# Iodine-Catalyzed Cross-Coupling of Isocyanides and Thiols for the synthesis of *S*-Thiocarbamates

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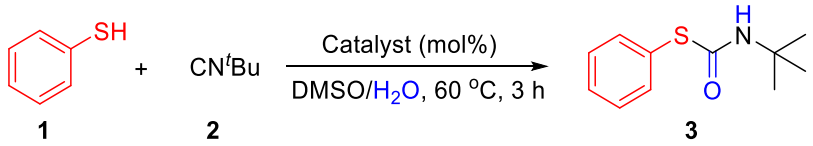
## 1. General Consideration:

Unless stated otherwise, all solvents and commercially available reagents were used as received. Hexane, which was used for column chromatography, was distilled prior to use. Non-commercial starting materials were prepared as described below or according to literature procedures. Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Advance 500 MHz at ambient temperature using the deuterated solvent and TMS as internal standard ($^1$H: δ 2.50 ppm and $^{13}$C[$^1$H]: δ 39.52 ppm for DMSO-$d_6$, $^1$H: δ 7.26 ppm and $^{13}$C[$^1$H]: δ 77.16 ppm for $CDCl_3$). Chemical shifts (δ) are given in ppm and coupling constants (J) are quoted in hertz (Hz). Multiplicities are described as s (singlet), d (doublet), t (triplet), q (quartet), hp (heptuplet), m (multiplet), br (broad) or com-binations thereof. $^{13}$C-NMR spectra were recorded with complete proton decoupling. For high resolution mass-spectrometric analysis, samples were dissolved in MeOH or $CH_3CN$ and diluted to a concentration of approximately 10-5 mol/L. 2 µL was injected using a CapLC system and electrosprayed through the nanoelectrospray source. The nanoelectrospray source was operated in positive ion mode at an electrospray potential of 1.7 kV. Colunm chromatography was performed by manual on $SiO_2$ (particle size 100-200 mesh) using the indicated eluent and visualized by UV detection (254 nm).

## 2. Detailed results of Screening

### 2.1 *Table S1:* Screening of Catalyst[a]:

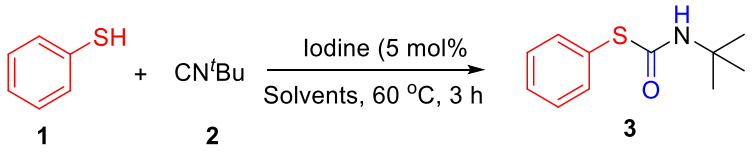



1 2 3

| S. No. | Catalyst (mol %) | Temp. (°C) | Time (h) | Yield (%)[b] |
|---|---|---|---|---|
| 1 | CuI (20) | 60 | 3 h | 15[c] |
| 2 | NaI (20) | 60 | 3 h | 20[c] |
| 3 | KI (20) | 60 | 3 h | 25[c] |
| 4 | TBAI (20) | 60 | 3 h | 60 |
| 5 | - | 60 | 3 h | nr[c] |
| 6 | Iodine (50) | 60 | 3 h | 75 |
| 7 | Iodine (20) | 60 | 3 h | 87 |
| 8 | Iodine (10) | 60 | 3 h | 87 |
| **9** | **Iodine (5)** | **60** | **3 h** | **85** |

[a]Reaction conditions: Thiophenol (**1a**, 30 mg, 0.27 mmol, 1.0 equiv), *tert*-butyl isocyanide (**2a**, 0.32 mmol, 27 mg, 1.2 equiv), DMSO/$H_2O$ (99/1, 0.2 mL), temperature (60 °C), 3 h, [b] Yields are of isolated product after column chromatography. [c]starting material recovered; nr: No Reaction

**2.2 *Table S2:* Effect of solvents[a]**

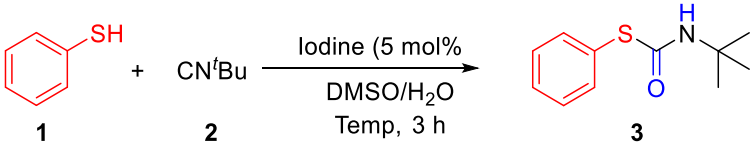



**1** **2** **3**

| S. No. | Solvents | Conditions | Yield (%)[b] |
|---|---|---|---|
| 1 | DMF/$H_2O$ (99/1) | 60 °C, 3 h | nr[c] |
| 2 | THF/$H_2O$ (99/1) | 60 °C, 3 h | trace[c] |
| 3 | Acetonitrile/$H_2O$ (99/1) | 60 °C, 3 h | nr[c] |
| 4 | toluene/$H_2O$ (99/1) | 60 °C, 3 h | trace[c] |
| 5 | DCE/$H_2O$ (99/1) | 60 °C, 3 h | 15[c] |
| 6 | EtOH/$H_2O$ (99/1) | 60 °C, 3 h | 65[c] |
| **7** | **DMSO/$H_2O$ (99/1)** | **60 °C, 3 h** | **85** |
| 8 | 1,4-Dioxane/$H_2O$ (99/1) | 60 °C, 3 h | nr[c] |
| 9 | Methanol/$H_2O$ (99/1) | 60 °C 3 h | 70[c] |
| 10 | DMSO/$H_2O$ (1/1) | 60 °C 3 h | 40 |
| 11 | DMSO/$H_2O$ (20/1) | 60 °C 3 h | 30 |
| 12 | DMSO/$H_2O$ (9/1) | 60 °C 3 h | 15 |
| 13 | DMSO/$H_2O$ (7/3) | 60 °C 3 h | 20 |
| 14 | Water | 60 °C 3 h | 0 |

[a]Reaction conditions: Thiophenol (**1a**, 30 mg, 0.27 mmol, 1.0 equiv), *tert*-butyl isocyanide (**2a**, 0.32 mmol, 27 mg, 1.2 equiv), DMSO/$H_2O$ (99/1, 0.2 mL), temperature (60 °C), 3 h, [b] Yields are of isolated product after column chromatography. [c]starting material recovered.

**2.3 *Table S3:* Effect of Temperature[a]**

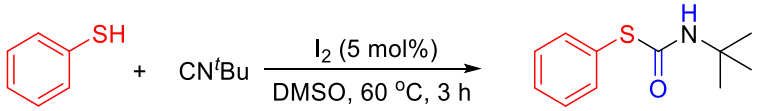



**1** **2** **3**

| S. No. | Condition (99/1) | Temperature | Yield (%)[b] |
|---|---|---|---|
| 1 | DMSO/$H_2O$ | rt, 3 h | 30[c] |
| 2 | DMSO/$H_2O$ | 40 °C, 3 h | 50[d] |
| **3** | **DMSO/$H_2O$** | **60 °C, 3 h** | **85** |
| 4 | DMSO/$H_2O$ | 80 °C, 3 h | 75 |
| 5 | DMSO/$H_2O$ | 100 °C, 3 h | 70 |
| 6 | DMSO/$H_2O$ | 60 °C, 8 h | 55 |
| 7 | DMSO/$H_2O$ | 60 °C 12 h | 45 |

[a]Reaction conditions: Thiophenol (**1a**, 30 mg, 0.27 mmol, 1.0 equiv), *tert*-butyl isocyanide (**2a**, 0.32 mmol, 27 mg, 1.2 equiv), DMSO/$H_2O$ (99/1, 0.2 mL), temperature (60 °C), 3 h, [b] Yields are of isolated product after column chromatography. [c]NR: No reaction, [d]starting material recovered.

**2.4 *Table S4*: Blank Experiment**




**1a** **2a** **3a**

| S. No. | 1a | 2a | Iodine (5 mol %) | DMSO:$H_2O$ (0.2 mL) | 3a (%) |
|---|---|---|---|---|---|
| 1 | ✓ | ✓ | ✓ | ✓ | 85 |
| 2 | × | ✓ | ✓ | ✓ | 0 |
| 3 | ✓ | × | ✓ | ✓ | 0 |
| 4 | ✓ | ✓ | × | ✓ | 0 |
| 5 | ✓ | ✓ | ✓ | × | 0 |

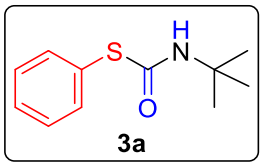
**3. General procedure for the synthesis of 3:**

A 10 mL schlenk tube equipped with a stir-bar was charged with thiophenol (0.03 g, 0.27 mmol), *tert*-butyl isocyanide (0.026 g, 0.32 mmol) in DMSO/$H_2O$ (99/1, 0.2 mL) as a solvent. Then after 5-10 min. Iodine (0.003 g, 0.01 mmol) was added to the reaction mixture. The mixture was stirred it at 60 °C for 3 h. After completion of the reaction on TLC, the reaction mixture was diluted with water and extracted three times with EtOAc. Collected organic layers were washed with water, sodium thiosulphate solution and brine successively, dried over anhydrous sodium sulphate,

filtered, and concentrated in vacuo. Purification by silica gel (100-200 mesh) chromatography (EtOAc: Hexane) to yield the desired product **3**.

## 4. Analytical data of compound 3a-3n

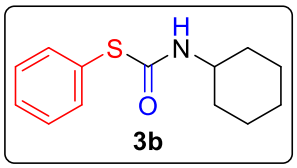
### 3a: *S*-phenyl *tert*-butylcarbamothioate[1]



**3a**

Off-White solid, Yield: 0.047 g (85%); m.p.: 114-115 $^{o}$C; $R_f$ 0.8 (1:9 EtOAc/hexane); $^{1}$H NMR, (δ ppm): (500 MHz, $CDCl_3$): 7.54-7.41 (m, 5H, aromatic *C-H),* 5.19 (br s, 1H, N-*H*), 1.33 (s, 9H, $Sp^3$ C-*H*). $^{13}$C NMR (δ ppm): (125 MHz, $CDCl_3$): 164.0, 135.4, 129.4, 129.3, 129.1, 53.5, 28.9. HRMS (ESI): calcd for $C_{11}H_{16}NOS$ $[M+H]^+$ 210.0947, found 210.0948.

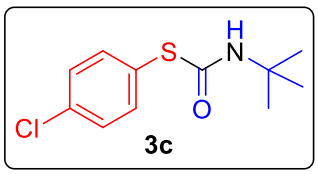
### 3b: *S*-phenyl cyclohexylcarbamothioate[1]



**3b**

Off-White solid, Yield: 0.058 g (91%); m.p.: 112-113 $^{o}$C; $R_f$ 0.6 (1:9 EtOAc/hexane); $^{1}$H NMR, (δ ppm): (500 MHz, $CDCl_3$): 7.56 (t, 2H, aromatic *C-H*, *J* = 3.0 Hz), 7.42-7.41 (m, 3H, aromatic *C-H*), 5.21 (br s, 1H, N-*H*), 3.74 (s, 1H, $Sp^3$ C-*H*), 1.89 (d, 2H, $Sp^3$ C-*H*, *J* = 9.4 Hz), 1.64-1.55 (m, 3H, $Sp^3$ C-*H*), 1.36-1.28 (m, 2H, $Sp^3$ C-*H*), 1.17-1.07 (m, 3H, $Sp^3$ C-*H*). $^{13}$C NMR (δ ppm): (125 MHz, $CDCl_3$): 164.9, 135.4, 129.6, 129.5, 129.4, 50.5, 32.9, 25.4, 24.6. HRMS (ESI): calcd for $C_{13}H_{18}NOS$ $[M+H]^+$ 236.1104, found 236.1085.

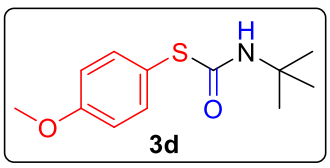
### 3c: *S*-(4-chlorophenyl) *tert*-butylcarbamothioate[1]



**3c**

White solid, Yield: 0.037 g (75%); m.p.: 145-146 $^{o}$C; $R_f$ 0.6 (1:9 EtOAc/hexane); $^{1}$H NMR, (δ ppm): (500 MHz, $CDCl_3$): 7.45 (d, 2H, aromatic *C-H*, *J* = 8.4 Hz*),* 7.36 (d, 2H, aromatic *C-H*, *J* = 8.4 Hz), 5.20 (br s, 1H, N-*H*), 1.35 (s, 9H, $Sp^3$ C-*H*). $^{13}$C NMR (δ ppm): (125 MHz, $CDCl_3$): 163.2, 136.6, 135.7, 129.3, 127.4, 53.7, 28.9.

### 3d: *S*-(4-methoxyphenyl) *tert*-butylcarbamothioate[1]

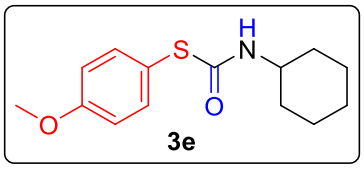


**3d**

White solid, Yield: 0.043 g (85%); m.p.: 83-84 $^{o}$C; $R_f$ 0.7 (1:9 EtOAc/hexane); $^{1}$H NMR, (δ ppm): (500 MHz, $CDCl_3$): 7.45 (d, 2H, aromatic *C-H*, *J* = 8.4 Hz), 6.93 (d, 2H, aromatic *C-H*, *J* = 8.4 Hz), 5.15 (br s, 1H, N-*H*), 3.83 (s, 3H, $Sp^3$ C-H), 1.32 (s, 9H, $Sp^3$ C-*H*). $^{13}$C

NMR (δ ppm): (125 MHz, $CDCl_3$): 164.9, 160.7, 137.2, 119.9, 114.9, 55.4, 53.4, 28.8. HRMS (ESI): calcd for $C_{12}H_{18}NO_2S$ $[M+H]^+$ 240.1053, found 240.1043

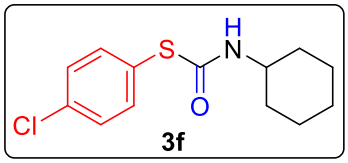
**3e: *S*-(4-methoxyphenyl) cyclohexylcarbamothioate**



**3e**

White solid, Yield: 0.051 g (90%); m.p.: 148-150 $^oC$; $R_f$ 0.6 (1:9 EtOAc/hexane); $^1H$ NMR, (δ ppm): (500 MHz, $CDCl_3$): 7.47 (d, 2H, aromatic *C-H*, *J* = 8.5 Hz), 6.93 (d, 2H, aromatic *C-H*, *J* = 8.7 Hz), 5.21 (br s, 1H, N-*H*), 3.84 (s, 3H, $Sp^3$ C-*H*), 3.73-3.69 (m, 1H, $Sp^3$ C-*H*), 1.87 (d, 2H, $Sp^3$ C-*H*, *J* =9.6 Hz), 1.63-1.54 (m, 3H, $Sp^3$ C-*H*), 1.32-1.29 (m, 2H, $Sp^3$ C-*H*), 1.16-1.07 (m, 3H, $Sp^3$ C-*H*). $^{13}C$ NMR (δ ppm): (125 MHz, $CDCl_3$): 165.9, 160.9, 137.2, 119.5, 115.1, 55.4, 50.4, 29.7, 25.4, 24.6. HRMS (ESI): calcd for $C_{14}H_{20}NO_2S$ $[M+H]^+$ 266.1209, found 266.1208.

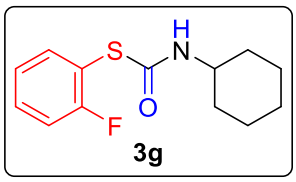
**3f: *S*-(4-chlorophenyl) cyclohexylcarbamothioate[2]**



**3f**

White solid, Yield: 0.045 g (82%); m.p.: 140-142 $^oC$; $R_f$ 0.5 (1:9 EtOAc/hexane); $^1H$ NMR, (δ ppm): (500 MHz, $CDCl_3$): 7.39 (d, 2H, aromatic *C-H*, *J* = 8.3 Hz), 7.34-7.28 (m, 2H, aromatic *C-H*), 5.19 (br s, 1H, N-*H*), 3.66 (s, 1H, $Sp^3$ C-*H*), 1.85 (d, 2H, $Sp^3$ C-*H*, *J* = 8.5 Hz), 1.61-1.51 (m, 3H, $Sp^3$ C-*H*), 1.27-1.18 (m, 2H, $Sp^3$ C-*H*), 1.07 (t, 3H, $Sp^3$ C-*H*, *J* = 6.6 Hz). $^{13}C$ NMR (δ ppm): (125 MHz, $CDCl_3$): 164.1, 136.5, 135.8, 129.4, 127.2, 50.9, 29.7, 25.3, 24.7.

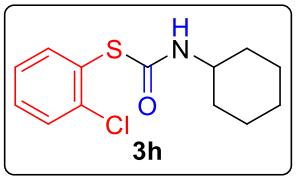
**3g: *S*-(2-fluorophenyl) cyclohexylcarbamothioate**



**3g**

Off-White solid, Yield: 0.048g (81%); m.p.: 118-120 $^oC$; $R_f$ 0.8 (1:9 EtOAc/hexane); $^1H$ NMR, (δ ppm): (500 MHz, $CDCl_3$): 7.54 (t, 1H, aromatic *C-H*, *J* = 6.7 Hz), 7.45-7.41 (m, 1H, aromatic *C-H*), 7.17 (dd, 1H, aromatic *C-H*, *J* = 14.0, 6.9 Hz), 5.27 (br s, 1H, N-*H*), 3.74 (s, 1H, $Sp^3$ C-*H*), 1.94 (d, 2H, $Sp^3$ C-*H*, *J* = 8.6 Hz), 1.69-1.58 (m, 3H, $Sp^3$ C-*H*), 1.34-1.29 (m, 2H, $Sp^3$ C-*H*), 1.19-1.15 (m, 3H, $Sp^3$ C-*H*). $^{13}C$ NMR (δ ppm): (125 MHz, $CDCl_3$): 163.4, 162.9, 161.5, 137.6, 132.0 ($J_{C-F}$ = 35 Hz), 124.7, 116.2 ($J_{C-F}$ = 90 Hz), 56.7, 32.8, 25.4, 24.6. HRMS (ESI): calcd for $C_{13}H_{17}FNOS$ $[M+H]^+$ 254.1010, found 254.1026.

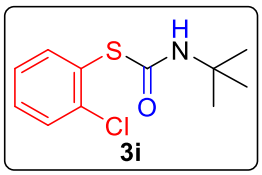
**3h: *S*-(2-chlorophenyl) cyclohexylcarbamothioate**



3h

Off-White solid, Yield: 0.041 g (74%); m.p.: 125-127 $^{o}$C; $R_f$ 0.6 (1:9 EtOAc/hexane); $^{1}$H NMR, (δ ppm): (500 MHz, $CDCl_3$): 7.67 (d, 1H, aromatic *C-H*, *J* = 7.4 Hz), 7.52 (d, 1H, aromatic *C-H*, *J* = 7.9 Hz), 7.36 (td, 1H, aromatic *C-H*, *J* = 7.5, 1.2 Hz), 7.30 (t, 1H, aromatic *C-H*, *J* = 7.5 Hz), 5.30 (br s, 1H, N-*H*), 3.79 (s, 1H, $Sp^3$ C-*H*), 1.94 (d, 2H, $Sp^3$ C-*H*, *J* = 9.2 Hz), 1.69-1.58 (m, 3H, $Sp^3$ C-*H*), 1.37-1.30 (m, 2H, $Sp^3$ C-*H*), 1.19-1.12 (m, 3H, $Sp^3$ C-*H*). $^{13}$C NMR (δ ppm): (125 MHz, $CDCl_3$): 162.9, 139.1, 137.7, 131.0, 130.3, 128.3, 127.4, 50.9, 32.9, 25.4, 24.6. HRMS (ESI): calcd for $C_{13}H_{17}ClNOS$ $[M+H]^+$ 270.0714, found 270.0731.

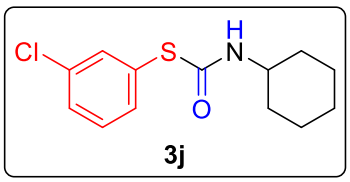
**3i: *S*-(2-chlorophenyl) *tert*-butylcarbamothioate**



3i

Colourless liquid, Yield: 0.038 g (76%); $R_f$ 0.8 (1:9 EtOAc/hexane); $^{1}$H NMR, (δ ppm): (500 MHz, $CDCl_3$): 7.65 (dd, 1H, aromatic *C-H*, *J* = 7.6, 1.4 Hz), 7.51 (d, 1H, aromatic *C-H*, *J* = 7.8 Hz), 7.35 (td, 1H, aromatic *C-H*, *J* = 7.3, 1.3 Hz), 7.30 (td, 1H, aromatic *C-H*, *J* = 7.6, 1.2 Hz), 5.27 (br s, 1H, N-*H*), 1.36 (s, 9H, $Sp^3$ C-*H*). $^{13}$C NMR (δ ppm): (125 MHz, $CDCl_3$): 162.0, 139.1, 137.7, 130.8, 130.2, 128.6, 127.3, 53.8, 28.8. HRMS (ESI): calcd for $C_{11}H_{15}ClNOS$ $[M+H]^+$ 244.0558, found 244.0562.

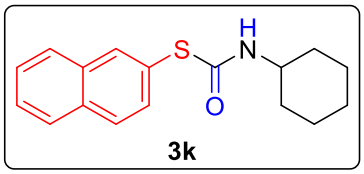
**3j: *S*-(3-chlorophenyl) cyclohexylcarbamothioate**



3j

White solid, Yield: 0.049 g (88%); m.p.: 110-112 $^{o}$C; $R_f$ 0.6 (1:9 EtOAc/hexane); $^{1}$H NMR, (δ ppm): (500 MHz, $CDCl_3$): 7.55 (s, 1H, aromatic *C-H*), 7.42 (d, 1H, aromatic *C-H*, *J* = 7.3 Hz), 7.38 (d, 1H, aromatic *C-H*, *J* = 7.8 Hz), 7.33 (t, 1H, aromatic *C-H*, *J* = 7.6 Hz), 5.26 (br s, 1H, N-*H*), 3.74 (s, 1H, $Sp^3$ C-*H*), 1.93 (d, 2H, $Sp^3$ C-*H*, *J* = 8.6 Hz), 1.69-1.61 (m, 3H, $Sp^3$ C-*H*), 1.35-1.30 (m, 2H, $Sp^3$ C-*H*), 1.16-1.14 (m, 3H, $Sp^3$ C-*H*). $^{13}$C NMR (δ ppm): (125 MHz, $CDCl_3$): 163.7, 134.9, 134.7, 133.3, 130.5, 130.1, 125.5, 50.9, 29.7, 25.3, 24.7. HRMS (ESI): calcd for $C_{13}H_{17}ClNOS$ $[M+H]^+$ 270.0714, found 270.0714.

**3k: *S*-(naphthalen-2-yl) cyclohexylcarbamothioate**

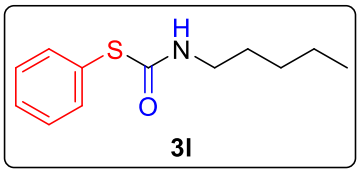


3k

White solid, Yield: 0.047 g (88%); m. p.: 88-91 $^{o}$C; $R_f$ 0.8 (1:9 EtOAc/hexane). $^{1}$H NMR, (δ ppm): (500 MHz, $CDCl_3$): 7.57-7.56 (m, 2H, aromatic *C-H*), 7.43-7.42 (m, 3H, aromatic *C-H*), 5.30 (br

s, 1H, N-*H*), 3.26 (q, 2H, $Sp^3$ C-*H*, *J* = 6.6 & 13.0 Hz), 1.48-1.45 (m, 2H, $Sp^3$ C-*H)*, 1.29-1.25 (m, 4H, $Sp^3$ C-*H)*, 0.87 (t, 3H, $Sp^3$ C-*H*, *J* = 6.9 Hz). $^{13}$C NMR (δ ppm): (125 MHz, $CDCl_3$): 164.9, 135.2, 133.6, 133.4, 131.6, 128.9, 128.0, 127.8, 127.2, 126.7, 126.2, 50.7, 32.9, 25.4, 24.6. HRMS (ESI): calcd for $C_{17}H_{20}NOS$ $[M+H]^+$ 286.1260, found 286.1261.

