# Supporting Information

## Identification of 6,8-Ditrifluoromethyl Halogenated Phenazine as a Potent Bacterial Biofilm-Eradicating Agent

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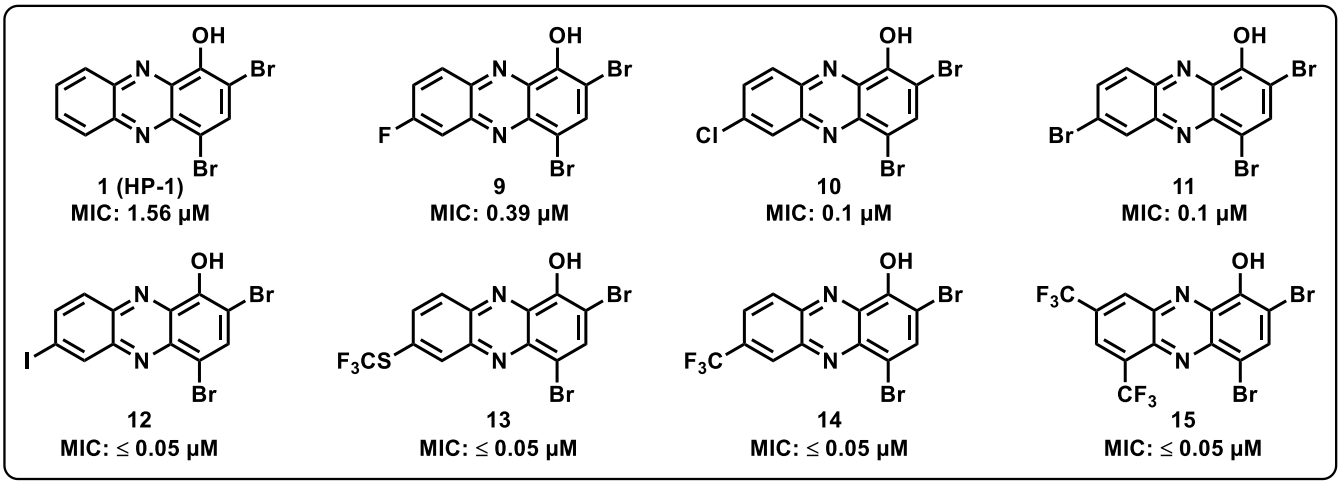
**1.) Supporting Figure 1. MIC Assay against MRSA 44.**

## MIC against MRSA 44

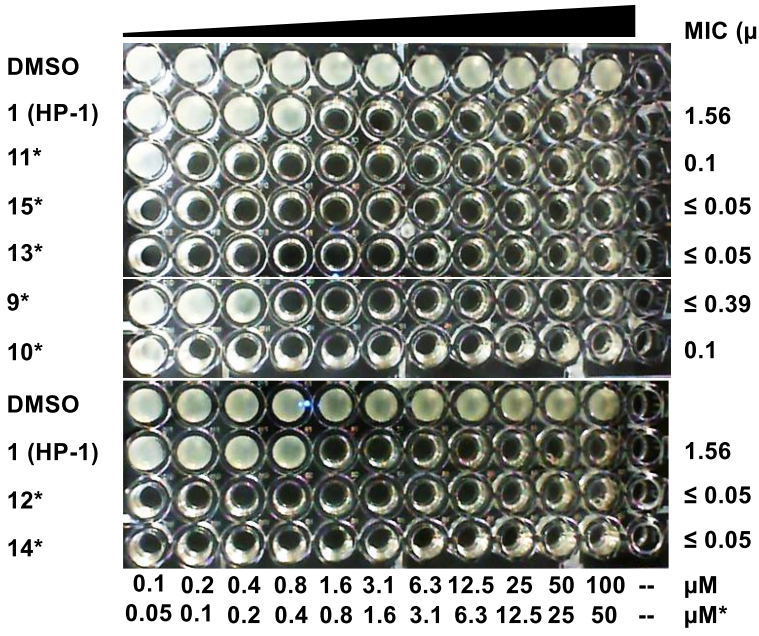



| | 12 | 11 | 10 | 9 | 8 | 7 | 6 | 5 | 4 | 3 | 2 | 1 | | MRSA 44 | MIC |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 600 | 0.669 | 0.537 | 0.609 | 0.632 | 0.605 | 0.612 | 0.586 | 0.573 | 0.577 | 0.679 | 0.729 | 0.047 | A | DMSO | OD600: 0.572 |
| 600 | 0.596 | 0.642 | 0.566 | 0.434 | 0.06 | 0.055 | 0.065 | 0.057 | 0.062 | 0.077 | 0.097 | 0.049 | B | 1 (HP-1) | 1.56 |
| 600 | 0.337 | 0.05 | 0.066 | 0.05 | 0.053 | 0.053 | 0.052 | 0.054 | 0.06 | 0.069 | 0.102 | 0.048 | C | 11* | 0.1 |
| 600 | 0.049 | 0.049 | 0.049 | 0.049 | 0.049 | 0.052 | 0.053 | 0.054 | 0.058 | 0.068 | 0.076 | 0.048 | D | 15* | ≤ 0.05 |
| 600 | 0.051 | 0.052 | 0.052 | 0.052 | 0.054 | 0.052 | 0.052 | 0.051 | 0.054 | 0.059 | 0.078 | 0.047 | E | 13* | ≤ 0.05 |
| 600 | 0.49 | 0.433 | 0.305 | 0.051 | 0.054 | 0.053 | 0.054 | 0.055 | 0.06 | 0.065 | 0.079 | 0.036 | G | 9* | 0.39 |
| 600 | 0.287 | 0.053 | 0.051 | 0.052 | 0.051 | 0.051 | 0.053 | 0.054 | 0.062 | 0.062 | 0.083 | 0.048 | H | 10* | 0.1 |

| | 12 | 11 | 10 | 9 | 8 | 7 | 6 | 5 | 4 | 3 | 2 | 1 | | MRSA 44 | MIC |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 600 | 0.451 | 0.484 | 0.474 | 0.445 | 0.398 | 0.451 | 0.463 | 0.438 | 0.436 | 0.404 | 0.356 | 0.038 | A | DMSO | OD600: 0.398 |
| 600 | 0.539 | 0.535 | 0.475 | 0.357 | 0.104 | 0.054 | 0.055 | 0.058 | 0.064 | 0.081 | 0.105 | 0.039 | B | 1 (HP-1) | 1.56 |
| 600 | 0.051 | 0.05 | 0.051 | 0.05 | 0.052 | 0.053 | 0.054 | 0.058 | 0.069 | 0.083 | 0.119 | 0.041 | C | 12* | ≤ 0.05 |
| 600 | 0.05 | 0.051 | 0.051 | 0.051 | 0.05 | 0.052 | 0.052 | 0.054 | 0.058 | 0.063 | 0.07 | 0.039 | D | 14* | ≤ 0.05 |

DMSO stock with test range: 10 mM (0.1 - 100 µM), *5 mM (0.05 - 50 µM)

## MIC against MRSA 44

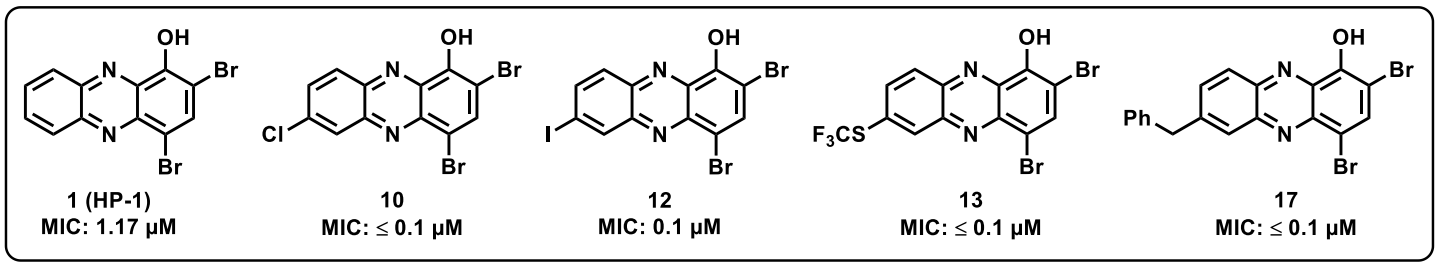



| MRSA 44 | Replicate A | Replicate B | Replicate C | MIC | OD600 |
|---|---|---|---|---|---|
| DMSO (OD600) | 0.321 | 0.431 | 0.572 | | 0.441 |
| 1 (HP-1) | 1.56 | 1.56 | 1.56 | 1.56 | |
| 11* | 0.1 | 0.1 | 0.1 | 0.1 | |
| 15* | ≤ 0.05 | ≤ 0.05 | ≤ 0.05 | ≤ 0.05 | |
| 13* | ≤ 0.05 | ≤ 0.05 | ≤ 0.05 | ≤ 0.05 | |
| 9* | 0.39 | 0.39 | 0.39 | 0.39 | |
| 10* | 0.1 | 0.1 | 0.1 | 0.1 | |
| | | | | | |
| DMSO (OD600) | 0.483 | 0.398 | 0.473 | | 0.451 |
| 1 (HP-1) | 1.56 | 1.56 | 1.56 | 1.56 | |
| 12* | ≤ 0.05 | ≤ 0.05 | ≤ 0.05 | ≤ 0.05 | |
| 14* | ≤ 0.05 | ≤ 0.05 | ≤ 0.05 | ≤ 0.05 | |

$OD_{600}$ values for DMSO controls were calculated by averaging turbidity readings from microtiter wells and subtracting blank microtiter well readings. MIC values were determined as the lowest concentration required to demonstrate ≥ 90% growth inhibition compared to the DMSO control (for each MIC assay).

**2.) Supporting Figure 2. MIC Assay against *S. epidermidis* 12228.**

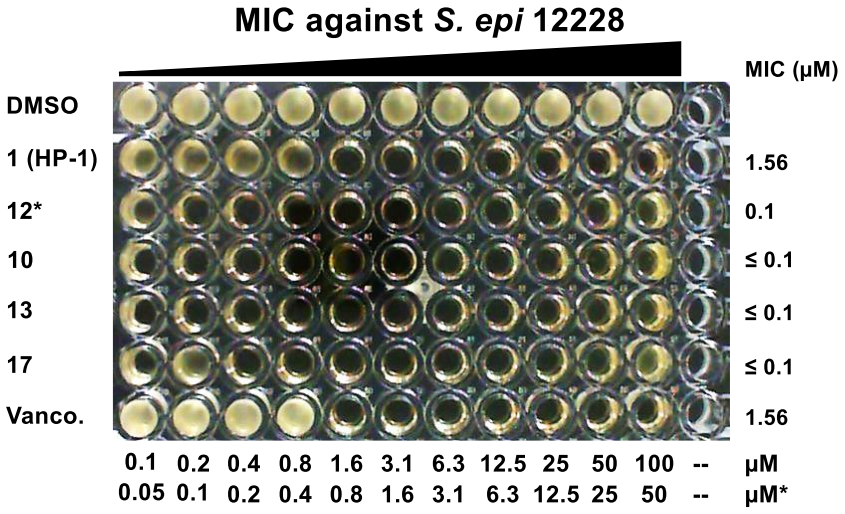
## MIC against *S. epidermidis* 12228




| | 12 | 11 | 10 | 9 | 8 | 7 | 6 | 5 | 4 | 3 | 2 | 1 | | *S. epi* 12228 | MIC |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 600 | 0.593 | 0.617 | 0.689 | 0.664 | 0.65 | 0.612 | 0.733 | 0.654 | 0.685 | 0.555 | 0.621 | 0.048 | A | DMSO | OD600: 0.595 |
| 600 | 0.2 | 0.232 | 0.292 | 0.211 | 0.089 | 0.09 | 0.091 | 0.096 | 0.104 | 0.124 | 0.146 | 0.056 | B | 1 (HP-1) | 1.56 |
| 600 | 0.125 | 0.094 | 0.094 | 0.093 | 0.089 | 0.09 | 0.088 | 0.093 | 0.099 | 0.107 | 0.123 | 0.05 | C | 12* | 0.1 |
| 600 | 0.092 | 0.093 | 0.096 | 0.1 | 0.104 | 0.109 | 0.117 | 0.118 | 0.127 | 0.15 | 0.186 | 0.08 | D | 10 | ≤ 0.1 |
| 600 | 0.129 | 0.13 | 0.129 | 0.128 | 0.129 | 0.127 | 0.124 | 0.123 | 0.127 | 0.138 | 0.158 | 0.077 | E | 13 | ≤ 0.1 |
| 600 | 0.138 | 0.255 | 0.133 | 0.134 | 0.134 | 0.135 | 0.14 | 0.144 | 0.152 | 0.171 | 0.23 | 0.1 | F | 17 | ≤ 0.1 |
| 600 | 0.611 | 0.649 | 0.708 | 0.726 | 0.14 | 0.139 | 0.138 | 0.137 | 0.139 | 0.136 | 0.135 | 0.098 | G | Vancomycin | 1.56 |

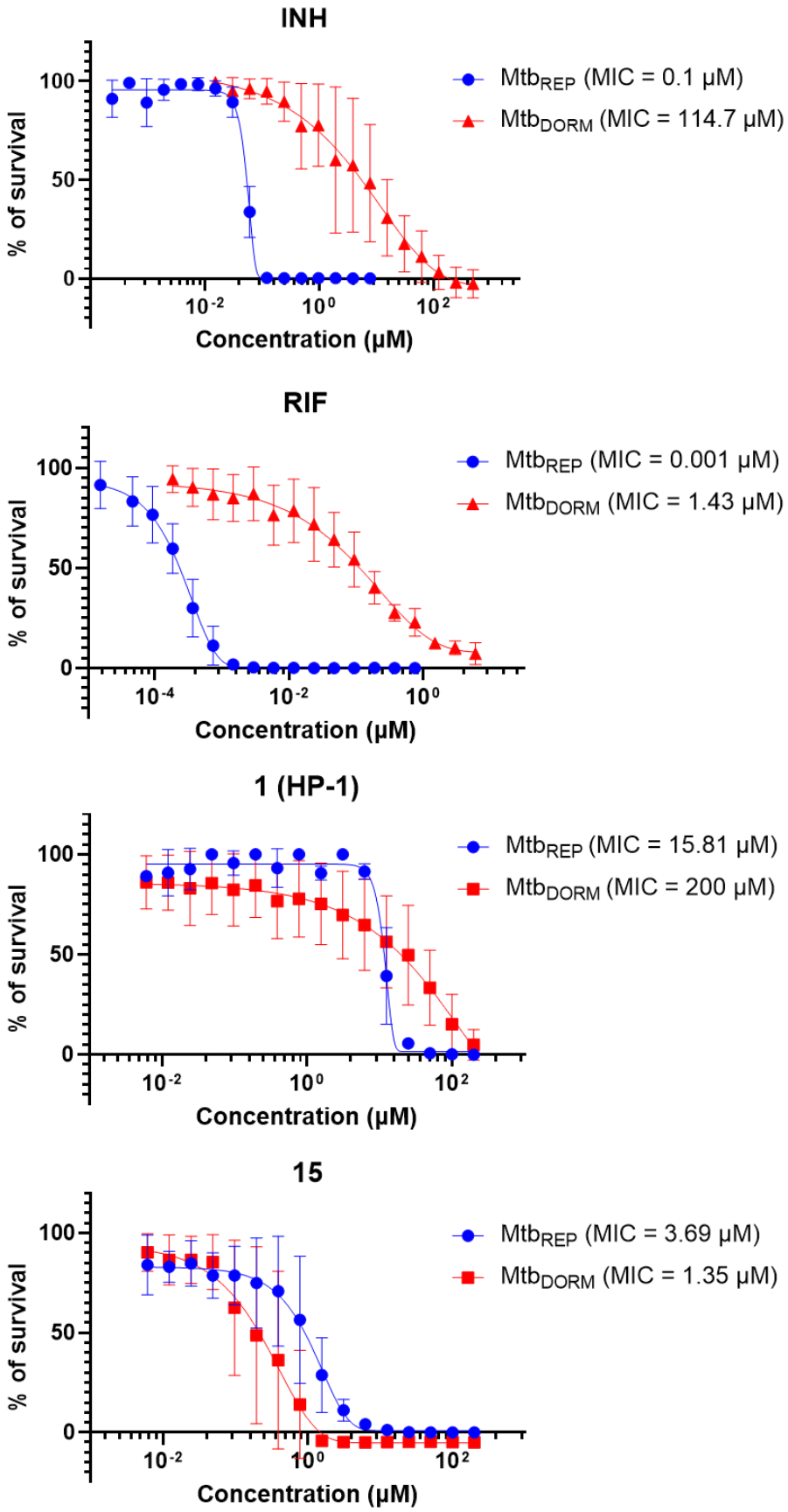
**DMSO stock with test range: 10 mM (0.1 - 100 µM), *5 mM (0.05 - 50 µM)**

| *S. epi* 12228 | Replicate A | Replicate B | Replicate C | MIC | OD600 |
|---|---|---|---|---|---|
| DMSO (OD600) | 0.591 | 0.595 | 0.494 | | 0.560 |
| 1 (HP-1) | 0.78 | 1.56 | 0.78 | 1.17 | |
| 12* | 0.1 | 0.1 | 0.1 | 0.1 | |
| 10 | ≤ 0.1 | ≤ 0.1 | ≤ 0.1 | ≤ 0.1 | |
| 13 | ≤ 0.1 | ≤ 0.1 | ≤ 0.1 | ≤ 0.1 | |
| 17 | ≤ 0.1 | ≤ 0.1 | ≤ 0.1 | ≤ 0.1 | |
| Vancomycin | 1.56 | 1.56 | 1.56 | 1.56 | |

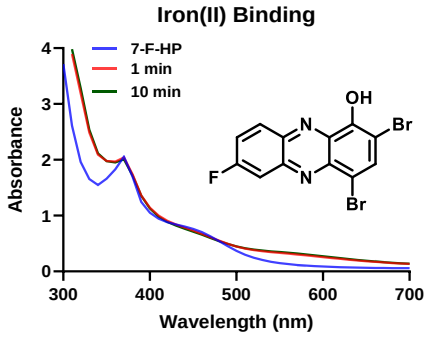


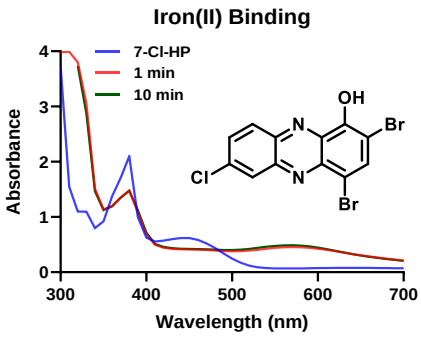

$OD_{600}$ values for DMSO controls were calculated by averaging turbidity readings from microtiter wells and subtracting blank microtiter well readings. MIC values were determined as the lowest concentration required to demonstrate ≥ 90% growth inhibition compared to the DMSO control (for each MIC assay).

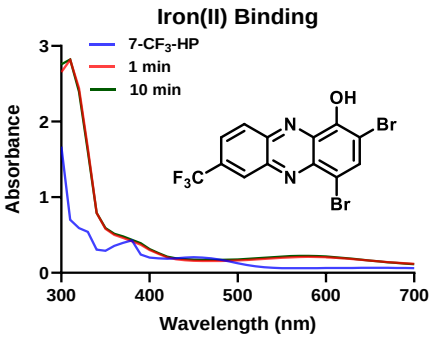
**3.) Supporting Figure 3. Dose-response Curves from MIC Assays against Mtb.**

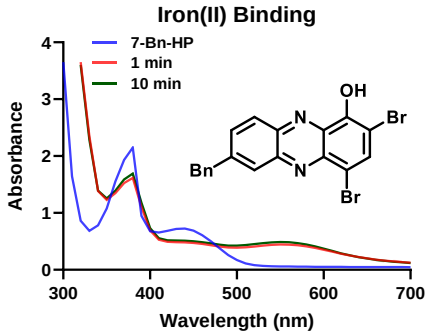


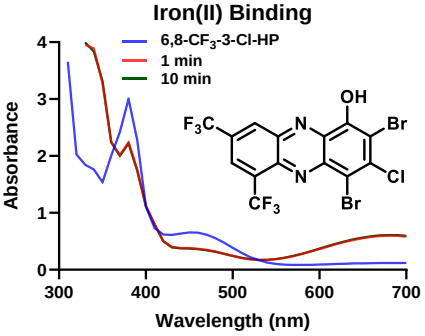
## 4.) Supporting Figure 4. UV-vis Spectroscopy Results.



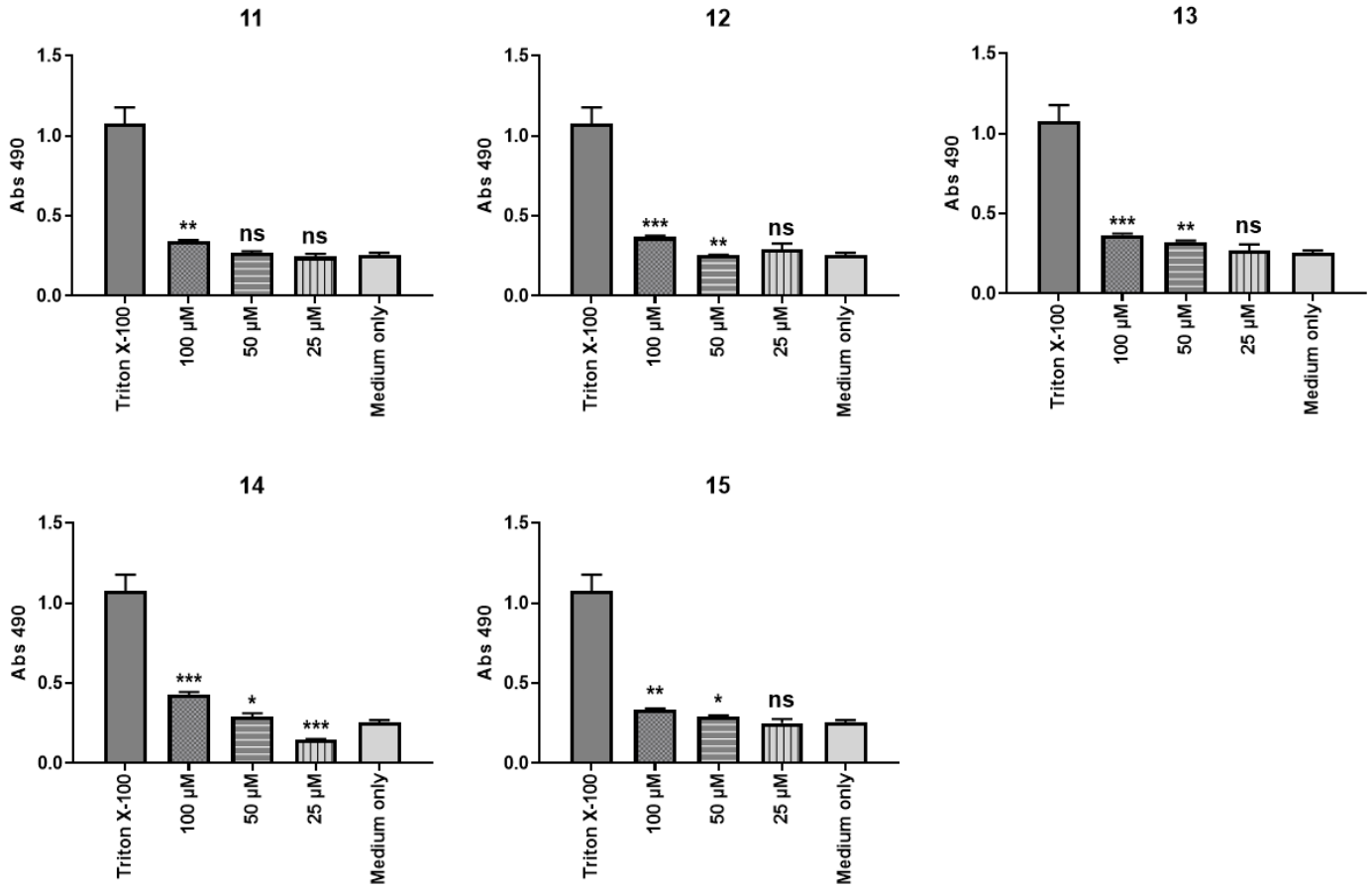



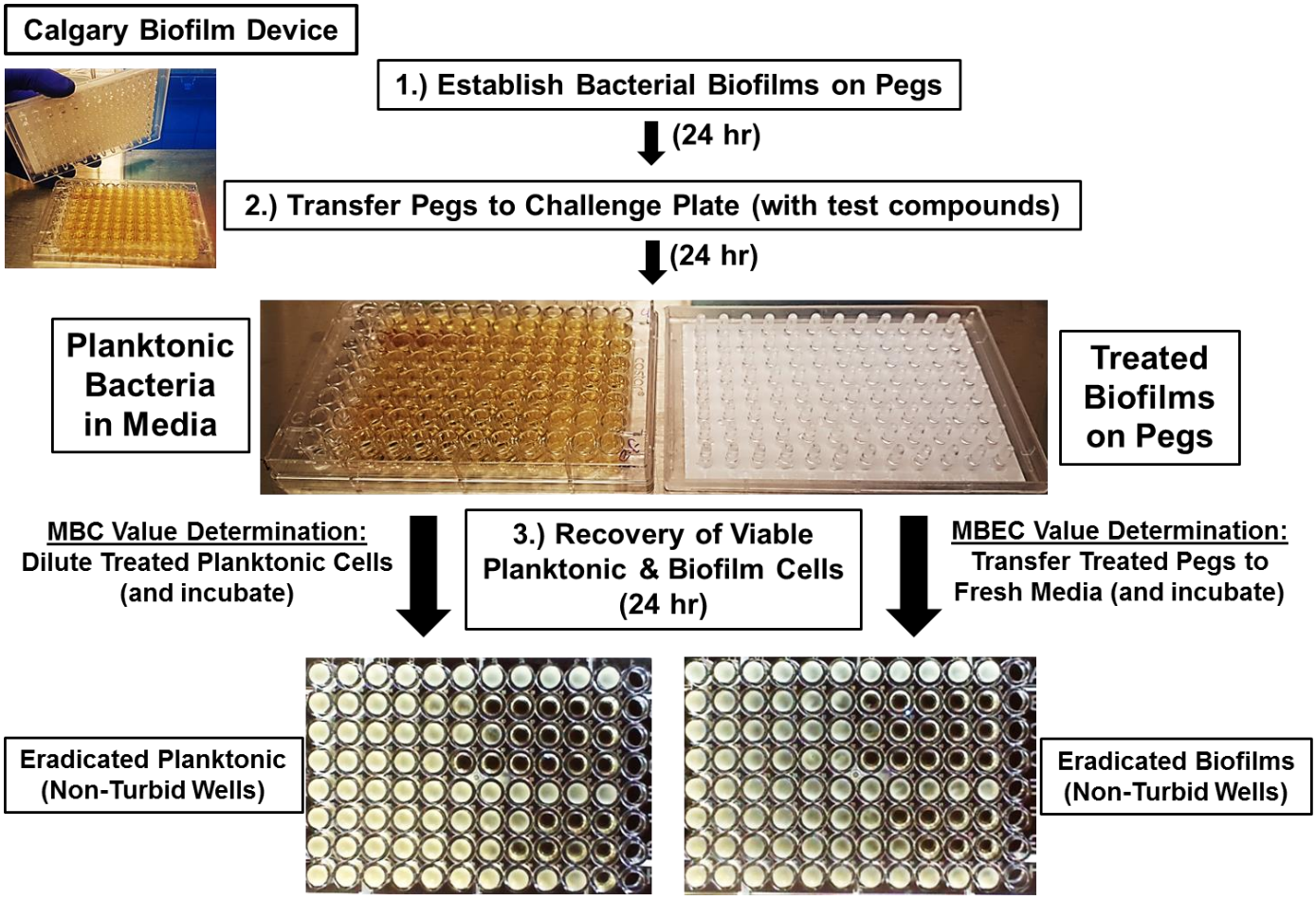



**5.) Supporting Figure 5. LDH Release Assay Results.**




Halogenated Phenazine cytotoxicity results (Triton-X = 100% cell death; Medium Only: 0% cell death).

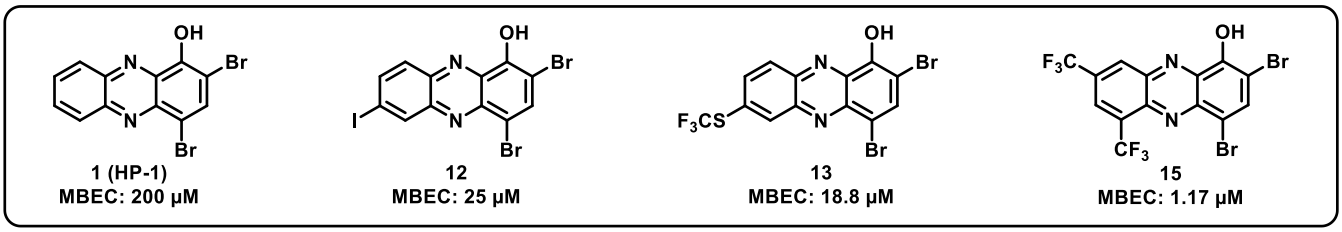
**6.) Supporting Figure 6. Calgary Biofilm Device Assay.**




Assay workflow to determine MBC and MBEC values of test compounds using the Calgary Biofilm Device.

**7.) Supporting Figure 7. Calgary Biofilm Device Assay against *S. aureus* 138.**

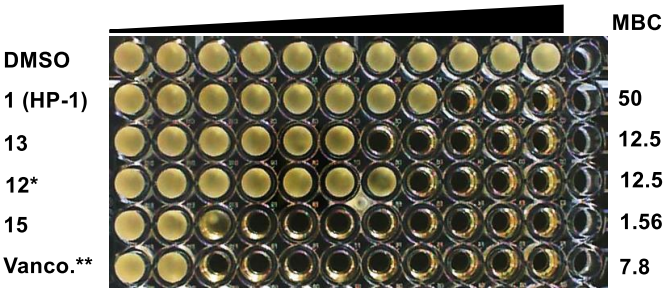
## Calgary Biofilm Device (CBD) Assay against *S. aureus* 138 (Media: TSBG)




| | 12 | 11 | 10 | 9 | 8 | 7 | 6 | 5 | 4 | 3 | 2 | 1 | | *S. aureus* 138 | MBC |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 600 | 0.872 | 0.869 | 0.839 | 0.805 | 0.861 | 0.85 | 0.85 | 0.776 | 0.849 | 0.794 | 0.789 | 0.05 | A | DMSO | OD600: 0.782 |
| 600 | 0.846 | 0.873 | 0.794 | 0.797 | 0.799 | 0.782 | 0.781 | 0.848 | 0.119 | 0.121 | 0.129 | 0.083 | B | 1 (HP-1) | 50 |
| 600 | 0.904 | 0.881 | 0.919 | 0.818 | 1.061 | 0.791 | 0.129 | 0.127 | 0.129 | 0.128 | 0.123 | 0.082 | C | 13 | 12.5 |
| 600 | 0.856 | 0.919 | 0.847 | 0.841 | 0.853 | 0.918 | 0.607 | 0.155 | 0.158 | 0.159 | 0.166 | 0.12 | D | 12* | 12.5 |
| 600 | 0.886 | 0.791 | 0.435 | 0.167 | 0.166 | 0.165 | 0.164 | 0.161 | 0.163 | 0.164 | 0.169 | 0.118 | E | 15 | 1.56 |
| 600 | 0.9 | 0.925 | 0.174 | 0.175 | 0.177 | 0.178 | 0.18 | 0.182 | 0.183 | 0.183 | 0.185 | 0.147 | F | Vancomycin** | 7.8 |

DMSO stock with test range: 10 mM (0.2 - 200 µM), *5 mM (0.1 - 100 µM), **100 mM (2 - 2000 µM)

### Planktonic Eradication (MBC)



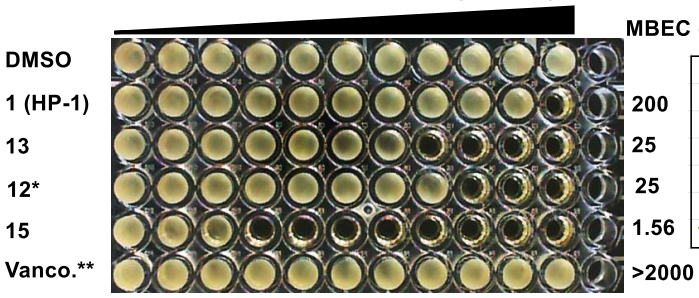

| *S. aureus* 138 | Replicate A | Replicate B | Replicate C | MBC | OD600 |
|---|---|---|---|---|---|
| DMSO | 0.782 | 0.689 | 0.643 | | 0.705 |
| 1 (HP-1) | 50 | 50 | 50 | 50 | |
| 13 | 12.5 | 12.5 | 12.5 | 12.5 | |
| 12* | 12.5 | 12.5 | 12.5 | 12.5 | |
| 15 | 1.56 | 1.56 | 1.56 | 1.56 | |
| Vancomycin** | 7.8 | 7.8 | 7.8 | 7.8 | |

DMSO stock with test range: 10 mM (0.2 - 200 µM), *5 mM (0.1 - 100 µM), **100 mM (2 - 2000 µM)

| | 12 | 11 | 10 | 9 | 8 | 7 | 6 | 5 | 4 | 3 | 2 | 1 | | *S. aureus* 138 | MBEC |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 600 | 0.646 | 0.712 | 0.58 | 0.617 | 0.593 | 0.691 | 0.628 | 0.682 | 0.625 | 0.667 | 0.642 | 0.05 | A | DMSO | OD600: 0.594 |
| 600 | 0.71 | 0.711 | 0.664 | 0.714 | 0.757 | 0.73 | 0.649 | 0.632 | 0.566 | 0.457 | 0.081 | 0.053 | B | 1 (HP-1) | 200 |
| 600 | 0.646 | 0.66 | 0.58 | 0.59 | 0.576 | 0.477 | 0.318 | 0.077 | 0.077 | 0.075 | 0.072 | 0.052 | C | 13 | 25 |
| 600 | 0.769 | 0.63 | 0.557 | 0.629 | 0.633 | 0.615 | 0.594 | 0.43 | 0.11 | 0.097 | 0.106 | 0.078 | D | 12* | 25 |
| 600 | 0.624 | 0.441 | 0.411 | 0.113 | 0.112 | 0.109 | 0.108 | 0.107 | 0.106 | 0.105 | 0.103 | 0.074 | E | 15 | 1.56 |
| 600 | 0.7 | 0.7 | 0.58 | 0.716 | 0.665 | 0.559 | 0.591 | 0.623 | 0.604 | 0.593 | 0.672 | 0.098 | F | Vancomycin** | > 2000 |

DMSO stock with test range: 10 mM (0.2 - 200 µM), *5 mM (0.1 - 100 µM), **100 mM (2 - 2000 µM)

### Biofilm Eradication (MBEC)



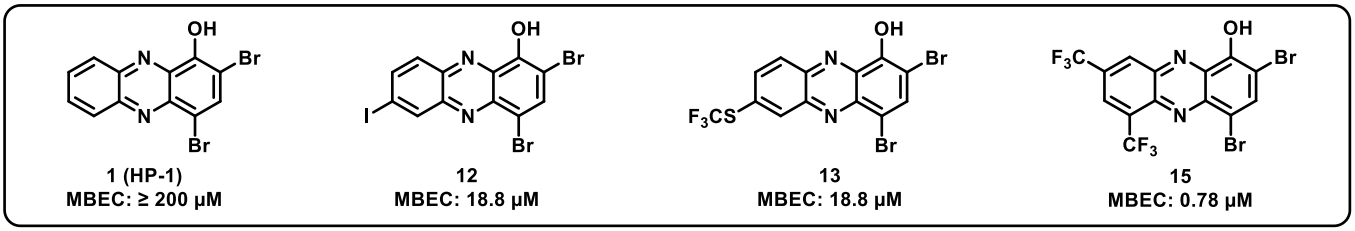

| *S. aureus* 138 | Replicate A | Replicate B | Replicate C | MBEC | OD600 |
|---|---|---|---|---|---|
| DMSO | 0.594 | 0.707 | 0.589 | | 0.630 |
| 1 (HP-1) | 200 | 200 | 200 | 200 | |
| 13 | 25 | 25 | 25 | 25 | |
| 12* | 25 | 25 | 12.5 | 18.8 | |
| 15 | 1.56 | 1.56 | 0.78 | 1.17 | |
| Vancomycin** | > 2000 | > 2000 | > 2000 | > 2000 | |

DMSO stock with test range: 10 mM (0.2 - 200 µM), *5 mM (0.1 - 100 µM), **100 mM (2 - 2000 µM)

$OD_{600}$ values for DMSO controls were calculated by averaging turbidity readings from microtiter wells and subtracting blank microtiter well readings. MBC & MBEC values were determined as the lowest test concentration required to demonstrate ≥ 90% reduction in turbidity compared to the DMSO control.

