Organic Heterocyclothiazenes. Part 7.[1] Chemistry of 1,3,5,2,4,6-Trithiatriazepines

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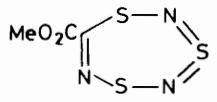
Methyl trithiatriazepine-7-carboxylate (**1**), obtained from tetrasulphur tetranitride and dimethyl acetylenedicarboxylate, is hydrolysed to the carboxylic acid (**3**) which is decarboxylated in boiling dioxane to give the parent 1,3λ⁴δ²,5,2,4,6-trithiatriazepine (**4**). Trithiatriazepine (**4**) is a remarkably stable 10π aromatic system similar to, although less polar than, the trithiadiazepine(**2b**). The triazepine (**4**) is less reactive towards electrophilic substitution than the diazepine (**2b**) but it can be nitrated with nitronium tetrafluoroborate, and brominated with *N*-bromosuccinimide in acetonitrile at 110 °C. The thermal stability of compounds (**2b**) and (**4**) suggests that the unknown sulphur nitride trithiatetrazepine (**8**) would be thermodynamically stable.

In Part 1 of this series we reported that two minor products of the reaction of tetrasulphur tetranitride, S_4N_4, with dimethyl acetylenedicarboxylate (DMAD) in boiling toluene were methyl 1,3,5,2,4,6-trithiatriazepine-7-carboxylate (**1**) and dimethyl 1,3,5,2,4-trithiadiazepine-6,7-dicarboxylate (**2a**).[2] Subsequently the parent trithiadiazepine (**2b**) was synthesized independently[3] and shown to undergo ready electrophilic substitution in agreement with the proposed 10π aromatic structure.[4]



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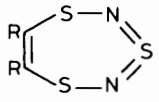


(**2**) **a**; R = CO_2Me
b; R = H

The only trithiatriazepines yet reported are the methyl (**1**), ethyl, and t-butyl esters and the 7-acetyl and formyl derivatives, all prepared from S_4N_4–acetylene reactions.[3,5] We now describe the optimisation of the preparation of the methyl ester (**1**) and its conversion into the parent trithiatriazepine (**4**) whose chemical properties are also in accord with a 10π aromatic system.

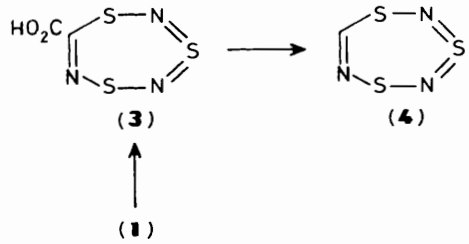
Results and Discussion

In S_4N_4–acetylene reactions, relatively high temperatures (156 °C in bromobenzene) favour formation of trithiadiazepines and markedly disfavour formation of trithiatriazepines.[1] Thus lower reaction temperatures were indicated for the preparation of compound (**1**) from S_4N_4 and DMAD. Reactions in boiling benzene were unacceptably slow, but a solvent mixture of benzene and toluene (2:1), b.p. 93 °C, was found to be more convenient, reproducibly giving a 28% yield of the ester (**1**) in 24 h. Thus the ester (**1**), the starting point for all our subsequent work on trithiatriazepine, is now readily available.

Base-catalysed hydrolysis of the ester (**1**) was unsuccessful because of the instability of the trithiatriazepine ring towards hydroxide ion. Demethylation of the ester with trimethylsilyl chloride and sodium iodide in acetonitrile[6] was also unsuccessful but treatment with boron tribromide in dichloromethane[7] did cause demethylation to the colourless crystalline acid (**3**) in 63% yield. Its i.r. spectrum showed strong absorptions for acidic hydrogen (3 500—2 200 cm^{-1}), for C=N and C=O (1 747 and 1 703 cm^{-1}), and for N=S=N (1 151 cm^{-1}), and the exchangeable proton resonated at δ 5.2 (br) in the n.m.r. spectrum. The mass spectrum showed the molecular ion at *m/z* 195 and peaks at 151 ($M^+ - CO_2$), 92 ($N_2S_2^+$), and 59 ($CHNS^+$).

