Reaction of nitrones with internal fluoroalkenes and with tetrafluorobenzyne

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Abstract

Reaction of *C,N*-diphenylnitrone with octafluorobut-2-ene and octafluoronorbornadiene at room temperature affords the corresponding isoxazolidines (**8**) (96%) and (**9**) (28%), respectively; perfluoro-(2,3-dimethylbut-2-ene) and octafluorocyclopentene are unreactive under comparable conditions. Rearranged 1:1 adducts, i.e. *C*-phenyl-*C*-(2-hydroxytetrafluorophenyl)imines (**10**), are formed from reaction of tetrafluorobenzyne with the nitrones $PhCH=^{+}NR-O^{-}$ (R = Ph, Bu^{t} and Me), although the t-butylnitrone reaction also gives the benzo[*b*]isoxazolidine (**11**). The imine **10c** formed from the methylnitrone is converted into an unidentified fibrous 1:1 adduct on attempted recrystallization [EtOH] and this hydrolyses readily to 2-hydroxytetrafluorobenzophenone (**13**).

Introduction

Cycloaddition of nitrones to fluoroalkenes and fluorobenzynes has received only limited attention.

In 1972 the reactions of hexafluoropropene and octafluoroisobutene with *C*-phenyl-*N*-benzyl- and *C*-methyl-*N*-ethyl-nitrone were reported [1] to give the isoxazolidines **1** (where X = F or CF_3 and R = Ph, R′ = CH_2Ph or R = Me, R′ = Et). In contrast, it was stated in 1978 that reaction between *C,N*-diphenylnitrone and hexafluoropropene afforded the 2-azetidinone **2** [2].

Further work in this department on the latter reaction indicated that the isoxazolidine **3** was the initial unstable product [3] and on attempted purification of the reaction product by DCFC the β-lactam **2** (30%) was isolated [4]. Similarly, the reaction involving chlorotrifluoroethylene gave a low yield (13%) of isoxazolidine **4** and this on DCFC afforded azetidinone **5** [4].

Several reports [5–7] have appeared on the reaction of benzyne with various nitrones to give the corresponding benzo[*b*]isoxazolidines, e.g. **6** [5], but to the best of our knowledge the only such reaction involving tetrafluorobenzyne is that with *C*-phenyl-*N*-4-fluorophenylnitrone [4]. This gave

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a mixture of products from which a 1:1 adduct (30%) was isolated and this was tentatively assigned the isoxazolidine structure **7**.

In the present work the reactions of *C,N*-diphenylnitrone with a number of internal perfluoroalkenes and the nitrones $PhCH=^{+}NR-O^{-}$ (R = Ph, Bu^t and Me) with tetrafluorobenzyne have been investigated.

Experimental

Starting materials

The perfluoroalkenes used were research samples prepared in the department and the purity of each was checked before use. Pentafluorobenzene (Fluorochem Ltd.), *C,N*-diphenylnitrone (Lancaster Synthesis) and *C*-phenyl-*N*-t-butylnitrone (Lancaster Synthesis) were commercial samples.

C-Phenyl-*N*-methylnitrone was prepared as reported [8] in 85% yield by reaction of benzaldehyde with *N*-methylhydroxylamine hydrochloride in the presence of base.

Tetrafluorobenzyne was generated *in situ* in the presence of the nitrone by the following procedure. A solution of n-butyl-lithium (1.55 M in hexane) in anhydrous diethyl ether (40 cm^3) contained in a three-necked flask (*c.* 250 cm^3) fitted with a nitrogen inlet, a pressure-equalizing dropping funnel and a reflux condenser surmounted by a cold finger (−78 °C) connected to a nitrogen exit, was cooled to −78 °C and stirred. Pentafluorobenzene in ether (40 cm^3) was added dropwise during 30 min, stirring was continued at *c.* −70 °C (2 h) and then a solution of the nitrone in anhydrous THF (130 cm^3) was added dropwise during 30 min with the temperature kept below −65 °C. The resulting solution was stirred at *c.* −70 °C (2 h), allowed to warm slowly to room temperature (*c.* 3 h) and then stirred overnight (12 h).

General techniques

Individual components of mixtures were separated by dry column flash chromatography (DCFC) using silica (Kieselgel 60H) after examination by TLC.

Products were examined by IR spectroscopy (Perkin-Elmer 783 instrument), ^1H and ^{19}F NMR spectroscopy [Perkin-Elmer R32 instrument operating at 90 MHz (^1H) and 84.6 MHz (^{19}F) with references Me_4Si and CF_3CO_2H, respectively; shifts to low field of reference are designated positive], ^{13}C NMR spectroscopy (Bruker WP80 spectrometer operating at 20.1 MHz with broad band proton decoupling using D_2O as the deuterium lock signal and Me_4Si as internal reference) and mass spectrometry (Kratos MS45 instrument with an electron beam energy of 70 eV).

