

Conversion of enamines, enamides and triazoles by trithiazyl trichloride into 1,2,5-thiadiazoles

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Trithiazyl trichloride **1** converts primary and secondary enamines, enamides and 1,2,3-triazoles into 1,2,5-thiadiazoles. These mild reactions provide one-pot routes to various alkyl, aryl, functional and quaternary 1,2,5-thiadiazoles, in moderate to good yields. The trimer **1** reacts as a 1,2-bis-electrophile adding an N–S unit across C=C–N. For primary enamines ¹⁵N-labelling reveals an additional, minor pathway in which N–S–N is added across C=C, with elimination of the enamine nitrogen. With *N*-alkylated enamines the alkyl group is retained in a quaternised thiadiazole, but this can be dealkylated *in situ*. Enamides react similarly but with spontaneous *N*-deacylation. 1,2,3-Triazoles with electron withdrawing groups to stabilise their acyclic diazoimine tautomers also give 1,2,5-thiadiazoles, with loss of dinitrogen. Mechanisms are proposed for these new reactions.

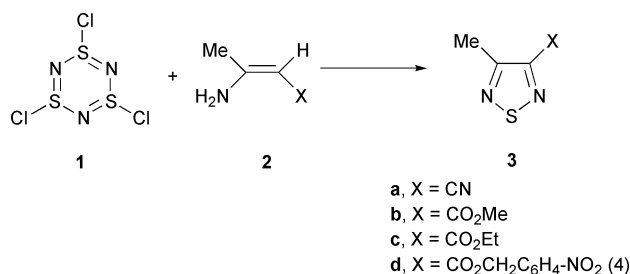
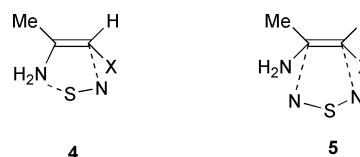
We have shown that trithiazyl trichloride, (NSCl)₃, “the trimer” **1** reacts readily with nucleophilic unsaturated substrates, by electrophilic attack or by cycloaddition, to give a useful range of sulfur–nitrogen heterocyclic compounds.¹ Thus pyrroles, for example, are converted into isothiazoles or fused 1,2,5-thiadiazoles.² It seemed that enamines might undergo somewhat analogous reactions, with addition of the trimer across the bisnucleophilic enamine group or across the carbon–carbon double bond, and we now describe these and related reactions.

Results and discussion

Reactions with primary enamines

We first treated the stable primary enamines 3-aminocrotonitrile **2a** and methyl, ethyl and *p*-nitrobenzyl 3-aminocrotonates **2b–d** with the trimer **1** (1 equiv.) in tetrachloromethane at RT for 16 h (Scheme 1). Moderate yields of the 1,2,5-

latter with the amino group, being eliminated, presumably as ammonia, as in **5**. We have distinguished between these possibilities by ¹⁵N-labelling experiments. ¹⁵N-Labelled primary enamine **2b** was made by treatment of methyl acetoacetate in aqueous ethanol with labelled ammonia gas which was generated from ¹⁵N-labelled ammonium sulfate (98% enriched). The mass spectrum of the enamine **2b** showed 97% ¹⁵N incorporation.



Scheme 1

thiadiazoles **3** (28, 62, 40 and 56% respectively) were obtained after chromatographic purification, and their structures followed from their mass spectra, infrared, ¹H and ¹³C NMR spectra. This reaction provides a new, simple one-pot preparation for 1,2,5-thiadiazoles with electron withdrawing groups in the 3-position.

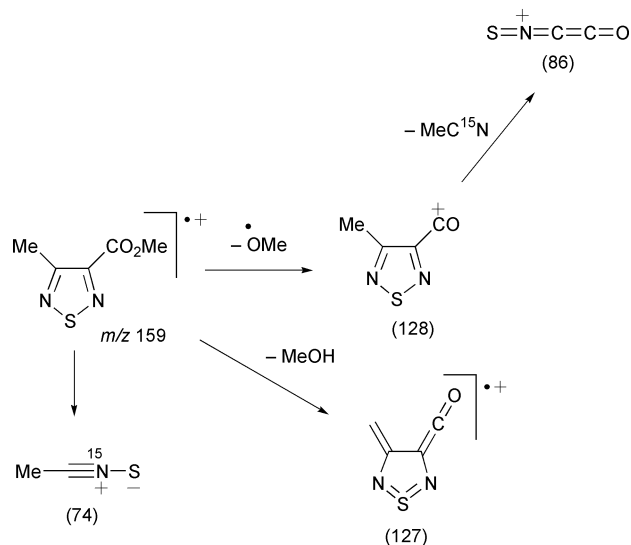
Since the trimer **1** is known to contribute either an S–N or an N–S–N unit in its ring-forming reactions,¹ formation of the 1,2,5-thiadiazoles could involve the former with incorporation of the primary amino group into the product, as in **4**, or the

The labelled enamine **2b** and trimer **1** under the same conditions as before gave the thiadiazole **3b** (60%) which showed the same *R_p*, mp and ¹H NMR spectrum as the unlabelled compound. Analysis of the mass spectrum of labelled **3b** using an isotopic abundance calculation program showed 87% incorporation of a single ¹⁵N label, 13% of unlabelled thiadiazole and a negligibly small amount of doubly labelled material. The fragment peak at *m/z* 74, which corresponds to ¹⁵N-acetonitrile sulfide, was observed in the mass spectrum of labelled thiadiazole **3b**; the same fragment in unlabelled **3b** was observed at *m/z* 73. This strongly suggested that the ¹⁵N label is at N-5 rather than N-2 (Scheme 2), indicating retention of the nitrogen of the enamine in the thiadiazole with no scrambling of the label during reaction. This assignment was further supported by the ¹⁵N NMR spectrum which showed one singlet at 341 ppm with nitromethane as external reference.