**8.) Supporting Figure 8. Calgary Biofilm Device Assay against MRSA 2.**

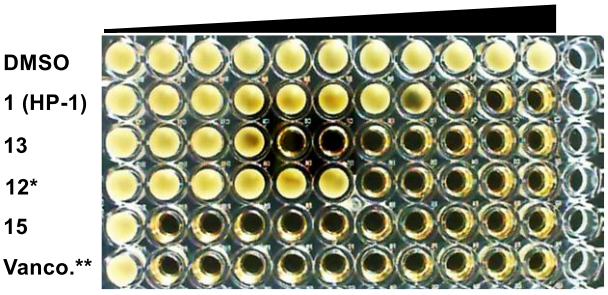
## Calgary Biofilm Device (CBD) Assay against MRSA 2 (Media: TSBG)




| | 12 | 11 | 10 | 9 | 8 | 7 | 6 | 5 | 4 | 3 | 2 | 1 | | MRSA 2 | MBC |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 600 | 0.719 | 0.732 | 0.716 | 0.704 | 0.71 | 0.715 | 0.728 | 0.723 | 0.708 | 0.693 | 0.71 | 0.049 | A | DMSO | OD600: 0.665 |
| 600 | 0.695 | 0.683 | 0.696 | 0.708 | 0.818 | 0.752 | 0.706 | 0.335 | 0.142 | 0.144 | 0.15 | 0.053 | B | 1 (HP-1) | 50 |
| 600 | 0.805 | 0.615 | 0.661 | 0.476 | 0.138 | 0.138 | 0.135 | 0.139 | 0.138 | 0.138 | 0.137 | 0.049 | C | 13 | 3.13 |
| 600 | 0.715 | 0.722 | 0.822 | 0.628 | 0.633 | 0.628 | 0.149 | 0.153 | 0.156 | 0.159 | 0.161 | 0.069 | D | 12* | 6.25 |
| 600 | 0.785 | 0.171 | 0.17 | 0.168 | 0.165 | 0.163 | 0.162 | 0.157 | 0.157 | 0.158 | 0.167 | 0.065 | E | 15 | 0.39 |
| 600 | 0.71 | 0.169 | 0.173 | 0.171 | 0.173 | 0.173 | 0.177 | 0.176 | 0.178 | 0.177 | 0.176 | 0.091 | F | Vancomycin** | 3.9 |

DMSO stock with test range: 10 mM (0.2 - 200 µM), *5 mM (0.1 - 100 µM), **100 mM (2 - 2000 µM)

### Planktonic Eradication (MBC)



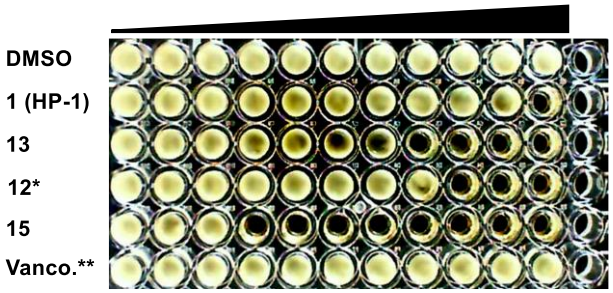

| MRSA 2 | Replicate A | Replicate B | Replicate C | MBC | OD600 |
|---|---|---|---|---|---|
| DMSO (OD600) | 0.662 | 0.665 | 0.622 | | 0.650 |
| 1 (HP-1) | 25 | 50 | 25 | 37.5 | |
| 13 | 3.13 | 3.13 | 6.25 | 4.69 | |
| 12* | 6.25 | 6.25 | 6.25 | 6.25 | |
| 15 | 0.78 | 0.39 | 0.39 | 0.59 | |
| Vancomycin** | 3.9 | 3.9 | 7.8 | 5.9 | |

DMSO stock with test range: 10 mM (0.2 - 200 µM), *5 mM (0.1 - 100 µM), **100 mM (2 - 2000 µM)

| | 12 | 11 | 10 | 9 | 8 | 7 | 6 | 5 | 4 | 3 | 2 | 1 | | MRSA 2 | MBEC |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 600 | 0.694 | 0.56 | 0.63 | 0.637 | 0.679 | 0.669 | 0.659 | 0.628 | 0.669 | 0.625 | 0.643 | 0.048 | A | DMSO | OD600: 0.597 |
| 600 | 0.676 | 0.541 | 0.657 | 0.572 | 0.494 | 0.605 | 0.547 | 0.475 | 0.427 | 0.376 | 0.087 | 0.05 | B | 1 (HP-1) | 200 |
| 600 | 0.46 | 0.484 | 0.393 | 0.396 | 0.328 | 0.276 | 0.172 | 0.093 | 0.088 | 0.086 | 0.085 | 0.049 | C | 13 | 25 |
| 600 | 0.682 | 0.497 | 0.465 | 0.507 | 0.413 | 0.412 | 0.421 | 0.481 | 0.092 | 0.092 | 0.093 | 0.055 | D | 12* | 25 |
| 600 | 0.509 | 0.31 | 0.369 | 0.091 | 0.091 | 0.088 | 0.086 | 0.084 | 0.083 | 0.086 | 0.086 | 0.05 | E | 15 | 1.56 |
| 600 | 0.483 | 0.406 | 0.429 | 0.398 | 0.457 | 0.545 | 0.55 | 0.547 | 0.443 | 0.517 | 0.525 | 0.061 | F | Vancomycin** | > 2000 |

DMSO stock with test range: 10 mM (0.2 - 200 µM), *5 mM (0.1 - 100 µM), **100 mM (2 - 2000 µM)

### Biofilm Eradication (MBEC)

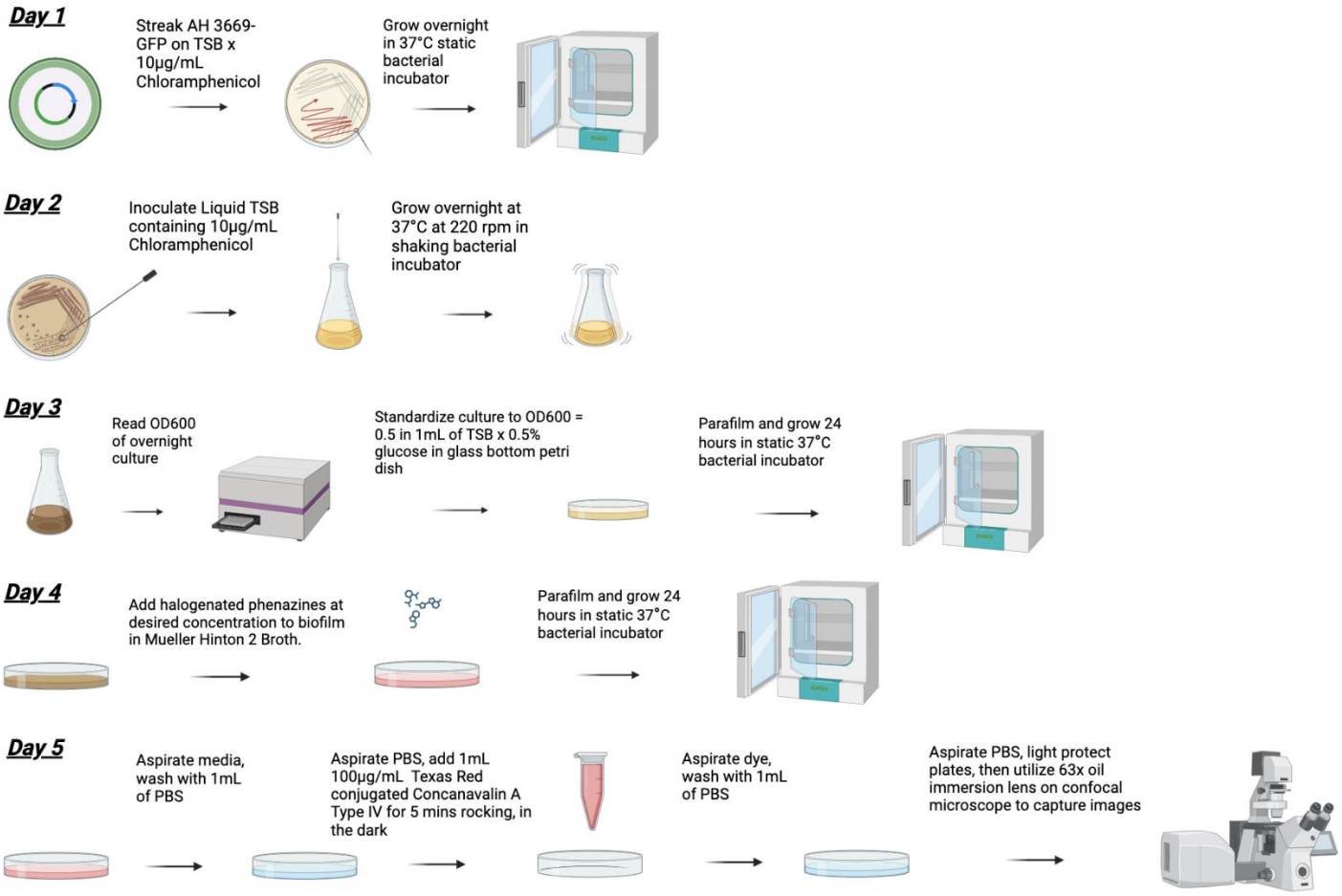



| MRSA 2 | Replicate A | Replicate B | Replicate C | MBEC | OD600 |
|---|---|---|---|---|---|
| DMSO (OD600) | 0.560 | 0.597 | 0.469 | | 0.542 |
| 1 (HP-1) | > 200 | 200 | 200 | ≥ 200 | |
| 13 | 12.5 | 25 | 12.5 | 18.8 | |
| 12* | 12.5 | 25 | 12.5 | 18.8 | |
| 15 | 0.78 | 1.56 | 0.39 | 0.78 | |
| Vancomycin** | > 2000 | > 2000 | > 2000 | > 2000 | |

DMSO stock with test range: 10 mM (0.2 - 200 µM), *5 mM (0.1 - 100 µM), **100 mM (2 - 2000 µM)

$OD_{600}$ values for DMSO controls were calculated by averaging turbidity readings from microtiter wells and subtracting blank microtiter well readings. MBC & MBEC values were determined as the lowest test concentration required to demonstrate ≥ 90% reduction in turbidity compared to the DMSO control.

## 9.) Supporting Figure 9. General Workflow for Confocal Microscopy Experiments.



**10.) Supporting Table 1. Antibacterial Activity Profiles against MRSA Clinical Isolates.**

Summary of halogenated phenazines antibacterial activity profiles (MIC values) against multi-drug resistant *Staphylococcus aureus* clinical isolates.

| Compound | MRSA 1 | MRSA 2 | *S. aureus* 129 | *S. aureus* 138 | *S. aureus* 147 | *S. aureus* 156 |
|---|---|---|---|---|---|---|
| **1 (HP-1)** | 2.35[a] | 2.35[a] | 2.35[a] | 2.35[a] | 2.35[a] | 2.35[a] |
| **9** | 0.59[a] | 1.56 | 2.35[a] | 0.78 | 1.17[a] | 1.17[a] |
| **10** | 0.05[b] | 0.20 | 0.15[a] | 0.10 | 0.10 | 0.10 |
| **12** | 0.15[a] | 0.39 | 0.20 | 0.20 | -- | 0.20 |
| **13** | 0.10 | 0.20 | 0.30[a] | 0.15[a] | 0.10 | 0.15[a] |
| **14** | 0.05[b] | 0.08[a] | 0.05[b] | 0.05[b] | 0.08[a] | 0.05[b] |
| **15** | 0.10 | 0.10 | 0.10 | 0.10 | 0.10 | 0.10 |
| **17** | 0.30[a] | 1.17[a] | 0.39 | 0.59[a] | 0.39 | 0.59[a] |
| **Vancomycin** | 0.39 | 0.39 | 0.39 | 0.39 | 0.59[a] | 0.39 |
| **Methicillin** | 37.5[a] | > 100 | 37.5[a] | 37.5[a] | 6.25 | 25 |
| **Ciprofloxacin** | 0.78 | > 100 | > 100 | > 100 | 1.17[a] | 0.78 |
| **Tetracycline** | 0.10[b] | 0.10[b] | 0.10[b] | 0.15[a] | 0.10[b] | 0.15[a] |
| **Erythromycin** | 100 | 18.8[a] | > 100 | > 100 | 37.5[a] | > 100 |
| **Tobramycin** | 6.25 | 6.25 | > 100 | 12.5 | 6.25 | 12.5 |

Note: All biological results are reported in micromolar (μM) concentrations and acquired from three or more independent experiments. The clinical isolates used in this panel are all resistant to methicillin. [a]Midpoint value for 2-fold range in MIC values observed. [b]Lowest concentration tested.

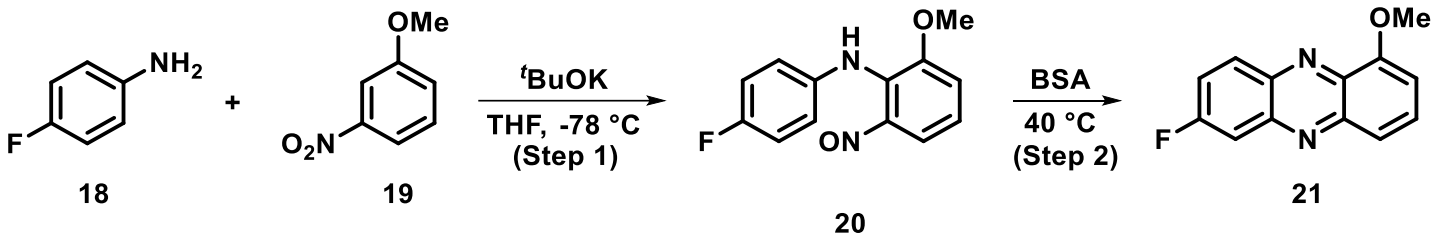
**11.) Supporting Table 2. Antibacterial Activities against Gram-Negative Pathogens.**

Summary of antibacterial activities for select HPs against Gram-negative pathogens (MIC values reported).

| Compound | *A. baumannii* 19606 | *A. baumannii* 17978 | *A. baumannii* 1794 | PA01 | *E. coli* UAEC-1 |
|---|---|---|---|---|---|
| **1 (HP-1)** | 37.5[a] | > 100 | > 100 | > 100 | > 100 |
| **15** | 12.5 | 75[a] | 75[a] | ≥ 100 | > 100 |
| **Colistin** | 0.39 | 0.78 | 2.35[a] | -- | -- |
| **Nitroxoline** | 1.56 | 9.38[a] | 9.38[a] | > 100 | 12.5 |

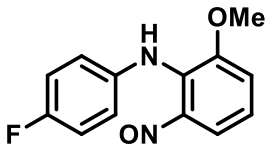
Note: MIC values are reported in micromolar (μM) concentrations and were acquired from three or more independent experiments. [a]Midpoint value for a 2-fold range observed from independent MIC experiments.

**12.) Synthetic Procedures and Characterization Data.**




**Procedure (Step 1).** A solution of 4-fluoroaniline (260 µL, 2.75 mmol) dissolved in 1 mL tetrahydrofuran was added dropwise to a stirring solution of potassium *tert*-butoxide (721 mg, 7.50 mmol) in tetrahydrofuran (12 mL) at -78 °C. Next, a solution of 3-nitroanisole (383 mg, 2.50 mmol) dissolved in 2 mL tetrahydrofuran was added to the reaction mixture which was then stirred at -78 °C until starting material was consumed (monitored by TLC). Upon completion, the reaction contents were transferred to a separatory funnel containing brine and the crude product was extracted with ethyl acetate (3 x 30 mL). The resulting organic layer was then dried with sodium sulfate, filtered, and concentrated *in vacuo* resulting in nitroso intermediate **20** (red solid) which was taken to the next step without purification. Note: Nitroso compound **20** was isolated and fully characterized below; however, other nitroso intermediates synthesized during these studies were advanced to the next step directly due to general stability concerns.

**Procedure (Step 2).** Nitroso **20** was dissolved in *N*,*N*-dimethylformamide (10 mL) before *N*,*O*-bis(trimethylsilyl)acetamide (2 mL, 8.1 mmol) was added to the mixture and the reaction was allowed to stir at 40 °C for 19 hours. Upon completion of the reaction, the contents were transferred to a separated funnel containing brine (50 mL) and the crude product was extracted with ethyl acetate (3 x 30 mL). The organic layer was then washed with water (3 x 50 mL), dried over sodium sulfate, filtered, and concentrated *in vacuo*. The resulting material was purified via column chromatography using 5:1 to 3:1 hexanes:ethyl acetate to afford 183 mg of **21** (32% yield) as a yellow solid. Note: This procedure was derived from published protocols and used throughout this study.[1-3]



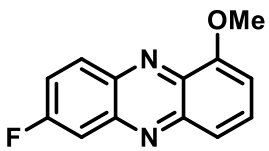
**20**

**$^{1}$H NMR (600 MHz, $CDCl_3$):** δ 10.16 (br. s, 1H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.04 - 7.00 (m, 3H), 6.98 - 6.90 (m, 3H), 3.71 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$):** δ 159.7 (d, *J* = 242.9 Hz), 159.4, 151.2, 138.0 (d, *J* = 2.8 Hz), 130.4, 123.6 (d, *J* = 8.2 Hz), 118.9, 118.0, 117.9, 115.2 (d, *J* = 22.8 Hz), 56.3.

**HRMS (ESI):** calc. for $C_{13}H_{12}FN_2O_2$ $[M+H]^+$: 247.0877, found: 247.0866.

**MP:** 113 - 115 °C.



**21**

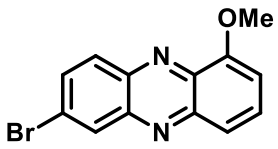
**Yield:** 32%; 183 mg of **21** was isolated as a yellow solid.

**$^{1}$H NMR (600 MHz, $CDCl_3$):** δ 8.28 (dd, *J* = 9.5, 5.9 Hz, 1H), 7.71 - 7.61 (m, 3H), 7.53 (ddd, *J* = 9.6, 7.9, 2.8 Hz, 1H), 6.93 (dd, *J* = 7.1, 1.2 Hz, 1H), 4.07 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$):** δ 163.3 (d, *J* = 255.7 Hz), 155.2, 144.4, 144.0 (d, *J* = 13.8 Hz), 139.6, 136.3 (d, *J* = 2.6 Hz), 132.6 (d, *J* = 10.4 Hz), 131.2, 122.1 (d, *J* = 28.2 Hz), 121.1, 111.4 (d, *J* = 21.1 Hz), 106.4 (d, *J* = 0.9 Hz), 56.5.

**HRMS (ESI):** calc. for $C_{13}H_{10}FN_2O$ $[M+H]^+$: 229.0772, found: 229.0767.

**MP:** 164 - 166 °C.




**22**

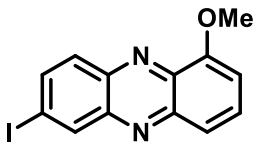
**Yield:** 34%; 249 mg of **22**; yellow solid.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.43 (d, *J* = 2.1 Hz, 1H), 8.26 (d, *J* = 9.3 Hz, 1H), 7.88 (dd, *J* = 9.3, 2.1 Hz, 1H), 7.84 - 7.74 (m, 2H), 7.10 (dd, *J* = 6.9, 1.3 Hz, 1H), 4.18 (s, 3H).

**$^{13}$C NMR (101 MHz, $CDCl_3$):** δ 155.2, 144.5, 143.7, 140.8, 136.9, 134.0, 131.5, 131.4, 131.4, 125.4, 121.5, 106.9, 56.6.

**HRMS (ESI):** calc. for $C_{13}H_{10}BrN_2O$ $[M+H]^+$: 288.9971, found: 288.9965.

**MP:** 183 - 185 °C.




**23**

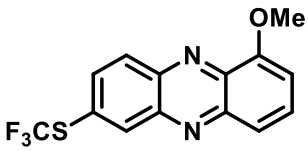
**Yield:** 45%; 1.05 g of **23**; yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$):** δ 8.68 (d, *J* = 1.8 Hz, 1H), 8.08 (d, *J* = 9.1 Hz, 1H), 8.02 (dd, *J* = 9.1, 1.8 Hz, 1H), 7.79 (dd, *J* = 8.9, 1.2 Hz, 1H), 7.76 (dd, *J* = 8.9, 7.3 Hz, 1H), 7.08 (dd, *J* = 7.3, 1.2 Hz, 1H), 4.17 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$):** δ 155.3, 144.4, 144.1, 141.3, 139.1, 138.6, 137.2, 131.5, 131.4, 121.7, 107.1, 97.9, 56.8.

**HRMS (ESI):** calc. for $C_{13}H_{10}IN_2O$ $[M+H]^+$: 336.9832, found: 336.9821.

**MP:** 193 - 195 °C.




**24**

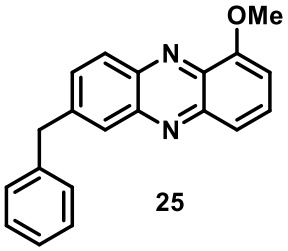
**Yield:** 27%; 130 mg of **24**; yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$):** δ 8.57 (d, *J* = 1.5 Hz, 1H), 8.41 (d, *J* = 9.1 Hz, 1H), 7.93 (dd, *J* = 9.1, 1.4 Hz, 1H), 7.82 (d, *J* = 8.7 Hz, 1H), 7.78 (dd, *J* = 8.7, 7.3 Hz, 1H), 7.09 (d, *J* = 7.3 Hz, 1H), 4.17 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$):** δ 155.3, 144.8, 142.8, 142.1, 137.8, 137.5, 134.8, 131.7, 131.5, 129.5 (q, *J* = 309.2 Hz), 128.1 (q, *J* = 1.9 Hz), 121.7, 107.6, 56.8.

**HRMS (ESI):** calc. for $C_{14}H_{10}F_3N_2OS$ $[M+H]^+$: 311.0460, found: 311.0473.

**MP:** 176 - 178 °C.




**25**

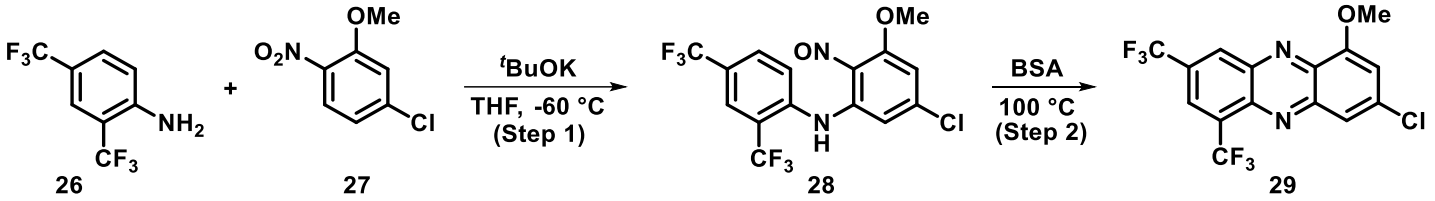
**Yield:** 29%; 219 mg of **25**; yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$):** δ 8.14 (d, *J* = 9.0 Hz, 1H), 7.81 (s, 1H), 7.62 (d, *J* = 8.8 Hz, 1H), 7.55 - 7.44 (m, 2H), 7.22 - 7.02 (m, 5H), 6.80 (d, *J* = 7.5 Hz, 1H), 4.05 (s, 2H), 3.95 (s, 3H). Note: TMS was used as a reference (0.00 ppm) in this experiment due to the $CHCl_3$ signal being buried by compound **25** protons (concentrated sample).

**$^{13}$C NMR (151 MHz, $CDCl_3$):** δ 155.0, 144.5, 144.1, 143.5, 141.2, 139.2, 136.4, 132.3, 130.3, 130.0, 129.2, 128.7, 127.4, 126.6, 121.1, 106.1, 56.3, 42.2.

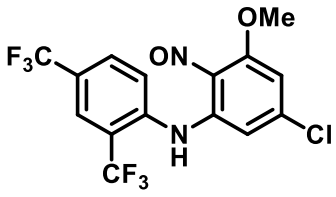
**HRMS (ESI):** calc. for $C_{20}H_{17}N_2O$ $[M+H]^+$: 301.1335, found: 301.1346.

**MP:** 148 - 150 °C.




**Procedure (Step 1).** 2,5-Bis(trifluoromethyl)aniline (338 µL, 2.18 mmol) was added to a stirring solution of potassium *tert*-butoxide (668 mg, 5.95 mmol) in 3 mL tetrahydrofuran at -60 °C. Then, a solution of 5-Chloro-2-nitroanisole (372 mg, 1.98 mmol) in 1.8 mL tetrahydrofuran was added to the reaction mixture at -60 °C and allowed to react at this temperature until complete (by TLC analysis). After the reaction was finished, the reaction contents were transferred to a separatory funnel containing brine and the crude product was extracted with ethyl acetate (3 x 30 mL). The resulting organic layer was collected and dried with sodium sulfate, filtered, and concentrated *in vacuo* resulting in crude nitroso **28**, which was taken directly to the next step (this intermediate was purified at a later stage in the project for characterization purposes; full data set below).

**Procedure (Step 2).** Nitroso **28** was dissolved in *N*,*N*-dimethylformamide (4.8 mL) before *N*,*O*-bis(trimethylsilyl)acetamide (2.4 mL, 9.9 mmol) was added, and the resulting mixture was allowed to stir at 100 °C for two hours. Upon completion, the reaction contents were transferred to a separated funnel containing brine (50 mL) and the crude product was extracted with ethyl acetate (3 x 30 mL). The organic layer was then washed with water (3 x 50 mL), dried over sodium sulfate, filtered, and concentrated *in vacuo*. The resulting solid was purified via column chromatography using 10:1 hexanes:ethyl acetate to afford 145 mg of **29** (29% yield) as a yellow solid.



28

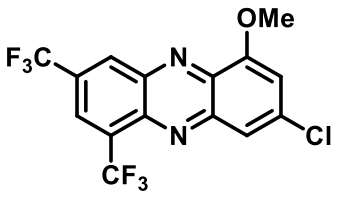
**Yield:** 51%; 406 mg of **28** was isolated as a dark brown solid.

**$^{1}$H NMR (600 MHz, $CDCl_3$):** δ 12.72 (s, 1H), 7.90 (d, *J* = 8.2 Hz, 1H), 7.76 (s, 1H), 7.66 (d, *J* = 8.2 Hz, 1H), 6.52 (d, *J* = 1.8 Hz, 1H), 6.38 (d, *J* = 1.8 Hz, 1H), 4.19 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$):** δ 164.7, 148.7, 147.8, 136.5 (q, *J* = 1.4 Hz), 135.5 (q, *J* = 33.6 Hz), 132.6, 129.2 (q, *J* = 30.9 Hz), 128.6 (q, *J* = 5.0 Hz), 125.3 (q, *J* = 3.7 Hz), 123.7 (q, *J* = 3.7 Hz), 122.9 (q, *J* = 273.3), 122.7 (q, *J* = 273.9), 105.4, 102.4, 57.3.

**HRMS (ESI):** calc. for $C_{15}H_{10}ClF_6N_2O_2$ $[M+H]^+$: 399.0330, found: 399.0322.

**MP:** 117 - 119 °C.




**29**

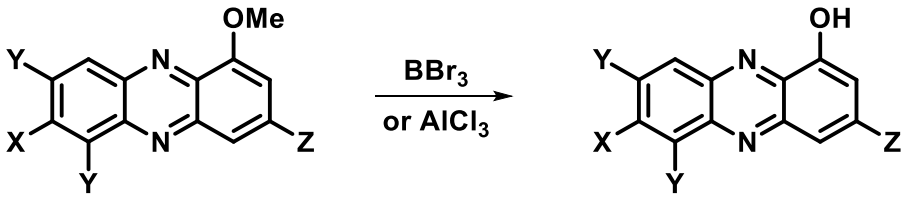
**Yield:** 29%; 145 mg of **29**; yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$):** δ 8.26 (d, *J* = 7.4 Hz, 1H), 8.22 (d, *J* = 7.4 Hz, 1H), 7.94 (d, *J* = 1.2 Hz, 1H), 7.09 (d, *J* = 1.2 Hz, 1H), 4.18 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$):** δ 156.2, 143.8, 140.2, 139.7, 138.2, 135.8, 132.8 (q, *J* = 30.8 Hz), 132.2 (q, *J* = 30.8 Hz), 128.3 (q, *J* = 5.6 Hz), 127.2 (q, *J* = 5.6 Hz), 123.0 (q, *J* = 274.6 Hz), 122.9 (q, *J* = 274.4 Hz), 120.5, 110.8, 57.4.

**HRMS (DART):** calc. for $C_{15}H_8ClF_6N_2O$ $[M+H]^+$: 381.0224, found: 381.0215.

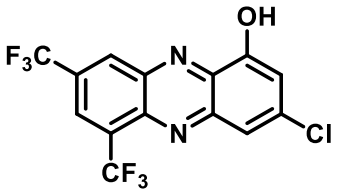
**MP:** 227 - 229 °C.




**7** **30**

**Procedure with $BBr_3$:** A solution of **29** (138 mg, 0.362 mmol) dissolved in anhydrous dichloromethane (3.6 mL) was added to a round bottom flask and cooled to -78 °C before a 1M solution of boron tribromide in dichloromethane (2.17 mL, 2.17 mmol) was added dropwise to the solution. The resulting reaction mixture was then allowed to stir at -78 °C for one hour being warmed to room temperature for 20 hours. After that time, the reaction was further heated to reflux for an additional four hours until complete (as monitored by TLC). Following this, brine (50 mL) was added to the mixture to quench the reaction, and the contents of the resulting biphasic mixture were transferred to a separated funnel and extracted with dichloromethane (3 x 30 mL). The resulting organic layers were then combined, dried with sodium sulfate, filtered, and concentrated *in vacuo*. The resulting solid was purified via column chromatography using 4:1 hexane:dichloromethane to afford 122 mg of **31** (92% yield) as a yellow solid.

**Procedure with $AlCl_3$:** Compound **23** (976 mg, 2.91 mmol) was dissolved in benzene (10 mL) in a round bottom flask before aluminum(III) chloride (2.14 g, 17.4 mmol) was added to the solution. The resulting mixture stirred at room temperature for seven hours until complete (as monitored by TLC). Following this time, the mixture was cooled to 0 °C and cold water (5 mL) was slowly added to quench the reaction. The contents of the resultant biphasic mixture were transferred to a separatory funnel with cold water (50 mL) and extracted using dichloromethane (3 x 30 mL). The organic layers were then combined, dried with sodium sulfate, filtered, and concentrated *in vacuo*. The crude mixture was purified via column chromatography using 9:1 hexane:ethyl acetate to afford 850 mg of **34** as a yellow solid (91% yield).



31

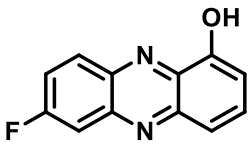
**Yield:** 92%, 122 mg of **31** using $BBr_3$; yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$):** δ 8.28 (d, *J* = 7.5 Hz, 1H), 8.25 (d, *J* = 7.5 Hz, 1H), 8.05 (s, 1H), 7.88 (d, *J* = 1.9 Hz, 1H), 7.30 (d, *J* = 1.9 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$):** δ 152.2, 143.5, 141.0 (2), 136.9, 133.0, 132.5 (q, *J* = 31.1 Hz), 131.9 (q, *J* = 31.1 Hz), 128.4 (q, *J* = 5.5 Hz), 127.7 (q, *J* = 5.5 Hz), 122.9 (q, *J* = 274.4 Hz), 122.8 (q, *J* = 274.4 Hz), 119.5, 113.1. Note: HMBC was used to characterize two carbon signals overlapping at 141.0 ppm (see spectra).

**HRMS (ESI):** calc. for $C_{14}H_4ClF_6N_2O$ $[M-H]^-$: 364.9922, found: 364.9918.

**MP:** 154 - 156 °C.



32

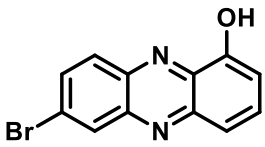
**Yield:** 53%; 78 mg of **32** using $BBr_3$; yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$):** δ 8.22 (dd, *J* = 9.4, 5.9 Hz, 1H), 8.13 (s, 1H), 7.84 (dd, *J* = 9.4, 2.6 Hz, 1H), 7.78 (dd, *J* = 8.7, 7.3 Hz, 1H), 7.74 (d, *J* = 8.7 Hz, 1H), 7.64 (ddd, *J* = 9.8, 7.8, 2.6 Hz, 1H), 7.23 (d, *J* = 7.3 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$):** δ 163.4 (d, *J* = 256.3 Hz), 152.0 (d, *J* = 1.1 Hz), 144.8 (d, *J* = 13.6 Hz), 144.2, 138.8, 134.3 (d, *J* = 2.7 Hz), 132.8 (d, *J* = 0.6 Hz), 131.7 (d, *J* = 10.3 Hz), 122.7 (d, *J* = 28.5 Hz), 119.8, 112.0 (d, *J* = 21.3 Hz), 109.1 (d, *J* = 1.4 Hz).

**HRMS (ESI):** calc. for $C_{12}H_8FN_2O$ $[M+H]^+$: 215.0615, found: 215.0610.

**MP:** 187 - 189 °C.



33

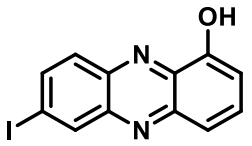
**Yield:** 100%, 102 mg of **33** using $BBr_3$; yellow solid.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.45 (s, 1H), 8.12 (s, 1H), 8.07 (d, *J* = 8.5 Hz, 1H), 7.87 (d, *J* = 8.9 Hz, 1H), 7.83 - 7.71 (m, 2H), 7.25 (d, *J* = 8.5 Hz, 1H). Note: TMS was used as a reference (0.00 ppm) due to the $CHCl_3$ signal being buried in a concentrated NMR sample.

**$^{13}$C NMR (101 MHz, $CDCl_3$):** δ 151.9, 144.5, 144.3, 139.9, 134.8, 134.4, 132.8, 131.9, 130.5, 125.5, 120.2, 109.6.

**HRMS (ESI):** calc. for $C_{12}H_8BrN_2O$ $[M+H]^+$: 276.9795, found: 276.9792.

**MP:** 198 - 200 °C.



34

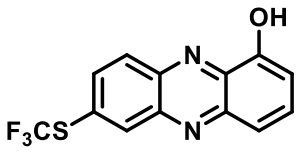
**Yield:** 91%, 230 mg of **34** using $BBr_3$ (91%, 853 mg using $AlCl_3$); yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$):** δ 8.73 (d, *J* = 1.8 Hz, 1H), 8.10 (s, 1H), 8.04 (dd, *J* = 9.1, 1.8 Hz, 1H), 7.93 (d, *J* = 9.1 Hz, 1H), 7.79 (dd, *J* = 8.9, 7.1 Hz, 1H), 7.76 (dd, *J* = 8.9, 1.4 Hz, 1H), 7.25 (m, 1H, partially buried).

**$^{13}$C NMR (151 MHz, $CDCl_3$):** δ 151.9, 144.8, 144.1, 140.2, 139.3, 139.0, 135.0, 132.8, 130.3, 120.3, 109.6, 97.7.