Reactions of C,N-*diphenylnitrone*

(a) With octafluorobut-2-ene

The alkene (*cis/trans* mixture) (6.15 g, 30.7 mmol) was condensed *in vacuo* into a Rotaflo tube (*c.* 250 cm^3) cooled to −196 °C and which

contained the nitrone (4.01 g, 20.3 mmol) and anhydrous diethyl ether (60 cm^3). After warming to room temperature, the tube was shaken in the dark (16 h). The volatile material was removed *in vacuo* and the resulting solid/liquid mixture was filtered to afford unchanged nitrone (1.87 g, 9.4 mmol, 47% recovered).

Traces of solvent remaining in the filtrate were removed *in vacuo* and the remaining brown oil, which rapidly darkened in light, was identified as 3,4-difluoro-3,4-bis(trifluoromethyl)-2,5-diphenylisoxazolidine (**8**) (n.c.) (4.18 g, 10.5 mmol, 96%) (Analysis: Found: C, 51.3; H, 3.0; N, 3.8; F, 38.6%; M^+, 397. $C_{17}H_{11}F_8NO$ requires C, 51.3; H, 2.8; N, 3.5; F, 38.3%; M, 397) as a mixture of three diastereoisomers in the ratio 80:13:7 (^{19}F NMR). IR $\nu_{max.}$: 3090, 3065 m (arom. C–H str.); 1605, 1500 m (arom. C=C str.); 1370 s (aryl C–N str.); 1250–1190 s (C–F str.); 1155 m (aliph. C–N str.); 1125 s (C–O str.); 960 s (N–O str.); 770, 695 s (arom. C–H out of plane def.); 760 s (CF_3 bending) cm^{-1}. ^1H NMR neat δ: 7.4–6.8 (mult., 10H, $2C_6H_5$); 5.17 (dd, 1H, >C*H*Ph, J=24.3 and 5.4 Hz) ppm*. ^{19}F NMR neat δ: isomer 1 (80%), multiplets at +5.0 (3F, CF_3); +0.5 (3F, CF_3); −39.5 (1F, >CF–O); −107 (1F, >CF–C) ppm; isomer 2 (13%), multiplets at +5.8; +0.1; −47.5; −89.5 ppm (ratio 3:3:1:1); and isomer 3 (7%), multiplets at +2.0; −3.5; −44.0; −94.5 ppm (ratio 3:3:1:1). MS *m/z*: 397 (100%, M^+); 328 [5.8, $(M-CF_3)^+$]; 181 [99.6, $(M-C_4F_8O)^+$]; 180 [35.2, $(M-C_4HF_8O)^+$]; 104 (16.6, $C_7H_6N^+$); 91 (48.3, $C_7H_7^+$); 77 (40.3, $C_6H_5^+$).

(b) With octafluoronorbornadiene

The diene (4.40 g, 19.0 mmol) was added to a stirred solution of the nitrone (3.00 g, 15.2 mmol) in anhydrous THF (70 cm^3) under nitrogen and the mixture was stirred further until the nitrone had reacted completely (TLC, 10 d) to give a yellow solution. Removal of the solvent below 45 °C under reduced pressure resulted in sudden darkening to give a black liquid (5.10 g) which TLC (CH_2Cl_2:pentane 1:4 v/v) showed was a complex mixture of products.

Separation of the mixture by DCFC gave (i) a yellow oil (eluant CH_2Cl_2:pentane 1:4 v/v) which was identified as 4,5-diphenyl-1,2,6,7,8,9,10,10-octafluoro-3-oxa-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene (**9**) (n.c.) (1.81 g, 4.18 mmol, 28%) (Analysis: Found: C, 55.6; H, 2.6; N, 3.0; F, 34.8%; M^+, 433. $C_{20}H_{11}F_8NO$ requires C, 55.4; H, 2.5; N, 3.2; F, 35.1%; M, 433) as a mixture of two isomers in the ratio 77:23 (^1H and ^{19}F NMR). IR $\nu_{max.}$: 3060, 3030 w (arom. C–H str.); 1755 m (CF=CF str.); 1595, 1480 m (arom. C=C str.); 1380 s (aryl C–N str.); 1300–1180 s (C–F str.); 1160 m (aliph. C–N str.); 1135 s (C–O str.); 960 s (N–O str.); 760, 680 s (arom. C–H out of plane def.) cm^{-1}. ^1H NMR $CDCl_3$ δ: 7.5–7.15 (mult., 10H, $2C_6H_5$); 5.07 [dd, 0.77H, >C*H*Ph, J=22.5 (H–F *trans*) and 2.7 Hz]; 5.18 [dd, 0.23H, >C*H*Ph, J=36.2 (H–F *cis*) and 3.0 Hz] ppm. ^{19}F NMR $CDCl_3$ δ: major isomer, −40.5, −61.4 (AB, 2F, CF_AF_B, J=195 Hz); −51.7 (1F, >CF–O);

