

Unsaturated nitrogen compounds containing fluorine. Part 11 [1]. Reaction of 2,5-dichloro- and 2,5-di-iodo-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene with diamines [2]

Ahmed O.A. Eltoun, Neil J. O'Reilly and Anthony E. Tipping*

Chemistry Department, University of Manchester, Institute of Science and Technology, Manchester M60 1QD (UK)

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Abstract

Treatment of the azines $\text{CF}_3\text{CX}=\text{N}-\text{N}=\text{CXCF}_3$ [$\text{X}=\text{Cl}$ (**1a**) and $\text{X}=\text{I}$ (**1b**)] with diamines $\text{H}_2\text{N}(\text{CH}_2)_n\text{NH}_2$ ($n=2, 3, 4, 6, 9, 12$) gives 2:1 substitution products, the open-chain dihalogenotetraenes $\text{CF}_3\text{CX}=\text{NN}=\text{C}(\text{CF}_3)\text{NH}(\text{CH}_2)_n\text{NHC}(\text{CF}_3)=\text{NN}=\text{CXCF}_3$, and/or 2:2 substitution products, the cyclotetraenes $\text{CF}_3\text{C}=\text{NN}=\text{C}(\text{CF}_3)\text{NH}(\text{CH}_2)_n\text{NHC}(\text{CF}_3)=\text{NN}=\text{C}(\text{CF}_3)\text{NH}(\text{CH}_2)_n\text{NH}$; the former compounds are the precursors of the cyclic compounds. In the reaction of azine **1a** with 1,6-diaminohexane, a further product, the bis(triazole) $\text{CF}_3\text{C}=\text{NN}=\text{C}(\text{CF}_3)\text{N}(\text{CH}_2)_6\text{N}(\text{CF}_3)=\text{NN}=\text{C}(\text{CF}_3)$, is also formed. The reaction of azine **1a** with 1,2-diaminobenzene gives 2-(trifluoromethyl)benzimidazole in excellent yield

Introduction

The reactions of the dichloroazine **1a** with primary and secondary amines [3, 4], halide ion (F^- and I^-) [1] and oxygen and sulphur-centred nucleophiles [1] to give mono- and/or di-substitution products have been reported and reactions with triethylamine in light [5] and phenyl-lithium [6] have been investigated. Substitution reactions of the di-iodoazine **1b** with aniline and diethyl phenylmalonate have also been carried out [1].

In an extension of this work, we now report the results of an investigation of the reactions of azines **1a** and **1b** with aliphatic diamines and of azine **1a** with 1,2-diaminobenzene.

Experimental

General techniques

Reaction products were purified or separated from mixtures as described in the text [dry column 'flash' chromatography (DCFC) used silica gel (60H Merck GF₂₅₆) purchased from BDH Chemicals Ltd.]. ¹H nuclear magnetic resonance (NMR) spectra were run either on Perkin-Elmer R32 (90 MHz) or R34 (220 MHz) spectrometers [reference internal tetramethylsilane (TMS)] and ¹⁹F NMR spectra were recorded on a Perkin-Elmer R32 (84.6 MHz) spectrometer [ref-

erence external trifluoroacetic acid (TFA)]. The NMR spectra were run as solutions [in CDCl_3 or $(\text{CD}_3)_2\text{CO}$ as indicated in the text] and chemical shifts to low field of reference are designated positive.

Infrared (IR) spectra were recorded on Perkin-Elmer 197 or 257 spectrophotometers using KBr discs for solid samples and NaCl plates for liquid films.

Low-resolution electron impact (EI) mass spectra were run on an AEI MS 902 instrument operating at 70 eV.

Melting points are uncorrected.

Elemental analyses (for C, H, N and F) were carried out by the Departmental analytical service using standard methods.

Starting materials

The diamines were commercial samples (Aldrich). The dichloroazine **1a** was prepared (60%) by reaction of TFA with hydrazine and treatment of the resulting 1,2-bis(trifluoroacetyl)hydrazine with *N,N*-dimethylaniline hydrochloride and phosphoryl chloride [2, 4]. Azine **1a** was converted into the corresponding di-iodoazine **1b** (94%) by treatment with a solution of sodium iodide (1:2.5 molar ratio) in acetone [1].

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

(a) With 1,2-diaminoethane in the presence of triethylamine

A solution of the dichloroazine **1a** (1.90 g, 7.3 mmol) in diethyl ether (25 cm³) and a solution of 1,2-

*To whom all correspondence should be addressed.

diaminoethane (0.44 g, 7.3 mmol) in diethyl ether (25 cm³) were added simultaneously over a period of 2 h to a stirred solution of triethylamine (3.64 g, 36.0 mmol) in diethyl ether (30 cm³) and stirring was continued (69 h). The white precipitate of triethylamine hydrochloride (1.61 g, 11.7 mmol, 80%) was filtered off and the solvent was removed from the filtrate under reduced pressure to give a residue (1.32 g) which was recrystallized first from light petroleum/chloroform and then from aqueous ethanol to afford a beige solid identified as 1,4,9,12-tetrakis(trifluoromethyl)-2,3,5,8,10,11,13,16-octa-azacyclohexadeca-1,3,9,11-tetraene (**2a**) (nc) (0.54 g, 1.10 mmol, 30%). (Analysis: Found: C, 29.1; H, 2.2; F, 46.3; N, 22.3%; mol.wt., 496. C₁₂H₁₂F₁₂N₈ requires: C, 29.0; H, 2.4; F, 46.0; N, 22.6%; mol.wt., 496). ¹H NMR [(CD₃)₂CO] δ: 7.2 (br., 2H, 2NH); 6.7 (br., 2H, 2NH); 3.7 (mult., 4H, 2CH₂N); and 3.5 (mult., 4H, 2CH₂N) ppm. ¹⁹F NMR δ: +15.8 to +8.2 (10s, CF₃) ppm. IR (ν_{max}) (cm⁻¹): 3450 and 3350 (m) (N–H str.); 1630 (s) (C=N str.); 1540 (m) (N–H bend); and 1205–1120 (s) (C–F str.). Mass spectrum *m/z*: 496 (11.2%, M⁺); 436 [28.7, (M–H₂NCH₂NH₂)⁺]; 219 (25.7, C₅H₃F₆N₃⁺); 218 (36.4, C₅H₂F₆N₃⁺); 139 (46.1, C₄H₆F₃N₂⁺); 137 (51.8, C₄H₄F₃N₂⁺); 125 (32.8, C₃H₄F₃N₂⁺); 110 (28.4, C₃HF₃N₂⁺); 96 (33.2, C₂HF₃N⁺); 69 (100.0, CF₃⁺); 43 (62.7, C₂H₅N⁺); 42 (41.9, C₂H₄N⁺); 30 (91.6, CH₄N⁺); and 29 (50.2, CH₃N⁺). The structure was confirmed by an X-ray crystallographic study [7].

