Bromofluorination of Vinyloxiranes

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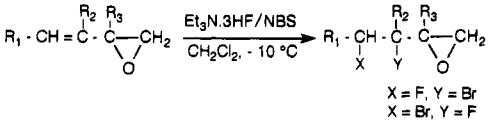
The action of *N*-bromosuccinimide/triethylamine tris(hydrofluoride) (NBS/Et_3N·3HF) on vinyloxiranes leads to the corresponding bromofluorinated oxiranes. The regioselectivity and yield of the reaction can be related to the degree of substitution on the vinyl group.

Introduction

The halofluorinating reagent XF (X = Cl, Br, I) is generally generated in situ from fluorine and bromine,[1-3] from silver fluoride and halogen,[4] or by combination of a positive halogen precursor, such as alkyl hypochlorite, *N*-halosuccinimide or *N*-bromoacetamide, with HF,[5-7] HF/pyridine,[8-10] or $Bu_4NH_2F_3$.[11,12] The XF addition using the mixture NBS/Et_3N·3HF has been realized on simple olefins[13,14] and allylic alcohols.[15] In the present work this reaction is carried out on the vinyloxiranes and yields the corresponding bromofluorooxiranes. The formation of these simple building-block molecules may prove useful in syntheses of fluorine-substituted products.

Results and Discussion

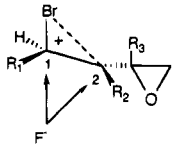
At room temperature, the action of triethylamine tris(hydrofluoride) on the vinyloxiranes leads, via oxirane ring opening, to the corresponding fluorohydrins[16] whereas the mixture NBS/Et_3N·3HF yields from the same vinyloxiranes, at −10 °C in dichloromethane, the corresponding bromofluorooxiranes, as shown below.



The synthesised products are shown in Table 1.

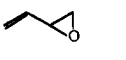
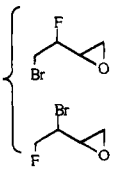
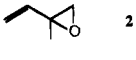
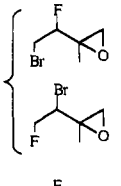
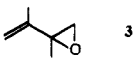
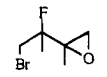
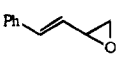
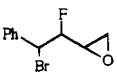
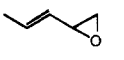
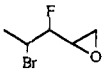
The results shown in Table 1 allow us to make the following comments: (i) The regioselectivity of the reaction, partial when the vinyl group of the starting vinyloxiranes is not substituted, becomes total for vinyloxiranes, where this group is substituted. (2) The formation of only two diastereoisomers D1 and D2 from each of compounds **4** and **5** excludes the existence of a bromonium ring ⇌ β-brominated carbocation equilibrium for which four diastereoisomers are expected for each of the derivatives and the bromofluorinated oxirane, with benzylic fluorine atom, must be present from compound **4**.

As shown below, the results may be rationalized with an unsymmetrical bromonium ring intermediate. The action of fluoride ion on this ring takes place preferably on the C2 carbon for compounds **1** and **2** and exclusively on this carbon for the other products.



Notice that, contrary to what has been observed in the case of compound **4** (R_1 = Ph), styrene derivative bro-

Table 1. Preparation of Bromofluoroepoxides

Vinyloxirane		Product		R.C (%)[a]	D1 : D2[b]	bp (°C/Torr)	Yield[c] (%)
	1		1c	73	49:51[d]	70/15	55
			1c'	27	58:42[d]		
	2		2c	61	29:71[d]	72/15	66
			2c'	39	55:45[d]		
	3		3c	-	31:69[d]	81/15	79
	4		4c	-	79:21	98/0.3	93
	5		5c	-	77:23	73/15	67

[a] R.C.: regioisomer composition based on ^{19}F NMR and GC. [b] D1: D2: diastereoisomer composition based on ^{19}F NMR. [c] Isolated yield. [d] D1 = *erythro*, D2 = *threo* based on ^{19}F NMR.

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mofluorination yields the corresponding bromofluorinated compounds with the fluorine atom at the benzylic position.[17,18]

Experimental Section

^1H NMR spectra were recorded in $CDCl_3$ on a JEOL NM-PMX apparatus at 60 MHz, and ^{19}F NMR spectra were obtained in $CDCl_3$ on a Bruker AC200 instrument at 188.313 MHz. The chemical shifts are reported in ppm relative to TMS and $CFCl_3$ used as internal standards for the ^1H and ^{19}F, respectively. IR spectra were carried out on a Perkin-Elmer 681 spectrophotometer. GC analyses were performed on an Intersmat IGC 120 DFL gas chromatograph with a SE 30 (10%) column. Mass spectral (MS) data were obtained on a Nermag R 10-10-B mass spectrometer operating at 70 eV in the impact mode.

Preparation of Bromofluorinated Oxiranes: General Procedure. A 100-mL three-necked round-bottomed flask equipped with a mechanical stirrer, pressure equalizing addition funnel, and nitrogen inlet was charged with 10 mmol of vinyloxirane and 20 mL of dry CH_2Cl_2. The flask was cooled to −10 °C. N-bromosuccinimide (1.78 g, 10 mmol) was added. The reaction mixture was stirred while $Et_3N{\cdot}3HF$ (3.22 g, 20 mmol) dissolved in CH_2Cl_2 (6 mL) was added dropwise. Stirring was kept overnight at −10 °C. The mixture was then diluted with water and extracted with ether. The organic layer was washed with sodium bicarbonate until basic pH and then with water. After the organic layer was dried on Na_2SO_4, the solvents were removed and the residue obtained was distilled.

