Studies of Heterocyclic Compounds. Part 31.[1] 4-Alkyl-5-alkylimino-Δ²-1,2,4-thiadiazolines: Synthesis and Cycloaddition Reactions with Nitriles in Attempts to Prepare 3aλ⁴-Thia-1,3,4,6-tetraazapentalenes

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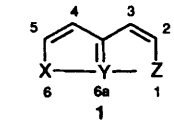
Several 4-alkyl-5-alkylimino-Δ²-1,2,4-thiadiazolines have been synthesized from 1,2,4-thiadiazoles, namely 3,4-dimethyl-5-methylimino-Δ²-1,2,4-thiadiazoline **9**, 3-methyl-6,7-dihydro-5*H*-1,2,4-thiadiazolo[4,5-*a*]pyrimidine **24**, 6,7-dihydro-5*H*-1,2,4-thiadiazolo[4,5-*a*]pyrimidine **26**, and 3-methyl-5,10-dihydrobenzo[*e*]-1,2,4-thiadiazolo[4,5-*a*][1,3]diazepine **34**. Cycloaddition reactions of compounds **9**, **24**, **26** and **34** were carried out in order to synthesize 1*H*,6*H*-3aλ⁴-thia-1,3,4,6-tetraazapentalenes **6**, whose system is a hitherto unknown variation of the 1,6,6aλ⁴-triheterapentalene structure. Compound **9** failed to react with nitriles and decomposed under forcing conditions. Compounds **24**, **26** and **34** underwent cycloaddition with nitiriles, with elimination of acetonitrile from **24** and **34** and of hydrogen cyanide from **26**, and incorporation of the nitrile into the product 4-alkyl-5-alkylimino-Δ²-1,2,4-thiadiazoline. 1*H*,6*H*-3aλ⁴-Thia-1,3,4,6-tetraazapentalenes **6** were not isolated or detected spectroscopically but it is proposed that they are intermediates in the cycloaddition of 4-alkyl-5-alkylimino-Δ²-1,2,4-thiadiazolines with nitriles. The heterocyclic system **34** is a new one.

1,6,6aλ⁴-Triheterapentalenes and their aza analogues comprise a large number of systems based on structure **1**, in which Y = S, Se or Te and X and Z are O, S, Se or NR. The essential structural feature in compounds **1** is the heteroatom unit **2** which employs four-electron three-centre bonding. In a previous paper[2] we formulated possible variations of the triheterapentalene structure which contain the structural element **3** or **4**. Attempts to synthesize compounds **5** which contain the unit **3** (X = Y = S, Z = N) gave instead 5-thioacylmethylene-Δ²-1,2,4-thiadiazolines, showing that the triheterapentalene structure **5** is energetically disfavoured relative to the monocyclic 5-thioacylmethylene-Δ²-1,2,4-thiadiazoline structure. The aim of the work described in this paper was to synthesize and study the structure of the hitherto unknown 1*H*,6*H*-3aλ⁴-thia-1,3,4,6-tetraazapentalenes **6**, which contain the unit **4** (X = Z = N, Y = S).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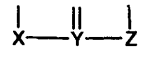
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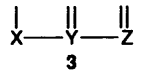
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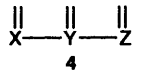
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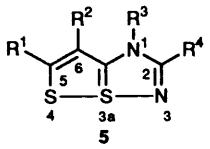
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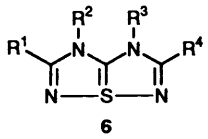
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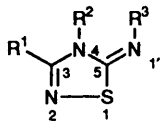
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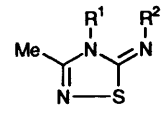
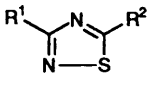
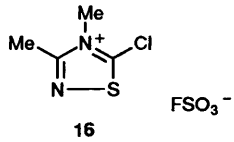

8 R^1 = Me, R^2 = H
9 R^1 = R^2 = Me
10 R^1 = $[CH_2]_3Br$, R^2 = H


11 R^1 = Me, R^2 = Cl
12 R^1 = Me, R^2 = NH_2
13 R^1 = Me, R^2 = NHCHO
14 R^1 = Ph, R^2 = NH_2
15 R^1 = H, R^2 = NH_2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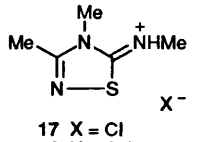
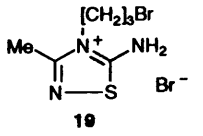

17 X = Cl
18 X = ClO_4

Results and Discussion

Synthesis of 4-Alkyl-5-alkylimino-Δ²-1,2,4-thiadiazolines.— Our synthetic objective was to prepare 4-alkyl-5-alkylimino-Δ²-1,2,4-thiadiazolines **7** for the purpose of carrying out cycloaddition with nitriles R^4CN to give the triheterapentalenes **6**. Attempts to obtain the methylimine **9** by methylation of the imine **8**[3,4] with iodomethane or methyl fluorosulfonate were unsatisfactory since mixtures of salts were obtained which, when deprotonated, gave mixtures of bases. The methylimine **9** was eventually obtained by successive methylation of 5-chloro-3-methyl-1,2,4-thiadiazole **11**[5] with methyl fluorosulfonate and treatment of the resulting salt **16** with ethanolic methylamine. The structure of the methylimine **9** was established indirectly by an X-ray single-crystal structure determination[6] of the corresponding hydrochloride **17**.

In order to obtain other 4-alkyl-5-alkylimino-Δ²-1,2,4-thiadiazolines **7**, 5-amino-3-methyl-1,2,4-thiadiazole **12** was allowed to react with 1,3-dibromopropane in hot dimethylformamide (DMF) in the expectation that alkylation would take place exclusively at position 4 to give the intermediate bromide **19**, analogously to the methylation[3] of compound **12**. Deprotonation of the bromide **19** and thermal cyclisation of the resulting

imine **10** would give the pyrimidinium bromide **20**. In the event the salt **20** was produced directly, but in modest yield (24%), and on being deprotonated afforded the 1,2,4-thiadiazolo[4,5-*a*]pyrimidine **24**. The reaction also gave the formamide **13** as the main reaction product (37%) together with dimethylammonium bromide (21%). The formamide **13** and the dimethylammonium bromide arise by condensation of the thiadiazole **12** with the solvent followed by solvolysis involving HBr and water. The use of the less reactive aprotic solvents *N*-methylpyrrolidinone and 1,3-dimethyl-1,3-propyleneurea (DMPU) in place of DMF raised the yield of the base **24** to ~35%.



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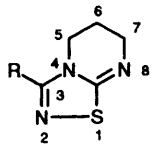
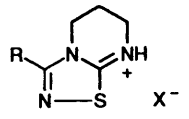


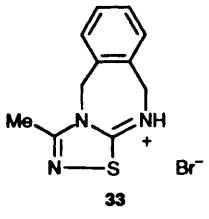
24 R = Me
25 R = Ph
26 R = H
27 R = 4-$NO_2C_6H_4$
28 R = 4-pyridyl
29 R = $MeOCH_2$
30 R = 2-HOC_6H_4
31 R = CD_3
32 R = CH=CHCN (*E*)



20 R = Me, X = Br
21 R = Ph, X = Br
22 R = H, X = Br
23 R = Me, X = PhC(O⁻)=CHCN

5-Amino-3-phenyl-1,2,4-thiadiazole **14** and 5-amino-1,2,4-thiadiazole **15** also reacted with 1,3-dibromopropane in boiling DMF, giving the bromides **21** and **22**, respectively, which, when deprotonated, yielded the corresponding bases **25** and **26**.