(b) *With 1,2-diaminoethane in the absence of triethylamine*

A solution of the dichloroazine **1a** (0.80 g, 3.1 mmol) in diethyl ether (10 cm³) was added during 15 min to stirred 1,2-diaminoethane (0.40 g, 6.5 mmol) and stirring was continued for 15 min. The volatile material was removed under reduced pressure and the residue was treated with aqueous sodium hydroxide (2 M, 3 cm³), extracted with diethyl ether (3 × 10 cm³), dried (MgSO₄) and the solvent evaporated. The resulting solid was further dried (vacuum desiccator) and was identified as tetraene **2a** (0.40 g, 0.81 mmol, 52%).

(c) *With 1,3-diaminopropane*

A solution of the dichloroazine **1a** (4.0 g, 15.3 mmol) in diethyl ether (30 cm³) was added dropwise to a stirred solution of 1,3-diaminopropane (2.27 g, 30.6 mmol) in diethyl ether (40 cm³) and stirring was continued (16 h). The precipitate of 1,3-diaminopropane hydrochloride (2.02 g, 13.7 mmol, 45%) was filtered off and the solvent was removed from the filtrate under reduced pressure to give a solid (3.47 g). Sublimation of the product (1.73 g) *in vacuo* at 110 °C gave an unidentified sublimate (0.75 g) which contained little fluorine (IR spectroscopy) and a residue identified

as 1,4,10,13-tetrakis(trifluoromethyl)-2,3,5,9,11,12,14,18-octa-azacyclo-octadeca-1,3,10,12-tetraene (**2b**) (nc) (0.90 g, 1.7 mmol, 44%). (Analysis: Found: C, 32.1; H, 3.3; F, 43.7; N, 21.2%; mol.wt., 524. C₁₄H₁₆F₁₂N₈ requires: C, 32.1; H, 3.1; F, 43.5; N, 21.4%; mol.wt., 524). ¹H NMR [(CD₃)₂CO] δ: 6.58 (br., 2H, 2NH); 3.43 (mult., 4H, 2CH₂N); and 1.80 (mult., 2H, CH₂) ppm. ¹⁹F NMR δ: major singlet bands at +14.9 and +11.4 and minor bands at +9.8, +9.4 and +9.0 ppm. IR (ν_{max}) (cm⁻¹): 3325 (s) (N–H str.); 1630 (s) (C=N str.); 1530 (m) (N–H bend); and 1230–1120 (s) (C–F str.). Mass spectrum *m/z*: 524 (3.5%, M⁺); 171 (4.7, C₄F₅N₂⁺); 153 (100.0, C₅H₈F₃N₂⁺); 152 (27.9, C₅H₇F₃N₂⁺); 151 (11.0, C₅H₆F₃N₂⁺); 96 (5.8, C₂HF₃N⁺); 69 (9.3, CF₃⁺); 56 (8.8, C₂H₄N₂⁺); 30 (18.7, CH₄N⁺); and 29 (17.0, CH₃N⁺).

(d) *With 1,6-diaminohexane*

A solution of 1,6-diaminohexane (1.85 g, 15.9 mmol) in diethyl ether (40 cm³) was added to a stirred solution of the dichloroazine **1a** (4.15 g, 15.9 mmol) in diethyl ether (10 cm³) and stirring was continued (16 h). The white precipitate (A) (2.95 g) was filtered off and was shown to contain fluorine [IR: 1220–1160 cm⁻¹ (C–F str.)] and it and the filtrate (B) were examined further.

The solid A was stirred with water (20 cm³) and dilute sodium hydroxide (2 M) was added until the solution was basic to litmus. Attempted extraction with dichloromethane gave an emulsion which could not be cleared by the addition of ether. The mixture was therefore acidified with dilute sulphuric acid (2 M) and filtered to produce a white solid C (0.50 g). Extraction of the filtrate with diethyl ether (2 × 50 cm³), followed by drying (MgSO₄) and removal of the solvent under reduced pressure, afforded a further amount of solid C (0.40 g). The combined solid C was treated with ether (30 cm³) and the insoluble product (D) [*R_F* = 0.15; light petroleum/dichloromethane (1:1 v/v)] was filtered off and the filtrate (E) stored.

The solid D was identified as the monohydrate of 1,6-bis[3,5-bis(trifluoromethyl)-4*H*-1,2,4-triazolo]hexane (**5b**) (0.36 g, 0.70 mmol, 10%). (Analysis: Found: C, 32.7; H, 3.1; N, 16.1%. C₁₄H₁₂F₁₂N₆·H₂O requires: C, 33.0; H, 2.8; N, 16.5%; m.p. 89 °C. IR (ν_{max}) (cm⁻¹): 3700–3120 (br.) (O–H str.). The NMR and mass spectra were virtually identical to those of the anhydrous bis-triazole **5a** (see below).