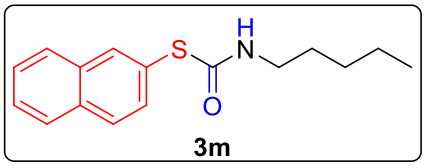
**3l: *S*-phenyl pentylcarbamothioate[1]**



**3l**

White solid, Yield: 0.048 g (80%); m.p.: 36-38 ºC; $R_f$ 0.7 (1:9 EtOAc/hexane); $^1$H NMR, (δ ppm): (500 MHz, $CDCl_3$): 7.57-7.56 (m, 2H, aromatic *C-H*), 7.43-7.42 (m, 3H, aromatic *C-H*), 5.30 (br s, 1H, N-*H*), 3.26 (q, 2H, $Sp^3$ C-*H*, *J* = 6.6 & 13.0 Hz), 1.48-1.45 (m, 2H, $Sp^3$ C-*H)*, 1.29-1.25 (m, 4H, $Sp^3$ C-*H)*, 0.87 (t, 3H, $Sp^3$ C-*H*, *J* = 6.9 Hz). $^{13}$C NMR (δ ppm): (125 MHz, $CDCl_3$): 165.9, 135.5, 129.7, 129.5, 128.7, 41.5, 29.2, 28.8, 22.3, 13.9.

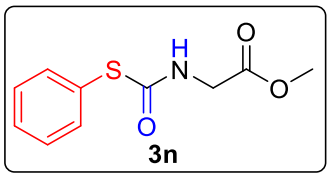
**3m: *S*-(naphthalen-2-yl) pentylcarbamothioate**



**3m**

White solid, Yield: 0.044 g (87%); m.p.: 82-84 ºC; $R_f$ 0.5 (1:9 EtOAc/hexane); $^1$H NMR, (δ ppm): (500 MHz, $CDCl_3$): 8.10 (s, 1H, aromatic *C-H*), 7.89-7.84 (m, 3H, aromatic *C-H*), 7.61-7.52 (m, 3H, aromatic *C-H*), 5.38 (br s, 1H, N-*H*), 3.26 (q, 2H, $Sp^3$ C-*H*, *J* = 6.5 & 12.9 Hz), 1.48-1.43 (m, 2H, $Sp^3$ C-*H)*, 1.30-1.23 (m, 4H, $Sp^3$ C-*H)*, 0.87 (t, 3H, $Sp^3$ C-*H*, *J* = 6.7 Hz). $^{13}$C NMR (δ ppm): (125 MHz, $CDCl_3$): 165.9, 135.4, 135.3, 133.6, 133.4, 131.7, 129.1, 128.0, 127.8, 127.3, 126.8, 41.6, 28.8, 22.2, 13.9, 13.88. HRMS (ESI): calcd for $C_{16}H_{20}NOS$ $[M+H]^+$ 274.1260, found 274.1262.

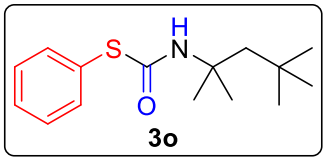
**3n: methyl ((phenylthio)carbonyl)glycinate[1]**



**3n**

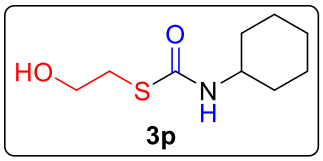
White solid, Yield: 0.046 g (79%); m.p.: 116-118 ºC; $R_f$ 0.25 (1:9 EtOAc/hexane); $^1$H NMR, (δ ppm): (500 MHz, $CDCl_3$): 7.59-7.44 (m, 5H, aromatic *C-H*), 5.92 (br s, 1H, N-*H*), 4.09 (s, 2H, $Sp^3$ C-*H*), 3.75 (s, 3H, $Sp^3$ C-*H)*. $^{13}$C NMR (δ ppm): (125 MHz, $CDCl_3$): 169.8, 166.9, 135.6, 130.0, 129.6, 127.9, 52.6, 42.5.

**3o: *S*-phenyl (2,4,4-trimethylpentan-2-yl)carbamothioate[1]**




White solid, Yield: 0.057 g (79%); m.p.: 85-86 $^{o}$C; $R_f$ 0.35 (1:9 EtOAc/hexane); $^{1}$H NMR, (δ ppm): (500 MHz, $CDCl_3$): 7.54-7.41 (m, 5H, aromatic *C-H*), 5.16 (br s, 1H, N-*H*), 1.66 (s, 2H, $Sp^3$ C-*H*), 1.37 (s, 6H, $Sp^3$ C-*H)*, 0.95 (s, 9H, $Sp^3$ C-*H*). $^{13}$C NMR (δ ppm): (125 MHz, $CDCl_3$): 163.9, 135.6, 129.5, 129.4, 129.2, 57.3, 51.8, 31.4, 29.2.

**3p: S-(2-hydroxyethyl) cyclohexylcarbamothioate**

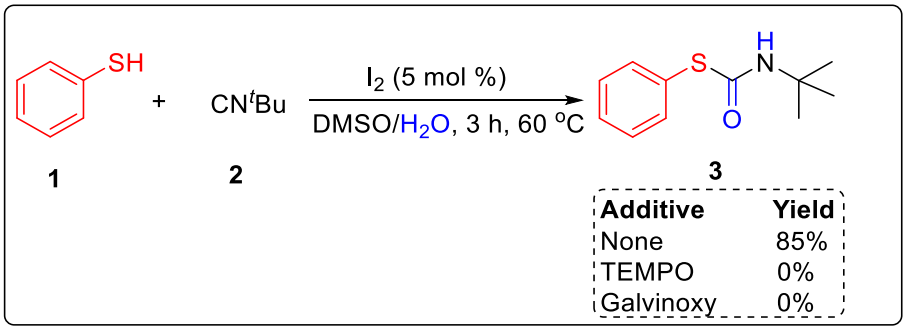



White solid, Yield: 0.09 g (74%); m.p.: 110-112 $^{o}$C; $R_f$ 0.25 (1:9 EtOAc/hexane); $^{1}$H NMR, (δ ppm): (500 MHz, $CDCl_3$): 5.22 (br s, 1H, N-*H*), 3.75 (s, 1H, $Sp^3$ C-*H*), 3.33 (s, 4H, $Sp^3$ C-*H*), 1.94 (d, 2H, $Sp^3$ C-*H*, *J* = 9.9 Hz), 1.71 (d, 3H, $Sp^3$ C-*H*, *J* = 13.2 Hz), 1.36-1.30 (m, 2H, $Sp^3$ C-*H*), 1.17 (t, 3H, $Sp^3$ C-*H*, *J* = 9.3 Hz). $^{13}$C NMR (δ ppm): (125 MHz, $CDCl_3$): 164.3, 50.8, 33.1, 25.4, 24.7, 3.9.

**3r: S-decyl cyclohexylcarbamothioate**


White solid, Yield: 0.06 g (71%); m.p.: 118-120 $^{o}$C; $R_f$ 0.2 (1:9 EtOAc/hexane); $^{1}$H NMR, (δ ppm): (500 MHz, $CDCl_3$): 5.17 (br s, 1H, N-*H*), 3.75 (s, 1H, $Sp^3$ C-*H*), 2.89 (d, 2H, $Sp^3$ C-*H*, *J* = 2.3 Hz), 1.94 (d, 2H, $Sp^3$ C-*H*, *J* = 10.3 Hz), 1.72-1.57 (m, 11H, $Sp^3$ C-*H*), 1.39-1.28 (m, 10H, $Sp^3$ C-*H*), 1.17-1.10 (m, 3H, $Sp^3$ C-*H*), 0.88 (t, 3H, $Sp^3$ C-*H*, *J* = 6.7 Hz). $^{13}$C NMR (δ ppm): (125 MHz, $CDCl_3$):160.3, 50.5, 33.2, 31.9, 29.7, 29.65, 29.61, 29.5, 29.4, 29.2, 28.8, 25.4, 24.8, 22.7, 14.1.

**5. Radical trap experiment:**




A 10 mL schlenk tube equipped with a stir-bar was charged with thiophenol (0.03 g, 0.27 mmol), *tert*-butyl isocyanide (0.026 g, 0.32 mmol) in DMSO/$H_2O$ (99/1, 0.2 mL) as a solvent. Then after

5-10 min. Iodine (0.003 g, 0.01 mmol) and radical scavengers [TEMPO/Galvinoxy (0.27 mmol)] was added to the reaction mixture. The mixture was stirred it at 60 $^{o}$C for 3 h. After completion of the reaction on TLC, the reaction mixture was diluted with water and extracted three times with EtOAc. Collected organic layers were washed with water, sodium thiosulphate solution and brine successively, dried over anhydrous sodium sulphate, filtered, and concentrated in vacuo. Purification by silica gel (100-200 mesh) chromatography (EtOAc: Hexane) to yield the desired product **3**.

**Table *S*5. Observation of radical trap experiment**

| S. No. | Additive | Yield |
|---|---|---|
| 1 | None | 85% |
| 2 | TEMPO | 0% |
| 3 | Galvinoxyl | 0% |

**6. General procedure for the control experiments:**

**6.1 Reaction under anhydrous conditions:**

1) Reaction under inert atmosphere: A 10 mL schlenk tube equipped with a stir-bar was charged with thiophenol (0.05 g, 0.42 mmol), *tert*-butyl isocyanide (0.041 g, 0.50 mmol) in DMSO/$H_2O$ (99/1, 0.5 mL) as a solvent under nitrogen atmosphere. Then after 5-10 min. Iodine (0.004 g, 0.021 mmol) was added to the reaction mixture and degased using nitrogen. The mixture was stirred at 60$^{o}$ C for 4 h under inert atmosphere. After completion of the reaction, the reaction mixture was passed through celite bed and washed with EtOAc. The reaction mixture was diluted with EtOAc, which was washed with water, sodium thiosulphate solution and brine successively, dried over anhydrous sodium sulphate, filtered, and concentrated in vacuo. Purification by silica gel (100-200 mesh) chromatography (EtOAc: Hexane) to yield the desired product **3**.

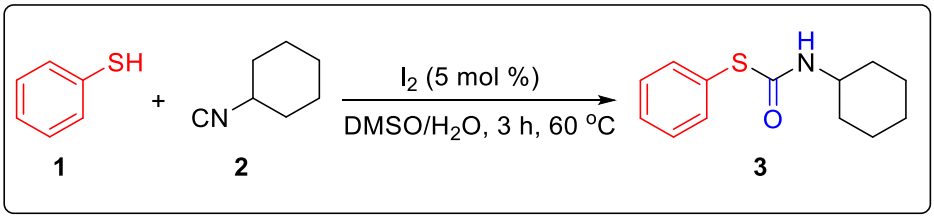
2) Reaction with anhydrous DMSO: A 10 mL schlenk tube equipped with a stir-bar was charged with thiophenol (0.05 g, 0.42 mmol), *tert*-butyl isocyanide (0.041 g, 0.50 mmol) in anhydrous DMSO (0.5 mL) as a solvent. Then after 5-10 min. Iodine (0.004 g, 0.021 mmol) was added to the reaction mixture. The mixture was stirred at 60$^{o}$ C for 4 h. After completion of the reaction, the reaction mixture was passed through celite bed and washed with EtOAc. The reaction mixture was

diluted with EtOAc, which was washed with water, sodium thiosulphate solution and brine successively, dried over anhydrous sodium sulphate, filtered, and concentrated in vacuo. Purification by silica gel (100-200 mesh) chromatography (EtOAc: Hexane) to yield the desired product **3**.

**6.2 Reaction with diphenyl disulphide:** A 10 mL schlenk tube equipped with a stir-bar was charged with thiophenol (0.05 g, 0.42 mmol), *tert*-butyl isocyanide (0.041 g, 0.50 mmol) in DMSO/$H_2O$ (99/1, 0.5 mL) as a solvent. Then after 5-10 min. Iodine (0.004 g, 0.021 mmol) was added to the reaction mixture. The mixture was stirred it at 60$^o$ C for 4 h. After completion of the reaction, the reaction mixture was passed through celite bed and washed with EtOAc. The reaction mixture was diluted with EtOAc, which was washed with water, sodium thiosulphate solution and brine successively, dried over anhydrous sodium sulphate, filtered, and concentrated in vacuo. Purification by silica gel (100-200 mesh) chromatography (EtOAc: Hexane) to yield the desired product **3**.

**6.3 Intermolecular competition Experiment:** A 10 mL schlenk tube equipped with a stir-bar was charged with thiophenol (0.05 g, 0.42 mmol), *tert*-butyl isocyanide (0.041 g, 0.50 mmol) in anhydrous DMSO/$H_2O$ (99/1, 0.5 mL) as a solvent. Then after 5-10 min. Iodine (0.004 g, 0.021 mmol) was added to the reaction mixture. The mixture was stirred it at 60$^o$ C for 4 h. After completion of the reaction, the reaction mixture was passed through celite bed and washed with EtOAc. The reaction mixture was diluted with EtOAc, which was washed with water, sodium thiosulphate solution and brine successively, dried over anhydrous sodium sulphate, filtered, and concentrated in vacuo. Purification by silica gel (100-200 mesh) chromatography (EtOAc: Hexane) to yield the desired product 3.

**7. Experimental procedure for gram scale synthesis:**




A 10 mL schlenk tube equipped with a stir-bar was charged with thiophenol (0.5 g, 4.55 mmol), cyclohexyl isocyanide (0.595 g, 5.46 mmol) in DMSO/$H_2O$ (99/1, 1.0 mL) as a solvent. Then after 5-10 min. Iodine (0.058 g, 0.23 mmol) was added to the reaction mixture. The mixture was stirred

it at 60 °C for 3 h. After completion of the reaction on TLC, the reaction mixture was diluted with water and extracted three times with EtOAc. Collected organic layers were washed with water, sodium thiosulphate solution and brine successively, dried over anhydrous sodium sulphate, filtered, and concentrated in vacuo. Purification by silica gel (100-200 mesh) chromatography (EtOAc: Hexane) to yield the desired product **3** [Yield: 0.93 g (88%)]

## 8. Crystal Data:

Colourless plate crystals of compound **3b** was grown by evaporation of mixed solvents of petroleum ether and dichloromethane at room temperature. The determination of unit cell and intensity data collection was performed using a *Xcalibur, Atlas* diffractometer at 293(2) K. Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm was performed with CrysAlisPro 1.171.38.46 (Rigaku Oxford Diffraction, 2015). Structure was solved with the SHELXT (Sheldrick, 2015) and refined with the SHELXL (Sheldrick, 2015).[1] Crystallographic data (excluding structure factors) for the structures in this manuscript have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC **1845513.** This data can be obtained free of charge from the Cambrige Crystallographic Data Centers *via* www.ccdc.cam.ac.uk/data_request/cif.

1: (a) Rigaku Oxford Diffraction. CrysAlisPro Software system, version 1.171.38.46. Rigaku Corporation Oxford, UK; 2015; (b) Sheldrick, G.M. *Acta Cryst*., **2015**, *A71*, 3-8.

### 8.1: Crystal structure of 3b:

Figure S1 represents an ORTEP diagram with 50% probability displacement ellipsoids. X-ray crystallographic analysis of **3b** [$C_{12}H_{14}N_6$] also confirmed the stereochemistry of the desired product.

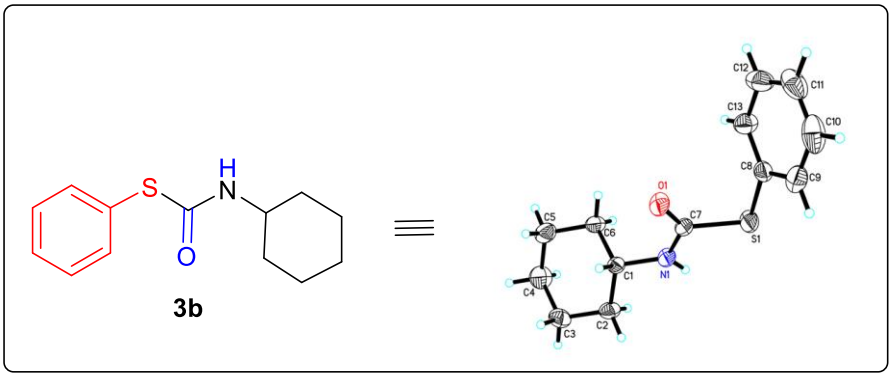


**Figure S1**: The X-ray crystal structure of compound **3b** showing with ORTEP diagram using 50% ellipsoidal plot.

| | |
|---|---|
| Identification code | CCDC Number: 1845513 |
| Empirical formula | $C_{13}H_{17}NOS$ |
| Formula weight | 235.34 |
| Temperature/K | 298.2 |
| Crystal system | Monoclinic |
| Space group | $P2_1/n$ |
| a/Å | 6.3713 (3) |
| b/Å | 23.7413 (12) |
| c/Å | 8.8276 (4) |
| α/° | 90.000 (0) |
| β/° | 103.695 (5) |
| γ/° | 90.000 (0) |
| Volume/$Å^3$ | 1297.33 (11) |
| Z | 4 |
| μ/$mm^{-1}$ | 0.23 |
| F(000) | 500 |
| Crystal size/$mm^3$ | 0.31 × 0.25 × 0.20 |
| Reflections collected | 6708 |
| Independent reflections | 3026 |
| Data/restraints/parameters | 2287/0/109 |
| Goodness-of-fit on $F^2$ | 1.044 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0708, $wR_2$ = 0.1991 |
| Final R indexes [all data] | $R_1$ = 0.1123, $wR_2$ = 0.2566 |
| Largest diff. peak/hole / e $Å^{-3}$ | 0.52/-0.31 |

**9. References:**

[1] P. Mampuys, Y. Zhu, S. Sergeyev, E. Ruijter, R. V. A. Orru, S. V. Doorslaer, B. U. W. Maes, *Org. Lett.* 2016, **18**, 2808-2811.

[2] H.-K. Kim, A. Lee, *Org. Biomol. Chem*., 2016, **14**, 7345-7353.

## 10. Copies of $^{1}H$ and $^{13}C$ NMR data:

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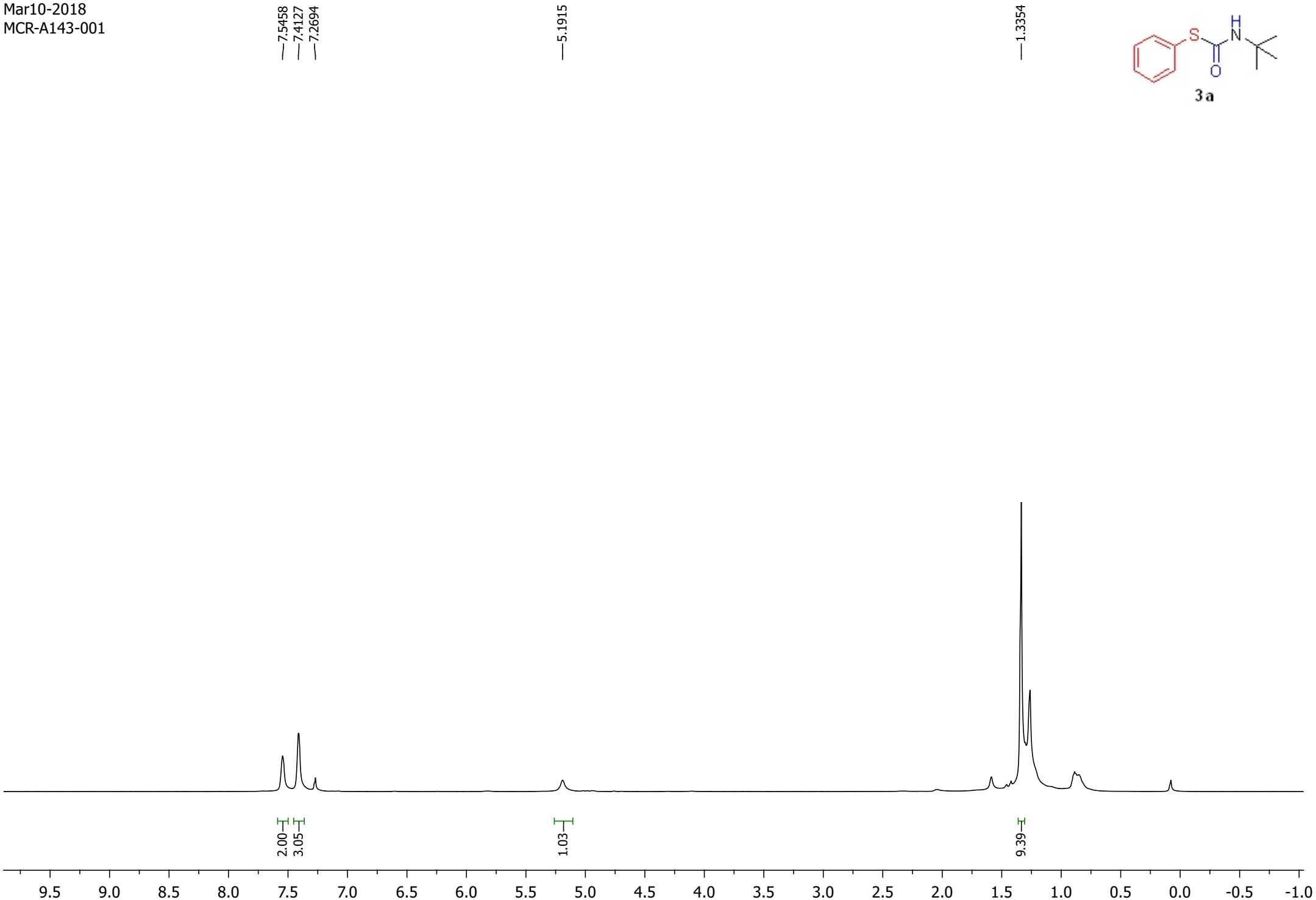

Mar10-2018
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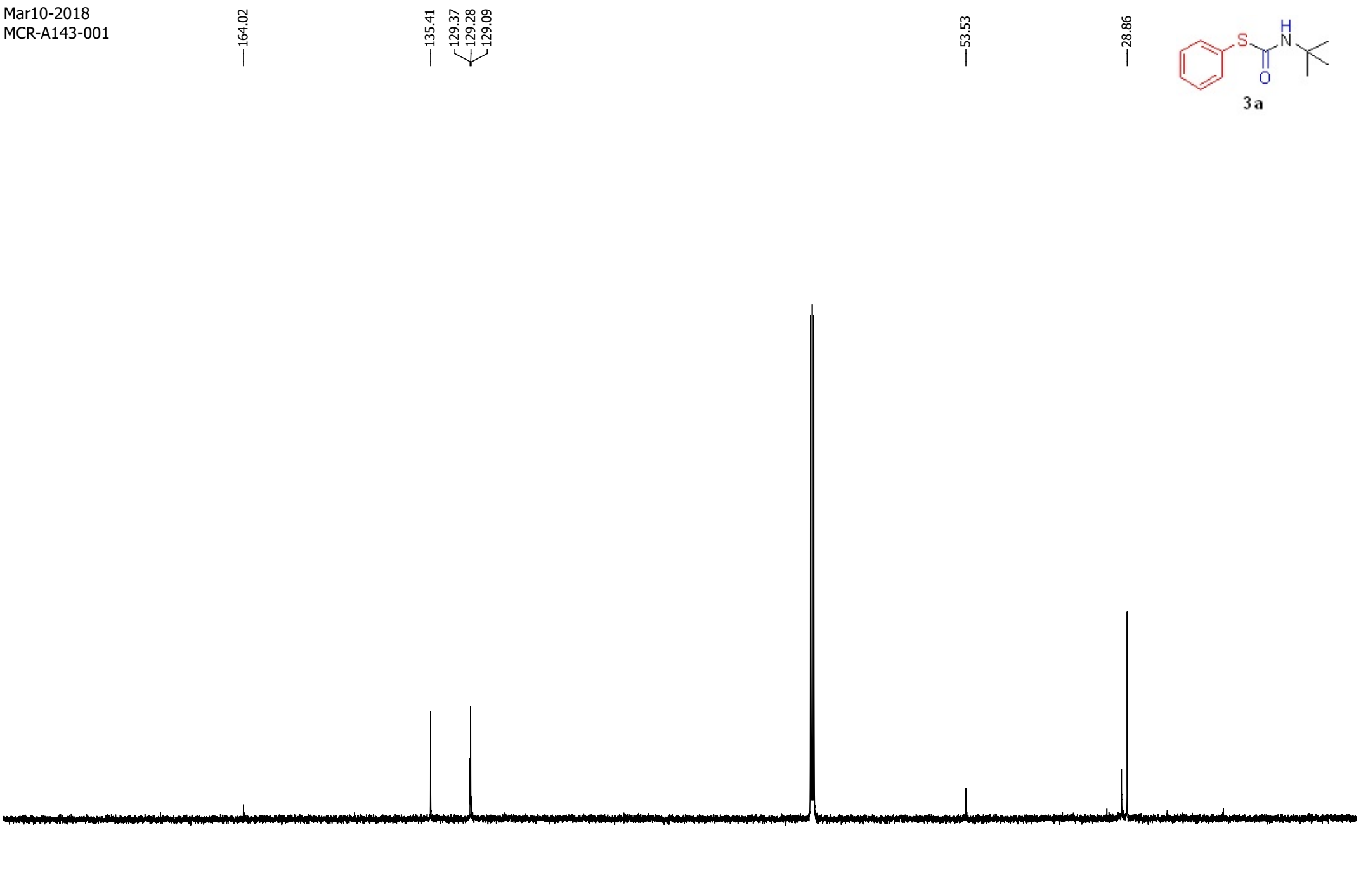

