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Supplementary Information

Synthesis and Evaluation of Peptidic Thrombin Inhibitors Bearing Acid-Stable Sulfotyrosine Analogues

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1 GENERAL MATERIALS

Peptide grade *N,N*-dimethylformamide (DMF) and dichloromethane (CH_2Cl_2) for peptide synthesis were purchased from RCI Labscan and Merck, respectively. Gradient grade acetonitrile (MeCN) for chromatography was purchased from Sigma Aldrich and ultrapure water (Type 1) was obtained from a Merck Millipore Direct-Q 5 water purification System. All chromatography solvents were supplemented with either trifluoroacetic acid (TFA) or formic acid (FA) purchased from Sigma-Aldrich as indicated. Standard Fmoc-protected amino acids (Fmoc-Xaa-OH), coupling reagents and resins were purchased from Mimotopes and Novabiochem. Fmoc-SPPS was performed manually in polypropylene Teflon-fritted syringes purchased from Torviq or through automated synthesis on a Gyros Protein Technologies® Symphony automated peptide synthesiser or a CEM® Liberty Blue automated microwave peptide synthesiser at temperatures as specified. All other reagents were purchased from Sigma Aldrich, AK Scientific or Merck and used as received.

All reactions were carried out under an argon atmosphere and at room temperature (22 °C) unless the reaction was performed under aqueous conditions or unless otherwise specified. Reactions undertaken at -78 °C utilised a bath of dry ice and acetone. Reactions carried out at 0 °C employed a bath of water and ice. Anhydrous THF, CH_2Cl_2 and MeOH were obtained using a PureSolv solvent purification system with water detectable only in low ppm levels. Reactions were monitored by thin layer chromatography (TLC) on aluminium backed silica plates (Merck Silica Gel 60 F254). Visualisation of TLC plates was undertaken with an ultraviolet (UV) light at λ = 254 nm and staining with solutions of vanillin, ninhydrin, phosphomolybdic acid (PMA), potassium permanganate or sulfuric acid, followed by exposure of the stained plates to heat. Silica flash column chromatography (Merck Silica Gel 60 40 – 63 μm) was undertaken to purify crude reaction mixtures using solvents as specified.

2 GENERAL PROCEDURES

2.1 RESIN LOADING

2.1.1 2-CHLOROTRITYL CHLORIDE (2-CTC) RESIN

2-CTC resin (1.14 mmol g^{-1} loading unless otherwise specified, Novabiochem) was swollen in CH_2Cl_2 for 30 min and then washed with CH_2Cl_2 (4 x 2 mL). The resin was treated with a solution of thionyl chloride in CH_2Cl_2 (2 vol%) for 30 minutes and then thoroughly washed with CH_2Cl_2 (10 x 2 mL). The washed resin was then treated with a solution of Fmoc-protected amino acid (2 equiv.) and *i*Pr_2NEt (8 equiv.) in CH_2Cl_2 (*c* = 0.1 M) for 16 h at room temperature. The resin was then filtered and washed with CH_2Cl_2 (4 x 2 mL) before being treated with a solution of methanol and *i*Pr_2NEt in CH_2Cl_2 (17:2:1 v/v/v CH_2Cl_2:MeOH:*i*Pr_2NEt) for 30 min at room temperature. The resin was finally filtered and washed with CH_2Cl_2 (4 x 2 mL) and DMF (4 x 2 mL) prior to iterative peptide assembly.

2.1.2 WANG RESIN

Wang resin (0.92 mmol g^{-1} loading unless otherwise specified, Bachem) was swollen in CH_2Cl_2 for 30 min and then washed with CH_2Cl_2 (4 x 2 mL). While the resin was swelling, the Fmoc-Xaa-OH (10 equiv.) to be loaded was dissolved in CH_2Cl_2 (*c* = 0.2 M) and cooled to 0 °C. *N,N'*-Diisopropylcarbodiimide (DIC) (5 equiv.) was then added to the amino acid solution, which was subsequently warmed to room temperature and stirred for 30 min until a white precipitate formed. The mixture was then concentrated under a stream of nitrogen gas to form a crude solid. The solid was then dissolved in 1:1 v/v CH_2Cl_2:DMF (*c* = 1 M), to which a small amount of 4-dimethylaminopyridine (DMAP) (cat.) was then added. The loading solution was then applied to the swollen resin which was shaken at room temperature for 16 h. The loading solution was then ejected, and the resin washed with CH_2Cl_2 (4 x 2 mL), DMF (4 x 2 mL) and CH_2Cl_2 (5 x 2 mL) before being treated with a capping solution of 10 vol% Ac_2O in CH_2Cl_2 (with cat. DMAP) for 45 min at room temperature. Finally, the capping solution was ejected, and the resin was washed with CH_2Cl_2 (4 x 2 mL) and DMF (4 x 2 mL) prior to iterative peptide assembly.

2.2 ITERATIVE PEPTIDE ASSEMBLY

2.2.1 DEPROTECTION CYCLES

Automated Deprotection (Symphony): The resin was treated with a solution of 20 vol% piperidine in DMF (2 x 2 mL x 3 min), filtered and then washed with DMF (4 x 2 mL).

Automated Deprotection (Liberty Blue): The resin was treated with a solution of 20 vol% piperidine in DMF (1 x 10 mL) at 90 °C for 50 s, then filtered and washed with DMF (4 x 4 mL).

Manual Deprotection: The resin was treated with a solution of 20 vol% piperidine in DMF (3 x 2 mL x 3 min), filtered and then washed with DMF (4 x 2 mL).

2.2.2 COUPLING CYCLES

Automated Coupling (Symphony): The resin was treated with a solution of Fmoc-Xaa-OH (4 equiv.), DIC (4 equiv.) and Oxyma (4 equiv.) in DMF ([Fmoc-Xaa-OH] = 0.3 M) for 40 min at room temperature. The resin was then filtered and washed with DMF (4 x 2 mL).

Automated Coupling (Liberty Blue): The resin was treated with a solution of Fmoc-Xaa-OH (5 mL, 0.2 M), DIC (2 mL, 0.5 M) and Oxyma (1 mL, 1 M) at 90 °C for 2 min,* then filtered and subjected immediately to the next deprotection cycle.

> **All Fmoc-Arg(Pbf)-OH residues were coupled twice before subsequent deprotection.*
>
> **All Fmoc-His(Trt)-OH residues were coupled at 50 °C for 10 min.*

Manual Coupling (Non-Standard): The resin was treated with a solution of Fmoc-Xaa-OH (1.5 equiv.), DIC (1.5 equiv.) and 1-hydroxy-7-azabenzotriazole (HOAt) (3 equiv.) in DMF ([Fmoc-Xaa-OH] = 0.1 M) for 16 h at room temperature. The resin was then filtered and washed with DMF (4 x 2 mL).

2.2.3 CAPPING CYCLES

Automated Capping (Symphony): The resin was treated with a solution of Ac_2O (2.5 vol%) and *i*Pr_2NEt (5 vol%) in DMF for 5 min at room temperature then washed with DMF (4 x 2 mL).

Manual Capping: The resin was treated with a solution of Ac_2O (10 vol%) in piperidine for 5 min at room temperature then washed with DMF (4 x 2 mL).

2.2.4 CLEAVAGE FROM RESIN

The resin was washed with CH_2Cl_2 (10 x 2 mL) then treated with an acidic cocktail of TFA:*i*Pr_3SiH:H_2O (90:5:5 v/v/v, 1-5 mL) for 2-3 h at room temperature with agitation. The cleavage cocktail was then ejected into a 50 mL centrifuge tube and concentrated under a gentle stream of N_2 gas. Once reduced to a small volume (~0.5 mL), pre-cooled Et_2O (~ 40 mL) was added to precipitate crude peptide. The resulting precipitate was pelleted by centrifugation (4000 x g, 5 min, 4 °C), the ether supernatant decanted and the remaining peptide pellet allowed to dry under a gentle stream of N_2 gas. This dry pellet was then stored at -20 °C until purification or further use.

2.3 PREPARATIVE CHROMATOGRAPHY

2.3.1 REVERSED-PHASE HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (RP-HPLC)

Preparative and semi-preparative reversed-phase high performance liquid chromatography (HPLC) was performed using a Waters 600E multisolvent delivery system with a Rheodyne 7725i injection valve (5 mL loading loop) with a Waters 500 pump and a Waters 490E programmable wavelength detector operating at 214 nm and 254 nm. Preparative reversed-phase HPLC was performed using a Waters Sunfire C18 column (5 µm, 19 x 150 mm or 5 µm, 30 x 150 mm) at a flow rate of either 14 mL min^{-1} or 38 mL min^{-1}. Semi-preparative reversed-phase HPLC was performed using a Waters Sunfire C18 column (5 µm, 10 x 250 mm) at a flow rate of 4 mL min^{-1}. All preparative and semi-preparative HPLC used a mobile phase of ultrapure (type 1) water (Solvent A) and MeCN (Solvent B) with 0.1 vol% trifluoroacetic acid (TFA) on linear gradients, unless otherwise specified.

2.4 Analytical Chromatography-Mass Spectrometry

2.4.1 Ultra performance Liquid Chromatography-Mass Spectrometry (UPLC-MS)

Ultra-performance liquid Chromatography-Mass Spectrometry (UPLC-MS) was performed on a Shimadzu 2020 UPLC-MS instrument with a Nexera X2 LC-30AD pump, Nexera X2 SPD-M30A UV/Vis diode array detector and a Shimadzu 2020 (ESI) mass spectrometer operating in positive mode. Separations were performed on a Waters Acquity BEH300 1.7 μm, 2.1 x 50 mm (C18) column at a flow rate of 0.6 mL min^{-1} unless otherwise specified. All separations were performed using a mobile phase of 0.1 vol% FA in water (Solvent A) and 0.1 vol% FA in MeCN (Solvent B) using linear gradients as specified.

2.4.2 Analytical Ultra Performance Liquid Chromatography (UPLC)

Analytical UPLC was performed on a Waters Acquity UPLC system equipped with a PDA eλ detector (λ = 210 – 400 nm), a sample manager FAN and Quaternary Solvent Manager (H-Class) modules. Separations were performed on a Waters Acquity BEH300 1.7 μm, 2.1 x 50 mm (C18) column at a flow rate of 0.6 mL min^{-1}. All separations were performed using a mobile phase of 0.1 vol% TFA in water (Solvent A) and 0.1 vol% TFA in MeCN (Solvent B) using linear gradients as specified.

2.5 Nuclear Magnetic Resonance (NMR) Spectroscopy

^{1}H NMR spectra were obtained at 300 K using a Bruker Avance DRX 400 or DRX 500 at frequencies of 400 MHz or 500 MHz, respectively, in $CDCl_3$, MeOD or D_2O. Chemical shifts are reported in parts per million (ppm) and coupling constant(s) (*J*) in Hertz (Hz). The residual solvent peaks were used as internal standards (e.g. $CDCl_3$ δ: 7.26 ppm) without the use of tetramethylsilane (TMS). ^{1}H NMR data are reported as follows: chemical shift values (ppm), relative integral, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), *J* in Hz, and assignments where possible. ^{13}C $\{^{1}H\}$ NMR spectra were obtained using a Bruker DRX 400 or DRX 500 at 100 MHz or 126 MHz in $CDCl_3$, D_2O or MeOD unless otherwise specified. ^{13}C $\{^{1}H\}$ NMR data are reported as chemical shift values (ppm) referenced to the solvent resonance (e.g. $CDCl_3$ δ: 77.2 ppm).

2.6 MASS SPECTROMETRY (MS)

2.6.1 ELECTROSPRAY IONISATION (ESI) LOW RESOLUTION MS

Low resolution mass spectra for novel compounds were recorded on a Bruker amaZon SL mass spectrometer (ESI) operating in positive mode or on a Shimadzu 2020 (ESI) mass spectrometer operating in positive mode for previously reported compounds.

2.6.2 ELECTROSPRAY IONISATION (ESI) HIGH RESOLUTION MS

High resolution mass spectra were recorded on a Bruker-Daltronics Apex Ultra 7.0 T Fourier transform (FTICR) mass spectrometer using a matrix of α-cyano-4-hydroxycinnamic acid in 1:1 v/v water:MeCN containing 0.1 vol% TFA.

2.7 INFRARED (IR) SPECTROSCOPY

Infrared (IR) spectra were obtained on a Bruker ALPHA spectrometer with Attenuated Total Reflection (ATR) capability and using OPUS 6.5 software.

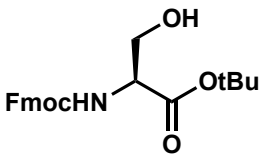
2.8 POLARIMETRY

Optical rotation measurements were obtained on a Perkin-Elmer 341 polarimeter at 589 nm (sodium D line) with a cell path length of 1 dm. Concentrations are reported in g/100 mL.

2.9 MELTING POINT MEASUREMENT

Melting point measurements were obtained on a Stanford Research Systems OptiMelt automated melting point system by visual inspection of the material.

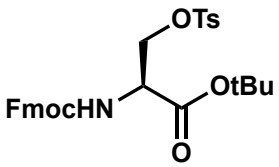
3 SYNTHESIS OF FMOC-PROTECTED SULFONATED TYROSINE BUILDING BLOCKS



***tert*-butyl (((9*H*-fluoren-9-yl)methoxy)carbonyl)-L-serinate**

A solution of *tert*-butyl 2,2,2-trichloroacetimidate (21.8 mL, 122 mmol) in cyclohexane (125 mL) was added to a solution of Fmoc-L-serine (10.0 g, 30.6 mmol) in EtOAc (250 mL) and the resulting reaction mixture was stirred at room temperature for 16 h. The mixture was concentrated *in vacuo* and re-dissolved in 25 vol% EtOAc in hexane for purification by flash silica gel chromatography (20-40 vol% EtOAc in hexane) to afford the pure product as a white foam (6.82 g, 17.8 mmol, 58%).

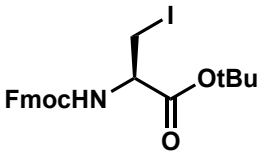
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.60 (d, *J* = 7.5 Hz, 2H), 7.40 (td, *J* = 7.5, 1.0 Hz, 2H), 7.31 (tt, *J* = 7.4, 1.4 Hz, 2H), 5.79 (d, 1H), 4.41 (d, *J* = 7.2 Hz, 2H), 4.33 (d, *J* = 7.0 Hz, 1H), 4.22 (t, *J* = 7.0 Hz, 1H), 3.93 (s, 2H), 2.47 (s, 1H), 1.49 (s, 9H); **^{13}C{^{1}H} NMR:** (126 MHz, $CDCl_3$) δ 169.59, 163.74, 156.37, 143.85, 143.73, 141.34, 141.31, 127.76, 127.12, 127.09, 125.12, 120.02, 120.00, 91.90, 82.95, 67.18, 63.68, 56.65, 47.17, 28.02; **LRMS:** (+ESI) *m/z* 406 $[M+Na]^+$; **HRMS:** (+ESI) Calc. for $C_{22}H_{25}NO_5Na$: 406.16249 $[M+Na]^+$, Found: 406.16182 $[M+Na]^+$; **IR (ATR):** ν_{max} = 3430, 3343, 3066, 2978, 2945, 2889, 1702, 1606, 1516, 1477, 1450, 1369, 1341, 1229, 1153, 1058, 912, 826, 759, 739, 621, 536, 426 cm^{-1}; **$[\alpha]_D$:** +0.023° (*c* 0.3, CH_2Cl_2). These data are in agreement with those published by Jobron and Hummel.[1]



***tert*-butyl *N*-(((9*H*-fluoren-9-yl)methoxy)carbonyl)-*O*-tosyl-*L*-serinate**

Fmoc-L-Ser-OtBu (6.82 g, 17.8 mmol) was dissolved in anhydrous pyridine (70 mL) and cooled to -10 °C. TsCl (6.78 g, 35.6 mmol) was then added to the reaction mixture, which was stirred at -10 °C for 16 h. After 16 h, the reaction mixture was poured onto ice-cold water (100 mL) and the aqueous mixture was extracted with EtOAc (100 mL). The organic phase was washed with 1 M citric acid (3 x 100 mL), saturated aqueous $NaHCO_3$ (2 x 100 mL), brine (100 mL), 1 M aqueous HCl (2 x 100 mL), saturated aqueous sodium bicarbonate (2 x 100 mL) and brine (3 x 100 mL). The washed organic phase was then dried over $MgSO_4$, filtered and concentrated *in vacuo* to a yellow oil. The resulting crude material was purified by flash silica gel chromatography (15-30 vol% EtOAc in hexane) affording the pure product as a white foam (7.85 g, 14.6 mmol, 82%).

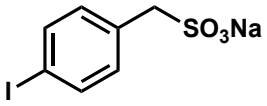
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.80 – 7.73 (m, 4H), 7.59 (dd, J = 10.3, 7.4 Hz, 2H), 7.41 (td, J = 7.4, 2.6 Hz, 2H), 7.36 – 7.29 (m, 2H), 7.26 (d, J = 8.2 Hz, 2H), 5.62 (d, J = 7.5 Hz, 1H), 4.49 – 4.41 (m, 2H), 4.37 – 4.22 (m, 3H), 4.18 (t, J = 7.3 Hz, 1H), 2.35 (s, 3H), 1.46 (s, 9H); **^{13}C{^{1}H} NMR:** (126 MHz, $CDCl_3$) δ 167.08, 155.57, 145.15, 143.78, 143.65, 141.29, 132.39, 129.94, 128.00, 127.81, 127.14, 125.24, 125.16, 120.02, 83.79, 69.53, 67.42, 53.78, 47.01, 27.87, 21.56; **LRMS:** (+ESI) *m/z* 560.19 $[M+Na]^+$; **IR (ATR):** ν_{max} = 3434, 3326, 3064, 2979, 2931, 2896, 1721, 1598, 1509, 1450, 1367, 1344, 1248, 1223, 1190, 1177, 1156, 1086, 1056, 995, 974, 908, 842, 816, 760, 740, 665, 554 cm^{-1}; **$[\alpha]_D$:** +0.093° (*c* 0.3, CH_2Cl_2).



***tert*-butyl (*R*)-2-((((9*H*-fluoren-9-yl)methoxy)carbonyl)amino)-3-iodopropanoate (6)**

Fmoc-L-Ser(OTs)-O*t*Bu (**6**) (1.91 g, 3.55 mmol) was dissolved in acetone (8 mL) and to this solution was added a solution of sodium iodide (1.07 g, 7.11 mmol) in acetone (4 mL). The reaction mixture was stirred under nitrogen for 24 h at room temperature then filtered. The filtrate was concentrated *in vacuo* and the resulting foam was redissolved in $CHCl_3$ (50 mL) and washed with H_2O (3 x 50 mL), saturated sodium thiosulfate (2 x 50 mL) and brine (50 mL). The washed organic layer was concentrated *in vacuo* to afford a white foam which was purified by flash chromatography (10-30 vol% EtOAc in hexane) to afford the pure product **6** as a white foam (1.31 g, 2.66 mmol, 75%).

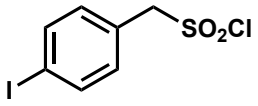
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.78 (d, J = 7.5 Hz, 2H), 7.63 (d, J = 7.5 Hz, 2H), 7.41 (t, J = 7.4 Hz, 2H), 7.34 (tdd, J = 7.5, 3.4, 1.2 Hz, 2H), 5.74 (d, J = 7.2 Hz, 1H), 4.44 (td, J = 7.4, 3.6 Hz, 2H), 4.37 (dd, J = 10.6, 7.2 Hz, 1H), 4.26 (t, J = 7.3 Hz, 1H), 3.67 – 3.57 (m, 2H), 1.54 (s, 9H); **^{13}C{^{1}H} NMR:** (126 MHz, $CDCl_3$) δ 168.21, 155.43, 143.82, 143.74, 141.33, 127.79, 127.16, 127.13, 125.25, 125.18, 120.05, 83.63, 67.34, 54.13, 47.13, 28.04, 8.46; **LRMS:** (+ESI) *m/z* 516.07 $[M+Na]^+$; **IR (ATR):** ν_{max} = 3419, 3329, 3065, 3040, 2977, 2943, 2900, 1710, 1502, 1449, 1369, 1338, 1299, 1249, 1216, 1152, 1118, 1060, 987, 909, 843, 758, 736, 647, 621, 544, 473, 425 cm^{-1}; **$[\alpha]_D$:** +0.15° (*c* 0.3, CH_2Cl_2). These data are in agreement with those published by Jobron and Hummel.[1]



Sodium 4-iodobenzylsulfonate

4-iodobenzyl bromide (25.31 g, 85.24 mmol) was dissolved in acetone (185 mL) and to this solution was added a solution of sodium sulfite (10.74 g, 85.24 mmol) in water (185 mL). The reaction was refluxed at 110 °C for 24 h. After 24 h the reaction mixture was concentrated under a stream of nitrogen gas to approximately half its original volume, during which a white precipitate formed. The precipitated solution was filtered the resulting solid was washed with acetone (500 mL), yielding the pure product as a white crystalline solid (23.44 g, 73.23 mmol, 86%).

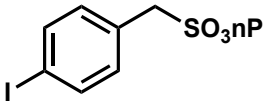
^{1}H NMR: (500 MHz, D_2O) δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 2H), 4.08 (s, 2H); **^{13}C{^{1}H} NMR:** (126 MHz, D_2O) δ 137.65, 132.29, 131.54, 93.24, 56.39; **LRMS:** (-ESI) *m/z* 297 $[M-H]^-$; **HRMS:** (-ESI) Calc. for $C_7H_6IO_3S$: 296.90878 $[M]^-$, Found: 296.90845 $[M]^-$; **IR (ATR):** ν_{max} = 2942, 1480, 1414, 1215, 1189, 1142, 1042, 1003, 892, 819, 762, 704, 636, 580, 536, 523 cm^{-1}; **m.p.:** >400 °C (decomp.). These data are in agreement with those published by Liu *et al*.[2]



(4-iodophenyl)methanesulfonyl chloride

Sodium (4-iodophenyl)methanesulfonate (2.07 g, 6.47 mmol) was dissolved in a mixture of sulfolane and MeCN (1:1 v/v, 8.30 mL) and heated to 60 °C. Phosphorus oxychloride (3.62 mL, 38.8 mmol) was added to the mixture which was then stirred at 60 °C for 4 h. The mixture was cooled to room temperature and poured over ice-cold H_2O (50 mL) to form a white precipitate. The resulting suspension was filtered, and the solid product was re-dissolved in CH_2Cl_2 (100 mL). The CH_2Cl_2 solution was washed with H_2O (3 x 100 mL) and brine (2 x 100 mL), then dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford the pure product as a white crystalline solid (1.82 g, 5.75 mmol, 89%).

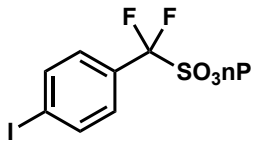
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.73 (d, J = 8.3 Hz, 2H), 7.14 (d, J = 8.4 Hz, 2H), 4.72 (s, 2H); **^{13}C{^{1}H} NMR:** (126 MHz, $CDCl_3$) δ 138.51, 132.94, 125.76, 96.96, 70.25; **LRMS:** (-ESI) *m/z* 314 $[M-H]^-$; **HRMS:** (-ESI) Calc. for $C_{12}H_{17}IO_3SNa$: 314.87489 $[M-H]^-$, Found: 314.87515 $[M-H]^-$; **IR (ATR):** ν_{max} = 3344, 3001, 2946, 1634, 1482, 1405, 1354, 1153, 1101, 630, 562, 512 cm^{-1}; **m.p.:** 145-147 °C. These data are in agreement with those published by Liu *et al*.[2]



Neopentyl (4-iodophenyl)methanesulfonate (4)

(4-iodophenyl)methanesulfonyl chloride (3.64 g, 11.4 mmol) was dissolved in dry THF (40 mL) and cooled to 0 °C. Neopentyl alcohol (1.12 g, 12.6 mmol) was added to the solution followed by Et_3N (1.75 mL, 12.6 mmol). The reaction mixture was warmed to room temperature and stirred for 20 h before being concentrated under a stream of nitrogen gas to afford a crude solid. The solid was re-dissolved in CH_2Cl_2 (100 mL) and washed with H_2O (3 x 100 mL) and brine (2 x 100 mL) before being dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford the pure product **4** as an off-white solid (3.58 g, 9.72 mmol, 85%).

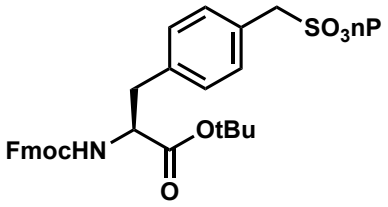
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.66 (d, J = 8.4 Hz, 2H), 7.08 (d, J = 8.3 Hz, 2H), 4.21 (s, 2H), 3.69 (s, 2H), 0.85 (s, 9H); **^{13}C{^{1}H} NMR:** (126 MHz, $CDCl_3$) δ 138.07, 132.43, 127.67, 95.14, 79.57, 55.99, 31.84, 26.00; **LRMS:** (+ESI) *m/z* 391 $[M+Na]^+$; **HRMS:** (+ESI) Calc. for $C_{12}H_{17}IO_3SNa$: 390.98353 $[M+Na]^+$, Found: 390.98326 $[M+Na]^+$; **IR (ATR):** ν_{max} = 2959, 2905, 2869, 1588, 1482, 1402, 1366, 1345, 1266, 1166, 954, 936, 832, 705, 632, 522, 475 cm^{-1}; **m.p.:** 112-114 °C. These data are in agreement with those published by Liu *et al.*[2]



Neopentyl difluoro(4-iodophenyl)methanesulfonate (5)

Neopentyl (4-iodophenyl)methanesulfonate (**4**) (2.70 g, 7.33 mmol) and *N*-fluorobenzensulfonimide (5.55 g, 17.6 mmol) were dissolved in dry THF (100 mL) and cooled to -78 °C. A 1 M solution of NaHMDS in THF (16.1 mL, 16.1 mmol) was added dropwise over 10 min and the reaction mixture was stirred at -78 °C for 2 h before being warmed to room temperature and stirred for an additional 2 h. The reaction was quenched with saturated aqueous NH_4Cl (100 mL) and extracted with Et_2O (3 x 100 mL). The ethereal extracts were washed with 5% w/v $NaHCO_3$ in H_2O (2 x 300 mL) and brine (300 mL), then dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford a crude white oil which was purified by flash silica gel chromatography (0-20 vol% EtOAc in hexane) to afford the pure product **5** as a yellow oil (2.51 g, 6.21 mmol, 85%).

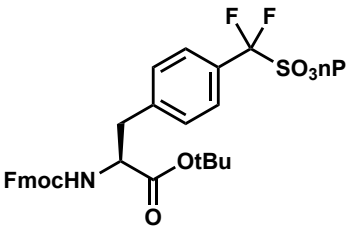
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.78 (d, J = 8.8 Hz, 2H), 7.32 (d, J = 8.5 Hz, 2H), 4.04 (s, 2H), 0.92 (s, 9H); **^{13}C{^{1}H} NMR:** (126 MHz, $CDCl_3$) δ 137.02, 127.61, 127.56, 127.51, 126.72, 126.54, 126.36, 122.06, 119.81, 117.55, 98.81, 98.79, 98.77, 83.55, 31.08, 24.79; **^{19}F{^{1}H} NMR:** (471 MHz, $CDCl_3$) δ -100.53; **LRMS:** (+ESI) *m/z* 427 $[M+Na]^+$; **HRMS:** (+ESI) Calc. for $C_{12}H_{15}F_2IO_3SNa$: 426.96469 $[M+Na]^+$, Found: 426.96451 $[M+Na]^+$; **IR (ATR):** ν_{max} = 2962, 2872, 1590, 1486, 1384, 1368, 1275, 1195, 1139, 1085, 1010, 971, 950, 922, 628, 599, 534 cm^{-1}. These data are in agreement with those published by Liu *et al*.[2]



tert-butyl (_S_)-2-((((9_H_-fluoren-9-yl)methoxy)carbonyl)amino)-3-(4-(((neopentyloxy)sulfonyl)methyl)phenyl)propanoate (7)

Zinc dust (1.07 g, 16.4 mmol) and a magnetic stirrer were added to a 25 mL round bottom flask and dried *in vacuo* under heat. The flask was cooled to room temperature and iodine (416 mg, 1.64 μmol) was added followed by a solution of Fmoc-iodoalanine-O*t*Bu (**6**) (2.69 g, 5.46 mmol) in dry degassed DMF (5 mL) and another catalytic amount of iodine. The reaction was stirred at room temperature for 20 min at which point TLC analysis showed formation of the zincate. A solution of $Pd_2(dba)_3$ (125 mg, 137 μmol) and SPhos (112 mg, 273 μmol) in dry degassed DMF (2.5 mL) was added to the zincate mixture. The flask was washed with additional dry DMF (1 mL) and this wash was added to the reaction mixture. A solution of neopentyl (4-iodophenyl)methanesulfonate **4** (2.61 g, 7.10 mmol) in dry degassed DMF (2.5 mL) was then added to the reaction mixture. The reaction mixture was stirred at room temperature for 24 h then filtered through a celite plug, concentrated under nitrogen, re-dissolved in EtOAc (50 mL) and washed with H_2O (2 x 50 mL), saturated aqueous NH_4Cl (2 x 50 mL) and brine (50 mL). The washed organic phase was dried over $MgSO_4$, filtered and concentrated *in vacuo,* affording a crude solid purified by flash chromatography (5-30 vol% EtOAc in hexane) to afford the pure product **7** as a yellow foam (1.31 g, 2.16 mmol, 39%).

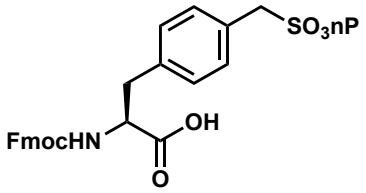
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.77 (d, J = 7.6 Hz, 2H), 7.58 (dd, J = 7.5, 4.7 Hz, 2H), 7.41 (t, J = 7.5 Hz, 2H), 7.36 – 7.29 (m, 4H), 7.19 (d, J = 7.7 Hz, 2H), 5.31 (d, J = 8.0 Hz, 1H), 4.58 – 4.51 (m, 1H), 4.35 (dd, J = 10.6, 6.9 Hz, 1H), 4.38 – 4.34 (m, 1H), 4.32 (s, 2H), 4.21 (t, J = 6.9 Hz, 1H), 3.73 (s, 2H), 3.17 – 3.05 (m, 2H), 1.42 (s, 9H), 0.91 (s, 9H); **^{13}C{^{1}H} NMR:** (126 MHz, $CDCl_3$) δ 170.45, 155.63, 143.97, 143.90, 141.44, 137.37, 130.82, 130.17, 127.86, 127.82, 127.18, 126.76, 125.24, 125.16, 120.13, 120.11, 82.77, 79.64, 67.03, 56.32, 55.14, 47.31, 47.28, 38.26, 31.91, 28.14, 28.10, 26.10; **LRMS:** (+ESI) *m/z* 630 $[M+Na]^+$; **IR (ATR):** ν_{max} = 3351, 3067, 3041, 2972, 2940, 2871, 1719, 1513, 1478, 1450, 1354, 1251, 1223, 1168, 1154, 1107, 1053, 963, 937, 913, 889, 844, 760, 740, 590, 533 cm^{-1}; **$[\alpha]_D$:** +0.035° (*c* 0.3, CH_2Cl_2).



tert-butyl (_S_)-2-((((9_H_-fluoren-9-yl)methoxy)carbonyl)amino)-3-(4-(difluoro((neopentyloxy)sulfonyl)methyl)phenyl)propanoate (8)

Zinc dust (543 mg, 8.32 mmol) and a magnetic stirrer were added to a 10 mL round bottom flask and dried *in vacuo* under heat. The flask was cooled to room temperature, iodine (208 mg, 819 μmol) was added and the flask again heated until a purple haze was visible. A solution of Fmoc-iodoalanine-O*t*Bu (**6**) (1.37 g, 2.78 mmol) in DMF (2 mL) was added to the zinc mixture and stirred at room temperature for 2 h, with zincate formation proceeding exothermically. A solution of $Pd_2(dba)_3$ (63.9 mg, 79.9 μmol) and SPhos (57.1 mg, 139 μmol) in DMF (1 mL) was then added to the zincate mixture followed by a solution of neopentyl difluoro(4-iodophenyl)methanesulfonate (**5**) (1.46 g, 3.63 mmol) in DMF (2 mL). The reaction mixture was then stirred at room temperature for 16 h. The mixture was filtered through celite and concentrated under a stream of N_2 gas before being re-dissolved in EtOAc (10 mL), washed with H_2O (2 x 10 mL), saturated NH_4Cl (2 x 10 mL) and brine (10 mL). The organic layer was dried over $MgSO_4$, then filtered and concentrated *in vacuo* to give crude material which was purified by silica flash chromatography (5-30 vol% EtOAc in hexane) to afford the product **8** as a white foam (449 mg, 0.912 mmol, 33%).

