Supplementary Information

Wittig reagents for chemoselective sulfenic acid ligation enables global site stoichiometry analysis and redox-controlled mitochondrial targeting

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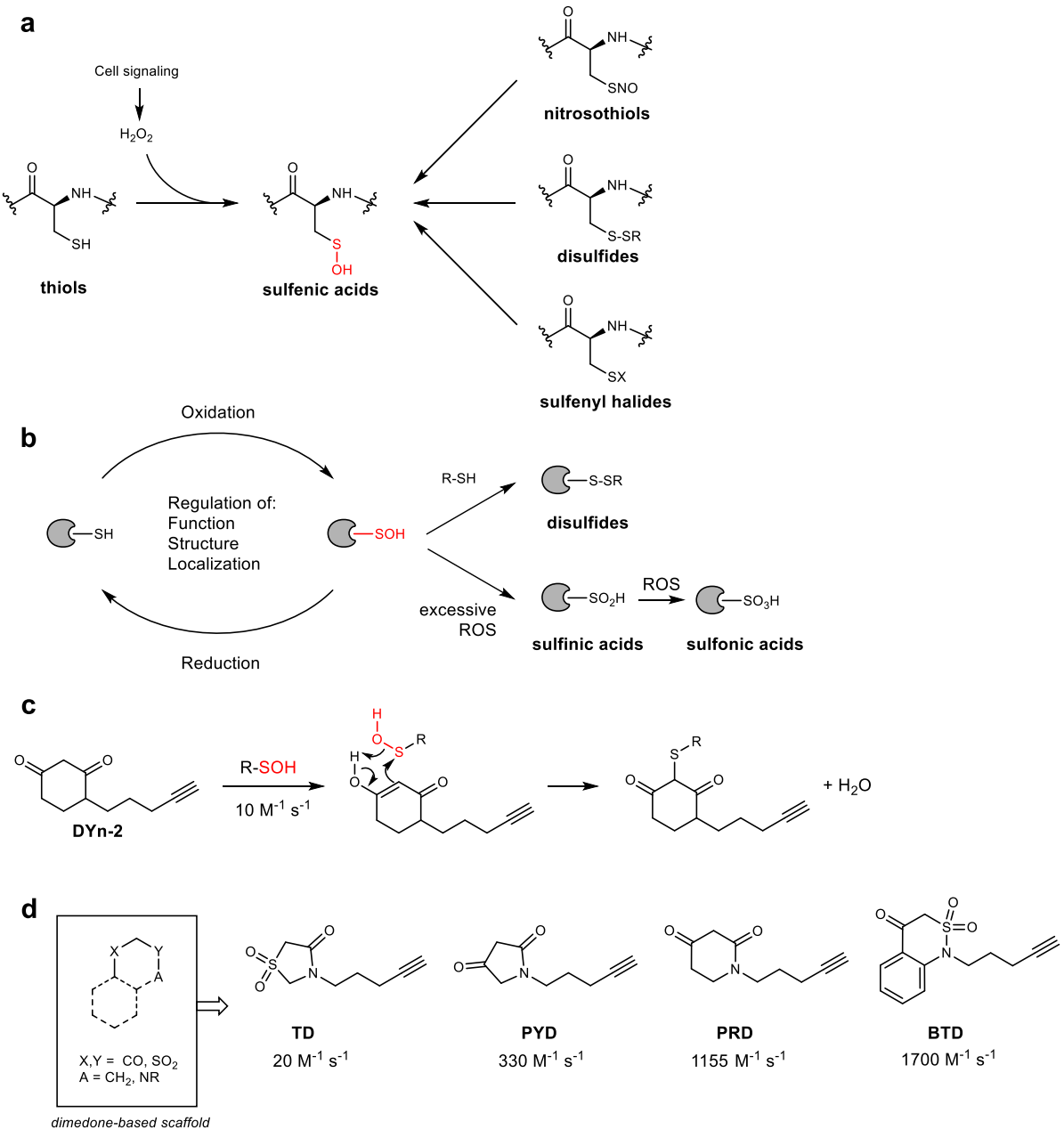
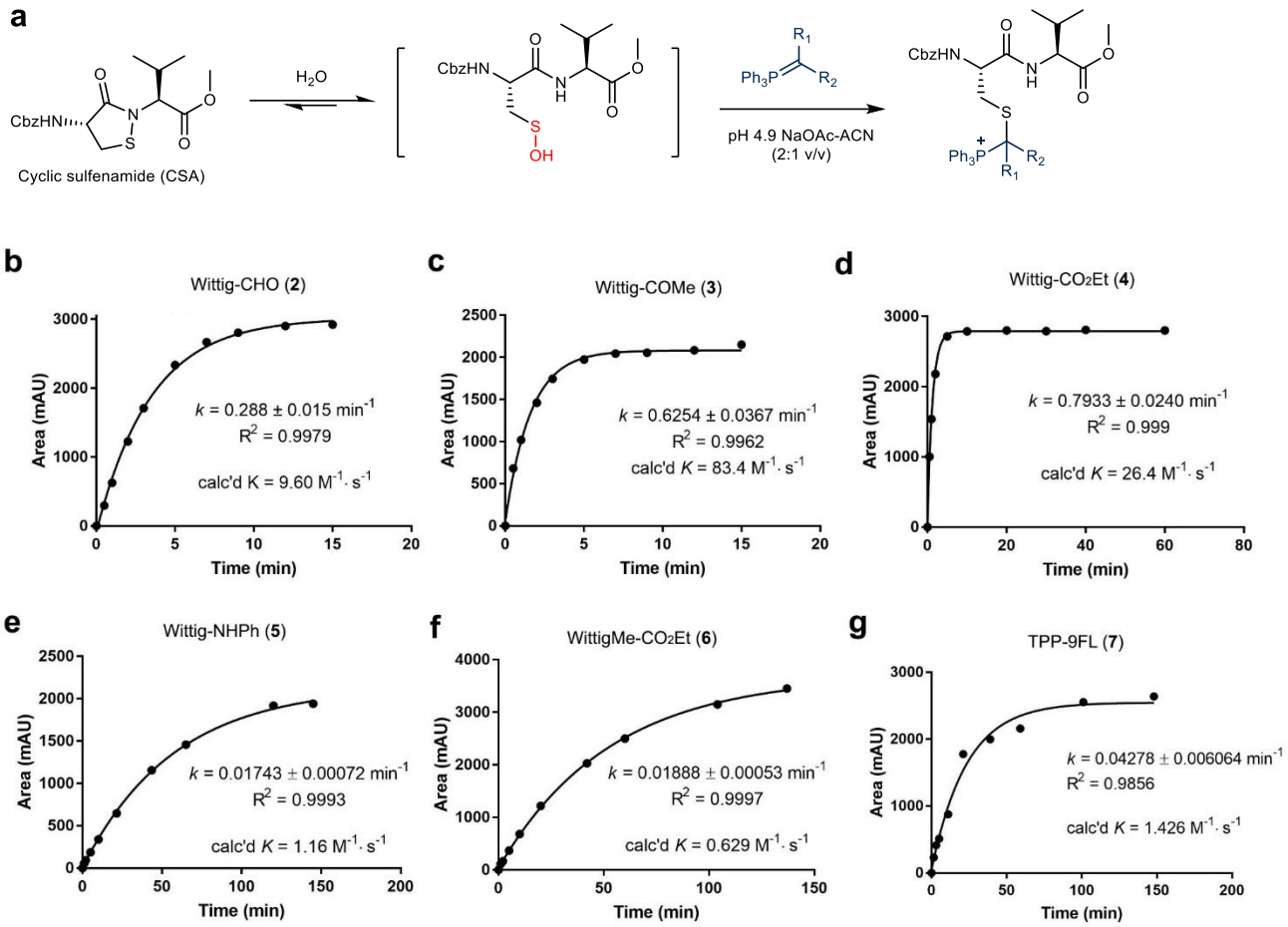
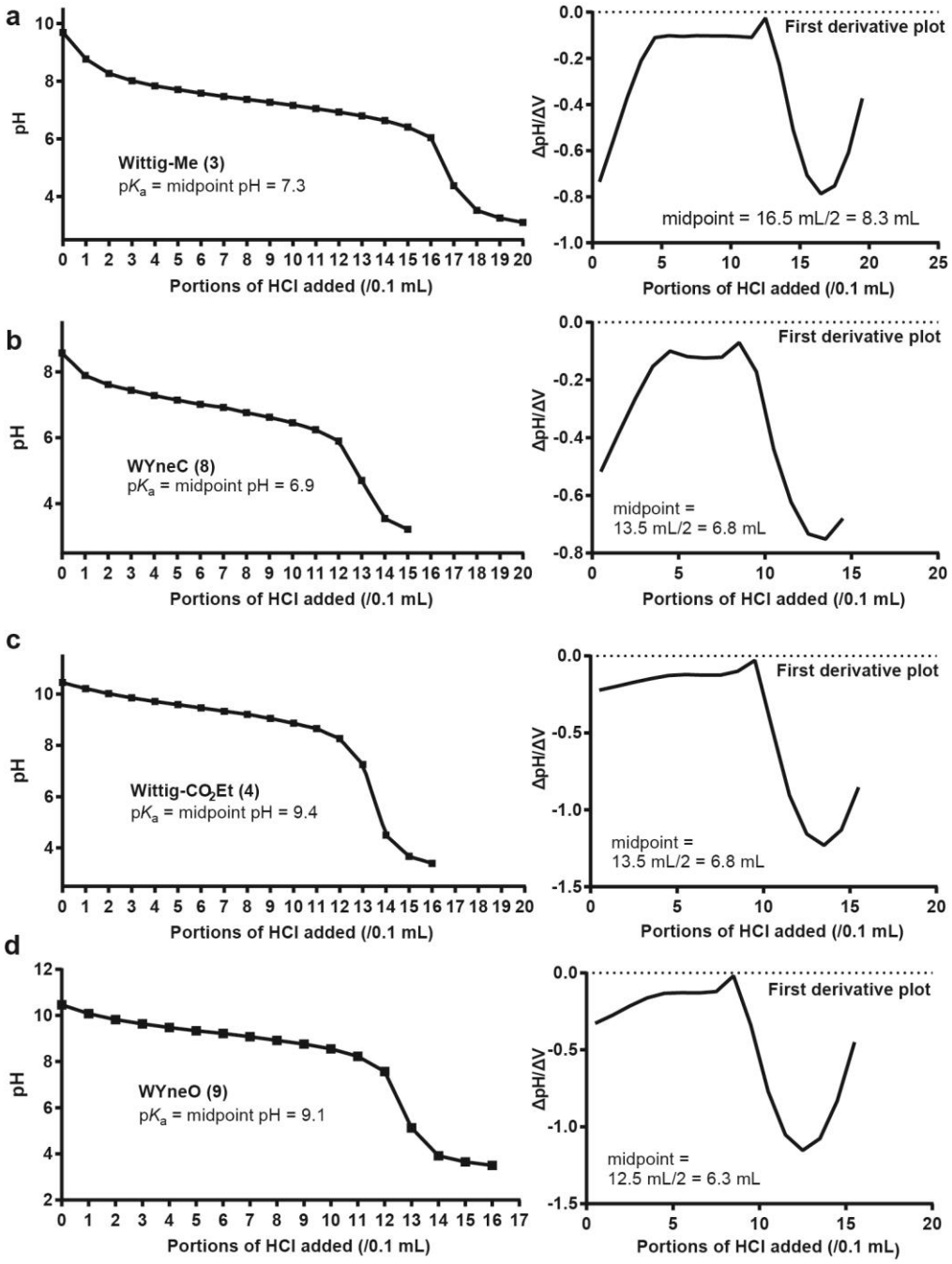


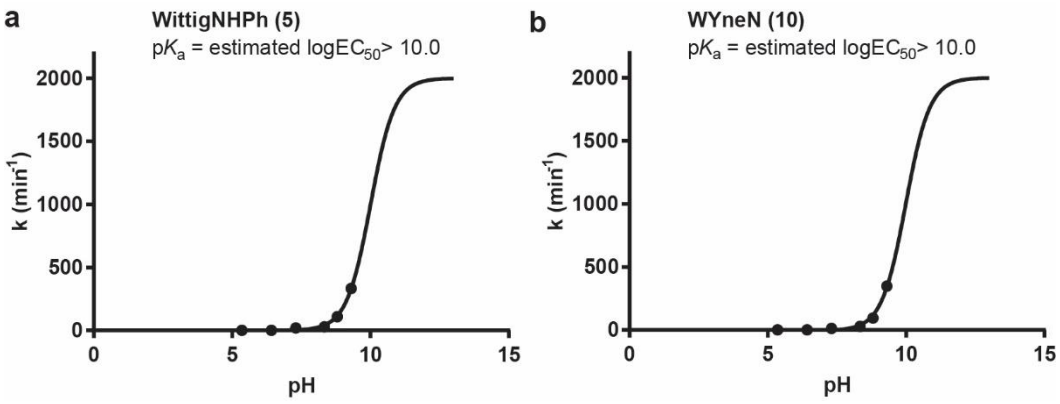
Supplementary Fig. 1 | *C*-Nucleophiles as probes for sulfenic acids. **a**, Two routes to the generation of the cysteine *S*-sulfenylation posttranslational modifications, including the oxidation of thiols and the hydrolysis of polarized sulfur species. **b**, The fates of protein sulfenic acids. They can play a role as a redox switch, forming disulfide bonds, or underwent irreversible oxidation to sulfinic and sulfonic acids under stress conditions. **c**, Mechanism of sulfenic acid labeling by DYn-2, a nucleophilic probe based on the 1,3-cyclohexadione scaffold. **d**, A functional group diversification strategy generates a library of nucleophiles with diverse reactivity.



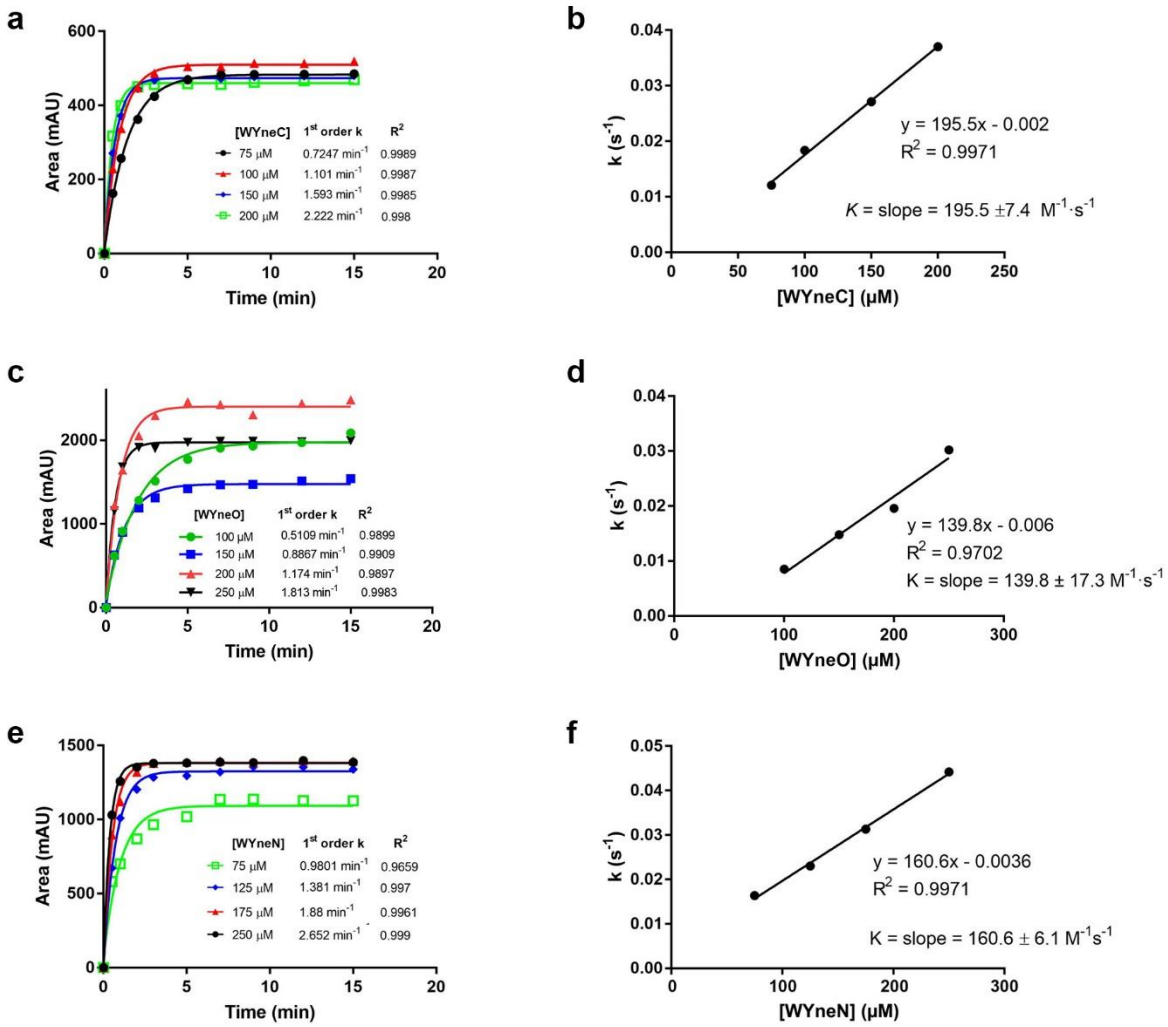
Supplementary Fig. 2 | Pseudo-first order rate plots of reactions between Wittig reagents and a cyclic sulfenamide (CSA). Detailed experimental procedure is described in supplementary methods. **a**, A small molecule dipeptide model of sulfenic acid was used to evaluate the kinetics of Wittig reagents. All reactions were carried in 25 mM NaOAc-ACN (2:1 v/v), pH 4.9 buffer. **b**, First order kinetic plot of 500 µM Wittig-CHO (**2**) and 100 µM CSA. **c**, First order kinetic plot of 125 µM Wittig-COMe (**3**) and 25 µM CSA. **d**, First order kinetic plot of 500 µM Wittig-CO_2Et (**4**) and 100 µM CSA. **e**, First order kinetic plot of 250 µM Wittig-NHPh (**5**) and 25 µM CSA. **f**, First order kinetic plot of 500 µM WittigMe-CO_2Et (**6**) and 100 µM CSA. **g**, First order kinetic plot of 500 µM TPP-9FL (**7**) and 50 µM CSA.



Supplementary Fig. 3 | Titration and pK_a determination of Wittig reagents. A solution (3 mL, ACN:H_2O = 1:2) of Wittig reagent (5 mM) was prepared in a glass reaction vial. HCl solution (ACN:H_2O = 1:2, approx. 10 mM) was added with 0.1 mL interval with stirring while the pH of the solution was recorded. pK_a was determined to be the pH at midpoint (halfway of the equivalence point where pH drastically decreases). **a**, Titration of Wittig-Me (**3**). **b**, Titration of WYneC (**8**). **c,** Titration of Wittig-CO_2Et (**4**). **d,** Titration of WYneO (**9**).

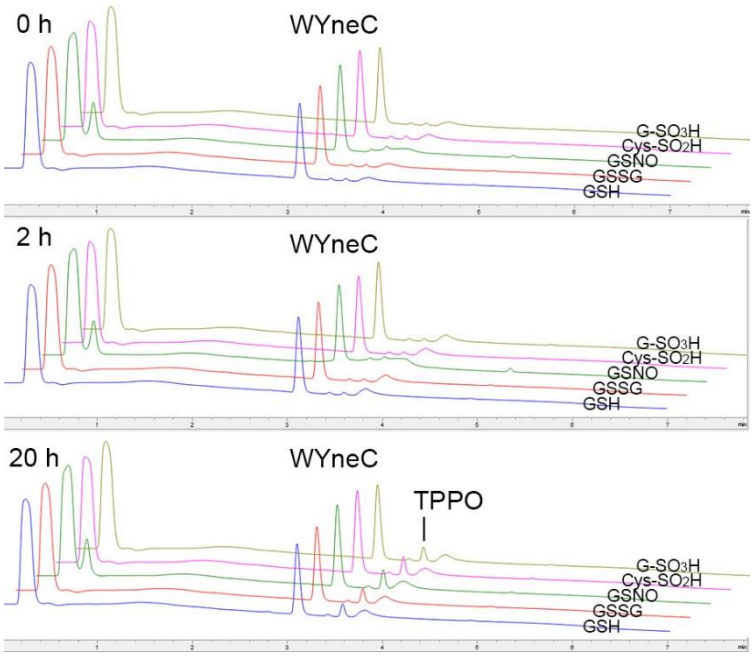


Supplementary Fig. 4 pK_a determination of amide derivatives of Wittig reagents. Due to instability in basic solutions, pK_a cannot be determined by titration. Instead, their reaction rates with CSA at various pH were fitted as sigmoid functions (upper limit set at 2,000 min^{-1}) and pK_a was derived from the $logEC_{50}$ of the curve. **a**, Estimated pK_a of WittigNHPh (**5**). **b**, Estimated pK_a of WYneN (**10**).



Supplementary Fig. 5 | Second order rate plots of reactions of WYne probes. Calculation is described in supplementary methods. **a**, First order rate constants of WYneC (**8**) at pH 4.9. **b**, Second order rate of WYneC (**8**) was obtained from linear regression of first order reaction rates vs. concentrations of the probe. **c**, First order rate constants of WYneO (**9**) at pH 4.9. **d**, Second order rate of WYneO (**9**) was obtained from linear regression of first order reaction rates vs. concentrations of the probe. **e**, First order rate constants of WYneN (**10**) at pH 7.4. **f**, Second order rate of WYneN (**10**) was obtained from linear regression of first order reaction rates vs. concentrations of the probe.

a



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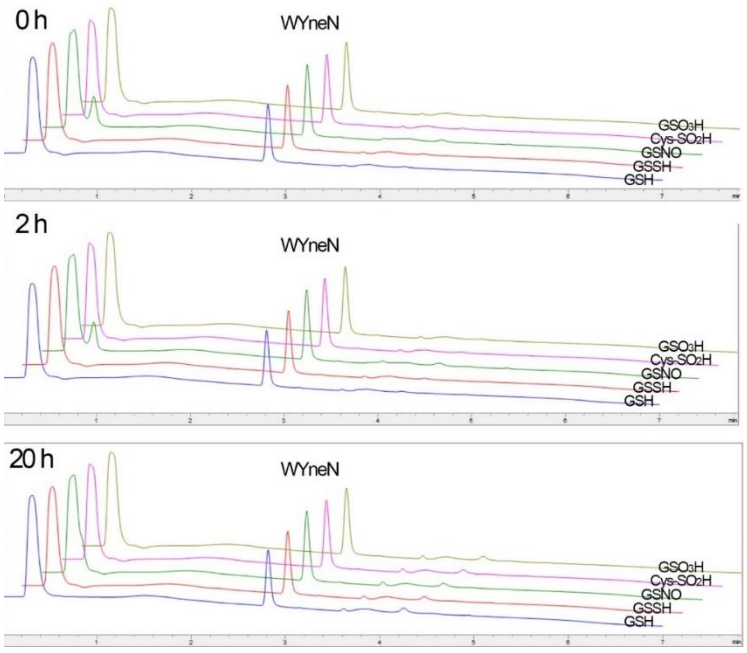
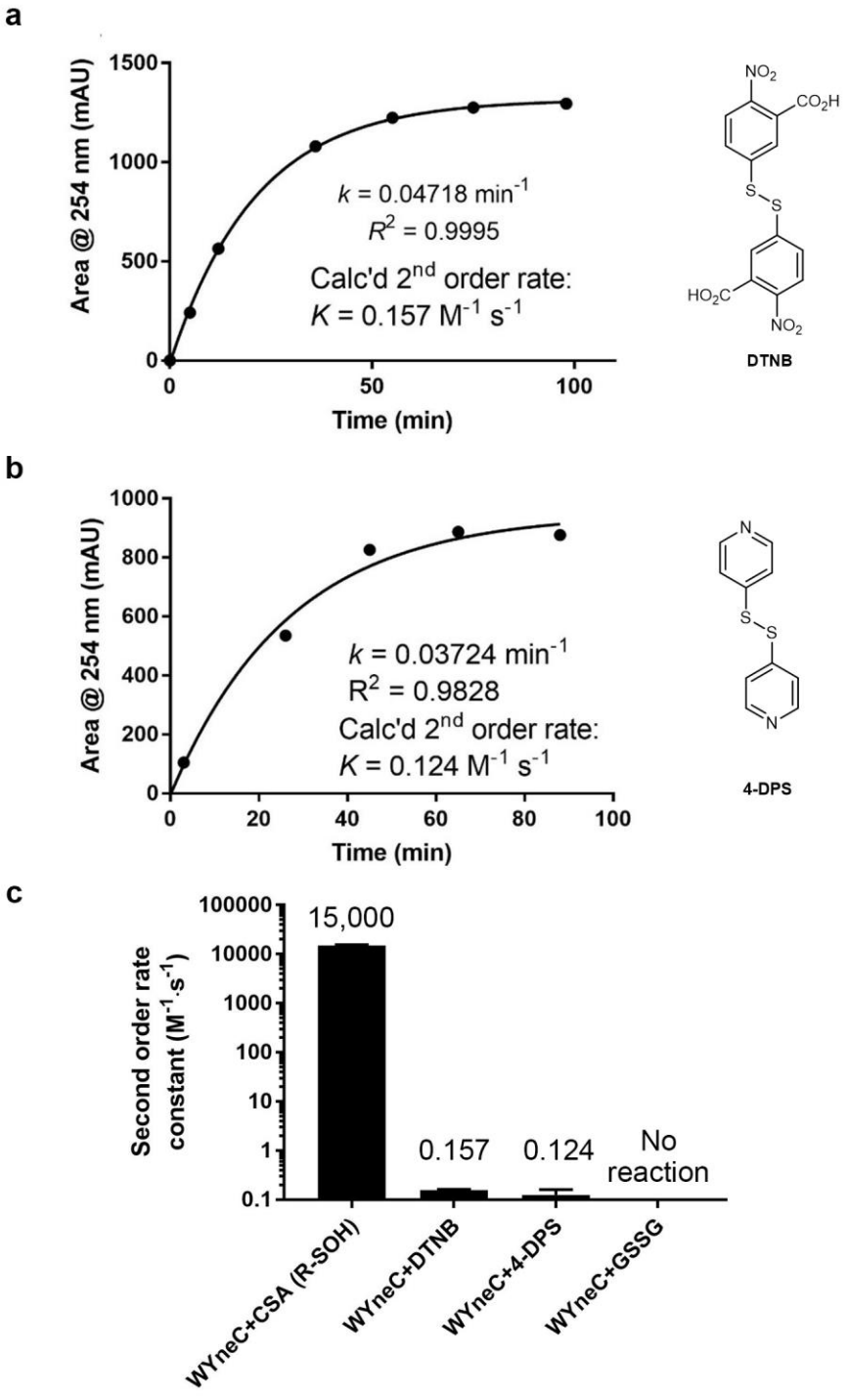
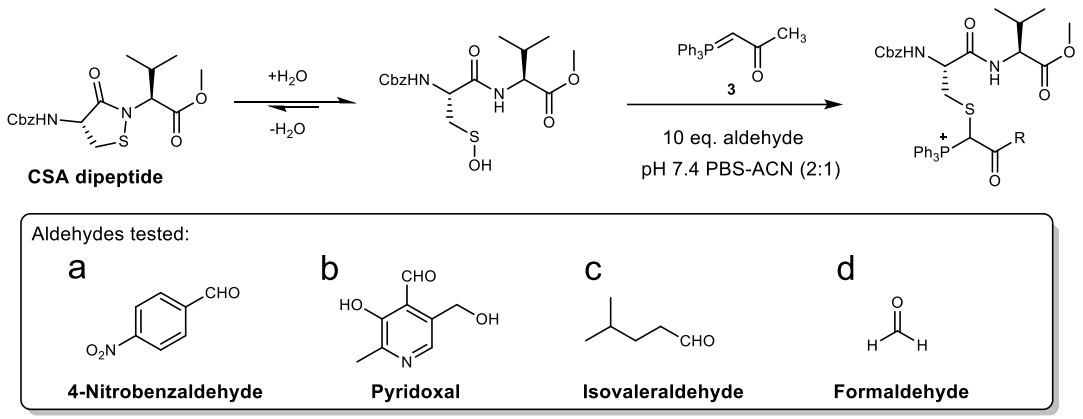


Supplementary Fig. 6 | Cross-reactivity study of WYne probes with cysteine oxoforms. Except that a small amount of WYneC was decomposed to triphenylphosphine oxide (TPPO) due to hydrolysis, the peak sizes of WYneC/N did not change over time, indicating no reactivity with these sulfur compounds. Studies were performed with 0.1 mM solutions of WYneC/N in 1 mL HEPES buffer (degas by N_2, 2:1 HEPES:ACN (v/v), 50 mM HEPES, 100 mM NaCl, pH 7.4) with one of the sulfur-containing compounds (1 mM, GSH: glutathione reduced; GSSG: glutathione disulfide; GSNO: *S*-nitrosoglutathione; Cys-SO_2H: cysteine sulfinic acid; G-SO_3H: glutathionesulfonic acid). The resulting solutions were kept at room temperature and analyzed on LC-MS after 0, 2 and 20 h. **a**, LC traces (190 nm) of WYneC (**8**) and cysteine oxoforms. **b**, LC traces (190 nm) of WYneN (**10**) and cysteine oxoforms.



Supplementary Fig. 7 | Reaction kinetics between WYneC and disulfides. **a**, Reaction between 0.25 mM of WYneC (**3**) and 5 mM of DTNB in 50 mM HEPES buffer, pH 7.4. **b**, Reaction between 0.25 mM of WYneC (**3**) and 5 mM of 4-DPS in 50 mM HEPES buffer, pH 7.4. **c**, Reaction rate of WYneC (**3**) with CSA (R-SOH) is much higher than "activated" disulfides DTNB (95,500-fold) and 4-DPS (120,000-fold), while an "inert" disulfide (GSSG) did not react with WYneC.



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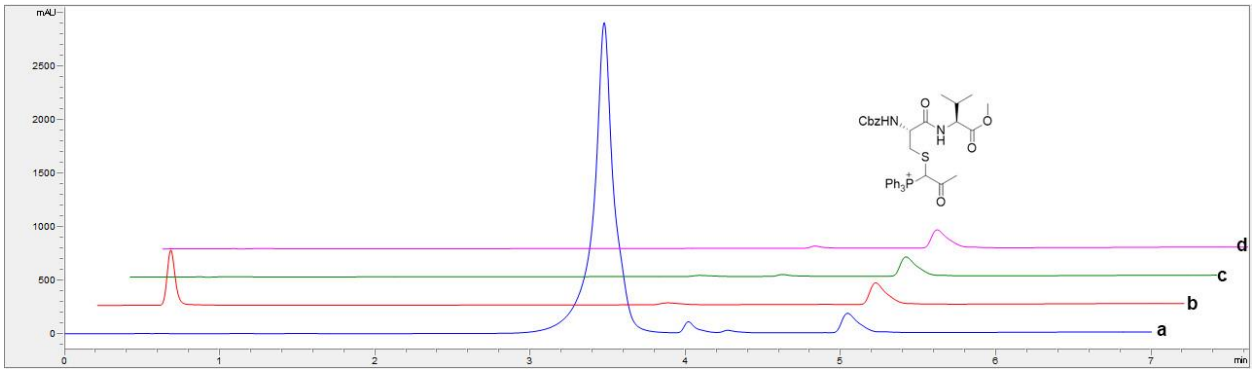

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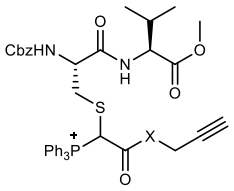
99 **Supplementary Fig. 8 | Reaction of Wittig-Me (3) in presence of aldehydes.** Wittig-Me (1 mM)
100 reacted with CSA dipeptide (1 mM) in PBS-ACN (2:1 v/v, pH 7.4) buffer with various aldehydes (10 mM):
101 4-nitrobenzaldehyde (**a**); pyridoxal (**b**); isovaleraldehyde (**c**) and formaldehyde (**d**). Quantitative product
102 formation was observed in all four cases, indicating no interference from aldehydes.

WYne-S dipeptide adducts:
(X=CH_2, NH, O)



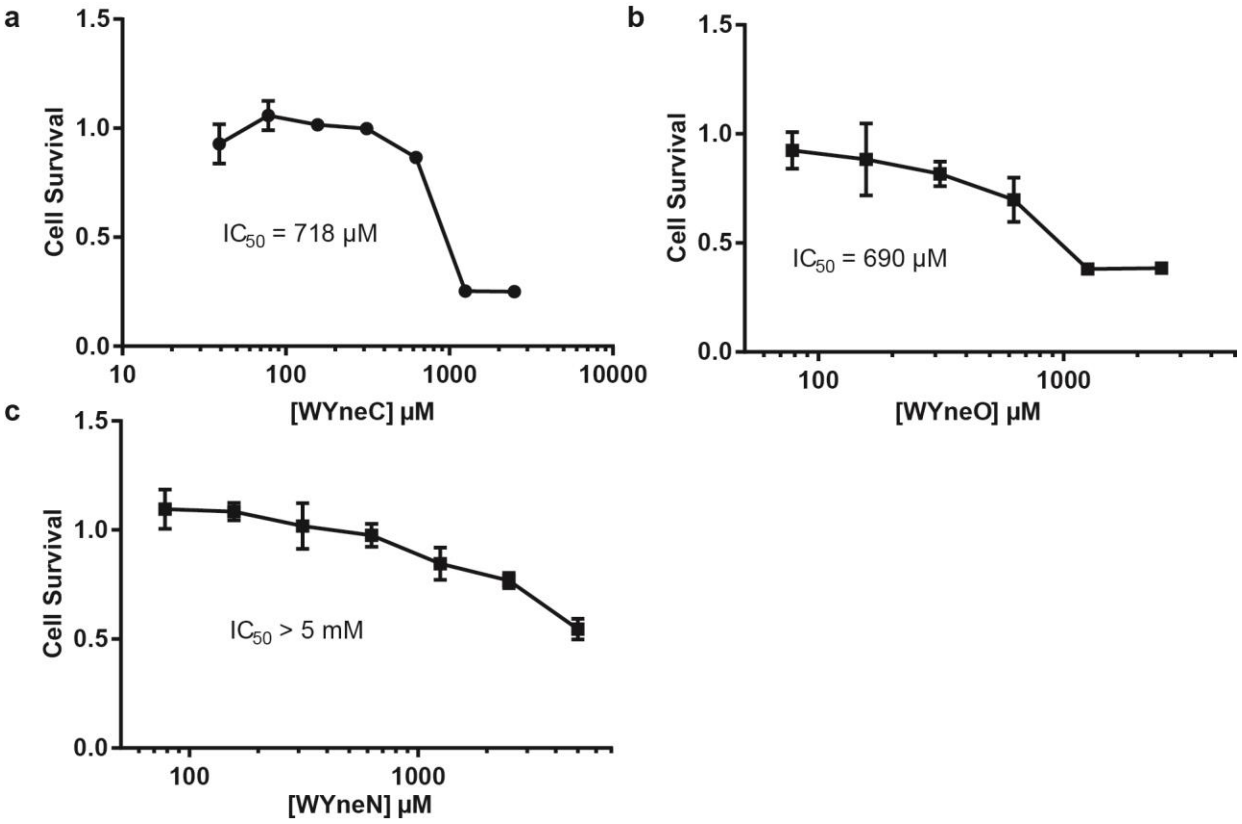
	Adduct stability 0.25 mM in HEPES buffer	Adduct stability 0.25 mM in HEPES with 10 mM DTT	Adduct stability 0.25 mM in pH 9.5 NH_4HCO_3 buffer[a]	Adduct stability 0.25 mM in pH 3.0 SCX buffer[b]
WYneC-S-Adduct X = CH_2	stable[c]	stable	stable	stable
WYneO-S-Adduct X = O	stable	$t_{1/2}$ = 0.5 h	stable	stable
WYneN-S-Adduct X = NH	stable	$t_{1/2}$ < 0.5 h	20% TPP cleavage after 20 h	stable

[a] 25 mM NH_4HCO_3, 33% ACN, pH 9.5.

