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Unsaturated nitrogen compounds containing fluorine. Part 16 ☆. The synthesis of 3,5-bis(trifluoromethyl)-1*H*-1,2,4-triazole and some 4-substituted derivatives from 2,5-dichloro-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene ☆☆

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Abstract

The dichloroazine **5** has been converted into the monoaminoazines $CF_3C(NHR)=NN=CClCF_3$ (**6**) [**a**, R = Ph (89%); **b**, R = H (81%); **c**, R = Me (89%); **d**, $R=CH_2CO_2Me$ (96%); **e**, $R=CH_2CO_2Et$ (95%)] and the diaminoazines $CF_3C(NHR)=NN=C(NHR)CF_3$ (**4**) [**c**, R = H (96%); **d**, R = Me (94%); **e**, $R=CH_2CO_2Me$ (50%); **f**, $R=CH_2CO_2Et$ (77%)] by reaction with ammonia or the appropriate primary amino compound; with hydroxylamine the *syn*-oxime $CF_3CCl=NNHC(CF_3)=NOH$ (**8**) (86%) was formed. The mixed diaminoazines $CF_3C(NHR)=NN=C(NHR')CF_3$ (**4**) [**g**, R = H, R' = Ph; **h**, R = Me, R' = H; **i**, R = Me, $R'=CH_2CO_2Me$; **j**, $R=CH_2CO_2Me$, R' = Ph (92%–96%)] have been synthesised from the monoaminoazines **6a–d**. A solution of the diaminoazine **4c**, heated in ethanol under reflux, gave 3,5-bis(trifluoromethyl)-1*H*-1,2,4-triazole (**1a**) (28%) and its ammonium salt $NH_4^+[C_2N_3(CF_3)_2]^-$ (**7b**) (54%), while the azines **4g** and **4j** under the same conditions each afforded 4-phenyl-3,5-bis(trifluoromethyl)-4*H*-1,2,4-triazole (**2c**) (ca. 85%).

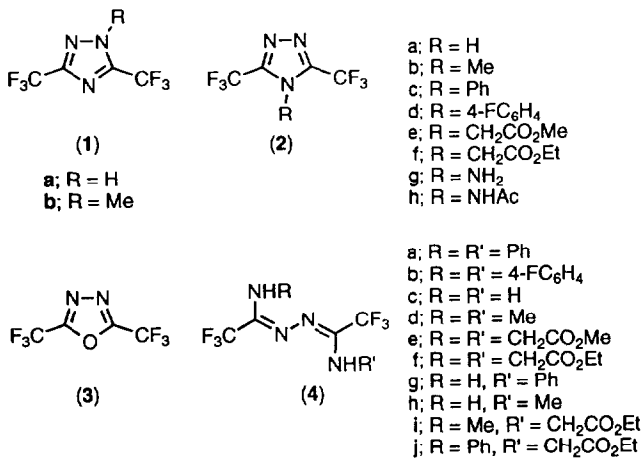
Thermolysis of the diaminoazines **4c–f** and **4h** in vacuo over the range 120–150 °C gave the following results: **4c** → **7b** (98%); **4d** → $MeNH_3^+[C_2N_3(CF_3)_2]^-$ (**7c**) (ca. 26%) + $Me_4N^+[C_2N_3(CF_3)_2]^-$ (**7d**) (ca. 13%) + 4-methyl-3,5-bis(trifluoromethyl)-4*H*-1,2,4-triazole (**2b**) (54%) + 1-methyl-3,5-bis(trifluoromethyl)-1*H*-1,2,4-triazole (**1b**) (1.5%); **4e** → the 4-carbomethoxymethyltriazole (**2e**) (93%); **4f** → the 4-carboethoxymethyltriazole (**2f**) (82%); **4h** → **1a** (11%) + **2b** (54%) + **7c** (31%). Treatment of salt **7b** with aqueous hydrochloric acid afforded the triazole **1a** (75%).

Keywords: Unsaturated nitrogen compounds; Synthesis; Bis(trifluoromethyl)triazole; NMR spectroscopy; Mass spectrometry

1. Introduction

It has been reported [3] that 3,5-bis(trifluoromethyl)-1*H*-1,2,4-triazole (**1a**) and its 4-methyl derivative **2b** can be obtained by heating the oxadiazole **3** with ammonia and methylamine, respectively. This route was later extended to the preparation of a range of 4-alkyl-, 4-alkenyl- and 4-aryl-3,5-bis(trifluoromethyl)-4*H*-1,2,4-triazoles [4].

Work in this Department has shown that the corresponding 4-aryl-1,2,4-triazoles **2c** (R = Ph) and **2d** ($R=4\text{-}FC_6H_4$) can be synthesised in good yield by thermolysis of diaminoazines of type $CF_3C(NHR)=NN=C(NHR)CF_3$ (**4**) (**a**, R = Ph; **b**, $R=4\text{-}FC_6H_4$) obtained from reaction of the dichlo-



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☆ For Part 15, see Ref. [1].

☆☆ Reported, in part, in a preliminary communication; see Ref. [2].

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roazine **5** with an excess of aniline and 4-fluoroaniline, respectively [5,6]; a lower yield of triazole **2c** was obtained from thermolysis of the monoaminoazine $CF_3C(NHPh)=NN=CClCF_3$ (**6a**) [5,6].

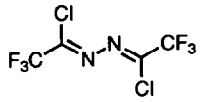
In the present investigation, a number of monoaminoazines **6** and diaminoazines **4** have been prepared from the dichloroazine **5**, and the azines **4** have been used to synthesize the parent 1,2,4-triazole **1a**, its ammonium salt **7b** and a range of 4-substituted-3,5-(bis(trifluoromethyl)-4*H*-1,2,4-triazoles of type **2**.

2. Results and discussion

The results obtained from the reaction of the dichloroazine **5** and monoaminoazines **6** with ammonia and primary amino compounds are summarised in Table 1.

Use of a 2:1 molar ratio of amine/azine **5** (or a 1:1 ratio in the presence of Et_3N) gave the monoaminoazines **6a–e** in high yield whilst employment of a higher molar ratio (>4:1) in the ammonia and methylamine reactions gave only the diaminoazines **4c** and **4d**, respectively. However, use of a higher molar ratio (≥4:1) in the reactions of the glycine esters afforded mixtures of the mono- and di-aminoazines after extended reaction periods, indicating that further reaction of the monoaminoazines **6d** and **6e** with the glycine esters to afford the diaminoazines **4e** and **4f** was slow under the conditions used (Scheme 1).

The diaminoazines **4g–j**, containing two different amino groups, were readily prepared in excellent yield by reaction of the isolated monoaminoazines **6a–d** with the appropriate amino compounds (Scheme 1).



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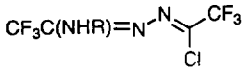


(6)

a; R = Ph
b; R = H
c; R = Me
d; R = CH_2CO_2Me
e; R = CH_2CO_2Et

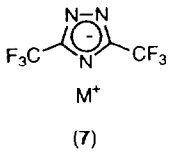
The diaminoazines **4c–j** were each formed as a single isomer as observed previously for compounds **4a** and **4b** [5,6], and an X-ray crystallographic study on compound **4g** has shown it is the (*ZZ*)-isomer with both of the bulky CF_3 groups *anti* and with considerable intermolecular hydrogen bonding present in the crystal state [7]. A previous X-ray study on compound **4g** had been incorrectly analysed [8] and this resulted in the compound being assigned the tautomeric imidoyl structure (**10**) [6]. It is considered that all the diaminoazines **4a–j** have the (*ZZ*)-conformation.

The only monoaminoazine **6** to be formed as a single isomer was compound **6b** and this was shown to have the (*ZZ*)-conformation (**6A**) by an X-ray study [9]. The

Table 1
Reaction of azines **5** and **6** with ammonia and primary amino compounds

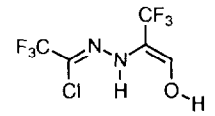
Azine	Amine	Molar ratio azine/amine	Temp. (°C)	Time (h)	Products (%) [c]
5	NH_2Ph	1:2	0	1.5	**6a**(89) [d]
5	NH_3	1:2	0	2.5	**6b**(81)
5	NH_3	1:7:5	0	2	**4c**(96)
			20	24	
5	NH_2Me	1:2	0	3.5	**6c**(89) [e]
5	NH_2Me	1:6	20	24	**4d**(94)
5	$NH_2CH_2CO_2Me$ [a]	1:1	20	3.5	**6d**(96) [d]
5	$NH_2CH_2CO_2Me$ [a]	1:4	20	72	**4e**(50); **6d**(41) [d]
5	$NH_2CH_2CO_2Et$ [a]	1:1	20	3.5	**6e**(95) [d]
5	$NH_2CH_2CO_2Et$ [b]	ca. 1:5	20	72	**4f**(77); **6e**(16) [f]
5	NH_2OH	1:4	20	24	**8**(86)
5	NH_2NH_2	ca. 1:4	0	24	**9**(89)
6a	NH_3	ca. 1:8	20	48	**4g**(92)
6b	NH_2Ph	1:3	20	72	**4g**(94)
6c	NH_3	ca. 1:10	20	48	**4h**(96)
6c	$NH_2CH_2CO_2Et$ [b]	ca. 1:35	20	72	**4i**(95) [g]
6d	NH_2Ph	1:3	20	53	**4j**(94)

[a] Amine liberated from hydrochloride salt by treatment with Et_3N in Et_2O/H_2O (1:1 v/v).
[b] Amine liberated from hydrochloride salt by treatment with NaOH in Et_2O/H_2O (1:1 v/v).
[c] Based on azine reacted, i.e. not recovered.
[d] Mixture of two isomers (ratio 55:45).
[e] Mixture of two isomers (ratio 62:38).
[f] Mixture of two isomers (ratio 52:48).
[g] Unchanged azine **6c** (26% recovered) also isolated.



