

Electronic Supplementary Information

Synthetic routes for a variety of halogenated (chiral) acetic acids from diethyl malonate

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1 General conditions

A flow or an atmosphere of dry nitrogen was used with a schlenk-apparatus for all water- and/or air-sensitive reactions. For the same purpose the glassware was dried with a heat gun. The quantitative and qualitative characterization was performed with GC-MS and NMR (500 MHz). For the gas chromatography with mass spectrometry a capillary column with InterCap 5MS/NP was used and the signals were recorded as the total ion current of the ions between m/z 50 and 500. The temperature method started isothermal at 60 °C for 1 minute and was increased to 150 °C with 15 °C per minute. With 40 °C per minute the oven was heated to 300 °C and kept for 1 minute. This resulted in a method length of 11 minutes and 45 seconds. ^1H , ^{13}C and ^{19}F NMR are recorded in parts per million and the data was reported as chemical shift (δ) in parts per million (ppm), multiplicity, coupling constant (J) in Hz and integration. The ^{13}C NMR are ^1H decoupled.

Commercial reagents were used with the given purity of the supplier. The purification of the intermediates was done by column chromatography if necessary. The given yields are the ^1H NMR purity corrected values. For comparison we list the ^1H NMR and GC-MS purities.

2 Monohalogenated malonates 9

Diethyl bromomalonate 9a: The reaction apparatus was heated under vacuum and flushed with nitrogen before usage. Sodium hydride (12.9 g, 60 %, 321.8 mmol) was suspended in dimethylsulfoxide (500 ml, anhydrous). Diethylmalonate **8** (50.2 g, 99 %, 310.3 mmol) was slowly dropped to the suspension. The resulting mixture was added dropwise to a vigorously stirred solution of CuBr₂ (150.3 g, 99 %, 666.0 mmol) in dimethylsulfoxide (275 ml, anhydrous). After the addition of ice water (200 ml) and H₂SO₄ (200 ml, 5 %), the mixture was extracted with dichloromethane (3 × 200 ml). The combined organic layer was washed with water (3 × 200 ml), dried over Na₂SO₄ and was then completely evaporated. The total yield was 81.0 g (99 %) of a colorless liquid with a purity of 91.7 % according to ¹H NMR (90.9 % GC-MS).

¹H NMR (500 MHz, CDCl₃): δ 4.84 (s, 1H), 4.31 (q, *J* = 7.1 Hz, 4H), 1.33 (t, *J* = 7.1 Hz, 6H). ¹³C NMR (126 MHz, CDCl₃): δ 164.58 (s, 2C), 63.23 (t, 2C), 42.41 (d, 1C), 13.88 (q, 2C). GC-MS *t*_R 8.60 min.

Diethyl chloromalonate 9b: The reaction apparatus was heated under vacuum and flushed with nitrogen before usage. Diethyl bromomalonate **9a** (6.9 g, 98 %, 28.2 mmol) was dissolved in dimethylsulfoxide (25 ml, anhydrous). *N*-chlorosuccinimide (6.7 g, 99 %, 49.0 mmol) was added and the mixture was stirred at room temperature over night. After the addition of saturated ammoniumchloride solution (20 ml) and water (50 ml), the mixture was extracted with ethyl acetate (3 × 20 ml). The combined organic layers were washed with saturated NaCl-solution (3 × 20 ml). The solvent was completely evaporated after drying with Na₂SO₄. The crude product was purified by column chromatography (cyclohexane:ethyl acetate, 5:1). The yield was 6.2 g (99.4 %) with a purity of 88.0 % according to ¹H NMR (83.4 % GC-MS).

¹H NMR (500 MHz, CDCl₃): δ 4.86 (s, 1H), 4.32 (dq, *J* = 7.1 Hz ; 1.1 Hz, 4H), 1.34 (t, *J* = 7.1 Hz, 6H). ¹³C NMR (126 MHz, CDCl₃): δ 164.50 (s, 2C), 63.18 (t, 2C), 55.47 (d, 1C),

13.91 (q, 2C). GC-MS t_R 7.89 min.

3 Dihalogenated malonates 10

Diethyl bromochloromalonate 10a via chlorination: Diethyl bromomalonate **9a** (5.1 g, 89 %, 19.0 mmol) was dissolved in acetone (40.0 ml) and acetic acid (16.0 ml). Sodium hypochlorite solution (19.0 ml, 10 %, 25.5 mmol) was added dropwise during 30 min at 0 °C. Saturated NaHCO₃-solution (100 ml) was added to the reaction mixture. When the CO₂ evolution stopped (approximately 15 min) the organic product layer was separated and the aqueous layer was extracted with dichloromethane (3 × 30 ml). The combined organic layers were washed with water (3 × 30 ml), dried over Na₂SO₄ and were completely evaporated. The yield was 5.5 g (98.0 %) with a purity of 92.6 % according to ¹H NMR (91.8 % GC-MS). ¹H NMR (500 MHz, CDCl₃): δ 4.39 (q, *J* = 7.1 Hz, 4H), 1.36 (t, *J* = 7.1 Hz, 6H). ¹³C NMR (126 MHz, CDCl₃): δ 163.05 (s, 2C), 65.00 (s, 1C), 64.68 (t, 2C), 13.74 (q, 2C). GC-MS *t*_R 9.40 min.

Diethyl bromochloromalonate 10a via bromination: For the preparation of the sodium hypobromite solution, sodium hydroxide (3.0 g, 85 %, 63.8 mmol) was dissolved in water (50 ml) and cooled to 0 °C. Bromine (3.3 g, 99 %, 20.3 mmol) was added to the ice cold mixture and stirred for 30 min. In a separate flask diethyl chloromalonate **9b** (3.4 g, 99 %, 17.3 mmol) was dissolved in acetone (10 ml) and acetic acid (5 ml) and cooled to 0 °C. The prepared sodium hypobromite solution was added dropwise to **9b**. The reaction mixture was stirred at RT over night. The reaction mixture was added to saturated NaHCO₃-solution (20 ml) and extracted with dichloromethane (3 × 25 ml). The combined organic layers were washed with water (2 × 20 ml) and with saturated NaHCO₃-solution (2 × 20 ml), dried over Na₂SO₄ and were then completely evaporated. The total yield was 4.8 g (99.9 %) of a light brown liquid with a purity of 98.5 % according to ¹H NMR (99.1 % GC-MS). ¹H NMR (500 MHz, CDCl₃): δ 4.38 (q, *J* = 7.1 Hz, 4H), 1.35 (t, *J* = 7.1 Hz, 6H). ¹³C NMR (126 MHz, CDCl₃): δ 163.02 (s, 2C), 64.99 (s, 1C), 64.67 (t, 2C), 13.73 (q, 2C). GC-MS *t*_R 9.40 min.

Diethyl bromofluoromalonate 10b via fluorination: Sodium hydride (80.0 mg, 60 %, 2.0 mmol) was dissolved in tetrahydrofuran (5.0 ml, anhydrous). To the mixture diethyl bromomalonate **9a** (0.50 g, 99 %, 2.0 mmol) was added carefully. After 3 h the hydrogen evolution has stopped and a clear solution was obtained. This solution was cooled to 0 °C. Then N-fluoro-2,4,6-trimethylpyridinium triflate (0.605 g, 99 %, 2.1 mmol) was added. The reaction mixture was stirred at 0 °C for 30 min. To the reaction mixture water (10 ml) and hydrochloric acid (10 ml, 1 M) were added and it was then extracted with dichloromethane (3 × 20 ml). The combined organic layers were washed with saturated NaHCO₃-solution (2 × 10 ml) and water, respectively. They were subsequently dried with Na₂SO₄ and evaporated completely. The yield was 0.57 g (85.5 %) of a light brown liquid with a purity of 81.0 % according to ¹H NMR (93.4 % GC-MS).

¹H NMR (500 MHz, CDCl₃): δ 4.40 (q, *J* = 7.1 Hz, 4H), 1.37 (t, *J* = 7.1 Hz, 6H). ¹³C NMR (126 MHz, CDCl₃): δ 162.33 (d, *J*_{CF} = 26.46 Hz, 2C), 89.95 (d, *J*_{CF} = 270.9 Hz, 1C), 64.29 (t, 2C), 13.78 (q, 2C). ¹⁹F NMR (470 MHz, CDCl₃): δ - 122.38 (s, 1F). GC-MS *t*_R 7.45 min.

Diethyl bromofluoromalonate 10b via bromination: The reaction procedure was similar to the bromination of **9b** to **10a**. Diethyl fluoromalonate **9c** (1.0 g, 97 %, 5.4 mmol) was the reactant. 2 equivalent of NaOBr were used. The total yield was 1.25 g (84.9 %) of a light brown liquid with a purity of 94.3 % according to ¹H NMR (97.8 % GC-MS).

¹H NMR (500 MHz, CDCl₃): δ 4.38 (q, *J* = 7.1 Hz, 4H), 1.34 (t, *J* = 7.1 Hz, 6H). ¹³C NMR (126 MHz, CDCl₃): δ 162.28 (d, *J*_{CF} = 26.46 Hz, 2C), 89.93 (d, *J*_{CF} = 270.9 Hz, 1C), 64.27 (t, 2C), 13.74 (q, 2C). ¹⁹F NMR (470 MHz, CDCl₃): δ - 122.39 (s, 1F). GC-MS *t*_R 7.45 min.

Diethyl chlorofluoromalonate 10c via fluorination: The reaction procedure was similar to the fluorination of **9a** to **10b**. Diethyl chloromalonate **9b** (0.52 g, 97 %, 2.6 mmol) was the reactant. The yield was 0.42 g (72.7 %) of a light brown liquid with a purity of 97.5 % according to ¹H NMR (97.4 % GC-MS).

¹H NMR (500 MHz, CDCl₃): δ 4.38 (q, *J* = 7.2 Hz, 4H), 1.35 (t, *J* = 7.2 Hz, 6H). ¹³C NMR

(126 MHz, CDCl₃): δ 161.83 (s, 2C), 97.89 (d, $J_{CF} = 261.4$ Hz, 1C), 64.24 (t, 2C), 13.76 (q, 2C). ¹⁹F NMR (470 MHz, CDCl₃): δ - 161.83 (s, 1F). GC-MS t_R 6.68 min.

Diethyl chlorofluoromalonate 10c via chlorination: The reaction procedure was similar to the chlorination of **9a** to **10a**. Diethyl fluoromalonate **9c** (103.8 g, 97 %, 565 mmol) was the reactant. The yield was 106.2 g (85.8 %) of a light brown liquid with a purity of 97.1 % according to ¹H NMR (93.9 % GC-MS).

¹H NMR (500 MHz, CDCl₃): δ 4.38 (q, $J = 7.2$ Hz, 4H), 1.35 (t, $J = 7.2$ Hz, 6H). ¹³C NMR (126 MHz, CDCl₃): δ 161.83 (s, 2C), 97.89 (d, $J_{CF} = 261.4$ Hz, 1C), 64.24 (t, 2C), 13.76 (q, 2C). ¹⁹F NMR (470 MHz, CDCl₃): δ - 161.83 (s, 1F). GC-MS t_R 6.68 min.

4 Dihalogenated acetic acids 5

Deutero bromochloroacetic acid 5a: NaOD (0.75 g, 99%, 99% d-Atom, 18.6 mmol) was dissolved in MeOD (10 ml) and dropwise added at room temperature to a solution of diethyl bromochloromalonate **10a** (1.5 g, 99%, 5.4 mmol) in MeOD (5 ml). The reaction mixture was stirred at room temperature for 30 min and a white suspension was formed. D₂SO₄-solution (5 g, 30 %, 99% d-Atom, 15.0 mmol) was added to the reaction mixture and the solid dissolved. H₂SO₄-solution (20 ml, 10 %) was added and the reaction mixture was extracted with diethyl ether (3 × 20 ml). The combined organic layers were dried over Na₂SO₄ and evaporated to dryness. The yield was 0.75 g (75.7 %) of a light brown liquid with a purity of 95.1 % according to ¹H NMR (95.5 % GC-MS). The degree of deuteration is ~89 % and was determined by the abundance ratio of *m/z* 172 and 173.

¹H NMR (500 MHz, CDCl₃): δ 8.80 (s, 1H). ¹³C NMR (126 MHz, CDCl₃): δ 169.27 (s, 1C), 48.09 (t, *J*_{CD} = 27.7 Hz, 1C). GC-MS *t*_R 9.35 min.

Deutero bromofluoroacetic acid 5b: Diethyl bromofluoromalonate (1.25 g, 94 %, 4.8 mmol) was dropwise added at room temperature to a solution of D₂SO₄ (5.0 g, 99 %, 99 % d-Atom 50.0 mmol) and D₂O (5.0 g). The reaction mixture was stirred at 120 °C for 5 hours. A solution of H₂SO₄ (20 ml, 5 %) was added to the mixture and then extracted with diethyl ether (3 × 20 ml). The combined organic layers were dried over Na₂SO₄ and evaporated to dryness. The yield was 0.44 g (50.8 %) of a light brown liquid with a purity of 84.0 % according to ¹H NMR (90.3 % GC-MS). The degree of deuteration is ~97 % and was determined by the abundance ratio of *m/z* 156 and 157.

¹H NMR (400 MHz, CDCl₃): δ 8.08 (s, 1H). ¹³C NMR (126 MHz, CDCl₃): δ 166.50 (d, *J*_{CF} = 25.5 Hz, 1C), 81.25 (dt, *J*_{CF} = 262.1 Hz, *J*_{CD} = 29.0 Hz, 1C). ¹⁹F NMR (470 MHz, CDCl₃): δ -151.96 (t, *J*_{CDF} = 9.4, 1F). GC-MS *t*_R 8.11 min.

Deutero chlorofluoroacetic acid 5c: Diethyl chlorofluoromalonate (1.5 g, 98 % 6.9 mmol) was dropwise added at room temperature to a solution of D₂SO₄ (7.0 g, 99 %, 99 % d-Atom, 70.0 mmol) and D₂O (7.0 g). The reaction mixture was stirred at 120 °C over night. A solution of H₂SO₄ (20 ml, 5 %) was added to the mixture and then extracted with diethyl ether (3 × 20 ml). The combined organic layers were dried over Na₂SO₄ and evaporated to dryness. The yield was 0.41 g (48.5 %) of a light brown liquid with a purity of 92.0 % according to ¹H NMR (94.2 % GC-MS). The degree of deuteration is ~94 % and was determined by the abundance ratio of *m/z* 61 and 62.

¹H NMR (500 MHz, CDCl₃): δ 10.81 (s, 1H). ¹³C NMR (126 MHz, CDCl₃): δ 168.99 (d, *J*_{CF} = 27.7 Hz, 1C), 90.15 (dt, *J*_{CF} = 253.3 Hz, *J*_{CD} = 29.0 Hz, 1C). ¹⁹F NMR (470 MHz, CDCl₃): δ -147.77 (t, *J*_{CDF} = 4.7, 1F). GC-MS *t*_R 7.11 min.

5 Synthesis path to bromochlorofluoromethane 7

Potassium monoethyl chlorofluoromalonate: Diethyl chlorofluoromalonate **10c** (87.2 g, 93.9 %, 385.3 mmol) was dissolved in absolute ethanol (250 ml). Potassium hydroxide (24.5 g, 86 %, 374.9 mmol) was dissolved in absolute ethanol (250 ml) and added dropwise at room temperature within 4 h to the vigorously stirred solution of **3c**. The resulting suspension was filtered and the residue was washed with absolute ethanol (100 ml). The filtrate was completely evaporated. The solid product was washed with dichloromethane (150 ml) to remove the starting material. The pure product was obtained by a second filtration and drying. The yield was 52.3 g (61 %) of a white crystalline solid with a purity of approximately 100 %.

^1H NMR (500 MHz, D_2O): δ 4.31 (q, $J = 7.1$ Hz, 2H), 1.25 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (126 MHz, D_2O): δ 166.71 (d, $J_{\text{CF}} = 24.1$ Hz, 1C), 165.62 (d, $J_{\text{CF}} = 28.4$ Hz, 1C), 99.85 (d, $J_{\text{CF}} = 260.0$ Hz, 1C), 65.01 (t, 1C), 13.11 (q, 1C). ^{19}F NMR (470 MHz, D_2O): δ - 114.85 (s, 1F).

Silver monoethyl chlorofluoromalonate 11c: A highly acidic ion exchange resin (100 ml, Amberlite IR 120, Na^+ form) was filled into a glass column. A solution of silver nitrate (400 ml, 0.4 M) was used to load the resin with silver ions. Before usage the resin was washed until the eluting water was free of silver ions. An aqueous solution of potassium monoethyl chlorofluoromalonate (4.0 g, 0.018 mol, 0.03 g/L) was eluted through the resin. The complete evaporation of the aqueous fraction gave 5.2 g (99 %) of the silver monoethyl chlorofluoromalonate **11c** as a grey solid with a purity of 100 % (XRF and ^{19}F NMR).

^1H NMR (500 MHz, D_2O): δ 4.44 (q, $J = 7.1$ Hz, 2H), 1.40 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (126 MHz, D_2O): δ 165.70 (d, $J_{\text{CF}} = 28.5$ Hz, 1C), 161.81 (d, $J_{\text{CF}} = 31.3$ Hz, 1C), 97.29 (d, $J_{\text{CF}} = 262.3$ Hz, 1C), 65.00 (t, 1C), 13.72 (q, 1C). ^{19}F NMR (470 MHz, D_2O): δ - 121.17 (s, 1F).

Ethyl bromochlorofluoroacetate 4: Bromine (3.8 g, 99 %, 23.7 mmol) was dissolved in CCl_4 (40 ml). At 0 °C, silver monoethyl chlorofluoromalonate **11c** (6.0 g, 98 %, 20.2 mmol) was added portion-wise (about 1.5 g per hour), while the reaction mixture was prevented from humidity. After 1.5 h a continuous evolve of CO_2 has started. When all the reactant was added the mixture was allowed to warm to room temperature and was then hold at that temperature over night. The precipitate was filtered and washed with CCl_4 (20 ml). The bromine was removed with NaHSO_3 -solution (8 %, 3×10 ml) and washed with saturated NaHCO_3 (3×10 ml). After drying with Na_2SO_4 the solvent was completely evaporated. The yield was 1.39 g (26.1 %) of a light brown liquid with a purity of 82.6 % according to ^1H NMR (82.0 % GC-MS).

^1H NMR (500 MHz, CDCl_3): δ 4.45 (q, $J = 7.1$ Hz, 2H), 1.43 (t, $J = 7.1$ Hz, 4H). ^{13}C NMR (126 MHz, CDCl_3): δ 161.90 (d, $J_{CF} = 27.7$ Hz, 1C), 96.12 (s, 1C), 64.83 (t, 1C), 13.75 (q, 1C). ^{19}F NMR (470 MHz, CDCl_3): δ - 64.23 (s, 1F). GC-MS t_R 4.38 min.

Bromochlorofluoroacetic acid 5d: NaOH (3.5 g, 85 %, 74.4 mmol) was dissolved in water (30 ml). At 0 °C methyl bromochlorofluoroacetate **4** (12.9 g, 59 %, 34.7 mmol) was added. After 3 h the acetate was quantitatively converted. The basic solution was acidified with concentrated H_2SO_4 (3 ml) and extracted with diethylether (3×20 ml). After drying with Na_2SO_4 the organic layer was completely evaporated. The yield was 9.0 g (99 %) of a colorless liquid with a purity of 73.0 % according to ^1H NMR (73.0 % GC-MS).

^1H NMR (500 MHz, CDCl_3): δ 11.36 (s, 1H). ^{13}C NMR (126 MHz, CDCl_3): δ 166.36 (d, $J_{CF} = 28.0$ Hz, 1C), 94.47 (d, $J_{CF} = 315.0$ Hz, 1C). ^{19}F NMR (470 MHz, CDCl_3): δ - 66.02 (s, 1F). GC-MS t_R 6.69 min.

Bromochlorofluoromethane 7: Bromochlorofluoroacetic acid **5d** (9.0 g, 74 %, 34.7 mmol) was dissolved in CHCl_3 (30 ml). Strychnin (11.6 g, 98 %, 34.0 mmol) was dissolved in CHCl_3 (80 ml) and added to the acid at 0 °C over 30 minutes. After 1 h the CHCl_3 was evaporated and the strychnin salt was obtained quantitatively as a brownish solid. A part of the strychn-

nine bromochlorofluoroacetate (5.2 g, 99 %, 8.76 mmol) was suspended in ethylene glycol (10 ml). The apparatus, which consisted of an Anschuetz head, Liebig condenser, collecting flask and cooling trap, was heated and flushed with nitrogen. The collecting flask and cooling trap were cooled with a mixture of acetone and dry ice to -78 °C. The suspension was heated to 80 °C and slowly increased to 100 °C as the gas formation also increased. After 45 min the gas formation stopped and the suspension was stirred at 140 °C for 1 h. The yield was 0.6 g (46.2 %) of a colorless liquid with a purity of 95.2 % according to ^1H NMR (99.0 % GC-MS).

