Electronic supporting information

Iridium catalyzed C2 site-selective methylation of indoles using pivaloyl directing group through weak chelation-assistance

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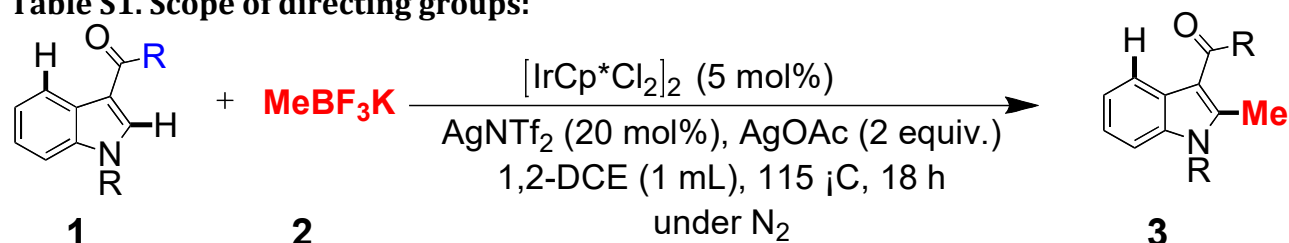
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1. General information

All the catalytic reactions were conducted under nitrogen atmosphere using standard Schlenk technique. The solvents and chemicals were purchased from Aldrich (Germany) and Chemtronica (Sweden). All glassware was dried overnight at 120 °C and if needed flame dried further. Column chromatography was performed on silica gel (Carlo Erba, 60Å). Thin layer chromatography was performed on silica gel precoated on aluminum foil containing a fluorescence indicator (254 nm). Preparative thin layer chromatography was performed on plates from Aldrich (Analtech, UV_{254} 20×20 cm, 500 micron). Yields refer to isolated compounds, and ^1H NMR was used to determine their purity. Nuclear magnetic resonance (NMR) spectroscopy was performed at 400 MHz (^1H NMR), 101 MHz (^{13}C NMR), and 376 MHz (^{19}F NMR) on a Bruker Ascend 400 instrument. Chemical shifts (δ) are provided in ppm and spectra referenced to non-deuterated solvent signals. Mass spectra (HRMS) were obtained from Lund University Kemi Centrum Mass Spectrometry facility. Instrument: Waters XEVO-G2 QTOF. ESI+: Capillary voltage 3 kV, Cone voltage 35V, Ext 4, Source Temp 120, Des Temp 300, Cone gas 50, Des gas 400. Continuum resolution mode, m/z 100-1200, manual lock mass correction using Leucine Enkephalin (m/z 556.2771).

N-Methylation and benzylation of indoles and installation of directing groups were preformed following our previously described procedure.[1] Indoles **1a-u**,[1] **v-w**,[2] **A-C**,[1] **D-E**,[3] **F**,[1] **G**[4] were prepared according to the literature. $MeBF_3K$, $Me(BO)_3$, and $MeB(OH)_2$ were commercially available and purchased from Merck and Chemtronica.

Table S1. Scope of directing groups:

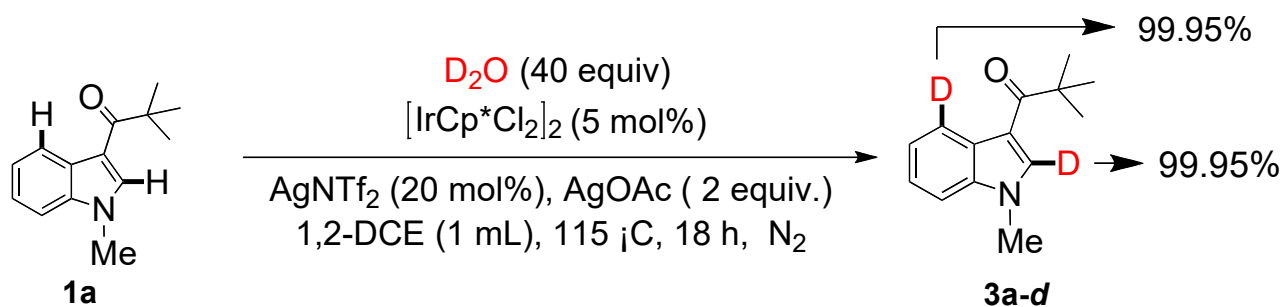| S. No	Indole		Yield (3) (NR = No reaction)
1	*N-methyl-3-pivaloyl indole* (C(O)tBu, N-Me)	**1a**	89%
2	acetyl (C(O)CH₃, N-Me)	**A**	Trace
3	aldehyde (C(O)H, N-Me)	**B**	NR
4	adamantanoyl (C(O)-bicyclic, N-Me)	**C**	NR
5	carboxylic acid (C(O)OH, N-Me)	**D**	NR
6	amide (C(O)NEt₂, N-Me)	**E**	NR
7	ester (C(O)OEt, N-Me)	**F**	NR
8	N-pivaloyl indole	**G**	NR
9	3-methyl, N-pivaloyl indole	**H**	NR
10	3-methyl indole (N-H)	**I**	NR

Mechanistic studies

A series of isotope experiments (Scheme SI-1a-c) were conducted to study the mechanism of the iridium-catalyzed methylation reaction. The initial experiments involved H/D scrambling studies with deuterated solvents under optimized reaction conditions. In a control experiment, N-methyl-3-pivaloyl indole (1a) was treated with co-solvent D2O (40 equiv.)

without the methylation reagent, resulting in almost complete deuterium incorporation at the C2 and C4 positions in the isolated product, indicating the reversible formation of a five and six-membered iridacycle at these positions (Scheme SI-1a). However, in an additive-free experiment with D2O (20 equiv.), there was negligible H/D exchange, indicating that the additive is a key component for the reversible formation of the iridacycle, as observed during the initial optimization reactions (Scheme-SI-1b). Under optimized conditions, a study without oxidant revealed 12% leaching, as observed by deuterium incorporation at the C5, C6, and C7 positions of the arene ring, in addition to around 85% D/H scrambling at the C2 and C4 positions. This result indicates that the C5, C6, and C7 C-H bonds are also capable of undergoing considerable reversible C-H activation (Scheme-SI-1c), offering opportunities for future studies using these catalytic systems for the synthesis of metal-catalyzed undirected reactions.[5]
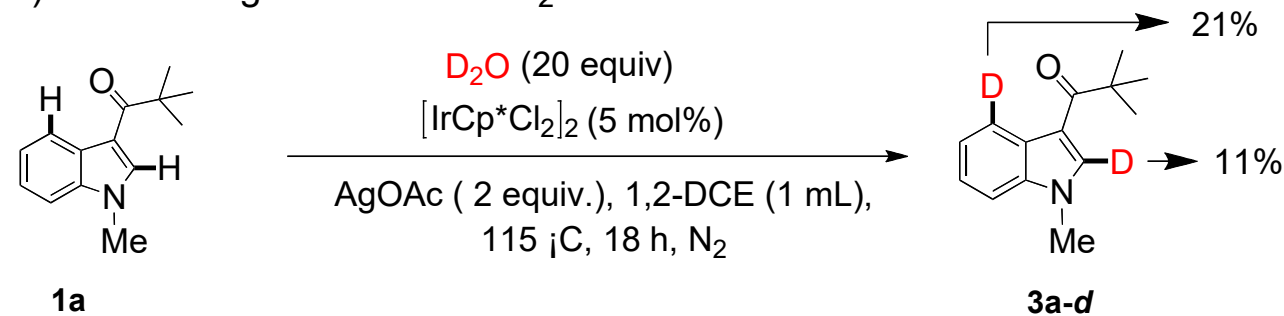
Furthermore, when the 2-protected indole (**1x**) was subjected to the methylation reactions. The isolation of unreacted starting material indicates that the reaction happens exclusively at C2 position (Scheme-SI-1d). In order to understand the working mechanism of this reaction, we performed intermolecular competition experiments with differently substituted indoles. This study showed that the electron donating group (OMe) substituted indole gave product in 52% isolated yield by having higher reactivity than electron withdrawing group substituted (COOMe) indole, which afforded only 25% product formation (Scheme-SI-1e). This result suggests that the electrophilic substitution type mechanism is could operative in this case.[6] Higher efficiency was also observed upon scale-up, with a 1 mmol scale reaction furnishing the isolated product (**3a**) in 94% yield, 0.200 g of product (Scheme-SI-1f).

a) H/D exhange studies with D_2O under standard reaction conditions

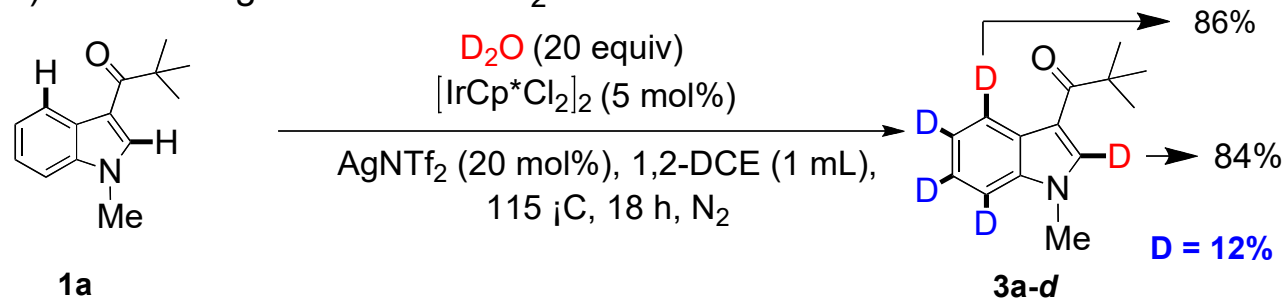Reagents above arrow: D_2O (40 equiv), $[IrCp*Cl_2]_2$ (5 mol%), AgNTf$_2$ (20 mol%), AgOAc (2 equiv.), 1,2-DCE (1 mL), 115 ¡C, 18 h, N$_2$. Starting material **1a**, product **3a-*d***, with 99.95% and 99.95% deuterium incorporation.

Scheme SI-a

b) H/D exhange studies with D$_2$O without additive

1a

Scheme SI-b

D$_2$O (20 equiv)
[IrCp*Cl$_2$]$_2$ (5 mol%)

AgOAc (2 equiv.), 1,2-DCE (1 mL),
115 ¡C, 18 h, N$_2$

21%

11%

3a-*d*

c) H/D exhange studies with D$_2$O without oxidant

1a

Scheme SI-c

D$_2$O (20 equiv)
[IrCp*Cl$_2$]$_2$ (5 mol%)

AgNTf$_2$ (20 mol%), 1,2-DCE (1 mL),
115 ¡C, 18 h, N$_2$

86%

84%

D = 12%

3a-*d*

d) Methylataion studies with C2 protected indole derivative

1x

MeBF$_3$K
[IrCp*Cl$_2$]$_2$ (5 mol%)

AgNTf$_2$ (20 mol%), AgOAc (2 equiv.)
1,2-DCE (1 mL), 115 ¡C, 18 h, N$_2$

3x
No reaction
Starting material recovered

e) Competition study

R = 6-OMe, **1k**
R = 6-COOMe, **1l**

Scheme SI a-e

MeBF$_3$K
[IrCp*Cl$_2$]$_2$ (5 mol%)

AgNTf$_2$ (20 mol%), AgOAc (2 equiv.)
1,2-DCE (1 mL), 115 ¡C, 18 h, N$_2$

R = 6-OMe, **3k**, 52%
R = 6-COOMe, **3l**, 25%

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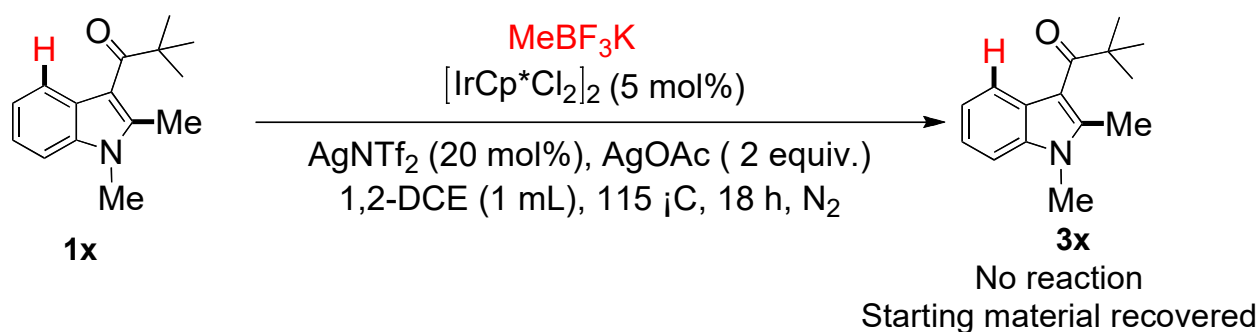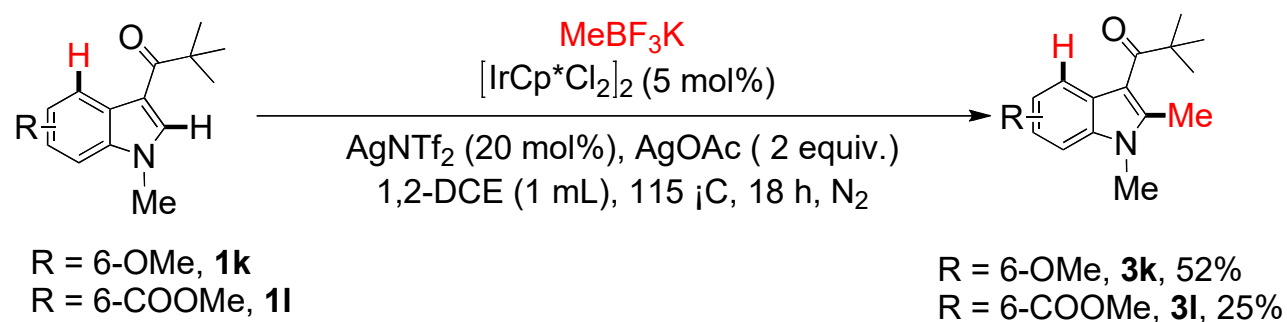
Procedure for mechanistic studies
In a 10 mL screw cap reaction tube, pivaloyl indole (1 equiv.), potassium trifluoromethylborate (5 equiv.), AgNTf$_2$ (20 mol%), Ir(III) catalyst (5 mol%), and silver acetate (2 equiv.) were added together. Then the reaction tube was evacuated and filled with nitrogen (three times). 1,2-dicloroethane (1 mL) and D2O (40 equiv) was added under nitrogen to the reaction mixture and then allowed to warm to 115 °C for 23h. Then the tube was cooled down to room temperature and filtered through celite by washing with acetone (30 mL) and the resulting crude reaction mixture was evaporated under reduced pressure. Then the residue was subjected to preparative thin layer chromatography.
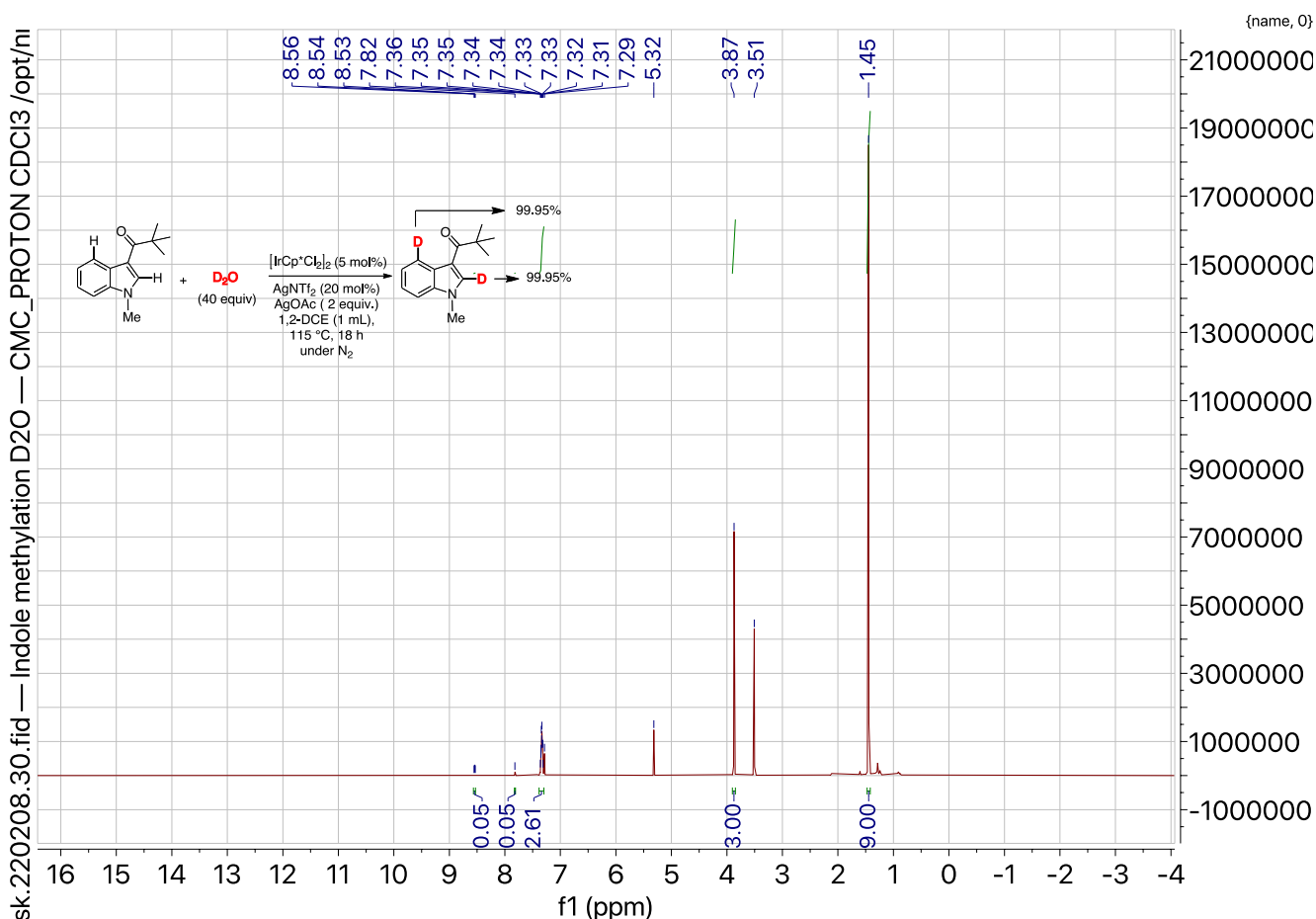

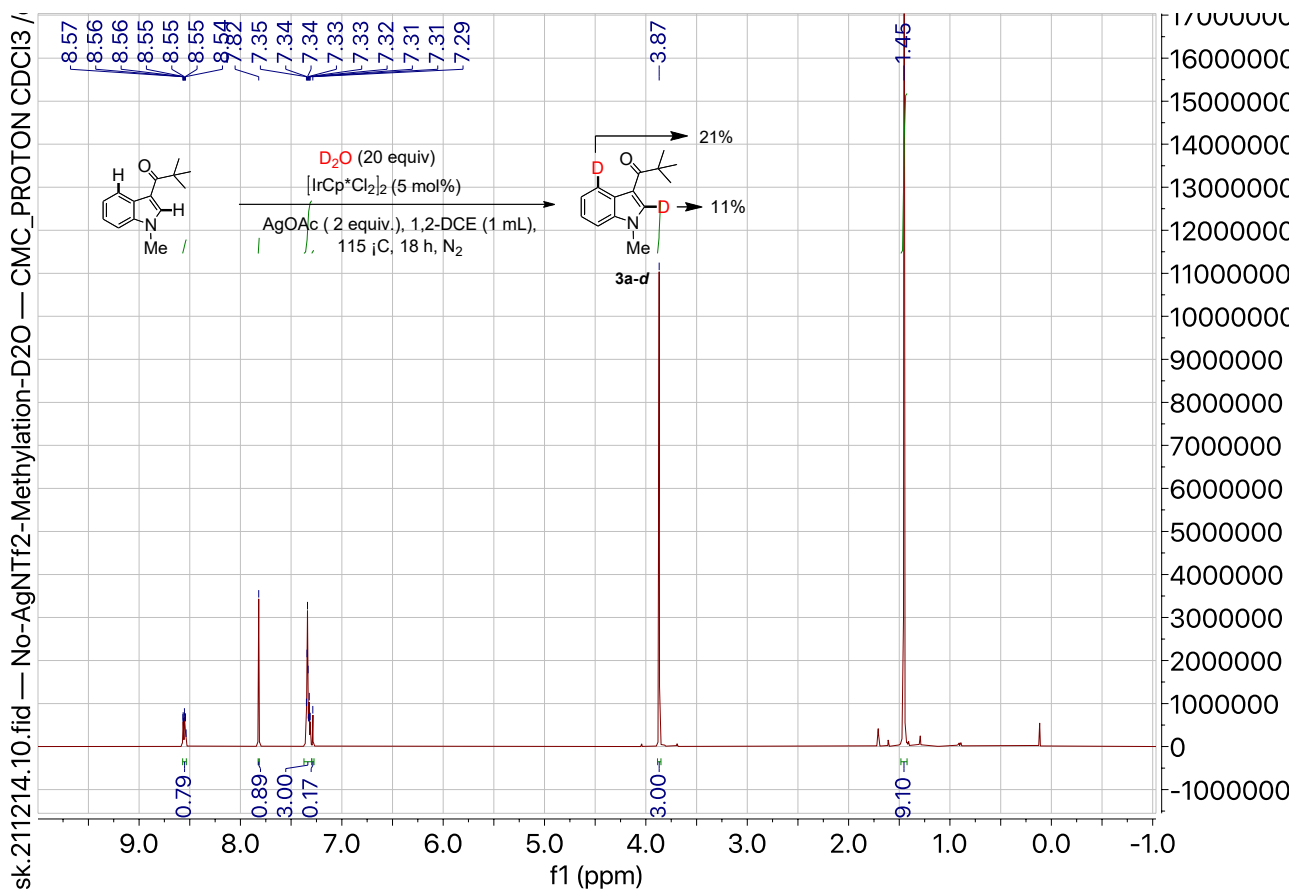Fig S1 – Deuterium studies under optimized conditions

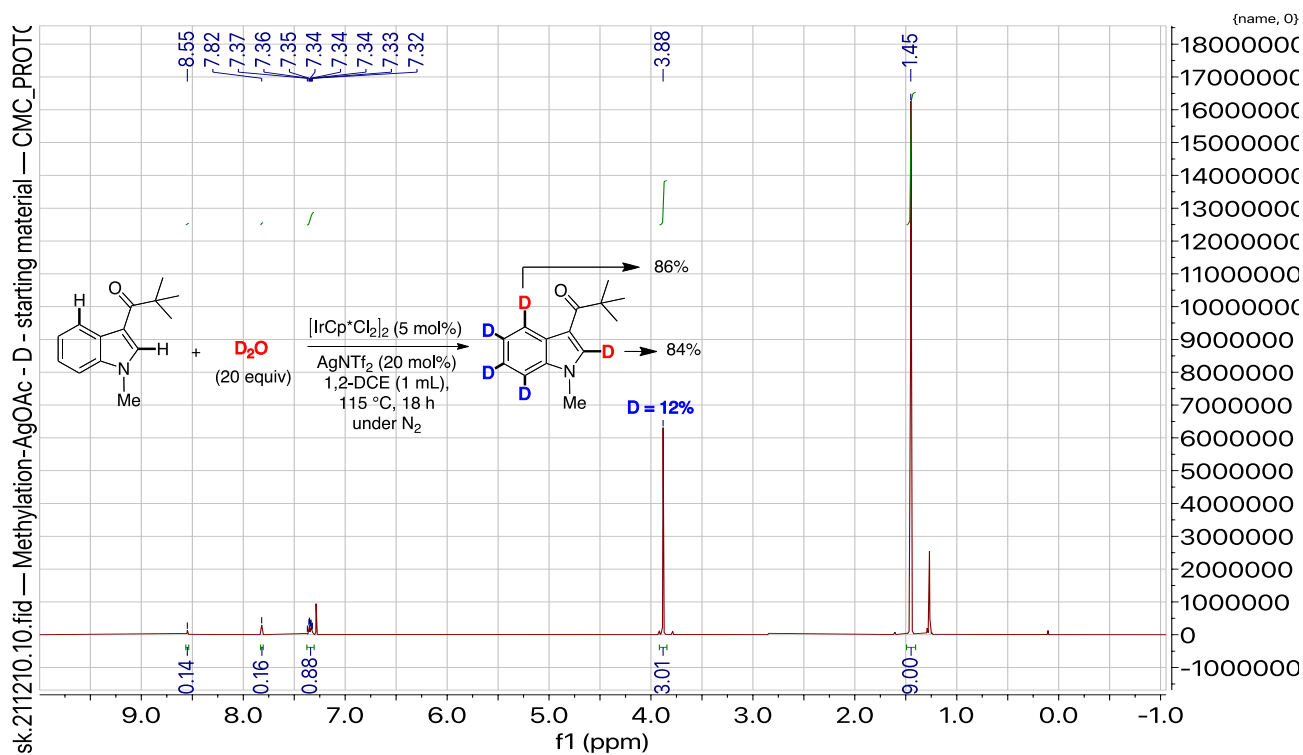**Fig S2** – Deuterium studies under optimized conditions without additive
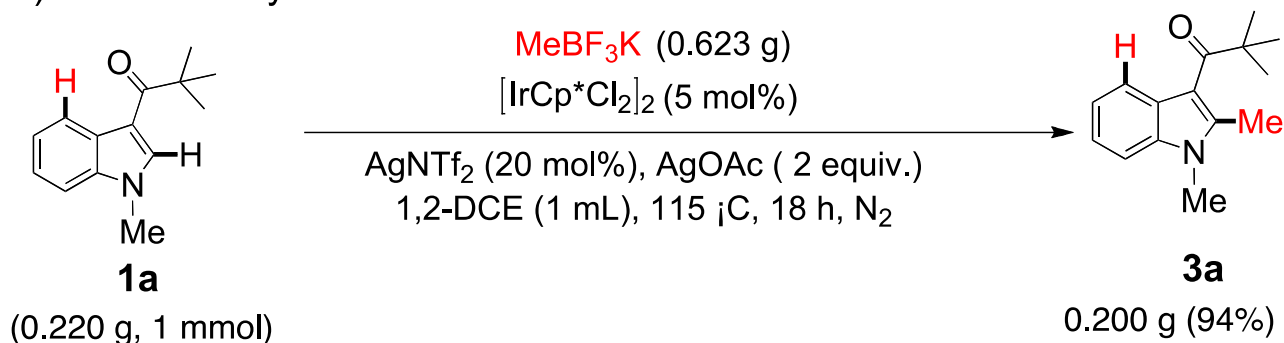

Fig S3 – Deuterium studies under optimized conditions without oxidant

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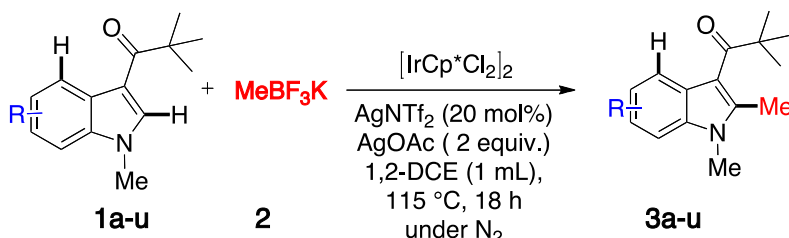## General procedure for the C-H methylation of indole – 1mmol scales

f) 1 mmol study

1a
(0.220 g, 1 mmol)

MeBF$_3$K (0.623 g)
[IrCp*Cl$_2$]$_2$ (5 mol%)

AgNTf$_2$ (20 mol%), AgOAc (2 equiv.)
1,2-DCE (1 mL), 115 ℃, 18 h, N$_2$

3a
0.200 g (94%)

Scheme SI-f

In an 50 mL screw cap reaction tube, pivaloyl indole (0.22 g, 1 mmol, 1 equiv.), potassium methyltrifluoroborate (0.623 g, 5 equiv.), AgNTf$_2$ (0.038g, 20 mol%), Ir(III) catalyst (0.0178g, 2.5 mol%), and silver acetate (0.33g, 2 equiv.) were added together. Then the reaction tube was evacuated and filled with nitrogen (three times). 1,2-dicloroethane (4 mL) was added under nitrogen to the reaction mixture and then allowed to warm to 115 °C for 24 h. Then the tube was cooled down to room temperature and filtered through celite by washing with acetone (30 mL) and the resulting crude reaction mixture was evaporated under reduced pressure. Then the residue was subjected to column chromatography using petroleum ether and acetone as an eluent (90:10 mL).

General procedure for the C-H methylation of indole

1a-u   **2**

[IrCp*Cl$_2$]$_2$
AgNTf$_2$ (20 mol%)
AgOAc (2 equiv.)
1,2-DCE (1 mL),
115 °C, 18 h
under N$_2$

3a-u

In an 10 mL screw cap reaction tube, pivaloyl indole (1 equiv.), potassium trifluoromethylborate (5 equiv.), AgNTf2 (20 mol%), Ir(III) catalyst (5 mol%), and silver acetate (2 equiv.) were added together. Then the reaction tube was evacuated and filled with nitrogen (three times). 1,2-dicloroethane (1 mL) was added under nitrogen to the reaction mixture and then allowed to warm to 115 °C for 23h. Then the tube was cooled down to room temperature and filtered through celite by washing with acetone (30 mL) and the resulting crude reaction mixture was evaporated under reduced pressure. Then the residue was subjected to preparative thin layer chromatography.

4. NMR data

1-(1,2-dimethyl-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3a)
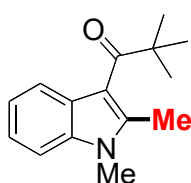
General procedure was followed using **1a** (50 mg, 23 mmol, 1.0 equiv.), **2** (140 mg, 1.15 mmol, 5 equiv.), AgNTf$_2$ (15 mg, 20 mol%), [IrCp*Cl$_2$]$_2$ (8.2 mg, 5 mol%), AgOAc (76 mg, 0.46 mmol, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3a** (47 mg, 89%). M. pt – 61-63°C; Yellow solid; **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.72 – 7.67 (m, 1H),

7.33 – 7.28 (m, 1H), 7.25 – 7.16 (m, 2H), 3.70 (s, 3H), 2.51 (s, 3H), 1.41 (s, 9H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 209.41, 140.0, 136.2, 125.3, 121.3, 121.1, 120.4, 115.1, 109.2, 44.5, 29.5, 27.4, 12.3. **HRMS (ESI):** Exact mass calculated for C$_{15}$H$_{19}$NO [M+H]$^+$: 230.1547, found: 230.1545
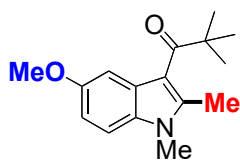
1-(1,2-dimethyl-5-methoxy-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3b)

General procedure was followed using **1b** (57 mg, 23 mmol, 1.0 equiv.), **2** (140 mg, 1.15 mmol, 5 equiv.), AgNTf$_2$ (15 mg, 20 mol%), [IrCp*Cl$_2$]$_2$ (8.2 mg, 5 mol%), AgOAc (76 mg, 0.46 mmol, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3b** (23 mg, 39%). Yellow solid.
M. pt – 111-113 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.18 (d, *J* = 2.2 Hz, 1H), 6.88 (dd, *J* = 8.8, 2.5 Hz, 1H), 3.88 (s, 3H), 3.67 (s, 3H), 2.50 (s, 3H), 1.40 (s, 9H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 208.8, 154.6, 140.7, 131.6, 125.7, 114.8, 110.5, 109.7, 104.3, 55.9, 44.4, 29.7, 27.4, 12.6. **HRMS (ESI):** Exact mass calculated for C$_{16}$H$_{21}$NO$_2$ [M+H]$^+$: 260.1653, found: 260.1651
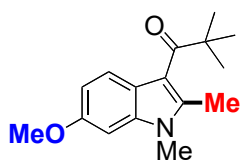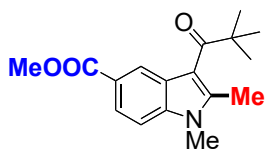
1-(1,2-dimethyl-6-methoxy-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3c)

General procedure was followed using **1c** (57 mg, 23 mmol, 1.0 equiv.), **2** (140 mg, 1.15 mmol, 5 equiv.), AgNTf$_2$ (15 mg, 20 mol%), [IrCp*Cl$_2$]$_2$ (8.2 mg, 5 mol%), AgOAc (76 mg, 0.46 mmol, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3c** (18 mg, 31%). Yellow solid. M. Pt – 90-94°C. **^{1}H NMR (400 MHz, Methanol-*d$_4$*)** δ 7.50 (d, *J* = 8.8 Hz, 1H), 6.91 (d, *J* = 2.3 Hz, 1H), 6.80 (dd, *J* = 8.8, 2.4 Hz, 1H), 3.87 (s, 3H), 3.67 (s, 3H), 2.44 (s, 3H), 1.35 (s, 9H). **^{13}C NMR (101 MHz, MeOD)** δ 210.4, 156.1, 139.6, 137.3, 121.1, 119.2, 114.2, 109.7, 92.9, 43.9, 28.5, 26.4, 11.0. **HRMS (ESI):** Exact mass calculated for C$_{16}$H$_{21}$NO [M+H]$^+$: 260.1654, found: 260.1651

1-(1,2-dimethyl-5-methylcarboxylate-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3d)

General procedure was followed using **1d** (65 mg, 23 mmol, 1.0 equiv.), **2** (140 mg, 1.15 mmol, 5 equiv.), AgNTf$_2$ (15 mg, 20 mol%), [IrCp*Cl$_2$]$_2$ (8.2 mg, 5 mol%), AgOAc (76 mg, 0.46 mmol, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3d** (54 mg, 82%). Colorless solid. M. Pt – 125-126°C. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.38 (d, *J* = 1.6 Hz, 1H), 7.91 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.28 (d, *J* = 8.7 Hz, 1H), 3.94 (s, 3H), 3.70 (s, 3H), 2.46 (s, 3H), 1.38 (s, 9H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 209.7, 167.9, 140.1, 138.6, 125.0, 123.4, 122.8, 122.3, 116.1, 108.8, 51.9, 44.8, 29.8, 27.3, 12.2. **HRMS (ESI):** Exact mass calculated for C$_{17}$H$_{21}$N$_2$O$_3$ [M+H]$^+$: 288.1599, found: 288.1600
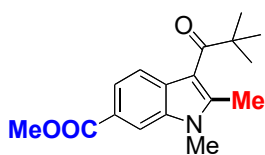
1-(1,2-dimethyl-6-methylcarboxylate-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3e)

General procedure was followed using **1e** (65 mg, 23 mmol, 1.0 equiv.), **2** (140 mg, 1.15 mmol, 5 equiv.), AgNTf$_2$ (15 mg, 20 mol%), [IrCp*Cl$_2$]$_2$ (8.2 mg, 5 mol%), AgOAc (76 mg, 0.46 mmol, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3e** (40 mg, 60%). Green solid. M. Pt – 117-117°C. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.07 – 8.05 (m, 1H), 7.85 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.64 (d, *J* = 8.5 Hz, 1H), 3.96 (s, 3H), 3.77 (s, 3H), 2.50 (s, 3H), 1.37 (s, 9H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 209.5, 167.8, 142.5, 135.6, 128.8, 122.9, 121.5, 120.3, 115.5, 111.4, 52.0, 44.7, 29.8, 27.3, 12.4. HRMS (ESI): Exact mass calculated for C$_{17}$H$_{21}$N$_2$O$_3$ [M+H]$^+$: 288.1599, found: 288.1600

1-(1,2-dimethyl-5-nitro-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3f)

General procedure was followed using **1f** (60 mg, 23 mmol, 1.0 equiv.), **2** (140 mg, 1.15 mmol, 5 equiv.), AgNTf$_2$ (15 mg, 20 mol%), [IrCp*Cl$_2$]$_2$ (8.2 mg, 5 mol%), AgOAc (76 mg, 0.46 mmol, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3f** (40 mg, 60%). Yellow solid. M. Pt – 138-142°C. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.54 (d, *J* = 2.2 Hz, 1H), 8.10 (dd, *J* = 9.1, 2.2 Hz, 1H), 7.33 (d, *J* = 9.1 Hz, 1H), 3.76 (s, 3H), 2.48 (s, 3H), 1.37 (s, 9H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 209.2, 142.1, 141.4, 138.9, 124.7, 117.4, 117.0, 116.9, 109.0, 45.0, 30.2, 27.3, 12.4. **HRMS (ESI):** Exact mass calculated for C$_{15}$H$_{18}$N$_2$O$_3$ [M+H]$^+$: 275.1392, found: 275.1396
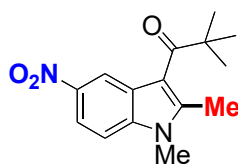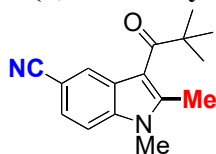
1-(1,2-dimethyl-5-cyano-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3g)

General procedure was followed using **1g** (56 mg, 23 mmol, 1.0 equiv.), **2** (140 mg, 1.15 mmol, 5 equiv.), AgNTf$_2$ (15 mg, 20 mol%), [IrCp*Cl$_2$]$_2$ (8.2 mg, 5 mol%), AgOAc (76 mg, 0.46 mmol, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3g** (17 mg, 30%). Colorless solid. M. Pt – 103-109 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.92 (d, *J* = 1.1 Hz, 1H), 7.45 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.36 (dd, *J* = 8.5, 0.7 Hz, 1H), 3.74 (s, 3H), 2.48 (s, 3H), 1.35 (s, 9H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 209.3, 140.7, 137.7, 125.8, 125.2, 124.5, 120.5, 115.7, 110.0, 103.5, 29.9, 27.3, 12.3. **HRMS (ESI):** Exact mass calculated for C$_{16}$H$_{18}$N$_2$O$_2$ [M+H]$^+$: 255.1497, found: 255.1497

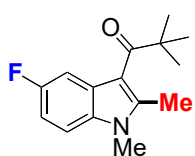## 1-(1,2-dimethyl-5-fluoro-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3h)

General procedure was followed using **1h** (55 mg, 23 mmol, 1.0 equiv.), **2** (140 mg, 1.15 mmol, 5 equiv.), AgNTf$_2$ (15 mg, 20 mol%), [IrCp*Cl$_2$]$_2$ (8.2 mg, 5 mol%), AgOAc (76 mg, 0.46 mmol, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3h** (43 mg, 78%). Yellow solid M. pt –74-77 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.35 (dd, *J* = 10.4, 2.5 Hz, 1H), 7.20 (dd, *J* = 8.9, 4.5 Hz, 1H), 6.95 (td, *J* = 9.0, 2.5 Hz, 1H), 3.68 (s, 3H), 2.49 (s, 3H), 1.38 (s, 9H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 208.7, 159.4, 157.1, 141.7, 132.8, 125.5, 125.4, 115.1, 109.8, 109.7, 109.5, 109.2, 106.5, 106.3, 44.4, 29.8, 27.3, 12.6. **^{19}F NMR (376 MHz, CDCl$_3$)** δ -123.17, -123.18, -123.19, -123.19, -123.20, -123.22, -123.23. **HRMS (ESI):** Exact mass calculated for C$_{15}$H$_{18}$FNO [M+H]$^+$: 248.1450, found: 248.1451.

1-(1,2-dimethyl-5-chloro-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3i)

General procedure was followed using **1i** (58 mg, 23 mmol, 1.0 equiv.), **2** (140 mg, 1.15 mmol, 5 equiv.), AgNTf$_2$ (15 mg, 20 mol%), [IrCp*Cl$_2$]$_2$ (8.2 mg, 5 mol%), AgOAc (76 mg, 0.46 mmol, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3i** (37 mg, 61%). Yellow solid. M. pt –89-91 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.61 (d, *J* = 1.9 Hz, 1H), 7.23 – 7.12 (m, 2H), 3.68 (s, 3H), 2.47 (s, 3H), 1.37 (s, 9H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 209.1, 140.6, 134.6, 126.3, 126.2, 121.5, 120.3, 114.7, 110.1, 44.6, 29.7, 27.4, 12.4. **HRMS (ESI):** Exact mass calculated for C$_{15}$H$_{18}$ClNO [M+H]$^+$: 264.1154, found: 264.1155.

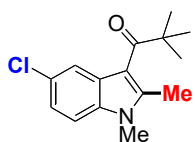## 1-(1,2-dimethyl-6-chloro-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3j)

General procedure was followed using **1j** (58 mg, 23 mmol, 1.0 equiv.), **2** (140 mg, 1.15 mmol, 5 equiv.), AgNTf$_2$ (15 mg, 20 mol%), [IrCp*Cl$_2$]$_2$ (8.2 mg,

11

5 mol%), AgOAc (76 mg, 0.46 mmol, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3j** (40 mg, 68%). Yellow solid. M.Pt – 129-133 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.52 (d, *J* = 8.6 Hz, 1H), 7.27 (d, *J* = 1.9 Hz, 1H), 7.10 (dd, *J* = 8.6, 1.9 Hz, 1H), 3.63 (s, 3H), 2.44 (s, 3H), 1.34 (s, 9H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 209.6, 140.2, 136.7, 127.3, 123.8, 121.7, 120.9, 115.0, 109.2, 44.6, 29.6, 27.3, 12.2. **HRMS (ESI):** Exact mass calculated for C$_{15}$H$_{18}$ClNO [M+H]$^+$: 264.1153, found: 264.1153.

