Haloaldehyde polymers: 45. Separation of fluorochlorobromoacetic acid into its antipodes; synthesis of optically active fluorochlorobromoacetaldehyde and its polymerization*

Thomas R. Doyle and Otto Vogl†
Polytechnic University, 333 Jay Street, Brooklyn, NY 11201, USA
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Racemic fluorochlorobromoacetic acid (FCBAA) was separated into its antipodes by recrystallization of the strychnine salts. Optically active FCBAA with a maximum enantiomeric purity of 66% was obtained. The enantiomeric purity was determined by ^{19}F nuclear magnetic resonance spectroscopy of the bornyl esters of FCBAA. The (+)-ethyl ester and the (−)-methyl/ethyl ester of FCBAA were reduced with diisobutyl aluminium hydride and, after work-up, gave a mixture of the hydrates and the hemiacetals of (+)- and (−)-fluorochlorobromoacetaldehyde (FCBA), which was dehydrated to optically active FCBA. The optical rotation of (+)- and (−)-FCBA indicated its enantiomeric purity to be similar to that of the parent FCBAA. Optically active FCBA was polymerized and the resulting polymer was characterized.

(Keywords: haloaldehyde polymers; fluorochlorobromoacetic acid; synthesis; polymerization; fluorochlorobromoacetaldehyde)

INTRODUCTION

Fluorochlorobromoacetaldehyde (FCBA) is the only perhaloacetaldehyde, based on fluorine, chlorine and bromine substituents, that is capable of existing in optically active form because it has a chiral centre at the carbon atom of the trihalomethyl substituent. Although precursors of FCBA have been synthesized previously[1–5], the racemic aldehyde has not been synthesized until recently[6–9]. The key intermediate is fluorochlorobromoacetic acid (FCBAA), for which a facile synthesis has been developed[10]; the methyl ester was reduced with diisobutyl aluminium hydride (DIBAL-H) to FCBA and its polymerization was studied[7,9].

Our interest in the polymerization of optically active FCBA stems from our work on the synthesis of optically active polychloral, an isotactic polymer whose optical activity is based on macromolecular asymmetry, helicity of one screw sense[11–15]. Since the steric bulk of the fluorochlorobromomethyl group of polyfluorochlorobromoacetaldehyde (PFCBA) is similar to that of the trichloromethyl group of polychloral, it was of interest to study the effect that the chiral centre has on the helicity (optical activity) of PFCBA.

When chloral is polymerized, it forms an exclusively isotactic polymer[16–18]. By analogy it was expected that FCBA assumes a similar exclusive configurational preference in the polymer[9]. The steric restriction based on the side-chain bulk (the trihalomethyl group) found in these polymers requires that the polyacetal backbone adopt the rigid helical conformation. Because of the chirality of the trihalomethyl side-group in PFCBA, the helical polymer chain was expected to exist exclusively in a one-handedness, causing optical activity based not only on the contribution of the chiral fluorochlorobromomethyl group but also on macromolecular asymmetry.

This condition was expected to be met if the predecessor of FCBA, namely FCBAA, could be separated into its optical antipodes. If only partial separation were achieved, it was expected that even a small amount of the 'impurity' of the other antipode would cause the formation of a polymer whose optical activity based on macromolecular asymmetry would be completely or partially eliminated. On the other hand, should only one antipode be capable of polymerization and the other antipode not be incorporated, the PFCBA would be composed of monomer units of only one enantiomer (stereoselective polymerization) and the polymer should show optical activity based on macromolecular asymmetry.

In a previous publication we reported that the polymerization of racemic FCBA by chiral initiators resulted in the formation of a polymer with a low to negligible optical activity[7]. Since PFCBA is an insoluble polymer, it was not possible to determine whether the polymer existed primarily as a mixture of polyenantiomers or as a copolymer of the enantiomeric units (the degree of stereoselectivity). Based on these experiments, it was possible to rule out a largely stereoselective polymerization because of the absence of a high optical rotation. The optical activity was contributed to PFCBA from the chiral side-group of the monomer unit alone and was expected to be in the range of 10–20° (refs 7–9).

In 1896, Swarts reported the optical resolution of FCBAA by fractional precipitation of its strychnine salt, but was unable to isolate the free acid[19,20]. This was attributed to racemization and decarboxylation of

* This paper is dedicated to Professor Gerhard Reinisch on the occasion of his 60th birthday with our warmest wishes
† To whom correspondence should be addressed

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FCBAA. The separation of the strychnine salts of FCBAA by crystallization was wasteful because of the similarity in the solubility of the strychnine salts of the (+)- and (−)-antipodes of FCBAA and strychnine itself.

It was the objective of this work to separate the antipodes of FCBAA to 100% optical purity and to develop a method to determine its optical purity; ^{19}F n.m.r. spectroscopy of the bornyl ester was considered the most promising method[21]. It was our further objective to convert optically active FCBAA to optically active FCBA by hydride reduction, to purify the aldehyde to polymerization-grade FCBA, to polymerize it with anionic initiators and to characterize the polymer.

MATERIALS AND MEASUREMENTS

Materials

All chemicals were used as received. Aldrich anhydrous-grade solvents were found to be adequate for all reactions except polymerizations.

n-Butyl lithium (1.6 M in hexane) and diisobutyl aluminium hydride (DIBAL-H) (1.0 M in dichloromethane) were obtained from the Aldrich Chemical Co.; both reagents were handled with gas-tight syringes and under a nitrogen atmosphere.

Measurements

Infra-red spectra were recorded on Perkin–Elmer model 1320 or Shimadzu IR-435 spectrophotometers. Peak assignments were made to the nearest 5 cm^{-1}.

The ^1H n.m.r. spectra were recorded at 89.56 MHz on a JEOL JNM-FX90Q multinuclear *FT* n.m.r. spectrometer or a Varian EM 390 n.m.r. spectrometer. The ^{13}C n.m.r. spectra were recorded at 22.50 MHz on a JEOL JNM-FX90Q multinuclear *FT* n.m.r. spectrometer with complete proton decoupling. The ^{19}F n.m.r. spectra were recorded at 84.26 MHz on a JEOL JNM-FX90Q multinuclear *FT* n.m.r. spectrometer, at 188.3 MHz on a Bruker W.P. 200 spectrometer, or at 84.67 MHz on a Varian EM 390 n.m.r. spectrometer.

The decomposition temperature of PFCBA was determined on a Perkin–Elmer DSC-F differential scanning calorimeter. The instrument was calibrated against an indium standard.

Gas chromatograms were obtained on a Varian Associates model 920 gas chromatograph. The purity of FCBA (water content) was determined by gas chromatography (g.c.) using 36% w/w diisodecyl phthalate coated on Chromosorb W (100/120 mesh) as a stationary phase and was reported in area per cent. A typical procedure involved injecting 10 μl of sample into the gas chromatograph. This method for the detection of impurities was estimated to be sensitive to 10 ppm.

Polarimetric measurements were carried out using a Perkin–Elmer 241 polarimeter at a temperature of 22 ± 1°C using the sodium D line as a light source. Solution measurements were done in glass cells with a path length of 10 mm. Suspension measurements were made in an isorefractive mixture of two miscible liquids, one with a smaller and the second with a higher refractive index than the powder. The liquid mixtures were prepared in a volumetric flask and their refractive indices were measured on an Abbe refractometer (Erma, Japan). Measurements were carried out in a 4 ml rectangular glass cell with a path length of 10 mm, which was closed with a Teflon stopper. The sodium lamp used as a light source had a 6 mm beam diameter and 1 s integration time. The suspension was stirred on the bottom of the cell with a 9 mm × 3 mm Teflon stirring bar. The speed of stirring was approximately 900 rpm regulated by an autotransformer and controlled by a digital stroboscope (Pioneer, model DS-303). All suspensions were prepared from polymer powders with particle sizes of less than 45 μm.

