (80%; 157 mg, 5 equiv.) added in one portion at 22 °C. The reaction mixture was stirred at 22 °C for 16 h and then adsorbed directly onto silica and separated by flash chromatography on silica. Elution with diethyl ether (50%) and then diethyl ether (90%), methanol (9%) and glacial acetic acid (1%) gave the *title compound* (7.6 mg, 27%) as cream crystals, m.p. 210–213 °C (decomp.), recrystallised from methanol–diethyl ether to give m.p. 240–242 °C (decomp.) (Found: M^+, 193.9279. $C_3H_2N_2O_2S_3$ requires *M*, 193.9278); λ_{max}(EtOH)/nm 246 (log ε 4.07) and 337 (3.70); ν_{max}(Nujol)/cm^{-1} 3375, 1674, 1506, 1462, 1376, 1276, 1161, 1022, 895, 736 and 667; δ_H(90 MHz; [$^2H_6$]-DMSO) 8.80 (1 H, s); *m/z* (200 °C) 194 (M^+, 100), 150 (26), 148 (17), 135 (3), 130 (8), 124 (9), 118 (9), 104 (25), 78 (79), 77 (13), 59 (24), 58 (22), 57 (22), 46 (59), 45 (47) and 44 (64).

Nitration of 1,3,5,2,4-*Trithiadiazepine*-6-*carboxylic Acid*.—1,3,5,2,4-Trithiadiazepine-6-carboxylic acid (1.5 mg, 0.008 mmol) was dissolved in acetonitrile (0.5 ml) and nitronium tetrafluoroborate (5.1 mg, 0.039 mmol, 5 equiv.) added in one portion at 22 °C. After being stirred at 22 °C for 15 min, the reaction mixture was added to water (10 ml) and the solution extracted with diethyl ether (2 × 20 ml). The combined ether extracts were washed with water (10 ml), dried ($MgSO_4$) and evaporated to give a yellow oil. This oil was adsorbed onto silica and separated using flash chromatography on silica. Elution with diethyl ether (20%) in light petroleum gave 6-nitro-

1,3,5,2,4-trithiadiazepine (0.3 mg, 20%) and then 6,7-dinitro-1,3,5,2,4-trithiadiazepine (0.4 mg, 22%), both identical with authentic specimens.[3] Further elution with progressively more polar solvents failed to give the isolation of other products.

Methyl 7-Nitro-1,3,5,2,4-trithiadiazepine-6-carboxylate **17**.—Methyl 1,3,5,2,4-trithiadiazepine-6-carboxylate (77.3 mg, 0.372 mmol) was dissolved in dry acetonitrile (5 ml) and the solution added to a suspension of nitronium tetrafluoroborate (167.3 mg, 1.25 mmol, 3.4 equiv.) in acetonitrile (5 cm) at 0 °C over a period of 5 min. The suspension became brown and was stirred at 0 °C for 15 min. The reaction mixture was then adsorbed onto silica rapidly and separated by flash chromatography on silica. Elution with diethyl ether (10–30%) in light petroleum gave the *title compound* **17** (53.4 mg, 57%) as yellow plates, m.p. 95–96 °C (from light petroleum) (Found: C, 19.3; H, 1.1; N, 16.5. $C_4H_3N_3O_4S_3$ requires C, 19.0; H, 1.2; N, 16.6%); λ_{max}(EtOH)/nm 212 (log ε 3.87), 296 (4.03) and 362 (3.22); ν_{max}($CHCl_3$)/cm^{-1} 3030, 2960, 1728s, 1530, 1480, 1430, 1327, 1300, 1170, 1020, 980, 928 and 887; δ_H(90 MHz; $CDCl_3$) 3.92 (3 H, s); δ_C(62.9 MHz; $CDCl_3$) 54.9, 143.1, 152.3 and 160.7; *m/z* (160 °C) 253 (M^+, 100%), 222 (9), 163 (29), 103 (34), 102 (28), 78 (77), 59 (43) and 46 (62).

