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Reaction of sulphur tetrafluoride with *trans*-4,5-dibromo-*cis*-1,2-cyclohexanedicarboxylic anhydride. A route to 7,7,9,9-tetrafluoro-8-oxa-cis-bicyclo[4.3.0]non-3-ene

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Abstract

Treatment of *trans*-4,5-dibromo-*cis*-1,2-cyclohexanedicarboxylic anhydride (**2**) with SF_4 and HF resulted in fluorination of the carbonyl groups and the almost total replacement of one bromine atom by fluorine affording 3-bromo-4,7,7,9,9-pentafluoro-8-oxa-*cis*-bicyclo[4.3.0]nonane (**3**) and 1-bromo-2-fluoro-*cis*-4,5-bis(trifluoromethyl)cyclohexane (**4**) in a 5:1 ratio with only trace amounts of 1,2-dibromo-*cis*-4,5-bis-(trifluoromethyl)cyclohexane (**5**). Dehalogenation of this mixture with zinc gave a mixture of 7,7,9,9-tetrafluoro-8-oxa-*cis*-bicyclo[4.3.0]non-3-ene (**6**) and *cis*-4,5-bis(trifluoro-methyl)cyclohex-1-ene (**7**). Pure **6** was isolated by bromination and subsequent separation of the dibromo derivatives by crystallization and debromination. The structure of isomer **3a** was confirmed by X-ray analysis.

Keywords: 4,5-Dibromo-*cis*-1,2-cyclohexanedicarboxylic anhydride; Fluorination; Sulphur tetrafluoride; Bromine–fluorine exchange; Bicyclic tetrafluoroethers; 7,7,9,9-Tetrafluoro-8-oxa-*cis*-bicyclo[4.3.0]non-3-ene preparation

1. Introduction

It is well established that treatment of 1,2-dicarboxylic acids, both aliphatic [1] and aromatic [2], or their anhydrides, with sulphur tetrafluoride results in considerable or predominant formation of cyclic tetrafluoroethers with correspondingly limited yields of bis(trifluoromethyl) derivatives. The cyclization is particularly favoured when the carboxylic groups are fixed in the *cis*-configuration. Thus, *cis*-1,2-cyclohexanedicarboxylic acid afforded a 70% yield of 7,7,9,9-tetrafluoro-8-oxa-*cis*-bicyclo[4.3.0]nonane, practically as the only product [1], and a 40% yield of 7,7,9,9-tetrafluoro-8-oxa-bicyclo[4.3.0]non-1(6)-ene was recently achieved from 3,4,5,6-tetrahydrophthalic anhydride [3].

The aim of the present work was the preparation of 7,7,9,9-tetrafluoro-8-oxa-*cis*-bicyclo[4.3.0]non-3-ene (**6**) required for further studies. The most straightforward route seemed to be the fluorination of *cis*-1,2,3,6-tetrahydrophthalic anhydride (**1**) with sulphur tetrafluoride, but a complex mixture of products was formed. As an alternative method, anhydride **1** was brominated to *trans*-4,5-dibromo-*cis*-1,2-cyclohexanedicarboxylic anhydride (**2**) which was successfully converted to the required compound **6** by a fluorination–dehalogenation process.

2. Results and discussion

The reaction of dibromoanhydride **2** with sulphur tetrafluoride and anhydrous hydrogen fluoride proceeded in an unexpected manner [1]; besides fluorination of the carbonyl groups, almost total replacement of one bromine atom by fluorine occurred to give the isomeric bromo-pentafluoro-8-oxa-*cis*-bicyclo[4.3.0]nonanes **3** as the main product together with the bromo-fluoro-*cis*-4,5-bis(trifluoromethyl)cyclohexanes **4** and a small amount of 1,2-dibromo-*cis*-4,5-bis(trifluoromethyl)cyclohexane (**5**) (see Scheme 1).

The bromine–fluorine exchange occurred regardless of the HF concentration; hence, it appeared that the latter is

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[1] Bromine atoms in anhydride **2**, as in other compounds formed by the addition of bromine to a cyclohexene ring, are undoubtedly *trans*-diequatorial [4].

