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HETEROCYCLIC POLYFLUORO-COMPOUNDS. PART 35 [1] DEHYDROFLUORINATION OF 2,2-BIS(TRIFLUOROMETHYL)- AND 2-PERFLUOROALKYL-3,4-DIFLUORO-OXETANS

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SUMMARY

Solid potassium hydroxide dehydrofluorinates 2,2-bis-(trifluoromethyl)-3,4-difluoro-oxetan to 3-fluoro-4,4-bis-(trifluoromethyl)-2-oxete (59%), 2-pentafluoroethyl-3,4-difluoro-oxetan to 2-tetrafluoroethylidene-3,4-difluoro-oxetan, and r-2-heptafluoro-n-propyl-t-3,t-4-difluoro-oxetan to (Z)-2-hexafluoro-n-propylidene-cis-3,4-difluoro-oxetan. Factors which affect these reactions are discussed.

INTRODUCTION AND RESULTS

Dehydrofluorination of polyfluoro-compounds is frequently rather difficult, requiring strong base under vigorous conditions, is largely governed by the relative acidities of the various protons that can be removed, and usually follows an E1cb type mechanism [2]. It is, however, synthetically useful and has been used extensively to prepare olefinic and aromatic fluoro-compounds.

The availability of 2,2-bis(trifluoromethyl)- and 2-perfluoroalkyl-3,4-difluoro-oxetans by the photochemical addition of hexafluoroacetone [3] and perfluoroaldehydes [3], respectively, to 1,2-difluoroethylene, prompted a study of

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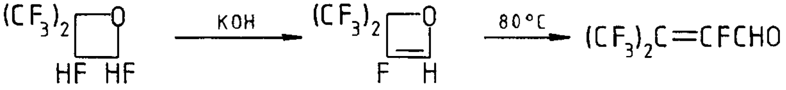
their dehydrofluorination. Here there is a balance of competing factors, the effect of the ring oxygen, of perfluoroalkyl versus a fluorine substituent, and of product stability, so far as the mode of elimination is concerned.

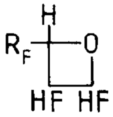
Treatment of 2,2-bis(trifluoromethyl)-3,4-difluoro-oxetan (1) with powdered potassium hydroxide yielded 3-fluoro-4,4-bis(trifluoromethyl)-2-oxete (2), (59%), which readily underwent ring opening at 80 °C:



(1) (2)

In the recovered oxetan, there was some enrichment of the relative amount of the cis-isomer, but it is difficult to attach significance to this, since much material was destroyed in the reaction.

Similar treatment of the trifluoromethyl-substituted oxetan (3, R_F=CF_3), as a mixture of three isomers, led to the destruction of the oxetan, and the formation of trifluoromethane,



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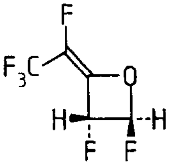

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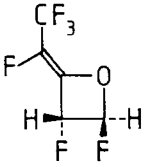
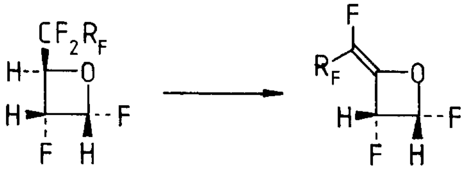


(5)

but no heterocyclic product was obtained. In contrast, the pentafluoroethyl-substituted oxetan (3, R_F=C_2F_5), as a mixture of two trans-3,4-difluoro-isomers and one cis-isomer, yielded some pentafluoroethane and a mixture of (Z)- and (E)-2-tetrafluoroethylidene-trans-3,4-difluoro-oxetan (4) and (5), in the ratio 92:8. There was some enhancement of the proportion of trans-isomers in the recovered oxetans, but no product was detected which possessed cis-fluorines. However, when the pure cis-oxetan (6) was similarly treated, the (Z)-ethylidene-



(6) (7)

substituted oxetan (7, R_F=CF_3) was obtained. Analogous to this, the perfluoro-n-propyl-substituted oxetan (6, R_F=C_2F_5) gave some 1H-perfluoropropane and the propylidene-oxetan (7, R_F=C_2F_5).

