Supplementary Information (SI)

Late-stage modification of peptides and proteins at cysteine with diaryliodonium salts

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Reagents and materials

Analytical thin layer chromatography (TLC) was performed on commercially prepared silica plates (Merck Kieselgel 60 0.25 mm F254). Flash column chromatography was performed using 230-400 mesh Kieselgel 60 silica eluting with analytical grade solvents as described. Ratios of solvents used for TLC and column chromatography are expressed in v/v as specified. Visualization of TLC plates was undertaken with an ultraviolet (UV) light at $\lambda = 254$ nm and by staining with solutions of vanillin, ninhydrin, phosphomolybdic acid (PMA), potassium permanganate or sulfuric acid, followed by exposure of the stained plates to heat. All buffers are aqueous unless stated otherwise.

All commercially available reagents were used as obtained from Sigma-Aldrich, Merck, Combi-Blocks, or AK Scientific and were used as received unless otherwise noted. Amino acids, coupling reagents and resins were obtained from Mimotopes. Reagents that were not commercially available were synthesized following literature procedures and referenced accordingly. *N,N*-Dimethylformamide (DMF) was obtained as peptide synthesis grade from Merck or Labscan. Reactions were carried out under an atmosphere of nitrogen or argon where specified.

Caution: diaryliodonium salts are high energy molecules thus caution should be taken with heat, friction, and impact (including sonication).

General experimental procedures

NMR spectra were recorded at 300 K or 330 K using a Bruker Avance DPX 200, 300, 400 or 500 MHz spectrometer at the magnetic field strengths indicated. Chemical shifts are reported in parts per million (ppm) upfield from tetramethylsilane and are calibrated to solvent residual signals: $CDCl_3$ (δ 7.26[H], 77.2[C]), D_2O (δ 4.79[H]), D_3OD (δ 3.31[H], 49.2[C]), DMSO-d_6 (δ 2.50[H], 39.52[C]). NMR data is reported as chemical shift (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, ddd = doublet of doublet of doublets), relative integral, coupling constant (*J*) and assignments are given where possible.

Low-resolution mass spectra were recorded on a Shimadzu 2020 mass spectrometer using electrospray ionization (ESI) operating in positive mode. ESI-MS spectra were deconvoluted using ESIprot.[1] High resolution ESI mass spectra were measured on a BrukerDaltonics Apex Ultra 7.0 T fourier transform mass spectrometer (FTICR). Infrared (IR) absorption spectra were recorded on a Bruker ALPHA Spectrometer with Attenuated Total Reflection (ATR) capability, using OPUS 6.5 software. Compounds were deposited as films on the ATR plate via solid compression. Matrix-Assisted Laser Desorption/Ionization Time-of-Flight (MALDI-TOF) mass spectra were measured on a Bruker Ultraflex MALDI-TOF instrument in linear positive (LP) mode using a matrix of 2,5-dihydroxyacetephenone and diammonium hydrogen citrate in 1:1 v/v with H_2O containing 1 vol% trifluoroacetic acid (TFA).

Analytical ultra-performance liquid chromatography (UPLC) was performed on a Waters System 2695 separations module with an Alliance series column heater at 30 ˚C and 2996 photodiode array detector at a flow rate of 0.2 mL min^{-1} using a mobile phase of 0.1 vol% TFA in H_2O (Solvent A) and 0.1 vol% TFA in MeCN (Solvent B) with a 1 min solvent A

equilibration step, unless otherwise noted. Results were analysed with Waters Empower software.

Ultra-performance liquid chromatography-mass spectrometry (UPLC-MS) was performed on a Shimadzu UPLC-MS 2020 system equipped with a Nexera X2 LC-30AD pump and a Nexera X2 SPD-M30A diode array detector coupled to a Shimadzu 2020 mass spectrometer (ESI) operating in positive mode at a flow rate of 0.6 mL min^{-1} using a mobile phase of 0.1% formic acid in H_2O (Solvent A) and 0.1% Formic acid in acetonitrile (Solvent B) with a 30 s Solvent A equilibration step.

Preparative reverse-phase HPLC was performed using a Waters 600 Multisolvent Delivery System and Waters 500 pump with 2996 photodiode array detector or Waters 490E Programmable wavelength detector operating at λ = 230 and 280 nm with a mobile phase of 0.1% TFA or formic acid in H_2O (Solvent A) and 0.1% TFA in MeCN (Solvent B) and a linear gradient as specified.

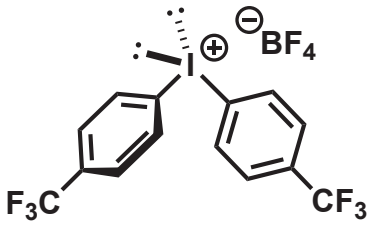
CD spectroscopy was performed using a Jasco J-815 CD Spectrometer (Jasco, Easton, MD) equipped with a temperature controller. Pre-aliquoted samples were dissolved in H_2O at room temperature to a final concentration of 10 μM. Protein solutions were transferred to a quartz cuvette (1 mm path length) and far-UV CD spectra were recorded at 20 °C with a scanning speed of 20 nm/min. A 4 s digital integration time and a 2 nm band width were used during data acquisition over a wavelength range of 180-260 nm. For each protein solution, four spectra were recorded, averaged and referenced by subtracting the average of four spectra obtained from H_2O alone. The data was smoothed with 6 neighbouring points on each side using Graphpad Prism 9.

Modified proteins were characterised by trypsin digestion and nanoLC-MS/MS as described previously.[2] Briefly, proteins were denatured, reduced using TCEP and alkylated with chloroacetamide followed by trypsin digestion. Peptides were purified using SDB-RPS Stagetips and analysed by nanoflow LC-MS/MS on 45 min gradients using data-dependent acquisition with HCD-MS2 analysis. Peptides were identified using the Byonic search engine (Protein Metrics, Cupertino, CA) with a 2% false-discovery rate and an error tolerance of 7 ppm at the precursor level and 30 ppm at the fragment level. Allowed modifications included the reaction-specific mass addition to cysteine, protein N-terminal acetylation, protein C-terminal amidation, and Gln/Glu pyro-glutamic acid formation at peptide N-termini. The Swissprot *E. coli* protein database was used in combination with the sequences of the zEGFR and H2A T120C proteins used in these experiments. This analysis allowed us to confirm for each reaction examined the correctly modified form of the protein constituted >99% of the observed signal intensity for the corresponding peptide sequence.

Plasma stability of peptide **6** was determined using a slightly modified method previously described by Teufel *et al.*[3] The peptides (5 mM stock in water) were added to human plasma (Sigma Aldrich pooled plasma, citrate as anticoagulant) to a concentration of 200 μM. The peptides were incubated at 37 °C for 0, 1, 4 and 24 h before being quenched with three volumes of 1:1 v/v MeOH: MeCN. The samples were centrifuged at 13,500 rpm for 5 minutes before removing an aliquot of the supernatant (20 μL) S37 that was diluted with water (20 μL) and analysed by UPLC-MS.

Synthesis of small molecules

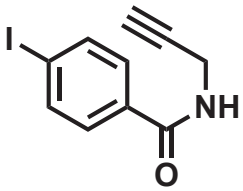
bis(4-trifluoromethylphenyl)iodonium tetrafluoroborate (1)



m-Chloroperbenzoic acid (1.12 g, 77 wt.% active oxidant, 5.5 mmol) and 4-iodobenzotrifluoride (1.37 g, 5.0 mmol) were dissolved in CH_2Cl_2 (18 mL), followed by the dropwise addition of boron trifluoride diethyl etherate (1.6 mL, 13 mmol). The reaction mixture was stirred at room temperature for 60 min, after which it was cooled to 0 °C and 4-(trifluoromethyl)phenylboronic acid (1.04 g, 5.5 mmol) was added. The reaction mixture was warmed to rt and stirred for 15 min. The crude reaction mixture was then filtered through a silica plug (6 g), eluting first with CH_2Cl_2 (50 mL) and then 20:1 v/v CH_2Cl_2/MeOH (180 mL). This solution was concentrated *in vacuo* and the remaining solid was immediately triturated with Et_2O (3 x 10 mL) to avoid decomposition, affording the diaryliodonium salt **1** as a white solid (886 mg, 38%).

^{1}H NMR (500MHz, DMSO-d_6) δ 8.52 (d, *J* = 8.3Hz, 4H), 7.93 (d, *J* = 8.5Hz, 4H); **^{13}C NMR** (126MHz, DMSO-d_6) δ 136.37, 132.12 (q, *J* = 32.6Hz), 128.52 (q, *J* = 3.7Hz), 123.39 (q, *J* = 273.0Hz), 120.95; **^{19}F NMR** (471MHz, DMSO-d_6) δ –61.78, –148.15, –148.20; **LRMS** (ESI+) *m/z* calculated for $C_{14}H_8BF_{10}I$ $[M - BF_4]^+$ 416.96; found 416.85. The above data is in agreement with those reported by Olofsson and co-workers.[4]

4-iodo-*N*-(prop-2-yn-1-yl)benzamide (S1)

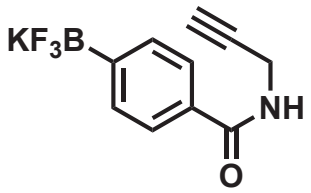


4-Iodobenzoic acid (10.1 g, 41 mmol), propargylamine (3.4 mL, 52 mmol), and triethylamine (8.4 mL, 61 mmol) were dissolved at rt in anhydrous DMF (120 mL). Following the addition of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (10.1 g, 52 mmol), the reaction mixture was heated at 90 °C for 60 min. Upon completion, the reaction mixture was allowed to cool to rt followed by the addition ice-cold water (300 mL). The resulting precipitate was collected *via* vacuum filtration and washed with additional water (600 mL). The precipitate was dissolved in EtOAc, dried over anhydrous $MgSO_4$, collected by vacuum filtration, and concentrated *in vacuo* afford amide **S1** as an off-white solid (2.81 g, 24%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.98 (t, *J* = 5.5 Hz, 1H), 7.86 (d, *J* = 8.5 Hz, 2H), 7.63 (d, *J* = 8.5 Hz, 2H), 4.04 (dd, *J* = 5.6, 2.5 Hz, 2H), 3.12 (t, *J* = 2.5 Hz, 1H); **^{13}C NMR** (101 MHz,

DMSO-d_6) δ 165.25, 137.22, 133.20, 129.19, 99.07, 81.08, 72.90, 28.50; **LRMS** (ESI+) *m/z* calculated for $C_{10}H_8INO$ $[M+H]^+$ 285.97; found 285.80. The above data is in agreement with those reported by Abell and co-workers.[5]

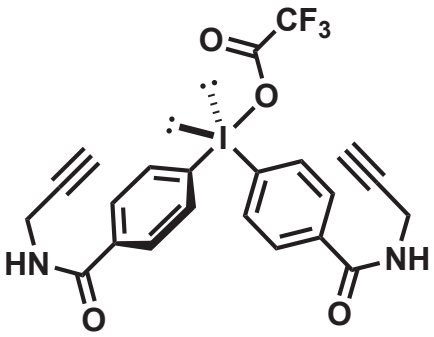
Potassium 4-iodo-*N*-(prop-2-yn-1-yl)-phenyltrifluoroborate (S2)



(4-(Prop-2-yn-1-ylcarbamoyl)phenyl)boronic acid (500 mg, 2.5 mmol) was dissolved in MeOH (24 mL) and cooled to 0 °C. Separately, KHF_2 (1.4 g, 17.9 mmol) was dissolved in H_2O (8 mL) and was added dropwise to the stirring MeOH solution. The reaction mixture was warmed to room temperature over 20 min and concentrated *in vacuo*. Acetone (40 mL) was added to the crude solid and the resulting suspension was filtered and the filtrate concentrated *in vacuo* to afford aryltrifluoroborate **S2** as a white solid (484 mg, 74%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.66 (t, *J* = 5.7 Hz, 1H), 7.61 (d, *J* = 7.7 Hz, 2H), 7.40 (d, *J* = 7.7 Hz, 2H), 4.02 (dd, *J* = 5.6, 2.5 Hz, 2H), 3.06 (t, *J* = 2.5 Hz, 1H); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 166.89, 131.07, 130.63, 125.26, 81.72, 72.46, 28.31; **^{19}F NMR** (376 MHz, DMSO-d_6) δ -139.56; **^{11}B NMR** (128 MHz, DMSO-d_6) δ 3.05; **LRMS** (ESI–) *m/z* calculated for $C_{10}H_8BF_3KNO$ $[M - K]^-$ 226.07; found 225.75l; **HRMS** (ESI–) *m/z* calculated for $C_{10}H_8BF_3KNO$ $[M - K]^-$ 226.0657; found 226.0656; **IR** ν_{max} (ATR, cm^{-1}) 3416, 3284, 1633, 1554, 1520, 1494, 1408, 1359, 1306, 1256, 1230, 1212, 1192, 1152, 1110, 1022, 953, 914, 866, 841, 814, 768, 711, 681, 648, 630, 581, 544, 481, 435.

bis(4-(prop-2-yn-1-ylcarbamoyl)phenyl)iodonium trifluoroacetate (4)

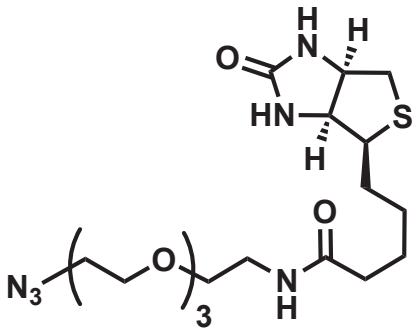


Under a nitrogen atmosphere aryl iodide **S1** (99 mg, 0.35 mmol) and Selectfluor^{TM} (165 mg, 0.47 mmol) were dissolved in anhydrous MeCN (2 mL), quickly followed by the addition of trimethylsilyl acetate (140 µL, 0.93 mmol). The reaction mixture was stirred at rt for 3 hr followed by the addition of aryltrifluoroborate **S2** (81 mg, 0.36 mmol) and trimethylsilyl triflate (60 µL, 0.33 mmol). After stirring at rt for 60 min, the reaction mixture was concentrated *in vacuo*. The crude product was purified by RP-HPLC with a Waters Sunfire®, C18, 180 Å, 30 x 150 mm column (0 to 20% MeCN over 50 min, 0.1 vol% TFA, 38 mL/min) and lyophilised to afford the diaryliodonium salt **4** as a yellow oil (26 mg, 14%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.13 (t, *J* = 5.5 Hz, 2H), 8.35 (d, *J* = 8.6 Hz, 4H), 7.91 (d, *J* = 8.4 Hz, 4H), 4.05 (dd, *J* = 5.5, 2.6 Hz, 4H), 3.13 (t, *J* = 2.6 Hz, 2H); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 164.69, 136.91, 135.28, 130.26, 119.60, 80.79, 73.13, 28.64; **^{19}F NMR** (376 MHz, DMSO-d_6) δ –74.01; **LRMS** (ESI+) *m/z* calculated for $C_{22}H_{16}F_3IN_2O_4$ $[M - C_2O_2F_3]^+$ 443.03; found 442.90; **HRMS** (ESI+) *m/z* calculated for $C_{22}H_{16}F_3IN_2O_4$ $[M - C_2O_2F_3]^+$ 443.0251; found 443.0252; **IR** ν_{max} (ATR, cm^{-1}) 3289, 1728, 1631, 1581, 1542, 1478, 1419, 1391, 1354, 1305, 1282, 1253, 1178, 1135, 1051, 998, 984, 923, 844, 828, 798, 753, 721, 705, 656, 618, 582, 514, 441, 412.

N.B. repeatedly dissolving this compound in acetonitrile leads to formation of an insoluble solid. This can be redissolved in H_2O and/or acetonitrile containing 1 vol% TFA additive.

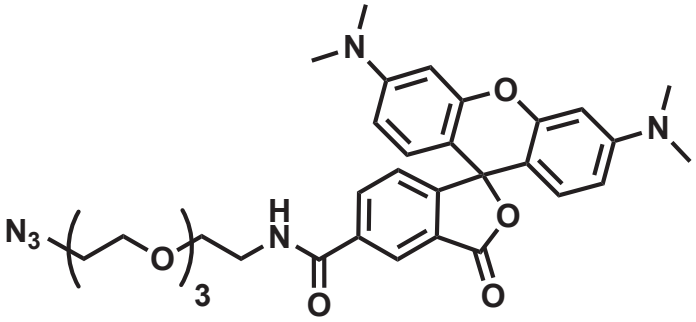
Azido-PEG$_3$-biotin (S3)



To a solution of azido-PEG$_3$-amine (240 µL, 1.2 mmol) and *i*-Pr$_2$EtN (340 µL, 2.0 mmol) in anhydrous CH_2Cl_2 (10 mL) was added biotin-NHS (341 mg, 1.0 mmol) at rt. The reaction mixture was stirred at rt for 2 h, after which it was concentrated under a stream of nitrogen. The crude residue was then purified by flash chromatography (eluent: 0 to 10 vol% MeOH in CH_2Cl_2) to afford azido-PEG$_3$-biotin **S3** as an off-white solid (288 mg, 63%).

^{1}H NMR (400 MHz, D_3COD) δ 4.49 (ddd, *J* = 7.9, 5.1, 1.0 Hz, 1H), 4.31 (dd, *J* = 7.9, 4.5 Hz, 1H), 3.71-3.58 (m, 10H), 3.55 (t, *J* = 5.5 Hz, 2H), 3.37 (dt, *J* = 8.5, 5.3 Hz, 4H), 3.21 (ddd, *J* = 8.9, 5.9, 4.4 Hz, 1H), 2.93 (dd, *J* = 12.7, 5.0 Hz, 1H), 2.75-2.65 (m, 1H), 2.22 (t, *J* = 7.4 Hz, 2H), 1.81-1.53 (m, 4H), 1.52-1.34 (m, 2H); **^{13}C NMR** (101MHz, D_3COD) δ 176.11, 166.09, 71.65, 71.62, 71.52, 71.52, 71.27, 71.11, 70.59, 63.36, 61.63, 56.98, 51.79, 49.64, 49.43, 49.21, 49.00, 48.79, 48.57, 48.36, 41.04, 40.36, 36.74, 29.74, 29.49, 26.82, –18.06; **LRMS** (ESI+) *m/z* calculated for $C_{18}H_{32}N_6O_5S$ $[M+H]^+$ 445.22; found 445.10. The above data is consistent with those reported by Tantama and co-workers.[6]

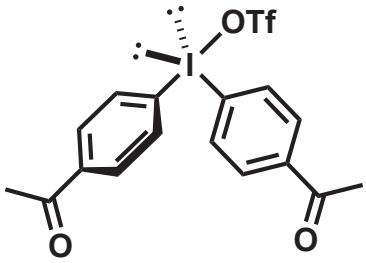
Azido-PEG$_3$-TAMRA (S4)



5-Carboxytetramethylrhodamine (14.0 mg, 33 μmol), NMM (15 μL, 140 μmol), Oxyma (7.0 mg, 49 μmol) and azido-PEG$_3$-amine (25 μL, 120 μmol) were dissolved in DMF (0.6 mL) and DIC (6 μL, 39 μmol) was added. The reaction was stirred at rt for 2 h and purified by RP-HPLC with a Waters Sunfire C18 19 x 150 mm column (0 to 50% MeCN, 0.1 vol% TFA over 30 min, 14 mL/min) to afford amide **S4** as an indigo oil (12 mg, 58%).

^{1}H NMR (400MHz, D_3COD) δ 8.77 (d, *J* = 1.9Hz, 1H), 8.26 (dd, *J* = 7.8, 1.9Hz, 1H), 7.52 (d, *J* = 7.9Hz, 1H), 7.16 (d, *J* = 9.4Hz, 2H), 7.06 (dd, *J* = 9.5, 2.5Hz, 2H), 6.98 (d, *J* = 2.4Hz, 2H), 3.74 (t, *J* = 5.4Hz, 2H), 3.72-3.57 (m, 12H), 3.34 (dd, *J* = 9.7, 4.8Hz, 14H)**; LRMS** (ESI+) *m/z* calculated for $C_{33}H_{38}N_6O_7$ $[M+H]^+$ 631.29; found 631.65. The above data is in agreement with those reported by Lahav and co-workers.[7]

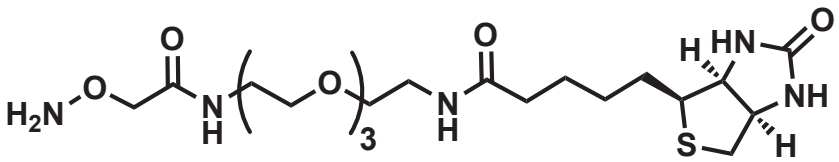
bis(4-acetylphenyl)iodonium triflate (14)



4-Acetophenone (491 mg, 2.0 mmol) and *m*-chloroperbenzoic acid (575 mg, 66 wt.% active oxidant, 2.2 mmol) were dissolved in CH_2Cl_2 (7.5 mL) in a sealed tube and heated to 80 ˚C for 18 hr. The reaction mixture was cooled to 0 °C, 4-(trifluoromethyl)phenylboronic acid (2.2 mg, 2.2 mmol) added, followed by the dropwise addition of boron trifluoride diethyl etherate (0.7 mL, 5.0 mmol). This was stirred for 15 min, warmed to r.t. and stirring for another 1 hr, followed by the dropwise addition of triflic acid (0.19 mL, 2.2 mmol). After stirring for 15 min the solution was concentrated *in vacuo*, triturated with diethyl ether (80 mL), centrifuged, the supernatant decanted leaving a solid which was then dried under vacuum to afford the pure diaryliodonium salt **14** as previously reported.[8]

^{1}H NMR (500 MHz, CD_3CN) δ 8.23 (d, J = 8.7 Hz, 4H), 8.02 (d, J = 8.7 Hz, 4H), 2.57 (s, 6H); **^{13}C NMR** (126 MHz, CD3CN) δ 197.9, 141.2, 136.8, 132.4, 118.7, 27.1; **^{19}F NMR** (471 MHz, CD_3CN) δ -79.2; **LRMS** (ESI+) *m/z* calculated for $C_{17}H_{14}F_3IO_5S$ $[M - CF_3O_3S]^+$ 365.00; found 365.00. The above data is in agreement with those reported by Liu and co-workers.[6]

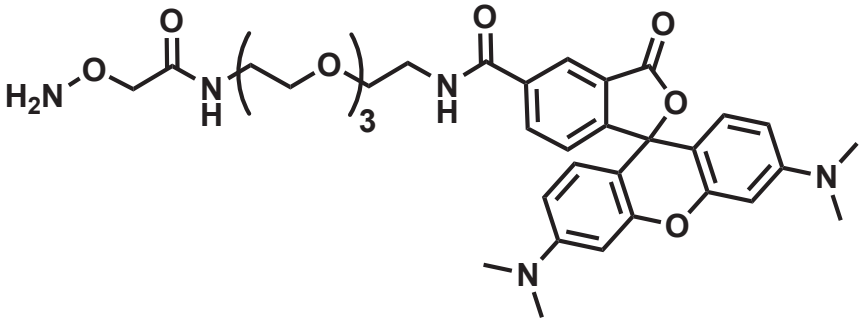
Alkoxyamine-PEG$_3$-biotin (S5)



Biotin-PEG$_3$-amine (104 mg, 0.25 mmol) and BocNHOCH$_2$CO$_2$Su (87 mg, 0.3 mmol) were dissolved in CH_2Cl_2 (20 mL), and triethylamine (70 µL, 0.5 mmol) was added. This was stirred for 2 h, concentrated *in vacuo*, dissolved in CH_2Cl_2 (1 mL), TFA (1 mL) added, then stirred for 2 h before concentrating under a stream of nitrogen and dried *in vacuo*. The crude material was purified by reverse phase flash chromatography (C18 stationary phase, 0 to 20% MeCN in H_2O over 15 column volumes, 0.1 vol% TFA) and the pure fraction lyophilised to afford the TFA salt of the alkoxyamine biotin derivative **S5** as a white solid (90 mg, 60%).

^{1}H NMR (400 MHz, D_2O) δ 4.59 (s, 2H, OCH$_2$CO), 4.55 (dd, *J* = 8.0, 5.0 Hz, 1H, CHN), 4.37 (dd, *J* = 8.0, 4.5 Hz, 1H, CHN), 3.67–3.55 (m, 12H, 12 x CH$_2$O), 3.43 (t, *J* = 5.4 Hz, 2H, CH$_2$N), 3.34 (t, *J* = 5.4 Hz, 2H, CH$_2$N), 3.31–3.25 (m, 1H, CHS), 2.94 (dd, *J* = 13.1, 5.0 Hz, 1H, CH$_2$S'), 2.73 (d, *J* = 13.0 Hz, 1H, CH$_2$S''), 2.22 (t, *J* = 7.3 Hz, 2H, CH$_2$CO), 1.73–1.47 (m, 4H 2 x CH$_2$), 1.41–1.33 (m, 2H, CH$_2$). **^{13}C NMR** (101 MHz, D_2O) δ 177.0 (CONH), 168.9 (CONH), 165.4 (NHCONH), 162.9 (q, J_{CF} = 36 Hz, CF_3CO_2), 116.4 (q, J_{CF} = 292 Hz, CF_3), 71.8 (OCH$_2$CO), 69.7 (CH$_2$O), 69.6 (CH$_2$O), 69.4 (2 x CH$_2$O), 68.9 (CH$_2$O), 68.7 (CH$_2$O), 62.1 (CHN), 60.3 (CHN), 55.4 (CHS), 39.7 (CH$_2$S), 38.9 (CH$_2$N), 38.8 (CH$_2$N), 35.5 (CH$_2$CO), 27.9 (CH$_2$), 27.7 (CH$_2$), 25.1 (CH$_2$). **HRMS** (ESI+) *m/z* calculated for $C_{20}H_{37}N_5O_7S$ $[M+H]^+$ m/z 492.2487; found: 492.2486. **IR** ν_{max} (ATR, cm^{-1}) 3293, 3093, 2933, 2873, 1671, 1557, 1199, 1182, 1137 cm^{-1}.

Alkoxyamine-PEG$_3$-TAMRA (S6)

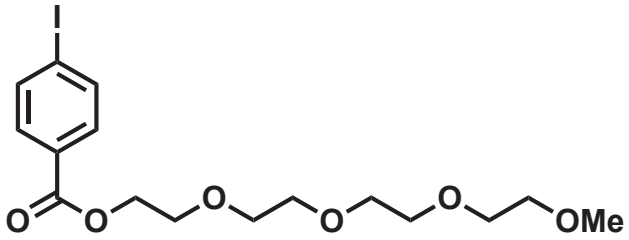


To a solution of azido-PEG$_3$-amine (100 mg, 0.458 mmol) in CH_2Cl_2 (2.3 mL) at 0 °C was added BocNHOCH$_2$CO$_2$Su (145 mg, 0.504 mmol), followed by triethylamine (93 µL, 0.916 mmol). The mixture was stirred at 0 °C for 25 min before treating with 1 M NaOH (1 mL) and stirring vigorously for 5 min. The mixture was partitioned between H_2O (10 mL) and EtOAc (15 mL), and the resulting organic layer was washed with 1 M HCl (2 x 10 mL), followed by H_2O (10 mL), and dried over $MgSO_4$. The filtrate was concentrated to dryness and the residue taken up in MeOH (5 mL). 10% w/w Pd/C (30 mg) was added and the mixture was vigorously stirred under an atmosphere of H_2 (1 atm) for 1 h. The suspension was filtered through celite and the filtrate concentrated to dryness, affording BocNHOCH$_2$CO-NH-PEG$_3$-amine as a low-melting colourless solid (138 mg, 82%), which was used without further purification.

To a solution of 5-carboxytetramethylrhodamine (22 mg, 0.05 mmol) in DMF (250 µL) was added HATU (19 mg, 0.05 mmol), followed by Et_3N (14 µL, 0.1 mmol). The mixture was stirred at rt for 5 min before adding a solution of the crude $BocNHOCH_2CO$-NH-PEG_3-amine (18 mg, 0.05 mmol) in DMF (250 µL). This mixture was stirred for 30 min at rt before concentrating under a stream of N_2. The residue was treated with 4 M HCl in dioxane (2 mL) and stirred at rt for 30 min before concentrating under a stream of N_2. The residue was purified by reverse phase flash chromatography (C18 stationary phase, 0 to 50% MeCN in H_2O over 20 column volumes, 0.1% TFA), affording the TFA salt of the TAMRA alkoxyamine derivative **S6** as a fluffy purple powder after lyophilisation (26 mg, 66%).

^{1}H NMR (500 MHz, D_2O) δ 8.54 (d, *J* = 1.9 Hz, 1H, ArCH), 8.11 (dd, *J* = 7.9, 1.9 Hz, 1H, ArCH), 7.49 (d, *J* = 7.9 Hz, 1H, ArCH), 7.02 (d, *J* = 9.5 Hz, 2H, 2 x ArCH), 6.72 (dd, *J* = 9.5, 2.5 Hz, 2H, 2 x ArCH), 6.21 (d, *J* = 2.4 Hz, 2H, 2 x ArCH), 4.52 (s, 2H, OC*H*$_2$CONH), 3.75 (t, *J* = 5.4 Hz, 2H, CH_2O), 3.72 – 3.68 (m, 2H, CH_2O), 3.67 – 3.60 (m, 6H, CH_2N, 2 x CH_2O), 3.60 – 3.56 (m, 2H, CH_2O), 3.54 (t, *J* = 5.4 Hz, 2H, CH_2O), 3.35 (t, *J* = 5.4 Hz, 2H, CH_2N), 2.98 (s, 12H, 4 x NCH_3); **^{13}C NMR** (126 MHz, D_2O) δ 169.0 (OCH_2*C*ONH), 168.9 (CONH), 168.6 (ArC*C*OO), 163.0 (q, J_{CF} = 35 Hz, CF_3*C*O), 157.1 (ArC-O), 157.0 (2 x ArC-O), 156.9 (2 x ArC-N), 136.5 (ArC), 135.7 (ArC), 132.0 (ArC), 131.4 (ArCH), 131.1 (ArCH), 130.6 (2 x ArCH), 129.8 (ArCH), 116.5 (q, J_{CF} = 292 Hz, CF_3) 114.2 (2 x ArCH), 112.9 (2 x ArC), 96.2 (2 x ArCH), 71.9 (O*C*H_2CONH), 69.8 (CH_2O), 69.8 (CH_2O), 69.7 (CH_2O), 69.6 (CH_2O), 69.0 (CH_2O), 68.8 (CH_2O), 40.1 (4 x NCH_3), 39.9 (CH_2N), 38.8 (CH_2N); **HRMS** (ESI+) *m/z* calculated for $C_{35}H_{44}N_5O_9$ $[M+H]^+$ m/z 678.3134; found: 678.3132; **IR** ν_{max} (ATR, cm^{-1}) 3294, 3083, 2929, 2876, 1667, 1647, 1594, 1561, 1536, 1493, 1409, 1366, 1348, 1184, 1132, 1083 cm^{-1}.

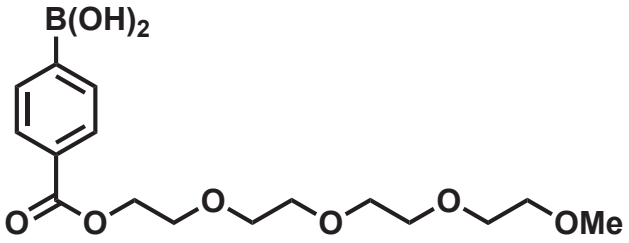
mPEG$_4$ 4-iodobenzoate (S7)



Under a nitrogen atmosphere 4-iodobenzoic acid (238 mg, 0.91 mmol), 4-dimethylaminopyridine (6 mg, 0.05 mmol), and mPEG$_4$-OH (100 mg, 0.48 mmol) were dissolved in anhydrous CH_2Cl_2 (2 mL) and stirred over activated 4 Å molecular sieves (140 mg) for 2 h before the addition of *N*-Ethyl-*N*′-(3-dimethylaminopropyl)carbodiimide hydrochloride (184 mg, 0.96 mmol). The reaction was stirred for 7 h, filtered through celite, and the filtrate concentrated *in vacuo*. The crude product was purified by flash chromatography (eluent: 50 vol% EtOAc in hexanes) to afford the pure ester **S7** as a colourless oil (183 mg, 87%).

^{1}H NMR (400 MHz, CD_3CN) δ 7.89 (d, *J* = 8.7 Hz, 2H), 7.74 (d, *J* = 8.5 Hz, 2H), 4.42 – 4.38 (m, 2H), 3.80 – 3.74 (m, 2H), 3.63 – 3.59 (m, 2H), 3.58 – 3.48 (m, 8H), 3.45 – 3.41 (m, 2H), 3.27 (s, 3H); **^{13}C NMR** (101 MHz, CD_3CN) δ 166.76, 138.95, 131.92, 131.00, 101.17, 72.63, 71.33, 71.23, 71.16, 71.15, 71.02, 69.65, 65.42, 58.91; **HRMS** (ESI+) *m/z* calculated for $C_{16}H_{23}IO_6$ $[M+Na]^+$ 461.0432; found 461.0436; **IR** ν_{max} (ATR, cm^{-1}) 2871, 1717, 1585, 1451, 1392, 1351, 1267, 1199, 1177, 1098, 1029, 1007, 944, 845, 753, 698, 682, 626, 613, 546, 464.

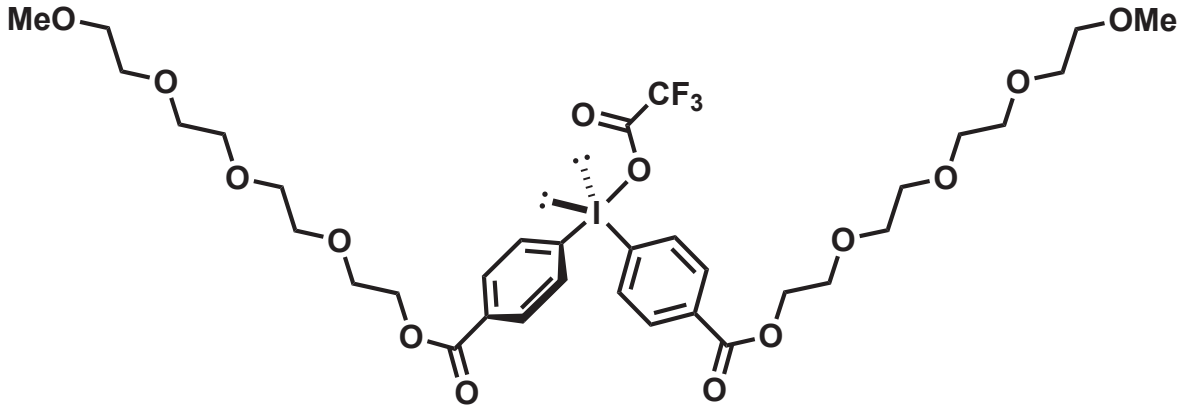
(4-(mPEG$_4$-carbonyl)phenyl)boronic acid (S8)



To a solution of 4-carboxyphenylboronic acid (200 mg, 1.21 mmol) in dry DMF (4 mL) was added 4-dimethylaminopyridine (113 mg, 0.542 mmol), followed by *N*-ethyl-*N*′-(3-dimethylaminopropyl)carbodiimide hydrochloride (393 mg, 2.05 mmol). The mixture was stirred for 1 h at rt before adding mPEG$_4$-OH (254 µL, 1.21 mmol) and stirring for a further 16 h at rt. The mixture was diluted with H_2O (20 mL) and extracted with EtOAc (5 x 20 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated to dryness. The residue was azeotroped with toluene (4 x 20 mL) and then purified by silica gel flash chromatography (0 to 15% MeOH in CH_2Cl_2 with 1% AcOH), affording the ester **S8** as a colourless oil (305 mg, 73%).

^{1}H NMR (300 MHz, MeOD) δ 8.00 (d, *J* = 7.8 Hz, 2H), 7.72 (m, 2H), 4.49–4.42 (m, 2H), 3.88–3.79 (m, 2H), 3.73–3.55 (m, 10H), 3.53–3.47 (m, 2H), 3.33 (s, 3H); **^{13}C NMR** (75 MHz, MeOD) δ 168.1, 134.5, 129.5 (2 aromatic signals too broad to be observed), 72.9, 71.7, 71.6 (2 overlapping signals), 71.5, 71.3, 70.2, 65.3, 59.1; **HRMS** (ESI+) *m/z* calculated for $C_{16}H_{25}BO_8$ $[M+Na]^+$ *m/z* 379.1535; found: 379.1534; **IR** ν_{max} (ATR, cm^{-1}) 3409, 2878, 1715, 1348, 1269, 1092, 1017, 711.

bis(4-mPEG$_4$ benzoate)iodonium trifluoroacetate (20)

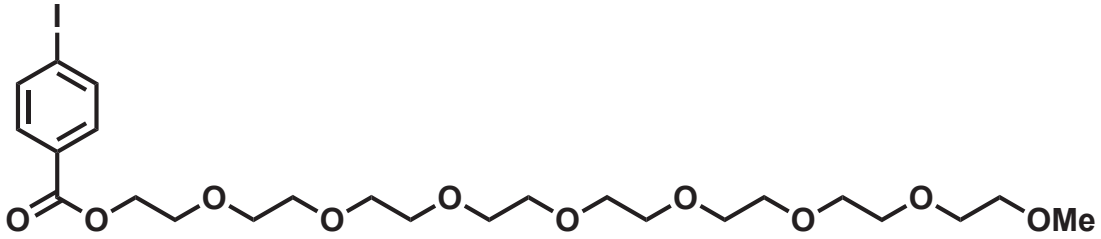


Boron trifluoride diethyl etherate (85 µL, 0.687 mmol) was added dropwise to a solution of aryl iodide **S5** (120 mg, 0.275 mmol) and *m*-chloroperbenzoic acid (77 wt%, 80 mg, 0.357 mmol) in CH_2Cl_2 (1.3 mL) and the mixture was stirred for 1.5 h at rt. The resulting solution was cooled to 0 °C and treated dropwise with a solution of arylboronic acid **S6** (108 mg, 0.302 mmol) in CH_2Cl_2 (1.3 mL). The solution was allowed to warm to rt and stirred for a further 1 h. TFA (42 µL, 0.542 mmol) was added and the mixture was stirred for a further 30 min. The resulting solution was concentrated to dryness and the solid residue washed with Et_2O (x3), leaving behind a viscous orange oil (105 mg, *ca.* 85% pure diaryliodonium tetrafluoroborate salt by ^{1}H NMR). The material could be further purified by reverse phase flash chromatography

(C18 stationary phase, 0 to 30% MeCN in H_2O over 15 column volumes, 0.1 vol% TFA) affording the diaryliodonium salt **20** as a viscous colourless oil after lyophilisation (60 mg, 25%).

^{1}H NMR (400 MHz, CD_3CN) δ 8.18 (d, *J* = 8.7 Hz, 4H), 8.05 (d, *J* = 8.6 Hz, 4H), 4.44 – 4.40 (m, 4H), 3.80 – 3.73 (m, 4H), 3.62 – 3.58 (m, 4H), 3.56 – 3.47 (m, 16H), 3.45 – 3.41 (m, 4H), 3.26 (s, 6H); **^{13}C NMR** (101 MHz, CD_3CN) δ 164.77, 135.56, 133.88, 132.39, 120.22, 71.58, 70.27, 70.15, 70.08, 69.94, 68.53, 64.90, 57.89; **^{19}F NMR** (376 MHz, CD_3CN) δ -76.26; **LRMS** (ESI+) *m/z* calculated for $C_{34}H_{46}IF_3O_{14}$ $[M–C_2O_2F_3]^+$ 749.2; found 749.6; **HRMS** (ESI+) *m/z* calculated for $C_{34}H_{46}IF_3O_{14}$ $[M–C_2O_2F_3]^+$ 749.2029; found 749.2039; **IR** ν_{max} (ATR, cm^{-1}) 2877, 1722, 1663, 1584, 1452, 1395, 1351, 1272, 1197, 1101, 998, 945, 831, 798, 754, 719, 679, 518, 481, 428.

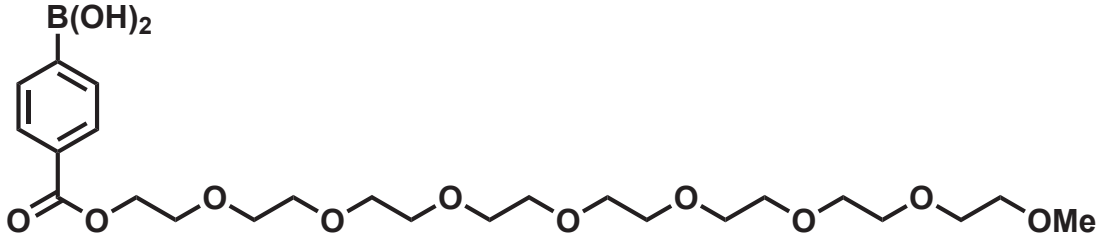
mPEG$_8$ 4-iodobenzoate (S9)



Under a nitrogen atmosphere 4-iodobenzoic acid (388 mg, 1.6 mmol), 4-dimethylaminopyridine (20 mg, 0.17 mmol), and mPEG$_8$-OH (315 mg, 0.82 mmol) were dissolved in anhydrous CH_2Cl_2 (7.5 mL), and stirred over activated 4 Å molecular sieves (500 mg) for 2 h before the addition of *N*,*N'*-dicylohexylcarbodiimide (322 mg, 1.57 mmol). The reaction was stirred overnight for 18 h, quenched with ethanol, and filtered through celite, and the filtrate concentrated *in vacuo*. The crude product was purified by flash chromatography (eluent: 0 to 100 vol% EtOAc in hexanes, then 20 vol% MeOH in hexanes) to afford the pure ester **S9** as a colourless oil (429 mg, 85%).

^{1}H NMR (400 MHz, CD_3CN) δ 7.87 (d, *J* = 8.5 Hz, 2H), 7.73 (d, *J* = 8.5 Hz, 2H), 4.43 – 4.37 (m, 2H), 3.79 – 3.73 (m, 2H), 3.64 – 3.59 (m, 2H), 3.58 – 3.48 (m, 24H), 3.47 – 3.43 (m, 2H), 3.28 (s, 3H); **^{13}C NMR** (126 MHz, CD_3CN) δ 138.09, 131.06, 130.12, 100.32, 71.76, 70.46, 70.34, 70.31, 70.28, 70.14, 68.78, 64.56, 58.05; **HRMS** (ESI+) *m/z* calculated for $C_{24}H_{39}IO_{10}$ $[M+Na]^+$ 637.1480; found 637.1482; **IR** ν_{max} (ATR, cm^{-1}) 2870, 1718, 1638, 1585, 1451, 1392, 1349, 1268, 1199, 1177, 1095, 1007, 945, 846, 754, 683, 605, 545, 489, 423.

(4-(mPEG$_8$-carbonyl)phenyl)boronic acid (S10)

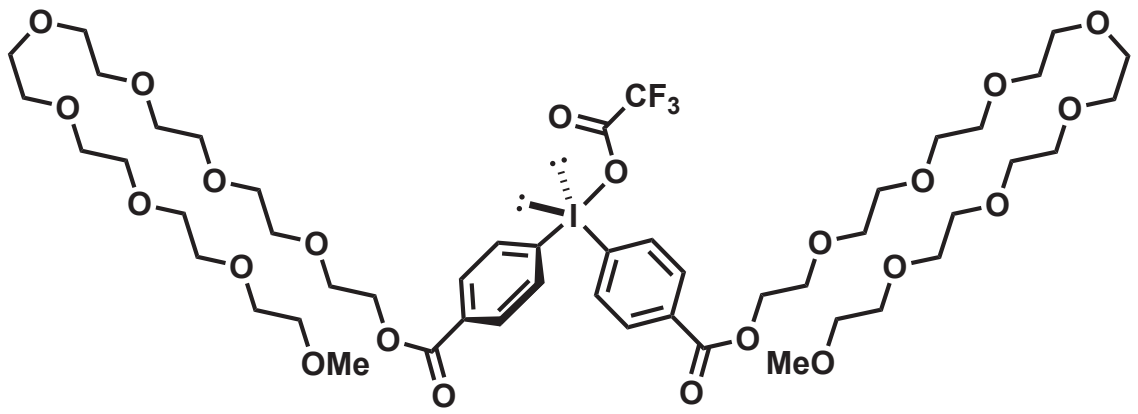


To a solution of 4-carboxyphenylboronic acid (47 mg, 0.28 mmol) in dry DMF (1 mL) was added 4-dimethylaminopyridine (26 mg, 0.13 mmol), followed by *N*-ethyl-*N'*-(3-

dimethylaminopropyl)carbodiimide hydrochloride (91 mg, 0.7 mmol). The mixture was stirred for 1 h at rt before adding $mPEG_8$-OH (59 μL, 0.28 mmol) and stirring for a further 16 h at rt. The mixture was diluted with H_2O (10 mL) and extracted with EtOAc (5 x 10 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated to dryness. The residue was azeotroped with toluene (4 x 10 mL) and then purified by silica gel flash chromatography (0 to 15% MeOH in CH_2Cl_2 with 1% AcOH), affording the ester **S10** as a colourless oil (85 mg, 55%).

^{1}H NMR (500 MHz, MeOD) δ 7.98 (d, *J* = 8.3 Hz, 2H), 7.69 (d, *J* = 7.7 Hz, 2H), 4.48 – 4.42 (m, 2H), 3.86 – 3.83 (m, 2H), 3.72 – 3.69 (m, 2H), 3.68 – 3.57 (m, 24H), 3.55 – 3.51 (m, 2H), 3.35 (s, 3H); **^{13}C NMR** (126 MHz, MeOD) δ 168.4, 134.4, 129.3 (2 aromatic signals too broad to be observed), 73.0, 71.7, 71.6 – 71.5 (10 overlapping signals), 71.3, 70.3, 65.3, 59.1; **HRMS** (ESI+) *m/z* calculated For $C_{24}H_{41}BO_{12}$ $[M+Na]^+$ *m/z* 555.2583; found: 555.2581; **IR** ν_{max} (ATR, cm^{-1}) 2870 3403, 2871, 1716, 1349, 1269, 1092, 1017, 712 cm^{-1}.

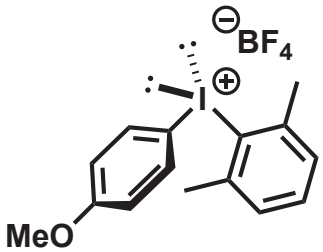
bis(4-mPEG$_8$ benzoate)iodonium trifluoroacetate (21)



Boron trifluoride diethyl etherate (43 μL, 0.35 mmol) was added dropwise to a solution of aryl iodide **S9** (85 mg, 0.14 mmol) and *m*-chloroperbenzoic acid (77 wt%, 31 mg, 0.18 mmol) in CH_2Cl_2 (0.7 mL) and the mixture was stirred for 1.5 h at rt. The resulting solution was cooled to 0 °C and treated dropwise with a solution of arylboronic acid **S10** (82 mg, 0.15 mmol) in CH_2Cl_2 (0.7 mL). The solution was allowed to warm to rt and stirred for a further 1 h. TFA (21 μL, 0.28 mmol) was added and the mixture was stirred for a further 30 min. The resulting solution was concentrated to dryness and the solid residue washed with Et_2O (x3), leaving behind a viscous oil, which could be further purified by reverse phase flash chromatography (C18 stationary phase, 0 to 30% MeCN in H_2O over 15 column volumes, 0.1 vol% TFA) affording the diaryliodonium salt **21** as a viscous colourless oil after lyophilisation (18 mg, 15%).

^{1}H NMR (500 MHz, CD_3CN) δ 8.19 (d, *J* = 8.4 Hz, 4H), 8.05 (d, *J* = 8.3 Hz, 4H), 4.48 – 4.41 (m, 4H), 3.78 (dd, *J* = 5.6, 3.6 Hz, 4H), 3.65 – 3.52 (m, 48H), 3.48 (dd, *J* = 5.8, 3.2 Hz, 4H), 3.29 (s, 6H); **^{19}F NMR** (471 MHz, CD_3CN) δ -76.58; **^{13}C NMR** (126 MHz, CD_3CN) δ 166.34 (HMBC), 136.60, 134.74, 133.37, 122.74 (HMBC), 72.05, 70.92, 70.66, 70.39, 70.37, 70.27, 70.24, 70.21, 70.18, 70.13, 70.04, 69.53, 65.75, 59.05; **LRMS** (ESI+) *m/z* calculated for $C_{50}H_{78}IF_3O_{22}$ $[M–C_2O_2F_3]^+$ 1101.4; found 1101.8; **HRMS** (ESI+) *m/z* calculated for $C_{50}H_{78}IF_3O_{22}$ $[M–C_2O_2F_3]^+$ 1101.4126; found 1101.4133; **IR** ν_{max} (ATR, cm^{-1}) 3398, 1676, 1430, 1374, 1277, 1183, 1131, 947, 836, 800, 755, 721, 601, 554, 483, 460, 420.

(4-methoxyphenyl)(2,6-dimethylphenyl)iodonium tetrafluoroborate (S12)



m-Chloroperbenzoic acid (610 mg, 85 wt.% active oxidant, 3.0 mmol) and 4-methoxyiodobenzene (632 mg, 2.7 mmol) were dissolved in wet CH_2Cl_2 (10 mL), followed by the dropwise addition of boron trifluoride diethyl etherate (0.85 mL, 6.9 mmol). The reaction mixture was stirred at room temperature for 30 min, after which it was cooled to 0 °C and 2,6-dimethyphenylboronic acid (450 mg, 3.0 mmol) was added. The reaction mixture warmed to rt stirred for 15 min. The reaction mixture was then filtered through a silica plug (6 g), eluting first with CH_2Cl_2 (50 mL) and then 20:1 v/v CH_2Cl_2/MeOH (180 mL). This solution was concentrated *in vacuo* and the remaining solid was immediately triturated with Et_2O (3 x 10 mL) to avoid decomposition, affording diaryl iodonium salt **S12** as a yellow solid (335 mg, 29%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.96 (d, J = 9.0 Hz, 1H), 7.46 (dd, J = 8.2, 6.6 Hz, 1H), 7.38 (d, J = 7.5 Hz, 1H), 7.05 (d, J = 9.1 Hz, 1H), 3.79 (s, 2H), 2.66 (s, 3H); **^{13}C NMR** (101 MHz, DMSO) δ 161.80, 141.53, 136.78, 132.65, 129.03, 126.66, 117.57, 103.16, 55.66, 26.45; **^{19}F NMR** (376 MHz, DMSO) δ -148.22, -148.28; **HRMS** (ESI+) *m/z* calculated for $C_{15}H_{16}BF_4IO$ $[M - BF_4]^+$ 339.0240; found 339.0240. **IR** ν_{max} (ATR, cm^{-1}) 1571, 1484, 1461, 1446, 1407, 1386, 1302, 1251, 1179, 1122, 1049, 1025, 989, 972, 904, 826, 799, 786, 744, 688, 619, 583, 549, 521, 511.

Solid-phase peptide synthesis (SPPS)

General procedure A; Automated peptide synthesis (SYRO I peptide synthesiser)

Rink amide resin was treated with 40 vol% piperidine (1.6 mL) in DMF for 3 min, drained, and then treated with 20 vol% piperidine in DMF for 10 min (1.6 mL), drained, and washed with DMF (4 x 1.6 mL). The resin was then treated with a solution of Fmoc-Xaa-OH (400 μmol, 4 eq.) and Oxyma (57 mg, 400 μmol, 4 eq.) in DMF (800 μL), followed by a solution of DIC (63 μL, 400 μmol, 4 eq.) in DMF (800 μL) and shaken at 75 ˚C for 1 h. The resin was then drained and washed with DMF (4 x 1.6 mL) before being treated with a solution of 5 vol% Ac_2O and 10 vol% *i*-Pr_2NEt in DMF (1.6 mL) for 5 min at room temperature, drained, washed with DMF (4 x 1.6 mL) and drained.

General procedure B; Automated microwave-assisted peptide synthesis (liberty blue peptide synthesiser)

Rink amide resin was treated with 20 vol% piperidine (10 mL) for 65 s at 90 °C before being drained and washed with DMF (4 x 7 mL). The resin was then treated with a solution of Fmoc-Xaa-OH (1 mmol, 4 eq.) in DMF (5 mL), Oxyma (284 mg, 2 mmol, 8 eq.) and DIC (313 μL, 2 mmol, 8 eq.) in DMF (8 mL) at 75 °C for 15 s before the temperature was increased to 90 ˚C for an additional 110 s before being drained. The resin was then re-treated with Fmoc-Xaa-OH (1 mmol, 4 eq.) in DMF (5 mL), Oxyma (284 mg, 2mmol, 8 eq.) and DIC (313 μL, 2 mmol, 8 eq.) in DMF (8mL) at 75 ˚C for 15 s and then at 90 ˚C for an additional 110 s and drained.

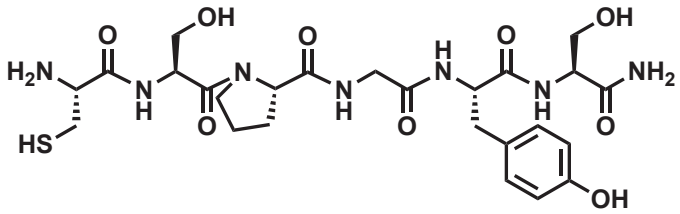
General procedure C; standard peptide cleavage

Rink amide resin was thoroughly washed with CH_2Cl_2 (5 x 5 mL) before being treated with 90:5:5 v/v/v TFA:triisopropylsilane:H_2O and shaken at rt for 2 h. The resin was filtered and washed with TFA (2 x 3 mL). The filtrate was concentrated under a stream of nitrogen before addition of diethyl ether (40 mL) to precipitate the peptide. The peptide was pelleted by centrifugation (5 min at 5000 rcf), the ether decanted, and the resulting crude peptide dried under a gentle stream of nitrogen.

General procedure D; peptide cleavage with reagent H

Rink amide was thoroughly washed with CH_2Cl_2 (5 x 5 mL) before being treated with TFA:phenol:thioanisole:EDT:H_2O:dimethyl sulfide:NH_4I (81:5:5:2.5:3:2:1.5 w/w/w/w/w/w/w) and shaken at rt for 4 h.[9] The resin was filtered and washed with TFA (2 x 3 mL). The filtrate was concentrated under a stream of nitrogen before addition of diethyl ether (40 mL) to precipitate the peptide. The peptide was pelleted by centrifugation (5 min at 5000 rcf), the ether decanted, and the resulting crude peptide dried under a gentle stream of nitrogen.

H-CSPGYS-NH_2 (2)



Rink amide resin (175 mg, 100 μmol, 0.57 mmol g^{-1}) was loaded with Fmoc-Ser(*t*Bu)-OH and synthesised on the Liberty Blue peptide synthesiser according to general procedure **B**. The resin-bound peptide was cleaved according to general procedure **C** and purified *via* preparative HPLC with a Waters X-Bridge®, C18, 300 Å, 30 x 150 mm column (0 to 30% MeCN over 30 min, 0.1 vol% TFA, 38 mL/min). Lyophilisation of the pure fractions afforded the pure peptide **2** (47.3 mg, 65% yield).