(7)

a; M = H
b; M = NH_4
c; M = NH_3Me
d; M = NMe_4
e; M = Na



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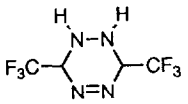

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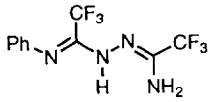

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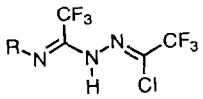


(11)

other monoaminoazines **6a** and **6c–e** were formed as mixtures of two isomers and the ^{19}F NMR chemical shift for the CF_3 group in the $CF_3C(NHR)=N-$ grouping of the major isomer was at higher field in each case than that for the corresponding CF_3 group in the minor isomer. Previous ^{19}NMR studies on other mono- and di-substituted azines derived from dichloroazine **5** have concluded that (i) CF_3 groups *syn* to a nitrogen lone pair have higher ^{19}F NMR chemical shifts than CF_3 groups *anti* to a nitrogen lone pair and (ii) the $CF_3CCl=N-$ grouping when present has the (*Z*)-configuration [6,10]. Analogous assignments to compounds **6a** and **6c–e** infer that the major isomers have the (*ZZ*)-configuration **6A** and the minor isomers have the (*EZ*)-configuration **6B**. The possibility that the products were the monoimidoyl tautomers (**11**) was discounted because of the observed ^1H NMR couplings between the NH proton and the adjacent CH_3 or CH_2 protons in the spectra of compounds **6c–e**.

Isomerisation of the (*E*)-$CF_3C(NHR)=$ grouping in the monoaminoazines **6** to the corresponding (*Z*)-grouping which is preferred in the diaminoazines **4** can occur readily on attack by amine (Scheme 2).

The reaction of hydroxylamine with dichloroazine **5** (4:1 molar ratio) gave only the (*ZZ*)-oxime **8** which was shown by X-ray crystallography to exist as the intermolecularly hydrogen-bonded dimer **12** in the solid state [11]. Attempts to replace the remaining chlorine atom in **8** by further reaction with hydroxylamine were unsuccessful.

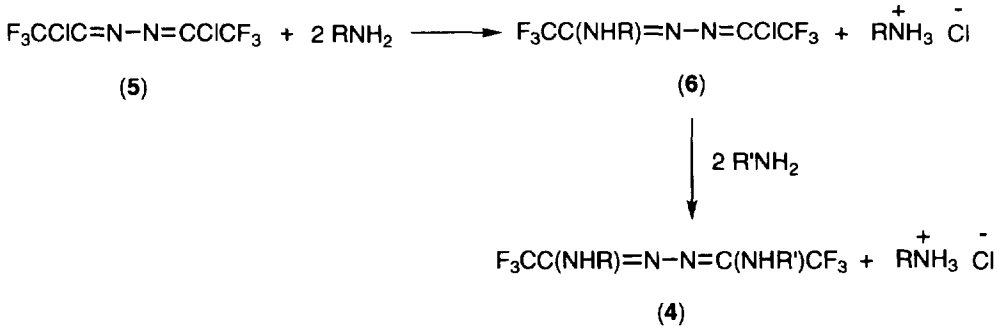
Treatment of dichloroazine **5** with hydrazine afforded the dihydro-s-tetrazine (**9**) in good yield. This compound has been prepared previously by reaction of the oxadiazole **3** with hydrazine [12].

Thermal cyclisation reactions carried out on the amino substituted azines are summarised in Table 2.

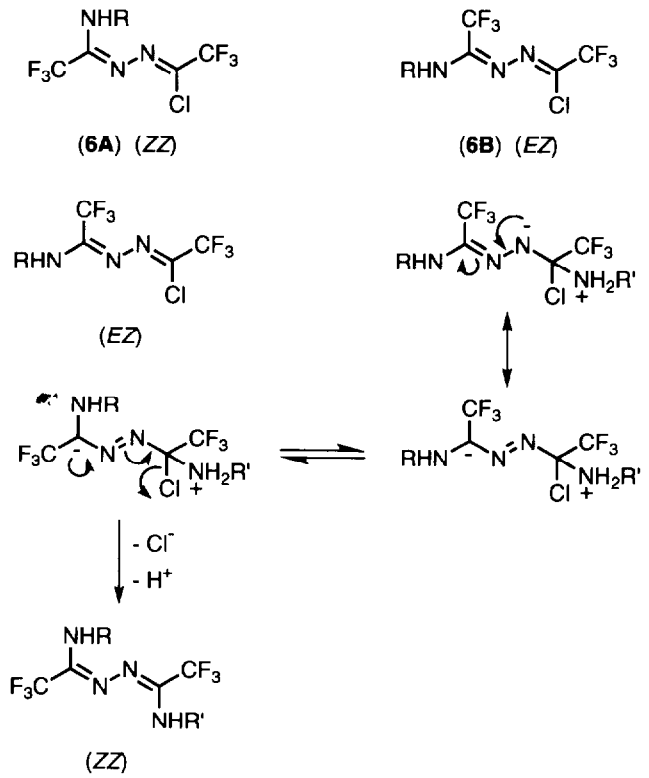
Thermolysis of the bis(4-fluoroanilino)azine **4b** in ethanol/water under reflux has been reported to give the 4-(4-fluorophenyl)-4*H*-1,2,4-triazole **2d** (96%) [6]. In the present work, the corresponding thermolysis of the bis(amino)azine **4c** afforded a mixture of the parent 1*H*-1,2,4-triazole **1a** and its ammonium salt **7b**, while the unsymmetrical bis(amino)azines **4g** and **4j** each gave the 4-phenyl-4*H*-1,2,4-triazole (**2c**). Cyclisation of azine **4g** had been expected to afford triazole **1a** via internal attack by the more nucleophilic nitrogen in the NH_2 group and elimination of the weaker base aniline. Intramolecular elimination of hydrogen chloride from the monoaminoazine **6b** was also successful under these conditions to give the triazole **1a** in moderate yield.

An alternative thermolysis procedure was then investigated in which various bis(amino)azines **4** were heated in the range 120–150 °C in vacuo in the absence of solvent. Compounds **4c**, **4e** and **4f**, as expected, gave high yields of the ammonium salt **7b** and the 4-carboalkoxymethyl-4*H*-1,2,4-triazoles **2e** and **2f**, respectively. The bis(methylamino)azine **4d** gave the expected products, methylamine and the 4-methyl-4*H*-1,2,4-triazole **2b**, in reasonable yield, but the remaining isolated compounds, salts **7c** and **7d** and the 1-methyl-1*H*-1,2,4-triazole **1b**, were unexpected.

It is considered that compounds **7c**, **7d** and **1b** arose via initial nucleophilic attack by methylamine on the methyl carbon of the 4-methyltriazole **2b** as shown in Scheme 3. This gave triazole **1a** together with dimethylamine and the latter compound should be more



Scheme 1.



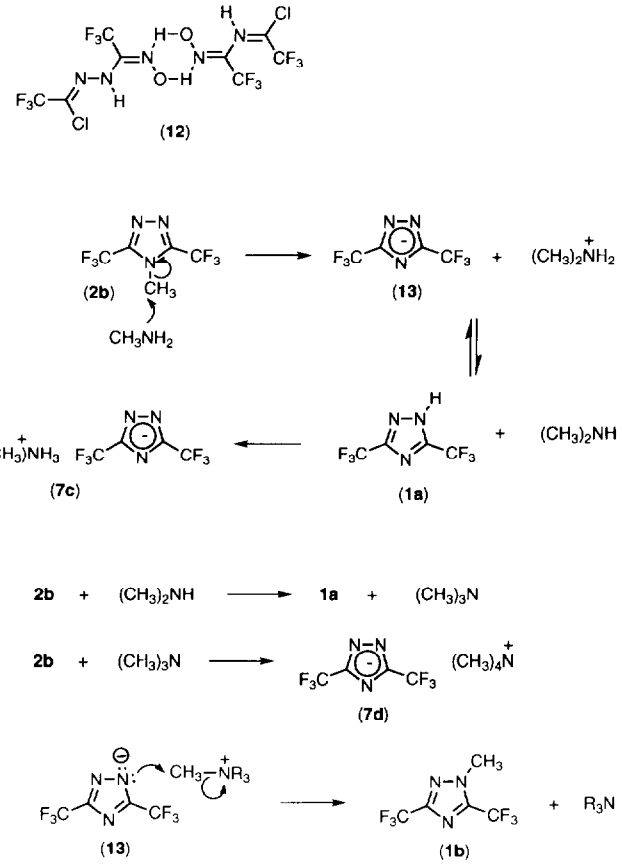
Scheme 2.

