Addition Reaction of 3,3,3-Trifluoropropene to Tetrahydrofuran. Telomeric Growth *via* Free-radical Rearrangements

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Tetrahydrofuran and 3,3,3-trifluoropropene react at 20 °C to give a homologous series of compounds in which one to four trifluoropropyl side chains are linked to THF. The principal product is tetrahydro-2-(3,3,3-trifluoropropyl)furan (1), but tetrahydro-2-(3,3,3-trifluoropropyl)-2-(5,5,5-trifluoro-2-trifluoromethylpentyl)furan (3) and tetrahydro-2,5-bis(3,3,3-trifluoropropyl)-2-(5,5,5-trifluoro-2-trifluoromethylpentyl)furan (4) are also formed in substantial yields. We propose that the adduct (3) is the end result of a free radical rearrangement in which a hydrogen atom is transferred *via* a 1,5-shift from C-2 of the tetrahydrofuranyl moiety of 1,1,1-trifluoro-5-(tetrahydrofuran-2-yl)-4-trifluoromethyl-2-pentyl radical (ii). Reaction of the resulting rearranged radical (iii) with 3,3,3-trifluoropropene followed by intermolecular hydrogen atom transfer gives (3). Formation of the adduct (4) requires that there be a 1,5-hydrogen shift from C-5 of intermediate (iv) across the ring to the $CH_2\dot{C}HCF_3$ side chain on C-2. Two 2:1 trifluoropropene–THF adducts, *cis*- and *trans*-tetrahydro-2,5-bis(3,3,3-trifluoropropyl)furan (2c) and (2d), are formed *via* a secondary reaction initiated by hydrogen abstraction from C-5 of (1).

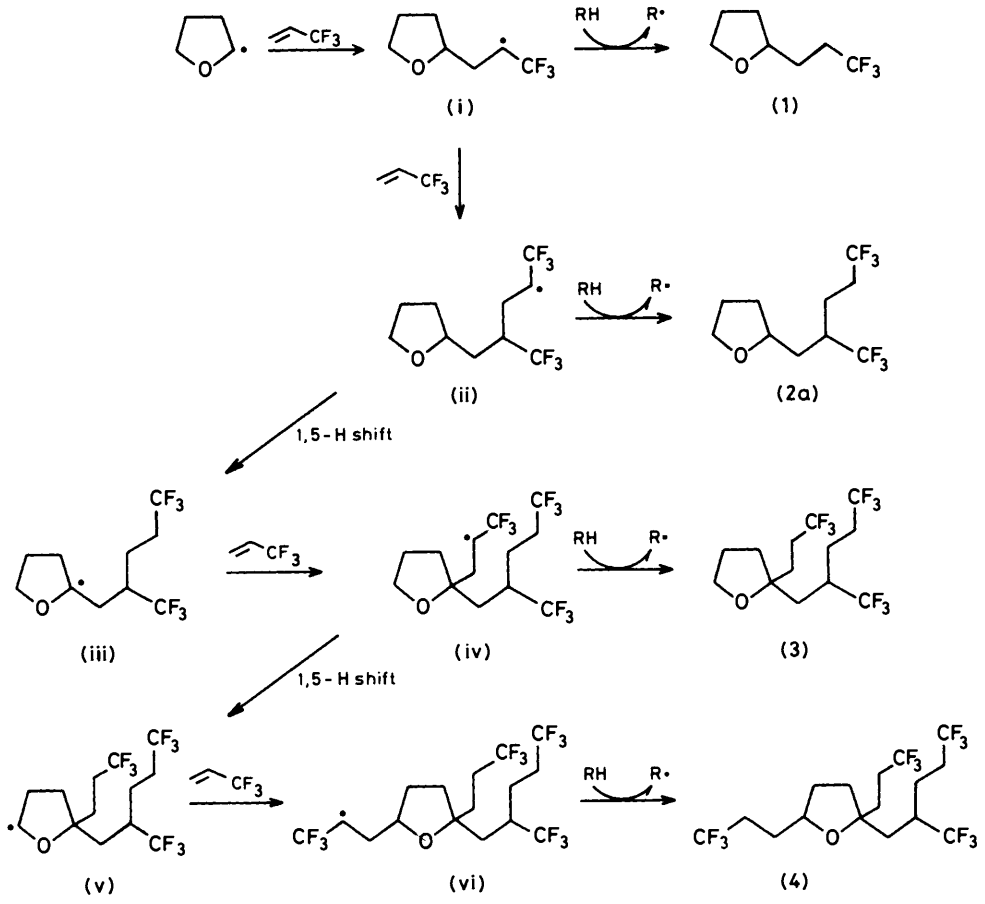
During a study of reactions of 3,3,3-trifluoropropene with organometallic reagents we found that tetrahydrofuran (THF) solutions of 3,3,3-trifluoropropene were unstable. Dry THF (distilled from Na) and 3,3,3-trifluoropropene react at room temperature to give a homologous series of compounds in which one, two, three, and four trifluoropropyl units were linked to THF. At 1.0M the reaction was virtually complete within 48 h. Addition of the free-radical inhibitor 4-methyl-2,6-di-t-butylphenol prevented the reaction from occurring, whereas warming the THF solution with benzoyl peroxide greatly accelerated the rate of the reaction without affecting the product composition. A great many free-radical coupling reactions of olefins with THF initiated by benzoyl peroxide or γ-radiation have been studied. However, 3,3,3-trifluoropropene may be unique both in the rate at which it reacts and in the product composition it gives. For example, chlorotrifluoroethylene (0.75M) in tetrahydrofuran, on γ-irradiation, gave a greater than 80% yield of a single product, tetrahydro-2-(2-chloro-1,1,2-trifluoroethyl)furan.[1,2] We confirmed these results and found that even in the absence of initiator there is evidence of reaction within a few hours, even though less than 20% of the chlorotrifluoroethylene reacts within ten days. Dedek and Fikar found that at higher concentrations (1.2—2.6M) small amounts of the telomeric by-products tetrahydro-2-(2,4-dichloro-1,1,2,3,3,4-hexafluorobutyl)furan and tetrahydro-2-(2,4,6-trichloro-1,1,2,3,3,4,5,5,6-nonafluorohexyl)furan were formed. Other authors using structurally similar olefins also have found higher molecular weight products, but claim that they are 2,5-disubstituted.[3] For example, THF and hexafluoropropene reportedly give tetrahydro-2-(1,1,2,3,3,3-hexafluoropropyl)furan and tetrahydro-2,5-bis(1,1,2,3,3,3-hexafluoropropyl)furan on γ-irradiation. The latter product predominates at higher total radiation doses. At low total γ-irradiation doses Muramatsu and co-workers found the monoadduct, tetrahydro-2-(1,1,2,3,3,3-hexafluoropropyl)furan, as the only product.[4]