A better route to the carboxylic acid (**3**) proved to be acid-catalysed hydrolysis of the ester (**1**), readily accomplished with 5M hydrochloric acid at 80 °C for 4 h. On cooling, the acid crystallised directly in high yield (77%). At higher hydrolysis temperatures the acid was appreciably decarboxylated.

Decarboxylation of trithiatriazepine-7-carboxylic acid (**3**) was best achieved by heating under reflux in dry dioxane for 3.5 h; evaporation gave trithiatriazepine (**4**) in 83% yield (Scheme 1). This reaction was very clean (t.l.c.) with no by-products, and

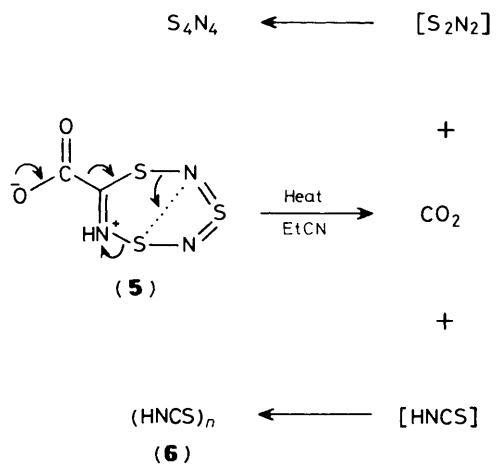


Scheme 1.

presumably some of the volatile trithiatriazepine (**4**) was being lost by evaporation. To prevent this loss, decarboxylation was attempted in propionitrile which has a similar boiling point (97 °C) to dioxane but would be more suitable for direct use, without evaporation, in subsequent reactions such as nitration with nitronium tetrafluoroborate. Surprisingly, when the carboxylic acid (**3**) was heated in refluxing propionitrile for 4 h, no trithiatriazepine (**4**) was formed, but S_4N_4 (32%) and a red intractable solid considered to be polymeric thiocyanic acid (**6**)[8] (60%) were isolated.

The ready decarboxylation in dioxane under such mild conditions may indicate that the acid (**3**) exists in equilibrium with the zwitterion (**5**). Pyridine-2-carboxylic acid which exists largely as the zwitterion undergoes smooth decarboxylation at the somewhat higher temperature of 140 °C. The formation of S_4N_4 and the polymer (**6**) could be explained by an alternative fragmentation of the zwitterion (**5**), as shown, to give S_2N_2, which dimerises to S_4N_4, and thiocyanic acid (Scheme 2).[8] This fragmentation was exactly paralleled in the mass spectrum of the acid (**3**), mentioned above.

1,3λ⁴δ²,5,2,4,6-Trithiatriazepine (**4**) crystallised from light petroleum as stable, colourless, highly volatile plates, m.p. 43 °C. Its i.r. and u.v. spectra were similar to those of trithiadiazepine (**2b**) with an asymmetric NSN vibration at $\nu_{max.}$ 1 136 cm^{-1} [1 152 cm^{-1} in (**2b**)] and a long wavelength absorption at $\lambda_{max.}$ 327 nm [330 nm in (**2b**)] typical of an aromatic π to π* transition. The mass spectrum showed the

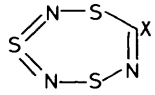


Scheme 2.

molecular ion at *m/z* 151 with peaks at 93 ($HN_2S_2^+$), 78 (NS_2^+), and 61 (HN_2S^+), but not for the loss of the fragment NS which is seen in the mass spectra of all trithiadiazepines.[3,5] The methyl ester (**1**), the corresponding ethyl and t-butyl esters, and the 7-formyl and acetyl trithiatriazepines all had spectroscopic properties similar to the parent (**4**), and showed no loss of NS in their mass spectra. The trithiatriazepine ring proton resonates at δ 9.0 and the carbon atom at δ 145 in the n.m.r. spectra, supporting a diamagnetic ring current and aromatic character for the heterocyclic ring. We assume that the ring is planar, by analogy with the ester (**1**)[9] and the trithiadiazepine (**2b**)[10] and from the general similarity of their spectral properties.