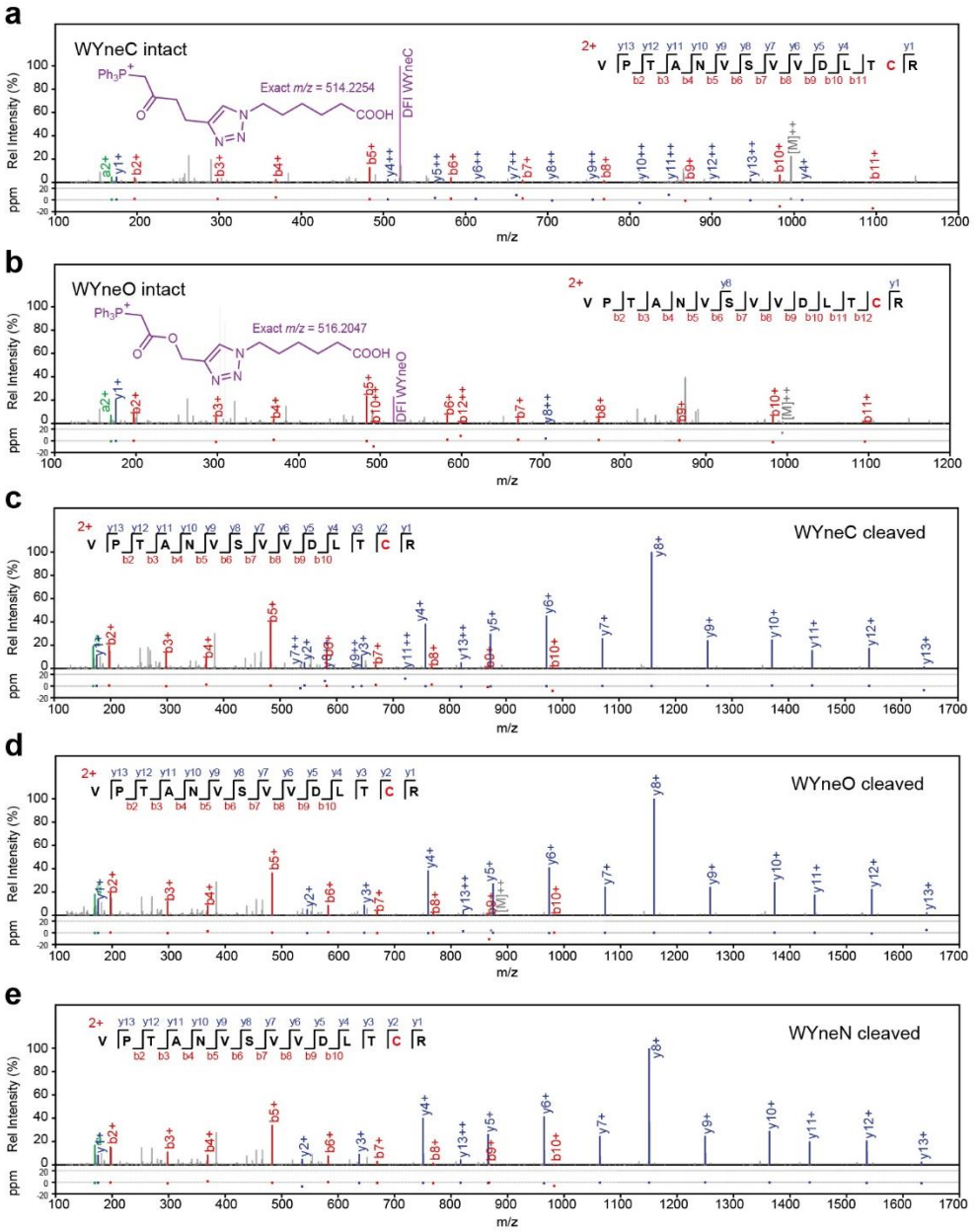
[b] 5 mM NaH_2PO_4, 25% ACN, pH 3.0.

[c] Indicates no degradation after 20 h at room temperature.

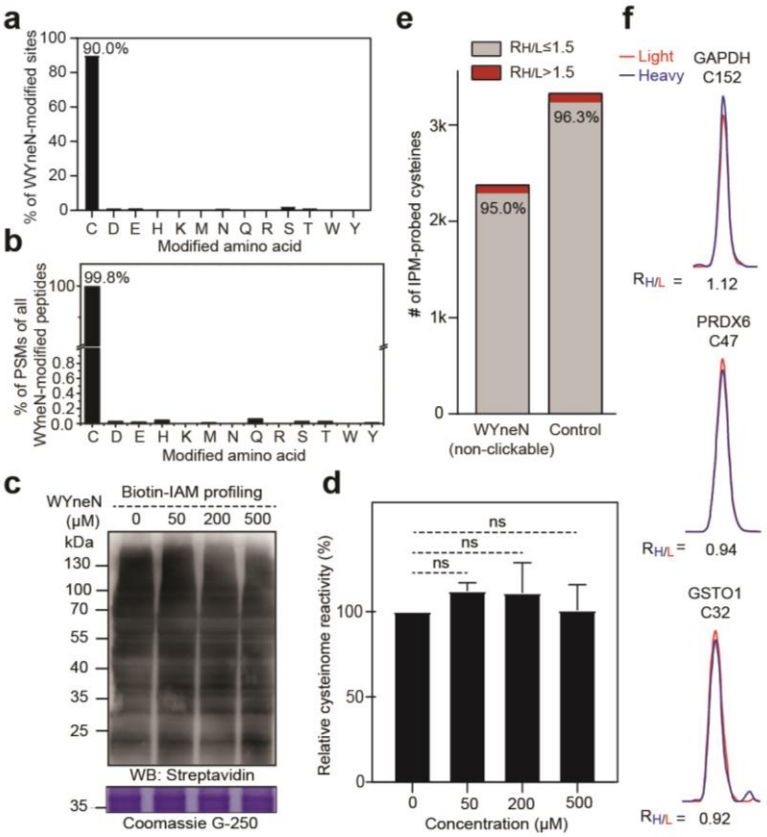
Supplementary Fig. 9 | Stability of WYne-S-dipeptide adducts at room temperature. The probes and their labeling products (WYne-S-dipeptide adducts) were studied under various conditions as indicated above. Compound stability was evaluated by periodic LC-MS analyses over a time period of 20 h.



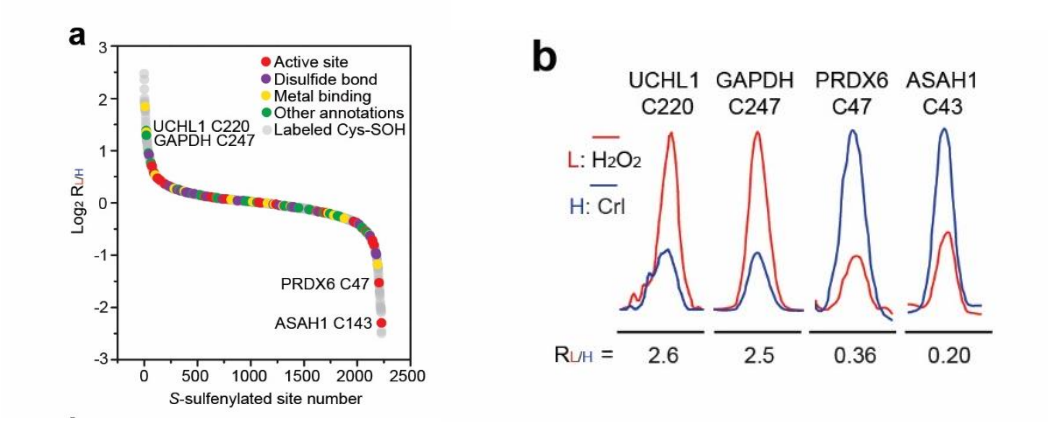
Supplementary Fig. 10 | Cytotoxicity of WYne probes in A549 cells. Exponentially growing HeLa cells were seeded in a 96-well plate at a density of 6,000 cells/well. After 16 h, culture media were replaced with 100 μL media containing test compounds or vehicle (2% DMSO). After 2 h incubation, culture media were replaced with 100 μL fresh media and 20 μL MTS reagent (CellTiter 96 AQ_{ueous} One Solution Cell Proliferation Assay, Promega). After 1.5 h incubation at 37°C, the absorbance at 490 nm was recorded. Data was plotted as survival (A_{490} ratio of treatment/control) vs. concentration by GraphPad Prism 7 using the "Inhibitor vs. response -- Variable slope (four parameters)" function. **a**, Cytotoxicity assay of WYneC. **b**, Cytotoxicity assay of WYneO. **c**, Cytotoxicity assay of WYneN.



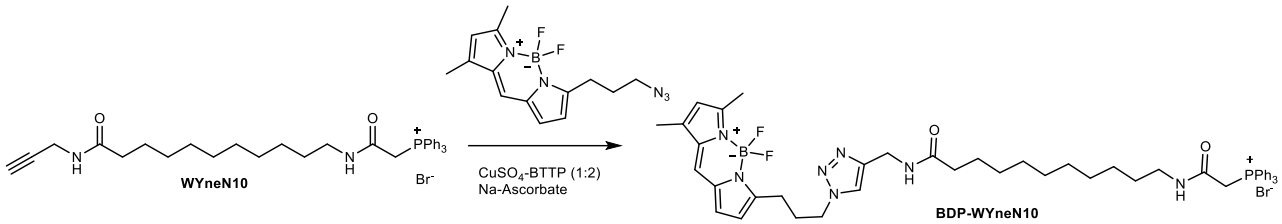
Supplementary Fig. 11 | Representative MS/MS spectra of the GAPDH peptides bearing WYne probes-derived cysteine adduction. **a**-**b**, MS/MS spectra of the GAPDH peptides bearing intact WYneC and WYneO probe, respectively. Diagnostic fragment ions (DFIs) provided by C-S bond cleavage from the intact probe-peptide adducts are shown in purple color. **c**-**e**, MS/MS spectra of the GAPDH peptides bearing WYne probes with a loss of triphenylphosphine.

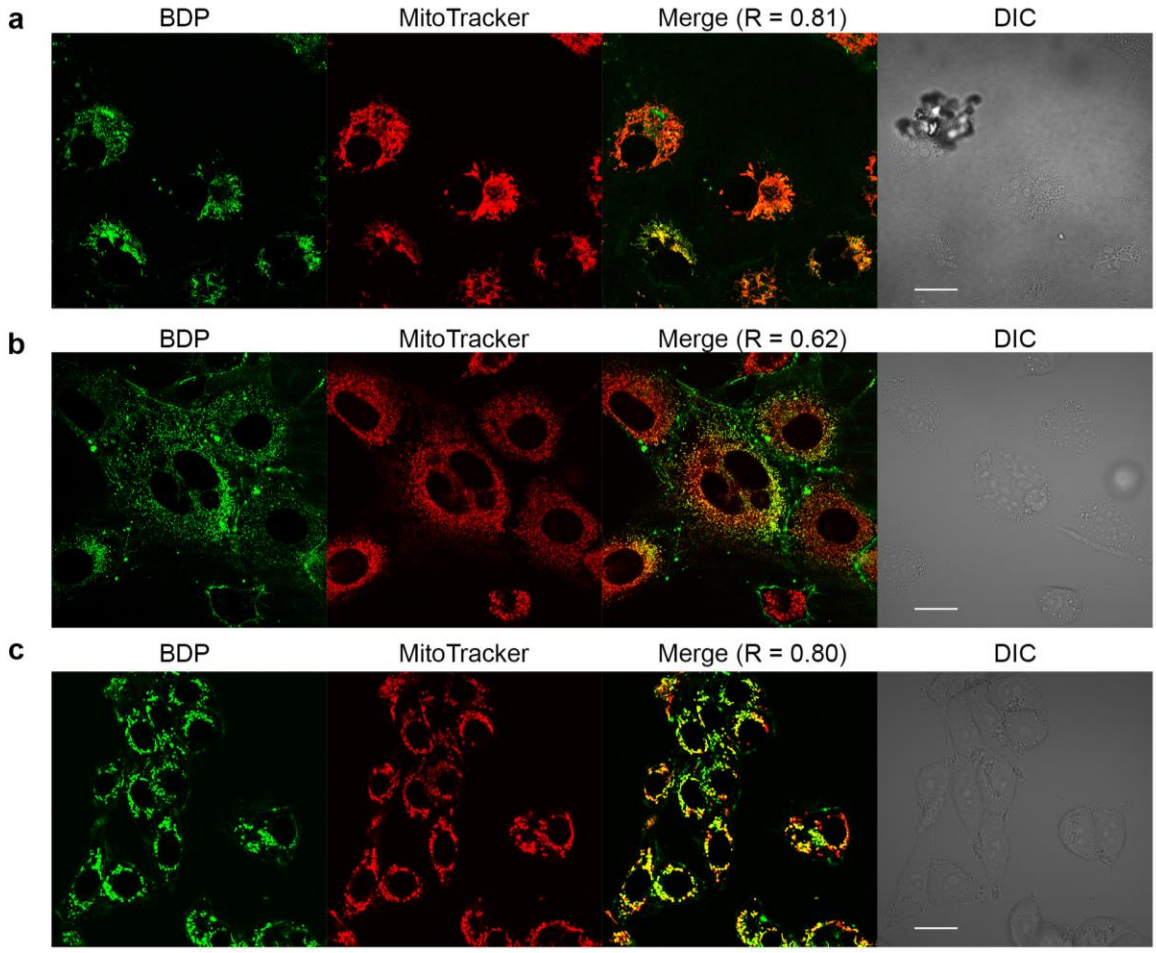


Supplementary Fig. 12 Proteome-wide selectivity of WYneN. **a**-**b**, Analysis of the amino acid specificity of WYneN. A549 cells labeled with WYneN were processed and analyzed as described in the methods section of this Supporting Information. pFind software was used to allowing the modification on any potentially polar amino acid. Bar charts showing the percentages of probe-modified sites (**a**) or the percentages of spectral counts of probe-modified sites (**b**) for individual amino acids. **c**-**d**, Representative western blot (**c**) and quantification (**d**) demonstrating that *in situ* WYneN treatment does not perturb the cysteinome. A549 cells were labeled with WYneN at the indicated concentrations at 37°C for 2h. Then the cell lysates were harvested and labeled with a thiol-reactive probe, namely biotin-IAM, separated with SDS-PAGE, and analyzed with streptavidin-HRP-based western blotting. ns, not significant. Student's t-test. **e**, QTRP-based site-specific analysis showing that both non-clickable WYne warhead and vehicle control had no significant impact on the cysteinome. A549 cells treated with or without WYneN warhead were labeled in *vitro* with a "clickable" thiol-reactive probe IPM. The probe-tagged proteomes were processed and analyzed as previously described[1]. In principle, only high heavy-to-light ratio ($R_{H/L}$, control versus treatment) values are indicative of cysteines that have less free thiol being available after WYneN warhead treatment. Not unexpectedly, those cysteines perturbed by either control or WYneN warhead treatment comprised only ~5% of all quantified sites, when a common cutoff (1.5-fold change) was applied. **f**, Representative extracted-ion chromatograms from (**e**) showing no change in IPM-tagged peptides from three well-known redox sensors, including GAPDH (C152), PRDX6 (C47) and GSTO1 (C32), from A549 cells treated with the non-clickable WYneN. The profiles for light- and heavy-labeled peptides are shown in red and blue, respectively. Heavy (Control)/light(treatment) ratios were calculated from biological duplicates and are displayed below the individual chromatograms.

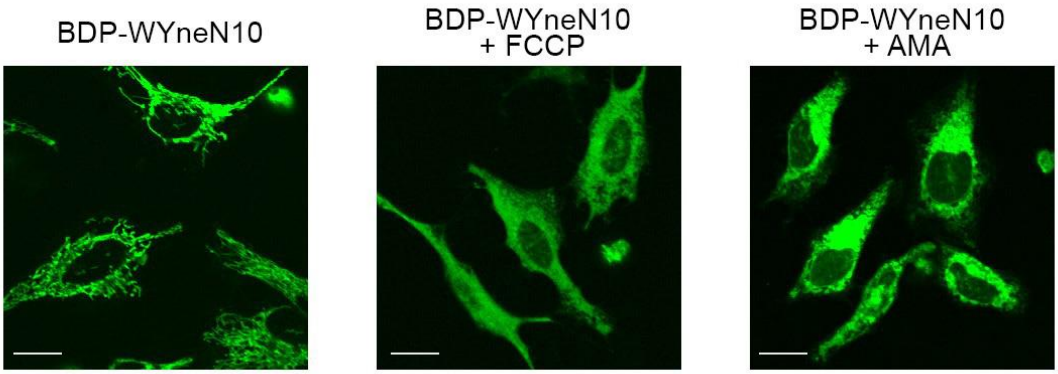


Supplementary Fig. 13 | WYneN-based in situ *S*-sulfenylome analysis. **a**, Rank plot showing site-specific changes in cysteine S-sulfenylation in A549 cells proteome in response to H_2O_2 treatment. Those sites with known functions retrieved from the Uniprot database are labeled in different colors as indicated. **b**, Extracted-ion chromatograms showing changes in WYneN-tagged peptides from UCHL1 (C220), GAPDH (C247), PRDX6 (C47) and ASAH1 (C43) from H_2O_2 stimulation of A549 cells. The profiles for light- and heavy-labeled peptides are shown in red and blue, respectively. Heavy (H_2O_2)/light (control) ratios were calculated from biological duplicates and are displayed below the individual chromatograms.

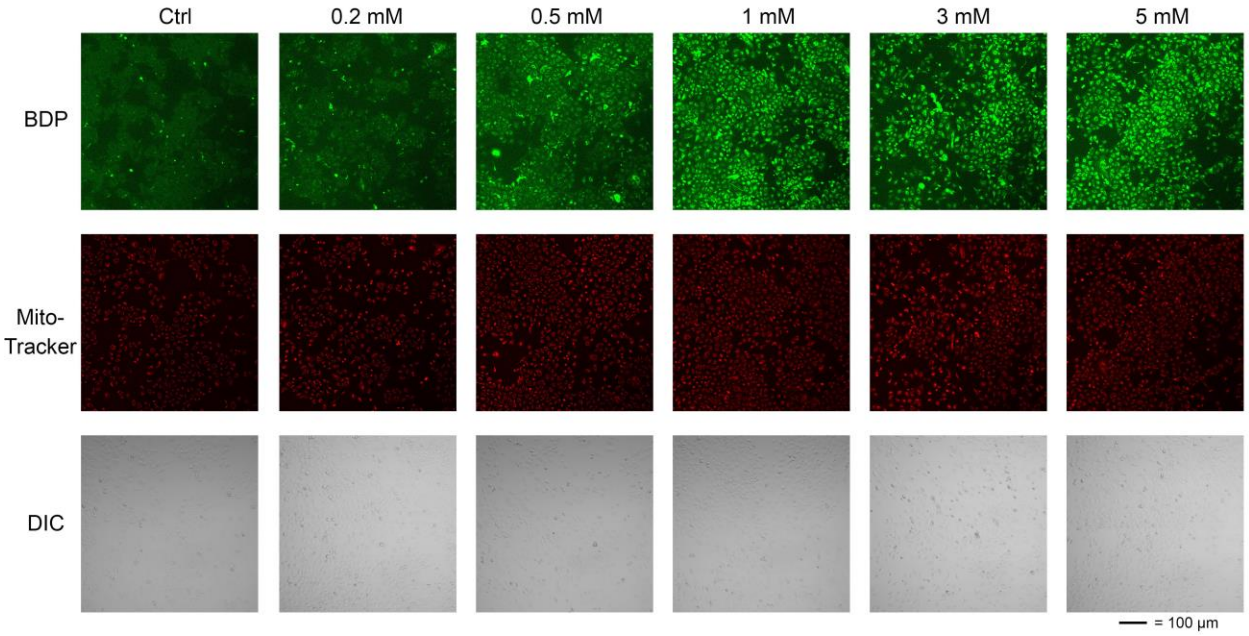




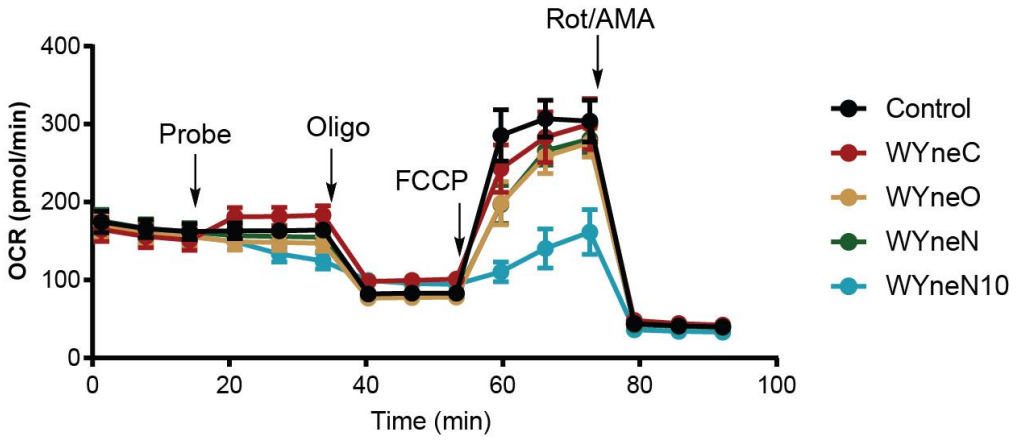
Supplementary Fig. 14 | Confocal live cell imaging of BDP-WYneN10 (500 nM) and MitoTracker Deep Red (100 nM) in cells. Confocal live cell images of BDP (green channel), MitoTracker Deep Red (red channel), merged and DIC (with a scale bar of 20 μm) were shown. Pearson's correlation coefficients (R) were calculated from the average of five regions of interest (ROIs) in representative cells. **a**, Live cell imaging of A549 cells. **b**, Live cell imaging of NIH3T3 cells. **c**, Live cell imaging of RKO cells.



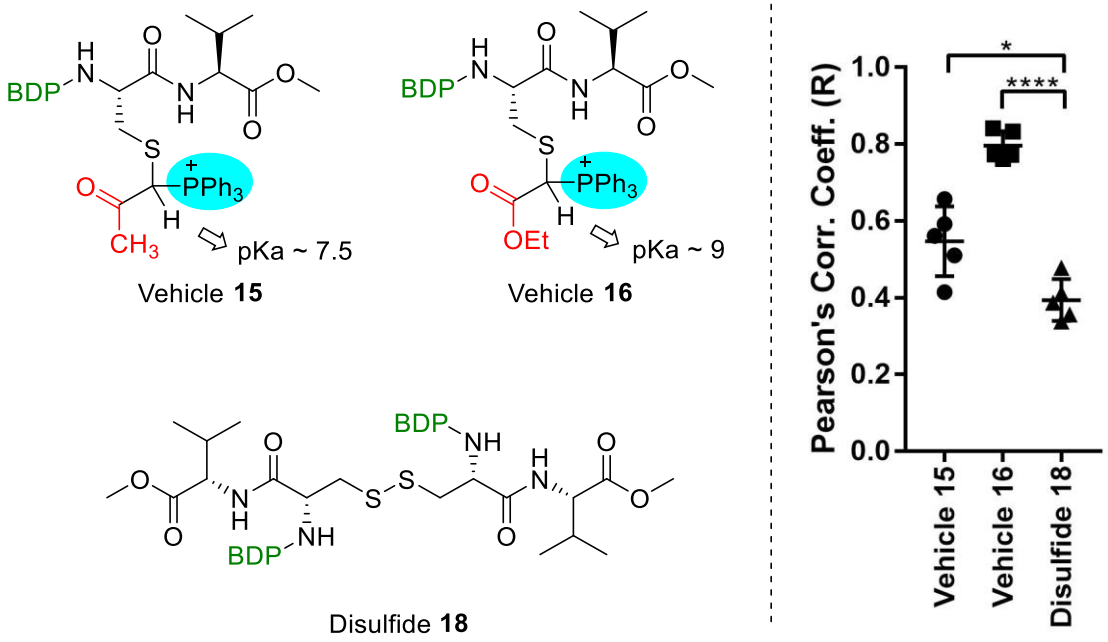
Supplementary Fig. 15 | Effect of mitochondrial uncouplers on localization of BDP-WYneN10. HeLa cells were incubated in DPBS, with FCCP (50 µM) or antimycin A (AMA, 15 µM) for 1 h at 37 °C, then treated with 1 µM BDP-WYneN10 and live cell images were acquired after 15 min. Disruption of mitochondrial respiration resulted in poor localization of the fluorescent probe. A scale bar of 20 µm is shown on each image.



Supplementary Fig. 16 | Effect of external H_2O_2 on the fluorescence of BDP-WYneN10. A549 cells were incubated with BDP-WYneN10 (1 μM) and MitoTracker Deep Red (0.1 μM) in DBPS, with various concentrations of H_2O_2. Live cell imaging was performed after 1 h. An increase in BODIPY fluorescence was observed along with increasing oxidant concentration, whereas the MitoTracker fluorescence stayed at a similar level.



Supplementary Fig. 17 | Effect of WYne probes on mitochondrial respiration. Oxygen consumption rates (OCR) were obtained on a Seahorse XF96 following manufacturer's protocol. A plate of 95% confluent A549 cells in 180 µL RPMI assay media were injected with the following compounds (12 replicates) in the order of: Port A: WYne probes (50 µM final concentration). Port B: Oligomycin A (1.5 µM). Port C: FCCP (1.5 µM). Port D: Antimycin A and rotenone (0.5 µM each). Three cycles consisting 3 min mixing and 3 min measurements were performed after each addition.



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220 **Supplementary Fig. 18 | Structures of vectors 15 and 16, and a disulfide control compound 18,**
221 **and their colocalization with MitoTracker™ Deep Red FM.** Live cell images were acquired from HeLa
222 cells stained with BODIPY (BDP)-tagged probes (0.5 μM) and MitoTracker (0.1 μM) in DPBS. Pearson's
223 correlation coefficients were calculated from five regions of interest (ROIs). Statistical significance of
224 Pearson's correlation coefficients between the vehicle and the control was shown (unpaired t-test, * $P \leqslant$
225 0.05, **** $P \leqslant 0.0001$).

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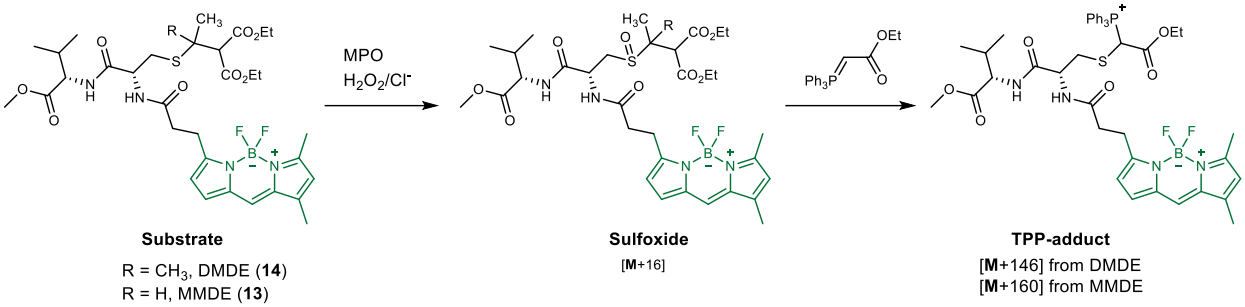
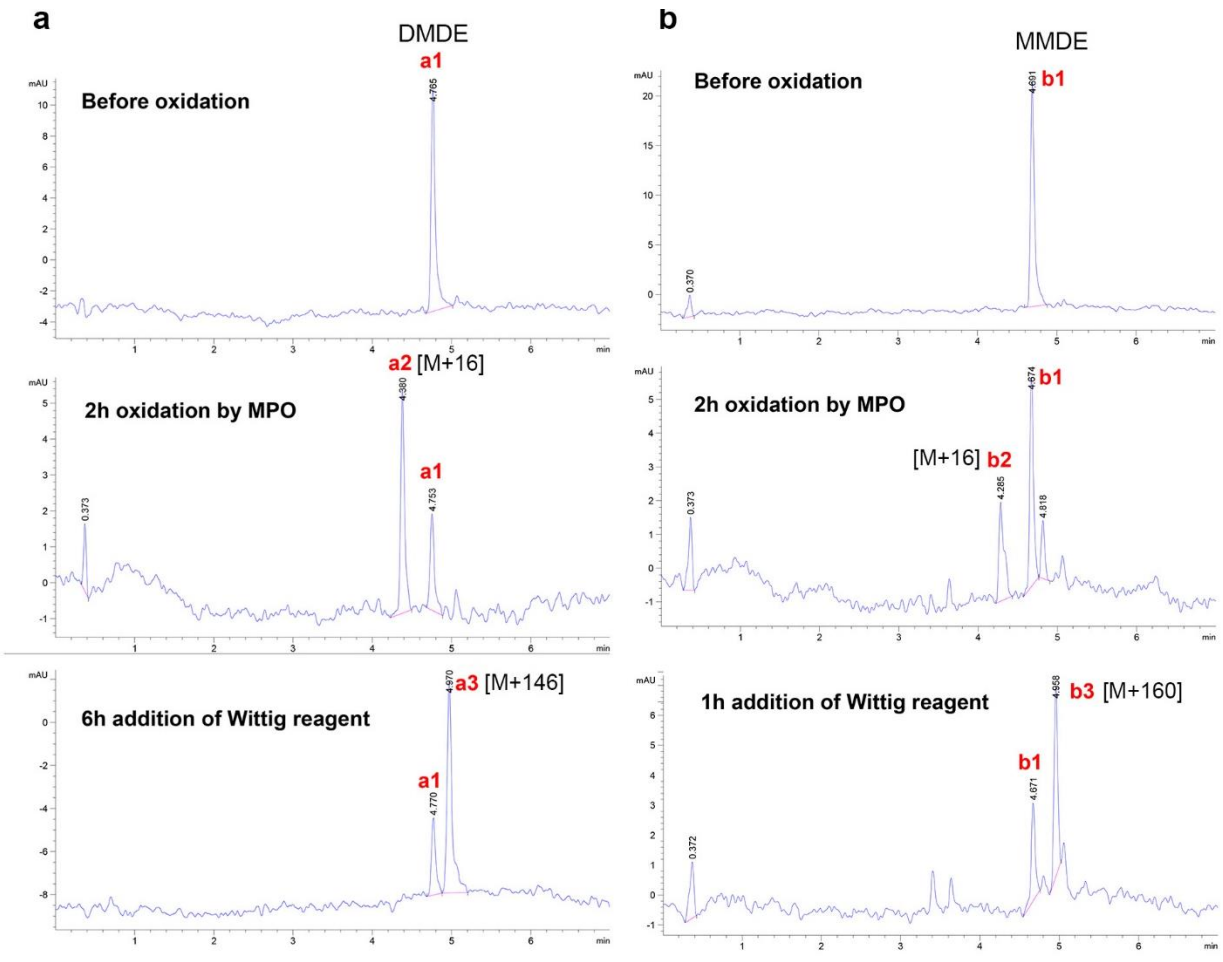
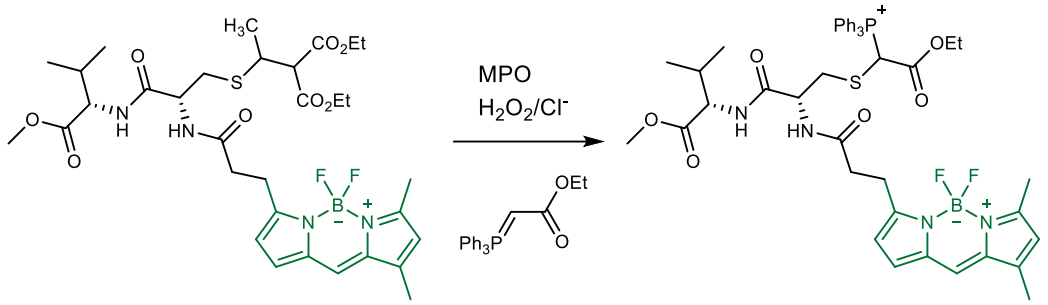
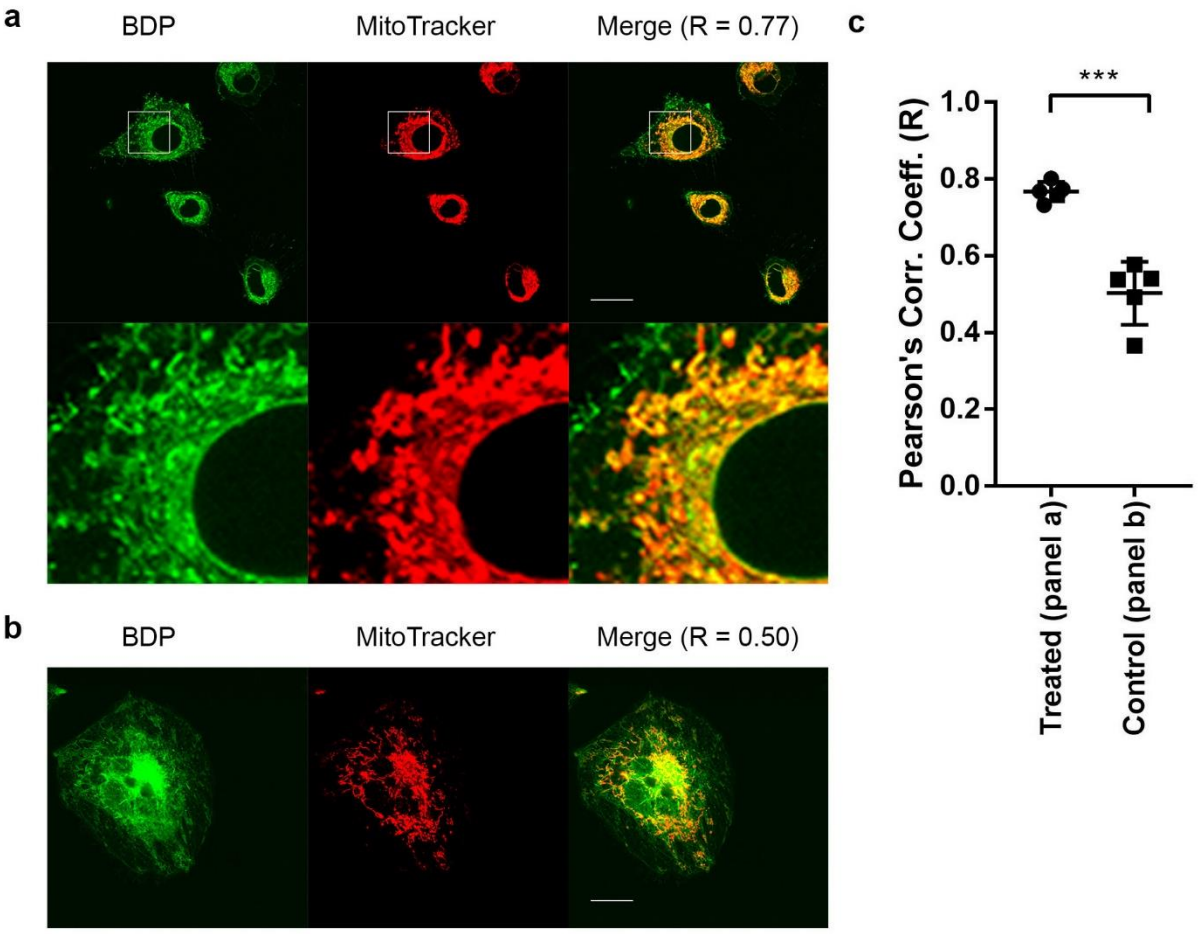


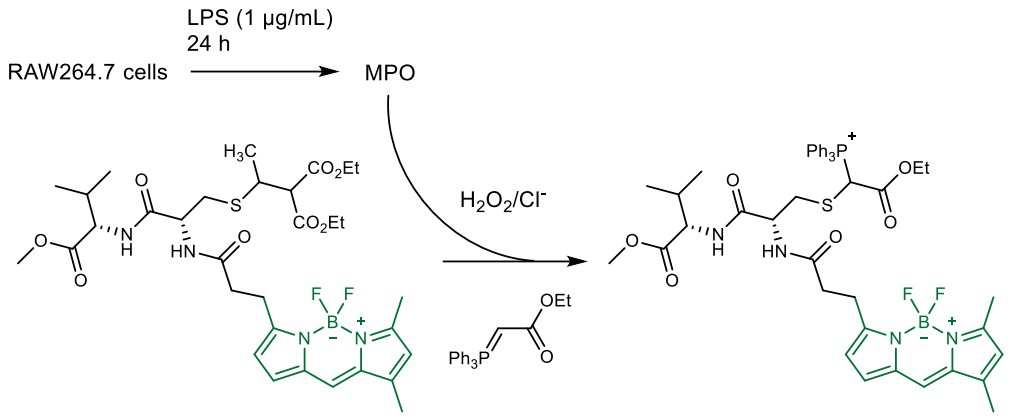


Supplementary Fig. 19 | Enzymatic generation of HOCl triggered redox-decaging and TPP-conjugation of a fluorescent dipeptide substrate. Myeloperoxidase produced HOCl which oxidized the substrates DMDE or MMDE (5 μM) in pH 7.4 PBS solution (0.1 mL). The resulting sulfoxide product reacted with Wittig reagent in 1 h (MMDE, panel **a**) or 6 h (DMDE, panel **b**) at 37 °C. Reaction progresses were monitored by LC-MS (absorption at 493 nm). LC peaks corresponding to DMDE (compound **14**, labeled as "a1"), its sulfoxide (a2) and TPP-adduct (a3); and MMDE (compound **13**, labeled as "b1"), its sulfoxide (b2) and TPP-adduct (b3) are labeled with corresponding mass shifts.