*A second minor absorption assigned to >C*H*Ph was observed at *c.* 5.3 ppm.

−69.2 (1F, =CF); −73.3 (1F, =CF); 90.8 (d mult., 1F, $\gtrless$CF−CH$\lessgtr$, J_{HF}= 22.5 Hz); −147.4 (1F, $\gtrless$CF), −151.5 (1F, $\gtrless$CF) ppm, minor isomer, −40.2, −63.0 (J_{AB}= 192 Hz); −52.0; −70.8; −72.7; −96.0 (d, J_{HF}= 36 Hz); −142.8, −146.1 ppm MS *m/z*: 433 (71.8%, M^+); 414[1.8, $(M-F)^+$]; 394 [1.5, $(M-HF_2)^+$]; 259 [8.1, $(M-C_5F_6)^+$]; 239 [8.7, $(M-CHF_7)^+$]; 212 [14.7, $(M-C_6F_7O)^+$]; 181 (26.2, $C_{13}H_{11}N^+$); 180 (28.7, $C_{13}H_{10}N^+$); 109 (14.2, $PhNCO^+$); 104 (58.1, $C_7H_6N^+$); 91 (80.4, $C_7H_7^+$); 77 (100, $C_6H_5^+$), (ii) a black liquid (0.74 g) (eluant Me_2CO) and (iii) a black gum (2.05 g) (eluant MeOH). Both the latter fractions were shown (TLC and ^{19}F NMR) to be complex mixtures and they were not examined further.

(c) With other perfluoroalkenes

Attempted reaction *in vacuo* in a Rotaflo tube (*c.* 250 cm^3) in the dark at room temperature, between (i) perfluoro-(2,3-dimethylbut-2-ene) (4.12 g, 13.1 mmol) and the nitrone (2.01 g, 10.1 mmol) in ether (50 cm^3) for 14 d, and (ii) octafluorocyclopentene (3.47 g, 16.3 mmol) and the nitrone (2.65 g, 13.5 mmol) in ether (50 cm^3) for 30 d gave only unchanged reactants.

(d) With tetrafluorobenzyne

Reaction between the benzyne [generated from pentafluorobenzene (2.10 g, 12.5 mmol) and n-butyl-lithium (14.0 mmol)] and the nitrone (2.46 g, 12.5 mmol) gave a small amount of a dark brown solid and a yellow solution. Filtration and then removal of the solvent *in vacuo* gave a yellow oil (3.10 g) which contained unchanged nitrone (IR). Purification of the product by DCFC [eluant CH_2Cl_2 and petrol (b.p., 40–60 °C) 1:1 v/v] gave a yellow solid 1:1 adduct identified as *C,N*-diphenyl-*C*-(2-hydroxytetrafluorophenyl)imine (**10a**) (n.c.) (1.20 g, 3.48 mmol, 28%) (Analysis: Found: C, 65.9; H, 3.6; N, 4.0; F, 21.8%; M^+, 345. $C_{19}H_{11}F_4NO$ requires C, 66.0; H, 3.8; N, 4.0; F, 22.0%; M, 345); m.p., 123–125 °C. IR $\nu_{max.}$: 3500–3300 m (O−H str.); 3060, 3020 w (arom. C−H str.); 1720 m (C=N str.); 1595, 1490 m (arom. C=C str.); 1340–1200 s (C−F str.); 1120 s (C−O str.); 755, 685 s (arom. C−H out of plane def.) cm^{-1}. ^1H NMR $CDCl_3$ δ: 7.6–6.9 (mult., $2C_6H_5$ and OH) ppm. ^{19}F NMR $CDCl_3$ δ: −55.6 (ddd, 1F, F−6, $J_{5-6} \approx 20$, $J_{3-6} \approx 10$ and $J_{4-6} \approx 6$ Hz); −71.3 (td, 1F, F−4, $J_{3-4} \approx J_{5-4} \approx$ 20 Hz); −85.5 (ddd, 1F, F−3, $J_{5-3} \approx 5.5$ Hz); −94.6 (td, 1F, F−5)ppm. MS *m/z*: 345 (88.4%, M^+); 344 [17.0, $(M-H)^+$]; 326 [5.7, $(M-HF)^+$]; 268 [16.7, $(M-C_6H_5)^+$]; 257 (100%, $C_{12}H_7F_4NO^+$); 239 (22.8, $C_{12}H_4F_4N^+$); 180 (43.8, $C_{13}H_{10}N^+$); 105 (41.2, $C_7H_7N^+$); 77 (70.2, $C_6H_5^+$).