Table 2
Thermal cyclisation reactions of amino-substituted azines

Azine	Method [a]	Temp. (°C)	Time (h)	Products (%) [b]
4c	A	79	84	**1a**(28); **7b**(54)
4g	A	79	72	**2c**(86)
4j	A	79	80	**2c**(85)
6b	A	79	72	**1a**(50)
4c	B	150	12	**7b**(98)
4d	B	120	24	**1b**(1.5); **2b**(54); **7c**(ca. 26); **7d**(ca. 13) [c]
4e	B	120	12	**2e**(93) [d]
4f	B	140	6	**2f**(82)
4h	B	120	48	**1a**(11); **2b**(54); **7c**(31) [e]

[a] Method A: Heated in ethanol under reflux. Method B: Heated in sealed ampoules or bulbs in vacuo.
[b] Based on azine reacted, i.e. not recovered.
[c] Methylamine (54%) also isolated.
[d] Unchanged azine **4e** (41% recovered) also isolated.
[e] A volatile mixture of ammonia and methylamine also isolated.

effective (more nucleophilic) than methylamine towards attack on the methyl carbon of the 4-methyltriazole **2b**, leading to the formation of trimethylamine. Attack by trimethylamine on the 4-methyltriazole **2b** then afforded the salt **7d**, while reaction of methylamine with triazole **1a** gave the salt **7c**. The 1-methyl-1*H*-1,2,4-triazole **1b** can be formed by S_N2 attack of the triazolide anion **13** on a methyl carbon in the cations $MeNH_3^+$ and/or Me_4N^+. In the triazolide anion **13**, N-1 would be expected to be more nucleophilic than N-4 because of the α-effect of the adjacent nitrogen atom (N-2), and it has been observed that reactions of both the triazole **1a** and its sodium salt **7e** with electrophiles result in the formation of 1-substituted-1*H*-1,2,4-triazoles [2,12].



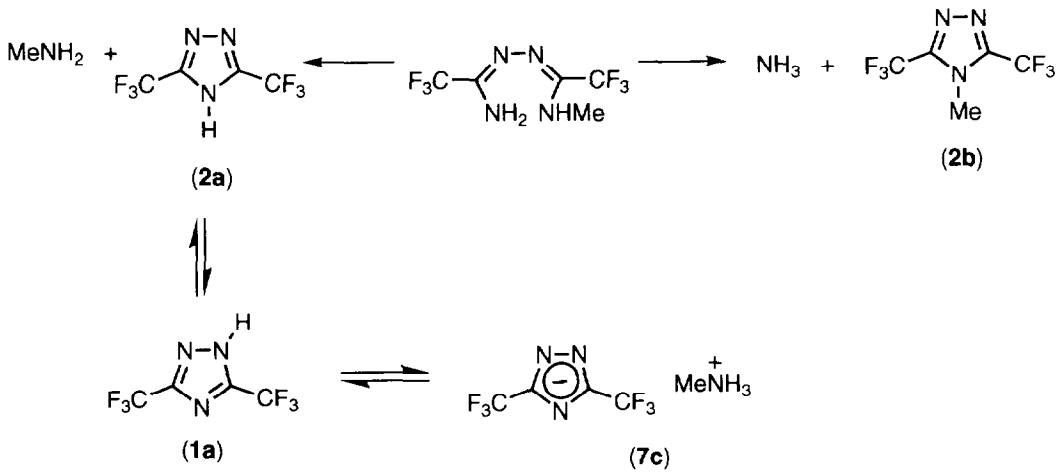
Scheme 3.

Thermolysis of the mixed diaminoazine **4h** resulted in competitive elimination of ammonia and methylamine (ratio 54:42) to give the 4-methyltriazole **2b** and a mixture of the triazole **1a** and its methylammonium salt **7c**, respectively (Scheme 4).

The ammonium salt **7b** was conveniently converted into the parent triazole **1a** (75%) by treatment with aqueous hydrochloric acid.

The structures of the 4-substituted 1,2,4-triazoles **2b**, **2c** and **2e–h** were established from their NMR spectra which showed only one absorption for the equivalent CF_3 groups and for the equivalent imino carbons. In contrast, 1-substituted 1,2,4-triazoles, i.e. **1b**, and products obtained from the reaction of the parent 1,2,4-triazole and its sodium salt **7e** with electrophiles [2,12] showed two absorptions for both the non-equivalent CF_3 groups and the non-equivalent imino carbons in their NMR spectra.

When the parent 1,2,4-triazole was first prepared, it was considered to be the 4*H*-1,2,4-triazole tautomer **2a**



Scheme 4.

[3]. The NMR spectra of the compound in solution ($CDCl_3$) [δ_H: 10.80 (br., NH) ppm. δ_F: +12.8 (s, 2 CF_3) ppm. δ_C: 150.9 (q, 2 C=N, ^2J = 41.1 Hz); 117.4 (q, 2 CF_3, ^1J = 270.0 Hz) ppm] are in agreement with structure **2a**. However, thermodynamic data reported recently are consistent with the compound being the 1*H*-1,2,4-triazole tautomer **1a** [13] and it has been calculated that the 1*H*-1,2,4-triazole tautomer **1a** is 32.6 kJ mol^{-1} lower in energy than tautomer **2a** [13]. The NMR observations can be explained by a fast equilibrium in solution for tautomer **1a** in which the proton shifts between N-1 and N-2 or, less likely, a fast equilibrium between tautomers **1a** and **2a**. It is therefore probable that the parent 1,2,4-triazole exists as tautomer **1a** in solution.

It has been reported [14] that heating the dihydro-s-tetrazine **9** [15] in acetic acid under reflux (6 h) resulted in rearrangement to the 4-amino-4*H*-1,2,4-triazole **2g**. In our hands, extended reflux (60 h) did result in rearrangement, but besides compound **2g** (61%) its acetyl derivative **2h** (25%) was also formed.

3. Experimental details

3.1. Starting materials

The dichloroazine **5** was synthesised by reaction of trifluoroacetic acid with hydrazine (2:1 molar ratio) to afford the bishydrazide $CF_3CONHNHCOCF_3$ which was treated with phosphoryl chloride and *N,N*-dimethylaniline hydrochloride [5,6]. The amino compounds or amine hydrochlorides employed were commercial samples and, where necessary, they were distilled before use and their purity checked (IR and ^1H NMR spectroscopy).

3.2. General techniques

Reactions involving the dichloroazine **5** and the monoaminoazines **6** were carried out at room temperature or at 0 °C (ice bath) in solvent (diethyl ether or diethyl ether/water as stated in the text), the solutions being stirred magnetically. The thermal cyclisation reactions of the diaminoazines **4** were performed either in anhydrous ethanol under reflux (method A) or in vacuo in sealed tubes or bulbs heated to the appropriate temperature (method B).

Where necessary, products were separated or purified by dry column flash chromatography (DCFC) using silica gel (Fluka 60 GF_{254}) and eluants as given in the text (light petroleum is the petroleum ether fraction b.p. 30–40 °C) or by sublimation in vacuo. The pure products were examined by IR spectroscopy (Perkin-Elmer DE783 instrument), ^1H NMR spectroscopy [Bruker AC-300 (300 MHz) spectrometer; external reference Me_4Si], ^{19}F NMR spectroscopy [Bruker AC-200 (188.3 MHz) instrument; external reference CF_3CO_2H], ^{13}C NMR (including DEPT 135°) spectroscopy [Bruker AC-300 (75.0 MHz) instrument with broad-band proton decoupling and D_2O as the deuterium lock signal; external reference Me_4Si] and mass spectroscopy [Kratos MS-25 or MS-45 instruments for electron impact (EI) and Kratos MS-50 instrument for fast atom bombardment (FAB) spectra each operating with an electron beam energy of 70 eV]. The NMR spectra were run on solutions in $CDCl_3$ (unless stated to the contrary) and chemical shifts to low field of reference are designated positive.

Melting points are uncorrected.

3.3. Reactions of 2,5-dichloro-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (5)

(a) With aniline

Aniline (4.20 g, 45.2 mmol), freshly distilled from zinc dust, in diethyl ether (20 cm^3) was added slowly

(0.5 h) to a stirred solution of the dichloroazine **5** (6.00 g, 22.99 mmol) in diethyl ether (30 cm^3) at 0 °C. Diethyl ether (20 cm^3) was added and stirring continued (1 h). The precipitate of aniline hydrochloride (2.92 g, 22.55 mmol, 98%) was filtered off and the solvent was removed from the filtrate in vacuo to give 2-anilino-5-chloro-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (**6a**) (6.49 g, 20.44 mmol, 89%) present as two isomers in the ratio 6:5 (^{19}F NMR spectroscopy); the IR and ^1H and ^{19}F NMR spectra were identical to those reported [6].

(b) With ammonia

An aqueous solution of ammonia (35% w/w) containing ammonia (0.78 g, 45.9 mmol) in diethyl ether (25 cm^3) was added slowly (0.5 h) to a stirred solution of the dichloroazine **5** (6.0 g, 23.0 mmol) in diethyl ether (50 cm^3) and water (25 cm^3) cooled to 0 °C, and stirring was continued (2 h). The ether layer was separated, dried ($MgSO_4$) and the ether removed in vacuo to give (*ZZ*)-1-amino-5-chloro-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (**6b**) (nc) (4.50 g, 18.63 mmol, 81%) (Analysis: Found: C, 19.6; H, 0.7; N, 17.1%; M^+, 241/243. $C_4H_2ClF_6N_3$ requires: C, 19.9; H, 0.8; N, 17.4%; M, 241.5), m.p. 58–60 °C, the stereochemistry of which was established by an X-ray structure determination [9].

In a second experiment, a mixture of aqueous ammonia (35% w/w) containing ammonia (5.1 g, 300 mmol) and dichloroazine **5** (10.0 g, 40.0 mmol) was stirred in diethyl ether (75 cm^3) at 0 °C (2 h) and then at room temperature (24 h). Water (50 cm^3) was added to dissolve the precipitate of ammonium chloride, the ether layer separated and worked-up as in the first experiment to afford (*ZZ*)-2,5-bis(amino)-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (**4c**) (nc) (8.17 g, 36.8 mmol, 96%) (Analysis: Found: C, 21.6; H, 1.8; N, 24.9%; M^+, 222. $C_4H_4F_6N_4$ requires C, 21.6; H, 1.8; N, 25.2%; M, 222), m.p. 114–116 °C.