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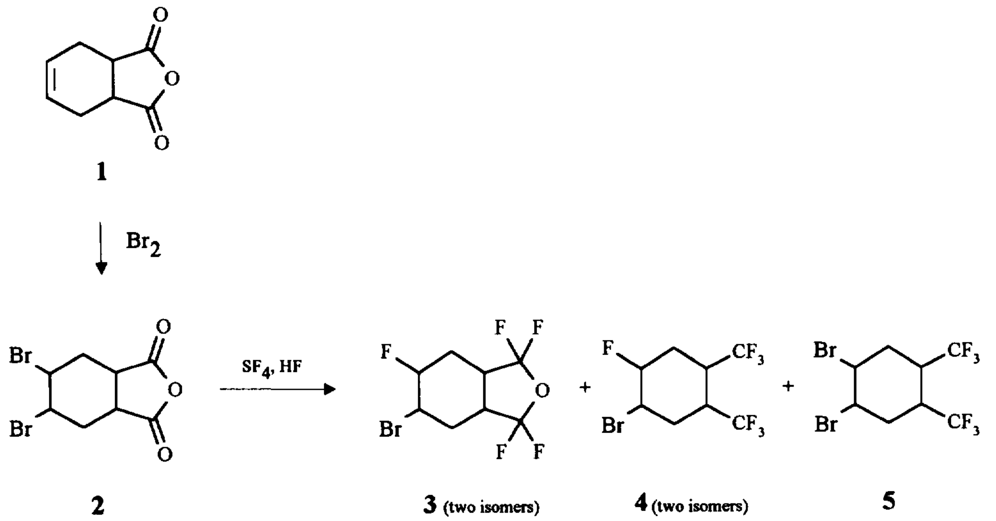


	3 (two isomers)	4 (two isomers)	5
HF : 2 = 3; 60°C ; 48 h	67%	7.5%	1.5%
HF : 2 = 0.5; 80°C ; 96 h	66%	13%	trace

Scheme 1.

regenerated by an SF_4 oxidation of the evolved HBr. The following reaction scheme may be considered:

$$RBr + HF \longrightarrow R\text{–}F + HBr$$

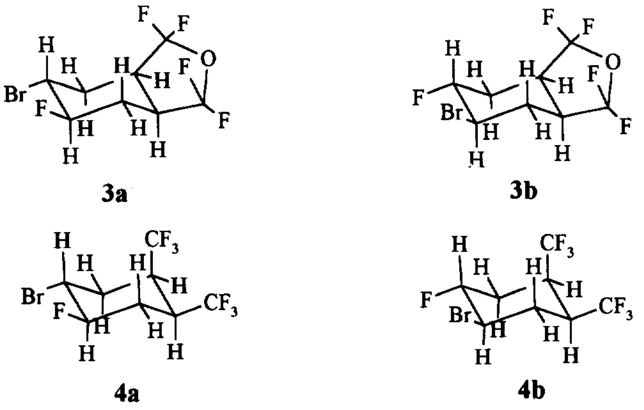
$$HBr + SF_4 \longrightarrow HF + SBr_4$$

$$SBr_4 \longrightarrow SBr_2 + Br_2$$

The formation of considerable amounts of elemental bromine was indeed observed in each experiment. Thus the bromine–fluorine exchange is caused by SF_4, with HF acting as a catalyst.

The fact that only one bromine is replaced can be interpreted in terms of anchimeric group assistance exerted by the second neighbouring bromine atom. Participation of the bromonium ions is confirmed by the almost total retention of the configuration and by the formation of equimolar amounts of regioisomers. Both compounds **3** and **4** were 1:1 mixtures of isomers **3a,b** and **4a,b** which derived from nucleophilic attack of the fluoride ion on either carbon atom C-3 or C-4 (Fig. 1). The structure of **3a** has been fully confirmed by an X-ray analysis (Tables 1 and 2, Fig. 2) and the structure of **3b** is the only rational alternative. Trace amounts of four other isomers of **3**, probably with inverted configuration at carbon atoms C-3 or C-4, were also detected by GC–MS. Structures **4a** and **4b**, although not proved, seem to be the most probable.

Compounds **3** and **4** readily undergo dehalogenation when treated with zinc dust in acetic anhydride. Dehalogenation of isolated pure **3a** gave the required alkene **6** almost quantitatively. For preparative purposes, however, the more efficient way is the dehalogenation of the crude mixture of compounds **3**–**5**. Bromination of the mixture of alkenes **6** and **7** thus obtained gave a mixture of dibromo derivatives **8** and **5**, from which bicyclic compound **8** was effectively separated by



3a **3b**

4a **4b**

Fig. 1. The structures of compounds 3 and 4.