The structure of the oxete (2) rests upon its spectroscopic properties, and its isomerisation to an aldehyde, rather than the acid fluoride, $(CF_3)_2C{=}CHCOF$, which would have been obtained from the 2-fluoro-isomer. The cis- and trans-isomers of 3,4-difluoro-oxetans such as (1) and (3) are readily distinguished on the basis of the n.m.r. parameters of the CHFCHF fragment [3,4]. For ^{19}F chemical shifts, the cis-isomers show ranges of -54.2 to -56.9 (CHFO) and -123.9 to -133.7 p.p.m. (CHFC) and the trans-isomers -37.4 to -42.9 (CHFO) and -117.3 to -126.1 p.p.m. (CHFC). For the H,H-coupling constants, $|{}^3J_{cis}|$ = 3-4 Hz and $|{}^3J_{trans}|$ = 1.5-2.5 Hz, and for the H,F-coupling constants $|{}^3J_{cis}|$ = 6-8 Hz for the CCFCHO grouping and 10-12 Hz for the OCFCHC grouping, and $|{}^3J_{trans}|$ = 3-4 Hz for the CCFCHO grouping and 6.5-11 Hz for the OCFCHC grouping. For the trans-isomers (4) and (5), the fluorine chemical shifts are close to the expected ranges, with the CHF group adjacent to the double bond, not unexpectedly, a little to low field of its saturated counterparts. The major isomer (4) shows the expected trans-H,H-coupling, and for the cis-H,F-coupling constants, that for the CCFCHO grouping is as expected, but that for OCFCHC is rather smaller than expected. The partial data obtained for the minor isomer clearly support its trans-assignment. For the cis-oxetans (7), the CHFO chemical shifts are as expected, and again the CHF absorptions adjacent to the double bond are a little to low field of their saturated counterparts. The H,H-coupling constants, and H,F-couplings for the CCFCHC grouping are as expected, but for oxetan (7, $R_F=C_2F_5$), again it is lower for the OCFCHC grouping. Spectral intensity was poor for the very limited quantity available of the ethylidene-substituted oxetan (7, $R_F=CF_3$), and no figure was obtained for this, but the many similarities shown leave no doubt that it is the *cis*-isomer. The (*Z*)-configuration assigned to oxetans (4) and (7) rests upon the observation of substantial long-range couplings involving the CF_3 and C_2F_5 groups and the nearby CHF group [4]. Oxetan (4) shows five-bond coupling constants of 7 and 1.5 Hz to the fluorine and proton of the nearby CHF group, and a similar ^5J (F,F) is seen in oxetan (7, $R_F=CF_3$). In the oxetan (7, $R_F=C_2F_5$) the corresponding coupling constants involving the CF_2 group have magnitudes of 10 and 3 Hz, and there is a ^6J (F,F) involving the CF_3 group of 2 Hz.

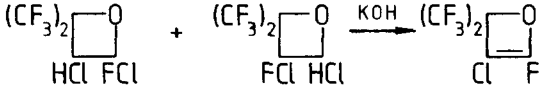
Unlike their saturated counterparts, the compounds (2), (4), and (7) all showed molecular ions of appreciable intensity in their mass spectra.

In oxetan (1), the acidity of the hydrogen next to the ring oxygen is affected by two competing factors, the σ-inductive effect (-*I*) of the electronegative oxygen, counter-balanced by lone-pair repulsion effects ($+I_\pi$). In these essentially planar, rigid structures, the $+I_\pi$ effect should be at a maximum [5], and as a consequence it is the other hydrogen which is removed. This is not apparently so for acyclic ethers [6], *e.g.*,

$$(CHF_2CHF)_2O \xrightarrow[200\text{-}220\,^\circ C]{KOH} CHF{=}CFOCHFCHF_2 + (CHF{=}CF)_2O$$

where the $+I_\pi$ effect of the oxygen can be minimised by appropriate bond rotations, and now the -*I* effect dominates.