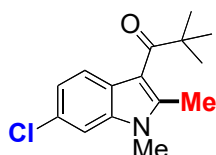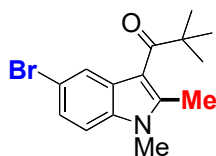### 1-(1,2-dimethyl-5-bromo-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3k)

General procedure was followed using **1k** (68 mg, 23 mmol, 1.0 equiv.), **2** (140 mg, 1.15 mmol, 5 equiv.), AgNTf$_2$ (15 mg, 20 mol%), [IrCp*Cl$_2$]$_2$ (8.2 mg, 5 mol%), AgOAc (76 mg, 0.46 mmol, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3k** (46 mg, 66%). Yellow solid. M. pt –110-113 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.75 (d, *J* = 1.8 Hz, 1H), 7.31 – 7.27 (m, 1H), 7.15 (d, *J* = 8.6 Hz, 1H), 3.67 (s, 3H), 2.47 (s, 3H), 1.37 (s, 9H).
^{13}C NMR (101 MHz, CDCl$_3$) δ 209.2, 140.3, 134.9, 126.9, 124.1, 123.3, 114.6, 113.7, 110.5, 44.6, 29.7, 27.4, 12.4. **HRMS (ESI):** Exact mass calculated for C$_{15}$H$_{18}$BrNO [M+H]$^+$: 308.0650, found: 308.0650

1-(1,2-dimethyl-5-iodo-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3l)

General procedure was followed using **1l** (80 mg, 23 mmol, 1.0 equiv.), **2** (140 mg, 1.15 mmol, 5 equiv.), AgNTf$_2$ (15 mg, 20 mol%), [IrCp*Cl$_2$]$_2$ (8.2 mg, 5 mol%), AgOAc (76 mg, 0.46 mmol, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3l** (59 mg, 72%). Brown solid. M. Pt – 133-135 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.91 (d, *J* = 1.7 Hz, 1H), 7.42 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.03 (d, *J* = 8.6 Hz, 1H), 3.63 (s, 3H), 2.43 (s, 3H), 1.33 (s, 9H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 209.7, 139.9, 135.3, 129.7, 129.4, 127.7, 114.2, 111.1, 84.0, 44.7, 29.6, 27.3, 12.3. **HRMS (ESI):** Exact mass calculated for C$_{15}$H$_{18}$INO [M+H]$^+$: 356.0503, found: 356.0500

1-(1,2-dimethyl-1,6,7,8-tetrahydrocyclopenta[*g*]-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3m)

General procedure was followed using **1m** (59 mg, 23 mmol, 1.0 equiv.), **2** (140 mg, 1.15 mmol, 5 equiv.), AgNTf$_2$ (15 mg, 20 mol%), [IrCp*Cl$_2$]$_2$ (8.2 mg, 5 mol%), AgOAc (76 mg, 0.46 mmol, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3m** (33 mg, 54%). Yellow solid. M. Pt – 147-149 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.40 (d, *J* = 8.1 Hz, 1H), 7.05 (d, *J* = 8.1 Hz, 1H), 3.87 (s, 3H), 3.41 (t, *J* = 7.4 Hz, 2H), 3.03 (t, *J* = 7.5 Hz, 2H), 2.42 (s, 3H), 2.21 (p, *J* = 7.5 Hz, 2H), 1.37 (s, 9H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 210.7, 138.6, 137.6, 133.6, 124.8, 124.4, 119.1, 117.1, 115.8, 44.7, 32.5, 31.9, 31.6, 27.5, 25.4, 12.2. **HRMS (ESI):** Exact mass calculated for C$_{18}$H$_{23}$NO [M+H]$^+$: 270.1860, found: 270.1858.

1-(1,2-dimethyl-7-bromo-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3n)
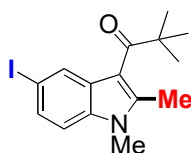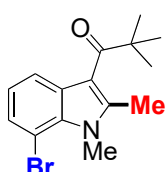
General procedure was followed using **1n** (68 mg, 23 mmol, 1.0 equiv.), **2** (140 mg, 1.15 mmol, 5 equiv.), AgNTf$_2$ (15 mg, 20 mol%), [IrCp*Cl$_2$]$_2$ (8.2 mg, 5 mol%), AgOAc (76 mg, 0.46 mmol, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3n** (51 mg, 73%).

Yellow solid. M. Pt – 67-70 °C. **¹H NMR (400 MHz, Chloroform-*d*)** δ 7.42 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.34 (dd, *J* = 7.7, 1.0 Hz, 1H), 6.94 (t, *J* = 7.8 Hz, 1H), 4.09 (s, 3H), 2.39 (s, 3H), 1.32 (s, 9H). **¹³C NMR (101 MHz, CDCl₃)** δ 211.3, 138.0, 132.6, 128.7, 126.9, 121.0, 119.6, 115.9, 103.5, 45.3, 32.6, 27.4, 12.6. **HRMS (ESI):** Exact mass calculated for $C_{15}H_{18}BrNO$ [M+H]⁺: 308.0648, found: 308.0650
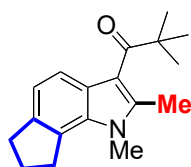
1-(1,2-dimethyl-7-methyl-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3o)

General procedure was followed using **1o** (54 mg, 23 mmol, 1.0 equiv.), **2** (140 mg, 1.15 mmol, 5 equiv.), AgNTf₂ (15 mg, 20 mol%), [IrCp*Cl₂]₂ (8.2 mg, 5 mol%), AgOAc (76 mg, 0.46 mmol, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3o** (35mg, 63%). Brown solid. M. Pt – 121-126 °C. **¹H NMR (400 MHz, Chloroform-*d*)** δ 7.39 (d, *J* = 8.0 Hz, 1H), 7.03 – 6.97 (m, 1H), 6.92 – 6.88 (m, 1H), 3.96 (s, 3H), 2.80 (s, 3H), 2.40 (s, 3H), 1.35 (s, 9H). **¹³C NMR (101 MHz, CDCl₃)** δ 211.4, 137.4, 135.0, 126.3, 124.6, 120.6, 120.1, 118.7, 115.9, 45.0, 32.7, 28.1, 27.4, 20.5, 12.4. **HRMS (ESI):** Exact mass calculated for $C_{16}H_{21}NO$ [M+H]⁺: 244.1703, found: 244.1701

1-(1-ethyl-2-methyl-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3p)
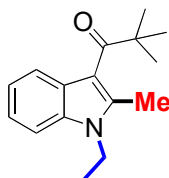
General procedure was followed using **1p** (54 mg, 23 mmol, 1.0 equiv.), **2** (140 mg, 1.15 mmol, 5 equiv.), AgNTf₂ (15 mg, 20 mol%), [IrCp*Cl₂]₂ (8.2 mg, 5 mol%), AgOAc (76 mg, 0.46 mmol, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3p** (54 mg, 96%). Yellow liquid. **¹H NMR (400 MHz, Chloroform-*d*)** δ 7.72 – 7.69 (m, 1H), 7.35 – 7.32 (m, 1H), 7.25 – 7.16 (m, 2H), 4.18 (q, *J* = 7.3 Hz, 2H), 2.52 (s, 2H), 1.41 (s, 9H), 1.38 (d, *J* = 7.2 Hz, 3H). **¹³C NMR (101 MHz, CDCl₃)** δ 209.4, 139.2, 135.1, 125.5, 121.2, 120.3, 115.1, 109.2, 44.5, 37.8, 27.4, 14.9, 12.1. **HRMS (ESI):** Exact mass calculated for $C_{16}H_{21}NO$ [M+H]⁺: 244.1701, found: 244.1701.

1-(1-pentyl-2-methyl-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3q)

General procedure was followed using **1q** (65 mg, 23 mmol, 1.0 equiv.), **2** (140 mg, 1.15 mmol, 5 equiv.), AgNTf₂ (15 mg, 20 mol%), [IrCp*Cl₂]₂ (8.2 mg, 5 mol%), AgOAc (76 mg, 0.46 mmol, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3q** (40 mg, 61%). Yellow liquid. **¹H NMR (400 MHz, Chloroform-*d*)** δ 7.72 – 7.68 (m, 1H), 7.34 – 7.30 (m, 1H), 7.24 – 7.14 (m, 2H), 4.14 – 4.06 (m, 2H), 2.51 (s, 3H), 1.79 (dd, *J* = 9.2, 5.9 Hz, 2H), 1.44 – 1.41 (m, 2H), 1.41 (s, 9H), 1.39 (d, *J* = 3.2 Hz, 3H), 0.94 (td, *J* = 5.6, 4.4, 2.0 Hz, 3H). **¹³C NMR (101 MHz, CDCl₃)** δ 209.4, 139.5, 135.6, 125.4, 121.2, 121.2, 120.3, 115.1, 109.4, 44.5, 43.3, 29.5, 29.1, 27.4, 22.4, 13.9, 12.3. **HRMS (ESI):** Exact mass calculated for $C_{19}H_{27}NO$ [M+H]⁺: 286.2168, found: 286.2171.
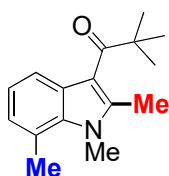
1-(1-hexyl-2-methyl-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3r)
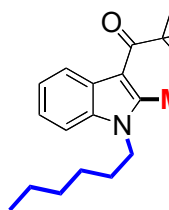
General procedure was followed using **1r** (77 mg, 27 mmol, 1.0 equiv.), **2** (140 mg, 1.15 mmol, 5 equiv.), AgNTf₂ (15 mg, 20 mol%), [IrCp*Cl₂]₂ (8.2 mg, 5 mol%), AgOAc (76 mg, 0.46 mmol, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3r** (52 mg, 84%). Yellow liquid. **¹H NMR (400 MHz, Chloroform-*d*)** δ 7.70 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.34 – 7.30 (m, 1H), 7.24 – 7.15 (m, 2H), 4.14 – 4.07 (m, 2H), 2.51 (s, 3H), 1.78 (p, *J* = 7.6 Hz, 2H), 1.42 (d, *J*

= 1.2 Hz, 2H), 1.41 (s, 9H), 1.38 – 1.29 (m, 5H), 0.92 (t, J = 6.9 Hz, 3H). **^{13}C NMR (101 MHz, CDCl$_3$) δ** 209.4, 139.5, 135.6, 125.4, 121.2, 121.2, 120.3, 115.1, 109.4, 44.5, 43.3, 31.5, 29.8, 27.4, 26.7, 22.5, 14.0, 12.3. **HRMS (ESI):** Exact mass calculated for C$_{20}$H$_{29}$NO [M+H]$^+$: 300.2322, found: 300.2327.

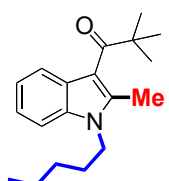## 1-(1-benzyl-2-methyl-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3s)
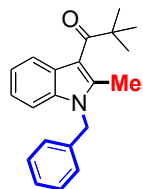
General procedure was followed using **1s** (68 mg, 23 mmol, 1.0 equiv.), **2** (140 mg, 1.15 mmol, 5 equiv.), AgNTf$_2$ (15 mg, 20 mol%), [IrCp*Cl$_2$]$_2$ (8.2 mg, 5 mol%), AgOAc (76 mg, 0.46 mmol, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3s** (39 mg, 56%). Yellow liquid.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.35 – 7.26 (m, 5H), 7.22 – 7.17 (m, 2H), 7.02 (d, J = 6.7 Hz, 2H), 5.37 (s, 2H), 2.45 (s, 3H), 1.43 (s, 9H). **^{13}C NMR (101 MHz, CDCl$_3$) δ** 209.83, 139.2, 136.8, 136.1, 128.9, 127.5, 125.9, 121.6, 121.1, 120.6, 115.7, 109.6, 46.5, 44.7, 27.4, 12.3. **HRMS (ESI):** Exact mass calculated for C$_{21}$H$_{23}$NO [M+H]$^+$: 306.1861, found: 306.1858.

1-(1-(4-methylbenzyl-2-methyl-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3t)
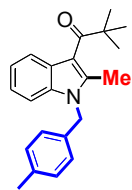
General procedure was followed using **1t** (70 mg, 23 mmol, 1.0 equiv.), **2** (140 mg, 1.15 mmol, 5 equiv.), AgNTf$_2$ (15 mg, 20 mol%), [IrCp*Cl$_2$]$_2$ (8.2 mg, 5 mol%), AgOAc (76 mg, 0.46 mmol, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3t** (54 mg, 74%). Brown liquid. **^{1}H NMR (400 MHz, Chloroform-d)** δ 7.75 – 7.69 (m, 1H), 7.27 (dt, J = 2.8, 1.4 Hz, 1H), 7.22 – 7.16 (m, 2H), 7.12 (d, J = 7.9 Hz, 3H), 6.92 (d, J = 7.7 Hz, 3H), 5.33 (s, 2H), 2.45 (s, 3H), 2.34 (s, 4H), 1.42 (s, 9H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 209.8, 139.3, 137.2, 136.1, 133.7, 129.5, 125.9, 125.6, 121.6, 121.1, 120.6, 115.6, 109.7, 46.3, 44.7, 27.4, 21.0, 12.3. **HRMS (ESI):** Exact mass calculated for C$_{22}$H$_{25}$NO [M+H]$^+$: 320.2010, found: 320.2014.

## 1-(1-(2,6-dichloro-2-methylbenzyl-4-methyl-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3u)
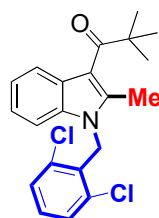
General procedure was followed using **1u** (63 mg, 23 mmol, 1.0 equiv.), **2** (140 mg, 1.15 mmol, 5 equiv.), AgNTf$_2$ (15 mg, 20 mol%), [IrCp*Cl$_2$]$_2$ (8.2 mg, 5 mol%), AgOAc (76 mg, 0.46 mmol, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3u** (44 mg, 51%).

Yellow solid. **^{1}H NMR (400 MHz, Chloroform-d)** δ 7.58 (dd, J = 8.3, 1.6 Hz, 1H), 7.36 (d, J = 7.6 Hz, 2H), 7.30 – 7.20 (m, 1H), 7.15 – 7.07 (m, 3H), 5.58 (s, 2H), 2.45 (s, 3H), 1.36 (s, 9H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 210.9, 138.6, 136.2, 135.9, 131.5, 129.8, 129.1, 125.8, 121.3, 120.7, 120.2, 116.1, 110.0, 45.0, 43.8, 27.4, 12.7. **HRMS (ESI):** Exact mass calculated for C$_{21}$H$_{21}$Cl$_2$NO [M+H]$^+$: 374.1073, found: 374.1078.

1-(1-phenyl-2-methyl-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3v)
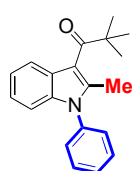
General procedure was followed using **1v** (50 mg, 18 mmol, 1.0 equiv.), **2** (100 mg, 5 equiv.), AgNTf$_2$ (20 mg, 20 mol%), [IrCp*Cl$_2$]$_2$ (7,5 mg, 5 mol%), AgOAc (60 mg, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3u** (44 mg, 85%).

Yellow liquid. **^{1}H NMR (400 MHz, Chloroform-d)** δ 7.61 (d, J = 8.0 Hz, 1H), 7.50 – 7.38 (m, 4H), 7.27 – 7.22 (m, 2H), 7.09 (ddd, J = 8.1, 7.0, 1.3 Hz, 1H), 7.05 – 7.00 (m, 1H), 6.94 (dt, J = 8.1, 1.0 Hz, 1H), 2.23 (s, 3H), 1.33 (s, 9H). **^{13}C NMR (101 MHz, CDCl$_3$) δ** 209.7, 139.6, 137.3, 136.9, 129.7, 128.5, 128.3, 125.5, 121.8, 121.0, 120.9, 116.0, 110.5, 44.7, 27.4, 13.3. **HRMS (ESI):** Exact mass calculated for C$_{20}$H$_{21}$NO [M+Na]$^+$: 314.1521, found: 314.1525.

**1-(1-(2-methoxyphenyl-2-methyl-1H-indol-3-yl)-2,2-dimethyl-1-propanone (3w)**
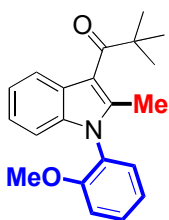
General procedure was followed using **1v** (56 mg, 16 mmol, 1.0 equiv.), **2** (97 mg, 5 equiv.), AgNTf$_2$ (12 mg, 20 mol%), [IrCp*Cl$_2$]$_2$ (6.3 mg, 5 mol%), AgOAc (53 mg, 2 equiv), 1,2-DCE (1 mL), at 115°C for 23 h. Preparative thin layer chromatography was eluted using 90 mL petroleum ether and 10 mL acetone combination yielded **3w** (28 mg, 55%).

Yellow liquid. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.72 (d, *J* = 8.0 Hz, 1H), 7.51 – 7.45 (m, 1H), 7.29 – 7.24 (m, 1H), 7.19 – 7.13 (m, 1H), 7.13 – 7.06 (m, 4H), 6.91 – 6.87 (m, 1H), 3.71 (s, 3H), 2.26 (s, 3H), 1.42 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 209.0, 156.0, 141.7, 137.3, 130.3, 130.2, 125.5, 125.3, 121.4, 121.0, 120.9, 120.7, 115.3, 112.3, 110.4, 55.6, 44.6, 27.4, 13.0. **HRMS (ESI):** Exact mass calculated for C$_{21}$H$_{23}$NO$_2$ [M+Na]$^+$: 344.1646, found: 344.1641.

Copies of spectra

3a, ^{1}H NMR, CDCl$_3$, 400 MHz
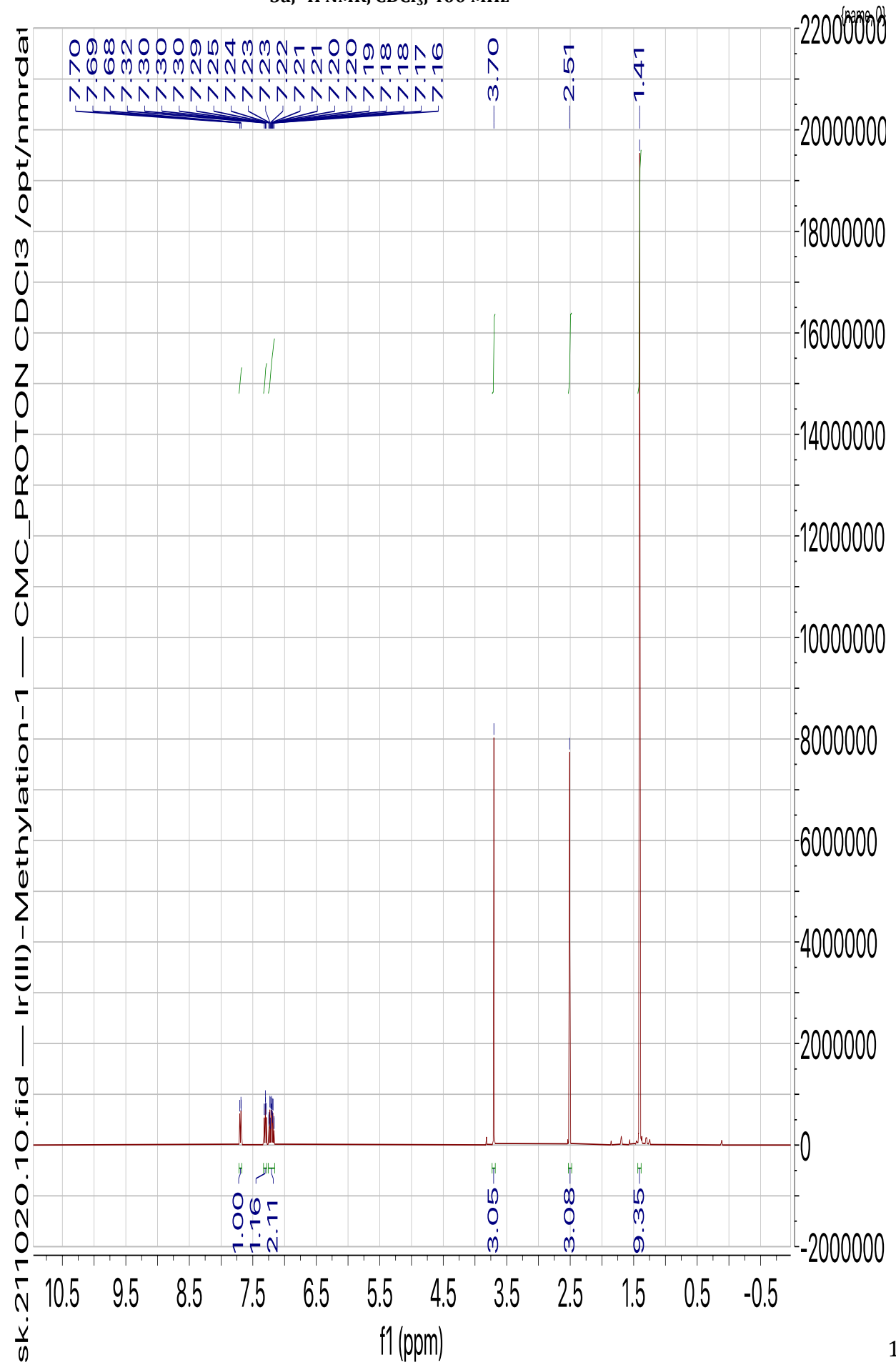
3a, ¹³C NMR (101 MHz, CDCl₃)
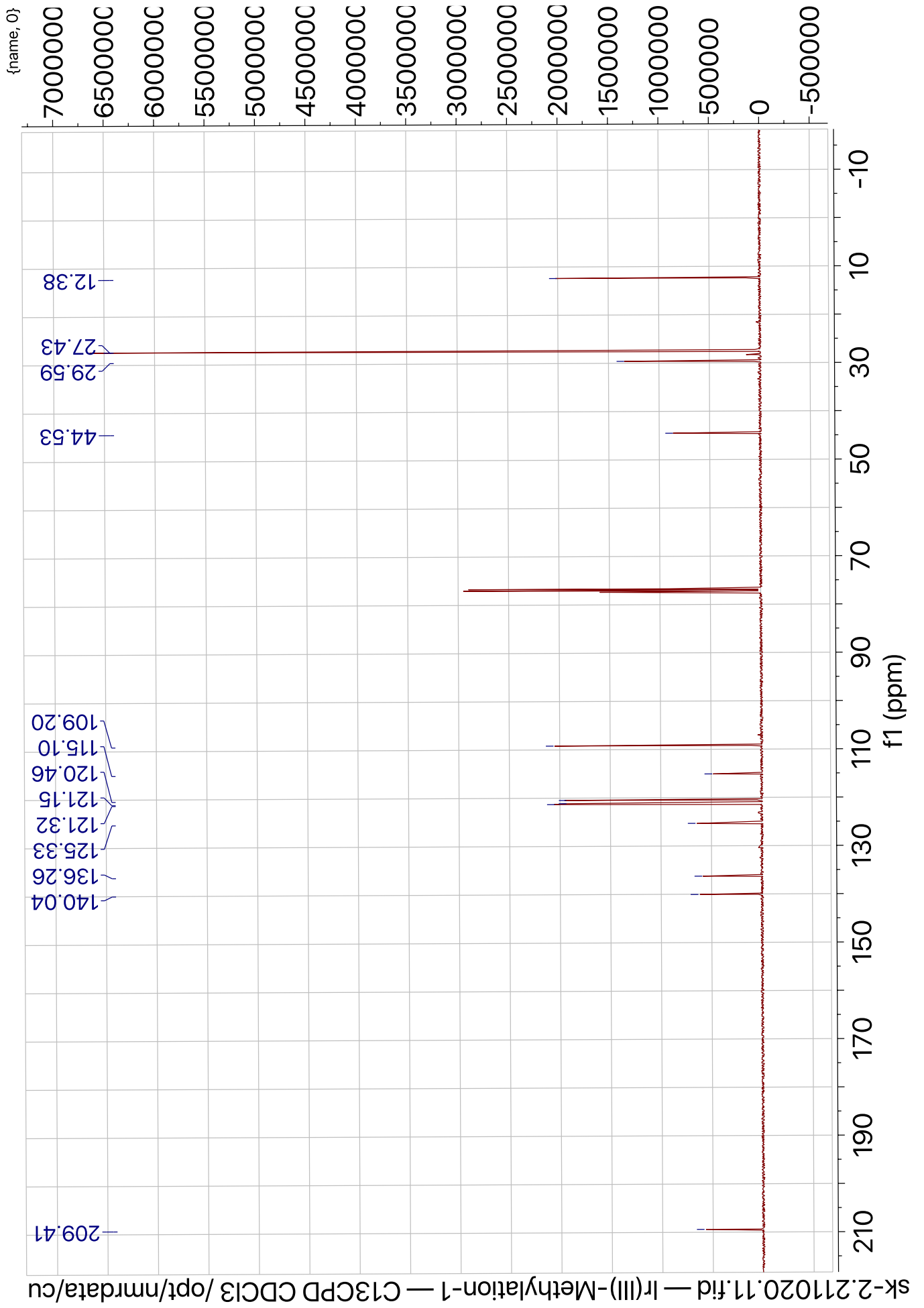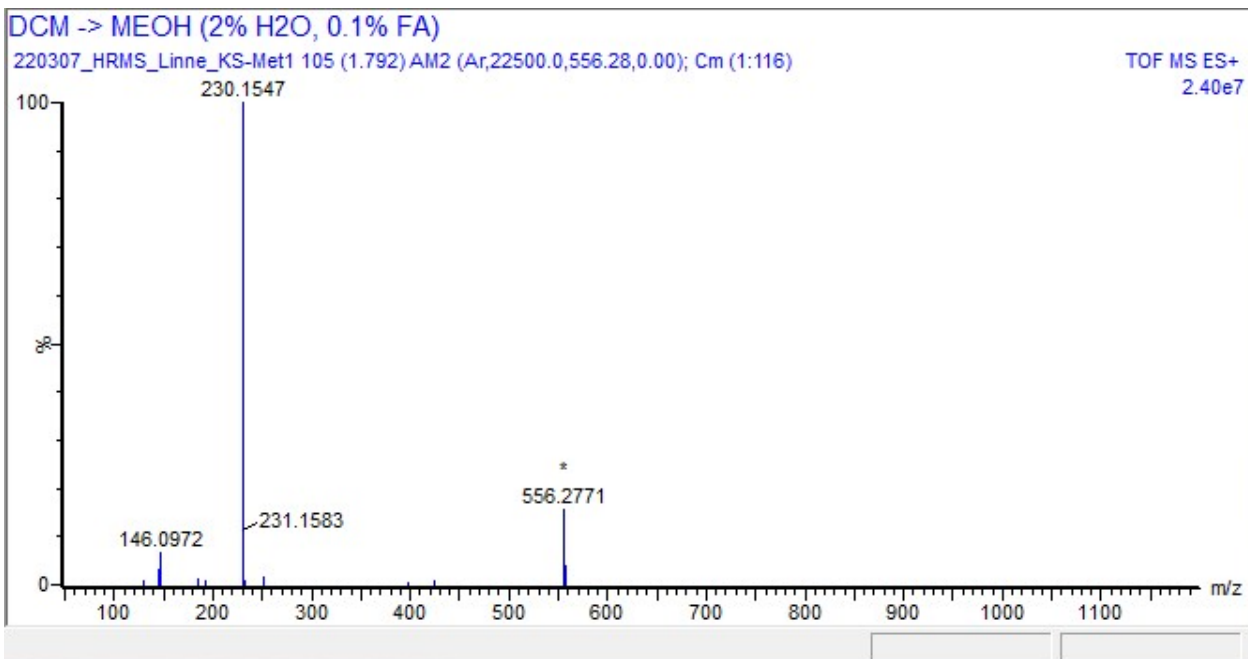
209.41
140.04
136.26
125.33
121.32
121.15
120.46
115.10
109.20
44.53
29.59
27.43
12.38

f1 (ppm)

230.1547

146.0972

231.1583

*
556.2771

Single Mass Analysis

Tolerance = 2.0 mDa / DBE: min = -1.5, max = 100.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 2

Monoisotopic Mass, Even Electron Ions

62 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 0-60   H: 0-100   N: 0-3   O: 0-4

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
230.1547	230.1545	0.2	0.9	6.5	C15 H20 N O	54.1	n/a	n/a	15	20	1	1

230.1547

231.1583

232.1620

252.1373

HRMS spectra of **3a**

3b, ^{1}H NMR, CDCl$_3$, 400 MHz

sk-7.22O1O1.4O.fid — 5-OMe/7-Br-indole methylationR — CMC_PROTON CI

Peaks: 7.29, 7.21, 7.18, 7.18, 6.89, 6.88, 6.87, 6.86, 3.88, 3.67, 2.50, 1.40

Integrals: 0.29, 0.45, 1.47, 1.00, 3.05, 2.93, 2.95, 9.00

{name, 0}

19

3b, ^{13}C NMR (101 MHz, CDCl$_3$)

sk-8.220101.41.fid — 5-OMe/7-Br-indole methylationR — C13CPD CDCl3 /o

208.89

154.62

140.79
131.63
125.79

114.82
110.54
109.71
104.31

55.94

44.40

29.72
27.42

12.65

{name, 0}

1700000
160000C
150000C
140000C
130000C
120000C
110000C
100000C
900000
800000
700000
600000
500000
400000
300000
200000
100000
0
-100000

f1 (ppm)

210 190 170 150 130 110 90 70 50 30 10 -10

220307_HRMS_Linne_KS-Met17 111 (1.894) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)   TOF MS ES+
1.23e7

100-

260.1653

%-

*
556.2771

176.1079   282.1475   557.2795

408.7165

0-

100   200   300   400   500   600   700   800   900   1000   1100   m/z

Print spectrum in landscape

Single Mass Analysis
Tolerance = 2.0 mDa   /   DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 2
Monoisotopic Mass, Even Electron Ions
183 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-60   H: 0-100   N: 0-3   O: 0-4   Cl: 0-2

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O	Cl
260.1653	260.1651	0.2	0.8	6.5	C16 H22 N O2	50.6	n/a	n/a	16	22	1	2	

DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met17 111 (1.894) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)   TOF MS ES+
1.23e+007

100-

260.1653

%-

176.1079   282.1475
177.1110   283.1516   308.0660

0-

180   200   220   240   260   280   300   320   340   360   380   m/z

HRMS spectra of **3b**

3c, ^{1}H NMR, CDCl$_3$, 400 MHz
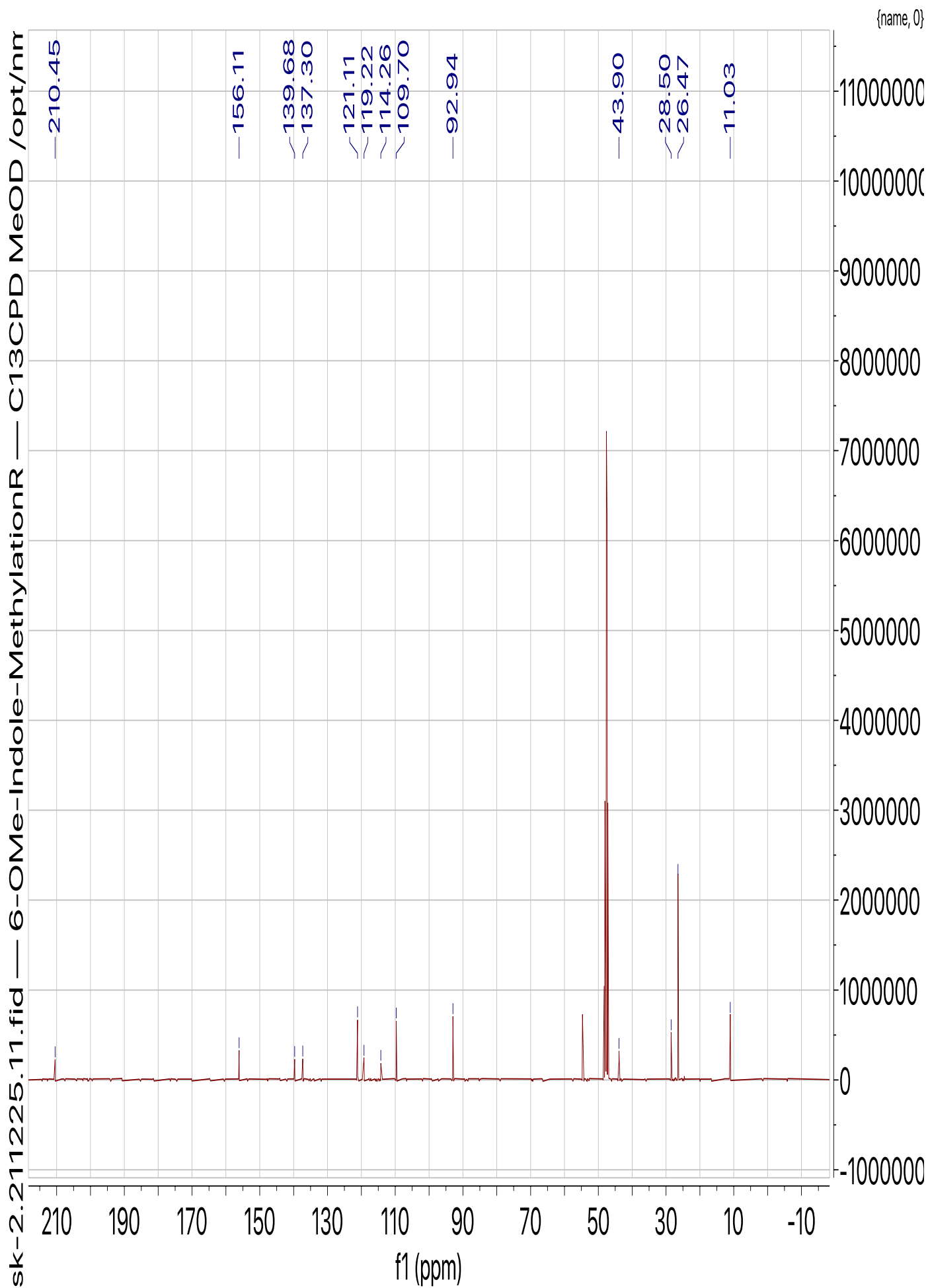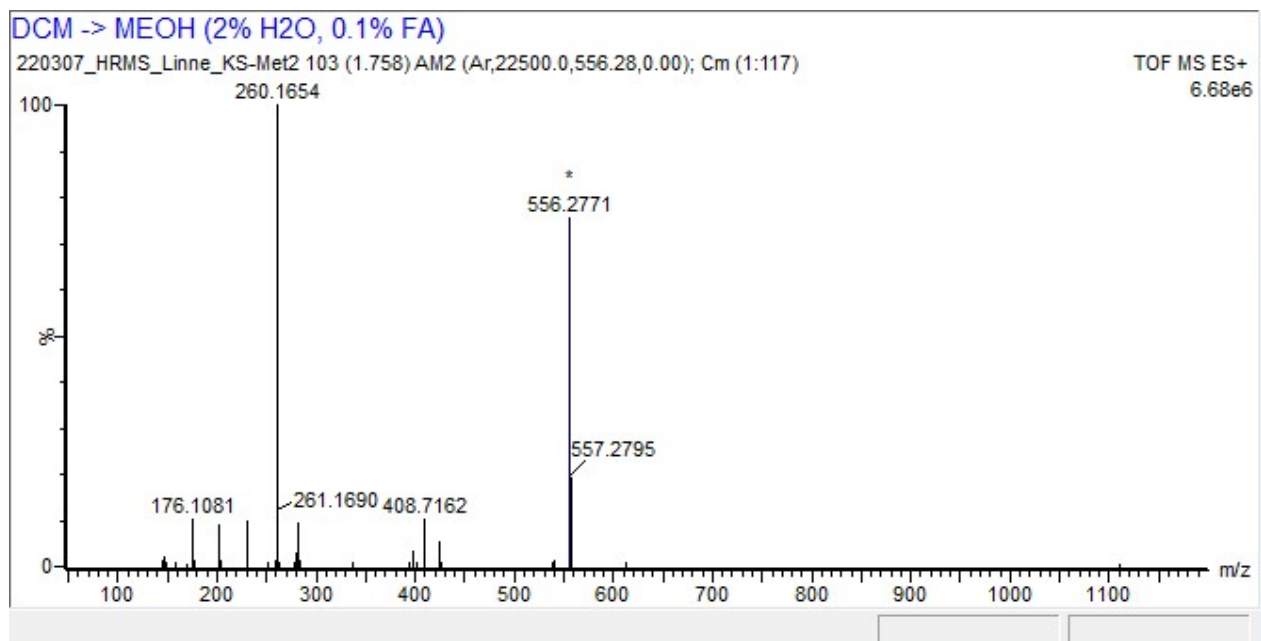
sk.211225.10.fid — 6-OMe-Indole-MethylationR — CMC_PROTON MeOD /or

{name, 0}

7.51
7.49
6.92
6.91
6.81
6.81
6.79
6.78
4.89
3.87
3.67
2.44
1.35

0.94
0.94
0.97
3.06
2.92
2.82
9.00

22

3c, ^{13}C NMR (101 MHz, CDCl$_3$)

210.45
156.11
139.68
137.30
121.11
119.22
114.26
109.70
92.94
43.90
28.50
26.47
11.03

sk-2.211225.11.fid — 6-OMe-Indole-MethylationR — C13CPD MeOD /opt/nmr

f1 (ppm)

{name, 0}

DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met2 103 (1.758) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)   TOF MS ES+
6.68e6

Single Mass Analysis
Tolerance = 2.0 mDa   /   DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 2
Monoisotopic Mass, Even Electron Ions
69 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-60   H: 0-100   N: 0-3   O: 0-4

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
260.1654	260.1651	0.3	1.2	6.5	C16 H22 N O2	47.1	n/a	n/a	16	22	1	2

DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met2 103 (1.758) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)   TOF MS ES+
6.68e+006
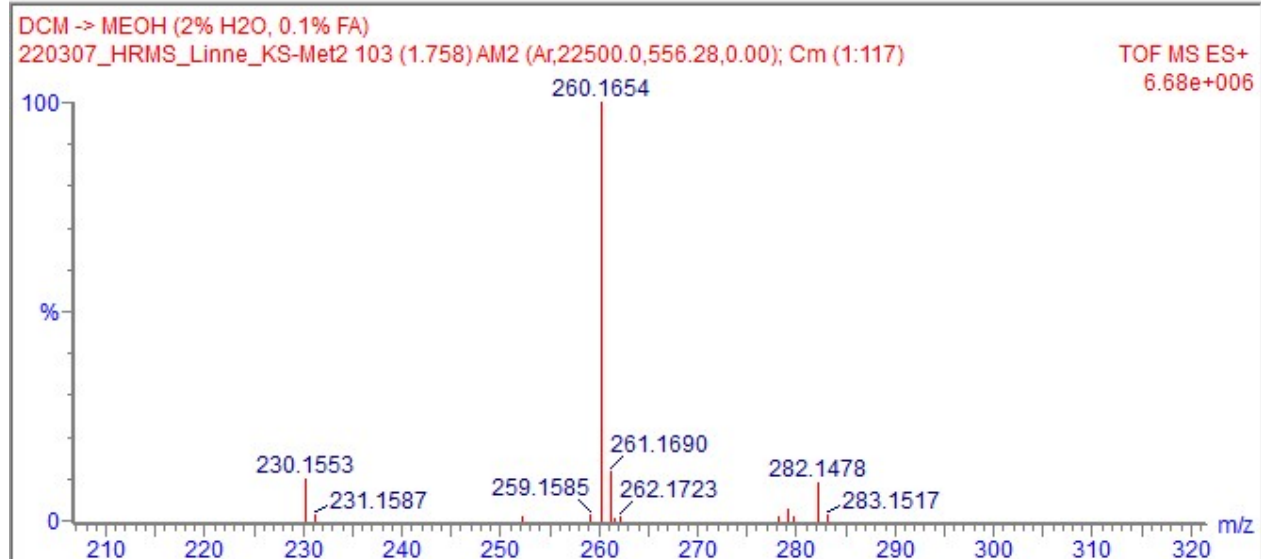
HRMS spectra of **3c**

3d, ¹H NMR, CDCl₃, 400 MHz

3d, ^{13}C NMR (101 MHz, CDCl$_3$)

sk-6.220101.31.fid — 5-COOMe-Indole methylation — C13CPD CDCl3 /opt/

{name, 0}

209.75

167.97

140.17
138.67
125.01
123.42
122.80
122.37
116.16
108.83

51.95
44.86

29.85
27.39

12.29

DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met14 102 (1.741) AM2 (Ar,22500.0,556.28,0.00); Cm (2:117)   TOF MS ES+
1.11e7

100 288.1599

* 556.2771

% 310.1421

557.2795

0

100 200 300 400 500 600 700 800 900 1000 1100   m/z

Single Mass Analysis

Tolerance = 2.0 mDa   /   DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 2
Monoisotopic Mass, Even Electron Ions
75 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-60   H: 0-100   N: 0-3   O: 0-4

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Nor...	Fit Conf %	C	H	N	O
288.1599	288.1600	-0.1	-0.3	7.5	C17 H22 N O3	50.3	n/a	n/a	17	22	1	3

DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met14 102 (1.741) AM2 (Ar,22500.0,556.28,0.00); Cm (2:117)   TOF MS ES+
1.12e+007

100 288.1599

%   289.1637   310.1421
                          290.1668   311.1458
256.1349   275.1407   336.1930
0

