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A Facile Synthesis of Fluorochlorobromoacetic Acid**

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Abstract. Fluorochlorobromoacetic acid was sythesized in the sequence of four steps from 1,1,2-trifluoro-2-chloroethylene in an overall yield of approximately 25%. 1,1,2-Trifluoro-2-chloroethylene was first allowed to react with sodium methoxide to form 1,2-difluoro-1-chloro-2-methoxyethylene, which was then brominated with elemental bromine and the reaction product treated with concentrated sulfuric acid to give methyl fluorochlorobromoacetate. This compound was hydrolized with a diluted sodium hydroxide solution to fluorochlorobromoacetic acid.

Keywords. Fluorochlorobromoacetic acid; 1,1,2-Trifluoro-2-chloroethylene, bromination; 1,2-Difluoro-1-chloro-2-methoxyethylene.

Eine einfache Synthese von Fluorchlorbromessigsäure

Zusammenfassung. Fluorchlorbromessigsäure wurde aus 1,1,2-Trifluor-2-chlorethylen in vier Stufen mit einer Gesamtausbeute von ca. 25% hergestellt. 1,1,2-Trifluor-2-chlorethylen wurde zuerst mit Natriummethoxid zu 1,2-Difluor-1-chlor-2-methoxyethylen umgesetzt, das dann mit elementarem Brom bromiert wurde. Das Reaktionsprodukt daraus ergab nach Behandlung mit konzentrierter Schwefelsäure Methyl-fluorchlorbromacetat, das nach Hydrolyse mit verdünnter Natronlauge zur Zielverbindung führte.

Introduction

Fluorochlorobromoacetic acid (*FCBAA*) is one of the simplest perhaloacetic acids, it is a racemate and capable of being separated into its antipodes. Although perhaloacetic acids are of considerable theoretical interest little efforts have been undertaken to study them in detail, especially in their optically active form. Of the three possible perhaloacetic acids (*XYZ*CCOOH) based on fluorine, chlorine, bromine and iodine as the halogen substituents, only fluorochlorobromoacetic acid (*FCBAA*) has been mentioned in the literature. The first and only reported synthesis of *FCBAA* was carried out by F. Swarts in the late 1890's and involved the substitution of a fluorine atom for a bromine atom in chlorodibromoacetic acid derivatives [1–3]. This method is somewhat complicated and not suitable for the preparation of larger amounts of *FCBAA*.

** This paper is dedicated to Professor Karl Schlögl on the occasion of his 65th birthday with warmest personal wishes

The optical resolution of *FCBAA* was also attempted, however, the optically active free acid could not be isolated, which was attributed to its tendency to racemize [1–3].

Our interest in the preparation of *FCBAA* results from its potential use as an intermediate in the synthesis and polymerization of optically active fluorochlorobromoacetaldehyde and the synthesis of optically active fluorochlorobromomethane [4–7].

It is the objective of this work to develop a facile synthesis for the preparation of *FCBAA* in large quantities and to characterize it, as well as its intermediate by infrared, ^{1}H, ^{13}C, and ^{19}F NMR spectroscopy.

Experimental Part

Materials

1,1,2-Trifluoro-2-chloroethylene was obtained from Specialty Chemicals. All other chemicals were obtained from the Aldrich Chemical Company and were used as received. The use of Aldrich anhydrous-grade solvents (using the "sure seal" system) was found to be adequate for all reactions.

Measurements

Infrared spectra were recorded on Perkin-Elmer Model 1320 or Shimadzu IR-435 spectrophotometers. Liquid samples were measured as 5% *w/w* samples in CCl_4 using matched KBr liquid cells. Peak assignments were made to the nearest 5 cm^{-1}.

^{1}H NMR spectra were recorded on a JEOL JNM-FX 90Q multinuclear FT NMR spectrometer on a Varian FM 390 NMR spectrometer.

^{13}C NMR spectra were recorded on a JEOL JNM-FX 90Q multinuclear FT NMR spectrometer with complete proton decoupling. Common instrument parameters used during the acquisition of spectral data included a pulse width of 12 µs, a pulse delay of 10 seconds, and an acquisition time of 0.68 seconds.

^{19}F NMR spectra were recorded on a JEOL JNM-FX 90Q multinuclear FT NMR spectrometer.

Gas chromatograms were obtained with a Varian Associates model 920 Gas Chromatograph. The following packed columns were used: 36% *w/w* diisodecyl phthalate coated on Chromosorb W (100/120 mesh), 20% *w/w* DC-200 silicon oil on Anakrom AS (70/80 mesh), 10% *w/w* Carbowax on Anakron AS (70/80 mesh), and 10% *w/w* FFAP on Anakrom AS (70/80 mesh).

Melting points were determined on a MEL-TEMP capillary melting point apparatus and are uncorrected.

Microanalysis were carried out by the Microlytis Laboratory, South Deerfield, MA. The halogens were determined using three instrumental procedures after Schoeninger oxygen flask decompositions of the sample had been performed: (1) Ion chromatographic procedures were employed for the determination of fluoride content. (2) Potentiometry using a bromide ion selective electrode enabled the determination of bromide content. (3) By determining the "total halide" content through the use of silver coulombetry, the chloride content could be determined by subtraction of the bromide content previously determined.