Results and Discussion

3,3,3-Trifluoropropene reacts differently with tetrahydrofuran. On the basis of the structures of the three major products (1), (3), and (4), we propose that free-radical rearrangements *via* intramolecular 1,5-hydrogen shifts represent a primary reaction pathway (Scheme 1).

The structures of the products were established by ^1H and ^{13}C n.m.r. and mass spectrometry following separation of the components by preparative gas chromatography. The molecular weights and the elemental composition were established by high resolution mass spectrometry. The ^1H n.m.r. spectra were exceptionally complex, even at 360 MHz and decoupling studies were not fruitful. The complexity of the ^1H n.m.r. spectra results partially because of the existence of diastereoisotopic protons and complex mixtures of diastereoisomers. Courtieu *et al.* have described a detailed ^1H and ^{19}F n.m.r. study on diastereoisomeric tetrahydro-2-(1,1,2,3,3,3-hexafluoropropyl)furans.[5] They were able to effectively use decoupling and INDOR techniques to assign coupling constants. Most of our structures were too complex to allow such an analysis. Simultaneous proton- and fluorine-decoupling was not possible. However, the ^1H n.m.r. data did confirm the substitution pattern on C-2 and C-5 of the THF ring. ^{13}C N.m.r. spectra provided the best evidence for the structure. The spectra were proton-decoupled but not fluorine-decoupled. Hence, some carbon assignments were made on the basis of the carbon-fluorine coupling constants. The coupling constants observed in the trifluoropropyl group are shown in Figure 1. Eliel *et al.* have assigned ^{13}C shifts for the four carbons on the tetrahydrofuran ring for every possible pattern of disubstitution and some patterns of trisubstitution.[6] On the basis of this information we were able to assign virtually every carbon atom in adducts (1), (2), and (3). The ^{13}C shift values for tetrahydro-2-ethylfuran and tetrahydro-2-methylfuran [6] may be compared to those for tetrahydro-2-(3,3,3-trifluoropropyl)furan (1) (Figure 2). The signals at 27.6 and 29.9 were assigned on the basis of the C-F coupling constant which was 3.0 Hz for the δ 27.6 resonance and 28.2 Hz for the signal centred at δ 29.9.