Microanalyses were carried out by the Microlytics Laboratory, South Deerfield, MA.

EXPERIMENTAL PROCEDURES

(a) Synthesis of FCBAA

FCBAA was synthesized in a sequence of four reaction steps in an overall yield of 35% from chlorotrifluoroethylene[9,10].

(b) Crystallization of FCBAA salts

Crystallization of FCBAA/R(+)-α-methylbenzylamine (RMBA) salt from carbon tetrachloride. In a 25 ml flask a solution of FCBAA (1.4 g, 7.4 mmol) in diethyl ether (6 ml) was cooled in a dry ice/acetone bath and an RMBA (1.0 g, 8.2 mmol) solution in diethyl ether (6 ml) was added. The solution was concentrated under reduced pressure and yielded a white crystalline solid of the FCBAA/RMBA salt, which was recrystallized from carbon tetrachloride. $[\alpha]_D^{22} = +2.16°$ to $+2.60°$ (5.0 g dl^{-1}, MeOH).

Crystallization of FCBAA/RMBA salt from benzene. An FCBAA (2.5 g, 13.3 mmol) solution in diethyl ether (15 ml) was cooled in a dry ice/acetone bath. The addition funnel was charged with RMBA (1.7 g, 14.0 mmol) and diethyl ether (15 ml). The solution was warmed to room temperature and concentrated on a rotary evaporator; it yielded a white crystalline solid. The FCBAA/RMBA salt was recrystallized from benzene. Elemental analysis: calculated for $C_{10}H_{12}Br \cdot ClFNO_2$, C 38.43%, H 3.87%, N 4.48%; found, C 38.38%, H 4.01%, N 4.46%. $[\alpha]_D^{22} = +2.79°$ to $+2.99°$ (4.5 g dl^{-1}, MeOH).

Crystallization of FCBAA/strychnine (STRY) salt from methanol(I). The solution of FCBAA (7.5 g, 39 mmol) in chloroform (30 ml) was cooled in an ice bath. STRY (13.1 g, 39 mmol) dissolved in chloroform (80 ml) was added. The resulting solution was warmed to room temperature, evaporated to dryness and yielded a white crystalline FCBAA salt, which was recrystallized from methanol. Elemental analysis: calculated for $C_{23}H_{22}Br \cdot ClFN_2O_4$, C 52.54%, H 4.42%, N 5.33%; found, C 52.61%, H 4.30%, N 5.48%. After a second recrystallization $[\alpha]_D^{22} = -15.8°$ (4.56 g dl^{-1}, $CHCl_3$).

Crystallization of the FCBAA/STRY salt from isopropyl alcohol (IPA). The FCBAA/STRY salt fractions from the methanol crystallization (I) were combined (16.3 g, 31 mmol of the salt) and recrystallized from IPA (see *Table 1*).

Crystallization of the FCBAA/brucine (BRU) salt from methanol. A solution of FCBAA (6.2 g, 32 mmol) in chloroform (30 ml) was cooled in an ice bath and a solution of BRU (13.9 g, 32 mmol) in chloroform (100 ml) was added. The solution was warmed to room

Table 1 Crystallization of the FCBAA/STRY salt from IPA and elemental analysis calculated for $C_{23}H_{22}BrClFN_2O_4$

Fraction[a]	Yield (g)	Yield (%)	$[\alpha]_D^{22}$[b] (deg)	Conc. (g dl^{-1})
1C	10.4	64	−17.2	2.28
1M	4.6	28	−34.4	2.30
2C	8.1	79	−16.1	2.45
2M	1.7	17	−26.3	2.30
3C	5.2	67	−16.6	2.32
3CC[c]	0.5	7	−16.3	2.16
3M	1.7	22	−35.1	2.15
X1C[d]	1.0	17	−13.6	0.75
X1CC	1.6	27	−18.9	2.25
X1M	2.2	37	−57.7	2.25

Fraction	C (%)	H (%)	N (%)
Calcd	52.54	4.42	5.33
2C	52.58	4.31	5.22
X1C	52.74	4.43	5.41
X1M	61.49	6.22	6.95

[a]C = crystalline fraction; M = soluble fraction
[b]Solvent $CHCl_3$
[c]Crystallized from the mother liquor
[d]X = combination of fractions 1M and 2M

Table 2 Crystallization of the FCBAA/BRU salt from methanol

Fraction	Yield (g)	Yield (%)	$[\alpha]_D^{22}$[a] (deg)	Conc. (g dl^{-1})
1C	12.2	68	−19.4	4.97
1CC[b]	2.8	16	−19.6	5.33
1M	2.1	12	−19.2	5.06
2C	9.0	76	−19.1	4.56
2M	1.9	16	−19.2	5.33
3C	6.2	73	−19.2	5.24
3M	1.8	21	−19.4	5.16

[a]Solvent chloroform
[b]Crystallized from the concentrated mother liquor

temperature, evaporated to dryness and yielded a white crystalline solid of the FCBAA/BRU salt, which was recrystallized from methanol (see *Table 2*). Elemental analysis: calculated for $C_{25}H_{28}BrClFN_2O_6$, C 51.25%, H 4.66%, N 4.78%; found, C 51.08%, H 4.70%, N 4.75%.

Crystallization of the FCBAA/BRU salt from isopropyl alcohol (IPA). The FCBAA salt fractions from the methanol crystallization were combined and gave 13.7 g (23 mmol) of the salt; the recrystallization was attempted using toluene and then acetone as solvents. The salt was then recrystallized from isopropyl alcohol. Elemental analysis: calculated for $C_{25}H_{28}BrClFN_2O_8$, C 51.25%, H 4.66%, N 4.78%; found, C 57.74%, H 6.19%, N 5.90%.

Crystallization of the FCBAA/STRY salt from methanol(II). A STRY (70.2 g, 0.21 mol) solution in chloroform (350 ml) was cooled in an ice bath. The solution of FCBAA (40.2 g, 0.21 mol) in chloroform (50 ml) was added. The solution was warmed to room temperature and the solvent was removed; it yielded a white crystalline solid of the STRY/FCBAA salt, which was recrystallized from methanol (see *Table 3*).

Crystallization of the FCBAA/STRY salt from methanol(III). A STRY (108 g, 0.32 mol) solution in chloroform (600 ml) was cooled in an ice bath. Then FCBAA (62 g, 0.32 mol) in chloroform (50 ml) was added. The resulting solution was warmed to room temperature and the solvent was evaporated to yield a white crystalline solid of the STRY/FCBAA salt; it was recrystallized from methanol (see *Table 4*).

