

Supporting Information

Efficient α -Selective Chlorination of Phenylacetic Acid and its *para*-Substituted Analogues

Camillo Morano,^a Alessandro Giraudo,^a Gabriella Roda,^a Edoardo Armano,^a
Giulia Nasta,^a Massimiliano Sipala,^a Marco Pallavicini,^a Cristiano Bolchi ^{*a}

Dipartimento di Scienze Farmaceutiche, Università degli Studi di Milano, via Mangiagalli 25, I-20133,
Milano, Italy

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1. General experimental details

Phenylacetic acids **1-11** were purchased from commercial sources. An aluminum reaction block was used as the heating source for reactions that required heating. Flash chromatography purifications were performed by using Sfar Silica D 60 μm cartridges. ^1H NMR and $^{13}\text{C}\{^1\text{H}\}$ -NMR spectra were recorded in CDCl_3 at 300 and 75 MHz respectively, with a Varian Mercury 300 Spectrometer. Chemical shifts are reported in ppm relative to residual solvent as an internal standard. Melting points were determined by a Buchi Melting Point B-540 apparatus. Thin-layer chromatography (TLC) analyses were carried out on alumina sheets precoated with silica gel 60 F254. High Resolution Mass Spectra (HRMS) were acquired by direct infusion on a Waters Q-ToF Synapt G2-Si HDMS (Waters Corporation, Milford, MA, United States) operated in negative ElectroSpray Ionization (ESI-).

2. General procedure for the preparation of **1a**, **2a**, **4a**, **5a,6a**, **7a**, **8a**, and **9a**

PCl_3 (0.3 equiv) was added to the appropriate phenylacetic acid (1 g) and the mixture was heated to the melting temperature (as below specified for each compound) in an aluminium reaction block and allowed to react for 10 min under stirring. At the same temperature, TCCA (1.5 equiv) was added portion wise over 15 min and allowed to react for 1.5 hours. The reaction mixture was cooled to room temperature, diluted with ethyl acetate and filtered. The filtrate was washed with 0.5 M aqueous solution of sodium metabisulfite and brine, dried over anhydrous sodium sulphate and concentrated under vacuum to give the crude product that was purified by crystallization or chromatography on silica gel.

*2-Chloro-2-phenylacetic acid (1a).*¹ Obtained from phenylacetic acid (**1**) (1 g, 7.34 mmol), PCl_3 (64 μL , 0.73 mmol) and TCCA (850 mg, 3.7 mmol) at 85 °C according to the general procedure. The crude product, a wax-like whitish solid (1.25 g), was purified by flash chromatography on silica gel eluting with dichloromethane/methanol/formic acid (95:5:1) to yield **1a** as a white solid (1.04 g, 83%): R_f (dichloromethane/methanol 8:2) 0.51; mp 76.5-77.2 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.72 (br s, 1H), 7.54-7.50 (m, 2H), 7.41-7.38 (m, 3H), 5.38 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 174.3, 135.1, 129.7, 129.1, 128.1, 58.8.

2-Chloro-2-(4-nitrophenyl)acetic acid (2a). Obtained from 4-nitrophenylacetic acid (**2**) (1 g, 5.52 mmol), PCl_3 (48 μL , 0.55 mmol) and TCCA (641 mg, 2.76 mmol) at 105 °C according to the general procedure. The crude product, a yellow solid (1.16 g), was purified by crystallization from cyclohexane/ethyl acetate (9:1 v/v) to yield **2a** as a light yellow solid (0.94 g, 79%): R_f (dichloromethane/methanol 8:2) 0.55; mp 132.1-133.3 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.26 (d, $J=8.5$ Hz, 2H), 7.71 (d, $J=8.5$ Hz, 2H), 6.99 (br s, 1H), 5.45 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.8, 148.7, 141.7, 129.3, 124.3, 57.4; HRMS (ESI-) m/z calcd for $\text{C}_7\text{H}_5\text{ClNO}_2$ [$\text{M}-\text{COOH}$] $^-$ 170.0008, found 170.0010.

*2-Chloro-2-(4-(trifluoromethyl)phenyl)acetic acid (4a).*¹ Obtained from 4-(trifluoromethyl)phenylacetic acid (**4**) (1 g, 4.90 mmol), PCl₃ (43 μ L, 0.49 mmol) and TCCA (569 mg, 2.45 mmol) at 85 °C according to the general procedure. The crude product, a wax-like whitish solid (1.12 g), was purified by flash chromatography on silica gel (gradient of dichloromethane/methanol from 0% to 10% methanol) to yield **4a** as a white solid (910 mg, 78%): *R*_f (dichloromethane/methanol 8:2) 0.57; mp 85.3-86.0 °C; ¹H NMR (300 MHz, CDCl₃) δ 10.77 (br s, 1H), 7.66 (s, 4H), 5.42 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 173.3, 138.8, 131.9 (q, *J*=32.8 Hz), 128.6, 126.1 (q, *J*=3.7 Hz), 123.8 (q, *J*=272.4 Hz), 57.9.

2-Chloro-2-(4-(methoxycarbonyl)phenyl)acetic acid (5a). Obtained from 4-(methoxycarbonyl)phenylacetic acid (**5**) (1 g, 5.18 mmol), PCl₃ (45 μ L, 0.52 mmol) and TCCA (602 mg, 2.59 mmol) at 95 °C according to the general procedure. The crude product, a wax-like white solid (1.11 g), was purified by trituration with cyclohexane to yield **5a** as a white solid (860 mg, 73%): *R*_f (dichloromethane/methanol 8:2) 0.3; mp 77.7-78.9 °C; ¹H NMR (300 MHz, CDCl₃) δ 9.46 (br s, 1H), 8.05 (d, *J*=8.0 Hz, 2H), 7.59 (d, *J*=8.0 Hz, 2H), 5.41 (s, 1H), 3.93 (s, 3 H); ¹³C NMR (75 MHz, CDCl₃) δ 172.4, 166.6, 139.9, 131.3, 130.3, 128.2, 58.2, 52.6; HRMS (ESI⁻) *m/z* calcd for C₉H₈ClO₂ [M-COOH]⁻ 183.0213, found 183.0218.

*2-Chloro-2-(4-fluorophenyl)acetic acid (6a).*¹ Obtained from 4-fluorophenylacetic acid (**6**) (1 g, 6.49 mmol), PCl₃ (57 μ L, 0.65 mmol) and TCCA (754 mg, 3.25 mmol) at 85 °C according to the general procedure. The crude product, a wax-like yellow solid (1.16 g), was purified by flash chromatography on silica gel (gradient of dichloromethane/methanol from 0% to 10% methanol) to yield **6a** as a whitish solid (960 mg, 78%): *R*_f (dichloromethane/methanol 8:2) 0.77; mp 82.4-83.3 °C; ¹H NMR (300 MHz, CDCl₃) δ 10.40 (br s, 1H), 7.54-7.47 (m, 2H), 7.12-7.04 (m, 2 H), 5.36 (s, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 174.1, 163.5 (d, *J*=250 Hz), 130.9 (d, *J*=3.5 Hz), 130.2 (d, *J*=8.6 Hz), 116.2 (d, *J*=22.2 Hz), 58.0.

*2-Chloro-2-(4-chlorophenyl)acetic acid (7a).*² Obtained from 4-chlorophenylacetic acid (**7**) (1 g, 5.86 mmol), PCl₃ (51 μ L, 0.59 mmol) and TCCA (681 mg, 2.93 mmol) at 90 °C according to the general procedure. The crude product, a colorless oil (1.13 g), was purified by crystallization from hexane to yield **7a** as a white solid (860 mg, 72%): *R*_f (dichloromethane/methanol 8:2) 0.85; mp 76.9-77.7 °C; ¹H NMR (300 MHz, CDCl₃) δ 10.32 (br s, 1H), 7.45 (d, *J*=8.6 Hz, 2H), 7.37 (d, *J*=8.6 Hz, 2H), 5.34 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 173.7, 135.9, 133.6, 129.5, 129.3, 58.0. HRMS (ESI⁻) *m/z* calcd for C₈H₅Cl₂O₂ [M-H]⁻ 202.9667, found 202.9669.

*2-Chloro-2-(4-bromophenyl)acetic acid (8a).*² Obtained from 4-bromophenylacetic acid (**8**) (1 g, 4.65 mmol), PCl₃ (41 μ L, 0.47 mmol) and TCCA (542 mg, 2.33 mmol) at 90 °C according to the general procedure. The crude product, a wax-like whitish solid (1.26 g), was purified by crystallization from hexane to yield **8a** as a white solid (850 mg, 73%): *R*_f (dichloromethane/methanol 8:2) 0.67; mp 77.4-

78.2 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.53 (d, $J=8.5$ Hz, 2H), 7.39 (d, $J=8.5$ Hz, 2H), 5.32 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 174.0, 134.0, 132.3, 129.8, 124.1, 58.0.

2-Chloro-2-(4-iodophenyl)acetic acid (9a). Obtained from 4-iodophenylacetic acid (**9**) (1 g, 3.82 mmol), PCl_3 (33 μL , 0.38 mmol) and TCCA (443 mg, 1.91 mmol) at 110 °C according to the general procedure. The crude product, a yellow solid (1.04 g), was purified by crystallization from cyclohexane/ethyl acetate (9:1, v/v) to yield **9a** as a yellow solid (760 mg, 67%): R_f (dichloromethane/methanol 8:2) 0.55; mp 108.8 °C (dec); ^1H NMR (300 MHz, CDCl_3) δ 7.74 (d, $J=8.4$ Hz, 2H), 7.25 (d, $J=8.4$ Hz, 2H), 5.87 (br s, 1H), 5.30 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 172.6, 138.3, 134.9, 129.9, 95.9, 58.2, 52.6; HRMS (ESI $^-$) m/z calcd for $\text{C}_8\text{H}_5\text{ClIO}_2$ [$\text{M}-\text{H}$] $^-$ 294.9023, found 294.9024.

3. General procedure for the preparation of **10a** and **11a**

The procedure was identical to the general procedure adopted for **1a**, **2a**, and **4a-9a**, but using 0.6 equivalents of PCl_3 instead of 0.3 and 1.8 equivalents of TCCA instead of 1.5 and purifying the crude product by vacuum distillation.

2-Chloro-2-(p-tolyl)acetic acid (10a).¹ Obtained from *p*-tolylacetic acid (**10**) (1 g, 6.66 mmol), PCl_3 (116 μL , 1.33 mmol) and TCCA (934 mg, 4.02 mmol) at 85 °C according to the general procedure. The crude product, a wax-like white solid (1.16 g), was purified by distillation under vacuum (0.5 with a kugelrohr apparatus at 150-155 °C (0.5 mbar) to yield **10a** as a white solid (760 mg, 62%): R_f (dichloromethane/methanol 8:2) 0.56; mp 81.5-82.3 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.40 (d, $J=8.0$ Hz, 2H), 7.20 (d, $J=8.0$ Hz, 2H), 5.36 (s, 1H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 174.0, 139.9, 132.2, 129.8, 128.0, 58.7, 21.4.

2-Chloro-2-(4-isopropylphenyl)acetic acid (11a). Obtained from 4-isopropylphenylacetic acid (**11**) (1 g, 5.61 mmol), PCl_3 (98 μL , 1.12 mmol) and TCCA (782 mg, 3.37 mmol) at 85 °C according to the general procedure. The crude product, a wax-like white solid (1.29 g), was purified by distillation under vacuum (0.5 mbar) with a kugelrohr apparatus at 150-155 °C to yield **11a** as a white solid (850 mg, 71%): R_f (dichloromethane/methanol 8:2) 0.56; mp 76.4-77.6 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.43 (d, $J=8.0$ Hz, 2H), 7.25 (d, $J=8.0$ Hz, 2H), 5.37 (s, 1H), 2.92 (hep, $J=6.9$ Hz, 1H), 1.25 (d, $J=6.9$ Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 174.2, 151.1, 132.9, 128.6, 127.7, 59.2, 34.5, 24.4; HRMS (ESI $^-$) m/z calcd for $\text{C}_{11}\text{H}_{12}\text{ClO}_2$ [$\text{M}-\text{H}$] $^-$ 211.0526, found 211.0530.