**HRMS (ESI):** calc. for $C_{12}H_8IN_2O$ $[M+H]^+$: 322.9676, found: 322.9672.

**MP:** 196 - 198 °C.




35

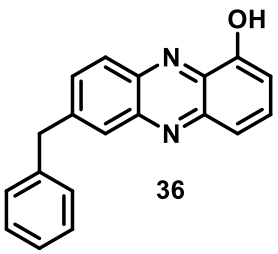
**Yield:** 100%, 54 mg of **35** using $BBr_3$; yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$):** δ 8.63 (d, *J* = 2.0 Hz, 1H), 8.26 (dd, *J* = 9.0, 0.4 Hz, 1H), 8.14 (br. s, 1H), 7.96 (dd, *J* = 9.0, 1.9 Hz, 1H), 7.83 (dd, *J* = 8.9, 7.0 Hz, 1H), 7.80 (dd, *J* = 8.9, 1.6 Hz, 1H), 7.29 (dd, *J* = 7.0, 1.6 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$):** δ 151.9, 144.5, 143.5, 141.1, 137.9, 135.6, 135.2, 133.1, 130.5, 129.5 (q, *J* = 309.0 Hz), 128.2 (q, *J* = 2.1 Hz), 120.3, 110.3.

**HRMS (ESI):** calc. $C_{13}H_8F_3N_2OS$ for $[M+H]^+$: 297.0304, found: 297.0307.

**MP:** 181 - 183 °C.




36

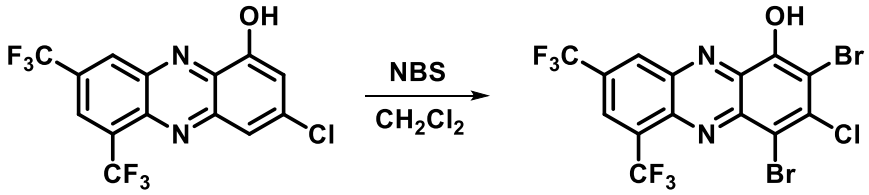
**Yield:** 78%, 71 mg of **36** using $BBr_3$; yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$):** δ 8.20 (br. s, 1H), 7.90 (d, *J* = 8.9 Hz, 1H), 7.87 (s, 1H), 7.64 - 7.55 (m, 2H), 7.49 (dd, *J* = 8.9, 1.7 Hz, 1H), 7.24 - 7.18 (m, 2H), 7.17 - 7.11 (m, 3H), 7.07 (dd, *J* = 6.8, 1.5 Hz, 1H), 4.10 (s, 2H). Note: TMS was used as a reference (0.00 ppm) in this experiment due to the $CHCl_3$ signal being buried by compound **36** protons (concentrated sample).

**$^{13}$C NMR (151 MHz, $CDCl_3$):** δ 151.9, 144.7, 144.3, 143.9, 140.4, 139.4, 134.4, 132.8, 131.9, 129.4, 129.1, 128.9, 128.0, 126.8, 119.9, 108.9, 42.5.

**HRMS (ESI):** calc. $C_{19}H_{15}N_2O$ for $[M+H]^+$: 287.1179, found: 287.1189.

**MP:** 138 - 140 °C.




31 16

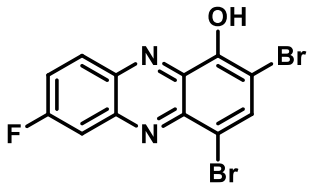
**Procedure.** Compound **31** (86.0 mg, 0.24 mmol) was dissolved in anhydrous dichloromethane (4 mL) in an oven-dried round bottom flask. *N*-bromosuccinimide (85.6 mg, 0.48 mmol) was then added to the solution and the resulting reaction mixture was stirred at room temperature for two hours. Upon completion (monitored by TLC), the reaction mixture was transferred to a separatory funnel containing 10% sodium thiosulfate (15 mL) and the crude product was extracted with dichloromethane (3 x 20 mL). The combined organic layers were dried over sodium sulfate and concentrated *in vacuo*. The resulting crude material was purified via column chromatography with 4:1 hexanes:dichloromethane to afford 113 mg of **16** (92% yield) as a red solid. Note: This bromination procedure was used for the synthesis of other halogenated phenazines used in this study.

**$^1$H NMR (600 MHz, $CDCl_3$):** δ 8.52 (br. s, 1H), 8.36 (d, *J* = 7.5 Hz, 1H), 8.33 (d, *J* = 7.5 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$):** δ 149.8, 141.5, 140.8, 140.1, 137.3, 132.9 (q, *J* = 31.7 Hz), 132.2, 131.6 (q, *J* = 31.5 Hz), 129.1 (q, *J* = 5.4 Hz), 129.0 (q, *J* = 5.4 Hz), 122.7 (q, *J* = 274.4 Hz), 122.6 (q, *J* = 274.5 Hz), 114.9, 108.6.

**HRMS (ESI):** calc. for $C_{14}H_2Br_2ClF_6N_2O$ $[M-H]^-$: 522.8111, found: 522.8103.

**MP:** 171 - 173 °C.




**9**

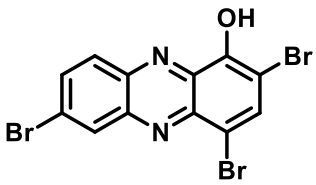
**Yield:** 39%, 41 mg of **9** was isolated as a yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$):** δ 8.42 (s, 1H), 8.29 (dd, *J* = 9.5, 5.8 Hz, 1H), 8.26 (s, 1H), 8.00 (dd, *J* = 9.2, 2.7 Hz, 1H), 7.74 (ddd, *J* = 9.5, 7.8, 2.7 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$):** δ 164.0 (d, *J* = 258.4 Hz), 149.3 (d, *J* = 0.9 Hz), 144.9 (d, *J* = 14.0 Hz), 140.4, 139.1, 138.1, 133.9 (d, *J* = 2.7 Hz), 131.3 (d, *J* = 10.4 Hz), 124.4 (d, *J* = 28.6 Hz), 112.8 (d, *J* = 4.3 Hz), 112.6, 103.3 (d, *J* = 1.4 Hz).

**HRMS (ESI):** calc. $C_{12}H_4Br_2FN_2O$ for $[M-H]^-$: 370.8660, found: 370.8644.

**MP:** 183 - 185 °C.




**11**

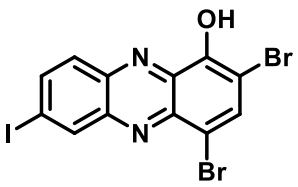
**Yield:** 28%, 15.5 mg of **11** was isolated as a yellow solid.

**$^1$H NMR (500 MHz, $CDCl_3$):** δ 8.64 (d, *J* = 2.1 Hz, 1H), 8.42 (s, 1H), 8.28 (s, 1H), 8.15 (d, *J* = 9.2 Hz, 1H), 7.98 (dd, *J* = 9.2, 2.1 Hz, 1H).

**$^{13}$C NMR (101 MHz, $CDCl_3$):** δ 149.3, 144.3, 140.4, 140.3, 138.1, 136.1, 134.4, 132.4, 130.1, 126.7, 113.2, 103.8.

**HRMS (ESI):** calc. $C_{12}H_4Br_3N_2O$ for $[M-H]^-$: 430.7843, found: 430.7840.

**MP:** 234 - 236 °C.




**12**

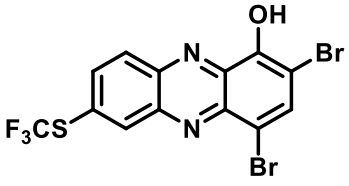
**Yield:** 62%, 74 mg of **12** was isolated as a yellow solid.

**$^1$H NMR (600 MHz, DMSO-*$d_6$*):** δ 11.61 (s, 1H), 8.77 (d, *J* = 1.8 Hz, 1H), 8.45 (s, 1H), 8.25 (dd, *J* = 9.1, 1.8 Hz, 1H), 8.09 (d, *J* = 9.1 Hz, 1H).

**$^{13}$C NMR (151 MHz, DMSO-*$d_6$*):** δ 151.0, 143.2, 140.3, 140.3, 139.6, 137.8, 137.5, 135.6, 130.2, 111.4, 104.9, 100.4.

**HRMS (ESI):** calc. $C_{12}H_4Br_2IN_2O$ for $[M-H]^-$: 478.7721, found: 478.7740.

**MP:** 236 - 238 °C.




**13**

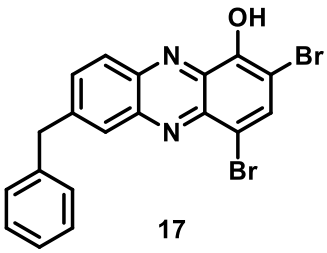
**Yield:** 93%, 270 mg of **13** was isolated as a yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$):** δ 8.76 (d, *J* = 1.8 Hz, 1H), 8.43 (s, 1H), 8.30 (d, *J* = 9.1 Hz, 1H), 8.29 (s, 1H), 8.05 (dd, *J* = 9.1, 1.8 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$):** δ 149.2, 143.4, 141.4, 140.6, 138.3, 138.1, 136.6, 135.1, 130.1, 129.4 (q, *J* = 2.2 Hz), 129.4 (q, *J* = 309.3 Hz), 113.4, 104.7.

**HRMS (ESI):** calc. $C_{13}H_4Br_2F_3N_2OS$ for $[M-H]^-$: 452.8348, found: 452.8362.

**MP:** 181 - 183 °C.




**17**

**Yield:** 70%, 76 mg of **17** was isolated as a yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$):** δ 8.49 (br. s, 1H), 8.22 (s, 1H), 8.18 (d, *J* = 0.8 Hz, 1H), 8.14 (d, *J* = 8.9 Hz, 1H), 7.75 (dd, *J* = 8.9, 1.8 Hz, 1H), 7.36 - 7.32 (m, 2H), 7.30 - 7.24 (m, 3H, partially buried), 4.27 (s, 2H).

**$^{13}$C NMR (151 MHz, $CDCl_3$):** δ 149.3, 145.9, 144.4, 140.7, 140.1, 139.2, 137.2, 134.6, 134.0, 129.4, 129.1, 128.8, 128.6, 127.0, 113.0, 102.9, 42.6.

**HRMS (ESI):** calc. $C_{19}H_{13}Br_2N_2O$ for $[M+H]^+$: 444.9370, found: 444.9377.

**MP:** 189 - 191 °C.

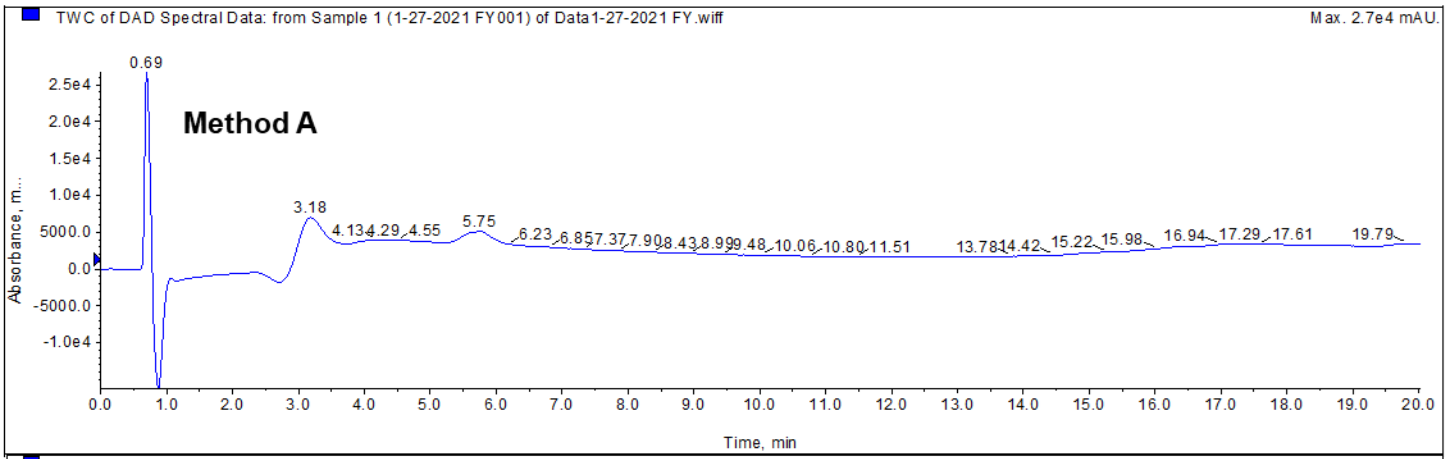
**13.) Compound Purity Analysis Using LC-MS.**

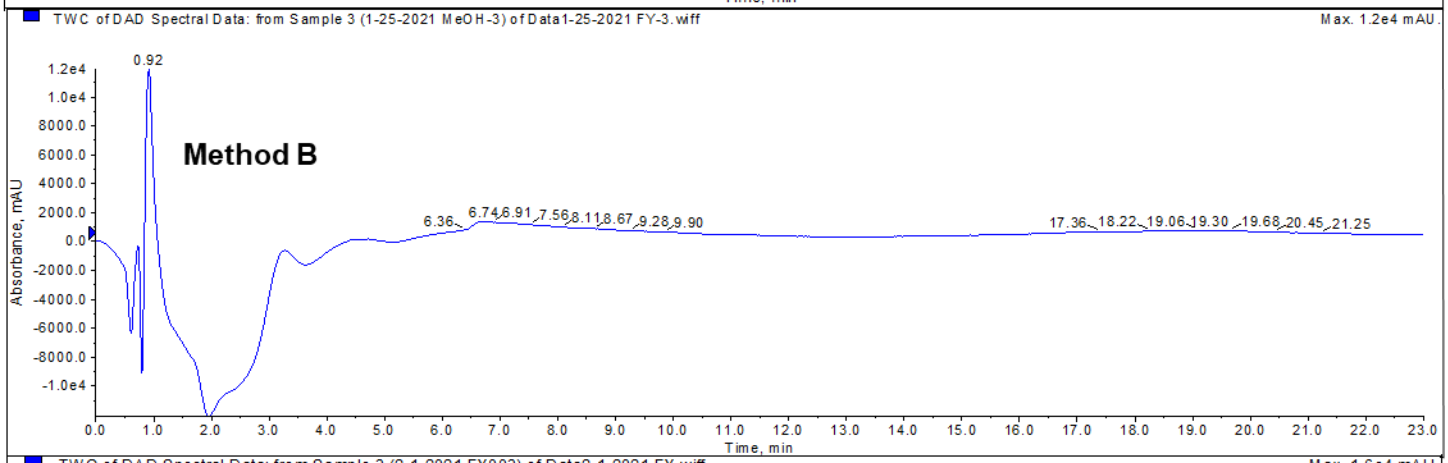
Select compounds evaluated in biological assays were determined to be ≥ 95% pure via LC-MS using a Shimadzu Prominence HPLC system, AB Sciex 3200 QTRAP spectrometer and a Kinetex C18 column (50 mm × 2.1 mm × 2.6 µm) with acetonitrile (B) and water (A) in 0.1% formic acid at a flow rate of 0.25 mL/minutes. Each LC-MS experiment was carried out with corresponding LC method. A blank methanol run was used to remove background noise from the purity assessment for each compound. The purity range for these test compounds was determined to be 94.9 - 99.9% pure, based on LC-MS results.

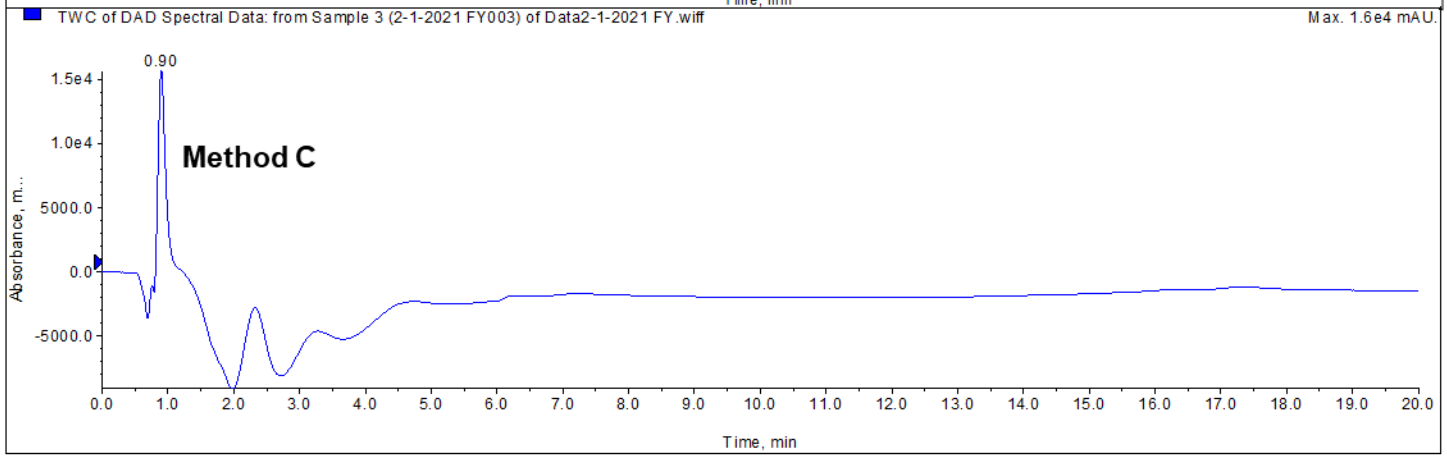
LC method **A**: Ramp up from 10% to 60% of B over 14 minutes, staying at 60% B for 5 minutes, ramp down to 10% of B over 1 minute.

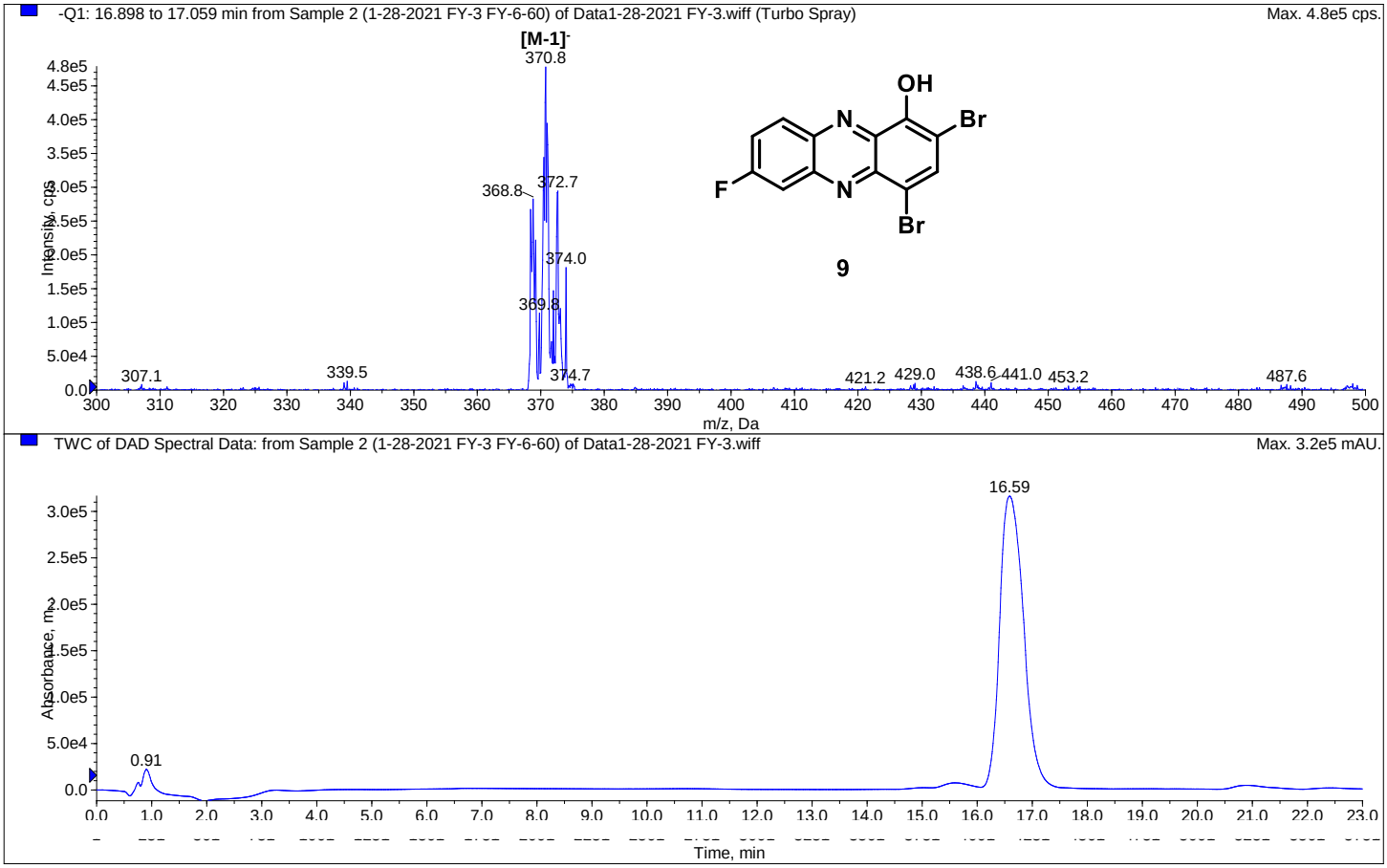
LC method **B**: Ramp up from 10% to 50% of B over 15 minutes, staying at 50% B for 6 minutes, ramp down to 10% of B over 2 minutes.

LC method **C**: Ramp up from 10% to 55% of B over 14 minutes, staying at 55% B for 5 minutes, ramp down to 10% of B over 1 minute.


TWC of DAD Spectral Data: from Sample 1 (1-27-2021 FY001) of Data1-27-2021 FY.wiff
Max. 2.7e4 mAU.
Method A
Absorbance, m...
Time, min

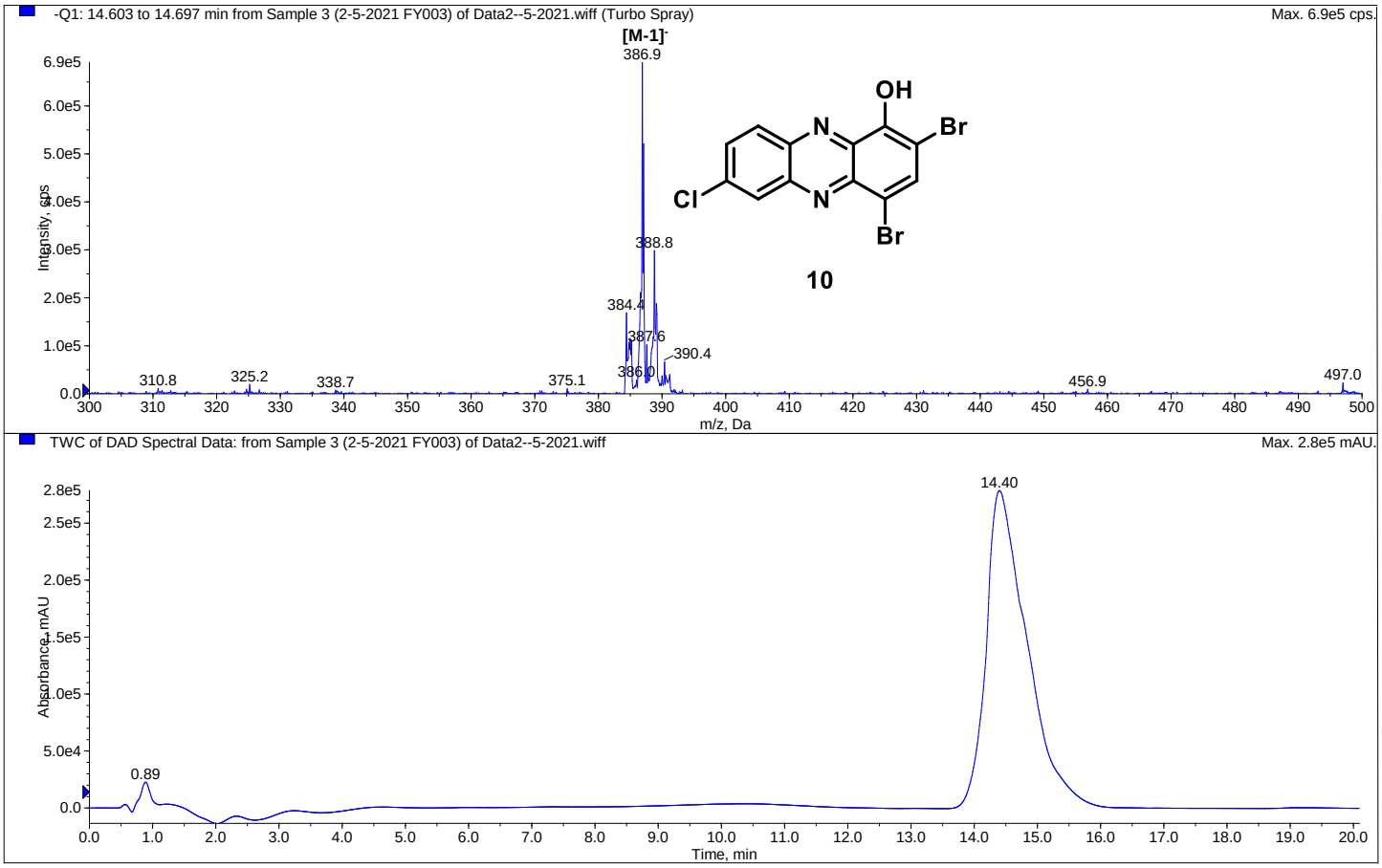

TWC of DAD Spectral Data: from Sample 3 (1-25-2021 MeOH-3) of Data1-25-2021 FY-3.wiff
Max. 1.2e4 mAU.
Method B
Absorbance, mAU
Time, min


TWC of DAD Spectral Data: from Sample 3 (2-1-2021 FY003) of Data2-1-2021 FY.wiff
Max. 1.6e4 mAU.
Method C
Absorbance, m...
Time, min



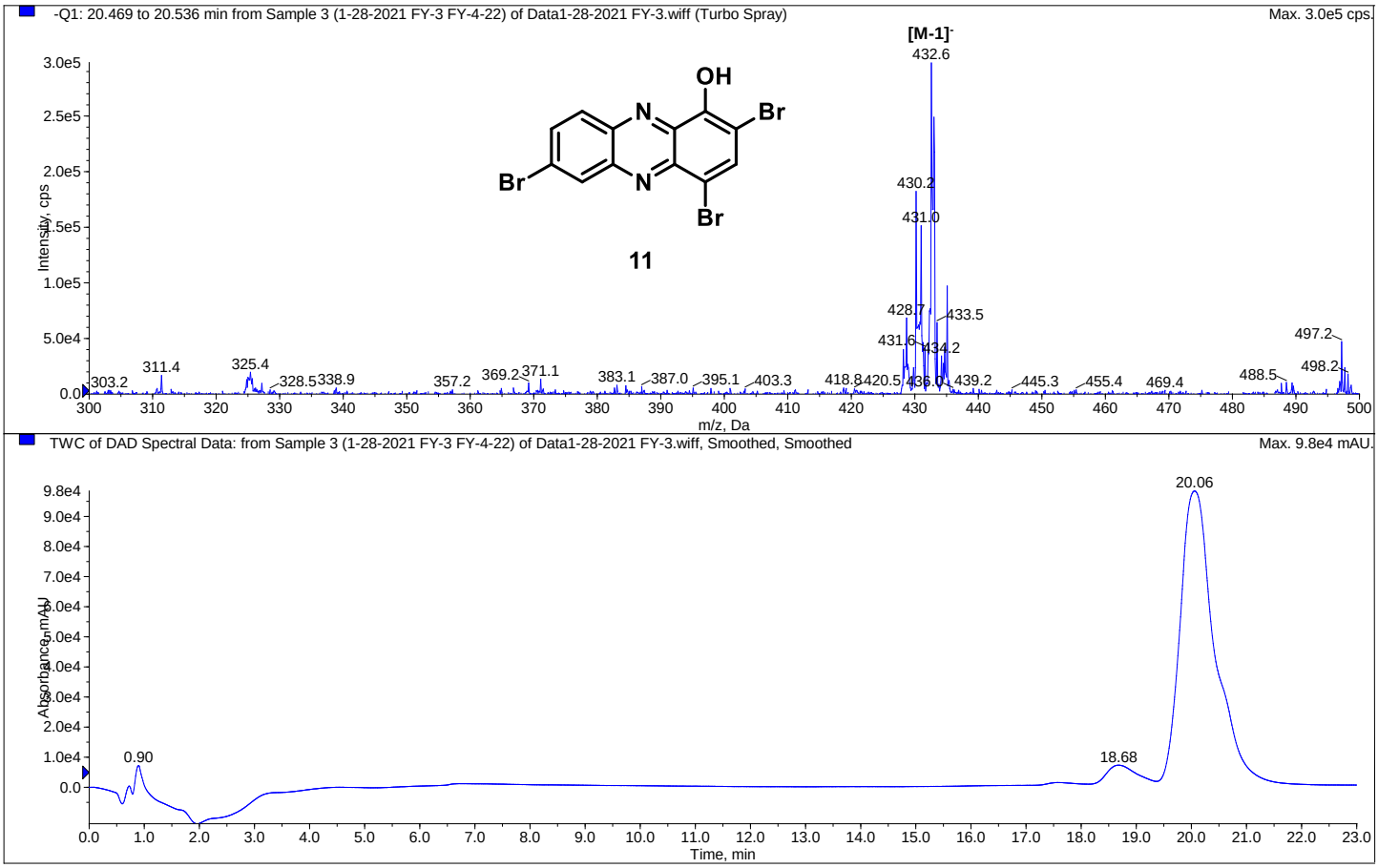

LC Method **B**; **MS (ESI):** found for $C_{12}H_4Br_2FN_2O$ for $[M-H]^-$: 370.8

| Retention Time (Min) | Peak Area |
|---|---|
| 15.6 | 143230 |
| 16.59 (**9**) | 9399000 |
| 19.16 | 2333 |
| 20.91 | 16040 |
| **Sum of Area** | 9560603 |
| **% Purity** | **98.3%** |



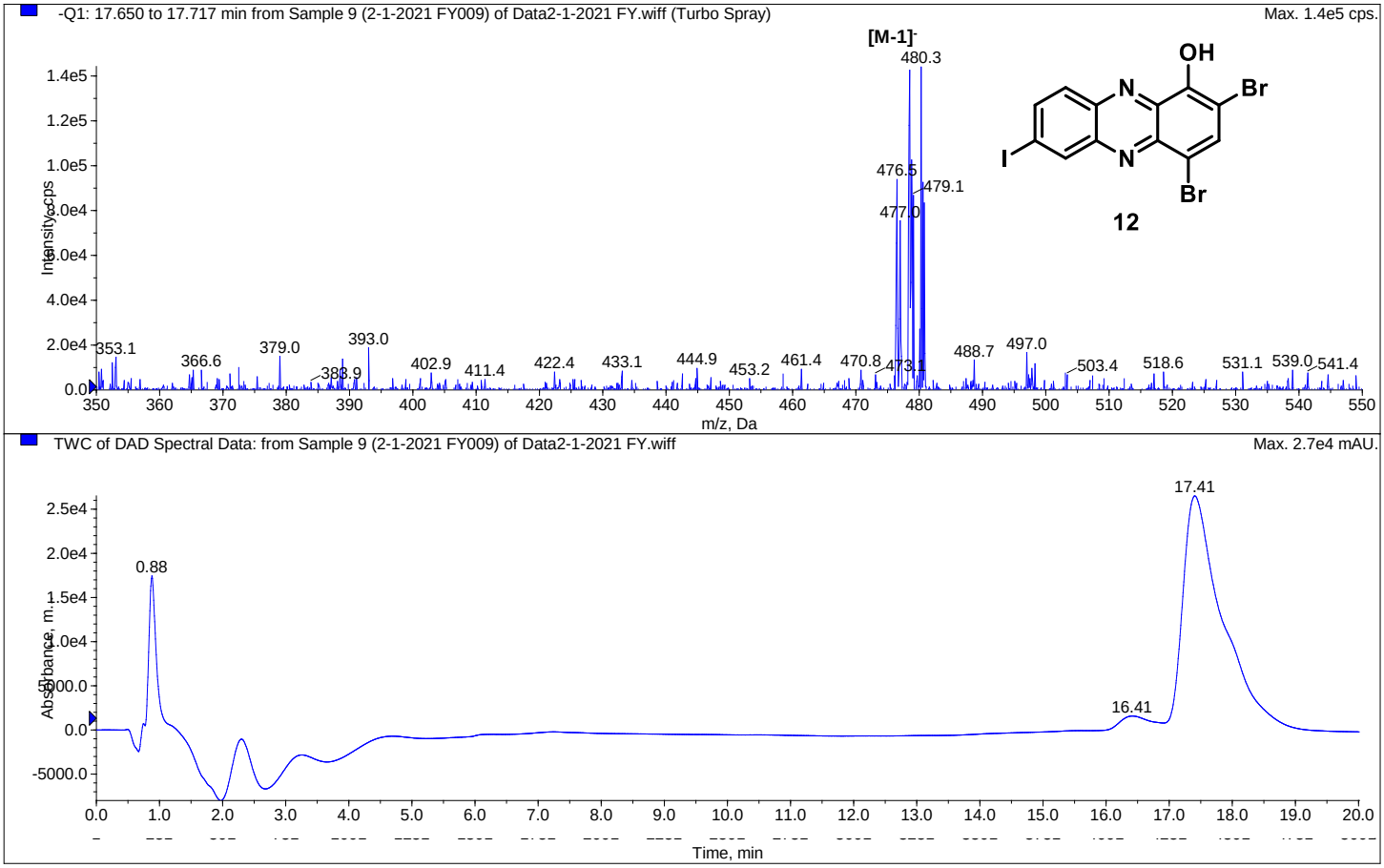

LC Method **A**; **MS (ESI):** found for $C_{12}H_4Br_2ClN_2O$ for $[M-H]^-$: 386.9

| Retention Time (Min) | Peak Area |
|---|---|
| 10.36 | 109305 |
| 14.40 (**10**) | 12475000 |
| 19.40 | 18233 |
| **Sum of Area** | 12602538 |
| **% Purity** | **99.0%** |



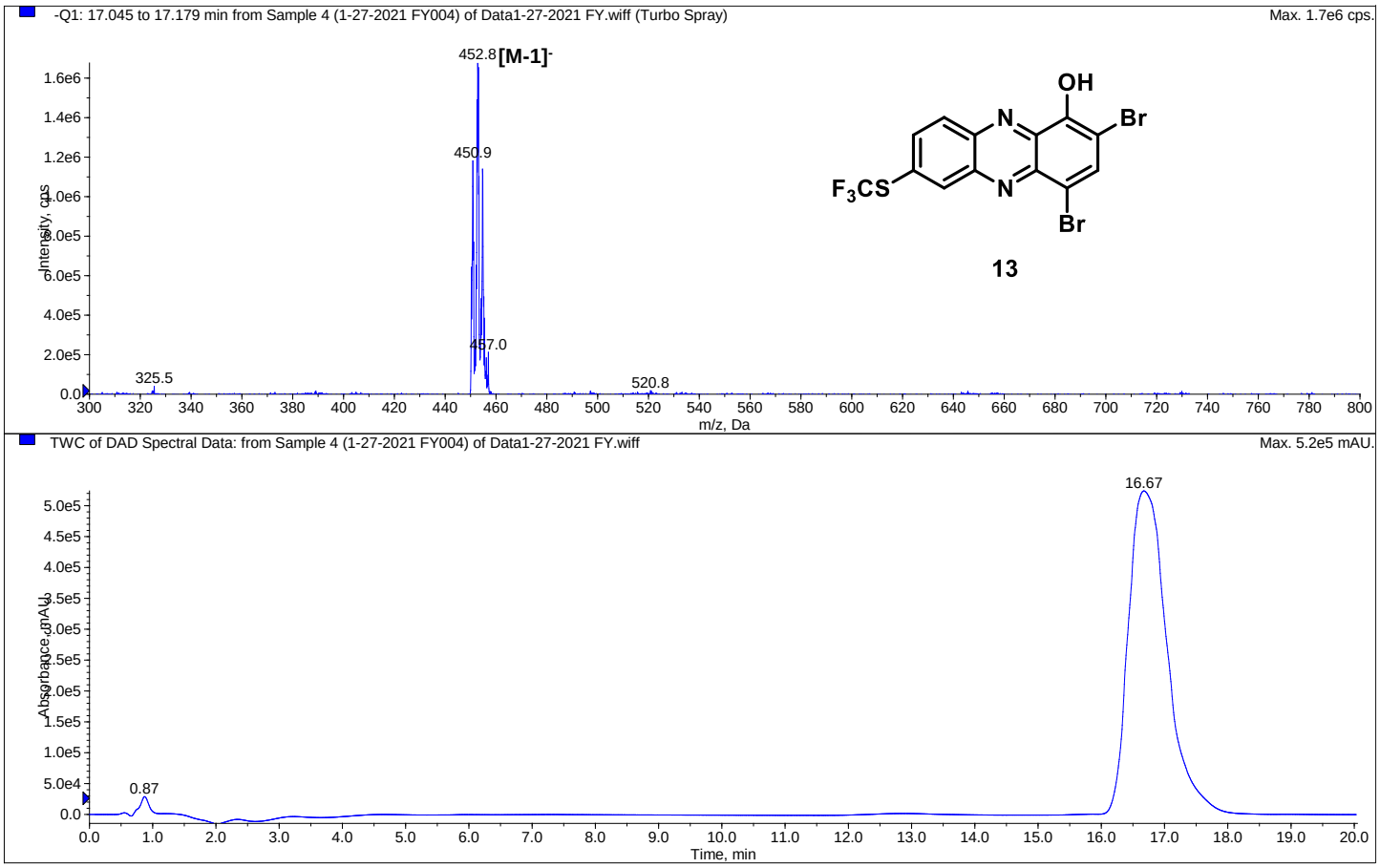

LC Method **B**; **MS (ESI):** found for $C_{12}H_4Br_3N_2O$ for $[M-H]^-$: 432.6

| Retention Time (Min) | Peak Area |
|---|---|
| 17.57 | 21441 |
| 18.68 | 202240 |
| 20.06 (**11**) | 4160100 |
| **Sum of Area** | 4383781 |
| **% Purity** | **94.9%** |