(c) With methylamine

An ethanolic solution of methylamine (33% w/w) containing methylamine (1.43 g, 45.98 mmol) in diethyl ether (15 cm^3) was added slowly (0.5 h) to a stirred solution of dichloroazine **5** (6.00 g, 22.98 g) in diethyl ether (50 cm^3) cooled to 0 °C and stirring continued (3 h). The white precipitate of methylamine hydrochloride (1.38 g, 20.4 mmol, 88%) was filtered off and the solvent removed from the filtrate in vacuo to afford a viscous yellow liquid identified as 2-chloro-1,1,1,6,6,6-hexafluoro-5-methylamino-3,4-diazahexa-2,4-diene (**6c**) (nc) (5.24 g, 20.4 mmol, 89%) (Analysis: Found: C, 23.8; H, 1.7; N, 16.4; F, 45.0%; M^+, 255/257. $C_5H_4ClF_6N_3$ requires: C, 23.5; H, 1.6; N, 16.4; F, 44.6%; M, 255.5), b.p. 168–170 °C, as a mixture of two isomers in the ratio 8:5 (^{19}F NMR spectroscopy).

In a second experiment, an excess of an ethanolic solution of methylamine (33% w/w) containing methylamine (5.60 g, 181.0 mmol) in diethyl ether (25 cm^3) was added slowly (0.5 h) to a stirred solution of dichloroazine **5** (8.00 g, 30.7 mmol) in diethyl ether (50 cm^3) and stirring continued (24 h). Water (50 cm^3) was added to dissolve the precipitate of methylamine hydrochloride, the ether layer separated, dried ($MgSO_4$) and the ether removed in vacuo to give a white solid identified as (*ZZ*)-2,5-bis(methylamino)-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (**4d**) (nc) (7.22 g, 28.8 mmol, 94%) (Analysis: Found: C, 29.1; H, 3.2; N, 22.2; F, 45.8%; M^+, 250. $C_6H_8F_6N_4$ requires: C, 28.8; H, 3.2; N, 22.4; F, 45.6%; M, 250), m.p. 64–66 °C.

(d) With methyl glycinate

A solution of dichloroazine **5** (10.40 g, 39.8 mmol) in diethyl ether (50 cm^3) was added slowly (0.5 h) to a stirred solution of methyl glycinate hydrochloride (5.0 g, 39.8 mmol) and triethylamine (8.05 g, 79.7 mmol) in diethyl ether (50 cm^3) and water (50 cm^3), and stirring continued (3 h). The ether layer was separated, dried ($MgSO_4$) and the ether removed in vacuo to give a light yellow solid identified as methyl 2-chloro-5-glycinato-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (**6d**) (nc) (11.5 g, 38.0 mmol, 96%) (Analysis: Found: C, 27.0; H, 1.8; N, 13.3%; M^+, 313/315. $C_7H_6ClF_6N_3O_2$ requires: C, 26.8; H, 2.0; N, 13.4%; M, 313.5), m.p. 85–87 °C, present as two isomers in the ratio 6:5 (^{19}F NMR spectroscopy).

A second reaction between dichloroazine **5** (3.0 g, 11.5 mmol) in diethyl ether (25 cm^3) and methyl glycinate hydrochloride (5.77 g, 46.2 mmol) in diethyl ether (100 cm^3) and water (100 cm^3) in the presence of triethylamine (4.66 g, 46.2 mmol), with the resultant mixture stirred (72 h), gave a white precipitate A (2.09 g). Work-up of the ether layer as in the first experiment afforded a yellowish solid B (1.65 g) and solids A and B were shown by TLC ($CHCl_3$) and ^{19}F NMR spectroscopy to consist of compound **6d** and a second component in the ratio 3:79 and 89:11, respectively. Separation of the two products by repeated DCFC (eluant $CHCl_3$) from the solids A and B gave compound **6d** (0.06 g and 1.42 g; total 1.48 g, 4.72 mmol, 41%), present as two isomers in the ratio 6:5 (^{19}F NMR spectroscopy), and dimethyl (*ZZ*)-2,5-bis(glycinato)-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (**4e**) (nc) (1.96 g and 0.15 g; total 2.11 g, 5.76 mmol, 50%) (Analysis: Found: C, 32.8; H, 3.3; N, 15.2%; M^+, 366. $C_{10}H_{12}F_6N_4O_4$ requires: C, 32.8; H, 3.3; N, 15.3%; M, 366), m.p. 157–159 °C.

(e) With ethyl glycinate

A solution of dichloroazine **5** (2.26 g, 10.0 mmol) in diethyl ether (25 cm^3) was added slowly (0.5 h) to a stirred solution of ethyl glycinate hydrochloride (1.40

g, 10.0 mmol) and triethylamine (2.03 g, 20.0 mmol) in diethyl ether (25 cm^3) and water (25 cm^3), and stirring continued (3 h). The ether layer was separated, dried ($MgSO_4$) and the ether removed in vacuo to give a white solid identified as ethyl 2-chloro-5-glycinato-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (**6e**) (nc) (3.10 g, 9.47 mmol, 95%) (Analysis: Found: C, 29.6; H, 2.6; N, 12.5%; M^+, 327/329. $C_8H_8ClF_6N_3O_2$ requires: C, 29.3; H, 2.4; N, 12.8%; M, 327.5), m.p. 75 °C, present as two isomers in the ratio 45:55.

In a second experiment, a solution of dichloroazine **5** (10.0 g, 38.3 mmol) in diethyl ether (20 cm^3) was added slowly (0.5 h) to a stirred solution of ethyl glycinate hydrochloride (26.7 g, 191.5 mmol) and sodium hydroxide (7.66 g, 191.5 mmol) in diethyl ether (100 cm^3) and water (100 cm^3), and stirring continued (72 h). The white precipitate C (5.3 g) was filtered off and a further quantity of ethyl glycinate hydrochloride (16.5 g, 114.7 mmol) and sodium hydroxide (4.59 g, 114.7 mmol) in water (50 cm^3) was added to the stirred filtrate, and stirring continued (72 h). The resulting precipitate (3.4 g) was collected and combined with the original product C. The ether layer was separated from the filtrate and the aqueous layer was extracted with diethyl ether (2×50 cm^3) and the combined ether extracts were dried ($MgSO_4$) and the ether removed in vacuo to give a second solid D (4.9 g).

The solids C and D were shown by TLC (eluant $CHCl_3$) and ^{19}F NMR spectroscopy to contain the same two components in the ratio 11:89 and 40:60, respectively, and these were separated by repeated DCFC (eluant $CHCl_3$) to afford component A (0.8 g and 1.2 g) and component B (7.9 g and 3.7 g).

Component A was identified as the monochloroazine **6e** (2.0 g, 6.11 mmol, 16%), present as two isomers in the ratio 48:52 (^{19}F NMR spectroscopy) and component B was identified as diethyl (*ZZ*)-2,5-bis(glycinato)-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (**4f**) (nc) (11.6 g, 29.4 mmol, 77%) (Analysis: Found: C, 36.3; H, 4.0; N, 14.0; F, 28.8%; M^+, 394. $C_{12}H_{16}F_6N_4O_4$ requires: C, 36.5; H, 4.1; N, 14.2; F, 28.9%; M, 394), m.p. 140–142 °C.

(f) With hydroxylamine

A solution of dichloroazine **5** (5.00 g, 19.2 mmol) in diethyl ether (15 cm^3) was added slowly to a stirred solution of hydroxylamine hydrochloride (5.33 g, 76.7 mmol) and sodium hydroxide (3.06 g, 76.5 mmol) in diethyl ether (100 cm^3) and water (100 cm^3), and stirring continued (24 h). The ether layer was separated and the aqueous layer washed with diethyl ether (2×50 cm^3). The combined ether extracts were dried ($MgSO_4$) and the ether removed in vacuo to afford a white solid (4.46 g), which was purified by sublimation in vacuo at 50 °C to give (*ZZ*)-2-chloro-1,1,1,6,6,6-hexafluoro-3,4-diazahex-4-en-5-one oxime (**8**) (nc) (4.24 g, 16.4 mmol, 86%) (Analysis: Found: C, 18.9; H, 0.8; N, 16.3; F, 44.7%; M^+, 257/259. $C_4H_2ClF_6N_3O$ requires: C, 18.6; H, 0.8; N, 16.3; F, 44.3%; M, 257.5), m.p. 118–120 °C, the structure of which was confirmed by X-ray crystallography [11].

(g) With hydrazine

A solution of hydrazine (2.57 g, 80.3 mmol) in diethyl ether (20 cm^3) was added slowly (0.25 h) to a stirred solution of dichloroazine **5** (6.00 g, 22.98 mmol) at 0 °C and stirring was continued (24 h). The precipitate of hydrazine hydrochloride (2.88 g, 42.04 mmol, 91%) was filtered off and the solvent removed from the filtrate under reduced pressure to give a yellow solid (5.10 g). This was purified by sublimation in vacuo at room temperature to afford 3,6-bis(trifluoromethyl)-1,2-dihydro-s-tetrazine (**9**) (4.54 g, 20.64 mmol, 89%), identified by a comparison of its IR and NMR spectra with those reported [15].

3.4. Reaction of 2-anilino-5-chloro-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (6a) with ammonia

An aqueous solution of ammonia (35% w/w) containing ammonia (1.75 g, 102.9 mmol) in diethyl ether (25 cm^3) was added in one portion to a stirred solution of the monoanilinoazine **6a** (4.00 g, 12.59 mmol) in diethyl ether (50 cm^3) and stirring was continued (48 h). Water (50 cm^3) was added, the ether layer separated and the aqueous layer extracted with diethyl ether (2×25 cm^3). The combined ether extracts were dried ($MgSO_4$) and the ether removed in vacuo to give a white solid (3.69 g), which on recrystallisation from n-pentane/dichloromethane (2:1 v/v), afforded azine **4g** (3.48 g, 11.67 mmol, 92%).

