Supporting Information

Table of Contents

1. General Methods:

Flash chromatography: was performed with 40-63-μm particle size silica gel.

NMR Spectroscopy: NMR data was acquired with Bruker Avance 400, Bruker Avance 500 MHz Bruker, or Avance 600 instrument. ^{1}H and ^{13}C NMR spectra were referenced relative to residual solvent or TMS.

Mass spectroscopy: ESI-MS was performed on Bruker Daltonics micrOTOF instrument.

Chemicals: The following chemicals were purchased and used as received: thiophenol (Aldrich), 4-aminonaphthol hydrochloride (TCI),pentafluorobenzene sulfonamide (Sigma), diisopropylethylamine (Fisher), $Rh_2(OAc)_4$ (Pressure Chemical), 2,2,2-trifluoroethanol (Aldrich), Iodobenzene diacetate (Aldrich), butyric acid (Acros), $MgSO_4$ (Fischer). All solvents were reagent grade. Solvents used in inert atmosphere reactions were purified and degassed by the glass contour solvent system from SG waters USA.

Synthesis of known compounds: $Rh_2(tfa)_4$,[1] methyl 4-(chlorosulfonyl)butanoate,[2] and BP-1-102[3] were prepared according to previously reported protocols. The complex $Rh_2(O_2C^nPr)_3(tfa)$ was prepared from rhodium(II) butanoate dimer[4] by the standard method.[5] The azide–alkyne **1**[9] and 3-azido-7-hydroxycoumarin[6] were synthesized as described previously.

STAT3 expression: The dimeric (pSTAT3) and monomeric (STAT3) recombinant core fragments of STAT3 (AA 127-722) were expressed, purified, and analyzed according to a previously described method.[7]

HPLC: HPLC was performed on a Shimadzu CBM-20A instrument with Phenomenex Jupiter 4 μ Proteo 90A (250 mm × 15 μm) and Phenomenex Jupiter 4 μ Proteo 90A (250 mm × 4.6 μm) columns. Flow rates of 8 mL/min and 1 mL/min were used for preparative and analytical columns, respectively. Analytical and preparative HPLC were performed with gradients of acetonitrile and water. All samples were run on a gradient of increasing (40-90%) MeCN/H_2O from 2-22 min. The absorbance was monitored at 320 nm during each run.

Proteomics analysis

a) **LC/MS-MS Sample preparation A.** Reaction solutions containing protein, probe, and catalyst were buffer-exchanged into aq ammonium bicarbonate (50 mM, pH 8.0) via repeated dilution and centrifugation through a centrifugal filter (3,000 MWCO, Amicon Ultra 3K, Millipore Corp.). The filtered reaction mixture was then subjected to overnight digestion at 37 °C with either sequencing-grade trypsin (Promega Corp.) or sequencing grade Asp-N (Protea Biosciences) protease at a 1:25 enzyme/substrate ratio.

b) **LC/MS-MS Sample preparation B.** The modification site was verified by a second analysis at the Rice MS facility, conducted blind of the results or conclusion of the initial analysis. STAT3 samples were digested with trypsin (20:1 μg protein/μg trypsin) without reduction or alkylation. Sample (50 μL) was diluted to 150 μL with aq ammonium bicarbonate (25 mM) and digested at 37 °C. An aliquot (50 μL) was taken after 3 h for LC-MS/MS analysis and the remaining sample was allowed to digest overnight for 13 additional h. After overnight digestion a second aliquot (50 μL) was taken and subjected to LC–MS/MS analysis.

c) **Data collection and analysis**.The resulting peptide digests were diluted in aq formic acid (1%) for injection onto a UPLC/MS system and resolved by nanoflow liquid chromatography reverse-phase gradient separation (3–40% acetonitrile/0.1% formic acid linear gradient over 30 min at 300 nL/min flow rate) on a 75 μm x 250 mm NanoAcquity BEH C-18 UPLC column (1.7 μm particle size; waters Corp.) using a NanoAcquity® UPLC system (Waters Corp.) before being introduced via a nanoelectrospray ionization source into a Synapt® mass spectrometer (Waters Corp.) for analysis. Mass spectrometry analysis to determine the site of modification by the alkyne diazo-containing probe moiety was carried out by MS precursor/product ion analysis accomplished using positive ion mode in the Synapt® instrument utilizing a data-independent parallel ion fragmentation strategy using alternating low and high collision energies in successive MS

scans, termed MS^E, LC/MS instrument control and data acquisition was accomplished using MassLynx software (v4.1, Waters Corp.).

The site of modification on the STAT3 core was localized by first identifying potentially modified precursor molecular ions from all of the observed low-energy MS^E spectra derived from STAT3 core digest peptides containing a delta mass of +415.19 Da (monoisotopic) associated with the reactive probe. The actual amino acid site of modification on the precursor ion was then identified by comparing the observed high energy MS^E spectra derived from the precursor molecular ion by the ramped CID collision energies to theoretical b-ion and y-ion fragmentation patterns predicted by in-silico MS spectral search algorithms with the probe modification being used as a potential "variable modification" allowable on any amino acid side chain (except glycine). MS spectral analysis was accomplished by a computerized protein database search strategy, after internal lock-mass correction of the raw MS data, using ProteinLynx Global Server (PLGS v3.0, Waters Corp.) software. All MS spectra used for localizing sites of modification were manually verified for accuracy.

Surface plasmon resonance (SPR) inhibition measurements:

a) **Phosphopeptide binding**. The ability of MM-206 to inhibit STAT3 binding to phosphopeptide (P1068) was assessed by SPR analysis on a Biacore 3000 instrument as previously described.[8]

b) **DNA binding**. Biotinylated, double-stranded probes were created by annealing complementary APRE oligonucleotides linked by a hairpin loop.[9] The STAT3 consensus binding sequence was immobilized on channel 2 of the SA sensor chip. As a reference, channel 1 was immobilized with a control mutant oligonucleotide lacking STAT3-binding activity due to key nucleotide substitutions. All DNA-binding experiments were performed in HEPES (20 mM at pH 7.5), containing (50 mM) NaCl, (10 mM) $MgCl_2$, and 0.005% Tween 20. To assess DNA-binding inhibition, aliquots of purified, phosphorylated pSTAT3 dimer were mixed with increasing concentrations of MM-206 (0–50 uM) and incubated at rt for 2 h before being passed over the surface of the DNA immobilized SA chip. Regeneration of the chip was achieved by injecting aq glycine (30 µL, 10 mM at pH 1.5). The resulting sensograms were corrected for bulk effects by subtracting the reference signal prior to analysis. RU signal at a single saturation time point was then chosen for all the samples and normalized to that of the untreated sample (100% binding). IC_{50} values were obtained by fitting the data to a competitive binding model with a four parameter logistic equation using Biacore Evaluation software.

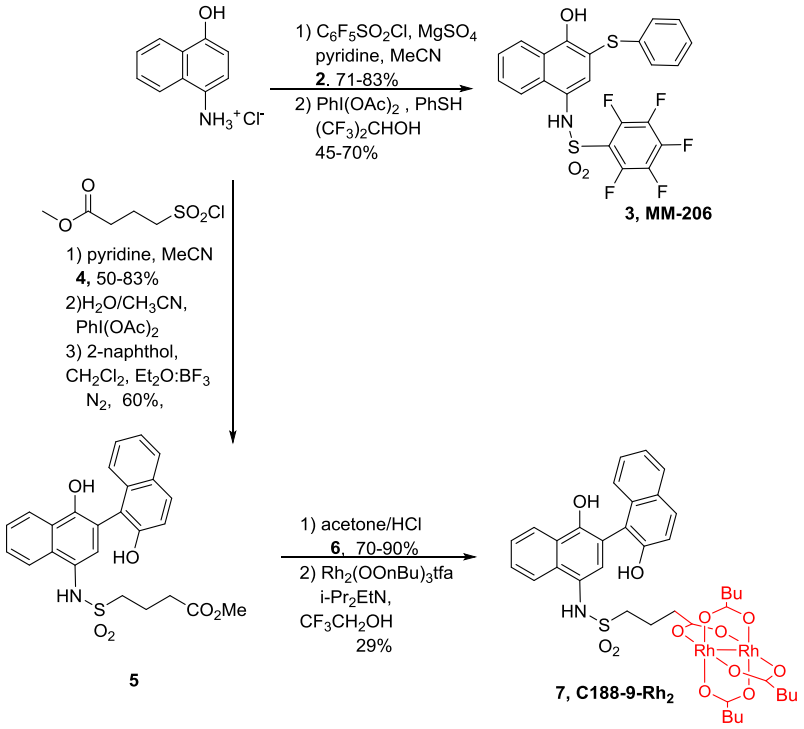
Standard procedure for protein modification and the inhibition thereof. pSTAT3 or STAT3 (2 µL, 40 µM in 0.1 M HEPES) was added into aq iodoacetamide (38 µL, 2 mM in 0.1 M HEPES, pH 7.4). It was allowed to sit in the dark at rt for 1 h. From this stock solution 2-µL protein samples were taken and diluted in modification reaction buffer (36.5 µL, 0.1 M HEPES), and into each an aq soln of a rhodium catalyst (0.5 µL, 40 µM in 0.1 M HEPES) was added. The modification reaction was initiated by addition of aq alkyne-diazo **1** (1 µL of 25 mM soln in 1:1 tBuOH/0.1 M HEPES). For measuring inhibition of modification, an inhibitor small molecule or phosphopeptide was added as an aq soln prior to addition of the diazo compound. Each reaction was shaken at rt for 6 h (unless noted otherwise), after which it was subjected to analysis as outlined below.

Fluorogenic analysis of blot membranes. Following established protocols,[10] the protein modification reaction samples were mixed with 4× LDS loading buffer and 20× reducing agent (XT, Biorad) and heated in boiling water for 3 min. Samples were loaded into SDS-PAGE (12% Bis-tris gel, Life Technologies). Resolved protein bands were then transferred onto a PVDF membrane (GE Healthcare), which had been preactivated in MeOH for 5 min. After transfer the membrane was bathed in a reaction mixture which contained 3-azido-7-hydroxycoumarin (500 µM), *tris*[(1-benzyl-1H-1,2,3-triazol-4-yl)methyl]amine (20 µM), sodium ascorbate (5 mM), and $CuSO_4$ (500 µM) in aq DMSO (50%). The membrane was incubated for 1 h in the dark and then rinsed thrice with aq EtOH (70%). The membrane was imaged with a Fujifilm LAS-4000 instrument using epi-UV light source (370 nm LED) and a L41 filter set. After imaging, the membrane was air dried and stained with Ponceau S solution.

Mouse methods. Animal studies were conducted according to a protocol approved by the Baylor College of Medicine IACUC (Institutional Animal Care and Use Committee, Assurance number A3823-01). Human leukemia samples were obtained from the Texas Children's Cancer Center, in accord with a research protocol approved by the Baylor College of Medicine IRB (Institutional Review Board, Assurance number 00000286). Patients/guardians gave written informed consent, in accordance with the Declaration of Helsinki, for banking of bone marrow for future research.

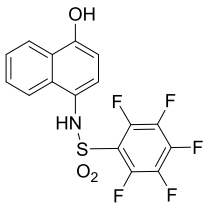
AML xenografts were established by tail vein injection of 1×10^7 MV4-11 cells stably transduced with firefly luciferase (MV4-11.ffluc) into 6-8 week old female NOD-SCID-IL2Rγ-/- (NSG) mice. Disease progression was monitored weekly by bioluminescence imaging (IVIS). Two weeks after cell injection, mice were randomized to receive MM-206 (30 mg/kg IP, once daily Mon–Fri) or the same concentration and volume of DMSO on the same schedule. For the first experiment, mice were treated for two weeks (10 doses), and for the second experiment mice were treated for four weeks (20 doses). Mice were humanely sacrificed when they appeared moribund, or ten weeks after cell injection for surviving mice. At the time of sacrifice, bone marrow cells were harvested and the percent of MV4-11 cells in the nucleated cell fraction was determined by flow cytometry for GFP (encoded by the ffluc vector).

2. Chemical synthesis procedures and characterization



Scheme S 1. The synthesis of MM-206 and C188-9-Rh2.

