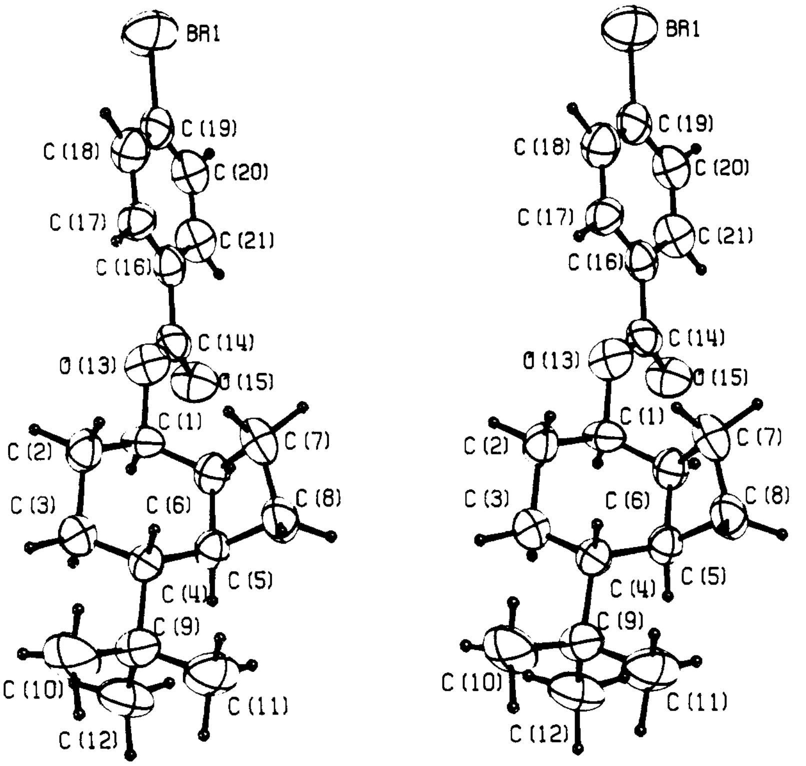
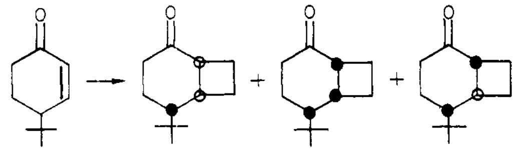
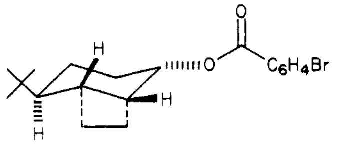


Figure 1. Stereoview of 5.



1 2 (61%) 3 (15%) 4 (24%)



5

radical intermediate(s) seems to be as much as 15 times more rapid than closure,[3] the validity of any model that ignores the complex set of rate constants involved in photochemical cycloadditions is suspect.

X-ray Analysis. The structure of compound 5 was unambiguously established by a routine single-crystal X-ray analysis. Crystals of this compound belonged to the monoclinic space group $P2_1/c$ with $a = 13.590$ (3), $b = 20.706$ (3), $c = 6.670$ (1) Å, $\beta = 106.50$ (1)°. The density was measured by flotation in aqueous KI as 1.36 g/cm^3. On the basis of four molecules per unit cell, the calculated density was 1.348 g/cm^3. A 1-Å data set (maximum $\sin \theta/\lambda = 0.5$) was collected on a Syntex P$\bar{1}$ diffractometer using copper radiation ($\lambda = 1.5418$ Å). The diffractometer was equipped with an incident-beam graphite monochromator. All diffraction data were collected at room temperature.

All crystallographic calculations were facilitated by the CRYM crystallographic computer system.[13] A trial structure was obtained by using conventional Patterson and Fourier techniques. This trial structure routinely refined to a final R index ($R = \sum||F_o| - |F_c||/\sum|F_o|$) of 0.078. The final cycles of full-matrix least-squares refinement contained the nonhydrogen coordinates in one matrix and the nonhydrogen anisotropic temperature factors, scale factor, and secondary extinction coefficient in a second matrix. The shifts calculated in the final cycle of refinement were in every case less than one-tenth the corresponding standard deviation. Hydrogen positions were calculated where possible. Methyl hydrogens were located by difference Fourier techniques. While the hydrogen parameters were added to the structure factor calculations during the later stages of refinement, they were not refined. A final difference Fourier revealed no missing or misplaced electron density. A stereoview of the molecule is given in Figure 1. Other pertinent crystallographic data are included as supplementary material.

Supplementary Material Available: Crystallographic data including coordinates and anisotropic temperature factors for nonhydrogen atoms, hydrogen coordinates, distances, and angles (2 pages). Ordering information is given on any current masthead page.