In solution trithiazyl trichloride **1** exists in equilibrium with the dissociated monomer, thiazyl chloride, N≡S–Cl, the position of equilibrium depending on the solvent, the temperature and the purity of the sample.³ The reactive species could therefore be the trimer, the monomer or both. We have argued that the monomer is the reactive species in many reactions of the trimer in hot solutions where an N–S unit is transferred and where only one-third of an equivalent of trimer is required for complete conversion, as in the almost quantitative rearrange-

Table 1 Effect of temperature on yield and ^{15}N incorporation in the conversion of enamine **2b** (1 mmol) and trithiazyl trichloride **1** (1 mmol) into the thiadiazole **3b**

Temperature/ °C	Solvent	Yield of 3b (%)	^{15}N -label incorporation (%)
−78	DCM	37	93
20	CCl_4	60	87
77	CCl_4	55	87
111	PhMe	25	92

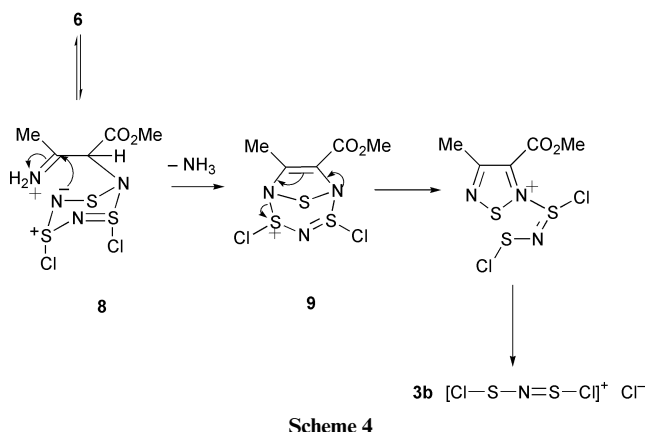
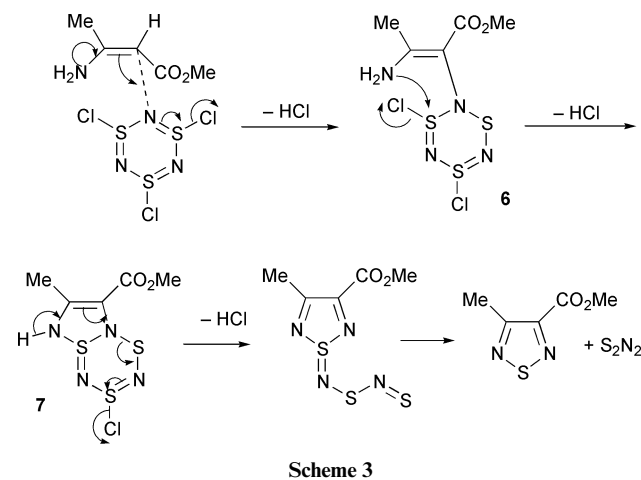


ment of 2,5-diphenylfuran into 5-benzoyl-3-phenylisothiazole.⁴ Treatment of the enamine **2b** with trimer was therefore repeated, in boiling tetrachloromethane, with 0.33 and 1.0 equiv. of trimer; thiadiazole **3b** was obtained in 19 and 55% of yield respectively, making it less likely that the reaction occurs *via* the monomer. Furthermore, **3b** was obtained in 37% yield from **2b** and trimer (1 equiv.) in DCM at -78°C at which temperature the monomer would be formed extremely slowly from pure trimer.³

The effect of temperature on the ^{15}N -incorporation as well as on the yield was studied, and the results are shown in Table 1. The maximum yield of thiadiazole **3b** was obtained at room temperature. In boiling toluene the yield was much reduced, possibly because of the faster decomposition of trimer to sulfur and S_4N_4 at this temperature; the resulting complex reaction mixture was also more difficult to separate in this experiment. The percentage of ^{15}N incorporated remained essentially constant over the temperature range studied.