Assigning structures to the four isomeric disubstituted tetrahydrofuran adducts (Scheme 2) presented a more complex problem. On the basis of the ^{13}C signals for the ring C-2 and C-5 carbons, all four possible arrangements of substitution are present. The major products by far, however, are (2c) and (2d). One shows the C-2 resonance at 76.20 and the other at 76.78 p.p.m. The 76.20 p.p.m. signal is about twice the intensity of the 76.78 p.p.m. signal, but we were not able to determine which signal belongs to which of the two isomers (2c)



Scheme 1

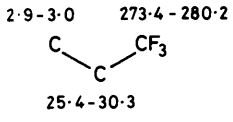


Figure 1. Coupling constants (Hz) observed for the 3,3,3-trifluoropropyl group

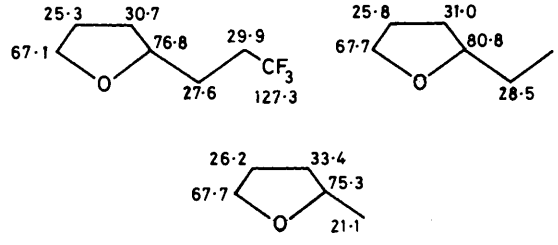


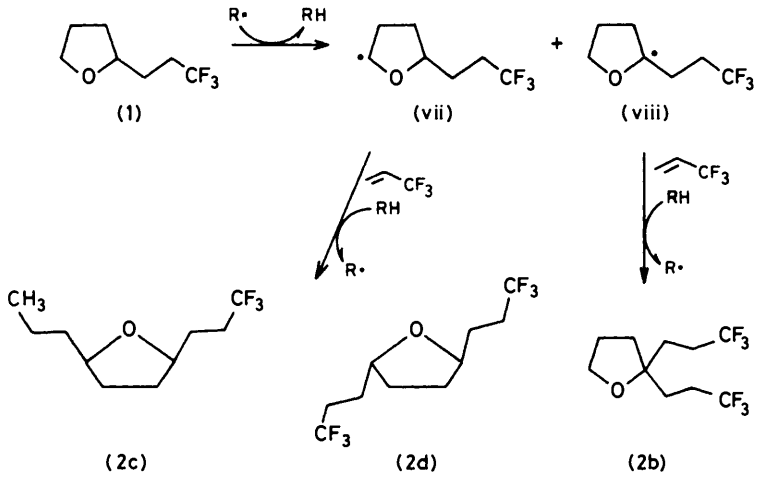
Figure 2. Comparison of ^{13}C shifts (p.p.m. relative to $SiMe_4$) for 2-methyl-, 2-ethyl-, and 2-(3,3,3-trifluoropropyl)-tetrahydrofuran

and (2d). Peaks at 67.19 and 81.39 p.p.m. correspond to signals for the unsubstituted and disubstituted carbons, respectively, of (2b). The telomeric adduct (2a) is present in the least amount. Peaks of nearly the same intensity fall at 74.84 (C-2 monosubstituted) and 66.83 p.p.m. (C-5 unsubstituted).

The 4 : 1 trifluoropropene–THF adduct can be assigned structure (4). Although there are too many overlapping carbon resonances in the ^{13}C spectrum to assign them all, the ^{1}H, ^{13}C, and mass spectral data taken altogether are strongly supportive of this structure (4). One other structure, tetrahydro-2,2-bis(3,3,3-trifluoropropyl)-5-(5,5,5-trifluoro-2-trifluoromethylpentyl)furan, that would possibly fit the available data is highly improbable on the basis of mechanistic rationale.

Integration of the three partially resolved g.c. peaks due to 2 : 1 trifluoropropene–THF adducts gave a ratio of 1 : 9 : 5. The two larger of these must be due to the 2,5-bis(trifluoropropyl) derivatives (2c) and (2d) in correspondence to the ^{13}C spectral results. Graphing the amounts of trifluoropropene, and adducts (1)—(4) *versus* time illustrates two important points (Figure 3). The rate of formation of (2c) and (2d) is coupled to the concentration of tetrahydro-2-(3,3,3-trifluoropropyl)furan (1). The 3 : 1 trifluoropropene–THF and 4 : 1 trifluoropropene–THF adducts (3) and (4) are formed at a relatively greater rate early in the reaction [*i.e.* the maximum rate of formation of (1) occurs between 24 and 30 h, while (3) and (4) are formed relatively more rapidly between 10 and 24 h after the reaction was started].