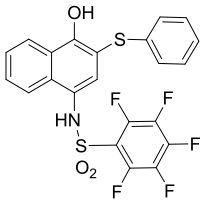
Preparation of 2,3,4,5,6-pentafluoro-N-(4-hydroxynaphthalen-1-yl)benzenesulfonamide (2)



Solid 4-amino-1-naphthol hydrochloride (2.0 g, 10.2 mmol, TCI) was placed in a round-bottomed flask containing $MgSO_4$ (2.0 g) and a stir bar. The reaction vessel was evacuated and back-filled with nitrogen. Both pyridine (40 mL) and acetonitrile (5 mL) were transferred by syringe to the round-bottomed flask. Pentafluorobenzenesulfonylchloride (1.0 mL, 6.7 mmol) was added via syringe. The reaction was monitored by TLC and was complete after 2 h The reaction mixture was taken up in CH_2Cl_2 and washed with aq HCl (3 × 20 mL, 2M). The CH_2Cl_2 layer was loaded directly onto a silica gel column and was eluted (1:1 ether/hexane). The solvent was evaporated to afford 2.4 g (92% yield) of a yellowish white powder, **2**. ^{1}H NMR (500 MHz, acetone-*d*6) ppm 6.84 (d, *J* = 8.0 Hz, 1H) 7.21 (d, *J* = 8.0 Hz, 1H) 7.49 - 7.54 (m, 1H) 7.54 - 7.60

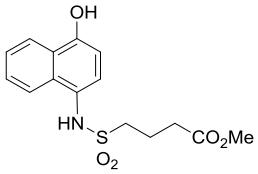
(m, 1H) 8.11 - 8.15 (m, 1H) 8.23 - 8.29 (m, 1H) (387). ^{13}C NMR (150 MHz, acetonitrile-*d*3) ppm 107.5, 120.3, 122.2, 123.1, 124.6, 126.6, 128.4, 128.6, 137.01, 145.4. MS (ESI), $[M-H]^-$ calcd for $C_{16}H_7F_5NO_3S^-$ 388.01, found 388.01.

Preparation of 2,3,4,5,6-pentafluoro-N-(4-hydroxy-3-(phenylthio)naphthalen-1-yl)benzenesulfonamide (3)



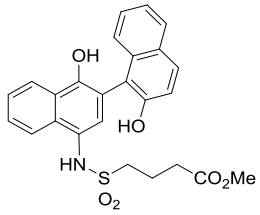
Iodobenzene diacetate (27 mg, 0.084 mmol) and benzenesulfonamide ,2 (25 mg, 0.064 mmol) were placed into a 4-ml vial. The two reactants were dissolved in 1,1,1,3,3,3-hexafluoroisopropanol (0.25 mL). After 5 minutes, thiophenol (35 µl, 0.321 mmol) was added to the yellow solution. The reaction was monitored by TLC. After 2 h, the reaction was taken up in CH_2Cl_2. The organic layer was loaded directly onto a silica gel column (eluent: 10% ether/hexane) to yield **3** (21 mg, 65%). ^{1}H NMR (500 MHz, acetone - *d*6) ppm 7.03 - 7.10 (m, 2H) 7.16 - 7.23 (m, 1H) 7.23 - 7.30 (m, 2H) 7.37 (s, 1H) 7.60 - 7.65 (m, 1H) 7.65 - 7.71 (m,1H) 8.22 (d, *J* = 8.3 Hz, 1H) 8.34 (dd, *J* = 8.33, 0.6 Hz, 1H) ^{13}C NMR (150 MHz, acetonitrile - *d*3) ppm 110.1, 123.5, 123.6, 123.8, 125.4, 127.00, 127.4, 128.0, 129.2, 129.8, 132.00, 133.3, 136.6, 155.6, MS (ESI), $[M-H]^-$ calcd for $C_{22}H_{11}F_5NO_3S_2$- 496.01, found 496.01.

Preparation of methyl 4-(N-(4-hydroxynaphthalen-1-yl)sulfamoyl)butanoate (4)



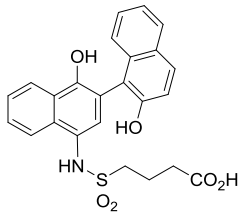
The naphthol sulfonamide ester, **4,** was made adding **3** and $MgSO_4$ to a round-bottomed flask. This flask was evacuated and then backfilled with nitrogen. Dry degassed pyridine was added to the reaction vessel. Next, methyl 4-(chlorosulfonyl)butanoate was added to the brown slurry. After 1 hour the reaction was complete by TLC. CH_2Cl_2 was added to the reaction which was then washed with aq HCl (3×, 4 M soln). The product was precipitated from the organic layer by addition of hexane (83% yield). ^{1}H NMR (600 MHz, MeCN-*d*3) ppm 2.09 (dtd, *J* = 9.7, 7.4, 5.7 Hz, 2H) 2.46 (t, *J* = 7.2 Hz, 2H) 3.11 - 3.20 (m, 2H) 3.63 (s,3H) 6.89 (d, *J* = 8.1 Hz, 1H) 7.34 - 7.41 (m, 2H) 7.51 - 7.57 (m, 1H) 7.60 - 7.64 (m, 1H) 7.77 (s, 1H) 8.18 (d, *J* = 8.4 Hz, 1H) 8.22 (d, *J* = 8.1 Hz, 1H) 13C NMR (150 MHz, MeCN -*d*3) ppm 20.0, 32.4, 51.5, 52.1, 108.4 , 123.1 , 124.1, 124.9 , 126.1, 126.3, 126.7 , 127.9 , 133.0, 153.3 , 173.7 MS (ESI), $[M-H]^-$ calcd for $C_{15}H_{16}NO_5S^-$: 322.1, found 322.1.

Preparation of methyl 4-(N-(1',2-dihydroxy-[1,2'-binaphthalen]-4'-yl)sulfamoyl)butanoate (4)



Sulfonamide **3** (339 mg, 1.05 mmol) was added to a flask with iodobenzene diacetate (356 mg, 1.14 mmol). Acetonitrile (5ml) was added to this flask. While the solution was stirring, water (5ml) was added. After 2 h the reaction was taken up in CH_2Cl_2 and washed with water (3 × 20 mL). The CH_2Cl_2 layer was then dried with Na_2SO_4, filtered through cotton, and concentrated in vacuo. The crude brown solid (414 mg) was placed under an inert atmosphere (N_2) with 2-naphthol (165 mg, 1.14 mmol). CH_2Cl_2 (4 ml) was added to form a brown solution. While stirring the solution, BF_3•Et_2O (8 mL, 8 mmol) was added. After 30 min the reaction was complete, as determined by TLC. More CH_2Cl_2 (20 mL) was added to this reaction, and then it was quenched with water. The CH_2Cl_2 layer was washed three timeswith H_2O, dried with $MgSO_4$, filtered, and concentrated in vacuo. The brown solid was recrystallized overnight from $CHCl_3$, filtered, and dried to yield a white powder (270 mg, 57% yield over 2 steps). ^{1}H NMR (500 MHz, acetone-*d*6) ppm 2.08 - 2.17 (m, 2H) 2.44 - 2.50 (m, 2H) 3.24 - 3.30 (m, 2 H) 3.51 (s, 3H) 7.29 - 7.40 (m, 4 H) 7.42 - 7.45 (m,1H) 7.59 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H) 7.65 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H) 7.85 - 7.89 (m, 2H) 8.36 - 8.40 (m, 1H) 8.42 (dq, *J* = 8.4, 0.7 Hz, 1H) 8.46 (s, 1H) ^{13}C NMR (126 MHz, acetone – *d*6) ppm 20.1,32.5,51.0,51.7, 115.7, 116.6, 119.6,123.8, 123.9 124.7, 125.4, 125.6, 126.3, 127.1, 127.5, 127.5, 129.0, 129.8, 130.0, 130.9, 133.0, 135.2, 154.3, 173.3, 206.4, 206.4, 206.4, 206.4 MS (ESI), $[M-H]^-$ calcd for $C_{25}H_{22}NO_6S_1^-$: 464.1, found 464.1.

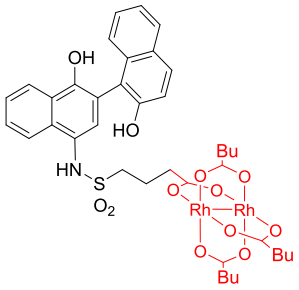
Preparation of 4-(N-(1',2-dihydroxy-[1,2'-binaphthalen]-4'-yl)sulfamoyl)butanoic acid, (6)



Acetone (10 ml) was purged with nitrogen for 30 min. The binaphthol carboxylate **4** (37 mg, 0.0796 mmol) was added along with aq HCl (10 mL, 4 M), and the resulting solution was heated to 60 °C. After 14 h the reaction vessel was cooled to rt and the acetone was evaporated under

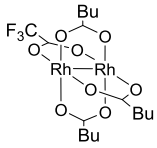
reduced pressure, resulting in precipitation of a pinkish-white solid. This slurry was extracted twice with CH_2Cl_2. The combined organic layers were loaded directly onto a silica gel column (eluent: 0→10% MeOH/CH_2Cl_2), affording the desired acid (30 mg, 83% yield). ^{1}H NMR (500 MHz, MeCN - *d*3) ppm 1.97 - 2.07 (m, 2H) 2.38 (t, *J* = 7.2 Hz, 2H) 3.14 - 3.20 (m, 2H) 7.26 - 7.32 (m, 3H) 7.33 - 7.39 (m, 2H) 7.48 (s, 1H) 7.56 - 7.59 (m, 1H) 7.59 - 7.63 (m, 1H) 7.63 - 7.70 (m, 1H) 7.87 - 7.91 (m, 1H) 7.93 (d, *J* = 9.0 Hz, 1H) 8.27 - 8.34 (m, 2H). ^{13}C NMR (150 MHz, MeCN - *d*3) ppm 20.1, 32.5, 51.3, 115.6, 116.3, 119.8, 123.8, 124.5, 124.8, 125.3, 125.7, 127.0, 127.1, 128.0, 128.2, 129.3,130.0, 130.4, 131.6, 133.2, 135.2, 151.6, 154.4, 174.3 MS (ESI), [M-H]$^-$ calcd for $C_{24}H_{20}NO_6S^-$: 450.1, found 450.1.

Preparation of dirhodium(II) trisbutyrate mono-4-(N-(1',2-dihydroxy-[1,2'-binaphthalen]-4'-yl)sulfamoyl)butanoate (7)



To a scintillation vial containing acid **5 (**21 mg, 0.047 mmol**)** and $Rh_2(O_2C^nPr)_3$(tfa), **8** (24 mg 0.041 mmol), 2,2,2 trifluoroethanol (4 mL) was added. A solution of Hünig's base (40 µl, 0.4 mmol, 1 M in hexafluoroisopropanol) was subsequently added to this vial. The reaction mixture was heated to 50 °C and stirred continuously for 14 h, after which the reaction was purified by preparative HPLC (eluent: 40→90 MeCN/H_2O) to yield (11 mg, 29%) the desired product. ^{1}H NMR (500 MHz, MeCN-*d*3) ppm 0.63 (t, *J* = 7.4 Hz, 6H) 0.69 (t, *J* = 7.4 Hz, 3H) 1.29 - 1.41 (m, 6H) 1.85 (td, *J* = 7.5, 4.49 Hz, 2H) 1.96 - 2.01 (m, 7H) 2.10 - 2.17 (m, 2H) 2.93 - 3.01 (m, 2H) 7.20 - 7.23 (m, 1H) 7.27 - 7.33 (m, 2H) 7.33 - 7.38 (m, 2H) 7.41 (s, 1H) 7.60 (ddd, *J* = 8.3, 7.0, 1.3 Hz, 1H) 7.65 - 7.70 (m, 1H) 7.88 - 7.94 (m, 2H) 8.26 - 8.31 (m, 2H). ^{13}C NMR (150 MHz, MeCN - *d*3) ppm 13.8, 13.8, 20.0, 20.8 , 35.7, 39.7, 39.7, 51.4, 115.5, 116.2, 119.6, 123.7, 124.4, 124.6, 125.2, 125.6, 126.9, 126.9, 128.0, 128.1, 129.2, 129.8, 130.3, 131.5, 133.1, 135.1, 151.4, 154.1, 192.9, 194.9 , MS (ESI), [M-H]$^-$ calcd for $C_{36}H_{40}NO_{12}Rh_2S$: 916.0, found: 916.1.