Reaction mechanism

The evidence available supports, but does not prove, that the trimer is the reactive species in the conversion of **2b** into **3b**, and we offer a mechanistic explanation for the extensive, but incomplete, incorporation of the isotopic label on this basis. Mechanisms are proposed for a *major* pathway (Scheme 3) which involves incorporation of the enamine nitrogen into the product and a *minor* pathway (Scheme 4) in which this nitrogen is eliminated. Both mechanisms start by electrophilic attack of the enamine carbon by the trimer, through nitrogen, with loss of chlorine from the adjacent sulfur atom, to give intermediate **6**; this process would be favoured by the S^{IV} to S^{II} transformation. In the major pathway the 1,3-bisnucleophilic enamine cyclises onto the heterocyclic ring to give the bicyclic intermediate **7**, the trimer having acted as a 1,2-bis-electrophile. The final elimination of HCl, as shown in **7**, is accompanied by fragmentation to the aromatic thiadiazole and S_2N_2 ; the latter is

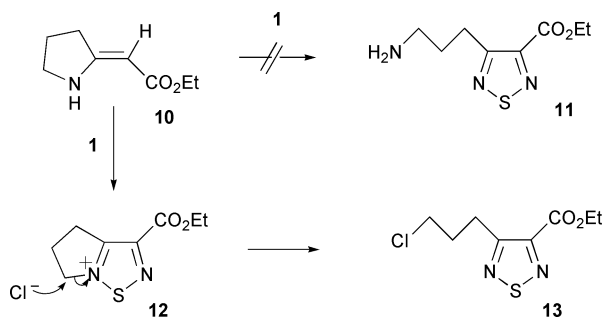


thermally unstable and dimerises very readily to S_4N_4 and polymerises to poly(sulfur nitride).⁵ Variable amounts of S_4N_4 were isolated in these experiments. A control experiment showed that S_4N_4 did not convert enamine **2b** into thiadiazole **3b**, even on prolonged boiling in tetrachloromethane.

In the minor pathway (Scheme 4) protonation of the same intermediate enamine **6**, on carbon or on nitrogen, would make it vulnerable to intramolecular nucleophilic attack by the neighbouring trimer nitrogen, shown in dipolar form in **8**. Further protonation by the HCl generated could lead to loss of ammonia to give a sulfur-bridged intermediate **9** which could fragment to thiadiazole **3b** and the known bis(chlorothio)-nitronium {IUPAC name: chloro[(chlorothio)imino]sulfonium} cation $[\text{Cl}-\text{S}-\text{N}=\text{S}-\text{Cl}]^+$.⁶ In this minor pathway the trimer has acted as an N(1)electrophile–N(3)nucleophile, and it should be noted that for this transfer of N–S–N the trimer is a much more reasonable reagent than the monomer.

Reactions with secondary enamines

Evidence for the minor pathway mechanism (Scheme 4) could be provided by detection of the eliminated ammonia. We considered that support for this elimination would be more feasible, and more interesting, if the eliminated amino group remained attached to the thiadiazole produced, by starting with a cyclic enamine. The enamino-ester **10** (Scheme 5) was therefore prepared from 2-methoxy-1-pyrroline and Meldrum's acid and ethanolsis of the product.⁷ If **10** reacted with the trimer **1** by the "minor" pathway, the aminopropylthiadiazole **11** would be produced as its hydrochloride. However, no formation of **11** was observed in this reaction at RT. The only product isolated was the chloropropylthiadiazole **13**, in very low yield (6%). This had a molecular ion peak at m/z 234 with the characteristic isotopic cluster for one chlorine atom, a loss of ethanol from the molecular ion by a McLafferty-type rearrangement (*cf.* Scheme 2), and the formula $\text{C}_8\text{H}_{11}\text{ClN}_2\text{O}_2\text{S}$ from HRMS;



Scheme 5

^1H and ^{13}C NMR indicated the presence of a chloropropyl group.

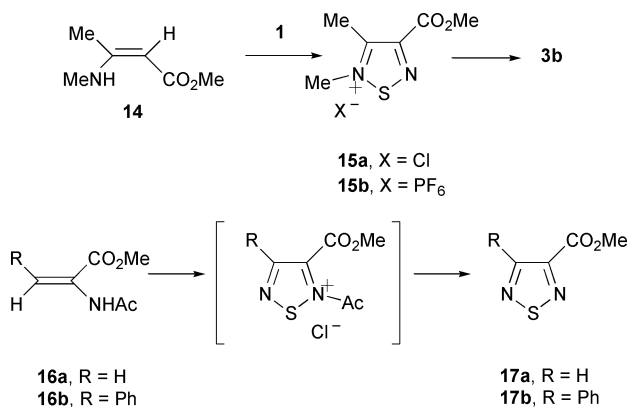
In contrast with the primary enamine reactions, an increase in temperature for the reaction of trimer **1** with **10**, in boiling tetrachloromethane, gave a substantial increase in the yield of **13** (50%). Clearly the major pathway (Scheme 3) has predominated since this mechanism would lead to the thiadiazolium salt **12** as the primary product which would be susceptible to “dealkylation” by chloride ion, slowly at RT and more rapidly in boiling tetrachloromethane. In the light of this reaction, an acyclic secondary enamine, methyl 3-*N*-methylaminocrotonate **14**, was treated with trimer in tetrachloromethane. At RT, traces of a product with an R_f value identical to that of thiadiazole **3b** were observed; from a reaction in the boiling solvent, **3b** was isolated in 19%. This was presumably formed *via* the corresponding *N*-methylthiadiazolium chloride **15a**.