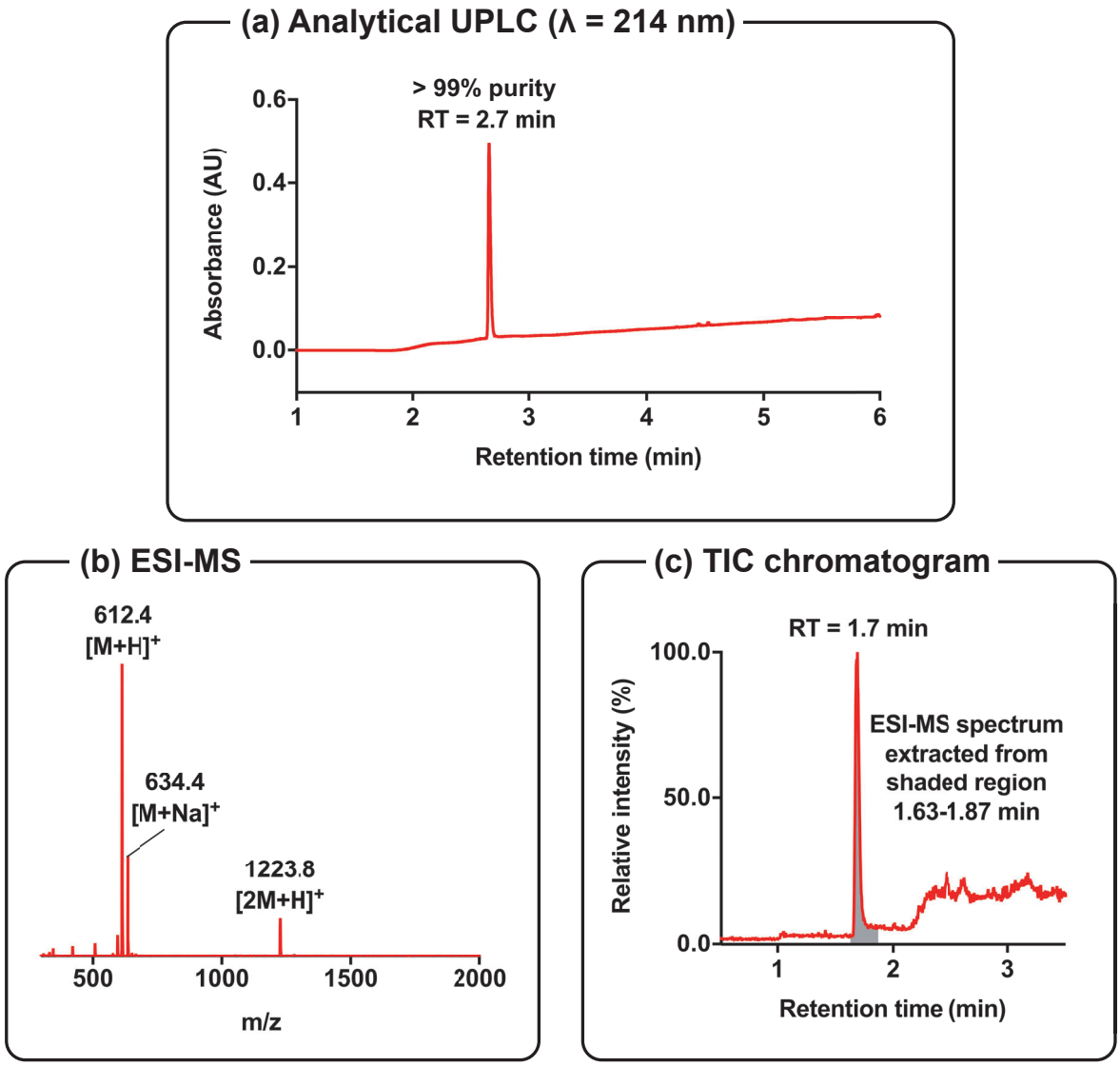
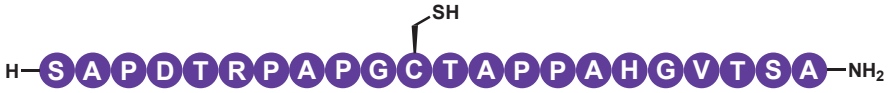


Figure S1: (a) Analytical ultra-performance liquid chromatography (UPLC) chromatogram of pure peptide **2**: retention time (RT) = 2.7 min (0 to 60% MeCN in H_2O over 5 min, 0.1% TFA, λ = 214 nm, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column); **(b) ESI-MS** spectrum (ESI+) of pure peptide **2** extracted from total ion current (TIC) chromatogram 1.63-1.87 min: *m/z* calculated for $C_{25}H_{37}N_7O_9S$ $[2M+H]^+$ 1223.5, $[M+Na]^+$ 634.2, $[M+H]^+$ 612.3; found (ESI+) $[2M+H]^+$ 1223.8, $[M+Na]^+$ 634.4, $[M+H]^+$ 612.4; **(c) TIC chromatogram** of pure peptide **2**: RT = 1.7 min (0 to 60% MeCN in H_2O over 3 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column).

MUC1 VNTR (5)



Rink amide resin (175 mg, 100 µmol, 0.57 mmol g^{-1}) was loaded with Fmoc-Ala-OH and the peptide synthesised on the Liberty Blue peptide synthesiser according to general procedure **B**. The resin-bound peptide was cleaved according to general procedure **C** and purified *via* preparative HPLC with an Waters X-Bridge®, C18, 300 Å, 30 x 150 mm column (0 to 30% MeCN over 30 min, 0.1 vol% TFA, 38 mL/min). Lyophilisation of the pure fractions afforded the pure peptide **5** (59 mg, 26% yield).

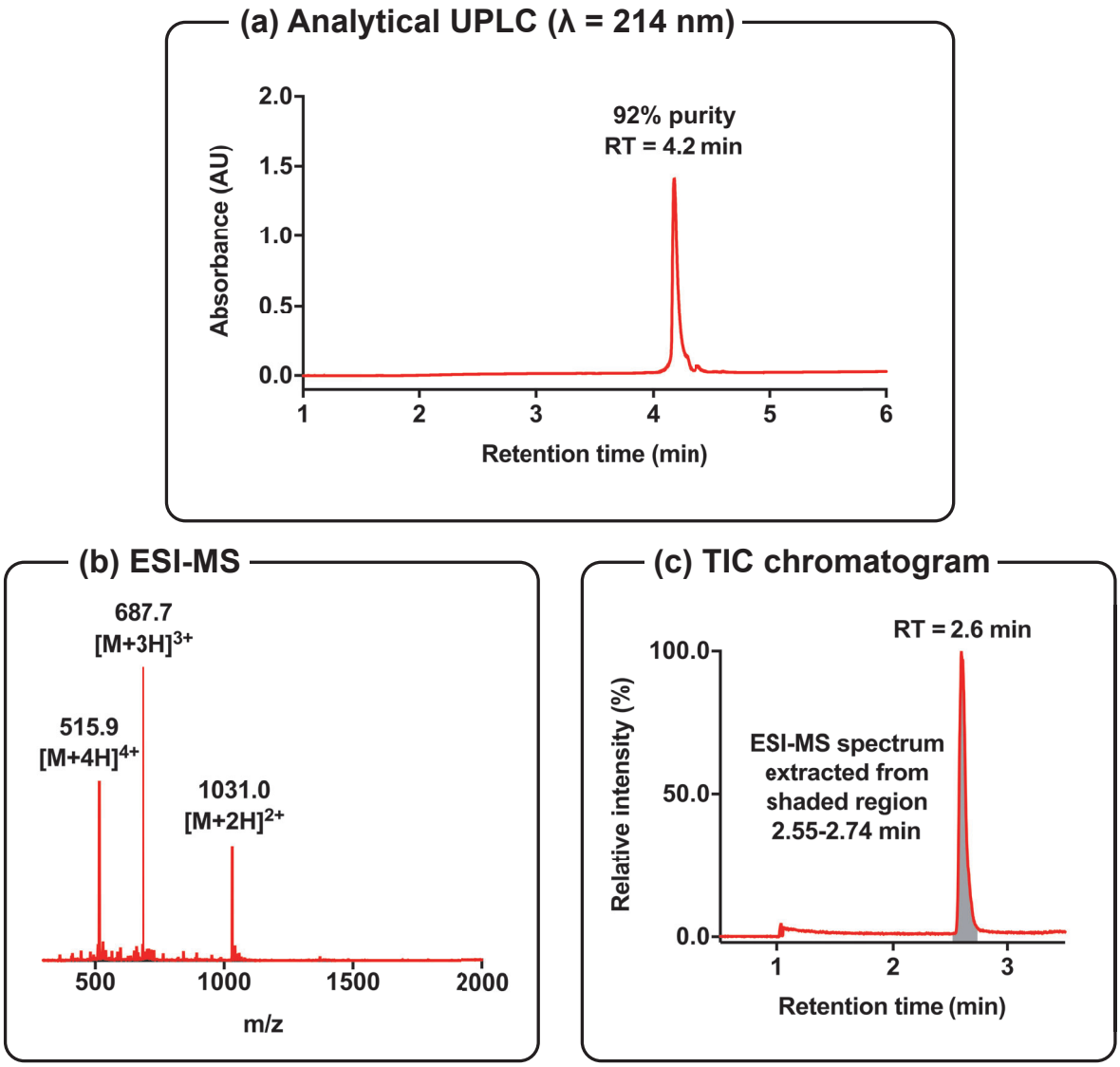
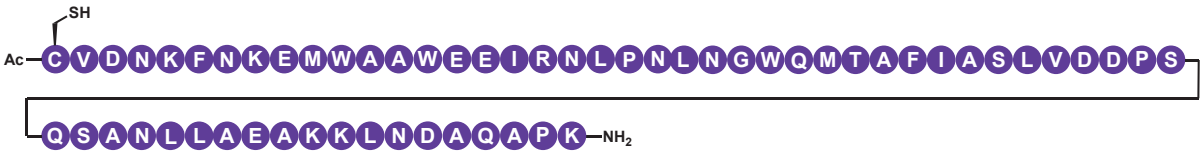


Figure S2: (a) Analytical UPLC chromatogram of pure peptide **5**: retention time (RT) = 4.2 min (0 to 30% MeCN in H_2O over 5 min, 0.1% TFA, λ = 214 nm, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column); **(b) ESI-MS** spectrum (ESI+) of pure peptide **5** extracted from TIC chromatogram 2.55-2.74 min: *m/z* calculated for $C_{86}H_{138}N_{28}O_{29}S$ $[M+2H]^{2+}$ 1030.5, $[M+3H]^{3+}$ 687.3, $[M+4H]^{4+}$ 515.8; found (ESI+) $[M+2H]^{2+}$ 1031.0, $[M+3H]^{3+}$ 687.7, $[M+4H]^{4+}$ 515.9; deconvoluted mass of 2059.9 +/– 0.3 Da; **(c) TIC chromatogram** of pure peptide **5**: RT = 2.6 min (0 to 40% MeCN in H_2O over 3 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column).

zEGFR (11)



Rink amide resin (88 mg, 50 μmol, 0.57 mmol g^{-1}) was loaded with Fmoc-Lys(Boc)-OH and the protein synthesised on the SYRO I peptide synthesiser according to general procedure **A**. The resin-bound peptide was split in half and 25 μmol was cleaved according to general procedure **D**. The crude peptide was dissolved in 2 vol% AcOH in 1:1 MeCN:H_2O and lyophilised to remove carbamic acid on Trp, followed by purification *via* preparative HPLC with a Waters X-Bridge® C18, 300 Å, 10 x 250 mm column (0 to 50% MeCN over 60 min, 0.1 vol% TFA, 38 mL/min, 55 ˚C). Lyophilisation of the pure fractions afforded the pure protein **11** (9 mg, 5% isolated yield).

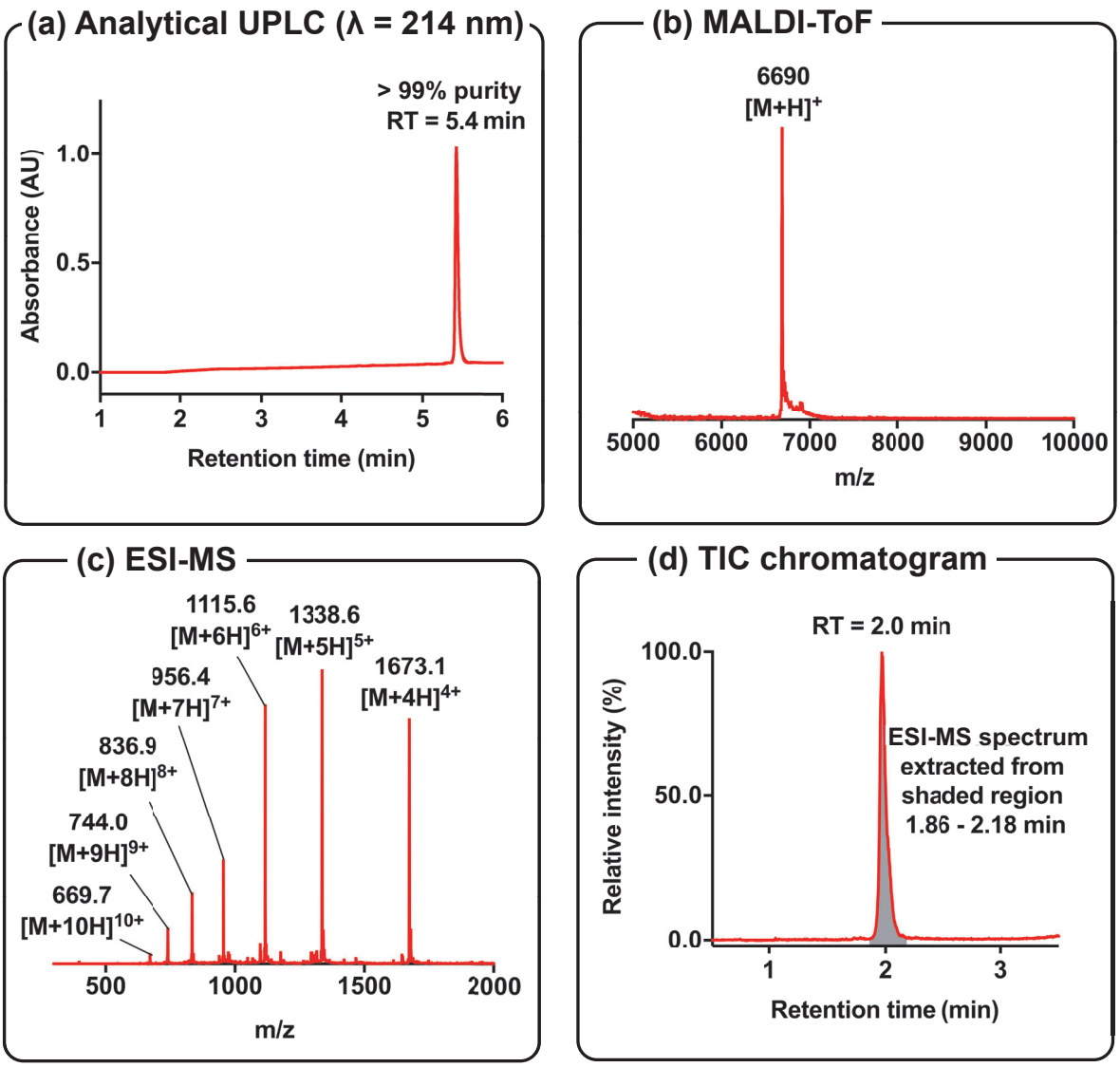


Figure S3: (a) Analytical UPLC chromatogram of pure protein **11**: retention time (RT) = 5.4 min (0 to 60% MeCN in H_2O over 5 min, 0.1% TFA, λ = 214 nm, Waters Acquity ® BEH, C18, 300Å, 2.1x50 mm column); **(b) MALDI-ToF** (LP) of pure protein: *m/z* calculated for $C_{296}H_{459}N_{81}O_{90}S_3$ $[M+H]^+$ 6685; found (LP) $[M+H]^+$ 6690; **(c) ESI-MS** spectrum (ESI+) of pure protein **11** extracted from TIC chromatogram 1.86-2.18 min: *m/z* calculated for $C_{296}H_{459}N_{81}O_{90}S_3$ $[M+4H]^{4+}$ 1672.1, $[M+5H]^{5+}$ 1337.9, $[M+6H]^{6+}$ 1115.1, $[M+7H]^{7+}$ 955.9, $[M+8H]^{8+}$ 836.6, $[M+9H]^{9+}$ 743.7, $[M+10H]^{10+}$ 669.7; found (ESI+) $[M+4H]^{4+}$ 1673.1, $[M+5H]^{5+}$ 1338.6, $[M+6H]^{6+}$ 1115.6, $[M+7H]^{7+}$ 956.4, $[M+8H]^{8+}$ 836.9, $[M+9H]^{9+}$ 744.0, $[M+10H]^{10+}$ 669.7; deconvoluted mass of 6687.5 +/– 0.6 Da; **(d) TIC chromatogram** of pure protein **11**: RT = 2.0 min (0 to 100% MeCN in H_2O over 3 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column)**.** The above data is consistent with that reported by Zhong *et al.*[7]

Alkoxyamine-PEG$_3$-penetratin (S11)

Rink amide resin (88 mg, 50 µmol, 0.57 mmol g^{-1}) was loaded with Fmoc-Lys(Boc)-OH and the peptide synthesised up to Fmoc-RQIKIWFQNRRMKWKK-NH_2 on the SYRO I peptide synthesiser according to general procedure A. The resin was treated with 20 vol% piperidine in DMF for 3 min, drained, and these steps repeated once more before washing with DMF (x3), CH_2Cl_2 (x3), and then DMF (x3). The resin was then treated with a solution of Fmoc-NH-PEG$_3$-CO_2H (195 mg, 400 µmol, 4 eq.) and Oxyma (57 mg, 400 µmol, 4 eq.) in DMF (800 µL), followed by a solution of DIC (63 µL, 400 µmol, 4 eq.) in DMF (800 µL) and shaken for 2 h, then washed with DMF (x3), CH_2Cl_2 (x3), and then DMF (x3). The resin was treated with 20 vol% piperidine in DMF for 3 min, drained, and these steps repeated once more before washing with DMF (x3), CH_2Cl_2 (x3), and then DMF (x3). The resin was then treated with a solution of $BocNHOCH_2CO_2Su$ (58 mg, 200 µmol, 2 eq.) and N,N-diisopropylethylamine (70 µL, 400 µmol, 2 eq.) in CH_2Cl_2 (4 mL) and shaken for 16 h. After washing with DMF (x3), CH_2Cl_2 (x3), and then DMF (x3), the resin-bound peptide was cleaved according to general procedure C and purified *via* preparative HPLC with a Waters X-Bridge™, C18, 130 Å, 19 x 100 mm column (0 to 40% MeCN over 40 min, 0.1 vol% TFA, 15 mL/min). Lyophilisation of the pure fractions afforded the pure peptide S11 (9 mg, 5% yield).

HR-ESI-MS spectrum (ESI+) of pure peptide S11 *m/z* calculated for $C_{115}H_{194}N_{37}O_{25}S$ $[M+5H]^+$ 505.0948; found (ESI+) $[M+5H]^+$ 505.0950.

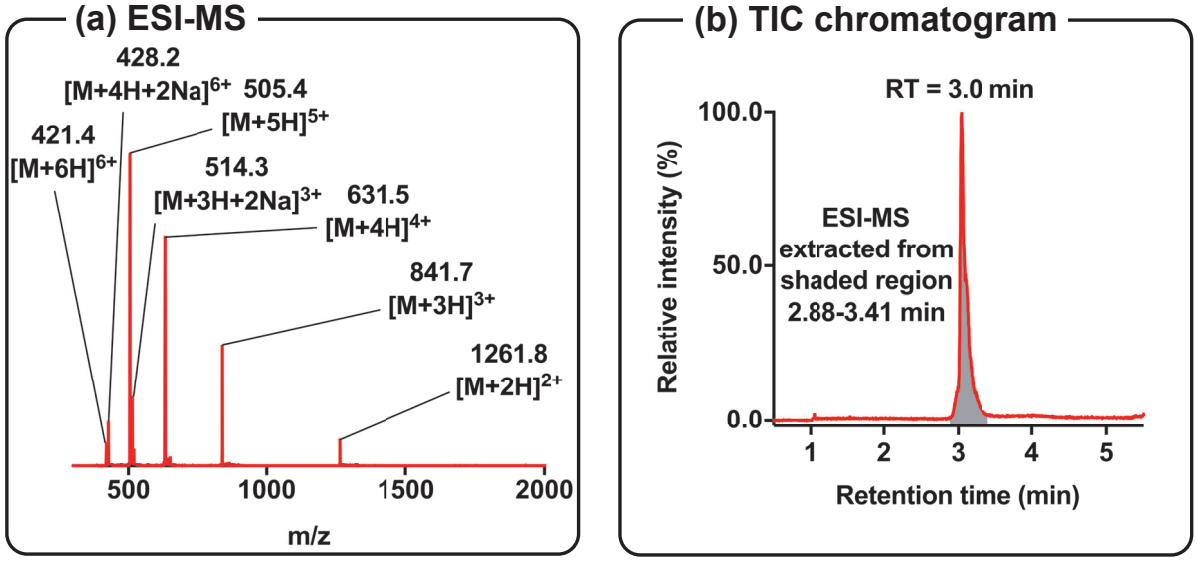
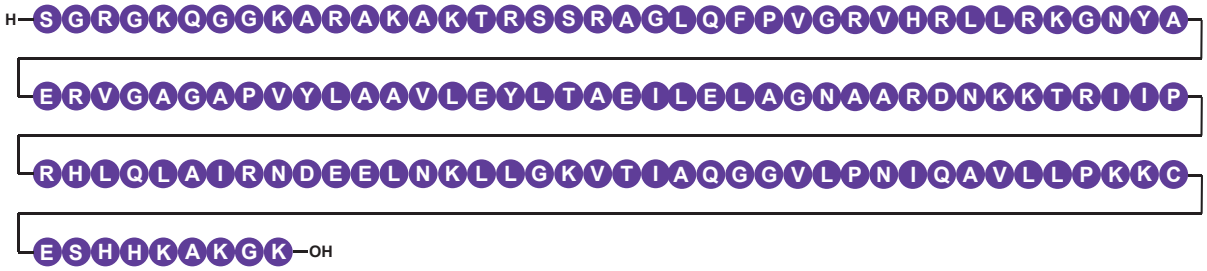


Figure S4: (a) ESI-MS spectrum (ESI+) of pure peptide **S11** extracted from TIC chromatogram 2.88-2.41 min: *m/z* calculated for $C_{115}H_{189}N_{37}O_{25}S$ $[M+2H]^{2+}$ 1261.2, $[M+3H]^{3+}$ 841.2, $[M+4H]^{4+}$ 631.1, $[M+3H+2Na]^{5+}$ 513.9, $[M+5H]^{5+}$ 505.1, $[M+4H+2Na]^{6+}$ 428.4, $[M+6H]^{6+}$ 421.1; found (ESI+) $[M+2H]^{2+}$ 1261.8, $[M+3H]^{3+}$ 841.7, $[M+4H]^{4+}$ 631.5, $[M+3H+2Na]^{5+}$ 514.3, $[M+5H]^{5+}$ 505.4, $[M+4H+2Na]^{6+}$ 428.2, $[M+6H]^{6+}$ 421.4; deconvoluted mass of 2522.0 +/– 0.3 Da; **(b) TIC chromatogram** of pure peptide **S11**: RT = 3.0 min (0 to 30% MeCN in H_2O over 5 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column).

Protein expression

H2A T120C (15)



H2A T120C was expressed in *E. coli* BL21 (DE3) pLysS cells and purified from inclusion bodies as previously reported.[10] Briefly, competent cells were transformed with histone expression plasmids (pET28a, Novagen) and grown in Luria-Bertani (LB) medium at 37 °C until reaching an OD600 of 0.6. Protein expression was induced by the addition of 1 mM isopropyl β-d-1-thiogalactopyranoside (IPTG) for 4 h at 37 ˚C. Cell pellets were harvested and lysed by sonication in histone lysis buffer containing 50 mM Tris-HCl pH 7.5, 100 mM NaCl, 1 mM β-mercaptoethanol (BME), and the insoluble fraction after clarification (30 min at 15,000 Å~ g at room temperature) was washed twice with histone lysis buffer containing 1% (v/v) Triton X-100, and then twice without Triton X-100. The pellet was dissolved in 10 mL of unfolding buffer (20 mM Tris-HCl pH 7.5, 6 M guanidinium HCl and 1mM dithiothreitol (DTT)) per L of culture by stirring at room temperature overnight. Resuspended pellets were then centrifuged at 20,000 Å~ g for 30 min at 4 ˚C. Filtered supernatants were purified *via* RP-HPLC with a Vydac, C18, 300 Å, 22x250 mm (0 to 70% MeCN over 40 min, 0.1 vol% TFA, 7 mL/min). Lyophilisation of the pure fractions afforded the pure protein **15**, which was stored at –20 °C in sealed protein low-binding tubes.

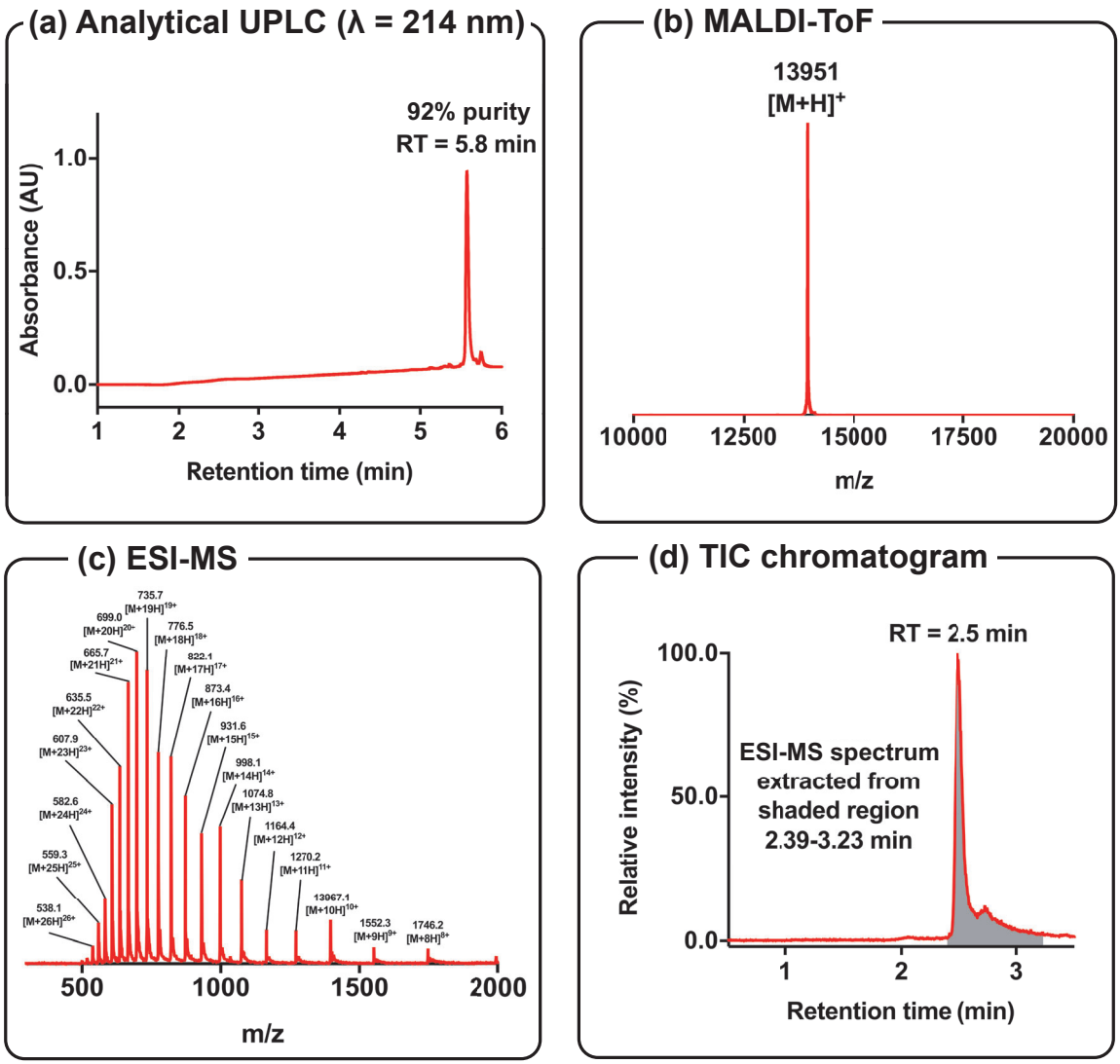
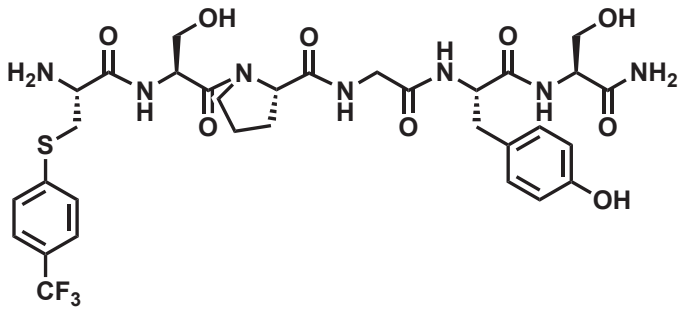


Figure S5: (a) Analytical UPLC chromatogram of pure protein **15**: retention time (RT) = 5.8 min (0 to 60% MeCN in H_2O over 5 min, 0.1% TFA, λ = 214 nm, Waters Acquity ® BEH, C18, 300Å, 2.1x50 mm column); **(b) MALDI-ToF** (LP) of pure protein **15**: *m/z* calculated for $C_{615}H_{1042}N_{198}O_{170}S$ $[M+H]^+$ 13954; found (LP) $[M+H]^+$ 13951; **(c) ESI-MS** spectrum (ESI+) of pure protein **15** extracted from TIC chromatogram 2.39-3.23 min: *m/z* calculated for $C_{615}H_{1042}N_{198}O_{170}S$ $[M+8H]^{8+}$ 1745.2, $[M+9H]^{9+}$ 1551.4, $[M+10H]^{10+}$ 1396.4, $[M+11H]^{11+}$ 1296.4, $[M+12H]^{12+}$ 1163.8, $[M+13H]^{13+}$ 1074.4, $[M+14H]^{14+}$ 997.7, $[M+15H]^{15+}$ 931.3, $[M+16H]^{16+}$ 873.1, $[M+17H]^{17+}$ 821.8, $[M+18H]^{18+}$ 776.2, $[M+19H]^{19+}$ 735.4, $[M+20H]^{20+}$ 698.7, $[M+21H]^{21+}$ 665.5, $[M+22H]^{22+}$ 635.3, $[M+23H]^{23+}$ 607.7, $[M+24H]^{24+}$ 582.4, $[M+25H]^{25+}$ 559.2, $[M+26H]^{26+}$ 537.7; found (ESI+) $[M+8H]^{8+}$ 1746.2, $[M+9H]^{9+}$ 1552.3, $[M+10H]^{10+}$ 13967.1, $[M+11H]^{11+}$ 1270.2, $[M+12H]^{12+}$ 1164.4, $[M+13H]^{13+}$ 1074.8, $[M+14H]^{14+}$ 998.1, $[M+15H]^{15+}$ 931.6, $[M+16H]^{16+}$ 873.4, $[M+17H]^{17+}$ 822.1, $[M+18H]^{18+}$ 776.5, $[M+19H]^{19+}$ 735.7, $[M+20H]^{20+}$ 669.0, $[M+21H]^{21+}$ 665.7, $[M+22H]^{22+}$ 635.5, $[M+23H]^{23+}$ 607.9, $[M+24H]^{24+}$ 582.6, $[M+25H]^{25+}$ 559.3, $[M+26H]^{26+}$ 538.1; deconvoluted mass of 13,959.0 +/– 0.5 Da; **(d) TIC chromatogram** of pure protein **15**: RT = 2.5 min (0 to 60% MeCN in H_2O over 3 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column).

Peptide and protein modification with diaryliodonium salts

C(*S*-(4-(trifluoromethyl)phenyl))SPGYS-NH_2 (3)



A protein low-binding Eppendorf tube containing peptide **2** (8.0 mg, 11.0 μmol) in HEPES buffer (2.0 mL, 0.1 M, pH 8.0) containing EDTA (1 mM) and TCEP (3.7 mg, 3.2 μmol) was warmed to 37 ˚C, and diaryliodonium salt **1** (24.4 mg, 43.8 μmol) in MeCN (220 μL) added. The reaction was monitored by UPLC-MS and analytical UPLC by taking an aliquot (3 μL) and diluting it in 0.1 vol% TFA in H_2O (50 μL). The reaction was 90% complete after 90 min as judged by analytical UPLC, quenched with 0.1 vol% TFA in H_2O (2.0 mL), and purified by RP-HPLC with a Waters SunFire™, C18, 180 Å, 10 x 250 mm column with 4 mL/min flow rate (0 to 30% MeCN over 30 min, 0.1 vol% TFA) (0 to 30% MeCN over 30 min, 0.1 vol% TFA, 4 mL/min) followed. Lyophilisation of the pure fractions afforded the pure peptide **3** (5.7 mg, 60% isolated yield).

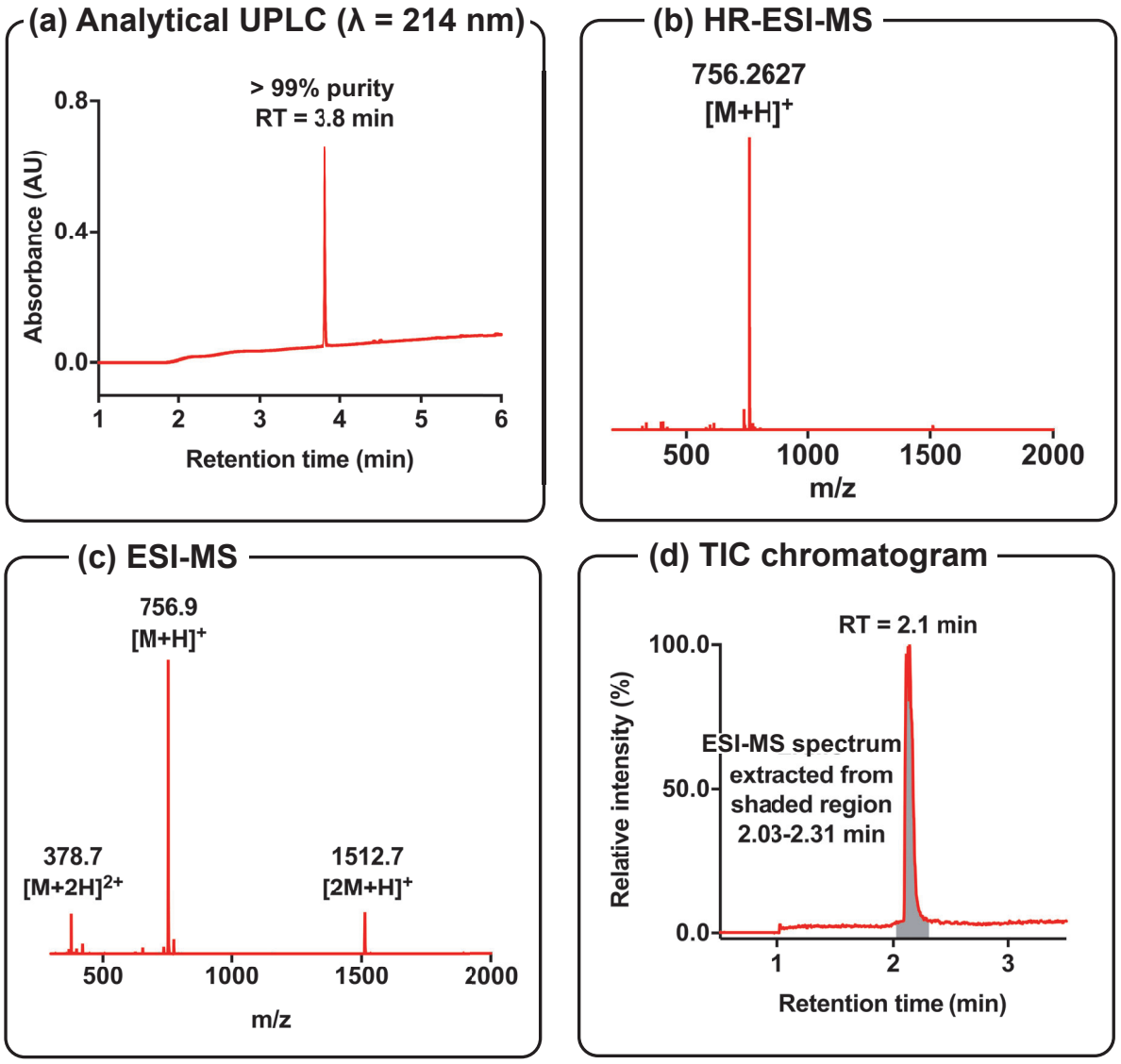
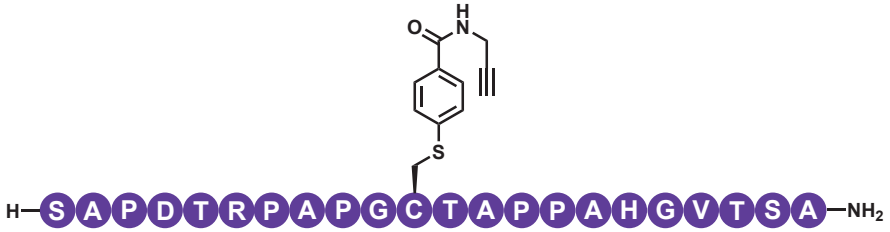


Figure S6: (a) Analytical UPLC chromatogram of pure peptide **3**: retention time (RT) = 3.8 min (0 to 60% MeCN in H_2O over 5 min, 0.1% TFA, λ = 214 nm, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column); **(b) HR-ESI-MS** spectrum (ESI+) of pure peptide **3** *m/z* calculated for $C_{32}H_{40}F_3N_7O_9S$ $[M+H]^+$ 756.2633; found (ESI+) $[M+H]^+$ 756.2627; **(c) ESI-MS** spectrum (ESI+) of pure peptide **3** extracted from TIC chromatogram 2.03-2.31 min: *m/z* calculated for $C_{32}H_{40}F_3N_7O_9S$ $[2M+H]^+$ 1511.5, $[M+H]^+$ 756.3, $[M+2H]^{2+}$ 378.7; found (ESI+) $[2M+H]^+$ 1512.7, $[M+H]^+$ 756.9, $[M+2H]^{2+}$ 378.7; **(d) TIC chromatogram** of pure peptide **3**: RT = 2.1 min (0 to 50% MeCN in H_2O over 5 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.92 (d, *J* = 7.6Hz, 1H, SerA2NH), 8.50 – 8.37 (m, 2H, Cys2NH_2), 8.07 (*app*.t, *J* = 5.8Hz, 1H, Gly2NH), 7.95 (d, *J* = 7.9Hz, 1H, SerB2NH), 7.91 (d, *J* = 8.1Hz, 1H, Tyr2NH), 7.67 (d, *J* = 8.3Hz, 2H, SAr3a, SAr3b), 7.57 (d, *J* = 8.2Hz, 2H, SAr2a, Sar2b), 7.11 – 7.05 (m, 2H, SerB1NH_2), 7.01 (d, *J* = 8.3Hz, 2H, Tyr5b, Tyr5a), 6.62 (d, *J* = 8.4Hz, 2H, Tyr6b, Tyr6a), 4.62 (*app*.q, *J* = 6.9Hz, 1H, SerA2), 4.45 (ddd, *J* = 8.9, 4.5Hz, 1H, Tyr2), 4.32 (dd, *J* = 8.4, 3.9Hz, 1H, Pro2), 4.18 (ddd, *J* = 8.1, 5.5Hz, 1H, SerB2), 4.11 – 4.05 (m, 1H, Cys2), 3.75 – 3.44 (m, 9H, Cys3', SerA3', SerA3'', Pro5', Pro5'', Gly2', Gly2'', SerB3', SerB3''), 3.35 (dd, *J* = 14.2, 7.2Hz, 1H, Cys3''), 2.93 (dd, *J* = 13.9, 4.5Hz, 1H, Tyr3'), 2.66 (dd, *J* = 13.9, 9.3Hz, 1H, Tyr3''), 2.04 – 1.97 (m, 1H, Pro3'), 1.95 – 1.87 (m, 1H, Pro4'),

1.86 – 1.79 (m, 2H, Pro3'', Pro4''). **^{13}C NMR** (126MHz, DMSO-d_6) δ 171.8 (Pro1), 171.6 (SerB1), 171.0 (Tyr1), 168.5 (Gly1), 168.3 (SerA1), 166.6 (Cys1), 155.8 (Tyr7), 140.4 (SAr1), 129.8 (Tyr5a/Tyr5b), 127.7 (Tyr4), 127.5 (SAr2a/SAr2b), 126.4 (SAr4), 125.3 (SAr3a/SAr3b), 124.0 ($SArCF_3$), 114.6 (Tyr6a/Tyr6b), 61.6 (SerB3), 61.3 (SerA3), 59.6 (Pro2), 54.7 (SerB2), 54.0 (Tyr2), 53.1 (SerA2), 50.5 (Cys2), 46.6 (Pro5), 41.5 (Gly2), 36.3 (Tyr3), 32.4 (Cys3), 28.8 (Pro3), 23.9 (Pro4).

MUC1-alkyne (6)



A protein low-binding Eppendorf tube containing peptide **5** (5.0 mg, 2.1 μmol) in HEPES buffer (378 μL, 0.1 M, pH 8.0) was warmed to 37 ˚C, and diaryliodonium salt compound **4** (5.8 mg, 10.4 μmol) in MeCN (42 μL) added. The reaction was monitored by UPLC-MS by taking an aliquot (2 μL) and diluting it in 0.1 vol% TFA in H_2O (38 μL). The reaction was 91% complete after 120 min as judged by UPLC-MS, quenched with 0.1 vol% TFA in H_2O (1.0 mL), and purified by RP-HPLC with a Waters XBridge ®, C18, 300 Å, 10 x 250 mm column (0 to 30% MeCN over 60 min, 0.1 vol% formic acid, 4 mL/min) followed. Lyophilisation of the pure fractions afforded the pure peptide **6** (2.50 mg, 52% isolated yield).

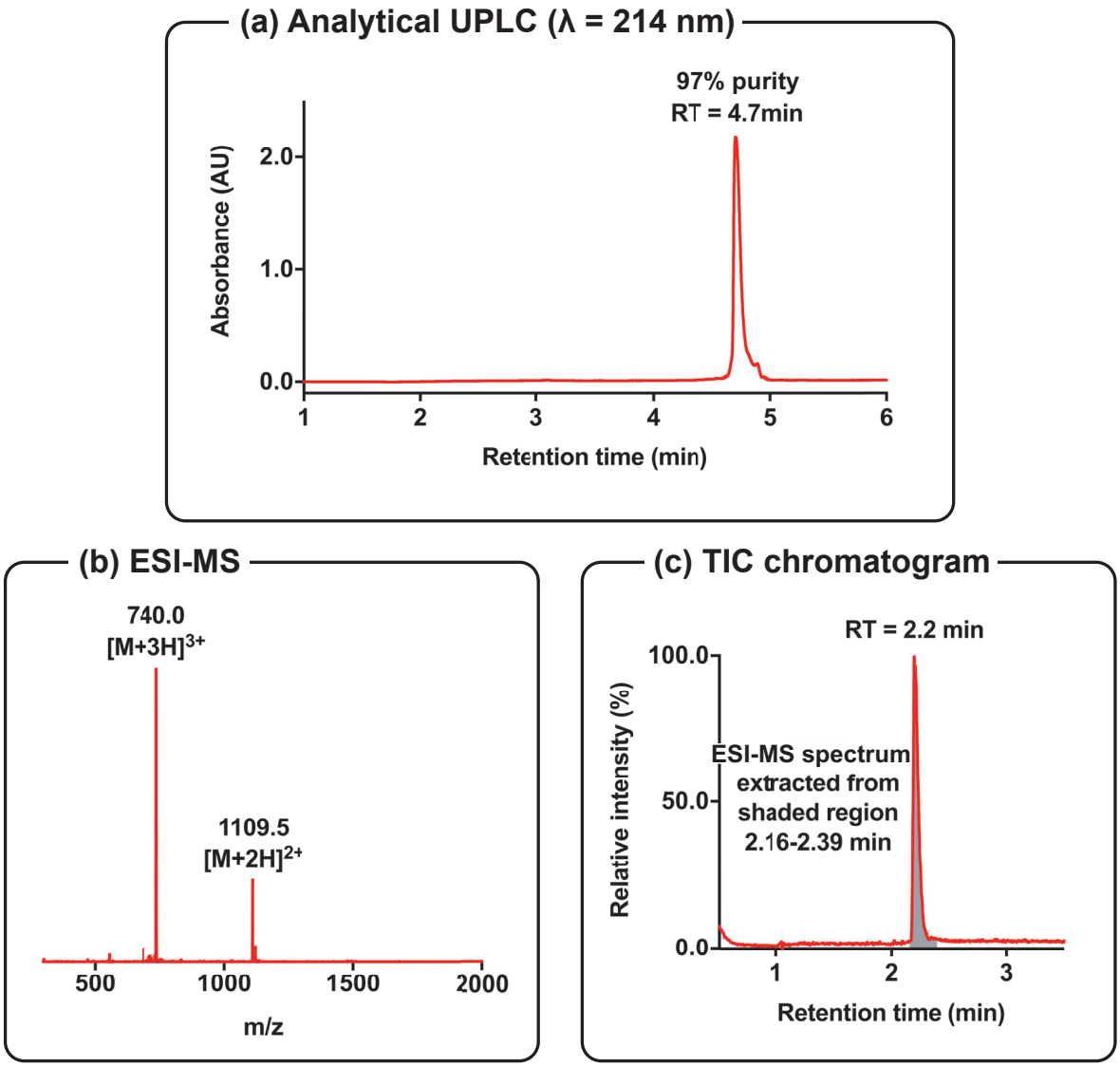
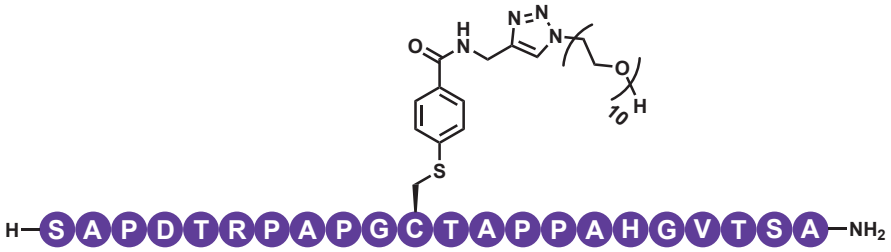


Figure S7: (a) Analytical UPLC chromatogram of pure peptide **6**: retention time (RT) = 4.7 min (0 to 30% MeCN in H_2O over 3 min, 0.1% TFA, λ = 214 nm, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column); **(b) ESI-MS** spectrum (ESI+) of pure peptide **6** extracted from TIC chromatogram 2.16-2.39 min: *m/z* calculated for $C_{96}H_{145}N_{29}O_{30}S$ $[M+2H]^{2+}$ 1109.1, $[M+3H]^{3+}$ 739.7; found (ESI+) $[M+2H]^{2+}$ 1109.5, $[M+3H]^{3+}$ 740.0; deconvoluted mass of 2217.0 Da; **(c) TIC chromatogram** of pure peptide **6**: RT = 2.2 min (0 to 40% MeCN in H_2O over 3 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column).

MUC1-PEG$_{10}$-OH (7)



Procedure 1 (One-pot arylation and CuAAC)

A protein low-binding binding Eppendorf tube containing peptide **5** (1.0 mg, 0.4 μmol) in HEPES buffer (95 μL, 0.1 M, pH 8.0) was warmed to 37 ˚C, and diaryliodonium salt compound **4** (0.6 mg, 1.0 μmol) in MeCN (8 μL) was added. The reaction was monitored by UPLC-MS by taking an aliquot (0.5 μL) and diluting it in 0.1 vol% TFA in H_2O (10 μL). The arylation reaction was 91% complete after 180 min as judged by UPLC-MS, then azido-PEG$_{10}$-OH (1.5 mg, 3.0 μmol), $CuSO_4$/THPTA (2.1 μL, 18.9/189 mM, HEPES (0.1 M) pH 8.0 buffer) followed by ascorbate (2.1 μL, 189 mM, HEPES (0.1 M) buffer pH 8.0) were added. The reaction was monitored by UPLC-MS by taking an aliquot (2 μL) and diluting it in 0.1 vol% TFA in H_2O (38 μL). The CuAAC reaction was >99% complete after 60 min as judged by UPLC-MS, and quenched with 0.1 vol% TFA in H_2O (0.8 mL), and purified by RP-HPLC with a Waters SunFire™, C18, 180 Å, 10 x 250 mm column (0 to 30% MeCN over 30 min, 0.1 vol% TFA, 4 mL/min, 50 ˚C). Lyophilisation of the pure fractions afforded the pure peptide **7** (0.33 mg, 28% isolated yield).

Procedure 2 (CuAAC)

A protein low-binding Eppendorf tube containing peptide **6** (1.0 mg, 0.4 μmol) in buffer (80 μL, phosphate (0.1 M), pH 7.0) was warmed to 37 ˚C, then azido-PEG$_{10}$-OH (1.0 mg, 2.1 μmol) in DMSO (8 μL), $CuSO_4$/THPTA (24μL, 1.7/8.3 mM, phosphate (0.1 M) pH 7.0 buffer) followed by ascorbate (20 μL, 10 mM, phosphate (0.1 M) pH 7.0 buffer) were added. The reaction was monitored by UPLC-MS by taking an aliquot (1 μL) and diluting it in 0.1 vol% TFA in H_2O (38 μL). The CuAAC reaction was >99% complete after 60 min as judged by UPLC-MS, and quenched with 0.1 vol% TFA in H_2O (1.0 mL). The peptide was purified by RP-HPLC with a Waters SunFire™, C18, 180 Å, 10 x 250 mm column (0 to 30% MeCN over 30 min, 0.1 vol% TFA, 4 mL/min). Lyophilisation of the pure fractions afforded the pure peptide **7** (0.91 mg, 78% isolated yield, 41% isolated yield over two steps from peptide **5**).

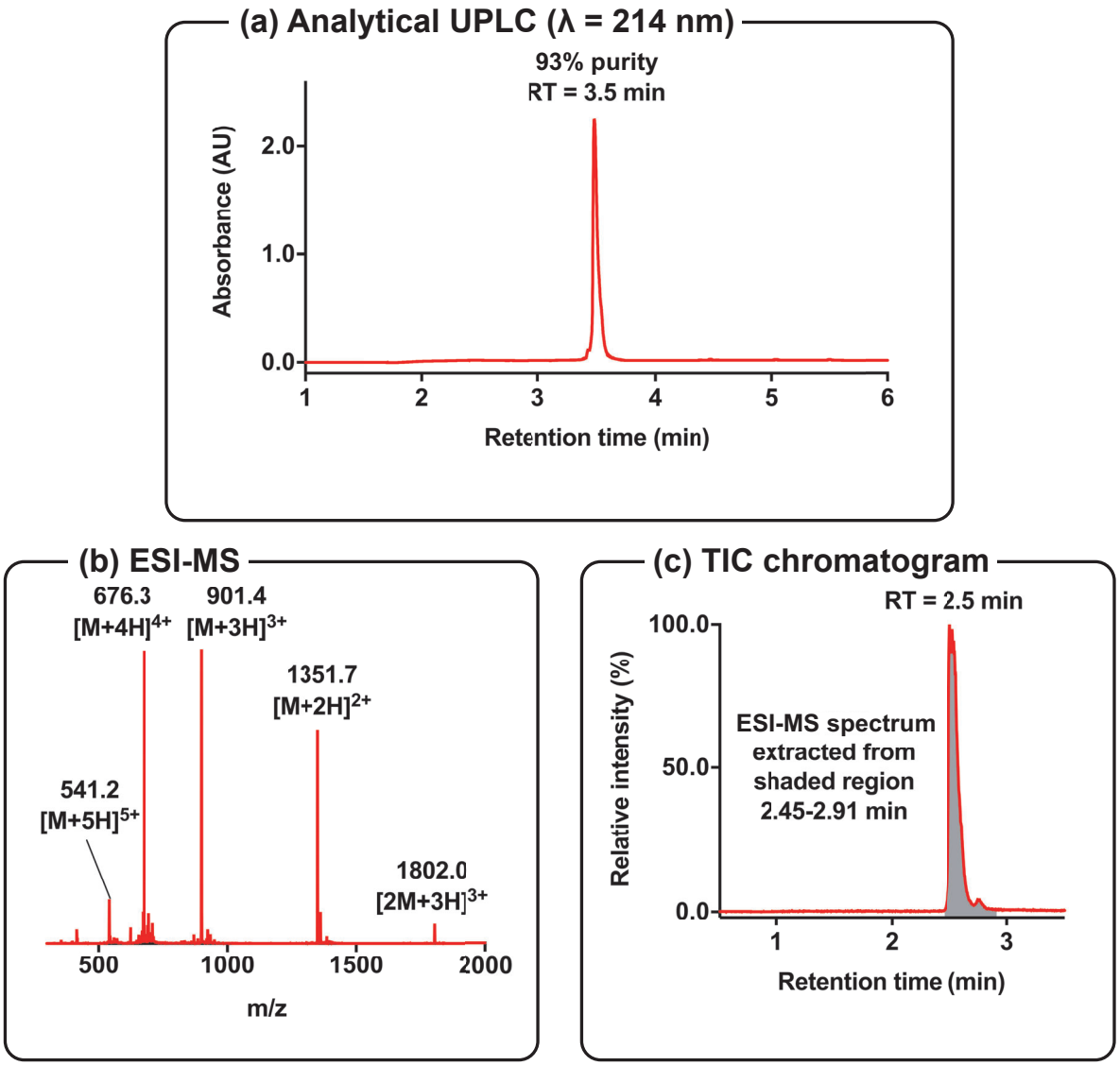
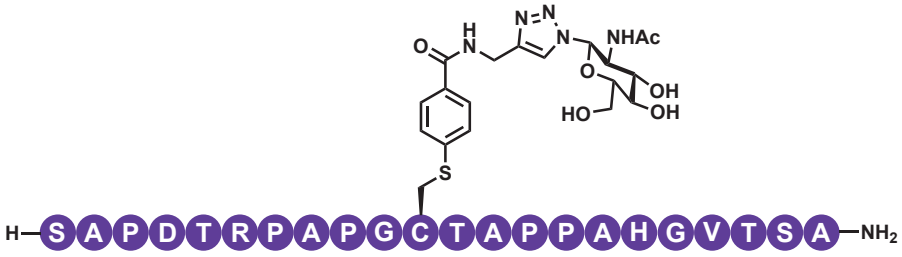


Figure S8: (a) Analytical UPLC chromatogram of pure peptide **7**: retention time (RT) = 3.5 min (0 to 60% MeCN in H_2O over 5 min, 0.1% TFA, λ = 214 nm, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column); **(b) ESI-MS** spectrum (ESI+) of pure peptide **7** extracted from TIC chromatogram 2.45-2.91 min: *m/z* calculated for $C_{116}H_{186}N_{32}O_{40}S$ $[2M+3H]^{3+}$ 1800.6, $[M+2H]^{2+}$ 1350.7, $[M+3H]^{3+}$ 900.8, $[M+4H]^{4+}$675.8, $[M+5H]^{5+}$ 540.9; found (ESI+) $[2M+3H]^{3+}$ 1802.0, $[M+2H]^{2+}$ 1351.7, $[M+3H]^{3+}$ 901.4, $[M+4H]^{4+}$676.3, $[M+5H]^{5+}$ 541.2; deconvoluted mass of 2701.2 +/– 0.2 Da; **(c) TIC chromatogram** of pure peptide **7**: RT = 2.5 min (0 to 30% MeCN in H_2O over 3 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column).

MUC1-GlcNAc-OH (8)



Procedure 1 (One -pot arylation and CuAAC)

A protein low-binding binding Eppendorf tube containing peptide **5** (1.0 mg, 0.4 μmol) in HEPES buffer (95 μL, 0.1 M, pH 8.0) was warmed to 37 ˚C, and diaryliodonium salt compound **4** (0.6 mg, 1.0 μmol) in MeCN (8 μL) was added. The reaction was monitored by UPLC-MS by taking an aliquot (0.5 μL) and diluting it in 0.1 vol% TFA in H_2O (10 μL). The arylation reaction was 91% complete after 180 min as judged by UPLC-MS, then β-azido-GlcNAc (0.8 mg, 3.1 μmol), $CuSO_4$/THPTA (2.1 μL, 18.9/189 mM, HEPES (0.1 M) pH 8.0 buffer) followed by ascorbate (2.1 μL, 189 mM, HEPES (0.1 M) buffer pH 8.0) were added. The reaction was monitored by UPLC-MS by taking an aliquot (2 μL) and diluting it in 0.1 vol% TFA in H_2O (38 μL). The CuAAC reaction was >99% complete after 60 min as judged by UPLC-MS, and quenched with 0.1 vol% TFA in H_2O (0.8 mL), and purified by RP-HPLC with a Waters SunFire™, C18, 180 Å, 10 x 250 mm column (0 to 30% MeCN over 30 min, 0.1 vol% TFA, 4 mL/min, 50 ˚C). Lyophilisation of the pure fractions afforded the pure peptide **8** (0.39 mg, 36% isolated yield).

Procedure 2 (CuAAC)

A protein low-binding Eppendorf tube containing peptide **6** (1.0 mg, 0.4 μmol) in buffer (80 μL, phosphate (0.1 M), pH 7.0) was warmed to 37 ˚C, then azido-β-GlcNAc (0.5 mg, 2.1 μmol) in DMSO (8μL), $CuSO_4$/THPTA (24μL, 1.7/8.3 mM, phosphate (0.1 M) pH 7.0 buffer) followed by ascorbate (20 μL, 10 mM, phosphate (0.1 M) pH 7.0 buffer) were added. The reaction was monitored by UPLC-MS by taking an aliquot (1 μL) and diluting it in 0.1 vol% TFA in H_2O (38 μL). The CuAAC reaction was >99% complete after 60 min as judged by UPLC-MS, and quenched with 0.1 vol% TFA in H_2O (1.0 mL). The peptide was purified by RP-HPLC with a Waters SunFire™, C18, 180 Å, 10 x 250 mm column (0 to 30% MeCN over 30 min, 0.1 vol% TFA, 7 mL/min, 50 ˚C). Lyophilisation of the pure fractions afforded the pure peptide **8** (0.27 mg, 25% isolated yield, 13% isolated yield over two steps from peptide **5**).