These results are consistent with a mechanism in which the more highly substituted products, (3) and (4), are formed in higher relative yield early in the reaction when the concentration of 3,3,3-trifluoropropene is greatest That is, the rate of coupling of radical (i) (Scheme 1) with 3,3,3-trifluoropropene to give radical (ii) is proportional to the concentration of the olefin, whereas the rate of intermolecular hydrogen radical transfer to (i) from tetrahydrofuran is relatively insensitive to concentration because the THF is present in such a large excess.



Scheme 2

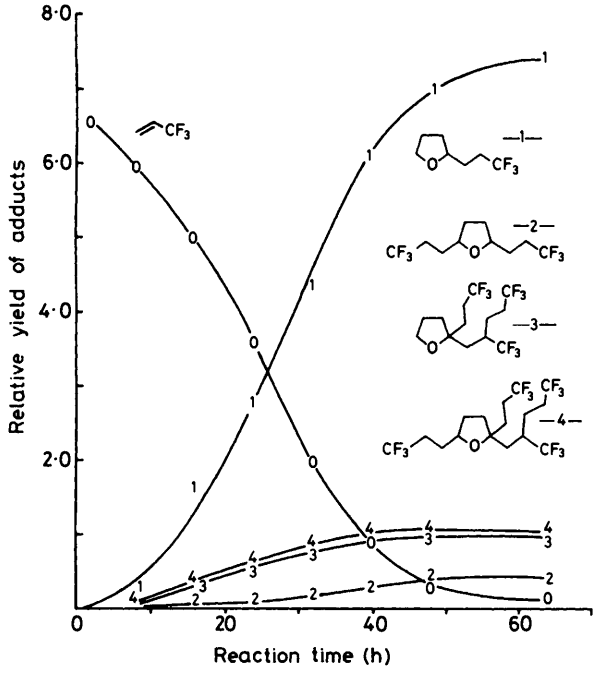
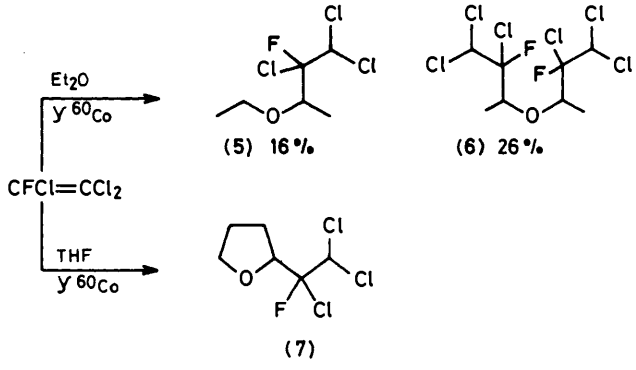


Figure 3. Relative amounts of adducts (1)—(4) as a function of reaction time. The initial concentration of 3,3,3-trifluoropropene was 1.04M



Scheme 3

On the basis of the g.c. analysis and determination of non-volatile components products of higher molecular weight (>455) constituted less than 6% of the total products. These results can be reasonably interpreted on the basis of the reactivity of intermediate (i), which abstracts hydrogen from THF to give (1) in preference to coupling to trifluoropropene to give radical (ii). The intermolecular hydrogen-abstraction pathway leading from radical (iv) to (4) should likewise predominate over a coupling pathway which leads to higher molecular weight products. The mechanism outlined in Scheme 1 is somewhat speculative since the postulated free radical intermediates were not verified spectroscopically.

