Reaction of tetrafluoroethene oligomers. Part 17.[1] Some reactions of (*E*/*Z*)-perfluoro-2,3-dimethylpenta-1,3-diene

Graham D. Burns, Paul L. Coe* and Colan L. Andrews

School of Chemistry, The University of Birmingham, Edgbaston, Birmingham, UK B15 2TT

Received (in Cambridge, UK) 21st August 2000, Accepted 3rd January 2001
First published as an Advance Article on the web 8th February 2001

(*E*/*Z*)-Perfluoro-2,3-dimethylpenta-1,3-diene has been reacted with cold methanol to afford a monosubstituted product, whereas reaction in methanol containing triethylamine, even at ice temperature, formed a single multi-substituted product containing seven methoxy groups; these products have been fully characterised and their formation rationalised. Reactions of the diene with aniline and substituted anilines formed either pyrroloquinolines, azetines or oxoazetines. A rationalisation of the different reaction pathways in terms of the substitution pattern and electron demand of the substituents in the anilines is presented.

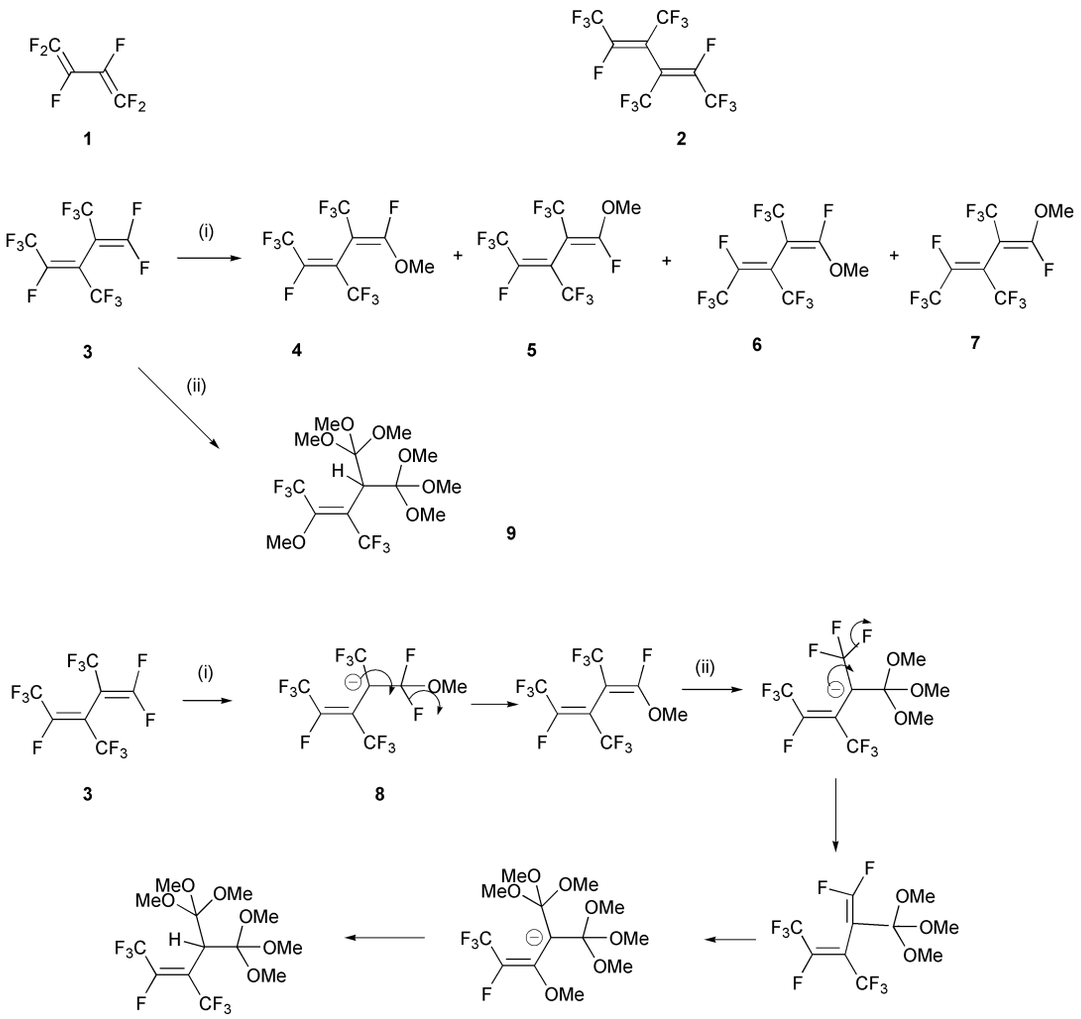
Introduction

Although perfluorobutadiene **1**[2] has been known for many years and the chemistry of cyclic perfluorodienes has been well described and reviewed by Tatlow,[3] until relatively recently few acyclic perfluorodienes were readily available. We have described a pyrolytic reaction of TFE oligomers which led to the isolation of a number of interesting cyclic perfluorodienes[4] and have reported part of our work with these dienes.[5] More recently Chambers has described the preparation and reactions of some related compounds either by a pyrolytic process[6] or by a very elegant electron transfer reaction.[7] With this lack of availability of starting materials most of the chemistry of acyclic perfluorodienes which has been described has been confined to cycloaddition or electrocyclic reactions.[8] Recently, Chambers[7,9,10] has reported some reactions of nucleophiles with perfluoro-1,3-dienes, in particular with perfluoro-3,4-dimethylhexa-2,4-diene **2** using oxygen, sulfur and nitrogen nucleophiles. In certain cases (see below) these reactions led to the formation of unexpected heterocycles. In our earlier papers[4] we reported a viable preparative route to (*E*/*Z*)-perfluoro 2,3-dimethylpenta-1,3-diene **3,** which was previously prepared by Haszeldine[11] as a byproduct in studies of perfluoroallenes, by pyrolysis of perfluoro-4-ethyl-3,5-dimethylhex-2-ene (TFE pentamer). We have described some intramolecular cyclisations of these dienes and also reported on the chemistry of the product cyclobutenes.[4] We now report on the reaction chemistry of a 50 : 50 (*E*/*Z*) mixture of **3**. As we described earlier[4] it is possible to separate the isomers into their single isomers by very careful preparative GLC but for the initial studies we used the mixture and as will be seen the separation proved to be unnecessary.