The solvent was removed from the filtrate E under reduced pressure and the residue was again treated with ether (30 cm³) and the ether-insoluble solid F (*R_F* = 0.24; eluant as before) was filtered off and the filtrate G retained. The solid F was identified as 1,6-bis[3,5-bis(trifluoromethyl)-4*H*-1,2,4-triazolo]hexane (**5a**) (nc) (0.17 g, 0.35 mmol, 4%) (nc). (Analysis:

Found: C, 34.3; H, 2.6; F, 46.0; N, 17.1%; $C_{14}H_{12}F_{12}N_6$ requires: C, 34.2; H, 2.5; F, 46.3; N, 17.1%; m.p. 104–105 °C. 1H NMR ($CDCl_3$) δ : 4.20 (t, 4H, $2CH_2N$, $J=8$ Hz); 1.86 (mult, 4H, $2CH_2$); and 1.50 (mult., 4H, $2CH_2$) ppm. ^{19}F NMR δ : +16.4 (s, CF_3) ppm. IR (ν_{max}) (cm^{-1}): 1620–1600 (s) ($C=N$ str.); 1250–1100 (s) ($C-F$ str.); and 760 (s) (CF_3 def.). Mass spectrum m/z : 493 [1.0%, ($M+H$) $^+$]; 423 [1.7, ($M-CF_3$) $^+$]; 218 (56.2, $C_5H_2F_6N_3^+$); 208 (8.0, $C_4H_2F_6N_3^+$); 95 (8.6, $C_2F_3N^+$); 83 (19.3, $C_6H_{11}^+$ and $C_3H_9N^+$); 69 (33.8, CF_3^+); 55 (100.0, $C_3H_5N^+$); 43 (19.5, $C_2H_5N^+$); and 41 (74.4, $C_2H_3N^+$).

Removal of the solvent from filtrate G under reduced pressure gave a dark unidentified solid (0.13 g) [m.p. 98 °C (decomp.)] which gave only one spot on TLC [$R_F=0.59$; light petroleum/dichloromethane (1:1 v/v)]. IR (ν_{max}) (cm^{-1}): 1760–1700 (s) ($C=O$ str.?). and 1240–1220 (s) ($C-F$ str.). Mass spectrum m/z : 331 (0.1%); 224 (4.1); 155 (31.0); 99 (7.5); 97 (10.5, CF_3CO^+); 69 (100.0, CF_3^+); 50 (13.0, CF_2^+); and 45 (10.9).

Examination of the original filtrate B by TLC (diethyl ether) showed the presence of a major ($R_F=0.90$) and a minor baseline component. Separation of the major component by DCFC [light petroleum/dichloromethane (1:1 v/v)] gave an orange oil (2.04 g) which on re-examination by TLC (diethyl ether) was shown to consist of a major ($R_F=0.89$) and a minor ($R_F=0.95$) component. The material was identified as a mixture of 5,14-bis(trifluoromethyl)-2,17-dichloro-1,1,1,18,18,18-hexafluoro-3,4,6,13,15,16-hexa-azaoctadeca-2,4,14,16-tetraene (**3a**) (nc) (1.64 g, 2.90 mmol, 36%) [Analysis: Found: mol.wt., 565/567/569 for ($M+H$) $^+$. Calc. for $C_{14}H_{14}Cl_2F_{12}N_6$: mol.wt., 565.2] and 1,4,13,16-tetrakis(trifluoromethyl)-2,3,5,12,14,15,17,24-octa-azacyclobutaecosa-1,3,13,15-tetraene (**2d**) (nc) (0.40 g, 0.65 mmol, 8%) (Analysis: Found: mol.wt., 608. Calc. for $C_{20}H_{28}F_{12}N_8$: mol.wt., 608) present in the ratio 9:2 (Analysis: Found: C, 31.5; H, 2.9; Cl, 10.5; F, 40.2; N, 15.7%). Calc. for a 9:2 mixture of $C_{14}H_{14}Cl_2F_{12}N_6$ and $C_{20}H_{28}F_{12}N_8$: C, 31.5; H, 2.9; Cl, 10.3; F, 39.8; N, 15.5%). 1H NMR ($CDCl_3$) δ : 6.10–5.65 (broad, 2H, 2NH); 3.60–3.15 (complex, 4H, $2CH_2N$); and 2.00–1.10 (complex 8H, $4CH_2$) ppm. ^{19}F NMR δ : for **3a**: +11.8 (s, CF_3); +9.9 (s, CF_3); +9.3 (s, CF_3CCl); +9.13 (s, CF_3CCl); and +9.11 (s, CF_3CCl) ppm in the ratio 2:3:2:1:2; δ : for **2d**: +16.3; +16.2; +10.6; and +10.5 ppm in the ratio 5:7:7:3. IR (ν_{max}) (cm^{-1}): 3460 and 3400–3200 (m) ($N-H$ str.); 1660–1610 (s) ($C=N$ str.); 1250–1120 (s) ($C-F$ str.); and 755 (s) (CF_3 def.). Mass spectrum m/z : 608 [1.1%, $C_{20}H_{28}F_{12}N_8^+$ (M_B^+)]; 565/567/569 [100.0, $C_{14}H_{14}Cl_2F_{12}N_6^+$ (M_A+H) $^+$]; 529/531 [48.2, $C_{14}H_{14}ClF_{12}N_6^+$ (M_A-Cl) $^+$]; and 69 (14.1, CF_3^+).

(e) With 1,6-diaminohexane in the presence of triethylamine

A solution of the dichloroazine **1a** (2.61 g, 10.0 mmol) in diethyl ether (20 cm^3) was added to a stirred solution of the diamine (1.16 g, 10.0 mmol) and triethylamine (2.04 g, 20.1 mmol) in diethyl ether (20 cm^3) and since an exothermic reaction took place the mixture was cooled (ice bath). Stirring was continued (2 h), the white precipitate (1.39 g) filtered off, and the filtrate washed with water (2×40 cm^3), dried ($MgSO_4$) and the solvent removed under reduced pressure to give a low-melting solid (2.38 g). Recrystallization (aqueous ethanol) gave a mixture (1.85 g) of compounds **3a** (1.27 g, 2.24 mmol, 45%) and **2d** (0.58 g, 0.96 mmol, 19%) (Analysis: Found: C, 32.8; H, 3.1; N, 15.9%. Calc. for a mixture of $C_{14}H_{14}Cl_2F_{12}N_6$ and $C_{20}H_{28}F_{12}N_8$ in the ratio 7:3: C, 32.7; H, 3.1; N, 15.9%).

