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VICINAL BROMOFLUOROALKANES : THEIR REGIOSELECTIVE FORMATION AND THEIR CONVERSION TO FLUOROOLEFINS

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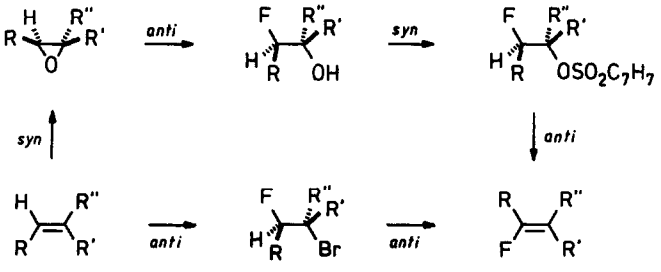
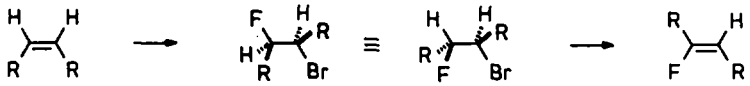
Summary : The reaction of alkenes with *N*-bromosuccinimide and triethylamine tris(hydrofluoride) produces *vic*-bromofluoroalkanes (1) with high yields. As long as the addition to the double bond is sterically unhindered, bromine and fluorine get attached with very high regioselectivity, the latter halogen occupying the more substituted, carbocation stabilizing position. 2-Fluoro-1-alkenes give 1-bromo-2,2-difluoroalkanes (4). The heavier halogen may be removed by base promoted dehydrofluorination, to afford fluoroolefins (2), or by reduction with tributyltin hydride, leading to mono- or difluoroalkanes (*e.g.*, 5).

In the preceding article [1] an improved access to fluoroolefins is described. The method relies on a four step sequence : epoxidation of an alkene, ring opening of the epoxide by addition of hydrogen fluoride, conversion of the resulting fluorohydrin to the *p*-toluenesulfonate and finally base promoted elimination. We realized that the same goal could be reached more directly. The simultaneous addition of a bromine and a fluorine atom to a carbon-carbon double bond is a facile and strictly *anti*-periplanar process [2, 3]. The subsequent selective elimination of hydrogen bromide should cause no difficulties.



The results confirmed the expectation. When treated with *N*-bromosuccinimide and triethylamine tris(hydrofluoride), *cis*- and *trans*-6-dodecene gave *threo*- and, respectively, *erythro*-6-bromo-7-fluorododecane (**1a**) in almost quantitative yield. Dehydrobromination proceeded smoothly with potassium *tert*-butoxide in tetrahydrofuran at 0 °C to afford (*Z*)- and (*E*)-6-fluoro-6-dodecene (**2a**), respectively. In the same way, *trans*-4-octene was converted to *erythro*-4-bromo-5-fluorooctane (**1b**) and to (*E*)-4-fluoro-4-octene (**2b**).

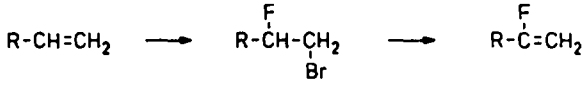


***threo*-1** **Z-2**

***erythro*-1** **E-2**

a: R = $H_{11}C_5$; **b:** R = H_7C_3

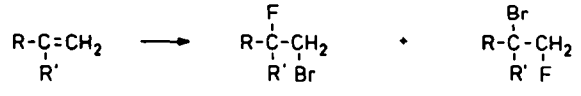
One crucial problem had still to be clarified: the regioselectivity of bromonium fluoride addition to asymmetric, notably terminal alkenes. The scarce literature data available were not very encouraging : 3-phenyl-1-propene was reported to produce a 11 : 89 mixture of 2-bromo-1-fluoro-3-phenylpropane and 1-bromo-2-fluoro-3-phenylpropane [2]. Fortunately, the bromine-fluorine addition turned out to perfectly regioselective, as it should, if suitable reaction conditions were chosen. Thus, 1-decene gave pure 1-bromo-2-fluoro-decane (**1c**) and styrene pure 2-bromo-1-fluoro-1-phenyl-ethane (**1d**). The treatment with potassium *tert*-butoxide led to 2-fluoro-1-decene (**2c**) and 1-fluoro-1-phenylethylene (**2d**, α-fluorostyrene).