The liberation of FCBAA from diastereoisomeric amine salts

A typical liberation of FCBAA from the salt proceeded as follows. A 100 ml round-bottomed flask was charged with FCBAA/STRY (4.8 g, 9.1 mmol) and water (35 ml), and the resulting suspension was cooled in an ice bath. Sulphuric acid (6.4 g, 65.7 mmol) was added to the mixture over a 20 min period. The aqueous phase was extracted for one day using diethyl ether (Et_2O) in a continuous liquid/liquid extractor. The Et_2O solution was dried over magnesium sulphate, filtered and concentrated on a rotary evaporator under reduced pressure. The residue was distilled using a short path distillation head at a pressure of 2 mmHg; the yield was 1.23 g, b.p. = 45°C. The distillate was analysed by ^1H n.m.r. spectroscopy (CCl_4) and was shown to contain 93% FCBAA and 7% diethyl ether. The overall yield of FCBAA was 1.2 g, 6.3 mmol (68%).

Table 3 Crystallization of the FCBAA/STRY salt from methanol(II)

Fraction	Yield (g)	Yield (%)	$[\alpha]_D^{22}$[a] (deg)	Conc. (g dl^{-1})
1C	68.5	62	−17.2	2.52
1M	39.5	36	−20.1	2.20
2C	40.9	60	−15.5	2.04
2M	26.5	39	−21.8	1.88
3C	26.1	64	−15.0	1.87
3M	14.0	34	−21.8	1.89
X1C[b]	39.3	60	−19.3	1.84
X1M	25.0	38	−26.1	1.89
X2C	19.5	50	−17.6	1.67
X2M	19.3	49	−21.2	1.98
X3C	21.1	63	−16.7	1.98
X3M	6.9	35	−22.2	1.57
Y1C[c]	15.3	59	−15.9	1.73
Y1M	10.1	39	−23.4	1.97

[a]Solvent chloroform
[b]X = combination of fractions 1M and 2M
[c]Y = combination of fractions X1M and X2M

Table 4 Crystallization of FCBAA/STRY salt from methanol(III)

Fraction	Yield (g)	Yield (%)	$[\alpha]_D^{22}$[a] (deg)	Conc. (g dl^{-1})
1C	109.5	64	−16.9	1.63
1CC[b]	42.8	25	−20.3	2.22
1M	14.7	9	−33.7	1.64
2C	68.7	63	−15.3	1.56
2M	36.5	33	−19.3	1.63
3C	46.0	67	−14.4	1.58
3M	22.2	32	−19.3	1.62
4C	31.9	69	−13.5	1.16
4M	13.4	29	−18.3	1.09

[a]Solvent chloroform
[b]Crystallized from the concentrated mother liquor

Esterification of optically active FCBAA

Ethyl fluorochlorobromoacetate (EFCBA). A 50 ml round-bottomed flask was equipped with a magnetic stirrer, a Dean–Stark trap filled with benzene and a reflux condenser. The flask was charged with FCBAA (9.2 g, 47 mmol; $[\alpha]_D^{22} = +7.6°$ (6.36 g dl^{-1}, Et_2O)), ethanol (6.6 g, 0.14 mol) and benzene (10 ml). The mixture was heated to reflux for 10 h using an oil bath; 0.8 ml of water was collected (0.86 ml of water was the theoretical amount). The solution was concentrated on a rotary evaporator, and the residue was distilled under reduced pressure. EFCBA was obtained as a clear colourless liquid; it was analysed by g.c. and showed a purity greater than 99.5%. The overall yield of EFCBA was 8.5 g, 38 mmol (79%), b.p. = 78–80°C/51 mmHg, $[\alpha]_D^{22} = +4.8°$ (6.3 g dl^{-1}, CCl_4). The infra-red spectrum showed absorptions at 2976, 2920, 2885 cm^{-1} (C–H stretching) and 1760 cm^{-1} (C=O stretching). The ^{1}H n.m.r. spectrum ($CDCl_3$) showed δ: 1.17, 1.25 and 1.33 ppm (–CH_3, 3H); and 4.16, 4.24, 4.32 and 4.39 ppm (–CH_2–, 2H). The ^{13}C n.m.r. spectrum ($CDCl_3$) showed δ: 13.31 ppm (–CH_3); 64.68 ppm (–CH_2–); 88.96 and 102.93 ppm (FClBr*C*–); and 161.67 and 160.43 ppm (–*C*OOEt). The ^{19}F n.m.r. spectrum ($CDCl_3$) ($CFCl_3$ as internal reference) showed δ: −64.83 ppm (*F*ClBrC–). Elemental analysis: calculated for $C_4H_5BrClFO_2$, C 21.89%, H 2.30%, Cl 16.16%; found, C 21.86%, H 2.32%, Cl 16.13%.

Mixed methyl(ethyl) fluorochlorobromoacetate (MFCBA/EFCBA). Into a 50 ml round-bottomed flask were placed FCBAA (9.5 g, 50 mmol; $[\alpha]_D^{22} = -6.3°$ (6.16 g dl^{-1}, Et_2O)), methanol (48 g, 0.15 mol) and benzene (10 ml). The esterification was carried out similarly to the esterification described in the last subsection. A clear colourless liquid was obtained, which was analysed by g.c.: MFCBA (80%), EFCBA (19%) and benzene (1%). The yield of mixed esters was 8.3 g, 39 mmol (79%). The b.p. was 63–78°C/49 mmHg, and the optical rotation $[\alpha]_D^{22}$ was −4.6° (5.1 g dl^{-1}, CCl_4).

(c) Determination of the optical purity of FCBAA by ^{19}F n.m.r. spectroscopy of its diastereoisomeric esters

Synthesis of [(1S)-endo]-(−)-bornyl fluorochlorobromoacetate (BFCBA) and R(−)-2-octyl fluorochlorobromoacetate (RFCBA)

Synthesis of BFCBA using the imidazolide of FCBAA. A 15 ml round-bottomed flask was equipped with a magnetic stirrer, a reflux condenser and a flow control adaptor, which was fitted with an argon-filled balloon. In the round-bottomed flask was placed FCBAA (0.7 g, 3.8 mmol; $[\alpha]_D^{22} = +4.0°$ (3.05 g dl^{-1}, Et_2O)), tetrahydrofuran (5 ml) and CDI (0.78 g, 4.6 mmol). The solution was warmed to 50°C and the evolution of carbon dioxide was noticed. When the evolution of carbon dioxide ceased, borneol (0.69 g, 4.5 mmol) was added to the reaction mixture and the solution was heated to reflux for 4 h. The product was worked up by pouring the reaction solution into water (30 ml), extracting with Et_2O washing with water and drying the ether solution over magnesium sulphate. The solution was concentrated and the residue distilled at 0.03 mmHg. BFCBA was collected as a clear colourless liquid, 0.59 g, 1.8 mmol (40%), b.p. = 130°C/0.03 mmHg, $[\alpha]_D^{22} = -52.30°$ ($\alpha_D^{22} = -0.706° \pm 0.001°$, 1.35 g dl^{-1}, Et_2O). The infra-red spectrum (4% in CCl_4, using matched KBr liquid cells) showed absorptions at 2950 cm^{-1} (C–H stretching) and 1755 cm^{-1} (C=O stretching). The ^{1}H n.m.r. spectrum (benzene-d_6) showed δ: 0.7 to 2.5 ppm (complex, 16H); and 5.00 and 5.15 ppm (multiplets, 1H). The ^{19}F n.m.r. spectrum (benzene-d_6, $CFCl_3$ internal reference) showed δ: −63.70 and −63.85 ppm (*F*ClBrC–).