Trithiatriazepine (**4**), with an R_F value of 0.37 (light petroleum on silica), is less polar than trithiadiazepine (**2b**) (R_F 0.30), despite its additional heteroatom. This agrees with the smaller dipole moment calculated for the triazepine (**4**) than for the diazepine (**2b**); these were respectively 0.47 and 1.52 debye by the MNDO method, and 1.01 and 2.29 debye by the *ab initio* (3-21 G*) method.[11] The extra ring nitrogen atom in trithiatriazepine (**4**) presumably introduces an additional dipole into the molecule which is in opposition to the net dipole of trithiadiazepine (**2b**). The corresponding methyl and t-butyl esters followed the same trend, with the trithiatriazepines again being less polar than the trithiadiazepines.

In spite of its extra ring nitrogen atom, trithiatriazepine (**4**) has similar thermal stability to trithiadiazepine (**2b**) surviving over 20 h heating in *o*-dichlorobenzene (180 °C); this is striking for a ring with six of its seven members being heteroatoms. However, the extra nitrogen atom did, as expected, decrease the reactivity of the trithiatriazepine relative to the trithiadiazepine towards electrophilic substitution. Treatment of trithiatriazepine (**4**) with nitronium tetrafluoroborate in acetonitrile at 0 °C gave the 7-nitro compound (**7a**) as stable, pale yellow

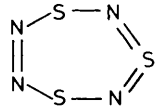


(**7**) **a** ; X = NO_2
b ; X = Br

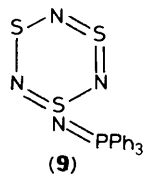
crystals, m.p. 60 °C, in 60% yield, comparable to the nitration of 6-nitrotrithiadiazepine to the 6,7-dinitro compound. The long wavelength u.v. absorption at 345 nm and the i.r. absorption at 1 150 cm^{-1} suggested that the ring was still intact, and there was a strong absorption at 1 305 cm^{-1} for the nitro group. Elemental analysis and the mass spectrum confirmed the molecular formula $CN_4O_2S_3$, and the mass spectrum showed loss of NO_2 and the presence of fragments NS_2 and NS typical of trithiatriazepines. The ^{13}C signal for the nitro compound (**7a**) resonated at 154.4 p.p.m., 9.4 p.p.m. downfield relative to the signal for the parent compound.

The differences between trithiatriazepine (**4**) and trithiadiazepine (**2b**) towards electrophilic attack were most noticeable in bromination and thalliation reactions. The diazepine (**2b**) gave an almost quantitative yield of 6-bromotrithiadiazepine with 1 mol equiv. of *N*-bromosuccinimide in acetonitrile at room temperature for 1 day.[4] The triazepine (**4**) required 20 mol equiv. of *N*-bromosuccinimide in acetonitrile at 110 °C (sealed tube) for 3 days to give only 30% of 7-bromotrithiatriazepine (**7b**), and some trithiatriazepine (**4**) (12%) could still be recovered. Similarly, the diazepine (**2b**) reacted rapidly with bromine in tetrachloromethane at room temperature whereas the triazepine (**4**) was virtually inert to bromine in boiling tetrachloromethane in the dark and on irradiation with a tungsten lamp. The triazepine (**4**) required an excess of bromine in boiling tetrachloromethane in the presence of an iron–iron(III) chloride catalyst for significant reaction, thus supporting the electrophilic nature of the substitution, and still gave only 22% of the bromide (**7b**). Thallium tris(trifluoroacetate) in acetonitrile converted trithiadiazepine (**2b**) into its bis(trifluoroacetoxy) derivative in high yield:[12] trithiatriazepine was inert to these and more vigorous conditions (refluxing trifluoroacetic acid). Lithiation of trithiatriazepine was equally unsuccessful, either by hydrogen–lithium or bromine–lithium exchange with n-butyl- or t-butyl-lithium in tetrahydrofuran under standard reaction conditions; again starting material (**4**) or (**7b**) was recovered. Further consequences of the differing reactivities of trithiadiazepines and trithiatriazepines will be explored in a later part of this series.