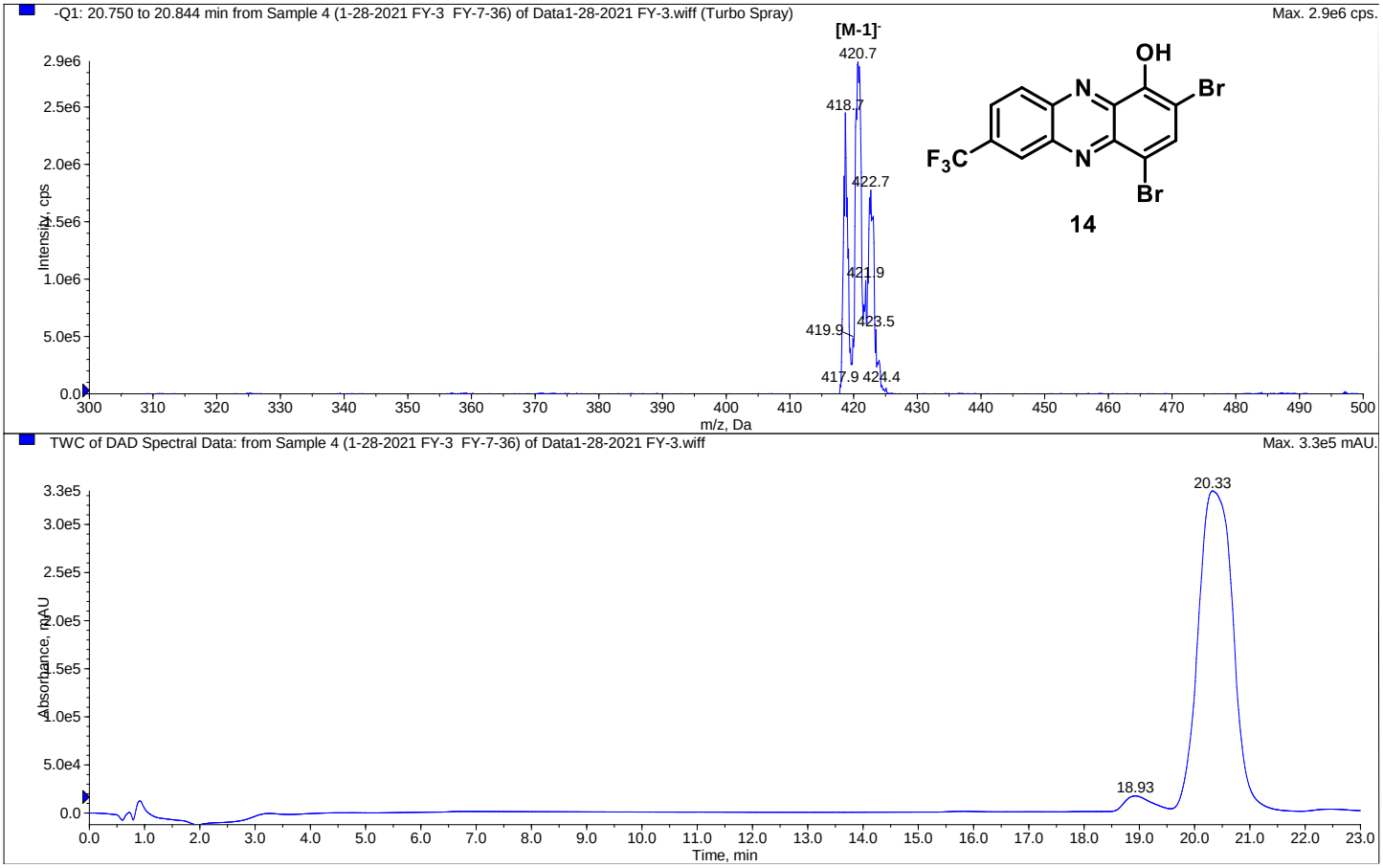

LC Method **C**; **MS (ESI):** found for $C_{12}H_4Br_2IN_2O$ for [M-H]: 480.3

| Retention Time (Min) | Peak Area |
|---|---|
| 16.41 | 33052 |
| 17.41 (**12**) | 1102800 |
| **Sum of Area** | 1135852 |
| **% Purity** | **97.1%** |



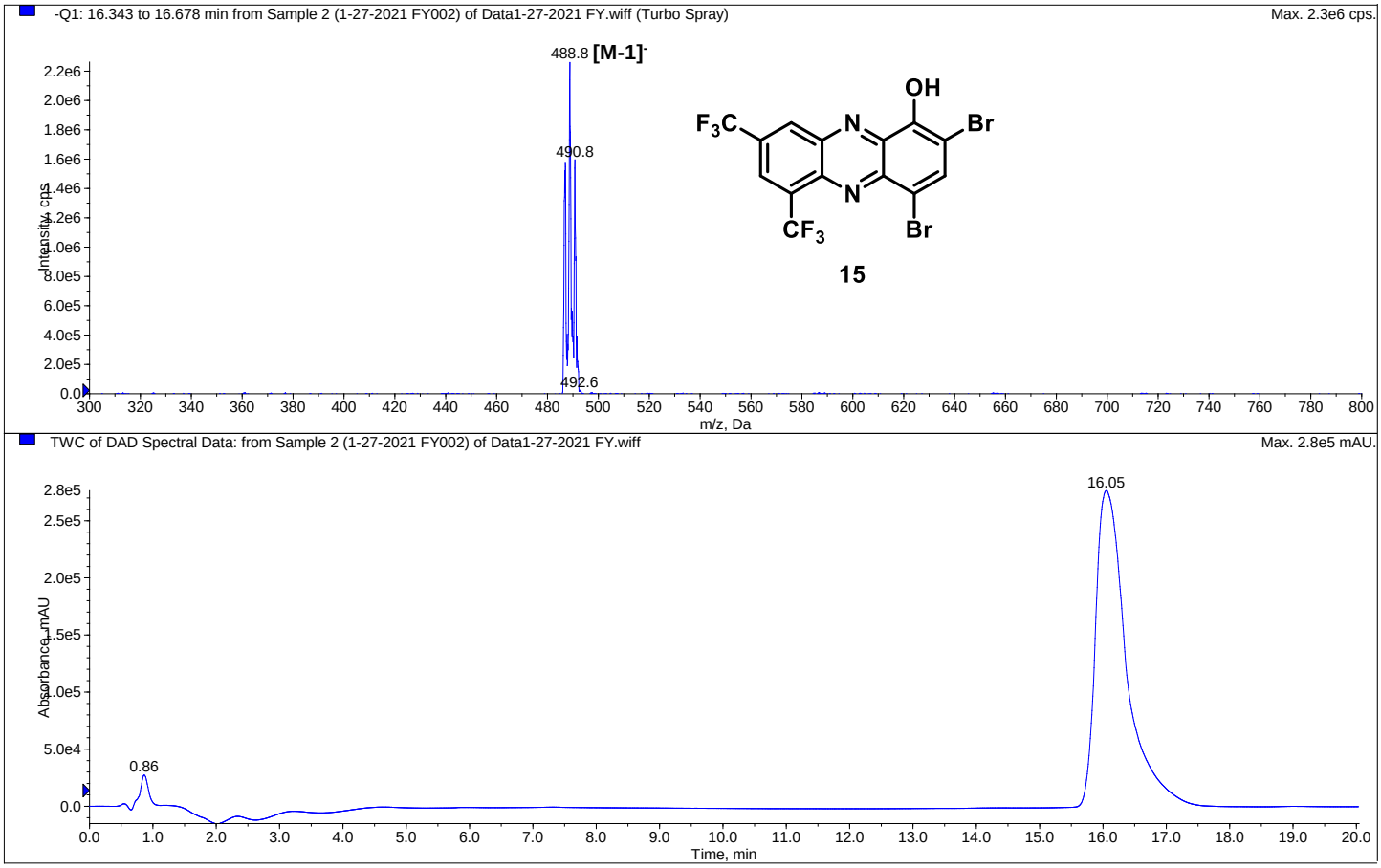

LC Method **A**; **MS (ESI):** found for $C_{13}H_4Br_2F_3N_2OS$ $[M-H]^-$: 452.8

| Retention Time (Min) | Peak Area |
|---|---|
| 12.87 | 90860 |
| 15.87 | 5594 |
| 16.67 (**13**) | 22171000 |
| **Sum of Area** | 22267454 |
| **% Purity** | **99.6%** |



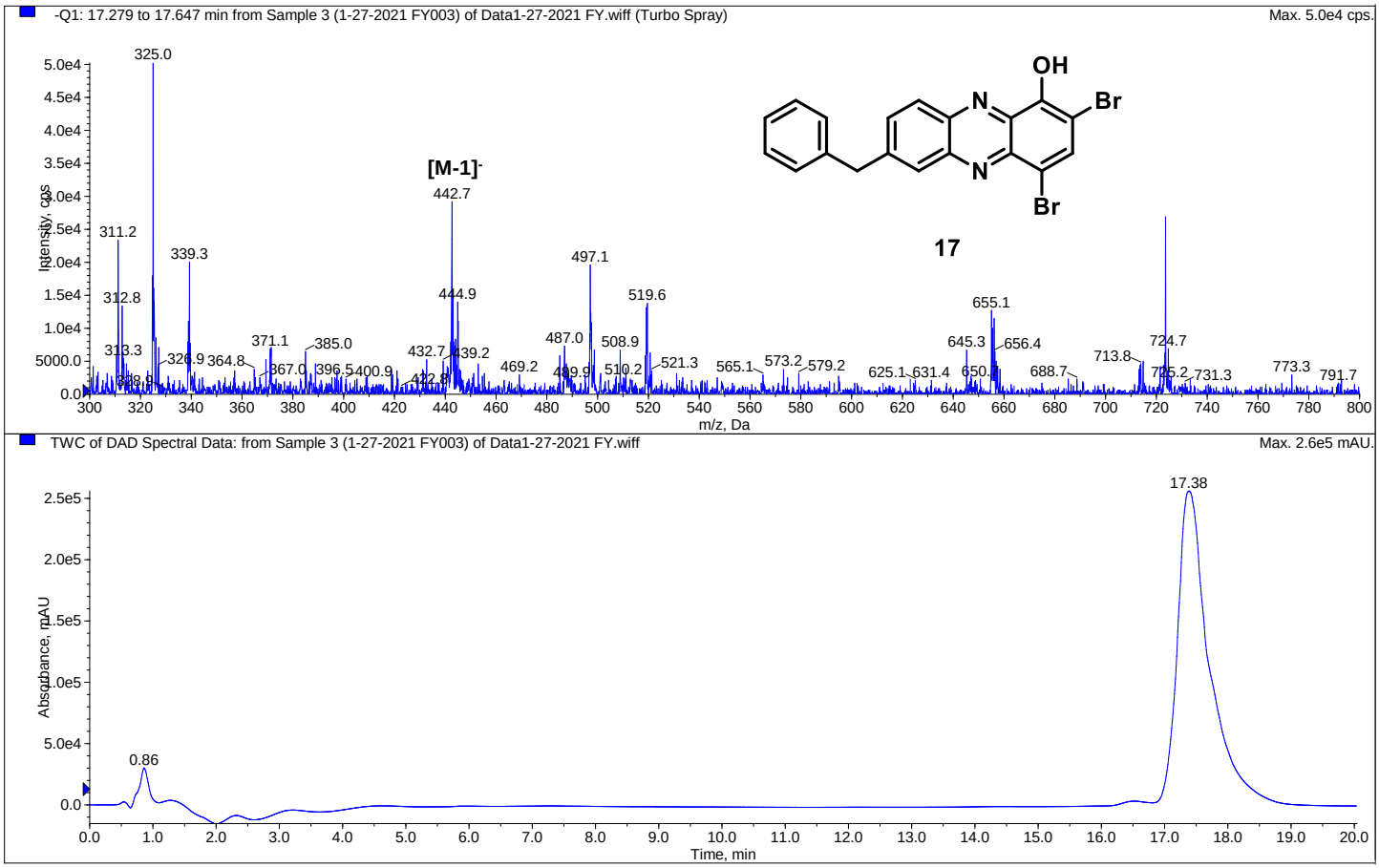

LC Method **B**; **MS (ESI):** found for $C_{13}H_4Br_2F_3N_2O$ $[M-H]^-$: 420.7

| Retention Time (Min) | Peak Area |
|---|---|
| 15.81 | 20849 |
| 18.93 | 468290 |
| 20.33 (**14**) | 14337000 |
| **Sum of Area** | 14826139 |
| **% Purity** | **96.7%** |




LC Method **A**; **MS (ESI):** found for $C_{14}H_3Br_2F_6N_2O$ $[M-H]^-$: 488.8

| Retention Time (Min) | Peak Area |
|---|---|
| 7.34 | 7552 |
| 16.05 (**15**) | 9358000 |
| 19.12 | 4299 |
| **Sum of Area** | 9369851 |
| **% Purity** | **99.9%** |




LC Method **A**; **MS (ESI):** found for $C_{19}H_{13}Br_2N_2O$ $[M-H]^-$: 442.7

| Retention Time (Min) | Peak Area |
|---|---|
| 7.35 | 2816 |
| 16.52 | 48675 |
| 17.38 (**17**) | 8835600 |
| **Sum of Area** | 8887091 |
| **% Purity** | **99.4%** |

**14.) Literature References.**

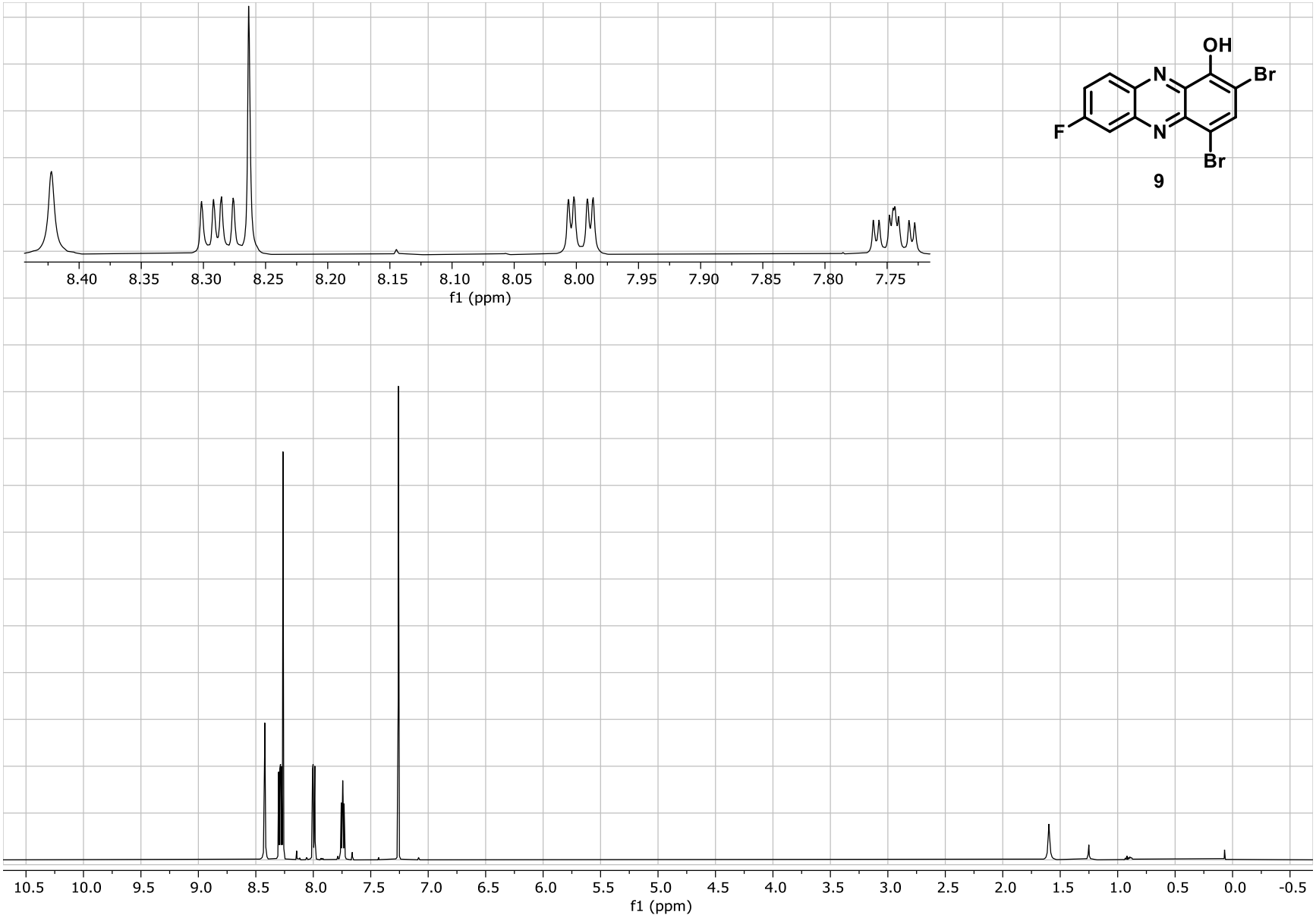
1) Kwast, A.; Stachowska, K.; Trawczyński, A.; Wróbel, Z. *N*-Aryl-2-Nitrosoanilines as Intermediates in the Synthesis of Substituted Phenazines from Nitroarenes. *Tetrahedron Lett.* **2011**, *52*, 6484-6488.

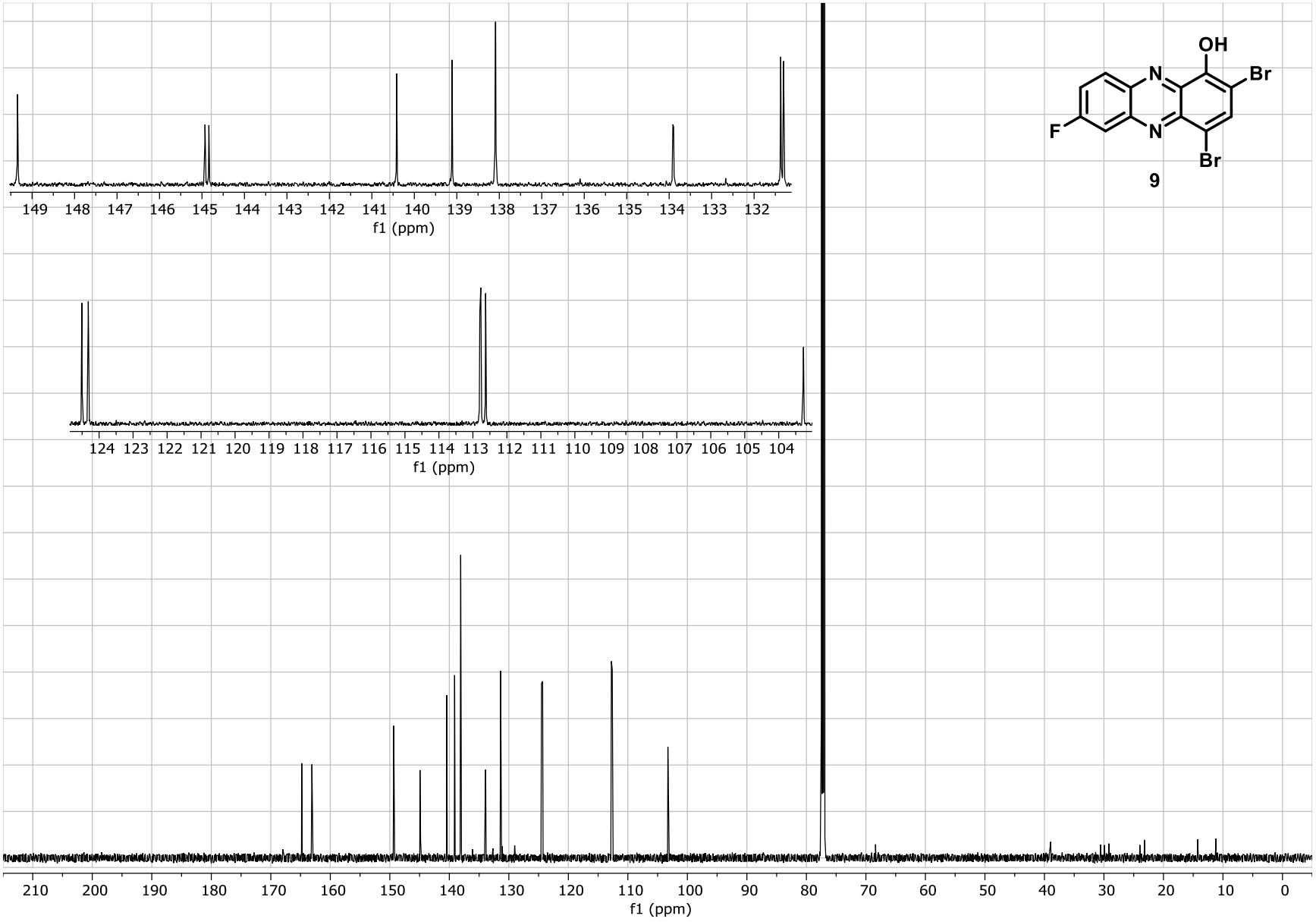
2) Wróbel, Z.; Plichta, K.; Kwast, A. Reactivity and Substituent Effects in the Cyclization of *N*-Aryl-2-Nitrosoanilines to Phenazines. *Tetrahedron* **2017**, *73*, 3147-3152.

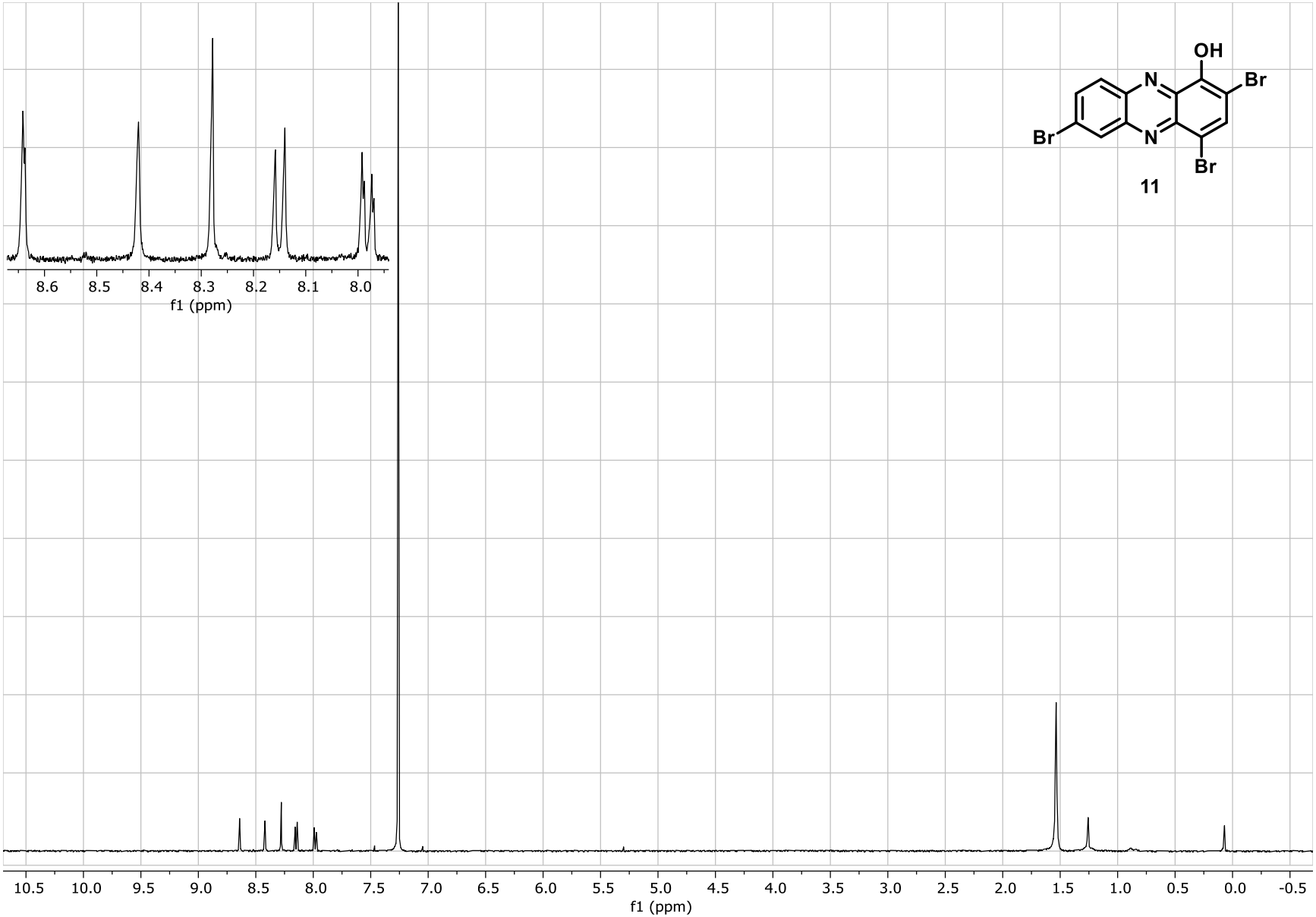
3) Liu, K.; Xiao, T.; Yang, H.; Chen, M.; Gao, Q.; Brummel, B. R.; Ding, Y.; Huigens III, R. W. Design, Synthesis and Evaluation of Halogenated Phenazine Antibacterial Prodrugs Targeting Nitroreductase Enzymes for Activation. *RSC Med. Chem.* **2023**, *14*, 1472-1481.

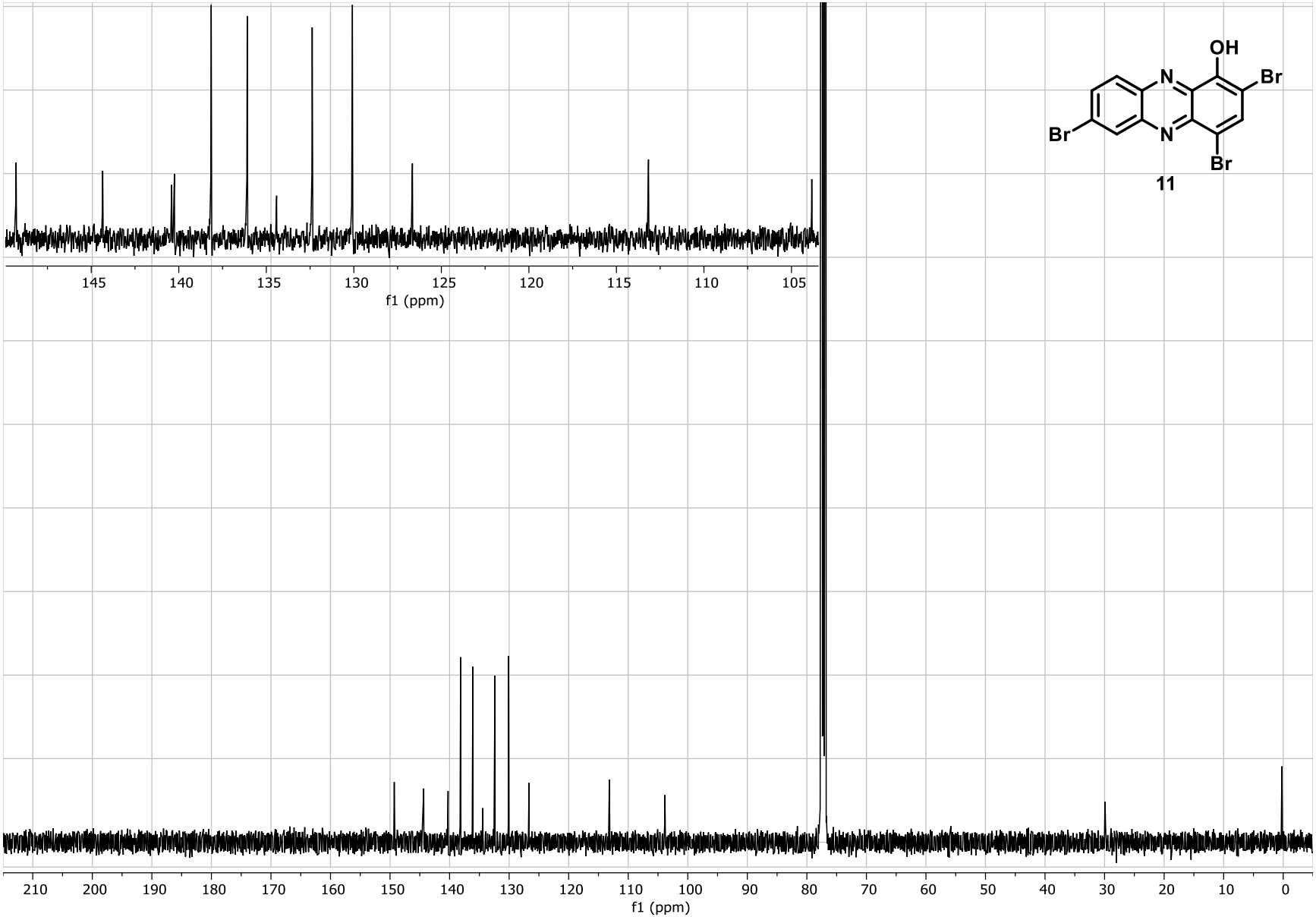
**15.) NMR Spectra.**

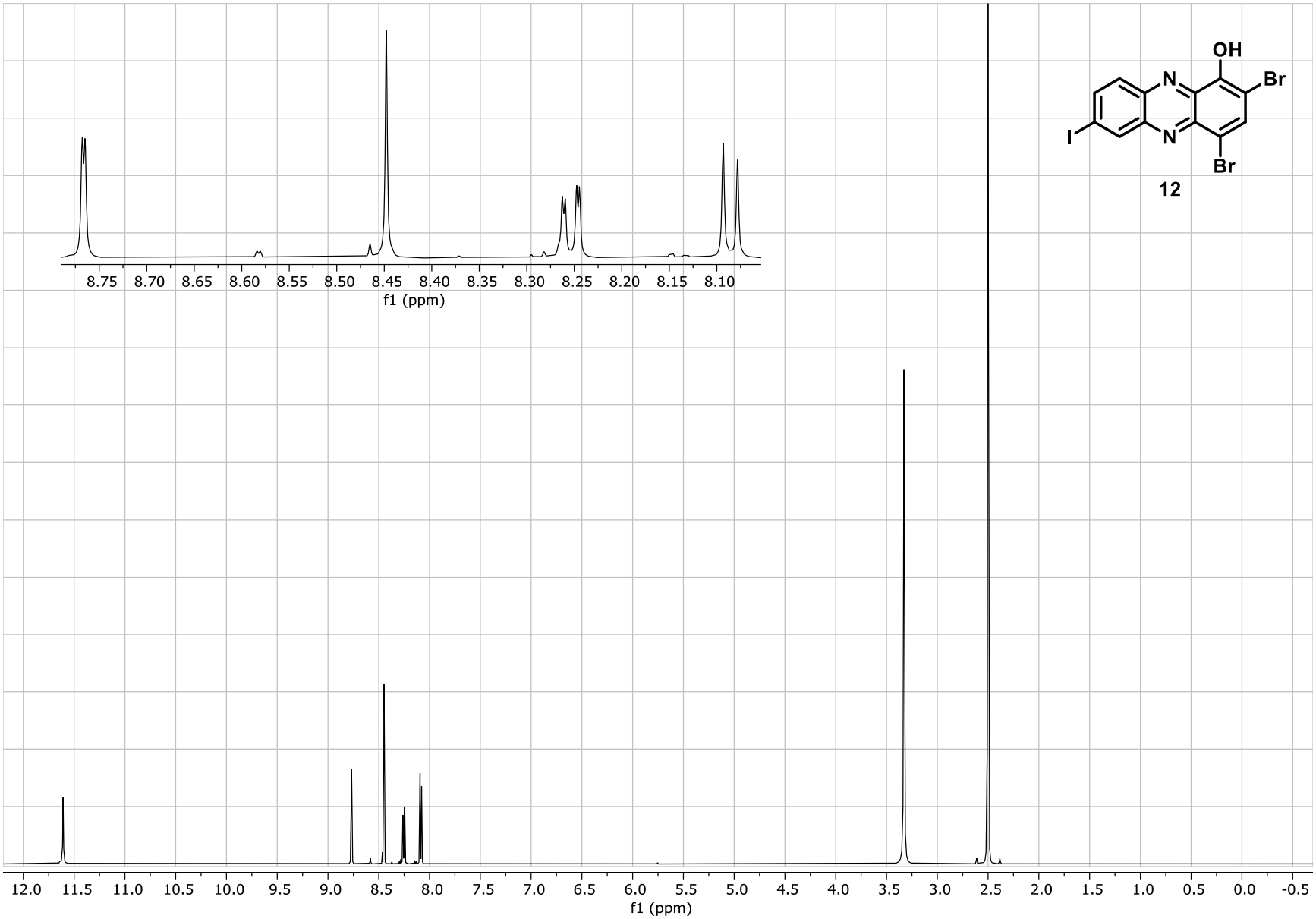
NMR spectra for all new compounds synthesized during these studies are presented on the following pages, including $^{1}H$ NMR, $^{13}C$ NMR, and 2-D NMRs (HSQC & HMBC for **31**).