5-Amino-3-methyl-1,2,4-thiadiazole **12** also reacted with 1,2-bis(bromomethyl)benzene in boiling DMF to give the diazepinium bromide **33** directly, together with much dimethylammonium bromide. Deprotonation of the bromide **33** afforded the diazepine **34** in 45% overall yield. The diazepine **34** is the first member of the benzo[*e*]-1,2,4-thiadiazolo[4,5-*a*][1,3]diazepine system to be reported and isolated. Compounds **24–26** and **34** are moderately strong bases [pK_a (5% EtOH–water): **24**, 8.48; **25**, 8.24; **34**, 7.46].



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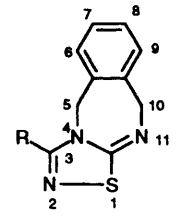
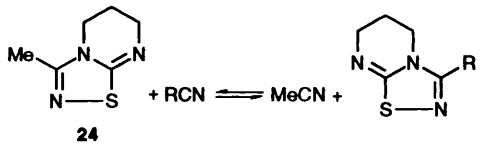


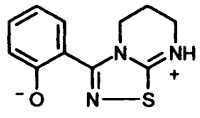
34 R = Me
35 R = CD_3
36 R = CH=CHCN (*E*)

Cycloaddition of the Pyrimidines **24** *and* **26** *and the Diazepine* **34** *with Nitriles.*—The reaction of the methyl base **24** with a series of nitriles was investigated. 1*H*,6*H*-3aλ^4-Thia-1,3,4,6-tetraazapentalenes **6** have not been found in any of these reactions nor has their presence been detected by NMR spectroscopy. In the majority of reactions the overall process involved the incorporation of the reactant nitrile into the reaction product and concomitant elimination of acetonitrile from the reactant (Scheme 1). Thus the base **24** reacted with boiling benzonitrile to give the same compound **25** as had been obtained by the sequence **14** → **21** → **25**. Reaction of the base **24** with 4-nitrobenzonitrile, 4-cyanopyridine and methoxyacetonitrile gave the thiadiazolo[4,5-*a*]pyrimidines **27–29**, respectively. The product from the reaction of the base **24** with 2-hydroxybenzonitrile in boiling toluene had a high melting point (228–229 °C) and was sparingly soluble in polar organic solvents. Its IR spectrum displayed a broad band centred at 2550 cm^{-1}. These properties suggest that the compound possesses the zwitterion structure **37** or an intermolecularly hydrogen-bonded structure held by OH---N-8 interactions. In solution it appears to exist in the neutral monomeric form **30**. The ^1H NMR spectrum [$(CD_3)_2SO$] shows a CH_2 triplet at δ 3.57, which is close to the range (δ 3.83–3.89) in which the 5-H_2 triplets of compounds **25**, **27** and **28** occur. The 5-H_2 triplet of the zwitterion **37** would be expected to occur further downfield in the region in which the 5-H_2 signal of the salt **21** occurs (δ 4.12).



24

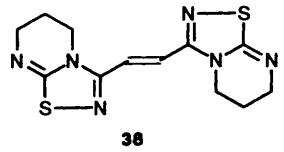
Scheme 1



37

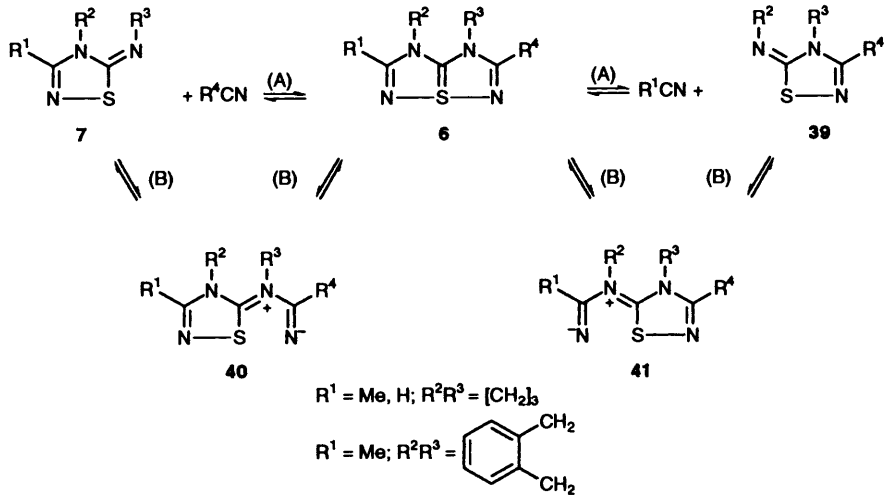
The methyl base **24** reacted with boiling trideuterioacetonitrile to give the trideuteriomethyl analogue **31** in high yield (84%). The base **31**, when boiled in acetonitrile, gave back the methyl base **24** (86%). The results of these experiments demonstrate the reversibility of the process (Scheme 1). Periodic examination of a solution of the base **24** in CD_3CN (CD_3CN:**24**, 38:1) by ^1H NMR spectroscopy showed that the base **24** reacts with CD_3CN at a measurable rate at ambient temperature. Conversion of the base **24** into compound **31** was 50% complete after 6.5 days.

The methyl base **24** reacted slowly with fumaronitrile (1:2 ratio) in toluene at room temperature at both cyano groups to give the stable yellow ethene **38** (79% yield). With a larger excess of fumaronitrile (1:5 ratio), the nitrile **32** was isolated (65%), together with the ethene **38** (11%). The nitrile **32** undergoes slow, continuous self-cycloaddition to give the ethene **38** along with polar decomposition products. It could not be freed entirely (TLC) from impurities for elemental analysis but was characterised by its ^1H NMR and mass spectra.



38

The base **24** failed to react with boiling pivalonitrile (105 °C). Reaction took place between the base **24** and benzoylacetonitrile but did not involve the cyano group. Instead an acid–base reaction occurred to give the ion-pair **23** which was insoluble in non-polar organic solvents. Its IR spectrum (KBr) did not show C=O stretching absorption but instead showed a broad band at 2700–2400 cm^{-1} arising from =NH– and a strong band at 2150 cm^{-1} originating from the unit $^-O–C=C–C\equiv N \leftrightarrow O=C–C=C=N^-$ [*cf.* $PhCOCH_2CN$: ν(C=O) 1690 cm^{-1}; ν(C≡N) 2258 cm^{-1}]. The ion-pair dissolved in $(CD_3)_2SO$ to give a solution whose ^1H NMR spectrum showed that virtually complete reversion to the



Scheme 2

base **24** and benzoylacetonitrile had occurred. Boiling of a suspension of the ion-pair **23** in toluene did not give any useful product.

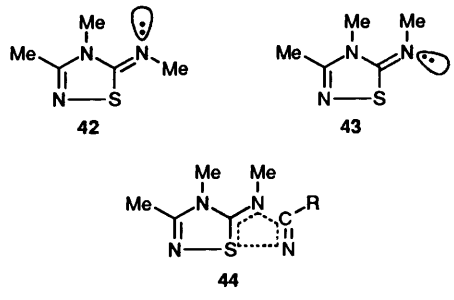
The base **26** reacted with nitriles in a similar manner to the base **24**, with elimination of hydrogen cyanide. It reacted with boiling acetonitrile to give the methyl base **24** and with benzonitrile in boiling toluene to give the phenyl base **25**.