^1H NMR (500 MHz, CDCl_3): δ 7.64 (d, $J = 52.0$ Hz, 1H). ^{13}C NMR (126 MHz, CDCl_3): δ 89.72 (dd, $J_{CF} = 304.6$ Hz, 1C). ^{19}F NMR (470 MHz, CDCl_3): δ - 81.66 (d, $J = 52.0$ Hz, 1F). GC-MS t_R 1.81 min.

6 ^1H , ^{13}C and ^{19}F NMR spectra of all products

6.1 NMR spectra of monohalogenated malonates 9

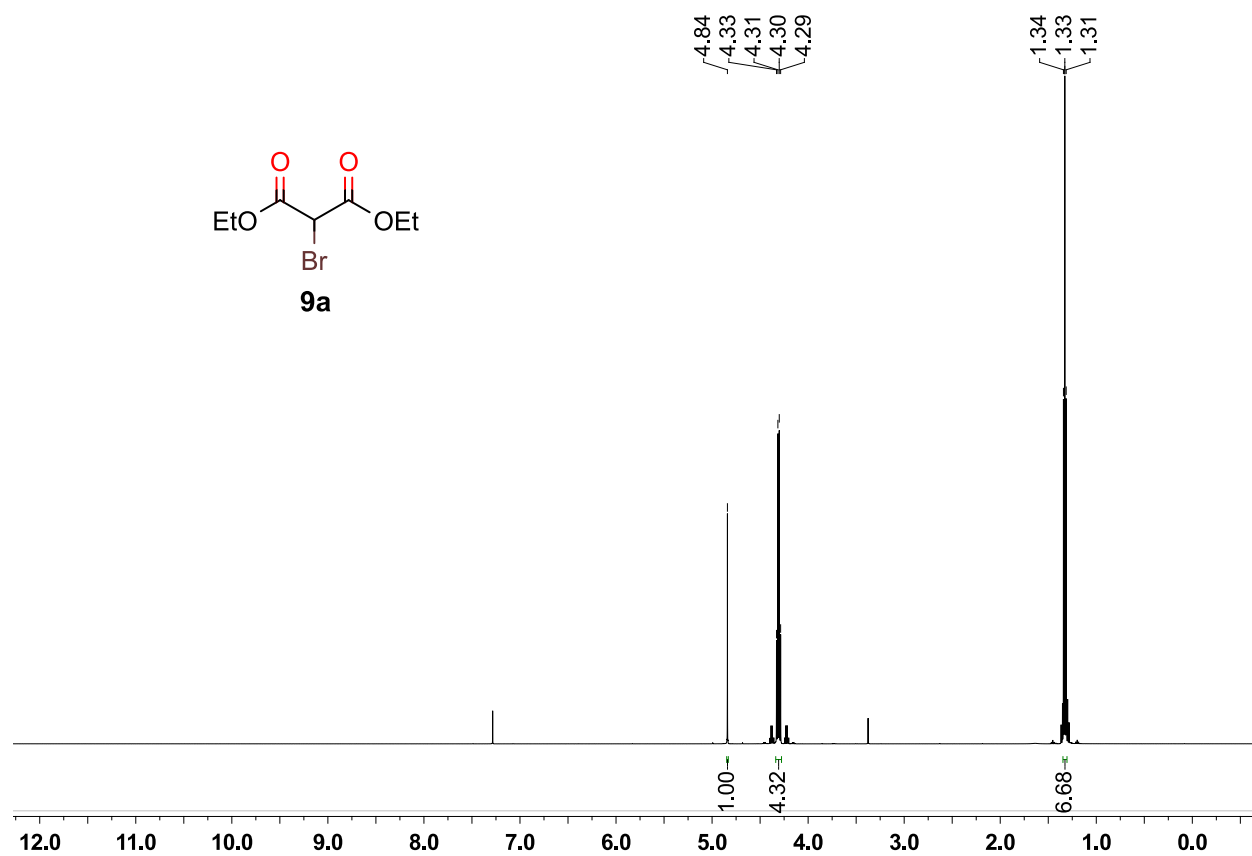


Figure 1 ^1H NMR (500 MHz) spectrum of diethyl bromomalonate (**9a**) in CDCl_3 (7.26 ppm).

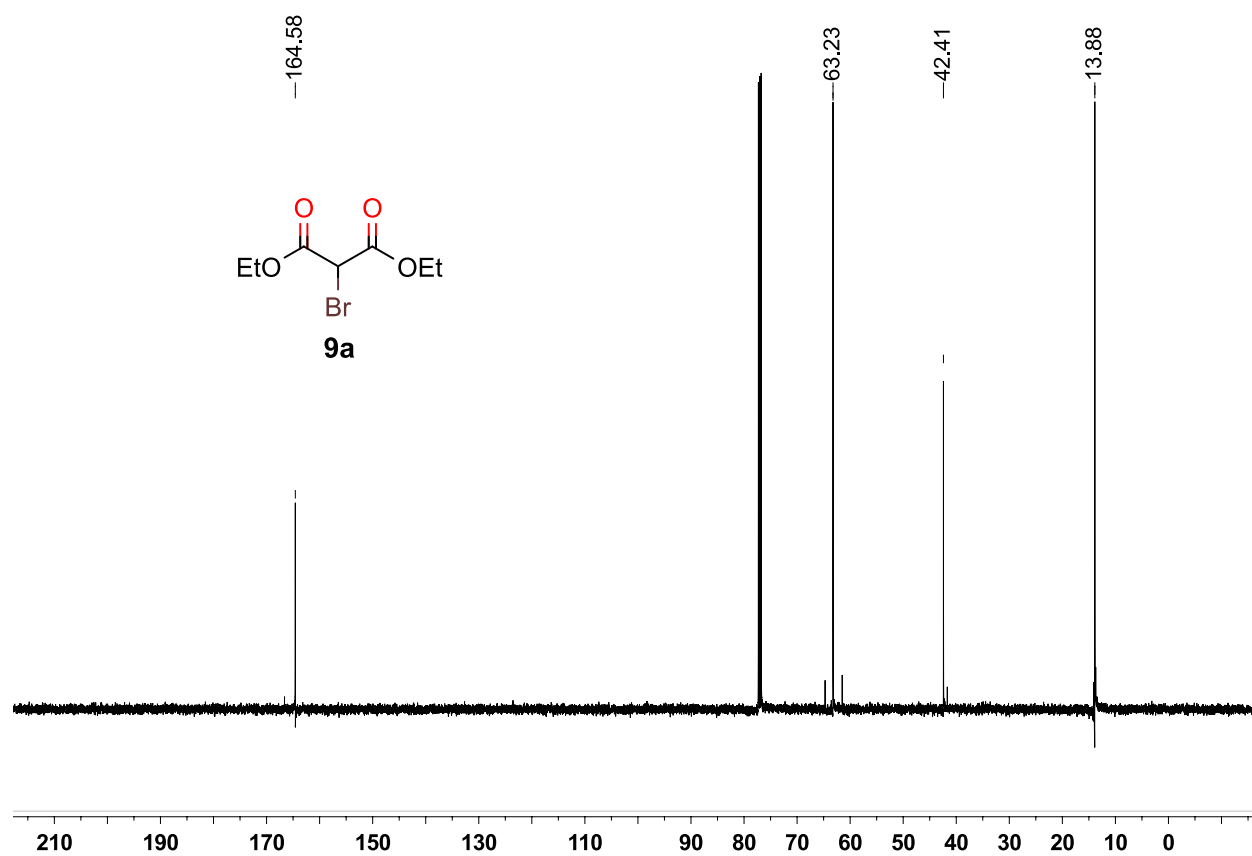


Figure 2 ^{13}C NMR (126 MHz) spectrum of diethyl bromomalonate (**9a**) in CDCl_3 (77.2 ppm).

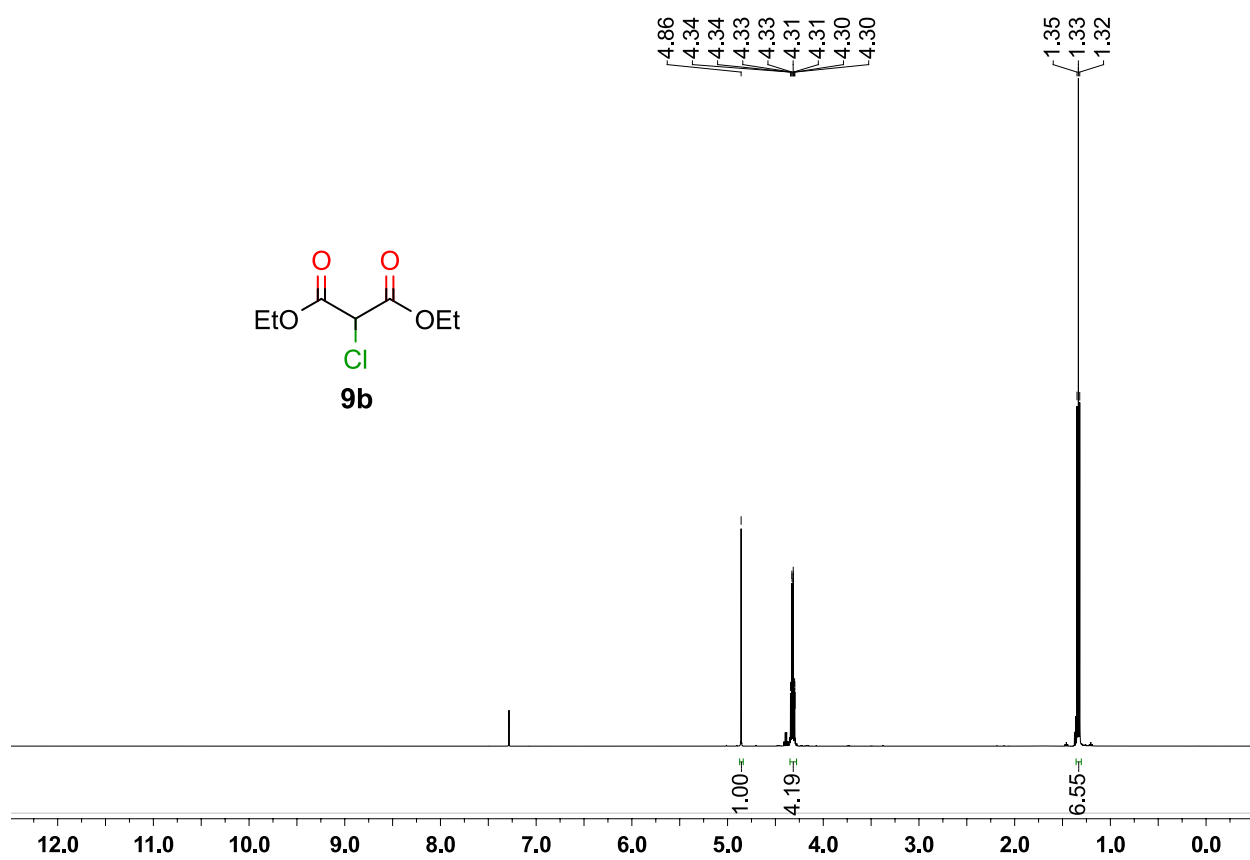


Figure 3 ^1H NMR (500 MHz) spectrum of diethyl chloromalonate (**9b**) in CDCl_3 (7.26 ppm).

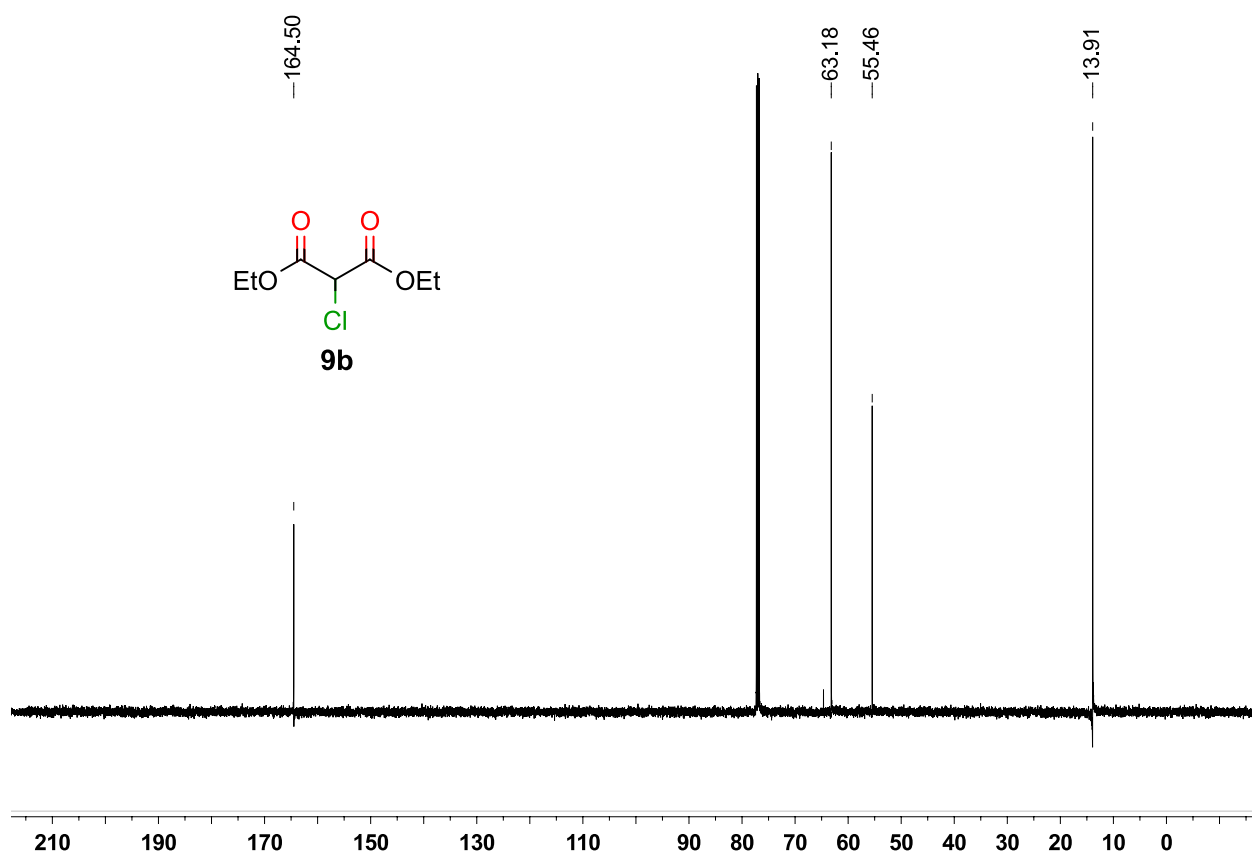


Figure 4 ^{13}C NMR (126 MHz) spectrum of diethyl chloromalonate (**9b**) in CDCl_3 (77.2 ppm).

6.2 NMR spectra of dihalogenated malonates 10

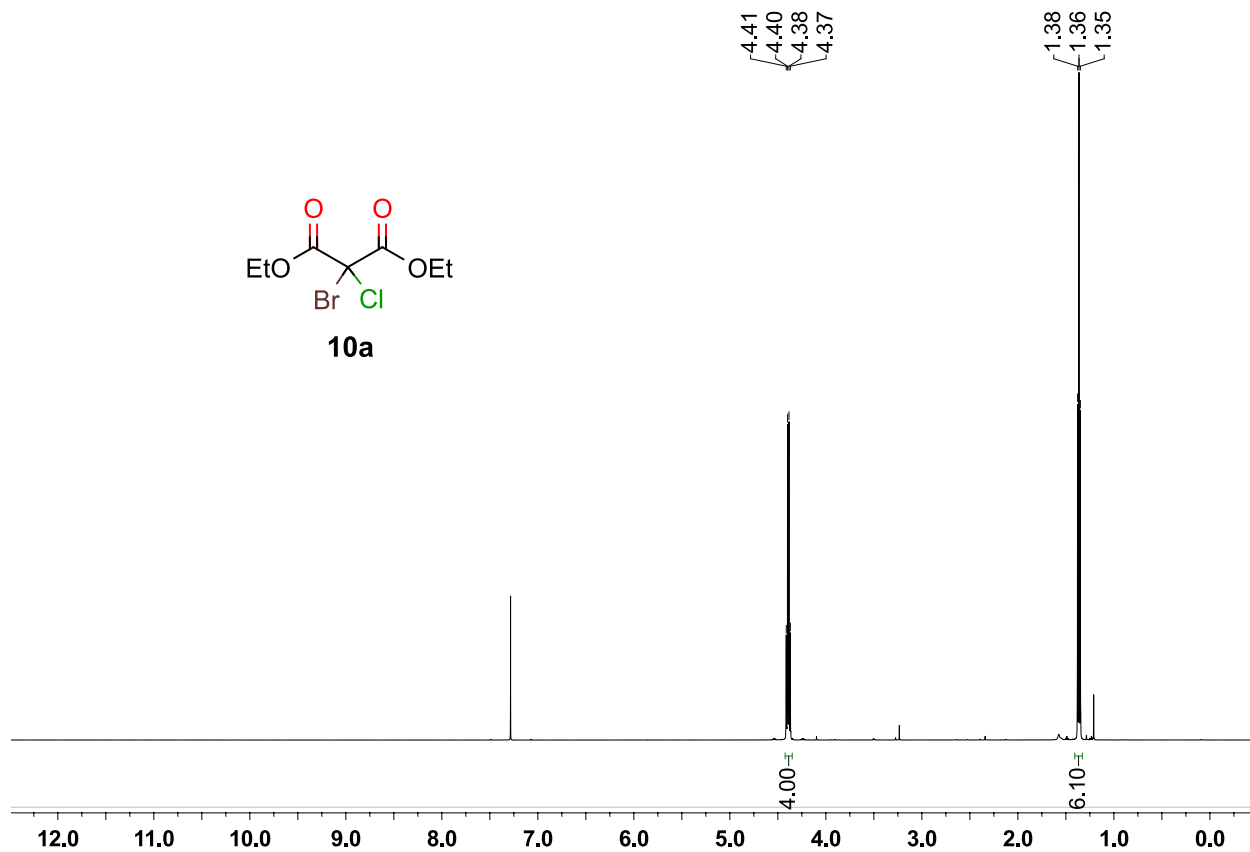


Figure 5 ¹H NMR (500 MHz) spectrum of diethyl bromochloromalonate (**10a**) in CDCl₃ (7.26 ppm) obtained from **9a**.

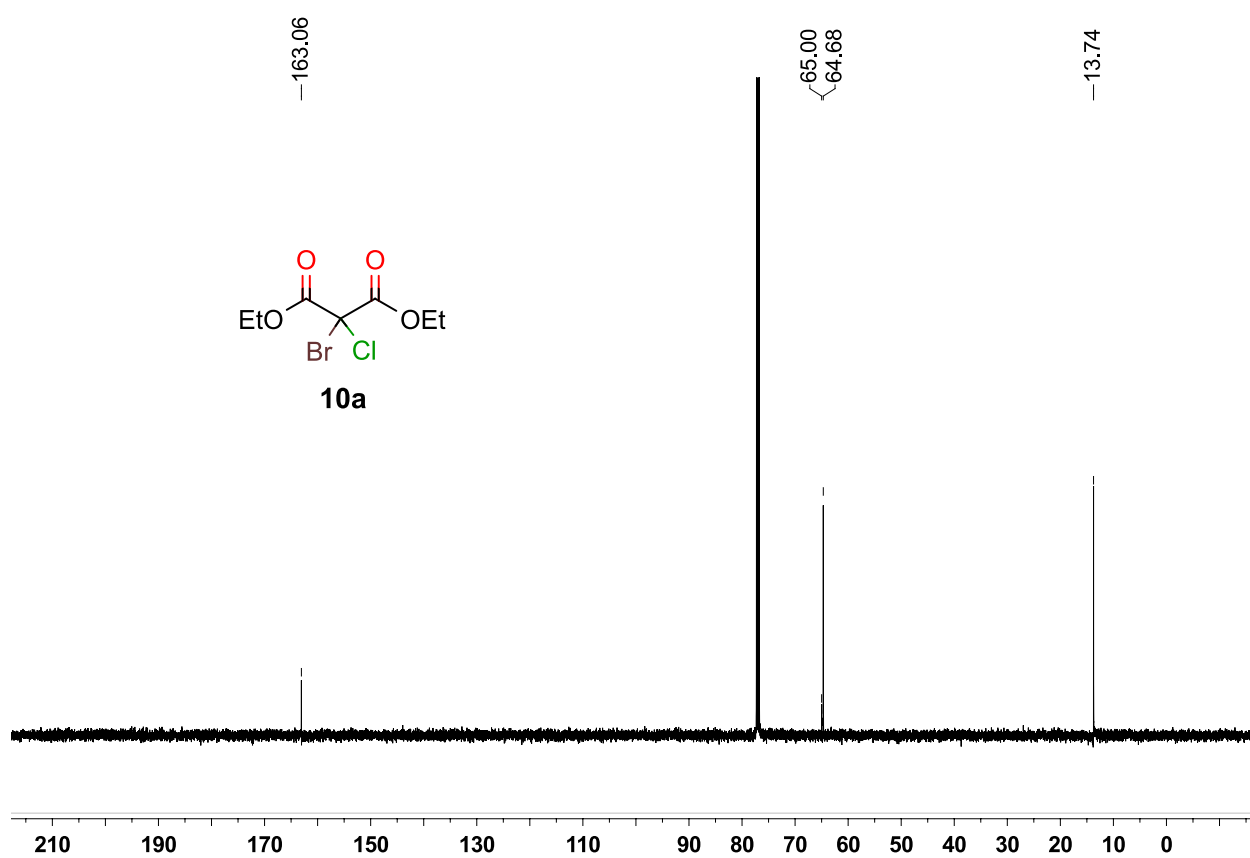


Figure 6 ^{13}C NMR (126 MHz) spectrum of diethyl bromochloromalonate (**10a**) in CDCl_3 (77.2 ppm) obtained from **9a**.