240 250 260 270 280 290 300 310 320 330 340   m/z

HRMS spectra of **3d**

3e, ^{1}H NMR, CDCl$_3$, 400 MHz
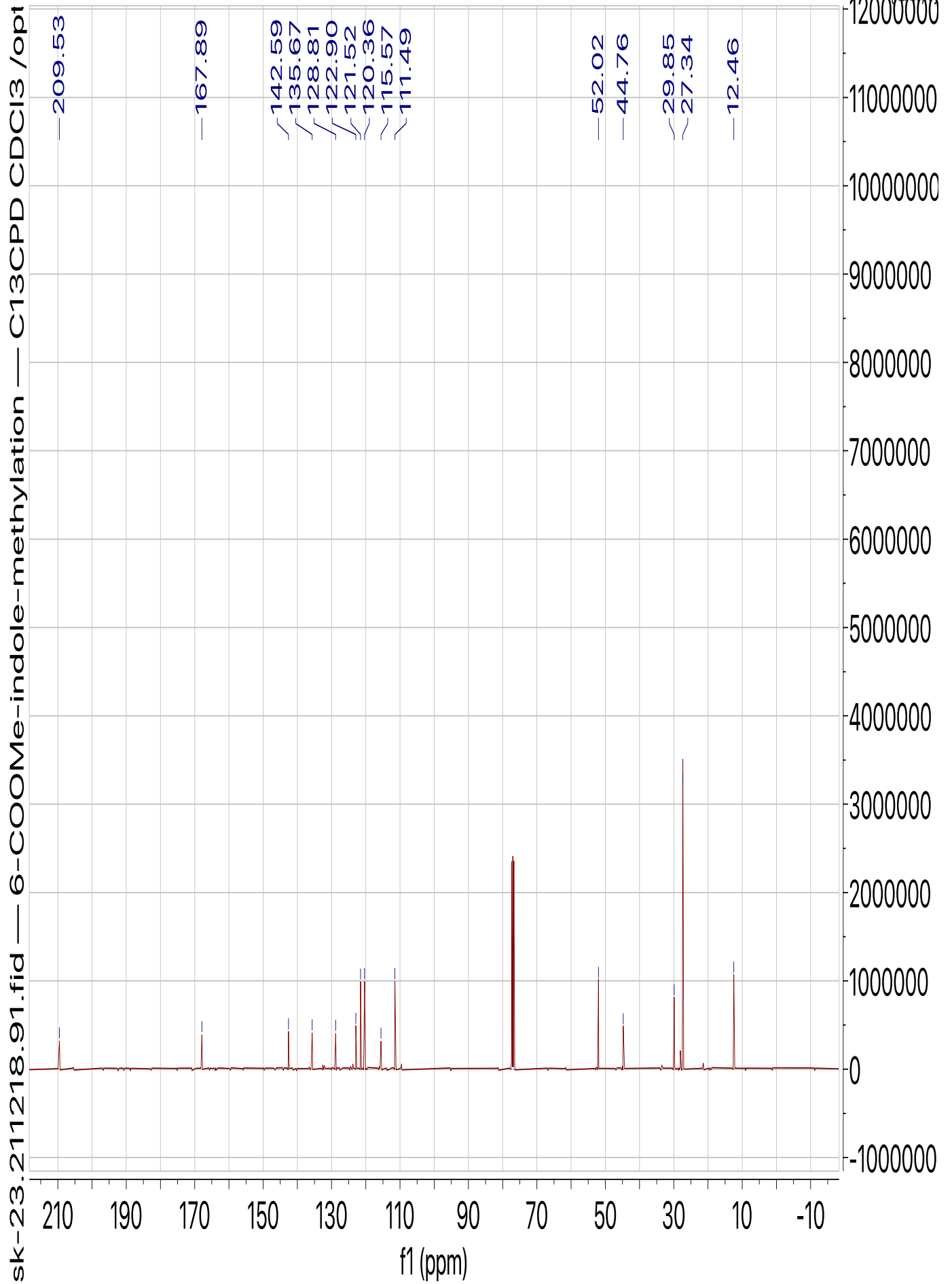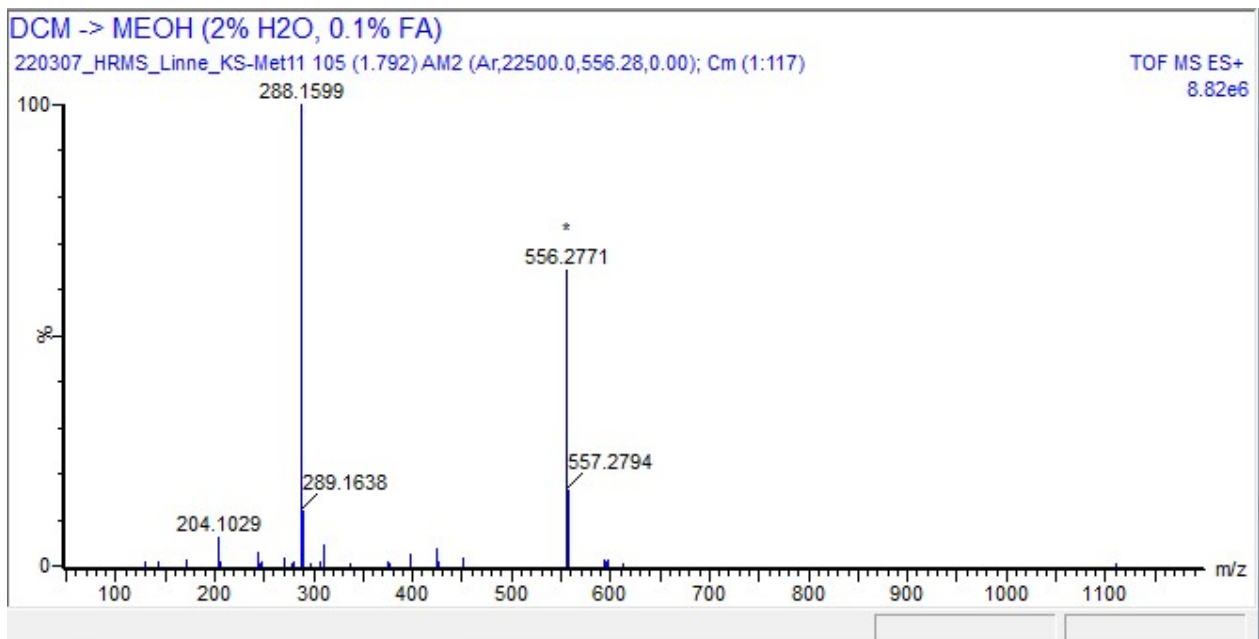
3e, ¹³C NMR (101 MHz, CDCl₃)

sk-23.211218.91.fid — 6-COOOMe-indole-methylation — C13CPD CDCl3 /opt

Peaks: 209.53, 167.89, 142.59, 135.67, 128.81, 122.90, 121.52, 120.36, 115.57, 111.49, 52.02, 44.76, 29.85, 27.34, 12.46

DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met11 105 (1.792) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)
TOF MS ES+
8.82e6

288.1599

556.2771 *

557.2794

289.1638

204.1029

100 200 300 400 500 600 700 800 900 1000 1100 m/z

Single Mass Analysis
Tolerance = 2.0 mDa / DBE: min = -1.5, max = 100.0
Element prediction: Off
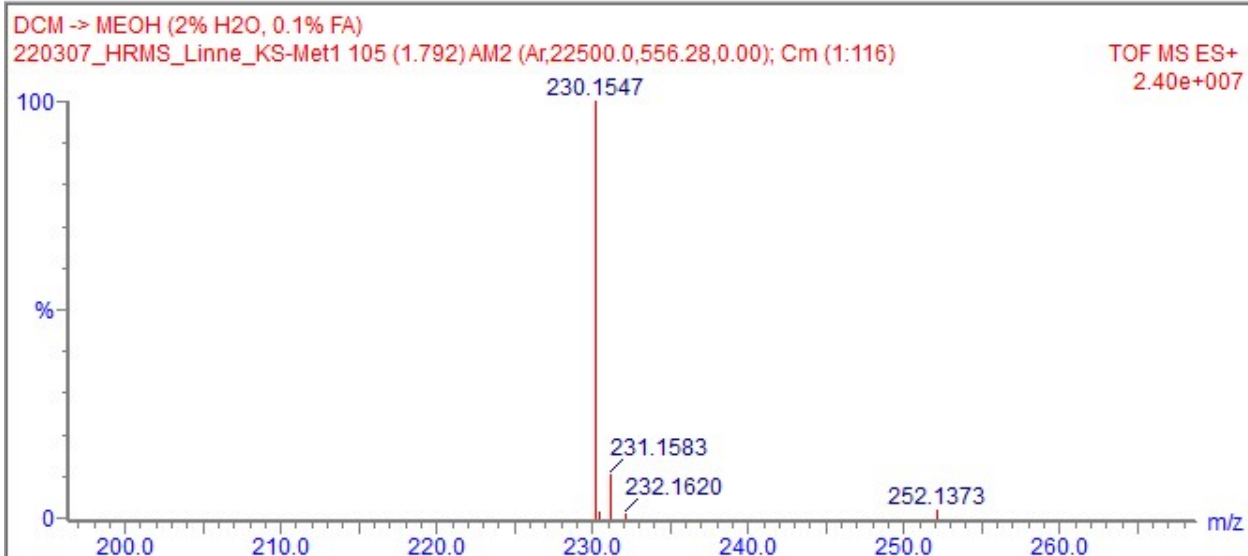Number of isotope peaks used for i-FIT = 2
Monoisotopic Mass, Even Electron Ions
75 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
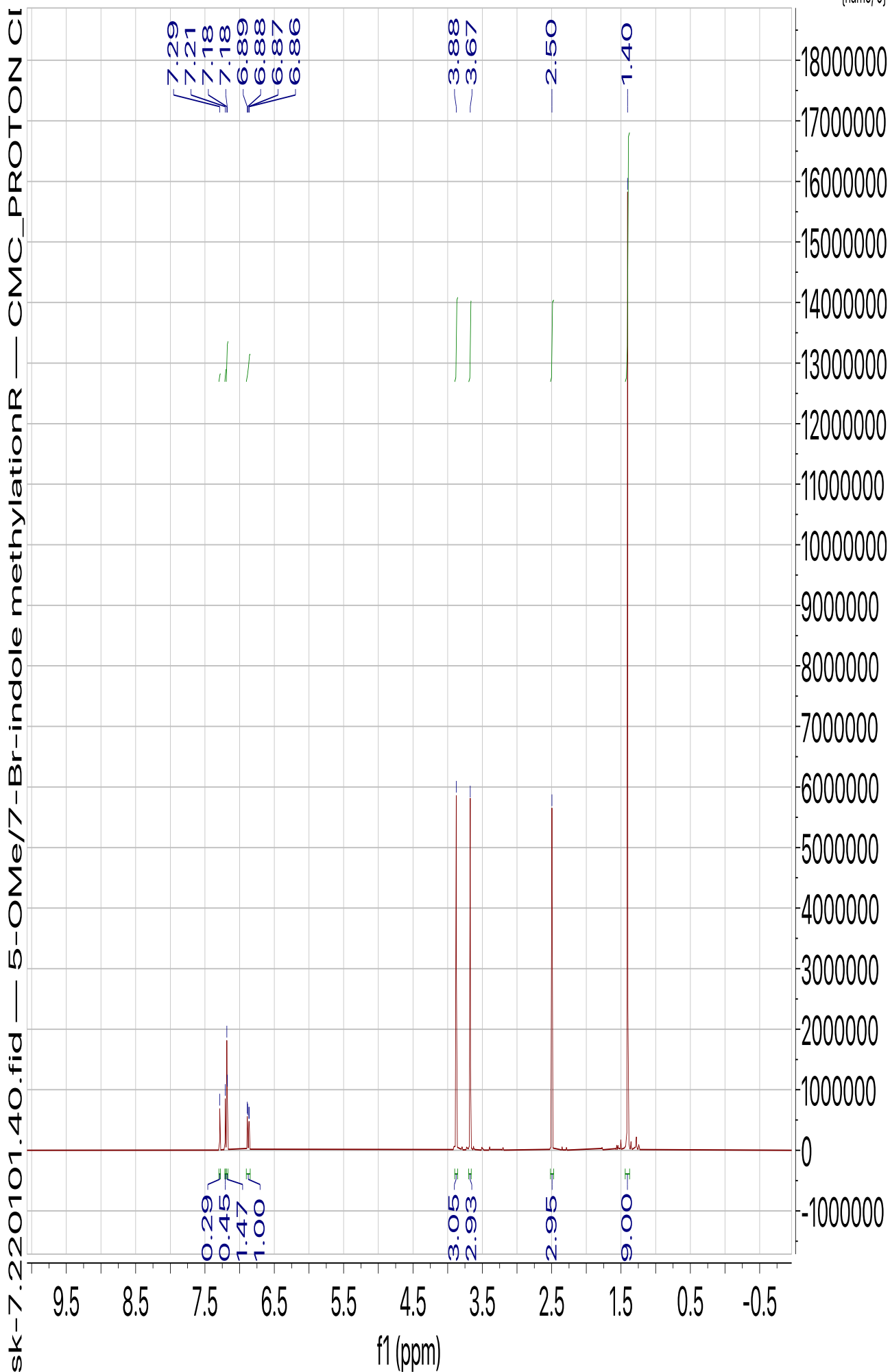Elements Used:
C: 0-60   H: 0-100   N: 0-3   O: 0-4

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
288.1599	288.1600	-0.1	-0.3	7.5	C17 H22 N O3	27.8	n/a	n/a	17	22	1	3

DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met11 105 (1.792) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)
TOF MS ES+
8.82e+006

288.1599

289.1638

204.1029

244.1708

270.1867

310.1424

336.1929

374.1088

200 210 220 230 240 250 260 270 280 290 300 310 320 330 340 350 360 370 380 m/z

HRMS spectra of **3e**

3f, ^{1}H NMR, CDCl$_3$, 400 MHz

sk.211230.10.fid — CMC_PROTON CDCl3 / — 5-NO2-indolemethylation-pdt — CMC_PROTON CDCl3 /

8.54, 8.54, 8.12, 8.11, 8.09, 8.09, 7.34, 7.31, 7.29, 3.76, 2.48, 1.37

1.00, 1.03, 1.06, 3.16, 3.20, 9.74

3f, ¹³C NMR (101 MHz, CDCl₃)

209.27

142.15
141.45
138.99
124.76
117.41
117.09
116.97
109.09

45.06

30.20
27.31

12.46

sk-2.211230.11.fid — 5-NO2-indolemethylation-pdt — C13CPD CDCl3 /opt/r

f1 (ppm)

220307_HRMS_Linne_KS-Met13 103 (1.758) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)

TOF MS ES+
1.33e7

100

%

0

275.1392

*
556.2771

261.1240 276.1426

557.2795

191.0822

100   200   300   400   500   600   700   800   900   1000   1100   m/z

Single Mass Analysis
Tolerance = 2.0 mDa   /   DBE: min = -1.5, max = 100.0
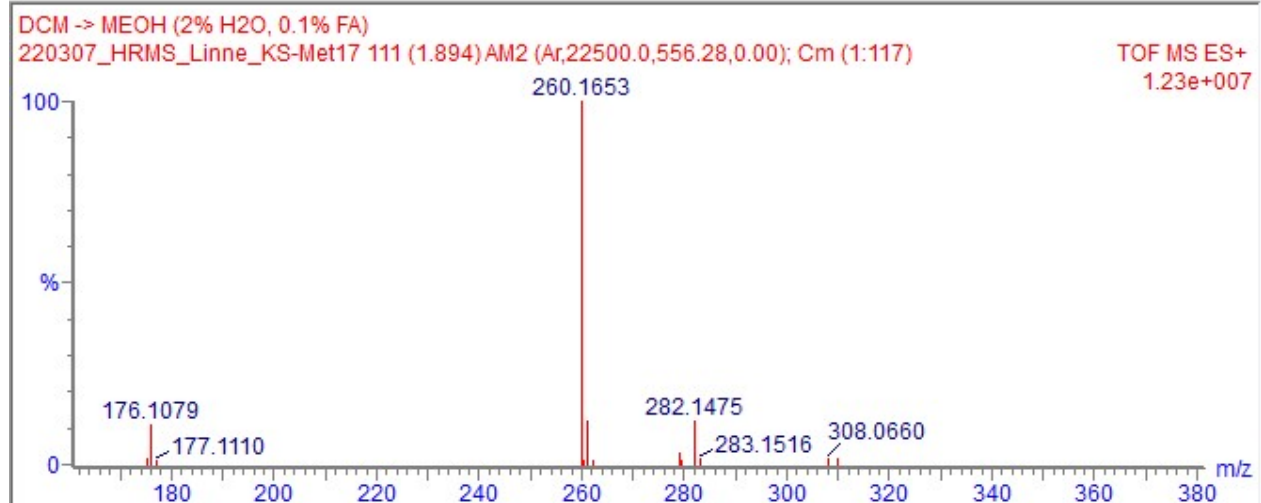Element prediction: Off
Number of isotope peaks used for i-FIT = 2
Monoisotopic Mass, Even Electron Ions
74 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
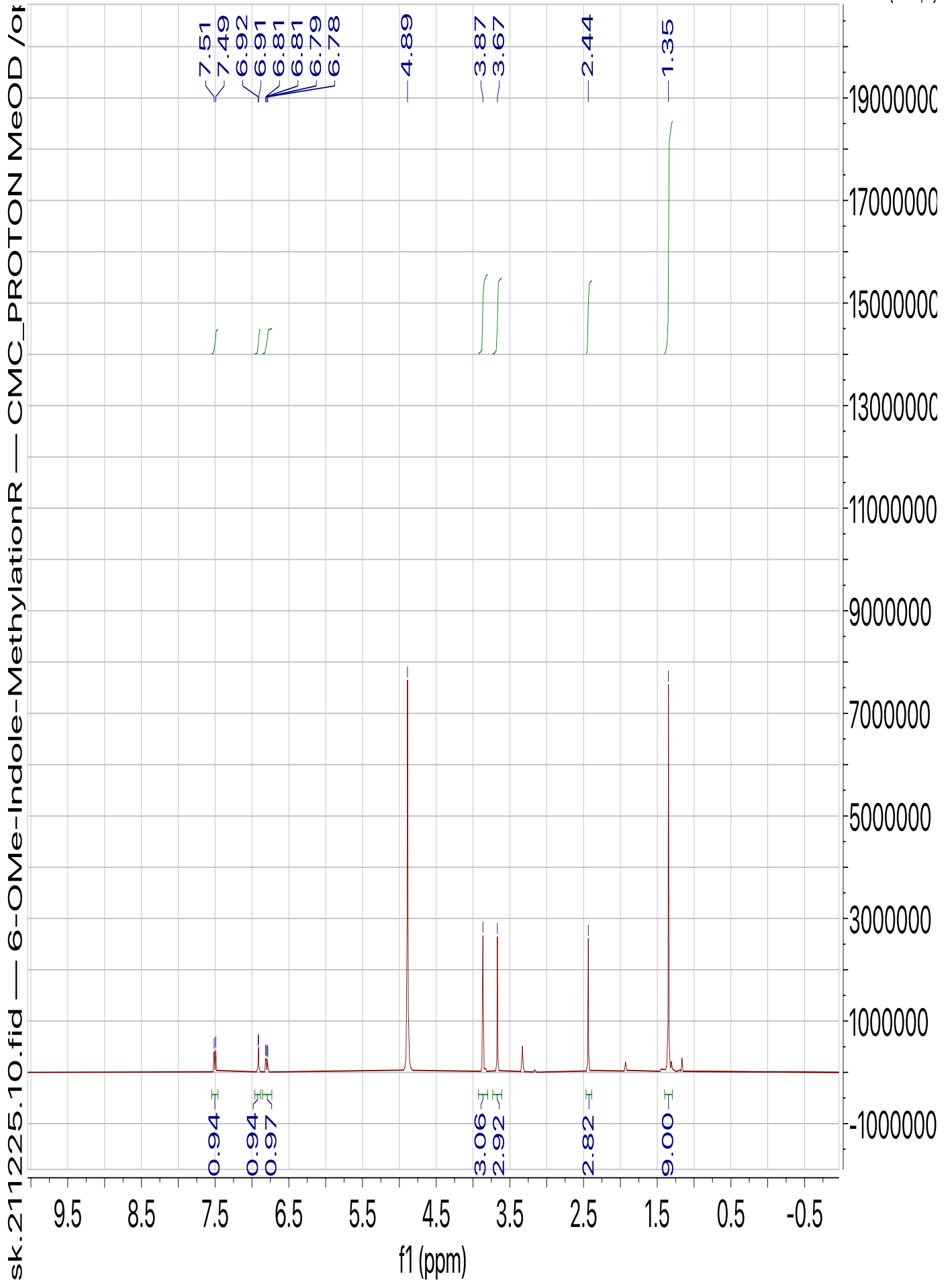Elements Used:
C: 0-60   H: 0-100   N: 0-3   O: 0-4

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O.
275.1392	275.1396	-0.4	-1.5	7.5	C15 H19 N2 O3	50.0	n/a	n/a	15	19	2	3

DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met13 103 (1.758) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)

TOF MS ES+
1.33e+007

275.1392

100

%

0

244.1707   255.1502   261.1240
262.1271

276.1426
289.1562

297.1216

240.0   250.0   260.0   270.0   280.0   290.0   300.0   310.0   320.0   m/z

HRMS spectra of **3f**

3g, ^{1}H NMR, CDCl$_3$, 400 MHz
Minor C4 isomer also observed

{name, 0}

sk-3_221220.20.fid — 5-CN-indole-methylation — PROTON CDCl3 {D:\nmr

7.83 7.83 7.83 7.43 7.41 7.38 7.37 7.36 7.35 7.28 7.27 7.25 7.25 7.19

3.77 3.65

2.59 2.39

1.30 1.26

1.00 1.52 1.12 0.68 3.24 0.64 3.31 2.04 10.39

f1 (ppm)

34

3g, ^{13}C NMR (101 MHz, CDCl$_3$)
Minor C2 isomer also observed
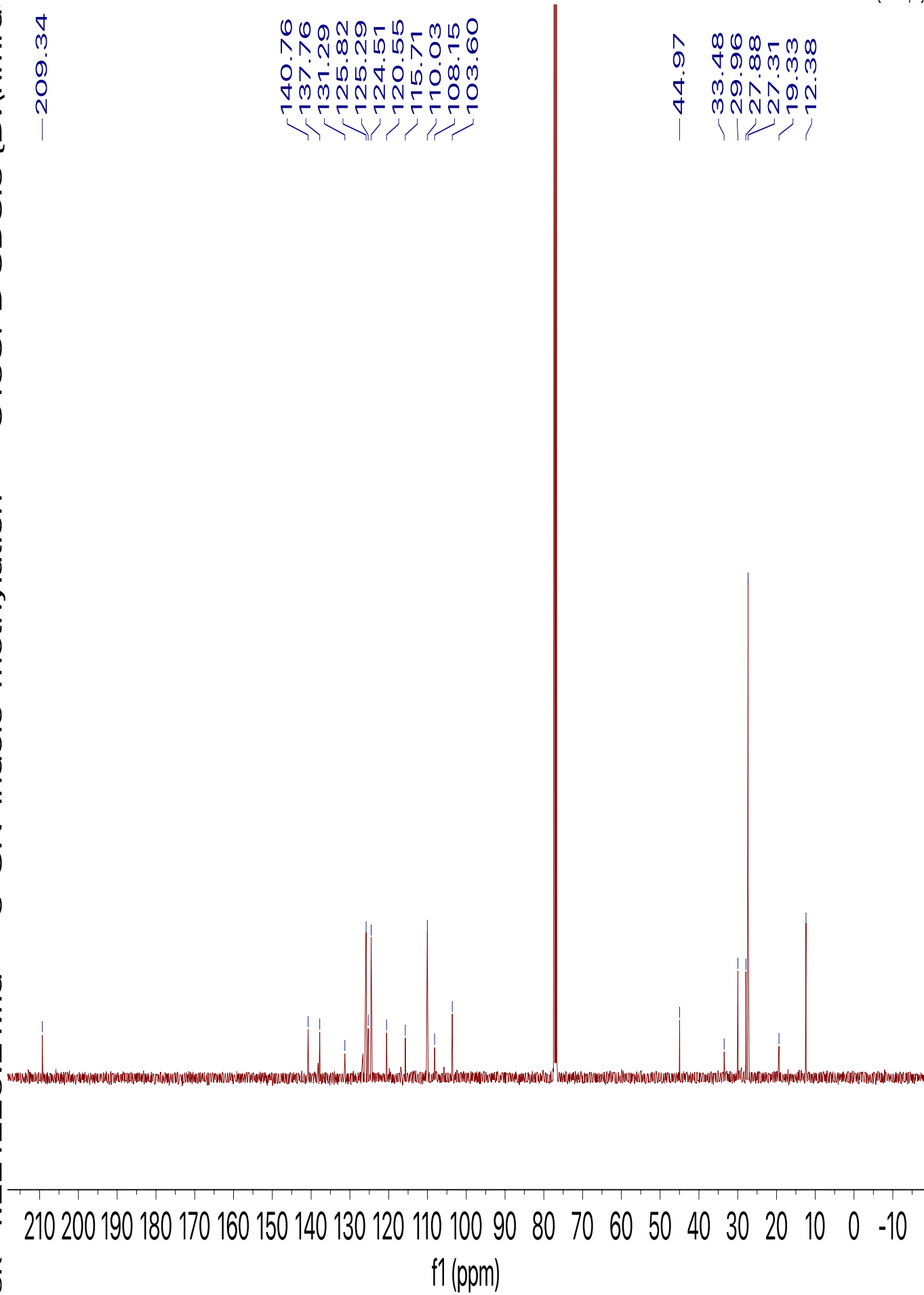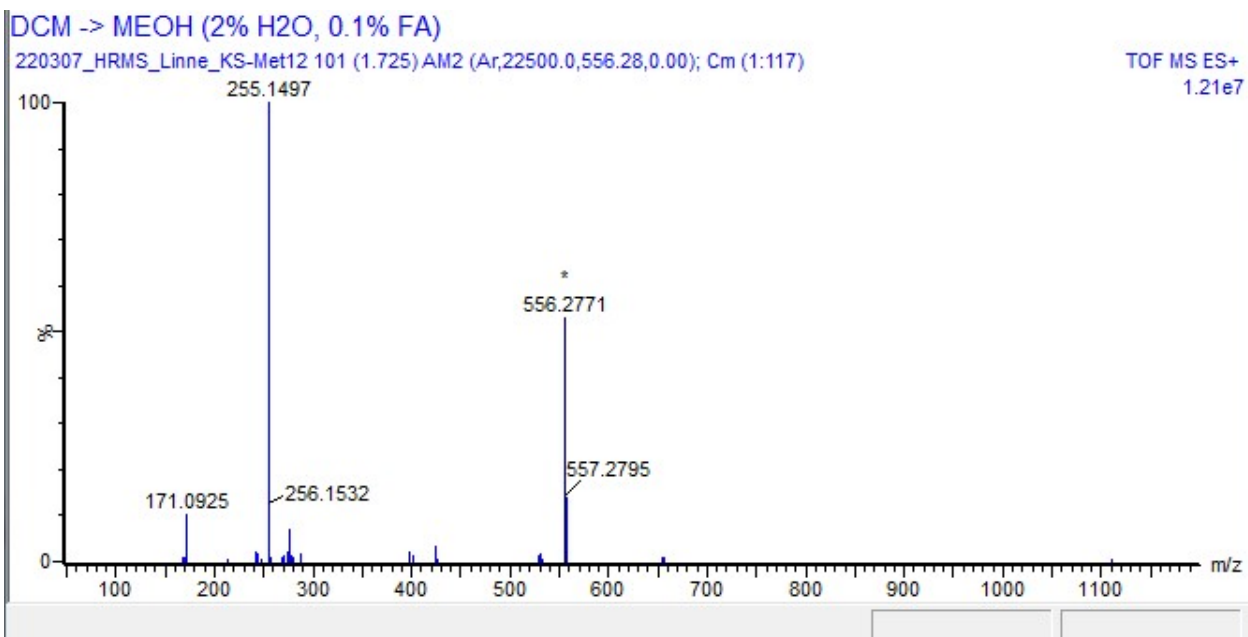
{name, 0}

209.34

140.76
137.76
131.29
125.82
125.29
124.51
120.55
115.71
110.03
108.15
103.60

44.97

33.48
29.96
27.88
27.31
19.33
12.38

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met12 101 (1.725) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)   TOF MS ES+
                                                                                                      1.21e7

100-   255.1497

                                              *
                                          556.2771

%-

            171.0925   256.1532   557.2795

0-
        100   200   300   400   500   600   700   800   900   1000   1100   m/z

Single Mass Analysis
Tolerance = 2.0 mDa   /   DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 2
Monoisotopic Mass, Even Electron Ions
72 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
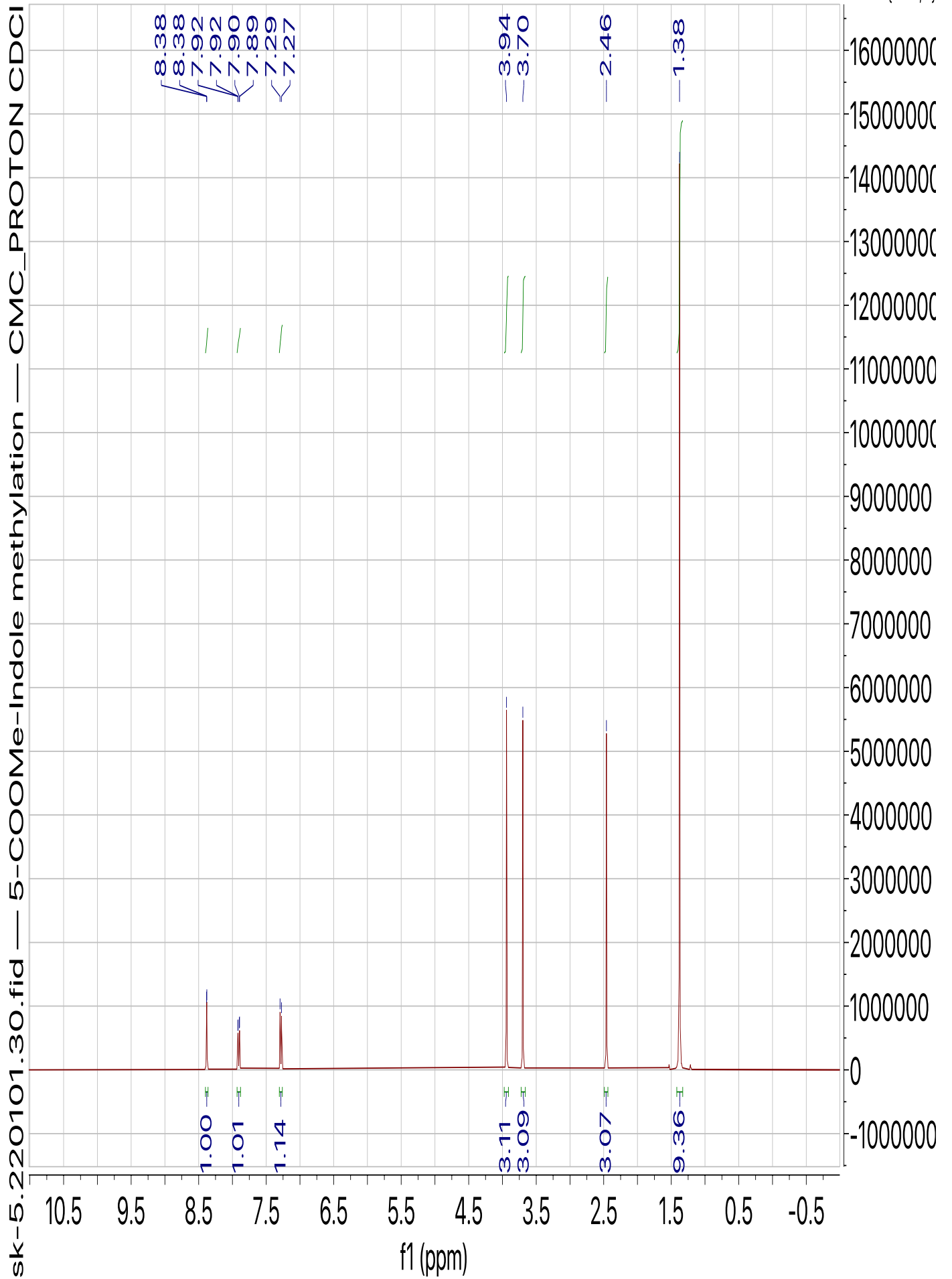Elements Used:
C: 0-60   H: 0-100   N: 0-3   O: 0-4

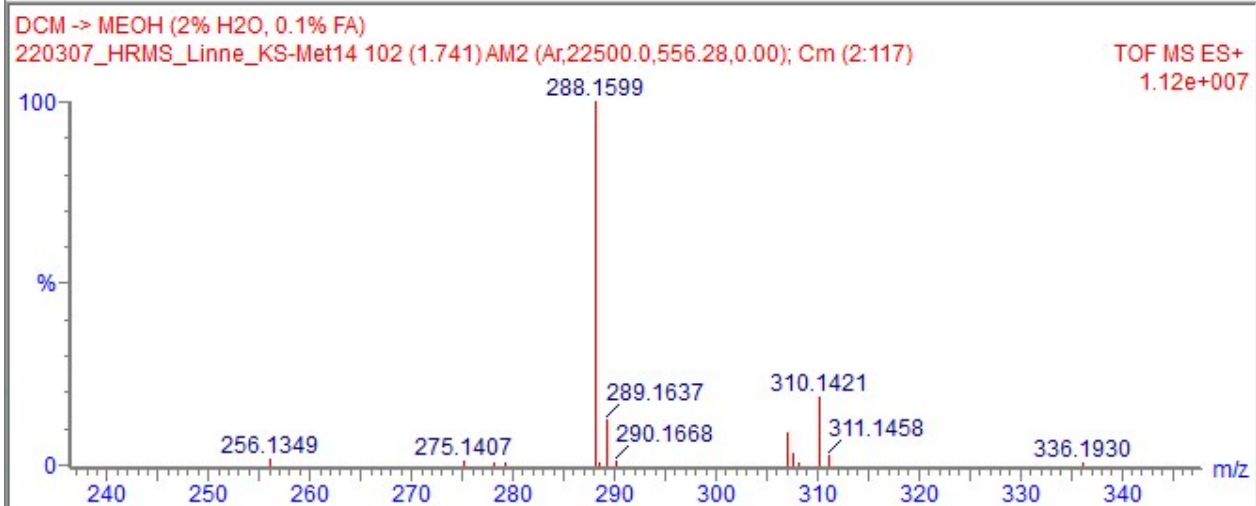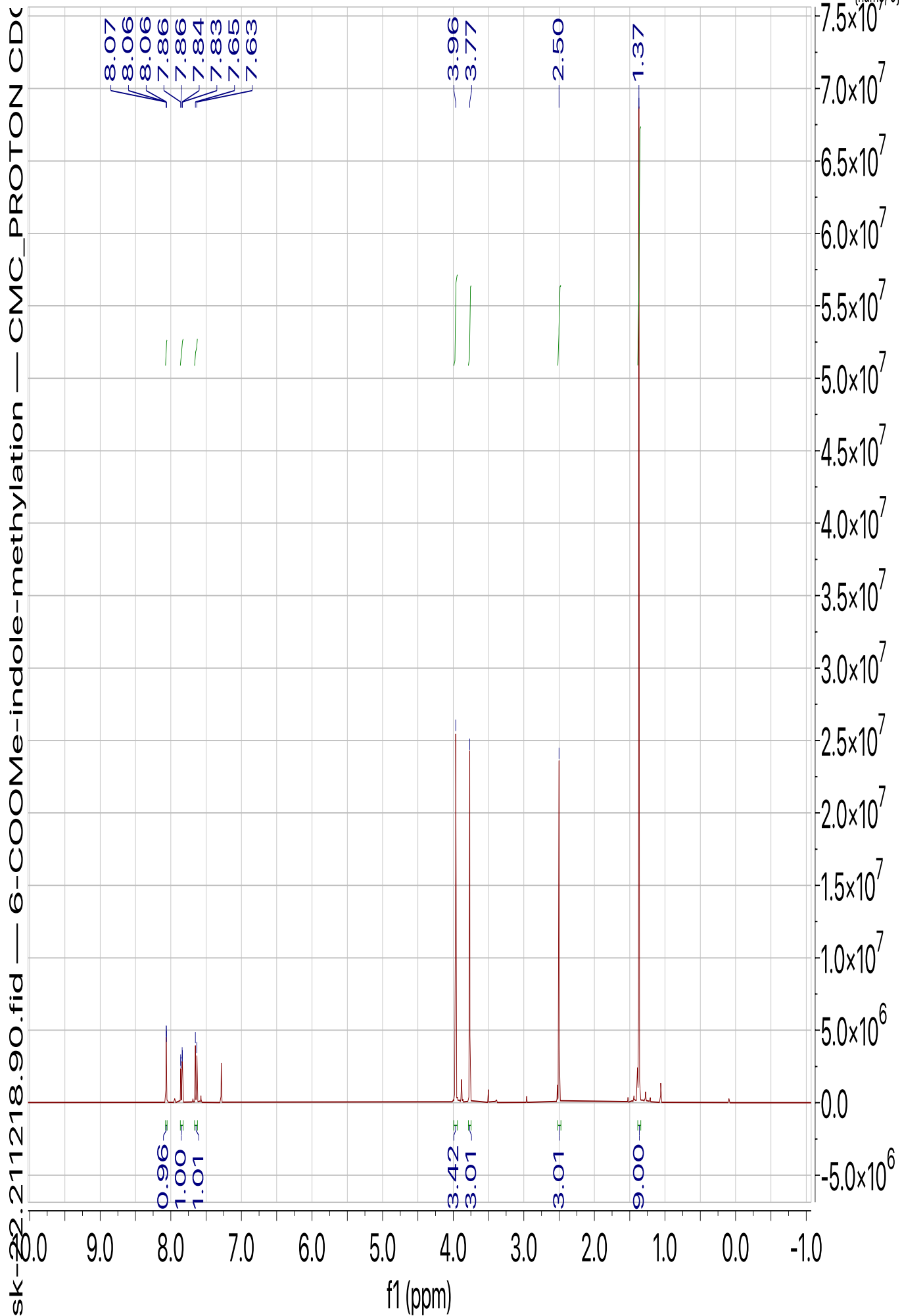| Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Nor...	Fit Conf %	C	H	N	O
255.1497	255.1497	0.0	0.0	8.5	C16 H19 N2 O	50.3	n/a	n/a	16	19	2	1

DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met12 101 (1.725) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)   TOF MS ES+
                                                                                                      1.21e+007

100-   255.1497

%-

        171.0925   256.1532   277.1320
        172.0958   213.1399   241.1345
0-
    170 180 190 200 210 220 230 240 250 260 270 280 290 300 310 320 330 340 350   m/z

HRMS spectra of **3g**

3h, ^{1}H NMR, CDCl$_3$, 400 MHz

{name, 0}

7.36, 7.36, 7.34, 7.33, 7.22, 7.21, 7.20, 7.18, 6.98, 6.97, 6.96, 6.95, 6.93, 6.93

3.68

2.49

1.38

0.99, 1.05, 1.07

3.06

3.06

9.00

sk.211229.10.fid — 5F-indole methylation — CMC_PROTON CDCl3 /opt/nmr

37

3h, ^{13}C NMR (101 MHz, CDCl$_3$)

sk-2.211229.11.fid — 5F-indole methylation — C13CPD CDCl3 /opt/nmrdata/

{name, 0}

Peaks: 208.72, 159.46, 157.12, 141.71, 132.87, 125.57, 125.47, 115.11, 109.81, 109.71, 109.55, 109.29, 106.56, 106.31, 44.46, 29.82, 27.36, 12.60

3h, ¹⁹F NMR, CDCl₃

{name, 0}

-123.17
-123.18
-123.19
-123.19
-123.20
-123.22
-123.23

sk-3_211229.12.fid — 5F-indole methylation — F19 CDCl3 /opt/nmrdata/curre

9000000
8000000
7000000
6000000
5000000
4000000
3000000
2000000
1000000
0

20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220

f1 (ppm)

DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met7 103 (1.758) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)   TOF MS ES+
                                                                                                1.08e7

100 ─
        248.1450

                                                    *
                                              556.2771

%─

                                                  557.2795
          249.1485
    164.0879

0 ─────┬────┬────┬────┬────┬────┬────┬────┬────┬────┬────┬──── m/z
      100 200 300 400 500 600 700 800 900 1000 1100