1 **2**

c: R = $H_{17}C_8$; **d:** R = H_5C_6

Steric bulk may jeopardize the regioselective outcome of the bromonium fluoride addition. 3,3-Dimethyl-1-butene gives a 9 : 91 mixture of 1-bromo-2-fluoro-3,3-dimethylbutane (**1e**) and 2-bromo-1-fluoro-3,3-dimethylbutane (**3e**), 2,4,4-trimethyl-1-pentene a 84 : 16 mixture of 1-bromo-2-fluoro-2,4,4-trimethylpentane (**1f**) and 2-bromo-1-fluoro-2,4,4,-trimethylpentane (**3f**).



1 **3**

e: R = $(H_3C)_3C$; R' = H; **f:** R = $(H_3C)_3C$-CH_2; R' = CH_3

In all ordinary cases, the fluorine gets exclusively attached to the more substituted olefinic carbon atom which can better sustain the transient positive charge. This rule holds also for branched olefins of the 1,1,2-trialkylethylene type [4]. Geraniol, for example, is quantitatively converted to (*E*)-6-bromo-7-fluoro-3,7-dimethyl-2-octen-1-ol (*E*-**1g**).

***E*-1g**

Fluorine is known to stabilize carbenium ions by an electron donating resonance effect [5]. This led us to predict for 2-fluoro-1-alkenes an enhanced reactivity and a perfect regiocontrol in electrophilic addition processes. 2-Fluoro-1-decene (**2c**) and 1-fluoro-1-phenylethylene (**2d**) did indeed react quite smoothly with *N*-bromosuccinimide in the presence of triethylamine tris(hydrofluoride) to afford 1-bromo-2,2-difluorodecane (**4c**) and 2-bromo-1,1-difluoro-1-phenylethane (**4d**) as the exclusive products.

2 **4**

c: R = $H_{17}C_8$; **d:** R = H_5C_6

As already demonstrated previously [3, 6], treatment with tributyltin hydride allows to replace bromine by a hydrogen atom without affecting adjacent carbon-fluorine bonds. In the same way, we were able to reduce 2-bromo-1,1-difluoro-1-phenylethane (**4d**) to 1,1-difluoro-1-phenylethane (**5**, α,α-difluoroethylbenzene).

4 d **5**

EXPERIMENTAL PART

Generalities : see preceding article.[1] - Typical ^{1}H-NMR spectra of *vic*-bromofluoroalkanes reveal some anomalities as illustrated by a few examples below (see figure). In particular, the left-hand and right-hand parts of the α-fluoromethine signal are not identical. This phenomenon can serve as a sensitive probe for conformational analysis. As computer simulations [7] reveal, only the conformer in which the two unequal alkyl substituent at the fluoromethine/methylene axis occupy *anti*-periplanar positions exhibit such an asymmetry (a twin signal composed of a doublet of doublets on the low-field side and of a triplet on the high-field side). In this array, one methylene hydrogen is *gauche* with respect to the fluorine atom and *anti* with respect to the fluoromethine

hydrogen atom, while the other methylene hydrogen has the opposite spatial relationship to the same vicinal neighbors. In each of the two other staggered conformations one methylene hydrogen is gauche with respect to both nuclei of the fluoromethine group. Under these circumstances a symmetrical methine (H_x) signal must result (doublet of triplets in the case of an *anti*-periplanar H,F-, doublet of doublets of doublets in the case of an *anti*-periplanar H,H_x-interactions).