Methyl 2,4-Dihydro-7-hydroxyamino-1,3,5,2,4-trithiadiazepine-6-carboxylate **18**.—The ester **17** (10.0 mg, 0.04 mmol) was dissolved in absolute ethanol (1 ml) and tin(II) chloride dihydrate (44.6 mg, 0.20 mmol, 5 equiv.) added in one portion at 22 °C. The reaction mixture was stirred at 22 °C for 100 min and then added to a solution of sodium hydrogen carbonate (16.8 mg, 0.2 mmol) in water (5 ml) at 0 °C. Brine (5 ml) was added to the system and the suspension extracted with diethyl ether (2 × 25 ml). The ether layers were washed with water (5 ml), dried ($MgSO_4$) and evaporated to give a clear oil which was adsorbed onto silica and separated by flash chromatography on silica. Elution with diethyl ether (70%) in light petroleum gave the *title compound* **18** (6.4 mg, 66%) as a colourless waxy solid, m.p. 40–43 °C (from light petroleum) (Found: M^+, 240.9644. $C_4H_7N_3O_3S_3$ requires *M*, 240.9649); λ_{max}(EtOH)/nm 260 (log ε 4.23) and 368 nm (3.92); ν_{max}(CCl_4)/cm^{-1} 3587, 3330, 2978, 2930, 2866, 1736s, 1436, 1382, 1333, 1299, 1252, 1205, 1148, 1120, 955 and 858; δ_H(250 MHz; $CDCl_3$) 3.88 (3 H, s), 4.75 (1 H, s), 4.93 (1 H, br s), 5.52 (1 H, s) and 7.60 (1 H, br s); *m/z* (100 °C) 241 (M^+, 33%), 224 (6), 211 (8), 207 (2), 195 (100), 193 (80), 179 (51), 163 (3), 135 (19), 117 (9), 80 (14), 78 (25), 68 (16), 64 (23), 62 (14), 59 (30), 48 (7), 47 (40), 46 (27) and 45 (15).

6-Acetoxymercuri-1,3,5,2,4-trithiadiazepine **19** *and 6,7-Bis(acetoxymercuri)-1,3,5,2,4-trithiadiazepine* **20**.—(a) *With an excess of mercuriating agent.* Trithiadiazepine **3** (100 mg, 0.67 mmol) was dissolved in glacial acetic acid (2 ml) and the solution added to a suspension of mercury (II) acetate (424.9 mg, 1.33 mmol, 2 equiv.) in glacial acetic acid (3 ml). The reaction mixture became almost clear and was stirred at 22 °C for 96 h. The resulting cream precipitate was filtered off, washed with acetic acid and ethanol, and dried at 22 °C under high vacuum overnight to give the *title compound* **20** (395.6 mg, 89%) as needles, m.p. 256–260 °C (decomp.) (from ethanol) (Found: C, 11.1; H, 0.9; N, 4.2. $C_6H_6Hg_2N_2O_4S_3$ requires C, 10.8; H, 0.9; N, 4.2%); ν_{max}(Nujol)/cm^{-1} 1698w, 1630, 1583s, 1563s, 1435, 1386, 1367, 1329s, 1136, 1024, 752, 690, 647 and 599; δ_H(90 MHz; [$^2H_6$]-DMSO) 1.98 (6 H, s).

(b) *With an excess of trithiadiazepine.* Trithiadiazepine **3** (200 mg, 1.33 mmol) was dissolved in glacial acetic acid (5 ml) and the solution added to a solution of mercury(II) acetate (84.9 mg, 0.267 mmol, 0.2 equiv.) in glacial acetic acid (5 ml) at 22 °C. The reaction mixture was then stirred for 20 h at 22 °C. The resulting white precipitate was filtered off, washed with acetic acid and ethanol, and dried at 22 °C under high vacuum overnight to give 6,7-bis(acetoxymercuri)-1,3,5,2,4-trithiadiazepine **20** (67.1 mg, 75% based on mercury(II) acetate), identical with that described previously. The filtrate (without the acetic acid and ethanol washings) was evaporated on a rotary evaporator under high vacuum to give colourless oily crystals. This material was triturated repeatedly with light petroleum to extract trithiadiazepine **3** and the solids were dried *in vacuo* to give the title compound **19** [11.8 mg, 11% based on mercury(II) acetate] as crystals, m.p. 224–227 °C (decomp.) (from light petroleum) (Found: C, 12.0; H, 0.9; N, 7.2. $C_4H_4N_2O_2S_3Hg$ requires C, 11.8; H, 1.0; N, 6.9%); ν_{max}(Nujol)/cm^{-1} 1562, 1470, 1455, 1448, 1379, 1366, 1320, 1149, 1018, 688 and 648; δ_H(90 MHz; [$^2H_6$]-DMSO) 2.05 (3 H, s) and 8.15 (1 H, s). The light petroleum extract was filtered and evaporated to give recovered trithiadiazepine (140.0 mg, 70%).