The diazepine **34** reacted with nitriles less readily than did the bases **24** and **26**. Reaction with boiling trideuterioacetonitrile occurred slowly, only 25% conversion into the deuteriated analogue **35** taking place after 26 h. Conversion of compound **34** into the trideuterio analogue **35** was achieved to a greater extent (77%) by reflux of a solution of the diazepine **34** in a mixture of CD_3CN and $(CD_3)_2SO$. The diazepine **34** reacted readily with fumaronitrile in boiling toluene to give the nitrile **36**. There was no evidence of reaction at both cyano groups of fumaronitrile. Heating of the diazepine **34** in boiling benzonitrile resulted in the disappearance of the diazepine but did not yield any identifiable product, while prolonged boiling of the diazepine **34** with benzonitrile in toluene or benzene led to the recovery of starting material.

In contrast to the successful cycloadditions of the bases **24**, **26** and **34** with nitriles, the methylimine **9** failed to react with boiling trideuterioacetonitrile or with benzonitrile in boiling toluene and was recovered in high yield. In boiling benzonitrile, the methylimine **9** decomposed.

Conclusions.—1*H*,6*H*-3aλ^4-Thia-1,3,4-6-tetraazapentalenes **6** are not stable isolable species but may be higher-energy intermediates formed in low concentration in a reversible cycloaddition–elimination process in the reactions of 4-alkyl-5-alkylimino-Δ^2-1,2,4-thiadiazolines **7** with nitriles R^4CN which give the product 4-alkyl-5-alkylimino-Δ^2-thiadiazolines **39** (Scheme 2). Possible pathways for this process are (A) a two-step sequence in which the cycloaddition and cycloreversion steps are concerted, or (B) a four-step sequence involving charged intermediates **40** and **41**. It is also possible that the reactions of compound **7** with R^4CN and its analogue **39** with R^1CN do not involve the intermediate **6** but instead proceed through a transition state whose structure resembles structure **6**.

We propose the following explanation for the failure of the methylimine **9** to react with nitriles. The methylimine **9** is likely to exist in the *anti* form **42** rather than the *syn* form **43** since repulsion between methyl groups at positions 4 and N-1′ is avoided in configuration **42**. However, access to the lone pair of the imino nitrogen atom by the nitrile is more sterically hindered in the *anti* form **42** than in the *syn* form **43**. Also, a stabilised cyclic 10π-electron transition state, depicted by structure **44**, can arise in the reactions of the *syn* form **43** (and in the reactions of the bases **24**, **26** and **34**) but not in the reactions of the *anti* form **42**. We have been unable to obtain crystals of the methylimine **9** suitable for a crystal-structure determination but it is noteworthy that the hydrogen atom on N-1′ in the hydrochloride **17** is closer than is the methyl group on N-1′ to the methyl group at position 4.[6]



Experimental

M.p.s were determined with a Kofler hot-stage apparatus and are uncorrected. ^1H NMR spectra were determined at 200 MHz and ^{13}C NMR spectra at 50 MHz with a Bruker AC 200 spectrometer. ^1H NMR chemical shifts δ_H are given in ppm downfield from tetramethylsilane as internal reference. *J*-Values are given in Hz. ^{13}C NMR chemical shifts δ_C are given in ppm relative to the central peak of the $CDCl_3$ triplet taken as δ_C 77.00 or the central peak of the $(CD_3)_2SO$ multiplet taken as δ_C 39.9, and are proton-decoupled values. Extracts were dried over sodium sulfate. Solvents were removed from dried extracts and chromatographic eluates at reduced pressure with a rotary film evaporator. Ether denotes diethyl ether. The following anhydrous solvents were redistilled before use: acetone, DMPU, ethanol, methanol, propan-1-ol, pyridine. The following solvents were dried by standard procedures and were redistilled before use: cyclohexane, dichloromethane, ether, ethyl acetate, hexane. Benzene, toluene and xylene (mixture of isomers) were refluxed over sodium for 2 h, then distilled. DMF and *N*-methylpyrrolidinone were dried over powdered calcium hydride for several days and were then distilled at ~20 mmHg. Acetonitrile was boiled over sodium hydride for 30 min, distilled, then boiled over phosphoric anhydride for 1 h, distilled, and redistilled. Triethylamine was refluxed over

powdered calcium hydride and then distilled before use. Column chromatography was carried out with silica (85–200 mesh).

Synthesis of 3,4-*Dimethyl*-5-*methylimino*-4,5-*dihydro*-1,2,4-*thiadiazole* **9**.—Methyl fluorosulfonate (1.94 cm^3, 24 mmol) was added to a solution of 5-chloro-3-methyl-1,2,4-thiadiazole **11**[5] (2.692 g, 20 mmol) in dichloromethane (20 cm^3) and the resulting solution was kept for 24 h. The salt **16** (4.53 g, 91%) which had crystallised was filtered off, washed with ether, dried, and added to 33% (w/w) ethanolic methylamine (12 cm^3) cooled to −50 °C. The temperature of the mixture was allowed to rise to room temperature, 1 mol dm^{-3} aq. sodium hydroxide (40 cm^3) was added, and the resulting mixture was extracted with dichloromethane (4 × 100 cm^3). The residue from the dried and evaporated extracts was dissolved in acetonitrile (5 cm^3) and 70% (w/w) perchloric acid (4 cm^3) was added followed by ether (200 cm^3). 3,4-*Dimethyl*-5-*methylamino*-1,2,4-*thiadiazolium perchlorate* **18** (3.38 g, 69% from **11**) was obtained as plates, m.p. 204–206 °C (Found: C, 24.6; H, 4.1; N, 17.35. $C_5H_{10}ClN_3O_4S$ requires C, 24.65; H, 4.14; N, 17.25%); δ_H[$(CD_3)_2SO$] 2.48 (3 H, s, 3-Me), 3.06 (3 H, s, 4-Me), 3.57 (3 H, s, 5-NMe) and 10.48 (1 H, s, NH); δ_C[$(CD_3)_2SO$] 20.6 (3-Me), 37.5 (4-Me), 37.9 (5-NMe), 164.1 (C-3) and 181.3 (C-5).

1 Mol dm^{-3} aq. sodium hydroxide (20 cm^3) was added to an aqueous solution of the foregoing salt (3.38 g in 20 cm^3) and the mixture was extracted with dichloromethane (4 × 100 cm^3). The residue from the dried and evaporated extracts was distilled at 125 °C/3 mmHg (heating block), giving 3,4-dimethyl-5-methylimino-4,5-dihydro-1,2,4-thiadiazole **9** (1.138 g, 39.8% from **11**) as plates, m.p. 39–41 °C, which gradually change in air to a grey solid; δ_H($CDCl_3$) 2.21 (3 H, s, 3-Me), 2.91 (3 H, s, 5-NMe) and 3.22 (3 H, s, 4-Me); δ_C($CDCl_3$) 17.4 (3-Me), 32.4 (4-Me), 41.0 (5-NMe), 158.7 (C-3) and 164.6 (C-5); *m*/*z* 143.0513 (M^+).