Single Mass Analysis
Tolerance = 2.0 mDa   /   DBE: min = -1.5, max = 100.0
Element prediction: Off
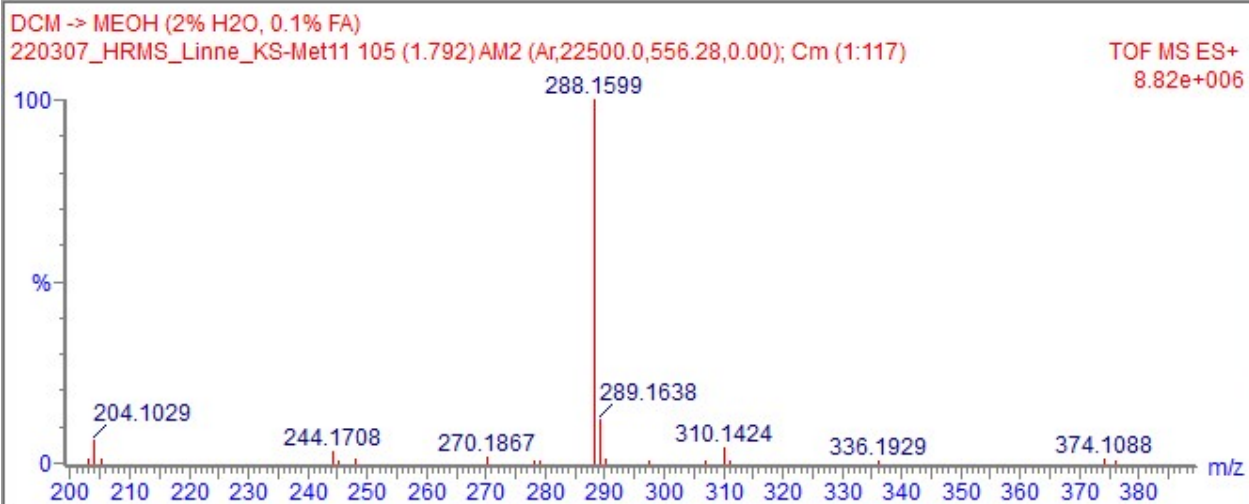Number of isotope peaks used for i-FIT = 2
Monoisotopic Mass, Even Electron Ions
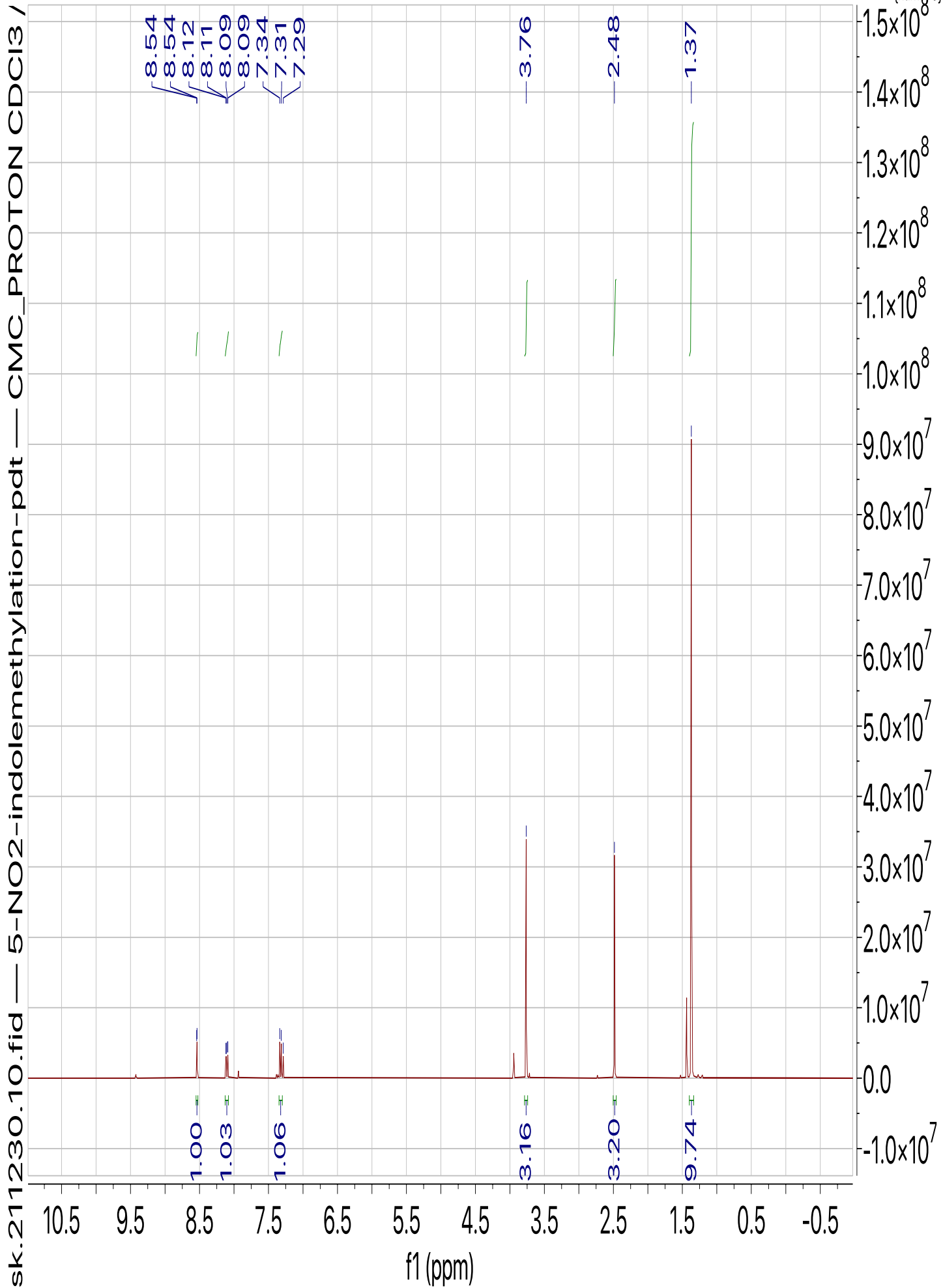129 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)
Elements Used:
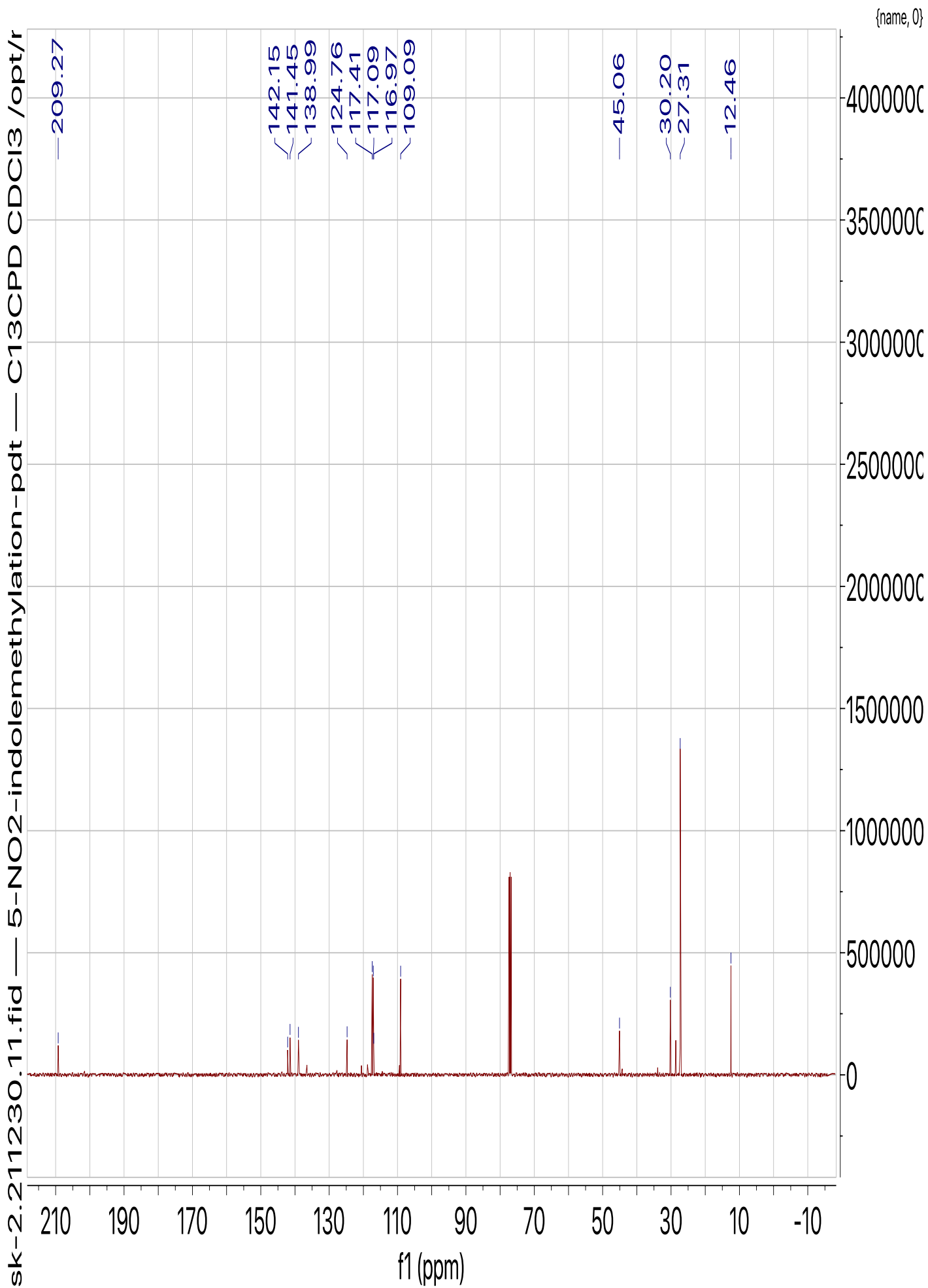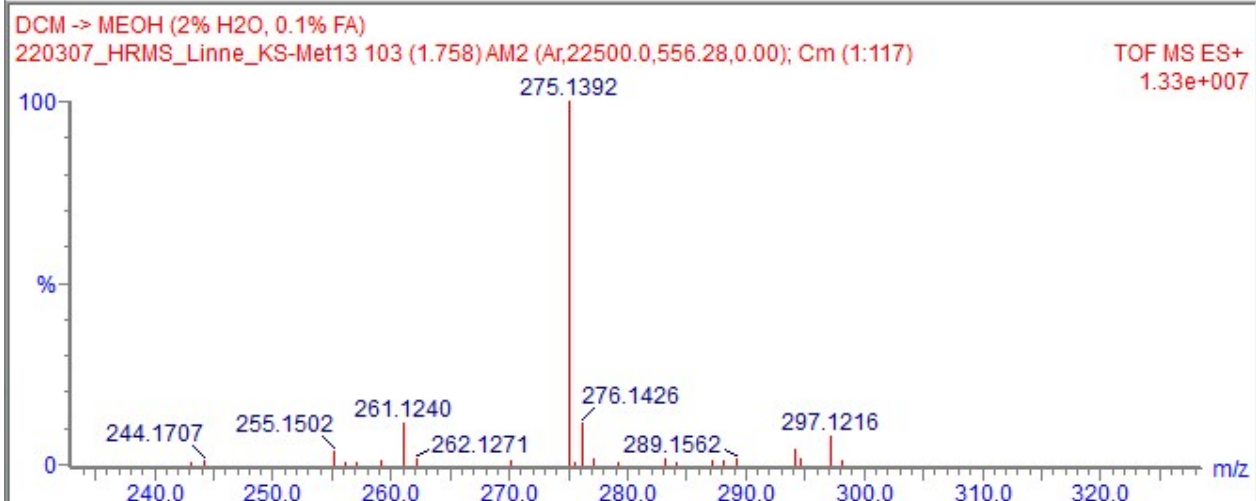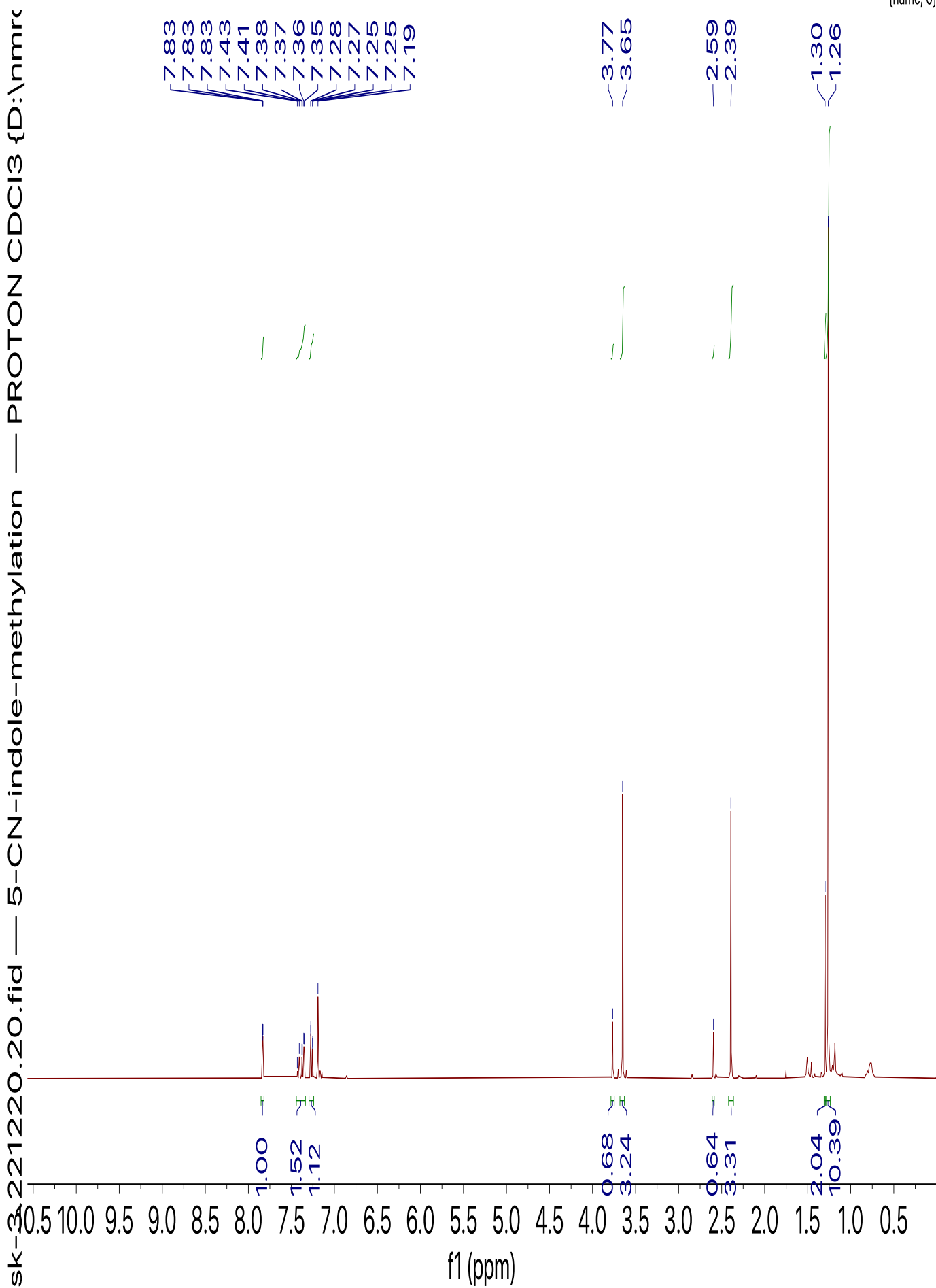C: 0-60   H: 0-100   N: 0-3   O: 0-4   F: 0-1

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT ...	Fit Conf %	C	H	N	O	F
248.1450	248.1451	-0.1	-0.4	6.5	C15 H19 N O F	50.4	0.093	91.15	15	19	1	1	1
	248.1439	1.1	4.4	10.5	C18 H18 N	52.8	2.425	8.85	18	18	1		
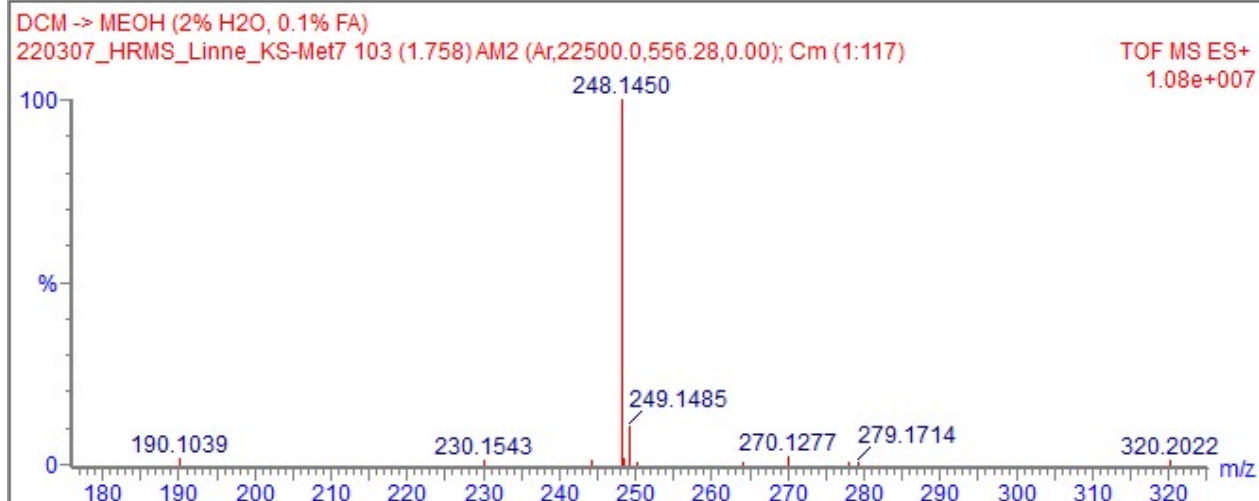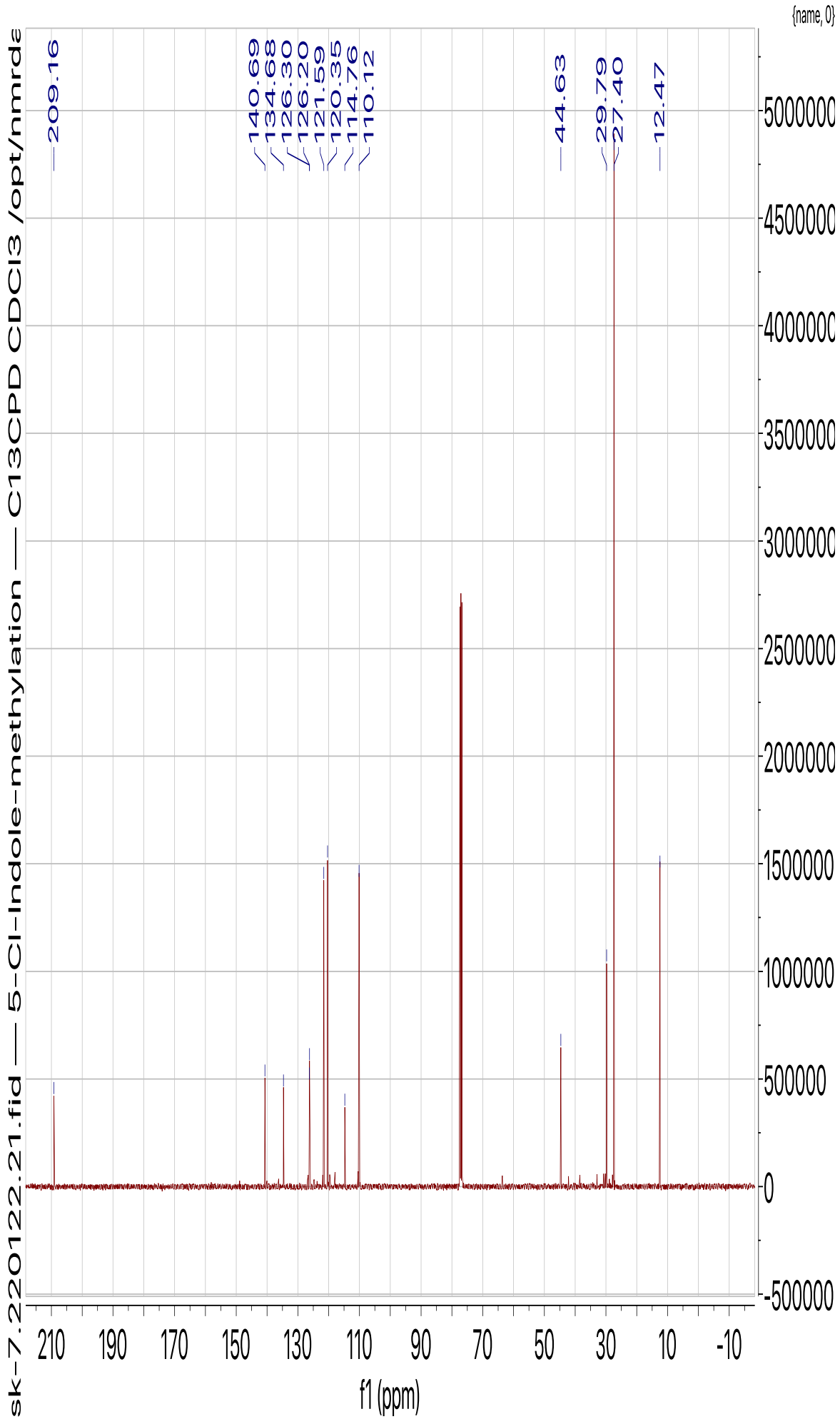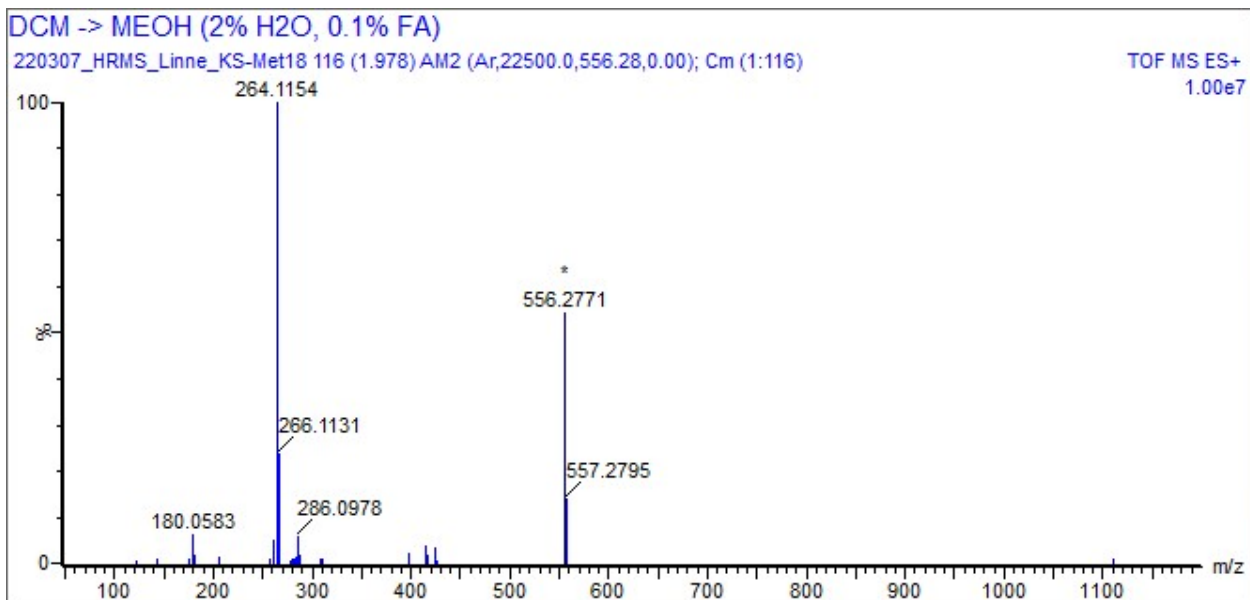
DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met7 103 (1.758) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)   TOF MS ES+
                                                                                                1.08e+007

100 ─
                                    248.1450

%─

                                      249.1485

    190.1039   230.1543   270.1277 279.1714   320.2022
0 ──┬────┬────┬────┬────┬────┬────┬────┬────┬────┬────┬────┬────┬────┬────┬── m/z
   180 190 200 210 220 230 240 250 260 270 280 290 300 310 320

HRMS spectra of **3h**

3i, ^{1}H NMR, CDCl$_3$, 400 MHz

sk-2.220122.20.fid — 5-Cl-Indole-methylation — CMC_PROTON CDCl3 /op1

7.61
7.61
7.29
7.21
7.19
7.17
7.17
7.15
7.14

3.68

2.47

1.37

{name, 0}

1.00
2.38
3.23
3.26
9.68

f1 (ppm)

3i, ^{13}C NMR (101 MHz, CDCl$_3$)

sk-7.220122.21.fid — 5-Cl-Indole-methylation — C13CPD CDCl3 /opt/nmrda

{name, 0}

209.16

140.69
134.68
126.30
126.20
121.59
120.35
114.76
110.12

44.63

29.79
27.40

12.47

Single Mass Analysis
Tolerance = 2.0 mDa   /   DBE: min = -1.5, max = 100.0
Element prediction: Off
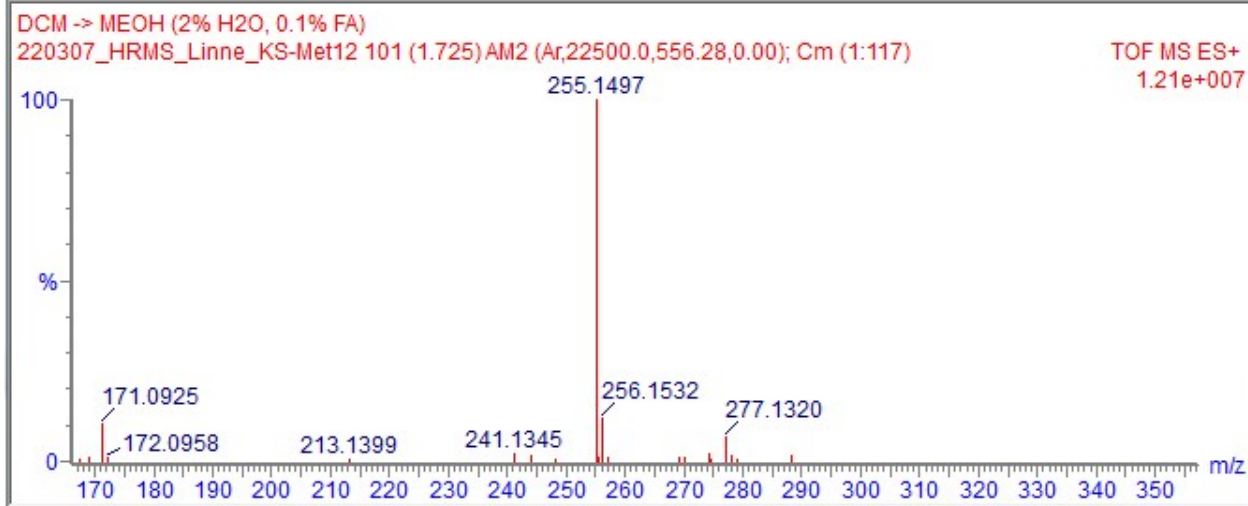Number of isotope peaks used for i-FIT = 2
Monoisotopic Mass, Even Electron Ions
189 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-60   H: 0-100   N: 0-3   O: 0-4   Cl: 0-2

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-F...	i-FIT ...	Fit Conf %	C	H	N	O	Cl
264.1154	264.1155	-0.1	-0.4	6.5	C15 H19 N O Cl	27.7	0.050	95.10	15	19	1	1	1
	264.1137	1.7	6.4	11.5	C16 H14 N3 O	30.6	3.016	4.90	16	14	3	1	

HRMS spectra of **3i**

{name, 0}

sk-5.221220.30.fid — 6-Cl-indole-methylation — PROTON CDCl3 {D:\nmrd:

7.45
7.43
7.19
7.19
7.19
7.04
7.04
7.02
7.01

3.56

2.37

1.26

1.00
1.17
1.00

3.21

3.28

10.06

f1 (ppm)

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.

3j, ¹³C NMR (101 MHz, CDCl₃)
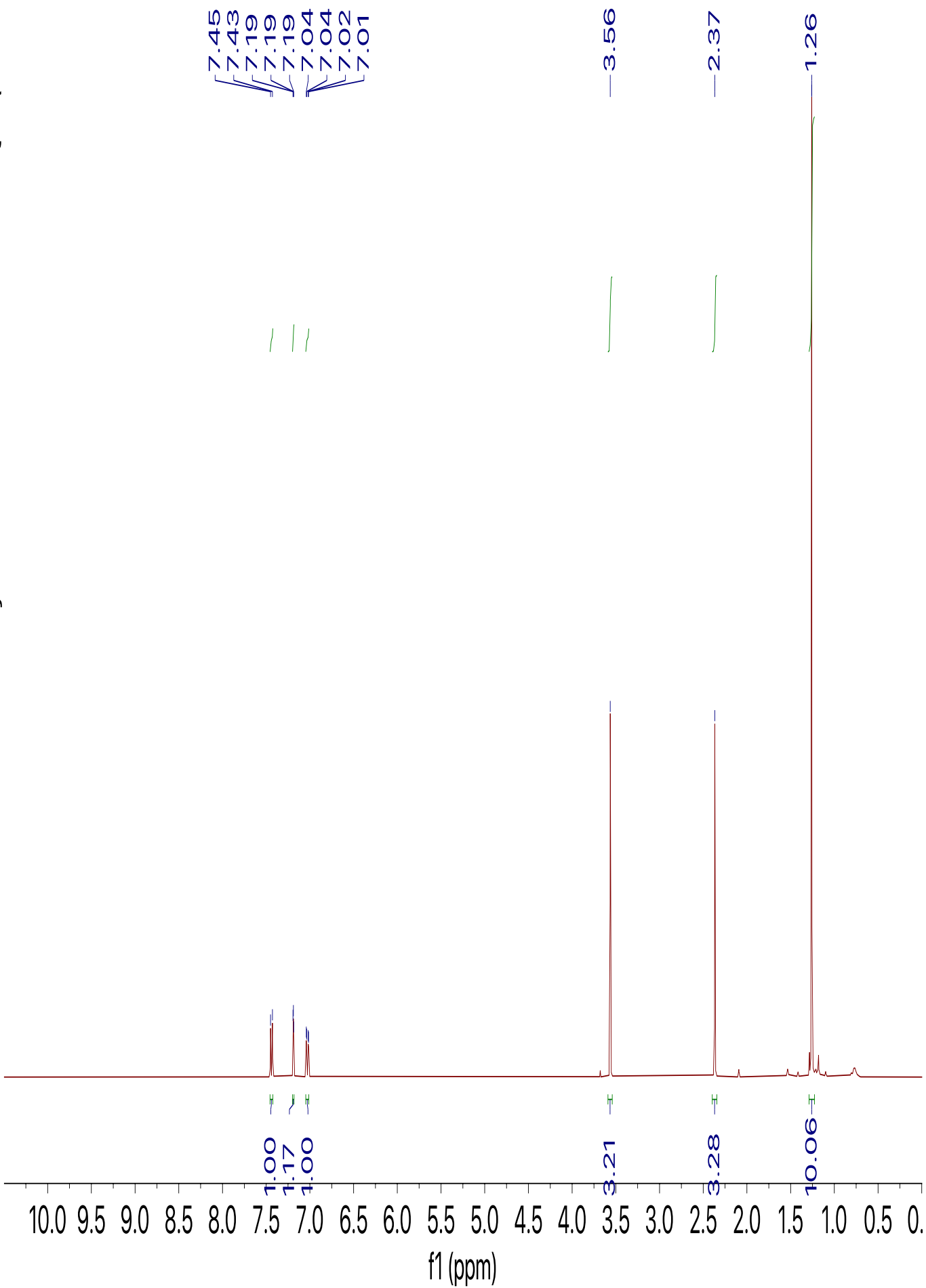
sk-6.221220.31.fid — 6-Cl-indole-methylation — C13CPD CDCl3 {D:\nmrda
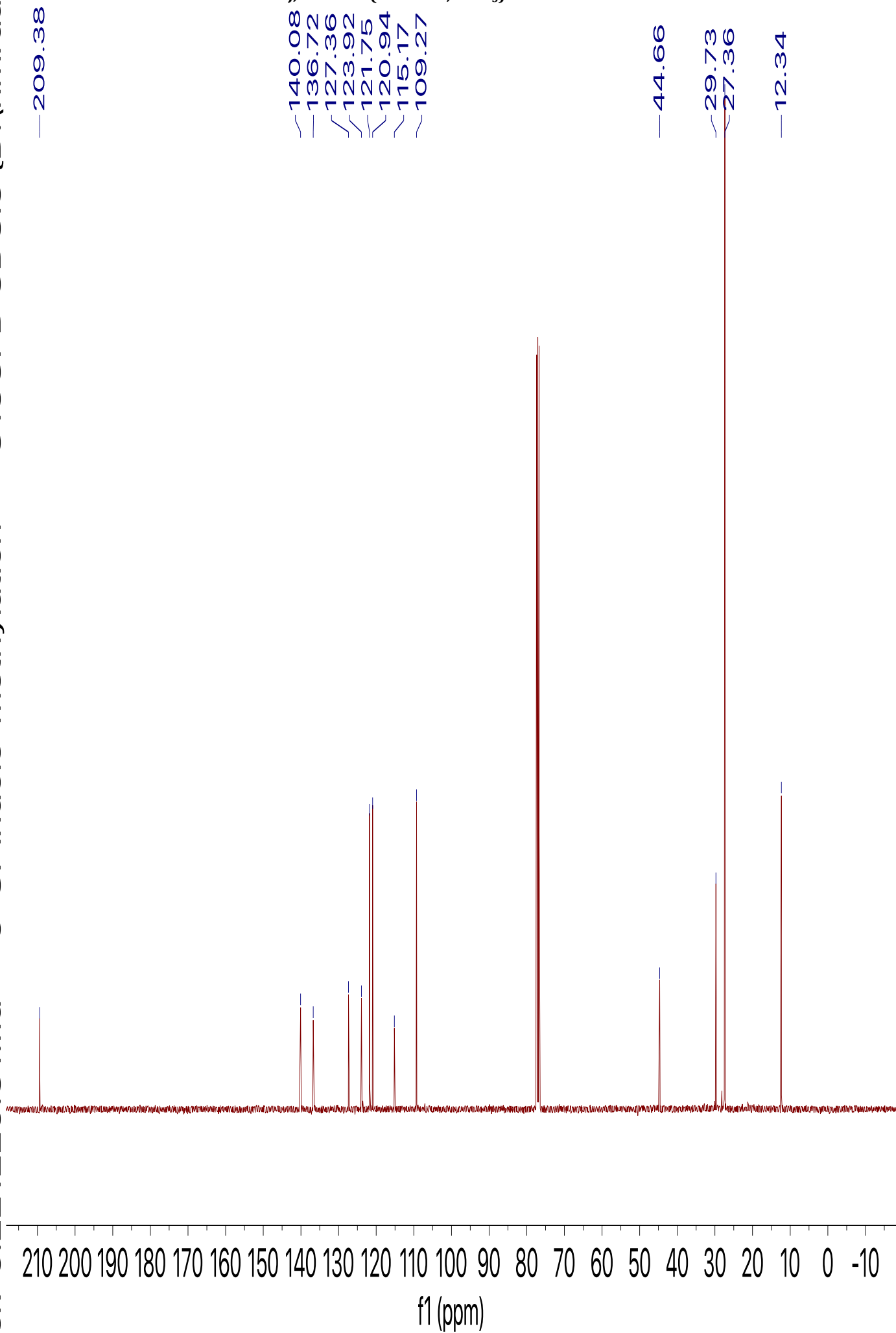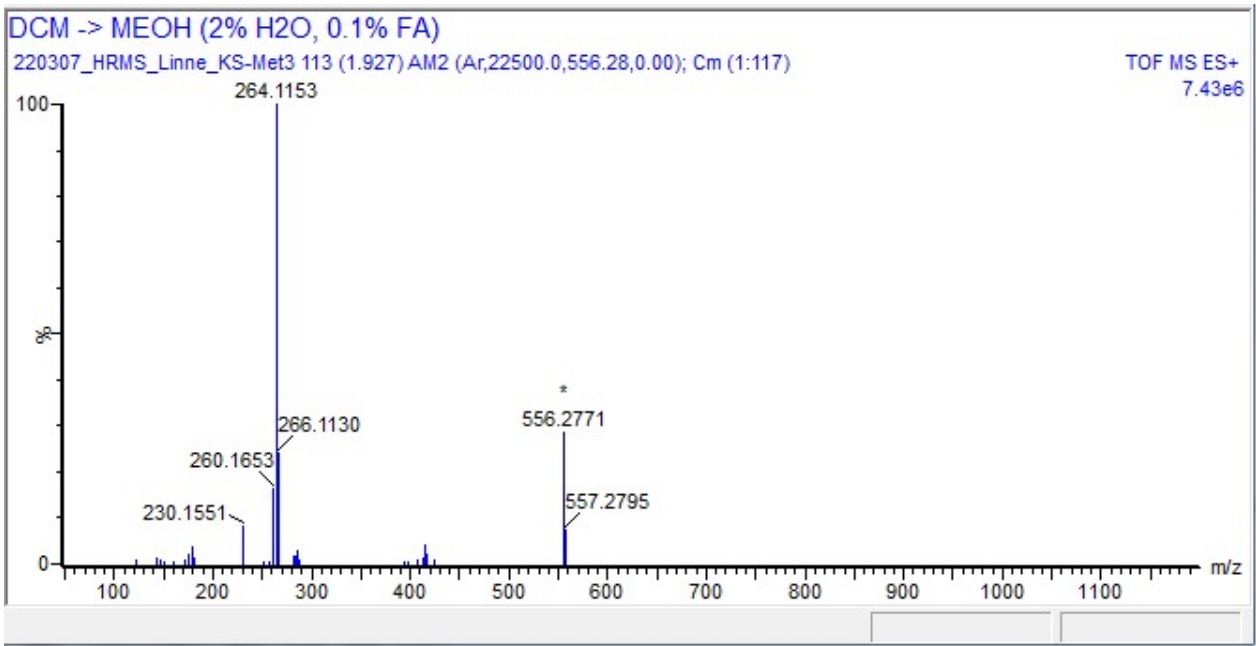
209.38

140.08
136.72
127.36
123.92
121.75
120.94
115.17
109.27

44.66

29.73
27.36

12.34

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

Single Mass Analysis

Tolerance = 2.0 mDa / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 2
Monoisotopic Mass, Even Electron Ions
189 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)
Elements Used:

C: 0-60	H: 0-100	N: 0-3	O: 0-4	Cl: 0-2

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i...	Fit Conf %	C	H	N	O	Cl
264.1153	264.1155	-0.2	-0.8	6.5	C15 H19 N O Cl	20...	92.79	15	19	1	1	1
	264.1137	1.6	6.1	11.5	C16 H14 N3 O	32...	7.21	16	14	3	1	
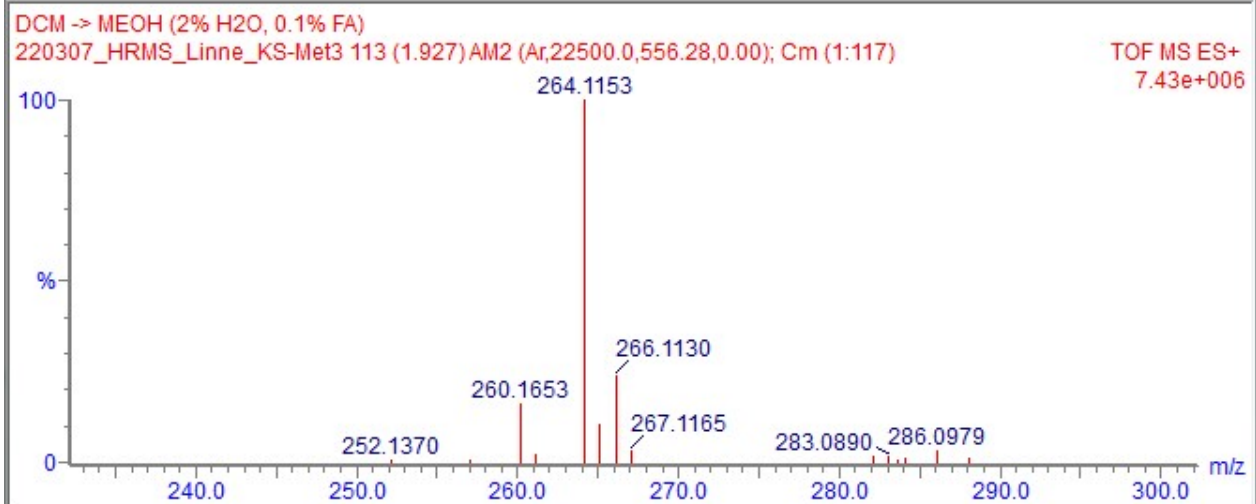
HRMS spectra of **3j**
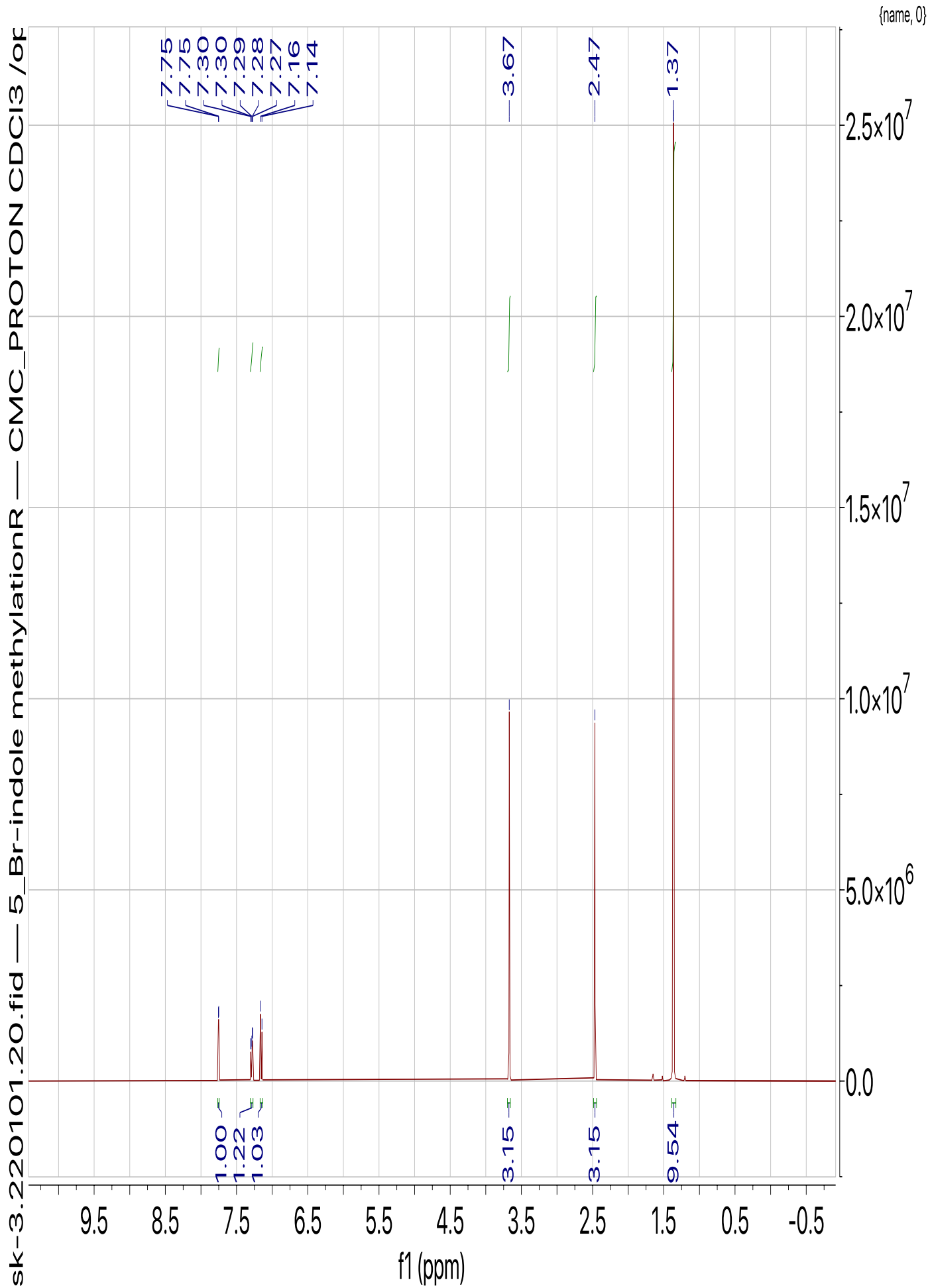
3k, ^{1}H NMR, CDCl$_3$, 400 MHz

sk-3.220101.20.fid — 5_Br-indole methylationR — CMC_PROTON CDCl3 /of

{name, 0}

7.75
7.75
7.30
7.30
7.29
7.28
7.27
7.16
7.14

3.67

2.47

1.37

2.5×10^7

2.0×10^7

1.5×10^7

1.0×10^7

5.0×10^6

0.0

1.00
1.22
1.03

3.15

3.15

9.54

f1 (ppm)

3k, ^{13}C NMR (101 MHz, CDCl$_3$)

sk-4.220101.21.fid — 5_Br-indole methylationR — C13CPD CDCl3 /opt/nmrd

{name, 0}

209.24
140.37
134.94
126.96
124.19
123.32
114.67
113.79
110.56
44.67
29.77
27.40
12.43

