ELSEVIER

Journal of Fluorine Chemistry 69 (1994) 171–183

JOURNAL OF FLUORINE CHEMISTRY

Unsaturated nitrogen compounds containing fluorine. Part 15 [1]. The reactions of 2,5-dichloro-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene and its 2-amino derivative with enamines

Mohamad M. Abdul-Ghani, Salim H.A. Benomar (in part), Anthony E. Tipping*

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

Received 22 September 1993; accepted 25 January 1994

Abstract

Reaction of the title dichloroazine (**1**) with the enamines $CH_2(CH_2)_nCH{=}CNR_2$ [(**4**), $NR_2{=}NEt_2$, $n{=}2$; (**6**), $NR_2{=}NEt_2$, $n{=}3$; (**7**), $NR_2{=}N(CH_2)_2OCH_2CH_2$, $n{=}2$] gives initially the 2-substituted enamines $CH_2(CH_2)_nC(NR_2){=}CC(CF_3){=}NN{=}CClCF_3$ (**19a–c**) which can undergo tautomerisation to the rearranged enamines $R_2NC{=}CH(CH_2)_nC{=}C(CF_3)NHN{=}CClCF_3$ (**20a–c**). Further reaction of amine **20a** takes place with dichloroazine **1** to afford the bicyclic compound $CF_3CCl{=}NNHCH(CF_3)C{=}CNEtCHMeN(N{=}CClCF_3)C(CF_3){=}CCH_2CH_2$ (**5**) (34%). All the other isolated products are formed via hydrolysis on attempted purification on silica gel, i.e. **19a** → $Et_2NCH(CH_2)_3C{=}C(CF_3)N{=}NCOCF_3$ (**9**) (23%); **19b** → $O{=}C(CH_2)_4CHC(CF_3){=}NN{=}CRCF_3$ [$R{=}NEt_2$ (**11**) (21%); $R{=}NHEt$ (**12**) (17%)]; **19c** → $O{=}C(CH_2)_3C{=}C(CF_3)NHN{=}CClCF_3$ (**15**) (21%) and $CH_2CH_2O(CH_2)_2NCH(CH_2)_3C{=}C(CF_3)N{=}NCOCF_3$ (**17**) (9%); **20b** → $O{=}C(CH_2)_4CHCH(CF_3)NHN{=}CClCF_3$ (**10**) (28%) and $CH(CH_2)_4C{=}C(CF_3)NHNCOCF_3$ (**13**) (9%); **20c** → $CF_3CCl{=}NN{=}C(CF_3)C{=}C{-}O{-}CH(CH_2)_3C{=}C(CF_3)N{=}NC(CF_3){=}CCH_2CH_2$ (**14**) (8%) and $CH_2(CH_2)_2C(NCH_2CH_2OCH_2CH_2){=}CC(CF_3){=}NNHC(CF_3){=}C(CH_2)_2CH[C(CF_3){=}NN{=}CClCF_3]C{=}O$ (**16**) (18%). Reaction of the 2-aminoazine **8** with enamine **4** affords the 2-substituted enamine $CH_2(CH_2)_2C(NEt_2){=}CC(CF_3){=}NN{=}C(NH_2)CF_3$ (**18**) (36%) on separation on neutral alumina, but on silica gel the hydrolysis product $O{=}C(CH_2)_3CHC(CF_3){=}NN{=}C(NH_2)CF_3$ (**37**) (38%) is formed. The amides **9**, **13** and **17** resulting from hydrolysis of a $CF_3CCl{=}N$ grouping are unexpected products. Compounds **9**, **14** and **17** are fully conjugated and in cases where the products could contain a carbonyl group conjugated with an olefinic double bond or a conjugated azine grouping, the isolated products have the former conjugation i.e. compounds **15** and **16**, except if an amino or substituted amino substituent is present when the azine conjugation is preferred, i.e., compounds **11**, **12** and **37**.

Keywords: Reactions; Dichloroazine; Enamines; Hydrolysis; NMR spectroscopy; IR spectroscopy; Mass spectrometry

1. Introduction

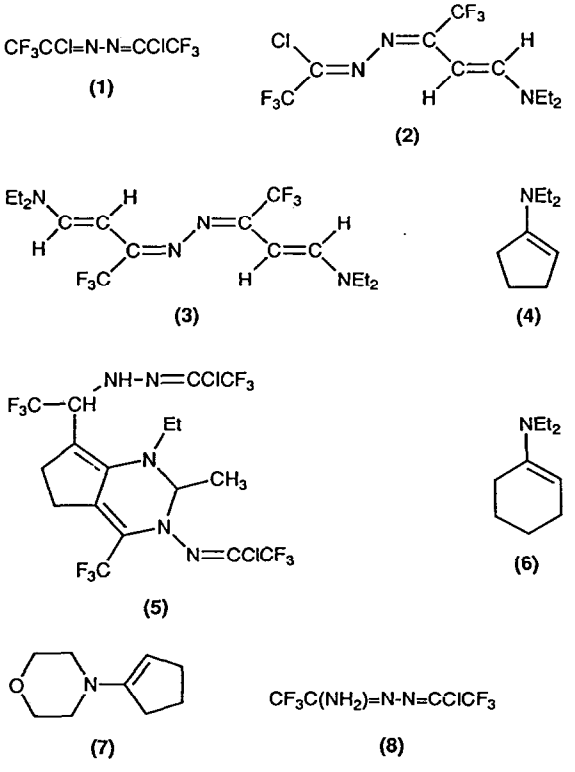
The dichloroazine **1** undergoes facile reaction with a range of nucleophiles including amines [2–4], halide ion [2,5], alkoxides, phenoxides and thiophenoxides [2,5] and phenyl-lithium [6] to replace one or both chlorine atoms depending on the reactant ratio employed. It was also shown that the enamine $Et_2NCH{=}CH_2$, generated via a single electron transfer (SET) reaction between triethylamine and dichloroazine **1** in light at room temperature, attacked azine **1** to give the triazadecatriene **2** [1,7] and that under more extreme conditions (115 °C) further reaction occurred to afford the tetra-azatetradecatetraene **3** as one of the products [1]. A preliminary investigation of the reaction of the dichloroazine **1** with 1-diethylaminocyclopentene (**4**) has also been carried out and this gave two major products one of which was identified as the bicyclic compound **5**, but the second product could not be obtained sufficiently pure for its structure to be established [8].

In the present work, the reaction of enamine **4** with dichloroazine **1** has been repeated with the object of identifying the second major product, and reactions involving 1-diethylaminocyclohexene (**6**) and 1-morpholinocyclopentene (**7**) have been investigated. The reaction of the monoaminomonochloroazine **8** with enamine **4** has also been carried out to compare the results with those obtained previously for

*Corresponding author.

SSDI 0022-1139(94)03074-A

the reaction of the triazadecatriene **2** with this enamine [1].



2. Results and discussion

The results obtained from reaction of dichloroazine **1** with the enamines **4**, **6** and **7** and from reaction of azine **8** with enamine **4** are summarised in Table 1.

Compounds **5**, **9–18** and **37** are reaction products, while structures **19–36** represent postulated reaction intermediates in the following discussion.

The crude product mixtures after separation of the solid enamine hydrochloride all showed an absence of spectral bands for ketonic carbonyl [IR (ν_{max}) (cm^{-1}): 1680–1750. ^{13}C NMR δ: 200–220 ppm] and amide carbonyl [IR (ν_{max}) (cm^{-1}): ca. 1720. ^{13}C NMR δ: ca. 155 ppm] groups. Therefore, compounds **9–17** were formed by hydrolysis on silica gel of the initial products during separation/purification by dry column flash chromatography (DCFC).

All of the reactions involving dichloroazine **1** are considered to have resulted in the initial formation of the 2-substituted enamines **19**, which then underwent further reaction to give the observed products. The products **5** and **9**, isolated from the reaction involving enamine **4**, can be explained as arising by the mechanistic route shown in Scheme 1.

The initial product, the 2-substituted enamine **19a**, on acid catalysis gave the tautomeric enamine **20a**, which reacted with dichloroazine **1** to afford the immonium salt **21a** and hence its tautomer **22**. Cyclisation of salt **22** with elimination of hydrogen chloride then yielded the bicyclic compound **5**. Competing protonation of enamine **19a** at the imino nitrogen of the $CF_3CCl{=}N-$ grouping gave the immonium cation **23** which underwent attack by water (on silica gel) at the immonium carbon, followed by elimination of hydrogen chloride and deprotonation to afford the amide **24a**, tautomerisation of which gave the isolated amide **9**.

The bicycle **5** was isolated as a mixture of two diastereomers in the ratio ca. 4:1 (NMR spectroscopy),

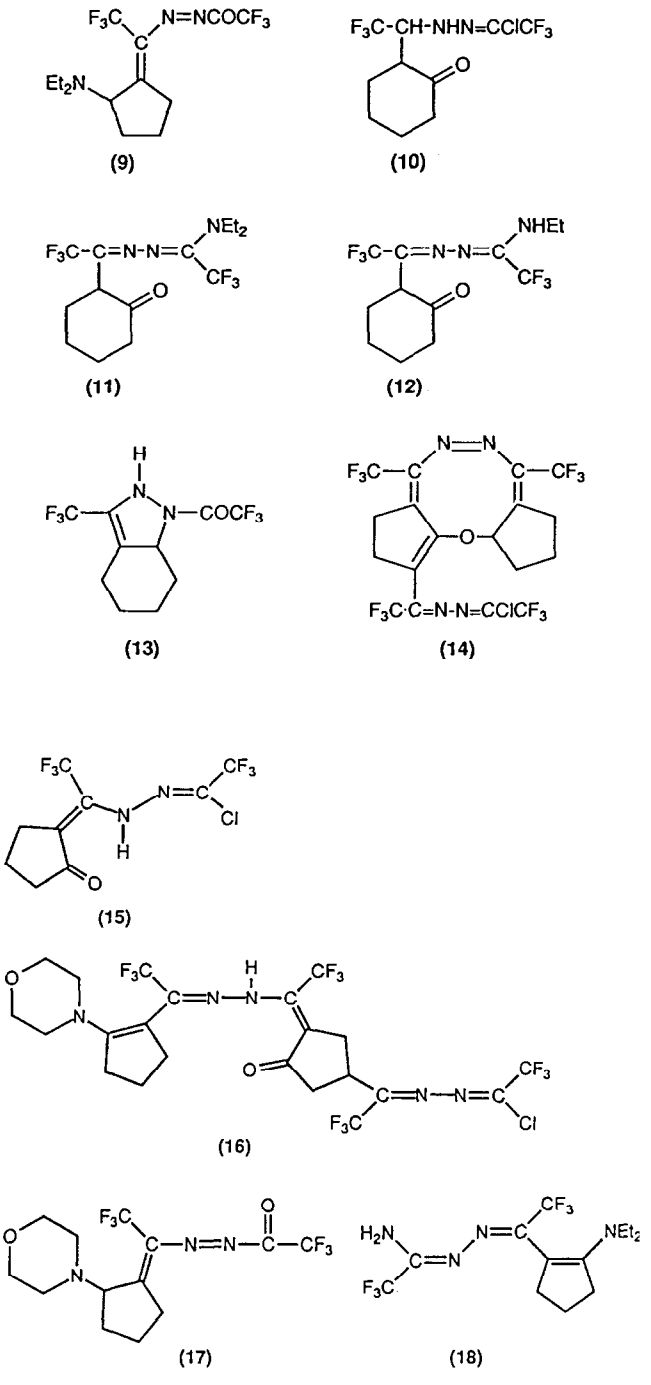
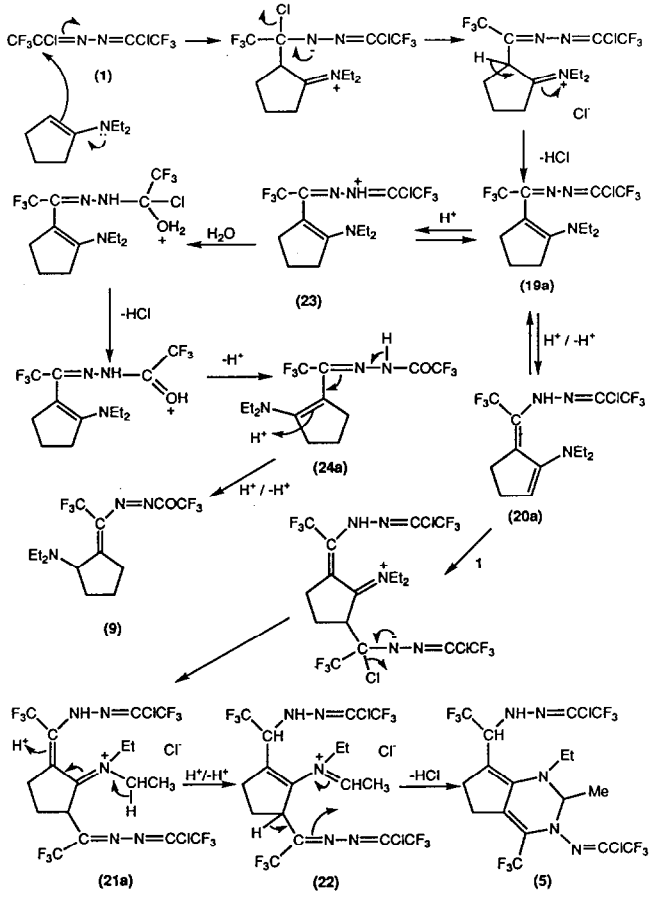


