Reactions of tetrafluoroethene oligomers. Part 15.[1] Reactions of perfluoro-3,4-dimethylhex-3-en-2-one; a highly reactive α,β-unsaturated ketone

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Perfluoro-3,4-dimethylhex-3-en-2-one **1** has been shown to react with nucleophiles both at the double bond and at the carbonyl group depending on the type of nucleophilic centre and also on the steric requirements of the attacking reagent. In many cases the first formed product undergoes further reactions either with the original nucleophile or by intramolecular processes. Thus, reaction of **1** with primary amines afforded azetines **3** and **4** in the cases of ethylamine and cyclohexylamine and a mixture of the azetine **5** and a ketenimine **6** from *tert*-butylamine. The ketenimine **6** either on standing at room temperature or more quickly on heating cyclised quantitatively to the azetine **5** found in the original reaction. Reaction of the enone with secondary amines took a different course; the products from reaction with diethylamine were an unsaturated amide **8** and *N*,*N*-diethyltrifluoroethanamide **7**, and piperidine afforded not only an unsaturated amide **11** and the corresponding ethanamide **10** but also a piperidyl ketone **12**. This intermediate is postulated to be the archetype of the first formed product for all the reactions reported. Reaction with dimethylamine yielded a different product, a disubstituted unsaturated ketone **9**, but none of the corresponding amides as seen with other secondary amines. The reaction with hydrazine afforded a substituted pyrazolidine **2**. When the enone was treated either with triethylamine or with fluoride ion cyclisation to yield a perfluorotetramethyldihydrofuran **13** occurred. Reaction with sodium methoxide or sodium phenoxide yielded the corresponding bis-ethers **14**, **15**, whilst reaction with sodium hypochlorite gave a hydrogen containing epoxide **16**, postulated to arise from a haloform type reaction from the first formed epoxide. Finally, reaction with methylmagnesium iodide gave a dimethyl substituted derivative **17**. A mechanistic rationale based on a series of addition–elimination reactions with or without subsequent cyclisation is proposed to explain these reactions.

Introduction

The use of reactive fluorinated building blocks for the *de novo* synthesis of a wide range of compounds both in the pharmaceutical and agrochemical areas is becoming increasingly important and this area of chemistry has recently been comprehensively reviewed by Percy.[2] We have demonstrated this recently by reporting a short simple stereospecific synthesis of fluorodeoxyribose derivatives starting from trifluorovinyllithium.[3] The use of α,β-unsaturated ketones as building blocks in synthesis is well established but the chemistry of the corresponding polyfluoro derivatives, which could be potentially a rich source of useful building blocks for the introduction of fluorine regio- and possibly stereospecifically, has been sparsely reported.[4]

The main reason for this lack of information is the relatively few reliable synthetic methods available hitherto. The first reported work by Anderson[5] and Tarrant *et al.*[6] led to the formation of perfluoromethyl vinyl ketone in very low yield in a multistep process. Knunyants and Snergirev reported two methods of synthesis, the first from hexafluoropropene oligomers[7] and the second by the reaction of fluoride ion with perfluoroethers.[8] England[9] also reported similar work to the latter. However the yields in all of these processes were either small or the starting materials were very difficult to obtain and very little chemistry was discussed. In a previous paper[10] in this series we have described the formation of perfluoro(3,4-dimethylhex-3-en-2-one) **1** by pyrolysis of perfluoro(4-ethyl-2,5-dihydro-2,3,4,5-tetramethylfuran) which in turn was obtained from the pentamer of tetrafluoroethene. We now describe some of the chemistry of this readily available example of a little studied class of compounds which may give an insight into the potentially important use of such compounds in the synthesis of bioactive compounds containing fluorine atoms or fluoroalkyl groups.

Our process gave us multi-gram quantities of **1**, and we were thus able to study in detail some of the chemistry of this class of materials. Since it is well known that both perfluoroalkenes and ketones react readily with nucleophiles we were able to study the relative reactivity of each of the functionalities with such reagents within the same molecule.

Results and discussion

We began our investigation by reacting **1** with a series of nitrogen nucleophiles using a selection of primary (Scheme 1), secondary (Scheme 2) and tertiary amines of differing steric requirements as nucleophiles. Thus, in a strongly exothermic reaction, ethylamine yielded a single product in good yield. The product, a white crystalline solid, showed strong bands in its IR spectrum at 1690, 1605 and 3260 cm^{-1}. The ^1H NMR spectrum showed signals attributable to an NH group exchangeable with D_2O, and two different ethyl groups. The ^{19}F spectrum showed three complex signals attributable to a CF_3, a C_2F_5 and a further sharp singlet corresponding to a second CF_3 group. These data, together with elemental analysis and mass spectral data, suggest that the compound is the azetine **3**. Similar structures have been observed previously[1] from the reaction of TFE trimer with certain amines. In a similar reaction with cyclohexylamine the azetine **4** was obtained which was characterised as above.

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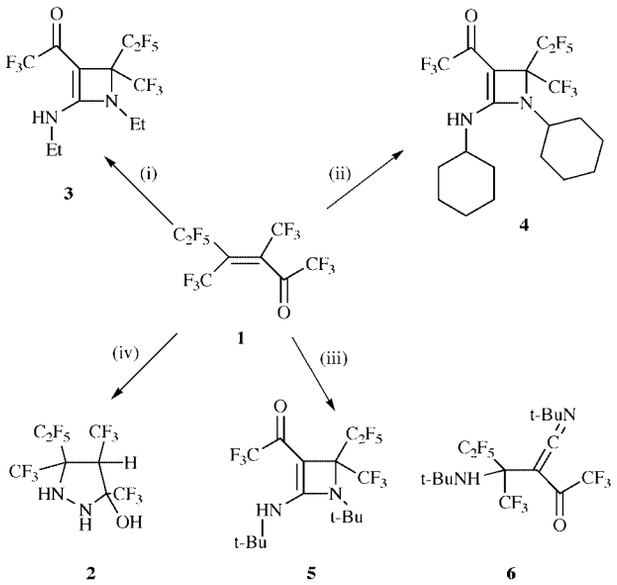
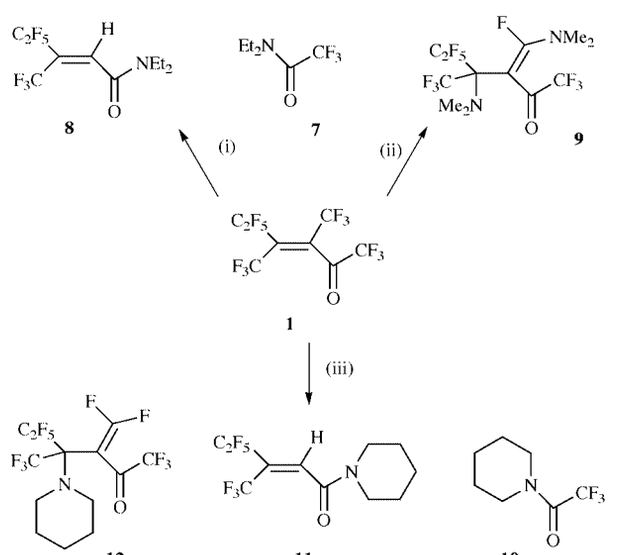