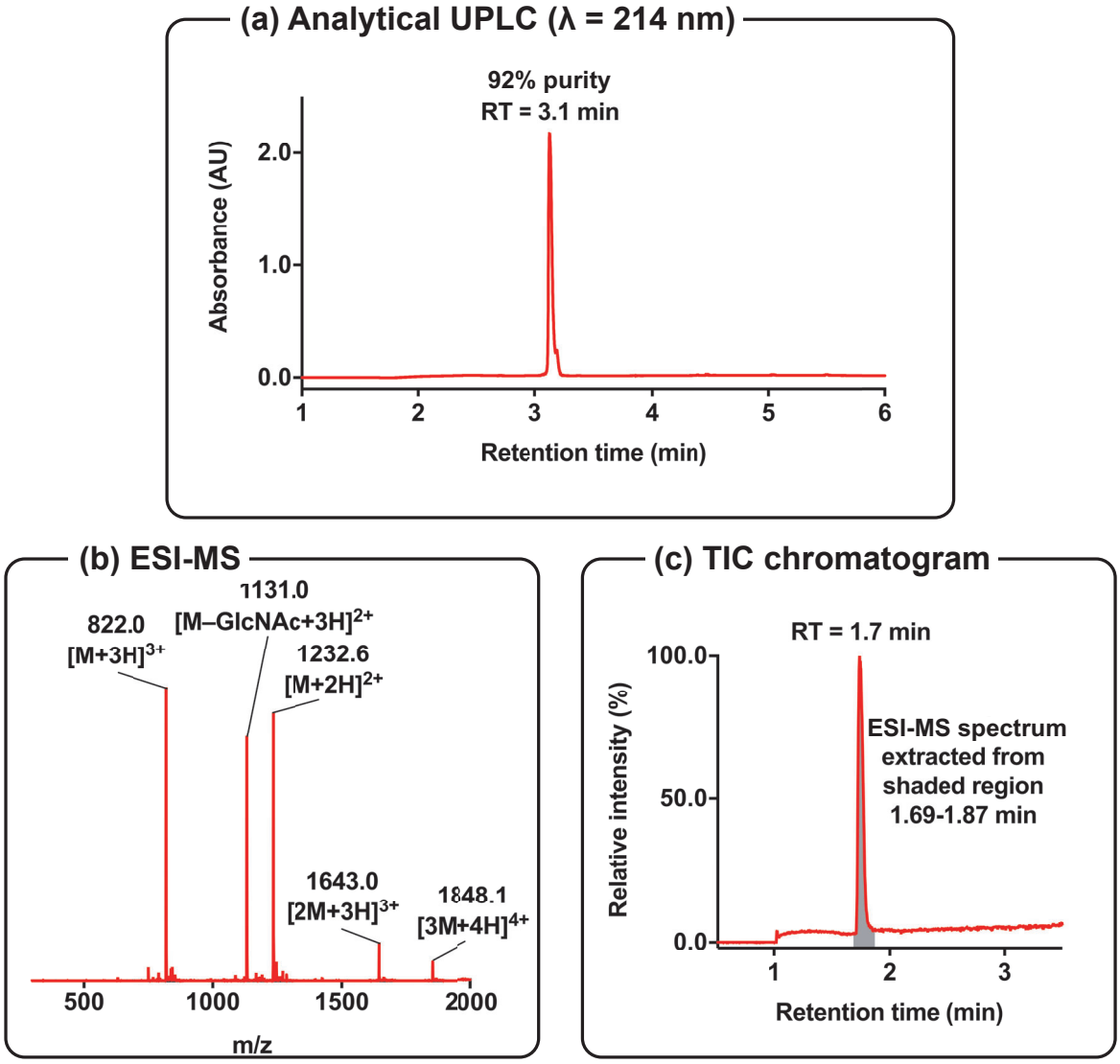
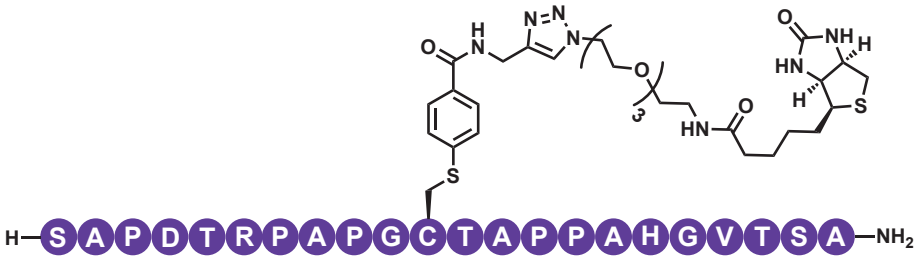


Figure S9: (a) Analytical UPLC chromatogram of pure peptide **8**: retention time (RT) = 3.1 min (0 to 60% MeCN in H_2O over 5 min, 0.1% TFA, λ = 214 nm, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column); **(b) ESI-MS** spectrum (ESI+) of pure peptide **8** extracted from TIC chromatogram 1.69-1.87 min: *m/z* calculated for $C_{104}H_{159}N_{33}O_{35}S$ $[3M+4H]^{4+}$ 1847.6, $[2M+3H]^{+}$ 1642.4, $[M+2H]^{2+}$ 1232.1, $[M–GlcNAc+3H]^{2+}$ 1130.5, $[M+3H]^{3+}$ 821.7; found (ESI+) $[3M+4H]^{4+}$ 1848.1, $[2M+3H]^{+}$ 1643.0, $[M+2H]^{2+}$ 1232.6, $[M–GlcNAc+3H]^{2+}$ 1131.0, $[M+3H]^{3+}$ 822.0; deconvoluted mass of 2463.1 +/– 0.2 Da; **(c) TIC chromatogram** of pure peptide **8**: RT = 1.7 min (0 to 50% MeCN in H_2O over 3 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column).

MUC1-PEG$_3$-biotin (9)



Procedure 1 (One-pot arylation and CuAAC)

A protein low-binding binding Eppendorf tube containing peptide **5** (1.0 mg, 0.4 μmol) in HEPES buffer (95 μL, 0.1 M, pH 8.0) was warmed to 37 ˚C, and diaryliodonium salt compound **4** (0.6 mg, 1.0 μmol) in MeCN (8 μL) was added. The reaction was monitored by UPLC-MS by taking an aliquot (0.5 μL) and diluting it in 0.1 vol% TFA in H_2O (10 μL). The arylation reaction was 91% complete after 180 min as judged by UPLC-MS, then azido-PEG$_3$-biotin (**S3**) (0.9 mg, 2.0 μmol), $CuSO_4$/THPTA (2.1 μL, 18.9/189 mM, HEPES (0.1 M) pH 8.0 buffer) followed by ascorbate (2.1 μL, 189 mM, HEPES (0.1 M) buffer pH 8.0) were added. The reaction was monitored by UPLC-MS by taking an aliquot (2 μL) and diluting it in 0.1 vol% TFA in H_2O (38 μL). The CuAAC reaction was >99% complete after 120 min as judged by UPLC-MS, and quenched with 0.1 vol% TFA in H_2O (0.8 mL), and purified by RP-HPLC with a Waters SunFire™, C18, 180 Å, 10 x 250 mm column (0 to 30% MeCN over 30 min, 0.1 vol% TFA, 4 mL/min, 50 ˚C). Lyophilisation of the pure fractions afforded the pure peptide **9** (0.41 mg, 36% isolated yield).

Procedure 2 (CuAAC)

A protein low-binding Eppendorf tube containing peptide **6** (1.0 mg, 0.4 μmol) in buffer (80 μL, phosphate (0.1 M), pH 7.0) was warmed to 37 ˚C, then azido-PEG$_3$-biotin (**S3**) (0.9 mg, 2.1 μmol) in DMSO (8 μL), $CuSO_4$/THPTA (24μL, 1.7/8.3 mM, phosphate (0.1 M) pH 7.0 buffer) followed by ascorbate (20 μL, 10 mM, phosphate (0.1 M) pH 7.0 buffer) were added. The reaction was monitored by UPLC-MS by taking an aliquot (1 μL) and diluting it in 0.1 vol% TFA in H_2O (38 μL). The CuAAC reaction was >99% complete after 120 min as judged by UPLC-MS, and quenched with 0.1 vol% TFA in H_2O (1.0 mL). The peptide was purified by RP-HPLC with a Waters SunFire™, C18, 180 Å, 10 x 250 mm column (0 to 30% MeCN over 30 min, 0.1 vol% TFA, 7 mL/min). Lyophilisation of the pure fractions afforded the pure peptide **9** (0.80 mg, 69% isolated yield, 36% isolated yield over two steps from peptide **5**).

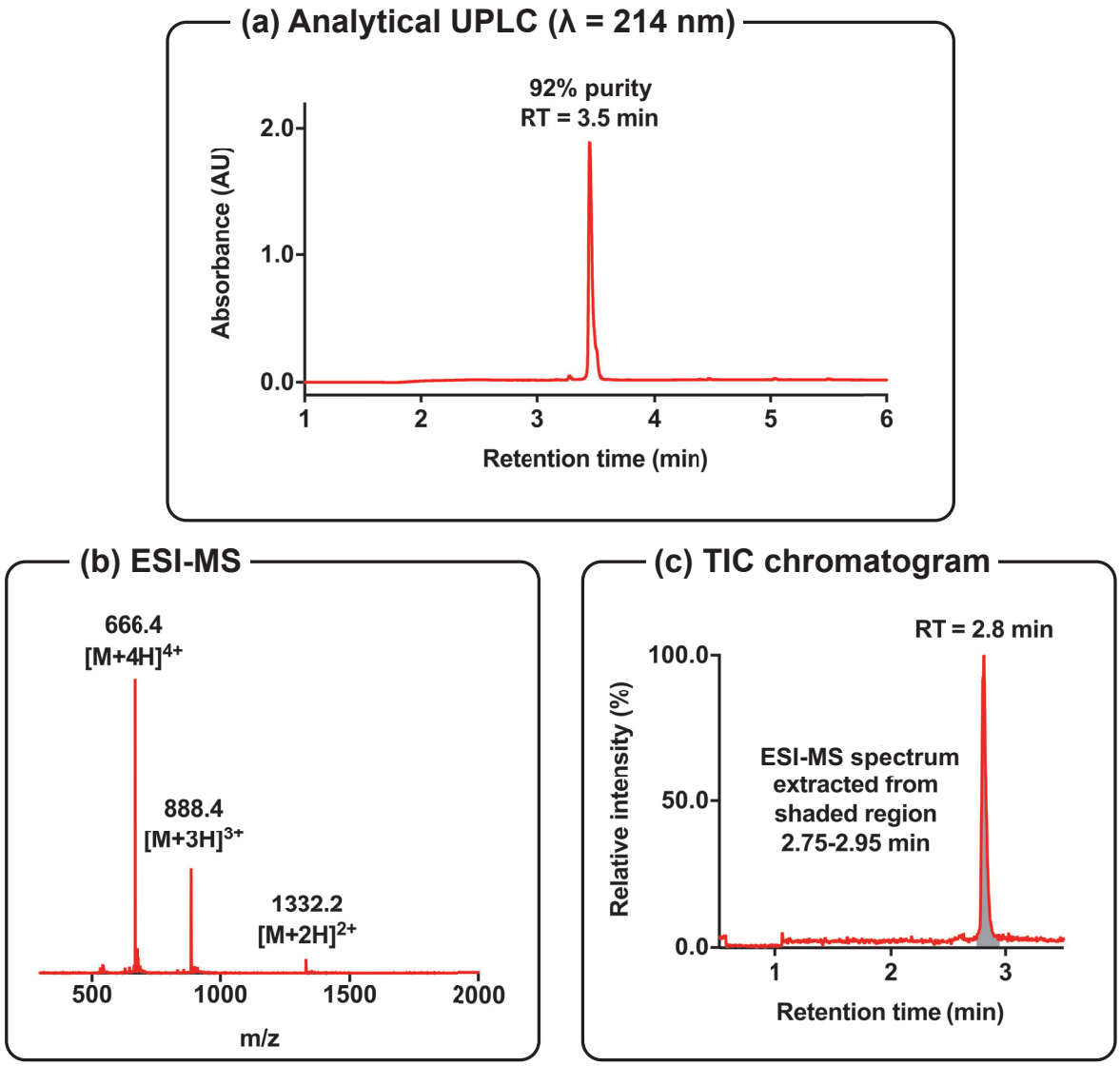
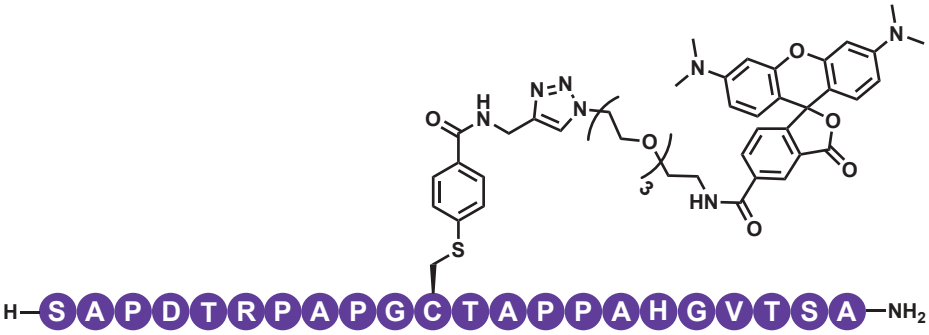


Figure S10: (a) Analytical UPLC chromatogram of pure peptide **9**: retention time (RT) = 3.5 min (0 to 60% MeCN in H_2O over 5 min, 0.1% TFA, λ = 214 nm, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column); **(b) ESI-MS** spectrum (ESI+) of pure peptide **9** extracted from TIC chromatogram 2.75-2.95 min: *m/z* calculated for $C_{114}H_{177}N_{35}O_{35}S_2$ $[M+2H]^{2+}$ 1331.1, $[M+3H]^{3+}$ 887.8, $[M+H]^{4+}$ 666.1; found (ESI+) $[M+2H]^{2+}$ 1331.2, $[M+3H]^{3+}$ 888.4, $[M+H]^{4+}$ 666.4; deconvoluted mass of 2662.1 +/– 0.4 Da; **(c) TIC chromatogram** of pure peptide **9**: RT = 2.8 min (0 to 30% MeCN in H_2O over 3 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column).

MUC1-PEG$_3$-TAMRA (10)



Procedure 1 (One-pot arylation and CuAAC)

A protein low-binding binding Eppendorf tube containing peptide **5** (1.0 mg, 0.4 μmol) in buffer (95 μL, 0.1 M, pH 8.0) was warmed to 37 ˚C, and diaryliodonium salt compound **4** (0.6 mg, 1.0 μmol) in MeCN (8 μL) was added. The reaction was monitored by UPLC-MS by taking an aliquot (0.5 μL) and diluting it in 0.1 vol% TFA in H_2O (10 μL). The arylation reaction was 91% complete after 180 min as judged by UPLC-MS, then azido-PEG$_3$-tamra (**S4**) (1.53 mg, 2.43 μmol, 29 mM), $CuSO_4$/THPTA (2.1 μL, 18.9/189 mM, HEPES (0.1 M) pH 8.0 buffer) followed by ascorbate (2.1 μL, 189 mM, HEPES (0.1 M) buffer pH 8.0) were added. The reaction was monitored by UPLC-MS by taking an aliquot (2 μL) and diluting it in 0.1 vol% TFA in H_2O (38 μL). The CuAAC reaction was >99% complete after 180 min as judged by UPLC-MS, and quenched with 0.1 vol% TFA in H_2O (0.8 mL), and purified by RP-HPLC with a Waters SunFire™, C18, 180 Å, 10 x 250 mm column (0 to 30% MeCN over 30 min, 0.1 vol% TFA, 4 mL/min, 50 ˚C). Lyophilisation of the pure fractions afforded the pure peptide **10** (0.7 mg, 57% isolated yield).

Procedure 2 (CuAAC)

A protein low-binding Eppendorf tube containing peptide **6** (1.0 mg, 0.4 μmol) in buffer (80 μL, phosphate (0.1 M), pH 7.0) was warmed to 37 ˚C, then azido-PEG$_3$-TAMRA (**S4**) (0.9 mg, 2.1 μmol) in DMSO (8 μL), $CuSO_4$/THPTA (24 μL, 1.7/8.3 mM, phosphate (0.1 M) pH 7.0 buffer) followed by ascorbate (20 μL, 10 mM, phosphate (0.1 M) pH 7.0 buffer) were added. The reaction was monitored by UPLC-MS by taking an aliquot (1 μL) and diluting it in 0.1 vol% TFA in H_2O (38 μL). The CuAAC reaction was >99% complete after 180 min as judged by UPLC-MS, and quenched with 0.1 vol% TFA in H_2O (1.0 mL). The peptide was purified by RP-HPLC with a Waters SunFire™, C18, 180 Å, 10 x 250 mm column (0 to 30% MeCN over 30 min, 0.1 vol% TFA, 7 mL/min, 50 ˚C). Lyophilisation of the pure fractions afforded the pure peptide **10** (0.8 mg, 65% isolated yield, 34% isolated yield over two steps from peptide **5**).

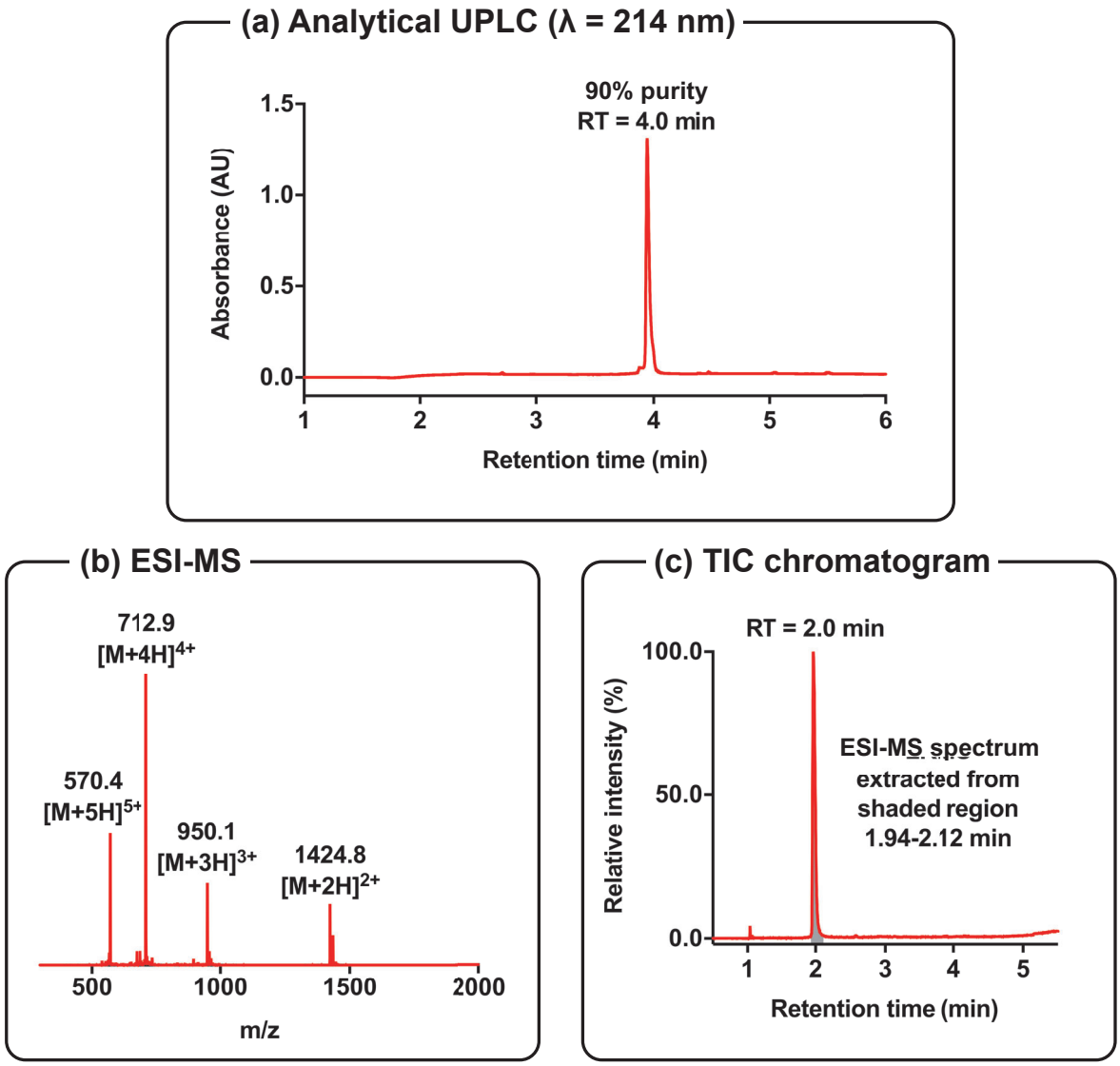
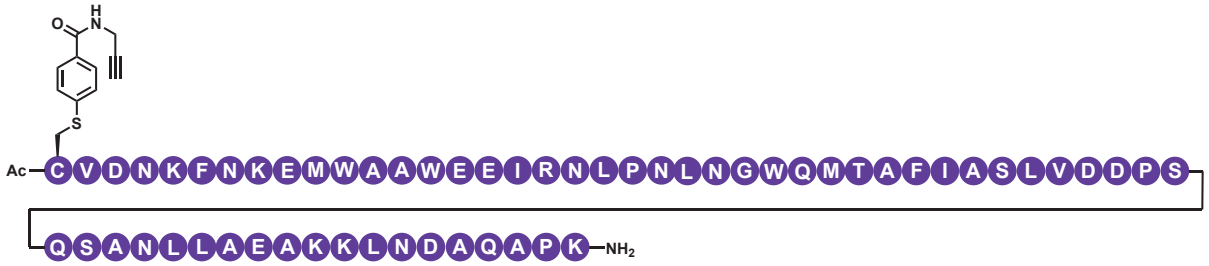


Figure S11: (a) Analytical UPLC chromatogram of pure peptide **9**: retention time (RT) = 4.0 min (0 to 60% MeCN in H_2O over 5 min, 0.1% TFA, λ = 214 nm, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column); **(b) ESI-MS** spectrum (ESI+) of pure peptide **9** extracted from TIC chromatogram 1.94-2.12 min: *m/z* calculated for $[M+2H]^{2+}$ 1424.2, $[M+3H]^{3+}$ 949.8, $[M+4H]^{4+}$ 712.9, $[M+5H]^{5+}$ 570.4; found (ESI+) $[M+2H]^{2+}$ 1424.8, $[M+3H]^{3+}$ 950.1, $[M+4H]^{4+}$ 712.9, $[M+5H]^{5+}$ 570.4; deconvoluted mass of 2847.4 +/– 0.3 Da; **(c) TIC chromatogram** of pure peptide **9**: RT = 2.0 min (0 to 100% MeCN in H_2O over 5 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column)**.**

zEGFR-alkyne (12)



A protein low-binding Eppendorf tube containing protein **11** (1.7 mg, 223 nmol) in buffer (2.0 mL, phosphate (0.2 mM), EDTA (1 mM), pH 8.0) was warmed to 37 ˚C. Diaryliodonium salt **4** (5.4 mg, 9.6 µmol) in MeCN (204 µL) was added and the reaction monitored by UPLC-MS and MALDI-ToF by taking an aliquot (1 µL) and diluting it in 0.1 vol% TFA in H_2O (20 µL). The reaction was 95% complete after 240 min as judged by UPLC-MS, quenched with 0.1 vol% TFA in H_2O (0.5 mL), and purified by RP-HPLC with a Waters X-Bridge® C18, 300 Å, 10 x 250 mm column (0 to 60% MeCN over 50 min, 0.1 vol% TFA, 4 mL/min, 55 ˚C). Lyophilisation of the pure fractions afforded the pure protein **12** (0.82 mg, 45% isolated yield).

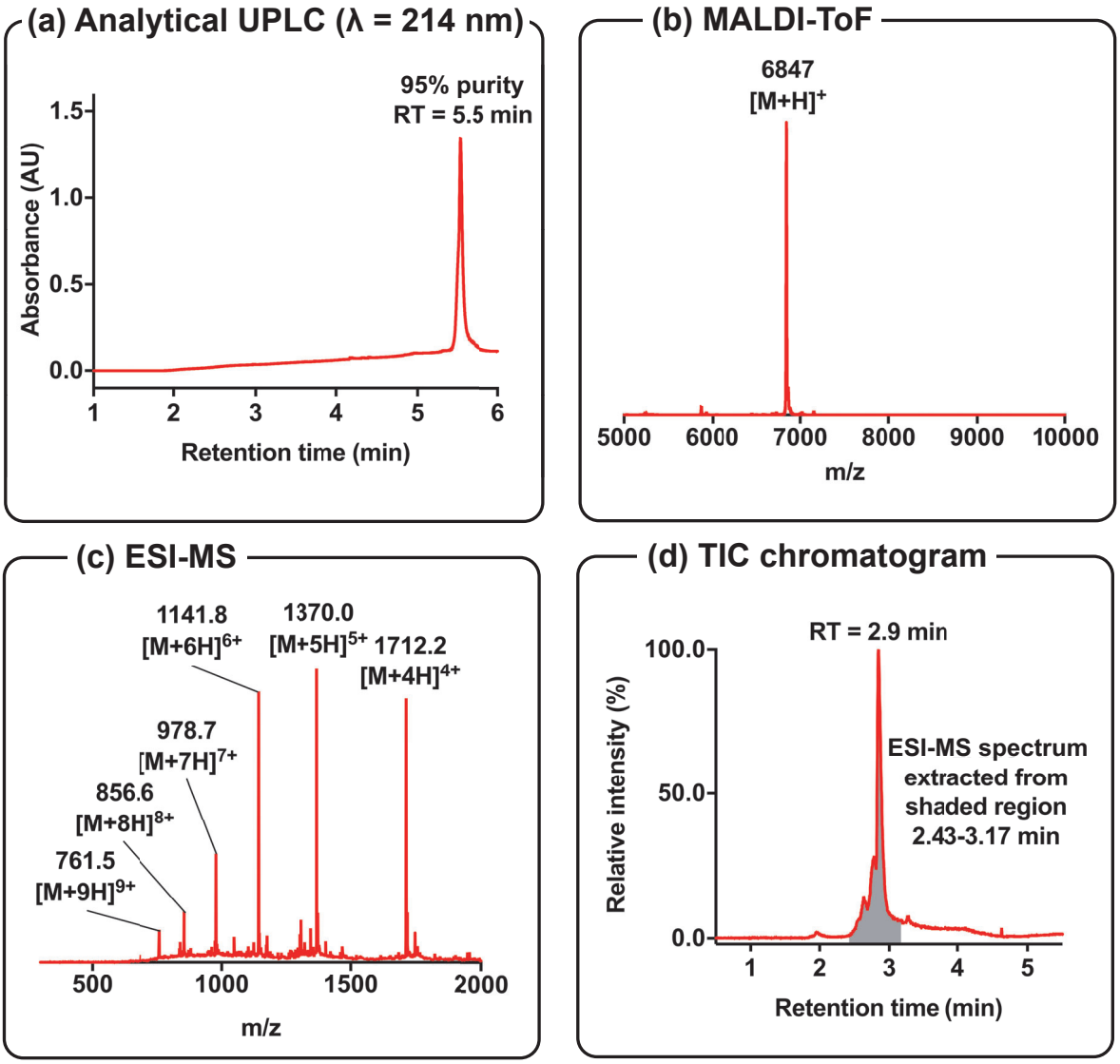
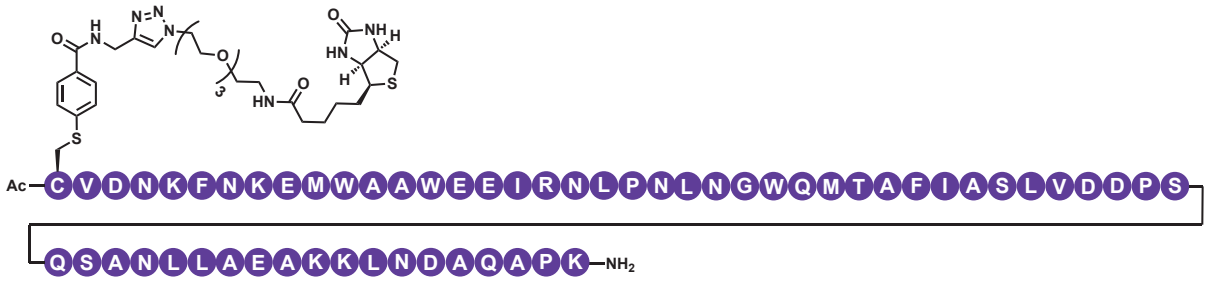


Figure S12: (a) Analytical UPLC chromatogram of pure protein **12**: retention time (RT) = 2.9 min (0 to 60% MeCN in H_2O over 5 min, 0.1% TFA, λ = 214 nm, Waters Acquity ® BEH, C18, 300Å, 2.1x50 mm column); **(b) MALDI-ToF** (LP) of pure protein **12**: *m/z* calculated for $C_{306}H_{466}N_{82}O_{91}S_3$ $[M+H]^+$ 6842; found (LP) $[M+H]^+$ 6847; **(c) ESI-MS** spectrum (ESI+) of pure protein **12** extracted from TIC chromatogram 2.43-3.17 min: *m/z* calculated for $C_{306}H_{466}N_{82}O_{91}S_3$ $[M+4H]^+$ 1704.6, $[M+5H]^{5+}$ 1363.9, $[M+6H]^{6+}$ 1136.7, $[M+7H]^{7+}$ 974.5, $[M+8H]^{8+}$ 852.8, $[M+9H]^{9+}$ 758.2; found (ESI+) $[M+4H]^+$ 1712.2, $[M+5H]^{5+}$ 1370.0, $[M+6H]^{6+}$ 1141.8, $[M+7H]^{7+}$ 978.7, $[M+8H]^{8+}$ 856.6, $[M+9H]^{9+}$ 761.5; deconvoluted mass of 6844.6 +/– 0.4 Da; **(d) TIC chromatogram** of pure protein: RT = 2.9 min (0 to 100% MeCN in H_2O over 5 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column).

zEGFR-PEG$_3$-biotin (13)



A protein low-binding binding Eppendorf tube containing protein **11** (1.0 mg, 140 nmol) in HEPES buffer (630 µL, 0.1 M, pH 8.0) was warmed to 37 ˚C, and diaryliodonium salt compound **4** (1.9 mg, 3.3 µmol) in MeCN (70 µL) was added. The reaction was monitored by UPLC-MS by taking an aliquot (2 µL) and diluting it in 0.1 vol% TFA in H_2O (18 µL). The arylation reaction was 95% complete after 240 min as judged by UPLC-MS, then azido-PEG$_3$-biotin (**S3**) (3.8 mg, 8.6 µmol), $CuSO_4$/THPTA (9.1 µL, 18.9/189 mM, HEPES (0.1 M) pH 8.0 buffer) followed by ascorbate (9.1 µL, 189 mM, HEPES (0.1 M) buffer pH 8.0) were added. The reaction was monitored by UPLC-MS by taking an aliquot (2 µL) and diluting it in 0.1 vol% TFA in H_2O (18 µL). The CuAAC reaction was >99% complete after incubating for 15 h as judged by UPLC-MS, and quenched with 0.1 vol% TFA in H_2O (0.8 mL), and purified by RP-HPLC with a Waters X-Bridge® C18, 300 Å, 10 x 250 mm column (15 to 50% MeCN over 90 min, 0.1 vol% TFA, 7 mL/min, 50 ˚C). Lyophilisation of the pure fractions afforded the pure protein **13** (0.37 mg, 35% isolated yield).

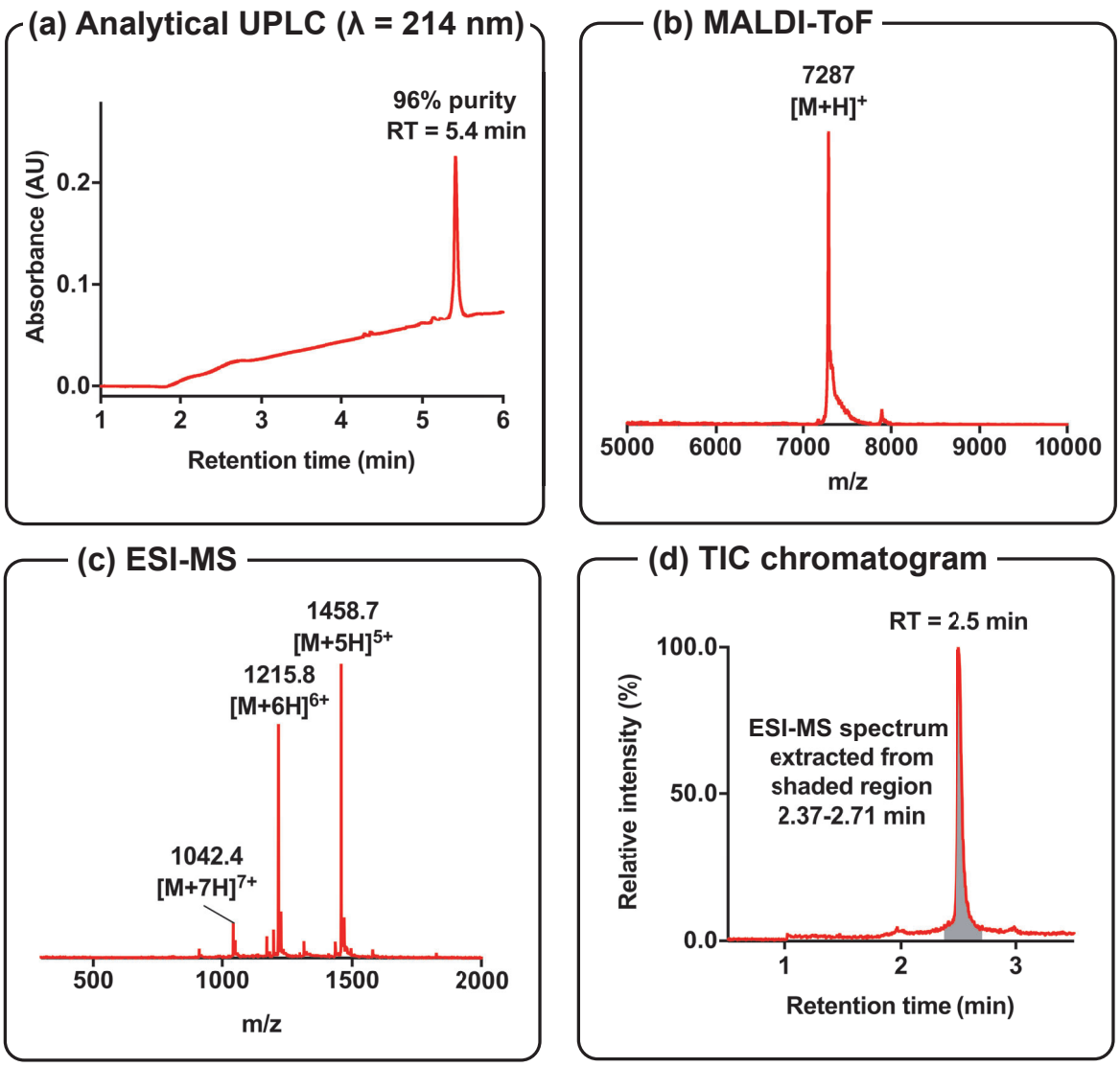
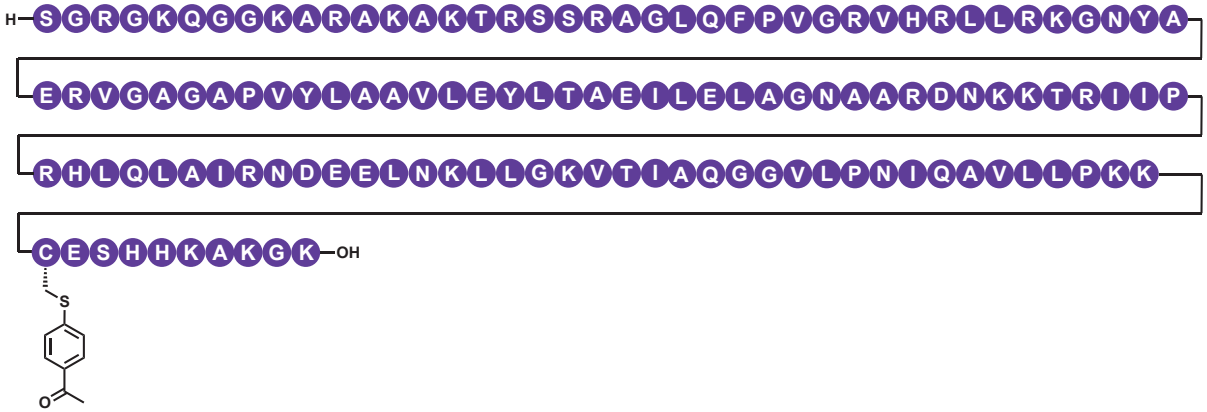


Figure S13: (a) Analytical UPLC chromatogram of pure protein **13**: retention time (RT) = 5.4 min (0 to 60% MeCN in H_2O over 5 min, 0.1% TFA, λ = 214 nm, Waters Acquity ® BEH, C18, 300Å, 2.1x50 mm column); **(b) MALDI-ToF** (LP) of pure protein **13**: *m/z* calculated for $C_{324}H_{498}N_{88}O_{96}S_4$ $[M+H]^+$ 7287; found (LP) $[M+H]^+$ 7287; **(c) ESI-MS** spectrum (ESI+) of pure protein **13** extracted from TIC chromatogram 2.37-2.71 min: *m/z* calculated for $C_{324}H_{498}N_{88}O_{96}S_4$ $[M+5H]^{5+}$ 1458.1, $[M+6H]^{6+}$ 1215.3, $[M+7H]^{7+}$ 1041.8; found (ESI+) $[M+5H]^{5+}$ 1458.7, $[M+6H]^{6+}$ 1215.8, $[M+7H]^{7+}$ 1042.4; deconvoluted mass of 7289.0 +/– 0.3 Da; **(d) TIC chromatogram** of pure protein **13**: RT = 2.5 min (0 to 60% MeCN in H_2O over 3 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 300Å, 2.1x50 mm column)

H2A-ketone (16)



A protein low-binding Eppendorf tube containing protein **15** (2.0 mg, 120 nmol) in buffer (236 µL, phosphate (0.2 mM), EDTA (1 mM), pH 8.0) was warmed to 37 ˚C, and diaryliodonium salt compound **14** (0.3 mg, 0.5 µmol) in MeCN (35 µL) was added. The reaction was monitored by UPLC-MS and MALDI-ToF by taking an aliquot (2 µL) and diluting it in 0.1 vol% TFA in H_2O (80 µL). The reaction was 98% complete after 60 min as judged by MALDI-ToF-MS, quenched with 0.1 vol% TFA in H_2O (2 mL), and purified by RP-HPLC with a Vydac, C18, 300 Å, 22x250 mm (15 to 70% acetonitrile over 40 min, 0.1% TFA, 7 mL/min). Lyophilisation of the pure fractions afforded the pure protein **16** (1.1 mg, 54% isolated yield).

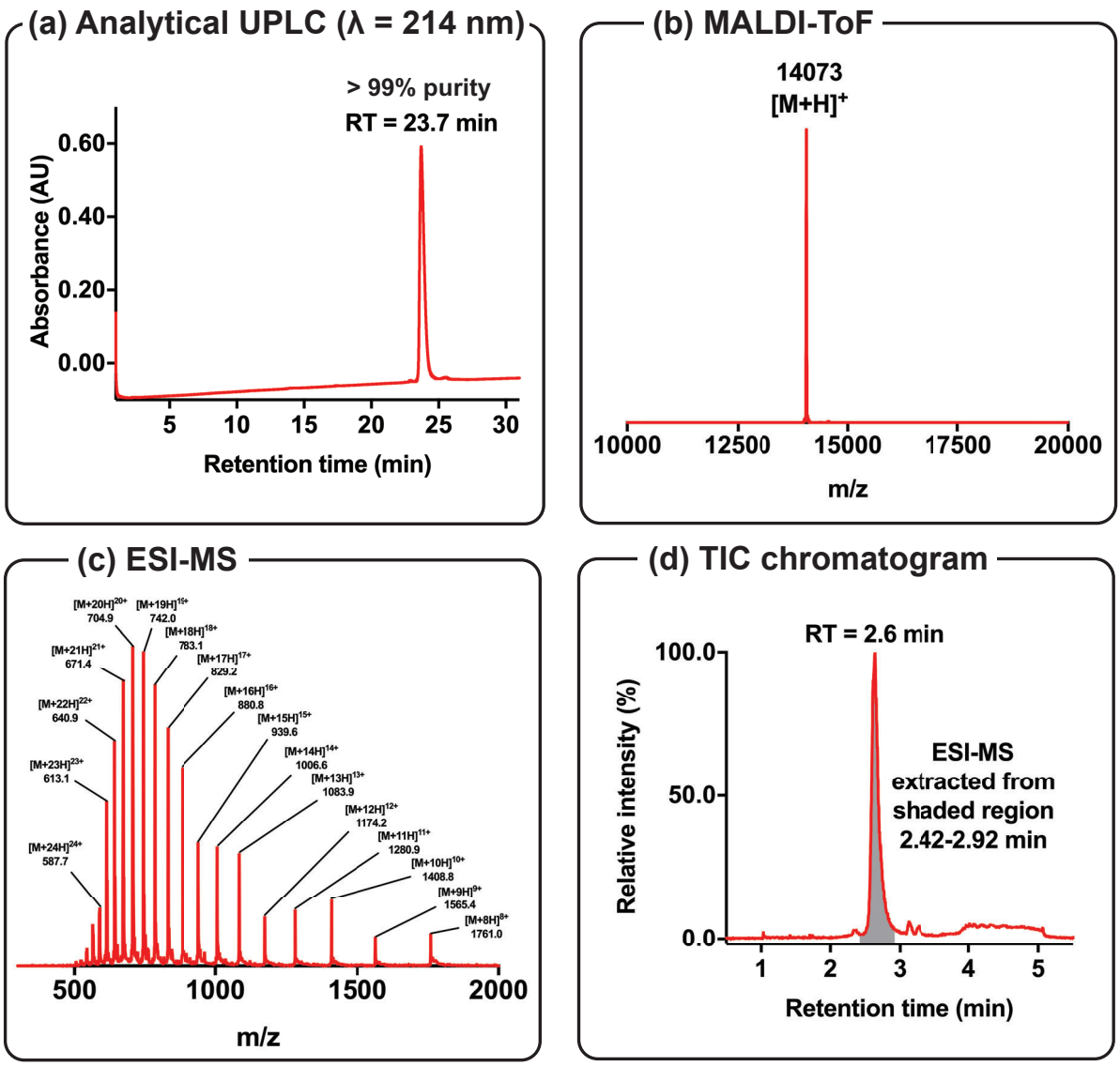
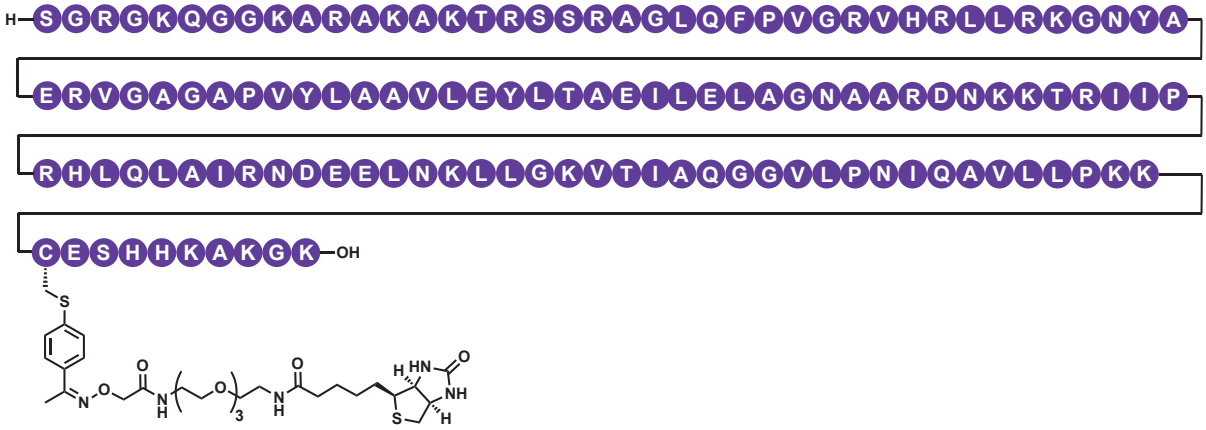


Figure S14: (a) Analytical UPLC chromatogram of pure protein **16**: retention time (RT) = 23.7 min (1 to 50% MeCN in H_2O over 30 min, 0.1% TFA, λ = 214 nm, Symmetry™, C4, 300 Å, 2.1x150 mm column); **(b) MALDI-ToF** (LP) of pure protein **16**: *m/z* calculated for $C_{623}H_{1048}N_{198}O_{171}S$ $[M+H]^+$ 14073; found (LP) $[M+H]^+$ 14073; **(c) ESI-MS** spectrum (ESI+) of pure protein **16** extracted from TIC chromatogram 2.42-2.92 min: *m/z* calculated for $C_{623}H_{1048}N_{198}O_{171}S$ $[M+8H]^{8+}$ 1760.0, $[M+9H]^{9+}$ 1564.6, $[M+10H]^{10+}$ 1408.2, $[M+11H]^{11+}$ 1280.3, $[M+12H]^{12+}$ 1173.7, $[M+13H]^{13+}$ 1083.5, $[M+14H]^{14+}$ 1006.1, $[M+15H]^{15+}$ 939.1, $[M+16H]^{16+}$ 880.5, $[M+17H]^{17+}$ 828.8, $[M+18H]^{18+}$ 782.8, $[M+19H]^{19+}$ 741.6, $[M+20H]^{20+}$ 704.6, $[M+21H]^{21+}$ 671.1, $[M+22H]^{22+}$ 640.6, $[M+23H]^{23+}$ 612.8, $[M+24H]^{24+}$ 597.3; found (ESI+) $[M+8H]^{8+}$ 1761.0, $[M+9H]^{9+}$ 1565.4, $[M+10H]^{10+}$ 1408.8, $[M+11H]^{11+}$ 1280.9, $[M+12H]^{12+}$ 1174.2, $[M+13H]^{13+}$ 1083.9, $[M+14H]^{14+}$ 1006.6, $[M+15H]^{15+}$ 939.6, $[M+16H]^{16+}$ 880.8, $[M+17H]^{17+}$ 829.2, $[M+18H]^{18+}$ 783.1, $[M+19H]^{19+}$ 742.0, $[M+20H]^{20+}$ 704.9, $[M+21H]^{21+}$ 671.4, $[M+22H]^{22+}$ 640.9, $[M+23H]^{23+}$ 613.1, $[M+24H]^{24+}$ 587.7; deconvoluted mass of 14077.7 +/– 0.7 Da; **(d) TIC chromatogram** of pure protein **16**: RT = 2.6 min (0 to 60% MeCN in H_2O over 3 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column).

H2A-PEG$_3$-biotin (17)



A protein low-binding Eppendorf tube containing protein **16** (1.0 mg, 65 nmol) in buffer (126 µL, citric acid (85 mM), phosphate (30 mM), pH 3) was warmed to 37 ˚C, and alkoxyamine-PEG$_3$-biotin (**S5**) (2.0 mg, 3.3 µmol) in MeCN (14 µL) was added followed by the catalyst 5-methoxyanthranilic acid (0.22 mg, 1.3 µmol). The reaction was monitored by UPLC-MS by taking an aliquot (0.5 µL) and diluting it in 0.1 vol% TFA in H_2O (20 µL). The reaction was 93% complete after 60 min as judged by UPLC-MS, diluted with H_2O (1 mL), and purified by RP-HPLC with a Vydac, C18, 300 Å, 22x250 mm (15 to 70% acetonitrile over 40 min, 0.1% TFA, 7 mL/min). Lyophilisation of the pure fractions afforded the pure protein **17** (0.93 mg, 82% isolated yield).

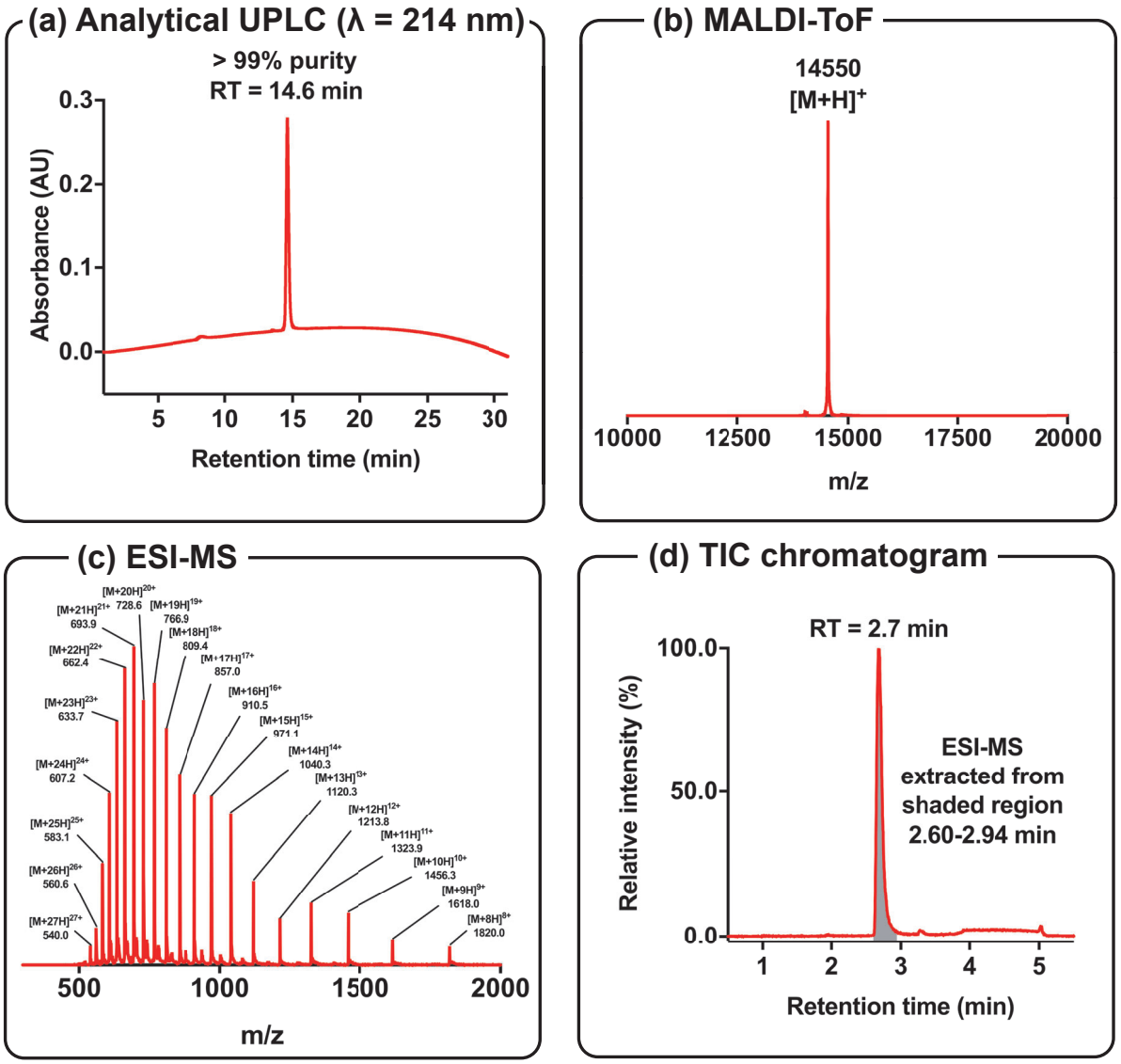
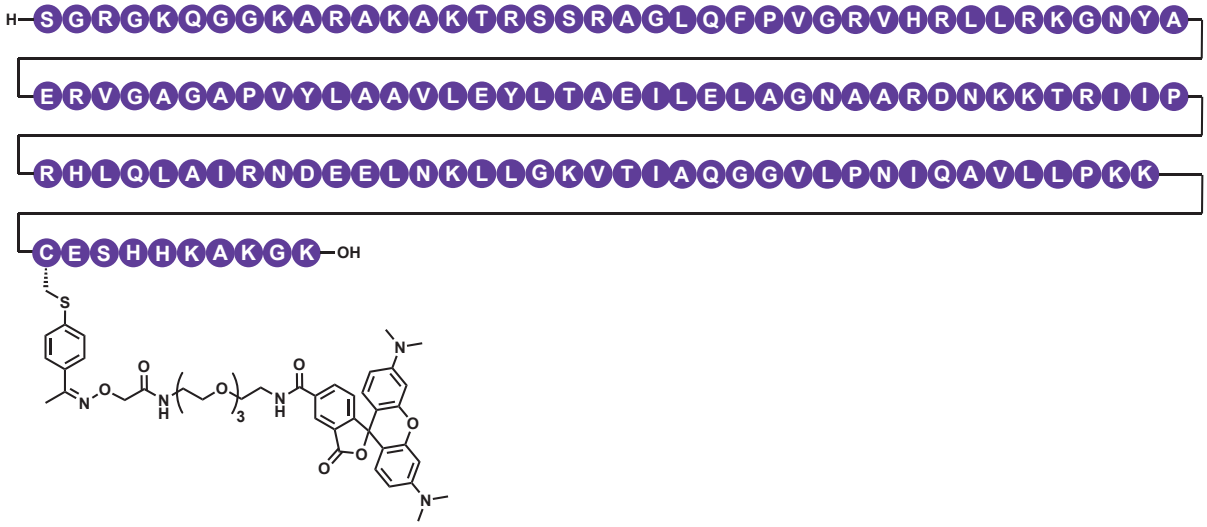


Figure S15: (a) Analytical UPLC chromatogram of pure protein **17**: retention time (RT) = 14.6 min (1 to 80% MeCN in H_2O over 30 min, 0.1% TFA, λ = 214 nm, Symmetry™, C4, 300 Å, 2.1x150 mm column); **(b) MALDI-ToF** (LP) of pure protein **17**: *m/z* calculated for $C_{643}H_{1083}N_{203}O_{177}S_2$ $[M+H]^+$ 14546; found (LP) $[M+H]^+$ 14550; **(c) ESI-MS** spectrum (ESI+) of pure protein **17** extracted from TIC chromatogram 2.60-2.94 min: *m/z* calculated for $C_{643}H_{1083}N_{203}O_{177}S_2$ $[M+8H]^{8+}$ 1819.2, $[M+9H]^{9+}$ 1617.1, $[M+10H]^{10+}$ 1455.5, $[M+11H]^{11+}$ 1323.3, $[M+12H]^{12+}$ 1213.1, $[M+13H]^{13+}$ 1119.9, $[M+14H]^{14+}$ 1040.0, $[M+15H]^{15+}$ 970.7, $[M+16H]^{16+}$ 910.1, $[M+17H]^{17+}$ 856.6, $[M+18H]^{18+}$ 809.1, $[M+19H]^{19+}$ 766.5, $[M+20H]^{20+}$ 728.3, $[M+21H]^{21+}$ 693.6, $[M+22H]^{22+}$ 662.2, $[M+23H]^{23+}$ 633.4, $[M+24H]^{24+}$ 607.1, $[M+25H]^{25+}$ 582.8, $[M+26H]^{26+}$ 560.4, $[M+27H]^{27+}$ 539.7; found (ESI+) $[M+8H]^{8+}$ 1820.0, $[M+9H]^{9+}$ 1618.0, $[M+10H]^{10+}$ 1456.3, $[M+11H]^{11+}$ 1323.9, $[M+12H]^{12+}$ 1213.8, $[M+13H]^{13+}$ 1120.3, $[M+14H]^{14+}$ 1040.3, $[M+15H]^{15+}$ 971.1, $[M+16H]^{16+}$ 910.5, $[M+17H]^{17+}$ 857.0, $[M+18H]^{18+}$ 809.4, $[M+19H]^{19+}$ 766.9, $[M+20H]^{20+}$ 728.6, $[M+21H]^{21+}$ 693.9, $[M+22H]^{22+}$ 662.4, $[M+23H]^{23+}$ 633.7, $[M+24H]^{24+}$ 607.2, $[M+25H]^{25+}$ 583.1, $[M+26H]^{26+}$ 560.6, $[M+27H]^{27+}$ 540.0; deconvoluted mass of 14551 +/– 0.4 Da; **(d) TIC chromatogram** of pure protein **17**: RT = 2.7 min (0 to 60% MeCN in H_2O over 3 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column).

H2A-PEG$_3$-TAMRA (18)



A protein low-binding Eppendorf tube containing protein **16** (1.0 mg, 65 nmol) in buffer (100 µL, citric acid (85 mM), phosphate (30 mM), pH 3) was warmed to 37 ˚C, and alkoxyamine-PEG$_3$-TAMRA (**S6**) (1.86 mg, 2.4 µmol) in MeCN (35 µL) was added followed by the catalyst 5-methoxyanthranilic acid (0.22 mg, 1.3 µmol) in H_2O/MeCN (35 µL, 1:1 (v/v)). The reaction was monitored by UPLC-MS by taking an aliquot (0.5 µL) and diluting it in 0.1 vol% TFA in H_2O (20 µL). The reaction was 86% complete after 3 h as judged by UPLC-MS, diluted with H_2O (1 mL), and purified by RP-HPLC with a Vydac, C18, 300 Å, 22x250 mm (15 to 70% acetonitrile over 40 min, 0.1% TFA, 7 mL/min). Lyophilisation of the pure fractions afforded the pure protein **18** (0.94 mg, 82% isolated yield).