Further elution (CH_2Cl_2) gave a yellowish solid (1.24 g) which was identified as impure unchanged nitrone.

Reaction of C-phenyl-N-t-butylnitrone with tetrafluorobenzyne

The benzyne [generated from pentafluorobenzene (2.00 g, 11.9 mmol) and n-butyl-lithium (14.0 mmol)] and the nitrone (2.11 g, 12.0 mmol) gave a turbid solution, which on filtration afforded a clear yellow filtrate. Removal of the solvent under reduced pressure gave a yellow semi-solid (2.15 g),

the ^{19}F NMR spectrum of which showed the presence of four tetrafluorophenyl compounds (A–D) (^{19}F NMR δ: −65, −76, −84, −87; −58, −71, −86, −101; −63, −82, −90, −102; and −55, −74, −86, −101.3 in the ratio 41:32:18:9) and which on treatment with diethyl ether (15 cm^3) gave crystals (0.62 g) of unchanged nitrone contaminated with compound B.

The resulting filtrate on removal of the ether *in vacuo* gave a yellow solid (1.43 g) which was separated by DCFC into (i) a white crystalline solid [eluant petrol (b.p., 40–60 °C)] which was identified as 2-t-butyl-3-phenyl-4,5,6,7-tetrafluorobenzo[*b*]isoxazolidine (**11**) (n.c.) (0.95 g, 2.92 mmol, 25%) (Analysis: Found: C, 62.3; H, 4.8; N, 4.2; F, 23.0%; M^+, 325.1076. $C_{17}H_{15}F_4NO$ requires C, 62.2; H, 4.6; N, 4.3; F, 23.4%; M, 325.1090); m.p., 99–100 °C (recrystallised from EtOH). IR $\nu_{max.}$: 3040 w (arom. C−H str.); 2980, 2920 m (aliph. C−H str.); 1540, 1505, 1455 m (arom. C=C str.); 1340–1180 s (C−F str.); 1095 s (C−O str.); 955 s (N−O str.); 690 s, 750 m (arom. C−H out of plane def.) cm^{-1}. ^1H NMR $CDCl_3$ δ: 7.47 (broad s, 5H, Ph); 5.73 (s, 1H, $\diagdown CH\diagup$Ph); 1.1 (s, 9H, CMe_3) ppm. ^{19}F NMR $CDCl_3$ δ: −65.2 (dd, 1F, F−4, $J_{5-4} \approx 22$, $J_{7-4} \approx 14.7$ Hz); −76.1 (mult., 1F, F−6); −84.0 (ddd, 1F, F−7, $J_{6-7} \approx 20$, $J_{4-7} \approx 14.6$, $J_{5-7} \approx 4.7$ Hz); −87.35 (ddd, 1F, F−5, $J_{4-5} \approx 22$, $J_{6-5} \approx 19$, $J_{7-5} \approx 4.7$ Hz) ppm. ^{13}C NMR $CDCl_3$ δ: 143–129 (complex multiplets, arom. CF); 140.7 (s, *ipso*-C_6H_5); 128.8, 128.2, 127.0 (3×s, *o*-, *m*- and *p*-C_6H_5); 113.9 (d, arom. $=CF-\underset{|}{C}=$, $^2J_{F-C} = 16$Hz); 65.2 (s, $\diagdown CHN\diagup$); 62.0 (s, Me_3CN); 25.1 (s, Me) ppm. MS *m/z*: 325 (33.7%, M^+); 310 [2.2, $(M-CH_3)^+$]; 269 [57.1, $(M-C_4H_8)^+$]; 268 [29.3, $(M-C_4H_9)^+$]; 253 (24.9, $C_{13}H_5F_4O^+$); 77 (19.7, $C_6H_5^+$); 57 (100, $C_4H_9^+$), (ii) a yellow solid [eluant CH_2Cl_2 and petrol (b.p., 40–60 °C) 1:1 v/v], which was identified as *C*-phenyl-*C*-(2-hydroxytetrafluorophenyl)-*N*-t-butylimine (**10b**) (n.c.) (0.26 g, 0.80 mmol, 7%) (Analysis: Found: C, 62.4; H, 4.4; N, 4.0; F, 23.5%; M^+, 325. $C_{17}H_{15}F_4NO$ requires C, 62.1; H, 4.6; N, 4.3; F, 23.4%; M, 325); m.p., 172–174 °C. IR $\nu_{max.}$: 3600–3350 m (O−H str.); 3140, 3080 m (arom. C−H str.); 2980, 2880 m (aliph. C−H str.); (1650 s (C=N str.); 1580, 1545, 1500 m (arom. C=C str.); 1330–1220 s (C−F str.); 1150 s (C−O str.); 760, 690 s (arom. C−H out of plane def.) cm^{-1}. ^1H NMR $CDCl_3$ δ: 7.60–7.25 (mult., 6H, C_6H_5 and OH); 1.27 (s, 9H, CMe_3) ppm. ^{19}F NMR $CDCl_3$ δ: −58.5 (ddd, 1F, F−6, $J_{5-6} = 22.7$, $J_{3-6} = 11.1$, $J_{4-6} = 6.1$ Hz); −71.7 (td, 1F, F−4, $J_{3-4} \simeq J_{5-4} = 21.9$, $J_{6-4} = 6.0$ Hz); −86.7 (ddd, 1F, F−3, $J_{4-3} = 21.2$, $J_{6-3} = 10.9$, $J_{5-3} = 8.2$ Hz); −101.0 (td, 1F, F−5, $J_{4-5} \simeq J_{6-5} = 21.9$, $J_{3-5} = 8.1$ Hz) ppm. ^1H NMR $CDCl_3$ δ: 171.6 (d, C=N, $^3J_{F-C} = 4$ Hz); 160.9 (mult., FC=*C*); 160.4 (mult., FC=*C*); 146–130 (4×dmult., 4×FC=, $J \approx 250$ Hz); 129.7, 128.9, 127.8, 126.5 (4×s, C_6H_5); 57.9 (N−*C*Me_3); 30.7 (Me) ppm. MS *m/z*: 325 (23.1%, M^+); 310 [7.6, $(M-Me)^+$]; 268 [100, $(M-C_4H_9)^+$]; 77 (38.7, $C_6H_5^+$); 57 (69.8, CMe_3^+), and (iii) a yellow solid (eluant Me_2CO) (0.10 g), which the ^{19}F NMR spectrum showed contained the 1:1 adduct (**10b**) and a new unidentified tetrafluorophenyl compound [^{19}F NMR $CDCl_3$ δ: −61.1 (dd, $J = 24$ and 8 Hz); −74.3 (td, $J = 21$ and 3 Hz); −82.6 (ddd, $J = 21.9$ and 4 Hz); −92.6 (t, $J = 23$ Hz) ppm. ^1H NMR δ: 7.6–7.3 (mult.,