3.5. Reaction of 2-amino-5-chloro-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (6b) with aniline

An excess of aniline (2.30 g, 24.7 mmol) in diethyl ether (10 cm^3) was added in one portion to a stirred solution of the monoaminoazine **6b** (2.00 g, 8.28 mmol) in diethyl ether and stirring was continued (24 h) before the mixture was stored (48 h). The resulting precipitate of aniline hydrochloride (1.08 g, 8.28 mmol, 100%) was filtered off and the ether removed from the filtrate in vacuo to give a slushy solid (3.14 g). Purification of the material by DCFC (eluant n-hexane/diethyl ether 1:1 v/v) gave (*ZZ*)-2-amino-5-anilino-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (**4g**) (nc) (2.32 g, 7.76 mmol, 94%) (Analysis: Found: C, 40.5; H, 2.7: N, 18.5%; M^+, 298. $C_{10}H_8F_6N_4$ requires: C, 40.3; H, 2.7; N, 18.8%; M, 298), m.p. 110–112 °C. A later component which was also obtained was identified as unchanged aniline (0.54 g).

Table 3
^{1}H, ^{19}F and ^{13}C NMR spectral data

Compound	NMR δ (ppm) [a]
1a	δ_H: 10.80 (s, NH). δ_F: +12.8 (s, CF_3). δ_C: 150.9 (q, C=N, ^2J=41.4 Hz); 117.4 (q, CF_3, ^1J=270.9 Hz)
1b	δ_H: 3.71 (s, NCH_3). δ_F: +13.7 (s, 3F, CF_3); +11.4 (s, 3F, CF_3). δ_C: 152.4 (q, C=N, ^2J=41.0 Hz); 145.5 (q, C=N, ^2J=42.1 Hz); 118.2 (q, CF_3, ^1J=269.3 Hz); 117.3 (q, CF_3, ^1J=271.1 Hz); 37.0 (s, NCH_3)
2e	δ_H: 4.98 (s, 2H, NCH_2); 3.84 (s, 3H, OCH_3). δ_F: +15.2 (s, CF_3). δ_C: 163.8 (s, OC=O); 146.4 (q, C=N, ^2J=40.6 Hz); 116.7 (q, CF_3, ^1J=272.0 Hz); 53.1 (s, OCH_3); 45.5 (s, NCH_2)
2f	δ_H: 5.10 (s, 2H, NCH_2); 4.31 (q, 2H, OCH_2, J=7.2 Hz); 1.32 (t, 3H, CH_3, J=7.2 Hz). δ_F: +14.5 (s, CF_3). δ_C: 164.3 (s, OC=O); 146.7 (q, C=N, ^2J=40.0 Hz); 117.4 (s, CF_3, ^1J=271.6 Hz); 63.1 (s, OCH_2); 46.5 (s, NCH_2); 13.4 (s, CH_3)
2h [b]	δ_H: 12:65 (s, 1H, NH); 2.13 (s, 3H, CH_3). δ_F: +15.8 (s, CF_3). δ_C: 173.2 (s, NC=O); 150.2 (q, C=N, ^2J=40.6 Hz); 120.8 (q, CF_3, ^1J=271.6 Hz); 23.8 (s, CH_3)
4c	δ_H: 5.45 (s, NH_2). δ_F: +7.0 (s, CF_3). δ_C: 147.9 (q, C=N, ^2J=34.5 Hz); 118.5 (q, CF_3, ^1J=274.8 Hz)
4d	δ_H: 6.01 (br., 1H, NH); 2.99 (d, 3H, NCH_3, J=5.5 Hz). δ_F: +9.2 (s, CF_3). δ_C: 148.2 (q, C=N, ^2J=32.5 Hz); 118.9 (q, CF_3, ^1J=275.6 Hz); 29.6 (s, NCH_3)
4e	δ_H: 6.35 (br., 1H, NH); 4.19 (d, 2H, NCH_2, J=5.5 Hz); 3.80 (s, 3H, OCH_3). δ_F: +10.0 (s, CF_3). δ_C: 169.7 (s, OC=O); 146.2 (q, C=N, ^2J=32.9 Hz); 118.7 (q, CF_3, ^1J=275.7 Hz); 52.6 (s, OCH_3); 44.5 (s, NCH_2)
4f	δ_H: 6.39 (br., 1H, NH); 4.24 (q, 2H, OCH_2, J=7.1 Hz); 4.18 (d, 2H, NCH_2, J=5.5 Hz); 1.30 (t, 3H, CH_3, J=7.1 Hz). δ_F: +10.0 (s, CF_3). δ_C: 169.3 (s, OC=O); 146.3 (q, C=N, ^2J=32.9 Hz); 118.2 (s, CF_3, ^1J=275.8 Hz); 61.9 (s, OCH_2); 44.7 (s, NCH_2); 14.1 (s, CH_3)
4g	δ_H: 7.82 (s, 1H, NH); 7.30 (mult., 5H, C_6H_5); 5.62 (s, 2H, NH_2). δ_F: +12.7 [s, 3F, $CF_3C(NHPh)$=]; +6.2 [s, 3F, $CF_3C(NH_2)$=]. δ_C: 148.1 (q, PhNHC=N, ^2J=35.3 Hz); 146.7 (q, H_2NC=N, ^2J=33.1 Hz); 137.0 (s, *ipso*-C_6H_5); 129.0, 126.9, 126.3 (3s, *m*-, *p*-, *o*-C_6H_5); 118.7 (q, CF_3, ^1J=274.5 Hz); 118.5 (q, CF_3, ^1J=275.0 Hz)
4h	δ_H: 5.98 (br., 1H, NH); 5.45 (s, 2H, NH_2); 3.01 (d, 3H, NCH_3, J=5.5 Hz). δ_F: +9.2 [s, 3F, $CF_3C(NHMe)$=]; +6.1 [s, 3F, $CF_3C(NH_2)$=]. δ_C: 148.7 (q, MeNHC=N, ^2J=32.1 Hz); 147.5 (q, H_2NC=N, ^2J=34.0 Hz); 118.9 (q, CF_3, ^1J=275.7 Hz); 118.7 (q, CF_3, ^1J=274.8 Hz); 29.4 (s, NCH_3)
4i	δ_H: 6.37 (br., 1H, N*H*CH_2); 5.98 (br., 1H, N*H*CH_3); 4.22 (q, 2H, OCH_2, J=7.1 Hz); 4.13 (d, 2H, NCH_2, J=6.0 Hz); 3.00 (d, 3H, NCH_3, J=5.8 Hz); 1.27 (t, 3H, CH_3, J=7.1 Hz). δ_F: +9.2 (s, 3F, CF_3); +8.9 (s, 3F, CF_3). δ_C: 169.7 (s, OC=O); 148.2 (q, MeNHC=N, ^2J=32.4 Hz); 145.6 (q, EtO_2CCH_2NHC=N, ^2J=32.9 Hz); 118.7 (q, CF_3, ^1J=275.7 Hz); 118.5 (q, CF_3, ^1J=275.7 Hz); 61.4 (s, OCH_2); 44.2 (s, NCH_2); 29.0 (q, NCH_3, ^4J=2.9 Hz); 13.4 (s, CH_3)
4j	δ_H: 7.75 (s, 1H, PhN*H*); 7.27 (mult., 5H, C_6H_5); 6.38 (br., 1H CH_2NH); 4.23 (d, 2H, NCH_2, J=5.5 Hz); 3.74 (s, 3H, OCH_3). δ_F: +13.6 [s, 3F, $CF_3C(NHPh)$=]; +10.0 [s, 3F, $CF_3C(NHCH_2CO_2Me)$=]. δ_C: 169.8 (s, OC=O; 146.5 (q, C=N, ^2J=32.8 Hz); 146.4 (q, C=N, ^2J=33.2 Hz); 137.0 (s, *ipso*-C_6H_5); 128.9, 126.8, 126.1 (3s, *m*-, *p*-, *o*-C_6H_5); 118.7 (q, 2 CF_3, J=275.7 Hz); 52.5 (s, OCH_3); 44.6 (s, NCH_2)
6b	δ_H: 5.80 (s, NH_2). δ_F: +9.0 [s, 3F, $CF_3C(NH_2)$=]; +6.8 (s, 3F, CF_3CCl=). δ_C: 152.6 (q, H_2NC=N, ^2J=35.3 Hz); 134.9 (q, ClC=N, ^2J=40.5 Hz); 118.0 (q, CF_3, ^1J=276.3 Hz); 117.6 (q, CF_3, ^1J=274.3 Hz)
(*ZZ*)-**6c**	δ_H: 6.09 (br., 1H, NH); 3.14 (d, 3H, NCH_3, J=6.0 Hz). δ_F: +8.6 [s, 3F, $CF_3C(NHMe)$=]; +7.9 (s, 3F, CF_3CCl=). δ_C: 147.1 (q, MeNHC=N, ^2J=35.8 Hz); 128.4 (q, ClC=N, ^2J=41.3 Hz); 117.9 (q, CF_3, ^1J=272.9 Hz); 117.2 (q, CF_3, ^1J=285.1 Hz); 30.5 (s, NCH_3)
(*EZ*)-**6c**	δ_H: 5.92 (br., 1H, NH); 3.06 (d, 3H, NCH_3, J=5.0 Hz). δ_F: +10.7 [s, 3F, $CF_3C(NHMe)$=]; +8.1 (s, 3F, CF_3CCl=). δ_C: 152.2 (q, MeNHC=N, ^2J=42.1 Hz); 133.4 (q, ClC=N, ^2J=32.3 Hz); 118.4 (s, 3F, ^1J=277.3 Hz); 117.6 (q, CF_3, ^1J=276.7 Hz); 28.9 (s, NCH_3)
(*ZZ*)-**6d**	δ_H: 6.70 (br., 1H, NH); 4.19 (d, NCH_2, J=5.0 Hz); 3.83 (s, OCH_3). δ_F: +9.2 [s, 3F, $CF_3C(NHCH_2CO_2Me)$=]; +9.0 (s, 3F, CF_3CCl=). δ_C: 168.9 (s, OC=O); 149.3 (q, MeO_2CCH_2NHC=N, ^2J=34.3 Hz); 125.9 (q, ClC=N, ^2J=40.4 Hz); 117.8 (q, CF_3, ^1J=273.3 Hz); 116.9 (q, CF_3, ^1J=284.9 Hz); 52.5 (s, OCH_3); 45.1 (s, NCH_2)
(*EZ*)-**6d**	δ_H: 6.70 (br., 1H, NH); 4.28 (d, NCH_2, J=5.5 Hz); 3.85 (s, OCH_3). δ_F: +11.8 [s, 3F, $CF_3C(NHCH_2CO_2Me)$=]; +9.0 (s, 3F, CF_3CCl=). δ_C: 169.2 (s, OC=O); 152.9 (q, MeO_2CCH_2NHC=N, ^2J=40.6 Hz); 130.1 (q, ClC=N, ^2J=41.2 Hz); 118.3 (q, CF_3, ^1J=277.7 Hz); 117.6 (q, CF_3, ^1J=274.0 Hz); 52.6 (s, OCH_3); 46.0 (s, NCH_2)
(*ZZ*)-**6e**	δ_H: 6.48 (br., 1H, NH); 4.39 (q, 2H, OCH_2, J=7.1 Hz); 4.32 (d, 2H, NCH_2, J=5.5 Hz); 1.28 (t, 3H, CH_3, J=7.1 Hz). δ_F: +9.1 [s, 3F, $CF_3C(NHCH_2CO_2Et)$=]; +8.9 (s, 3F, CF_3CCl=). δ_C: 168.5 (s, OC=O); 149.1 (q, EtO_2CCH_2NHC=N, ^2J=34.7 Hz); 125.6 (q, ClC=N, ^2J=39.6 Hz); 117.8 (q, CF_3, ^1J=273.5 Hz); 116.9 (q, CF_3, ^1J=284.9 Hz); 62.2 (s, OCH_2); 43.6 (s, NCH_2); 13.9 (s, CH_3)
(*EZ*)-**6e**	δ_H: 6.38 (br., 1H, NH); 4.50 (q, 2H, OCH_2, J=7.2 Hz); 4.15 (d, 2H, NCH_2, J=5.0 Hz); 1.26 (t, 3H, CH_3, J=7.2 Hz). δ_F: +11.7 [s, 3F, $CF_3C(NHCH_2CO_2Et)$=]; +8.9 (s, 3F, CF_3CCl=). δ_C: 168.6 (s, OC=O); 152.7 (q, EtO_2CCH_2NHC=N, ^2J=40.5 Hz); 130.4 (q, ClC=N, ^2J=40.0 Hz); 118.4 (q, CF_3, ^1J=277.5 Hz); 117.6 (q, CF_3, ^1J=274.4 Hz); 62.4 (s, OCH_2); 45.2 (s, NCH_2); 13.8 (s, CH_3)