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06-Jun-2018
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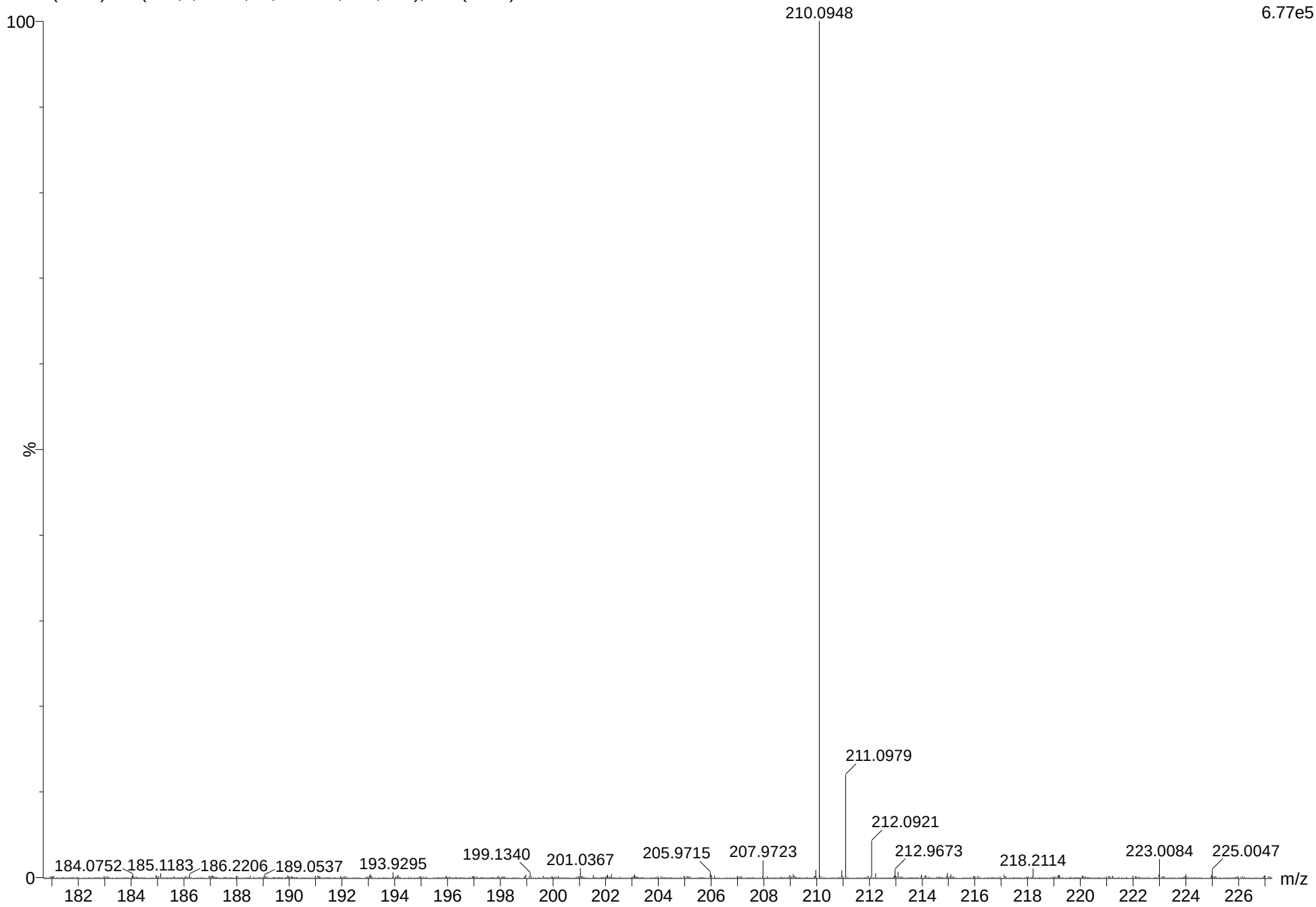

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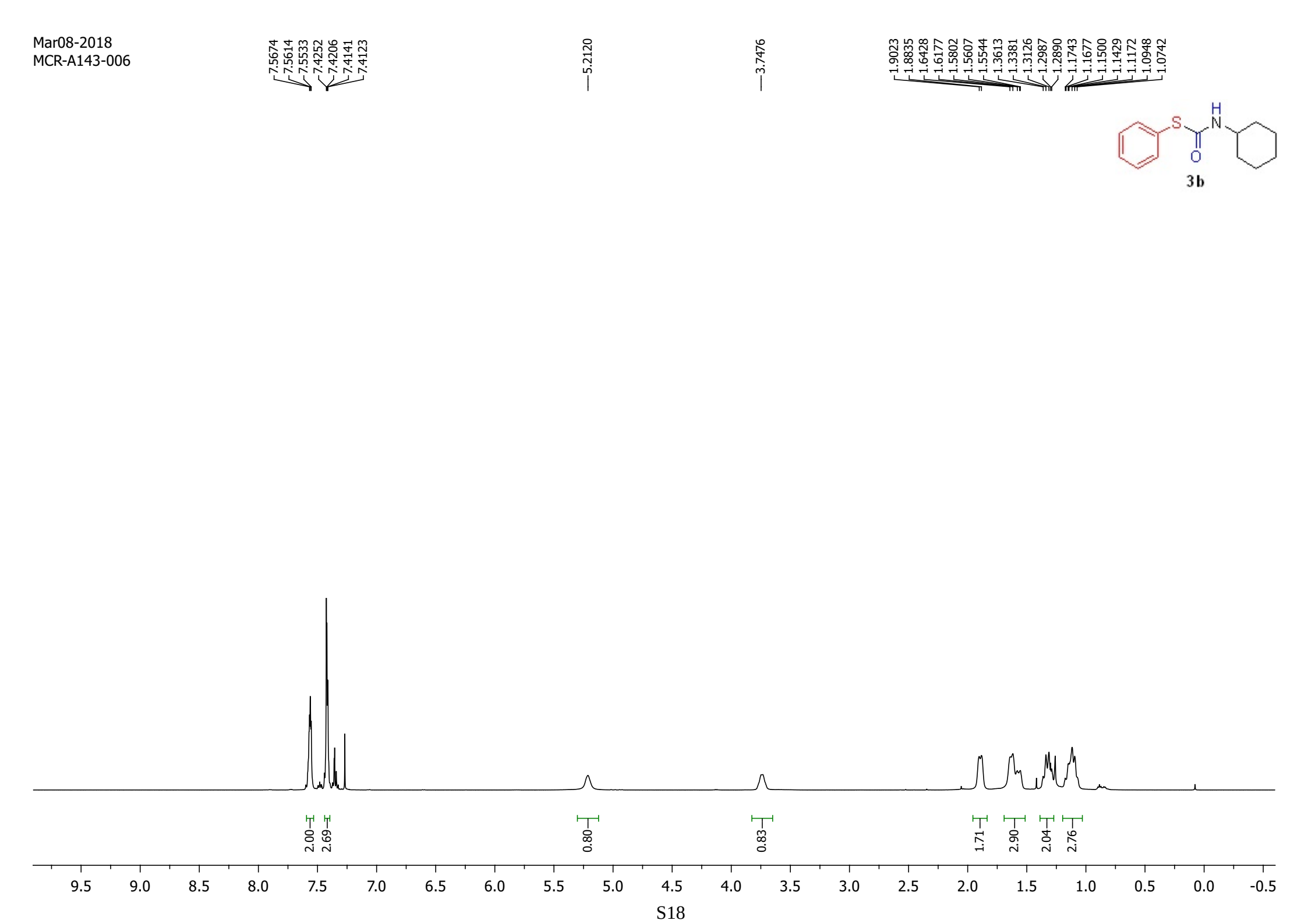

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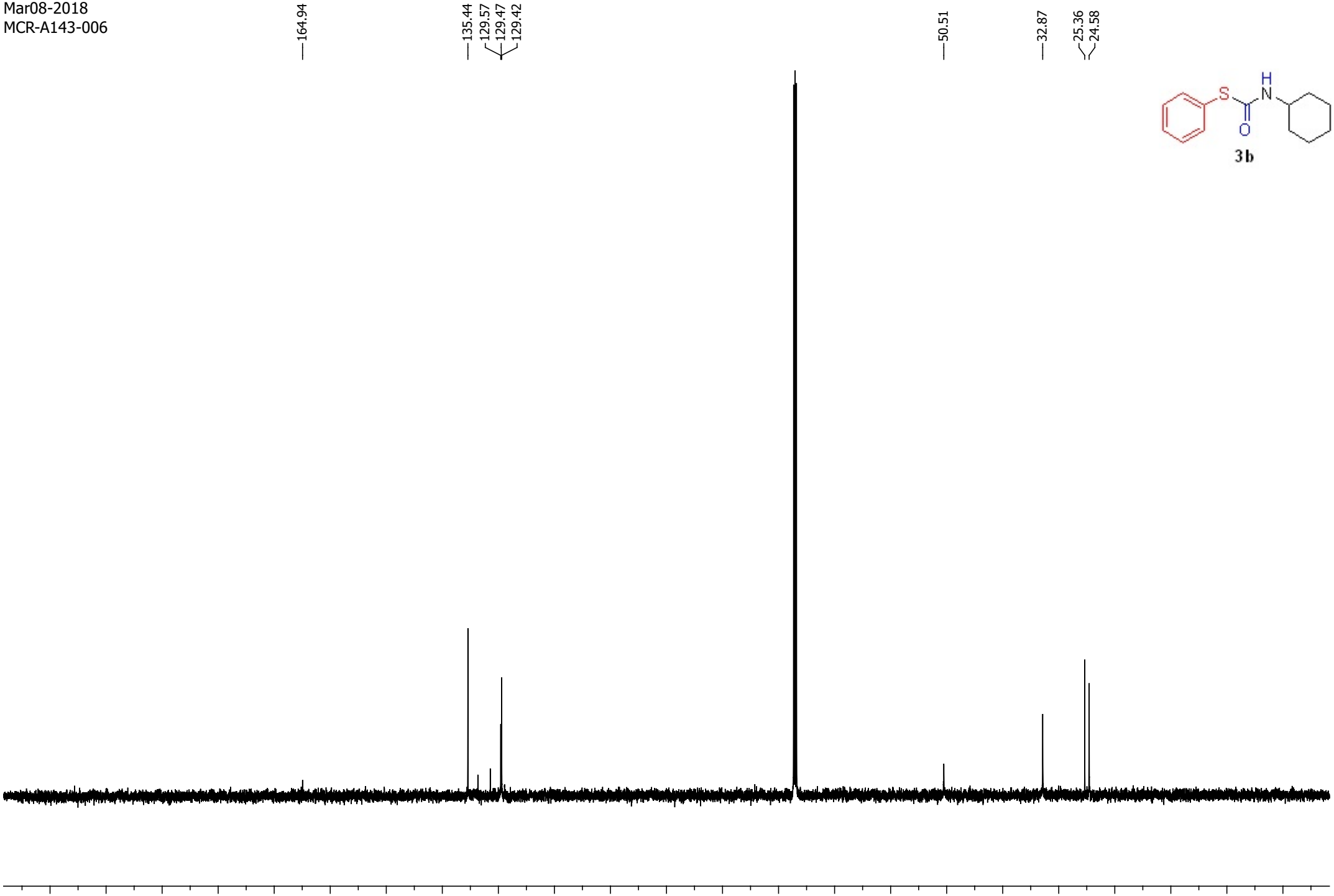

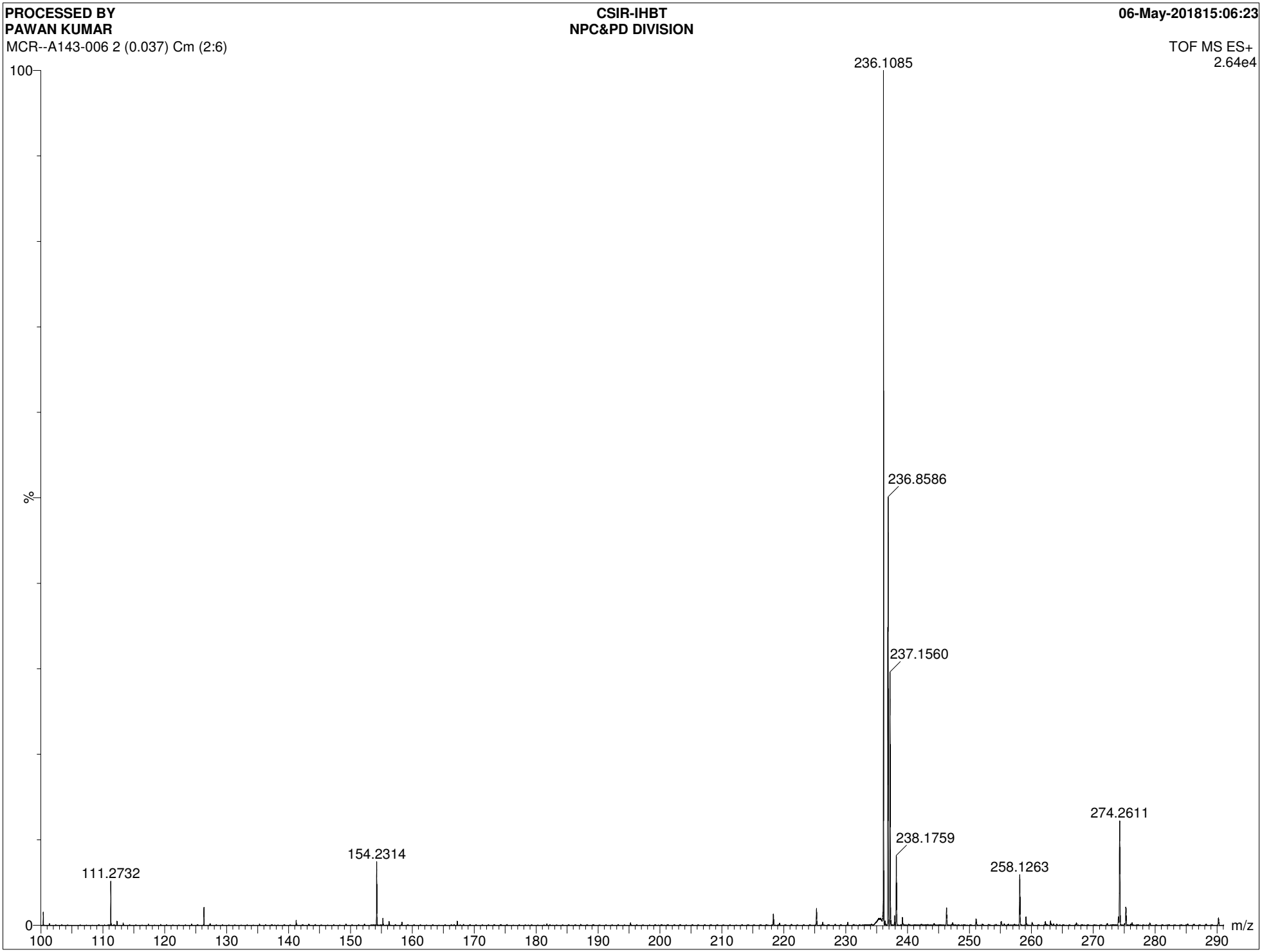
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PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
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Mar05-2018
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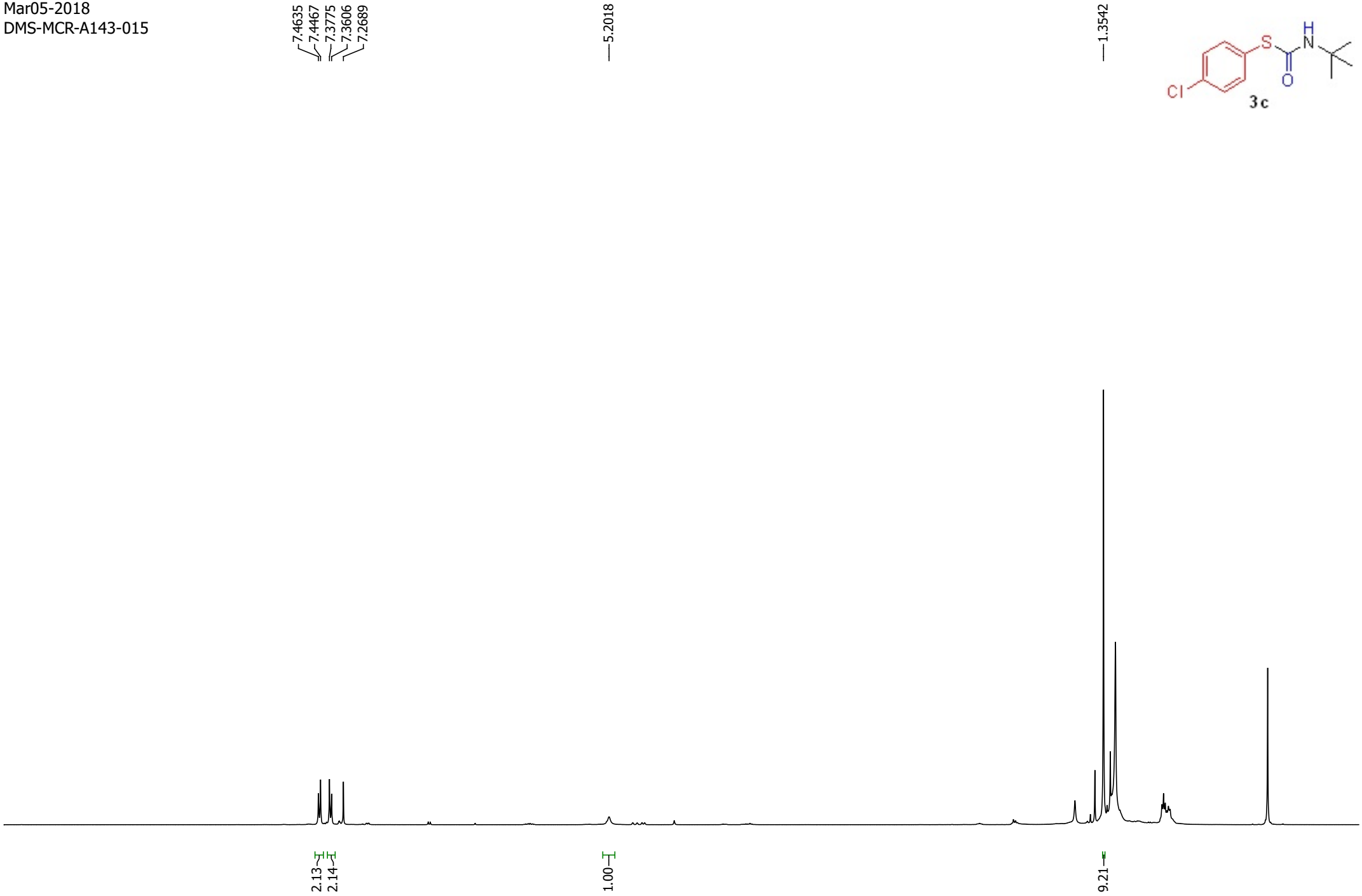

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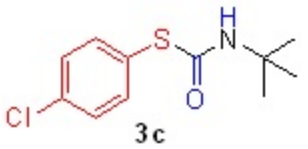
28.88



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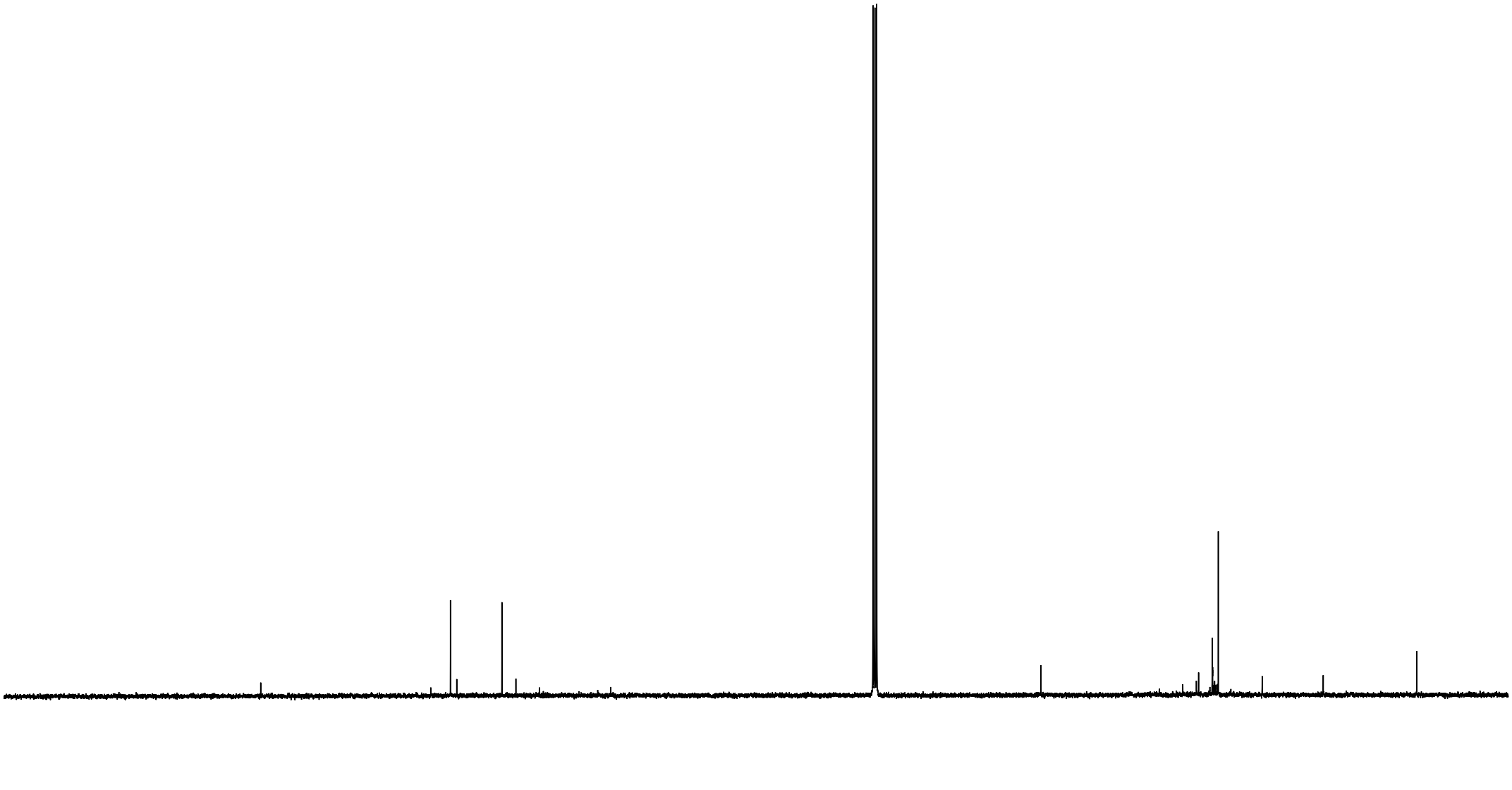