Trithiatetrazepine.—Since both the diazepine (**2b**) and triazepine (**4**) are thermally stable, it is worth considering the consequences of replacing the remaining carbon atom in the triazepine (**4**) by nitrogen to give the trithiatetrazepine (trisulphur tetranitride) (**8**). This sulphur nitride, S_3N_4, is unknown, and it may be significant that it has never been reported as a by-product in any of the very large number of reactions of S_4N_4 and related species, even in the reaction of S_4N_4 with triphenylphosphine[13] which might have been expected to cause desulphurisation to S_3N_4. The product of this last reaction was the trithiatriazine (**9**) which is, formally at least, the triphenylphosphine adduct of a trithiatriazino–nitrene, isomeric with trithiatetrazepine (**8**). It is possible that contraction of the 8-membered ring of S_4N_4 to the 6-membered ring of product (**9**) could have proceeded through the intermediate 7-membered ring (**8**), which then reacts further with triphenylphosphine.



(**8**)



(**9**)

A possible decomposition pathway available to trithiatetrazepine (**8**) is the extrusion of dinitrogen, and indeed polysulphur–nitrogen rings with nitrogen–nitrogen bonds are very rare. Nevertheless, if compound (**8**) were planar and delocalised, like the isoelectronic rings of compounds (**2b**) and (**4**), it should have 10π aromatic character and thus be stabilised, and possibly isolable. According to MNDO and *ab initio* MO calculations, the three rings (**2b**), (**4**), and (**8**) all have very comparable bond lengths, bond angles, π bond orders, and sets of distinct π orbitals characteristic of 10π aromatic systems.[11] The synthesis of this unknown trisulphur tetranitride is thus an interesting challenge.

Experimental

For general points see reference 2. Light petroleum refers to the fraction, b.p. 40—60 °C.

Reaction of Tetrasulphur Tetranitride with Dimethyl Acetylenedicarboxylate.—Tetrasulphur tetranitride (4.14 g, 22.5 mmol), dimethyl acetylenedicarboxylate (5.5 ml, 45 mmol), benzene (66 ml), and toluene (33 ml) were heated under nitrogen at reflux (93 °C) for 24 h, behind a safety screen. Two such reaction mixtures were combined, filtered, and the solvents evaporated. Dichloromethane (100 ml) was added and the resulting solution decanted from the sulphur residue which was washed with further portions of dichloromethane (5 × 20 ml). The combined dichloromethane fractions were pre-adsorbed onto silica (60 g) and separated by dry flash chromatography on silica (350 g). Light petroleum eluted sulphur. Dichloromethane (30—80%) in light petroleum eluted methyl 1,3,5,2,4,6-trithiatriazepine-7-carboxylate (**1**)[2] (2.639 g, 28%). Dichloromethane (85—100%) in light petroleum eluted dimethyl 1,3,5,2,4-trithiadiazepine-6,7-dicarboxylate (**2a**)[2] (1.061 g, 9%). The major product from this reaction, dimethyl 1,2,5-thiadiazole-3,4-dicarboxylate,[14] and a minor product, dimethyl 1,2,4-thiadiazole-3,5-dicarboxylate,[14] were detected by t.l.c. but not isolated.