Supplementary Fig. 20 | Enzymatic oxidative decaging of MMDE and in vivo delivery of a fluorescent cargo to mitochondria. HeLa cells in 8-well culture slides (ibidi µ-slide) were incubated with MMDE (0.2 µM), Wittig-CO_2Et (5 µM), H_2O_2 (1 mM) and myeloperoxidase (MPO, 0.15 mg/mL) in DPBS containing MitoTracker Deep Red (50 nM). After 1 h incubation at 37 °C, live cells were imaged under a confocal microscope. A scale bar of 20 µm, and a zoom-in area of 20x20 µm was shown. Pearson's correlation coefficients (R) were calculated from the average of five regions of interest (ROIs) in representative cells. **a**, Confocal images of HeLa cells after treatment. A scale bar of 20 µm was added on the merged image. **b**, Control experiment with the same setup excluding MPO. **c**, Statistical significance of Pearson's correlation coefficients between the two experiments (unpaired t-test, P = 0.0001).



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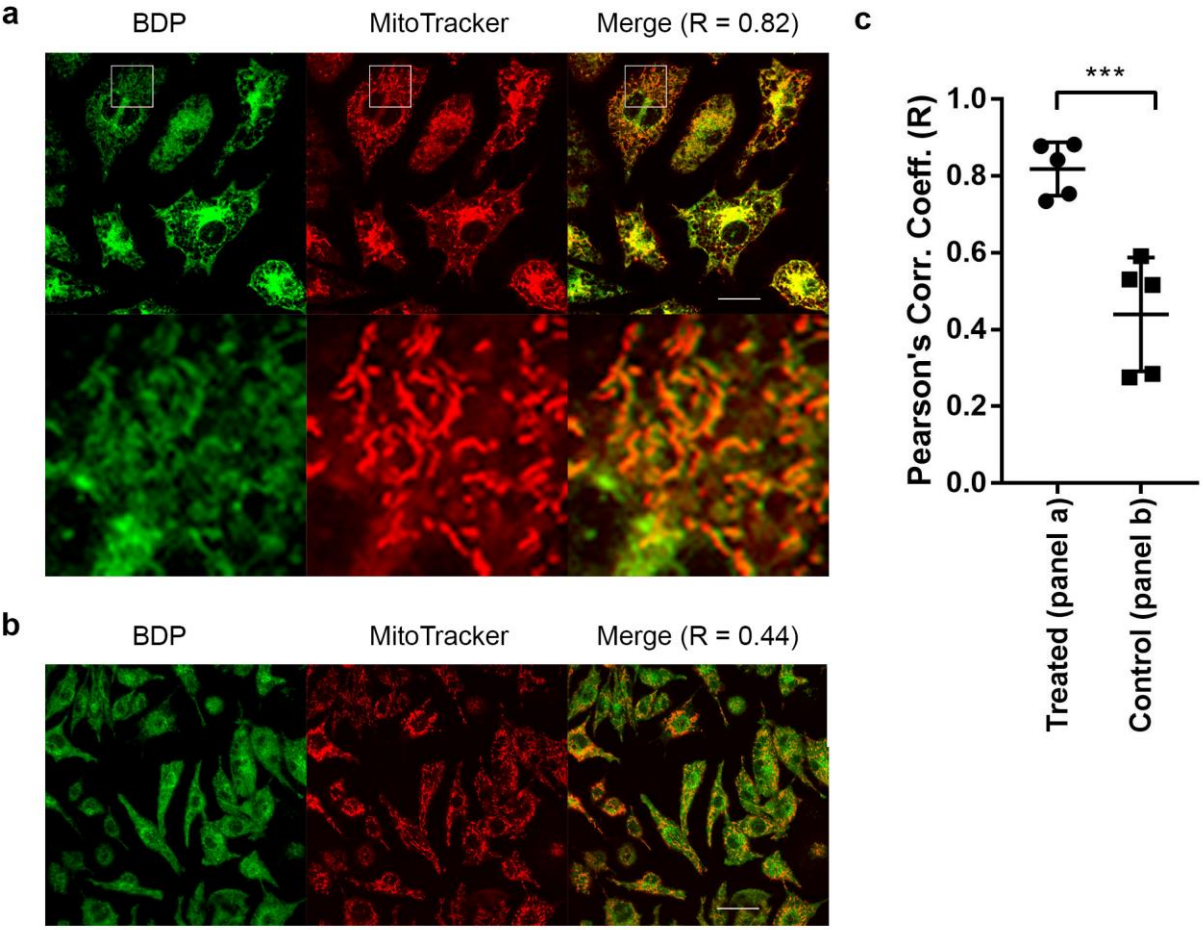

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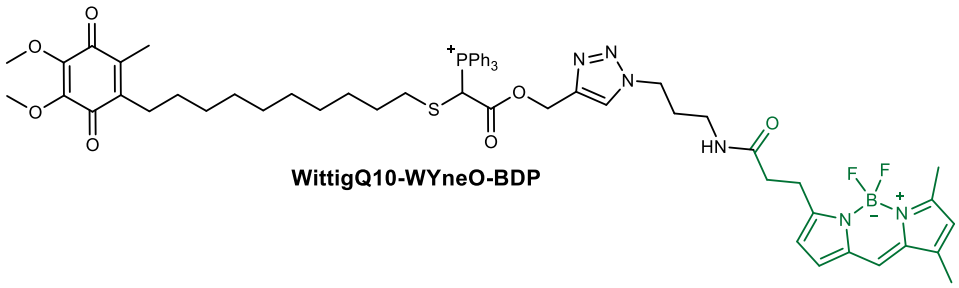
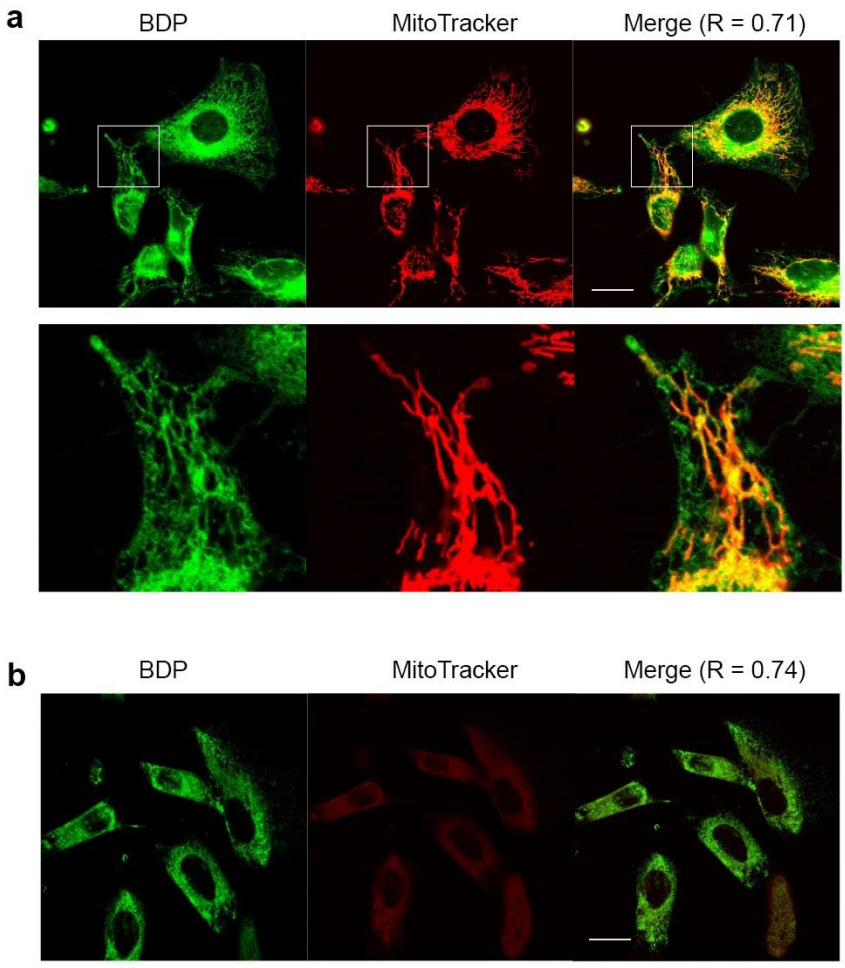
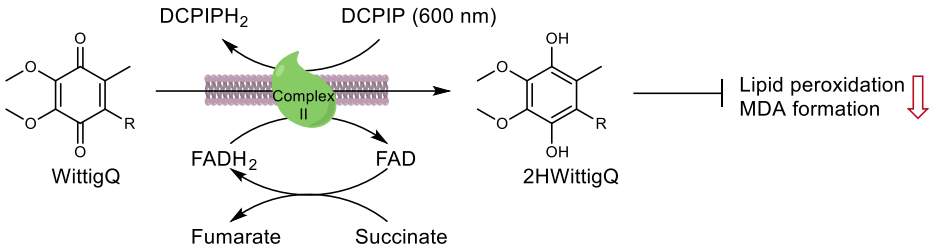
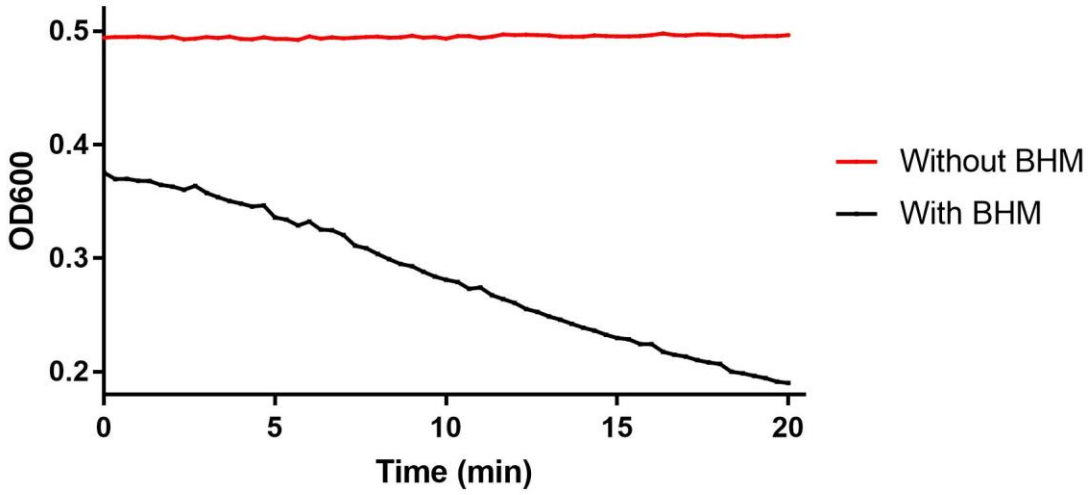
259 **Supplementary Fig. 21 | Oxidative decaging of MMDE and mitochondrial delivery in macrophage**
260 **cells**. RAW 264.7 cells were stimulated with 1 μg/mL LPS for 24 h, then treated with MMDE (0.2 μM),
261 Wittig-CO_2Et (5 μM) and H_2O_2 (1 mM) in DPBS containing MitoTracker Deep Red (50 nM). After 1 h
262 incubation at 37 °C, live cells were imaged under a confocal microscope. A scale bar of 20 μm, and a
263 zoom-in area of 20x20 μm were shown. Pearson's correlation coefficients (R) were calculated from the
264 average of five regions of interest (ROIs) in representative cells. **a**, Confocal images of RAW 264.7 cells
265 after treatment. **b**, Control experiment without the Wittig reagent and H_2O_2. **c**, Statistical significance of
266 Pearson's correlation coefficients between the two experiments (unpaired t-test, P = 0.0008).





Supplementary Fig. 22 | Live cell confocal imaging of WittigQ10-WYneO-BDP showed signs of localization to mitochondria. A scale bar of 20 μm, and a zoom-in area of 30x30 μm were shown. Pearson's correlation coefficients (R) were calculated from the average of five regions of interest (ROIs) in representative cells. **a**, HeLa cells were treated with 1 μM of WittigQ10-WYneO-BDP (prepared via click chemistry protocol and HPLC purified) and 50 nM of MitoTracker Deep Red in DPBS. **b**, HeLa cells were pre-incubated with FCCP (50 μM) for 1 h and treated with the aforementioned probes in DPBS.





Supplementary Fig. 23 | Mitochondrial complex II assay with WittigQ in presence of quinone depleted bovine heart mitochondria (BHM) or control at 37 °C. Complex II activity resulted in reduction of WittigQ and a steady decrease in OD600. Detailed experimental procedure is described in supplementary methods.

Supplementary Methods

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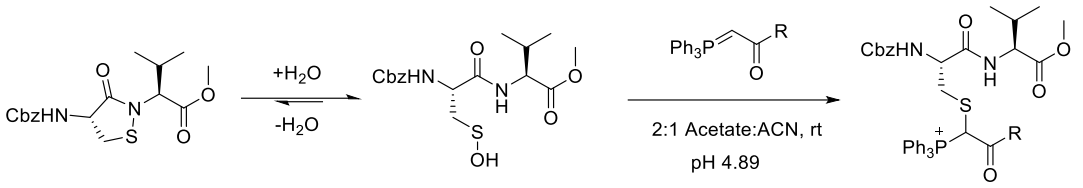
SI 1. Reaction kinetics study



The rate studies measuring the reaction between nucleophiles with a model dipeptide-SOH were performed as previously described (Gupta, V.; Carroll, K. S. *Chem. Sci.* **2016**, *7*, 400). To a 2 mL solution of a nucleophile in an appropriate buffer (10 mM PBS pH 7.4, or sodium acetate pH 4.9) was added 1 mL solution of cyclic sulfenamide (CSA) in acetonitrile. In order to obtain pseudo first-order kinetics, the concentration of nucleophile was maintained at least 5 times higher than CSA. An aliquot (300 µL) of the reaction was collected at regular intervals (a total of 9 data points) and immediately quenched by addition of formic acid (100 µL). First order rate constant (*k*) was obtained by plotting the UV peak area (*Y*-axis) of the product against time (*X*-axis) and analyzing the plot using the "Dissociation - One phase exponential decay" function in GraphPad Prism 7:

$$Y = (Y0 - NS) \cdot e^{-kX} + NS$$

For initial survey of the reactivity of Wittig reagents, second-order rate constants (*K*) was calculated from first order rate constants (*k*) and the concentration of nucleophiles (*C*):

$$K = \frac{k}{C}$$

For WYne probes, second-order rate constant (*K*) was obtained from the linear regression of first order rate constants (*k*) vs. concentrations of nucleophiles (*C*):

$$k = K \cdot C + intercept$$

SI 2. Cell culture and labeling

A549, HeLa, RKO and NIH3T3 cells were sourced from ATCC. Cells were cultured in corresponding media (HeLa and RKO cells in EMEM; NIH3T3 cells in DMEM; A549 cells in RPMI-1640) supplemented with 10% (vol/vol) FBS (Invitrogen), maintained at 37 °C under 5% CO_2 humidified atmosphere.

For in situ labeling, cells at ~80% confluency were cultured in serum-free medium overnight, then switched to fresh serum-free medium containing vehicle (2% DMSO) or probes. After incubation for a certain peroid of time, cells were washed with cold PBS (3 mL x 4), then treated with HEPES lysis buffer (50 mM HEPES, 150 mM NaCl, pH 7.4, 1% NP-40 (Igepal CA-630), 0.5 % sodium deoxycholate, 0.1% SDS, with 1X freshly added protease inhibitor (Roche cOmplete™, EDTA-free Protease Inhibitor) and 200 U/mL catalase). The flasks were kept on ice with occasional swirling for 10 min. The lysates were transferred to 1.5 mL Eppendorf tubes and cell debris were removed by centrifugation (16,000 x g, 15 min). Protein concentration of the supernatant was determined by BCA assay (Thermo Scientific) and adjusted to an approriate concentration (0.4-1.0 mg/mL) with HEPES buffer (50 mM HEPES, 150 mM NaCl, pH 7.4).

SI 3. Click chemistry (CuAAC)

To 89 µL alkyne-tagged lysate solutions were added: 2 µL azide reporter compound (e.g. TAMRA-N_3, 5 mM), 7 µL premixed $CuSO_4$-BTTP (2 µL 12.5 mM $CuSO_4$, 5 µL 10 mM BTTP) then 2 µL sodium ascorbate (125 mM). The Click reactions were rocked at room temperature for 1 h, then quenched with addition of 1 µL EDTA (100 mM).

Reagents for CuAAC	**Effective final concentration (µM)**
TAMRA-N_3	100
$CuSO_4$	250
BTTP	500
Sodium ascorbate	2500

For CuAAC of small molecules with BDP-FL-azide (Lumiprobe Inc.), reactions were performed in 1 mL DMSO-H_2O (1:1 v/v) using a similar procedure as above. After reaction completion, the mixture was purified by prep-HPLC (5-100% ACN-H_2O gradient) to afford BDP conjugates.

Reagents for CuAAC (small molecules)	**Effective final concentration (μM)**
BDP-FL-azide	200
Small molecule alkynes	1000
$CuSO_4$	1000
BTTP	2000
Sodium ascorbate	2500

SI 4. In-gel fluorescence

After conjugation with TAMRA-N_3, the labeled protein samples were mixed with non-reducing SDS sample buffer and separated by SDS-PAGE (4-20%), washed twice with water and MeOH-H_2O-AcOH (4:5:1 v/v/v, 5 min per wash) and imaged (Azure Sapphire™ Biomolecular Imager) at 520 nm (TAMRA) and 658 nm (protein ladder), followed by staining (coomassie brilliant blue R-250) to ensure equal protein loading.

SI 5. Inact protein mass spectrometry

Protein samples were buffer exchanged (50 mM ammonium bicarbonate, with Zeba™ Spin Desalting Columns (7k molecular weight cutoff, Thermo Scientific) and diluted with ammonium bicarbonate (50 mM) to a final concentration of 3 μM. 10 μL of each sample was separated by HPLC (GRACE VyDAC C4 protein column, 50x4.6 mm, 5-100% ACN in H_2O gradient) and analyzed by mass spectrometry (Thermo

Scientific LTQ Linear Ion Trap MS). Obtained mass spectra were deconvoluted using the MagTran software (Dr. Zhongqi Zhang, Amgen Inc., Thousand Oaks, CA).

SI 6. Chemoproteomic workflow

SI 6.1 Cell culture and treatment

A549 cells were purchased from the ATCC, cultured in DMEM supplemented with 10% FBS (Invitrogen),1% penicillin-streptomycin (Invitrogen) and 1% Glutagro (Corning), maintained at 37°C in a 5% CO_2 humidified atmosphere. For H_2O_2 treatment, cells were grown to ~80% confluency and subjected to serum-deprivation overnight. Then, cells were washed with fresh and pre-warmed serum-free medium and incubated with medium containing 1mM H_2O_2 at 37°C for 15 min.

SI 6.2 Chemoselective labeling the S-sulfenylome

For *in vitro* labeling, A549 cells without stimuli were harvested, lysed in pre-chilled NETN buffer (50 mM HEPES (pH 7.6), 150 mM NaCl, and 1% IGEPAL) supplemented with 1 x protease and phosphatase inhibitors (Thermo Scientific, A32961) containing 200 unit/mL catalase (Sigma-Aldrich), and then incubated with 5 mM of the SOH-specific probe as indicated (WYneC, WYneO, WYneN, BTD, or DYn-2) at 37°C for 2 h with rotation and light protection. For *in situ* labeling, intact A549 cells treated with or without H_2O_2 (1 mM, 15 min, 37°C) were incubated with 0.5 mM probe as indicated (WYneN, $^{13}C_5$ WYneN, or BTD) at 37°C for 1 h and then were lysed with aforementioned NETN buffer.

SI 6.3 Subsequent labeling of the nucleophilic cysteinome

A549 cells labeled with $^{13}C_5$ WYneN were harvested and lysed as described above. The same protein samples were then reduced with 10 mM TECP at room temperature (RT, 25°C) for 30 min to reduce

reversible oxidations other than sulfenic acids and subsequently labeled with 20 mM IPM, a 'clickable' thiol-reactive probe, at RT for 1 h.

SI 6.4 Preparing the probe-labeled protein samples

The probe-labeled protein samples were incubated with 40 mM iodoacetamide at 37 °C for 1 h with light protection. To remove all the excess small molecules, proteins were then precipitated with a methanol-chloroform system (aqueous phase/methanol/chloroform, 4:4:1 (v/v/v)). The precipitated proteins were resuspended with 50 mM ammonium bicarbonate containing 0.2 M urea and digested with sequencing grade trypsin (Promega) at a 1:50 (enzyme/substrate) ratio overnight at 37°C. The tryptic digests were desalted with HLB extraction cartridges (Waters) and evaporated to dryness. For qualitative and ratiometric analyses, dried peptides were resuspended in a water solution containing 30% acetonitrile (MeCN). For stoichiometric quantification, dried peptides were resuspended in a water solution containing 50% MeCN. CuAAC reaction was then performed as described previously[1] by subsequently adding 1 mM either light or heavy Azido-UV-biotin (1 µL of a 40 mM stock), 10 mM sodium ascorbate (4 µL of a 100 mM stock), 1 mM TBTA (1 µL of a 50 mM stock, and 10 mM $CuSO_4$ (4 µL of a 100 mM stock). After 2h incubation at RT, the light and heavy isotopic tagged samples were then mixed immediately following CuAAC reaction. The samples were cleaned by strong cation exchange (SCX) spin columns and then subject to the enrichment with streptavidin beads for 2 h at RT. Streptavidin beads were washed with 50 mM NaAc (pH4.5), 50 mM NaAc containing 2 M NaCl (pH4.5), and deionized water twice each with vortexing and/or rotation to remove non-specific binding substances, then resuspended in 25 mM ammonium bicarbonate, transferred to glass tubes (VWR), and irradiated with 365 nm UV light (Entela, Upland, CA) for 2 h at RT with magnetic stirring. The supernatant was collected, dried under vacuum, and stored at −20°C until LC-MS/MS analysis.

SI 6.5 Liquid chromatography-tandem mass spectrometry (LC-MS/MS) analysis

LC-MS/MS analyses were performed on a Q Exactive plus instrument (Thermo Fisher Scientific). Peptide samples were reconstituted in 0.1% formic acid and pressure-loaded onto a 2-cm microcapillary precolumn packed with C18 (3-μm, 120 Å, SunChrom, USA) operated with an Easy-nLC1000 system (Thermo Fisher Scientific). The precolumn was connected to a 12-cm 150-μm-inner diameter microcapillary analytical column packed with C18 (1.9-μm, 120 Å, Dr. Maisch GebH, Germany) and equipped with a homemade electrospray emitter tip. The spray voltage was set to 2.0 kV and the heated capillary temperature to 320°C. LC gradient consisted of 0 min, 7% B; 14 min, 10% B; 51 min, 20% B; 68 min, 30% B; 69-75 min, 95% B (A = water, 0.1% formic acid; B = MeCN, 0.1% formic acid) at a flow rate of 600 nL/min. MS1 spectra were recorded with a resolution of 70,000, an AGC target of 3e6, a max injection time of 20 ms, and a mass range from *m/z* 300 to 1400. HCD MS/MS spectra were acquired with a resolution of 17,500, an AGC target of 1e6, a max injection time of 60 ms, a 1.6 *m/z* isolation window and normalized collision energy of 30. Peptide *m/z* that triggered MS/MS scans were dynamically excluded from further MS/MS scans for 18 s.

SI 6.6 Peptide identification and quantification.

For blind search, raw data files were searched against *Homo sapiens* Uniprot canonical database using DirecTag-TagRecon as previously described[2,3]. the maximum modification mass was 600 Da, precursor ion mass tolerance was 0.01 Da, and fragmentation tolerance was 0.1 Da. The blind search results were visualized and analyzed with IDPicker[4].

For targeted search, raw data files were searched against *Homo sapiens* Uniprot canonical database using pFind studio[5]. Precursor ion mass and fragmentation tolerance were set as 10 ppm and 20 ppm, respectively. The maximum number of modifications and missed cleavages allowed per peptide were both set as three. For all analyses, mass shifts of + 15.9949 Da (methionine oxidation) and + 57.0214 Da (iodoacetamide alkylation) were searched as variable modifications. For site-specific mapping of probe-modified SOH sites, mass shifts of + 511.202 ($C_{30}H_{30}N_3O_3P$, Intact) and +265.142 ($C_{13}H_{19}N_3O_3$, cleaved) for WYneC, + 513.181 ($C_{29}H_{28}N_3O_4P$, intact) and +267.121 ($C_{12}H_{17}N_3O_4$,

cleaved) for WYneO, +512.197 (intact) and +252.122 ($C_{11}H_{16}N_4O_3$, cleaved) for WYneN, +418.131 ($C_{19}H_{22}N_4O_5S$) for BTD, and +333.169 ($C_{17}H_{23}N_3O_4$) for DYn-2 were searched as variable modifications, respectively. For stoichiometric quantification of %SOH, mass shift of +252.122 ($C_{11}H_{16}N_4O_3$, for both TPP-cleaved adduct derived from WYneN and the adduct derived from IPM) was searched as variable variable modification.

For qualitative and ratiometric analyses, a differential modification of 6.020 Da on probe-derived modification was used for stable-isotopic quantification. For stoichiometric analysis, a differential modification of 5.017 Da on probe-derived modification was used for stable-isotopic quantification. The FDRs were estimated by the program from the number and quality of spectral matches to the decoy database. The FDRs at spectrum, peptide, and protein level were < 1%. Quantitative analyses were performed using pQuant[6], which calculates light to heavy ratios ($R_{L/H}$) based on each identified MS scan with a 15 ppm-level *m/z* tolerance window and assigns an interference score (Int. Score) to each value from zero to one. The median values of probe-modified peptide ratios with σ less than or equal 0.5 were considered to calculate site-level ratios. Quantification results were obtained from two or four biological replicates.

SI 7. Confocal microscopy

Cells were cultured in 35 mm dishes (Ibidi µ-Dish, cell culture treated) at 50-75% confluency. The media was replaced with DPBS (VWR, with Ca^{2+} and Mg^{2+}) containing fluorescent probes. After 10 min of incubation at 37 °C, live cell images were acquired on a confocal microsope (Olympus Fluoview 1000) with preset channel settings (FITC channel for BODIPY-containing probes; Cy5 channel for MitoTracker™ Deep Red). Pixel intensity and colocalization analysis were performed with the ImageJ software (Wayne Rasband, NIH).

SI 8. Redox-decaging and capture of sulfenic acids with Wittig reagents

Redox-caged sulfenic acids (50 µM in PBS, pH 7.4) was treated with HOCl (50 µM, 1 eq.). Immediate formation of corresponding sulfoxide product was observed by LC-MS analysis. Wittig reagent (500 µM, 1 eq.) was then added, and the solution was incubated at 37 °C for an indicated time and analyzed on LC-MS. Yield of the TPP-linked product was calculated based on the ratio of peak area (product/starting material) at 493 nm. Assumption was made that all BODIPY fluorescent compounds have the same molar extinction coefficient at 493 nm.

For myeloperoxidase (MPO)-induced generation of HOCl, recombiant human MPO (R&D Systems, 3174) was treated with 2 mM H_2O_2 in PBS (0.1 mg/mL) for 2 h at 37 °C, then redox-caged sulfenic acids (5 µM) and Wittig reagent (100 µM, 20 eq.) was added succeedingly. The reactions were performed at 37 °C and tracked by LC-MS (493 nm absorption).

SI 9. Preparation of HeLa mitochondria

HeLa cells from a 150 mm culture dish ($2x10^7$ cells) were washed and harvested (via scraping) in cold PBS. Fractionating of intact mitochondria was performed with the Mitochondria Isolation Kit for Cultured Cells (Thermo Scientific, 89874) with slight modification to manufacturer's protocol. In brief, at 4 °C, pelleted cells were mixed with 700 µL of Mitochondria Isolation Reagent A with 1X protease inhibitor (Roche) for 2 min, homogenized in a dounce tissue grinder, and mixed with 700 µL of Mitochondria Isolation Reagent C with 1X protease inhibitor. Cell debris were removed by centrifugation at 700 x g for 10 min. The supernatant was then centrifugated at 7,000 x g for 15 min to give pelleted mitochondria, which were washed with 500 µL of Reagent C and centrifugated again at 12,000 x g for 15 min. The mitochondria pellet was resuspended in appropriate buffer and used immediately for further studies.

SI 10. Assay of lipid peroxidation

100 µL aliquots of intact HeLa mitochondria (0.5 mg protein/mL) in KCl buffer (100 mM KCl, 10 mM Tris·HCl, pH 7.6) was pre-treated with succinate (10 mM), rotenone (10 µM), and quinone antioxidant (MitoQ or WittigQ, at 20/10/5/2.5/0 µM in duplicate). After 30 min incubation at 37 °C, lipid peroxidation was induced by addition of $FeSO_4$ (50 µM), sodium ascorbate (150 µM) and H_2O_2 (1 mM). After 40 min incubation at 37 °C, MDA assay solution (300 µL, Sigma-Aldrich MAK085) was added. The mixture was heated at 95 °C for 1 h, cooled to room temperature and analyzed on a fluorescence spectrometer (Ex/Em = 535/555 nm). Amount of MDA formed by lipid peroxidation was calculated from a standard curve, and plotted against the concentration of the antioxidant.

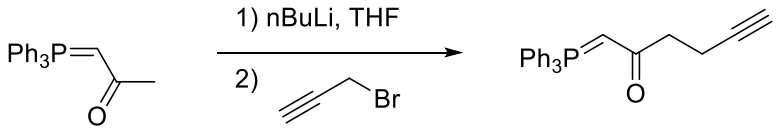
SI 11. Assay of complex II activity

Activity of mitochondrial complex II was assayed via a commercial kit (Cayman Chemical 700940). Bovine heart mitochondria (1 µL, kit provided) were added to 50 µL reaction mixture containing 100 µM WittigQ, 10 mM succinate, 10 µM rotenone, 1 mM KCN in KCl buffer (100 mM KCl, 10 mM Tris·HCl, pH 7.6), then mixed with 2.5 % DCPIP solution (50 µL). OD600 was plotted over time on a plate reader at room temperature or 37 °C. Control experiment was performed in parallel without mitochondria.

Synthetic Procedures

General All reactions were conducted in flame-dried glassware under nitrogen pressure with dry solvents, unless otherwise noted. All chemicals were purchased from Sigma-Aldrich (St. Louis, MO), or Acros Organics (Fair Lawn, NJ) and used as received. Column chromatography was performed with silica gel P60 (Sorbent Technologies) on an automated flash chromatography system (CombiFlash Nextgen 300+). Reactions were monitored by thin layer chromatography (TLC) carried out using Analtech 60 F254 silica gel (precoated sheets, 0.25 mm thick). ^{1}H-NMR and ^{13}C-NMR spectra were collected in $CDCl_3$ or DMSO-d6 (Cambridge Isotope Laboratories, Cambridge, MA) at 400 and 100 MHz respectively, using a Bruker AM-400 instrument with chemical shifts relative to residual $CHCl_3$ (7.26 and 77.16 ppm) or DMSO (2.50 and 39.52 ppm). Low resolution mass spectroscopy analyses were carried out on an Agilent LC/MS system (Agilent 1220 HPLC with InfinityLab Poroshell 120 SB-C18 column and Agilent 6120 Quad MS). Preparative HPLC was performed on an Agilent 1260 HPLC system with ZORBAX SB-C18 column (21.2x150 mm) using a gradient of 5-100% acetonitrile in water. All HPLC solvents were supplied with 0.1% (v/v) formic acid.