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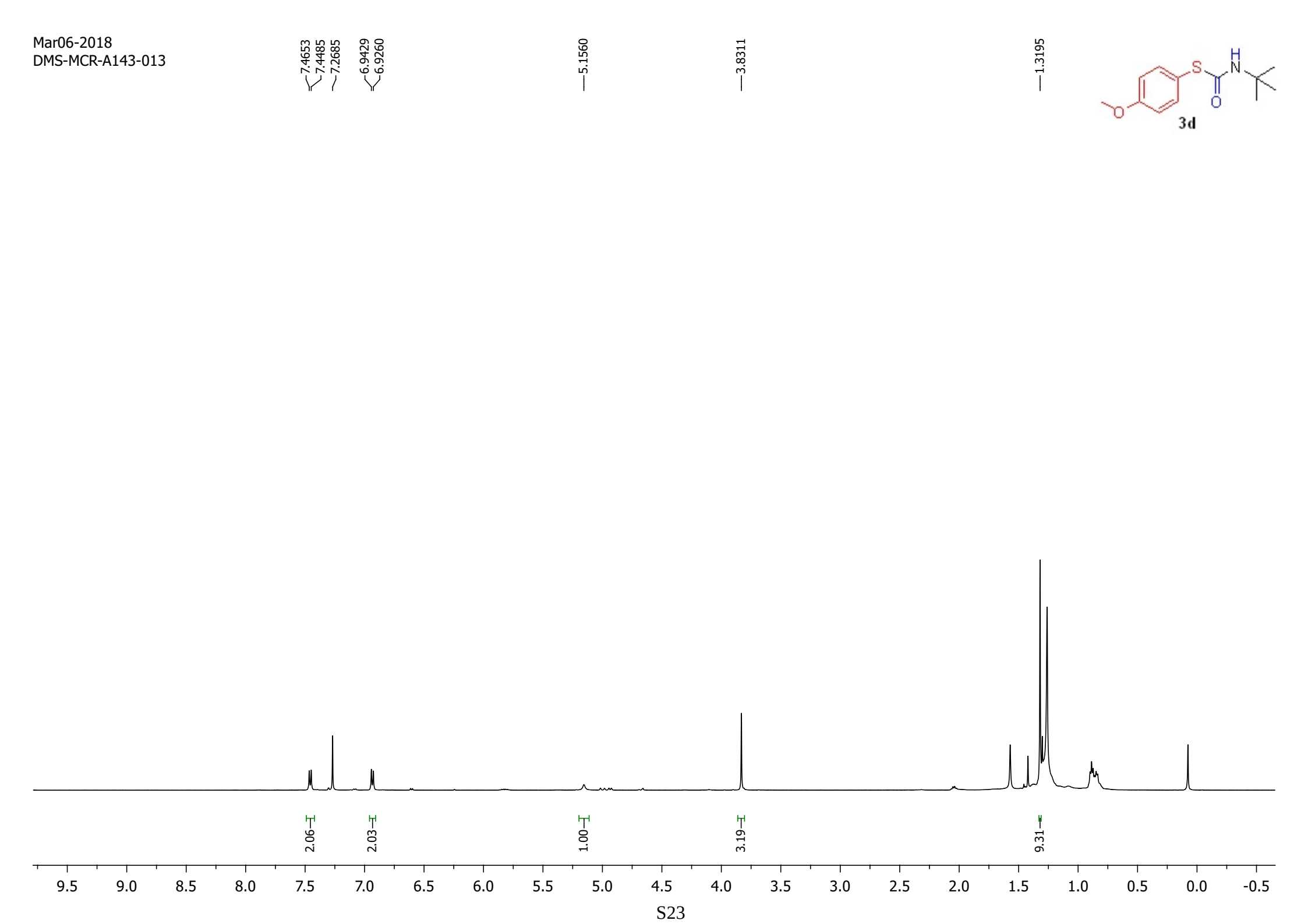

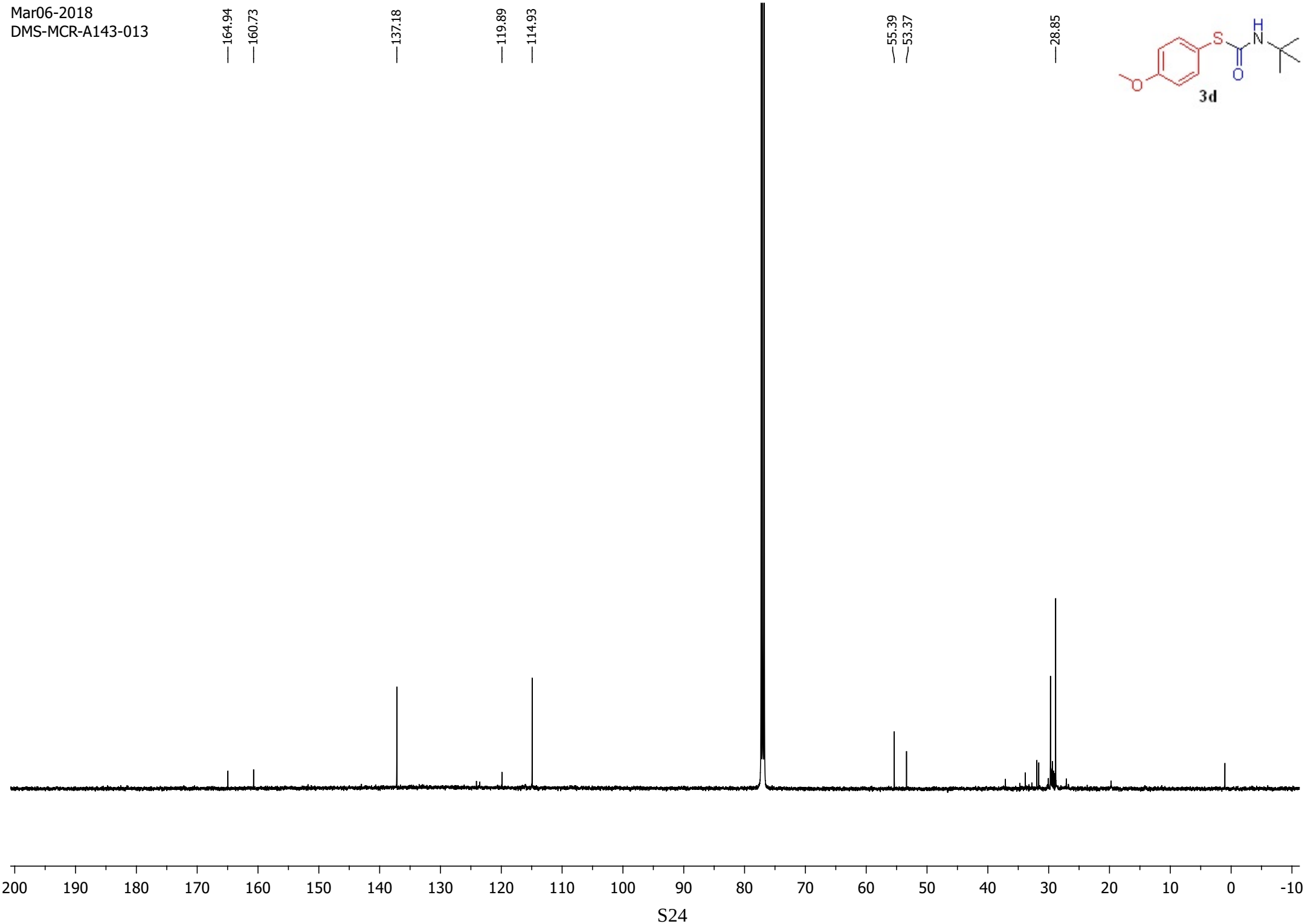
Mar06-2018
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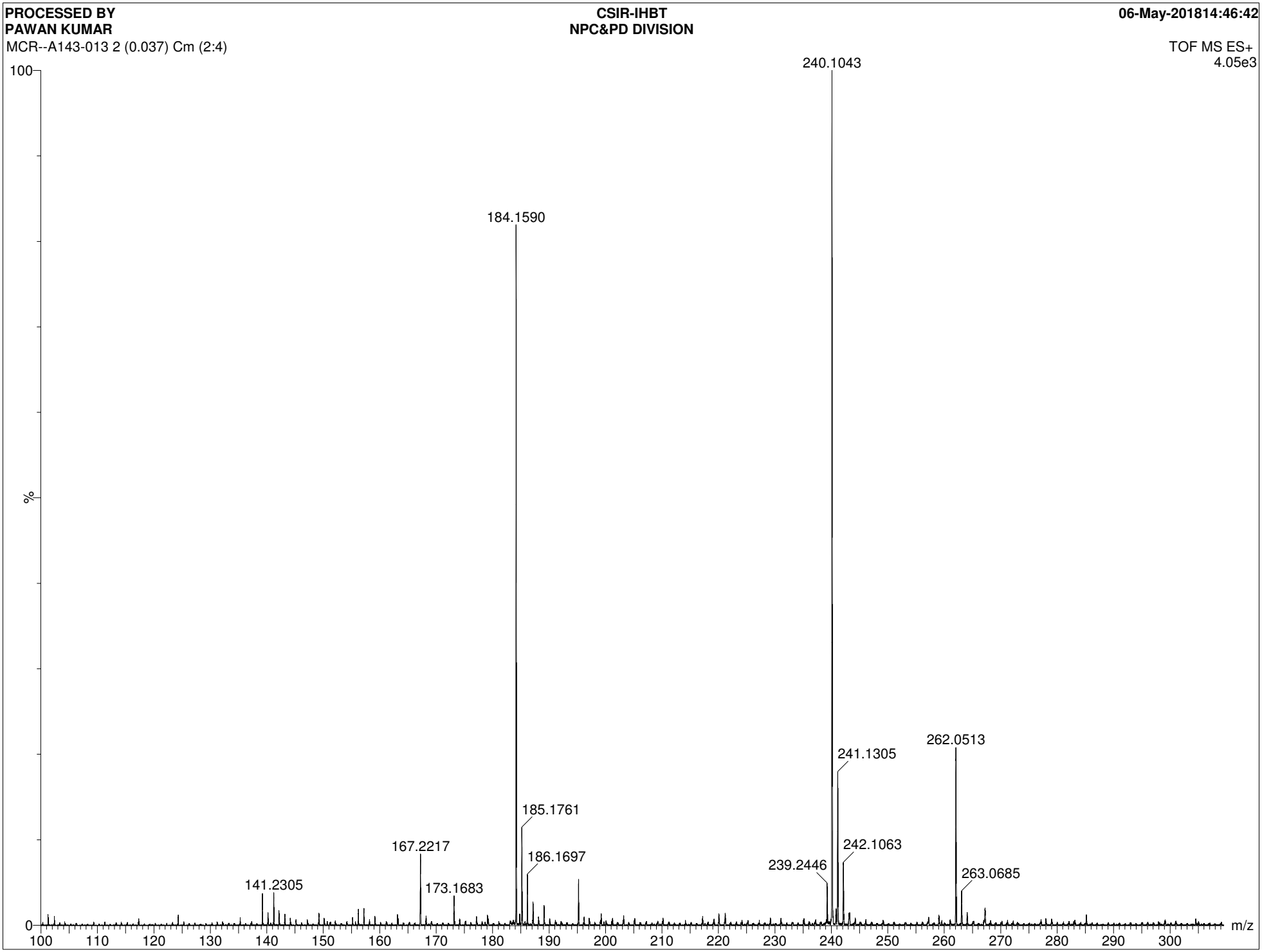
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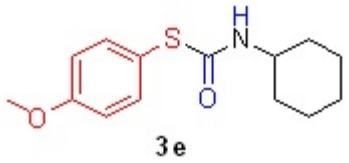
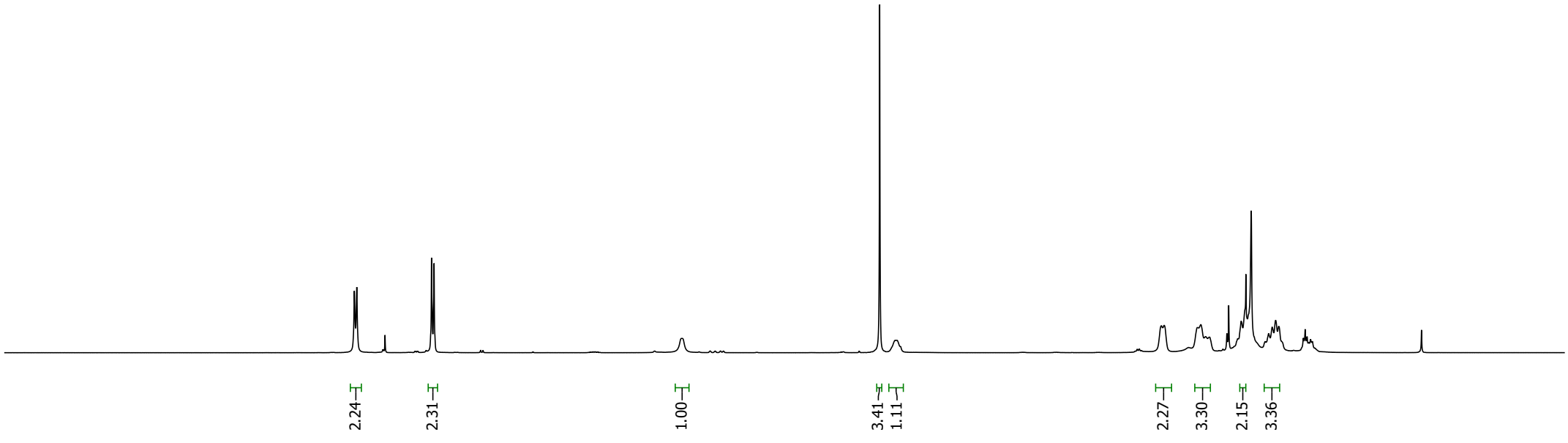
Feb27-2018
MCR-A143-014




3e



Feb27-2018
MCR-A143-014

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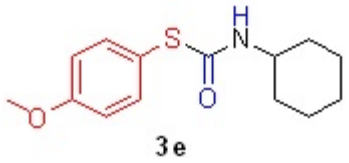
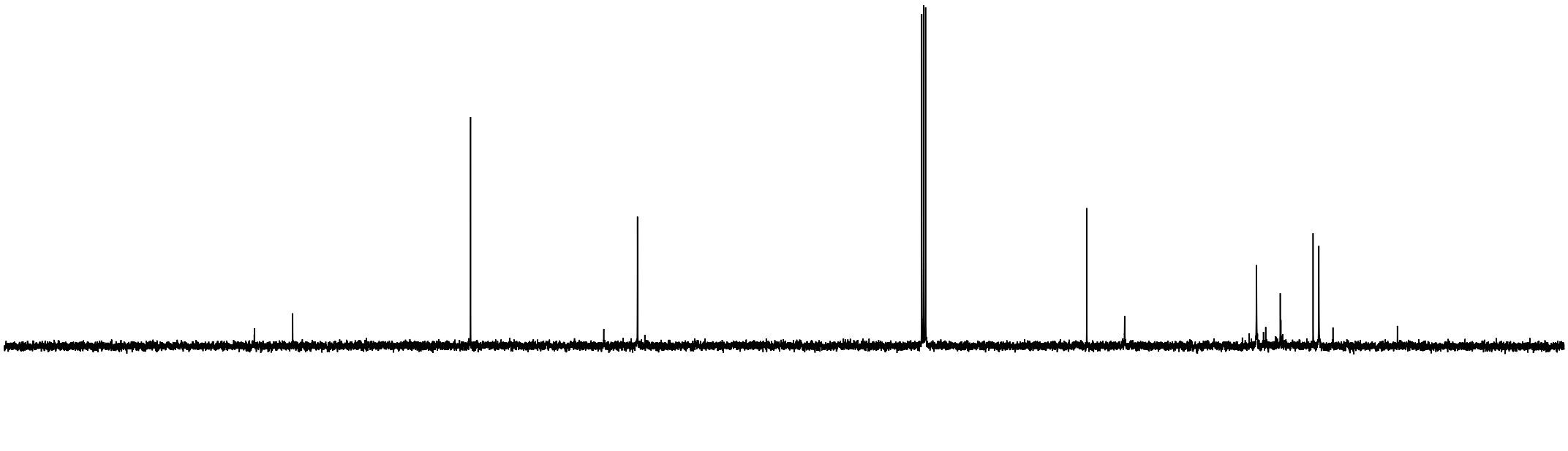
55.43
50.38
32.88
25.37
24.60




3e



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

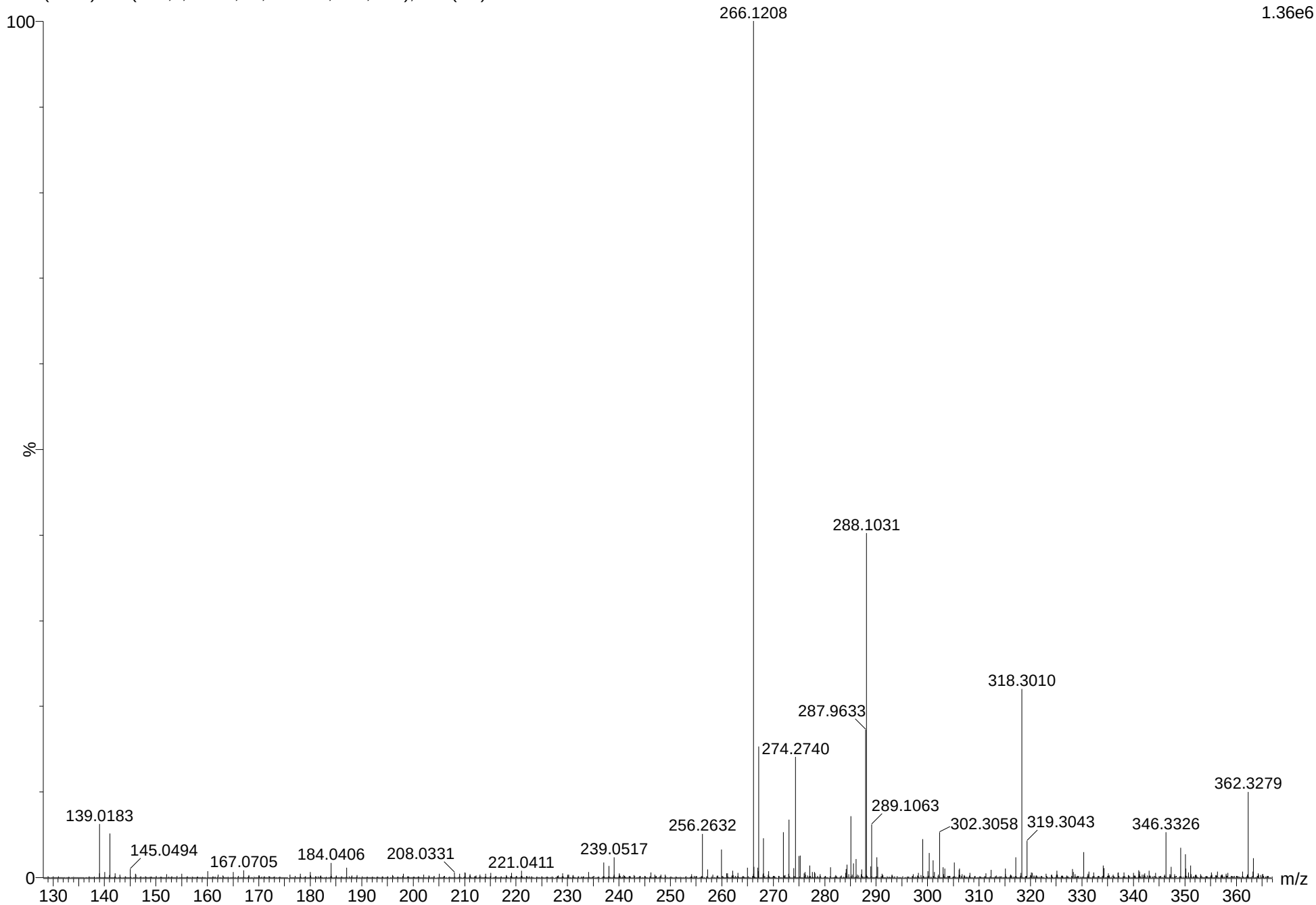
XEVO-G2SQTOF#NotSet

06-Jun-2018
11:28:18

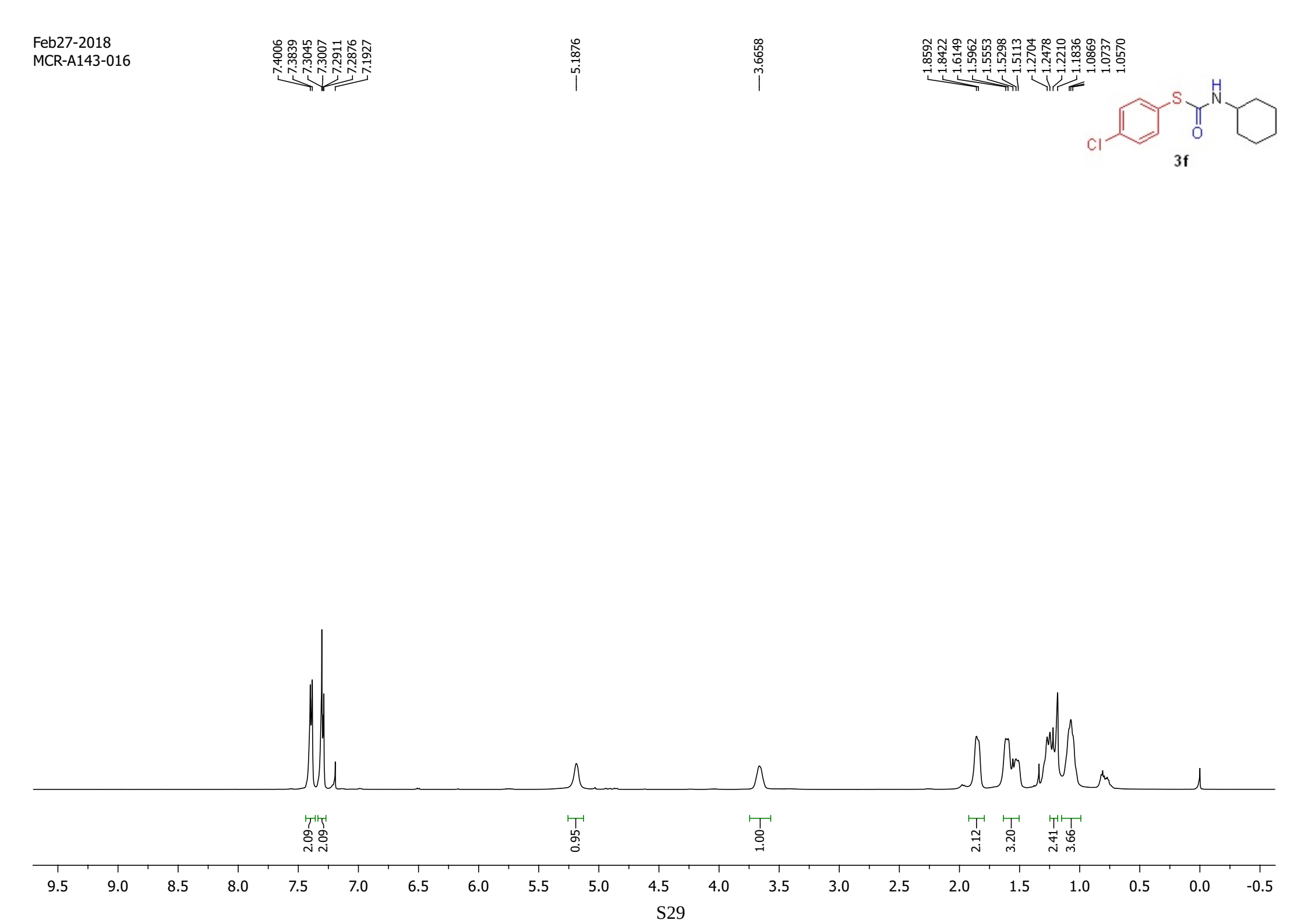
USER NAME: BHAGWAN

3E 6 (0.118) AM (Cen,4, 80.00, Ht,10000.0,0.00,0.00); Cm (4:8)