Results and discussion

We began our study by reacting **3** with neutral methanol at 0 °C (see Scheme 1). An exothermic reaction took place and the starting material had all reacted within 2 minutes to yield a mixture of two major products in almost equal amounts and two very minor products, as shown by GLC. Such a rapid reaction parallels a similar reaction of **2**.[9] ^{1}H NMR spectroscopy of the crude mixture showed signals for four methyl ethers corresponding to the two major and two minor isomers. The ^{19}F NMR spectrum of the crude mixture was very complex and only certain resonances could be assigned. The elemental analysis of the mixture gave good values for a monomethoxylated product. The two major products were separated by preparative GLC but we could not isolate a sufficient amount of the minor products for full characterisation (no separate elemental analysis could be obtained). Compound **4**, which eluted from the column first, gave a ^{1}H NMR signal at δ 3.56 as a complex doublet assigned as a methoxy group on a double bond with a fluorine atom on the same carbon atom. The ^{19}F spectrum of the separated isomers was less complex and could, with the aid of the spectrum of the starting material, be readily interpreted since one significant part of the spectrum was essentially unaltered by the reaction. Thus, we were able immediately to show that **4** was the product from the reaction of the *Z* isomer of the starting material and that the reaction had taken place, as would be expected, at the CF_2= group. An important feature of the spectrum was the nature of the signal for the CF_3 group at position 2 which appeared as a doublet $^4J_{FF}$ 18 Hz, and was assigned as a *cis* F to CF_3 coupling *cf.* the corresponding coupling in **3** of 17 Hz. We therefore believe that the methoxy group and the CF_3 are in the *trans* arrangement and that **4** is (*Z*,*Z*)-1-methoxyperfluoro-2,3-dimethylpenta-1,3-diene **4**. Elemental analysis and mass spectrometry were consistent with this structure. The second component, one of the minor products, which eluted from the column was shown similarly by ^{1}H and ^{19}F NMR spectroscopy (see Experimental section for details) to be a methyl ether and by a comparison of the chemical shift and coupling patterns with the *Z* isomer of the starting material, to be (*E*,*Z*)-1-methoxyperfluoro-2,3-dimethylpenta-1,3-diene **5**. The structure was further supported by mass spectrometric data. The third component isolated (the second major product) was similarly shown to be the (*Z*,*E*) isomer **6**, and the final product **7**, a minor isomer, had (*E*,*E*) stereochemistry; this pattern fits with the suggestion that the major isomers are formed by the favourable elimination process from the intermediate **8** (Scheme 1) and the minor products from the unfavourable intermediate. We next reacted **3** with methanol containing 10% w/w of triethylamine at 0 °C. After a highly exothermic reaction we were able to isolate a thick oil which very slowly crystallised to a low melting solid indicated by GLC and TLC to be a single product. ^{1}H NMR spectroscopy showed three singlets in the ratio of 1 : 3 : 18 at δ 3.7, 3.8 and 4 these we assigned to a single proton, one and six methoxy groups, respectively. The signal at δ 3.8 corresponds well with that observed for a methoxy group on an sp^2 carbon also attached to a CF_3 group.[9] The band at δ 4 corresponds to a

 DOI: 10.1039/b006825j

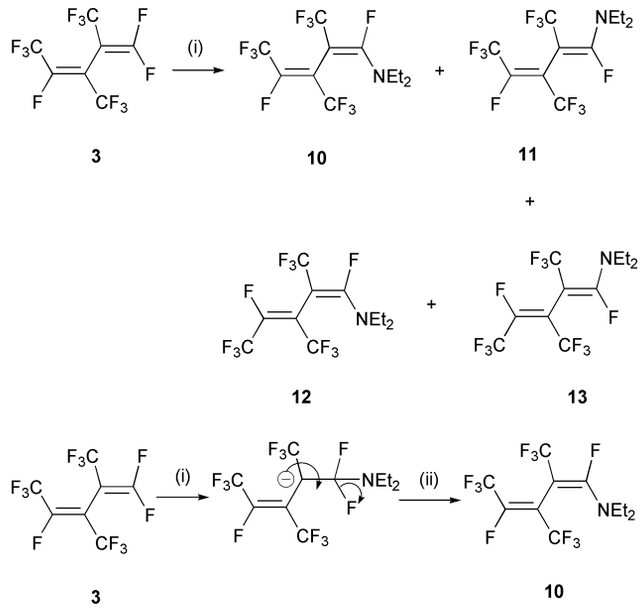


Scheme 1 *Reagents and conditions*: (i) MeOH; (ii) MeOH–Et_3N.