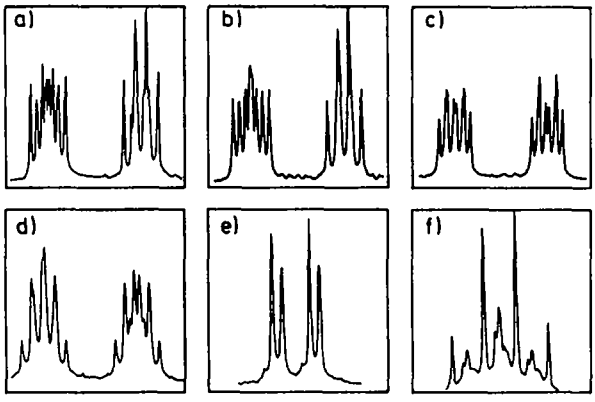


Figure. ^{1}H-Nuclear magnetic resonance subspectra of *vic*-bromofluoroalkanes

a) *erythro*-**1b** : -CHF- b) *erythro*-**1a** : -CHF- c) *threo*-**1a** : -CHF-

d) **1c** : -CHF- e) **1c** : $-CH_2Br$ f) **4a** : $-\overset{|}{\underset{|}{C}}-CH_2-CF_2-$

1. *vic*-Bromofluoroalkanes

General procedure : At 0 °C, triethylamine tris(hydrofluoride) (32 mL, 32 g, 0.20 mol) in dichloromethane (50 mL) was added dropwise, in the course of 15 min, to a suspension of *N*-bromosuccinimide (21 g, 0.12 mol) in dichloromethane (50 mL), in which the olefin (0.10 mol) had been dissolved. After 2 h of additional stirring at 0 °C, the reaction mixture was absorbed on silica gel (50 g) which was dried by evaporation and poured on top of a column filled with fresh silica gel (150 g) and hexane. Elution with hexane and distillation afforded the product, the purity of which was checked by gas chromatography (50 m OV-1701, 100 → 190 °C).

erythro-**6-Bromo-7-fluorododecane** (*erythro*-**1a**) : 92% (diastereomeric purity 97%); mp -23 to -22 °C; bp 110 - 111 °C/3 mmHg; n_D^{20} 1.4507. - ^{1}H-NMR ($CDCl_3$) : 4.50 (1 H, d of symm. m, J_{HF} 48.7), 4.02 (1 H, symm. m), 1.8 (4 H, m), 1.3 (12 H, m, narrow), 0.90 (6 H, t, *J* 6.7). - MS : 166 (5%, M^+ - HBr - HF - 1), 125 (5%), 111 (32%), 97 (50%), 55 (100%). - Analysis : calc. for $C_{12}H_{24}BrF$ (267.23) C 53.94, H 9.05; found C 53.68, H 9.10%.

threo-**6-Bromo-7-fluorododecane** (*threo*-**1a**) : 90% (diastereomeric purity (97%); mp -8 to -7 °C; bp 112 - 114 °C/ 3 mmHg; n_D^{20} 1.4524. - ^{1}H-NMR ($CDCl_3$) : 4.46 (1 H, ddt, *J* 47.7, 8.6, 3.5), 3.98 (1 H, dddd, *J* 22.2, 7.5, 6.6, 3.4), 1.89 (2 H, q, *J* 7.5), 1.8 (1 H, m), 1.7 (1 H, m), 1.3 (12 H, m), 0.92 (6 H, t, *J* 6.9). - MS : 166 (3%), 55 (100%). - Analysis : calc. for $C_{12}H_{24}BrF$ (267.23) C 53.94, H 9.05; found C 53.79, H 9.11%.

erythro-**4-Bromo-5-fluorooctane** (*erythro*-**1b**) : 97% (diastereomeric purity >99%); bp 40 - 41 °C/3 mmHg; n_D^{20} 1.4441. - ^{1}H-NMR (C_6D_6) : 4.52 (1 H, d of symm. m, J_{HF} 48.7), 4.02 (1 H, symm. m), 1.7 (8 H, m, broad), 0.97 (3 H, t, *J* 7.4), 0.95 (3 H, t, *J* 7.4). - MS : 111 (2%, M^+ - HBr, - HF), 69 (8%), 55 (100%). - Analysis : calc. for $C_8H_{16}BrF$ (211.12) C 45.51, H 7.64; found C 45.58, H 7.85%.