(*continued*)

Table 3 (*continued*)

Compound	NMR δ (ppm) [a]
7b [c]	δ_H: 6.02 (s, NH_4). δ_F: +14.5 (s, CF_3). δ_C: 155.0 (q, C=N, ^2J=36.9 Hz); 120.8 (q, CF_3, ^1J=269.1 Hz)
7c [c]	δ_H: 3.68 (br., 3H, NH_3); 3.08 (br., 3H, NCH_3). δ_F: +15.2 (s, CF_3). δ_C: 154.9 (q, C=N, ^2J=34.7 Hz); 122.5 (q, CF_3, ^1J=268.5 Hz); 58.1 (s, NCH_3)
7d [c]	δ_H: 3.62 (s, Me_4N). δ_F: +15.2 (s, CF_3). δ_C: 155.6 (q, C=N, ^2J=35.5 Hz); 122.6 (q, CF_3, ^1J=268.6 Hz); 56.3 (s, NCH_3)
8	δ_H: 8.84 (s, 1H, OH); 8.30 (s, 1H, NH). δ_F: +10.8 (s, 3F, CF_3C=NOH); +9.4 (s, 3F, CF_3CCl=). δ_C: 140.9 (q, C=NOH, ^2J=35.3 Hz); 119.7 (q, CF_3, ClC=N, ^2J=39.6 Hz); 118.3 (q, CF_3, ^1J=274.5 Hz); 118.2 (q, CF_3, ^1J=272.5 Hz)

[a] In $CDCl_3$ solvent.
[b] In DMSO-d_6 solvent.
[c] In acetone-d_6 solvent.

3.6. Reactions of 2-chloro-1,1,1,6,6,6-hexafluoro-5-methylamino-3,4-diazahexa-2,4-diene (6c)

(a) With ammonia

An excess of aqueous ammonia (35% w/w) containing ammonia (3.50 g, 205.8 mmol) in diethyl ether (10 cm^3) was added in one portion to a stirred solution of the monomethylaminoazine **6c** (5.00 g, 19.57 mmol) in diethyl ether (25 cm^3) and stirring was continued (48 h). The resulting precipitate of ammonium chloride was dissolved in water (10 cm^3), the ether layer separated and the aqueous layer extracted with ether (2×50 cm^3). The combined ether extracts were dried ($MgSO_4$) and the ether removed in vacuo to afford (*ZZ*)-2-amino-1,1,1,6,6,6-hexafluoro-5-methylamino-3,4-diazahexa-2,4-diene (**4h**) (nc) (4.45 g, 18.86 mmol, 96%) (Analysis: Found: C, 25.3; H, 2.4; N, 23.9; F, 48.1%; M^+, 236. $C_5H_6F_6N_4$ requires: C, 25.4; H, 2.5; N, 23.7; F, 48.3%; M, 236), m.p. 68–70 °C.

(b) With ethyl glycinate

A solution of the monomethylaminoazine **6c** (4.00 g, 15.65 mmol) in diethyl ether (15 cm^3) was added rapidly to a stirred solution of ethyl glycinate hydrochloride (8.0 g, 57.3 mmol) and sodium hydroxide (2.25 g, 56.2 mmol) in diethyl ether (50 cm^3) and water (50 cm^3), and stirring continued (72 h). The ether layer was separated and the aqueous layer extracted with ether (2×25 cm^3), the extracts combined and then dried ($MgSO_4$). Removal of the ether in vacuo gave a thick yellow oil which was shown by TLC (eluant: light petroleum/CH_2Cl_2 2:1 v/v) to contain two components one of which was the unchanged azine **6c**. Separation of the two components by DCFC (same eluant) gave ethyl (*ZZ*)-2-glycinato-1,1,1,6,6,6-hexafluoro-5-methylamino-3,4-diazahexa-2,4-diene (**4i**) (nc) (3.56 g, 11.05 mmol, 95%) (Analysis: Found: C, 33.7; H, 3.5; N, 17.1; F, 35.6%; M^+, 322. $C_9H_{12}F_6N_4O_2$ requires: C, 33.5; H, 3.7; N, 17.4; F, 35.4%; M, 322), m.p. 52–54 °C, and unchanged monomethylaminoazine **6c** (1.03 g, 4.03 mmol, 26% recovered).

3.7. Reaction of methyl 2-chloro-5-glycinato-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (6d) with aniline

Aniline (1.80 g, 19.4 mmol) was added in one portion to a stirred solution of the monoglycinatoazine **6d** (2.00 g, 6.4 mmol) in diethyl ether (10 cm^3) and stirring was continued (5 h) before the material was stored (48 h). The white precipitate of aniline chloride (0.80 g, 6.18 mmol, 96%) was filtered off and the ether removed from the filtrate in vacuo to give a mixture (2.85 g) of a product and unchanged aniline as shown by TLC ($CHCl_3$). Separation of the mixture by DCFC (eluant: $CHCl_3$) gave methyl 1-anilino-4-glycinato-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (**4j**) (nc) (2.22 g, 6.1 mmol, 94%) (Analysis: Found: C, 42.3; H, 3.4; N, 15.0%; M^+, 370. $C_{13}H_{12}F_6N_4O_2$ requires: C, 42.2; H, 3.2; N, 15.1%; M, 370), m.p. 62 °C, and unchanged aniline (0.43 g, 4.0 mmol, 24% recovered).

3.8. Thermal cyclisation experiments

3.8.1. Method A in refluxing ethanol

(a) 2.5-Diamino-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (4c)

A solution of diaminoazine **4c** (3.12 g, 14.1 mmol) in ethanol (7 cm^3) was heated under reflux (84 h) and the ethanol was then removed in vacuo. Addition of diethyl ether (10 cm^3) to the residue gave insoluble material which was filtered off and washed with diethyl ether and then chloroform to afford ammonium 3,5-bis(trifluoromethyl)-1,2,4-triazolide (**7b**) (nc) (1.70 g, 7.66 mmol, 54%) (Analysis: Found: C, 21.5; H, 1.8; N, 24.9%; M^+, 222. $C_4H_4F_6N_4$ requires: C, 21.6; H, 1.8; N, 25.2%; M, 222), m.p. 132 °C.