A further illustration of this is provided by the dehydrochlorination of a mixture of the oxetans (8) and (9), where only the former reacts to give an oxete [1]:



(8) (9)

In the oxetans (3) and (6), the perfluoroalkyl group will cause a substantial increase in the acidity of the adjacent hydrogen compared with fluorine [7], and this more than outweighs the $+\underline{I}_{\pi}$ effect of the oxygen. Here, however, a further factor enters, in that there is formed an _exo_-methylene double bond, rather than one in the ring. Presumably, factors of product stability dominate here, and the less strained species with an external double bond is formed, despite the need to lose a fluorine from a CF_2 group rather than a CHF group.

EXPERIMENTAL

Techniques similar to those described earlier were employed [3]. The oxetans were prepared by the photochemical addition of hexafluoroacetone [3], or the appropriate perfluoroaldehyde [3] to 1,2-difluoroethylene.

Dehydrofluorination Reactions of Polyfluoro-oxetans using Potassium Hydroxide

(a) Of 2,2-bis(trifluoromethyl)-3,4-difluoro-oxetan

A 1:1 mixture of _cis_- and _trans_-isomers of the oxetan (3.00 g, 13.00 mmol) was added in two portions to finely powdered potassium hydroxide (7.40 g, 130.0 mmol), contained in a Pyrex flask (25 cm^3) fitted with a water condenser and dropping funnel. The mixture was refluxed with vigorous stirring for 8 h, and volatile product, identified as trifluoromethane (1 mg, 0.02 mmol, 0.3%) by i.r. spectroscopy, was condensed in a trap cooled to -196 °C, attached *via* a tap to the condenser. The liquid fraction which remained in the flask was then removed *in vacuo*, dried (molecular sieve type 3A), and shown by g.l.c. (4m Kel-F No 10 oil on Celite at 66 °C) to comprise unreacted *trans*- (0.727g, 3.16 mmol) and *cis*-2,2-bis(trifluoromethyl)-3,4-difluoro-oxetan (0.902g, 3.92 mmol), and 3-fluoro-4,4-bis(trifluoromethyl)-2-oxete (nc) (0.740g, 3.50 mmol, 59% yield band upon oxetan consumed).

A sample of the oxete (Found: *M*, 209.9921. C_5HF_7O requires *M*, 209.9916) was separated by g.l.c., and identified by i.r., with $\nu_{max.}$ 3160 m (C-H str.) and 1714 vs cm^{-1} (C=C str.), and n.m.r. spectroscopy, with δ_F (positive values to low field of external CF_3CO_2H) 0.6 (CF_3) and -59.1 p.p.m. (CF, ^3J (H,F) = 8.0 Hz) and δ_H (internal $SiMe_4$) 5.98 p.p.m., by mass spectrometry, with *m/e* ($\geqslant$ 10%) 210 (*M*, 21.2), 163 (C_4HF_6, 42.6), 162 (C_4F_6, 59.4), 113 (C_3HF_4, 16.2), 112 (C_3F_4, 19.1), 93 (C_3F_3, 74.4) 75 (C_3HF_2, 20.0), 71 (C_3FO, 27.7), 69 (CF_3, 100.0), 51 (CHF_2, 38.0), 44 (C_2HF, 19.9), 43 (C_2F, 32.6), 41 (C_2HO, 19.6), 40 (C_2O, 22.0) and 31 (CF, 23.3%), and by its ready and complete isomerisation at 80 °C during 45 min to 2,4,4,4-tetrafluoro-3-trifluoromethylbut-2-en-1-al. This aldehyde was identified by i.r., with $\nu_{max.}$ 1665 s (C=C str.) and 1730 s cm^{-1} (C=O str.), and n.m.r. spectroscopy, with δ_F 20.8 [CF_3 *cis* to C=O, *J* (CF_3,CF_3) = *J* (CF_3,F) = 9 Hz], 16.2 [CF_3 *trans* to C=O, *J* (CF_3,F) = 26 Hz], and -28.2 p.p.m. [CF, *J* (H,F) = 14 Hz], and δ_H 9.44 p.p.m. (CH=C), and mass spectrometry, with *m/e* 210 (*M*, 4.1) and (>10%) 163 (C_4HF_6, 14.4), 162 (C_4F_6, 24.2), 93 (C_3F_3, 19.0), 81 (C_2F_3, 13.3), 69 (CF_3, 32.5), 44 (C_2HF, 100.0), 40 (C_2O, 38.3), and 29 (CHO, 36.5%).

