Far-Red and Near-Infrared Seminaphthofluorophores for Targeted Pancreatic Cancer Imaging

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Supporting Information

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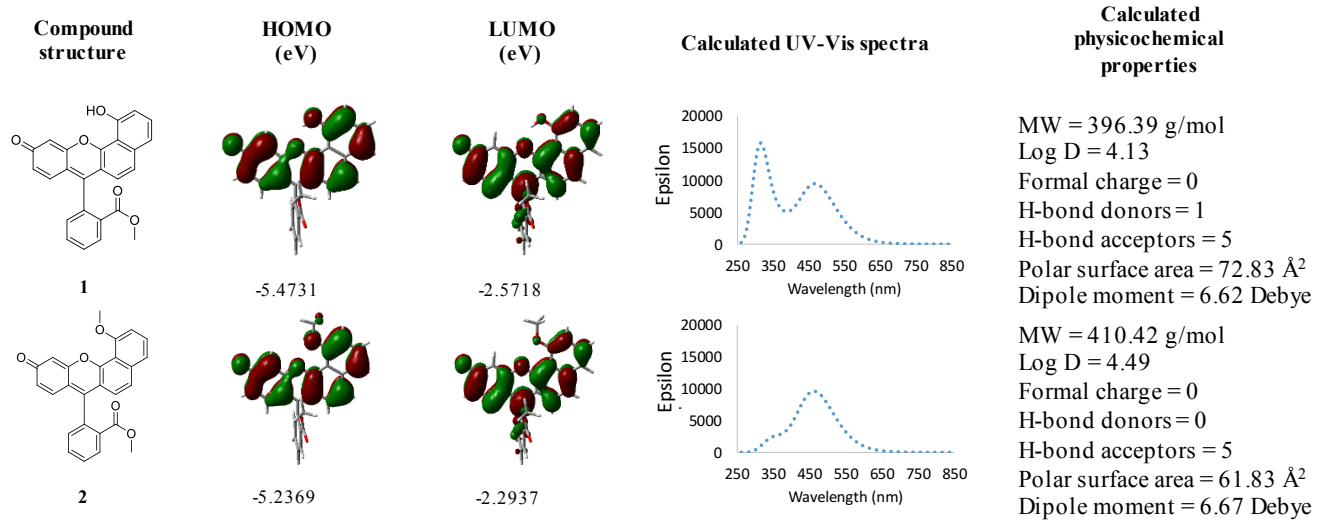


Figure S1. Energy levels and depiction of frontier molecular orbitals (HOMO and LUMO), calculated absorption spectra and physicochemical properties of seminaphthofluorescein. Molecular orbital, dipole moment and UV-Vis spectra calculations were carried out using time-dependent density functional theory (TD-DFT) on the gas-phase at the B3LYP/6-31G(d,p) level of the optimized geometries. Log D values at pH 7.4 and polar surface area were calculated using Marvin and JChem calculator plugins (ChemAxon, Budapest, Hungary).

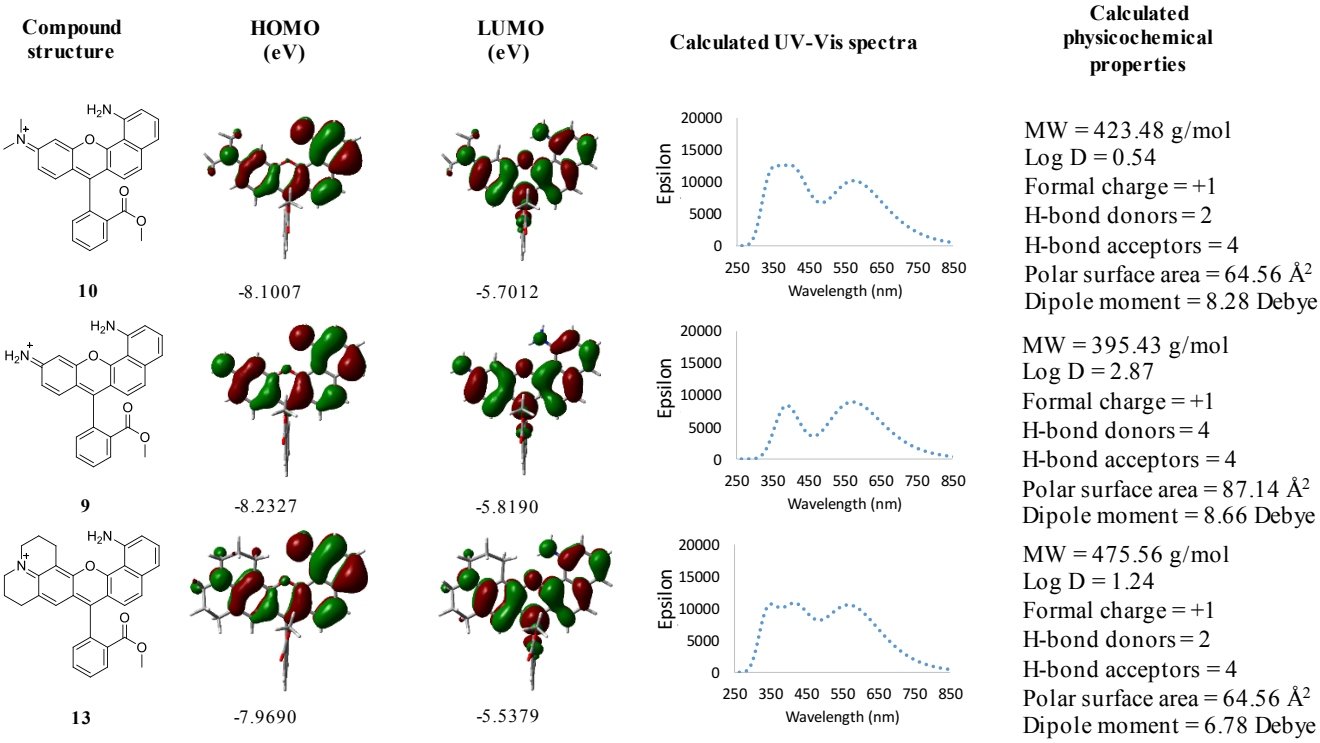


Figure S2. Energy levels and depiction of frontier molecular orbitals (HOMO and LUMO), calculated absorption spectra and physicochemical properties of seminaphthorhodamines. Molecular orbital, dipole moment and UV-Vis spectra calculations were carried out using time-dependent density functional theory (TDDFT) on the gas-phase at the B3LYP/6-31G(d,p) level of the optimized geometries. Log D values at pH 7.4 and polar surface area were calculated using Marvin and JChem calculator plugins (ChemAxon, Budapest, Hungary).

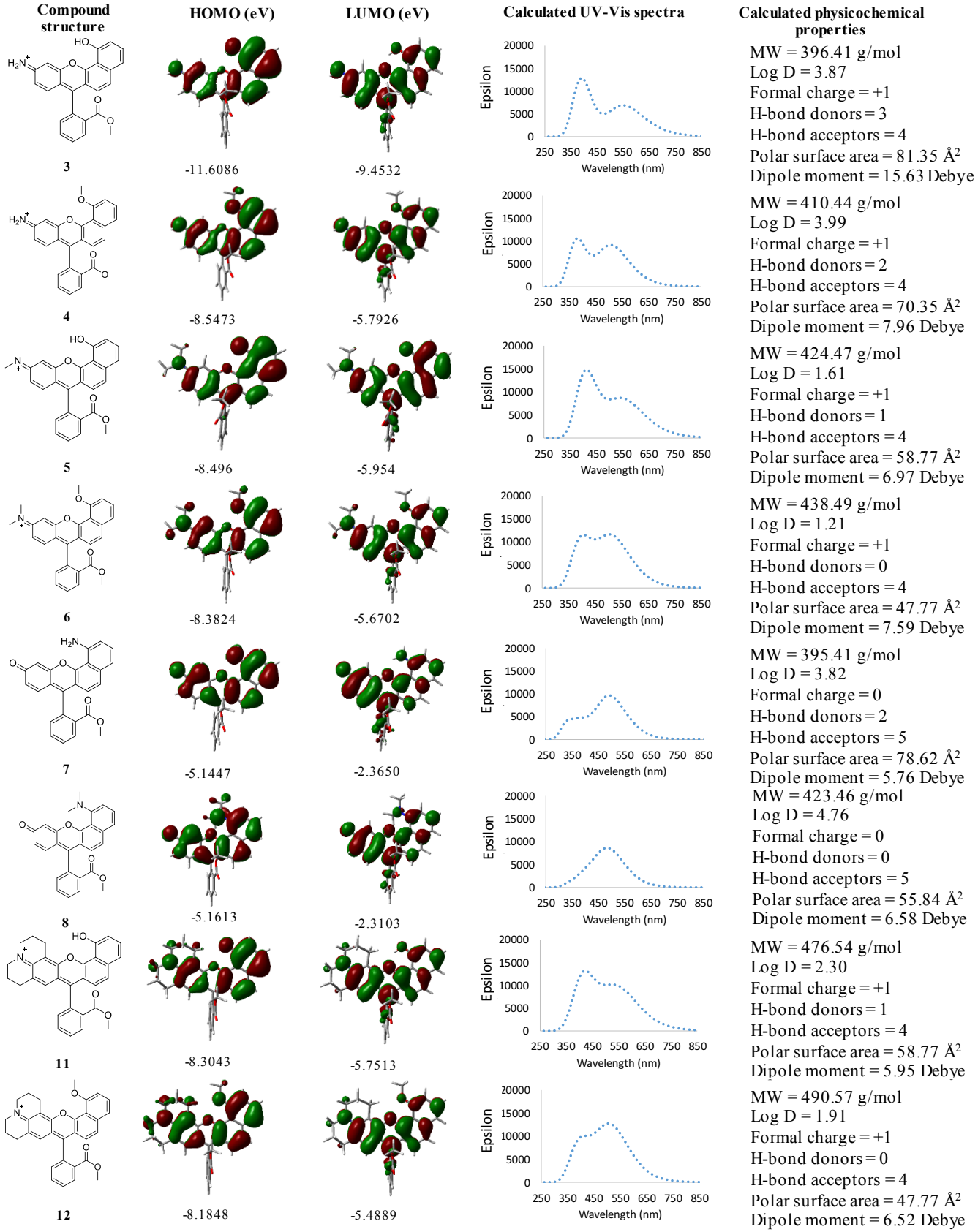
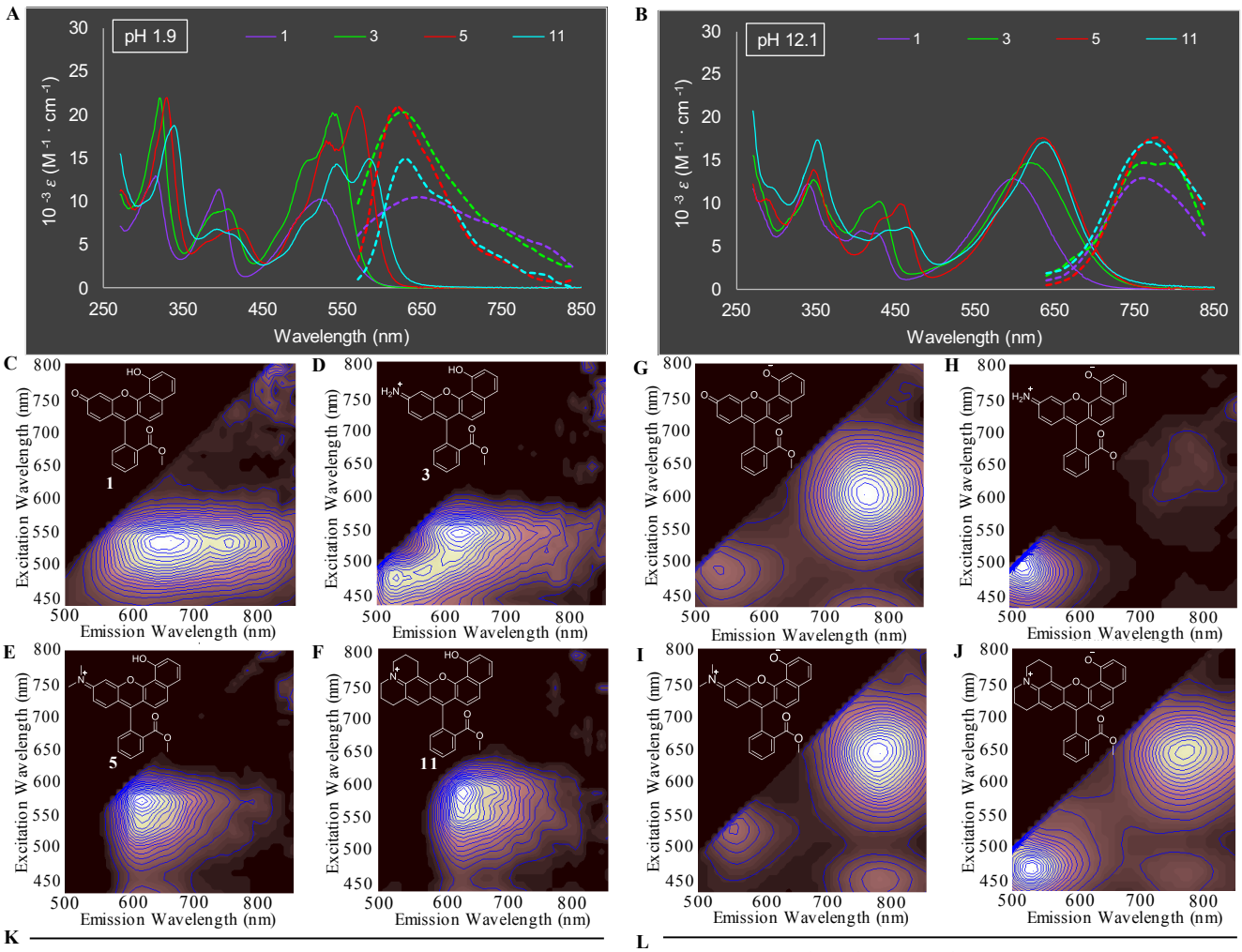


Figure S3. Energy levels and depiction of frontier molecular orbitals (HOMO and LUMO), calculated absorption spectra and physicochemical properties of seminaphthorhodafluors. Molecular orbital, dipole moment and UV-Vis spectra calculations were carried out using time-dependent density functional theory (TDDFT) on the gas-phase at the B3LYP/6-31G(d,p) level of the optimized geometries. Log D values at pH 7.4 and polar surface area were calculated using Marvin and JChem calculator plugins (ChemAxon, Budapest, Hungary).



K

Compound	λ_{max} abs (Extinction Coefficient) (nm) ($M^{-1}\cdot cm^{-1}$)	λ_{max} em (Quantum Yield) (nm) (%)	Stokes Shift (nm)	Brightness	pK_a
1	530 (12,167)	600 (1.17)	70	142	7.72 +/- 0.04
3	542 (19,787)	604 (1.14)	62	226	6.67 +/- 0.11
5	567 (20,399)	614 (4.09)	47	834	6.82 +/- 0.06
11	585 (15,134)	624 (15.3)	39	2314	7.84 +/- 0.11

L

Conjugate base of	λ_{max} abs (Extinction Coefficient) (nm) ($M^{-1}\cdot cm^{-1}$)	λ_{max} em (Quantum Yield) (nm) (%)	Stokes Shift (nm)	Brightness
1	599 (8,613)	760 (0.19)	161	16
3	621 (15,589)	770 (0.11)	149	17
5	632 (17,252)	780 (0.17)	148	29
11	643 (14,454)	770 (0.30)	127	43

Figure S4. pH-dependent spectral properties of dual-emitting seminaphthofluorescein (**1**) and seminaphthorhodafluors (**3**, **5** and **11**). (A) Absorption spectra (solid lines) and normalized fluorescence emission spectra (dash lines) of **1**, **3**, **5** and **11** in acidic solution (pH 1.9, HCl). (B) Absorption spectra and normalized fluorescence emission spectra of the conjugate bases in basic solution (pH 12.1, NaOH). (C-F) Excitation Emission Matrices (EEMs), of **1** (C), **3** (D), **5** (E) and **11** (F) in acidic solution. (G-J) EEMs of the conjugate bases in basic solution. (K) Tabulated spectral properties of **1**, **3**, **5** and **11** in acidic solution. (L) Tabulated spectral properties of the conjugate bases in basic solution. Fluorophore concentrations range from 10 to 15 μM. Aqueous solutions contain 10% DMSO and 12.5 mM HCl or NaOH. Red emitting species in (A) were excited at 480 nm or 510 nm. NIR emitting species in (B) were excited at 630 nm. Emission spectra in (A and B) are normalized to their corresponding absorption peaks. The color scale of EEMs (C-J) are normalized to the maximum of each plot. The spectral properties of compounds **1**, **3**, **5**, and **11** are pH sensitive as a result of the hydroxyl groups with pK_a values in the physiological range. In acid, the hydroxyl forms of the compounds display structured absorption peaks with maxima ranging from 530 to 585 nm, modest Stokes shifts, and fluorescence emission maxima between 600 and 624 nm. The conjugate bases of these compounds display broad featureless absorption peaks ranging from 599-643 nm, large Stokes shifts, and broad fluorescence emission peaks in the NIR. Quantum yields of the NIR emitting species were generally ~3-5 times higher in the organic solvents MeOH and DMSO as compared to aqueous solution.

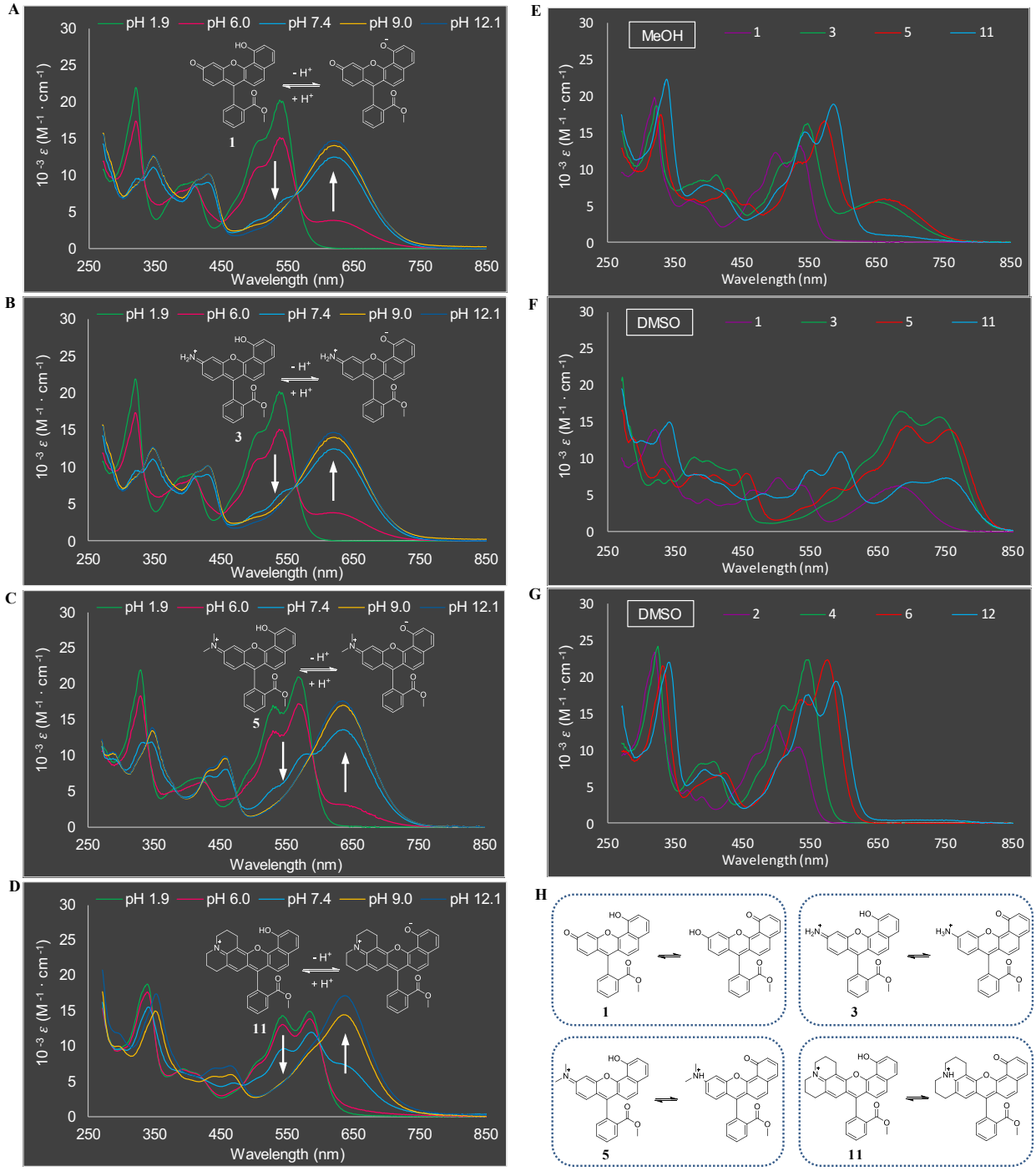
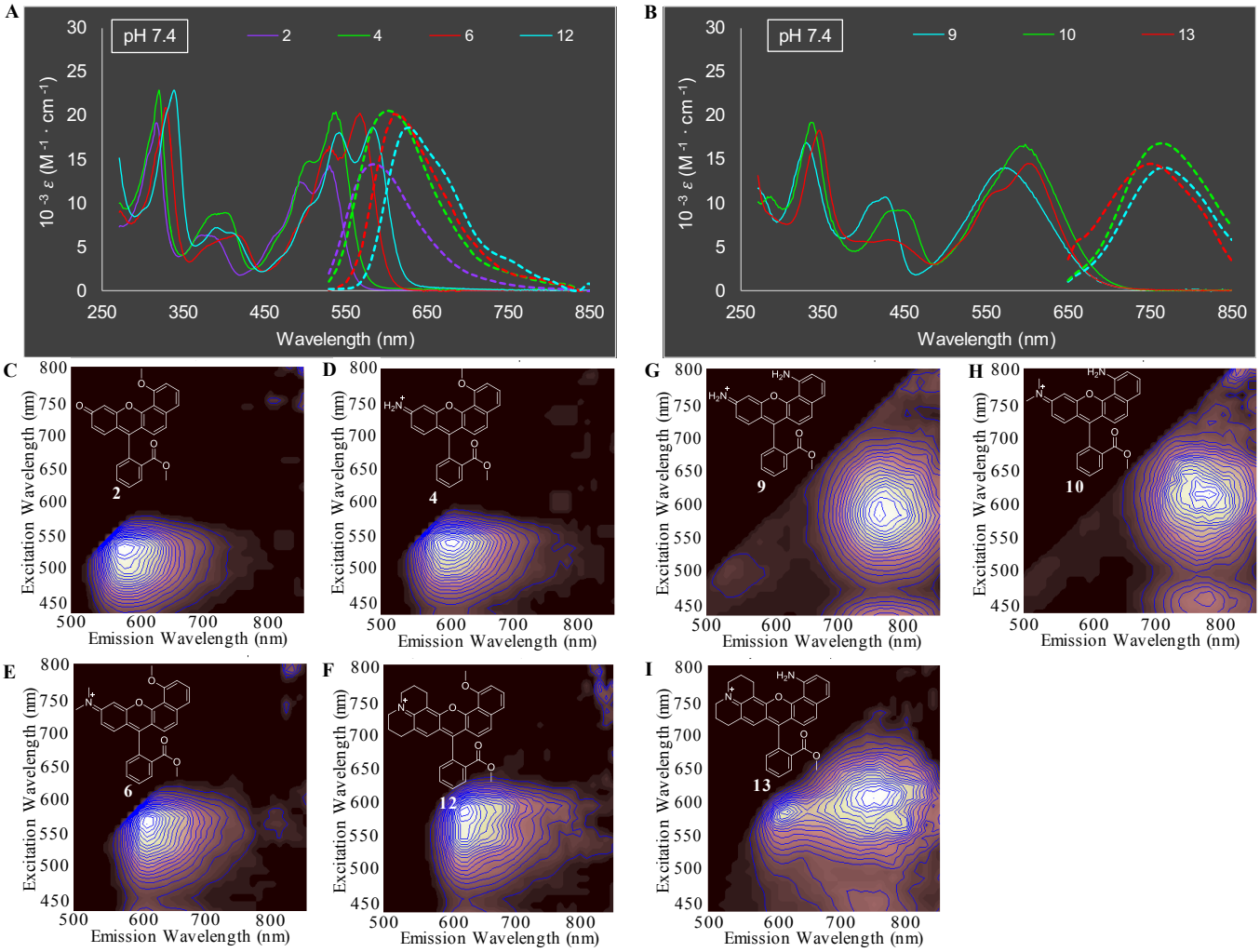


Figure S5. pH- and solvent-dependent absorption spectra of seminaphthofluorescein (**1**) and seminaphthorhodafluors (**3**, **5** and **11**). (A-D) Absorption spectra as a function of pH for **1** (A), **3** (B), **5** (C) and **11** (D). (E-F) Absorption spectra of **1**, **3**, **5** and **11** as a function of solvents including MeOH (E) and DMSO (F) display short and long wavelength absorption bands attributed to tautomer formation. (G) Absorption spectra of methyl ether derivatives (**2**, **4**, **6** and **12**) in DMSO do not exhibit tautomer formation. (H) Tautomerization equilibria. Chromophore concentrations range from 10 to 15 μM. Aqueous solutions contain 10% DMSO and 12.5 mM HCl, phosphate buffer, or NaOH. Ratiometric absorption spectra with pK_a values in the physiological range were observed for **1**, **3**, **5** and **11**. Well defined isosbestic points indicate spectral changes result from acid-base equlibria between two species. In aqueous solution at low pH, a single tautomer with hydroxyls on the annulated ring dominate. Absorptions from both tautomers are apparent in organic solvents. Long wavelength tautomers are more pronounced in **3** and **5** as compared to **1** and **11**; and in DMSO as compared to MeOH. Methyl ether derivatives **2**, **4**, **6** and **12** approximate naphthol tautomers , existing as single species similar to short wavelength tautomers of **1**, **3**, **5**, and **11** in organic solvents.



J

Compound	λ_{max} abs (Extinction Coefficient) (nm) ($M^{-1}\cdot cm^{-1}$)	λ_{max} em (Quantum Yield) (nm) (%)	Stokes shift (nm)	Brightness
2	530 (15,610)	580 (46.49)	50	7257
4	538 (21,742)	596 (34.42)	58	7484
6	568 (22,470)	606 (9.32)	38	2094
12	582 (17,764)	622 (11.38)	40	2022

K

Compound	λ_{max} abs (Extinction Coefficient) (nm) ($M^{-1}\cdot cm^{-1}$)	λ_{max} em (Quantum Yield) (nm) (%)	Stokes Shift (nm)	Brightness
9	576 (13,872)	760 (0.18)	184	25
10	598 (17,066)	770 (0.20)	172	34
13	601 (12,808)	740 (0.66)	139	85

Figure S6. pH-independent spectral properties of red-emitting methyl ether derivatives (**2**, **4**, **6** and **12**) and NIR-emitting seminaphthorhodamines (**9**, **10** and **13**) in pH 7.4 buffer. (A) Absorption spectra (solid lines) and normalized fluorescence emission spectra (dash lines) of methyl ether derivatives (**2**, **4**, **6** and **12**). (B) Absorption spectra and normalized fluorescence emission spectra of seminaphthorhodamines (**9**, **10** and **13**). (C-F) EEMs of methyl ether derivatives **2** (C), **4** (D), **6** (E) and **12** (F), (G-I) EEMs of seminaphthorhodamines **9** (G), **10** (H) and **13**(I). (J) Tabulated spectral properties of methyl ether derivatives. (K) Tabulated spectral properties of seminaphthorhodamines. Fluorophore concentrations range from 10 to 15 µM. Aqueous solutions contain 10% DMSO and 12.5 mM pH 7.4 phosphate buffer. Red emitting methyl ether derivatives in **a** were excited at 480 nm. NIR emitting seminaphthorhodamines in (B) were excited at 630 nm. Emission spectra in (A and B) are normalized to their corresponding absorption peaks. The color scale of EEMs (C-I) are normalized to the maximum of each plot. Replacing the ionizable hydroxyl groups with a methyl ether (compounds **2**, **4**, **6**, **12**) removes both the pH and tautomeric equilibria of compounds **1**, **3**, **5**, **11**, thus approximating naphthol tautomers in a range of solvents and pH values. Absorption spectra of the methyl ether derivatives are nearly identical to their corresponding hydroxyl analogs. Emission wavelengths of the methyl ethers remain in the orange/red region. Quantum yields of the methyl ethers range from ~10-45% and are generally improved as compared to their hydroxyl analogs (improvements of ~40 fold for **2**,

30 fold for **4** and more than 2 fold for **6**). Alternatively, replacing the hydroxyl group with an NH_2 group (compounds **9**, **10** and **13**) provides another method to remove the pH dependence while maintaining the long wavelength NIR emission observed in the conjugate bases of compounds **3**, **5**, and **11** in a range of pH values for the resulting seminaphthorhodamines. The seminaphthorhodamines show no sensitivity to pH over a wide range encompassing physiological pH. Emission maxima are all greater than 740 nm with large Stokes shifts. The seminaphthorhodamines are approximately twice as bright as the corresponding long wavelength emissions observed for the conjugate bases of compounds **3**, **5** and **11**. Quantum yields of the NIR emitting species were generally ~3-5 times higher in the organic solvents MeOH and DMSO as compared to aqueous solution.

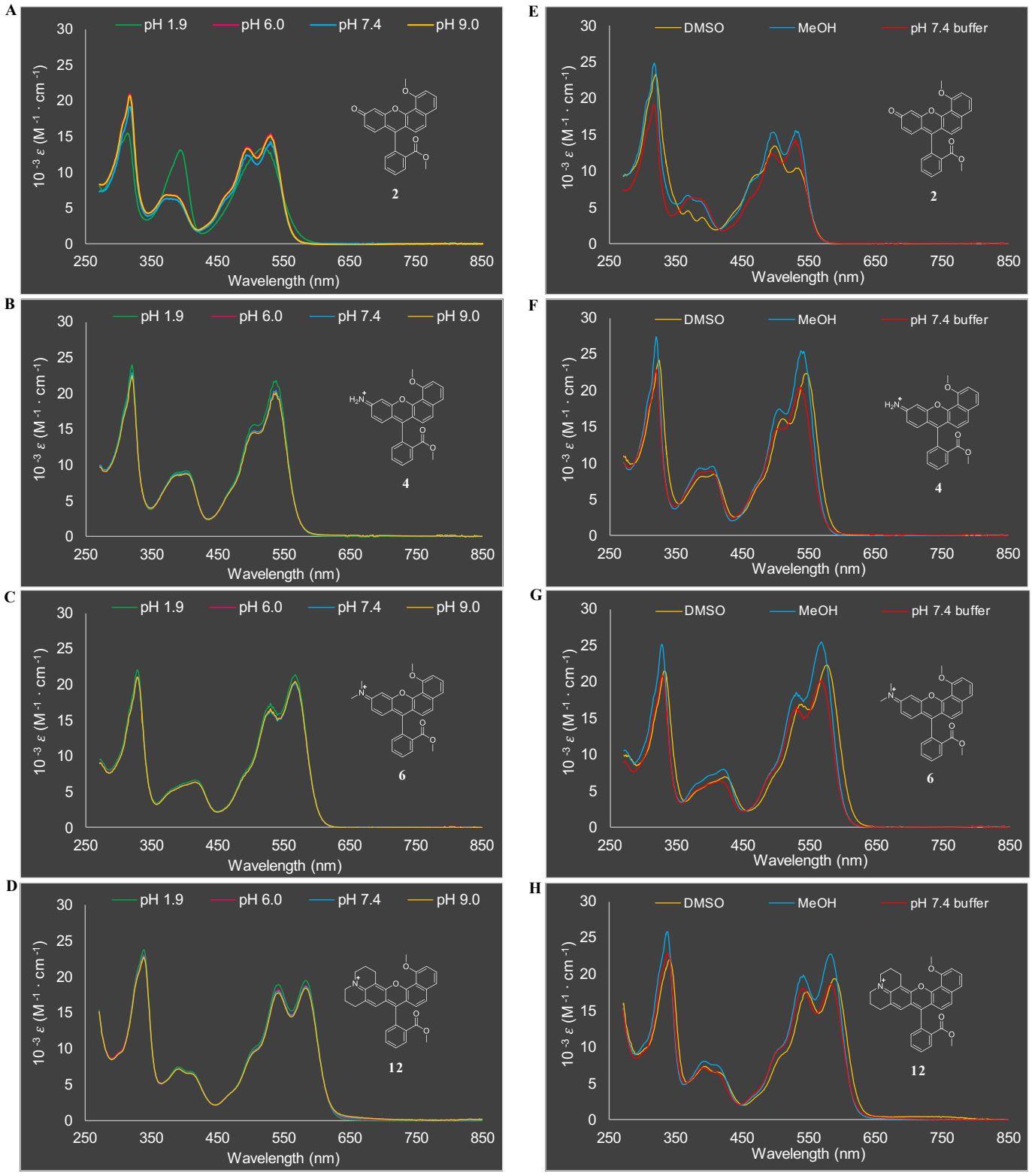


Figure S7. pH- and solvent independent absorption spectra of methyl ether derivatives (**2**, **4**, **6** and **12**). (A-D) Absorption spectra as a function of pH for methyl ether derivatives **2** (A), **4** (B), **6** (C) and **12** (D). (E-H) Absorption spectra of methyl ether derivatives as a function of solvents including DMSO, MeOH and pH 7.4 phosphate buffer. Chromophore concentrations range from 10 to 15 µM. Aqueous solutions contain 10% DMSO and 12.5 mM HCl, phosphate buffer, or NaOH. No pH or tautomeric equilibria are observed for the methyl ether derivatives. There was no significant change in wavelength upon changing solvents from DMSO to MeOH to aqueous solution.

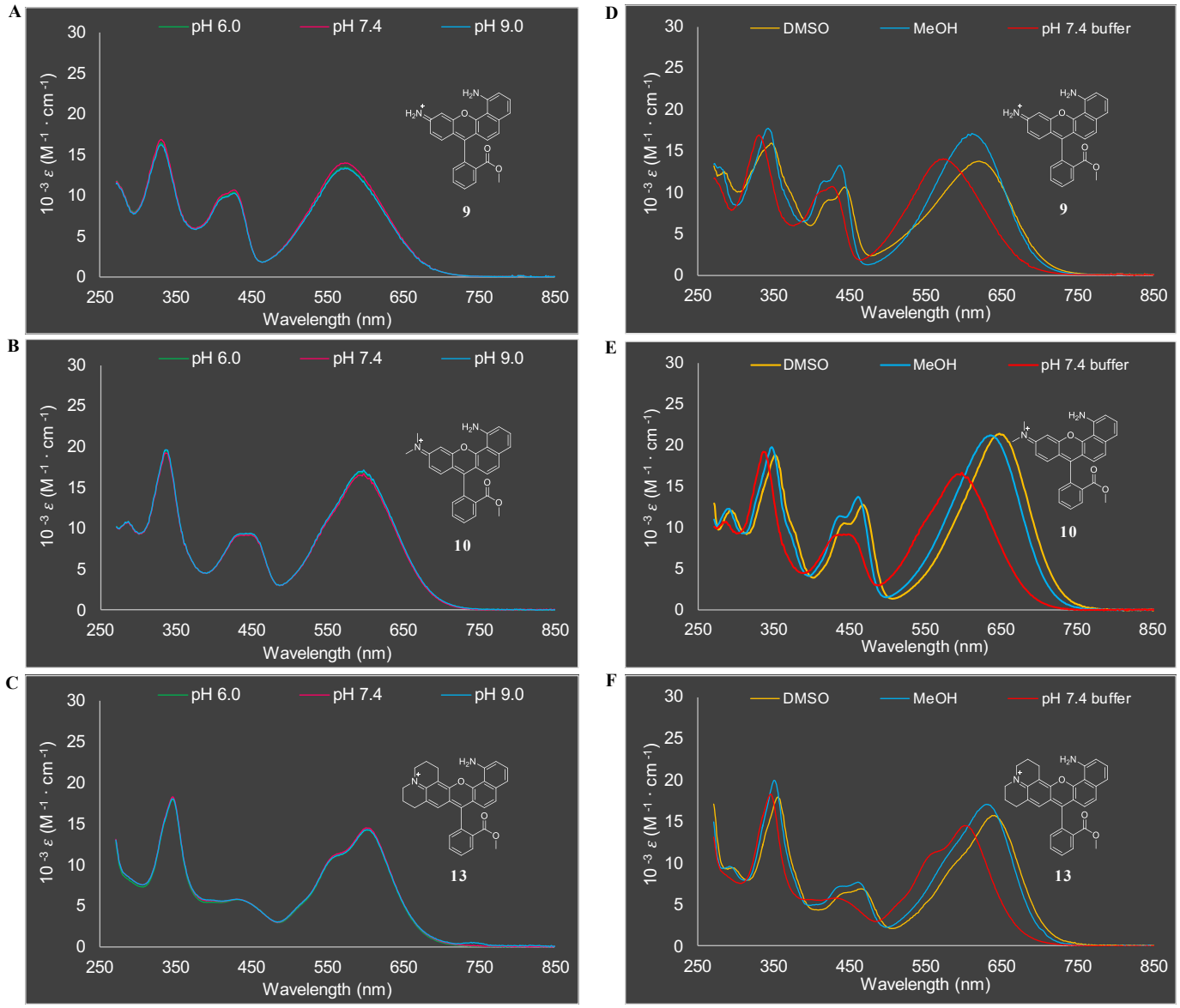
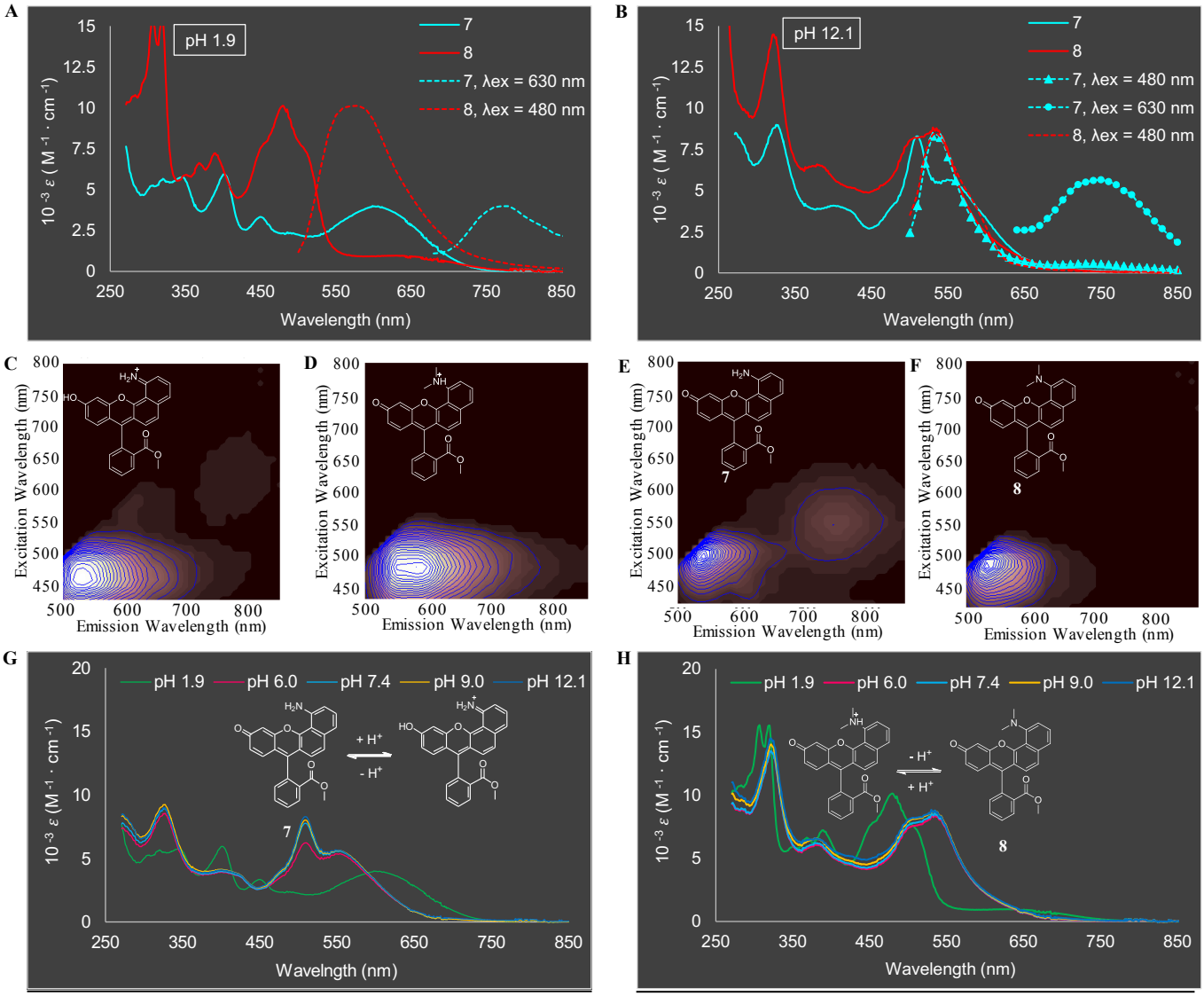


Figure S8. Absorption spectra of seminaphthorhodamines (**9**, **10** and **13**) as a function of pH and solvent. (A-C) Absorption spectra as a function of pH for pH independent seminaphthorhodamines **9** (A), **10** (B) and **13** (C). (D-F) Absorption spectra of seminaphthorhodamines as a function of solvents including DMSO, MeOH, and pH 7.4 phosphate buffer. Chromophore concentrations range from 10 to 15 µM. Aqueous solutions contain 10% DMSO and 12.5 mM HCl, phosphate buffer, or NaOH. No pH equilibria are observed for the seminaphthorhodamine derivatives. Seminaphthorhodamines **9**, **10** and **13** display moderate sensitivity to polarity with the longest wavelengths in DMSO and the shortest in aqueous solution.



I

Conjugate acid of	λ_{max} abs (Extinction Coefficient) (nm) ($M^{-1}\cdot cm^{-1}$)	λ_{max} em (nm)	Stokes Shift (nm)	pK_a
7	598 (3,996)	770	172	4.99 +/- 0.13
8	480 (10,132)	580	100	4.36 +/- 0.04

J

Compound	λ_{max} abs (Extinction Coefficient) (nm) ($M^{-1}\cdot cm^{-1}$)	λ_{max} em (nm)	Stokes Shift (nm)
7	509 (8,300)	530	21
7	549 (5,664)	750	201
8	530 (8,834)	530	21

Figure S9. pH dependent spectral properties of transposed seminaphthorhodafluors (**7** and **8**). (A) Absorption spectra (solid lines) and normalized fluorescence emission spectra (dash lines) of conjugate acids in acidic solution (pH 1.9, HCl). (B) Absorption spectra and normalized fluorescence emission spectra of **7** and **8** in basic solution (pH 12.1, NaOH). (C-D) EEMs of conjugate acids in acidic solution. (E-F) EEMs of **7** (E) and **8** (F) in basic solution. (G) Absorption spectra as a function of pH for **7**. (H) Absorption spectra as a function of pH for **8**. (I) Tabulated spectral properties of the conjugate acids in acidic solution. (J) Tabulated spectral properties of **7** and **8** in basic solution. Fluorophore concentrations are 15 μM. Aqueous solutions contain 10% DMSO and 12.5 mM HCl, phosphate buffer, or NaOH. Red emitting species in (A) and (B) were excited at 480 nm. NIR emitting species in (A) and (B) were excited at 630 nm. Emission spectra in (A) and (B) are normalized to their corresponding absorption peaks. The color scale of EEMs (C-F) are normalized to the maximum of each plot. Compared to seminaphthorhodafluors **3** and **5**, the hydroxyl and amine groups are transposed in compounds **7** and **8**. Seminaphthorhodafluors **3** and **5** were isolated as acidic salts with pK_a values in the physiological range, resulting in ratiometric spectral properties (short wavelength absorption and emission for the acids with long wavelength absorption and emission for the conjugate bases). The transposed compounds were isolated as neutral species, having pK_a values

approximately 2 units lower, thus displaying no sensitively to pH over the physiological range. At physiological pH and in organic solvents, both **7** and **8** displayed an absorption maxima near 525 nm. Protonation leads to a long wavelength absorption near 600 nm for **7** and short wavelength absorption near 450 nm for **8**. Compound **8** was short wavelength absorbing and emitting as both the base and conjugate acid with no long wavelength species observed. Interestingly, **7** displayed dual emission as both the base and conjugate acid. These dual emissions are attributed to different tautomeric forms exhibiting less strained geometries.

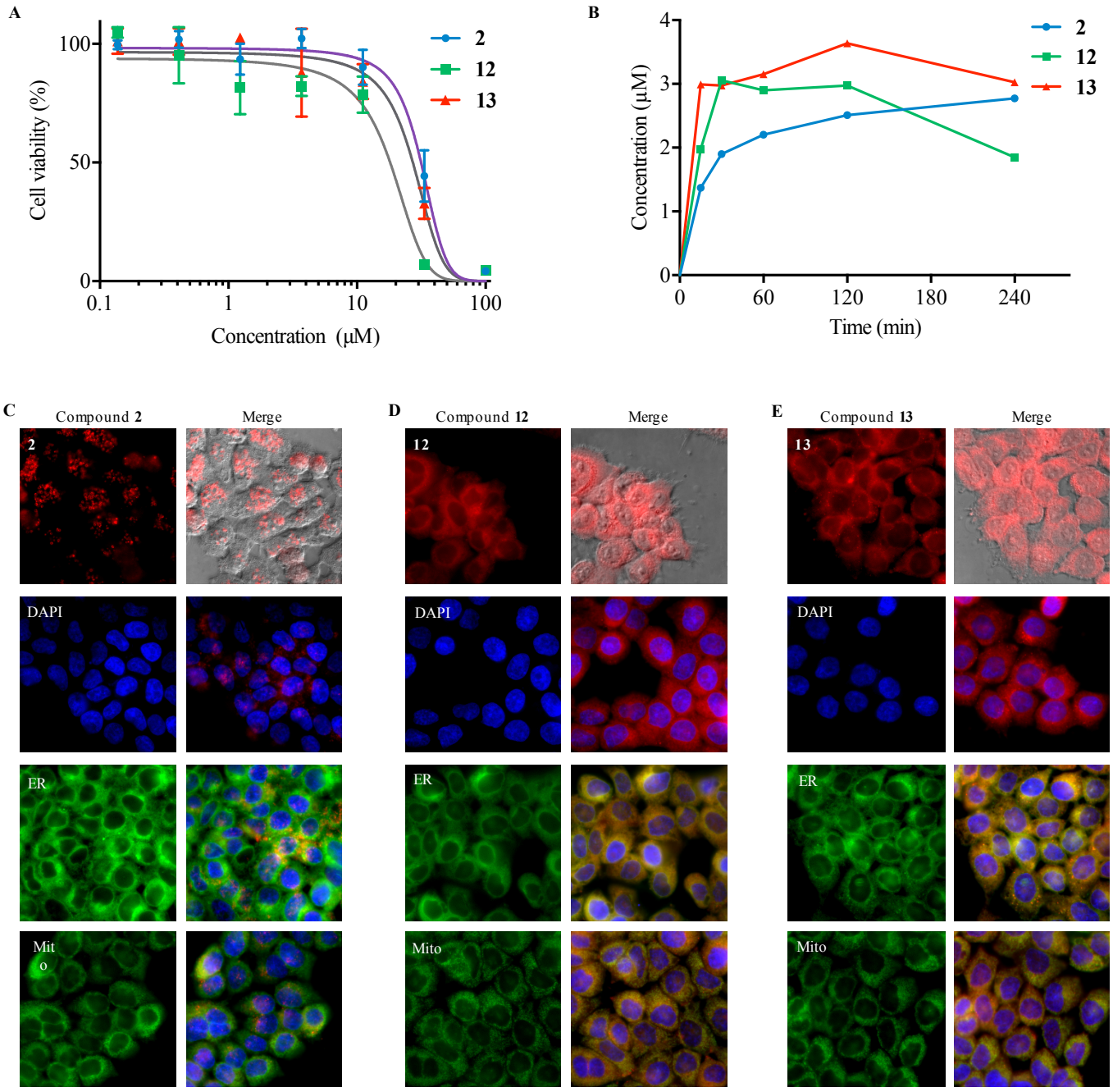


Figure S10. Cell viability, cellular uptake and subcellular localization of compounds **2**, **12**, and **13** in Capan-1 cells. **a**, Cytotoxicity of **2**, **12**, and **13**. **b**, Cellular uptake of **2**, **12**, and **13**. **c-e**, Subcellular localization of compounds **2** (**c**), **12** (**d**) and **13** (**e**). Fluorescence images containing synthesized fluorophores are labeled as **2**, **12** or **13** (red). Images of subcellular organelles stained with commercial fluorescent trackers are labeled as DAPI (blue), ER (green) or Mito (green). The merge columns show images of (top) phase contrast of the compound of interest, followed successively below by colocalization of DAPI + the compound of interest, colocalization of DAPI + ER + the compound of interest, and colocalization of DAPI + Mito + the compound of interest. Compounds **12** and **13** demonstrated extensive accumulation in the mitochondria and limited accumulation in the nucleus and ER.