Table 1

Atomic coordinates (×10^4) and equivalent isotropic displacement parameters (Å^2×10^3) for compound **3a**

Atom	x	y	z	U_{eq}[a]
Br	5427.1(2)	7691.1(3)	4685.2(2)	31.9(1)
O	8372.9(15)	1543(2)	2955(2)	44.0(5)
F1	7732.8(11)	7551(2)	5660.7(14)	44.1(4)
F2	9867.0(12)	2937(2)	3404(2)	55.5(5)
F3	9299.3(13)	2875(2)	1488(2)	55.5(5)
F4	6758.4(13)	869(2)	2315(2)	49.9(4)
F5	7034.6(12)	1864(2)	4185.7(13)	37.1(4)
C1	7258(2)	4051(3)	2524(2)	23.6(5)
C2	6351(2)	5210(3)	2981(2)	23.4(5)
C3	6538(2)	5944(3)	4308(2)	20.3(5)
C4	7588(2)	6874(3)	4434(2)	26.1(5)
C5	8454(2)	5513(3)	4210(2)	25.9(5)
C6	8356(2)	4792(3)	2864(2)	25.3(5)
C7	8986(2)	3054(4)	2684(2)	37.7(6)
C8	7334(2)	2086(3)	2997(2)	32.1(6)

[a] U_{eq} is defined as one-third of the trace of the orthogonalized U_{ij} tensor.

Table 2
Bond lengths (Å) and angles (°) for compound **3a**

Br–C3	1.958(2)	O–C7	1.384(3)
O–C8	1.390(3)	F1–C4	1.405(3)
F2–C7	1.346(3)	F3–C7	1.358(3)
F4–C8	1.347(3)	F5–C8	1.348(3)
C1–C8	1.513(3)	C1–C2	1.527(3)
C1–C6	1.538(3)	C2–C3	1.525(3)
C3–C4	1.507(3)	C4–C5	1.510(3)
C5–C6	1.530(3)	C6–C7	1.513(3)
C7–O–C8	109.5(2)	C8–C1–C2	116.9(2)
C8–C1–C6	101.7(2)	C2–C1–C6	115.6(2)
C3–C2–C1	113.1(2)	C4–C3–C2	110.5(2)
C4–C3–Br	110.23(14)	C2–C3–Br	109.00(14)
F1–C4–C3	109.1(2)	F1–C4–C5	107.6(2)
C3–C4–C5	110.6(2)	C4–C5–C6	109.6(2)
C7–C6–C5	112.2(2)	C7–C6–C1	99.6(2)
C5–C6–C1	112.7(2)	F2–C7–F3	105.2(2)
F2–C7–O	107.5(2)	F3–C7–O	108.0(2)
F2–C7–C6	114.9(2)	F3–C7–C6	112.1(2)
O–C7–C6	108.8(2)	F4–C8–F5	105.2(2)
F4–C8–O	107.7(2)	F5–C8–O	107.5(2)
F4–C8–C1	114.1(2)	F5–C8–C1	114.2(2)
O–C8–C1	107.9(2)		

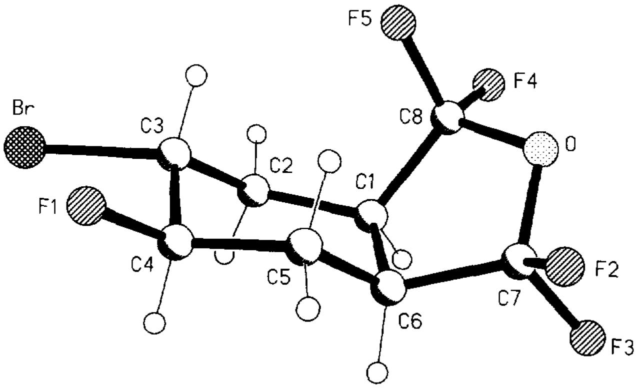
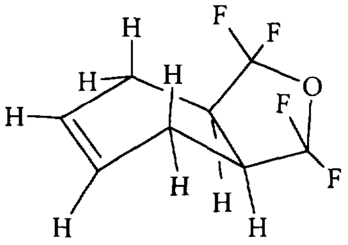


Fig. 2. X-Ray molecular structure of compound **3a** with crystallographic numbering.

crystallization and then debrominated to alkene **6** (see Scheme 2).