(b) Of 2-trifluoromethyl-3,4-difluoro-oxetan

A 1.0:1.1:1.4 mixture of the isomeric oxetans, *r*-2-trifluoromethyl-*t*-3,*c*-4-, *t*-3,*t*-4-, and *c*-3,t-4-difluoro-oxetan, (9.00 g, 55.5 mmol) was added to finely powdered potassium hydroxide (6.72 g, 120.0 mmol), as above, and the mixture was refluxed for 4.5 h. Trifluoromethane (2.10 g, 30.0 mmol) was collected in the cold trap, and the remaining liquid was shown by g.l.c. (2 m tritolyl phosphate on Celite at 27 °C) to comprise the above oxetans (3.70 g, 22.80 mmol), together with a trace (10 mg) of unidentified material.

(c) Of 2-pentafluoroethyl-3,4-difluoro-oxetan

A 1.0:1.9:2.7 mixture of the isomeric oxetans, *r*-2-pentafluoroethyl-*t*-3,*c*-4-, *t*-3,*t*-4-, and *c*-3,t-4-difluoro-oxetan, (16.24 g, 76.6 mmol) was added to potassium hydroxide (7.50 g, 134.0 mmol) in four portions as above, and the mixture refluxed for 8 h. Pentafluoroethane (0.45 g, 3.8 mmol) collected in the cold trap, and the liquid fraction which remained was removed *in vacuo*, dried, and separated by g.l.c. (3.5 m trixylyl phosphate on Celite at 37 °C) to give the recovered oxetans, as above (12.26 g, 57.8 mmol), in the ratio 1.0:1.1:2.9, and 2-tetrafluoroethylidene-*trans*-3,4-difluoro-oxetan (nc) (2.02 g, 10.5 mmol, 56% yield based upon oxetans consumed) (Found: C, 30.7; H, 1.2; F, 59.3. $C_5H_2F_6O$ requires C, 31.2; H, 1.0; F, 59.4%), as a 92:8 mixture of (*Z*)- and (*E*)- isomers, together with a number of minor components (*ca*. 0.60 g), which were examined by g.l.c. coupled i.r. spectroscopy, but only 3,3,3-trifluoropropyne (0.11 g, 1.2 mmol, 6%) was identified.

The ethylidene oxetan was identified by i.r., with $\nu_{max.}$ 1772 s cm^{-1} (C=C str.), and n.m.r. spectroscopy, with the (*Z*)-isomer showing δ_F 5.6 [CF_3, ^3J (F,F) = 16.0, ^5J (F,F) = 7.0, ^5J (H,F) = 1.5 Hz], -44.9 [CHFO, ^2J (H,F) = 62, ^3J (H,F) = ^3J (F,F) = 7 Hz], -90.3 (=CF), and -111.5 p.p.m. [CHFC, ^2J (H,F) = 52; ^3J (H,F) = 7 Hz] and δ_H 5.80 [CHFC, ^3J (H,H) = 1.5 Hz] and 5.22 p.p.m. (CHFC), and the (*E*)-isomer showing δ_F 6.7 [CF_3, ^3J (F,F) = 13.2 Hz], -44.5 (CHFO, ^2J (H,F) = 62.4, ^3J (H,F) = ^3J (F,F) = 7 Hz], -90.0 (=CF), and -111.5 p.p.m. [CHFC, ^2J (H,F) = 52.5 Hz] and δ_H 5.54 (CHFO) and 4.94 p.p.m. (CHFC), and mass spectrometry, with *m/e* 192 (*M*, 7.1) and (>10%) 128 (C_3F_4O, 15.4), 109 (C_3F_3O, 74.1), 100 (C_2F_4, 10.1), 75 (C_3HF_2, 59.9), 73 (C_3H_2FO, 26.3), 69 (CF_3, 48.1), 64 ($C_2H_2F_2$, 25.1), 59 (C_2FO, 100.0), 45 (C_2H_2F, 12.2), 32 (CHF, 51.2), and 31 (CF, 39.6%).