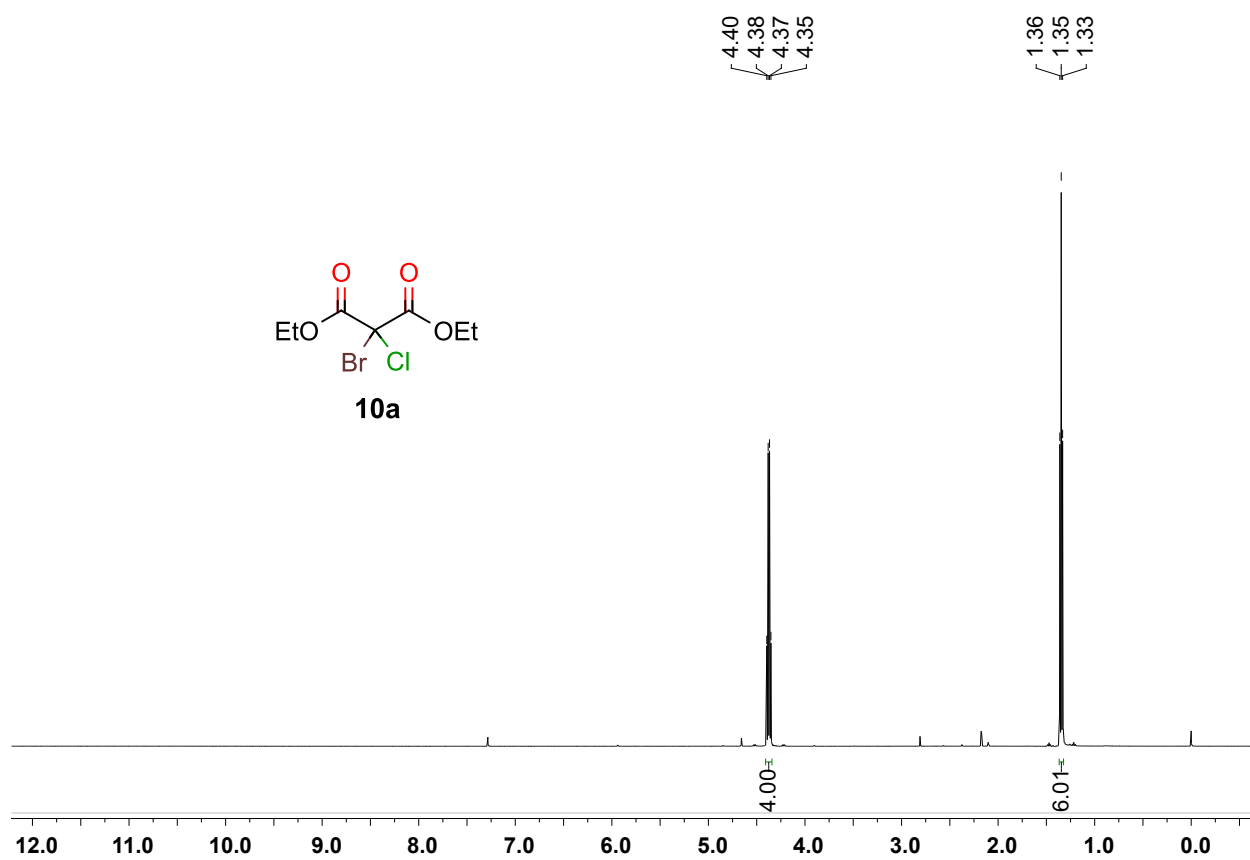


Figure 7 ^1H NMR (500 MHz) spectrum of diethyl bromochloromalonate (**10a**) in CDCl_3 (7.26 ppm) obtained from **9b**.

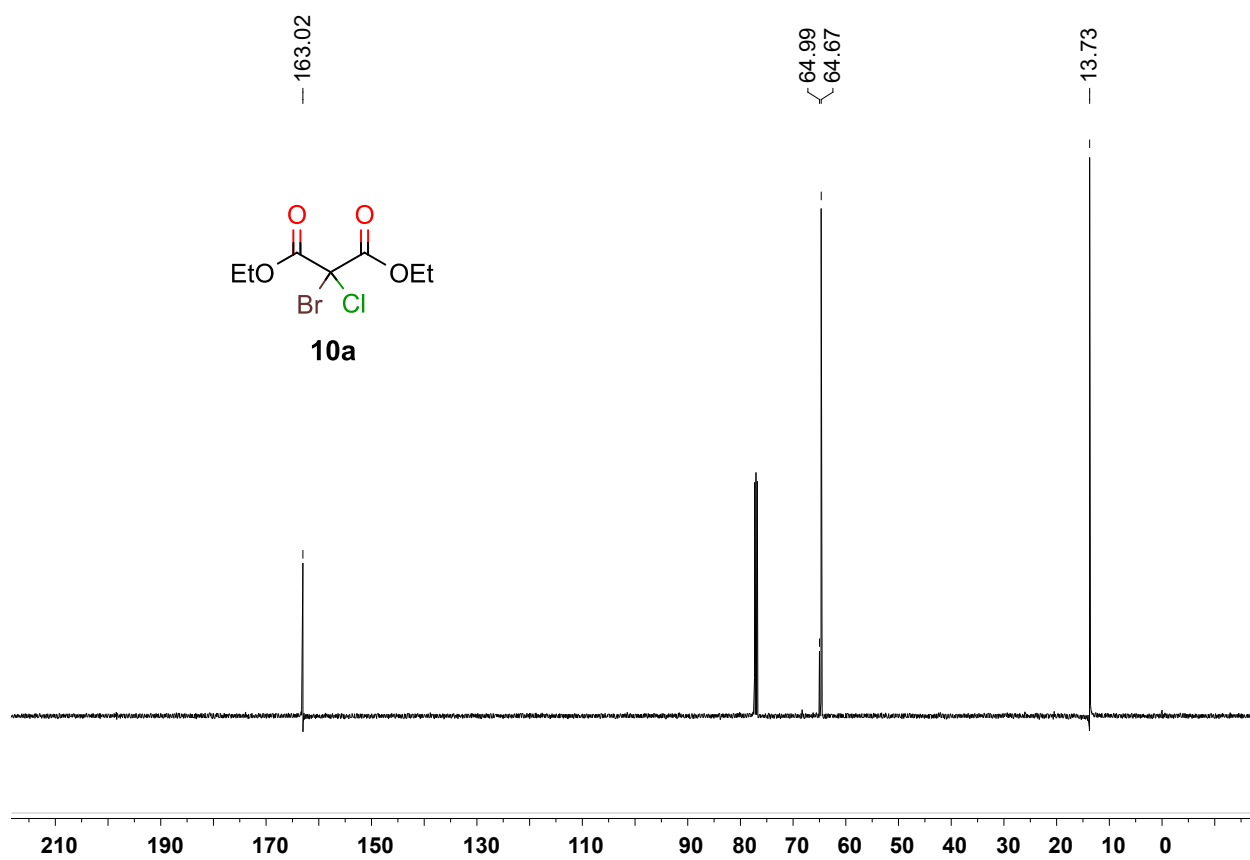


Figure 8 ^{13}C NMR (126 MHz) spectrum of diethyl bromochloromalonate (**10a**) in CDCl_3 (77.2 ppm) obtained from **9b**.

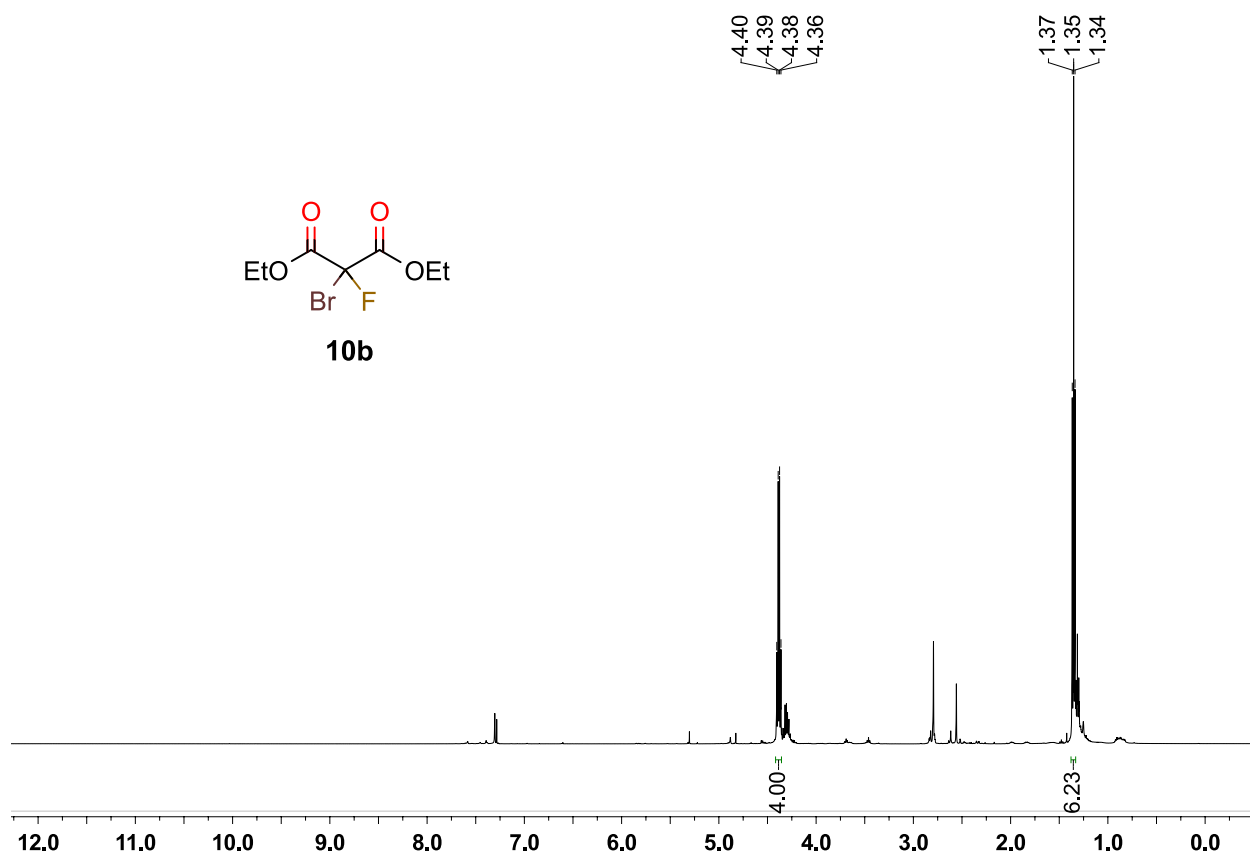


Figure 9 ¹H NMR (500 MHz) spectrum of diethyl bromofluoromalonate (**10b**) in CDCl₃ (7.26 ppm) obtained from **9a**.

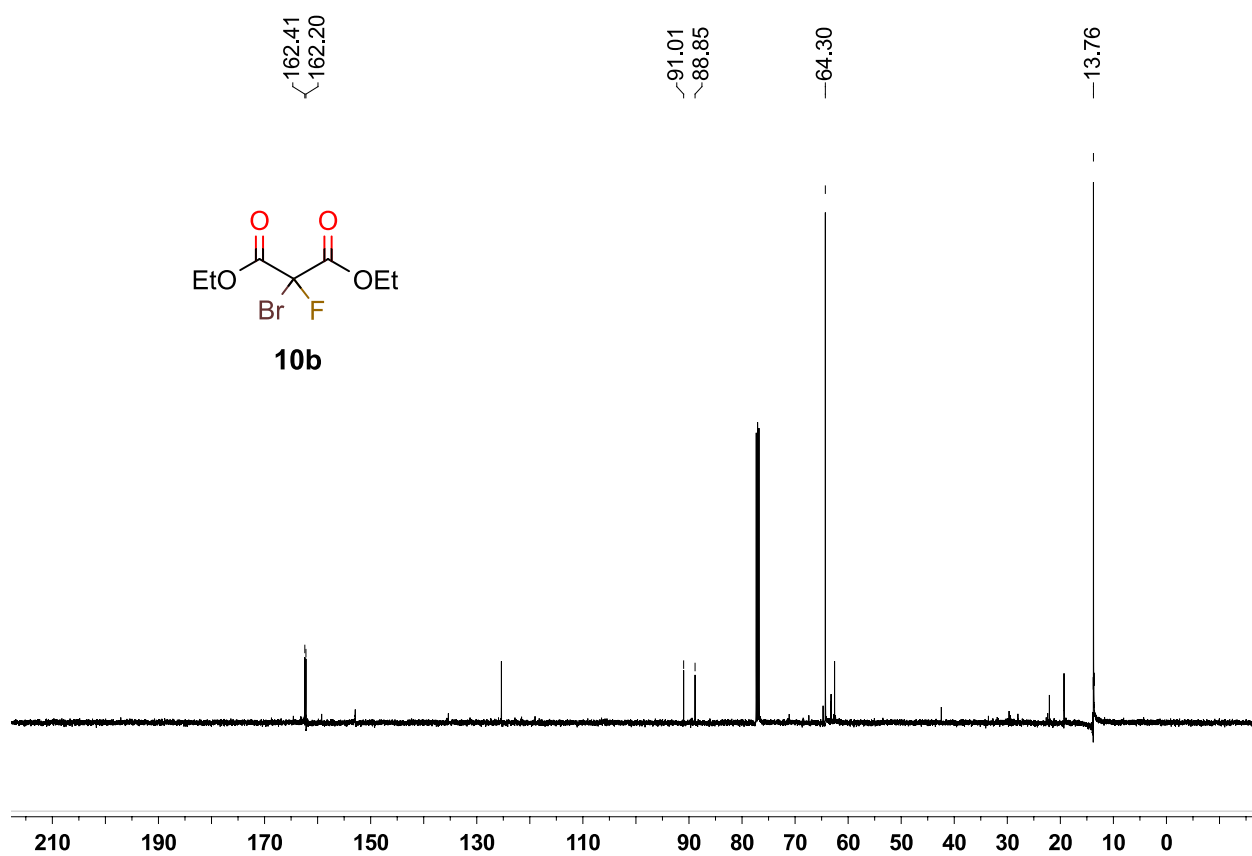


Figure 10 ¹³C NMR (126 MHz) spectrum of diethyl bromofluoromalonate (**10b**) in CDCl₃ (77.2 ppm) obtained from **9a**.

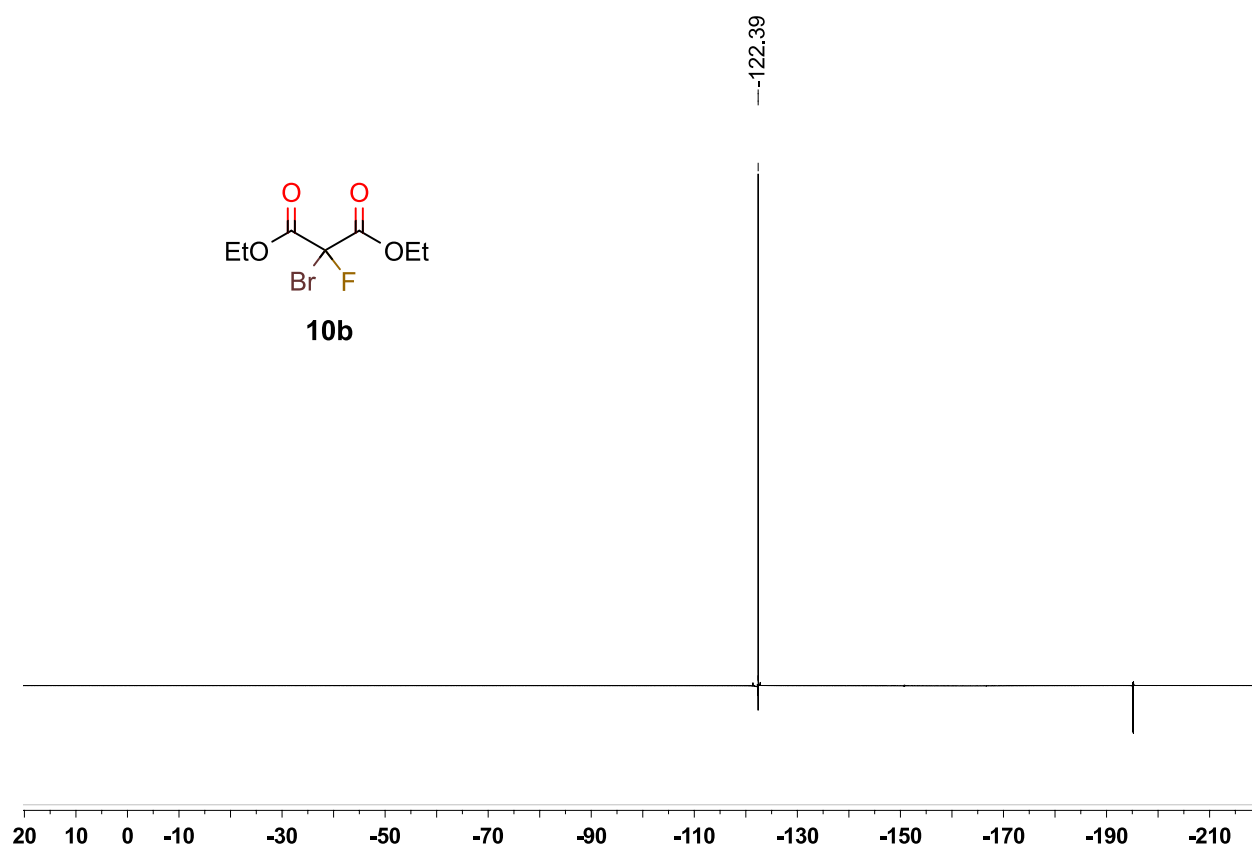


Figure 11 ^{19}F NMR (470 MHz) spectrum of diethyl bromofluoromalonate (**10b**) in CDCl_3 obtained from **9a**.

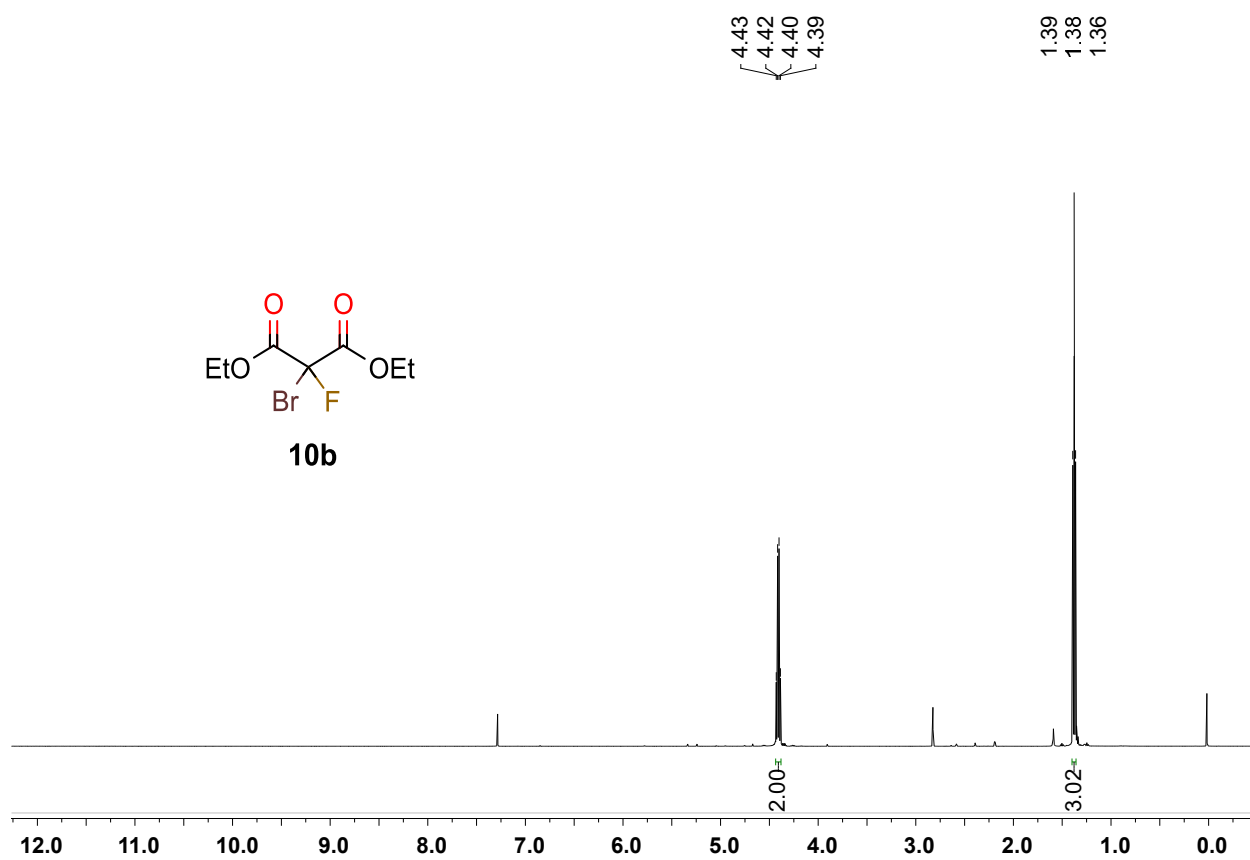


Figure 12 ¹H NMR (500 MHz) spectrum of diethyl bromofluoromalonate (**10b**) in CDCl₃ (7.26 ppm) obtained from **9c**.