The most interesting phenomena associated with the addition reaction are the postulated 1,5-hydrogen shifts. Very little quenching of radical (ii) occurs. Instead a 1,5-hydrogen shift leads to the more stable radical (iii), which couples with another molecule of 3,3,3-trifluoropropene to give radical (iv). This less stable radical more readily abstracts hydrogen from THF to give addition product (3), or undergoes a 1,5-hydrogen shift to give radical (v). This latter rearrangement is unusual because of the geometric requirements of 1,5-hydrogen shifts. Hydrogen migration requires a linear transition state (C–H · · · C).[7] In an open-chained linear molecule the 1,5-hydrogen shift occurs more readily than 1,2-, 1,3-, or 1,4-shifts because of this constraint. Free-radical rearrangements *via* a 1,5-hydrogen shift are common,[8-11] particularly in telomerization reactions of ethylene with carboxylic acids and alcohols.[8] Rearrangement occurs to generate free radical intermediates at a carbon attached to a stabilizing substituent.

$$\cdot(CH_2CH_2)_2CHRX \xrightarrow{1,5\text{-H shift}} H(CH_2CH_2)_2\dot{C}RX$$

R = Alkyl group X = OH, CO_2R', CN

1,5-Hydrogen shifts from H–C–O–C–C–Ċ to Ċ–O–C–C–C–H have been noted less frequently. Muramatsu *et al.* isolated the 1 : 2 adduct (6) from the γ-radiation-induced reaction of diethyl ether with fluorotrichloroethylene, but tetrahydrofuran gave only the monoadduct (7) under the same conditions (Scheme 3). Dedek and Fikar made a similar observation with addition reactions of chlorotrifluoroethylene and diethyl ether and proposed that the diadducts were a result of an intramolecular 1,5-H shift.[1] Tetrahydrofuran does not commonly give a 2,5-bisadduct, probably because the 5-membered ring constrains the molecule in a conformation which makes 1,5-H shift *via* a linear transition state difficult.

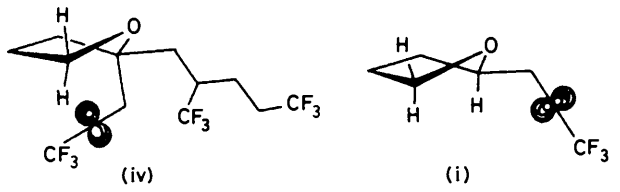


Figure 4. Predominant conformations for radicals (i) and (iv) (equatorial- and axial-type, respectively)

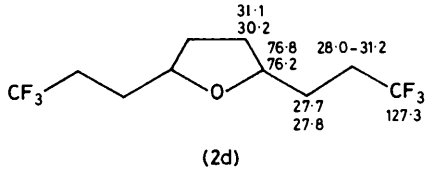
One exception recently noted in the literature is the reaction of the 2-tetrahydrofuranyl radical with butynedioic acid to give an open chain product which is postulated to have followed a pathway involving abstraction of hydrogen at C-5 by the intermediate radical (tetrahydrofuran-2-yl)-$\dot{C}(CO_2H)=\dot{C}CO_2H$.[12]

Our results are consistent with Muramatsu's, and Dedek and Fikar's. Intermediate radical (i) (Scheme 1) would exist predominantly in a conformation in which the side chain is in an equatorial-type location (Figure 4) and hence the radical would not rearrange. Consequently the diadducts (2c) and (2d) are not formed in significant amounts. Only when the concentration of (1) has built up sufficiently, do (2c) and (2d) appear as secondary reaction products formed *via* hydrogen-atom abstraction from C-5 on (1) (Scheme 2). However, the 1,5-H shift on rearrangement of radical (iv) to (v), which would also require hydrogen abstraction across the 5-membered ring, appears to be a reasonable pathway because the predominant conformation of (*iv*) must be one in which the $CH_2\dot{C}HCF_3$ side chain is in an axial-type position (Figure 4). The larger side chain should preferentially occupy a position in space that would force the $CH_2\dot{C}HCF_3$ group into closer proximity to the α-CH. After rearrangement, radical (v) couples with 3,3,3-trifluoropropene to give the less stable radical (vi) which abstracts a hydrogen atom from another THF molecule in preference to further oligomerization. Since, except in cases where a 1,5-hydrogen shift can occur to give a stable C–O–$\dot{C}$ radical, the $\dot{C}$–CF_3 preferentially abstracts hydrogen from the THF, (4) is a logical end product.

These results provide a significantly more complete picture of the complexities of free-radical oligomerization reactions on THF than suggested by related studies [1-4] where only 2-monosubstituted or 2,5-disubstituted adducts were obtained.