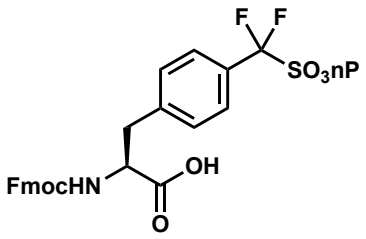
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.77 (d, 7.55 Hz, 2H), 7.62 (d, 7.84 Hz, 4H), 7.58 (d, 7.64 Hz, 2H), 7.41 (t, 7.55 Hz), 7.31 (m, 4H), 5.34 (d, 7.57 Hz, 1H), 4.56 (dd, 6.75 Hz, 6.44 Hz, 1 H), 4.47 (m, 1H), 4.37 (m, 1H), 4.22 (t, 6.80 Hz, 1H), 4.10 (s, 2H), 3.16 (m, 2H), 1.39 (s, 9H), 1.01 (s, 9H); **^{13}C{^{1}H} NMR:** (126 MHz, $CDCl_3$) δ 169.9, 155.3, 143.5, 141.1, 129.7, 127.5, 127.0, 127.0, 126.9, 126.9, 124.9, 124.8, 119.8, 119.8, 84.2, 82.7, 66.7, 54.7, 47.0, 38.2, 31.9, 27.7, 25.6; **^{19}F{^{1}H} NMR:** (471 MHz, $CDCl_3$) δ -99.81; **LRMS:** (+ESI) *m/z* 666 $[M+Na]^+$; **HRMS:** (+ESI) Calc. for $C_{34}H_{39}F_2NO_7SNa$: 666.23075 $[M+Na]^+$, Found: 666.22952 $[M+Na]^+$; **IR (ATR):** ν_{max} = 3330, 3067, 3041, 2978, 2937, 2886, 1720, 1518, 1478, 1450, 1384, 1369, 1341, 1251, 1224, 1156, 1106, 1077, 974, 954, 927, 846, 759, 740, 605, 537, 427 cm^{-1}; **$[\alpha]_D$:** +0.062° (*c* 0.3, CH_2Cl_2).



(*S*)-2-((((9*H*-fluoren-9-yl)methoxy)carbonyl)amino)-3-(4-(((neopentyloxy)sulfonyl)methyl)phenyl)propanoic acid (2)

Fmoc-L-Smp(nP)-O*t*Bu (**7**) (1.26 g, 2.07 mmol) was dissolved in a 1:1 v/v mixture of TFA and CH_2Cl_2 (10 mL). The reaction mixture was stirred at room temperature for 2 h. The reaction mixture was concentrated under a stream of nitrogen and then azeotroped with CH_2Cl_2 (x 2), toluene (x 3) and $CHCl_3$ (x 2), affording the crude product which was purified by flash silica gel chromatography (0-10 vol% MeOH in CH_2Cl_2 with 1 vol% acetic acid), affording the pure product **2** as an orange foam (879 mg, 1.59 mmol, 77%).

^{1}H NMR: (500 MHz, MeOD) δ 7.81 (d, *J* = 7.6 Hz, 2H), 7.63 (t, *J* = 7.1 Hz, 2H), 7.44 – 7.36 (m, 4H), 7.36 – 7.28 (m, 3H), 7.29 (d, *J* = 6.0 Hz, 1H), 4.48 (s, 2H), 4.44 (dd, *J* = 9.2, 4.6 Hz, 1H), 4.34 – 4.23 (m, 2H), 4.17 (t, *J* = 6.9 Hz, 1H), 3.76 (s, 2H), 3.25 (dd, *J* = 13.9, 4.7 Hz, 1H), 2.99 (dd, *J* = 13.9, 9.3 Hz, 1H), 0.90 (s, 9H); **^{13}C{^{1}H} NMR:** (126 MHz, MeOD) δ 173.72, 156.93, 143.83, 143.81, 141.15, 138.26, 130.61, 129.28, 127.38, 126.98, 126.78, 124.91, 124.86, 119.50, 79.57, 66.57, 55.36, 54.98, 36.86, 31.19, 24.91; **LRMS:** (+ESI) *m/z* 596 $[M+2Na]^{2+}$; **HRMS:** (+ESI) Calc. for $C_{30}H_{33}NO_7SNa$: 574.18699 $[M+Na]^+$, Found: 574.18633 $[M+Na]^+$; **IR (ATR):** ν_{max} = 3060, 2962, 2872, 1712, 1515, 1451, 1427, 1349, 1169, 1106, 1051, 961, 937, 891, 842, 760, 741, 593, 538, 426 cm^{-1}; **$[\alpha]_D$:** +0.191° (*c* 0.3, CH_2Cl_2).



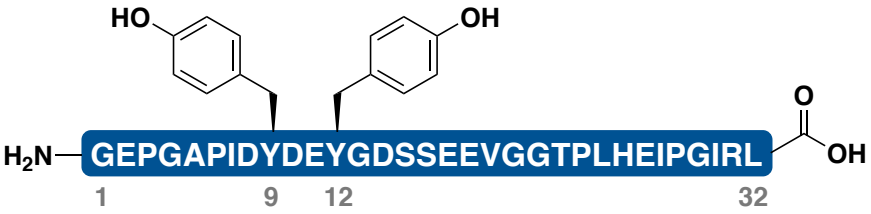
(*S*)-2-((((9*H*-fluoren-9-yl)methoxy)carbonyl)amino)-3-(4-(difluoro((neopentyloxy)sulfonyl)methyl)phenyl)propanoic acid (3)

Fmoc-L-F_2Smp(nP)-O*t*Bu (**8**) (238 mg, 370 μmol) was dissolved in a 1:1 v/v mixture of TFA and CH_2Cl_2 (10 mL). The reaction mixture was stirred at room temperature for 2 h. The reaction mixture was concentrated under a stream of nitrogen and then azeotroped with CH_2Cl_2 (x 2), toluene (x 3) and $CHCl_3$ (x 2), affording the crude product which was purified by flash silica gel chromatography (0-10 vol% MeOH in CH_2Cl_2 with 1 vol% acetic acid), affording the pure product **3** as an orange foam (132 mg, 231 μmol, 62%).

^{1}H NMR: (500 MHz, MeOD) δ 7.75 (d, *J* = 7.6 Hz, 2H), 7.58 (t, *J* = 8.1 Hz, 4H), 7.44 – 7.32 (m, 4H), 7.31 – 7.24 (m, 2H), 4.43 (dd, *J* = 9.1, 4.9 Hz, 1H), 4.32 (dd, *J* = 10.6, 7.1 Hz, 1H), 4.22 (dd, *J* = 10.6, 6.9 Hz, 1H), 4.12 (t, *J* = 7.0 Hz, 1H), 4.03 (s, 2H), 3.34 – 3.27 (m, 1H), 3.05 (dd, *J* = 13.8, 9.0 Hz, 1H), 0.94 (s, 9H); **^{13}C{^{1}H} NMR:** (126 MHz, MeOD) δ 174.92, 156.87, 143.84, 143.77, 143.11, 141.17, 129.61, 127.40, 126.83, 126.77, 124.85, 124.78, 123.24, 120.99, 119.55, 118.75, 84.14, 66.47, 55.66, 37.18, 31.50, 24.74; **^{19}F{^{1}H} NMR:** (471 MHz, MeOD) δ -76.87 (TFA-C$\underline{F}_3$), -100.75; **LRMS:** (+ESI) *m/z* 586 $[M+H]^+$; **HRMS:** (+ESI) Calc. for $C_{30}H_{31}F_2NO_7SNa$: 610.16815 $[M+Na]^+$, Found: 610.16708 $[M+Na]^+$; **IR (ATR):** ν_{max} = 3392, 3067, 2962, 2872, 2495, 2228, 2074, 1694, 1614, 1589, 1450, 1423, 1384, 1368, 1279, 1195, 1105, 1084, 973, 925, 806, 759, 740, 606, 536, 454, 424 cm^{-1}; **$[\alpha]_D$:** +0.317° (*c* 0.3, CH_2Cl_2). These data are in agreement with those published by Liu *et al*.[2]

4 SYNTHESIS OF PEPTIDIC THROMBIN INHIBITORS

4.1 TTI



TTI (Y9, Y12) (9)

Wang resin (0.28 mmol g^{-1} loading) was loaded with Fmoc-Leu-OH according to the general procedures. Synthesis of the G13-R31 fragment was then performed using automated coupling protocols *(see General Procedures – Automated Coupling (Liberty Blue)*) on a CEM Liberty Blue® peptide synthesiser with a double coupling of R31. Fragment G1-Y12 was then synthesised manually (*see General Procedures – Manual Coupling (Standard)*) with double couplings for E2, I7, D8 and E11. After completion of the synthesis, the peptide was cleaved from the resin and deprotected by treatment with an acidic cleavage cocktail (90:5:5 v/v/v TFA:*i*Pr_3SiH:H_2O) at room temperature for 2 h. The deprotection solution was concentrated under a stream of nitrogen until a small volume remained (<0.5 mL). Cold Et_2O (40 mL) was then added to the remaining deprotection solution to precipitate peptidic material. The resulting suspension was then centrifuged at 4 °C (2000 x g, 5 min) and the ether supernatant was decanted, leaving the crude peptide material to dry under a gentle stream of nitrogen. The crude peptide was dissolved in 5 vol% MeCN in H_2O (0.1 vol% FA) (5 mL) and purified by preparative reversed-phase chromatography (Waters Sunfire C18, 30 x 150 mm, 38 mL min^{-1}) on a 0-50%B gradient over 45 min (*see general procedures*). Subsequent lyophilisation afforded the purified TTI (Y9, Y12) (**9**) (16.2 mg, 4.61 µmol, 23% from resin loading [64 steps]).

See analytical data on next page.

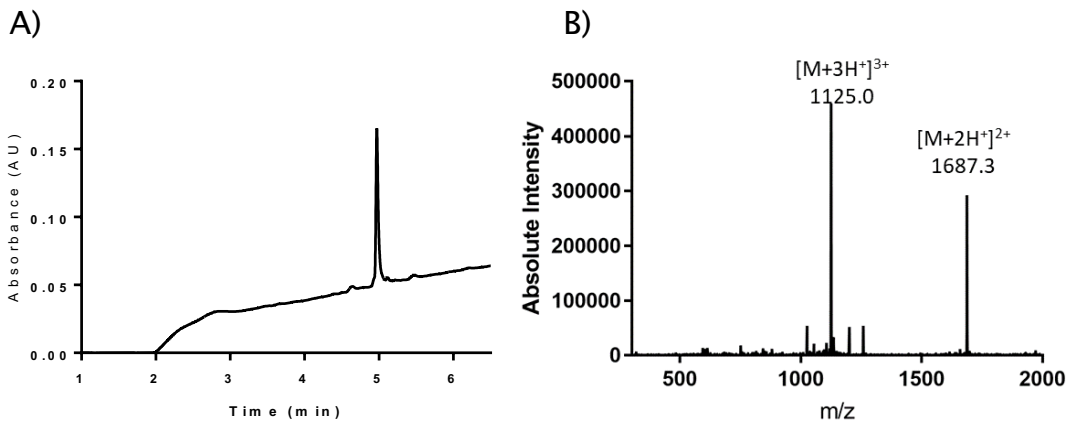
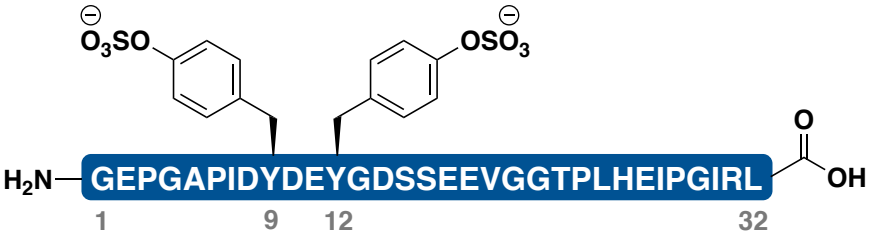


Figure S1. A) Analytical reversed-phase HPLC analysis of purified TTI (Y9, Y12) (**9**) (0-50%B over 5 min, λ = 214 nm) collected on a Waters Acquity UPLC system, as per general procedures. **B)** Mass spectrum (ESI+) of purified TTI (Y9, Y12) (**9**) collected on a Shimadzu 2020 (ESI) mass spectrometer, as per general procedures.



TTI (sY9, sY12) (10)

Wang resin (0.28 mmol g^{-1} loading) was loaded with Fmoc-Leu-OH according to the general procedures. Synthesis of the G13-R31 fragment was then performed using automated coupling protocols (*see General Procedures – Automated Coupling (Liberty Blue)*) on a Liberty Blue® peptide synthesiser with double coupling of R31. Coupling of Fmoc-Tyr(SO_3nP)-OH was then performed manually according to *General Procedures (Manual Coupling (Non-Standard))*. Fragment D10-E11 was then synthesised manually (*see General Procedures – Manual Coupling (Standard)*) with double coupling of E11, before a second manual coupling of Fmoc-Tyr(SO_3nP)-OH according to *General Procedures (Manual Coupling (Non-Standard))*. The resin-bound peptide was then transferred to a Liberty Blue® peptide synthesiser for completion of the G1-D8 fragment with 50 °C single couplings of all residues and a final Fmoc-deprotection. After completion of the synthesis, the peptide was cleaved from the resin and deprotected by treatment with an acidic cleavage cocktail (90:5:5 v/v/v TFA:*i*Pr_3SiH:H_2O) at room temperature for 2 h. The deprotection solution was concentrated under a stream of nitrogen until a small volume remained (<0.5 mL). Cold Et_2O (40 mL) was then added to the remaining deprotection solution to precipitate peptidic material. The resulting suspension was then centrifuged at 4 °C (2000 x g, 5 min) and the ether supernatant was decanted, leaving the crude peptide material to dry under a gentle stream of nitrogen. The precipitated material was dissolved in 1.5 mL of NH_4OAc buffer (1 M NH_4OAc, 6 M Gn.HCl, 0.1 M Na_2HPO_4) at pH 7 and incubated at 37 °C for 3 h to facilitate the removal of the sulfonyl neopentyl protecting group. After complete neopentyl removal, as judged by UPLC-MS analysis, the reaction mixture was diluted to 5 mL total volume with H_2O (0.1 vol% FA) and purified by preparative reversed-phase chromatography (Waters Sunfire C18, 30 x 150 mm, 38 mL min^{-1}) on a 0-50%B gradient over 45 min (*see general procedures*). Subsequent lyophilisation afforded the purified TTI (sY9, sY12) (**10**) (5.2 mg, 1.4 μmol, 7% from resin loading [65 steps]).

See analytical data on next page.

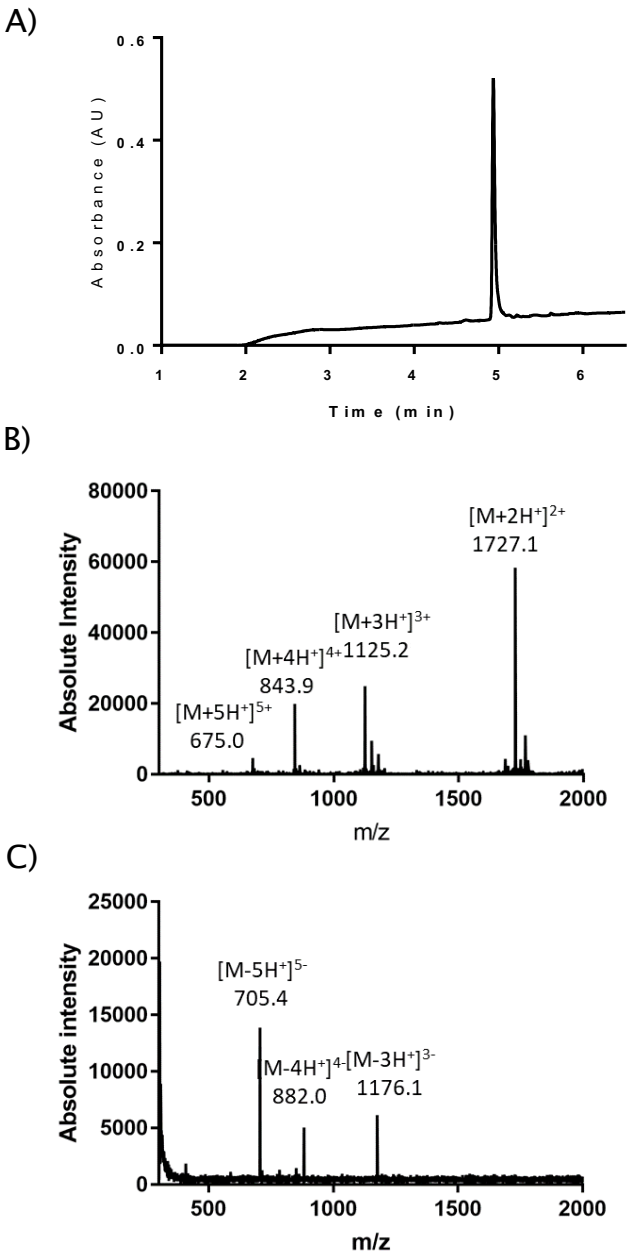
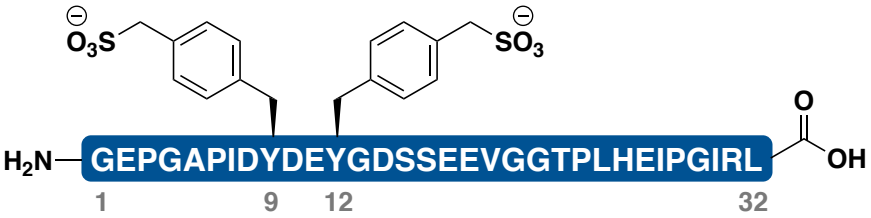


Figure S2. A) Analytical reversed-phase HPLC analysis of purified TTI (sY9, sY12) (**10**) (0-50%B over 5 min, λ = 214 nm) collected on a Waters Acquity UPLC system, as per general procedures. **B)** Mass spectrum (ESI+) of purified TTI (sY9, sY12) (**10**) collected on a Shimadzu 2020 (ESI) mass spectrometer, as per general procedures. **C)** Mass spectrum (ESI-) of purified TTI (sY9, sY12) (**10**) collected on a Shimadzu 2020 (ESI) mass spectrometer, as per general procedures.



TTI (Smp9, Smp12) (11)

Wang resin (0.28 mmol g^{-1} loading) was loaded with Fmoc-Leu-OH according to the general procedures. Synthesis of the G13-R31 fragment was then performed using automated coupling protocols (*see General Procedures – Automated Coupling (Liberty Blue)*) on a Liberty Blue® peptide synthesiser with double coupling of R31. Coupling of Fmoc-Smp(nP)-OH (**2**) was then performed manually according to the *General Procedures (Manual Coupling (Non-Standard))*. Fragment D10-E11 was then synthesised manually (*see General Procedures – Manual Coupling (Standard)*) with double coupling of E11, before a second manual coupling of Fmoc-Smp(nP)-OH (**2**) according to *General Procedures (Manual Coupling (Non-Standard))*. The resin-bound peptide was then transferred to a Liberty Blue® peptide synthesiser for completion of the G1-D8 fragment with 50 °C single couplings of all residues and a final Fmoc-deprotection. After completion of the synthesis, the peptide was cleaved from the resin and deprotected by treatment with an acidic cleavage cocktail (90:5:5 v/v/v TFA:*i*Pr_3SiH:H_2O) at room temperature for 2 h. The deprotection solution was concentrated under a stream of nitrogen until a small volume remained (<0.5 mL). Cold Et_2O (40 mL) was then added to the remaining deprotection solution to precipitate peptidic material. The resulting suspension was then centrifuged at 4 °C (2000 x g, 5 min) and the ether supernatant was decanted, leaving the crude peptide material to dry under a gentle stream of nitrogen. The precipitated material was dissolved in 1.5 mL of NH_4OAc buffer (1 M NH_4OAc, 6 M Gn.HCl, 0.1 M Na_2HPO_4) at pH 7 and incubated at 70 °C for 15 h to facilitate the removal of the sulfonyl neopentyl protecting group. After complete neopentyl removal, as judged by UPLC-MS analysis, the reaction mixture was diluted to 5 mL total volume with H_2O (0.1 vol% FA) and purified by preparative reversed-phase chromatography (Waters Sunfire C18, 30 x 150 mm, 38 mL min-1) on a 0-50%B gradient over 45 min (*see general procedures*). Subsequent lyophilisation afforded the purified TTI (Smp9, Smp12) (**11**) (8.6 mg, 2.3 μmol, 23% from resin loading [65 steps]).

See analytical data on next page.

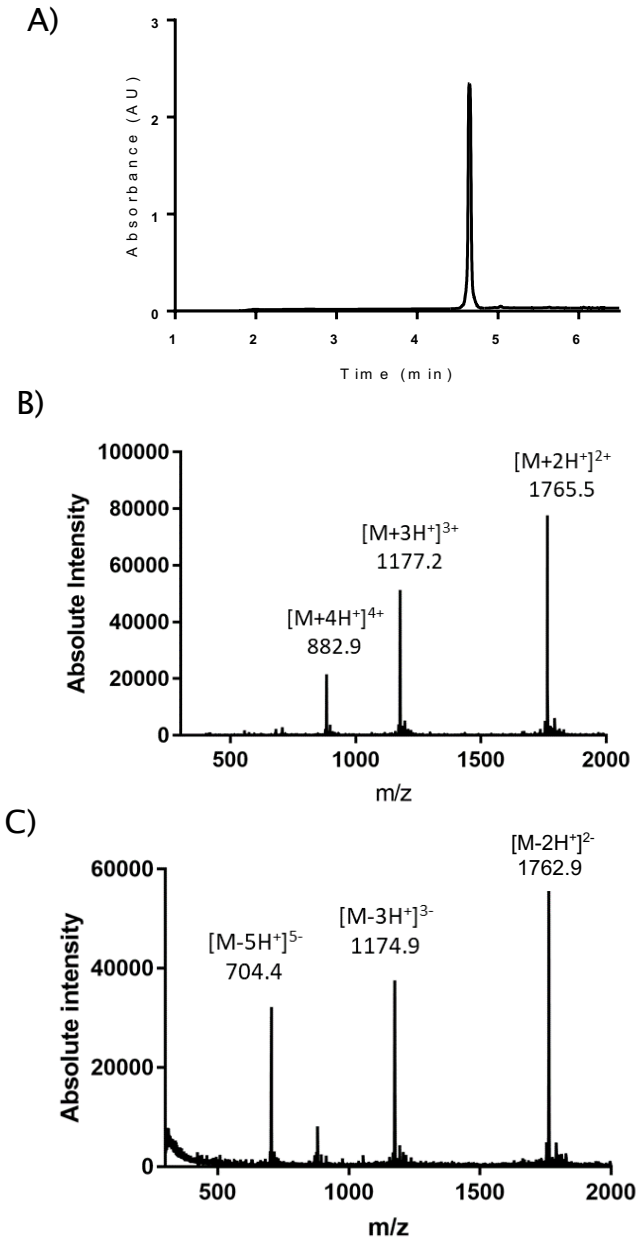
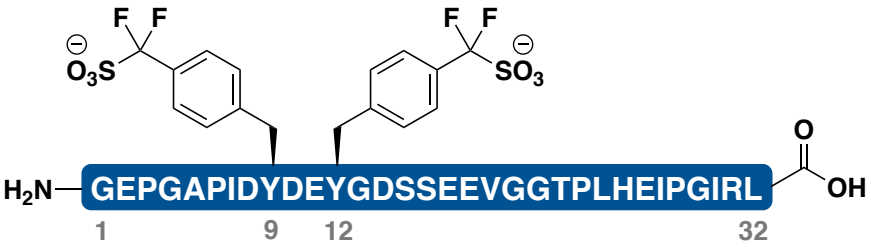


Figure S3. A) Analytical UPLC analysis of purified TTI (Smp9, Smp12) (**11**) (0-50%B over 5 min, λ = 214 nm) collected on a Waters Acquity UPLC system, as per general procedures. **B)** Mass spectrum (ESI+) of purified TTI (Smp9, Smp12) (**11**) collected on a Shimadzu 2020 (ESI) mass spectrometer, as per general procedures. **C)** Mass spectrum (ESI-) of purified TTI (Smp9, Smp12) (**11**) collected on a Shimadzu 2020 (ESI) mass spectrometer, as per general procedures.



TTI (F_2Smp9, F_2Smp12) (12)

Wang resin (0.28 mmol g^{-1} loading) was loaded with Fmoc-Leu-OH according to the general procedures. Synthesis of the G13-R31 fragment was then performed using automated coupling protocols (*see General Procedures – Automated Coupling (Liberty Blue)*) on a Liberty Blue® peptide synthesiser with a double coupling of R31. Coupling of Fmoc-F_2Smp(nP)-OH (**3**) was then performed manually according to the General Procedures (*Manual Coupling (Non-Standard)*). Fragment D10-E11 was then synthesised manually (*see General Procedures – Manual Coupling (Standard)*) with double coupling of E11, before a second manual coupling of Fmoc-F_2Smp(nP)-OH (**3**) according to *General Procedures (Manual Coupling (Non-Standard))*. The resin-bound peptide was then transferred to a Liberty Blue® peptide synthesiser for completion of the G1-D8 fragment with 50 °C single couplings of all residues and a final Fmoc-deprotection. After completion of the synthesis, the peptide was cleaved from the resin and deprotected by treatment with an acidic cleavage cocktail (90:5:5 v/v/v TFA:*i*Pr_3SiH:H_2O) at room temperature for 3 h. The deprotection solution was concentrated under a stream of nitrogen until a small volume remained (<0.5 mL). Cold Et_2O (40 mL) was then added to the remaining deprotection solution to precipitate peptidic material. The resulting suspension was then centrifuged at 4 °C (2000 x g, 5 min) and the ether supernatant was decanted, leaving the crude peptide material to dry under a gentle stream of nitrogen. The precipitated material was dissolved in 1.5 mL of NH_4OAc buffer (1 M NH_4OAc, 6 M Gn.HCl, 0.1 M Na_2HPO_4) at pH 7 and incubated at 37 °C for 3 h to facilitate the removal of the sulfonyl neopentyl protecting group. After complete neopentyl removal, as judged by UPLC-MS analysis, the reaction mixture was diluted to 5 mL total volume with H_2O (0.1 vol% FA) and purified by preparative RP-HPLC (Waters Sunfire C18, 19 x 150 mm, 14 mL min^{-1}) on a 0-50%B gradient over 45 min (*see general procedures*). Subsequent lyophilisation afforded the purified TTI (F_2Smp9, F_2Smp12) (**12**) (4.8 mg, 1.3 μmol, 13% from resin loading [65 steps]).

See analytical data on next page.

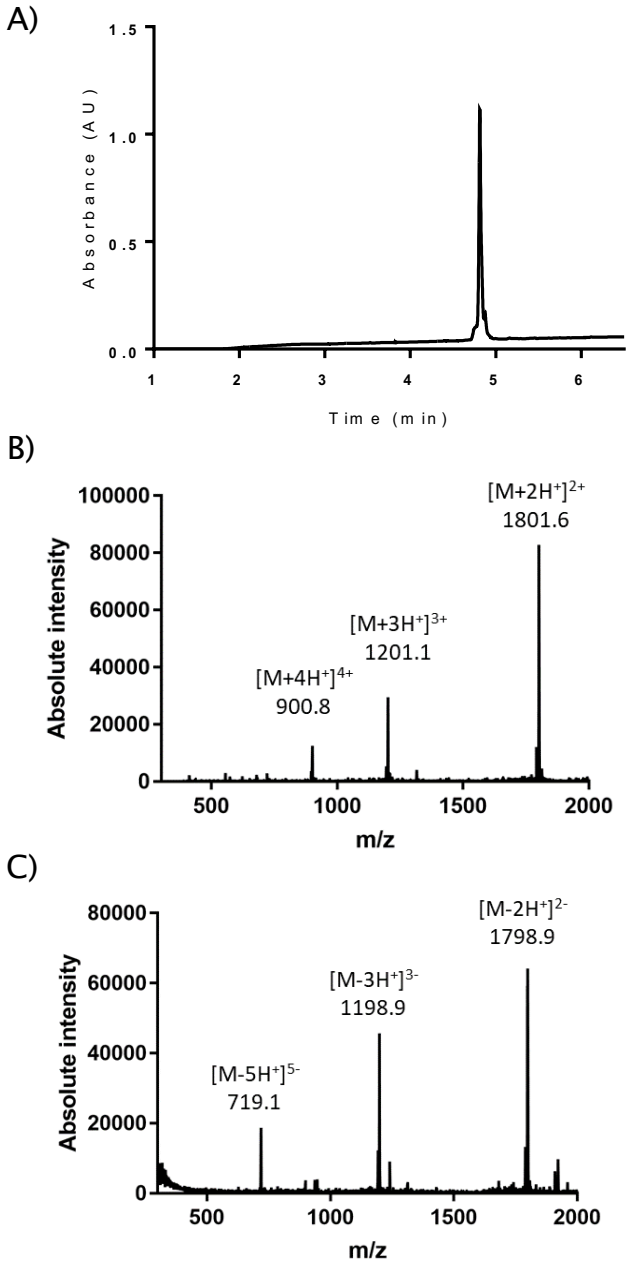
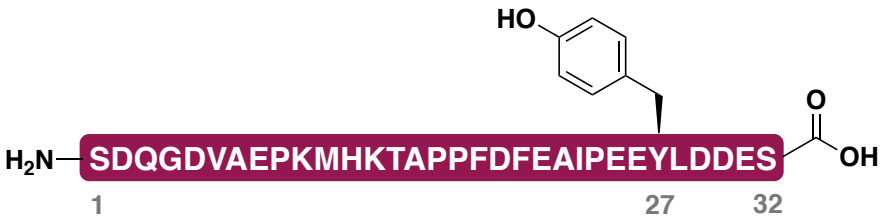


Figure S4. A) Analytical UPLC analysis of purified TTI (F_2Smp9, F_2Smp12) (**12**) (0-50%B over 5 min, λ = 214 nm) collected on a Waters Acquity UPLC system, as per general procedures. **B)** Mass spectrum (ESI+) of purified TTI (F_2Smp9, F_2Smp12) (**12**) collected on a Shimadzu 2020 (ESI) mass spectrometer, as per general procedures. **C)** Mass spectrum (ESI-) of purified TTI (F_2Smp9, F_2Smp12) (**12**) collected on a Shimadzu 2020 (ESI) mass spectrometer, as per general procedures.

4.2 VARIEGIN



Variegin (Y27) (13)

2-CTC resin (0.51 mmol g^{-1} loading) was loaded with Fmoc-Ser(*t*Bu)-OH according to the general procedures. Synthesis of the S1-E31 fragment was then performed using automated coupling protocols (*see General Procedures – Automated Coupling (Symphony)*) on a Gyros Protein Technologies Symphony® peptide synthesiser, with double couplings at Q3, D5, V6, E8, H12, K13, A15, P16, A22, I23 and E26. After completion of the synthesis, the peptide was cleaved from the resin and deprotected by treatment with an acidic cleavage cocktail (90:5:5 v/v/v TFA:*i*Pr_3SiH:H_2O) at room temperature for 3 h. The deprotection solution was concentrated under a stream of nitrogen until a small volume remained (<0.5 mL). Cold Et_2O (40 mL) was then added to the remaining deprotection solution to precipitate peptidic material. The resulting suspension was then centrifuged at 4 °C (2000 x g, 5 min) and the ether supernatant was decanted, leaving the crude peptide material to dry under a gentle stream of nitrogen. The crude peptide was dissolved in 5 vol% MeCN in H_2O (0.1 vol% FA) (5 mL) and purified by preparative reversed-phase chromatography (Waters Sunfire C18, 30 x 150 mm, 38 mL min^{-1}) on a 0-50%B gradient over 45 min (*see general procedures*). Subsequent lyophilisation afforded the purified Variegin (Y27) (**13**) (5.7 mg, 1.5 μmol, 6% from resin loading [64 steps]).

See analytical data on next page.