Removal of the ether from the filtrate in vacuo gave a waxy solid which was purified by DCFC (eluant: $CHCl_3$) and identified as 3,5-bis(trifluoromethyl)-1*H*-1,2,4-triazole (**1a**) (0.80 g, 3.90 mmol, 28%) (Analysis: Found: C, 23.1; H, 0.6; N, 20.8%; M^+, 205. Calc. for $C_4HF_6N_3$: C, 23.4; H, 0.5; N, 20.5%; M, 205), m.p. 74–75 °C, lit. [3], m.p. 76–77 °C for the compound which had been assigned the tautomeric 4*H*-1,2,4-triazole structure (**2a**).

Table 4
Mass spectral data [a]

Compound	MS: *m/z* (%, assignment) [b]
1b	219 (98, M^+); 200 [41, $(M-F)^+$]; 110 (10, $C_2HF_3N_2^+$); 105 (11, $C_2HF_2N_3^+$); 88 (10, $C_3F_2N^+$); 86 (50, $C_2HFN_3^+$); 84 (70, $C_3HFN_2^+$); 76 (12, $C_2F_2N^+$); 69 (91, CF_3^+); 50 (11, CHF_2^+); 31 (25, CF^+)
2e	277 (15, M^+); 218 [14, $(M-CO_2Me)^+$]; 190 (12, $C_4F_6N_2^+$); 110 (48); 95 (11, $C_2F_3N^+$); 76 (18); 69 (100); 59 (96, $C_2H_3O_2^+$); 54 (16, $C_2H_2N_2^+$); 53 (15, $C_2HN_2^+$); 45 (40, CHO_2^+); 43 (24, $C_2H_3O^+$); 42 (21, $C_2H_2O^+$); 31 (17); 29 (23, CHO^+)
2f	291 (37, M^+); 247 [12, $(M-C_2H_4O)^+$]; 219 [80, $(M-C_2H_4CO_2)^+$]; 218 [27, $(M-CO_2Et)^+$]; 96 (9, $C_2HF_3N^+$); 95 (7); 76 (9); 69 (48); 29 (100, $C_2H_5^+$/CHO^+)
2h	262 (4, M^+); 223 [15, $(M-HF_2)^+$]; 220 (18, $C_4H_2F_6N_4^+$); 205 (6, $C_4HF_6N_3^+$); 69 (11); 43 (100)
4c	222 (76, M^+); 206 [4, $(M-NH_2)^+$]; 203 [12, $(M-F)^+$]; 153 [82, $(M-CF_3)^+$]; 138 (10, $C_3H_3F_3N_3^+$); 133 (24, $C_3H_3F_2N_4^+$); 96 (21); 77 (23, $C_2HF_2N^+$); 69 (100); 66 (13, $C_2N_3^+$); 50 (12, CF_2^+); 31 (17)
4d	250 (43, M^+); 220 [15, $(M-NHMe)^+$]; 181 [52, $(M-CF_3)^+$]; 125 (29, $C_3H_4F_3N_2^+$); 110 (92); 96 (30); 69 (85); 57 (60, C_2FN^+); 55 (11, $C_2H_3N_2^+$); 42 (21, $C_2H_4N^+$); 31 (8); 30 (100, CH_3NH^+); 29 (44, CH_3N^+)
4e [c]	367 [42, $(M+H)^+$]; 366 (5, M^+); 335 [17, $(M-CH_3O)^+$]; 297 [11, $(M-CF_3)^+$]; 278 [21, $(M-NHCO_2Me)^+$]; 183 (14, $C_5H_6F_3N_2O_2^+$); 168 (6, $C_4H_3F_3N_2O_2^+$); 125 (7, $C_3H_4F_3N_2^+$)
4f	394 (46, M^+); 349 [4, $(M-EtO)^+$]; 325 [39, $(M-CF_3)^+$]; 321 [63, $(M-CO_2Et)^+$]; 292 [18, $(M-NHCH_2CO_2Et)^+$]; 247 (13, $C_6H_3F_6N_3O^+$); 197 (63, $C_6H_8F_3N_2O_2^+$); 154 (33, $C_6H_8N_3O^+$); 126 (27, $C_4H_4N_3O_2^+$); 118 (17, $C_4H_4F_3N_2^+$); 110 (34); 104 (15, $C_3H_2F_3N_2^+$); 91 (16, $C_2HF_2N_2^+$); 77 (24); 71 (23, $C_2H_2FN_2^+$); 69 (46); 56 (12, $C_2H_2NO^+$); 45 (35, EtO^+); 41 (21, $C_2H_3N^+$); 29 (100)
4g [c]	299 [63, $(M+H)^+$]; 298 (5, M^+); 282 [17, $(M-NH_2)^+$]; 279 [14, $(M-F)^+$]; 260 [8, $(M-2F)^+$]; 229 [23, $(M-CF_3)^+$]; 206 [28, $(M-NHPh)^+$]; 187 [12, $(M-F-NHPh)^+$]; 172 (14, $C_9H_8N_4^+$)
4h	236 (2, M^+); 220 [5, $(M-NH_2)^+$]; 167 [2, $(M-CF_3)^+$]; 125 (8, $C_3H_4F_3N_2^+$); 110 (22); (96 (14); 69 (27); 57 (20); 43 (100); 42 (15); 30 (21, CH_3NH^+); 29 (16)
4i	322 (8, M^+); 253 [4, $(M-CF_3)^+$]; 249 [5, $(M-CO_2Et)^+$]; 220 [15, $(M-NHCH_2CO_2Et)^+$]; 197 (9, $C_6H_8F_3N_2O_2^+$); 179 (5, $C_5H_6F_3N_4^+$); 125 (11, $C_3H_4F_3N_2^+$); 110 (20); 69 (20); 58 (25, $C_2H_2O_2^+$); 43 (12); 30 (15, CH_3NH^+); 29 (100, $C_2H_5^+$/CHO^+/CH_3N^+)
4j [c]	371 [72, $(M+H)^+$]; 370 (6, M^+); 339 [31, $(M-MeO)^+$]; 311 [22, $(M-CO_2Me)^+$]; 301 [18, $(M-CF_3)^+$]; 282 [36, $(M-NHCO_2Me)^+$]; 278 [27, $(M-NHPh)^+$]; 263 (12, $C_6H_3F_6N_3O_2^+$); 242 (14, $C_{10}H_9F_3N_4^+$); 187 (8, $C_8H_6F_3N_2^+$)
6b	241/243 (31, M^+); 222/224 [3, $(M-F)^+$]; 206 [47, $(M-Cl^+$]; 172/174 [9, $(M-CF_3)^+$]; 111 (11, $C_2H_2F_3N_2^+$); 96 (5); 77 (15); 69 (100); 42 (15, $CH_2N_2^+$); 31 (8)
6c	255/257 (13, M^+); 236/238 [2, $(M-F)^+$]; 220 [16, $(M-Cl)^+$]; 219 [5, $(M-HCl)^+$]; 125 (6); 110 (14); 96 (8); 69 (43); 58 (27); 43 (100; 31 (9); 30 (18); 29 (27)
6d	313/315 (51, M^+); 294/296 [3, $(M-F)^+$]; 282/284 [4, $(M-MeO)^+$]; 278 [29, $(M-Cl)^+$]; 254/256 [81, $(M-CO_2Me)^+$]; 225/227 (63, $C_4F_6ClN^+$); 218 (13, $C_4H_2F_6N_3^+$); 140 (13, $C_5H_6N_3O_2^+$); 69 (100); 59 (18, $C_2H_3O_2^+$); 43 (11)
6e	327/329 (40, M^+); 292 [15, $(M-Cl)^+$]; 281/283 [15, $(M-EtOH)^+$]; 254/256 (97, $(M-CO_2Et)^+$]; 225/227 (68); 218 (10); 154 (11, $C_8H_8N_3O_2^+$); 69 (100); 29 (99, $C_2H_5^+$/CHO^+)
7b	205 (84, M^+); 186 [59, $(M-F)^+$]; 138 (12, $C_4NF_4^+$); 110 (98); 100 (26, $C_2F_4^+$); 91 (14); 69 (100); 50 (6); 31 (13)
7c [c]	32 (100, $CH_3NH_3^+$)
7c [d]	409 [45, (2, $C_4N_3F_6+H)^-$]; 204 (100, $C_4N_3F_6^-$); 176 (4, $C_4NF_6^-$)
7d [c]	74 (100, Me_4N^+)
8	257/259 (19, M^+); 238/240 [5, $(M-F)^+$]; 222 [78, $M-Cl)^+$]; 127 (9, $C_2H_2F_3N_2O^+$); 116 (10, $C_3F_2N^+$); 112 (11, $C_2HF_3NO^+$); 110 (13); 96 (36); 77 (8); 76 (10); 69 (100)

[a] EI spectra unless stated otherwise.
[b] Expressed as a percentage of the base peak.
[c] FAB (positive ion spectra).
[d] FAB (negative ion spectrum).

(b) 2-Amino-5-anilino-1,1,1,6,6,6-hexafluoro-3,4-diaza-hexa-2,4-diene (4g)

A solution of the 2-amino-5-anilinoazine **4g** (0.76 g, 2.55 mmol) in ethanol (10 cm^3) was heated under reflux (72 h) and the product (0.70 g) obtained after removal of the ethanol and volatile material in vacuo purified by sublimation at 50 °C in vacuo to give 4-phenyl-3,5-bis(trifluoromethyl)-4*H*-1,2,4-triazole (**2c**) (0.62 g, 2.21 mmol, 86%) which was identified by a comparison of its NMR and mass spectra with those reported [6].

(c) Methyl 2-anilino-5-glycinato-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (4j)

A solution of azine **4j** (0.50 g, 1.35 mmol) in ethanol (8 cm^3) was heated under reflux (80 h) and the product (0.42 g) obtained after removal of the ethanol and volatile material in vacuo purified by sublimation in vacuo to afford triazole **2c** (0.34 g, 1.15 mmol, 85%).