100   308.0650

%

556.2771

244.1706

557.2797

311.0668

0

100   200   300   400   500   600   700   800   900   1000   1100   m/z

Single Mass Analysis
Tolerance = 2.0 mDa / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 2
Monoisotopic Mass, Even Electron Ions
147 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
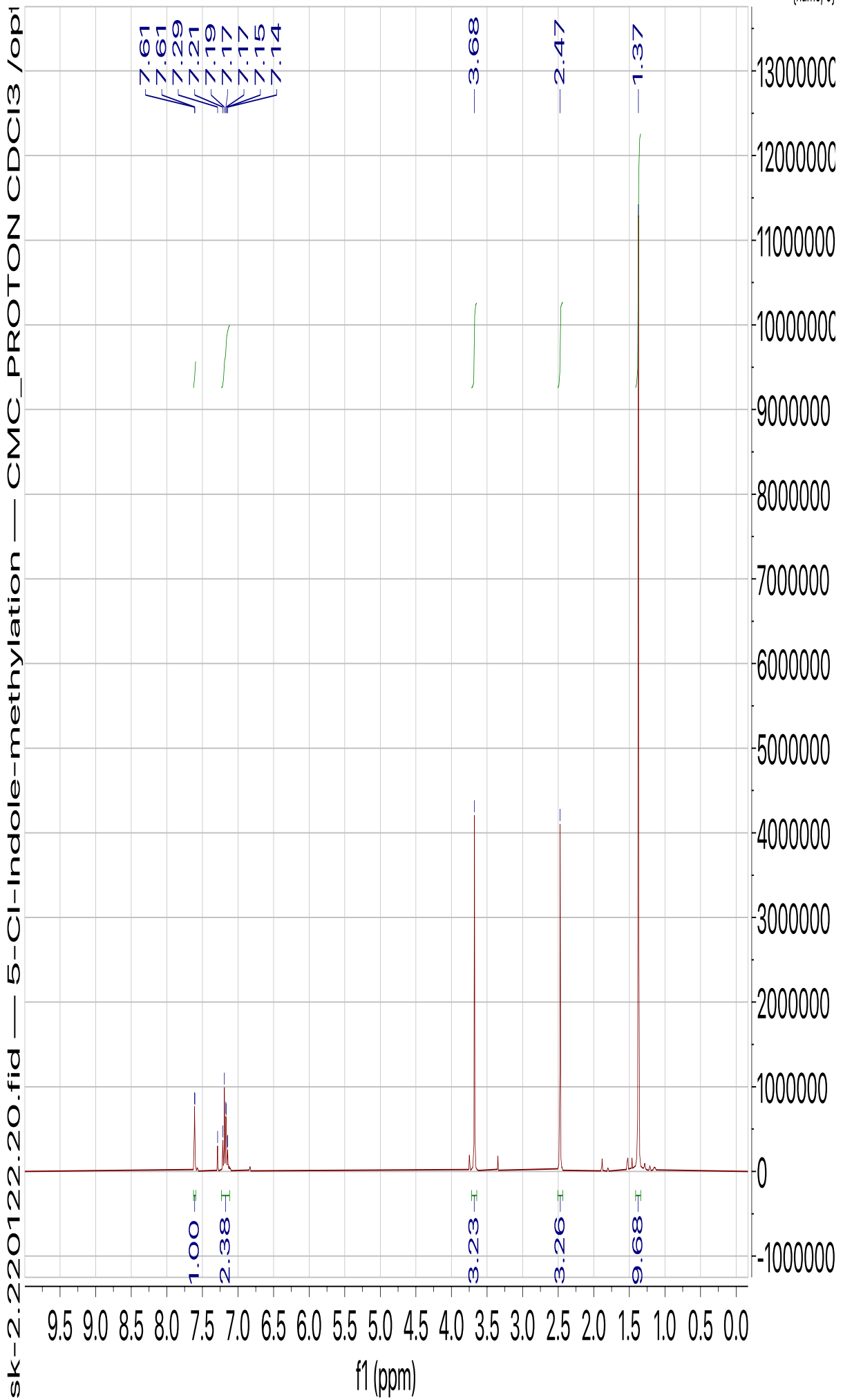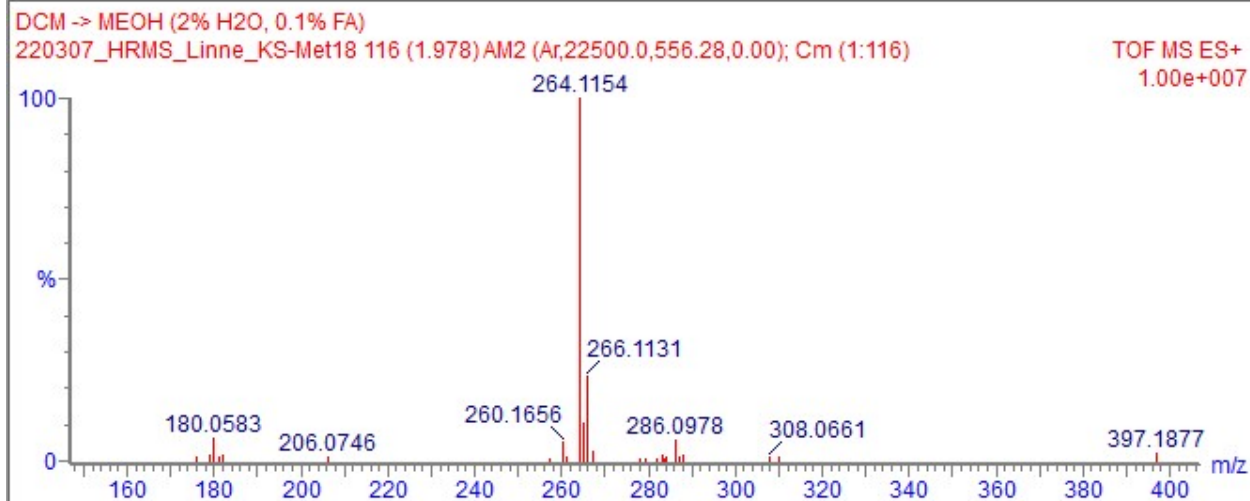Elements Used:
C: 0-60   H: 0-100   N: 0-3   O: 0-4   Br: 0-1

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i...	Fit Conf %	C	H	N	O	Br
308.0650	308.0650	0.0	0.0	6.5	C15 H19 N O Br	28.4	n...	n/a	15	19	1	1	1

100   308.0650

%

311.0668
266.1529   279.1711   320.2022   330.0479   356.0526   397.1875

0
250   260   270   280   290   300   310   320   330   340   350   360   370   380   390   400   m/z

HRMS spectra of **3k**

3l, ^{1}H NMR, CDCl$_3$, 400 MHz
Minor C2 isomer also observed

7.91, 7.91, 7.43, 7.43, 7.41, 7.41, 7.04, 7.02
3.63
2.43
1.33

0.89, 0.92, 0.94
2.88
2.90
9.00

sk-5-211225.30.fid — 5-Iodoindole-methylationR — CMC_PROTON CDCl3 /c

{name, 0}

3l, ^{13}C NMR (101 MHz, CDCl$_3$)

209.75
139.97
135.36
129.72
129.42
127.75
114.27
111.14
84.06
44.70
29.67
27.36
12.30

sk-6.211225.31.fid — 5-Iodoindole–methylationR — C13CPD CDCl3 /opt/nmr

{name, 0}

356.0503

556.2771

357.0545   552.5447   557.2795

Single Mass Analysis
Tolerance = 2.0 mDa / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 2
Monoisotopic Mass, Even Electron Ions
155 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-60   H: 0-100   N: 0-3   O: 0-4   I: 0-1

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT ...	Fit Conf %	C	H	N	O	I
356.0503	356.0500	0.3	0.8	26.5	C28 H6 N	32.491	8.28	28	6	1		
	356.0511	-0.8	-2.2	6.5	C15 H19 N O I	20.086	91.72	15	19	1	1	1

356.0503

357.0545

336.1932   375.0232   378.0329   394.2187 397.1877

HRMS spectra of **3l**

3m, ¹H NMR, CDCl₃, 400 MHz

sk-3.211228.30.fid — cyclopentylindole-methylation — CMC_PROTON CDCl

7.41 7.39 7.29 7.06 7.04

3.87 3.43 3.41 3.40 3.05 3.03 3.01 2.42 2.25 2.23 2.21 2.19 2.18 1.37

1.00 1.00 3.11 2.14 2.15 3.11 2.20 9.59

3m, ^{13}C NMR (101 MHz, CDCl$_3$)

{name, 0}

sk-4.211228.31.fid — cyclopentylindole-methylation — C13CPD CDCl3 /opt/...

210.71

138.67
137.62
133.68
124.82
124.46
119.11
117.11
115.85

44.78
32.57
31.90
31.61
27.52
25.42
12.27

f1 (ppm)

54

DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met9 109 (1.860) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)   TOF MS ES+
6.76e6

100-
270.1860

                                    *
                                556.2771

%-

                                          557.2794

                            271.1896
    244.1708
          292.1686

0-
    100   200   300   400   500   600   700   800   900   1000   1100   m/z

Single Mass Analysis
Tolerance = 2.0 mDa   /   DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 2
Monoisotopic Mass, Even Electron Ions
74 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
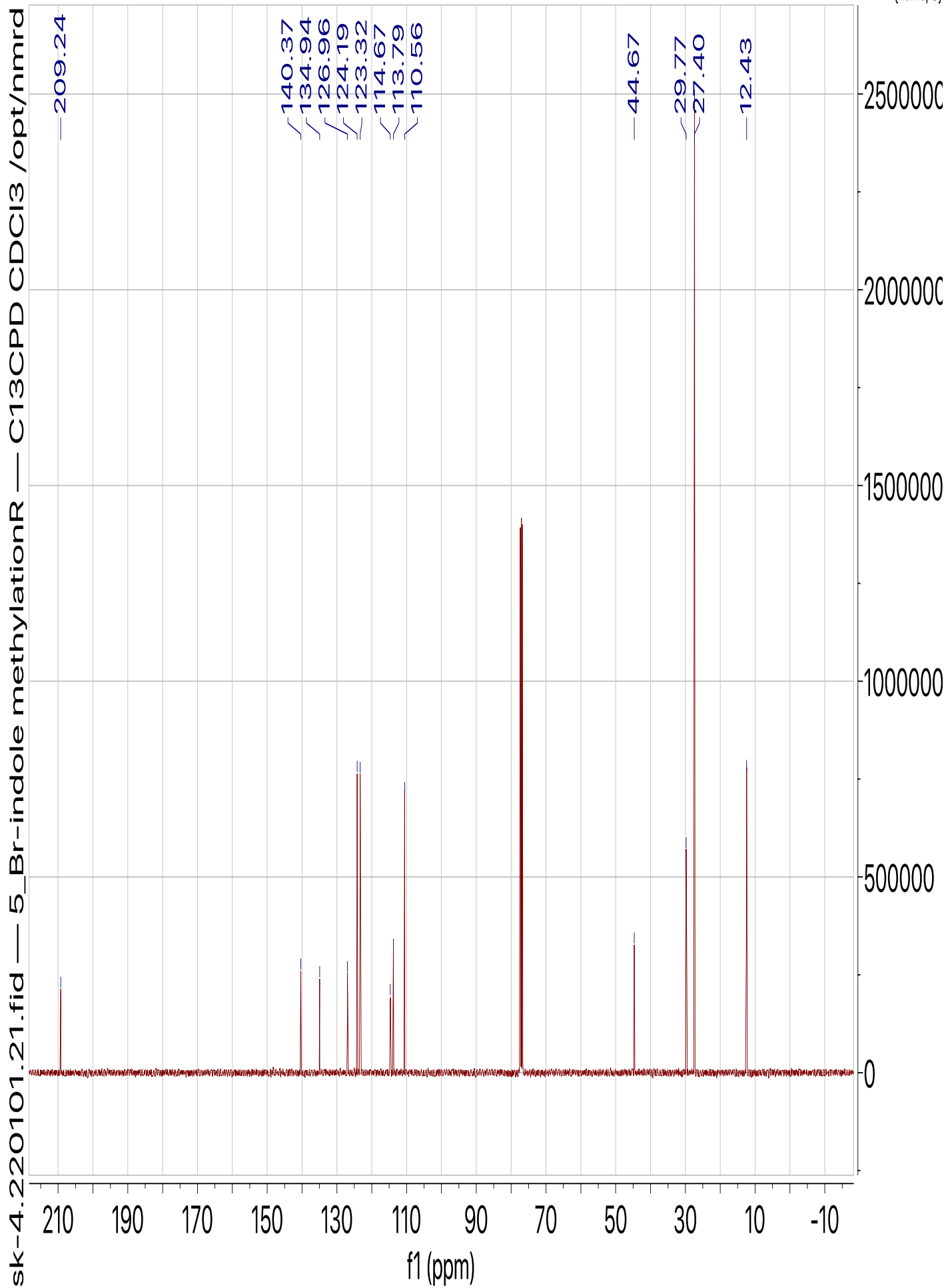Elements Used:
C: 0-60   H: 0-100   N: 0-3   O: 0-4
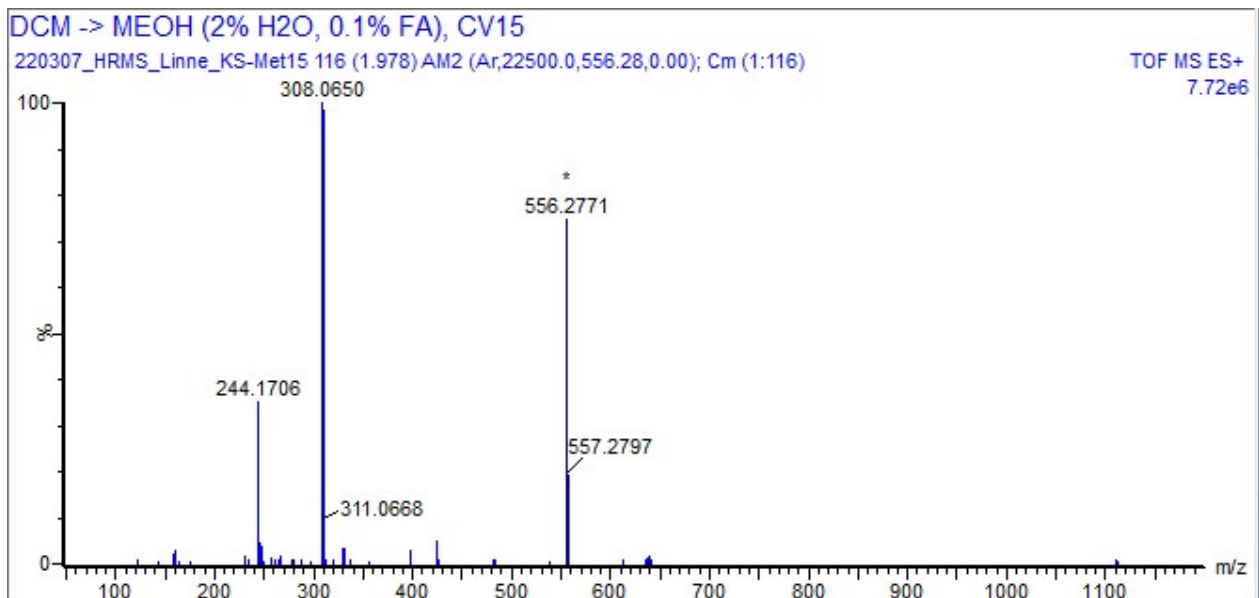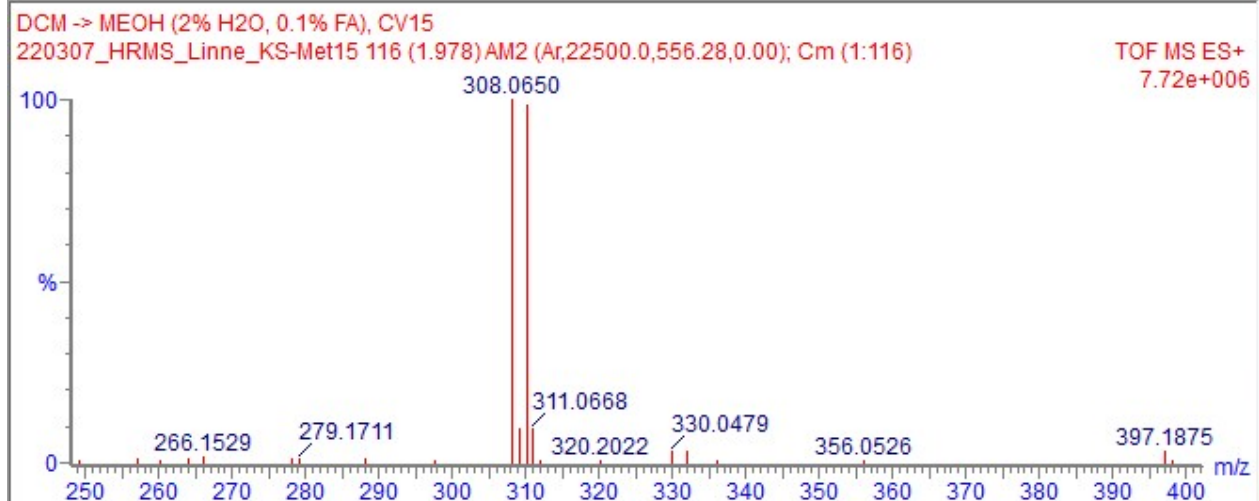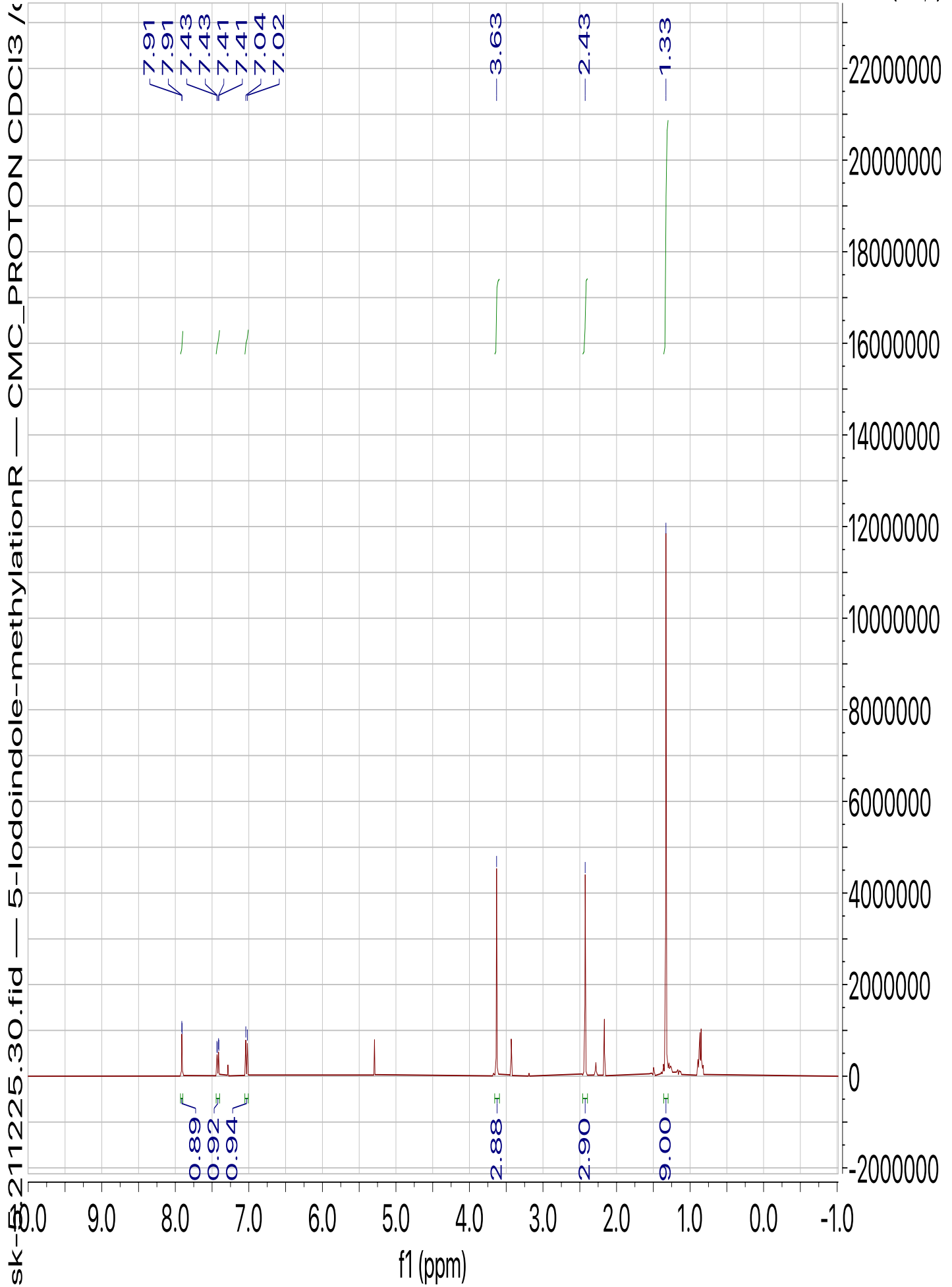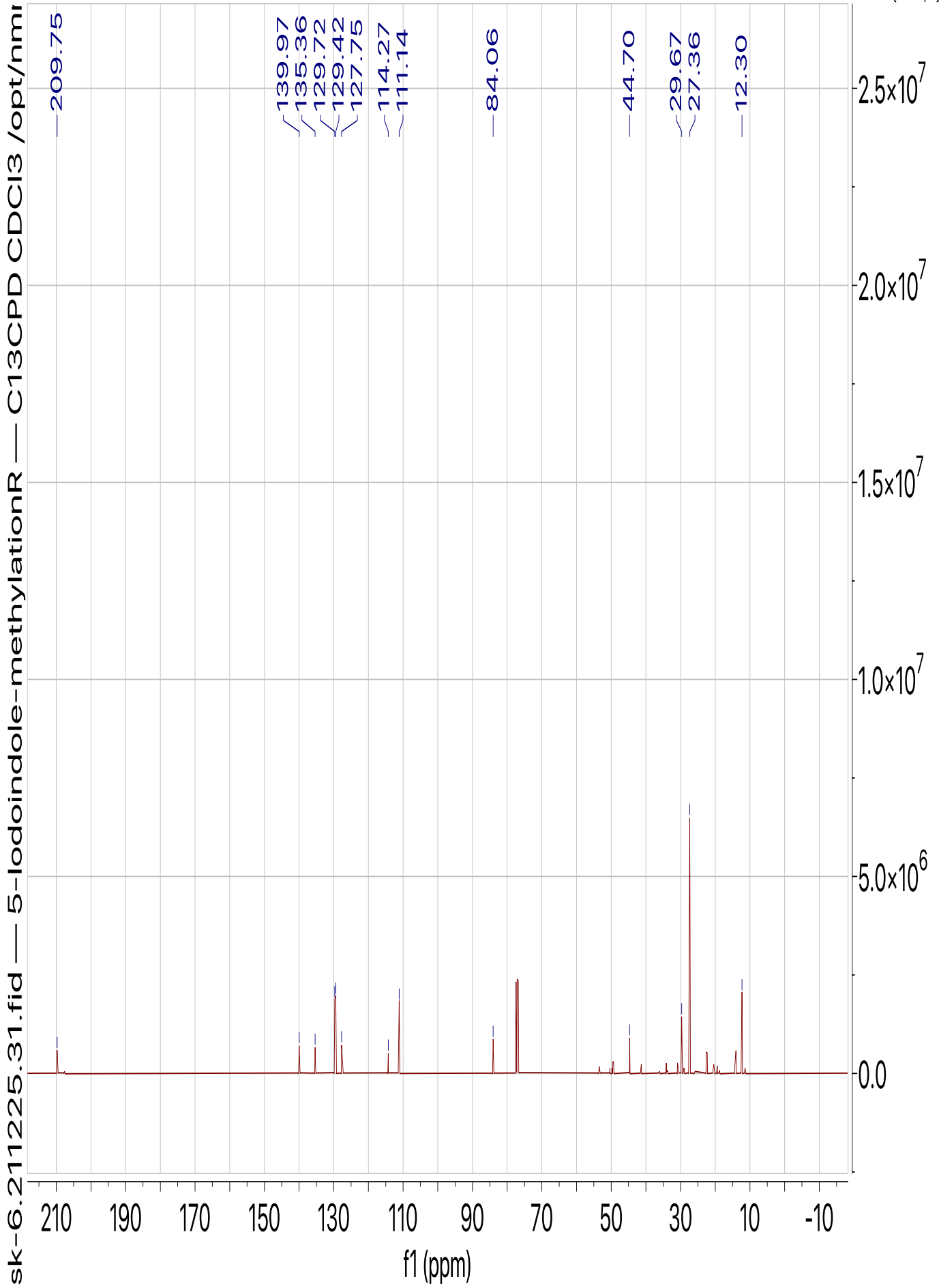
Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
270.1860	270.1858	0.2	0.7	7.5	C18 H24 N O	26.1	n/a	n/a	18	24	1	1

DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met9 109 (1.860) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)   TOF MS ES+
6.76e+006
                                270.1860

100-

%-

                            271.1896

    212.1083   244.1708   269.1790   292.1686
                                              297.6154   336.1932

0-
    200 210 220 230 240 250 260 270 280 290 300 310 320 330 340 350 360   m/z

HRMS spectra of **3m**

3n, ¹H NMR, CDCl₃, 400 MHz

{name, 0}

sk-7-221220.40.fid — 7-Br-indole-methylation — PROTON CDCl3 {D:\nmrd:

7.33
7.33
7.31
7.31
7.24
7.24
7.22
7.22
7.22
7.18
6.85
6.83
6.81

3.98

2.28

1.22

1.00
1.19
1.03

3.12

3.55

9.63

f1 (ppm)

3n, ^{13}C NMR (101 MHz, CDCl$_3$)

{name, 0}

sk-8.221220.41.fid — 7-Br-indole-methylation — C13CPD CDCl3 {D:\nmrda

211.32

138.03
132.63
128.71
126.95
121.07
119.62
115.97

103.58

45.35

32.65
27.40

12.63

f1 (ppm)

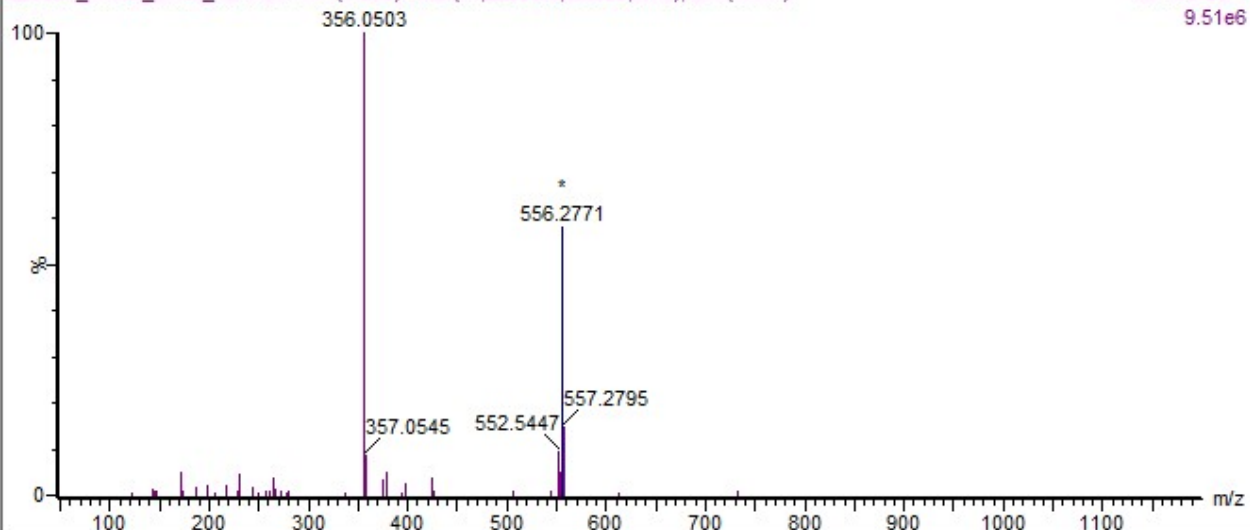210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met16 101 (1.725) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)   TOF MS ES+
8.57e6

308.0648
556.2771
557.2796
288.1604
311.0668
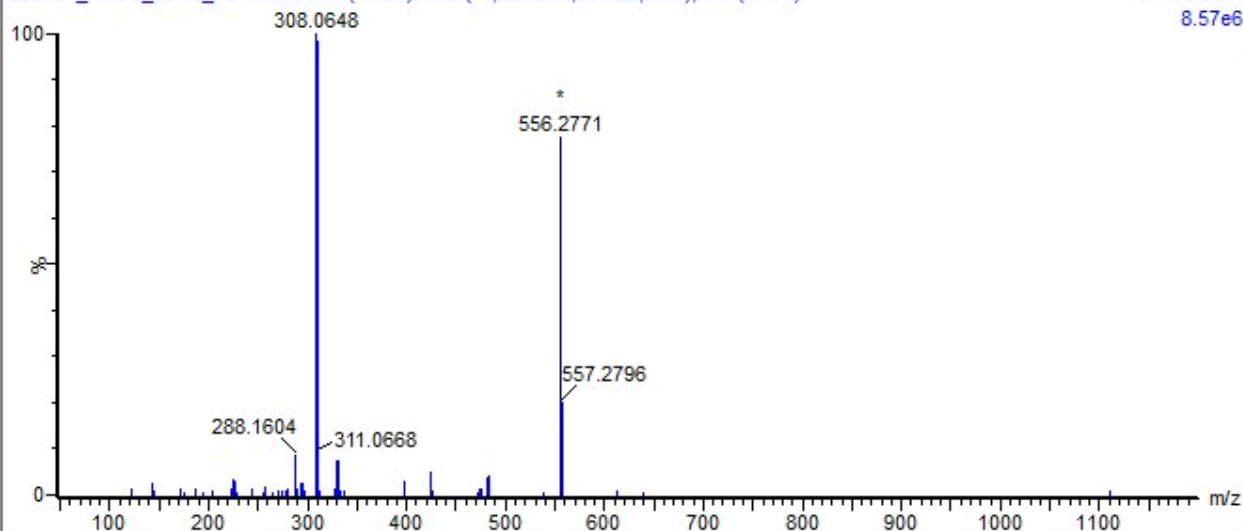
Single Mass Analysis
Tolerance = 2.0 mDa   /   DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 2
Monoisotopic Mass, Even Electron Ions
147 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
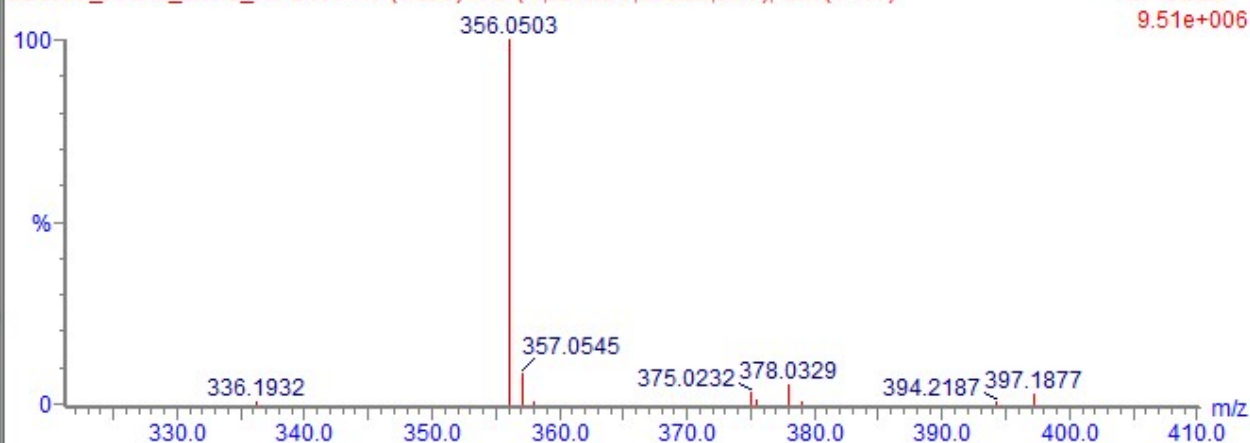Elements Used:
C: 0-60   H: 0-100   N: 0-3   O: 0-4   Br: 0-1

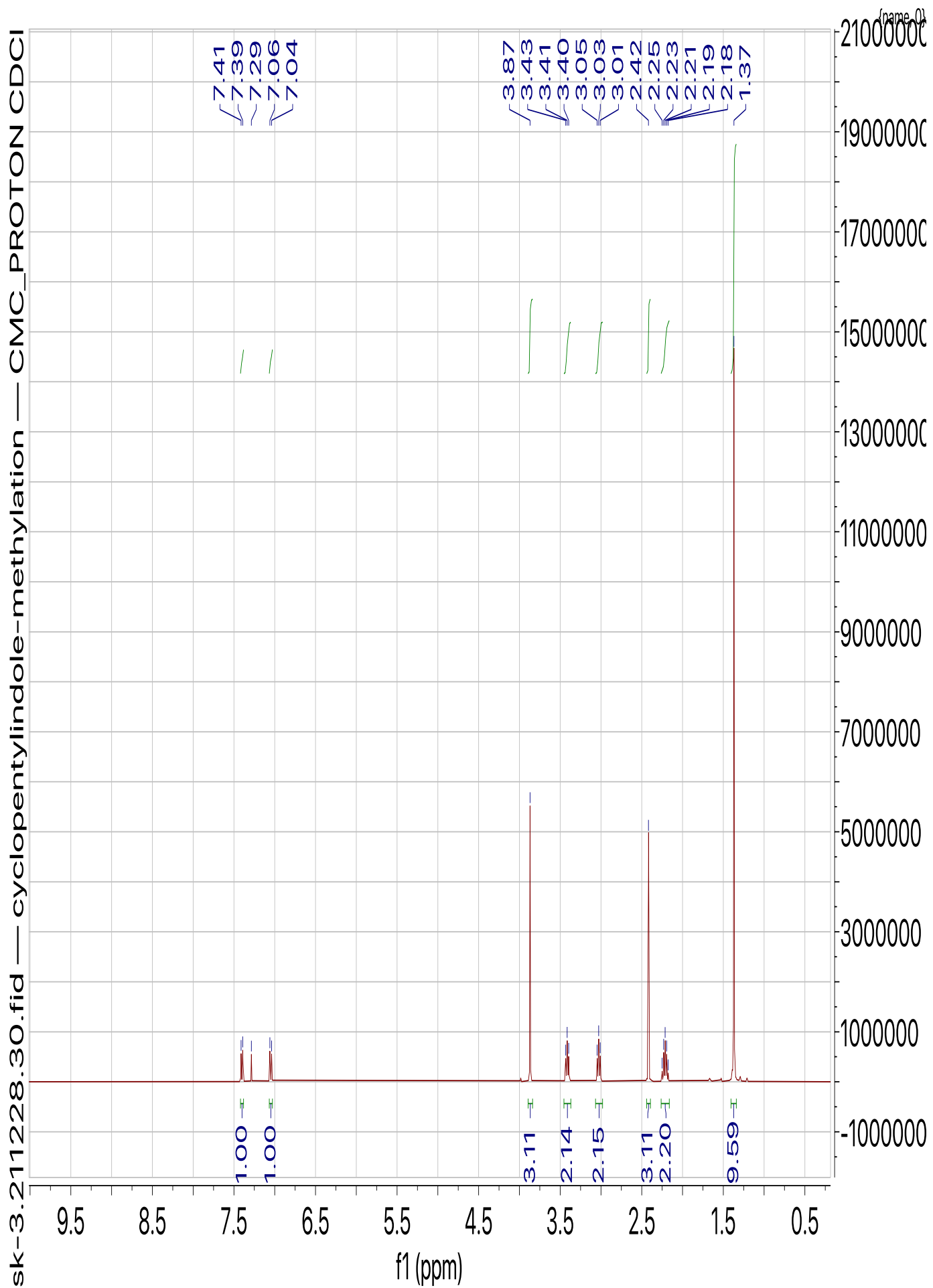| Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-...	i-FIT Norm	Fit Conf %	C	H	N	O	Br
308.0648	308.0650	-0.2	-0.6	6.5	C15 H19 N O Br	2...	n/a	n/a	15	19	1	1	1

DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met16 101 (1.725) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)   TOF MS ES+
8.57e+006

308.0648
224.0077
257.0645
288.1604
311.0668 330.0473
397.1878

HRMS spectra of **3n**

3o, ¹H NMR (400 MHz, CDCl₃)

{name, 0}

3o, ^{13}C NMR (101 MHz, CDCl$_3$)

{name, 0}

sk.211221.31.fid — 7-Meindole methylation-A-R — C13CPD CDCl3 /opt/nmrc

211.48

137.44
135.07
126.36
124.63
120.68
120.11
118.75
115.94

45.05

32.74
28.13
27.49
20.57
12.46

f1 (ppm)

60

DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met5 112 (1.911) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)   TOF MS ES+
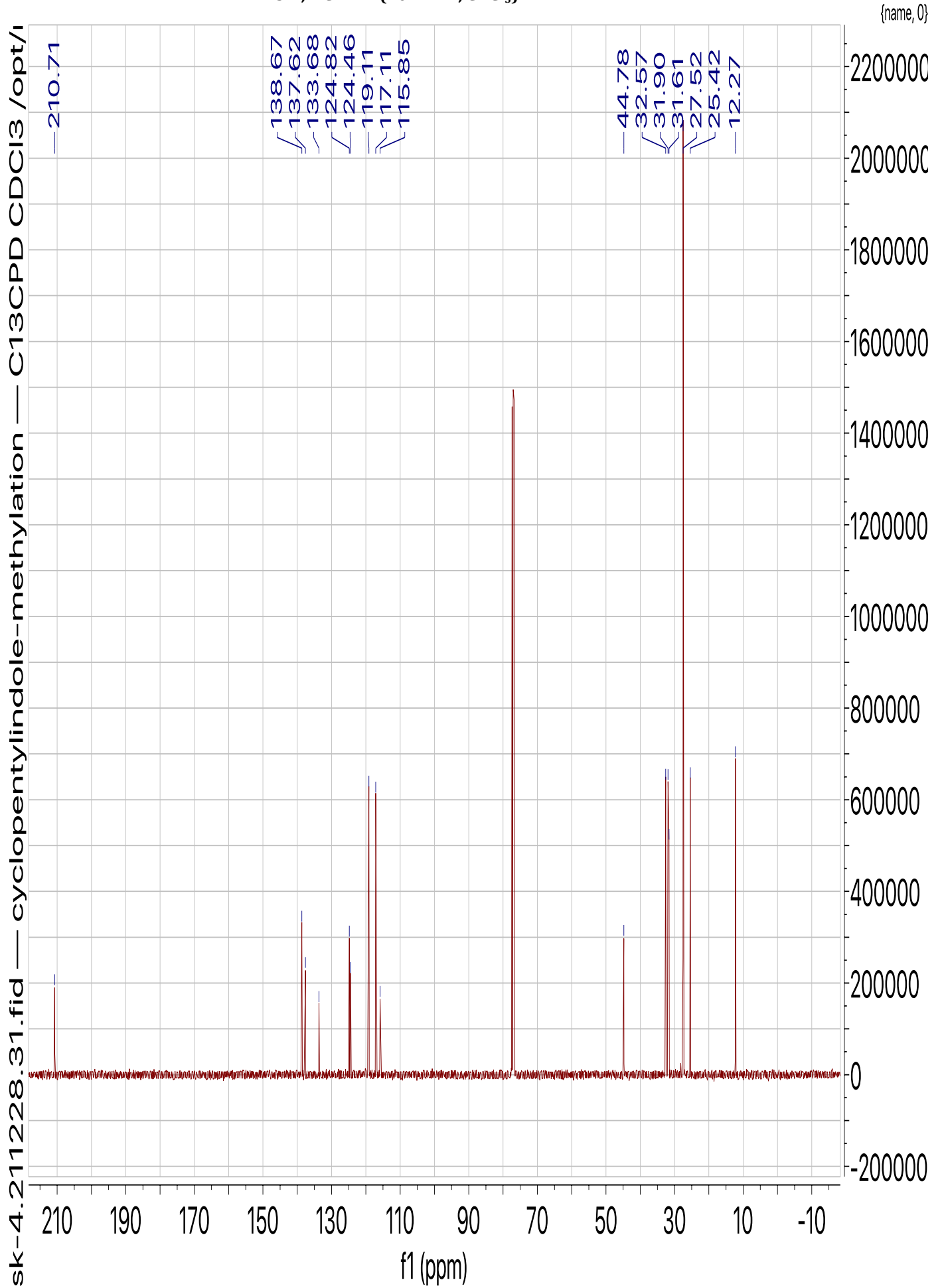   7.92e6

Single Mass Analysis
Tolerance = 2.0 mDa   /   DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 2
Monoisotopic Mass, Even Electron Ions
66 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-60   H: 0-100   N: 0-3   O: 0-4

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
244.1703	244.1701	0.2	0.8	6.5	C16 H22 N O	26.3	n/a	n/a	16	22	1	1

DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met5 112 (1.911) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)   TOF MS ES+
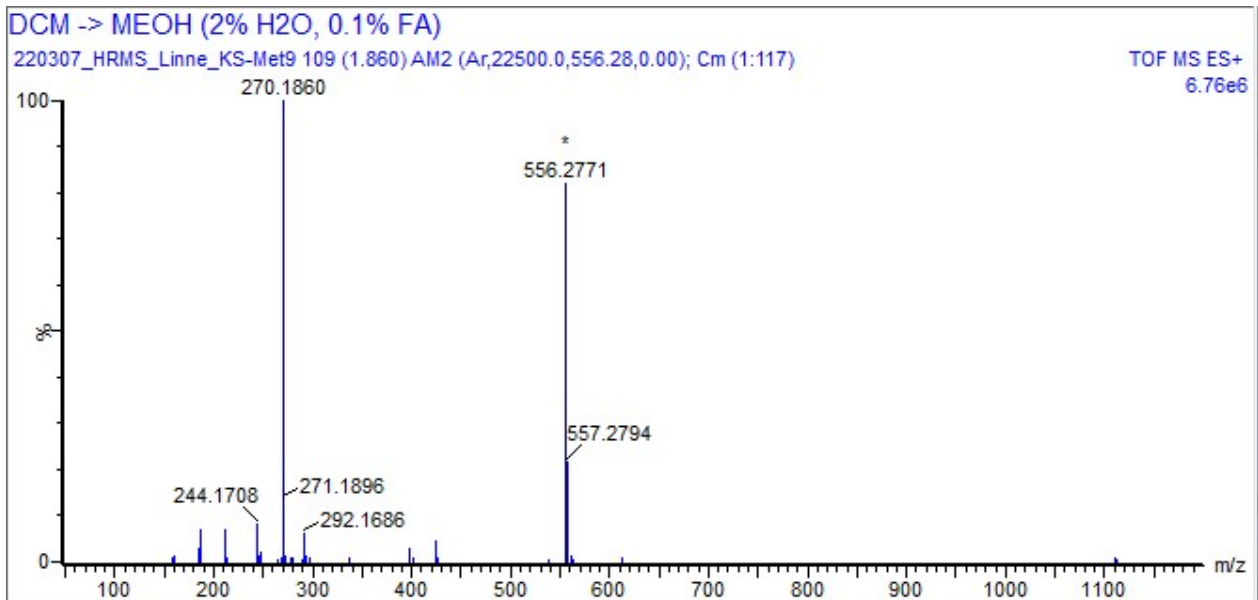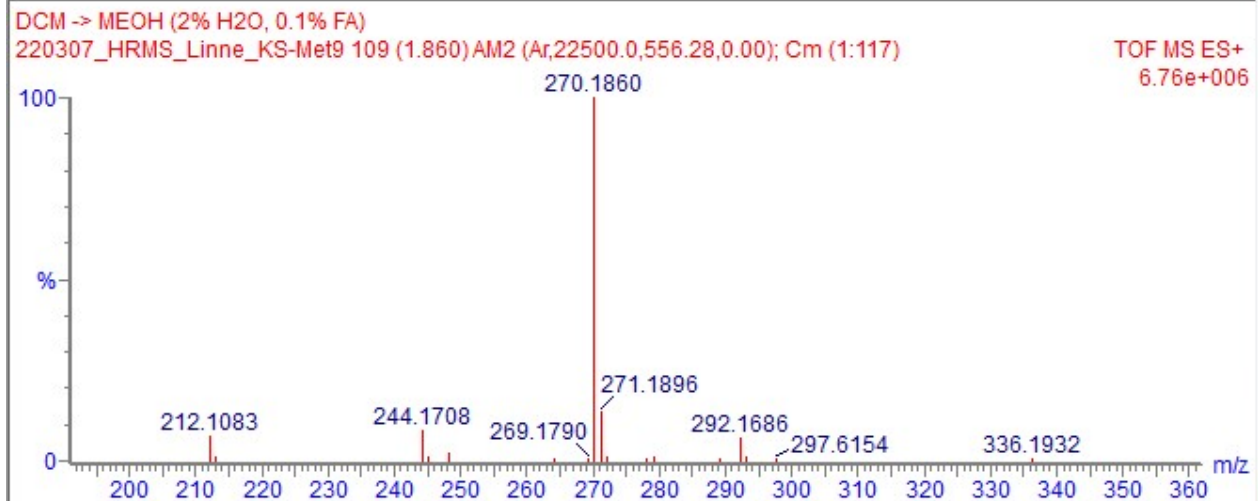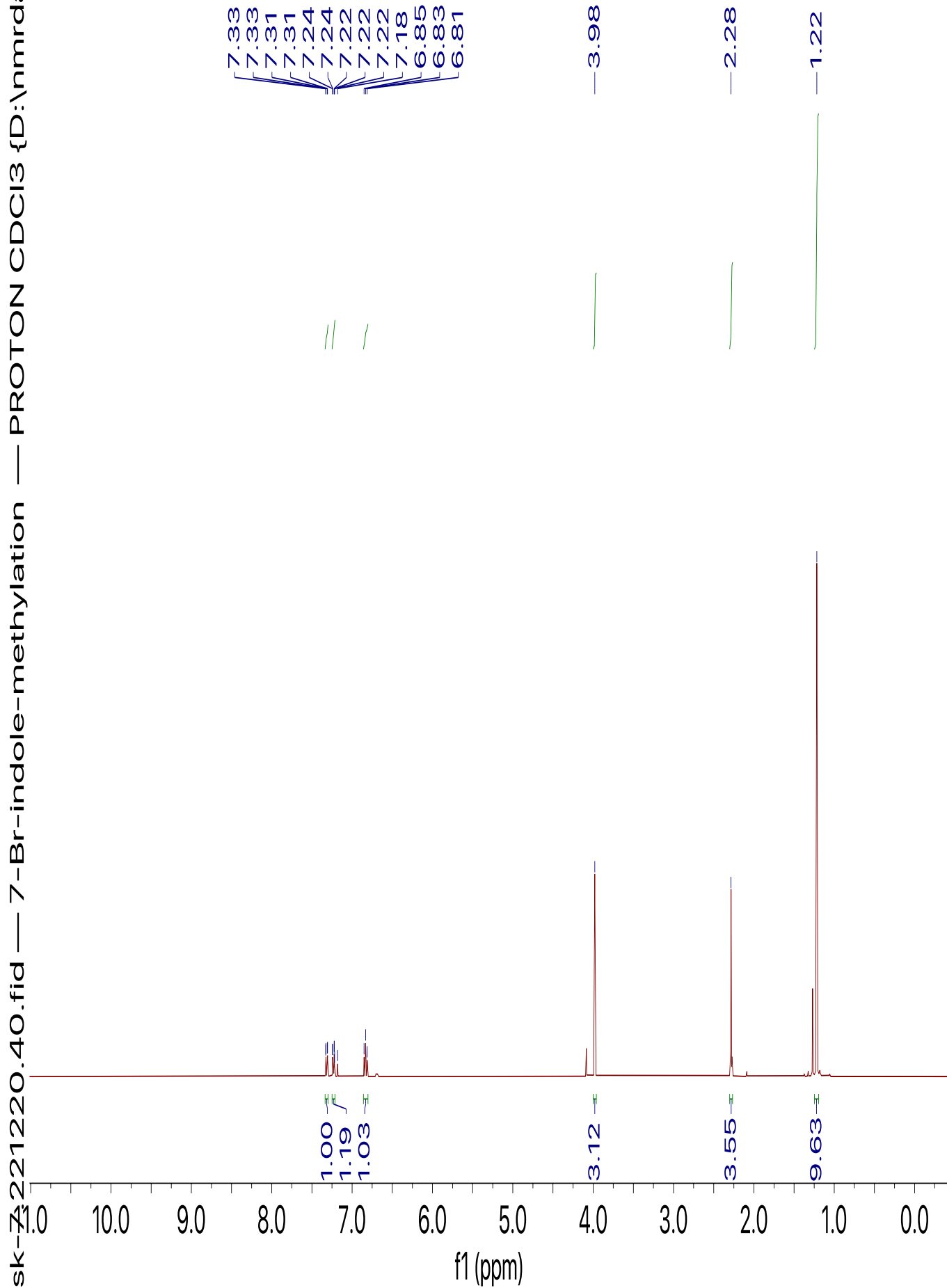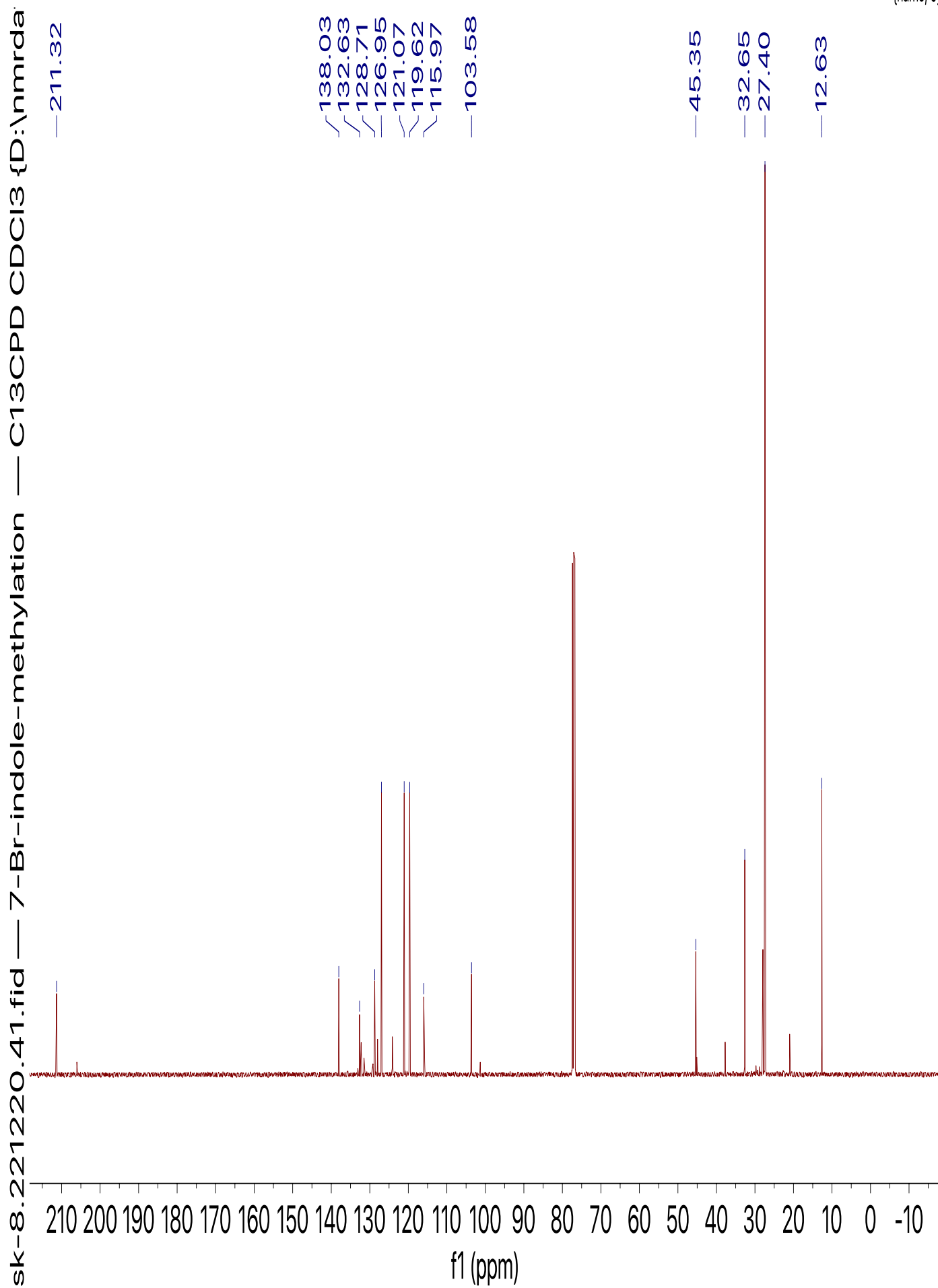   7.92e+006
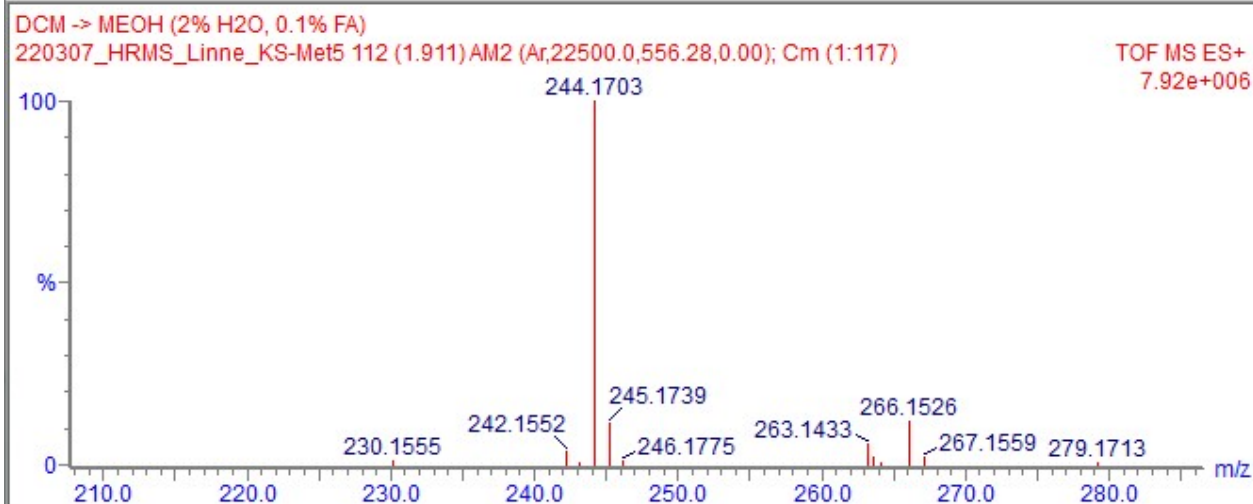
HRMS spectra of **3o**

3p, ^{1}H NMR, CDCl$_3$, 400 MHz
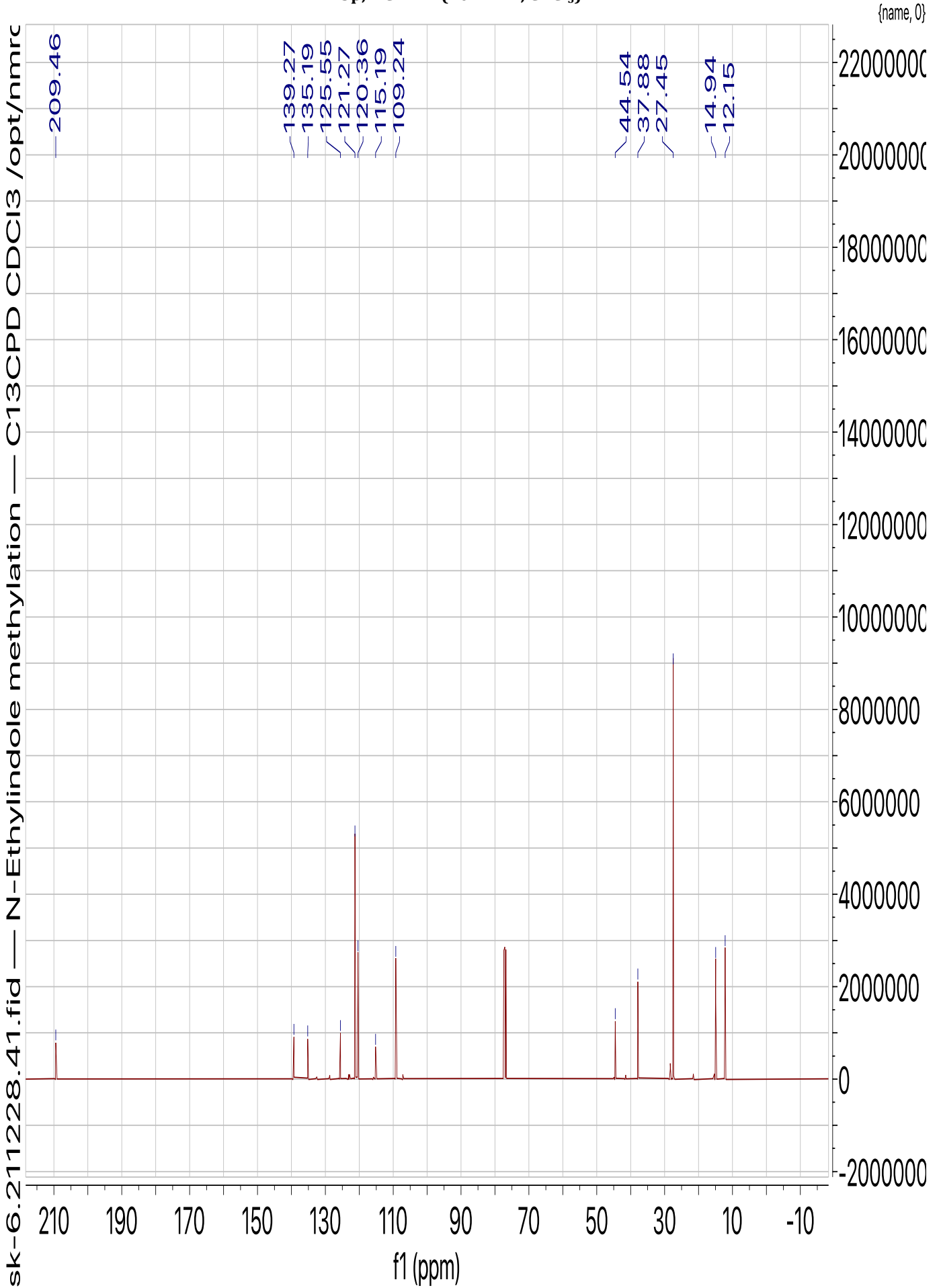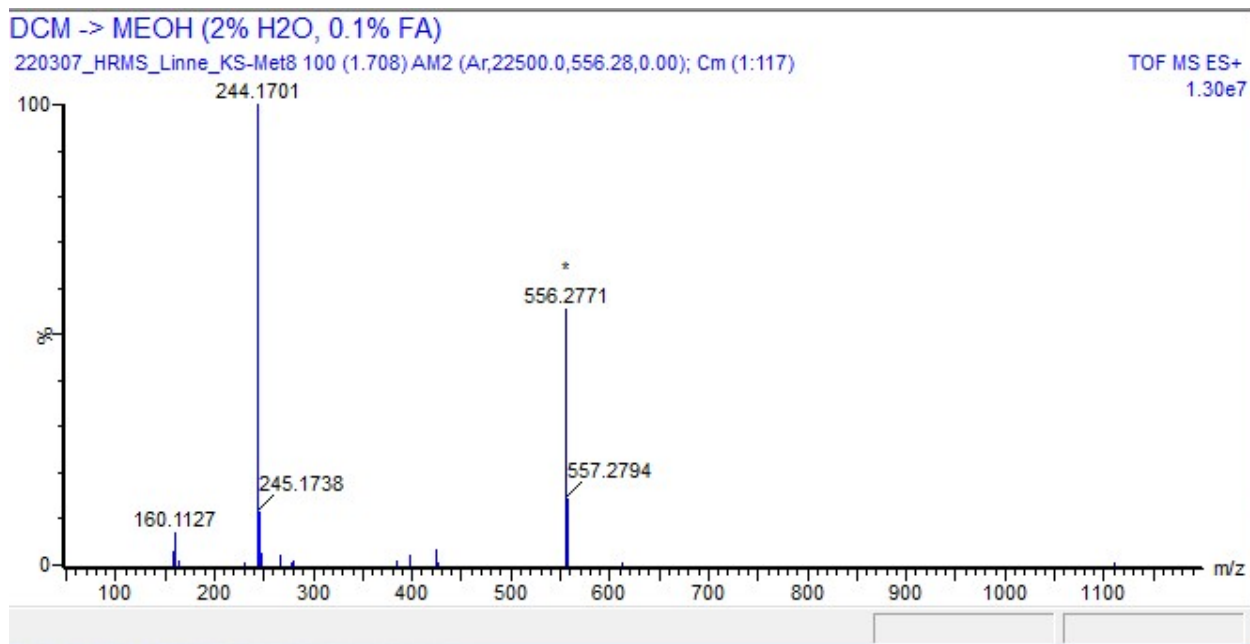
sk-5.211228.40.fid — N-Ethylindole methylation — CMC_PROTON CDCl3 /ol

{name, 0}

Peaks (ppm): 7.72, 7.70, 7.70, 7.34, 7.32, 7.32, 7.29, 7.24, 7.24, 7.23, 7.22, 7.21, 7.20, 7.20, 7.18, 7.18, 7.17, 7.16, 4.21, 4.19, 4.17, 4.16, 2.52, 1.41

Integrations: 1.00, 1.01, 2.22, 2.22, 3.13, 9.35, 2.66

3p, ^{13}C NMR (101 MHz, CDCl$_3$)

sk-6.211228.41.fid — N-Ethylindole methylation — C13CPD CDCl3 /opt/nmrc

209.46

139.27
135.19
125.55
121.27
120.36
115.19
109.24

44.54
37.88
27.45

14.94
12.15

f1 (ppm)

220307_HRMS_Linne_KS-Met8 100 (1.708) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)   TOF MS ES+
                                                                                                   1.30e7

100   244.1701

                                      *
                              556.2771

%

                                      557.2794
      160.1127   245.1738

0
      100   200   300   400   500   600   700   800   900   1000   1100   m/z

Single Mass Analysis
Tolerance = 2.0 mDa   /   DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 2
Monoisotopic Mass, Even Electron Ions
66 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
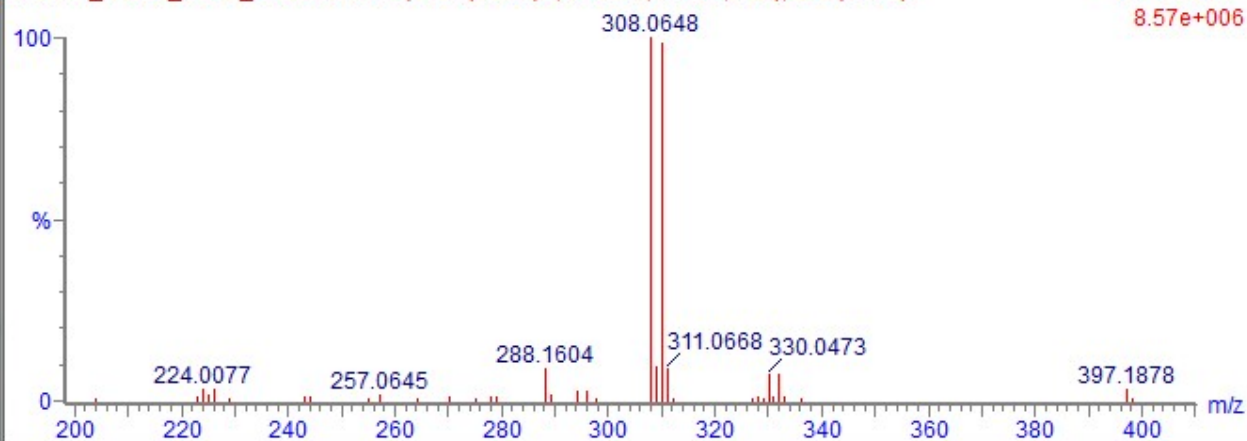Elements Used:
C: 0-60   H: 0-100   N: 0-3   O: 0-4

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Nor...	Fit Conf %	C	H	N	O
244.1701	244.1701	0.0	0.0	6.5	C16 H22 N O	50.8	n/a	n/a	16	22	1	1

DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met8 100 (1.708) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)   TOF MS ES+
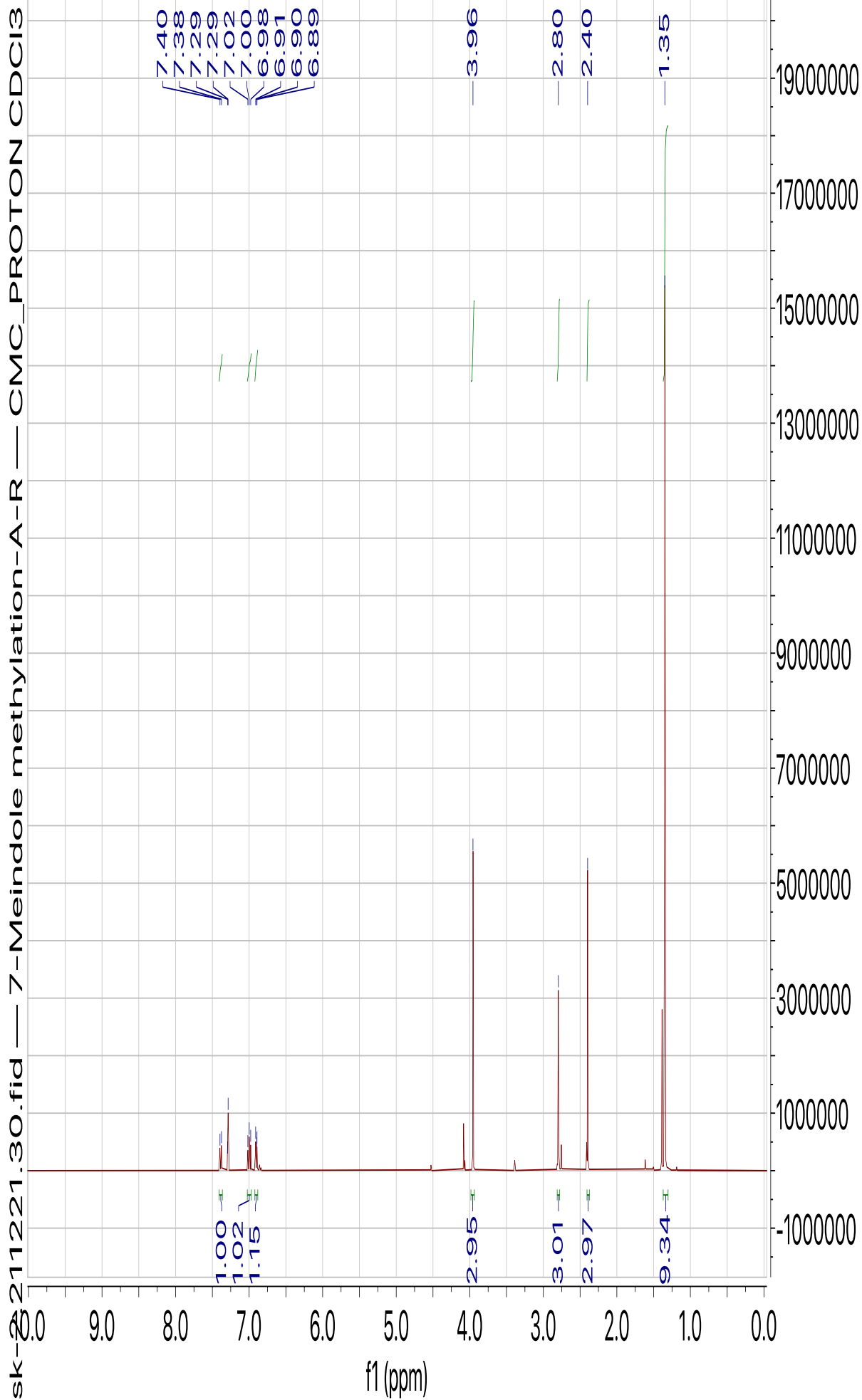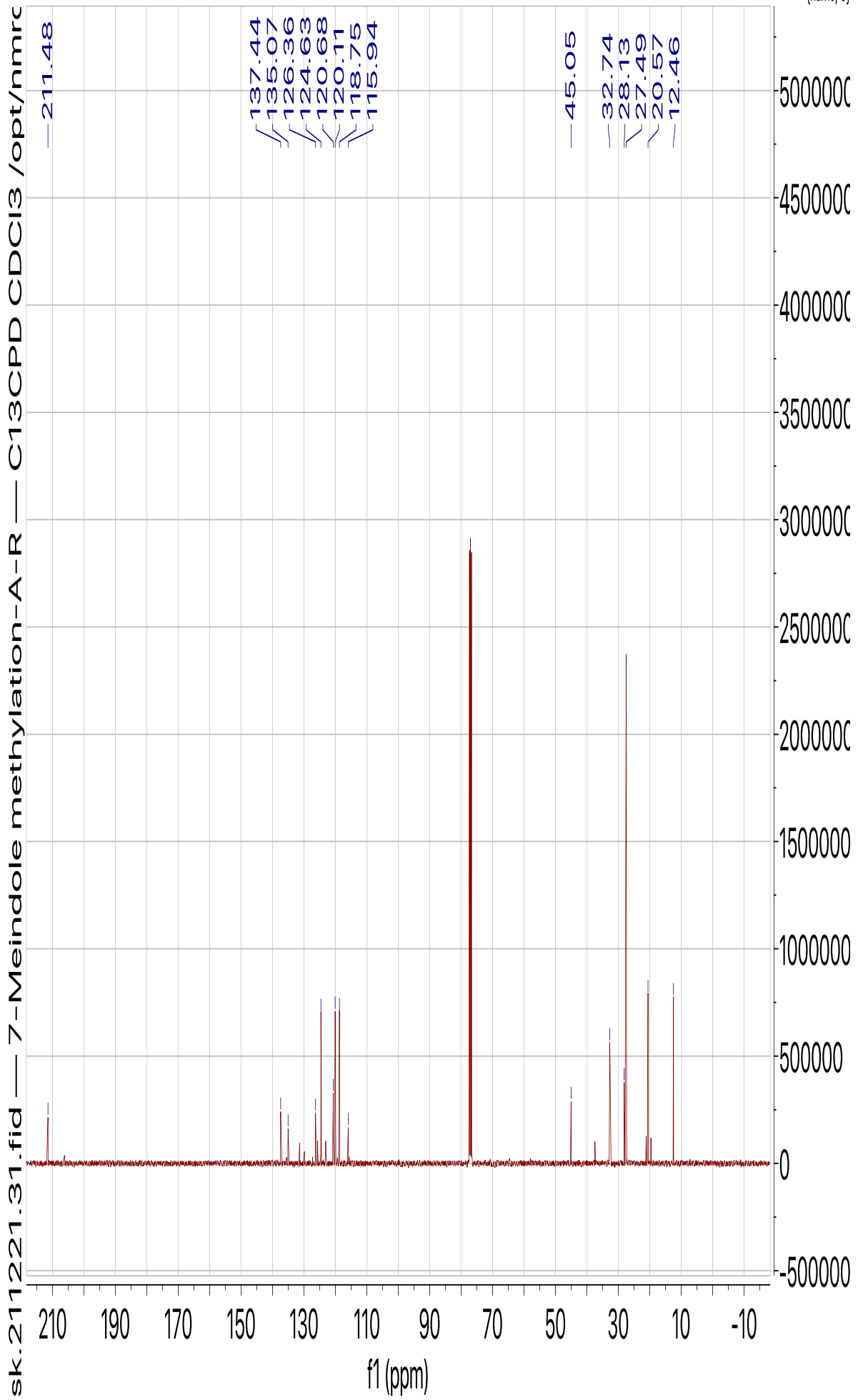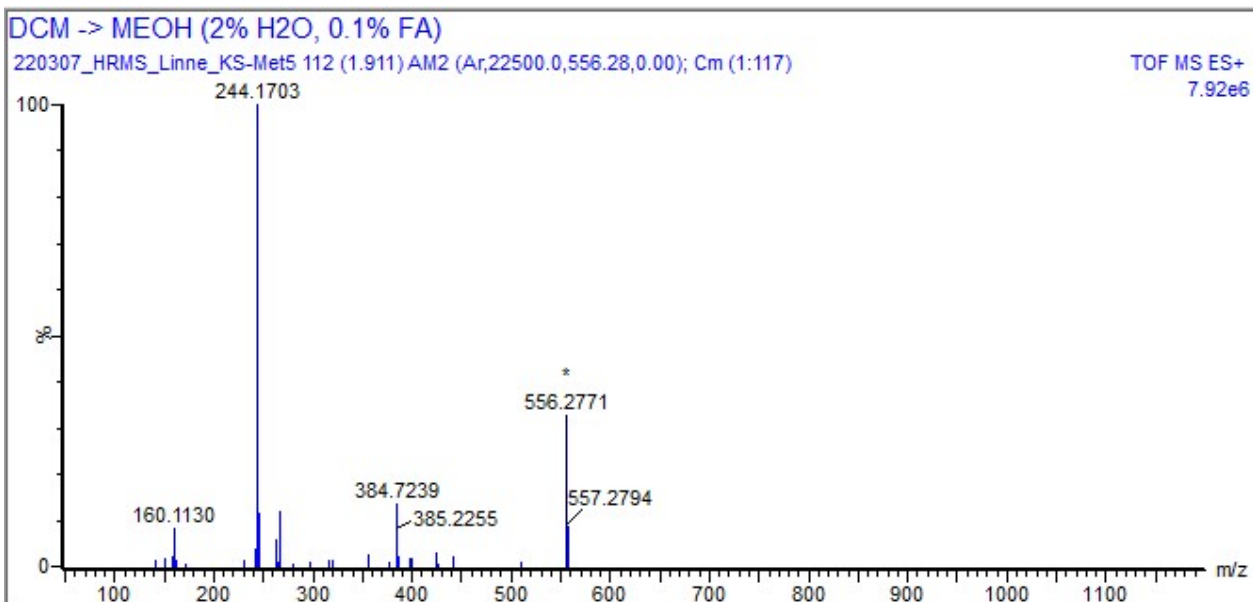   1.30e+007
100   244.1701

%

                          245.1738
                                    248.1456   266.1527
         230.1554   279.1710
0
   170 180 190 200 210 220 230 240 250 260 270 280 290 300 310 320   m/z

HRMS spectra of **3p**

3q, ^{1}H NMR, CDCl$_3$, 400 MHz
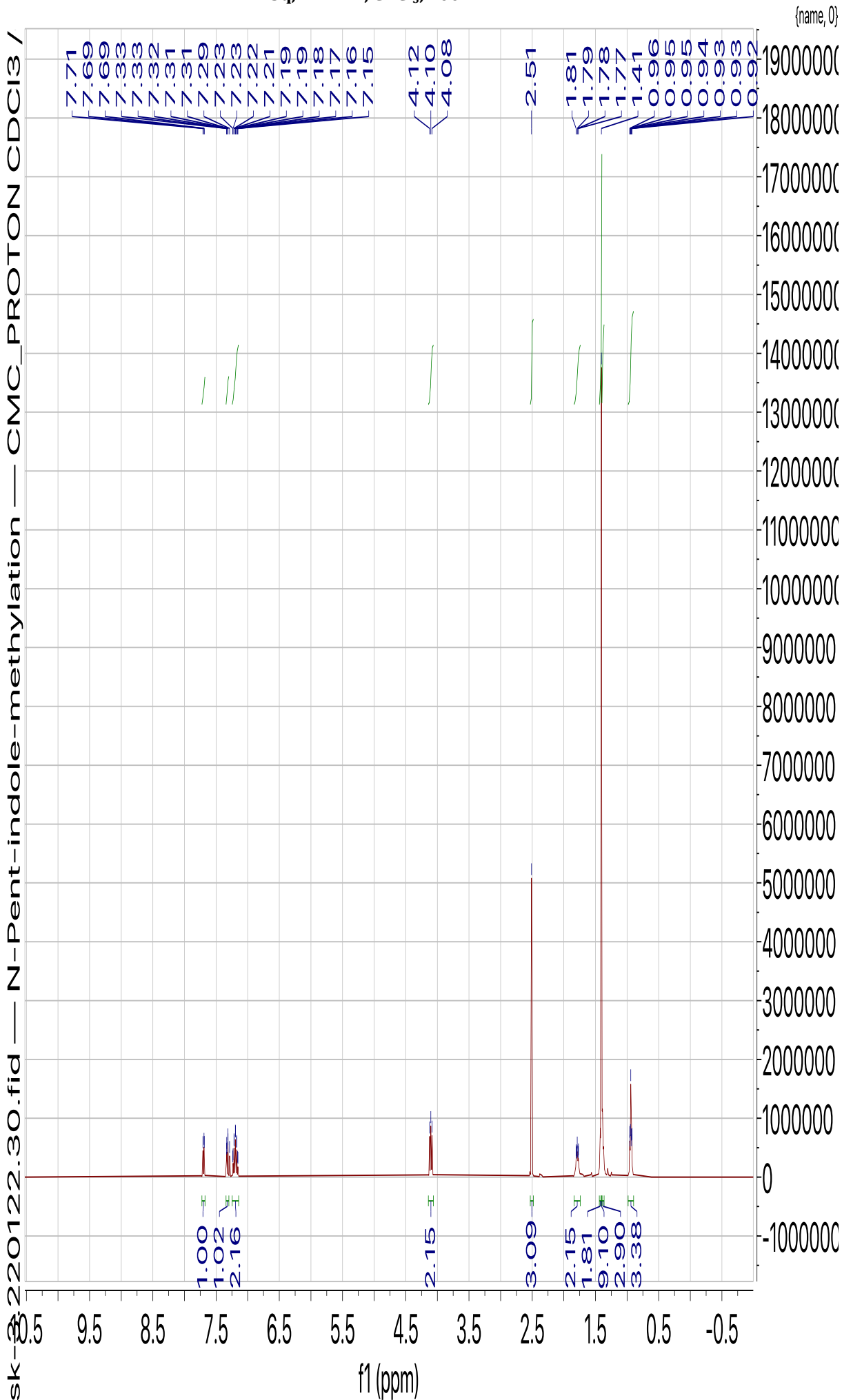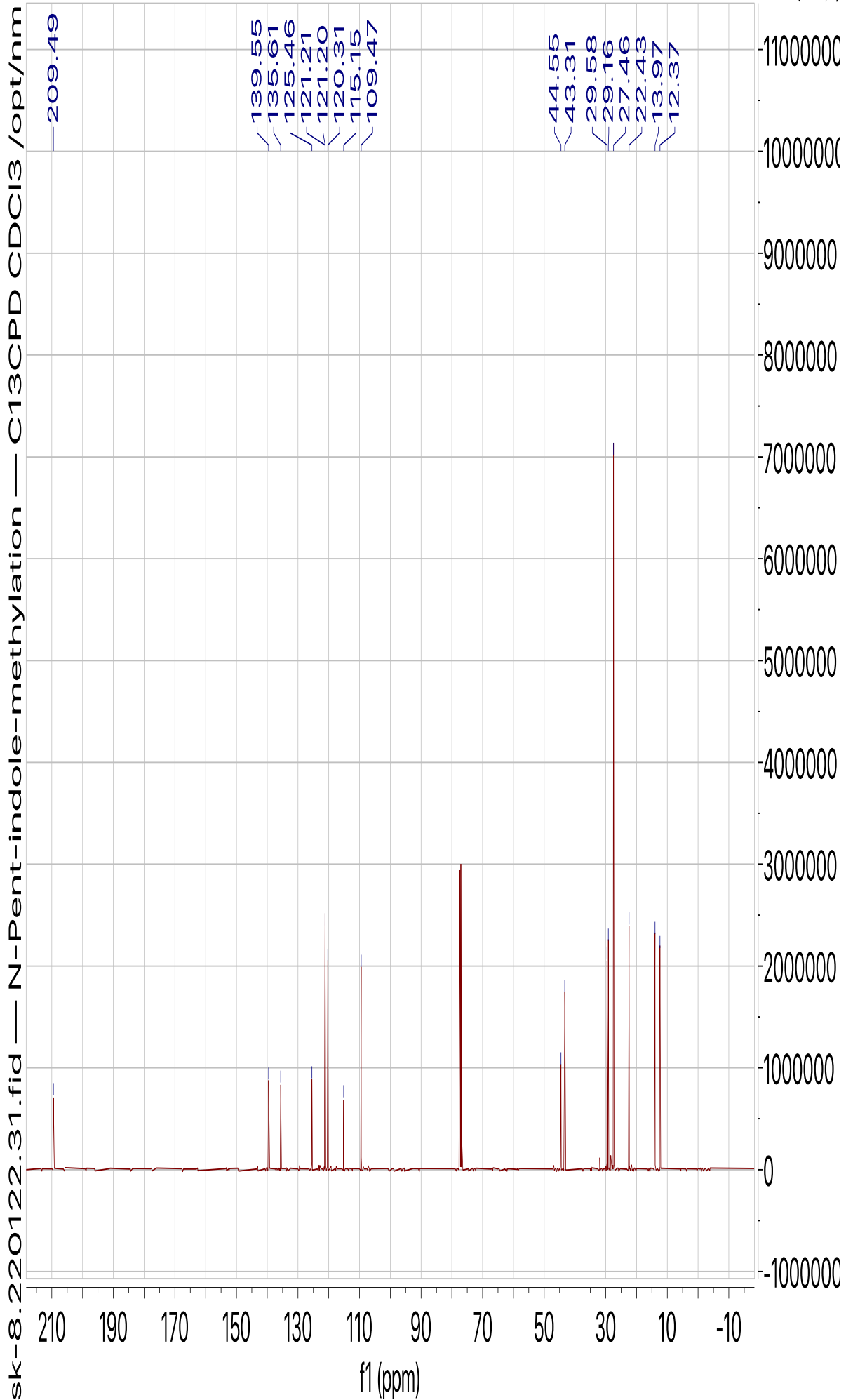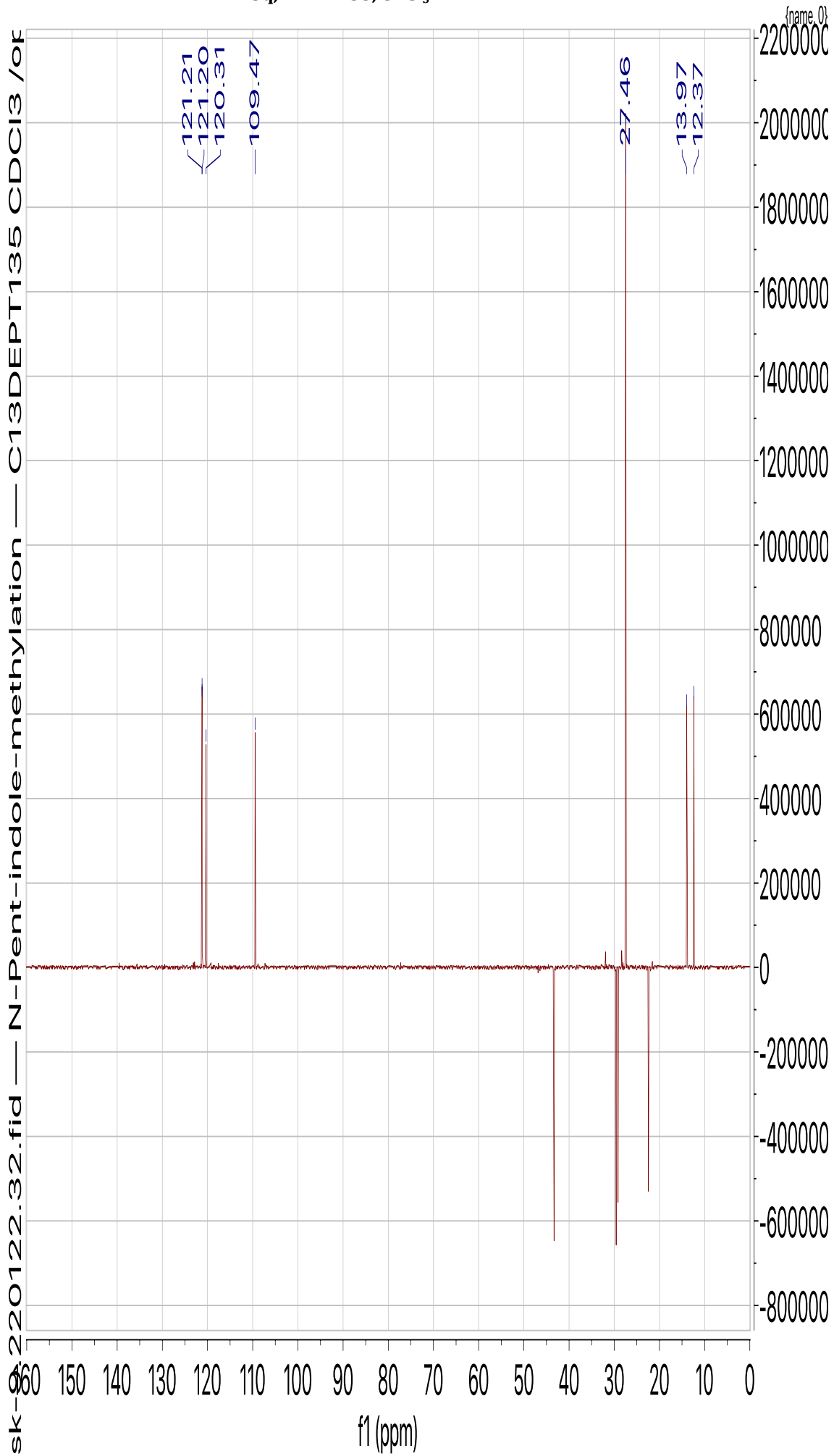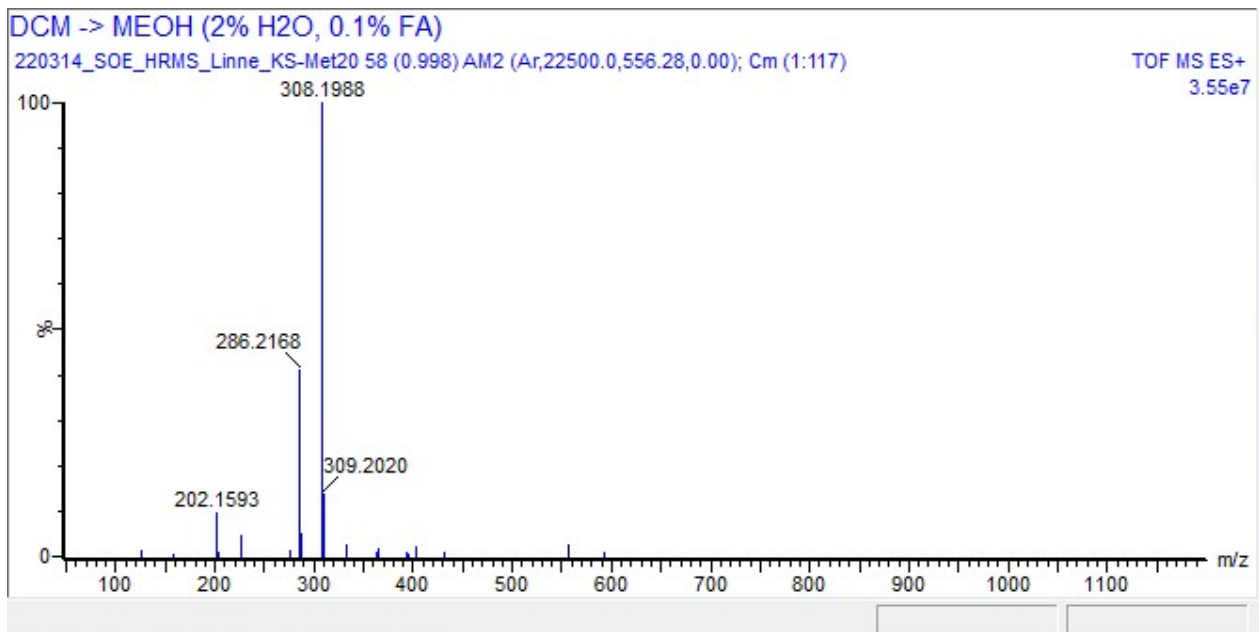
sk-3q 220122.30.fid — N-Pent-indole-methylation — CMC_PROTON CDCl3 /