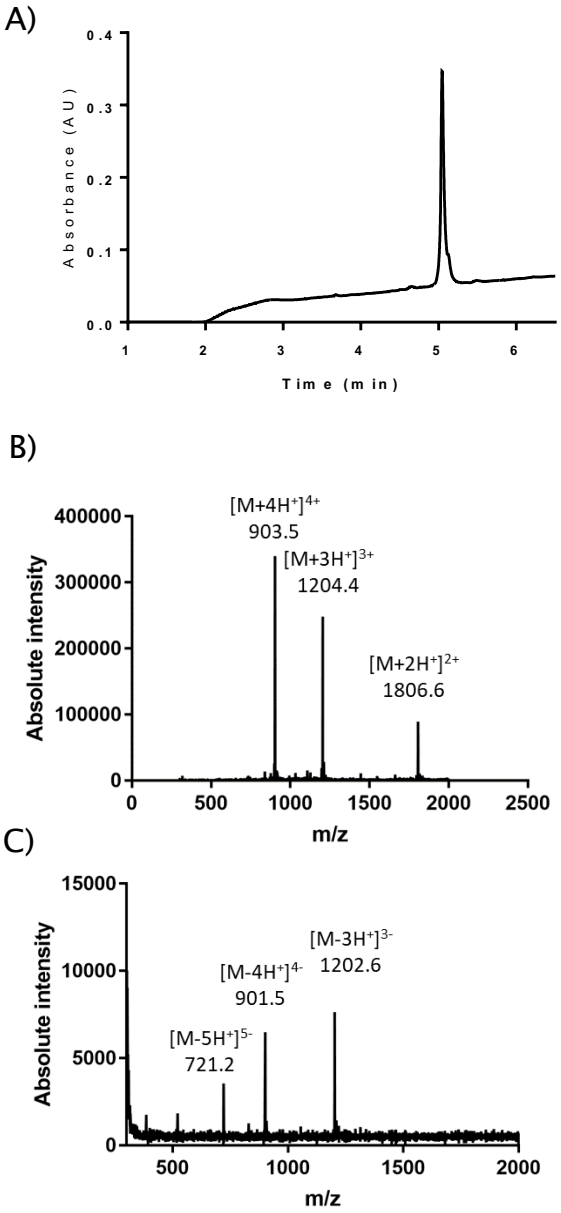
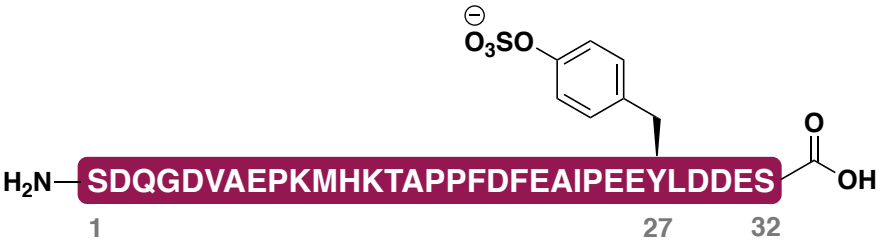


Figure S5. A) Analytical reversed-phase HPLC analysis of purified Variegin (Y27) (**13**) (0-50%B over 5 min, λ = 214 nm) collected on a Waters Acquity UPLC system, as per general procedures. **B)** Mass spectrum (ESI+) of purified Variegin (Y27) (**13**) collected on a Shimadzu 2020 (ESI) mass spectrometer, as per general procedures. **C)** Mass spectrum (ESI-) of purified Variegin (Y27) (**13**) collected on a Shimadzu 2020 (ESI) mass spectrometer, as per general procedures.



Variegin (sY27) (14)

2-CTC resin (0.28 mmol g^{-1} loading) was loaded with Fmoc-Ser(*t*Bu)-OH according to the general procedures. Synthesis of the L28-E31 fragment was then performed using automated coupling protocols (*see General Procedures – Automated Coupling (Symphony)*) on a Gyros Protein Technologies Symphony® peptide synthesiser. Coupling of Fmoc-Tyr(SO_3nP)-OH was then performed manually according to the *General Procedures (Manual Coupling (Non-Standard))*. Fragment S1-E26 was then completed using automated coupling protocols (*see General Procedures – Automated Coupling (Symphony)*) with double couplings at Q3, D5, V6, E8, H12, K13, A15, P16, A22, I23 and E26. After completion of the synthesis, the peptide was cleaved from the resin and deprotected by treatment with an acidic cleavage cocktail (90:5:5 v/v/v TFA:*i*Pr_3SiH:H_2O) at room temperature for 3 h. The deprotection solution was concentrated under a stream of nitrogen until a small volume remained (<0.5 mL). Cold Et_2O (40 mL) was then added to the remaining deprotection solution to precipitate peptidic material. The resulting suspension was then centrifuged at 4 °C (2000 x g, 5 min) and the ether supernatant was decanted, leaving the crude peptide material to dry under a gentle stream of nitrogen. The precipitated material was dissolved in 2 mL of NH_4OAc buffer (1 M NH_4OAc, 6 M Gn.HCl, 0.1 M Na_2HPO_4) at pH 7 and incubated at 37 °C for 3 h to facilitate the removal of the sulfate neopentyl protecting group. After complete neopentyl removal, as judged by UPLC-MS analysis, the reaction mixture was diluted to 5 mL total volume with H_2O (0.1 vol% FA) and purified by preparative reversed-phase chromatography (Waters Sunfire C18, 30 x 150 mm, 38 mL min^{-1}) on a 0-50%B gradient over 45 min (*see general procedures*). Subsequent lyophilisation afforded the purified Variegin (sY27) (**14**) (18.2 mg, 4.6 μmol, 15% from resin loading [65 steps]).

See analytical data on next page.

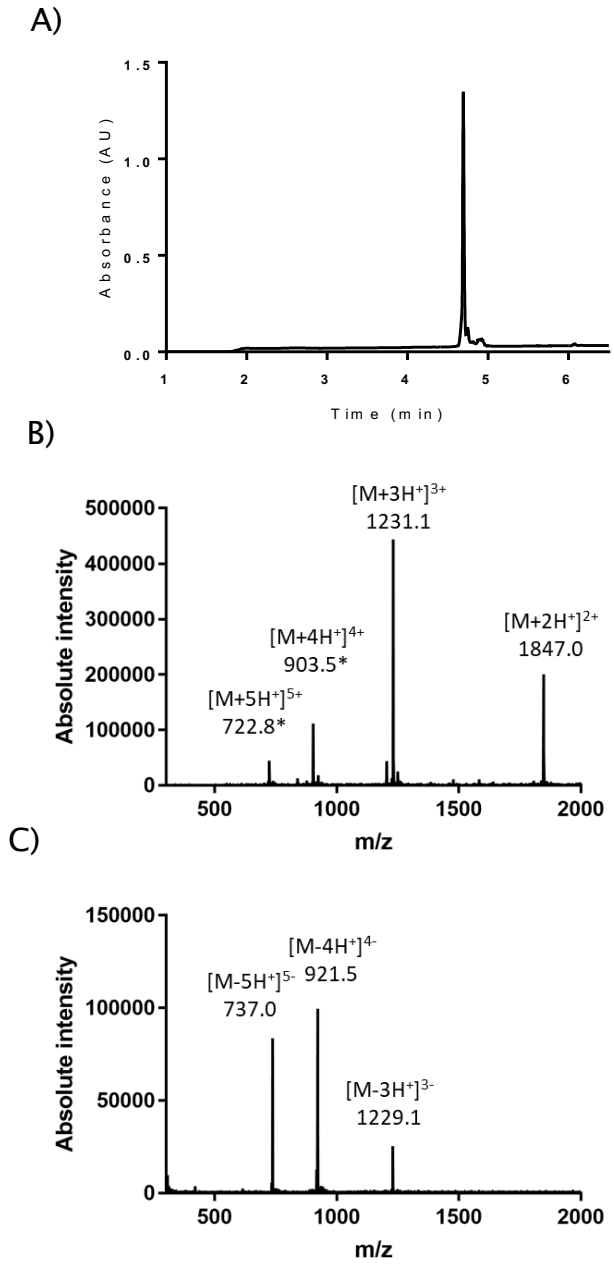
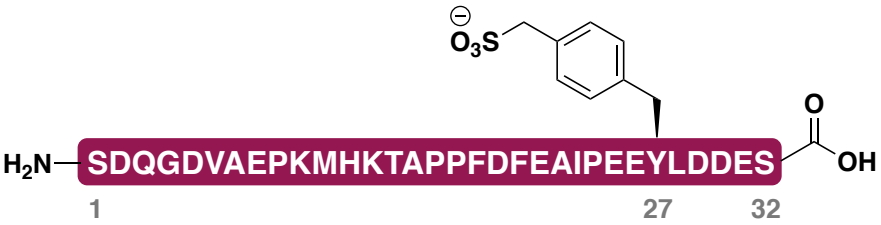


Figure S6. A) Analytical reversed-phase HPLC analysis of purified Variegin (sY27) (**14**) (0-50%B over 5 min, λ = 214 nm) collected on a Waters Acquity UPLC system, as per general procedures. **B)** Mass spectrum (ESI+) of purified Variegin (sY27) (**14**) collected on a Shimadzu 2020 (ESI) mass spectrometer, as per general procedures. **C)** Mass spectrum (ESI-) of purified Variegin (sY27) (**14**) collected on a Shimadzu 2020 (ESI) mass spectrometer, as per general procedures.



Variegin (Smp27) (15)

2-CTC resin (0.28 mmol g^{-1} loading) was loaded with Fmoc-Ser(*t*Bu)-OH according to the general procedures. Synthesis of the L28-E31 fragment was then performed using automated coupling protocols (*see General Procedures – Automated Coupling (Symphony)*) on a Gyros Protein Technologies Symphony® peptide synthesiser. Coupling of Fmoc-Smp(nP)-OH (**2**) was then performed manually according to the *General Procedures (Manual Coupling (Non-Standard))*. Fragment S1-E26 was then completed using automated coupling protocols (*see General Procedures – Automated Coupling (Symphony)*) with double couplings at Q3, D5, V6, E8, H12, K13, A15, P16, A22, I23 and E26. After completion of the synthesis, the peptide was cleaved from the resin and deprotected by treatment with an acidic cleavage cocktail (90:5:5 v/v/v TFA:*i*Pr_3SiH:H_2O) at room temperature for 3 h. The deprotection solution was concentrated under a stream of nitrogen until a small volume remained (<0.5 mL). Cold Et_2O (40 mL) was then added to the remaining deprotection solution to precipitate peptidic material. The resulting suspension was then centrifuged at 4 °C (2000 x g, 5 min) and the ether supernatant was decanted, leaving the crude peptide material to dry under a gentle stream of nitrogen. The precipitated material was dissolved in 2 mL of NH_4OAc buffer (1 M NH_4OAc, 6 M Gn.HCl, 0.1 M Na_2HPO_4) at pH 7 and incubated at 70 °C for 16 h to facilitate the removal of the sulfonyl neopentyl protecting group. After complete neopentyl removal, as judged by UPLC-MS analysis, the reaction mixture was diluted to 5 mL total volume with H_2O (0.1 vol% FA) and purified by preparative reversed-phase chromatography (Waters Sunfire C18, 19 x 150 mm, 14 mL min^{-1}) on a 0-50%B gradient over 45 min (*see general procedures*). Subsequent lyophilisation afforded the purified Variegin (Smp27) (**15**) (1.9 mg, 0.48 μmol, 4% from resin loading [65 steps]).

See analytical data on next page.

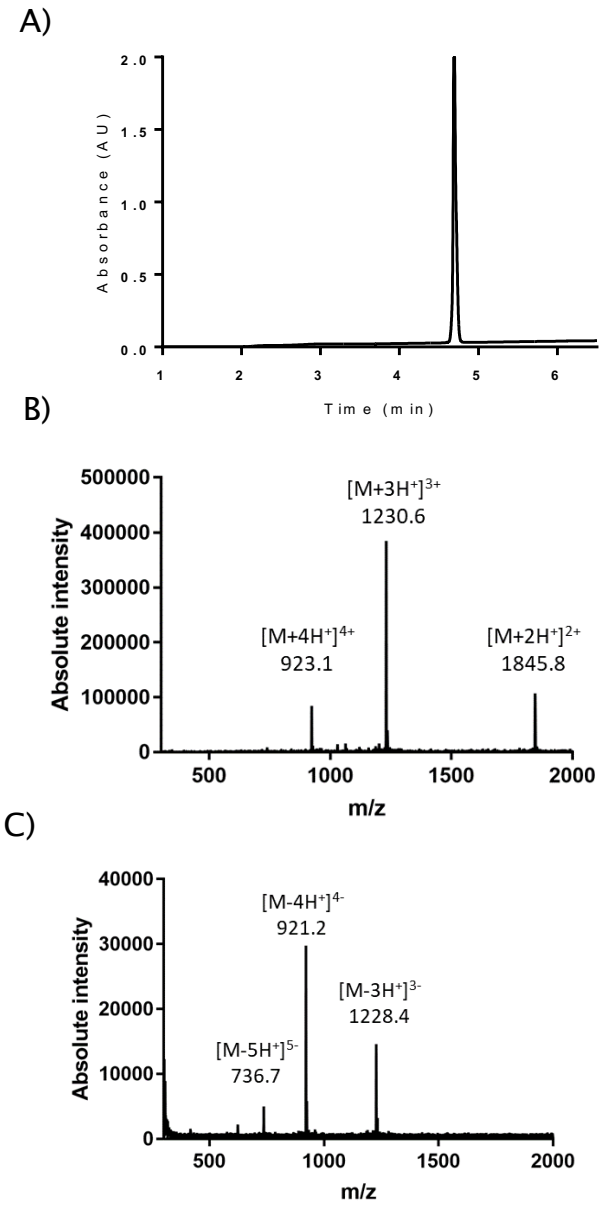
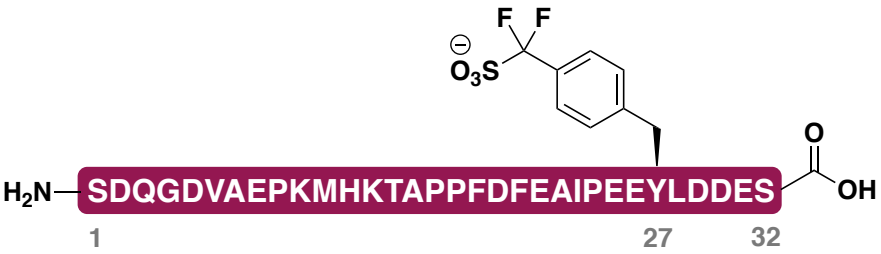


Figure S7. A) Analytical reversed-phase HPLC analysis of purified Variegin (Smp27) (**15**) (0-50%B over 5 min, λ = 214 nm) collected on a Waters Acquity UPLC system, as per general procedures. **B)** Mass spectrum (ESI+) of purified Variegin (Smp27) (**15**) collected on a Shimadzu 2020 (ESI) mass spectrometer, as per general procedures. **C)** Mass spectrum (ESI-) of purified Variegin (Smp27) (**15**) collected on a Shimadzu 2020 (ESI) mass spectrometer, as per general procedures.



Variegin (F_2Smp27) (16)

2-CTC resin (0.28 mmol g^{-1} loading) was loaded with Fmoc-Ser(*t*Bu)-OH according to the general procedures. Synthesis of the L28-E31 fragment was then performed using automated coupling protocols (*see General Procedures – Automated Coupling (Symphony)*) on a Gyros Protein Technologies Symphony® peptide synthesiser. Coupling of Fmoc-F_2Smp(nP)-OH (**3**) was then performed manually according to the *General Procedures (Manual Coupling (Non-Standard))*. Fragment S1-E26 was then completed using automated coupling protocols (*see General Procedures – Automated Coupling (Symphony)*) with double couplings at Q3, D5, V6, E8, H12, K13, A15, P16, A22, I23 and E26. After completion of the synthesis, the peptide was cleaved from the resin and deprotected by treatment with an acidic cleavage cocktail (90:5:5 v/v/v TFA:*i*Pr_3SiH:H_2O) at room temperature for 3 h. The deprotection solution was concentrated under a stream of nitrogen until a small volume remained (<0.5 mL). Cold Et_2O (40 mL) was then added to the remaining deprotection solution to precipitate peptidic material. The resulting suspension was then centrifuged at 4 °C (2000 x g, 5 min) and the ether supernatant was decanted, leaving the crude peptide material to dry under a gentle stream of nitrogen. The precipitated material was dissolved in 2 mL of NH_4OAc buffer (1 M NH_4OAc, 6 M Gn.HCl, 0.1 M Na_2HPO_4) at pH 7 and incubated at 37 °C for 3 h to facilitate the removal of the sulfonyl neopentyl protecting group. After complete neopentyl removal, as judged by UPLC-MS analysis, the reaction mixture was diluted to 5 mL total volume with H_2O (0.1 vol% FA) and purified by preparative reversed-phase chromatography (Waters Sunfire C18, 19 x 150 mm, 14 mL min^{-1}) on a 0-50%B gradient over 45 min (*see general procedures*). Subsequent lyophilisation afforded the purified Variegin (F_2Smp27) (**16**) (1.7 mg, 0.42 μmol, 4% from resin loading [65 steps]).

See analytical data on next page.

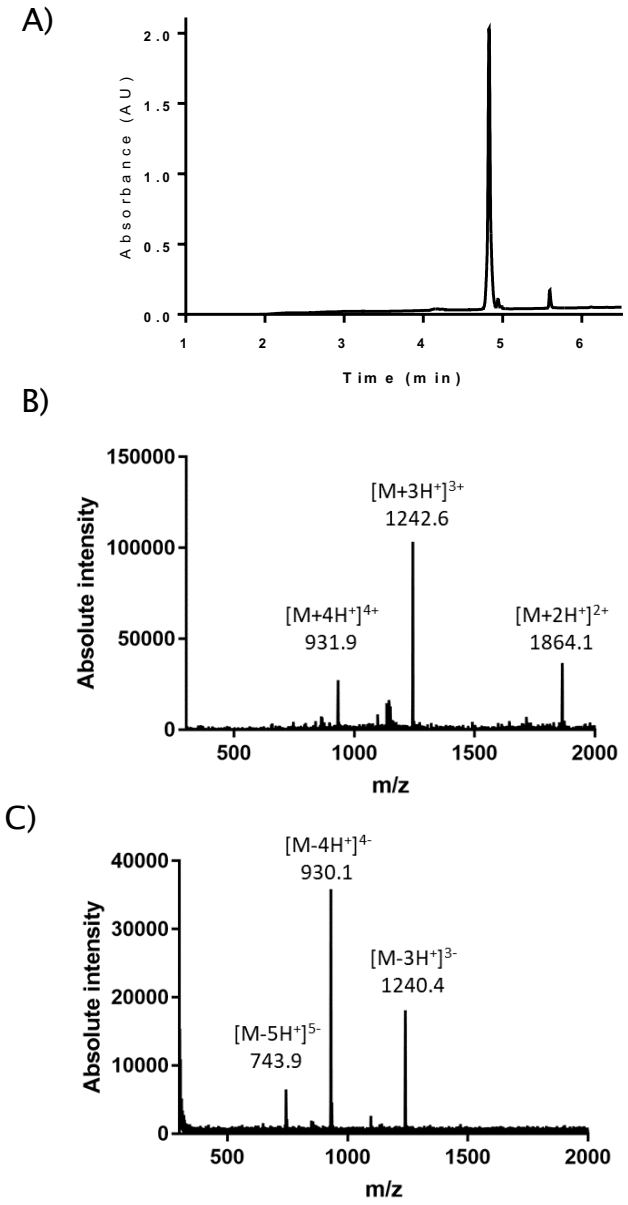


Figure S8. A) Analytical reversed-phase HPLC analysis of purified Variegin (F_2Smp27) (**16**) (0-50%B over 5 min, λ = 214 nm) collected on a Waters Acquity UPLC system, as per general procedures. **B)** Mass spectrum (ESI+) of purified Variegin (F_2Smp27) (**16**) collected on a Shimadzu 2020 (ESI) mass spectrometer, as per general procedures. **C)** Mass spectrum (ESI-) of purified Variegin (F_2Smp27) (**16**) collected on a Shimadzu 2020 (ESI) mass spectrometer, as per general procedures.

5 OPTIMISATION OF NEOPENTYL SULFONATE ESTER DEPROTECTION

Samples of neopentyl-protected TTI (sY9, sY12) (10 mg, 3 μmol) were dissolved in different mildly nucleophilic deprotection mixtures to a concentration of 10 mM:

1) NaN_3 (7.2 mg, 40 eq.) in DMSO (50 °C, 3 h)
2) NaN_3 (7.2 mg, 40 eq.) in DMF (50 °C, 3 h)
3) 1 M NH_4OAc, 6 M Gn.HCl, 0.1 M Na_2HPO_4, pH 7 (37 °C, 3 h)
4) 10 M NH_4OAc, 6 M Gn.HCl, 0.1 M Na_2HPO_4, pH 7 (37 °C, 3 h)

The different NaN_3 and NH_4OAc deprotection conditions were incubated for 3 h at 50 °C and 37 °C, respectively. *Condition 1* (40 eq. NaN_3 in DMSO) (*figure S9A*) led to successful nP deprotection over the 3 h, with some degree of peptide degradation. *Condition 2* (40 eq. NaN_3 in DMF) (*figure S9B*) led exclusively to degradation of the peptide over the 3 h. *Conditions 3 and 4* (1 M and 10 M NH_4OAc in aqueous buffer) (*figure S9C*) led to successful nP deprotection over the 3 h, with some degree of peptide degradation, with condition 3 (1 M NH_4OAc in aqueous buffer) leading to more consistent and complete deprotection (overlaid conditions: *figure S9D*). As such, *condition 3* (1 M NH_4OAc, 6 M Gn.HCl, 0.1 M Na_2HPO_4, pH 7) was chosen for subsequent nP deprotections.

The deprotection of nP-protected sulfonates (i.e. TTI (Smp9, Smp12) (**11**) and Variegin (Smp27) (**15**)) using the optimised conditions (1 M NH_4OAc, 6 M Gn.HCl, 0.1 M Na_2HPO_4, pH 7) were found to require elevated temperatures of 70 °C and extended reaction times of up to 16 h to reach completion. nP-protected difluorosulfonates (i.e. TTI (F_2Smp9, F_2Smp12) (**12**) and Variegin (F_2Smp27) (**16**)) were successfully deprotected under identical conditions to neopentyl-protected sulfates, as optimised above (1 M NH_4OAc, 6 M Gn.HCl, 0.1 M Na_2HPO_4, pH 7, 37 °C for 3 h).

See analytical data on next page.

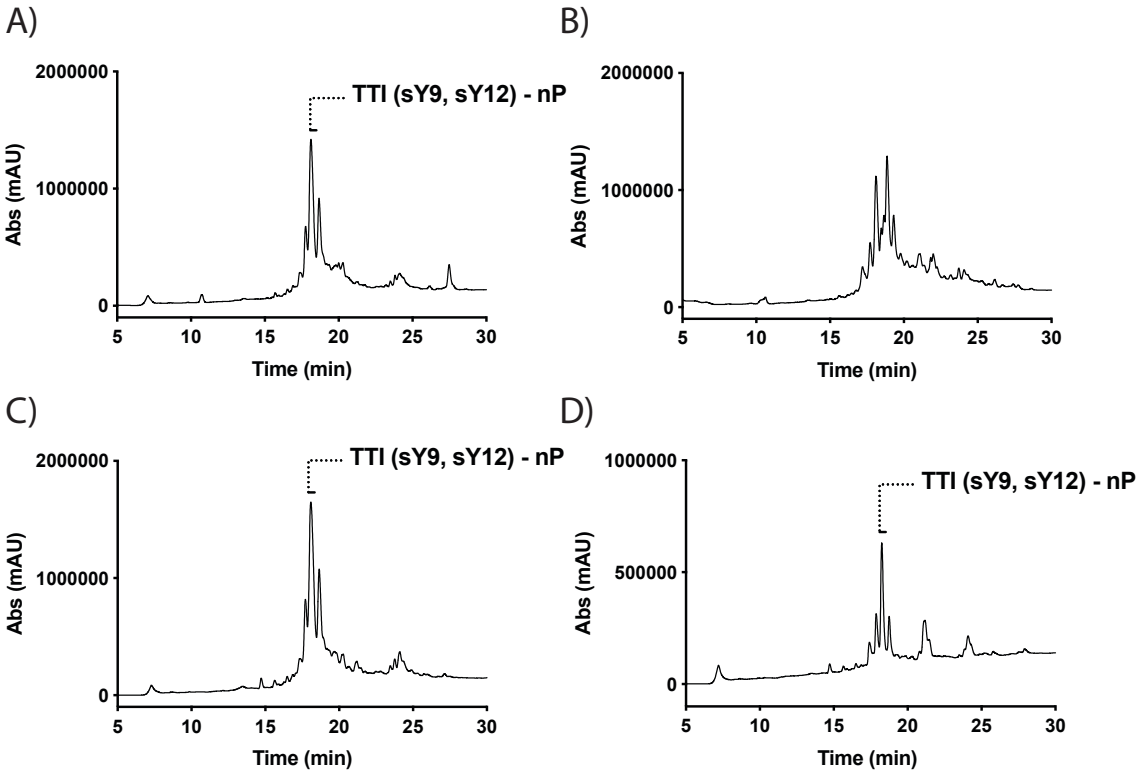


Figure S9. UPLC analysis (0-80%B over 30 min) of the trial deprotections of nP-protected TTI (sY9, sY12) (*c* = 10 mM) at t = 3 h under the following reaction conditions: **A)** NaN_3 (40 eq.) in DMSO at 50 °C, **B)** NaN_3 (40 eq.) in DMF at 50 °C, **C)** 1 M NH_4OAc in aqueous 6 M Gn.HCl (0.1 M Na_2HPO_4, pH 7) at 37 °C, and **D)** 10 M NH_4OAc in aqueous 6 M Gn.HCl (0.1 M Na_2HPO_4, pH 7) at 37 °C.

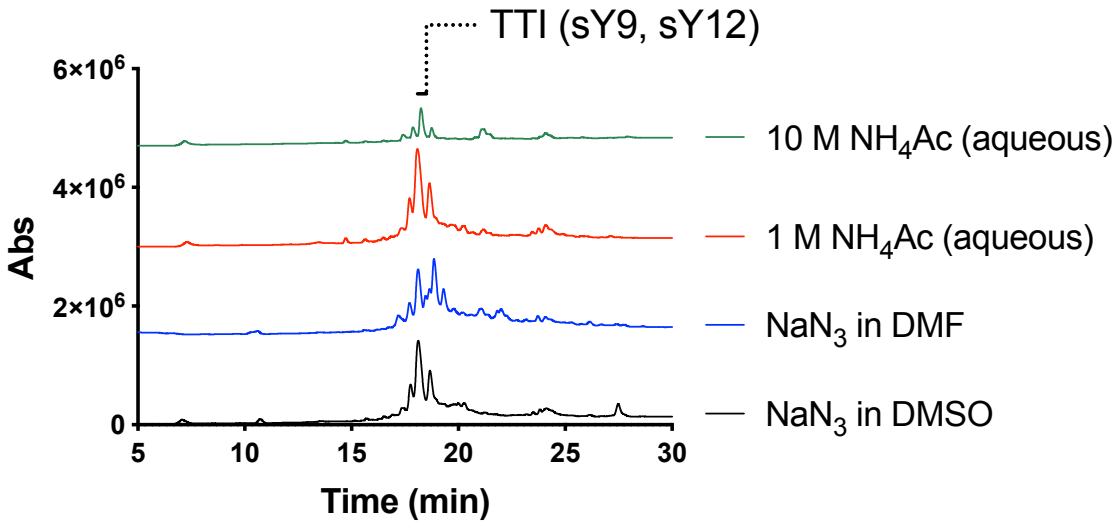


Figure S10. Overlaid conditions for the neopentyl deprotection of nP-protected TTI (sY9, sY12).

6 THROMBIN INHIBITION ASSAY

The inhibition of the amidolytic activity of human α- or γ-thrombin (Haematologic Technologies) was followed spectrophotometrically using Tos-Gly-Pro-Arg-*p*-nitroanilide (Chromozym TH, Roche) as chromogenic substrate. Inhibition assays were performed in 50 mM Tris.HCl pH 8.0, 50 mM NaCl and 1 mg mL^{-1} bovine serum albumin (BSA) with 0.2 nM enzyme, 100 μM substrate and varying concentrations of TTI and Variegin inhibitor variants **10-16** from 0-80 nM, except in the case of **9**, where concentration was varied from 0-1.25 μM. The inhibitory potency of Variegin variants **13-16** against human γ-thrombin was assessed varying concentrations of inhibitor from 0-83 nM. The concentration of each variant was determined by measuring the amide bonds using a Direct Detect Infrared Spectrometer (Millipore). All reactions were initiated by the addition of thrombin and carried out at 37 °C in 96-well microtiter plates. Reaction progress was monitored at 405 nm for 60 mins on a Synergy2 multi-mode microplate reader (Biotek). All measurements were made in duplicate. Inhibition constants (K_i) were determined according to a tight-binding inhibitor model, using the Morrison equation with Prism (GraphPad Software).

Table S1. Determined K_i values for the synthetic inhibitors **9-16** against human α- and γ-thrombin.

TTI variant	**α-Thrombin (pM)**	**R^2**	**γ-Thrombin (pM)**	**R^2**
Y9, Y12 (**9**)	826.9 ± 70.85	0.992	1042 ± 26.85	0.999
sY9, sY12 (**10**)	0.59 ± 0.05	0.999	1.00 ± 0.52	0.999
Smp9, Smp12 (**11**)	3.82 ± 0.34	0.999	2.85 ± 0.37	0.999
F_2Smp9, F_2Smp12 (**12**)	0.27 ± 0.02	0.999	0.61 ± 0.08	0.999
Variegin variant	**α-Thrombin (pM)**	**R^2**	**γ-Thrombin (nM)**	**R^2**
Y27 (**13**)	65.4 ± 6.5	0.992	854.1 ± 88.92	0.984
sY27 (**14**)	3.81 ± 0.60	0.996	1017 ± 31.02	0.998
Smp27 (**15**)	5.59 ± 1.81	0.981	1806 ± 146.1	0.985
F_2Smp27 (**16**)	6.27 ± 0.80	0.997	2626 ± 171.7	0.989

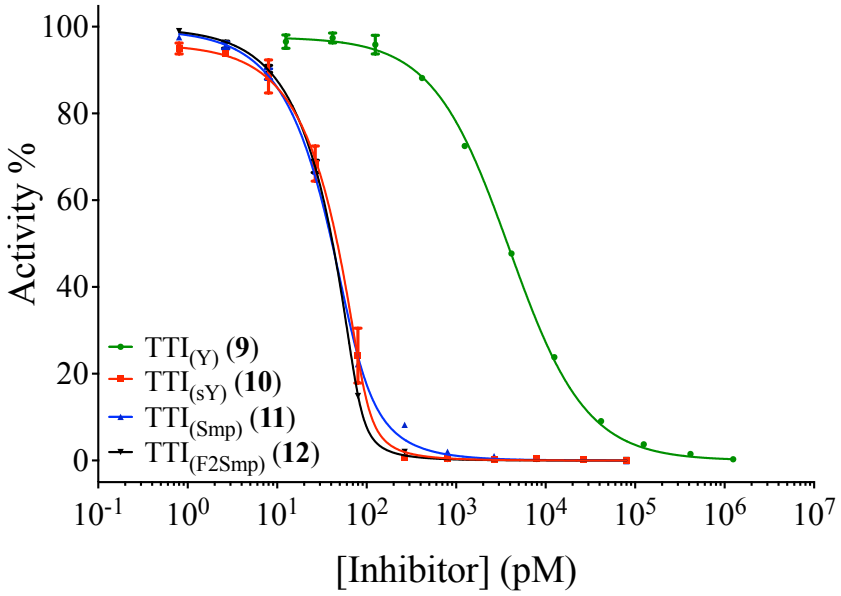


Figure S11. Effect of TTI tyrosine modification on human γ-thrombin amidolytic activity. Activity assays were performed as described (see above – Thrombin Inhibition Assay). Amidolytic activity of human γ-thrombin in the presence of TTI variants was measured at increasing concentrations of unsulfated **9** (green), disulfated **10** (red), Smp-containing **11** (blue) and F_2Smp-containing **12** (black). Activities are represented as a percentage assuming maximum activity (100%) in the absence of inhibitor. Error bars represent the standard deviation of two independent experiments. Data were fitted to the Morrison inhibition function using GraphPad Prism 6 (GraphPad Software).