Attempts were made to isolate the dithiazolium salt intermediates. Upon dropwise addition of a tetrachloromethane solution of trimer **1** to stirred solutions of the enamines **10** and **14** in the same solvent at RT, brown precipitates were formed. These were filtered, washed with dry tetrachloromethane under nitrogen, dissolved in water and extracted thoroughly with DCM to remove organic impurities. The resulting aqueous solutions were treated with activated charcoal, filtered and evaporated under high vacuum. The crude chloride salts, **12** and **15a**, which have appropriate infra red spectra, were purified by anion exchange; a saturated aqueous solution of ammonium hexafluorophosphate was slowly added to their concentrated aqueous solutions to give the hexafluorophosphate salts in low overall yields (8 and 15% respectively). The structures of these salts followed from their FAB-MS, IR and ^1H NMR spectra. The FAB-MS showed the expected molecular ion peaks and the IR spectra showed strong ester carbonyl absorption. In the ^1H NMR spectra of cations **12** and **15** the N-5 and C-4 substituent signals were at substantially lower field than for those of the neutral thiadiazoles **13** and **3b**; these latter were formed from the PF_6^- salts on treatment with benzyltriethylammonium chloride in suspension in boiling tetrachloromethane. All these results support the mechanisms proposed above. It is worth noting that, in contrast with the alkylation of 1,2,5-thiadiazoles, these trimer reactions provide a regiospecific synthesis of the thiadiazolium salts like **12** and **15** although the reactions have yet to be optimised.

Reactions with enamides

We next considered treatment of enamides with the trimer since although enamides are less nucleophilic than enamines, the deacylation of analogous intermediate *N*-acylthiadiazolium salts should proceed more readily than the *N*-dealkylations. Methyl 2-acetamidoacrylate **16a** was attractive since it is commercially available and a range of 3-aryl groups can be readily introduced by palladium coupling reactions.⁸

Methyl 2-acetamidoacrylate **16a** and methyl 2-acetamido-3-phenylacrylate **16b**, prepared by palladium catalysed coupling with iodobenzene,⁸ were treated with trimer in refluxing tetrachloromethane, and the expected thiadiazoles **17a** and **b** were

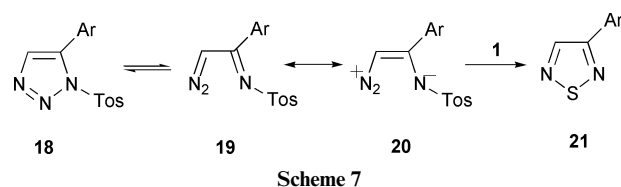


Scheme 6

obtained in 53 and 38% respectively (Scheme 6). Presumably these reactions proceed through the *N*-acylthiadiazolium salts but these were too sensitive to be readily isolated. This simple reaction provides a new route to aryl-1,2,5-thiadiazoles.

Reactions with 1,2,3-triazoles

1,2,3-Triazoles were also considered as a potential source of an enamine-like unit for condensation with the trimer. 1,2,3-Triazoles with an electron-withdrawing group on N(1), such as **18**, are in equilibrium with acyclic diazoimines⁹ *e.g.* **19** ↔ **20** which are 1,3-electrophile–nucleophiles activated by the loss of dinitrogen and hence potentially able to condense with the trimer to form 1,2,5-thiadiazoles **21** (Scheme 7). We therefore



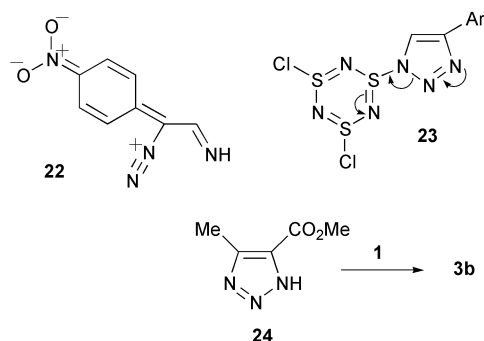
Scheme 7

prepared the 5-(*p*-nitrophenyl) derivative, **18a**, Ar = $\text{C}_6\text{H}_4\text{NO}_2$ -*p*,¹⁰ since the nitro group was expected to facilitate triazole ring opening and to confer crystallinity on reaction products.

The reaction between triazole **18a** and trimer **1** in boiling tetrachloromethane for 16 h gave the detosylated thiadiazole **21a**, Ar = $\text{C}_6\text{H}_4\text{NO}_2$ -*p*, in high yield (90%). If the triazole **18a** were first detosylated in boiling aqueous ethanol the product gave the same thiadiazole with trimer, at a comparable rate but in a lower yield (67%). The *N*-tosyl group is therefore not crucial to the reaction, and indeed it was probably removed under the acidic conditions generated; we found that **18a** was detosylated by dry hydrogen chloride gas.

However, the *p*-nitro group is crucial to the reaction since 4-phenyl-1,2,3-triazole¹⁰ did not give 3-phenyl-1,2,5-thiadiazole on treatment with trimer under the same conditions; only starting triazole, S_4N_4 and S_8 were isolated. This could indicate that the trimer does not react with the intact triazole but requires a very small amount (at least) of the diazoimine tautomer, the formation of which will be strongly favoured by delocalisation of charge onto the nitro group **22**. An alternative and perhaps more likely explanation is that the trimer does react with the triazole, through sulfur, to give a species like **23** in which the triazole is activated to ring opening (arrows in **23**) just as it is in the *N*-tosyl derivative. It is possible that this ring opening could occur with the extra activation provided by the *p*-nitro group, but not its absence.