Preparation of 1-(triphenylphosphaneylidene)hex-5-yn-2-one (8)



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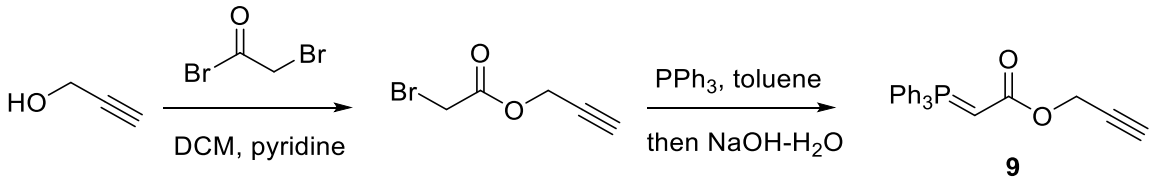
To an oven-dried and N_2-flushed flask was added a solution of 1-(triphenylphosphoranylidene)-2-propanone (954 mg, 3.00 mmol) in dry THF (20 mL). The solution was cooled to -78 °C then *n*-BuLi (2.33 mL, 1.8 M in hexane, 4.20 mmol) was slowly added and the resulting brown solution was stirred at -78 °C for 1 h. Then propargyl bromide (80 wt% in toluene, 400 µL, 4.20 mmol) was added and the solution was slowly warmed to room temperature and stirred overnight. Solvent was removed *in vacuo* and the mixture was diluted in DCM (30 mL), washed with water (20 mL x 3), dried (Na_2SO_4) and concentrated *in vacuo*.

The crude product was purified by flash chromatography (1-5% MeOH in DCM) and further purified by prep-HPLC (5-100% ACN in H_2O) to afford the title product as a white solid (557.1 mg, 1.56 mmol, 52% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 (m, 15H), 3.75 (d, *J* = 25.0 Hz, 1H), 2.55 (m, 4H), 1.95 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 190.71 (d, *J* = 2.2 Hz), 133.09 (d, *J* = 10.2 Hz), 132.06 (d, *J* = 2.9 Hz), 128.84 (d, *J* = 12.0 Hz), 127.01 (d, *J* = 90.3 Hz), 85.34, 67.81, 51.59 (d, *J* = 107.4 Hz), 39.90 (d, *J* = 15.8 Hz), 15.93. **MS** (ESI) Calculated for $C_{24}H_{22}OP$ [M+H$^+$] 357.1; observed 357.2

Preparation of prop-2-yn-1-yl 2-(triphenylphosphaneylidene)acetate (9)



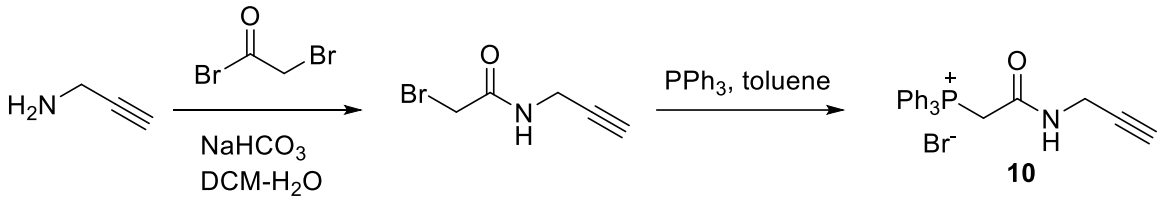
9

Step 1: To a solution of propargyl alcohol (58 µL, 1.0 mmol) and pyridine (81 µL, 1.0 mmol) in DCM (10 mL) at 0 °C, bromoacetyl bromide (87 µL, 1.0 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 20 min then warmed to room temperature and stirred for 30 min. After that, water (15 mL) was added and the mixture was extracted with DCM (10 mL x 3). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*.

Step 2: The crude bromoacetyl ester above was dissolved in 3 mL toluene, and slowly added into a solution of triphenylphosphine (262 mg, 1.0 mmol) in toluene (3 mL). The mixture was stirred at room temperature overnight. The white precipitate was filtered, washed with toluene (10 mL) and hexane (10 mL), and taken in water (10 mL). NaOH (2 M) was added until the pH of the solution reached 8-9. The mixture was extracted with DCM (10 mL x 3), dried (Na_2SO_4) and concentrated to give the title product as a yellow oil (282 mg, 79 % in two steps). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.58 (m, 15H), 4.46 (d, *J* = 2.4 Hz, 2H), 3.32 (t, *J* = 2.5 Hz, 1H), 2.85 (d, *J* = 21.9 Hz, 1H). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.95 (d, *J* = 15.0 Hz), 132.55 (d, *J* = 10.1 Hz), 132.33 (d, *J* = 2.8 Hz), 129.02 (d, *J* = 11.9 Hz), 126.91 (d, *J* =

91.5 Hz), 80.94, 75.64, 48.82 (d, *J* = 3.5 Hz), 29.14 (d, *J* = 127.6 Hz). **MS** (ESI) Calculated for $C_{23}H_{20}O_2P$ [M+H$^+$] 359.1; observed 359.0.

Preparation of (2-oxo-2-(prop-2-yn-1-ylamino)ethyl)triphenylphosphonium bromide (10)

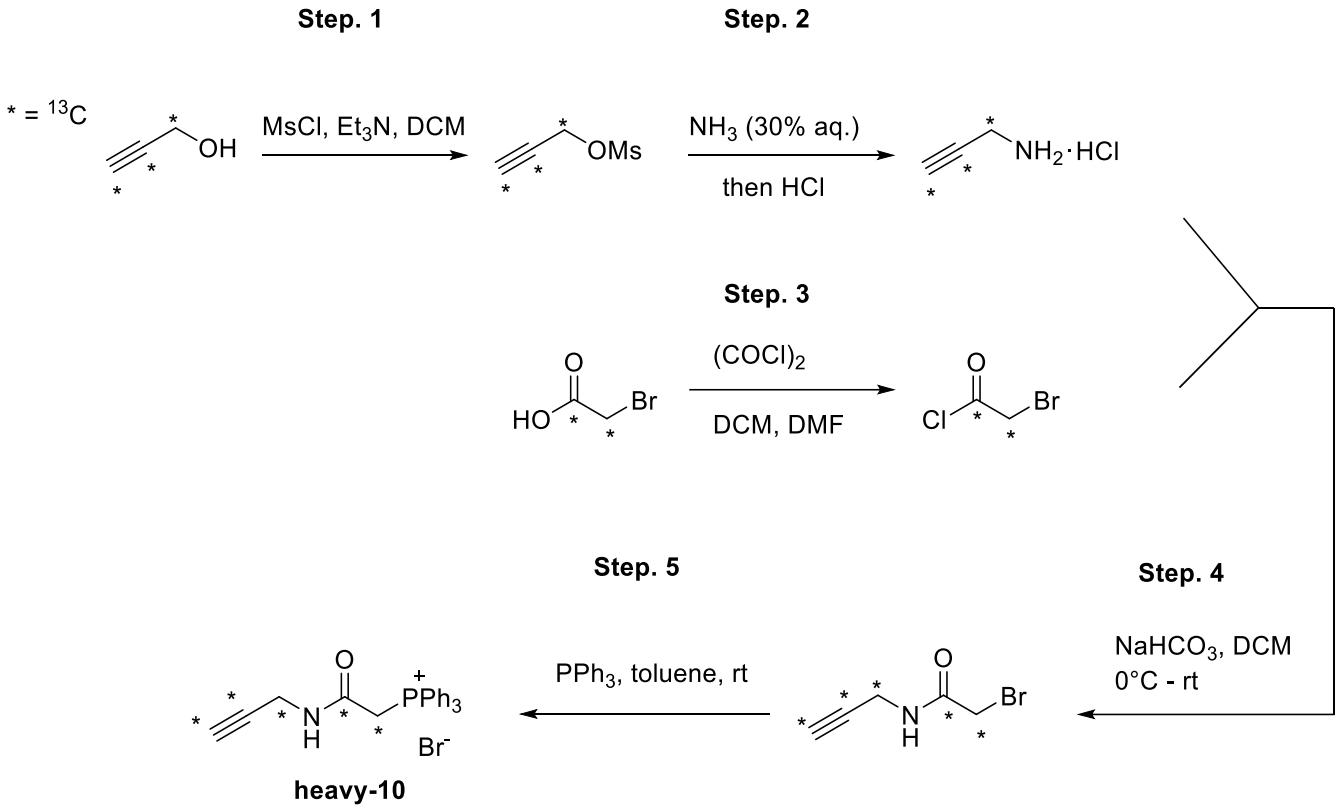


10

Step 1: Propargylamine (0.30 g, 5.45 mmol) was dissolved in 10 mL DCM and 10 mL $NaHCO_3$ (sat'd aq. soln.). The mixture was vigorously stirred at -10 °C and bromoaceytl bromide (0.7 mL, 8.17 mmol) was slowly added. The mixture was slowly warmed to rt and stirred for 3 h. DCM was removed *in vacuo* and the mixture was extracted with EtOAc (10 mL x 3). The combined organic layers were washed with sat'd $NaHCO_3$, 1 M HCl and brine (20 mL each), dried (Na_2SO_4) and concentrated to afford the bromoacetamide compound as an off-white solid.

Step 2: Part of the crude bromoacetamide compound above (176 mg) was treated with PPh_3 (262 mg, 1.0 mmol) in toluene (5 mL) overnight. The precipitate was filtered, washed with toluene (10 mL) and hexane (10 mL). The precipitate was purified by flash chromatography (1-7% MeOH in DCM), followed by prep-HPLC purification (5-100% ACN in H_2O) to afford the title compound as a white powder (352 mg, 0.804 mmol, 80% yield). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.01 (m, 1H), 7.83 (m, 15H), 5.03 (d, *J* = 15.0 Hz, 2H), 3.81 (dd, *J* = 5.5, 2.6 Hz, 2H), 3.16 (m, 1H)**. ^{13}C NMR** (100 MHz, DMSO-d_6) δ 162.67 (d, *J* = 4.6 Hz), 134.86 (d, *J* = 3.2 Hz), 133.73 (d, *J* = 10.4 Hz), 130.06, 118.65 (d, *J* = 88.7 Hz), 79.75, 73.63, 30.97 (d, *J* = 58.0 Hz), 28.47. **MS** (ESI) Calculated for $C_{23}H_{21}NOP$ [M$^+$] 358.1; observed 358.2.

584 **Preparation of $^{13}C_5$-WYneN (heavy-10)**



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586 **Step 1**: $^{13}C_3$-Propargyl alcohol (250 mg, 4.24 mmol) was dissolved in dry DCM (10 mL) and Et_3N (4.7
587 mmol) was added. The mixture was cooled to 0 °C then MsCl (4.7 mmol) was added dropwise. After
588 warming to rt (15 min), the mixture was stirred for another 2 h @ rt. The mixture was diluted with 5 mL
589 DCM and 15 mL NH_4Cl (sat'd aqueous solution). The organic layer was washed with 15 mL $NaHCO_3$
590 (sat'd aqueous solution) and 15 mL brine. The organic layer was dried and concentrated to afford the
591 crude mesylate as a yellow oil (595 mg, quantitative yield).

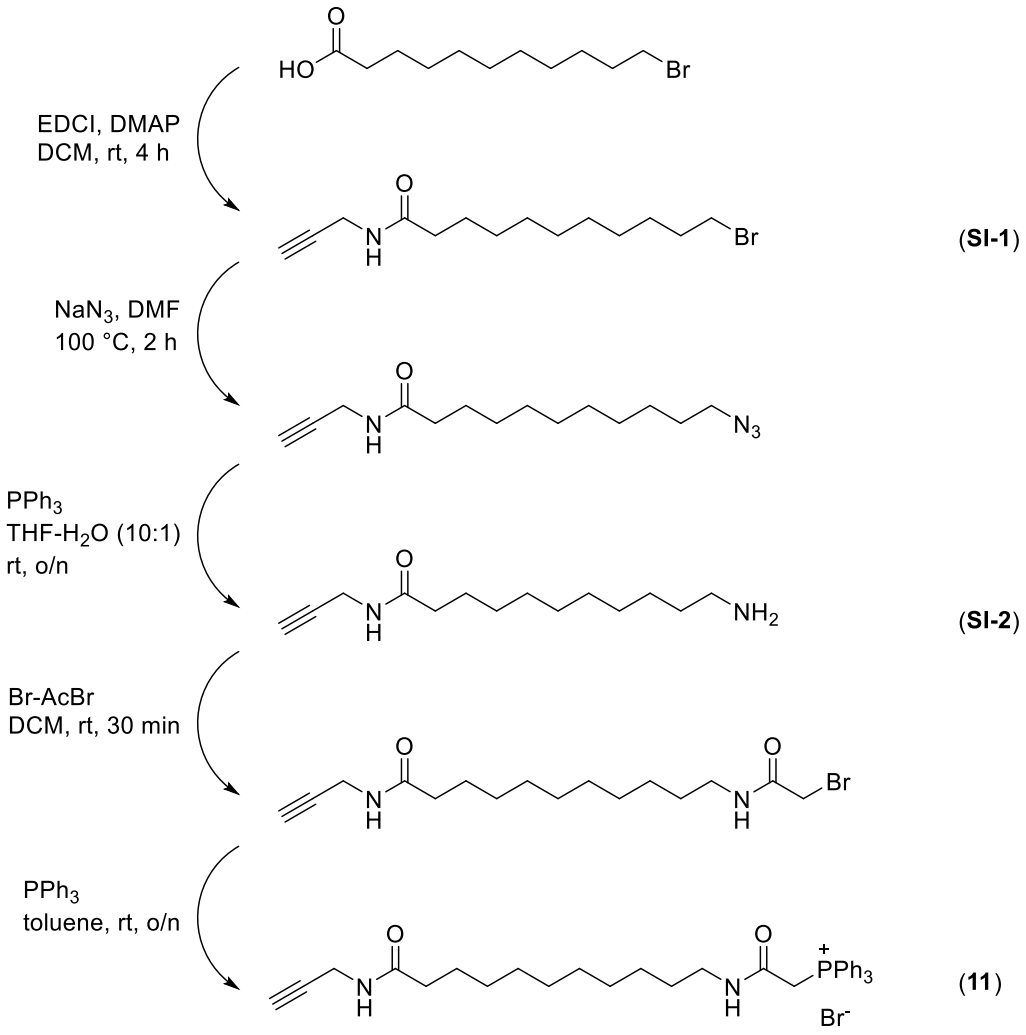
592 **Step 2**: 3.00 mmol of the mesylate above was dissolved in 10 mL aqueous ammonia (30%). The mixture
593 was stirred at room temperature for 3 h. After dilution with 5 mL NaOH (2 M), the aqueous layer was
594 extracted with DCM (10 mL x 3). Nitrogen gas was bubbled in the combined organic layers for 1 h, until
595 the vapor gave a negative alkali test (moist pH paper). 2 mL HCl (4 M in dioxane) was added, and the
596 solvent was removed *in vacuo*. The white precipitate was washed with cold ether (1 mL x 3) and dried to
597 afford $^{13}C_3$-propargylamine hydrochloride (127 mg, 1.35 mmol, 45% yield).

Step 3: $^{13}C_2$-bromoacetic acid (170 mg, 1.2 mmol) was dissolved in dry DCM (5 mL) with catalytic DMF (20 µL). Oxalyl chloride (2.4 mmol) was slowly added while stirring at room temperature. After 1 h, volatiles were removed *in vacuo* to afford the crude acid chloride which was used immediately in the next step.

Step 4: $^{13}C_3$-propargylamine hydrochloride (127 mg, 1.35 mmol) was dissolved in 5 mL DCM and 5 mL $NaHCO_3$ (sat'd aqueous solution) and cooled to 0 °C. The acid chloride above (1.2 mmol) in dry DCM (5 mL) was added dropwise. The reaction mixture was slowly warmed to rt and stirring was continued for 30 min. The mixture was diluted with sat'd $NaHCO_3$ (10 mL) and extracted with DCM (15 mL x 3). After drying (Na_2SO_4), the organic layer was concentrated and purified by flash chromatography (10-40% EtOAc in hexane gradient) to afford the amide product as a white solid (74.0 mg, 0.41 mmol, 34% yield).

Step 5: The purified $^{13}C_5$-amide above (0.41 mmol) and triphenylphosphine (107 mg, 0.41 mmol) was taken in toluene (5 mL). The mixture was stirred at room temperature overnight. After removal of solvent *in vacuo*, the white precipitate was washed with cold ether (1 mL x 5), then purified by flash chromatography (1-7% MeOH in DCM) to afford the title product **heavy-10** as a white solid (104.5 mg, 0.236 mmol, 58% yield). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.93 (brs, 1H), 7.88 (m, 3H), 7.75 (m, 12H), 5.13 (dd, *J* = 14.9, 6.2 Hz, 1H), 4.80 (dd, *J* = 14.9, 6.2 Hz, 1H), 3.99 (m, 1H), 3.65 (m, 1H), 3.16 (ddq, *J* = 244, 54.7, 2.6 Hz, 1H). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 162.72 (d, *J* = 48.2 Hz), 134.87, 133.74 (d, *J* = 10.6 Hz), 130.01 (d, *J* = 13.0 Hz), 118.69 (d, *J* = 89.4 Hz), 79.90 (dd, *J* = 169.1, 71.0 Hz), 73.46 (dd, *J* = 169.0, 13.3 Hz), 30.90 (dd, *J* = 58.1, 49.4 Hz), 28.46 (dd, *J* = 70.9, 13.3 Hz). **MS** (ESI) Calculated for $^{12}C_{18}{}^{13}C_5H_{21}NOP$ [M^+] 363.1; observed 363.2.

Preparation of WYneN10 (11):



Preparation of 11-bromo-*N*-(prop-2-yn-1-yl)undecanamide (SI-1):

To a solution of 11-bromoundecanoic acid (1.00 g, 3.77 mmol) and propargylamine (256 µL, 4.00 mmol) in dry DCM (10 mL) was added EDCI (767 mg, 4.00 mmol) and DMAP (48.8 mg, 0.40 mmol). The mixture was stirred at room temperature for 4 h. After concentration *in vacuo*, the residue was purified by flash chromatography (5-20% EtOAc in hexane) to afford the title compound as a white solid (0.95 g, 3.14 mmol, 85 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.65 (brs, 1H), 4.06 (dd, *J* = 5.3, 2.6 Hz, 2H), 3.41 (t, *J* = 6.9 Hz, 2H), 2.24 (t, *J* = 2.6 Hz, 1H), 2.20 (m, 2H), 1.85 (m, 2H), 1.64 (m, 2H), 1.42 (m, 2H), 1.29 (m, 10H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.07, 79.77, 76.85, 71.49, 36.45, 34.10, 32.86, 29.39, 29.32, 29.26,

29.18, 28.77, 28.19, 25.60. **MS** (ESI) Calculated for $C_{14}H_{25}BrNO$ [M+H$^+$] 302.1, 304.1; observed 302.1, 304.1.

Preparation of 11-amino-*N*-(prop-2-yn-1-yl)undecanamide (SI-2)

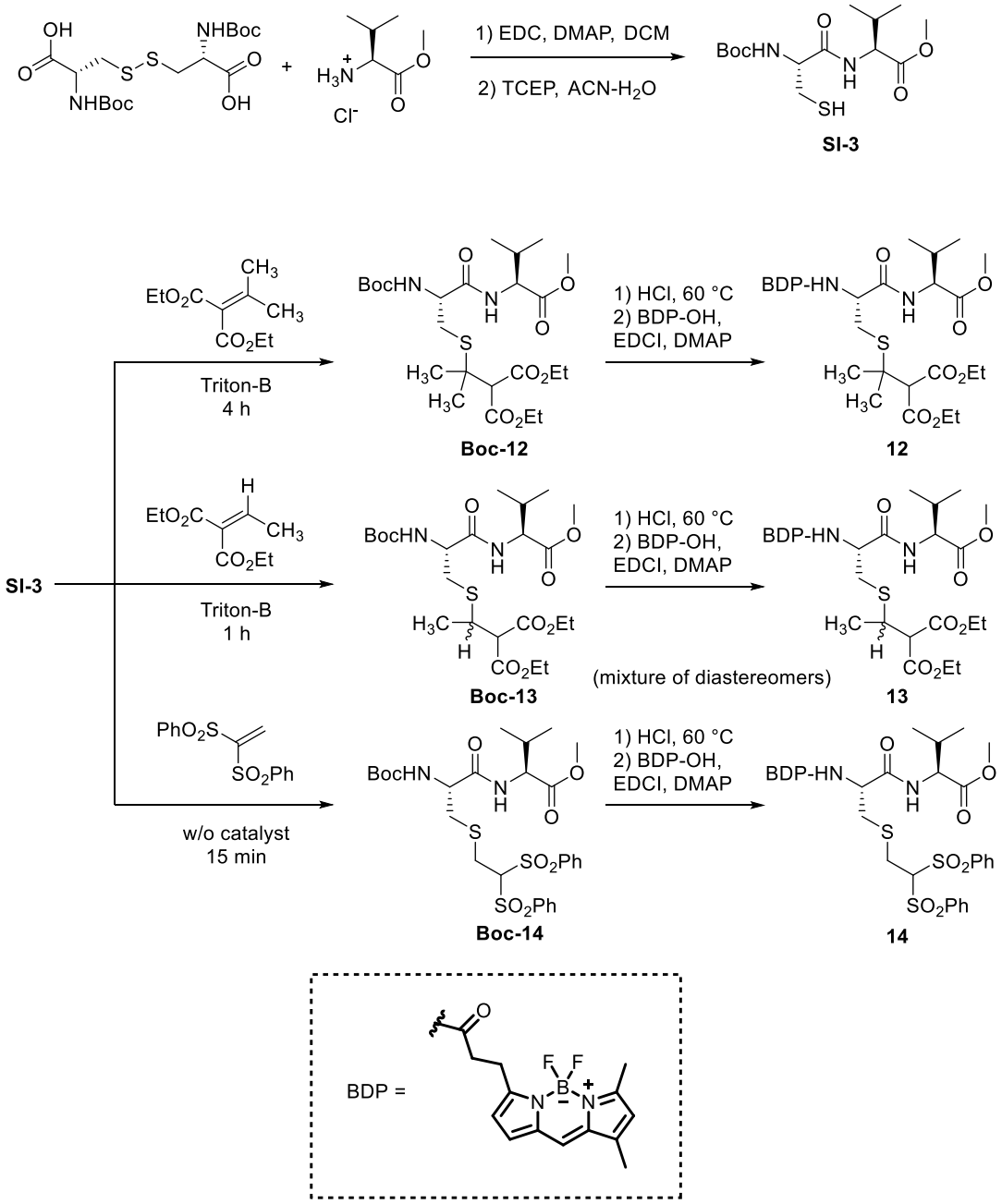
The product above (377.5 mg, 1.25 mmol) was dissolved in DMF and NaN_3 (163 mg, 2.5 mmol) was added. The mixture was heated to 100 °C with stirring in a sealed tube filled with N_2. After 2 h, the mixture was diluted with water (20 mL) and extracted with DCM (20 mL x 3). The combined organic layers were washed with brine and dried (Na_2SO_4) to afford the crude azido compound as a white solid (301.0 mg, 1.23 mmol), which was dissolved in THF (5 mL) and H_2O (0.5 mL). Triphenylphosphine (655 mg, 2.5 mmol) was added, and the solution was stirred at room temperature overnight. After concentrating *in vacuo*, the precipitate was washed several times in cold EtOAc to afford the title compound as a white solid (194.1 mg, 0.816 mmol, 65% yield in two steps). **^{1}H NMR** (400 MHz, Methanol-d_4) δ 3.94 (s, 2H), 3.04 (t, *J* = 7.1 Hz, 1H), 2.61 (t, *J* = 7.2 Hz, 2H), 2.19 (t, *J* = 7.5 Hz, 2H), 1.60 (t, *J* = 7.0 Hz, 2H), 1.45 (t, *J* = 7.1 Hz, 2H), 1.31 (m, 12H). **^{13}C NMR** (100 MHz, Methanol-d_4) δ 175.92, 80.32, 71.80, 42.65, 36.83, 34.00, 30.64, 30.60, 30.55, 30.40, 30.21, 29.34, 28.05, 26.87. **MS** (ESI) Calculated for $C_{14}H_{27}N_2O$ [M+H$^+$] 239.2; observed 239.2.

Preparation of (2-oxo-2-((11-oxo-11-(prop-2-yn-1-ylamino)undecyl)amino)ethyl)Triphenyl-phosphonium bromide (11)

Compound **SI-2** (22 mg, 0.092 mmol) was dissolved in dry DCM (1 mL) and treated with DIPEA (20 µL, 0.115 mmol) and bromoacetyl bromide (10 µL, 0.115 mmol). After 30 min, the mixture was diluted in brine (10 mL) and extracted with DCM (10 mL x 3). The organic layers were combined, dried (Na_2SO_4) and concentrated *in vacuo* to afford the crude product as a yellow oil (20.7 mg, 0.058 mmol, 63%). The yellow oil above (20.7 mg, 0.058 mmol) was taken in toluene (1 mL) and treated with triphenylphosphine (30.4 mg, 0.115 mmol). After stirring overnight at rt, the mixture was concentrated and dissolved in H_2O-ACN

(2 mL + 2 mL). The title compound **11** was obtained by HPLC purification (5-100% ACN in H_2O, eluted at 18-20 min) followed by lyophilization: (yield calculated as bromide salt) 12.3 mg, 0.020 mmol, 34 % yield). **^{1}H NMR (400 MHz, DMSO-d_6)** δ 9.53 (brs, 1H), 8.33 (brs, 1H), 7.78 (m, 15H), 5.07 (brs, 2H), 3.82 (dd, J = 5.5, 2.5 Hz, 2H), 3.06 (t, *J* = 2.5 Hz, 1H), 2.93 (q, *J* = 6.3 Hz, 2H), 2.07 (t, *J* = 7.4 Hz, 2H), 1.47 (m, 2H), 1.22 (m, 14H). **^{13}C NMR (100 MHz, DMSO-d_6)** δ 171.90, 171.90, 134.64, 134.61, 133.83, 133.72, 129.90, 129.77, 81.39, 72.66, 39.02, 35.03, 28.88, 28.83, 28.73, 28.61, 28.60, 28.58, 27.67, 26.20, 25.11. **MS** (ESI) Calculated for $C_{34}H_{42}N_2O_2P$ [M^+] 541.3; observed 541.3.

680 **Preparation of redox-caged sulfenic acids 12-14:**



681

682 **Preparation of Boc-Cys-Val-OMe dipeptide (SI-3)**

683 To a N_2-flushed flask containing (Boc-Cys-OH)$_2$ (440.5 mg, 1.0 mmol), *L*-Valine methyl ester
684 hydrochloride (502.9 mg, 3.0 mmol) in 20 mL dry DCM at 0 °C was added EDCI·HCl (575.1 mg, 3.0 mmol)
685 and DMAP (12.2 mg, 0.1 mmol). The mixture was slowly warmed and stirred at room temperature
686 overnight, diluted with EtOAc (60 mL) washed with sat'd $NaHCO_3$ (30 mL x 2) and brine (30 mL). The

687 organic layer was dried, concentrated and purified by chromatography (20-50% EtOAc in hexane) to
688 afford the disulfide (Boc-Cys-Val-OMe)$_2$ as a white solid, which was dissolved in ACN-H_2O (15 mL + 15
689 mL) was added tris(2-carboxyethyl)phosphine hydrochloride (TCEP·HCl, 573.3 mg, 2.0 mmol). The
690 solution was stirred at 37 °C for 5 h. After completion, it was diluted in DCM (20 mL) and washed with
691 sat'd $NaHCO_3$ (20 mL x 2) and brine (20 mL), dried (Na_2SO_4) and concentrated *in vacuo* to afford the title
692 compound **SI-3** as a white solid (185.1 mg, 0.553 mmol, 55% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.85
693 (brs, 1H), 5.48 (brs, 1H), 4.51 (dd, *J* = 8.7, 4.9 Hz, 1H), 4.34 (m, 1H), 3.73 (s, 3H), 3.05 (m, 1H), 2.73 (m,
694 1H), 2.19 (m, 1H), 1.69 (m, 1H), 1.45 (s, 9H), 0.92 (dd, *J* = 11.9, 6.9 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$)
695 δ 172.17, 170.38, 155.69, 80.83, 57.56, 55.69, 52.44, 31.28, 28.47, 26.82, 19.23, 17.92. **MS** (ESI)
696 Calculated for $C_{14}H_{26}N_2NaO_5S$ [M+Na^+] 357.1; observed 357.2.

697

698 **General procedure for the preparation of Boc-protected precursor Boc12-14**

699 To an oven-dried, N_2-flushed flask containing 66.8 mg (0.20 mmol) of dipeptide **SI-3** in 2 mL dry THF at
700 -78°C was added Triton-B (8 µL, 40% in methanol, 0.02 mmol) in 2 mL dry THF dropwise, then
701 corresponding electron-deficient alkene (0.15 mmol) in 2 mL dry THF was added dropwise. The reaction
702 mixture was then stirred at room temperature until completion of reaction (see scheme above), then
703 diluted with brine (20 mL) and extracted with DCM (20 mL x 3). The combined organic layers were dried
704 (Na_2SO_4), concentrated and purified by chromatography (20-50% EtOAc in hexane) to afford Boc-
705 protected compounds **Boc12-14**.

706

707 **Diethyl 2-(2-(((*R*)-2-((tert-butoxycarbonyl)amino)-3-(((*S*)-1-methoxy-3-methyl-1-oxobutan-2-**
708 **yl)amino)-3-oxopropyl)thio)propan-2-yl)malonate (Boc-12)**

709 Compound **Boc-12** was prepared as a colorless oil, 34.6 mg, 0.065 mmol, 43% yield. **^{1}H NMR** (400 MHz,
710 $CDCl_3$) δ 6.97 (brs, 1H), 5.49 (brs, 1H), 4.47 (dd, *J* = 8.7, 4.9 Hz, 1H), 4.18 (m, 4H), 3.70 (s, 3H), 3.04
711 (dd, *J* = 12.9, 6.6 Hz, 1H), 2.88 (dd, *J* = 12.9, 6.1 Hz, 1H), 2.15 (m, 1H), 1.55 (s, 3H), 1.53 (s, 3H), 1.43

(s, 9H), 1.25 (td, *J* = 7.1, 2.3 Hz, 6H), 0.91 (dd, J = 8.9, 6.9 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.91, 170.49, 167.36, 167.12, 80.40, 61.53, 61.45, 60.41, 57.42, 52.12, 46.06, 31.29, 30.32, 28.34, 26.88, 26.54, 19.02, 17.77, 14.11. **MS** (ESI) Calculated for $C_{24}H_{43}N_2O_9S$ [M+H$^+$] 535.3; observed 535.3.

Diethyl 2-(1-(((*R*)-2-((tert-butoxycarbonyl)amino)-3-(((*S*)-1-methoxy-3-methyl-1-oxobutan-2-yl)amino)-3-oxopropyl)thio)ethyl)malonate (Boc-13)

Compound **Boc-13** was isolated as an inseparable mixture of diastereomers. Off-white solid, 54.8 mg, 0.105 mmol, 70% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.05, 6.97 (brs, 1H), 5.63, 5.48 (brs, 1H), 4.50 (m, 1H), 4.40, 4.31 (m, 1H), 4.21 (m, 4H), 3.72, 3.70 (s, 3H), 3.51 (m, 2H), 2.92 (m, 2H), 2.17 (m, 1H), 1.45, 1.45 (s, 9H), 1.41, 1.39 (s, 3H), 1,27, 1.27 (t, *J* = 7.1 Hz, 6H), 0.94, 0.91 (t, *J* = 8.6 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.00, 171.89, 170.70, 170.55, 168.00, 167.69, 167.42, 80.47, 80.21, 61.85, 61.79, 58.28, 58.17, 57.60, 57.41, 52.22, 52.13, 40.11, 38.83, 31.35, 31.17, 28.40, 28.36, 20.11, 20.08, 19.07, 17.85, 17.80, 14.16. **MS** (ESI) Calculated for $C_{23}H_{41}N_2O_9S$ [M+H$^+$] 521.3; observed 521.3.

Methyl *S*-(2,2-bis(phenylsulfonyl)ethyl)-*N*-(tert-butoxycarbonyl)-*L*-cysteinyl-*L*-valinate (Boc-14)

Compound **Boc-14** was prepared as a white solid, 85.1 mg, 0.133 mmol, 88% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 (m, 4H), 7.71 (m, 2H), 7.58 (m, 4H), 7.07 (d, *J* = 8.8 Hz, 1H), 5.52 (m, 2H), 4.51 (m, 2H), 3.74 (s, 3H), 3.59 (dd, *J* = 16.2, 4.7 Hz, 1H), 3.16 (dd, *J* = 15.9, 6.6 Hz, 1H), 2.93 (dd, *J* = 14.6, 6.8 Hz, 1H), 2.74 (dd, *J* = 14.7, 6.6 Hz, 1H), 2.20 (m, 1H), 1.50 (s, 9H), 0.92 (dd, *J* = 15.1, 6.9 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.01, 170.44, 155.67, 138.06, 137.05, 134.93, 134.68, 130.24, 129.85, 129.18, 129.13, 83.23, 80.33, 57.59, 53.62, 52.26, 37.44, 30.83, 28.44, 19.12, 17.65. **MS** (ESI) Calculated for $C_{28}H_{39}N_2O_9S_3$ [M+H$^+$] 643.2 observed 643.3.

General procedure for the preparation of fluorescent redox-caged sulfenic acids 12-14

Boc12-14 (0.05 mmol) was treated with 2 mL HCl (4.0 M solution in dioxane) and microwaved at 60 °C for 20 min. After cooling, the solution was concentrated *in vacuo*, taken in DCM (10 mL) and washed with sat'd $NaHCO_3$ solution (10 mL). The aqueous layer was extracted with DCM (10 mL x 2). Combined organic solutions were dried (Na_2SO_4) and concentrated *in vacuo*. The product above and 3-BODIPY-propanoic acid (0.05 mmol) was dissolved in dry DCM at 0 °C, followed by addition of EDCI·HCl (0.05 mmol) and DMAP (0.01 mmol). The mixture was slowly warmed to room temperature while stirring for 3 h. After completion, the mixture was diluted with DCM (10 mL) and washed with sat'd $NaHCO_3$ (10 mL) and brine (10 mL). The organic layer was dried (Na_2SO_4), concentrated and purified by flash chromatography (10-50% EtOAc in hexane) to afford compound **12-14**.

Diethyl 2-(2-(((R)-2-(3-(5,5-difluoro-7,9-dimethyl-5*H*-5λ^4,6λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-3-yl)propanamido)-3-(((*S*)-1-methoxy-3-methyl-1-oxobutan-2-yl)amino)-3-oxopropyl)thio)propan-2-yl)malonate (12)

Compound **12** was prepared as a dark red solid, 19.8 mg, 0.028 mmol, 56% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.6 Hz, 1H), 7.07 (s, 1H), 6.86 (d, *J* = 4.0 Hz, 1H), 6.78 (d, *J* = 6.8 Hz, 1H), 6.28 (d, *J* = 4.1 Hz, 1H), 6.10 (s, 1H), 4.61 (td, *J* = 7.1, 5.8 Hz, 1H), 4.44 (dd, *J* = 8.6, 5.0 Hz, 1H), 4.20 (m, 4H), 3.79 (s, 1H), 3.71 (s, 3H), 3.30 (t, *J* = 7.5 Hz, 2H), 3.02 (dd, *J* = 13.6, 5.8 Hz, 1H), 2.72 (m, 3H), 2.55 (s, 3H), 2.24 (s, 3H), 2.17 (m, 1H), 1.58 (s, 3H), 1.55 (s, 3H), 1.26 (t, J = 7.1 Hz, 6H), 0.93 (t, *J* = 6.7 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.28, 171.83, 170.33, 167.82, 167.31, 160.52, 157.31, 143.96, 135.32, 133.50, 128.23, 123.91, 120.55, 117.28, 61.69, 61.55, 60.48, 57.75, 53.09, 52.18, 46.33, 35.52, 31.05, 30.17, 27.05, 26.37, 24.69, 19.14, 17.87, 15.06, 14.15, 11.42. **MS** (ESI) Calculated for $C_{33}H_{48}BF_2N_4O_8S$ [M+H$^+$] 709.3 observed 709.3.