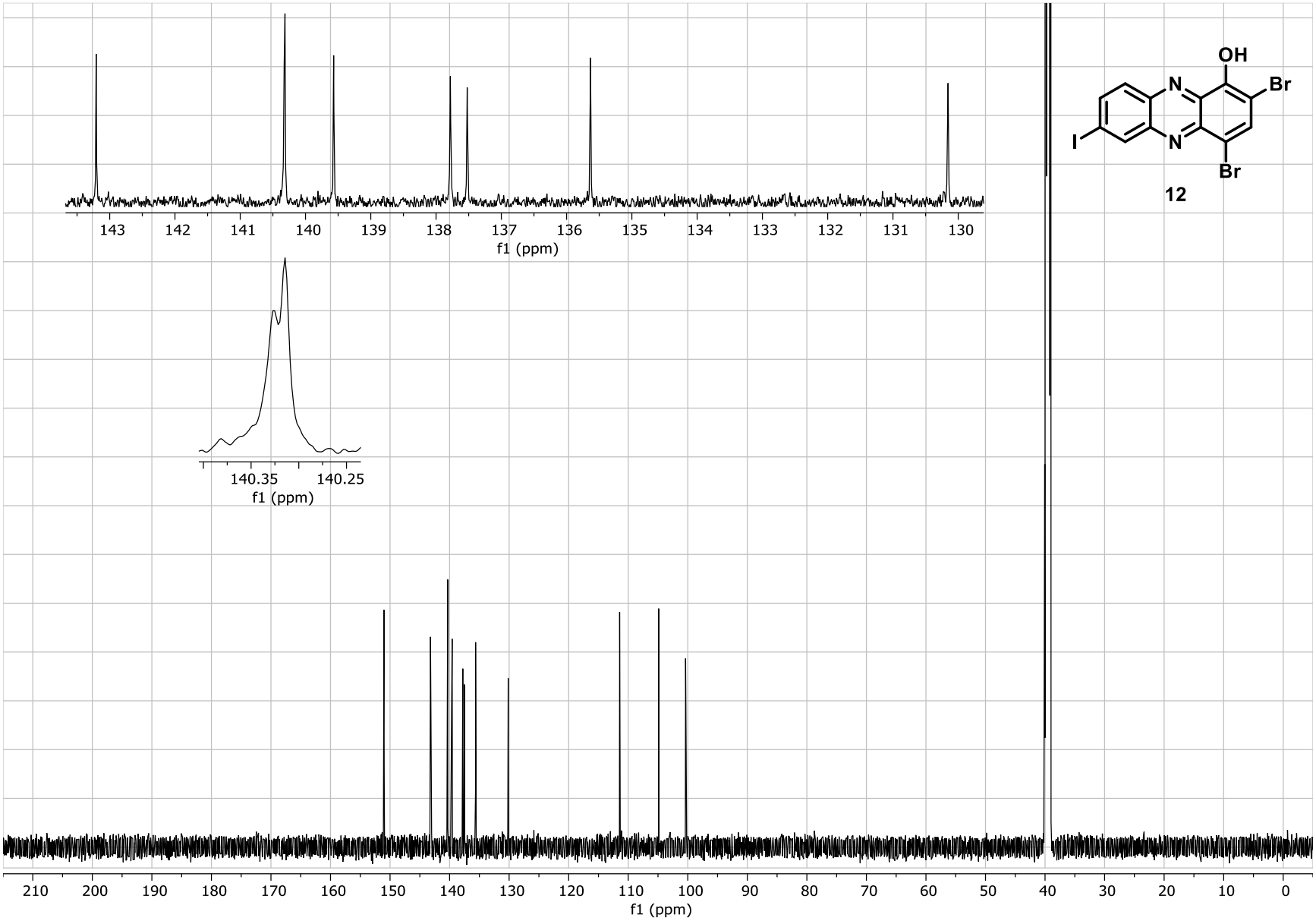

OH
Br
N
F
N
Br
9
8.40
8.35
8.30
8.25
8.20
8.15
8.10
8.05
8.00
7.95
7.90
7.85
7.80
7.75
f1 (ppm)
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

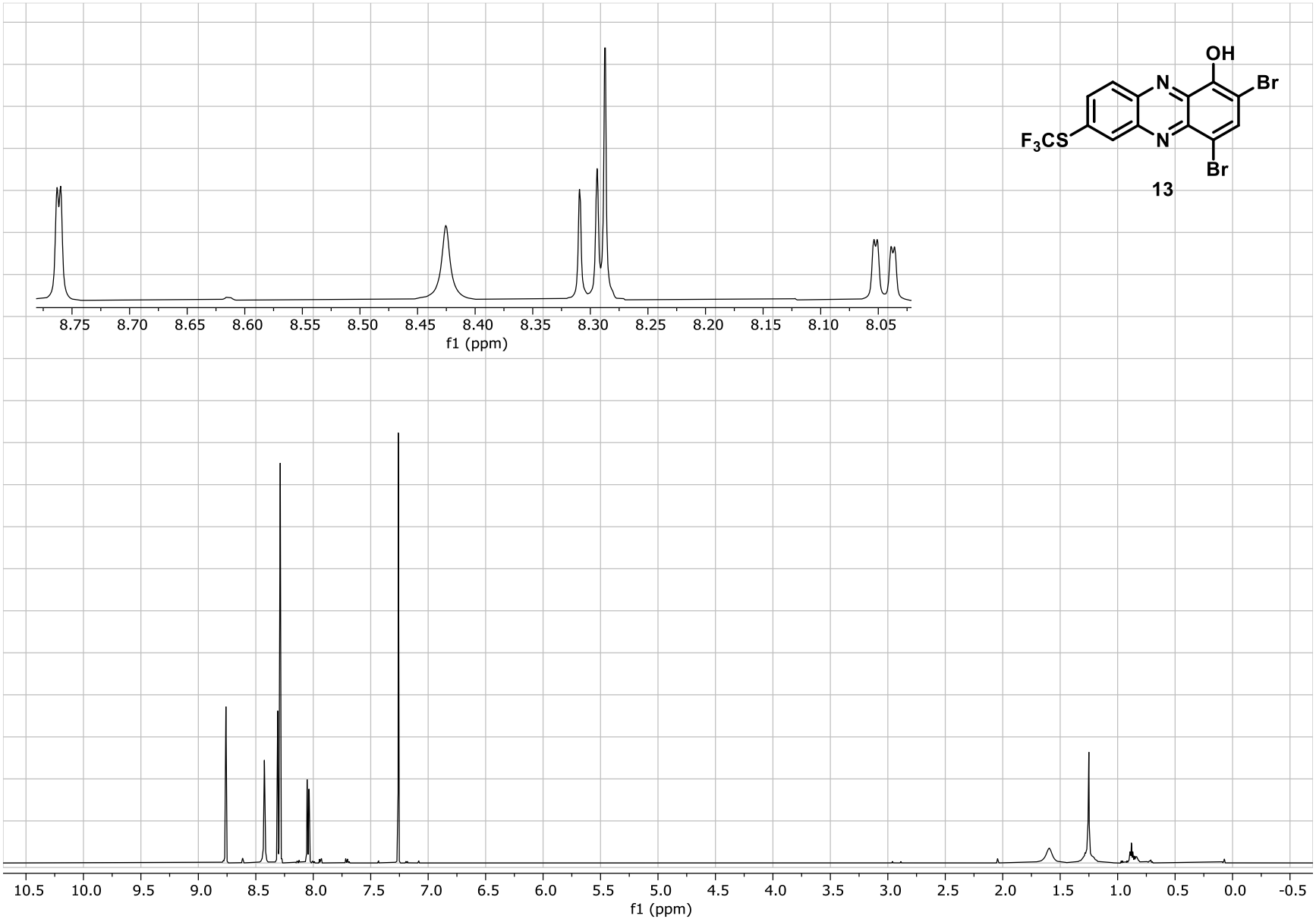

OH
Br
F
N
N
Br
9
149 148 147 146 145 144 143 142 141 140 139 138 137 136 135 134 133 132
f1 (ppm)
124 123 122 121 120 119 118 117 116 115 114 113 112 111 110 109 108 107 106 105 104
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

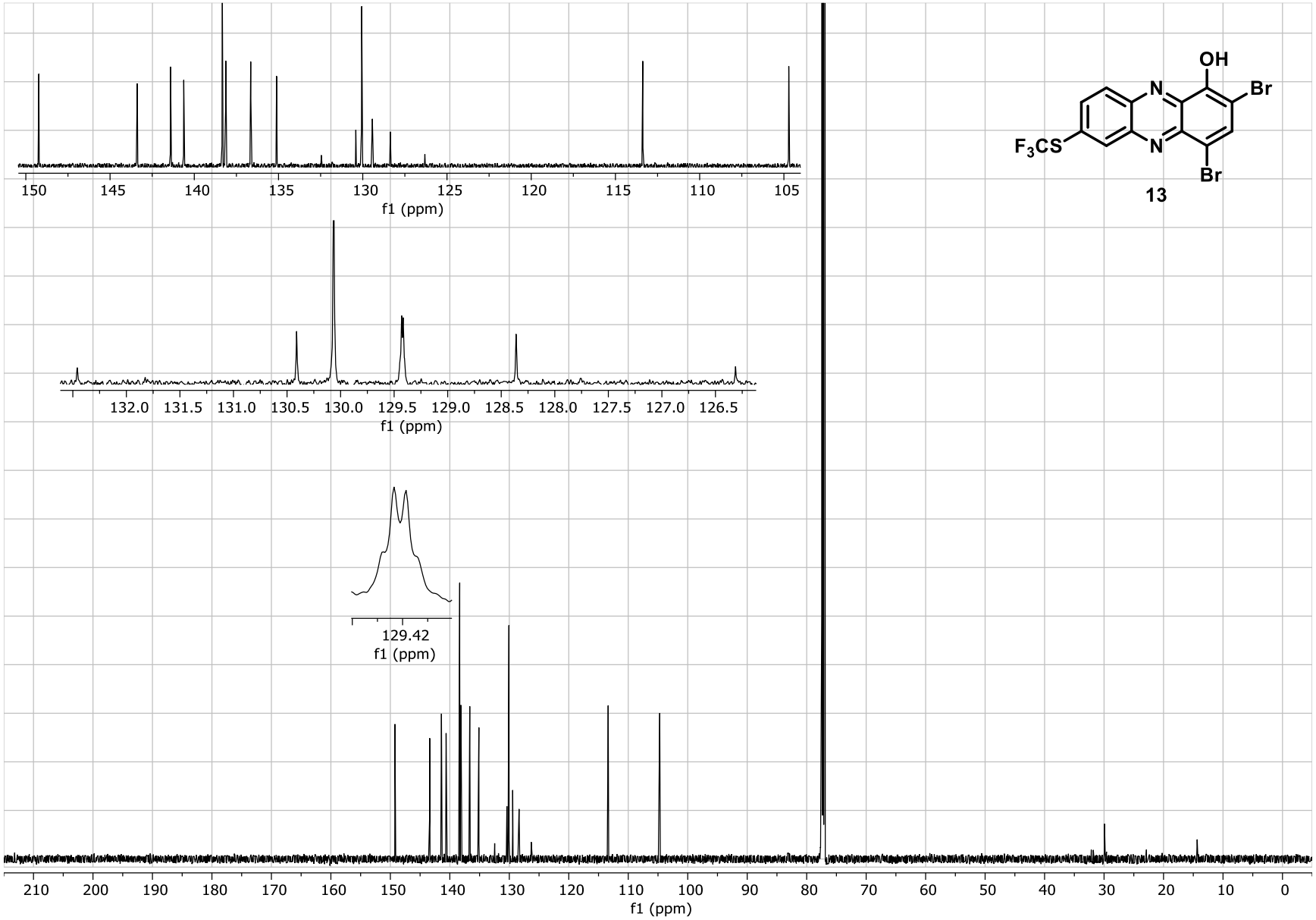

OH
Br
N
N
Br
Br
11
8.6
8.5
8.4
8.3
8.2
8.1
8.0
f1 (ppm)
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

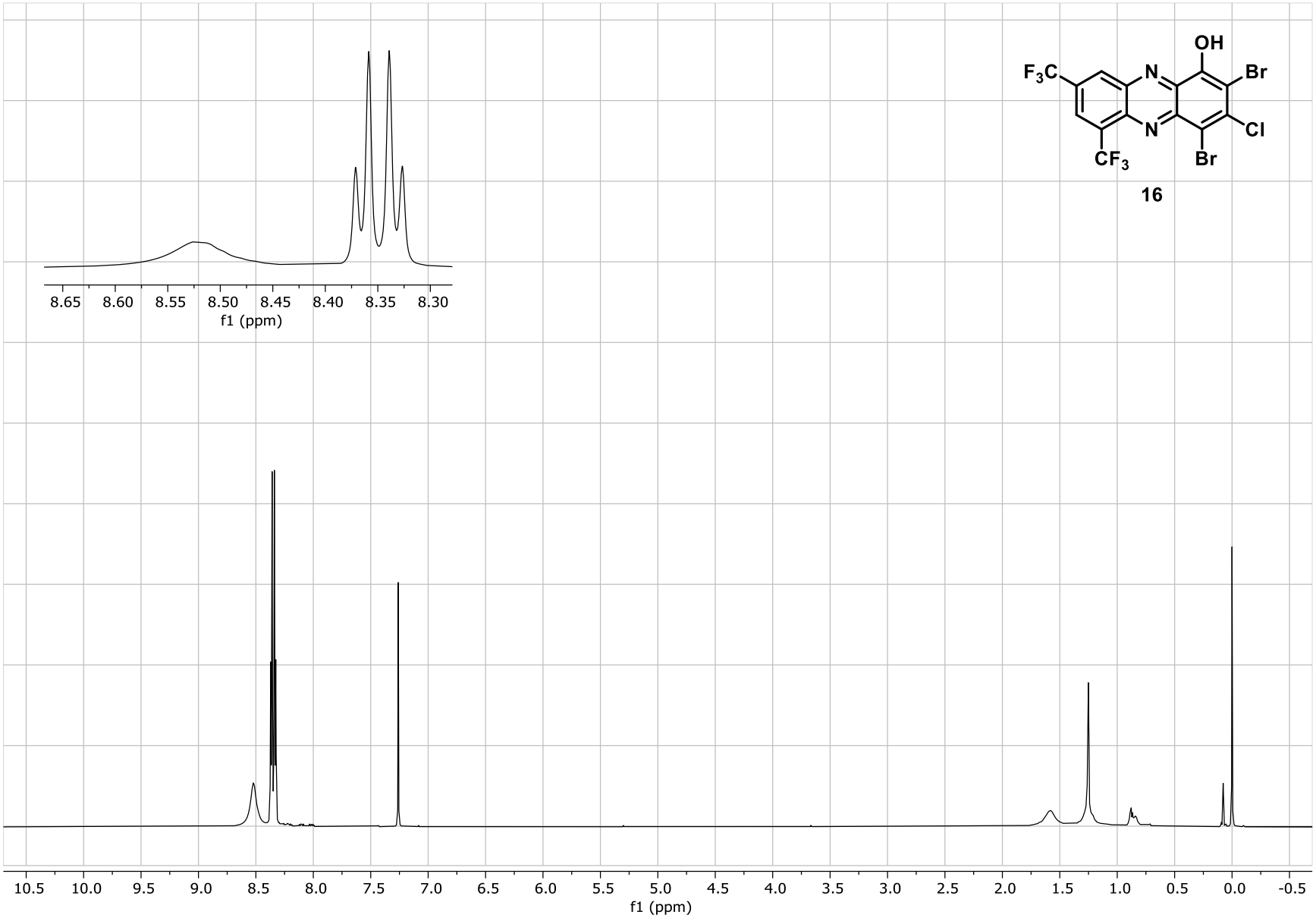

OH
Br
Br
N
N
Br
11
145
140
135
130
125
120
115
110
105
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

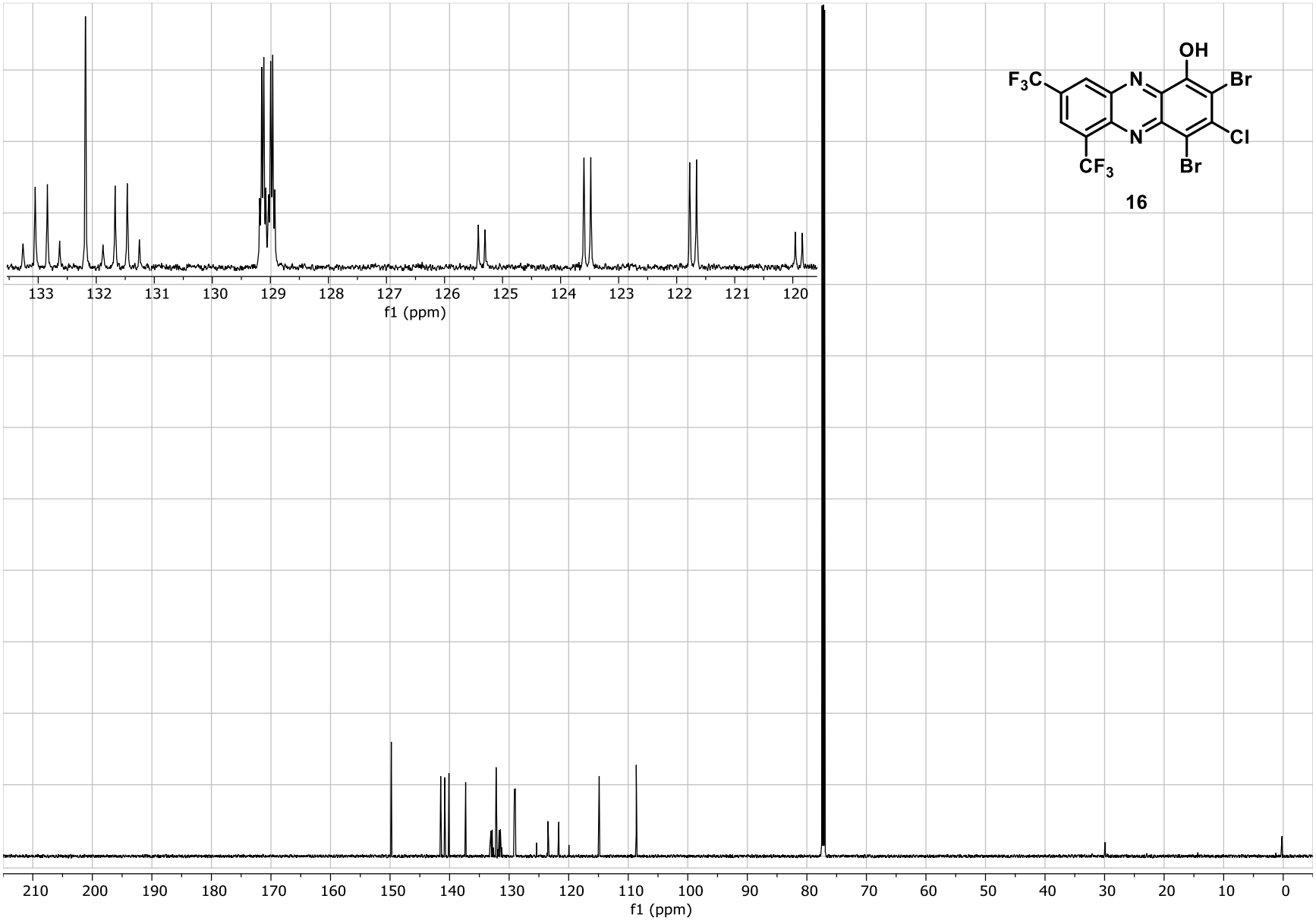

OH
Br
N
N
I
Br
12
8.75 8.70 8.65 8.60 8.55 8.50 8.45 8.40 8.35 8.30 8.25 8.20 8.15 8.10
f1 (ppm)
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

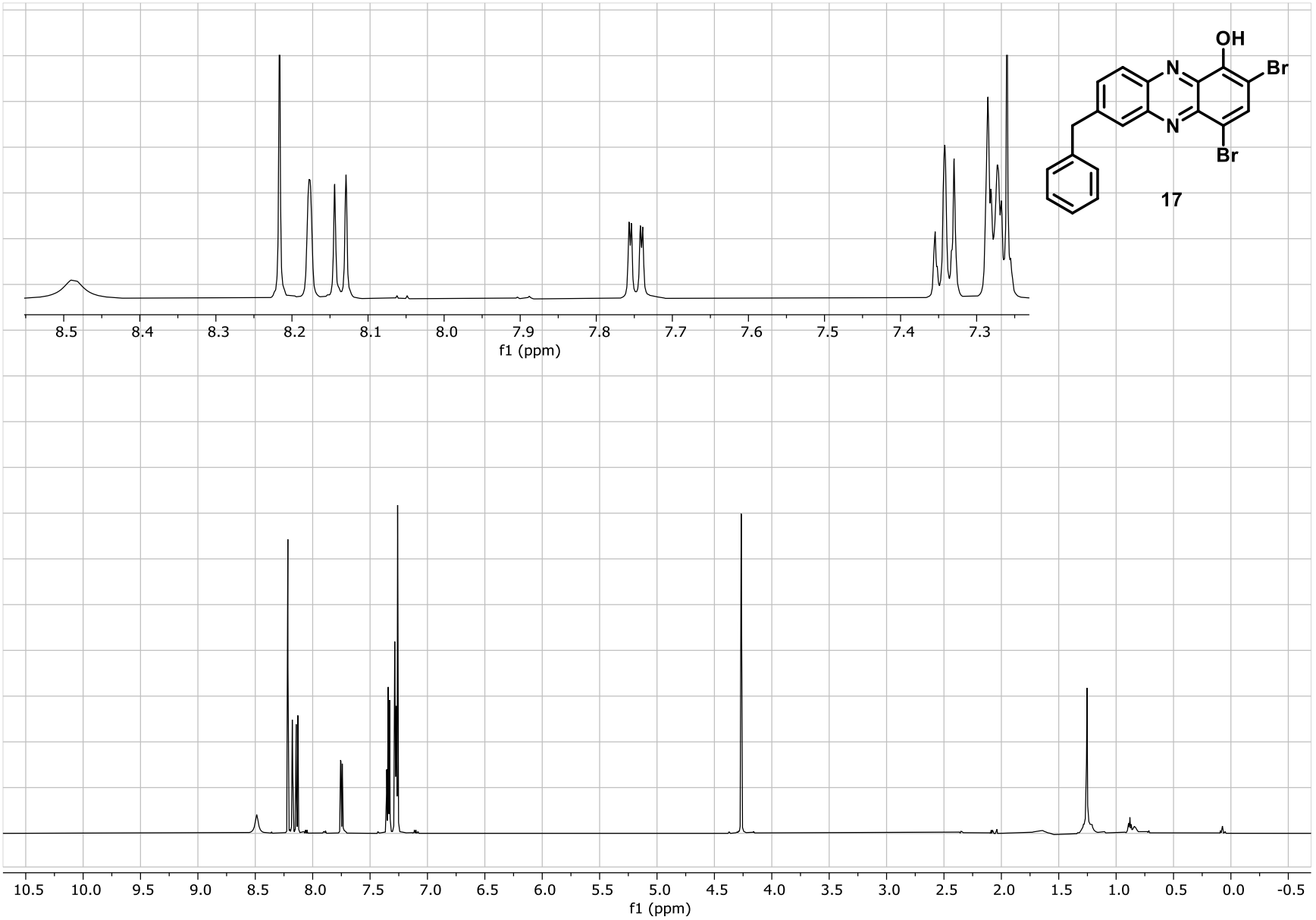

OH
Br
N
N
I
Br
12
143 142 141 140 139 138 137 136 135 134 133 132 131 130
f1 (ppm)
140.35 140.25
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

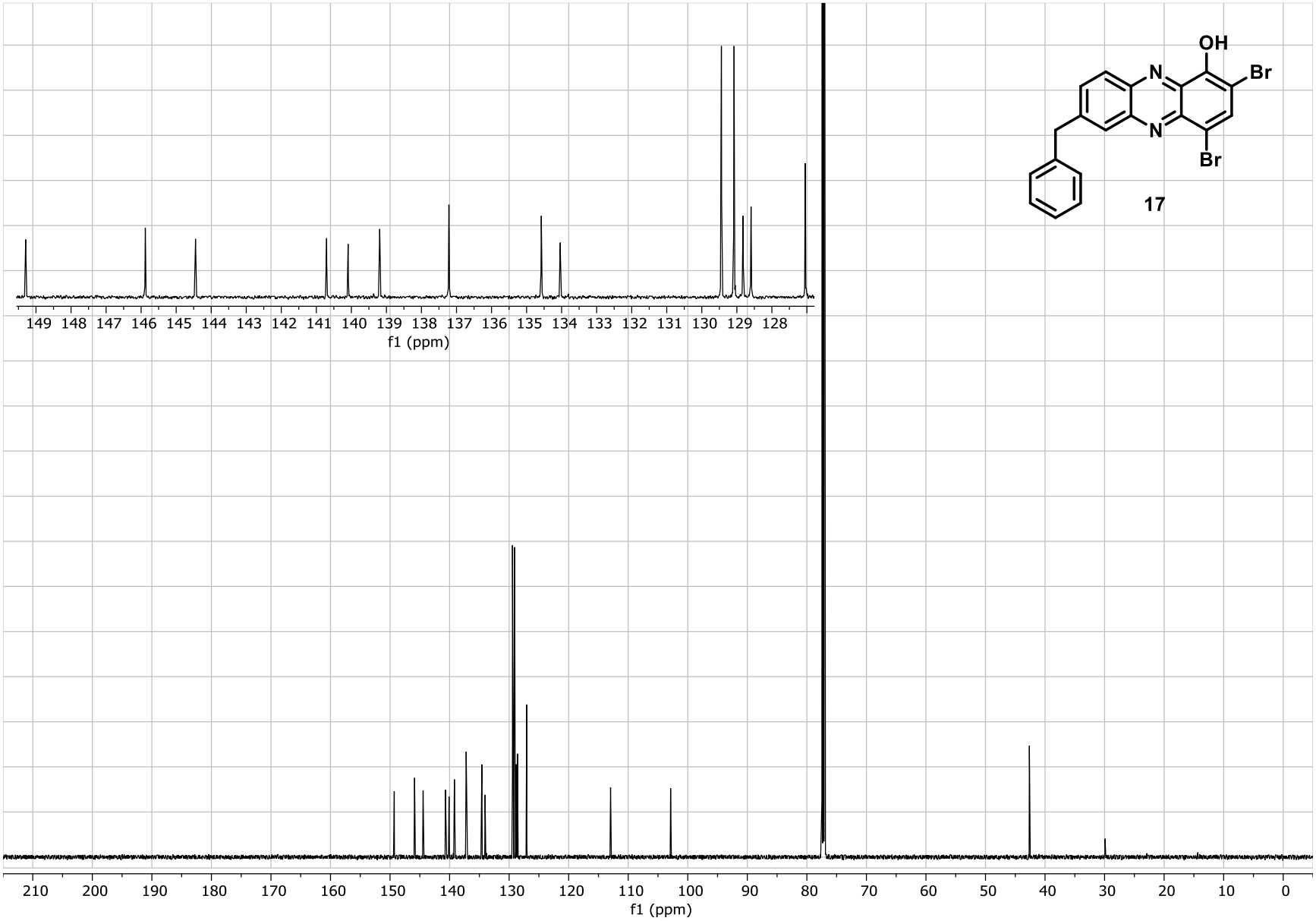

OH
Br
N
N
F3CS
Br
13
8.75 8.70 8.65 8.60 8.55 8.50 8.45 8.40 8.35 8.30 8.25 8.20 8.15 8.10 8.05
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

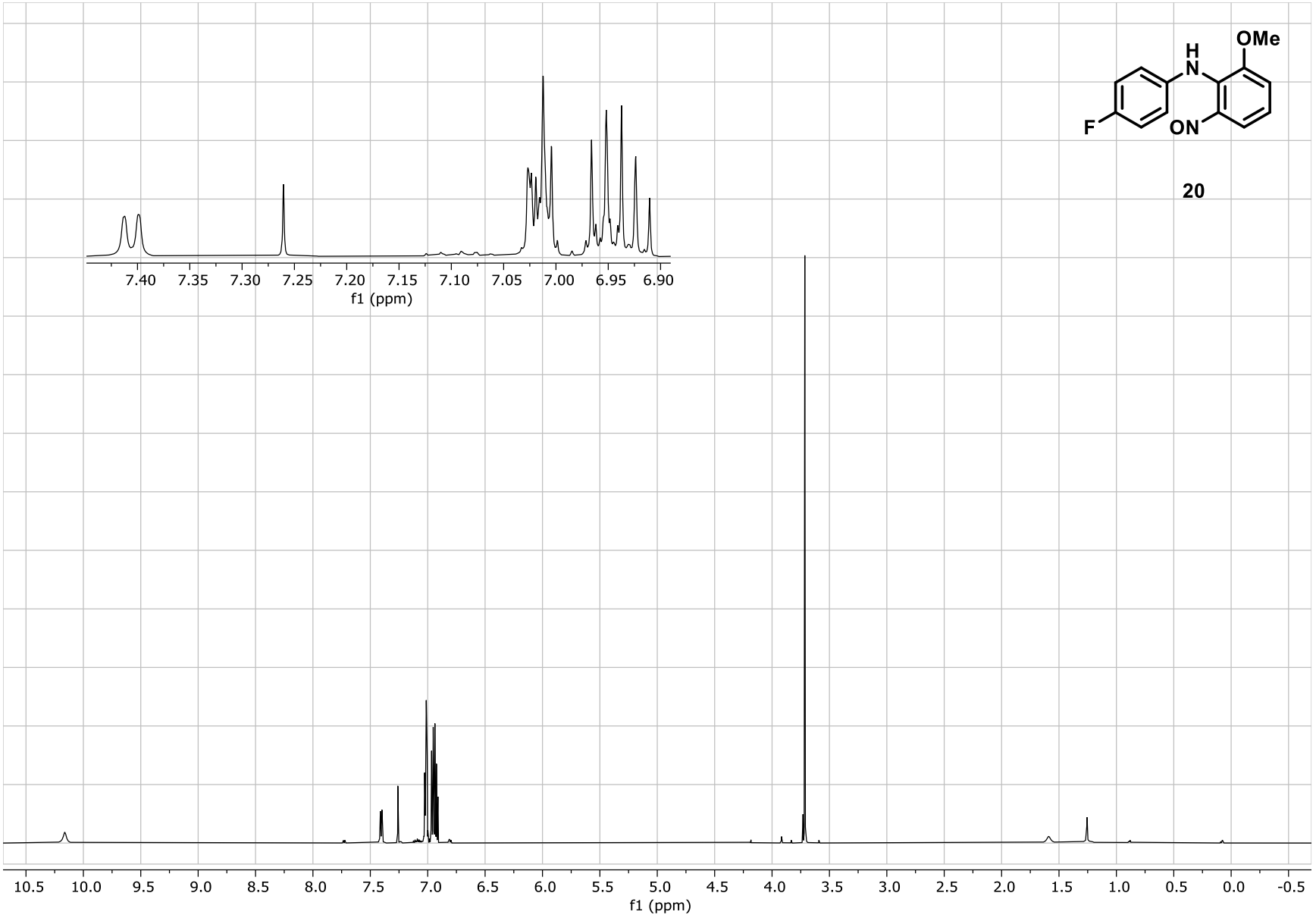

OH
Br
N
N
F3CS
Br
13
150 145 140 135 130 125 120 115 110 105
f1 (ppm)
132.0 131.5 131.0 130.5 130.0 129.5 129.0 128.5 128.0 127.5 127.0 126.5
f1 (ppm)
129.42
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

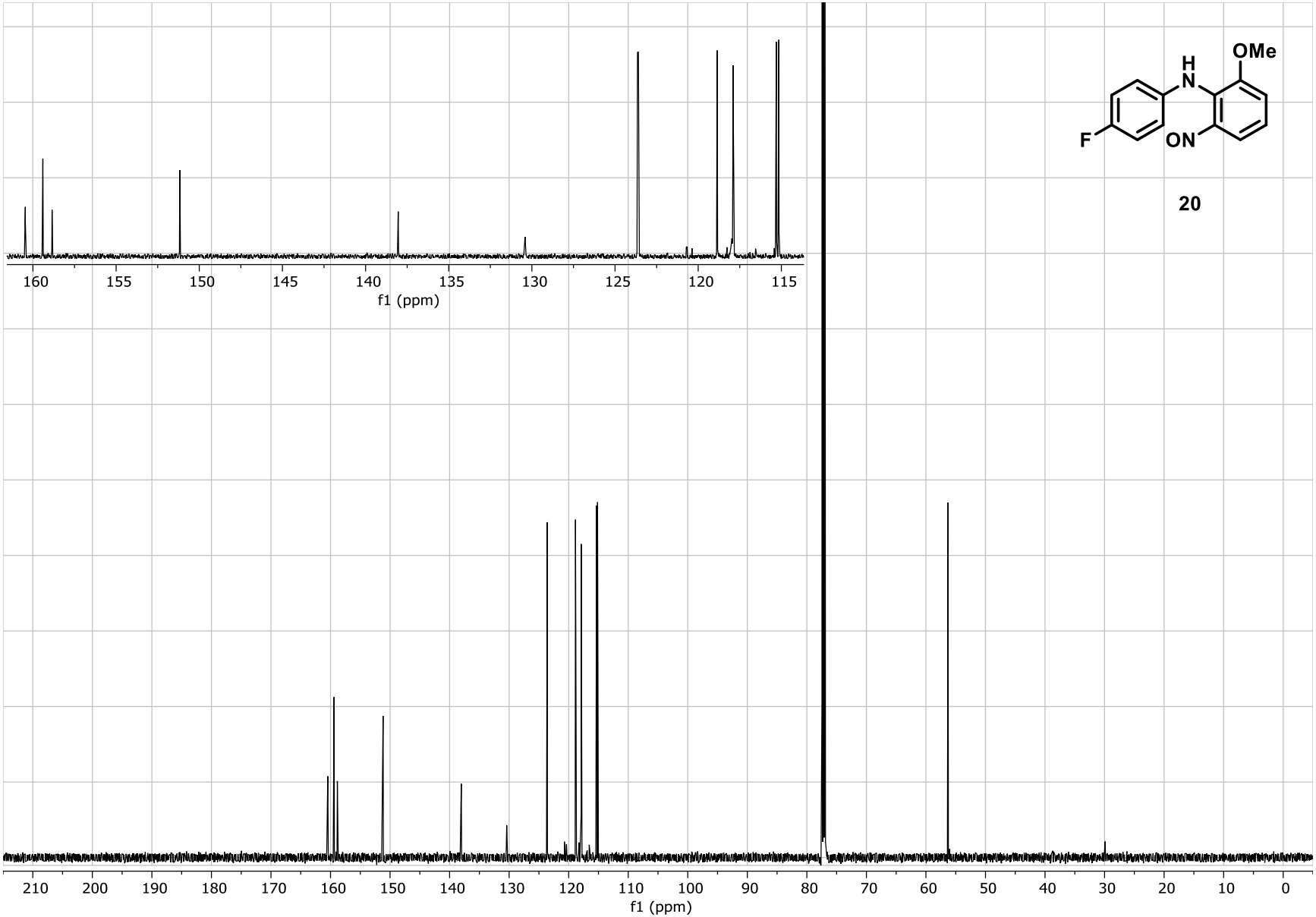

OH
F3C
N
Br
N
Cl
CF3
Br
16
8.65 8.60 8.55 8.50 8.45 8.40 8.35 8.30
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

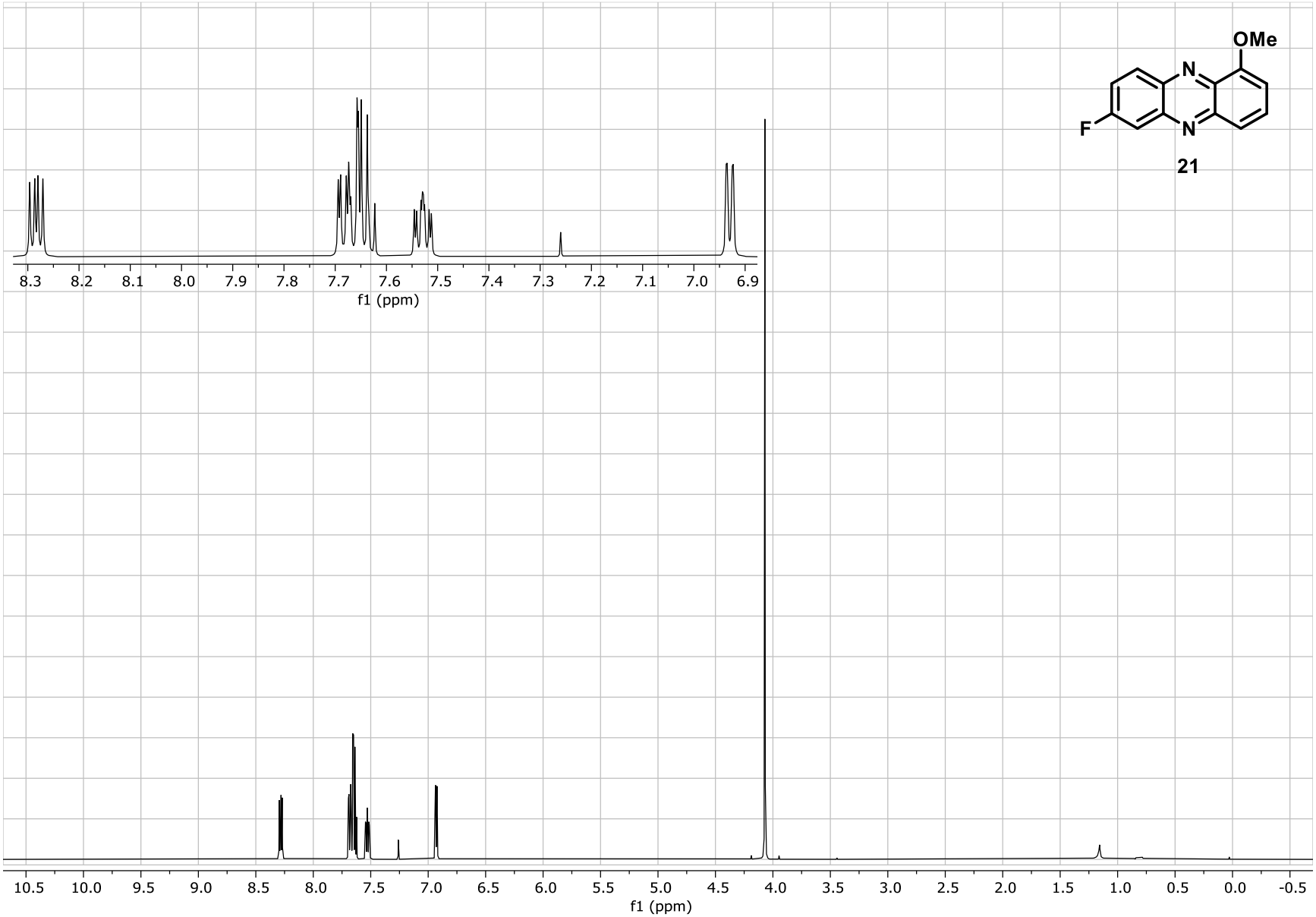

OH
F3C
N
Br
N
Cl
CF3
Br
16
133 132 131 130 129 128 127 126 125 124 123 122 121 120
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