A triazole with an intermediate electron withdrawing substituent gave intermediate results. Methyl 5-methyl-3*H*-1,2,3-triazole-4-carboxylate **24**, prepared by cycloaddition of trimethylsilyl azide and methyl tetrolate,¹¹ was treated with



trimer under the standard conditions in boiling tetrachloromethane; the reaction was slow giving only 9% of thiadiazole **3b** and recovered **24** (54%) after 16 h. Presumably a higher temperature is required for triazole ring opening; the reaction was still slow in boiling toluene, giving a 17% yield and 49% of **24**. Further improvement of the isolated yield to 34% was obtained by portionwise addition of the trimer, to minimise its decomposition at this higher temperature; starting triazole (46%) was recovered so the corrected yield of **3b** was 65%.

Although the scope of this 1,2,3-triazole to 1,2,5-thiadiazole transformation is limited, it does provide an attractive route to thiadiazoles with electron withdrawing substituents.

Experimental

For general information, see references 1, 2 and 4

Methyl 3-aminocrotonate **2b**,¹² methyl 3-*N*-methylamino-crotonate **14**,¹² ethyl α -(pyrrolidin-2-ylidene)acetate **10**,⁷ methyl 2-acetamido-3-phenylacrylate **16b**,⁸ 5-*p*-nitrophenyl-1,2,3-triazole¹⁰ and its 1-*p*-tolylsulfonyl derivative **18a**¹⁰ and methyl 5-methyl-3*H*-1,2,3-triazole-4-carboxylate (**24**)¹¹ were prepared by literature methods. Methyl 3-¹⁵N-aminocrotonate was prepared by treatment of a solution of methyl acetoacetate (900 mg, 7.8 mmol) in water (1 ml) and ethanol (1 ml) with ¹⁵N-enriched ammonia gas which was generated from ¹⁵N-enriched ammonium sulfate (500 mg, 3.9 mmol) (98% enriched) with sodium hydroxide solution. The labelled compound (319 mg, 26%) separated to give colourless crystals, mp 82–83°C, *m/z* 116 (*M*⁺, 38%), 85 (100, *M* – OMe) and 84 (26, *M* – MeOH).

p-Nitrobenzyl 3-aminocrotonate **2d**

Ethyl acetoacetate (4.0 g, 26 mmol) and *p*-nitrobenzyl alcohol (4.1 g, 31 mmol) were mixed and heated until ethanol was evolved. The ethanol was distilled off and excess of ethyl acetoacetate was distilled off *in vacuo*. The crude oil of *p*-nitrobenzyl acetoacetate (5.1 g) was used in the next step without further purification.

Crude *p*-nitrobenzyl acetoacetate (1.2 g, 5 mmol) and concentrated ammonia solution (*d* = 0.88) (3 ml) were dissolved in ethanol (3 ml). The reaction mixture was stirred at room temperature for 30 min. The yellow precipitate which separated was filtered off and dried. Recrystallization of the crude product from ethanol–water (1 : 1) afforded the *title compound* (380 mg, 32%) as pale yellow needles, mp 133–134°C (ethanol–water) (Found: C, 55.9; H, 5.1; N, 11.6. C₁₁H₁₂N₂O₄ requires C, 55.9; H, 5.1; N, 11.9%); ν_{\max} (Nujol mull)/cm^{−1} 1667vs (C=O), 1640s, 1567s, 1504s, 1289s and 1171s; δ_{H} (400 MHz; CDCl₃) 8.18 (2H, d, *J* 8.8), 7.90 (1H, br, *N*-H hydrogen bonded), 7.49 (2H, d, *J* 8.8), 5.18 (2H, s, CH₂), 4.76 (1H, br, *N*-H free), 4.61 (1H, s, alkene-H) and 1.92 (3H, s, CH₃); δ_{C} (101 MHz; CDCl₃) 169.3 (C=O ester), 161.0 (C-4'), 147.3 (C-1'), 145.0, 127.7, 123.6, 83.0, 62.9 (CH₂) and 22.3 (Me); *m/z* 236 (*M*⁺, 12%), 136 (6, O₂NC₆H₄CH₂), 106 (11, O₂NC₆H₄CH₂ – NO) and 84 (86, *M* – O₂NC₆H₄CH₂O) and 57 (100, H₂NC(CH₃)CH₂).

Reactions of trithiazyl trichloride with primary enamines

General procedure. The primary enamine (1 mmol) was dissolved in CCl₄ (10 ml), and trithiazyl trichloride (245 mg, 1 mmol) in CCl₄ (10 ml) was added dropwise. The reaction mixture was stirred at room temperature for 16 h. The reaction mixture was then filtered through a short pad of silica. The filtrate was concentrated under reduced pressure. The residue was then subjected to column chromatography on silica with DCM–light petroleum (1 : 1) mixture as eluent.

3-Cyano-4-methyl-1,2,5-thiadiazole 3a. 3-Aminocrotononitrile **2a** was treated with trithiazyl trichloride and the *title compound* (35 mg, 28%) was obtained as a light yellow oil (Found: *M*⁺ 125.0041. C₄H₃N₃S requires *M* 125.0048); ν_{\max} (neat)/cm^{−1} 2241vs (nitrile), 1483s, 1439s, 1405s, 1388s, 1292s, and 1150s; δ_{H} (250 MHz; CDCl₃) 2.76 (3H, s, Me); δ_{C} (63 MHz; CDCl₃) 163.5, 134.0, 111.9 (nitrile C) and 15.25 (Me); *m/z* 125 (*M*⁺, 43%), 84 (32, *M* – MeCN), 73 (100, *M* – NCCN) and 46 (26, NS).