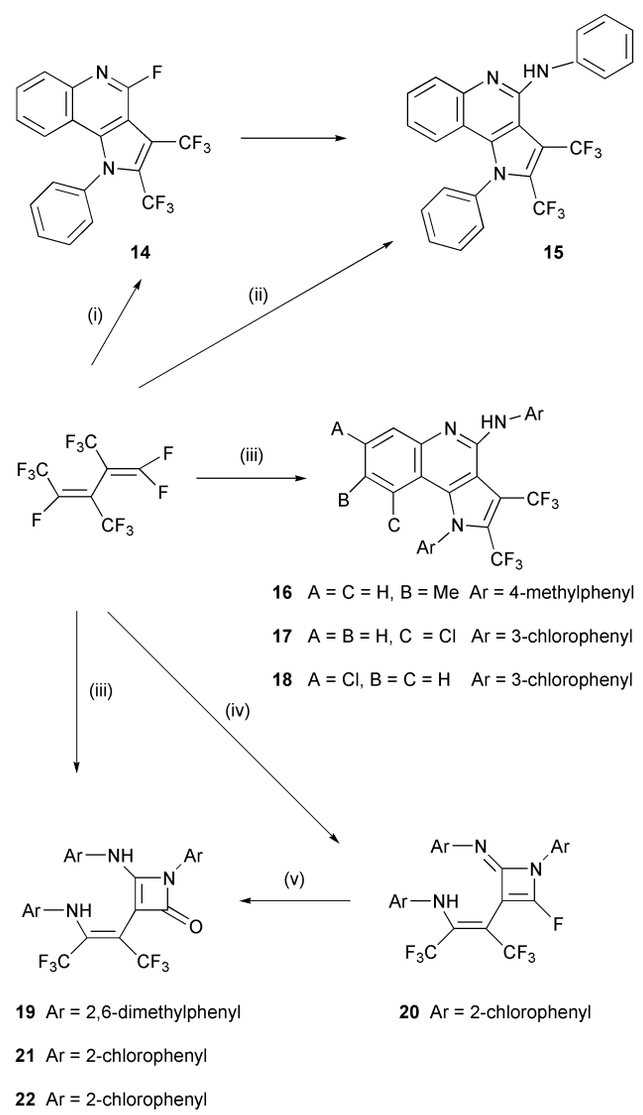
signal for two equivalent trimethoxymethyl groups and the signal at δ 3.7 for the single proton accords with a tertiary proton, the observed chemical shift and that calculated using shift parameters for a trimethoxymethyl group (calculated from the shifts for CH_3 and CH_2 groups in methyl orthoacetate and methyl orthobutyrate[12]) and for vinyl groups, are consistent with such a proton. The ^{19}F NMR spectrum showed bands for two CF_3 groups both on a double bond. The signal with a chemical shift of δ −64.2 is consistent with a CF_3 with a methoxy group on the same carbon atom and the second signal at δ −63.9 is consistent with a CF_3 *trans* to the latter. Elemental analysis and mass spectrometry were consistent with the compound being (*E*)-5,5,5-trifluoro-1,1,1,4-tetramethoxy-3-trifluoromethyl-2-(trimethoxymethyl)pent-3-ene **9**. Since we found no evidence for the corresponding (*Z*) isomer and as the yield of product (83%) is very high, we conclude that during the methoxylation step at carbon 4 the intermediate from the (*Z*) isomer in the starting material must have formed only the favourable product on loss of fluoride ion. This result parallels our previous report of the reaction of TFE trimer with methoxide ion when we also observed a complex series of addition–elimination reactions leading to multiply substituted products.[13] The significant difference in reactivity when the diene terminus is CF_2=, compared with Chambers' work when the terminus was =$CFCF_3$, is also clearly evident. The mechanisms of these reactions are shown graphically in Scheme 1.

We next considered the reaction of **3** with amines and found that ammonia and aliphatic primary amines, even at low temperature, produced intractable mixtures of products clearly due to multiple substitution even with an excess of **3**. It would seem that the first formed products are even more reactive than the starting diene which itself on the evidence of the methanol reaction is very reactive. We found that treatment of **3** with one equivalent of diethylamine at 0 °C afforded a yellow oil which was shown by TLC to be a mixture of four components which ran very closely together. We were able to separate only the two major isomers from the mixture by column chromatography so full characterisation of all the components was not possible. GC/MS on the mixture showed that they were all mono-substituted *N*,*N*-diethylamino derivatives of **3**. ^{19}F NMR spectroscopy confirmed that the substitution had occurred at the CF_2= group as expected and by comparison with the spectra of **4**, **5**, **6** and **7** we believe that the major products are (*Z*,*Z*)- and (*Z*,*E*)-1-(*N*,*N*-diethylamino)perfluoro-2,3-dimethylpenta-1,3-diene **10** and **12** and the minor products are the corresponding (*E*,*Z*) and (*E*,*E*) isomers **11** and **13**. The elemental analysis of the mixture was consistent with the structure. These results are summarised in Scheme 2. The products all rapidly hydrolysed in acidic solution to an intractable tar.

In the light of the high reactivity of aliphatic amines we next investigated reactions with the less nucleophilic aromatic amines. Reactions of fluoroalkenes with anilines have been reported previously by Haszeldine[14] with HFP dimer (perfluoro-2-methylpent-2-ene), by ourselves with TFE trimer (perfluoro-3-methylpent-2-ene) and more recently by Chambers[10] with **2**. Haszeldine reported that the HFP dimer yielded an iminoketenimine with 2,6-dimethoxyaniline, we showed that the TFE trimer and 1,4-dimethoxyaniline yielded a quinoline derivative and Chambers reported the formation of a pyrrole derivative as the major product with smaller amounts of pyrroloquinolines in the reaction of **2** with a number of aniline derivatives. As none of these alkenes have a terminal



Scheme 2 *Reagents and conditions*: (i) Et_2NH; (ii) $-F^-$.