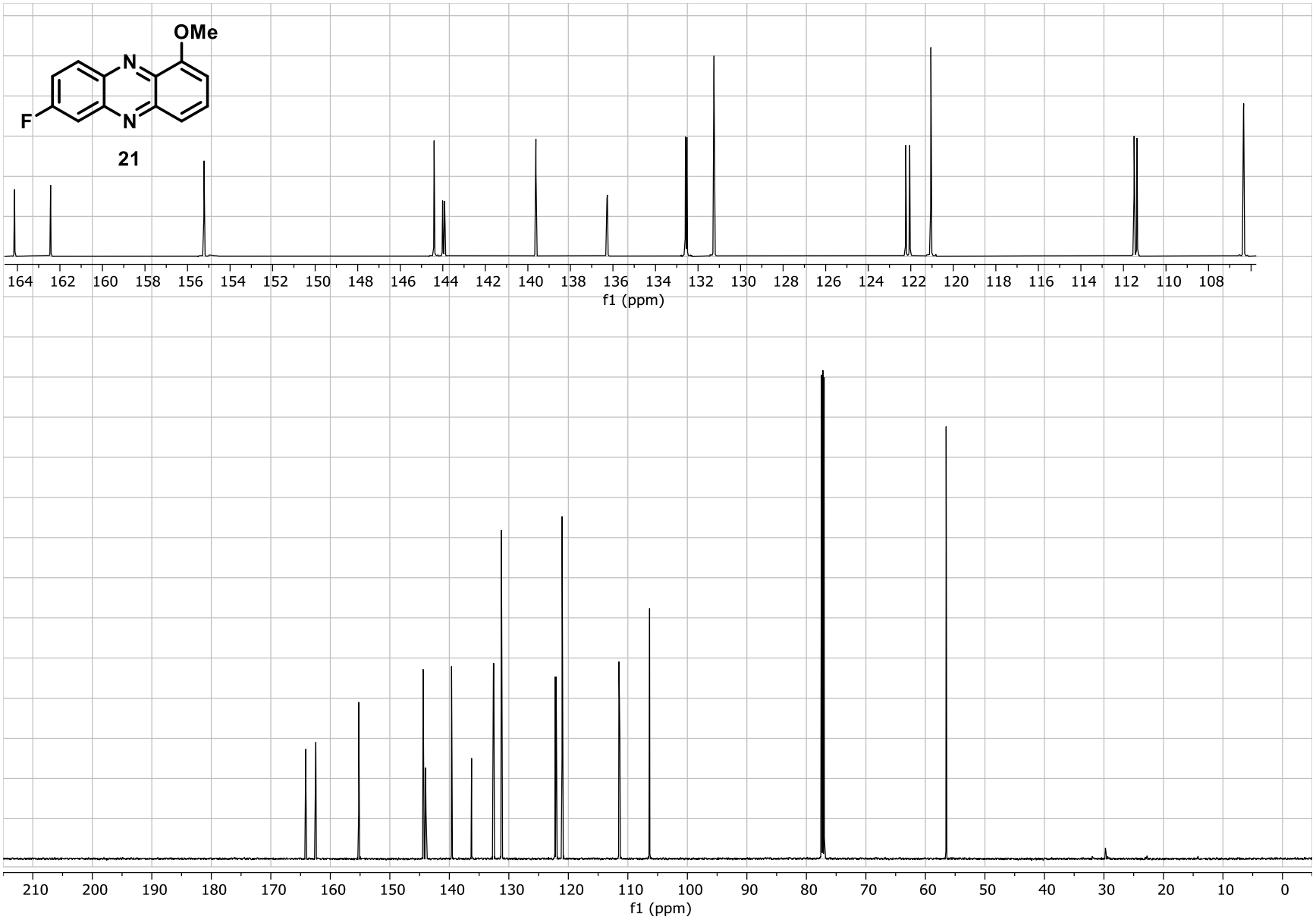

OH
Br
N
N
Br
17
8.5
8.4
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
f1 (ppm)
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

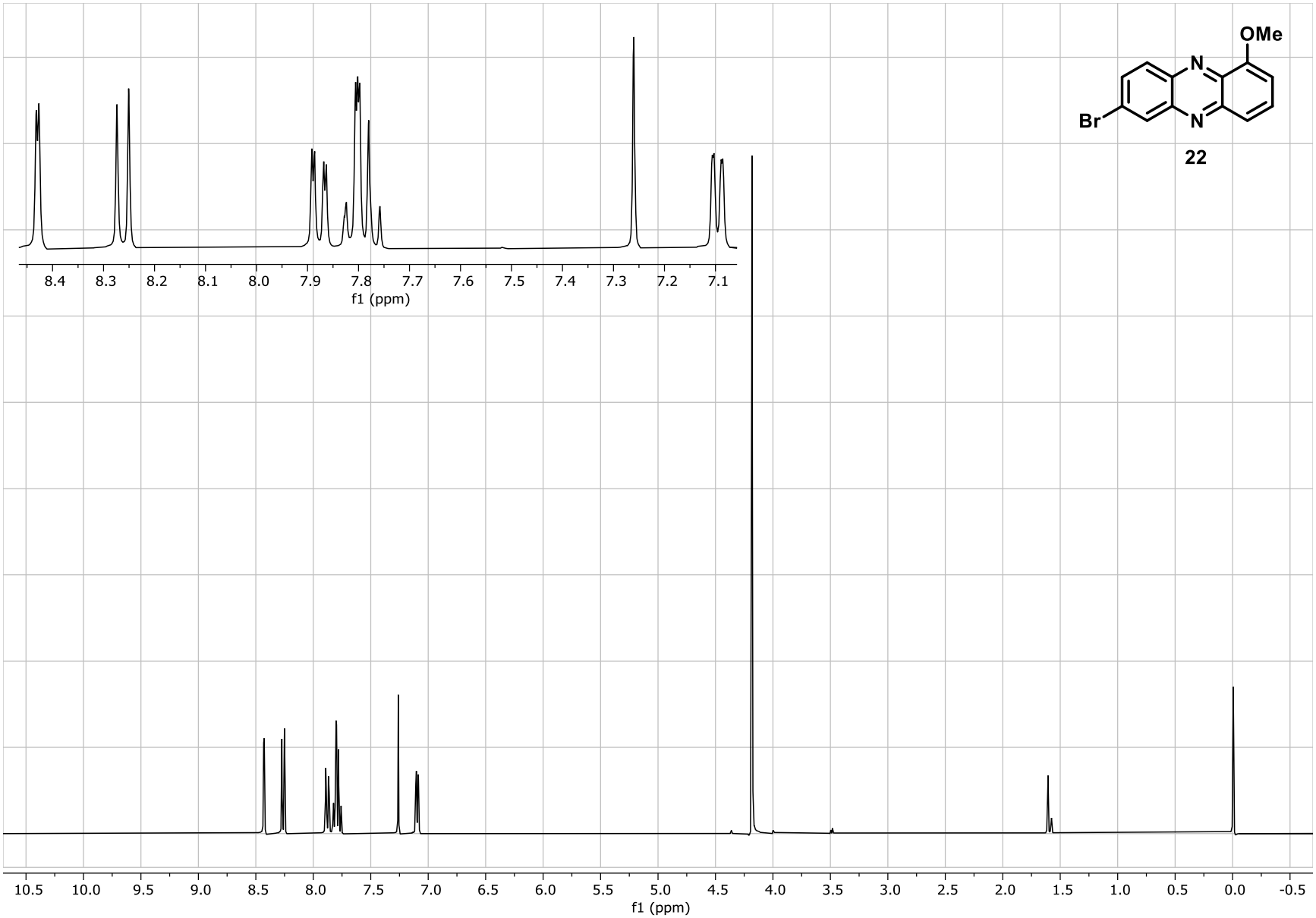

OH
Br
N
N
Br
17
149 148 147 146 145 144 143 142 141 140 139 138 137 136 135 134 133 132 131 130 129 128
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

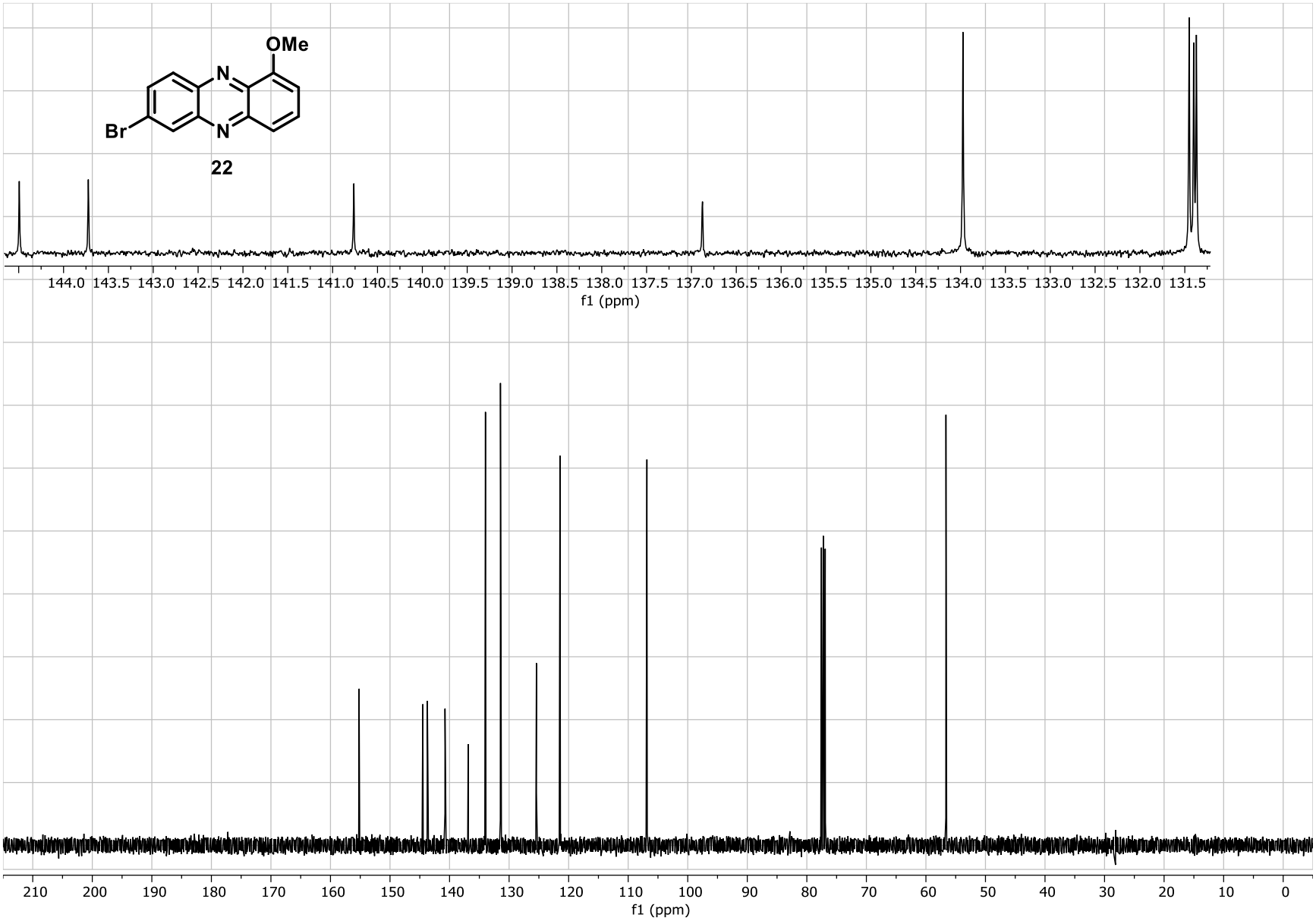

OMe
H
N
F
ON
20
7.40 7.35 7.30 7.25 7.20 7.15 7.10 7.05 7.00 6.95 6.90
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

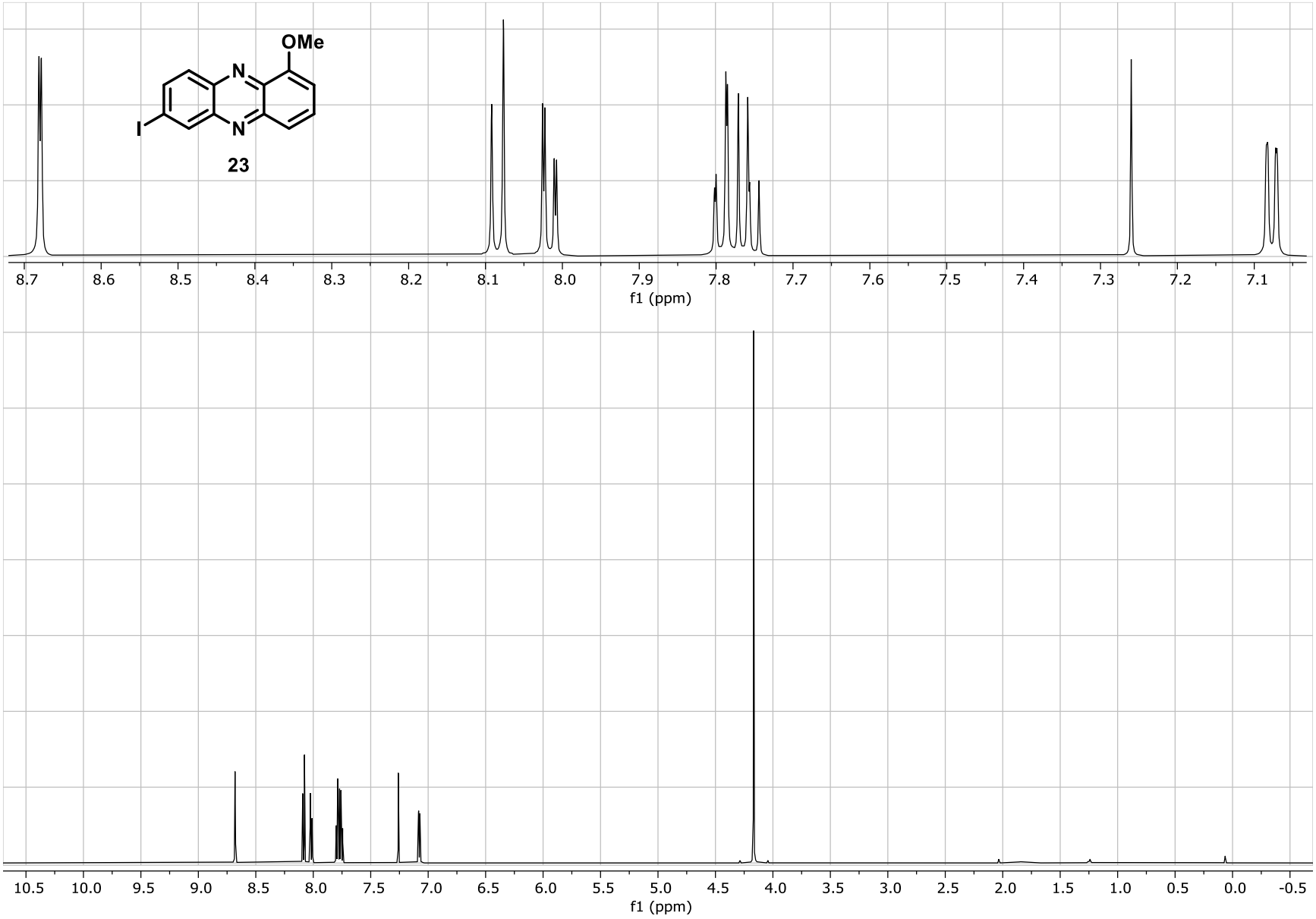

OMe
H
N
F
ON
20
160
155
150
145
140
135
130
125
120
115
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

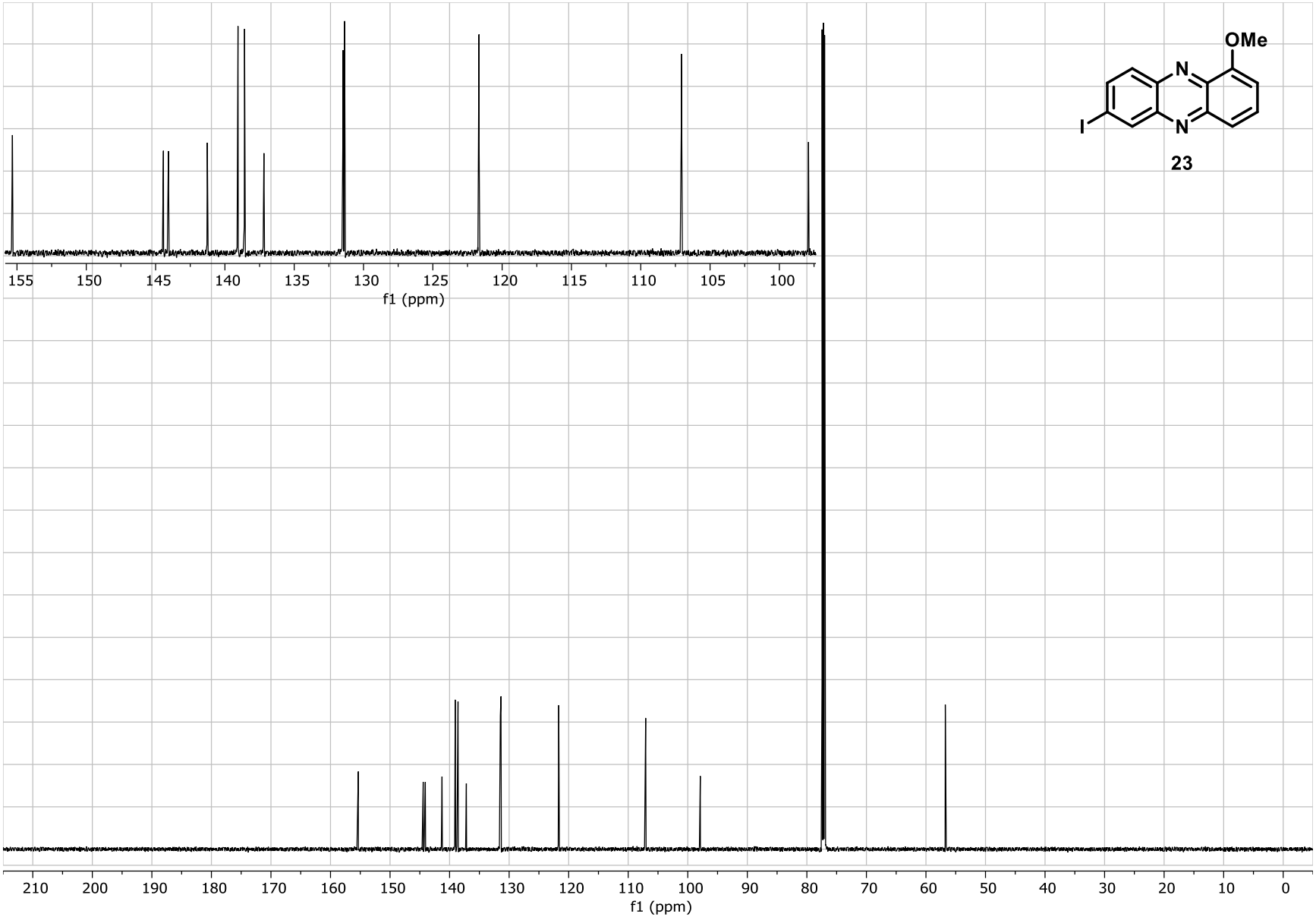

OMe
N
N
F
21
8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

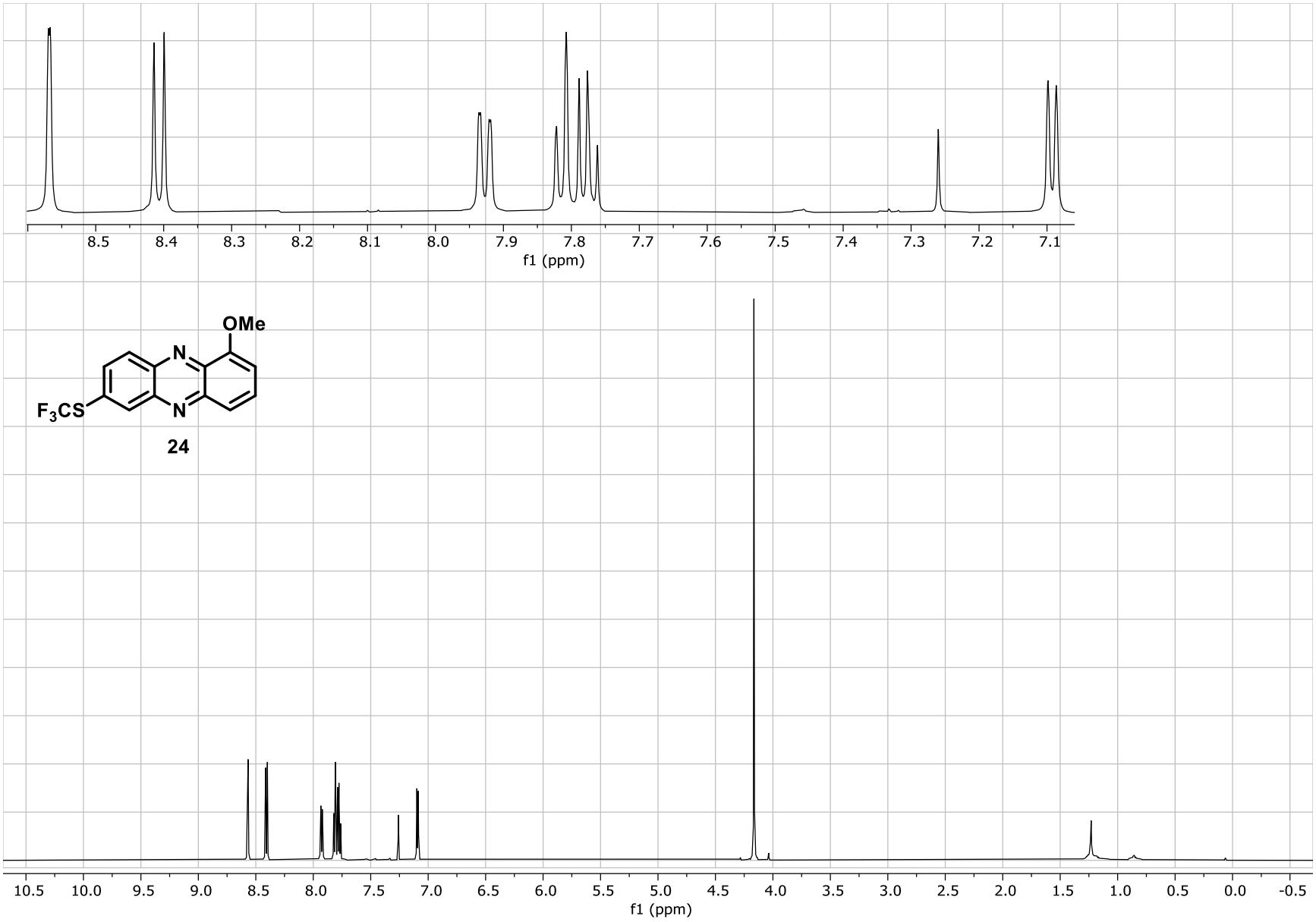

OMe
N
N
F
21
164 162 160 158 156 154 152 150 148 146 144 142 140 138 136 134 132 130 128 126 124 122 120 118 116 114 112 110 108
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

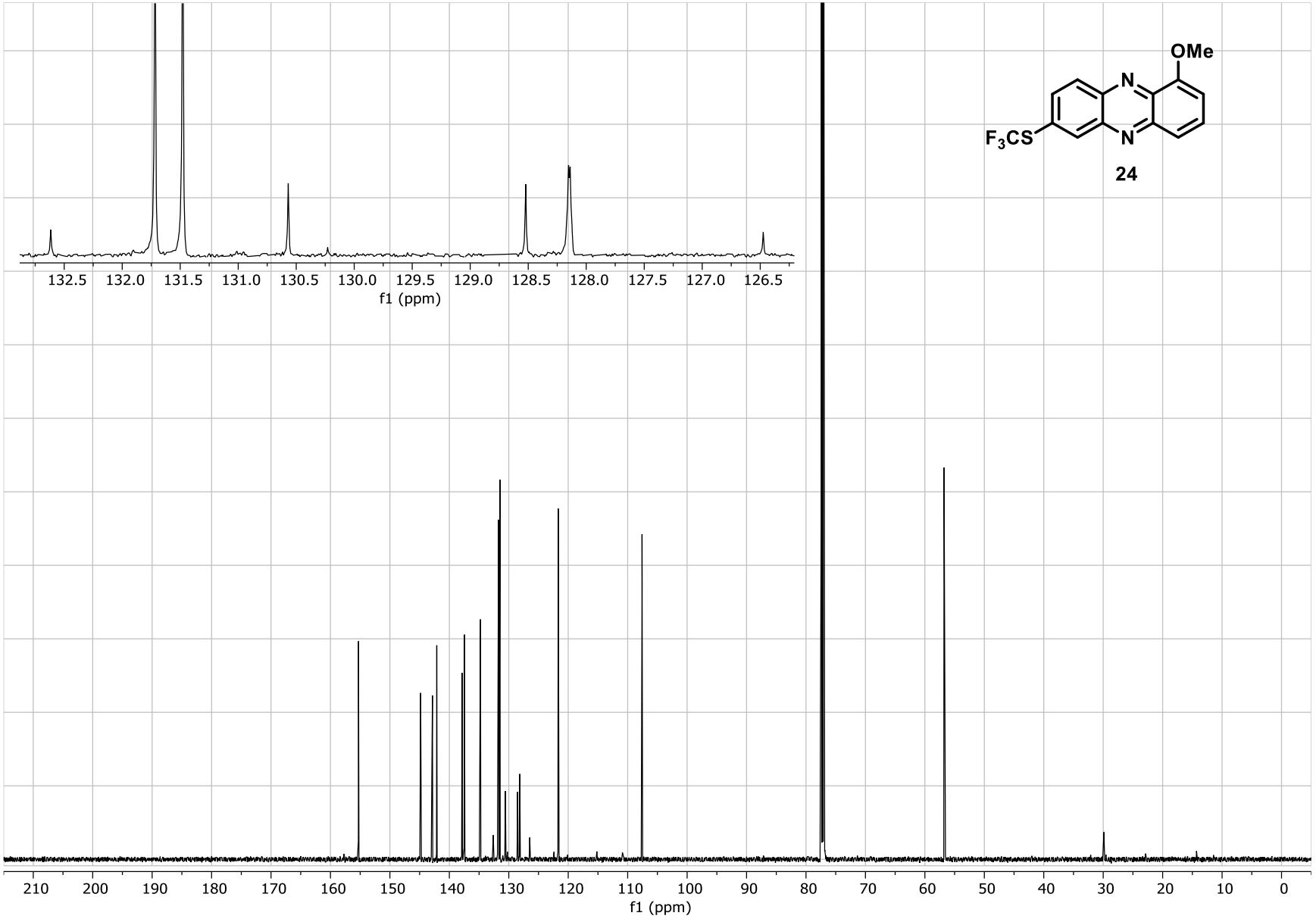

OMe
N
N
Br
22
8.4
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
f1 (ppm)
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

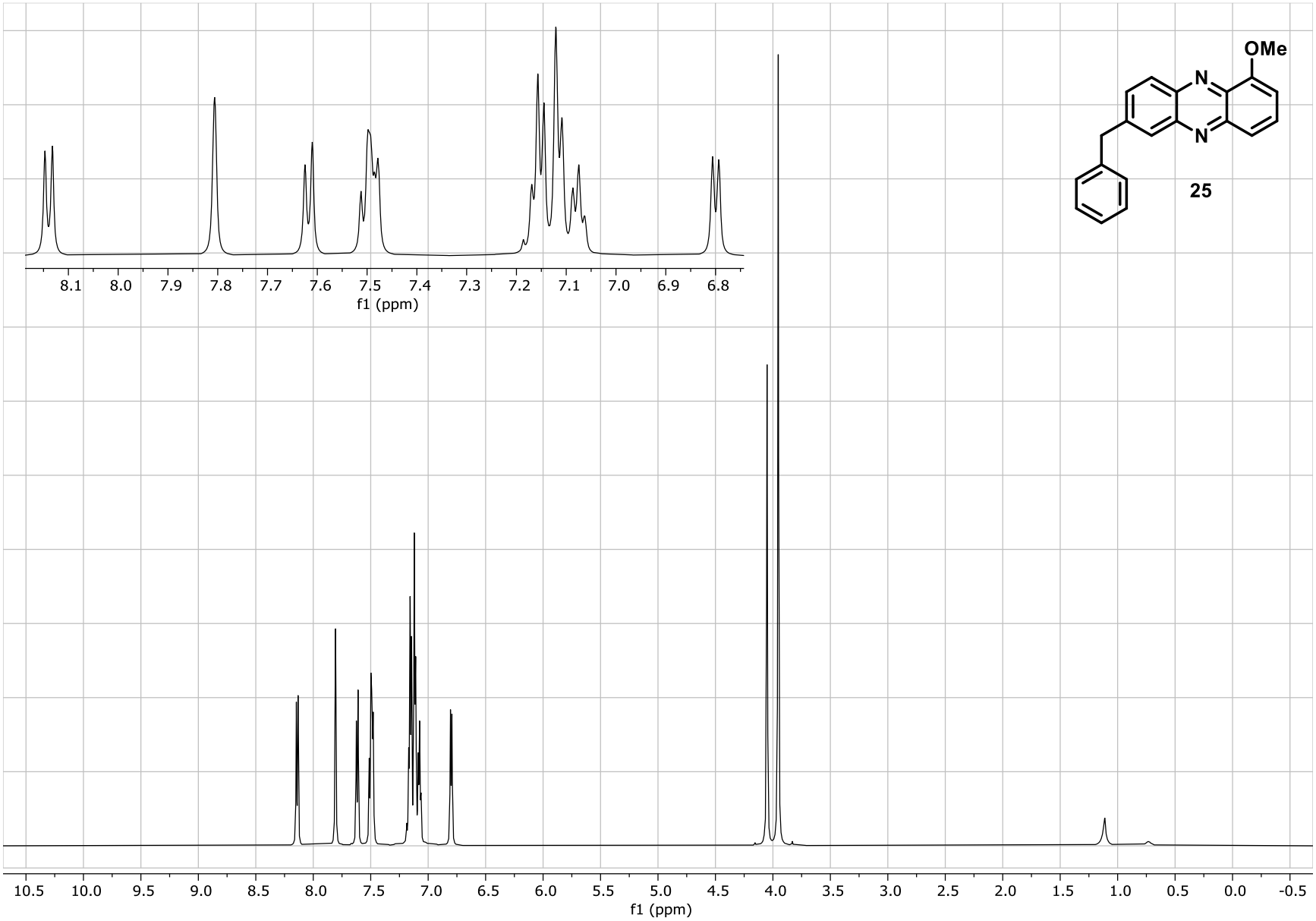

OMe
N
N
Br
22
144.0 143.5 143.0 142.5 142.0 141.5 141.0 140.5 140.0 139.5 139.0 138.5 138.0 137.5 137.0 136.5 136.0 135.5 135.0 134.5 134.0 133.5 133.0 132.5 132.0 131.5
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

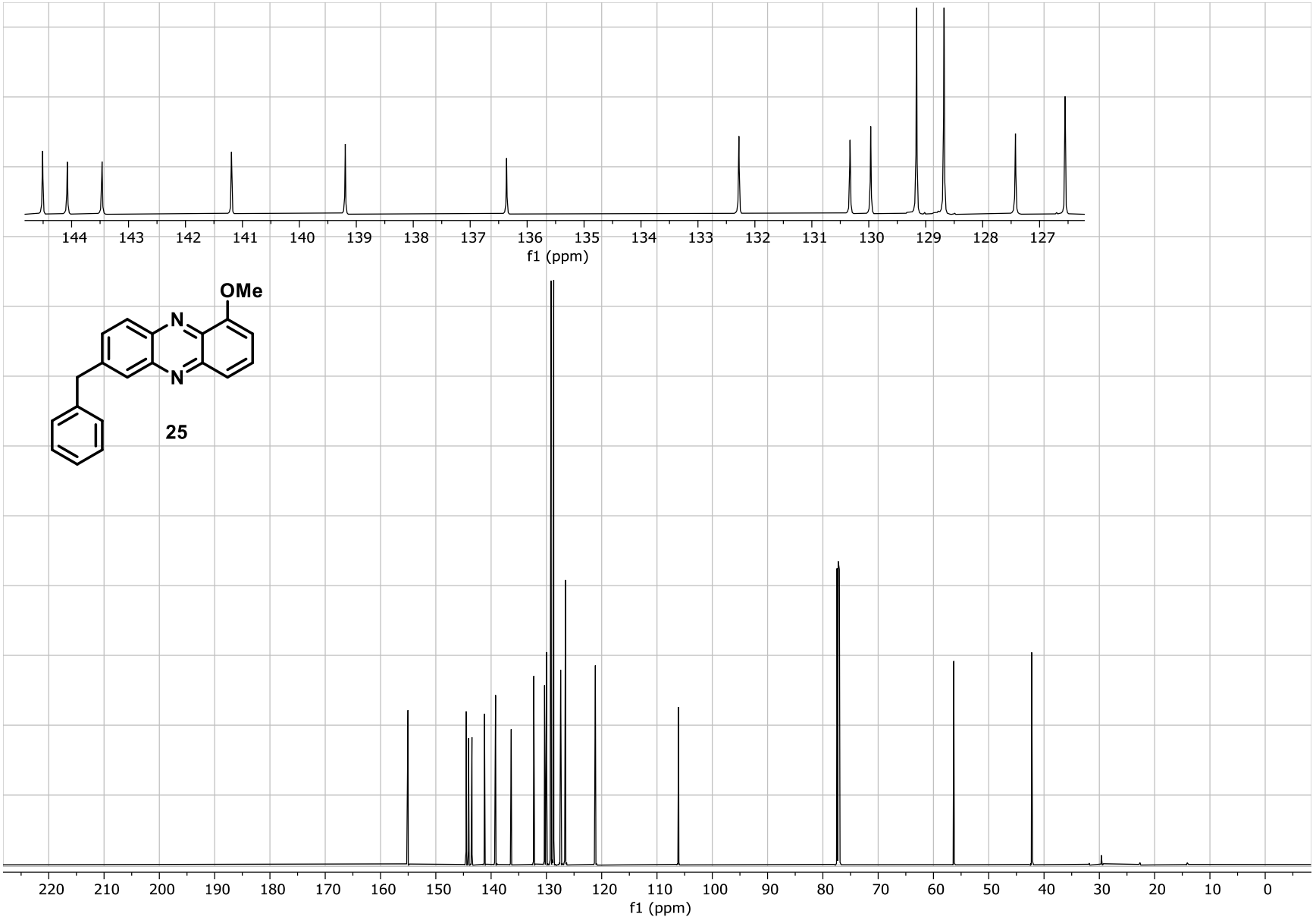

OMe
N
N
I
23
8.7
8.6
8.5
8.4
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
f1 (ppm)
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