6-Acetoxymercuri-7-bromo-1,3,5,2,4-trithiadiazepine **21**.—6-Bromotrithiadiazepine (100 mg, 0.437 mmol) was dissolved in THF (2 ml) and the solution added to a solution of mercuric acetate (139.2 mg, 0.437 mmol, 1 equiv.) in glacial acetic acid (2 ml) at 22 °C. The reaction mixture was then refluxed for 18 h. The resulting cream suspension was allowed to cool to ambient temperature when the product was filtered off, washed with acetic acid and ethanol and dried at 22 °C under high vacuum overnight to give the *title compound* **21** (113.8 mg, 44%) as crystals, m.p. 208–210 °C (decomp.) (from ethanol) (Found: C, 9.9; H, 0.6; N, 5.5. $C_4H_3BrHgN_2O_2S_3$ requires C, 9.9; H, 0.6; N, 5.7%); ν_{max}(Nujol)/cm^{-1} 1577, 1470, 1453, 1375, 1323, 1149, 1020, 901, 775 and 694; δ_H(90 MHz; [$^2H_6$]-DMSO) 2.10 (3 H, s).

Bis(7-nitro-1,3,5,2,4-trithiadiazepin-6-yl)-mercury **22**.—6-Nitrotrithiadiazepine **13** (100 mg, 0.512 mmol) was dissolved in glacial acetic acid (2 ml) and the solution added to a suspension of mercury(II) acetate (163.2 mg, 0.512 mmol, 1 equiv.) in glacial acetic acid (1 ml) at 22 °C. The solid dissolved to give a pale yellow solution which was then refluxed for 72 h. The resulting orange–yellow suspension was allowed to cool to ambient temperature when the product was filtered off, washed with acetic acid, water and ethanol and dried at 22 °C under high vacuum overnight to give the *title compound* **22** (73.9 mg, 49%) as yellow–orange crystals, m.p. 238–244 °C (decomp.) (from ethanol) (Found: C, 7.9; N, 13.0. $C_4N_6O_4S_6Hg$ requires C, 8.2; N, 14.3%); ν_{max}(Nujol)/cm^{-1} 1485, 1456, 1327, 1273, 1156, 1006, 978, 931, 774, 756, 728, 661 and 579. The structure was confirmed by X-ray diffraction.[8]

6-Iodo-7-nitro-1,3,5,2,4-trithiadiazepine.—(a) *From bis(6-nitro-1,3,5,2,4-trithiadiazepin-7-yl)mercury* **22**. Compound **22** (9.3 mg, 0.016 mmol was suspended in THF and a solution of iodine (26.7 mg, 0.21 mmol) in THF (1 ml) added at 22 °C. The reaction mixture was added to water (2 ml) and the resulting aqueous suspension extracted with diethyl ether (2 × 5 ml). The combined ether layers were washed with water (2 ml), dried ($MgSO_4$) and evaporated to give an oil which was adsorbed onto silica and separated by flash chromatography. Elution with light petroleum gave the *title compound* (4.5 mg, 89%) as yellow–orange crystals, m.p. 56–57 °C. Recrystallisation of this material from diethyl ether–light petroleum gave the product, m.p. 62–63 °C (Found: M^+, 320.8204. $C_2IN_3O_2S_3$ requires *M*, 320.8917); λ_{max}(EtOH)/nm 215 (log ε 4.04) and 306 (3.87); ν_{max}($CHCl_3$)/cm^{-1} 1530, 1420, 1310, 1285, 1165, 1018, 983, 925 and 910; *m/z* (120 °C) 321 (M^+, 100%), 275 (29), 195 (26), 183 (18), 171 (18), 148 (9), 127 (12), 102 (47), 78 (53), 46 (43) and 28 (37).

