Supporting Information

N-Arylated Peptide: Troponyl Residue Influences The Structure and Conformation of *N*-Troponylated *di-/tri*-Peptides

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1. Experimental Procedure

Material and Instrumentation: All required chemical materials were obtained from commercial and used without purification. Anhydrous DMF was freshly prepared by distilling over calcium hydride. The reaction was monitored by thin-layer chromatography (TLC), purification by Column chromatography (230-400/100-200 mesh silica). Mass spectra were recorded by Bruker MicrOTOF-Q II Spectrometer. NMR spectra were recorded on Bruker AV-700MHz and Bruker AV-400 (^{1}H:400MHz ,^{13}C:100.6 MHz),^{1}H and ^{13}C-NMR chemical shift were recorded in ppm downfield from tetramethylsilane, splitting patterns are abbreviated as: s, singlet; d, doublet; dd, doublet of doublet; t, triplet; q, quartet; dq, doublet of quartet; m, multiple. CD experiment were performed on JASCO-J 1500 all CD experiment were performed at 20°C.All CD spectra recorded two scans averaged, CD spectra recorded from 310-190 nm.

Syntheses of Troponyl monomer: A solution of 2-tosyloxy tropone (1.00g, 3.61 mmol) in ethanol (50mL), was added in neutralized amino methyl ester (1.2mg,7.23mmol) and refluxed. The reaction was monitored by using thin layer chromatography and found the completion of reactions after 36 hours. After that cooling the reaction mixture at room temperature and concentrated under reduced presser. The reaction mixture was dissolved in DCM(50mL) and washed with water(50ml) three times and then brine(50mL) solution one time using the separating flask. The organic layer was kept Na_2SO4 for 20 minutes and then concentrated under vacuum. The concentrated crude residue was purified by the column chromatography method. The product was purified by using solvent 30% ethyl acetate in hexane[1]; the N-troponyl aminomethyl ester was dissolved in EtOH and THF (1:1), to this reaction mixure 2 eq. of NaOH was dissolved in little amont of disstiled water was added and allow to stirring room temperature. The reaction mixture was monitered by TLC, after 15min. reaction was

completed .The solvent was removed under the reduced pressure and the crude product 1N HCl was added and extracted twice EtOAC. The organic layers were combined together, dried over Na_2SO_4 and concentrated under low pressure to afford the pure product as yellow gelatinous liquid. This Troponyl momnomer acid was futher used for peptide synthesis[2].

***General procedure for peptide synthesis*:** L-amino methyl ester (1.2 eq) was neutralized with Et_3N and to the reaction mixture of troponyl monomer amino acid (1.0 eq.) in anhydrous DMF (10 ml) with NMM (3.0 eq.), HOAT (1.3 eq.), and EDC-HCL (1.3 eq.) and then allow to stir overnight. After complication of reaction, the reaction mixture was concentrated under reduced pressure. Concentrated reaction mixture was extracted three times with methylene chloride. The organic layer was combined dried over saturated sodium bicarbonate. The washed organic layer was combined together and concentrated under reduced pressure and loaded silica gel column purification to obtained desired product. The obtained product was characterised by ^{1}H -/^{13}C-NMR and ESI-ToF-HRMS mass techniques. The characterization of all synthesized hybrid peptide data is provided in bellow.

2. Analytical data

methyl-(2-((7-oxocyclohepta-1,3,5-trien-1-yl)amino)acetamido)acetate ***(2a)****. (tr-Gly-Gly-OMe)* The Pure product was obtained as yellowish solid (60 mg, 80% yield,) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.35 – 7.16 (m, 4H), 6.92 (s, 1H), 6.81 (t, *J* = 9.5 Hz, 1H), 6.54 (d, *J* = 10.2 Hz, 1H), 4.12 (d, *J* = 6.3 Hz, 2H), 4.06 (d, *J* = 5.5 Hz, 2H), 3.71 (s, 3H), 3.49 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.34, 169.77, 168.64, 154.90, 137.90, 136.28, 130.75, 124.64, 110.24, 52.42, 47.04, 41.00. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd. For $C_{12}H_{14}N_2O_4$ 273.0846, found 273.0852.