Detailed NMR studies using lanthanide-induced shift techniques revealed that *cis*-8-oxabicyclo[4.3.0]non-3-ene and some of its derivatives, i.e. non-fluorinated analogues of **6**, exist exclusively or almost exclusively in the 'open' conformation [5]. This is in agreement with the X-ray structure of the nitrogen analogue, the methionide salt of *cis*-8-methyl-8-azabicyclo[4.3.0]non-3-ene [6]. The close structural analogy of alkene **6** to the above-mentioned compounds, particularly to *cis*-7,7,9,9-tetramethyl-8-oxabicyclo[4.3.0]non-3-ene [5], strongly suggests that **6** also exist exclusively in the 'open' conformation as shown in Fig. 3.



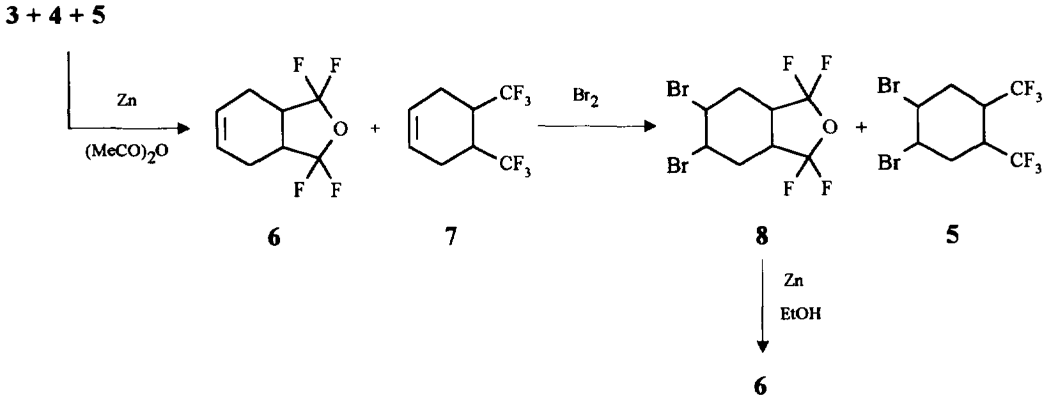
6

Fig. 3. The structure of compound **6**.

3. Experimental details

Melting points were determined in capillaries and boiling points were measured during distillation; both are uncorrected. ^1H spectra were recorded in $CDCl_3$ with a Varian 200 MHz or with a Bruker 500 MHz spectrometer, as indicated. ^{19}F and ^{13}C spectra were obtained with a Varian 200 MHz spectrometer at 188 and 50 MHz, respectively. Chemical shifts are quoted in ppm from internal TMS for protons and carbon nuclei (positive downfield) and from internal $CFCl_3$ for the fluorine nucleus (positive upfield). GC–MS analyses were performed with a Hewlett-Packard 5890 apparatus (70 eV) using a 30 m capillary column coated with a HP5 oil. For preparative GLC isolations, a GCHF-18.3 apparatus (Germany) equipped with a 4.0 m × 10 mm column filled with 5% silica oil SE-52 on Chromosorb G was used.

1,2,3,6-Tetrahydrophthalic anhydride (**1**) was a commercial reagent grade product (Riedel-deHaën) and *trans*-4,5-dibromo-*cis*-1,2-cyclohexanedicarboxylic anhydride (**2**)



Scheme 2.

was prepared by bromination of anhydride **1** according to the modified literature procedure (m.p. 138 °C) [7,8].