Methyl 4-methyl-1,2,5-thiadiazole-3-carboxylate 3b. Methyl 3-aminocrotonate **2b** was treated with trithiazyl trichloride and the *title compound* (98 mg, 62%) was obtained as colourless needles, mp 25–26°C (Found: *M*⁺ 158.0157. C₅H₆N₂O₂S requires *M* 158.0150); ν_{\max} (neat)/cm^{−1} 1728vs (C=O), 1590s (C=N), 1444vs, 1263vs and 1103vs; δ_{H} (250 MHz; CDCl₃) 4.00 (3H, s, ester Me), and 2.83 (3H, s, 4-Me); δ_{C} (63 MHz; CDCl₃) 163.0 (C=O, ester), 160.75, 150.0, 52.8 (ester Me) and 17.3 (4-Me); *m/z* 158 (*M*⁺, 31%), 127 (55, *M* – MeO), 126 (100, *M* – MeOH), 86 (24, SNCCO), 73 (14, CH₃CNS) and 72 (7, CH₂CNS).

¹⁵N Labelled methyl 3-aminocrotonate **2b** was treated with trithiazyl trichloride in different solvents and at different temperatures. Yields and isotopic incorporation are given in Table 1. The labelled *title compound* has identical mp, ¹H NMR and IR spectra to the unlabelled compound. For the labelled compound obtained from room temperature reaction, $\delta_{\text{N-15}}$ 341.0 (external reference MeNO₂); *m/z* 159 (*M*⁺, 31%), 158 (4), 128 (53, *M* – MeO), 127 (100, *M* – MeOH), 86 (27, S¹⁴NCCO), 74 (15, CH₃C¹⁵NS) and 73 (8, CH₂C¹⁵NS).

Ethyl 4-methyl-1,2,5-thiadiazole-3-carboxylate 3c. Ethyl 3-aminocrotonate **2c** was treated with trithiazyl trichloride to give the *title compound* (69 mg, 40%) as a light yellow oil (Found: *M*⁺ 172.0304. C₆H₈N₂O₂S requires *M* 172.0306); ν_{\max} (neat)/cm^{−1} 1723vs (C=O), 1422s, 1172vs and 1100vs; δ_{H} (250 MHz; CDCl₃) 4.47 (2H, q, *J* 7.2, ester CH₂) and 2.84 (3H, s, 4-Me) and 1.46 (3H, t, *J* 7.2, ester Me); δ_{C} (63 MHz; CDCl₃) 162.9 (C=O ester), 160.3, 150.3, 62.05 (ester CH₂), 17.4 (4-Me) and 14.1 (ester Me); *m/z* 172 (*M*⁺, 27%), 144 (25), 127 (84, *M* – EtO), 126 (100, *M* – EtOH), 86 (27, SNCCO) and 73 (20, MeCNS).

***p*-Nitrobenzyl 4-methyl-1,2,5-thiadiazole-3-carboxylate 3d.** *p*-Nitrobenzyl 3-aminocrotonate **2d** was treated with trithiazyl trichloride and the *title compound* (143 mg, 56%) was obtained as pale yellow prisms, mp 100–102°C (ethanol) (Found: C, 47.0; H, 2.9; N, 14.9. C₁₁H₉N₃O₄S requires C, 47.3; H, 3.25; N, 15.0%); ν_{\max} (Nujol)/cm^{−1} 1749vs (C=O), 1604vs, 1516vs, 1342vs, 1258s and 1112s; δ_{H} (400 MHz; CDCl₃) 8.25 (2H, dt, *J* 8.8, 2.1), 7.64 (2H, dt, *J* 8.8, 2.1), 5.51 (2H, s, CH₂) and 2.83 (3H, s, Me); δ_{C} (101 MHz; CDCl₃) 163.3 (C=O ester), 159.9, 149.3, 147.9, 142.1, 128.8, 123.95, 66.0 (CH₂) and 17.4 (Me); *m/z* 279 (*M*⁺, 2%) and 233 (2, *M* – NO₂)

Ethyl 4-(3-chloropropyl)-1,2,5-thiadiazole-3-carboxylate **13**

To a refluxing solution of ethyl α -(pyrrolidin-2-ylidene)acetate **10** (200 mg, 1.3 mmol) in CCl₄ (10 ml), trithiazyl trichloride (380 mg, 1.55 mmol) in CCl₄ (10 ml) was added dropwise. The