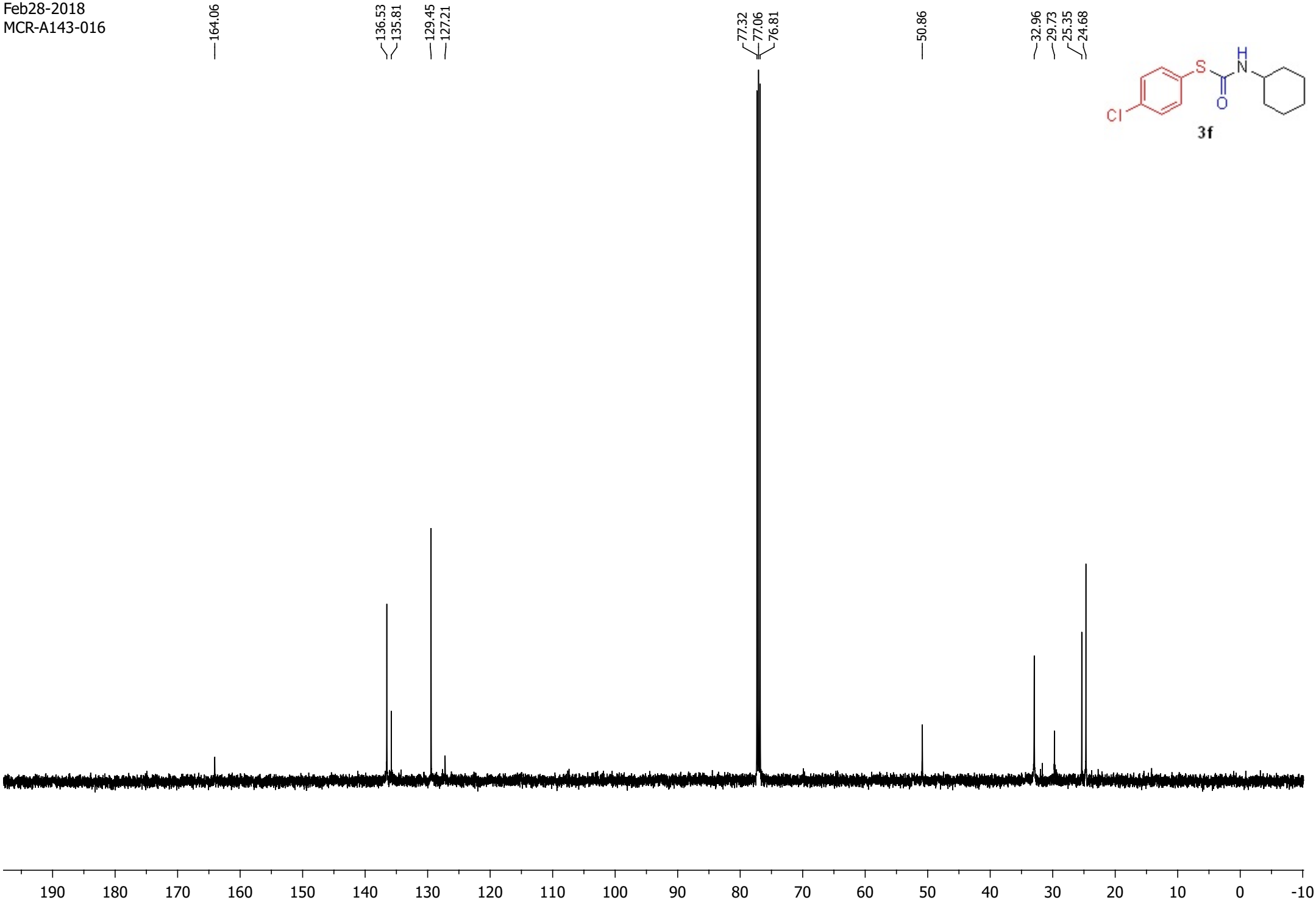
TOF MS ES+
1.36e6



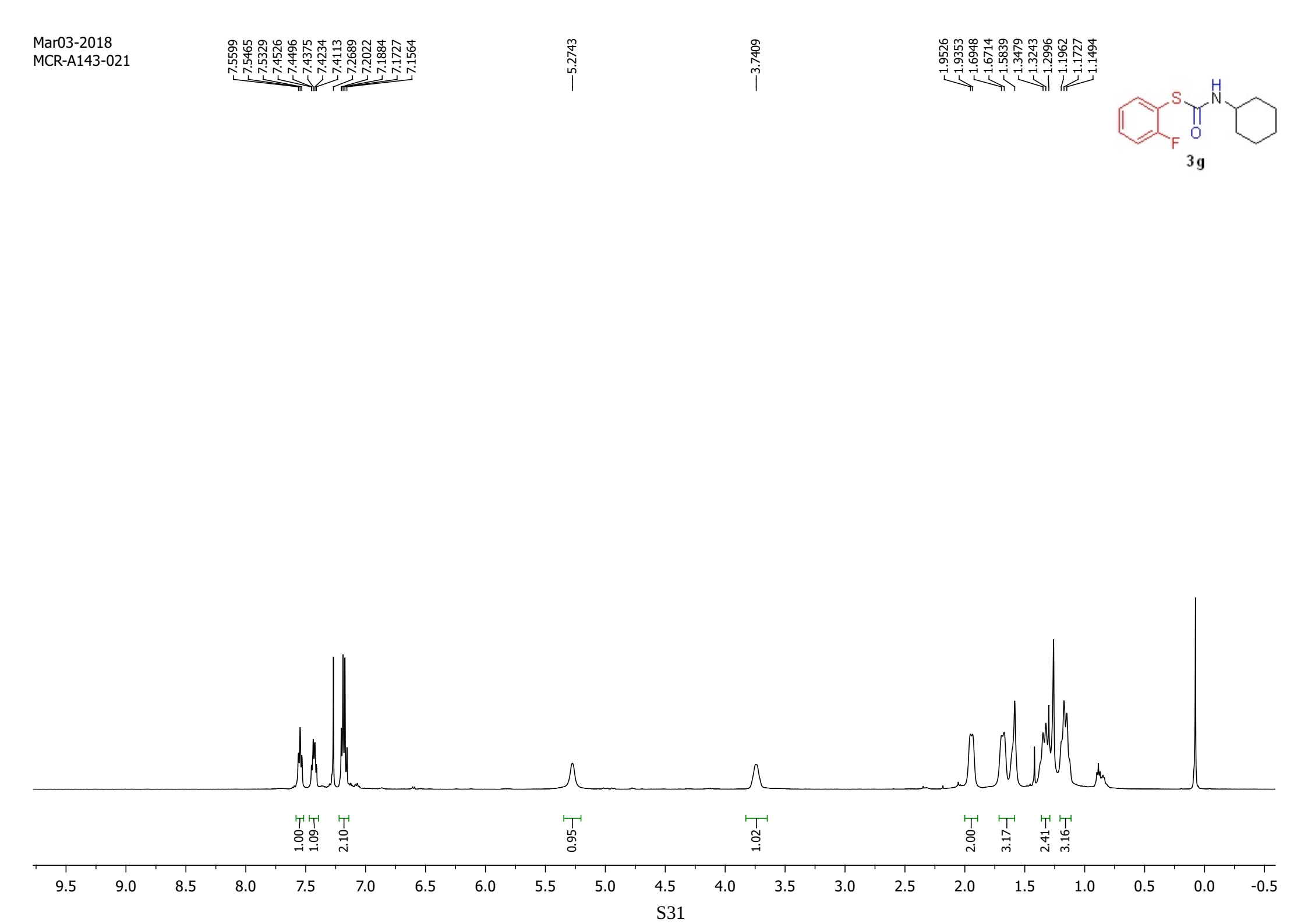
Feb27-2018
MCR-A143-016



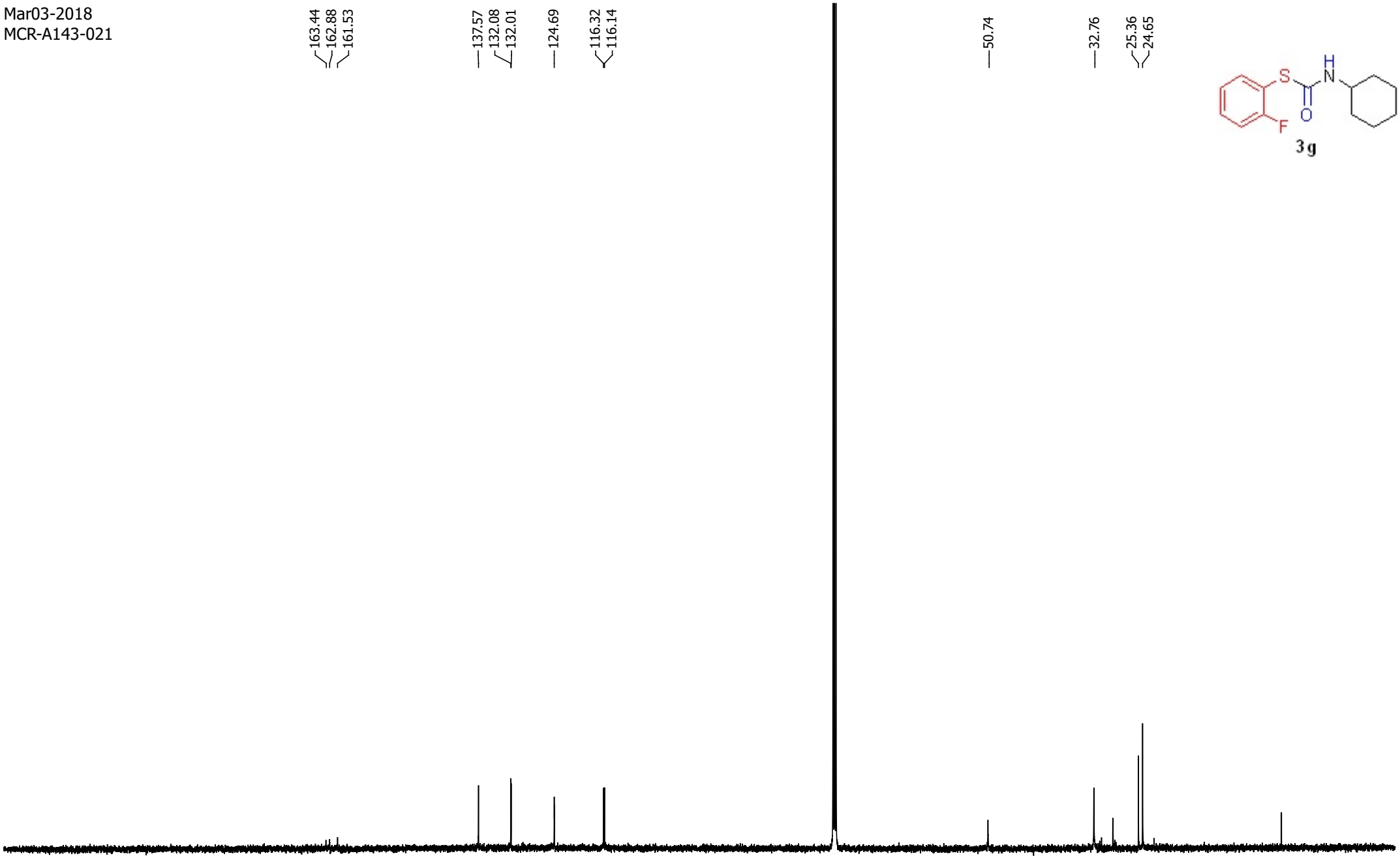
Feb28-2018
MCR-A143-016



Mar03-2018
MCR-A143-021



Mar03-2018
MCR-A143-021

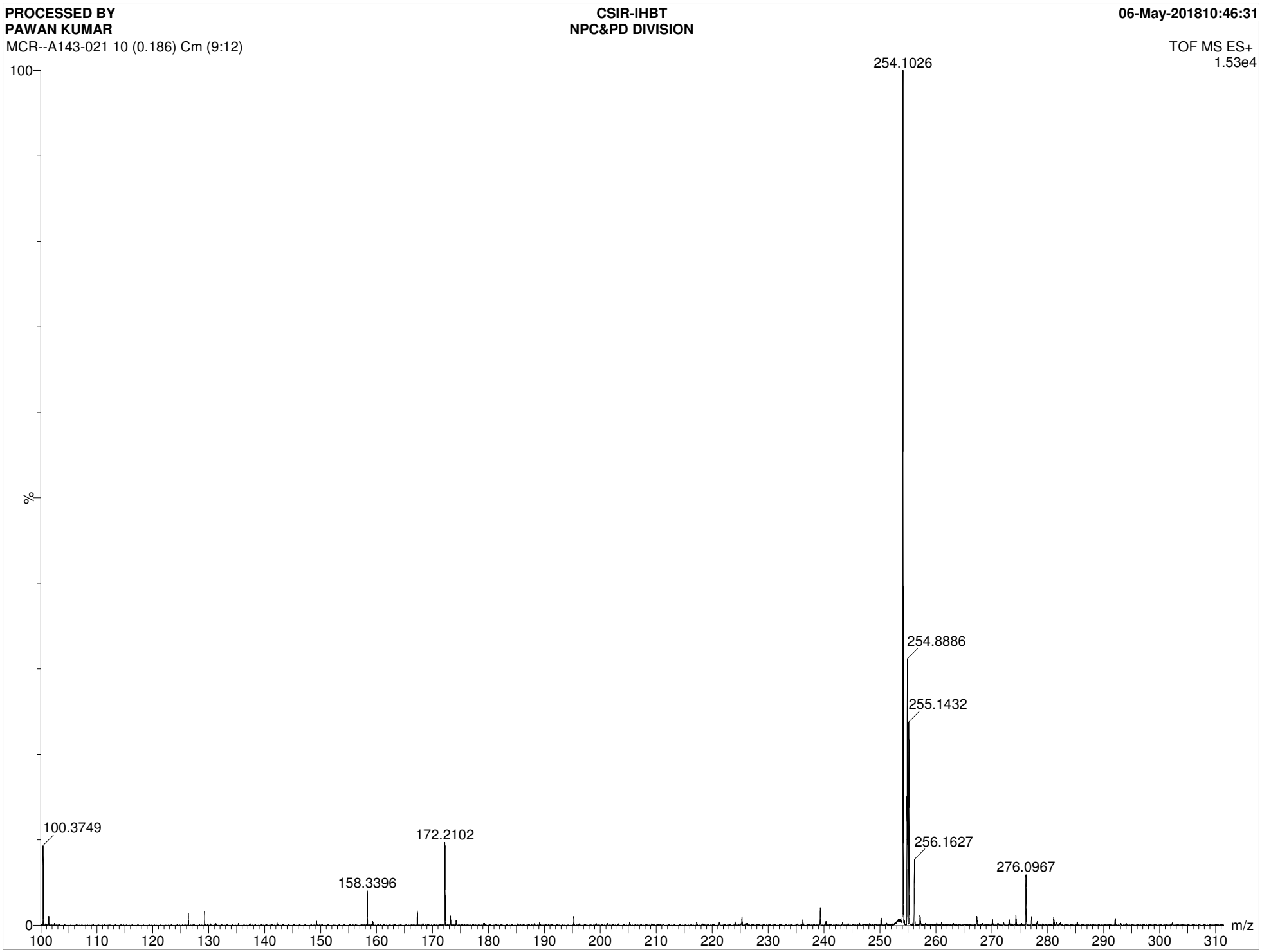


Mar03-2018
MCR-A143-021

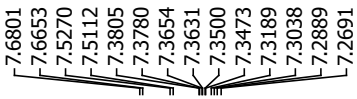
-105.75


3g

-91 -92 -93 -94 -95 -96 -97 -98 -99 -101 -103 -105 -107 -109 -111 -113 -115 -117 -119


PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
06-May-201810:46:31
MCR--A143-021 10 (0.186) Cm (9:12)
TOF MS ES+
1.53e4
100
%
0
254.1026
254.8886
255.1432
256.1627
276.0967
100.3749
158.3396
172.2102
100
110
120
130
140
150
160
170
180
190
200
210
220
230
240
250
260
270
280
290
300
310
m/z