Preparation of dirhodium(II) trisbutyrate mono-trifluoroacetate (8)



Rhodium tetratrifluoroacetate (297 mg, 0.45 mmole) and potassium butyrate (297 mg, 1.18 mmole) were added to a scintillation vial. Then THF (5ml) was added to two solids. The reaction was heated to 50 ^{o}C for 14hours. The resulting solution was rotovaped onto silica. The product was purified by column chromatography to yield, **8** (70 mg, 27%).^{1}H NMR (500 MHz, MeCN -*d3*) ppm 0.63 - 0.75 (m, 3 H) 1.35 - 1.45 (m, 2 H) 2.01 - 2.11 (m, 2 H) ^{13}C NMR (150 MHz, MeCN -*d*3) ppm 13.8, 13.8, 20.0, 20.1, 39.8, 39.9, 109.3, 111.2, 113.1, 115.0, 173.9, 174.1, 174.4, 174.6, 196.1, 196.8

3. Mass Spectrometry

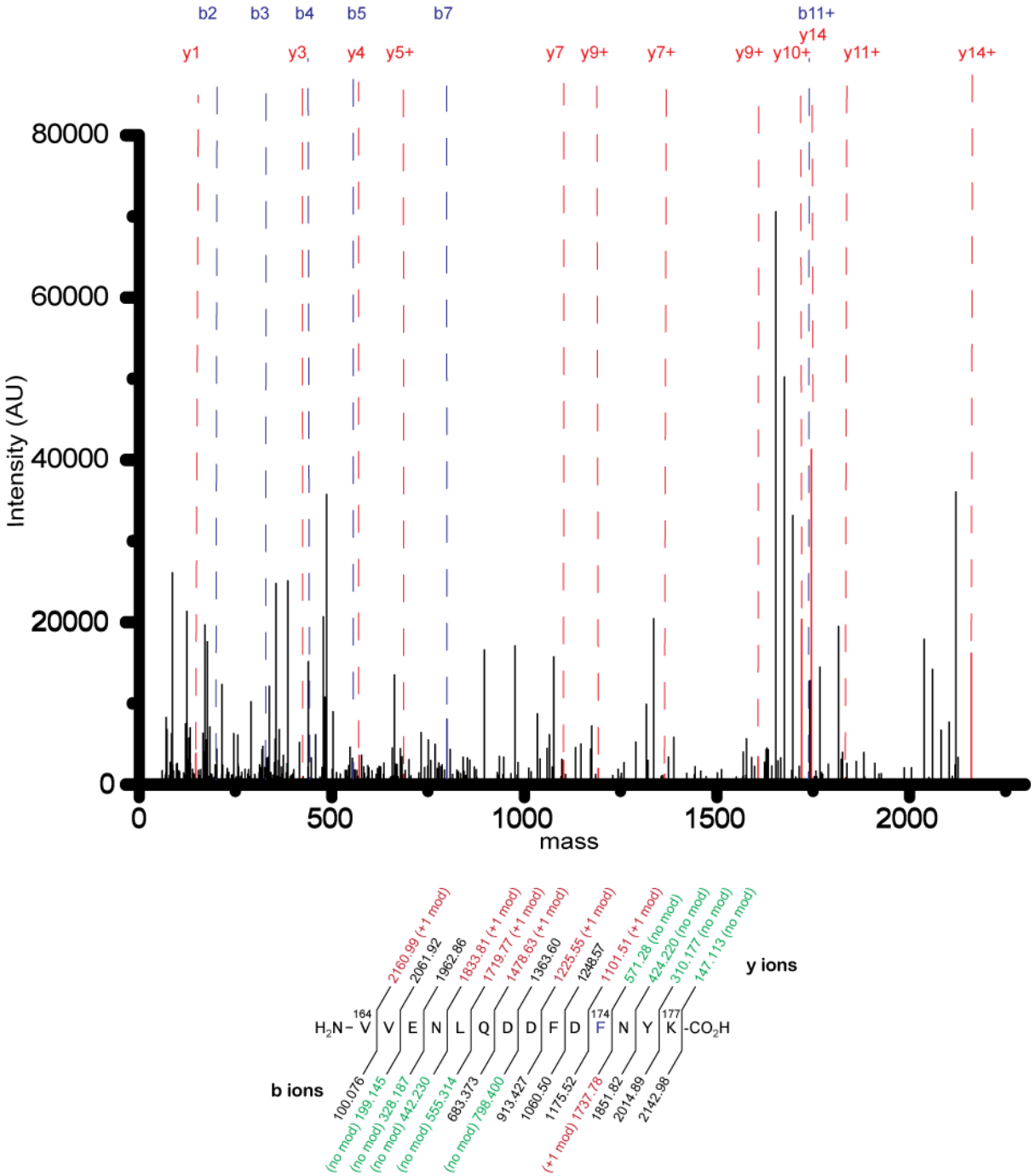


Figure S1. MS-MS spectrum of VVENLQDDFDFNYK+ 1 modification is shown below. Modification of the same peptide fragment was found at two different MS facilities.

4. Cellular assays

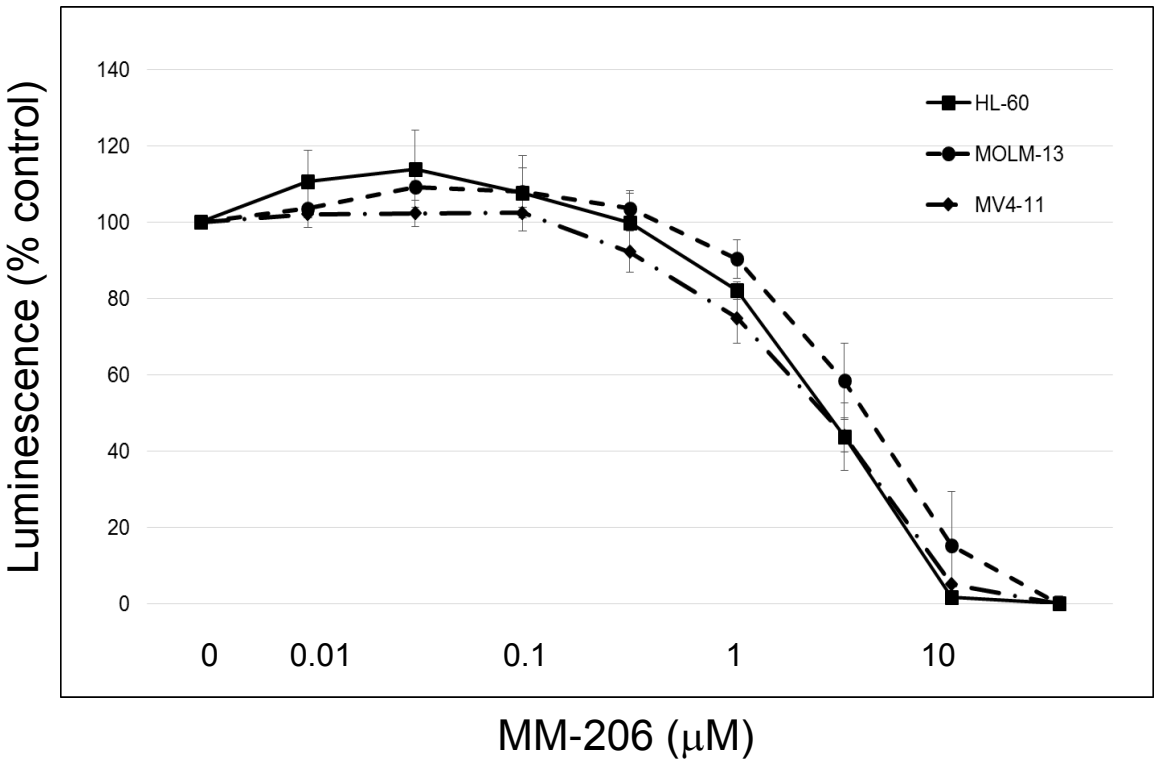
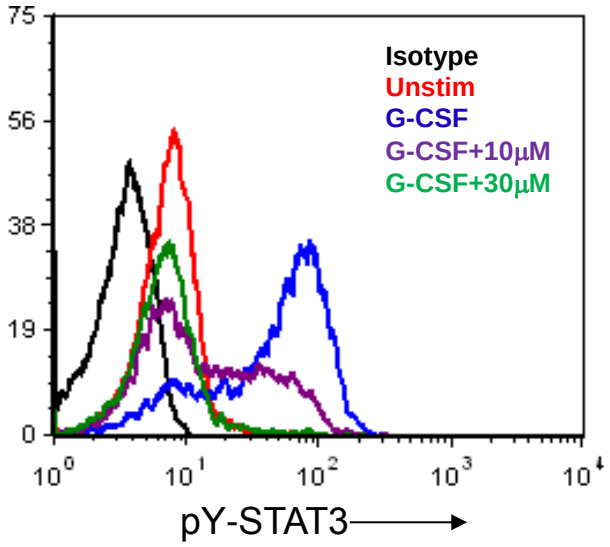


Figure S2. MM-206 reduces cell viability in a dose-dependent manner in human AML cells. Firefly luciferase-expressing AML cell lines were treated with increasing doses of MM-206 for 48 hours, then luminescence was measured. Background was subtracted and values were normalized to the untreated control. Each value was determined in triplicate. Mean ± SD for n = 3 independent assays per cell line.

a)



b)

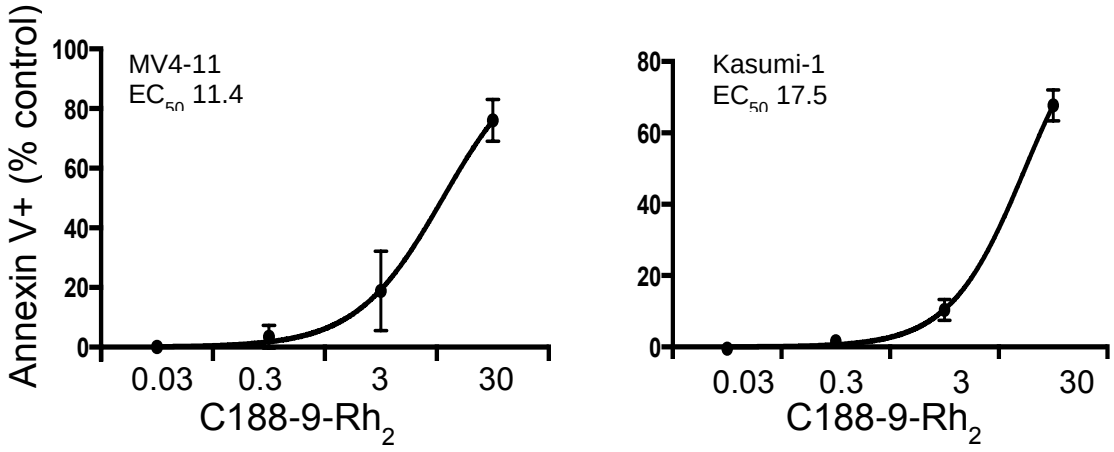


Figure S3. C188-9-Rh_2 inhibits G-CSF-induced STAT3 phosphorylation and induces apoptosis in human AML cells. (a) Representative histogram showing dose-dependent decrease in G-CSF-induced pY-STAT3 in Kasumi-1 cells. (b) AML cell lines were treated with C188-9-Rh_2 for 24 h. Cells were labeled with Annexin V-FITC for quantification of apoptosis. Mean ± SD for n = 3.