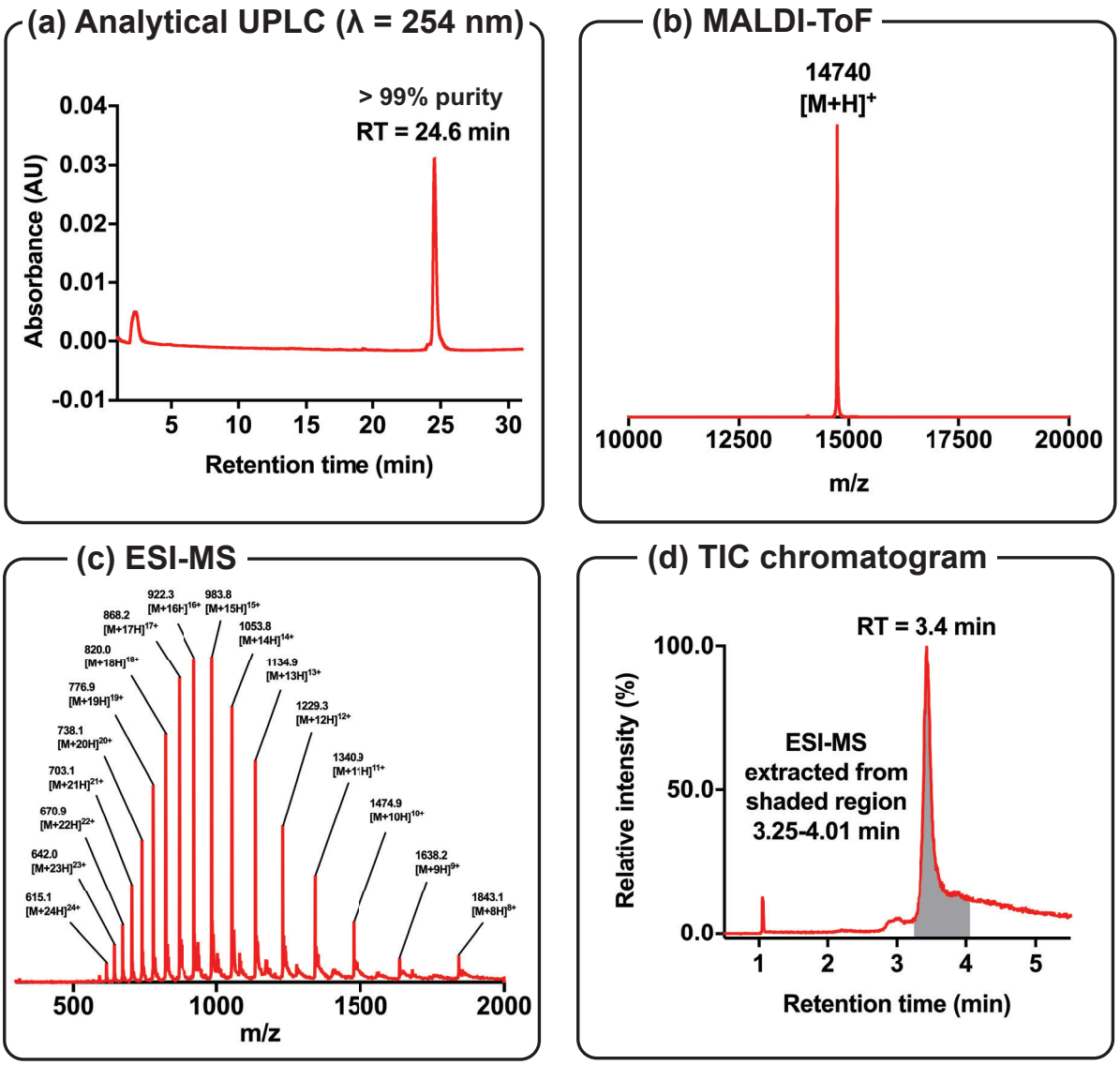
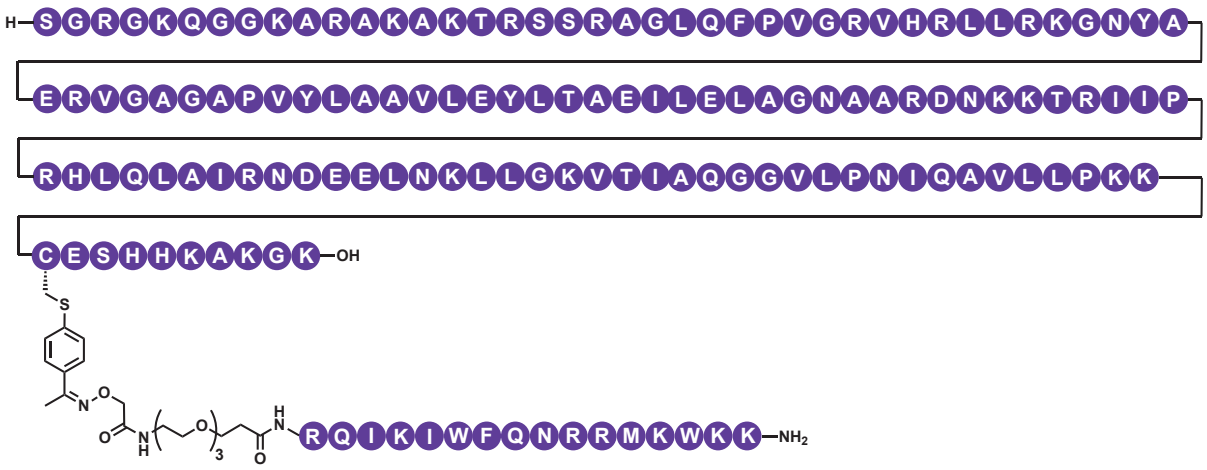


Figure S16: (a) Analytical UPLC chromatogram of pure protein **18**: retention time (RT) = 24.6 min (1 to 80% MeCN in H_2O over 30 min, 0.1% TFA, λ = 254 nm, Symmetry™, C4, 300 Å, 2.1x150 mm column); **(b) MALDI-ToF** (LP) of pure protein **18**: *m/z* calculated for $C_{658}H_{1089}N_{203}O_{179}S$ $[M+H]^+$ 14732; found (LP) $[M+H]^+$ 14740; **(c) ESI-MS** spectrum (ESI+) of pure protein **18** extracted from TIC chromatogram 3.25-4.01 min: *m/z* calculated for $C_{658}H_{1089}N_{203}O_{179}S$ $[M+8H]^{8+}$ 1842.4, $[M+9H]^{9+}$ 1637.8, $[M+10H]^{10+}$ 1474.1, $[M+11H]^{11+}$ 1340.2, $[M+12H]^{12+}$ 1228.6, $[M+13H]^{13+}$ 1134.2, $[M+14H]^{14+}$ 1053.2, $[M+15H]^{15+}$ 983.1, $[M+16H]^{16+}$ 921.7, $[M+17H]^{17+}$ 867.6, $[M+18H]^{18+}$ 819.4, $[M+19H]^{19+}$776.3, $[M+20H]^{20+}$ 737.6, $[M+21H]^{21+}$ 702.6, $[M+22H]^{22+}$ 670.6, $[M+23H]^{23+}$ 641.5, $[M+24H]^{24+}$614.8; found (ESI+) $[M+8H]^{8+}$ 1843.1, $[M+9H]^{9+}$ 1638.2, $[M+10H]^{10+}$ 1474.9, $[M+11H]^{11+}$ 1340.9, $[M+12H]^{12+}$ 1229.3, $[M+13H]^{13+}$ 1134.9, $[M+14H]^{14+}$ 1053.8, $[M+15H]^{15+}$ 983.8, $[M+16H]^{16+}$ 922.3, $[M+17H]^{17+}$ 868.2, $[M+18H]^{18+}$ 820.0, $[M+19H]^{19+}$ 776.9, $[M+20H]^{20+}$ 738.1, $[M+21H]^{21+}$ 703.1, $[M+22H]^{22+}$ 670.9, $[M+23H]^{23+}$ 642.0, $[M+24H]^{24+}$ 615.1; deconvoluted mass of 14740.4 +/– 1.4 Da; **(d) TIC chromatogram** of pure protein **18**: RT = 3.4 min (0 to 60% MeCN in H_2O over 5 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column).

H2A-PEG$_3$-penetratin (19)



A protein low-binding Eppendorf tube containing protein **16** (1.0 mg, 65 nmol) in buffer (112 µL, citric acid (85 mM), phosphate (30 mM), pH 3) was warmed to 37 ˚C, and alkoxyamine-PEG$_3$-penetratin (**S11**) (11.3 mg, 3.3 µmol) in H_2O/MeCN (28 µL, 1:1 (v/v)) was added followed by the catalyst 5-methoxyanthranilic acid (0.44 mg, 2.6 µmol). The reaction was monitored by UPLC-MS by taking an aliquot (0.5 µL) and diluting it in 0.1 vol% TFA in H_2O (20 µL). The reaction was 82% complete after 20 h as judged by UPLC-MS, diluted with H_2O (1 mL), and purified by RP-HPLC with a Vydac, C18, 300 Å, 22x250 mm (15 to 70% acetonitrile over 40 min, 0.1% TFA, 7 mL/min). Lyophilisation of the pure fractions afforded the pure protein **19** (1.1 mg, 83% isolated yield).

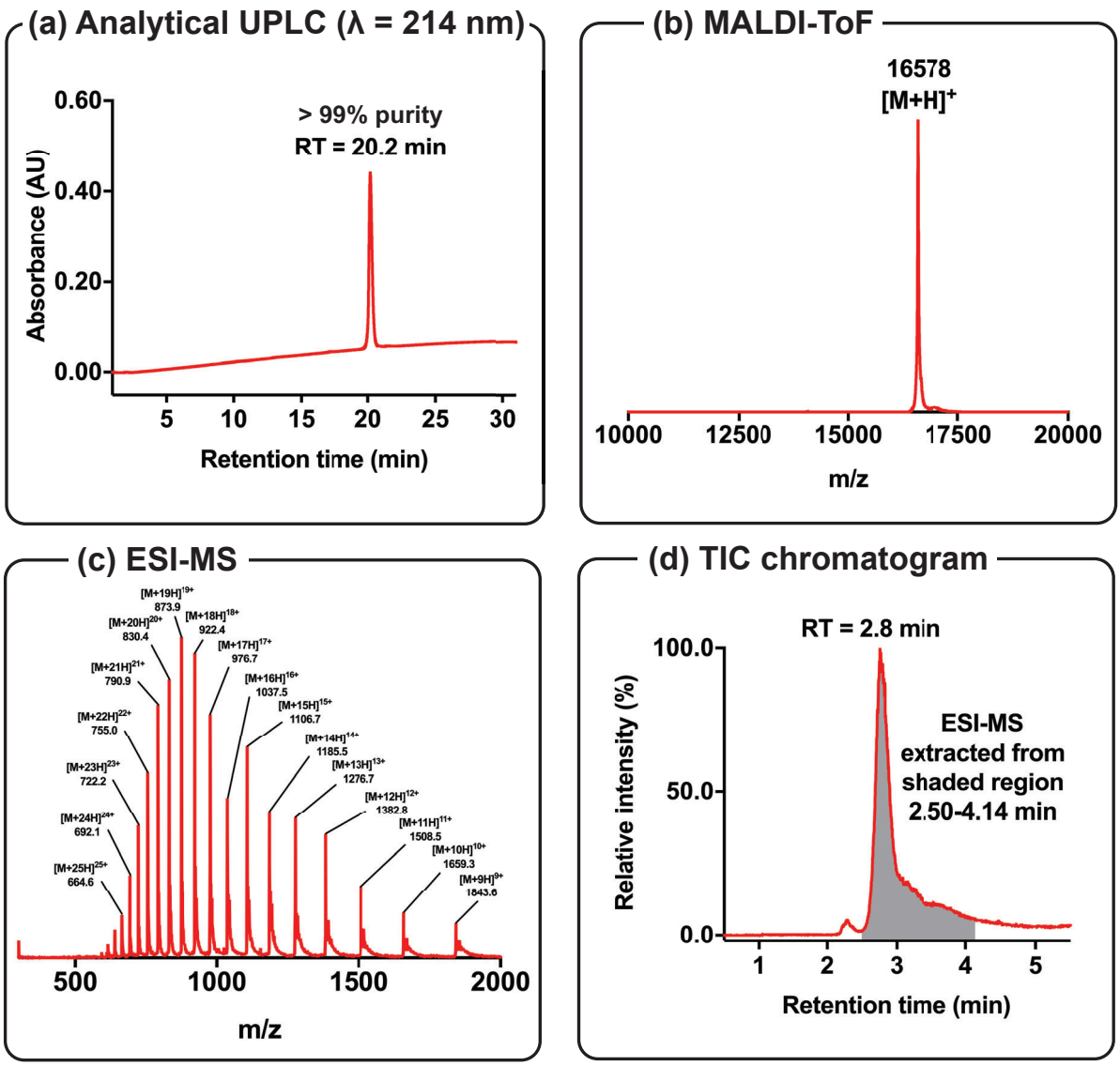
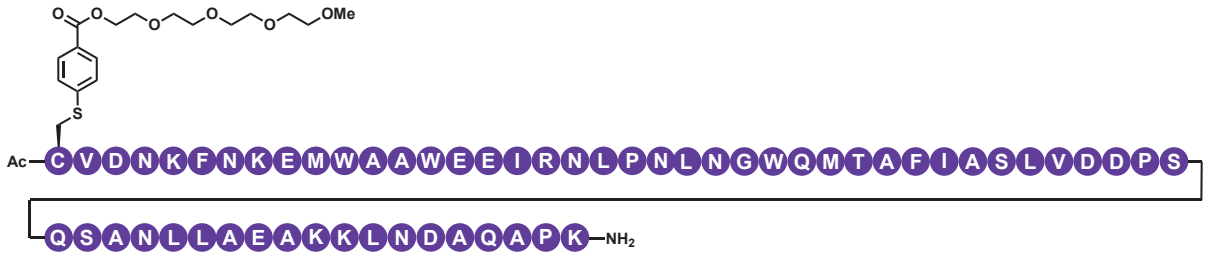


Figure S17: (a) Analytical UPLC chromatogram of pure protein **19**: retention time (RT) = 20.2 min (1 to 80% MeCN in H_2O over 30 min, 0.1% TFA, λ = 214 nm, Symmetry™, C4, 300 Å, 2.1x150 mm column); **(b) MALDI-ToF** (LP) of pure protein **19**: *m/z* calculated for $C_{738}H_{1235}N_{235}O_{195}S_2$ $[M+H]^+$ 16575; found (LP) $[M+H]^+$ 16578; **(c) ESI-MS** spectrum (ESI+) of pure protein **19** extracted from TIC chromatogram 2.50-4.14 min: *m/z* calculated for $C_{738}H_{1235}N_{235}O_{195}S_2$ $[M+9H]^{9+}$ 1842.6, $[M+10H]^{10+}$ 1658.4, $[M+11H]^{11+}$ 1507.8, $[M+12H]^{12+}$ 1382.2, $[M+13H]^{13+}$ 1276.0, $[M+14H]^{14+}$ 1184.9, $[M+15H]^{15+}$ 1106.0, $[M+16H]^{16+}$ 1036.9, $[M+17H]^{17+}$ 976.0, $[M+18H]^{18+}$ 921.8, $[M+19H]^{19+}$ 873.3, $[M+20H]^{20+}$ 829.7, $[M+21H]^{21+}$ 790.3, $[M+22H]^{22+}$ 754.4, $[M+23H]^{23+}$ 721.6, $[M+24H]^{24+}$ 691.6, $[M+25H]^{25+}$ 664.0; found (ESI+) $[M+9H]^{9+}$ 1843.6, $[M+10H]^{10+}$ 1659.3, $[M+11H]^{11+}$ 1508.5, $[M+12H]^{12+}$ 1382.8, $[M+13H]^{13+}$ 1276.7, $[M+14H]^{14+}$ 1185.5, $[M+15H]^{15+}$ 1106.7, $[M+16H]^{16+}$ 1037.5, $[M+17H]^{17+}$ 976.7, $[M+18H]^{18+}$ 922.4, $[M+19H]^{19+}$ 873.9, $[M+20H]^{20+}$ 830.4, $[M+21H]^{21+}$ 790.9, $[M+22H]^{22+}$ 755.0, $[M+23H]^{23+}$ 722.2, $[M+24H]^{24+}$ 692.1, $[M+25H]^{25+}$ 664.6; deconvoluted mass of 16584 +/– 1.9 Da; **(d) TIC chromatogram** of pure protein **19**: RT = 2.8 min (0 to 60% MeCN in H_2O over 5 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column).

zEGFR-mPEG$_4$ (22)



A protein low-binding Eppendorf tube containing protein **11** (1.0 mg, 136 nmol) in buffer (600 µL, phosphate (0.2 mM), EDTA (1 mM), pH 8.0), TCEP (1.4 µL, 100 mM, phopsphate buffer) was warmed to 37 ˚C. Diaryliodonium salt compound **20** (0.4 mg, 0.5 µmol) in MeCN (70 µL) was added. The reaction was monitored by UPLC-MS and MALDI-ToF by taking an aliquot (1 µL) and diluting it in 0.1 vol% TFA in H_2O (20 µL). The reaction was 90% complete after 180 min as judged by UPLC-MS, quenched with 0.1 vol% TFA in H_2O (0.5 mL), and purified by RP-HPLC with a Waters X-Bridge® C18, 300 Å, 10 x 250 mm column (0 to 60% MeCN over 55 min, 0.1 vol% TFA, 4 mL/min, 50 ˚C). Lyophilisation of the pure fractions afforded the pure protein **22** (0.34 mg, 32% isolated yield).

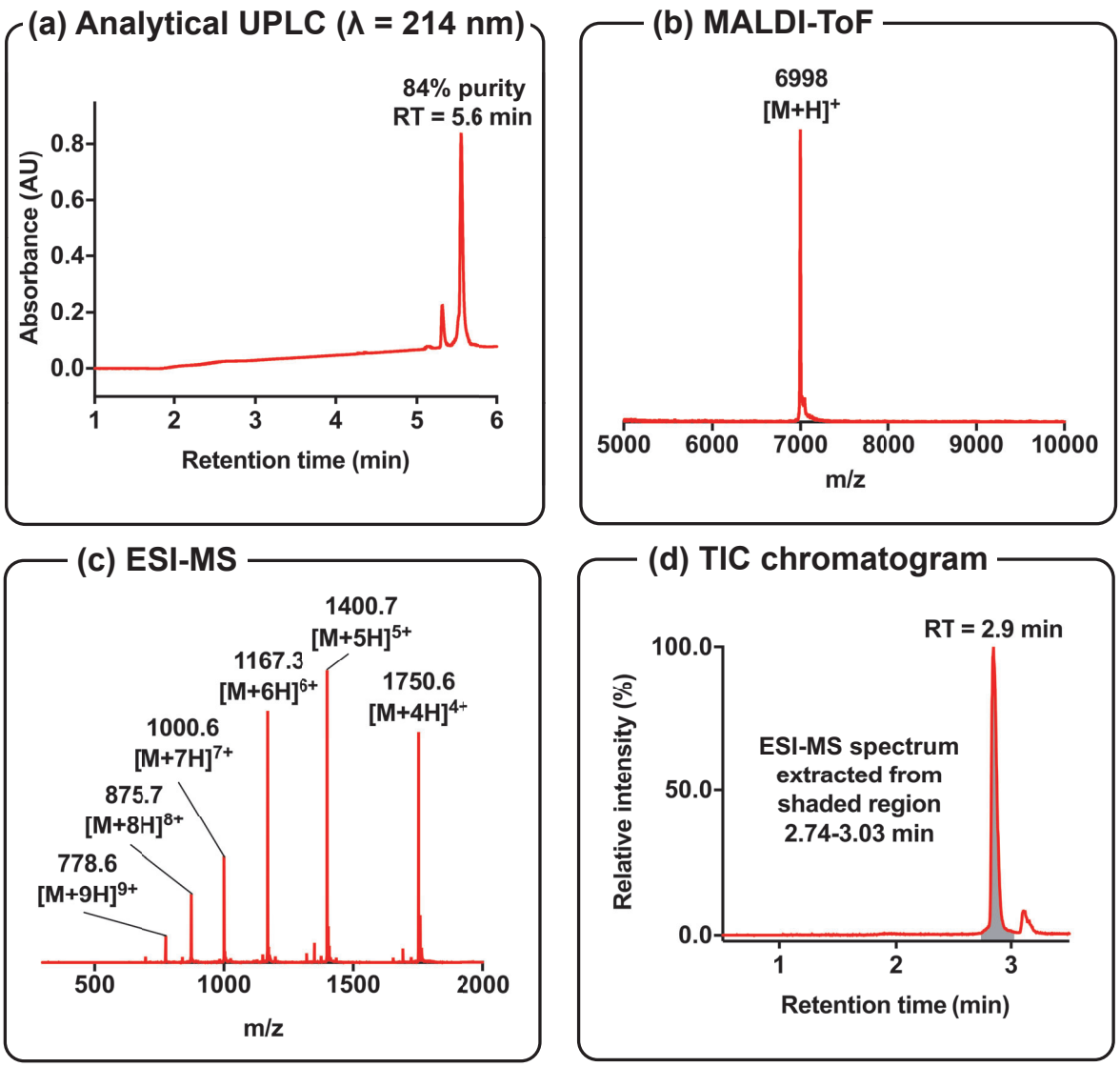
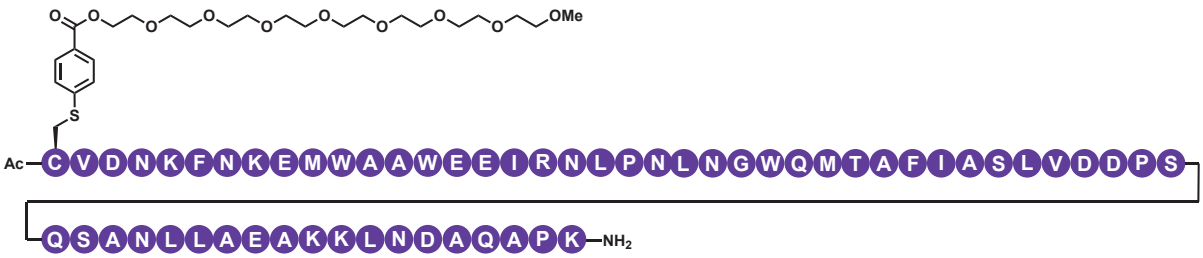


Figure S18: (a) Analytical UPLC chromatogram of pure protein **22**: retention time (RT) = 5.6 min (0 to 60% MeCN in H_2O over 5 min, 0.1% TFA, λ = 214 nm, Waters Acquity ® BEH, C18, 300Å, 2.1x50 mm column); **(b) MALDI-ToF** (LP) of pure protein **22**: *m/z* calculated for $C_{312}H_{418}N_{81}O_{96}S_3$ $[M+H]^+$ 6996; found (LP) $[M+H]^+$ 6998; **(c) ESI-MS** spectrum (ESI+) of pure protein **22** extracted from TIC chromatogram 2.74-3.03 min: *m/z* calculated for $C_{312}H_{418}N_{81}O_{96}S_3$ $[M+4H]^{4+}$ 1749.6, $[M+5H]^{5+}$ 1399.9, $[M+6H]^{6+}$ 1166.8, $[M+7H]^{7+}$ 1000.2, $[M+8H]^{8+}$ 875.3, $[M+9H]^{9+}$ 778.2; found (ESI+) $[M+4H]^{4+}$ 1750.6, $[M+5H]^{5+}$ 1400.7, $[M+6H]^{6+}$ 1167.3, $[M+7H]^{7+}$ 1000.6, $[M+8H]^{8+}$ 875.7, $[M+9H]^{9+}$ 778.6; deconvoluted mass of 6997.9 +/–0.5 Da; **(d) TIC chromatogram** of pure protein **22**: RT = 2.9 min (0 to 60% MeCN in H_2O over 3 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column).

zEGFR-mPEG$_8$ (23)



A protein low-binding Eppendorf tube containing protein **11** (1.0 mg, 136 nmol) in buffer (241 µL, phosphate (0.2 mM), EDTA (1 mM), TCEP (0.5 mM), pH 8.0)) was warmed to 37 ˚C. Diaryliodonium salt compound **21** (0.2 mg, 0.27 µmol) in MeCN (26 µL) was added. The reaction was monitored by UPLC-MS and MALDI-ToF by taking an aliquot (1 µL) and diluting it in 0.1 vol% TFA in H_2O (20 µL). The reaction was 90% complete after 120 min as judged by UPLC-MS, quenched with 0.1 vol% TFA in H_2O (0.5 mL), and purified by RP-HPLC with a Waters X-Bridge® C18, 300 Å, 10 x 250 mm column (0 to 50% MeCN over 50 min, 0.1 vol% TFA, 4 mL/min, 50 ˚C). Lyophilisation of the pure fractions afforded the pure protein **23** (0.22 mg, 21% isolated yield).

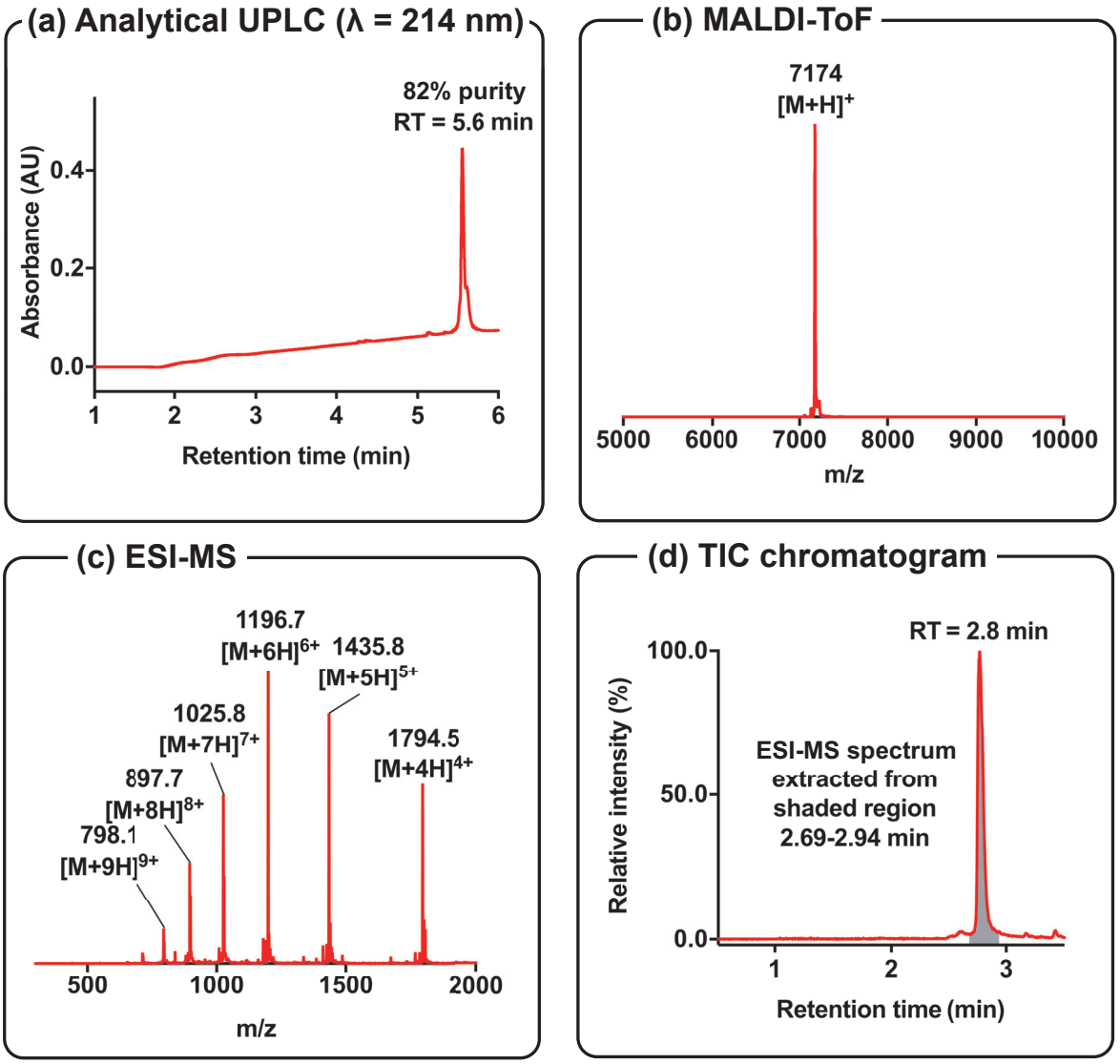
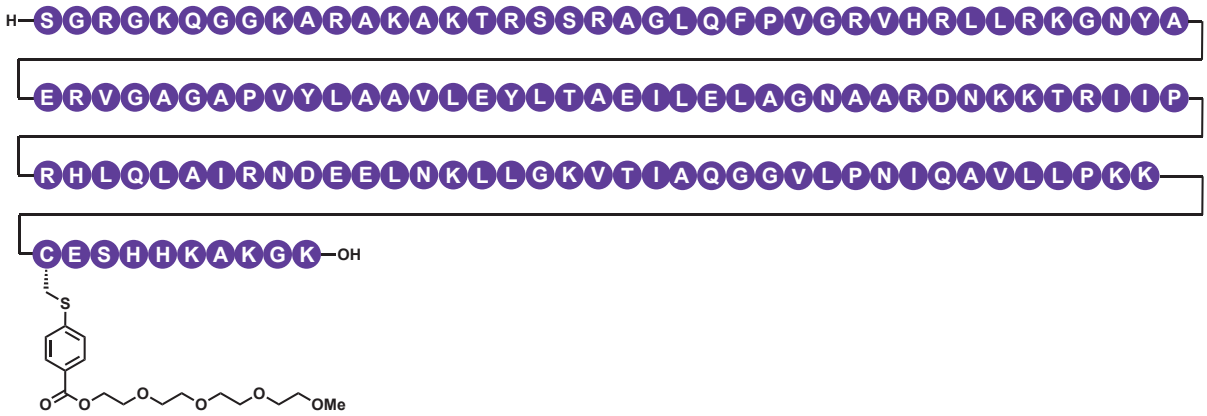


Figure S19: (a) Analytical UPLC chromatogram of pure protein **23**: retention time (RT) = 5.6 min (0 to 60% MeCN in H_2O over 5 min, 0.1% TFA, λ = 214 nm, Waters Acquity ® BEH, C18, 300Å, 2.1x50 mm column); **(b) MALDI-ToF** (LP) of pure protein **23**: *m/z* calculated for $C_{320}H_{497}N_{81}O_{100}S_3$ $[M+H]^+$ 7172; found (LP) $[M+H]^+$ 7174; **(c) ESI-MS** spectrum (ESI+) of pure protein **23** extracted from TIC chromatogram 2.69-2.94 min: *m/z* calculated for $[M+4H]^{4+}$ 1793.7, $[M+5H]^{5+}$ 1435.1, $[M+6H]^{6+}$ 1196.1, $[M+7H]^{7+}$ 1025.4, $[M+8H]^{8+}$ 897.3, $[M+9H]^{9+}$ 797.7; found (ESI+) $[M+4H]^{4+}$ 1794.5, $[M+5H]^{5+}$ 1435.8, $[M+6H]^{6+}$ 1196.7, $[M+7H]^{7+}$ 1025.8, $[M+8H]^{8+}$ 897.7, $[M+9H]^{9+}$ 798.1; deconvoluted mass of 7173.8 +/– 0.3 Da; **(d) TIC chromatogram** of pure protein **23**: RT = 2.8 min (0 to 60% MeCN in H_2O over 3 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column)**.**

H2A-mPEG$_4$ (24)



A protein low-binding Eppendorf tube containing protein **15** (1.5 mg, 90 nmol) in buffer (444 µL, phosphate (0.2 mM), EDTA (1 mM), pH 8.0) was warmed to 37 ˚C, and diaryliodonium salt compound **20** (0.3 mg, 0.4 µmol) in MeCN (48 µL) was added. The reaction was monitored by UPLC-MS and MALDI-ToF by taking an aliquot (1 µL) and diluting it in 0.1 vol% TFA in H_2O (20 µL). The reaction was 94% complete after 180 min as judged by MALDI-ToF, quenched with 0.1 vol% TFA in H_2O (0.5 mL), and purified by RP-HPLC with a Vydac, C18, 300 Å, 22x250 mm (15 to 70% acetonitrile over 40 min, 0.1% TFA, 7 mL/min). Lyophilisation of the pure fractions afforded the pure protein **24** (0.81 mg, 53% isolated yield).

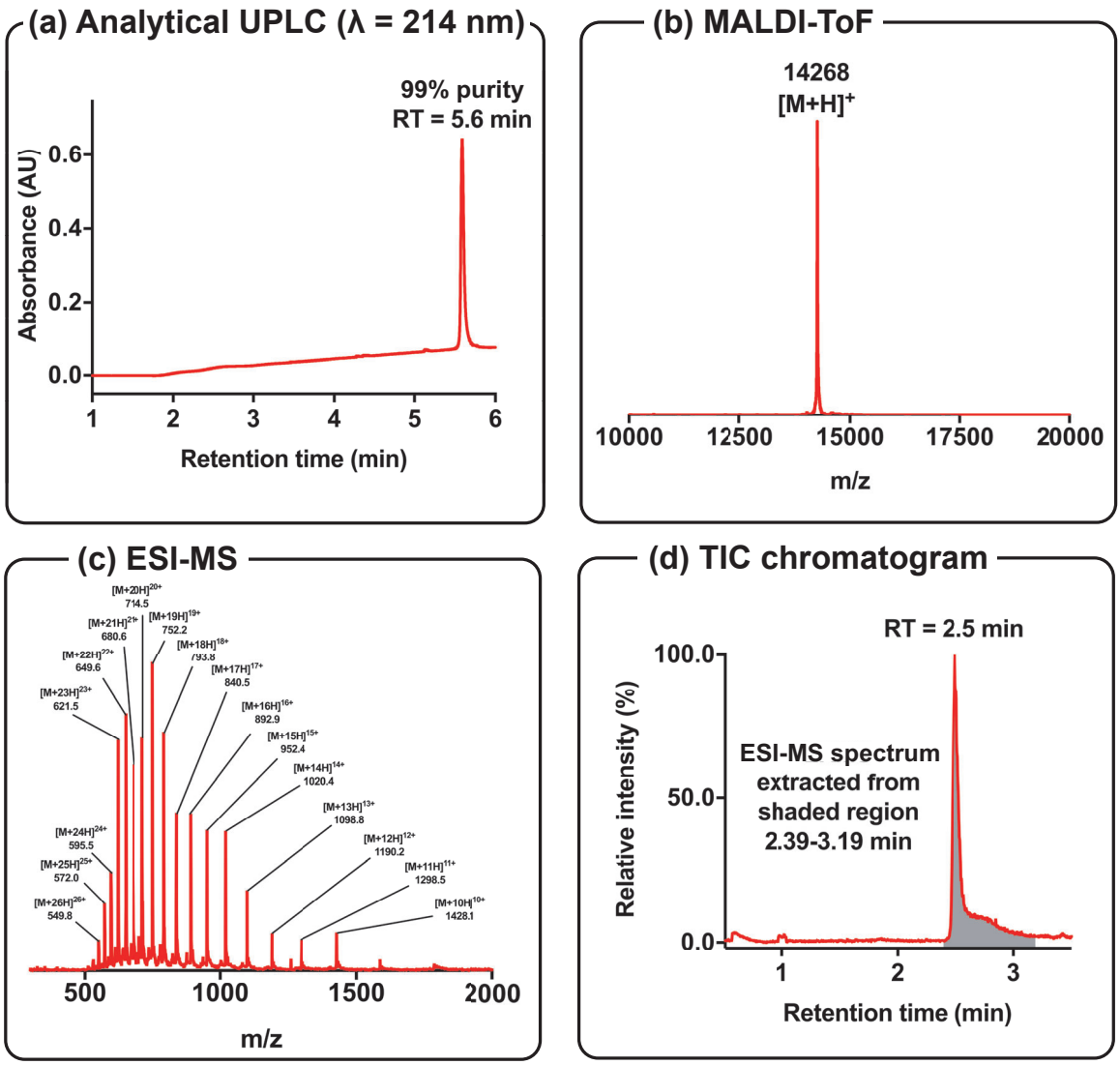
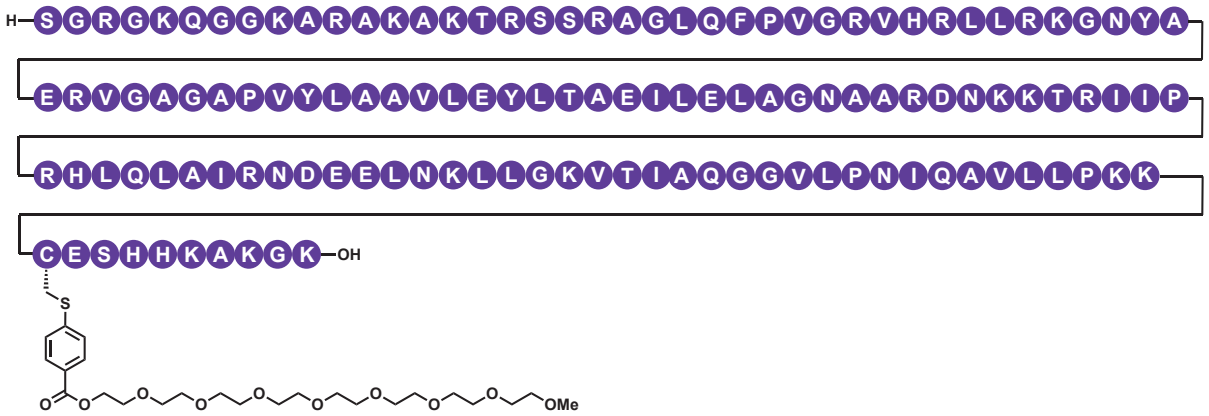


Figure S20: (a) Analytical UPLC chromatogram of pure protein **24**: retention time (RT) = 5.6 min (0 to 60% MeCN in H_2O over 5 min, 0.1% TFA, λ = 214 nm, Waters Acquity ® BEH, C18, 300Å, 2.1x50 mm column); **(b) MALDI-ToF** (LP) of pure protein **24**: *m/z* calculated for $C_{631}H_{1064}N_{198}O_{176}S$ $[M+H]^+$ 14265; found (LP) $[M+H]^+$ 14268; **(c) ESI-MS** spectrum (ESI+) of pure protein **24** extracted from TIC chromatogram 2.39.3.19 min: *m/z* calculated for $C_{631}H_{1064}N_{198}O_{176}S$ $[M+10H]^{10+}$ 1427.4, $[M+11H]^{11+}$ 1297.7, $[M+12H]^{12+}$ 1189.7, $[M+13H]^{13+}$ 1098.2, $[M+14H]^{14+}$ 1019.9, $[M+15H]^{15+}$ 951.9, $[M+16H]^{16+}$ 892.5, $[M+17H]^{17+}$ 840.1, $[M+18H]^{18+}$ 793.5, $[M+19H]^{19+}$ 751.8, $[M+20H]^{20+}$ 714.2, $[M+21H]^{21+}$ 680.3, $[M+22H]^{22+}$ 649.4, $[M+23H]^{23+}$ 621.2, $[M+24H]^{24+}$595.3, $[M+25H]^{25+}$ 571.6, $[M+26H]^{26+}$ 549.6; found (ESI+) $[M+10H]^{10+}$ 1428.1, $[M+11H]^{11+}$ 1298.5, $[M+12H]^{12+}$ 1190.2, $[M+13H]^{13+}$ 1098.8, $[M+14H]^{14+}$ 1020.4, $[M+15H]^{15+}$ 952.4, $[M+16H]^{16+}$ 892.9, $[M+17H]^{17+}$ 840.5, $[M+18H]^{18+}$ 793.8, $[M+19H]^{19+}$ 752.2, $[M+20H]^{20+}$ 714.5, $[M+21H]^{21+}$ 680.6, $[M+22H]^{22+}$ 649.6, $[M+23H]^{23+}$ 621.5, $[M+24H]^{24+}$ 595.5, $[M+25H]^{25+}$ 572.0, $[M+26H]^{26+}$ 549.8; deconvoluted mass of 14271.2 +/– 0.9 Da; **(d) TIC chromatogram** of pure protein **24**: RT = 2.5 min (0 to 60% MeCN in H_2O over 3 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column).

H2A-mPEG$_8$ (25)



A protein low-binding Eppendorf tube containing protein **15** (1.5 mg, 90 nmol) in buffer (177 µL, phosphate (0.2 mM), EDTA (1 mM), pH 8.0), TCEP (1.4 µL, 100 mM, phopsphate buffer) was warmed to 37 ˚C. Diaryliodonium salt compound **21** (0.8 mg, 0.7 µmol) in MeCN (26 µL) was added. The reaction was monitored by UPLC-MS and MALDI-ToF by taking an aliquot (1 µL) and diluting it in 0.1 vol% TFA in H_2O (20 µL). The reaction was 99% complete after 120 min as judged by MALDI-ToF, quenched with 0.1 vol% TFA in H_2O (0.5 mL), and purified by RP-HPLC with a Vydac, C18, 300 Å, 22x250 mm (15 to 70% acetonitrile over 40 min, 0.1% TFA, 7 mL/min). Lyophilisation of the pure fractions afforded the pure protein **25** (1.2 mg, 77% isolated yield).

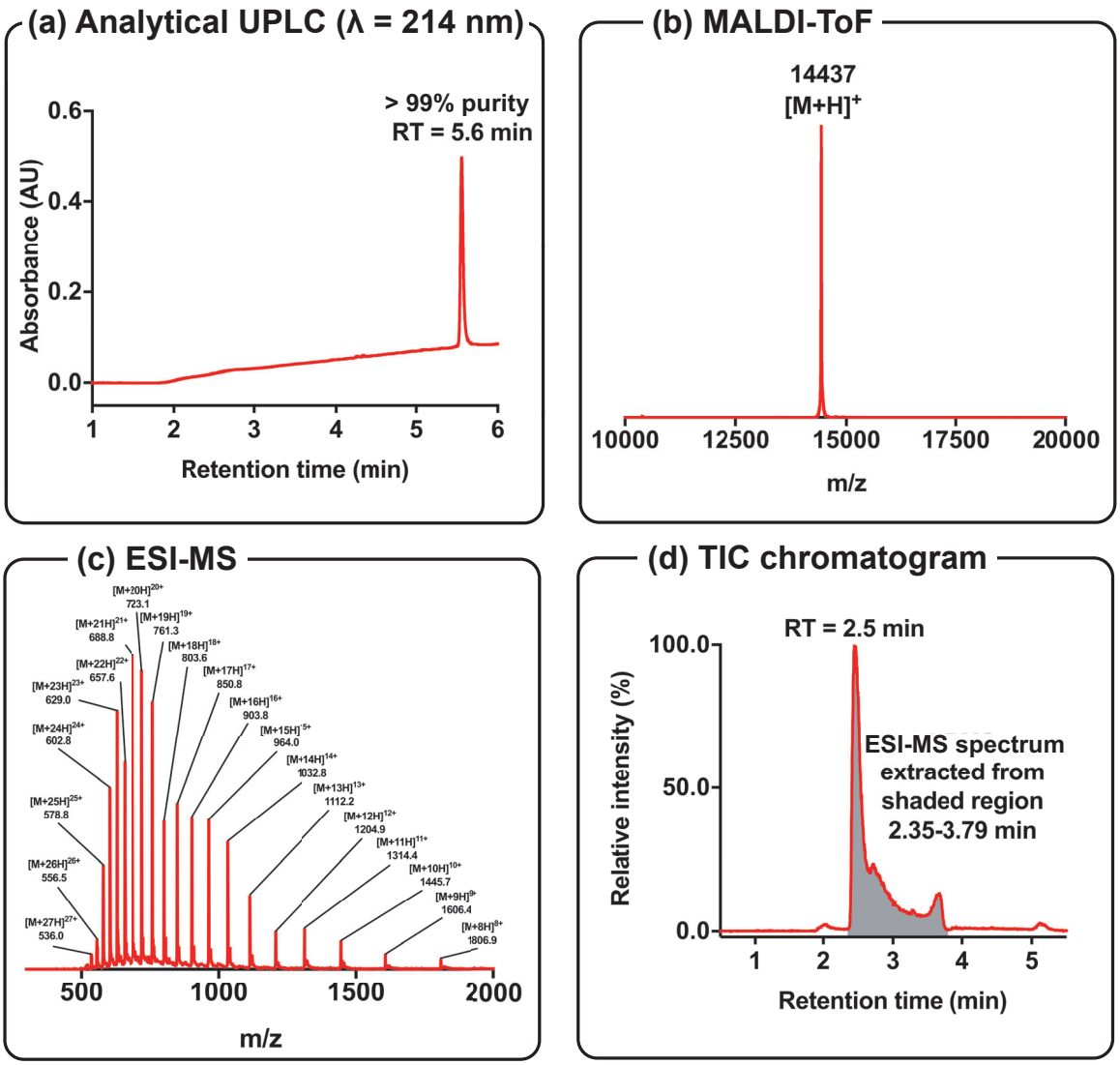
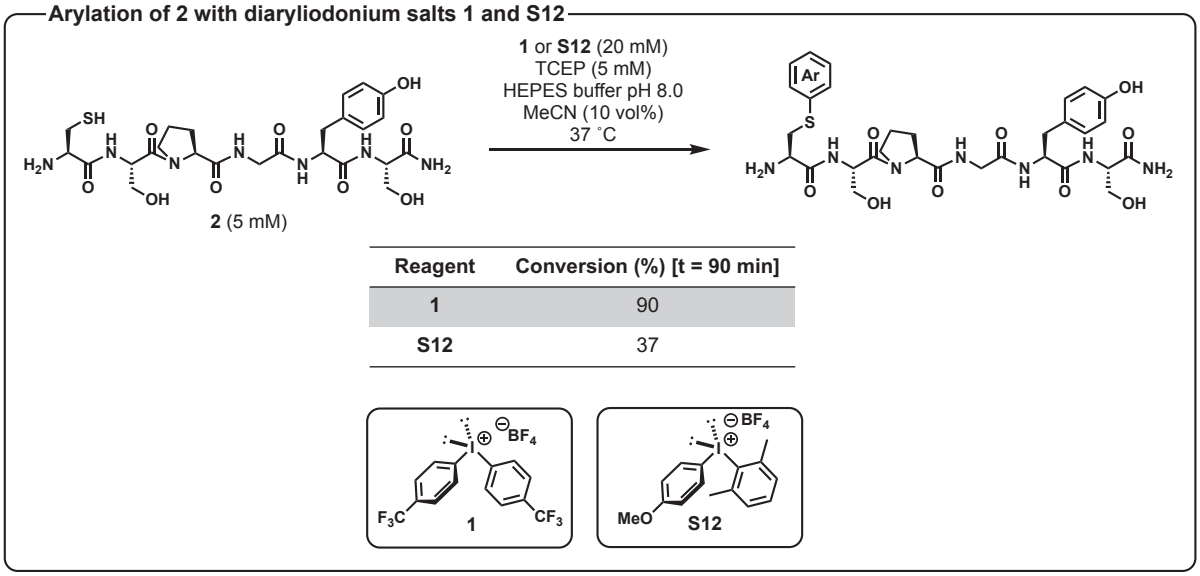


Figure S21: (a) Analytical UPLC chromatogram of pure protein **25**: retention time (RT) = 5.6 min (0 to 60% MeCN in H_2O over 5 min, 0.1% TFA, λ = 214 nm, Waters Acquity ® BEH, C18, 300Å, 2.1x50 mm column); **(b) MALDI-ToF** (LP) of pure protein **25**: *m/z* calculated for $[M+H]^+$ 14441; found (LP) $[M+H]^+$ 14437; **(c) ESI-MS** spectrum (ESI+) of pure protein **25** extracted from TIC chromatogram 2.35-3.79 min: *m/z* calculated for $C_{639}H_{1030}N_{198}O_{180}S$ $[M+8H]^{8+}$ 1806.0, $[M+9H]^{9+}$ 1605.5, $[M+10H]^{10+}$ 1445.0, $[M+11H]^{11+}$ 1313.8, $[M+12H]^{12+}$ 1204.4, $[M+13H]^{13+}$ 1111.8, $[M+14H]^{14+}$ 1032.5, $[M+15H]^{15+}$ 963.7, $[M+16H]^{16+}$ 903.5, $[M+17H]^{17+}$ 850.4, $[M+18H]^{18+}$ 803.2, $[M+19H]^{19+}$ 761.0, $[M+20H]^{20+}$ 723.0, $[M+21H]^{21+}$ 688.6, $[M+22H]^{22+}$ 657.4, $[M+23H]^{23+}$ 628.8, $[M+24H]^{24+}$ 602.7, $[M+25H]^{25+}$ 578.6, $[M+26H]^{26+}$ 556.4, $[M+27H]^{27+}$ 535.8; found (ESI+) $[M+8H]^{8+}$ 1806.9, $[M+9H]^{9+}$ 1606.4, $[M+10H]^{10+}$ 1445.7, $[M+11H]^{11+}$ 1314.4, $[M+12H]^{12+}$ 1204.9, $[M+13H]^{13+}$ 1112.2, $[M+14H]^{14+}$ 1032.8, $[M+15H]^{15+}$ 964.0, $[M+16H]^{16+}$ 903.8, $[M+17H]^{17+}$ 850.8, $[M+18H]^{18+}$ 803.6, $[M+19H]^{19+}$ 761.3, $[M+20H]^{20+}$ 723.1, $[M+21H]^{21+}$ 688.8, $[M+22H]^{22+}$ 657.6, $[M+23H]^{23+}$ 629.0, $[M+24H]^{24+}$ 602.8, $[M+25H]^{25+}$ 578.8, $[M+26H]^{26+}$ 556.5, $[M+27H]^{27+}$ 536.0; deconvoluted mass of 14444.7 +/– 1.5 Da; **(d) TIC chromatogram** of pure protein **25**: RT = 2.5 min (0 to 60% MeCN in H_2O over 5 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column).

Optimisation studies

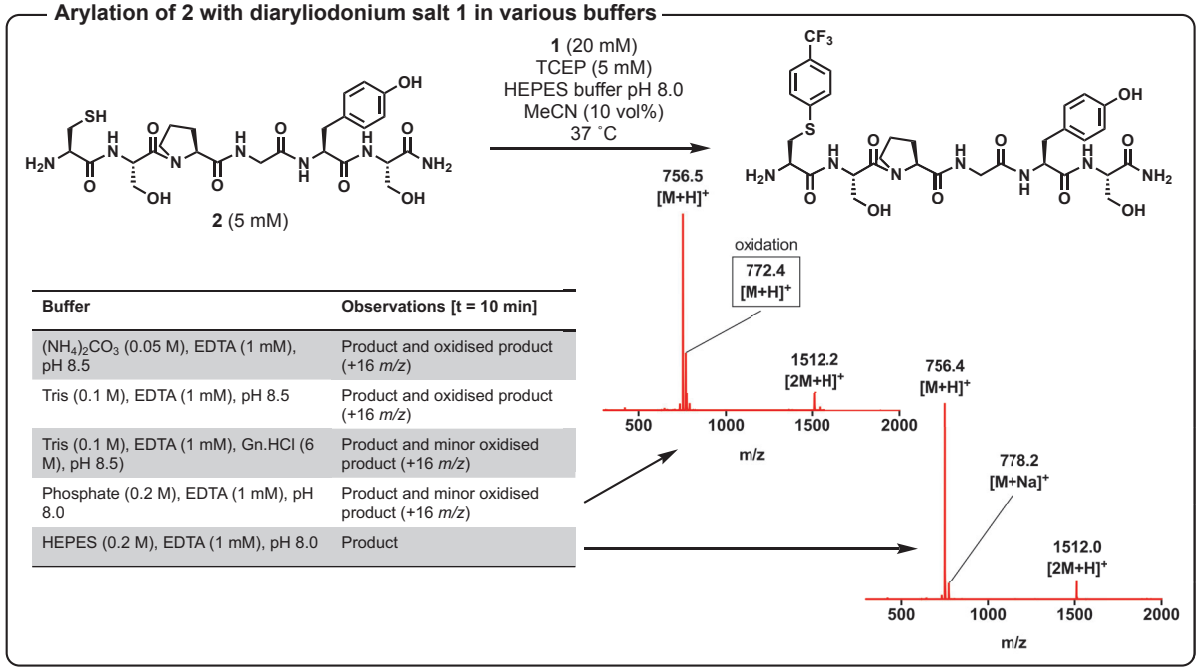
Influence of substituents on diaryliodonium salt reactivity



Reagent	Conversion (%) [t = 90 min]
1	90
S12	37

Scheme S1: Arylation of peptide **2** with diaryliodonium salts with differing electrophilicity. Conversions calculated by relative total ion current intensities in ESI-MS spectra obtained via UPLC-MS.

Influence of buffer on arylation chemistry

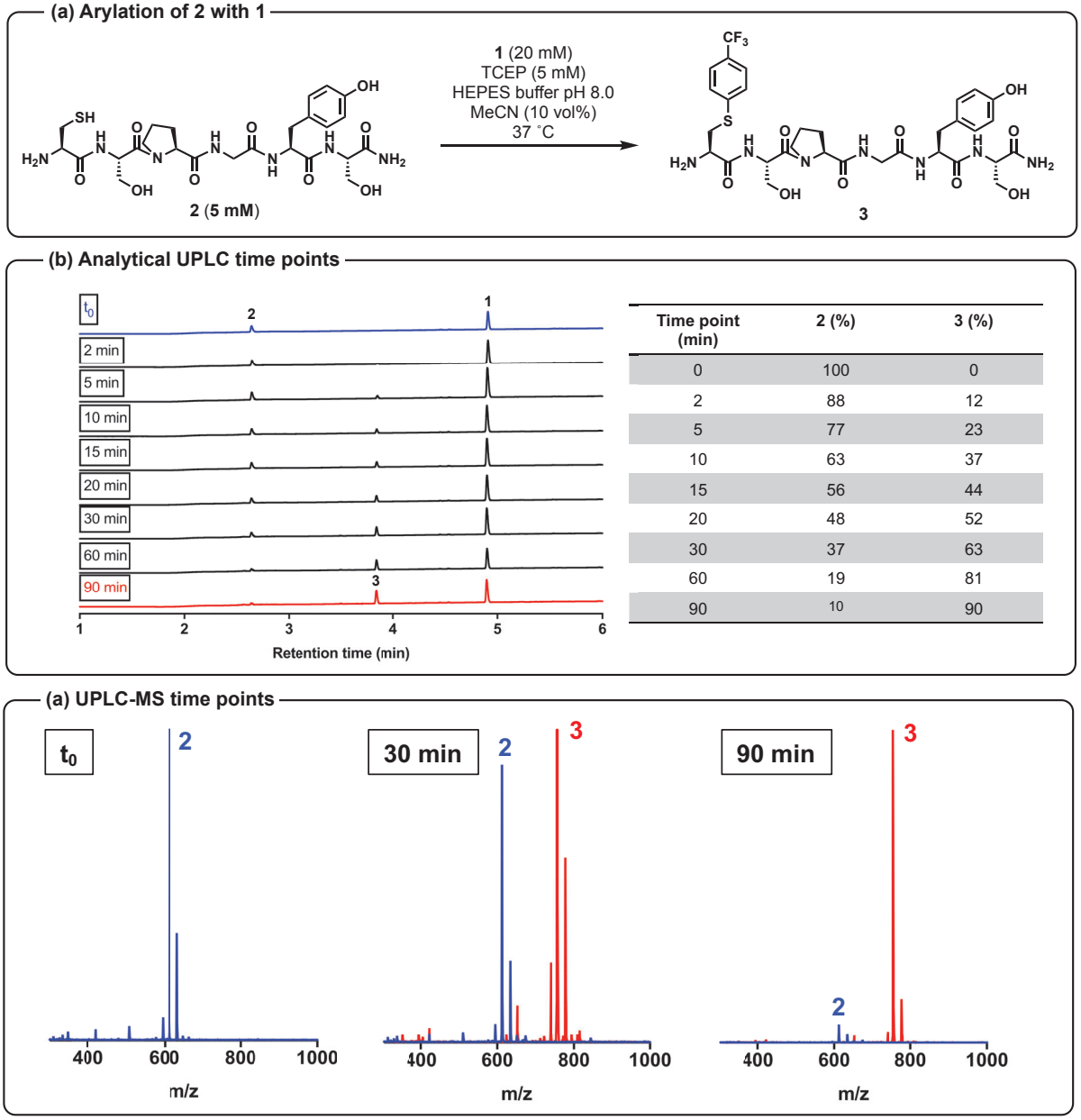


Buffer	Observations [t = 10 min]
$(NH_4)_2CO_3$ (0.05 M), EDTA (1 mM), pH 8.5	Product and oxidised product (+16 *m/z*)
Tris (0.1 M), EDTA (1 mM), pH 8.5	Product and oxidised product (+16 *m/z*)
Tris (0.1 M), EDTA (1 mM), Gn.HCl (6 M), pH 8.5)	Product and minor oxidised product (+16 *m/z*)
Phosphate (0.2 M), EDTA (1 mM), pH 8.0	Product and minor oxidised product (+16 *m/z*)
HEPES (0.2 M), EDTA (1 mM), pH 8.0	Product

Scheme S2: Arylation of peptide **2** with diaryliodonium salt **1** in various buffers; observations made by UPLC-MS analysis.