3.1. X-Ray structure determination of compound 3a

Crystal data: $C_8H_8BrF_5O$, M = 295.05, monoclinic, space group $P2_1/c$; $a = 12.8133(14)$, $b = 7.2481(6)$, $c = 10.6771(14)$ Å, $\beta = 91.996(10)°$; $V = 991.0$ Å^3; $Z = 4$, $D_x = 1.978$ mg/m^3; λ(Mo Kα) = 0.71073 Å; $\mu = 4.2$ mm^{-1}; $T = -100$ °C. Data collection and reduction: a colourless tablet 0.4 × 0.3 × 0.15 mm was mounted in an inert oil. Data were collected to $2\theta_{max} = 55°$ on a Siemens P4 diffractometer. An absorption correction based on ψ-scans gave transmission factors of 0.55–0.99. Of 4083 measured data, 2271 were unique ($R_{int} = 0.024$). Structure solution and refinement: the structure was solved by direct methods and refined anisotropically on F^2 (program SHELXL-93, G.E. Sheldrick, University of Göttingen). Hydrogen atoms were included with a riding model. The final $wR(F^2)$ was 0.056 for all 2271 unique reflections and 136 parameters, conventional $R(F) = 0.027$; $S = 0.89$; max. $\Delta/\sigma < 0.001$; max. $\Delta\rho = 0.31$ e Å^{-3}. Final atomic coordinates are presented in Table 1 with derived bond lengths and angles in Table 2 [2].

3.2. Reaction of trans-4,5-dibromo-cis-1,2-cyclohexanedicarboxylic anhydride (2) with sulphur tetrafluoride

Run 1

Anhydride **2** (45 g, 0.15 mol) and liquid hydrogen fluoride (10 ml, 0.5 mol) were placed in a 250 ml stainless-steel autoclave pre-cooled to ca. −30 °C and then, after cooling the autoclave to ca. −78 °C (acetone/Dry Ice bath), SF_4 (66 g, 0.55 mol) was condensed into it. The reaction was conducted at 180 °C for 48 h, the gases (SOF_2, SF_4, HF) were released (after cooling to ambient temperature) and the contents of the autoclave dissolved in CH_2Cl_2 (100 ml). The solution was washed with aqueous K_2CO_3, followed by water and dried over $MgSO_4$. Evaporation of the solvent gave a semicrystalline yellow solid composed of compounds **3**, **4** and **5** in a 45:5:1 ratio (GC–MS analysis). Total yield: 36 g (80%). Two GLC peaks of comparable intensity and identical mass spectrum appeared for each compound **3** and **4** indicating isomeric mixtures. Several crystallization from n-hexane gave a longer GLC retention time for isomer **3a** in the pure state. An analytical sample of an isomeric mixture of compounds **4** was isolated by preparative GLC.

Run 2

Anhydride **2** (60 g, 0.2 mol), hydrogen fluoride (2 ml, 0.1 mol) and sulphur tetrafluoride (90 g, 0.83 mol) were reacted at 70–80 °C for 96 h and worked-up as described above to give 46 g (yield 80%) of a mixture of compounds **3** and **4** in a 5:1 ratio with only a trace amount of **5**.

trans-4)(*e*)-Bromo-3(*e*),7,7,9,9-pentafluoro-8-oxa-*cis*-bicyclo[4.3.0]nonane (**3a**): Colourless crystals; m.p. 83–84 °C. Analysis: Found: C, 32.9; H, 2.8; Br, 27.8; F, 32.1%. $C_8H_8BrF_5O$ requires: C, 32.6; H, 2.7; Br, 27.1; F, 32.2%. ^1H NMR (500 MHz) δ: 1.95, 2.44 [AB system (m), CH_2, $J_{A-B} = 24$ Hz]; 2.22–2.62 [AB system (m), CH_2, $J_{A-B} = 15.3$ Hz]; 3.00 (m, 2H, CH); 4.24 (m, CHBr, $^3J_{H-H} =$ ca. 13.2, 8.5, 4.7 Hz); 4.58 (dm, CHF, $^2J_{H-F} = 47.3$ Hz, $^3J_{H-H} =$ ca. 9.0, 8.0, 4.3 Hz, $^4J_{H-F} = 1.0$ Hz) ppm. Decoupling of the 4.58 signal allowed J_{4H-5H} to be estimated as ca. 8 Hz (ax–ax). ^{19}F NMR (200 MHz) δ: 170.5 (dm, CHF, $^2J_{H-F} = 47.3$ Hz); 67.5, 81.1 [AB system (dm), CF_2, $J_{A-B} = 140.5$ Hz]; 71.3, 73.0 [AB system (dm), CF_2, $J_{A-B} = 143.5$ Hz] ppm. ^{13}C NMR (200 MHz) δ: 128.6 (t, CF_{22}, $^1J_{C-F} = 265.2$ Hz); 128.1 (t, CF_2, $^1J_{C-F} = 266.5$ Hz); 89.5 (d, CF, $^1J_{C-F} = 181.8$ Hz); 45.7 (dd, CHBr, $^2J_{C-F} = 21.6$ Hz, $^4J_{C-F} = 3.2$ Hz); 41.1 (t, C-2, $^2J_{C-F} = 26.0$ Hz); 40.8 (td, C-1, $^2J_{C-F} = 22.0$ Hz, $^3J_{C-F} = 8$ Hz); 28.2 (dt, C-3, $^3J_{C-F} = 3.5$ Hz); 26.1 (dt, C-6, $^2J_{C-F} = 23.2$ Hz, $^3J_{C-F} = 2.7$ Hz) ppm. GC–MS (m/z): 296 [<1% M^+ (^{81}Br)]; 215 [30, $(M-Br)^+$]; 195 [10, $(M-Br-HF)^+$]; 187 [15, $(M-Br-CO)^+$]; 167 [100, $(M-HBr-COF)^+$]; 147 (30, $C_7H_6F_3{}^+$); 127 (40, $C_7H_5F_2{}^+$); 97 (15, $C_6H_6F^+$); 77 (40, $C_6H_5{}^+$).