5. Fluorogenic analysis of blot membranes

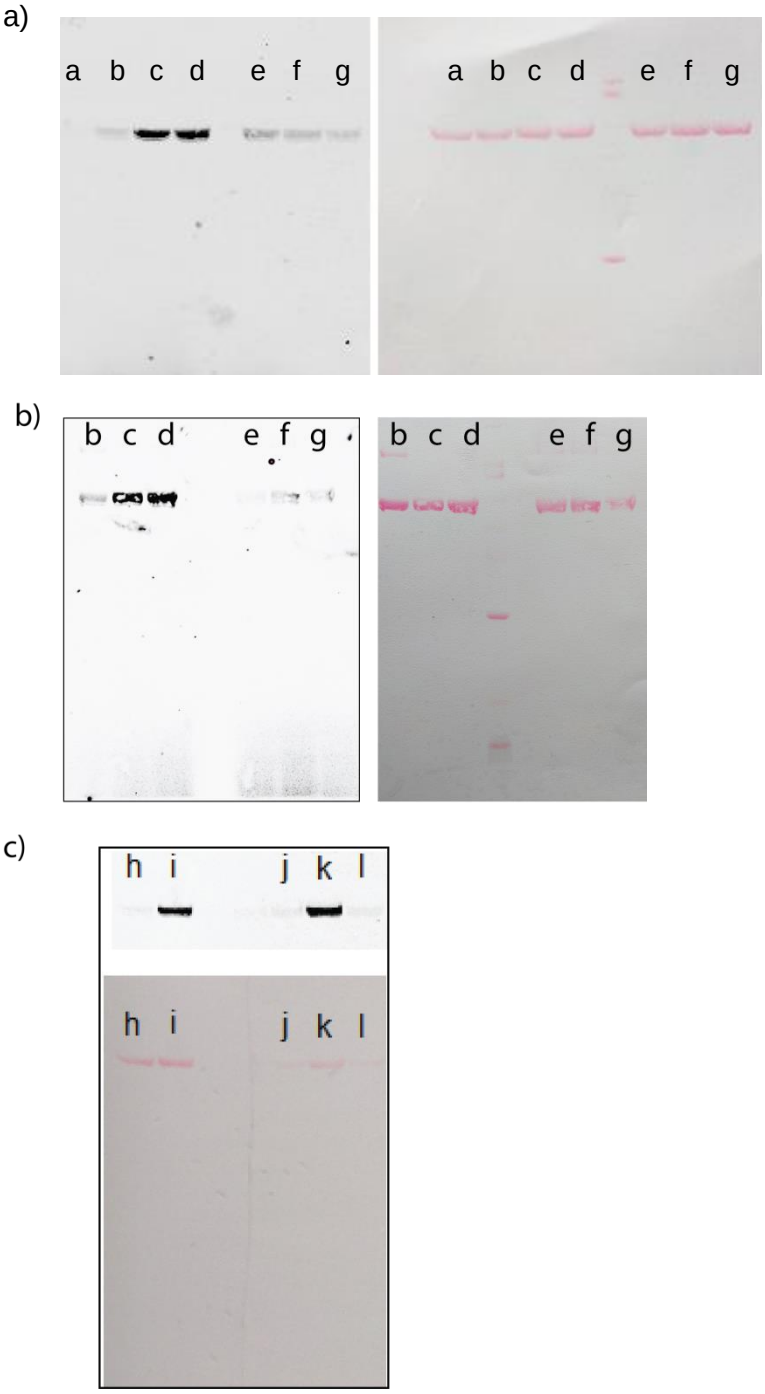
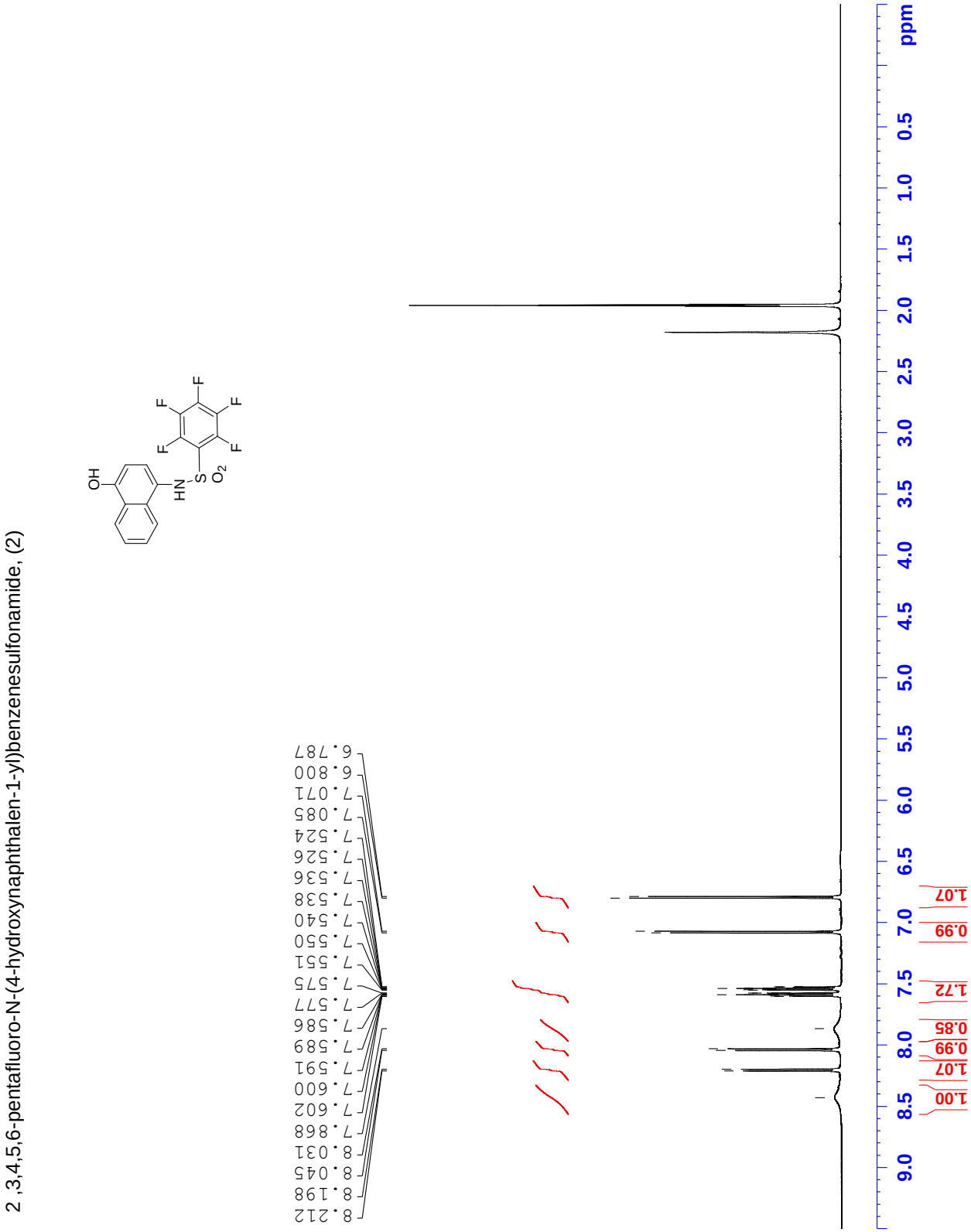
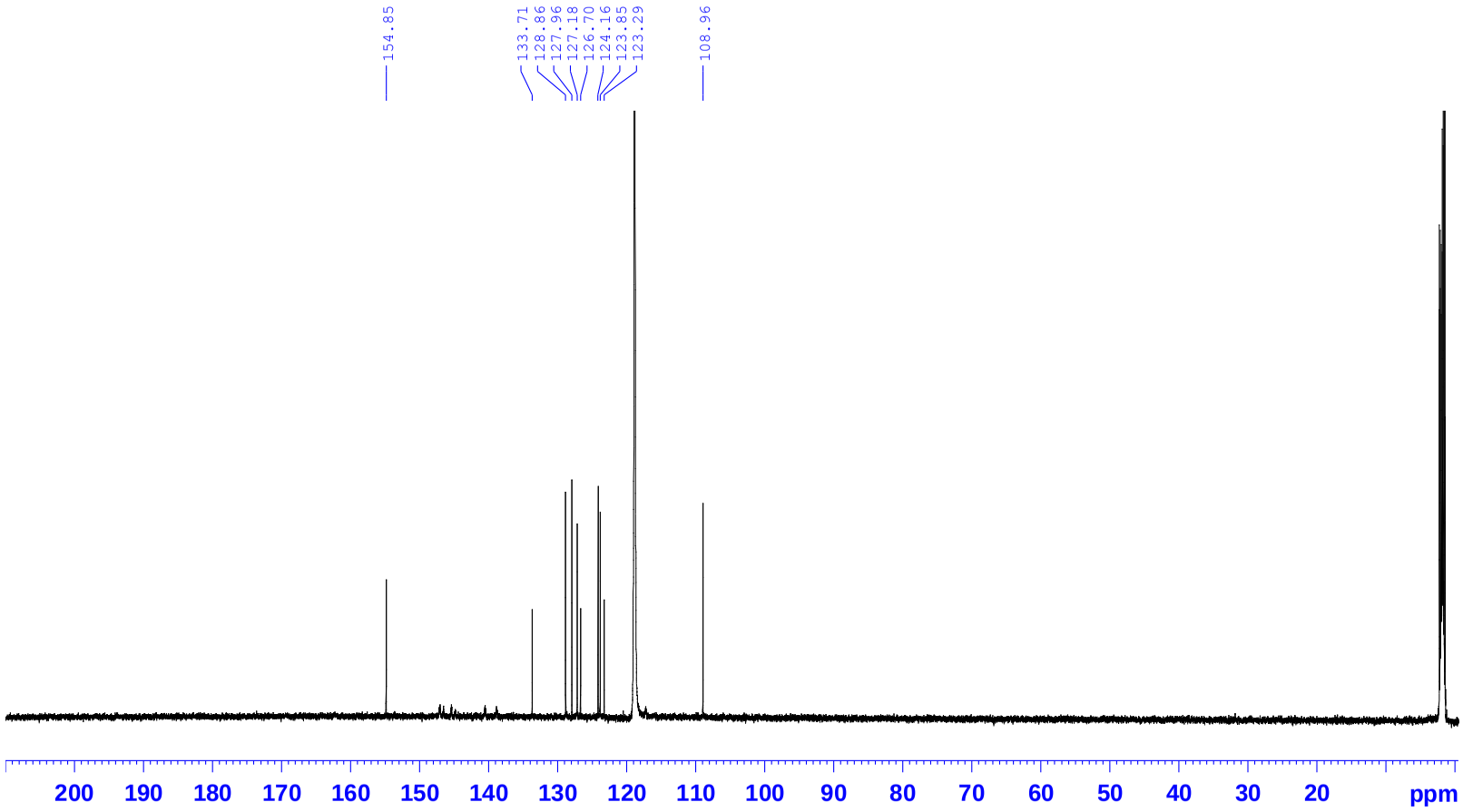


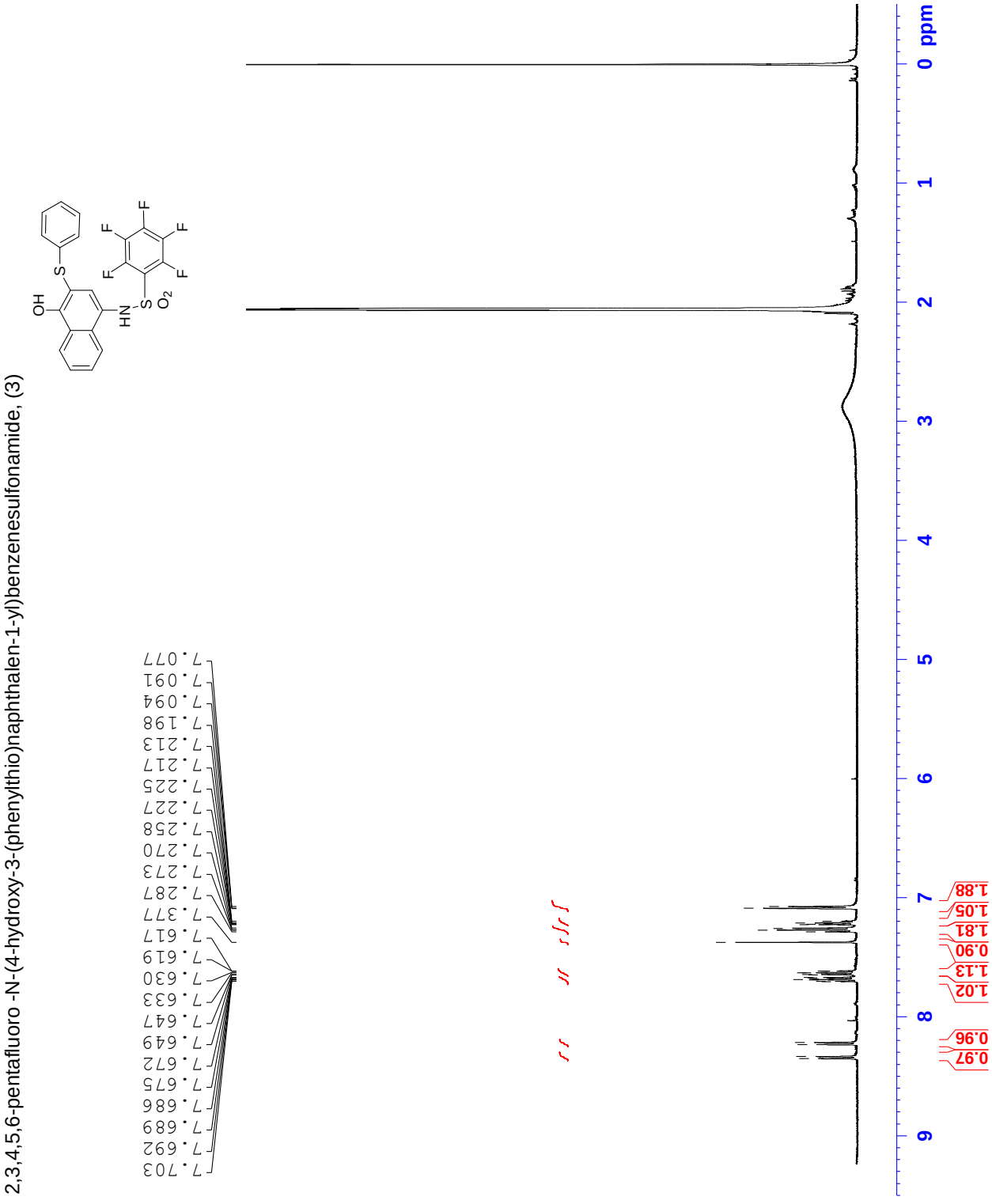
Figure S4. Gel images for protein modification, visualized by fluorescence (left) and total protein stain (Ponceau S, right). (a) Complete gels from STAT3 analysis in Fig. 3c. See main text for details. (b). Identical analysis performed with phosphorylated, dimeric protein (pSTAT3). (c) Complete gels from pSTAT3 analysis in Fig. 3c. Reaction time = 14 h.