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Received March 27, 1980

Reaction Modes of Fluorination of Cyclic Ethers by Potassium Fluoride-18-Crown-6

Summary: The reaction scheme of the chlorine substitution of epichlorohydrin or 3,3-bis(chloromethyl)oxetane by

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(13) D. J. Duchamp, American Crystallographic Association Meeting, Bozeman, MT, 1964, paper B-14, p 29.

0022-3263/80/1945-3930$01.00/0

Table I. Synthesis of Halomethyl Cyclic Ethers in the Presence of 18-CR-6[a]

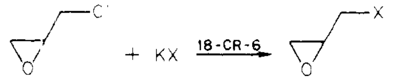
reaction	chloromethyl compd (g)	KX (g)	18-CR-6/KX, mol %	temperature, °C	solvent (mL)	time, h	product (% yield)
1	**1** (1.45)	KF (1.30)		215[b]		2	**2** (5)
2	**1** (9.11)	KF (10.34)	1.1	60	CH_2Cl_2 (20)/H_2O (20)	24	**2** (1)
3	**1** (1.13)	KF (1.09)	2.6	80	C_6H_6 (10)/H_2O (10)	24	**2** (8)
4	**1** (1.16)	KF (1.10)	2.2	100	C_7H_8 (11)/H_2O (11)	24	**2** (6)
5	**1** (1.09)	KF (1.20)	2.2	50	CH_3CN (10)	24	**2** (3)
6	**1** (2.92)	KF (2.92)	2.2	80	C_6H_6 (20)	24	**2** (9)
7	**1** (3.00)	KF (3.00)	1.1	100		23	**2** (54)[c]
8	**1** (12.48)	KF (12.77)	1.3	reflux		21	**2** (44)[c]
9	**1** (6.20)	KF (6.10)	2.2	reflux		23	**2** (47)[c]
10	**1** (12.18)	KF (10.03)	1.2	100		23	**2** (56)[d]
11	**1** (20.22)	KF (20.00)	0.9	reflux		23	**2** (45)[d]
12	**1** (20.23)	KF (20.02)	0.9	reflux		46	**2** (18)[d,e]
13	**1** (3.25)	KBr (4.00)	4.5	100		23	**6** (36)
14	**1** (2.82)	KI (5.07)	6.3	100		1.5	**7** (6)
15	**1** (2.82)	KI (5.07)	6.3	100		23	**7** (5)[f]
16	**1** (1.51)	KI (2.84)	6.4	50		3	**7** (20)
17	**1** (1.51)	KI (2.84)	6.4	50		6	**7** (42)
18	**3** (3.38)	KF (3.85)	6.4	100		8	**4** (6) + **5** (0)
19	**3** (3.38)	KF (2.85)	6.4	100		23	**4** (35) + **5** (18)

[a] The reaction was started by mixing all the reagents. [b] In an autoclave. [c] An unidentified side product, presumably a ring-opening product, was observed (15-25%) in the gas chromatogram. [d] Under nitrogen with dried reagents, only 1-2% of the side product was formed. [e] With prolonged reaction time, the formed **2** was polymerized to lower the yield. [f] Reaction system became very viscous.

potassium fluoride–18-crown-6 was elucidated by the aid of selectively deuterated compounds.

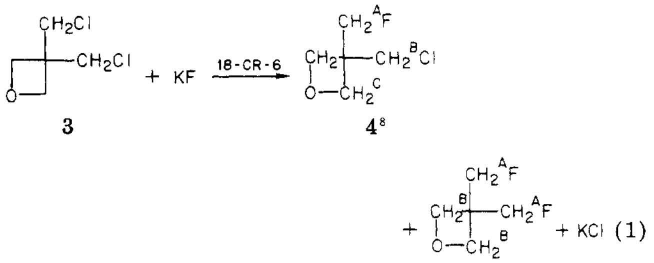
Sir: Epichlorohydrin (**1**) was reported to give new substituted methyloxiranes by nucleophilic attack.[1] Fluoride ion (F^-) solvated by a crown ether[2,3] or poly(ethylene glycol)–acetonitrile[4] was shown to be a strong nucleophile in aprotic organic solvents.

Epifluorohydrin (**2**) has been synthesized under vigorous conditions from **1** and potassium fluoride (KF) in polyhydroxylic solvents[5,6] at 180–200 °C or in an autoclave under pressure at 220 °C.[7] However, the yield was generally poor, ranging from 30 to 40%. We have found that direct displacement of the chlorine atom of **1** by F^- gave **2** in reasonable yield in the presence of catalytic amounts of 18-crown-6 (18-CR-6) without solvents. This procedure has some general utility for interconversion of a halomethyl cyclic ether into another halomethyl cyclic ether. Thus, epibromohydrin (**6**), epiiodohydrin (**7**), and (fluoromethyl)oxetanes could be synthesized by this procedure. The reactivity of the potassium salt seems to be in the order KI > KBr > KF > KCl. The reaction scheme for 3,3-bis(chloromethyl)oxetane (**3**) is shown in eq 1. The results are shown in Table I.