Preparation of Intermediates

1,1-Difluoro-2-chloro-1-methoxyethylene (DFCME). Synthesis of DFCME by in-situ generation of sodium methoxide. A typical procedure is as follows: A dry 5 liter, 3-neck, roundbottom flask was equipped with a mechanical stirrer, Dewar condenser, Claisen adaptor, thermometer, and a pressure equalizing funnel. The system was flushed through the Dewar condenser with dry nitrogen, and the nitrogen flow was monitored by a bubbler. The roundbottom flask was charged with 2.8 liters of anhydrous diethylene glycol dimethyl ether (diglyme). The pressure addition funnel was charged with anhydrous methanol (87 ml, 69 g, 2.16 mol). Sodium metal (39 g, 1.71 mol) was cut under hexanes and added to the reaction vessel. Using a heating mantle, the reaction temperature was raised to 120°C. The sodium metal melted and now existed in the form of small droplets. Methanol was added dropwise over a 2-hour period, during which time hydrogen gas was evolved and a fine white precipitate was formed. (Caution: The reaction must be carried out in a well-ventilated hood to effectively remove the hydrogen gas.) When sodium metal had been consumed, the Claisen adaptor was replaced by an inlet adaptor. The reaction mixture was heated to reflux (diglyme b. p. = 162°C) and much of the excess methanol was removed with a stream of dry nitrogen. This process took 45 min, and more than 50 ml of diglyme were also removed. The heating mantle was removed and the contents of the reaction flask were cooled to 45°C. Gaseous 1,1,2-trifluoro-2-chloroethylene (*TFCE*, b. p. = − 27°C) was condensed in a dry ice/acetone-filled Dewar condenser and added over a 1.5-hour period by allowing it to slowly evaporate. The addition of *TFCE* was adjusted such that the resulting exothermic reaction reached but did not exceed a maximum temperature of 85°C. The reaction mixture was allowed to cool to room temperature, the mechanical stirrer removed and replaced with a flow control adaptor and the reaction vessel connected to a 100 ml roundbottom flask. The Dewar condenser was connected to the reaction flask through the lower gas inlet using rubber tubing. A vacuum line was fitted to the upper gas inlet of the Dewar condenser, and the 100 ml collecting flask was immersed in a dry ice/acetone bath. The pressure was slowly reduced to 15 mm Hg and the reaction vessel was warmed using a heating mantle to keep the temperature of the mixture at 25°C. About 30 ml of a clear colorless liquid was collected in the 100 ml roundbottom flask (Fraction I). A second fraction was collected in the 250 ml roundbottom flask when the pressure of the system was slowly reduced to 1.5 mm Hg and the reaction vessel was warmed to 60°C. During this operation, about 100 ml of a clear colorless liquid was collected. Fractions I and II were combined and distilled under dry nitrogen at ambient pressure to yield 93 g, 0.73 mol, b. p. = 56–64°C; 43% yield (based on sodium metal). Gas chromatography showed the distillate to consist of 96% *DFCME*, 3% 1-chloro-2-methoxy-1,2,2-trifluoroethane (*CMTFE*) and three unknown peaks, which totaled 1%.

Purified *DFCME* was obtained by redistilling *DFCME* through a 15 cm Vigreux column fitted with a variable reflux distillation head. The center fraction boiled at 58.5°C and was analyzed by gas chromatography; it was 98.5% pure.

The infrared spectrum showed absorptions at 2980 cm^{-1} and 2950 cm^{-1} (C−H stretching), 1755 cm^{-1} (C=C stretch). The ^{1}H NMR spectrum (neat) showed a complex multiplet centered at 3.8 ppm ($-OCH_3$) (Fig. 1). The ^{13}C NMR spectrum (*acetone-d*$_6$) showed δ: 60.57, 60.77, 60.97 ppm ($-OCH_3$), 11.20, 118.46, 120.94, 121.47, 130.47, 131.06, 133.61, 133.74 ppm ($FClC=CFOCH_3$), and 142.68, 144.25, 144.57, 146.46, 154.95, 156.37, 156.58, 158.28 ppm ($FClC=CFOCH_3$). The ^{19}F NMR spectrum (benzene-d_6, $CFCl_3$ internal standard) was measured using a 30030 Hz window (347 ppm full width) and showed δ: −105.57, −106.01, −133.48, and −133.91 ppm ($=CFOCH_3$), and −119.75, −121.14, −139.22, and −140.61 ppm ($FClC=$).

Elem. Anal.: Calcd. for $C_3H_3ClF_2O$: C 28.04%, H 2.36%. Found: C 27.85%, H 2.31%.

The scale-up of the *DFCME* synthesis was carried out using the same general procedure as described above. It gave consistently a 45–55% yield of *DFCME* at purities of 98–99%.

Using commercial grade sodium methoxide from a freshly opened bottle gave *DFCE* in an overall yield of 26% with a purity of 75% with 25% chloro-2-methoxy-1,2,2-trifluoroethylene (*CMTFE*).

1-Chloro-2-methoxy-1,2-trifluoroethane (CMTFE). A 100 ml 3-neck, roundbottom flask was equipped with a magnetic stirrer, thermometer, and a Dewar condenser. The system was flushed through the Dewar condenser with dry nitrogen while the nitrogen flow was monitored by a bubbler. The flow was charged with anhydrous methanol (20 ml, 15 g, 0.49 mol), potassium hydroxide (1.4 g, 24 mmol), placed in an oil bath, and warmed to 50°C. 1,2,2-Trifluoro-2-chloroethylene (*TFCE*) was condensed on the dry ice/acetone-filled Dewar condenser and liquid *TFCE* was added dropwise to the reaction flask. The reaction was monitored by GC. After one hour, GC showed a 75% conversion, based on methanol consumption. After two hours, the conversion was found to be 95%, and after three hours a 98^{+}% conversion was obtained. The reaction was stopped and the potassium hydroxide suspension was filtered under dry nitrogen pressure. The yield of crude *CMTFE* was 61 g (0.42 mol), 85% of the theoretical yield; it was distilled through a 15 cm Vigreux column.