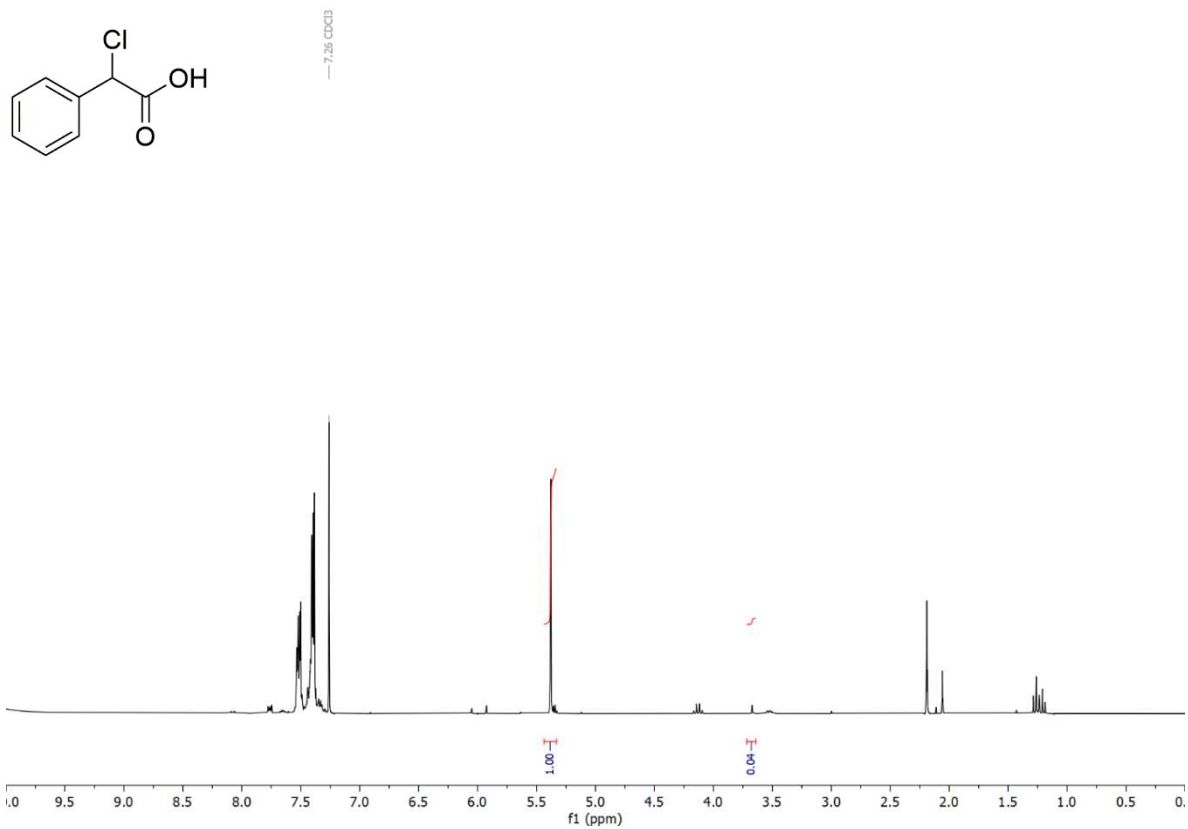
4. References

1. C. Maret, N. David, D. Pierrot, E. Leonel, V. Levacher, J. F. Briere, S. Oudeyer, Synthesis of α -chloroarylacetic acid via electrochemical carboxylation of α,α -dichloroarylmethane derivatives, *Molecules*, 2023, **28**, 6704.
2. W. Reeve, J. R. McKee, R. Brown, S. Lakshmanan, G. A. McKee, Studies on the rearrangement of (trichloromethyl)carbinols to α -chloroacetic acids, *Can. J. Chem.*, 1980, **58**, 485-493.

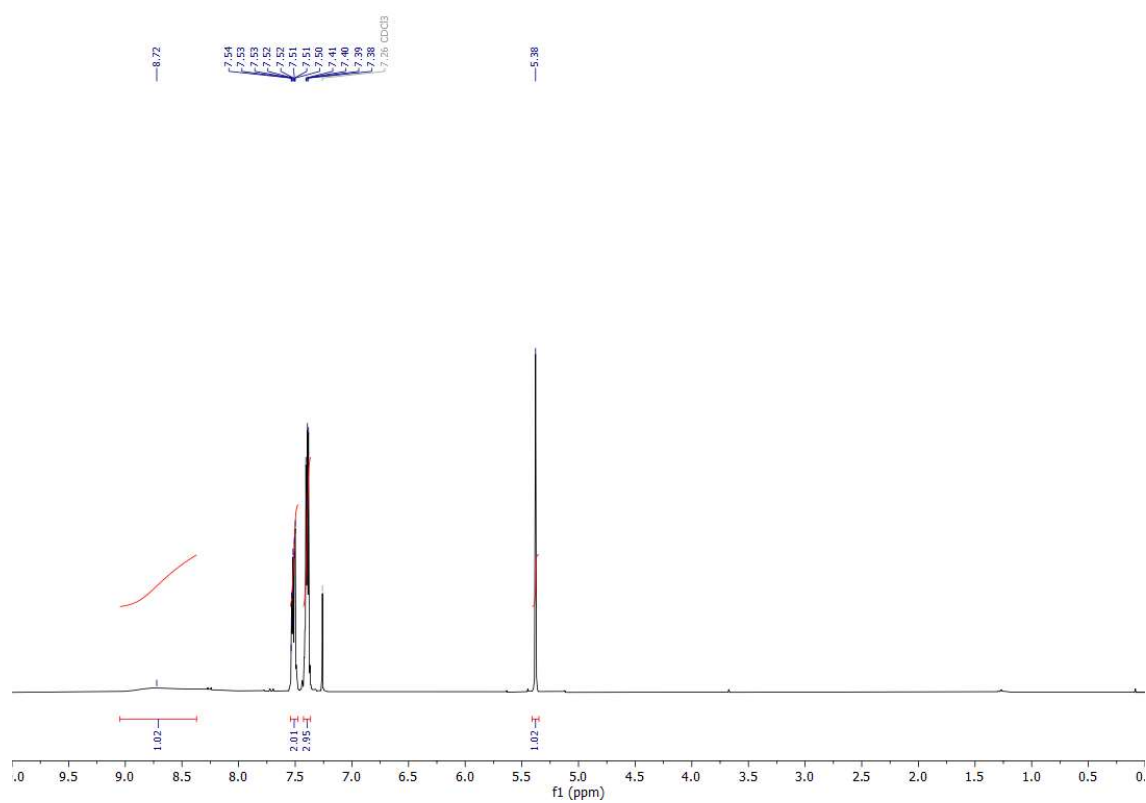
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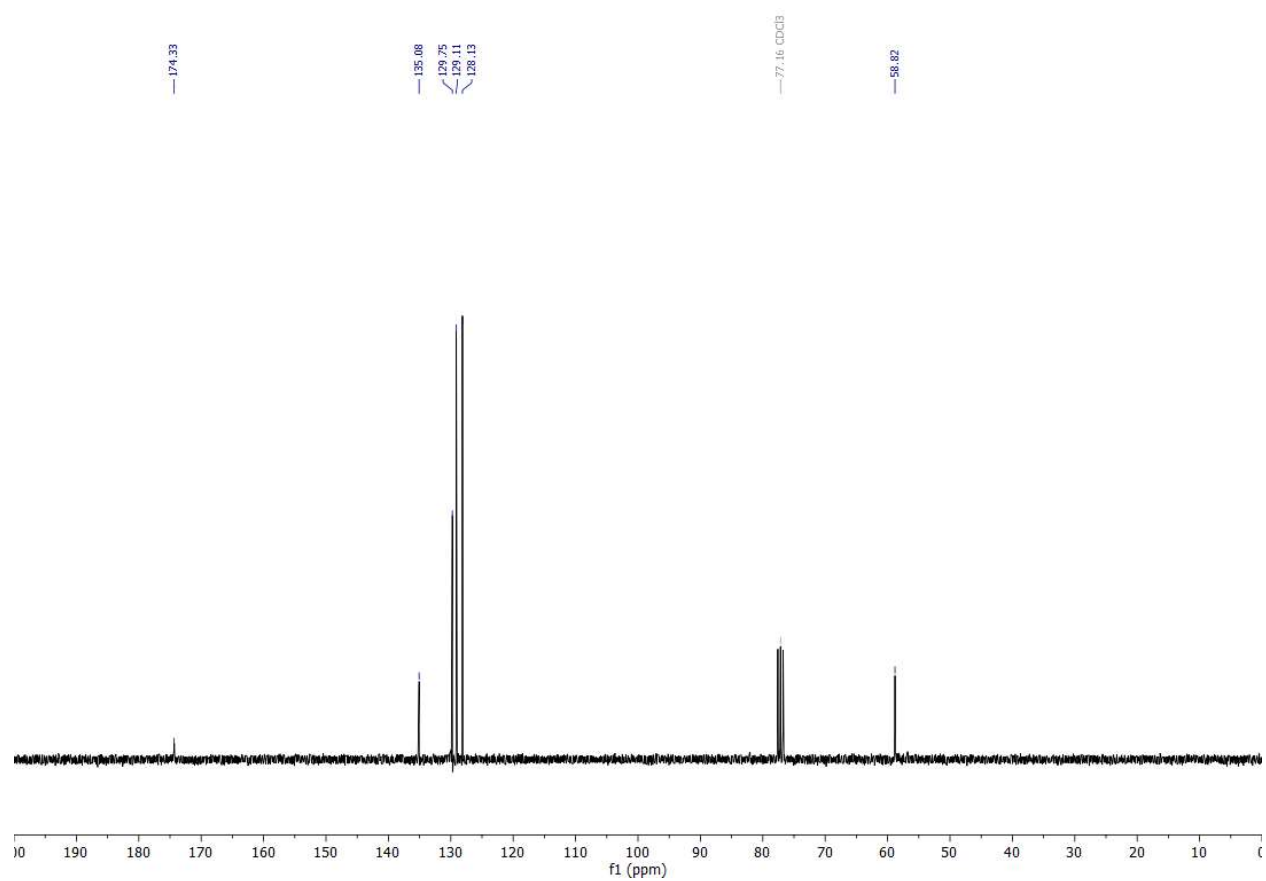
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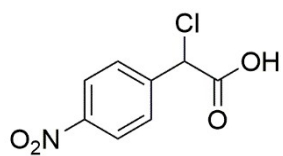
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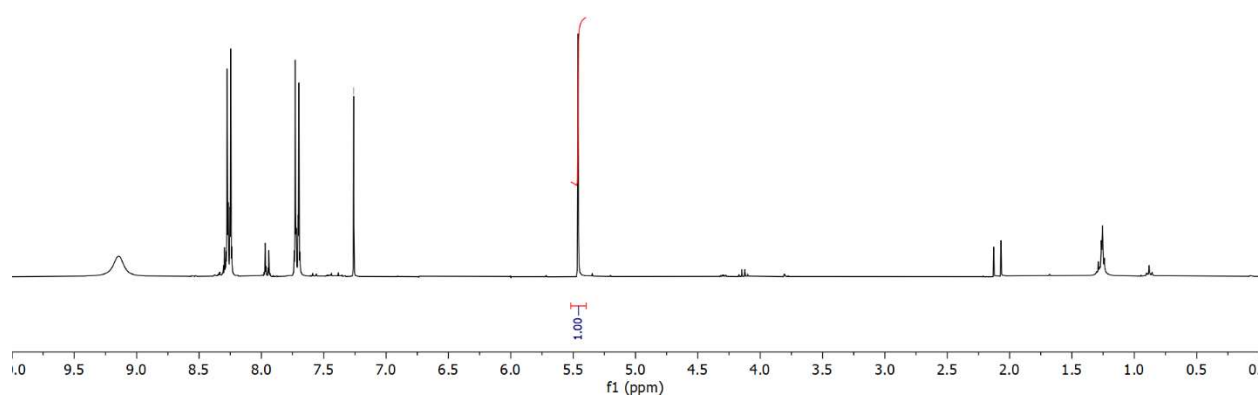


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crude



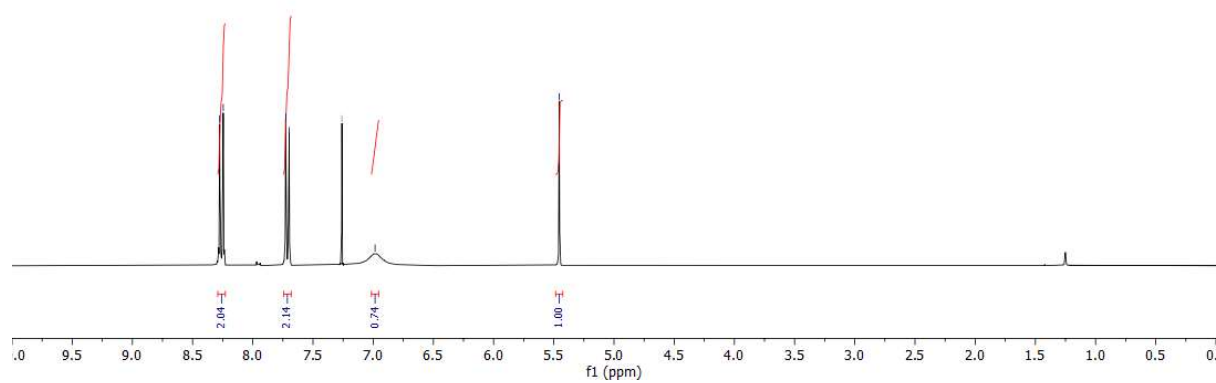
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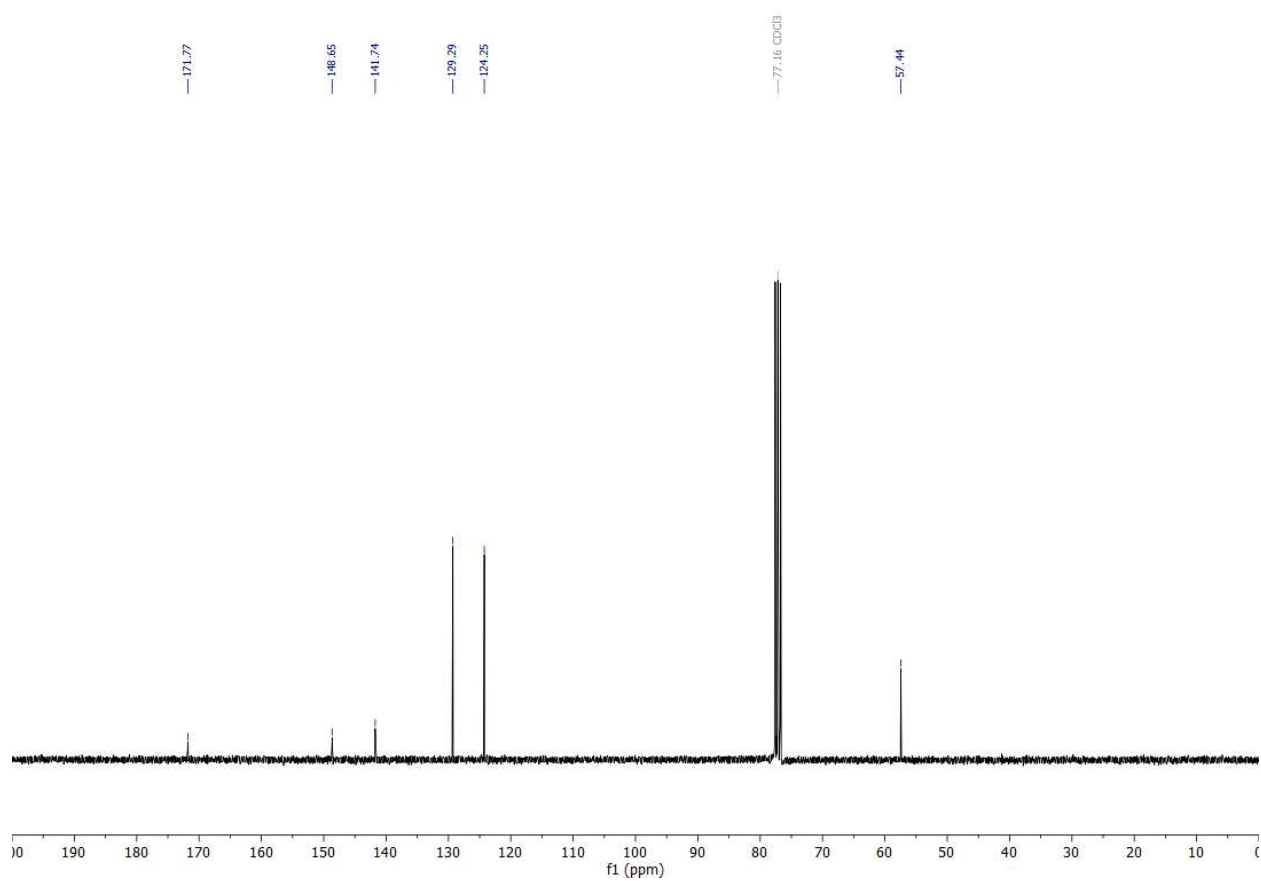