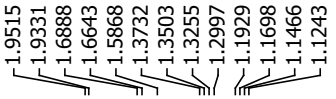
Mar03-2018
MCR-A143-019

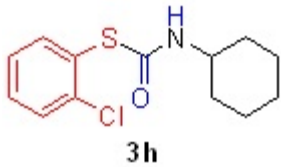




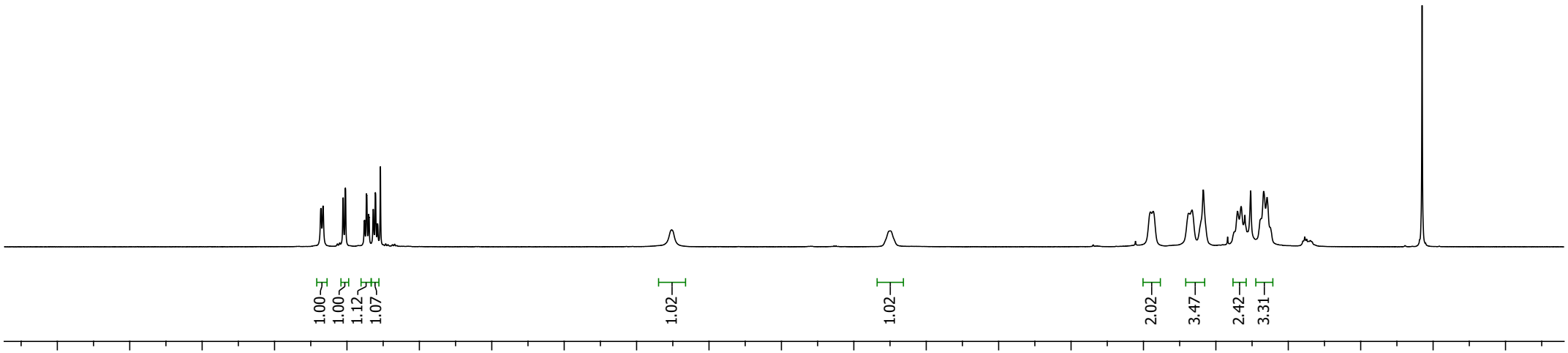




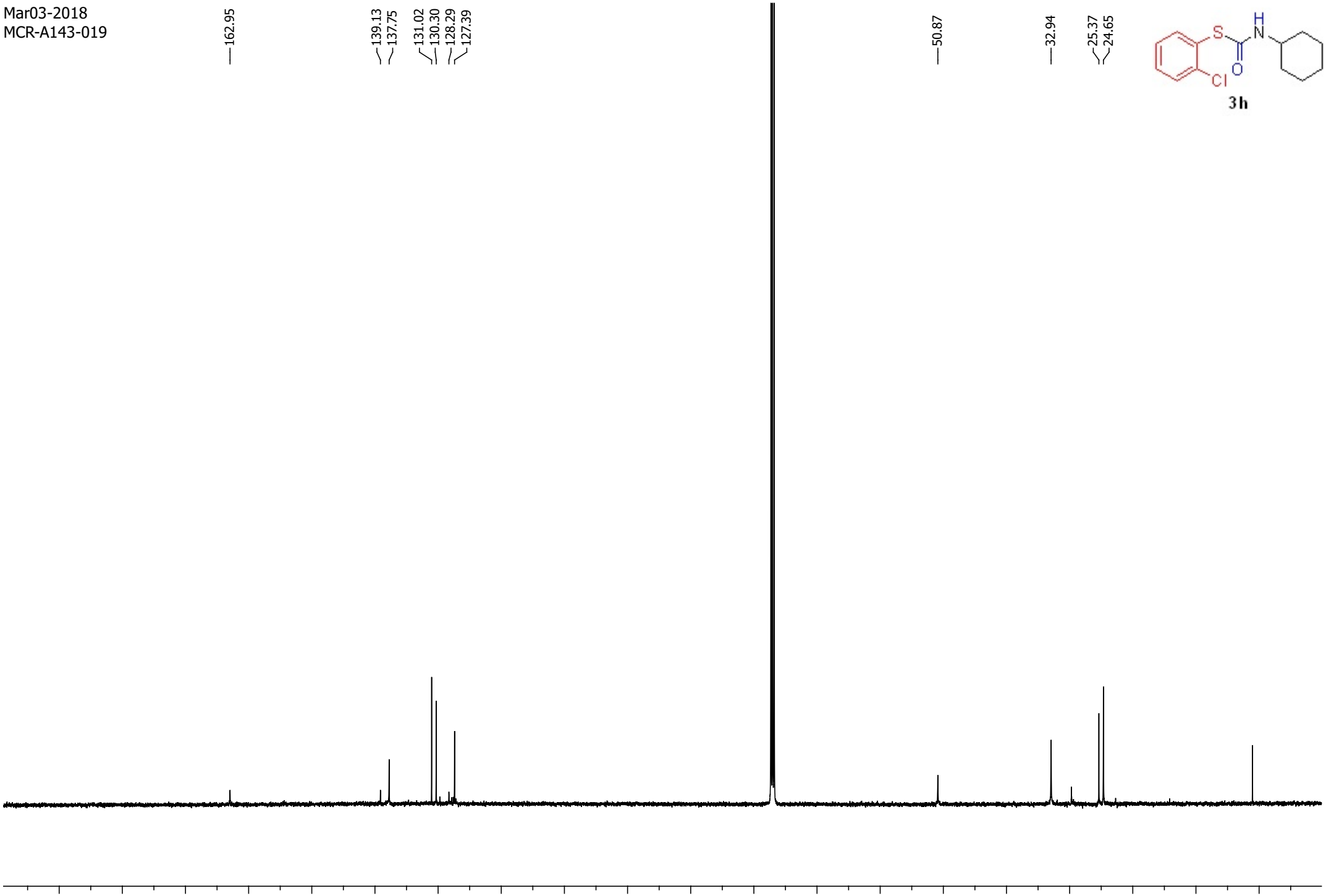



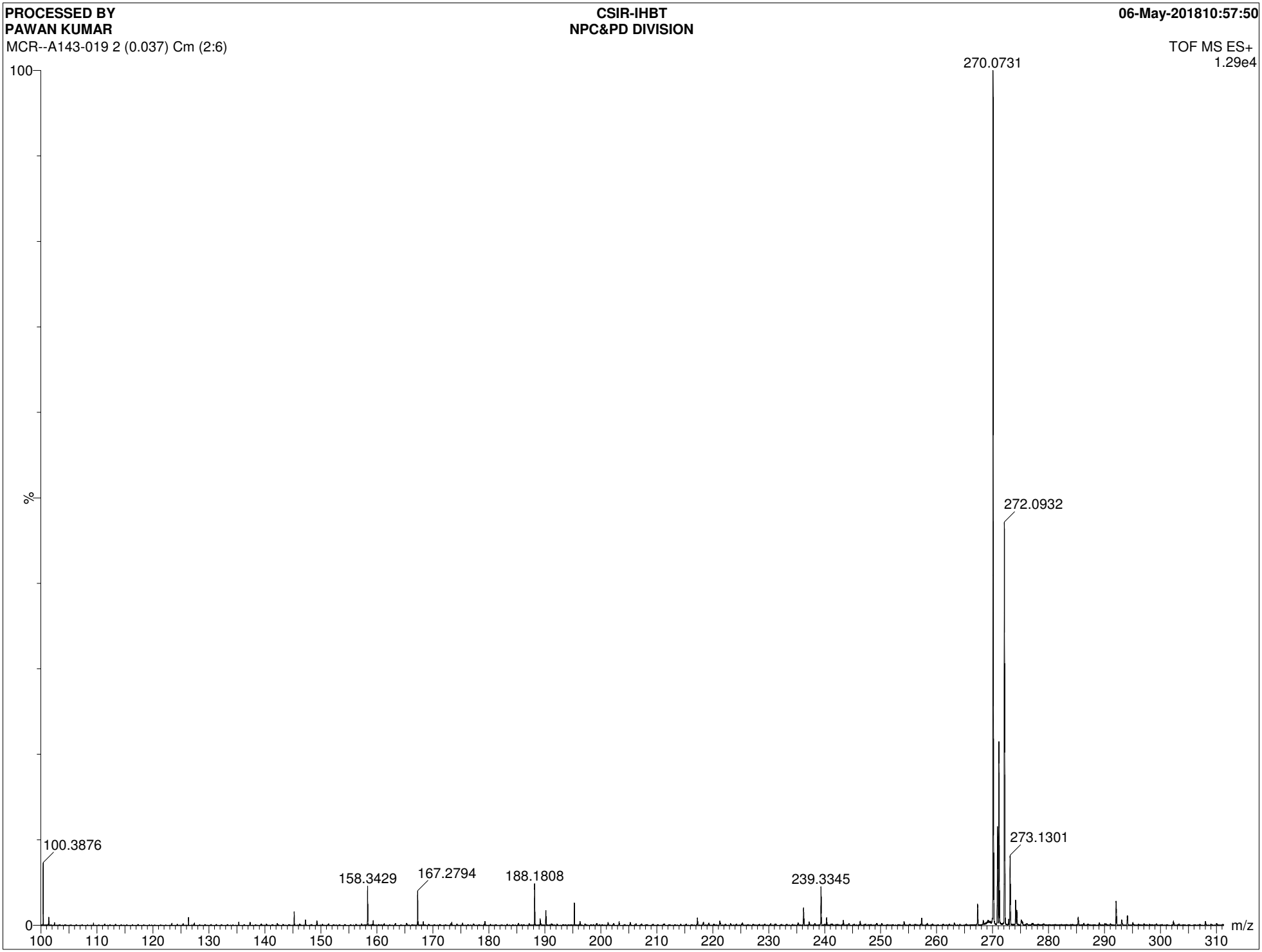




**3h**

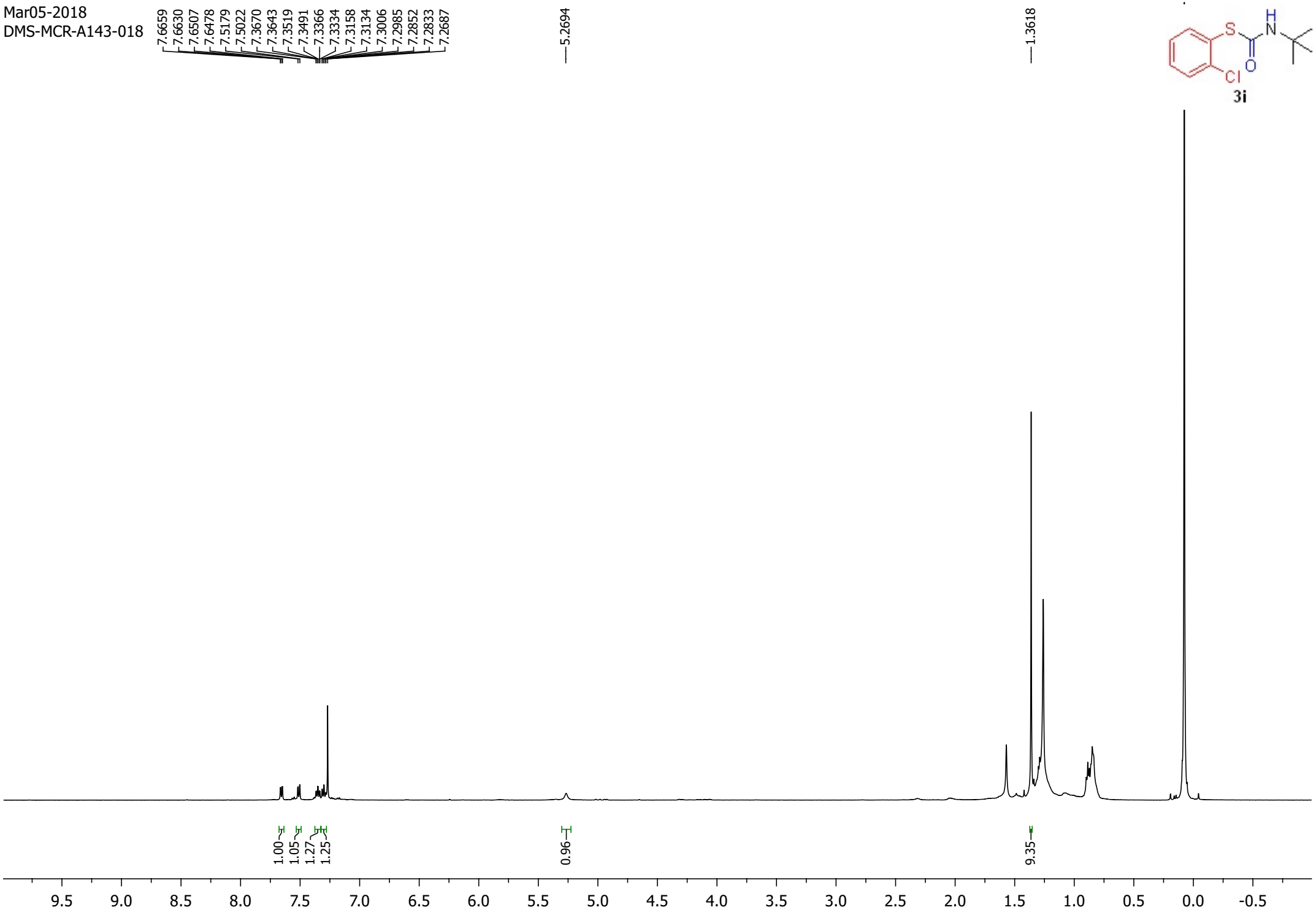


Mar03-2018
MCR-A143-019

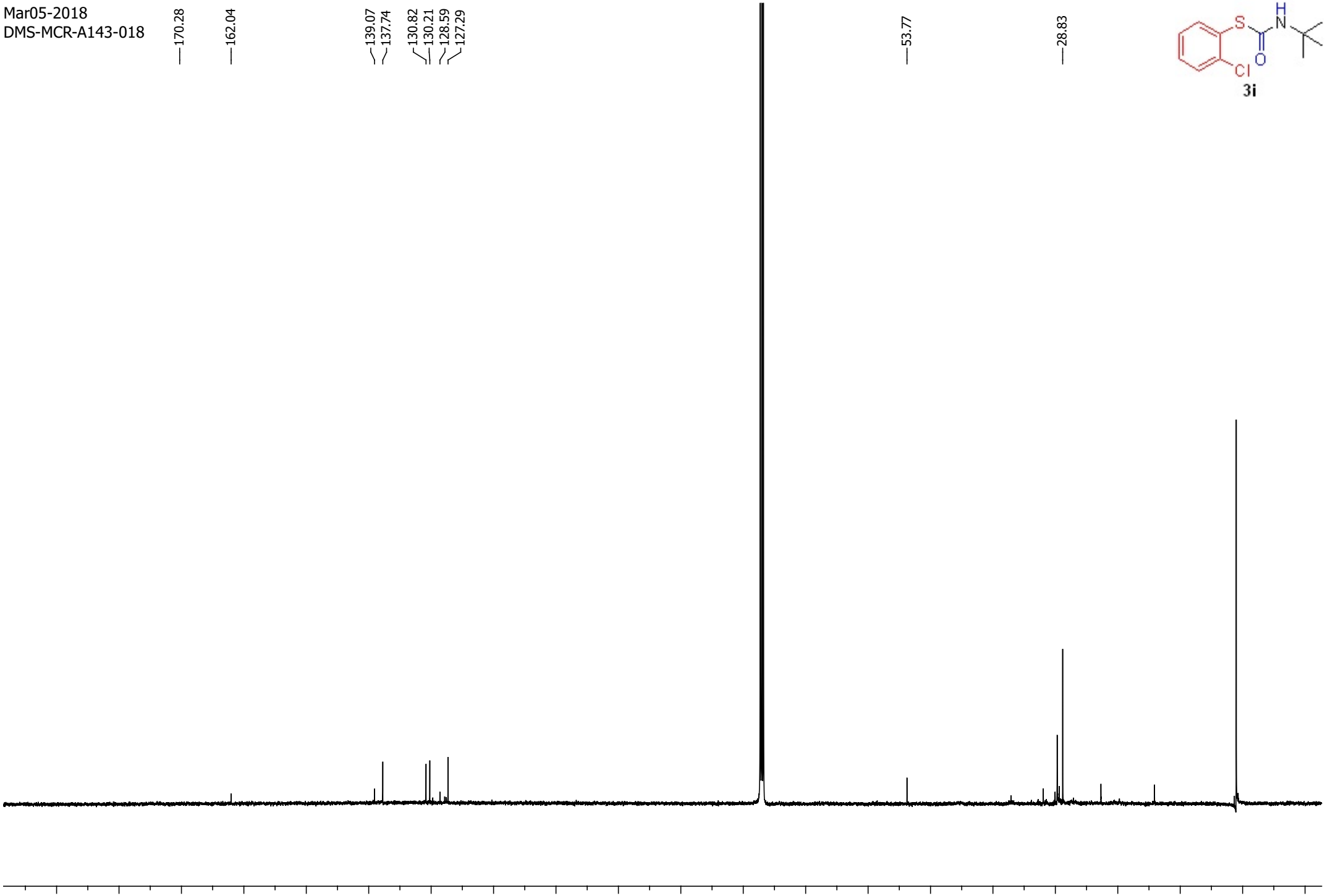


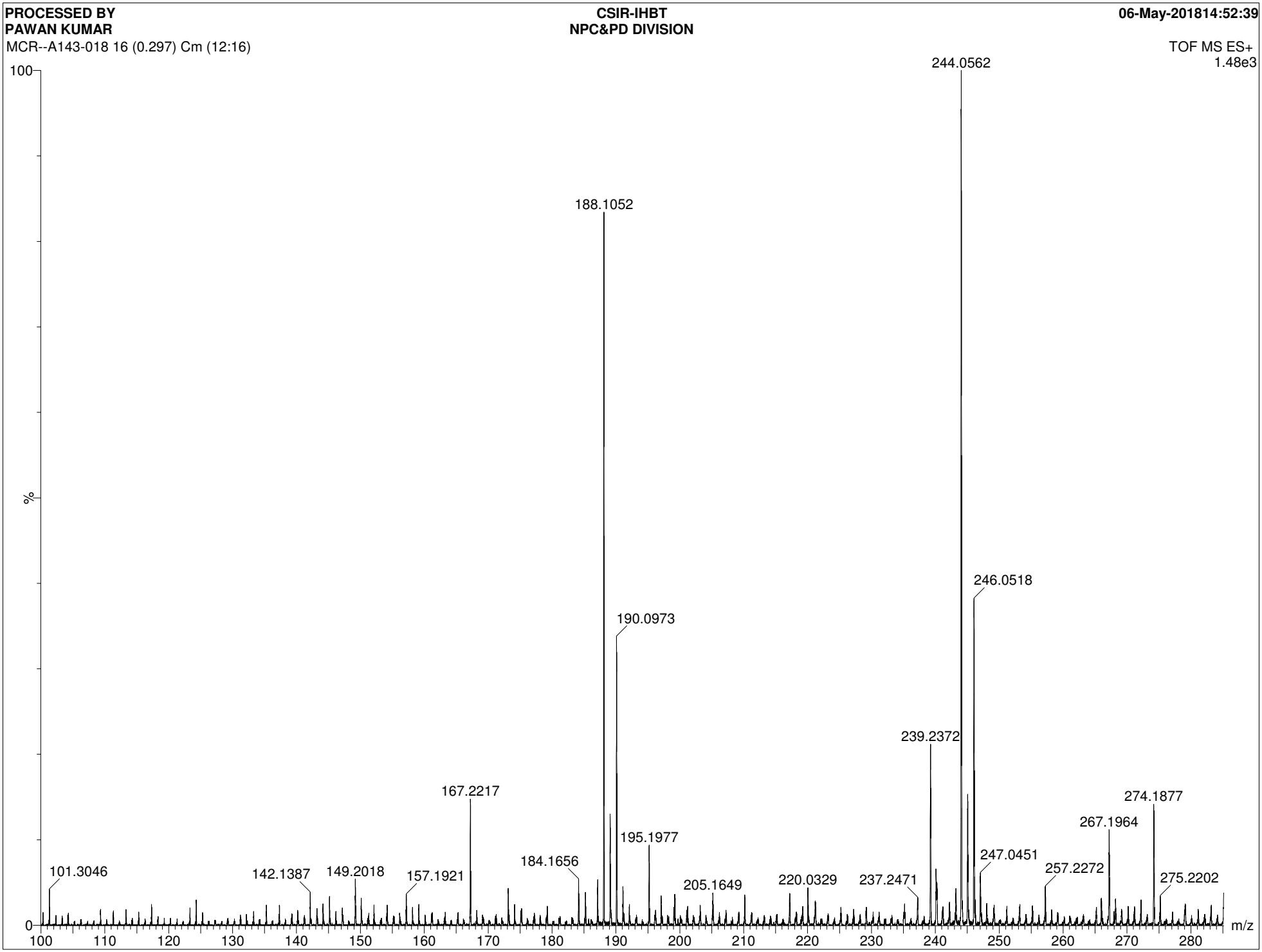

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
06-May-201810:57:50
MCR--A143-019 2 (0.037) Cm (2:6)
TOF MS ES+
1.29e4
270.0731
272.0932
273.1301
100.3876
158.3429
167.2794
188.1808
239.3345
%
m/z

Mar05-2018
DMS-MCR-A143-018

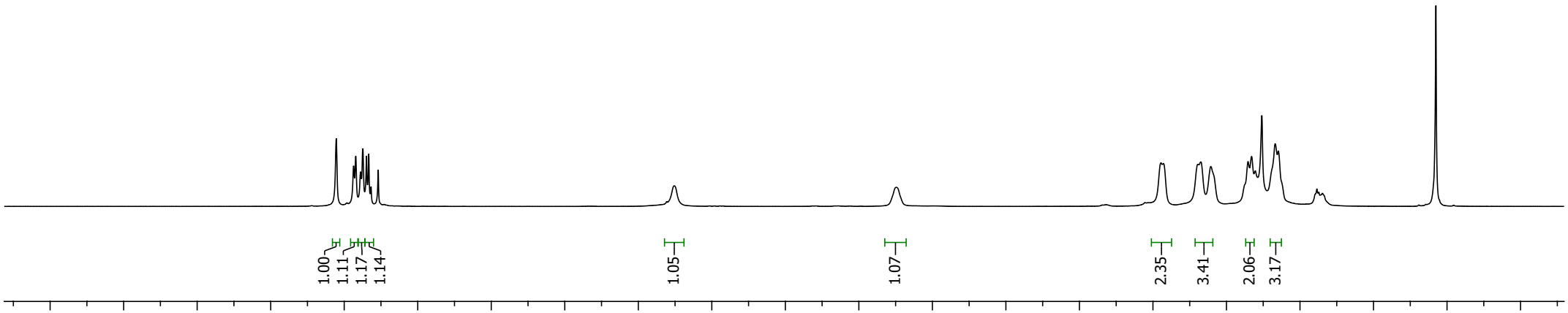


Mar05-2018
DMS-MCR-A143-018

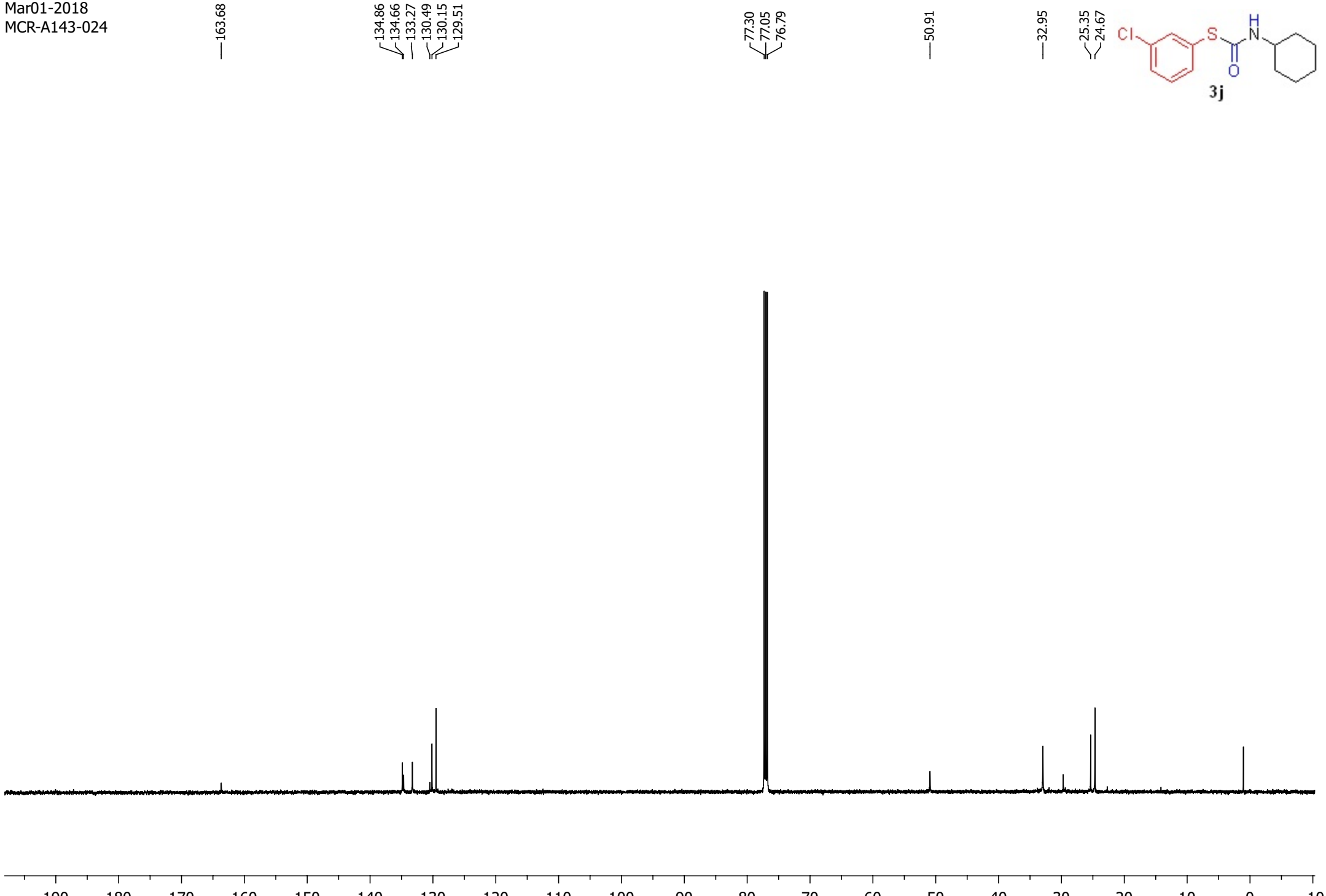



PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
06-May-201814:52:39
MCR--A143-018 16 (0.297) Cm (12:16)
TOF MS ES+
1.48e3
244.0562
188.1052
246.0518
190.0973
239.2372
167.2217
274.1877
267.1964
195.1977
247.0451
257.2272
184.1656
275.2202
101.3046
142.1387
149.2018
157.1921
205.1649
220.0329
237.2471
%
m/z

Feb28-2018
MCR-A143-024

Mar01-2018
MCR-A143-024



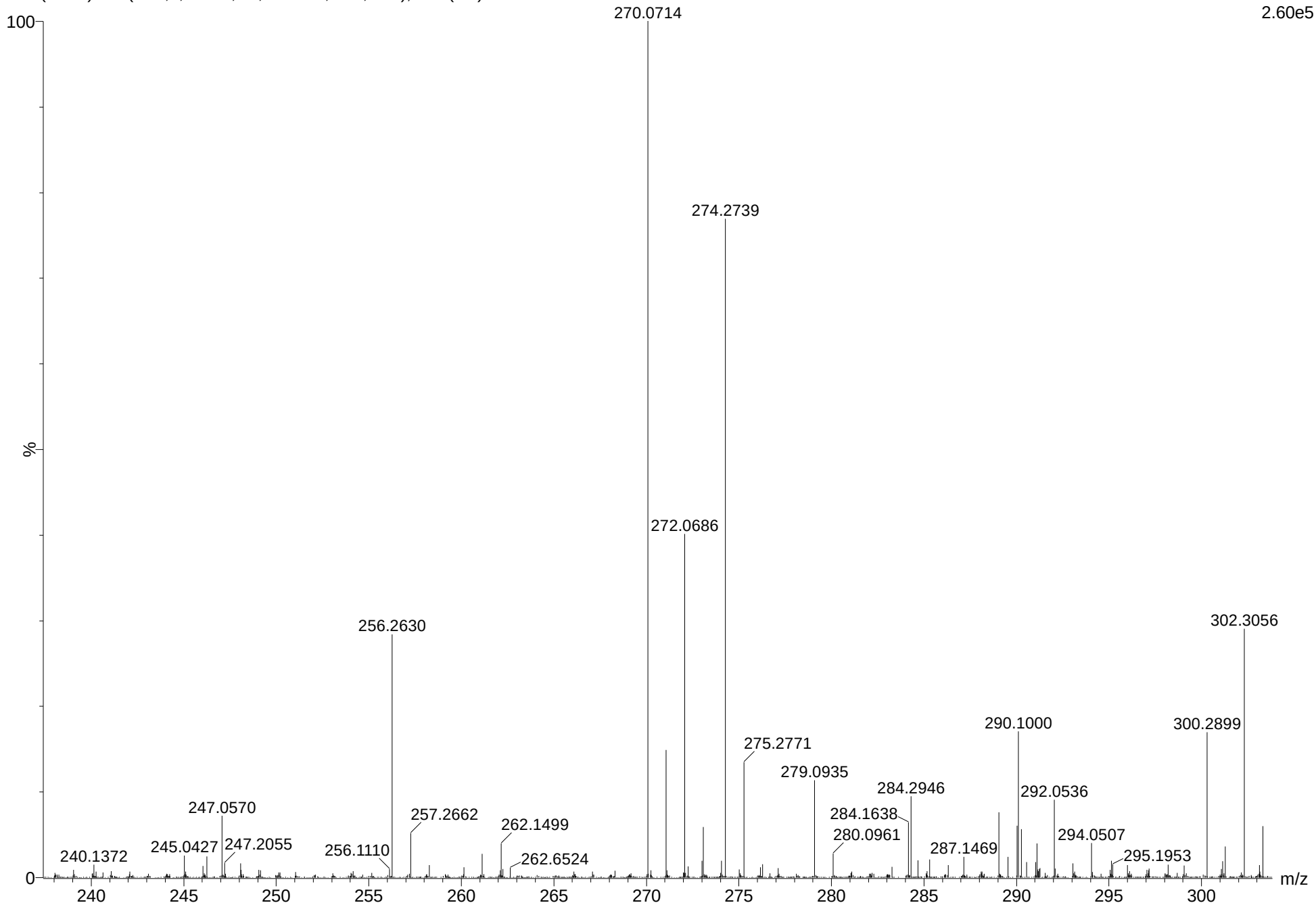
XEVO-G2SQTOF#NotSet

06-Jun-2018
11:22:08

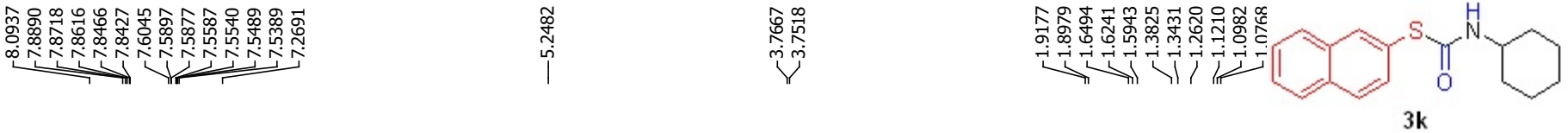
USER NAME: BHAGWAN

3J 6 (0.118) AM (Cen,4, 80.00, Ht,10000.0,0.00,0.00); Cm (4:8)