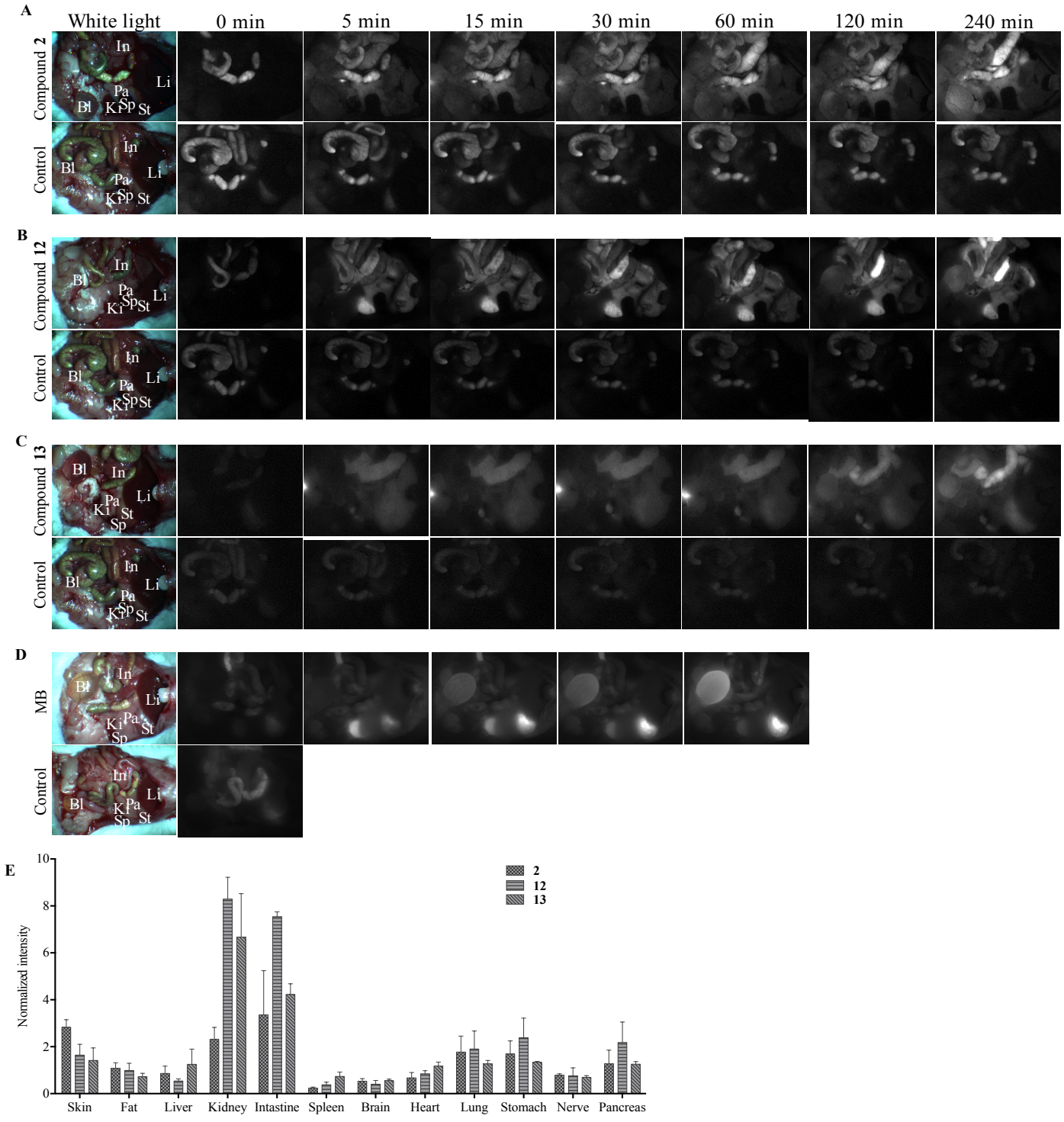


Figure S11. Biodistribution profile of compound **2**, **12**, **13** and MB in healthy CD-1 mice. Representative images of the fluorescence intensity in the peritoneal cavity over time following systemic administration of compound **2** (A), **12** (B), **13** (C), and MB (D). All images are representative of data collected for $n = 3$ systemically injected mice per compound. All fluorescence images were collected at 50 ms exposure time. All images are displayed with equivalent normalization between time points and to images of a control, uninjected mouse. In = Intestine; Li = liver; Pa = pancreas; Sp = spleen; St = stomach; Bl = Bladder; Ki = Kidney.(E) *Ex vivo* resected organ normalized fluorescence intensity comparison of compound **2**, **12**, and **13**. Mean resected organ fluorescence intensity 4 hours after systemic administration of compounds **2**, **12**, or **13**. All mean fluorescence intensity was calculated for $n = 3$ injected mice per compound. Fluorescence intensities for each organ were normalized to the muscle fluorescence intensity per animal. Data is presented as the mean ± S.D.

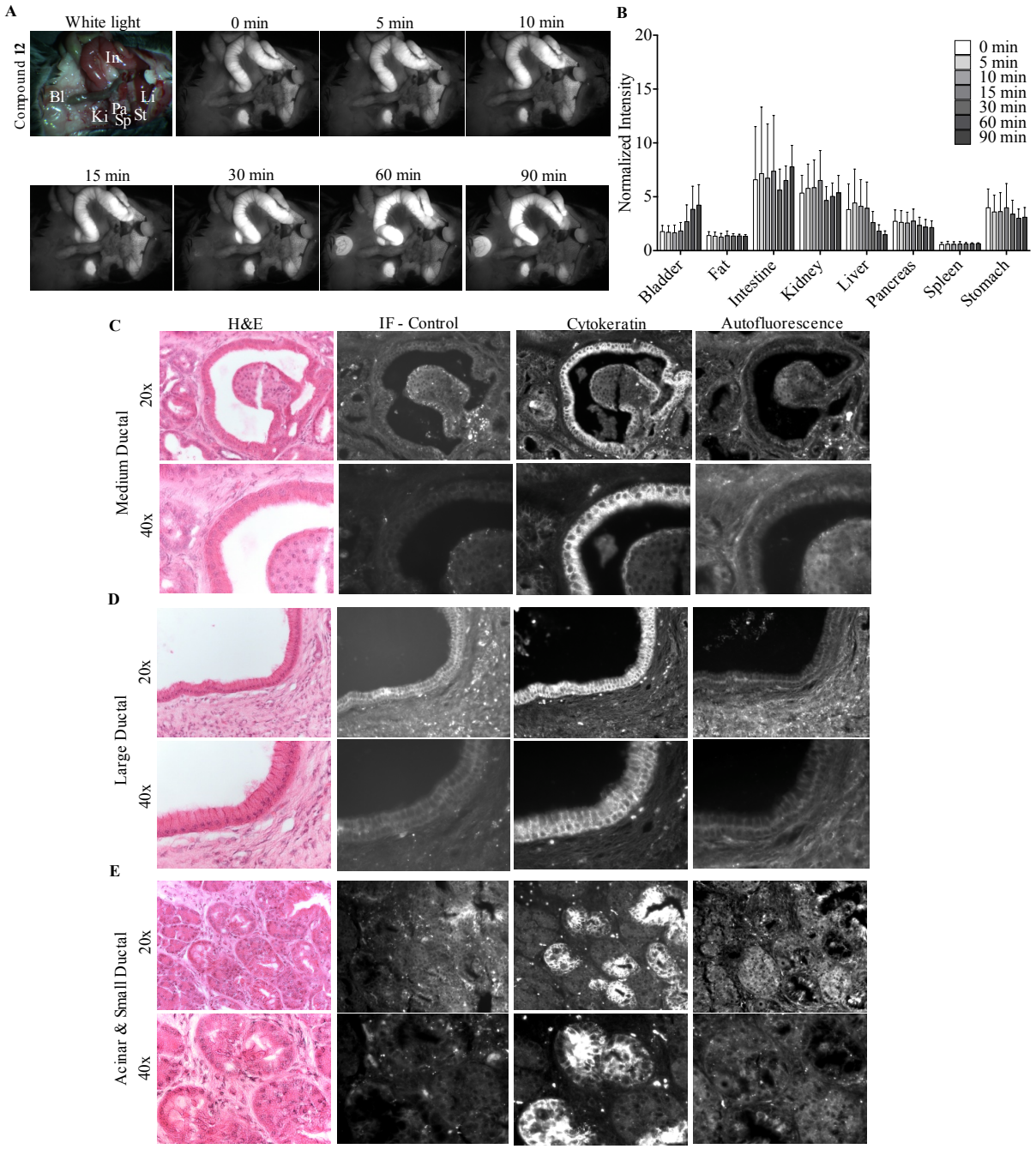
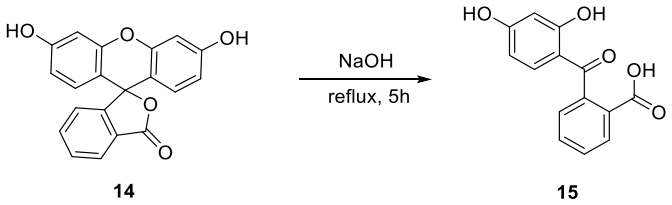


Figure S12. Biodistribution of compound **12** in PDAC mice and *ex vivo* pathology of resected PDAC tissue from uninjected control mice. (A) Representative images of the fluorescence intensity in the peritoneal cavity over time following systemic administration of compound **12** in PDAC tumor bearing mice and (B) corresponding mean fluorescence intensities measured for each organ. All images are representative of data collected for $n = 5$ systemically administered mice. All fluorescence images were collected at 50 ms exposure time. All images are displayed with equivalent normalization between time points. Quantified fluorescence intensity for each organ was normalized to the muscle intensity per animal per time point. Data is presented as the mean ± S.D. In = Intestine; Li = liver; Pa = pancreas; Sp = spleen; St = stomach; Bl = Bladder; Ki = Kidney. (C-E) Representative microscopy images of (C) medium and (D) large duct type adenocarcinoma tissue and of (E) normal pancreatic acinar cells next to small duct type adenocarcinoma tissue resected from uninjected PDAC tumor bearing mice. Control IF images were collected from serial sections that had been stained using the same procedure as those for cytokeratin visualization, but with blank staining solution to demonstrate antibody staining specificity. Images were collected in the compound **12** fluorescence channel and were normalized to compound **12** fluorescence images in Figure 7 for each respective tissue type to demonstrate autofluorescence in the compound **12** fluorescence channel in unstained PDAC tissue.

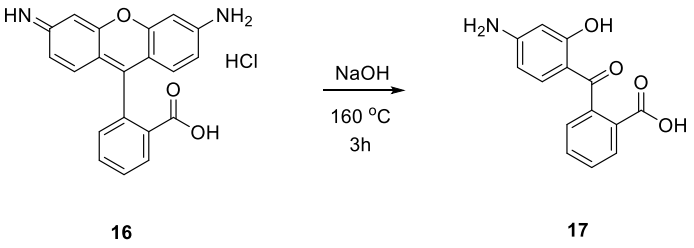
Synthesis and Characterization Data

General. Unless otherwise indicated, all commercially available starting materials were used directly without further purification. Silica gel Sorbent Technologies 32-63 μm was used for flash column chromatography. ^{1}H- and ^{13}C NMR were obtained on either a ARX-400 or ARX 600 Advance Bruker spectrometer. Chemical shifts (δ) are given in ppm relative to DMSO-d_6 (2.50 ppm, ^{1}H, 39.52 ^{13}C) unless otherwise indicated. MS (HRMS, ESI) spectra were obtained at the PSU Bioanalytical Mass Spectrometry Facility on a ThermoElectron LTQ-Orbitrap high resolution mass spectrometer with a dedicated Accela HPLC system. Compounds **1** and **2** were synthesized as described in the literature.[18]



Scheme S1. Synthesis of 2-(2,4-dihydroxybenzoyl)benzoic acid, **15**.

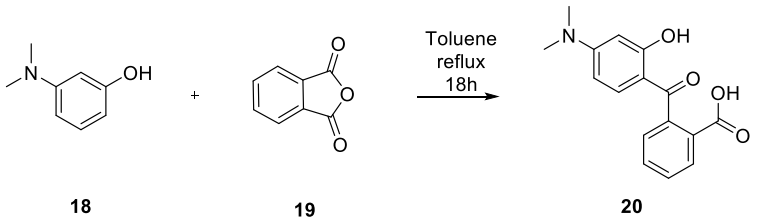
2-(2,4-dihydroxybenzoyl)benzoic acid, 15. NaOH (50 g, 1.25 mol) is dissolved in 100 mL of DI water while cooling in an ice bath. Fluorescein (**14**) is added in one portion and the mixture is refluxed 5h. The mixture is cooled down to room temperature and neutralized to pH 7 using concentrated HCl. The mixture is treated with 2% $NaHCO_3$ to dissolve the solid formed, and then extracted with ethyl ether (3 × 100 mL). The aqueous phase is acidified to pH 2 using concentrated HCl, then extracted with ethyl ether (300 mL). The ethyl ether is evaporated to leave a brown residue. The target compound **15** is isolated by recrystallization from water. Yield: 4.35 g, 56%. ^{1}H NMR (400 MHz, DMSO) δ 13.19 (s, 1H), 12.24 (s, 1H), 10.71 (s, 1H), 8.00 (dd, J = 7.7, 0.9 Hz, 1H), 7.74 – 7.67 (m, 1H), 7.65-7.61 (m, 1H), 7.42 (dd, J = 7.5, 1.0 Hz, 1H), 6.95 – 6.90 (m, 1H), 6.33 (d, J = 2.3 Hz, 1H), 6.29 (dd, J = 8.7, 2.3 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 200.51, 166.76, 165.01, 164.42, 140.00, 134.75, 132.32, 129.99, 129.74, 129.48, 127.45, 113.29, 108.34, 102.55. HR ESI $[M + H]^+$ *m/z* 259.0602, calc. for $C_{14}H_{11}O_5$ 259.0600.



Scheme S2. Synthesis of 2-(4-amino-2-hydroxybenzoyl)benzoic acid, **17**.

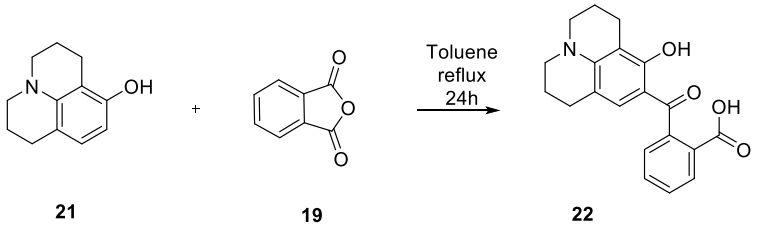
2-(4-amino-2-hydroxybenzoyl)benzoic acid, **17.** Rhodamine 110 hydrochloride (**16**) (0.2 g, 0.545 mmol) is mixed with NaOH (0.375g, 9.27 mmol) and 180 μL of water. The mixture is stirred and heated at 160 °C for 2 h,

0.5 mL of 50% NaOH is added in one portion and the mixture heated and stirred at 160 °C for an additional 1 h. The mixture is allowed to cool down to room temperature and diluted with 10 mL of water. The mixture is acidified to pH 1 with concentrated HCl. The resulting mixture is extracted with ethyl ether (2 × 50 mL), the organic extracts are combined, dried over anhydrous Na_2SO_4, filtered and the solvent evaporated under vacuum to leave **17** as a pale yellow solid. Yield: 0.130 g, 93%. ^{1}H NMR (400 MHz, DMSO) δ 13.01 (s, 1H), 12.59 (s, 1H), 7.95 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.67 (td, *J* = 7.5, 1.4 Hz, 1H), 7.60 (td, *J* = 7.6, 1.4 Hz, 1H), 7.36 (dd, *J* = 7.5, 1.0 Hz, 1H), 6.71 (d, *J* = 8.6 Hz, 1H), 6.44 (s, 2H), 6.05 – 5.97 (m, 2H). ^{13}C NMR (101 MHz, DMSO) δ 198.31, 166.92, 164.98, 156.82, 140.07, 134.48, 131.95, 129.84, 129.69, 129.31, 127.68, 109.79, 106.48, 98.16. HR ESI $[M + H]^+$ *m/z* 258.0754, calc for $C_{14}H_{12}NO_4$ 258.0760; HR ESI $[M + Na]^+$ *m/z* 280.0575, calc. for $C_{14}H_{11}NO_4Na^+$ 280.0580.



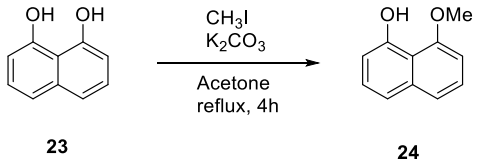
Scheme S3. Synthesis of 2-(4-(dimethylamino)-2-hydroxybenzoyl)benzoic acid, **20**.

2-(4-(dimethylamino)-2-hydroxybenzoyl)benzoic acid, 20. 3-dimethyl amino phenol (**18**) (5 g, 36.44 mmol) and phthalic anhydride (**19**) (5.39 g, 36.44 mmol) are dissolved in 150 mL of toluene and refluxed 18 h. The solvent is evaporated under vacuum to leave a purple residue. The residue is dissolved in ethyl acetate and the mixture passed through a plug of silica gel using EtOAc:Hexanes 1:1, EtOAc:Hexanes 3:1, and EtOAc for elution; 4.32 g, 42% of **20** are obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.51 (s, 1H), 8.09 (dd, *J* = 7.9, 0.9 Hz, 1H), 7.66 – 7.59 (m, 1H), 7.53 (td, *J* = 7.7, 1.3 Hz, 1H), 7.35 (dd, *J* = 7.5, 0.9 Hz, 1H), 6.88 (d, *J* = 9.1 Hz, 1H), 6.15 (d, *J* = 2.5 Hz, 1H), 6.06 (dd, *J* = 9.1, 2.5 Hz, 1H), 3.02 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.78, 170.69, 165.29, 156.10, 141.35, 134.44, 132.96, 131.23, 129.34, 128.15, 127.81, 110.45, 104.13, 97.89, 40.09. HR ESI $[M + H]^+$ *m/z* 286.1094, calc for $C_{16}H_{16}NO_4$ 286.1073; HR ESI $[M + Na]^+$ *m/z* 308.0915, calc. for $C_{16}H_{15}NO_4Na^+$ 308.0893.



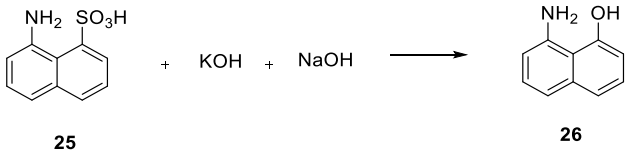
Scheme S4. Synthesis of 2-(8-hydroxy-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-9-carbonyl)benzoic acid, **22**.

2-(8-hydroxy-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-9-carbonyl)benzoic acid, 22. Phthalic anhydride (**19**) (0.392 g 2.64 mmol) and 8-hydroxyjulolidine (**21**) (0.5 g, 2.64 mmol) are dissolved in 12 mL of toluene. The mixture is refluxed 24 h, then the solvent evaporated under vacuum. The target compound **22** is isolated as a pale yellow solid by flash column chromatography on silica gel using CH_2Cl_2:MeOH 95:5 for elution. Yield: 622 mg, 70%. ^{1}H NMR (400 MHz, DMSO) δ 13.02 (s, 1H), 12.94 (s, 1H), 7.97 – 7.91 (m, 1H), 7.65 (dt, *J* = 7.5, 3.8 Hz, 1H), 7.59 (dt, *J* = 7.6, 3.8 Hz, 1H), 7.33 (d, *J* = 6.5 Hz, 1H), 6.39 (s, 1H), 3.24 (dd, *J* = 11.6, 7.0 Hz, 4H), 2.59 (t, *J* = 6.4 Hz, 2H), 2.41 (t, *J* = 6.1 Hz, 2H), 1.90 – 1.80 (m, 2H), 1.81 – 1.70 (m, 2H). ^{13}C NMR (101 MHz, DMSO) δ 197.98, 167.04, 159.77, 148.79, 140.16, 131.76, 129.85, 129.66, 129.19, 127.70, 112.43, 108.38, 104.61, 54.91, 49.39, 48.94, 26.66, 21.09, 20.09, 19.57. HR ESI $[M + H]^+$ *m/z* 338.1379, calc. for $C_{20}H_{20}NO_4$ 338.1386; HR ESI $[M + Na]^+$ *m/z* 360.1197, calc. for $C_{20}H_{19}NO_4Na^+$ 360.1206.



Scheme S5. Synthesis of 8-methoxynaphthalen-1-ol, **24**.

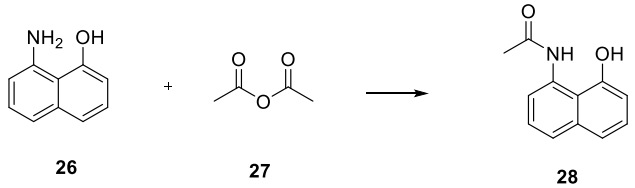
8-methoxynaphthalen-1-ol, 24. Under Ar atmosphere 1,8-dihydroxynaphthalene (**23**) (1 g, 6.24 mmol) and ground K_2CO_3 are suspended in 5 mL of acetone, CH_3I (0.88 g, 6.24 mmol) is added in one portion. The mixture is refluxed for 4 h. The mixture is allowed to cool down to room temperature, diluted with 15 mL of DI water and then acidified to pH 1 using 6M HCl. The aqueous phase is extracted with ethyl acetate (2 × 50 mL). The organic extracts are combined, dried over anhydrous Na_2SO_4, filtered and the solvent evaporated under vacuum. The target compound **24** is isolated by flash column chromatography on silica gel using EtOAc:Hexanes 25:75 for elution. Yield: 0.86 g, 79%. ^{1}H NMR (400 MHz, DMSO) δ 9.38 (s, 1H), 7.45 – 7.28 (m, 4H), 6.93 (dd, *J* = 7.6, 0.9 Hz, 1H), 6.78 (dd, *J* = 6.6, 2.1 Hz, 1H), 4.02 (d, *J* = 5.3 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 155.89, 154.00, 136.32, 127.46, 126.17, 120.95, 118.49, 114.56, 110.05, 104.44, 56.16, 40.12.



Scheme S6. Synthesis of 8-aminonaphthalen-1-ol, **26**.

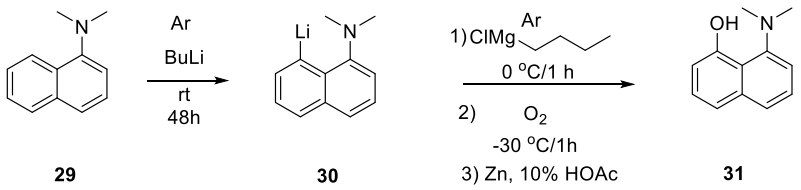
8-aminonaphthalen-1-ol, 26. Aminonaphthalene sulfonic acid (**25**) (12.5 g, 56 mmol) is made into a paste with 15 mL of water. KOH (22.3 g, 397 mmol) and NaOH (22.39 g, 560 mmol) are melted at 200 °C in a stainless steel beaker while being stirred using a mechanical stirrer (320 rpm). The aminonaphthalene sulfonic acid paste is added portion wise. The temperature is increased slowly to 260 °C while stirred. When the temperature reaches 260 °C, the mixture turns dark brown, then it liquefies and the thick melt turns black giving off white fumes. The

mixture is kept for additional 15 min at this temperature. The mixture is cooled rapidly to avoid further oxidation. The solidified cake is dissolved in 500 mL of DI water, and filtered. The filtrate is acidified with concentrated HCl to pH 1 and filtered again. The filtrate is neutralized by adding solid $NaHCO_3$ portion wise. The precipitate formed is filtered, washed with water (300 mL) and dried under vacuum. 5.3 g (59%) of **26** are obtained. ^{1}H NMR (600 MHz, DMSO) δ 7.11 – 7.03 (m, 3H), 6.86 (dd, *J* = 8.0, 1.1 Hz, 1H), 6.61 (dd, *J* = 5.0, 3.6 Hz, 1H), 6.45 (dd, *J* = 7.5, 1.1 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 155.37, 146.33, 137.19, 126.93, 125.78, 118.89, 114.39, 113.84, 107.33, 107.22. HR ESI $[M + H]^+$ *m/z* 160.0753, calc. for $C_{10}H_{10}NO$ 160.0756.



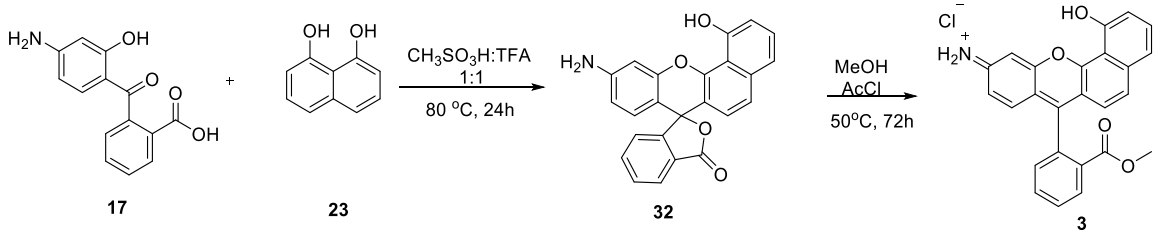
Scheme S7. Synthesis of N-(8-hydroxynaphthalen-1-yl)acetamide, **28**.

***N*-(8-hydroxynaphthalen-1-yl)acetamide, 28.** 8-amino-1-naphthol (**26**) (5 g, 31 mmol) is suspended in 100 mL of DI water. 6N HCl is added until a homogeneous solution is obtained, the mixture is sonicated to help to dissolve the solid. A yellow-black solution is obtained at pH around 1. Acetic anhydride (4.81 g, 47.12 mmol) is added in one portion and the mixture stirred at room temperature, after a few seconds a precipitate starts forming. Solid $NaHCO_3$ is added portion wise until pH 6-7 is reached. A cream precipitate is obtained. The precipitate is filtered and washed with water and dissolved in a minimum amount of ethanol. The solution is brought to boil and then activated carbon is added, the mixture is boiled for additional 3 min, then filtered and washed with cold ethanol. DI water is added to the filtrate until a turbid solution is obtained, after 30 min upon standing, the target compound precipitates as small yellow needles. The recrystallized product is filtered, washed with water and then dried under vacuum. 2.05 g, (33%) of **28** are obtained. ^{1}H NMR (400 MHz, DMSO) δ 11.23 (s, 1H), 11.08 (s, 1H), 8.41 (d, *J* = 7.6 Hz, 1H), 7.49 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.35 (ddd, *J* = 8.2, 6.4, 2.8 Hz, 2H), 6.89 (dd, *J* = 7.4, 1.3 Hz, 1H), 2.15 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 167.67, 153.34, 136.17, 135.60, 126.29, 126.05, 122.87, 119.94, 115.10, 114.67, 110.12, 25.29. HR ESI $[M + H]^+$ *m/z* 202.0856, calc. for $C_{12}H_{11}NO_2$ 202.8202; $[M + Na]^+$ *m/z* 224.0675, calc. for $C_{12}H_{10}NO_2Na$ 224.0675.



Scheme S8. Synthesis of 8-(dimethylamino)naphthalen-1-ol, **31**.

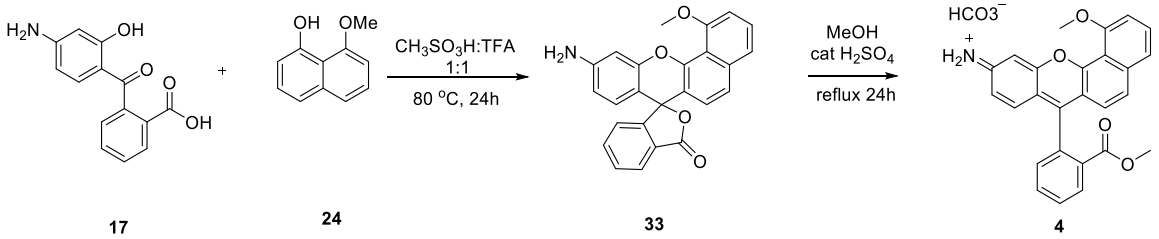
8-(dimethylamino)naphthalen-1-ol, 31. Under Ar atm, 1.7 M *n*-butyl lithium in hexanes (4.71 g, 73.6 mmol) is added in a continuous stream to a stirred solution of *N,N*-dimethyl-1-naphthylamine (**29**) (2.74 g, 16 mmol) in 35 mL of anhydrous ether. The mixture is stirred 48 h at room temperature. The lithiated naphthylamine (**30**) solution is cooled down to 0 °C and 2 M *n*-butyl magnesium chloride in hexanes (7.93 g, 67.9 mmol) is added slowly in order to keep the temperature at 0 °C. After 20 min, the reaction mixture is cooled down to -30 °C and maintained at this temperature for 4 h while dry O_2 is passed through the solution with stirring. A light yellow-grey precipitate forms and the mixture can not be longer stirred. A solution of 10% acetic acid in water (100 mL) is added under Ar atm, followed by the addition of Zn powder (1 g). The two phases are stirred for 30 min until effervescence had ceased and the aqueous phase is neutral. The flocculated Zn is filtered and the phases separated. The organic phase is washed with saturated $NaHCO_3$ solution (3 × 50 mL), water (1 × 50 mL), dried over anhydrous Na_2SO_4 and the solvent evaporated under vacuum. The target compound **31** is isolated by flash column chromatography on silica gel using 20% ether in hexanes, after pre-absorbing the crude mixture onto silica. Yield: 1.5 g, 50%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.36 (s, 1H), 7.66 (dd, J = 8.0, 1.2 Hz, 1H), 7.41 – 7.26 (m, 4H), 6.85 (dd, J = 7.5, 1.2 Hz, 1H), 2.84 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.91, 150.08, 136.40, 127.75, 126.80, 125.69, 119.06, 118.05, 116.87, 110.05, 46.47. HR ESI $[M + H]^+$ *m/z* 188.1072, calc. for $C_{12}H_{14}NO$ 188.1069.



Scheme S9. Synthesis of 1-hydroxy-7-(2-(methoxycarbonyl)phenyl)-10H-benzo[c]xanthen-10-iminium chloride, **3**.

1-hydroxy-7-(2-(methoxycarbonyl)phenyl)-10H-benzo[c]xanthen-10-iminium chloride, 3. Compound **17** (100 mg, 0.388 mmol) and 1,8-dihydroxynaphthalene (**23**) (93.4 mg, 0.583 mmol) are dissolved in 1.5 mL of methanesulfonic acid. 1.5 mL of TFA is added and the mixture heated at 80 °C for 24h. The mixture is allowed to cool down to room temperature and then poured into 20 mL of DI water. The precipitate formed is filtered and washed with water until the filtrate is neutral. The title compound is isolated by flash column chromatography on silica gel using CH_2Cl_2:MeOH 95:5 for elution. 144 mg, (97%) of **32** are obtained. ^{1}H NMR (600 MHz, DMSO)

δ 9.86 (s, 1H), 8.05 – 7.98 (m, 1H), 7.79 (td, *J* = 7.5, 1.1 Hz, 1H), 7.76 – 7.69 (m, 1H), 7.47 – 7.39 (m, 2H), 7.32 (d, *J* = 7.4 Hz, 1H), 7.27 (d, *J* = 7.6 Hz, 1H), 7.05 – 7.00 (m, 1H), 6.63 (d, *J* = 2.1 Hz, 1H), 6.59 (t, *J* = 6.5 Hz, 1H), 6.43 (d, *J* = 8.5 Hz, 1H), 6.39 (dd, *J* = 8.6, 2.2 Hz, 1H), 5.69 (s, 2H). ^{13}C NMR (151 MHz, DMSO) δ 168.80, 154.80, 152.95, 151.39, 151.24, 148.21, 136.56, 135.55, 130.01, 128.65, 128.18, 126.25, 124.55, 124.10, 123.87, 123.31, 118.68, 113.96, 112.20, 111.82, 111.72, 104.67, 99.58, 84.17. HR ESI $[M + H]^+$ *m/z* 382.1081, calc for $C_{24}H_{16}NO_4$ 382.1073. Compound **32** (50 mg, 131 μmol) is dissolved in 25 mL of anhydrous MeOH. 0.750 mL of acetyl chloride is added dropwise. The mixture is stirred and heated at 50 °C for 48h. 0.3 mL of acetyl chloride is added and the mixture is kept at 50 °C for additional 24 h. The solvent is evaporated under vacuum. The title compound **3** is purified in a C_{18} reversed phase SPE cartridge using MeOH:H_2O 2:8, MeOH:H_2O 1:1 for elution. Yield 45.44 mg (88%). ^{1}H NMR (400 MHz, DMSO) δ 11.47 (s, 1H), 8.91 (d, *J* = 15.4 Hz, 2H), 8.34 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.99 (td, *J* = 7.5, 1.3 Hz, 1H), 7.90 (td, *J* = 7.7, 1.3 Hz, 1H), 7.85 – 7.77 (m, 2H), 7.61 – 7.55 (m, 2H), 7.36 (d, *J* = 7.2 Hz, 1H), 7.29 (d, *J* = 9.3 Hz, 1H), 7.24 – 7.14 (m, 2H), 7.02 (d, *J* = 9.0 Hz, 1H), 3.56 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 165.09, 161.45, 160.00, 158.19, 157.57, 154.18, 138.39, 133.70, 133.59, 133.52, 131.77, 130.97, 130.75, 130.42, 129.08, 127.17, 122.51, 121.50, 119.26, 117.47, 117.10, 114.08, 112.28, 96.84, 52.48. HR ESI $[M]^+$ *m/z* 396.1240, calc. for $C_{25}H_{18}NO_4$ 396.1230.

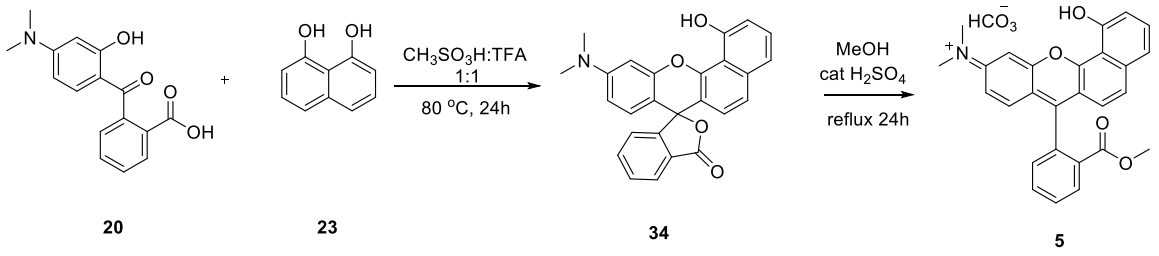


17 24 33 4

Scheme S10. Synthesis of 1-methoxy-7-(2-(methoxycarbonyl)phenyl)-10H-benzo[c]xanthen-10-iminium bicarbonate, **4**.

1-methoxy-7-(2-(methoxycarbonyl)phenyl)-10H-benzo[c]xanthen-10-iminium bicarbonate, 4. Compound **17** (150 mg, 0.583 mmol), and compound **24** (152 mg, 0.875 mmol) are dissolved in 1 mL of methanesulfonic acid, then 1 mL of TFA is added. The mixture is stirred at 80 °C for 16h. The mixture is cooled down to room temperature and poured into 50 mL of DI water. The mixture is neutralized to pH 6-7 by portion wise addition of solid $NaHCO_3$. The precipitate formed is filtered and washed with water (25 mL), then air dried. The title compound **33** is isolated by flash column chromatography using CH_2Cl_2:MeOH 9:1 for elution. Yield 157 mg (68%). ^{1}H NMR (400 MHz, DMSO) δ 8.05 – 7.99 (m, 1H), 7.78 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.73 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.56 (t, *J* = 7.9 Hz, 1H), 7.47 (dd, *J* = 13.7, 8.2 Hz, 2H), 7.29 – 7.24 (m, 1H), 7.16 (d, *J* = 7.2 Hz, 1H), 6.65 (d, *J* = 8.7 Hz, 1H), 6.60 (d, *J* = 2.0 Hz, 1H), 6.40 (dt, *J* = 8.6, 5.3 Hz, 2H), 5.68 (s, 2H), 4.05 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 168.83, 157.04, 153.02, 151.59, 151.31, 148.04, 136.49, 135.58, 130.04, 128.46,

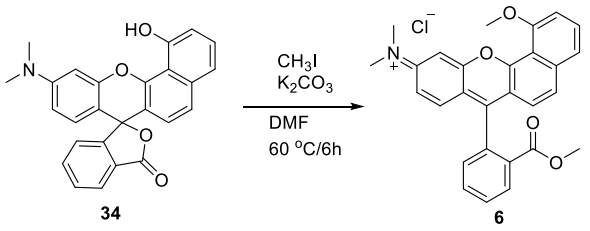
128.17, 126.22, 124.58, 124.42, 124.14, 123.19, 120.30, 114.95, 112.83, 111.72, 108.26, 104.64, 99.48, 84.29, 56.42. HR ESI $[M + H]^+$ *m/z* 396.1230, calc. for $C_{25}H_{18}NO_4$ 396.1230. Compound **33** (50 mg, 126 μmol) is dissolved in 2 mL of MeOH. To this solution is added concentrated H_2SO_4 (100 μL) dropwise, then the mixture is refluxed for 24h. The mixture is allowed to cool down to room temperature, then poured into 50 mL of ice water and 200 mg of $NaHCO_3$ is added in one portion. The precipitate formed is washed with 2% $NaHCO_3$ (2 × 10 mL). The solid is transferred to a flask containing 50 mL of 2% HOAc. The pH of the solution is adjusted to 6-7 using 1 M NaOH. The aqueous phase is extracted with $CHCl_3$ (3 x 100 mL). The organic phase is dried over anhydrous Na_2SO_4 and the solvent evaporated under vacuum to leave a dark purple solid. The title compound **4** is isolated by flash column chromatography on silica gel using CH_2Cl_2:MeOH 9:1 for elution. Yield 49 mg, 94%. ^{1}H NMR (400 MHz, DMSO) δ 8.97 (d, *J* = 5.3 Hz, 2H), 8.34 (dd, *J* = 7.9, 1.0 Hz, 1H), 8.04 – 7.85 (m, 4H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.57 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.30 (d, *J* = 9.3 Hz, 1H), 7.24 – 7.14 (m, 2H), 7.10 (d, *J* = 8.9 Hz, 1H), 4.22 (s, 3H), 3.54 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 165.07, 161.76, 160.07, 158.44, 158.33, 153.23, 138.40, 133.62, 133.54, 133.33, 131.96, 131.00, 130.80, 130.43, 129.09, 127.03, 123.23, 121.82, 120.86, 117.96, 117.43, 113.08, 109.82, 96.87, 56.82, 52.77, 52.48. HR ESI $[M]^+$ *m/z* 410.1400, calc. for $C_{26}H_{20}NO_4$ 410.1386.



Scheme S11. Synthesis of N-(1-hydroxy-7-(2-(methoxycarbonyl)phenyl)-10H-benzo[c]xanthen-10-ylidene)-N-N-dimethyl iminium bicarbonate, **5**.

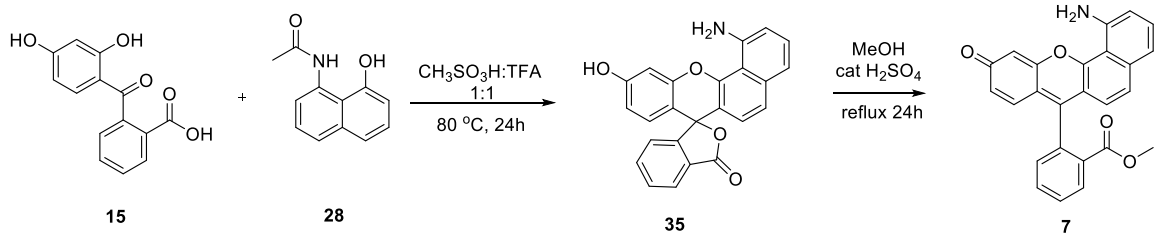
***N*-(1-hydroxy-7-(2-(methoxycarbonyl)phenyl)-10H-benzo[c]xanthen-10-ylidene)-N-N-dimethyl iminium bicarbonate, 5.** Compound **20** (0.750 g, 2.63 mmol) and **23** (0.632 g, 3.94 mmol) are dissolved in 6.5 mL of methanesulfonic acid, then TFA (6.5 mL) are added. The mixture is heated at 80 °C for 24h, then allowed to cool down to room temperature. The mixture is poured into 300 mL of DI water, the purple solid is filtered and washed with water (3 × 100 mL), then dried under vacuum. The target compound **34** is separated by flash chromatography on silica gel using $CHCl_3$:MeOH 9:1 for elution. Yield 0.778 g, 72%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.08 – 8.04 (m, 1H), 7.65 (dqd, *J* = 14.4, 7.3, 1.3 Hz, 2H), 7.47 (t, *J* = 7.9 Hz, 1H), 7.41 (d, *J* = 8.8 Hz, 1H), 7.32 (dd, *J* = 8.1, 0.9 Hz, 1H), 7.18 – 7.15 (m, 1H), 7.08 (dd, *J* = 7.7, 1.0 Hz, 1H), 6.69 (dd, *J* = 8.8, 4.2 Hz, 2H), 6.55 – 6.48 (m, 2H), 3.03 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.70, 154.32, 153.52, 152.23, 150.95, 148.59, 136.63, 135.18, 129.88, 129.16, 129.00, 126.97, 125.23, 124.43, 124.11, 124.06, 119.69, 113.38, 112.72, 112.56,

110.23, 105.84, 97.93, 83.39, 40.44. HR ESI $[M + H]^+$ found 410.1392, calc. for $C_{26}H_{20}NO_4$ 410.1368. Compound **34** (100 mg, 243 μmol) is dissolved in 2 mL of MeOH. To this solution is added concentrated H_2SO_4 (100 μL) dropwise, then the mixture is refluxed for 16 h. The mixture is allowed to cool down to room temperature, then poured into 50 mL of ice water and filtered. The precipitate is washed with 2% $NaHCO_3$ (2 × 10 mL). The solid is transferred to a flask containing 50 mL of 2% HOAc. The pH of the solution is adjusted to 6-7 using 1 M NaOH. The aqueous phase is extracted with $CHCl_3$ (3 × 100 mL). The organic phase is dried over anhydrous Na_2SO_4 and the solvent evaporated under vacuum to leave a dark purple solid. The target compound **5** is isolated by flash column chromatography. A dark purple band is eluted with $CHCl_3$:MeOH 9:1, 8:2; yield 36 mg. A second green band was eluted with $CHCl_3$:MeOH 1:1, then 1:3; yield 61 mg. Total yield of **34,** 97 mg, (94%). ^{1}H NMR (400 MHz, DMSO) δ 8.32 (d, *J* = 7.0 Hz, 1H), 7.97 (d, *J* = 7.5 Hz, 1H), 7.89 (t, *J* = 7.1 Hz, 1H), 7.72 (t, *J* = 8.6 Hz, 2H), 7.58 (d, *J* = 6.7 Hz, 1H), 7.43 – 7.34 (m, 2H), 7.26 (d, *J* = 8.1 Hz, 1H), 7.20 (d, *J* = 9.6 Hz, 1H), 7.09 (d, *J* = 2.4 Hz, 1H), 6.93 (d, *J* = 9.0 Hz, 1H), 3.54 (s, 3H), 3.39 (s, 6H). ^{13}C NMR (101 MHz, DMSO) δ 165.29, 158.40, 154.28, 153.85, 138.93, 135.22, 134.73, 133.24, 130.70, 129.87, 128.79, 127.72, 124.06, 120.52, 117.48, 113.21, 96.43, 94.54, 79.25, 52.13. HR ESI $[M^+]$ *m/z* 424.1540, calc for $C_{27}H_{22}NO_4^+$ 424.1543.



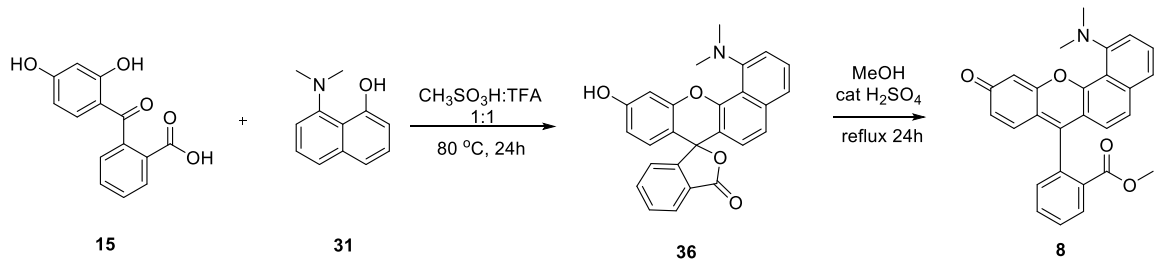
Scheme S12. Synthesis of *N*-(1-methoxy-7-(2-(methoxycarbonyl)phenyl)-10H-benzo[c]xanthen-10-ylidene)-N-methylmethanaminium chloride, **6**.

***N*-(1-methoxy-7-(2-(methoxycarbonyl)phenyl)-10H-benzo[c]xanthen-10-ylidene)-N-methylmethanaminium chloride, 6.** Compound **34** (50 mg, 0.122 mmol), K_2CO_3 (67.5 mg, 0.488 mmol) are suspended in 0.6 mL of anhydrous DMF, CH_3I (104 mg, 0.732 mmol) is added in one portion. The mixture is stirred at 60 °C for 6h, then allowed to cool down to room temperature. 2 mL of saturated NH_4Cl are added to quench the reaction. The precipitate formed is filtered and washed with 0.5% NaOH (2 mL), then with water (25 mL). The title compound **6** is isolated by flash column chromatography on silica gel using CH_2Cl_2:MeOH 9:1 for elution. Yield: 4.5 mg, (8%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 7.9 Hz, 1H), 7.87 (d, *J* = 7.5 Hz, 1H), 7.84 – 7.77 (m, 2H), 7.66 (d, *J* = 9.0 Hz, 1H), 7.61 (dd, *J* = 9.7, 2.0 Hz, 1H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.40 (d, *J* = 7.5 Hz, 1H), 7.35 (d, *J* = 9.7 Hz, 1H), 7.24 (s, 1H), 7.13 (s, 1H), 7.09 (d, *J* = 8.9 Hz, 1H), 4.30 (s, 3H), 3.63 (s, 3H), 3.59 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.45, 160.65, 159.55, 159.11, 158.31, 154.73, 139.21, 134.11, 133.58, 133.39, 131.66, 131.12, 130.89, 130.39, 129.82, 127.38, 123.24, 120.99, 119.99, 118.60, 117.63, 114.24, 109.24, 96.78, 57.11, 52.76, 42.53, 29.84. HR ESI $[M^+]$ *m/z* 438.1698, calc for $C_{28}H_{24}NO_4^+$; 438.1699.



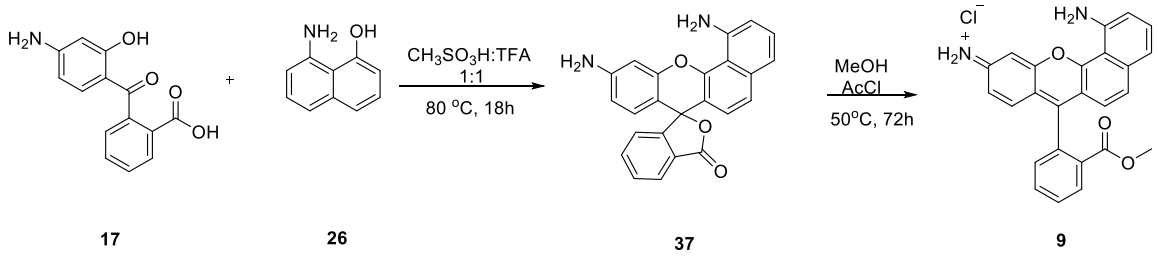
Scheme S13. Synthesis of methyl 2-(1-amino-10-oxo-10H-benzo[c]xanthen-7-yl)benzoate, **7**.

Methyl 2-(1-amino-10-oxo-10H-benzo[c]xanthen-7-yl)benzoate 7. Compound **15** (200 mg, 0.774 mmol), and compound **28** (234 mg, 1.16 mmol) are dissolved in 2.5 mL of methanesulfonic acid, then 2.5 mL of TFA are added. The mixture is stirred at 80 °C for 24h, then cooled down to room temperature. The mixture is poured into 50 mL of DI water, the precipitate obtained is filtered and washed with DI water, then air dried. The title compound is isolated by flash column chromatography on silica gel using CH_2Cl_2:MeOH 9:1. 33 mg of a mixed fraction containing the target product **35** is isolated. 17 mg of the **35** mixed fraction are dissolved in 1 mL of MeOH, 50 µL of concentrated sulfuric acid are added in one portion. The mixture is refluxed for 16h, the mixture is allowed to cool down to room temperature and poured into 10 mL of DI water. 200 mg of $NaHCO_3$ is added in one portion. The precipitate formed is filtered and washed with aqueous 2% $NaHCO_3$, the precipitate is then suspended in 25 mL of 2% HOAc, a dark brown black suspension is obtained, the mixture is neutralized to pH 6-7 by adding solid $NaHCO_3$ portion wise. The aqueous phase is extracted with $CHCl_3$ (3 x 50 mL), the organic extracts are combined, dried over anhydrous Na_2SO_4, filtered and the solvent evaporated under vacuum to leave a black precipitate. The title compound **7** is isolated by flash column chromatography on silica gel using CH_2Cl_2:MeOH 9:1 for elution. Yield 2.7 mg, 15%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.78 (td, *J* = 7.5, 1.4 Hz, 1H), 7.71 (td, *J* = 7.7, 1.4 Hz, 1H), 7.47 (t, *J* = 7.9 Hz, 1H), 7.41 (d, *J* = 8.9 Hz, 1H), 7.35 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.17 (d, *J* = 7.7 Hz, 1H), 6.94 (d, *J* = 9.6 Hz, 1H), 6.86 (d, *J* = 7.8 Hz, 1H), 6.82 (d, *J* = 8.9 Hz, 1H), 6.68 (dd, *J* = 9.6, 1.9 Hz, 1H), 6.63 (d, *J* = 1.9 Hz, 1H), 5.69 (s, 2H), 3.63 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.06, 158.17, 146.15, 137.97, 135.26, 132.99, 131.36, 131.30, 130.72, 129.90, 129.82, 125.81, 122.57, 117.43, 112.65, 111.41, 105.15, 52.60. HR ESI [M+ H^+] *m/z* 396.1240, calc for $C_{25}H_{18}NO_4^+$ 396.1230.



Scheme S14. Synthesis of Methyl 2-(1-(dimethylamino)-10-oxo-10H-benzo[c]xanthen-7-yl)benzoate, **8**.

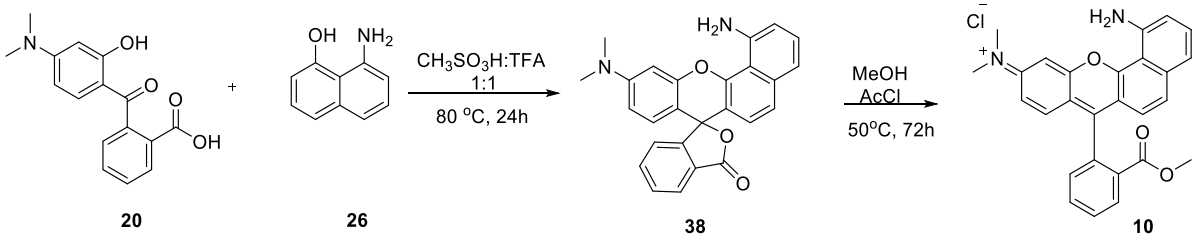
Methyl 2-(1-(dimethylamino)-10-oxo-10H-benzo[c]xanthen-7-yl)benzoate, 8. Compound **15** (200 mg, 0.774 mmol), compound **31** (217.5 mg, 1.16 mmol) are dissolved in 2.5 mL of methanesulfonic acid, then 2.5 mL of TFA is added. The mixture is stirred at 80 ^{o}C for 24 h, then cooled down to room temperature. The mixture is poured into 50 mL of DI water, the precipitate obtained is filtered and washed with DI water, then air dried. The crude mixture is separated by flash column chromatography on silica gel using CH_2Cl_2:MeOH 95:5 for elution; 15 mg of a mixed fraction containing **36** is isolated. 10 mg of the **36** mixed fraction are dissolved in 1 mL of MeOH, 50 µl of concentrated Sulfuric acid is added in one portion. The mixture is refluxed for 16 h, the mixture is allowed to cool down to room temperature and poured into 10 mL of DI water. 200 mg of $NaHCO_3$ are added in one portion. The precipitate formed is filtered and washed with aqueous 2% $NaHCO_3$, the precipitate is then suspended in 25 mL of 2% HOAc. The mixture is neutralized to pH 6-7 by adding solid $NaHCO_3$ portion wise. The aqueous phase is extracted with $CHCl_3$ (3 x 50 mL), the organic extracts are combined, dried over anhydrous Na_2SO_4, filtered and the solvent evaporated under vacuum. The crude mixture was separated by flash column chromatography on silica gel using CH_2Cl_2:MeOH 9:1 for elution. The isolated fraction (5.9 mg) containing the target product **8** was further separated by flash column chromatography on silica gel using EtOAc:MeOH 95:5 for elution. Yield, 1.5 mg, (14.5%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.77 (td, *J* = 7.5, 1.5 Hz, 1H), 7.70 (td, *J* = 7.7, 1.4 Hz, 1H), 7.56 (t, *J* = 7.9 Hz, 1H), 7.47 (d, *J* = 8.9 Hz, 1H), 7.39 (d, *J* = 7.3 Hz, 1H), 7.36 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.21 (dd, *J* = 7.8, 0.9 Hz, 1H), 6.92 (dd, *J* = 9.1, 7.4 Hz, 2H), 6.70 (s, 2H), 3.59 (s, 3H), 3.04 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.77, 158.79, 152.34, 138.80, 135.39, 132.90, 131.35, 131.12, 130.80, 130.54, 130.21, 129.80, 129.52, 125.54, 123.04, 121.50, 117.37, 116.79, 116.12, 105.25, 52.52, 45.39. HR ESI [M^+] *m/z* 424.1556, calc for $C_{27}H_{22}NO_4^+$ 424.1543.