Diethyl 2-(1-(((R)-2-(3-(5,5-difluoro-7,9-dimethyl-5*H*-5λ^4,6λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-3-yl)propanamido)-3-(((*S*)-1-methoxy-3-methyl-1-oxobutan-2-yl)amino)-3-oxopropyl)thio)ethyl)malonate (13)

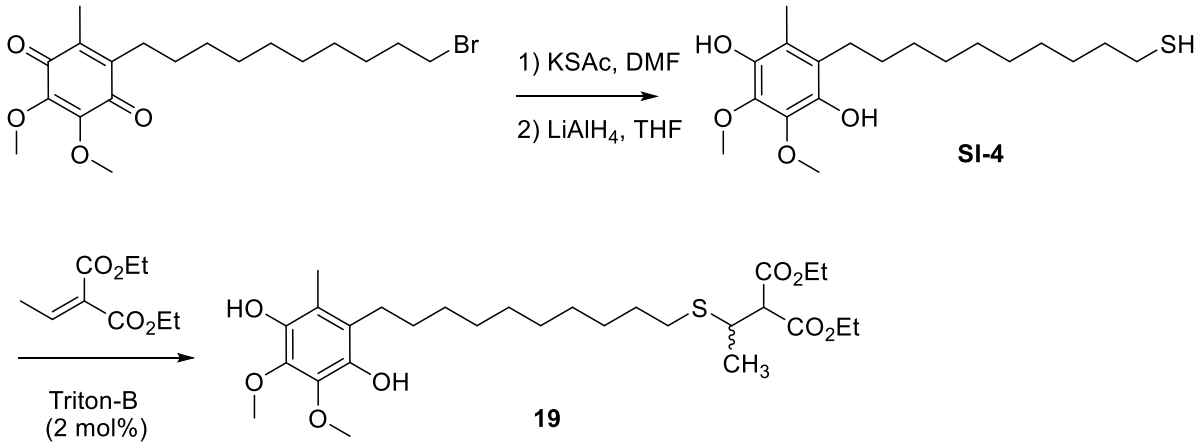
Compound **13** was isolated as an inseparable mixture of diastereomers. Dark red solid, 15.0 mg, 0.022 mmol, 43% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.15; 7.07 (d, *J* = 8.7 Hz, 1H), 7.07 (s, 1H), 6.87 (m, 1H), 7.03; 6.66 (d, *J* = 7.0 Hz, 1H), 6.30; 6.27(d, *J* = 4.1 Hz, 1H), 6.10 (s, 1H), 4.71 (m, 1H), 4.46 (m, 1H), 4.20 (m, 4H), 3.71; 3.70 (s, 3H), 3.55 (m, 2H), 3.32 (m, 2H), 3.17; 2.93 (dd, *J* = 14.1, 4.6 Hz, 1H), 2.69 (m, 3H), 2.55 (m, 3H), 2.24 (s, 3H), 2.17 (m, 1H), 1.43; 1.41 (d, *J* = 2.3 Hz, 3H), 1.26 (m, 6H), 0.93 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.52, 171.89, 171.78, 171.75, 170.47, 170.36, 168.46, 168.10, 167.77, 167.55, 160.56, 157.48, 157.30, 143.97, 135.34, 133.51, 128.20, 123.92, 120.54, 117.28, 67.23, 62.04, 61.89, 58.33, 57.92, 57.86, 57.64, 53.39, 52.27, 52.23, 52.15, 40.52, 38.70, 35.73, 35.41, 33.28, 32.33, 31.13, 31.00, 24.70, 20.12, 19.14, 19.13, 17.92, 17.86, 15.07, 14.19, 14.16, 14.13, 11.44. **MS** (ESI) Calculated for $C_{32}H_{46}BF_2N_4O_8S$ [M+H$^+$] 694.3 observed 694.3.

Methyl *S*-(2,2-bis(phenylsulfonyl)ethyl)-*N*-(3-(5,5-difluoro-7,9-dimethyl-5*H*-5λ^4,6λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-3-yl)propanoyl)-*L*-cysteinyl-*L*-valinate (14)

Compound **14** was prepared as a dark red solid, 17.3 mg, 0.021 mmol, 42% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12 (m, 2H), 8.07 (m, 2H), 7.68 (m, 2H), 7.58 (m, 4H), 7.09 (s, 2H), 6.88 (d, *J* = 4.1 Hz, 1H), 6.53 (d, *J* = 7.8 Hz, 1H), 6.28 (d, *J* = 4.0 Hz, 1H), 6.12 (s, 1H), 5.83 (dd, *J* = 6.5, 4.9 Hz, 1H), 4.87 (dt, J = 7.9, 6.7 Hz, 1H), 4.45 (dd, *J* = 8.7, 4.7 Hz, 1H), 3.74 (s, 3H), 3.63 (dd, *J* = 16.1, 4.9 Hz, 1H), 3.34 (t, *J* = 7.6 Hz, 2H), 3.18 (dd, *J* = 16.0, 6.5 Hz, 1H), 2.91 (dd, J = 14.8, 6.7 Hz, 1H), 2.70 (m, 3H), 2.57 (s, 3H), 2.25 (s, 3H), 2.20 (m, 1H), 0.91 (dd, *J* = 13.7, 6.9 Hz, 6H). **^{13}C NMR** (100 MHz, CDCl3) δ 171.92, 171.89, 170.25, 160.69, 157.08, 144.13, 138.00, 137.14, 135.42, 134.93, 134.69, 133.49, 130.30, 129.93, 129.23, 129.21, 128.26, 124.00, 120.65, 117.11, 82.89, 77.36, 57.75, 52.34, 52.32, 37.73, 35.31, 30.73, 28.64,

24.51, 19.20, 17.66, 15.11, 11.46. **MS** (ESI) Calculated for $C_{37}H_{44}BF_2N_4O_8S_3$ [M+H$^+$] 817.2 observed 817.2.

Preparation of redox-caged CoQ10 (Compound 19)



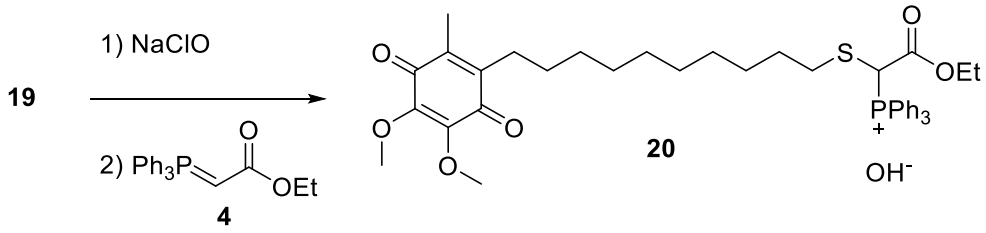
2-(10-mercaptodecyl)-5,6-dimethoxy-3-methylbenzene-1,4-diol (SI-4)

2-(10-bromodecyl)-5,6-dimethoxy-3-methylcyclohexa-2,5-diene-1,4-dione[7] (100 mg, 0.25 mmol) in 2 mL DMF was treated with potassium thioacetate (45 mg, 0.40 mmol). After stirring at room temperature for 15 min, the mixture was diluted in H_2O (15 mL) and extracted with EtOAc (15 mL x 3), dried (Na_2SO_4) and concentrated. The residue was taken in EtOH and filtered. The filtrate was concentrated again to give the crude thioacetate product as a yellow oil, which was re-dissolved in 5 mL dry THF. The resulting solution was cooled to -78 °C and $LiAlH_4$ (0.6 mL, 1.0 M in ether, 0.60 mmol) was added dropwise. After slowly warming to room temperature (30 min), the mixture was carefully quenched with 1.0 M HCl (2 mL), extracted with EtOAc (15 mL x 3), dried (Na_2SO_4) and concentrated. The product was purified by flash chromatography (10-30% EtOAc in hexane) to afford the title compound **SI-4** as a yellow oil (62.5 mg, 0.176 mmol, 70% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.89 (s, 6H), 2.59 (m, 2H), 2.53 (q, *J* = 7.5 Hz, 2H), 2.16 (s, 3H), 1.61 (m, 2H), 1.48 (m, 2H), 1.34 (m, 13H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 140.13, 139.94, 136.75, 136.73, 123.40, 117.81, 60.91, 60.85, 34.17, 29.99, 29.66, 29.63, 29.63, 29.59, 29.19, 28.49, 26.45, 24.78, 11.27. **MS** (ESI) Calculated for $C_{19}H_{33}O_4S$ [M+H$^+$] 357.2; observed 357.2.

Diethyl 2-(1-((10-(2,5-dihydroxy-3,4-dimethoxy-6-methylphenyl)decyl)thio)ethyl)malonate (19)

In a N_2-flushed oven-dried flask, compound **SI-4** (62.5 mg, 0.176 mmol) was dissolved in 2 mL dry THF. The solution was cooled to -78 °C, followed by dropwise addition of triton-B (40% w/w in MeOH, 1.6 µL, 3.52 µmol) in 1 mL dry THF, and diethyl 2-ethylidenemalonate (36.0 mg, 0.194 mmol) in 1 mL dry THF. The mixture was slowly warmed to 55 °C and stirred for 6 h, concentrated *in vacuo*, and purified by flash chromatography (10-50% EtOAc in hexane) to afford the title compound **19** as a yellow oil (59.1 mg, 0.109 mmol, 62% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.34 (d, *J* = 20.9 Hz, 2H), 4.22 (m, 4H), 3.89 (s, 6H), 3.49 (d, *J* = 9.2 Hz, 1H), 3.37 (m, 1H), 2.57 (m, 4H), 2.15 (s, 3H), 1.56 (m, 2H), 1.46 (m, 2H), 1.31 (m, 21H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.85, 167.71, 140.12, 139.94, 136.75, 136.72, 123.38, 117.77, 61.68, 61.66, 60.91, 60.85, 58.54, 39.35, 31.17, 30.00, 29.72, 29.68, 29.64, 29.64, 29.60, 29.33, 29.06, 26.45, 20.03, 14.20, 14.20, 11.27. **MS** (ESI) Calculated for $C_{28}H_{46}NaO_8S$ [M+Na^+] 565.3; observed 565.3.

Preparation of WittigQ (20)



Compound **19** (30 mg, 0.055 mmol) was dissolved in 5 mL ACN-H_2O (1:2), and treated with NaClO (0.055 mmol). With brief mixing, Wittig-CO_2Et (compound **4**, 0.55 mmol) was immediately added. The mixture was stirred at room temperature for 2 h, concentrated *in vacuo* and purified by prep-HPLC (5-100% ACN in H_2O) to afford the title compound **20** as a yellow oil (19.9 mg, 0.028 mmol, 50%). Note 1: The quinol moiety was oxidized to quinone under aerobic conditions. Note 2: At smaller scale (50 µM of **19** and NaClO, 500 µM of **4**, when NaClO was administrated slowly over 30 min *via* a syringe injector, the reaction yield was >90% as determined by LC-MS. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 (m, 15 H), 4.12 (m, 2H), 3.99 (d, J = 0.6 Hz, 6H), 2.45 (t, *J* = 7.8 Hz, 2H), 2.15 (m, 2H), 2.02 (s, 3H), 1.26 (m, 19H). **^{13}C NMR**

(100 MHz, $CDCl_3$) δ 184.88, 184.32, 144.47, 143.25, 138.81, 134.09, 133.99, 131.89, 131.86, 128.51, 128.39, 61.30, 30.02, 29.66, 29.65, 29.55, 29.49, 29.12, 28.91, 28.59, 26.57, 12.07. **MS** (ESI) Calculated for $C_{41}H_{50}O_6PS$ [M^+] 701.3; observed 701.2.

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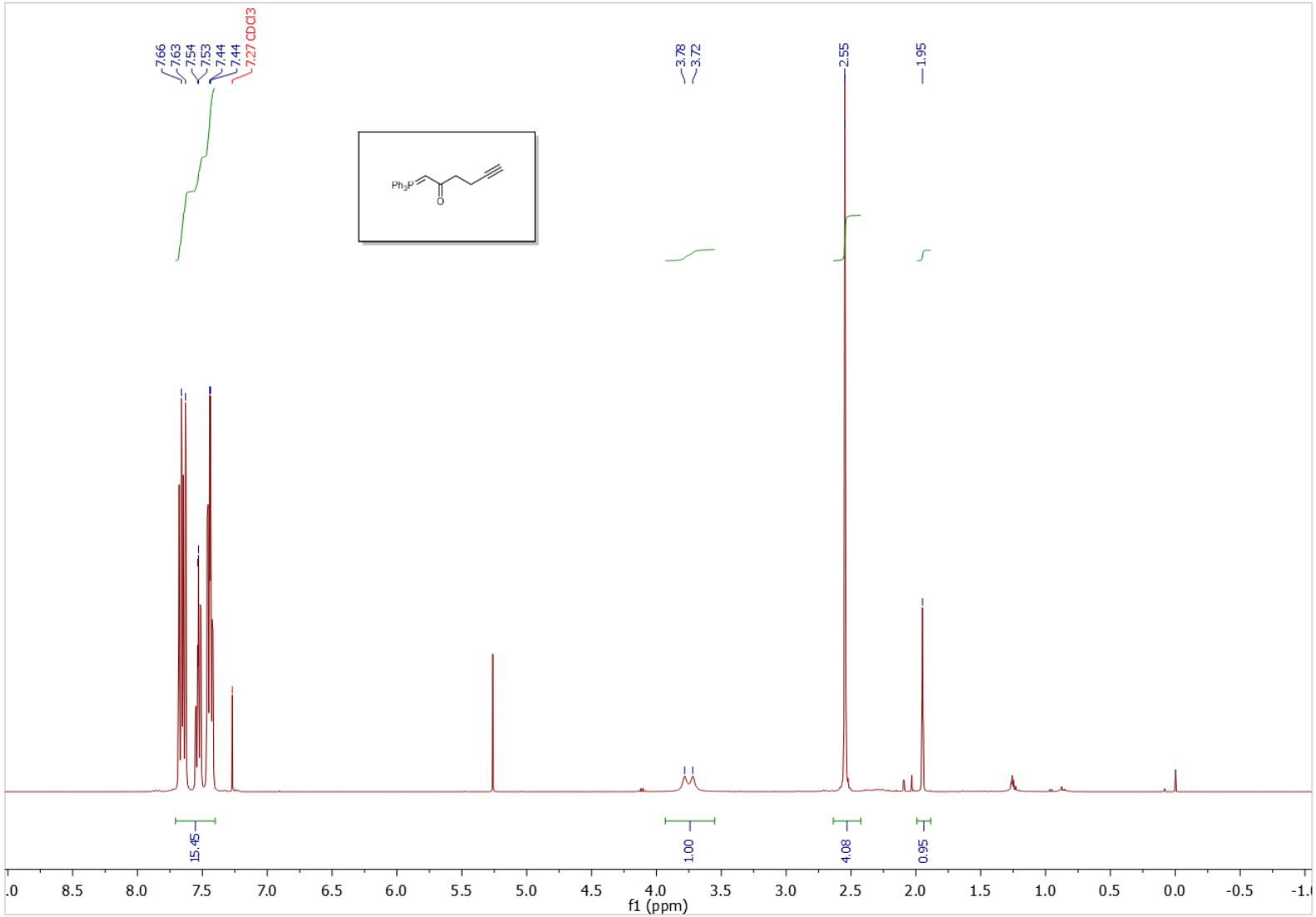
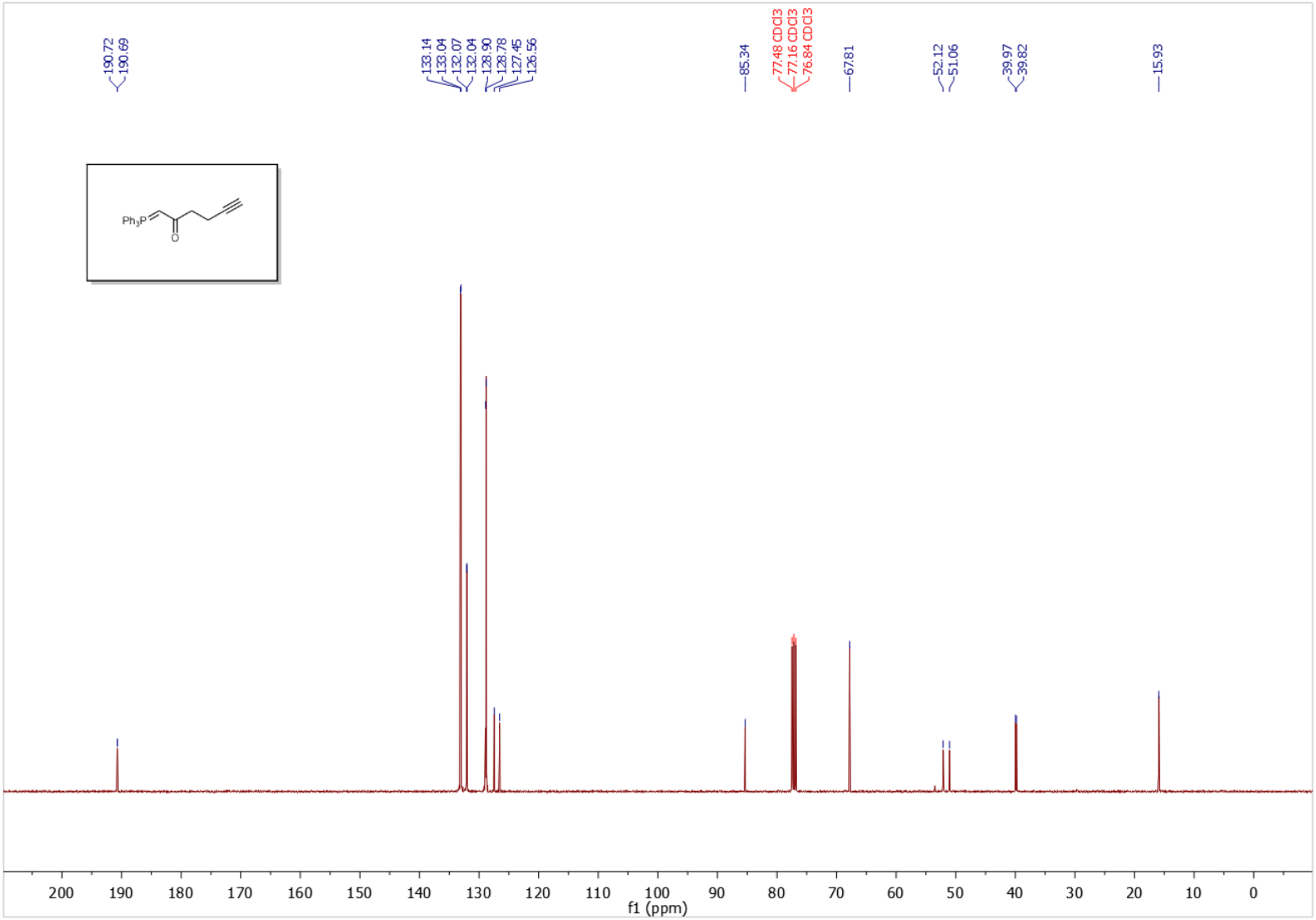
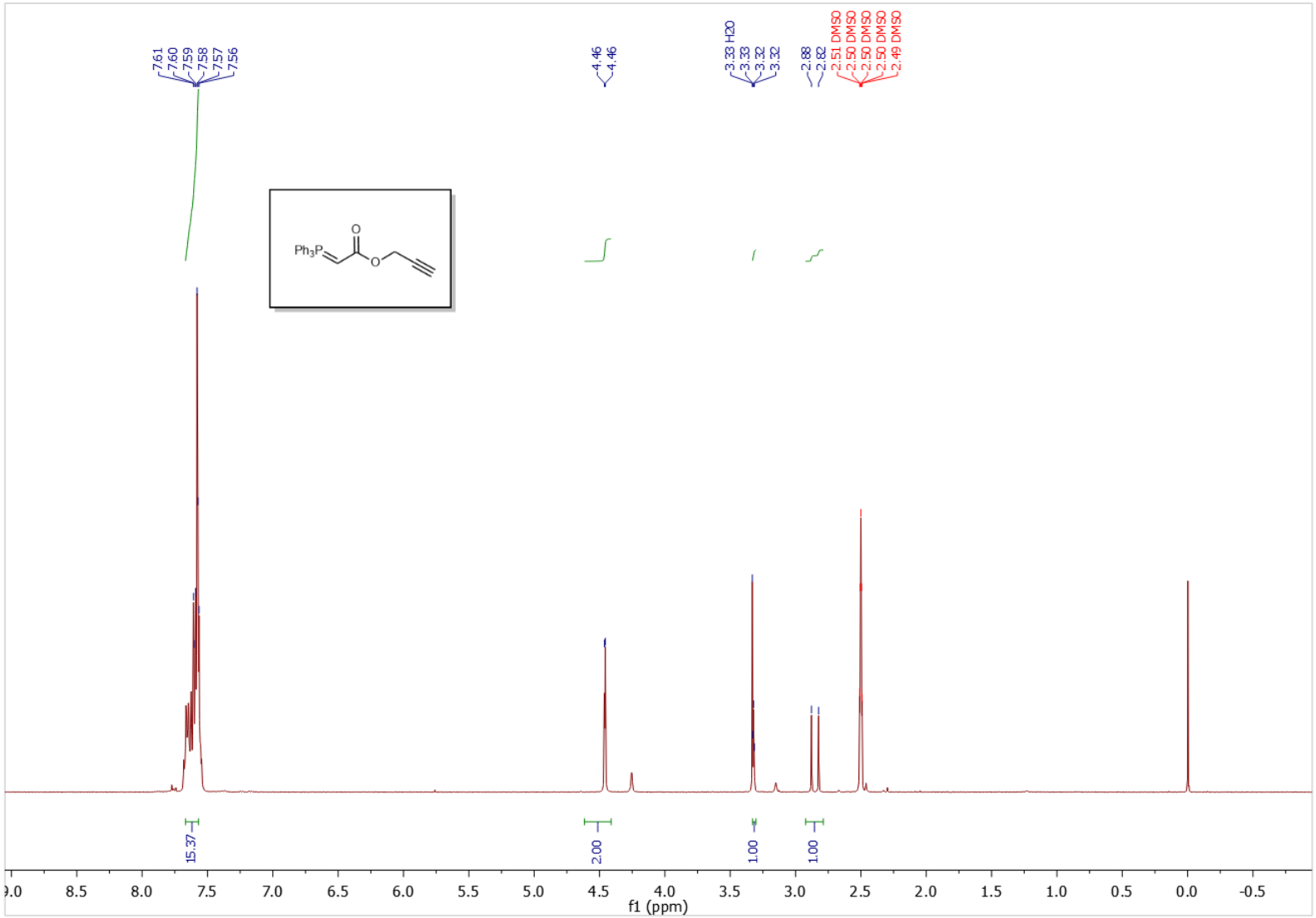


^{1}H NMR spectra of compound **8**



^{13}C NMR spectra of compound **8**



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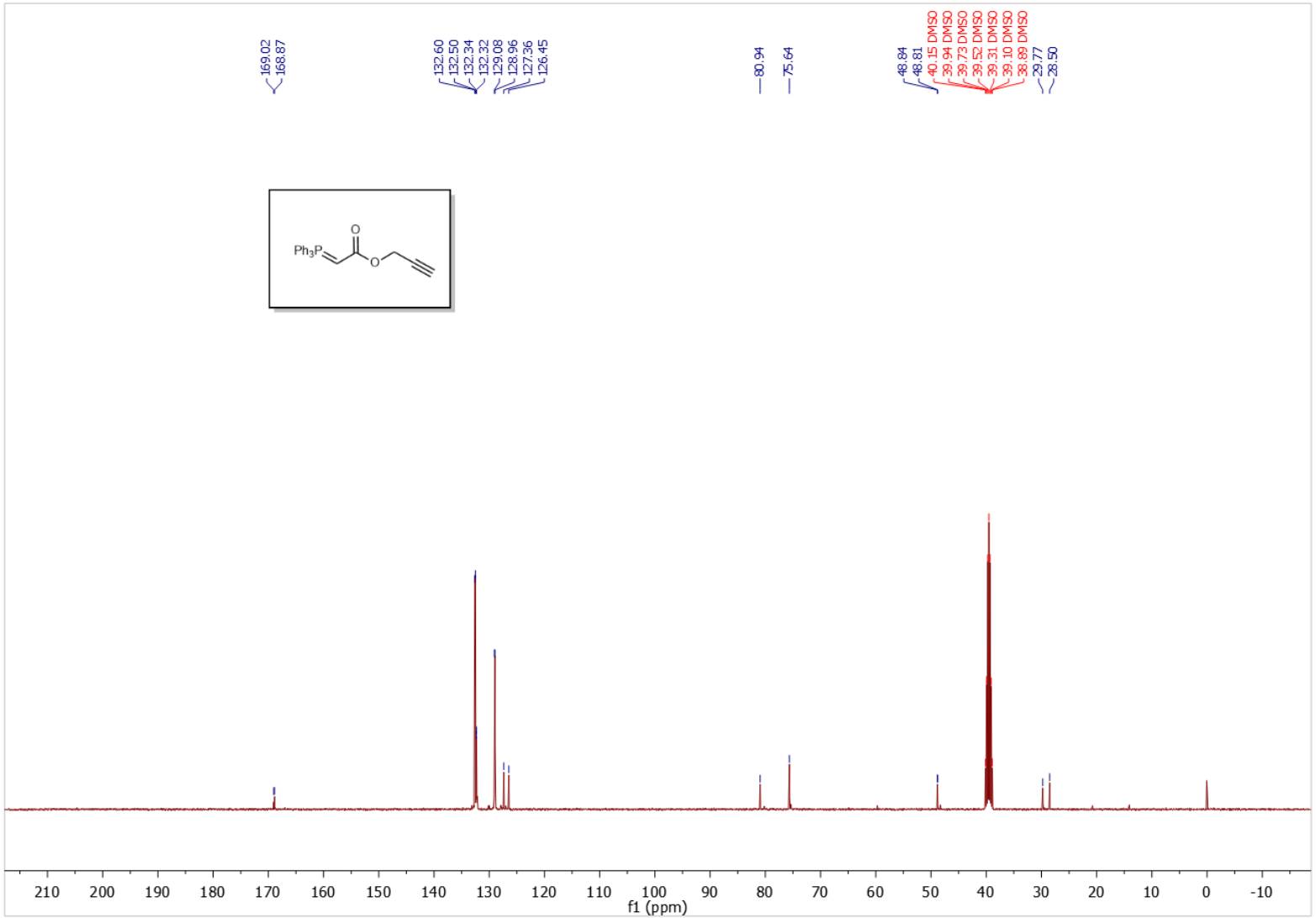
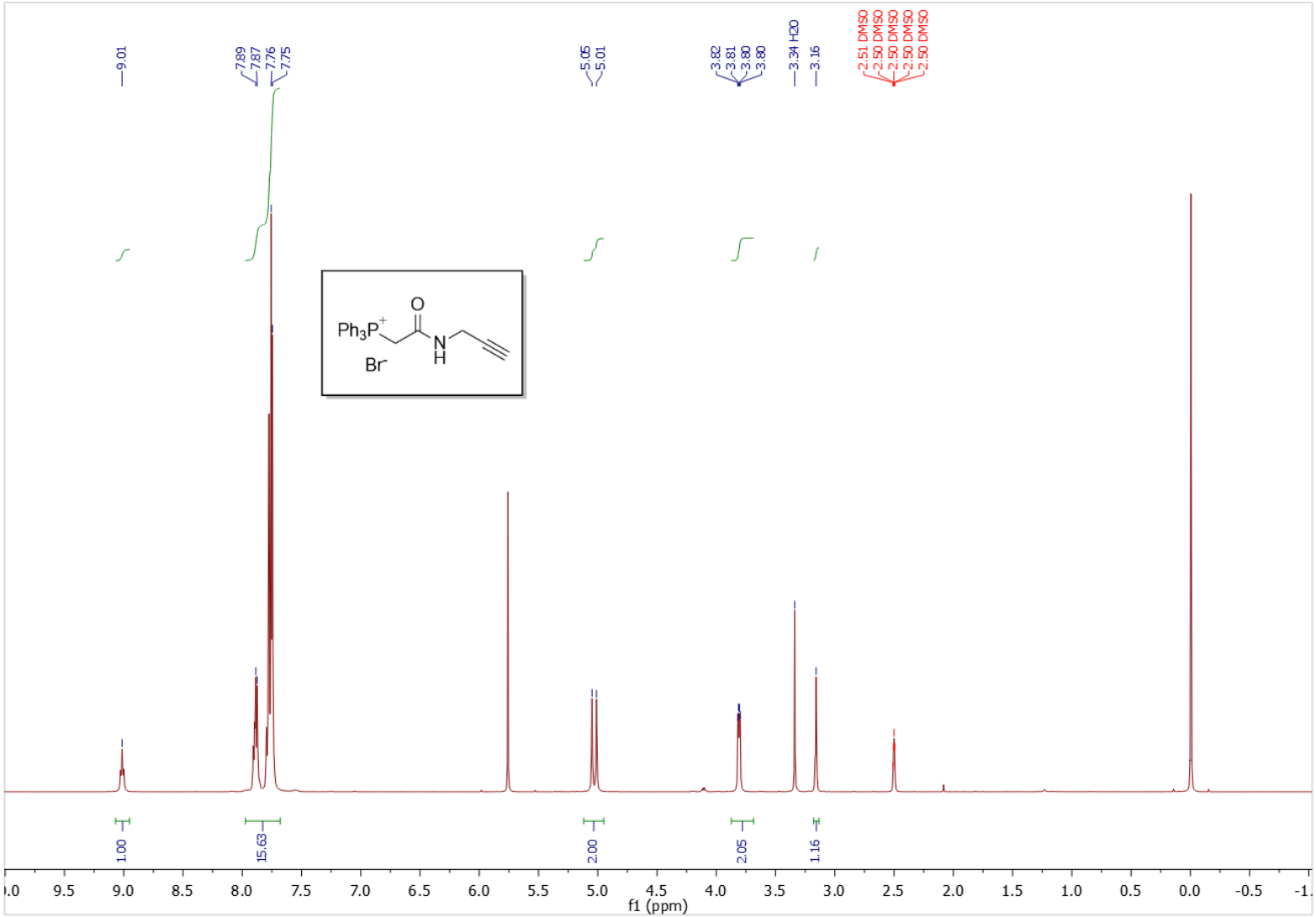
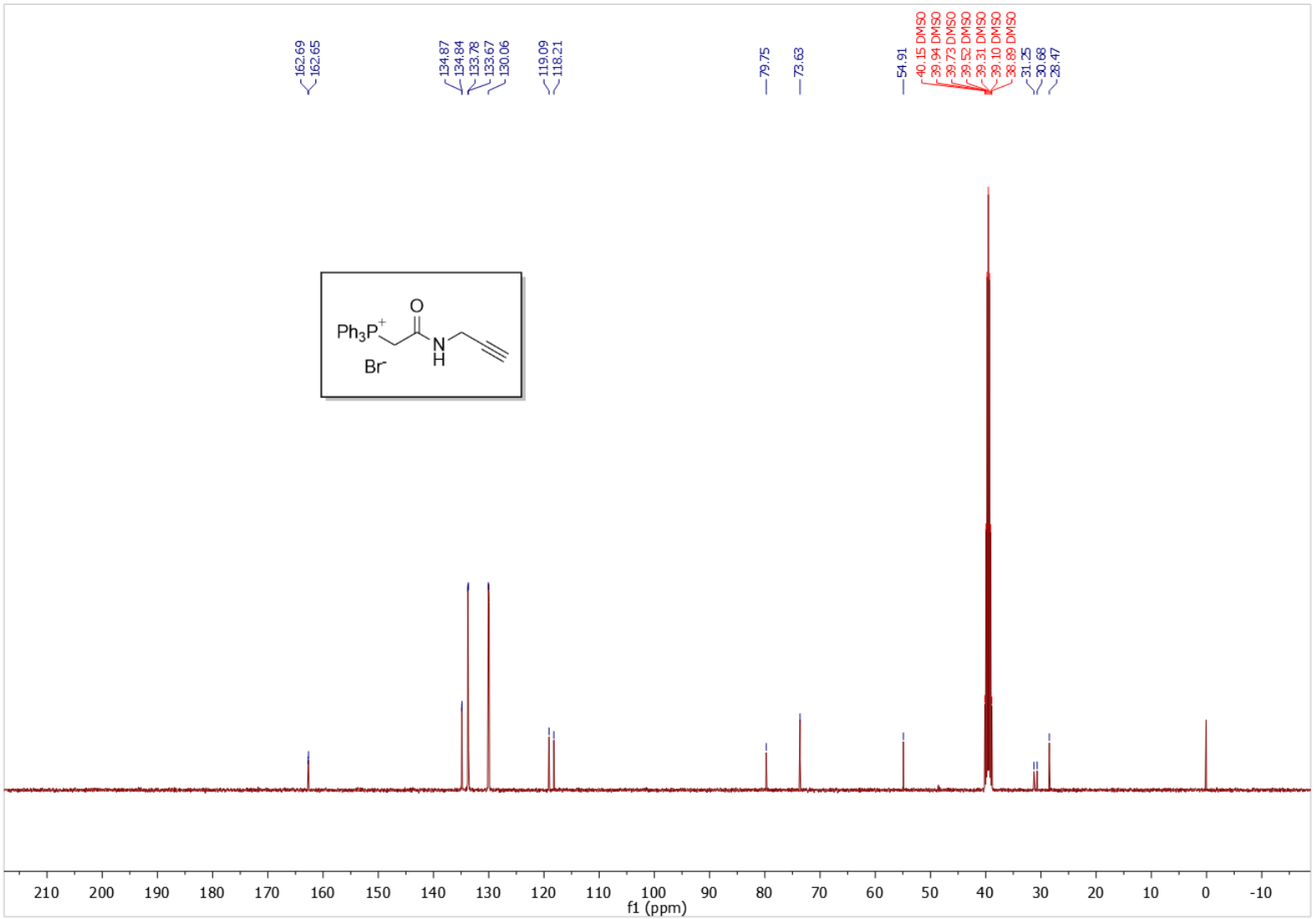