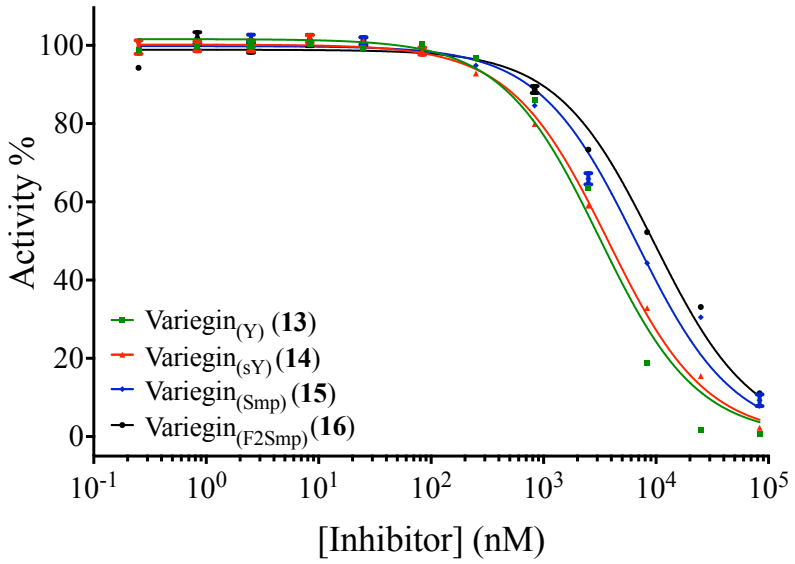


Figure S12. Effect of Variegin tyrosine modification on human γ-thrombin amidolytic activity. Activity assays were performed as described (see above – Thrombin Inhibition Assay). Amidolytic activity of human γ-thrombin in the presence of Variegin was measured at increasing concentrations of unsulfated **13** (green), sulfated **14** (red), Smp-containing **15** (blue) and F_2Smp-containing **16** (black) variants. Activities are represented as a percentage assuming maximum activity (100%) in the absence of inhibitor. Error bars represent the standard deviation of two independent experiments. Data were fitted to the Morrison inhibition function using GraphPad Prism 6 (GraphPad Software).

7 ACID STABILITY ASSAYS

To test the acid stability of the sulfonate moiety of TTI (Smp9, Smp12) (**11**) and TTI (F_2Smp9, F_2Smp12) (**12**), these thrombin inhibitors were dissolved in ultrapure H_2O (type 1) with 0.1 vol% TFA (pH 2) to a concentration of 100 mM and subsequently incubated at room temperature for 10 h. Aliquots were taken at 1 h intervals and analyzed by UPLC and UPLC-MS.

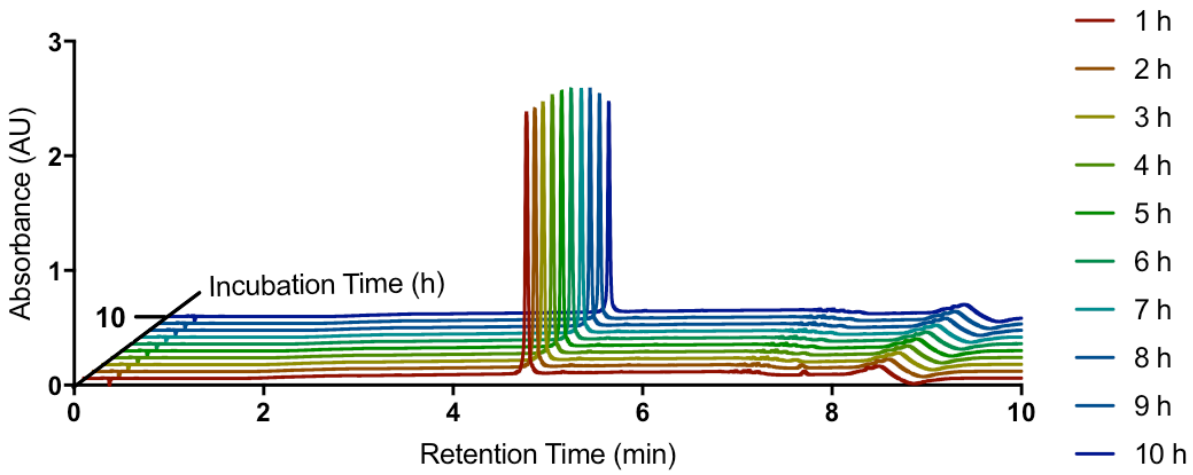


Figure S13. UPLC analysis of TTI (Smp9, Smp12) (**11**) at 1 h time intervals during incubation in H_2O with 0.1 vol% TFA (pH 2) to a concentration of 100 mM.

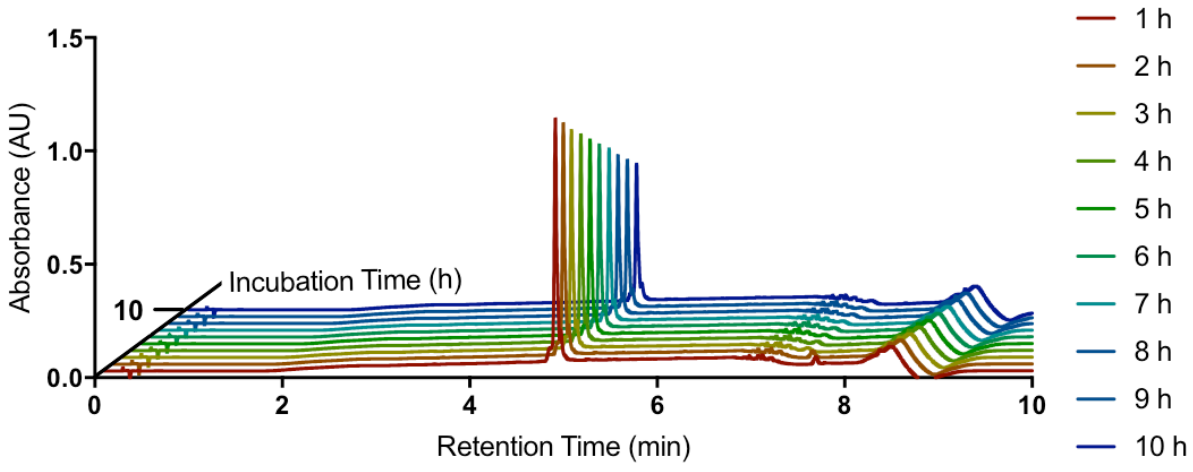


Figure S14. UPLC analysis of TTI (F_2Smp9, F_2Smp12) (**12**) at 1 h time intervals during incubation in H_2O with 0.1 vol% TFA (pH 2) to a concentration of 100 mM.

8 COMPLEX CRYSTALLISATION TRIALS

Human α-thrombin (Haematologic Technologies) was mixed in a 1:3 molar ratio with TTI (Smp9, Smp12) (**11**) in 0.02 M HEPES pH 7.5, 0.125 M NaCl. The solution was incubated on ice for 30 min and then concentrated to 14 mg/mL using a 2 kDa cut-off centrifugal ultrafiltration device (Sartorius). Crystallization conditions were screened at 20 °C in sitting drop geometry using 96-well plates. Drops were prepared with a dispensing robot (Mosquito, TTP LabTech Ltd) by mixing equal volumes (150 nL) of the complex and reservoir solutions and equilibrated against 80 μL of the latter. A crystallization condition yielding orthorhombic crystals (space group $P2_12_12_1$) was identified (0.1 M HEPES pH 7.5, 0.2 M ammonium acetate, 25% (w/v) PEG 3350). Crystals were recovered from the drops, cryopreserved in 0.1 M HEPES pH 7.5, 0.2 M ammonium acetate, 30% (w/v) PEG 3350, 15% (v/v) glycerol, and flash-cooled in liquid nitrogen.

9 X-RAY CRYSTALLOGRAPHY

X-ray diffraction data collection on crystals of human α-thrombin in complex with TTI (Smp9, Smp12) (**11**) was performed at 100K on the BL13-XALOC beamline[3] of the ALBA Synchrotron (Cerdanyola del Vallès, Spain) using a PILATUS 6M detector (Dectris) (900 images, 0.1º rotation, 0.097 s exposure).

Data was indexed and integrated with XDS[4] and reduced with utilities from the CCP4 suite.[5] The raw diffraction images were deposited with the Structural Biology Data Grid (doi: 10.15785/SBGRID/846).[6] The structure was solved by molecular replacement with PHASER[7] using the coordinates from human α-thrombin (PDB: 6TKG) as a search model.[8] Refinement and model building were conducted iteratively using COOT[9] and PHENIX, respectively.[10] The final refined three-dimensional coordinates and structure factors were deposited at the Protein Data Bank (PDB: 7PHX, doi: 10.2210/pdb7PHX/pdb). All structural representations were produced using PyMOL (Schrödinger).

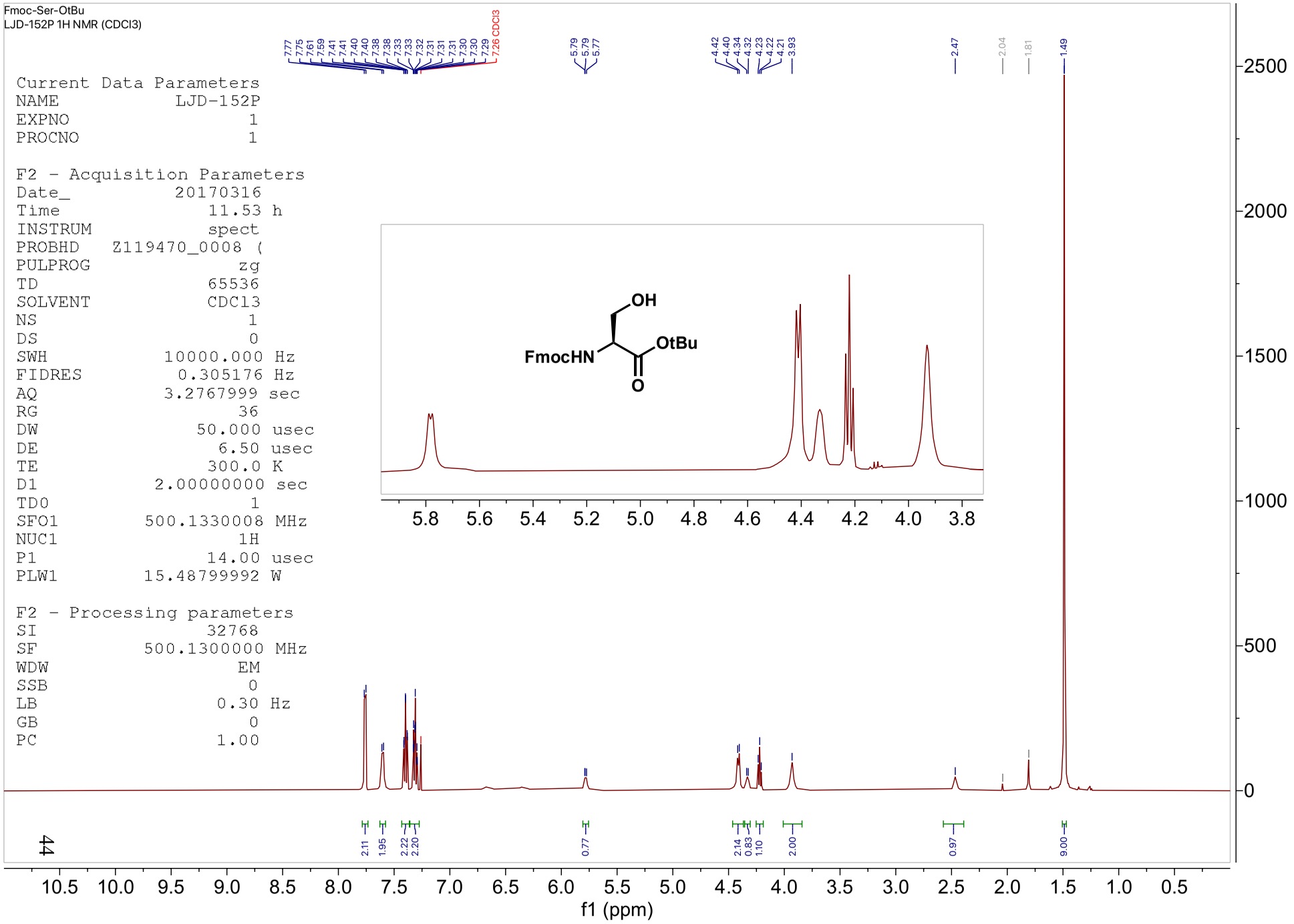
Table S2. Data collection and refinement statistics*.

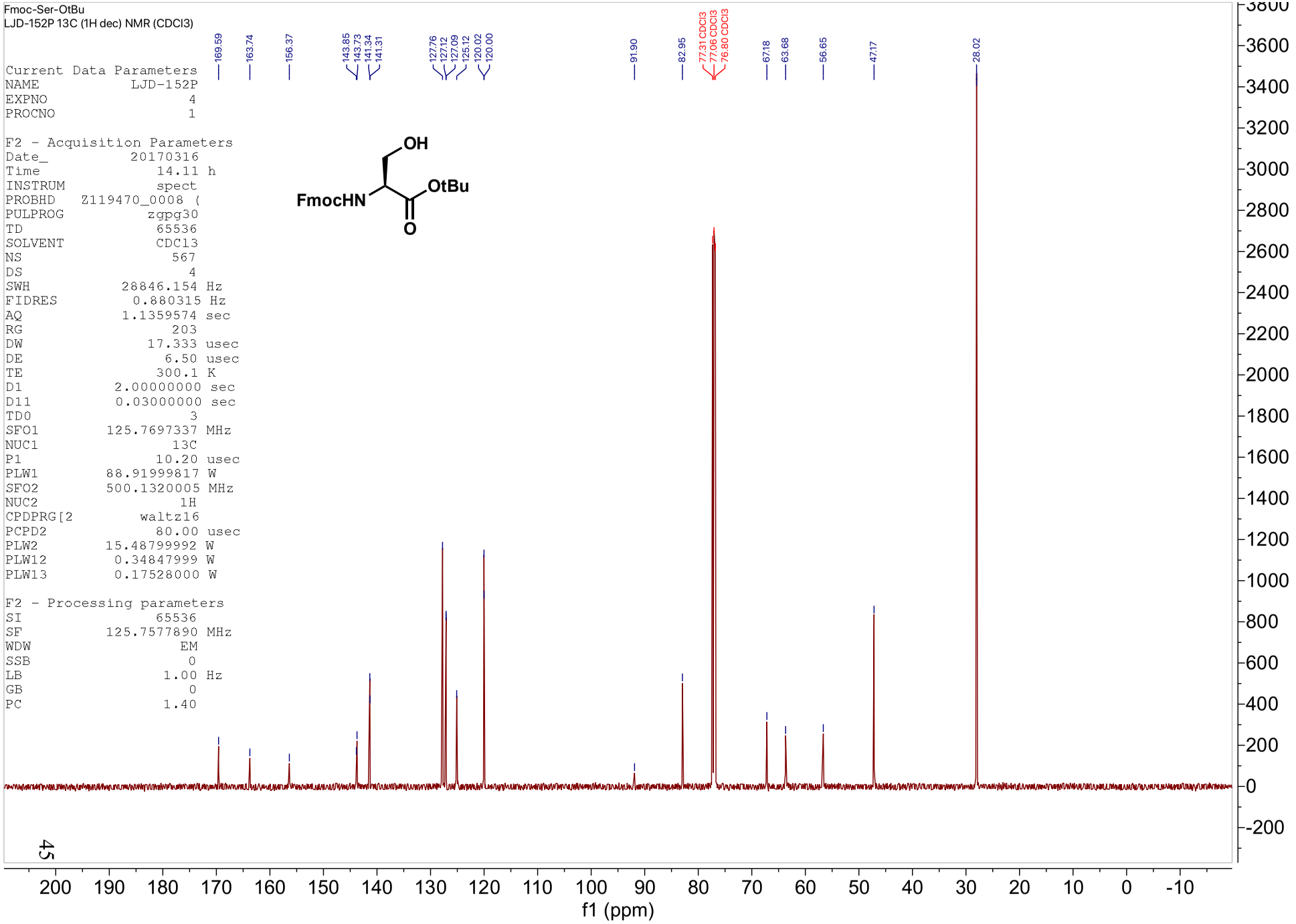
Dataset	**TB: TTI-Smp9,Smp12**
Data collection	
Beamline	ALBA BL13-XALOC
Wavelength (Å)	0.97926
Resolution range (Å)	42.95 -1.80 (1.84 - 1.80)
Space group	$P2_12_12_1$
Unit cell dimensions (Å)	a=43.7, b=80.8, c=85.9
Number of reflections (observed / unique)	92,228 / 27,532 (5,220 / 1,617)
Multiplicity	3.3 (3.2)
Completeness (%)	96.0 (97.0)
Mean I/σ(I)	14.8 (1.9)
R_{merge} (%)	3.9 (53.6)
$CC^{1/2}$	0.999 (0.834)
Complexes per a.u.	1
Matthews coefficient ($Å^3\ Da^{-1}$)	2.06
Solvent content (%)	40.2
Refinement	
R_{work}	0.183
R_{free}	0.221
Protein residues	300
Water molecules	133
r.m.s.d. bond lengths (Å)	0.008
r.m.s.d. bond angles (°)	1.005
Ramachandran favored (%)	97.6
Ramachandran outliers (%)	0.0
PDB code	7PHX

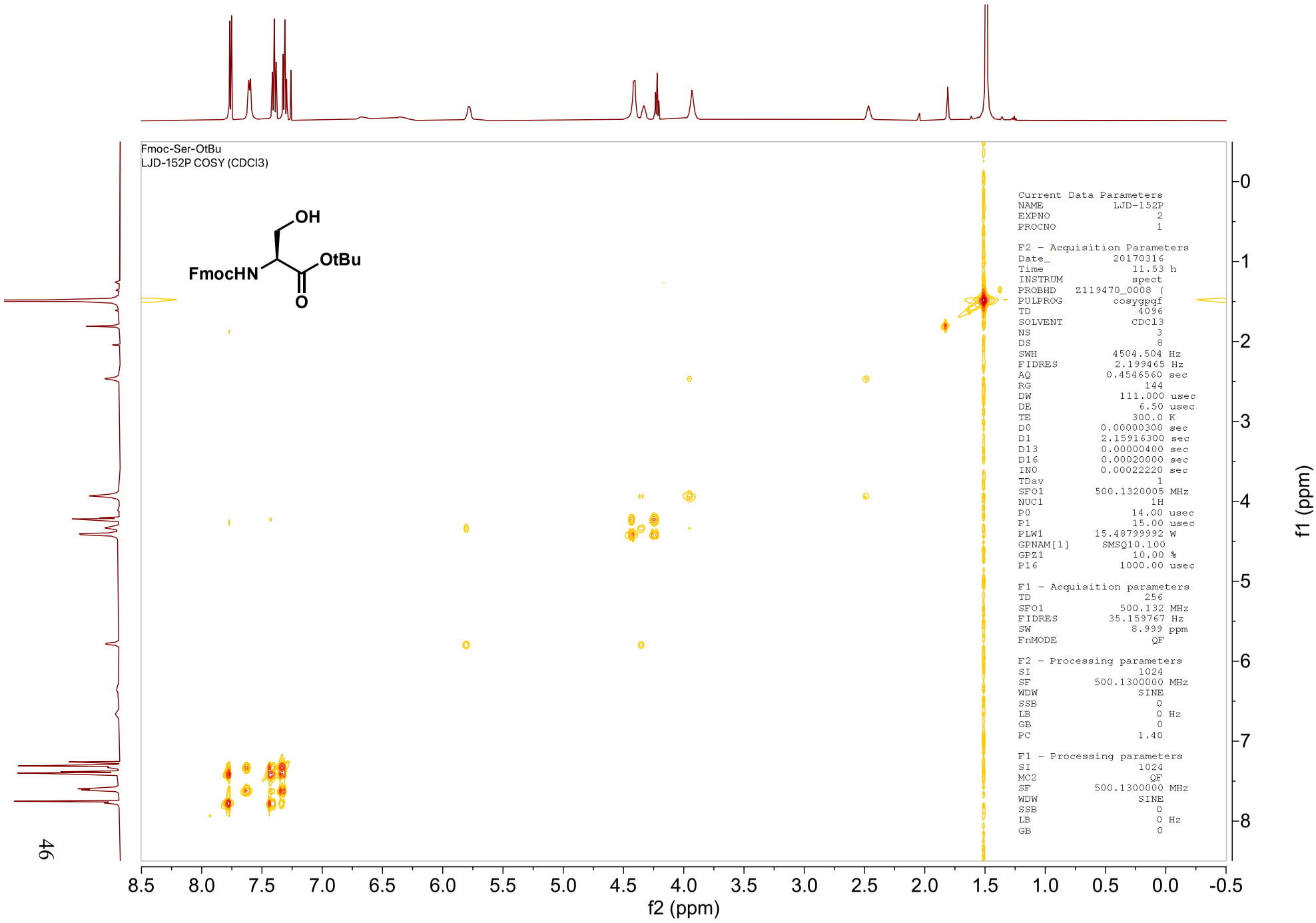
* Values in parenthesis correspond to the highest resolution shell.

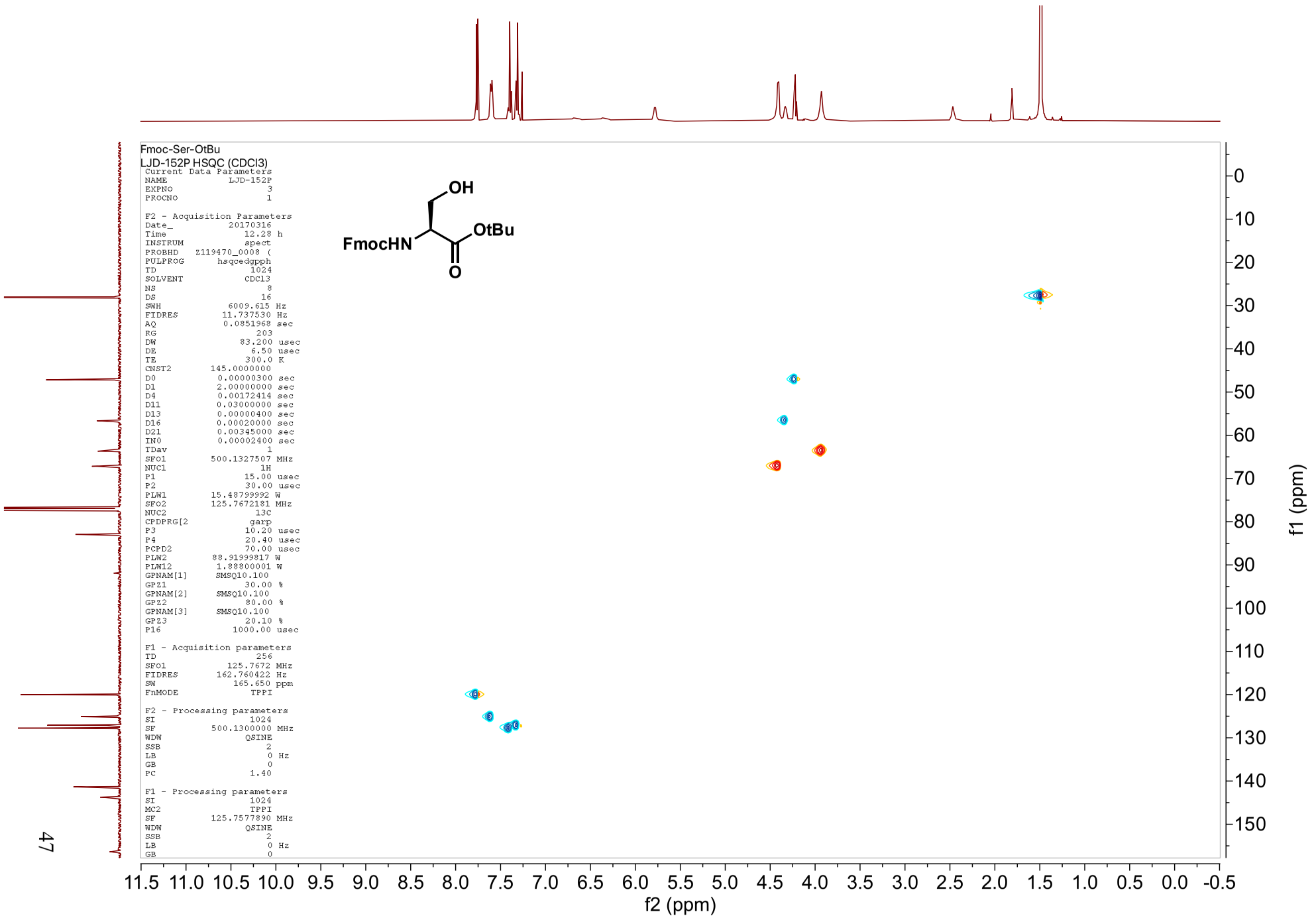
10 NMR SPECTRA FOR 2, 3 AND SYNTHETIC INTERMEDIATES

Continued on next page.


Fmoc-Ser-OtBu
LJD-152P 1H NMR (CDCl3)
Current Data Parameters
NAME LJD-152P
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170316
Time 11.53 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG zg
TD 65536
SOLVENT CDCl3
NS 1
DS 0
SWH 10000.000 Hz
FIDRES 0.305176 Hz
AQ 3.2767999 sec
RG 36
DW 50.000 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
TD0 1
SFO1 500.1330008 MHz
NUC1 1H
P1 14.00 usec
PLW1 15.48799992 W
F2 - Processing parameters
SI 32768
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.77 7.75 7.61 7.59 7.41 7.41 7.40 7.40 7.38 7.38 7.33 7.33 7.32 7.31 7.31 7.31 7.30 7.30 7.29 7.26 CDCl3
5.79 5.79 5.77
4.42 4.40 4.34 4.32 4.23 4.22 4.21 3.93
2.47 2.04 1.81 1.49
OH
FmocHN
OtBu
O
2.11 1.95 2.22 2.20 0.77 2.14 0.83 1.10 2.00 0.97 9.00
44
f1 (ppm)


Fmoc-Ser-OtBu
LJD-152P 13C (1H dec) NMR (CDCl3)
169.59
163.74
156.37
143.85
143.73
141.34
141.31
127.76
127.12
127.09
125.12
120.02
120.00
91.90
82.95
77.31 CDCl3
77.06 CDCl3
76.80 CDCl3
67.18
63.68
56.65
47.17
28.02
Current Data Parameters
NAME LJD-152P
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170316
Time 14.11 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 567
DS 4
SWH 28846.154 Hz
FIDRES 0.880315 Hz
AQ 1.1359574 sec
RG 203
DW 17.333 usec
DE 6.50 usec
TE 300.1 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 3
SFO1 125.7697337 MHz
NUC1 13C
P1 10.20 usec
PLW1 88.91999817 W
SFO2 500.1320005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 15.48799992 W
PLW12 0.34847999 W
PLW13 0.17528000 W
F2 - Processing parameters
SI 65536
SF 125.7577890 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
OH
FmocHN
OtBu
O
45
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)
3800 3600 3400 3200 3000 2800 2600 2400 2200 2000 1800 1600 1400 1200 1000 800 600 400 200 0 -200


Fmoc-Ser-OtBu
LJD-152P COSY (CDCl3)
OH
FmocHN
OtBu
O
Current Data Parameters
NAME LJD-152P
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170316
Time 11.53 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG cosygpqf
TD 4096
SOLVENT CDCl3
NS 3
DS 8
SWH 4504.504 Hz
FIDRES 2.199465 Hz
AQ 0.4546560 sec
RG 144
DW 111.000 usec
DE 6.50 usec
TE 300.0 K
D0 0.00000300 sec
D1 2.15916300 sec
D13 0.00000400 sec
D16 0.00020000 sec
IN0 0.00022220 sec
TDav 1
SFO1 500.1320005 MHz
NUC1 1H
P0 14.00 usec
P1 15.00 usec
PLW1 15.48799992 W
GPNAM[1] SMSQ10.100
GPZ1 10.00 %
P16 1000.00 usec
F1 - Acquisition parameters
TD 256
SFO1 500.132 MHz
FIDRES 35.159767 Hz
SW 8.999 ppm
FnMODE QF
F2 - Processing parameters
SI 1024
SF 500.1300000 MHz
WDW SINE
SSB 0
LB 0 Hz
GB 0
PC 1.40
F1 - Processing parameters
SI 1024
MC2 QF
SF 500.1300000 MHz
WDW SINE
SSB 0
LB 0 Hz
GB 0
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f2 (ppm)
0 1 2 3 4 5 6 7 8
f1 (ppm)