methyl-(2-((7-oxocyclohepta-1,3,5-trien-1-yl)amino)acetamido)propanoate ***(2b).*** *(tr-Gly-ala-OMe)* The Pure product was obtained as light-yellow solid (66 mg, 74% yield) ^{1}H NMR (400

MHz, $CDCl_3$) δ 7.68 (t, *J* = 5.7 Hz, 1H), 7.33 – 7.08 (m, 4H), 6.78 (t, *J* = 9.5 Hz, 1H), 6.53 (d, *J* = 10.2 Hz, 1H), 4.63 (p, *J* = 7.3 Hz, 1H), 4.10 (d, *J* = 6.2 Hz, 2H), 3.69 (s, 3H), 1.37 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.23, 172.88, 167.99, 155.04, 137.84, 136.29, 130.50, 124.40, 110.20, 52.48, 48.05, 47.06, 29.69, 17.92. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. For $C_{13}H_{16}N_2O_4$ 265.1183, found 265.1210.

methyl-(2-((7-oxocyclohepta-1,3,5-trien-1-yl)amino)propanamido)acetate ***(2c).*** *(tr-ala-Gly-OMe)* The Pure product was obtained as light red Viscous liquid (86 mg, 63% yield) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (dd, *J* = 6.5, 5.1 Hz, 1H), 7.27 – 7.15 (m, 3H), 7.09 (s, 1H), 6.80 (t, *J* = 9.5 Hz, 1H), 6.53 (d, *J* = 10.2 Hz, 1H), 4.13 – 4.04 (m, 1H), 4.01 (dd, *J* = 5.8, 2.3 Hz, 2H), 3.70 (s, 3H), 1.68 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.20, 172.69, 169.78, 154.24, 137.91, 136.44, 130.68, 124.64, 110.98, 77.36, 77.04, 76.72, 53.99, 52.33, 40.98, 19.14. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd. For $C_{13}H_{16}N_2O_4$ 287.1002, found 287.1026.

methyl-(3-methyl-2-((7-oxocyclohepta-1,3,5-trien-1-yl)amino)butanamido)acetate ***(2d).*** *(tr-Val-Gly-OMe)* The Pure product was obtained as yellowish solid (200 mg, 70% yield,) ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.48 – 7.44 (m, 1H), 7.44 – 7.36 (m, 1H), 7.29 – 7.20 (m, 3H), 7.15 – 7.07 (m, 1H), 6.80 (dd, *J* = 20.6, 11.1 Hz, 1H), 6.57 (d, *J* = 10.3 Hz, 1H), 4.59 (s, 1H), 4.09 (dd, *J* = 17.9, 6.0 Hz, 1H), 3.96 (dd, *J* = 17.9, 5.7 Hz, 1H), 3.87 (t, *J* = 5.7 Hz, 1H), 3.69 (s, 3H), 2.53 – 2.48 (m, 1H), 1.12 (dd, *J* = 30.4, 6.9 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.01, 171.43, 169.78, 155.00, 137.95, 136.68, 130.04, 126.74, 124.53, 111.08, 63.79, 52.26, 40.98, 31.26, 19.60, 17.87. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. For $C_{15}H_{20}N_2O_4$ 293.1496, found 293.1515.

methyl-(3-methyl-2-((7-oxocyclohepta-1,3,5-trien-1-yl)amino)butanamido)propanoate ***(2e).*** *(tr-Val-β-ala-OMe)* The Pure product was obtained as light red Viscous liquid (551 mg, 62% yield,) ^{1}H NMR (700 MHz, CDCl3) δ 7.44 (d, J = 6.3 Hz, 1H), 7.32 – 7.25 (m, 1H), 7.20 –