(b) *From 1,3,5,2,4-trithiadiazepin-6-ylthallium bis(trifluoroacetate)* **8**. 1,3,5,2,4-Trithiadiazepine **3** (100.0 mg, 0.66 mmol) was

added in one portion to a 0.34 mol dm^{-3} solution of thallium(III) tris(trifluoroacetate) in acetonitrile (2.2 ml, 0.75 mmol, 1.14 equiv.) and the resulting suspension was refluxed for 3 h. The reaction mixture was then allowed to cool and solvent removed on a rotary evaporator. The residue was triturated with dry, light petroleum to remove unchanged trithiadiazepine and to leave an oily solid which was dried *in vacuo* at 22 °C. A solution of acetyl nitrate was prepared by the addition of concentrated (70%; *d* 1.42) nitric acid (0.042 ml, 0.66 mmol) to acetic anhydride (1.5 ml) at 15 °C, the temperature being maintained < 20 °C. The solution was then cooled to 0–2 °C and concentrated sulphuric acid (0.01 ml) added in one portion with stirring. The cooled solution of acetyl nitrate thus prepared was added at 0 °C to the crude solid **8**, and the suspension allowed to warm to 22 °C. After being stirred for 2.5 h at 22 °C the reaction mixture was cooled to 5 °C and ice (1 g) added to destroy any residual acetyl nitrate. The suspension was stirred for 5 min and then 6 mol dm^{-3} aqueous sodium hydroxide added cautiously to adjust the pH of the mixture to 6.0, the temperature being maintained < 20 °C. A solution of iodine (266 mg, 1.05 mmol) in chloroform (20 ml) was then added and the two-phase mixture refluxed for 12 h. After the mixture had been allowed to cool to ambient temperature, a solution of sodium metabisulphite (660 mg) in water (5 ml) was added to destroy excess of iodine and the reaction mixture stirred for 5 min. The suspension was then filtered through Celite and the aqueous layer separated and extracted with chloroform (20 ml). The combined organic layers were washed with water (2 × 10 ml), dried ($MgSO_4$) and the solvent removed on a rotary evaporator. The residue was adsorbed onto silica and separated by flash chromatography. Elution with dichloromethane (10–30%) in light petroleum gave 6-iodo-7-nitro-1,3,5,2,4-trithiadiazepine (50.6 mg, 24%) as orange–yellow crystals, m.p. 60–61 °C, identical with that described previously. Recrystallisation from dichloromethane–light petroleum gave a pure specimen, m.p. 62–63 °C. Further elution gave 6-nitro-1,3,5,2,4-trithiadiazepine **13** (30.3 mg, 24%) and 6,7-dinitro-1,3,5,2,4-trithiadiazepine (4.0 mg, 3%), both identical with authentic specimens.