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 < 7.70
 — 7.36 CDCl₃
 — 6.98

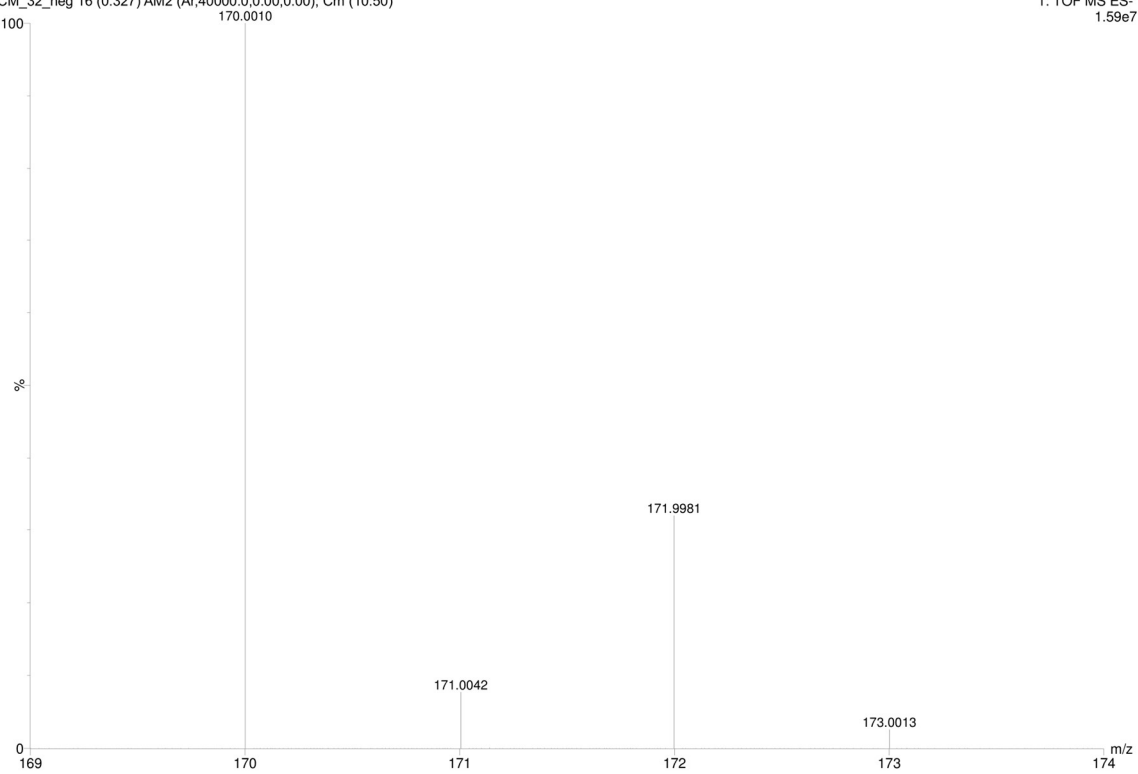
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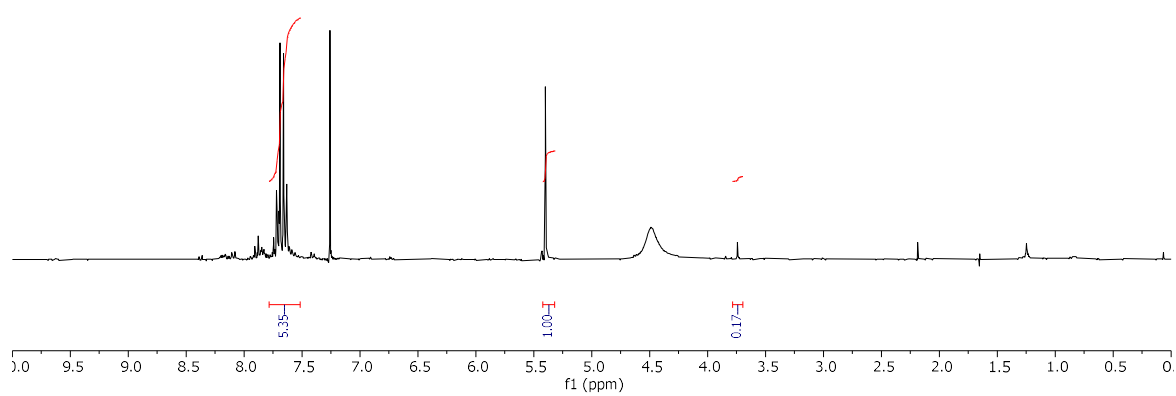
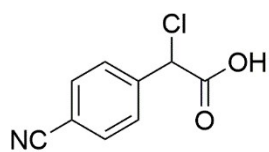
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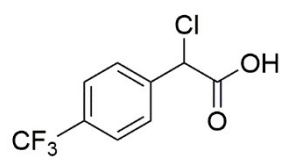
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crude

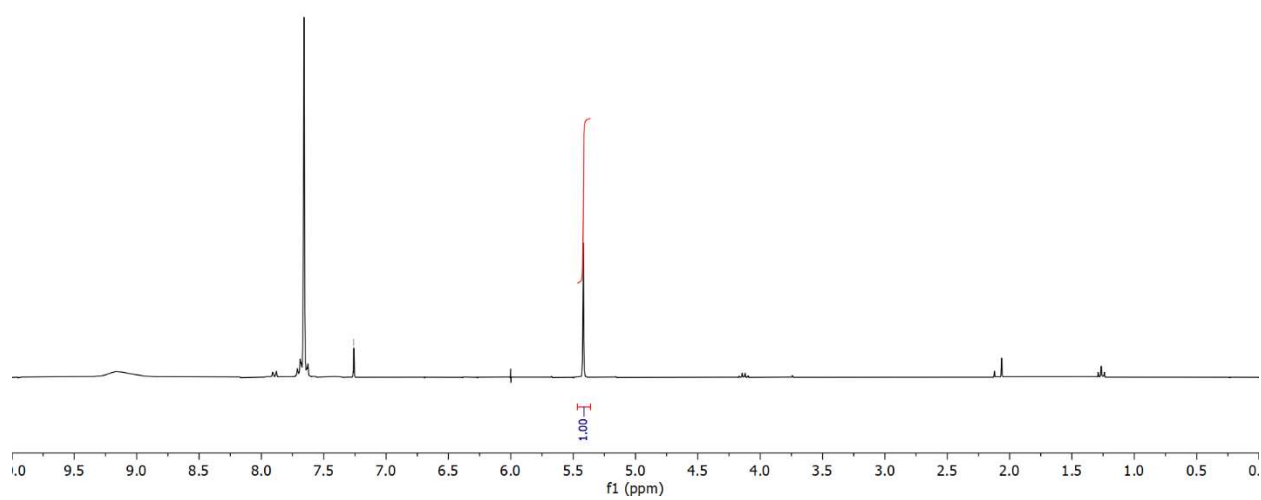


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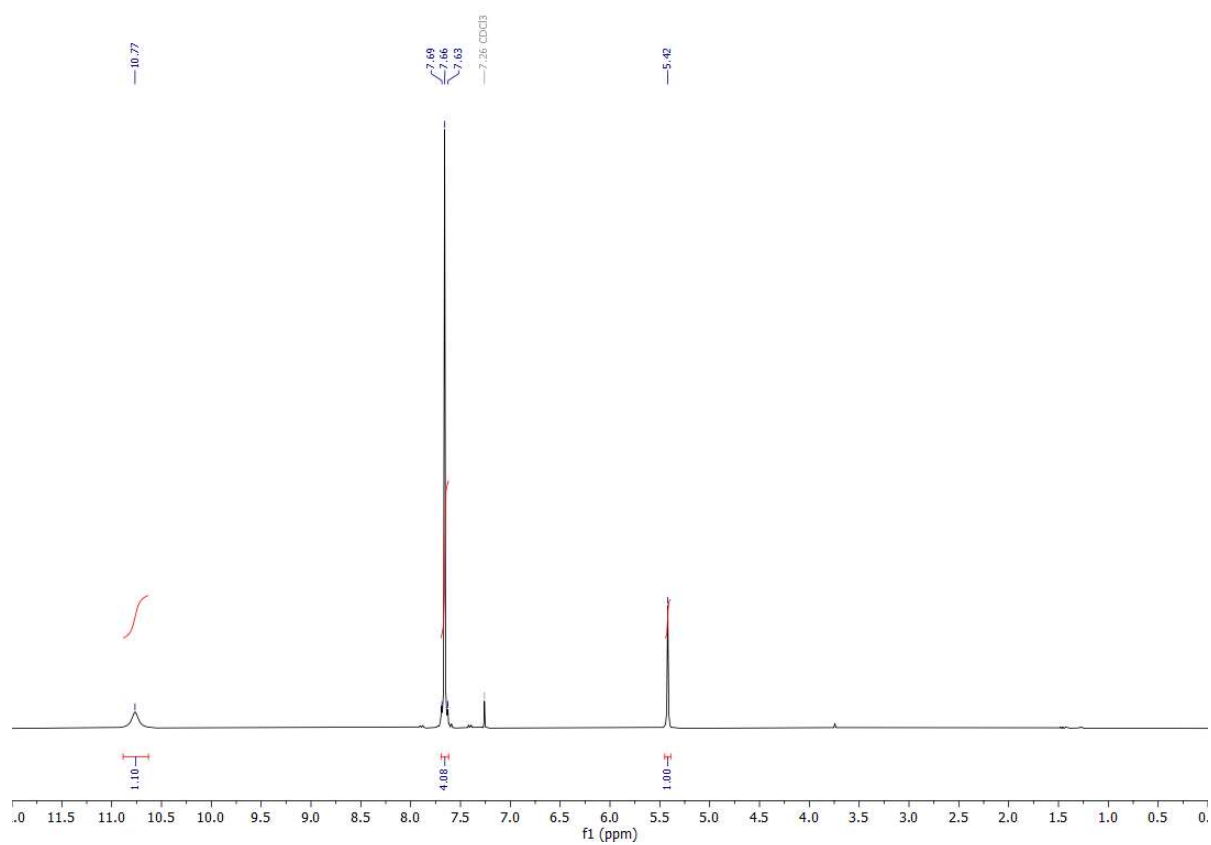
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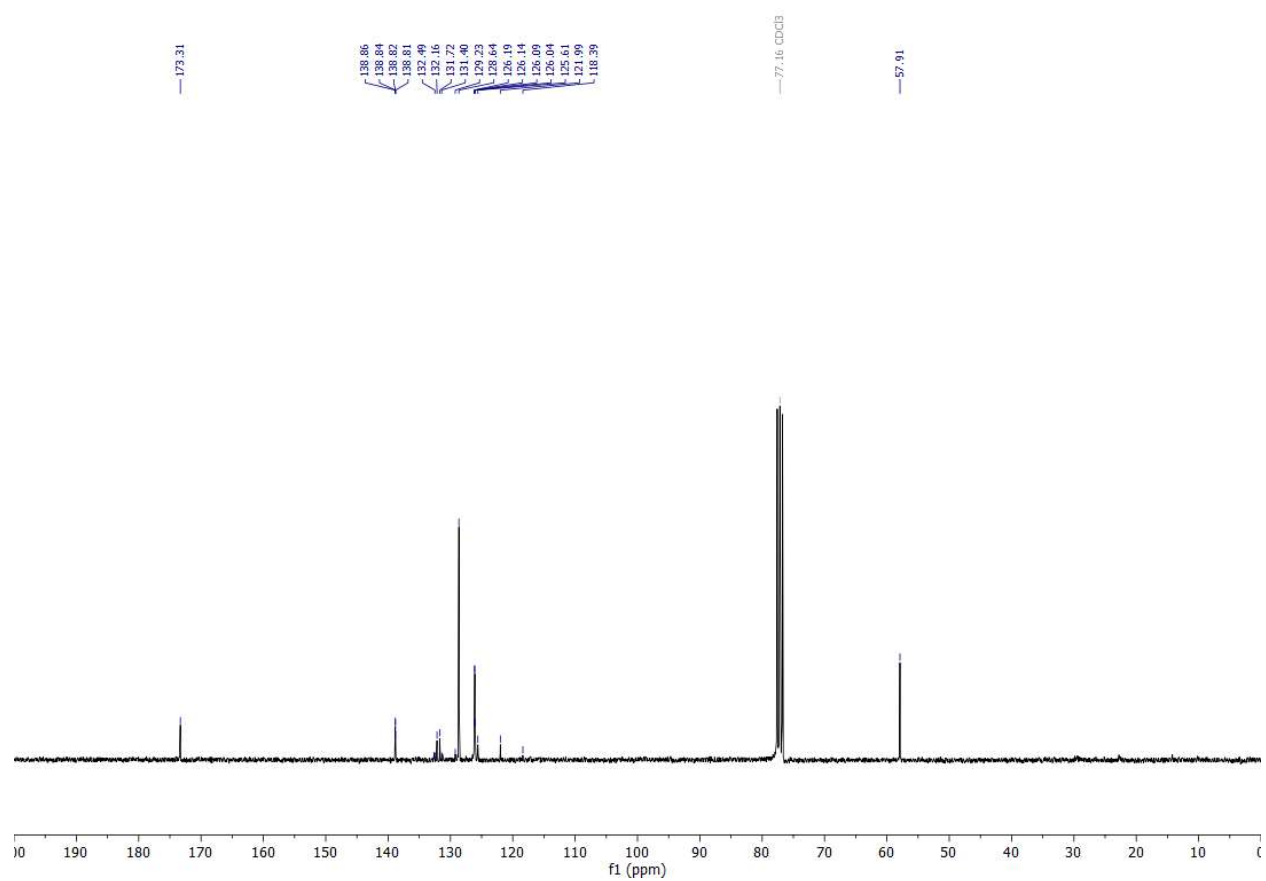