The main fraction (b.p. 71–71.5°C) was pure *CMTFE* (99%), and forecut showed a trace of *DFCME*. The yield after distillation (including the forecut) was 57 g, 0.39 mol (79%). The infrared spectrum showed absorptions at 3000 cm^{-1}, 2960 and 2850 cm^{-1} (C$-$H stretching), 1450 cm^{-1} (O$-$CH$_3$ stretching), 1370 to 1090 cm^{-1} (C$-$F stretching). The ^{1}H NMR spectrum (neat) showed δ: 3.70 ppm (CH$_3$O$-$, 3 H) and two triplets centered at 5.80 and 6.35 ppm (HFClC$-$, 1 H). The ^{13}C NMR spectrum (acetone-d_6, proton decoupled) showed 51.50, 51.82, and 52.15 ppm (CH$_3$O$-$), 89.03, 90.92, 92.81, 100.06, 101.95, 103.84 ppm (HFClC$-$), and 108.28, 109.39, 120.03, 121.21, 131.84, 132.95 ppm ($-$CF$_2-$). The ^{19}F NMR spectrum (benzene-d_6, CFCl$_3$ internal reference) was measured using a 30030 Hz window (347 ppm full width) and showed δ: -90.53 ppm ($-$CF$_2-$) and -152.96, -153.57 ppm (HFClC$-$).

Elem. Anal.: Calcd. for $C_3H_4ClF_3O$: C 24.26%, H 2.72%. Found: C 23.98%, H 2.65%.

1,2-Difluoro-2-chloro-1,2-dibromo-1-methoxyethane (DFCDM). A typical bromination procedure is as follows: A dry 250 ml 3-neck, roundbottom flask was equipped with a magnetic stirrer, a pressure addition funnel, a thermometer, and a flow control adaptor which was fitted with an argon-filled balloon. The flask was charged with *DFCME* (85 g, 0.66 mol) and carbon tetrachloride (65 ml), and the funnel was charged with bromine (106 g, 0.66 mol). The flask was cooled in an ice bath, and the bromine was added dropwise over a 75-minute period. Carbon tetrachloride was removed by distillation through a 15 cm Vigreux column at atmospheric pressure. Distillation was continued at reduced pressure; the main fraction boiled at 75–77°C/45 mm Hg. Yield of the clear colorless *DFCDM* (173 g, 0.60 mol) was 91% of the theoretical amount.

The infrared spectrum showed absorptions at 3000 cm^{-1}, 2940 cm^{-1}, and 2840 cm^{-1} (C$-$H ($-$OCH$_3$), 89.35, 103.86 ppm (FClBrC$-$), and 161.80, 163.04 ppm ($-$COOCH$_3$). The ^{19}F NMR 1010 cm^{-1} (C$-$F stretching). The ^{1}H NMR spectrum showed δ: 3.85 ppm ($-$OCH$_3$). The ^{13}C NMR spectrum (acetone-d_6) showed δ: 56.72, 56.98, 57.18 ppm ($-$OCH$_3$), 98.75, 98.95, 100.25, 100.45, 112.52, 112.85, 114.03, 114.29 ppm (FClBrC$-$), and 111.41, 112.85, 124.86, 126.30 ppm ($-$CFBrOCH$_3$). The ^{19}F NMR spectrum (benzene-d_6, CFCl$_3$ internal reference) showed δ: -59.48, -59.66, -62.00, -62.22 ppm [$-$CFBr(OCH$_3$)], and -65.70, -65.87, -66.35, -66.52 ppm (FClBrC$-$).

Elem. Anal.: Calcd. for $C_3H_3Br_2ClF_2O$: C 12.50%, H 1.05%. Found: C 12.58%, H 1.04%.

In several additional brominations the yields were 85–90%.

Methyl fluorochlorobromoacetate (MFCBA). General procedure. A 250 ml roundbottom flask was equipped with a magnetic stirrer, a 125 ml pressure equalizing addition funnel, and a flow control adaptor which was fitted with an argon-filled balloon. The flask was charged with sulfuric acid (93 ml, 170 g, 1.74 mol) (Fisher reagent grade from a freshly opened bottle) and was cooled to 0°C in an ice bath. The funnel was charged with *DFCDM* (167 g, 0.59 mol) which was added over a 30-minute period to the cilled sulfuric acid. The light-orange solution was then transferred to a 10° ± 1°C water bath. The two-phase system was stirred for 4 hours at 10°C. Work-up was done by pouring the dark fuming reaction mixture into 1.8 l of ice. The dense, cherry-red organic phase was separated and dried over magnesium sulfate; it gave a crude yield of 111 g, 0.54 mol (93%). The product was analyzed by GC which showed it to be of 98% purity. Distillation through a 15 cm Vigreux column gave a main fraction of *MFCBA* (97 g, 0.47 mol), boiling at 67.5°C and 65 mm Hg, which was obtained in 81% yield at a purity of $>99\%$.