1

2, X = F
6, X = Br
7, X = I



3 **4**[8] **5**[8]

Table II. Catalytic Activity of Amine and Polyethers in the Synthesis of **2**[a]

no.	**1**, g	KF, g	catalyst (g)	yield, %
1	20.22	20.00	18-CR-6 (0.85)	60
2	2.13	1.86	TMED (0.19)	1
3	2.00	2.20	pentaglyme (0.20)	1
4	2.03	2.05	PEG-100 (0.20)	5
5	2.03	2.00	DME (0.20)	1

[a] Under reflux conditions for 23 h. TMED = *N,N,N′,N′*-tetramethylethylenediamine, PEG = poly(ethylene glycol), DME = 1,2-dimethoxyethane.

The yield and selectivity of the reaction depends very much on anhydrous conditions in the bulk reaction. Dried reagents under nitrogen atmosphere gave reasonable yields and less side products (reactions 10, 11; Table I). The product can be isolated by simple distillation under vacuum followed by fractional distillation at ordinary pressure. The phase-transfer reactions (reactions 2–4) were messy and usually gave poor yields and large amounts of side products, although the initial disappearance of **1** was faster than the bulk reactions. Both **6** and **7** could be synthesized by this method, but in the case of **7**, the reaction time should be chosen properly to prevent further reaction giving a complex mixture of reaction products including polymeric material (reactions 14, 15). Lowering the reaction temperature may be better (reactions 16, 17). In the case of **3**, unsymmetrically substituted oxetane **4** could be selectively synthesized by using shorter reaction time. Longer reaction time gave the mixture of **4** and **5**. The catalytic activity of tertiary amine and linear polyethers

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(1) D. E. McClure, B. H. Arison, J. J. Baldwin, *J. Am. Chem. Soc.*, **101**, 3666 (1979).

(2) C. L. Liotta, H. P. Harris, *J. Am. Chem. Soc.*, **96**, 2250 (1974).

(3) T. A. Bianchi, L. A. Cate, *J. Org. Chem.*, **42**, 2031 (1977).

(4) T. Kitazume, N. Ishikawa, *Chem. Lett.*, 283 (1978).

(5) G. Olah, A. Pavlath, *Acta Chim. Acad. Sci. Hung.*, **3**, 425 (1953).

(6) E. D. Bergmann, S. Cohen, *J. Chem. Soc.*, 2259 (1958).

(7) F. L. Pattison, J. J. Norman, *J. Am. Chem. Soc.*, **79**, 2311 (1957).

(8) **4**: NMR ($CDCl_3$) δ 3.92 (s, 2 H, H^B, 4.49 (d, 2 H, H^C, $J_{(HCCCH_2F,\ trans)} = 1.4$ Hz), 4.50 (s, 2 H, H^C, J_{HH} and $J_{(HCCCH_2F,\ cis)} < J_{(HCCCH_2F,\ trans)}$, 4.73 (d, 2 H, H^A, $J_{HCF} = 47.2$ Hz). **5**: NMR ($CDCl_3$) δ 4.58 (q, 4 H, H^B, $J_{(HCCCH_2F)} = 1.4$ Hz, 0.8 Hz), 4.73 (d, 4 Hz, H^A, $J_{HCF} = 48.0$ Hz). Analyses of the ^1H NMR spectra of **1**, **6**, and **7** were reported.[9-11]

(9) W. A. Thomas, *J. Chem. Soc. B*, 1187 (1968).

(10) J. L. Pierre, P. Arnand, *Bull. Soc. Chim. Fr.*, 2868 (1969).

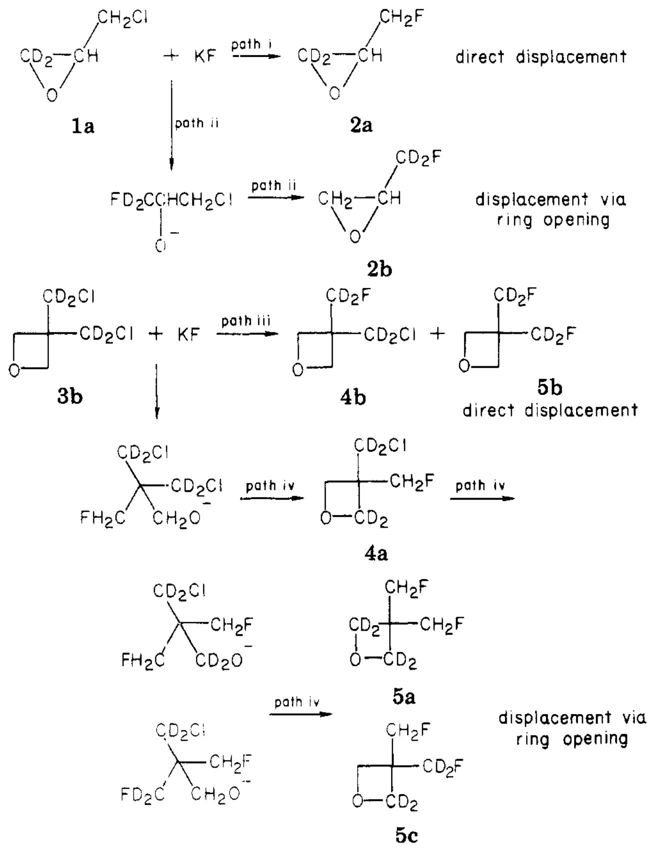
(11) C. L. Macdonald, W. F. Reynolds, *Can J. Chem.*, **48**, 1046 (1970).