Scheme S15. Synthesis of 1-amino-7-(2-(methoxycarbonyl)phenyl)-10H-benzo[c]xanthen-10-iminium chloride, **9**.

1-amino-7-(2-(methoxycarbonyl)phenyl)-10H-benzo[c]xanthen-10-iminium chloride, 9. Compound **17** (310 mg, 1.21 mmol), 8-aminonaphthalen-1-ol (**26**) (287.75 mg, 1.81 mmol) are dissolved in 4.5 mL of methanesulfonic acid, then 4.5 mL of TFA is added. The mixture is stirred at 80 ^{o}C for 18 h, then cooled down to room temperature. The mixture is poured into 60 mL of DI water, the mixture is brought to pH 5 by portion wise

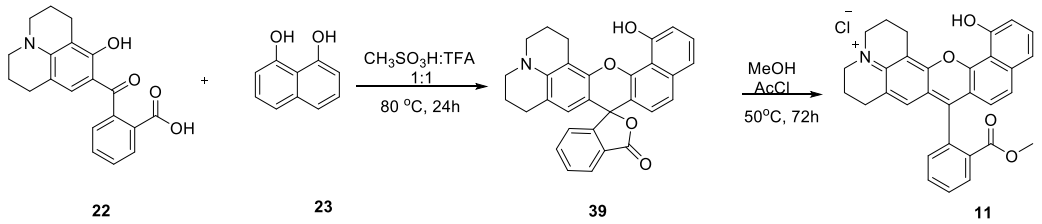
addition of solid $NaHCO_3$. The dark green precipitate obtained is filtered and washed with DI water. The title compound **37** is isolated by flash column chromatography on silica gel using CH_2Cl_2:MeOH 9:1 for elution. Yield 254.9 mg, 56%. ^{1}H NMR (400 MHz, DMSO) δ 8.01 (d, *J* = 7.6 Hz, 1H), 7.80 (td, *J* = 7.5, 1.1 Hz, 1H), 7.72 (td, *J* = 7.5, 0.7 Hz, 1H), 7.36 – 7.25 (m, 3H), 7.00 (d, *J* = 7.6 Hz, 1H), 6.82 (dd, *J* = 7.7, 0.7 Hz, 1H), 6.71 (d, *J* = 1.8 Hz, 1H), 6.48 (d, *J* = 8.7 Hz, 1H), 6.43 (d, *J* = 2.6 Hz, 1H), 6.35 (s, 2H), 5.69 (s, 2H). ^{13}C NMR (101 MHz, DMSO) δ 168.81, 152.83, 151.27, 150.99, 149.26, 146.12, 136.51, 135.56, 130.04, 128.83, 128.31, 126.32, 124.58, 124.11, 123.88, 123.27, 115.01, 111.96, 111.69, 110.79, 110.69, 104.78, 99.30, 84.15. HR ESI $[M + H]^+$ *m/z* 381.1232, calc. for $C_{24}H_{17}N_2O_3$ 381.1233. Compound **37** (25 mg, 66 μmol) is dissolved in 20 mL of anhydrous MeOH; 1.0 mL of acetyl chloride is added drop wise. The mixture is stirred and heated at 50 °C for 48 h; 0.5 mL of acetyl chloride is added and the mixture is kept at 50 °C for additional 24 h. The solvent is evaporated under vacuum. The title compound **9** is isolated by flash column chromatography on silica gel using CH_2Cl_2:MeOH 90:10, 85:15, 80:20 for elution. Yield 24 mg, 93%. ^{1}H NMR (400 MHz, DMSO) δ 8.70 (s, 2H), 8.32 (d, *J* = 6.9 Hz, 1H), 7.99 – 7.94 (m, 1H), 7.88 (dd, *J* = 10.9, 4.5 Hz, 1H), 7.70 – 7.63 (m, 1H), 7.55 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.47 (d, *J* = 2.0 Hz, 1H), 7.33 (s, 2H), 7.23-7.13 (m, 4H), 6.86 (d, *J* = 9.0 Hz, 2H), 3.56 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 165.08, 160.42, 158.80, 157.07, 156.39, 149.40, 137.94, 134.03, 133.90, 133.49, 131.31, 130.92, 130.64, 130.42, 129.10, 127.83, 121.75, 120.61, 116.80, 115.91, 115.79, 113.85, 108.57, 97.90, 52.46. HR ESI $[M]^+$ *m/z* 395.1386, calc. for $C_{25}H_{19}N_2O_3^+$ 395.1390.



Scheme S16. Synthesis of N-(1-amino-7-(2-(methoxycarbonyl)phenyl)-10H-benzo[c]xanthen-10-ylidene)-N-methylmethanaminium, **10**.

***N*-(1-amino-7-(2-(methoxycarbonyl)phenyl)-10H-benzo[c]xanthen-10-ylidene)-N-methylmethanaminium, 10.** Compound **20** (450 mg, 1.58 mmol), 8-aminonaphthalen-1-ol (**26)** (326.41 mg, 2.05 mmol) are dissolved in 2 mL of methanesulfonic acid, then 2 mL of TFA is added. The mixture is stirred at 80 °C for 24 h, then cooled down to room temperature. The mixture is poured into 150 mL of DI water, the mixture is neutralized by portion wise addition of $NaHCO_3$, the dark green precipitate obtained is filtered and washed with DI water then air dried. The target compound **38** is isolated by flash column chromatography on silica gel using CH_2Cl_2:MeOH 95:5, 9:1, Yield 265 mg, 41 %. ^{1}H NMR (400 MHz, DMSO) δ 8.03 (d, *J* = 7.4 Hz, 1H), 7.79 (dt, *J* = 7.5, 3.8 Hz, 1H), 7.73 (dt, *J* = 7.4, 3.7 Hz, 1H), 7.37 – 7.24 (m, 3H), 6.98 (dd, *J* = 10.7, 4.6 Hz, 2H), 6.87 (d, *J* = 7.8 Hz, 1H), 6.59 – 6.56 (m, 2H), 6.50 (d, *J* = 8.7 Hz, 1H), 6.37 (s, 2H), 2.99 (s, 6H). ^{13}C NMR (101 MHz, DMSO) δ 168.79, 152.91,

152.01, 151.05, 149.36, 146.15, 136.57, 135.59, 130.08, 128.84, 128.08, 126.21, 124.62, 124.08, 123.98, 123.20, 114.81, 111.57, 110.80, 110.48, 109.98, 105.01, 98.68, 83.95. HR ESI [M+ H^+] *m/z* 409.15743, calc. for $C_{26}H_{21}N_2O_3^+$ 409.15466. Under Ar, compound **38** (25 mg, 0.043 mmol) is dissolved in 12.5 mL of anhydrous MeOH. The solution is cooled down to 0 ^oC in an ice bath, 0.375 mL of acetyl chloride is added drop wise. The mixture is stirred and heated at 50 ^oC for 48 h; 0.2 mL of acetyl chloride is added and the mixture is kept at 50 ^oC for additional 24 h. The solvent is evaporated under vacuum. 27 mg (96%) of **10** are obtained. ^1H NMR (400 MHz, DMSO) δ 8.33 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.97 (td, *J* = 7.5, 1.3 Hz, 1H), 7.92 – 7.85 (m, 2H), 7.68 (dd, *J* = 16.6, 8.6 Hz, 2H), 7.56 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.43 – 7.34 (m, 3H), 7.26 – 7.16 (m, 3H), 6.87 (d, *J* = 9.0 Hz, 1H), 3.55 (s, 3H), 3.38 (d, *J* = 8.3 Hz, 6H). ^{13}C NMR (101 MHz, DMSO) δ 165.10, 158.47, 157.60, 156.82, 156.39, 149.34, 137.95, 133.89, 133.52, 130.96, 130.69, 130.41, 129.13, 127.95, 121.73, 117.08, 115.74, 115.55, 113.83, 108.24, 97.33, 52.77, 52.48. HR ESI [M^+] *m/z* 423.17298, calc. for $C_{27}H_{23}N_2O_3^+$ 423.17031.

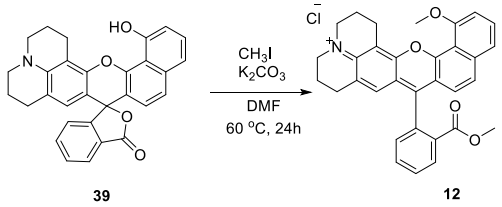


22 23 39 11

Scheme S17. Synthesis of 15-hydroxy-9-(2-(methoxycarbonyl)phenyl)-1,2,3,5,6,7-hexahydrobenzo[7,8]chromeno[2,3-f]pyrido[3,2,1-ij]quinolin-4-ium chloride, **11**.

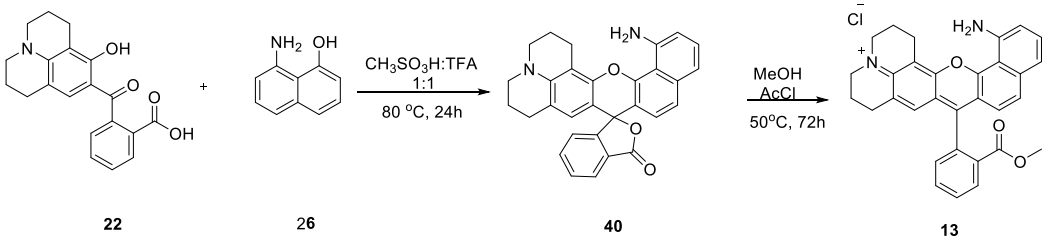
15-hydroxy-9-(2-(methoxycarbonyl)phenyl)-1,2,3,5,6,7-hexahydrobenzo[7,8]chromeno[2,3-f]pyrido[3,2,1-ij]quinolin-4-ium chloride, 11. Compound **22** (200 mg, 0.593 mmol), 1,8-dihydroxynaphthalene (**23**) (142 mg, 0.889 mmol) are dissolved in 1.5 mL of methanesulfonic acid, then 1.5 mL of TFA is added. The mixture is stirred at 80 ^oC for 24 h, then cooled down to room temperature. The mixture is poured into 50 mL of DI water, the precipitate obtained is filtered and washed with DI water then dried under vacuum. 256 mg (93%) of **39** are obtained. ^1H NMR (400 MHz, DMSO) δ 11.39 (s, 1H), 8.27 (d, *J* = 7.7 Hz, 1H), 7.90 (t, *J* = 7.3 Hz, 1H), 7.83 (t, *J* = 7.5 Hz, 1H), 7.70 (dd, *J* = 17.0, 8.5 Hz, 2H), 7.48 (t, *J* = 7.3 Hz, 2H), 7.24 (d, *J* = 7.8 Hz, 1H), 6.92 (d, *J* = 8.9 Hz, 1H), 6.85 (s, 1H), 3.63 (d, *J* = 22.7 Hz, 6H), 2.76 (s, 2H), 2.06 (s, 2H), 1.91 (s, 2H). ^{13}C NMR (101 MHz, DMSO) δ 166.46, 158.01, 157.68, 156.84, 137.90, 133.16, 130.38, 126.35, 125.32, 122.66, 119.13, 118.37, 115.38, 113.42, 112.67, 105.31, 50.94, 50.64, 26.89, 19.77, 18.86. HR ESI [M+ H^+] *m/z* 462.1690, calc. for $C_{30}H_{24}NO_4^+$ 462.17108. Compound **39** (50 mg, 0.108 mmol) is dissolved in 25 mL of anhydrous MeOH. 0.75 mL of acetyl chloride is added drop wise. The mixture is stirred and heated at 50 ^oC for 48 h. 0.3 mL of acetyl chloride is added and the mixture is kept at 50 ^oC for additional 24 h. The solvent is evaporated under vacuum, the target compound **11** is isolated by flash column chromatography on silica gel using CH_2Cl_2:MeOH 90:10 for elution. Yield 46 mg, 90%. ^1H NMR (400 MHz, DMSO) δ 11.50 (s, 1H), 8.33 (d, *J* = 7.8 Hz, 1H), 7.97 (t, *J* = 7.3

Hz, 1H), 7.92 – 7.85 (m, 1H), 7.73 (dd, *J* = 12.5, 8.5 Hz, 2H), 7.53 (t, *J* = 7.9 Hz, 2H), 7.31 (d, *J* = 7.9 Hz, 1H), 6.95 – 6.87 (m, 2H), 3.71 (s, 2H), 3.65 (s, 2H), 3.56 (s, 3H), 3.33 (s, 2H), 2.78 (s, 2H), 2.08 (s, 2H), 1.92 (s, 2H). ^{13}C NMR (101 MHz, DMSO) δ 201.26, 164.65, 157.10, 156.33, 152.34, 130.52, 129.06, 116.89, 113.67, 113.39, 112.24, 105.24, 103.61, 52.59, 50.51, 19.55, 18.60. HR ESI $[M]^+$ *m/z* 476.1858, calc. for $C_{31}H_{26}NO_4^+$ 476.1856.



Scheme S18. Synthesis of 15-methoxy-9-(2-(methoxycarbonyl)phenyl)-1,2,3,5,6,7-hexahydrobenzo[7,8]chromeno[2,3-f]pyrido[3,2,1-ij]quinolin-4-ium chloride, **12**.

15-methoxy-9-(2-(methoxycarbonyl)phenyl)-1,2,3,5,6,7-hexahydrobenzo[7,8]chromeno[2,3-f]pyrido[3,2,1-ij]quinolin-4-ium chloride, 12. Under Ar atm, compound **39** (25 mg, 0.054 mmol) is dissolved in 0.5 mL of anhydrous DMF, to this solution is added K_2CO_3 (22.5 mg, 0.162 mmol) and CH_3I (31 mg, 0.217 mmol). The mixture is heated at 60 °C for 24 h, then allowed to cool down to room temperature. 2 mL of saturated NH_4Cl is added to quench the reaction. The precipitate formed is filtered and washed with 0.5% NaOH (2 mL), then with water (25 mL). The title compound **12** is isolated by flash column chromatography on silica gel using CH_2Cl_2:MeOH 90:10 for elution. Yield: 16 mg, 59%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.91 – 7.84 (m, 1H), 7.82 – 7.72 (m, 2H), 7.60 (d, *J* = 8.9 Hz, 1H), 7.50 (d, *J* = 7.9 Hz, 1H), 7.39 (d, *J* = 6.7 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 1H), 7.01 (d, *J* = 8.9 Hz, 1H), 6.78 (s, 1H), 4.22 (s, 3H), 4.05 – 3.89 (m, 2H), 3.84 – 3.69 (m, 2H), 3.64 (s, 3H), 3.38 (dd, *J* = 12.8, 7.2 Hz, 2H), 2.95 – 2.74 (m, 2H), 2.39 – 2.01 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.59, 158.81, 156.53, 154.52, 153.32, 138.73, 134.59, 133.58, 132.36, 131.54, 130.76, 130.56, 129.86, 129.77, 126.66, 125.79, 123.21, 120.99, 118.11, 117.86, 114.58, 108.74, 106.16, 56.79, 52.74, 52.32, 52.05, 28.08, 20.40, 20.18, 19.65. HR ESI $[M]^+$ *m/z* 490.2026, calc. for $C_{32}H_{28}NO_4^+$ 490.2012.



Scheme S19. Synthesis of 15-amino-9-(2-(methoxycarbonyl)phenyl)-1,2,3,5,6,7-hexahydrobenzo[7,8]chromeno[2,3-f]pyrido[3,2,1-ij]quinolin-4-ium chloride, **13**.

15-amino-9-(2-(methoxycarbonyl)phenyl)-1,2,3,5,6,7-hexahydrobenzo[7,8]chromeno[2,3-f]pyrido[3,2,1-ij]quinolin-4-ium chloride, 13. Compound **22** (100 mg, 0.296 mmol) and compound **26** (71 mg, 0.444 mmol)

are dissolved in 1.5 mL of methanesulfonic acid, then 1.5 mL of TFA is added. The mixture is stirred at 80 ^{o}C for 24 h, then cooled down to room temperature. The mixture is poured into 50 mL of DI water, then neutralized by portion wise addition of $NaHCO_3$, the green precipitate obtained is filtered and washed with DI water then air dried. The target compound is isolated by flash column chromatography on silica gel using CH_2Cl_2:MeOH 90:10, 80:20, and then 100% MeOH to elute the last dark green band that corresponds to the target compound **40**. The MeOH fraction is evaporated under vacuum, and the resulting solid is dissolved in a mixture of CH_2Cl_2:MeOH 90:10 and filtered trough a 0.22 µm filter to remove any dissolved silica. Yield 52 mg, 39 %. ^{1}H NMR (400 MHz, DMSO) δ 8.01 (d, *J* = 7.4 Hz, 1H), 7.79 (td, *J* = 7.5, 1.2 Hz, 1H), 7.72 (td, *J* = 7.5, 0.9 Hz, 1H), 7.37 – 7.25 (m, 3H), 7.01 (d, *J* = 7.3 Hz, 1H), 6.81 (d, *J* = 6.7 Hz, 1H), 6.47 (d, *J* = 8.7 Hz, 1H), 6.38 (s, 2H), 6.13 (s, 1H), 3.23 – 3.10 (m, 2H), 2.98 (d, *J* = 5.0 Hz, 1H), 2.02 (d, *J* = 2.9 Hz, 2H), 1.85 – 1.75 (m, 2H). ^{13}C NMR (101 MHz, DMSO) δ 168.83, 153.34, 152.90, 149.78, 149.33, 147.24, 146.83, 145.90, 145.24, 144.55, 136.55, 135.57, 130.04, 128.76, 126.35, 124.61, 124.19, 123.96, 123.31, 118.66, 115.22, 115.01, 112.06, 110.74, 110.65, 108.55, 106.10, 104.40, 84.50, 63.19, 49.20, 48.32, 26.76, 21.64, 21.13, 20.73, 18.57. HR ESI $[M+ H]^+$ *m/z* 461.1869, calc. for $C_{30}H_{25}N_2O_3^+$ 461.1859. Compound **40** (20 mg, 0.043 mmol) is dissolved in 15 mL of anhydrous MeOH; 0.75 mL of acetyl chloride is added drop wise. The mixture is stirred and heated at 50 ^{o}C for 48 h; then 0.2 mL of acetyl chloride is added and the mixture is kept at 50 ^{o}C for additional 24 h. The solvent is evaporated under vacuum. 21 mg (100%) of the target compound **13** are obtained. ^{1}H NMR (400 MHz, DMSO) δ 8.32 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.96 (td, *J* = 7.5, 1.3 Hz, 1H), 7.92 – 7.84 (m, 1H), 7.69 – 7.63 (m, 2H), 7.50 (d, *J* = 6.6 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 7.22 (d, *J* = 7.9 Hz, 1H), 6.90 – 6.79 (m, 2H), 3.73 – 3.61 (m, 4H), 3.57 (s, 1H), 3.27 (d, *J* = 5.9 Hz, 2H), 2.82 – 2.74 (m, 2H), 2.10 (dd, *J* = 12.5, 6.5 Hz, 2H), 1.91 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.57, 156.75, 156.60, 153.20, 152.80, 148.90, 138.31, 134.80, 133.87, 133.38, 131.49, 130.59, 130.39, 129.97, 128.08, 127.94, 125.73, 121.57, 117.28, 116.96, 116.34, 114.91, 110.34, 106.08, 54.50, 52.75, 51.76, 51.26, 28.00, 21.21, 20.38, 19.56.. HR ESI $[M^+]$ m/z 475.2029, calc. for $C_{31}H_{27}N_2O_3^+$ 475.2016.

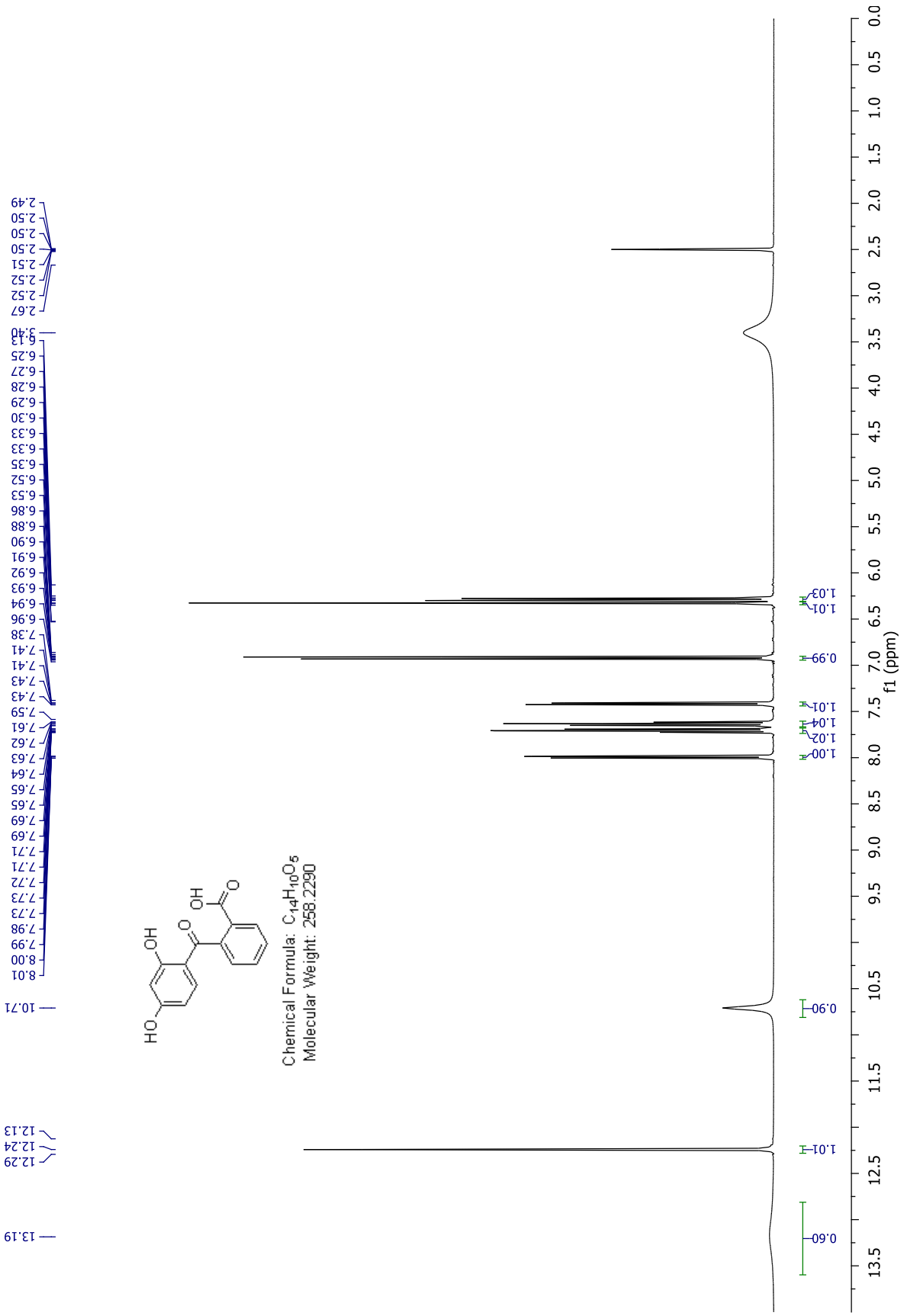


Figure S13. [1]H NMR spectrum of compound **15**.

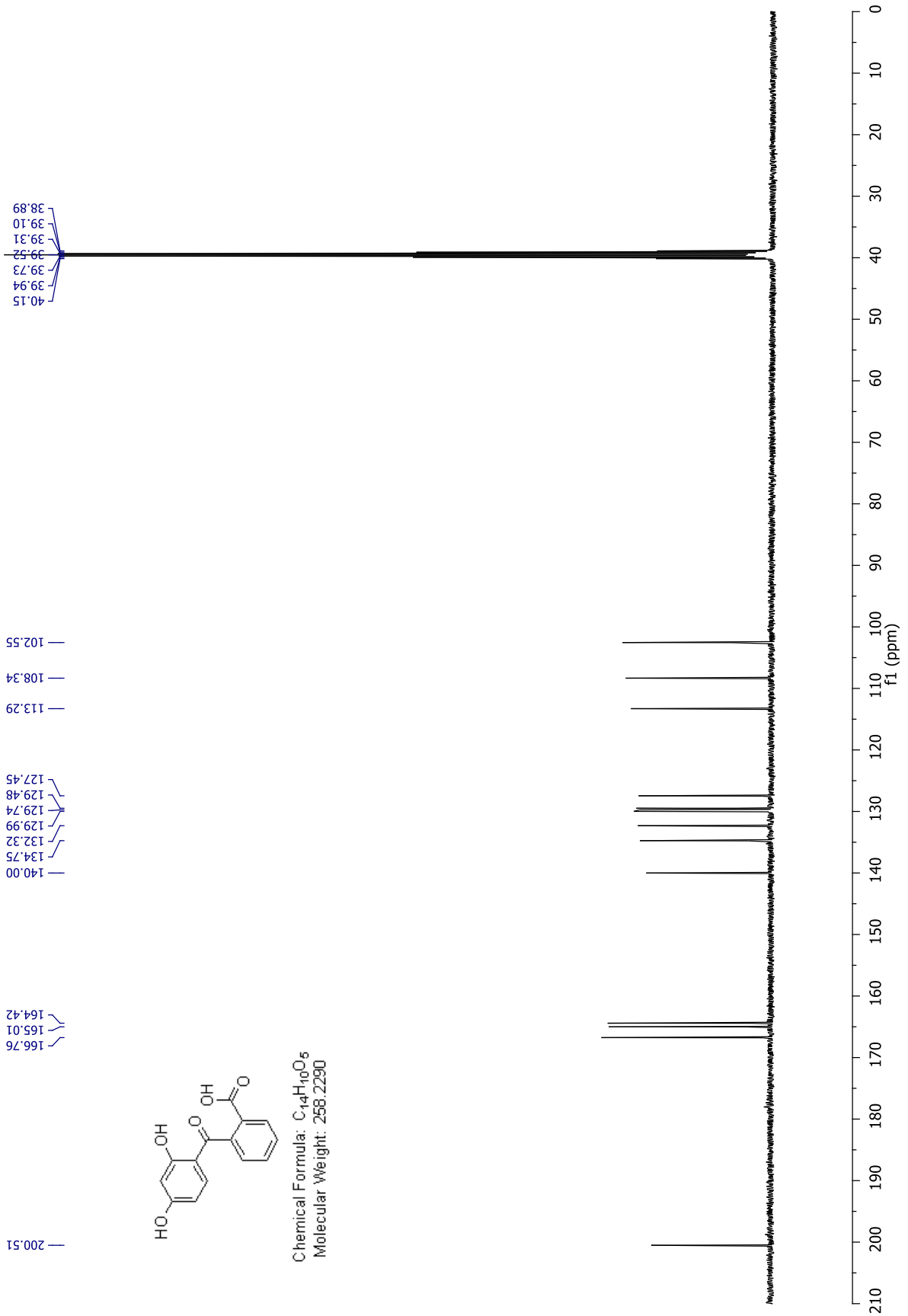
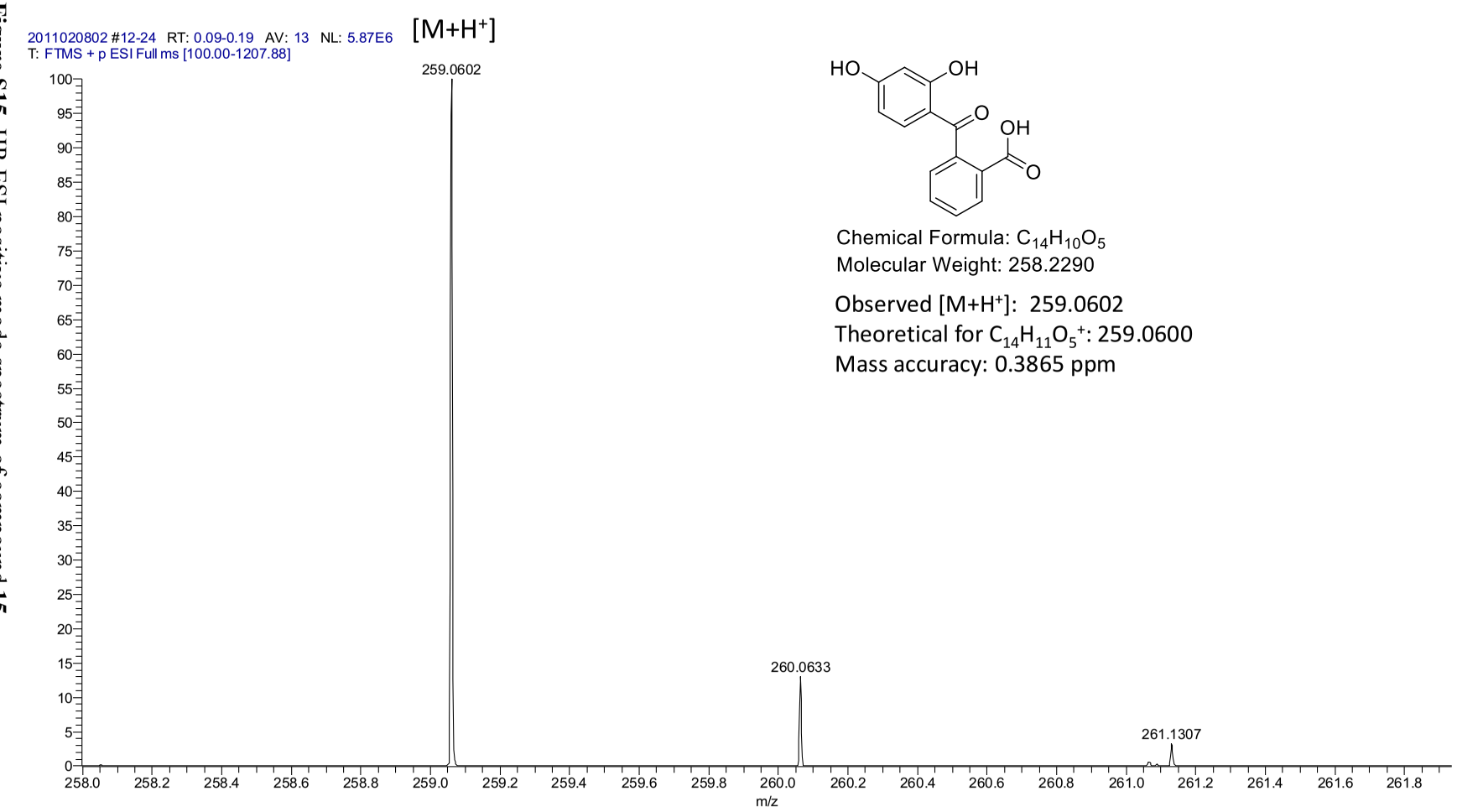


Figure S14. ^{13}C NMR spectrum of compound **15**.

Figure S15. HR ESI positive mode spectrum of compound **15**.



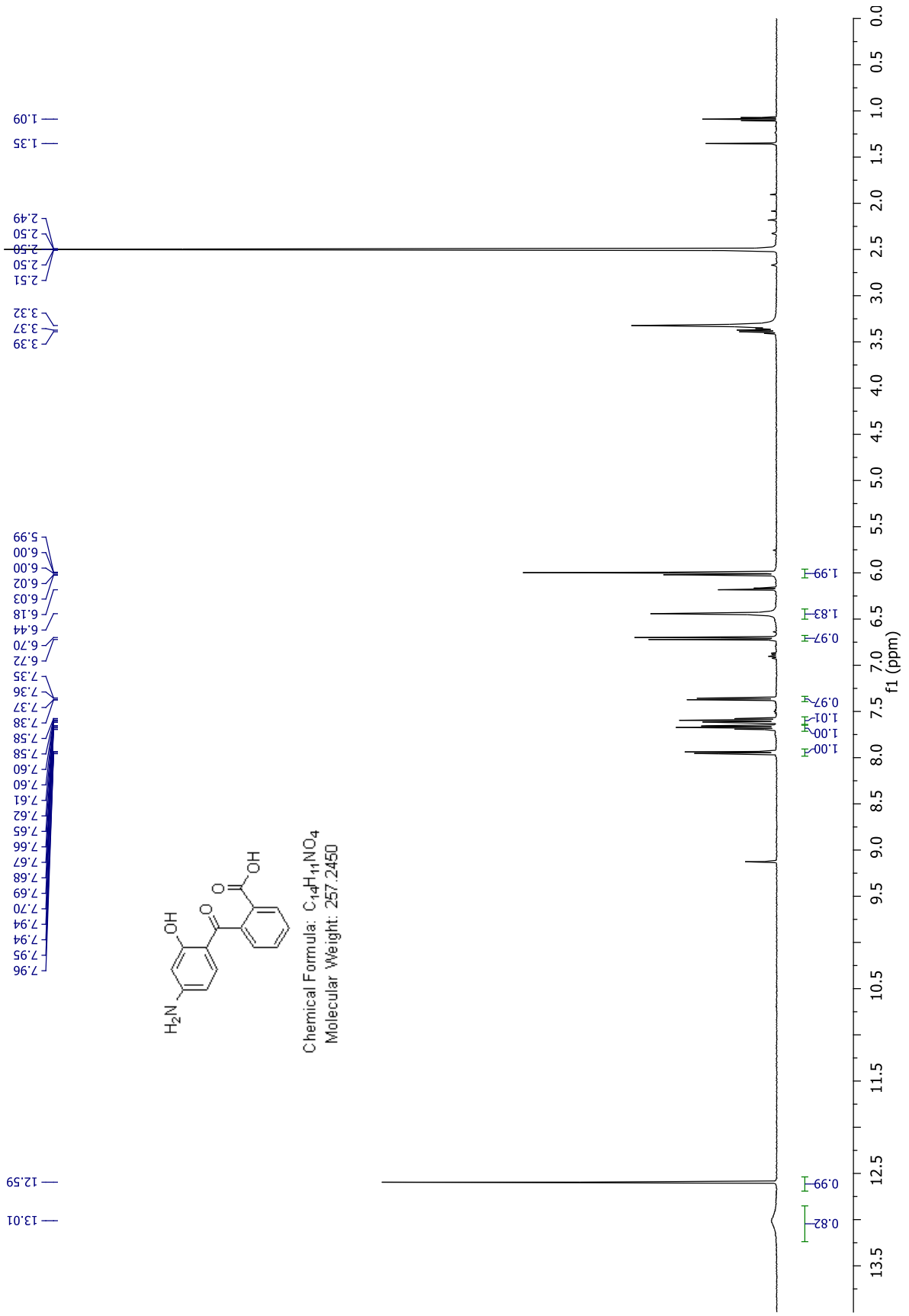


Figure S16. ^{1}H NMR spectrum of compound **17**.

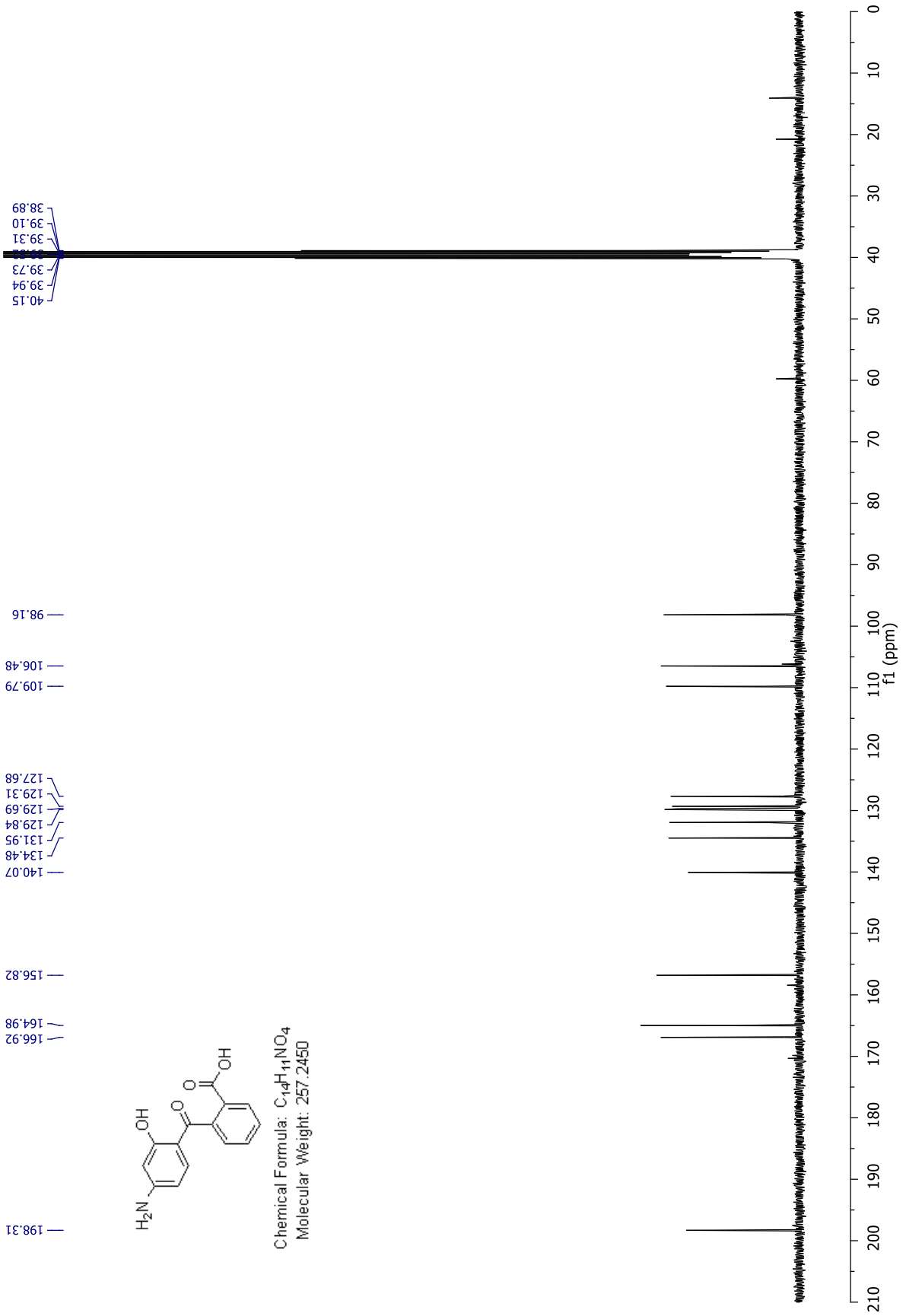


Figure S17. ^{13}C NMR spectrum of compound **17**.

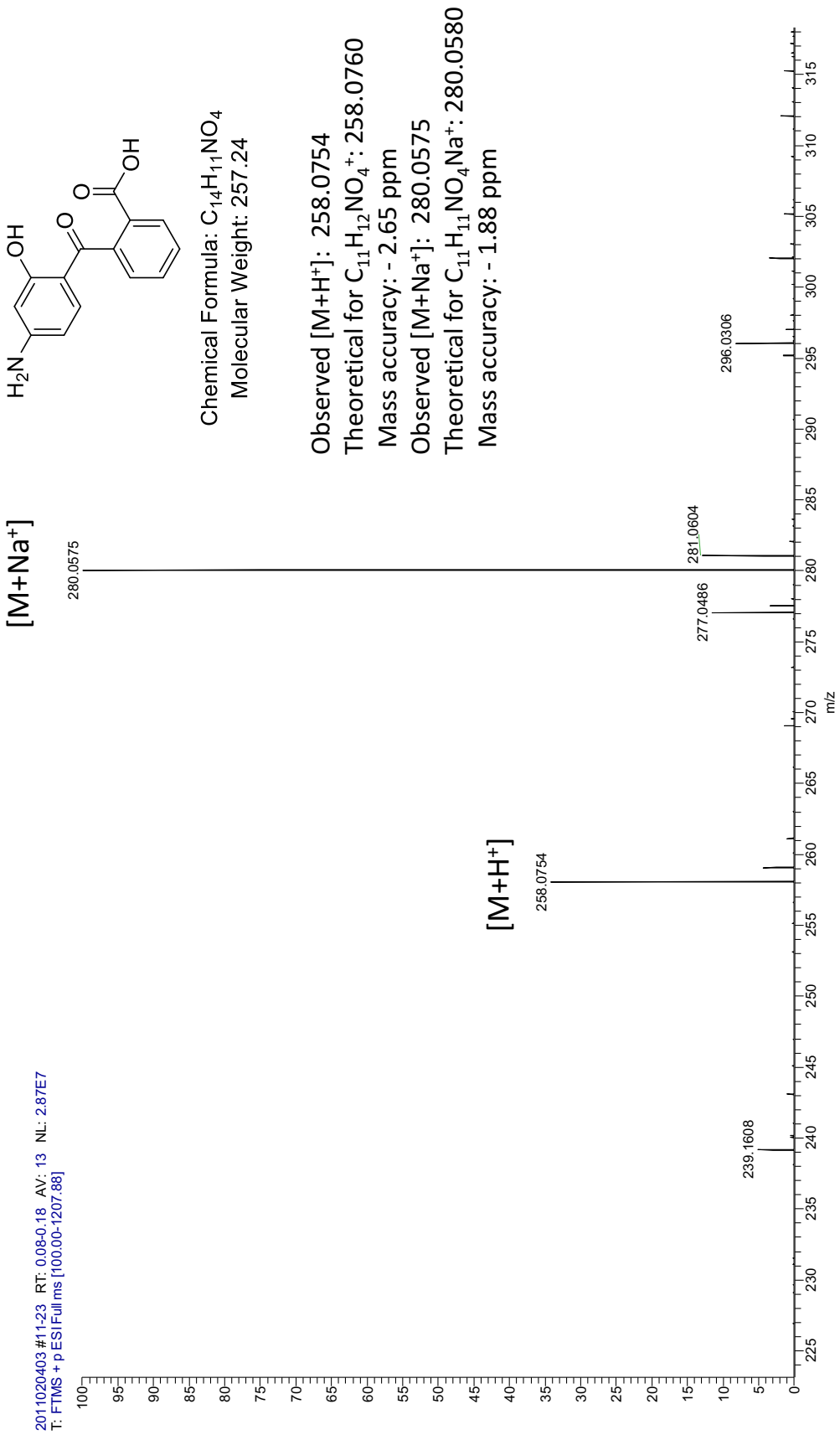


Figure S18. HR ESI positive mode spectrum of compound **17**.

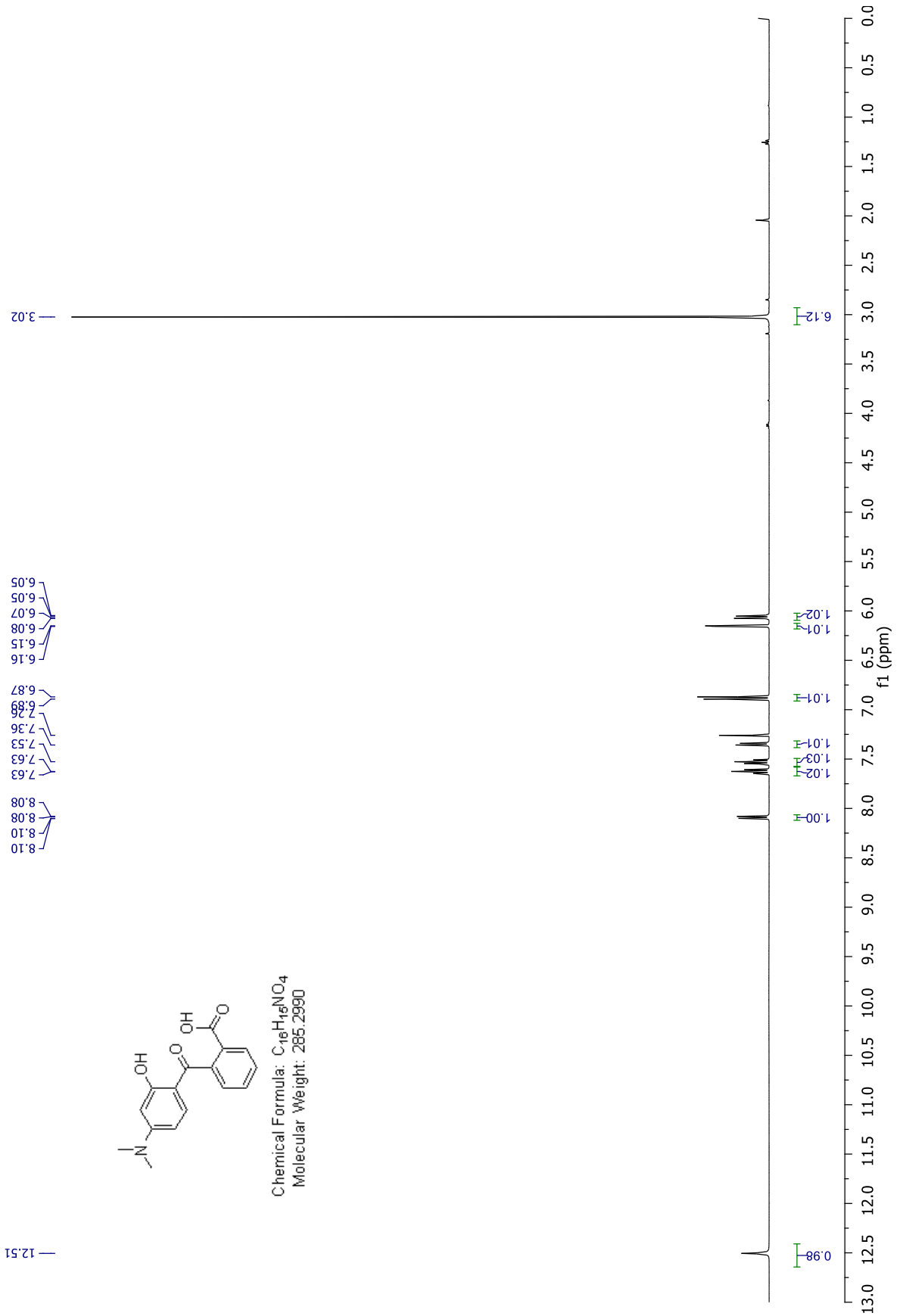


Figure S19. ^{1}H NMR spectrum of compound **20**.

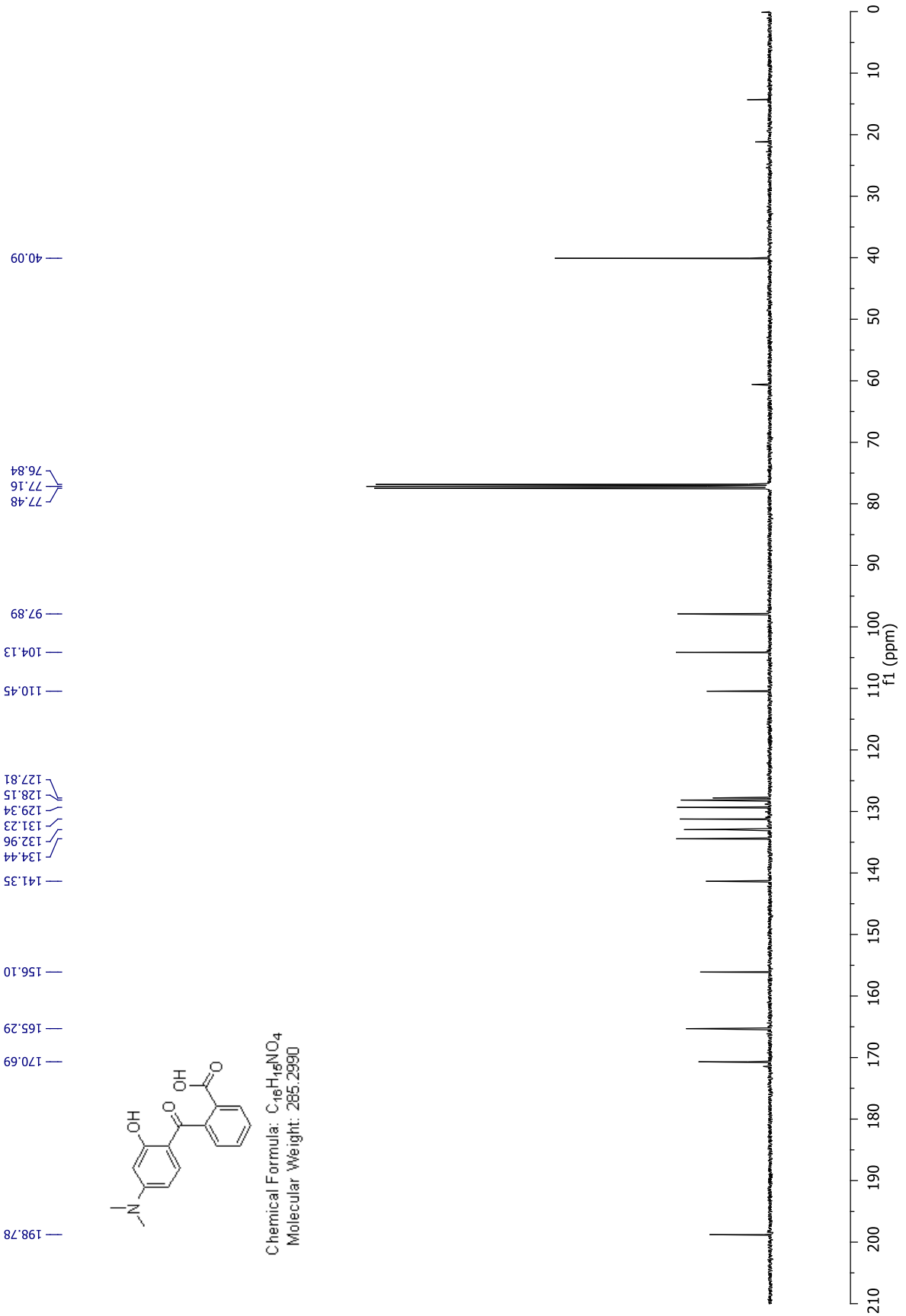


Figure S20. ^{13}C NMR spectrum of compound **20**.