The infrared spectrum showed absorptions at 3100 cm^{-1}, 2940 cm^{-1}, and 2840 cm^{-1} (C$-$H stretching), 1770 cm^{-1} (C=O stretching), 1430 cm^{-1} (C$-$F stretching). The ^{1}H NMR spectrum (neat) showed δ: 4.0 ppm ($-$OCH$_3$). The ^{13}C NMR spectrum (acetone-d_6) showed δ: 55.61 ppm ($-$OCH$_3$), 89.35, 103.86 ppm (FClBrC$-$), and 161.80, 163.04 ppm ($-$COOCH$_3$). The ^{19}F NMR spectrum (benzene-d_6, CFCl$_3$ internal reference, 15015 Hz window, 178 ppm full width) showed δ: -64.13 ppm (FClBrC$-$).

Elem. Anal.: Calcd. for $C_3H_3BrClFO_2$: C 17.54%, H 1.48%. Found: C 17.56%, H 1.48%.

Several additional runs in 0.5 mol quantities gave *MFCBA* in 80–85% yield. In a separate study, it was shown that the reaction was essentially complete in 1 hour (97%); after 3 hours the conversion was >99%.

Fluorochlorobromoacetic acid (FCBAA). Typical hydrolysis experiments proceeded as follows: A 250 ml roundbottom flask was equipped with a magnetic stirrer and a flow control adaptor which was fitted with an argon-filled balloon. The flask was charged with 1.0 *M* aqueous potassium hydroxide (140 ml), which was cooled in an ice bath to 3°C. Methyl fluorochlorobromoacetate (*MFCBA*) (24.6 g, 0.12 mol) was added over a 5-minute period where whereby a two-phase system formed; *MFCBA* was essentially hydrolyzed in 10 minutes, but the mixture continued to be stirred for an additional 30 minutes in the ice bath. The mixture was acidified with sulfuric acid (8.5 g, 0.09 mol) in 25 ml of distilled water. The aqueous solution was extracted with diethyl ether in a continuous liquid/liquid extractor for one day. The diethyl ether solution was dried over magnesium sulfate, filtered, and concentrated on a rotary evaporator under reduced pressure. The residue was distilled through a 15 cm Vigreux column reflux distillation head at 15 mm Hg. *FCBAA* was obtained as a clear colorless liquid (22 g, b. p. = 70–80°C/15 mm Hg). The distillate was analyzed by ^{1}H NMR spectroscopy which showed it to consist of 93% *FCBAA* and 7% of diethyl ether. The overall yield of *FCBAA* was 20 g, 0.11 mol (89% of theory). In several additional hydrolysis experiments, *FCBAA* was routinely obtained in 85–90% yield.

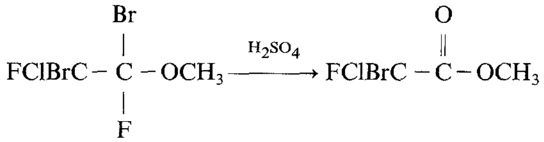
Pure *FCBAA* was obtained more easily by dichloromethane extraction of the aqueous phase (b. p. = 65°C/6 mm Hg; purity = 99%). The infrared spectrum of *FCBAA* showed absorption at 2900 cm^{-1} (O−H stretch, broad), 1750 cm^{-1} (C=O, stretch), 1415 cm^{-1} (O−H bending). The ^{1}H NMR spectrum (neat) showed δ: 11.6 ppm (−COOH). The ^{13}C NMR spectrum (acetone-d_6) showed δ: 89.91, 103.65 ppm (FClBrC−) and 161.74, 162.98 ppm (−COOH). The ^{19}F NMR spectrum (acetone-d_6, $CFCl_3$ internal reference) showed δ: −63.70 ppm (FClBrC−).

Results and Discussion

Fluorochlorobromoacetic acid was synthesized in a four-step process from 1,1,2-trifluoro-2-chloroethylene. Reaction of the 1,1,2-trifluoro-2-chloroethylene (*TFCE*) with commercially available sodium methoxide (from a freshly opened bottle) resulted in a 80/20 mixture of the substitution product *DFCME* and the saturated addition product 1-chloro-2-methoxy-1,2,2-trifluoroethane (*CMTFE*).

$$NaOCH_3 + FClC{=}CF_2 \xrightarrow{Diglyme} FClC{=}CFOCH_3$$

$$FClC{=}CFOCH_3 \xrightarrow[CCl_4]{Br_2} FClBrC{-}CFBrOCH_3$$



$$FClBrC-\underset{\displaystyle F}{\overset{\displaystyle Br}{C}}-OCH_3 \xrightarrow{H_2SO_4} FClBrC-\overset{\displaystyle O}{\overset{\|}{C}}-OCH_3$$

$$FClBrCCOOCH_3 \xrightarrow[0°C]{10\%\ KOH,\ H_2SO_4} FClBrCCOOH$$

The overall yield of *DFCME* using this procedure was about 25%. We greatly modified the procedure of Meier and Bohler [8] by freshly preparing alcohol-free

Table 1. ^{13}C NMR spectral data of 1,2-difluoro-2-chloro-1-methoxyethylene (acetone-d_6; *TMS*).
$FClC=CFOCH_3$
Carbon type 1 2 3