Fmoc-Ser-OtBu
LJD-152P HSQC (CDCl3)
Current Data Parameters
NAME LJD-152P
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170316
Time 12.28 h
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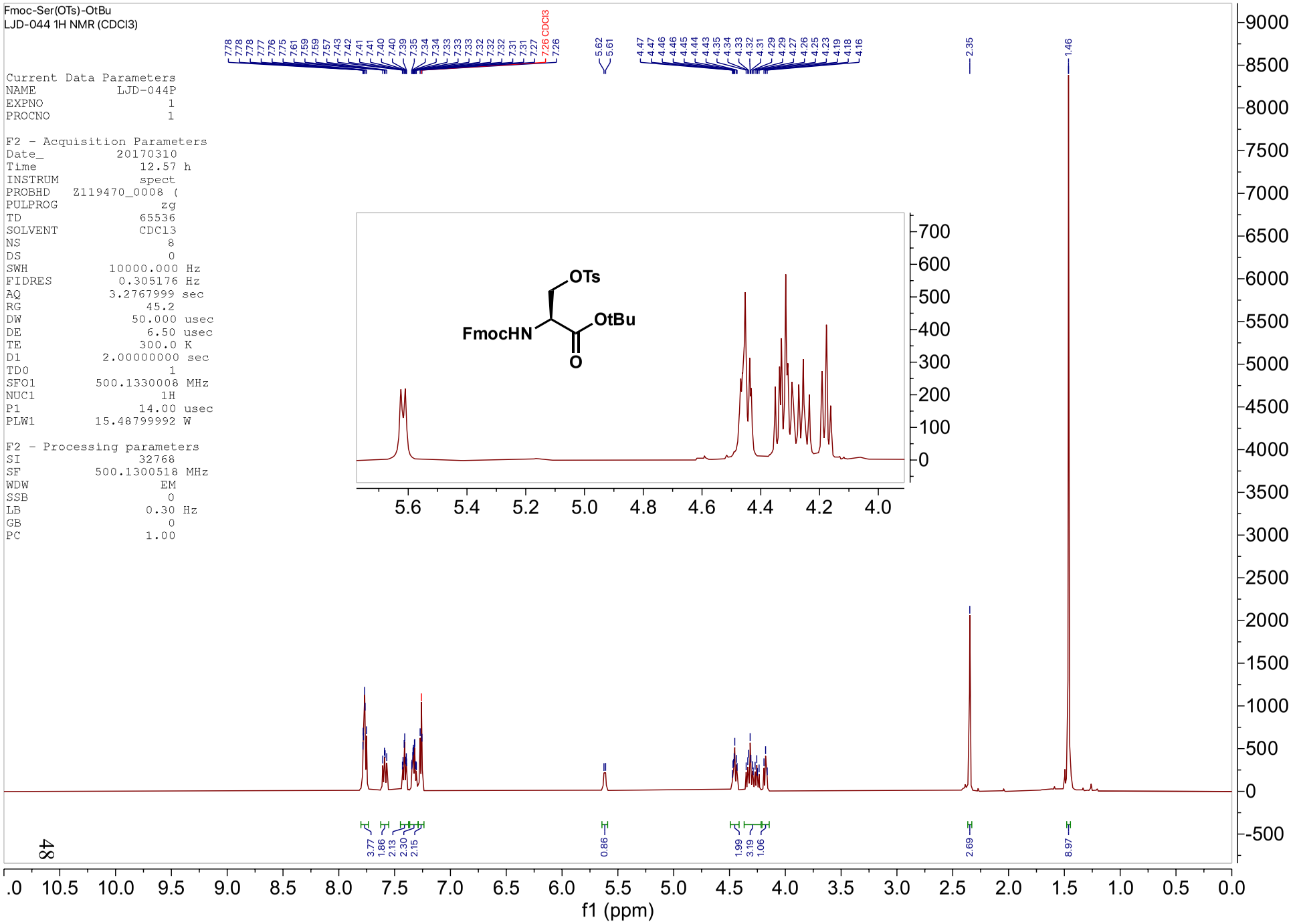
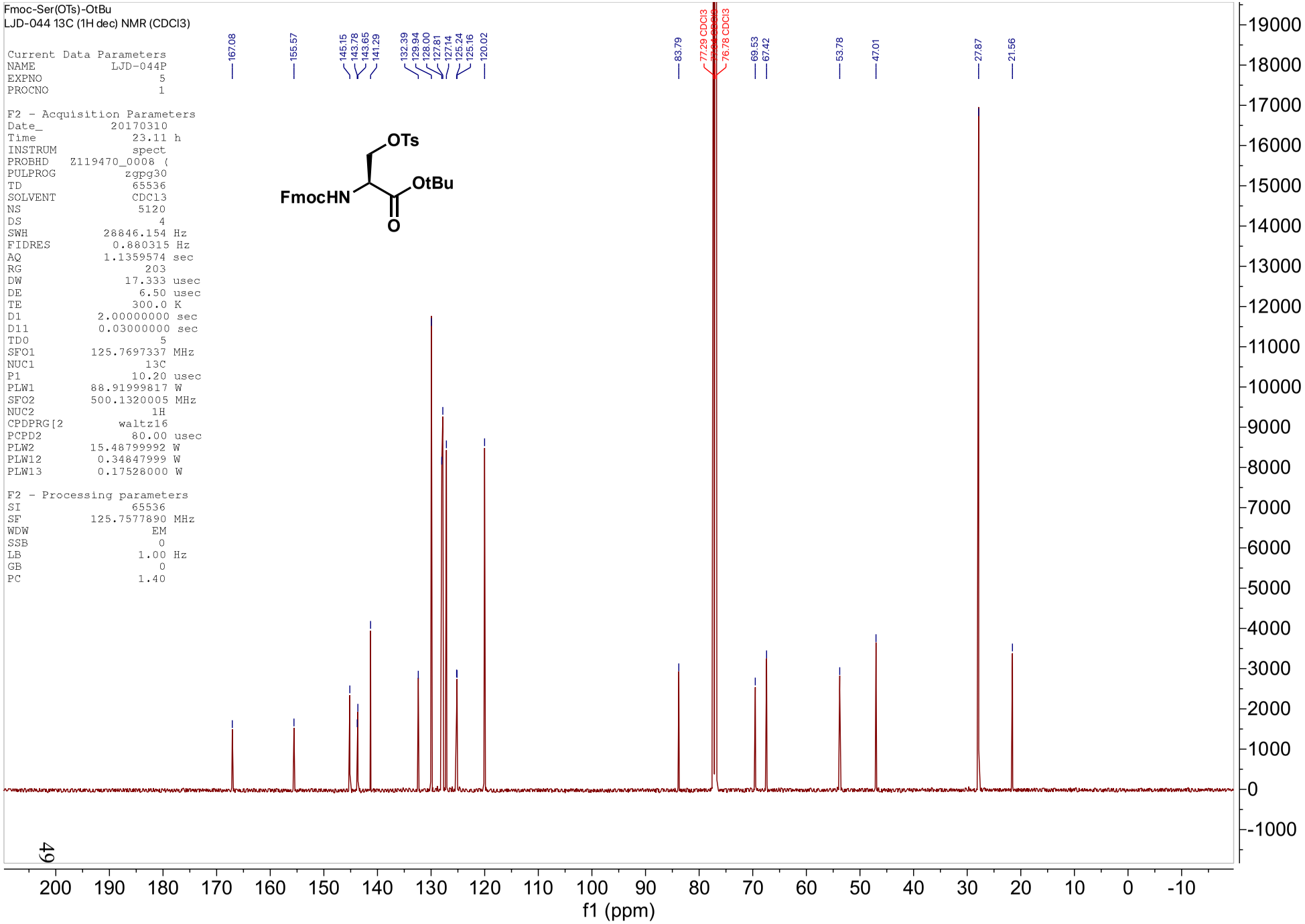
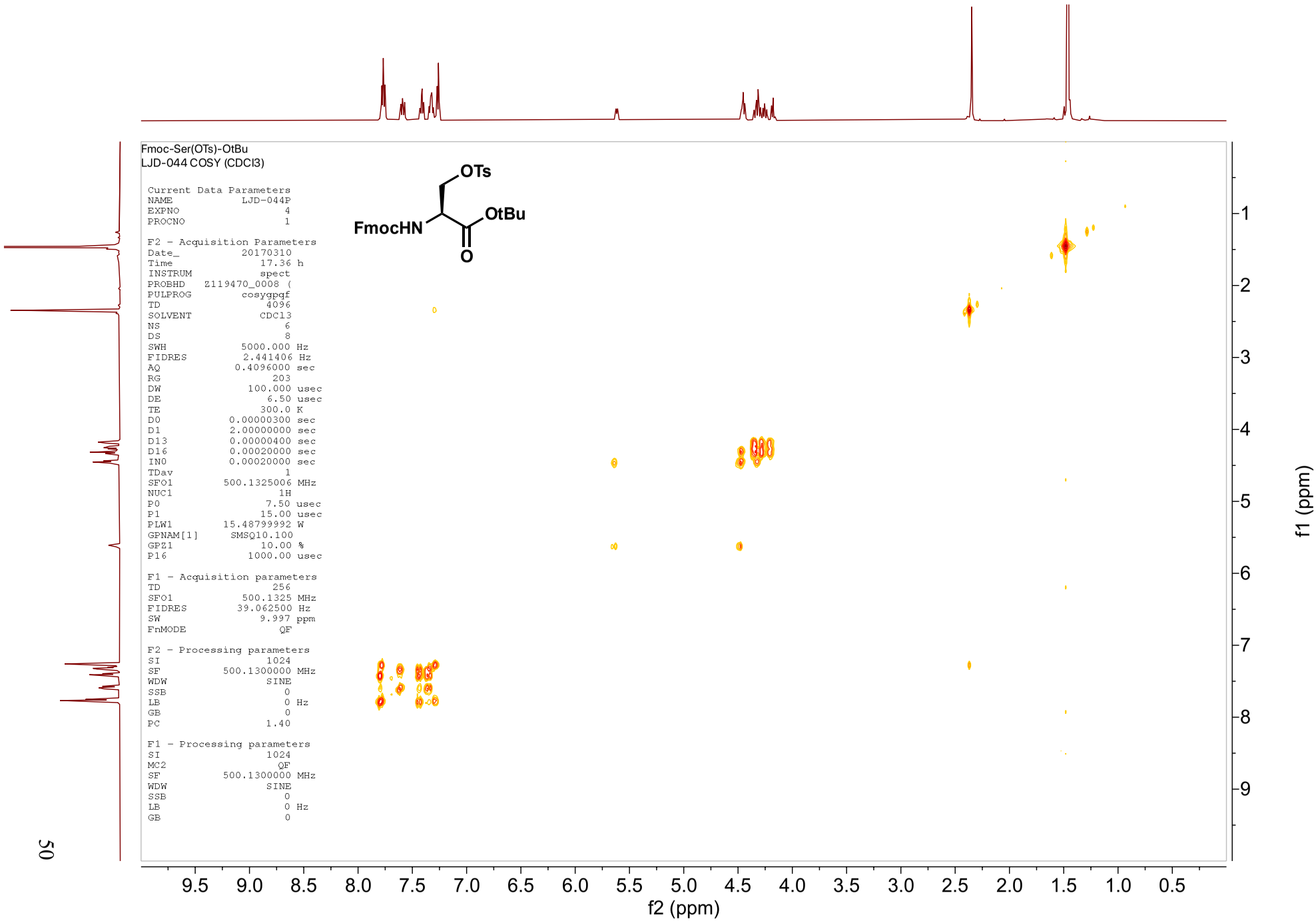
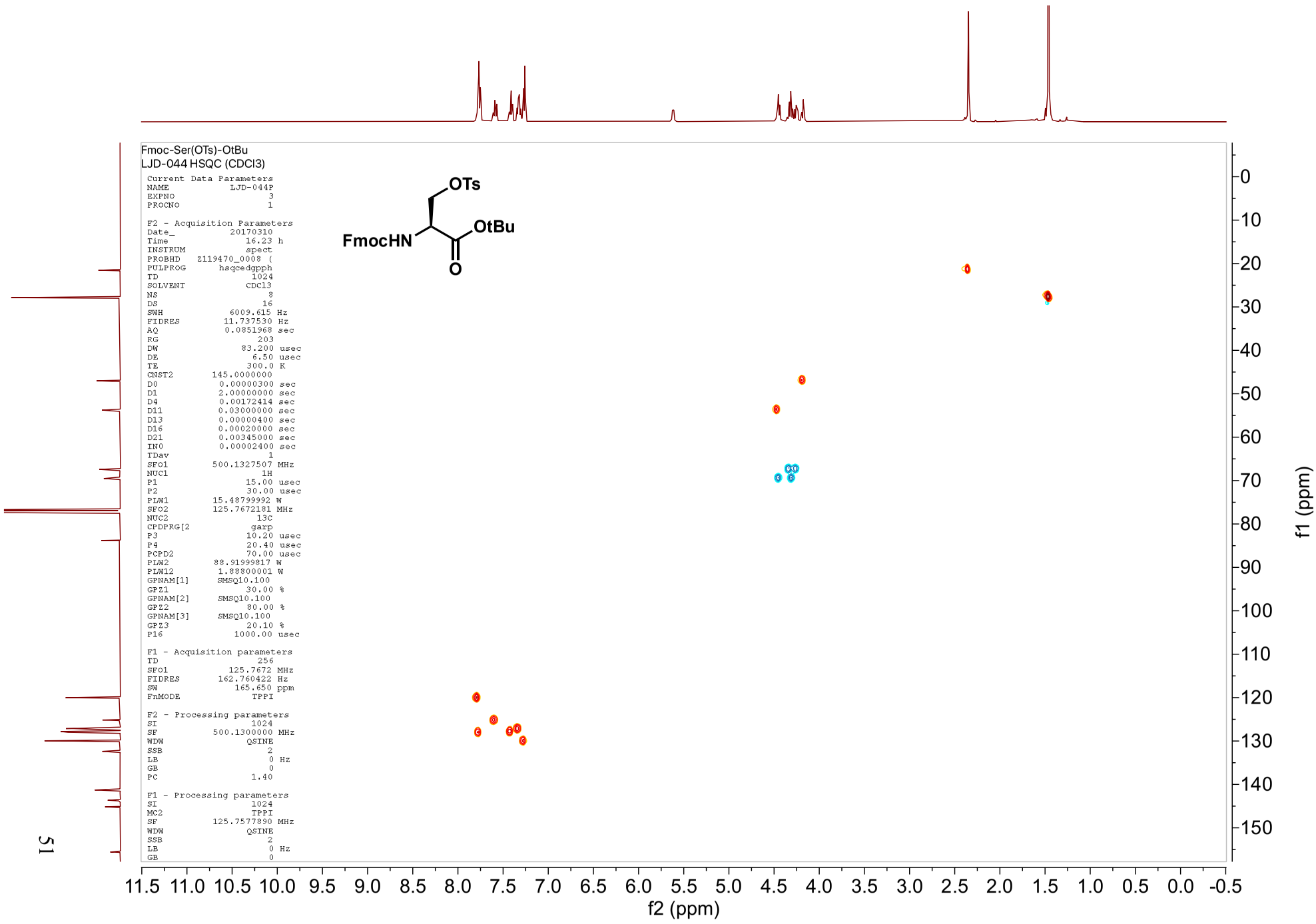
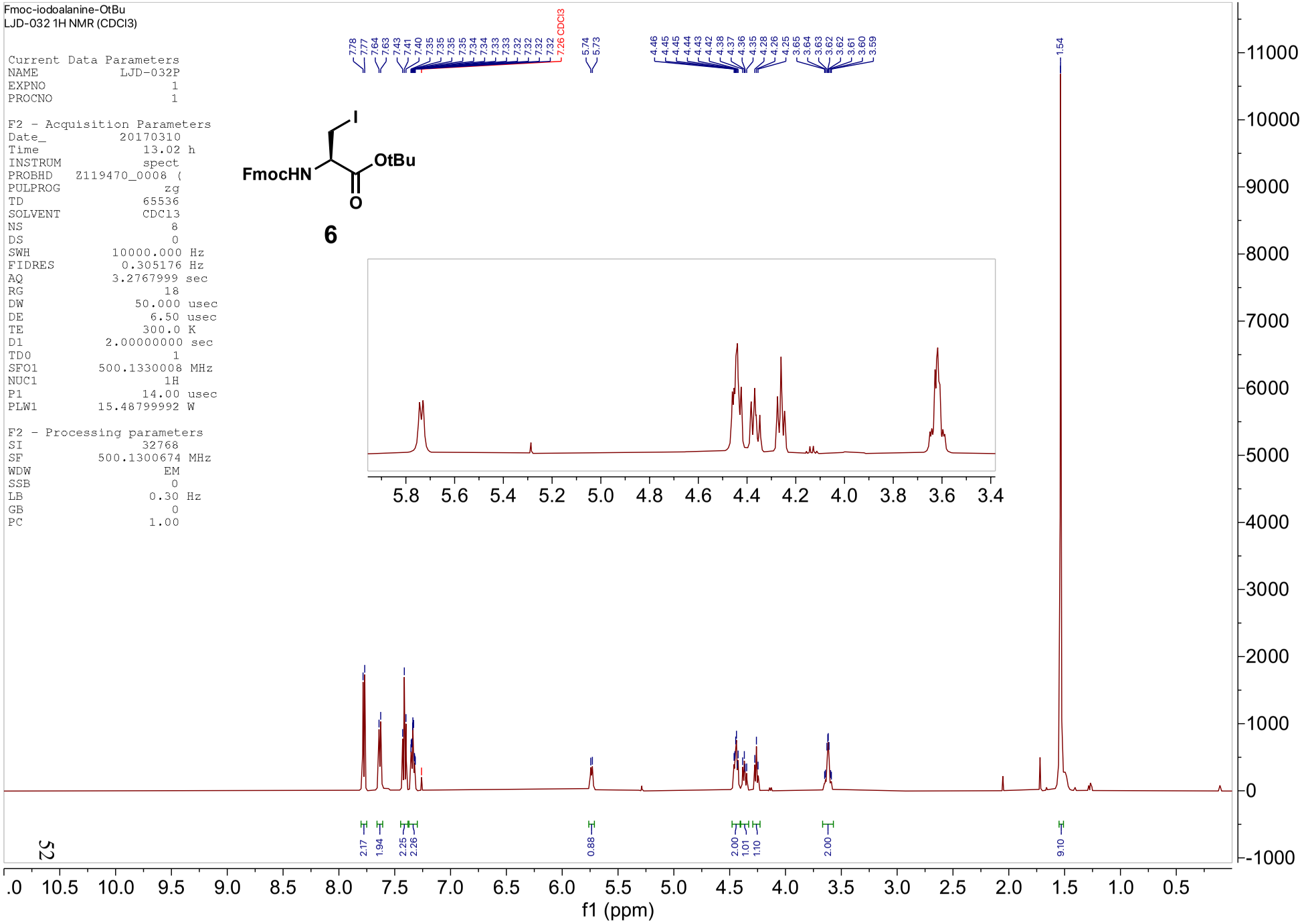
PROBHD Z119470_0008 (
PULPROG hsqcedgpph
TD 1024
SOLVENT CDCl3
NS 8
DS 16
SWH 6009.615 Hz
FIDRES 11.737530 Hz
AQ 0.0851968 sec
RG 203
DW 83.200 usec
DE 6.50 usec
TE 300.0 K
CNST2 145.0000000
D0 0.00000300 sec
D1 2.00000000 sec
D4 0.00172414 sec
D11 0.03000000 sec
D13 0.00000400 sec
D16 0.00020000 sec
D21 0.00345000 sec
IN0 0.00002400 sec
TDav 1
SFO1 500.1327507 MHz
NUC1 1H
P1 15.00 usec
P2 30.00 usec
PLW1 15.48799992 W
SFO2 125.7672181 MHz
NUC2 13C
CPDPRG[2 garp
P3 10.20 usec
P4 20.40 usec
PCPD2 70.00 usec
PLW2 88.91999817 W
PLW12 1.88800001 W
GPNAM[1] SMSQ10.100
GPZ1 30.00 %
GPNAM[2] SMSQ10.100
GPZ2 80.00 %
GPNAM[3] SMSQ10.100
GPZ3 20.10 %
P16 1000.00 usec
F1 - Acquisition parameters
TD 256
SFO1 125.7672 MHz
FIDRES 162.760422 Hz
SW 165.650 ppm
FnMODE TPPI
F2 - Processing parameters
SI 1024
SF 500.1300000 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.40
F1 - Processing parameters
SI 1024
MC2 TPPI
SF 125.7577890 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
OH
OtBu
FmocHN
O
47
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f2 (ppm)
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150
f1 (ppm)


Fmoc-Ser(OTs)-OtBu
LJD-044 1H NMR (CDCl3)
Current Data Parameters
NAME LJD-044P
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170310
Time 12.57 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG zg
TD 65536
SOLVENT CDCl3
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.305176 Hz
AQ 3.2767999 sec
RG 45.2
DW 50.000 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
TD0 1
SFO1 500.1330008 MHz
NUC1 1H
P1 14.00 usec
PLW1 15.48799992 W
F2 - Processing parameters
SI 32768
SF 500.1300518 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OTs
OtBu
FmocHN
O
7.78 7.78 7.78 7.77 7.76 7.75 7.61 7.59 7.59 7.57 7.43 7.42 7.41 7.41 7.40 7.40 7.39 7.35 7.34 7.34 7.33 7.33 7.33 7.32 7.32 7.32 7.31 7.31 7.27 7.26 CDCl3 7.26
5.62 5.61
4.47 4.47 4.46 4.46 4.45 4.44 4.43 4.35 4.34 4.33 4.32 4.31 4.29 4.29 4.27 4.26 4.25 4.23 4.19 4.18 4.16
2.35
1.46
3.77 1.86 2.13 2.30 2.15
0.86
1.99 3.19 1.06
2.69
8.97
48
f1 (ppm)


Fmoc-Ser(OTs)-OtBu
LJD-044 13C (1H dec) NMR (CDCl3)
Current Data Parameters
NAME LJD-044P
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170310
Time 23.11 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 5120
DS 4
SWH 28846.154 Hz
FIDRES 0.880315 Hz
AQ 1.1359574 sec
RG 203
DW 17.333 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 5
SFO1 125.7697337 MHz
NUC1 13C
P1 10.20 usec
PLW1 88.91999817 W
SFO2 500.1320005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 15.48799992 W
PLW12 0.34847999 W
PLW13 0.17528000 W
F2 - Processing parameters
SI 65536
SF 125.7577890 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
OTs
OtBu
FmocHN
O
167.08
155.57
145.15
143.78
143.65
141.29
132.39
129.84
128.00
127.81
127.14
125.24
125.16
120.02
83.79
77.29 CDCl3
76.78 CDCl3
69.53
67.42
53.78
47.01
27.87
21.56
f1 (ppm)


Fmoc-Ser(OTs)-OtBu
LJD-044 COSY (CDCl3)
OTs
OtBu
FmocHN
O
Current Data Parameters
NAME LJD-044P
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170310
Time 17.36 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG cosygpqf
TD 4096
SOLVENT CDCl3
NS 6
DS 8
SWH 5000.000 Hz
FIDRES 2.441406 Hz
AQ 0.4096000 sec
RG 203
DW 100.000 usec
DE 6.50 usec
TE 300.0 K
D0 0.00000300 sec
D1 2.00000000 sec
D13 0.00000400 sec
D16 0.00020000 sec
IN0 0.00020000 sec
TDav 1
SFO1 500.1325006 MHz
NUC1 1H
P0 7.50 usec
P1 15.00 usec
PLW1 15.48799992 W
GPNAM[1] SMSQ10.100
GPZ1 10.00 %
P16 1000.00 usec
F1 - Acquisition parameters
TD 256
SFO1 500.1325 MHz
FIDRES 39.062500 Hz
SW 9.997 ppm
FnMODE QF
F2 - Processing parameters
SI 1024
SF 500.1300000 MHz
WDW SINE
SSB 0
LB 0 Hz
GB 0
PC 1.40
F1 - Processing parameters
SI 1024
MC2 QF
SF 500.1300000 MHz
WDW SINE
SSB 0
LB 0 Hz
GB 0
50
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f2 (ppm)
1 2 3 4 5 6 7 8 9
f1 (ppm)


Fmoc-Ser(OTs)-OtBu
LJD-044 HSQC (CDCl3)
Current Data Parameters
NAME LJD-044P
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170310
Time 16.23 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG hsqcedgpph
TD 1024
SOLVENT CDCl3
NS 8
DS 16
SWH 6009.615 Hz
FIDRES 11.737530 Hz
AQ 0.0851968 sec
RG 203
DW 83.200 usec
DE 6.50 usec
TE 300.0 K
CNST2 145.0000000
D0 0.00000300 sec
D1 2.00000000 sec
D4 0.00172414 sec
D11 0.03000000 sec
D13 0.00000400 sec
D16 0.00020000 sec
D21 0.00345000 sec
IN0 0.00002400 sec
TDav 1
SFO1 500.1327507 MHz
NUC1 1H
P1 15.00 usec
P2 30.00 usec
PLW1 15.48799992 W
SFO2 125.7672181 MHz
NUC2 13C
CPDPRG[2 garp
P3 10.20 usec
P4 20.40 usec
PCPD2 70.00 usec
PLW2 88.91999817 W
PLW12 1.88800001 W
GPNAM[1] SMSQ10.100
GPZ1 30.00 %
GPNAM[2] SMSQ10.100
GPZ2 80.00 %
GPNAM[3] SMSQ10.100
GPZ3 20.10 %
P16 1000.00 usec
F1 - Acquisition parameters
TD 256
SFO1 125.7672 MHz
FIDRES 162.760422 Hz
SW 165.650 ppm
FnMODE TPPI
F2 - Processing parameters
SI 1024
SF 500.1300000 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.40
F1 - Processing parameters
SI 1024
MC2 TPPI
SF 125.7577890 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
OTs
OtBu
FmocHN
O
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f2 (ppm)
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150
f1 (ppm)


Fmoc-iodoalanine-OtBu
LJD-032 1H NMR (CDCl3)
Current Data Parameters
NAME LJD-032P
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170310
Time 13.02 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG zg
TD 65536
SOLVENT CDCl3
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.305176 Hz
AQ 3.2767999 sec
RG 18
DW 50.000 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
TD0 1
SFO1 500.1330008 MHz
NUC1 1H
P1 14.00 usec
PLW1 15.48799992 W
F2 - Processing parameters
SI 32768
SF 500.1300674 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
FmocHN
OtBu
I
O
6
7.78 7.77 7.64 7.63 7.43 7.41 7.40 7.35 7.35 7.35 7.35 7.34 7.34 7.33 7.33 7.32 7.32 7.32 7.32 7.26 CDCl3
5.74 5.73
4.46 4.45 4.45 4.44 4.43 4.42 4.38 4.37 4.36 4.35 4.28 4.26 4.25
3.65 3.64 3.63 3.62 3.62 3.61 3.60 3.59
1.54
2.17 1.94 2.25 2.26 0.88 2.00 1.01 1.10 2.00 9.10
f1 (ppm)

Fmoc-iodoalanine-OtBu
LJD-032 13C (1H dec) NMR (CDCl3)

```
Current Data Parameters
NAME            LJD-032P
EXPNO                  5
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170311
Time                5.45 h
INSTRUM             spect
PROBHD    Z119470_0008 (
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  5120
DS                     4
SWH            28846.154 Hz
FIDRES          0.880315 Hz
AQ              1.1359574 sec
RG                   203
DW                17.333 usec
DE                 6.50 usec
TE                 300.0 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    5
SFO1         125.7697337 MHz
NUC1                13C
P1                10.20 usec
PLW1         88.91999817 W
SFO2         500.1320005 MHz
NUC2                1H
CPDPRG[2         waltz16
PCPD2             80.00 usec
PLW2         15.48799992 W
PLW12         0.34847999 W
PLW13         0.17528000 W

F2 - Processing parameters
SI                 65536
SF           125.7577890 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
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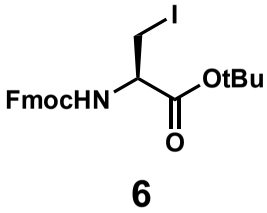
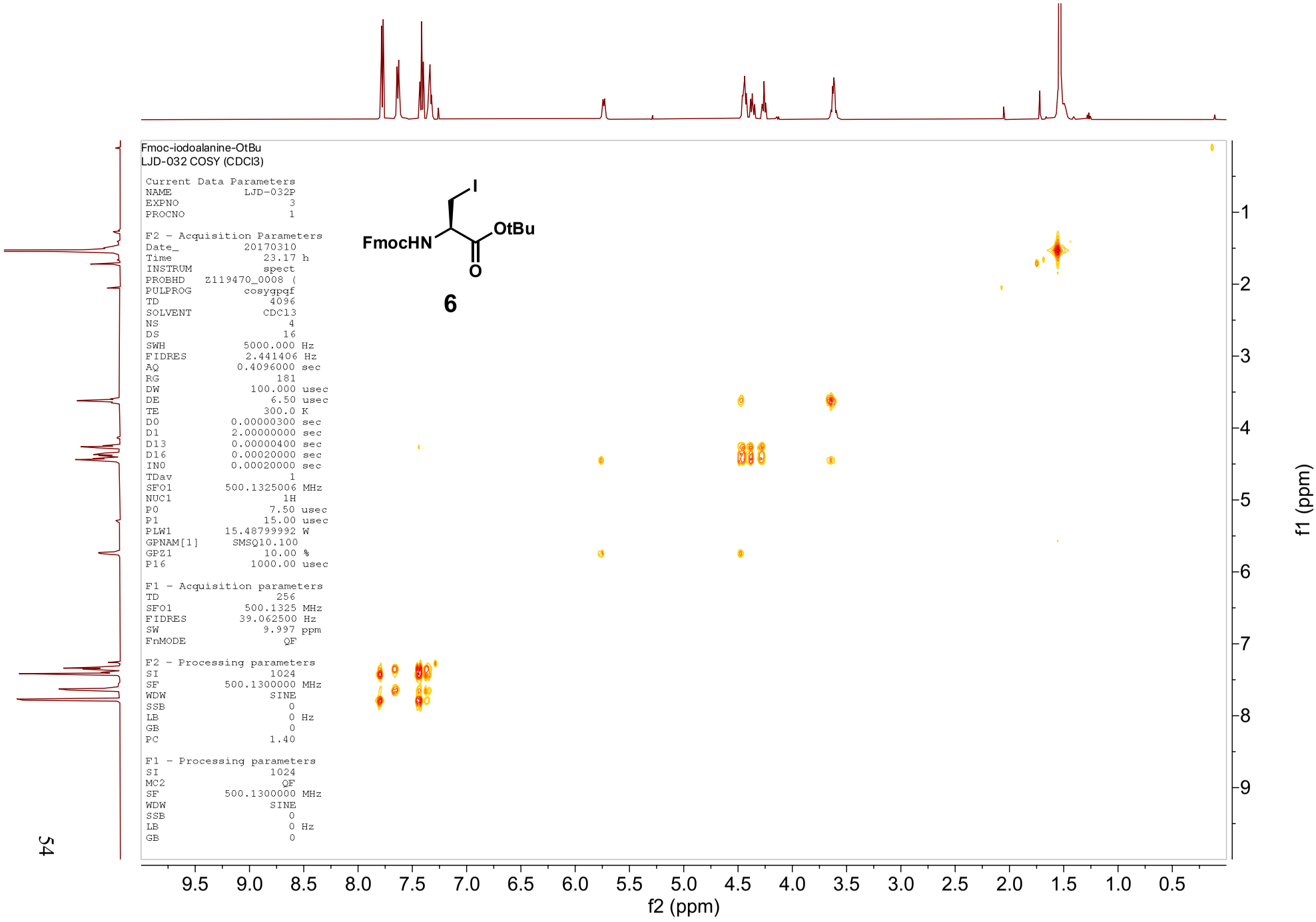


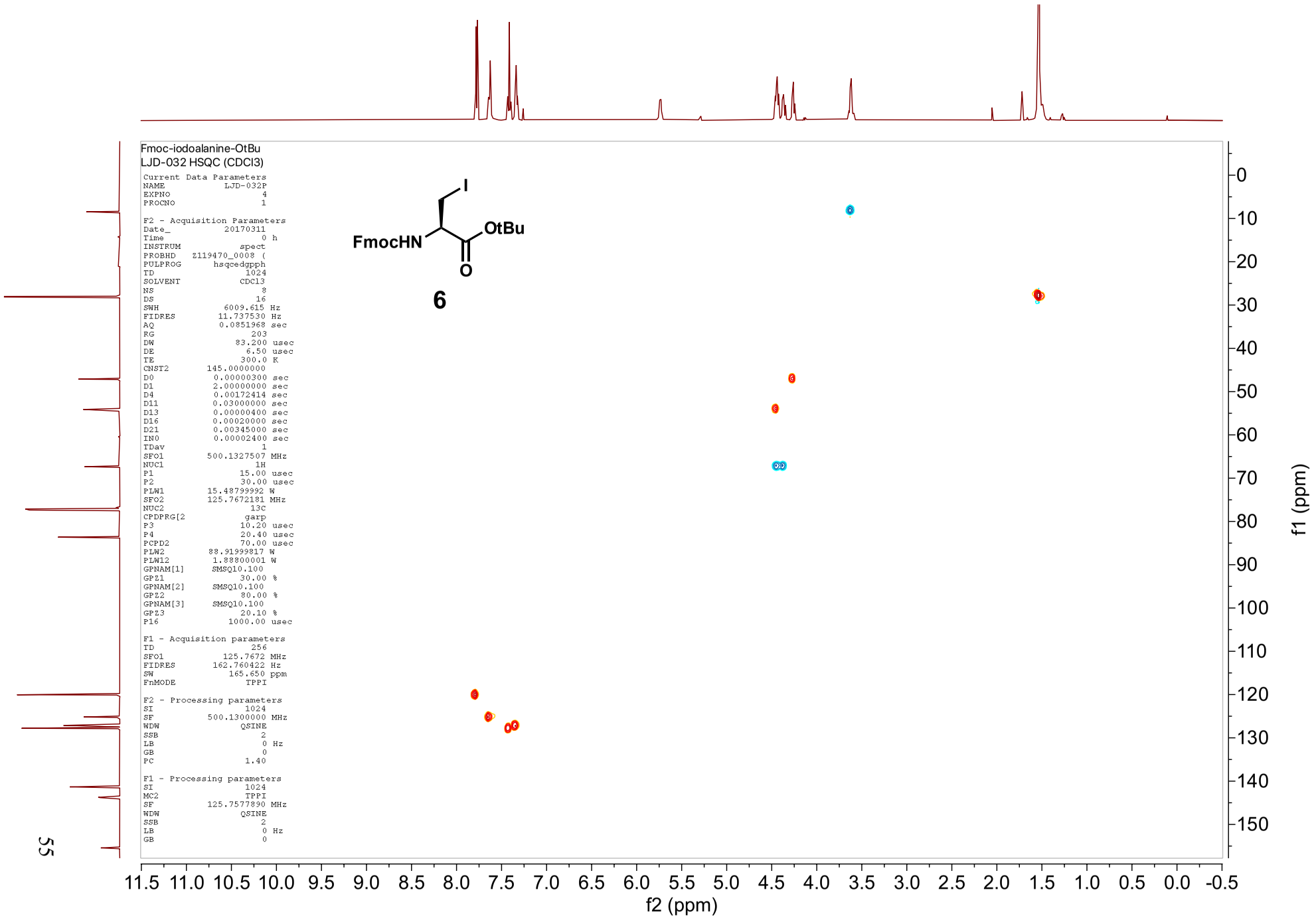
6

168.21 155.43 143.82 143.74 141.33 127.79 127.16 127.13 125.25 125.18 120.05 83.63 77.37 CDCl3 77.12 CDCl3 76.86 CDCl3 67.34 54.13 47.13 28.04 8.46

53

f1 (ppm)


Fmoc-iodoalanine-OtBu
LJD-032 COSY (CDCl3)
Current Data Parameters
NAME LJD-032P
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170310
Time 23.17 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG cosygpqf
TD 4096
SOLVENT CDCl3
NS 4
DS 16
SWH 5000.000 Hz
FIDRES 2.441406 Hz
AQ 0.4096000 sec
RG 181
DW 100.000 usec
DE 6.50 usec
TE 300.0 K
D0 0.00000300 sec
D1 2.00000000 sec
D13 0.00000400 sec
D16 0.00020000 sec
IN0 0.00020000 sec
TDav 1
SFO1 500.1325006 MHz
NUC1 1H
P0 7.50 usec
P1 15.00 usec
PLW1 15.48799992 W
GPNAM[1] SMSQ10.100
GPZ1 10.00 %
P16 1000.00 usec
F1 - Acquisition parameters
TD 256
SFO1 500.1325 MHz
FIDRES 39.062500 Hz
SW 9.997 ppm
FnMODE QF
F2 - Processing parameters
SI 1024
SF 500.1300000 MHz
WDW SINE
SSB 0
LB 0 Hz
GB 0
PC 1.40
F1 - Processing parameters
SI 1024
MC2 QF
SF 500.1300000 MHz
WDW SINE
SSB 0
LB 0 Hz
GB 0
I
FmocHN
OtBu
O
6
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f2 (ppm)
1 2 3 4 5 6 7 8 9
f1 (ppm)

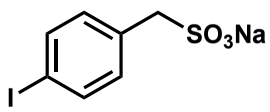

Fmoc-iodoalanine-OtBu
LJD-032 HSQC (CDCl3)
Current Data Parameters
NAME LJD-032P
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170311
Time 0 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG hsqcedgpph
TD 1024
SOLVENT CDCl3
NS 8
DS 16
SWH 6009.615 Hz
FIDRES 11.737530 Hz
AQ 0.0851968 sec
RG 203
DW 83.200 usec
DE 6.50 usec
TE 300.0 K
CNST2 145.0000000
D0 0.00000300 sec
D1 2.00000000 sec
D4 0.00172414 sec
D11 0.03000000 sec
D13 0.00000400 sec
D16 0.00020000 sec
D21 0.00345000 sec
IN0 0.00002400 sec
TDav 1
SFO1 500.1327507 MHz
NUC1 1H
P1 15.00 usec
P2 30.00 usec
PLW1 15.48799992 W
SFO2 125.7672181 MHz
NUC2 13C
CPDPRG[2 garp
P3 10.20 usec
P4 20.40 usec
PCPD2 70.00 usec
PLW2 88.91999817 W
PLW12 1.88800001 W
GPNAM[1] SMSQ10.100
GPZ1 30.00 %
GPNAM[2] SMSQ10.100
GPZ2 80.00 %
GPNAM[3] SMSQ10.100
GPZ3 20.10 %
P16 1000.00 usec
F1 - Acquisition parameters
TD 256
SFO1 125.7672 MHz
FIDRES 162.760422 Hz
SW 165.650 ppm
FnMODE TPPI
F2 - Processing parameters
SI 1024
SF 500.1300000 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.40
F1 - Processing parameters
SI 1024
MC2 TPPI
SF 125.7577890 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
I
FmocHN
OtBu
O
6
f2 (ppm)
f1 (ppm)

Sodium 4-iodobenzylsulfonate
LJD-138C 1H NMR (D2O)