Dissolution of the methylimine **9** (5 mmol) in ethanol saturated with hydrogen chloride (5 cm^3), followed by addition of ether, gave 3,4-dimethyl-5-methylamino-1,2,4-thiadiazolium chloride **17** (840 mg, 94%) as needles, m.p. 181–183 °C; X-ray single-crystal structure determination given in ref. 6.

Reactions of 5-*Amino*-3-*methyl*-1,2,4-*thiadiazole with* 1,3-*Dibromopropane: Synthesis of* 3-*Methyl*-6,7-*dihydro*-5H-1,2,4-*thiadiazolo*[4,5-a]*pyrimidine* **24**.—(*a*) A solution of the thiadiazole **12**[3] (5.755 g, 50 mmol) and 1,3-dibromopropane (25.4 cm^3, 250 mmol) in DMF (20 cm^3) was heated at 130 °C for 30 min. The solution was allowed to cool overnight at room temperature. The solid which had crystallised was filtered off, washed successively with ether–methanol (3:1; 4 × 10 cm^3) and ether (30 cm^3), and dried *in vacuo* over P_4O_{10}. Recrystallisation of a sample of the solid from methanol (charcoal) gave 3-*methyl*-6,7-*dihydro*-5H-1,2,4-*thiadiazolo*[4,5-a]*pyrimidin*-8-*ium bromide* **20** as needles, m.p. 290–292 °C (decomp.) (Found: C, 30.4; H, 4.3; N, 17.8. $C_6H_{10}BrN_3S$ requires C, 30.52; H, 4.27; N, 17.79%); δ_H[$(CD_3)_2SO$] 2.09 (2 H, quint, 6-H_2), 2.44 (3 H, s, 3-Me), 3.56 (2 H, t, 7-H_2), 4.13 (2 H, t, 5-H_2) and 10.75 (1 H, br, NH); δ_H(CF_3CO_2D) 2.41 (2 H, quint, 6-H_2), 2.64 (3 H, s, 3-Me), 3.85 (2 H, t, 7-H_2) and 4.35 (2 H, t, 5-H_2).

The solid (2.872 g) was dissolved in water, 1 mol dm^{-3} aq. sodium hydroxide (20 cm^3) was added, and the mixture was extracted with dichloromethane (4 × 150 cm^3). Solvent was removed from the dried extracts and the solid residue was extracted with hot ether–cyclohexane (9:1; 4 × 50 cm^3). Solvent was distilled from the combined extracts until the residual volume was ~50 cm^3. 3-*Methyl*-6,7-*dihydro*-5H-1,2,4-*thiadiazolo*[4,5-a]*pyrimidine* **24** (1.615 g) crystallised from the cooled solution as needles, m.p. 72–73 °C, sublimes at 125–130 °C/0.7 mmHg (Found: C, 46.3; H, 5.5; N, 27.0. $C_6H_9N_3S$ requires C, 46.4; H, 5.84; N, 27.07%); λ_{max}(cyclohexane)/nm 269.5 (ε/dm^3 mol^{-1} cm^{-1} 3715), 253.5 (5250) and 233.5 (4470); δ_H($CDCl_3$) 1.92 (2 H, quint, 6-H_2), 2.20 (3 H, s, 3-Me), 3.49 (2 H, t, 7-H_2) and 3.80 (2 H, t, 5-H_2); δ_H(CD_3CN) 1.81 (2 H, quint, 6-H_2), 2.11 (3 H, s, 3-Me), 3.36 (2 H, t, 7-H_2) and 3.77 (2 H, t, 5-H_2); δ_C($CDCl_3$) 16.0 (CH_3), 19.1 (C-6), 42.9 and 44.7 (C-5 and -7), 154.8 (C-3) and 162.4 (C-8a); *m*/*z* 155.0508 (M^+).

The DMF and the excess of 1,3-dibromopropane were removed at reduced pressure from the reaction mother liquors. The residue was dissolved in methanol (100 cm^3), charcoal was added, and the mixture was boiled for 30 min, then filtered while hot, and solvent was removed from the filtrate. A solution of the residue in dichloromethane–acetone (3:1; 50 cm^3) was chromatographed [silica (38 × 4.0 cm)]. Elution gave the following fractions: (i) dichloromethane–acetone (3:1; 1000 cm^3); (ii) dichloromethane–acetone (3:1; 1000 cm^3) and (iii) methanol (1500 cm^3). Fraction (i) afforded 5-*formamido*-3-*methyl*-1,2,4-*thiadiazole* **13** (2.625 g, 36.7%) as crystals, m.p. 195–197 °C (sublimation > 189 °C) (Found: C, 33.3; H, 3.3; N, 29.3. $C_4H_5N_3OS$ requires C, 33.56; H, 3.52; N, 29.35%); δ_H[$(CD_3)_2SO$] 2.50 (3 H, s, 3-Me), 8.79 (1 H, s, CHO) and 12.98 (1 H, br, NH); δ_C[$(CD_3)_2SO$] 22.6 (CH_3), 165 (CHO) and 171.6 and 177.3 (C-3 and -5); *m*/*z* 143.0145 (M^+). Fraction (ii) gave back starting material **12** (475 mg, 8.3%). The solid residue from fraction (iii) was a 10:1 mixture (^1H NMR) of dimethylammonium bromide and the salt **20**. It was dissolved in water (40 cm^3), 1 mol dm^{-3} aq. sodium hydroxide (1.5 cm^3) was added, and the mixture was extracted with dichloromethane (4 × 30 cm^3). The combined dichloromethane extracts yielded another crop (189 mg) of the base **24** (total yield 1.804 g, 23.2%). The aqueous solution was evaporated to dryness and the residue was extracted with acetonitrile to leave undissolved sodium bromide. Removal of acetonitrile from the extracts and recrystallisation of the residue from acetonitrile–acetone (2:1) gave dimethylammonium bromide (1.32 g, 21%) as plates, m.p. and mixed m.p. with an authentic sample 133–135 °C; δ_H[$(CD_3)_2SO$] 2.20 (6 H, s, 2 × Me) and 7.76 (2 H, s, NH_2); δ_C[$(CD_3)_2SO$] 38.16 (Me).

(*b*) A solution of 5-amino-3-methyl-1,2,4-thiadiazole **12** (5.755 g, 50 mmol) and 1,3-dibromopropane (25.4 cm^3, 250 mmol) in *N*-methylpyrrolidinone (40 cm^3) was heated at 110 °C for 3 h, then at 123 °C for 2 h, and finally allowed to cool to room temperature overnight. The bromide **20** which had crystallised (4.494 g, 38.1%) was filtered off, washed with acetone (3 × 10 cm^3) and dried *in vacuo* over P_4O_{10}. The salt was dissolved in water (40 cm^3), 1 mol dm^{-3} aq. sodium hydroxide (40 cm^3) was added, and the mixture was extracted with dichloromethane (4 × 150 cm^3). Solvent was removed from the dried extracts and the residue was extracted with boiling ether–cyclohexane (9:1; 4 × 80 cm^3). Solvent was distilled from the combined extracts until the residual volume was ~50 cm^3. 3-Methyl-6,7-dihydro-5*H*-1,2,4-thiadiazolo[4,5-*a*]pyrimidine **24** (2.763 g, 35.6%) crystallised from the cooled solution as crystals, identical [m.p. and mixed m.p. 70–72 °C; ^1H NMR spectrum ($CDCl_3$)] with the product **24** of the preceding experiment.