Carbon type	$^2J_{CF}$		Average		$^1J_{CF}$ (Hz)
	(ppm)	(Hz)	(ppm)	(Hz)	
2	158.28	42.65	157.34	3 545.13	266.20
2	156.39				
2	146.46	42.65	145.52	3 278.93	
2	144.57				
2	156.58	36.77	155.77	3 509.83	277.23
2	154.95				
2	144.25	35.30	143.47	3 232.60	
2	142.68				
1	133.74	73.54	132.11	2 976.70	276.42
1	130.47				
1	121.47	73.54	119.84	2 700.21	
1	118.20				
1	133.61	57.35	132.34	2 981.85	284.58
1	131.06				
1	120.94	55.89	119.70	2 697.27	
1	118.46				
3	60.96	Four overlapping peaks			
3	60.77				
3	60.57				

methoxide in diglyme. Liquid *TFCE* was added over a two-hour period and gave *DFCME* in about 50% yield based on sodium metal in a purity (by GC) as high as 99%. A number of reactions were carried out ranging in size from 0.25 mol to 1.70 mol of sodium metal. Low yields of *DFCME* seem to be caused by the physical occlusion of suspended sodium methoxide by sodium fluoride, which is generated during the reaction. ^1H, ^{13}C, and ^{19}F spectroscopic studies show that *DFCME* is a mixture of *cis* and *trans* isomers.

Meier and Bohler [8] reported the synthesis of 1,2-difluoro-2-chloro-1-ethoxyethylene (*DFCFE*) in a one pot reaction starting from *in situ* generation of sodium ethoxide in diethyl ether. Their method suffers from the impractical addition of gaseous *TFCE* (4 days) and the presence of excess ethanol, which gave about 15% 1-chloro-2-ethoxy-1,2,2-trifluoroethane (*CETFE*) as a byproduct.

As reported by Sheppard and Sharts [9], nucleophilic attack on unsymmetrical fluorohaloolefins almost always occurs on the $=CF_2$ group because: (a) the largest induced positive charge is on a carbon atom bearing two fluorine atoms, (b) steric repulsion is least on the $=CF_2$ group, and (c) chlorine or other halogen atoms in the β-position can stabilize an α-negative charge by d orbital resonance and inductive electron withdrawal.

The infrared spectrum of *DFCME* shows the inductive effect of fluorine on the carbon carbon double bond by the high frequency of 1 755 cm^{-1}. The ^1H NMR

Table 2. ^{19}F NMR spectral data of 1,2-difluoro-2-chloro-1-methoxyethylene (benzene-d_6; $CFCl_3$).
$FClC=CFOCH_3$
Fluorine type 1 2

Fluorine type	Isomer	ppm	$^3J_{FF}$ (Hz)
1	*cis*	−105.57	36.66
1	*cis*	−106.01	
1	*trans*	−119.75	117.30
1	*trans*	−121.14	
2	*cis*	−133.48	36.66
2	*cis*	−133.91	
2	*trans*	−139.92	117.31
2	*trans*	−140.61	

spectrum (neat) shows the $-OCH_3$ group as a complicated multiplet (centered at 3.8 ppm). The multiplicity of this peak is due to the presence of *cis* and *trans* isomers and proton/fluorine coupling. The ^{13}C NMR spectrum shows the $-OCH_3$ resonance of *DFCME* as three peaks of two overlapping doublets. The observed multiplet is due to carbon/fluorine coupling and the presence of *cis*/*trans* isomers in the *DFCME*. The ^{13}C NMR spectrum of the vinyl carbon atoms of *DFCME* shows the expected 16 peaks; 8 peaks for $FClC=$ ranging from 118.20 to 133.74 ppm and $H_3COFC=$ ranging from 142.68 to 158.28 ppm (Table 1). The ^{19}F NMR spectrum of *DFCME* shows a total of 8 peaks, 4 for each *cis*/*trans* isomer; the chemical shift values are tabulated in Table 2.

The base catalyzed addition of methanol to *TFCE* had been improved over the literature procedure [10]; it resulted in an 85% yield of *CMTFE*. Like the *DFCME* synthesis, the nucleophile added exclusively to the carbon atom substituted with two fluorine atoms [10–14].

The ^{1}H NMR spectrum (neat) of *CMTFE* shows the $-OCH_3$ proton as a singlet at 3.70 ppm. The $FClHC-$ proton is split into a doublet of triplets centered at 5.80 and 6.35 ppm. The coupling constants are $^2J_{FH} = 49.5$ Hz and $^3J_{FH} = 4.5$ Hz. The ^{13}C NMR spectrum of *CMTFE* was analyzed and shows a total of 15 peaks, which is the theoretical amount. The results are shown in Table 3. The ^{19}F NMR spectrum (benzene-d_6) of *CMTFE* shows the $-CF_2-$ fluorine atoms as a singlet at -90.53 ppm and the $-CFOCH_3$ fluorine atom as a doublet of -152.96 and -153.57 ppm, $^2J_{FH} = 51.32$ Hz. Expanding the $-CFHOCH_3$ fluorine resonance by a factor of 10 indicated the presence of fine structure due to fluorine/fluorine coupling. Vicinal fluorine/fluorine coupling constants range between 15.7 and 24.6 Hz [13] and are not observed in this spectrum since a 30 030 Hz window was used.

Kane and coworkers [14] described the dehydrofluorination of *CMTFE* by heating neat *CMTFE* to reflux with powdered potassium hydroxide for 22 hours; they obtained *DFCME* in 22% yield. We have followed this procedure and monitored the reaction conversion by GC. The GC analysis showed a 10% conversion to *DFCME* was obtained after 2 hours of heating, but prolonged heating caused no increase in the reaction conversion. A number of dehydrofluorinating techniques

Table 3. ^{13}C NMR spectral data of 1-chloro-2-methoxy-1,2,2-trifluoroethane (benzene-d_6; *TMS*).