trans-3(*e*)-bromo-4(*e*),7,7,9,9-pentafluoro-8-oxa-*cis*-bicyclo[4.3.0]nonane (**3b**): MS identical with **3a**.

trans-1-bromo-2-fluoro-*cis*-4,5-bis(trifluoromethyl)cyclohexanes **4** (two isomers): GC–MS (m/z): 318 [<1% M^+ (^{81}BR)]; 237 [100, $(M-BR)^+$]; 217 [70, $(M-HBr-F)^+$]; 127 (40, $C_7H_5F_2{}^+$).

trans-1,2-dibromo-*cis*-4,5-bis(trifluoromethyl)cyclohexane (**5**); GC–MS (m/z): 380 [10%, M^+ (^{81}Br)]; 299 [25, $(M-Br)^+$, (^{81}Br)]; 217 [100, $(M-HBr-Br)^+$]; 127 (40, $C_7H_5F_2{}^+$).

3.3. Preparation of 7,7,9,9-tetrafluoro-8-oxa-cis-bicyclo[4.3.0]non-3-ene (6)

A. From pure 3a

Compound **3a** (15 g, 0.05 mol), acetic anhydride (15 g, 0.15 mol) and activated zinc dust (30 g, 0.46 mol) were placed in a 250 ml flask fitted with a mechanical stirrer and a reflux condenser. The mixture was carefully heated until rapid reaction occured. Gentle warming was prolonged for a further 15 min. After cooling to ambient temperature, water (100 ml) was added and the product steam-distilled. The organic layer of the distillate was separated, washed with aqueous Na_2CO_3 solution followed by water and dried over $MgSO_4$. Distillation (b.p. 30–32 °C/1.5 Torr) gave pure alkene **6** (GLC estimate) as a colourless liquid. Yield 9.7 g (98%). Analysis: Found: C, 49.1; H, 4.0; F, 38.6%. $C_8H_8F_4O$ requires: C, 49.0; H, 4.1; F, 38.7%. ^1H NMR (200 MHz) δ: 2.1–2.5 (m, 4H, CH_2); 2.8–3.0 (m, 2H, CH); 5.75 (narrow m, 2H, CH=CH) ppm. ^{19}F NMR (200 MHz) δ: 71.3, 81.1

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[2] Full details of the structure determination have been deposited at the Fachinformationszentrum Karlsruhe, Gesellschaft für Wissenschaftlich-technische Information mbH, 76344 Eggenstein-Leopoldshafen, Germany. Any request for this material should quote a full literature citation and the reference number CSD 401714.

(AB system, 2×dt, $2CF_2$, $^2J_{F-F}=141.1$ Hz, $^4J_{F-F}=9.2$ Hz) ppm. ^{13}C NMR (200 MHz) δ: 19.4 (s, CH_2); 38.4 (t, CH, $^3J_{C-F}=25.2$ Hz); 123.3 (s, CH=CH); 129.5 (tdd, CF_2, $^1J_{C-F}=265.0$ Hz, $J=5.3$, 2.5 Hz) ppm. GC–MS (m/z): 196 (25%, M^+); 176 [15 $(M-HF)^+$]; 148 [25, $(M-HF-CO)^+$]; 79 (100, $C_6H_7^+$).