Scheme 1 *Reagents and conditions*: (i) $EtNH_2$; (ii) $C_6H_{11}NH_2$; (iii) t-$BuNH_2$; (iv) NH_2NH_2.



Scheme 2 *Reagents and conditions*: (i) Et_2NH; (ii) Me_2NH; (iii) Piperidine.

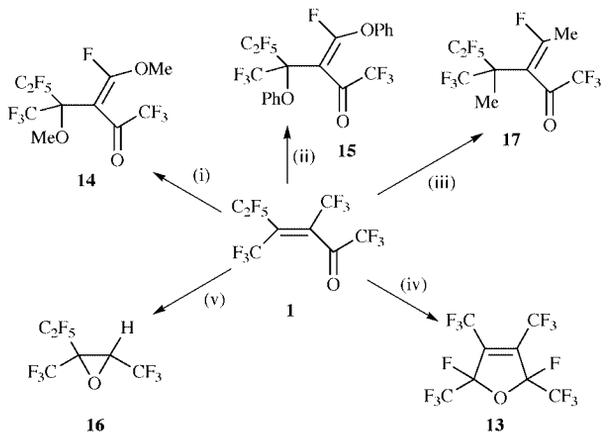
Reaction of **1** with *tert*-butylamine gave a mixture of two products, a liquid and a solid, and the latter on filtration and recrystallisation was readily characterised as the corresponding azetine **5**. The liquid fraction either on prolonged standing at room temperature or by heating for a short time at 100 °C converted to **5** quantitatively. The liquid fraction showed two very strong bands in its IR spectrum at 2060 and 1650 cm^{-1} which from a comparison with some of our previous work [11] we could attribute to the C=C=N structure and to a C=O group respectively. ^1H NMR spectroscopy indicated the presence of two different *tert*-butyl groups and ^{19}F NMR spectroscopy indicated there were two different CF_3 groups present, one signal, a sharp singlet, being characteristic of the CF_3CO function. These data along with the elemental analysis suggest that the product is the ketenimine **6**.

The reaction of **1** with secondary amines followed an entirely different pattern to that of primary amines. Reaction of **1** with diethylamine afforded a mixture of two products, readily separated by column chromatography. The first product which was eluted from the column was identified by comparison with an authentic sample as *N*,*N*-diethyltrifluoroethanamide **7**. The second product, an oil, gave a strong band at 1650 cm^{-1} in its IR spectrum, characteristic of an amide. ^1H NMR spectroscopy showed two sets of signals in the ratio of 1:4 due to a pair of isomers. These we assigned from chemical shift and coupling constant data to ethyl groups attached to nitrogen and somewhat unexpectedly a signal for a single olefinic proton. ^{19}F NMR spectroscopy again showed two sets of signals, in the same ratio, assigned as a C_2F_5 and a CF_3 group both attached to a double bond. The mass spectral and elemental analysis data confirmed the structure as an inseparable mixture of (*E*/*Z*)-*N*,*N*-diethyl-4,4,5,5,5-pentafluoro-3-trifluoromethylpent-2-enamide **8**. Reaction of **1** with dimethylamine produced an entirely different product with no evidence of any of the analogous amides obtained from the previous reaction. The single product we obtained showed bands at 1680 and 1620 cm^{-1} in the IR spectrum corresponding to a C=O group and C=C system respectively. The ^1H NMR spectrum showed signals for two different dimethylamino functions one of which appeared to be attached to an olefinic system with a coupling to fluorine. The ^{19}F spectrum showed signals for two CF_3 groups one of which, a sharp singlet, was assigned as a CF_3CO group and a signal for a CF_2 group as part of a C_2F_5 group and a signal for a single olefinic fluorine atom with an HF coupling constant identical to that found in the ^1H spectrum associated with the dimethylamino groups. The mass spectral and elemental analysis data confirmed the structure as 4-(*N*,*N*-dimethylamino)-3-(*N*,*N*-dimethylaminofluoromethylene)perfluoro(4-methylhexan-2-one) **9**. The striking difference in the reaction of **1** with the homologous amines suggested that either steric factors or nucleophilicity/basicity differences are involved in the change of reaction pathway. To gain further insight into this possibility we investigated a similar reaction of **1** with piperidine. In this case we obtained three products which were readily separated by column chromatography. Two were readily identified as *N*-trifluoroethanoylpiperidine **10** and (*E*/*Z*)-1-piperidino-4,4,5,5,5-pentafluoro-3-trifluoromethylpent-2-en-1-one enamide **11**. Their structures were determined by comparison with an authentic sample in the case of **10** and by the spectral similarities in **11** with respect to **8**. The third product did not show the presence of an amide in its IR spectrum, but gave bands at 1760 and 1670 cm^{-1} corresponding to those expected for a CF_2=C group and a C=O group respectively. The ^1H NMR spectrum showed only signals for the cyclohexane ring protons. The ^{19}F NMR spectrum was much more interesting, it showed signals for two CF_3 groups, a C_2F_5 group and a complex signal for two olefinic fluorine atoms. Mass spectral and elemental analysis data confirmed the structure as the keto-olefin **12**—a somewhat unexpected product. Difluoromethylene groups are normally very reactive towards nucleophiles and we might have expected therefore not to see such a product under the reaction conditions we were using. However it should be noted that there are some rare examples of such compounds being obtained in the TFE oligomer chemistry.[1] The origin of compounds **8** and **11** is interesting since we have lost the trifluoroethanoyl group and a trifluoromethyl group from **1**. The presence of **12** in the product mixture from the piperidine reaction suggested to us that this could be an intermediate in the process leading to the formation of **11** and thus a similar intermediate could lead to the formation of **8**. We therefore reacted **12** with piperidine as in the original experiment but at reflux in ether as solvent. After 18 h no starting material remained and the reaction was worked up as in the original experiment. Pure **11** was isolated in good yield. We therefore conclude that **12** is almost certainly an intermediate in the formation of **11** as discussed below.