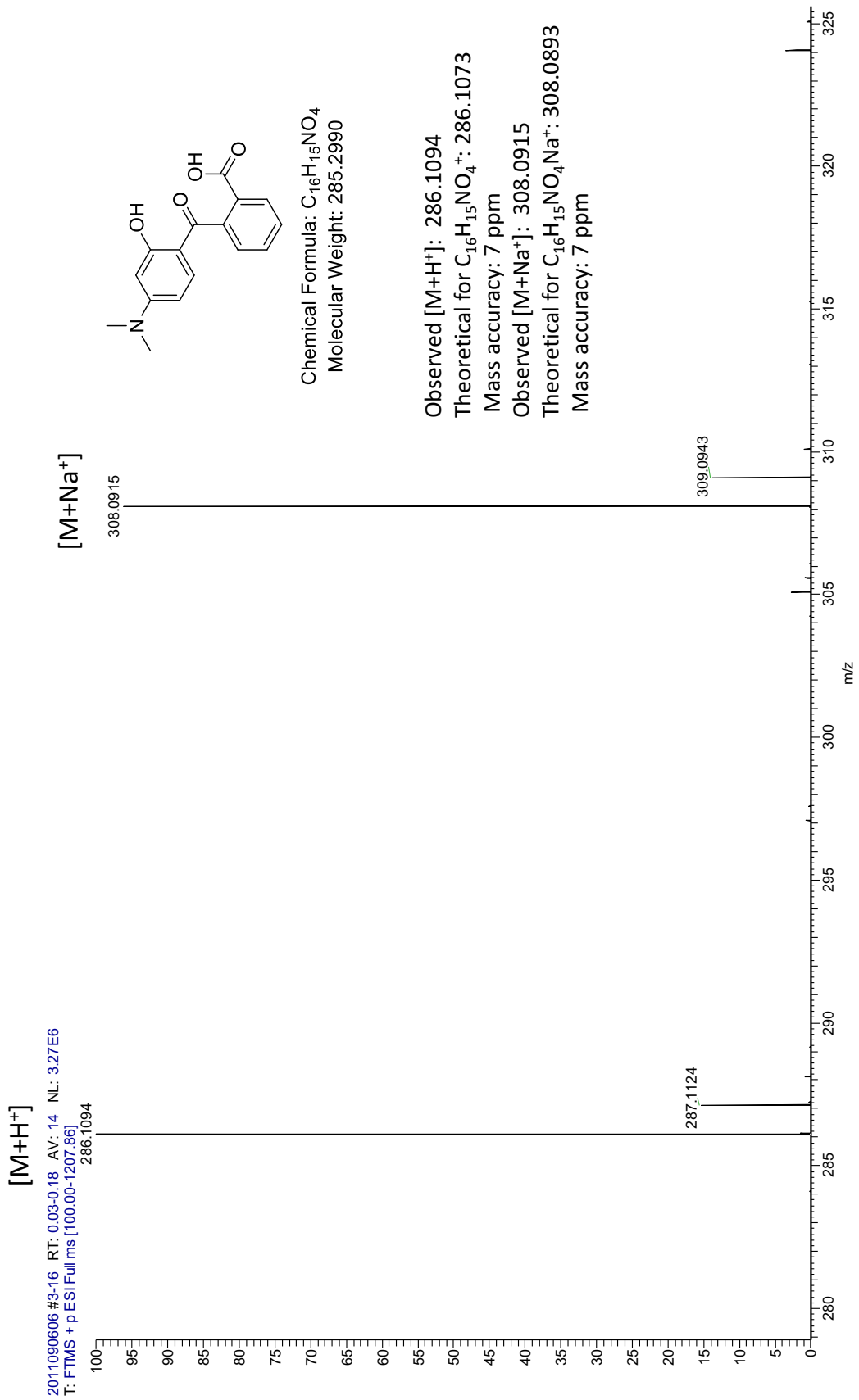


Figure S21. HR ESI positive mode spectrum of compound **20**.

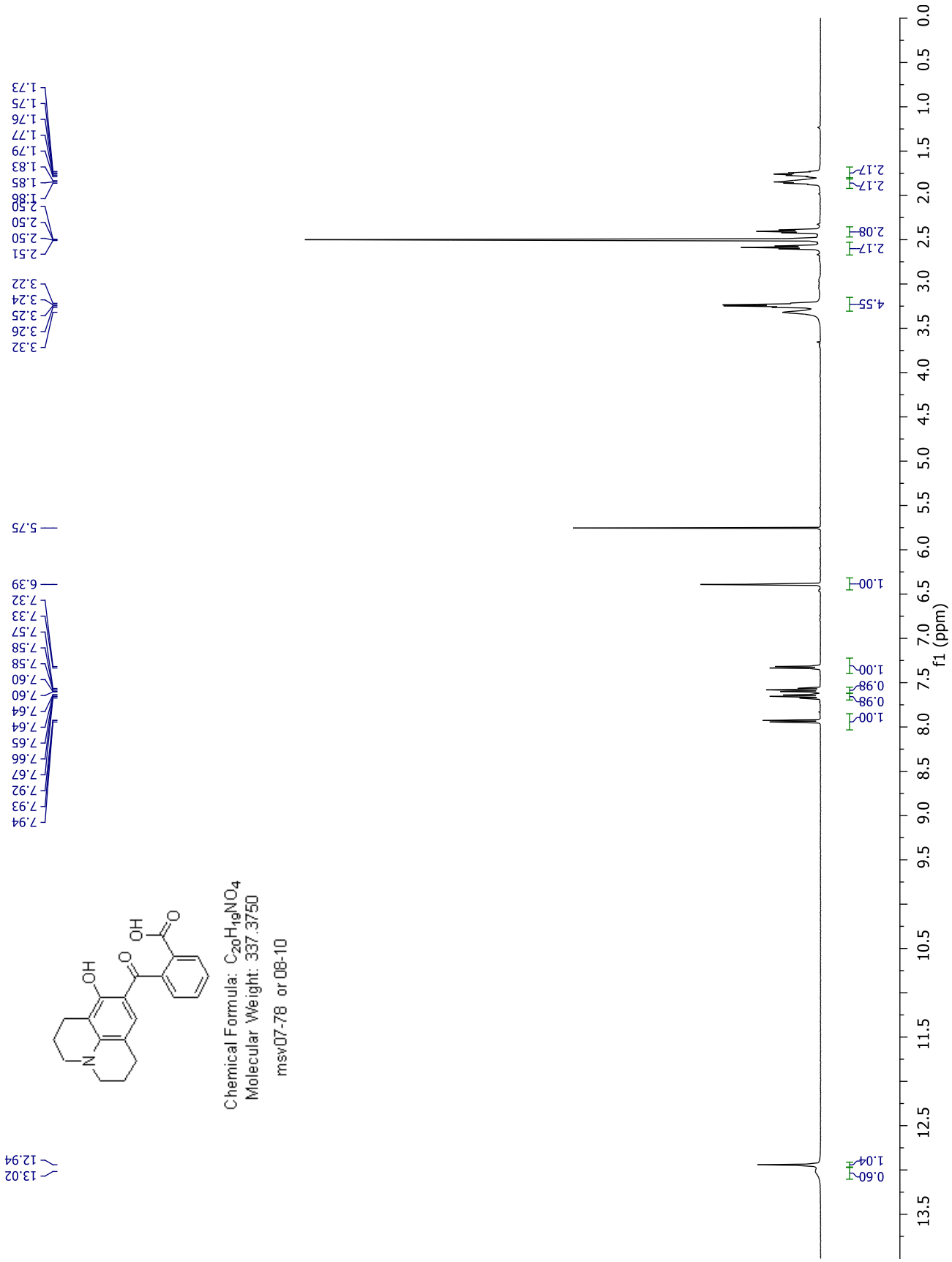


Figure S22. ^{1}H NMR spectrum of compound **22**.

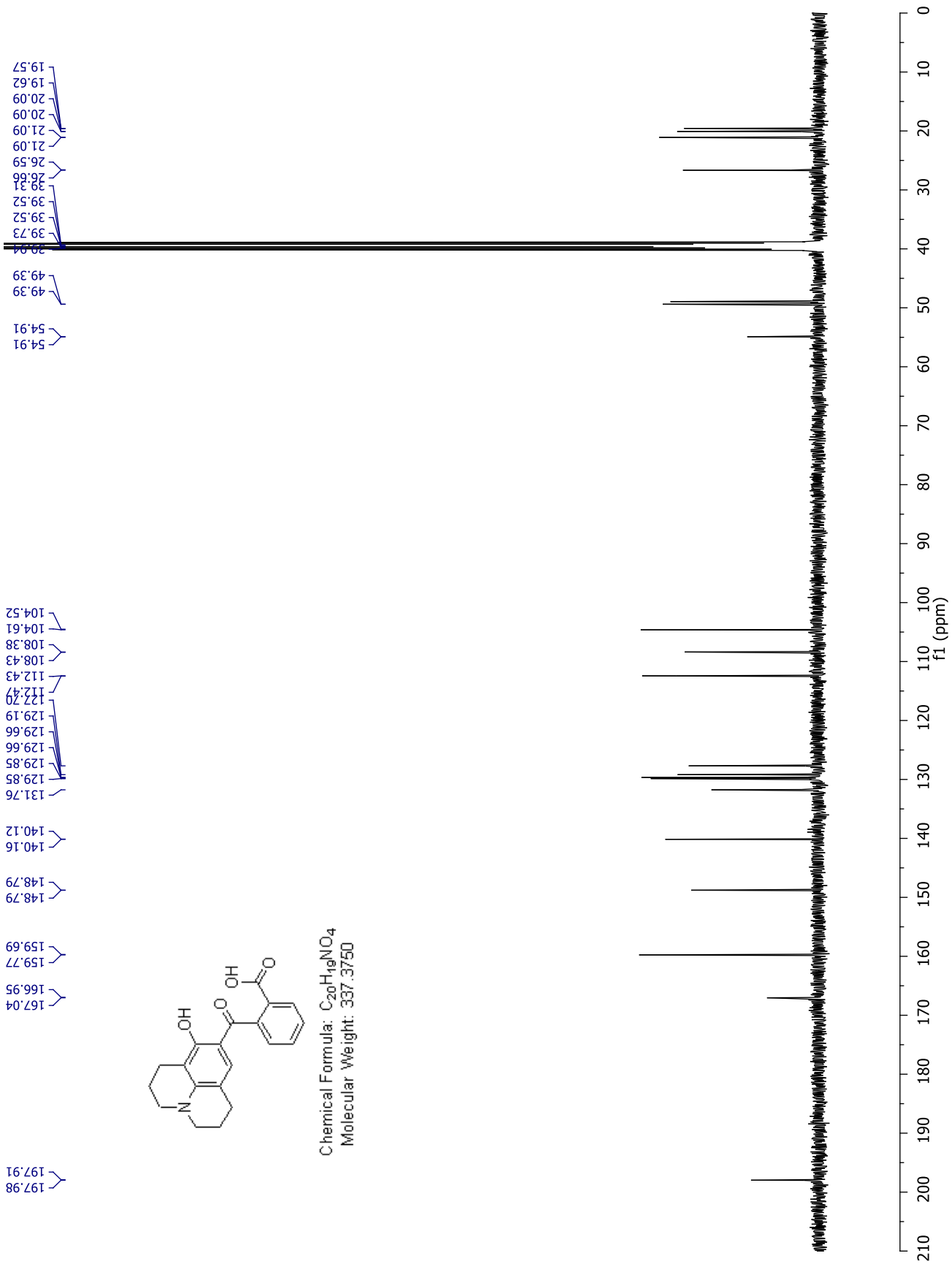
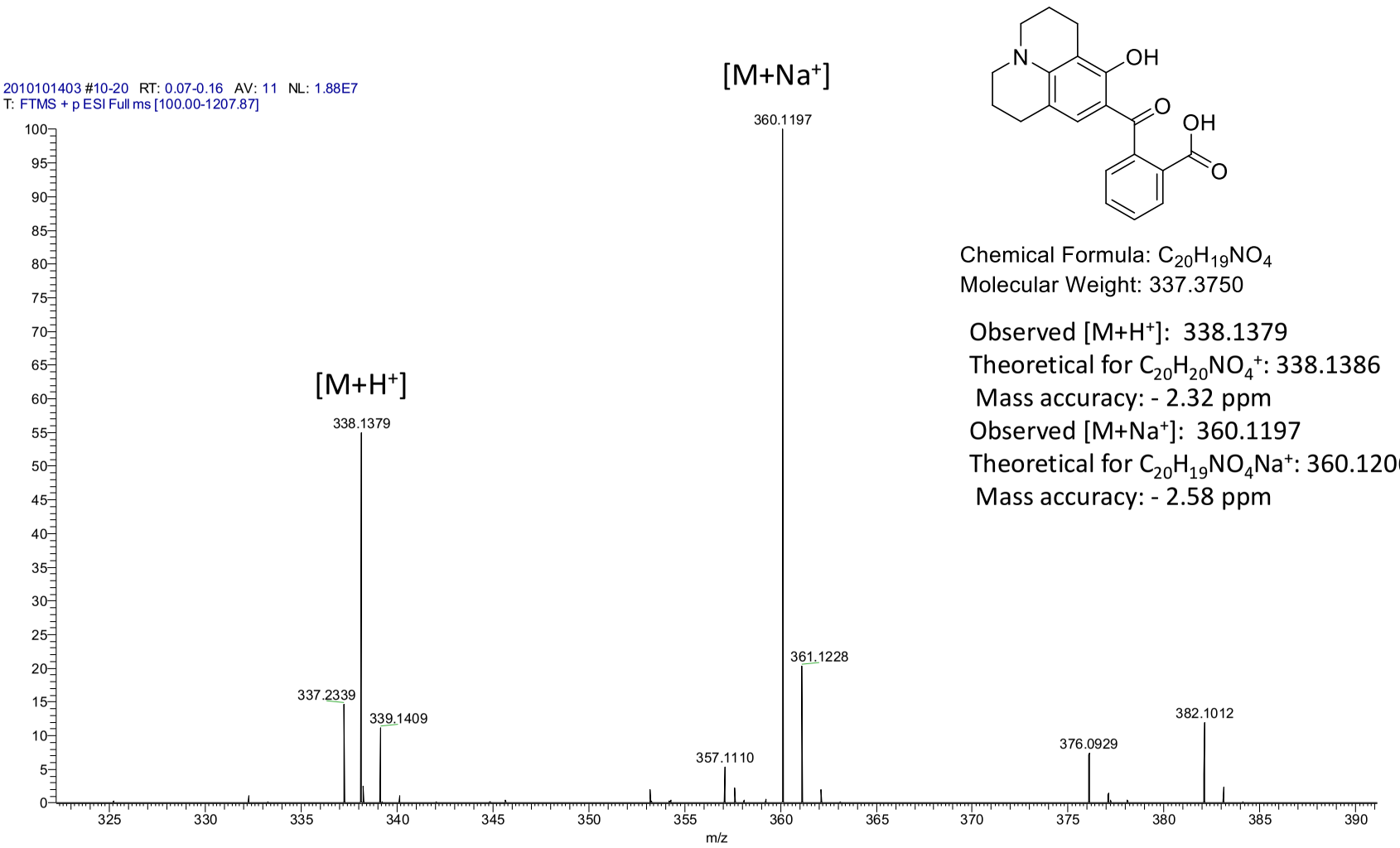


Figure S23. ^{13}C NMR spectrum of compound **22**.

Figure S24. HR ESI positive mode spectrum of compound **22**.



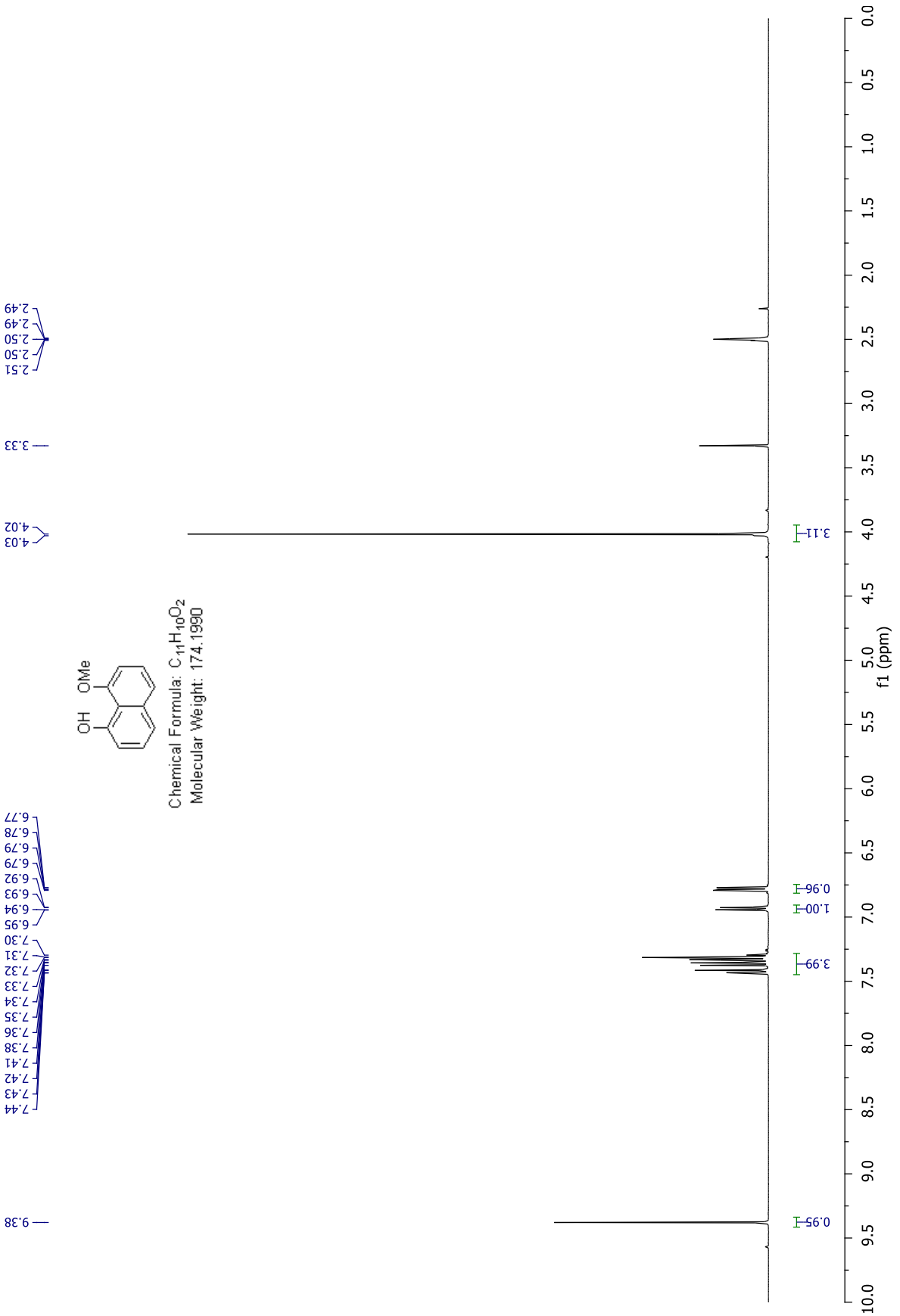


Figure S25. ^{1}H NMR spectrum of compound **24**.

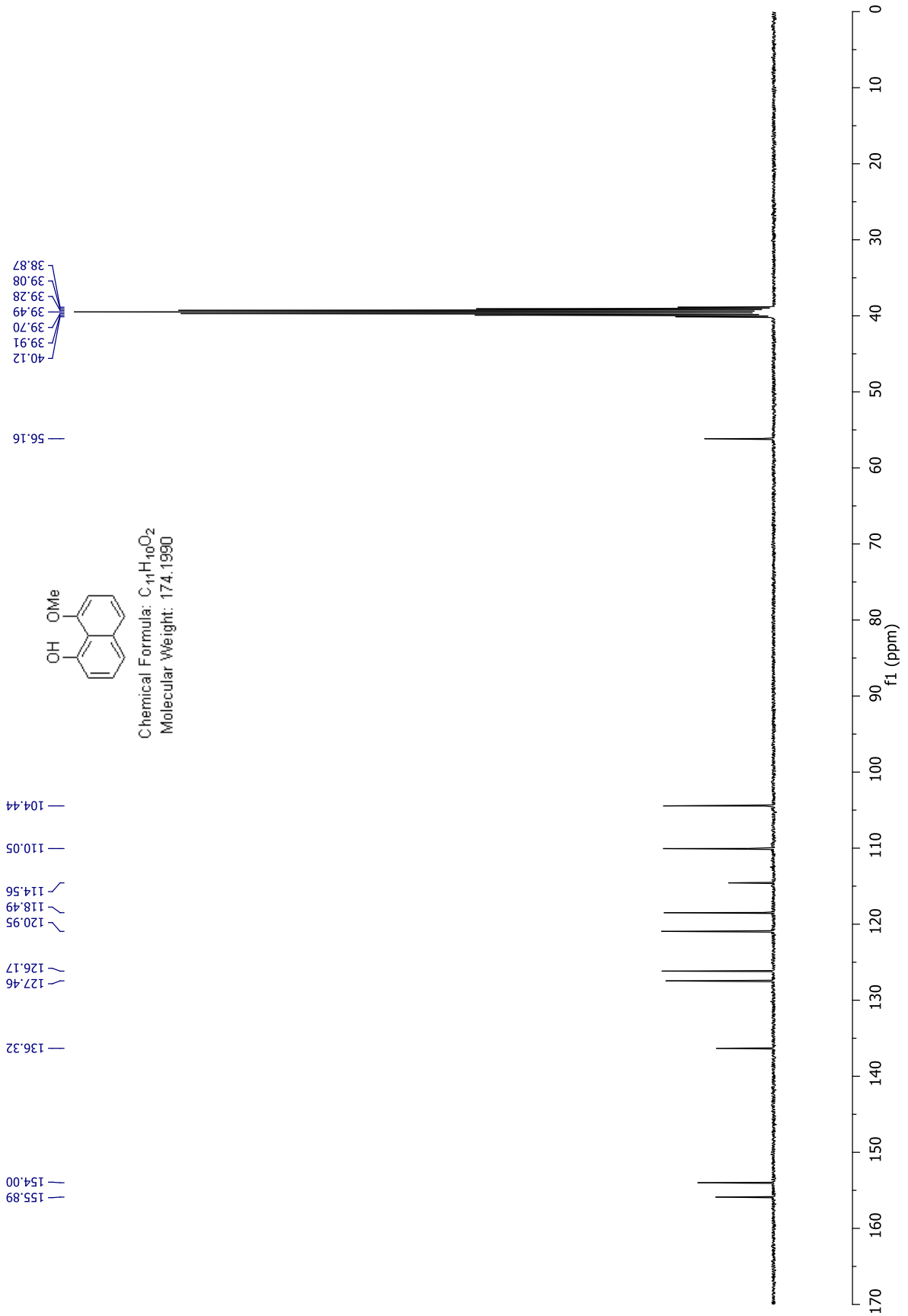


Figure S26. ^{13}C NMR spectrum of compound **24**.

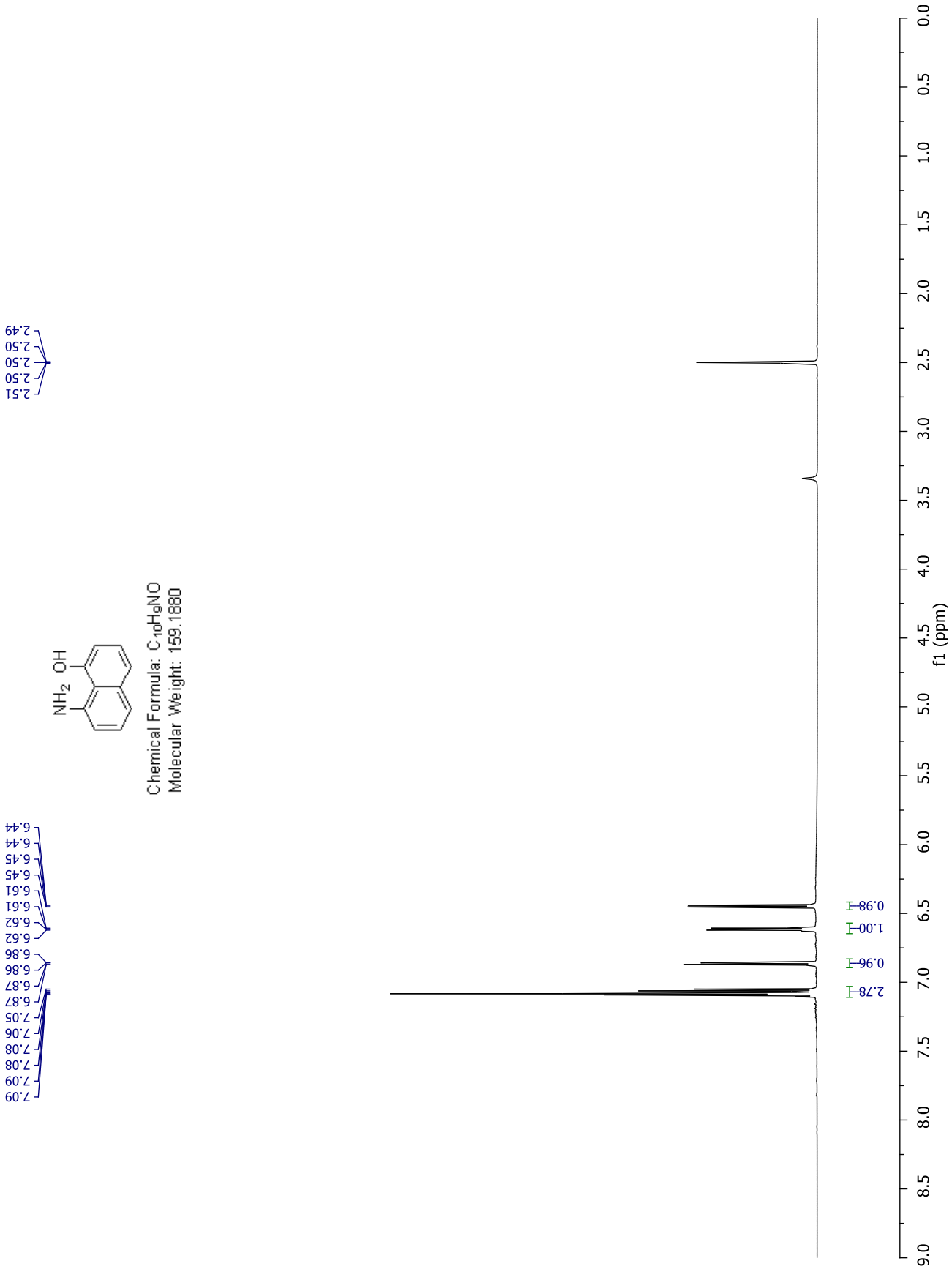


Figure S27. ^{1}H NMR spectrum of compound **26**.

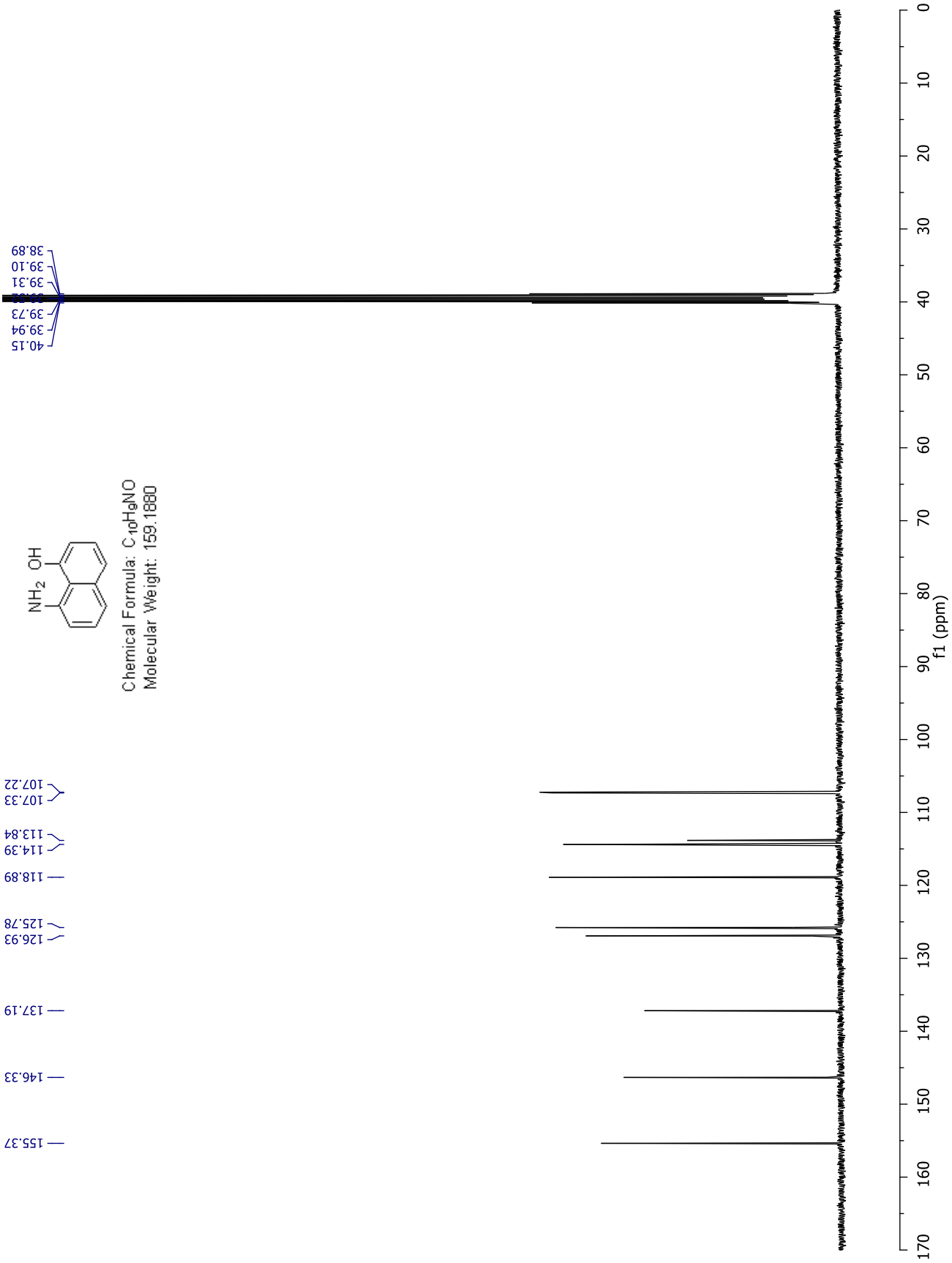


Figure S28. ^{13}C NMR spectrum of compound **26**.

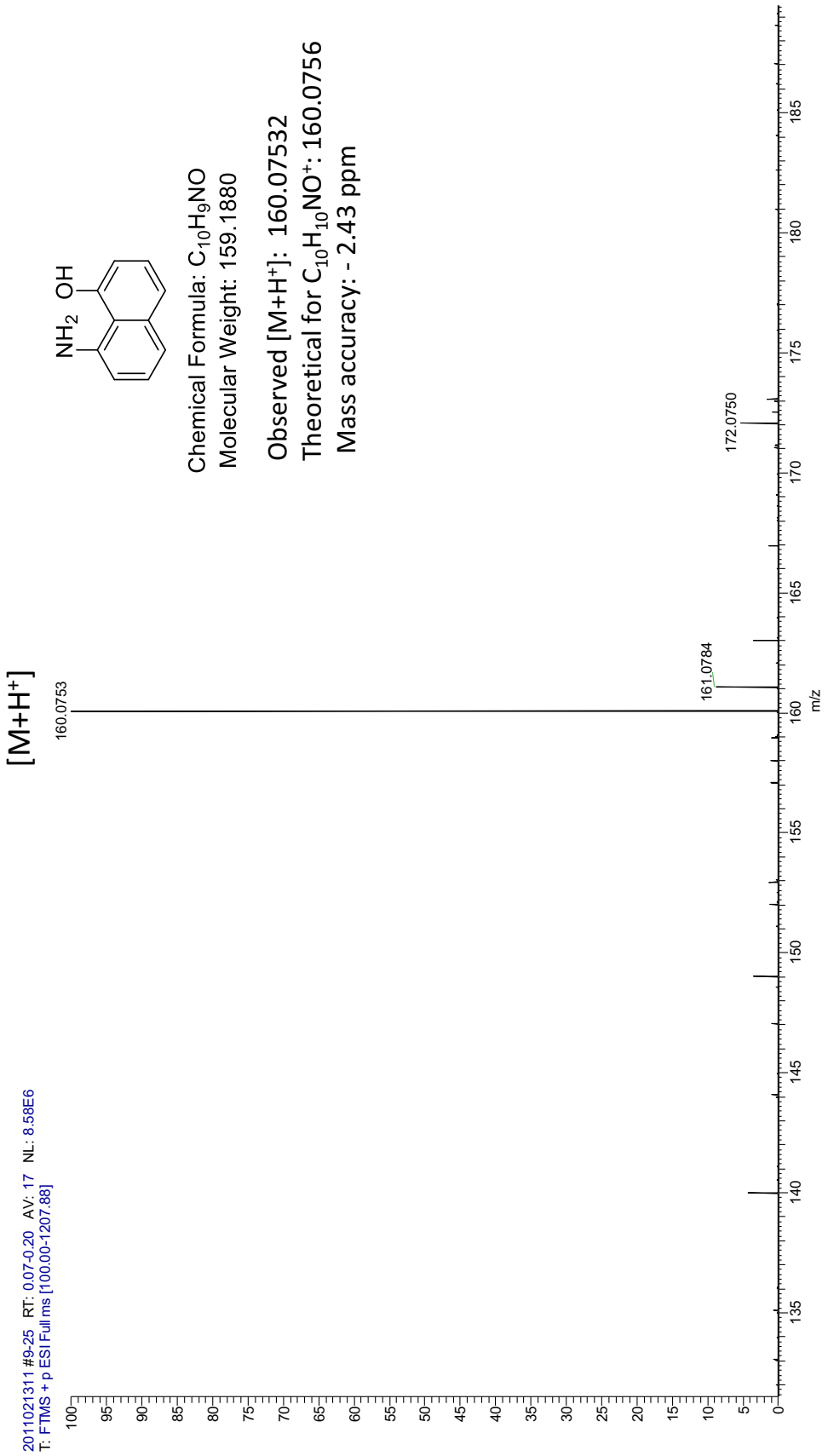


Figure S29. HR ESI positive mode spectrum of compound **26**.

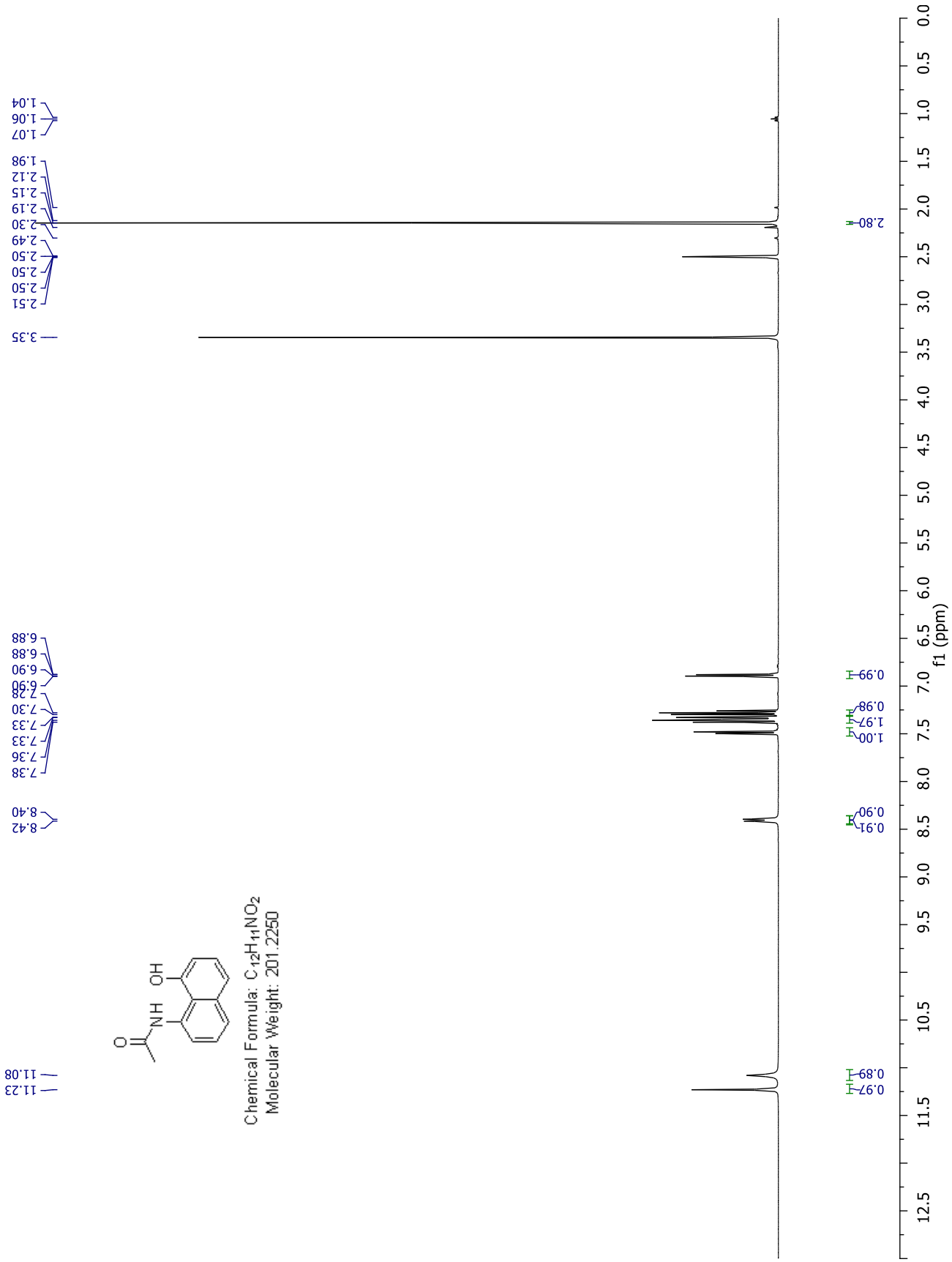


Figure S30. ^{1}H NMR spectrum of compound **28**.

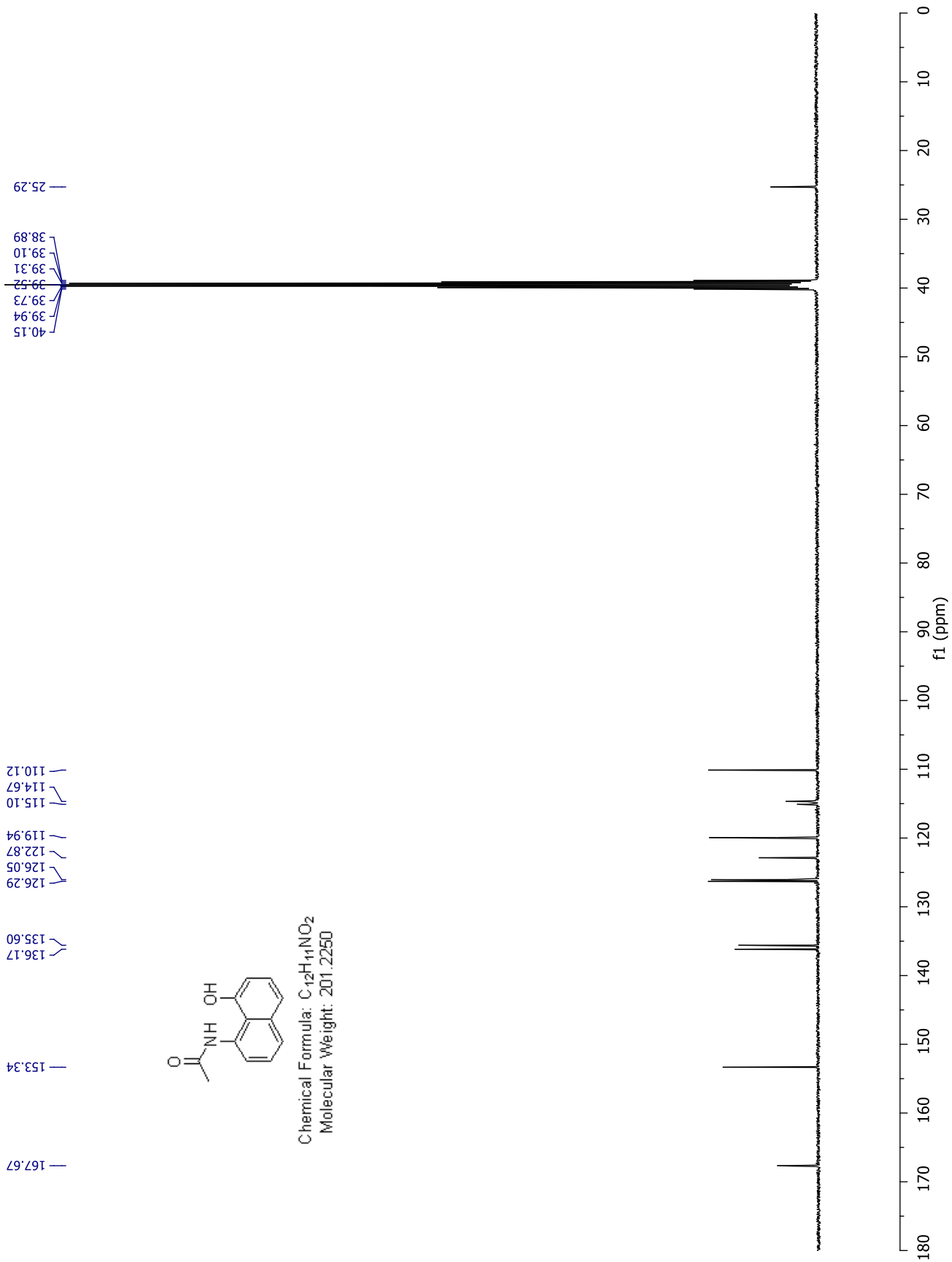


Figure S31. ^{13}C NMR spectrum of compound **28**.

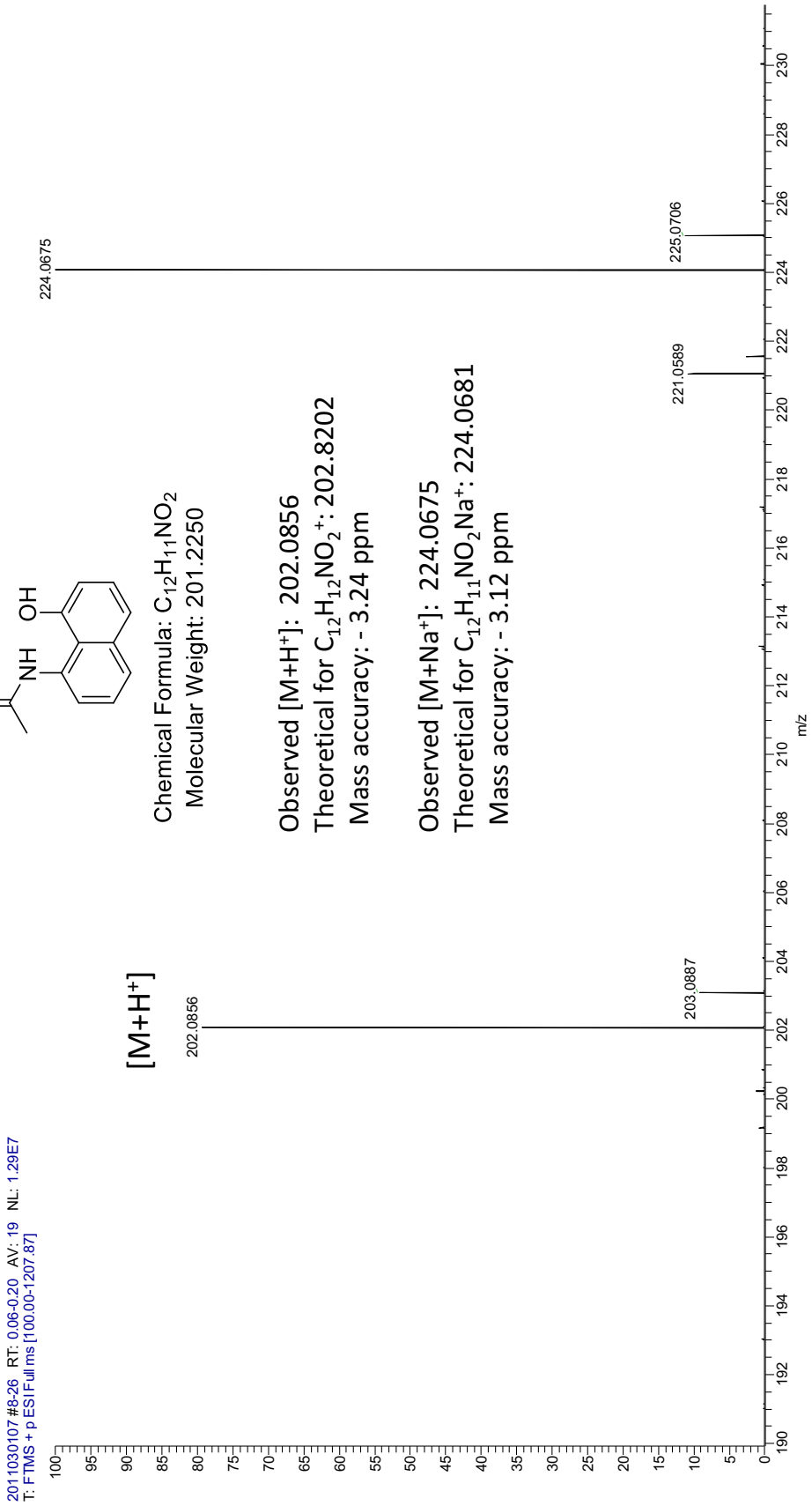


Figure S32. HR ESI positive mode spectrum of compound **28**.

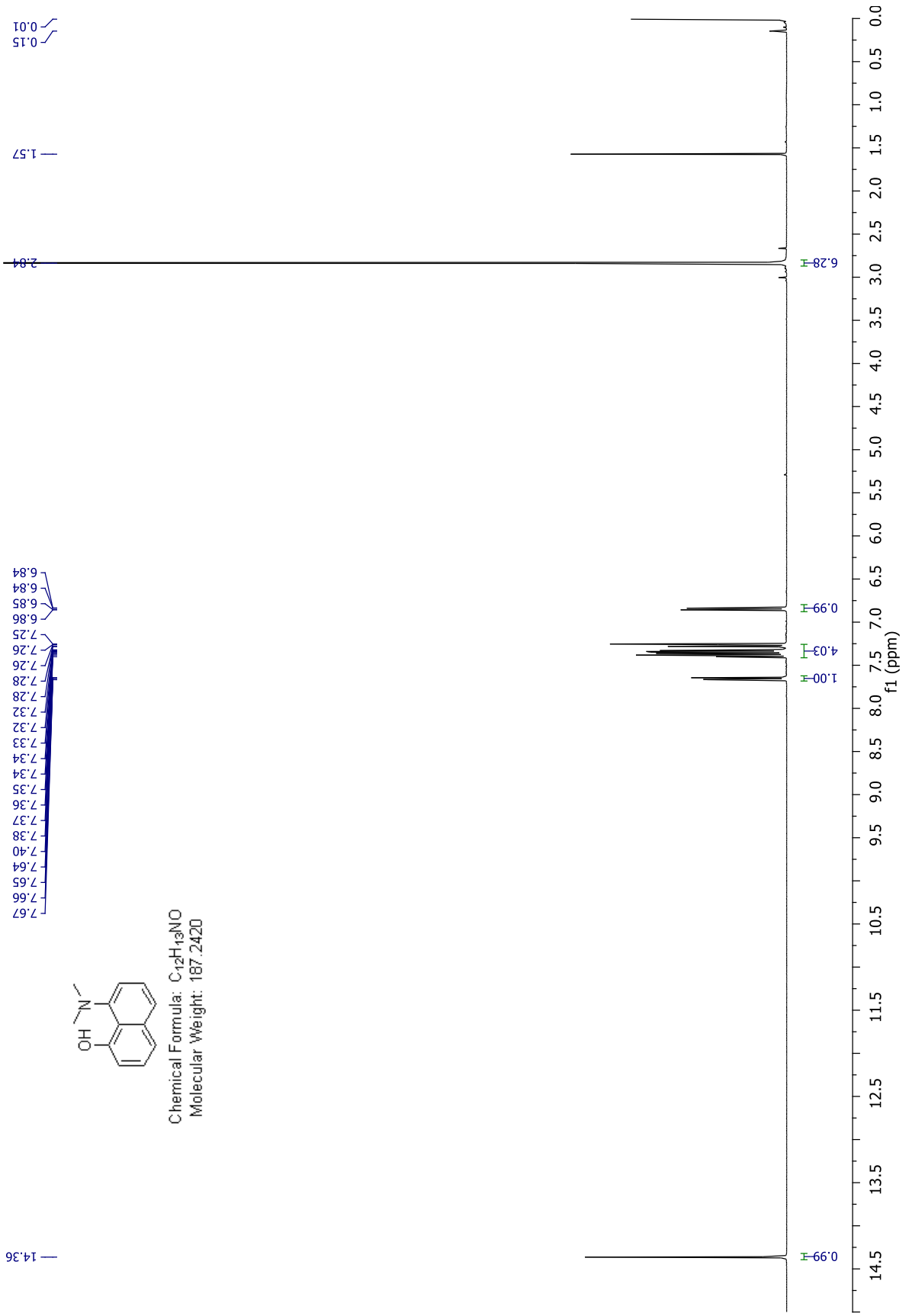


Figure S33. ^{1}H NMR spectrum of compound **31**.

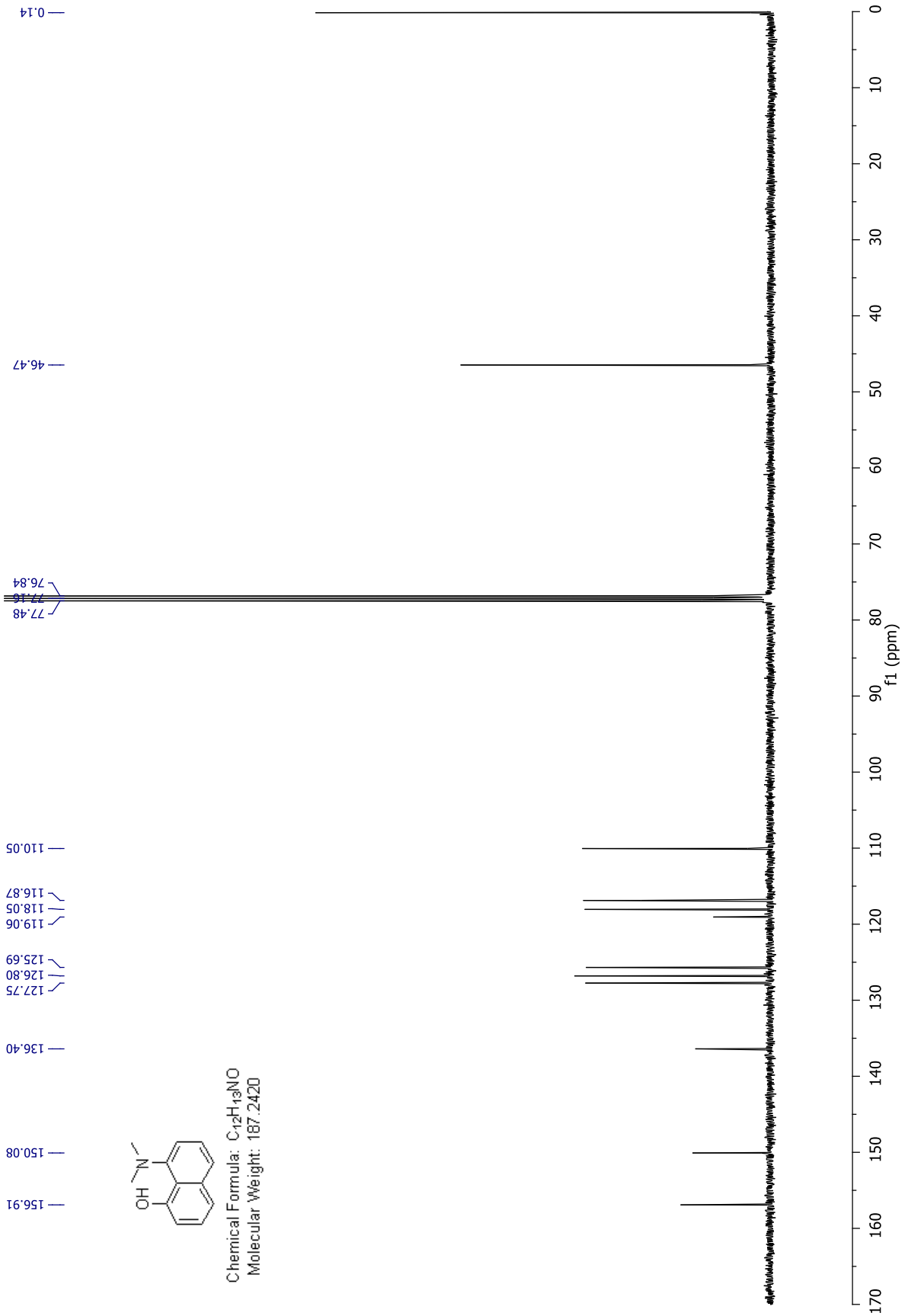


Figure S34. ^{13}C NMR spectrum of compound **31**.