Table 5 Synthesis of BFCBA and RFCBA

Acid (g)	Acid (mmol)	$[\alpha]_D^{22}$ (deg)	Solvent[a] (ml)
1.17	6.11	Racemic	15 (B)
1.16	6.06	Racemic	10 (O)
0.80	4.18	+7.6	10 (B)
0.74	3.87	−6.3	10 (B)
1.07	5.58	−5.2	15 (B)
0.75	3.92	−3.1	10 (B)
1.10	5.75	+1.5	10 (B)
0.50	2.61	+10.3	8 (B)

[a]Samples 1, 3–8, B = [(*S*)-endo]-(−)-borneol; sample 2, O = R(−)-2-octanol

Table 6 Optical purity of fluorochlorobromoacetic acid

Ester	$[\alpha]_D^{22}$[a] (deg)	Window (ppm)	Integration[b]
BFCBA	+4.0	5.9	38/62
BFCBA	0	5.9	50/50
RFCBA	0	5.9	50/50
RFCBA[c]	0	2.0	50/50
BFCBA[d]	+7.6	5.9	26/74
BFCBA[e]	−6.3	5.9	71/29
BFCBA	−5.2	3.0	67/33
BFCBA	−3.1	3.0	61/39
BFCBA	+1.5	3.0	46/54
BFCBA	+10.3	3.0	17/83

[a]Optical rotation of the parent acid (about 5.0 g dl^{-1}, Et_2O)
[b]Integration was measured by peak height
[c]The n.m.r. spectrum was measured using a continuous-wave n.m.r. spectrometer and was electronically integrated
[d]Parent acid of (+)-FCBA
[e]Parent acid of (−)-FCBA

Synthesis of BFCBA by azeotropic removal of water. A typical esterification proceeded as follows. A round-bottomed flask was equipped with a magnetic stirrer, a Dean–Stark trap and a reflux condenser. The flask was charged with FCBAA, the appropriate alcohol and benzene. The mixture was heated to reflux for 7 h using an oil bath. The solution was concentrated under reduced pressure (20 mmHg). The crude mixture was dissolved in benzene-d_6 for n.m.r. measurements.

The syntheses of BFCBA and RFCBA are summarized in *Table 5*.

Determination of the optical purity of FCBAA

^{19}F n.m.r. spectra of BFCBA and RFCBA were determined using a 10% solution of the appropriate ester in benzene-d_6[9,21] (*Table 6*).

(d) Synthesis and polymerization of optically active FCBA

Synthesis and polymerization of (−)-FCBA

DIBAL-H reduction of (−)-MFCBA/EFCBA. A dry 250 ml round-bottomed flask was equipped with a

magnetic stirrer, a pressure addition funnel, a thermometer and a flow control adaptor. Under an argon blanket, the round-bottomed flask was charged with MFCBA/EFCBA (which was an 80/20 mixture of the methyl and ethyl esters, respectively) (8.1 g, 39 mmol; $[\alpha]_D^{22} = -4.6°$) and dry dichloromethane (DCM) (20 ml); the mixture was cooled in a dry ice/acetone bath. An addition funnel capped with a septum was charged with DIBAL-H (1.0 M in DCM (50 mmol, 50 ml)) which was transferred with a dry syringe. The DIBAL-H solution was added over a 1.5 h period; during the addition of DIBAL-H the reaction temperature reached a maximum of −70°C. Upon completion of the DIBAL-H addition, the solution was stirred for 1 h at −78°C. The clear, colourless, cold solution was poured onto 150 ml of 2% sulphuric acid; DCM was removed on a rotary evaporator and the aqueous phase was extracted with a continuous liquid/liquid extractor for 17 h using Et_2O. The ether solution was dried over magnesium sulphate, filtered, concentrated under reduced pressure and the residue distilled under reduced pressure and analysed by g.c. The distillate contained 4% Et_2O and 96% hydrate/methyl and ethyl hemiacetal. The overall yield of the product was 6.6 g, 32 mmol (83%), b.p. = 60–75°C/50 mmHg.

Synthesis of (−)-FCBA. All glassware was dried overnight at 120°C, rapidly assembled and cooled under a flow of dry argon. A dehydrating mixture prepared by weighing phosphorus pentoxide (1.5 g, 11 mmol) in a tared, septum-capped, 10 ml round-bottomed flask, connected to a dry argon gas manifold, and the flask was cooled in a dry ice/acetone bath. The flask was charged with sulphuric acid (1.1 g, 11 mmol) followed by the hydrate/hemiacetal (6.6 g, 33 mmol). The mixture was warmed to room temperature and distilled onto sulphuric acid (0.5 ml). FCBA was obtained as a clear colourless liquid (b.p. = 75–82°C), which was fractionally distilled. The yield of FCBA was 3.9 g, 22 mmol (67%). The optical rotation was $-1.29° \pm 0.01°$, $[\alpha]_D^{22} = -10.5°$ (12.31 g dl^{-1}, CCl_4).

Polymerization of (−)-FCBA with R(−)-Li-2-octanoxide (RLO) or S(+)-Li-2-octanoxide (SLO). All glassware was dried overnight at 120°C, rapidly assembled and cooled under a flow of dry argon. The appropriate alcohol was weighed in a tared 5 ml round-bottomed flask under an argon atmosphere and connected to a dry argon gas manifold; the flask was cooled in a dry ice/acetone bath and charged with the appropriate amount of n-butyl lithium (1.6 M in hexane). The flask was warmed to room temperature and the evolution of butane gas was noted.

The preparation of the initiators (RLO and SLO) is summarized in *Table 7*. The initiating solutions were clear and colourless. FCBA was transferred with a dry syringe to two dry, argon-blanketed, septum-capped test tubes (10 ml). FCBA was weighed, warmed to 80°C in an oil bath and initiated with the appropriate alkoxide (*Table 8*). To achieve polymerization, 2.0 mol% of initiator was used. The initiated monomer (FCBA) was polymerized by cooling the mixture in an ice bath; a rapid polymerization was observed. The polymerization vessels were stored overnight at 0°C. The polymer samples were isolated as solid plugs, which readily crumbled into powder. PFCBA powder was stabilized by stirring it for 6 days in methanol saturated with dry HCl at room temperature. PFCBA was isolated, washed with methanol and dried at room temperature for 16 h (0.1 mmHg). The polymer was ground into a fine powder and sieved through a 63 μm sieve. The optical activity of PFCBA was measured in suspension using an isorefractive mixture of carbon tetrachloride/carbon disulphide ($n_D = 1.547$) in a 10 mm glass cell; the suspension was stirred at 1200 rpm. Results are shown in *Table 9*.