Monitoring of peptide and protein arylations

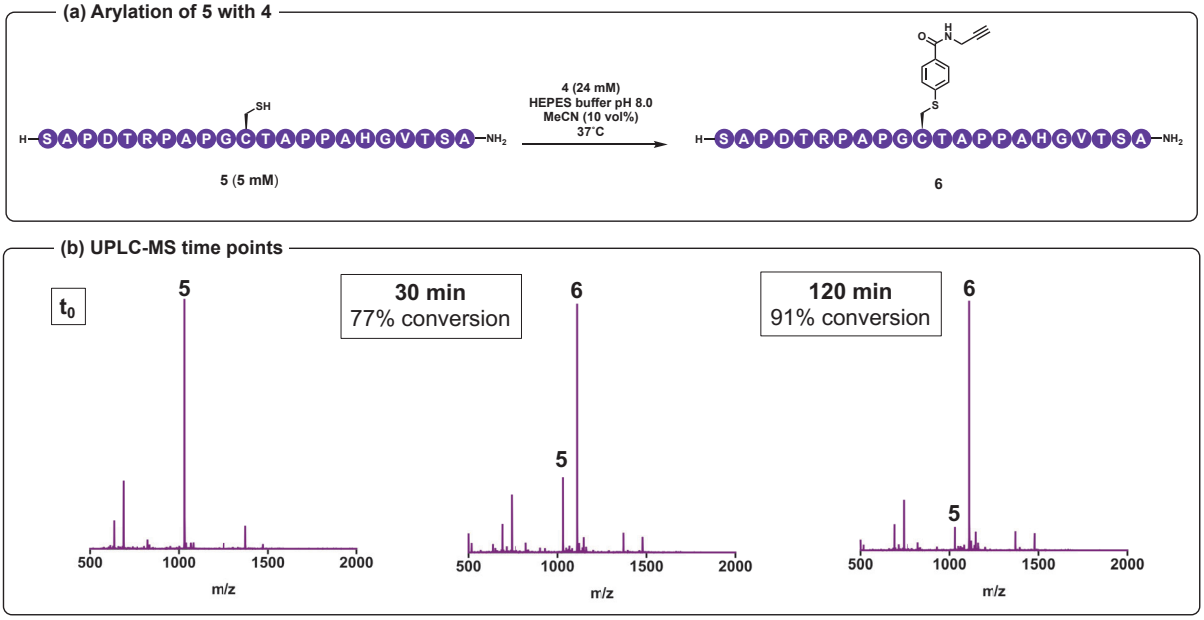
CSPGYS (2) arylation with diaryliodonium salt 1



Time point (min)	2 (%)	3 (%)
0	100	0
2	88	12
5	77	23
10	63	37
15	56	44
20	48	52
30	37	63
60	19	81
90	10	90

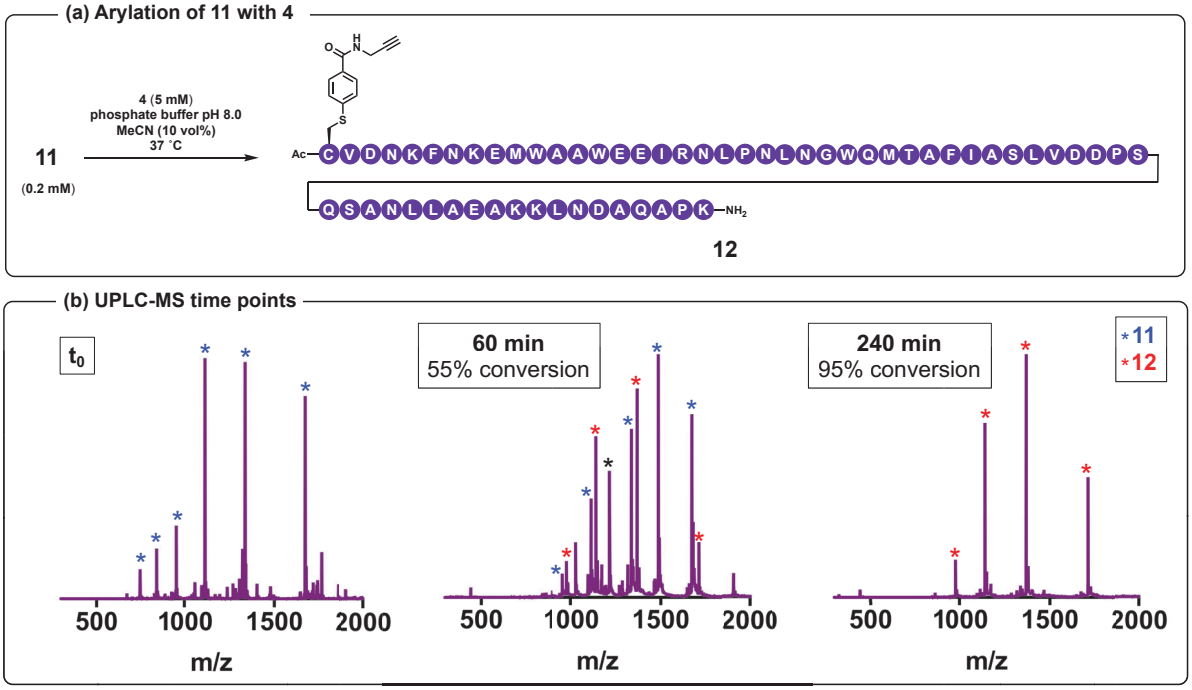
Scheme S3: (a) Arylation of peptide **2** with the diaryliodonium salt **1**; **(b)** Analytical UPLC chromatograms of **2** arylation: retention time (RT) = 3.5 min (0 to 60% MeCN in H_2O over 5 min, 0.1% TFA, λ = 214 nm, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column); conversions based on integration of UV absorption peaks corresponding to **2** and **3**; **(c) ESI-MS** spectra (ESI+) extracted from TIC chromatograms (0 to 60% MeCN in H_2O over 3 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column).

MUC1 VNTR (5) arylation with diaryliodonium salt 4



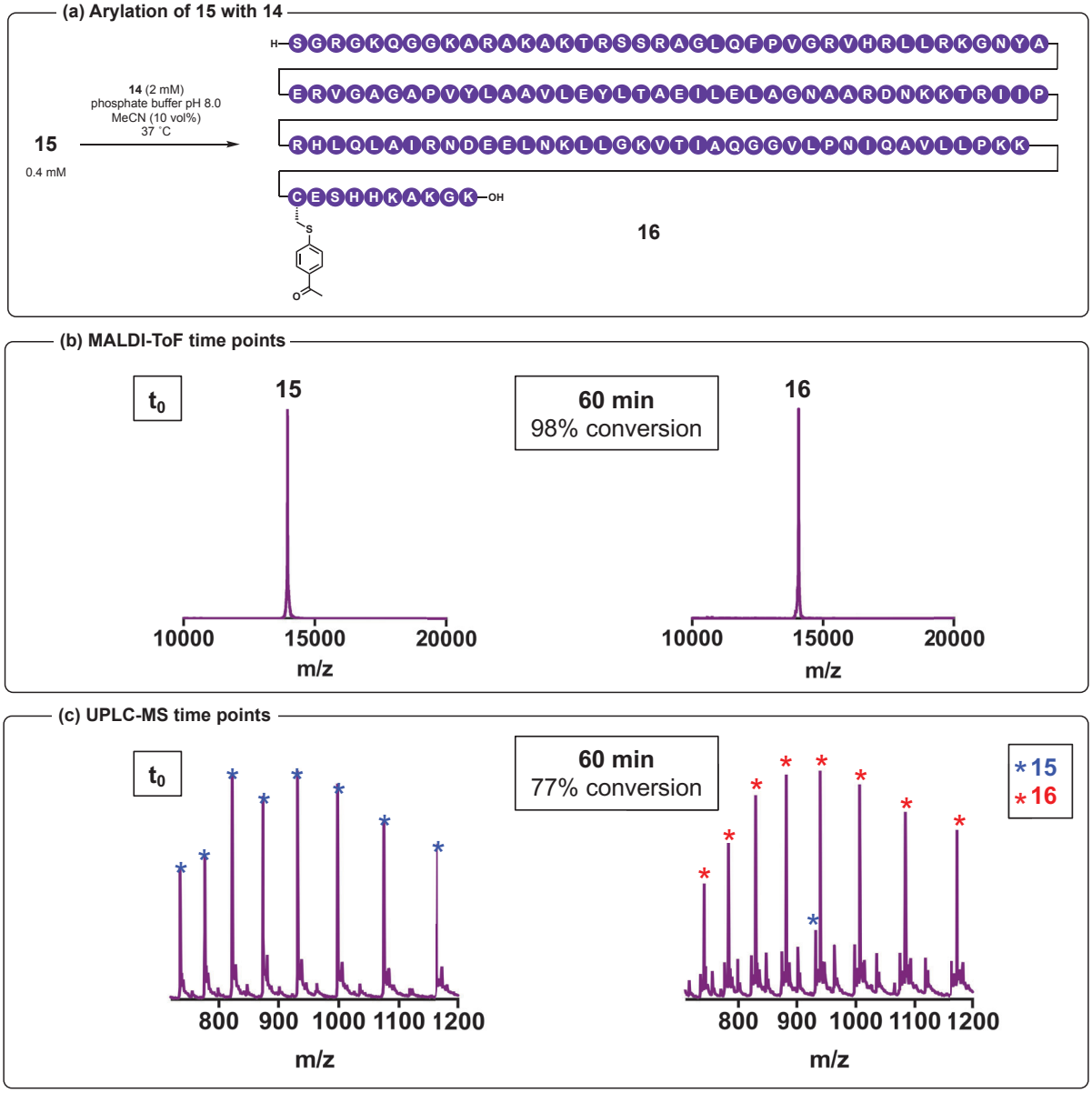
Scheme S4: (a) Arylation of peptide **5** with the diaryliodonium salt **4**; **(b) ESI-MS** spectra (ESI+) extracted from TIC chromatograms (0 to 20% MeCN in H_2O over 3 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column): Conversions calculated based on relative intensities of 1031 m/z $[M+2H]^{2+}$ (**5**) and 1109 m/z $[M+2H]^{2+}$ (**6**).

zEGFR (11) arylation with diaryliodonium salt 4



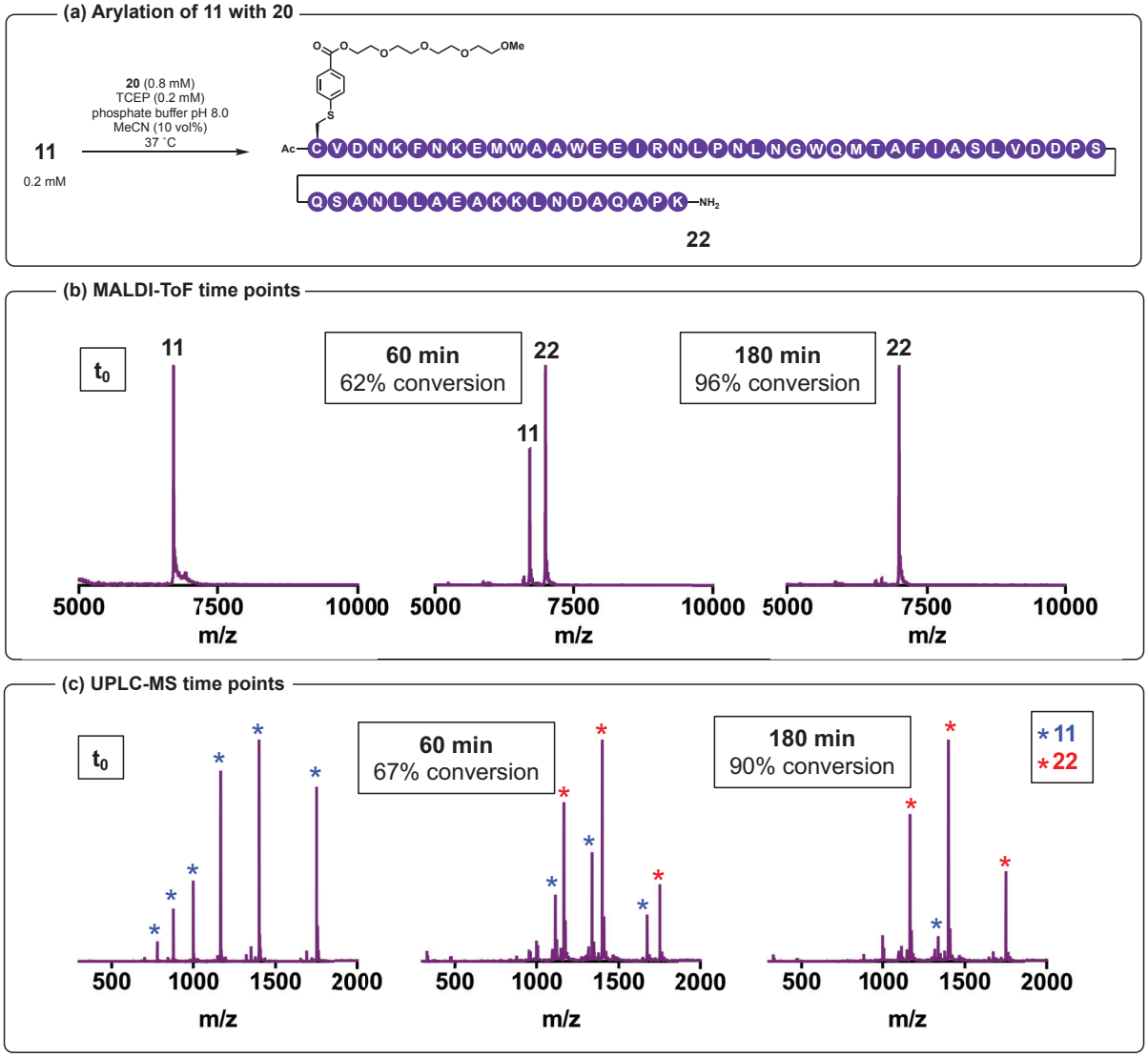
Scheme S5: **(a)** Arylation of protein **11** with the diaryliodonium salt **4**; **(c) ESI-MS** spectra (ESI+) extracted from TIC chromatograms (0 to 60% MeCN in H_2O over 5 min, 0.1% formic acid, Waters Acquity ® BEH, C8, 300 Å, 2.1x50 mm column): Conversions calculated based on relative intensities of 1339 *m/z* $[M+5H]^{5+}$ (**11**) and 1370 *m/z* $[M+5H]^{5+}$ (**12**); * impurity on UPLC-MS.

H2A (15) arylation with diaryliodonium salt 14



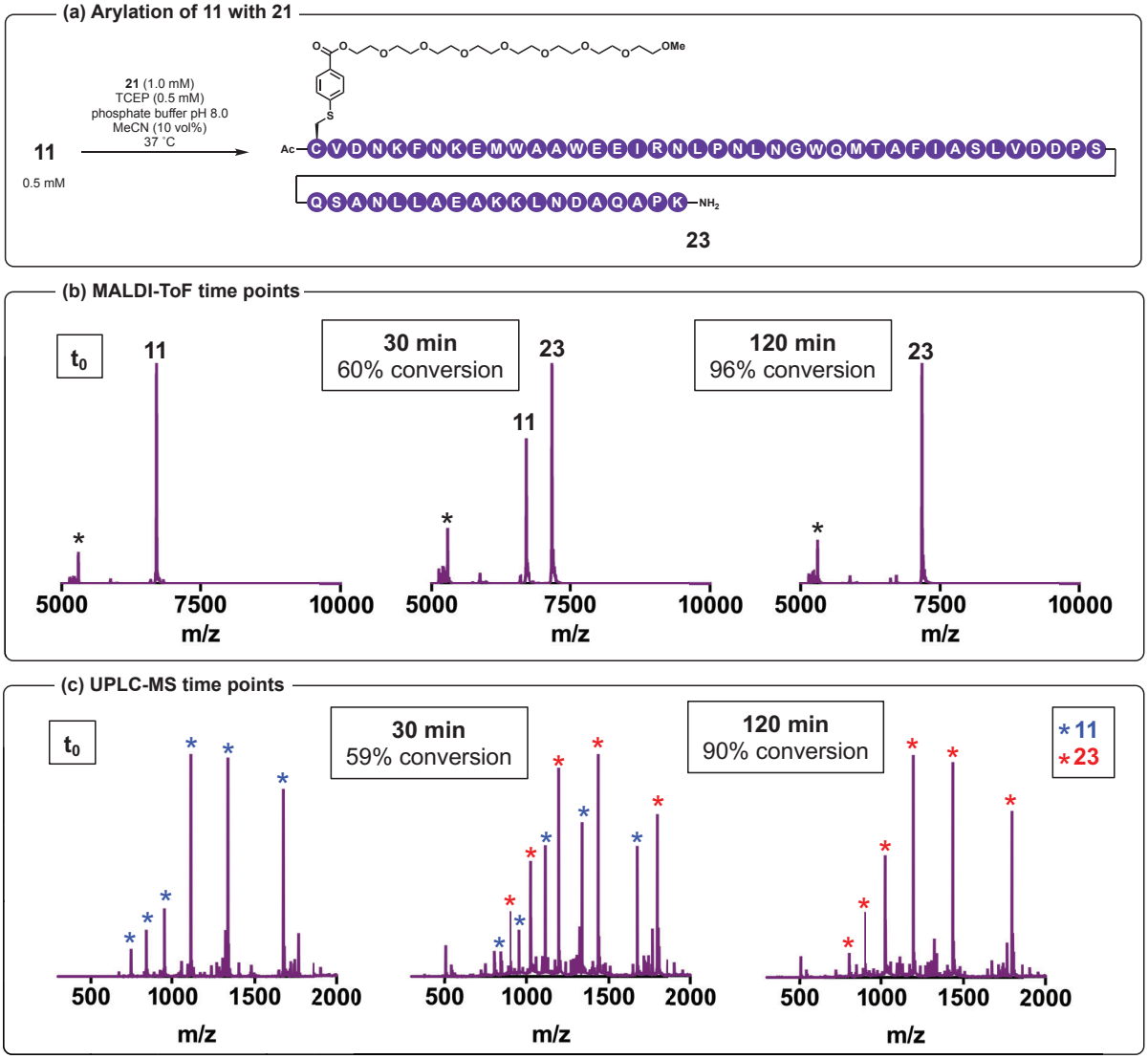
Scheme S6. Arylation of protein **15** with the diaryliodonium salt **14**; **(b) MALDI-ToF** (LP) of arylation time points: conversions calculated based on relative intensities of 13951 m/z (**15**) and 14073 m/z (**22**); **(c) ESI-MS** spectra (ESI+) extracted from TIC chromatograms (0 to 60% MeCN in H_2O over 5 min, 0.1% formic acid, Waters Acquity ® BEH, C8, 300 Å, 2.1x50 mm column): Conversions calculated based on relative intensities of 932 *m/z* $[M+15H]^{15+}$ (**15**) and 940 *m/z* $[M+15H]^{15+}$ (**24**); measured 300-2000 *m/z*, 720-1200 *m/z* presented for clarity.

zEGFR (11) arylation with diaryliodonium salt 20



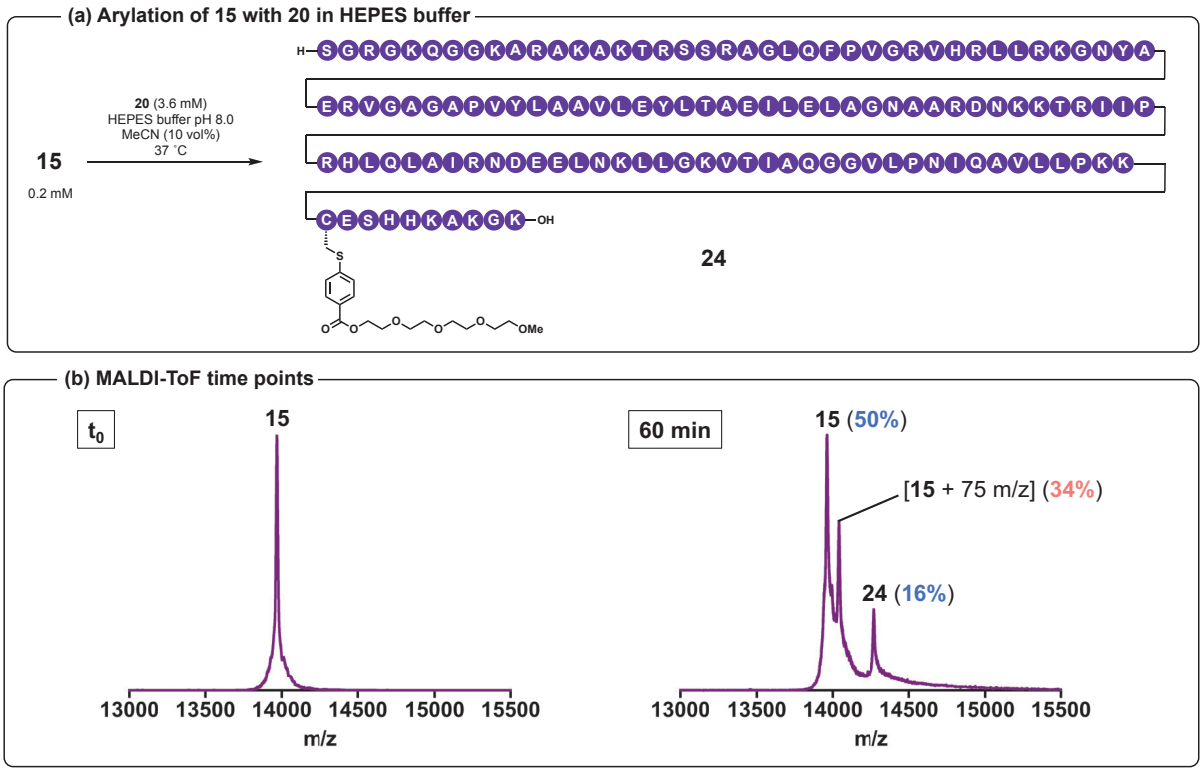
Scheme S7: **(a)** Arylation of protein **11** with the diaryliodonium salt **20**; **(b) MALDI-ToF** (LP) of arylation time points: conversions calculated based on relative intensities of 6690 m/z (**11**) and 6998 m/z (**22**); **(c) ESI-MS** spectra (ESI+) extracted from TIC chromatograms (0 to 60% MeCN in H_2O over 5 min, 0.1% formic acid, Waters Acquity ® BEH, C8, 300 Å, 2.1x50 mm column): Conversions calculated based on relative intensities of 1339 *m/z* $[M+5H]^{5+}$ (**11**) and 1400 *m/z* $[M+5H]^{5+}$ (**22**).

zEGFR (11) arylation with diaryliodonium salt 21

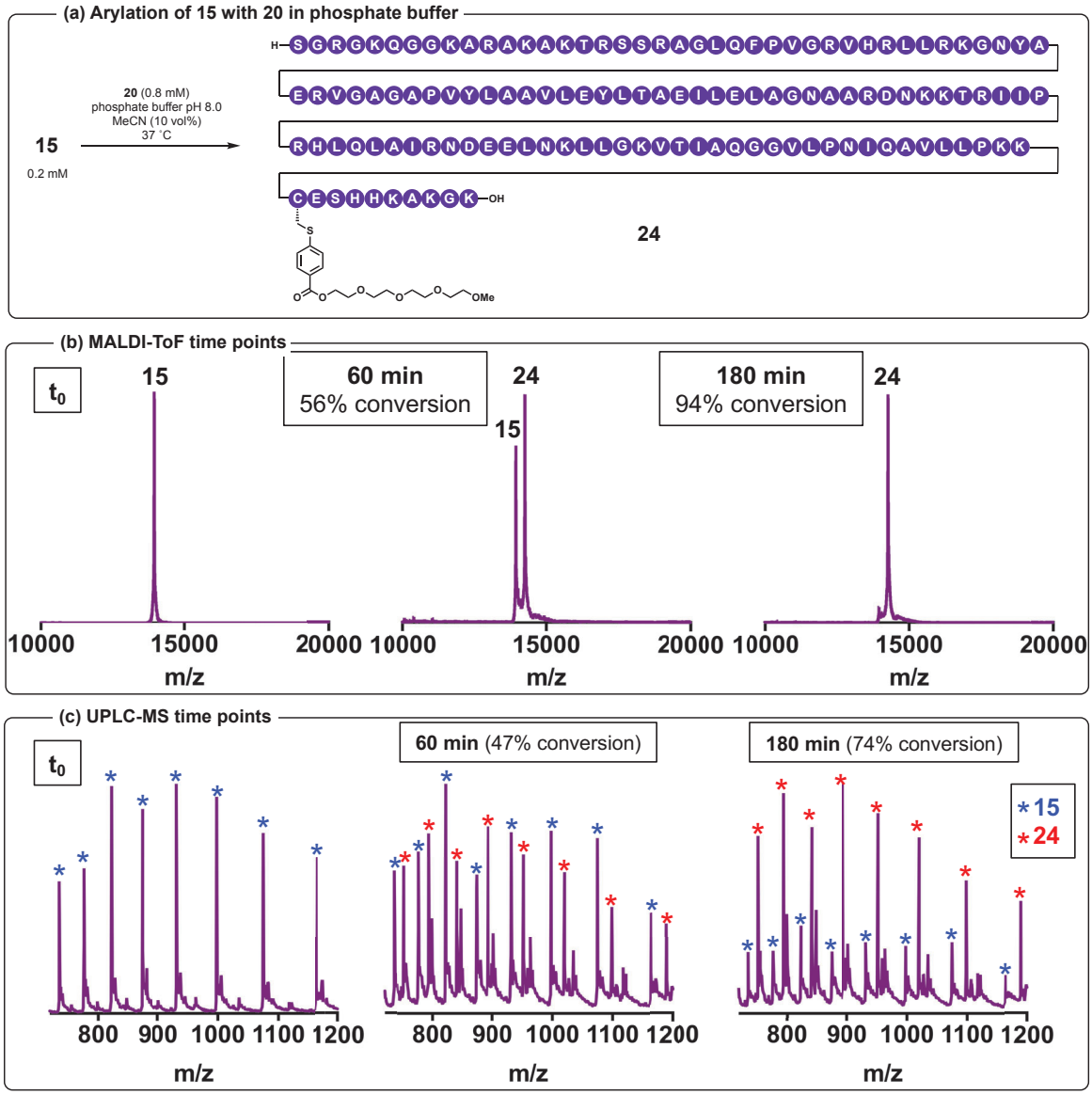


Scheme S8: **(a)** Arylation of protein **11** with the diaryliodonium salt **23**; **(b) MALDI-ToF** (LP) of arylation time points: conversions calculated based on relative intensities of 6690 m/z (**11**) and 7174 m/z (**23**); * truncation from SPPS of **11**; **(c) ESI-MS** spectra (ESI+) extracted from TIC chromatograms (0 to 60% MeCN in H_2O over 5 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column): Conversions calculated based on relative intensities of 1339 *m/z* $[M+5H]^{5+}$ (**11**) and 1436 *m/z* $[M+5H]^{5+}$ (**23**).

H2A T120C (15) arylation with diaryliodonium salt 20

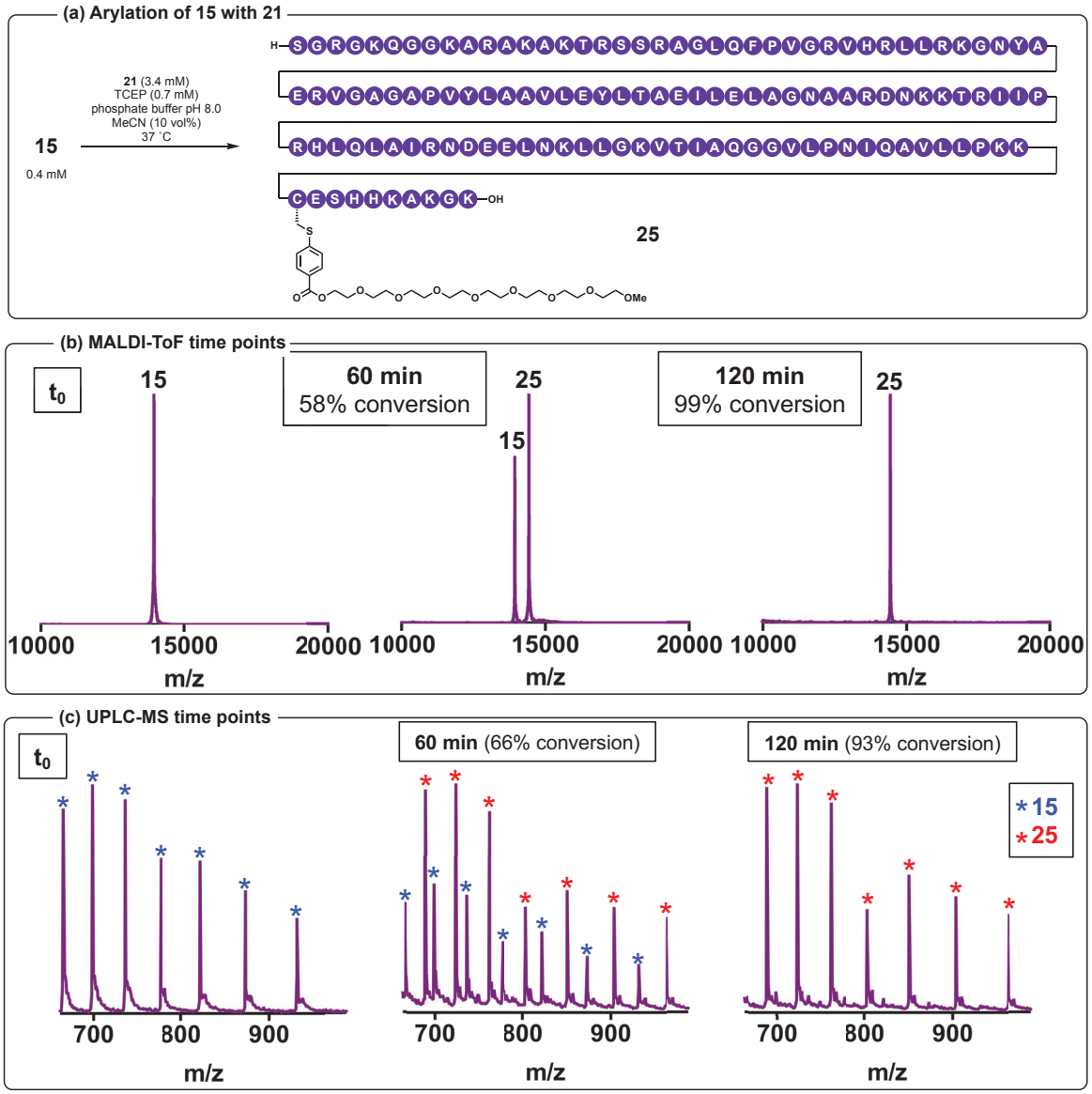


Scheme S9. (a) (a) Arylation of protein **15** with the diaryliodonium salt **20** in HEPES buffer; **(b) MALDI-ToF** (LP) of reaction mixture showing undesired adduct (+ 75 m/z) formation: conversions calculated based on relative intensities of 13951 m/z (**15**), 14026 m/z (undesired adduct), and 14268 m/z (**24**).



Scheme S10: **(a)** Arylation of protein **15** with the diaryliodonium salt **20**; **(b) MALDI-ToF** (LP) of arylation time points: conversions calculated based on relative intensities of 13951 m/z (**15**) and 14268 m/z (**24**); **(c) ESI-MS** spectra (ESI+) extracted from TIC chromatograms (0 to 60% MeCN in H_2O over 3 min, 0.1% formic acid, Waters Acquity ® BEH, C8, 300 Å, 2.1x50 mm column): Conversions calculated based on relative intensities of 932 *m/z* $[M+15H]^{15+}$ (**15**) and 952 *m/z* $[M+15H]^{15+}$ (**24**); measured 300-2000 *m/z*, 720-1200 *m/z* presented for clarity.

H2A T120C (15) arylation with diaryliodonium salt 21



Scheme S11: **(a)** Arylation of protein **15** with the diaryliodonium salt **15**; **(b) MALDI-ToF** (LP) of arylation time points: conversions calculated based on relative intensities of 13951 m/z (**15**) and 14437 m/z (**25**); **(c) ESI-MS** spectra (ESI+) extracted from TIC chromatograms (0 to 60% MeCN in H_2O over 5 min, 0.1% formic acid, Waters Acquity ® BEH, C18, 130 Å, 2.1x50 mm column): Conversions calculated based on relative intensities of 932 *m/z* $[M+15H]^{15+}$ (**15**) and 964 *m/z* $[M+15H]^{15+}$ (**25**); measured 300-2000 *m/z*, 662-990 *m/z* presented for clarity.

Stability studies

Chemical and plasma stability of MUC1-alkyne (6)

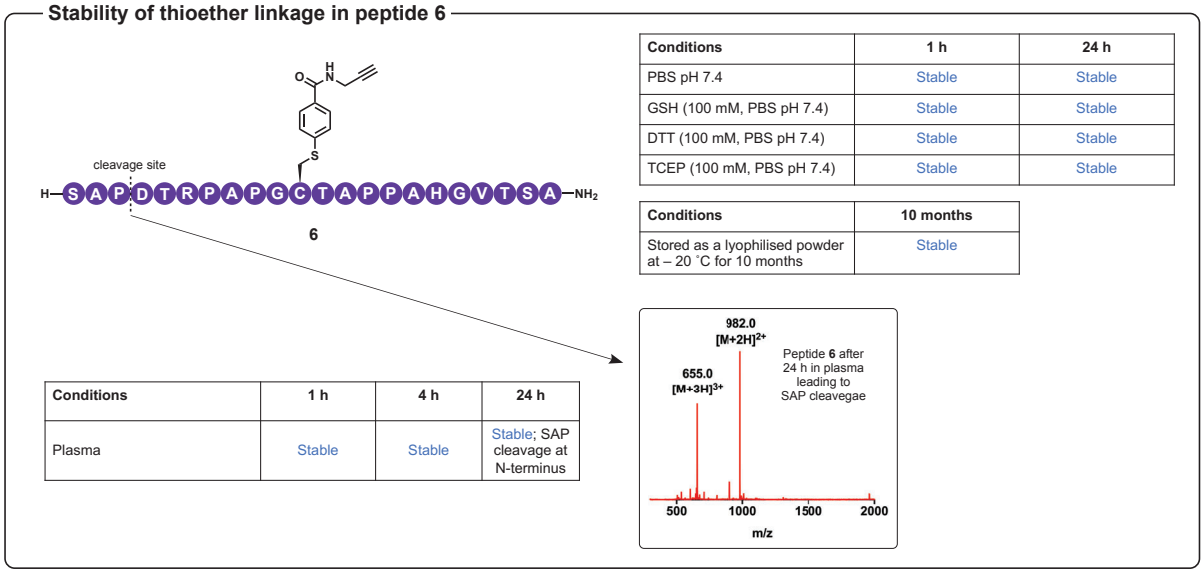


Figure S22. Stability of thioether linkage in peptide **6** under various conditions; observations made by UPLC-MS analysis. Phosphate buffered saline (PBS).

Circular dichroism (CD) spectroscopy

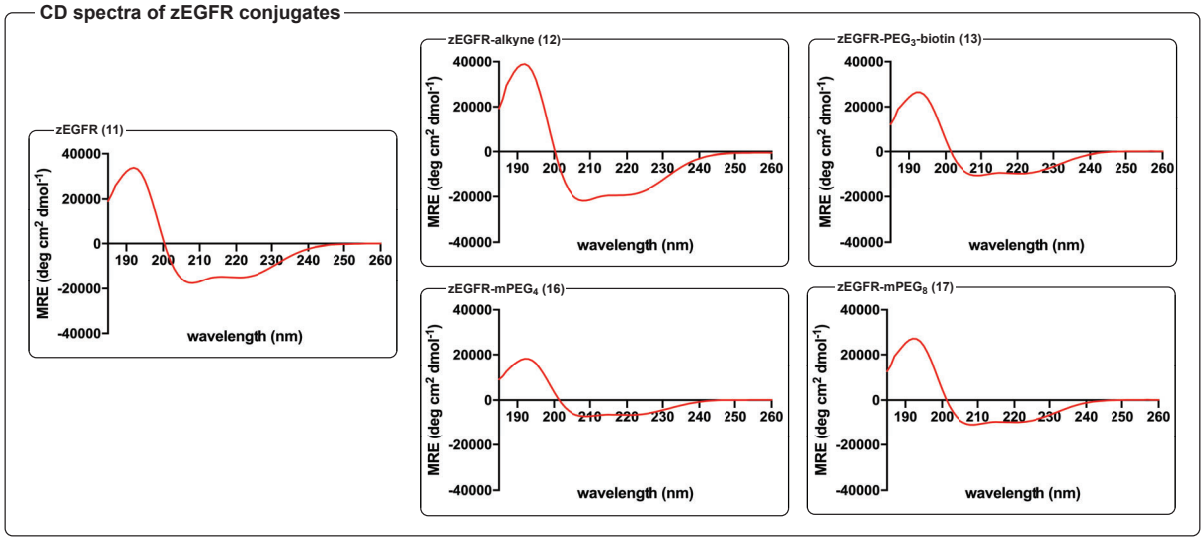


Figure S23: CD spectra of zEGFR conjugates **11**, **12**, **13**, **22**, and **23** measured in H_2O. Spectra for all conjugates are characteristic for a folded alpha-helical secondary structure expected for zEGFR.

LC-MS/MS of protein conjugates

zEGFR-alkyne (12)

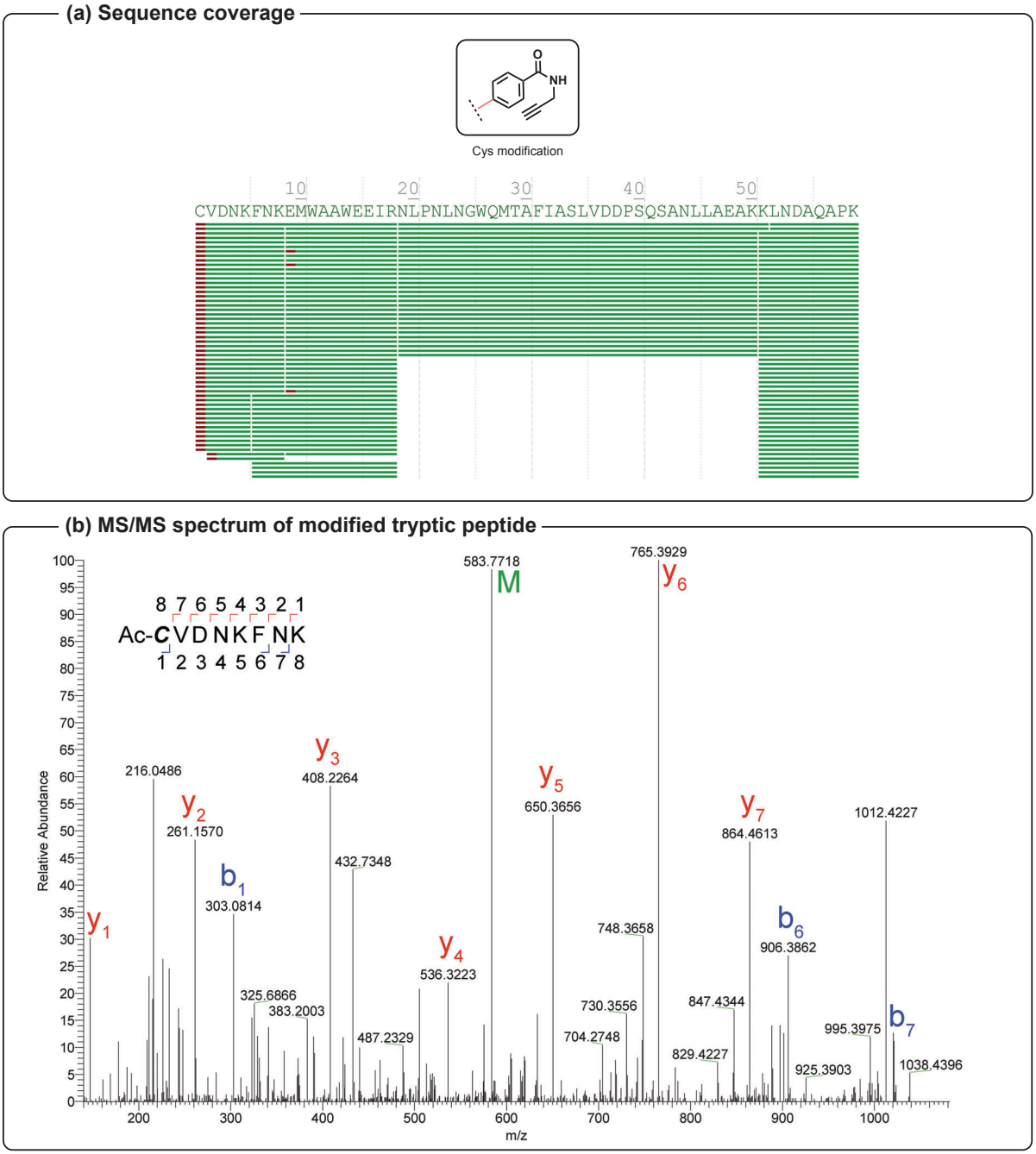


Figure S24. MS/MS analysis of protein conjugate **12** after tryptic digestion. **(a)** Sequence coverage; **(b)** MS/MS spectrum of modified tryptic peptide. note: a separate minor peak corresponding to a diastereomer of the peptide Ac-CVDNKFNK-OH was observed in the zEGFR (**11**) precursor due to minor epimerisation during SPPS.

H2A-ketone (16)

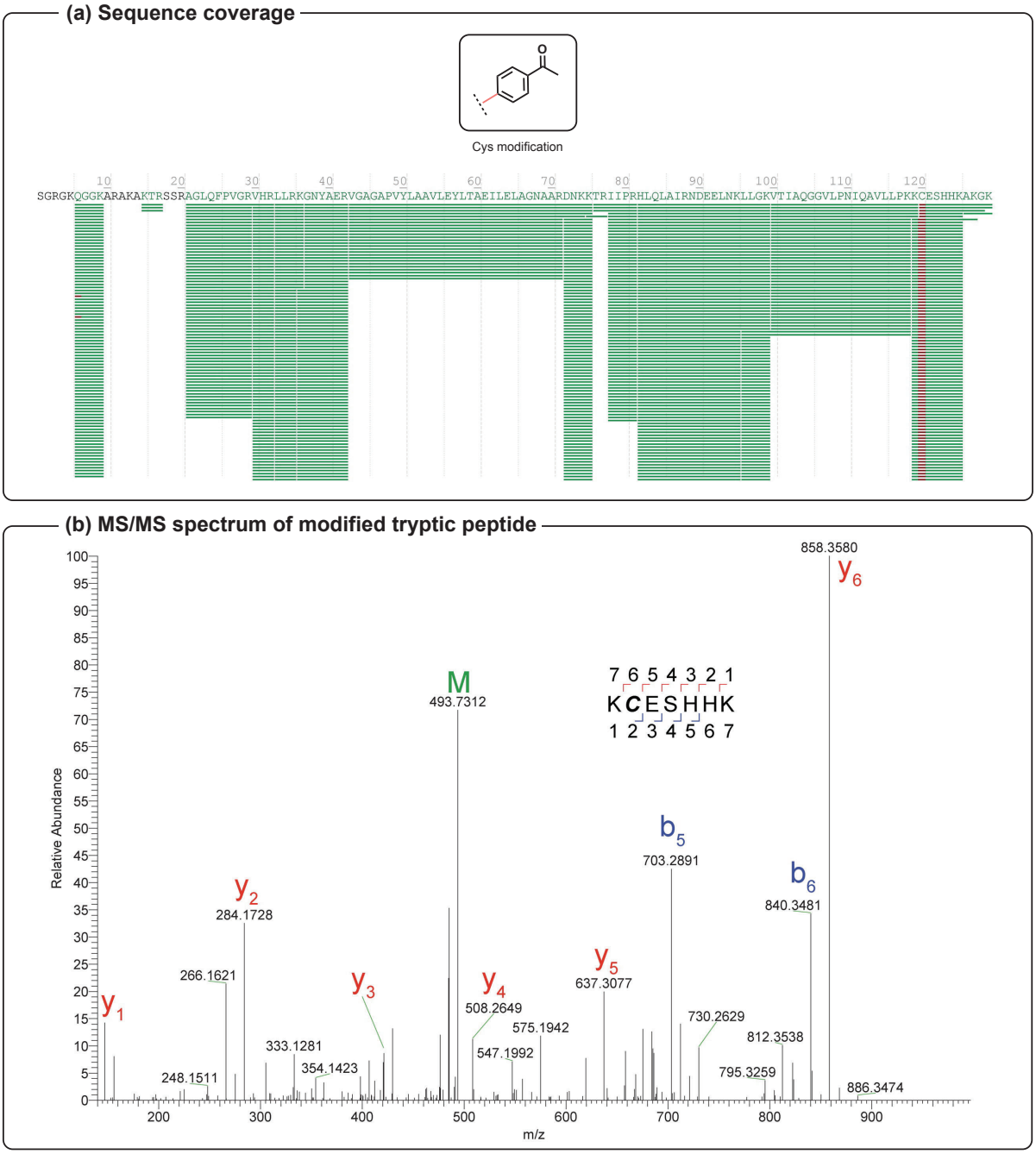


Figure S25. MS/MS analysis of protein conjugate **16** after tryptic digestion. **(a)** Sequence coverage; **(b)** MS/MS spectrum of modified tryptic peptide.

H2A-PEG$_3$-biotin (17)

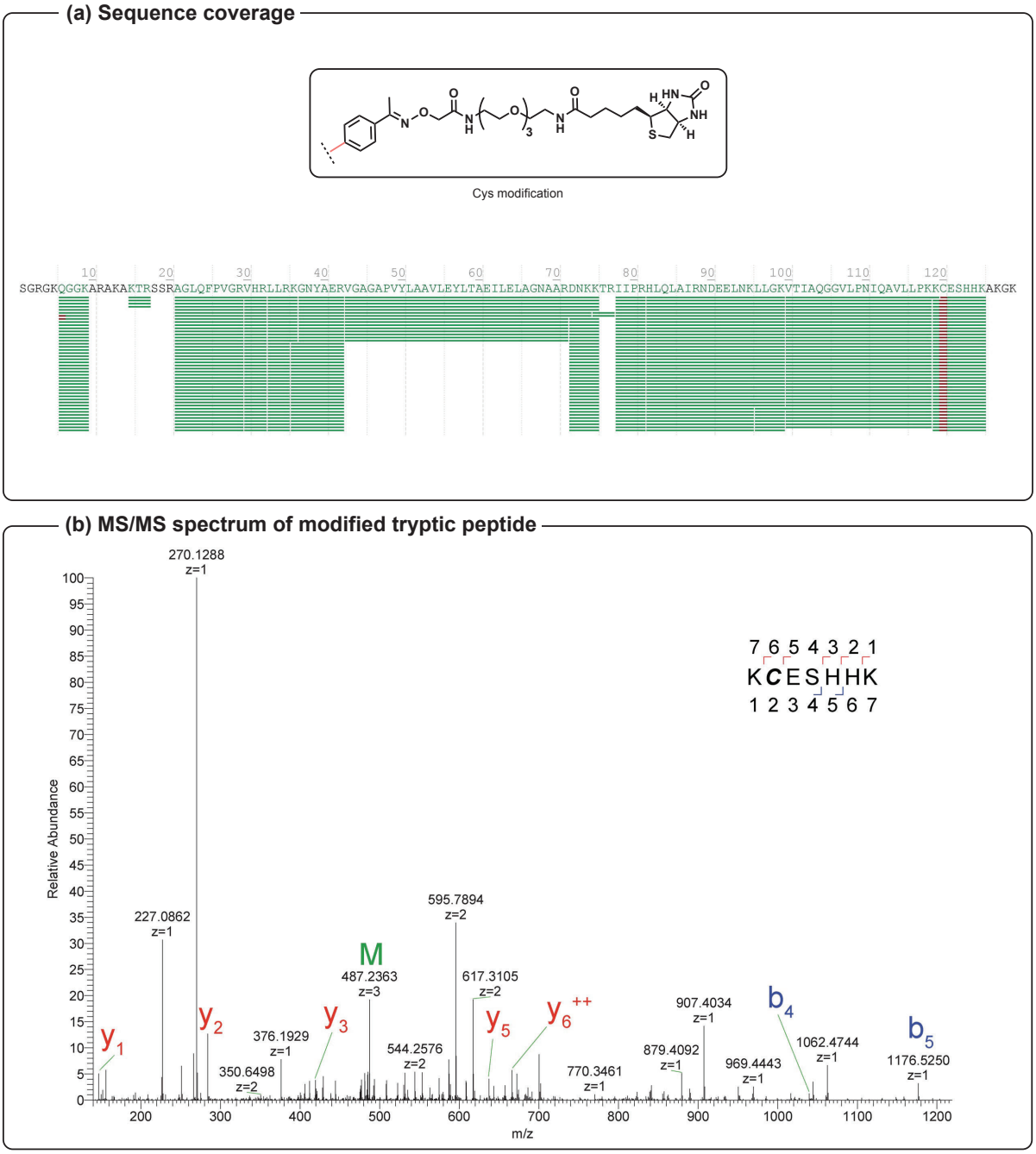


Figure S26. MS/MS analysis of protein conjugate **17** after tryptic digestion. **(a)** Sequence coverage; **(b)** MS/MS spectrum of modified tryptic peptide.

H2A-PEG$_3$-penetratin (19)

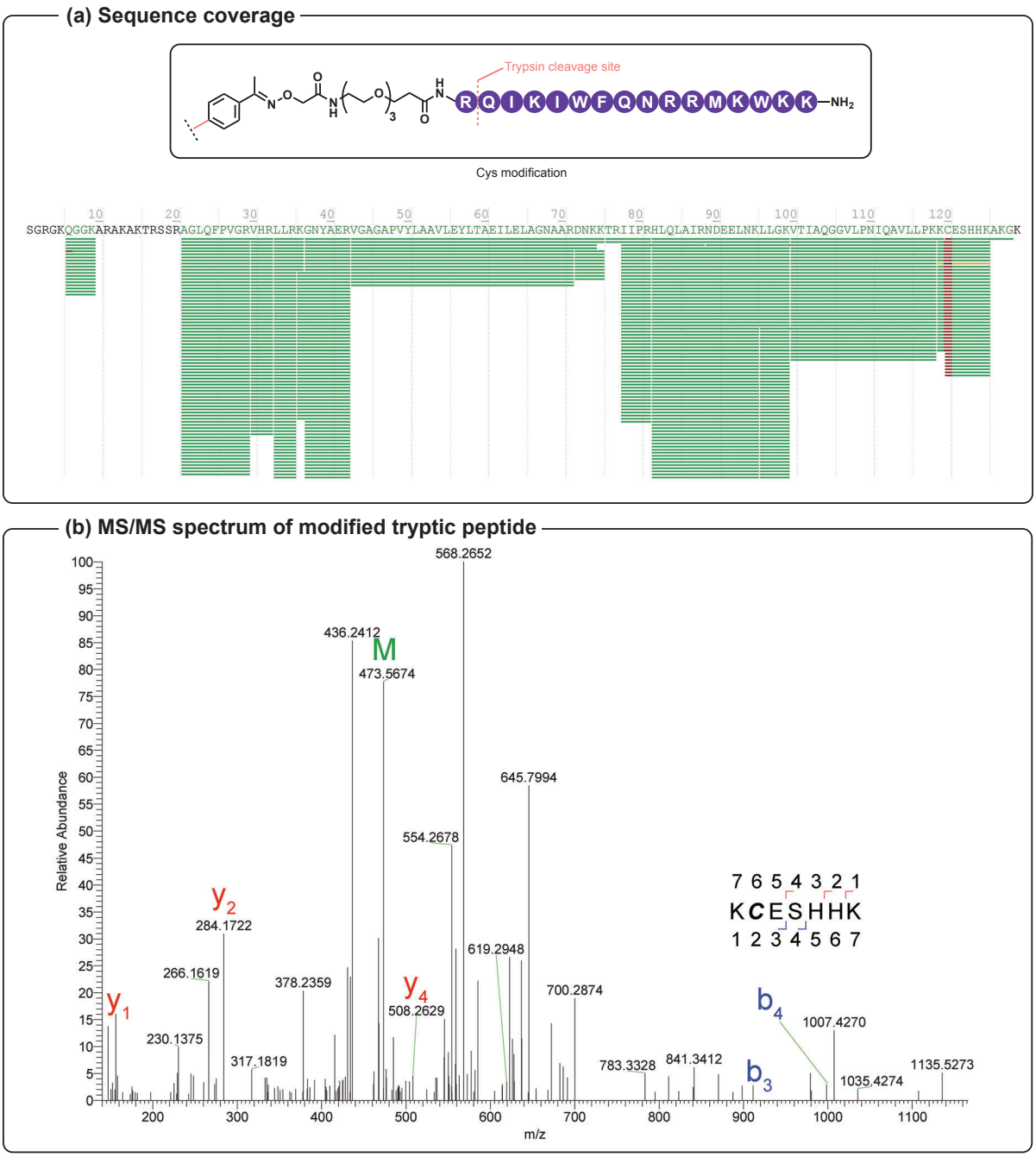


Figure S27. MS/MS analysis of protein conjugate **19** after tryptic digestion. **(a)** Sequence coverage; **(b)** MS/MS spectrum of modified tryptic peptide wherein the Cys modification was also cleaved in the tryptic digest at its RQ junction.

zEGFR-mPEG$_4$ (22)

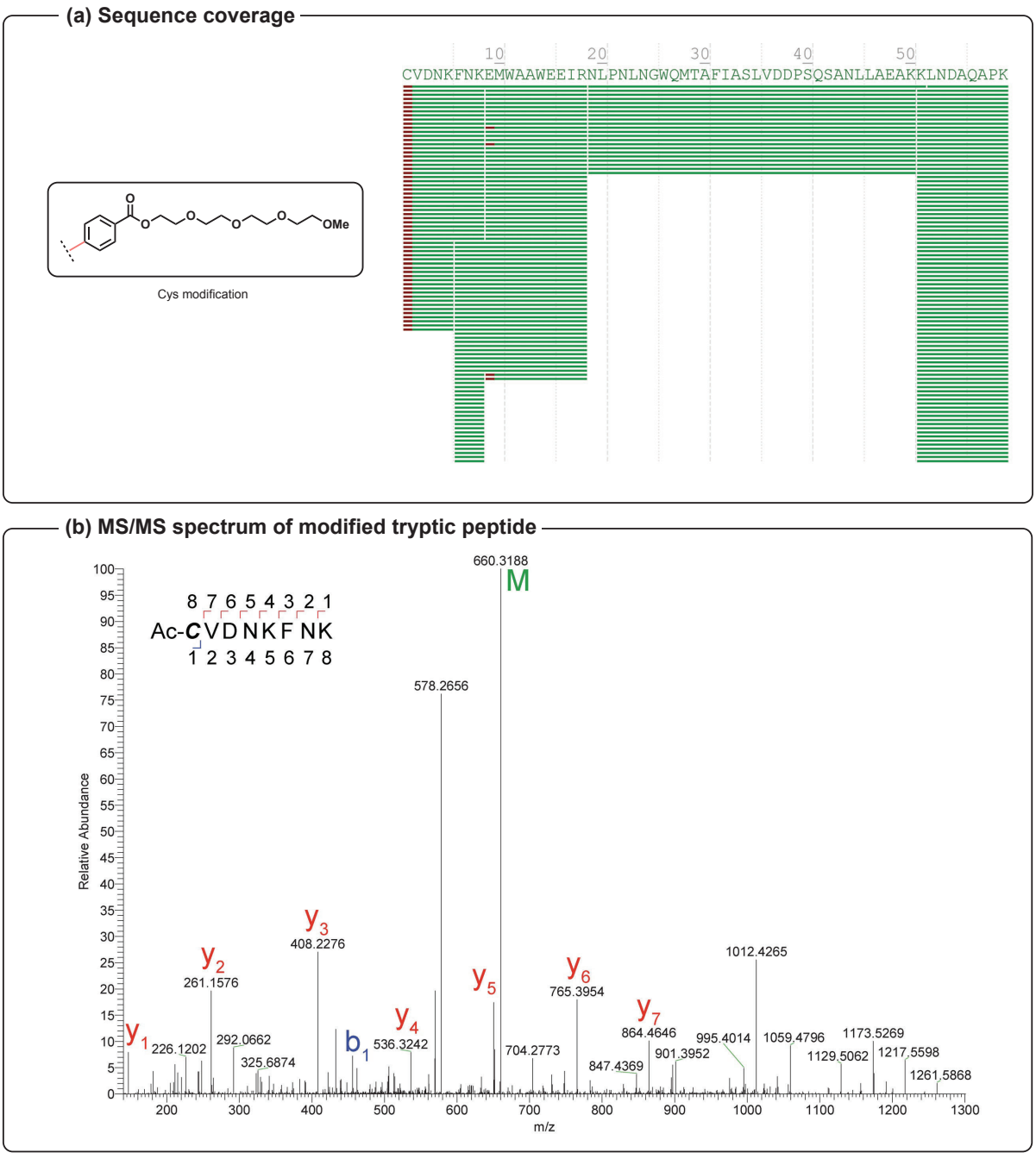


Figure S28. MS/MS analysis of protein conjugate **22** after tryptic digestion. **(a)** Sequence coverage; **(b)** MS/MS spectrum of modified tryptic peptide.

zEGFR-mPEG$_8$ (23)

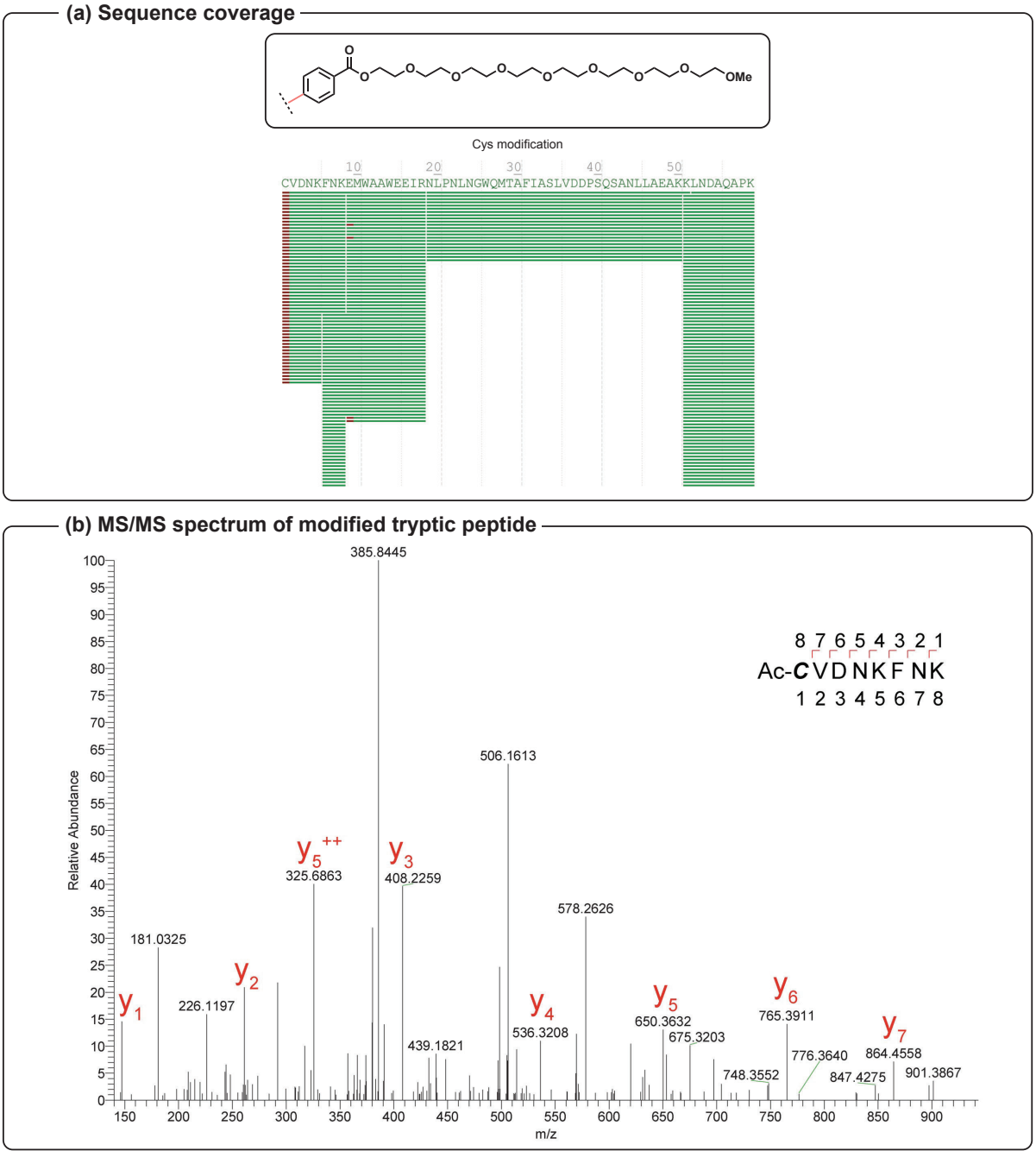


Figure S29. MS/MS analysis of protein conjugate **23** after tryptic digestion. **(a)** Sequence coverage; **(b)** MS/MS spectrum of modified tryptic peptide.