(*c*) A solution of 5-amino-3-methyl-1,2,4-thiadiazole **12** (5.755 g, 50 mmol) and 1,3-dibromopropane (25.4 cm^3, 250 mmol) in DMPU (40 cm^3) was heated at 110 °C for 3 h, then at 123 °C for 2 h, and subsequently worked up according to the procedure of the preceding experiment (*b*). The base **24** (2.675 g, 34.5%) was obtained as crystals, identical [m.p. and mixed m.p. 70–72 °C; ^1H NMR spectrum ($CDCl_3$)] with the product of the two preceding experiments.

Synthesis of 3-*Phenyl*-6,7-*dihydro*-5H-1,2,4-*thiadiazolo*[4,5-a]*pyrimidine* **25**.—A solution of 5-amino-3-phenyl-1,2,4-thiadiazole **14**[3] (1.773 g, 10 mmol) and 1,3-dibromopropane (10.2 cm^3,

100 mmol) in DMF (6 cm^3) was boiled for 1.5 h. The cream powder (1.626 g) which separated from the cooled solution was filtered off, washed with ether, and dried *in vacuo* over P_4O_{10}. Recrystallisation of a sample from ethanol gave 3-*phenyl*-6,7-*dihydro*-5H-1,2,4-*thiadiazolo*[4,5-a]*pyrimidin*-8-*ium bromide* **21** as needles, m.p. 295–297 °C (decomp.) (Found: C, 44.1; H, 4.0; N, 13.9. $C_{11}H_{12}BrN_3S$ requires C, 44.30; H, 4.06; N, 14.09%); $\delta_H[(CD_3)_2SO]$ 2.07 (2 H, quint, 6-H_2), 3.63 (2 H, t, 7-H_2), 4.12 (2 H, t, 5-H_2), 7.68 (5 H, br m, Ph) and 8.43 (1 H, v br, NH).

1 Mol dm^{-3} aq. sodium hydroxide (15 cm^3) was added to a suspension of the bromide (1.626 g) in water (50 cm^3) and the mixture was extracted with dichloromethane (5 × 100 cm^3). The dried and evaporated extracts gave a solid, which was extracted with boiling ether–cyclohexane (9:1; 2 × 50 cm^3). Solvent was distilled from the combined extracts until crystallisation began. The cooled solution yielded 3-*phenyl*-6,7-*dihydro*-5H-1,2,4-*thiadiazolo*[4,5-a]*pyrimidine* **25** (378 mg, 17.4% yield from **14**) as granules, m.p. 114–115 °C (Found: C, 60.6; H, 4.9; N, 19.5. $C_{11}H_{11}N_3S$ requires C, 60.83; H, 5.10; N, 19.34%); λ_{max}(cyclohexane)/nm 312.5 (ε dm^3 mol^{-1} cm^{-1} 2340), 252.9 (6610) and 227 (12 880); $\delta_H(CDCl_3)$ 1.82 (2 H, quint, 6-H_2), 3.54 (2 H, t, 7-H_2), 3.83 (2 H, t, 5-H_2) and 7.51 (5 H, s, Ph); $\delta_C(CDCl_3)$ 19.5 (C-6), 45.3 and 45.6 (C-5 and -7), 128.3, 128.8, 129.5 and 130.7 (4 C of Ph), 157.4 (C-3) and 162.8 (C-8a); *m/z* 217.0673 (M^+).

Synthesis of 6,7-*Dihydro*-5H-1,2,4-*thiadiazolo*[4,5-a]*pyrimidine* **26**.—A solution 5-amino-1,2,4-thiadiazole **15**[3] (1.01 g, 10 mmol) and 1,3-dibromopropane (10 cm^3, 98.4 mmol) in DMF (2.5 cm^3) was boiled for 15 min, then allowed to cool spontaneously to room temperature. The supernatant liquid was decanted off and the sticky brown residue was recrystallised from propan-1-ol to give an impure brown powder. Recrystallisation of a sample from ethanol (charcoal) and then from ethanol again gave 6,7-*dihydro*-5H-1,2,4-*thiadiazolo*[4,5-a]*pyrimidin*-8-*ium bromide* **22** as straw-coloured needles, m.p. 242–245 °C (decomp. > 230 °C) (Found: C, 26.9; H, 3.6; N, 18.7. $C_5H_8BrN_3S$ requires C, 27.04; H, 3.63; N, 18.92%); $\delta_H[(CD_3)_2SO]$ 2.10 (2 H, quint, 6-H_2), 3.62 (2 H, t, 7-H_2), 4.27 (2 H, t, 5-H_2), 8.62 (1 H, s, 3-H) and 10.68 (1 H, v br, N–H).

1 Mol dm^{-3} aq. sodium hydroxide (10 cm^3) was added to a solution of the brown powder (1.61 g) in water (25 cm^3) and the mixture was extracted with dichloromethane (4 × 100 cm^3). Solvent was removed from the combined dried extracts with the minimum of heating, and the residual red solid was extracted with boiling ether–cyclohexane (9:1; 2 × 50 cm^3). The combined extracts were concentrated to ~30 cm^3 by gentle warming (water-bath). 6,7-*Dihydro*-5H-1,2,4-*thiadiazolo*[4,5-a]*pyrimidine* **26** (310 mg, 22% overall yield from **15**) crystallised as flakes, m.p. 90–92 °C (decomp.) (Found: C, 42.2; H, 4.95; N, 29.6. $C_5H_7N_3S$ requires C, 42.53; H, 5.00; N, 29.76%); $\delta_H(CDCl_3)$ 1.90 (2 H, quint, 6-H_2), 3.54 (2 H, t, 7-H_2), 3.89 (2 H, t, 5-H_2) and 7.32 (1 H, s, 3-H); $\delta_C(CDCl_3)$ 19.4 (C-6), 43.0 and 46.2 (C-5 and -7), 147.1 (C-3) and 161.3 (C-8a); *m/z* 141.0361 (M^+).

Synthesis of 3-*Methyl*-5,10-*dihydrobenzo*[e]-1,2,4-*thiadiazolo*[4,5-a][1,3]*diazepine* **34**.—A solution of 5-amino-3-methyl-1,2,4-thiadiazole **12** (5.755 g, 50 mmol) and 1,2-bis(bromomethyl)benzene (33 g, 125 mmol) in DMF (100 cm^3) was boiled for 30 min. Solvent was removed at reduced pressure from the cooled solution and the residue was dissolved in methanol–acetone (1:1; 300 cm^3). Charcoal was added and the mixture was boiled for 10 min, then filtered while hot. Solvent was removed from the filtrate, the residue was dissolved in acetone (200 cm^3), and the solution was set aside at room temperature for 6 h. 3-*Methyl*-5,10-*dihydrobenzo*[e]-1,2,4-*thiadiazolo*[4,5-a][1,3]*diazepin*-11-*ium bromide* **33** (7.6 g, 51%) crystallised as needles, m.p. 272–273 °C (Found: C, 44.1; H, 4.0; N, 14.1. $C_{11}H_{12}BrN_3S$ requires C, 44.31; H, 4.06; N, 14.09%); $\delta_H[(CD_3)_2SO]$ 2.63 (3 H, s, Me), 5.02 (2 H, s, 10-H_2), 5.63 (2 H, s, 5-H_2), 7.38–7.76 (4 H, m, benzo H) and 11.5 (1 H, br s, $w_{\frac{1}{2}}$ 12 Hz, NH).