Experimental

3,3,3-Trifluoropropene, purchased from P.C.R. Research Chemicals, Inc., was homogeneous by g.c. and used without further purification. Tetrahydrofuran was dried and purified immediately prior to use by distillation over sodium metal. ^{1}H N.m.r. spectra were obtained on a Nicolet 360-MHz pulsed Fourier-Transform n.m.r. spectrometer using up to 32K points over a 20-KHz bandwidth. ^{13}C N.m.r. spectra were obtained on a Jeol Model PS 100-MHz Fourier-Transform n.m.r. spectrometer operating at 25.14 MHz and on a Joel FX60 60-MHz Fourier-Transform n.m.r. spectrometer operating at 15.03 MHz. Tetramethylsilane was used as the internal standard. High resolution electron-impact mass spectra were obtained on a modified Kratos/AEI MS90 mass spectrometer, operating at a dynamic resolution of $M/\Delta M$ 10 000. Low resolution mass spectra were obtained with a consolidated 12-110B mass spectrometer. Chemical ionization spectra were recorded on a Finigian 4000 using isobutane as reactant gas.



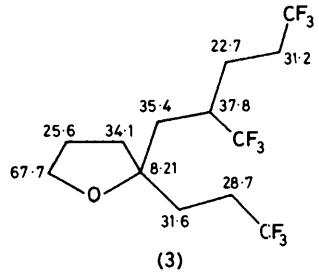


Figure 5. ^{13}C N.m.r. assignments (δ/p.p.m.) for compounds (2d) and (3)

G.l.c. analysis and preparative g.c. were performed with a Hewlett-Packard 5710A gas chromatograph and a 12-ft × ¼-in 10% SE-30 on Gas-Chrom Q column, at a flow rate of 40 ml He/min.

Reaction of THF with $CF_3CH=CH_2$.—3,3,3-Trifluoropropene (5.0 g) was taken up in 50 ml of dry THF (1.04M) and the mixture stirred at room temperature in a closed flask. 2-ml Samples were removed from the reaction mixture at t = 0, 2, 4, 8, and 16 h and every 8 h thereafter up to 112 h. The samples were inhibited by addition of a solution of 2,6-di-t-butyl-*p*-cresol (0.2 mg) in THF (2 μl), and stored in the dark at 5 °C until g.l.c. analysis. After 112 h, the THF was partially removed on a rotary evaporator and the products separated by g.c. 80-μl Samples were injected at a column temperature of 155 °C and the temperature allowed to increase after 12.5 min at a rate of 32 °C/min up to 300 °C.

The monoadduct (1) eluted at 2.91 min, (2a—d) at 7.11 min, (3) at 9.77 min, and (4) at 15.64 min. Products (1)—(4) were characterized by ^{1}H and ^{13}C n.m.r. and mass spectrometry. Additional reactions carried out at concentrations of $CH_2=CHCF_3$ in THF of 0.42, 0.31, 0.21, and 0.105M, gave qualitatively similar results.

Tetrahydro-2-(3,3,3-*trifluoropropyl*)*furan* (1), δ($CDCl_3$) 1.47 (m, 1 H), 1.71 (m, 2 H), 1.88 (m, 2 H), 1.99 (m, 1 H), 2.09 (m, 1 H), 2.26 (m, 1 H), 3.69 (m, 1 H), and 3.82 (m, 2 H); δ(^{13}C) ($CDCl_3$) 25.33 (s), 27.59 (q, J_{C-F} 3.0 Hz), 29.93 (q, J_{C-F} 28.2 Hz), 30.69 (s), 67.09 (s), 76.81 (s), and 126.26 p.p.m. (q, J_{C-F} 275.4 Hz) [Found: $(M-1)^+$, 167.0680. Calc. for $C_7H_{10}OF_3$: $(M-1)$ 167.0684]; Mass spectrum (low resolution) *m/e* (rel. intensity) 167 (2), 125 (26), 97 (16), 85 (22), 77 (16), 71 (100), 57 (16), and 55 (31); mass spectrum (C.I.) *m/e* (rel. intensity) 170 (39) ($M+2$), 169 (100), 167 (53), 152 (23), 151 (100), 150 (33), 149 (100), and 107 (100).