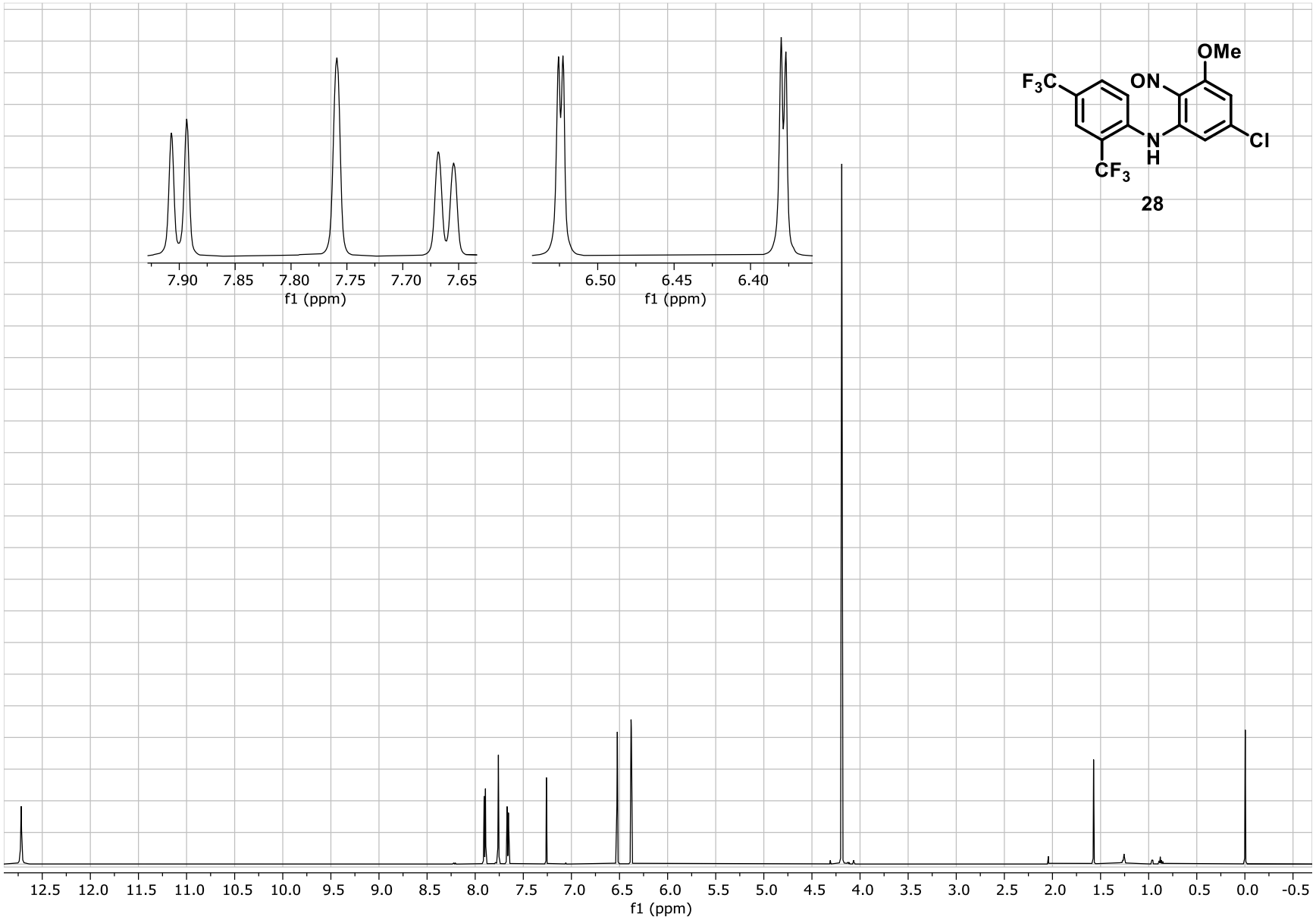

OMe
N
N
I
23
155 150 145 140 135 130 125 120 115 110 105 100
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

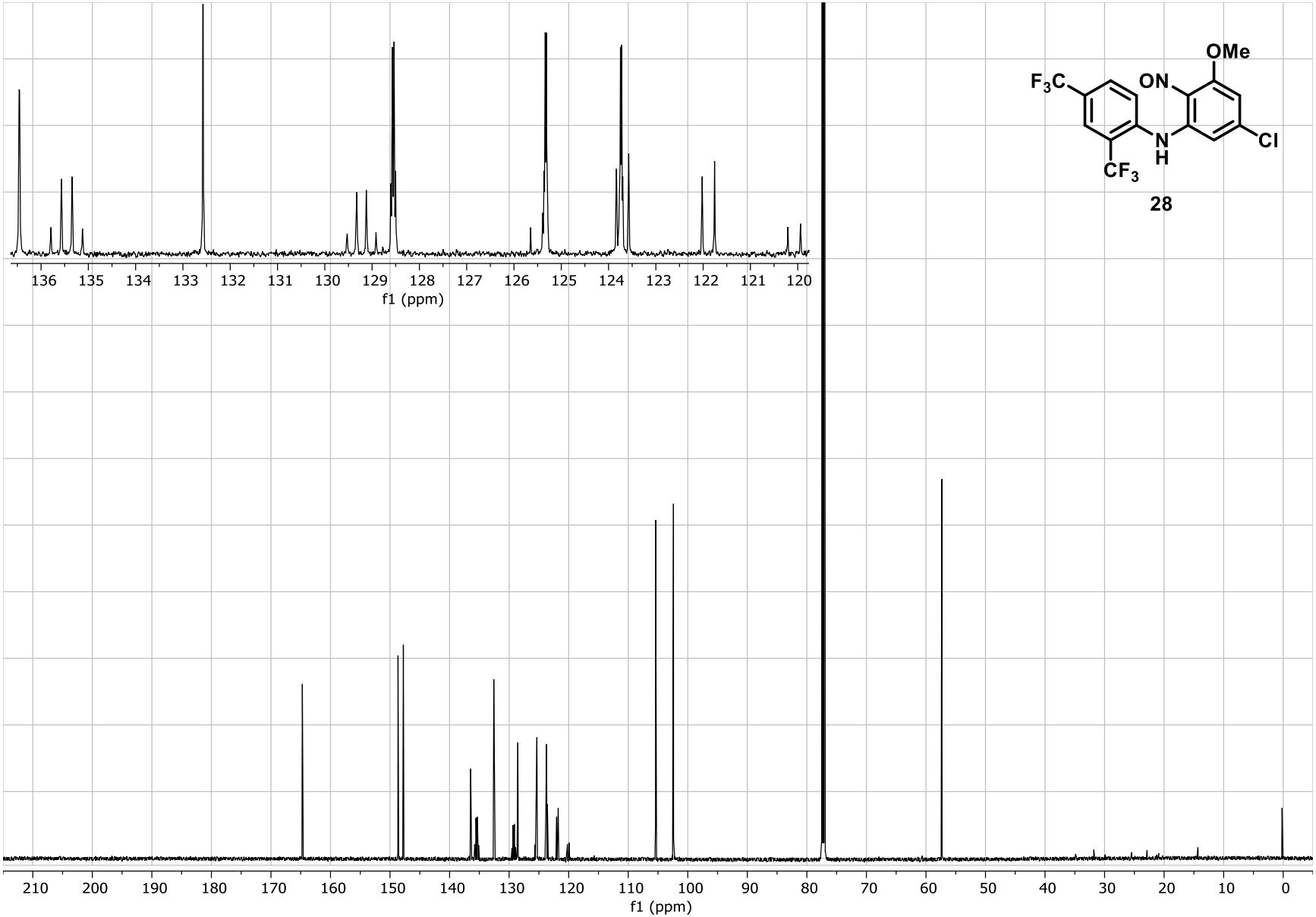

8.5
8.4
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
f1 (ppm)
OMe
N
N
F3CS
24
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

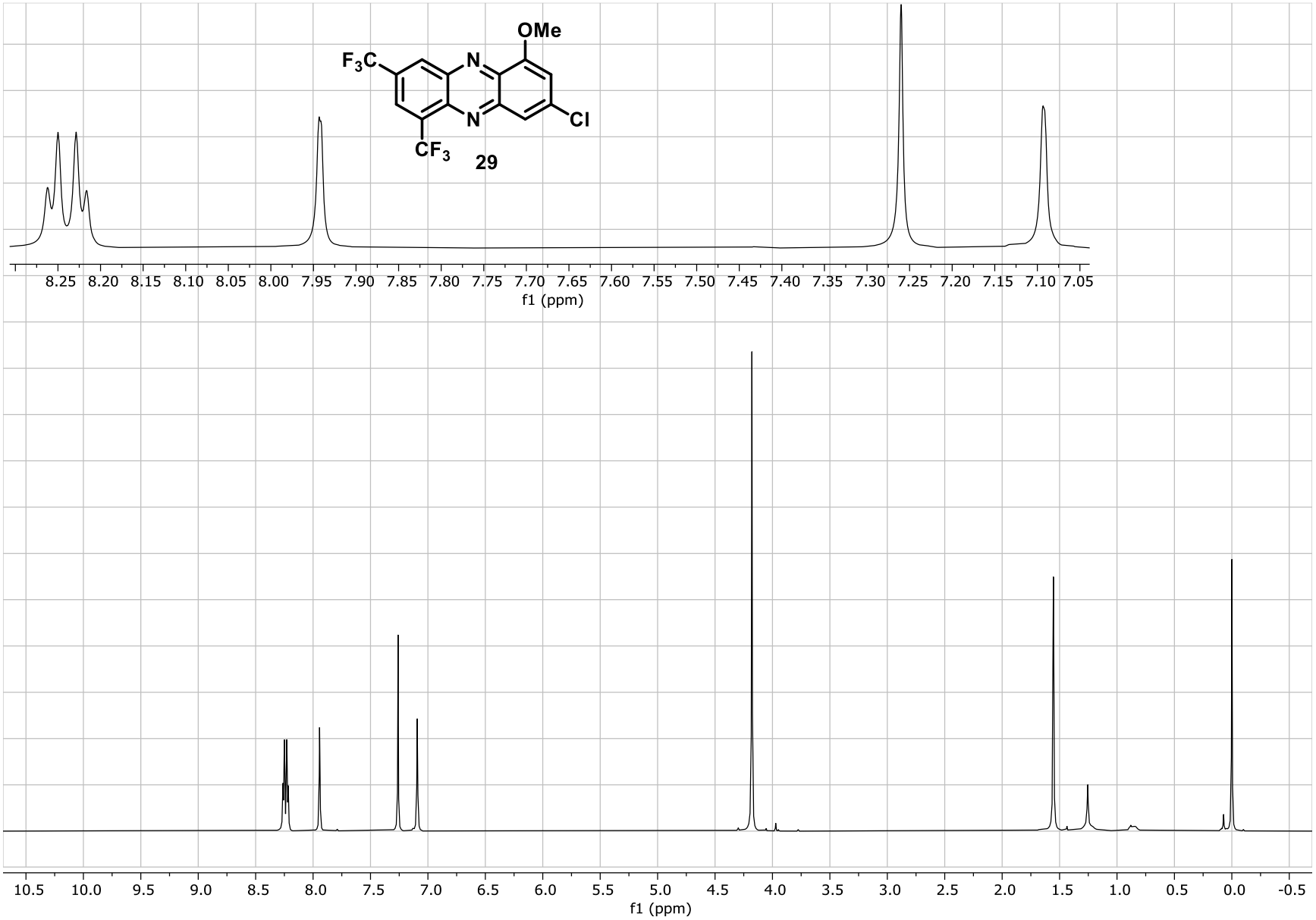

OMe
N
N
F3CS
24
132.5
132.0
131.5
131.0
130.5
130.0
129.5
129.0
128.5
128.0
127.5
127.0
126.5
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

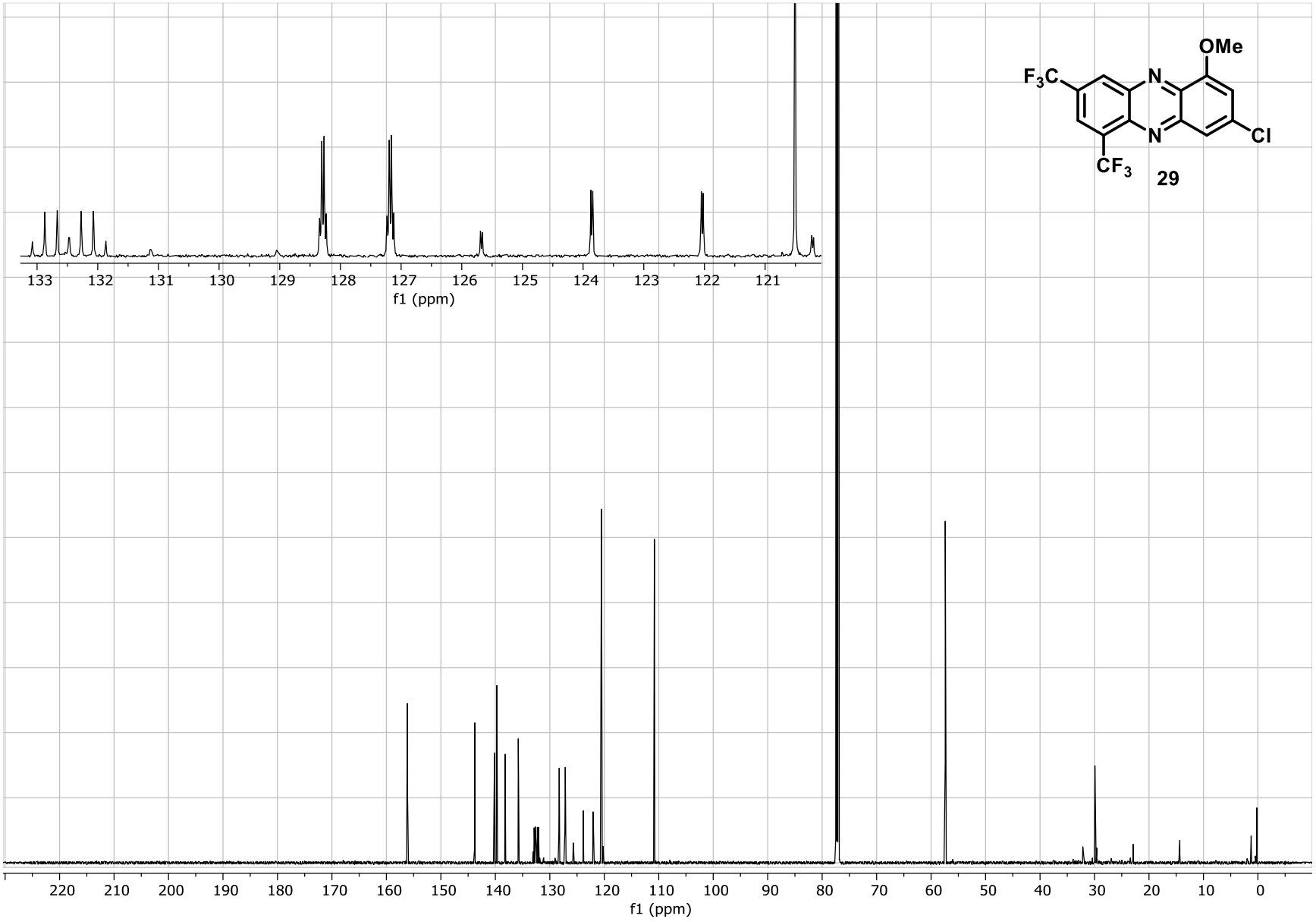

OMe
N
N
25
8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

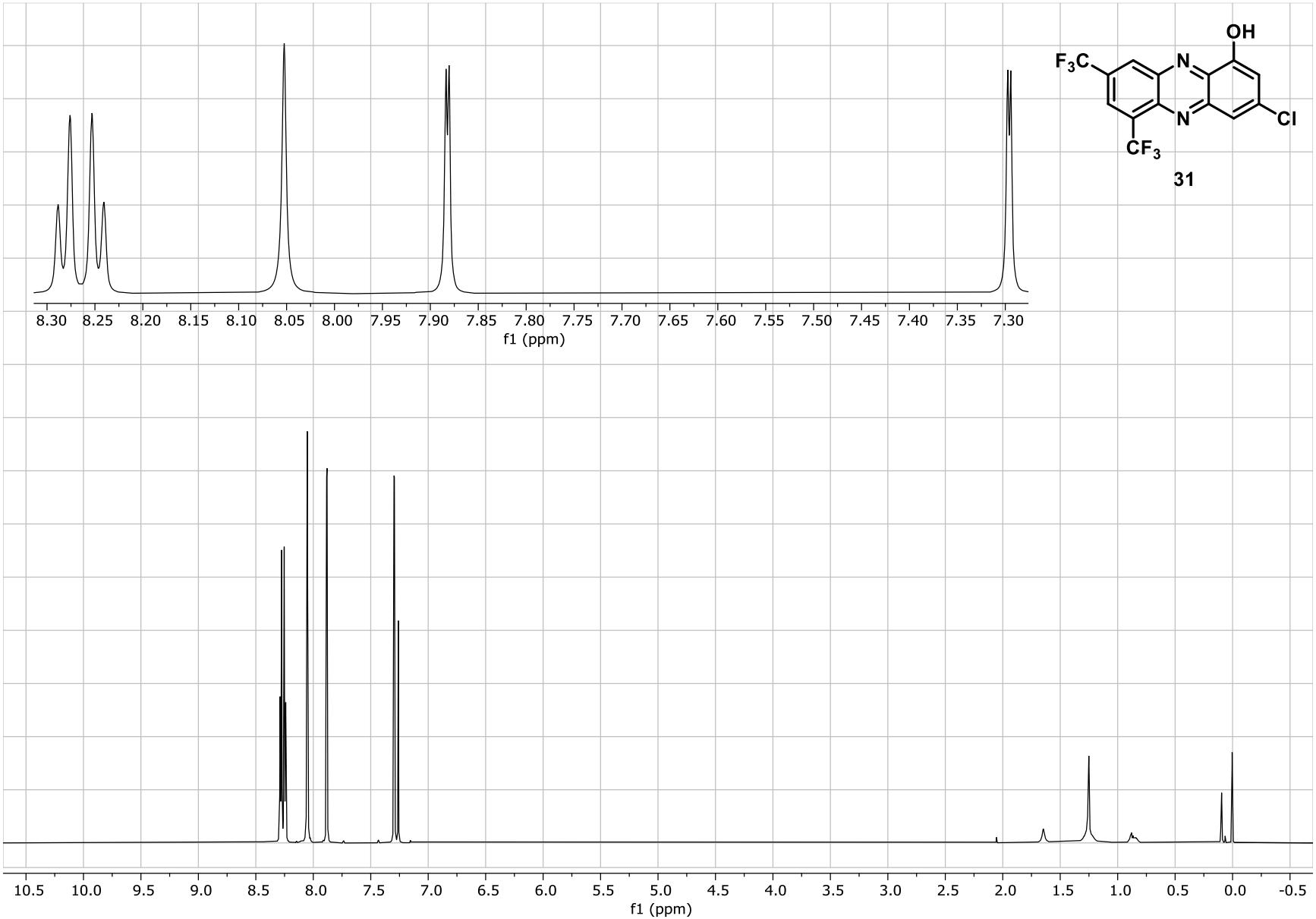

OMe
N
N
25
144 143 142 141 140 139 138 137 136 135 134 133 132 131 130 129 128 127
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

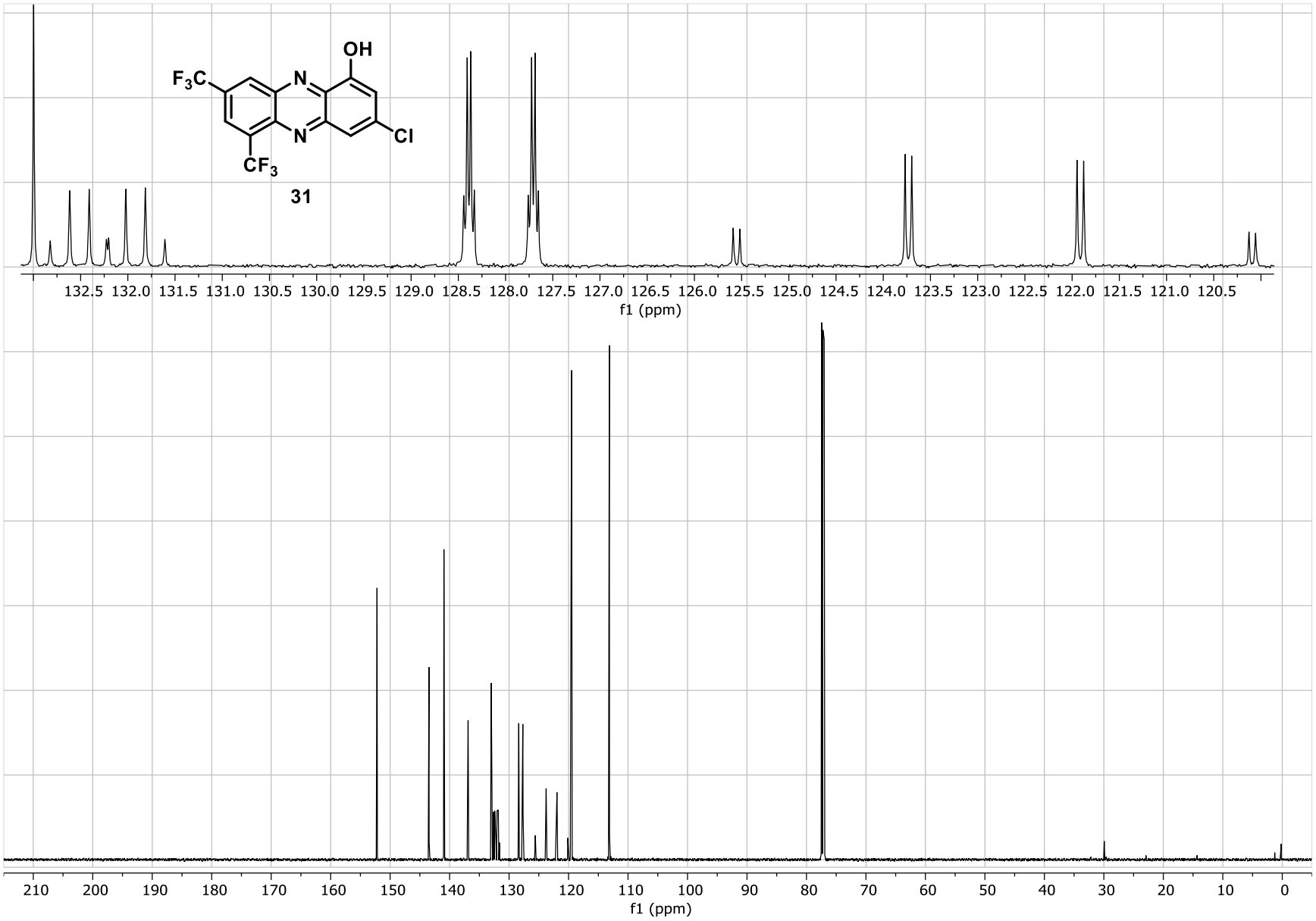

7.90
7.85
7.80
7.75
7.70
7.65
f1 (ppm)
6.50
6.45
6.40
f1 (ppm)
OMe
F3C
ON
N
H
Cl
CF3
28
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

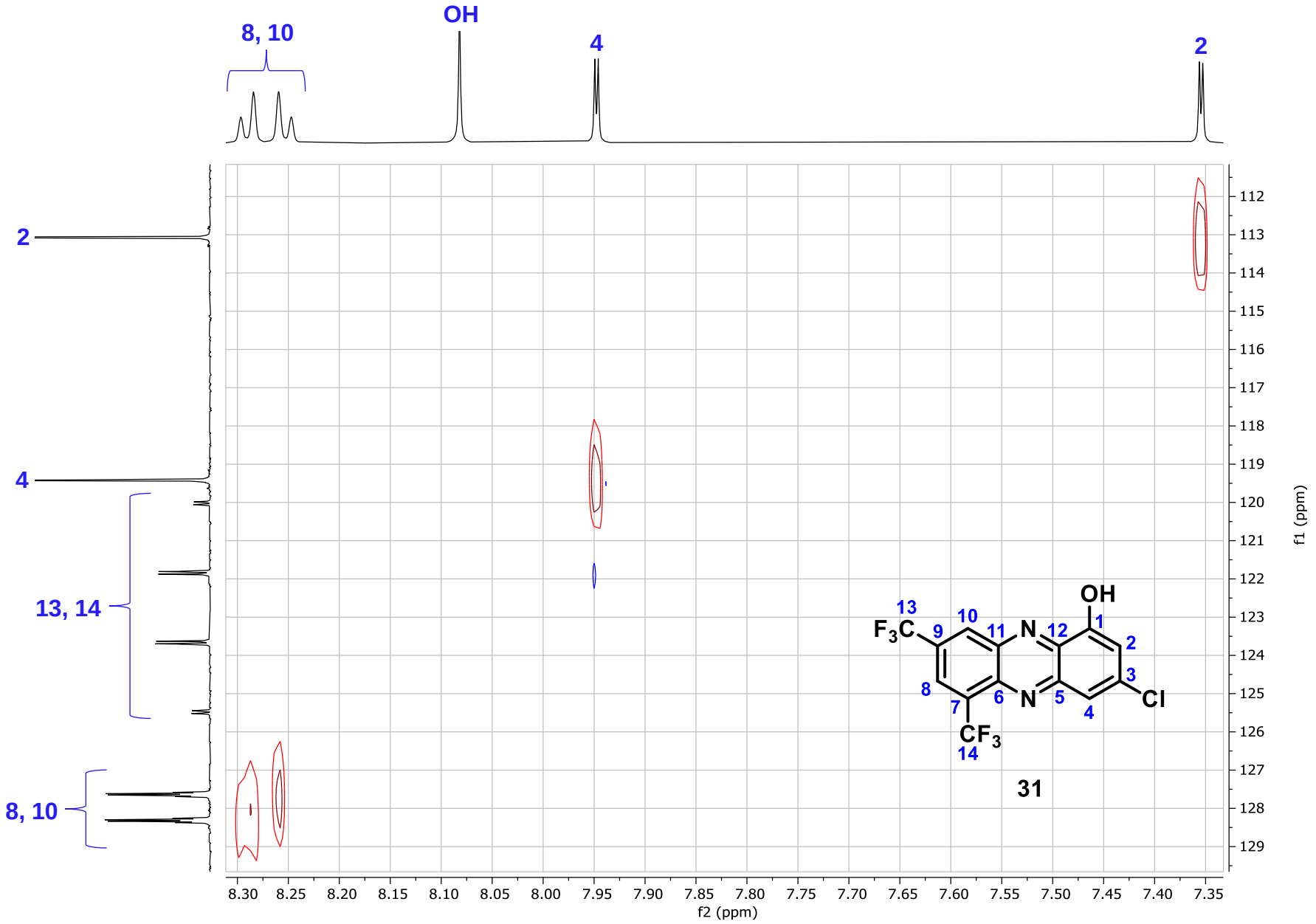

OMe
F3C
ON
N
H
Cl
CF3
28
136 135 134 133 132 131 130 129 128 127 126 125 124 123 122 121 120
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


OMe
F3C
N
N
Cl
CF3
29
8.25 8.20 8.15 8.10 8.05 8.00 7.95 7.90 7.85 7.80 7.75 7.70 7.65 7.60 7.55 7.50 7.45 7.40 7.35 7.30 7.25 7.20 7.15 7.10 7.05
f1 (ppm)
10.5 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 0.0 -0.5
f1 (ppm)

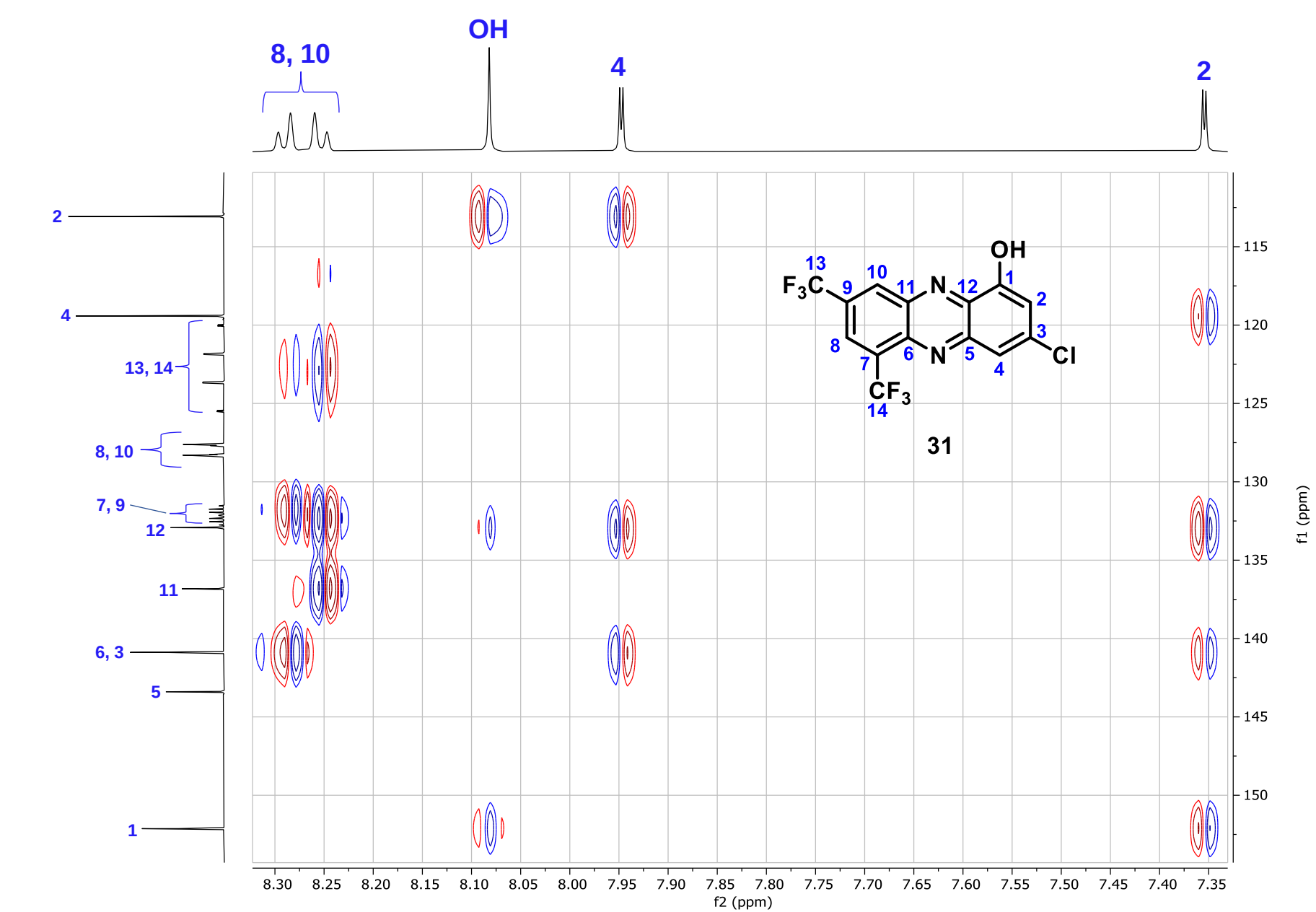

OMe
F3C
N
N
Cl
CF3
29
133
132
131
130
129
128
127
126
125
124
123
122
121
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


OH
F3C
N
N
Cl
CF3
31
8.30 8.25 8.20 8.15 8.10 8.05 8.00 7.95 7.90 7.85 7.80 7.75 7.70 7.65 7.60 7.55 7.50 7.45 7.40 7.35 7.30
f1 (ppm)
10.5 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 0.0 -0.5
f1 (ppm)

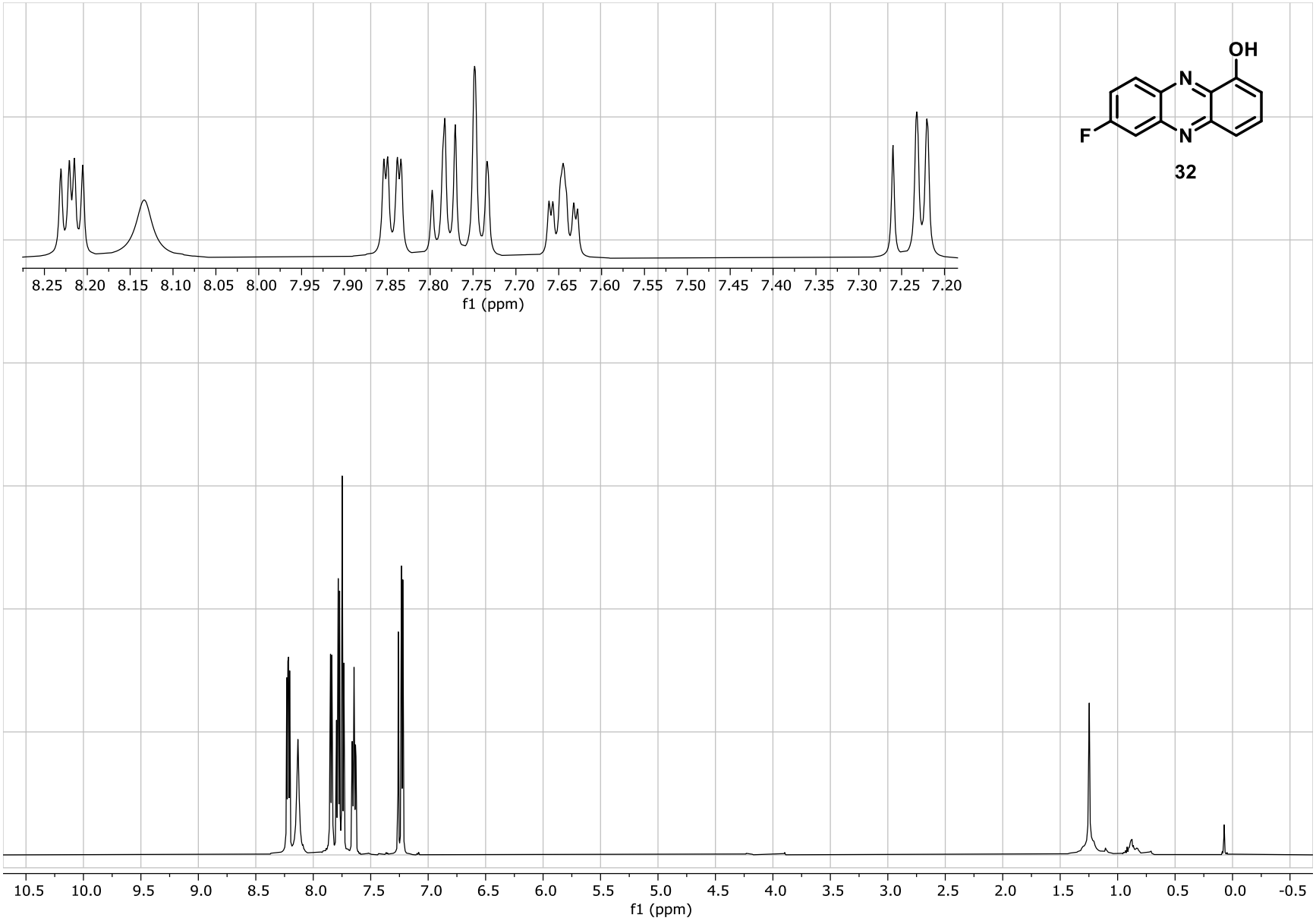

OH
F3C
N
N
Cl
CF3
31
132.5 132.0 131.5 131.0 130.5 130.0 129.5 129.0 128.5 128.0 127.5 127.0 126.5 126.0 125.5 125.0 124.5 124.0 123.5 123.0 122.5 122.0 121.5 121.0 120.5
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