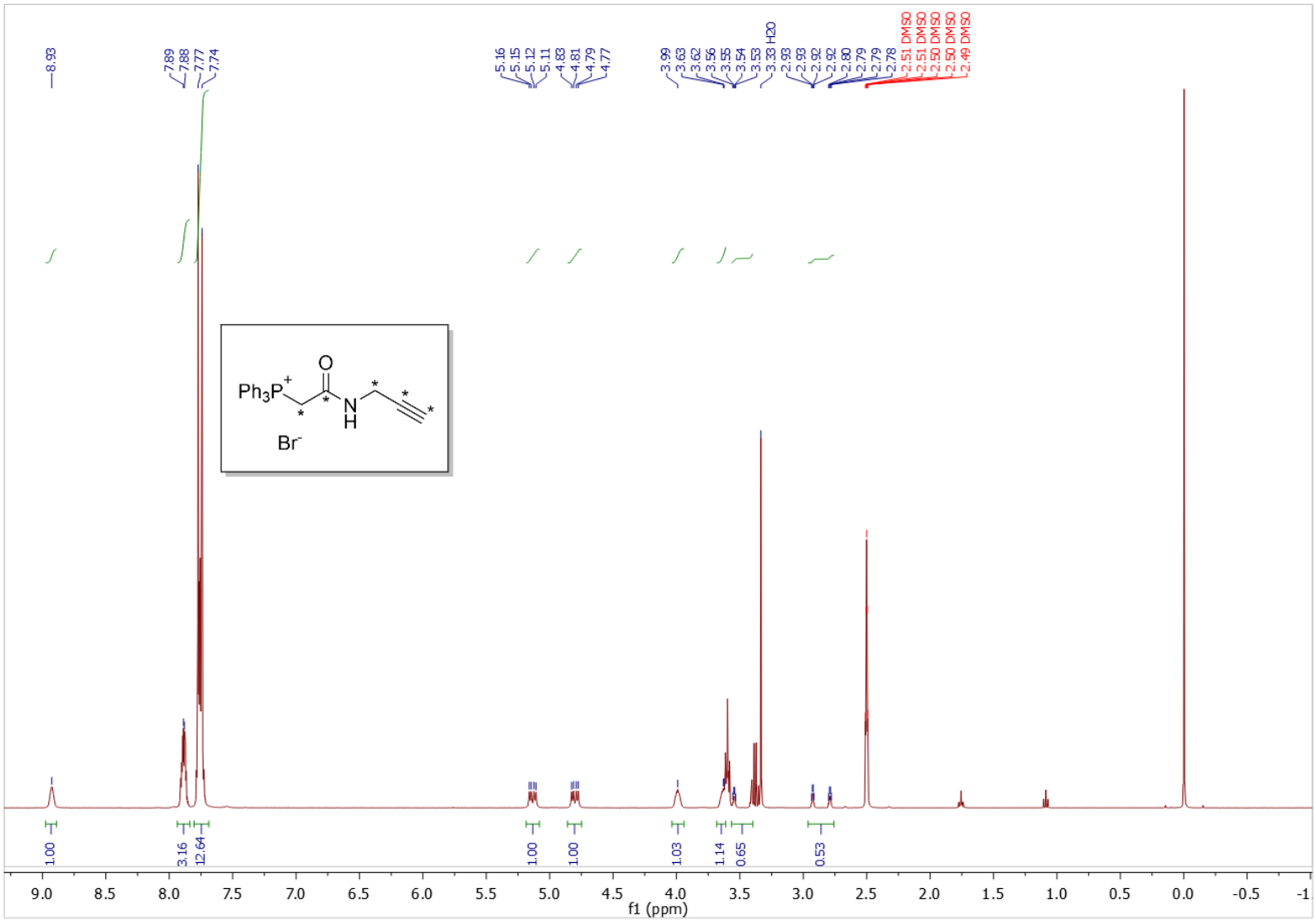
^{13}C NMR spectra of compound **9**



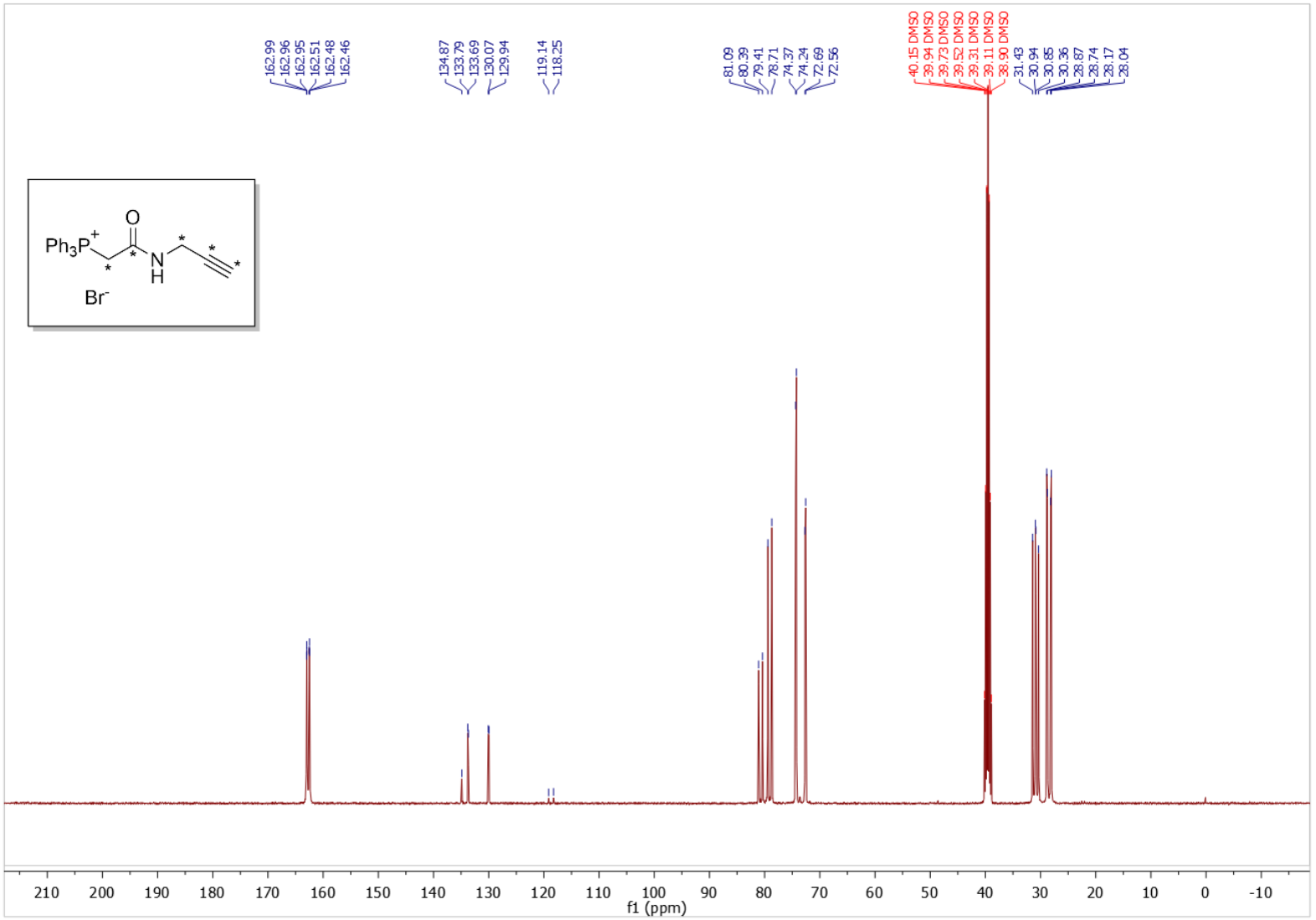
^{1}H NMR spectra of compound **10**



^{13}C NMR spectra of compound **10**



^{1}H NMR spectra of compound **heavy-10**



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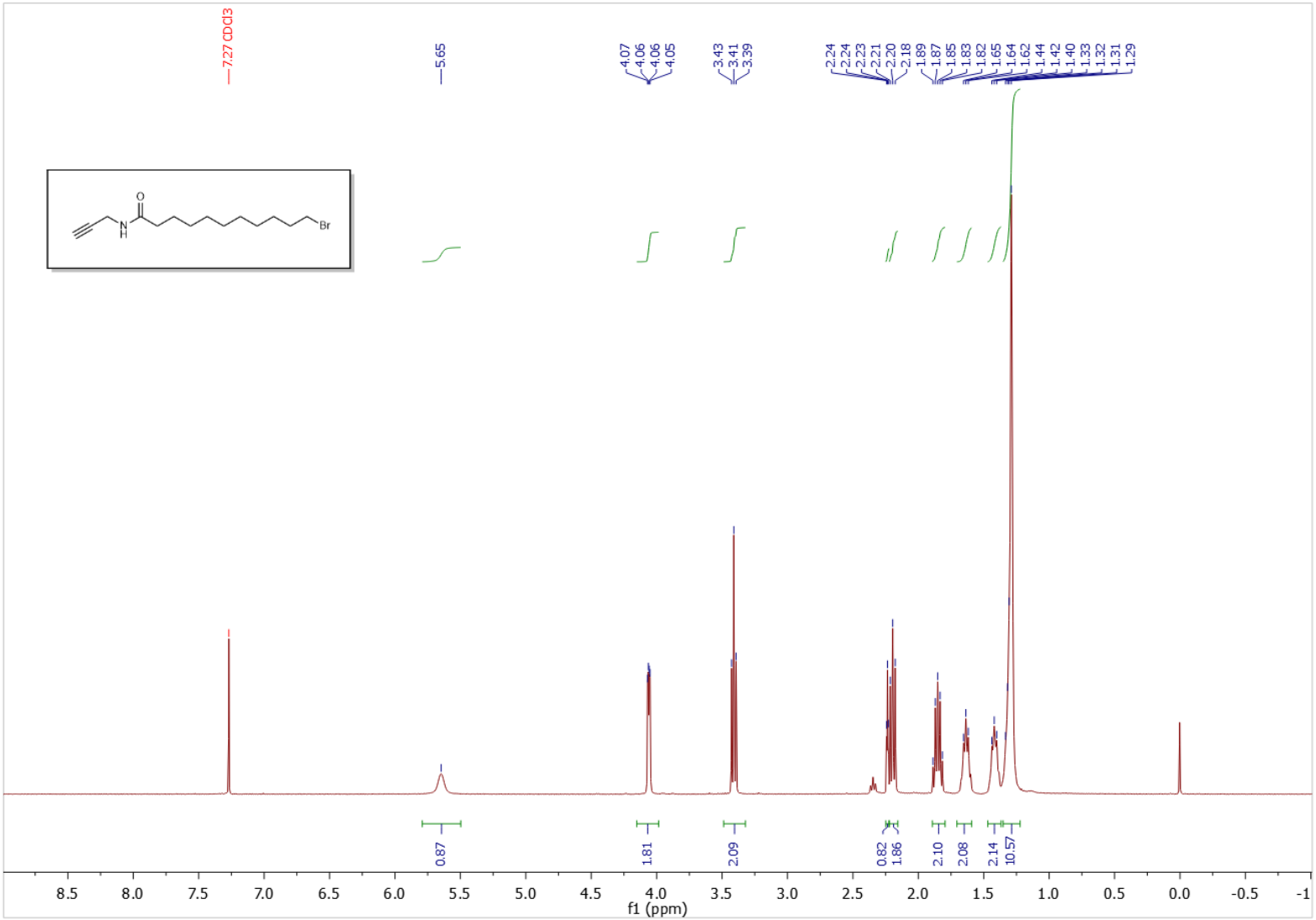
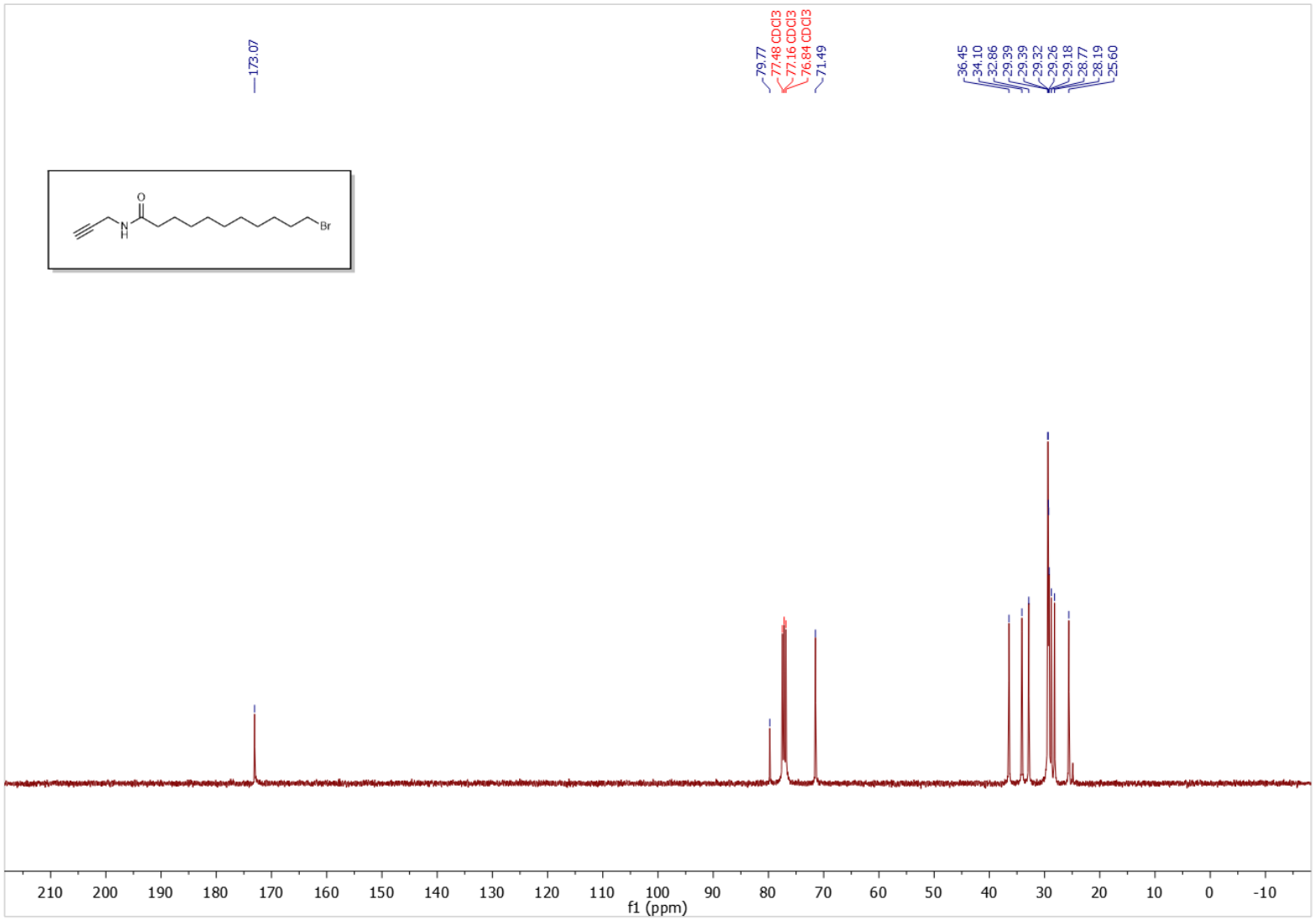
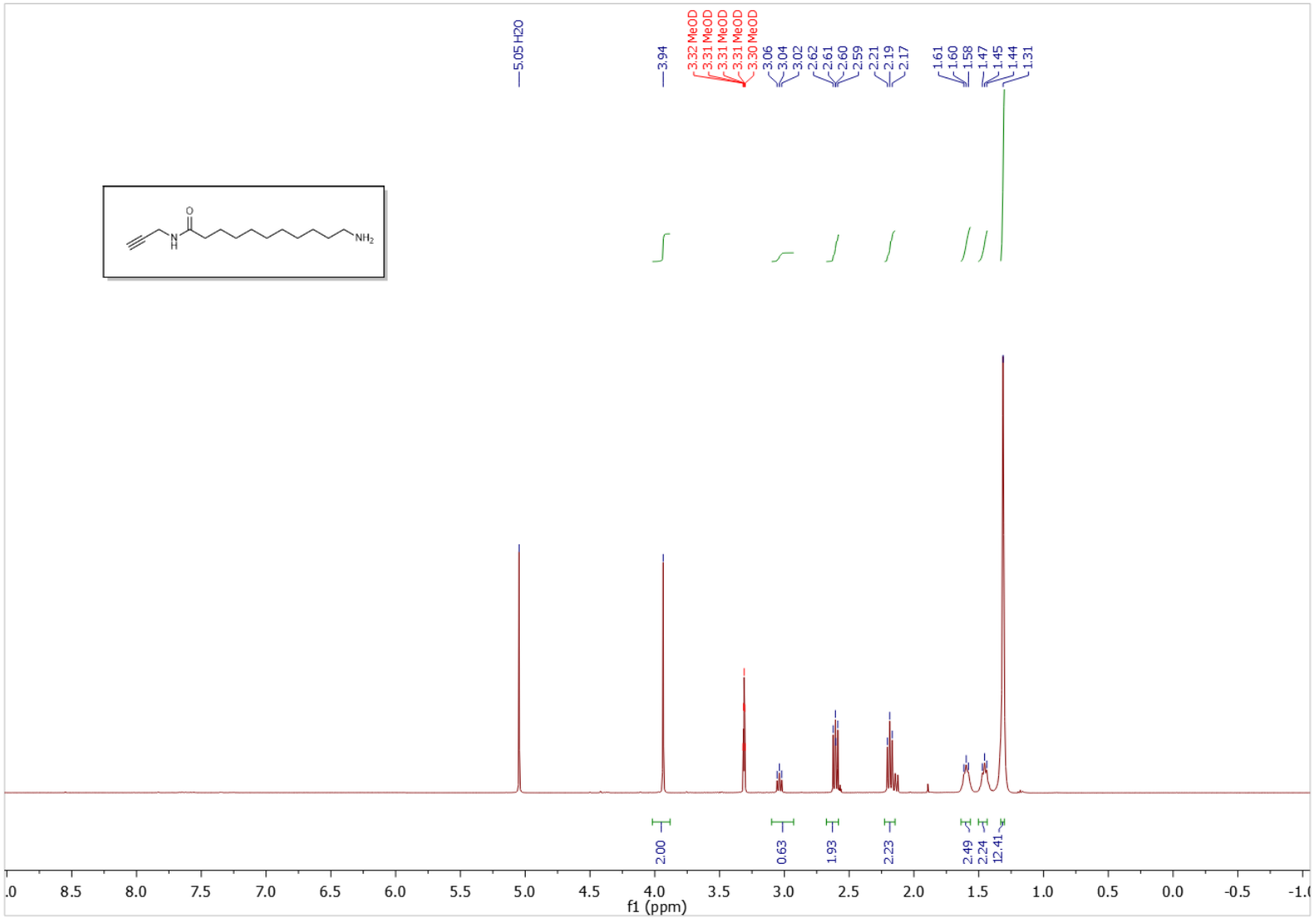