Table 1
Reactions of azines **1** and **8** with enamines (1:2 molar ratio) in anhydrous diethyl ether[a]

Azine	Enamine	Time (min)	Enamine hydrochloride (%)[b]	Products (%)[c]
1	**4**	60	55	**5** (34[d]); **9** (23)
1[e]	**4**	10		**5** (13[d]); **9** (56)
1	**6**	60	42	**10** (28[f]); **11** (21); **12** (17): **13** (9)
1	**7**	60	50	**14** (8); **15** (21); **16** (18); 17 (9)
8	**4**	30	50	**18** (36)

[a]Carried out under a nitrogen atmosphere.
[b]Yields based on enamine used.
[c]Yields based on azine used.
[d]Mixture of two diastereomers (ratio ca. 4:1).
[e]Carried out in air with diethyl ether which had not been dried.
[f]Mixture of two diastereomers which were separated (10% and 16% yield).



Scheme 1.

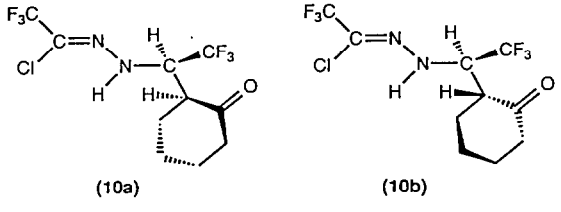
but on the evidence available it was not possible to determine the stereochemistry of the individual isomers.

The two experiments involving dichloroazine **1** and enamine **4** afforded very different yields of the products **5** and **9**, i.e. experiment 1 carried out under anhydrous conditions (60 min) gave a **5**/**9** ratio of 34:23, while in experiment 2 using non-anhydrous conditions (10 min) the ratio was 13:56. These observations can be explained by a slow conversion of enamine **19a** into the bicycle **5**, so that in the 10-min reaction considerably more enamine **19a** was present in the product mixture when it was hydrolysed on silica gel and hence a much higher yield of amide **9** was obtained than in the 60-min reaction.

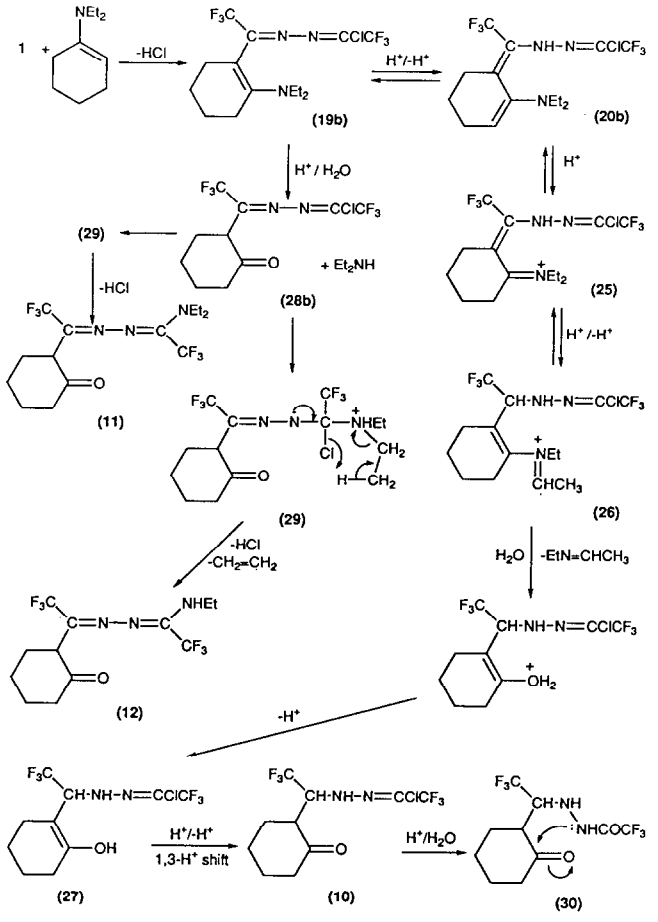
Only hydrolysis products, i.e. compounds **10–13**, were obtained from the reaction involving dichloroazine **1** and the six-membered ring enamine **6** and these are considered to have been formed via the 2-substituted enamine **19b** (Scheme 2).

Acid-catalysed rearrangement of enamine **19b** to enamine **20b** followed by protonation afforded the immonium cation **25** and hence the tautomeric cation **26**, which was hydrolysed to the 2-substituted ketone **10** via the enol **27**. Competing hydrolysis of enamine **19b** gave the ketone **28b** together with diethylamine which then attacked ketone **28b** at the imino carbon of the $CF_3CCl{=}N-$ grouping to afford the intermediate **29**. Loss of hydrogen chloride from intermediate **29** gave the diethylamino-substituted azine **11**, while concerted loss of hydrogen chloride and ethene yielded the ethylamino-substituted azine **12**.

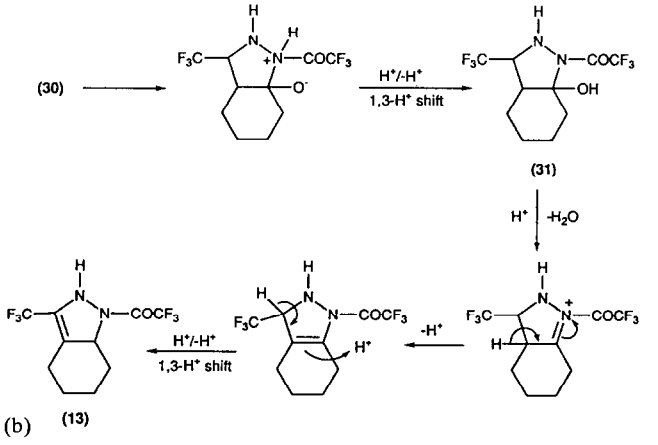
Further hydrolysis of product **10** gave the ketoamide **30** which cyclised to the bicyclic alcohol **31**. Acid-catalysed dehydration of alcohol **31** followed by tautomerisation then yielded the bicyclic amide **13**.



The cyclohexanone derivative **10** was formed as two isomers, which were separated in 10% and 16% yield, respectively, and these are considered to be the diastereomers **10a** and **10b**, but it was not possible to assign any stereochemistry to the isolated isomers.



(a)



(b)

Scheme 2.

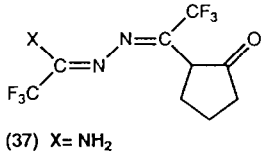
Only hydrolysis products, i.e. compounds **14–17**, were isolated from the reaction of dichloroazine **1** with the morpholine enamine **7** (Scheme 3).

The initial product, the 2-substituted enamine **19c**, underwent competing acid-catalysed rearrangement and acid-catalysed hydrolysis. Rearrangement gave enamine **20c**, which was converted to the immonium salt **32** either by reaction with a second molecule of enamine **19c** or by reaction with dichloroazine **1** to afford the immonium salt **21c**, which was then attacked by enamine **7** with elimination of hydrogen chloride. Loss of hydrogen chloride from salt **32** gave the bisenamine **33** which on hydrolysis gave a mixture of the bisketone **34** and the monoketone **35**. Diketone **34** on acid-catalysed cyclisation and dehydration gave the fully-conjugated tricyclic compound **14** via its tautomer **36**, while rearrangement of the monoketone **35** gave the isolated tautomer **16**.

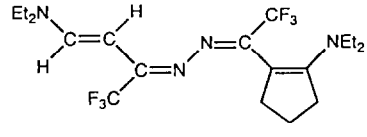
Hydrolysis of the enamine grouping in compound **19c** gave the conjugated ketone **15** via its tautomer **28**, while hydrolysis of the $CF_3CCl{=}N-$ grouping afforded amide **17** via its tautomer **24b**.

Amide **17** is analogous to amide **9** formed in the reaction involving enamine **4**, and the pathway leading eventually to compounds **14** and **16** (Scheme 3) is identical in its early stages to the pathway leading to bicycle **5** (Scheme 1). The remaining product arising from the enamine **7** reaction, i.e. ketone **15**, was not detected in the products from the enamine **4** reaction, indicating that the enamine grouping in the substituted morpholine enamine **19c** is more readily hydrolysed than the enamine grouping in the diethylamino enamine **19a** as expected.

In the above reactions, the expected hydrolysis products of the enamines **19**, i.e. the non-rearranged ketones **28a** and **28b**, were not isolated nor detected. In contrast, treatment of the monoaminomonochloroazine **8** with enamine **4** afforded the 2-substituted enamine **18c** after DCFC on neutral alumina, while DCFC on silica gel gave the non-rearranged ketone **37** as the only product isolated. It has been reported previously that hydrolysis on silica gel of the corresponding 2-substituted enamine **38**, formed from reaction of triazadecatriene **2** with enamine **4**, afforded the non-rearranged ketone **39** [1].