Treatment of 6-*Acetoxymercuri*-7-*bromo*-1,3,5,2,4-*trithiadiazepine* **21** *with Copper(II) Thiocyanate.*—6-Acetoxymercuri-7-bromo-1,3,5,2,4-trithiadiazepine **21** (36.2 mg, 0.074 mmol) and copper(II) thiocyanate (66.6 mg, 0.37 mmol, 5 equiv.) were suspended in benzene (2 ml) and the suspension refluxed for 72 h. The mixture was allowed to cool to ambient temperature when the suspension was adsorbed onto silica and separated by flash chromatography. Elution with diethyl ether (5–10%) in light petroleum gave 6-*bromo*-7-*thiocyanato*-1,3$\lambda^4\delta^2$,5,2,4-*trithiadiazepine* (4.5 mg, 21%) as a pale yellow oil (Found: M^+, 284.8164. $C_3BrN_3S_4$ requires *M*, 284.8158); λ_{max}(EtOH)/nm 250 (log ε 4.32) and 338 (3.86); $\nu_{max}(CCl_4)/cm^{-1}$ 2929, 2163, 1448, 1161s, 1009 and 931; *m/z* (80 °C) 285 (M^+, 69%), 241 (18), 239 (16), 124 (87), 102 (31), 88 (35), 78 (100), 70 (30) and 46 (51). Further elution gave 6-*thiocyanato*-1,3$\lambda^4\delta^2$,5,2,4-*trithiadiazepine* (2.3 mg, 15%) as cream crystals, m.p. 39–41 °C (Found: M^+, 206.9055. $C_3HN_3S_4$ requires *M*, 206.9053); λ_{max}(EtOH)/nm 239 (log ε 4.19) and 328 (3.90); $\nu_{max}(CCl_4)/cm^{-1}$ 3004, 2161s, 1163s and 1004; *m/z* (130 °C) 207 (M^+, 100%), 161 (21), 124 (24), 78 (75), 57 (20), 46 (46) and 45 (36). Further elution gave 6,7-*dithiocyanato*-1,3$\lambda^4\delta^2$,5,2,4-*trithiadiazepine* (4.1 mg, 21%) as crystals, m.p. 148–152 °C (sublimes) (Found: M^+, 263.8720. $C_4N_4S_5$ requires *M*, 263.8727); λ_{max}(EtOH) 260 (log ε 3.84) and 322 (3.38); $\nu_{max}(CHCl_3)/cm^{-1}$ 2164s, 1603 and 1161; *m/z* (160 °C) 264 (M^+, 100%), 218 (16), 124 (95), 102 (32), 88 (49), 78 (84), 76 (21), 70 (37), 46 (58) and 44 (16).

Further reactions of 6-acetoxymercuri-7-bromo-1,3,5,2,4-trithiadiazepine **21** with copper(II) thiocyanate were carried out using a similar chromatographic work-up (see Table 4).

Treatment of 6,7-*Bis*(*acetoxymercuri*)-1,3,5,2,4-*trithiadiazepine* **20** *with Copper(II) Thiocyanate.*—6,7- Bis(acetoxymercuri)-1,3,5,2,4-trithiadiazepine **20** (100 mg, 0.15 mmol) and copper (II) thiocyanate (134.6 mg, 0.75 mmol, 5 equiv.) were suspended in xylene (2 ml) and the suspension was refluxed for 16 h. The reaction mixture was allowed to cool and then adsorbed onto silica and separated by flash chromatography. Elution with diethyl ether (10–20%) in light petroleum gave 6-thiocyanato-1,3,5,2,4-trithiadiazepine (5.8 mg, 19%), identical with that described previously. Further elution gave 6,7-dithiocyanato-1,3,5,2,4-trithiadiazepine (4.4 mg, 11%) also identical with that described previously.

6-*Iodo*-1,3$\lambda^4\delta^2$5,2,4-*trithiadiazepine*.[14]—(*cf.* Ref. 15) 1,3,5,2,4-Trithiadiazepine **3** (30 mg, 0.20 mmol) was added in one portion to thallium tris(trifluoroacetate) (326 mg, 0.60 mmol) in dry acetonitrile (2.0 ml), and the mixture was heated at reflux under nitrogen for 3 h. When cool, a solution of potassium iodide (246 mg, 1.5 mmol) in water (1.0 ml) was added. The product was extracted into ether and then washed with water, dried ($MgSO_4$) and chromatographed on silica, eluting with light petroleum, to give the *title compound* (37 mg, 80% based on unrecovered **3**) as pale yellow plates, m.p. 92–94 °C (from light petroleum) (Found: C, 8.8; H, 0.35; N, 9.95. $C_2HIN_2S_3$ requires C, 8.7; H, 0.4; N, 10.1%); λ_{max}(EtOH)/nm 224 (log ε 3.74), 244 (3.57), 325 (3.22) and 345 (3.24); $\nu_{max}(CHCl_3)/cm^{-1}$ 2920, 2850, 1150, 993, 905, 855 and 640; δ_H(90 MHz; $CDCl_3$) 7.66(s); *m/z* 276 (M^+, 100%), 230 (25), 184 (11), 127 (17), 124 (25), 105 (20), 103 (26), 78 (54) and 46 (59). Further elution with light petroleum gave unchanged trithiadiazepine **3** (5 mg, 17%).