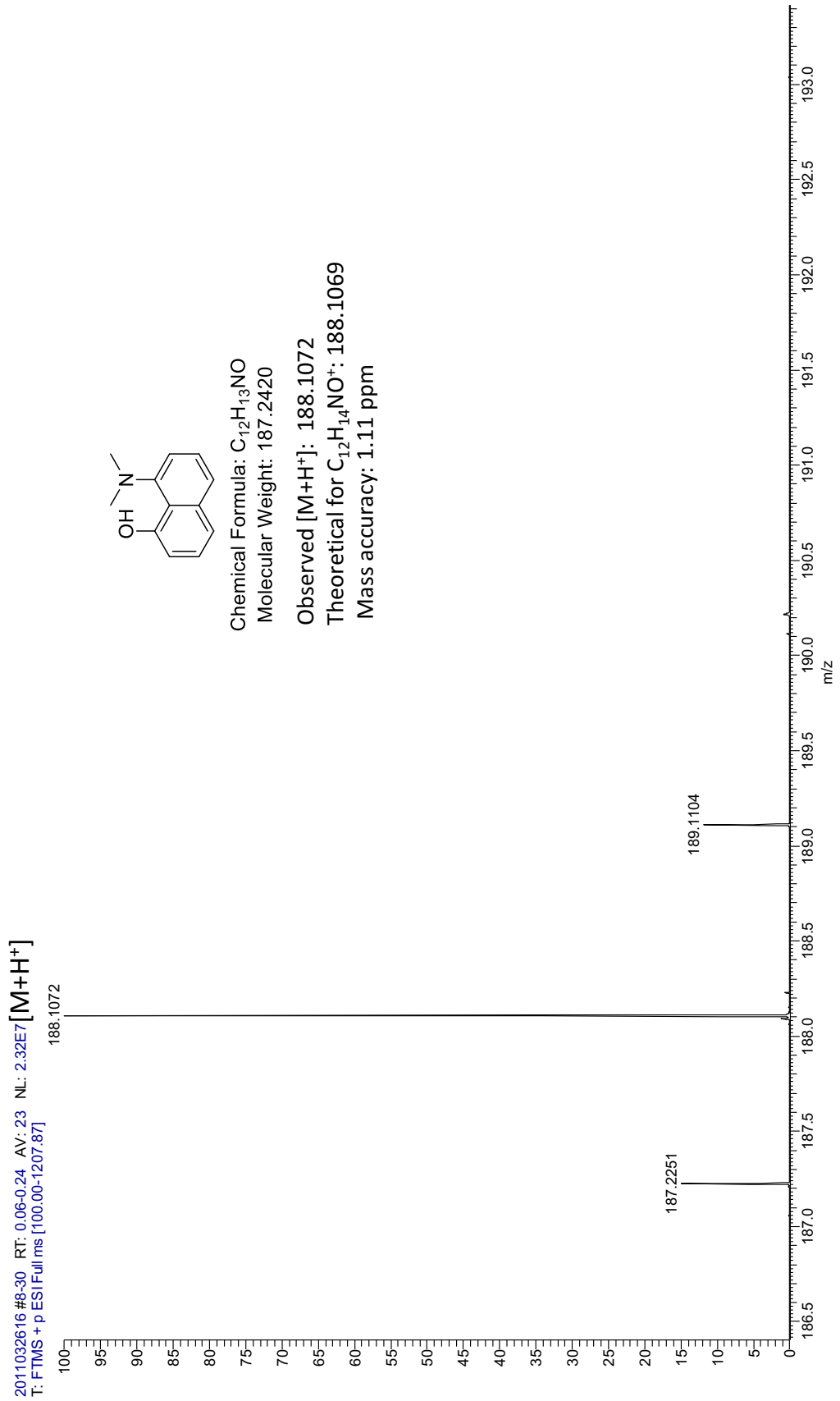


Figure S35. HR ESI positive mode spectrum of compound **31**.

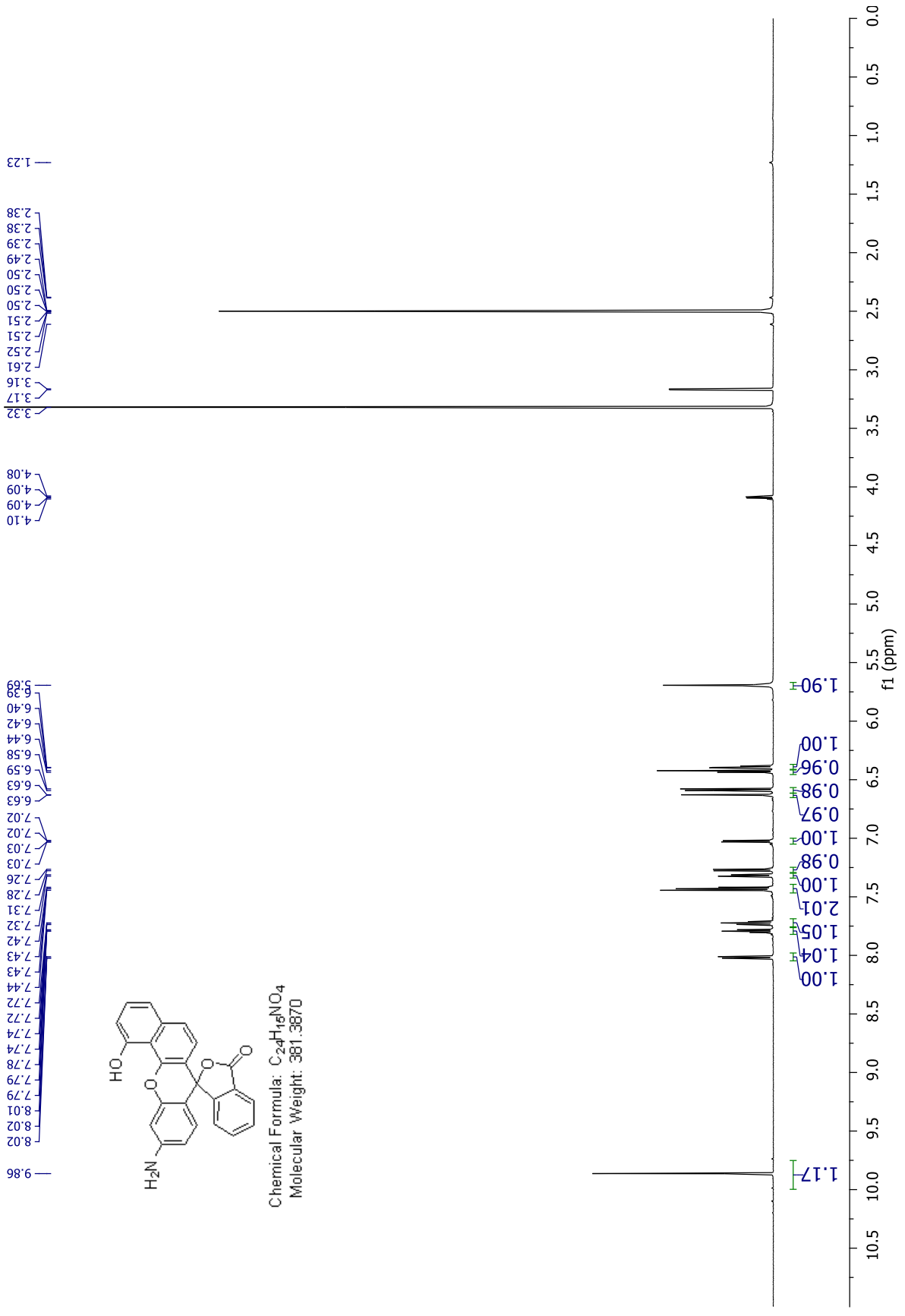


Figure S36. ^{1}H NMR spectrum of compound **32**.

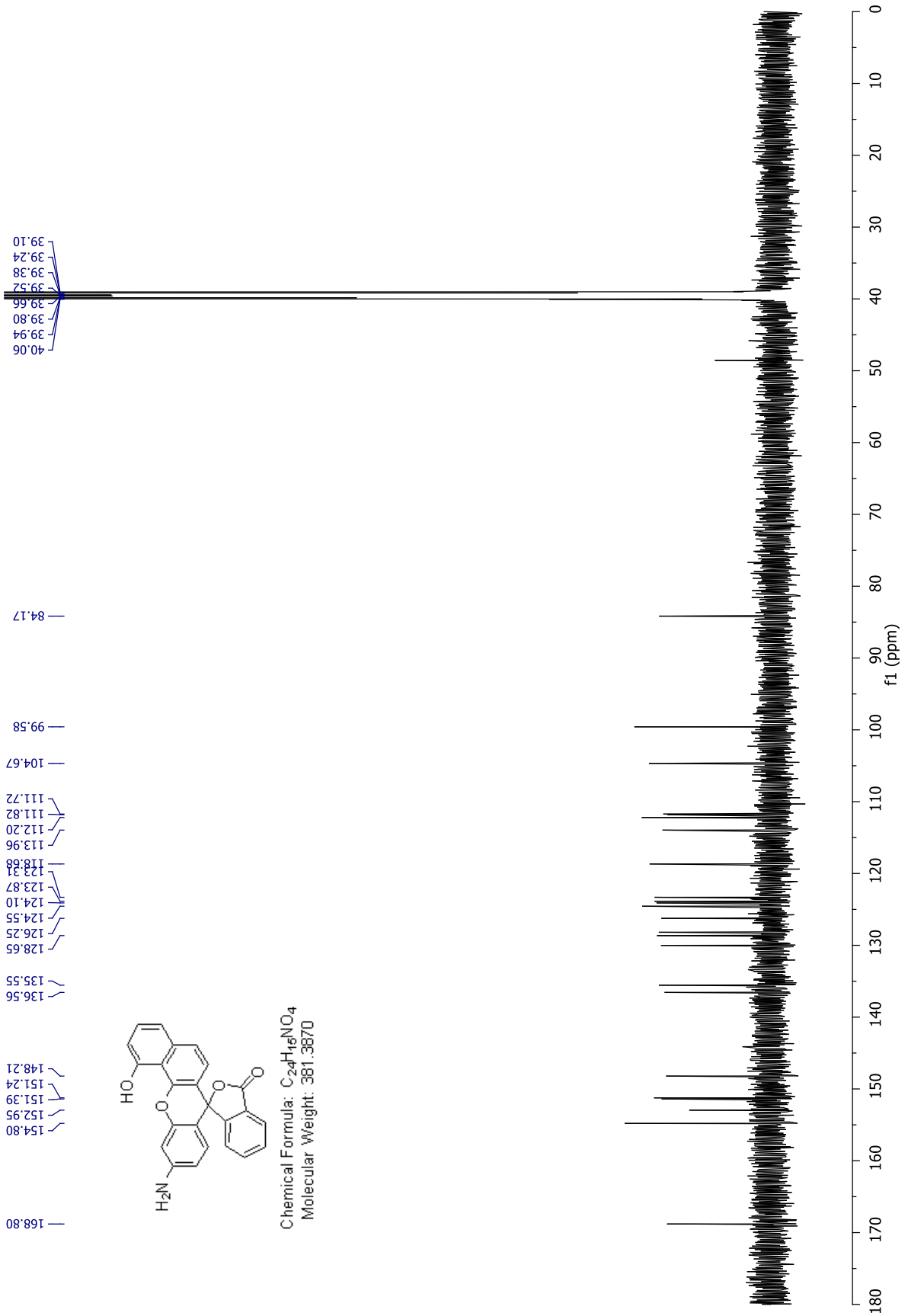


Figure S37. ^{13}C NMR spectrum of compound **32**.

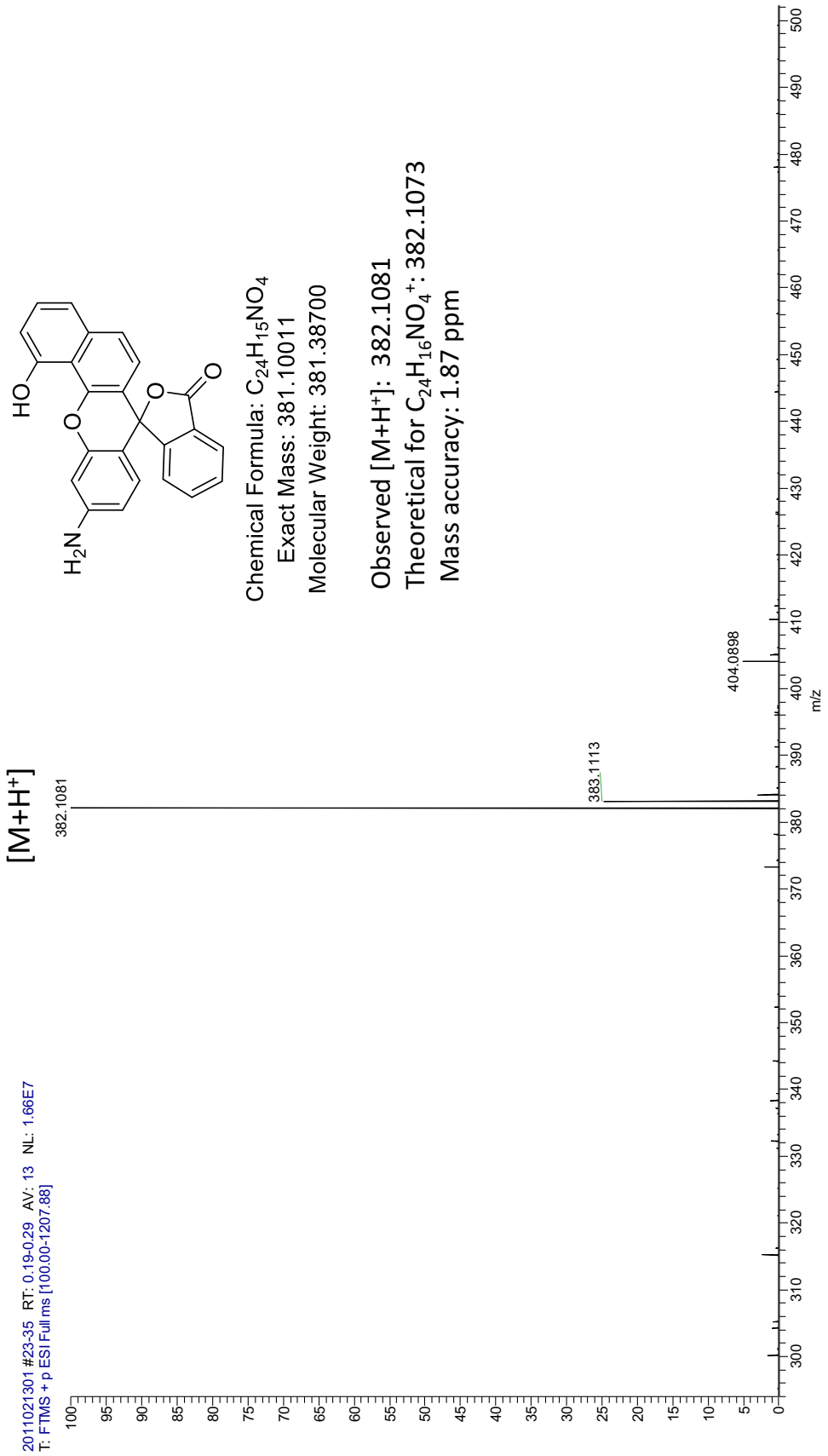


Figure S38. HR ESI positive mode spectrum of compound **31**.

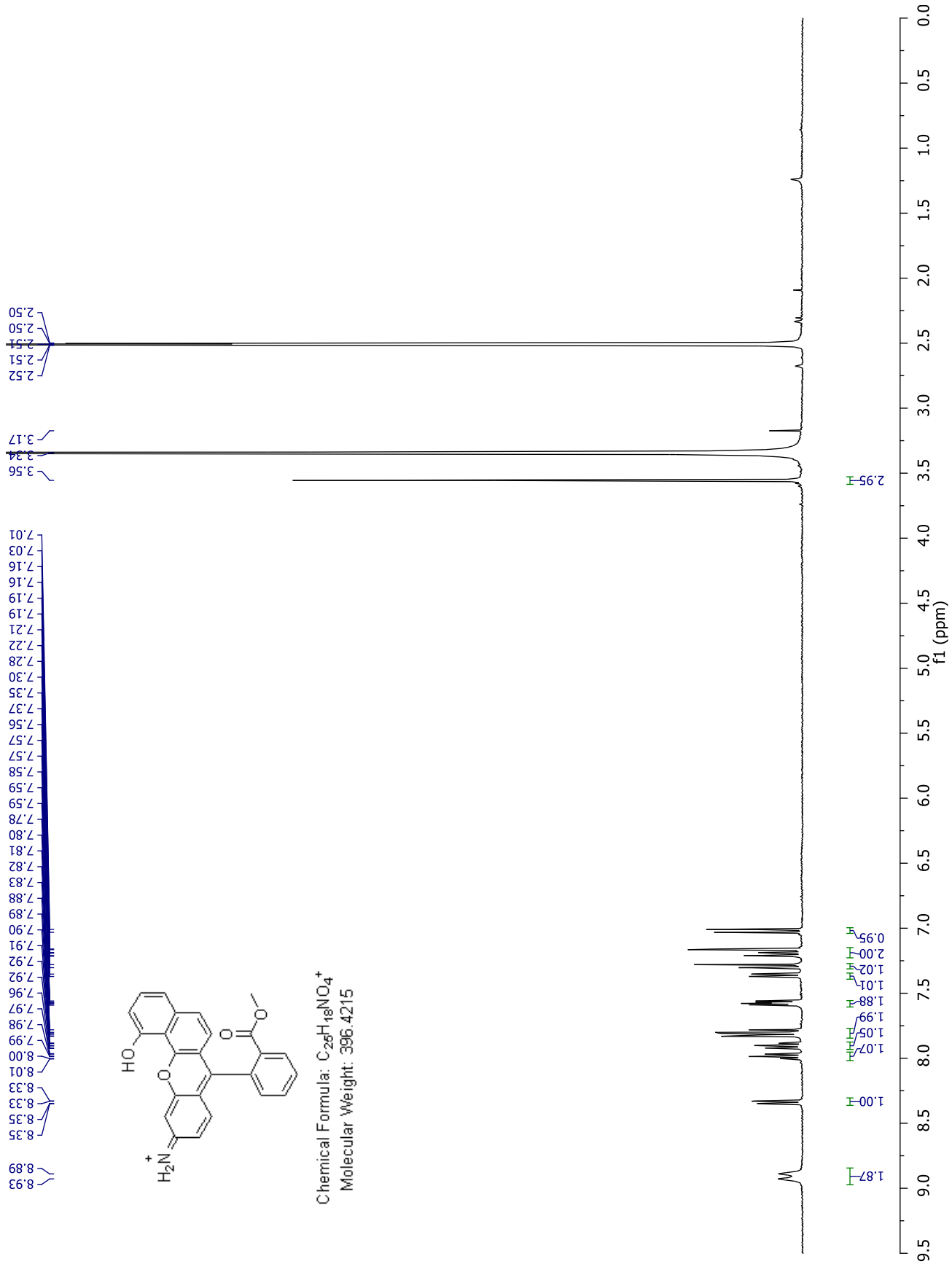


Figure S39. ^{1}H NMR spectrum of compound **3**.

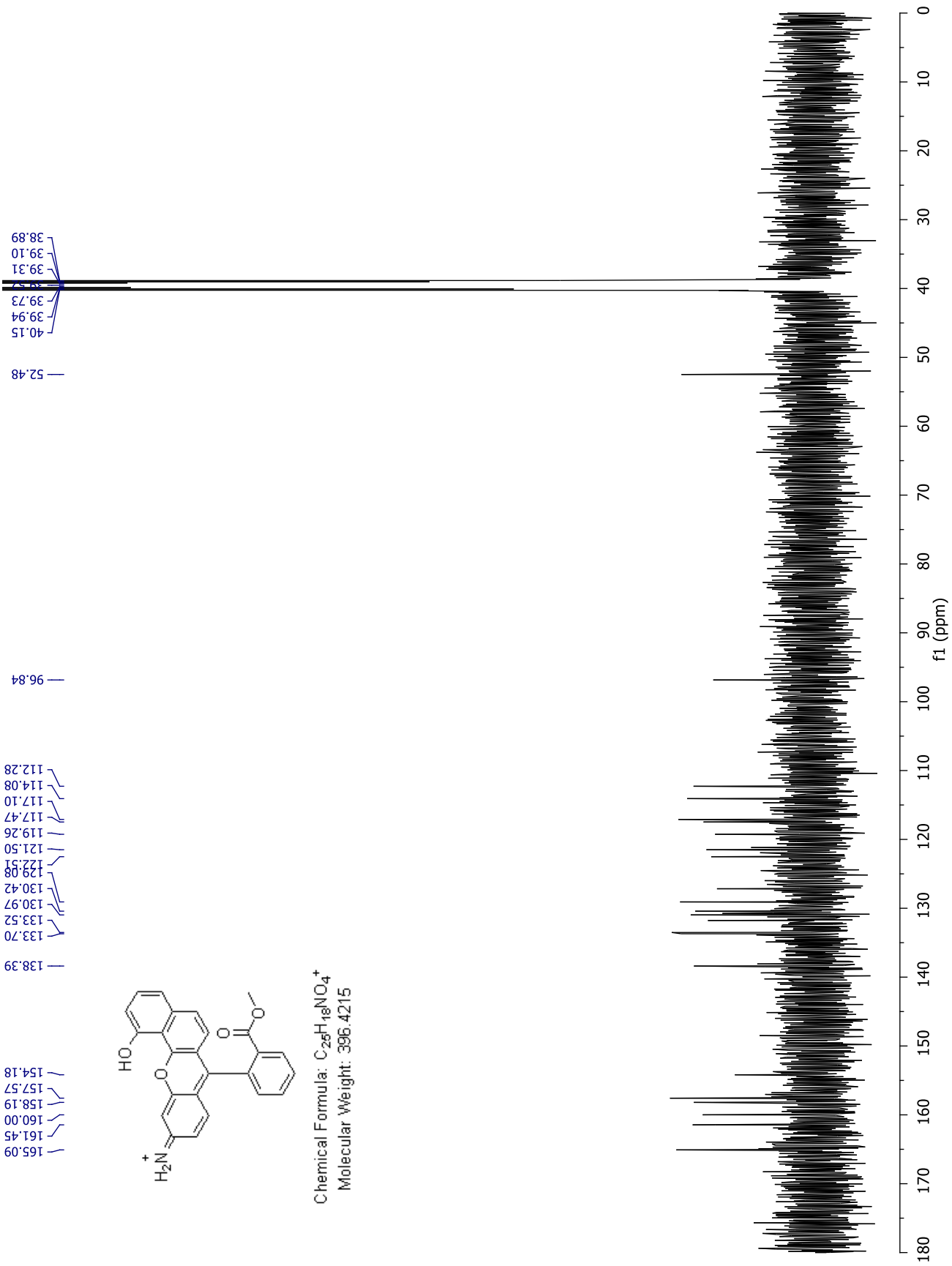


Figure S40. ^{13}C NMR spectrum of compound **3**.

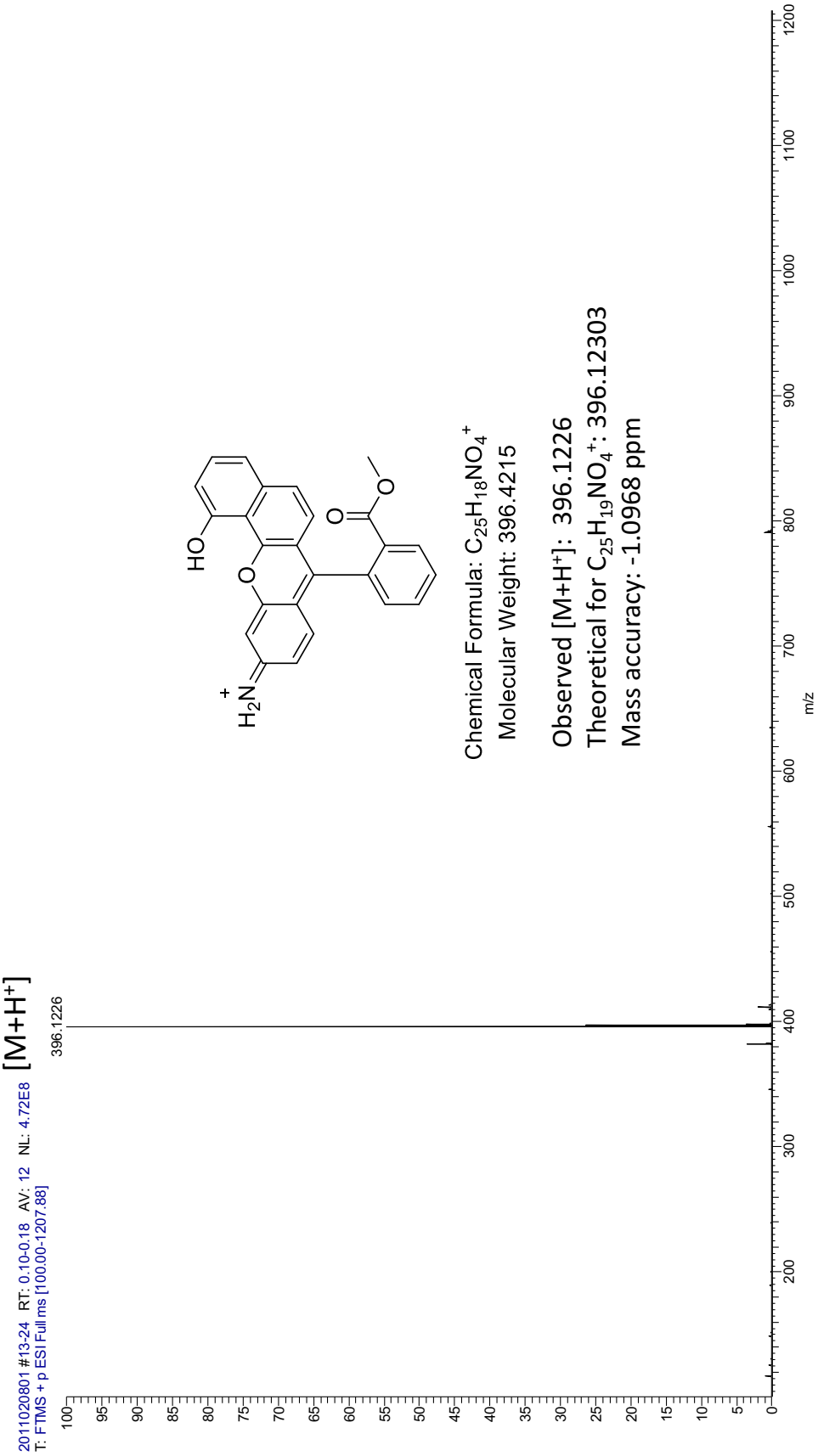


Figure S41. HR ESI positive mode spectrum of compound **3**.

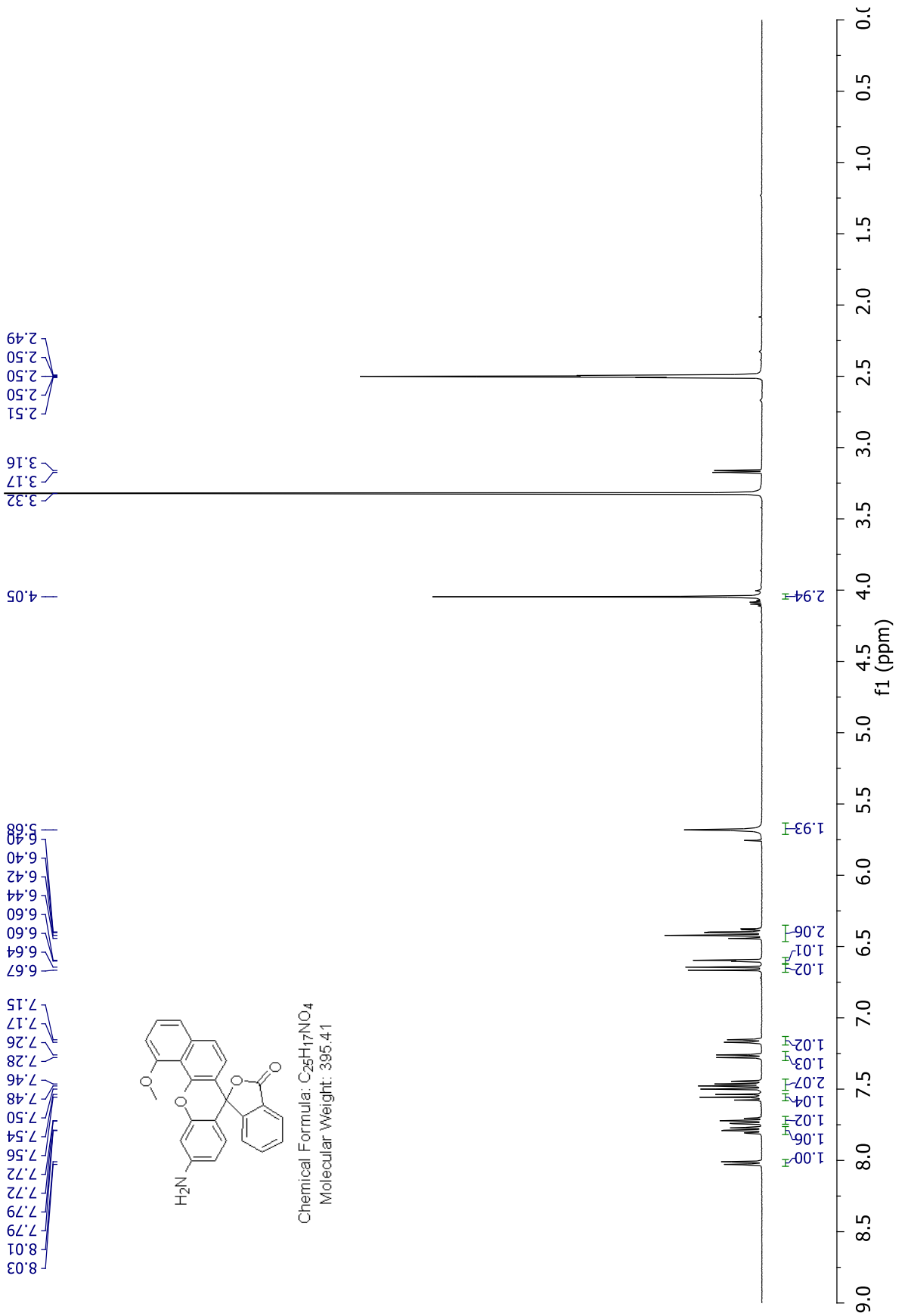


Figure S42. ^{1}H NMR spectrum of compound **33**.

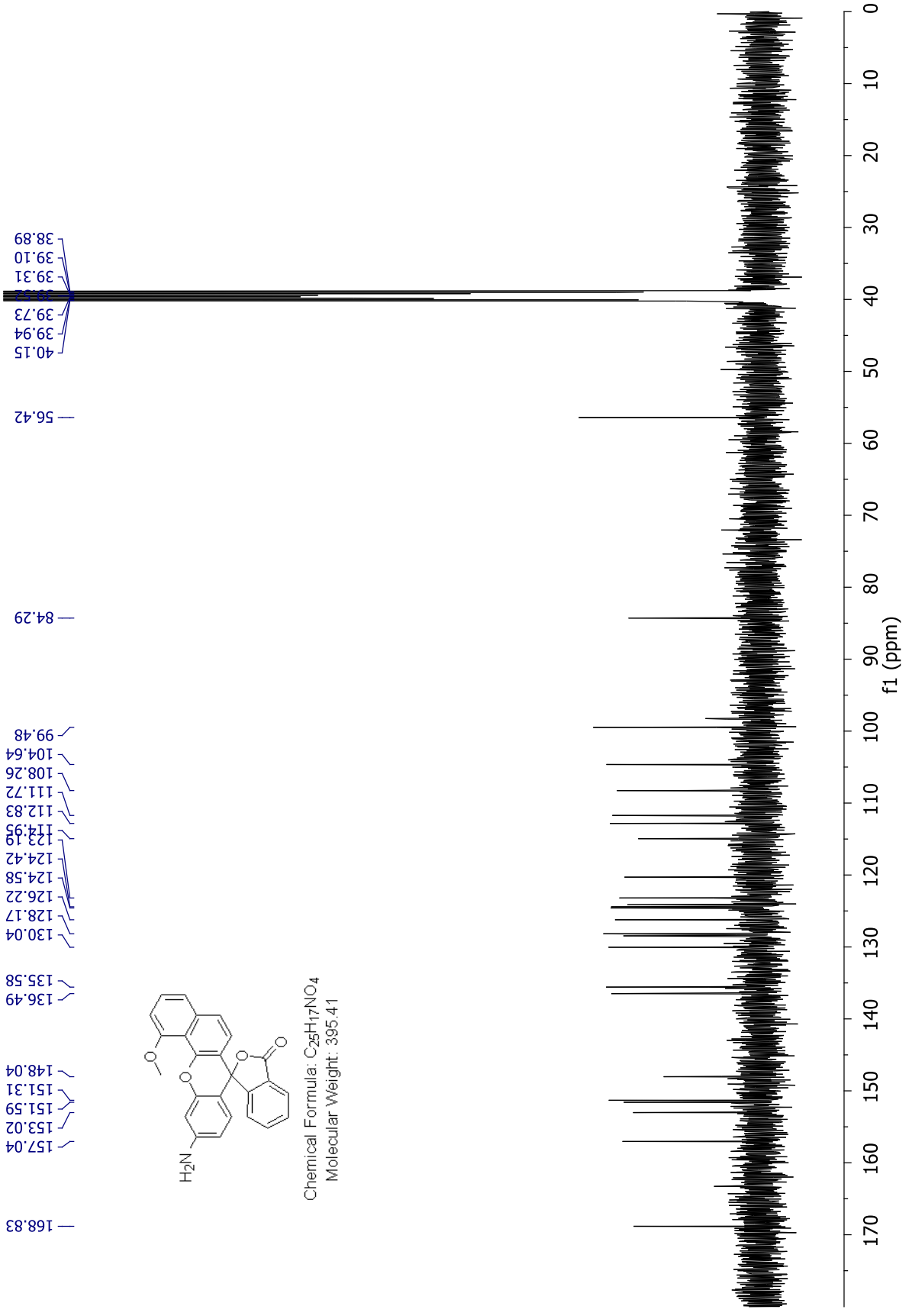


Figure S43. ^{13}C NMR spectrum of compound **33**.

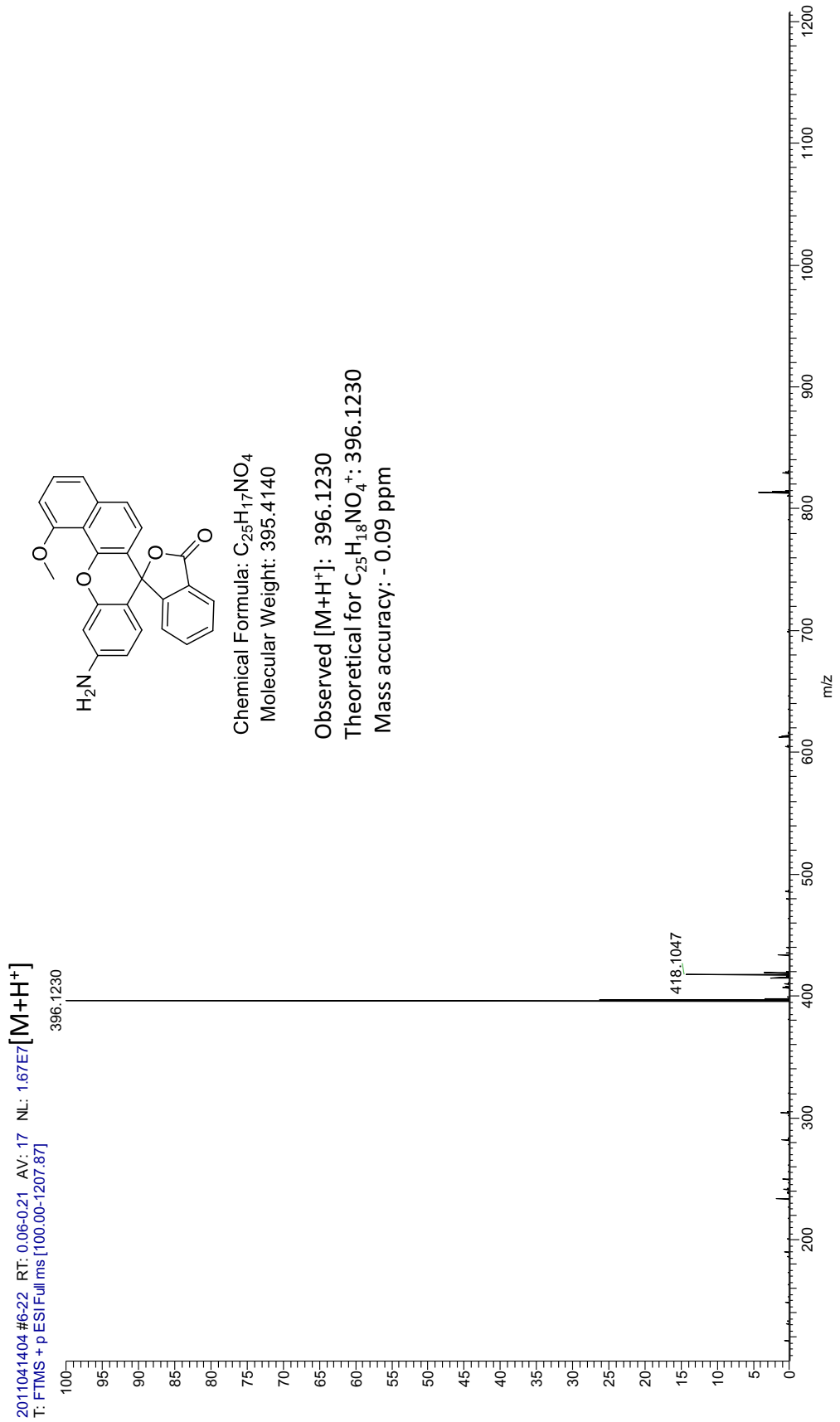


Figure S44. HR ESI positive mode spectrum of compound **33**.

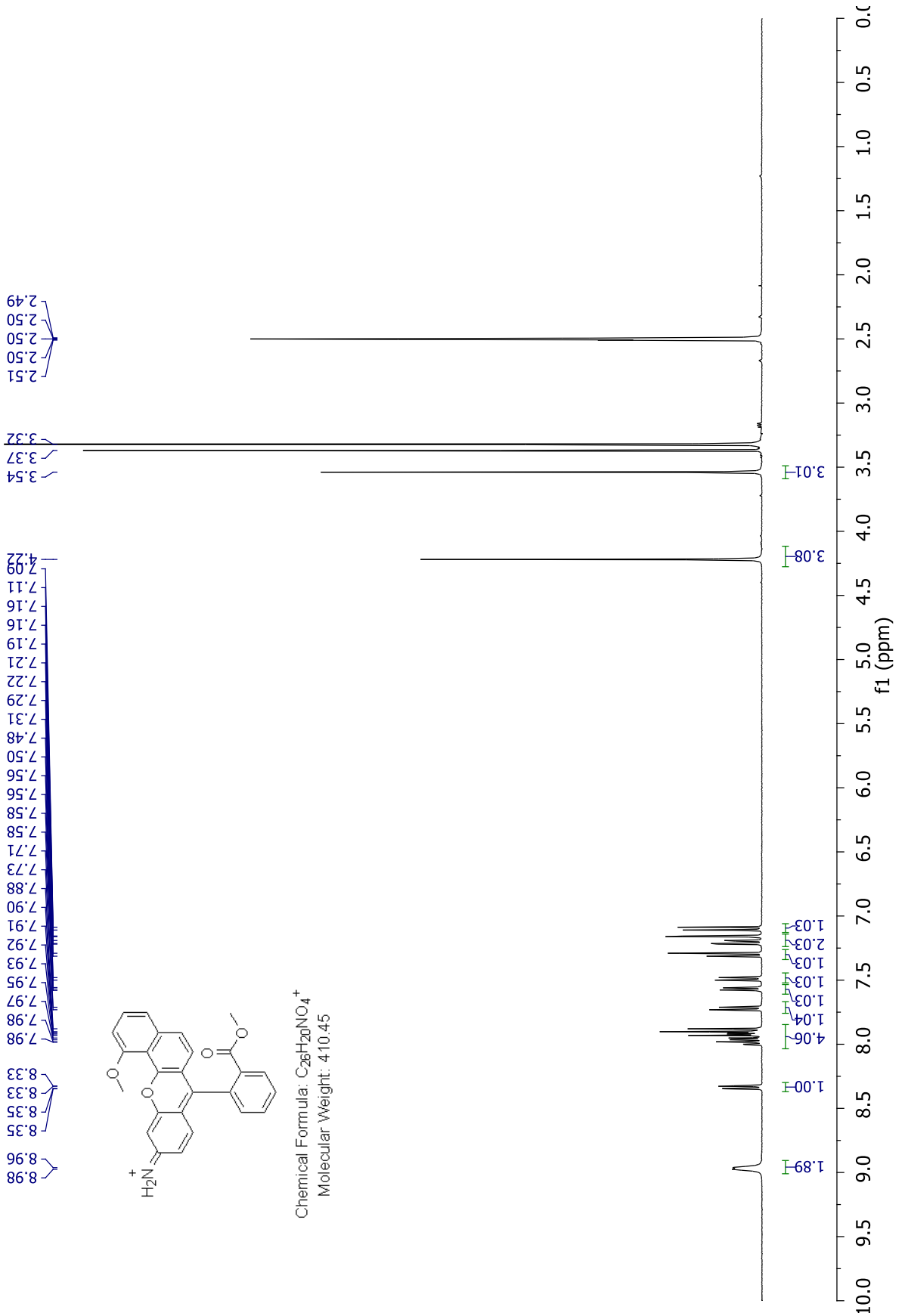


Figure S45. ^{1}H NMR spectrum of compound **4**.

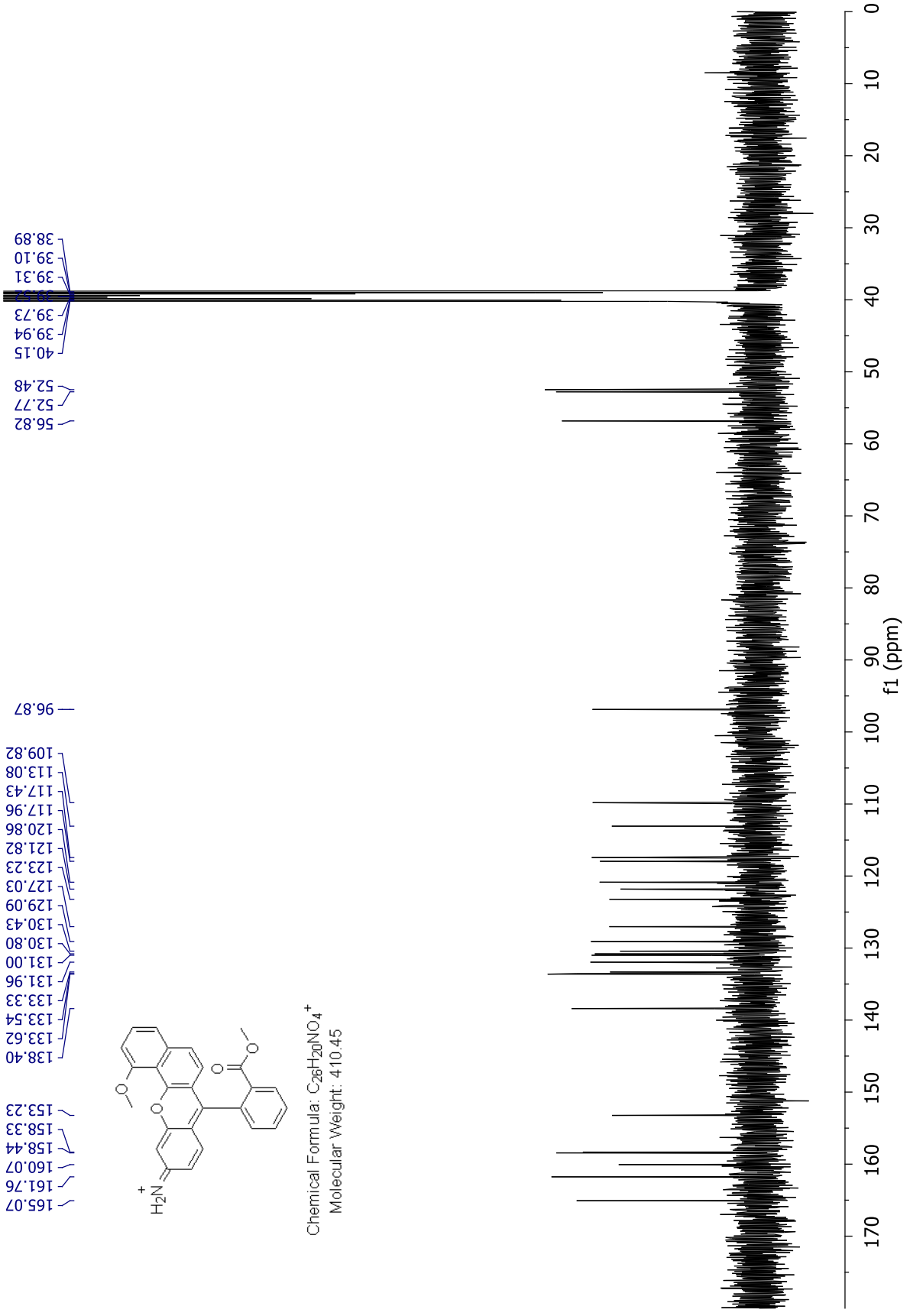


Figure S46. ^{13}C NMR spectrum of compound **4**.

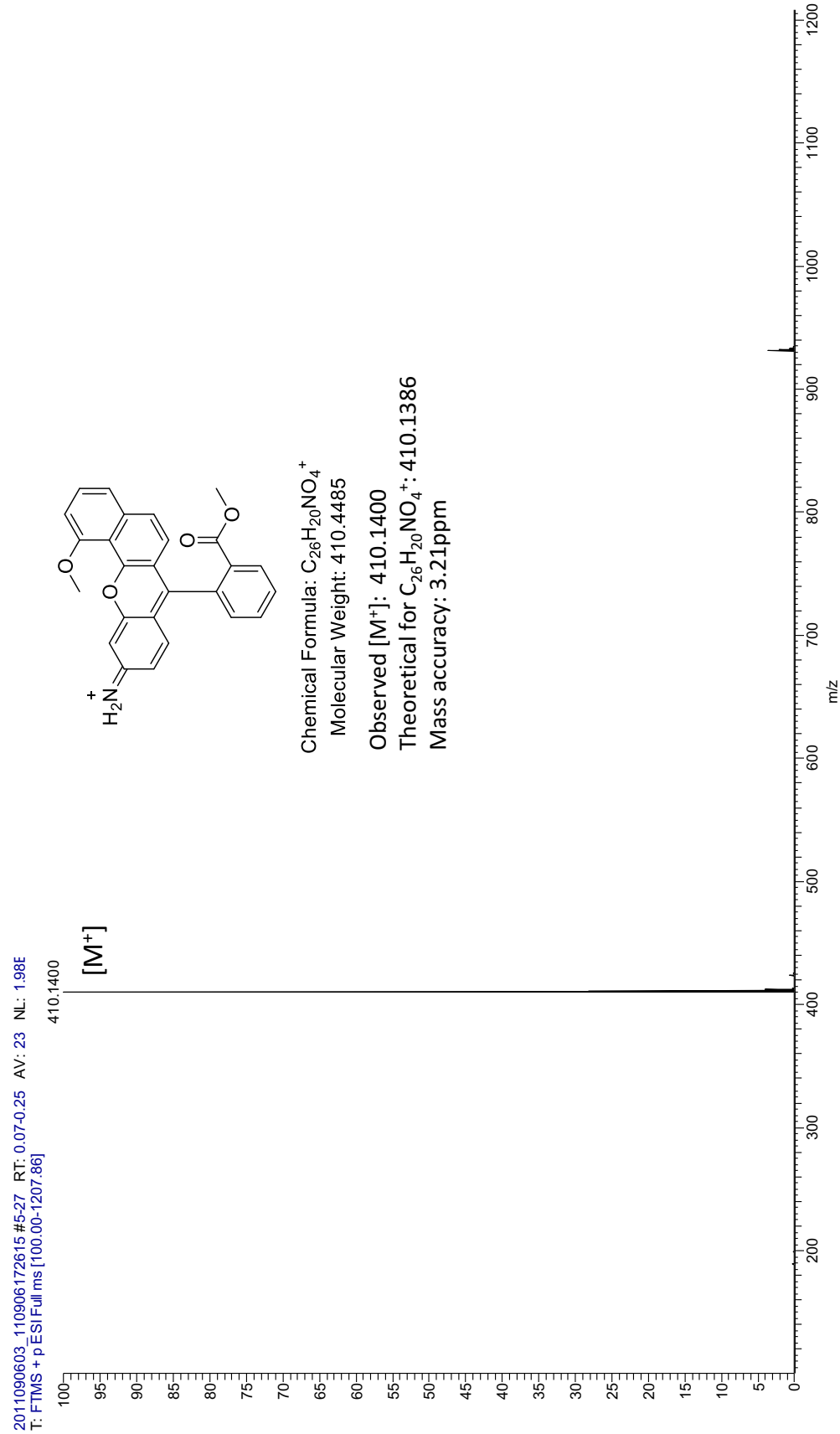


Figure S47. HR ESI positive mode spectrum of compound **4**.

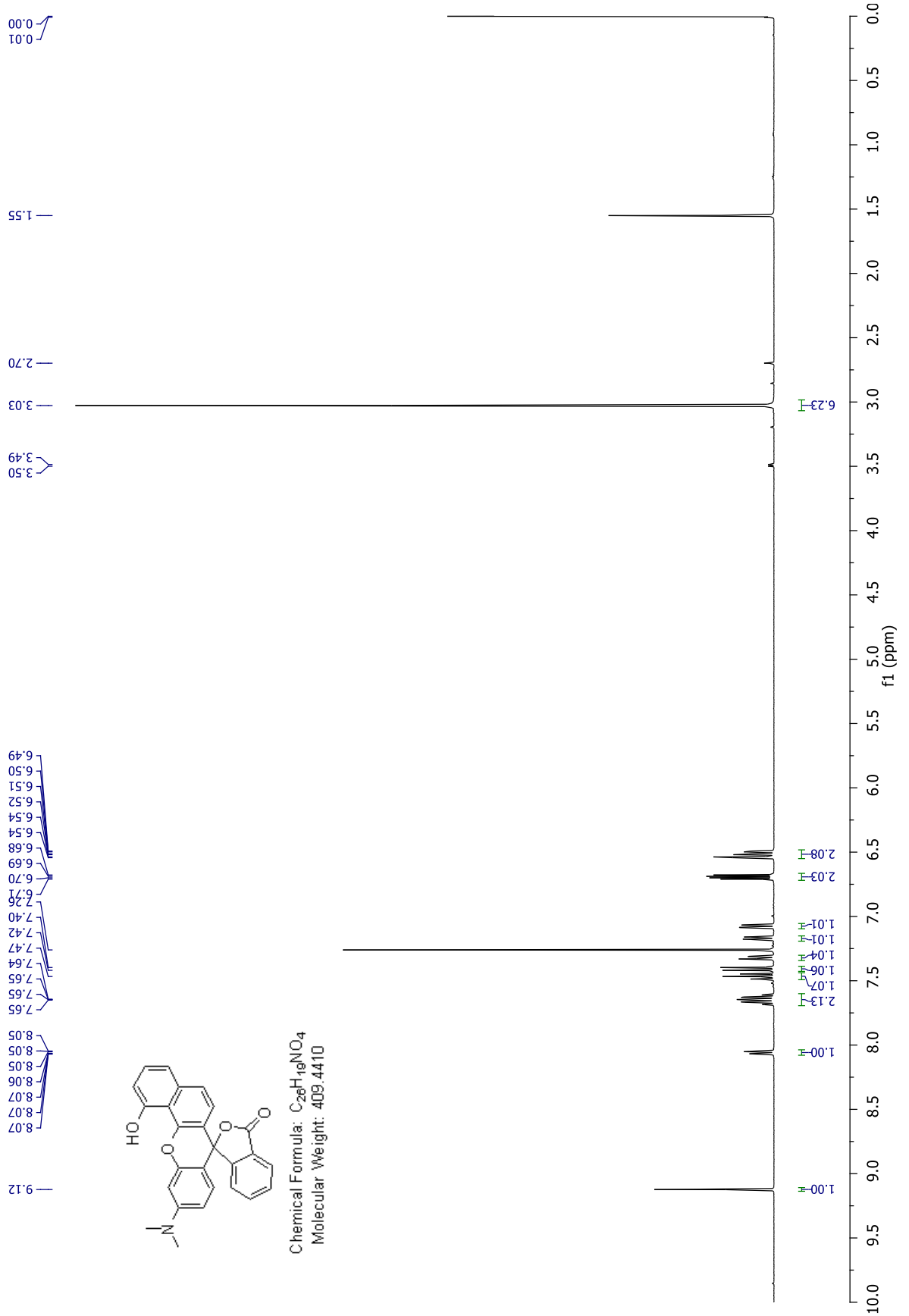


Figure S48. ^{1}H NMR spectrum of compound **34**.