1c: IR ($CHCl_3$) 3000, 1095, 860 cm^{-1}; ^1H NMR δ 4.60 (dm, 1 H, J = 47.1 Hz), 3.58 (dd, 2 H, J = 20.8, 5.0 Hz), 3.26 (dm, 1 H, J = 9.8 Hz), 2.83 (m, 2 H); ^{19}F NMR δ *erythro* −189.5 (dtd, 1 F, J = 47.1, 20.8, 9.8 Hz), *threo* −184.5 (dtdd, 1 F, J = 47.0, 16.8, 13.4, 4.0 Hz); MS (*m/z*) 138/140 (M − CH_2O, 1.79/1.40), 93/95 (CH_2Br, 6.33/5.71), 89 (M − Br, 19.21), 60 (16.44), 51 (60.10), 41 (100.00).

1c': IR ($CHCl_3$) 3000, 1095, 860 cm^{-1}; ^1H NMR δ 4.70 (dd, 2 H, J = 47.0, 18.3 Hz), 4.26 (m, 1 H), 3.26 (m, 1 H), 2.83 (m, 2 H); ^{19}F NMR δ *erythro* −217.3 (td, 1 F, J = 47.0, 18.3 Hz), *threo* −210.3 (td, 1 F, J = 47.2, 14.0 Hz); MS (*m/z*) 89 (M − Br, 18.36), 60 (13.46), 51 (75.86), 41 (100.00).

2c: IR ($CHCl_3$) 2990, 1090, 865 cm^{-1}; ^1H NMR δ 4.57 (dm, 1 H, J = 49.0 Hz), 3.59 (dm, 2 H, J = 25.3 Hz), 3.05 (m, 2 H), 1.38 (s, 3 H, *threo*), 1.23 (s, 3 H, *erythro*); ^{19}F NMR δ *erythro* −198.3 (dt, 1 F, J = 49.0, 25.4 Hz), *threo* −194.2 (dt, 1 F, J = 49.4, 21.2 Hz); MS (*m/z*) 102 (M − HBr, 1.03), 93/95 (CH_2Br, 3.53/2.61), 69 (2.38), 55 (100.00).

2c': IR ($CHCl_3$) 2990, 1090, 865 cm^{-1}; ^1H NMR δ 4.73 (dm, 2 H, J = 49.5 Hz), 4.05 (dm, 1 H, J = 14.1 Hz), 3.05 (m, 2 H), 1.60 (s, 3 H, *threo*), 1.48 (s, 3 H, *erythro*); ^{19}F NMR δ *erythro* −223.4 (td, 1 F, J = 49.0, 14.1 Hz), *threo* −217.5 (td, 1 F, J = 49.0, 15.0 Hz); MS (*m/z*) 103 (M − Br, 4.89), 84 (7.14), 69 (3.28), 55 (100.00).

3c: IR ($CHCl_3$) 3000, 1090, 855 cm^{-1}; ^1H NMR δ 3.58 (m, 2 H), 2.65−3.08 (m, 2 H), 1.56 (d, 3 H, *erythro*, J = 19.0 Hz), 1.47 (d, 3 H, *threo*, J = 22.1 Hz), 1.40 (s, 3 H); ^{19}F NMR δ *erythro* −159.6 (qt, 1 F, J = 21.3, 20.0 Hz), *threo* −154.3 (qdd, 1 F, J = 21.9, 21.8, 11.4 Hz); MS (*m/z*) 196 ($M^{\bullet+}$, 0.1), 181/183 (M − CH_3, 1.95/1.77), 117 (M − Br, 100.00), 103 (8.92), 93/95 (6.69/6.16), 87 (19.66), 57 (39.20).

4c: IR ($CDCl_3$) 2980, 1670, 1100, 865 cm^{-1}; ^1H NMR δ 7.30 (s, 5 H), 4.70 (dm, 1 H, J = 50.0 Hz), 4.26 (dm, 1 H, J = 25.0 Hz), 3.25−3.00 (m, 3 H); ^{19}F NMR D1 −182.0 (ddd, 1 F, J = 50.0, 25.0, 13.6 Hz), D2 −170.7 (ddd, 1 F, J = 49.6, 24.4, 15.0 Hz); MS (*m/z*) 244/246 ($M^{\bullet+}$, 14.03/13.46), 165 (M − Br, 58.67), 164 (M − HBr, 43.21), 145 (29.58), 105 (100.00), 77 (44.35).

5c: IR ($CHCl_3$) 2990, 1090, 860 cm^{-1}; ^1H NMR δ 4.90 (dm, 1 H, J = 48.0 Hz), 4.21 (dm, 1 H, J = 27.5 Hz), 3.80−3.20 (m, 3 H), 1.71 (d, 3 H, D2, J = 6.6 Hz), 1.35 (d, 3 H, D1, J = 5.8 Hz); ^{19}F NMR δ D1 − 179.9 (ddd, 1 F, J = 48.1, 27.4, 24.4 Hz), D2 −169.0 (ddd, 1 F, J = 48.0, 24.6, 23.1 Hz); MS (*m/z*) 182/184 ($M^{\bullet+}$, 0.61/0.58), 181/183 (M − 1, 0.85/1.25), 167/169 (M − CH_3, 5.39/4.30), 107/109 (CH_3 − $CHBr^+$, 0.64/0.73), 103 (M − Br, 17.61), 59 ($C_3H_4F^+$, 56.92), 53 ($C_4H_5^+$, 100.00).

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