$FClHC-CF_2OCH_3$
Carbon type 1 2 3

Carbon type	$^2J_{CF}$		Average		$^1J_{CF}$ (Hz)
	(ppm)	(Hz)	(ppm)	(Hz)	
2	132.95	25.00	132.40	2 983.32	265.46
2	131.84				
2	121.21	26.47	120.62	2 717.86	265.47
2	120.03				
2	109.39	25.00	108.84	2 452.39	
2	108.28				
1	103.84	42.65			
1	101.95	42.65	101.95	2 297.22	248.55
1	100.06				
1	92.81	42.65			
1	90.92	42.65	90.92	2 048.67	
1	89.03				
		$^3J_{CF}$			
3	52.15	7.36			
3	51.82	7.35			
3	51.50				

were tried using phase transfer catalyst [15] and potassium hydroxide (aqueous and powdered), but the conversion to *DFCME* was never greater than 15%; this route to *DFCME* was consequently abandoned.

DFCME was brominated with elemental bromine in carbon tetrachloride. The yields of *DFCDM* (after distillation) were between 85 and 90%. The ^{1}H NMR spectrum of *DFCDM* (neat) shows the $-OCH_3$ proton as a singlet at 3.85 ppm and the ^{13}C NMR spectrum of *DFCDM* shows a total of 14 peaks. The diastereomeric $-OCH_3$ carbon shows three peaks (instead of the expected two doublets) which is due to overlapping resonances. The resonances of the diastereomeric carbon atoms of the $-CFBrOCH_3$ group are observed at 118.41 and 119.58 ppm. The calculated value for this group is 123 ppm [16, 17]. Each of the carbon atoms is split into doublets and shows $^1J_{CF}$ coupling. $^2J_{CF}$ couplings were not observed for this carbon atom. The diastereomeric carbon atoms of the $-CFClBr$ group were observed at 105.78 and 107.26 ppm. The calculated value for this group is 99.7 ppm [16, 17]. This carbon atom shows both $^1J_{CF}$ and $^2J_{CF}$ coupling (Table 4). The ^{19}F NMR spectrum of *DFCDM* shows a total of 8 peaks, which is the theoretical amount. Four different fluorine atoms are present, two for each belong to the diastereomers (Table 5).

MFCBA was synthesized by a modified literature procedure [18], which resulted in greatly improved yields (85% vs. 53%). Our method involved minimizing contact time with water during workup and varying the molar ratio of *DFCDM* to sulfuric acid. The optimal ratio was found to be three mol of sulfuric acid to one mol of *DFCDM*. Other reaction conditions were explored; it was found that the addition

Table 4. ^{13}C NMR spectral data of 1,2-difluoro-2-chloro-1,2-dibromo-1-methoxyethane (acetone-d_6; *TMS*).

$FClBrC-CFBrOCH_3$
Carbon type 1 2 3

Carbon type	$^2J_{CF}$ (ppm)	(Hz)	Average (ppm)	(Hz)	$^1J_{CF}$ (Hz)
2	126.30	–	–	–	302.97
2	112.85	–	–	–	
2	124.86	–	–	–	302.96
2	114.41	–	–	–	
1	114.29	5.89	114.16	2572.25	311.05
1	114.03				
1	100.45	4.41	100.35	2261.21	
1	100.25				
1	112.85	7.35	112.70	2539.17	311.79
1	112.54				
1	98.95	4.41	98.85	2227.38	
1	98.75				
3	57.18	Four overlapping peaks			
3	56.98				
3	56.72				

Table 5. ^{19}F NMR spectral data of 1,2-difluoro-2-chloro-1,2-dibromo-1-methoxyethane (benzene-d_6; $CFCl_3$).

$FClBrC-CFBrOCH_3$
Fluorine type 1 2

Fluorine type	ppm	$^3J_{FF}$ (Hz)
1	−66.52	14.66
1	−66.35	
1	−65.87	14.66
1	−65.70	
2	−62.22	18.33
2	−62.00	
2	−59.66	14.67
2	−59.48	

of methanol (0.3 eq) slowed the reaction rate, and the addition of silica (0.3 eq, based on SiO_2), in order to allow HF to react, resulted in a lower yield.

The infrared spectra of *MFCBA* show the inductive effect of the fluorine atom on the carbon oxygen double bond by its high frequency (1 770 cm^{-1}). The ^{1}H NMR spectrum of *MFCBA* (neat) shows the $-OCH_3$ protons as a singlet (4.00 ppm). The ^{13}C NMR spectrum of *MFCBA* (acetone-d_6) shows: 55.61 ppm ($-OCH_3$); 89.42 and 103.26 ppm ($FClBrC-$), $^1J_{CF} = 311.79$ HZ; 161.80 and 163.11 ($C=O$),

${}^2J_{CF} = 29.41$ Hz. The ^{19}F NMR spectrum of *MFCBA* (benzene-d_6) shows a singlet at -64.13 ppm (FClBrC$-$).

Fluorocarbon ethers of the type $-CF_2-OR$ (R = alkyl, aryl) have been found to be readily hydrolyzed at 10°C with concentrated sulfuric acid to the corresponding esters [19].

The synthesis of ethyl fluorochlorobromoacetate was described [18] by treating 1,2-difluoro-2-chloro-1,2-dibromo-1-ethoxyethane with sulfuric acid (53% yield). The authors postulated that the reaction proceeded by the abstraction of a bromide ion to form a fluorocarbenium-oxonium ion, which was then hydrolyzed by a water workup to the ester and hydrogen fluoride. Olah [20] has shown that α-fluorine atoms stabilize carbenium ions by back coordination of its unshared electron pairs into the vacant p orbital of the carbon atom.