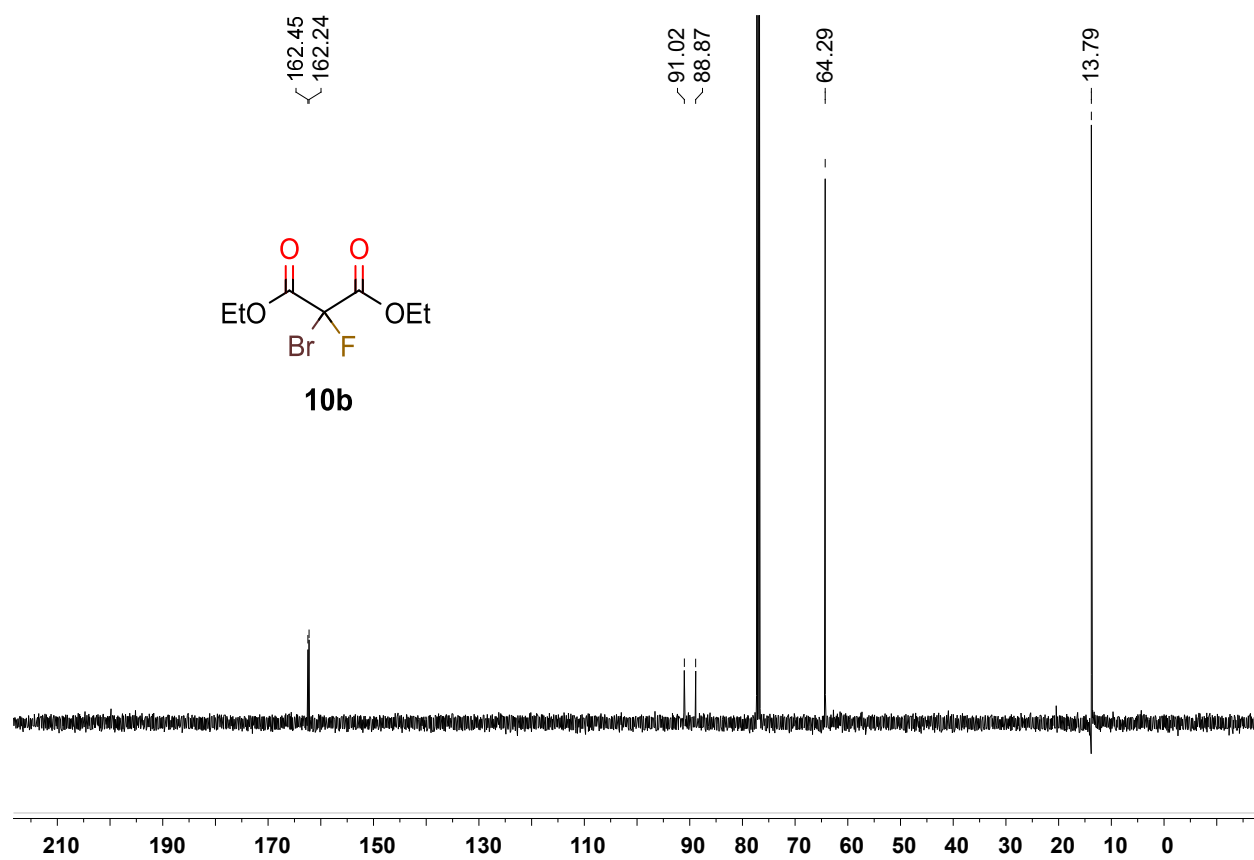


Figure 13 ^{13}C NMR (126 MHz) spectrum of diethyl bromofluoromalonate (**10b**) in CDCl_3 (77.2 ppm) obtained from **9c**.

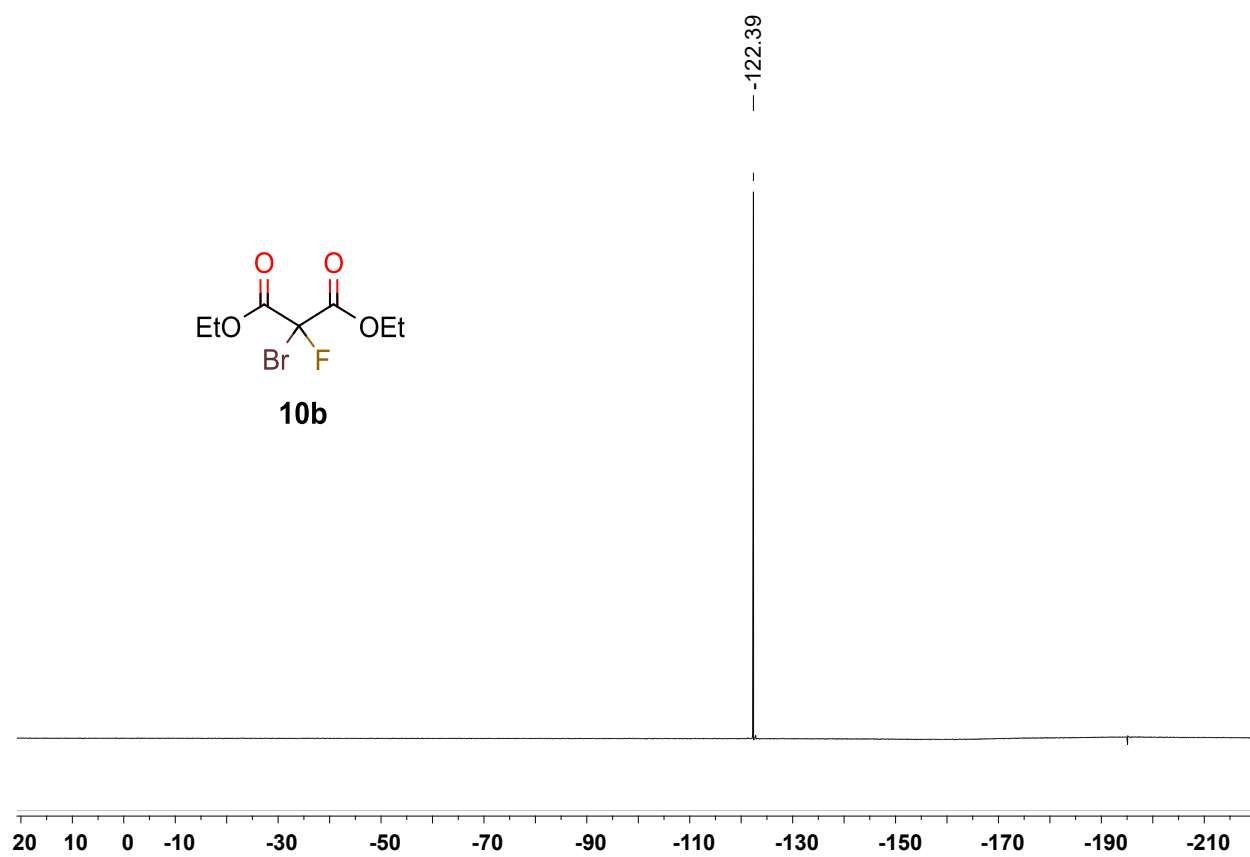


Figure 14 ^{19}F NMR (470 MHz) spectrum of diethyl bromofluoromalonate (**10b**) in CDCl_3 obtained from **9c**.

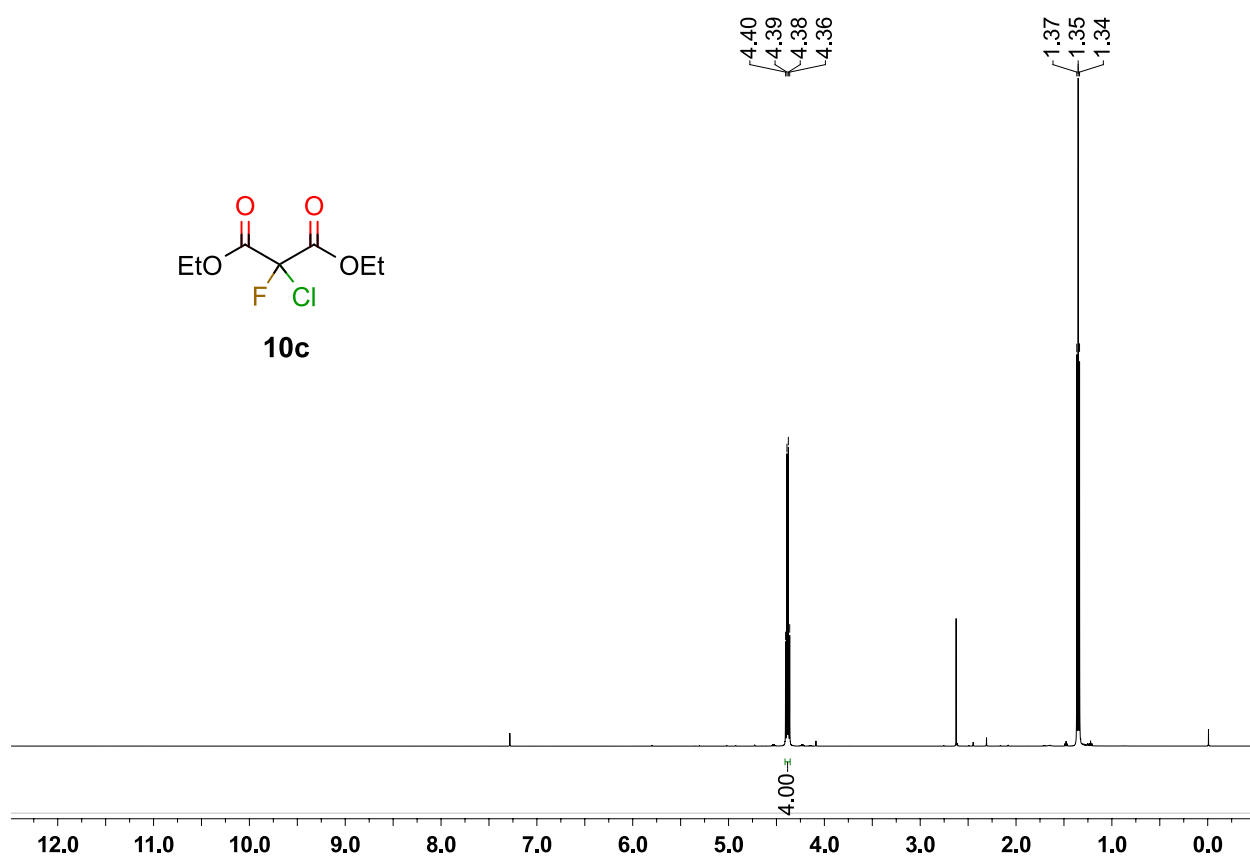


Figure 15 ¹H NMR (500 MHz) spectrum of diethyl chlorofluoromalonate (**10c**) in CDCl₃ (7.26 ppm) obtained from **9b**.

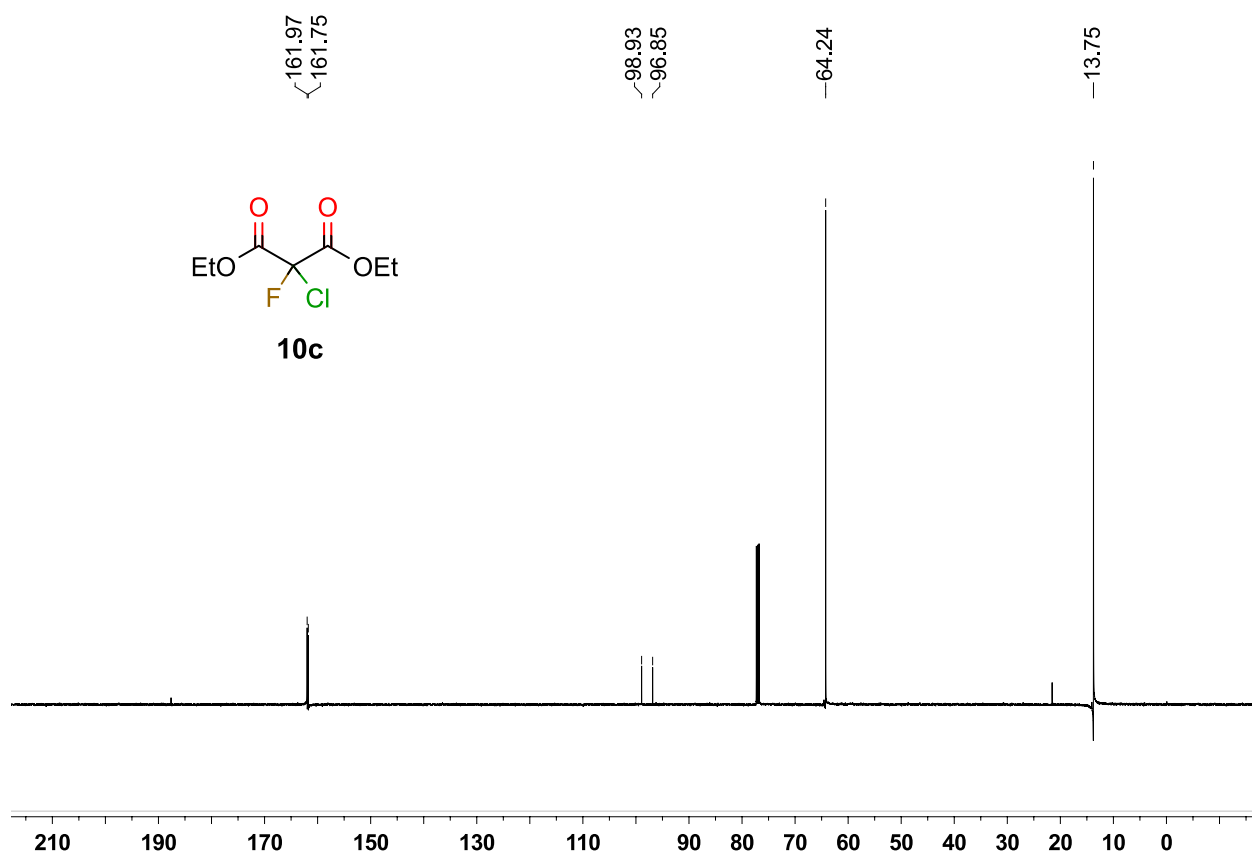


Figure 16 ^{13}C NMR (126 MHz) spectrum of diethyl chlorofluoromalonate (**10c**) in CDCl_3 (77.2 ppm) obtained from **9b**.

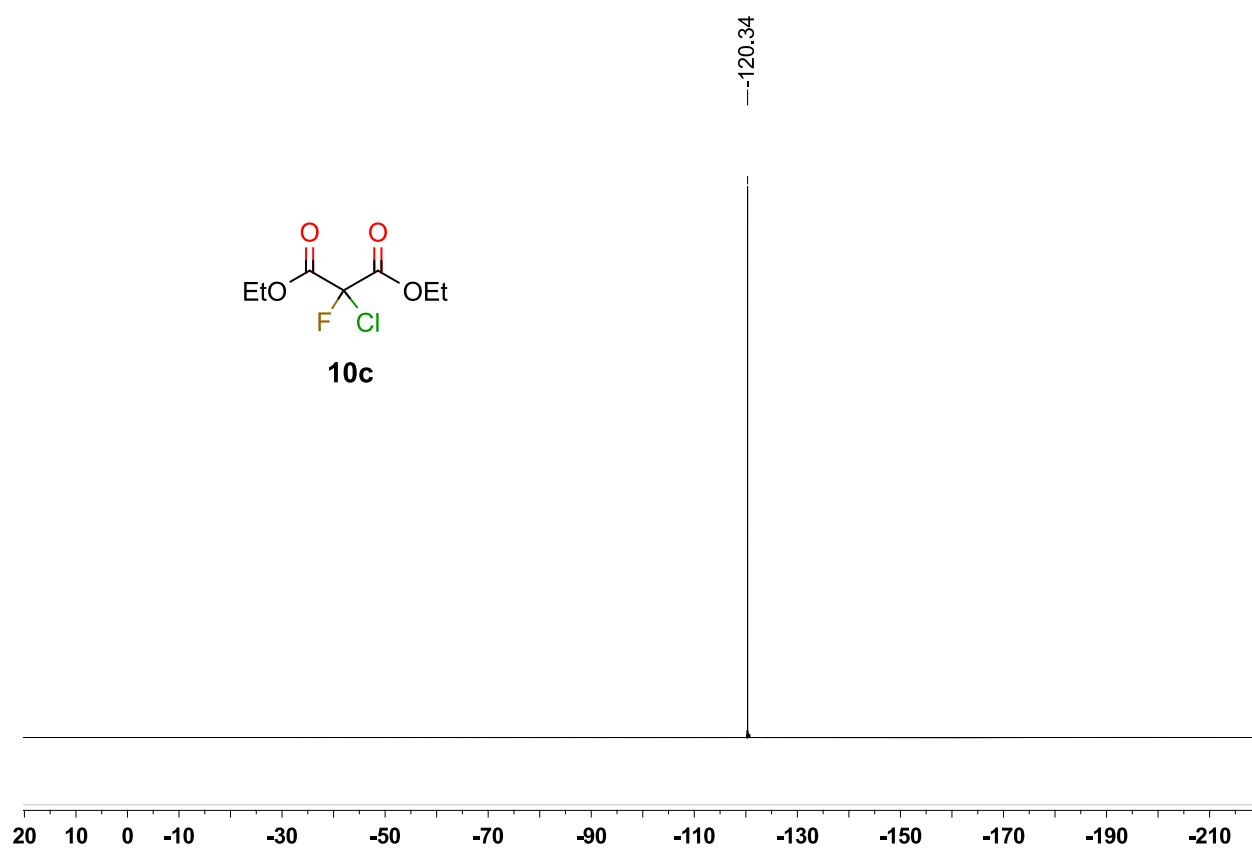


Figure 17 ^{19}F NMR (470 MHz) spectrum of diethyl chlorofluoromalonate (**10c**) in CDCl_3 obtained from **9b**.

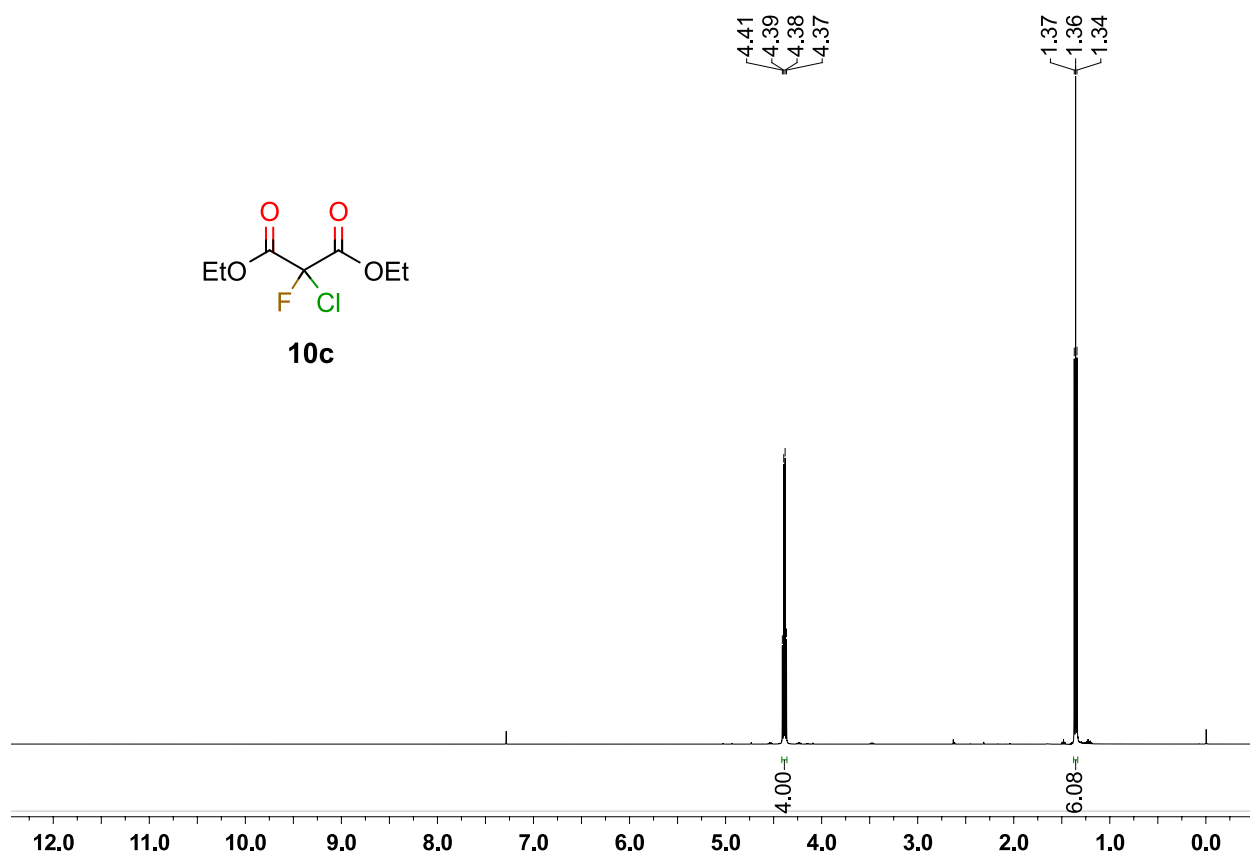


Figure 18 ¹H NMR (500 MHz) spectrum of diethyl chlorofluoromalonate (**10c**) in CDCl₃ (7.26 ppm) obtained from **9c**.