(37) X= NH_2

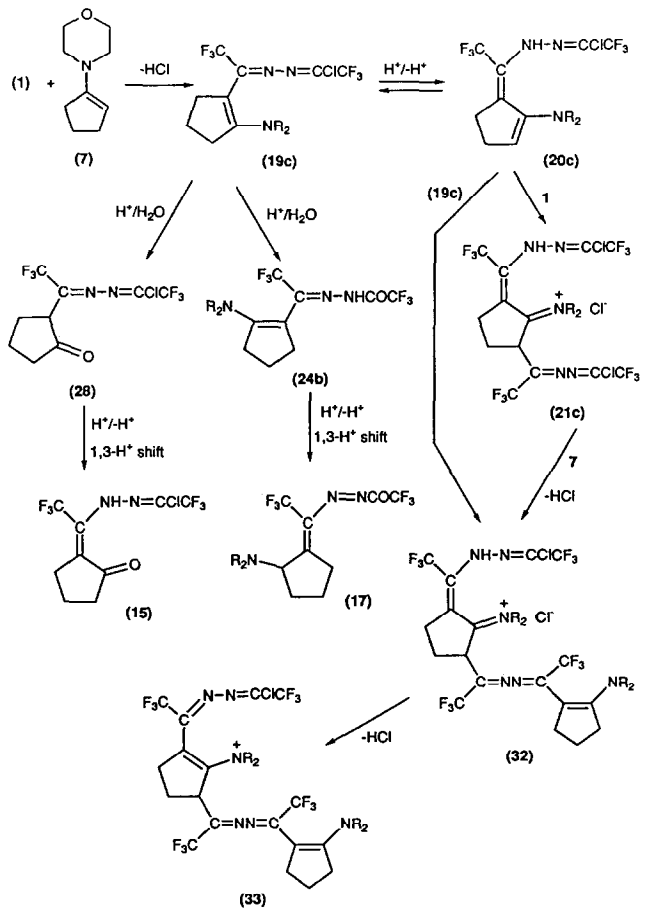


(38)

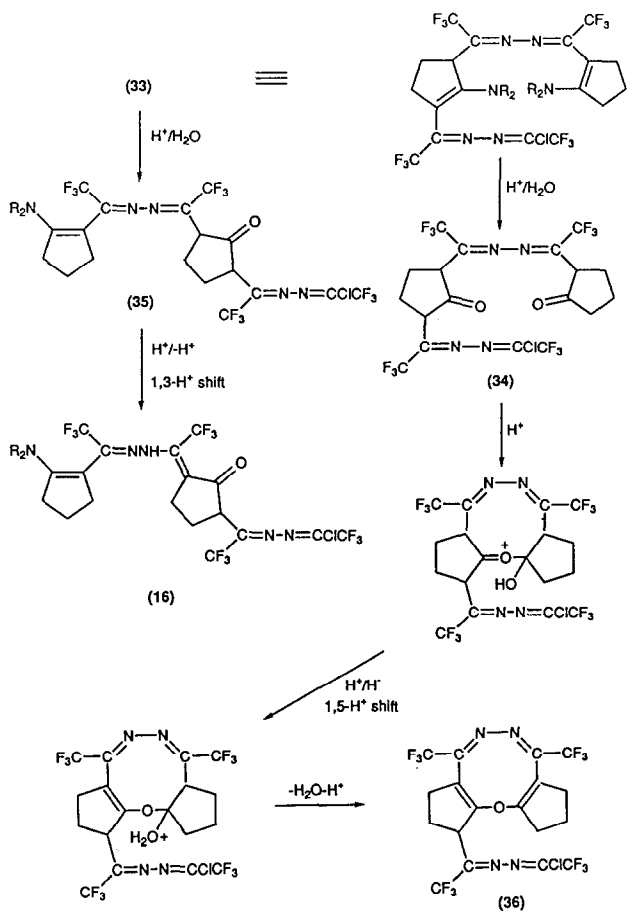
(39) X= Et_2N-CH=CH-

It was considered that hydrolysis of the initial products involving the enamine grouping to give 2-substituted ketones and the formation of the amides **9**, **13** and **17**, via hydrolysis of the $CF_3CCl{=}N-$ grouping, would be most unexpected, since hydrolysis of this grouping had not been observed in any other reactions of the dichloroazine **1** carried out previously.

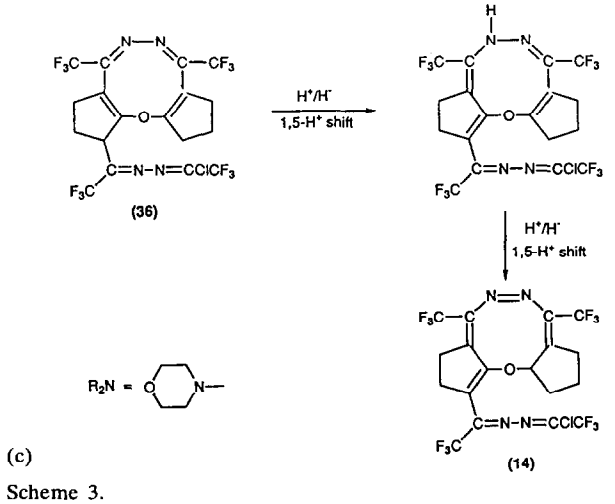
It is apparent that the stabilisation afforded by conjugation plays an important role in determining which hydrolysis products are formed. Thus, compounds **9**, **14** and **17** are fully conjugated and compounds in which a carbonyl group is conjugated with an olefinic double



(a)



(b)



(c)

Scheme 3.

bond, i.e. **15** and **16**, are more stable than their azine tautomers, unless an amino or substituted amino bonded to an azine carbon is present, i.e. compounds **11**, **12** and **37**.

The molecular formulae of the products were determined by accurate mass measurements on compounds **14** and **18** and elemental analysis together with the presence of a molecular ion peak in the mass spectrum of each of the compounds **5**, **9**, **10** (both isomers), **11–13**, **15–17** and **37**, and their structures were established by a consideration of the spectral data given in Tables 2–6.

Compound **5**, a 2:1 adduct–2HCl of dichloroazine **1** and enamine **4**, was a mixture of two isomers (ratio

Table 2
IR spectral data

Compound	IR (ν_{max}) (cm^{-1}) (assignment)
5	3300 (w, N–H str.); 2915/2860 (m, aliph. C–H str.); 1620 (m, C=N/C=C str.); 1205–1120 (s, C–F str.); 740 (m, CF_3 def.)
9	2980/2885 (m, aliph. C–H str.); 1718 (s, C=O str.); 1630 (m, C=C str.); 1450 (m, CH_2 bend); 1245–1090 (s, C–F str.); 1035 (m, C–N str.); 740 (m, CF_3 def.)
10 (minor isomer)	3300 (m, N–H str.); 2940 (m, aliph. C–H str.); 1710 (s, C=O str.); 1610 (s, C=N str.); 1450 (m, CH_2 bend); 1270 (s, =C–N str.); 1230/1090 (s, C–F str.); 970 (s, C–Cl str.); 750 (m, CF_3 def.)
10 (major isomer)	3300 (m, N–H str.); 2980 (m, aliph. C–H str.); 1710 (s, C=O str.); 1610 (s, C=N str.); 1450 (m, CH_2 bend); 1270 (m, =C–N str.); 1200–1100 (s, C–F str.); 970 (s, C–Cl str.); 740 (m, CF_3 def.)
11	2980 (m, aliph. C–H str.); 1710 (s, C=O str.); 1620 (s, C=N str.); 1450 (m, CH_2 bend); 1380 (m, CH_3 bend); 1280 (m, =C–N str.); 1230–1080 (s, C–F str.); 745 (m, CF_3 def.)
12	3345 (m, N–H str.); 2950 (m, aliph. C–H str.); 1720 (s, C=O str.); 1590 (m, C=N str.); 1450 (w, CH_2 bend); 1365 (w, CH_3 bend); 1280 (m, =C–N str.); 1220–1110 (s, C–F str.); 730 (m, CF_3 def.)
13	3440 (m, N–H str.); 2960/2940 (m, aliph. C–H str.); 1610 (m, C=C str.); 1450 (m, CH_2 bend); 1300 (m, =C–H str.); 1240–1100 (s, C–F str.); 750 (m, CF_3 def.)
14	2980/2960 (m, aliph. C–H str.); 1610 (m, C=N/C=C str.); 1440 (m, CH_2 bend); 1310 (m, =C–O str.); 1280 (m, =C–N str.); 1230–1120 (s, C–F str.); 750 (m, CF_3 def.)
15	3220 (m, N–H str.,); 2980/2940 (m, aliph. C–H str.); 1680 (s, C=O str.); 1610 (s, C=N/C=C str.); 1460 (m, CH_2 bend); 1290 (s, =C–N str.); 1240–1130 (s, C–F str.); 740 (m, CF_3 def.);
16	3400 (m, N–H str.); 2980/2920 (m, aliph. C–H str.); 1680 (s, C=O str.); 1610 (s, C=N str.); 1600 (s, C=C str.); 1450 (m, CH_2 bend); 1280 (s, =C–N str.); 1250–1100 (s, C–F str.); 920 (m, C–Cl str.); 750 (m, CF_3 def.);
17	2970 (m, aliph. C–H str.); 1720 (s, C=O str.); 1630 (m, C=C str.); 1460 (m, CH_2 bend); 1270 (s, =C–N str.); 1230–1120 (s, C–F str.); 1035 (m, C–O str.); 740 (m, CF_3 def.)
18	3420/3150 (m, N–H str.); 2980 (m, aliph. C–H str.); 1650 (s, C=C str.); 1620 (m, C=N str.); 1550 (m, N–H bend); 1450 (m, CH_2 bend); 1375 (m, CH_3 bend); 1275 (m, =C–N str.); 1240–1110 (s, C–F str.); 740 (m, CF_3 def.)
37	3420/3300 (m, N–H str.); 2980 (m, aliph. C–H str.); 1730 (m, C=O str.); 1620 (m, C=N str.); 1550 (m, N–H bend); 1450 (m, CH_2 bend); 1280 (m, =C–N str.); 1220/1120 (s, C–F str.); 740 (m, CF_3 def.)

ca. 4:1) and the NMR spectra showed the presence of the groupings $-CH(CF_3)NHN=CClCF_3$ and $=C(CF_3)NN=CClCF_3$ derived from the azine **1** {data for major isomer: ^1H NMR δ: 7.58 (d, 1H, NH, $J=7$ Hz); 4.84 (pentet, 1H, CF_3CHNH, $J=7$ Hz) ppm. ^{19}F NMR δ: (d, 3F, CF_3CH, $J=7$ Hz); 10.1 and 9.5 (2s, $2\times3F$, $2CF_3CCl=N$); 15.2 [s, 3F, $=C(CF_3)-N$] ppm. ^{13}C NMR δ: 124.2 and 124.1 (2q, $2CF_3CCl=N$, $^1J=282$–284 Hz); 121.6 [q, $=C(CF_3)N$, $^1J=273$ Hz]; 120.2 [q, $=C(CF_3)N$, $^2J=34.5$ Hz]; 118.2 (q, CF_3CH, $^1J=273$ Hz); 117.9 and 114.3 (2q, $2CF_3CCl=N$, $^2J=42$–43.5 Hz); 60.9 (q, CF_3CH, $^2J=36$ Hz) ppm} and the grouping $N-CHMeNEt\overline{C=C(CH_2)_2C}=$ derived from the enamine [data for major isomer: ^1H NMR δ: 5.36 (q, 1H, $N-CHMe-N$, $J=6.5$ Hz); 2.98 and 2.68 (4H, 2 ring CH_2); 2.74 (q, 2H, NCH_2CH_3, $J=7$ Hz); 1.24 (t, 3H, NCH_2CH_3, $J=7$ Hz); 1.22 (d, 3H, $CHCH_3$, $J=6.5$ Hz) ppm. ^{13}C NMR δ: 144.6 (=C–N); 134.9 and 129.8 (2 $=C-C$); 70.9 (N–CH–N); 49.8 (NCH_2); 30.8 and 24.5 (2 ring CH_2); 18.9 ($NCHCH_3$); 12.6 (NCH_2CH_3) ppm] thus confirming the structure.