7.16 (m, 1H), 7.13-7.10 (m, 2H, 6.75 (q, J = 9.5 Hz, 1H), 6.45 (d, J = 10.3 Hz, 1H), 3.78 (t, J = 6.0 Hz, 1H), 3.54 – 3.45 (m, 5H), 2.53 – 2.47 (m, 2H), 2.47 – 2.38 (m, 1H), 1.11 – 1.05 (m, 6H). ^{13}C NMR (176 MHz, CDCl3) δ 176.89, 172.17, 170.88, 154.95, 137.62, 136.46, 129.69, 123.79, 110.15, 63.97, 51.60, 35.22, 33.85, 31.11, 19.58, 18.24. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. For $C_{16}H_{22}N_2O_4$ 307.1652, found 307.1674.

methyl-(2-((7-oxocyclohepta-1,3,5-trien-1-yl)amino)acetamido)propanoate ***(2f).*** *(tr-Gly-β-ala-OMe)* The Pure product was obtained as light-yellow solid (160 mg, 95% yield) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 2H), 7.14 (d, *J* = 11.6 Hz, 1H), 6.82 (t, *J* = 9.5 Hz, 1H), 6.60 (d, *J* = 10.4 Hz, 1H), 4.14 (s, 2H), 4.03 (s, 2H), 3.82 (s, 2H), 3.71 (d, *J* = 2.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.03, 170.11, 169.23, 155.12, 150.47, 138.02, 136.75, 129.85, 128.86, 124.36, 120.46, 110.63, 76.83, 52.23, 46.30, 40.84. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. For $C_{13}H_{16}N_2O_4$ 265.1183, found 265.1196.

methyl-(4-methyl-2-((7-oxocyclohepta-1,3,5-trien-1yl)amino)pentanamido)propanoate ***(2g).*** *(tr-leu-β-ala-OMe)* The Pure product was obtained as light yellow Viscous liquid (392 mg, 62% yield) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.31 (m, 1H), 7.29 (d, *J* = 4.7 Hz, 1H), 7.27 – 7.18 (m, 3H), 6.88 – 6.76 (m, 2H), 6.45 (d, *J* = 10.2 Hz, 1H), 3.99 – 3.95 (m, 1H), 3.54 – 3.44 (m, 5H), 2.49 (t, *J* = 6.1 Hz, 2H), 1.96 – 1.78 (m, 3H), 1.01 (d, *J* = 6.0 Hz, 1H), 0.91 (d, *J* = 6.0 Hz, 3H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 177.32, 172.30, 172.01, 154.53, 137.86, 136.36, 130.63, 124.35, 110.17, 57.14, 51.79, 42.13, 35.07, 25.24, 23.14, 21.52. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. For $C_{17}H_{24}N_2O_4$ 321.1809, found 321.1820.

methyl-(2-((7-oxocyclohepta-1,3,5-trien-1-yl)amino)propanamido)propanoate ***(2h).*** (*Tr-Ala-β-Ala-OMe*) The Pure product was obtained as light red Viscous liquid (200 mg, 70% yield) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.28 (m, 1H), 7.24 – 7.16 (m, 3H), 6.84 (s, 1H), 6.78 (t, *J* = 9.5 Hz, 1H), 6.40 (d, *J* = 10.2 Hz, 1H), 4.05-3.99 (m, 1H), 3.56 – 3.42 (m, 5H), 2.49 (t, *J* =

6.1 Hz, 2H), 1.64 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.20, 172.18, 171.97, 154.12, 137.72, 136.12, 130.74, 124.27, 110.17, 77.37, 77.05, 76.74, 54.07, 51.70, 34.94, 33.70, 29.70, 19.11. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd. For $C_{14}H_{18}N_2O_4$ 301.1159, found 301.1184.