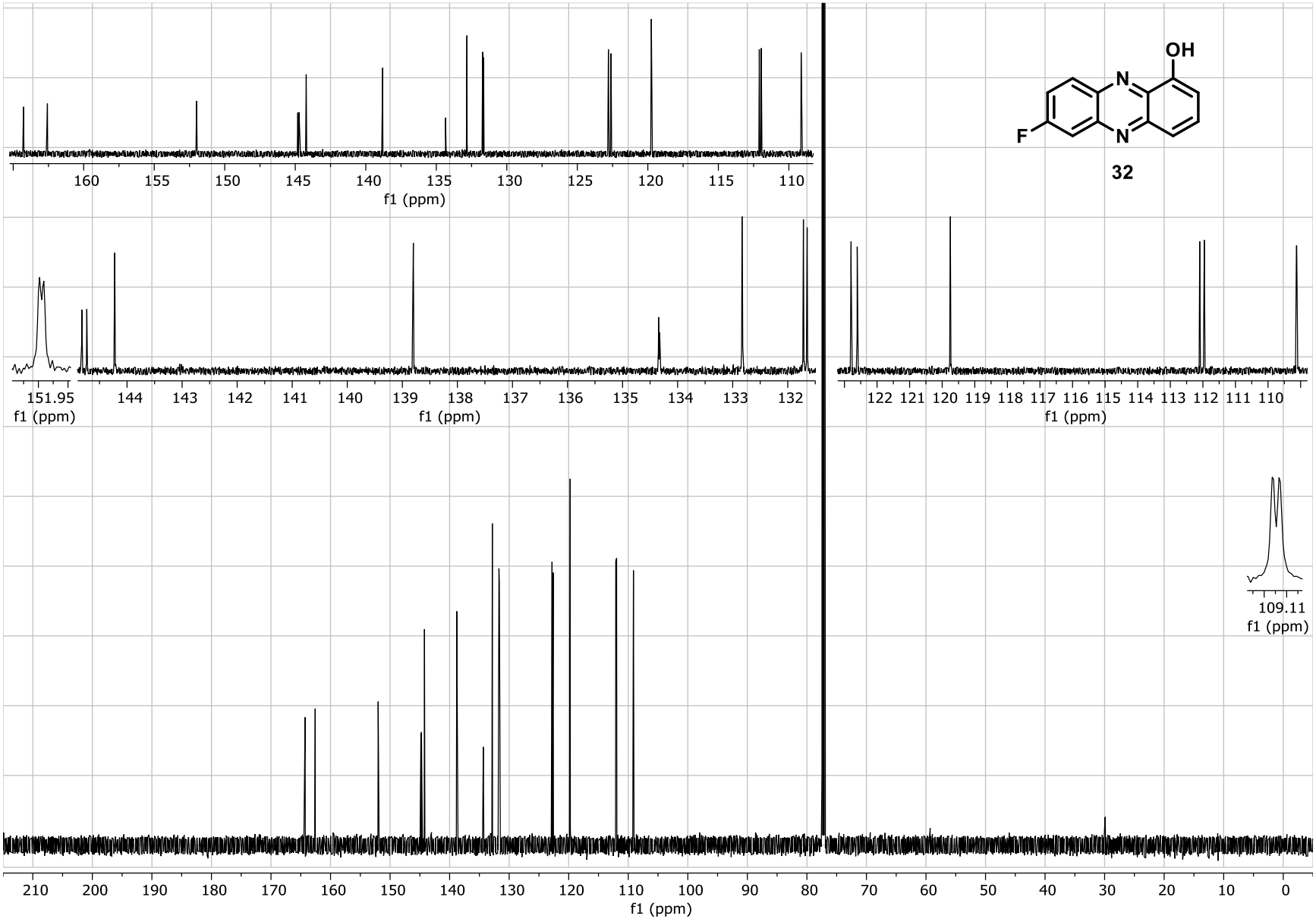


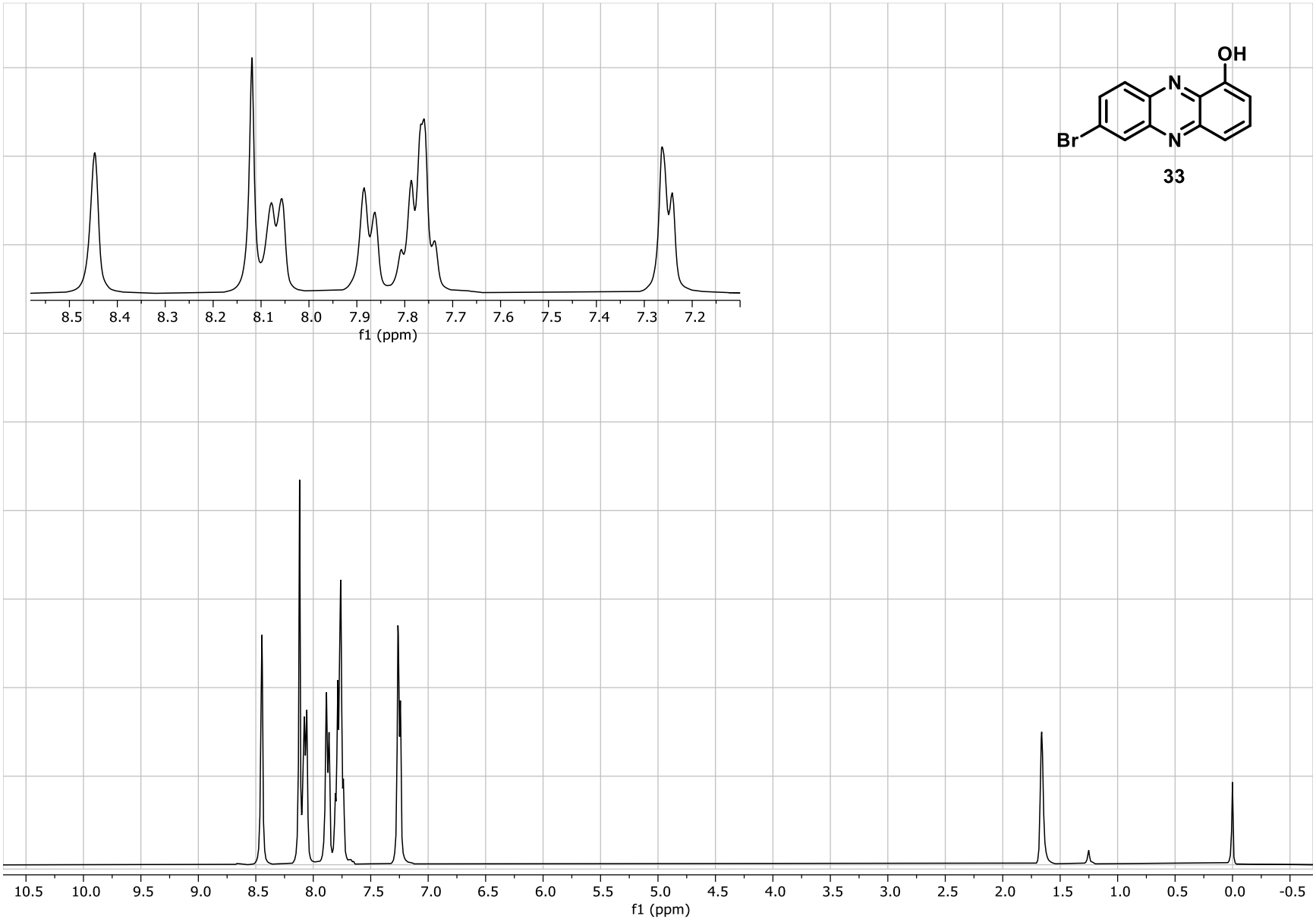

**Zoomed In Version: HSQC of 31 (unable to differentiate signals at positions 8 & 10, and positions 13 &14)**

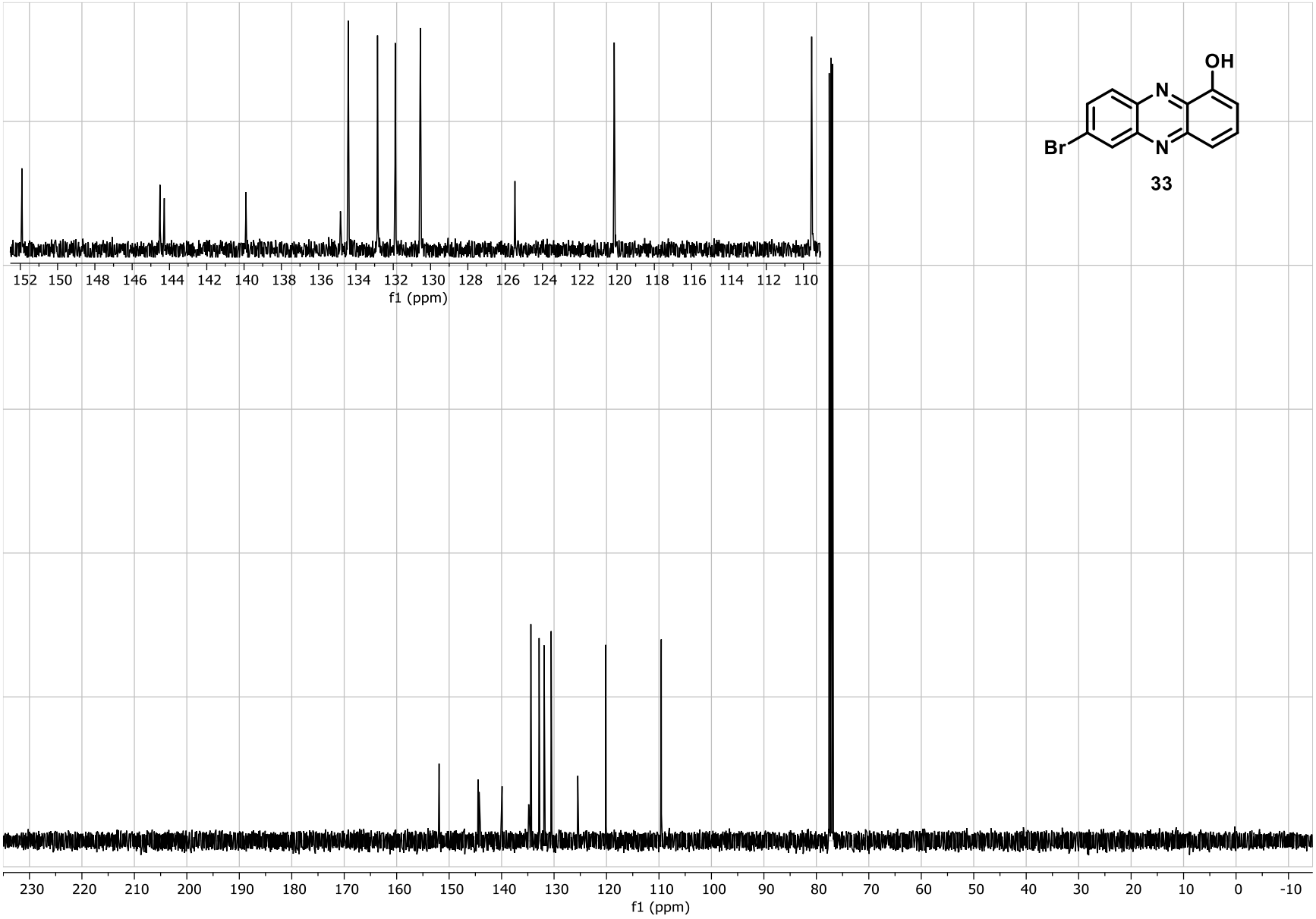


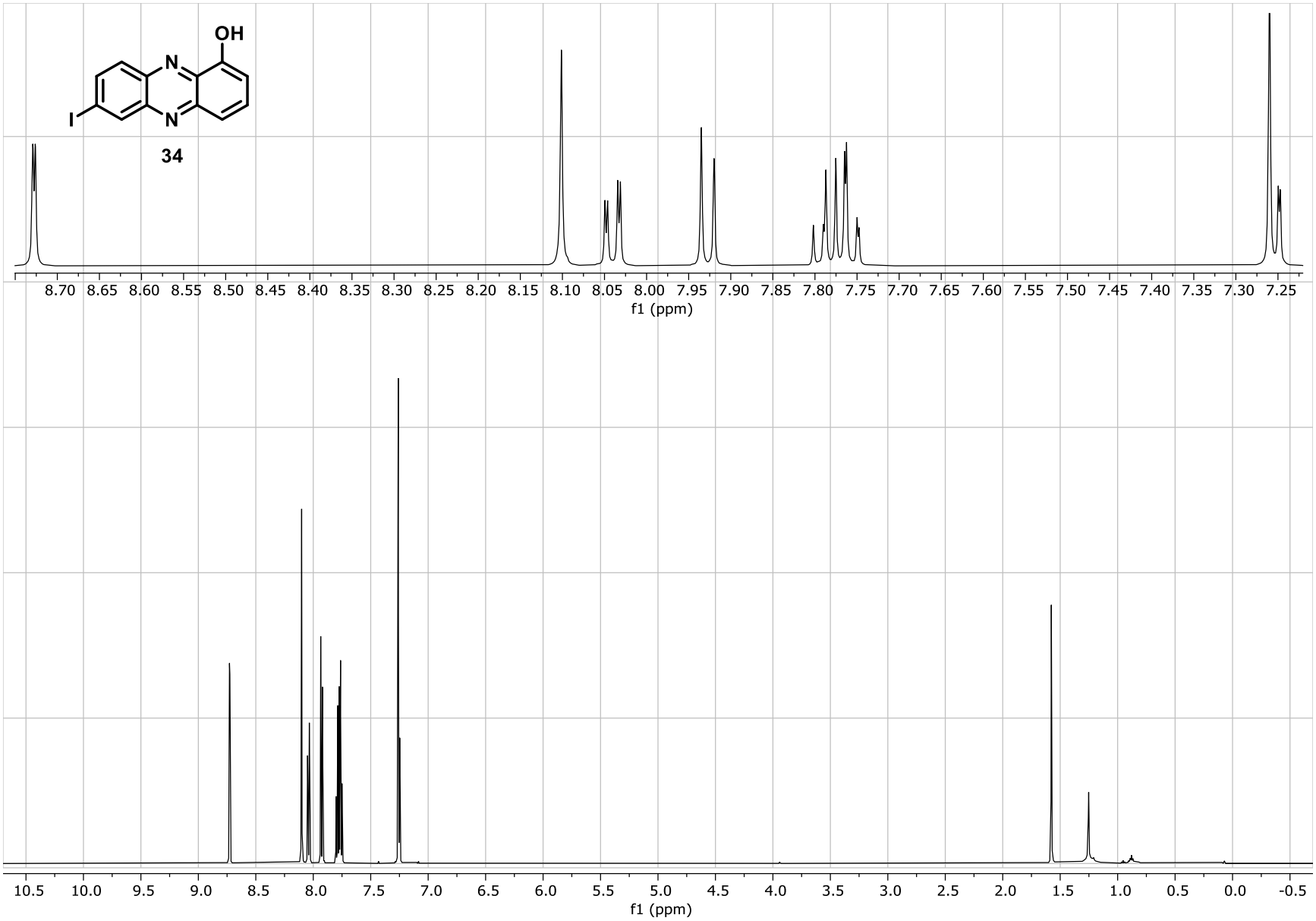

**Zoomed In Version: HMBC of 31 shows 2 overlapping carbon signals at 141.0 ppm (unable to differentiate signals at positions 7 & 9, 8 & 10, and 13 & 14)**

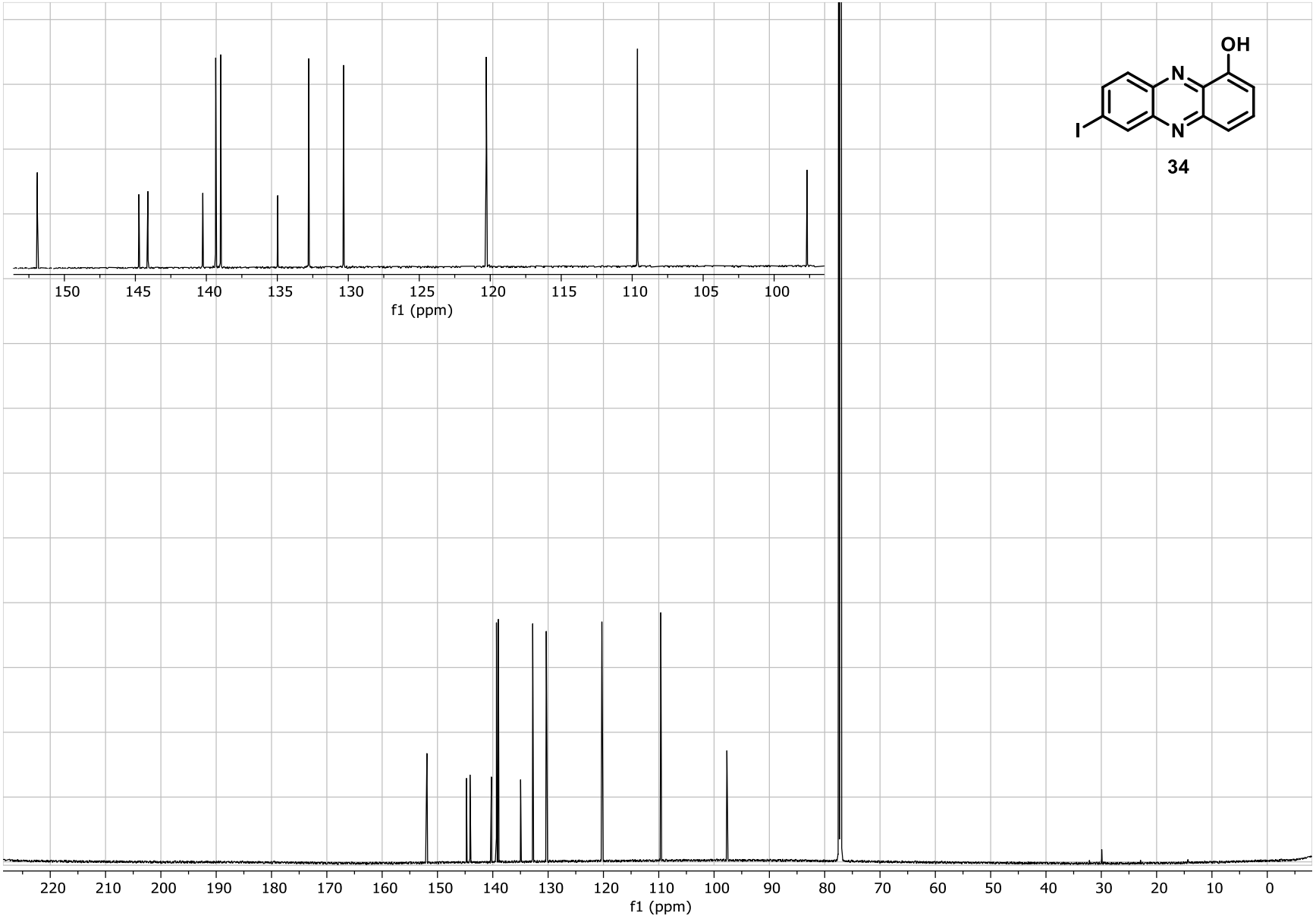

OH
N
N
F
32
8.25 8.20 8.15 8.10 8.05 8.00 7.95 7.90 7.85 7.80 7.75 7.70 7.65 7.60 7.55 7.50 7.45 7.40 7.35 7.30 7.25 7.20
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

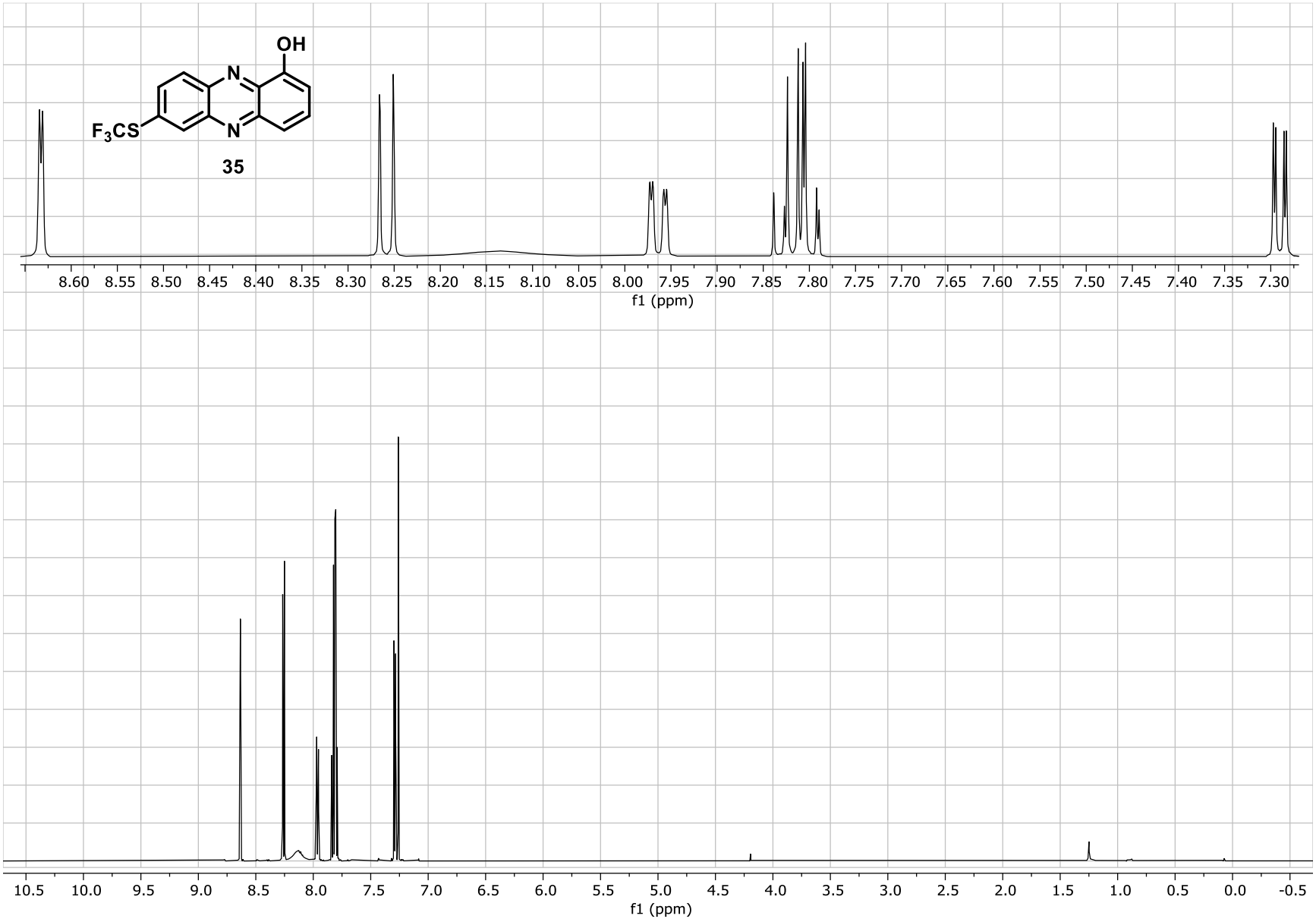

OH
N
F
N
32
160 155 150 145 140 135 130 125 120 115 110
f1 (ppm)
151.95
f1 (ppm)
144 143 142 141 140 139 138 137 136 135 134 133 132
f1 (ppm)
122 121 120 119 118 117 116 115 114 113 112 111 110
f1 (ppm)
109.11
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

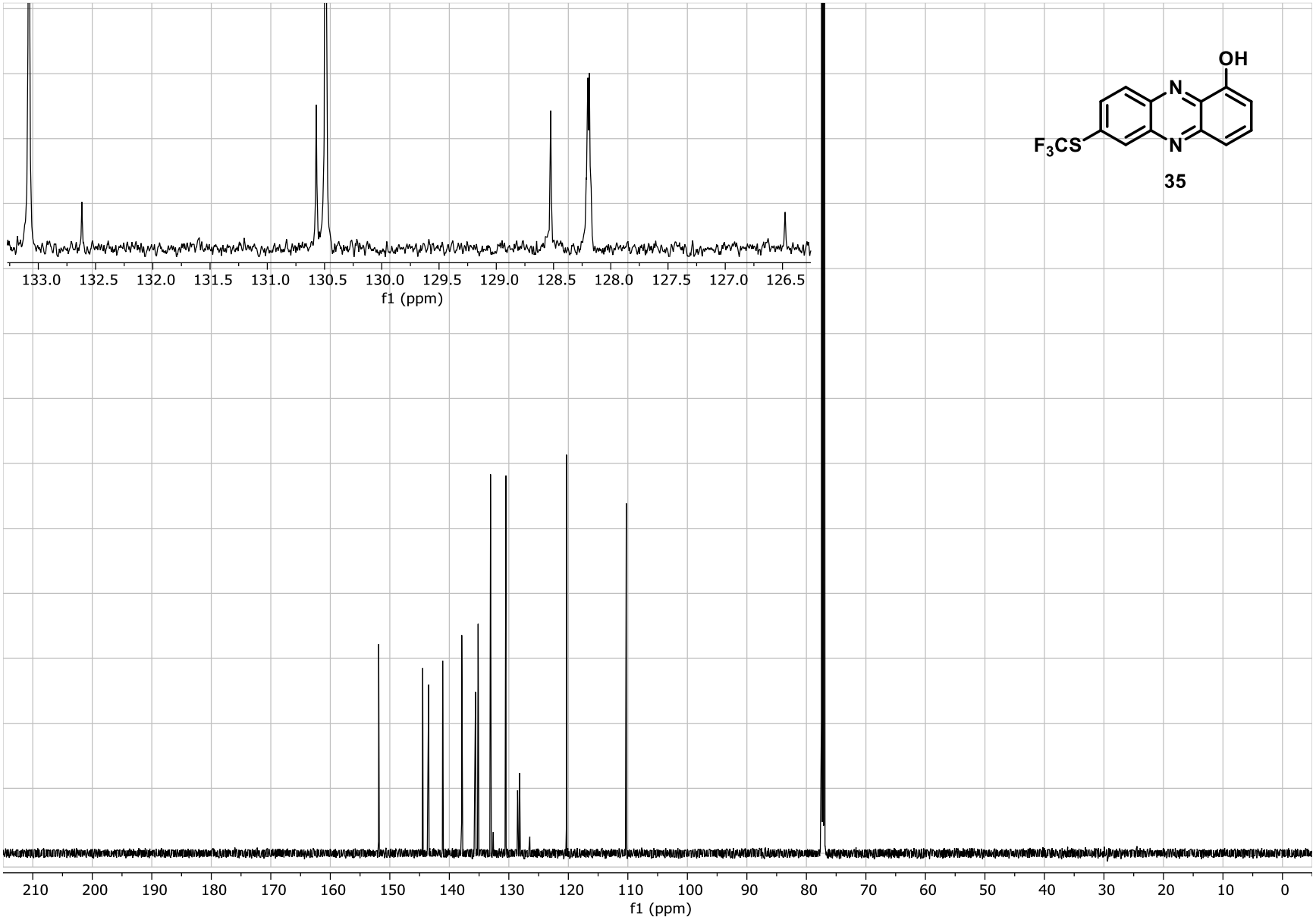

OH
N
N
Br
33
8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

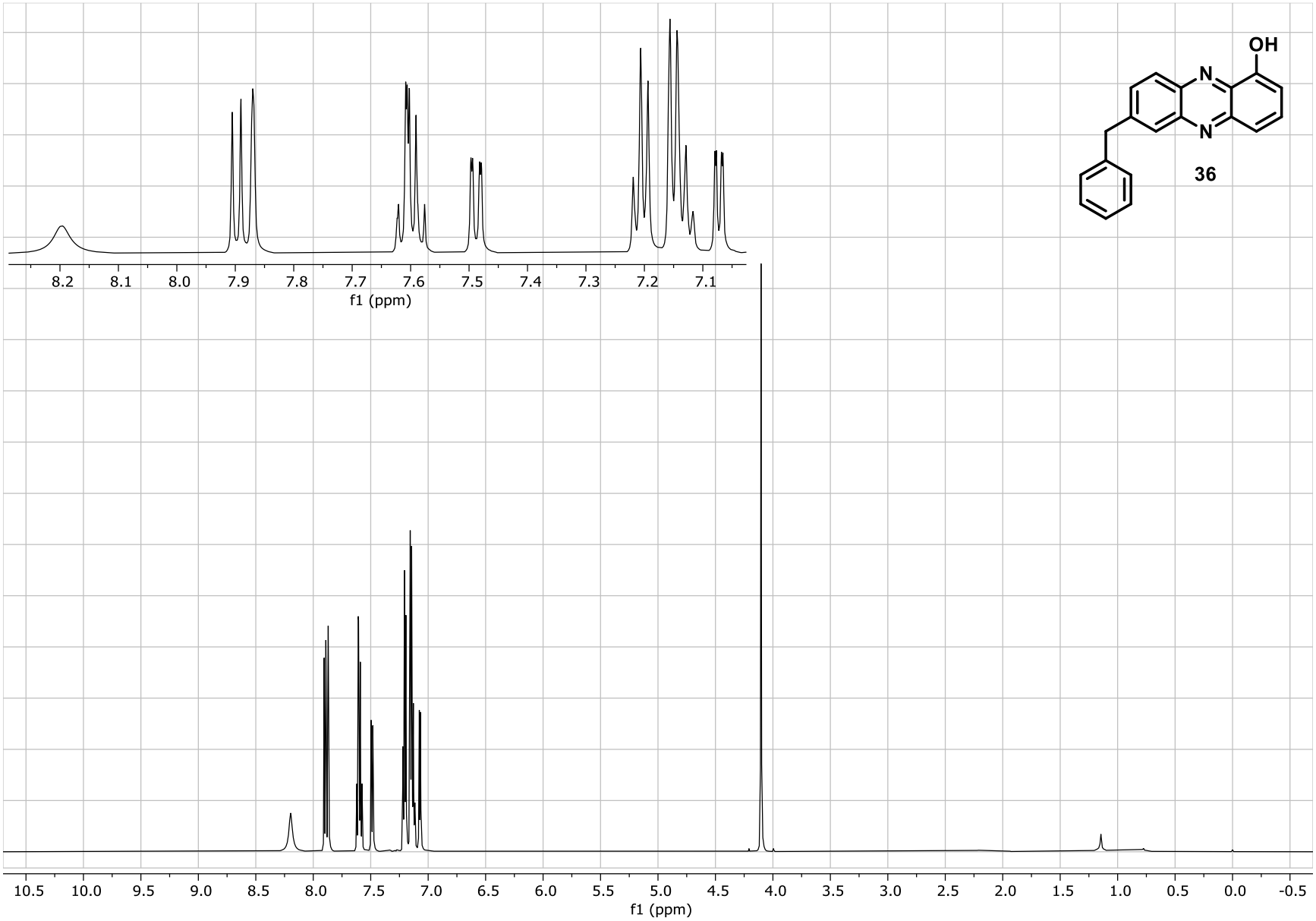

OH
N
N
Br
33
152 150 148 146 144 142 140 138 136 134 132 130 128 126 124 122 120 118 116 114 112 110
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

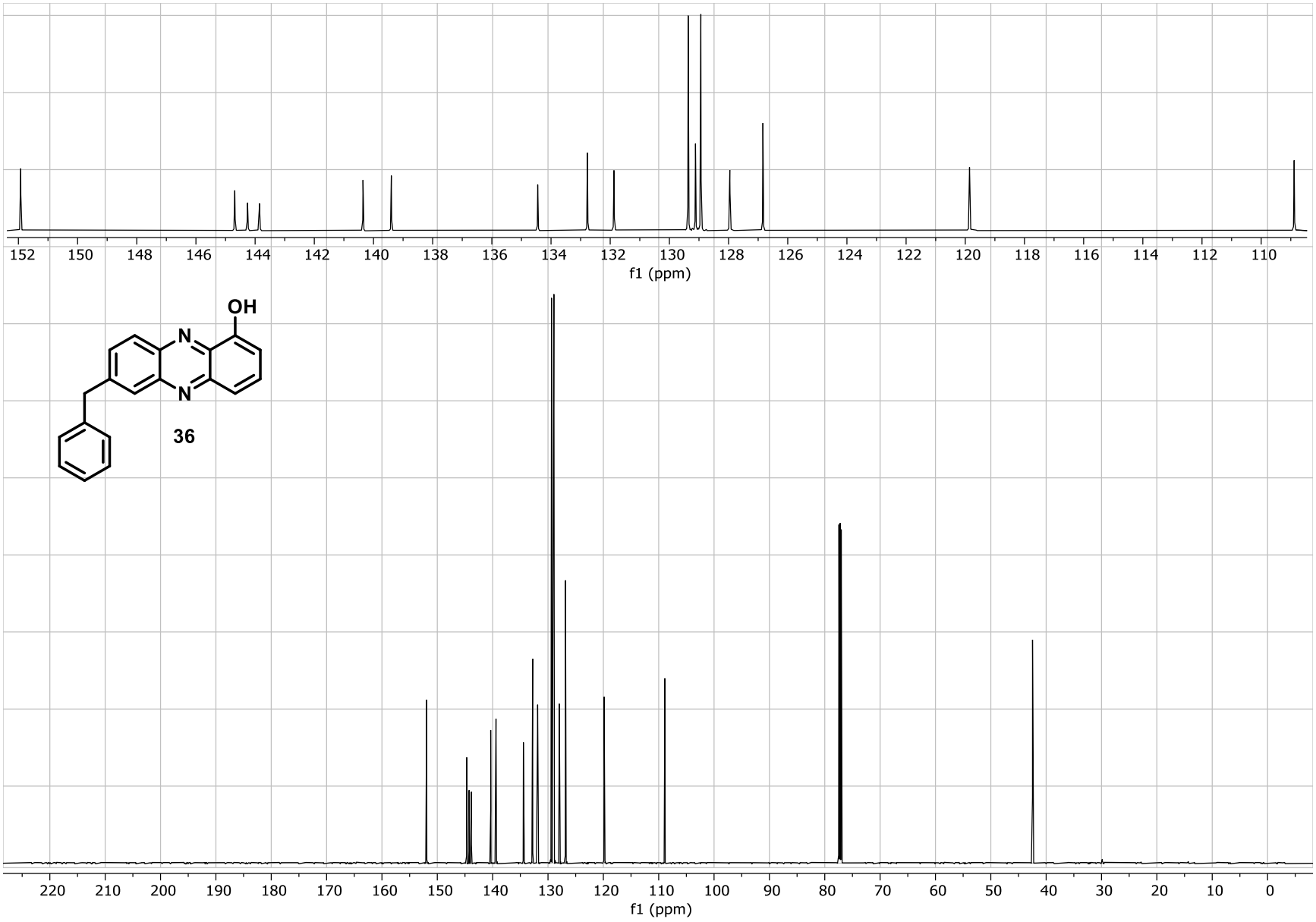

OH
N
N
I
34
8.70 8.65 8.60 8.55 8.50 8.45 8.40 8.35 8.30 8.25 8.20 8.15 8.10 8.05 8.00 7.95 7.90 7.85 7.80 7.75 7.70 7.65 7.60 7.55 7.50 7.45 7.40 7.35 7.30 7.25
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


OH
N
N
I
34
150
145
140
135
130
125
120
115
110
105
100
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


OH
N
N
F3CS
35
8.60 8.55 8.50 8.45 8.40 8.35 8.30 8.25 8.20 8.15 8.10 8.05 8.00 7.95 7.90 7.85 7.80 7.75 7.70 7.65 7.60 7.55 7.50 7.45 7.40 7.35 7.30
f1 (ppm)
10.5 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 0.0 -0.5
f1 (ppm)


OH
N
N
F3CS
35
133.0 132.5 132.0 131.5 131.0 130.5 130.0 129.5 129.0 128.5 128.0 127.5 127.0 126.5
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


OH
N
N
36
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
f1 (ppm)
10.5
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
0.0
-0.5
f1 (ppm)


OH
N
N
36
152 150 148 146 144 142 140 138 136 134 132 130 128 126 124 122 120 118 116 114 112 110
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)