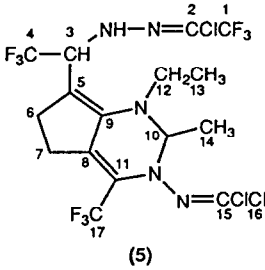
The NMR spectra of compounds **9** and **17** were very similar, except for absorptions for the different amino groups (Et_2N and morpholino), and showed the presence of the groupings $=C(CF_3)N=NCOCF_3$ {^{19}F NMR δ: ca. 12.5 [s, 3F, $=C(CF_3)-N$]; 7.5 (s, 3F, $COCF_3$) ppm. ^{13}C NMR δ: ca. 156 (q, $NCOCF_3$, $^2J=38$ Hz); ca. 150 [q, $=C(CF_3)-N$, $^2J=37$ Hz]; ca. 120 [q, $=C(CF_3)-N$, $^1J=272$–275 Hz]; ca. 116 (q, $NCOCF_3$, $^1J=289$ Hz) ppm} and $R_2N\overline{CH(CH_2)_3C}=$ [^1H NMR δ: ca. 3.4 (t, 1H, CH_2CH-N, $J=7$ Hz); ca. 3–1.2 (6H, 3 ring CH_2) ppm. ^{13}C NMR δ: ca. 103 (=C); ca. 54 (CHN); ca. 35, ca. 31 and ca. 25 (3 ring CH_2) ppm together with the expected absorptions for the R_2N groups] which proved the structures.

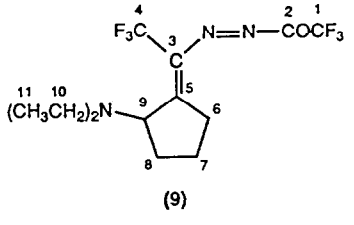
Compounds **10–12** were shown to be 2-substituted cyclohexanones [^1H NMR δ: ca. 3.7–3.0 (1H, CHC=O); 2.55–1.60 (8H, 4 ring CH_2) ppm. ^{13}C NMR δ: 210–204 (ketonic C=O) ca. 50 ($CHC=O$); ca. 40 ($CH_2C=O$); 33–24 (3 ring CH_2) ppm] and the substituent groupings were $-CH(CF_3)NHN=CClCF_3$ in compound **10** (with comparable ^1H, ^{13}C and ^{19}F NMR data to those found for the same grouping in compound **5**), $-C(CF_3)=NN=C(CF_3)NEt_2$ in compound **11** {^1H NMR δ: ca. 3.5 (q, 4H, $2CH_2N$); 1.2 (t, 6H, $2CH_3$) ppm. ^{19}F

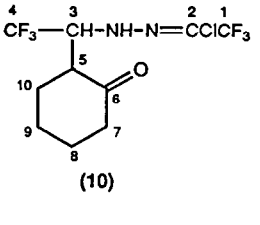
Table 3
^{1}H NMR spectral data

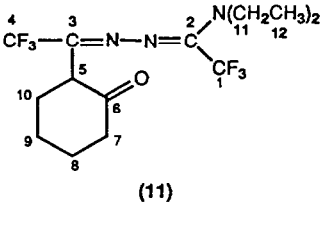
Compound[a]	^{1}H NMR δ: ppm (assignment)
5 major (minor) isomer	7.58 (6.51) (d, 1H, NH, $J_{3\text{-NH}}$=7.0 Hz); 5.36 (5.34) (q, 1H, H-10; $J_{14\text{-}10}$=6.5 Hz); 4.84 (4.96) (pentet, 1H, H-3, $J_{\text{NH-3}}=J_{4\text{-}3}$=7.0 Hz); 2.89 (2.79) (mult., 2H, H-6 or H-7); 2.68 (2.51) (mult., 2H, H-7 or H-6); 2.74 (q, 2H, H-12, $J_{13\text{-}12}$=7.0 Hz) 1.24 (1.21) (t, 3H, H-13, $J_{12\text{-}13}$=7.0 Hz); 1.22 (1.20) (d, 3H, H-14, $J_{10\text{-}14}$=6.5 Hz)
9	3.34 (t, 1H, H-9, $J_{8\text{-}9}$=6.5 Hz); 2.93 and 2.51 (ABq, 4H, H-10, $J_{\text{A-B}}$=14.0 Hz, $J_{11\text{-}10}$=7.0 Hz); 2.78 (dd, 1H, H-8a, $J_{8b\text{-}8a}$=14.0 Hz, $J_{9\text{-}8a}$=5.5 Hz); 2.03, 1.94, 1.87 and 1.37 (4 mult., 2H and 3×1H, H-6/7/8b); 1.04 (t, 6H, H-11, $J_{10\text{-}11}$=7.0 Hz)
10 minor isomer	7.46 (d, 1H, NH, $J_{3\text{-NH}}$=8.0 Hz); 4.01 (pentet, d, 1H, H-3, $J_{\text{NH-3}}\simeq J_{4\text{-}3}$=8.0 Hz, $J_{5\text{-}3}$=3.5 Hz); 3.03 (ddd, 1H, H-5, $J_{10a\text{-}5}$=12.0 Hz, $J_{10b\text{-}5}$=5.2 Hz, $J_{3\text{-}5}$=3.5 Hz); 2.44 (dd, 2H, H-7, $J_{8a\text{-}7}$=10.0 Hz, $J_{8b\text{-}7}$=4.5 Hz); 2.19 (mult., 2H, H-10); 2.04 (mult., 1H, H-9a); 1.84 (mult., 1H, H-9b); 1.78 (mult., 2H, H-8)
10 major isomer	6.45 (d, 1H, NH, $J_{3\text{-NH}}$=8.0 Hz); 4.76 (pentet, d, 1H, H-3, $J_{\text{NH-3}}\simeq J_{4\text{-}3}$=8.0 Hz, $J_{5\text{-}3}$=4.1 Hz); 2.87 (ddd, 1H, H-5, $J_{10a\text{-}5}$=10.0 Hz, $J_{10b\text{-}5}$=5.0 Hz; $J_{3\text{-}5}$=4.1 Hz); 2.54 (mult., 1H, H-7a); 2.42 (mult., 1H, H-7b); 2.27, 2.13, 2.04 and 1.78 (4 mult., 3×1H and 3H, H-8/9/10)
11	3.74 (dd, 1H, H-5, $J_{10a\text{-}5}$=12.5 Hz, $J_{10b\text{-}5}$=6.0 Hz); 3.57 and 3.39 (2q, 4H, H-11, $J_{12\text{-}11}$=7.0 Hz); 2.54 and 2.31 (2 mult., 2H, H-7); 2.19, 2.13, 2.06, 1.97, 1.74 and 1.62 (6 mult., 6×1H, H-8/9/10); 1.20 (t, 6H, H-12, $J_{11\text{-}12}$=7.0 Hz)
12	5.74 (br., 1H, NH); 3.61 (dd, 1H, H-5, $J_{10a\text{-}5}$=12.0 Hz, $J_{10b\text{-}5}$=7.0 Hz); 3.58 (pentet, 1H, H-11, $J_{\text{NH-11}}\simeq J_{12\text{-}11}$=7.0 Hz); 2.48 and 2.30 (ABmult., H-7, $J_{7a\text{-}7b}$=16 Hz); 2.26, 2.23, 2.07, 2.03, 1.77 and 1.64 (6 mult., 6×1H, H-8/9/10); 1.26 (t, 3H, H-12, $J_{11\text{-}12}$=7.0 Hz)
13	4.38 (br., 1H, NH); 3.29 (t, 1H, H-10, $J_{9\text{-}10}$=6.5 Hz); 2.42 (ddd, 1H, H-6a, $J_{6b\text{-}6a}$=14.5 Hz, $J_{7a\text{-}6a}$=7.5 Hz, $J_{7b\text{-}6a}$=5.0 Hz); 2.16 (ddd, 1H, H-6b, $J_{6a\text{-}6b}$=14.5 Hz, $J_{7a\text{-}6b}$=8.5 Hz, $J_{7b\text{-}6b}$=5.0 Hz); 2.00, 1.73, 1.62, 1.58, 1.47 and 1.45 (6 mult., 6×1H, H-7/8/9)
14	3.61 (dd, 1H, H-10), $J_{11a\text{-}10}$=4.0, $J_{11b\text{-}10}$=1.5 Hz); 2.94 (mult., 2H, H-6 or H-7); 2.83 (mult., 2H, H-7 or H-6); 2.23, 2.05, 2.01, 1.96, 1.84 and 1.80 (6 mult., 6×1H, H-11/12/13)
15	12.75 (br., 1H, NH); 2.93 (tq, 2H, H-9, $J_{8\text{-}9}$=7.8 Hz, $J_{4\text{-}9}$=3.5 Hz); 2.48 (t, 2H, H-7, $J_{8\text{-}7}$=7.8 Hz); 2.02 (pentet, 2H, H-8, $J_{7\text{-}8}\simeq J_{9\text{-}8}$=7.8 Hz)
16	12.02 (br., 1H, NH); 4.43 (mult., 1H, H-5); 3.44 (t, 4H, H-20, $J_{19\text{-}20}$=5.0 Hz); 2.98 (t, 4H, H-19, $J_{20\text{-}19}$=5.0 Hz); 2.84 (mult., 2H, H-17); 2.75 and 2.45 (ABmult., 2H, H-8); 2.42 (t, 2H, H-15, $J_{16\text{-}15}$=7.5 Hz); 1.98 (pentet, 2H, H-16, $J_{16\text{-}15}\simeq J_{17\text{-}15}$=7.5 Hz); 1.92 and 1.88 (ABmult., 2H, H-9)
17	3.68 and 3.66 (ABdd, 4H, H-11, $J_{11a\text{-}11b}$=13.0 Hz, $J_{10a\text{-}11a}=J_{10b\text{-}11b}$=6.0 Hz, $J_{10b\text{-}11a}=J_{10a\text{-}11b}$=3.2 Hz); 3.43 (t, 1H, H-9, $J_{8\text{-}9}$=7.0 Hz); 3.02 (mult., 1H, H-6a); 2.80 and 2.64 (ABdd, 4H, H-10, $J_{10a\text{-}10b}$=11.0 Hz, $J_{11a\text{-}10a}=J_{11b\text{-}10b}$=6.0 Hz, $J_{11a\text{-}10b}=J_{11b\text{-}10a}$=3.2 Hz), 2.08–1.85 (complex, 3H, H-6b, H-8); 1.40 and 1.18 (ABmult., 2H, H-7)
18	5.34 (br., 2H, NH_2); 2.88 (q, 4H, H-10, $J_{11\text{-}10}$=7.0 Hz); 2.58 (t, 2H, H-8, $J_{7\text{-}8}$=7.5 Hz); 2.47 (t, 2H, H-6, $J_{7\text{-}6}$=7.5 Hz); 1.89 (pentet, 2H, H-7, $J_{6\text{-}7}\simeq J_{8\text{-}7}$=7.5 Hz); 1.02 (t, 6H, H-11, $J_{10\text{-}11}$=7.0 Hz)
37	5.84 (br., 2H, NH_2); 3.29 (t, 1H, H-5, $J_{9\text{-}5}$=10.0 Hz); 2.53 (ddd, 1H, H-7a, $J_{7b\text{-}7a}$=13.5 Hz, $J_{8a\text{-}7a}$=12.0 Hz, $J_{8b\text{-}7a}$=8.5 Hz); 2.31–2.17 and 1.85 (complex, 4H and mult., 1H, H-7b/8/9)