The reaction **1** with hydrazine hydrate gave, in an exothermic reaction, a crystalline solid which showed no band for a carbonyl group, but did show bands for NH_2 and OH groups in the IR spectrum. The ^1H NMR spectrum gave four signals of equal intensity, three of which disappeared on exchange with D_2O and a signal at δ 4.05 for a non-exchangeable proton as a quartet due to a proton on a carbon atom bearing a CF_3 group. The

^{19}F spectrum showed signals for a C_2F_5 and two CF_3 groups. The mass spectral and elemental analysis data confirmed the structure as the pyrazolidine **2**. Related reactions with TFE trimer and hexafluoropentane-2,4-dione afford similar products.[1]

We next turned our attention to the reactions of **1** with oxygen nucleophiles (Scheme 3). Reaction with sodium methoxide



Scheme 3 *Reagents and conditions*: (i) MeO^-; (ii) PhO^-; (iii) MeMgBr; (iv) F^- or Et_3N; (v) NaOCl.

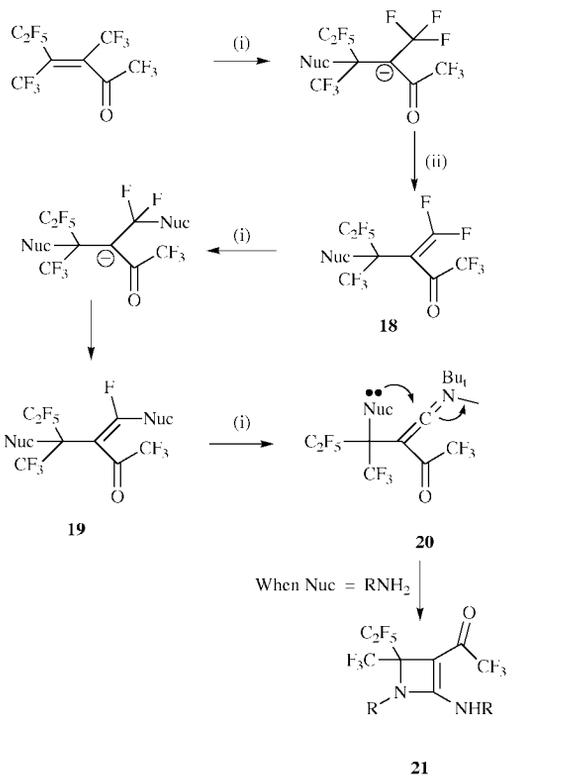
afforded a single component which showed some similar spectral characteristics to compound **9** with bands in its IR spectrum at 1735 and 1650 cm^{-1} attributable to CFX=C and C=O respectively. The ^1H NMR spectrum showed the presence of two different methoxy groups. The ^{19}F spectrum was almost identical to that of compound **9** and we thus concluded that the disposition of the fluorinated moieties in both compounds were the same. Elemental analysis and mass spectrometry confirmed the proposed structure as the keto-olefin **14**. The product from the reaction of **1** with sodium phenoxide had similar spectral characteristics compound **14** with phenoxy groups replacing the methoxy groups and is assigned the structure as the keto-olefin **15**.

The formation of fluorinated epoxides and their subsequent reactions has led to some unusual and useful compounds[11] and we were interested to see if **1** would react to give what would be a very interesting epoxide. We chose to use sodium hypochlorite as the epoxidising agent as it has been highly successful in previous work. Thus, reaction of **1** afforded a single product. The IR spectrum immediately showed that the carbonyl group was no longer present but a new band characteristic of fluorinated epoxides at 1510 cm^{-1} had appeared. The ^1H NMR spectrum indicated the presence of two CF_3 groups one of which was highly coupled and a C_2F_5 group. The ^1H spectrum surprisingly gave a signal resonance at δ 4.15 as a quartet indicating a proton on a carbon bearing a CF_3 group. An accurate mass measurement gave the correct mass for the epoxide **16** as a *cis*/*trans* mixture. Because of the volatility of **16** we were unable to obtain an elemental analysis.

The reactions of fluoroalkenes with organometallic compounds and indeed Michael additions to them are well known processes. We therefore reacted **1** with methylmagnesium iodide to see which mode of reaction was preferred. A single product was obtained which showed again the presence of a CFX=C group and a C=O group in its IR spectrum. The ^1H NMR spectrum showed signals for two methyl groups, one of which was attached to a double bond. The ^{19}F spectrum again was very similar to compounds **9**, **14** and **15** suggesting similar base structures. Elemental analysis and mass spectrometry confirmed the structure as being consistent with the keto-olefin **17** as an *E*/*Z* mixture.

We and others[1,12–15] have shown that certain TFE oligomer derivatives will readily cyclise in the presence of either triethylamine or fluoride ion to yield furan, pyrrole, pyran or dioxane derivatives. With this in mind we reacted **1** either with triethylamine in dry ether or with fluoride ion in acetonitrile to yield a single product in good yield which was shown to be identical with the perfluorodihydrofuran derivative **13** previously prepared by Chambers *et al*.[16]