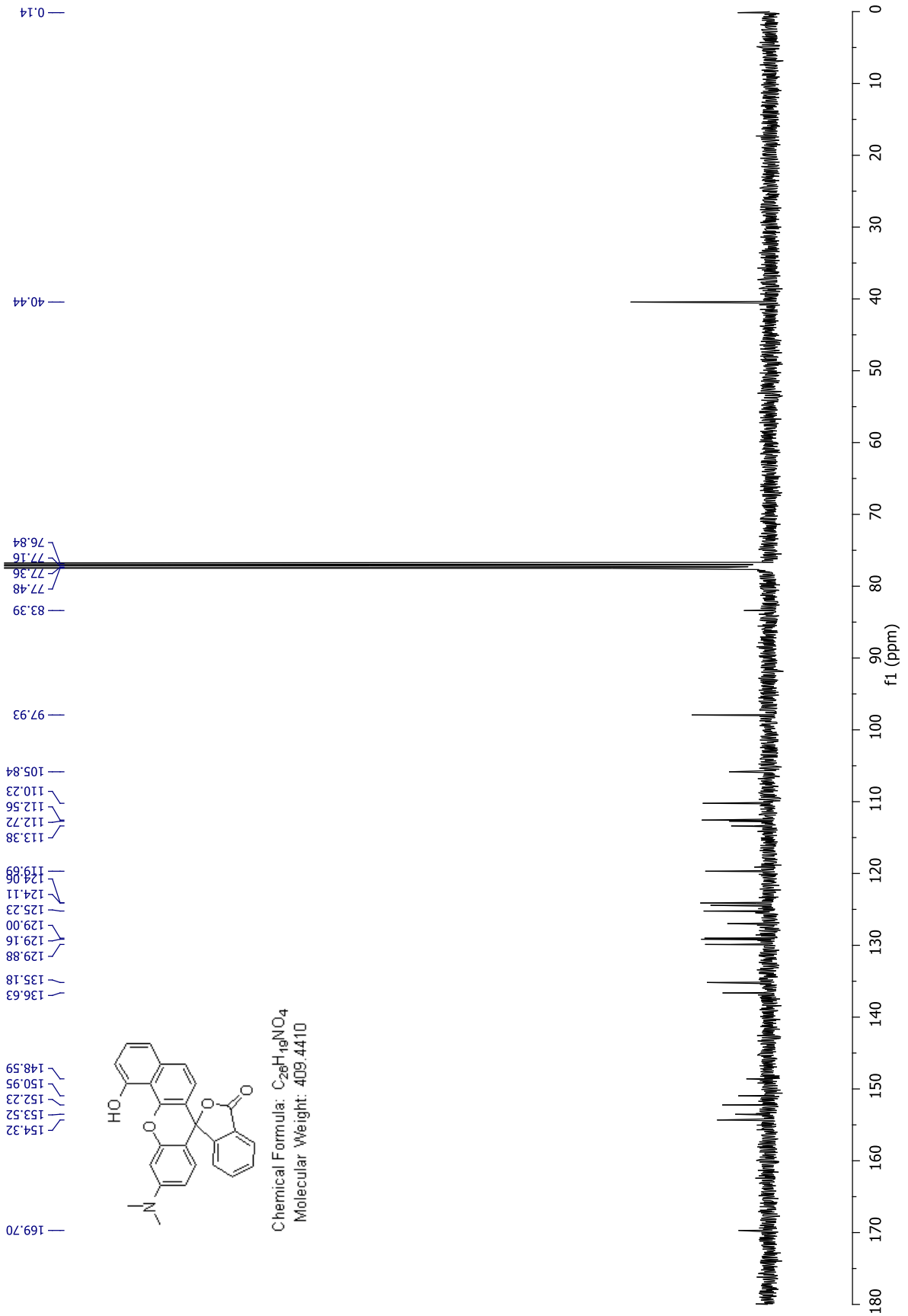


Figure S49. ^{13}C NMR spectrum of compound **34**.

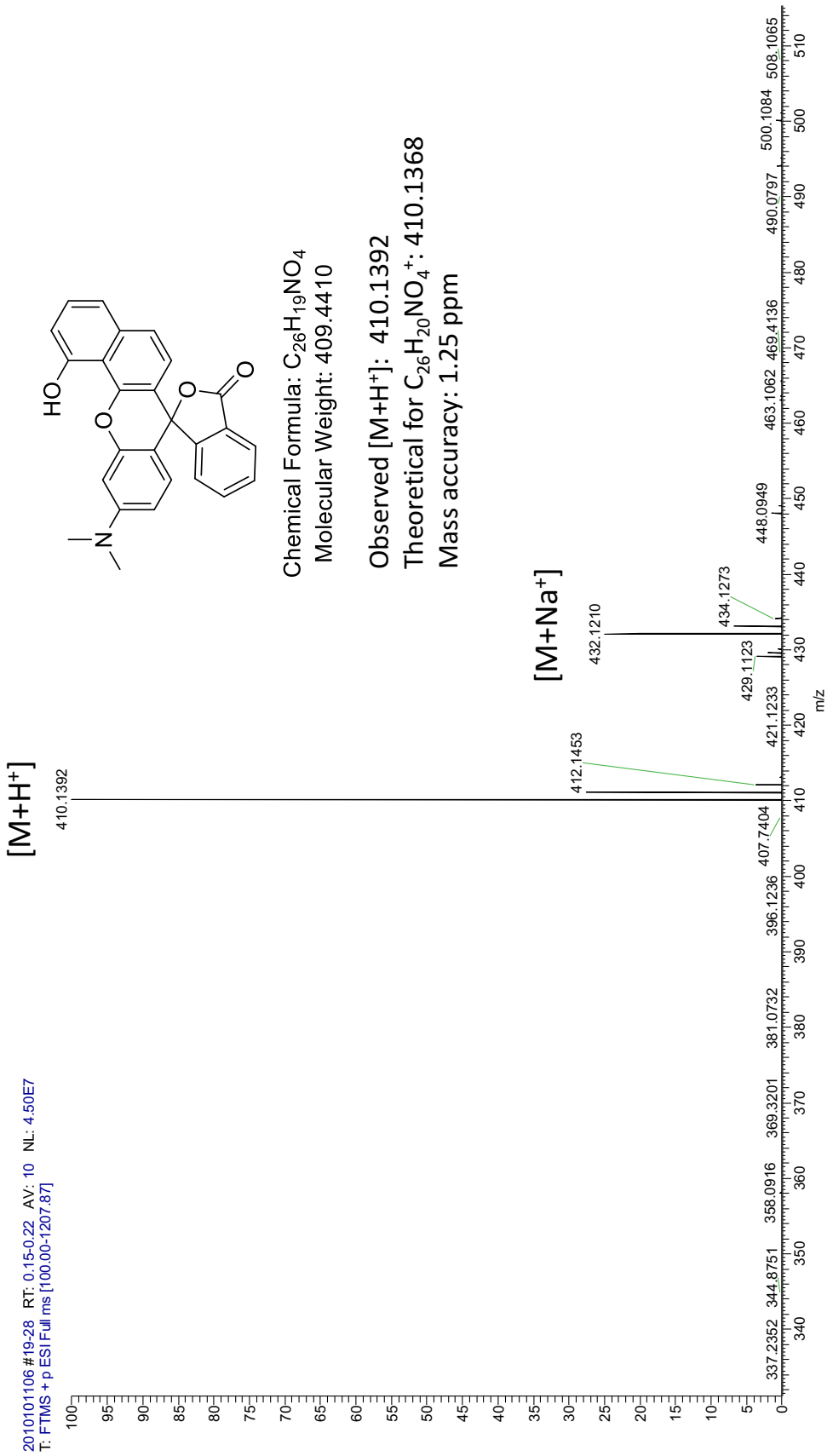


Figure S50. HR ESI positive mode spectrum of compound **34**.

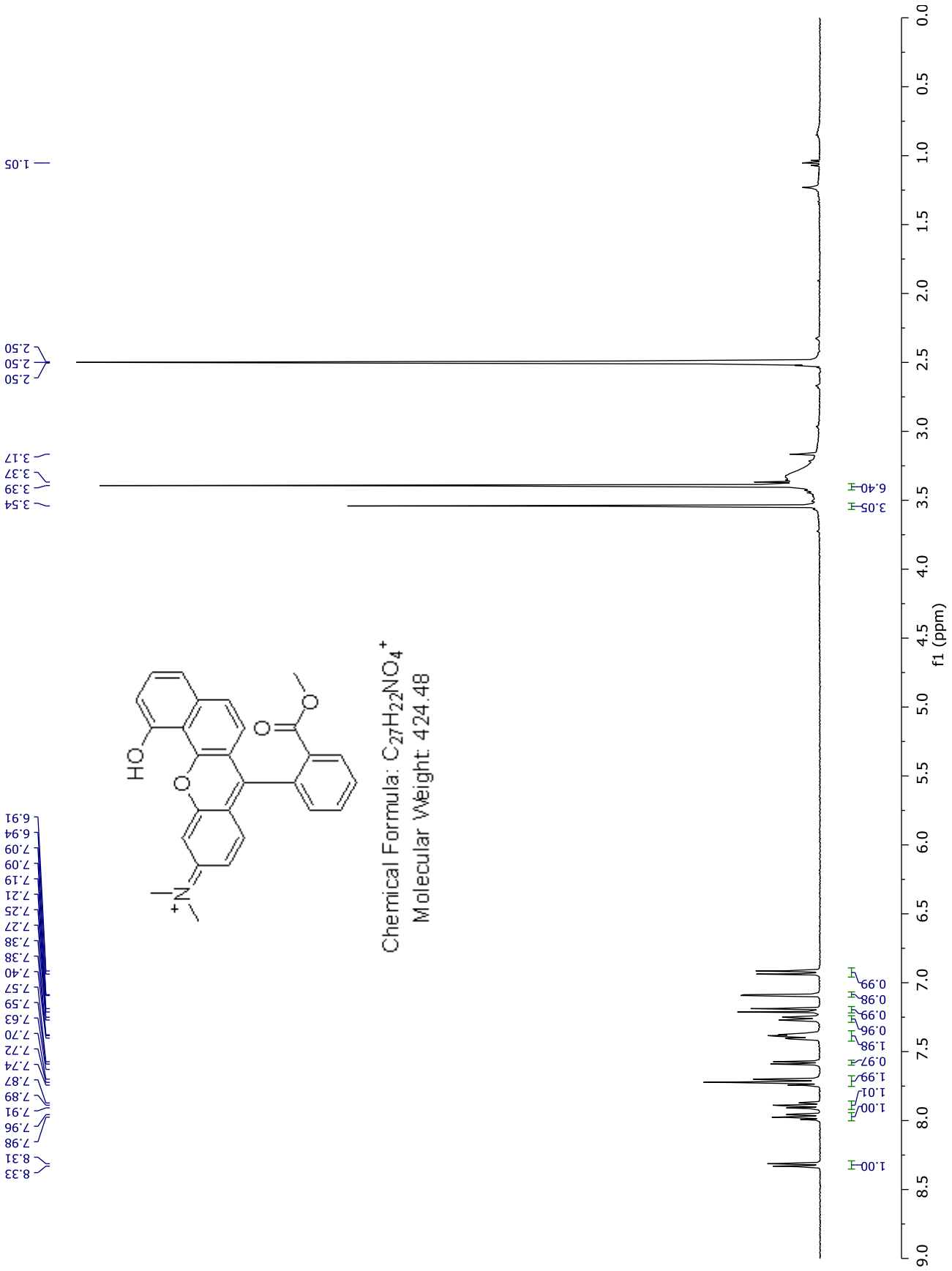


Figure S51. ^{1}H NMR spectrum of compound **5**.

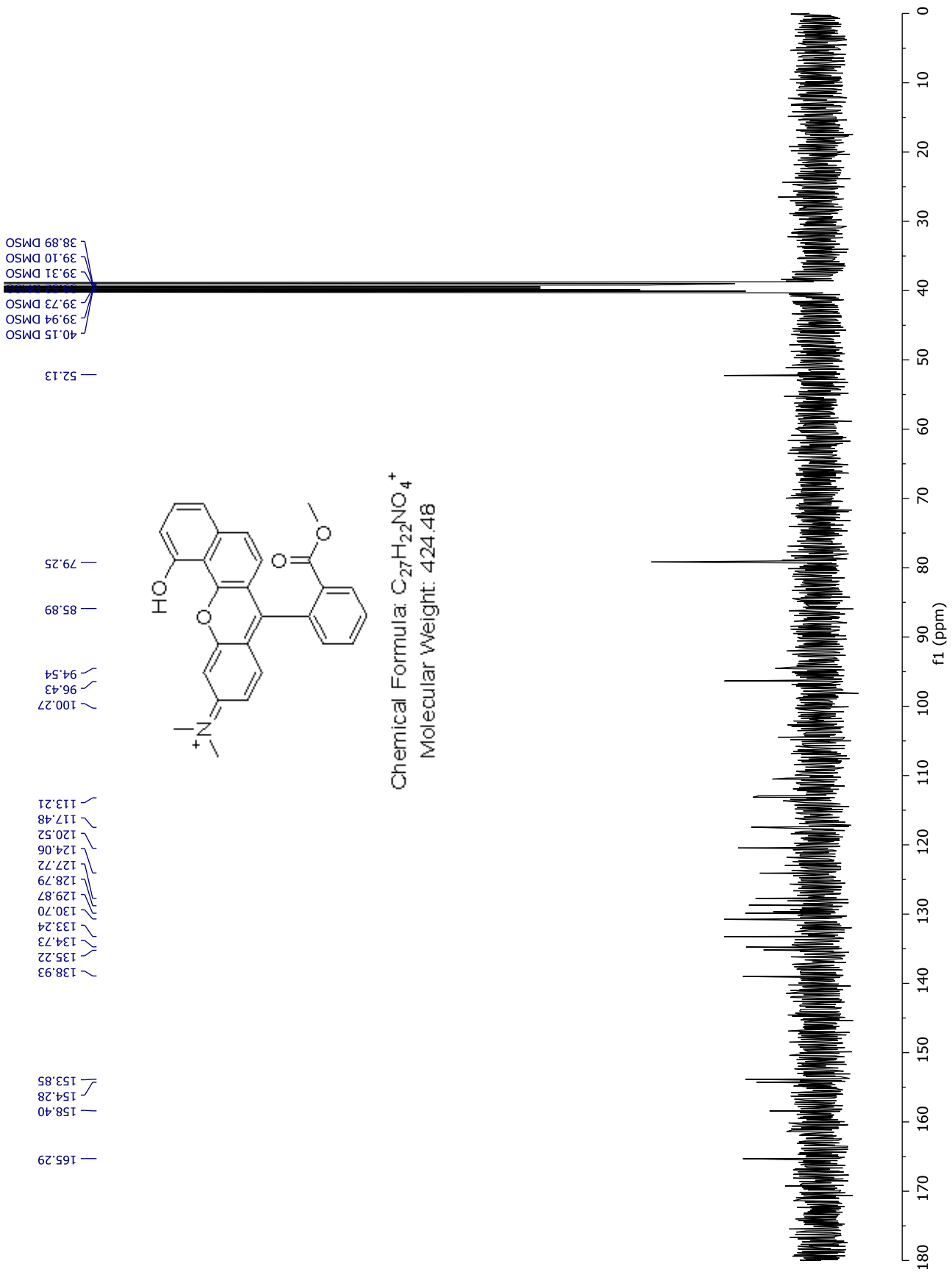
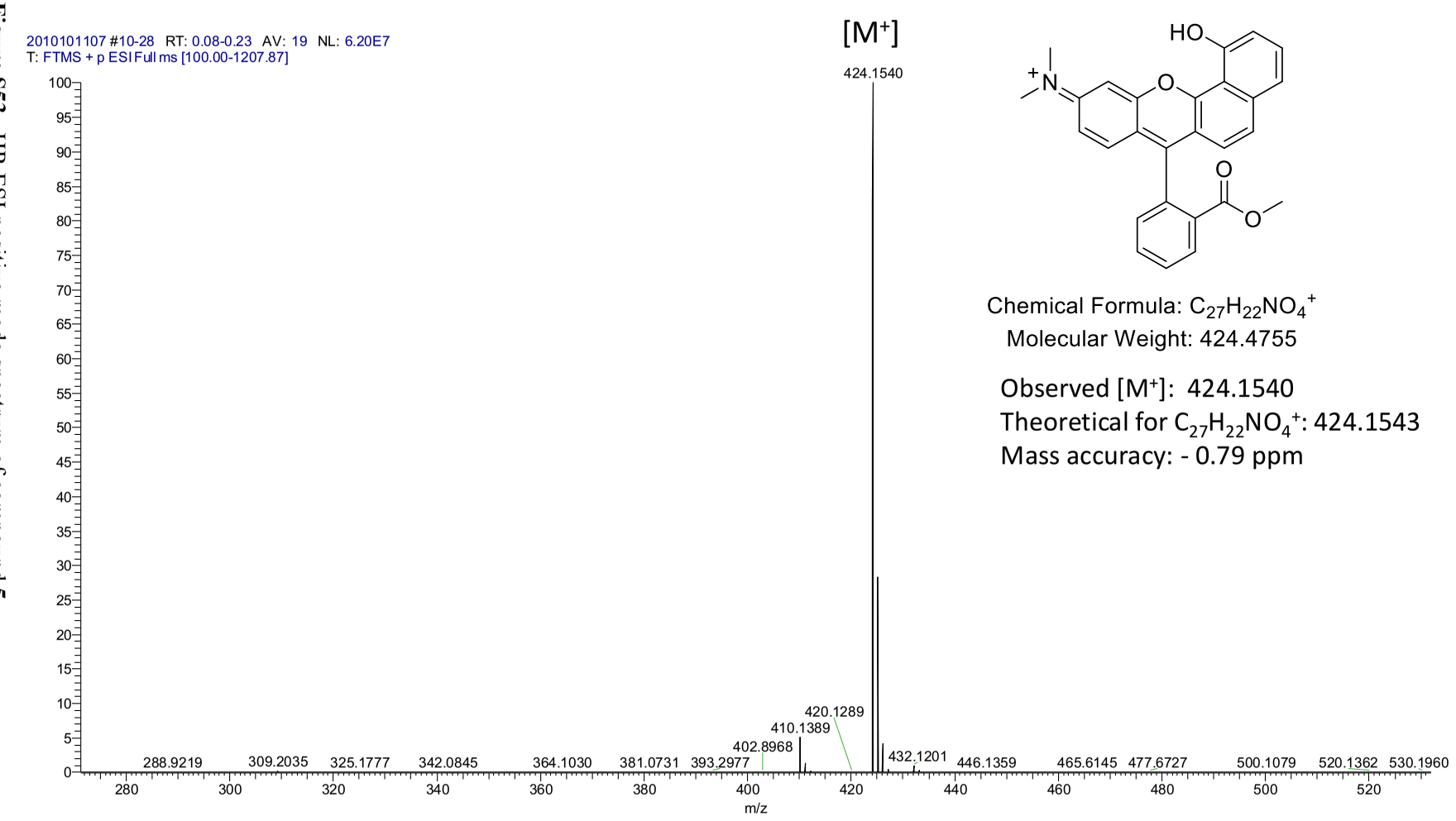


Figure S52. ^{13}C NMR spectrum of compound **5**.

Figure S53. HR ESI positive mode spectrum of compound **5**.



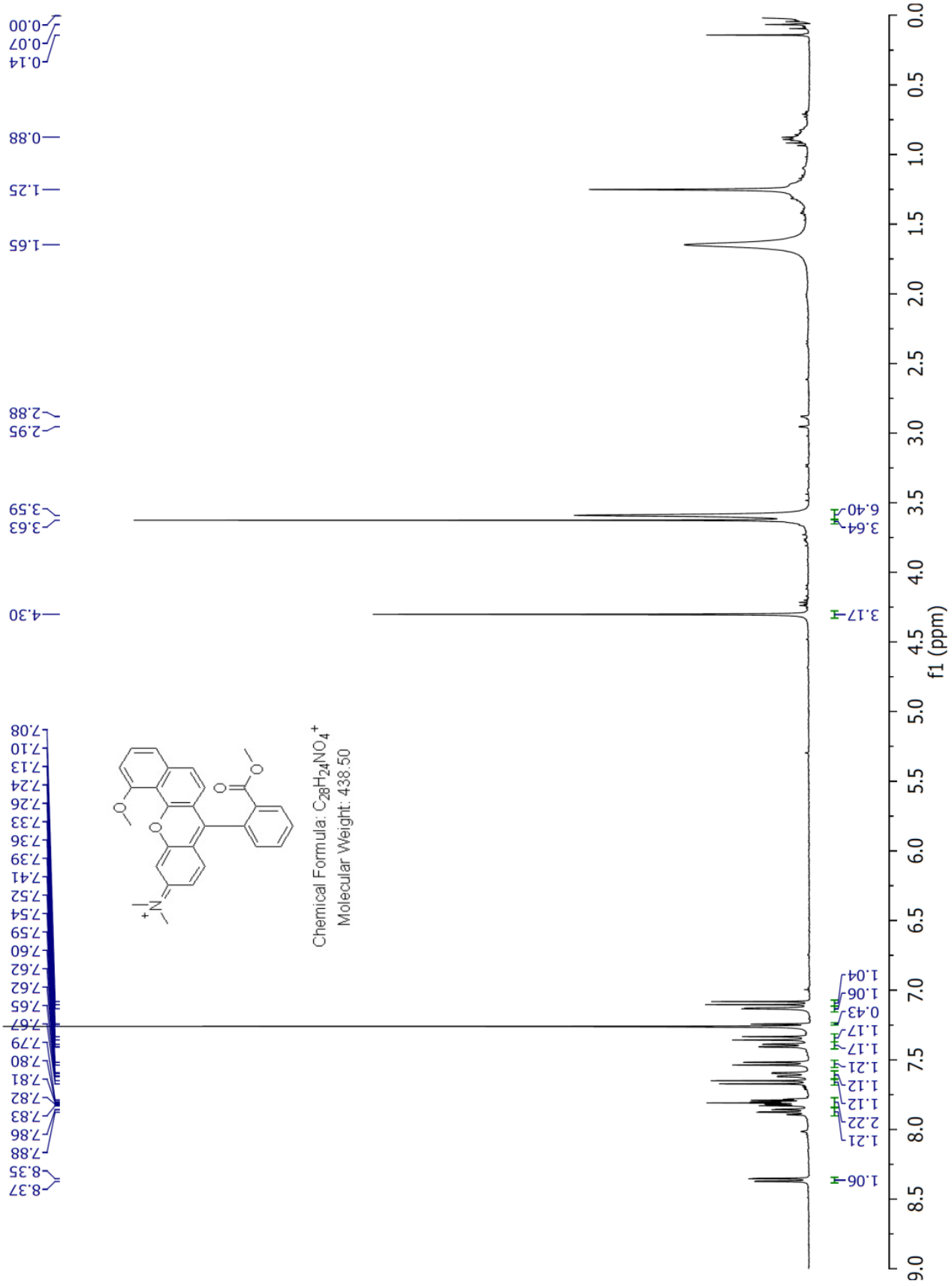


Figure S54. ^{1}H NMR spectrum of compound **6**.

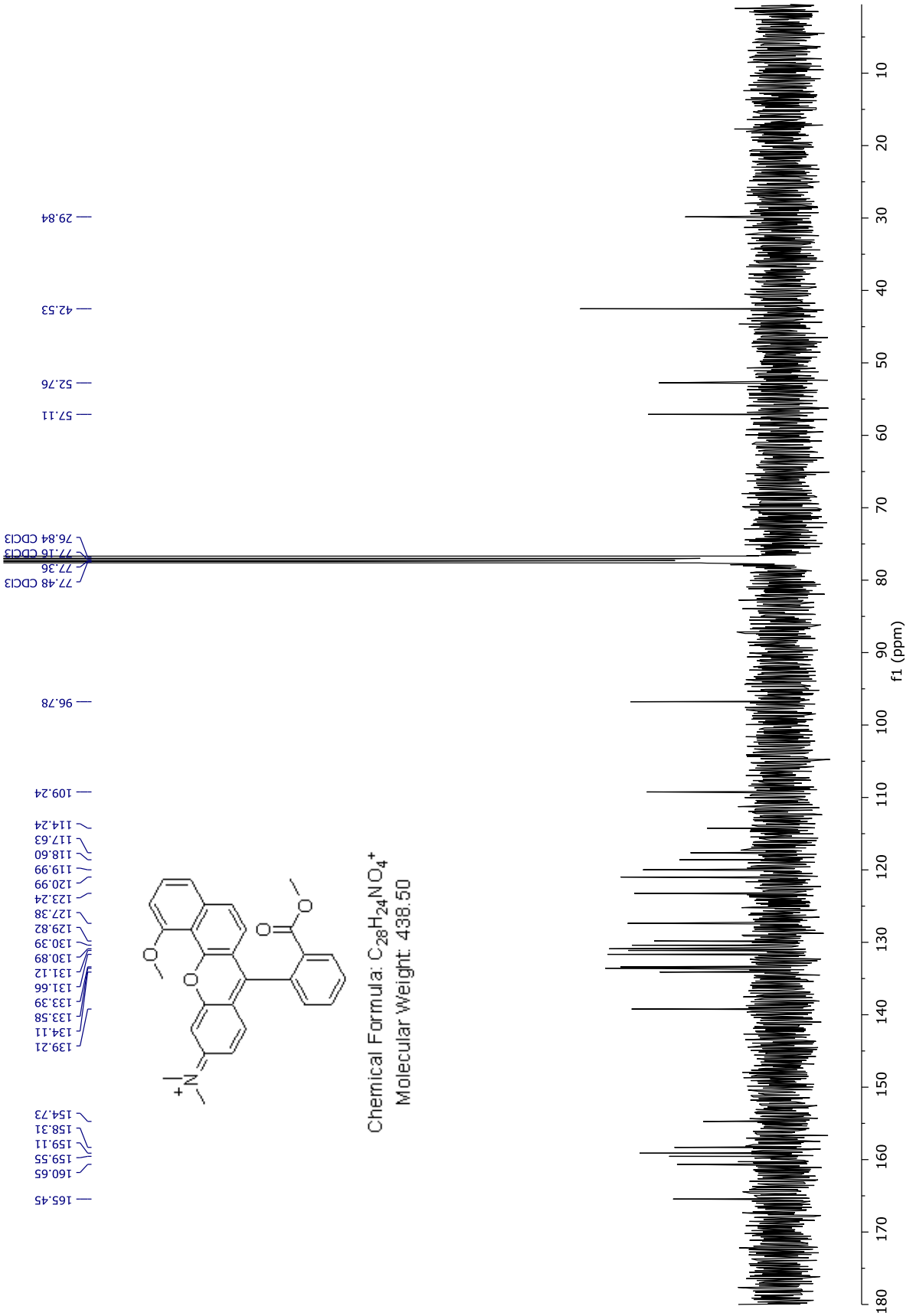


Figure S55. ^{13}C NMR spectrum of compound **6**.

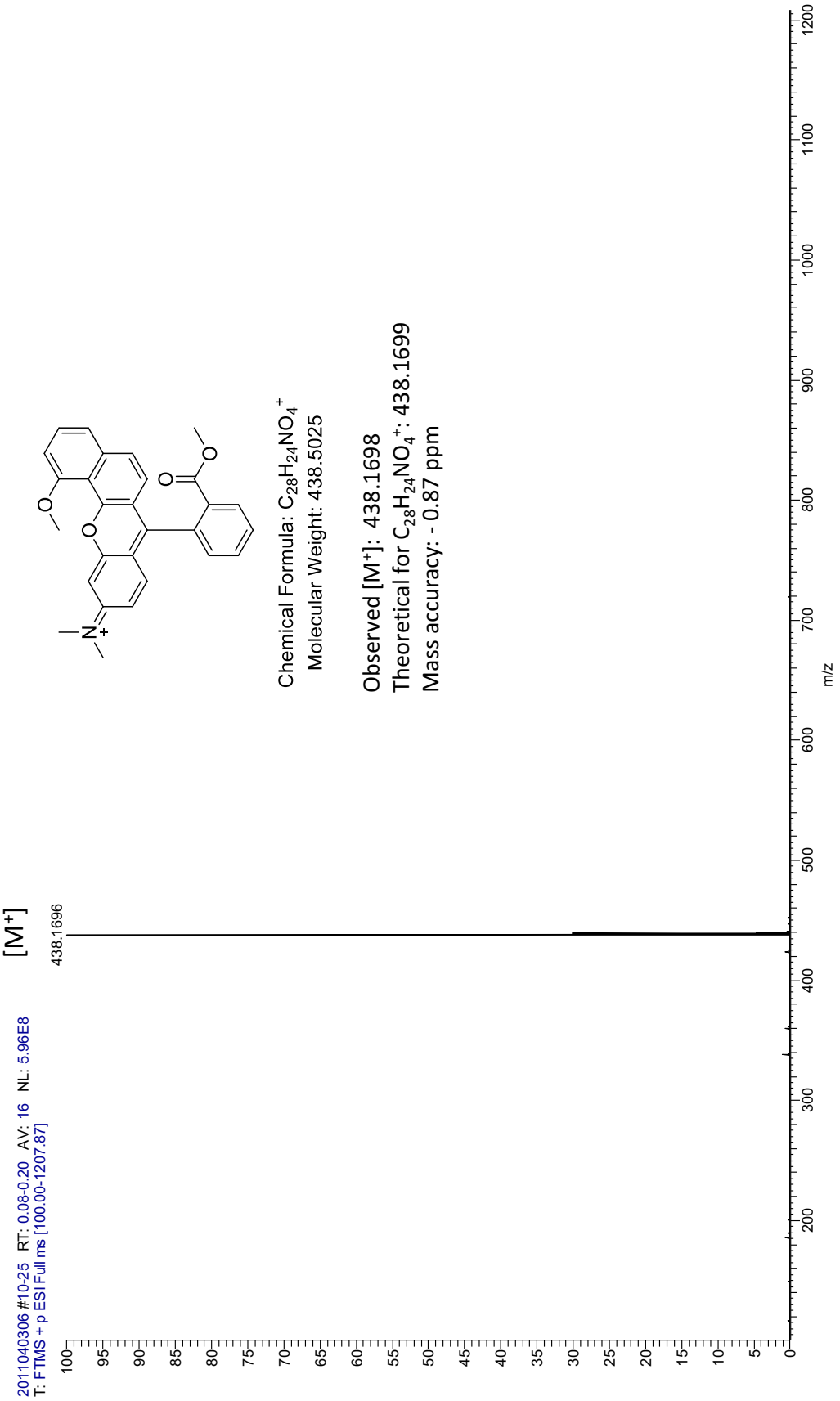


Figure S56. HR ESI positive mode spectrum of compound **6**.

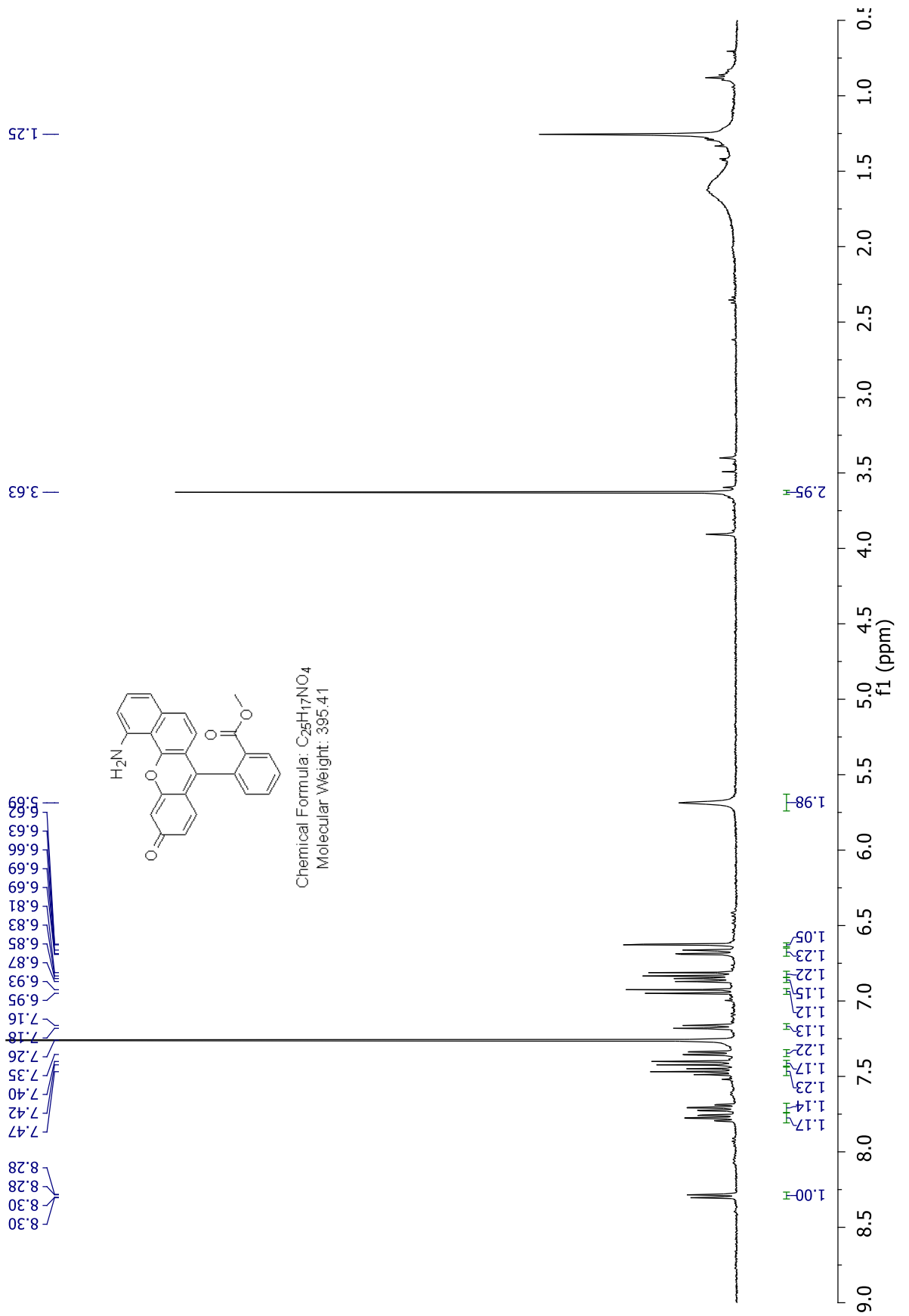


Figure S57. ^{1}H NMR spectrum of compound **7**.

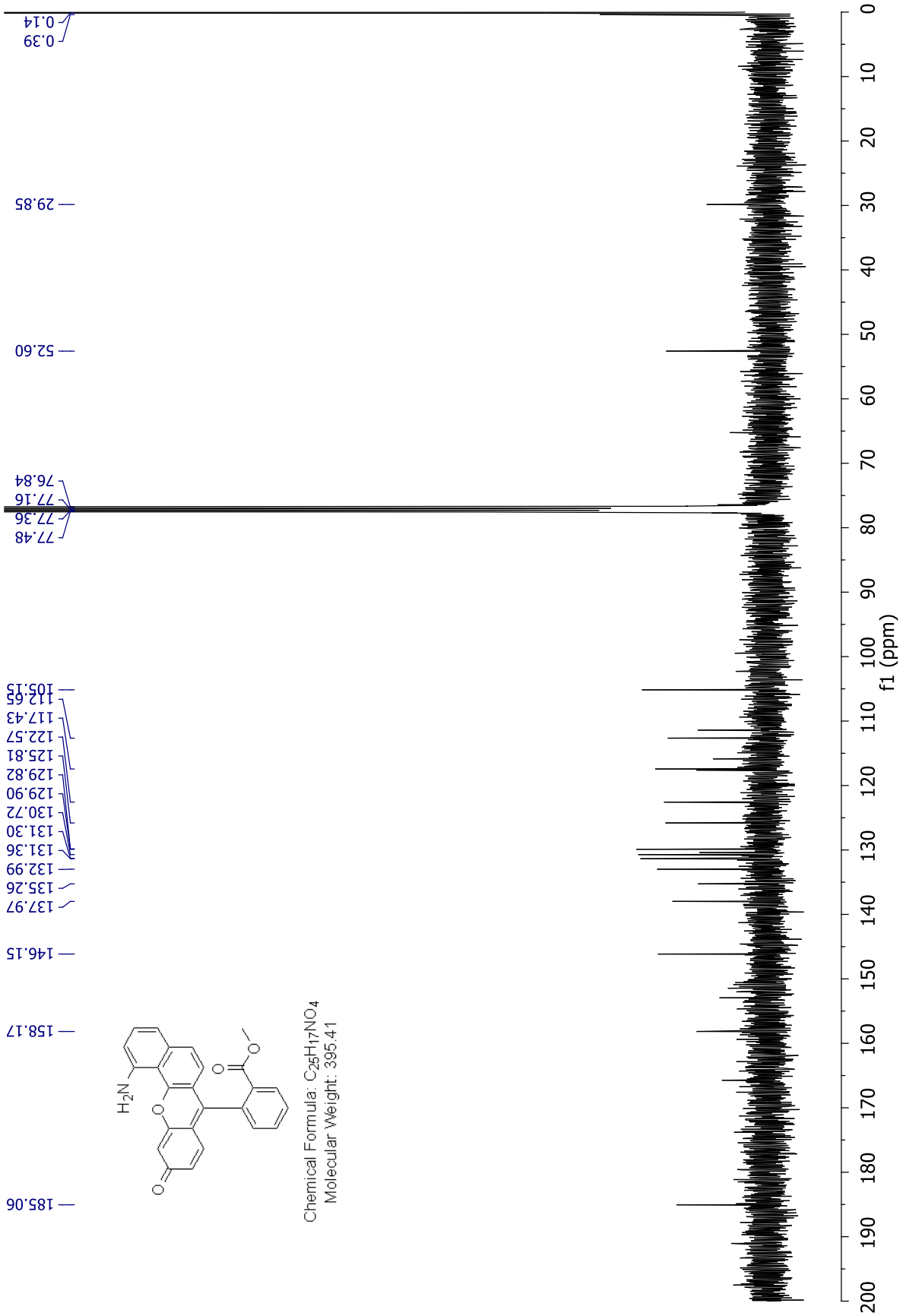


Figure S58. ^{13}C NMR spectrum of compound **7**.

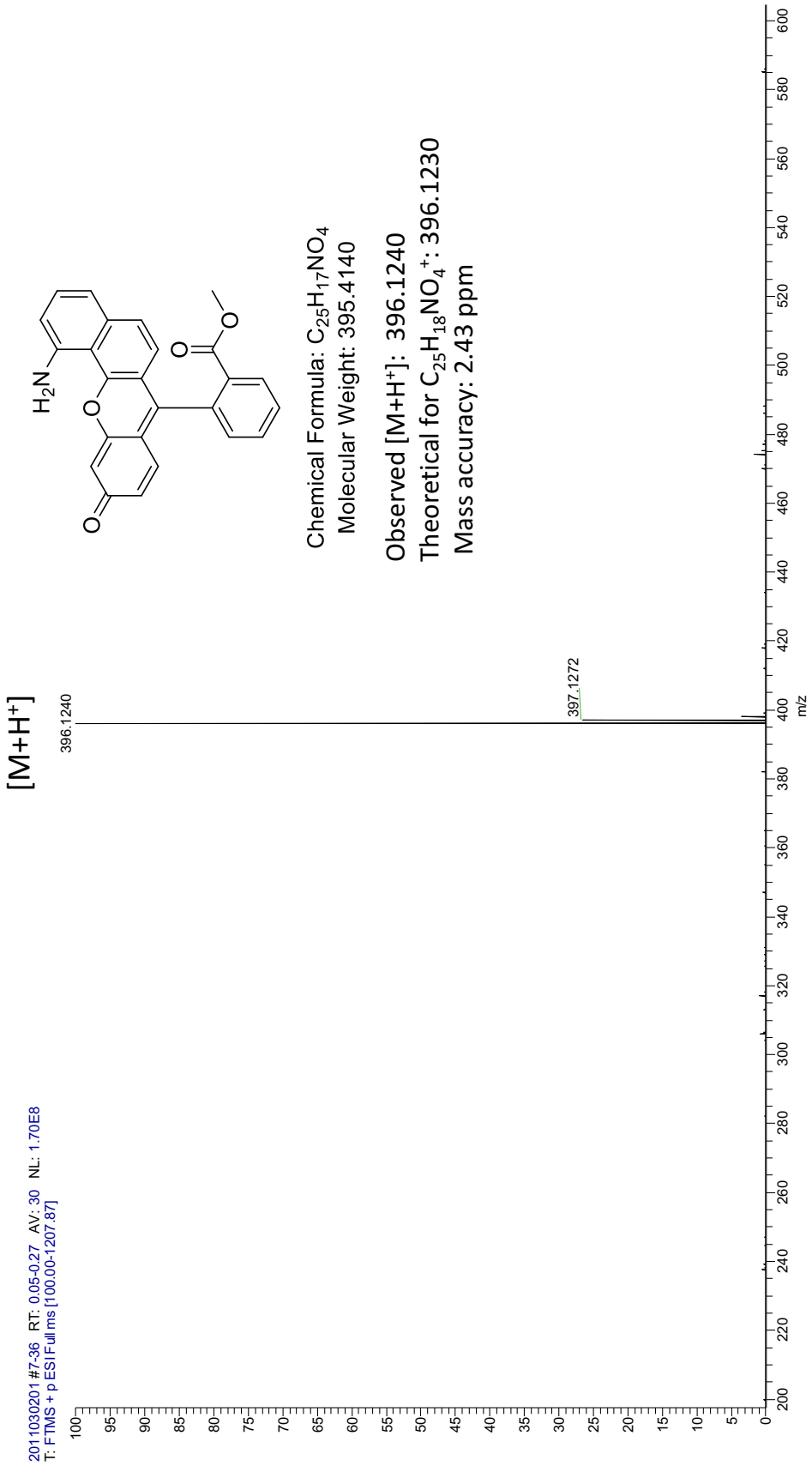


Figure S59. HR ESI positive mode spectrum of compound **7**.

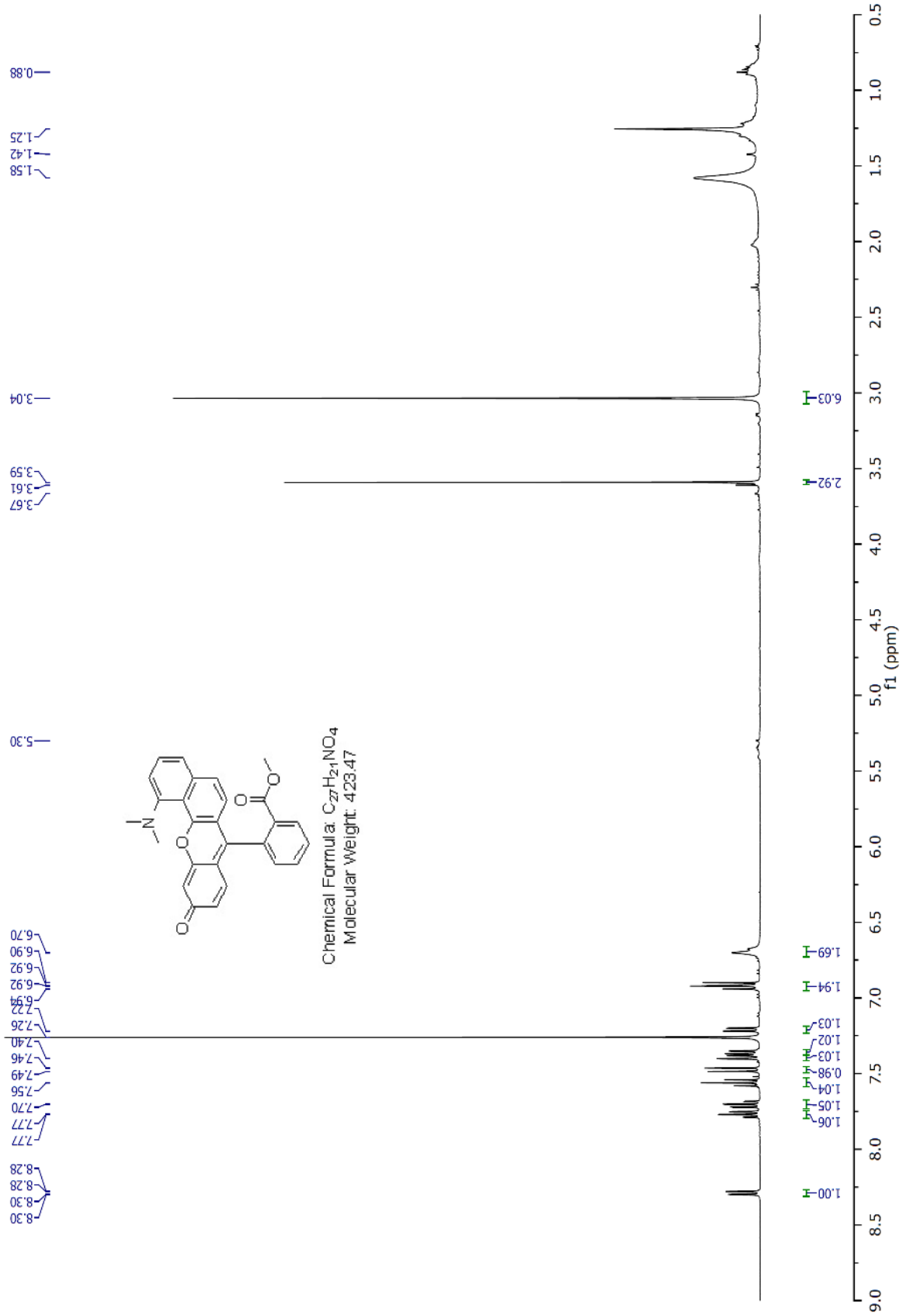


Figure S60. ^{1}H NMR spectrum of compound **8**.

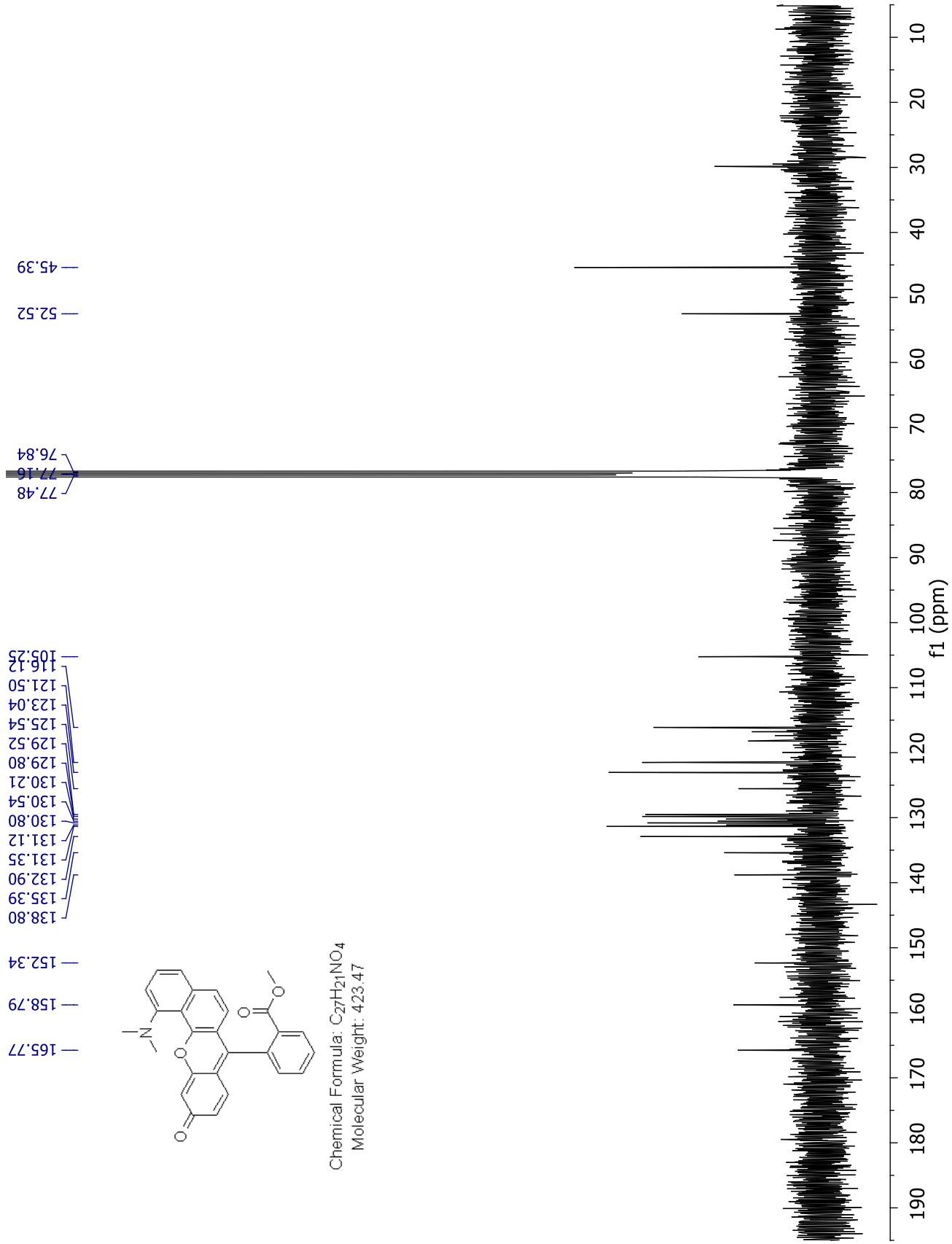


Figure S61. ^{13}C NMR spectrum of compound **8**.