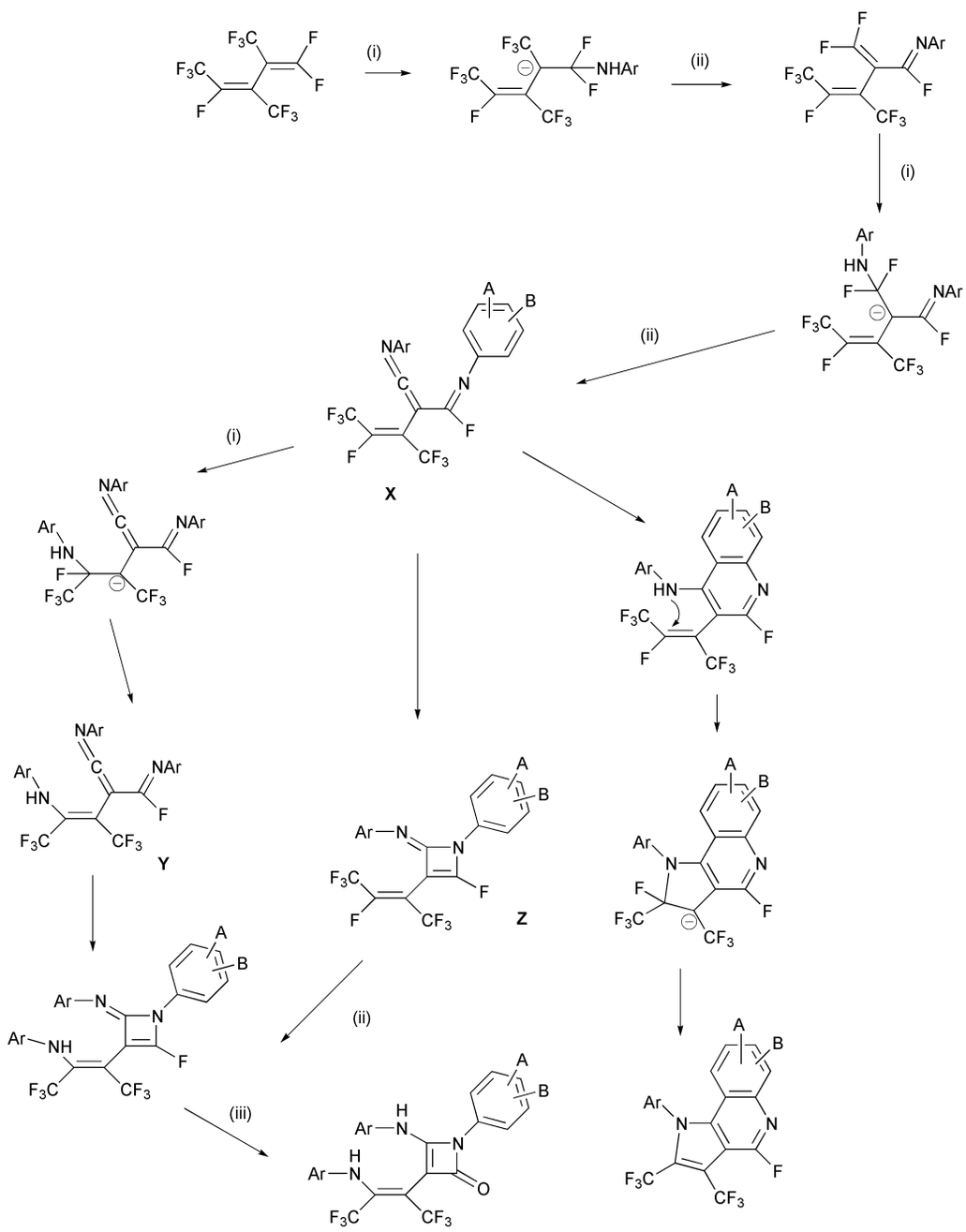
Scheme 3 *Reagents and conditions*: (i) aniline; (ii) aniline–CsF; (iii) $ArNH_2$, Ar is indicated above; (iv) 2-chloroaniline; (v) H_2O–H_2SO_4.

CF_2= group, it was of interest to see if **3** showed a different reaction profile and secondly to see if the aniline substitution pattern was important. We first reacted **3** (Scheme 3) with aniline in ether–triethylamine at 0 °C to yield a beige solid which by TLC analysis was shown to consist of mainly one compound. After column chromatography and recrystallisation a pale yellow crystalline solid was obtained. ^{1}H NMR spectroscopy showed a group of peaks between δ 6.6 and 8.0 which were attributed to aromatic protons and analysed (see Experimental for details) as derived from a quinoline moiety and a phenyl group; this was confirmed by the ^{13}C NMR spectrum. The ^{19}F NMR spectrum showed the presence of two signals for CF_3 groups and a signal for a fluorine atom on an aromatic ring as a quartet, a doublet of quartets and a quartet. This coupling pattern allowed us to define the structural relationship of the three groups. These data indicate that the product is 4-fluoro-1-phenyl-2,3-bis(trifluoromethyl)-1*H*-pyrrolo[3,2-*c*]quinoline **14**. Elemental analysis and mass spectrometry confirmed this structure. This result is in accord with those recently reported by Chambers.[10] Interestingly we found none of the corresponding pyrrole derivatives, the main product in Chambers' reaction as noted above. To test out the effect of reaction conditions we repeated the reaction with a large excess of aniline and obtained the same result.

We next considered the effect of fluoride ion on the reaction in the hope that it might suppress the elimination of fluoride from the first formed intermediates. We thus repeated the reaction in the presence of caesium fluoride. We obtained a slightly different product to **14**, analysis of the structure as above (see Experimental for details) revealed the absence of the fluorine atom at position 4 and the incorporation of a further *N*-phenyl group to yield 1-phenyl-4-phenylamino-2,3-bis-(trifluoromethyl)-1*H*-pyrrolo[3,2-*c*]quinoline **15**. We believe this reaction is due to the fluoride ion acting as a base in the production of more reactive anilide ion which reacts in a standard nucleophilic displacement process. Pyrrolo[3,2-*c*]quinolines are known to act as anti-hypertension agents and it was interesting to extend the range of products in this series to a potential biological investigation as well as to try to define the reaction mechanism of these somewhat unexpected results. We thus embarked on a series of reactions with anilines of differing substitutions. Reaction of *p*-toluidine and 3-chloroaniline with **3** in the presence of triethylamine gave the expected pyrroloquinolines **16**, **17** and **18**, corresponding to **15**. In the case of 3-chloroaniline the two possible isomers **17** and **18** with respect to the chlorine atoms were separated and characterised. We next reacted 2,6-xylidine with **3** in the same manner but did not obtain a pyrroloquinoline. The ^{1}H NMR spectrum showed a complex band, which could not be analysed (it was equivalent to nine protons), three singlets in the ratio 1 : 1 : 1 consistent with 18 methyl protons and two signals which were exchangeable with D_2O (NH protons). The ^{19}F spectrum showed quartets for two non-equivalent CF_3 groups with no other fluorine signals observable. The ^{13}C spectrum showed a very complex series of signals in the range δ 117–145 (mainly arene carbon atoms), signals for the CF_3 carbons and signals for the methyl groups and importantly a signal at δ 156 for a carbonyl function. This latter was confirmed by a band in the IR spectrum at 1760 cm^{-1} consistent with a four membered lactam. The mass spectrum showed an *m*/*z* at 573 with a base peak at *m*/*z* 105 equivalent to the xylidine moiety. The elemental analysis was in accord with these data and the structure was assigned to (*E*)-1-(2,6-dimethylphenyl)-4-(2,6-dimethylphenylamino)-3-[3-(2,6-dimethylphenylamino)hexafluoro-(*E*)-but-2-en-2-yl]-2-oxoazetine **19**. Similar four membered ring structures have been observed previously.[13] This result confirms the observation of Haszeldine (above) that the formation of quinoline derivatives requires free *ortho*-positions in the aniline. Interestingly when we repeated this reaction with 2- and 4-chloroaniline the products obtained were again the azetine **20** and the oxoazetine **21** respectively and not the pyrroloquinolines. It is noteworthy that in the reaction with 2-chloroaniline we did not use an aqueous work up and were able to obtain the