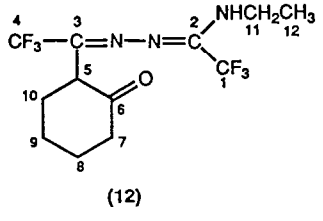
[a]Numbering for NMR tables:

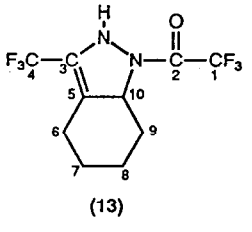

(5)

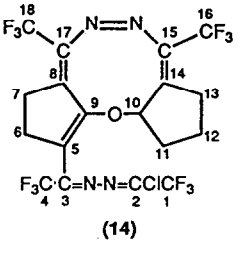

(9)

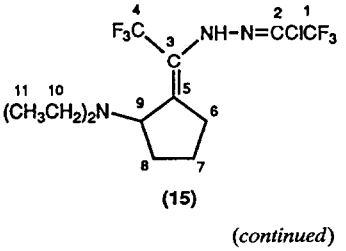

(10)


(11)


(12)

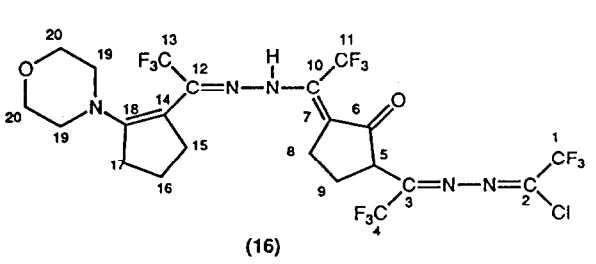

(13)


(14)

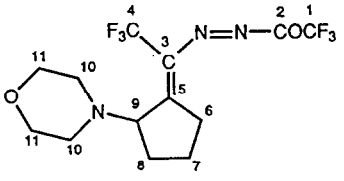

(15)

(continued)

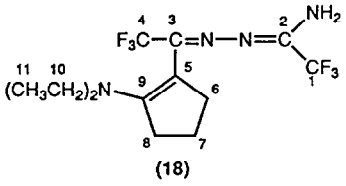
Table 3 (*continued*)



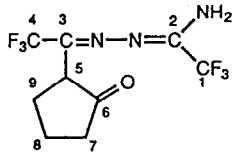
(16)



(17)



(18)



(37)

Table 4
^{19}F NMR spectral data

Compound[a]	^{19}F NMR δ: ppm (assignment)
5 major (minor) isomer	15.2 (15.2) (s, 3.75F, F-17); 10.1 (9.7) [s, 3F (0.75F), F-1 or F-16]; 9.5 (9.5) (s, 3.75F, F-16 or F-1); 6.1 (6.8) [d, 3F (0.75F), F-4, $J_{3\text{-}4}$=7.0 (7.0) Hz]
9	12.6 (s, 3F, F-4); 7.5 (s, 3F, F-1)
10 minor isomer	9.3 (s, 3F, F-1); 5.8 (d, 3F, F-4, $J_{3\text{-}4}$=8.0 Hz)
10 major isomer	9.3 (s, 3F, F-1); 5.6 (d, 3F, F-4, $J_{3\text{-}4}$=8.0 Hz)
11	12.8 (s, 3F, F-4); 8.6 (s, 3F, F-1)
12	8.9 (s, 3F, F-4); 8.6 (s, 3F, F-1)
13	11.3 (s, 3F, F-4); 5.7 (s, 3F, F-1)
14	13.7 (s, 3F, F-4); 12.2 (s, 3F, F-16 or F-18); 10.5 (s, 3F, F-18 or F-16); 7.7 (s, 3F, F-1)
15	16.2 (t, 3F, F-4, $J_{9\text{-}4}$=3.5 Hz); 9.1 (s, 3F, F-1)
16	17.1 (s, 3F, F-4); 11.7 (s, 3F, F-11); 8.3 (s, 3F, F-13); 7.4 (s, 3F, F-1)
17	12.4 (s, 3F, F-4); 7.5 (s, 3F, F-1)
18	13.3 (s, 3F, F-4); 9.2 (s, 3F, F-1)
37	10.1 (s, 3F, F-4); 8.6 (s, 3F, F-1)

[a]For numbering, see footnote to Table 3.

NMR δ: 12.8 (s, 3F, CF_3C=N); 8.6 [s, 3F, $Et_2NC(CF_3)$=N] ppm. ^{13}C NMR δ: 150.6 [q, $Et_2NC(CF_3)$=N, ^2J=32.5 Hz]; 144.4 (q, CF_3C=N, ^2J=31 Hz); 120.9 (q, CF_3C=N, ^1J=276 Hz); 119.3 [q, $Et_2NC(CF_3)$=N, ^1J=279 Hz]; ca. 45 (NCH_2); 14.3 (CH_3) ppm} and $-C(CF_3)$=NN=$C(CF_3)$NHEt in compound **12** with comparable chemical shifts and coupling constants for the azine residue as observed in the spectra of compound **11**, together with absorptions for the NHEt group [^{1}H NMR δ: 5.74 (br., 1H, NH); 3.58 (pentet, 2H, NCH_2, J=7.0 Hz); 1.25 (t, 3H, CH_3) ppm. ^{13}C NMR δ: ca. 40 (NCH_2); 15.8 (CH_3) ppm].

The NMR spectra of compound **13** established that it contained a =$C(CF_3)NHN(COCF_3)$– grouping {^{1}H NMR δ: 4.38 (br., 1H, NH) ppm. ^{19}F NMR δ: 11.3 [s, 3F, =$C(CF_3)$NH]; 5.7 (s, 3F, $COCF_3$) ppm. ^{13}C NMR δ: 156.2 (q, CF_3CON, ^2J=41 Hz]; 151.6 [q, =$C(CF_3)$NH, ^2J=38 Hz]; 119.4 [q, =$C(CF_3)$NH, ^1J=273 Hz]; 115.2 (q, CF_3CON, ^1J=278 Hz) ppm} and a =$\overline{C(CH_2)_4}$CH– grouping derived from enamine **6** [^{1}H NMR δ: 3.29 (t,

Table 5
^{13}C NMR spectral data

Compound[a]	^{13}C NMR δ: ppm (assignment)[b]
5 major (minor) isomer	144.6 (144.3) (C-9); 134.9 (134.8) and 129.8 (127.4) (C-5/8); 124.2 (124.2) (q, C-1 or C-16), ^1J=282.3 Hz); 124.1 (124.1) (q, C-16 or C-1, ^1J=284.4 Hz); 121.6 (121.55) [q, C-17, ^1J=273.3 (273.1) Hz]; 120.7 (120.8) [q, C-11, ^2J=34.6 (34.7) Hz]; 118.2 (118.1) [q, C-4, ^1J=273.1 (271.9) Hz]; 117.9 (117.8) [q, C-2 or C-15, ^2J=42.0 (41.8) Hz]; 114.3 (113.2) [q, C-15 or C-2, ^2J=43.5 (43.5) Hz]; 70.9 (70.5) (C-10); 60.9 (59.4) [q, C-3, ^2J=36.4 (36.9) Hz]; 49.8 (49.6) (C-12); 30.8 (30.5) (C-6 or C-7); 24.5 (24.8) (C-7 or C-6); 18.2 (18.3) (C-14); 12.6 (12.7) (C-13)
9	155.9 (q, C-2, ^2J=37.9 Hz); 149.8 (q, C-3, ^2J=36.7 Hz); 119.7 (q, C-4, ^1J=274.7 Hz); 116.0 (q, C-1, ^1J=288.9 Hz); 104.3 (C-5); 54.4 (C-9); 44.9 (C-10); 35.6 (C-8); 30.9 (C-6); 24.7 (C-7); 15.6 (C-11)
10 minor isomer	210.0 (C-6); 124.4 (q, C-1, ^1J=284.3 Hz); 177.9 (q, C-4, ^1J=271.8 Hz); 112.5 (q, C-2, ^2J=43.1 Hz); 62.4 (q, C-3, ^2J=30.2 Hz); 51.7 (C-5); 42.7 (C-7); 32.7, 28.0 and 25.6 (C-8/9/10)
10 major isomer	207.6 (C-6); 125.3 (q, C-1, ^1J=284.4 Hz); 118.1 (q, C-4, ^1J=271.2 Hz); 113.0 (q, C-2, ^2J=43.2 Hz); 58.5 (q, C-3, ^2J=29.9 Hz); 49.3 (C-5); 41.9 (C-7); 28.6, 27.0 and 24.9 C-8/9/10)
11	204.7 (C-6); 150.0 (q, C-2, ^2J=32.5 Hz); 144.4 (q, C-3, ^2J=31.1 Hz); 120.9 (q, C-4, ^1J=275.8 Hz); 119.3 (q, C-1, ^1J=279.2 Hz); 49.8 (C-5); 45.5 and 45.4 (C-11); 40.8 (C-7); 27.4, 24.7 and 24.1 (C-8/9/10); 14.3 (C-12)
12	204.5 (C-6); 154.1 (q, C-2, ^2J=32.3 Hz); 148.3 (q, C-3, ^2J=35.8 Hz); 120.5 (q, C-4, ^1J=275.1 Hz); 118.5 (q, C-1, ^1J=277.6 Hz); 49.9 (C-5); 40.7 (C-7 or C-11); 38.7 (C-11 or C-7); 28.0, 25.1 and 24.4 (C-8/9/10); 15.8 (C-12)
13	156.2 (q, C-2, ^2J=41.2 Hz); 151.6 (q, C-3, ^2J=38.0 Hz); 119.4 (q, C-4, ^1J=272.6 Hz); 115.2 (q, C-1, ^2J=287.4 Hz); 96.3 (C-5); 50.7 (C-10); 29.8 (C-6); 21.9, 17.8 and 17.3 (C-7/8/9)
14	154.2 (C-9); 147.6 (q, C-3, ^2J=37.5 Hz); 146.0 (q, C-17, ^2J=32.2 Hz); 131.9 (q, C-15, ^2J=41.8 Hz); 128.9 (C-5); 121.4 (q, C-2, ^2J=37.7 Hz); 120.6 (q, C-4, ^1J=273.9 Hz); 119.9 (q, C-18, ^1J=271.2 Hz); 119.5 (q, C-16, ^1J=277.7 Hz); 117.2 (q, C-1, ^1J=275.0 Hz); 112.6 (C-8); 109.4 (C-14); 54.4 (C-10); 35.8 (C-7); 29.8, 28.6, 26.4 and 23.6 (C-6/11/12/13)
15	211.4 (C-6); 137.4 (q, C-3, ^2J=33.6 Hz); 120.9 (q, C-4, ^1J=278.2 Hz); 118.6 (q, C-1, ^1J=272.5 Hz); 117.9 (q, C-2, ^2J=43.6 Hz); 113.9 (C-5); 39.6 (C-7); 28.2 (q, C-9, ^4J=3.5 Hz); 20.9 (C-8)
16	210.6 (C-6); 153.4 (q, C-12, ^2J=32.7 Hz); 150.8 (C-18); 138.3 (q, C-10; ^2J=32.8 Hz); 136.7 (q, C-3, ^2J=34.7 Hz); 129.6 (q, C-2, ^2J=38.2 Hz); 120.8 (q, C-13); ^1J=274.8 Hz); 120.4 (q, C-11, ^1J=278.8 Hz); 119.7 (q, C-4, ^1J=278.2 Hz); 116.8 (q, C-1, ^1J=275.6 Hz); 110.2 (C-7); 98.4 (C-14); 66.4 (C-20); 47.4 (C-19); 44.2 (C-5); 39.0 (C-17); 32.0 (C-15); 29.4, 28.4 and 20.3 (C-8/9/16)
17	156.4 (q, C-2, ^2J=38.0 Hz); 149.8 (q, C-3, ^2J=36.9 Hz); 119.4 (q, C-4, ^1J=272.5 Hz); 115.7 (q, C-1, ^1J=288.9 Hz); 102.1 (C-5); 66.9 (C-11); 53.5 (C-9); 48.5 (C-10); 33.9 (C-6); 30.7 (C-8); 24.9 (C-7)
18	158.7 (C-9); 155.3 (q, C-2, ^2J=30.6 Hz); 146.8 (q, C-3, ^2J=34.6 Hz); 121.2 (q, C-4, ^1J=278.0 Hz); 118.8 (q, C-1, ^1J=275.2 Hz); 93.8 (C-5); 44.6 (C-10); 35.4 (C-8); 33.2 (C-6); 21.3 (C-7); 13.3 (C-11)
37	213.9 (C-6); 156.1 (q, C-2, ^2J=32.9 Hz); 151.1 (q, C-3, ^2J=34.9 Hz); 121.0 (q, C-4, ^1J=275.3 Hz); 118.9 (q, C-1, ^1J=276.0 Hz); 49.5 (C-5); 38.1 (C-7); 29.0 (C-9); 22.8 (C-8)