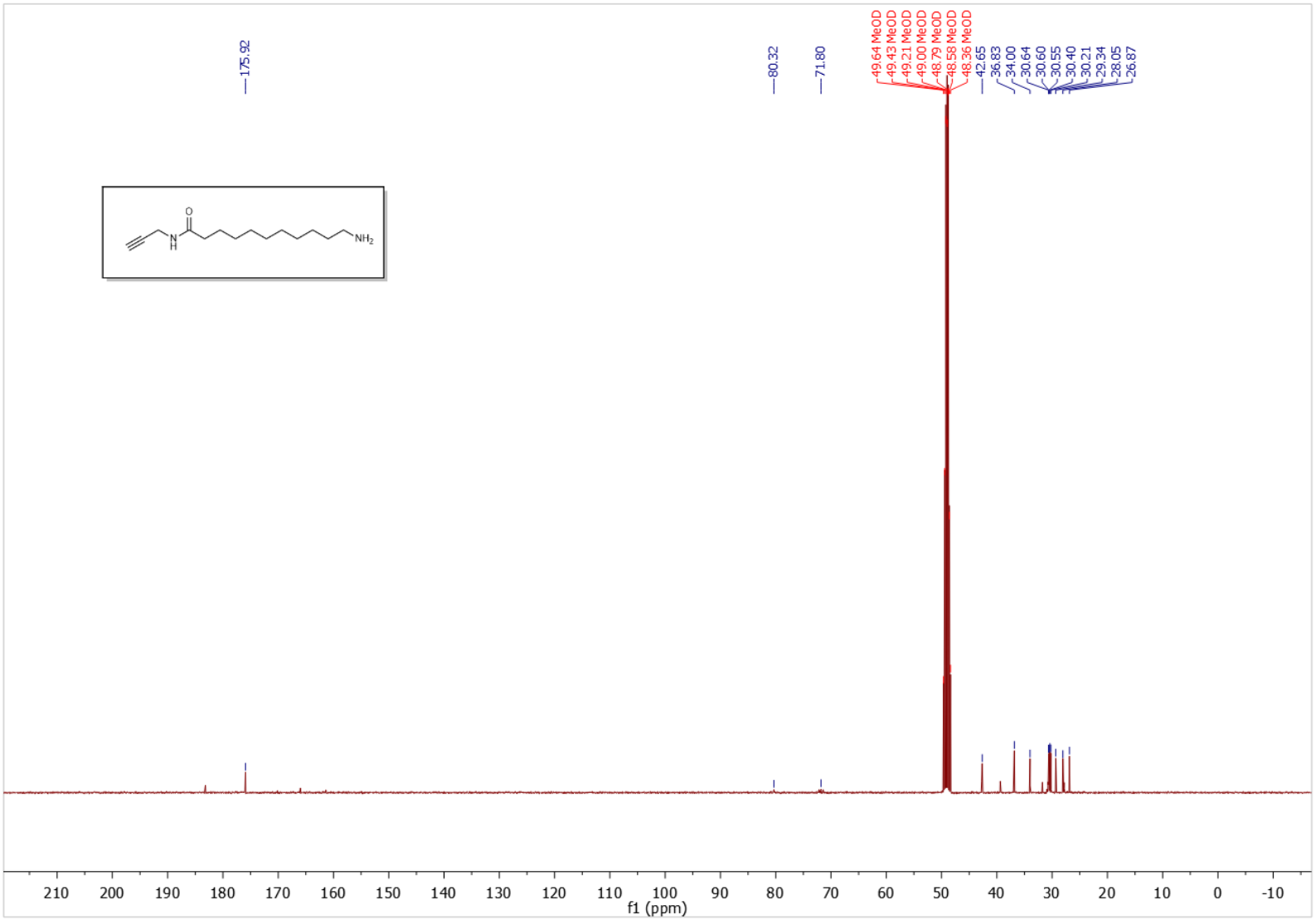
^{1}H NMR spectra of compound **SI-1**



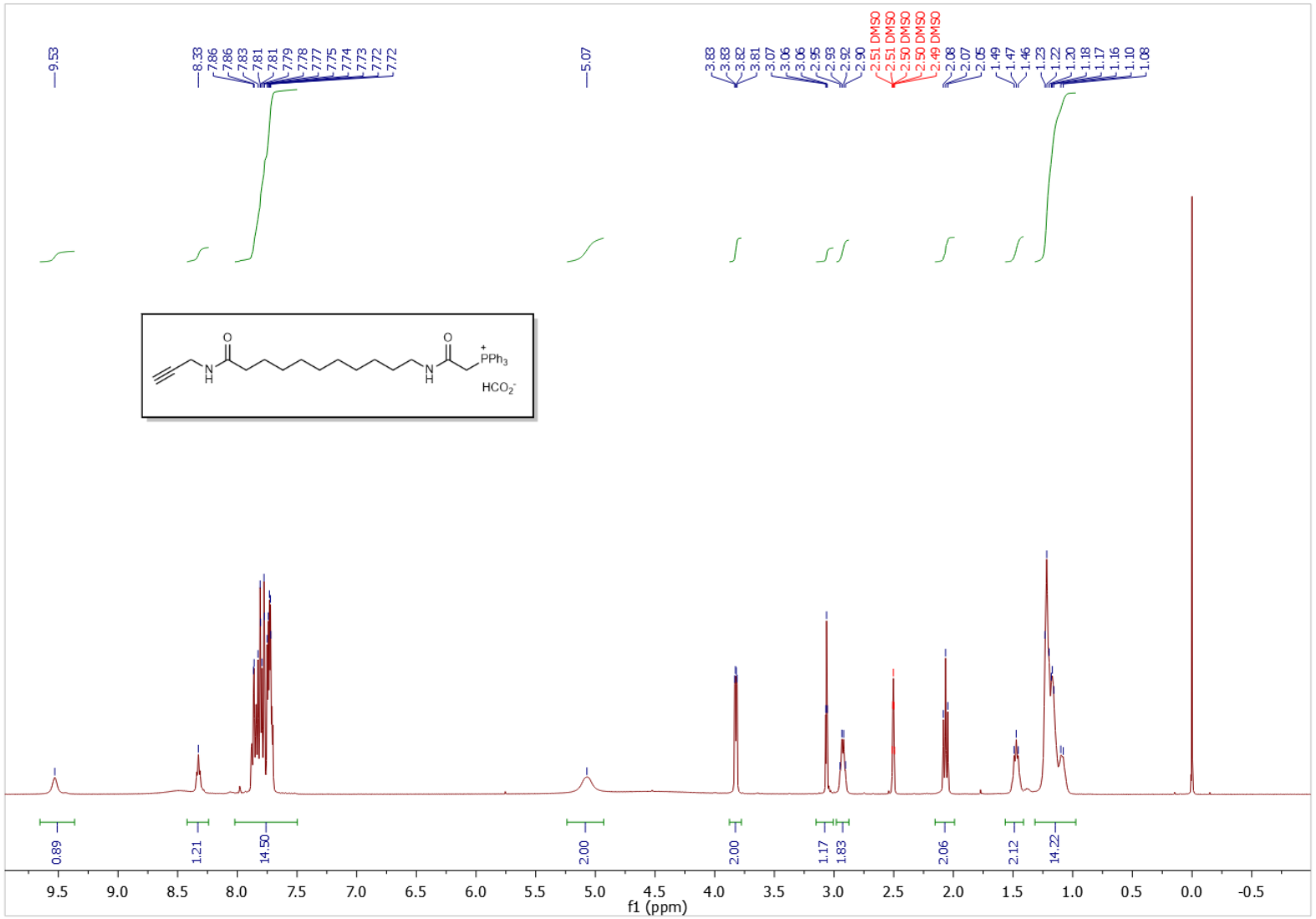
^{13}C NMR spectra of compound **SI-1**



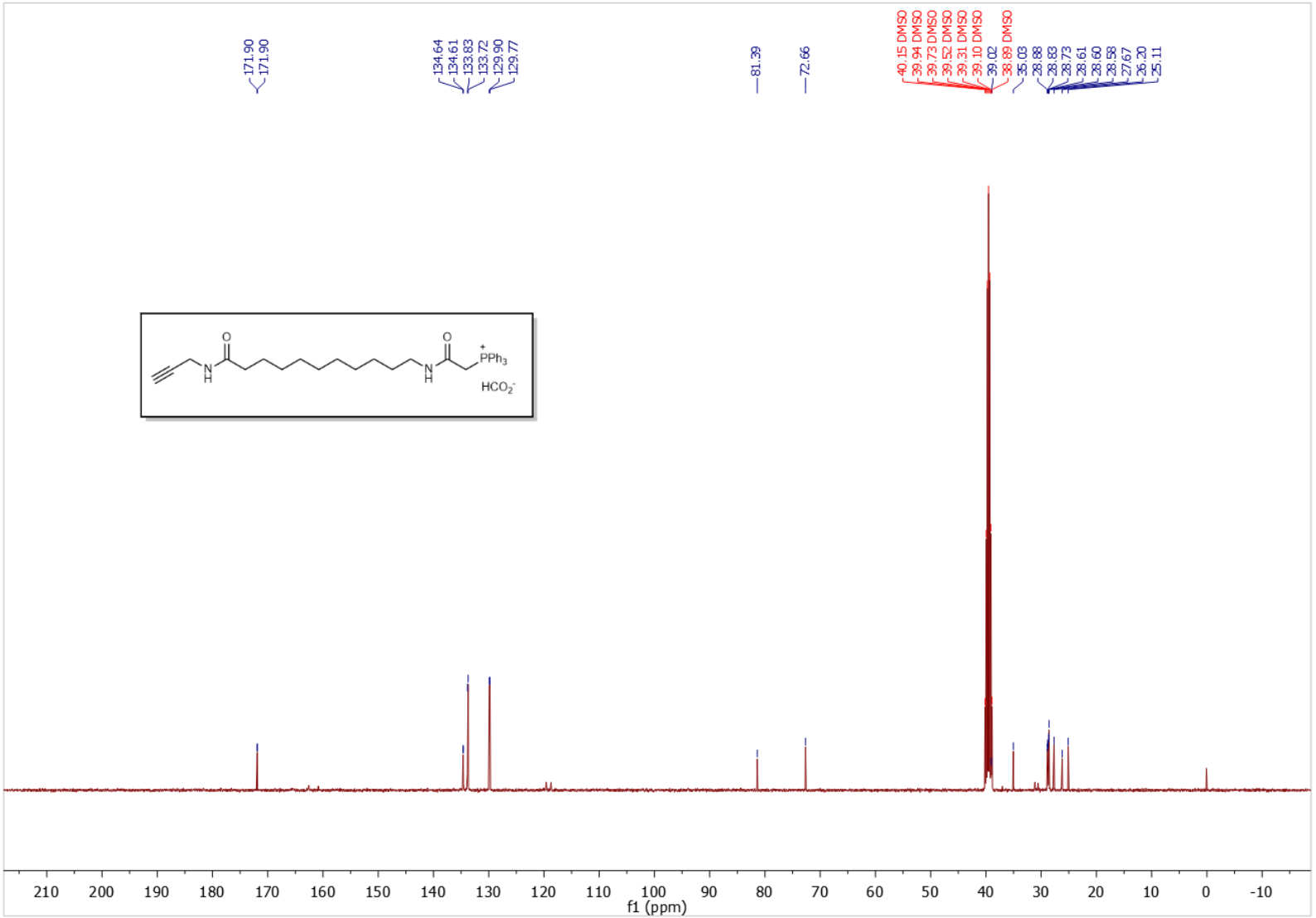
^{1}H NMR spectra of compound **SI-2**



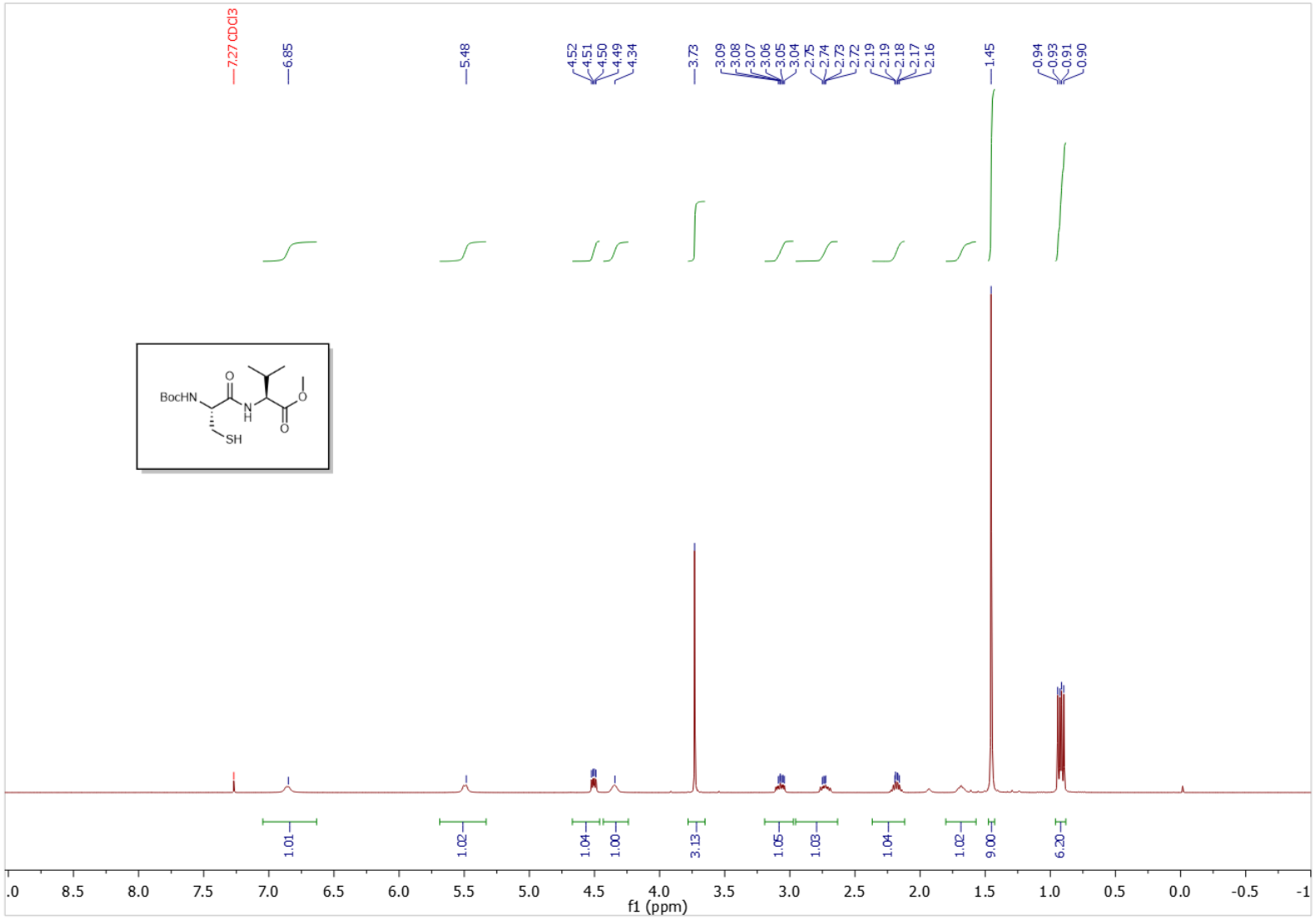
^{13}C NMR spectra of compound **SI-2**



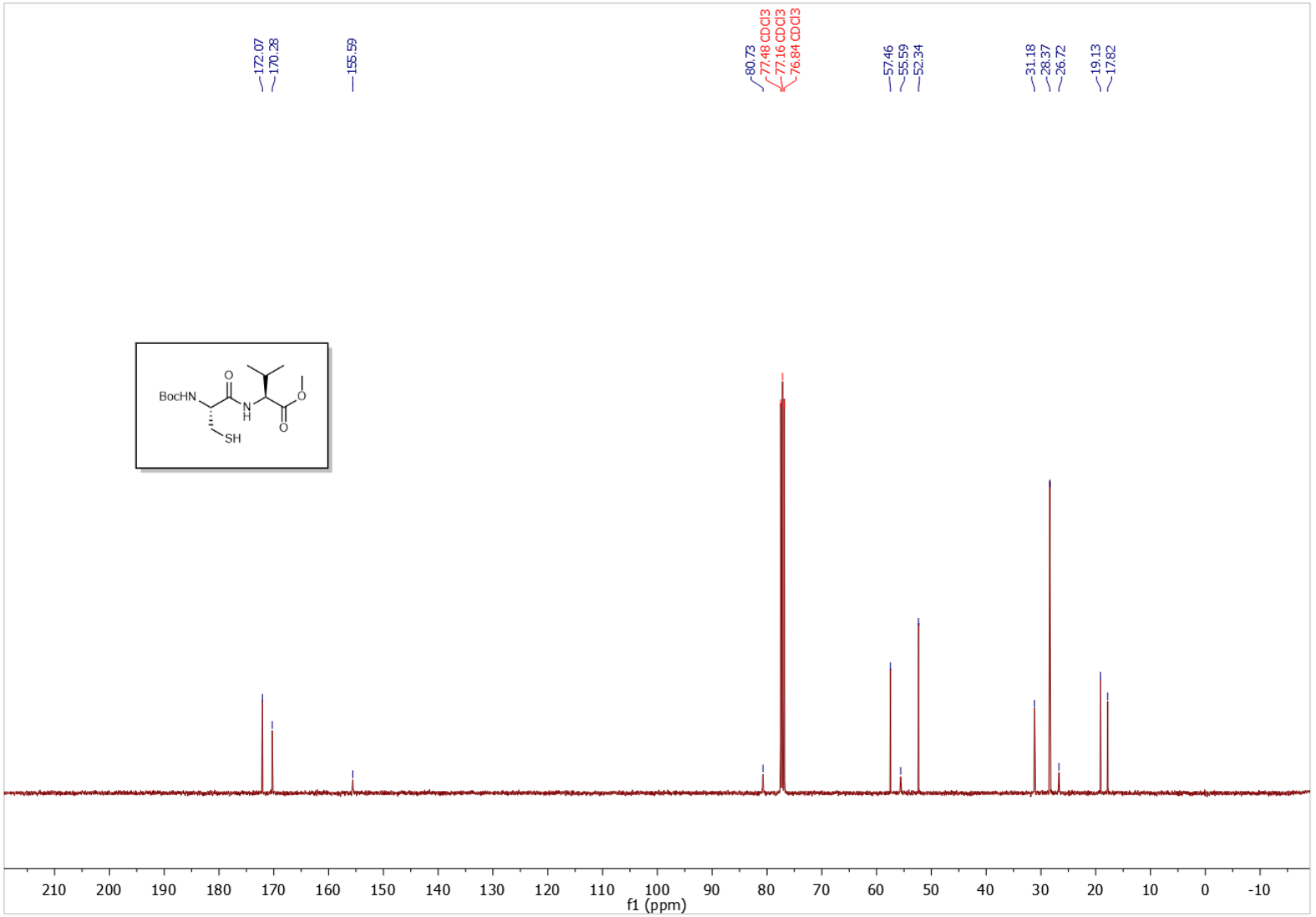
^{1}H NMR spectra of compound **11**



^{13}C NMR spectra of compound **11**



^{1}H NMR spectra of compound **SI-3**



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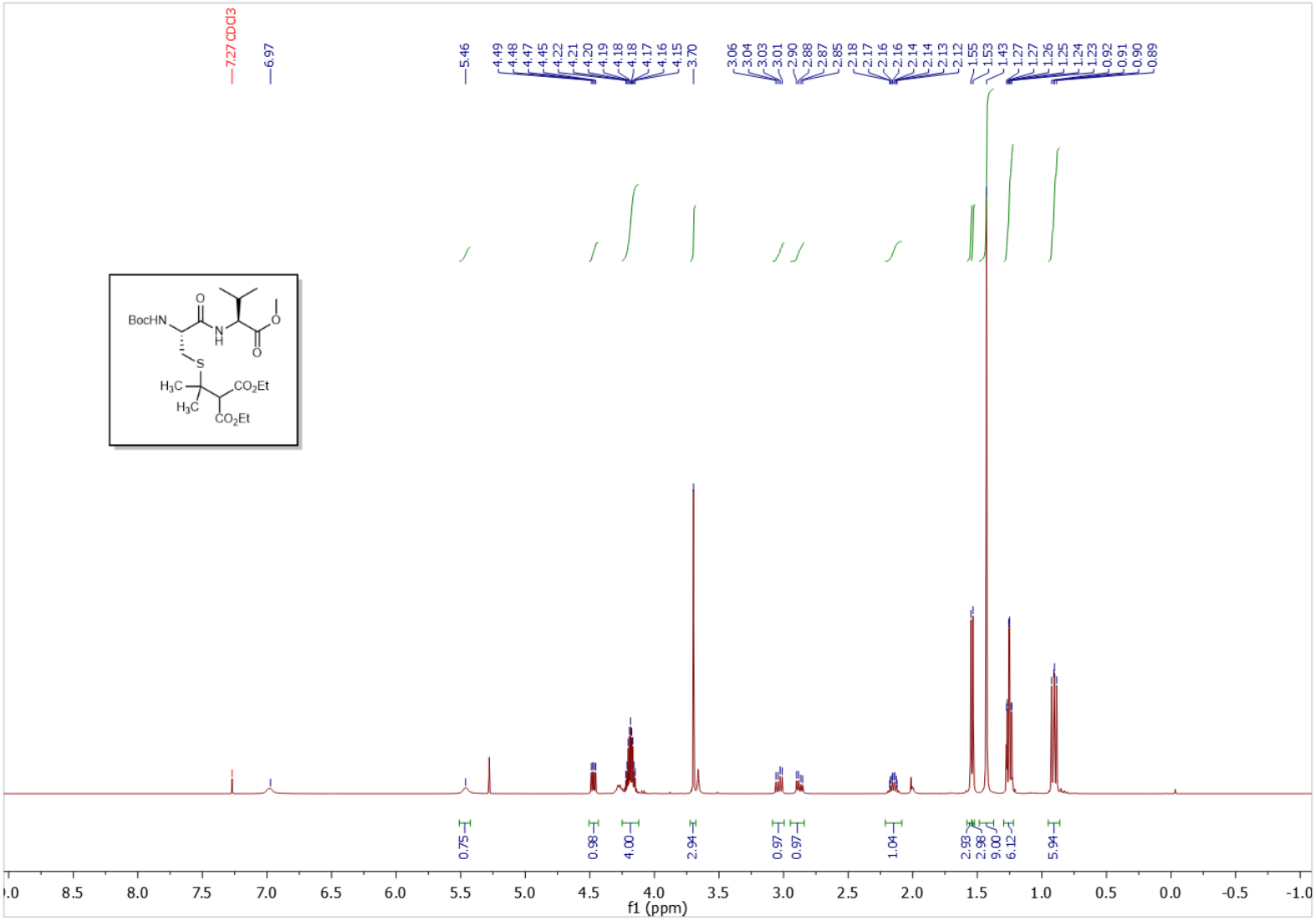

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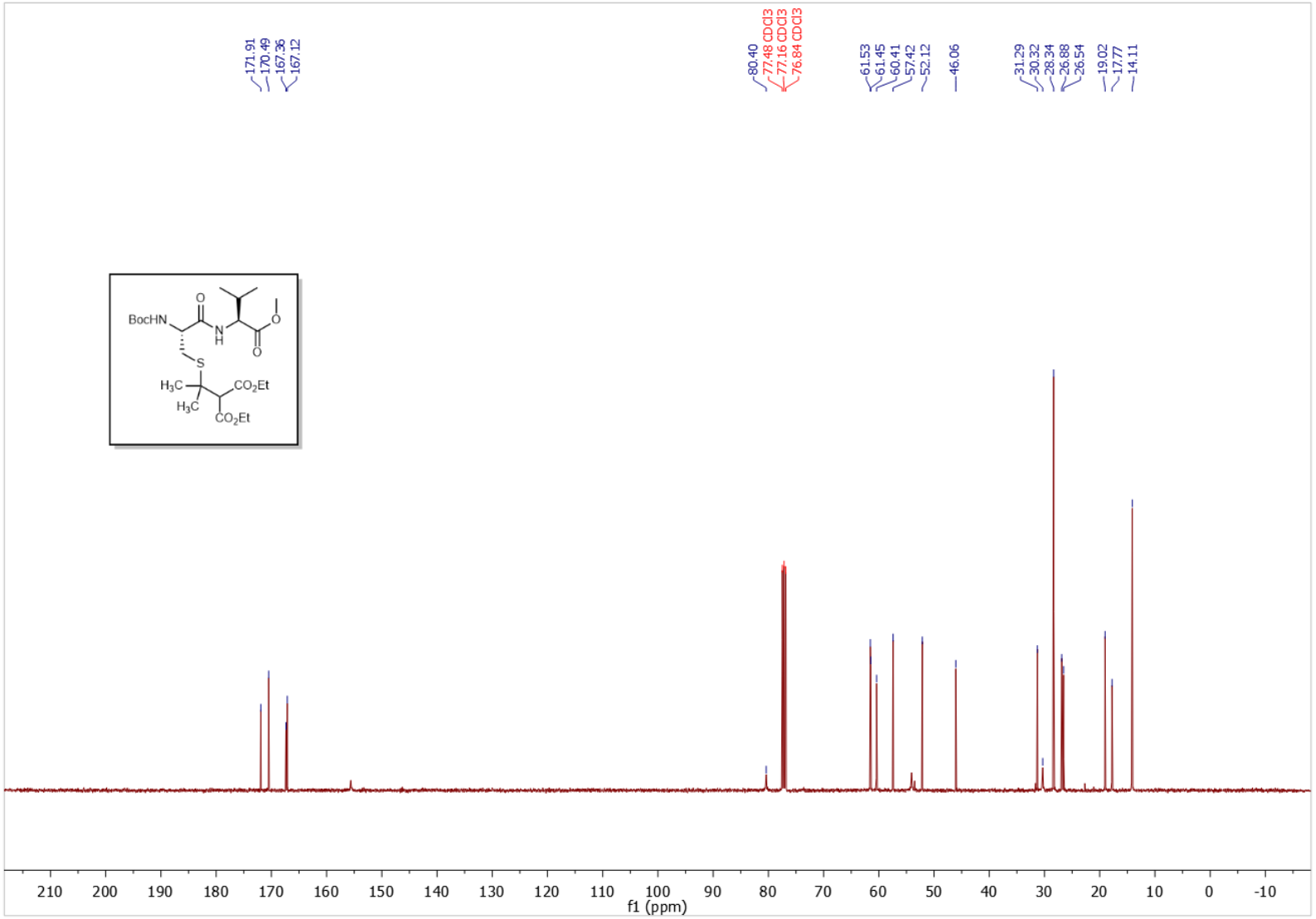
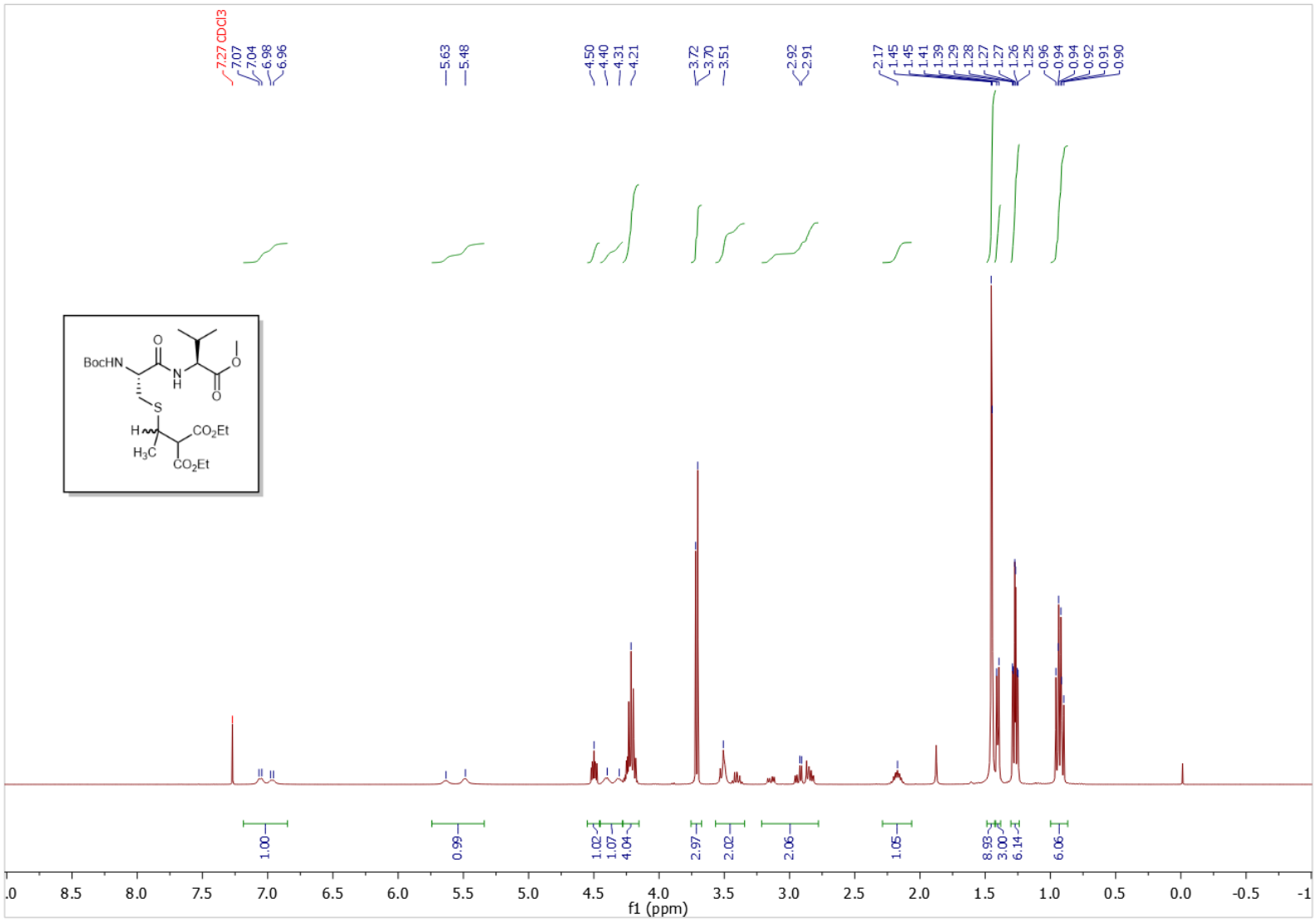


^{13}C NMR spectra of compound **Boc12**



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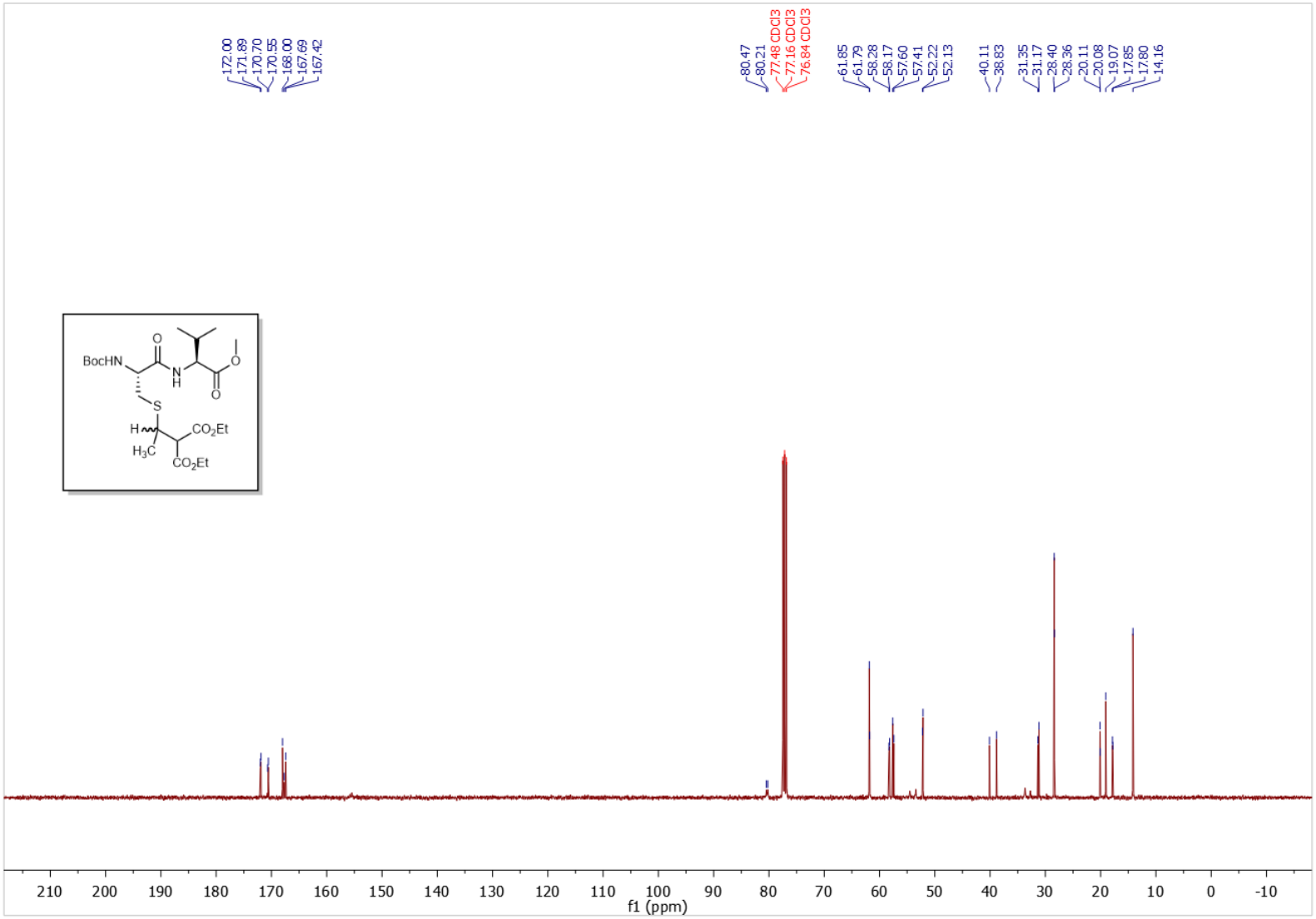
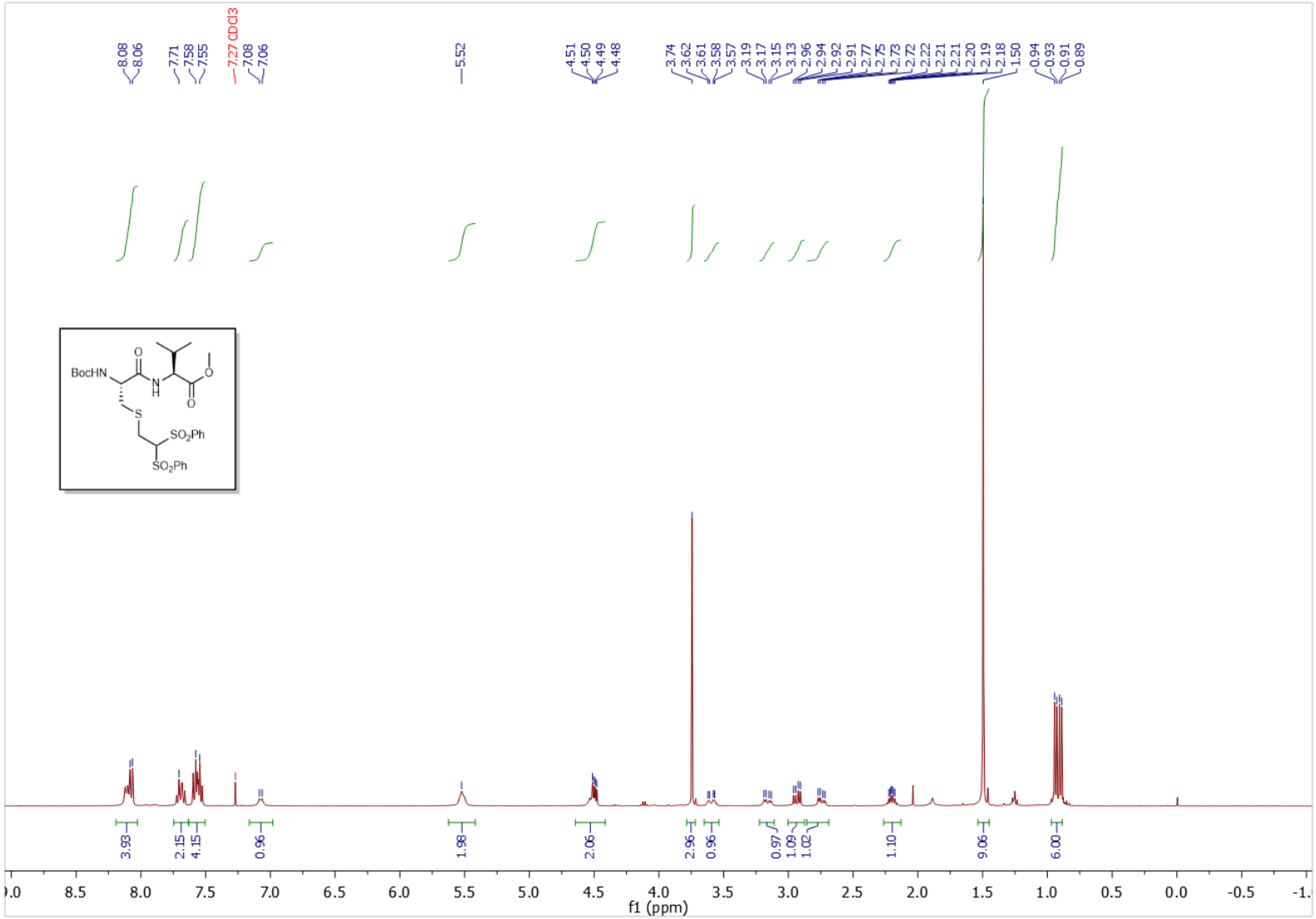
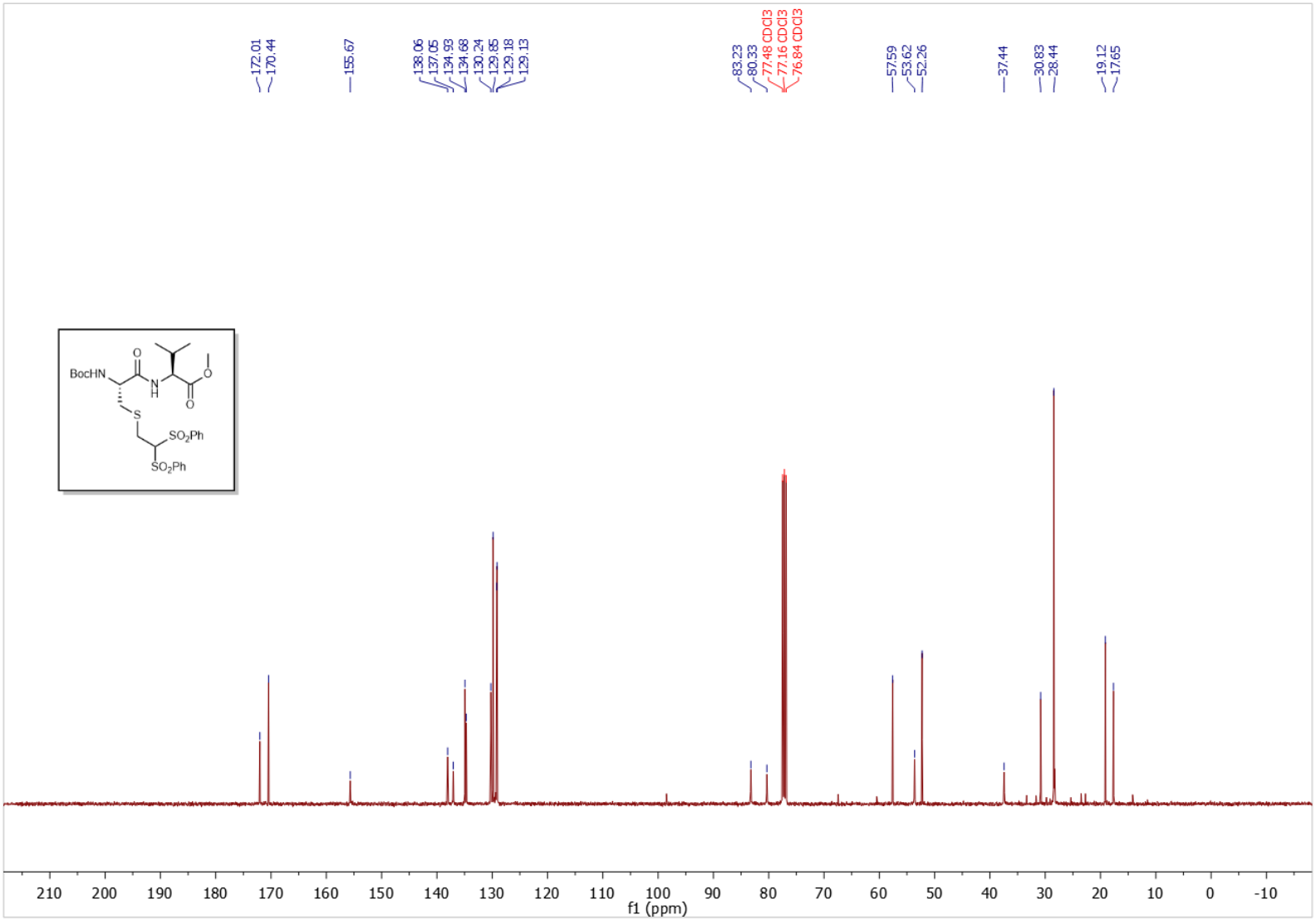


^{13}C NMR spectra of compound **Boc13**



^{1}H NMR spectra of compound **Boc14**



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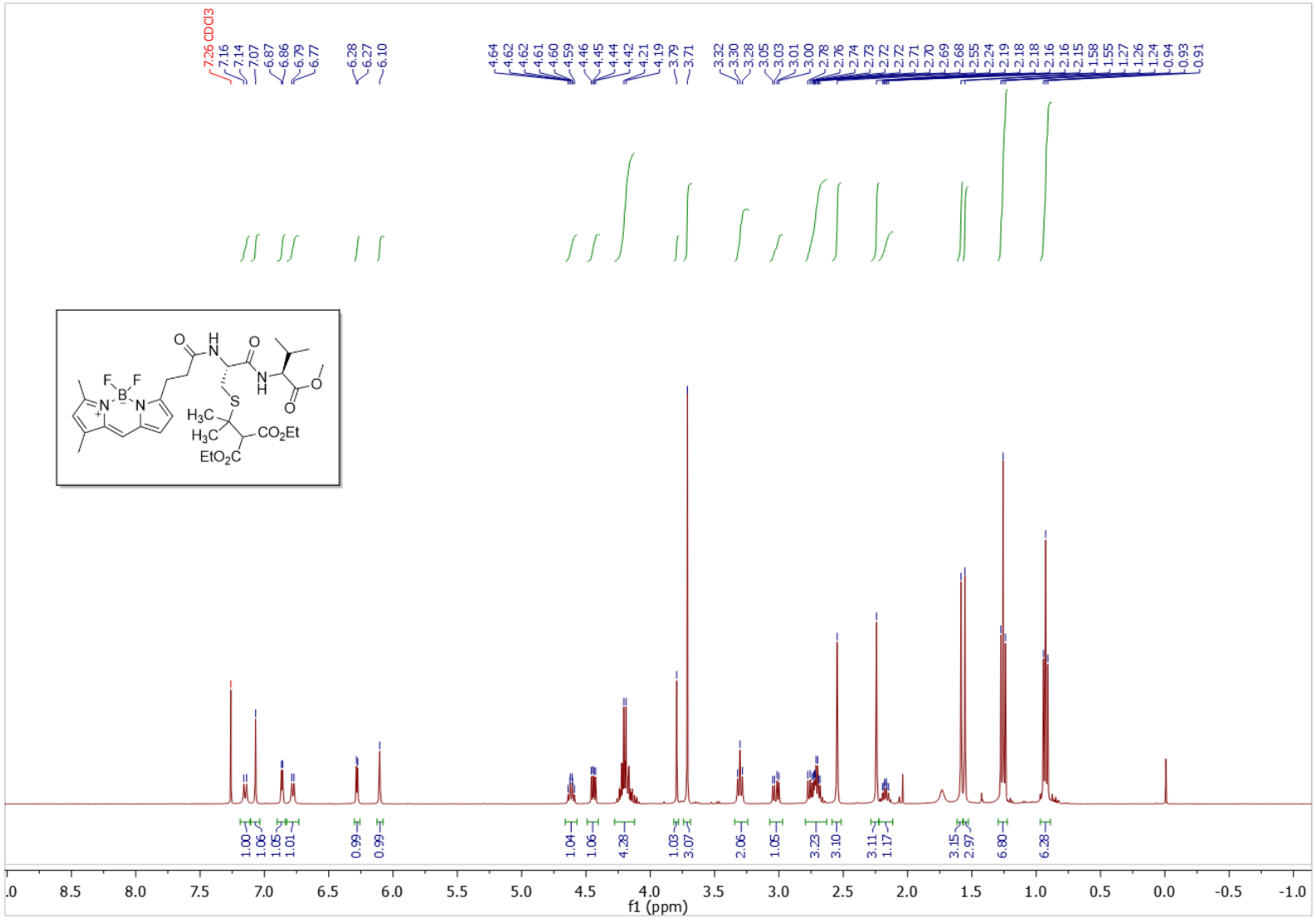
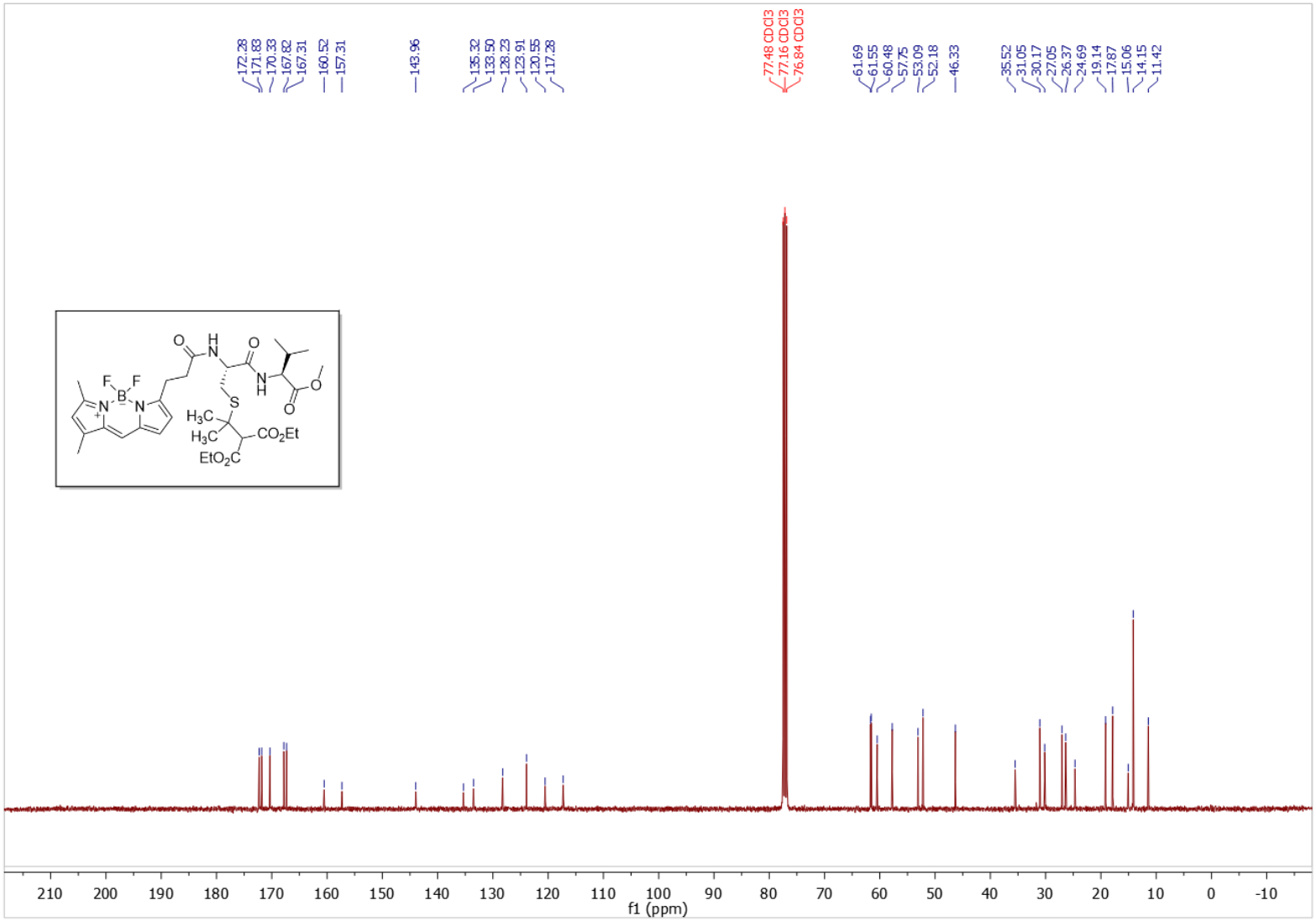
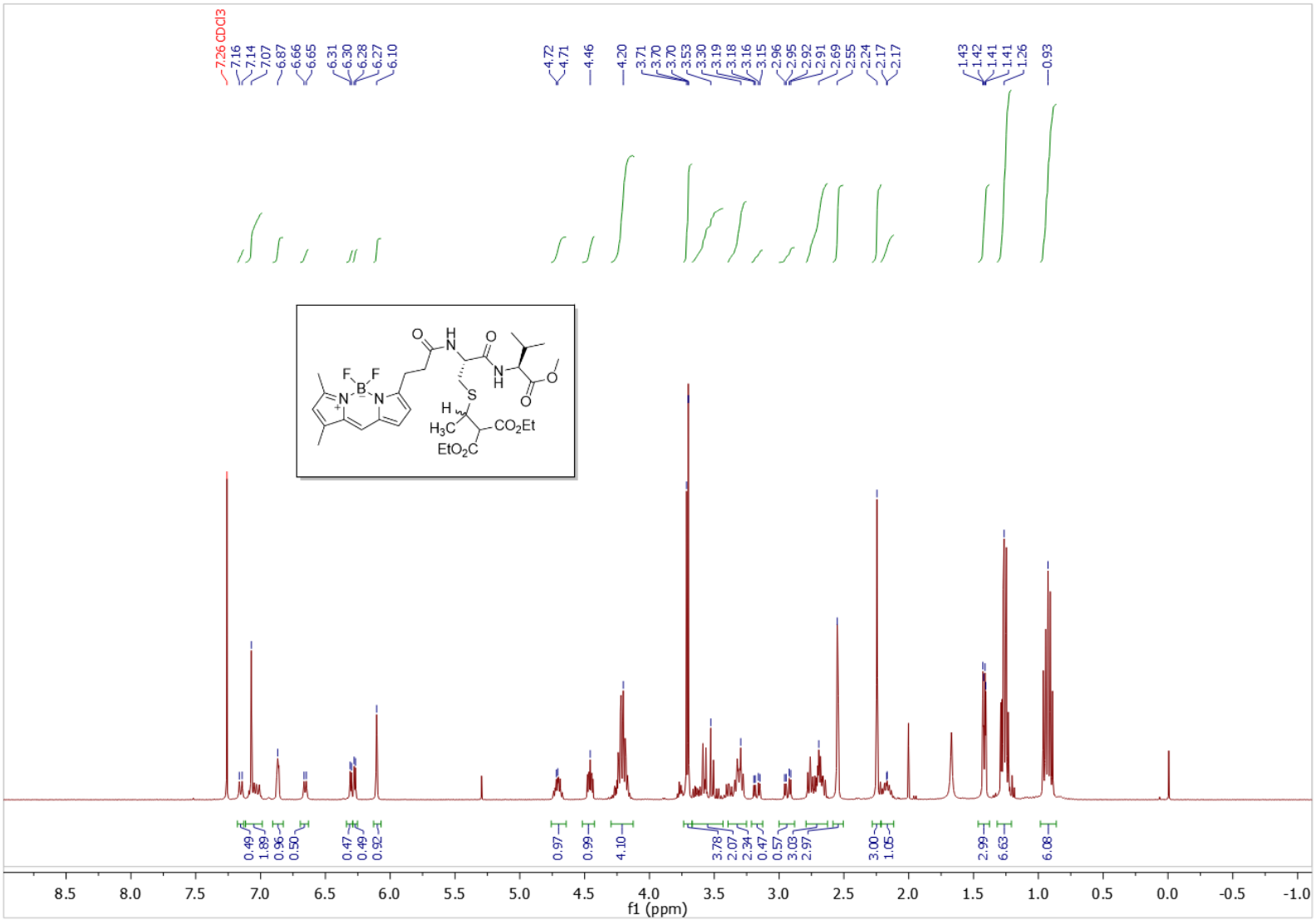