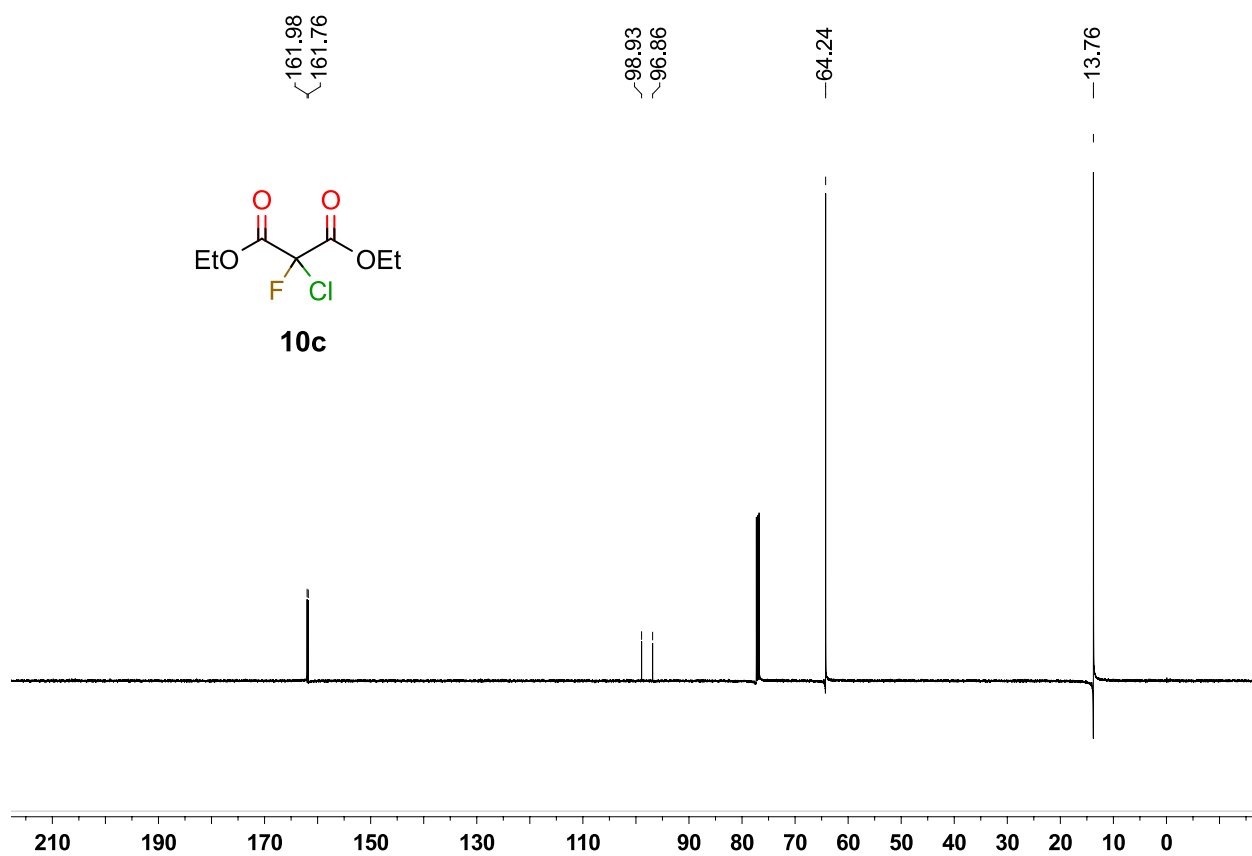


Figure 19 ^{13}C NMR (126 MHz) spectrum of diethyl chlorofluoromalonate (**10c**) in CDCl_3 (77.2 ppm) obtained from **9c**.

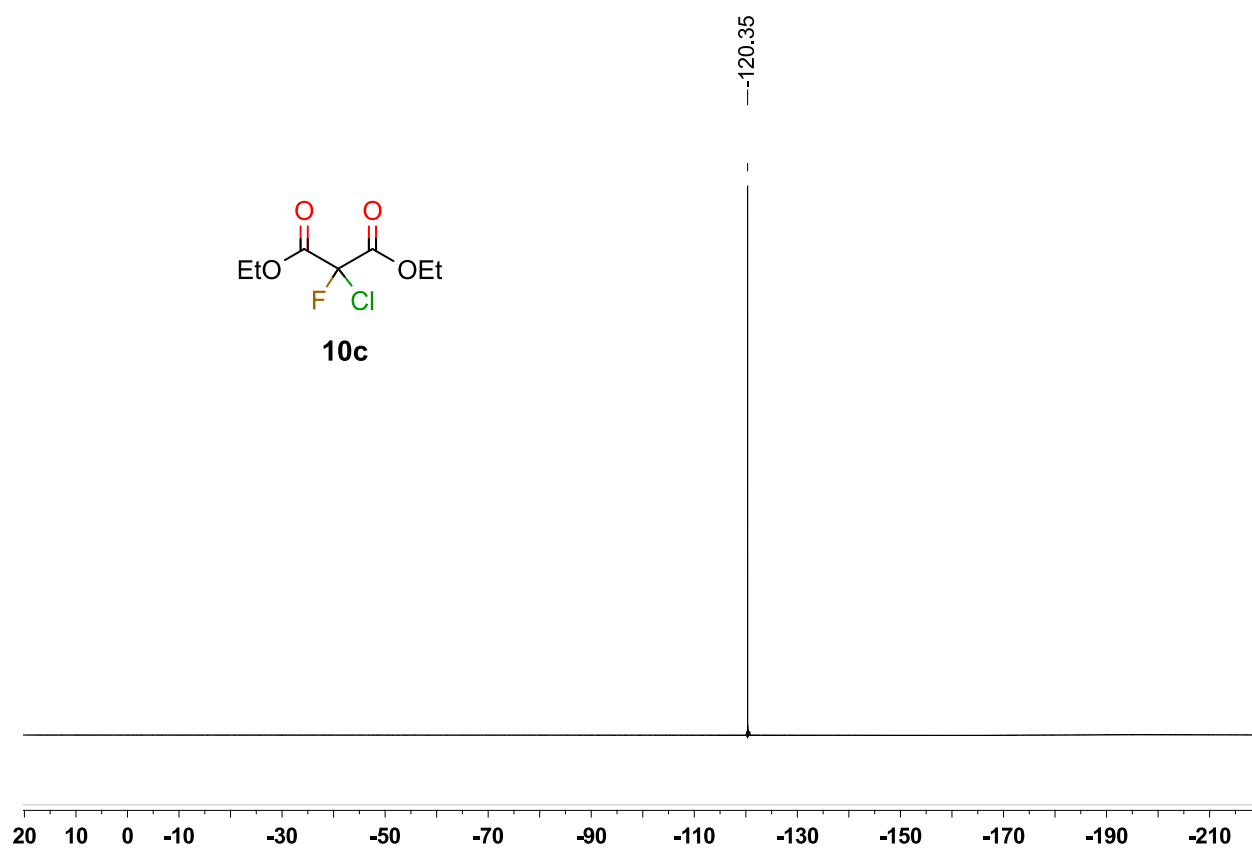


Figure 20 ^{19}F NMR (470 MHz) spectrum of diethyl chlorofluoromalonate (**10c**) in CDCl_3 obtained from **9c**.

6.3 NMR spectra of monoethyl malonate salts 11

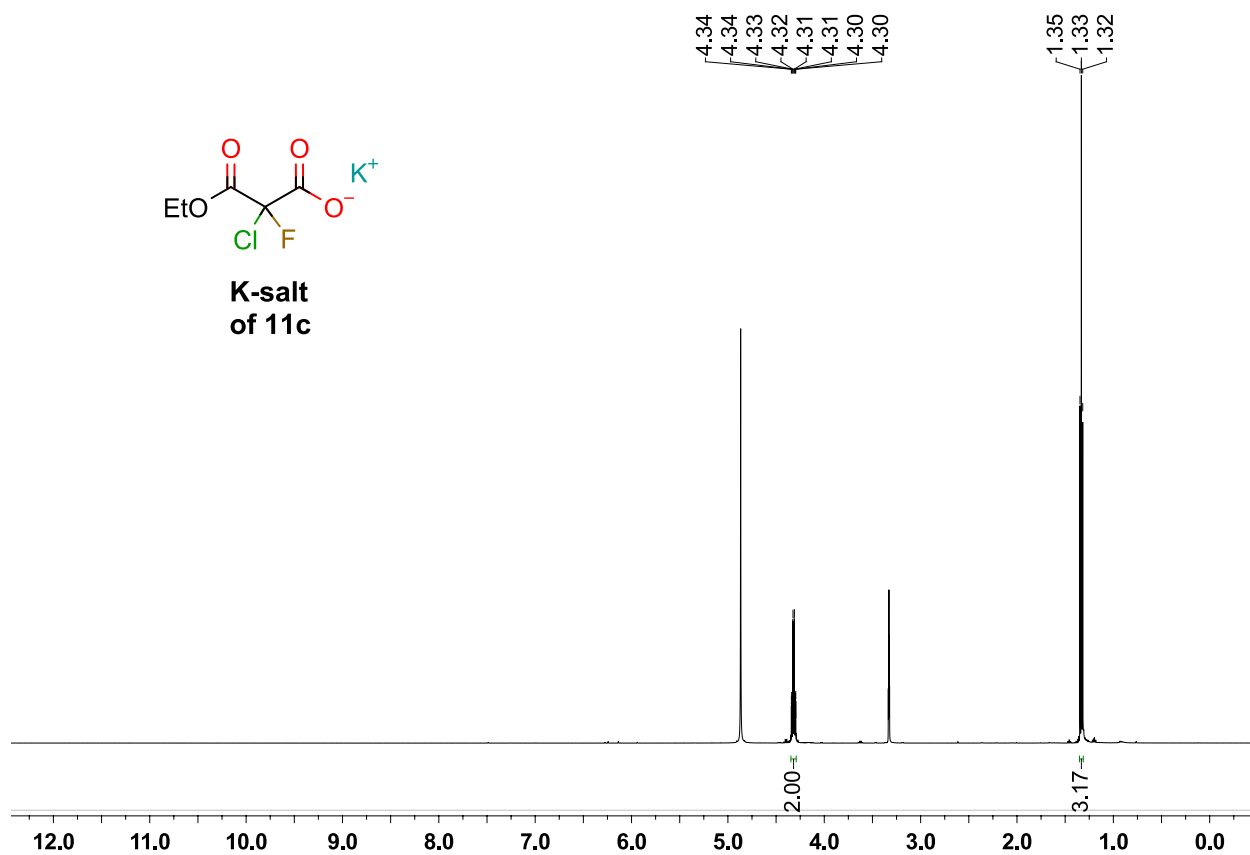


Figure 21 ¹H NMR (500 MHz) spectrum of potassium monoethyl chlorofluoromalonate in D₂O/DMSO-d₆ mixture (3.33 ppm H₂O in DMSO, 4.79 ppm H₂O in D₂O).

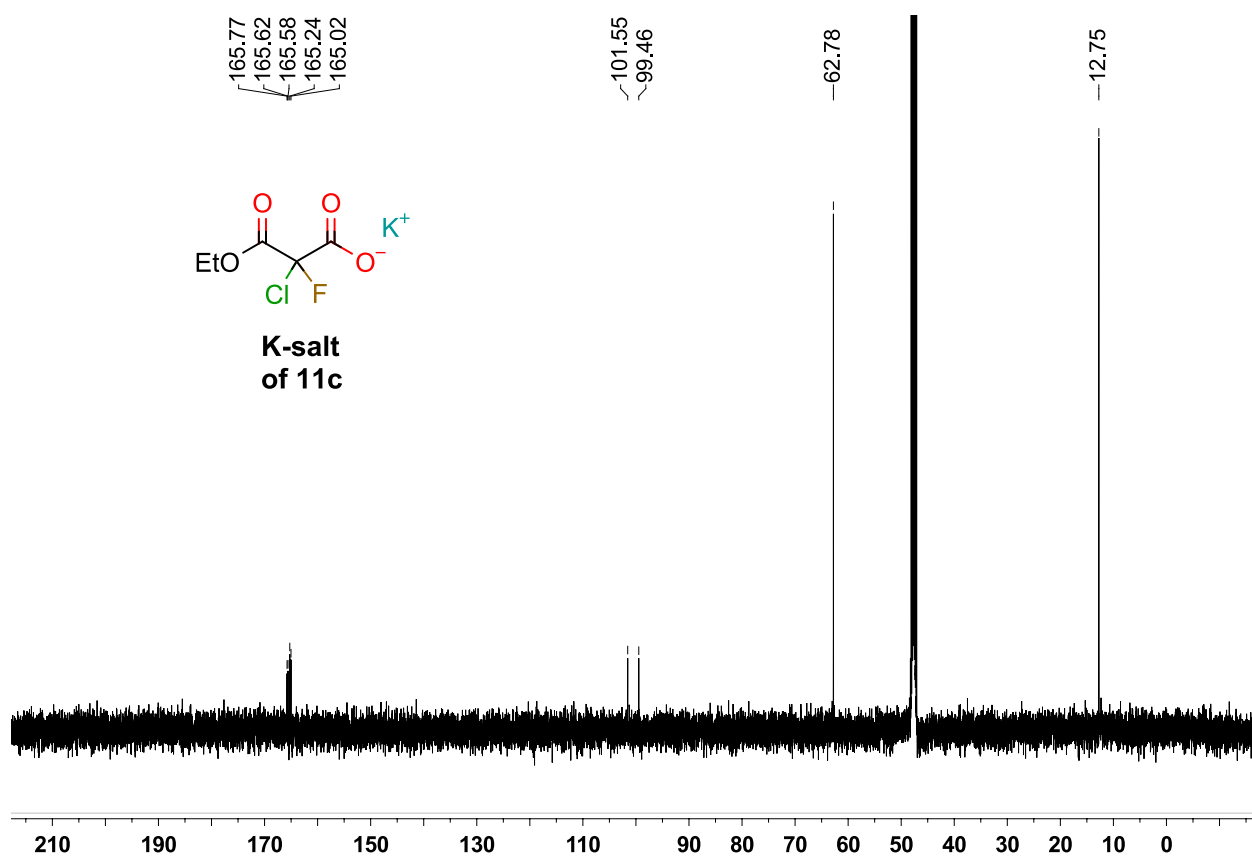


Figure 22 ^{13}C NMR (126 MHz) spectrum of potassium monoethyl chlorofluoromalonate in $\text{D}_2\text{O}/\text{DMSO-d}_6$ mixture (47.6 ppm DMSO).

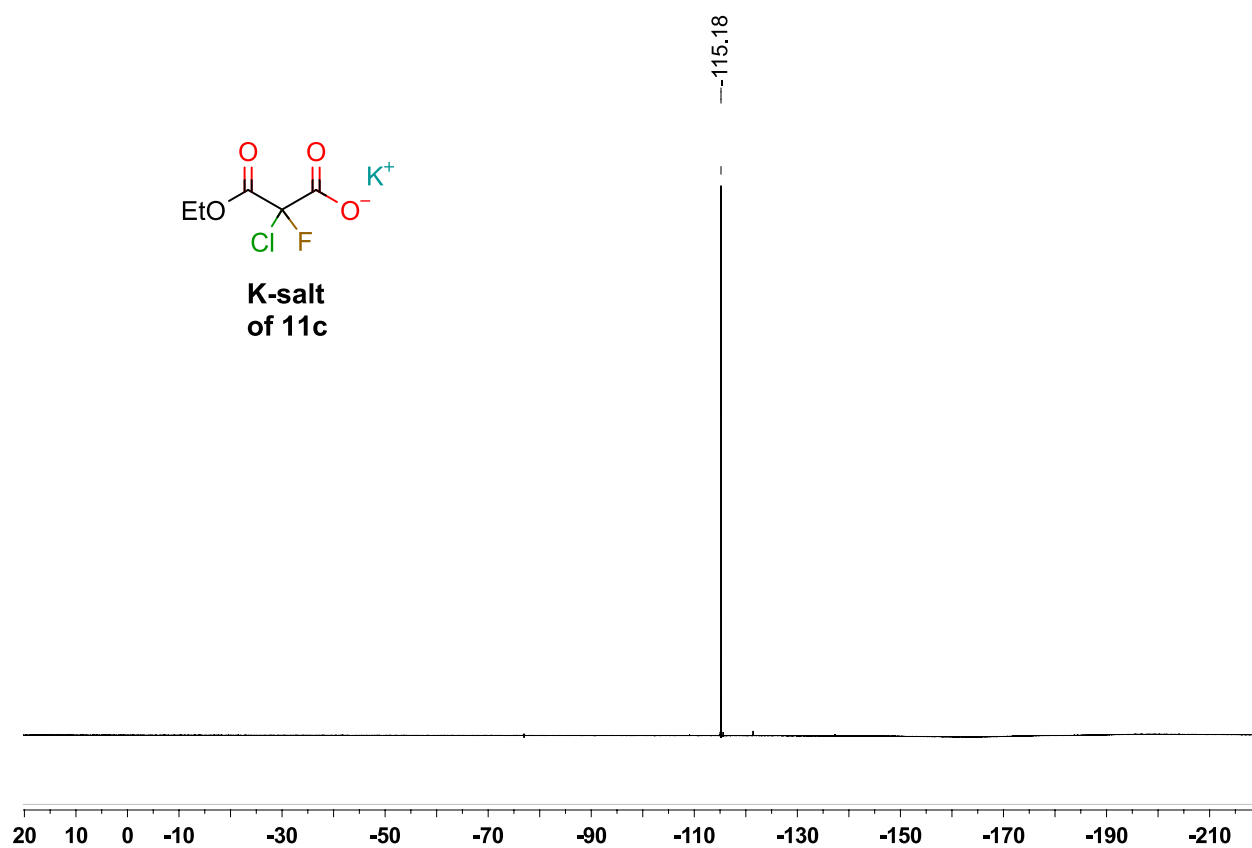


Figure 23 ¹⁹F NMR (470 MHz) spectrum of potassium monoethyl chlorofluoromalonate in D₂O.

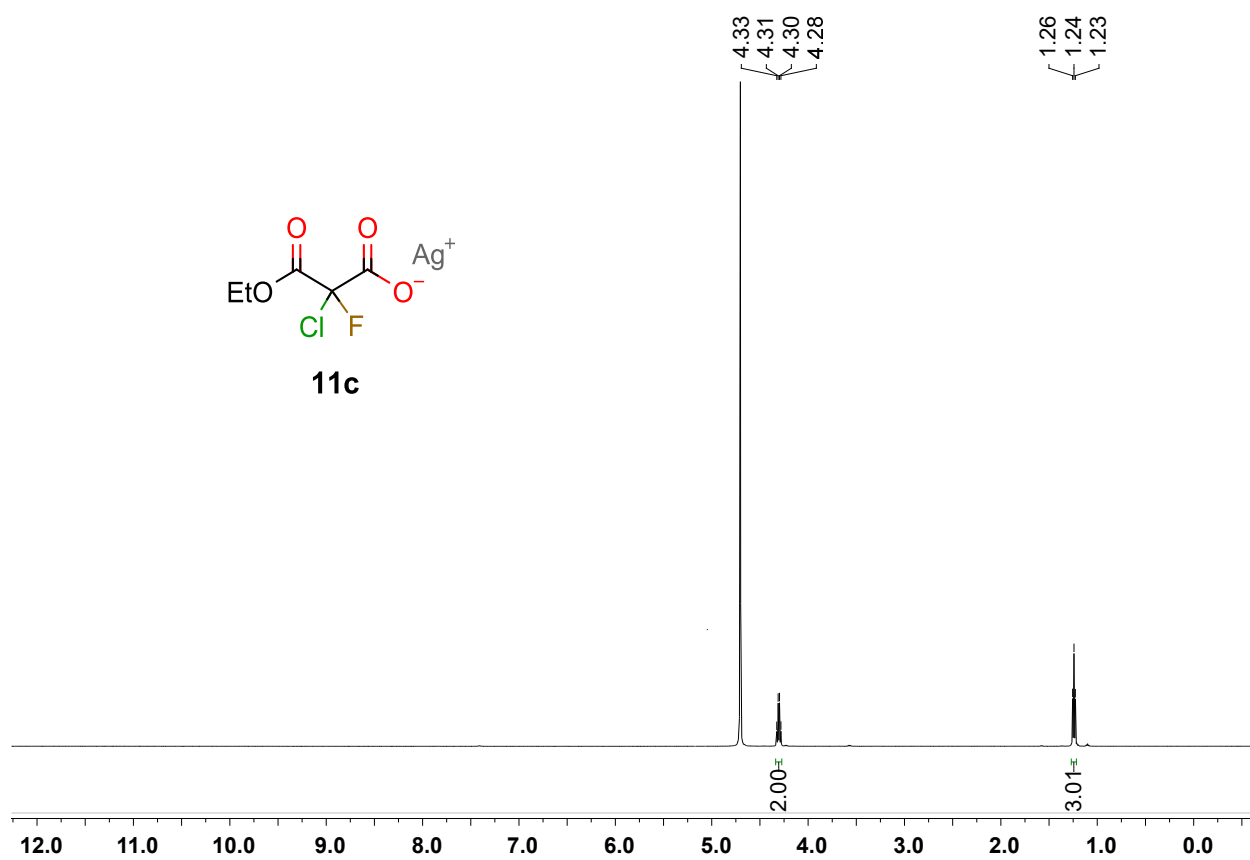


Figure 24 ¹H NMR (500 MHz) spectrum of silver monoethyl chlorofluoromalonate (**11c**) in D₂O (4.79 ppm).