Table 7 Initiator preparation

	R(−)-2-octanol		n-Butyl lithium	
RLO	0.46 g	3.50 mmol	0.21 g	3.33 mmol
	S(+)-octanol		n-Butyl lithium	
SLO	0.49 g	3.74 mmol	0.23 g	3.44 mmol

Table 8

	FCBA		Initiator	
Tube	(g)	(mmol)	Type	Amount
R	1.69	9.64	RLO	4 × 0.5 mol%
S	1.67	9.52	SLO	4 × 0.5 mol%

Table 9

	PFCBA			Optical rotation (deg)	
Initiator	(g)	(%)	(g dl^{-1})	α_D^{22}	$[\alpha]_D^{22}$
RLO	0.68	46	3.26	$+0.02 \pm 0.03$	6 ± 10
SLO	0.79	55	3.04	$+0.04 \pm 0.03$	13 ± 10

Thermal degradation of PFCBA to (−)-FCBA. PFCBA (0.31 g; 0.15 g RLO + 0.16 g SLO) was weighed in a tared 10 ml round-bottomed flask which was equipped with a flow control adaptor and a magnetic stirrer. The flow control adaptor was connected by a piece of rubber tubing to a Dewar condenser, which was equipped with a vacuum adaptor and a 15 ml Schlenk tube. The pressure was reduced to 30 mmHg and regulated with a nitrogen gas line. The Dewar condenser was filled with dry ice/acetone and the Schlenk tube was cooled in a dry ice bath. The 10 ml flask was immersed in a silicone oil bath which was preheated to 185°C. After 30 min, PFCBA had substantially degraded, and heating was stopped (0.050 g of PFCBA was recovered as a white powder). The Schlenk tube was warmed to room temperature; the liquid was transferred with a gas-tight syringe to a dry, tared, septum-capped 5 ml round-bottomed flask. FCBA (0.14 g, 0.80 mmol) (45%) was collected and analysed by g.c.: the purity was greater than 99.9%. The optical rotation was measured in CCl_4 at 10.38 g dl^{-1} ($\alpha_D^{25} = -0.99° \pm 0.01°$) and $[\alpha]_D^{25} = -9.6°$.

Synthesis and polymerization of (+)-FCBA

DIBAL-H reduction of (+)-EFCBA. A dry, 250 ml, three-necked round-bottomed flask was equipped with a magnetic stirrer, pressure addition funnel and thermometer. The flask was blanketed with argon gas, charged with EFCBA (8.2 g, 37 mmol; $[\alpha]_D^{22} = +4.8°$) and dry dichloromethane (DCM) (20 ml), and cooled in a dry ice/acetone bath. The septum-capped addition funnel was charged with DIBAL-H, 1.0 M in DCM (48 mmol,

48 ml) with a dry syringe. The DIBAL-H solution was added over a 1.5 h period; during the addition of DIBAL-H the reaction temperature reached a maximum of −70°C. After stirring for one additional hour at −78°C, the clear, colourless, cold solution was poured onto 150 ml of 2% sulphuric acid/water. DCM was removed on a rotary evaporator and the aqueous phase was extracted with diethyl ether in a continuous liquid/liquid extractor for 12 h. The ether solutions were dried and concentrated; the residue was distilled under reduced pressure and analysed by g.c. The distillate contained 3% Et_2O and 97% hydrate/ethyl hemiacetal. The overall yield of the product was 6.9 g (32 mmol, 88%), b.p. 56–78°C/85 mmHg.

Synthesis of (+)-FCBA. A dehydrating mixture of phosphorus pentoxide (1.7 g, 12 mmol) and sulphuric acid (1.1 ml, 11 mmol) was placed in a 10 ml round-bottomed flask, which was cooled in a dry ice/acetone bath; hydrate/hemiacetal (6.0 g, 30 mmol) was added. The mixture was warmed to room temperature and distilled under an argon atmosphere onto phosphorus pentoxide (0.5 g). FCBA was obtained as a colourless liquid (b.p. = 80–82°C); redistillation gave a main fraction which was collected in a Schlenk tube and analysed by g.c. The purity of FCBA was 99.9%, with water/MeOH below 10 ppm. The yield of FCBA was 2.8 g, 16 mmol; it was 54% of the theoretical amount. The optical rotation was $\alpha_D^{25} = +1.32° \pm 0.01°$, $[\alpha]_D^{25} = +10.9°$ (12.11 g dl^{-1} in CCl_4).

Polymerization of (+)-FCBA with R(−)-Li-2-octanoxide (RLO) and S(+)-Li-2-octanoxide (SLO). The alcohol was weighed in a tared 5 ml round-bottomed flask, which was connected to a dry argon gas manifold. The flask was cooled in a dry ice/acetone bath and charged with the appropriate amount of n-butyl lithium (1.6 M in hexane). The flask was warmed to room temperature and butane evolution was noted.

The preparation of the initiators (RLO and SLO) is outlined in *Table 10*. The initiator solutions were clear and colourless. FCBA was transferred with a dry syringe to dry, argon-blanketed, septum-capped test tubes (two). The tubes were warmed to 80°C in an oil bath, and the warm initiator solution was added (*Table 11*). Clear solutions were obtained. Polymerization was achieved by cooling the initiated monomer in an ice bath. The polymerization vessels were stored overnight at 0°C. The polymers were isolated as solid plugs, which consisted of a glassy hard exterior and a brittle interior that was readily ground into powder. The glassy polymer portion was cut into small pieces and stabilized by treating for several days with a saturated solution of dry HCl in methanol at room temperature. PFCBA was isolated, washed with methanol and dried at room temperature (0.1 mmHg). The PFCBA was ground into a fine powder and sieved through a 63 μm sieve. The optical activity was measured in suspension using an isorefractive mixture of carbon tetrachloride/carbon disulphide ($n_D = 1.547$) in a 10 mm glass cell, which was stirred at 1200 rpm. Results are shown in *Table 12*. The optical rotation of the polymers synthesized from (−)-FCBA using RLO and SLO as initiators was measured as a function of wavelength. The results are tabulated in *Table 13*.

Thermal decomposition of PFCBA to (+)-FCBA. PFCBA (0.37 g; 0.18 g RLO + 0.19 g SLO) was weighed in a tared 10 ml round-bottomed flask and thermally decomposed as described previously for the recovery of (−)-FCBA. After 30 min, the PFCBA was substantially

Table 10 Initiator preparation

	R(−)-2-octanol		n-Butyl lithium	
RLO	0.66 g	5.03 mmol	0.31 g	4.78 mmol
	S(+)-2-octanol		n-Butyl lithium	
SLO	0.65 g	4.98 mmol	0.30 g	4.73 mmol

Table 11

	FCBA		Initiator	
Tube	(g)	(mmol)	Type	Amount
R	1.43	8.15	RLO	1 × 0.5 mol%
S	1.20	6.84	SLO	1 × 0.5 mol%

Table 12

	PFCBA			Optical rotation (deg)	
Initiator	(g)	(%)	(g dl^{-1})	α_D^{22}	$[\alpha]_D^{22}$
RLO	0.93	65	0.65	0 ± 0.025	0 ± 38
SLO	0.73	61	0.76	+0.010 ± 0.030	0 ± 40

Table 13 Optical activity of PFCBA as a function of wavelength

Initiator	Conc. (g dl^{-1})	Wavelength (nm)	α_D[a] (deg)	Tr[b] (%)	$[\alpha]_D^{22}$ (deg)
RLO	0.66	589	+0.015 ± 0.020	75 ± 5	+23 ± 30
RLO	0.66	578	+0.015 ± 0.020	80 ± 5	+23 ± 30
RLO	0.66	546	+0.015 ± 0.030	80 ± 5	+23 ± 45
RLO	0.66	436	+0.020 ± 0.030	80 ± 5	+30 ± 45
RLO	0.66	365	–	15 ± 5	–
SLO	0.74	589	+0.015 ± 0.020	75 ± 5	+20 ± 27
SLO	0.74	578	+0.020 ± 0.030	75 ± 5	+27 ± 40
SLO	0.74	546	+0.020 ± 0.020	75 ± 5	+20 ± 27
SLO	0.74	436	+0.030 ± 0.020	75 ± 5	+20 ± 27
SLO	0.74	365	–	15 ± 5	–

[a]Measured in suspension using an isorefractive mixture of carbon tetrachloride/carbon disulphide ($n = 1.547$)
[b]Tr = transmission; 80 ± 5% is the maximum transmission

decomposed to monomer and heating was stopped (0.075 g of PFCBA was recovered as a white powder). The receiving tube was warmed to room temperature and FCBA was transferred with a gas-tight syringe to a dry, tared, septum-capped, 5 ml round-bottomed flask. The FCBA obtained (0.10 g, 27% of the theoretical amount) was analysed by g.c. and showed a purity greater than 99.9%. The optical rotation was measured in carbon tetrachloride, $\alpha_D^{22} = +1.05° \pm 0.01°$, 8.91 g dl^{-1} and $[\alpha]_D^{22} = +11.8°$. The carbon tetrachloride solution was charged with water (2.0 μl, 0.002 g, 0.11 mmol), which was 20 mol% and 2 wt% of the (+)-FCBA. The optical rotation of the hydrate of FCBA (HFCBA) thus obtained was measured and gave a $\alpha_D^{22} = +0.88° \pm 0.01°$, 8.91 g dl^{-1} and $[\alpha]_D^{22} = +9.9°$.