(f) With 1,2-diaminobenzene

A solution of freshly recrystallized 1,2-diaminobenzene (0.57 g, 5.29 mmol) in diethyl ether (50 cm^3) and a solution of the dichloroazine **1a** (1.38 g, 5.29 mmol) in diethyl ether (30 cm^3) were added simultaneously over a period of 45 min to a stirred solution of triethylamine (0.53 g, 5.29 mmol) in diethyl ether (25 cm^3) at 0 °C and stirring was continued (3 h). The precipitate of triethylamine hydrochloride (0.64 g, 4.7 mmol, 89%) was filtered off and the solvent removed under reduced pressure from the filtrate to give a white solid (1.12 g) which was recrystallized from aqueous ethanol and identified as 2-(trifluoromethyl)-benzimidazole (**11**) (0.95 g, 5.1 mmol, 97%) (Analysis: Found: C, 52.0; H, 2.7; F, 30.6; N, 15.1%; mol.wt., 186. Calc. for $C_8H_5F_3N_2$: C, 51.6; H, 2.7; F, 30.6; N, 15.1%; mol.wt., 186), m.p. 208 °C; lit. value [8] m.p. 210 °C, by a comparison of its IR spectrum with that reported [9].

Reactions of 2,5-di-iodo-1,1,1,6,6,6-hexafluoro-3,4-diaza-hexa-2,4-diene (**1b**)

(a) With 1,4-diaminobutane

A solution of the diamine (0.39 g, 4.40 mmol) in diethyl ether (40 cm^3) was added dropwise (0.5 h) to a stirred solution of the di-iodoazine **1b** (1.58 g, 3.56 mmol) in diethyl ether (10 cm^3) and stirring continued (2 h), when examination of the reaction mixture by TLC indicated an absence of azine **1b**. The precipitate (0.76 g) of 1,4-diaminobutane hydroiodide (0.05 g, 0.23 mmol) and 1,4-diaminobutane dihydroiodide (0.71 g, 2.07 mmol) (ratio 1:9) (Analysis: Found: C, 14.8; H, 4.3; N, 8.5%. Calc. for a mixture of $C_4H_{13}IN_2$ and $C_4H_{14}I_2N_2$ in the ratio 1:9: C, 14.8; H, 4.3; N, 8.6%) was filtered off and removal of the solvent under reduced pressure from the filtrate gave a non-volatile oil (1.34 g). This oil was purified by DCFC (light petroleum/

diethyl ether) to give a major fraction (1.16 g) identified as a mixture (ratio 7:2) of 2,15-di-iodo-1,1,1,16,16,16-hexafluoro-4,11-bis(trifluoromethyl)-3,4,6,11,13,14-hexa-azaheptadeca-2,4,12,14-tetraene (**4a**) (nc) (0.96 g, 1.33 mmol, 75%) and 1,4,11,14-tetrakis(trifluoromethyl)-2,3,5,10,12,13,15,20-octa-azacycloicos-1,3,11,13-tetraene (**2c**) (nc) (0.20 g, 0.38 mmol, 21%) (Analysis: Found: C, 23.3; H, 1.9; N, 13.3%. Calc. for a 7:2 mixture of $C_{12}H_{10}F_{12}I_2N_6$ and $C_{16}H_{20}F_{12}N_8$: C, 23.3; H, 1.9; N, 13.6%). 1H NMR ($CDCl_3$) δ : 5.95 (br., 2H, NH); 3.65–3.30 (complex, 4H, CH_2N); and 1.90–1.55 (complex, 4H, CH_2) ppm. ^{19}F NMR δ : for **4a**: singlets at +12.7 (9F); +12.3 and +12.2 (6F); +11.6 and +11.5 (9F); and +9.8 (5F) ppm; for **2c**: major singlets at +10.8 and +10.7; and minor singlets at +16.2; +13.1; +11.9; +11.2; and +10.4 ppm. IR (ν_{max}) (cm^{-1}): 3450 and 3350 (s) (N–H str.); 1640–1620 (s) (C=N str.); 1570 and 1540 (s) (N–H bend); 1210–1120 (s) (C–F str.); and 785, 760 and 725 (s) (CF_3 def.). Mass spectrum m/z : 593 [5.0%, ($M_A - I$) $^+$]; 552 (3.2, M_B^+); 388 [7.8, ($M_B - CF_3 - CF_3N$) $^+$]; 386; 219 (22.7, $C_5H_3F_6N_3^+$); 139 (26.0, $C_5H_8F_3N^+$); 137 (20.7, $C_5H_6F_3N^+$); 128 (24.0, $C_6H_9FN_2^+$); 127 (37.6, I^+ and $C_6H_8FN_2^+$); 72 (29.9, $C_4H_{10}N^+$); 70 (41.7, $C_4H_8N^+$); 69 (100.0, CF_3^+ and $C_4H_7N^+$); 55 (76.7, $C_3H_5N^+$); and 43 (26.5, $C_2H_5N^+$).

(b) With 1,6-diaminohexane

A solution of the diamine (0.42 g, 3.65 mmol) in diethyl ether (20 cm^3) was added dropwise (0.5 h) to a stirred solution of the azine **1b** (1.62 g, 3.65 mmol) in diethyl ether (15 cm^3) and stirring was continued (26 h). The white precipitate of 1,6-diaminohexane dihydrochloride (0.68 g, 1.83 mmol, 50%) (Analysis: Found: C, 19.6; H, 5.2; N, 7.8%. $C_6H_{18}I_2N_2$ requires: C, 19.4; H, 4.9; N, 7.5%) was filtered off and the solvent removed from the filtrate under reduced pressure to give a solid (1.47 g). This was shown by TLC to contain a major product and a small amount of reactant diamine. The product was purified by DFC (light petroleum/diethyl ether) to afford a pale yellow solid identified as 2,17-di-iodo-1,1,1,18,18,18-hexafluoro-5,14-bis(trifluoromethyl)-3,4,6,13,15,16-hexa-azaoctadeca-2,4,14,16-tetraene (**4b**) (nc) (1.36 g, 1.82 mmol, 99%). (Analysis: Found: C, 22.8; H, 2.0; F, 30.3; N, 11.5%. $C_{14}H_{14}F_{12}I_2N_6$ requires: C, 22.5; H, 1.9; F, 30.5; N, 11.2%), m.p. 67–68 °C. 1H NMR ($CDCl_3$) δ : 5.82 and 5.70 (2br., 2H, 2NH); 3.48 (complex, 4H, $2CH_2N$); 1.72 (complex, 2H, CH_2); 1.62 (complex, 2H, CH_2); and 1.42 (complex, 4H, $2CH_2$) ppm. ^{19}F NMR δ : singlets at +12.7 (6F); +12.3 (3F); +12.2 (3F); +11.4 (6F); and +9.7 (6F) ppm. IR (ν_{max}) (cm^{-1}): 3450 (s) (N–H str.); 1628 (s) C=N str.); 1562 (s) (N–H bend); and 1210–1120 (s) (C–F str.). Mass spectrum m/z : 621 [6.7%, ($M - I$) $^+$]; 219 (9.7, $C_5H_3F_6N_3^+$); 195 (100.0, $C_8H_{14}F_3N_2^+$); 100 (16.3, $C_6H_{14}N^+$); 83 (17.4, $C_6H_{11}^+$);