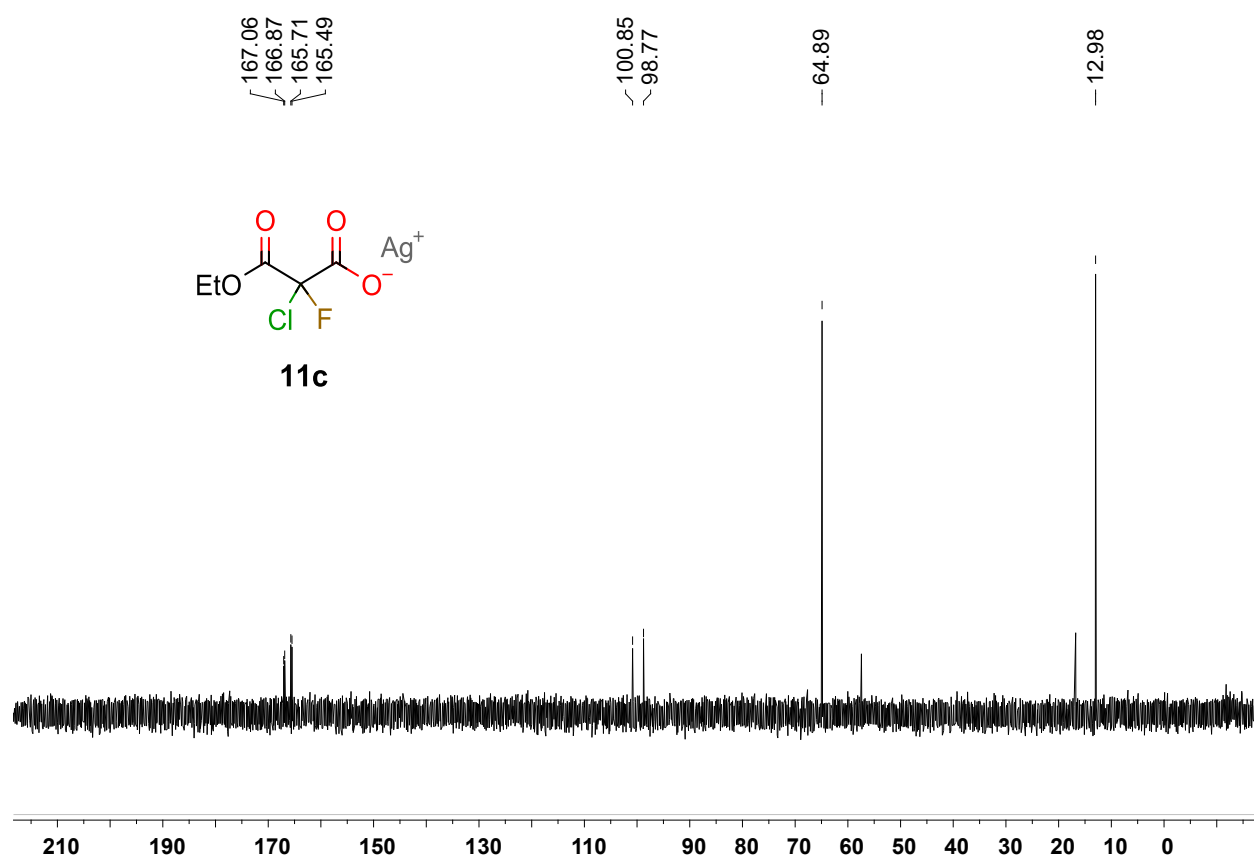


Figure 25 ^{13}C NMR (126 MHz) spectrum of silver monoethyl chlorofluoromalonate (**11c**) in D_2O .

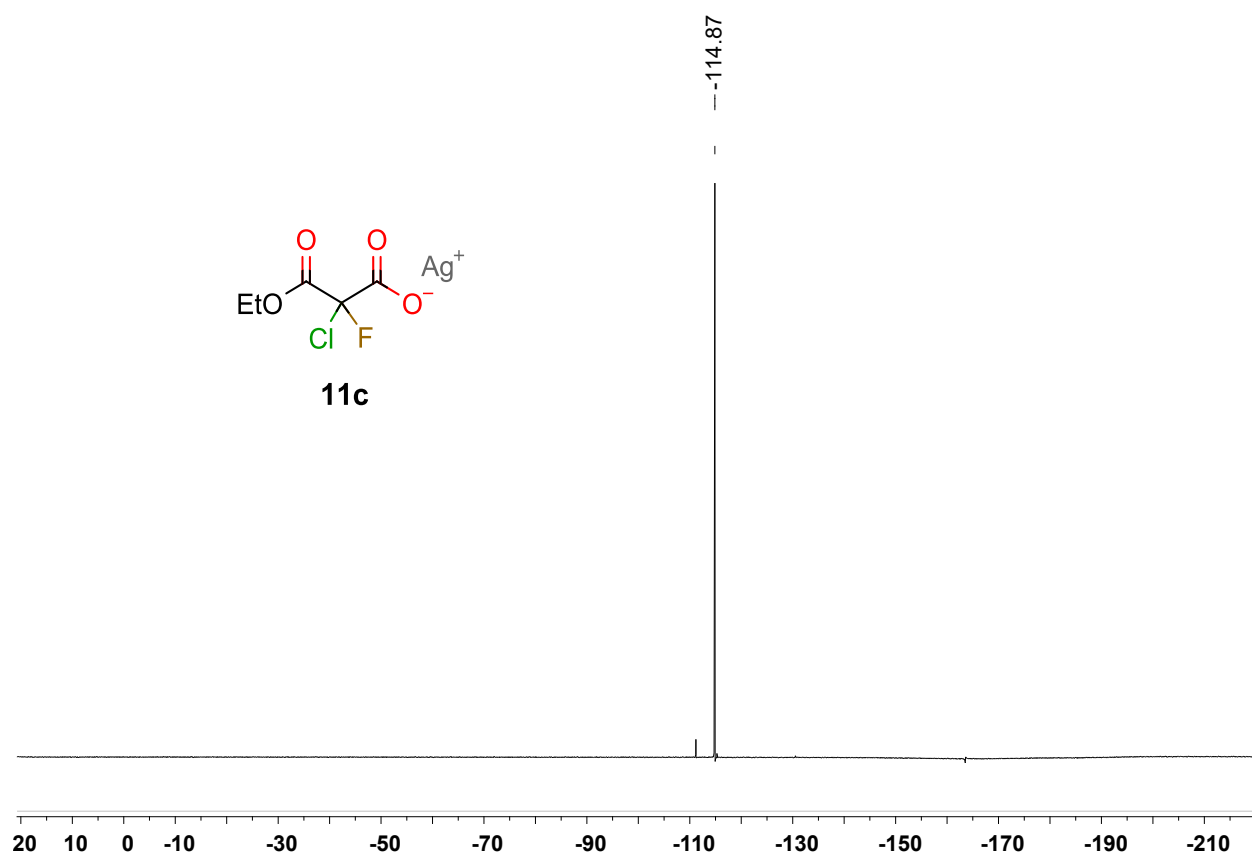


Figure 26 ^{19}F NMR (470 MHz) spectrum of silver monoethyl chlorofluoromalonate (**11c**) in D_2O .

6.4 NMR spectra of halogenated acetic acids 5

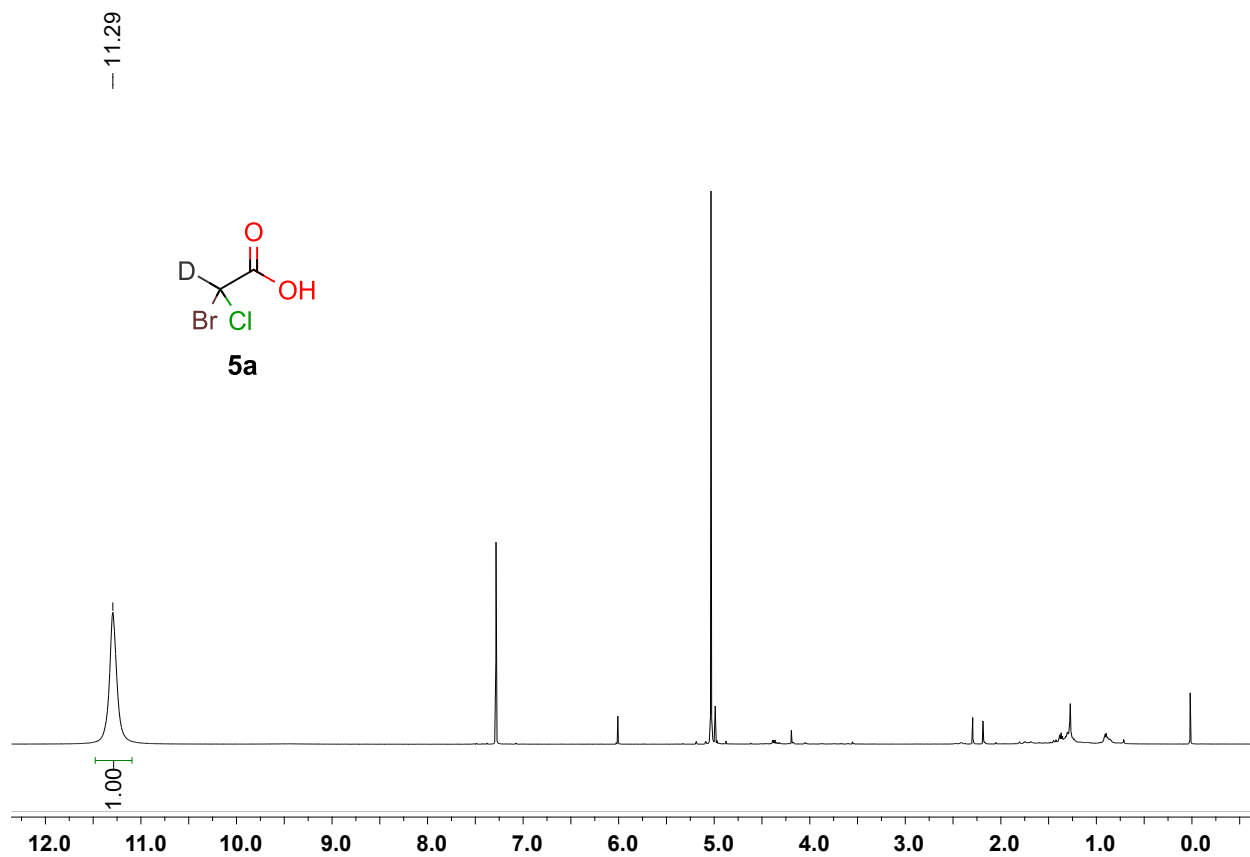


Figure 27 ^1H NMR (500 MHz) spectrum of deuterio bromochloroacetic acid (**5a**) in CDCl_3 (7.26 ppm). The signal at 5.03 ppm results from the undeuterated product.

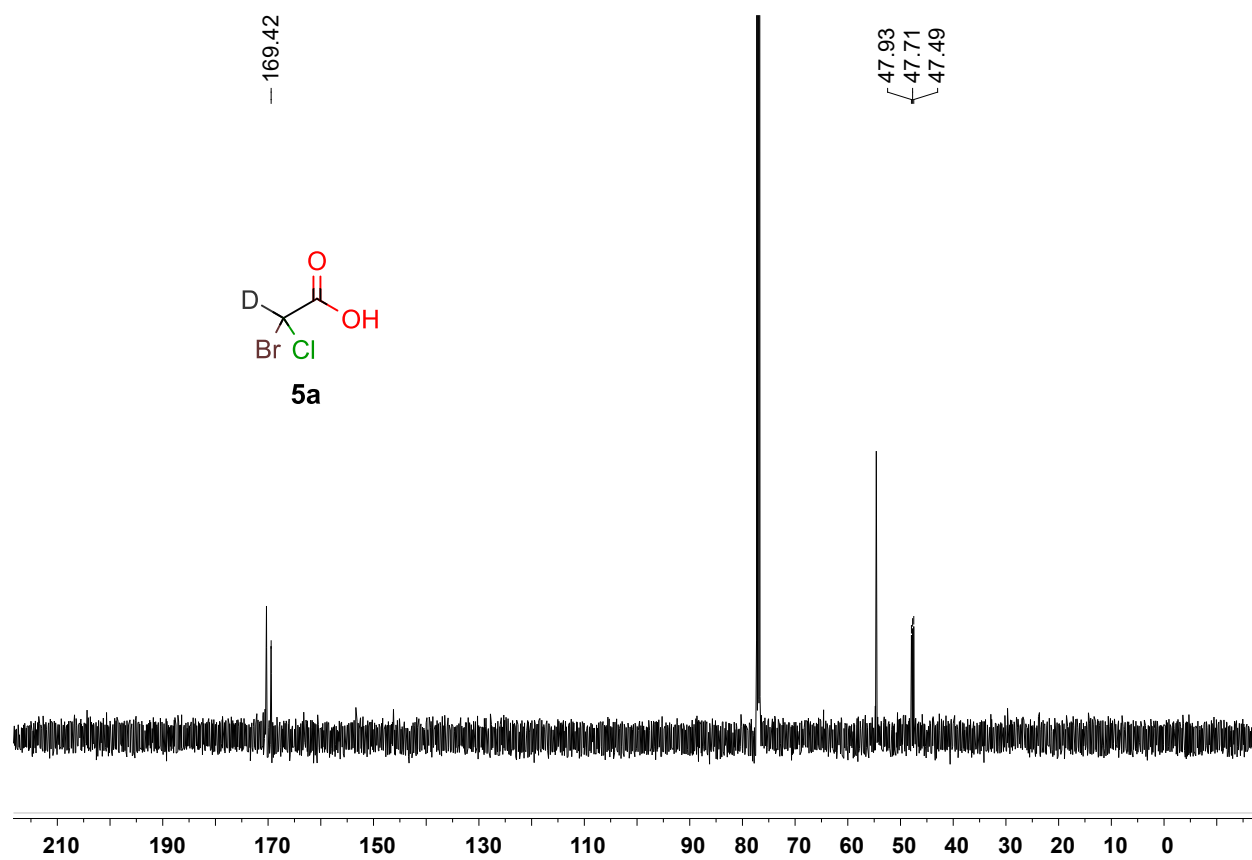


Figure 28 ^{13}C NMR (126 MHz) spectrum of deuterio bromochloroacetic acid (**5a**) in CDCl_3 (77.2 ppm). The signals at 54.6 and 170.3 ppm belong to the undeuterated product.

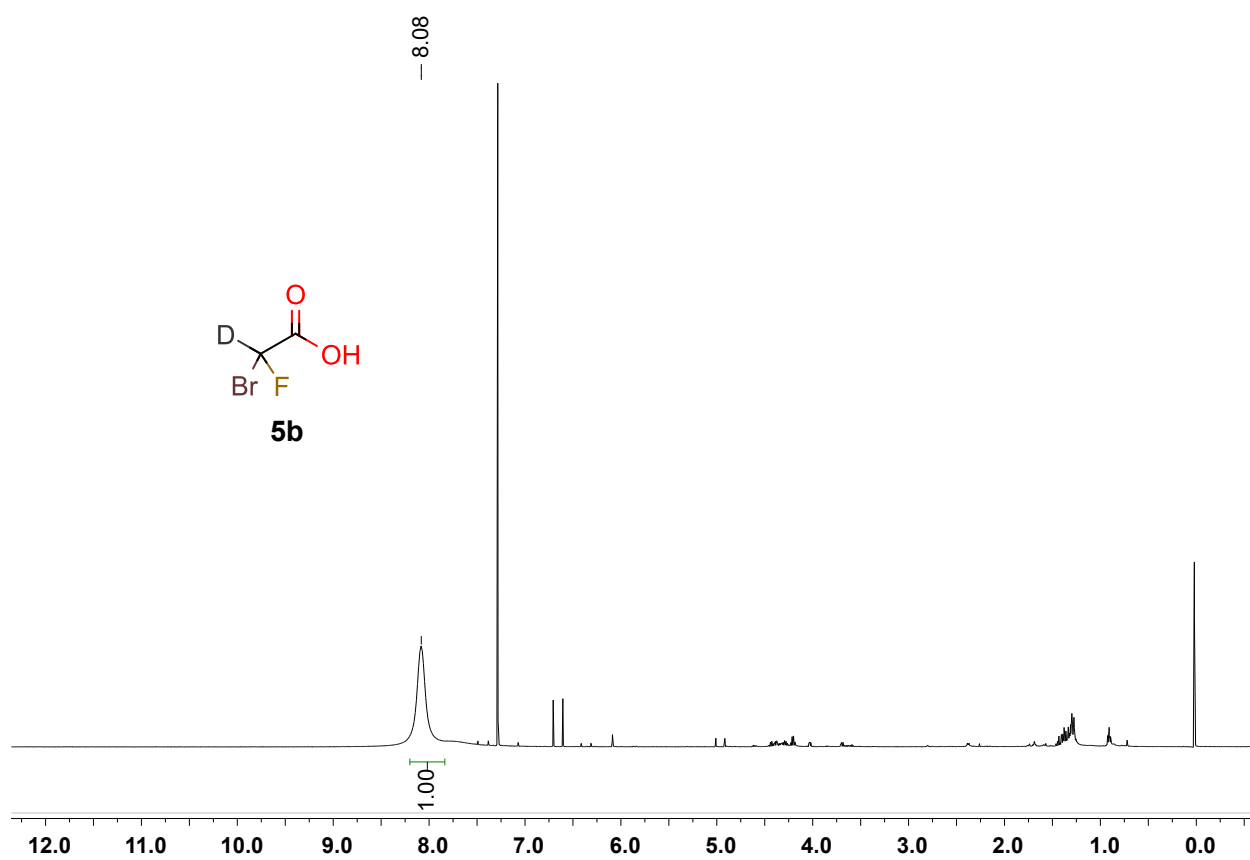


Figure 29 ^1H NMR (500 MHz) spectrum of deuterio bromofluoroacetic acid (**5b**) in CDCl_3 (7.26 ppm). The signal at 6.69 ppm belongs to the undeuterated product.