The bromide **33** (7.6 g) was added to water (200 cm^3) and 1 mol dm^{-3} aq. sodium hydroxide (50 cm^3), and the mixture was extracted with dichloromethane (400 cm^3 + 2 × 100 cm^3). The residue from the dried and evaporated extracts was recrystallised from cyclohexane–dichloromethane (9:1). 3-*Methyl*-5,10-*dihydrobenzo*[e]-1,2,4-*thiadiazolo*[4,5-a][1,3]*diazepine* **34** (4.90 g, 88.5%; overall yield from **12**, 45%) was obtained as crystals, m.p. 206–209 °C (Found: C, 60.9; H, 5.1; N, 19.4. $C_{11}H_{11}N_3S$ requires C, 60.83; H, 5.10; N, 19.34%); $\delta_H(CDCl_3)$ 2.29 (3 H, s, Me), 4.78 (2 H, s, 10-H_2), 5.03 (2 H, s, 5-H_2) and 7.24–7.38 (4 H, m, benzo H); $\delta_C(CDCl_3)$ 17.2 (C-3), 49.2 and 50.7 (C-5 and -10), 127.7, 128.1, 128.4 and 132.9 (C-6–9), 132.7 and 139.9 (C-5a and -9a), 154.5 (C-3) and 163.3 (C-11a); *m/z* 217.0675 (M^+).

The acetone mother liquors from which the bromide **33** had crystallised were evaporated and the residue was extracted with boiling hexane (4 × 200 cm^3). 1,2-Bis(bromomethyl)benzene (4.65 g, 14.3%) was recovered from the hexane extracts. The undissolved residue was triturated with acetone, filtered off, and recrystallised from acetonitrile, to give dimethylammonium bromide (8.33 g, 66.1 mmol) as needles, m.p. and mixed m.p. with an authentic sample 133–135 °C.

Reactions of 3-*Methyl*-6,7-*dihydro*-5H-1,2,4-*thiadiazolo*[4,5-a]*pyrimidine* **24** *with Nitriles.*—*With benzonitrile.* A solution of the base **24** (777 mg, 5 mmol) in benzonitrile (2.5 cm^3, 24.5 mmol) was boiled for 30 min, cooled, and chromatographed [silica (41 × 2.5 cm)]. Elution with ether gave eluates (200 cm^3) containing benzonitrile. Further elution with ether–methanol (9:1) brought through homogeneous eluates (1500 cm^3) which yielded 3-phenyl-6,7-dihydro-5*H*-1,2,4-thiadiazolo[4,5-*a*]pyrimidine **25** (594 mg, 55%), crystals from cyclohexane–benzene (~1:1), identical [m.p. and mixed m.p. 113–114.5 °C; ^1H NMR spectrum ($CDCl_3$)] with the product from the reaction of 5-amino-3-phenyl-1,2,4-thiadiazole **14** with 1,3-dibromopropane.

With p-*nitrobenzonitrile.* A solution of the base **24** (776 mg, 5 mmol) and *p*-nitrobenzonitrile (741 mg, 5 mmol) in toluene (15 cm^3) was boiled for 4 h, cooled, and chromatographed [silica (41 × 2.7 cm)]. Elution with methanol–ether (3:2) gave, initially, eluates (250 cm^3) containing *p*-nitrobenzonitrile, and subsequently homogeneous yellow eluates (900 cm^3) which yielded 3-p-*nitrophenyl*-6,7-*dihydro*-5H-1,2,4-*thiadiazolo*[4,5-a]*pyrimidine* **27** (835 mg, 64%), as yellow spars from cyclohexane–dichloromethane (~4:1), m.p. 172–174 °C (Found: C, 50.3; H, 3.7; N, 21.4. $C_{10}H_{11}N_4O_2S$ requires C, 50.37; H, 3.84; N, 21.36%); $\delta_H(CDCl_3)$ 1.90 (2 H, quint, 6-H_2), 3.59 (2 H, t, 7-H_2), 3.91 (2 H, t, 5-H_2), 7.76 and 7.87 (2 H, 2 × *o*-protons of 3-Ar) and 8.33 and 8.44 (2 H, 2 × *m*-protons of 3-Ar); $\delta_H[(CD_3)_2SO]$ 1.75 (2 H, quint, 6-H_2), 3.41 (2 H, t, 7-H_2), 3.89 (2 H, t, 5-H_2), 7.94 and 8.05 (2 H, 2 × *o*-protons of 3-Ar) and 8.35 and 8.46 (2 H, 2 × *m*-protons of 3-Ar); $\delta_C(CDCl_3)$ 19.3 (C-6), 45.2 and 45.8 (C-5 and -7), 124.0 and 129.5 (C-2′ and -3′), 135.1 (C-1′), 149.1 (C-4′), 155.1 (C-3) and 162.0 (C-8a); *m/z* 262.0532 (M^+).

With 4-*cyanopyridine.* A solution of the base **24** (777 mg, 5 mmol) and 4-cyanopyridine (5.21 g, 50 mmol) in toluene (100 cm^3) was boiled for 30 h. Chromatography [silica (28 × 2.2 cm)] of the cooled solution gave the following eluates: (i) ether–methanol (17:8; 200 cm^3) (ii) ether–methanol (17:8; 3150 cm^3) (iii) methanol (1500 cm^3). The reddish oily residue from the combined homogeneous fractions (ii) and (iii) slowly solidified. The solid was extracted with ether–cyclohexane (9:1; 5 × 50 cm^3) and the combined extracts were concentrated by

distillation (water-bath) to ~100 cm^3. 3-(4'-*Pyridyl*)-6,7-*dihydro*-5H-1,2,4-*thiadiazolo*[4,5-a]*pyrimidine* **28** (900 mg, 82.5%) was obtained as granules, m.p. 143–145 °C (Found: C, 55.2; H, 4.7; N, 26.0. $C_{10}H_{10}N_4S$ requires C, 55.02; H, 4.62; N, 25.67%); $\delta_H(CDCl_3)$ 1.86 (2 H, quint, 6-H_2), 3.55 (2 H, t, 7-H_2), 3.88 (2 H, t, 5-H_2), 7.44 and 7.51 (2 H, 3'- + 5'-H) and 8.74 and 8.82 (2 H, 2'- + 6'-H); $\delta_H[(CD_3)_2SO]$ 1.74 (2 H, quint, 6-H_2), 3.39 (2 H, t, 7-H_2), 3.88 (2 H, t, 5-H_2), 7.61 and 7.69 (2 H, 3'- + 5'-H) and 8.73 and 8.80 (2 H, 2'- + 6'-H); $\delta_C(CDCl_3)$ 19.3 (C-6), 45.2 and 45.6 (C-5 and -7), 122.2, 136.6 and 150.5 (C-2', -3' and -4'), 154.9 (C-3) and 162.0 (C-8a); *m/z* 218.0619 (M^+).