[a]For numbering, see footnote to Table 3.
[b]Singlet absorptions unless stated otherwise.

1H, $=CCHCH_2$); 2.42–1.45 (8H, $4CH_2$) ppm. ^{13}C NMR δ: 96.3 (=C); 50.7 (CH); 29.8–17.3 ($4CH_2$) ppm].

Compound **14** contained two azine **1** residues and two enamine **6** residues, and the NMR spectra showed the presence of the groupings $-C(CF_3)=NN=CClCF_3$ [^{19}F NMR δ: 13.7 (s, 3F, $CF_3C=N$); 7.7 (s, 3F, $CF_3CCl=N$) ppm. ^{13}C NMR δ: 147.6 (q, $CF_3C=N$, ^2J=37.5 Hz); 121.4 (q, $CF_3CCl=N$, ^2J=38 Hz); 120.6 (q, $CF_3C=N$, ^1J=274 Hz); 117.2 (q, $CF_3CCl=N$, ^1J=275 Hz) ppm], $=C(CF_3)N=NC(CF_3)=$ {^{19}F NMR δ: 12.2 and 10.5 [2s, 2×3F, $2=C(CF_3)-N$] ppm. ^{13}C NMR δ: 146.0 [q, $=C(CF_3)-N$, ^2J=32 Hz]; 131.9 [q, $=C(CF_3)-N$, ^2J=42 Hz]; 119.9 (q, CF_3, ^1J=271 Hz); 119.5 (q, CF_3, ^1J=278 Hz) ppm} and $=\overbrace{C(CH_2)_2C}=C-O-\overbrace{CH(CH_2)_3C}=$ [^1H NMR δ: 3.61 (dd, 1H, $-CCHCH_AH_B$); 2.94 (mult., 2H, $=CCH_2$); 2.83 (mult., 2H, $=CCH_2$); 2.23–1.80 (6H, 3 ring CH_2) ppm. ^{13}C NMR δ: 154.2 (=C–O); 128.9 (C=C–O); 112.6 (=C); 109.4 (=C); 54.4 (CHO); 35.8–23.6 (5 ring CH_2) ppm] in agreement with the proposed structure.

The NMR spectra of compound **15** confirmed that it was derived from one azine **1** and one enamine **7** residue by the presence of the groupings $=C(CF_3)NHN=CClCF_3$ {^1H NMR δ: 12.75 (br., 1H, NH) ppm. ^{19}F NMR δ: 16.2 [t, 3F, $=C(CF_3)NH$, ^4J=3.5 Hz]; 9.1 (s, 3F, $CF_3CCl=N$) ppm. ^{13}C NMR δ: 137.4 [q, $=C(CF_3)NH$, ^2J=33.6 Hz]; 120.9 [q, $=C(CF_3)NH$, ^1J=278 Hz]; 118.6 (q, $CF_3CCl=N$, ^1J=272.5 Hz); 117.9 (q, $CF_3CCl=N$, ^2J=43.6 Hz) ppm} and $=\overbrace{C(CH_2)_3C}=O$ [^1H NMR δ: 2.93 (tq, $=CCH_2CH_2$, J=8 and 3.5 Hz); 2.48 (t, 2H, CH_2CO, J=8 Hz); 2.02 (pentet, 2H,

Table 6
Mass spectral data (EI unless stated otherwise)

Compound	MS *m/z* (%, assignment)
5	587/589/591 (72, M^+); 457/459 [17, $(M-CF_3CClN)^+$]; 442/444 [71, $(M-CF_3CClNNH)^+$]; 373/375 (9, $C_{14}H_{14}F_6ClN_3^+$); 297 (100, $C_{12}H_{11}F_6N_2^+$); 215 (10, $C_{10}H_{10}F_3N_2^+$); 69 (17, CF_3^+)
9	345 (32, M^+); 330 [5, $(M-Me)^+$]; 326 [10, $(M-F)^+$]; 276 [30, $(M-CF_3^+$]; 233 [59, $(M-Me-CF_3CO)^+$]; 220 [19, $(M-CF_3CON_2)^+$]; 218 (19, $C_9H_{11}F_3N_3^+$); 217 (12, $C_9H_{10}F_3N_3^+$); 192 (17, $C_9H_{13}NF_3^+$); 139 [100, $(M-CF_3CN_2COCF_3)^+$]; 69 (43); 58 (25, $C_3H_8N^+$); 54 (15, $C_4H_6^+$]; 44 (16, $C_2H_6N^+$); 29 (61, $C_2H_5^+$); 27 (48, $C_2H_3^+$)
10 (major isomer)	324/326 (100, M^+); 305/307 [9, $(M-F)^+$]; 289 [4, $(M-Cl)^+$]; 194 [9, $(M-CF_3CClN)^+$]; 97 (9, $C_6H_9O^+$); 84 (8, $C_5H_8O^+$)
10 (minor isomer)	324/326 (100); 305/307 (6); 289 (11); 194 (47); 166 (4, $C_7H_{11}F_3N^+$); 165 (10, $C_7H_{10}F_3N^+$); 96 (4, $C_6H_8O^+$)
11	359 (6, M^+); 344 [10, $(M-Me)^+$]; 167 [4, $(M-CF_3CNNEt_2)^+$]; 166 (5, $C_6H_9F_3N_2^+$); 124 (7, $C_3H_2F_3N_2^+$); 96 (5, $C_6H_8O^+$); 88 (10, $C_7H_4^+$); 84 (100, $C_5H_{10}N^+$]; 71 (19, $C_4H_9N^+$); 69 (6, CF_3^+); 56 (15, $C_3H_6N^+$); 51 (29, C_3HN^+)
12	331 (2, M^+); 262 [5, $(M-CF_3)^+$]; 234 [8, $(M-C_6H_9O)^+$]; 192 [59, $(M-CF_3CNNHEt)^+$]; 165 (20, $C_5H_6F_3N_3^+$); 139 (23, $C_4H_6F_3N_2^+$); 124 (72, $C_4H_5F_3N^+$); 96 (56, $C_6H_8O^+$); 94 (15, $C_6H_6O^+$); 84 (59, $C_5H_8O^+/C_3H_6N_3^+$); 77 (15, $C_6H_5^+$); 69 (100, CF_3^+); 68 (30, $C_4H_4O^+$); 67 (40, $C_4H_3O^+$); 56 (98, $C_3H_6N^+$); 55 (71, $C_3H_5N^+$); 51 (34, C_3HN^+); 44 (42, $C_2H_6N^+$); 43 (45, $C_2H_5N^+$); 29 (58, $C_2H_5^+$)
13	288 (1, M^+); 287 [17, $(M-H)^+$]; 261 [19, $(M-C_2H_3)^+$]; 235 [16, $(M-C_4H_5)^+$]; 191 [14, $(M-CF_3CO)^+$]; 162 [8, $(M-CF_3CON_2H]^+$]; 149 (8, $C_7H_8F_3^+$); 105 (24, $C_6H_9N_2^+$); 94 (43, $C_5H_6N_2^+$); 91 (17, $C_5H_3N_2^+$); 77 (24, $C_6H_5^+$); 69 (100, CF_3^+); 67 (27, $C_5H_7^+$); 55 (30, $C_4H_7^+$); 41 (26, $C_3H_5^+$)
14	562/564 (53, M^+); 543/545 [15, $(M-F)^+$]; 527 [6, $(M-Cl)^+$]; 493/495 [24, $(M-CF_3)^+$]; 432 [18, $(M-CF_3CClN)^+$]; 362 [81, $(M-CF_3CClN-CF_3-H)^+$; 337 [8, $(M-CF_3CN_2CClCF_3)^+$]; 294 (15, $C_{14}H_{11}F_3N_3O^+$); 267 (13, $C_{13}H_{10}F_3N_2O^+$); 213 (9, $C_{12}H_{11}N_3O^+$); 107 (16, $C_7H_7O^+$); 69 (100, CF_3^+); 55 (14, $C_4H_7^+$); 41 (46, $C_3H_5^+$)
15	308/310 (23, M^+); 273 [12, $(M-Cl)^+$]; 253 [5, $(M-Cl-HF)^+$]; 150 (6, $C_5H_3F_3NO^+$); 132 (16, $C_7H_4N_2O^+$); 108 (100, $C_6H_6NO^+$); 80 (22, $C_5H_4O^+$); 69 (38, CF_3^+); 55 (39, $C_3H_3O^+$); 54 (13, $C_3H_2O^+$); 39 (17, $C_3H_3^+$); 27 (26, $C_2H_3^+$)
16[a]	649/651 (100, M^+); 630/632 [20, $(M-F)^+$]; 563/565 [47, $(M-C_4H_8NO)^+$]; 402/404 (11, $C_{11}H_6F_9ClN_3O^+$)
17	359 (18, M^+); 290 [12, $(M-CF_3)^+$]; 247 [31, $(M-CF_3CONH)^+$]; 234 (19, $C_{11}H_{15}F_3NO^+$); 153 [100, $(M-CF_3CN_2COCF_3)^+$; 86 (76, $C_4H_8NO^+$); 84 (36, $C_4H_6NO^+$); 69 (66, CF_3^+); 67 (19, $C_5H_7^+$); 57 (44, $C_3H_5O^+$); 56 (34, $C_3H_4O^+$); 55 (26, $C_4H_7^+/C_3H_3O^+$); 51 (25, $C_4H_3^+$); 41 (64, C_2HO^+); 30 (17, CH_2O^+); 29 (69, CHO^+); 27 (46, $C_2H_3^+/CHN^+$)
18	344 (30, M^+); 315 [12, $(M-C_2H_5)^+$]; 233 (30, $C_{11}H_{16}F_6N_2^+$); 218 (56, $C_{10}H_{13}F_6N_2^+$); 217 (60, $C_{10}H_{12}F_6N_2^+$); 190 (14, $C_9H_{11}F_6N^+$); 189 (16, $C_9H_{10}F_6N^+$); 163 (93, $C_{10}H_{15}N_2^+$); 139 (28, $C_9H_{17}N^+$); 137 (30, $C_9H_{15}N^+$); 135 (17, $C_9H_{13}N^+$); 124 (26, $C_8H_{14}N^+$); 72 (39, $C_4H_{10}N^+$); 69 (72, CF_3^+); 58 (35, $C_3H_8N^+$); 54 (41, $C_2H_2N_2^+$); 43 (30, $C_2H_5N^+$); 29 (100, $C_2H_5^+$)
37[b]	290 [100, $(M+H)^+$]; 289 (5, M^+); 234 (3, $C_6H_5F_6N_3^+$); 220 [1, $(M-CF_3)^+$]; 113 (9, $C_4H_4FN_3^+$)