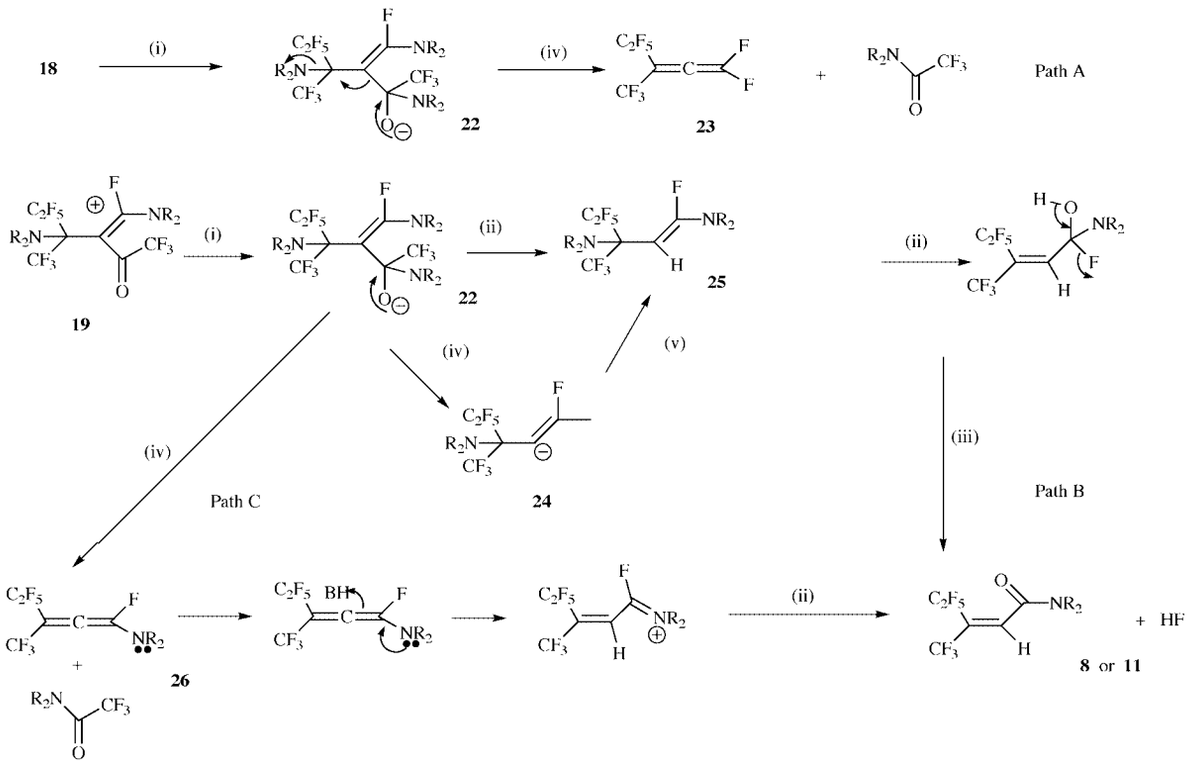
From a careful study of all of the above results it is clear that amongst the interesting reactions occurring there is an overall pattern leading to the observed products as shown in Scheme 4.



Scheme 4 *Reagents and conditions*: (i) Nuc; (ii) $-F^-$; (iii) H_2O; (iv) $-HF$; (v) $-Nuc^-$.

It seems that in all cases the first step is the Michael type reaction on the double bond system to give after elimination of fluoride ion intermediate **18** and this proposal is strengthened by the isolation of compound **11** from the reaction of piperidine with **1** *i.e* **18** when Nuc = piperidyl. This kind of elimination is quite common in the chemistry of TFE oligomers usually leading directly to product or, since **18** is likely to be more reactive towards nucleophiles than starting material, to further downstream products. Thus, **18** on further nucleophilic attack again in a Michael type reaction leads to products of the type **19** and such products, compounds **9**, **14**, **15** and **17** have been isolated in a number of the reactions we have studied. If however the attacking nucleophile, as in the case of primary amines, still has a hydrogen atom present, elimination of a further molecule of hydrogen fluoride takes place leading to ketenimines of the type **20** as exemplified by the isolation of compound **6** from the reaction with *tert*-butylamine. We have postulated and subsequently isolated such intermediates in our studies on the chemistry of TFE hexamer.[17] Without doubt, in the light of the ready ring closure of **6** to the azetine **5**, ketenimines of the type **6** are intermediates in the formation of the azetines **3** and **4**. In these cases we would expect the cyclisation reaction to be rapid compared with the corresponding reaction of **6** due to the steric effect of the bulky *tert*-butyl group. When the attacking nucleophile is not a primary amine the reaction appears either to stop after the formation of compounds of the type **19** as is the case in reactions with alkoxides and organometallic compounds.

A problem of mechanism arises however when the attacking nucleophile is a secondary amine since we clearly obtain



Scheme 5 *Reagents and conditions*: (i) R_2N; (ii) H_2O; (iii) −HF; (iv) $-R_2NH$; (v) BH.

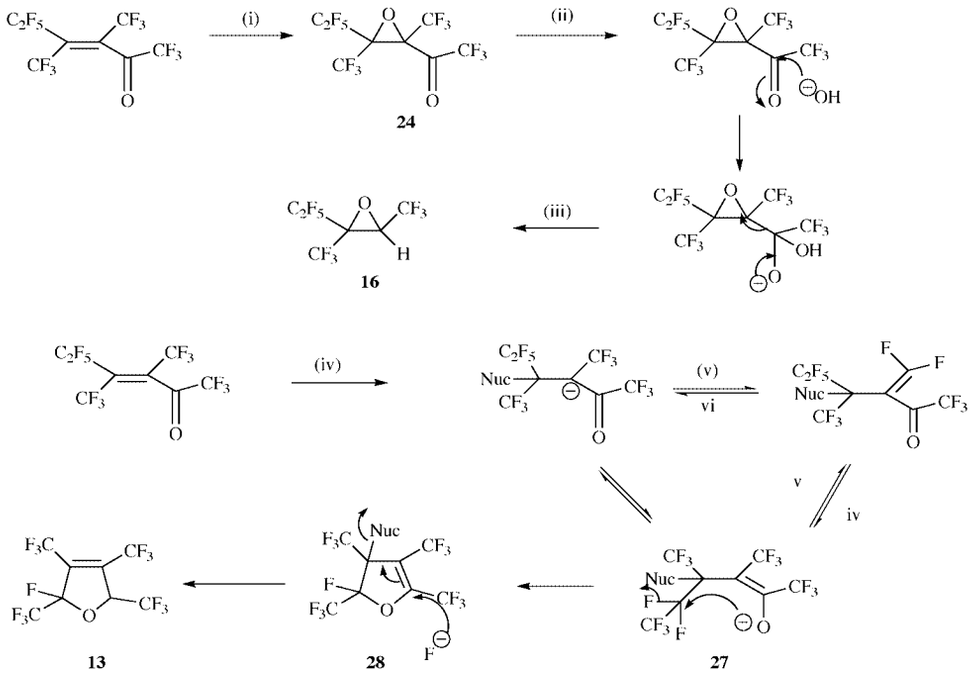
products of a different type *i.e.* **8**, **11** and **12**, and in particular **8** and **11**. Since we have shown that **12** is converted to **11** under similar reaction conditions which led to the formation of the mixture of **10**, **11** and **12** it is not unreasonable to suggest that **12** is an intermediate in the formation of **11**; further, the isolation of *N*,*N*-diethyltrifluoroethanamide and *N*-trifluoroethanoylpiperidine suggest these moieties are formed in the reaction leading to **8** and **11**. We considered two possibilities for the reaction as shown in Scheme 5. We assume not unreasonably that **18** (Scheme 4) is the common intermediate, as discussed above, which in some cases reacts further with nucleophiles leading to **19**. It appears that in certain cases, and in particular with the more strongly reactive secondary amines, a further set of reactions occurs (Scheme 5). The most obvious reaction, which also accounts for the formation of the trifluoroethanamides isolated, is a haloform-type reaction on the trifluoroacyl group leading ultimately to **23** from **18** (path A), or **25** from **19**. We discount the former pathway since it is known [18] that allenes of the type **20** react with nucleophiles at position 2 as shown and this would lead to the wrong product pattern. Thus, we are led to the conclusion that **22**, once formed, could decompose in three ways, firstly by loss of the amide to give the anion **24** which protonates to give **25** or secondly by a synchronous process leading as shown to give **25** directly. Hydrolysis of **25** with loss of the amine function as shown leads to the observed product, path B. Either of these processes seem to be energetically unlikely. The other alternative is for the loss of the amine function as shown leading to the allenamine **26** which could behave as an extended enamine, protonation and hydrolysis of which leads to the formation of **8** or **11** when the nucleophile is diethylamine or piperidine respectively. This mechanism has the merits that it satisfactorily accounts for all of the products observed and is chemically sound.