Tetrahydro-2-(5,5,5-*trifluoro*-2-*trifluoromethylpentyl*)*furan* (2a), *tetrahydro*-2,2-*bis*(3,3,3-*trifluoropropyl*)*furan* (2b), (±)-*tetrahydro*-2,5-*bis*(3,3,3-*trifluoropropyl*)*furan* (2d), and meso-*tetrahydro*-2,5-*bis*(3,3,3-*trifluoropropyl*)*furan* (2c); δ($CDCl_3$–CCl_4, 1 : 1) 1.5—2.3 (series of complex multiplets, 12 H) and 3.65—4.00 (m, 2 H); δ(^{13}C) [(CD_3)SO] (see Figure 5) 27.67 (br, s), 28.03, 28.58, 29.21, 29.97 (larger peaks of quartets), 30.24 (s), 31.09 (s), 76.20 (s), 76.78 (s), and 127.29 p.p.m. (q, J_{C-F} 276.3 Hz). Other peaks in the region 28.0—31.2 p.p.m. are unresolved because of the large number of signals in this region [Found: $(M-1)^+$, 263.0873. Calc. for $C_{10}H_{13}OF_6$:

(M − 1), 263.0870]; mass spectrum (low resolution) *m/e* (rel, intensity) 263 (3), 168 (6), 167 (77), 138 (27), 125 (47), 123 (10), 99 (13), 97 (17), 77 (28), 71 (30), 69 (17), 59 (20), 57 (10), 55 (100), 54 (11), and 47 (14); mass spectrum (C.I.) *m/e* (rel. intensity) 266 (3) (M + 2), 265 (34), 247 (18), 225 (23), 177 (22), 167 (39), 140 (23), 139 (100), 119 (22), 117 (32), and 100 (43).

Tetrahydro-2-(3,3,3-trifluoropropyl)-2-(5,5,5-trifluoro-2-trifluoromethylpentyl)furan (3), δ($CDCl_3$) 1.45—2.30 (series of complex multiplets, 15 H) and 3.81 (symmetrical multiplet, 2 H); δ(^{13}C) ($CDCl_3$) (see Figure 5 for assignments) 22.58 (quart, J_{C-F} 2.9 Hz), 25.60 (s), 28.72 (q, J_{C-F} 29.4 Hz) 31.16 (q, J_{C-F} 30.3 Hz), 31.64 (br s), 34.11 (s), 35.35 (br s), 37.81 (q, J_{C-F} 25.4 Hz), 67.70 (s), 82.13 (s), 126.80 (q, J_{C-F} 276.3 Hz) 127.25 (q, J_{C-F} 276.4 Hz), and 128.22 p.p.m. (q, J_{C-F} = 280.2 Hz) [Found: $(M - 1)^+$, 359.1061. Calc. for $C_{13}H_{16}OF_9$: (M − 1) 359.1057]; mass spectrum (low resolution) *m/e* (rel. intensity) 359 (1), 273 (11), 264 (22), 263 (74), 221 (57), 173 (56), 167 (75), 153 (29), 125 (77), 109 (24), 97 (51), 77 (57), 69 (23), 59 (25), and 55 (46); (C.I.) *m/e* (rel. intensity) 362 (M + 2) (6), 361 (17), 344 (27), 343 (100), 341 (39), 321 (35), 273 (35), and 167 (52).

Tetrahydro-2,5-bis(3,3,3-trifluoropropyl)-2-(5,5,5-trifluoro-2-trifluoromethylpentyl)furan (4), δ($CDCl_3$) 1.50—2.30 (series of complex multiplets, 19 H) and 3.92 (m, 1 H); δ(^{13}C) ($CDCl_3$) 22.80 (br s), 28.1—38.7 (series of overlapping s and quart), 78.89 (s), 82.65 (s), 127.09 (overlapping quart, J_{C-F} 273.44 Hz), and 128.13 p.p.m. (q, J_{C-F} 279.3 Hz) [Found: $(M - 1)^+$, 455.1248. Calc. for $C_{16}H_{19}OF_{12}$: (M − 1) 455.1244]; mass spectrum (low resolution) *m/e* (rel. intensity) 455 (2), 360 (25), 359 (75), 264 (20), 263 (75), 221 (81), 173 (59), 153 (29), 152 (26), 151 (29), 138 (70), 137 (25), 125 (94), 123 (41), 109 (25), 103 (33), 97 (60), 95 (20), 77 (73), 73 (37), 69 (30), 69 (21), 59 (62), 57 (21), 56 (22), 55 (100), 54 (26), 51 (24), and 47 (23); mass spectrum (C.I.) *m/e* (rel. intensity) 439 (M − 17) (11), 185 (13), 183 (13), 167 (100), 127 (35), and 125 (21).

Acknowledgements

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