We found in our study of the reaction of *DFCDM* with sulfuric acid that *MFCBA* forms in the absence of a water workup. This was done by separating the organic phase from sulfuric acid after the prescribed reaction time and analyzing it by GC, which showed *MFCBA*. This observation prompted a closer investigation of the reaction.

The reaction of *DFCDM* with sulfuric acid was studied by removing samples of the reaction mixture at various times, quenching them with water, separating the organic layer from water, drying them over anhydrous $MgSO_4$, and then studying their GC spectra. The GC data, given in area percent, showed that, after an 0.25 hour's reaction time, the product consisted of 70% *DFCDM,* 20% *MFCBA,* and 10% of an unknown compound. After 1.0, 2.25, and 3.0 hour's reaction time, the GC data showed that the water-quenched reaction product consisted of 97%, 99%, and 99% *MFCBA,* respectively. In addition, the ^{1}H, ^{13}C, and ^{19}F NMR spectra of the sample isolated after 0.25 hour were studied.

The ^{1}H NMR spectrum (neat) of the product shows *DFCDM* (3.85 ppm), a new singlet (3.95 ppm), and *MFCBA* (4.00 ppm) in a 67 : 9 : 24 ratio, respectively

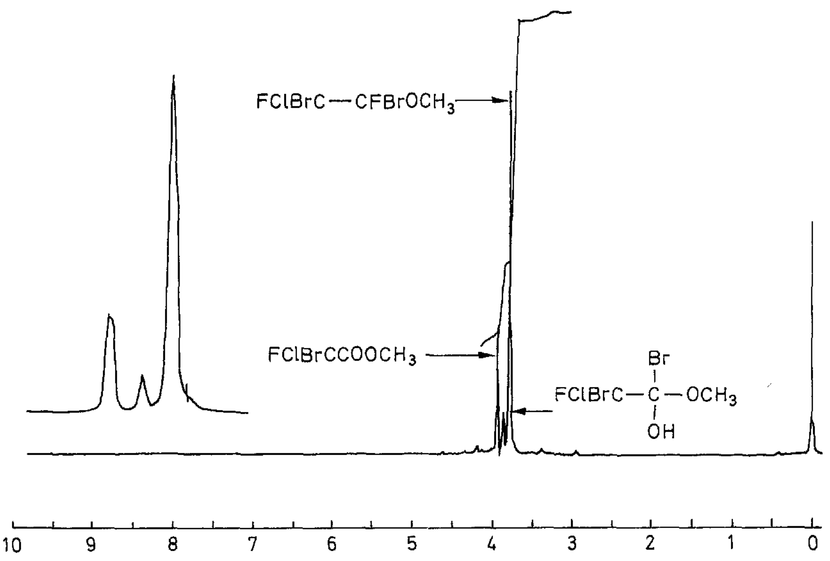


Fig. 1. Reaction of *DFCDM* with sulfuric acid; sample drawn at 0.25 hour; ^{1}H NMR

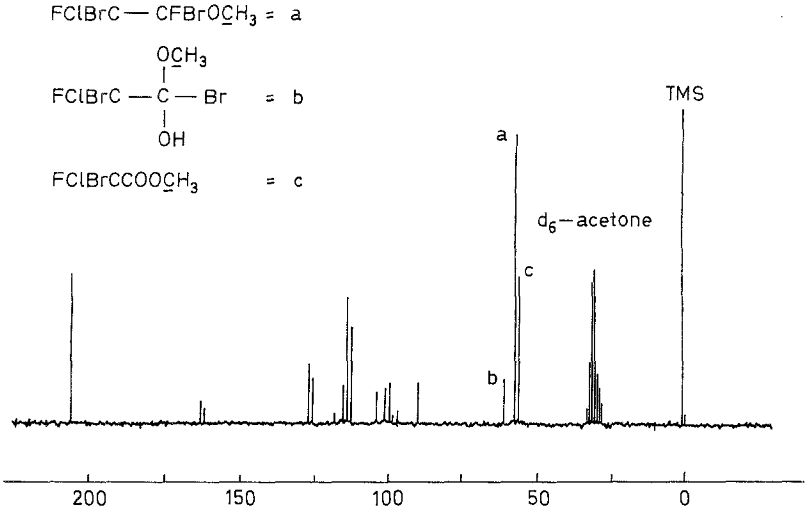


Fig. 2. Reaction of *DFCDM* with sulfuric acid; sample drawn at 0.25 hour; ^{13}C NMR

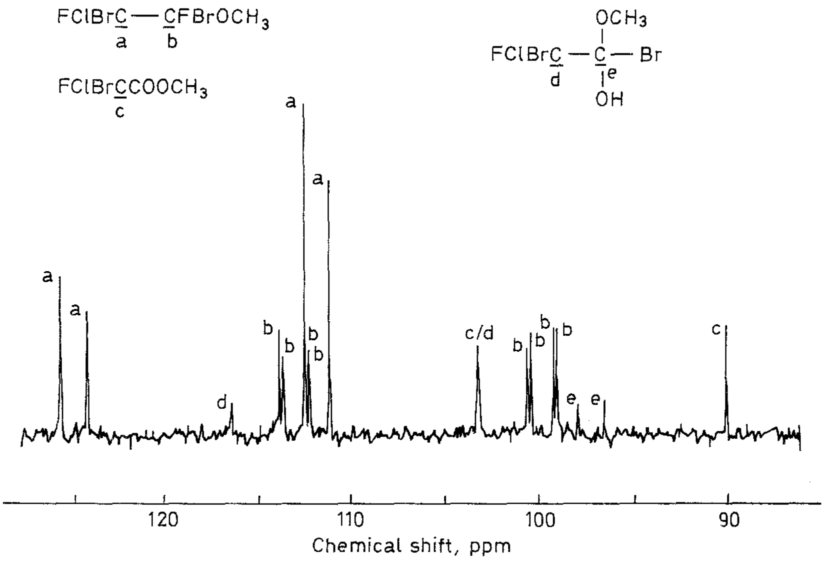


Fig. 3. Reaction of *DFCDM* with sulfuric acid; sample drawn at 0.25 hour; ^{13}C NMR, detail from 90 to 125 ppm