6. NMR Spectra

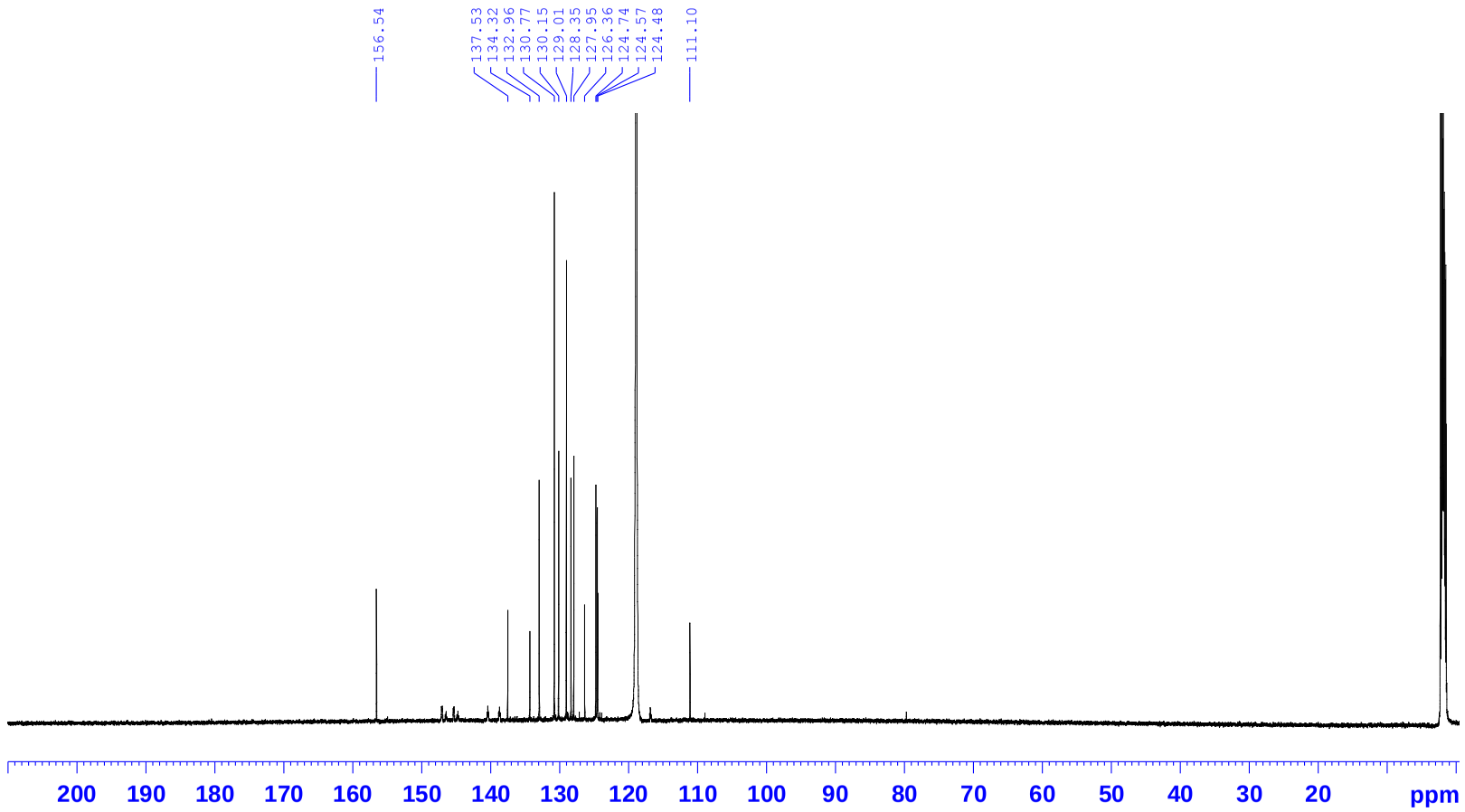


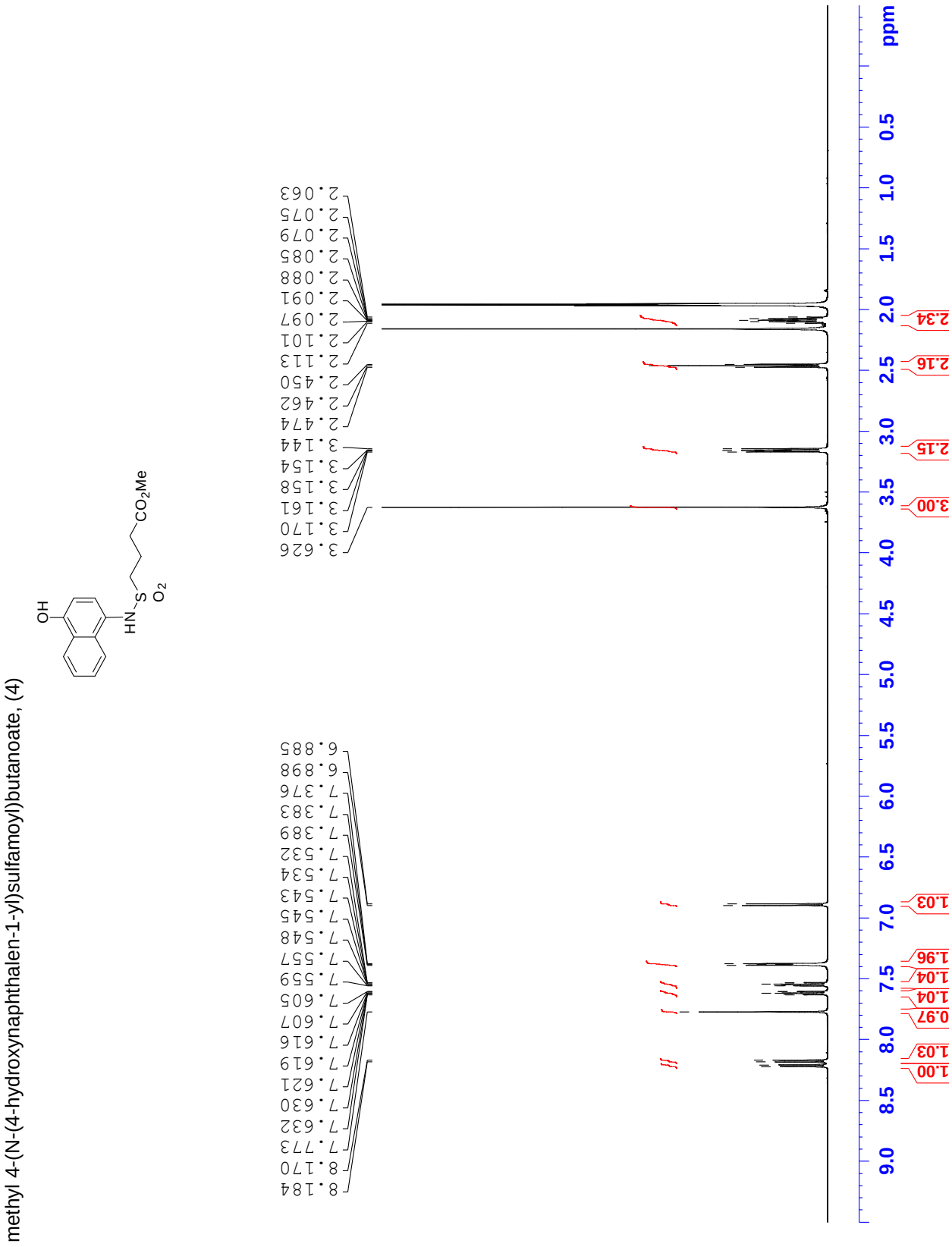
2 ,3,4,5,6-pentafluoro-N-(4-hydroxynaphthalen-1-yl)benzenesulfonamide, (2)



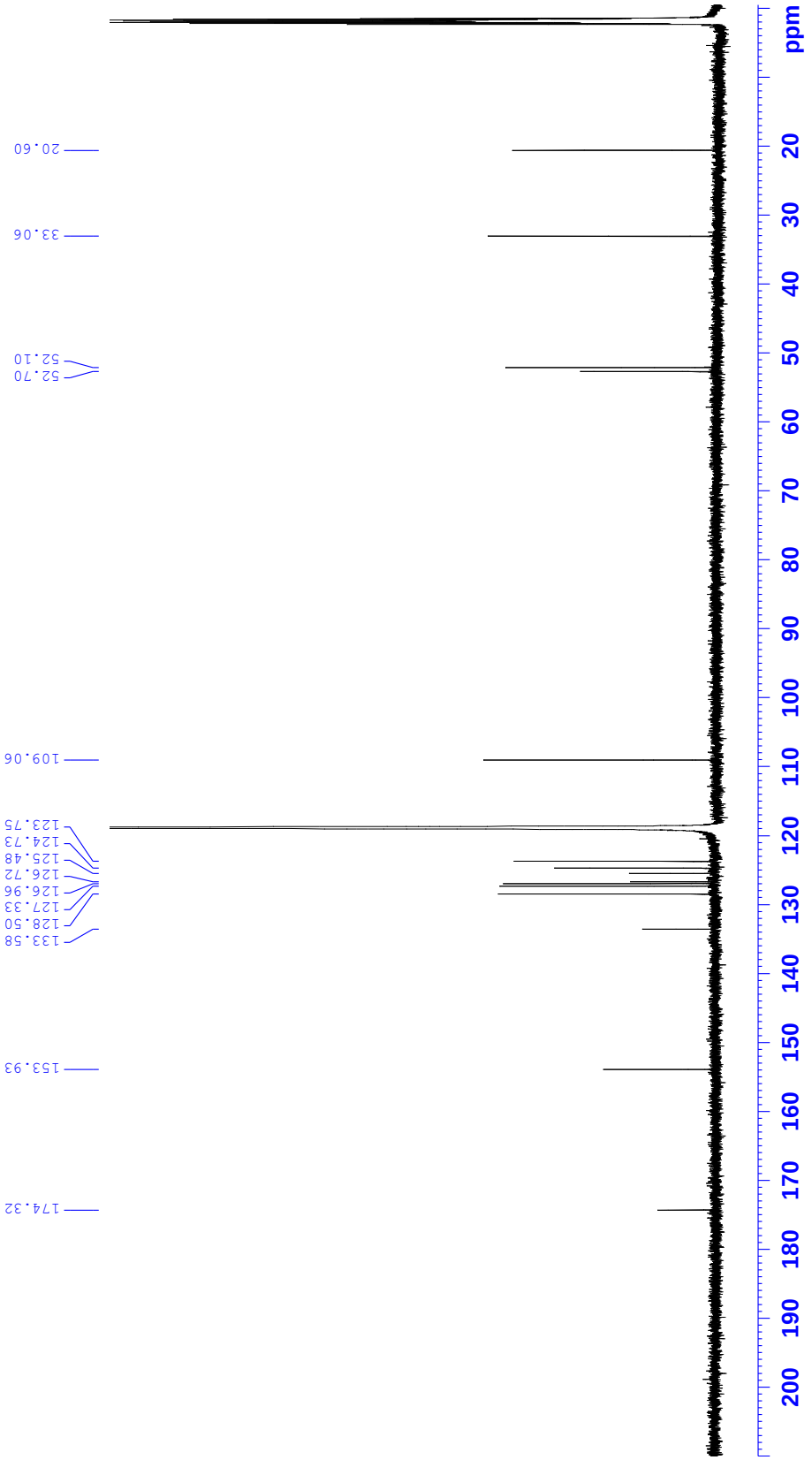

2,3,4,5,6-pentafluoro -N-(4-hydroxy-3-(phenylthio)naphthalen-1-yl)benzenesulfonamide, (3)
OH
S
HN
S
O2
F
F
F
F
F
7.703
7.692
7.689
7.686
7.675
7.672
7.649
7.647
7.633
7.630
7.619
7.617
7.377
7.287
7.273
7.270
7.258
7.227
7.225
7.217
7.213
7.198
7.094
7.091
7.077
0.97
0.96
1.02
1.13
0.90
1.81
1.05
1.88
ppm

2,3,4,5,6-pentafluoro -N-(4-hydroxy-3-(phenylthio)naphthalen-1-yl)benzenesulfonamide, (3)