The formation of the epoxide **16** and the cyclic ether **13** again poses some mechanistic problems. We propose, as shown in Scheme 6, that the epoxide **16** is formed *via* the expected epoxy ketone **24**. The solution in which the epoxidation is carried out is very strongly alkaline and we propose a simple haloform type cleavage of the ketone, a process well known in fluoroketone chemistry, leading to the observed epoxide (**16**). The formation of the cyclic ether we believe follows a pathway similar to that proposed by Chambers *et al.*[16] for its formation from the tetramer of tetrafluoroethene. Thus, attack of either fluoride ion or triethylamine at the vinylic centre of **1** leads to an intermediate enolate of the type **27** (Scheme 6). Intramolecular attack of the enol oxygen on the C_2F_5 group in an manner analogous to that reported earlier[11,16] affords intermediate **28** and fluoride ion catalysed rearrangement of **28** affords the observed cyclic ether **13**.

To see if there was any theoretical basis for our suppositions we carried out some molecular orbital calculations and found that, in spite of examining a number of possible parameters such as HOMO–LUMO interactions, possible transition state energy levels *etc.*, we could find no conclusive evidence to support any one of the possible pathways over any of the others and we can only put forward the suggestions we have made based on the literature precedents we have cited as the most plausible explanation of our results. We thus have shown that perfluoro α,β-unsaturated ketones do present some unusual and unexpected chemistry, providing a novel series of compounds with the potential for the incorporation of fluorinated moieties by suitable choice of nucleophiles into a range of interesting compounds.

Experimental

^{1}H NMR (300 MHz) and ^{13}C NMR spectra (75 MHz) were measured on a Bruker AC 300 NMR spectrometer unless stated otherwise. ^{1}H NMR spectra (400 MHz) were measured on a Bruker AMX 400 NMR spectrometer. ^{19}F NMR spectra were carried out either on a JEOL NMR spectrometer, type FX 90 Q (84.26 MHz) or on a Bruker AC 300 NMR spectrometer (282.4 MHz); tetramethylsilane and trichlorofluoromethane were used as internal references. For the characterisation of the signals the following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sext = sextet, h = heptet, m = multiplet, br = broad, c = complex, dd = doublet of doublets, dt = doublet of triplets, "quin" = pseudo quintet *etc*. The



Scheme 6 *Reagents and conditions*: (i) NaOCl; (ii) NaOH; (iii) H_2O; (iv) F^- or Et_3N; (v) $-F^-$; (vi) $+F^-$.

chemical shift values for multiplet signals are the centred values; *J* values are given in Hz. The mass spectra (CI-MS/EI-MS) were measured on a VG-Prospec triple focusing mass spectrometer. For GC-MS analysis, a Carlo Erba 8000 series GC was used with a 50 meter column, BPX 5 (helium carrier gas, 70 eV, electron impact).

Thin layer chromatography was performed on TLC plastic sheets silica gel 60 F_{254}, pre-coated with a layer thickness of 0.2 mm from Merck, Art. 5735. Gas chromatographic analysis was carried out using a Philips PYE Unicam, Series 304 chromatograph with a 50 metre CD-SIL-CB 19 column. The data were registered by a JCL 600 chromatography data system.

Reactions of perfluoro-3,4-dimethylhex-3-en-2-one 1 with primary amines

(a) Ethylamine. To a solution of ethylamine (5 cm^3) in dry ether (50 cm^3) was added, with magnetic stirring, a solution of **1** (5 g) in ether (10 cm^3) over a period of 10 min at 18 °C. After the strong exotherm had subsided the reaction was stirred for 10 h. The solution was washed with 4 M HCl, water and dried ($MgSO_4$). Evaporation of the solvent afforded a red oil (4.11 g) which crystallised on standing. Thin layer chromatography showed only one component to be present, purification by column chromatography (silica, with ether as eluant) afforded 1-ethyl-2-(*N*-ethylamino)-3-trifluoroethanoyl-4-pentafluoroethyl-4-trifluoromethyl-1,4-dihydroazete **3** (3.7 g), mp 112–113 °C as white crystals (Found: C, 35.6; H, 2.7; N, 6.2; F, 50.8%. $C_{12}H_{11}F_{11}N_2O$ requires C, 35.3; H, 2,7; N, 6.7; F, 51.2%); $\delta_H(CDCl_3)$ 1.3 (t, 6H, CH_3), 3.60 and 3.75 overlapping (q and q, 4H, $CH_2 \times 2$, CH_2-O and CH_2-N) 8.14 (br s, 1H, NH); δ_F ($CDCl_3$) −69.1, (m, 3F, CF_3), −74.7 (m, 3F, CF_3CF_2), −79.3 (s, 3F, CF_3CO), −114.2, (m, 2F, CF_3CF_2); IR 3260 cm^{-1} (NH), 1690 cm^{-1} (C=O), 1605 cm^{-1} (C=C); *m/z* 408 $[M]^+$, 339 $[M - CF_3]^+$.