1,3$\lambda^4\delta^2$,5,2,4,6-*Trithiatriazepine*-7-*carboxylic Acid* (**3**).—(*a*) *By demethylation of ester* (**1**). A solution of boron tribromide in dichloromethane (1M; 0.5 ml, 0.5 mmol BBr_3) was added dropwise to a stirred solution of the ester (**1**) (21 mg, 0.1 mmol) in dichloromethane (2.5 ml) previously cooled to −40 °C under nitrogen.[7] The reaction mixture became yellow; stirring was continued at −40 °C for 1 h, then at 25 °C for 2 h. The mixture was carefully diluted with water (5 ml) and extracted with dichloromethane. The combined dichloromethane extracts were washed with water and dried ($MgSO_4$). Evaporation of the solvent and crystallisation of the residue from hot water gave the *acid* (**3**) (12 mg, 63%) as needles, m.p. 149—150 °C (decomp.) (Found: C, 12.6; H, 0.4%; M^+, 194.9241. $C_2HN_3O_2S_3$ requires C, 12.3; H, 0.5%; *M*, 194.9231); $\lambda_{max.}$(EtOH) 264 (log ε 4.27) and 332 nm (3.60); $\nu_{max.}$($CHCl_3$) 3 500—2 200br, 1 747s, 1 703s, 1 326s, 1 263s, 1 151s, and 971s cm^{-1}; δ_H(250 MHz; $CDCl_3$) 5.2 (br); *m/z* (120 °C) 195 (M^+, 40%), 151 ($M - CO_2$, 24), 92 (N_2S_2, 57), and 78 (NS_2, 100), 59 (HNCS, 68), and 46 (NS, 86).

(*b*) *By hydrolysis of the ester* (**1**). The ester (**1**) (0.365 g, 1.87 mmol) was stirred with 5M hydrochloric acid (180 ml) and warmed in an oil-bath to 80 °C until all the starting material had dissolved (2 h); heating was then continued at 80 °C for 2 h. The solution was left to cool slowly to room temperature. Fine needles of the carboxylic acid (**3**) crystallised out and were filtered off (0.243 g, 71%); more acid (20 mg, 6%) was obtained by extraction of the filtrate with dichloromethane, followed by drying ($MgSO_4$), and evaporation. This acid (**3**) was identical with that described above.

1,3$\lambda^4\delta^2$,5,2,4,6-*Trithiatriazepine* (**4**).—The carboxylic acid (**3**) (150 mg, 0.77 mmol) was dissolved in dry dioxane (10 ml) and heated at gentle reflux under nitrogen for 3.5 h. Evaporation of the solvent gave the *trithiatriazepine* (**4**) (97 mg, 83%) as plates, m.p. 43 °C (light petroleum) (Found: C, 8.15; H, 0.55; N, 27.7. CHN_3S_3 requires C, 7.95; H, 0.65; N, 27.8%); $\lambda_{max.}$(EtOH) 228 (log ε 3.89), 295 (3.41), and 327 nm (3.54); $\nu_{max.}$($CHCl_3$) 2 925, 2 850, 1 602, 1 496, 1 450, 1 310, 1 136vs, 972, 825, 628s, and 606 cm^{-1}; $\nu_{max.}$(KBr) 418 and 290 cm^{-1}; δ_H(250 MHz; $CDCl_3$) 9.03 (s); δ_C(22.5 MHz; $CDCl_3$) 145.1; *m/z* (100 °C) 153 (M^+ + 2, 14%), 151 (M^+, 100), 78 (NS_2, 62), and 46 (NS, 33).

Thermolysis of Trithiatriazepine-7-*carboxylic Acid* (**3**) *in Propionitrile.*—Trithiatriazepine-7-carboxylic acid (**3**) (100 mg, 0.513 mmol) and propionitrile (10 ml) were heated under reflux for 4 h. After cooling, a red polymeric solid tentatively assigned structure (**6**) (18 mg, 60%) {$\lambda_{max.}$[NaOH (aq.), 3×10^{-4}M] 250sh, and 290sh nm; $\nu_{max.}$(Nujol) 3 207br, 1 527, 1 505, 1 407, 1 357, and 1 234s cm^{-1}} was filtered off. The filtrate was pre-adsorbed onto silica and subjected to dry flash chromatography on silica (5 g). Elution with dichloromethane (30—40%) in light petroleum gave tetrasulphur tetranitride (15 mg, 32%). Analysis of the reaction mixture (t.l.c.) showed that no trithiatriazepine (**4**) was formed.