6-*Cyano*-1,3$\lambda^4\delta^2$,5,2,4-*trithiadiazepine*.[14]—This compound was prepared according to a reported procedure for aromatic nitriles.[16] 1,3,5,2,4-Trithiadiazepine **3** (30 mg, 0.20 mmol) and thallium tris(trifluoroacetate) (326 mg, 0.60 mmol) were heated at reflux in dry acetonitrile (2.0 ml) under nitrogen for 3 h. Copper(I) cyanide (150 mg, 1.67 mmol) was added and heating was continued for a further 24 h. The solvent was then evaporated under reduced pressure and the residue redissolved in dichloromethane. The dichloromethane solution was washed with water, dried ($MgSO_4$) and evaporated, and the residue was chromatographed on silica; elution with light petroleum gave uncharged trithiadiazepine **3** (13 mg, 44%), and with 20% dichloromethane in light petroleum gave the *title compound* (17 mg, 86% based on unrecovered starting material) as needles, m.p. 71–71.5 °C (from light petroleum) (Found: C, 20.8; H, 0.55; N, 23.5. $C_3HN_3S_3$ requires C, 20.6; H, 0.6; N, 24.0%); λ_{max}(EtOH)/nm 248 (log ε 3.96) and 332 (3.43); $\nu_{max}(CHCl_3)/cm^{-1}$ 2920, 2850, 2220, 1600, 1160, 1002, 908 and 608; δ_H(90 MHz; $CDCl_3$) 8.27(s); *m/z* 175 (M^+, 100%), 129 (24), 124 (29), 102 (8), 83 (7), 80 (7), 78 (71) and 46 (44).

Methyl 1,3$\lambda^4\delta^2$,5,2,4-*trithiadiazepine*-6-*carboxylate*.[14]—This compound was prepared according to a reported procedure for methoxycarbonylation of aromatic compounds.[17] 1,3,5,2,4-Trithiadiazepine **3** (30 mg, 0.20 mmol) and thallium tris(trifluoroacetate) (326 mg, 0.60 mmol) were heated at reflux in dry acetonitrile (2.0 ml) under nitrogen for 3 h. When cool, the reaction mixture was added to the following mixture of anhydrous reagents: palladium(II) chloride (5 mg, 0.03 mmol), lithium chloride (17 mg, 0.40 mmol) and magnesium oxide (17 mg, 0.40 mmol), prepared as a suspension in dry methanol (2.0 ml), saturated with carbon monoxide gas. Carbon monoxide gas was bubbled through the combined mixture for *ca.* 5 min. The mixture was then stirred at room temperature overnight. After this the crude reaction mixture was filtered and evaporated and the residue chromatographed on silica. Elution with light petroleum gave unchanged trithiadiazepine **3** (7 mg,

22%) and with 20% dichloromethane in light petroleum gave the *title compound* (22 mg, 69% based on unrecovered starting material) as needles, m.p. 110–111.5 °C [after sublimation (75 °C/1 mmHg)] (Found: C, 23.3; H, 1.9; N, 13.3. $C_4H_4N_2O_2S_3$ requires C, 23.1; H, 2.0; N, 13.45%); λ_{max}(EtOH)/nm 262 (log ε 3.82) and 334 (3.30); $\nu_{max}(CHCl_3)/cm^{-1}$ 2950, 2920, 2850, 1710s, 1495, 1430, 1280–1180s, 1160s, 1003, 961, 908, 645 and 600; δ_H(90 MHz; $CDCl_3$) 3.94 (3 H, s) and 8.80 (1 H, s); *m/z* 208 (M^+, 100%), 177 (6), 162 (32), 130 (6), 124 (8), 103 (10), 88 (6), 80 (10), 78 (25), 76 (5), 71 (8), 59 (35), 57 (15) and 46 (36).

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