RESULTS AND DISCUSSION

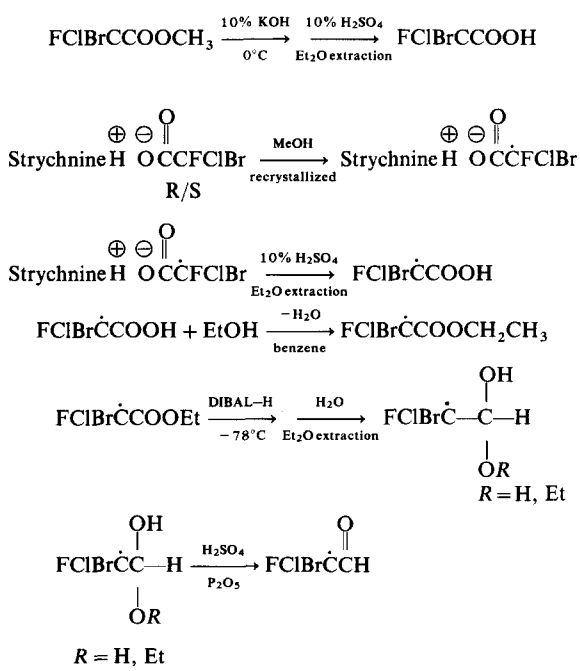
FCBAA was partially resolved into (+)-FCBAA and (−)-FCBAA via the strychnine salts, and the optical purity was determined via the bornyl esters. Partially resolved (+)- and (−)-FCBAA was converted into the (+)- and (−)-FCBA antipodes. The optical rotation of (+)- and (−)-FCBA indicated that racemization did not occur during its synthesis. The reaction scheme is shown below (*Scheme 1*).

The optical resolution of FCBAA was first attempted by fractional crystallization of its *R*(+)-α-methylbenzylamine salt (FCBAA/RMBA) from carbon tetrachloride and benzene. The salt was recrystallized four times from carbon tetrachloride. The cumulative yield from the first crystallization to the fourth crystallization was 50%, while the change in optical rotation during this process was 5% or 0.14°; the optical purity was not determined. FCBAA/RMBA was recrystallized in a similar manner from benzene. The change in optical rotation of FCBAA/RMBA after two crystallizations from benzene was 2% or 0.07°, while the cumulative yield for this process was 13%. The free acid was not isolated from FCBAA/RMBA salts when they were recrystallized from either carbon tetrachloride or benzene.

The brucine salt of FCBAA (FCBAA/BRU) was prepared and recrystallized from boiling methanol, which gave colourless needles. After three recrystallizations from methanol, the values of the optical rotation of the crystallized salt had not changed. Consequently, recrystallization of FCBAA/BRU was attempted from toluene and then from acetone, but neither of these solvents dissolved the FCBAA/BRU effectively; it was finally recrystallized four times from isopropyl alcohol (IPA). The optical rotations of all the salt fractions obtained from the IPA crystallizations were significantly different from that of the fractions recrystallized from methanol. Elemental analysis of the FCBAA/BRU salt recrystallized from methanol agreed with the calculated value, but the elemental analysis of the fractions crystallized from IPA were rich in carbon, nitrogen and hydrogen, suggesting that some decarboxylation of the FCBAA/BRU salt had probably occurred. Decarboxylation of the FCBAA/BRU salt had probably also occurred during its attempted recrystallization from toluene, since its boiling point is 111°C. It was later found that FCBAA salts start to decarboxylate thermally above 85°C[9,22].

The strychnine salt of FCBAA (FCBAA/STRY) was recrystallized from IPA and MeOH; in both cases the salt was isolated as needle-like crystals. After three recrystallizations of FCBAA/STRY from IPA, the change in optical rotation for the more soluble isomer was 1.1° or 6%, while the cumulative yield of the less soluble isomer was 34%. After two recrystallizations of the FCBAA/STRY salt from MeOH, the change in optical rotation for the more soluble isomer was 1.8° or 10%, while the cumulative yield of the less soluble isomer was 24%. The optical purities of the FCBAA/STRY salt obtained by recrystallization from IPA and MeOH were determined from the borneol esters of the resolved FCBAA to be 22% (61/39 mixture of isomers) and 34% (67/33 mixture of isomers), respectively.

The results of our preliminary studies on the optical resolution of FCBAA indicate that the best system for obtaining FCBAA of high optical purity was the crystallization of the strychnine salt from methanol.



Scheme 1 Synthesis of optically active fluorochlorobromoacetaldehyde (FCBA)

Two large-scale optical resolutions of FCBAA were carried out by recrystallization of its strychnine salt (110 g and 170 g of salt) from methanol. The greatest change in optical rotation for the less soluble FCBAA/STRY isomer was 3.4° or 20%, which was done in a cumulative yield of 19% in four recrystallizations. The free acid was liberated from the recrystallized salt and gave optically active FCBAA, which had an optical purity of 66% (83/17 mixture of the antipodes). The optical purity of PCBAA was determined by ^{19}F n.m.r. spectroscopy of its bornyl ester[9,21].

In all cases, it was necessary to minimize the time the salt remained in contact with the hot solvent, otherwise the salts started to decarboxylate.

FCBAA was liberated from the STRY salts by neutralizing their aqueous suspension with sulphuric acid and extracting the free FCBAA with diethyl ether.

(+)-FCBAA was esterified with ethanol (the esterification method was studied with trichloroacetic acid as the model); it resulted in a 79% yield of ethyl fluorochlorobromoacetate (EFCBA) ($[\alpha]_D^{22} = +4.8°$, 6.3 g dl^{-1} in CCl_4).

EFCBA was reduced with DIBAL-H (using the method developed for MFCBA) and gave HEFCBA. When HEFCBA was extracted from the aqueous phase by continuous liquid/liquid extraction with diethyl ether, water was simultaneously extracted, and the extraction time had to be limited.

(−)-FCBA was partially esterified with methanol and completed with ethanol; benzene was used as the solvent. The mixed esters were obtained in about 80% yield (MFCBA, 80%; EFCBA, 20%), $[\alpha]_D^{22} = -4.6°$ (5.1 g dl^{-1} in CCl_4), and were reduced with DIBAL-H. Water was not simultaneously extracted during the extraction of the hydrate/mixed methyl and ethyl hemiacetal.

The optical rotation of the pure antipodes of FCBAA and FCBA are unknown because neither FCBA nor FCBAA had been prepared in optically pure form. Hence it was necessary to devise a system which would allow us to determine the optical purity of FCBAA and FCBA.