With methoxyacetonitrile. A solution of the base **24** (776 mg, 5 mmol) and methoxyacetonitrile (1.7 cm^3, 22.9 mmol) in toluene (3 cm^3) was boiled for 4 h. The cooled solution was chromatographed [silica (40 × 2.2 cm)] with ether–methanol (4:1). The initial eluates (250 cm^3) were discarded and the succeeding eluates (2500 cm^3) yielded an oil, which was distilled at 150–160 °C/0.7 mmHg (heating block). 3-*Methoxymethyl*-6,7-*dihydro*-5H-1,2,4-*thiadiazolo*[4,5-a]*pyrimidine* **29** (573 mg, 62%) was obtained as an oil (Found: C, 45.2; H, 6.2; N, 22.35. $C_7H_{11}N_3OS$ requires C, 45.38; H, 5.98; N, 22.68%); $\delta_H(CDCl_3)$ 1.88 (2 H, quint, 6-H_2), 3.39 (3 H, s, Me), 3.52 (2 H, t, 7-H_2), 3.95 (2 H, t, 5-H_2) and 4.25 (2 H, s, CH_2O); $\delta_H[(CD_3)_2SO]$ 1.76 (2 H, quint, 6-H_2), 3.24 (2 H, t, 7-H_2), 3.27 (3 H, s, Me), 3.87 (2 H, t, 5-H_2) and 4.24 (2 H, s, CH_2O); $\delta_C(CDCl_3)$ 19.2 (C-6), 45.2 and 45.3 (C-5 and -7), 58.5 (Me), 68.2 (CH_2O), 154.6 (C-3) and 162.4 (C-8a); *m/z* 185.0612 (M^+).

With o-*hydroxybenzonitrile.* A solution of the base **24** (776 mg, 5 mmol) and *o*-hydroxybenzonitrile (1.193 g, 10 mmol) in toluene (36 cm^3) was boiled (oil-bath) for 6.5 h while a white solid slowly crystallised. The hot mixture was filtered, the solid was washed with toluene (25 cm^3), and solvent was removed from the combined filtrates. Addition of methanol to the resulting oil gave more solid. Recrystallisation of the combined solids (680 mg) from ethanol gave 3-o-*hydroxyphenyl*-6,7-*dihydro*-5H-1,2,4-*thiadiazolo*[4,5-a]*pyrimidine* **30** (partly in the form of its zwitterion **37**) (623 mg, 54%) as spars, m.p. 228–229 °C (decomp.) (Found: C, 56.8; H, 4.8; N, 18.3. $C_{11}H_{11}N_3OS$ requires C, 56.63; H, 4.75; N, 18.01%); ν_{max}(KBr)/cm^{-1} 2550v br (–$\overset{+}{N}$H=) and 1590s br (C=N); $\delta_H[(CD_3)_2SO$; 100 °C; $Me_3SiSiMe_3$] 1.66 (2 H, quint, 6-H_2), 3.31 (2 H, t, 7-H_2), 3.57 (2 H, t, 5-H_2), 5.70 (1 H, v br, OH) and 6.75–7.40 (4 H, m, ArH); *m/z* 233.0633 (M^+).

With trideuterioacetonitrile. (a) A solution of the methyl base **24** (776 mg, 5 mmol) in CD_3CN (5 cm^3, 96 mmol) was boiled for 7 h. Solvent was removed, the residual solid was dissolved in a fresh portion (5 cm^3) of CD_3CN, and the resulting solution was boiled for 7 h. Solvent was removed and the residue was recrystallised from ether–cyclohexane (2:1). 3-*Trideuteriomethyl*-6,7-*dihydro*-5H-1,2,4-*thiadiazolo*[4,5-a]*pyrimidine* **31** (668 mg, 84%) was obtained as needles, m.p. 72–74 °C (Found: C, 45.15; N, 27.0. $C_6H_6D_3N_3S$ requires C, 45.54; N, 26.55%); $\delta_H(CDCl_3)$ 1.91 (2 H, quint, 6-H_2), 3.49 (2 H, t, 7-H_2) and 3.80 (2 H, t, 5-H_2); $\delta_H(CD_3CN)$ 1.81 (2 H, quint, 6-H_2), 3.36 (2 H, t, 7-H_2) and 3.77 (2 H, t, 5-H_2); $\delta_C(CDCl_3)$ 19.1 (C-6), 43.1 and 45.0 (C-5 and -7), 154.9 (C-3) and 162.5 (C-8a) (the CD_3 signal was not observed); *m/z* 158.0695 (M^+).

(b) The base **24** (38.8 mg, 0.25 mmol) was dissolved in CD_3CN (0.5 cm^3, 9.6 mmol) and the solution was kept at ambient temperature. The progress of the reaction was followed by ^1H NMR spectroscopy, using the methyl signal of acetonitrile (δ_H 1.90) and the methyl base (δ_H 2.10) for monitoring. Conversion of the methyl base **24** into its trideuteriomethyl analogue **31** was 50% complete after 6.5 days and 80% complete after 17 days.

With fumaronitrile. (a) A solution of the base **24** (776 mg, 5 mmol) and fumaronitrile (781 mg, 10 mmol) in toluene (35 cm^3) was kept in the dark at room temperature for 14 days while olive-green rosettes of crystals formed. The yellow mother liquor was decanted, toluene (15 cm^3) was added, and the crystalline mass was crushed and filtered to give a homogeneous (TLC) yellow powder (606 mg, 79%). Recrystallisation from ethanol or methanol was accompanied by some decomposition and extensive loss of material to give 1,2-*bis*-(6,7-*dihydro*-5H-1,2,4-*thiadiazolo*[4,5-a]*pyrimidin*-3-*yl*)*ethene* **38** as deep yellow needles, m.p. 194–198 °C (gradual decomp. > 165 °C) (Found: C, 46.9; H, 4.65; N, 27.2. $C_{12}H_{14}N_6S_2$ requires C, 47.04; H, 4.61; N, 27.43%); $\delta_H(CDCl_3)$ 1.93 (2 H, quint, 6-H_2), 3.53 (2 H, t, 7-H_2), 3.93 (2 H, t, 5-H_2) and 7.19 (1 H, s, =CH).

(b) A solution of fumaronitrile (1.95 g, 25 mmol) in toluene (60 cm^3) was added to a solution of the base **24** (776 mg, 5 mmol) in toluene (25 cm^3). The resulting solution became yellow immediately and was kept at room temperature for 60 h, then was chromatographed [silica (37 × 2.2 cm)]. The following fractions were obtained: (i) toluene (1000 cm^3), discarded (ii) toluene–ether (4:1; 1000 cm^3), discarded (iii) toluene–ether (1:1; 500 cm^3), yellow (iv) ether (300 cm^3), yellow (v) ether–methanol (19:1; 2800 cm^3), yellow (vi) methanol (2000 cm^3), yellow. The homogeneous fractions (iii)–(v) were combined and gave 3-[(*E*)-2-*cyanovinyl*]-6,7-*dihydro*-5*H*-1,2,4-*thiadiazolo*[4,5-a]*pyrimidine* **32** (621 mg, 65%) as a yellow powder which decomposes gradually on being heated and could not be obained analytically pure (TLC) owing to disproportionation into the ethene **38** and fumaronitrile; $\delta_H(CDCl_3)$ 1.93 (2 H, quint, 6-H_2), 3.52 (2 H, t, 7-H_2), 3.88 (2 H, t, 5-H_2), 6.47 (1 H, d, *J* 16.1, CHCN) and 6.95 (1 H, d, *J* 16.1, C*H*=CHCN); $\delta_H[(CD_3)_2SO]$ 1.77 (2 H, quint, 6-H_2), 3.35 (2 H, t, 7-H_2), 3.94 (2 H, t, 5-H_2), 6.64 (1 H, d, *J* 16.1, CHCN) and 7.48 (1 H, d, *J* 16.1, C*H*=CHCN); *m/z* 192.0453. Fraction (vi) yielded the ethene **38** (163 mg, 11%).