(d) 2-Amino-5-chloro-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (6b)

A solution of monoaminoazine **6b** (5.0 g, 20.7 mmol) in ethanol (7 cm^3) was heated under reflux (72 h) and the ethanol then removed in vacuo to give a waxy solid (3.60 g), which on purification by DCFC (eluant: $CHCl_3$) gave triazole **1a** (2.12 g, 10.4 mmol, 50%).

3.8.2. Method B in vacuo

(a) 2,5-Diamino-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (4c)

Diaminoazine **4c** (10.0 g, 45.05 mmol) was heated in vacuo in a Pyrex tube (ca. 260 cm^3) at 150 °C (12 h) and the resultant material washed from the tube with diethyl ether in which it was insoluble. Removal of the ether in vacuo gave the ammonium salt **7b** (9.81 g, 44.1 mmol, 98%).

(b) 2,5-Bis(methylamino)-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (4d)

Bis(methylamino)azine **4d** (10.0 g, 40.0 mmol), heated in vacuo in a Pyrex bulb (ca. 1 dm^3) at 120 °C (24 h), gave methylamine (0.72 g, 23.22 mmol, 58%), which was identified by IR and mass spectroscopy, and a non-volatile material which was washed from the bulb with diethyl ether and then filtered. The ether-insoluble residue (3.91 g) was identified as a mixture of methylammonium 3,5-bis(trifluoromethyl)-1,2,4-triazolide (**7c**) (2.46 g, 10.42 mmol, 26%) and tetramethylammonium 3,5-bis(trifluoromethyl-(1,2,4-triazolide (**7d**) (1.45 g, 5.21 mmol, 13%) (Analysis: Found: M^+, 32 and 74 and M^-, 204. Calc. for $CH_3NH_3^+$: M, 32; $(CH_3)_4N^+$: M, 74 and $C_4F_6N_3^-$: M, 204) in the ratio 2:1 (NMR spectroscopy).

Removal of the ether from the filtrate gave a yellow liquid (5.25 g) which on low-pressure distillation at 12 mmHg afforded (i) 1-methyl-3,5-bis(trifluoromethyl)-1*H*-1,2,4-triazole (**1b**) (nc) (0.12 g, 0.55 mmol, 1.5%) (Analysis: Found: C, 27.5; H, 1.4; N, 19.1; F, 52.4%; M^+, 219. $C_5H_3F_6N_3$ requires: C, 27.4; H, 1.4; N, 19.2; F, 52.1%; M, 219), b.p. 52 °C/12 mmHg, and (ii) 4-methyl-3,5-bis(trifluoromethyl)-4*H*-1,2,4-triazole (**2b**) (4.74 g, 21.64 mmol, 54%) (Analysis: Found: C, 27.5; H, 1.3; N, 19.1; F, 52.3%; M^+, 219. Calc. for $C_5H_3F_6N_3$: C, 27.4; H, 1.4; N, 19.2; F, 52.1%; M, 219), b.p. 86 °C/12 mmHg, which was identified by a comparison of its NMR spectra with those reported [3].

(c) Dimethyl 2,5-bis(glycinato)-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (4e)

Dimethyl diglycinatoazine **4e** (2.0 g, 5.46 mmol), heated in vacuo in a Pyrex tube (ca. 50 cm^3) at 120 °C (12 h), gave material which was washed from the tube with diethyl ether. Removal of the ether afforded a waxy solid (1.81 g), which on sublimation at room temperature gave 4-carbomethoxymethyl-3,5-bis(trifluoromethyl)-4*H*-1,2,4-triazole (**2e**) (nc) (0.84 g, 3.03 mmol, 55% conversion, 93% yield) (Analysis: Found: C, 30.5; H, 1.6; N, 14.9; F, 41.4%; M^+, 277. $C_7H_5F_6N_3O_2$ requires: C, 30.3; H, 1.8; N, 15.2; F, 41.2%; M^+, 277), m.p. 35 °C, and a residue of unchanged azine **4e** (0.81 g, 2.21 mmol, 41% recovered).

(d) Diethyl 2,5-bis(glycinato)-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (4f)

Diethyl diglycinatoazine **4f** (5.0 g, 12.7 mmol), heated in vacuo in a Pyrex tube (ca. 260 cm^3) at 140 °C (6 h), and the reaction worked-up as in the previous experiment, gave a dark liquid (4.39 g). The liquid was dissolved in a mixture of chloroform and light petroleum (1:10 v/v) and heated under reflux in the presence of decolourising charcoal. Filtration and removal of the solvent (rotary evaporator) afforded a colourless solid identified as 4-carboethoxymethyl-3,5-bis(trifluoromethyl)-4*H*-1,2,4-triazole (**2f**) (nc) (3.03 g, 10.4 mmol, 82%) (Analysis: Found: C, 32.7; H, 2.5; N, 14.1; F, 39.6%; M^+, 291. $C_8H_7F_6N_3O_2$ requires: C, 33.0; H, 2.4; N, 14.4; F, 39.2%; M, 291), m.p. 28–30 °C.

(e) 2-Amino-5-methylamino-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (4h)

Diaminoazine **4h** (11.00 g, 46.61 mmol), heated in vacuo in a Pyrex bulb (ca. 1 dm^3) at 120 °C (48 h), gave a volatile mixture (0.54 g) of ammonia and methylamine (IR spectroscopy and mass spectrometry). The non-volatile residue was washed from the tube with diethyl ether and the insoluble product filtered off and identified as methylammonium 3,5-bis(trifluoromethyl)-1,2,4-triazolide (**7c**) (nc) (3.44 g, 14.58 mmol, 31%) (Analysis: Found: C, 25.6; H, 2.5; N, 23.6; F, 48.2%. $C_5H_6F_6N_4$ requires: C, 25.4; H, 2.5; N, 23.7; F, 48.3%), m.p. 222–224 °C. Removal of the ether from the filtrate (rotary evaporator) gave a residue (6.66 g) which was shown (^1H and ^{19}F NMR spectroscopy) to be a mixture of 3,5-bis(trifluoromethyl)-1*H*-1,2,4-triazole (**1a**) (1.10 g, 5.37 mmol, 11%) and 4-methyl-3,5-bis(trifluoromethyl)-4*H*-1,2,4-triazole (**2b**) (5.56 g, 25.39 mmol, 54%).

3.9. Rearrangement of 3,6-bis(trifluoromethyl)-1,2-dihydro-s-tetrazine (9)

A solution of the 1,2-dihydro-s-tetrazine **9** (5.00 g, 22.72 mmol) in acetic acid (35 cm^3), heated under

reflux (60 h) and the solvent then removed in vacuo, gave a waxy solid (4.88 g) which was separated by DCFC (eluant: $CHCl_3$) into its two components: (i) 4-amino-3,5-bis(trifluoromethyl)-4*H*-1,2,4-triazole (**2g**) (3.05 g, 13.86 mmol, 61%) (Analysis: Found: C, 22.1; H, 0.8; N, 25.1; F, 51.9%; M^+, 220. Calc. for $C_4H_2F_6N_4$: C, 21.8; H, 0.9; N, 25.4%; M, 220), m.p. 76–78 °C, lit. value [14] m.p. 77 °C, identified by a comparison of its IR and NMR spectra with those reported [14]; and (ii) 4-acetylamino-3,5-bis(trifluoromethyl)-4*H*-1,2,4-triazole (**2h**) (nc) (1.49 g, 5.69 mmol, 25%) (Analysis: Found: C, 27.8; H, 1.4; N, 21.4; F, 43.4%; M^+, 262. $C_6H_4F_6N_4O$ requires: C, 27.5; H, 1.5; N, 21.4; F, 43.5%; M, 262), m.p. 126–128 °C.

3.10. Reaction of ammonium 3,5-bis(trifluoromethyl)-1,2,4-triazolide (7b) with hydrochloric acid

A mixture of the ammonium salt **7b** (5.0 g, 22.5 mmol) and hydrochloric acid (20 cm^3, 4 M) was stirred at room temperature (0.5 h), then diethyl ether (50 cm^3) was added and stirring continued (5 min). The ether layer was separated, the aqueous layer extracted with diethyl ether (4×25 cm^3) and the combined ether extracts dried ($MgSO_4$). The ether was then removed (rotary evaporator) to give 3,5-bis(trifluoromethyl)-1*H*-1,2,4-triazole (**1a**) (3.46 g, 16.9 mmol, 75%).

All of the new compounds (**1b**, **2e**, **2f**, **2h**, **4c–j**, **6b–e**, **7b–d** and **8**) showed IR bands (ν_{max}) (cm^{-1}) at 1680–1620 (s) (C=N str.), 1250–1130 (s) (C–F str.) and 765–740 (CF_3 def.); additional bands were present in the spectra of (i) the aminoazines (**4c–j** and **6b–e**) at 3450–3320 (m) (N–H str.), (ii) the glycine derivatives (**2e**, **2f**, **4e**, **4f**, **6d** and **6e**) at 1760–1720 (s) (ester C=O str.), (iii) the amide (**2h**) at 3180 (m) (N–H str.) and 1700 (s) (C=O str.), (iv) the oxime (**8**) at 3300–3100 (br.) (O–H str.), (v) the compounds containing alkyl groups (**1b**, **2d**, **2e**, **4d–f**, **4h–j**, **6c–e**, **7c** and **7d**) at 2980–2850 (m) (alkyl C–H str.) and (vi) the anilino derivatives (**4g** and **4j**) at 3070–3050 (m) (aromatic C–H str.) and ca. 740 (m) and ca. 710 (m) (C–H out-of-plane bending). The ^1H, ^{19}F and ^{13}C NMR spectra are recorded in Table 3 and the MS data are summarised in Table 4.

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