Table III. Stereochemistry of Chlorine Substitution of Cyclic Ethers by KF in the Presence of 18-Crown-6

no.	starting material	temperature, °C	time, h	% conversion	product ratio
1[a]	**1a**	100	3	10	**2a**:**2b** = 50:50[d]
2[b]	**3b**	100	17	40	**4a**:**4b**:**5a**:**5b**:**5c** = 0:8:0:32:0
3[c]	**3b**	100	20	52	**4a**:**4b**:**5a**:**5b**:**5c** = 0:27:0:25:0

[a] **1a**, 0.1566 g; KF, 0.2235 g; 18-CR-6, 0.0489 g. [b] **3b**, 0.0620 g; KF, 0.0474 g; 18-CR-6, 0.0053 g. [c] **3b**, 0.0500 g; KF, 0.0572 g; 18-CR-6, 0.0087 g. [d] Unreacted **1** was converted into a 50:50 mixture of **1a** and **1b**.

Scheme I



was also studied. As can be seen in Table II, only crown ether has high catalytic activity.

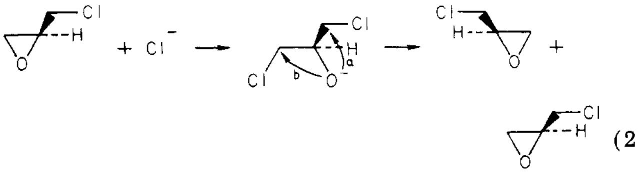
Two distinct reaction paths may be considered for the formation of fluoromethylated compounds (Scheme I).

The reaction mechanism can be determined by studying the deuterium incorporation in the product starting from selectively deuterated 1-chloro-2,3-epoxypropane-*3,3*-d_2 (**1a**)[12] or 1-chloro-2,3-epoxypropane-*1,1*-d_2 (**1b**) and 3,3-bis(chloromethyl-d_2)oxetane (**3b**).[12] The direct displacement should give **2a** from **1a** and **4b** from **3b** as initial products; on the other hand, **2b** from **1a** and **4a** from **3b** should be formed through a ring-opening mechanism. The back reaction from **2** to **1** was proved to be slow.

The results of the stereochemistry of the chlorine displacement reactions are shown in Table III.

In the case of **3**, deuterium in fluorinated oxetanes is seen only in the side chain (**4b**, **5b**) and not in the ring. It can be concluded that only direct displacement by F^- occurred. In the case of **1**, deuterium was found both in the ring (**2a**) and side chain (**2b**), almost in the same ratio. Moreover, recovered **1** (starting from 99% **1a** and 1% **1b**) was changed into an equimolar mixture of **1a** and **1b**. This fact indicates that the deuterium scrambling between ring (**1a**) and side chain (**1b**) is faster than the chlorine displacement by F^-. This process corresponds to racemization in optically active **1**. We feel that caution has to be taken in discussing the reaction mechanism of epichlorohydrin substitution. Absence of racemization is an essential requirement.[1]

At present, we can not determine the exact reaction paths of fluorination of epichlorohydrin. If we assume that the recemization proceeds via ring-opening, namely, that reaction paths a and b in eq 2 occur at the same rate, it is quite likely that both direct displacement and displacement via ring opening occurred in the case of **1**.


(2)

Registry No. 1, 106-89-8; **1a**, 42329-11-3; **2**, 503-09-3; **2a**, 74465-73-9; **2b**, 74465-74-0; **3**, 78-71-7; **3b**, 74465-75-1; **4**, 74465-76-2; **4b**, 74465-77-3; **5**, 338-61-4; **5b**, 74465-78-4; **6**, 3132-64-7; **7**, 624-57-7; 18-CR-6/KF, 38348-17-3; 18-CR-6/KBr, 38348-12-8; 18-CR-6/KI, 38348-19-5.

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Received March 7, 1980

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[12] The syntheses of these compounds will be published elsewhere.