azetine **20**. However, on standing in air this hydrolysed to the oxo-derivative **22**; alternatively, treatment of **20** under the normal work up conditions also led to the formation of **22**. These reactions suggest that an electronic effect, in addition to the blocking effect of *ortho*-substituents, determines the outcome of the reaction. The structures of **20** and **21** were determined by the same methods for the structure of **19** (details are shown in the Experimental section). These reactions are summarised in Scheme 3. We found no reaction of either type above occurred with a number of less basic anilines such as the 4-nitro, 2,4-dinitro, 3-trifluoromethyl, 2,6-dichloro and 3-fluoro derivatives. This result is somewhat different from those observed by Chambers[10] using perfluoro-3,4-dimethylhexa-2,4-diene **2** which with a number of arylamines afforded the pyrrole derivatives as the major products. We found no evidence for pyrrole formation in our reactions. Equally, Chambers does not report any evidence for the formation of azetines or oxoazetines and thus it would appear that our reactions, almost certainly by virtue of the presence of the highly reactive $=CF_2$ group, proceed by a different pathway to those reported. In the light of our recent report of the reactions of perfluoro-3,4-dimethylhex-3-en-2-one,[15] where we were able to isolate a ketenimine which cyclised to an azetine, we believe our reactions proceed *via* a ketenimine of the type **X** as shown in Scheme 4. We believe **X** is, as in the methoxide reaction above, formed by a series of addition–elimination reactions. Intermediate **X** may react at the remaining double bond with more amine to give **Y**. Equally this step could take place before formation of the ketenimine (see below) without altering the overall result. The next step in the sequence we believe is governed by the substitution pattern of the aromatic ring. If the 2 and 6 positions are blocked, as in the case of 2,6-xylidine, the initially formed product is the azetine **Z** which then reacts with more xylidine to form, after hydrolysis in the work up, the observed product. Similarly if the 2 or 6 positions are electron deficient or at least not activated to electrophilic attack azetine formation also occurs. If however the 2 and 6 positions are unblocked and are activated then pyrroloquinoline formation occurs. We believe the mechanisms presented in Scheme 4 are consistent with the results we have obtained.

We have thus shown, confirming Chambers' earlier reports, that perfluoro-1,3-dienes show extremely high reactivities



Scheme 4 *Reagents and conditions*: (i) $ArNH_2$; (ii) $-F^- -HF$; (iii) electrocyclisation; (iv) H_3O^+.

toward nucleophiles and further that relatively small structural changes both in the substrate and in the attacking nucleophile lead to considerably different results, probably due to the greater reactivity of a $=CF_2$ group *vs.* an $R_FCF=$ system towards nucleophiles.[16]

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 fluorotrichloromethane 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, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, "quin" = pseudo quintet, c = complex. *J* values are given in Hz. Ar refers to protons in pendant aromatic rings. 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 m 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 CP-SIL-CB 19 column. The data were registered by a JCL 600 chromatography data system.

Reaction of 3 with methanol

The diene mixture **3** (5.0 g) was added dropwise with stirring to methanol (25 cm^3) at 0 °C. The mixture was stirred for 3 h when a single phase had formed. The solution was poured into water and the lower fluorocarbon layer was separated and dried ($CaCl_2$). GC analysis of the product (4.9 g) indicated the presence of four components. Separation by preparative GLC [DNP on Celite 1 : 3 (9.1 m × 70 mm Column 100 °C)] afforded from 1 g of the mixture: (i) (*Z*,*Z*)-1-methoxyperfluoro-2,3-dimethylpenta-1,3-diene **4** (0.3 g); bp 123–125 °C (Found for the mixture of isomers: C, 29.7; H, 0.7; F, 64.8. $C_8H_3F_{11}O$ requires C, 29.9; H, 0.9; F, 64.5%); δ_H ($CDCl_3$) 3.56 (3H, cd, $^4J_{HF}$ 5.1, OMe); δ_F ($CDCl_3$) −62.3 (3F, d, $^4J_{FF}$ 21, 3-CF_3), −64.6 (3F, d, $^4J_{FF}$ 18, 2-CF_3), −69.7 (3F, c, 5-CF_3), −69.8 (1F, qq, $^4J_{FF}$ 17.5, $^3J_{HF}$ 5.1, 1-F), −104.8 (1F, dq, $^3J_{FF}$ 7, $^4J_{FF}$ 21, 4-F); *m*/*z* 324 (M^+). (ii) (*E*,*Z*)-1-Methoxyperfluoro-2,3-dimethylpenta-1,3-diene **5** (0.02 g); δ_H ($CDCl_3$) 3.7 (3H, cd, $^4J_{HF}$ 5.2, OMe); δ_F ($CDCl_3$) −59.2 (3F, m, 2-CF_3), −62.4 (3F, m, 3-CF_3), −69.5 (3F, cm, 5-CF_3), −70.1 (1F, qq, $^4J_{FF}$ 8, $^3J_{HF}$ 5.2, 1-F), −104.6 (1F, qq, $^4J_{FF}$ 20, $^3J_{FF}$ 6.9, 4-F); *m*/*z* 324 (M^+). Found 324.00079. $C_8H_3F_{11}O$ requires 324.00082. (iii) (*Z*,*E*)-1-Methoxyperfluoro-2,3-dimethylpenta-1,3-diene **6** (0.25 g) bp 124–125 °C; δ_H ($CDCl_3$) 3.8 (cd, $^4J_{HF}$ 5.0, OMe); δF ($CDCl_3$) −59.4 (3F, dq, $^5J_{FF}$ 11.7, $^3J_{FF}$ 11.4, 5-CF_3), −68.3 (3F, m, 3-CF_3), −68.4 (3F, d, $^4J_{FF}$ 17.5, 2-CF_3), −69.9 (1F, qq, $^4J_{FF}$ 17.5, $^3J_{HF}$ 5, 1-F), −101.3 (1F, m, 4-F); *m*/*z* 324 (M^+). (iv) (*E*,*E*)- 1-methoxyperfluoro-2,3-dimethylpenta-1,3-diene **7** (0.04 g); δ_H ($CDCl_3$) 3.9 (3H, m, OMe); δ_F ($CDCl_3$) −59.3 (3F, m, 4-CF_3), −60.1 (3F, m, 2-CF_3), −64.7 (3F, m, 3-CF_3), −70.1 (1F, qq, $^4J_{FF}$ 7, $^3J_{HF}$ 5.1, 1-F). Found 324.00080. $C_8H_3F_{11}O$ requires 324.00082.