A second crop of material (0.3 g) was shown to be a mixture of at least five products and was not further investigated.

(b) Cyclohexylamine. A similar reaction to the above, except that a solution of **1** (6 g) in ether (50 cm^3) was added to the amine (3 g) in ether (20 cm^3) at −20 °C, which had the effect of controlling the exotherm noted above, afforded cyclohexyl-2-(*N*-cyclohexylamino)-4-pentafluoroethyl-3-trifluoroethanoyl-4-trifluoromethyl-1,4-dihydroazete **4** (6.23 g), mp 140–141 °C (Found: C, 45.8; H, 4.8; N, 5.6%. $C_{20}H_{23}F_{11}N_2O$ requires C, 46.6; H, 4.5; N, 5.4%); δ_H ($CDCl_3$) 1.6 (cm, 22H), 7.2 (m, 1H, NH); δ_F ($CDCl_3$) −69.0, (m, 3F, CF_3), −74.3, (m, 3F, CF_3CF_2), −80.2 (s, 3F, CF_3CO), −113.5 (m, 2F, CF_3CF_2); *m/z* 516 $[M]^+$, 434 $[M - C_6H_{10}]^+$; IR 1660 cm^{-1} (C=O) 1585 cm^{-1} (C=C).

(c) *tert*-Butylamine. In the same manner as in (b) the ketone **1** (5 g) and *tert*-butylamine (1.93 g) afforded a mixture of two products readily separated by column chromatography, identified as (i) 1-*tert*-butyl-2-(*N*-*tert*-butylamino)-4-pentafluoroethyl-3-trifluoroethanoyl-4-trifluoromethyl-1,4-dihydroazete **5** (1.76 g), mp 135–136 °C (from ethanol) (Found: C, 39.8; H, 4.2; N, 6.3%. $C_{16}H_{19}F_{11}N_2O$ requires C, 40.1; H, 4.0; N, 6.0%); $\delta_H(CDCl_3)$ 1.25 (s, 9H, Bu_t), 1.50 (s, 9H, Bu_t), 8.75 (br s, 1H, NH); δ_F ($CDCl_3$) −72.4 (m, 3F, CF_3), −76.0 (m, 3F, CF_3CF_2), −80.6 (s, 3F, CF_3CO), −115.3 (m, 2F, CF_3CF_2); IR 1710 cm^{-1} (C=O), 1680 cm^{-1} (C=C); *m/z* 445 $[M - F]^+$, 407 $[M - C_4H_9]^+$, 393 $[M - C_4H_9N]^+$; (ii) a pale yellow oil, which on distillation *in vacuo* yielded *N*-(3-*tert*-butylamino-2-trifluoroethanoyl-3-trifluoromethylpentafluoropent-1-enylidine)-*tert*-butylamine **6** (2.15 g) bp 65 °C/0.1 mmHg (Found: C, 39.2; H, 3.7; N, 6.1%. $C_{16}H_{19}F_{11}N_2$ requires C, 40.1; H, 4.0, N, 6.0%); δ_H ($CDCl_3$) 1.52 (s + s, $2 \times 9H$, $2 \times Bu_t$); δ_F ($CDCl_3$) −73.9 (s, 3F, CF_3), −76 (cm, 3F, CF_3), −78.8 (cm, 3F, CF_3), −119.9 (cm, 2F, CF_3CF_2); IR 2060 cm^{-1} C=C=N, 1650 cm^{-1} C=O.

On standing for 100 h at rt or by heating at 100 °C for 30 min, **6** completely cyclised to the azete **4** in quantitative yield.

Reactions of 1 with secondary amines

(a) Diethylamine. A solution of diethylamine (1.93 g) in dry ether (50 cm^3) was added dropwise to a stirred solution of **1** in dry ether (100 cm^3) at 0 °C. The solution, which turned bright red, was stirred for a further 10 h at room temperature. The white precipitate of diethylamine hydrofluoride was filtered off and the filtrate concentrated to give a red oil (4.1 g). TLC showed the presence of two major components, column chromatography (silica, CCl_4–$CHCl_3$, 1:1) afforded from a portion of the oil (2 g) (i) *N*,*N*-diethyltrifluoroethanamide **7** (0.25 g) identical in all respects to a sample prepared from trifluoroethanoic anhydride and diethylamine; (ii) as a pale green oil (*E*/*Z*)-*N*,*N*-diethyl-4,4,5,5,5-pentafluoro-3-trifluoromethylpent-

2-enamide **8** (1.25 g) bp 62–64 °C/0.4 mmHg (Found: C, 38.6; H, 3.6; N, 4.3%. $C_{10}H_{11}F_8NO$ requires C, 38.3; H, 3.5; N, 4.5%); $\delta_H(CDCl_3)$ (isomer 1) 1.15 (t, 6H, CH_3CH_2), 3.35 (q, 4H, CH_3CH_2 N), 7.52 (s, 1H, =CH); (isomer 2) 1.18 (t, 6H, $^3J_{HH}$ 6.8, CH_3CH_2), 3.38 (q, 4H, $^3J_{HH}$ 6.8, CH_3CH_2N), 7.4 (s, 1H, =CH); $\delta_F(CDCl_3)$ (isomer 1) −62.2 (m, 3F, CF_3C=), −84.2 (m, 3F, CF_3CF_2), −110.2 (cq, 2F, CF_3CF_2); (isomer 2) −59.6 (m, 3F, CF_3C=), −84.3 (m, 3F, CF_3CF_2), −112.7 (m, 2F, CF_3CF_2); *m*/*z* 313 $[M]^+$, 293 $[M - HF]^+$, 194 $[M - C_2F_5]^+$.

The isomer ratio from these data was found to be isomer 1 : isomer 2 = 1 : 4. From previous results we tentatively suggest isomer 1 is the *E* isomer.