5H, C_6H_5); 1.4 (s, 9H, CMe_3) ppm. ^{13}C NMR δ: 133.1, 129.7, 128.4, 127.8 (4×s, C_6H_5); 70.4 (Me_3C); 27.9 (Me) ppm] present in the ratio 5:27.

Reaction of C-phenyl-N-methylnitrone with tetrafluorobenzyne

A mixture of the benzyne [generated from pentafluorobenzene (3.20 g, 19.0 mmol) and n-butyl-lithium (20.15 mmol)] and the nitrone (2.14 g, 15.8 mmol) gave solid material (0.40 g) and a yellow solution from which the solvent was removed *in vacuo* to afford a yellow gum (4.33 g), the ^{19}F NMR spectrum of which indicated that it contained two or three major and several minor components. Attempted separation of the mixture by DCFC gave (i) a yellow solid [eluant Me_2CO and petroleum ether (b.p., 40–60 °C) 1:9 v/v] identified as *C*-phenyl-*C*-(2-hydroxytetrafluorophenyl)-*N*-methylimine (**10c**) (n.c.) (1.31 g, 4.6 mmol, 29%) (Analysis: Found: C, 59.3; H, 2.9; N, 4.6; F, 26.6%; M^+, 283. $C_{14}H_9F_4NO$ requires C, 59.3; H, 3.1; N, 4.9; F, 26.8%; M, 283); m.p., 106–108 °C, as a mixture of the *E* and *Z* isomers in the ratio 5:1 (^{19}F NMR). ^1H NMR CCl_4 δ: 7.6–7.2 (mult. 6H, C_6H_5 + OH); 3.11 (s, 3H, NCH_3) ppm. ^{19}F NMR CCl_4 δ: major isomer −58.5 (ddd, 1F, 6−F, J_{5-6} = 21.1, J_{3-6} = 10.2, J_{4-6} = 5.9 Hz); −72.0 (td, 1F, 4−F, $J_{3-4} \simeq J_{5-4}$ = 21.6, J_{6-4} = 5.9 Hz); −85.2 (ddd, 1F, 3−F, J_{4-3} = 22.0, J_{6-3} = 10.2, J_{5-3} = 6.8 Hz); −98.0 (td, 1F, 5−F, $J_{4-5} \simeq J_{6-5}$ = 21.5, J_{3-5} = 6.8 Hz) ppm; and minor isomer −56.2 (ddd, 6−F, $J_{5-6} \approx 20$, $J_{3-6} \approx 10$, $J_{4-6} \approx 6$ Hz); −70.1 (td. 4−F, $J_{3-4} \simeq J_{5-4} \approx 20$, $J_{6-4} \approx 6$ Hz); −81.9 (ddd, 3−F, $J_{4-3} \approx 20$, $J_{6-3} \approx 10$, $J_{5-3} \approx 6$ Hz); −90.5 (td, 5−F, $J_{4-5} \simeq J_{6-5} \approx 20$, $J_{3-5} \approx 6$ Hz) ppm. MS *m/z*: 283 (88.8%, M^+); 282 [76.8, $(M-H)^+$]; 268 [12.4, $(M-Me)^+$]; 266 [13.5, $(M-OH)^+$]; 264 [24.7, $(M-F)^+$]; 253 [15.2, $(M-CH_4N)^+$]; 206 [66.3, $(M-C_6H_5)^+$]; 118 (100, $C_8H_8N^+$); 77 (35.8, $C_6H_5^+$), (ii) an unidentified yellow fibrous 1:1 adduct (eluant Me_2CO) (0.60 g, 2.12 mmol, 13%); m.p., 150–153 °C. ^1H NMR $(CD_3)_2CO$ δ: 7.8–7.2 (mult., 5H, C_6H_5); 3.25 (s, 3H, NCH_3) ppm. ^{19}F NMR $(CD_3)_2CO$ δ: −70.1 (dd, 1F, 6−F, J_{5-6} = 21.5, J_{3-6} = 8.4 Hz); −83.2 (t, 1F, 4−F, $J_{3-4} \simeq J_{5-4}$ = 21 Hz); −89.2 (dt, 1F, 3−F, J_{4-3} = 21.4, $J_{5-3} \simeq J_{6-3}$ = 8.4 Hz); −106.2 (td. 1F, 5−F, $J_{4-5} \simeq J_{6-5}$ = 21.8, J_{3-5} = 8.4 Hz) ppm. MS *m/z*: 283 (100%, M^+); 282 [77.8, $(M-H)^+$]; 268 [10.0, $(M-Me)^+$]; 266 [8.7, $(M-OH)^+$]; 264 [22.2, $(M-F)^+$], 253 [20.3, $(M-CH_4N)^+$]; 206 [58.8, $(M-C_6H_5)^+$]; 118 (88.5, $C_8H_8N^+$); 77 (37.0, $C_6H_5^+$), and (iii) a deep yellow gum (eluant MeOH) (0.65 g) which was shown (^{19}F NMR) to be a complex mixture and was not examined further.

Attempted recrystallisation of imine **10c** (0.50 g) from ethanol, to obtain a sample of the major isomer suitable for X-ray structural analysis, gave the unidentified, yellow fibrous 1:1 adduct (0.46 g), m.p., 150–152 °C, which was soluble in MeOH, EtOH, Me_2CO and DMSO, but relatively insoluble in $CHCl_3$ and CCl_4. ^1H NMR spectroscopic examination of a sample which had been kept in damp $(CD_3)_2CO$ for *c.* 4 weeks revealed an absence of the absorption at δ 3.25 ppm assigned to $N-CH_3$. Purification of the material by DCFC (eluant CH_2Cl_2) gave a white solid identified as 2-hydroxy-3,4,5,6-tetrafluorobenzophenone (**13**) (n.c.) (Analysis: Found: C, 57.5; H, 2.4; F,