```
Current Data Parameters
NAME            LJD-138C
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170310
Time              14.03 h
INSTRUM             spect
PROBHD   Z119470_0008 (
PULPROG               zg
TD                 65536
SOLVENT              D2O
NS                     8
DS                     0
SWH           10000.000 Hz
FIDRES         0.305176 Hz
AQ            3.2767999 sec
RG                  45.2
DW                50.000 usec
DE                 6.50 usec
TE                300.0 K
D1           2.00000000 sec
TD0                    1
SFO1         500.1330008 MHz
NUC1                  1H
P1                 14.00 usec
PLW1        15.48799992 W

F2 - Processing parameters
SI                 32768
SF          500.1300000 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

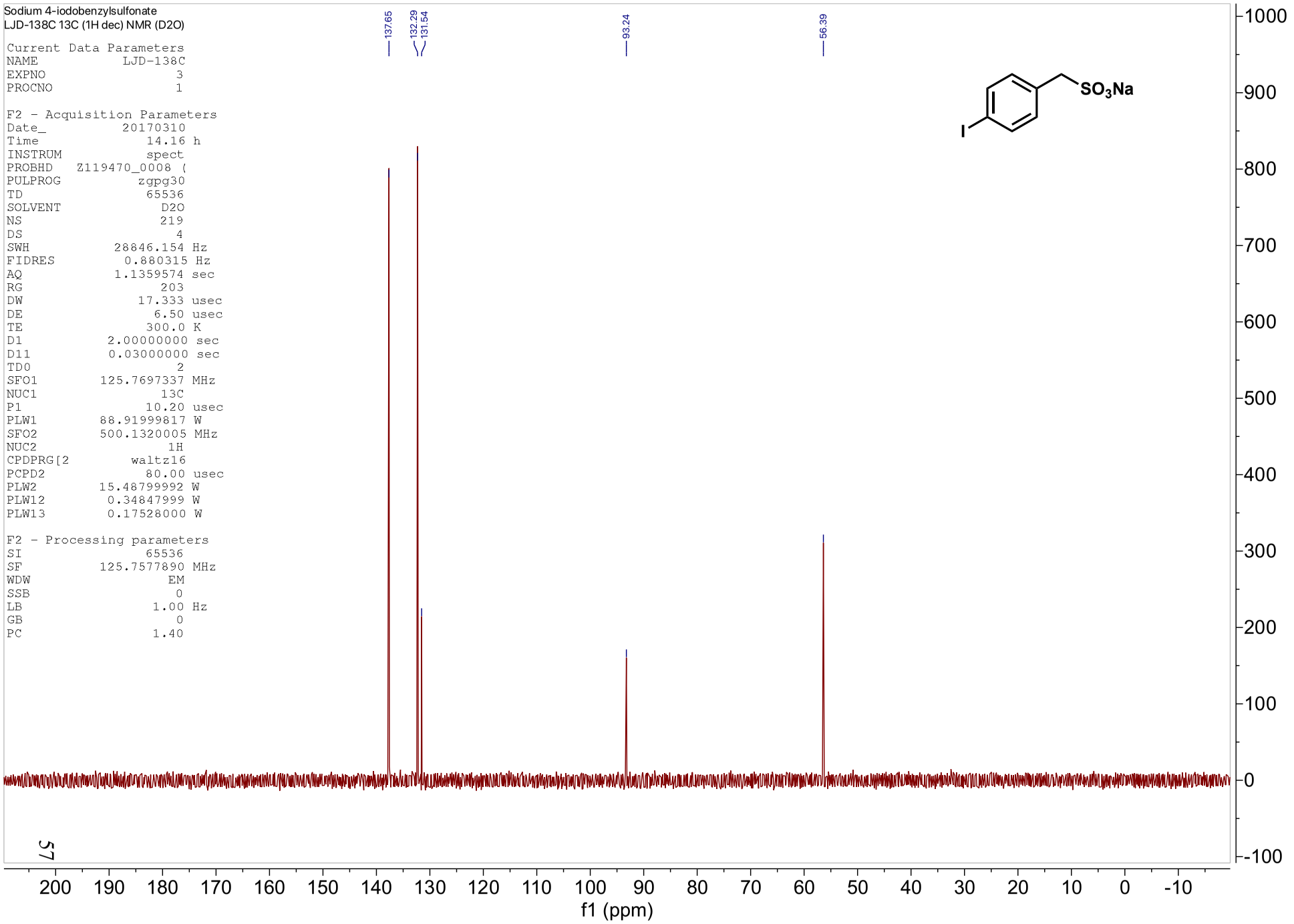


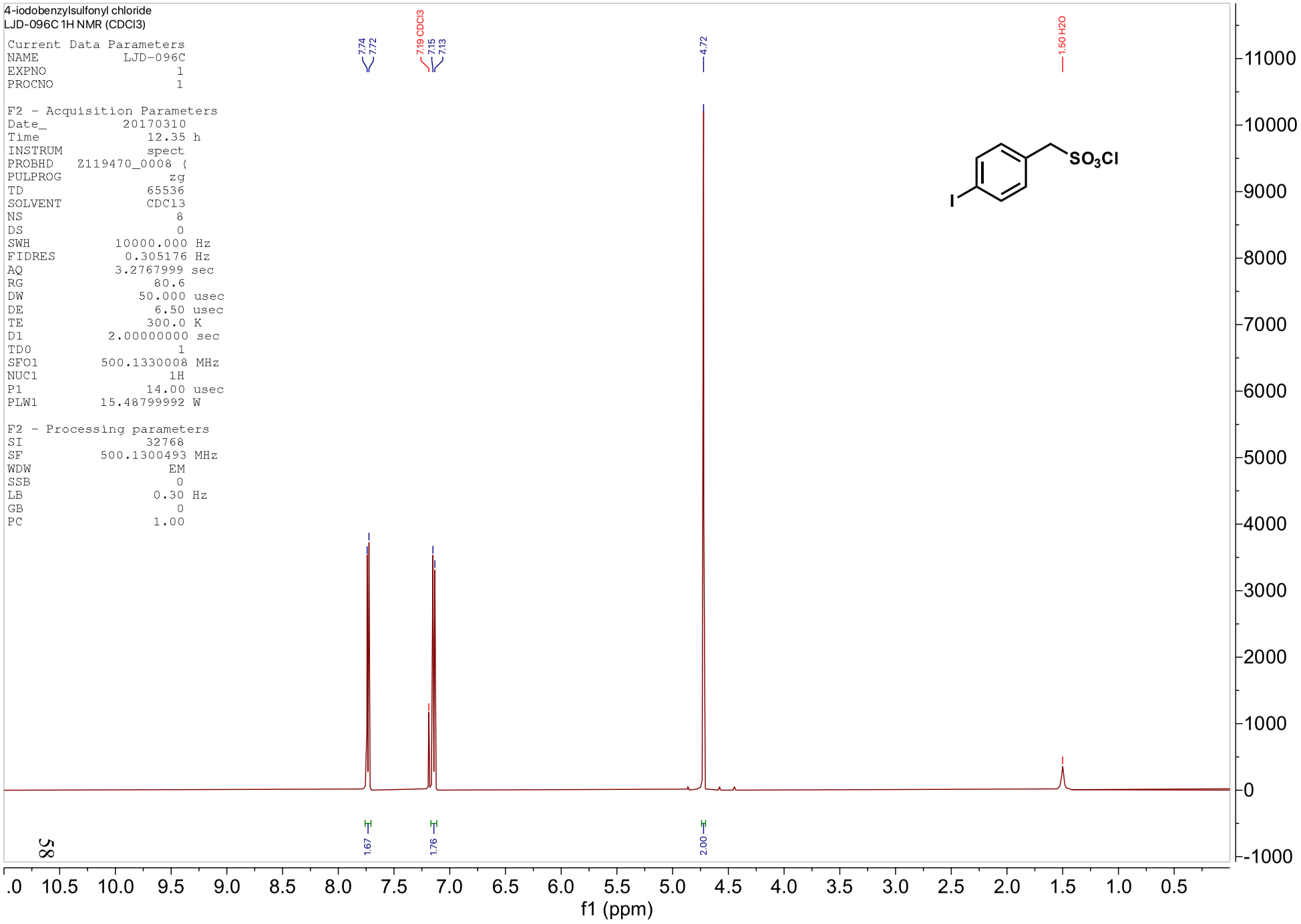
Sodium 4-iodobenzylsulfonate
LJD-138C 13C (1H dec) NMR (D2O)

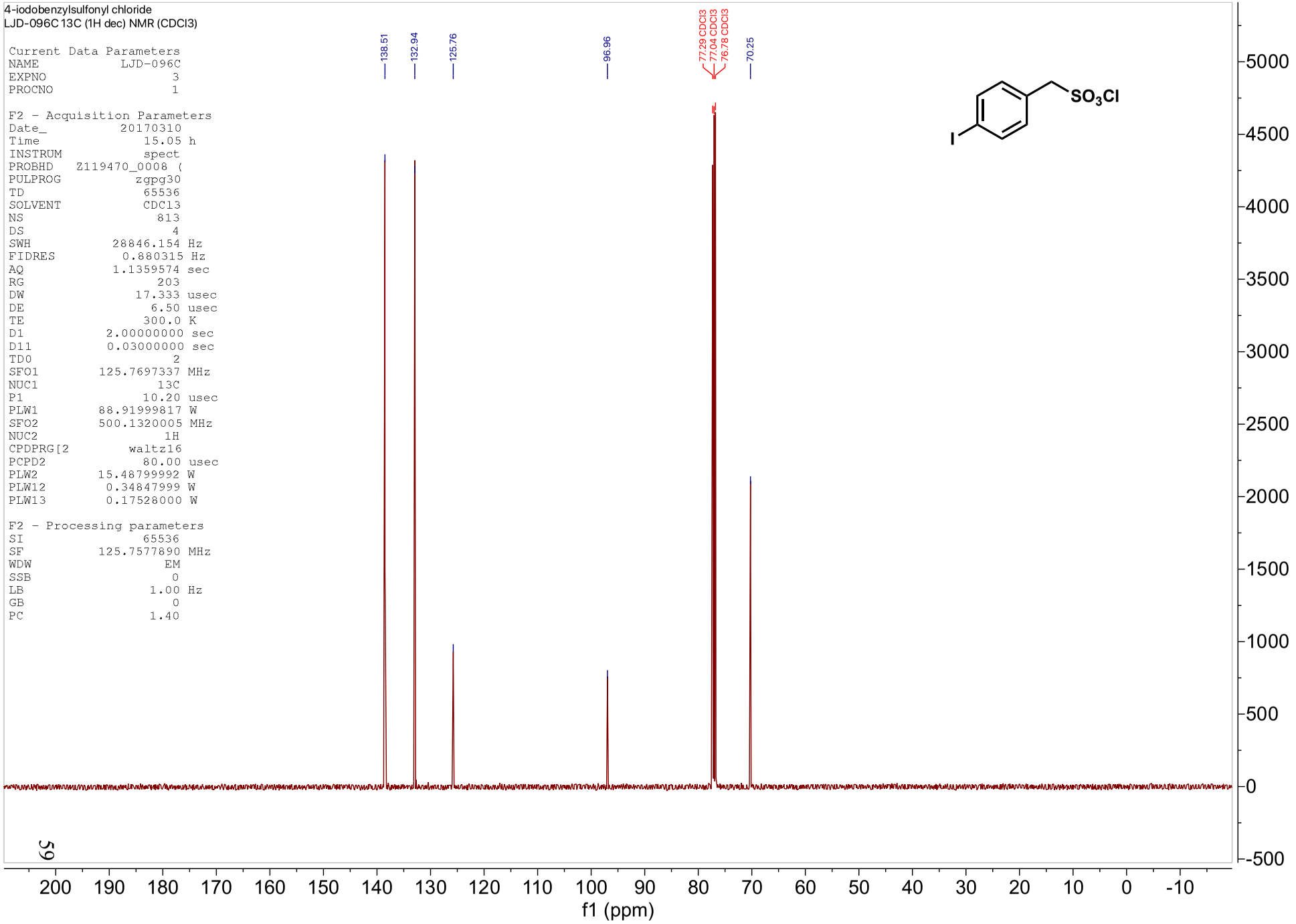
```
Current Data Parameters
NAME            LJD-138C
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170310
Time              14.16 h
INSTRUM             spect
PROBHD   Z119470_0008 (
PULPROG           zgpg30
TD                 65536
SOLVENT              D2O
NS                   219
DS                     4
SWH           28846.154 Hz
FIDRES         0.880315 Hz
AQ            1.1359574 sec
RG                   203
DW                17.333 usec
DE                 6.50 usec
TE                 300.0 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                    2
SFO1         125.7697337 MHz
NUC1                 13C
P1                10.20 usec
PLW1         88.91999817 W
SFO2         500.1320005 MHz
NUC2                 1H
CPDPRG[2         waltz16
PCPD2             80.00 usec
PLW2         15.48799992 W
PLW12         0.34847999 W
PLW13         0.17528000 W

F2 - Processing parameters
SI                 65536
SF          125.7577890 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```




4-iodobenzylsulfonyl chloride
LJD-096C 1H NMR (CDCl3)
Current Data Parameters
NAME LJD-096C
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170310
Time 12.35 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG zg
TD 65536
SOLVENT CDCl3
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.305176 Hz
AQ 3.2767999 sec
RG 80.6
DW 50.000 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
TD0 1
SFO1 500.1330008 MHz
NUC1 1H
P1 14.00 usec
PLW1 15.48799992 W
F2 - Processing parameters
SI 32768
SF 500.1300493 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.74
7.72
7.19 CDCl3
7.15
7.13
4.72
1.50 H2O
SO3Cl
I
1.67
1.76
2.00
f1 (ppm)

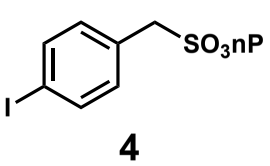

4-iodobenzylsulfonyl chloride
LJD-096C 13C (1H dec) NMR (CDCl3)
Current Data Parameters
NAME LJD-096C
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170310
Time 15.05 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 813
DS 4
SWH 28846.154 Hz
FIDRES 0.880315 Hz
AQ 1.1359574 sec
RG 203
DW 17.333 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 2
SFO1 125.7697337 MHz
NUC1 13C
P1 10.20 usec
PLW1 88.91999817 W
SFO2 500.1320005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 15.48799992 W
PLW12 0.34847999 W
PLW13 0.17528000 W
F2 - Processing parameters
SI 65536
SF 125.7577890 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
138.51
132.94
125.76
96.96
77.29 CDCl3
77.04 CDCl3
76.78 CDCl3
70.25
SO3Cl
I
59
f1 (ppm)

Neopentyl 4-iodobenzylsulfonate
LJD-073-1 1H NMR (CDCl3)

```
Current Data Parameters
NAME          LJD-073-1
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20170310
Time              12.39 h
INSTRUM           spect
PROBHD   Z119470_0008 (
PULPROG             zg
TD                65536
SOLVENT           CDCl3
NS                    8
DS                    0
SWH           10000.000 Hz
FIDRES        0.305176 Hz
AQ            3.2767999 sec
RG                   32
DW               50.000 usec
DE                6.50 usec
TE                300.0 K
D1           2.00000000 sec
TD0                   1
SFO1        500.1330008 MHz
NUC1                 1H
P1                14.00 usec
PLW1        15.48799992 W

F2 - Processing parameters
SI                32768
SF          500.1300474 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```



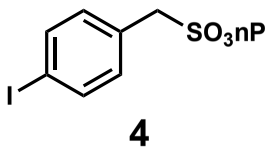
4

Neopentyl 4-iodobenzylsulfonate
LJD-073-1 13C (1H dec) NMR (CDCl3)

```
Current Data Parameters
NAME          LJD-073-1
EXPNO                 3
PROCNO                1

F2 - Acquisition Parameters
Date_          20170310
Time               15.15 h
INSTRUM            spect
PROBHD   Z119470_0008 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                   83
DS                    4
SWH           28846.154 Hz
FIDRES         0.880315 Hz
AQ            1.1359574 sec
RG                  203
DW               17.333 usec
DE                6.50 usec
TE                300.0 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        125.7697337 MHz
NUC1                13C
P1                10.20 usec
PLW1        88.91999817 W
SFO2        500.1320005 MHz
NUC2                 1H
CPDPRG[2         waltz16
PCPD2             80.00 usec
PLW2        15.48799992 W
PLW12        0.34847999 W
PLW13        0.17528000 W

F2 - Processing parameters
SI                65536
SF          125.7577890 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```



4

138.07 132.43 127.67 95.14 79.57 77.31 CDCl3 77.06 CDCl3 76.80 CDCl3 55.99 31.84 26.00

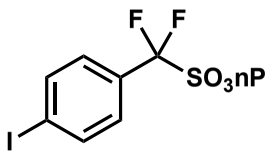
f1 (ppm)

Neopentyl difluoro(4-iodobenzyl)sulfonate
LJD-010 1H NMR (CDCl3)

```
Current Data Parameters
NAME            LJD-010P
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_          20170310
Time              12.48 h
INSTRUM            spect
PROBHD   Z119470_0008 (
PULPROG              zg
TD                65536
SOLVENT           CDCl3
NS                    8
DS                    0
SWH           10000.000 Hz
FIDRES         0.305176 Hz
AQ            3.2767999 sec
RG                 14.2
DW               50.000 usec
DE                6.50 usec
TE                300.0 K
D1           2.00000000 sec
TD0                   1
SFO1        500.1330008 MHz
NUC1                 1H
P1                14.00 usec
PLW1        15.48799992 W

F2 - Processing parameters
SI                32768
SF          500.1300567 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```



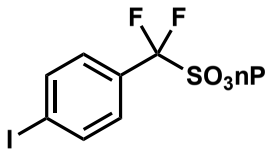
5

Neopentyl difluoro(4-iodobenzyl)sulfonate
LJD-010 13C (1H dec) NMR (CDCl3)

```
Current Data Parameters
NAME            LJD-010P
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_          20170310
Time               16.18 h
INSTRUM             spect
PROBHD   Z119470_0008 (
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH           28846.154 Hz
FIDRES         0.880315 Hz
AQ            1.1359574 sec
RG                   203
DW                17.333 usec
DE                 6.50 usec
TE                 300.0 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                    1
SFO1        125.7697337 MHz
NUC1                13C
P1                10.20 usec
PLW1        88.91999817 W
SFO2        500.1320005 MHz
NUC2                1H
CPDPRG[2         waltz16
PCPD2             80.00 usec
PLW2        15.48799992 W
PLW12        0.34847999 W
PLW13        0.17528000 W

F2 - Processing parameters
SI                 65536
SF          125.7579226 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
```



5

137.02
127.61
127.56
127.51
126.72
126.54
126.36
122.06
119.81
117.55
98.81
98.79
98.77
83.55
76.27 CDCl3
76.02 CDCl3
75.77 CDCl3
31.08
24.79

63

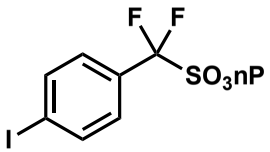
f1 (ppm)

Neopentyl difluoro(4-iodobenzyl)sulfonate
LJD-010 19F (1H dec) NMR (CDCl3)

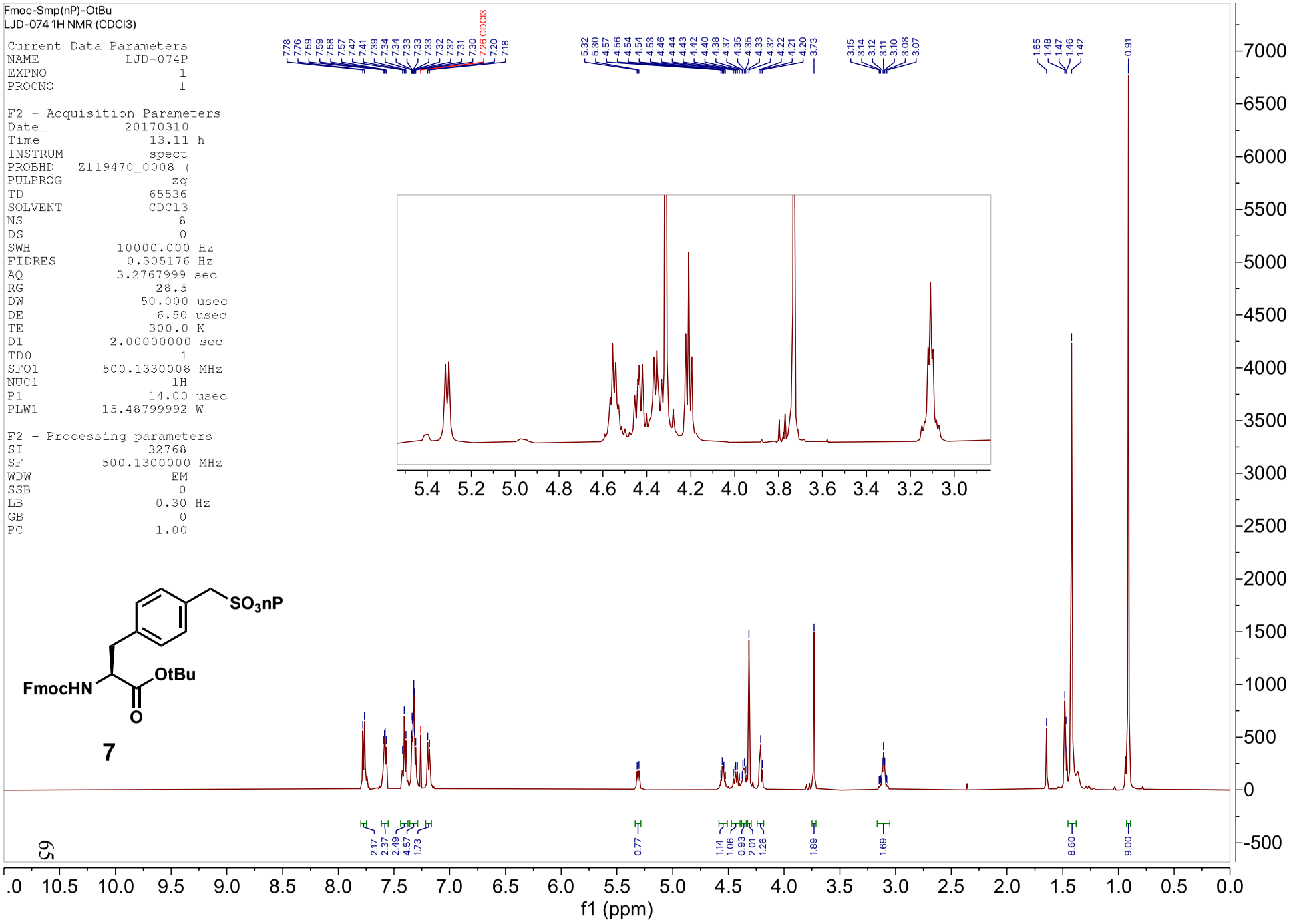
```
Current Data Parameters
NAME            LJD-010P
EXPNO                  3
PROCNO                 1

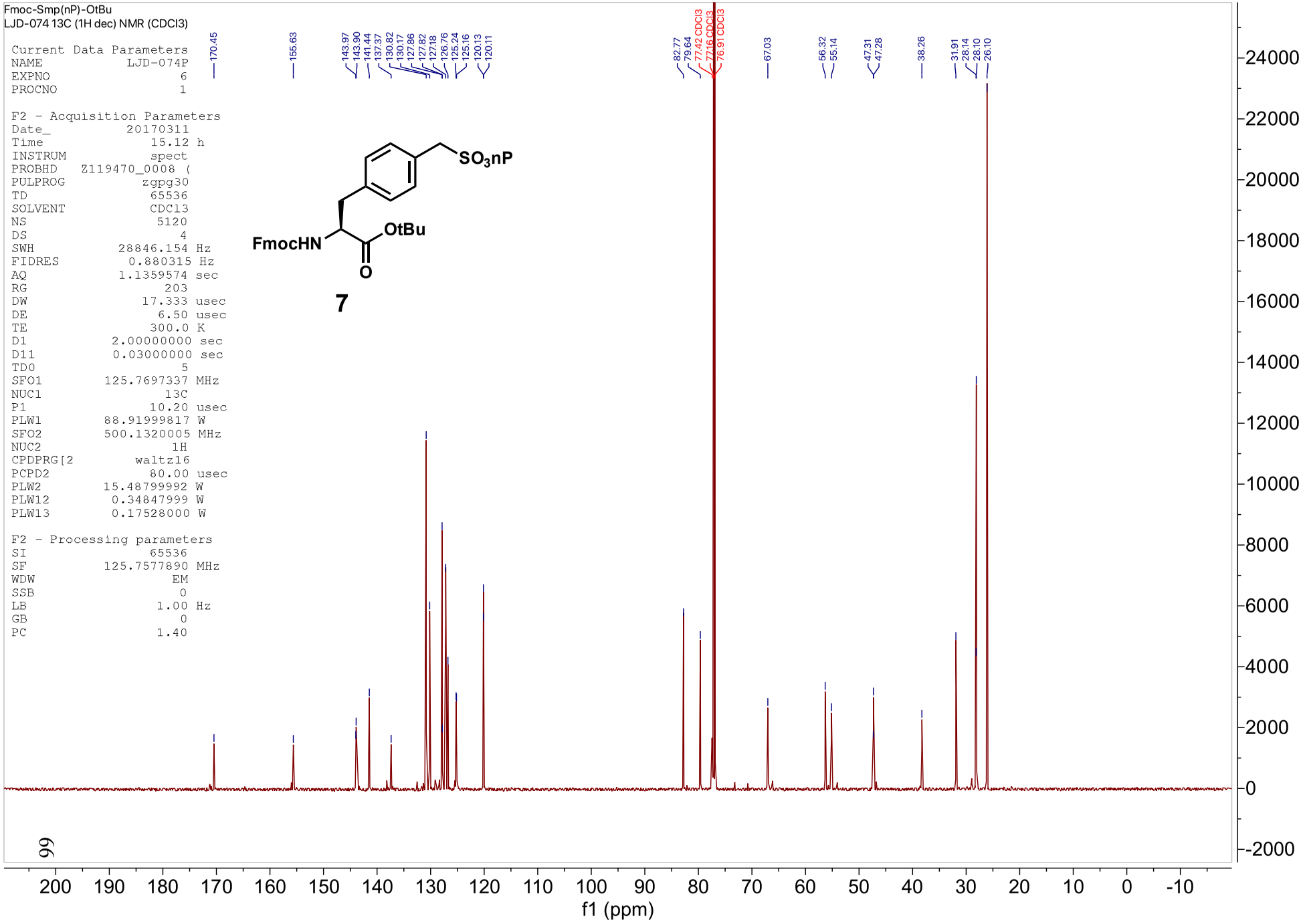
F2 - Acquisition Parameters
Date_           20170310
Time               15.22 h
INSTRUM             spect
PROBHD   Z119470_0008 (
PULPROG          zgfhigqn
TD                 46870
SOLVENT            CDCl3
NS                   128
DS                     0
SWH            46875.000 Hz
FIDRES          2.000213 Hz
AQ             0.4999467 sec
RG                   203
DW                10.667 usec
DE                 6.50 usec
TE                 300.0 K
D1            0.10000000 sec
D11           0.03000000 sec
D12           0.00002000 sec
TD0                    1
SFO1         470.5627297 MHz
NUC1                 19F
P1                 14.95 usec
PLW1         41.97600174 W
SFO2         500.1325006 MHz
NUC2                 1H
CPDPRG[2          waltz16
PCPD2              80.00 usec
PLW2         15.48799992 W
PLW12         0.34847999 W

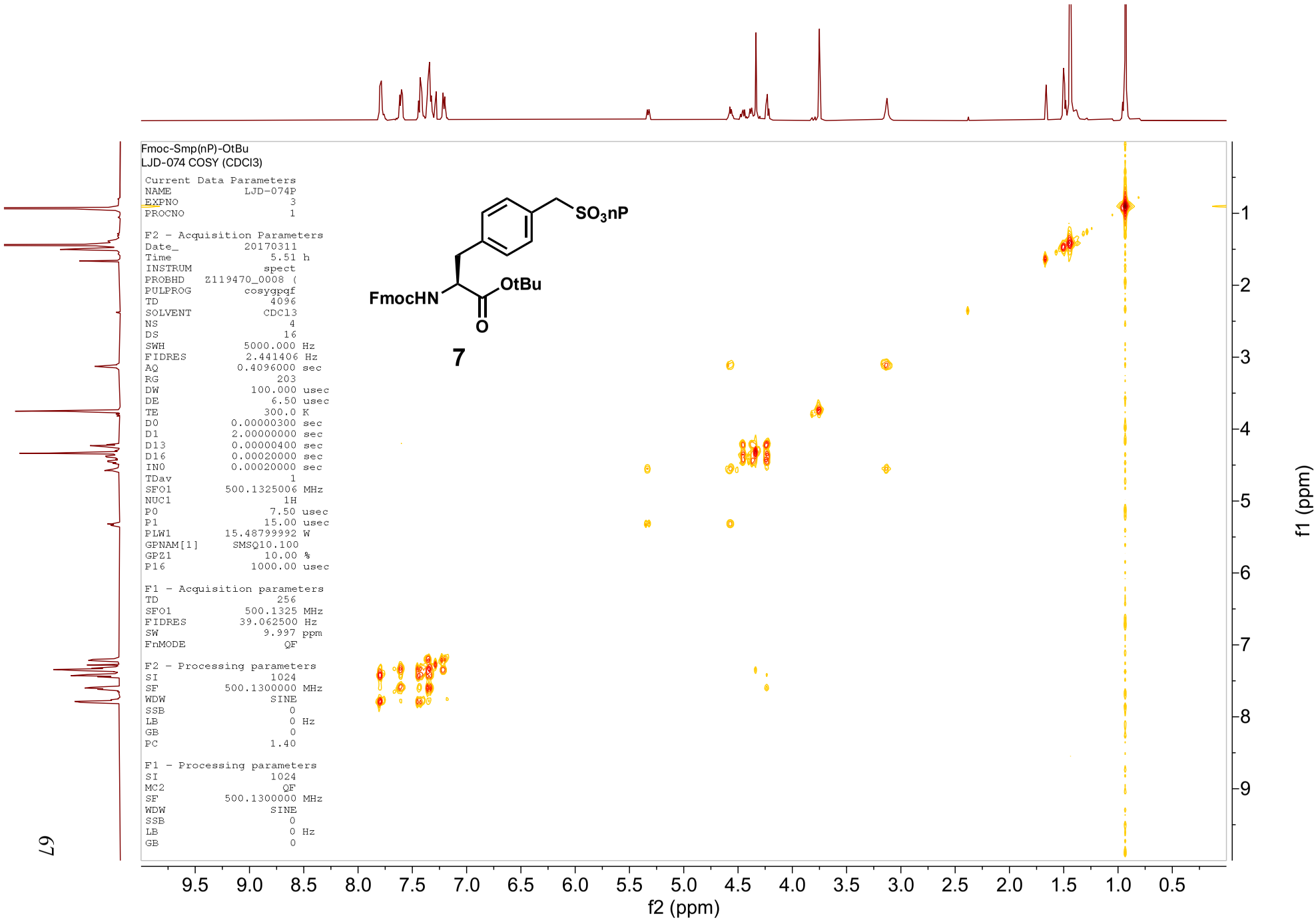
F2 - Processing parameters
SI                 32768
SF           470.5923770 MHz
WDW                   EM
SSB                    0
LB                  2.00 Hz
GB                     0
PC                  1.00
```