[a]CI spectrum.
[b]FAB spectrum.

$CH_2CH_2CH_2$, $J=8$ Hz) ppm. ^{13}C NMR δ: 211.4 (ketonic C=O); 113.9 (=C); 93.6 (CH_2CO); 28.2 (q, $=CCH_2$, $^4J=3.5$ Hz); 20.9 (CH_2) ppm]. The low-field absorption for the NH proton showed that it was hydrogen-bonded to the carbonyl oxygen, and the presence in the spectra of coupling between a CF_3 group and the allylic CH_2 group further confirmed that the product had structure **15** with *syn* NH and carbonyl groups.

Compound **16** was shown from its NMR spectra to be derived from two dichlorazine **1** and two enamine **7** residues by the presence of the groupings $CF_3C=NN=CClCF_3$ (with similar ^{19}F and ^{13}C NMR chemical shifts and coupling constants to those observed for the same group in compound **14**), $-C(CF_3)=NNHC(CF_3)=$ {^1H NMR δ: 12.02 (br., 1H, NH) ppm. ^{19}F NMR δ: 11.7 (s, 3F, $CF_3C=N$); 8.3 [s, 3F, $=C(CF_3)NH$] ppm, ^{13}C NMR δ: 153.4 (q, $CF_3C=N$, $^2J=33$ Hz]; 138.3 [q, $=C(CF_3)NH$, $^2J=33$ Hz); 120.8 (q, $CF_3C=N$, $^1J=275$ Hz); 120.4 [q, $=C(CF_3)NH$, $^1J=279$ Hz] ppm}, $=CC(=O)(CH_2)_2CH-$ [^1H NMR δ: 4.43 (mult., 1H CHCO); 2.75–2.45 (AB, 2H, $=CCH_2$); 1.92–1.88 (AB, 2H, $CH-CH_2$) ppm. ^{13}C NMR δ: 210.6 (ketonic C=O); 110.2 (=C); 44.2 (CH); 29–20 ($2CH_2$) ppm} and $CH_2CH_2OCH_2CH_2NC=C(CH_2)_2CH_2$ [^1H NMR δ: 3.44 (4H, $2CH_2O$); 2.98 (4H, $2CH_2N$); 2.84 (2H, $CH_2C=$); 2.42 (2H, $CH_2C=$), 1.98 (pentet, 2H, $CH_2CH_2CH_2$) ppm. ^{13}C NMR δ: 150.8 (=C–N); 98.4 (=C); 66.4 (OCH_2); 47.4 (NCH_2), 39–20 (3 ring CH_2) ppm]. These groupings confirmed structure **16** and the low-field absorption for the NH proton indicated it was

hydrogen-bonded to the carbonyl oxygen, and hence the NH and C=O groups were *syn*. However, in contrast to compound **15** no evidence was found in the NMR spectra for coupling between the *syn* CF_3 and allylic CH_2 groups.

The NMR spectra of compound **18** showed that it was a 2-substituted derivative of enamine **4** containing the groupings $Et_2NC{=}C(CH_2)_2CH_2$ [^{1}H NMR δ: 2.88 (q, 4H, $2CH_2N$, J=7.0 Hz); 2.58 (t, 2H, $=CCH_2$); 2.47 (t, 2H, $=CCH_2$); 1.89 (pentet, 2H, $CH_2CH_2CH_2$); 1.02 (t, 6H, $2CH_3$, J=7.0 Hz) ppm. ^{13}C NMR δ: 158.7 (=C–N); 93.8 (=C); 44.6 (NCH_2); 35.8, 33.2 and 21.3 (3 ring CH_2); 13.3 (CH_3) ppm] and $CF_3C{=}NN{=}C(CF_3)NH_2$ {^{1}H NMR δ: 5.34 (br., 2H, NH_2) ppm. ^{19}F NMR δ: 13.3 (s, 3F, $CF_3C{=}N$); 9.2 [s, 3F, $H_2NC(CF_3){=}N$] ppm. ^{13}C NMR δ: 155.3 (q, $H_2NC(CF_3){=}N$, ^2J=31 Hz); 146.8 (q, $CF_3C{=}N$, ^2J=35 Hz); 121.2 (q, $CF_3C{=}N$, ^1J=278 Hz); 118.8 (q, $H_2NC(CF_3){=}N$, ^1J=275 Hz) ppm} which confirmed the structure.

Compound **37**, the hydrolysis product of enamine **18**, exhibited comparable NMR chemical shifts and coupling constants for the $CF_3C{=}NN{=}C(CF_3)NH_2$ grouping to those for the same grouping in compound **18** and the compound was also a 2-substituted cyclopentanone [^{1}H NMR δ: 3.29 (t, 1H, $CH_2CHC{=}O$); 2.53–1.85 (6H, $3CH_2$) ppm. ^{13}C NMR δ: 213.9 (ketonic C=O)); 49.5 (CH); 38.1, 29.0 and 22.8 (3 ring CH_2) ppm]; these data established the structure.

3. Experimental

3.1. Starting materials

The dichloroazine **1** was synthesised by reaction of trifluoroacetic acid with hydrazine (2:1 molar ratio) to give the bishydrazide $CF_3CONHNHCOCF_3$ which was treated with phosphoryl chloride and *N*,*N*-dimethylaniline hydrochloride [2,3]. Azine **1** was converted into its monoamino derivative **8** by reaction with aqueous ammonia (1:2 molar ratio) in diethyl ether [9]. 1-Diethylaminocyclopentene (**4**) was prepared by treatment of diethylamine in diethyl ether with cyclopentanone and calcium chloride (12 mesh) [10] and 1-diethylaminocyclohexene (**6**) and the morpholine enamine **7** were made by reaction of the appropriate amine with cyclohexanone and cyclopentanone, respectively, in hexane in the presence of titanium(IV) chloride with the mixture heated under reflux (0.5 h) [11].

3.2. General techniques

The reactions of azines **1** and **8** with enamines were carried out in anhydrous diethyl ether under an atmosphere of nitrogen (unless stated otherwise). Products from azine **8** were purified by dry column flash chromatography (DCFC) using neutral alumina (Brockmann 1, standard grade) followed by sublimation in vacuo, while products from azine **1** were placed on the top of a DCFC column filled with silica gel (Fluka 60 GF_{254}) and the resulting hydrolysed components were separated by elution through the column (eluants as given in the text; light petroleum is the petroleum ether fraction b.p. 30–40 °C). Further purification of separated components was achieved by preparative-scale TLC using plates (24×20.5 cm) coated with silica gel (60 GF_{254}) on a <0.25 g scale.

The resulting pure products were examined by IR spectroscopy (Perkin-Elmer DE783 instrument), ^{1}H NMR spectroscopy [Bruker AC300 (300 MHz) spectrometer; external reference Me_4Si], ^{19}F NMR spectroscopy [Bruker AC200 (188.3 MHz) instrument; external reference CF_3CO_2H], ^{13}C NMR (including DEPT 135°) spectroscopy [Bruker AC300 (75.0 MHz) instrument with broad band proton decoupling and D_2O as the deuterium lock signal; external reference Me_4Si] and mass spectrometry [Kratos MS25 or MS45 instruments for electron impact (EI) or chemical ionisation (CI; NH_3 gas) spectra, Kratos MS50 instrument for fast atom bombardment (FAB) spectra and a Kratos Concept 1S spectrometer for accurate mass measurement; all instruments used an electron beam energy of 70 eV]. The NMR spectra were run on solutions in $CDCl_3$ and chemical shifts to low field of reference are designated positive.

Melting points are uncorrected.

The IR spectra are recorded in Table 2, the ^{1}H, ^{19}F and ^{13}C NMR spectra are given in Tables 3–5, and the mass spectra are summarised in Table 6.

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

(a) With 1-diethylaminocyclopentene (4) under anhydrous conditions

A solution of 1-diethylaminocyclopentene (**4**) (5.33 g, 38.35 mmol) in diethyl ether (50 cm^3) was added dropwise over 1 h to a stirred solution of the dichloroazine **1** (5.00 g, 19.16 mmol) in diethyl ether (150 cm^3) under an atmosphere of nitrogen. The resulting pale orange solid was filtered off under a nitrogen atmosphere and was identified (IR spectroscopy) as the enamine hydrochloride (3.70 g, 21.1 mmol, 55%). The filtrate was evaporated under reduced pressure to give a dark red oil (7.56 g), which was shown by TLC (eluant: light petroleum/ chloroform 2:1 v/v) to contain two major (R_F 0.69 and 0.23) and several minor components. The major components were separated by DCFC (same eluant) to afford (i) a mixture of two isomers (ratio ca. 4:1) of 3-(1-chloro-2,2,2-trifluoroethylidineamino)-7-[1-chloro-2,2,2-trifluoroethylidinehydrazono)-2,2,2-trifluoroethyl]-1-ethyl-2-methyl-4-tri-

fluoromethyl-5*H*,6*H*-cyclopenta[*e*][1,3]diazine (**5**) (nc) (1.89 g, 3.20 mmol, 34%) [Analysis: Found: C, 34.7, H, 2.6; N, 11.9; F, 38.8%; M^+, 587/589/591. $C_{17}H_{15}N_5Cl_2F_{12}$ requires: C, 35.0; H, 2.5; N, 11.9; F, 38.9%; M, 588] and (ii) 1,1,1,6,6,6-hexafluoro-3,4-diaza-2-(2-diethylaminocyclopentylidine)hex-3-en-5-one (**9**) (nc) (1.52 g, 4.41 mmol, 23%) [Analysis: Found: C, 44.9; H, 5.0; N, 12.5; F, 32.7%; M^+, 345. $C_{13}H_{17}N_3OF_6$ requires: C, 45.2; H, 4.9; N, 12.2; F, 33.3%; M, 345].