—7.26 CDCl₃



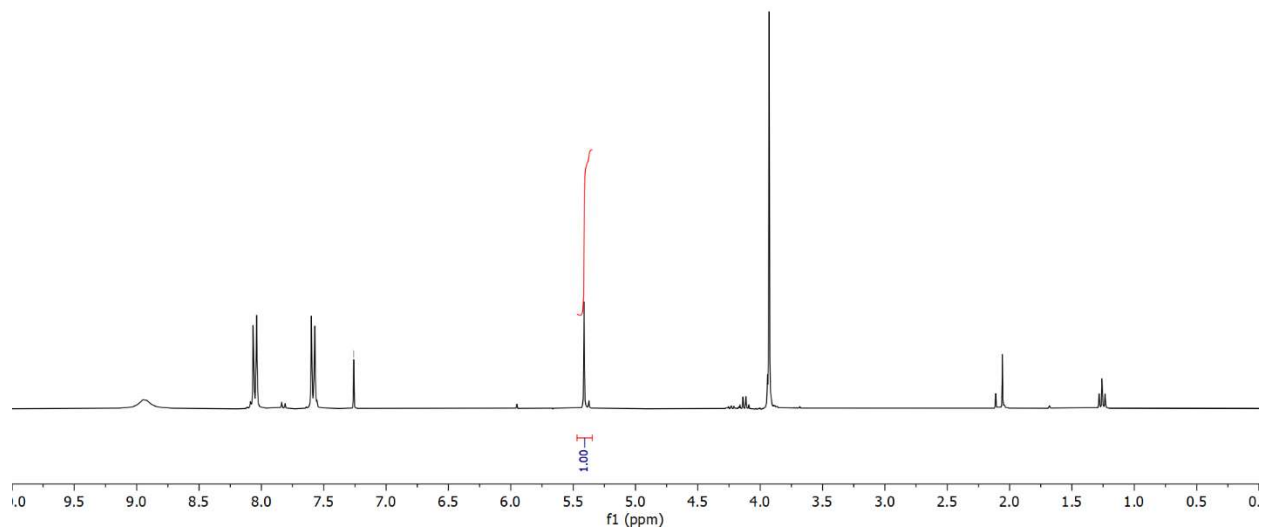
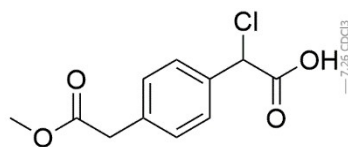
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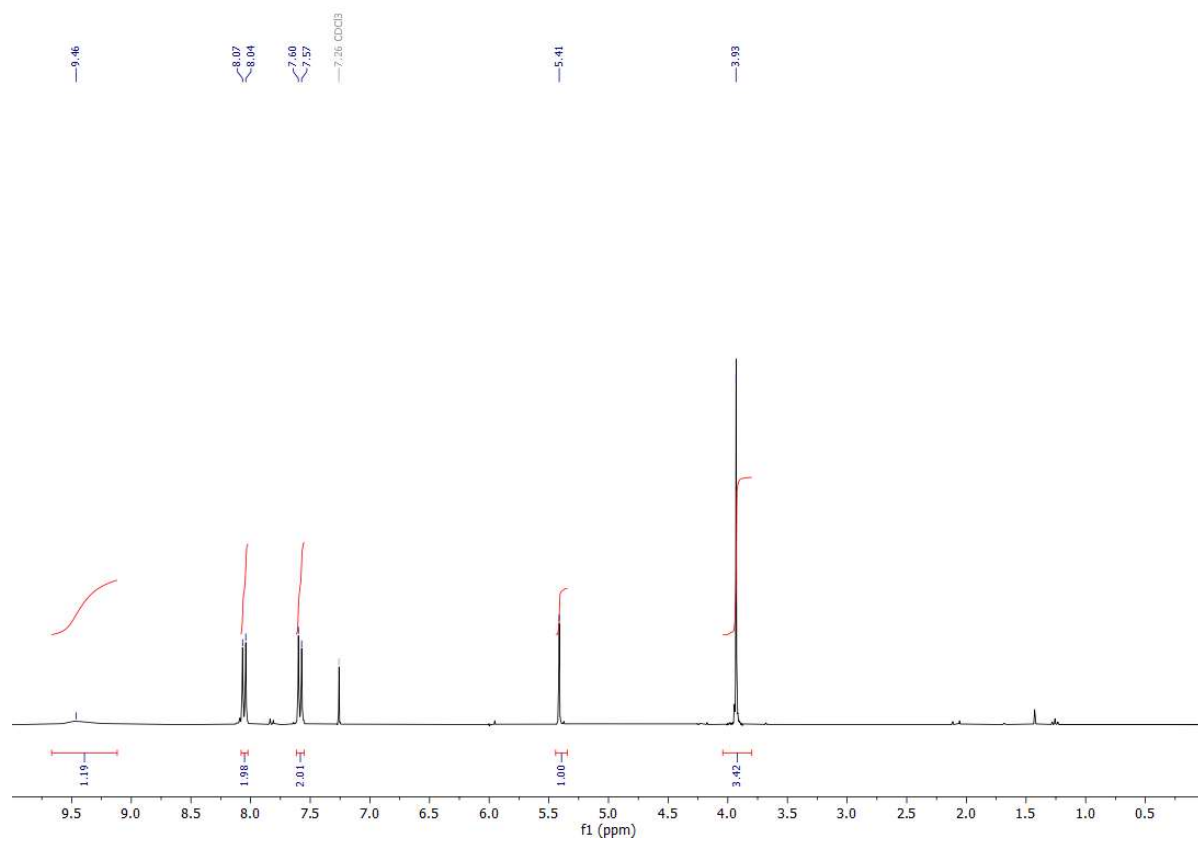


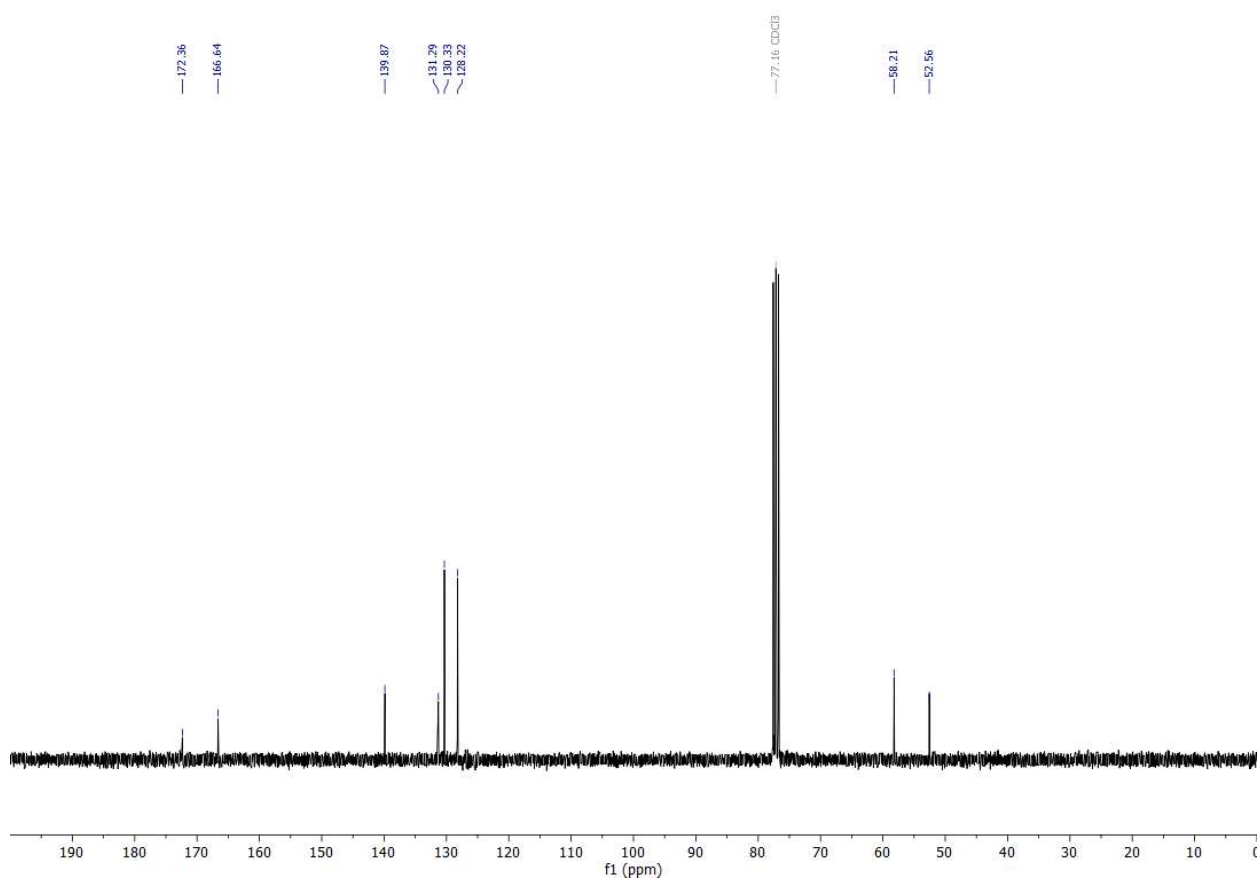
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crude



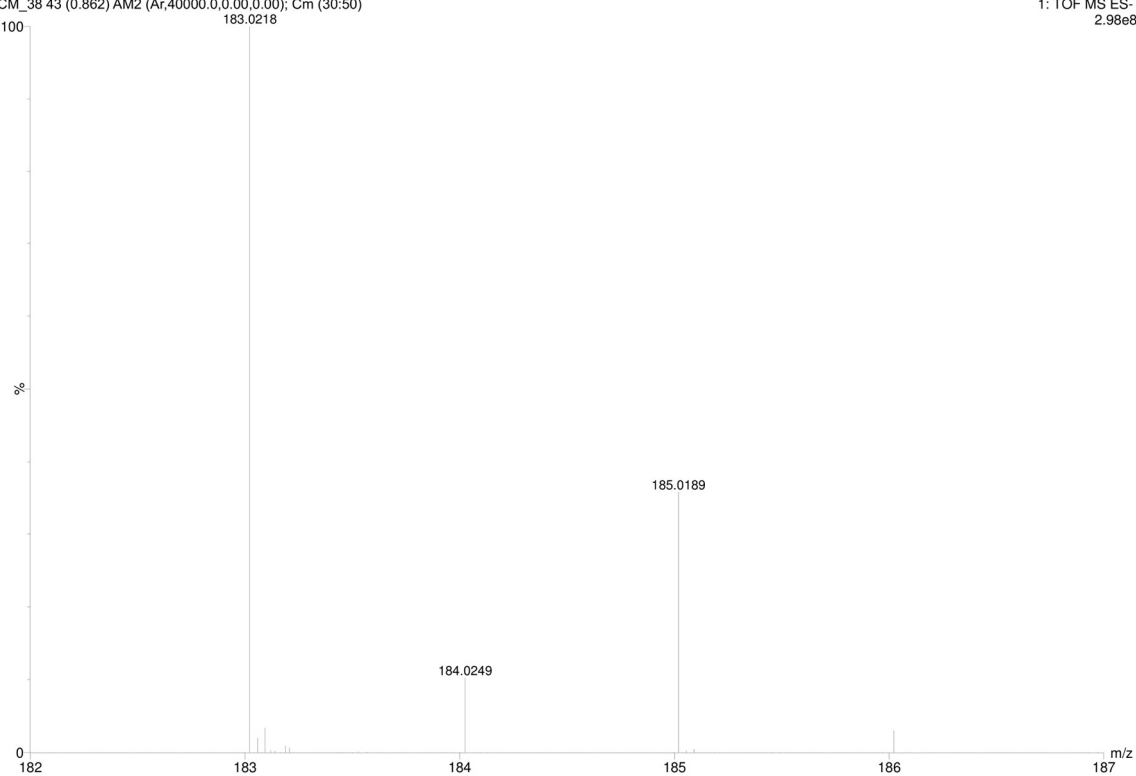
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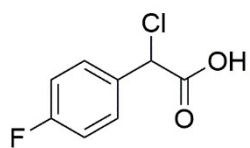
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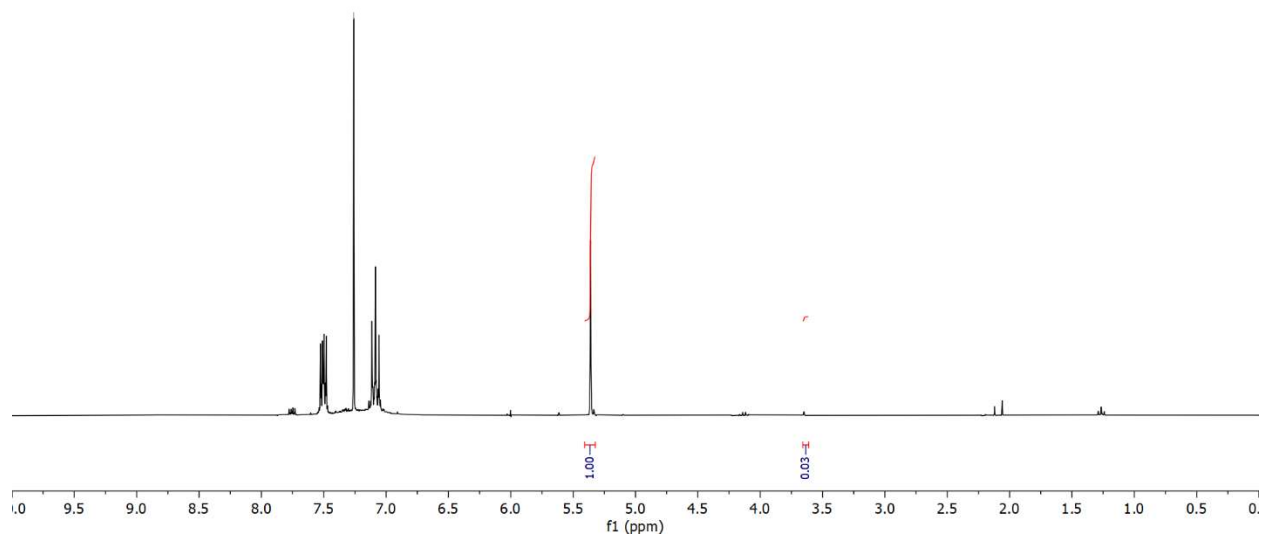