7-*Nitro*-1,3,5,2,4,6-*trithiatriazepine* (**7a**).—A mixture of nitronium tetrafluoroborate (115 mg, 0.86 mmol) and dry acetonitrile (2 ml) was added to trithiatriazepine (**4**) (0.087 g, 0.58 mmol) in dry acetonitrile (2 ml) and stirred for 2 h at 0 °C. The reaction mixture was pre-adsorbed onto silica and separated by dry flash chromatography on silica (9 g). Dichloromethane (15—30%) in light petroleum eluted unchanged trithiatriazepine (**4**) (5 mg, 6%); dichloromethane (35—40%) in light petroleum eluted 7-*nitrotrithiatriazepine* (**7a**) (63 mg, 55%) as yellow plates, m.p. 60 °C (light petroleum) (Found: C, 6.1; N, 28.4. $CN_4O_2S_3$ requires C, 6.1; N, 28.55·); $\lambda_{max.}$(EtOH) 277 log ε 3.75) and 345 nm (3.11); $\nu_{max.}$(CCl_4) 1 305vs, 1 150m, 990m, 950m, and 670m cm^{-1}; δ_C($CDCl_3$) 154.4; *m/z* (150 °C) 198 (M^+ + 2, 3.3%), 196 (M^+, 25), 150 ($M^+ - NO_2$, 63), 78 (NS_2, 40), and 46 (NS, 100).

7-*Bromo*-1,3,5,2,4,6-*trithiatriazepine* (**7b**).—(*i*) *From trithiatriazepine* (**4**) *and bromine.* Trithiatriazepine (40 mg, 0.265 mmol), bromine (13.7 μl, 0.265 mmol), iron dust (25 mg), iron(III) chloride (a trace), and tetrachloromethane (5 ml) were heated under reflux for 36 h, with more bromine (13.7 μl) added every 6 h. The reaction mixture was filtered and the filtrate separated by flash chromatography on silica (10 g). Light petroleum eluted sulphur (2 mg) followed by 7-*bromotrithiatriazepine* (**7b**) (13 mg, 22%) as colourless needles, m.p. 49—49.5 °C (light petroleum) (Found: M^+, 228.8441. C-$^{79}BrN_3S_3$ requires *M*, 228.8438); $\lambda_{max.}$(EtOH) 223 log ε 4.13), 252 (3.84), 280 (3.34), and 339 nm (3.60); $\nu_{max.}$(CCl_4) 1 500s, 1 140s, 985w, 880m, 660s, and 625m cm^{-1}; $\nu_{max.}$(KBr) 1 505s, 1 140s, 995m, 875m, 800s, 655s, 630m, 600s, 595m, 565m, 365m, and 295m cm^{-1}; *m/z* (170 °C) 231 and 229 (M^+, 66 and 60%), 150 (M^+ − Br, 8), 124 (N_2S_3, 11), 78 (NS_2, 100), and 46 (NS, 58).

(*ii*) *From trithiatriazepine* (**4**) *and* N-*bromosuccinimide.* Trithiatriazepine (15 mg, 0.1 mmol), *N*-bromosuccinimide (0.356 g, 2 mmol), and acetonitrile (2 ml) were heated in a sealed tube at 110 °C for 3 days. The reaction mixture was pre-adsorbed onto silica and separated by flash chromatography on silica (5 g). Light petroleum eluted 7-bromotrithiatriazepine (**7b**) (6.8 mg, 30%) identical with that obtained above, followed by unchanged trithiatriazepine (**4**) (1.8 mg, 12%).

Acknowledgements

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