1-Bromo-2-fluorodecane (1c) : 86%; mp -16 to -15 °C; bp 81 - 83 °C/3 mmHg; n_D^{20} 1.4486. - ^{1}H-NMR ($CDCl_3$): 4.64 (1 H, d of symm. m, J_{HF} 48.0), 3.47 (2 H, dd, *J* 19.2, 5.2), 1.7 (2 H, m), 1.4 (2 H, m), 1.3 (10 H, m, narrow), 0.88 (3 H, m, t-like, *J* ~ 7). - MS : 150 (4%), 55 (100%). - Analysis : calc. for $C_{10}H_{20}BrF$ (239.17) C 50.22, H 8.43; found C 50.29, H 8.16%.

2-Bromo-1-fluoro-1-phenylethane (1d) : 93%; bp 76 - 77 °C/3 mmHg; n_D^{20} 1.5430. - ^{1}H-NMR (C_6D_6) : 7.4 (5 H, m), 5.61 (1 H, ddd, *J* 47.0, 7.9, 4.2), 3.66 (1 H, ddd, *J* 15.3, 11.2, 7.8), 3.58 (1 H, ddd, *J* 26.0, 11.2, 4.4). - MS : 204 + 202 (20%, M^+ [^{80}Br + ^{78}Br]), 109 (100%). - Analysis : calc. for C_8H_8BrF (203.06) C 47.32, H 3.97; found C 47.51, H 3.98%.

2-Bromo-1-fluoro-3,3-dimethylbutane (3e) : 63% (9% regioisomeric contamination, by gas chromatography); bp 67 - 68 °C/ 288 mmHg. - ^{1}H-NMR ($CDCl_3$) : 4.80 (1 H, ddd, *J* ~ 32, 10.5, ~ 6), 4.67 (1 H, ddd, *J* ~ 32, ~ 10, ~ 6), 4.08 (1 H, ddd, *J* 16.5, 6.2, 5.3), 1.15 (9 H, s).

1-Bromo-2-fluoro-2,4,4-trimethylpentane (1f) : 71% (16% regioisomeric contamination, by gaschromatography); bp 31 - 33 °C/ 5 mmHg. - ^{1}H-NMR ($CDCl_3$) : 3.57 (1 H, dd, *J* 13.2, 10.7), 3.46 (1 H, dd, *J* 17.5, 10.7), 1.82 (1 H, dd, *J* 18.3, 15.0), 1.70 (1 H, dd, J 26.0, 15.0), 1.56 (3 H, d, *J* 21.5), 1.05 (9 H, d, *J* 0.8). - Analysis : calc. for $C_8H_{16}BrF$ (211.12) C 45.51, H 7.64; found C 45.84, H 7.82%.

(*E*)-6-Bromo-7-fluoro-2,7-dimethyl-2-octen-1-ol (*E*-1g) : 96%; isolation without distillation; n_D^{20} 1.4921. - ^{1}H-NMR ($CDCl_3$) : 5.50 (1 H, thex, *J* 6.7, 1.3), 4.18 (2 H, d, *J* 7.0), 3.88 (1 H, ddd, *J* 11.5 8.4, 2.0), 2.39 (1 H, symm. m), 2.15 (2 H, symm. m), 1.86 (1 H, s), 1.80 (1 H, symm. m), 1.69 (3 H, d, *J* 1.0), 1.56 (3 H, d, *J* 18.5), 1.49 (3 H, d, *J* 18.0). - Analysis : calc. for $C_{10}H_{18}BrFO$ (253.16) C 47.45, H 7.17; found C 49.23, H 7.05%.