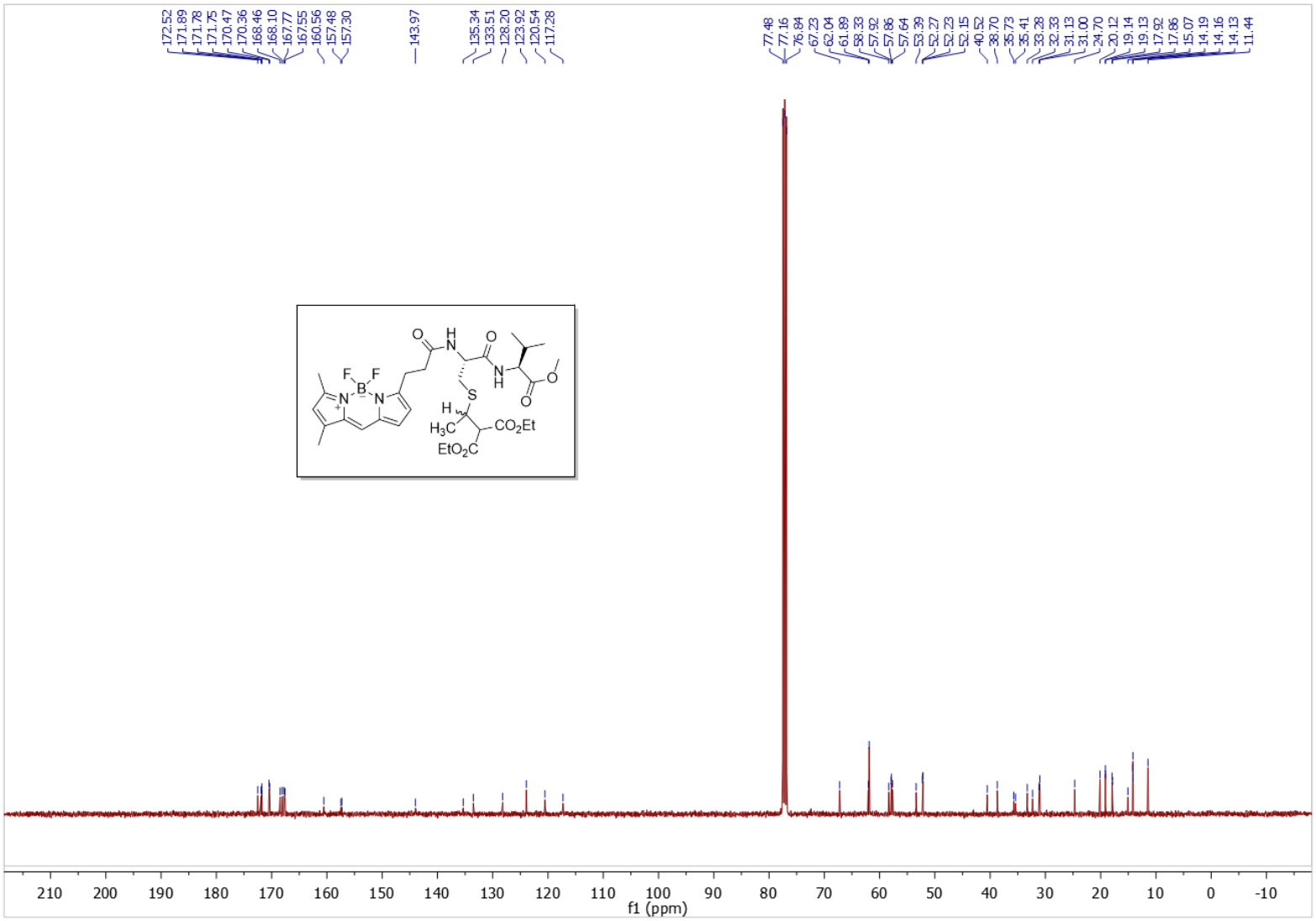
^{1}H NMR spectra of compound **12**



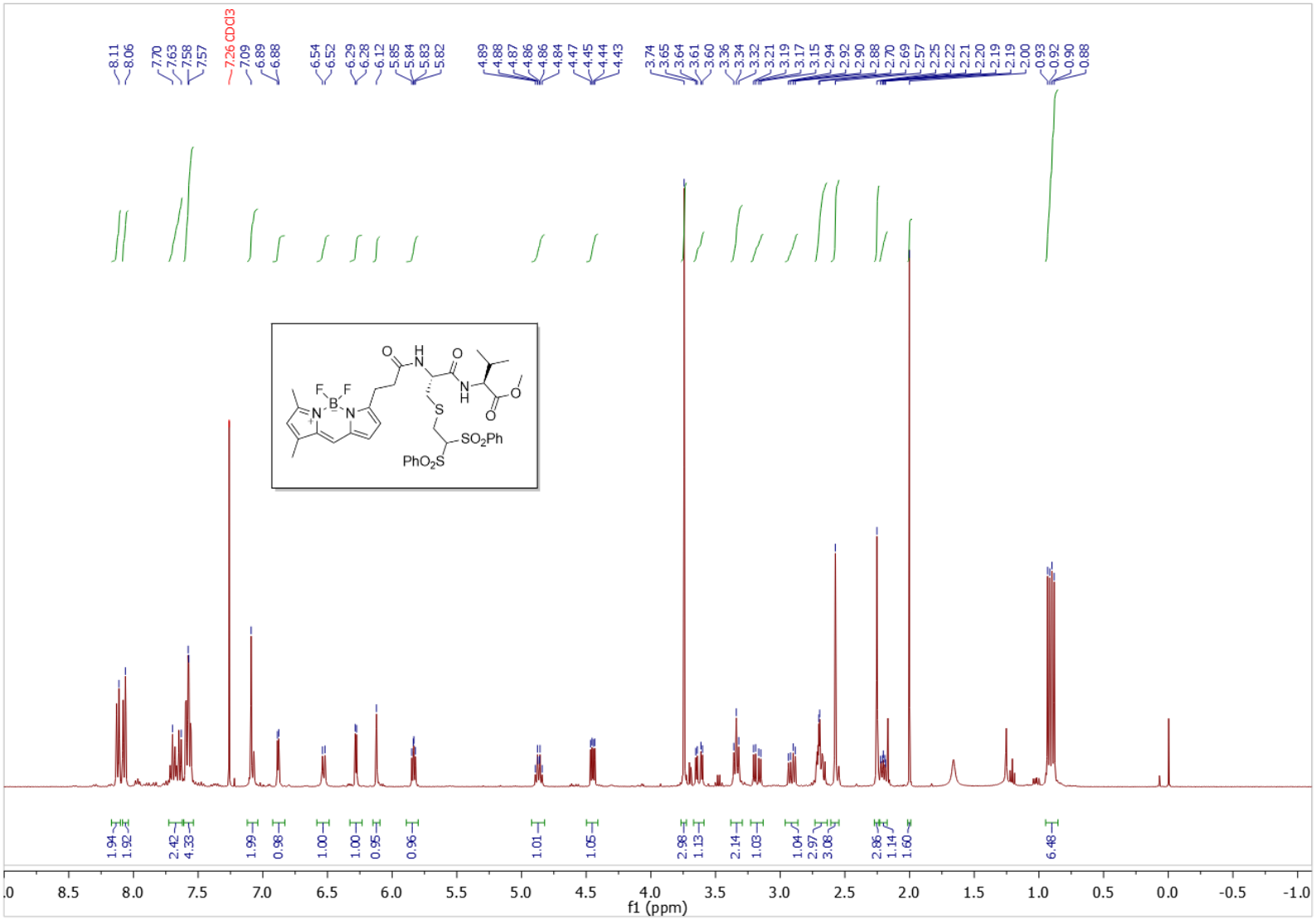
^{13}C NMR spectra of compound **12**



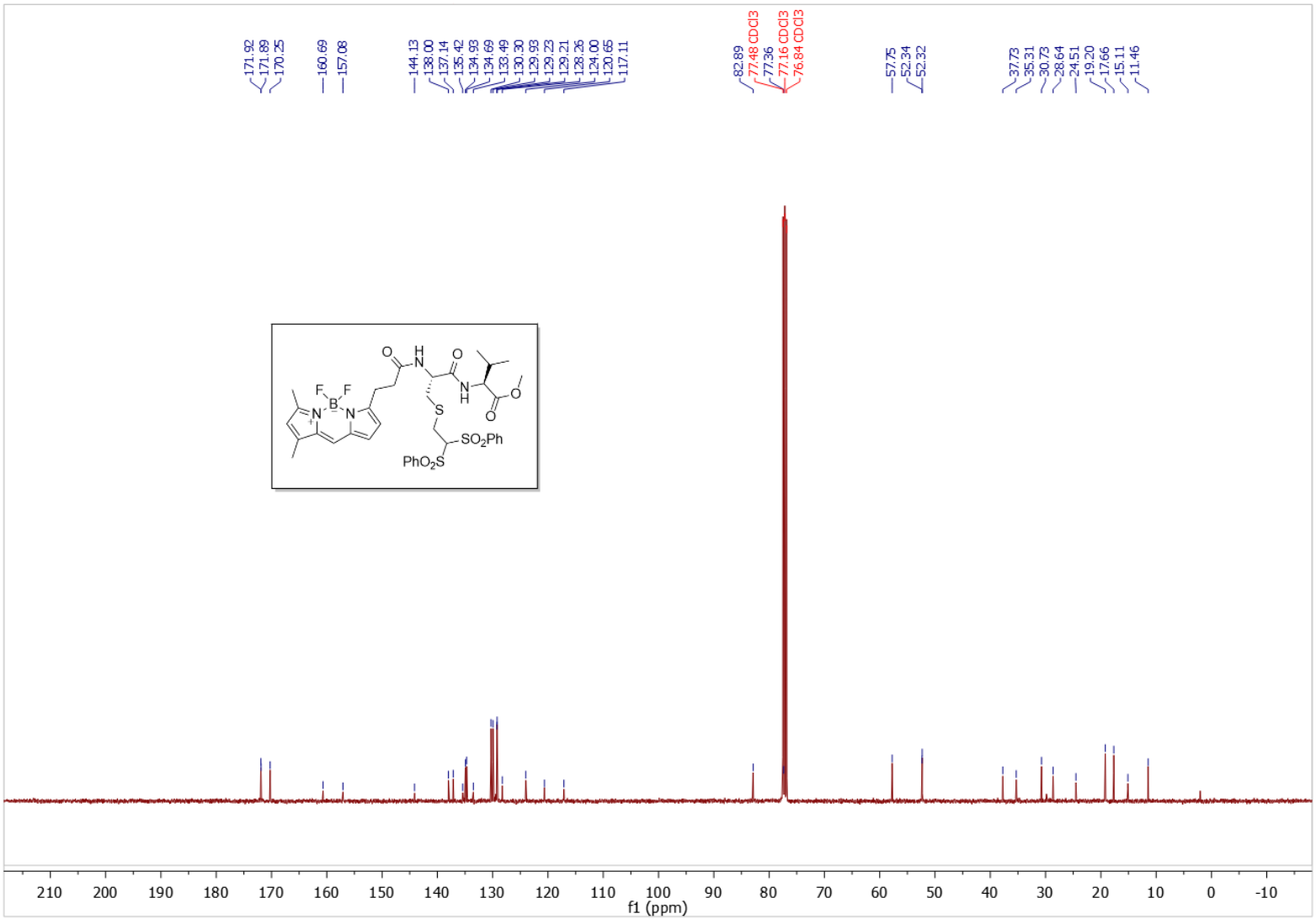
[1]H NMR spectra of compound **13**



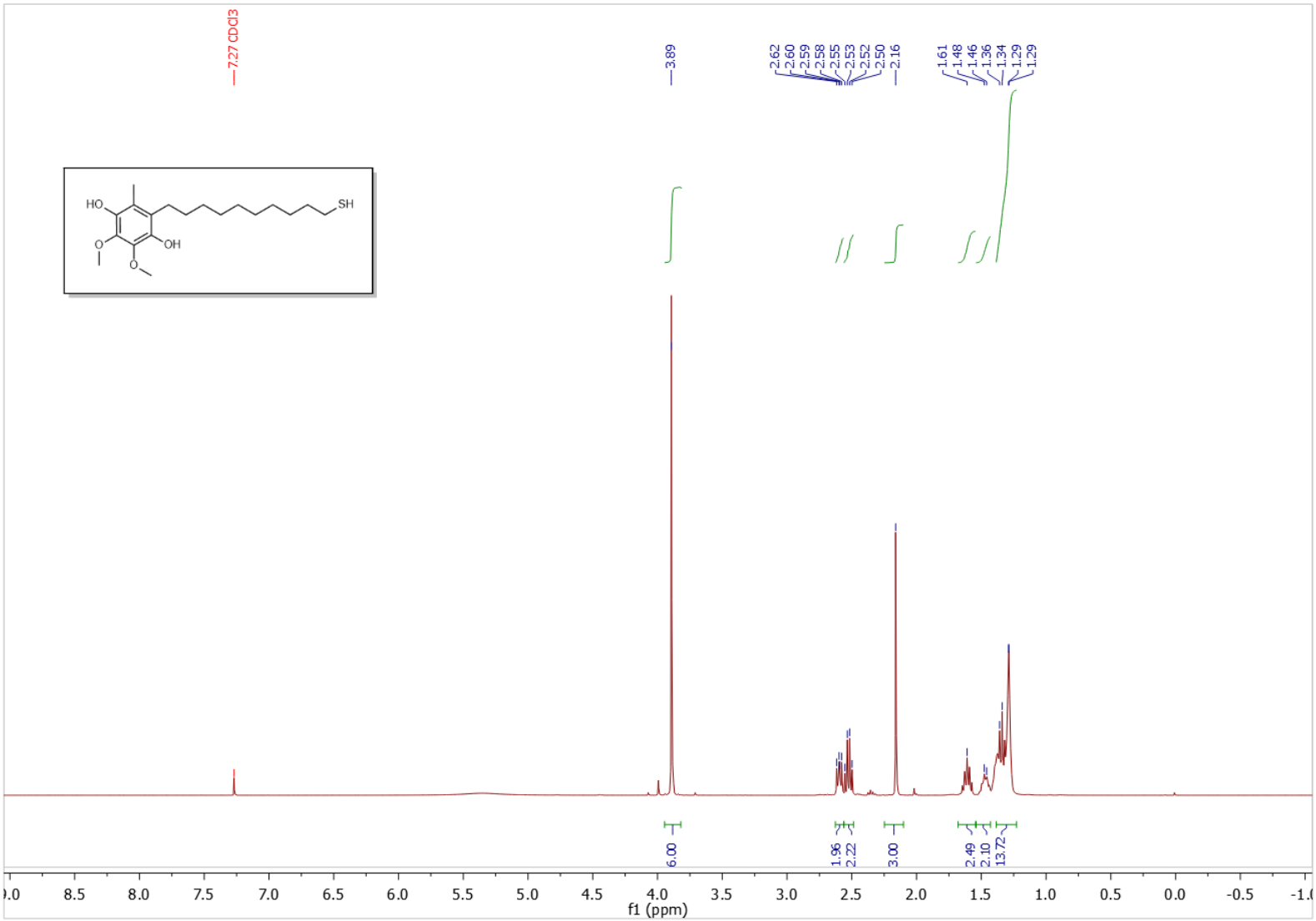
^{13}C NMR spectra of compound **13**



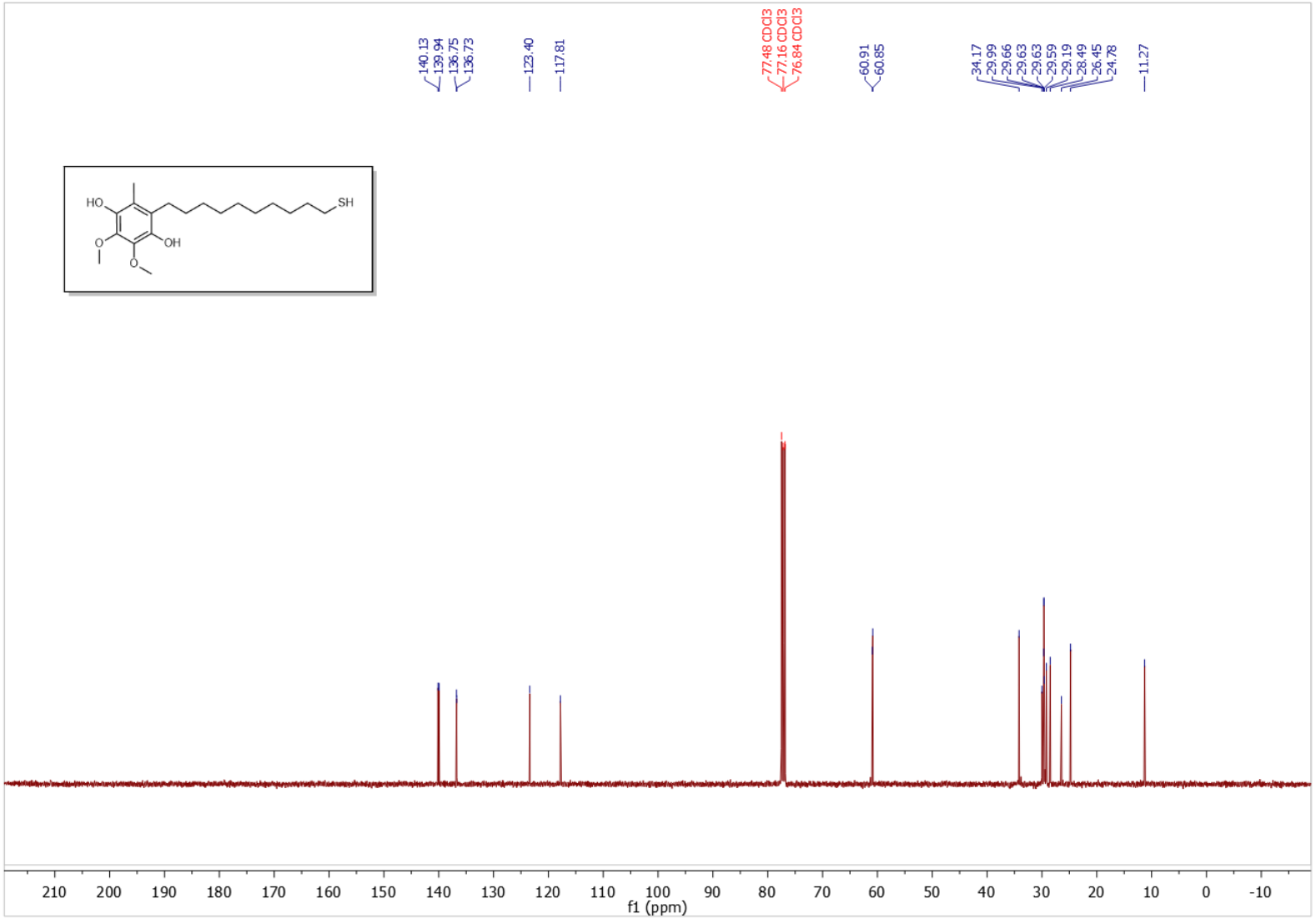
^{1}H NMR spectra of compound **14**



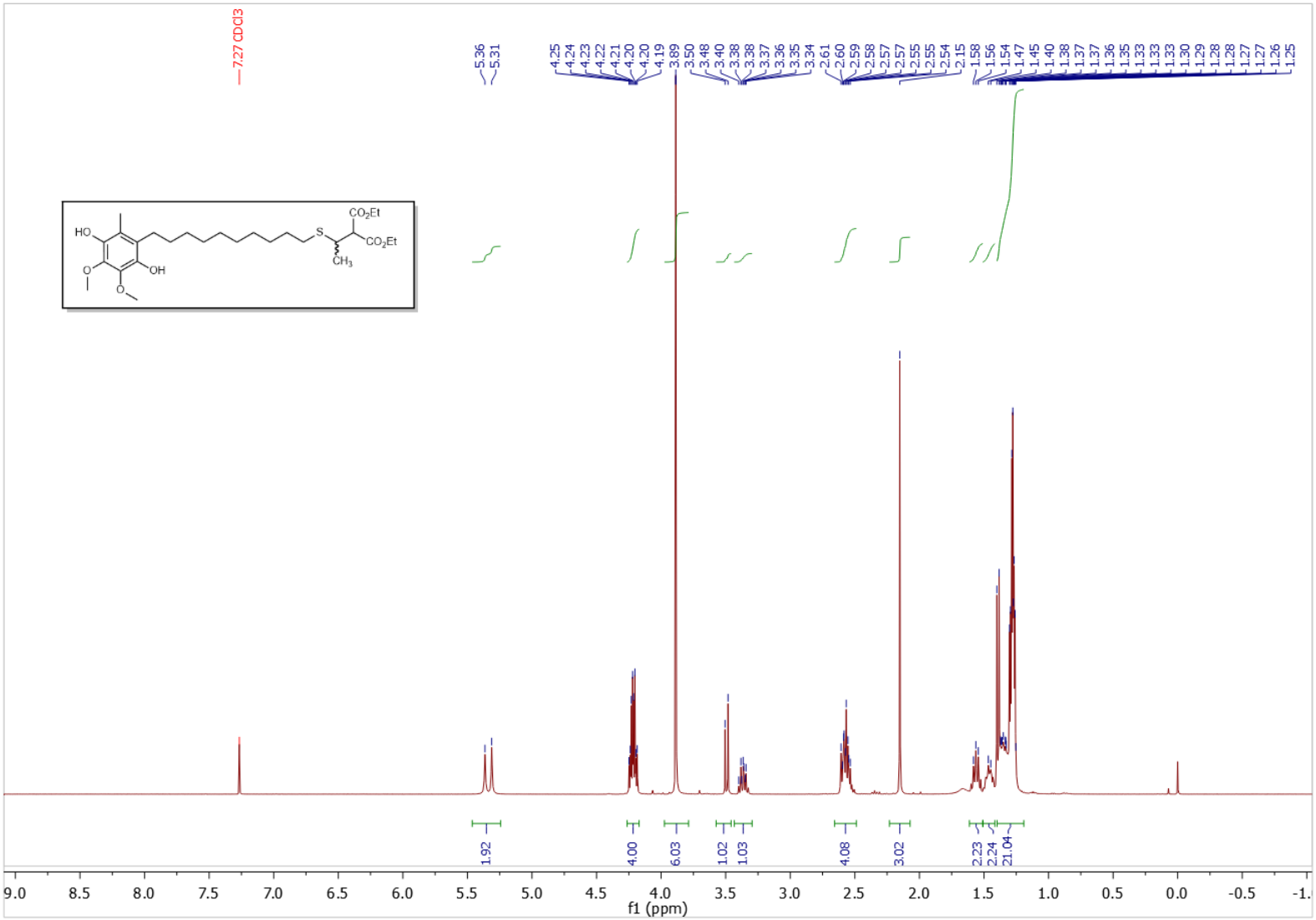
^{13}C NMR spectra of compound **14**



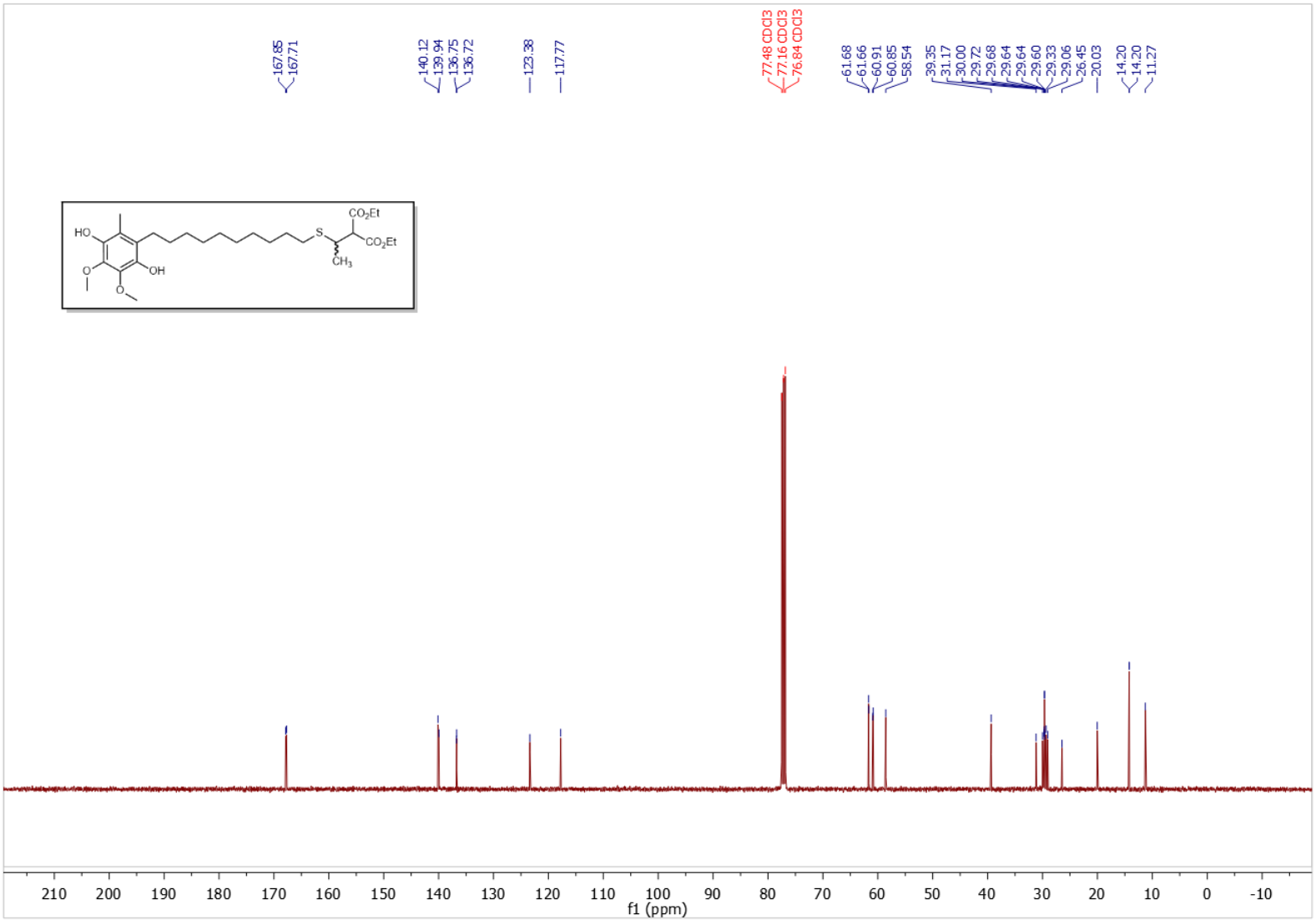
^{1}H NMR spectra of compound **SI-4**



^{13}C NMR spectra of compound **SI-4**



^{1}H NMR spectra of compound **19**



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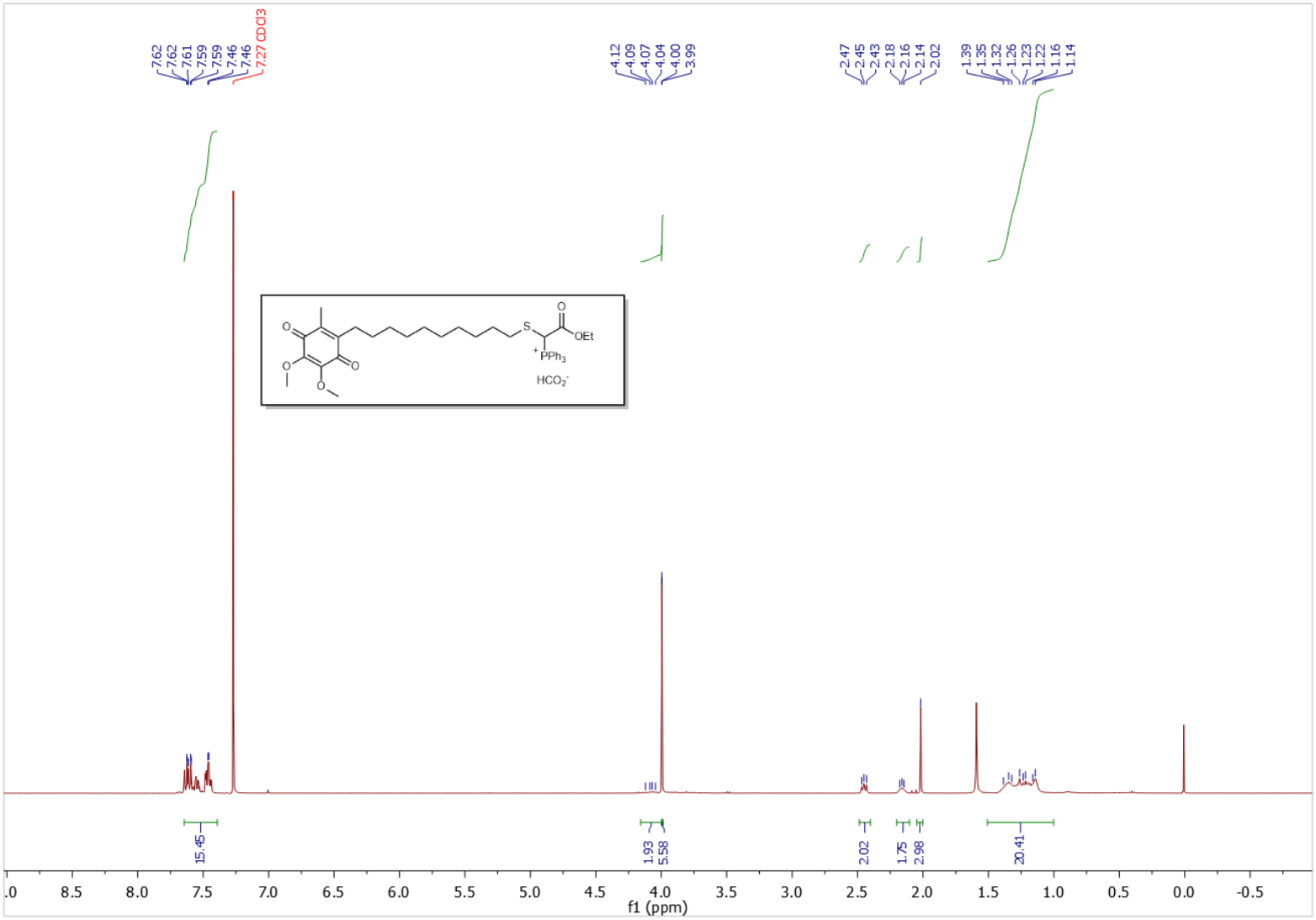

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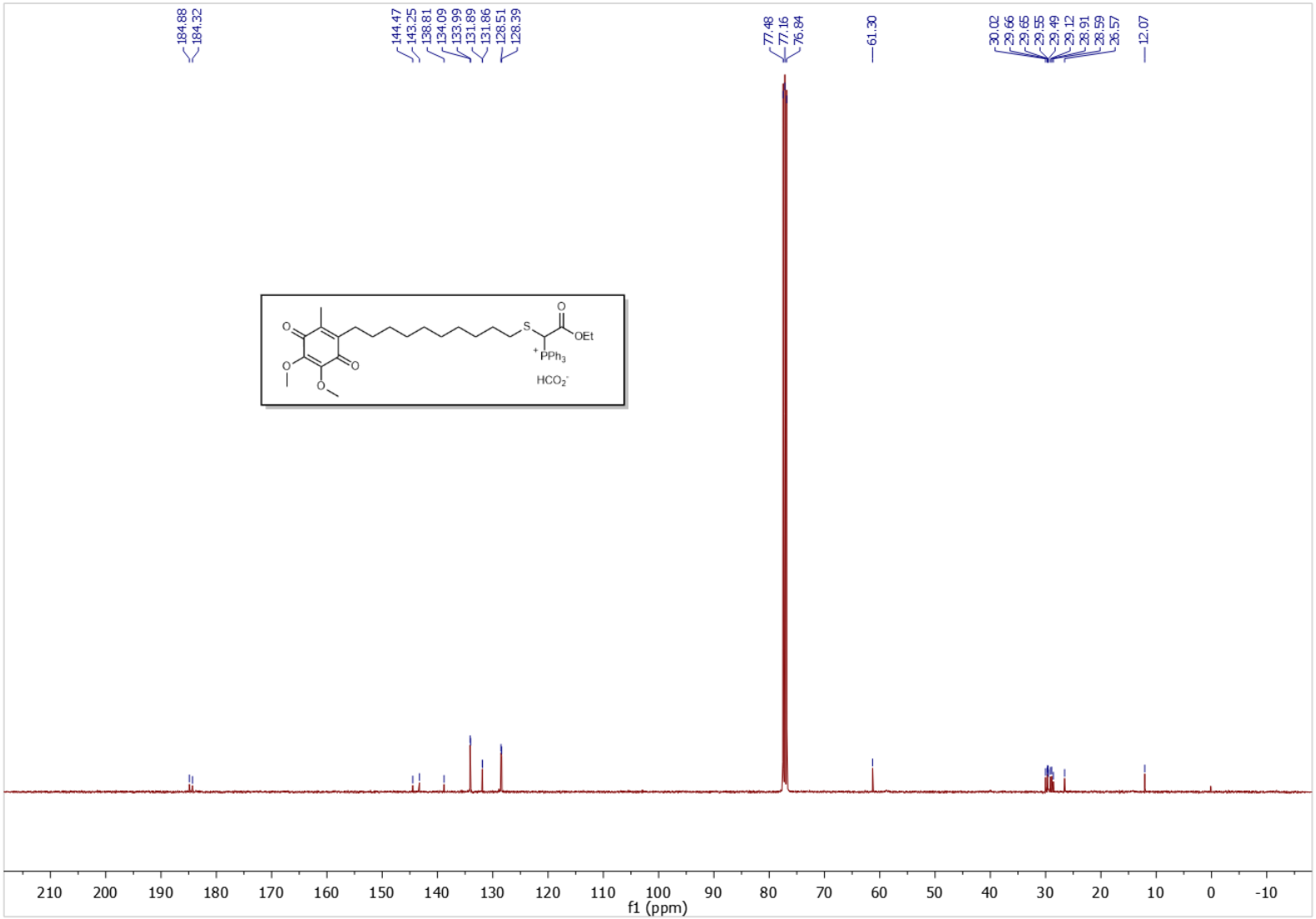

^{13}C NMR spectra of compound **20**