methyl-((2S,3R)-3-methyl-2-((7-oxocyclohepta-1,3,5-trien-1-yl)amino)pentanamido)propanoate ***(2i).*** *(tr-Ile-β-ala-Ome)* The Pure product was obtained as light red Viscous liquid (86 mg, 60% yield) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 20.5 Hz, 1H), 7.29 – 7.09 (m, 4H), 6.74 (t, *J* = 8.9 Hz, 1H), 6.46 (d, *J* = 9.4 Hz, 1H), 3.83 (s, 1H), 3.50 (s, 5H), 2.49 (s, 2H), 2.15 (s, 1H), 1.61 (s, 1H), 1.39 (ddd, *J* = 20.4, 13.4, 6.5 Hz, 1H), 1.08 – 0.83 (m, 7H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.15, 170.65, 154.87, 137.64, 136.31, 130.02, 123.93, 110.08, 77.41, 77.10, 76.78, 63.16, 51.62, 37.60, 35.06, 33.77, 25.15, 15.98, 11.51. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd. For $C_{17}H_{24}N_2O_4$ 343.1628, found 343.1603,

methyl-(2-((7-oxocyclohepta-1,3,5-trien-1-yl)amino)-3-phenylpropanamido)propanoate ***(2j).*** *(tr-Phe-β-ala-OMe)* The Pure product was obtained as light-yellow solid (150 mg, 78% yield) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 4.2 Hz, 1H), 7.36 – 7.21 (m, 6H), 7.15 (dd, *J* = 20.5, 10.8 Hz, 1H), 6.75 (dd, *J* = 20.1, 10.3 Hz, 2H), 6.40 (d, *J* = 10.2 Hz, 1H), 4.20 (d, *J* = 5.3 Hz, 1H), 3.56 – 3.38 (m, 5H), 3.27 (dt, *J* = 13.9, 10.3 Hz, 2H), 2.51 – 2.37 (m, 2H), 2.07 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.16, 172.04, 170.48, 154.19, 137.63, 136.05, 135.85, 130.50, 129.22, 128.92, 127.38, 124.19, 110.10, 59.27, 51.67, 38.68, 34.96, 33.66. HRMS (ESI-TOF) m/z:$[M+Na]^+$ Calcd. For $C_{20}H_{22}N_2O_4$ 377.1472, found 377.1476.

methyl-methyl-2-((-5-(7-oxocyclohepta-1,3,5-trien-1-yl)pyrrolidine-2-carboxamido)butanoate ***(2k).*** *(tr-Pro-val-OMe)* The Pure product was obtained as light red Viscous liquid (300 mg, 58% yield,) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 – 6.99 (m, 2H), 6.87 (d, *J* = 11.7 Hz, 1H), 6.70 (d, *J* = 8.5 Hz, 1H), 6.55 (t, *J* = 9.2 Hz, 1H), 6.47 (d, *J* = 10.5 Hz,

1H), 5.21 (d, *J* = 3.5 Hz, 1H), 4.50 – 4.43 (m, 1H), 3.75 (dd, *J* = 13.9, 8.4 Hz, 1H), 3.66 (s, 3H), 3.45 (dd, *J* = 16.7, 6.9 Hz, 1H), 2.29 – 1.90 (m, 6H), 0.91 (dd, *J* = 10.6, 7.3 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.30, 172.40, 172.09, 155.51, 135.69, 134.35, 132.48, 123.03, 113.97, 77.61, 77.29, 76.97, 63.54, 57.03, 51.94, 51.70, 31.35, 31.08, 23.23, 18.93, 17.76. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd. For $C_{18}H_{24}N_2O_4$ 355.1629, found 355.1627.

methyl-(3-((7-oxocyclohepta-1,3,5-trien-1-yl)amino)propanoyl)pyrrolidine-2-carboxylate ***(2l).*** *(tr-β-ala-Pro-OMe)* The Pure product was obtained as light red Viscous liquid (80 mg, 58% yield,) ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.33 (s, 1H), 7.27 – 7.24 (m, 1H), 7.22 (t, *J* = 9.5 Hz, 1H), 7.13 (d, *J* = 11.5 Hz, 1H), 6.67 (t, *J* = 9.5 Hz, 1H), 6.61 (d, *J* = 10.4 Hz, 1H), 4.49 (dd, *J* = 8.5, 3.8 Hz, 1H), 3.77 – 3.71 (m, 4H), 3.71-3.69 (m, 1H), 3.65 – 3.60 (m, 1H), 3.49-3.46 (m, 1H), 2.79 – 2.66 (m, 2H), 2.19-2.16 (m, 1H), 2.11 – 2.03 (m, 1H), 2.03 – 1.94 (m, 2H), 1.82 (s, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 176.84, 172.76, 169.13, 155.46, 137.42, 136.42, 128.86, 122.53, 108.77, 77.32, 77.14, 76.96, 58.81, 52.42, 47.13, 38.38, 33.39, 29.28, 24.81. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. For $C_{18}H_{24}N_2O_4$ 305.1496, found 305.1519.