69 (23.4, CF_3^+); 55 (70.7, $C_3H_5N^+$); and 41 (29.1, $C_2H_3N^+$).

(c) With 1,9-diaminononane

A suspension of the diamine (0.73 g, 4.6 mmol) in diethyl ether (30 cm^3) was added slowly (0.5 h) to a stirred solution of the azine **1b** (2.04 g, 4.59 mmol) in diethyl ether (10 cm^3) and stirring continued (16 h). The precipitate of the diamine dihydroiodide (0.92 g, 2.22 mmol, 48%) was filtered off and removal of the solvent under reduced pressure from the filtrate gave crude product (1.99 g) which TLC indicated contained a small amount of reactant diamine. The sample was dissolved in ether (10 cm^3), light petroleum (5 cm^3) then added and the resulting precipitate of the excess of diamine filtered off. Removal of the solvent from the filtrate under reduced pressure gave an orange oil identified as 2,20-di-iodo-1,1,1,21,21,21-hexafluoro-5,17-bis(trifluoromethyl)-3,4,6,16,18,19-hexa-azaheptacos-2,4,17,19-tetraene (**4c**) (nc) (1.72 g, 2.18 mmol, 95%). Analysis: Found: C, 26.1; H, 2.7; F, 29.1; N, 10.7%. $C_{17}H_{20}F_{12}I_2N_6$ requires: C, 25.8; H, 2.6; F, 28.9; N, 10.6%). 1H NMR ($CDCl_3$) δ : 5.83 and 5.68 (2br., 2H, 2NH); 3.49 (q, 4H, $2CH_2NH$, $J = 7.3$ Hz); 1.73 (complex, 2H, CH_2); 1.62 (complex, 2H); and 1.40–1.30 (complex, 10H, $5CH_2$) ppm. ^{19}F NMR δ : singlets at +12.9; +12.4; +11.6; and +9.9 ppm in the ratio 1:1:1:1. IR (ν_{max}) (cm^{-1}): 3450 (s) (N–H str.); 1630 (s) (C=N str.); 1200–1140 (s) (C–F str.); and 725 (s) (CF_3 def.). Mass spectrum m/z : 663 [7.7%, ($M - I$) $^+$]; 568 [2.5, ($M - I - CF_3CN$) $^+$]; 237 (49.9, $C_{11}H_{20}F_3N_2^+$); 219 (8.2, $C_{10}H_{14}F_3N_2^+$); 127 (8.4, I^+); 83 (22.8, CF_3N^+); 69 (58.0, CF_3^+); 55 (100.0, $C_3H_5N^+$); 43 (57.3, $C_2H_5N^+$); 41 (90.4, $C_2H_3N^+$); 30 (67.7, CH_4N^+); and 29 (94.2, CH_3N^+).

(d) With 1,12-diaminododecane

A solution of the diamine (2.19 g, 10.9 mmol) in diethyl ether (40 cm^3) was added slowly (0.5 h) to a stirred solution of the azine **1b** (2.42 g, 5.45 mmol) in diethyl ether (10 cm^3) and stirring continued (5 h). The white precipitate of the diamine dihydroiodide (2.50 g, 5.45 mmol, 50%) was filtered off and the solvent removed under reduced pressure from the filtrate to give a semi-solid material (2.13 g) which was shown by TLC to contain one major and two very minor components. The major component was purified by DFC (light petroleum/dichloromethane) to give a solid (2.03 g), m.p. 47–51 °C, which was identified as a 66:34 mixture of 2,23-di-iodo-1,1,1,24,24,24-hexafluoro-5,20-bis(trifluoromethyl)-3,4,6,19,21,22-hexa-azabutaeicos-2,4,20,22-tetraene (**4d**) (nc) (1.37 g, 1.65 mmol, 61%) and 1,4,19,22-tetrakis(trifluoromethyl)-2,3,5,18,20,21,23,36-octa-azacyclohexadecaicos-1,3,19,21-tetraene (**2e**) (nc) (0.66 g, 0.85 mmol, 31%). (Analysis: Found: C,

35.7; H, 4.3; F, 27.8; N, 11.4%. Calc. for a 66:34 mixture of $C_{20}H_{26}F_{12}I_2N_6$ and $C_{32}H_{52}F_{12}N_8$: C, 35.9; H, 4.4; F, 28.1; N, 11.6%. 1H NMR ($CDCl_3$) δ : 5.90 (br., 2H, 2NH); 3.34 (complex, 4H, 2CH₂N); and 1.40–1.28 (complex, 2OH, 10CH₂) ppm. ^{19}F NMR δ : for **4d**: singlets at +12.8; +12.4; +11.6; and +9.9 ppm in the ratio 1:1:1:1; for **2e**: +10.1 (s, CF₃) ppm. IR (ν_{max}) (cm^{-1}): 3460 (s) (N–H str.); 3360–3280 (m) (N–H str.); 1640–1610 (s) (C=N str.); 1570–1535 (s) (N–H bend); 1220–1120 (s) C–F str.; and 740–720 (s) (CF₃ def.). Mass spectrum m/z : 576 [5.4%, ($M_A - 2HI$)⁺]; 507 [6.0, ($M_A - 2HI - CF_3$)⁺]; 481 [3.6, ($M_A - 2HI - CF_3CN$)⁺]; 388 (4.3, $M_B^+/2$); 279 (19.3, $C_{14}H_{26}F_3N_2^+$); 149 (20.2, $C_{11}H_{17}^+$ and $C_{10}H_{15}N^+$); 128 (20.2, $C_9H_{20}^+$ and $C_8H_{18}N^+$); 111 (20.7, $C_8H_{15}^+$ and $C_7H_{13}N^+$); 97 (25.7, $C_7H_{13}^+$ and $C_6H_{11}N^+$); 95 (23.3, $C_7H_{11}^+$ and $C_6H_9N^+$); 83 (35.8, $C_6H_{11}^+$ and $C_5H_9N^+$); 81 (28.5, $C_6H_9^+$ and $C_5H_7N^+$); 77 (24.1, $C_6H_5^+$); 71 (28.9, $C_4H_9^+$); 69 (65.9, CF₃⁺); 59 (31.4, $C_3H_9N^+$); 57 (63.3, $C_3H_7N^+$); 56 (36.6, $C_3H_6N^+$); 55 (100.0, $C_3H_5N^+$); 43 (77.2, $C_2H_5N^+$); and 41 (90.0, $C_2H_3N^+$).