(d) Of r-2-pentafluoroethyl-t-3,t-4-difluoro-oxetan

The oxetan (0.878 g, 4.14 mmol) and potassium hydroxide (0.347 g, 6.20 mmol), sealed in a Pyrex ampoule (30 cm^3) *in vacuo* and shaken at 60 °C for 12 h, gave after fractionation by trap-to-trap distillation *in vacuo*, pentafluoroethane (22 mg, 0.18 mmol), and a mixture (by g.l.c.) of the recovered oxetan (0.649 g, 3.06 mmol, 74% recovery) and (*Z*)-2-tetrafluoroethylidene-*cis*-3,4-difluoro-oxetan (0.104 g, 0.54 mmol, 50% yield based upon oxetan consumed), which was identified by n.m.r. spectroscopy with δ_F 5.4 [CF_3, ^3J (F,F) = 14.2, ^5J (F,F) = 6.0 Hz], -58.6 [CHFO, ^2J (H,F) = 63.5 Hz], -90.4 (=CF), and -121.8 p.p.m. [CHFC, ^2J (H,F) = 52.2 Hz] and δ_H 5.85 [CHFO, ^3J (H,F) = ^3J (H,H) = 3.0 Hz] and 5.40 p.p.m. (CHFC).

(e) Of r-2-heptafluoro-n-propyl-t-3,t-4-difluoro-oxetan

The oxetan (0.915 g, 3.49 mmol) and potassium hydroxide (0.527 g, 9.58 mmol), sealed in a Pyrex ampoule (50 cm^3) *in vacuo* and shaken at 80 °C for 24 h, gave after fractionation by trap-to-trap distillation *in vacuo*, 1*H*-perfluoropropane (0.173 g, 1.02 mmol) which condensed at -130 °C, and a liquid fraction (0.552 g) which was separated by g.l.c. (4 m Kel-F No 10 oil on Celite at 65 °C) to give recovered oxetan (0.228 g, 0.87 mmol, 25%) and (*Z*)-2-hexafluoro-n-propylidene-*cis*-3,4-difluoro-oxetan (nc) (0.210 g, 0.87 mmol, 33% yield based upon oxetan consumed) (Found: C, 29.5; H, 0.8; F, 62.7. $C_6H_2F_8O$ requires C, 29.7; H, 0.8; F, 62.8%), b.p. (Siwoloboff) 101.5 °C at 760 mmHg, together with unidentified material comprising at least five components.

The propylidene-oxetan showed $\nu_{max.}$ 1767 s cm^{-1} (C=C str.), δ_F -8.6 [CF_3, ^4J (F,F) = 6.5, ^6J (F,F) = 2.0; ^3J (F,F) = 2.5 Hz], -45.9 [CF_2, ^3J (F,F) = 18, ^5J (F,F) = 10, ^6J (F,F) = 1, ^5J (H,F) = 3 Hz], -58.3 [CHFO, ^2J (H,F) 64, ^3J (F,F) = 13, ^3J (H,F) = 6, ^5J (F,F) = 3], -87.7 [=CF, ^4J (H,F) = 3 Hz], and

-120.8 p.p.m. CHFC, ^2J (H,F) = 53 Hz , and δ_H 5.84 [CHFO, ^3J (H,H) = ^3J (H,F) = 3 Hz] and 5.40 p.p.m. (CHFC), and *m/e* 242 (*M*, 6.7) and (>10%) 178 (C_4F_6O, 10.2), 159 (C_4F_5O, 24.5), 144 (C_4HF_5, 27.6), 125 (C_4HF_4, 34.8), 109 (C_3F_3O, 100.0), 100 (C_2F_4, 12.7), 75 (C_3HF_2, 61.6), 73 (C_3H_2FO, 22.2), 69 (CF_3, 45.0), 64 ($C_2H_2F_2$, 28.3), 45 (C_2H_2F, 11.4), 32 (CHF, 49.4), 31 (CF, 43.0), and 29 (CHO, 14.8%).

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