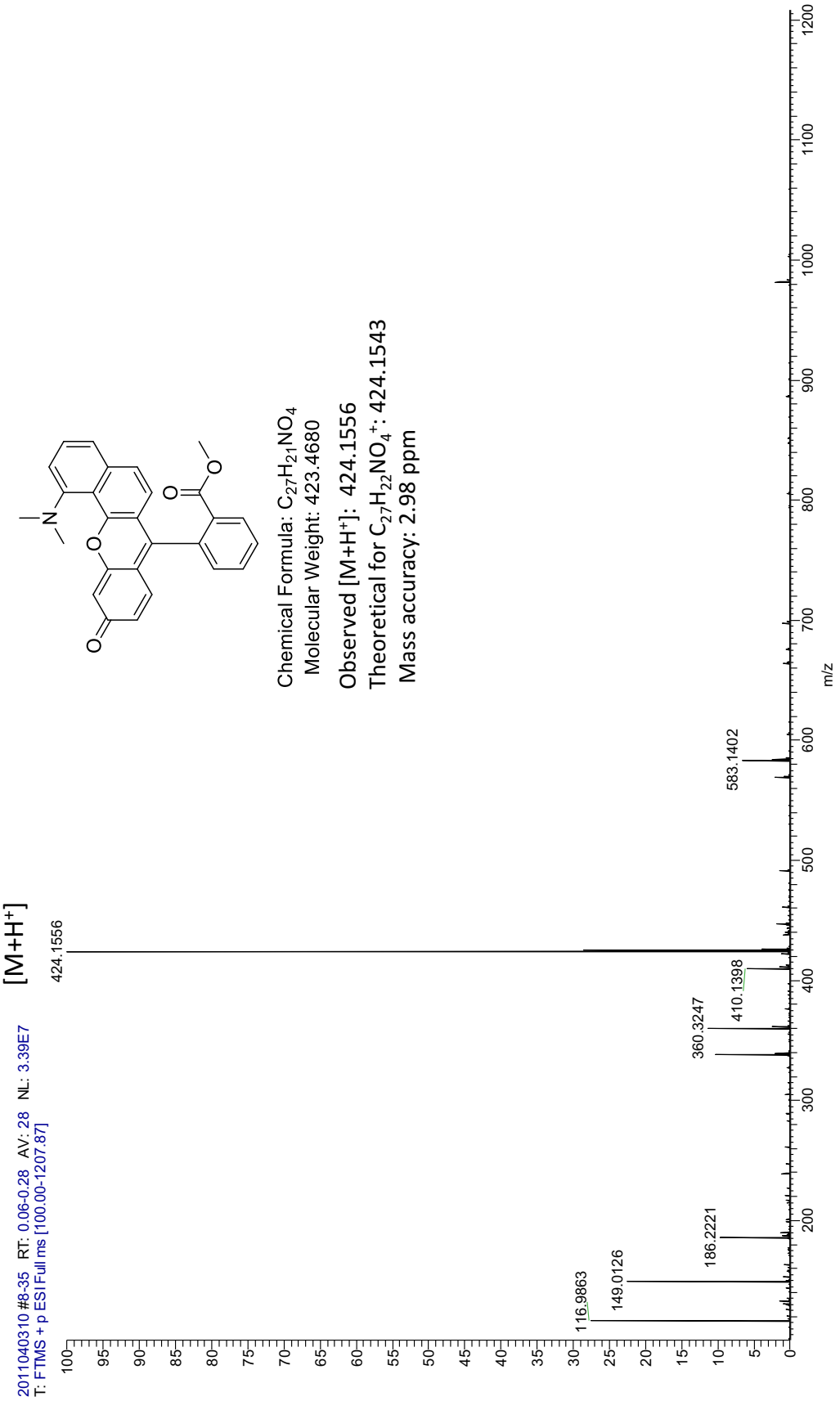


Figure S62. HR ESI positive mode spectrum of compound **8**.

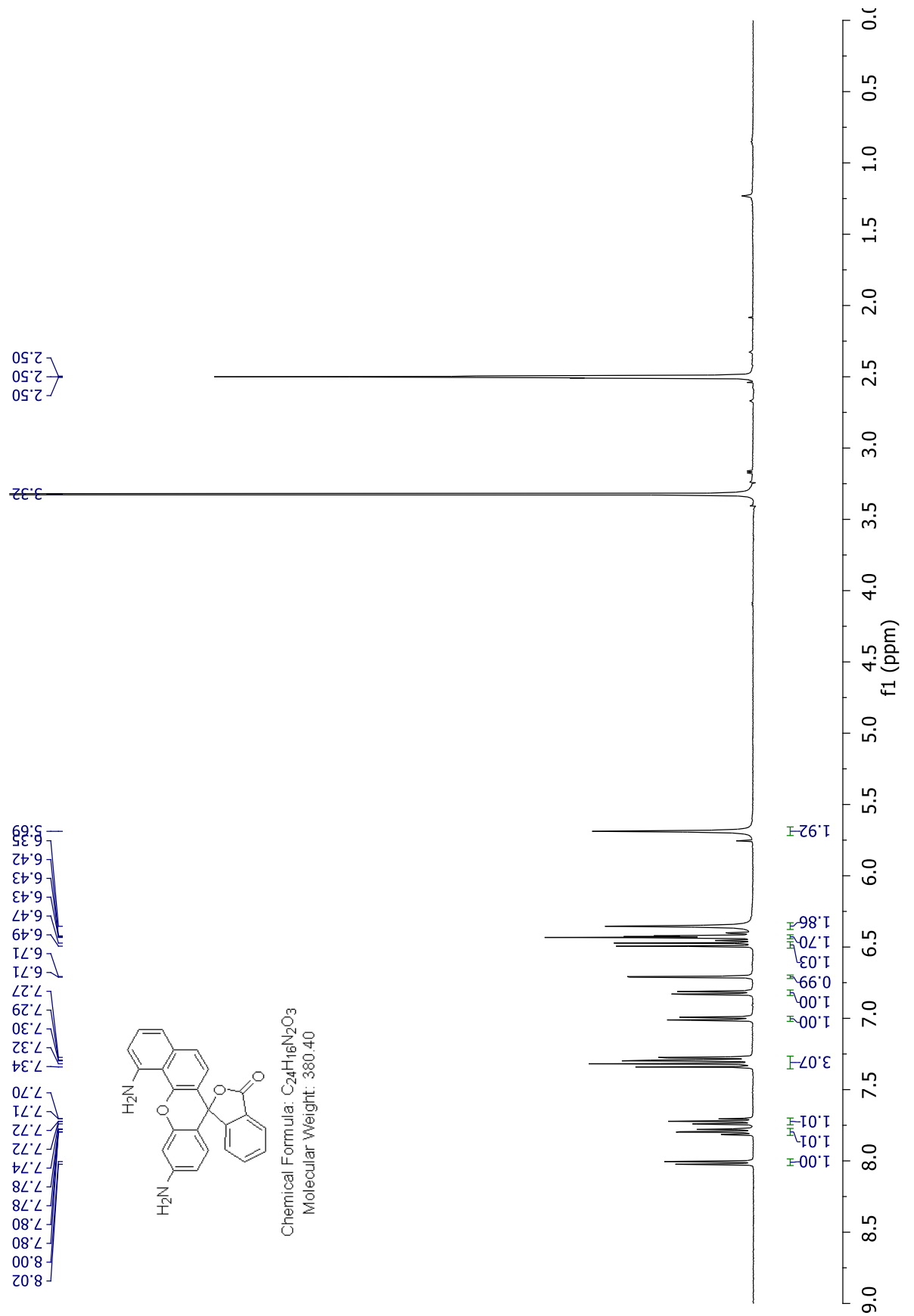


Figure S63. ^{1}H NMR spectrum of compound **37**.

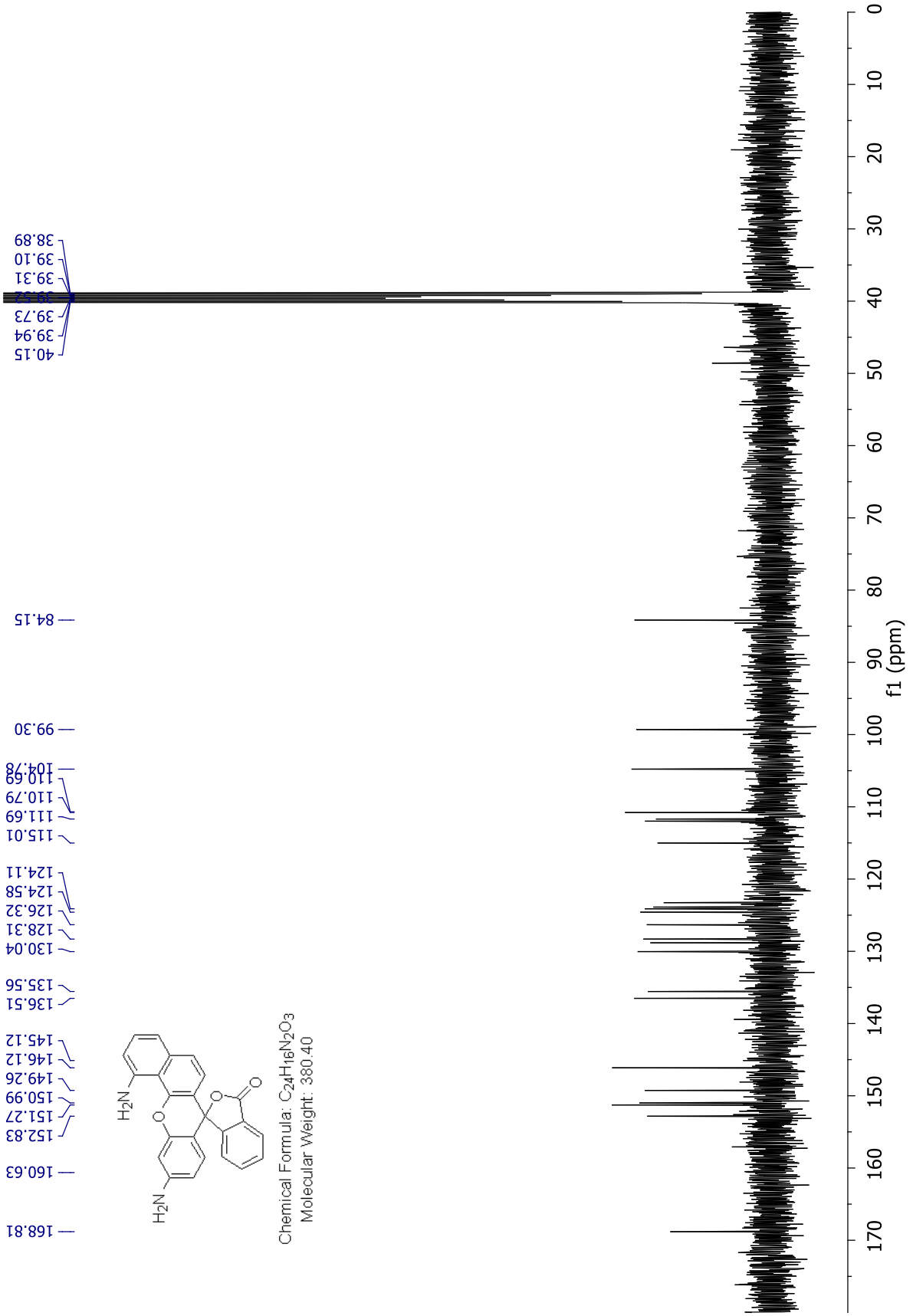


Figure S64. ^{13}C NMR spectrum of compound **37**.

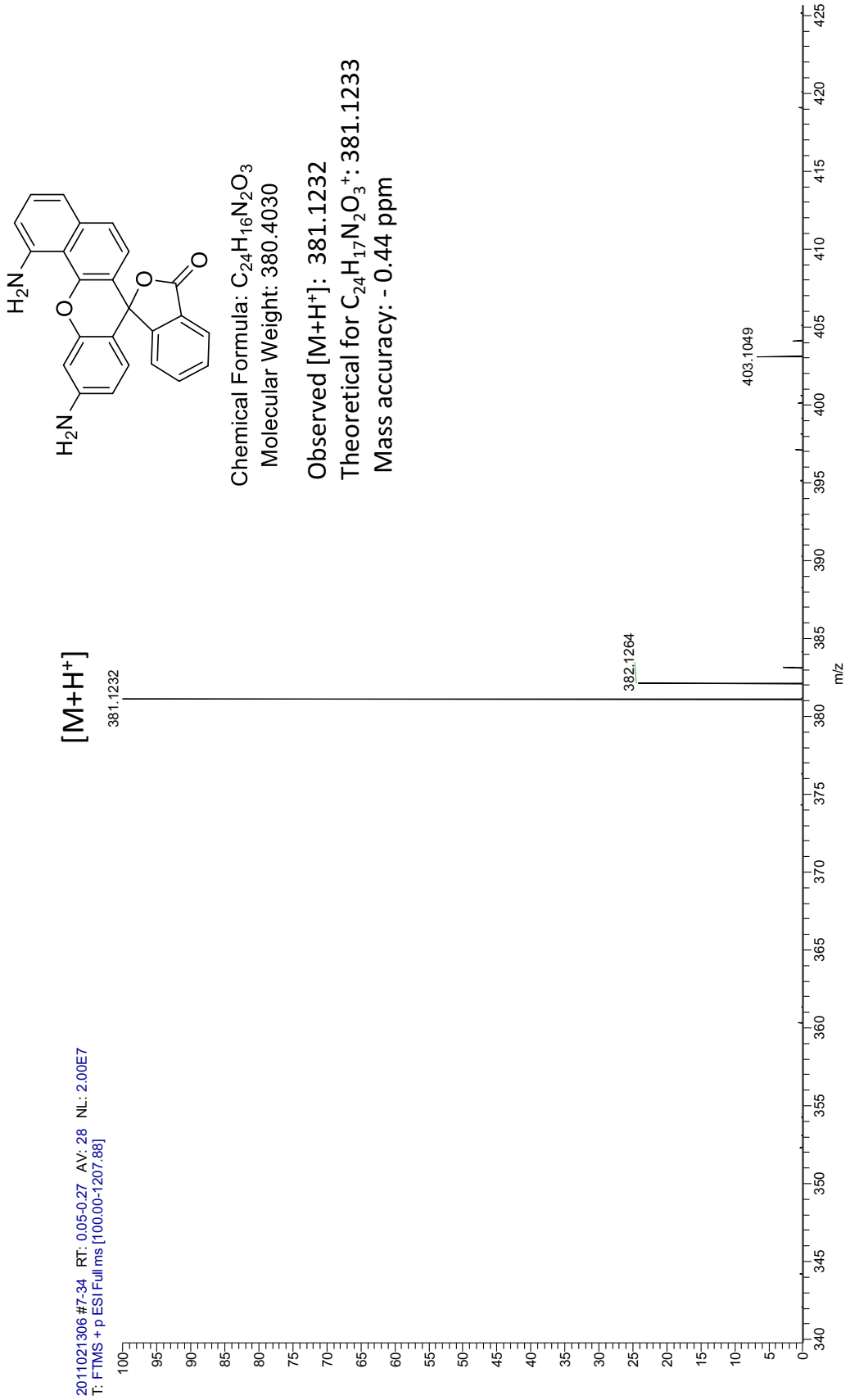


Figure S65. HR ESI positive mode spectrum of compound **37**.

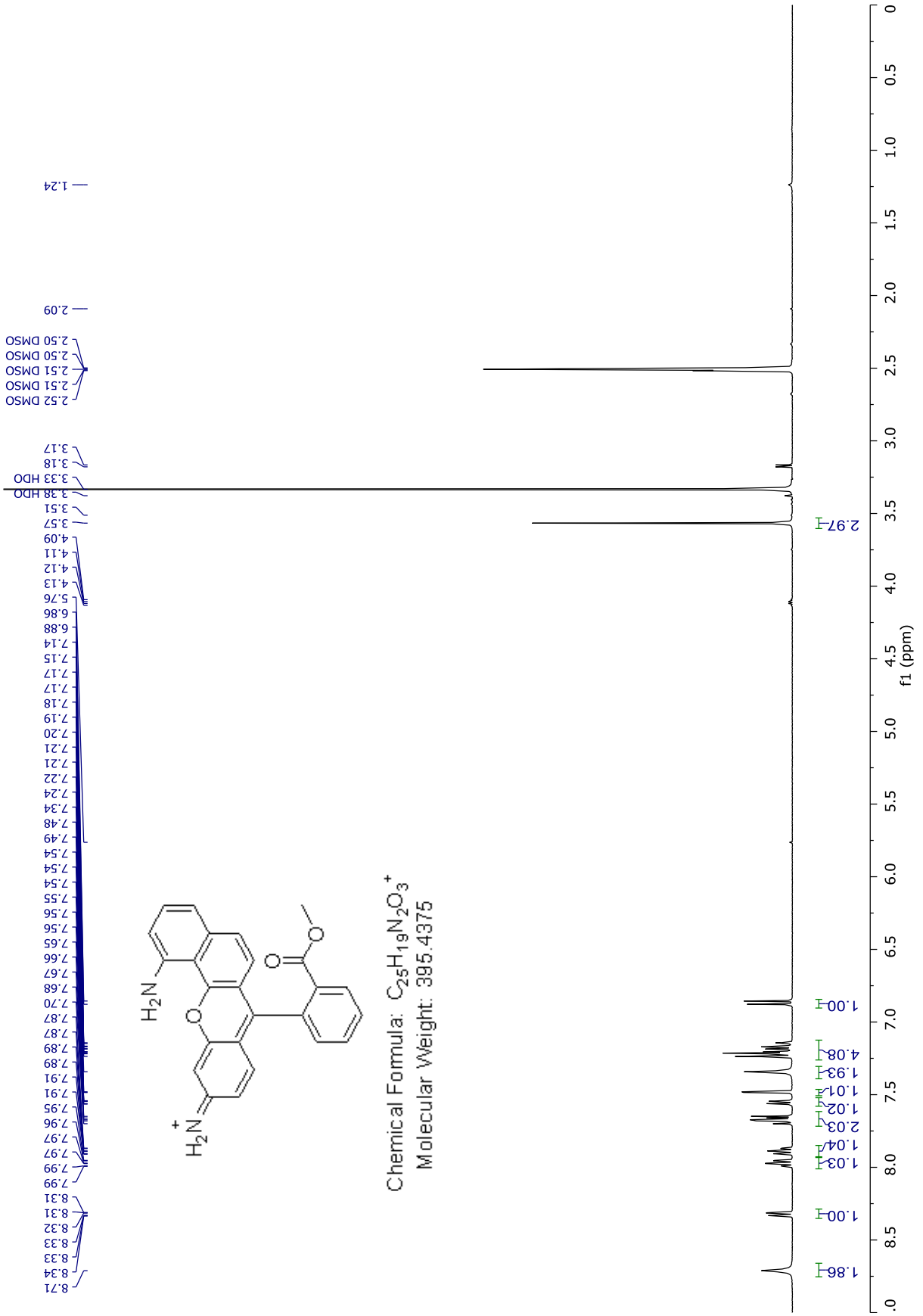


Figure S66. ^{1}H NMR spectrum of compound **9**.

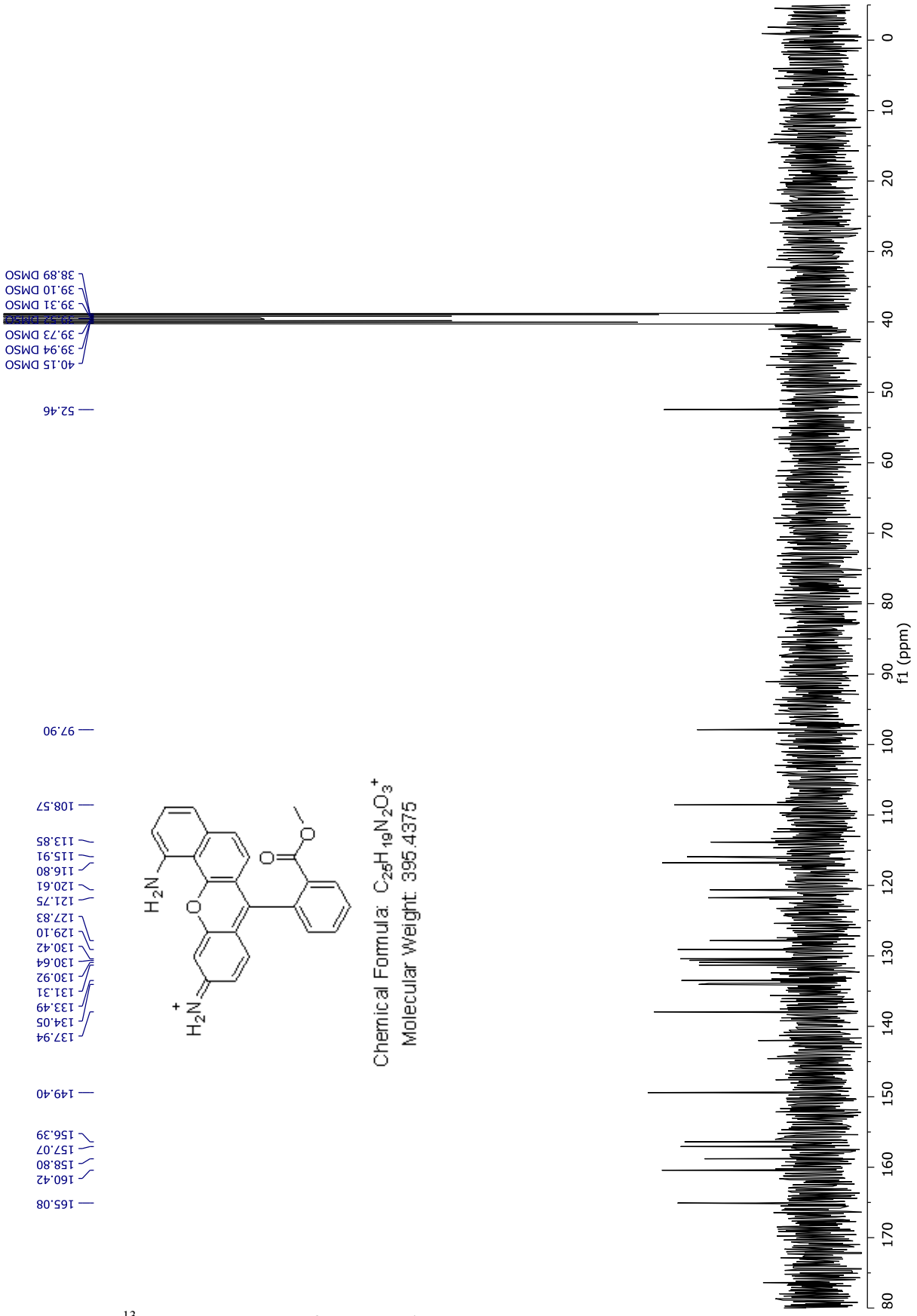
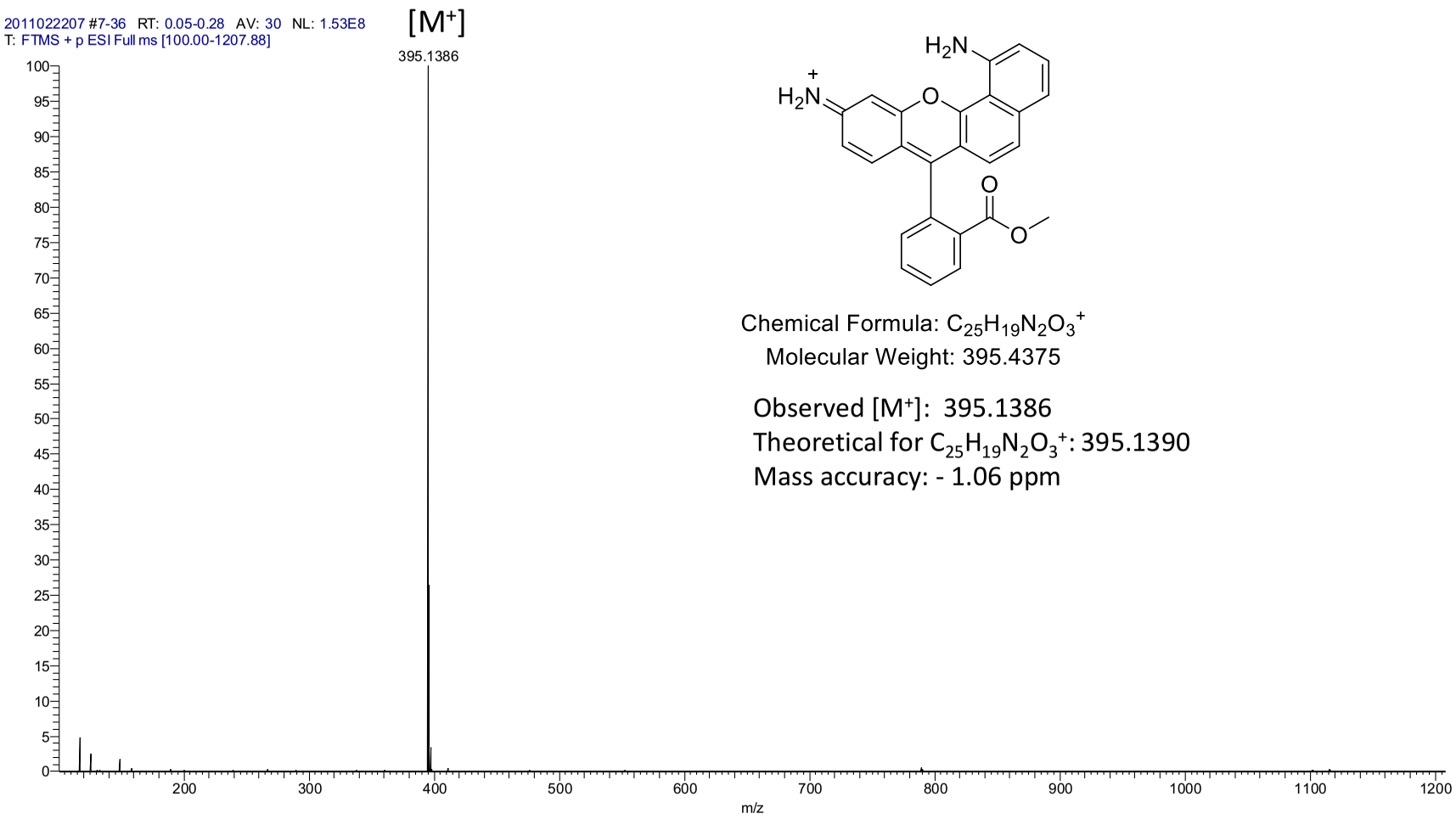


Figure S67. ^{13}C NMR spectrum of compound **9**.

Figure S68. HR ESI positive mode spectrum of compound **9**.



Chemical Formula: $C_{25}H_{19}N_2O_3^+$

Molecular Weight: 395.4375

Observed [M⁺]: 395.1386

Theoretical for $C_{25}H_{19}N_2O_3^+$: 395.1390

Mass accuracy: - 1.06 ppm

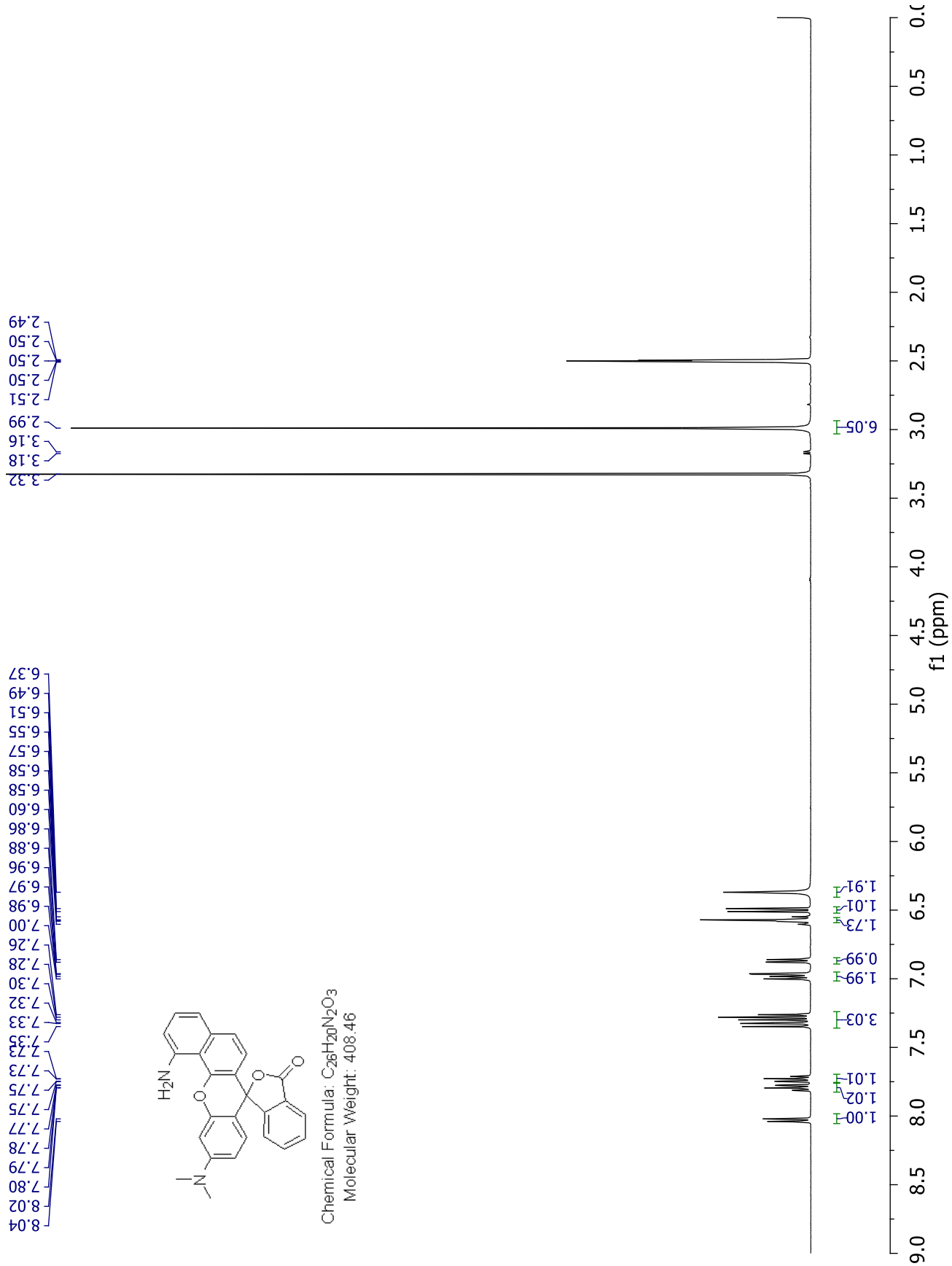


Figure S69. ^{1}H NMR spectrum of compound **38**.

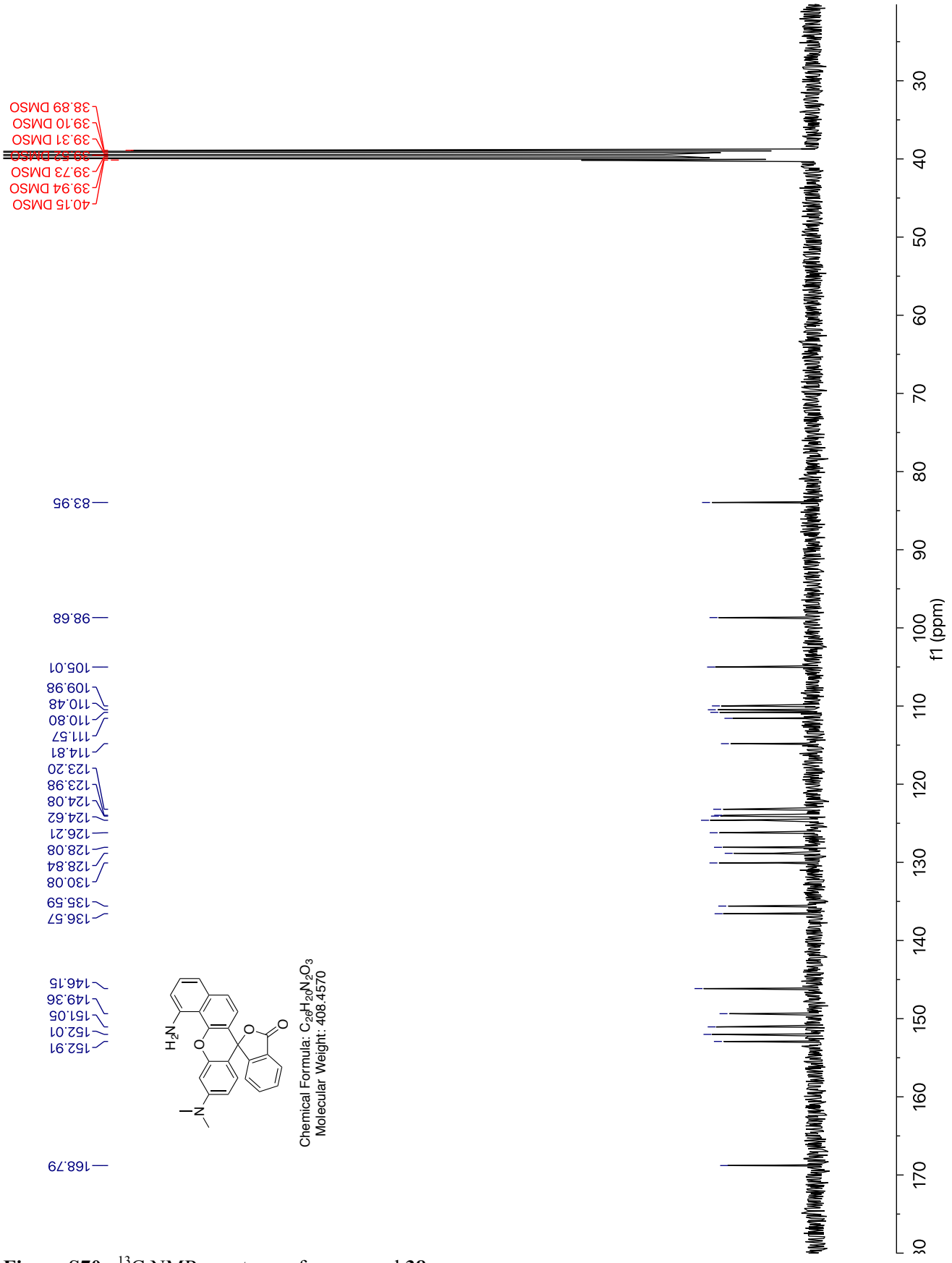


Figure S70. ^{13}C NMR spectrum of compound **38**.

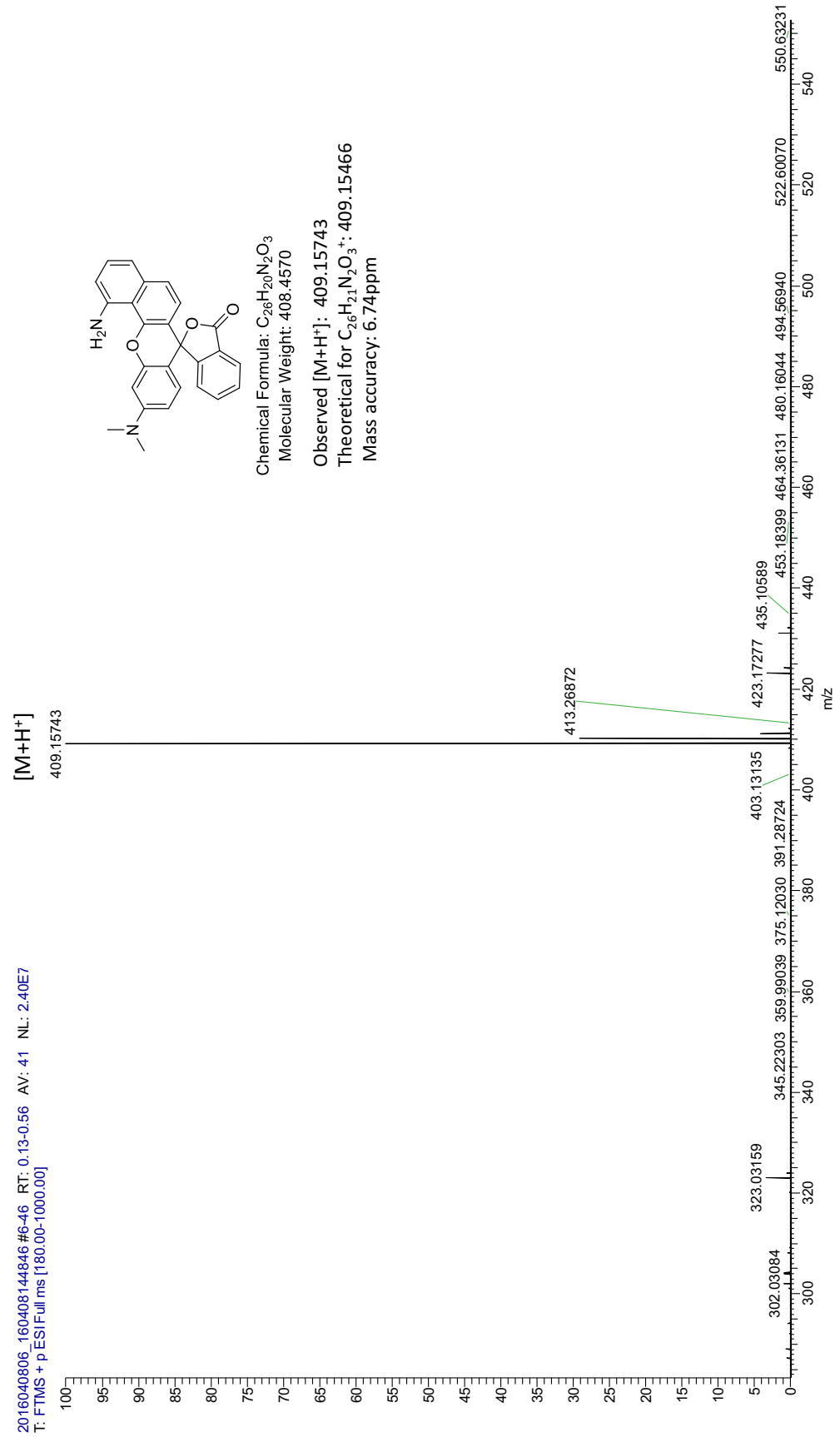


Figure S71. HR ESI positive mode spectrum of compound **38**.

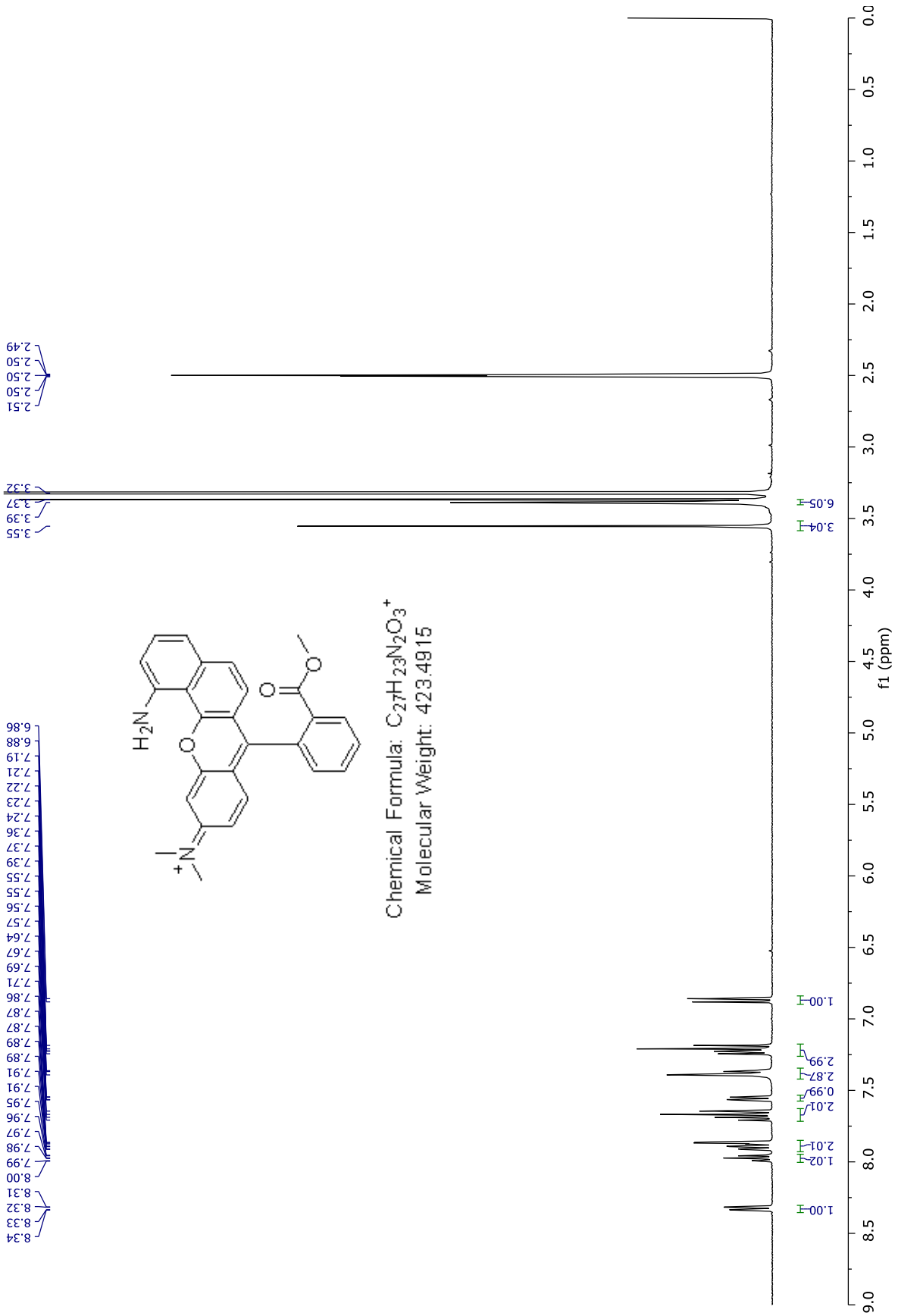


Figure S72. ^{1}H NMR spectrum of compound **10**.

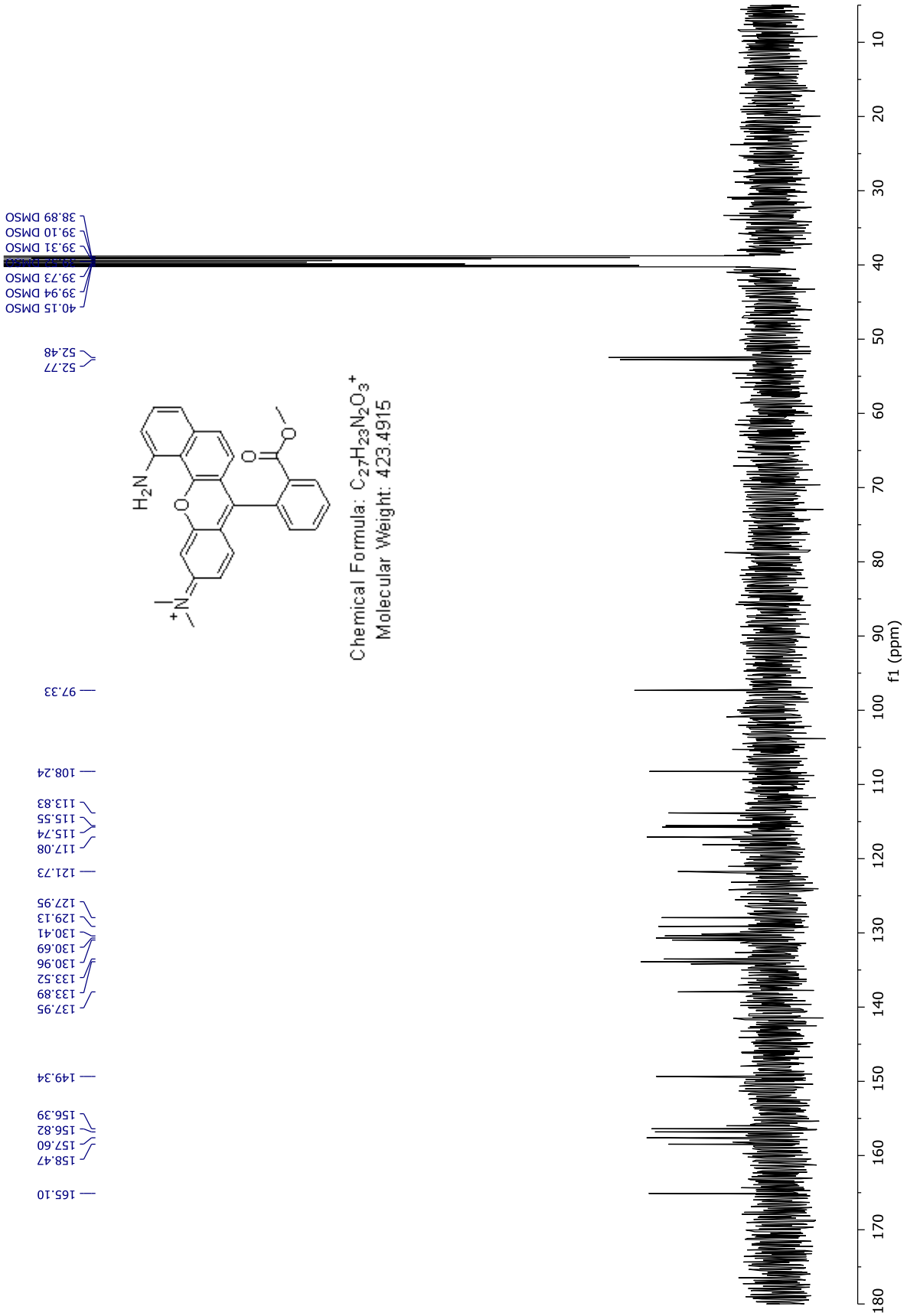
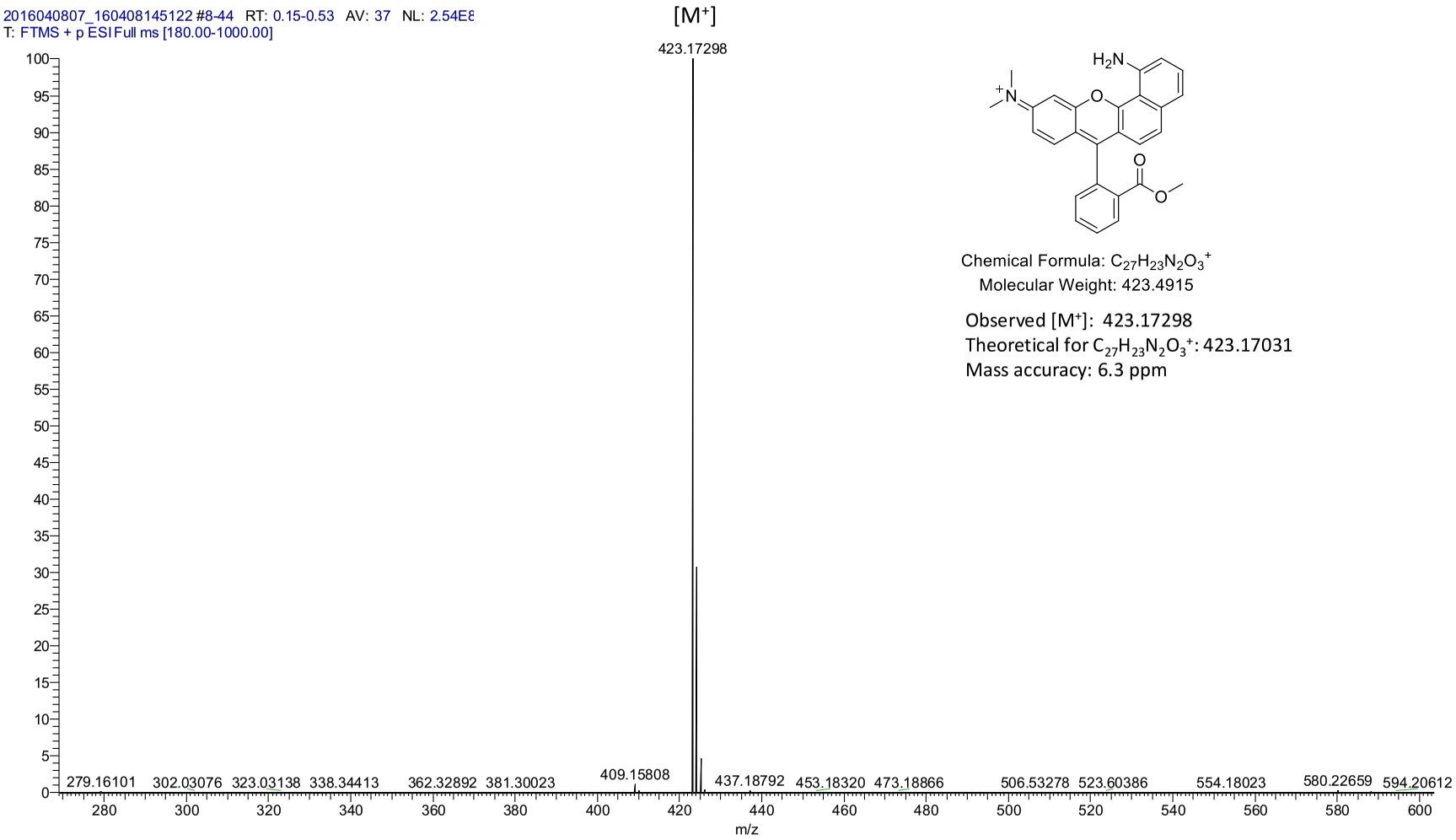


Figure S73. ^{13}C NMR spectrum of compound **10**.

Figure S74. HR ESI positive mode spectrum of compound **10**.



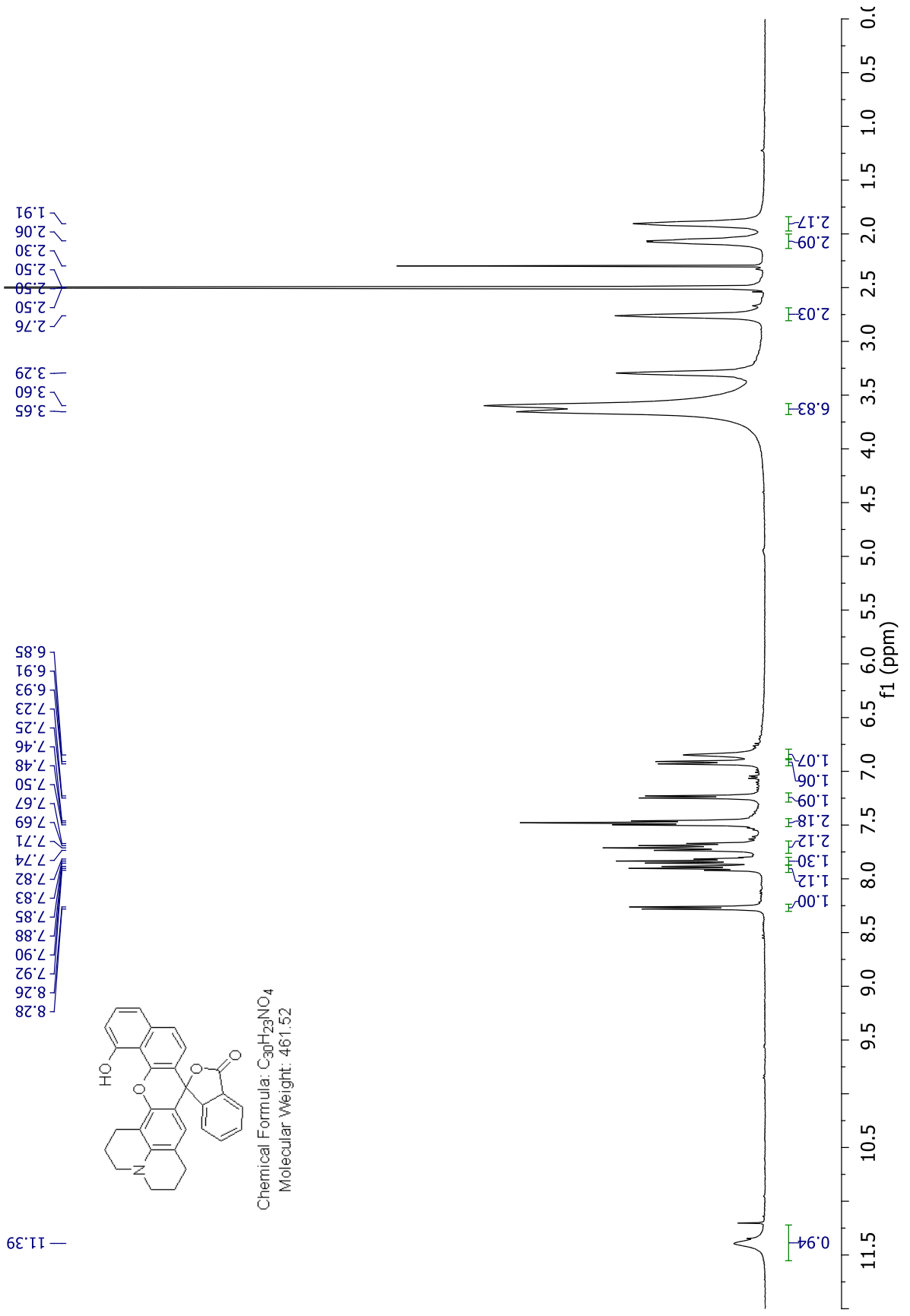


Figure S75. ^{1}H NMR spectrum of compound **39**.