The melting behaviour of the amine salts of FCBAA was not characteristic since the salts decompose without melting, and recrystallization to constant melting point was not feasible. Determination of the optical purity of the enantiomers of MFCBA and FCBA was attempted by g.c. Using several chiral packing materials, gas chromatography did not separate MFCBA or FCBA into the antipodes.

Two esters of FCBAA, borneol fluorochlorobromoacetate (BFCBA) and *R*(−)-2-octyl fluorochlorobromoacetate (RFCBA), were synthesized and analysed by g.c. using packed alumina columns, but no separation into the two individual diastereoisomeric esters was achieved.

The most convenient method of determining optical purity was thought to be by direct analysis of the diastereoisomeric amine salts of FCBAA by n.m.r. spectroscopy. The ^1H, ^{13}C and ^{19}F n.m.r. spectra of RMBA/FCBAA and STRY/FCBAA were determined in deuteriobenzene, deuteriopyridine and deuteriochloroform in the absence or presence of chiral or achiral lanthanide shift reagents; however, in all cases the hydrogen, carbon or fluorine atoms were magnetically equivalent[9].

The direct determination of the optical purity of FCBA was also attempted by n.m.r. spectroscopy, but in two different ways. The first attempt was the use of a shift reagent and the second attempt involved the synthesis of the diastereoisomeric hemiacetals.

The ^{19}F n.m.r. spectrum of FCBA (benzene-d_6, $CFCl_3$ reference) was observed at −77.52 ppm. The ^{19}F n.m.r. spectrum of FCBA (chloroform-d, $CFCl_3$ reference, 15015 Hz window), which contained a 7.0/1.0 molar ratio of FCBA/ytterbium TTF (YbTTF), was used; the ^{19}F resonance was observed at −77.42 ppm. When the molar ratio of FCBA/YbTTF was increased to 3.1/1.0, the ^{19}F n.m.r. resonance shifted upfield to −77.70 ppm. Magnetic equivalence was not observed in either case. The spectral window was then changed from 15015 Hz (186 ppm full width) to 125 Hz (1.5 ppm full width). The ^{19}F n.m.r. spectra of FCBA/YbTTF (7.0/1.0 and 3.1/1.0) showed F/H coupling, but magnetic non-equivalence was still not observed. The small induced shifts (estimated to be 0.98 ppm per molar equivalent of YbTTF) may be related to the lower electron density of the carbonyl oxygen caused by the electron-withdrawing capability of the trihalo group. This makes the carbonyl oxygen atom of FCBA a poor Lewis base, which does not complex well with the shift reagent (a Lewis acid).

The second attempt at the determination of the optical purity of FCBA was made by forming its diastereoisomeric *S*(+)-2-octyl hemiacetal. The ^{19}F n.m.r. spectrum (benzene-d_6, 15015 Hz, 178 ppm full width, $CFCl_3$ reference) of FCBA showed a single resonance at −77.52 ppm. The sample tube also contained a sealed capillary tube filled with a 90/10 mixture of carbon tetrachloride/trifluoroacetic acid which had a ^{19}F resonance at −78.26 ppm. Into the septum-capped n.m.r. tube was then injected a small amount of *S*(+)-2-octanol (0.5 mol% based on FCBA) and the ^{19}F n.m.r. spectrum was rerun while closing the spectral window to 2000 Hz (23.7 ppm full width) (external trifluoroacetic acid as reference). The ^{19}F n.m.r. resonance of the FCBA was observed at 0.92 and 0.96 ppm (H/F coupling). The ^{19}F n.m.r. resonance of the FCBA-2-*S*(+)-octyl hemiacetal was a complex multiplet centred at 13.15 ppm. The complex nature of the ^{19}F n.m.r. resonance of FCBA-2-*S*(+)-octyl hemiacetal precluded the determination of the optical purity.

The best solution to the problem of the determination of the optical purity of FCBAA was found to be the synthesis of diastereoisomeric esters of FCBAA using a chiral alcohol and measuring their ^{19}F n.m.r. spectra.

Borneol and *R*(−)-2-octyl esters of racemic FCBAA were synthesized (BFCBA and RFCBA, respectively) and the ^{19}F n.m.r. spectra (15015 Hz, 178 ppm full width) were measured. In both cases the ^{19}F n.m.r. fluorine resonances overlapped and did not allow accurate integration. The ^{19}F n.m.r. resonances of the BFCBA peaks were separated by 0.13 ppm, while the fluorine resonances in RFCBA were separated by only 0.08 ppm. When the spectral window was opened to 500 Hz (5.9 ppm full width) the ^{19}F n.m.r. resonances were well separated and allowed a direct integration of the diastereoisomeric esters. Both the borneol and *R*(−)-2-octyl esters of racemic FCBAA showed a 50/50 ratio of the diastereoisomeric esters. They were determined quantitatively by peak height and the 'cut and tare' method. Furthermore, RFCBA was measured with a continuous-wave instrument (2 ppm full width); direct integration of the ^{19}F n.m.r. resonance peaks could be carried out; they were found to be of equal intensity. These experiments established the validity of this tech-

nique for determining the optical purity of FCBAA.

Since the borneol ester has the largest peak separation, borneol esters of seven samples of partially resolved FCBAA were synthesized and their ^{19}F n.m.r. spectra (500 Hz, 5.9 ppm full width or 250 Hz, 3.0 ppm full width in benzene-d_6) were measured[9]. The plot of the optical rotation of FCBAA as a function of the optical purity of FCBAA (as determined by ^{19}F n.m.r. spectroscopy of the BFCBAs) resulted in a linear relationship (*Figure 1*). Extrapolating for the optical rotation of the pure enantiomer, an $[\alpha]_D^{22}$ of $\pm 15.5°$ (in diethyl ether) was obtained for optically pure FCBAA.

The synthesis of BFCBA was accompanied by esterification of FCBAA and borneol in benzene using the azeotropic removal of water. In one case, FCBAA was allowed to react with carbonyldiimidazole to form the imidazolide of FCBAA, which was then treated with borneol and formed BFCBA. The ^{19}F n.m.r. resonance of FCBAA was observed at -63.00 ppm and that of BFCBA was observed at -63.89 and -64.00 ppm (relative to $CFCl_3$).

The synthesis of RFCBA was accomplished by esterification of *R*(−)-2-octanol and FCBAA in benzene and removing the water by azeotropic distillation. Unlike the borneol esters synthesized under similar conditions, a small doublet was observed at -63.19 and -63.21 ppm (^{19}F n.m.r. resonance of RFCBA had been found at -63.61 and -63.70 ppm). The small multiplet is believed to be due to the presence of a small amount of FCBAA anhydride. Unlike the borneol esters, which were synthesized using a 1.5 molar excess of borneol, RFBCA had been prepared with only a 1.1 molar excess of *R*(−)-2-octanol.