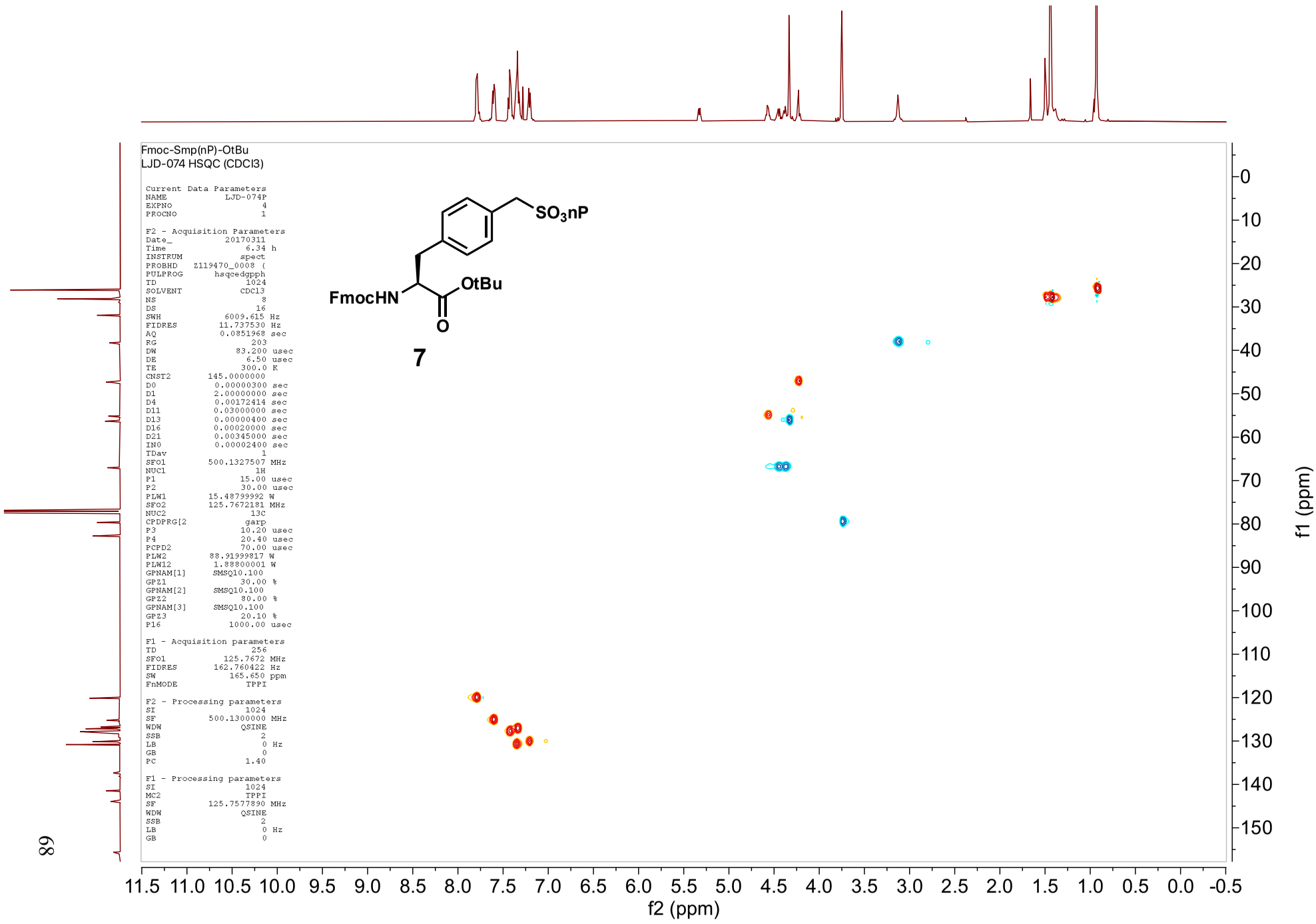


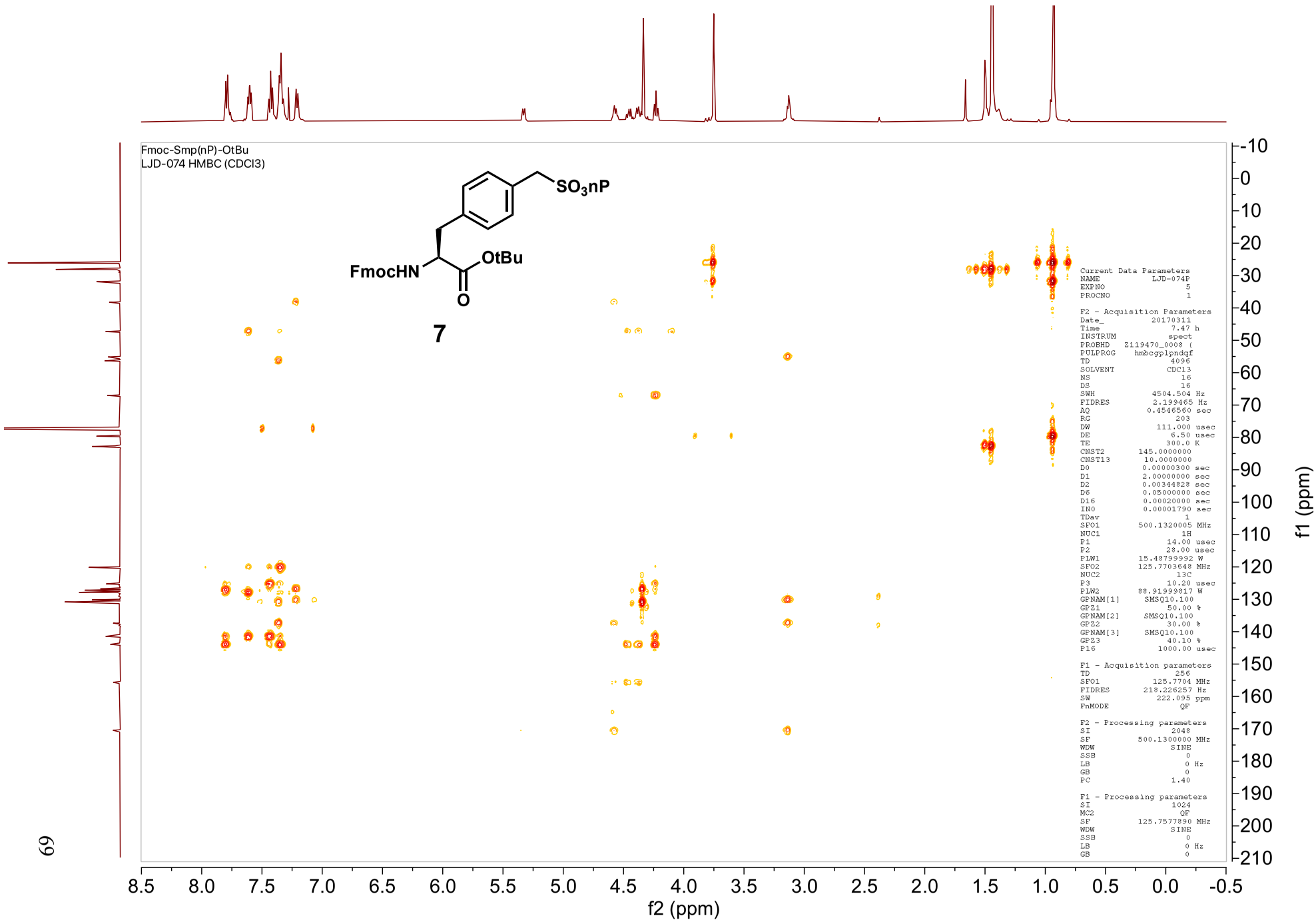
5

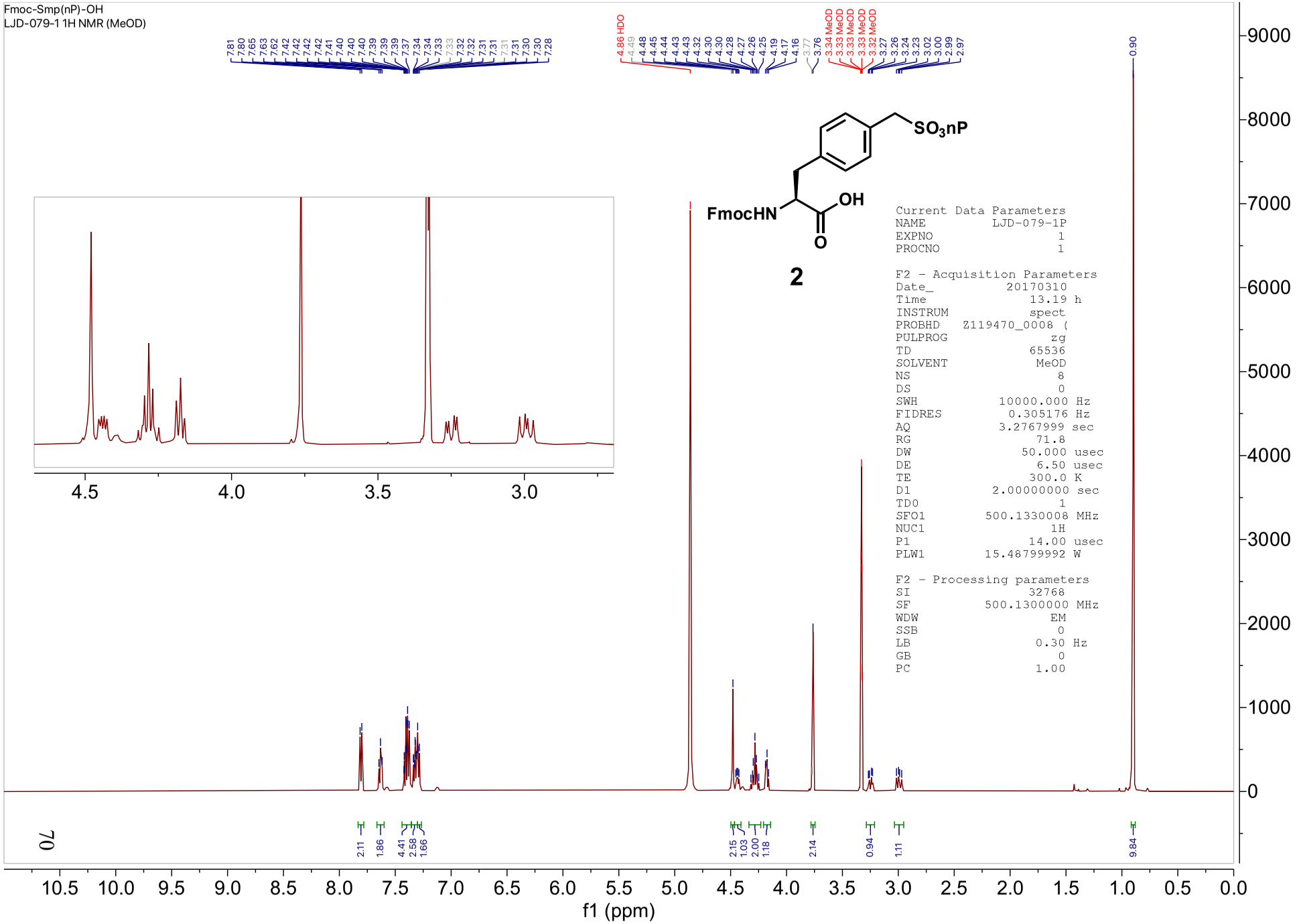

Fmoc-Smp(nP)-OtBu
LJD-074 1H NMR (CDCl3)
Current Data Parameters
NAME LJD-074P
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170310
Time 13.11 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG zg
TD 65536
SOLVENT CDCl3
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.305176 Hz
AQ 3.2767999 sec
RG 28.5
DW 50.000 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
TD0 1
SFO1 500.1330008 MHz
NUC1 1H
P1 14.00 usec
PLW1 15.48799992 W
F2 - Processing parameters
SI 32768
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.78 7.76 7.59 7.59 7.58 7.57 7.42 7.41 7.39 7.34 7.34 7.33 7.33 7.33 7.32 7.32 7.31 7.30 7.26 CDCl3 7.20 7.18
5.32 5.30 4.57 4.56 4.54 4.54 4.53 4.46 4.44 4.43 4.42 4.40 4.38 4.37 4.35 4.35 4.33 4.32 4.22 4.21 4.20 3.73
3.15 3.14 3.12 3.11 3.10 3.08 3.07
1.65 1.48 1.47 1.46 1.42
0.91
SO3nP
FmocHN
OtBu
O
7
2.17 2.37 2.49 4.57 1.73
0.77
1.14 1.06 0.93 2.01 1.26
1.89
1.69
8.60
9.00
f1 (ppm)

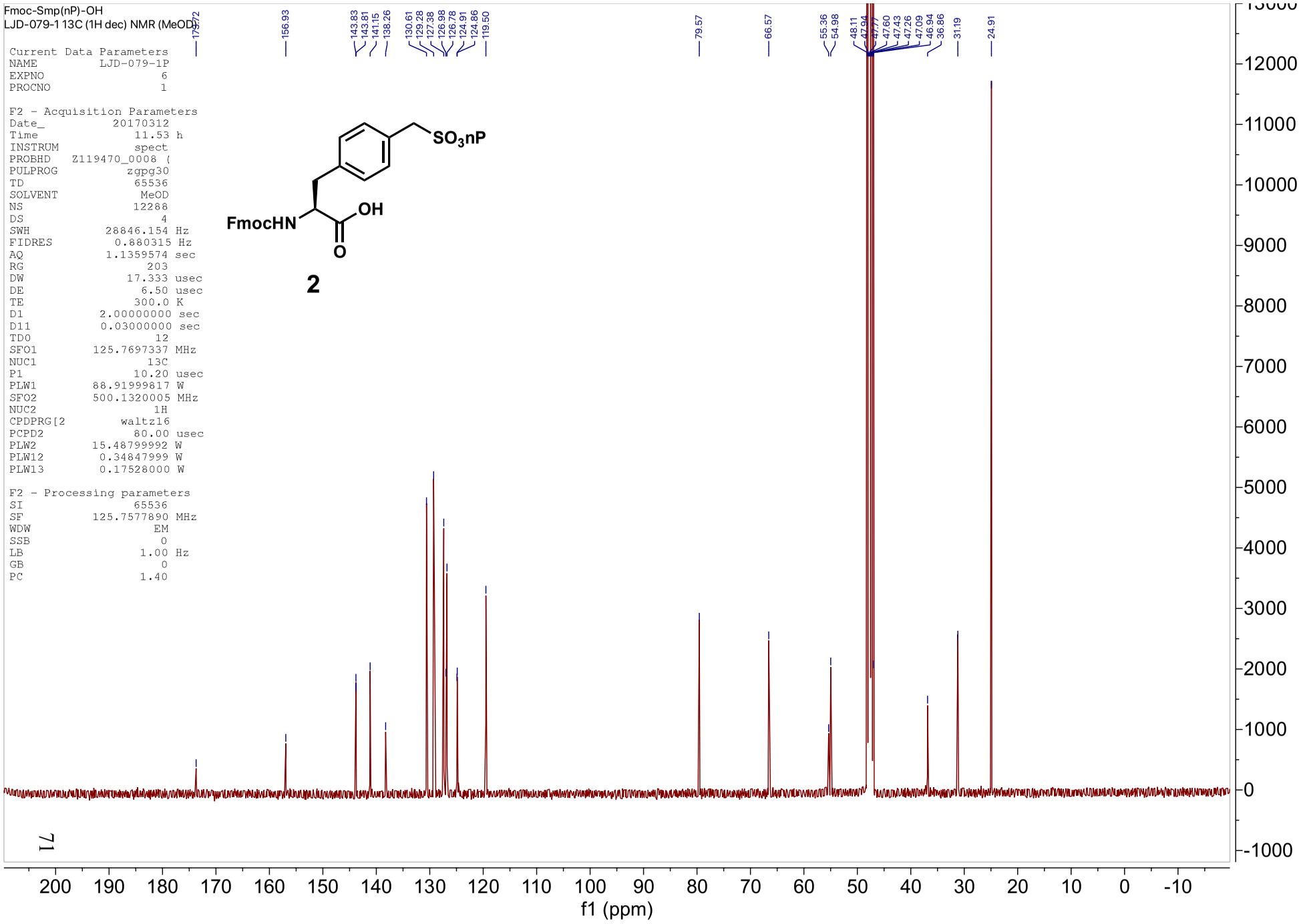

Fmoc-Smp(nP)-OtBu
LJD-074 13C (1H dec) NMR (CDCl3)
Current Data Parameters
NAME LJD-074P
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170311
Time 15.12 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 5120
DS 4
SWH 28846.154 Hz
FIDRES 0.880315 Hz
AQ 1.1359574 sec
RG 203
DW 17.333 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 5
SFO1 125.7697337 MHz
NUC1 13C
P1 10.20 usec
PLW1 88.91999817 W
SFO2 500.1320005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 15.48799992 W
PLW12 0.34847999 W
PLW13 0.17528000 W
F2 - Processing parameters
SI 65536
SF 125.7577890 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
170.45
155.63
143.97
143.90
141.44
137.37
130.82
130.17
127.86
127.82
127.18
126.76
125.24
125.16
120.13
120.11
82.77
79.64
77.42 CDCl3
77.16 CDCl3
76.91 CDCl3
67.03
56.32
55.14
47.31
47.28
38.26
31.91
28.14
28.10
26.10
SO3nP
FmocHN
OtBu
O
7
99
f1 (ppm)

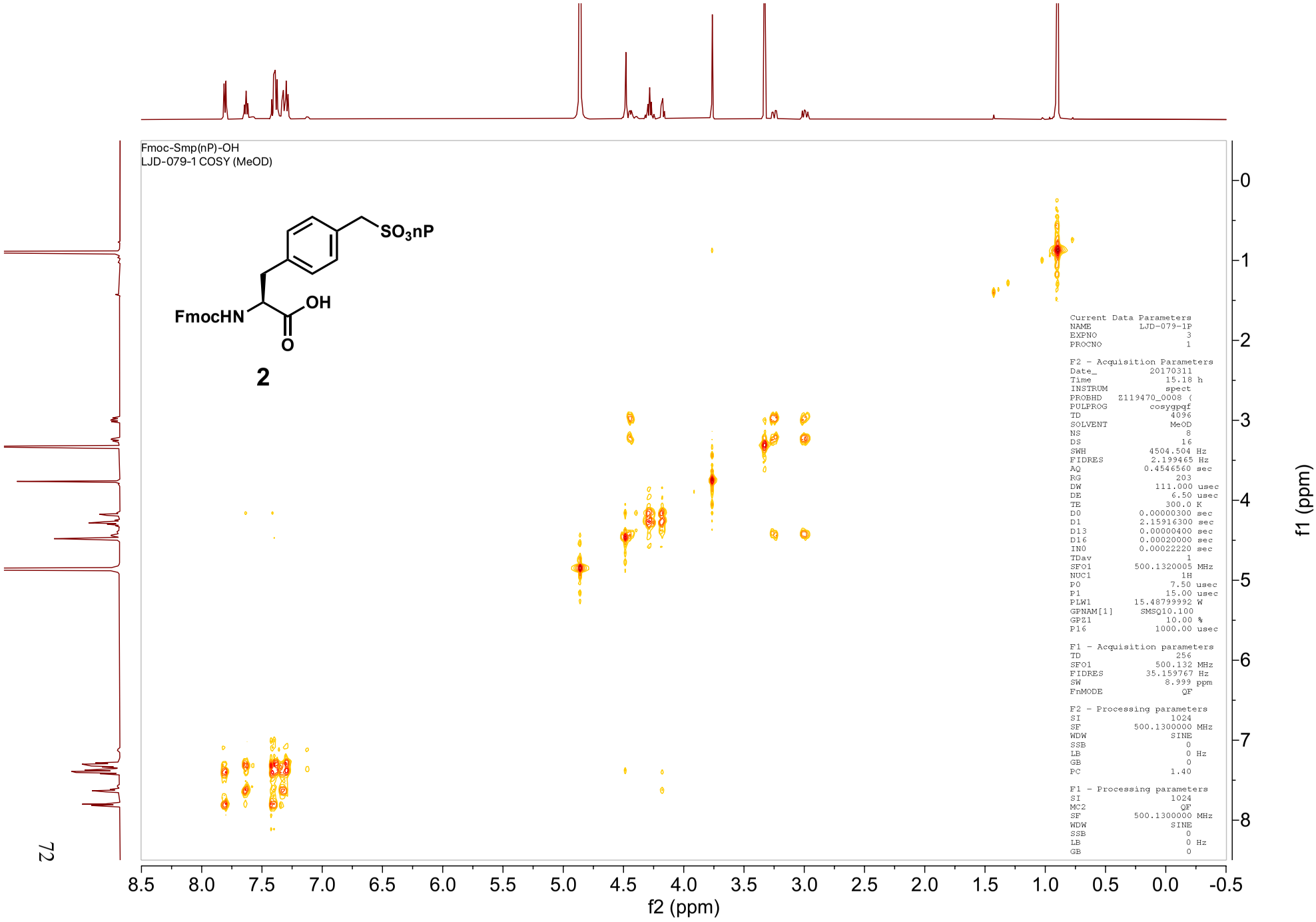

Fmoc-Smp(nP)-OtBu
LJD-074 COSY (CDCl3)
Current Data Parameters
NAME LJD-074P
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170311
Time 5.51 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG cosygpqf
TD 4096
SOLVENT CDCl3
NS 4
DS 16
SWH 5000.000 Hz
FIDRES 2.441406 Hz
AQ 0.4096000 sec
RG 203
DW 100.000 usec
DE 6.50 usec
TE 300.0 K
D0 0.00000300 sec
D1 2.00000000 sec
D13 0.00000400 sec
D16 0.00020000 sec
IN0 0.00020000 sec
TDav 1
SFO1 500.1325006 MHz
NUC1 1H
P0 7.50 usec
P1 15.00 usec
PLW1 15.48799992 W
GPNAM[1] SMSQ10.100
GPZ1 10.00 %
P16 1000.00 usec
F1 - Acquisition parameters
TD 256
SFO1 500.1325 MHz
FIDRES 39.062500 Hz
SW 9.997 ppm
FnMODE QF
F2 - Processing parameters
SI 1024
SF 500.1300000 MHz
WDW SINE
SSB 0
LB 0 Hz
GB 0
PC 1.40
F1 - Processing parameters
SI 1024
MC2 QF
SF 500.1300000 MHz
WDW SINE
SSB 0
LB 0 Hz
GB 0
SO3nP
FmocHN
OtBu
O
7
f2 (ppm)
f1 (ppm)

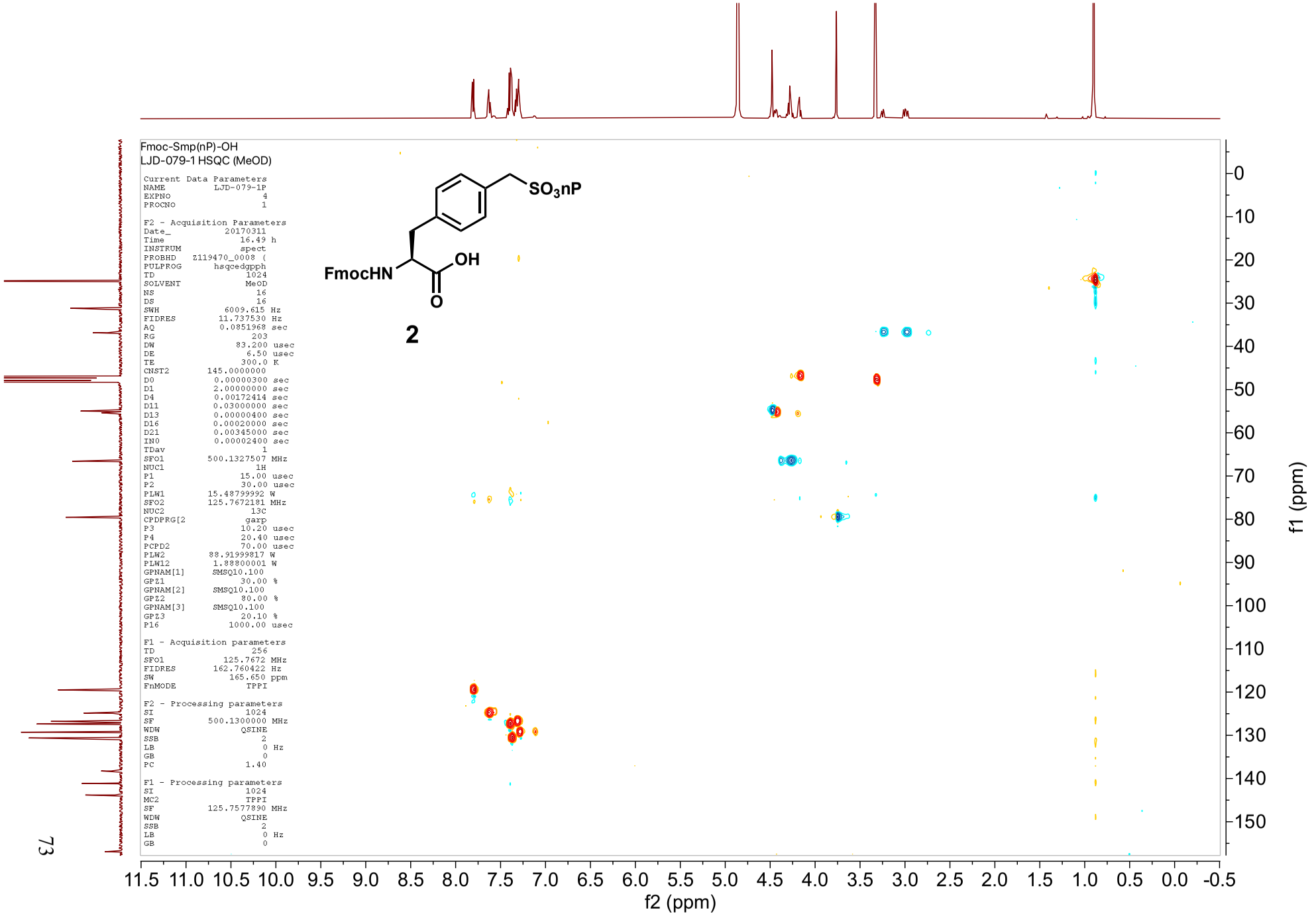

Fmoc-Smp(nP)-OtBu
LJD-074 HSQC (CDCl3)
Current Data Parameters
NAME LJD-074P
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170311
Time 6.34 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG hsqcedgpph
TD 1024
SOLVENT CDCl3
NS 8
DS 16
SWH 6009.615 Hz
FIDRES 11.737530 Hz
AQ 0.0851968 sec
RG 203
DW 83.200 usec
DE 6.50 usec
TE 300.0 K
CNST2 145.0000000
D0 0.00000300 sec
D1 2.00000000 sec
D4 0.00172414 sec
D11 0.03000000 sec
D13 0.00000400 sec
D16 0.00020000 sec
D21 0.00345000 sec
IN0 0.00002400 sec
TDav 1
SFO1 500.1327507 MHz
NUC1 1H
P1 15.00 usec
P2 30.00 usec
PLW1 15.48799992 W
SFO2 125.7672181 MHz
NUC2 13C
CPDPRG[2 garp
P3 10.20 usec
P4 20.40 usec
PCPD2 70.00 usec
PLW2 88.91999817 W
PLW12 1.88800001 W
GPNAM[1] SMSQ10.100
GPZ1 30.00 %
GPNAM[2] SMSQ10.100
GPZ2 80.00 %
GPNAM[3] SMSQ10.100
GPZ3 20.10 %
P16 1000.00 usec
F1 - Acquisition parameters
TD 256
SFO1 125.7672 MHz
FIDRES 162.760422 Hz
SW 165.650 ppm
FnMODE TPPI
F2 - Processing parameters
SI 1024
SF 500.1300000 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.40
F1 - Processing parameters
SI 1024
MC2 TPPI
SF 125.7577890 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
SO3nP
OtBu
FmocHN
O
7
89
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f2 (ppm)
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150
f1 (ppm)

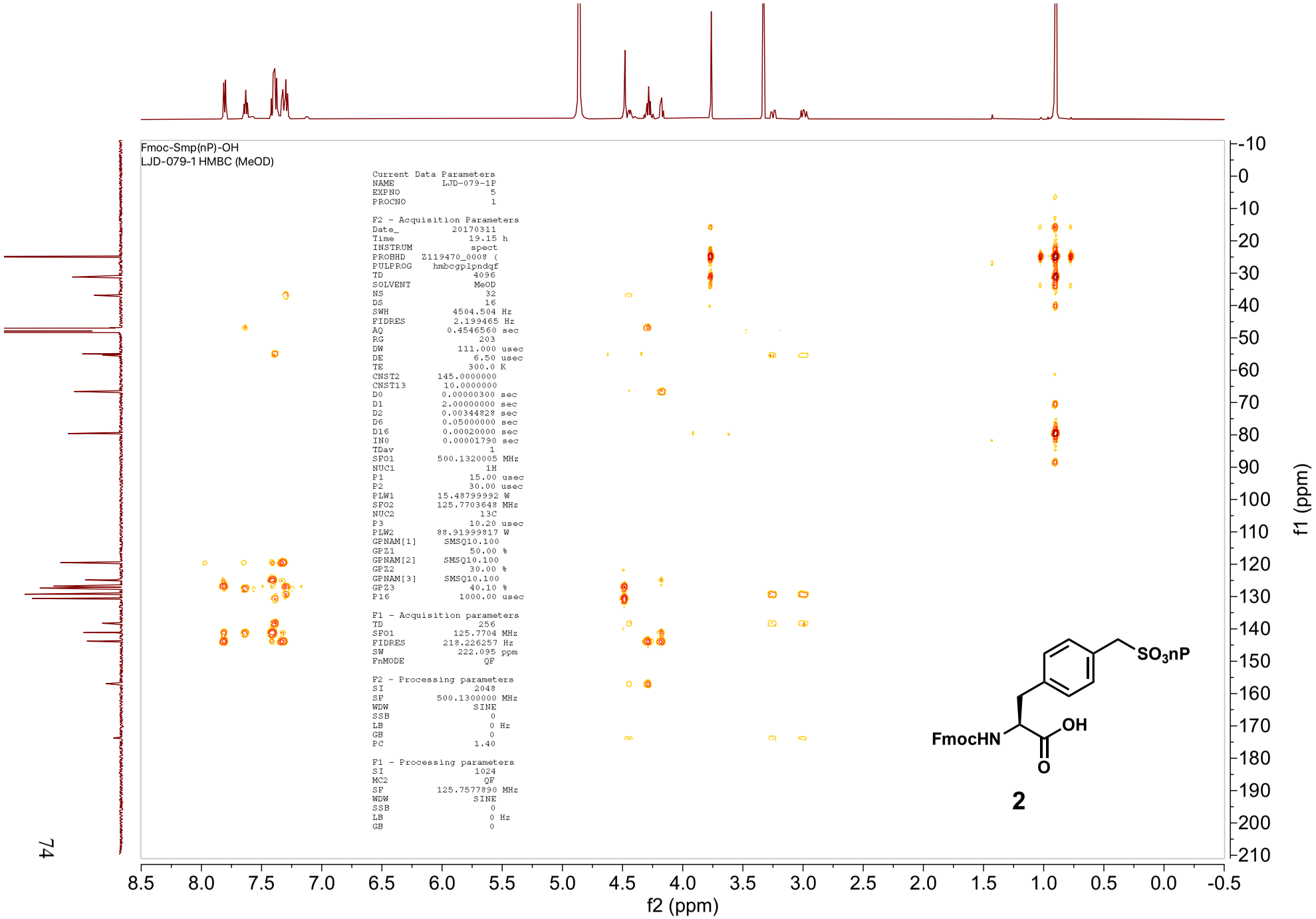

Fmoc-Smp(nP)-OtBu
LJD-074 HMBC (CDCl3)
SO3nP
FmocHN
OtBu
O
7
Current Data Parameters
NAME LJD-074P
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170311
Time 7.47 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG hmbcgplpndqf
TD 4096
SOLVENT CDCl3
NS 16
DS 16
SWH 4504.504 Hz
FIDRES 2.199465 Hz
AQ 0.4546560 sec
RG 203
DW 111.000 usec
DE 6.50 usec
TE 300.0 K
CNST2 145.0000000
CNST13 10.0000000
D0 0.00000300 sec
D1 2.00000000 sec
D2 0.00344828 sec
D6 0.05000000 sec
D16 0.00020000 sec
IN0 0.00001790 sec
TDav 1
SFO1 500.1320005 MHz
NUC1 1H
P1 14.00 usec
P2 28.00 usec
PLW1 15.48799992 W
SFO2 125.7703648 MHz
NUC2 13C
P3 10.20 usec
PLW2 88.91999817 W
GPNAM[1] SMSQ10.100
GPZ1 50.00 %
GPNAM[2] SMSQ10.100
GPZ2 30.00 %
GPNAM[3] SMSQ10.100
GPZ3 40.10 %
P16 1000.00 usec
F1 - Acquisition parameters
TD 256
SFO1 125.7704 MHz
FIDRES 218.226257 Hz
SW 222.095 ppm
FnMODE QF
F2 - Processing parameters
SI 2048
SF 500.1300000 MHz
WDW SINE
SSB 0
LB 0 Hz
GB 0
PC 1.40
F1 - Processing parameters
SI 1024
MC2 QF
SF 125.7577890 MHz
WDW SINE
SSB 0
LB 0 Hz
GB 0
69
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f2 (ppm)
-10 0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210
f1 (ppm)