Reaction of 3 with methanol and triethylamine

Triethylamine (2 g) was added dropwise with stirring to an ice cold suspension of the diene **3** (5 g) in methanol (25 cm^3). A vigorous reaction occurred with a considerable exotherm. After further stirring at 0 °C for 1 h the mixture was poured into water to give a two phase system. The lower fluorocarbon layer was separated and dried ($CaCl_2$). After filtration the oil was refrigerated to give a low melting white crystalline solid (3.9 g) which was shown by TLC and GC analysis to be a single component. Sublimation *in vacuo* (10 mmHg, 50 °C) afforded (*E*)-5,5,5-trifluoro-1,1,1,4-tetramethoxy-3-trifluoromethyl-2-trimethoxymethylpent-3-ene **9** (3.7 g); mp 41–42 °C (Found: C, 40.2; H, 5.1; F, 27.4. $C_{14}H_{22}F_6O_7$ requires C, 40.4; H, 5.3; F 27.4%); δ_H ($CDCl_3$) 3.7 (1H, m, $CH(COMe_3)_2$), 3.8 (3H, m, 4-OMe), 4.0 (18H, s, OMe × 6); δ_F ($CDCl_3$) −63.9 (3F, m, 3-CF_3), −64.2 (3F, q, $^5J_{FF}$ 11.7, 5-CF_3); *m*/*z* 416 (M^+).

Reaction of 3 with diethylamine

Diethylamine (6.0 g) in dry ether (10 cm^3) was added to an ice cold solution of **3** (5 g) in dry ether (25 cm^3) and the mixture was stirred for 2 h and was then filtered to remove precipitated diethylamine hydrofluoride. The solution was concentrated to a yellow oil (3.9 g) and was separated by column chromatography (chloroform–hexane 1 : 1 as eluant) to yield two major components and two very minor products which could not be isolated in sufficient quantity for characterisation. The latter products were shown by GC/MS to be the two minor isomers of the two main products. The separated major products from two similar reactions were combined and each was distilled *in vacuo* to yield (i) (*Z*,*Z*)-1-diethylaminoperfluoro-2,3-dimethylpenta-1,3-diene **10** (2.8 g); bp 85–87 °C (10 mmHg) (Found: C, 35.9; H, 2.6; F, 57.4. $C_{11}H_{10}F_{11}N$ requires C, 36.2; H, 2.8; F. 57.2%); δ_H ($CDCl_3$) 1.2 (3H, t, $^3J_{HH}$ 7.1, CH_3), 3.2 (2H, q, $^3J_{HH}$ 7.1, CH_2); δ_F ($CDCl_3$) −58.6 (3F, d, $^4J_{FF}$ 17.1, 3-CF_3), −64.6 (3F, m, 5-CF_3), −67.6 (3F, m, 2-CF_3), −102.7 (1F, m, 1-F), −150.8 (1F, m, 1-F); *m*/*z* 416 (M^+); and (ii) (*Z*,*E*)-1-diethylaminoperfluoro-2,3-dimethylpenta-1,3-diene **12** (2.6 g); bp 87–88 °C (10 mmHg) (Found: C, 36.3; H, 2.9; F, 57.5. $C_{11}H_{10}F_{11}N$ requires C, 36.2; H, 2.8; F, 57.2%); δ_H ($CDCl_3$) 1.3 (3H, t, $^3J_{HH}$ 7.0, CH_3), 3.3 (2H, q, $^3J_{HH}$ 7.0, CH_2); δ_F ($CDCl_3$) −59.4 (3F, m, 4-CF_3), −64.8 (3F, d, $^4J_{FF}$ 17.5, 2-CF_3), −68.4 (3F, dq, $^4J_{FF}$ 11, $^5J_{FF}$ 11.7, 3-CF_3), −101.6 (1F, m, 4-F), −147.3 (1F, m, 1-F); *m*/*z* 416 (M^+).

General reaction of 3 with anilines

The aniline (freshly distilled or recrystallised prior to use) (5.1 mmol) in dry ether (25 cm^3) was added dropwise to an ice cold solution of **3** (1.7 mmol) and triethylamine (11.9 mmol) in dry ether (25 cm^3) with stirring. After the addition was complete the mixture was stirred for 12 h at 18 °C. The solution was then filtered and concentrated by rotary evaporation. The residue was purified by column chromatography (chloroform–hexane 1 : 1 as eluant) to afford the products indicated below for specific anilines.

(a) With aniline. Pale yellow crystals (from petroleum ether bp 60–80 °C) of 4-fluoro-1-phenyl-2,3-bis(trifluoromethyl)-1*H*-pyrrolo[3,2-*c*]quinoline **14** (55%); mp 184–185 °C (Found: C, 57.1; H, 2.3; F, 33.7; N, 6.8. $C_{19}H_9F_7N_2$ requires C, 57.3; H, 2.3; F, 33.4; N, 7%); δ_H ($CDCl_3$) 6.82 (1H, d, $^3J_{HH}$ 8.7, 9-H), 7.45 (1H, d, $^3J_{HH}$ 7.5, 6-H), 7.7 (1H, m, 8-H), 7.8 (5H, m, Ar ring), 8.21 (1H, d, $^3J_{HH}$ 7.9, 7-H); δ_F ($CDCl_3$) −53.6 (3F, q, $^5J_{FF}$ 12.9, 2-CF_3), −54.0 (3F, dq, $^5J_{FF}$ 12.8, $^5J_{FF}$ 3.0, 3-CF_3), −58.1 (1F, q, $^5J_{FF}$ 3.0, 4-F); *m*/*z* 398 [M^+].