(Fig. 1). The ^{13}C NMR spectrum of the mixture (acetone-d_6) (Fig. 2) shows a new singlet at 67.57 ppm, which is assigned to a carbon atom of a $-CX_2-O-CH_3$ group, where $X \neq$ F ($-CFBrOCH_3$, $-CF_2OCH_3$, and $=CFOCH_3$ all show fluorine carbon coupling); the resonances observed at 96.08 and 97.58 ppm are assigned to a carbon atom of an $FClBrC-CX_2OCH_3$ group where $X \neq$ F ($^2J_{CF} = 33.83$ Hz and is indicative of an α-fluorine atom); the resonances observed at 103.13 and 116.90 ppm are assigned to the carbon atoms of the $FClBrC-CX_2$ group, where $X \neq$ F ($^1J_{CF} = 301.31$ Hz) and is indicative of a fluorine substituted carbon atom;

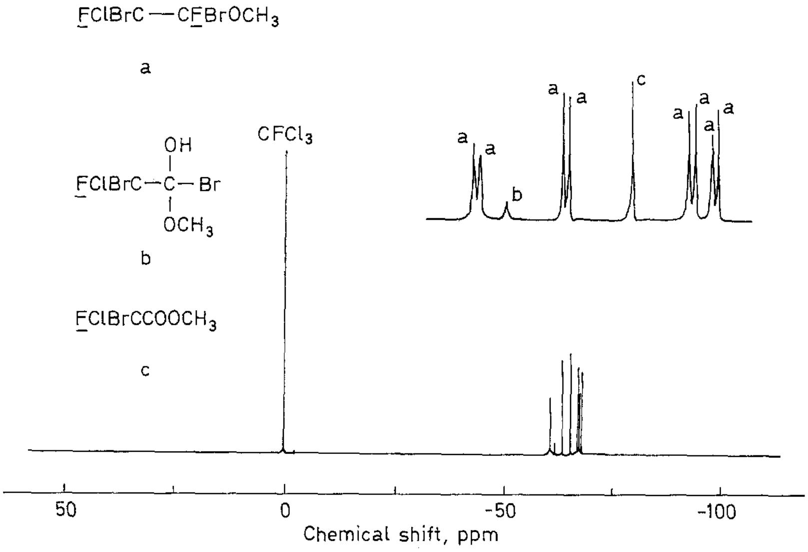


Fig. 4. Reaction of *DFCDM* with sulfuric acid; sample drawn at 0.25 hour; ^{19}F NMR

the peak at 103.13 ppm is overlapped by another signal. Fig. 3 shows the spectrum from 90 ppm to 125 ppm in more detail. The ^{19}F NMR spectrum of the mixture (benzene-d_6) shows a new singlet at -60.52 ppm; it indicates a new type of fluorine atom is present (Fig. 4).

^{1}H, ^{13}C, and ^{19}F NMR spectroscopy indicates the structures of the intermediate to be consistent with the product formed from the hydrolysis of a bromocarbenium-oxonium ion or the corresponding sulfonic acid-ester derivative shown. It implies that the first step in the reaction of *DFCDM* with H_2SO_4 is the abstraction of a fluoride ion. However, this study does not eliminate the possibility of bromine abstraction occurring simultaneously, since the fluorine-containing intermediates may be unstable. It is well known in organic fluorine chemistry that geminally substituted fluoroalcohols readily lose hydrogen fluoride [9, 13]. The abstraction of a fluoride ion is hindered by the high strength and low polarizability of the carbon fluorine bond, but is aided by the exceptionally strong hydrogen bonding ability of the fluoride ion [9].

Hydrolysis of *MFCBA* proceeded readily at 3°C using aqueous potassium hydroxide. The potassium salt was then neutralized with sulfuric acid and extracted with diethyl ether to give *FCBAA* in yields as high as 89%. Although *FCBAA* was purified by distillation (b. p. = 65°C/6 mm Hg), the acid still contained diethyl ether (4–7%); pure *FCBAA* was obtained by dichloromethane extraction of the aqueous phase.

The infrared spectrum of *FCBAA* shows a carbonyl function (at 1750 cm^{-1}), which demonstrates the inductive effect of the halogen atoms on the carbon oxygen double bond by its high absorption frequency. The ^{1}H NMR spectrum of *FCBAA* (neat) showed a singlet at 11.6 ppm (–COOH). The ^{13}C NMR spectrum of *FCBAA* (acetone-d_6) shows δ in ppm: 89.91 and 103.65 (FClBrC–) $^1J_{FC} = 311.79$ Hz; 161.74 and 162.98 (HOOC–) $^2J_{CF} = 27.94$ Hz. The ^{19}F NMR spectrum of *FCBAA* (acetone-d_6) shows a single absorption at -63.70 ppm (FClBrC–).

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