(b) With 1-diethylaminocyclopentene (4) under non-anhydrous conditions

A solution of 1-diethylaminocyclopentene (**4**) (2.13 g, 15.3 mmol) in diethyl ether (15 cm^3) was added dropwise over a period of 10 min to a stirred solution of the dichloroazine **1** (2.00 g, 7.66 mmol) in diethyl ether (50 cm^3). The precipitate of the enamine hydrochloride was filtered off to give a dark red oil (2.31 g) which was separated as in the previous experiment into its two major components, compounds **5** (0.29 g, 0.49 mmol, 13%) and **9** (1.48 g, 4.29 mmol, 56%).

(c) With 1-diethylaminocyclohexene (6)

A solution of the cyclohexenylamine **6** (7.03 g, 45.95 mmol) in diethyl ether (50 cm^3) was added dropwise (1 h) to a stirred solution of the dichloroazine **1** (6.00 g, 22.98 mmol) in diethyl ether (150 cm^3) under a nitrogen atmosphere. The resulting yellow solid was filtered off under a nitrogen atmosphere and identified (IR spectroscopy) as the enamine hydrochloride (3.66 g, 19.4 mmol, 42%), while the filtrate was evaporated under reduced pressure to give a dark yellow oil (6.26 g) which was shown by TLC (eluant: light petroleum/chloroform 4:3 v/v) to contain four major components (R_F 0.37, 0.22, 0.12 and 0.08). The major components were separated to afford (i) a mixture of two diastereomers of 2-chloro-1,1,1,6,6,6-hexafluoro-5-(cyclohexanon-2-yl)-3,4-diazahex-2-ene (**10**) (2.09 g, 6.44 mmol, 28%) in the ratio (ca. 1.0:1.4) as shown by ^1H NMR spectroscopy and from which the individual isomers were separated by preparative-scale TLC (eluant: light petroleum/diethyl ether 9:1 v/v) to give 2-chloro-1,1,1,6,6,6-hexafluoro-5-(cyclohexanon-2-yl)-3,4-diazahex-2-ene (**10**) (isomer 1) (nc) (R_F 0.50) (0.78 g, 2.40 mmol, 10%) [Analysis: Found: C, 37.3; H, 3.4; N, 8.6%; M^+, 324/326. $C_{10}H_{11}N_2OClF_6$ requires: C, 37.0; H, 3.4; N, 8.6%; M, 324.5] and 2-chloro-1,1,1,6,6,6-hexafluoro-5-(cyclohexanon-2-yl)-3,4-diazahex-2-ene (**10**) (isomer 2) (nc) (R_F 0.33) (1.18 g, 3.64 mmol, 16%) [Analysis: Found: C, 37.3; H, 3.4; N, 8.6%; M^+, 324/326. $C_{10}H_{11}N_2OClF_6$ requires: C, 37.0; H, 3.4; N, 8.6%; M, 324.5]; (ii) material (1.83 g) which was further purified by preparative scale TLC (eluant: light petroleum/dichloromethane 1:1 v/v) and identified as 2-(cyclohexanon-2-yl)-6-ethyl-1,1,1-trifluoro-5-trifluoromethyl-3,4,6-triazaocta-2,4-diene (**11**) (nc) (R_F 0.37) (1.72 g, 4.79 mmol, 21%) [Analysis: Found: C, 46.5; H, 5.4; N, 11.4%; M^+, 359. $C_{14}H_{19}N_3OF_6$ requires: C, 46.8; H, 5.3; N, 11.7%; M, 359]; (iii) material (1.37 g) which was further purified by preparative-scale TLC (eluant: light petroleum/chloroform 1:2 v/v) to give 2-(cyclohexanon-2-yl)-1,1,1-trifluoro-5-trifluoromethyl-3,4,6-triazaocta-2,4-diene (**12**) (nc) (R_F 0.20) (1.29 g, 3.91 mmol, 17%) [Analysis: Found: C, 43.8; H, 4.8; N, 12.8%; M^+, 331. $C_{12}H_{15}N_3OF_6$ requires: C, 43.5; H, 4.5; N, 12.7%; M, 331. M.p. 58–60 °C]; and (iv) material (0.68 g) which was further purified by preparative-scale TLC (eluant: light petroleum/chloroform 1:2 v/v) to give 4-trifluoroacetyl-2-trifluoromethyl-3,4-diazabicyclo[4.3.$0^{1,5}$]non-1-ene (**13**) (nc) (R_F 0.15) (0.58 g, 2.01 mmol, 9%) [Analysis: Found: C, 41.6; H, 3.3; N, 9.5%; M^+, 288. $C_{10}H_{10}N_2OF_6$ requires: C, 41.7; H, 3.5; N, 9.7%; M, 288. M.p. 34–36 °C].

(d) With 1-morpholinocyclopentene (7)

Treatment of the dichloroazine **1** (4.00 g, 15.32 mmol) in diethyl ether (100 cm^3) with a solution of the enamine **7** (4.70 g, 30.72 mmol) as in the previous experiment gave the enamine hydrochloride (2.98 g, 15.32 mmol, 50%) and a dark red oil (5.29 g) which was shown by TLC (eluant: light petroleum/dichloromethane 2:1 v/v) to contain four major components (R_F 0.84, 0.58, 0.43 and 0.18). These components were separated by DCFC (same eluant) to afford (i) a yellow solid identified as 9-(5-chloro-1,1,1,6,6,6-hexafluoro-3,4-diazahex-2,4-dien-2-yl)-2,5-bis(trifluoromethyl)-3,4-diaza-11-oxatricyclo[10.3.0.^{1,12}$0^{6,10}$]pentadeca-1,3,5,9-tetraene (**14**) (nc) (0.68 g, 1.21 mmol, 8%). [Analysis: Found: M^+, 562.0429. $C_{18}H_{11}N_4OClF_{12}$ requires: M, 562.0430]; (ii) a yellow liquid identified as 2-chloro-5-(cyclopentan-1-on-2-ylidine)-1,1,1,6,6,6-hexafluoro-3,4-diazahex-2-ene (**15**) (nc) (0.98 g, 3.17 mmol), 21%) [Analysis: Found: C, 35.1; H, 2.2; N, 9.4; F, 37.3%. M^+, 308/310. $C_9H_7N_2OClF_6$ requires: C, 35.0; H, 2.3; N, 9.1: F, 37.0%; M, 308.5]; (iii) a dark yellow liquid identified as 1,1,1,6,6,6-hexafluoro-2-[5-(5-chloro-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-dien-2-yl)cyclopentan-1-on-2-ylidine]-5-(2-morpholinocyclopenten-1-yl)-3,4-diazahex-2-ene (**16**) (nc) (1.78 g, 2.74 mmol, 18%) [Analysis: Found: M^+, 649.1091. $C_{22}H_{20}O_2N_5ClF_{12}$ requires: M, 649.1114]; and (iv) material (0.62 g) which was sublimed in vacuo at room temperature to give a white solid identified as 1,1,1,6,6,6-hexafluoro-5-(2-morpholinocyclopentanylidine)-3,4-diazahexa-3-en-2-one (**17**) (nc) (0.51 g, 1.42 mmol, 9%) [Analysis: Found: C, 43.8; H, 4.6; N, 11.4; F, 31.6%; M^+, 359. $C_{13}H_{15}N_3O_2F_6$ requires: C, 43.5; H, 4.2; N, 11.7; F, 31.8%; M, 359].

3.4. Reaction of 2-amino-5-chloro-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (8) with 1-diethylaminocyclopentene (4)

A solution of the enamine **4** (3.68 g, 26.5 mmol) in diethyl ether (25 cm^3) was added dropwise over a period

of 30 min to a stirred solution of the aminochloroazine **8** (3.20 g, 13.3 mmol) in diethyl ether (70 cm^3) under a nitrogen atmosphere and stirring was continued (15 h). The resulting precipitate of the enamine hydrochloride (2.31 g, 13.2 mmol, 50%) was filtered off and the solvent was removed from the filtrate to give a dark brown sticky solid (4.49 g) which was shown by TLC (eluant: light petroleum/dichloromethane 1:1 v/v) to contain one major component (R_F 0.37) and baseline material. Attempted purification by DCFC (same eluant) using alumina gave material (3.32 g) which was further purified by sublimation in vacuo at 40 °C to afford 2-amino-5-(2-diethylaminocyclopenten-1-yl)-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (**18**) (nc) (1.63 g, 4.74 mmol, 36%) [Analysis: Found: M^+, 344.1439. $C_{13}H_{18}N_4F_6$ requires: M, 344.1436].

3.5. Hydrolysis of 2-amino-5-(2-diethylaminocyclopenten-1-yl)-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (18)

A portion (1.0 g) of the crude reaction mixture obtained in the previous experiment and silica gel (3 g) in dichloromethane (40 cm^3) were poured on to the top of a DCFC sintered column and left (28 h) before eluting (light petroleum/diethyl ether 5:2 v/v) to give a compound (R_F 0.31) identified as 2-amino-5-(cyclopentanon-2-yl)-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (**37**) (nc) (0.32 g, 1.11 mmol, 38%) [Analysis: Found: C, 37.7; H, 3.4; N, 14.2%; M^+, 289. $C_9H_9N_3OF_6$ requires: C, 37.4; H, 3.1; N, 14.5%; M, 289].

Acknowledgement

We thank the Hariri Foundation for a grant (to M.M. A.-G.).

References

[1] For Part 14, see M.M. Abdul-Ghani and A.E. Tipping, *J. Fluorine Chem., 68* (1994) 211.
[2] M.G. Barlow, D. Bell, N.J. O'Reilly and A.E. Tipping, *J. Fluorine Chem., 23* (1983) 293.
[3] D. Bell, A.O.A. Eltoum, N.J. O'Reilly and A.E. Tipping, *J. Fluorine Chem., 64* (1993) 151.
[4] A.O.A. Eltoum, N.J. O' Reilly and A.E. Tipping, *J. Fluorine Chem., 65* (1993) 157.
[5] A.O.A. Eltoum, N.J. O'Reilly and A.E. Tipping, *J. Fluorine Chem., 65* (1993) 101.
[6] S.H. Benomar, B. Patel and A.E. Tipping, *J. Fluorine Chem., 50* (1990) 207.
[7] S.H. Benomar, N.H. O'Reilly and A.E. Tipping, *J. Fluorine Chem., 51* (1991) 207.
[8] S.H. Benomar, *M.Sc. Thesis,* University of Manchester, 1990.
[9] M.M. Abdul-Ghani, *Ph.D. Thesis,* University of Manchester, 1992.
[10] E.P. Blanchard, *J. Org. Chem., 28* (1963) 1397.
[11] R. Carlson and A. Nilsson, *Acta Chem. Scand., 38B* (1984) 49.