7.71, 7.69, 7.69, 7.33, 7.33, 7.32, 7.31, 7.31, 7.29, 7.23, 7.23, 7.22, 7.21, 7.19, 7.19, 7.18, 7.17, 7.16, 7.15

4.12, 4.10, 4.08

2.51

1.81, 1.79, 1.78, 1.77, 1.41

0.96, 0.95, 0.95, 0.94, 0.93, 0.93, 0.92

1.00, 1.02, 2.16

2.15

3.09

2.15, 1.81, 9.10, 2.90, 3.38

65

3q, ¹³C NMR (101 MHz, CDCl₃)

sk-8.220122.31.fid — N-Pent-indole-methylation — C13CPD CDCl3 /opt/nmr

209.49

139.55
135.61
125.46
121.21
121.20
120.31
115.15
109.47

44.55
43.31
29.58
29.16
27.46
22.43
13.97
12.37

66

3q, DPET-135, CDCl₃

100
308.1988

%
286.2168

309.2020
202.1593
0
m/z
100 200 300 400 500 600 700 800 900 1000 1100

Single Mass Analysis
Tolerance = 3.0 mDa / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 2
Monoisotopic Mass, Even Electron Ions
95 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
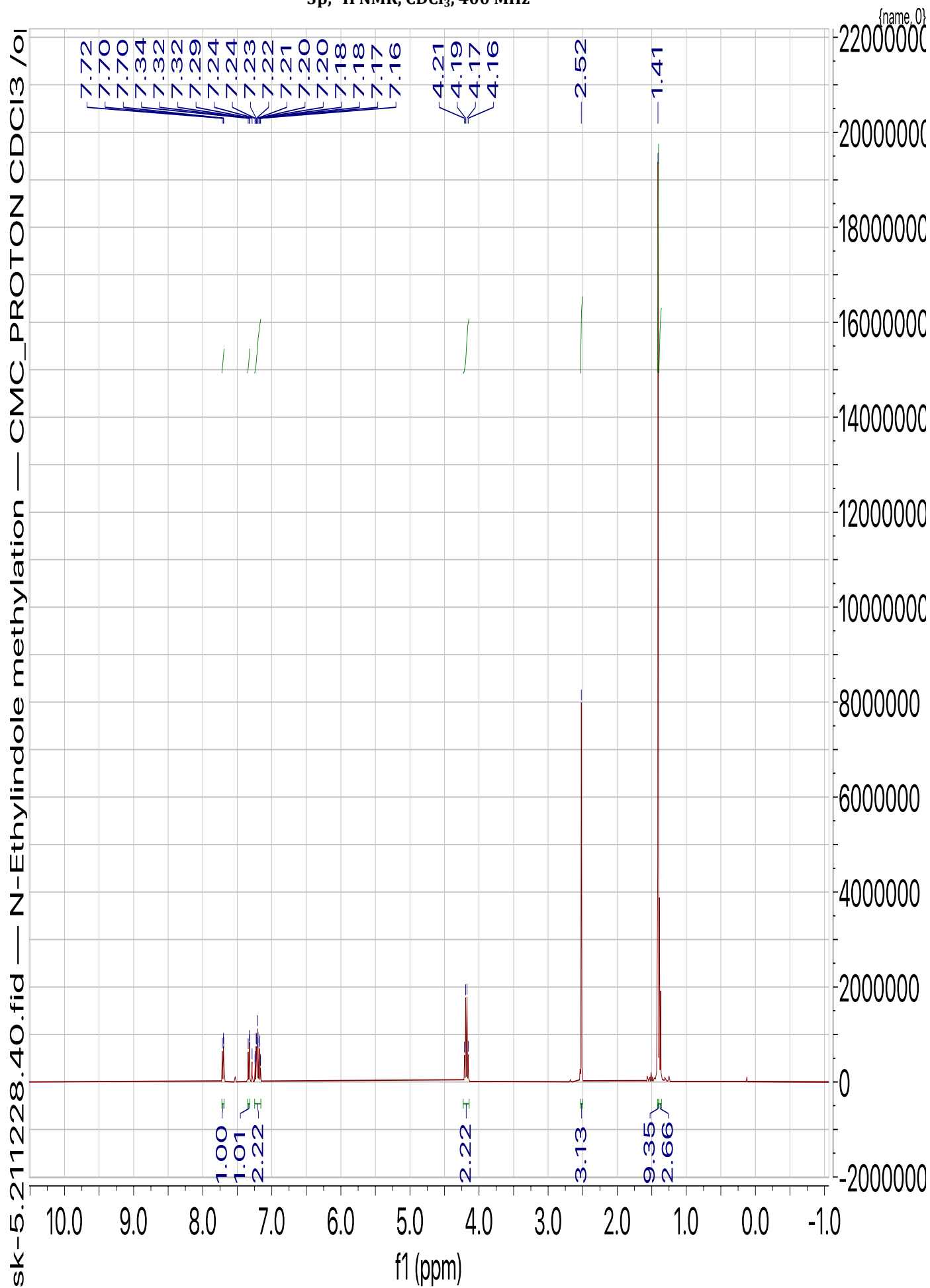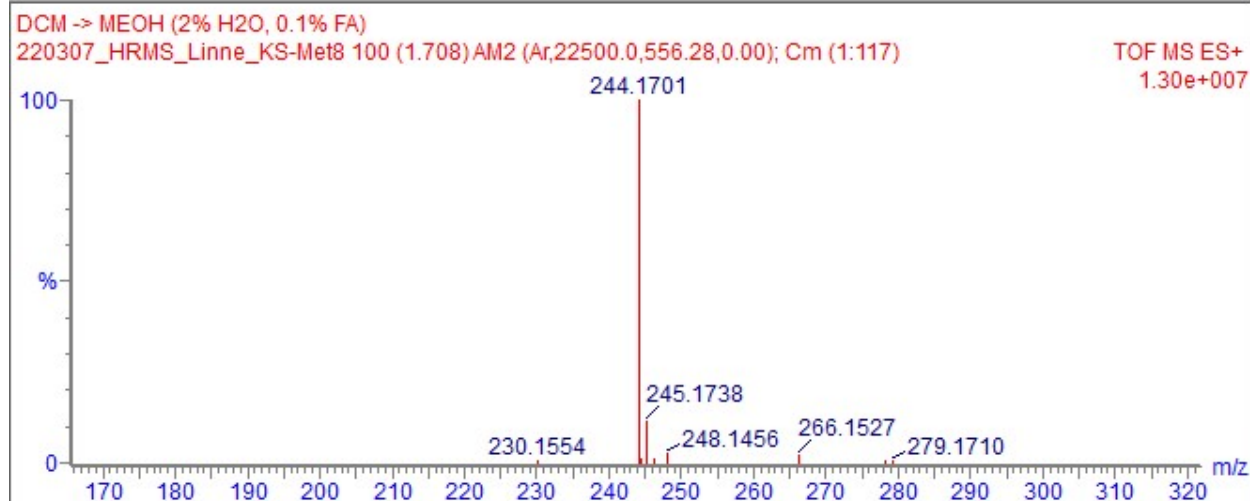Elements Used:
C: 0-60   H: 0-100   N: 0-1   O: 0-20

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
286.2168	286.2171	-0.3	-1.0	6.5	C19 H28 N O	29.1	n/a	n/a	19	28	1	1
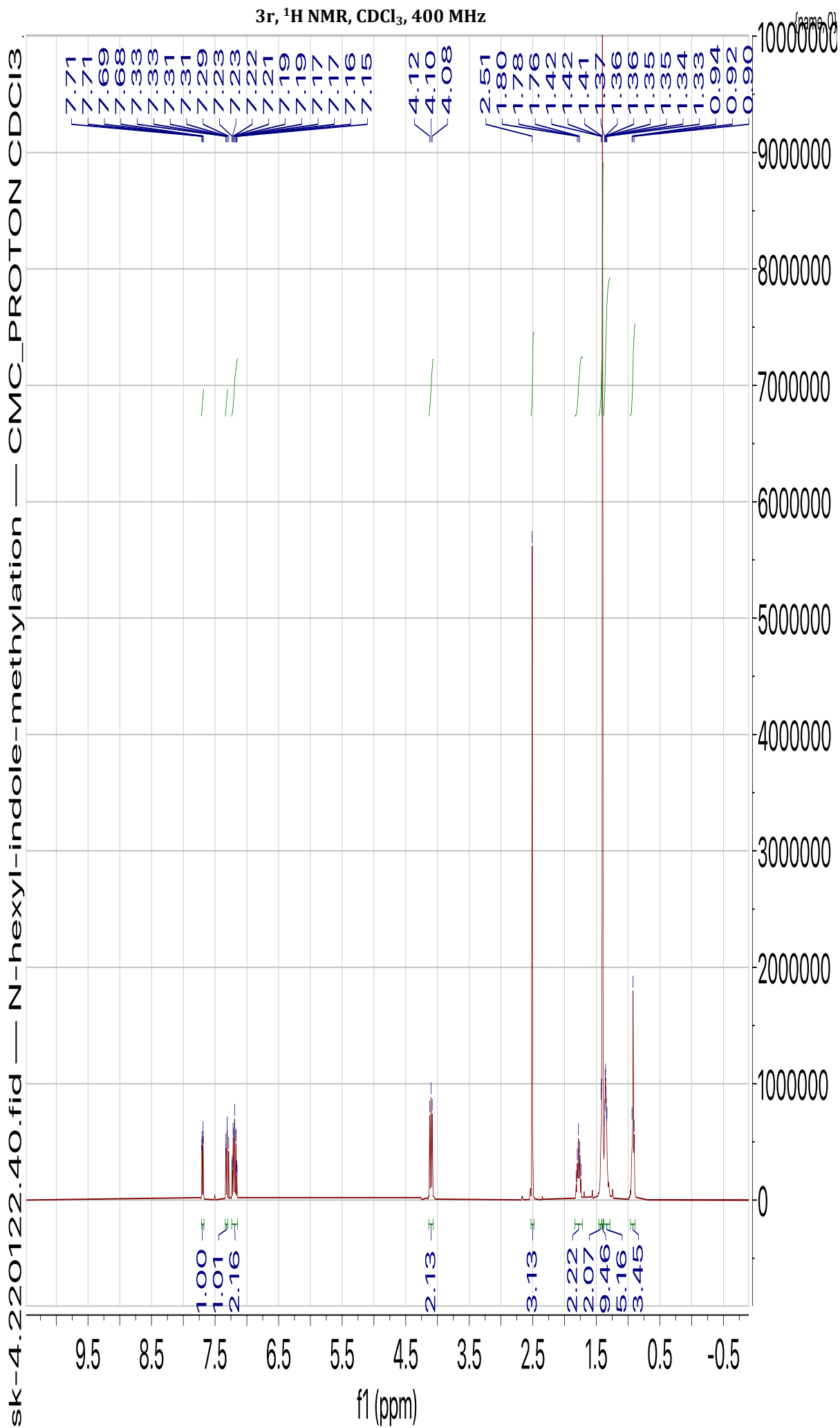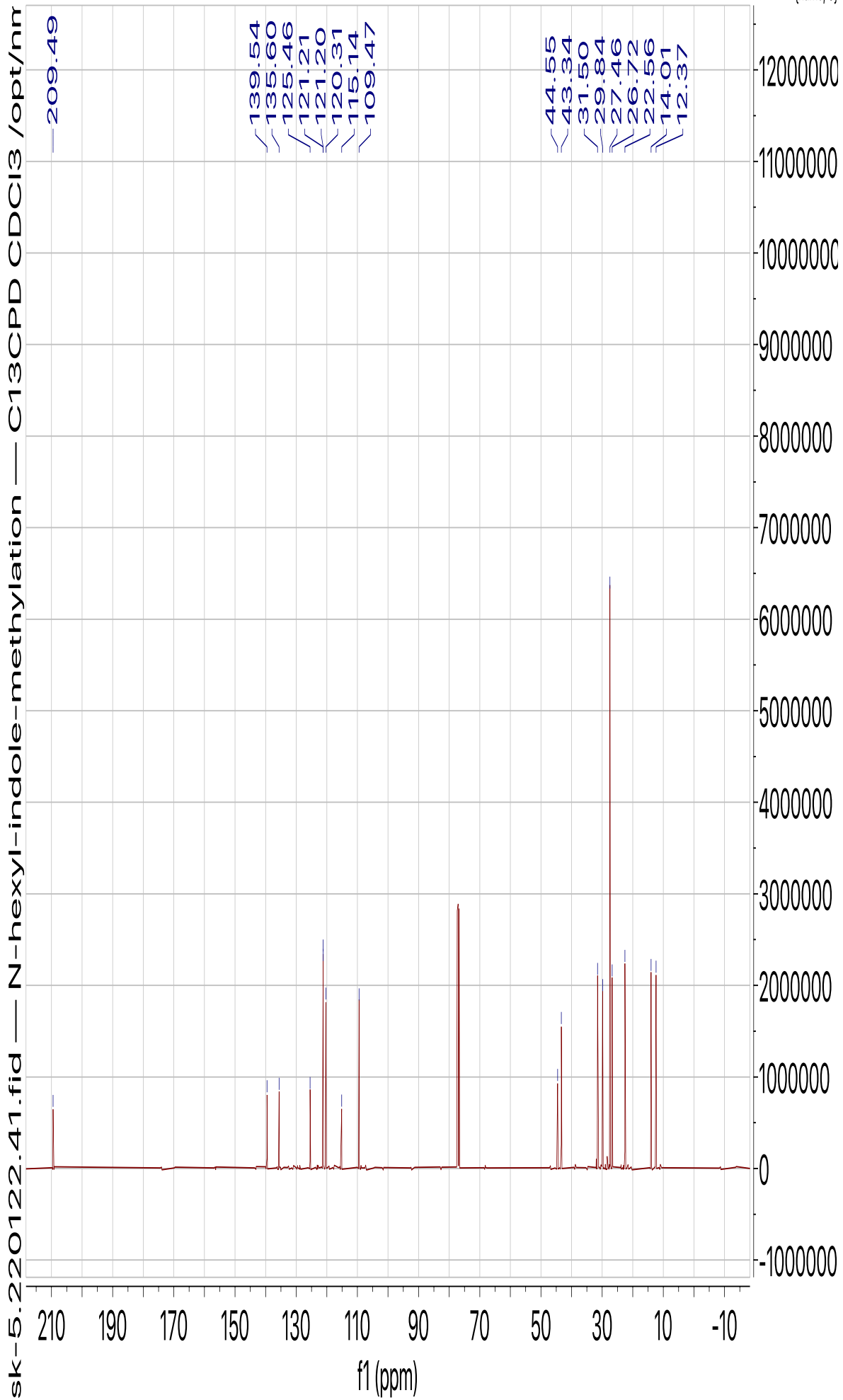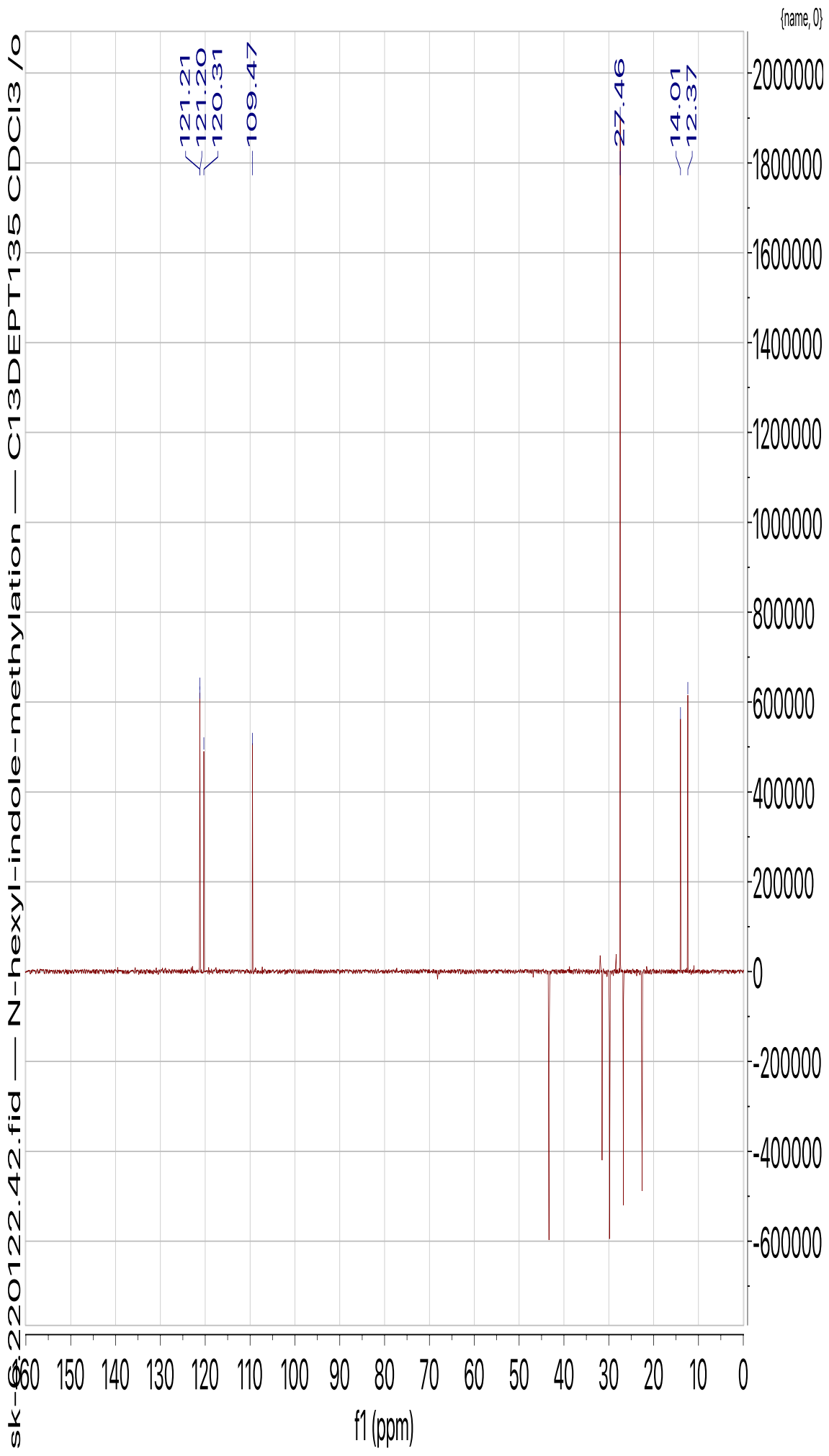
DCM -> MEOH (2% H2O, 0.1% FA)
220314_SOE_HRMS_Linne_KS-Met20 58 (0.998) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)
TOF MS ES+
3.55e+007

100
308.1988

%
286.2168
287.2206
309.2020
276.1602
310.2061
332.2224
0
m/z
250 260 270 280 290 300 310 320 330 340 350 360

HRMS spectra of **3q**

3r, ¹H NMR, CDCl₃, 400 MHz

sk-4.220122.40.fid — N-hexyl-indole-methylation — CMC_PROTON CDCl3

7.71, 7.71, 7.69, 7.68, 7.33, 7.33, 7.31, 7.31, 7.29, 7.23, 7.23, 7.22, 7.21, 7.19, 7.17, 7.17, 7.16, 7.15, 4.12, 4.10, 4.08, 2.51, 1.80, 1.78, 1.76, 1.42, 1.42, 1.41, 1.37, 1.36, 1.36, 1.35, 1.34, 1.33, 0.94, 0.92, 0.90

Integrals: 1.00, 1.01, 2.16, 2.13, 3.13, 2.22, 2.07, 9.46, 5.16, 3.45

f1 (ppm)

3r, ^{13}C NMR (101 MHz, CDCl$_3$)

209.49

139.54
135.60
125.46
121.21
121.20
120.31
115.14
109.47

44.55
43.34
31.50
29.84
27.46
26.72
22.56
14.01
12.37

sk-5.220122.41.fid — N-hexyl-indole-methylation — C13CPD CDCl3 /opt/nm

f1 (ppm)

70

sk-6-220122.42.fid — N-hexyl-indole-methylation — C13DEPT135 CDCl3 /o

121.21
121.20
120.31
109.47
27.46
14.01
12.37

{name, 0}

71

Single Mass Analysis

Tolerance = 3.0 mDa / DBE: min = -1.5, max = 100.0

Element prediction: Off

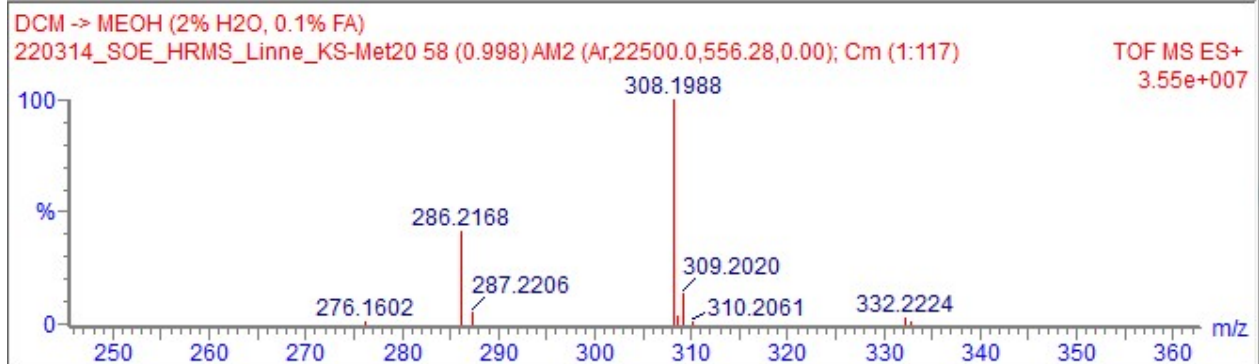Number of isotope peaks used for i-FIT = 2

Monoisotopic Mass, Even Electron Ions

102 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 0-60   H: 0-100   N: 0-1   O: 0-20

Mass	Calc. Mass	m...	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
300.2322	300.2327	-0.5	-1.7	6.5	C20 H30 N O	55.2	n/a	n/a	20	30	1	1

HRMS spectra of **3r**

3s, ^{1}H NMR, CDCl$_3$, 400 MHz
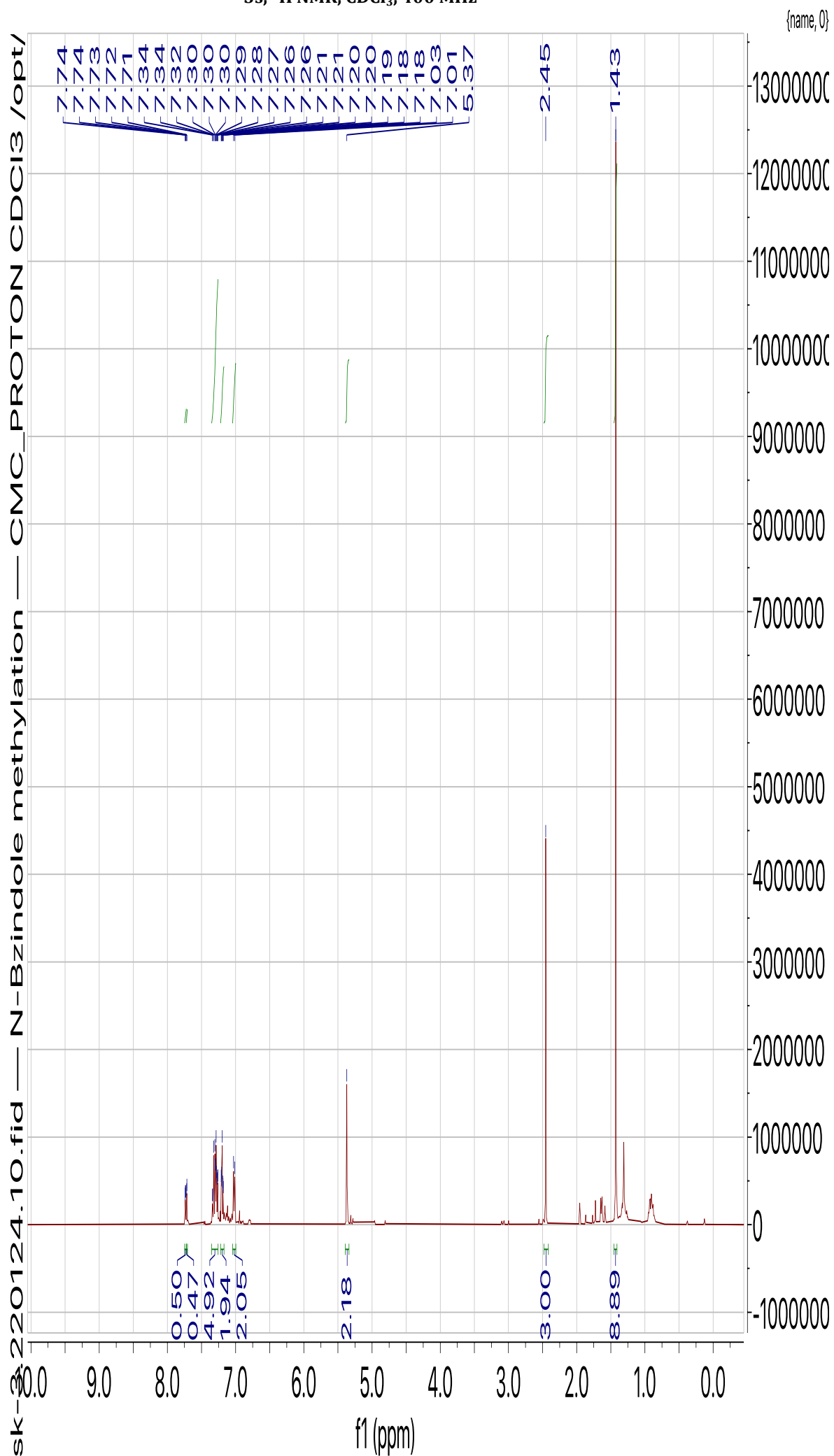
7.74, 7.74, 7.73, 7.72, 7.71, 7.34, 7.34, 7.32, 7.30, 7.30, 7.30, 7.30, 7.29, 7.28, 7.27, 7.26, 7.26, 7.21, 7.20, 7.20, 7.19, 7.18, 7.18, 7.03, 7.01, 5.37

2.45

1.43

0.50, 0.47, 4.92, 1.94, 2.05

2.18

3.00

8.89

sk-3_220124.10.fid — N-Bzindole methylation — CMC_PROTON CDCl3 /opt/

f1 (ppm)

3s, ^{13}C NMR (101 MHz, CDCl$_3$)

sk-5.220124.11.fid — N–Bzindole methylation — C13CPD CDCl3 /opt/nmrdat

{name, 0}

209.83

139.24
136.80
136.15
128.94
127.58
125.96
121.67
121.16
120.67
115.79
109.67

46.56
44.73

27.48

12.32
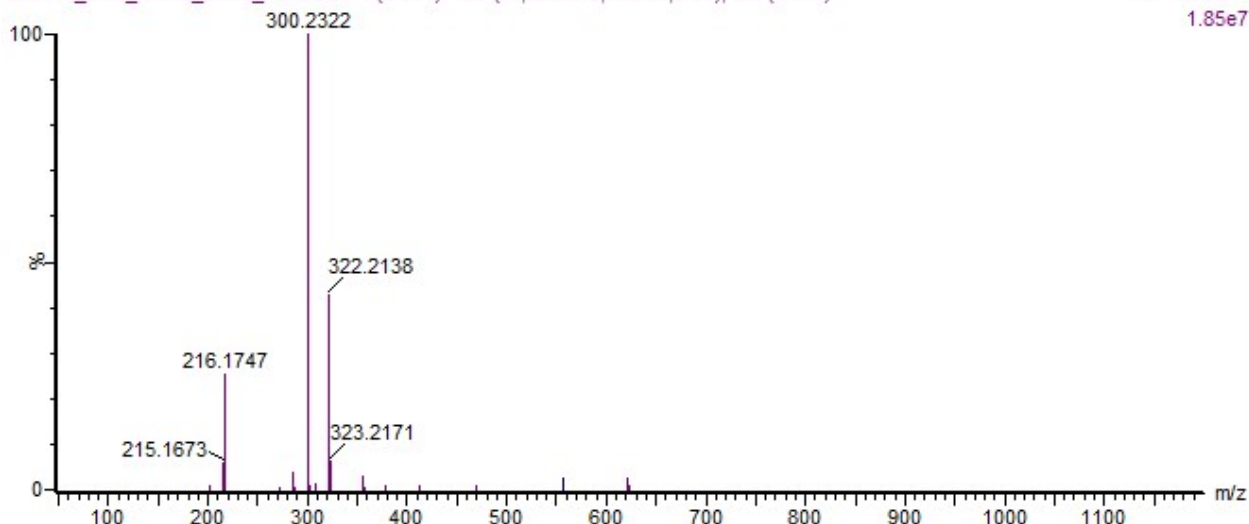
DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met19 111 (1.894) AM2 (Ar,22500.0,556.28,0.00); Cm (1:116)   TOF MS ES+
                                                                                          5.41e6

100-   306.1861

                                        *
                                     556.2771

 %-

                           307.1898
                           328.1686   557.2795
            222.1291

  0-
        100   200   300   400   500   600   700   800   900   1000   1100   m/z
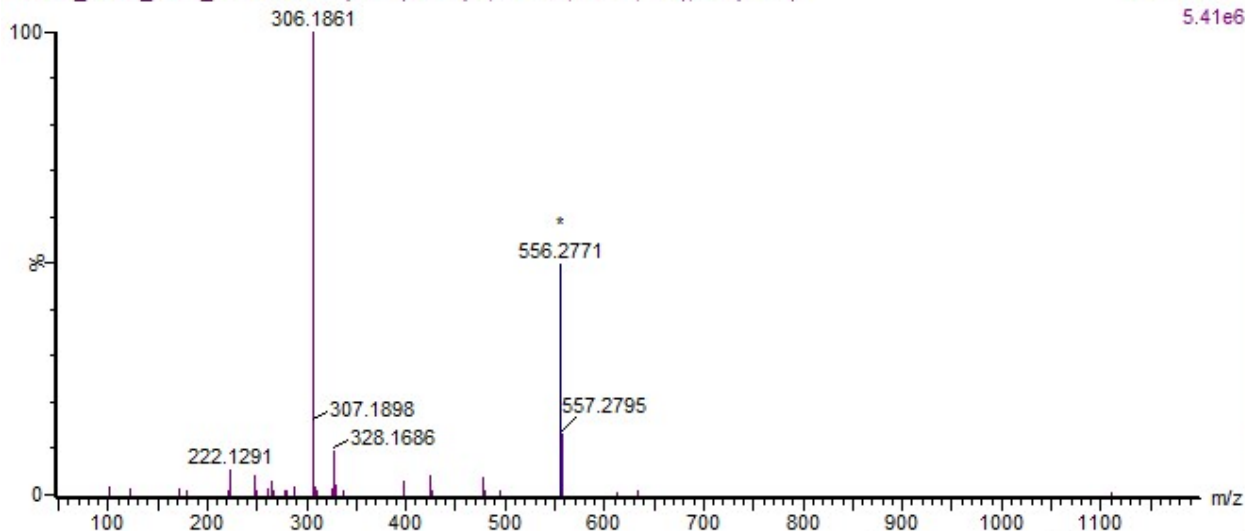
Single Mass Analysis
Tolerance = 2.0 mDa   /   DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 2
Monoisotopic Mass, Even Electron Ions
84 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
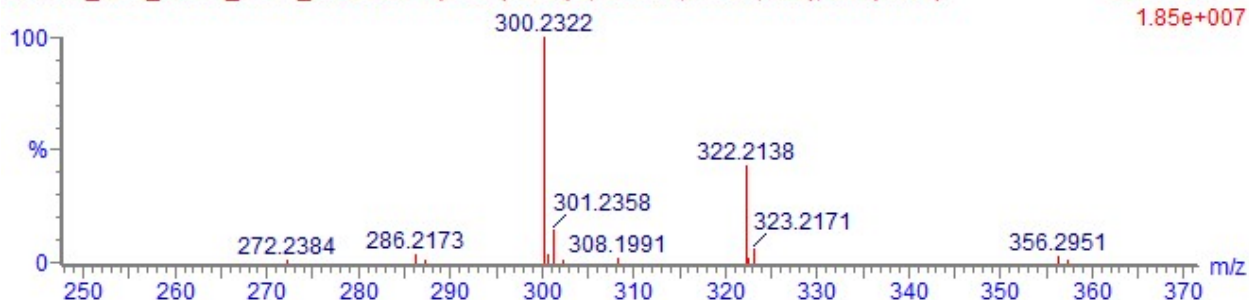Elements Used:
C: 0-60   H: 0-100   N: 0-3   O: 0-4

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-F...	Fit Conf %	C	H	N	O
306.1861	306.1858	0.3	1.0	10.5	C21 H24 N O	26.3	n/a	n/a	21	24	1	1

DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met19 111 (1.894) AM2 (Ar,22500.0,556.28,0.00); Cm (1:116)   TOF MS ES+
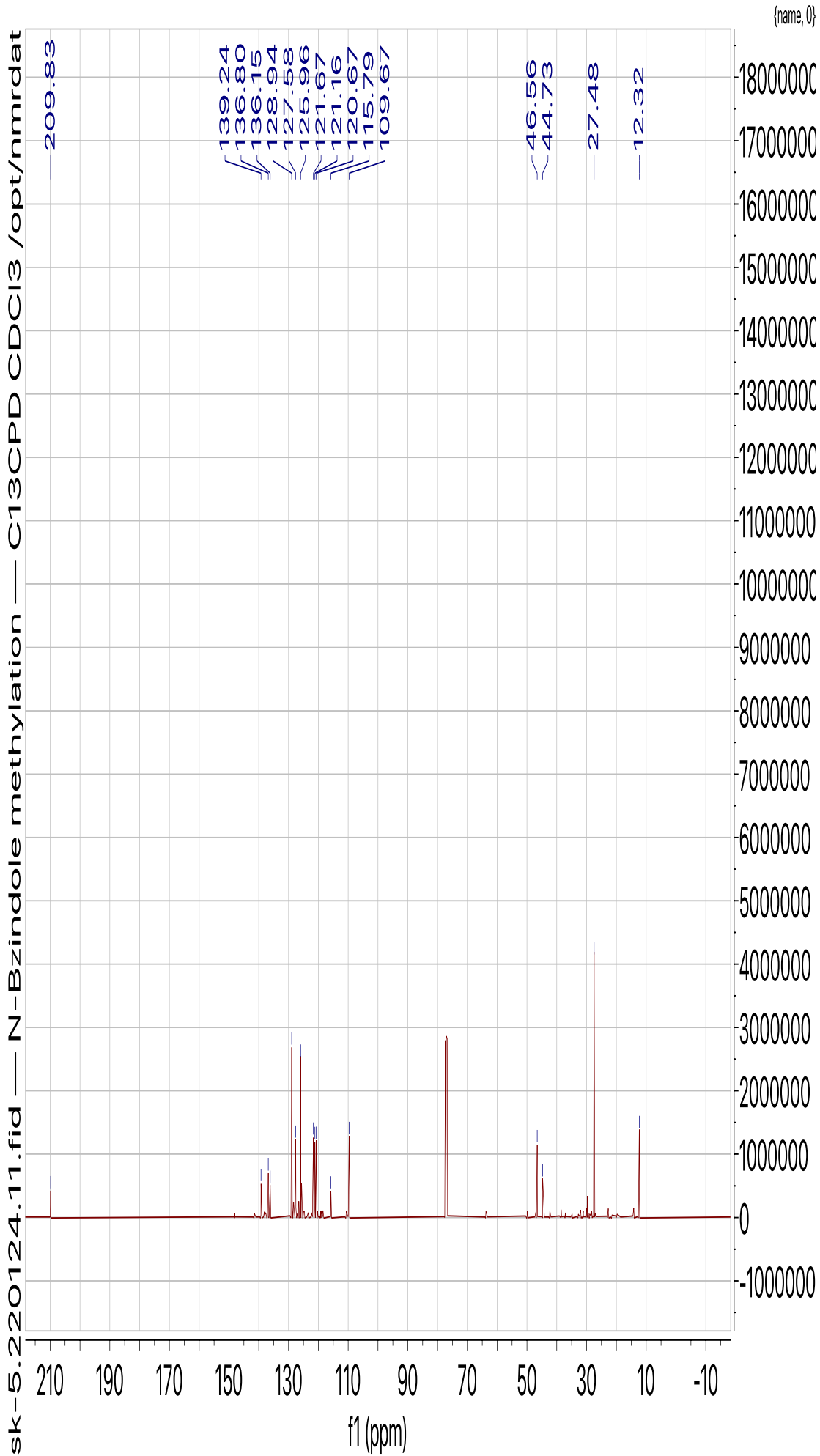   5.41e+006
100-   306.1861

 %-

                                  307.1898
                                         328.1686
        248.1450 264.1168   308.1935   397.1876
                          287.1684   329.1722
  0-
     240   250   260   270   280   290   300   310   320   330   340   350   360   370   380   390   400   m/z

HRMS spectra of **3s**

3t, ^{1}H NMR, CDCl$_3$, 400 MHz

sk-24.211218.100.fid — 4-Methylbenzylindole methylation — CMC_PROTON

{name, 0}

76

3t, ^{13}C NMR (101 MHz, CDCl$_3$)

sk-25.211218.101.fid — 4-Methylbenzylindole methylation — C13CPD CDCl3

209.80

139.34
137.27
136.15
133.75
129.59
125.93
125.60
121.61
121.14
120.60
115.69
109.70

46.37
44.70

27.48
21.07
12.34

f1 (ppm)

100—
320.2010

*
556.2771

%—

321.2047   557.2796
342.1836
262.1599

0—
                100   200   300   400   500   600   700   800   900   1000   1100   m/z

Single Mass Analysis
Tolerance = 2.0 mDa   /   DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 2
Monoisotopic Mass, Even Electron Ions
87 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
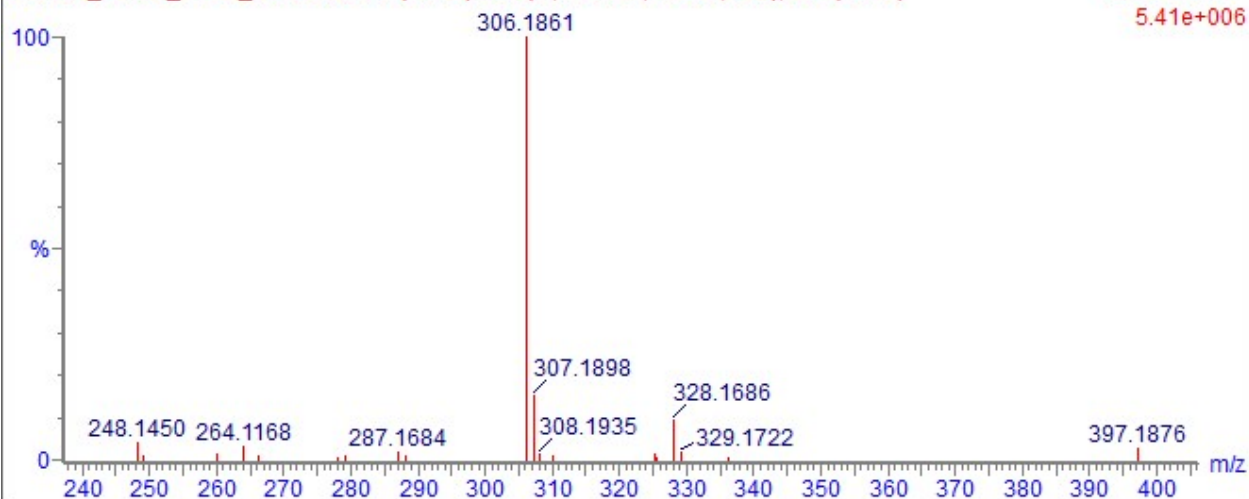Elements Used:
C: 0-60   H: 0-100   N: 0-3   O: 0-4