B. From the mixture of ***3–5***

The mixture of compounds **3–5** (36 g, ca. 0.12 mol) was dissolved in acetic anhydride (50 ml) and dehalogenated with zinc dust (70 g, 1.1 mol) as above. Steam-distillation gave an oily liquid (22 g) which was dissolved in $CHCl_3$ (50 ml) and dried over $MgSO_4$; then bromine (18 g, 0.225 mol) was added at 0–5 °C and the reaction mixture stirred for 0.5 h. The solid residue obtained after evaporation of the solvent was recrystallized three times from methanol to give *trans*-3,4-dibromo-7,7,9,9-tetrafluoro-8-oxa-*cis*-bicyclo-[4.3.0]nonane (**8**) as colourless prisms (25 g, 0.07 mol); m.p. 82–83 °C (GLC showed a single isomer). Analysis: Found: C, 26.7; H, 2.3; Br, 44.8; F, 21.3%. $C_8H_8Br_2F_4O$ requires: C, 27.0; H, 2.3; Br, 44.9; F, 21.4%. ^1H NMR (200 MHz) δ: 2.0–2.4, 2.6–2.9 (two complex AB systems, 4H, CH_2); ca. 3.0 (m, 2H, CH); 3.99 (m, 1H, CHBr, $^3J_{H-H}=$ ca. 10.3, 4.0, 1.7 Hz); 4.28 (m, 1H, CHBr, $^3J_{H-H}=$ ca. 10.7, 4.9, 1.9 Hz) ppm. ^{19}F NMR (200 MHz) δ: 65.9, 85.1 (AB system, dm, CF_2, $J_{A-B}=141.8$ Hz); 68.7, 73.4 (AB system, dm, CF_2, $J_{A-B}=143.2$ Hz) ppm. ^{13}C NMR (200 MHz) δ: 31.3 (s, CH_2); 32.5 (t, CH_2, $^3J_{C-F}=3.9$ Hz); 41.8 (t, CH, $^2J_{C-F}=26.0$ Hz); 42.5 (tt, CH, $^2J_{C-F}=20.5$ Hz, $^3J_{C-F}=2.0$ Hz); 50.5 (s, CHBr); 50.7 (d, CHBr, $^4J_{C-F}=0.8$ Hz); 127.7 (tm, CF_2, $^1J_{C-F}=264.8$ Hz); 128.4 (tm, CF_2, $^1J_{C-F}=262.2$ Hz) ppm. GC–MS (m/z): 358 [<1%, M^+ (^{81}Br)]; 277 [30, $(M-Br)^+$]; 167 (100, $C_7H_7F_4^+$); 147 (80, $C_7H_6F_3^+$); 127 (90, $C_7H_5F_2^+$).

The dibromo compound **8** was dissolved in ethanol (50 ml), the solution brought to boiling (under reflux) and zinc dust (50 g, 0.765 mol) added portionwise. The mixture was refluxed for 1 h, then cooled to ambient temperature and the solid material filtered off. The filtrate was distilled under reduced pressure to give a fraction (10 g, b.p. 30–32 °C; yield 71.4%) identified as alkene **6**.

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References

[1] W. Dmowski and R. Koliński, *Polish J. Chem., 52* (1978) 71.
[2] W. Dmowski, *J. Fluorine Chem., 65* (1993) 139, and references therein.
[3] W. Dmowski, *Polish J. Chem., 68* (1994) 2175.
[4] R.C. Fahey, in E.L. Eliel and N.L. Alinger (eds.), *Topics in Stereochemistry,* Wiley, New York, 1968, Vol. 3, p. 286.
[5] D.J. Bennett, A.C. Craig, B.P. Mundy, G.W. Dirks and K.B. Lipkowitz, *J. Org. Chem., 41* (1976) 469.
[6] G.D. Smoth, R.D. Otzenberger, B.P. Mundy and C.N. Caughlan, *J. Org. Chem., 39* (1974) 321.
[7] J.E. Gill and J. Munro, *J. Chem. Soc.,* (1952) 4630.
[8] R.S. Wilder and G.D. Martin, US Pat. 2 550 744, 1951; [*Chem. Abs., 46* (1952) 2574].