2-Chloro-2-(4-fluorophenyl)acetic acid (6a)

crude

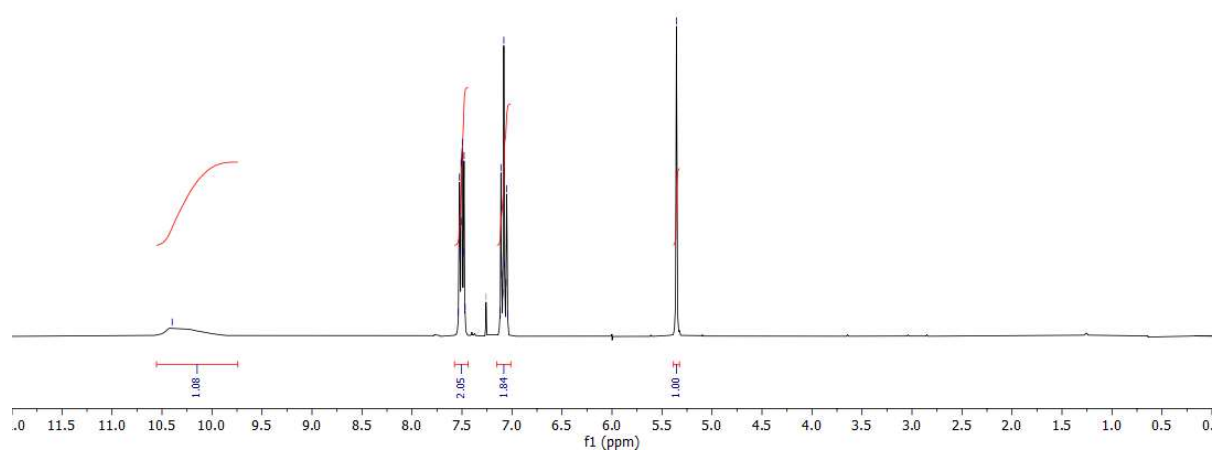


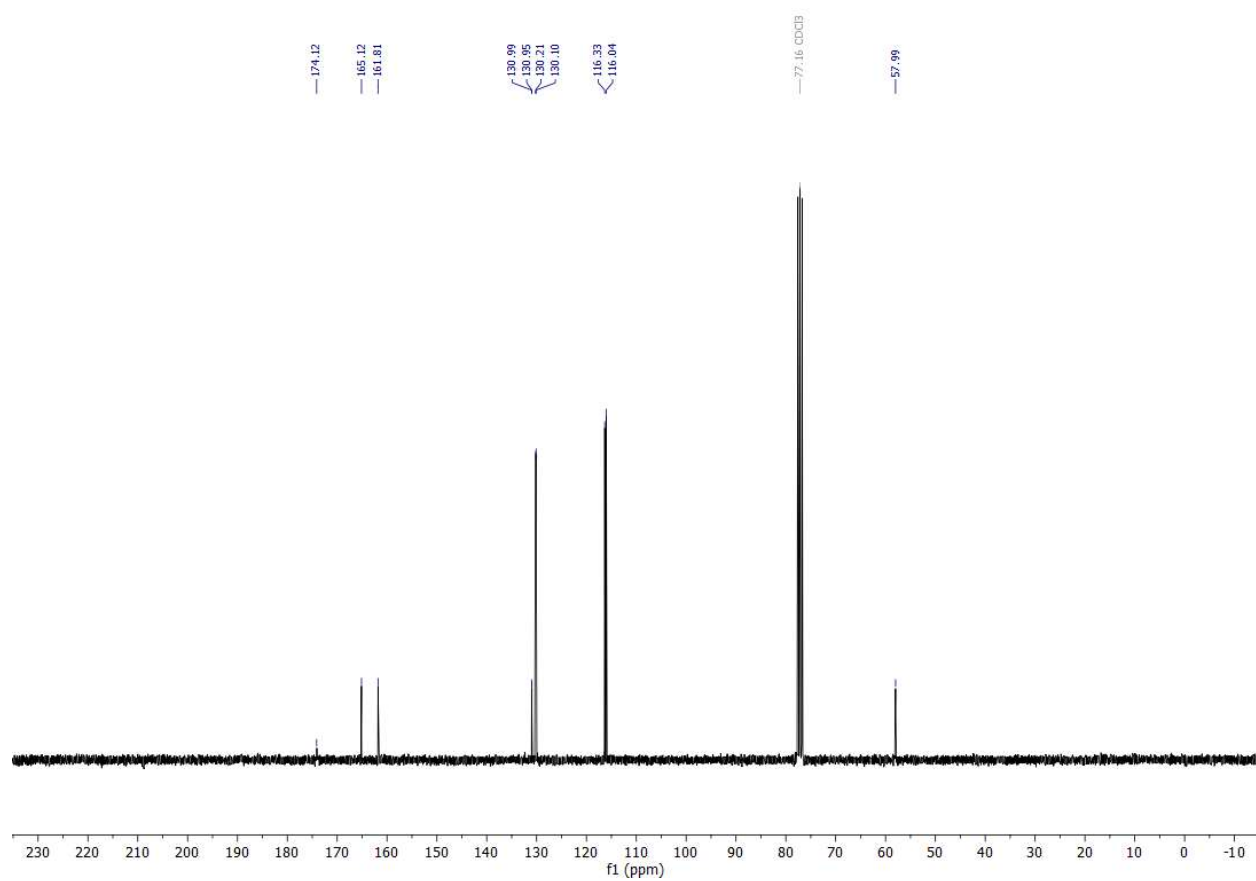
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purified

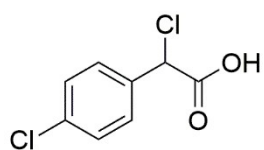
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7.06
7.05
7.04
— 5.36



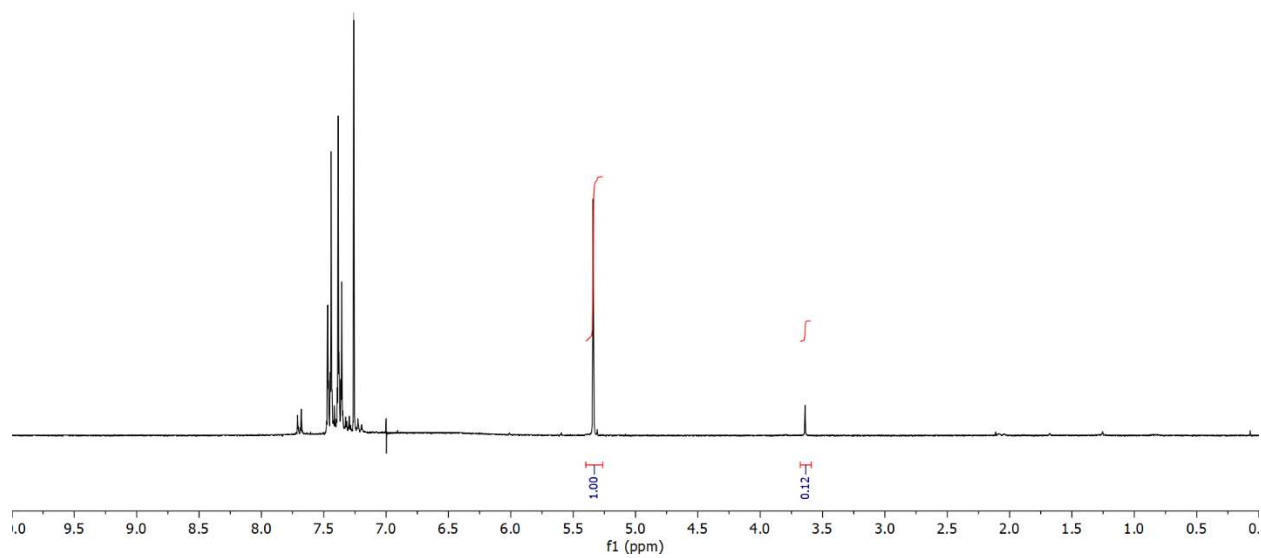


2-Chloro-2-(4-chlorophenyl)acetic acid (7a)

crude



— 7.26 CDCl₃

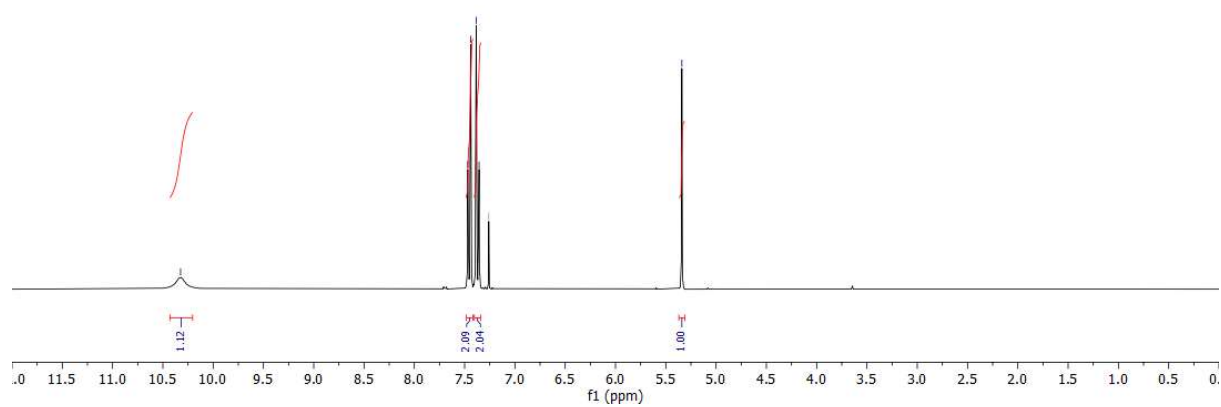


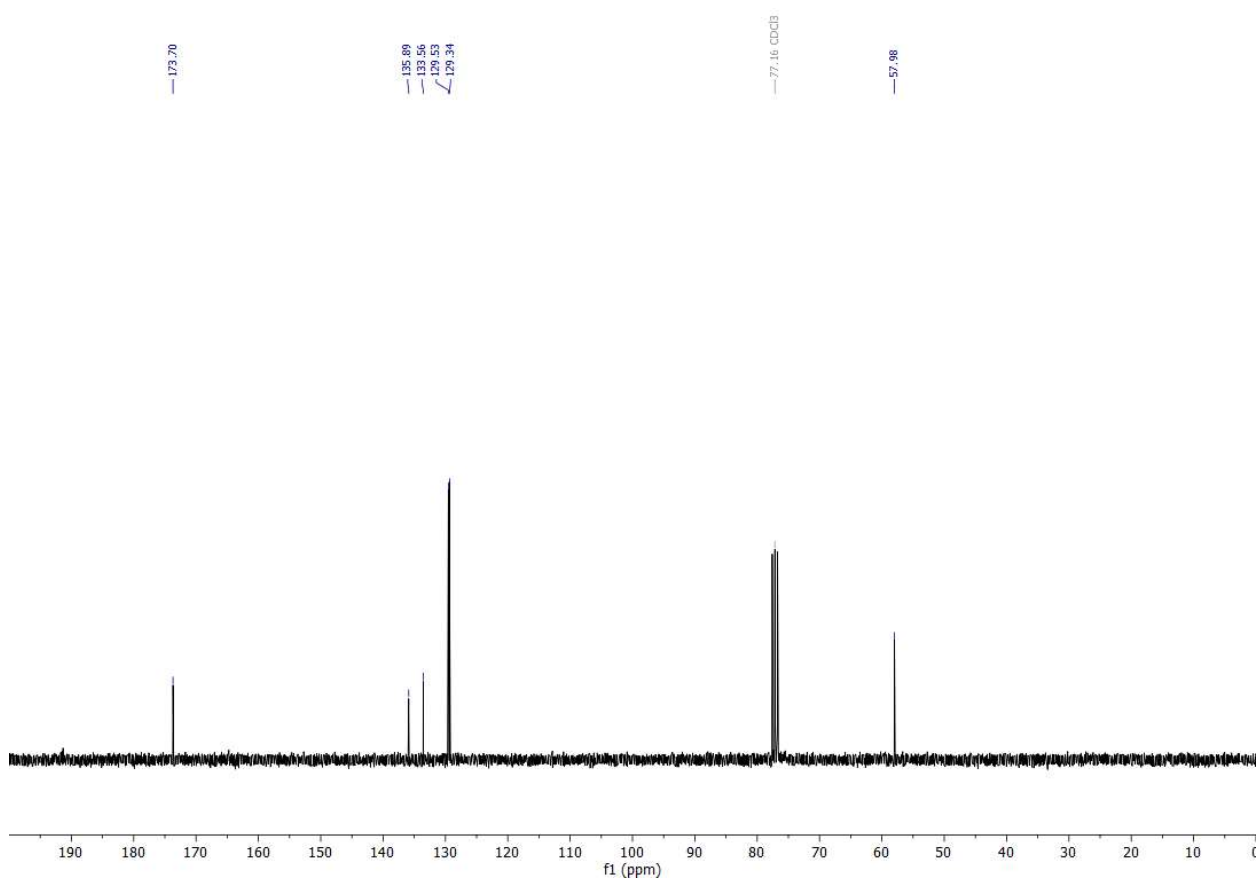
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— 10.32