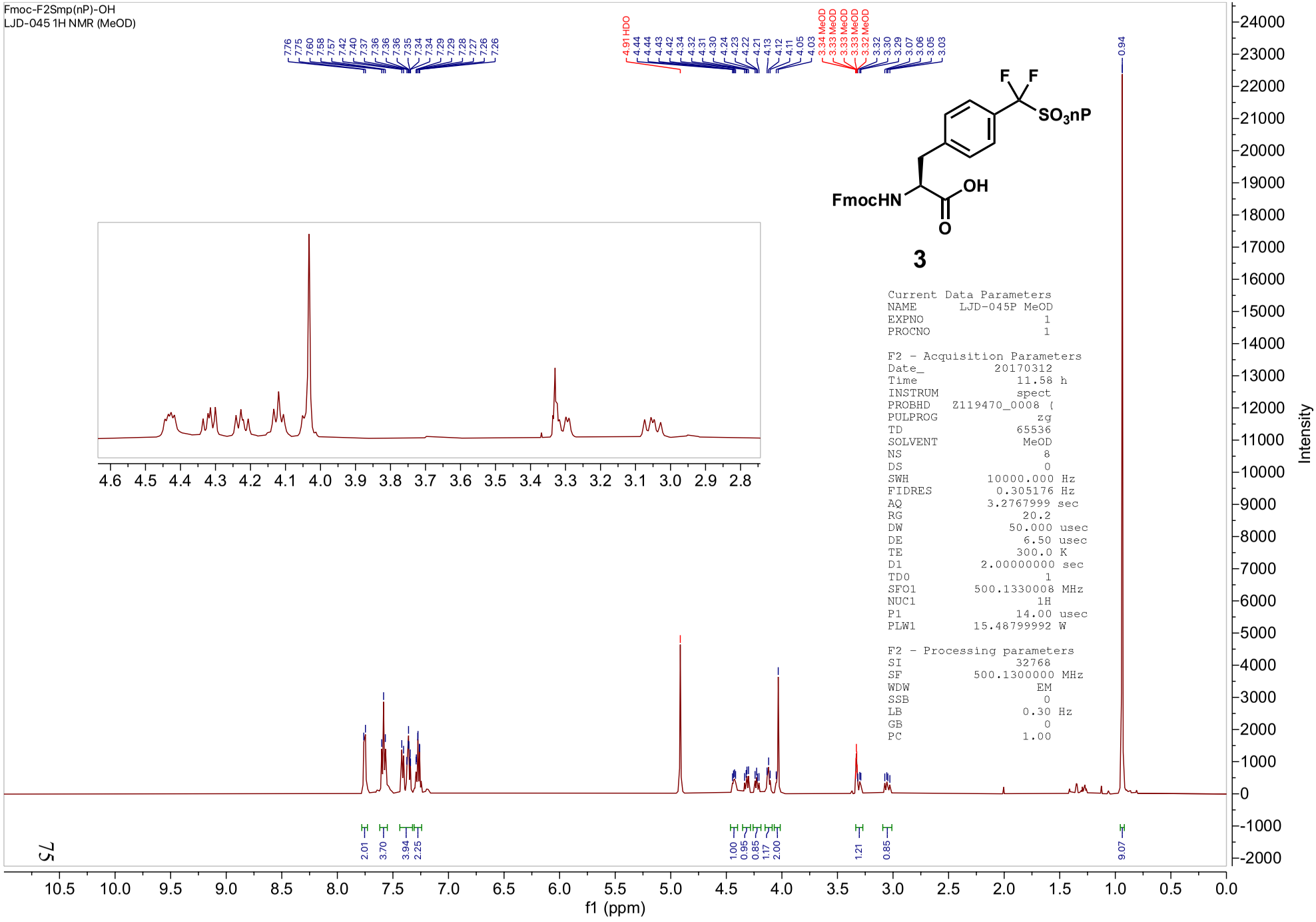

Fmoc-Smp(nP)-OH
LJD-079-1 1H NMR (MeOD)
7.81 7.80 7.65 7.63 7.62 7.42 7.42 7.42 7.42 7.41 7.40 7.40 7.40 7.39 7.39 7.39 7.37 7.34 7.34 7.33 7.33 7.32 7.32 7.31 7.31 7.31 7.31 7.30 7.30 7.28
4.86 HDO 4.49 4.48 4.45 4.44 4.43 4.43 4.32 4.30 4.28 4.27 4.26 4.25 4.19 4.17 4.16 3.77 3.76
3.34 MeOD 3.33 MeOD 3.33 MeOD 3.33 MeOD 3.32 MeOD
3.27 3.26 3.24 3.23 3.02 3.00 2.99 2.97
0.90
SO3nP
FmocHN
OH
O
2
Current Data Parameters
NAME LJD-079-1P
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170310
Time 13.19 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG zg
TD 65536
SOLVENT MeOD
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.305176 Hz
AQ 3.2767999 sec
RG 71.8
DW 50.000 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
TD0 1
SFO1 500.1330008 MHz
NUC1 1H
P1 14.00 usec
PLW1 15.48799992 W
F2 - Processing parameters
SI 32768
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
4.5 4.0 3.5 3.0
2.11 1.86 4.41 2.58 1.66 2.15 1.03 2.00 1.18 2.14 0.94 1.11 9.84
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
9000 8000 7000 6000 5000 4000 3000 2000 1000 0


Fmoc-Smp(nP)-OH
LJD-079-1 13C (1H dec) NMR (MeOD)
Current Data Parameters
NAME LJD-079-1P
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170312
Time 11.53 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG zgpg30
TD 65536
SOLVENT MeOD
NS 12288
DS 4
SWH 28846.154 Hz
FIDRES 0.880315 Hz
AQ 1.1359574 sec
RG 203
DW 17.333 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 12
SFO1 125.7697337 MHz
NUC1 13C
P1 10.20 usec
PLW1 88.91999817 W
SFO2 500.1320005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 15.48799992 W
PLW12 0.34847999 W
PLW13 0.17528000 W
F2 - Processing parameters
SI 65536
SF 125.7577890 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
179.72
156.93
143.83
143.81
141.15
138.26
130.61
129.28
127.38
126.98
126.78
124.91
124.86
119.50
79.57
66.57
55.36
54.98
48.11
47.94
47.77
47.60
47.43
47.26
47.09
46.94
36.86
31.19
24.91
SO3nP
OH
FmocHN
O
2
71
f1 (ppm)

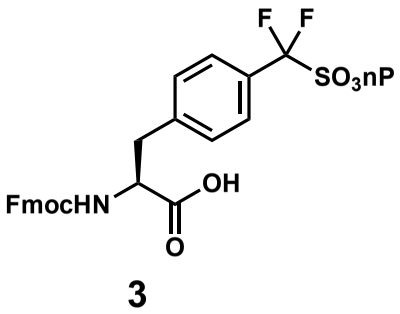

Fmoc-Smp(nP)-OH
LJD-079-1 COSY (MeOD)
SO3nP
OH
FmocHN
O
2
Current Data Parameters
NAME LJD-079-1P
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170311
Time 15.18 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG cosygpqf
TD 4096
SOLVENT MeOD
NS 8
DS 16
SWH 4504.504 Hz
FIDRES 2.199465 Hz
AQ 0.4546560 sec
RG 203
DW 111.000 usec
DE 6.50 usec
TE 300.0 K
D0 0.00000300 sec
D1 2.15916300 sec
D13 0.00000400 sec
D16 0.00020000 sec
IN0 0.00022220 sec
TDav 1
SFO1 500.1320005 MHz
NUC1 1H
P0 7.50 usec
P1 15.00 usec
PLW1 15.48799992 W
GPNAM[1] SMSQ10.100
GPZ1 10.00 %
P16 1000.00 usec
F1 - Acquisition parameters
TD 256
SFO1 500.132 MHz
FIDRES 35.159767 Hz
SW 8.999 ppm
FnMODE QF
F2 - Processing parameters
SI 1024
SF 500.1300000 MHz
WDW SINE
SSB 0
LB 0 Hz
GB 0
PC 1.40
F1 - Processing parameters
SI 1024
MC2 QF
SF 500.1300000 MHz
WDW SINE
SSB 0
LB 0 Hz
GB 0
f2 (ppm)
f1 (ppm)
72


Fmoc-Smp(nP)-OH
LJD-079-1 HSQC (MeOD)
Current Data Parameters
NAME LJD-079-1P
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170311
Time 16.49 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG hsqcedgpph
TD 1024
SOLVENT MeOD
NS 16
DS 16
SWH 6009.615 Hz
FIDRES 11.737530 Hz
AQ 0.0851968 sec
RG 203
DW 83.200 usec
DE 6.50 usec
TE 300.0 K
CNST2 145.0000000
D0 0.00000300 sec
D1 2.00000000 sec
D4 0.00172414 sec
D11 0.03000000 sec
D13 0.00000400 sec
D16 0.00020000 sec
D21 0.00345000 sec
IN0 0.00002400 sec
TDav 1
SFO1 500.1327507 MHz
NUC1 1H
P1 15.00 usec
P2 30.00 usec
PLW1 15.48799992 W
SFO2 125.7672181 MHz
NUC2 13C
CPDPRG[2 garp
P3 10.20 usec
P4 20.40 usec
PCPD2 70.00 usec
PLW2 88.91999817 W
PLW12 1.88800001 W
GPNAM[1] SMSQ10.100
GPZ1 30.00 %
GPNAM[2] SMSQ10.100
GPZ2 80.00 %
GPNAM[3] SMSQ10.100
GPZ3 20.10 %
P16 1000.00 usec
F1 - Acquisition parameters
TD 256
SFO1 125.7672 MHz
FIDRES 162.760422 Hz
SW 165.650 ppm
FnMODE TPPI
F2 - Processing parameters
SI 1024
SF 500.1300000 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.40
F1 - Processing parameters
SI 1024
MC2 TPPI
SF 125.7577890 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
SO3nP
OH
FmocHN
O
2
73
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f2 (ppm)
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150
f1 (ppm)


Fmoc-Smp(nP)-OH
LJD-079-1 HMBC (MeOD)
Current Data Parameters
NAME LJD-079-1P
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170311
Time 19.15 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG hmbcgplpndqf
TD 4096
SOLVENT MeOD
NS 32
DS 16
SWH 4504.504 Hz
FIDRES 2.199465 Hz
AQ 0.4546560 sec
RG 203
DW 111.000 usec
DE 6.50 usec
TE 300.0 K
CNST2 145.0000000
CNST13 10.0000000
D0 0.00000300 sec
D1 2.00000000 sec
D2 0.00344828 sec
D6 0.05000000 sec
D16 0.00020000 sec
IN0 0.00001790 sec
TDav 1
SFO1 500.1320005 MHz
NUC1 1H
P1 15.00 usec
P2 30.00 usec
PLW1 15.48799992 W
SFO2 125.7703648 MHz
NUC2 13C
P3 10.20 usec
PLW2 88.91999817 W
GPNAM[1] SMSQ10.100
GPZ1 50.00 %
GPNAM[2] SMSQ10.100
GPZ2 30.00 %
GPNAM[3] SMSQ10.100
GPZ3 40.10 %
P16 1000.00 usec
F1 - Acquisition parameters
TD 256
SFO1 125.7704 MHz
FIDRES 218.226257 Hz
SW 222.095 ppm
FnMODE QF
F2 - Processing parameters
SI 2048
SF 500.1300000 MHz
WDW SINE
SSB 0
LB 0 Hz
GB 0
PC 1.40
F1 - Processing parameters
SI 1024
MC2 QF
SF 125.7577890 MHz
WDW SINE
SSB 0
LB 0 Hz
GB 0
FmocHN
OH
O
SO3nP
2
f2 (ppm)
f1 (ppm)
74


Fmoc-F2Smp(nP)-OH
LJD-045 1H NMR (MeOD)
F F
SO3nP
FmocHN
OH
O
3
Current Data Parameters
NAME LJD-045P MeOD
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170312
Time 11.58 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG zg
TD 65536
SOLVENT MeOD
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.305176 Hz
AQ 3.2767999 sec
RG 20.2
DW 50.000 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
TD0 1
SFO1 500.1330008 MHz
NUC1 1H
P1 14.00 usec
PLW1 15.48799992 W
F2 - Processing parameters
SI 32768
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
f1 (ppm)
Intensity
75

Fmoc-F2Smp(nP)-OH
LJD-045 13C (1H dec) NMR (MeOD)



3

```
Current Data Parameters
NAME      LJD-045P MeOD
EXPNO                6
PROCNO               1

F2 - Acquisition Parameters
Date_          20170313
Time              10.07 h
INSTRUM            spect
PROBHD   Z119470_0008 (
PULPROG          zgpg30
TD                65536
SOLVENT             MeOD
NS                13993
DS                    4
SWH           28846.154 Hz
FIDRES         0.880315 Hz
AQ            1.1359574 sec
RG                  203
DW               17.333 usec
DE                6.50 usec
TE                300.0 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                  25
SFO1        125.7697337 MHz
NUC1                13C
P1                10.20 usec
PLW1        88.91999817 W
SFO2        500.1320005 MHz
NUC2                 1H
CPDPRG[2         waltz16
PCPD2             80.00 usec
PLW2        15.48799992 W
PLW12        0.34847999 W
PLW13        0.17528000 W

F2 - Processing parameters
SI                65536
SF          125.7577890 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

Fmoc-F2Smp(nP)-OH
LJD-045 19F (1H dec) NMR (MeOD)

```
Current Data Parameters
NAME      LJD-045P MeOD
EXPNO                2
PROCNO               1

F2 - Acquisition Parameters
Date_          20170312
Time              12.00 h
INSTRUM            spect
PROBHD   Z119470_0008 (
PULPROG         zgfhigqn
TD                46870
SOLVENT            MeOD
NS                   128
DS                     0
SWH           46875.000 Hz
FIDRES         2.000213 Hz
AQ            0.4999467 sec
RG                   203
DW               10.667 usec
DE                6.50 usec
TE               300.0 K
D1           0.10000000 sec
D11          0.03000000 sec
D12          0.00002000 sec
TD0                  1
SFO1         470.5627297 MHz
NUC1                19F
P1                14.95 usec
PLW1         41.97600174 W
SFO2         500.1325006 MHz
NUC2                1H
CPDPRG[2         waltz16
PCPD2             80.00 usec
PLW2         15.48799992 W
PLW12         0.34847999 W

F2 - Processing parameters
SI                32768
SF           470.5923770 MHz
WDW                  EM
SSB                   0
LB                 2.00 Hz
GB                    0
PC                 1.00
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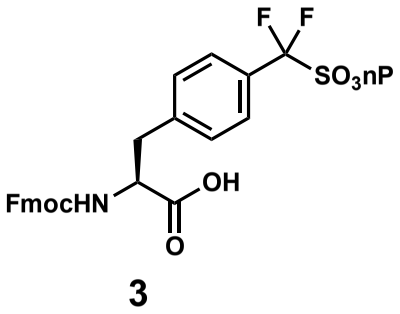
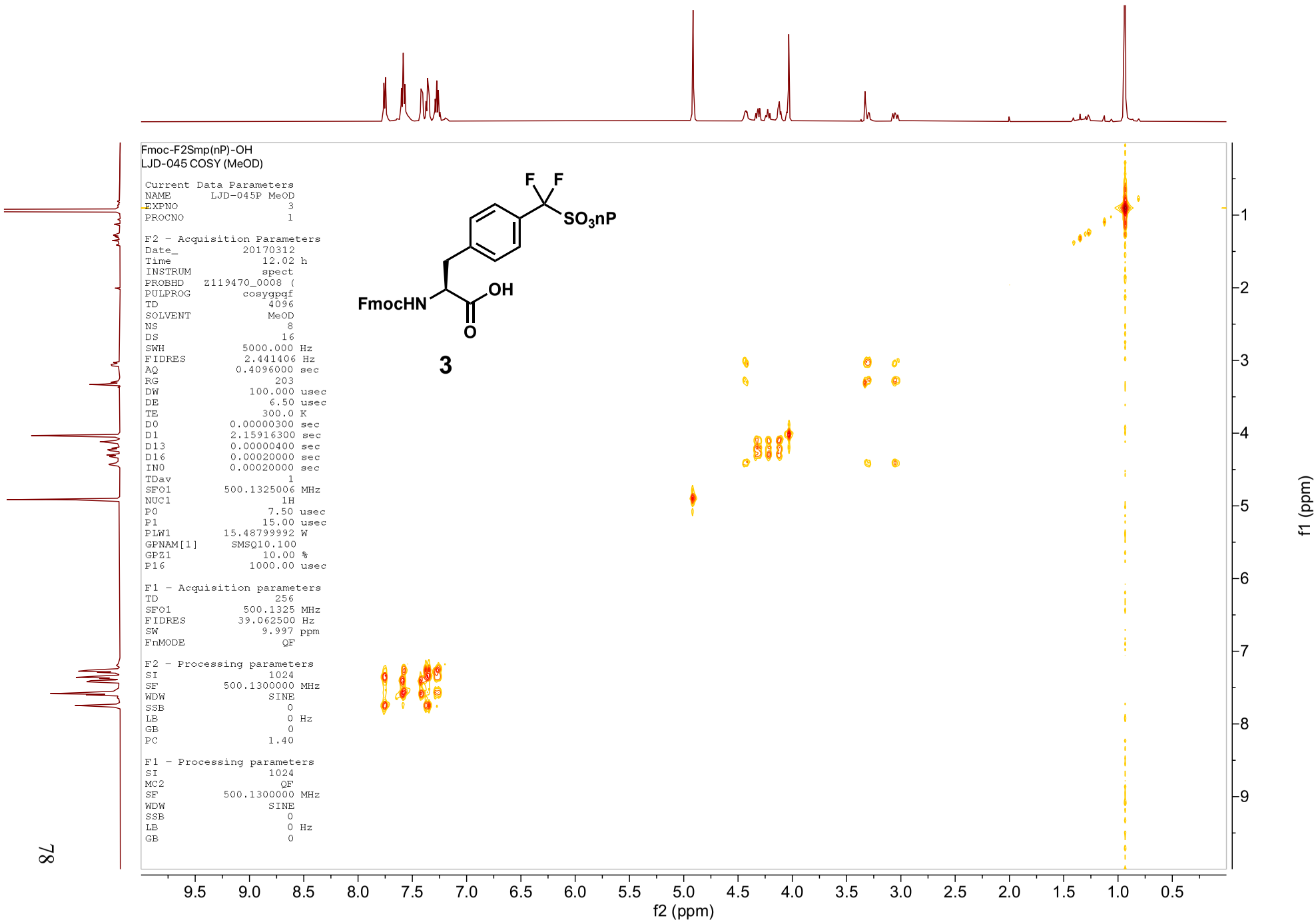
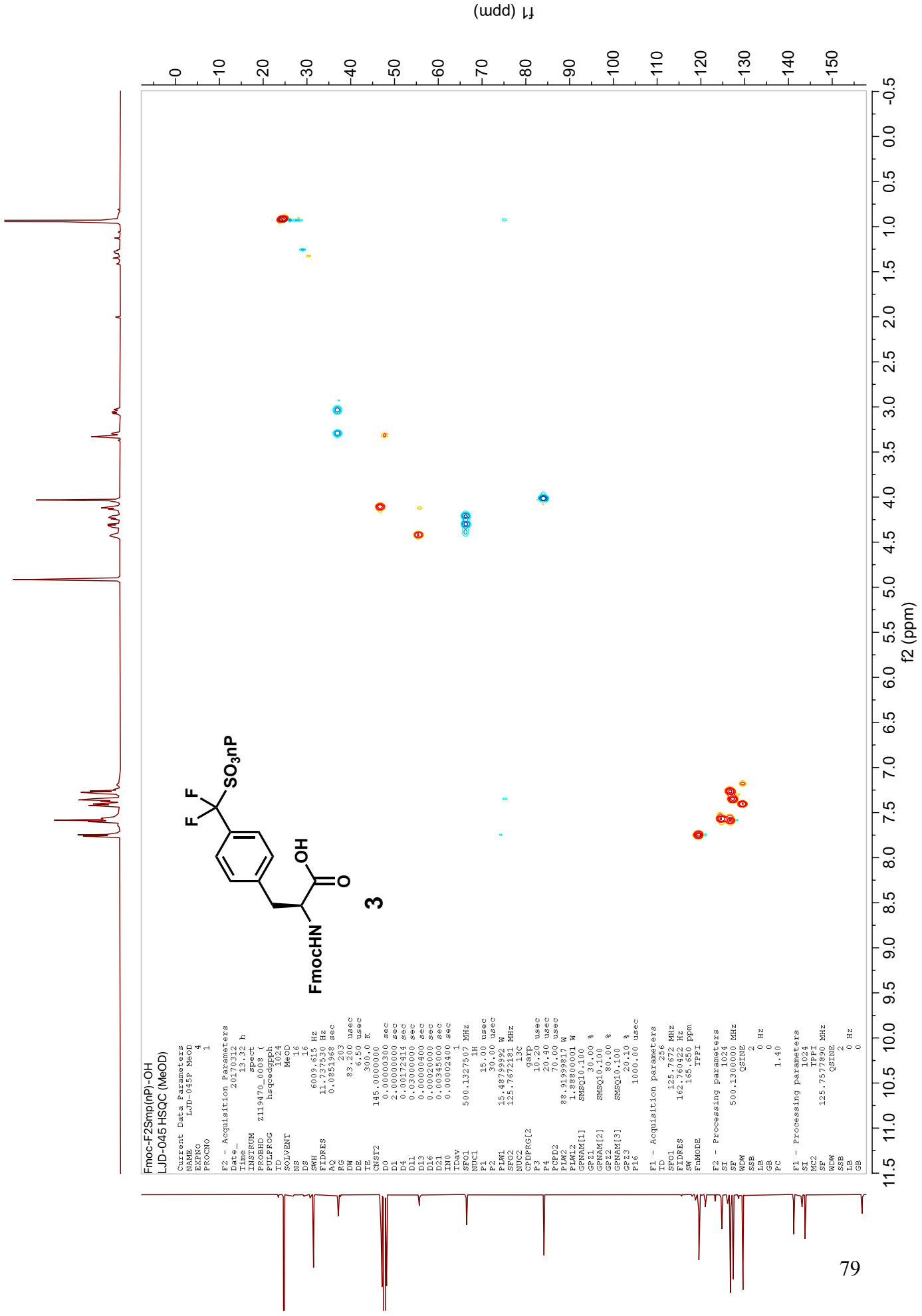
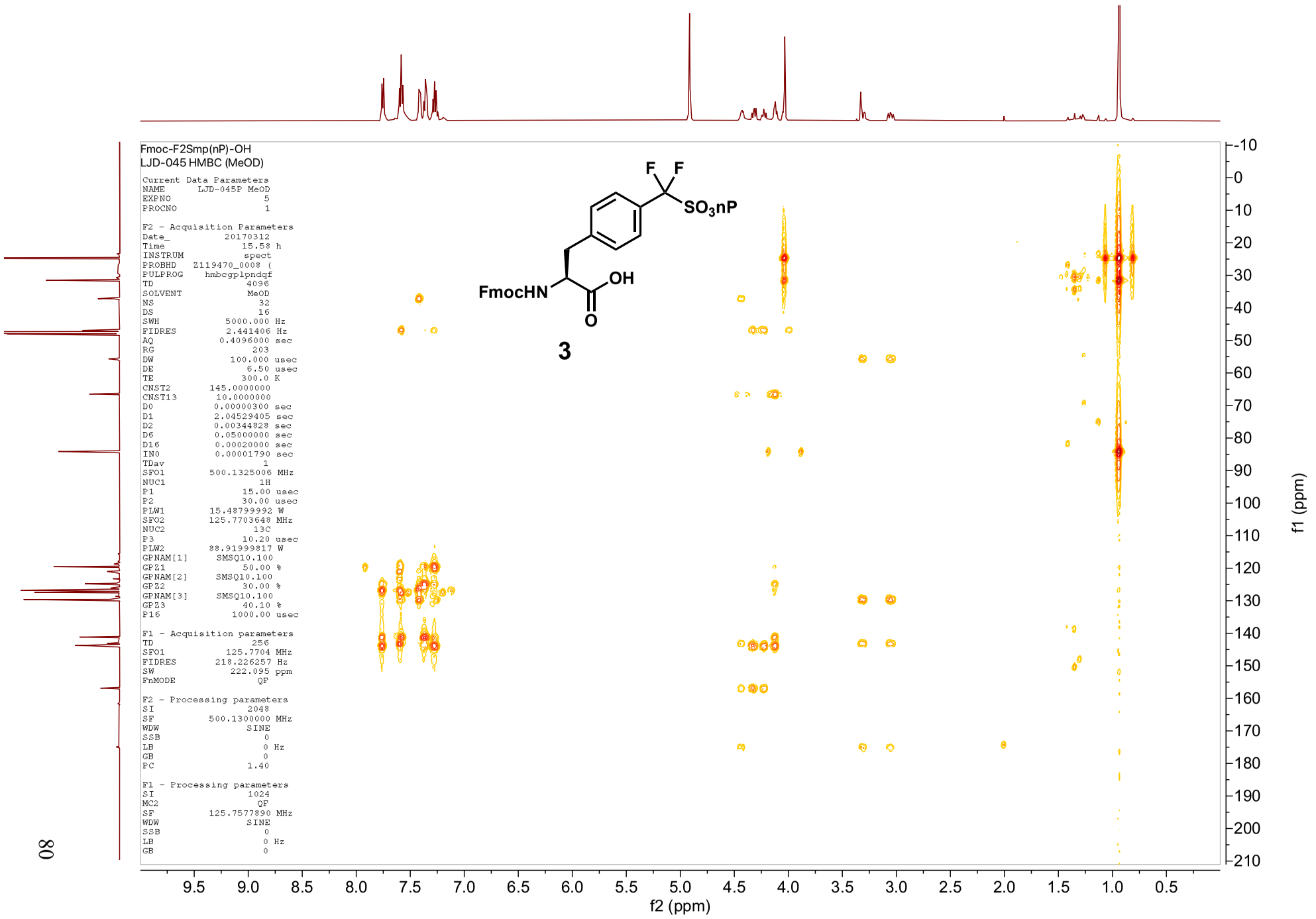


3


Fmoc-F2Smp(nP)-OH
LJD-045 COSY (MeOD)
Current Data Parameters
NAME LJD-045P MeOD
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170312
Time 12.02 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG cosygpqf
TD 4096
SOLVENT MeOD
NS 8
DS 16
SWH 5000.000 Hz
FIDRES 2.441406 Hz
AQ 0.4096000 sec
RG 203
DW 100.000 usec
DE 6.50 usec
TE 300.0 K
D0 0.00000300 sec
D1 2.15916300 sec
D13 0.00000400 sec
D16 0.00020000 sec
IN0 0.00020000 sec
TDav 1
SFO1 500.1325006 MHz
NUC1 1H
P0 7.50 usec
P1 15.00 usec
PLW1 15.48799992 W
GPNAM[1] SMSQ10.100
GPZ1 10.00 %
P16 1000.00 usec
F1 - Acquisition parameters
TD 256
SFO1 500.1325 MHz
FIDRES 39.062500 Hz
SW 9.997 ppm
FnMODE QF
F2 - Processing parameters
SI 1024
SF 500.1300000 MHz
WDW SINE
SSB 0
LB 0 Hz
GB 0
PC 1.40
F1 - Processing parameters
SI 1024
MC2 QF
SF 500.1300000 MHz
WDW SINE
SSB 0
LB 0 Hz
GB 0
F
F
SO3nP
FmocHN
OH
O
3
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f2 (ppm)
1
2
3
4
5
6
7
8
9
f1 (ppm)


Fmoc-F2Smp(nP)-OH
LJD-045 HSQC (MeOD)
Current Data Parameters
NAME LJD-045P MeOD
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170312
Time 13.32 h
INSTRUM spect
PROBHD 2119470_0008 (
PULPROG hsqcedqppi
TD 1024
SOLVENT MeOD
NS 16
DS 16
SWH 6009.615 Hz
FIDRES 11.737530 Hz
AQ 0.0851968 sec
RG 203
DW 83.200 usec
DE 6.50 usec
TE 300.0 K
CNST2 145.0000000
D0 0.00000300 sec
D1 2.00000000 sec
D4 0.00172414 sec
D11 0.03000000 sec
D13 0.00000400 sec
D16 0.00020000 sec
D21 0.00345000 sec
IN0 0.00002400 sec
TDav 1
SFO1 500.1327507 MHz
NUC1 1H
P1 15.00 usec
P2 30.00 usec
PLW1 15.48799992 W
SFO2 125.7672181 MHz
NUC2 13C
CPDPRG[2 garp
P3 20.00 usec
P4 20.40 usec
PCPD2 70.00 usec
PLW2 88.91999817 W
PLW12 1.88800001 W
GPNAM[1] SMSQ10.100
GPZ1 30.00 %
GPNAM[2] SMSQ10.100
GPZ2 80.00 %
GPNAM[3] SMSQ10.100
GPZ3 20.10 %
P16 1000.00 usec
F1 - Acquisition parameters
TD 256
SFO1 125.7672 MHz
FIDRES 162.760422 Hz
SW 165.650 ppm
FnMODE TPPI
F2 - Processing parameters
SI 1024
SF 500.1300000 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.40
F1 - Processing parameters
SI 1024
MC2 TPPI
SF 125.7577890 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
F F
SO3nP
OH
O
FmocHN
3
f2 (ppm)
f1 (ppm)


Fmoc-F2Smp(nP)-OH
LJD-045 HMBC (MeOD)
Current Data Parameters
NAME LJD-045P MeOD
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170312
Time 15.58 h
INSTRUM spect
PROBHD Z119470_0008 (
PULPROG hmbcgplpndqf
TD 4096
SOLVENT MeOD
NS 32
DS 16
SWH 5000.000 Hz
FIDRES 2.441406 Hz
AQ 0.4096000 sec
RG 203
DW 100.000 usec
DE 6.50 usec
TE 300.0 K
CNST2 145.0000000
CNST13 10.0000000
D0 0.00000300 sec
D1 2.04529405 sec
D2 0.00344828 sec
D6 0.05000000 sec
D16 0.00020000 sec
IN0 0.00001790 sec
TDav 1
SFO1 500.1325006 MHz
NUC1 1H
P1 15.00 usec
P2 30.00 usec
PLW1 15.48799992 W
SFO2 125.7703648 MHz
NUC2 13C
P3 10.20 usec
PLW2 88.91999817 W
GPNAM[1] SMSQ10.100
GPZ1 50.00 %
GPNAM[2] SMSQ10.100
GPZ2 30.00 %
GPNAM[3] SMSQ10.100
GPZ3 40.10 %
P16 1000.00 usec
F1 - Acquisition parameters
TD 256
SFO1 125.7704 MHz
FIDRES 218.226257 Hz
SW 222.095 ppm
FnMODE QF
F2 - Processing parameters
SI 2048
SF 500.1300000 MHz
WDW SINE
SSB 0
LB 0 Hz
GB 0
PC 1.40
F1 - Processing parameters
SI 1024
MC2 QF
SF 125.7577890 MHz
WDW SINE
SSB 0
LB 0 Hz
GB 0
F
F
SO3nP
OH
FmocHN
O
3
f2 (ppm)
f1 (ppm)

11 References

1. L. Jobron and G. Hummel, *Org. Lett.*, 2000, **2**, 2265-2267.
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