27.7; M^+, 270. $C_{13}H_6O_2F_4$ requires C, 57.8; H, 2.2; F, 28.1%; M, 270). ^1H NMR $CDCl_3$ δ: 10.78 (s, 1H, OH); 7.9–7.5 (mult., 5H, C_6H_5) ppm. ^{19}F NMR $CDCl_3$ δ: −67.0 (mult., 1F, 6−F); −79.3 (tmult., 1F, 4−F): −85.3 (mult., 1F, 3−F); −96.7 (td, 1F, 5−F) ppm. ^{13}C NMR $CDCl_3$ δ: 196.1 (C=O); 148–132 (4 dmult., 4 arom. FC=, $J \approx 250$ Hz); 138.3 (*ipso*-C_6H_5); 133.7, 128.7, 128.5 (*o*-, *m*- and *p*-C_6H_5); 108.1 (d, FC=C<, $J=18$ Hz); 103.4 (d, FC=C<, $J=14$ Hz) ppm. MS *m/z*: 270 (73.4%, M^+); 269 [52.5, $(M-H)^+$]; 193 [22.2, $(M-C_6H_5)^+$]; 105 (100, $C_7H_5O^+$); 77 (66.8, $C_6H_5^+$). IR $\nu_{max.}$: 3400–3100 m (O−H str.); 3080 m (arom. C−H str.); 1740 m (C=O str.); 1580, 1540 m (arom. C=C str.); 1350–1240 s (C−F str.); 1135 m (C−O str.); 750, 690 m (arom. C−H out of plane def.) cm^{-1}.

Results and discussion

Reaction of octafluorobut-2-ene (*cis/trans* mixture) with *C,N*-diphenylnitrone (3:2 molar ratio) in diethyl ether at room temperature (16 h) gave (i) volatile material consisting of unchanged alkene and ether, (ii) unchanged nitrone (47% recovered) and (iii) 3,4-difluoro-3,4-bis(trifluoromethyl)-2,5-diphenylisoxazolidine (**8**) (96%) as a mixture of 3-diastereoisomers in the ratio 80:13:7 (^{19}F NMR spectroscopy). The magnitude of the vicinal H−F coupling constant observed (24.3 Hz) in the ^1H NMR spectrum for the methine absorption of the major isomer was somewhat greater than expected for a *trans* $^3J_{HF}$ coupling. However, the coupling can depend on the dihedral angle, bond length, bond angle and electronegativity of neighbouring groups [8]. If the observed coupling is *trans*, then it is probable that the major isomer has the sterically favoured structure **8a** and is formed by concerted 1,3-dipolar cycloaddition of the nitrone to the *trans*-alkene.

A mixture of octafluoronorbornadiene and *C,N*-diphenylnitrone (5:4 molar ratio) in THF at room temperature (10 d) gave a yellow solution which, on removal of the excess of diene and the solvent under reduced pressure below 45 °C, suddenly underwent partial decomposition to afford a black liquid mixture. Separation of the major component by DCFC gave 4,5-diphenyl-1,2,6,7,8,9,10,10-octafluoro-3-oxa-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene (**9**) (28%) as a mixture of two isomers in the ratio 77:23 ($^3J_{HF}=22.5$ and 36 Hz, respectively). The large difference in the $^3J_{HF}$ couplings observed indicates possibly that one is *cis* and the other is *trans* ($^3J_{HF}$ *cis* > *trans*), but on the evidence available *exo* or *endo* structures could not be assigned to the isomers.

Surprisingly, reaction did not take place at room temperature in diethyl ether between the nitrone and perfluoro-(2,3-dimethylbut-2-ene) (14 d) or octafluorocyclopentene (30 d).

The reaction of *C,N*-diphenylnitrone with tetrafluorobenzyne {generated from treatment of pentafluorobenzene with n-butyl-lithium [9]} (1:1 molar ratio) in Et_2O/THF, whilst the stirred solution was warmed from *c.* −70 °C

to room temperature, gave a yellow oil from which a 1:1 adduct identified as the imine **10a** (28%) was separated by DCFC.

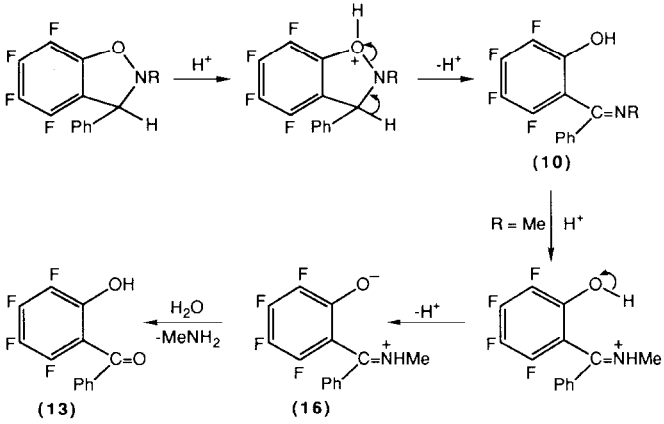
Comparable reaction with *C*-phenyl-*N*-t-butylnitrone gave a mixture of four tetrafluorophenyl compounds in the ratio 41:32:18:9 (^{19}F NMR spectroscopy). Separation by DCFC afforded pure samples of the two major components which were identified as the benzo[*b*]isoxazolidine **11** (25%) and the imine **10b** (7%), respectively. A mixture of unchanged nitrone and imine **10b** was also obtained, but the two minor products remain unidentified.