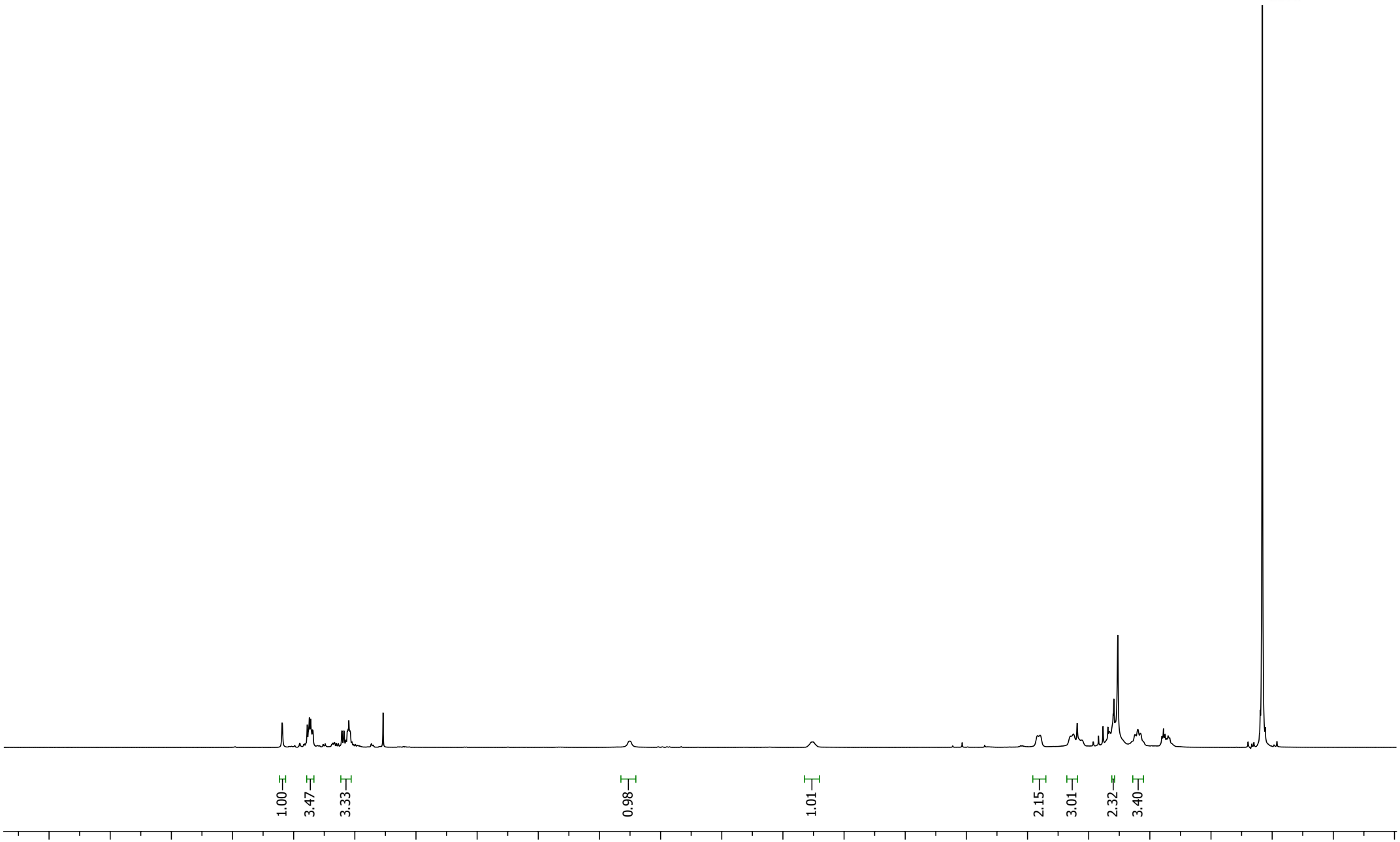
TOF MS ES+
2.60e5



Apr06-2018
DMS-MCR-A143-063

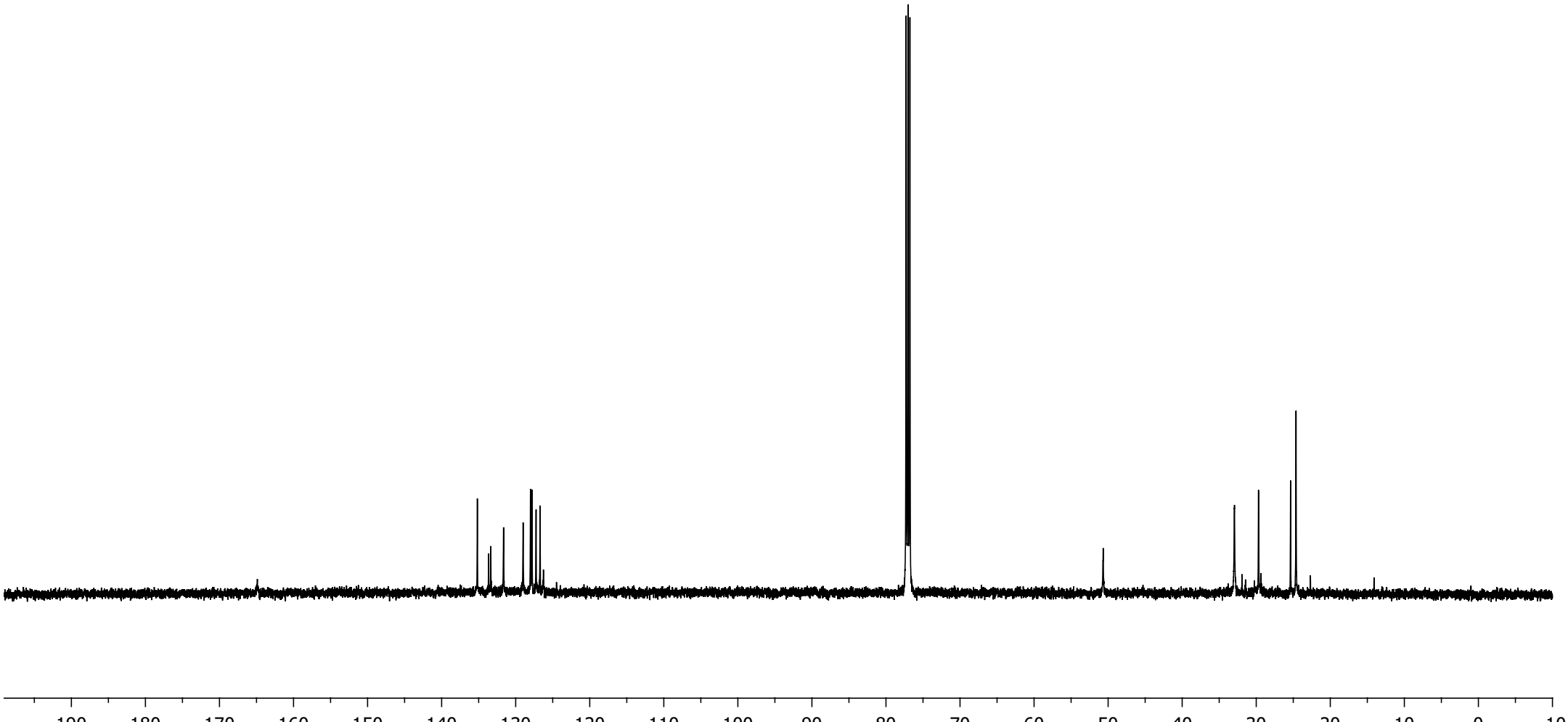



3k



Jun04-2018
DMS-MCR-A143-063


3k



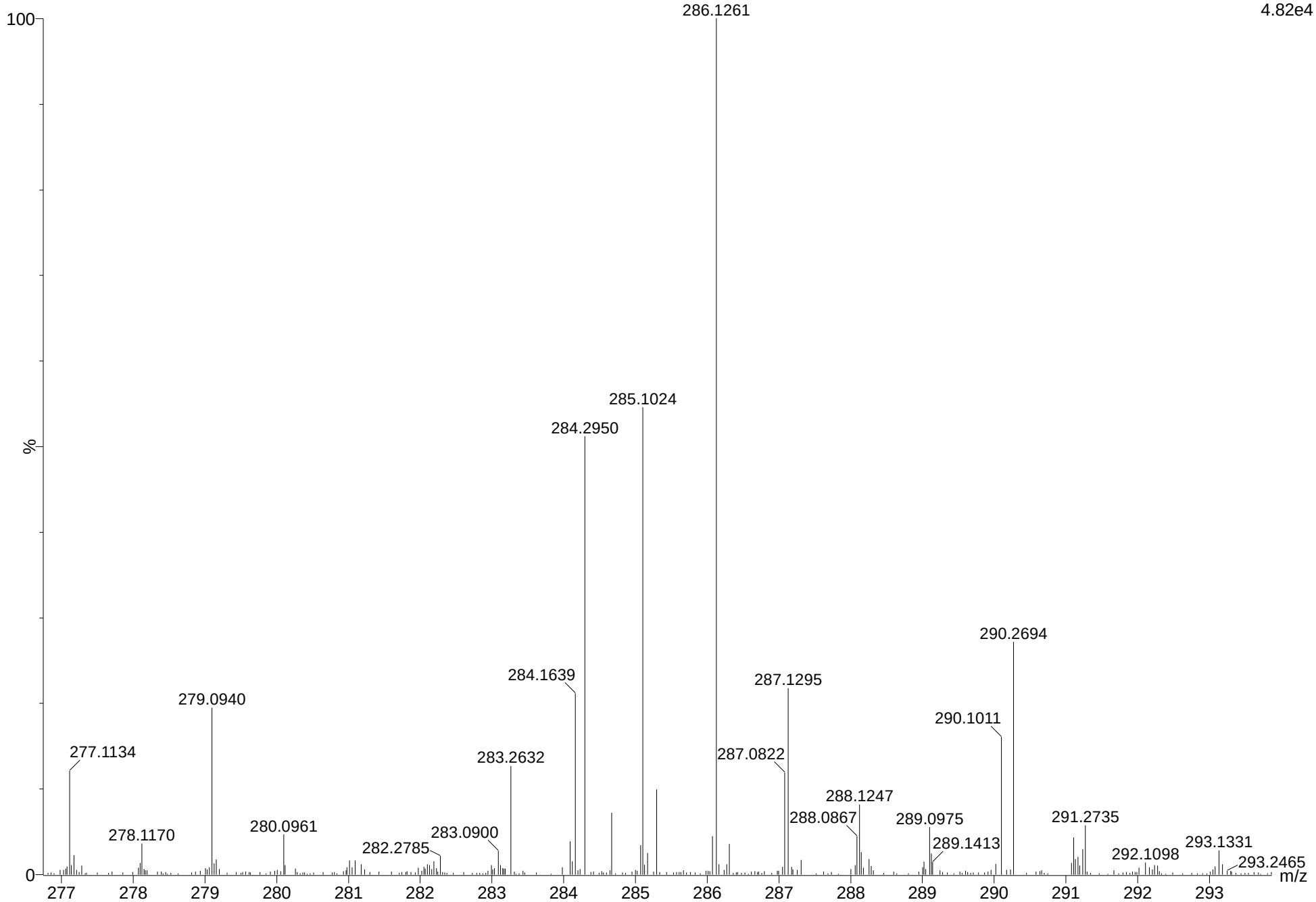
XEVO-G2SQTOF#NotSet

06-Jun-2018
11:24:10

USER NAME: BHAGWAN

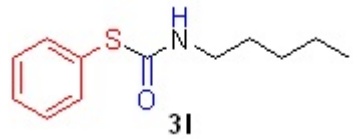
3K 6 (0.118) AM (Cen,4, 80.00, Ht,10000.0,0.00,0.00); Cm (4:8)

TOF MS ES+
4.82e4

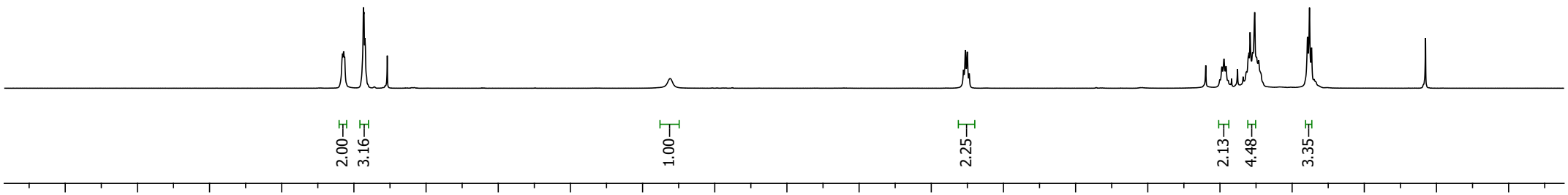


Apr03-2018
DMS-MCR-A143-059

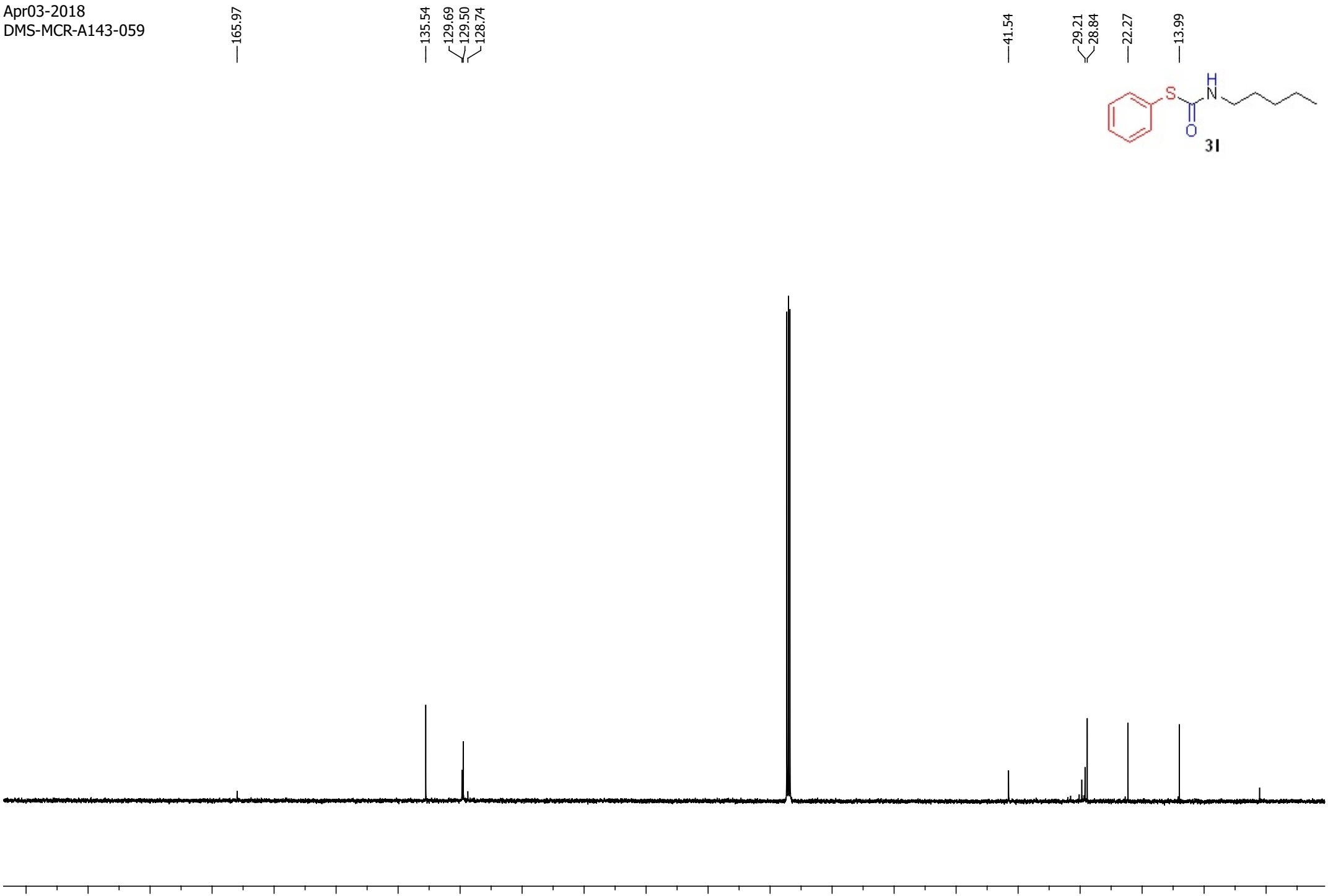
7.5783
7.5713
7.5643
7.4338
7.4305
7.4236
7.2688
5.3092
3.2766
3.2634
3.2505
3.2368
1.5984
1.4866
1.4723
1.4577
1.2996
1.2910
1.2738
1.2594
0.8934
0.8796
0.8651




**3l**



Apr03-2018
DMS-MCR-A143-059



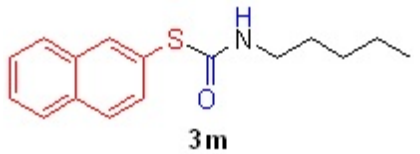
May23-2018
DMS-MCR-A143-111

8.1043 7.8903 7.8740 7.8613 7.8459 7.6168 7.5999 7.5725 7.5615 7.5582 7.5543 7.5490 7.5429 7.5394 7.5252 7.2689

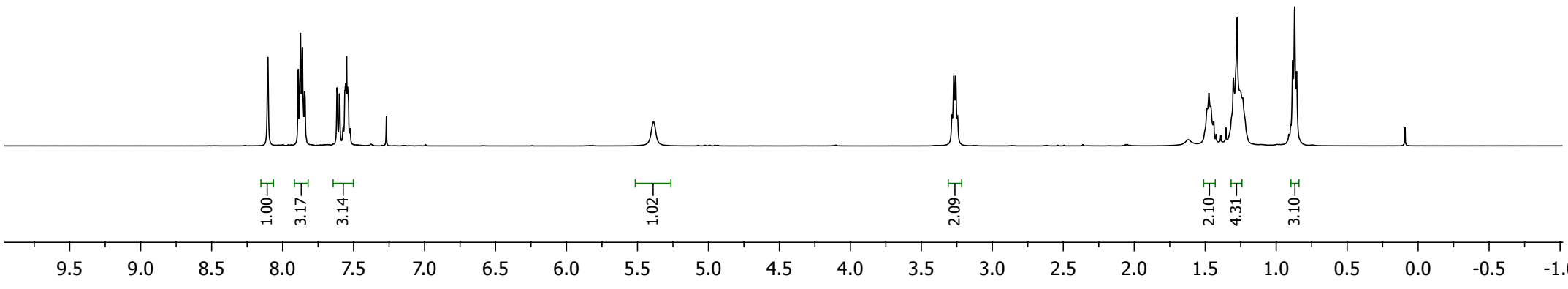
5.3867

3.2840 3.2710 3.2582 3.2450

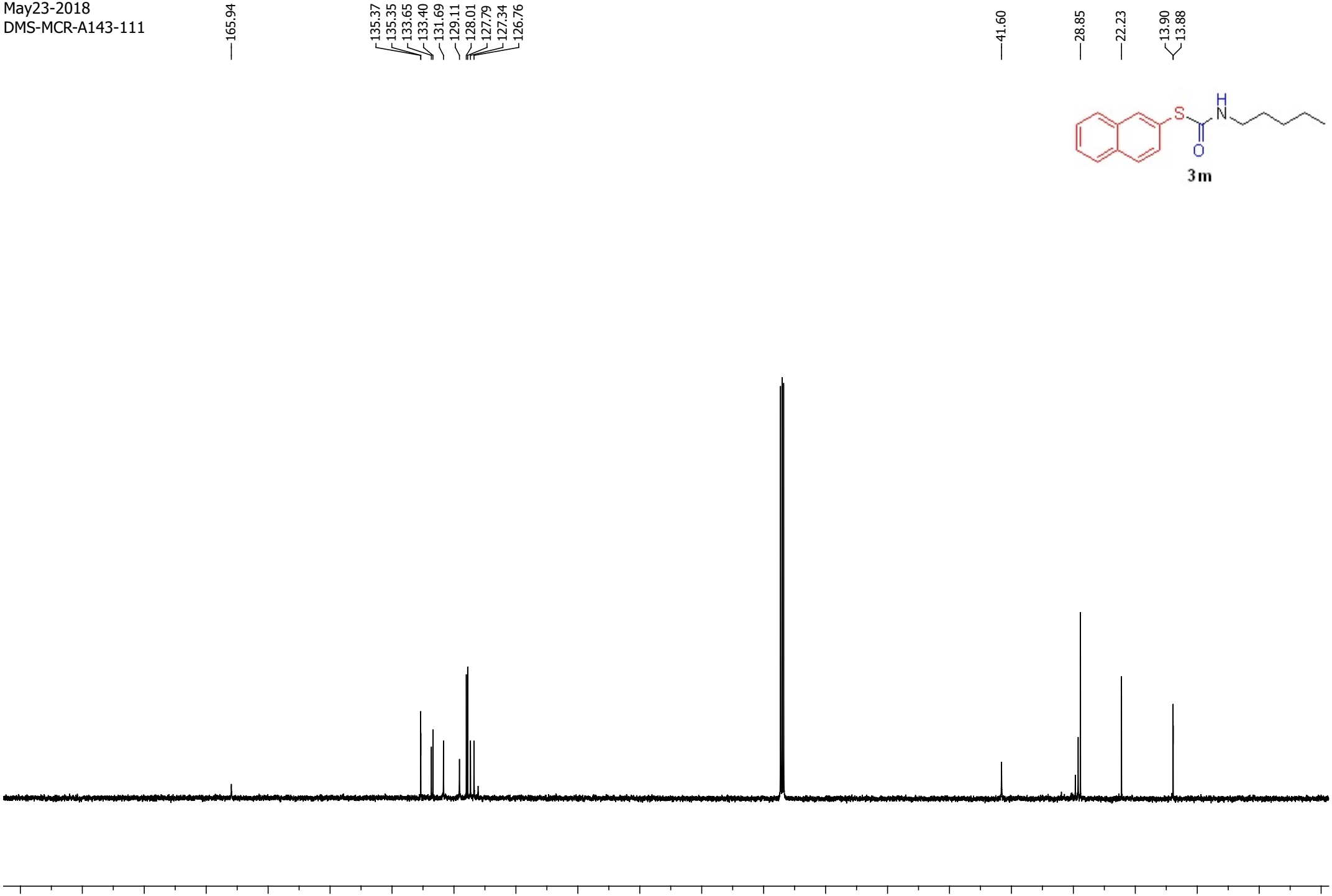
1.4867 1.4740 1.4614 1.4394 1.3013 1.2750 1.2537 1.2367 0.8836 0.8702 0.8561




3m



May23-2018
DMS-MCR-A143-111



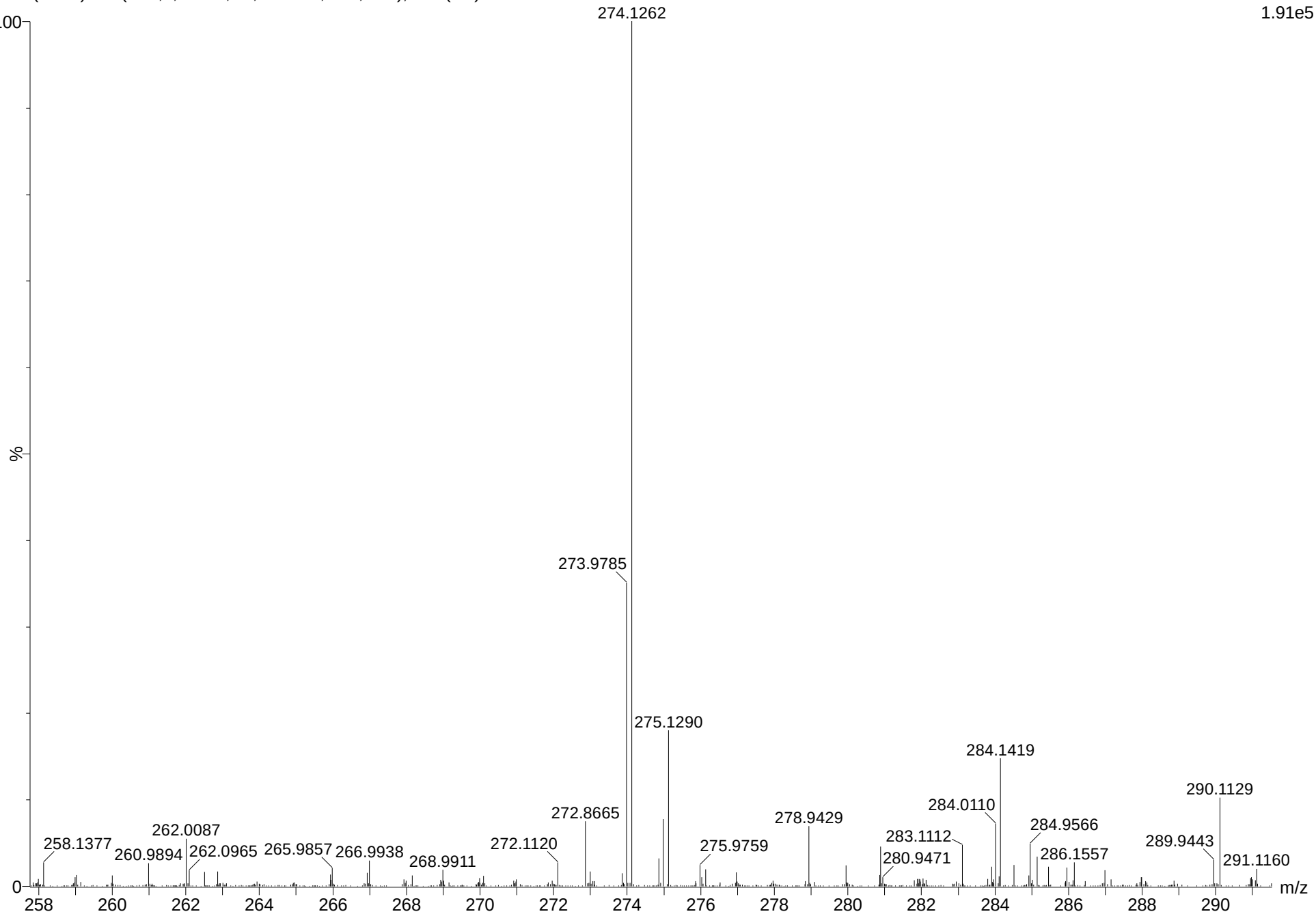
XEVO-G2SQTOF#NotSet

06-Jun-2018
11:26:11

USER NAME: BHAGWAN

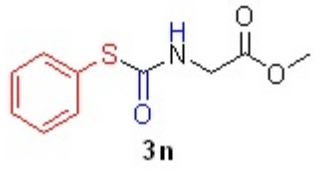
3M 6 (0.118) AM (Cen,4, 80.00, Ht,10000.0,0.00,0.00); Cm (4:9)