H2A-mPEG$_4$ (24)

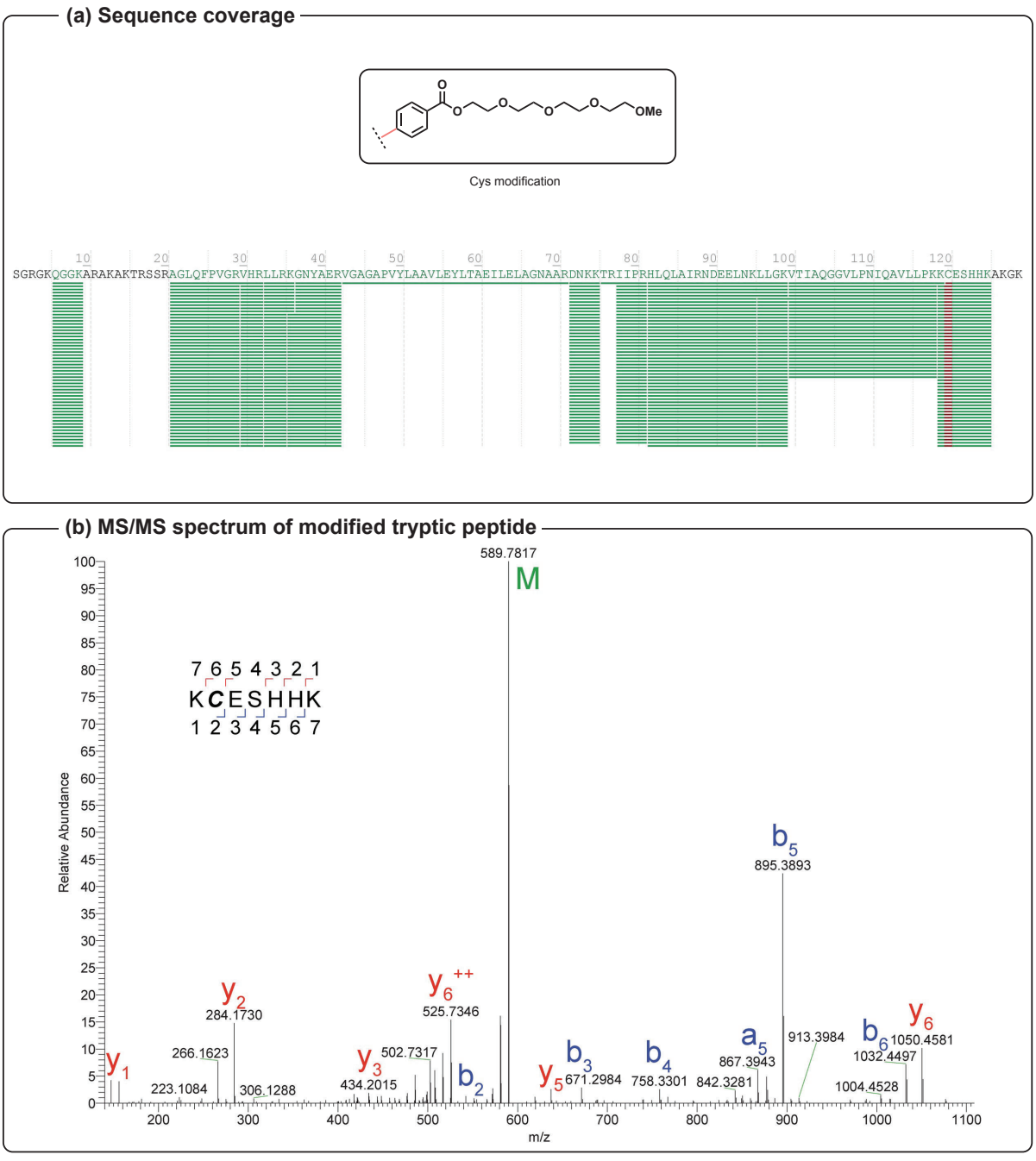


Figure S30. MS/MS analysis of protein conjugate **24** after tryptic digestion. **(a)** Sequence coverage; **(b)** MS/MS spectrum of modified tryptic peptide.

H2A-mPEG$_8$ (25)

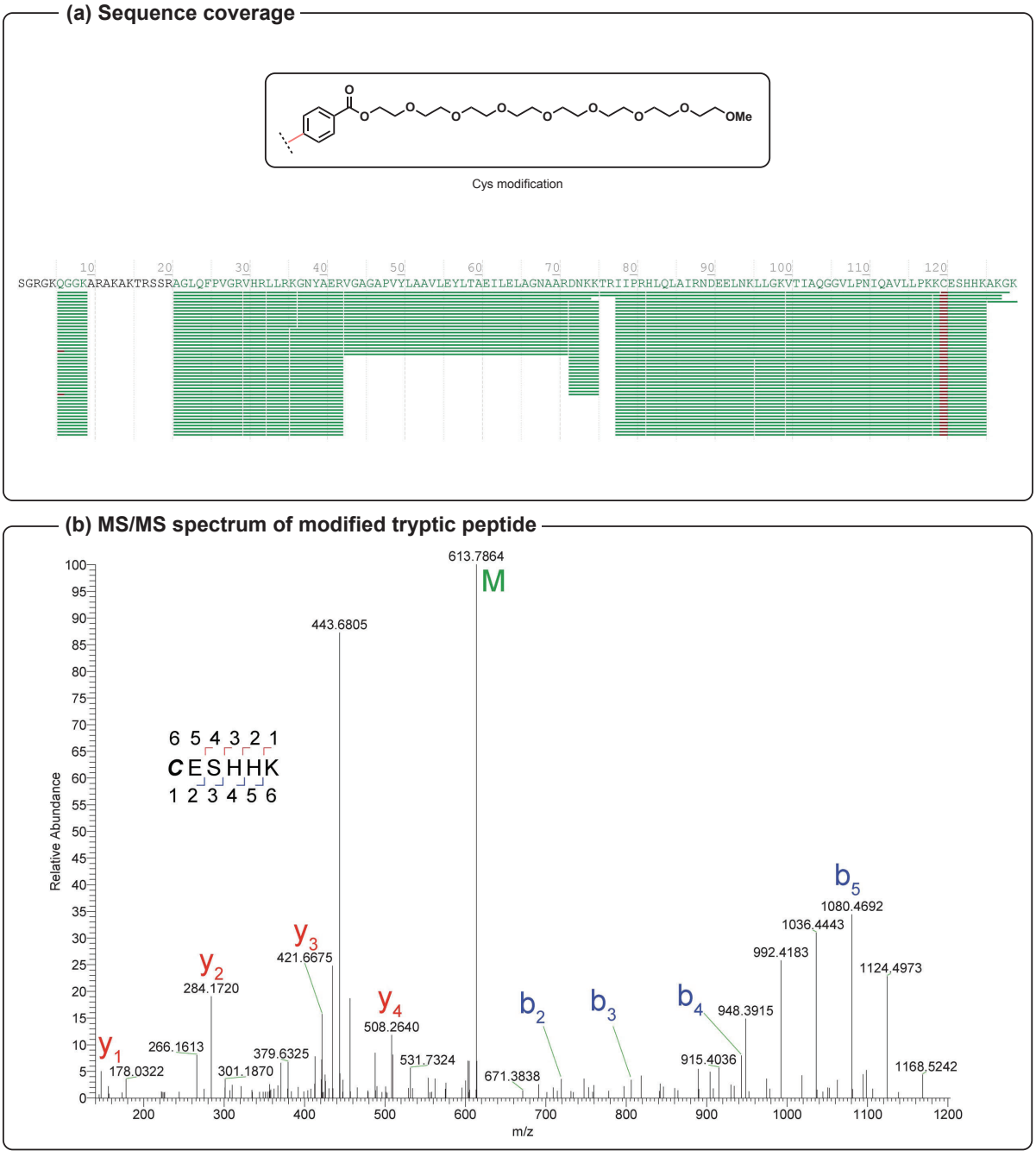


Figure S31. MS/MS analysis of protein conjugate **25** after tryptic digestion. **(a)** Sequence coverage; **(b)** MS/MS spectrum of modified tryptic peptide.

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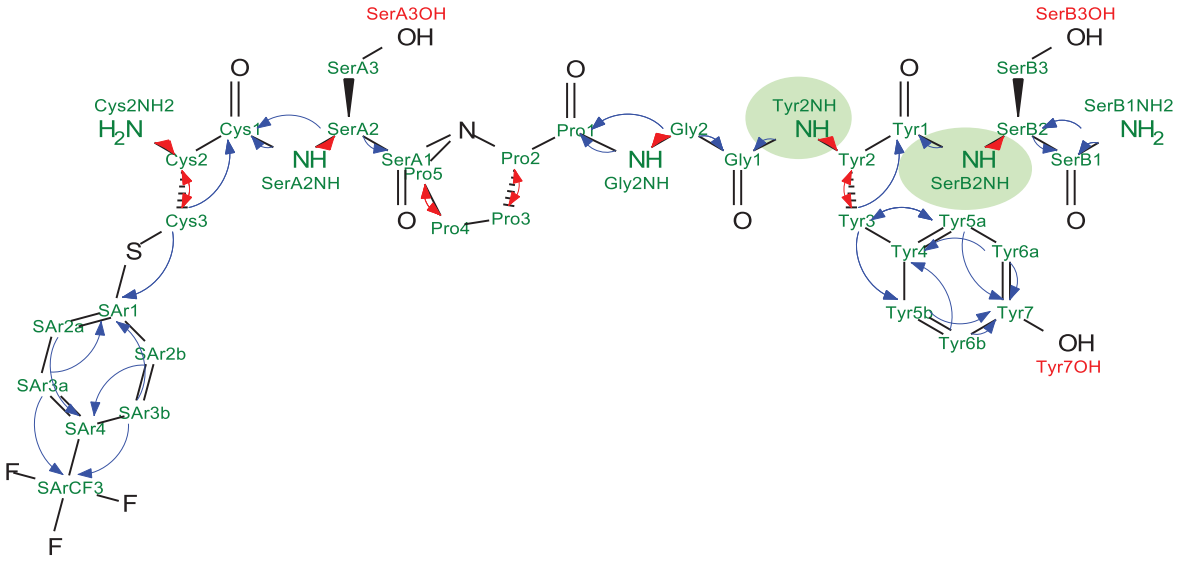
NMR Spectra

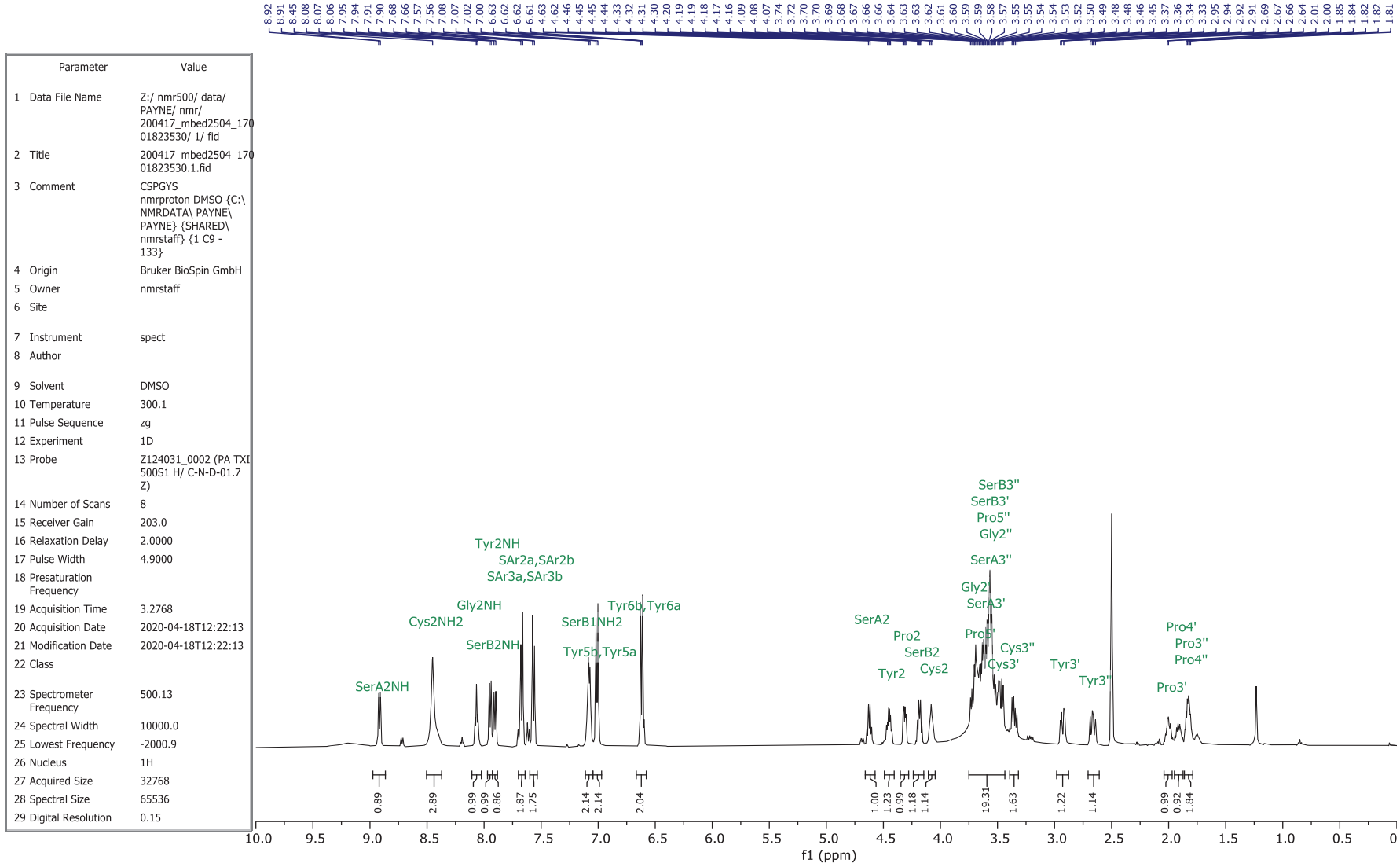
Figure S32: C(*S*-(4-(trifluoromethyl)phenyl))SPGYS-NH_2 (**3**) NMR correlations; HSQC in red arrows; HMBC in blue arrows.



No	δ_H	δ_C	HSQC-EDITED	HMBC	COSY
Cys1	-	166.6	-	3.35(Cys3"), 3.47(Cys3'), 4.62(SerA2), 8.92(SerA2NH)	-
Cys2	4.08	50.5	50.5(Cys2)	-	3.35(Cys3"), 3.47(Cys3'), 8.45(Cys2NH2)
Cys2NH2	8.45	-	-	-	4.08(Cys2)
Cys3'	3.47	32.4	32.4(Cys3)	140.4(SAr1),166.6(Cys1)	4.08(Cys2)
Cys3"	3.35	32.4	32.4(Cys3)	140.4(SAr1),166.6(Cys1)	4.08(Cys2)
Gly1	-	168.5	-	3.54(Gly2"), 3.71(Gly2'), 7.91(Tyr2NH)	-
Gly2'	3.71	41.5	41.5(Gly2)	168.5(Gly1),171.8(Pro1)	8.07(Gly2NH)
Gly2"	3.54	41.5	41.5(Gly2)	168.5(Gly1),171.8(Pro1)	8.07(Gly2NH)
Gly2NH	8.07	-	-	171.8(Pro1)	3.54(Gly2"), 3.71(Gly2')
Pro1	-	171.8	-	3.54(Gly2"), 3.71(Gly2'), 8.07(Gly2NH)	-
Pro2	4.31	59.6	59.6(Pro2)	-	1.82(Pro3"), 1.99(Pro3')
Pro3'	1.99	28.8	28.8(Pro3)	-	4.31(Pro2)
Pro3"	1.82	28.8	28.8(Pro3)	-	4.31(Pro2)
Pro4'	1.91	23.9	23.9(Pro4)	-	3.56(Pro5"), 3.67(Pro5')
Pro4"	1.83	23.9	23.9(Pro4)	-	3.56(Pro5"), 3.67(Pro5')
Pro5'	3.67	46.6	46.6(Pro5)	-	1.83(Pro4"), 1.91(Pro4')
Pro5"	3.56	46.6	46.6(Pro5)	-	1.83(Pro4"), 1.91(Pro4')
SAr1	-	140.4	-	3.35(Cys3"), 3.47(Cys3'), 7.67(SAr3a), 7.67(SAr3b)	-
SAr2a	7.57	127.5	127.5(SAr2a)	126.4(SAr4)	-
SAr2b	7.57	127.5	127.5(SAr2b)	126.4(SAr4)	-
SAr3a	7.67	125.3	125.3(SAr3a)	124.0(SArCF3),140.4(SAr1)	-
SAr3b	7.67	125.3	125.3(SAr3b)	124.0(SArCF3),140.4(SAr1)	-
SAr4	-	126.4	-	7.57(SAr2a), 7.57(SAr2b)	-
SArCF3	-	124	-	7.67(SAr3a), 7.67(SAr3b)	-
SerA1	-	168.3	-	4.62(SerA2)	-
SerA2	4.62	53.1	53.1(SerA2)	166.6(Cys1), 168.3(SerA1)	8.92(SerA2NH)
SerA2NH	8.92	-	-	166.6(Cys1)	4.62(SerA2)
SerA3'	3.62	61.3	61.3(SerA3)	-	-
SerA3"	3.58	61.3	61.3(SerA3)	-	-
SerB1	-	171.6	-	4.18(SerB2),7.08(SerB1NH2)	-
SerB1NH2	7.08	-	-	54.7(SerB2), 171.6(SerB1)	-
SerB2	4.18	54.7	54.7(SerB2)	171.6(SerB1)	7.95(SerB2NH)
SerB2NH	7.95	-	-	171.0(Tyr1)	4.18(SerB2)
SerB3'	3.59	61.6	61.6(SerB3)	-	-
SerB3"	3.51	61.6	61.6(SerB3)	-	-
Tyr1	-	171	-	2.66(Tyr3"), 2.93(Tyr3'), 7.95(SerB2NH)	-
Tyr2	4.45	54	54.0(Tyr2)	-	2.66(Tyr3"), 2.93(Tyr3'),7.91(Tyr2NH)
Tyr2NH	7.91	-	-	168.5(Gly1)	4.45(Tyr2)
Tyr3'	2.93	36.3	36.3(Tyr3)	129.8(Tyr5b), 129.8(Tyr5a),171.0(Tyr1)	4.45(Tyr2)
Tyr3"	2.66	36.3	36.3(Tyr3)	129.8(Tyr5b), 129.8(Tyr5a),171.0(Tyr1)	4.45(Tyr2)
Tyr4	-	127.7	-	6.62(Tyr6b), 6.62(Tyr6a)	-
Tyr5a	7.01	129.8	129.8(Tyr5a)	36.3(Tyr3),155.8(Tyr7)	-
Tyr5b	7.01	129.8	129.8(Tyr5b)	155.8(Tyr7)	-
Tyr6a	6.62	114.6	114.6(Tyr6a)	127.7(Tyr4),155.8(Tyr7)	-
Tyr6b	6.62	114.6	114.6(Tyr6b)	127.7(Tyr4),155.8(Tyr7)	-
Tyr7	-	155.8	-	6.62(Tyr6b), 6.62(Tyr6a),7.01(Tyr5b), 7.01(Tyr5a)	-

Table S1: Summary of NMR data for **3**

Figure S33: ^{1}H NMR (500MHz, DMSO-d_6) of C(*S*-(4-(trifluoromethyl)phenyl))SPGYS-NH_2 (**3**)



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2	Title	200417_mbed2504_170 01823530.1.fid
3	Comment	CSPGYS nmrproton DMSO {C:\ NMRDATA\ PAYNE\ PAYNE} {SHARED\ nmrstaff} {1 C9 - 133}
4	Origin	Bruker BioSpin GmbH
5	Owner	nmrstaff
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	DMSO
10	Temperature	300.1
11	Pulse Sequence	zg
12	Experiment	1D
13	Probe	Z124031_0002 (PA TXI 500S1 H/ C-N-D-01.7 Z)
14	Number of Scans	8
15	Receiver Gain	203.0
16	Relaxation Delay	2.0000
17	Pulse Width	4.9000
18	Presaturation Frequency	
19	Acquisition Time	3.2768
20	Acquisition Date	2020-04-18T12:22:13
21	Modification Date	2020-04-18T12:22:13
22	Class	
23	Spectrometer Frequency	500.13
24	Spectral Width	10000.0
25	Lowest Frequency	-2000.9
26	Nucleus	1H
27	Acquired Size	32768
28	Spectral Size	65536
29	Digital Resolution	0.15

Figure S34: ^{1}H-^{1}H COSY NMR (500 MHz, DMSO-d_6) of C(*S*-(4-(trifluoromethyl)phenyl))SPGYS-NH_2 (**3**)

	Parameter	Value
1	Data File Name	Z:/ nmr500/ data/ PAYNE/ nmr/ 200417_mbed2504 _17001823530/ 2/ ser
2	Title	200417_mbed2504 _17001823530.2.se r
3	Comment	CSPGYS nmrgrcosy DMSO {C:\ NMRDATA\ PAYNE\ PAYNE} {SHARED\ nmrstaff} {1 C9 - 133}
4	Origin	Bruker BioSpin GmbH
5	Owner	nmrstaff
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	DMSO
10	Temperature	300.0
11	Pulse Sequence	cosygpqf
12	Experiment	COSY
13	Probe	Z124031_0002 (PA TXI 500S1 H/ C- N-D-01.7 Z)
14	Number of Scans	12
15	Receiver Gain	203.0
16	Relaxation Delay	2.5000
17	Pulse Width	4.9000
18	Presaturation Frequency	
19	Acquisition Time	0.3408
20	Acquisition Date	2020-04-18T12:23: 51
21	Modification Date	2020-04-18T14:50: 09
22	Class	
23	Spectrometer Frequency	(500.13, 500.13)
24	Spectral Width	(6009.6, 6002.4)
25	Lowest Frequency	(-151.9, -155.2)
26	Nucleus	(1H, 1H)
27	Acquired Size	(2048, 256)
28	Spectral Size	(2048, 256)
29	Digital Resolution	(2.93, 23.45)

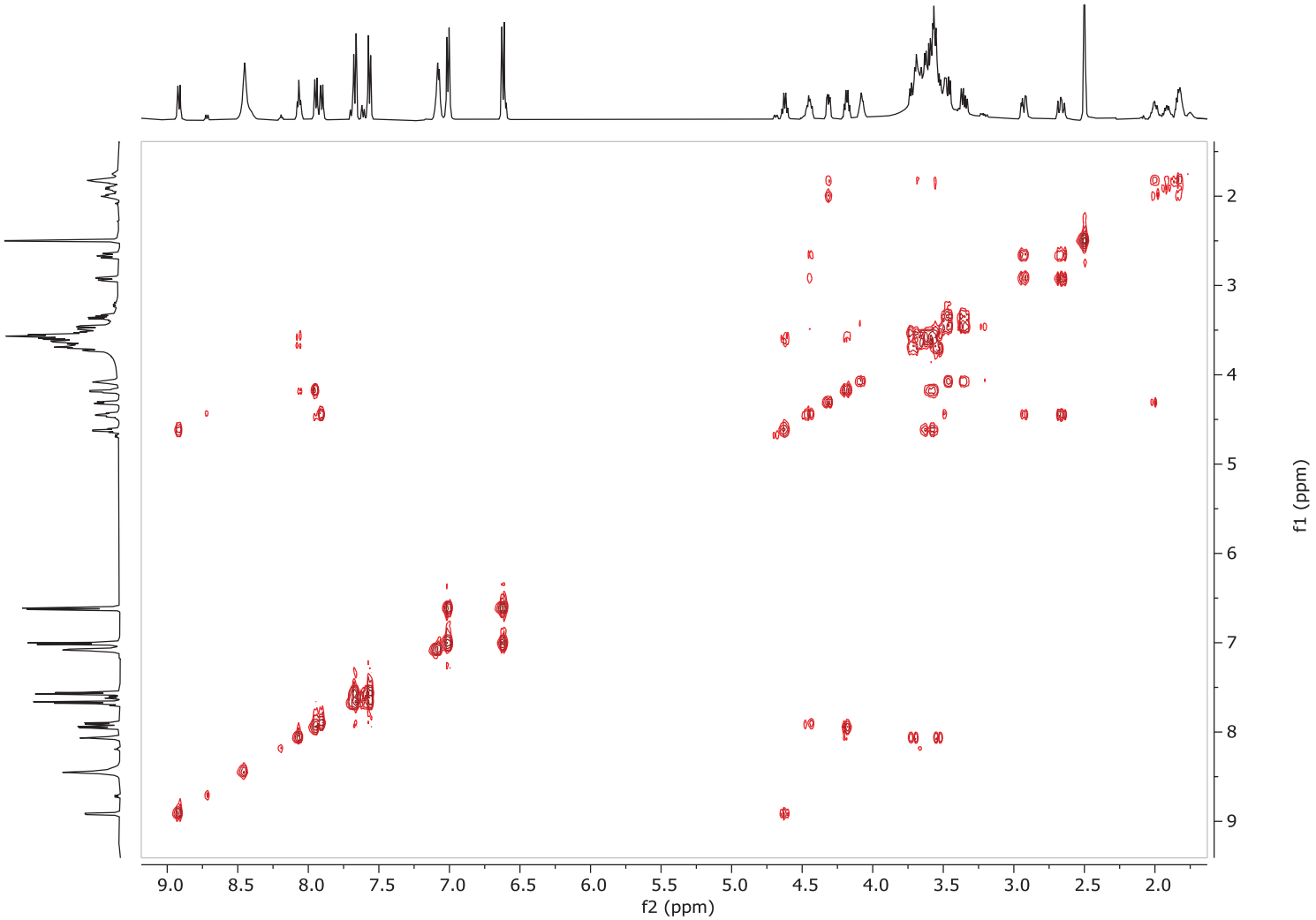
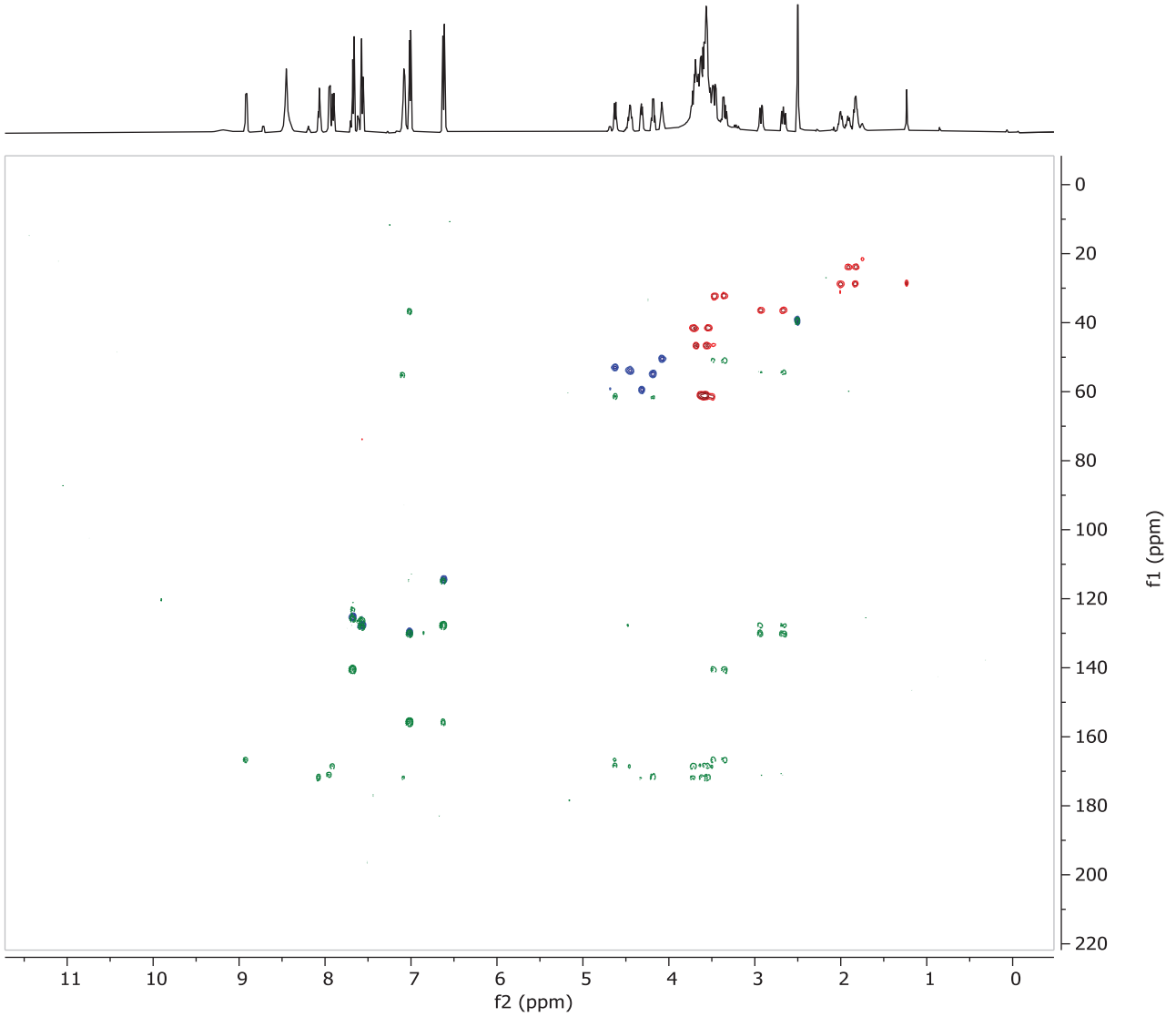


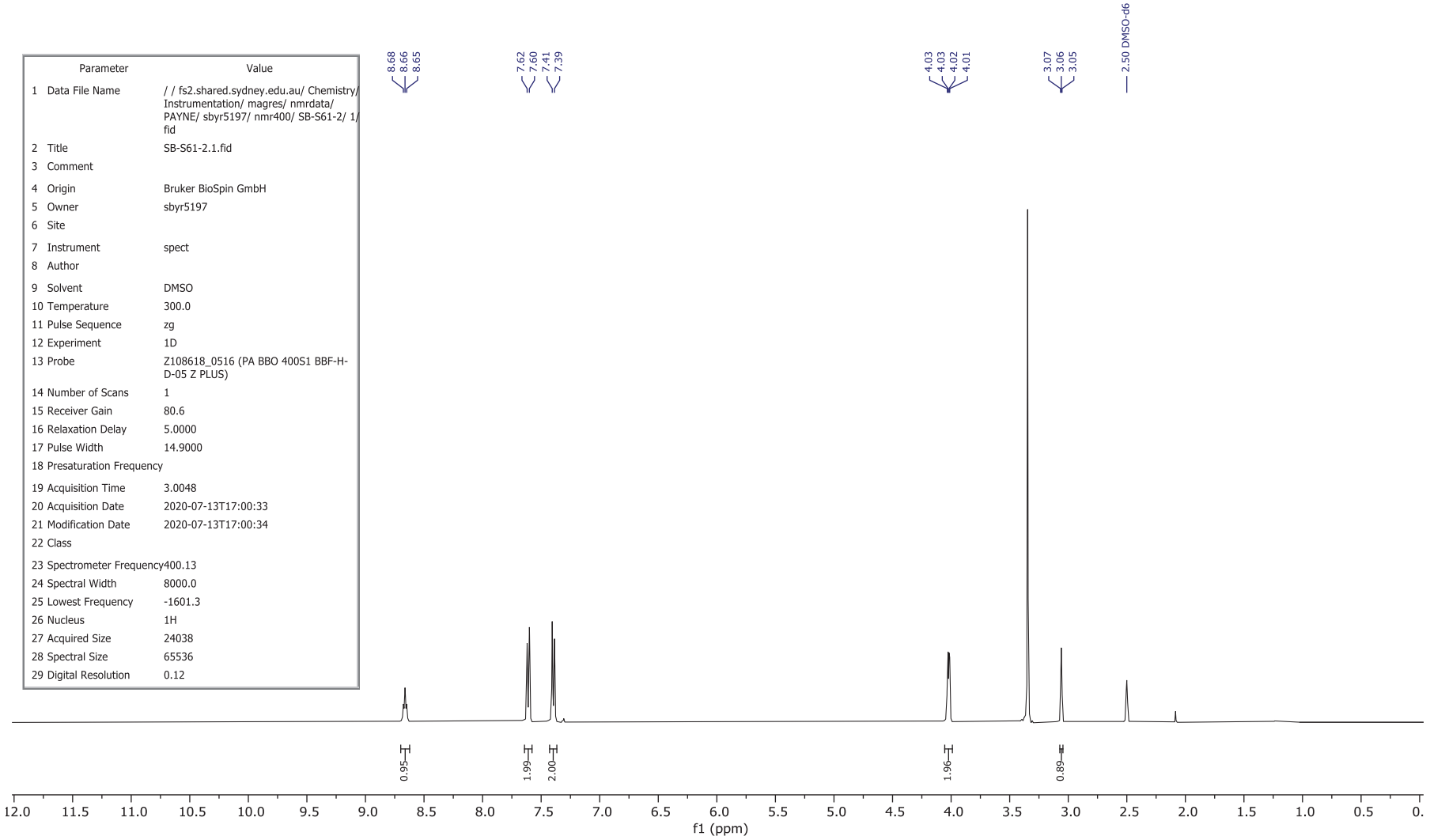
Figure S35: ^{1}H-^{13}C HSQC/HMBC NMR overlay (500/126MHz, DMSO-d_6) of C(*S*-(4-(trifluoromethyl)phenyl))SPGYS-NH_2 (**3**)

	Parameter	Value
1	Data File Name	Z:/ nmr500/ data/ PAYNE/ nmr/ 200417_mbed2504_17001823530/ 5/ ser
2	Title	200417_mbed2504_17001823530.5.ser
3	Comment	CSPGYS nmrgrhsqced DMSO {C:\ NMRDATA\ PAYNE\ PAYNE} {SHARED\ nmrstaff} {1 C9 - 133}
4	Origin	Bruker BioSpin GmbH
5	Owner	nmrstaff
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	DMSO
10	Temperature	300.0
11	Pulse Sequence	hsqcedgpph
12	Experiment	HSQC-EDITED
13	Probe	Z124031_0002 (PA TXI 500S1 H/ C-N-D-01.7 Z)
14	Number of Scans	20
15	Receiver Gain	203.0
16	Relaxation Delay	2.0000
17	Pulse Width	4.9000
18	Presaturation Frequency	
19	Acquisition Time	0.0852
20	Acquisition Date	2020-04-18T18:06:05
21	Modification Date	2020-04-18T21:05:09
22	Class	
23	Spectrometer Frequency	(500.13, 125.77)
24	Spectral Width	(6009.6, 20833.3)
25	Lowest Frequency	(-252.1, -1092.9)
26	Nucleus	(1H, 13C)
27	Acquired Size	(512, 256)
28	Spectral Size	(512, 512)
29	Digital Resolution	(11.74, 40.69)

	Parameter	Value
1	Data File Name	Z:/ nmr500/ data/ PAYNE/ nmr/ 200417_mbed2504_17001823530/ 6/ ser
2	Title	200417_mbed2504_17001823530.6.ser
3	Comment	CSPGYS nmrgrhmbclp DMSO {C:\ NMRDATA\ PAYNE\ PAYNE} {SHARED\ nmrstaff} {1 C9 - 133}
4	Origin	Bruker BioSpin GmbH
5	Owner	nmrstaff
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	DMSO
10	Temperature	300.0
11	Pulse Sequence	hmbcgplpndqf
12	Experiment	HMBC
13	Probe	Z124031_0002 (PA TXI 500S1 H/ C-N-D-01.7 Z)
14	Number of Scans	40
15	Receiver Gain	203.0
16	Relaxation Delay	2.0000
17	Pulse Width	4.9000
18	Presaturation Frequency	
19	Acquisition Time	0.3408
20	Acquisition Date	2020-04-18T21:07:41
21	Modification Date	2020-04-19T03:56:40
22	Class	
23	Spectrometer Frequency	(500.13, 125.77)
24	Spectral Width	(6009.6, 28248.6)
25	Lowest Frequency	(-146.5, -354.3)
26	Nucleus	(1H, 13C)
27	Acquired Size	(2048, 256)
28	Spectral Size	(2048, 1024)
29	Digital Resolution	(2.93, 27.59)

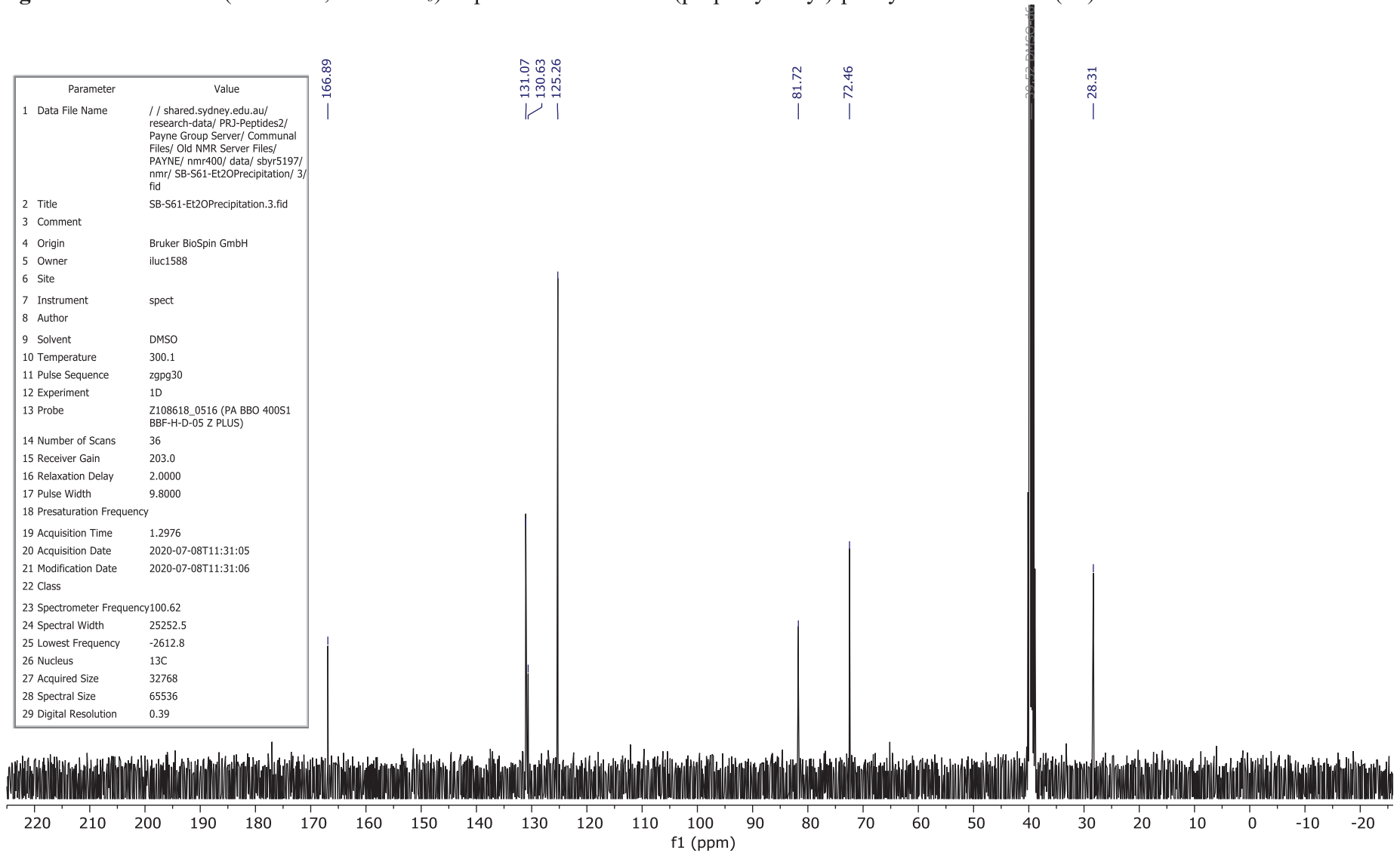


Fugure S36: ^{1}H-NMR (400 MHz, DMSO-d$_6$) of potassium 4-iodo-*N*-(prop-2-yn-1-yl)-phenyltrifluoroborate (**S2**)



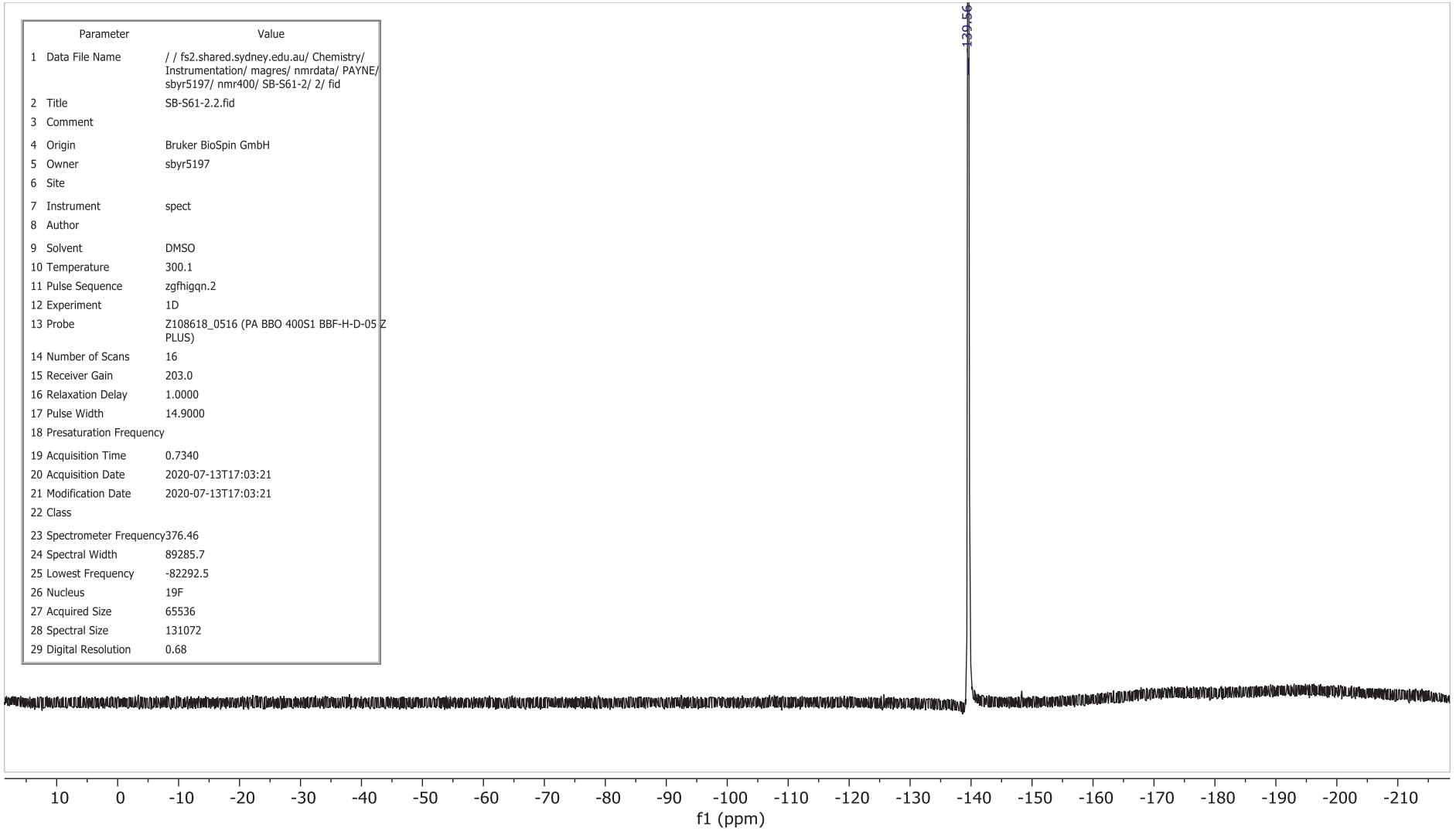
	Parameter	Value
1	Data File Name	/ / fs2.shared.sydney.edu.au/ Chemistry/ Instrumentation/ magres/ nmrdata/ PAYNE/ sbyr5197/ nmr400/ SB-S61-2/ 1/ fid
2	Title	SB-S61-2.1.fid
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	sbyr5197
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	DMSO
10	Temperature	300.0
11	Pulse Sequence	zg
12	Experiment	1D
13	Probe	Z108618_0516 (PA BBO 400S1 BBF-H-D-05 Z PLUS)
14	Number of Scans	1
15	Receiver Gain	80.6
16	Relaxation Delay	5.0000
17	Pulse Width	14.9000
18	Presaturation Frequency	
19	Acquisition Time	3.0048
20	Acquisition Date	2020-07-13T17:00:33
21	Modification Date	2020-07-13T17:00:34
22	Class	
23	Spectrometer Frequency	400.13
24	Spectral Width	8000.0
25	Lowest Frequency	-1601.3
26	Nucleus	1H
27	Acquired Size	24038
28	Spectral Size	65536
29	Digital Resolution	0.12

Figure S37: ^{13}C-NMR (101 MHz, DMSO-d$_6$) of potassium 4-iodo-*N*-(prop-2-yn-1-yl)-phenyltrifluoroborate (**S2**)



	Parameter	Value
1	Data File Name	/ / shared.sydney.edu.au/ research-data/ PRJ-Peptides2/ Payne Group Server/ Communal Files/ Old NMR Server Files/ PAYNE/ nmr400/ data/ sbyr5197/ nmr/ SB-S61-Et2OPrecipitation/ 3/ fid
2	Title	SB-S61-Et2OPrecipitation.3.fid
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	iluc1588
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	DMSO
10	Temperature	300.1
11	Pulse Sequence	zgpg30
12	Experiment	1D
13	Probe	Z108618_0516 (PA BBO 400S1 BBF-H-D-05 Z PLUS)
14	Number of Scans	36
15	Receiver Gain	203.0
16	Relaxation Delay	2.0000
17	Pulse Width	9.8000
18	Presaturation Frequency	
19	Acquisition Time	1.2976
20	Acquisition Date	2020-07-08T11:31:05
21	Modification Date	2020-07-08T11:31:06
22	Class	
23	Spectrometer Frequency	100.62
24	Spectral Width	25252.5
25	Lowest Frequency	-2612.8
26	Nucleus	13C
27	Acquired Size	32768
28	Spectral Size	65536
29	Digital Resolution	0.39

Figure S38: ^{19}F-NMR (376 MHz, DMSO-d_6) of potassium 4-iodo-*N*-(prop-2-yn-1-yl)-phenyltrifluoroborate (**S2**)



Parameter		Value
1	Data File Name	/ / fs2.shared.sydney.edu.au/ Chemistry/ Instrumentation/ magres/ nmrdata/ PAYNE/ sbyr5197/ nmr400/ SB-S61-2/ 2/ fid
2	Title	SB-S61-2.2.fid
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	sbyr5197
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	DMSO
10	Temperature	300.1
11	Pulse Sequence	zgfhigqn.2
12	Experiment	1D
13	Probe	Z108618_0516 (PA BBO 400S1 BBF-H-D-05 Z PLUS)
14	Number of Scans	16
15	Receiver Gain	203.0
16	Relaxation Delay	1.0000
17	Pulse Width	14.9000
18	Presaturation Frequency	
19	Acquisition Time	0.7340
20	Acquisition Date	2020-07-13T17:03:21
21	Modification Date	2020-07-13T17:03:21
22	Class	
23	Spectrometer Frequency	376.46
24	Spectral Width	89285.7
25	Lowest Frequency	-82292.5
26	Nucleus	19F
27	Acquired Size	65536
28	Spectral Size	131072
29	Digital Resolution	0.68

Figure S39: ^{11}B-NMR (128 MHz, DMSO-d_6) of potassium 4-iodo-*N*-(prop-2-yn-1-yl)-phenyltrifluoroborate (**S2**)

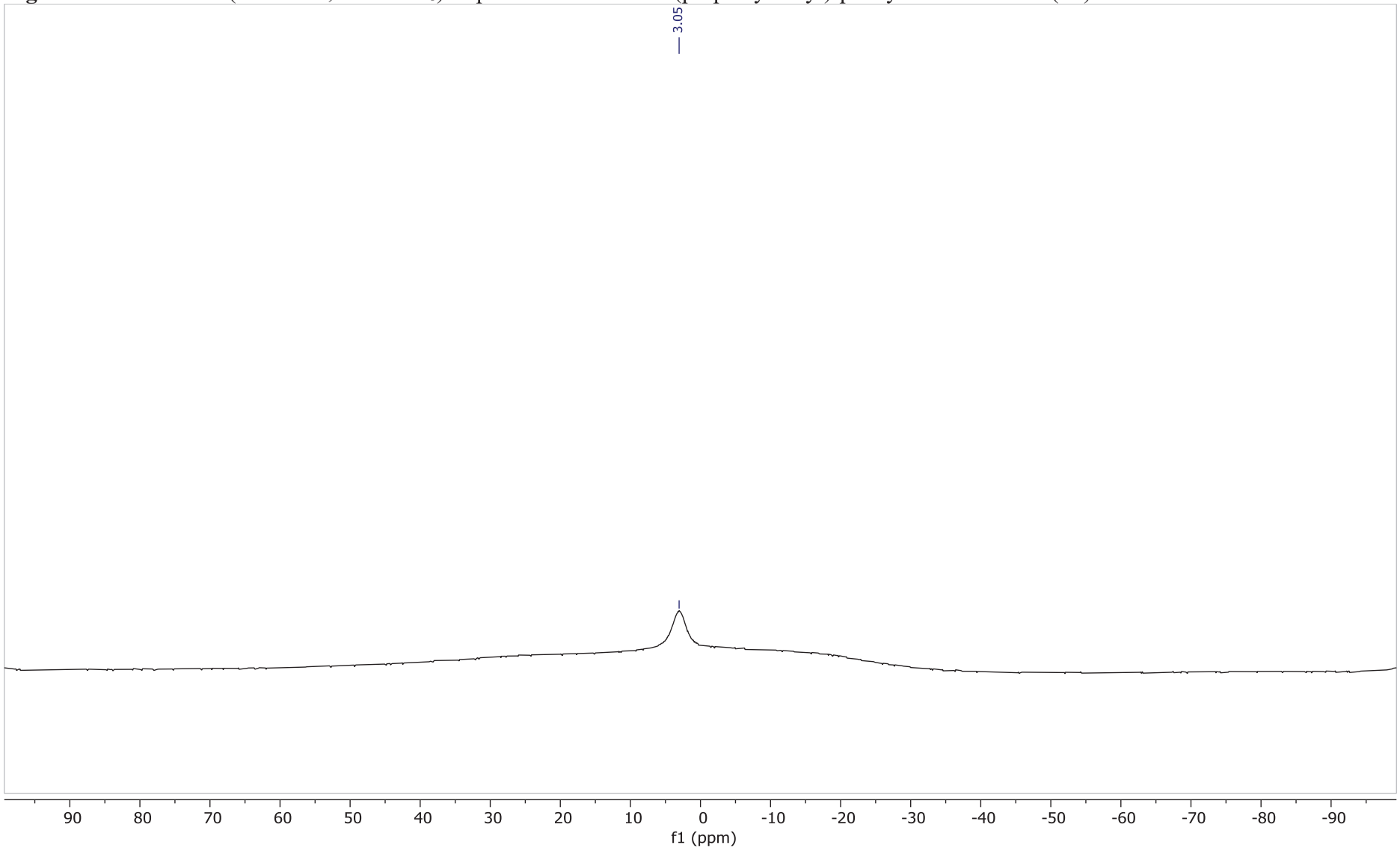


Figure S40: ^{1}H-NMR (400 MHz, DMSO-d_6) of Bis(4-(prop-2-yn-1-ylcarbamoyl)phenyl)iodonium trifluoroacetate (**4**)