(c) The base **24** (502 mg, 3.23 mmol) was added to a solution of the nitrile **32** (621 mg, 3.23 mmol) in toluene (25 cm^3) and the resulting solution was kept at room temperature for 10 days. The precipitated yellow solid (343 mg) was filtered off, and the filtrate was kept at room temperature for a further 10 days to give more yellow solid (215 mg). The combined yellow solids (558 mg, 56%) were identical (m.p., mixed m.p., ^1H NMR spectrum) with the ethene **38** prepared in the preceding experiment (*a*).

With benzoylacetonitrile. Filtered solutions of the base **24** (776 mg, 5 mmol) in toluene (10 cm^3) and benzoylacetonitrile (727 mg, 5 mmol) in toluene (7 cm^3) were mixed. Crystals formed rapidly and the mixture was kept at room temperature for 48 h. The solid was filtered off, washed with toluene followed by ether, and dried *in vacuo* over P_4O_{10}. The mother liquor contained only starting materials (TLC). 3-*Methyl*-6,7-*dihydro*-5H-1,2,4-*thiadiazolo*[4,5-a]*pyrimidin*-8-*ium benzoylacetonitrile enolate* **23** (1.255 g, 84%) was thereby obtained as rhombs, m.p. 90.5–92.5 °C (Found: C, 60.0; H, 5.4; N, 18.9. $C_{15}H_{17}N_4OS$ requires C, 59.98; H, 5.37; N, 18.65%); ν_{max}(KBr)/cm^{-1} 2550v br (=$\overset{+}{N}$H–), 2150s (conj. C≡N) and 1604br s (C=N, C=C). The ^1H NMR specrum [$(CD_3)_2SO$] consisted of the superimposed spectra of the base and benzoylacetonitrile.

Reaction of 3-*Trideuteriomethyl*-6,7-*dihydro*-5H-1,2,4-*thiadiazolo*[4,5-a]*pyrimidine* **31** *with Acetonitrile.*—The methyl base **24** (776 mg, 5 mmol) was converted into the trideuteriomethyl base **31** as previously described, and the entire product **31**, whose ^1H NMR spectrum ($CDCl_3$ and CD_3CN) showed no ring-methyl signal, was dissolved in acetonitrile (5 cm^3, 95.7 mmol). The solution was boiled for 7 h, solvent was removed, the solid residue was redissolved in a fresh portion of acetonitrile (5 cm^3), and the resulting solution was boiled for 7 h. Solvent was removed and the residue was

recrystallised from ether–cyclohexane, to give 3-methyl-6,7-dihydro-5*H*-1,2,4-thiadiazolo[4,5-*a*]pyrimidine **24** (671 mg, 86.5%) as spars, identical [m.p. and mixed m.p.; ^{1}H NMR spectrum ($CDCl_3$)] with an authentic sample.

Reaction of 6,7-*Dihydro*-5H-1,2,4-*thiadiazolo*[4,5-a]*pyrimidine* **26** *with Nitriles.*—*With acetonitrile.* A solution of the base **26** (710 mg, 5.03 mmol) in acetonitrile (25 cm^3, 479 mmol) was boiled for 14 h, cooled, and solvent was removed. Sublimation of the residue at 140 °C/0.1 mmHg and recrystallisation of the sublimate from ether–cyclohexane gave 3-methyl-6,7-dihydro-5*H*-1,2,4-thiadiazolo[4,5-*a*]pyrimidine **24** (359 mg, 46%) as needles, identical [m.p. and mixed m.p.; ^{1}H NMR spectrum ($CDCl_3$)] with an authentic sample.

With benzonitrile. A solution of the base **26** (707 mg, 5 mmol) and benzonitrile (5.1 cm^3, 50 mmol) in toluene (20 cm^3) was boiled for 8 h, cooled, and chromatographed [silica (43 × 2.5 cm)]. The initial eluates [ether–methanol (19:1; 700 cm^3)] were discarded and the succeeding eluates [ether–methanol (19:1; 1000 cm^3); methanol (1000 cm^3)] were combined to give a solid, which was recrystallised from benzene–cyclohexane (1:1). 3-Phenyl-6,7-dihydro-5*H*-1,2,4-thiadiazolo[4,5-*a*]pyrimidine **25** (640 mg, 59%) was obtained as granules, identical [m.p., mixed m.p.; ^{1}H NMR spectrum ($CDCl_3$)] with authentic sample.

Reaction of 3-*Methyl*-5,10-*dihydrobenzo*[e]-1,2,4-*thiadiazolo*[4,5-a][1,3]*diazepine* **34** *with Nitriles.*—*With trideuterioacetonitrile.* (a) A solution of the diazepine **34** (217 mg, 1 mmol) in CD_3CN (2 cm^3, 19.2 mmol) was refluxed for 6 h. More CD_3CN (3 cm^3) was added and the mixture was refluxed for another 20 h. Removal of solvent gave prisms (200 mg), m.p. 209–210 °C, whose ^{1}H NMR spectrum ($CDCl_3$; measurement of intensities of 3-Me, 5-H_2 and 10-H_2 signals) showed it to be a 1:3 mixture of the deuteriated base **35** and the starting base **34**.

(b) A solution of the diazepine **34** (217 mg, 1 mmol) in CD_3CN (5 cm^3, 96 mmol) and $(CD_3)_2SO$ (2.5 cm^3) was refluxed for 24 h (solution temperature 92 °C; vapour temperature 80 °C). Removal of solvent gave crystals, m.p. 209–210 °C, which was a mixture of the deuteriated base **35** (77%) and the base **34** (23%) [^{1}H NMR spectrum ($CDCl_3$): **35**:**34**, 7:2; mass spectrum: M^+ (**35**): M^+ (**34**), 6.7:2].

With fumaronitrile. A solution of the diazepine **34** (435 mg, 2 mmol) and fumaronitrile (781 mg, 10 mmol) in toluene (15 cm^3) was refluxed for 3 h. Solvent was removed and the residue was chromatographed [silica (20 × 2.5 cm)]. The initial eluates [dichloromethane (50 cm^3)] were discarded and the succeeding eluates [dichloromethane–acetone (4:1)] afforded 3-[(E)-2-*cyanovinyl*]-5,10-*dihydrobenzo*[e]-1,2,4-*thiadiazolo*[4,5-a]-[1,3]*diazepine* **36** (388 mg, 76%), bright yellow crystals from dichloromethane–ether, m.p. 189–191 °C (decomp.) (Found: C, 61.3; H, 3.8; N, 22.1. $C_{13}H_{10}N_4S$ requires C, 61.40; H, 3.96; N, 22.03%); δ_H($CDCl_3$) 4.79 (2 H, s, 10-H_2), 5.05 (2 H, s, 5-H_2), 6.45 (1 H, d, *J* 15.9, CHCN), 7.10 (1 H, d, *J* 15.9, C*H*=CHCN) and 7.26–7.41 (4 H, m, ArH); δ_C($CDCl_3$) 49.3 and 51.0 (C-5 and -10), 107.3 (*C*HCN), 116.3 (CN), 128.0, 128.4, 128.6, 129.9 and 133.9 (C-6–9 and *C*H=CHCN), 132.1 and 139.8 (C-5a and -9a), 150.5 (C-3) and 161.7 (C-11a).

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