7.47
7.44
7.38
7.36
— 7.26 CDCl₃

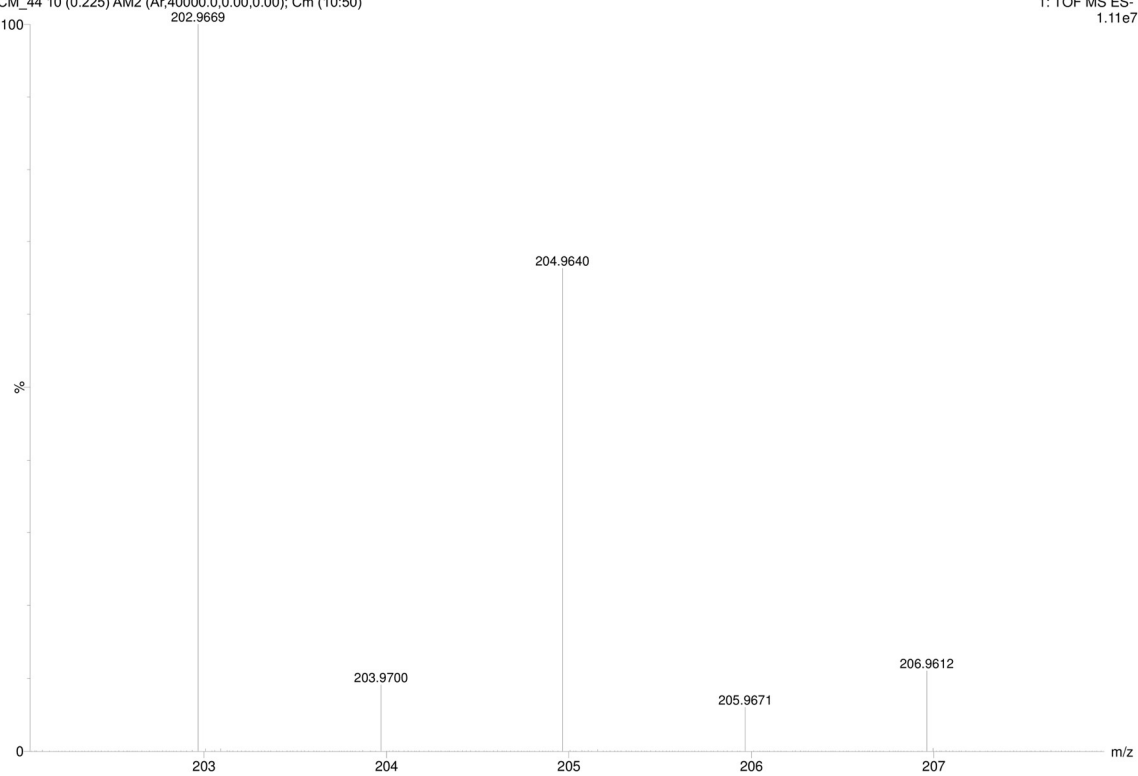
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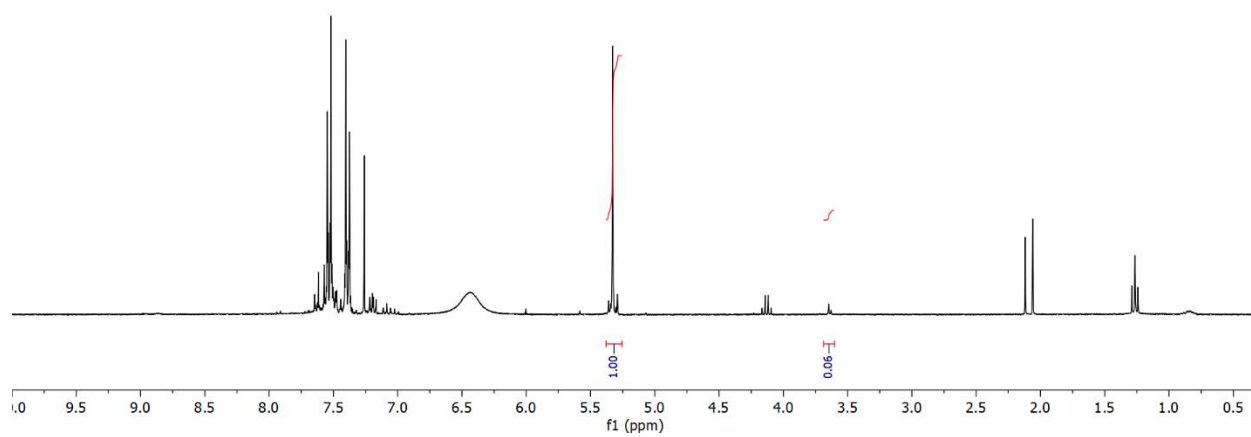
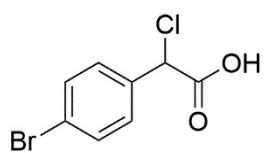
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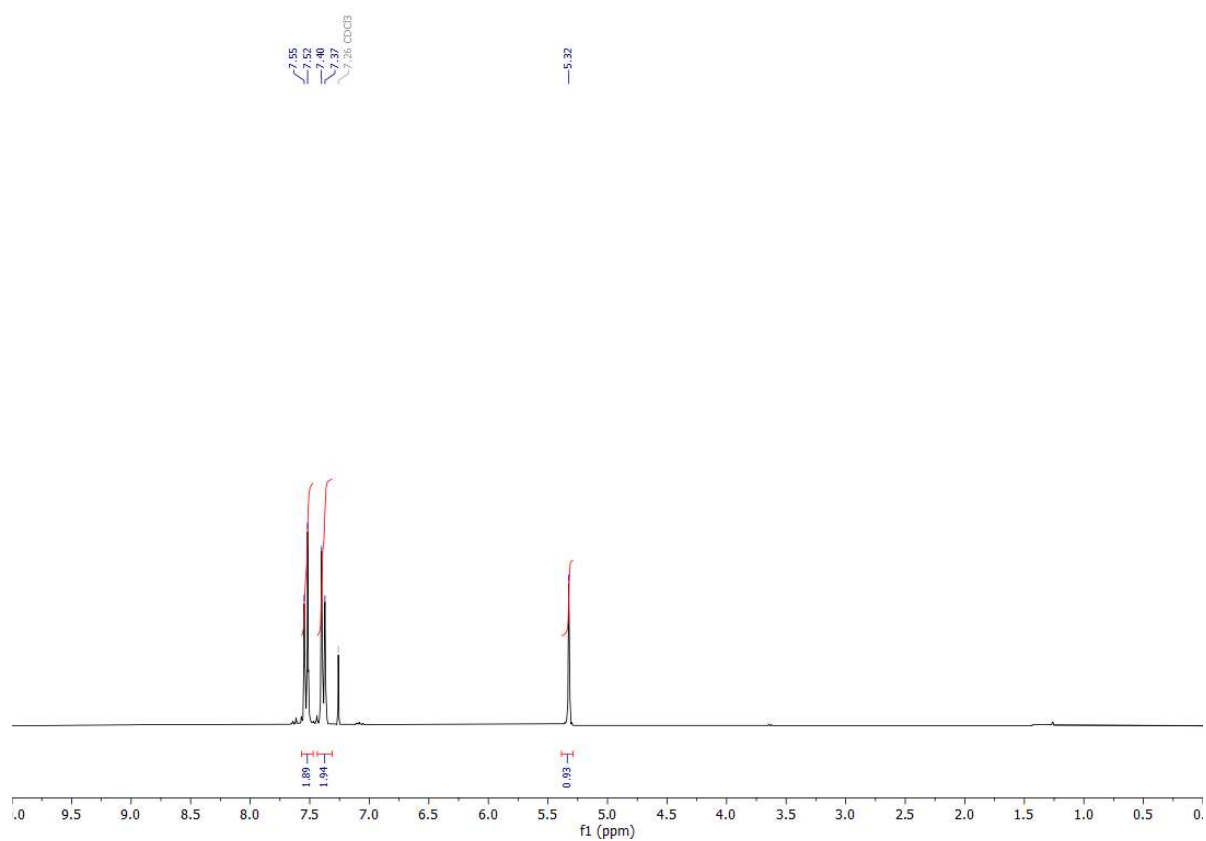


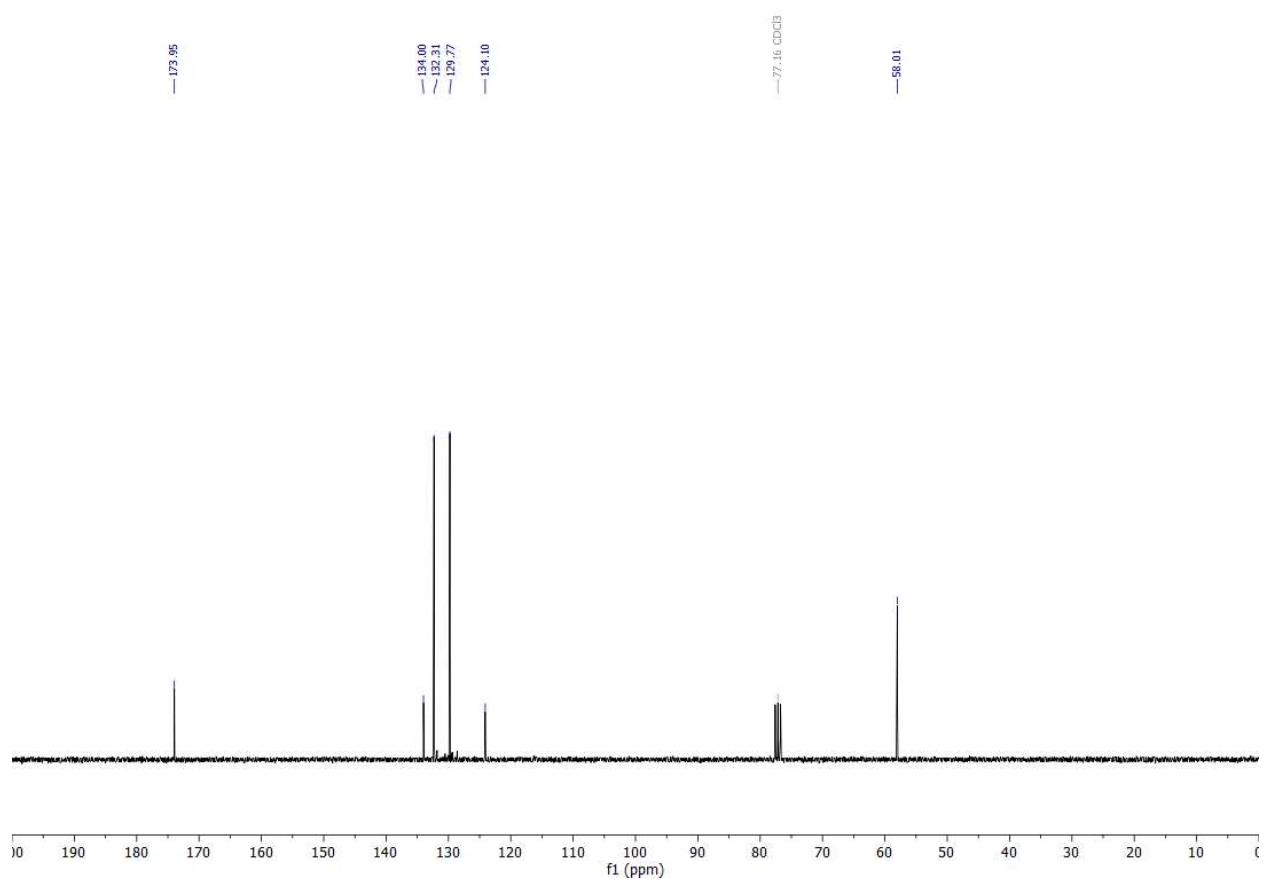
2-Chloro-2-(4-bromophenyl)acetic acid (8a)

crude



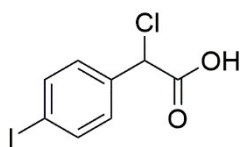
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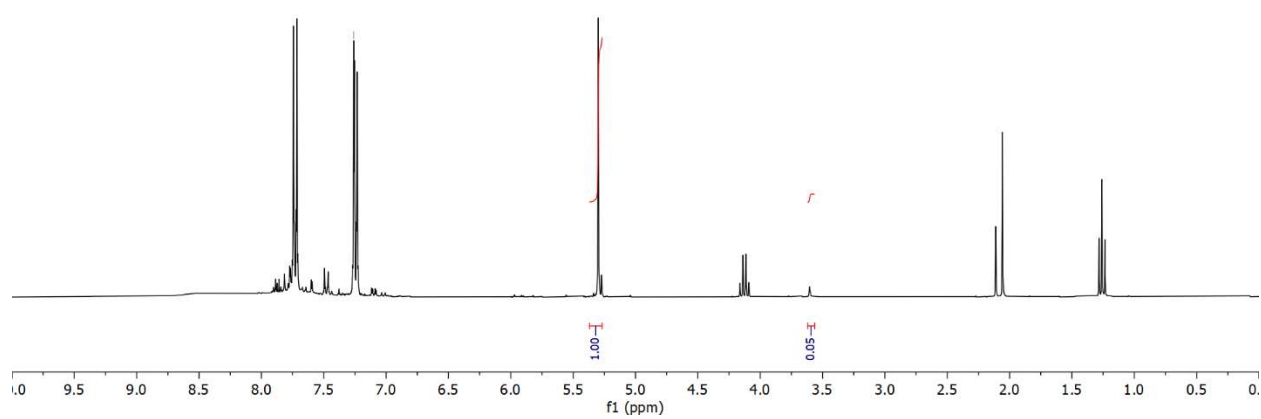