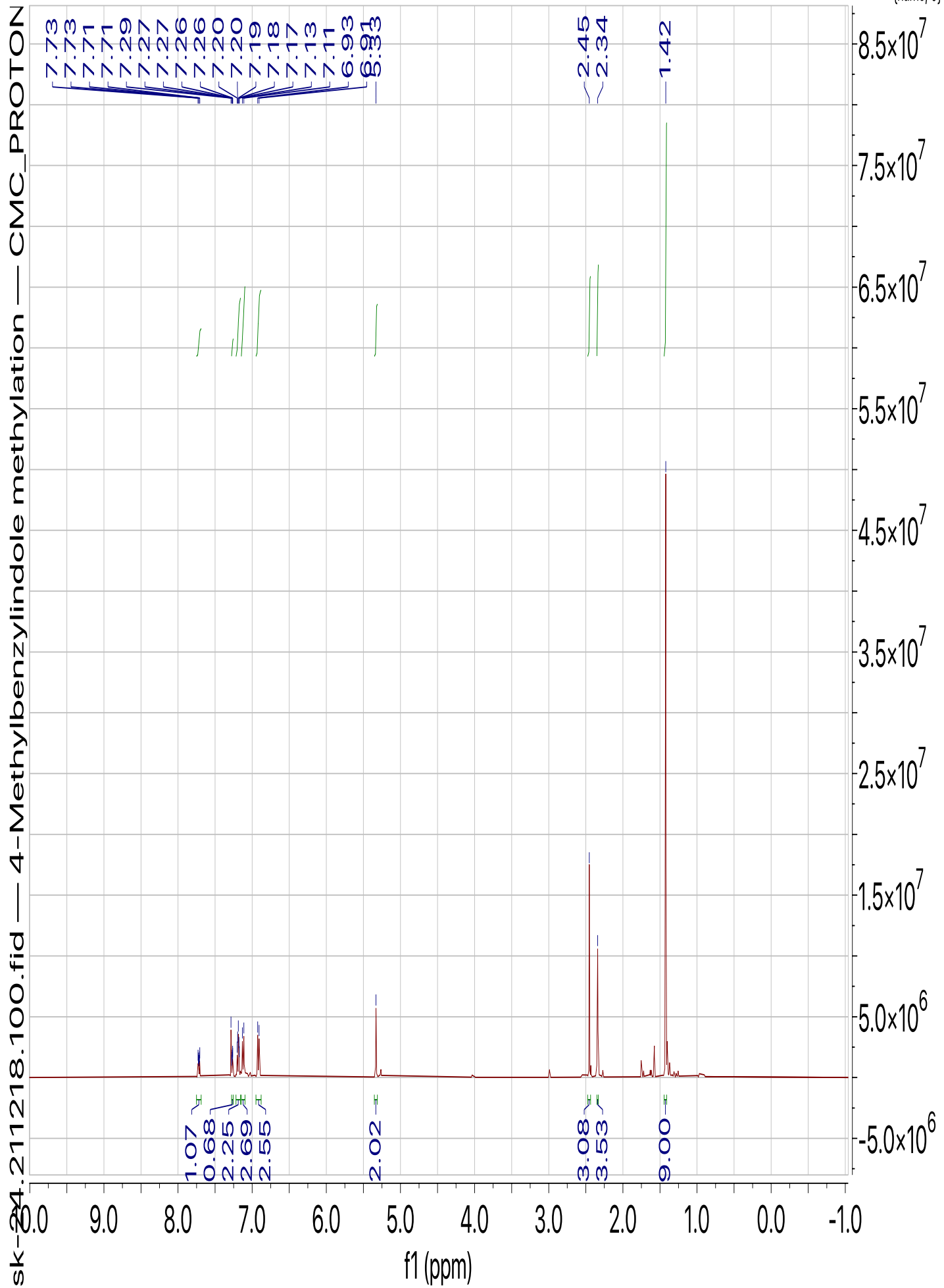| Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
320.2010	320.2014	-0.4	-1.2	10.5	C22 H26 N O	27.0	n/a	n/a	22	26	1	1

DCM -> MEOH (2% H2O, 0.1% FA)
220307_HRMS_Linne_KS-Met6 107 (1.826) AM2 (Ar,22500.0,556.28,0.00); Cm (1:117)   TOF MS ES+
7.90e+006
320.2010
100—

%—

321.2047
262.1599   322.2084   342.1836
278.1151   279.1712 297.6152   356.0525   376.2646   397.1875
0—
        270   280   290   300   310   320   330   340   350   360   370   380   390   m/z

HRMS spectra of **3t**

{name, 0}

sk.211228.20.fid — 2,6-dichlorobenzylindole methylation — CMC_PROTON

7.59
7.59
7.57
7.56
7.37
7.35
7.29
7.26
7.24
7.24
7.22
7.13
7.11
7.11
7.10
7.09
7.08
5.88

2.45

1.36

0.94
1.94
1.43
2.99

1.84

2.90

9.00

f1 (ppm)

3u, ¹³C NMR (101 MHz, CDCl₃)

sk-2.211228.21.fid — 2,6-dichlorobenzylindole methylation — C13CPD CDCl₃

{name, 0}

210.92

138.65
136.26
135.97
131.58
129.83
129.17
125.86
121.38
120.76
120.26
116.13
110.06

45.01
43.80

27.46

12.71

Single Mass Analysis
Tolerance = 2.0 mDa   /   DBE: min = -1.5, max = 100.0
Element prediction: Off
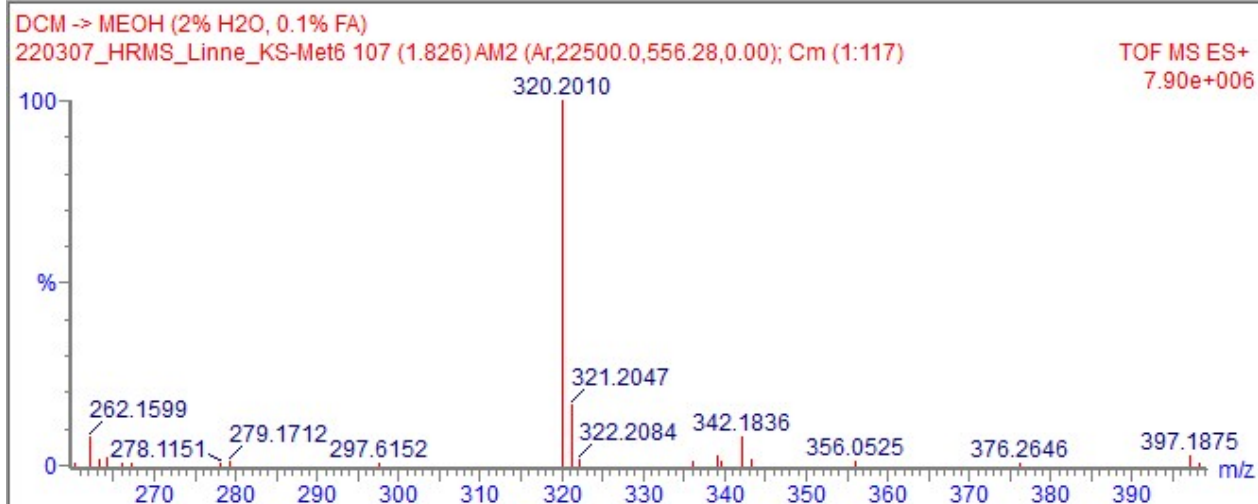Number of isotope peaks used for i-FIT = 2
Monoisotopic Mass, Even Electron Ions
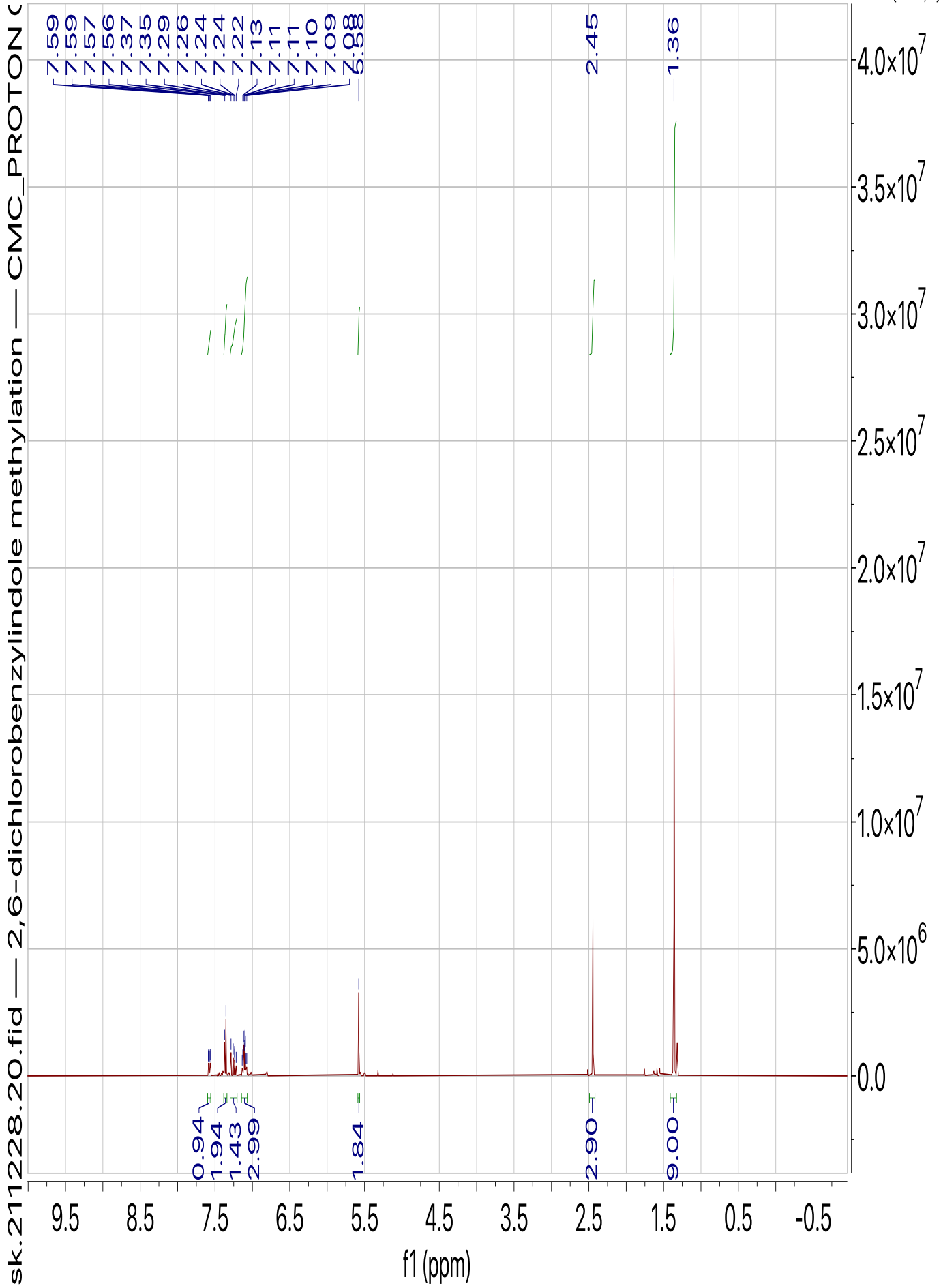266 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)
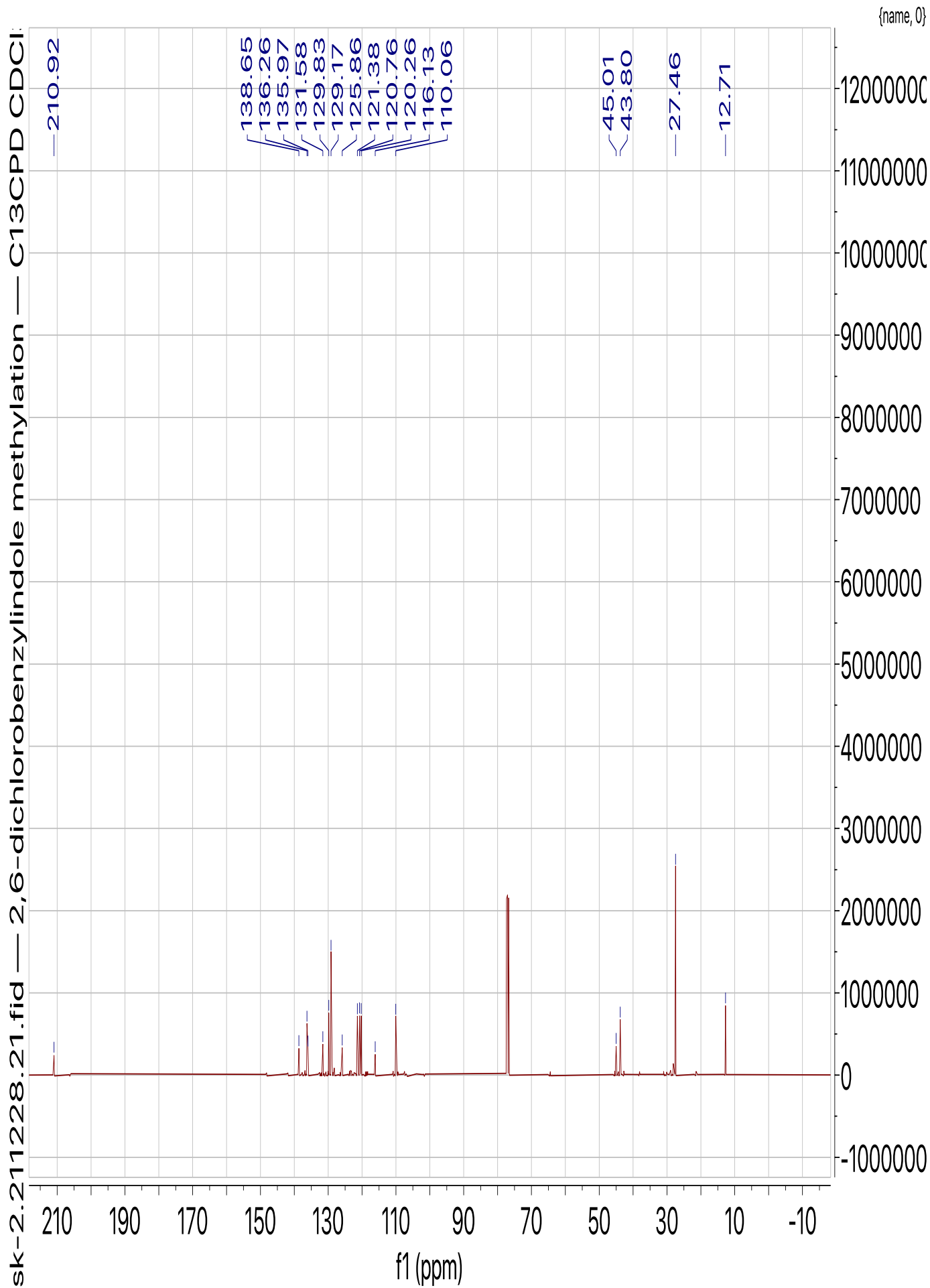Elements Used:
C: 0-60   H: 0-100   N: 0-3   O: 0-4   Cl: 0-2

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT ...	Fit Conf %	C	H	N	O	Cl
374.1073	374.1078	-0.5	-1.3	10.5	C21 H22 N O Cl2	0.105	90.00	21	22	1	1	2
	374.1060	1.3	3.5	15.5	C22 H17 N3 O Cl	3.302	10.00	22	17	3	1	1

HRMS spectra of **3u**

3v, ^{1}H NMR, CDCl$_3$, 400 MHz

{name, 0}

sk.230227.10.fid — N-Ph-Piv-Methyl — PROTON CDCl3 {D:\nmrdata\currer

Peaks: 7.62, 7.60, 7.49, 7.47, 7.45, 7.43, 7.43, 7.42, 7.41, 7.41, 7.26, 7.26, 7.24, 7.24, 7.24, 7.11, 7.11, 7.10, 7.09, 7.09, 7.08, 7.07, 7.04, 7.02, 7.02, 7.01, 7.00, 6.95, 6.95, 6.95, 6.93, 6.93, 6.93, 2.23, 1.33

Integrals: 1.00, 3.57, 2.18, 1.12, 1.04, 1.11, 3.01, 9.66

f1 (ppm)

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

3v, ^{13}C NMR (101 MHz, CDCl$_3$)

{name, 0}

sk-2.230227.11.fid — N-Ph-Piv-Methyl — C13CPD CDCl3 {D:\nmrdata\curre
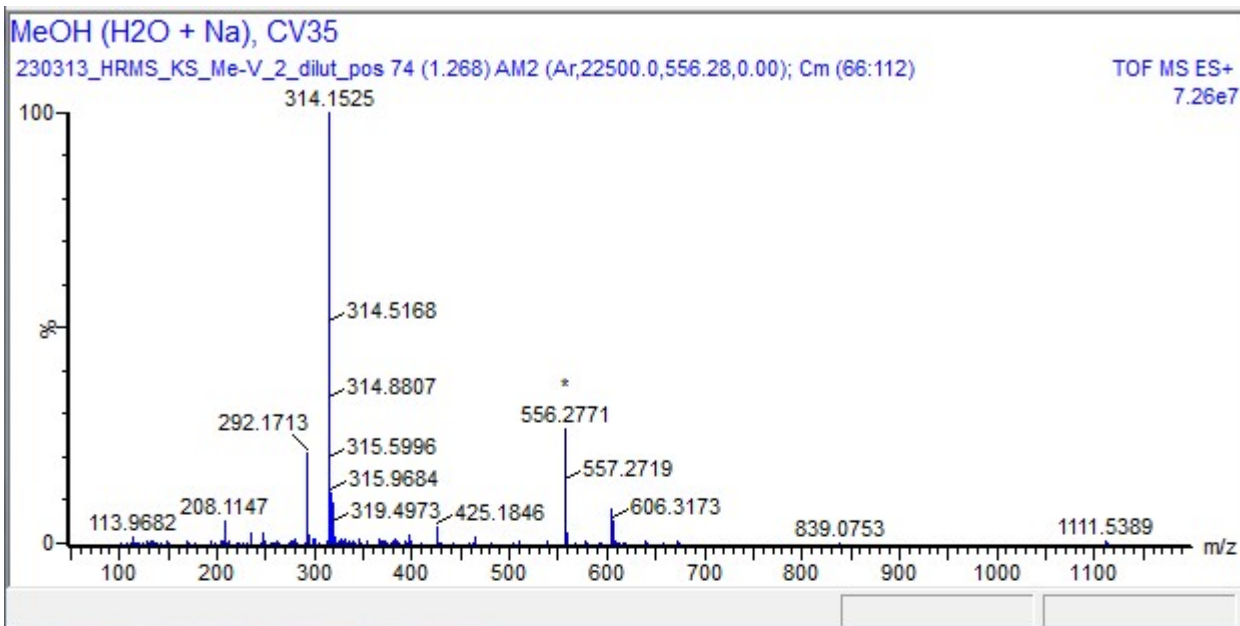
209.72

139.67
137.39
136.96
129.70
128.58
128.31
125.53
121.81
121.01
120.92
116.03
110.57

44.79

27.40

13.39

f1 (ppm)

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

MeOH (H2O + Na), CV35

230313_HRMS_KS_Me-V_2_dilut_pos 74 (1.268) AM2 (Ar,22500.0,556.28,0.00); Cm (66:112)　　TOF MS ES+
7.26e7

314.1525
314.5168
314.8807
292.1713
315.5996
315.9684
556.2771 *
557.2719
606.3173
113.9682　208.1147　319.4973　425.1846　839.0753　1111.5389

Single Mass Analysis
Tolerance = 2.0 mDa   /   DBE: min = -1.5, max = 100.0
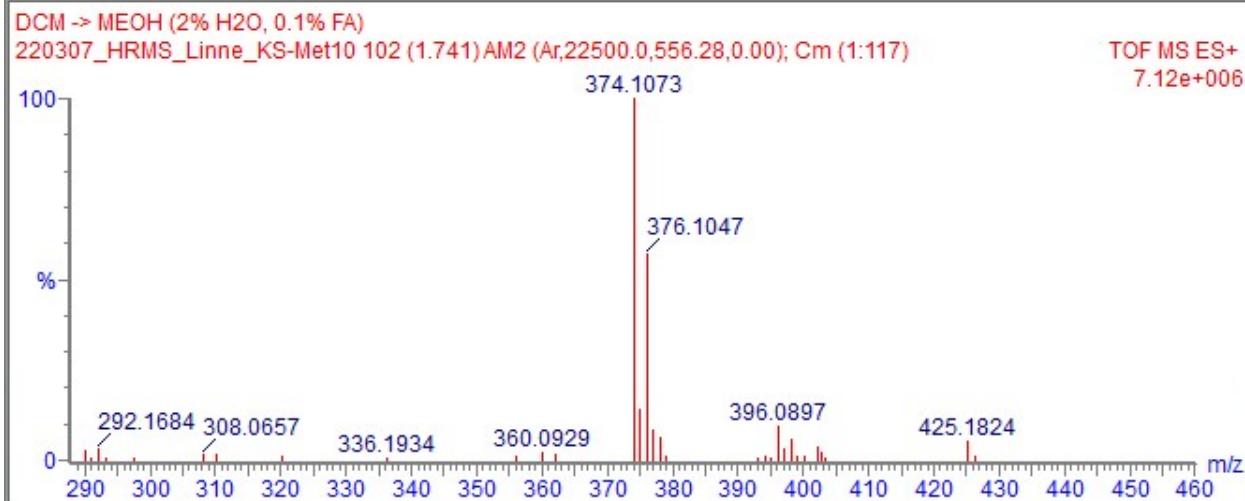Element prediction: Off
Number of isotope peaks used for i-FIT = 2
Monoisotopic Mass, Even Electron Ions
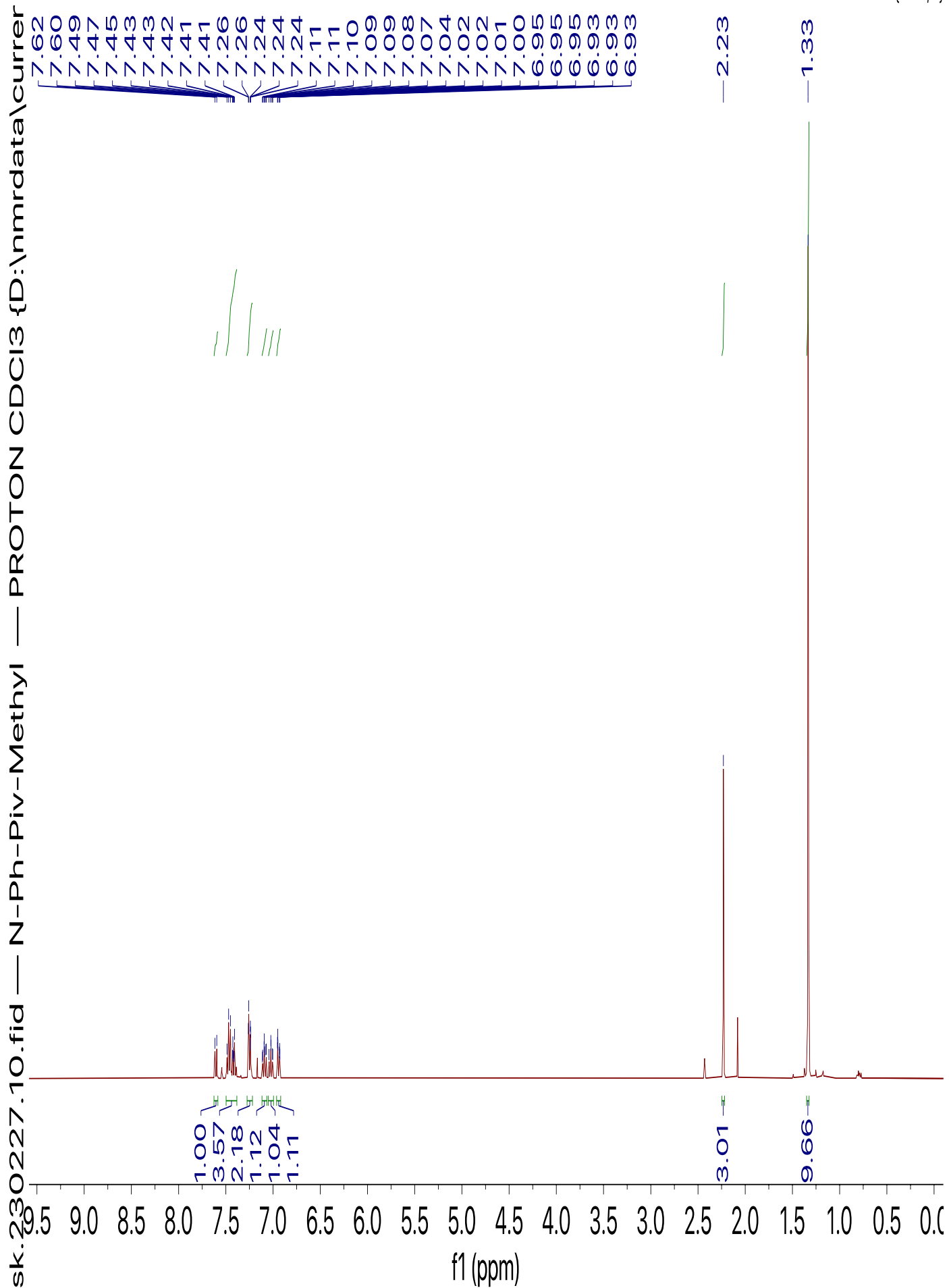17 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)
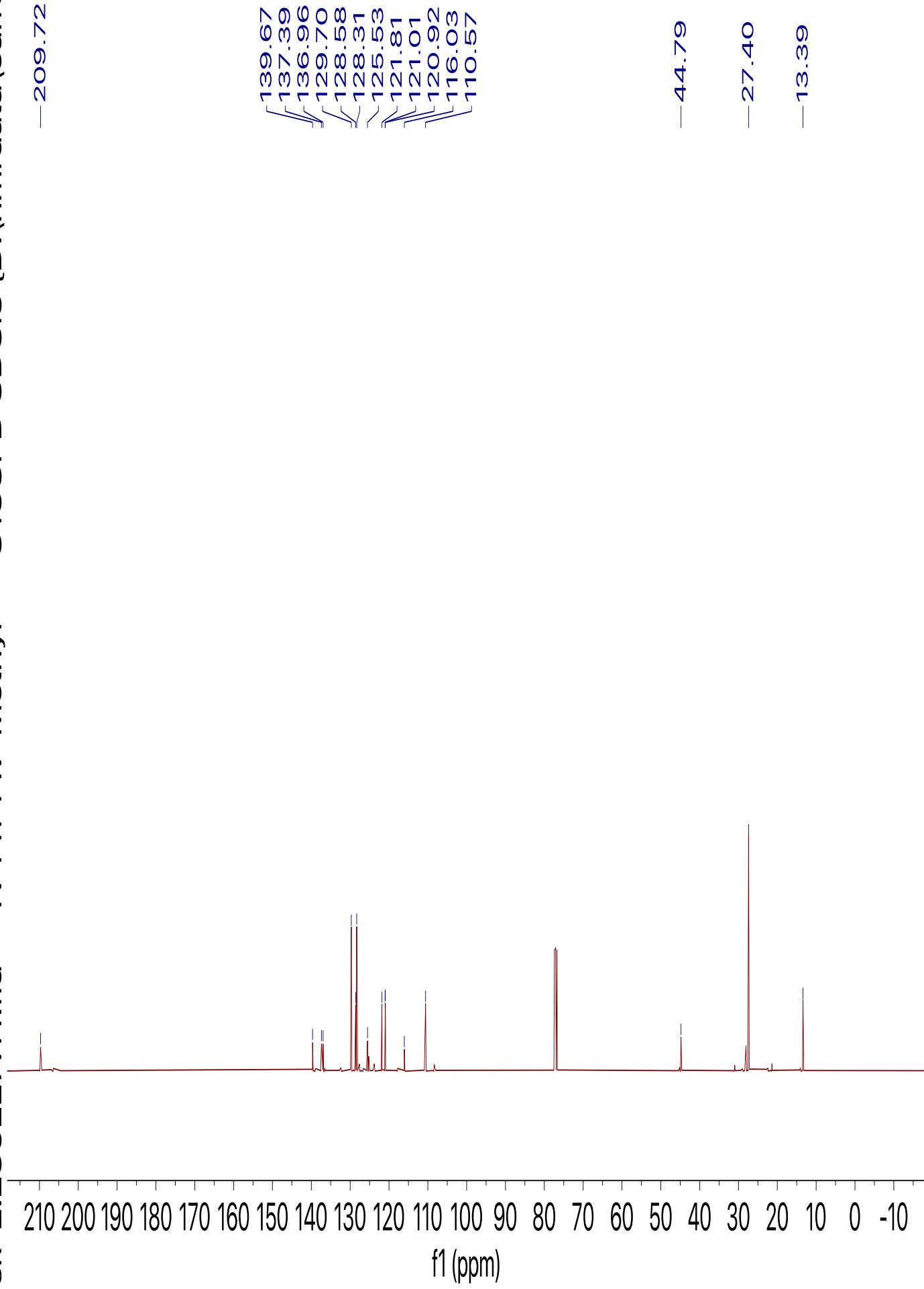Elements Used:
C: 18-26　　　H: 18-24　　　N: 0-3　　　O: 0-3　　　Na: 0-1

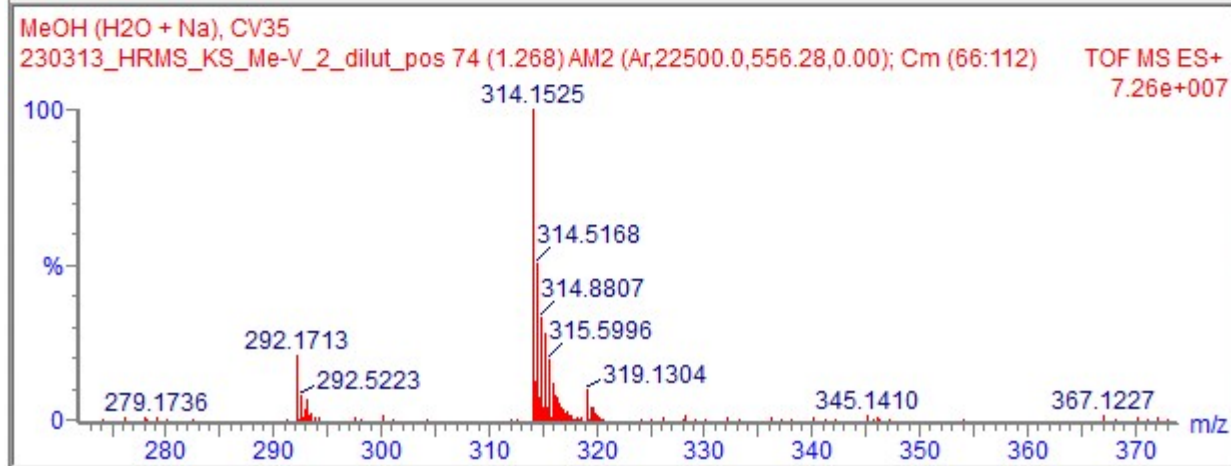| Mass	Calc. Mass	mDa	PPM	DBE	Formula	i.	i. Fit Conf %	C	H	N	O	Na
314.1525	314.1521	0.4	1.3	10.5	C20 H21 N O Na	5...0...99.90		20	21	1	1	1
	314.1545	-2.0	-6.4	13.5	C22 H20 N O	5...6...0.10		22	20	1	1	

MeOH (H2O + Na), CV35

230313_HRMS_KS_Me-V_2_dilut_pos 74 (1.268) AM2 (Ar,22500.0,556.28,0.00); Cm (66:112)　　TOF MS ES+
7.26e+007

314.1525
314.5168
314.8807
315.5996
292.1713
292.5223
319.1304
279.1736
345.1410
367.1227

HRMS spectra of **3V**

3w, ^{1}H NMR, CDCl$_3$, 400 MHz

sk.230301.10.fid — N-(2OMe)-Ph-Piv-Me — PROTON CDCl3 {D:\nmrdata\c

{name, 0}

Peaks: 7.73, 7.71, 7.50, 7.48, 7.48, 7.48, 7.46, 7.46, 7.28, 7.28, 7.26, 7.26, 7.25, 7.18, 7.16, 7.14, 7.14, 7.11, 7.10, 7.10, 7.09, 7.08, 7.07, 7.06, 6.91, 6.91, 6.89, 3.71, 2.26, 1.42

Integrals: 1.00, 1.11, 1.43, 1.17, 3.52, 1.04, 3.25, 3.14, 9.60

f1 (ppm)

3w, ^{13}C NMR (101 MHz, CDCl$_3$)

sk-2.230301.11.fid — N-(2OMe)-Ph-Piv-Me — C13CPD CDCl3 {D:\nmrdata}
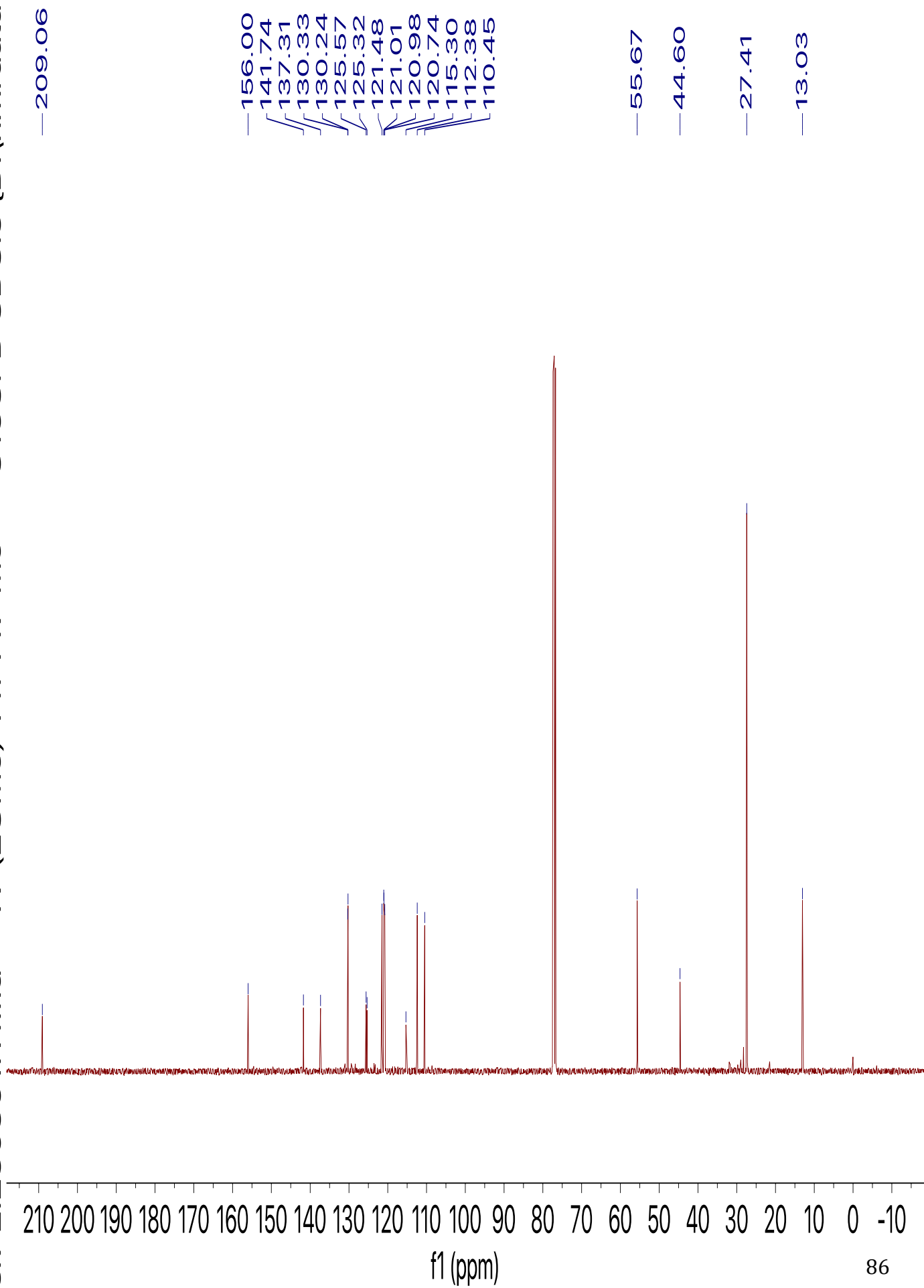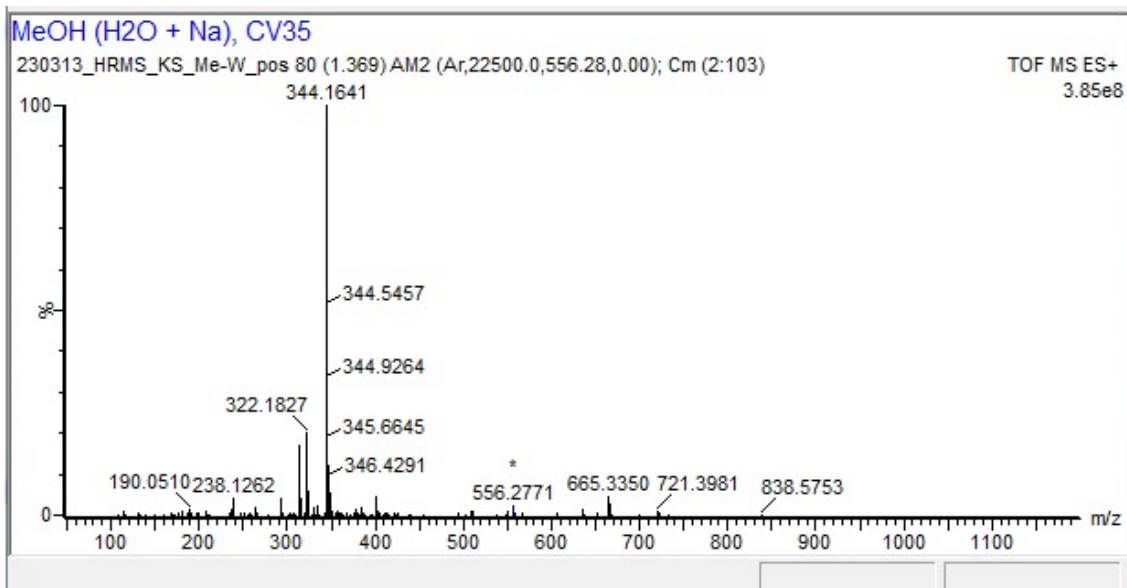
209.06

156.00
141.74
137.31
130.33
130.24
125.57
125.32
121.48
121.01
120.98
120.74
115.30
112.38
110.45

55.67

44.60

27.41

13.03

MeOH (H2O + Na), CV35
230313_HRMS_KS_Me-W_pos 80 (1.369) AM2 (Ar,22500.0,556.28,0.00); Cm (2:103)
TOF MS ES+
3.85e8

100-
344.1641
%-
344.5457
344.9264
322.1827
345.6645
346.4291
190.0510 238.1262
556.2771 665.3350 721.3981 838.5753
0-
m/z
100   200   300   400   500   600   700   800   900   1000   1100

Single Mass Analysis
Tolerance = 2.0 mDa / DBE: min = -1.5, max = 100.0
Element prediction: Off
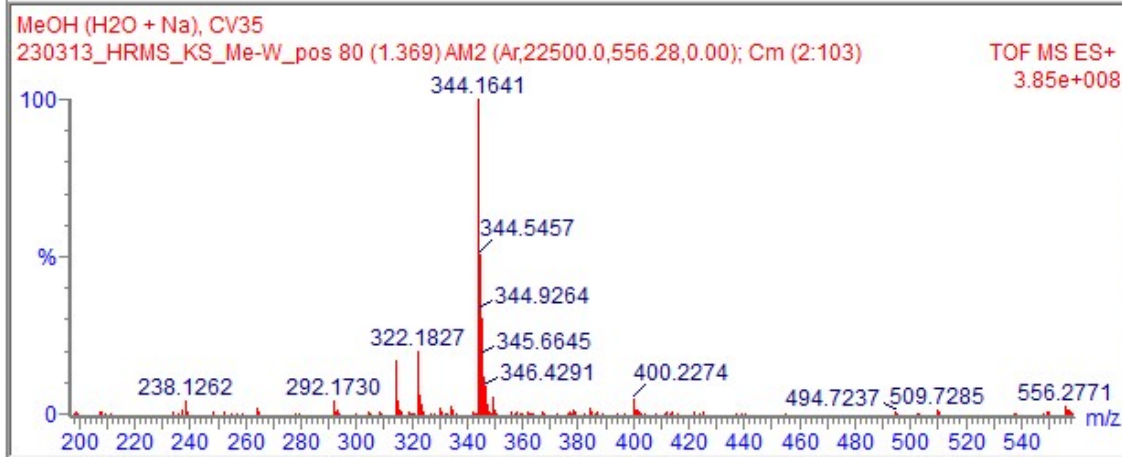Number of isotope peaks used for i-FIT = 2
Monoisotopic Mass, Even Electron Ions
11 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 18-27   H: 20-26   N: 1-2   O: 1-3   Na: 0-2

Mass	Calc. Mass	mDa	PPM	DBE	Formula		Fit Conf %	C	H	N	O	Na
344.1641	344.1651	-1.0	-2.9	13.5	C23 H22 N O2		4094.74	23	22	1	2	
	344.1626	1.5	4.4	10.5	C21 H23 N O2 Na		425.26	21	23	1	2	1

MeOH (H2O + Na), CV35
230313_HRMS_KS_Me-W_pos 80 (1.369) AM2 (Ar,22500.0,556.28,0.00); Cm (2:103)
TOF MS ES+
3.85e+008

100-
344.1641
%-
344.5457
344.9264
322.1827
345.6645
238.1262   292.1730
346.4291
400.2274
494.7237 509.7285
556.2771
0-
m/z
200 220 240 260 280 300 320 340 360 380 400 420 440 460 480 500 520 540

HRMS spectra of **3W**

6. References

1. S. Kathiravan, P. Anaspure, Z. Tianshu, and I. A. Nicholls, *Org. Lett.*, 2021, **23**, 3331-3336.

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3. D. A. Fernandez, M. Gulias, J. L. Mascarenas, and F. Lopez, *Angew. Chem. Int. Ed*. 2017, **56**, 9541-9545

4. D. R. Stuart, E. Villemure, and K. Fagnou, *J. Am. Chem. Soc.* 2007, **129**, 12072-12073.

5. M. Farizyan, A. Mondal, S. Mal, F. Deufel, M. van Gemmeren, *J. Am. Chem. Soc*. 2021, **143**, 16370-16376.

6. E. Tan, O. Quinonero, M. E. de Orbe, and A. M. Echavarren, *ACS Catal*. 2018, **8**, 2166-2172.