Reaction of the di-iodotetraene **4b** with 1,6-diaminohexane

A solution containing the di-iodotetraene **4b** (0.04 g, 0.053 mmol) and 1,6-diaminohexane (0.05 g, 0.43 mmol) in diethyl ether (5 cm³) was stirred (18.5 h) with the reaction monitored by TLC (diethyl ether). After this time, unchanged diamine ($R_F=0$) and unchanged di-iodotetraene ($R_F=0.91$) were still present, but a new spot ($R_F=0.98$) was observed and a white precipitate had been formed. The precipitate was filtered off and the solvent evaporated from the filtrate under reduced pressure to afford an oil (0.05 g). The oil was washed with water (2×10 cm³) to remove reactant diamine and then extracted with diethyl ether (2×12.5 cm³). The ethereal solution was dried (MgSO₄) and the ether removed *in vacuo* to give a solid (0.03 g) which was recrystallized (light petroleum/diethyl ether) to give a mixture (ratio 26:74) of unchanged di-iodotetraene **4b** and the cyclotetraene **2d**. (Analysis: Found: C, 35.1; H, 3.8; N, 15.8%. Calc. for a 26:74 mixture of $C_{14}H_{14}F_{12}I_2N_6$ and $C_{20}H_{28}F_{12}N_8$: C, 35.1; H, 3.9; N, 16.3%).

Pyrolysis of the di-iodotetraene **4c**

The di-iodotetraene **4c** (0.18 g, 0.23 mmol), heated *in vacuo* in a sealed Pyrex ampoule (*c.* 30 cm³) at 168 °C (312 h), charred to some extent and iodine was liberated. The tube cracked on opening, but the non-volatile material was extracted with ether (2×10 cm³), filtered to remove the charred material, and the filtrate treated with sodium metabisulphite (2 M, 10 cm³) and then with water (10 cm³). The ethereal solution was dried (MgSO₄) and the solvent removed *in vacuo* to

give a dark oil (0.07 g). 1H NMR ($CDCl_3$) δ : (complex absorptions) *c.* 4.3 (CH₂N); 1.9; 1.7; and 1.3 ppm. ^{19}F NMR δ : (singlet absorptions) +16.8; +16.4; +16.0; +13.9; +13.7; +13.4; +13.3; +12.9; and +2.6 ppm in the ratio 3:10:1:1:1:10:1:5. IR (ν_{max}) (cm^{-1}): 3100 (m) (N–H str.); 1700 (m) (C=O or C=N str.); and 1210–1160 (s) (C–F str.). Mass spectrum m/z : 535 (4.6%, $C_{17}H_{19}F_{12}N_6^+$); 465 (46.8, $C_{16}H_{18}F_9N_6^+$); 260 (18.7, $C_8H_8F_6N_3^+$); 218 (7.1, $C_5H_2F_6N_3^+$); 206 (21.3, $C_4H_2F_6N_3^+$); 69 (46.1, CF₃⁺); 55 (100.0, $C_3H_5N^+$); 43 (16.2, $C_2H_5N^+$); and 42 (25.4, $C_2H_4N^+$).

Results and discussion

The results obtained from reaction of the dihalogenazines **1a** and **1b** with the aliphatic diamines in diethyl ether are given in Table 1.

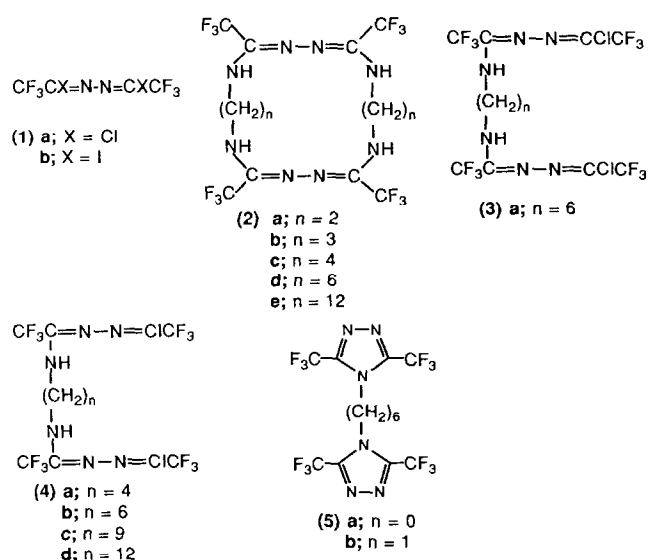


TABLE 1. Reaction of azines **1a** and **1b** at room temperature with diamines $H_2N(CH_2)_nNH_2$

Azine	Diamine	Molar ratio	Time (h)	Products	Yield (%)
1a ^a	n = 2	1:1	69	2a	30
1a	n = 2	1:2	0.5	2a	52
1a	n = 3	1:2	16	2b	44
1a	n = 6	1:1	16	2d	8
				3a	36
				5a	4
				5b	10
1a ^a	n = 6	1:1	2	2d	19
				3a	45
1b	n = 4	1:1.2	2	2c	21
				4a	75
1b	n = 6	1:1	26	4b	99
1b	n = 9	1:1	16	4c	95
1b	n = 12	1:2	5	2e	31
				4d	61

^aEt₃N also present.