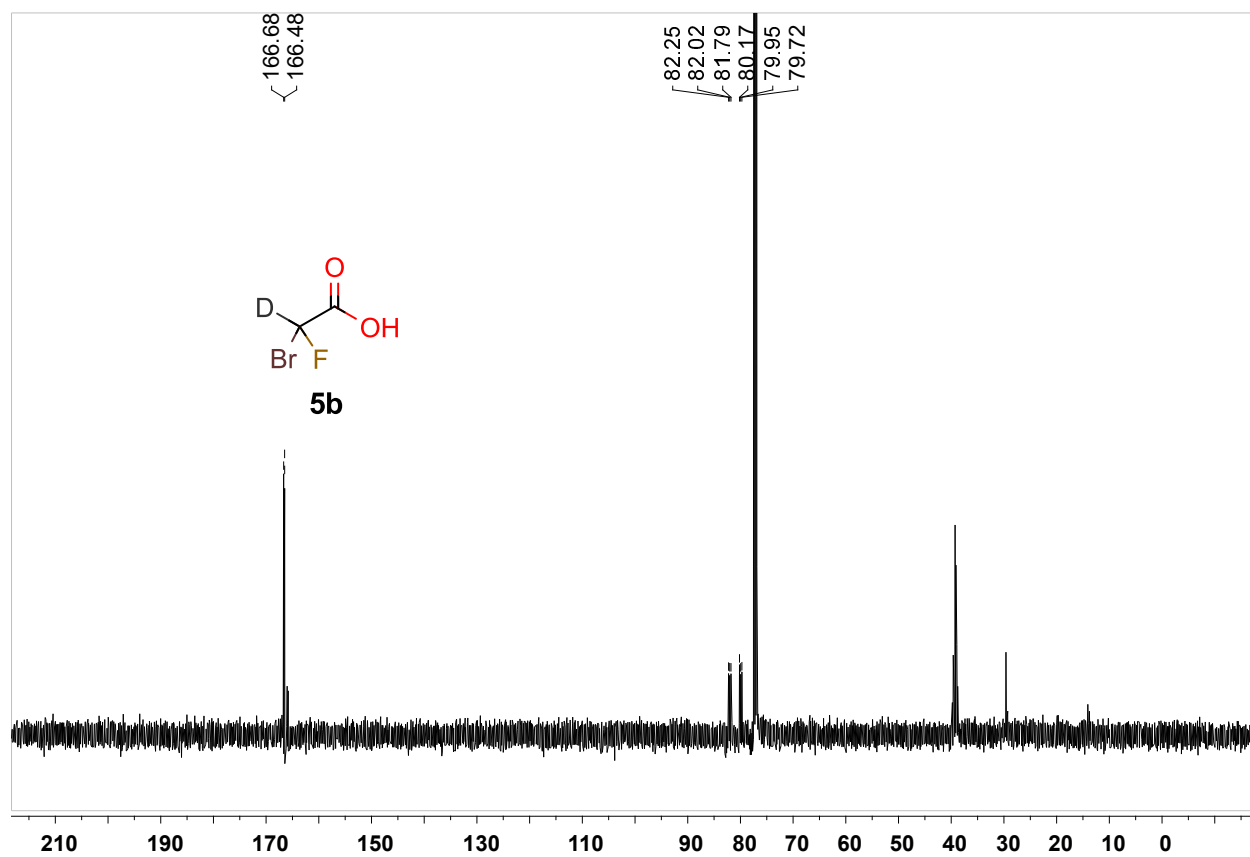


Figure 30 ^{13}C NMR (126 MHz) spectrum of deuterio bromofluoroacetic acid (**5b**) in CDCl_3 (77.2 ppm). At 39.3 ppm d-DMSO is visible, which was used to dissolve the deuterio bromofluoroacetic acid.

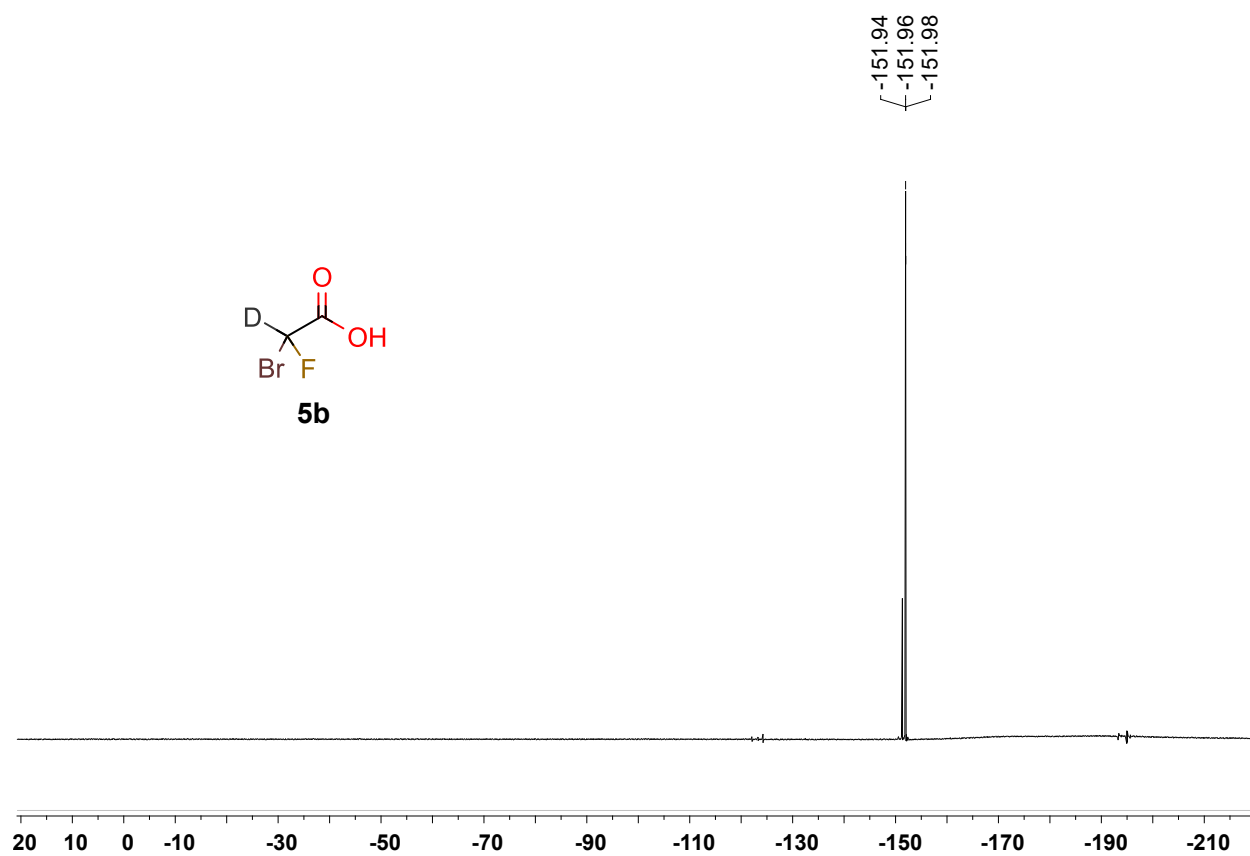


Figure 31 ^{19}F NMR (470 MHz) spectrum of deuterio bromofluoroacetic acid (**5b**) in CDCl_3 . The singlet at -151.28 belongs to the undeuterated product

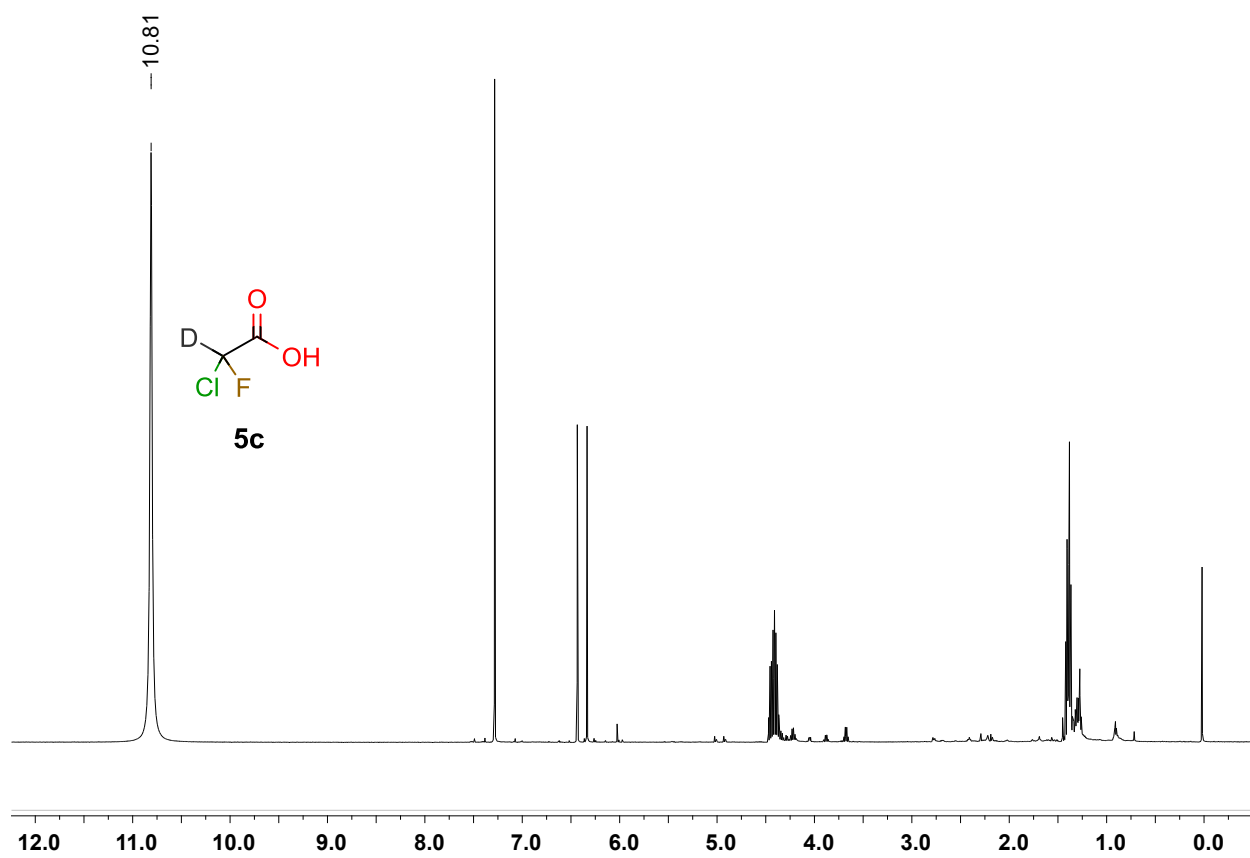


Figure 32 ^1H NMR (500 MHz) spectrum of deuterio chlorofluoroacetic acid (**5c**) in CDCl_3 (7.26 ppm). The signal at 6.41 ppm belongs to the undeuterated product. The impurities at 4.45 and 1.09 ppm result from the reactant and the intermediate.

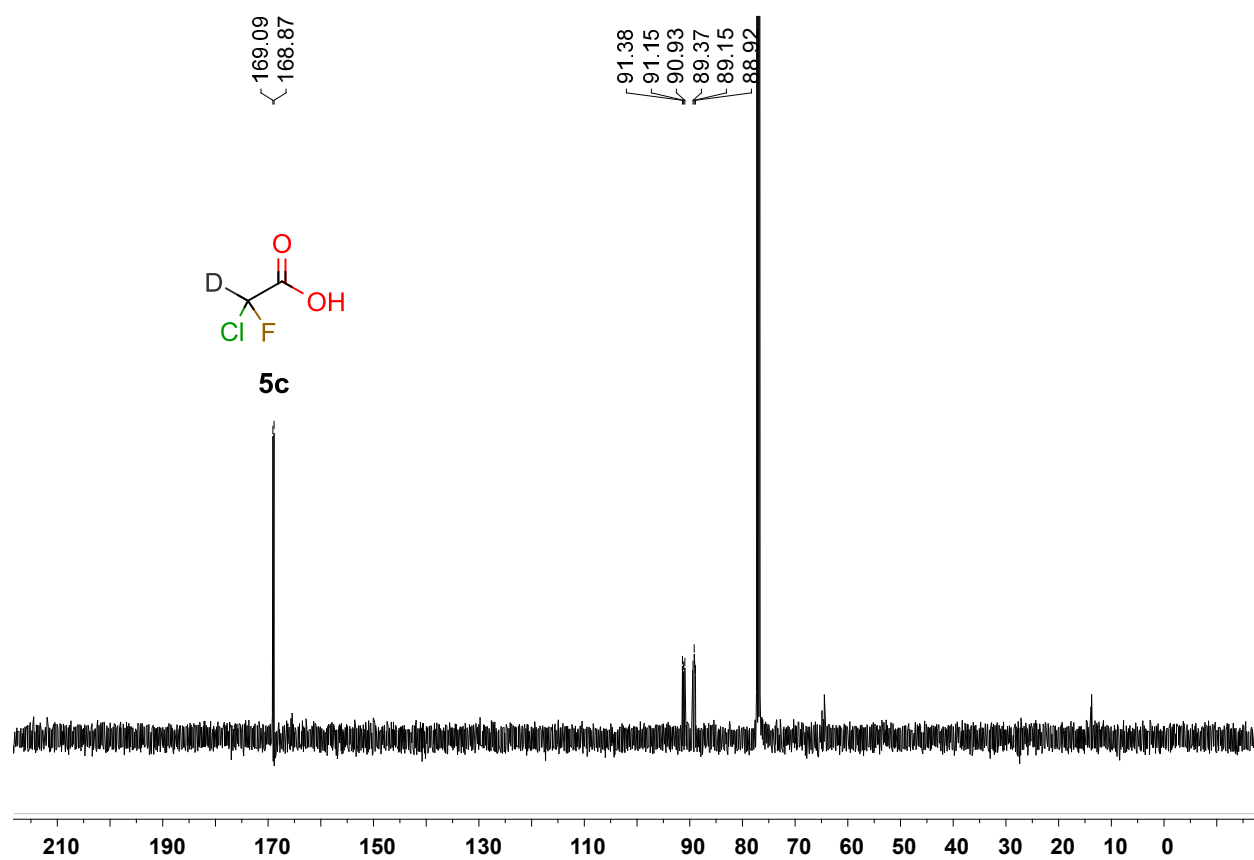


Figure 33 ^{13}C NMR (126 MHz) spectrum of deuterio chlorofluoroacetic acid (**5c**) in CDCl_3 (77.2 ppm). The impurities at 13.8 and 64.5 ppm result for the reactant and the intermediate.

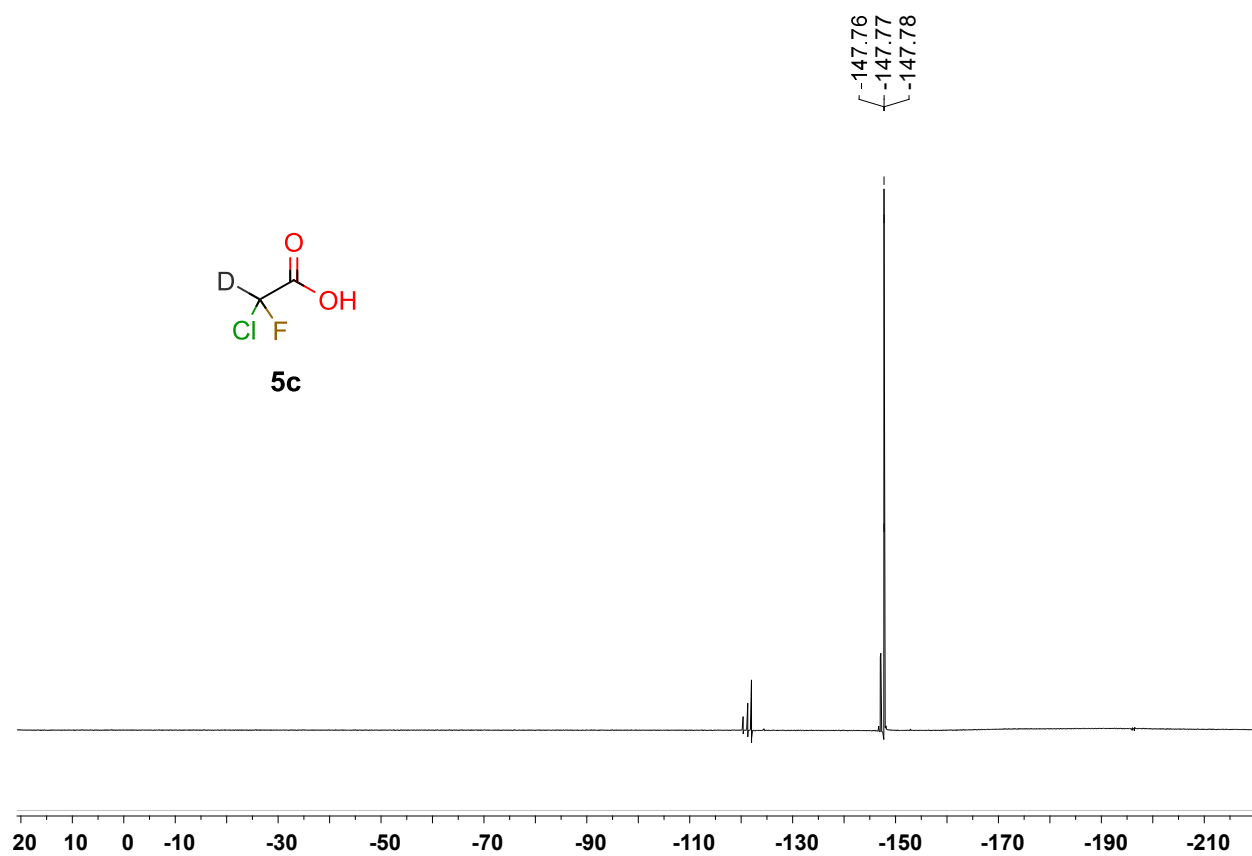


Figure 34 ^{19}F NMR (470 MHz) spectrum of deuterio chlorofluoroacetic acid (**5c**) in CDCl_3 . The impurities between 120.4 and 122.0 ppm result for the reactant and the intermediate.

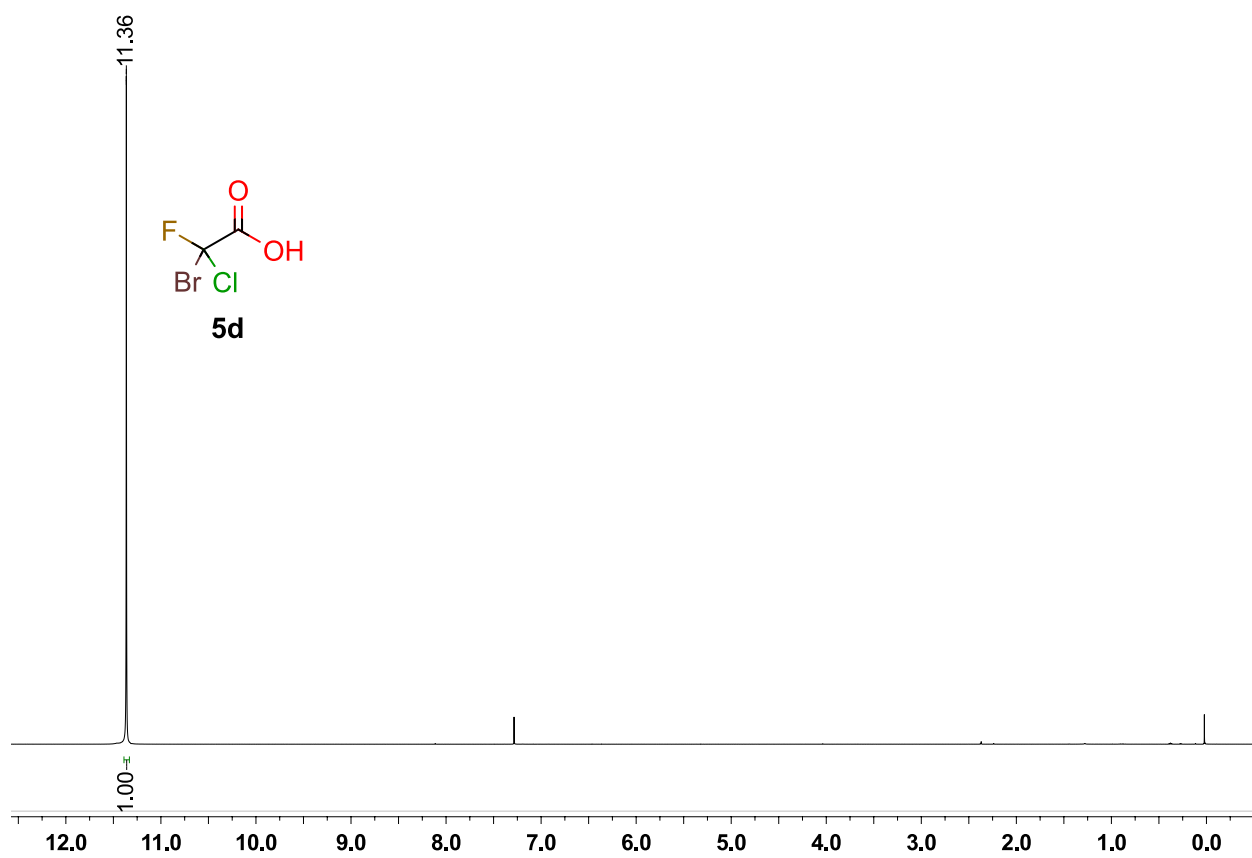


Figure 35 ^1H NMR (500 MHz) spectrum of bromochlorofluoroacetic acid (**5d**) in CDCl_3 (7.26 ppm).