	Parameter	Value
1	Data File Name	C:/ Users/ payne/ AppData/ Local/ Temp/ MeiPKZ1nS7CG $hh+Bov1Wg/ SB-S33-23-Run1/ 1/ pdata/ 1/ 1r
2	Title	SB-S33-23-Run1.1.1.1r
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	sbyr5197
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	DMSO
10	Temperature	300.0
11	Pulse Sequence	zg
12	Experiment	1D
13	Probe	Z108618_0516 (PA BBO 400S1 BBF-H-D-05 Z PLUS)
14	Number of Scans	16
15	Receiver Gain	80.6
16	Relaxation Delay	5.0000
17	Pulse Width	14.9000
18	Presaturation Frequency	
19	Acquisition Time	3.0048
20	Acquisition Date	2020-07-15T13:48:36
21	Modification Date	2020-10-15T13:11:18
22	Class	
23	Spectrometer Frequency	400.13
24	Spectral Width	8000.0
25	Lowest Frequency	-1601.4
26	Nucleus	1H
27	Acquired Size	24038
28	Spectral Size	32768
29	Digital Resolution	0.24

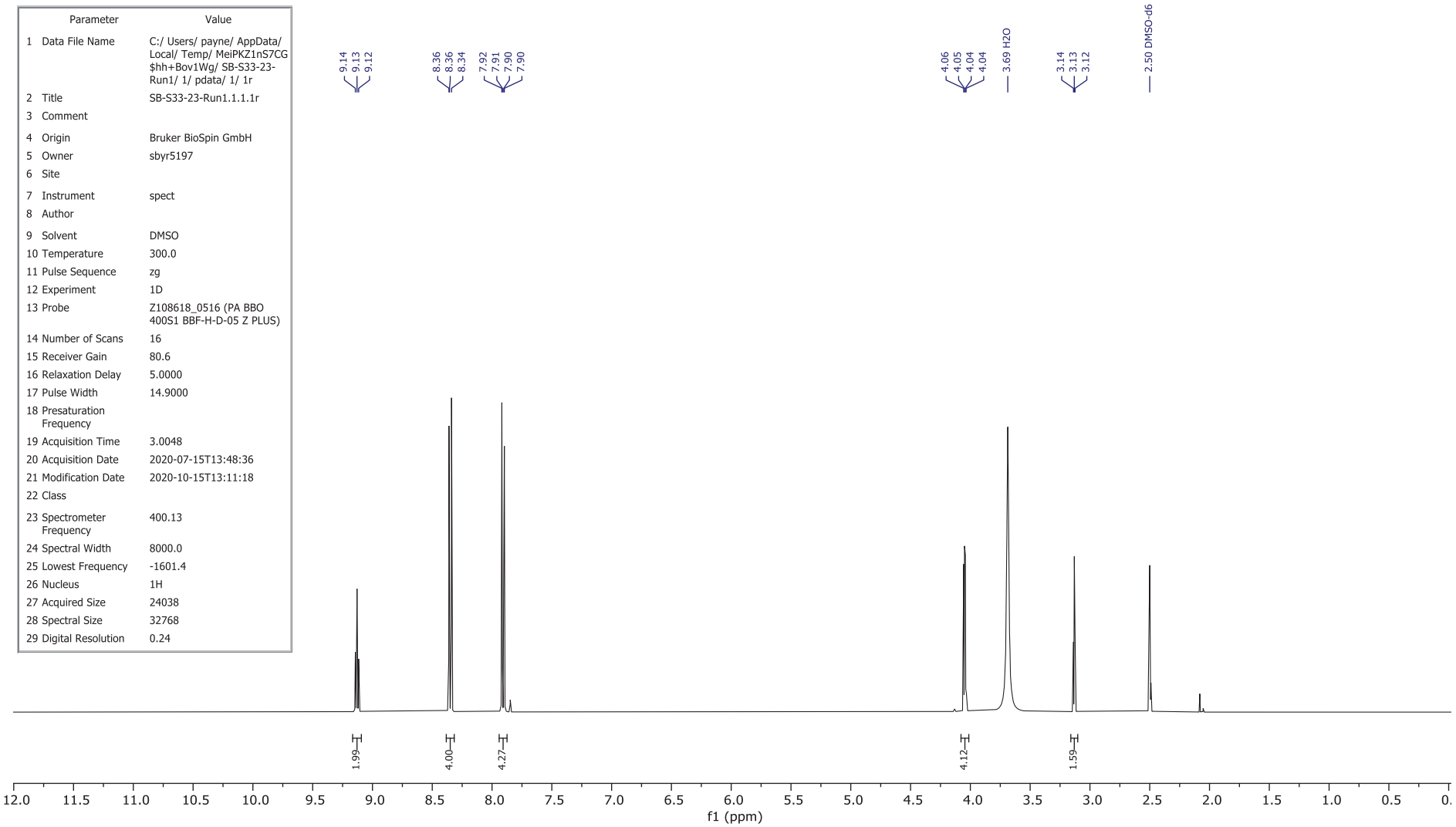
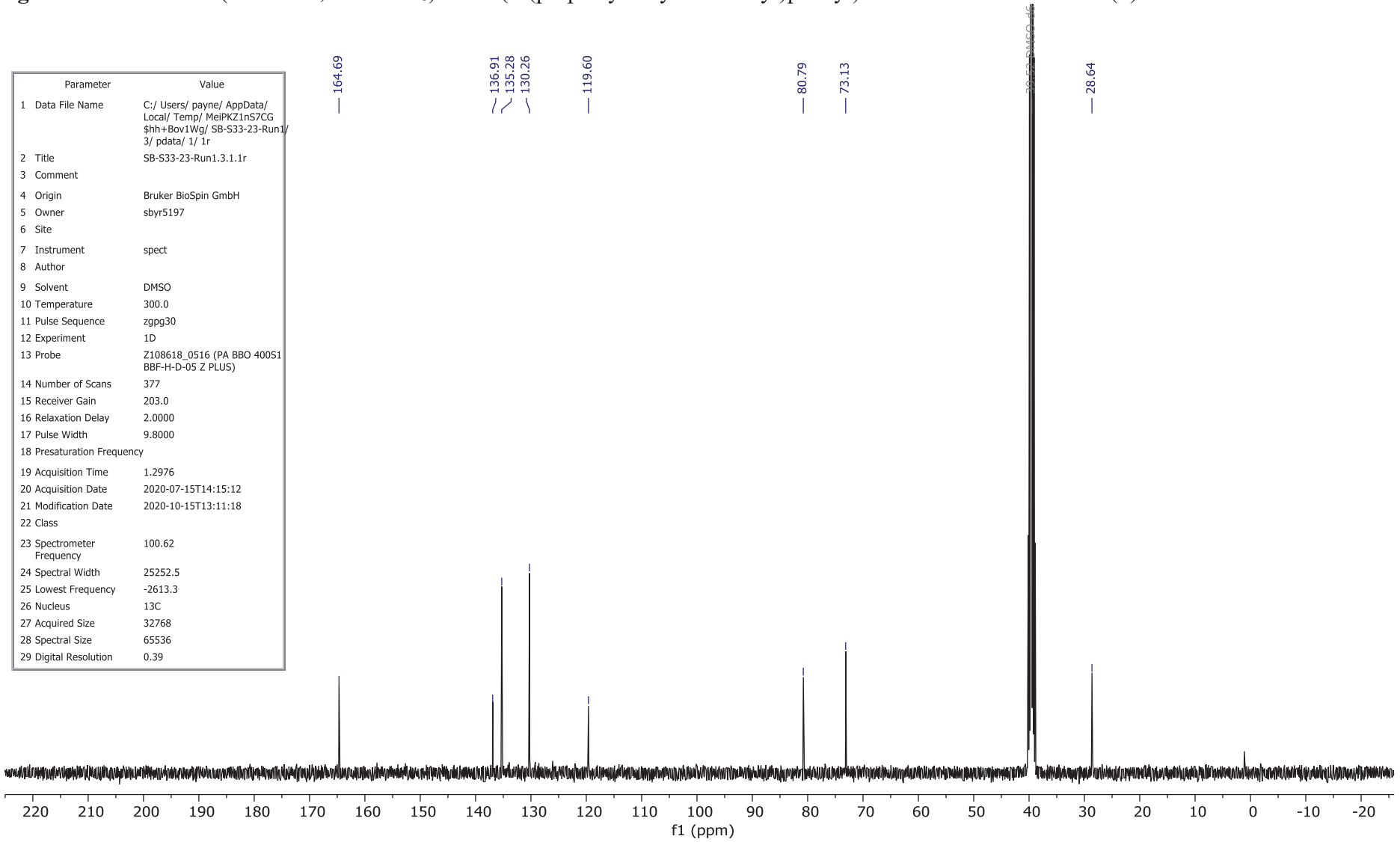
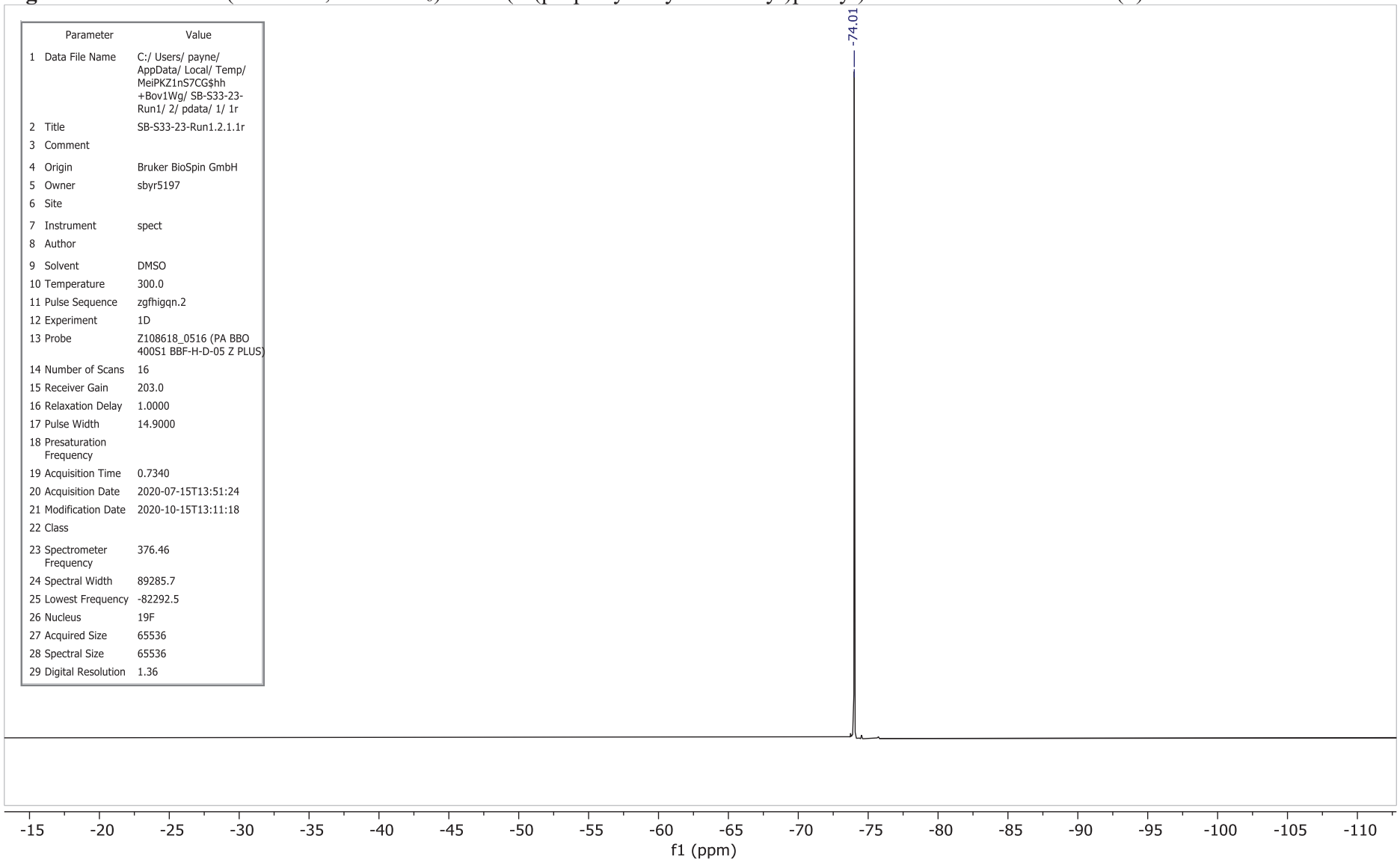


Figure S41: ^{13}C-NMR (101 MHz, DMSO-d$_6$) of Bis(4-(prop-2-yn-1-ylcarbamoyl)phenyl)iodonium trifluoroacetate (**4**)



	Parameter	Value
1	Data File Name	C:/ Users/ payne/ AppData/ Local/ Temp/ MeiPKZ1nS7CG $hh+Bov1Wg/ SB-S33-23-Run1/ 3/ pdata/ 1/ 1r
2	Title	SB-S33-23-Run1.3.1.1r
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	sbyr5197
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	DMSO
10	Temperature	300.0
11	Pulse Sequence	zgpg30
12	Experiment	1D
13	Probe	Z108618_0516 (PA BBO 400S1 BBF-H-D-05 Z PLUS)
14	Number of Scans	377
15	Receiver Gain	203.0
16	Relaxation Delay	2.0000
17	Pulse Width	9.8000
18	Presaturation Frequency	
19	Acquisition Time	1.2976
20	Acquisition Date	2020-07-15T14:15:12
21	Modification Date	2020-10-15T13:11:18
22	Class	
23	Spectrometer Frequency	100.62
24	Spectral Width	25252.5
25	Lowest Frequency	-2613.3
26	Nucleus	13C
27	Acquired Size	32768
28	Spectral Size	65536
29	Digital Resolution	0.39

Figure S42: ^{19}F-NMR (376 MHz, DMSO-d_6) of Bis(4-(prop-2-yn-1-ylcarbamoyl)phenyl)iodonium trifluoroacetate (**4**)



	Parameter	Value
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2	Title	SB-S33-23-Run1.2.1.1r
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	sbyr5197
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	DMSO
10	Temperature	300.0
11	Pulse Sequence	zgfhigqn.2
12	Experiment	1D
13	Probe	Z108618_0516 (PA BBO 400S1 BBF-H-D-05 Z PLUS)
14	Number of Scans	16
15	Receiver Gain	203.0
16	Relaxation Delay	1.0000
17	Pulse Width	14.9000
18	Presaturation Frequency	
19	Acquisition Time	0.7340
20	Acquisition Date	2020-07-15T13:51:24
21	Modification Date	2020-10-15T13:11:18
22	Class	
23	Spectrometer Frequency	376.46
24	Spectral Width	89285.7
25	Lowest Frequency	-82292.5
26	Nucleus	19F
27	Acquired Size	65536
28	Spectral Size	65536
29	Digital Resolution	1.36

Figure S43. Alkoxyamine-PEG$_3$-Biotin **S5** ^{1}H NMR (400 MHz, D_2O)

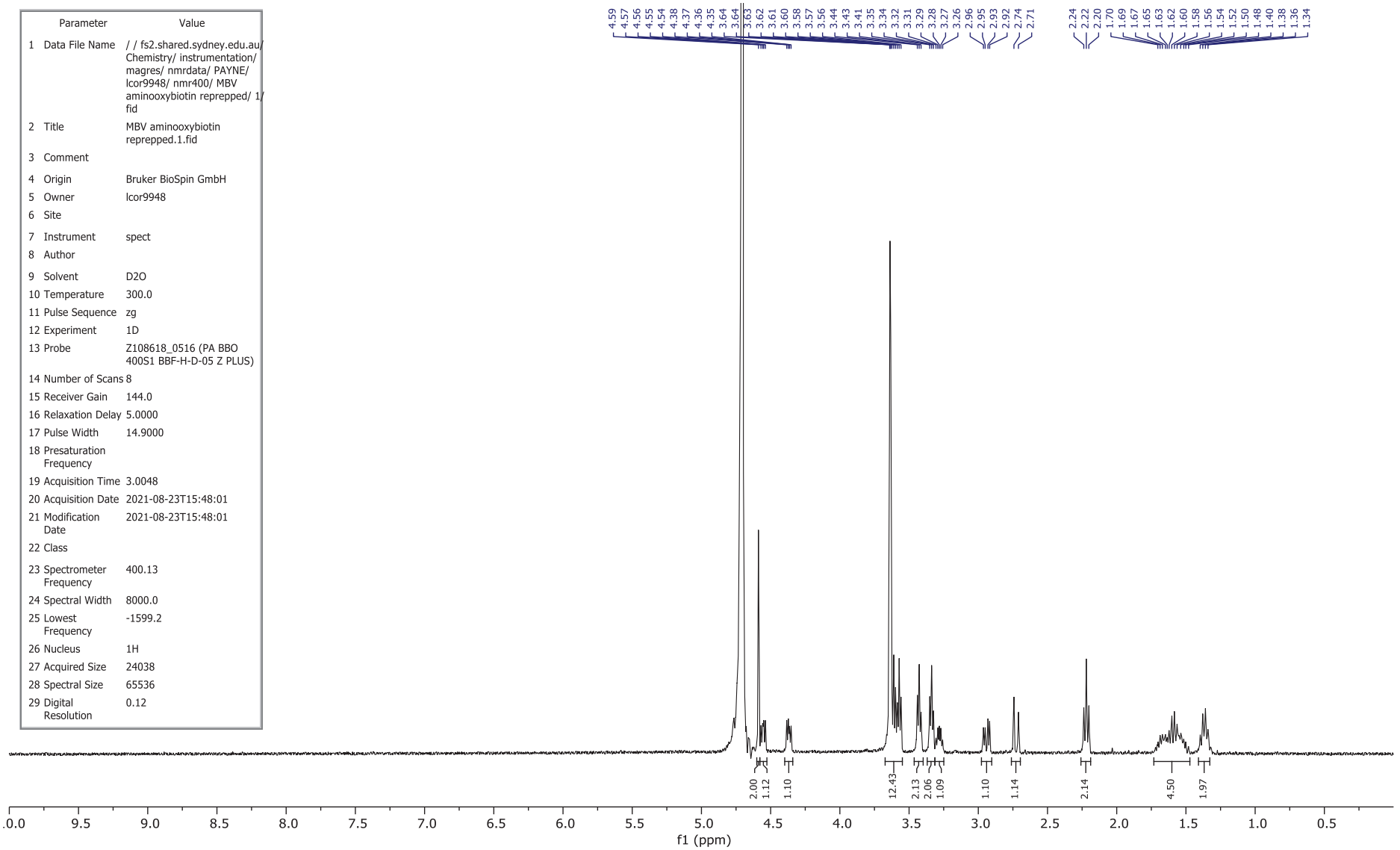
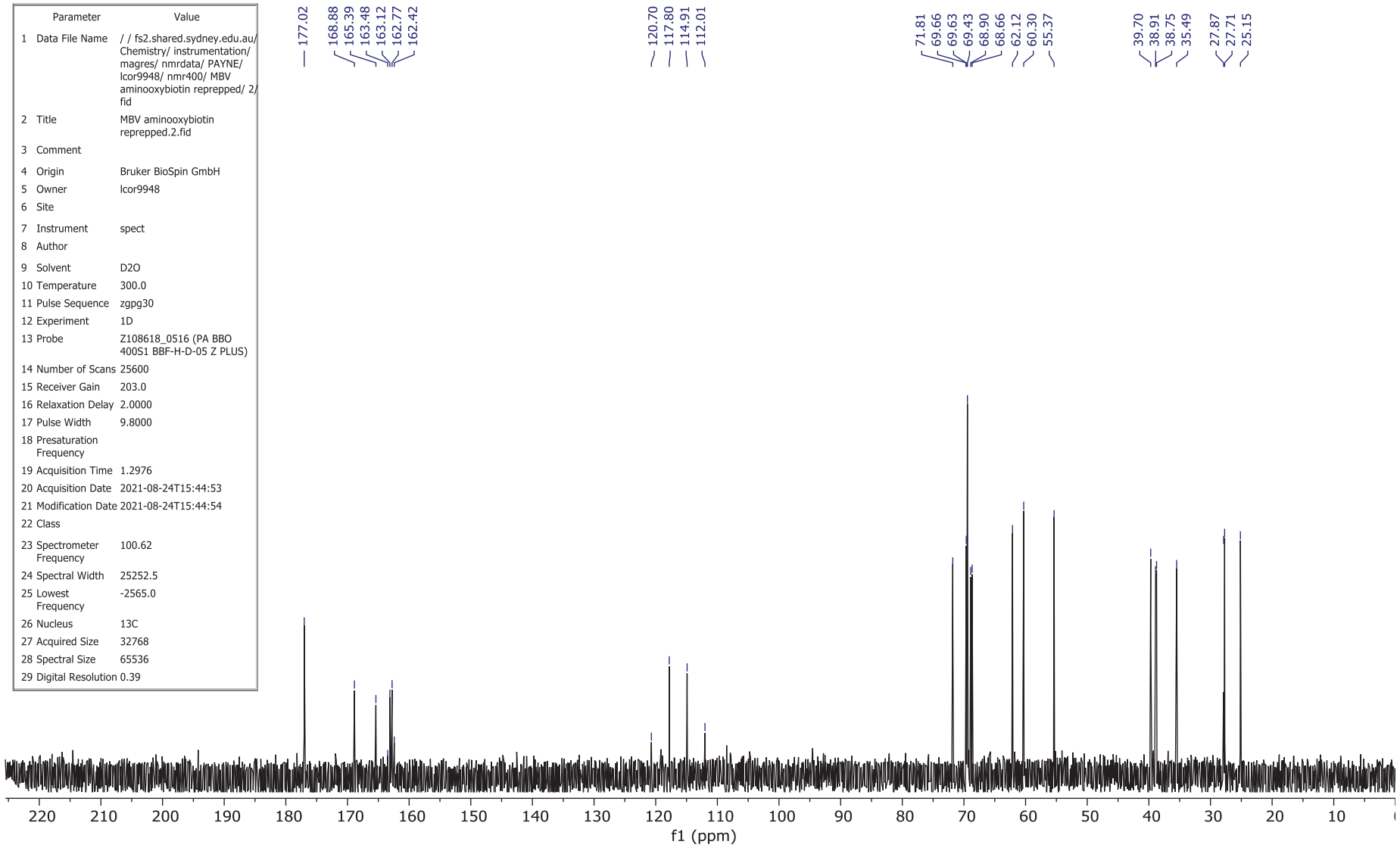
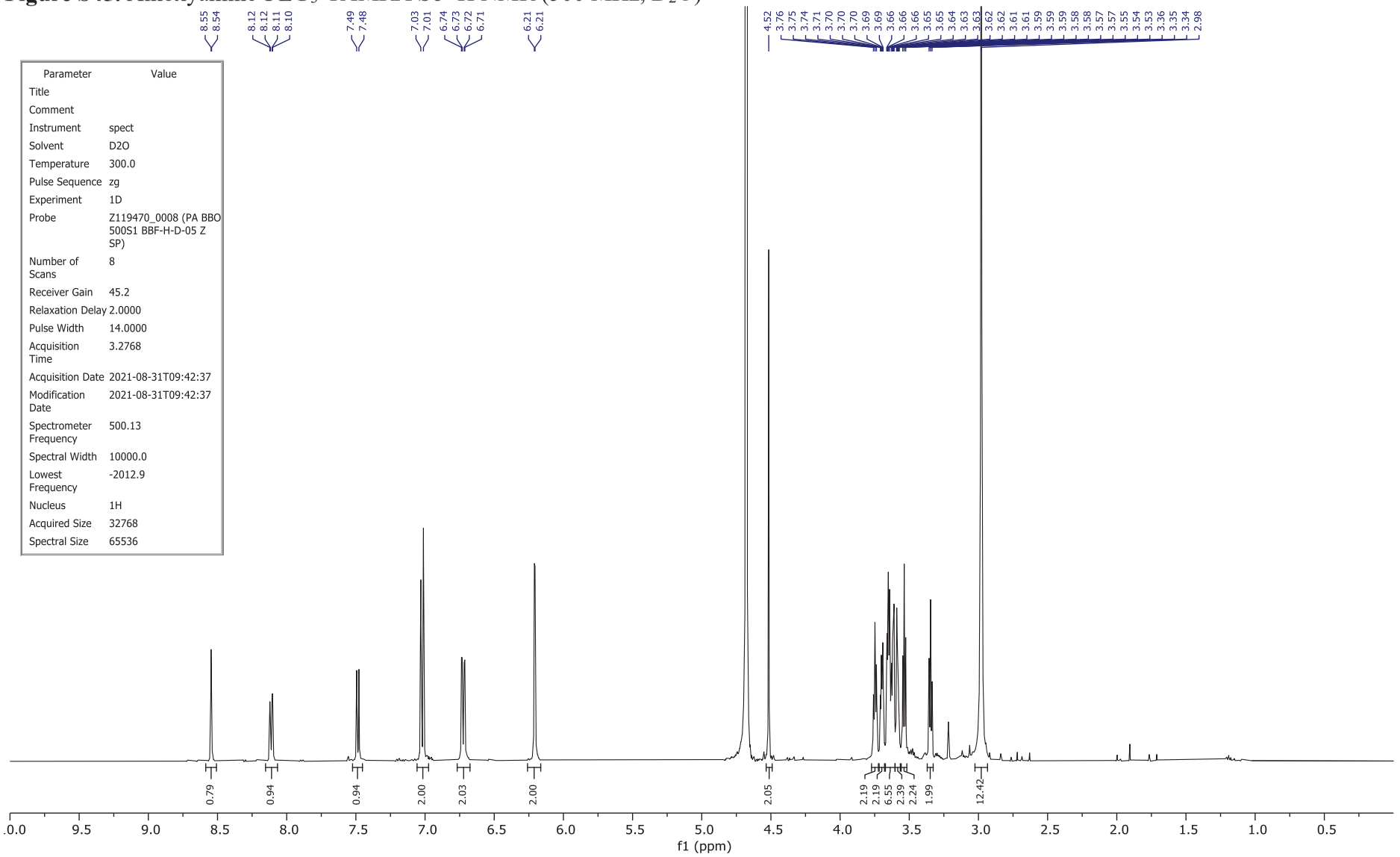


Figure S44. Alkoxyamine-PEG$_3$-Biotin **S5** ^{13}C NMR (101 MHz, D_2O)



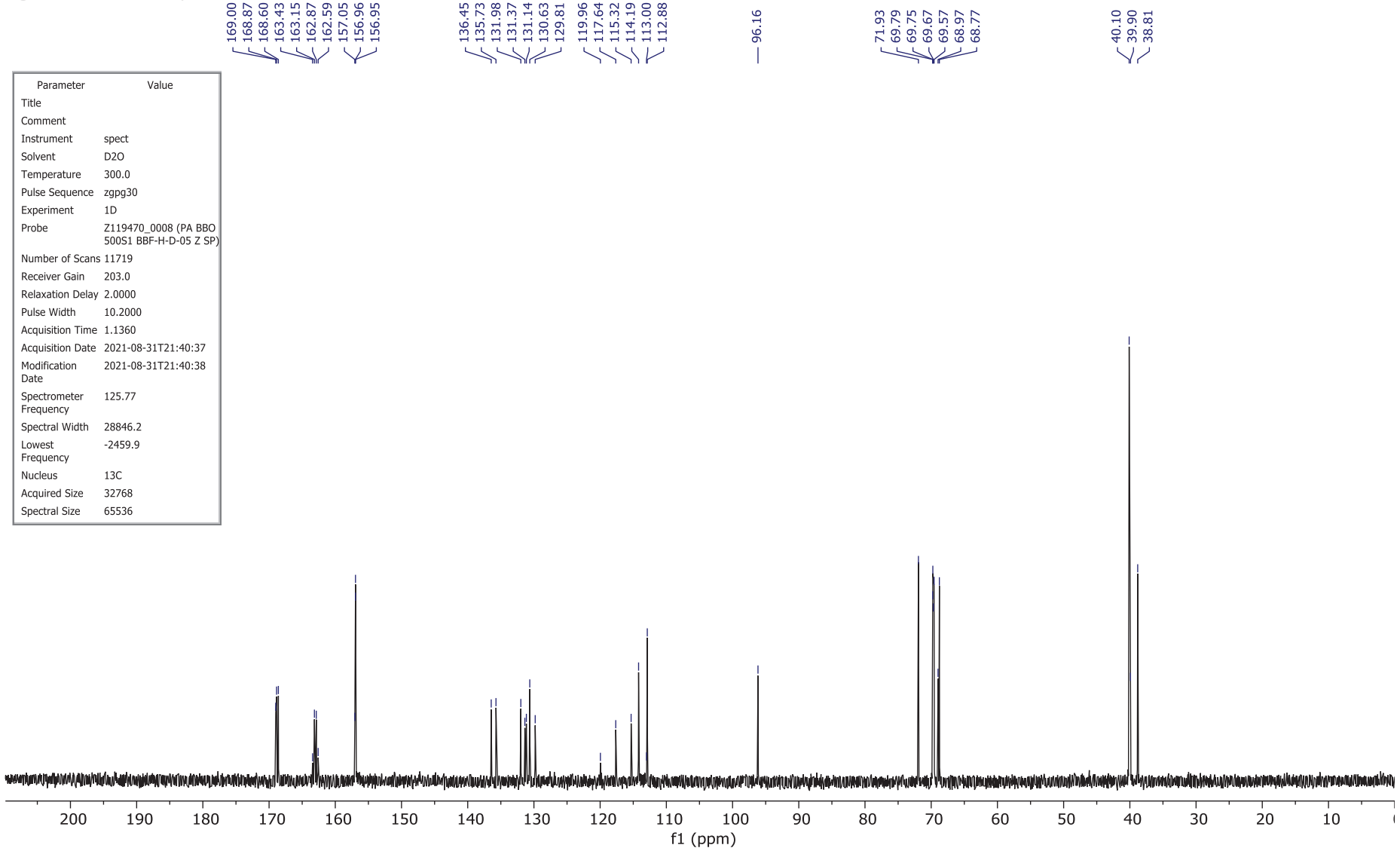
	Parameter	Value
1	Data File Name	/ / fs2.shared.sydney.edu.au/ Chemistry/ instrumentation/ magres/ nmrdata/ PAYNE/ lcor9948/ nmr400/ MBV aminooxybiotin reprepped/ 2/ fid
2	Title	MBV aminooxybiotin reprepped.2.fid
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	lcor9948
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	D2O
10	Temperature	300.0
11	Pulse Sequence	zgpg30
12	Experiment	1D
13	Probe	Z108618_0516 (PA BBO 400S1 BBF-H-D-05 Z PLUS)
14	Number of Scans	25600
15	Receiver Gain	203.0
16	Relaxation Delay	2.0000
17	Pulse Width	9.8000
18	Presaturation Frequency	
19	Acquisition Time	1.2976
20	Acquisition Date	2021-08-24T15:44:53
21	Modification Date	2021-08-24T15:44:54
22	Class	
23	Spectrometer Frequency	100.62
24	Spectral Width	25252.5
25	Lowest Frequency	-2565.0
26	Nucleus	13C
27	Acquired Size	32768
28	Spectral Size	65536
29	Digital Resolution	0.39

Figure S45. Alkoxyamine-PEG$_3$-TAMRA **S6** ^{1}H NMR (500 MHz, D_2O)



Parameter	Value
Title	
Comment	
Instrument	spect
Solvent	D2O
Temperature	300.0
Pulse Sequence	zg
Experiment	1D
Probe	Z119470_0008 (PA BBO 500S1 BBF-H-D-05 Z SP)
Number of Scans	8
Receiver Gain	45.2
Relaxation Delay	2.0000
Pulse Width	14.0000
Acquisition Time	3.2768
Acquisition Date	2021-08-31T09:42:37
Modification Date	2021-08-31T09:42:37
Spectrometer Frequency	500.13
Spectral Width	10000.0
Lowest Frequency	-2012.9
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

Figure S46. Alkoxyamine-PEG$_3$-TAMRA Trifluoroacetate **S6** ^{13} CNMR (126 MHz, D_2O)



Parameter	Value
Title	
Comment	
Instrument	spect
Solvent	D2O
Temperature	300.0
Pulse Sequence	zgpg30
Experiment	1D
Probe	Z119470_0008 (PA BBO 500S1 BBF-H-D-05 Z SP)
Number of Scans	11719
Receiver Gain	203.0
Relaxation Delay	2.0000
Pulse Width	10.2000
Acquisition Time	1.1360
Acquisition Date	2021-08-31T21:40:37
Modification Date	2021-08-31T21:40:38
Spectrometer Frequency	125.77
Spectral Width	28846.2
Lowest Frequency	-2459.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Figure S47. ^{1}H-NMR (400 MHz, CD_3CN) of mPEG$_4$ 4-iodobenzoate (**S7**)

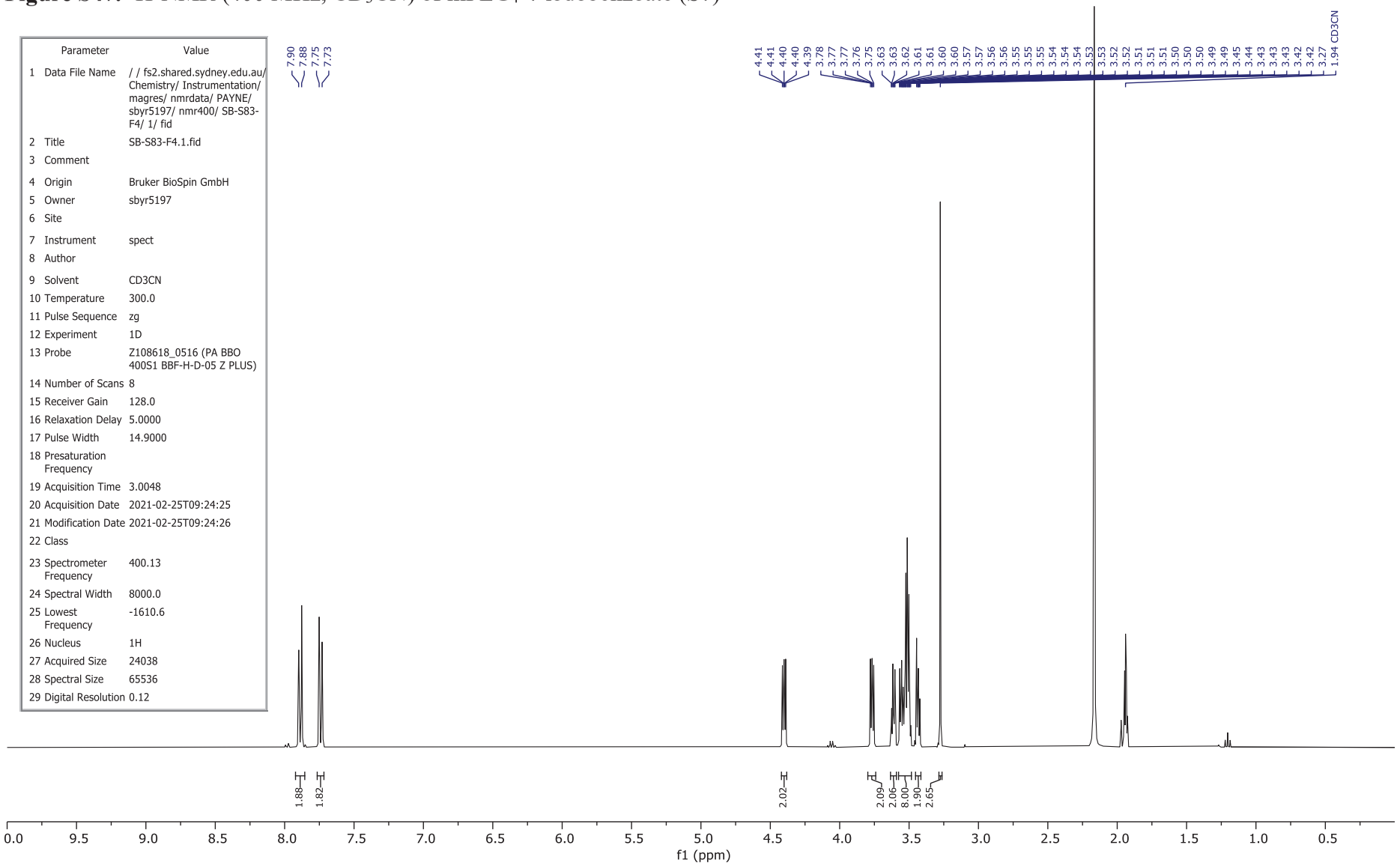


Figure S48. ^{13}C-NMR (101 MHz, CD_3CN) of mPEG$_4$ 4-iodobenzoate (**S7**)

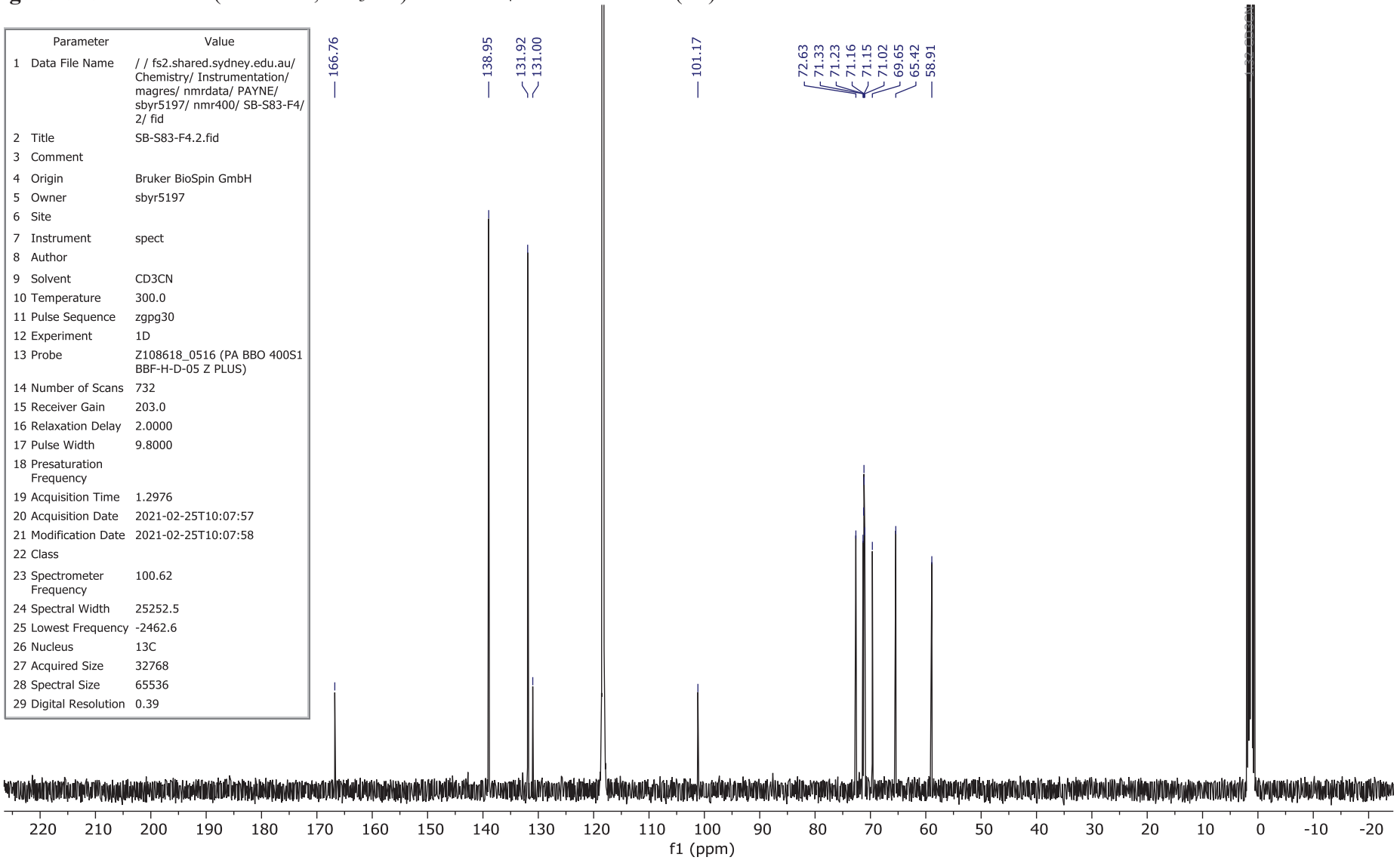
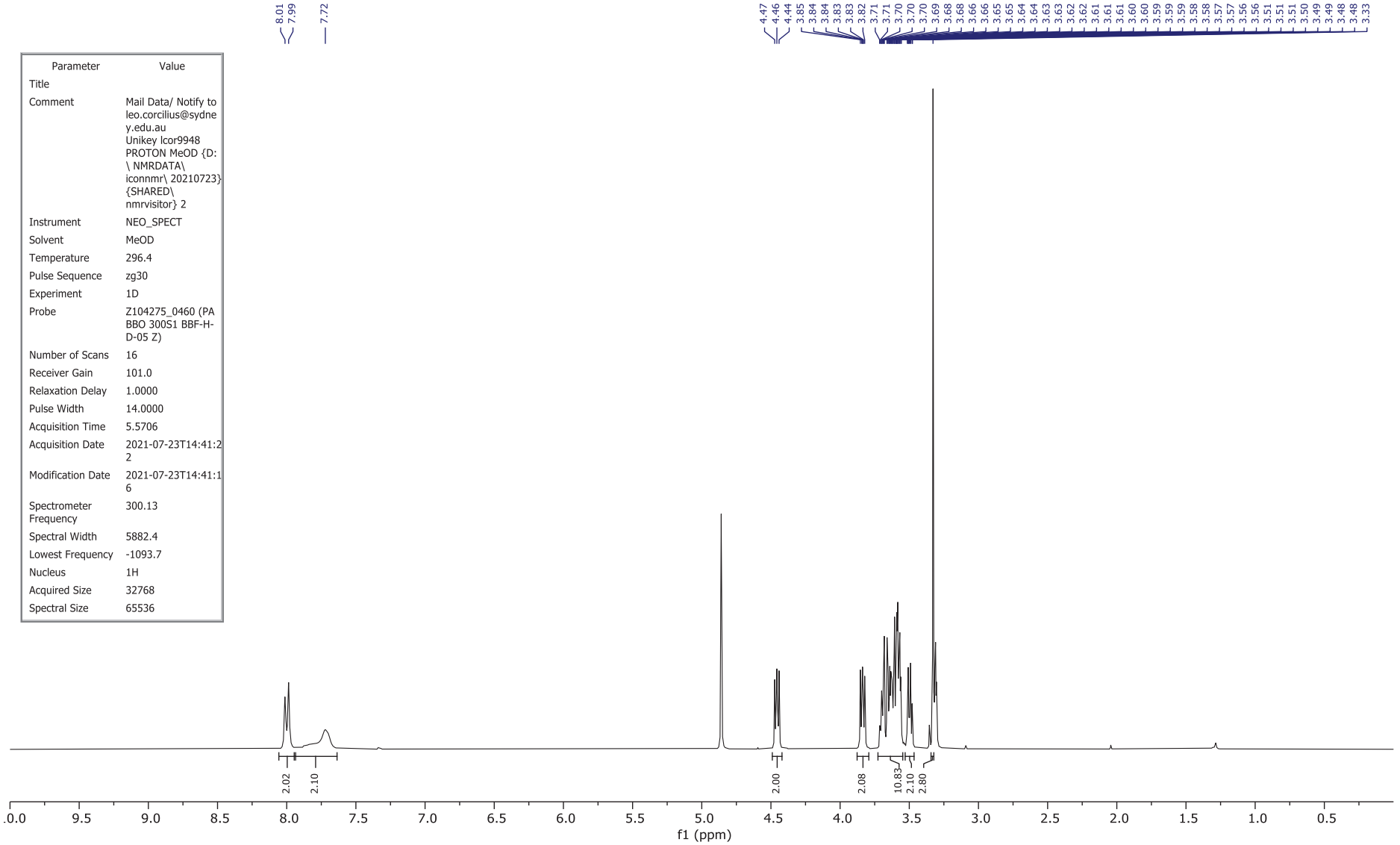
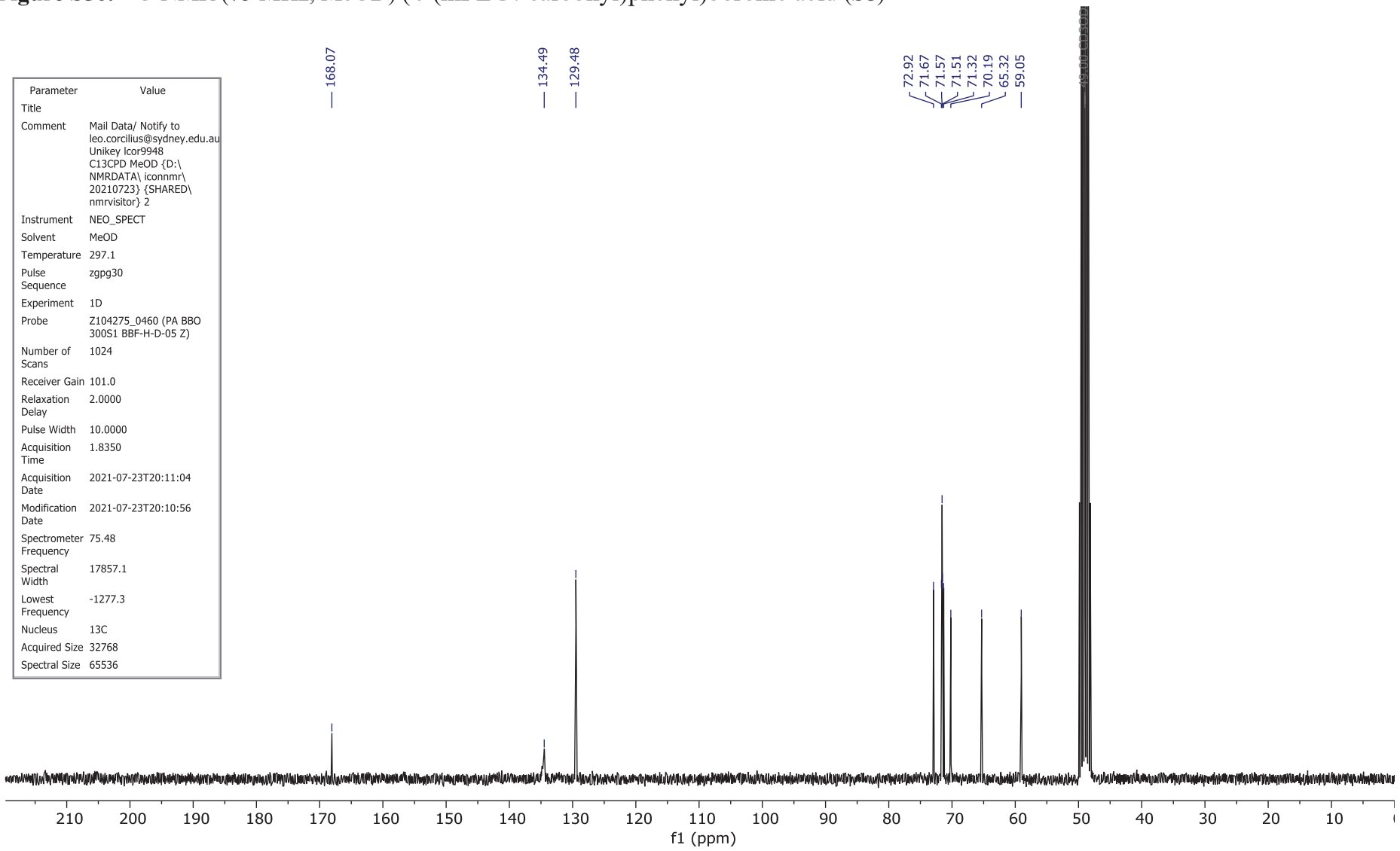


Figure S49. ^{1}H-NMR (300 MHz, MeOD) (4-(mPEG$_4$-carbonyl)phenyl)boronic acid (**S8**)



Parameter	Value
Title	
Comment	Mail Data/ Notify to leo.corcilius@sydney.edu.au Unikey lcor9948 PROTON MeOD {D:\ NMRDATA\ iconnmr\ 20210723} {SHARED\ nmrvisitor} 2
Instrument	NEO_SPECT
Solvent	MeOD
Temperature	296.4
Pulse Sequence	zg30
Experiment	1D
Probe	Z104275_0460 (PABBO 300S1 BBF-H-D-05 Z)
Number of Scans	16
Receiver Gain	101.0
Relaxation Delay	1.0000
Pulse Width	14.0000
Acquisition Time	5.5706
Acquisition Date	2021-07-23T14:41:22
Modification Date	2021-07-23T14:41:16
Spectrometer Frequency	300.13
Spectral Width	5882.4
Lowest Frequency	-1093.7
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

Figure S50. ^{13}C-NMR (75 MHz, MeOD) (4-(mPEG$_4$-carbonyl)phenyl)boronic acid (**S8**)



Parameter	Value
Title	
Comment	Mail Data/ Notify to leo.corcilius@sydney.edu.au Unikey lcor9948 C13CPD MeOD {D:\ NMRDATA\ iconnmr\ 20210723} {SHARED\ nmrvisitor} 2
Instrument	NEO_SPECT
Solvent	MeOD
Temperature	297.1
Pulse Sequence	zgpg30
Experiment	1D
Probe	Z104275_0460 (PA BBO 300S1 BBF-H-D-05 Z)
Number of Scans	1024
Receiver Gain	101.0
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.8350
Acquisition Date	2021-07-23T20:11:04
Modification Date	2021-07-23T20:10:56
Spectrometer Frequency	75.48
Spectral Width	17857.1
Lowest Frequency	-1277.3
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Figure S51: ^{1}H-NMR (400 MHz, CD_3CN) of Bis(4-mPEG$_4$ benzoate)iodonium trifluoroacetate (**20**)

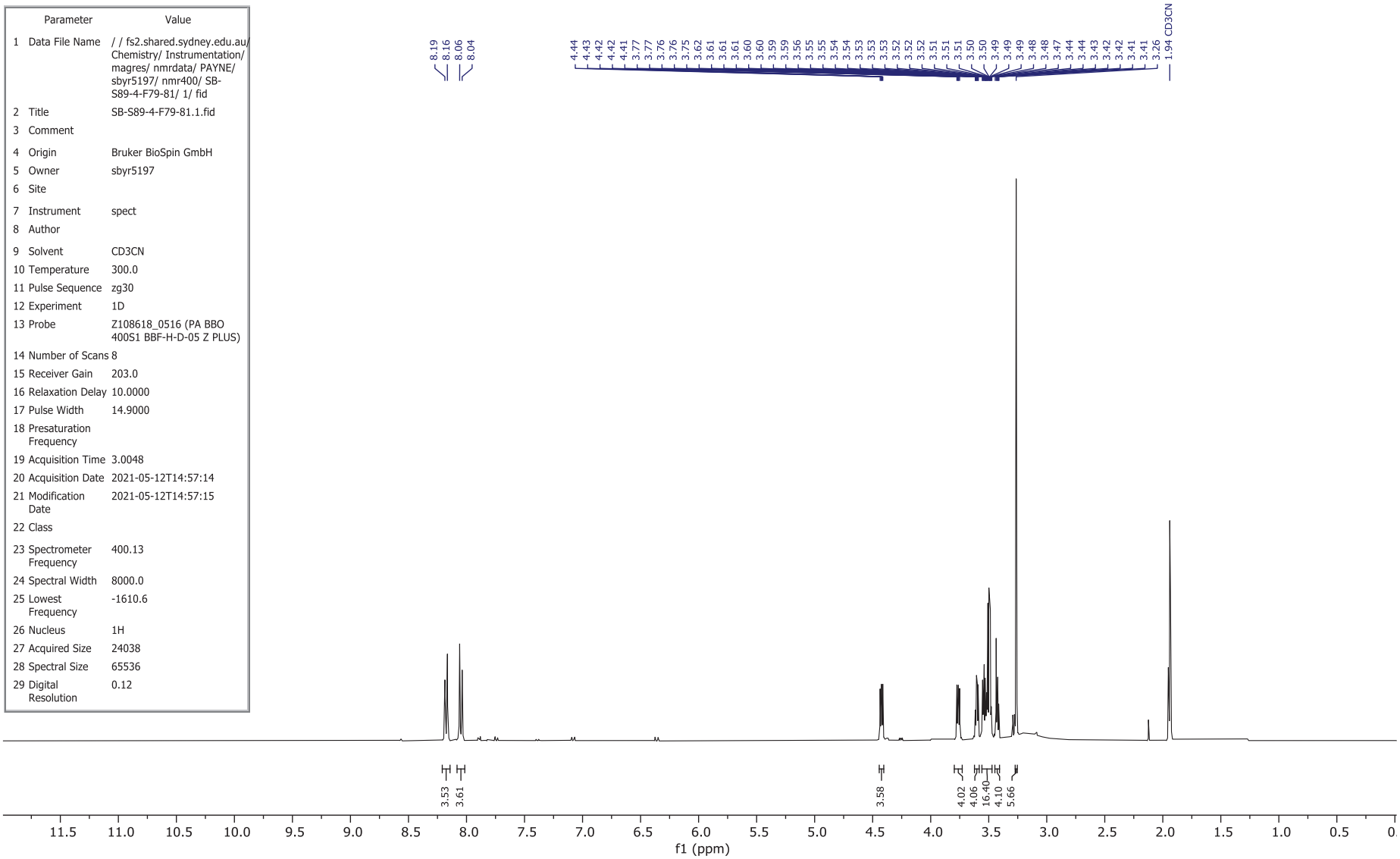


Figure S52: ^{13}C-NMR (101 MHz, CD_3CN) of Bis(4-mPEG$_4$ benzoate)iodonium trifluoroacetate (**20**)

	Parameter	Value
1	Data File Name	/ / fs2.shared.sydney.edu.au/ Chemistry/ Instrumentation/ magres/ nmrdata/ PAYNE/ sbyr5197/ nmr400/ SB-S89-4-F79-81/ 3/ fid
2	Title	SB-S89-4-F79-81.3.fid
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	sbyr5197
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	CD3CN
10	Temperature	300.0
11	Pulse Sequence	zgpg30
12	Experiment	1D
13	Probe	Z108618_0516 (PA BBO 400S1 BBF-H-D-05 Z PLUS)
14	Number of Scans	417
15	Receiver Gain	203.0
16	Relaxation Delay	2.0000
17	Pulse Width	9.8000
18	Presaturation Frequency	
19	Acquisition Time	1.2976
20	Acquisition Date	2021-05-12T15:26:48
21	Modification Date	2021-05-12T15:26:49
22	Class	
23	Spectrometer Frequency	100.62
24	Spectral Width	25252.5
25	Lowest Frequency	-2565.0
26	Nucleus	13C
27	Acquired Size	32768
28	Spectral Size	65536
29	Digital Resolution	0.39