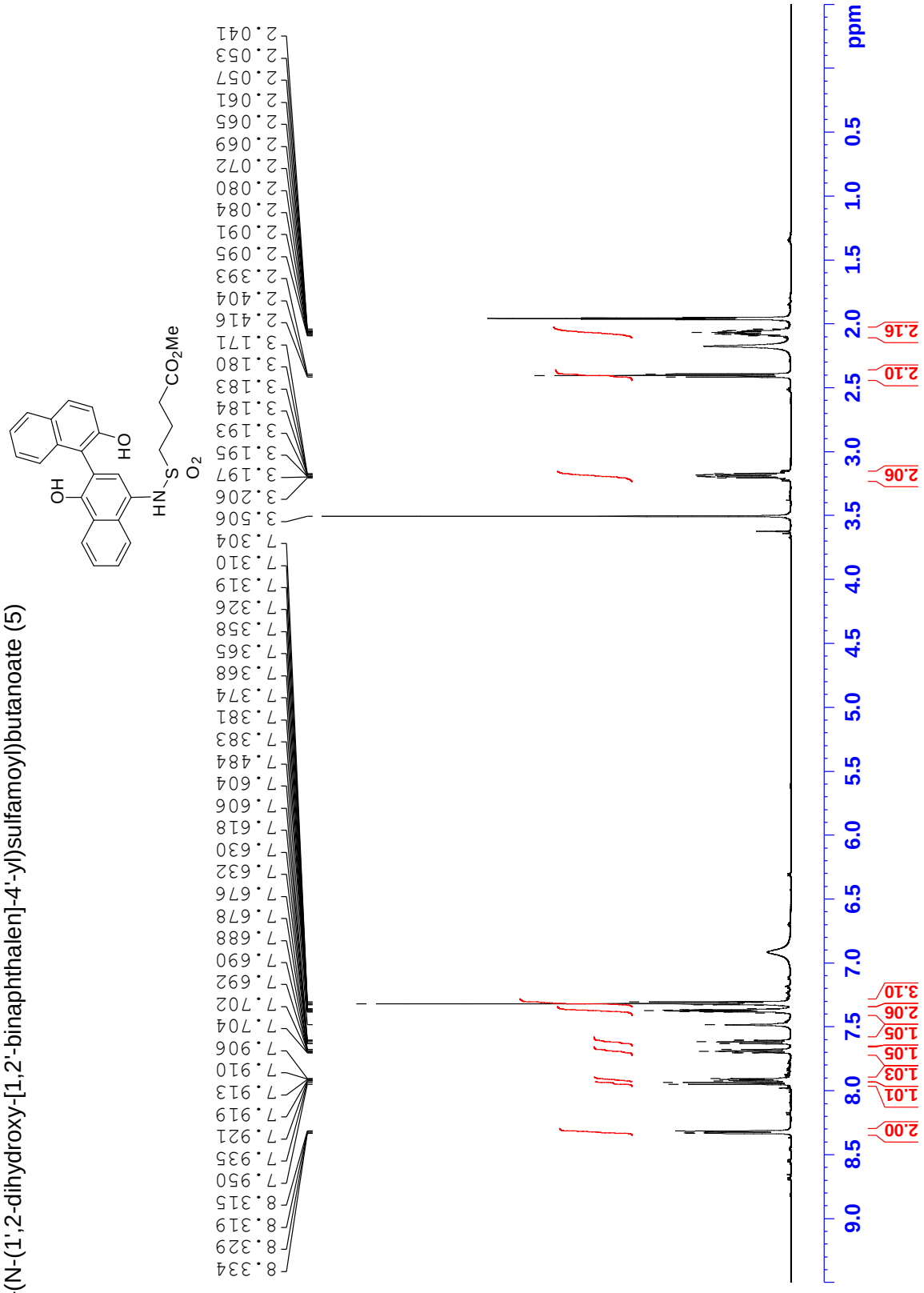



methyl 4-(N-(4-hydroxynaphthalen-1-yl)sulfamoyl)butanoate, (4)
OH
HN
S
O2
CO2Me
8.184
8.170
7.773
7.632
7.630
7.621
7.619
7.616
7.607
7.605
7.559
7.557
7.548
7.545
7.543
7.534
7.532
7.389
7.383
7.376
6.898
6.885
3.626
3.170
3.161
3.158
3.154
3.144
2.474
2.462
2.450
2.113
2.101
2.097
2.091
2.088
2.085
2.079
2.075
2.063
ppm
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
1.00
1.03
0.97
1.04
1.04
1.96
1.03
3.00
2.15
2.16
2.34

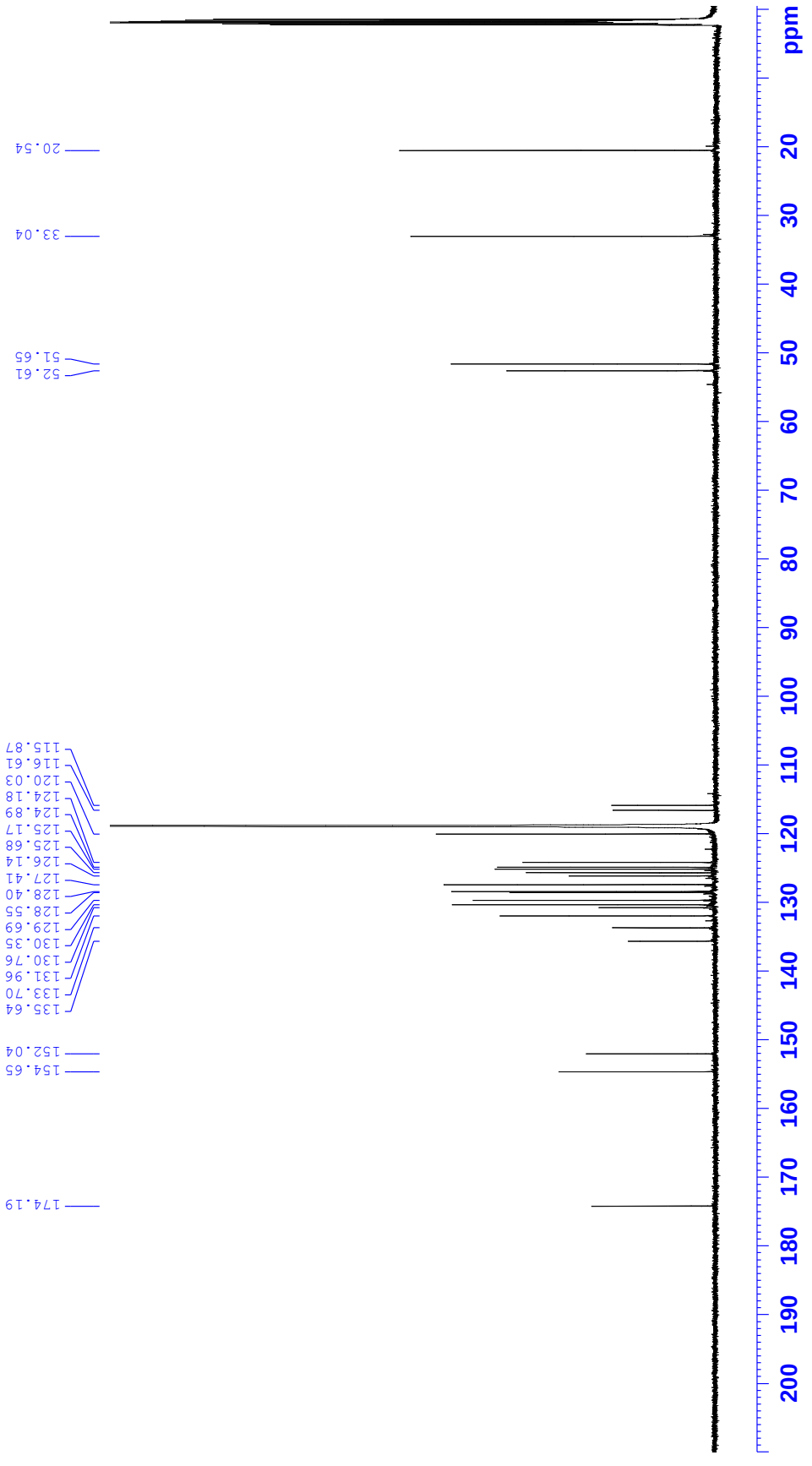
methyl 4-(N-(4-hydroxynaphthalen-1-yl)sulfamoyl)butanoate, (4)



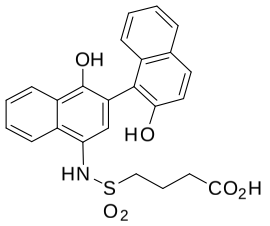
methyl 4-(N-(1',2-dihydroxy-[1,2'-binaphthalen]-4'-yl)sulfamoyl)butanoate (5)

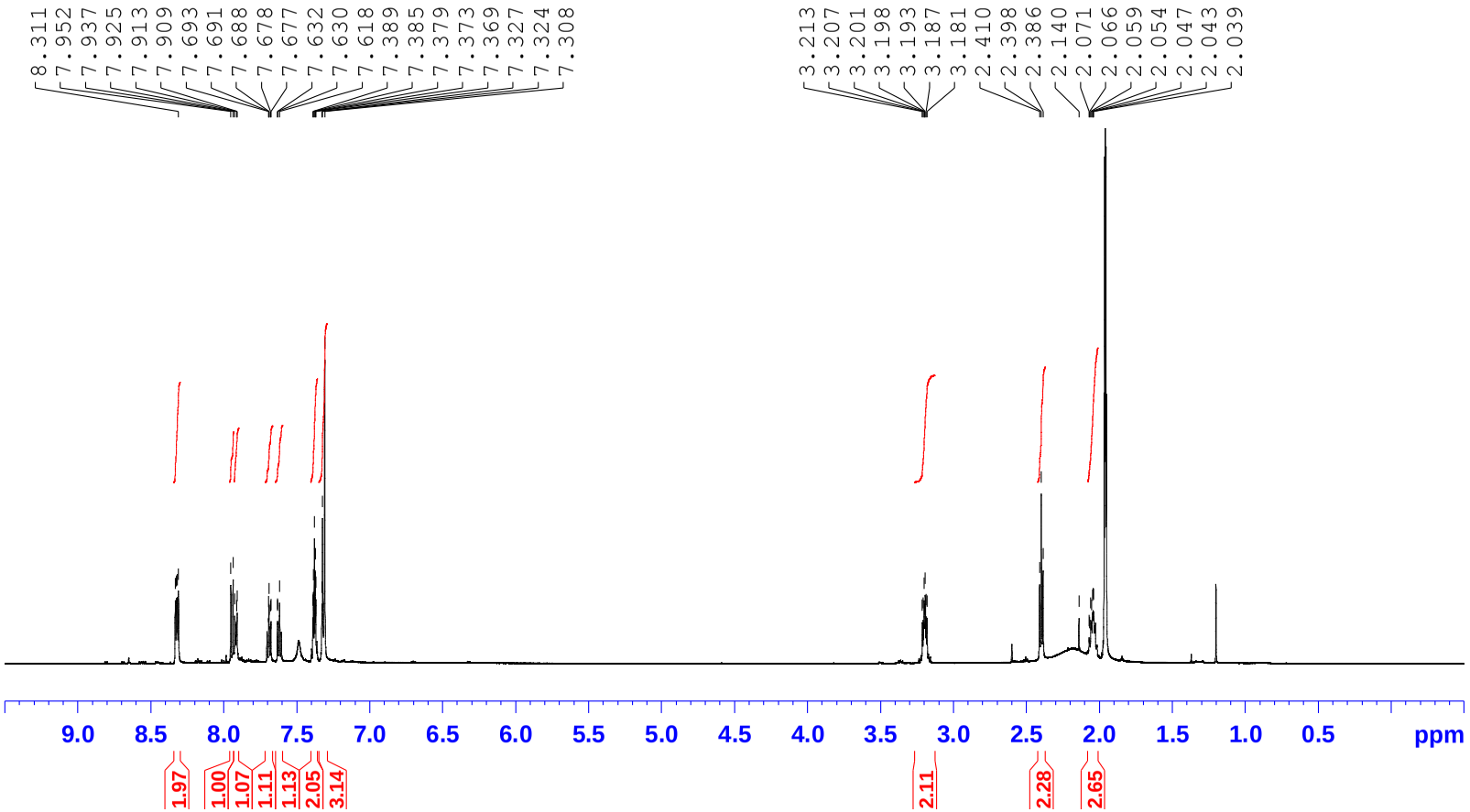


methyl 4-(N-(1',2-dihydroxy-[1,2'-binaphthalen]-4'-yl)sulfamoyl)butanoate (5)