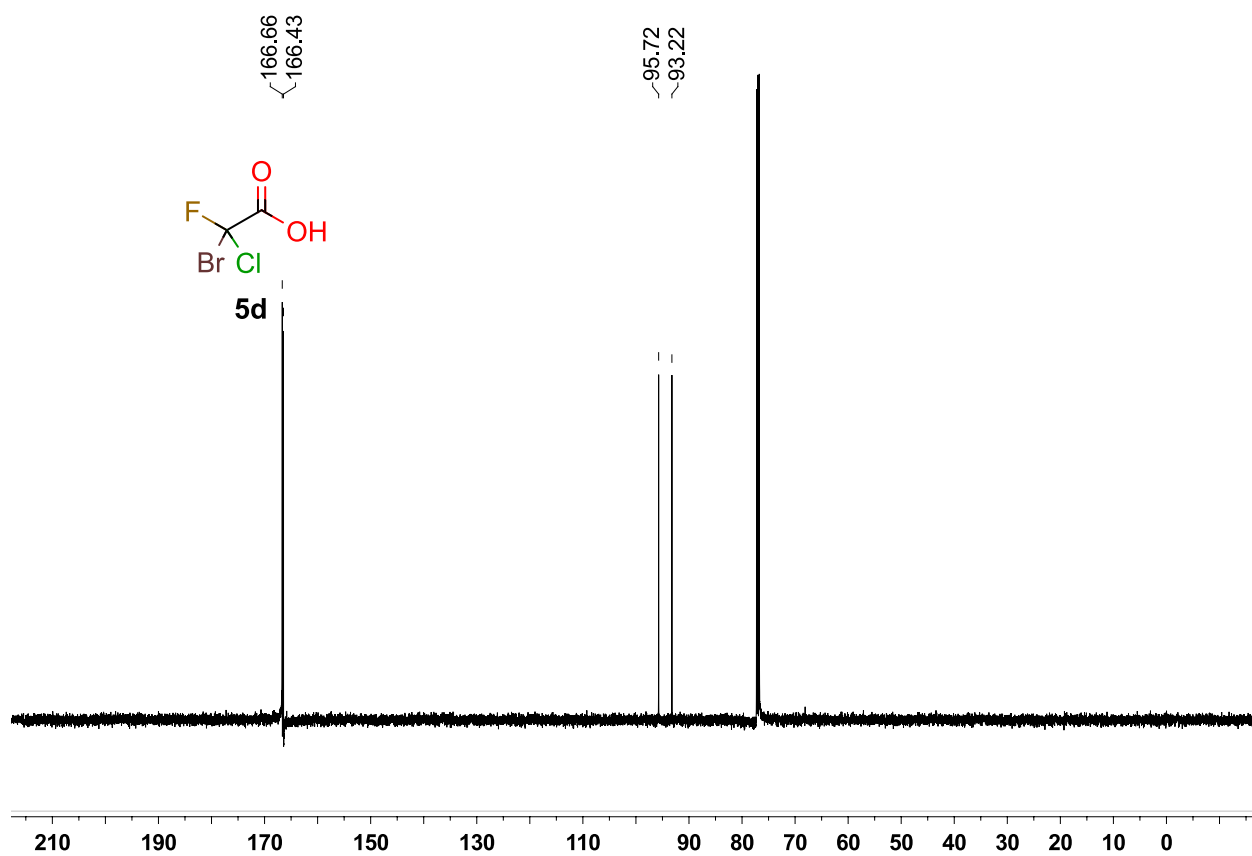


Figure 36 ^{13}C NMR (126 MHz) spectrum of bromochlorofluoroacetic acid (**5d**) in CDCl_3 (77.2 ppm).

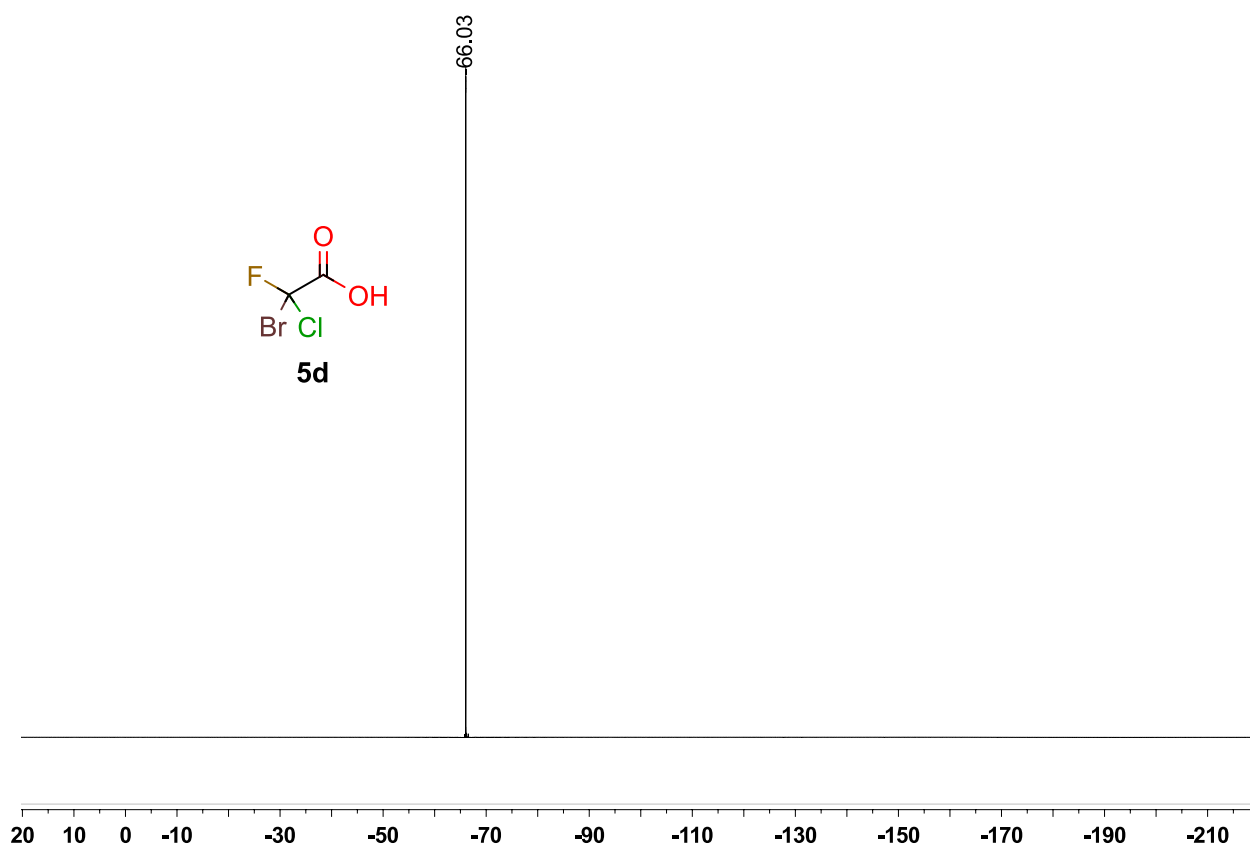


Figure 37 ^{19}F NMR (470 MHz) spectrum of bromochlorofluoroacetic acid (**5d**) in CDCl_3 .

6.5 NMR spectra of bromochlorofluoromethane **7**

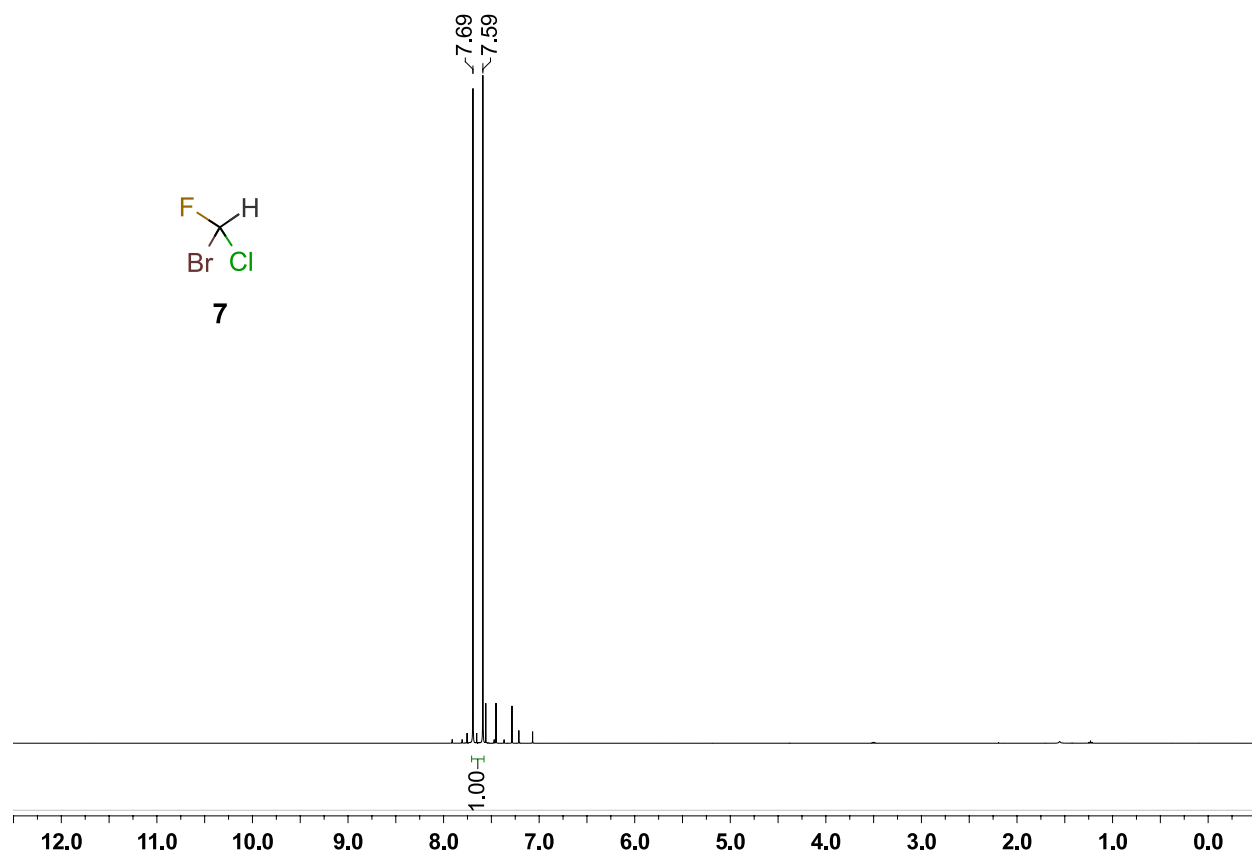


Figure 38 ^1H NMR (500 MHz) spectrum of bromochlorofluoromethane (**7**) in CDCl_3 (7.26 ppm). Impurity of probably CH_2ClF (7.5 ppm).

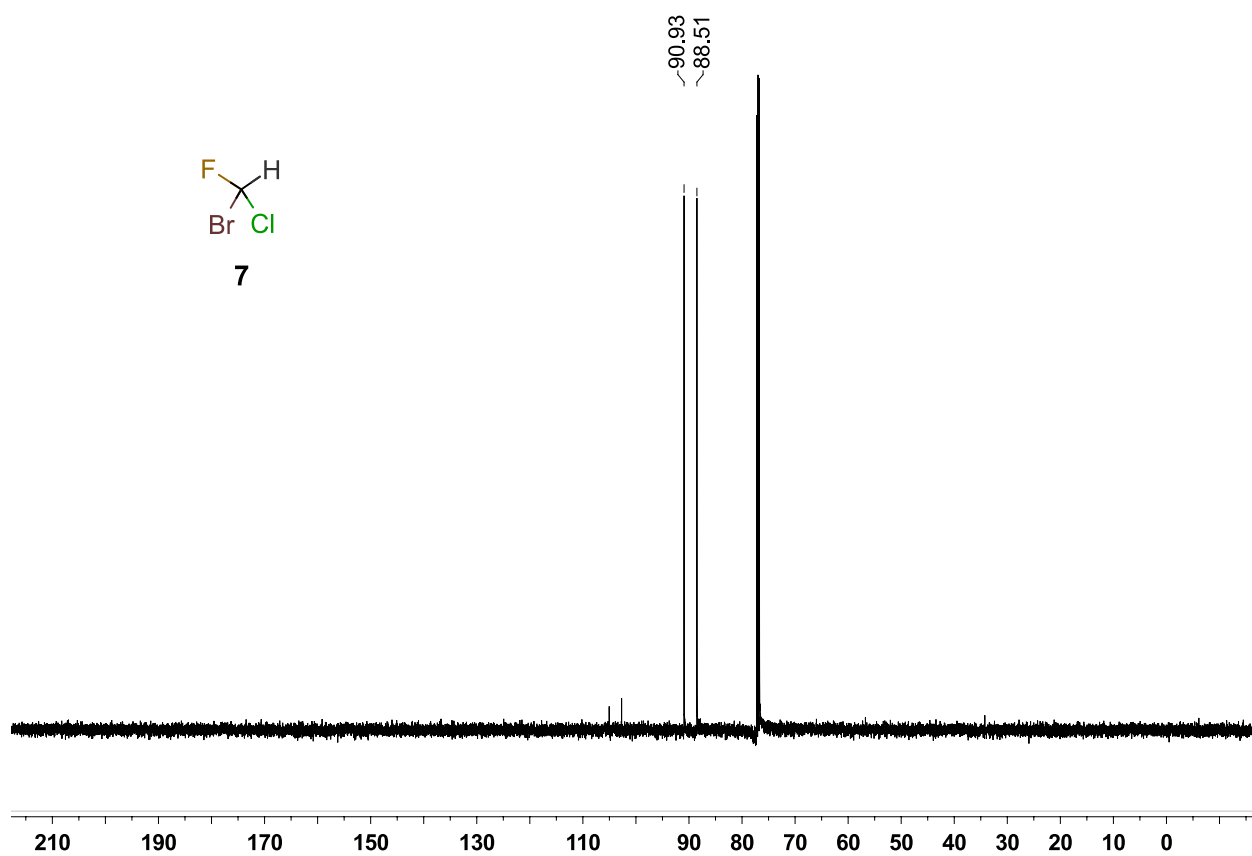


Figure 39 ^{13}C NMR (126 MHz) spectrum of bromochlorofluoromethane (**7**) in CDCl_3 (77.2 ppm). Impurity of probably CH_2ClF (104 ppm).

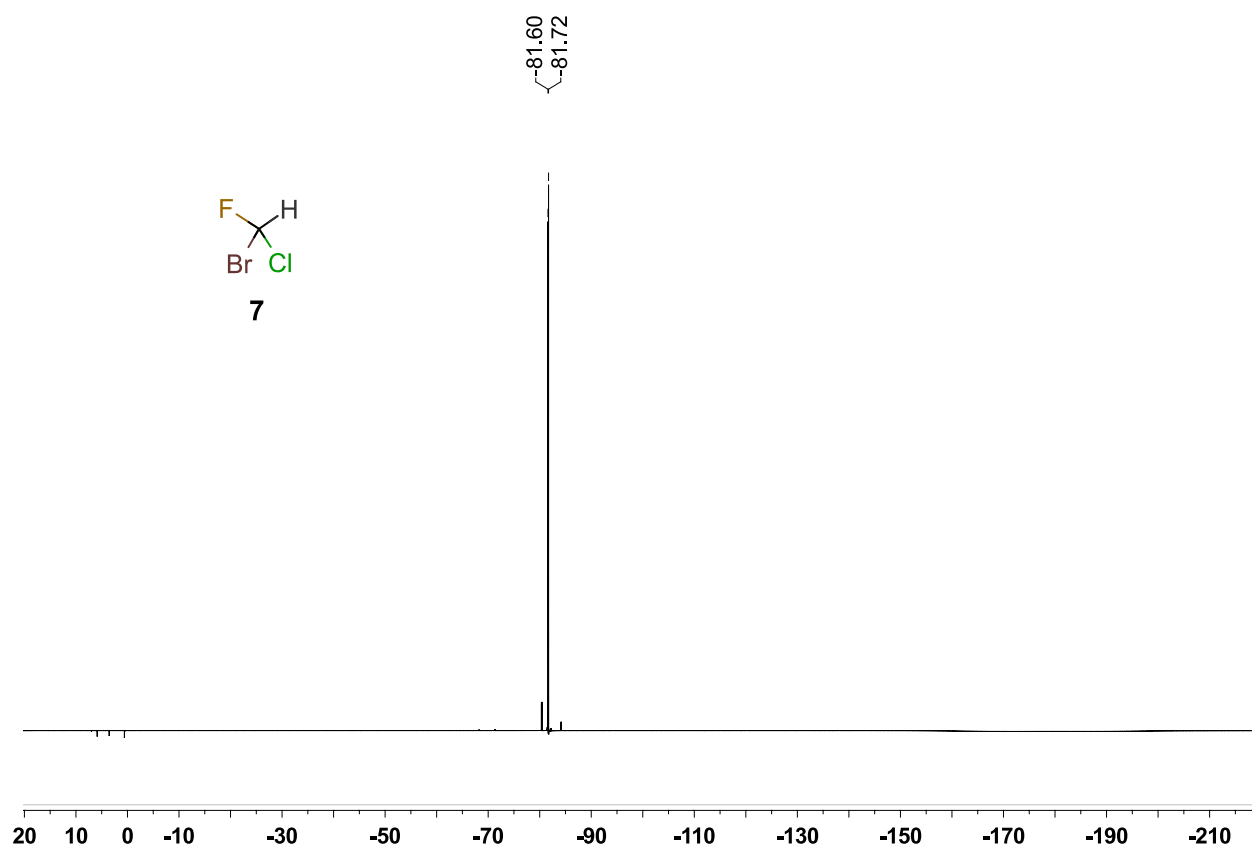


Figure 40 ^{19}F NMR (470 MHz) spectrum of bromochlorofluoromethane (**7**) in CDCl_3 . Impurity of probably CH_2ClF (-80.5 ppm).

7 XRF of potassium silver exchange

To determine the purity of this exchange NMR and XRF were used. In the NMR spectra the ^{19}F NMR has the best difference in the chemical shift between the potassium and silver salt. And thus the exchange yield to the silver salt has to be according to the ^{19}F NMR 100 %. To verify this result the quantity of silver was measured with a WD-XRF (Thermo fisher Scientific ADVANTX-2019 (11210)). The device parameter were ARL F45 goniometer, LiF200 crystal and FPC detector. The processing software was OXSAS v1.7.1.1729.

For the determination the K_α line was used, due to the lower detection limit of potassium. Furthermore, because of the higher energy needed for the excitation of silver, the potassium in a sample with both elements would interfere with its absorption and result in higher values for the silver lines. The calibration was performed with KNO_3 in water with the concentrations shown in Table 1.

Table 1: Calibration for potassium with a series of KNO_3 concentrations. The obtained intensities result from the K_α line.

Entry	$c/\text{mmol}\cdot\text{L}^{-1}$	I/cps
1	0.96	290
2	1.98	460
3	3.94	780
4	5.92	1090
5	7.89	1460
6	10.0	1760

The linear regression of the values from table 1 is shown in Figure 41 (right) next to their spectra (left). From the analysis of the linear regression (equation 1) the values for slope ($a = (164 \pm 11) \text{ cps}$) and intercept ($b = (134 \pm 57) \text{ cps}$) were obtained.

$$y = a \cdot x + b \quad (1)$$

The percentage of silver in the sample was calculated with the equation 2 with $I_s = 183 \text{ cps}$ (intensity of the sample) and $c_s = 77.4 \text{ mmol}\cdot\text{L}$ (sample concentration).

$$w_{\text{Ag}} = \left(1 - \frac{I_s - b}{c_s}\right) \cdot 100\% \quad (2)$$

The standard error was calculated with the error propagation of the values of equation 2 and corrected with the students-t-factor for 4 degrees of freedom ($N-2$, $N = 6$). The result was $w_{\text{Ag}} = (99.6 \pm 0.2) \%$ and conforms the results of the ^{19}F NMR (approximately 100 %).

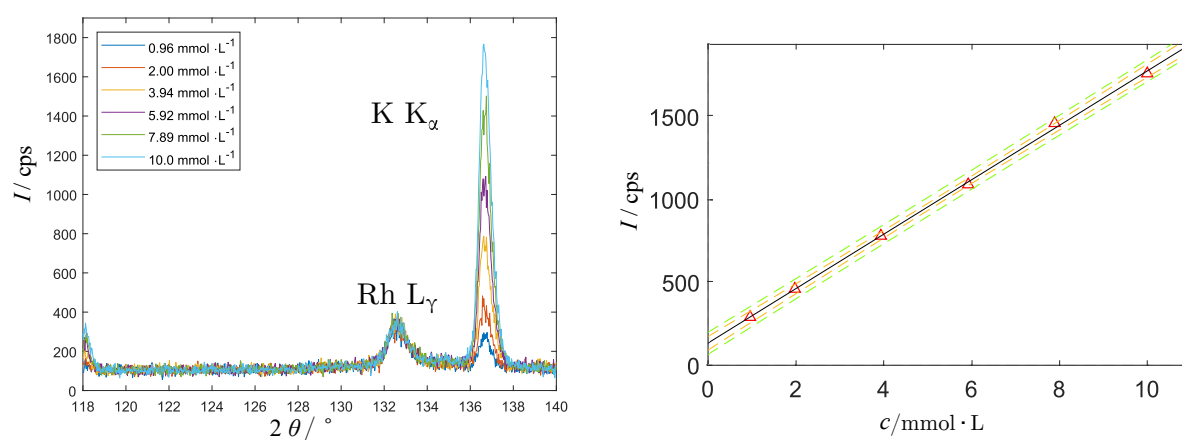


Figure 41 Measured XRF spectra of the standard series for Potassium with KNO_3 (left) and the linear regression (black line) for 6 measurements (red triangle) with the standard error (green dashed line) for the linear regression.