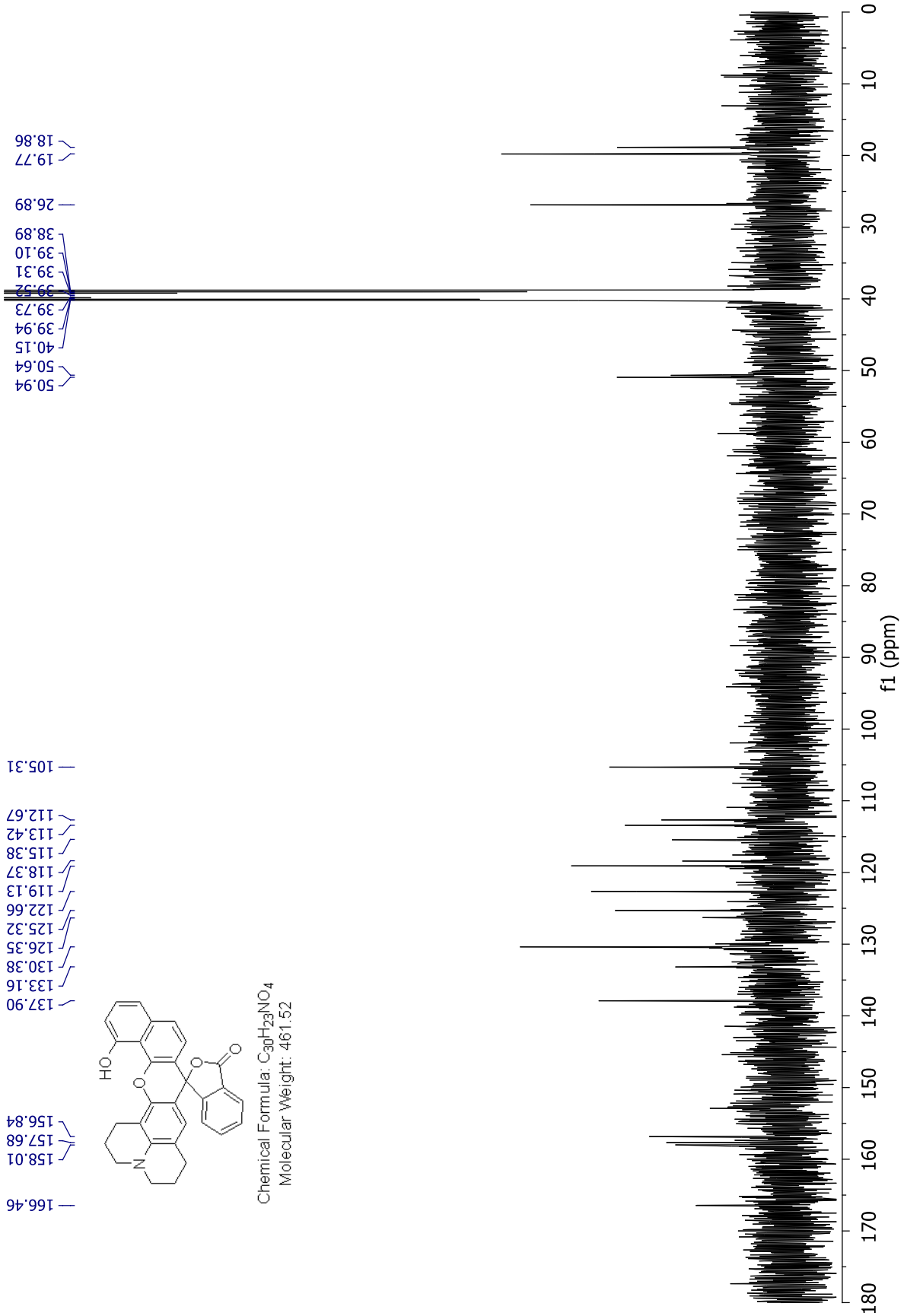


Figure S76. ^{13}C NMR spectrum of compound **39**.

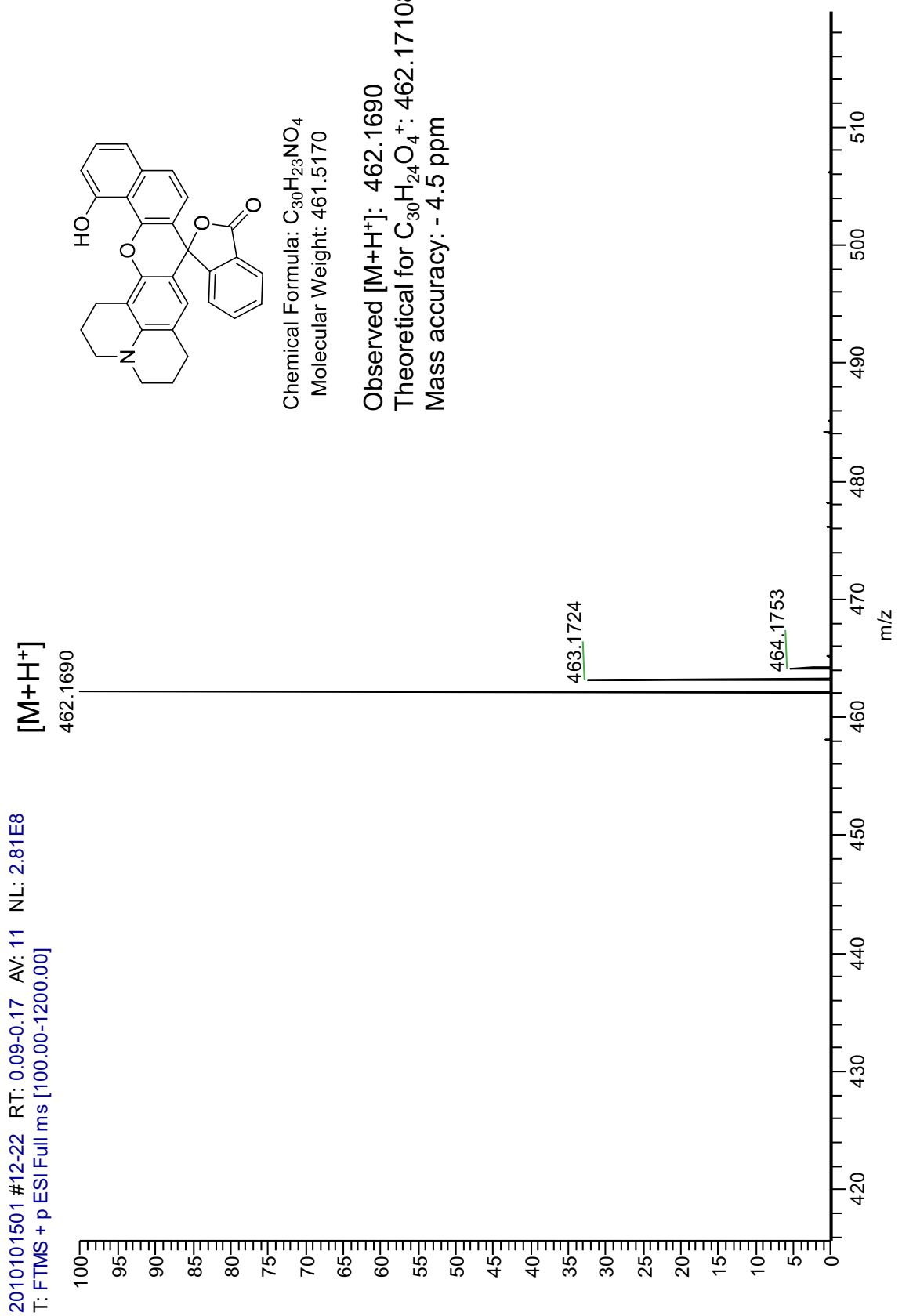


Figure S77. HR ESI positive mode spectrum of compound **39**.

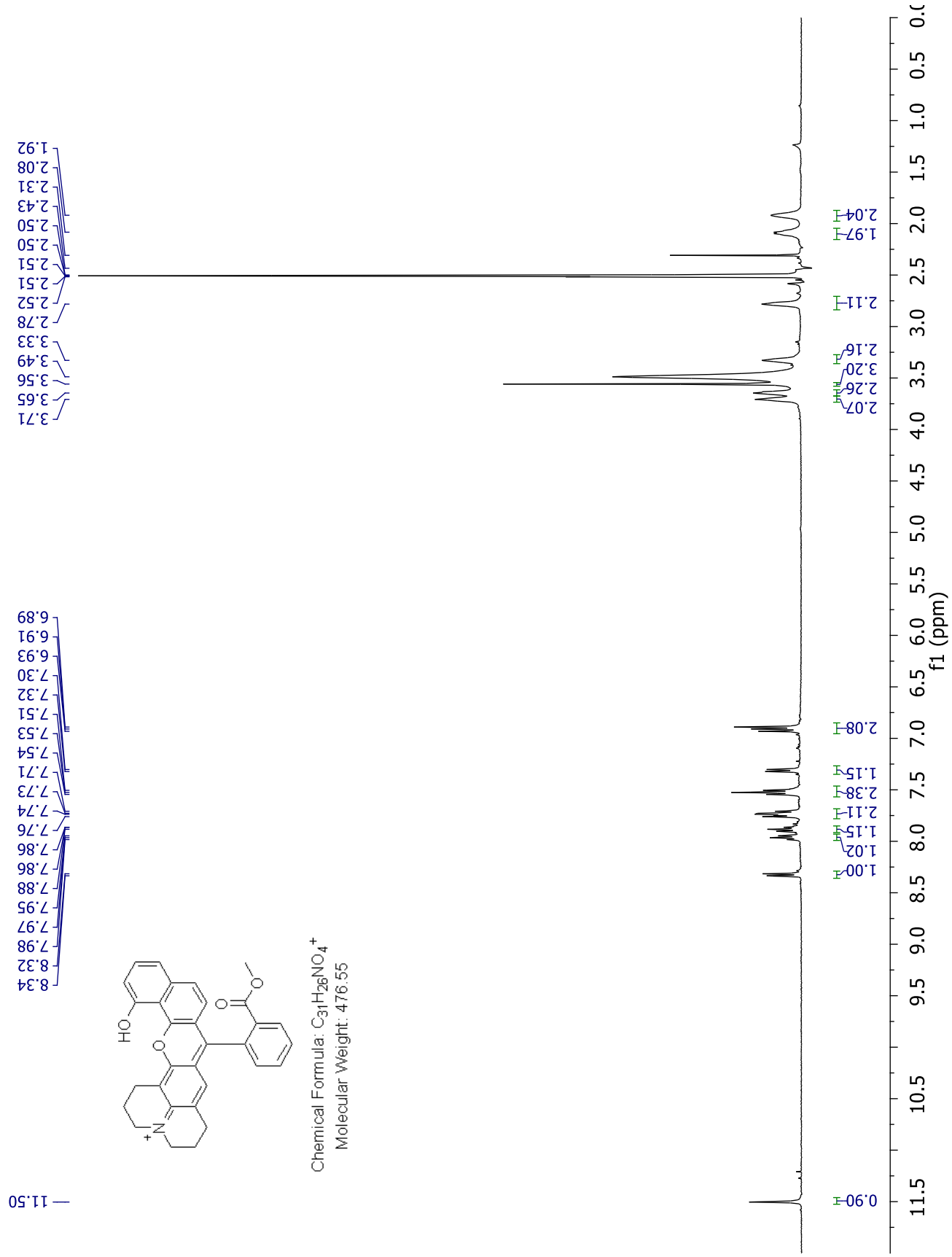


Figure S78. ^{1}H NMR spectrum of compound **11**.

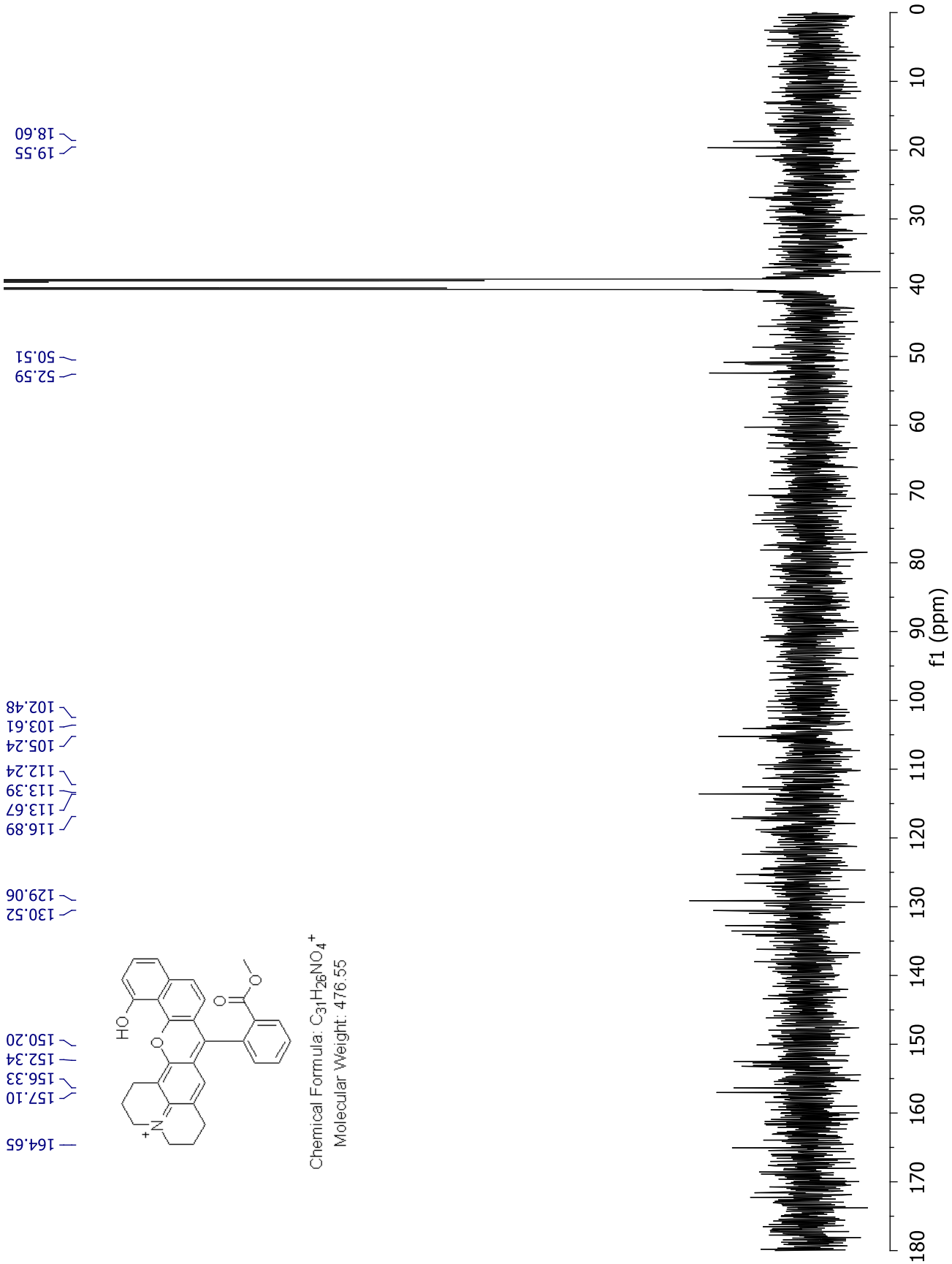
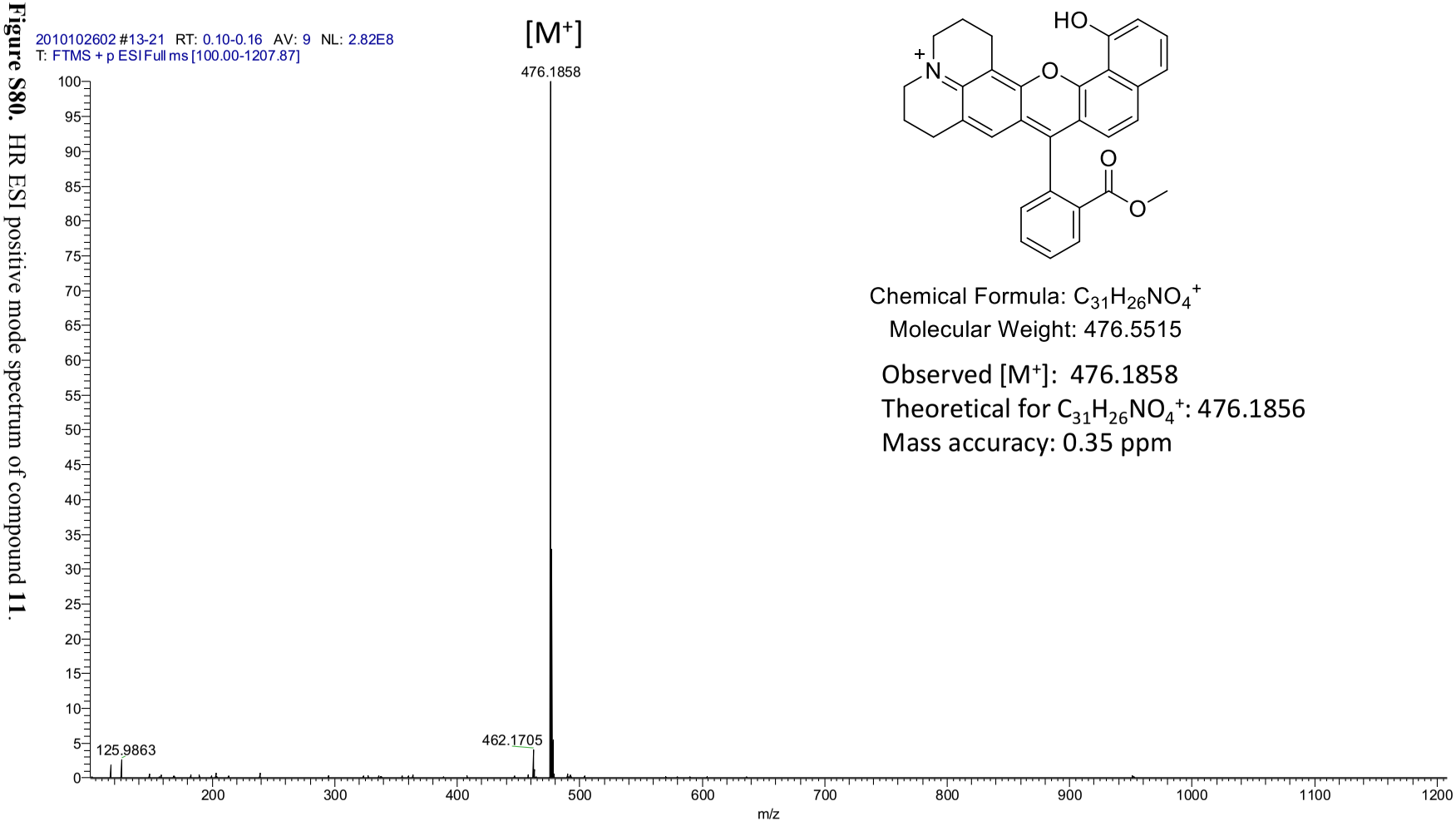


Figure S79. ^{13}C NMR spectrum of compound **11**.

Figure S80. HR ESI positive mode spectrum of compound **11**.



Chemical Formula: $C_{31}H_{26}NO_4^+$

Molecular Weight: 476.5515

Observed $[M^+]$: 476.1858

Theoretical for $C_{31}H_{26}NO_4^+$: 476.1856

Mass accuracy: 0.35 ppm

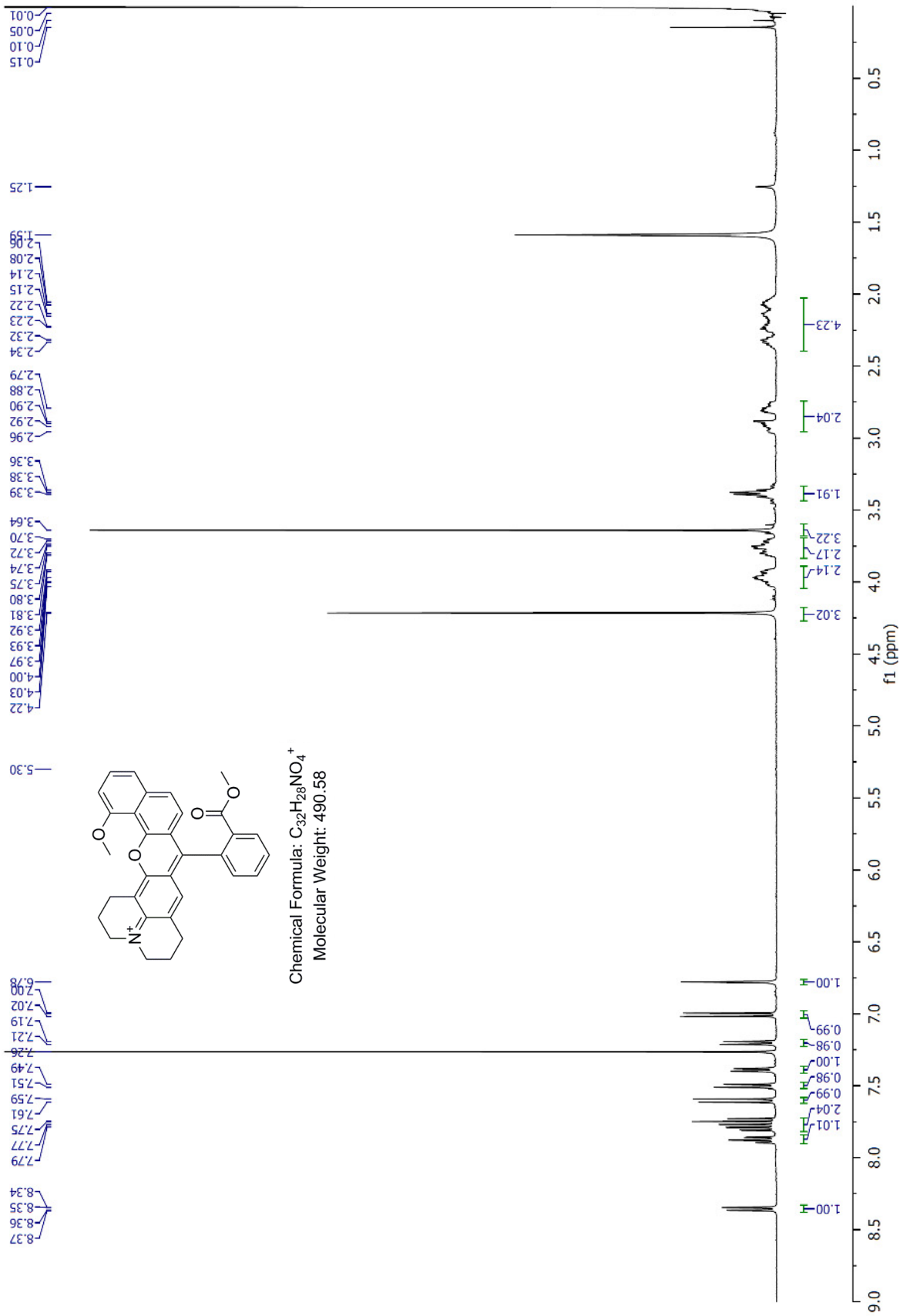


Figure S81. ^{1}H NMR spectrum of compound **12**.

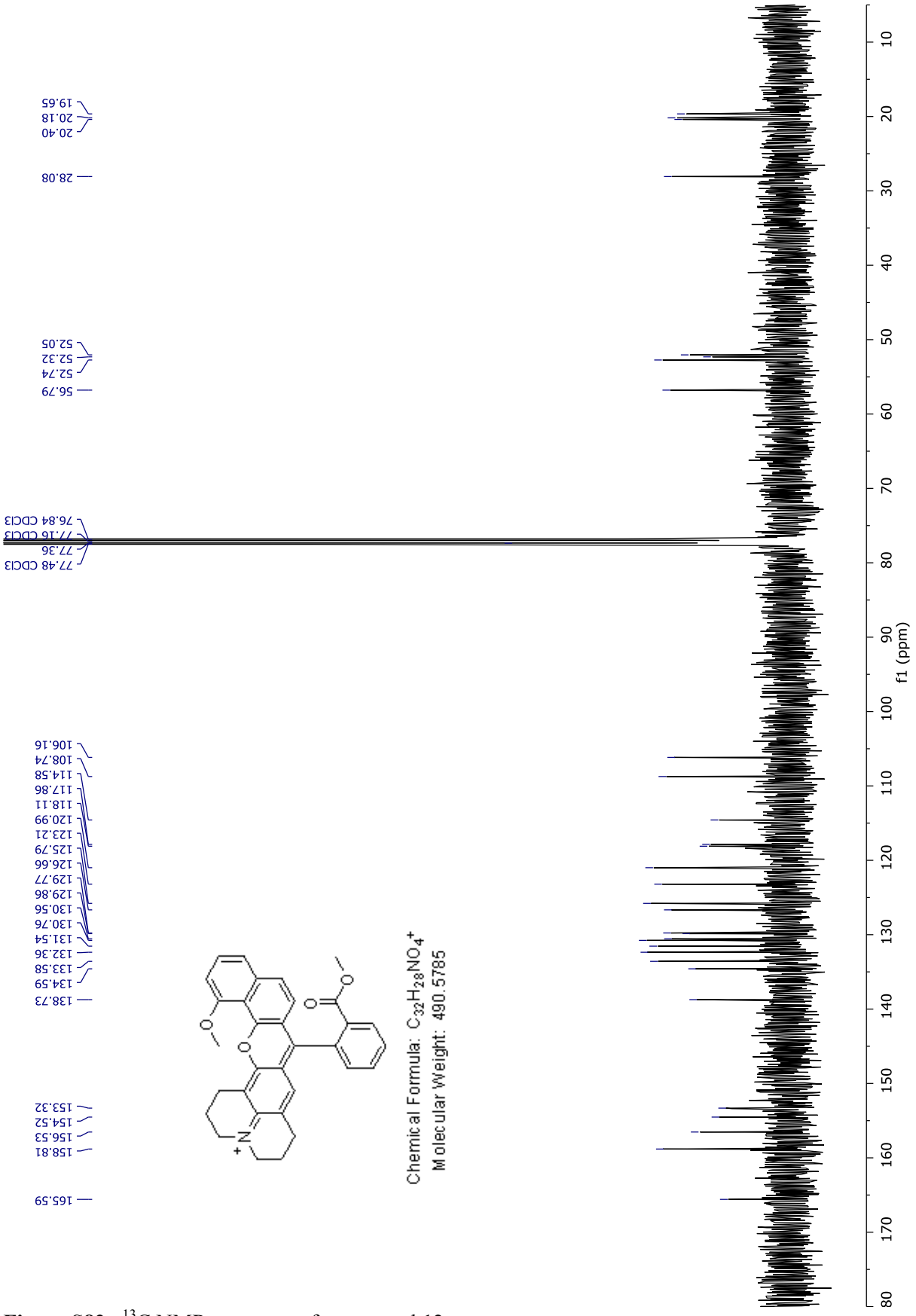


Figure S82. ^{13}C NMR spectrum of compound **12**.

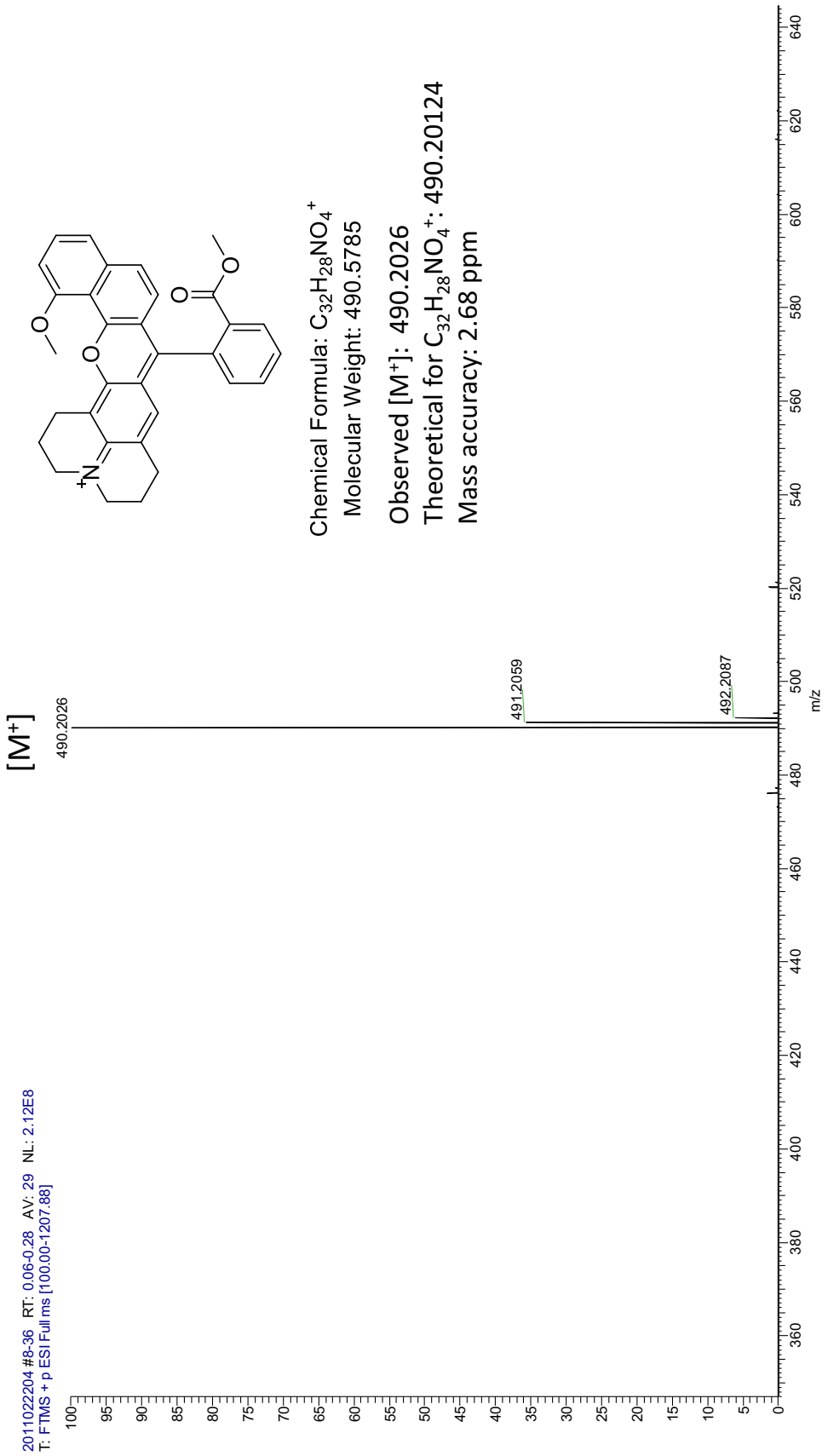


Figure S83. HR ESI positive mode spectrum of compound **12**.

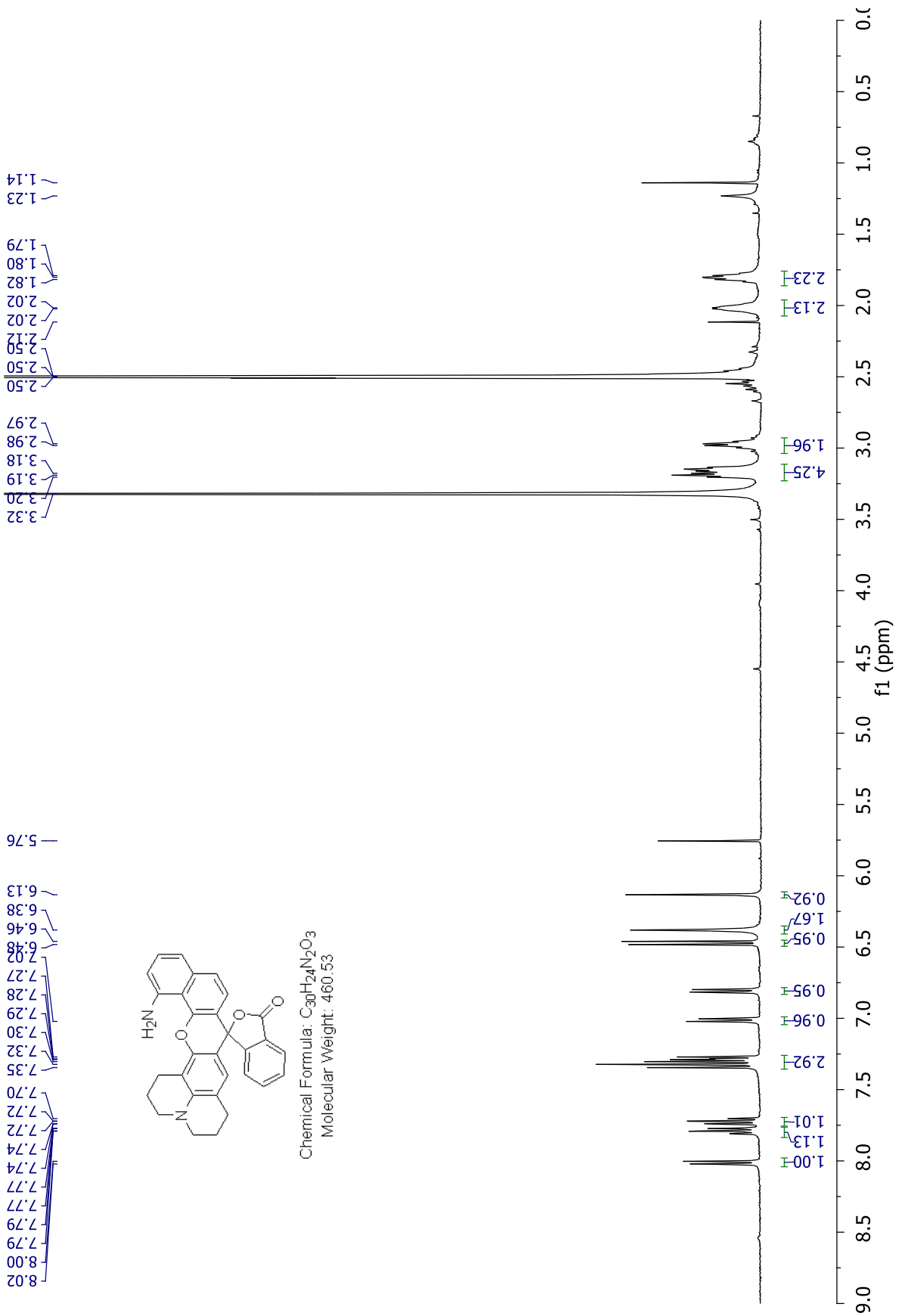


Figure S84. ^{1}H NMR spectrum of compound **40**.

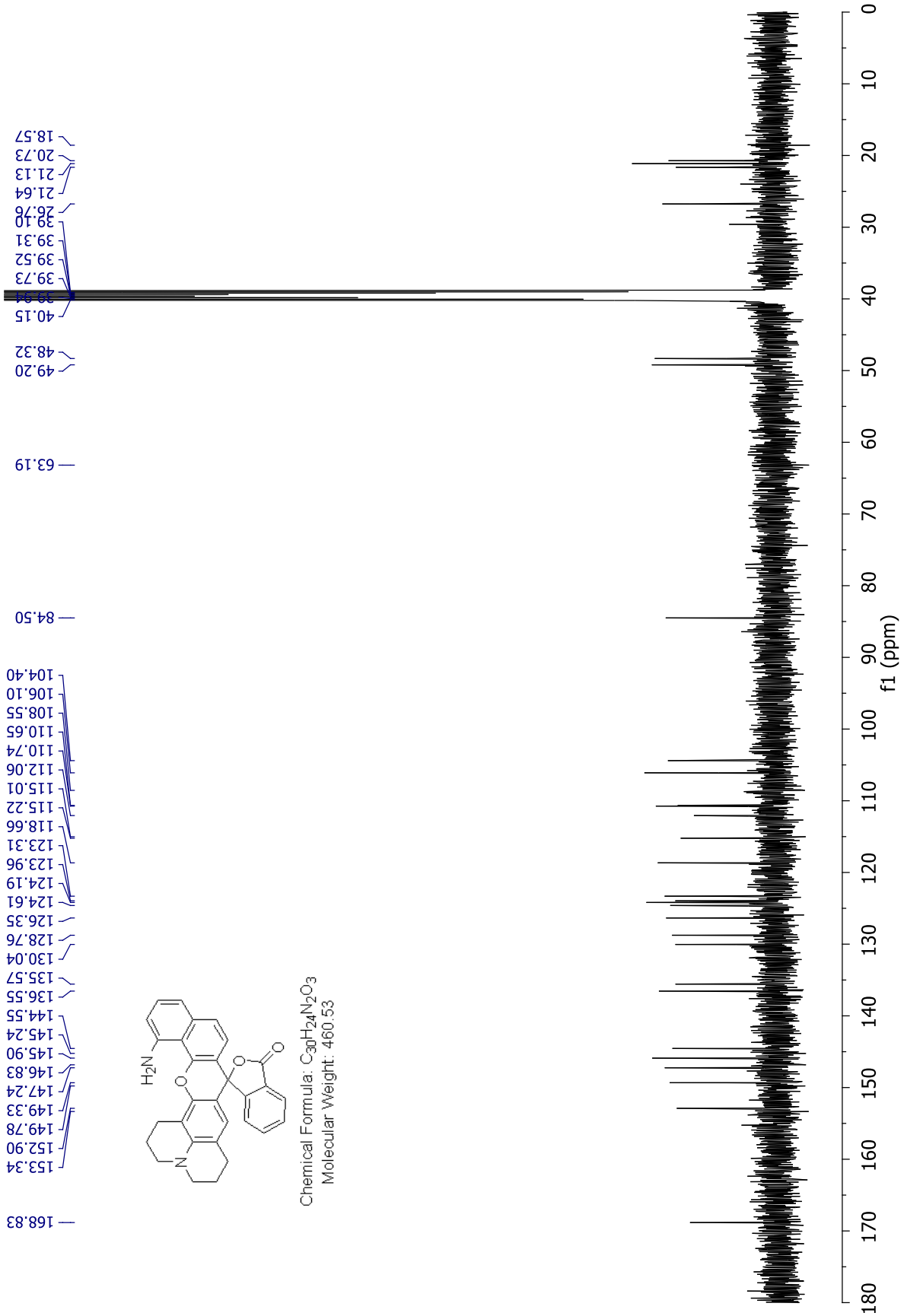
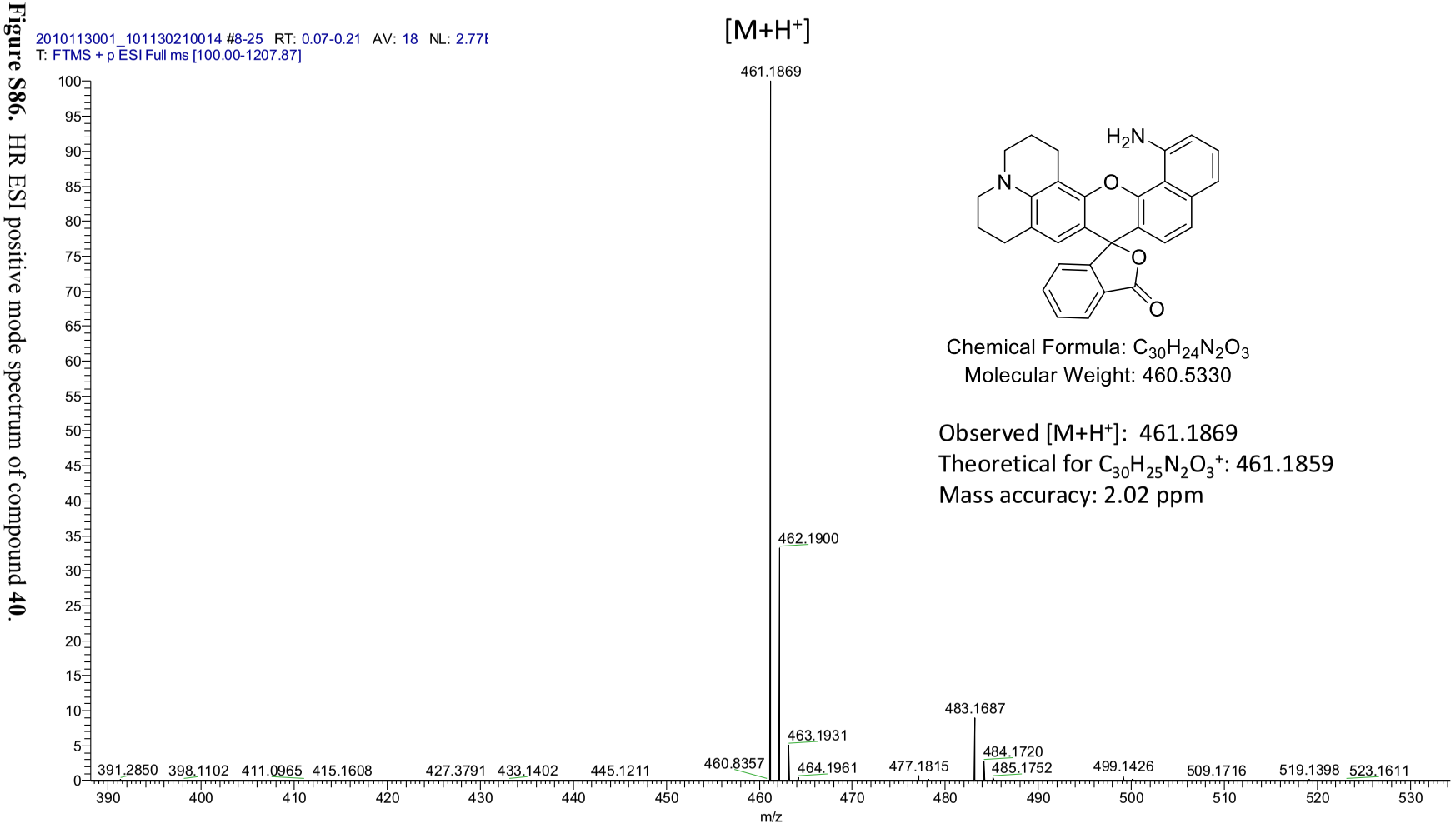


Figure S85. ^{13}C NMR spectrum of compound **40**.

Figure S86. HR ESI positive mode spectrum of compound **40**.



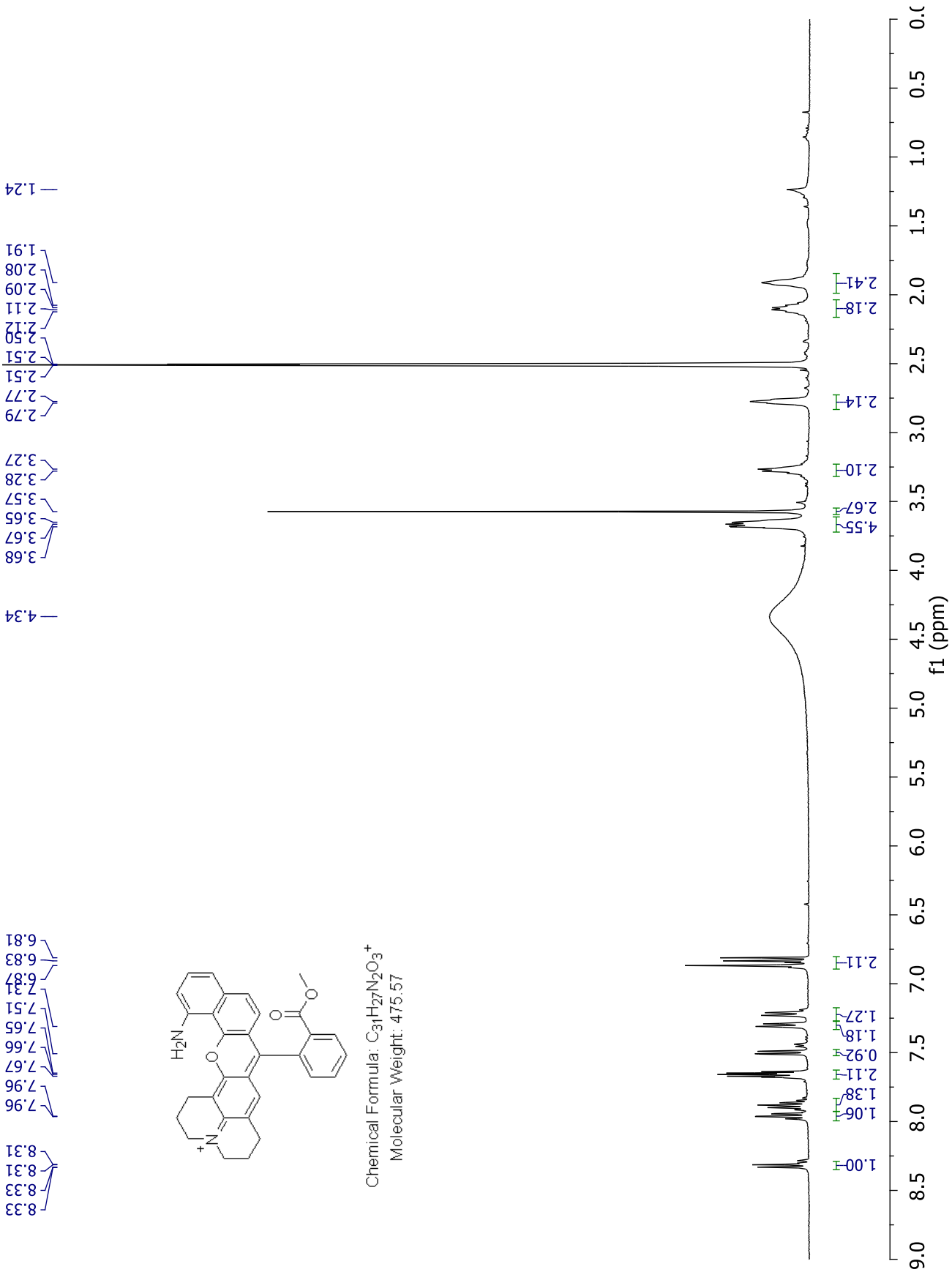


Figure S87. ^{1}H NMR spectrum of compound **13**.

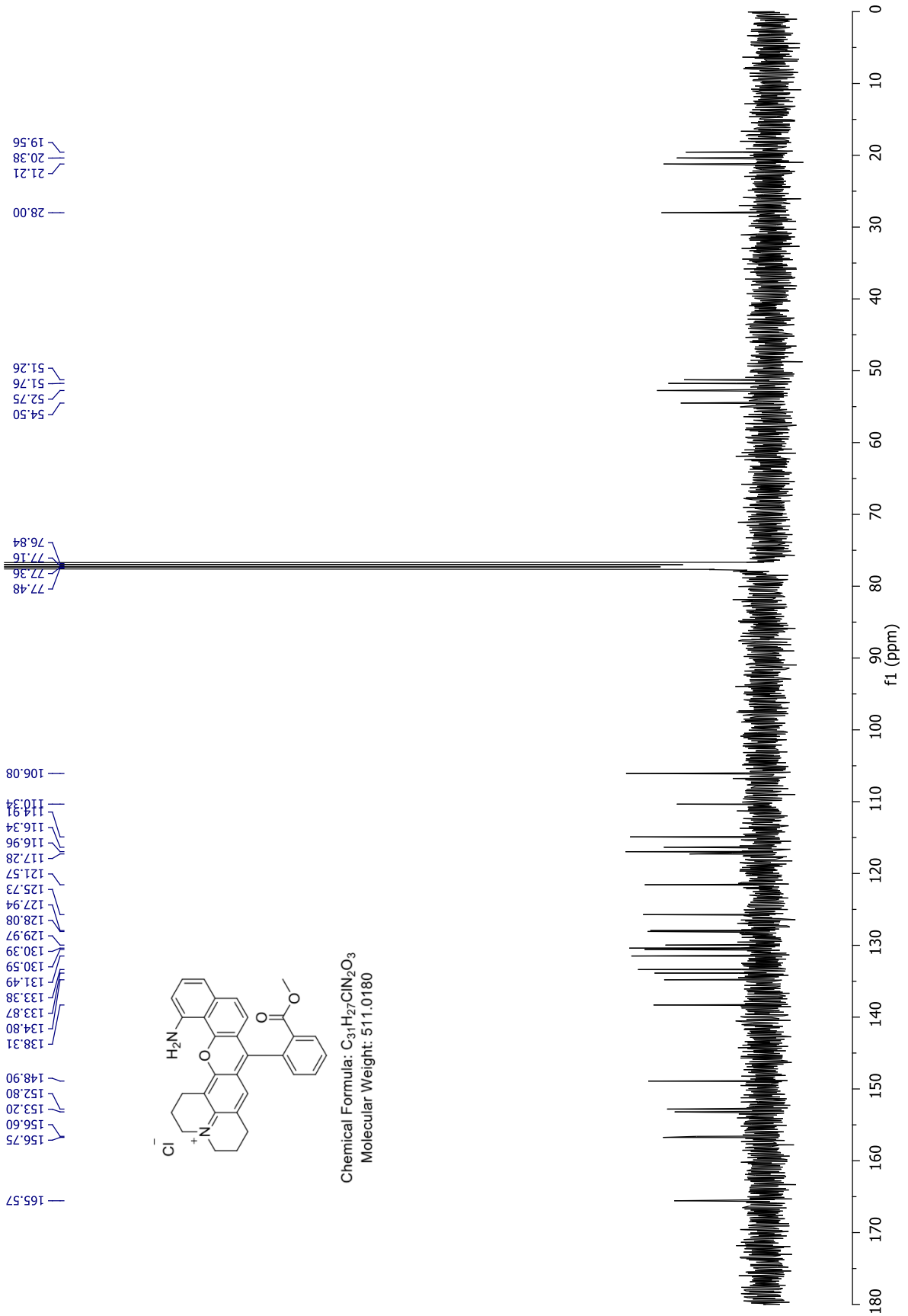


Figure S88. ^{13}C NMR spectrum of compound **13**.

Figure S89. HR ESI positive mode spectrum of compound **13**.