(b) Dimethylamine. A solution of excess dimethylamine (10 cm^3) in dry ether (100 cm^3) was cooled to −20 °C in a jacketed dropping funnel and was then added to a solution of **1** (10 g) in dry ether (20 cm^3) at −20 °C over 15 min, the solution was allowed to warm slowly to room temperature and was then stirred for a further 10 h. Water (50 cm^3) was added, the ether layer separated, combined with an ether extract of the aqueous layer and dried ($MgSO_4$). Evaporation of the ether afforded a red oil. TLC analysis using a number of solvent systems indicated only one product to be present. Distillation *in vacuo* yielded a yellow oil which crystallised on standing to give (*E*/*Z*)-4-(*N*,*N*-dimethylamino)-3-(*N*,*N*-dimethylaminofluoromethylene)perfluoro(4-methylhexan-2-one) **9** (4.1 g) mp 43–44 °C, bp 81–82 °C/0.04 mmHg (Found: C, 33.4; H, 2.8; N, 6.5; F, 53.6%. $C_{12}H_{12}F_{12}N_2O$ requires C, 33.7; H, 2.8; N, 6.5; F, 53.2%); δ_H 2.58 (s, 6H, $(CH_3)_2N$), 2.98 (d, 6H, $^4J_{HF}$ 4.5 Hz, $(CH_3)_2NCHF$=); δ_F −47.5 (h, 1F, $^4J_{HF}$ 4.6 Hz, =$CFN(CH_3)_2$), −61.5 (m, 3F, CF_3), −74.0 (s, 3F, CF_3CO), −78.6 (m, 3F, CF_3CF_2), −107.2 (m, 2F, CF_3CF_2); IR 1680 cm^{-1} C=O, 1620 cm^{-1} C=C.

(c) Piperidine. Piperidine (1.2 g) in dry ether (40 cm^3) was added dropwise with stirring to a solution of **1** (2.5 g) in dry ether (20 °C cm^3) at 0 °C. The mixture was stirred at 0 °C for 2 h and then at room temperature for a further 10 h. The resulting mixture was washed with water (2 × 25 cm^3) and the original ether layer and the extracts of the aqueous layer were combined and dried ($MgSO_4$). Evaporation of the ether afforded a red–yellow oil which was shown to contain three major components. Separation by column chromatography (silica, CCl_4–$CHCl_3$ 1 : 1) gave (i) *N*-trifluoroethanoylpiperidine **10** (0.49 g) identical to an authentic sample; (ii) 4-piperidinoperfluoro(4-methyl-3-methylenehexan-2-one) **12** (0.21 g) bp 66–67 °C 0.04 mmHg (Found: C, 35.1; H, 2.3; N, 3.4%. $C_{13}H_{10}F_{13}NO$ requires C, 35.2; H, 2.3; N, 3.2%); δ_H 1.62 (m, 6H), 3.38 (m, 4H); δ_F −58.4 (m, 2F, CF_2=), −59.7 (m, 3F, CF_3), −75 (s, 3F, $COCF_3$), −82.5 (m, 3F, CF_3CF_2), −106.1 (m, 2F, CF_3CF_2) and (iii) (*E*/*Z*)-1-piperidino-4,4,5,5,5-pentafluoro-3-trifluoromethylpent-2-en-1-one (**11**) (1.1 g) as a pale green liquid which decomposed on heating (Found: C, 41.2; H, 3.4; N, 4.4%. $C_{11}H_{11}F_8NO$ requires C, 40.7; H, 3.4; N, 4.3%); δ_H (isomer 1) 1.70 (m, 6H, CH_2 × 3), 3.55 (m, 4H, CH_2 × 2), 7.25 (m, 1H, =CH); δ_F −61.1 (m, 3F, CF_3), −83.2 (m, 3F, CF_3CF_2), −111.5 (m, 2F, CF_3CF_2); δ_H (isomer 2) 1.7 (m, 6H, 3 × CH_2), 3.30 (m, 4H, 2 × CH_2), 7.18 (m, 1H, =CH); δ_F −59 (m, 3F, CF_3), −84.9 (m, 3F, CF_3CF_2), −113.7 (m, 2F, CF_3CF_2).

Reaction of 12 with piperidine

A solution of **12** (0.4 g) in ether (25 cm^3) and piperidine (0.5 g) were heated at reflux for 18 h. The mixture was worked up exactly as in the previous experiment to give **11** (0.3 g) characterised by comparison of its NMR spectra.

Reaction of 1 with hydrazine

Hydrazine hydrate (0.7 g) was added dropwise over 5 min to a solution of **1** (5 g) in dry ether (100 cm^3) at 18 °C with vigorous stirring. The mixture was stirred for 10 h, the ether layer separated, dried ($MgSO_4$) and the solvent evaporated to leave a pale yellow solid (3.4 g). Sublimation *in vacuo* (20 mmHg) gave 3-hydroxy-5-pentafluoroethyl-3,4,5-tris(trifluoromethyl)pyrazolidine **2** (3.02 g) mp 71–72 °C (Found: C, 22.6; H, 1.2, N, 6.6%. $C_8H_4F_{14}N_2O$ requires C, 23.0, H, 1.0; N, 6.8%); δ_H ($CDCl_3$) 4.05 (q, 1H, $^4J_{HF}$ 9 Hz, CH), 4.88 (m, 1H, NH), 5.72 (m, 1H, NH), 7.18 (m, 1H, OH); δ_F ($CDCl_3$) −58.1 (m, 3F, CF_3), −70.7 (m, 3F, CF_3), −78.4 (m, 3F, CF_3), −82.9 (d, 3F, $^4J_{HF}$ 9 Hz, CF_3), −111 (cd, 2F, CF_2); *m*/*z* 410 $[M]^+$ 341, $[M - CF_3]^+$, 291 $[M - C_2F_5]^+$.