(−)-FCBA was liberated from its hydrated/hemiacetal in a two-step process. The first step consisted of the distillation of (−)-FCBA from a mixture of sulphuric acid/phosphorus pentoxide. The second step involved distillation of the crude (−)-FCBA from sulphuric acid,

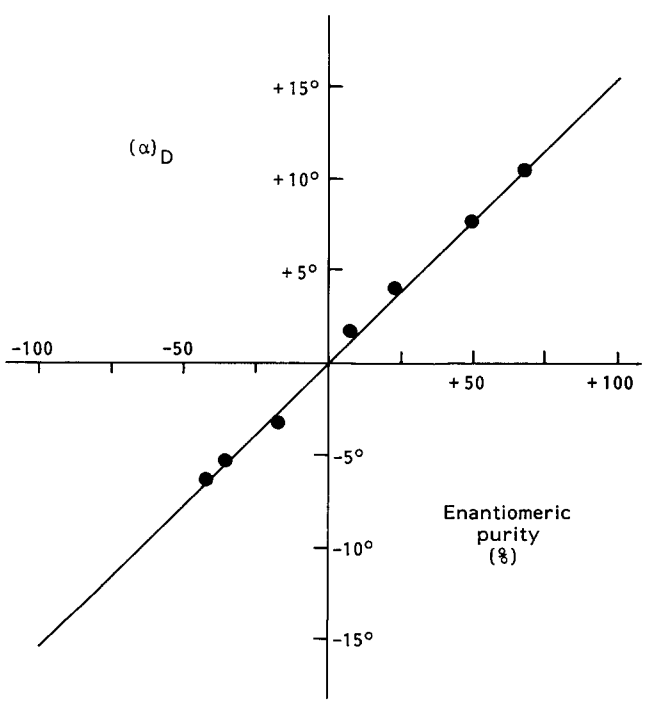


Figure 1 Optical rotation of fluorochlorobromoacetic acid (FCBAA) in diethyl ether

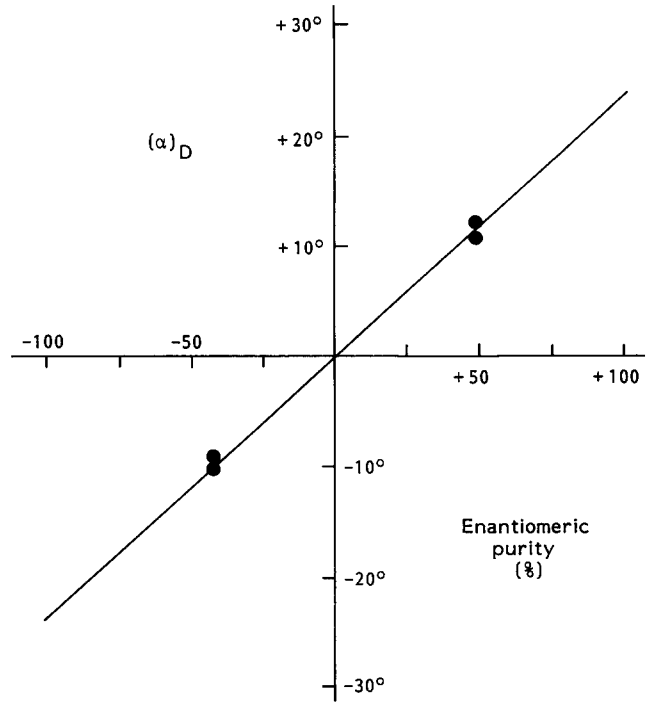


Figure 2 Optical rotation of fluorochlorobromoacetaldehyde (FCBA) in chloroform

which gave (−)-FCBA in an overall yield of 67%, $[\alpha]_D^{22} = -10.5°$ (12.31 g dl^{-1} in CCl_4). G.c. analysis of this sample of (−)-FCBA showed it to have a chemical purity of 98.6%.

(+)-FCBA was liberated from its hydrate/hemiacetal by a procedure similar to that of (−)-FCBA except that the crude (+)-FCBA was distilled from phosphorus pentoxide. (+)-FCBA was obtained in an overall yield of 54%, $[\alpha]_D^{22} = +10.9°$ (12.11 g dl^{-1} in CCl_4). G.c. analysis of (+)-FCBA showed it to have a chemical purity of 99.96%; the impurity was 0.04% diethyl ether. In comparing the g.c. analysis of (+)- and (−)-FCBA, it is evident that phosphorus pentoxide is a more effective dehydrating agent than sulphuric acid.

The optical rotation of (+)-FCBA and (−)-FCBA samples is plotted against the enantiomeric purity of FCBAA in *Figure 2* (as determined by ^{19}F n.m.r. spectroscopy of the borneol ester of the parent FCBAA, which was analysed to have an optical purity of 29/71 and 74/26, respectively); a linear relationship was established. The optical rotation of the pure antipodes of FCBA was extrapolated to be $\pm 24°$ ($\pm 1°$) (in CCl_4 at the Na D line). In all the extrapolations of optical purity it is assumed that the chiral centre was unaltered during the synthetic sequence leading from optically active FCBAA to optically active FCBA.

(+)-FCBA and (−)-FCBA were polymerized with both *R*(−)-Li-2-octanoxide (RLO) and *S*(+)-Li-2-octanoxide (SLO) using 0.5–2.0 mol% initiator respectively. The polymer samples were stabilized by treating them in methanol/HCl. PFCBA samples obtained from (+)-FCBA using RLO and SLO as initiators were isolated as solid plugs in yields of 65% and 61%, respectively. PFCBA samples obtained from (−)-FCBA using RLO and SLO as initiators were isolated also as solid plugs in 46% and 55% yields, respectively.

The optical rotation of PFCBA was measured in the solid state by suspending the polymer in an isorefractive

mixture of CCl_4/CS_2. A negligible optical rotation was found for PFCBA obtained from both (+)- and (−)-FCBA at the Na D line. Furthermore, the optical rotation of PFCBA obtained from (+)-FCBA was measured as a function of wavelength, at 578, 546 and 436 nm (it was not possible to measure the optical activity at 365 nm due to the low transmission of light from carbon disulphide absorption). The values of the polymer showed low, if any, optical activity. It should be noted that the optical activity contributed to the overall rotation of the polymer from the chiral side-group alone (from the optical purity of the starting monomer FCBA) was estimated to be a maximum of 10°; this value would be well within the experimental error for the measurement of optical activity in suspension.

Polymers obtained from both (+)- and (−)-FCBA were thermally degraded (180°C, 30 mmHg) and the optically active monomer was isolated. (−)-FCBA (purity >99.99% by g.c.) was isolated from PFCBA (obtained from (−)-FCBA) in 45% yield; it had an optical rotation $[\alpha]_D^{22} = -9.6°$ (10.4 g dl^{-1} in CCl_4); the original monomer had an optical rotation $[\alpha]_D^{22} = -10.5°$ (12.3 g dl^{-1} in CCl_4). (+)-FCBA (purity >99.99% by g.c.) was isolated (using the procedure described for (−)-FCBA) in 27% yield from PFCBA (obtained from (+)-FCBA) and had an optical rotation of $[\alpha]_D^{22} = +11.8°$ (8.91 g dl^{-1} in CCl_4); the original monomer had an optical rotation of $[\alpha]_D^{22} = +10.9°$ (12.11 g dl^{-1} in CCl_4). The low yields of the FCBA monomers obtained from the thermal degradation of PFCBA are probably due to volatilization and transfer losses, since only 0.31 g and 0.37 g, respectively, of polymer was used in the thermal degradation of the two samples of PFCBA. The optical rotation of (+)- and (−)-FCBA obtained by thermal degradation of PFCBA was compared with the enantiomeric composition of FCBA. The enantiomeric composition of FCBA was determined from the ^{19}F n.m.r. spectra of the borneol ester (assuming that the chiral centre was unaltered during subsequent synthesis steps); it is plotted in *Figure 2*.

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