reaction mixture was heated under reflux for 18 h. The reaction mixture was cooled and filtered through a short pad of silica and the filtrate was concentrated under reduced pressure. Column chromatography of the residue on silica with DCM–light petroleum (1 : 1) afforded the *title compound* (150 mg, 50%) as a light brown oil (Found: M^+ 234.0231. $C_8H_{11}ClN_2O_2S$ requires M 234.0230); ν_{\max} (neat)/ cm^{-1} 1723vs (C=O), 1424s, 1297s and 1097vs; δ_H (250 MHz; $CDCl_3$) 4.46 (2H, q, J 7.2, ester CH_2), 3.65 (2H, t, J 6.4, $ClCH_2CH_2CH_2$)*, 3.40 (2H, t, J 7.4, $ClCH_2CH_2CH_2$)*, 2.31 (2H, pentet, J 6.5, $ClCH_2CH_2CH_2$ *) and 1.46 (3H, t, J 7.1, ester Me); δ_C (63 MHz; $CDCl_3$) 165.4 (C=O ester), 160.2, 150.1, 62.2 (OCH_2CH_3), 44.1 ($ClCH_2$), 30.65, 28.25 and 14.15 (OCH_2CH_3); m/z 234 (M^+ , 16%), 188 (100, M – EtOH), 172 (30), 153 (67, M – EtOH – Cl) and 139 (89). (* assignments uncertain)

The reaction of ethyl α -(pyrrolidin-2-ylidene)acetate **10** (233 mg, 1.2 mmol) and trithiazyl trichloride (440 mg, 1.8 mmol) in CCl_4 at room temperature for 18 h afforded the *title compound* (17 mg, 6%).

The reaction of methyl 3-*N*-methylaminocrotonate **14** with trithiazyl trichloride

To a refluxing solution of methyl 3-*N*-methylaminocrotonate **14** (129 mg, 1 mmol) in CCl_4 (10 ml), trithiazyl trichloride (294 mg, 1.2 mmol) in CCl_4 (10 ml) was added dropwise. The reaction mixture was heated under reflux for 18 h. The reaction mixture was cooled and filtered through a short pad of silica and the filtrate was concentrated under reduced pressure. Column chromatography of the residue on silica with DCM–light petroleum (1 : 1) afforded methyl 4-methyl-1,2,5-thiadiazole-3-carboxylate **3b** (30 mg, 19%), identical with an authentic sample.

Ethyl 4*H*,5*H*,6*H*-pyrrolo[1,2-*b*][1,2,5]thiadiazol-7-ium-3-carboxylate chloride **12**

To a solution of ethyl α -(pyrrolidin-2-ylidene)acetate **10** (200 mg, 1.3 mmol) in CCl_4 (10 ml), trithiazyl trichloride (380 mg, 1.55 mmol) in CCl_4 (10 ml) was added dropwise with stirring at room temperature under nitrogen. A brown precipitate separated and the reaction mixture was stirred for 10 min. The reaction mixture was then allowed to stand and the supernatant solution was removed through a filter cannula, and the resulting brown solid was washed repeatedly with CCl_4 under nitrogen to remove excess of trithiazyl trichloride. The brown solid was then dissolved in water (20 ml) and extracted with DCM (3×30 ml). The aqueous solution was treated with activated charcoal and filtered. The resulting clear solution was evaporated to dryness in high vacuum to give a pale yellow solid. The yellow solid was dissolved in water (5 ml) and a saturated solution of ammonium hexafluorophosphate was added dropwise until a white precipitate started to appear. The *title compound* (35 mg, 8%) was filtered off, dried under vacuum and obtained as colourless microcrystalline needles, mp 160–162 °C (Found M^+ 199.0563. $C_8H_{11}N_2O_2S^+$ requires M 199.0541); ν_{\max} (Nujol mull)/ cm^{-1} 1742vs (C=O), 1456s, 1417s, 1380s and 1261s; δ_H (250 MHz; D_2O) 4.87 (2H, t, J 7.8, CH_2), 4.50 (2H, q, J 7.2, ester CH_2), 3.59 (2H, t, J 7.8, CH_2), 3.06 (2H, pentet, J 7.8, CH_2), 1.39 (3H, t, J 7.2, ester Me); m/z (FAB⁺) 199 (M^+ , 100%).

Methyl 4,5-dimethyl-1,2,5-thiadiazol-5-ium-3-carboxylate hexafluorophosphate **15b**

To a solution of methyl 3-*N*-methylaminocrotonate **14** (258 mg, 2 mmol) in CCl_4 (15 ml), trithiazyl trichloride (586 mg, 2.4 mmol) in CCl_4 (15 ml) was added dropwise with stirring at room temperature under nitrogen. A brown precipitate separated and the reaction mixture was stirred for 10 min. The reaction mixture was then allowed to stand and the supernatant

solution was removed through a filter cannula, and the resulting brown solid was washed repeatedly with CCl_4 under nitrogen to remove excess of trithiazyl trichloride. The brown solid was then dissolved in water (20 ml) and extracted with DCM (3×30 ml). The aqueous solution was treated with activated charcoal and filtered. The resulting clear solution was evaporated to dryness under high vacuum to give a pale yellow solid. The yellow solid was dissolved in water (10 ml) and a saturated solution of ammonium hexafluorophosphate was added dropwise until a white precipitate started to appear. The *title compound* (93 mg, 15%) was filtered off, dried under vacuum and obtained as colourless microcrystalline needles, mp 155–157 °C (Found: M^+ 173.0378. $C_6H_9N_2O_2S^+$ requires M 173.0385); ν_{\max} (Nujol mull)/ cm^{-1} 1740vs (C=O) 1445s, 1408vs, 1287vs and 1156vs; δ_H (250 MHz; D_2O) 4.40 (3H, s, 5-Me), 4.09 (3H, s, ester Me) and 3.05 (3H, s, 4-Me); m/z (FAB⁺) 173 (M^+ , 100%).