(b) With aniline and caesium fluoride. Reaction as above but with the addition of caesium fluoride (5 eq.) afforded, as a creamy solid (from petroleum ether bp 60–80 °C), 1-phenyl-4-phenylamino-2,3-bis(trifluoromethyl)-1*H*-pyrrolo[3,2-*c*]quinoline **15** (0.37 g, 46%); mp 186–187 °C (Found: C, 63.8; H, 3.1; N, 9.1. $C_{25}H_{15}F_6N_3$ requires C, 63.7; H, 3.2; F, 24.2; N, 8.9%); δ_H ($CDCl_3$) 6.4 (1H, br s, NH), 6.9 (1H, d, $^3J_{HH}$ 8.4, 9-H), 7.1–7.6 (11H, m, 8-H and 2 × Ar), 7.85 (1H, d, $^3J_{HH}$ 7.6, 6-H), 7.97 (1H, d, $^3J_{HH}$ 7.8, 7-H); δ_F ($CDCl_3$) −52.8 (3F, dq, $^5J_{FF}$ 13.5, $^6J_{HF}$ 6.8, 2-CF_3), −54.0 (3F, q, $^5J_{FF}$ 13.4, 3-CF_3); *m*/*z* 471 (M^+).

With *p*-toluidine. Reaction as above afforded as a cream solid 8-methyl-1-(4-methylphenyl)-4-(4-methylphenyl)amino-2,3-bis-(trifluoromethyl)-1*H*-pyrrolo[3,2-*c*]quinoline **16** (0.43 g, 50.6%); mp 174–175 °C (Found: C, 65.2; H, 4.2; N, 7.8. $C_{28}H_{21}F_6N_3$ requires C, 65.5; H, 4.1; N, 8.2%); δ_H ($CDCl_3$) 2.3–2.5 (9H, s, s, s, 3 × CH_3), 6.7 (2H, d, $^3J_{HH}$ 7.7, Ar), 7.0 (2H, d, $^3J_{HH}$ 8, Ar), 7.3–7.5 (5H, m, 5 × H-Ar), 7.7 (1H, s, 9-H), 7.8 (1H, d, $^3J_{HH}$ 8.5, 6-H); δ_F ($CDCl_3$) −50.8 (3F, q, $^5J_{FF}$ 12.9, 2-CF_3), −53.5 (3F, q, $^5J_{FF}$ 13.0, 3-CF_3); *m*/*z* 513 (M^+).

With 3-chloroaniline. In the same manner as above reaction of **3** (0.5 g) afforded a mixture which was separated by column chromatography (chloroform–hexane 1 : 1) to give: (i) 9-chloro-1-(3-chlorophenyl)-4-(3-chlorophenyl)amino-2,3-bis(trifluoromethyl)-1*H*-pyrrolo[3,2-*c*]quinoline **17** (0.06 g); mp 196–198 °C (Found for the mixture: C, 52.6; H, 2.5; F, 19.5; N, 6.9. $C_{25}H_{12}Cl_3F_6N_3$ requires C, 52.2; H, 2.1; F, 19.8; N, 7.3%); δ_H ($CDCl_3$) 7.0 (1H, dd, $^3J_{HH}$ 8.0, $^4J_{HH}$ 2.0, Ar), 7.1 (1H, dd, $^3J_{HH}$ 8, $^4J_{HH}$ 1, Ar), 7.2–7.4 (2H, c, 2 × Ar), 7.5–8.1 (7H, m, Ar); δ_F ($CDCl_3$) −52.1 (3F, dq, $^5J_{FF}$ 12.5, $^5J_{HF}$ 3.9, 3-CF_3), −54.7 (3F, $^5J_{FF}$ 12.5, 2-CF_3); *m*/*z* 573 [M^+] as a 3-chlorine isotopic cluster; and (ii) 7-chloro-1-(3-chlorophenyl)-4-(3-chlorophenyl)amino-2,3-bis(trifluoromethyl)-1*H*-pyrrolo[3,2-*c*]quinoline **18** (0.23 g) mp 156–159 °C; δ_H ($CDCl_3$) 6.8 (1H, ddd $^3J_{HH}$ 8, $^4J_{HH}$ 2, $^4J_{HH}$ 2, Ar), 6.85 (1H, ddd, $^3J_{HH}$ 8, $^4J_{HH}$ 2, $^4J_{HH}$ 2, Ar), 6.9 (1H, ddd, $^3J_{HH}$ 8, $^4J_{HH}$ 1, $^4J_{HH}$1, Ar), 7.1 (1H, t, $^3J_{HH}$ 8, Ar), 7.2–7.3 (2H, m, Ar), 7.4 (1H, dt, $^3J_{HH}$ 8,$^4J_{HH}$ 2, Ar), 7.5 (1H, d, $^4J_{HH}$ 2.5, 6-H), 7.6 (1H, dd, $^3J_{HH}$ 7.4, $^4J_{HH}$ 2, Ar), 7.9 (1H, dd, $^3J_{HH}$ 8, $^4J_{HH}$ 2.5, 8-H), 8.0 (1H, d, $^3J_{HH}$ 8, 9-H); δ_F ($CDCl_3$) −52.1 (3F, dq, $^5J_{FF}$ 12.5, $^5J_{HF}$ 3.9, 3-CF_3), −54.4 (3F, q, $^5J_{FF}$ 12.5, 2-CF_3); *m*/*z* 573 (M^+).

With 2,6-xylidine. Reaction as above afforded from **3** (0.52 g) with 2,6-xylidine, as a pale yellow solid, (*E*)-1-(2,6-dimethylphenyl)-4-(2,6-dimethylphenylamino)-3-[3-(*N*-2,6-dimethylphenylamino)hexafluorobut-2-en-2-yl]-2-oxoazetine **19** (0.15 g, 15.7%) mp 135–137 °C (Found: C, 64.6; H, 5.2; N, 7.1. $C_{31}H_{29}F_6N_3O$ requires C, 64.9; H, 5.1; N, 7.3%); δ_H ($CDCl_3$) 1.8 (6H, s, 2 × CH_3), 1.9 (6H, s, 2 × CH_3), 2.3 (6H, s, 2 × CH_3), 6.7–8.5 (9H, m, Ar); δ_F ($CDCl_3$) −52.5 (3F, q, $^5J_{FF}$ 12.6, CF_3), −55.5 (3F, q, $^5J_{FF}$ 12.9, CF_3); *m*/*z* 573 (M^+).