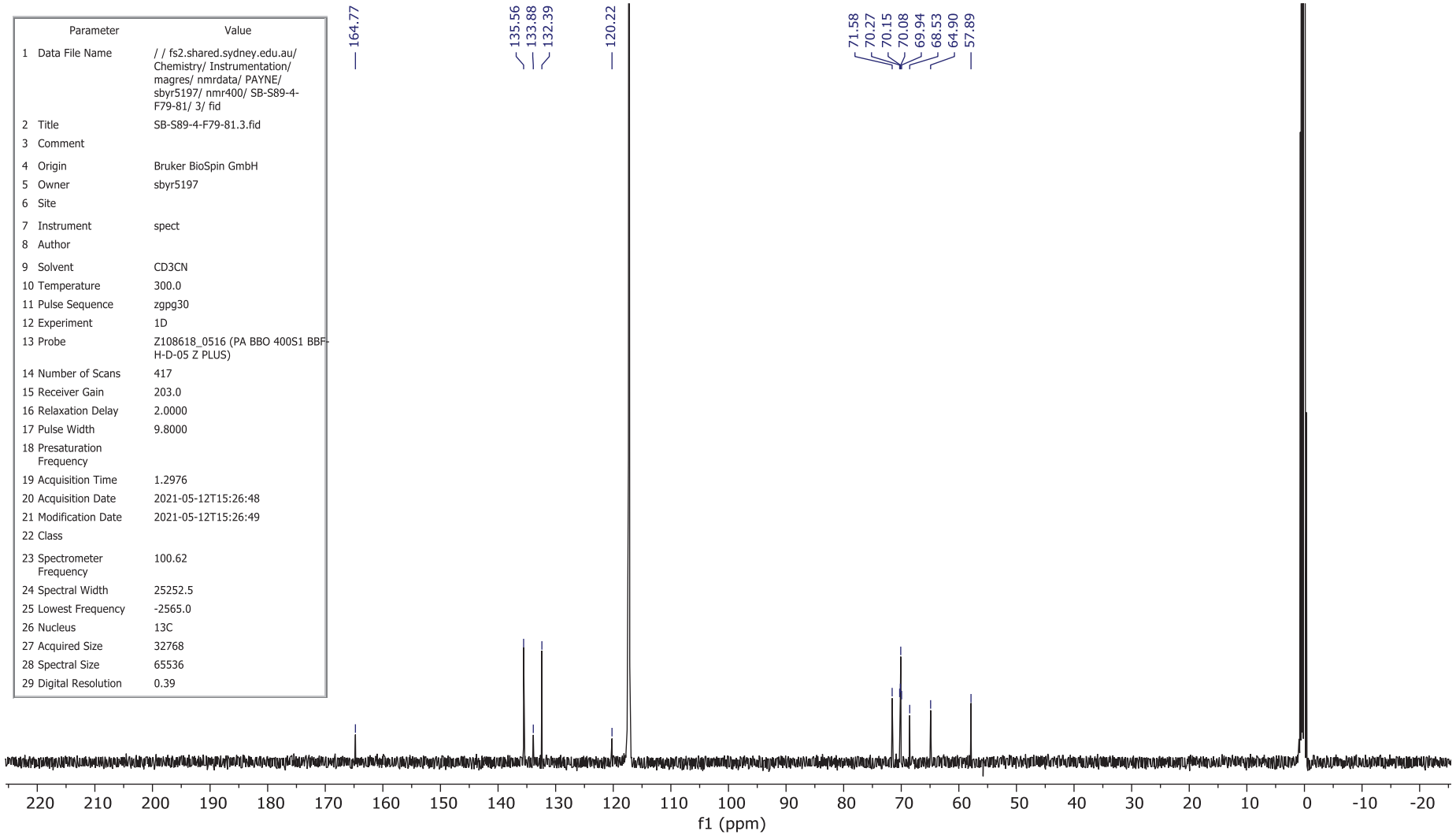
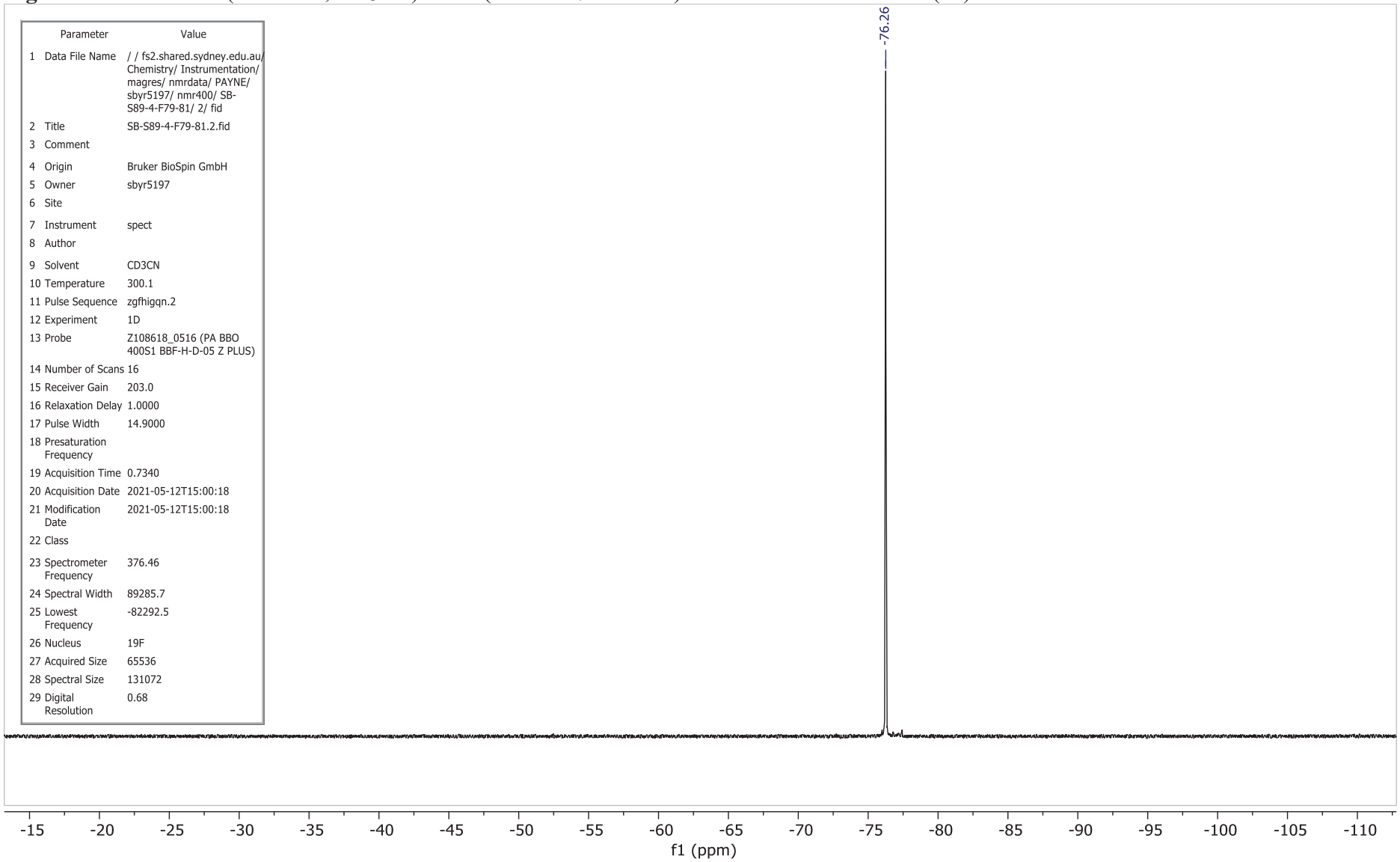


Figure S53: ^{19}F-NMR (376 MHz, CD_3CN) of Bis(4-mPEG$_4$ benzoate)iodonium trifluoroacetate (**20**)



	Parameter	Value
1	Data File Name	/ / fs2.shared.sydney.edu.au/ Chemistry/ Instrumentation/ magres/ nmrdata/ PAYNE/ sbyr5197/ nmr400/ SB-S89-4-F79-81/ 2/ fid
2	Title	SB-S89-4-F79-81.2.fid
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	sbyr5197
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	CD3CN
10	Temperature	300.1
11	Pulse Sequence	zgfhigqn.2
12	Experiment	1D
13	Probe	Z108618_0516 (PA BBO 400S1 BBF-H-D-05 Z PLUS)
14	Number of Scans	16
15	Receiver Gain	203.0
16	Relaxation Delay	1.0000
17	Pulse Width	14.9000
18	Presaturation Frequency	
19	Acquisition Time	0.7340
20	Acquisition Date	2021-05-12T15:00:18
21	Modification Date	2021-05-12T15:00:18
22	Class	
23	Spectrometer Frequency	376.46
24	Spectral Width	89285.7
25	Lowest Frequency	-82292.5
26	Nucleus	19F
27	Acquired Size	65536
28	Spectral Size	131072
29	Digital Resolution	0.68

Figure S54: ^{1}H-NMR (400 MHz, CD_3CN) of mPEG$_8$ 4-iodobenzoate (**S9**)

	Parameter	Value
1	Data File Name	/ / fs2.shared.sydney.edu.au/ Chemistry/ Instrumentation/ magres/ nmrdata/ PAYNE/ sbyr5197/ nmr400/ SB-S84-2/ 2/ fid
2	Title	SB-S84-2.2.fid
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	sbyr5197
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	CD3CN
10	Temperature	300.0
11	Pulse Sequence	zg
12	Experiment	1D
13	Probe	Z108618_0516 (PA BBO 400S1 BBF-H-D-05 Z PLUS)
14	Number of Scans	8
15	Receiver Gain	28.5
16	Relaxation Delay	5.0000
17	Pulse Width	14.9000
18	Presaturation Frequency	
19	Acquisition Time	3.0048
20	Acquisition Date	2021-03-25T16:47:40
21	Modification Date	2021-03-25T16:47:40
22	Class	
23	Spectrometer Frequency	400.13
24	Spectral Width	8000.0
25	Lowest Frequency	-1610.5
26	Nucleus	1H
27	Acquired Size	24038
28	Spectral Size	65536
29	Digital Resolution	0.12

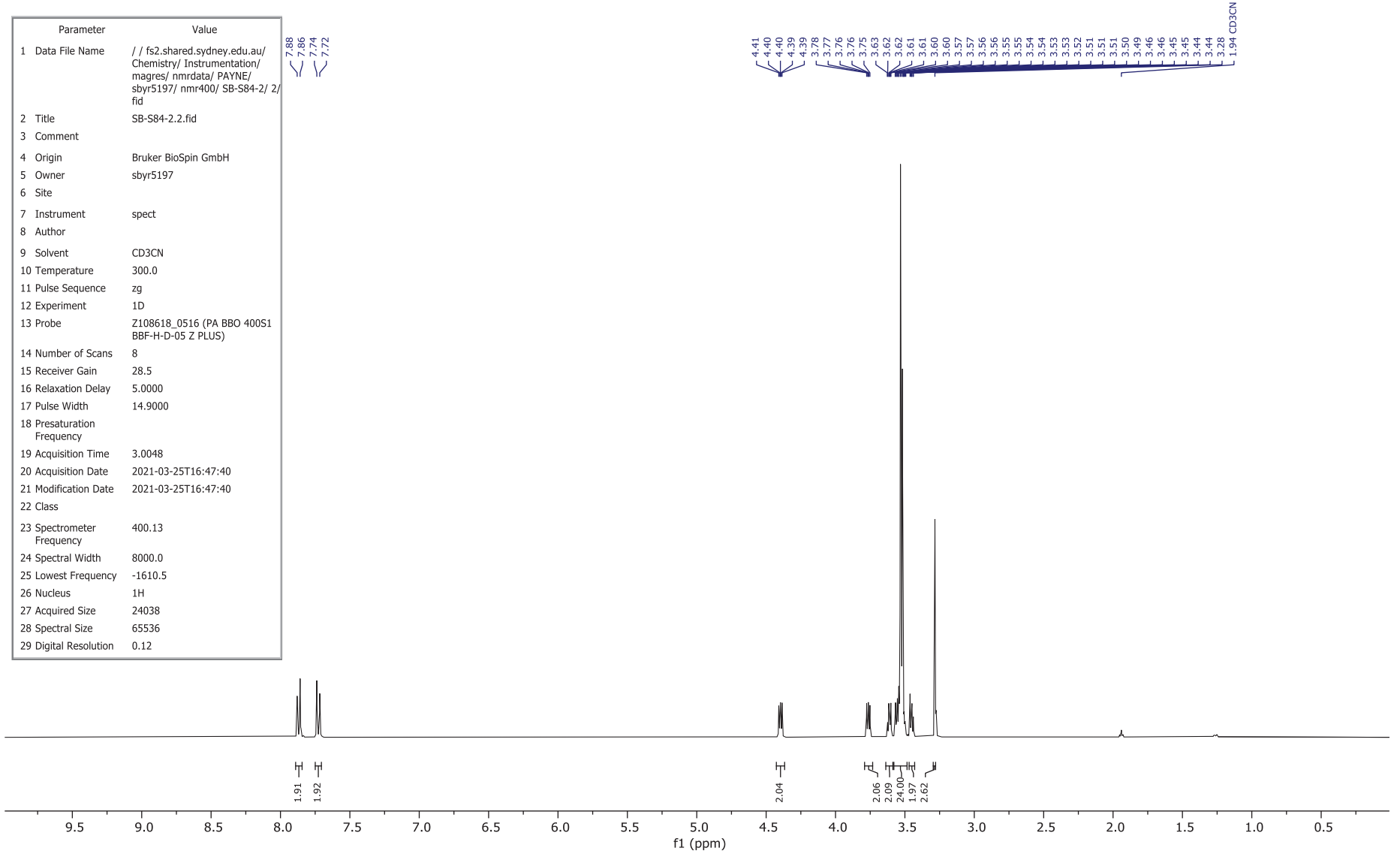
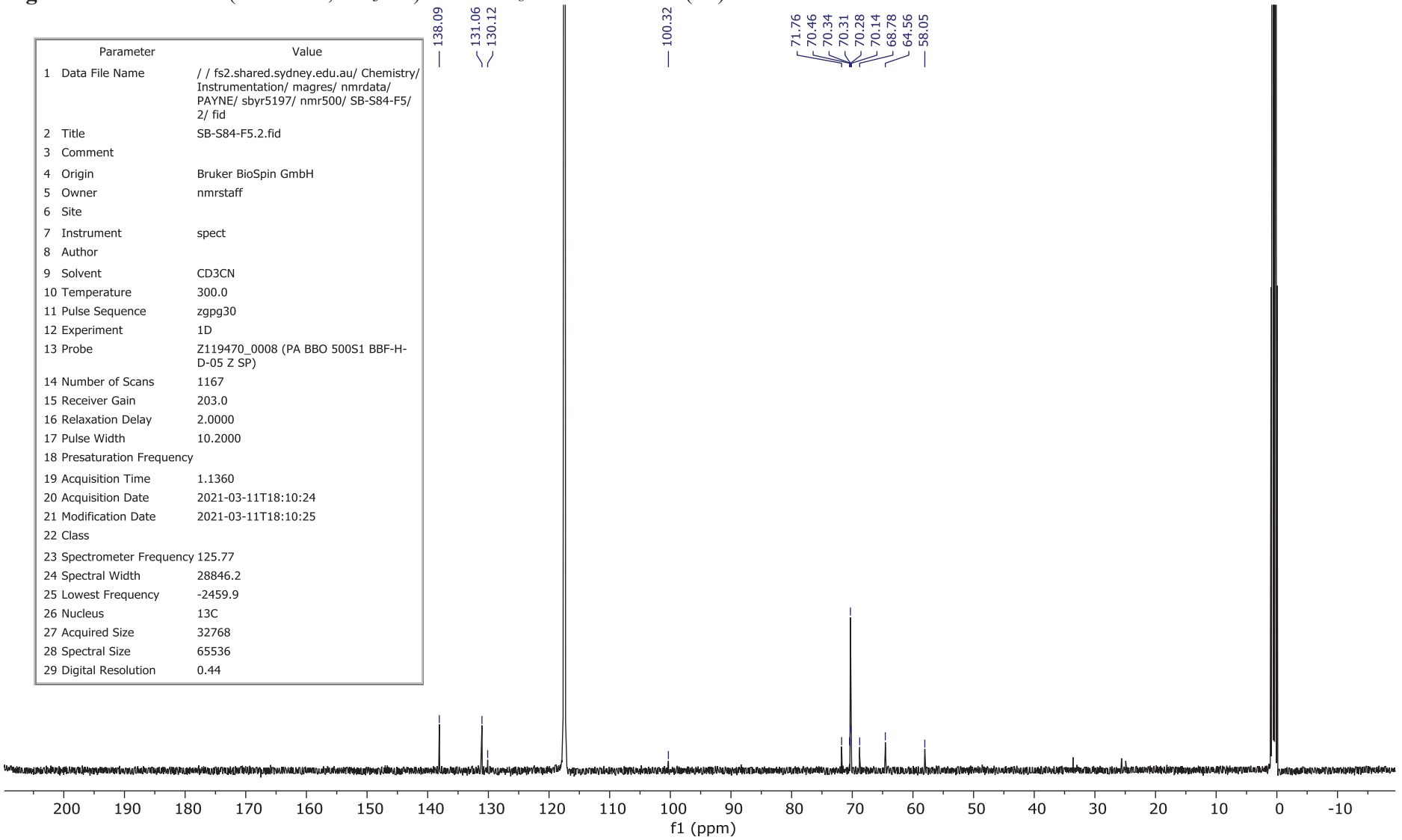


Figure S55: ^{13}C-NMR (126 MHz, CD_3CN) of mPEG$_8$ 4-iodobenzoate (**S9**)



	Parameter	Value
1	Data File Name	/ / fs2.shared.sydney.edu.au/ Chemistry/ Instrumentation/ magres/ nmrdata/ PAYNE/ sbyr5197/ nmr500/ SB-S84-F5/ 2/ fid
2	Title	SB-S84-F5.2.fid
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	nmrstaff
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	CD3CN
10	Temperature	300.0
11	Pulse Sequence	zgpg30
12	Experiment	1D
13	Probe	Z119470_0008 (PA BBO 500S1 BBF-H-D-05 Z SP)
14	Number of Scans	1167
15	Receiver Gain	203.0
16	Relaxation Delay	2.0000
17	Pulse Width	10.2000
18	Presaturation Frequency	
19	Acquisition Time	1.1360
20	Acquisition Date	2021-03-11T18:10:24
21	Modification Date	2021-03-11T18:10:25
22	Class	
23	Spectrometer Frequency	125.77
24	Spectral Width	28846.2
25	Lowest Frequency	-2459.9
26	Nucleus	13C
27	Acquired Size	32768
28	Spectral Size	65536
29	Digital Resolution	0.44

Figure S56. ^{1}H-NMR (500 MHz, MeOD) (4-(mPEG$_8$-carbonyl)phenyl)boronic acid (**S10**)

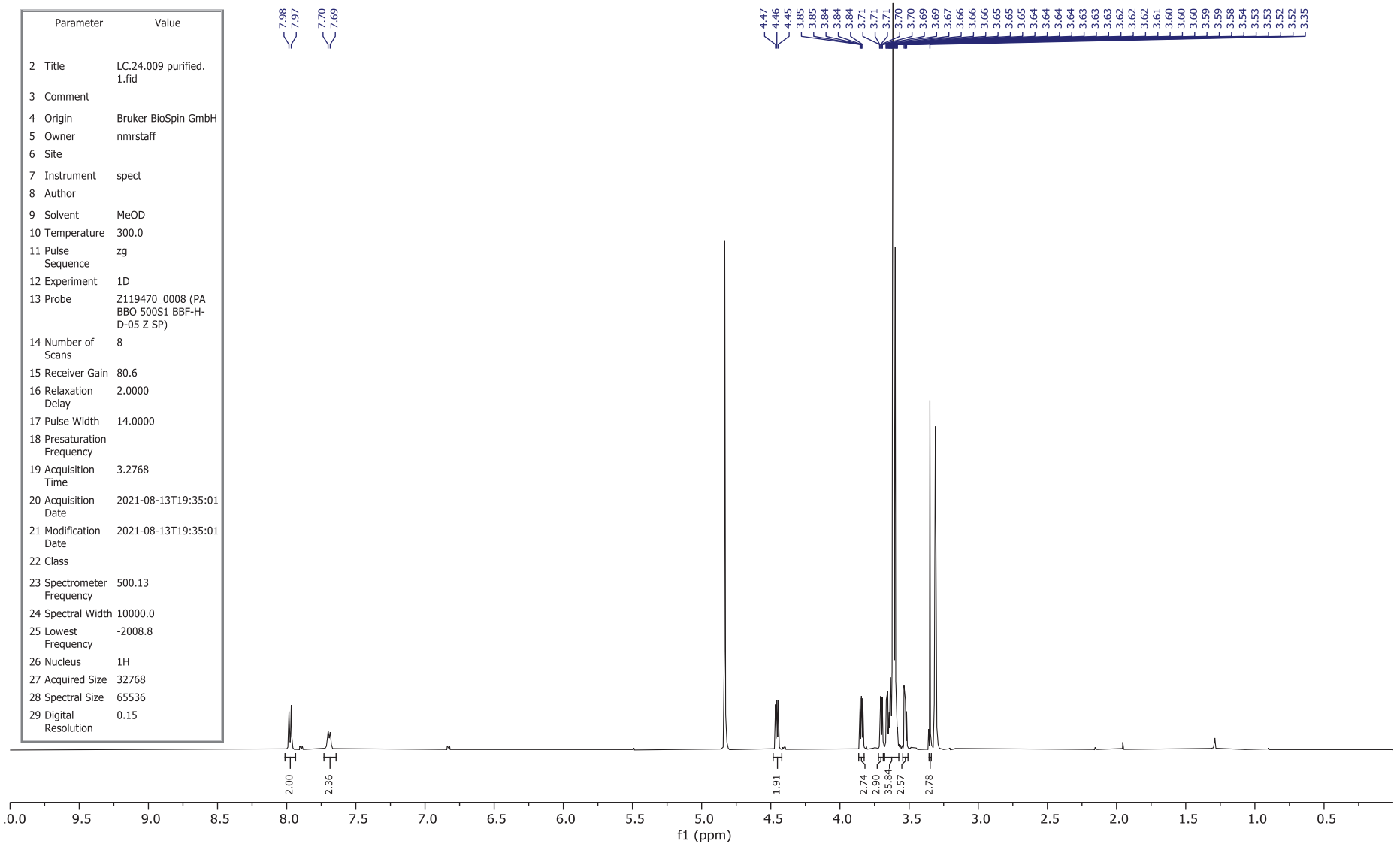


Figure S57. ^{13}C NMR (126 MHz, MeOD) (4-(mPEG$_8$-carbonyl)phenyl)boronic acid (**S10**)

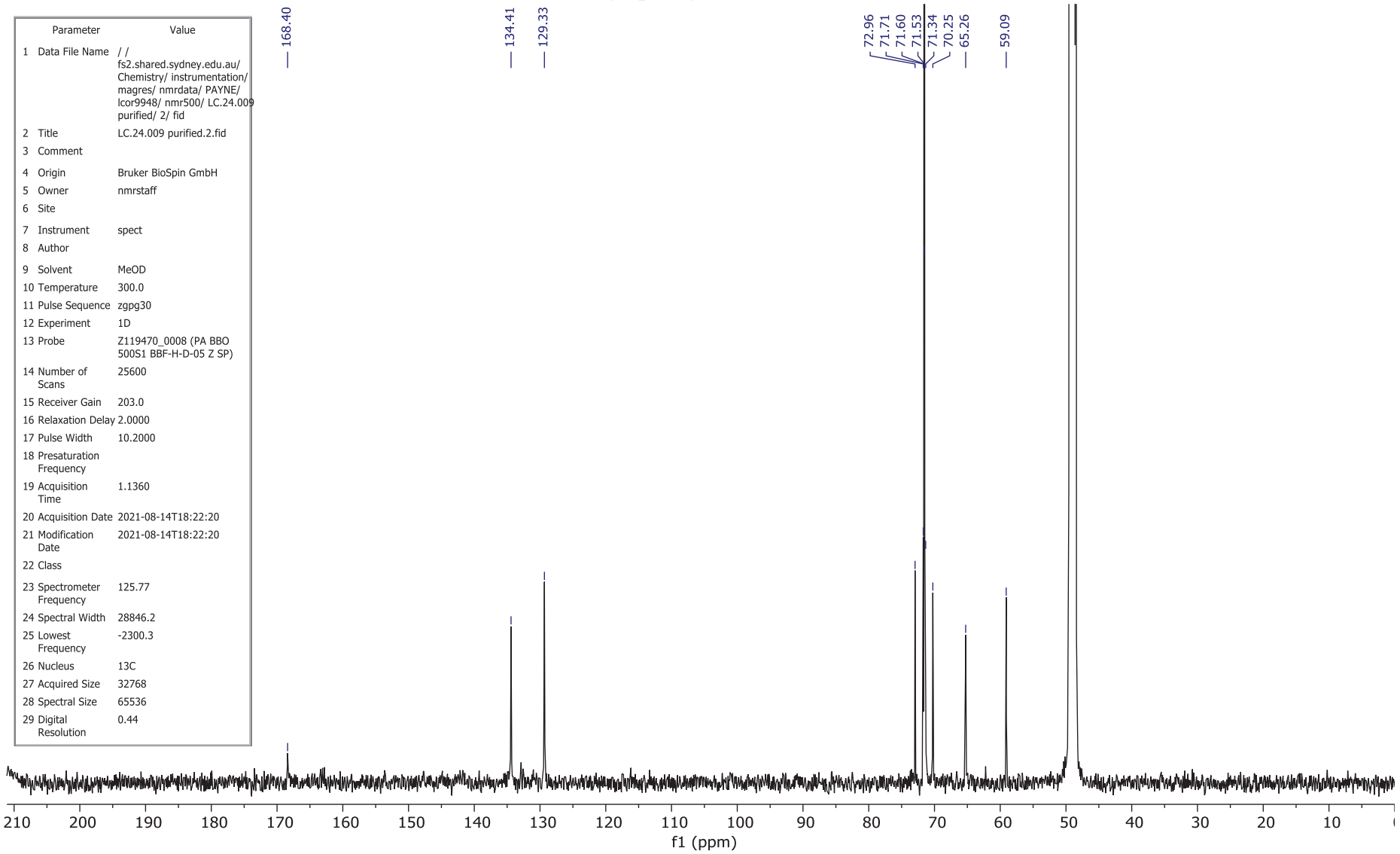


Figure S58: ^{1}H-NMR (500 MHz, CD_3CN) of Bis(4-mPEG$_8$ benzoate)iodonium trifluoroacetate (**21**)

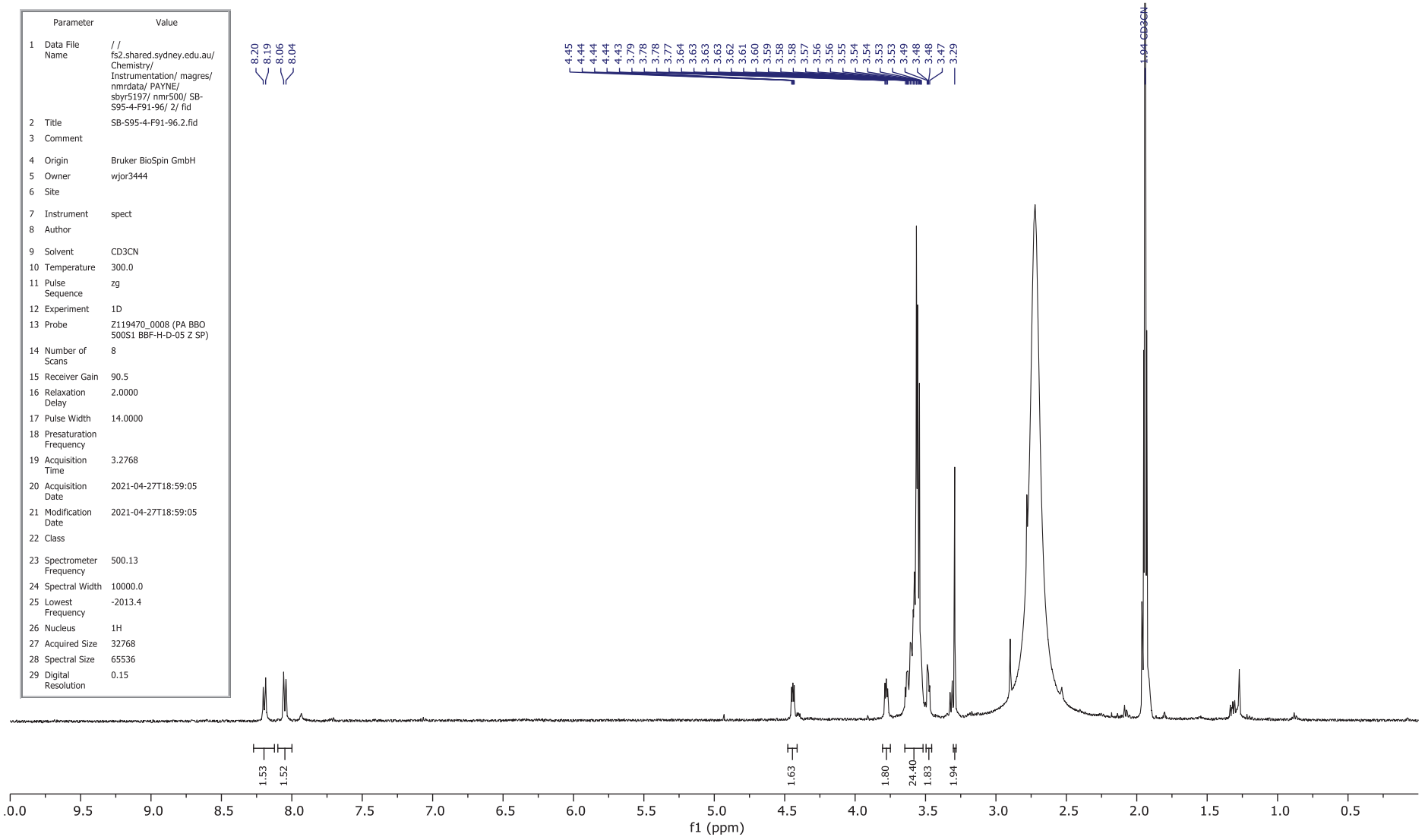
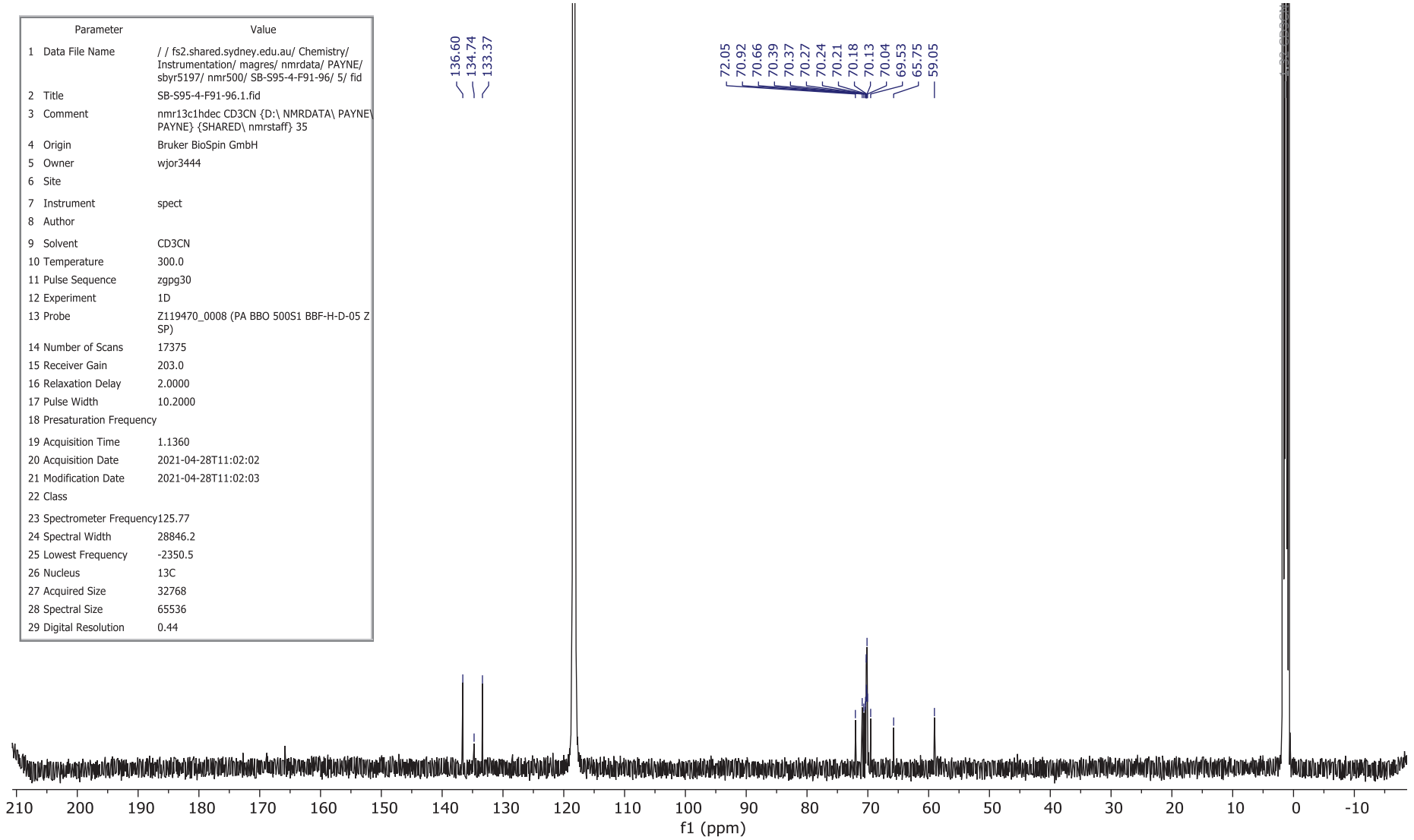
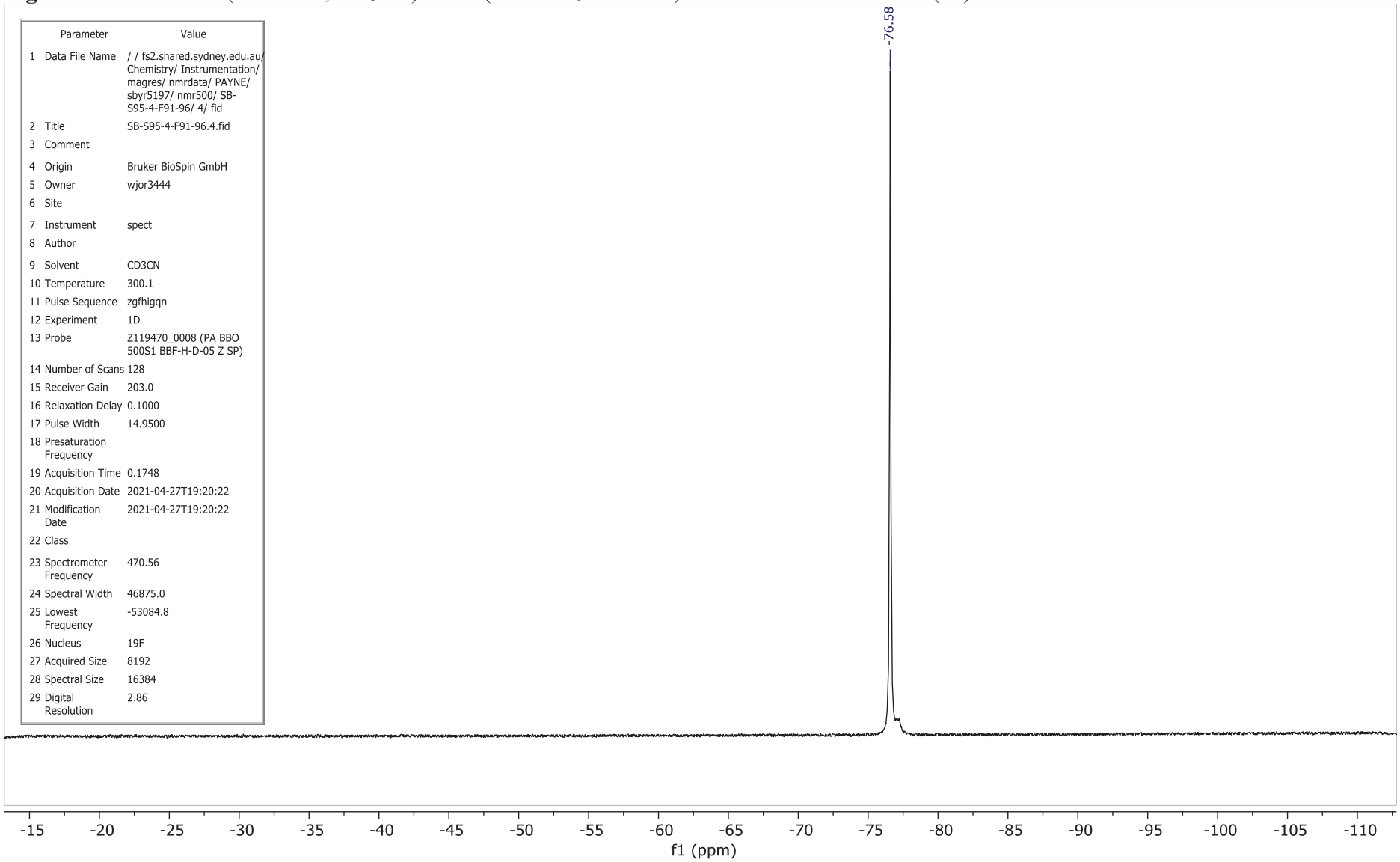


Figure S59: ^{13}C-NMR (126 MHz, CD_3CN) of Bis(4-mPEG$_8$ benzoate)iodonium trifluoroacetate (**21**)



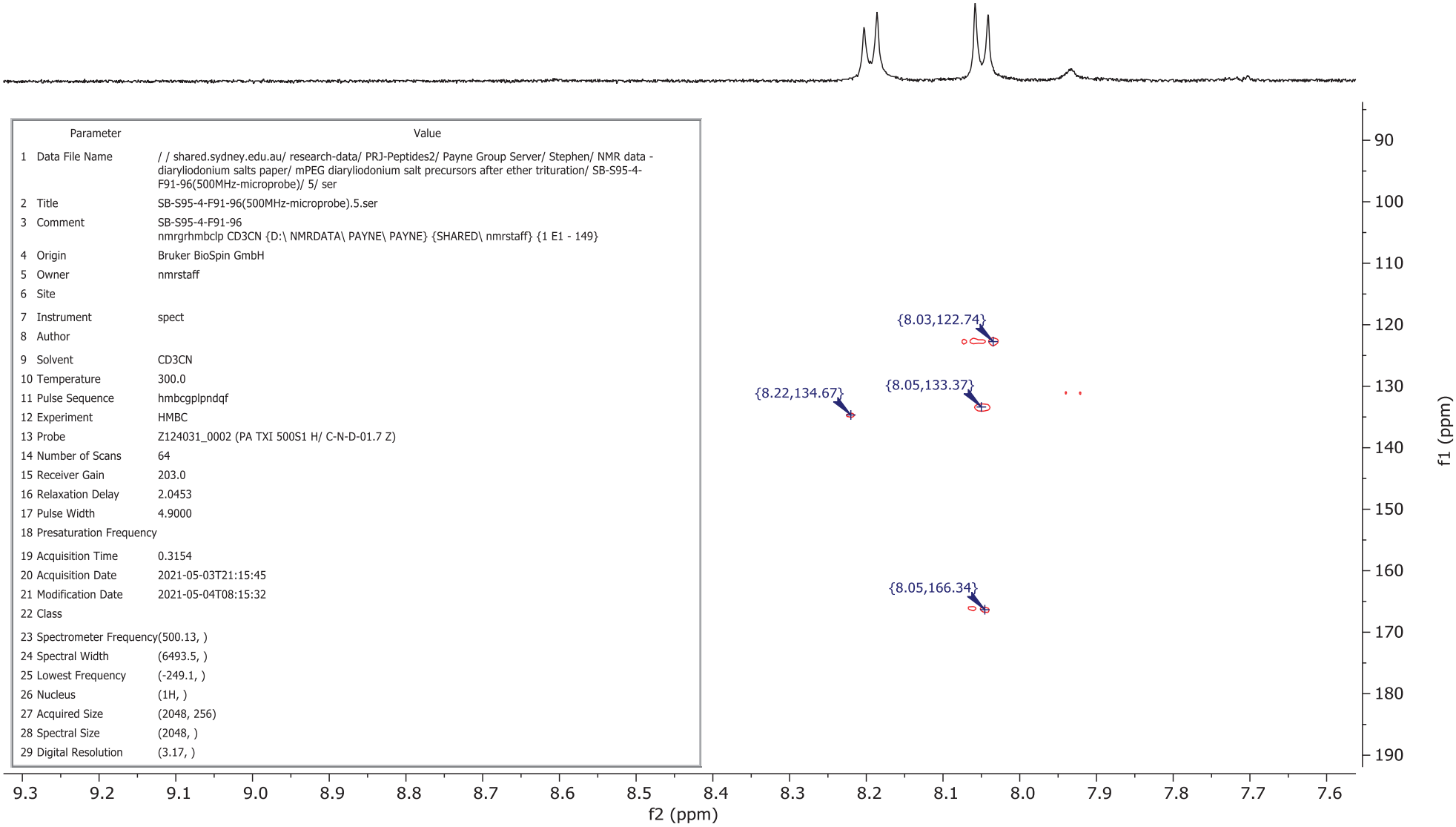
	Parameter	Value
1	Data File Name	/ / fs2.shared.sydney.edu.au/ Chemistry/ Instrumentation/ magres/ nmrdata/ PAYNE/ sbyr5197/ nmr500/ SB-S95-4-F91-96/ 5/ fid
2	Title	SB-S95-4-F91-96.1.fid
3	Comment	nmr13c1hdec CD3CN {D:\ NMRDATA\ PAYNE\ PAYNE} {SHARED\ nmrstaff} 35
4	Origin	Bruker BioSpin GmbH
5	Owner	wjor3444
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	CD3CN
10	Temperature	300.0
11	Pulse Sequence	zgpg30
12	Experiment	1D
13	Probe	Z119470_0008 (PA BBO 500S1 BBF-H-D-05 Z SP)
14	Number of Scans	17375
15	Receiver Gain	203.0
16	Relaxation Delay	2.0000
17	Pulse Width	10.2000
18	Presaturation Frequency	
19	Acquisition Time	1.1360
20	Acquisition Date	2021-04-28T11:02:02
21	Modification Date	2021-04-28T11:02:03
22	Class	
23	Spectrometer Frequency	125.77
24	Spectral Width	28846.2
25	Lowest Frequency	-2350.5
26	Nucleus	13C
27	Acquired Size	32768
28	Spectral Size	65536
29	Digital Resolution	0.44

Figure S60: ^{19}F-NMR (471 MHz, CD_3CN) of Bis(4-mPEG$_8$ benzoate)iodonium trifluoroacetate (**21**)



	Parameter	Value
1	Data File Name	/ / fs2.shared.sydney.edu.au/ Chemistry/ Instrumentation/ magres/ nmrdata/ PAYNE/ sbyr5197/ nmr500/ SB-S95-4-F91-96/ 4/ fid
2	Title	SB-S95-4-F91-96.4.fid
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	wjor3444
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	CD3CN
10	Temperature	300.1
11	Pulse Sequence	zgfhigqn
12	Experiment	1D
13	Probe	Z119470_0008 (PA BBO 500S1 BBF-H-D-05 Z SP)
14	Number of Scans	128
15	Receiver Gain	203.0
16	Relaxation Delay	0.1000
17	Pulse Width	14.9500
18	Presaturation Frequency	
19	Acquisition Time	0.1748
20	Acquisition Date	2021-04-27T19:20:22
21	Modification Date	2021-04-27T19:20:22
22	Class	
23	Spectrometer Frequency	470.56
24	Spectral Width	46875.0
25	Lowest Frequency	-53084.8
26	Nucleus	19F
27	Acquired Size	8192
28	Spectral Size	16384
29	Digital Resolution	2.86

Figure S61: ^{1}H-^{13}C- HMBC-NMR (500/126 MHz, CD_3CN) of Bis(4-mPEG$_8$ benzoate)iodonium trifluoroacetate (**21**)



	Parameter	Value
1	Data File Name	/ / shared.sydney.edu.au/ research-data/ PRJ-Peptides2/ Payne Group Server/ Stephen/ NMR data - diaryliodonium salts paper/ mPEG diaryliodonium salt precursors after ether trituration/ SB-S95-4-F91-96(500MHz-microprobe)/ 5/ ser
2	Title	SB-S95-4-F91-96(500MHz-microprobe).5.ser
3	Comment	SB-S95-4-F91-96 nmrgrhmbclp CD3CN {D:\ NMRDATA\ PAYNE\ PAYNE} {SHARED\ nmrstaff} {1 E1 - 149}
4	Origin	Bruker BioSpin GmbH
5	Owner	nmrstaff
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	CD3CN
10	Temperature	300.0
11	Pulse Sequence	hmbcgplpndqf
12	Experiment	HMBC
13	Probe	Z124031_0002 (PA TXI 500S1 H/ C-N-D-01.7 Z)
14	Number of Scans	64
15	Receiver Gain	203.0
16	Relaxation Delay	2.0453
17	Pulse Width	4.9000
18	Presaturation Frequency	
19	Acquisition Time	0.3154
20	Acquisition Date	2021-05-03T21:15:45
21	Modification Date	2021-05-04T08:15:32
22	Class	
23	Spectrometer Frequency	(500.13,)
24	Spectral Width	(6493.5,)
25	Lowest Frequency	(-249.1,)
26	Nucleus	(1H,)
27	Acquired Size	(2048, 256)
28	Spectral Size	(2048,)
29	Digital Resolution	(3.17,)

Figure S62: ^{1}H NMR (400 MHz, DMSO-d_6) of (4-methoxyphenyl)(2,6-dimethylphenyl)iodonium tetrafluoroborate (**S12**)

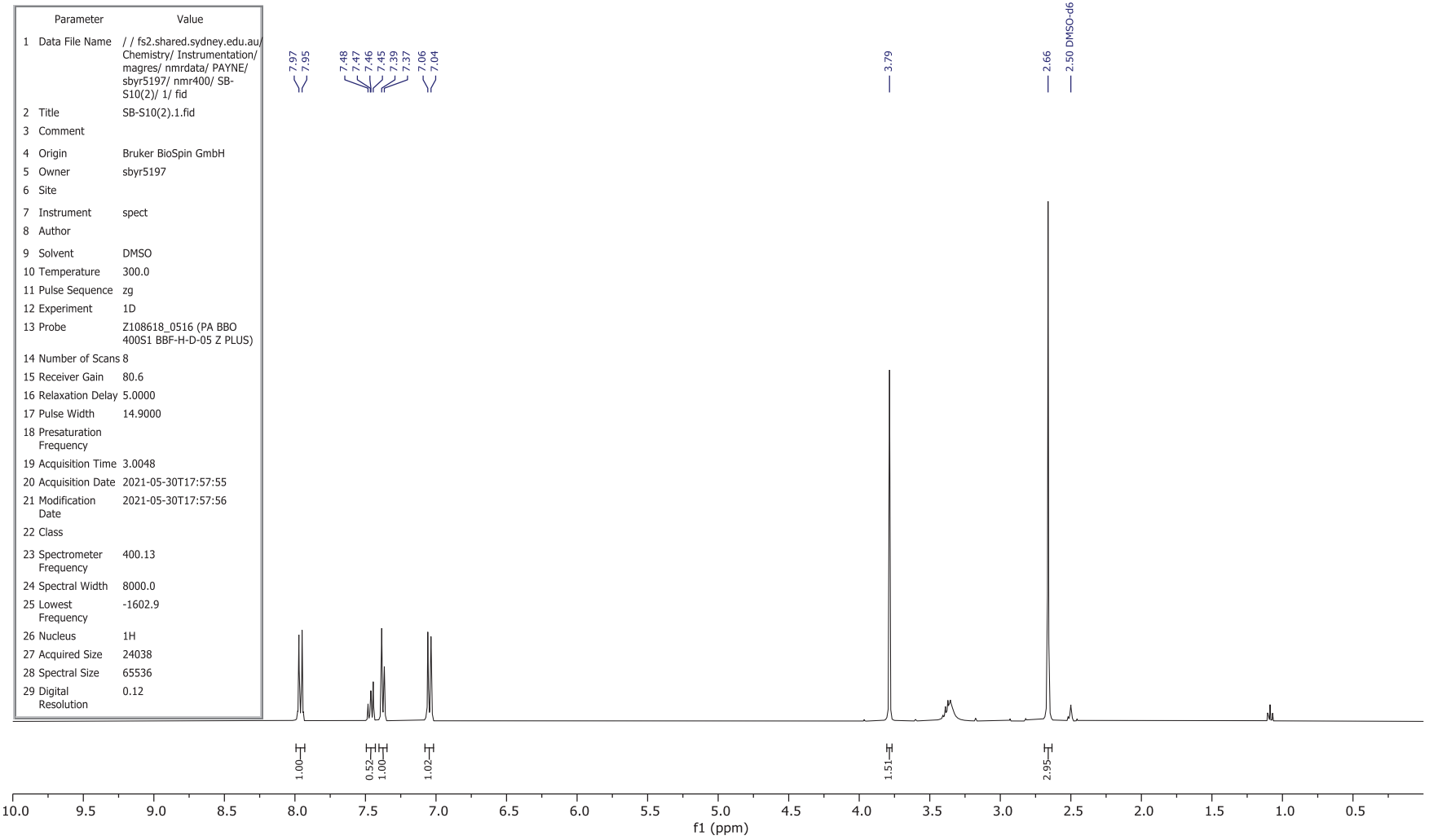
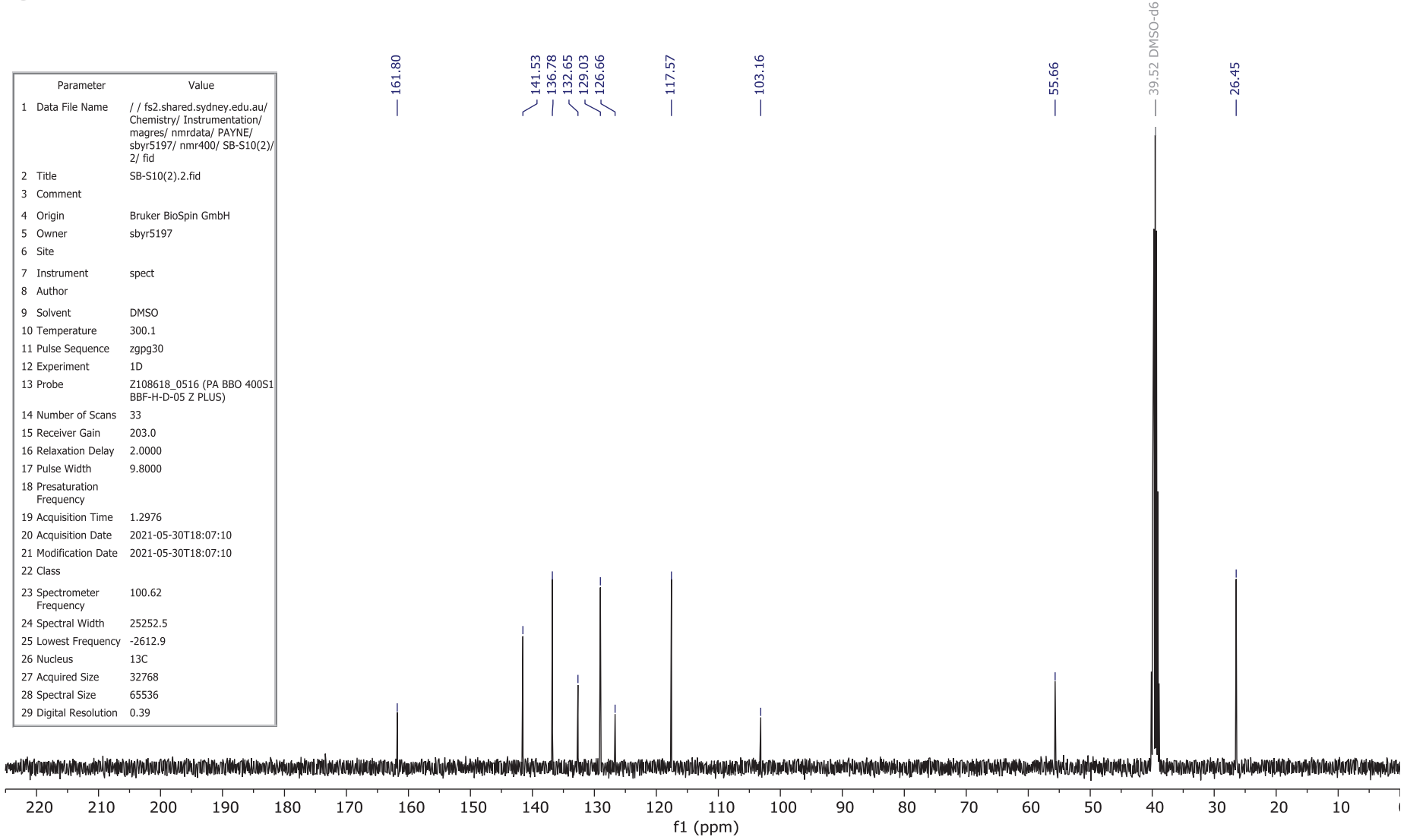
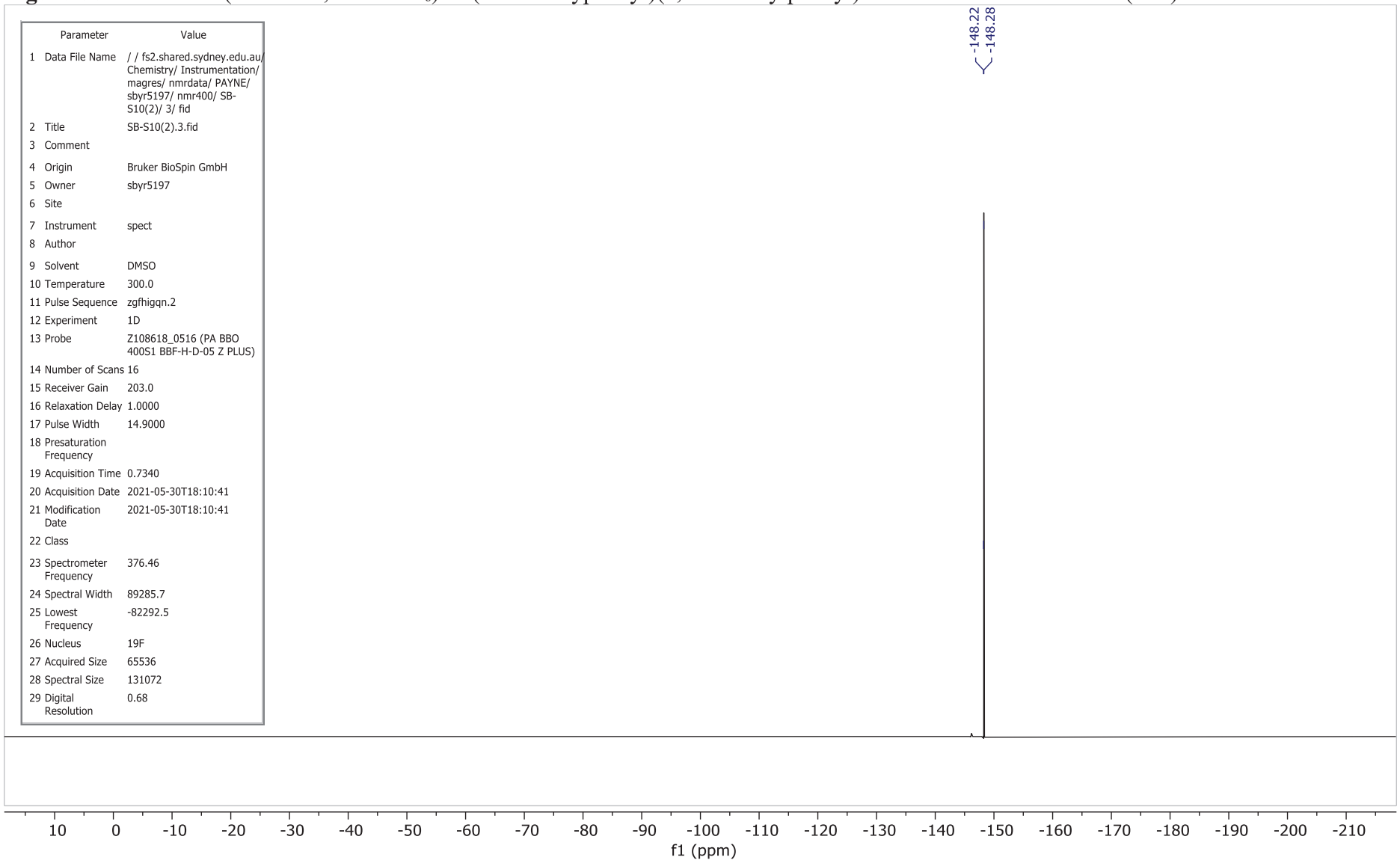


Figure S63: ^{13}C NMR (101 MHz, DMSO-d_6) of (4-methoxyphenyl)(2,6-dimethylphenyl)iodonium tetrafluoroborate (**S12**)



	Parameter	Value
1	Data File Name	/ / fs2.shared.sydney.edu.au/ Chemistry/ Instrumentation/ magres/ nmrdata/ PAYNE/ sbyr5197/ nmr400/ SB-S10(2)/ 2/ fid
2	Title	SB-S10(2).2.fid
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	sbyr5197
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	DMSO
10	Temperature	300.1
11	Pulse Sequence	zgpg30
12	Experiment	1D
13	Probe	Z108618_0516 (PA BBO 400S1 BBF-H-D-05 Z PLUS)
14	Number of Scans	33
15	Receiver Gain	203.0
16	Relaxation Delay	2.0000
17	Pulse Width	9.8000
18	Presaturation Frequency	
19	Acquisition Time	1.2976
20	Acquisition Date	2021-05-30T18:07:10
21	Modification Date	2021-05-30T18:07:10
22	Class	
23	Spectrometer Frequency	100.62
24	Spectral Width	25252.5
25	Lowest Frequency	-2612.9
26	Nucleus	13C
27	Acquired Size	32768
28	Spectral Size	65536
29	Digital Resolution	0.39

Figure S64: ^{19}F NMR (376 MHz, DMSO-d_6) of (4-methoxyphenyl)(2,6-dimethylphenyl)iodonium tetrafluoroborate (**S12**)



	Parameter	Value
1	Data File Name	/ / fs2.shared.sydney.edu.au/ Chemistry/ Instrumentation/ magres/ nmrdata/ PAYNE/ sbyr5197/ nmr400/ SB-S10(2)/ 3/ fid
2	Title	SB-S10(2).3.fid
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	sbyr5197
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	DMSO
10	Temperature	300.0
11	Pulse Sequence	zgfhigqn.2
12	Experiment	1D
13	Probe	Z108618_0516 (PA BBO 400S1 BBF-H-D-05 Z PLUS)
14	Number of Scans	16
15	Receiver Gain	203.0
16	Relaxation Delay	1.0000
17	Pulse Width	14.9000
18	Presaturation Frequency	
19	Acquisition Time	0.7340
20	Acquisition Date	2021-05-30T18:10:41
21	Modification Date	2021-05-30T18:10:41
22	Class	
23	Spectrometer Frequency	376.46
24	Spectral Width	89285.7
25	Lowest Frequency	-82292.5
26	Nucleus	19F
27	Acquired Size	65536
28	Spectral Size	131072
29	Digital Resolution	0.68