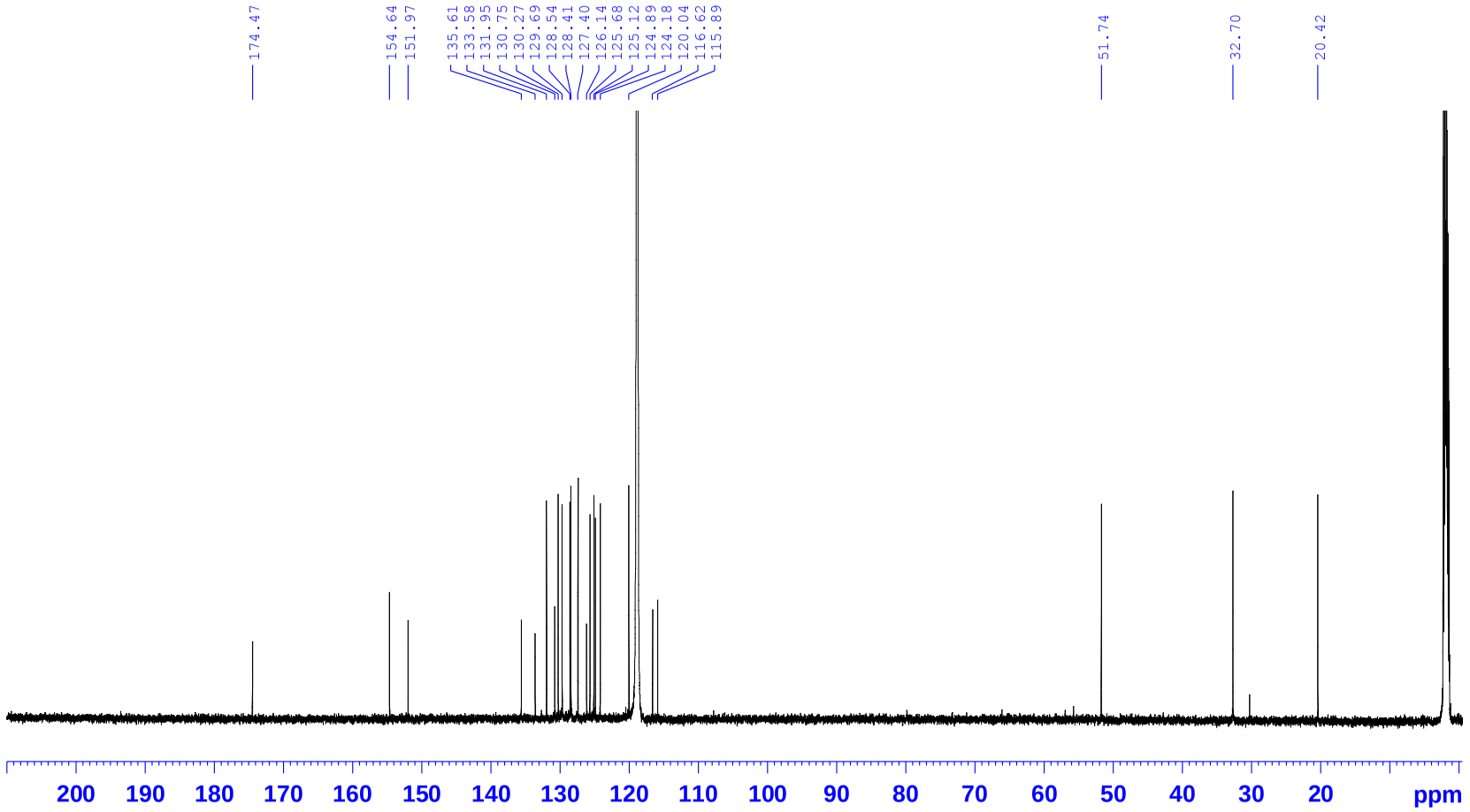


4-(N-(1',2-dihydroxy-[1,2'-binaphthalen]-4'-yl)sulfamoyl)butanoic acid, (6)

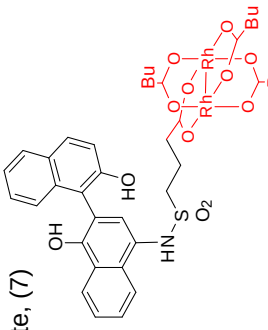




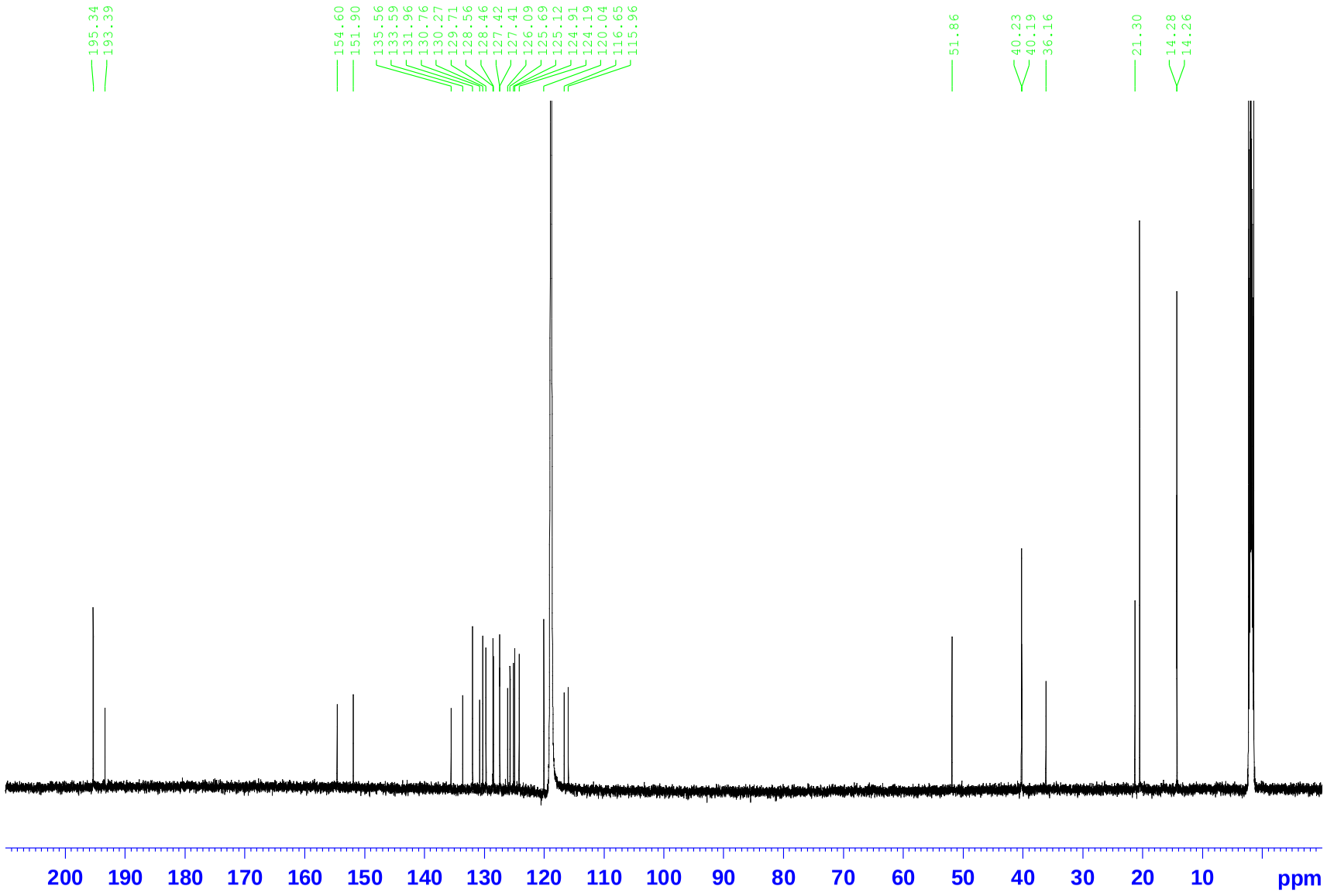
4-(N-(1',2-dihydroxy-[1,2'-binaphthalen]-4'-yl)sulfamoyl)butanoic acid, (6)



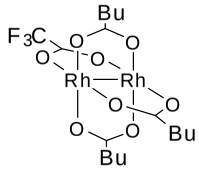
Dirhodium(II) trisbutyrate mono-4-(N-(1',2-dihydroxy-[1,2'-binaphthalen]-4'-yl)sulfamoyl)butanoate, (7)

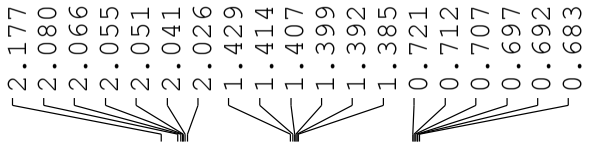


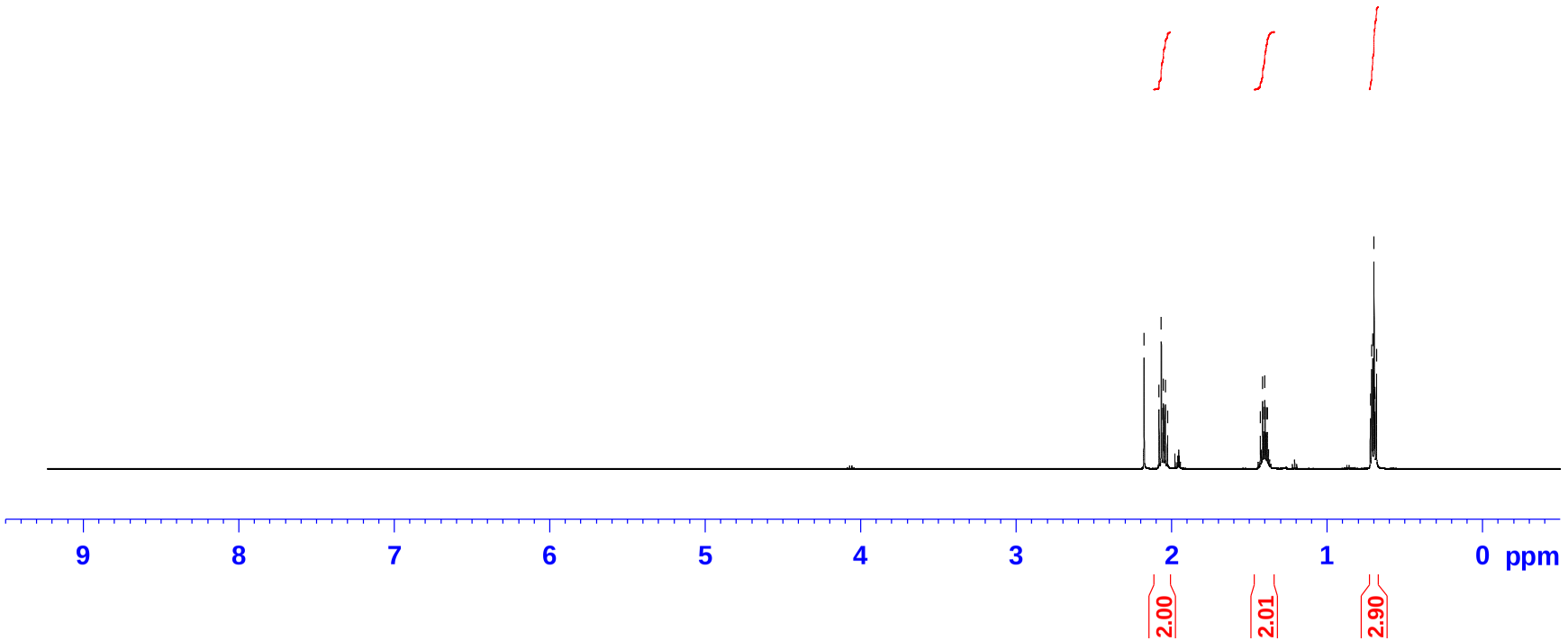
Dirhodium(II) trisbutyrate mono-4-(N-(1',2-dihydroxy-[1,2'-binaphthalen]-4'-yl)sulfamoyl)butanoate, (7)