Apart from the bis(triazole) **5**, the isolated products were cyclic 2:2 substitution products, i.e. the cyclo-tetraenes **2**, and open-chain 2:1 substitution products, i.e. the dihalogenotetraenes **3** and **4**. The structure of the cyclic compound **2a** was confirmed by an X-ray crystallographic study [7].

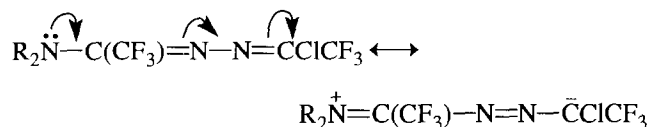
The reaction of the dichloroazine **1a** with the lower diamines $n=2$ and $n=3$ gave only the cyclic compounds **2** after purification, both when the theoretical molar ratio of reactants (1:2) was used or when a 1:1 ratio in the presence of triethylamine was employed; open chain 2:1 adducts **3** were not detected in these reactions. In the absence of triethylamine, 1 mol equiv. of diamine is consumed in forming the diamine dihydrochloride. A higher yield of compound **2a** was obtained in the reaction in which a short reaction time was used in the absence of triethylamine; later work showed that triethylamine reacted with azine **1a** (and **1b**) in the presence of light [5].

From the reaction of azine **1a** with the diamine $n=6$ (1:1 molar ratio 16 h), the yield of the cyclic compound **2d** was low as expected (amine consumed during formation of the dihydrochloride) and the 2:1 substitution compound **3a** was the major product. Surprisingly, the bis(triazole) **5** was also formed in this reaction. When the reaction was repeated in the presence of triethylamine for a much shorter time (2 h), only compounds **2d** and **3a** were isolated and the bis(triazole) **5** was not detected. This indicates that cyclization of the 2:1 substitution product **3a** to the triazole **5** is slow and an extended reaction period is required for compound **5** to be formed to any significant extent.

The notable feature of the reactions of the di-iodoazine **1b** with the diamines was the much higher yields of the products obtained ($\geq 92\%$) than from reactions involving azine **1a** (30–64%). When a 1:1 molar ratio of reactants was employed (with diamines $n=6$ and $n=9$), only the open-chain di-iodotetraenes **4b** and **4c** were produced, and when a 1:1.2 molar ratio was used with diamine $n=4$, the theoretical ratio of products **2c** and **4a** (21:75) was obtained. However, use of the theoretical 1:2 molar ratio with diamine $n=12$ gave only a relatively low yield (31%) of the cyclo-tetraene **2e** together with the di-iodotetraene **4d** (61%). It is apparent that a longer reaction time than that used (5 h) was needed for further reaction of **4d** to give **2e** in high yield.

When the reactions of the diamine $n=6$ with the two azines **1a** and **1b** are compared, it is clear that formation of the cyclo-tetraene **2d** is more favourable with dichloroazine **1a**. It has been observed previously in the reactions of azine **1a** with monoamines that monosubstitution products can be obtained in good yield by the use of a 1:2 molar ratio of reactants and that disubstitution products are formed, again in good

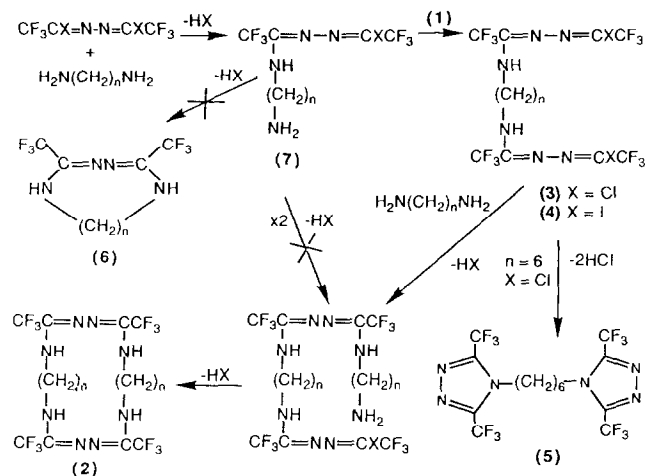
yield, by the use of a 1:4 molar ratio of reactants [3, 4]. Thus, the second halogen is more difficult to substitute than the first, and this has been explained on the basis that the +*M* effect of the amino nitrogen in the monosubstituted product renders the carbon atom bonded to chlorine in the remaining $-N=CClCF_3$ group more electron-rich (less electron-deficient) and hence less susceptible to nucleophilic attack, i.e.



This would also be the case with monosubstitution products derived from the di-iodoazine **1b**, and since iodine is less electronegative than chlorine, the imino carbon in the $-N=CXCF_3$ grouping would be more electron-rich when $X=I$ than when $X=Cl$. It would therefore be expected that nucleophilic attack on a monosubstituted azine derived from the dichloroazine **1a** would be faster than that by attack of the same nucleophile on the analogous monosubstituted azine derived from the di-iodoazine **1b**. The formation of cyclo-tetraenes **2** from azine **1a** should therefore be faster than their formation from azine **1b**.

This decreased reactivity towards substitution of the second halogen also explains why cyclic 1:1 substitution products of type **6** were not formed, i.e. the open-chain 1:1 substitution compound **7** underwent intermolecular reaction with azine **1** to give compounds **3** or **4** in preference to intramolecular cyclization to give compound **6**.

In order to confirm that the dihalogenotetraenes **3** and **4** were precursors to the cyclo-tetraenes **2**, rather than the open-chain 1:1 substitution compound **7**, the reaction of compound **4b** with an excess of the diamine $n=6$ was investigated. The reaction was slow, but after 18.5 h a mixture of unchanged **4b** and the cyclo-tetraene **2d** in the ratio 26:74 was obtained (Scheme 1).