2-Chloro-2-(4-iodophenyl)acetic acid (9a)

crude



— 7.26 CDCl₃

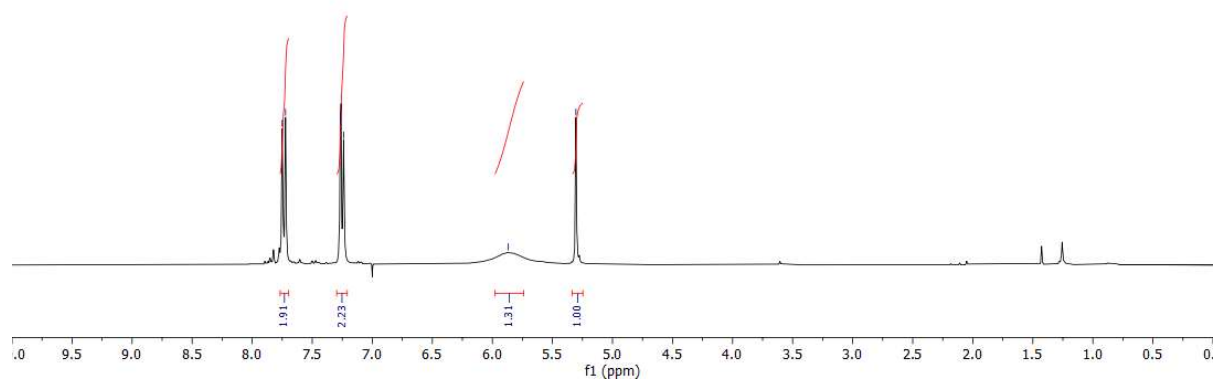


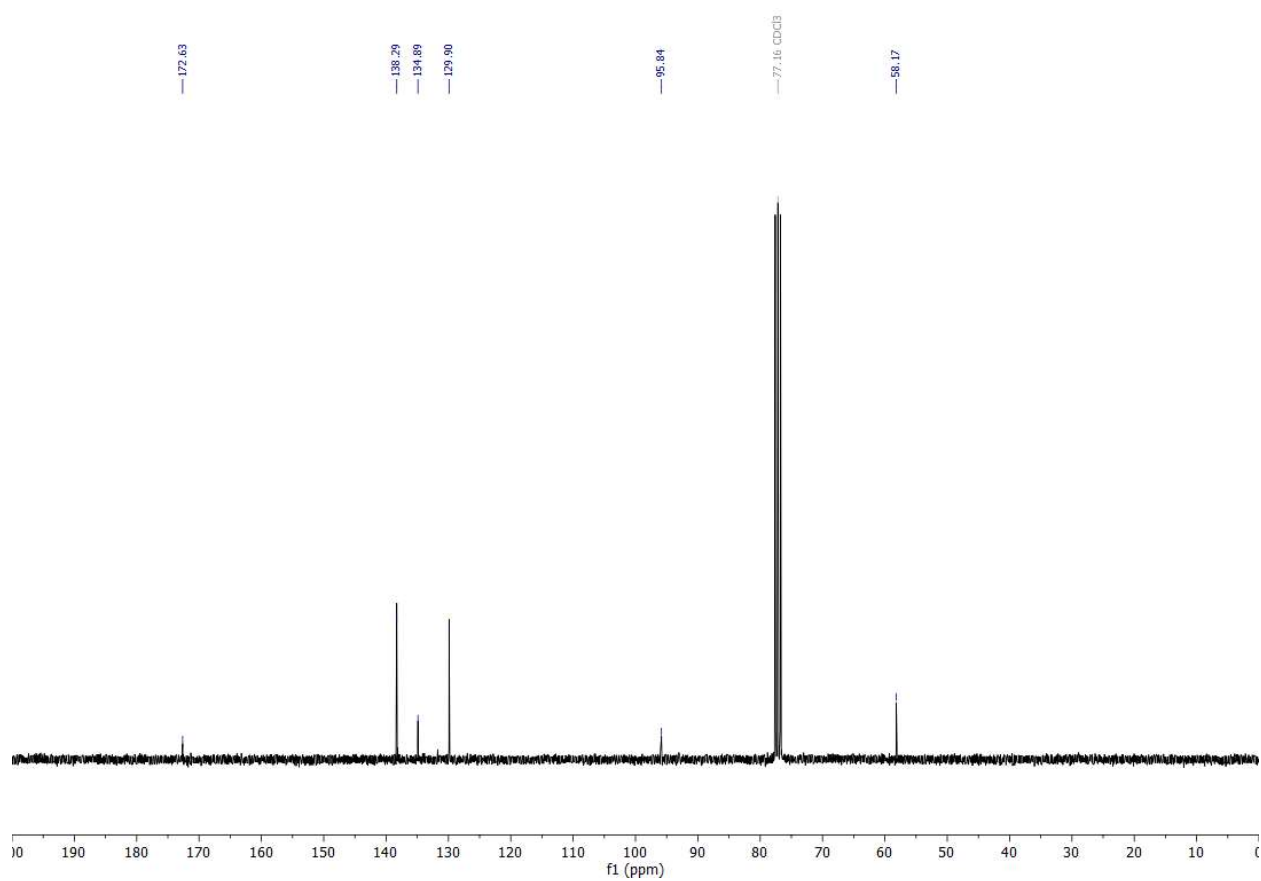
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7.75
7.72
7.27
7.26 CDCl₃
7.24

— 5.87

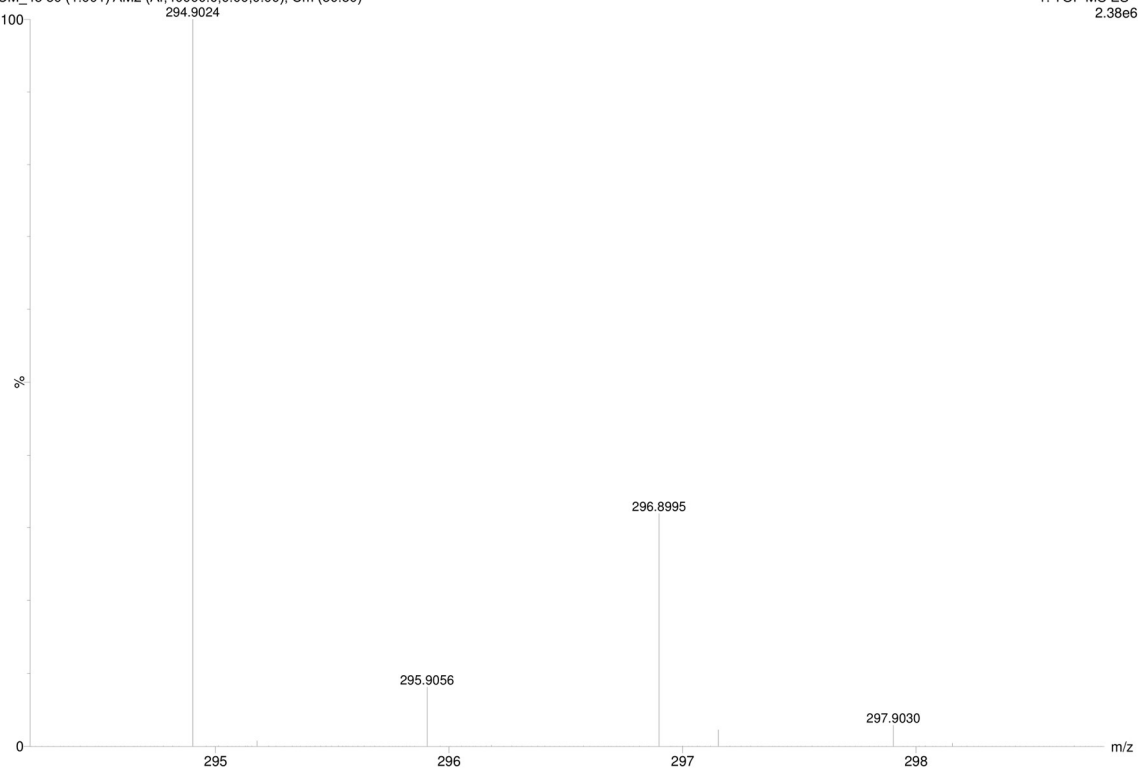
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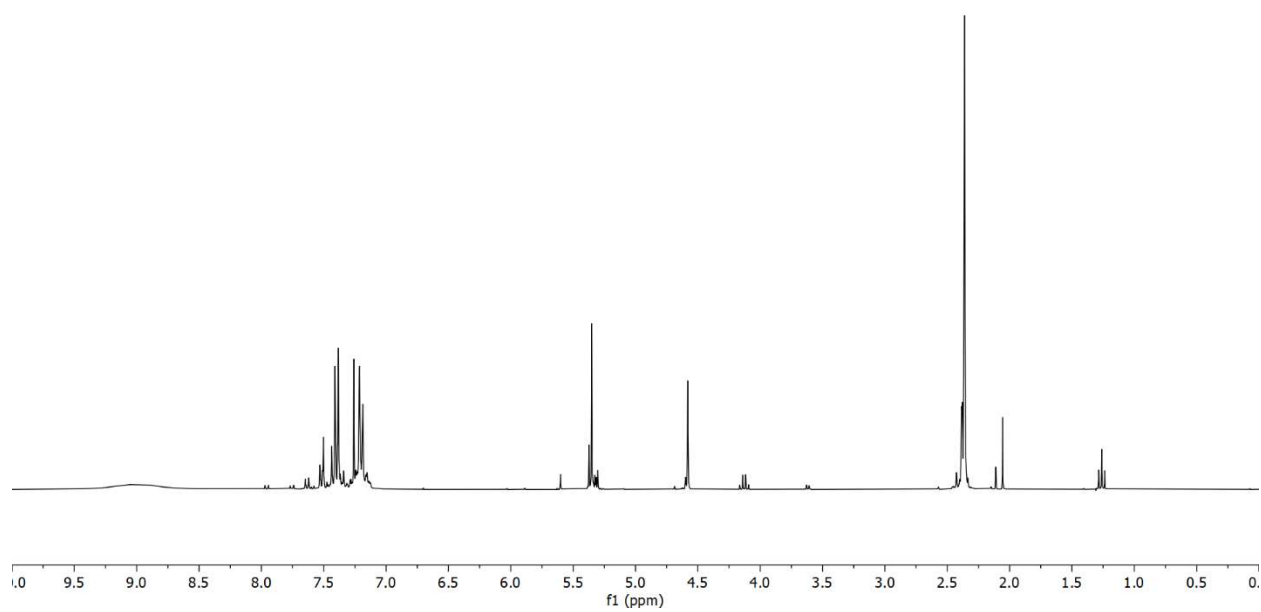
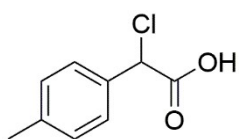
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2.38e6