Reaction of methyl 2-acetamidoacrylate **16a** with trithiazyl trichloride

To a refluxing solution of methyl 2-acetamidoacrylate **16a** (286 mg, 2 mmol) in CCl_4 (10 ml), trithiazyl trichloride (489 mg, 2 mmol) in CCl_4 (15 ml) was added dropwise. The reaction mixture was heated under reflux for 1 h. The reaction mixture was cooled to room temperature and filtered through a short pad of silica. The filtrate was concentrated under reduced pressure. Column chromatography of the residue on silica with DCM gave methyl 1,2,5-thiadiazole-3-carboxylate **17a** (151 mg, 53%) as a pale yellow solid, identical with an authentic sample, mp 40–41 °C (lit.,¹³ 41–42 °C).

The same reaction, carried out at room temperature for 4 h and worked up as above, afforded methyl 1,2,5-thiadiazole-3-carboxylate **17a** (15%).

Reaction of methyl 2-acetamido-3-phenylacrylate **16b** with trithiazyl trichloride

To a refluxing solution of methyl 2-acetamido-3-phenylacrylate **16b** (219 mg, 1 mmol) in CCl_4 (10 ml), trithiazyl trichloride (245 mg, 1 mmol) in CCl_4 (10 ml) was added dropwise. The reaction mixture was heated under reflux for 1 h. The reaction mixture was cooled to room temperature and filtered through a short pad of silica. The filtrate was concentrated under reduced pressure. Column chromatography of the residue on silica with DCM gave methyl 4-phenyl-1,2,5-thiadiazole-3-carboxylate **17b** (84 mg, 38%) as a pale yellow solid, mp 42–43 °C (lit.,¹³ 45–46 °C), m/z 220 (M^+ , 100%), 205 (29, M – Me), 189 (47, M – MeO), 135 (54, PhCNS) and 103 (19, PhCN).

3-*p*-Nitrophenyl-1,2,5-thiadiazole **21a**

To a refluxing solution of 1-tosyl-5-*p*-nitrophenyl-1,2,3-triazole **18a** (111 mg, 0.32 mmol) in CCl_4 (10 ml), trithiazyl trichloride (157 mg, 0.64 mmol) in CCl_4 (5 ml) was added dropwise. The reaction mixture was heated under reflux for 16 h. The reaction mixture was cooled to room temperature and filtered through a short pad of silica and the filtrate was concentrated under reduced pressure. Column chromatography of the residue on silica with DCM–light petroleum (1 : 1) gave the *title compound* (60 mg, 90%) as a colourless solid, mp 174–175 °C (lit.,¹⁴ 172 °C; δ_H 9.01 (1H, s, thiadiazole 4-H), 8.38 (2H, dt, J 8.9, 2.2) and 8.19 (2H, dt, J 8.9, 2.2); m/z 207 (M^+ , 100%), 180 (6, M – HCN), 177 (20, M – NO) and 161 (18, M – NO_2).

Treatment of 4-*p*-nitrophenyl-1,2,3-triazole (25 mg, 0.13 mmol) with trithiazyl trichloride (64 mg, 0.26 mmol) under the same conditions as described above afforded 3-*p*-nitrophenyl-1,2,5-thiadiazole **21a** (18 mg, 67%) identical to that described above.

Reaction of methyl 5-methyl-3*H*-1,2,3-triazole-4-carboxylate **24** with trithiazyl trichloride

To a refluxing solution of methyl 5-methyl-1,2,3-triazole-4-carboxylate **24** (90 mg, 0.64 mmol) in toluene (10 ml), trithiazyl trichloride (78 mg, 0.32 mmol) in toluene (5 ml) was added dropwise. Two more portions of trithiazyl trichloride (2 × 78 mg) in toluene (2 × 5 ml) were added dropwise after 1 and 2 h. The reaction mixture was heated under reflux for 16 h. The reaction mixture was cooled to room temperature and filtered through a short pad of silica. The filtrate was concentrated under reduced pressure. Column chromatography of the residue on silica with DCM–light petroleum (1 : 1) afforded methyl 4-methyl-1,2,5-thiadiazole-3-carboxylate **3b** (35 mg, 34%) as a pale yellow solid, identical with an authentic sample. Further elution with DCM–ethyl acetate (70 : 30) afforded the starting material **24** (41 mg, 46%).

Treatment of methyl 5-methyl-3*H*-1,2,3-triazole-4-carboxylate **24** (100 mg, 0.71 mmol) with trithiazyl trichloride (208 mg, 0.85 mmol) under the same conditions as described above, but with trithiazyl trichloride added in one portion afforded methyl 4-methyl-1,2,5-thiadiazole-3-carboxylate **3b** (19 mg, 17%) and unreacted starting material **24** (49 mg, 49%). The same reaction carried out in refluxing CCl₄ afforded methyl 4-methyl-1,2,5-thiadiazole-3-carboxylate **3b** (10 mg, 9%) and unreacted starting material **24** (54 mg, 54%).

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