Reaction of 1 with oxygen nucleophiles

(a) Sodium methoxide. Sodium methoxide (1.72 g) was added in one portion to a solution of **1** in dry ether (100 cm^3) at −78 °C. The mixture was stirred at −78 °C for 1 h, allowed to slowly warm to room temperature and then stirred for a further 12 h. The solution was filtered and the solvent evaporated to leave an oil (5.72 g). TLC (silica gel, CCl_4–$CHCl_3$ 1 : 1) showed the presence of one major component and a number of minor relatively fast running products. Separation of a portion (3 g) of the mixture by column chromatography (silica gel, CCl_4–$CHCl_3$ 1 : 1 as eluant) afforded (i) a complex mixture of at least six components not further investigated (0.8 g), (ii) (*E*/*Z*)-1,3-dimethoxyperfluoro(2-ethanoyl-3-methylpent-1-ene) **14** (1.86 g) bp 57–58 °C/0.2 mmHg (Found: C, 29.8; H, 1.6%. $C_{10}H_6F_{12}O_3$ requires C, 29.9; H, 1.5%); $\delta_H(CDCl_3)$ 3.55 (m, 3H, CH_3O), 4.02 (m, 3H, CH_3O); $\delta_F(CDCl_3)$ −66.5 (m, 3F, CF_3), −67.8 (m, 1F, =CF), −75.7 (m, 3F, CF_3), −81.8 (s, 3F, CF_3CO), −118.3 (m, 2F, CF_3CF_2); *m*/*z* 402 $[M]^+$, 331 $[M - CF_3]^+$.

(b) Sodium phenoxide. In the same way as in the preceding experiment **1** (5 g) was reacted with sodium phenoxide (3.2 g) to give a yellow oil (4.21 g). Purification of a portion (3 g) by column chromatography as above gave (i) a mixture of several unidentified compounds (0.1 g), (ii) (*E*/*Z*)-1,3-diphenoxyperfluoro(2-ethanoyl-3-methylpent-1-ene) **15** (2.6 g) bp 86–88 °C/0.5 mmHg (Found: C, 45.3; H, 1.9; F, 43.5%. $C_{20}H_{10}F_{12}O_3$ requires C, 45.0; H, 1.9; F, 43.3%); δ_H ($CDCl_3$) 6.82 (c Ar); δ_F ($CDCl_3$) −56.3 (cq, 1F, CF=), −64.6 (m, 3F, CF_3), −75 (m, 3F, CF_3CF_2), −78.8 (s, 3F, CF_3CO), −115.3 (m, 2F, CF_3CF_2); *m*/*z* 526 $[M]^+$, 457 $[M - CF_3]^+$, 433 $[M - C_6H_5O]^+$.

(c) Sodium hypochlorite. A suspension of **1** (15 g) in acetonitrile (30 cm^3) and sodium hypochlorite (14% available chlorine, 100 cm^3) was vigorously stirred at 0 °C. After 2 h the mixture was poured into water and the lower fluorocarbon layer (8.12 g) was separated off. Distillation afforded, as a 1 : 1 mixture by NMR spectroscopy of *cis*/*trans*-3-pentafluoroethyl-2,3-bis(trifluoromethyl)oxirane **16** (7.7 g) bp 57 °C; δ_H ($CDCl_3$) 4.15 (cq, 1H, $^3J_{HF}$ 6 Hz); δ_F ($CDCl_3$) −66.4 (m, 6F, CF_3 × 2), −66.4 (m, 3F, CF_3, *cis*-isomer), −72 (m, 3F, CF_3, *trans*-isomer), −81.4 (m, 6F, CF_3CF_2 × 2), −114 (m, 2F, CF_3CF_2, *trans*-isomer), −119.2 (m, 2F, CF_3CF_2 *cis*-isomer); *m*/*z* 279 $[M - F]^+$, 229 $[M - CF_3]^+$, 179 $[M - C_2F_5]^+$. Found mass, 297.98336. Required mass ($C_6HF_{11}O$), 297.98518.

Reaction of 1 with methylmagnesium iodide

An ether solution of methylmagnesium iodide (from magnesium (0.65 g) and iodomethane (3.80 g) was added to a solution of **1** (5 g) in dry ether (50 cm^3) with stirring at 0 °C over 5 min. The mixture was stirred for 2 h at 0 °C and was then slowly warmed to room temperature and stirred for a further 10 h. The solution was poured into 2 M H_2SO_4 (100 cm^3) and ice (50 g), and the ether layer was separated and combined with the ether extracts (2 × 100 cm^3) of the aqueous layer. The ether layer was washed with water (50 cm^3), dried ($MgSO_4$) and the ether distilled off. The residual red oil (3.2 g) was separated by preparative gas chromatography (10% DEGS/ChromasorbW at

100 °C, N_2 pressure 2 psi) to give two minor unidentified compounds (0.3 g) and an inseparable mixture of (*E*/*Z*)-4-methyl-1,1,1,5,5,6,6,6-octafluoro-4-trifluoromethyl-3-(2-fluoroethylidene)hexan-2-one **17** (2.1 g) bp 80–82 °C/12 mmHg (Found: C, 29.9; H, 1.5%. $C_{10}H_6F_{12}$ requires C, 30.2; H, 1.7%); δ_H ($CDCl_3$) 1.48 (m, 3H, CH_3), 2.93 (m, 3H, CH_3C=); δ_F ($CDCl_3$) −74.4 (m, 3F, CF_3), − 81.8 (m, 3F, CF_3), −82.9 (s, 3F, CF_3CO), −85 (m, 1F, CF=) −103.7 (m, 2F, CF_3CF_2); *m*/*z* 370 $[M]^+$, 301 $[M - CF_3]^+$, 251 $[M - C_2F_5]^+$.

Cyclisation reactions of 1

(a) Triethylamine. A mixture of **1** (10 g) and triethylamine (1 g) in dry ether (100 cm^3) was stirred at room temperature for 24 h. The mixture was poured into 2 M H_2SO_4 (100 cm^3) and ice (50 g). The ether layer was separated and washed with 2 M H_2SO_4, water, and dried ($MgSO_4$). The ether was distilled to leave an oil which on distillation afforded a mixture of the diasteroisomers of perfluoro(2,5-dihydro-2,3,4,5-tetramethylfuran) **13** (8.9 g) bp 81–82 °C (lit.,[14] 83 °C). The spectral data were identical to those reported by Chambers *et al.*

(b) Fluoride ion. In a similar experiment **1** (10 g) and dry KF (2 g) in acetonitrile (5 cm^3) were heated together in a Carius tube at 85 °C for 120 h. The contents of the cooled tube were then poured into water (10 cm^3) and the lower fluorocarbon layer (8.3 g) was shown to be pure **13** by spectroscopic analysis.

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