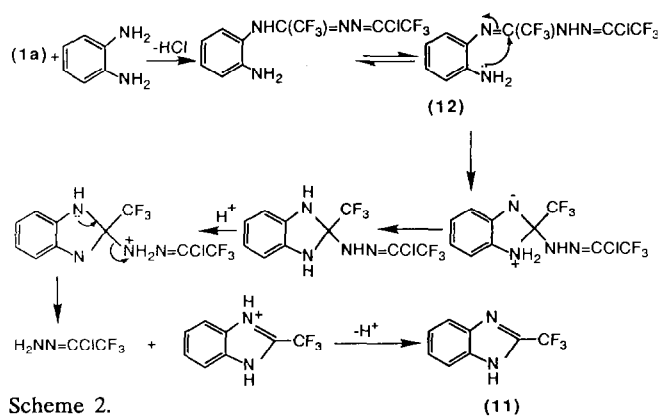
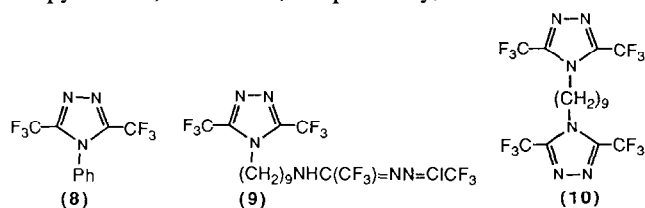
Scheme 1.

The successful reaction of **4b** with diamine $n=6$ to give **2d** indicates that unsymmetrical cyclotetraenes may be synthesized by the preparation of a dihalogenotetraene **3**, or better **4**, derived from one diamine followed by reaction with a different diamine.

The ^{19}F NMR spectra of the dihalogenotetraenes **3** and **4** in solution showed that isomers were present. Providing that the $\text{CF}_3\text{CX}=\text{N}-$ grouping has the (*Z*)-configuration, as has been demonstrated for the compound $\text{CF}_3\text{C}(\text{NH}_2)=\text{NN}=\text{CClCF}_3$ (X-ray study) [10], and has been suggested for azines of the type $\text{CF}_3\text{CR}=\text{NN}=\text{CICF}_3$ [1], there are three possible configurations for the two $\text{CF}_3(\text{NHR})=\text{N}-$ groupings, i.e. (*ZZ*), (*EZ*) and (*EE*). Three isomers were clearly present for compounds **3a**, **4a** and **4b** as shown by three absorptions for $\text{CF}_3\text{CCl}=\text{N}-$ ($\delta +9.1$ to $+9.3$ ppm) and three absorptions for $\text{CF}_3\text{CI}=\text{N}-$ ($\delta +12.2$ to $+12.7$ ppm), but only two absorptions were present for $\text{CF}_3\text{C}(\text{NHR})=\text{N}-$ ($\delta +9.9$ to $+11.8$ ppm) (total integration $\text{CF}_3\text{CX}=\text{N}-/\text{CF}_3\text{C}(\text{NHR})=\text{N}- = 1:1$); in the spectra of compounds **4c** and **4d**, only two absorptions for $\text{CF}_3\text{CI}=\text{N}-$ ($\delta +12.4$ to $+12.9$ ppm) and two absorptions for $\text{CF}_3\text{C}(\text{NHR})=\text{N}-$ ($\delta +9.9$ and $+11.6$ ppm) were observed. It was not possible to determine the isomer ratios because, although one $\text{CF}_3\text{CX}=\text{N}-$ absorption would be expected for each of the symmetrical compounds, i.e. when the two $\text{CF}_3\text{C}(\text{NHR})=\text{N}-$ groupings are either in the (*EE*)- or (*ZZ*)-configuration, two would be expected when the groupings are in the (*EZ*)-configuration. Therefore, certain absorptions are coincident.

The ^{19}F NMR spectra of the cyclotetraenes **2** in solution also indicated the presence of conformational isomers, except for the largest ring compound **2e**. The absorptions were in two regions, $\delta +13$ to $+16$ and $\delta +9$ to $+11$ ppm, and could possibly be assigned to $\text{CF}_3\text{C}(\text{NHR})=\text{N}-$ groupings in the (*E*)- and (*Z*)-configurations, respectively [CF_3 groups *anti* to a nitrogen lone pair absorb generally to lower field than CF_3 groups *syn* to a lone pair [1, 4]]; tautomerism of the type $\text{CF}_3\text{C}(\text{NHR})=\text{N}- \leftrightarrow \text{RN}=\text{C}(\text{CF}_3)-\text{NH}-$ is also possible.

It has been observed previously that thermolysis of the imidoyl compound $\text{PhN}=\text{C}(\text{CF}_3)\text{NHN}=\text{CClCF}_3$ at *c.* 120°C gave the 1,2,4-triazole **8** (33%) [4], and in the present work the thermolysis of the di-iodotetraene **4c** was investigated to determine if the mono- and/or bis-pyrazoles, **9** and **10**, respectively, were formed.



Scheme 2.

When compound **4c** was heated *in vacuo* in a sealed tube at 168°C (13 d), a dark oil (39% by weight of reactant) was obtained after removal of the iodine (NaHSO_3) formed. The ^{19}F NMR spectrum of the oil showed major absorptions at $\delta +16.8$; $+16.4$; $+13.3$; and $+2.6$ ppm (ratio *c.* 3:10:10:5); the low field absorptions ($\delta +16$ to $+17$ ppm) are in the region expected for CF_3 groups bonded to a triazole ring. The mass spectrum showed a highest mass peak at m/z 535 corresponding to $(\mathbf{9}-\text{I})^+$ or $(\mathbf{10}+\text{H})^+$, and a strong peak at m/z 465 [$(\mathbf{9}-\text{HI}-\text{CF}_3)^+$ or $(\mathbf{10}-\text{CF}_3)^+$] indicating that compounds **9** and/or **10** were present in the mixture.

Treatment of azine **1a** with 1,2-diaminobenzene (1:1 molar ratio) in diethyl ether in the presence of triethylamine gave 2-(trifluoromethyl)benzimidazole (**11**) (95%) (Scheme 2).

As expected, intramolecular nucleophilic attack by the primary amino group in intermediate **12** is more favoured on the substituted imidoyl carbon (5-centre transition state) than on the carbon bonded to chlorine (8-centre transition state); no attempt was made to isolate the other product of the reaction, the chlorohydrazone $\text{CF}_3\text{CCl}=\text{NH}_2$.

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