The corresponding reaction with *C*-phenyl-*N*-methylnitrone gave a complex mixture from which (i) the imine **10c** (29%), as a mixture of two isomers in the ratio *c.* 5:1, and (ii) an unidentified, yellow, fibrous 1:1 adduct (13%), m.p., 150–153 °C, were isolated; the latter compound was not the isoxazolidine **12**.

On attempted recrystallisation of imine **10c** from ethanol, it was converted into the same unidentified, yellow, fibrous adduct (m.p., 150–152 °C), which was almost insoluble in $CHCl_3$, and CCl_4 (contrast imine **10c**), but soluble in acetone and DMSO. When an NMR sample of this unknown material in damp $(CD_3)_2CO$ was stored (*c.* 4 weeks) and the resulting material purified by DCFC, 2-hydroxytetrafluorobenzophenone (**13**) was isolated.

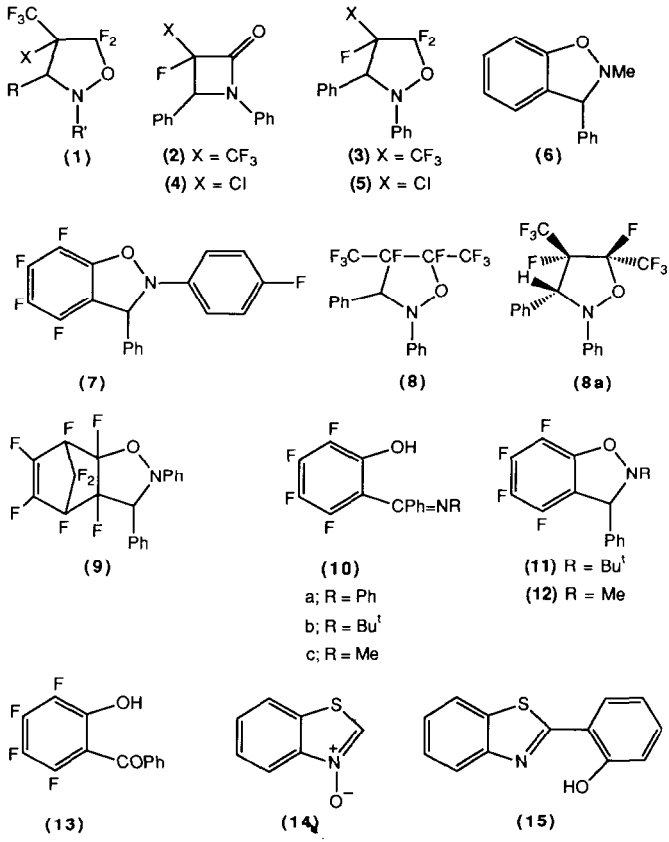
The imines **10** were each identified by the presence of a molecular ion peak in the mass spectrum, correct elemental analysis (C, H, N and F) for a 1:1 adduct, the absence of a methine absorption for ArC*H*Ph–N at $\delta \sim 5$ ppm in the ^{1}H NMR spectrum and broad hydrogen-bonded O–H (*c.* 3600–3300 cm^{-1}) and C=N (1650–1720 cm^{-1}) stretching absorptions in the IR spectrum. The phenolic OH proton absorption was not apparent in the ^{1}H NMR spectrum, being either coincident with that for the aromatic protons or broad and lost in the baseline.

It is considered that 1,3-dipolar cycloaddition first occurs to give the benzo[*b*]isoxazolidines which rearrange to the imines **10** by protonation at



Scheme 1.

oxygen followed by N–O bond scission and deprotonation at carbon (Scheme 1) with the *E* isomers (hydroxytetrafluorophenyl *anti* to the R group on N) sterically preferred; only when the R group was small (Me) was the less sterically favoured *syn* isomer detected. Isoxazolidines formed between heteroaromatic nitrones and benzyne cannot be isolated as they rearrange spontaneously to phenols, e.g. reaction involving nitrone **14** to give the substituted phenol **15** [10].



The unidentified fibrous 1:1 adduct, isolated after attempted recrystallisation of imine **10c**, was possibly the polar, resonance-stabilised zwitterion **16** which would be expected to undergo facile hydrolysis to the benzophenone **13** (Scheme 1).

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