With 2-chloroaniline. Reaction of **3** (0.5 g) with 2-chloroaniline (1.1 g) after reaction as above, except that the water washing step was omitted, afforded after purification by column chromatography and sublimation *in vacuo* (*E*)-1-(2-chlorophenyl)-4-(2-chlorophenylimino)-3-[3-(*N*-2-chlorophenylamino)hexafluorobut-2-en-2-yl]-2-fluoroazetine **20** (0.06 g); mp 243–244 °C (Found: C, 50.9; H, 2.0; N, 6.8. $C_{25}H_{13}F_7Cl_3$ requires C, 50.5; H, 2.2; N, 7.0%); δ_H ($CDCl_3$) 6.5 (1H, dd, $^4J_{HH}$ 15, $^4J_{HF}$ 3.8, NH), 6.9–9.5 (11H, m, Ar); δ_F ($CDCl_3$) −50.4 (3F, dq, $^5J_{FF}$ 12.9, $^4J_{HF}$ 3.8, CF_3), −53.7 (3F, q, $^4J_{FF}$ 12.9, CF_3), −112 (1F, s, CF=); *m*/*z* 573 (M^+).

With 4-chloroaniline. Reaction of **3** (0.5 g) with 4-chloroaniline (0.6 g) as above afforded a bright yellow solid which on purification by column chromatography and sublimation *in vacuo* yielded (*E*)-1-(4-chlorophenyl)-4-(4-chlorophenylamino)-3-[3-(*N*-4-chlorophenylamino)hexafluorobut-2-en-2-yl]-2-oxoazetine **21** (0.14 g); mp 190 °C decomp. (Found: C, 51.0; H, 2.4; N, 7.0. $C_{25}H_{14}Cl_3F_6N_3O$ requires C, 50.8; H, 2.4; N, 7.1%); δ_H ($CDCl_3$) 6.7 (1H, t, $^4J_{HH} = J_{HH}$ 2, NH × 2), 6.8–7.9 (12H, m, Ar); δ_F ($CDCl_3$) −51.5 (3F, q, $^5J_{FF}$ 14.3, CF_3), −53.5 (3F, q, $^5J_{FF}$ 14.3, CF_3); *m*/*z* 573 ($M - HF^+$).

Hydrolysis of 20

The azetine **20** (0.2 g) was stirred at 18 °C with 2 M sulfuric acid (5 cm^3) for 1 h and the mixture was then extracted with ether (3 × 10 cm^3). The combined extracts were dried ($MgSO_4$) and the solvent evaporated to leave a pale yellow solid. Purification by sublimation *in vacuo* afforded (*E*)-1-(2-chlorophenyl)-4-(2-chlorophenylamino)-3-[3-(*N*-2-chlorophenylamino)hexafluorobut-2-en-2-yl]-2-oxoazetine **22** (0.13 g); mp 211–215 °C (Found: C, 50.6; H, 2.2; N, 7.4. $C_{25}H_{14}Cl_3F_6N_3O$ requires C, 50.8; H, 2.4; N, 7.1%); δ_H ($CDCl_3$) 6.4 (1H, d, $^4J_{HH}$ 2.8, NH), 6.5 (1H, d, $^4J_{HH}$ 2.6, NH), 6.9–7.9 (12H, c, Ar); δ_F ($CDCl_3$) −51.6 (3F, q, $^5J_{FF}$ 13.7, CF_3), −53.4 (3F, q, $^5J_{FF}$ 13.7, CF_3); *m*/*z* 573 ($M - HF^+$).

References

1 Part 16. P. L. Coe and M. I. Cook, *J. Chem. Soc., Perkin. Trans. 1*, 2000, 1537.
2 R. N. Haszeldine, *J. Chem. Soc.*, 1952, 4423.
3 J. C. Tatlow, *J. Fluorine Chem.*, 1995, **75**, 7.
4 (*a*) P. L. Coe, S. F. Sellers, J. C. Tatlow, H. C. Fielding and G. Whittaker, *J. Fluorine Chem.*, 1981, **18**, 417; (*b*) P. L. Coe, M. I. Cook and I. R. Owen, *J. Fluorine Chem.*, 1998, **42**, 389.
5 P. L. Coe and C. L. Andrews, Presented in part at the American Chemical Society, Winter Fluorine Conference, St Petersburg, Florida, Jan. 1995.
6 (*a*) R. D. Chambers, A. A. Lindley, H. C. Fielding, J. S. Molliett and G. Whittaker, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1064; (*b*) M. R. Bryce, R. D. Chambers, A. A. Lindley and H. C. Fielding, *J. Chem. Soc., Perkin Trans. 1*, 1983, 2451.
7 M. W. Briscoe, R. D. Chambers, S. J. Mullins, T. Nakamura, J. F. S. Vaughan and F. G. Drakesmith, *J. Chem. Soc., Perkin Trans. 1*, 1994, 3115.
8 D. R. A. Perry, *Fluorine Chem. Rev.*, 1968, **1**, 253.
9 M. W. Briscoe, R. D. Chambers, S. J. Mullins, T. Nakamura and J. F. S. Vaughan, *J. Chem. Soc., Perkin Trans. 1*, 1994, 3119.
10 R. D. Chambers, W. K. Gray, S. J. Mullins and S. Korn, *J. Chem. Soc., Perkin Trans. 1*, 1997, 1457.
11 P. N. L. Bosbury, R. Fields and R. N. Haszeldine, *J. Chem. Soc., Perkin Trans. 1*, 1978, 422.
12 *The Aldrich Library of NMR Spectra*, 2nd edn., C. J. Ponchert, Aldrich Chemical Co., Milwaukee, USA, 1983, spectra 355C and 356C.
13 P. L. Coe and N. C. Ray, *J. Fluorine Chem.*, 1998, **88**, 169.
14 W. T. Flowers, R. N. Haszeldine, C. R. Owen and A. Thomas, *J. Chem. Soc., Chem. Commun.*, 1974, 134.
15 P. L. Coe, I. R. Owen and S. J. Till, *J. Chem. Soc., Perkin Trans. 1*, 2000, 1529.
16 M. R. Bryce, R. D. Chambers and G. Taylor, *J. Chem. Soc., Perkin Trans. 1*, 1984, 509.