TOF MS ES+
1.91e5



Jun30-2018
DMS-MCR-A143-120

7.5930
7.4489
7.2685
5.9219
4.0523
3.7500



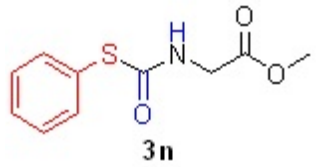

3n

1.98
2.85
1.00
2.04
2.95

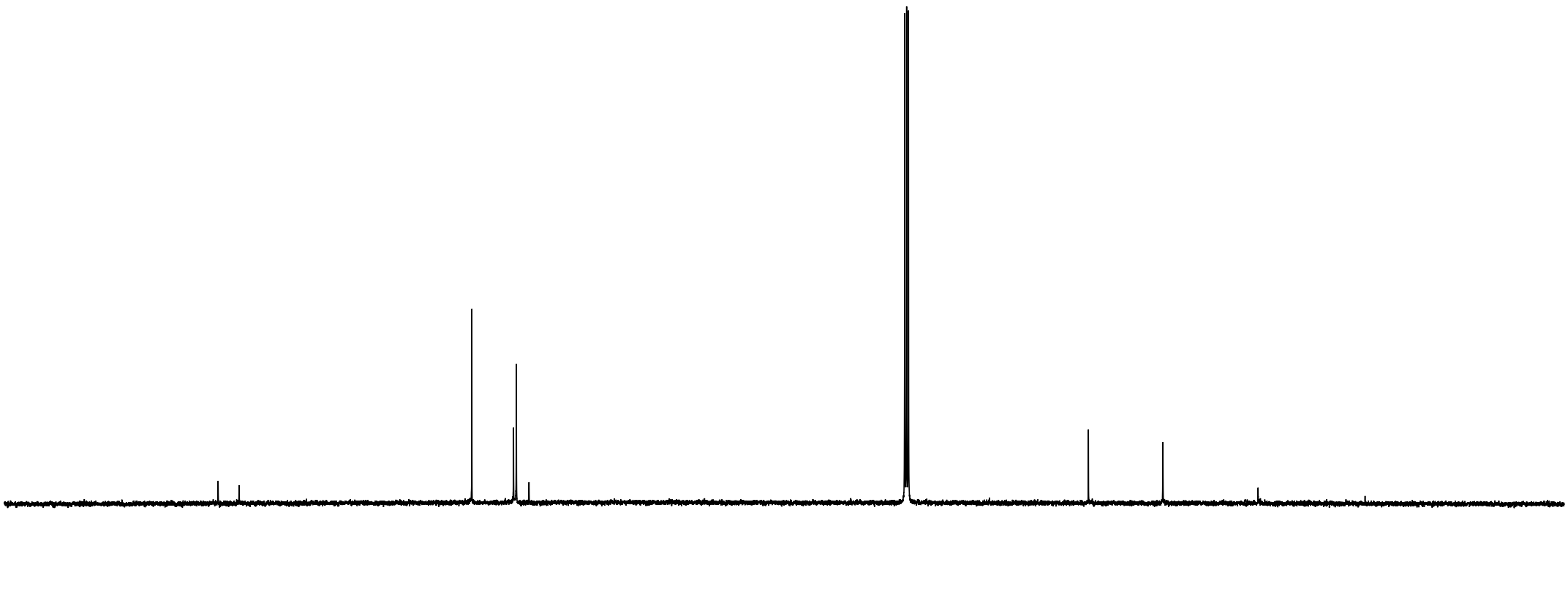
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5

Jun30-2018
DMS-MCR-A143-120

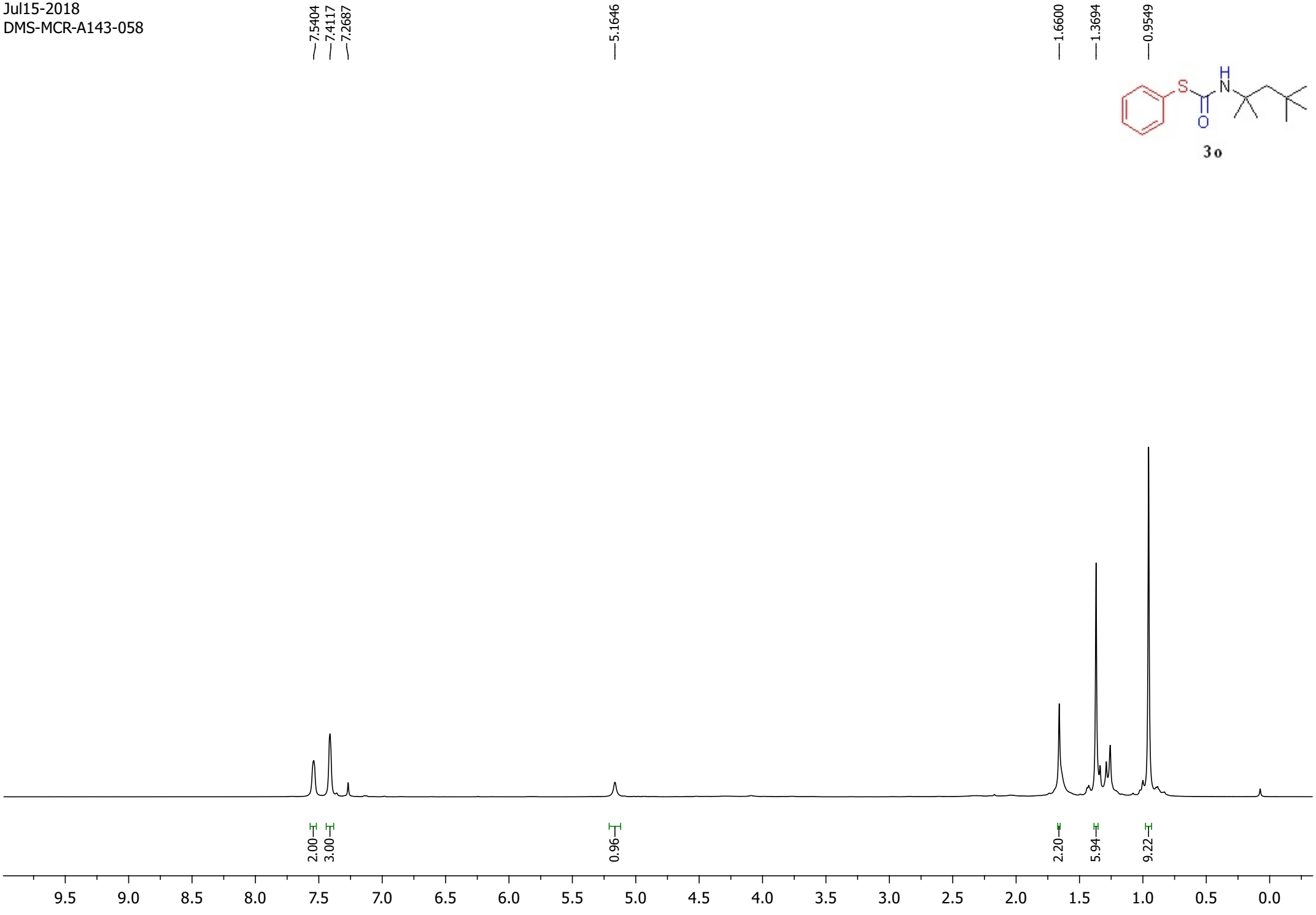
169.80
166.97
135.62
130.01
129.62
127.92
52.57
42.54



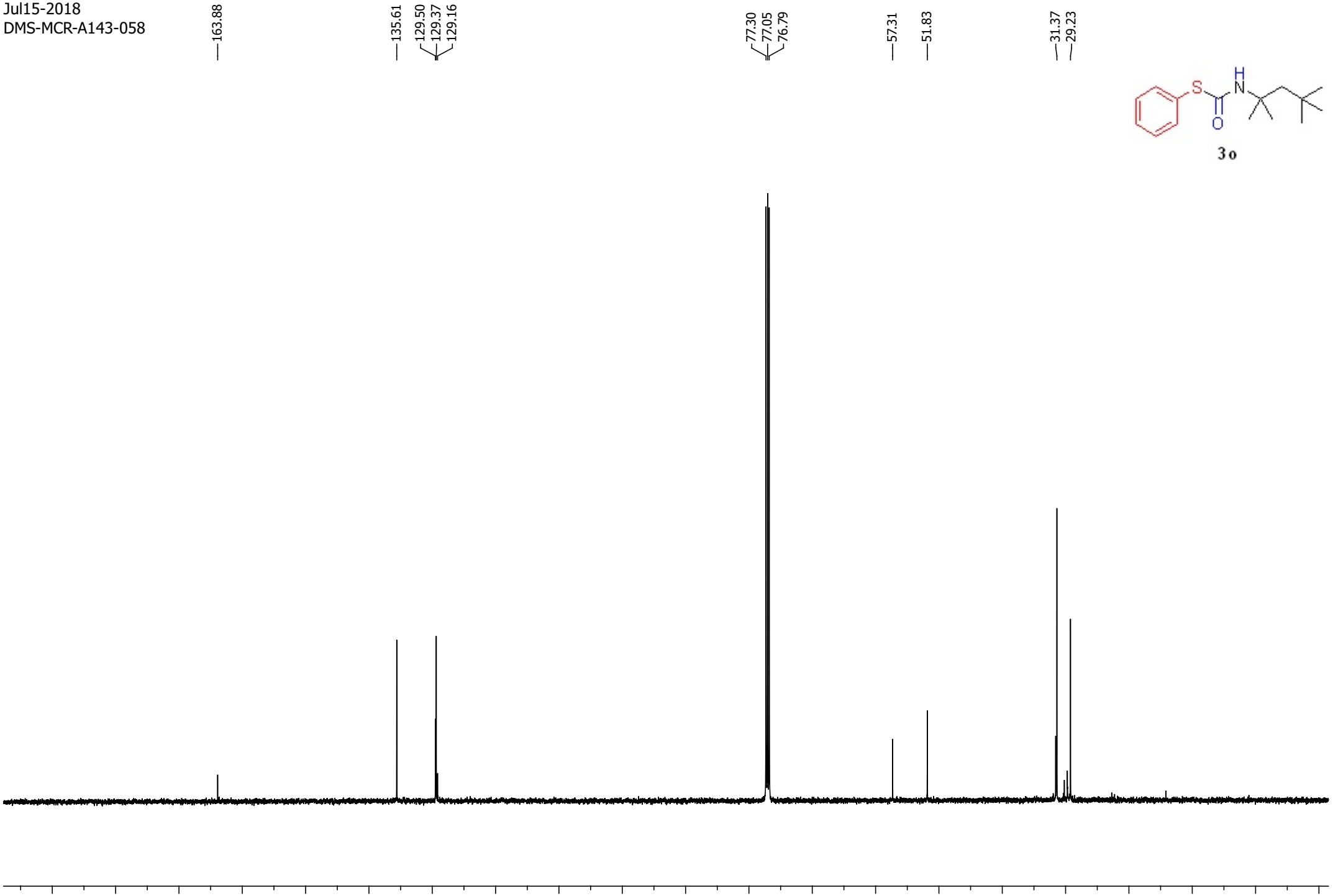

**3n**



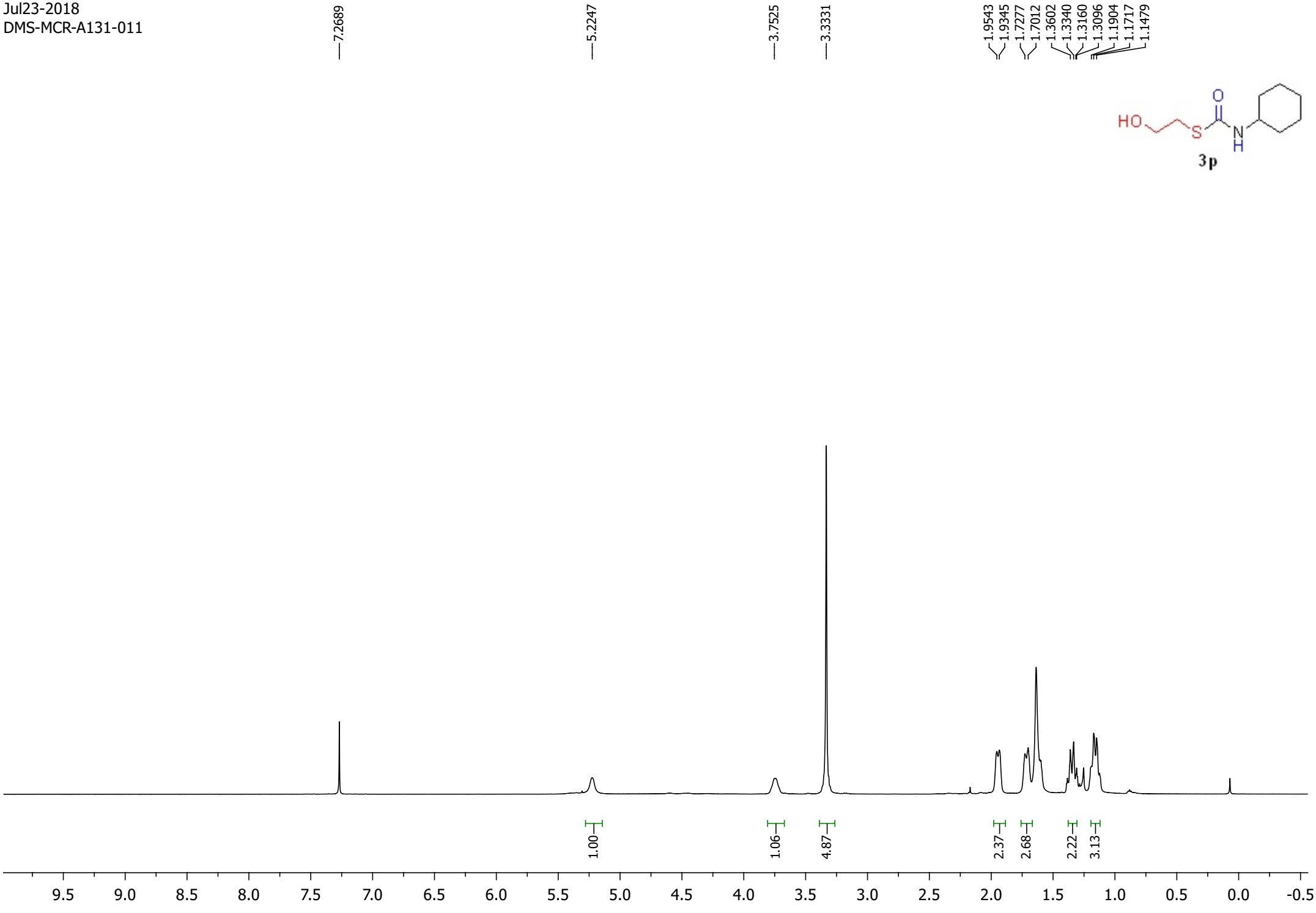
Jul15-2018
DMS-MCR-A143-058



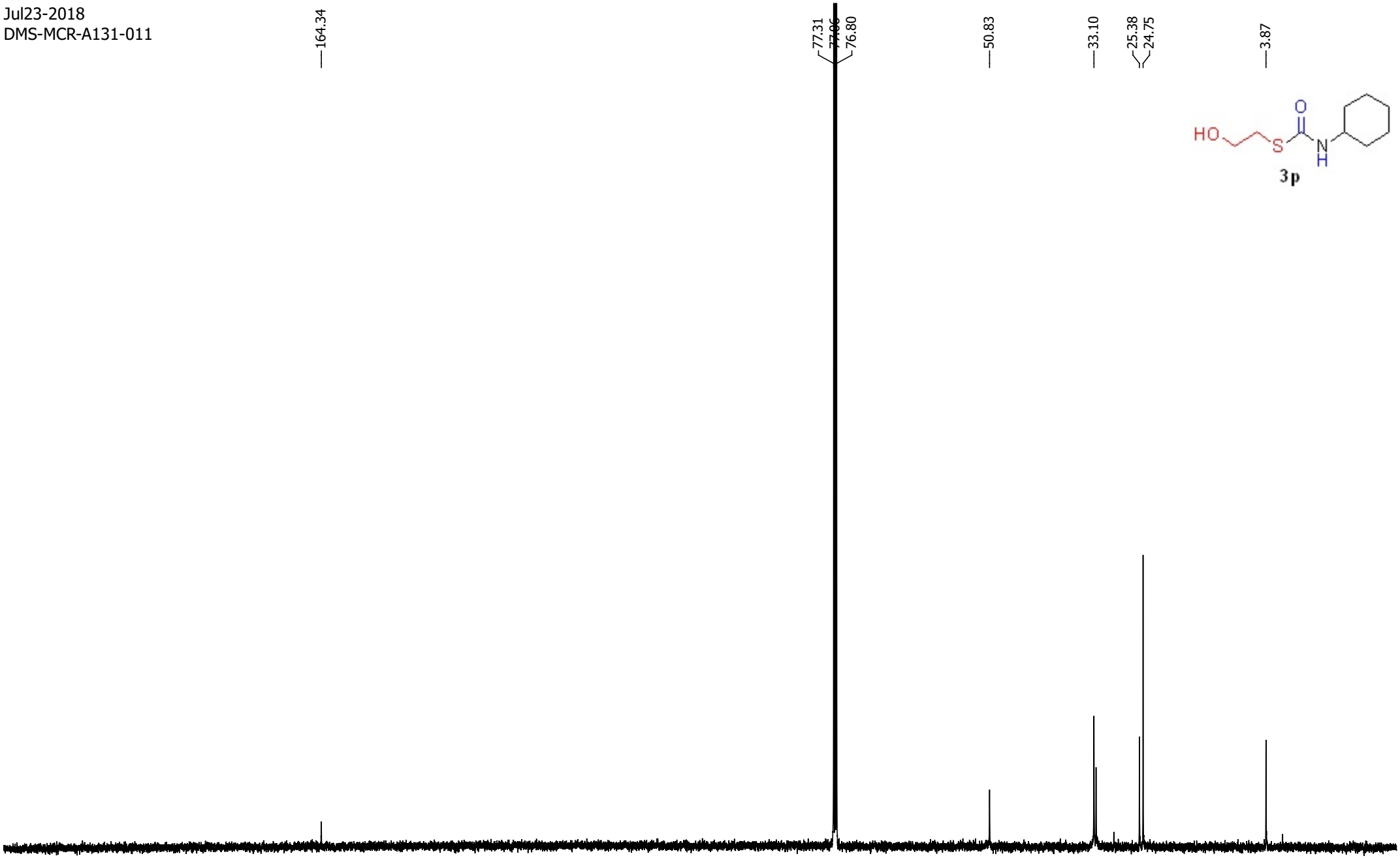
Jul15-2018
DMS-MCR-A143-058



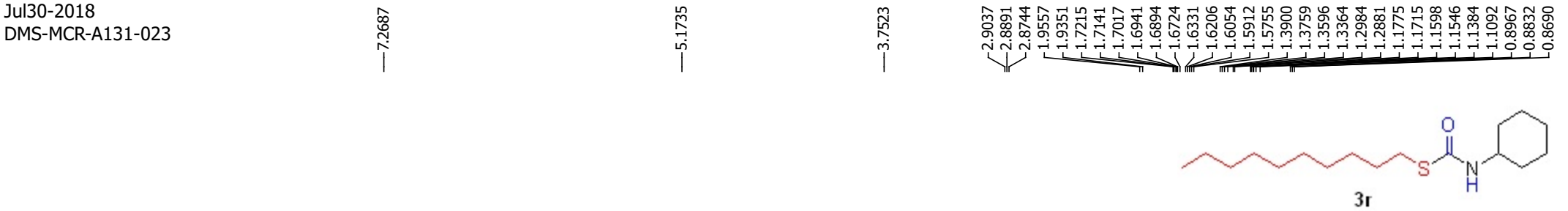
Jul23-2018
DMS-MCR-A131-011



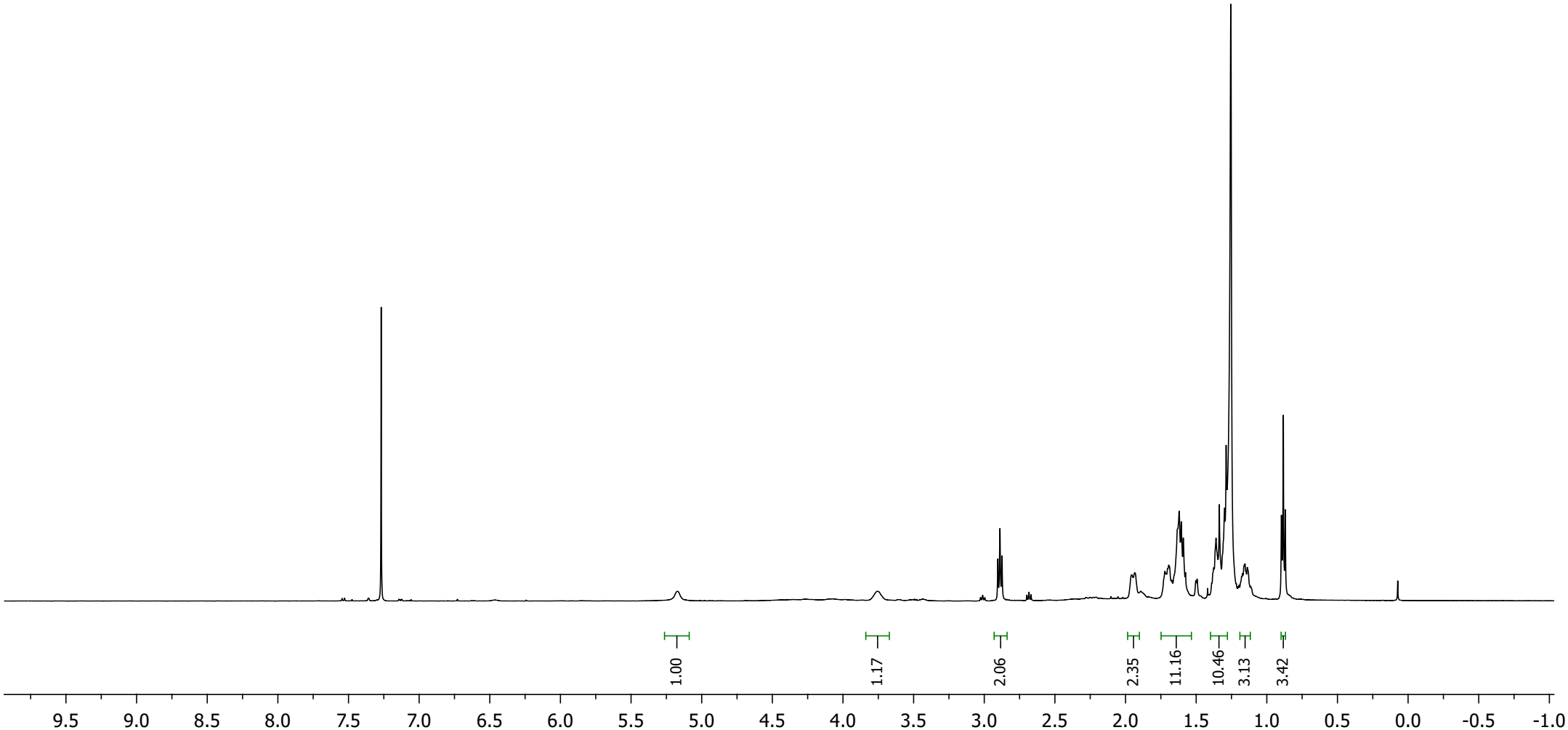
Jul23-2018
DMS-MCR-A131-011



Jul30-2018
DMS-MCR-A131-023




3r

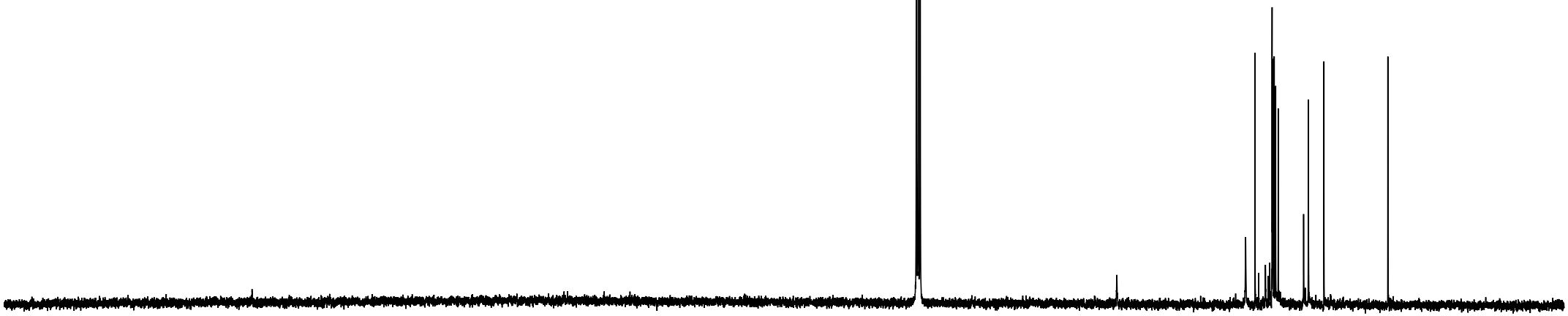


Jul30-2018
DMS-MCR-A131-023

166.27

50.46
33.20
31.94
29.67
29.65
29.61
29.55
29.37
29.18
28.84
25.44
24.79
22.71
14.15


3r



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