1-Bromo-2,2-difluorodecane (4c) : 85%; mp -8 to -7 °C; bp 62 - 63 °C/5 mmHg; n_D^{20} 1.4339. - ^{1}H-NMR ($CDCl_3$): 3.52 (2 H, t, *J* 13.1), 2.02 (2 H, symm. m), 1.48 (2 H, symm. m), 1.3 (10 H, m, narrow), 0.89 (3 H, t, *J* 6.9). - Analysis : calc. for $C_{10}H_{19}BrF_2$ (257.16) C 46.71, H 7.45; found C 46.71, H 7.69%.

2-Bromo-1,1-difluoro-1-phenylethane (4d) : 90%; bp 63 - 65 °C/5 mmHg; n_D^{20} 1.5126. - ^{1}H-NMR ($CDCl_3$) : 7.5 (5 H, m), 3.75 (2 H, t, *J* 13.9). - MS : 222 + 220 (11%, M^+ [^{80}Br + ^{78}Br]), 127 (100%). - Analysis : calc. for $C_8H_7BrF_2$ (221.04) C 43.47, H 3.19; found C 43.68, H 3.06%.

2. Replacement of Bromine by Hydrogen

1,1-Difluoro-1-phenylethane (5) : A mixture of 2-bromo-1,1-difluoro-1-phenylethane (3.3 g, 15 mmol) and tributyltin hydride (5.2 g, 18 mmol) was kept 2 h at 60 °C. Distillation afforded a colorless liquid; 1.35 g 5 [8] (63%); mp -61 to -60 °C; bp 64 - 65 °C/40 mmHg; n_D^{20} 1.4517. - ^{1}H-NMR ($CDCl_3$) : 7.5 (2 H, m), 7.4 (3 H, m), 1.96 (2 H, t, *J* 18.2).

3. Fluoroolefins

General procedure : The *vic*-bromofluoroalkane (50 mmol) was added to a solution of potassium *tert*-butoxide (6.7 g, 60 mmol) in tetrahydrofuran (50 mL). After 5 h at 0 °C, the fluoroolefin was isolated by distillation under reduced pressure.

(*Z*)-6-Fluoro-6-dodecene (*Z*-2a) [1, 9] : 91% (97% stereoisomeric purity).

(*E*)-6-Fluoro-6-dodecene (*E*-2a) [1, 9] : 94% (96% stereoisomeric purity).

(*E*)-4-Fluoro-4-octene (*E*-2b) : 82% (> 99% stereoisomeric purity), bp 66 - 68 °C/80 mmHg; n_D^{20} 1.4061. - ^{1}H-NMR ($CDCl_3$) : 5.01 (1 H, dt, *J* 22.9, 8.0), 2.19 (2 H, dt, *J* 23.4, 7.3), 1.90 (2 H, q, *J* 7.5), 1.54 (2 H, hex, *J* 7.3), 1.37 (2 H, hex, *J* 7.3), 0.94 (3 H, t, *J* 7.3), 0.90 (3 H, t, *J* 7.3). - MS : 130 (22%, M^+), 101 (44%), 81% (67%), 73 (39%), 59 (100%). - Analysis : calc. for $C_8H_{15}F$ (130.21) C 73.79, H 11.61; found C 73.77, H 11.67%.

2-Fluoro-1-decene (2c) [1] : 88%.

1-Fluoro-1-phenylethylene (2d) : 75%; mp -40 to -38 °C; bp 67 - 68 °C/30 mmHg; n_D^{20} 1.5222. ^{1}H-NMR (C_6D_6) : 7.6 (2 H, m), 7.5 (3 H, m), 5.03 (1 H, dd, *J* 49.8, 3.5), 4.85 (1 H, dd, *J* 18.0, 3.5). - MS : 122 (100%, M^+), 101 (27%), 96 (45%). - Analysis : calc. for C_8H_7F (122.14) C 78.67, H 5.78; found C 78.58, H 5.92%.

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