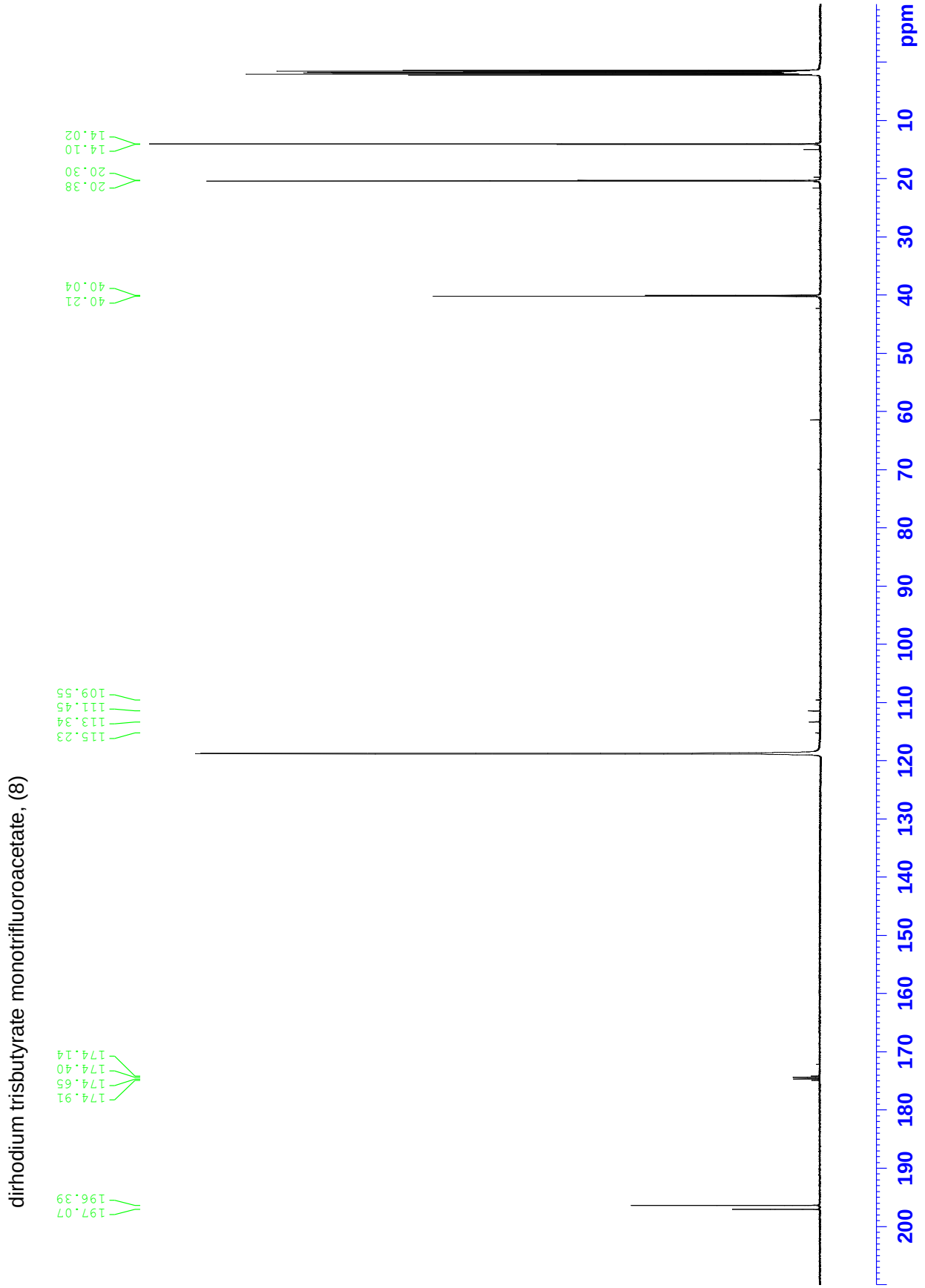


dirhodium trisbutyrate monotrifluoroacetate

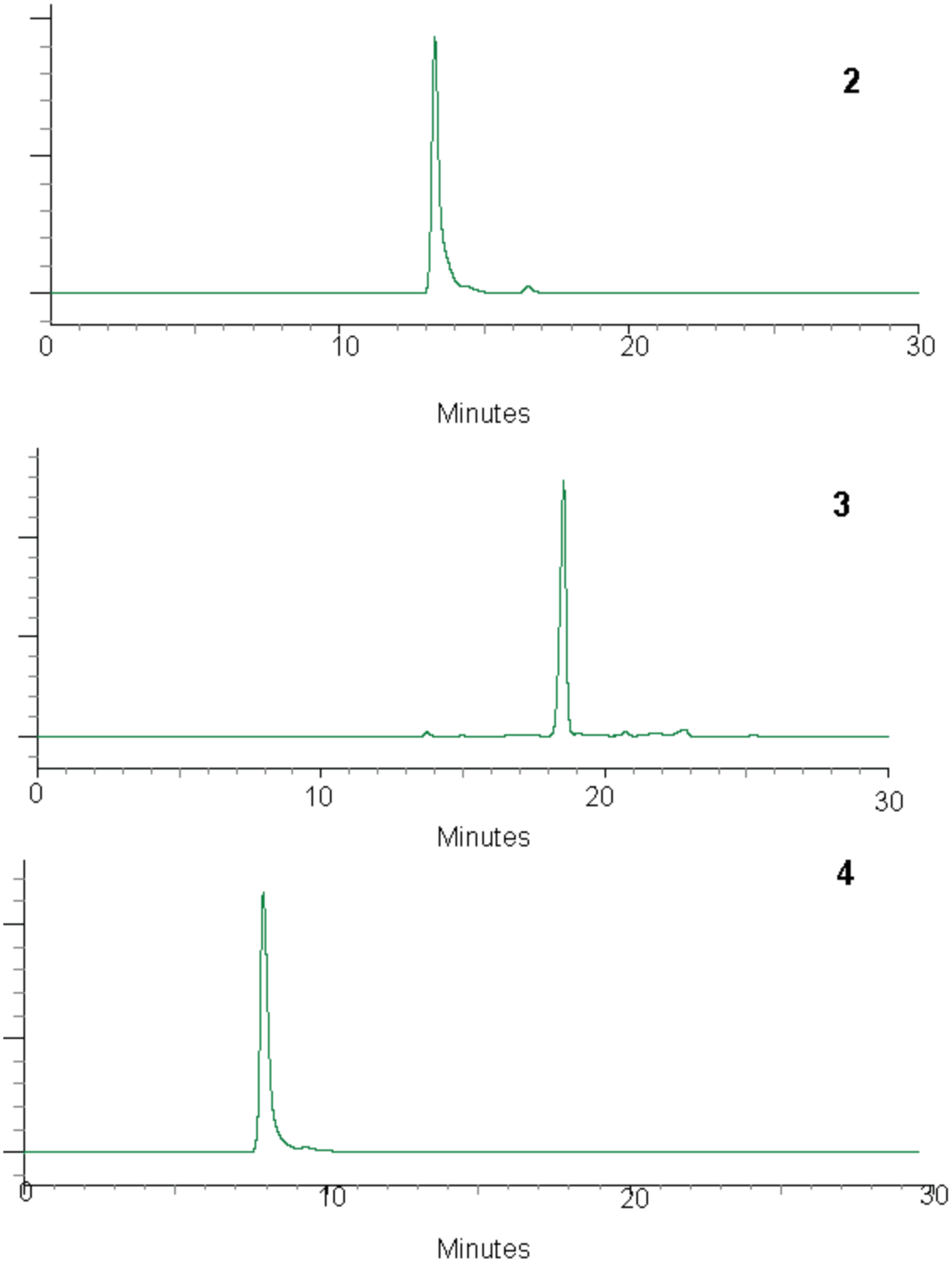


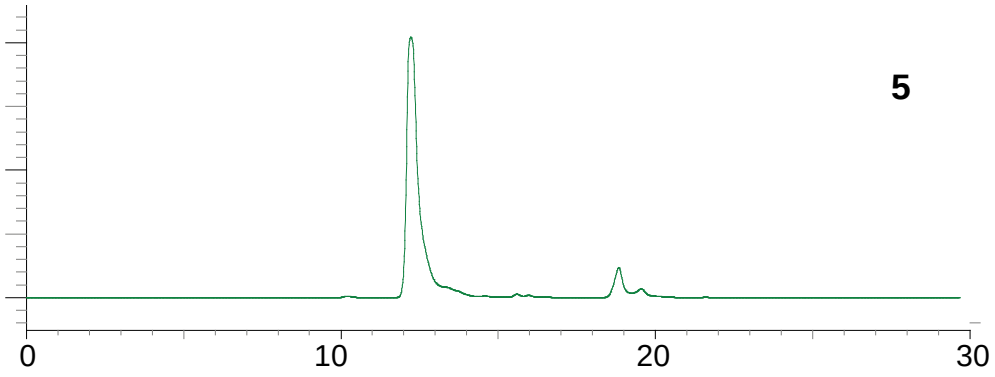


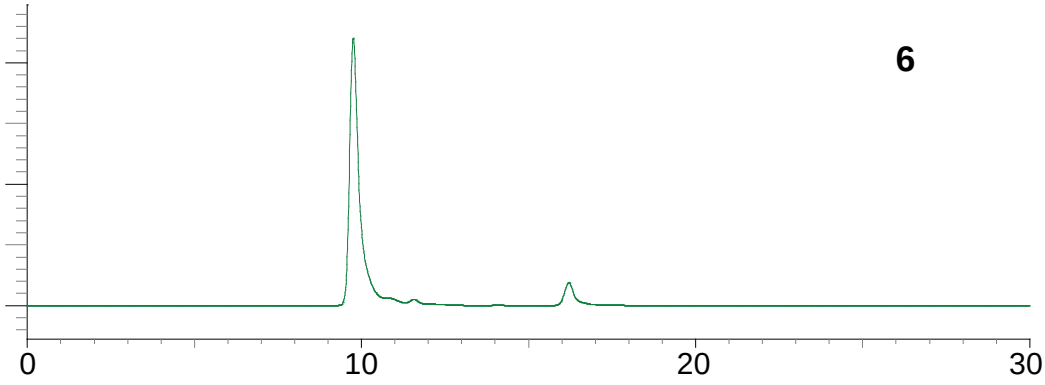


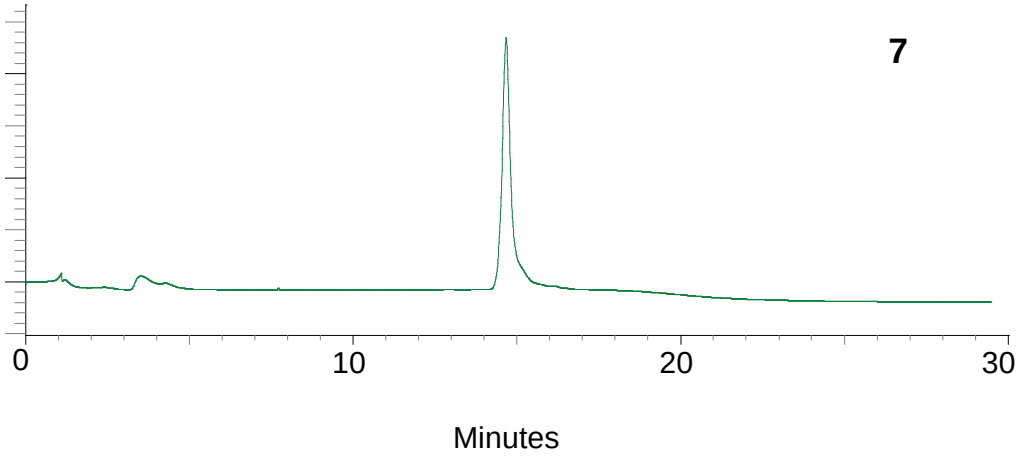

dirhodium trisbutyrate monotrifluoroacetate, (8)
14.02
14.10
20.30
20.38
40.04
40.21
115.23
113.34
111.45
109.55
174.14
174.40
174.65
174.91
196.39
197.07
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200

Analytical HPLC




5
0
10
20
30
Minutes


6
0
10
20
30
Minutes


7
0
10
20
30
Minutes

7. References

(1) Johnson, S. A.; Hunt, H. R.; Neumann, H. M. *Inorg. Chem.* **1963**, *2*, 960.

(2) Backes, B. J.; Ellman, J. A. *J. Org. Chem.* **1999**, *64*, 2322.

(3) Zhang, X.; Yue, P.; Page, B. D. G.; Li, T.; Zhao, W.; Namanja, A. T.; Paladino, D.; Zhao, J.; Chen, Y.; Gunning, P. T.; Turkson, J. *Proc. Natl. Acad. Sci. U. S. A.* **2012**, *109*, 9623.

(4) Zalatan, D. N.; Du Bois, J. *J. Am. Chem. Soc.* **2009**, *131*, 7558.

(5) Lou, Y.; Remarchuk, T. P.; Corey, E. J. *J. Am. Chem. Soc.* **2005**, *127*, 14223.

(6) Sivakumar, K.; Xie, F.; Cash, B. M.; Long, S.; Barnhill, H. N.; Wang, Q. *Org. Lett.* **2004**, *6*, 4603.

(7) Nkansah, E.; Shah, R.; Collie, G. W.; Parkinson, G. N.; Palmer, J.; Rahman, K. M.; Bui, T. T.; Drake, A. F.; Husby, J.; Neidle, S.; Zinzalla, G.; Thurston, D. E.; Wilderspin, A. F. *FEBS Lett.* **2013**, *587*, 833.

(8) Xu, X.; Kasembeli, M. M.; Jiang, X.; Tweardy, B. J.; Tweardy, D. J. *PLoS ONE* **2009**, *4*, e4783.

(9) Yu, C.; Meyer, D.; Campbell, G.; Larner, A.; Carter-Su, C.; Schwartz, J.; Jove, R. *Science* **1995**, *269*, 81.

(10) Vohidov, F.; Coughlin, J. M.; Ball, Z. T. *Angewandte Chemie International Edition* **2015**, *54*, 4587.