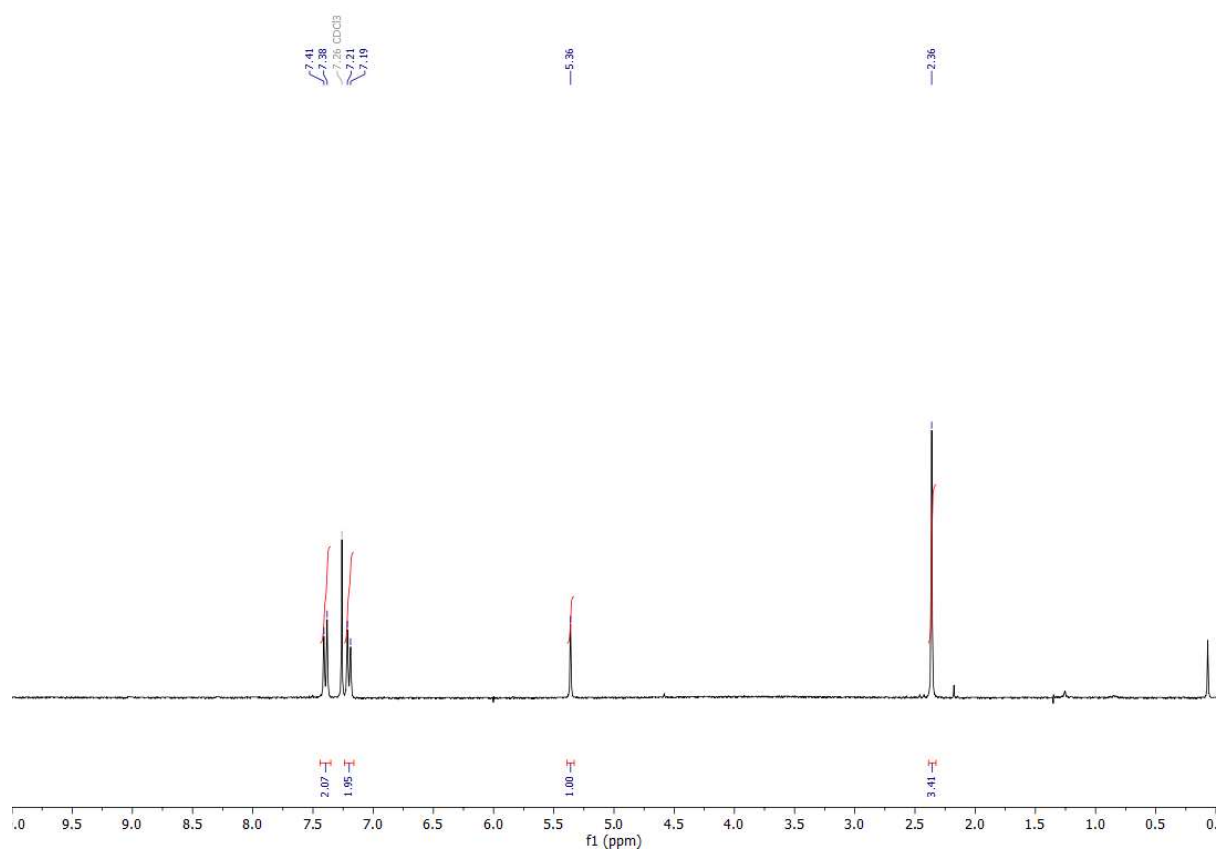


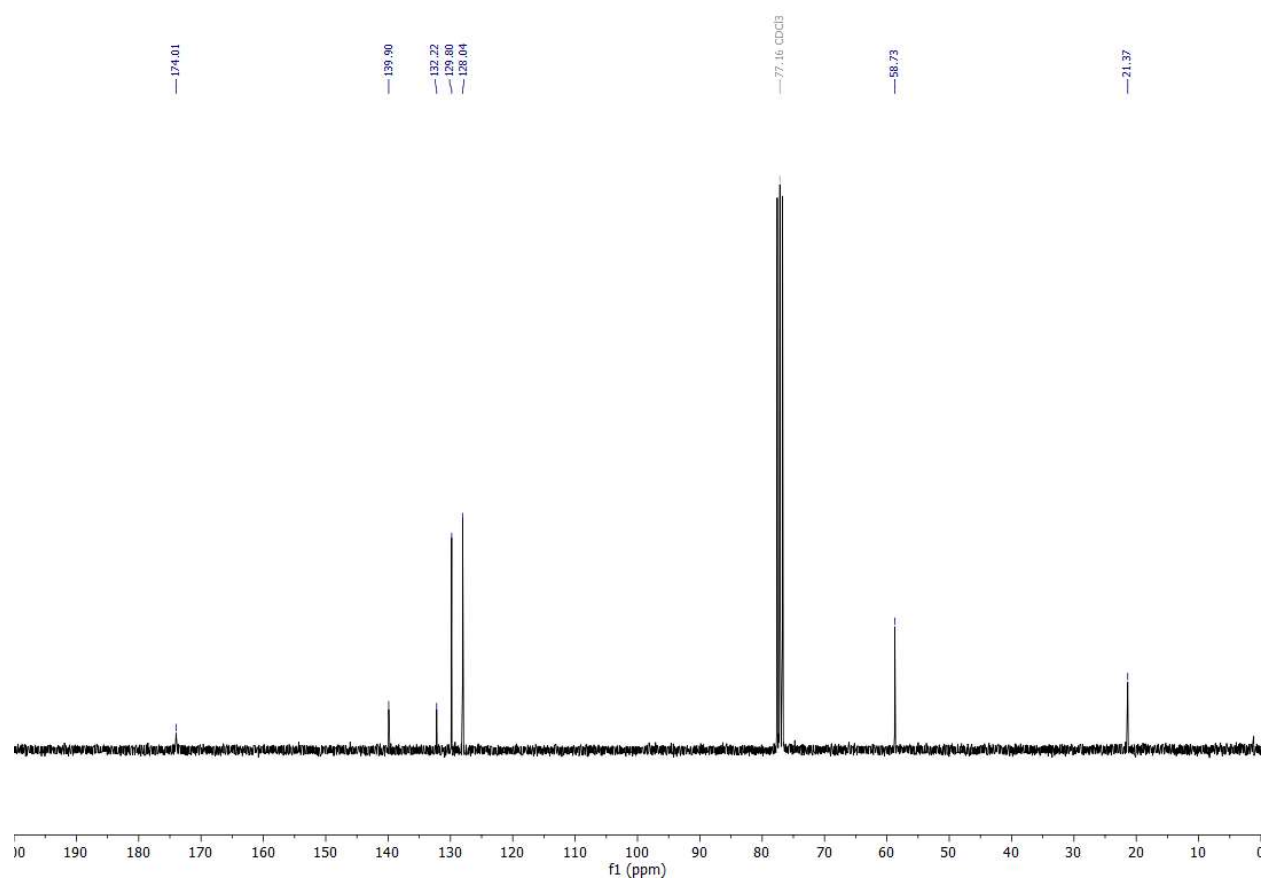
2-Chloro-2-(p-tolyl)acetic acid (10a)

crude



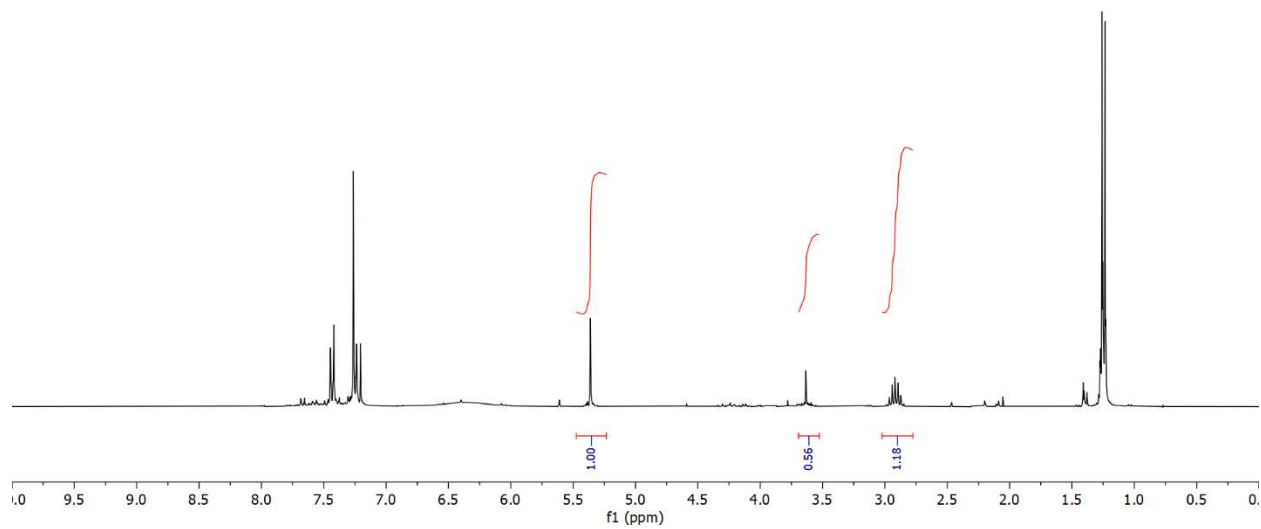
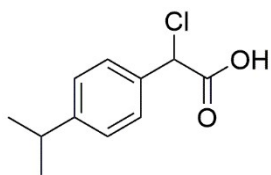
purified



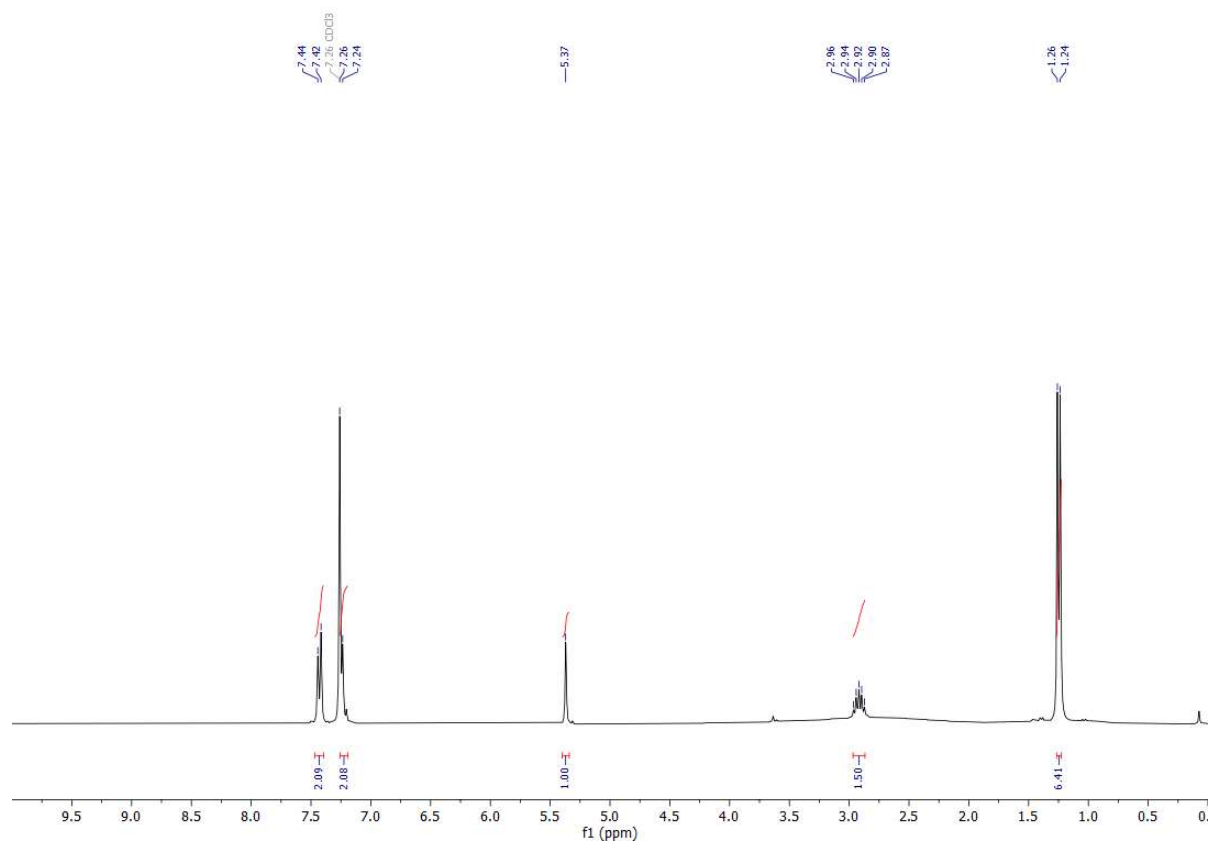


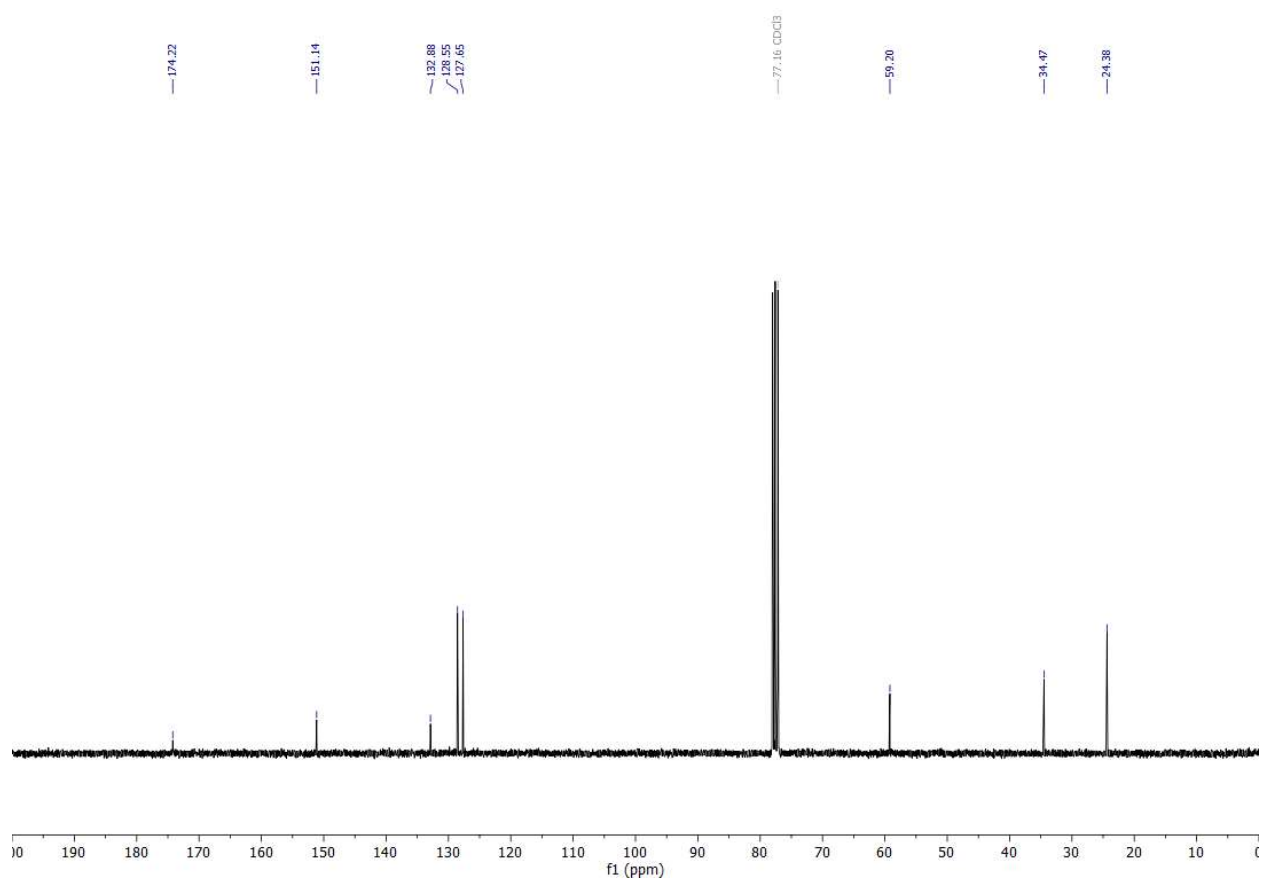
2-Chloro-2-(4-isopropylphenyl)acetic acid (11a)

crude



purified





CM_46 33 (0.674) AM2 (Ar,40000.0,0.00,0.00); Cm (20:50)

1: TOF MS ES-
1.15e7