methyl-(3-(2-((7-oxocyclohepta-1,3,5-trien-1-yl)amino)acetamido)propanamido)acetate ***(3a).*** *(tr-Gly-β-ala-Gly-OMe)* The Pure product was obtained as yellowish solid (155 mg, 75% yield,) ^{1}H NMR (700 MHz, MeOD) δ 7.41-7.44 (m, 4H), 7.14 (d, *J* = 11.5 Hz, 1H), 6.84 (t, *J* = 9.4 Hz, 1H), 6.69 (d, *J* = 10.3 Hz, 1H), 4.13 (s, 2H), 3.99 (d, *J* = 9.4 Hz, 1H), 3.93 – 3.88 (m, 3H), 3.81 (s, 2H), 3.74 – 3.68 (m, 4H), 3.54 (t, *J* = 6.4 Hz, 2H), 2.50 (t, *J* = 6.4 Hz, 2H). ^{13}C NMR (176 MHz, MeOD) δ 174.27, 172.00, 170.53, 169.06, 157.02, 149.86, 140.43, 139.38, 138.58, 136.41, 129.81, 129.30, 121.51, 46.64, 46.61, 46.57, 41.91, 41.87, 41.84, 41.03, 37.02, 36.29. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd. For $C_{15}H_{19}N_3O_5$ 344.1217, found 34401195.

methyl-(3-(2-((7-oxocyclohepta-1,3,5-trien-1-yl)amino)propanamido)propanamido)propanoate ***(3b).*** *(tr-Ala-β-ala-Ala-OMe)* The Pure

product was obtained as light red Viscous liquid (290 mg, 56% yield) ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.38 – 7.23 (m, 3H), 7.19 (t, *J* = 10.1 Hz, 1H), 7.13 (d, *J* = 11.6 Hz, 1H), 6.85 – 6.69 (m, 2H), 6.45 (dd, *J* = 19.6, 10.3 Hz, 1H), 4.44 (td, *J* = 7.2, 3.3 Hz, 1H), 4.08 – 4.04 (m, 1H), 3.72 (s, 3H), 3.63 – 3.41 (m, 2H), 2.43 (dtd, *J* = 21.5, 14.9, 8.6 Hz, 2H), 1.61 (d, *J* = 7.0 Hz, 3H), 1.43 – 1.22 (m, 4H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 176.95, 173.52, 172.38, 171.04, 154.32, 137.70, 136.39, 130.17, 123.96, 110.20, 110.11, 53.72, 52.53, 48.10, 35.77, 18.95, 17.87. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd. For $C_{17}H_{23}N_3O_5$ 372.1530, found 372.1518.

methyl-methyl-2-(3-(-3-methyl-2-((7-oxocyclohepta-1,3,5-trien-1-yl)amino)butanamido)propanamido)butanoate ***(3c).*** *(tr-Val-β-ala-Val-OMe)* The Pure product was obtained as light red Viscous liquid (250 mg, 56% yield) ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 14.0, 6.5 Hz, 1H), 7.30 (dd, *J* = 19.6, 9.1 Hz, 1H), 7.24 – 7.17 (m, 2H), 7.06 (s, 5H), 6.75 (t, *J* = 9.5 Hz, 1H), 6.48 (t, *J* = 11.4 Hz, 1H), 6.25 (d, *J* = 8.0 Hz, 1H), 4.45 (dd, *J* = 8.1, 5.3 Hz, 1H), 3.79 (t, *J* = 5.3 Hz, 1H), 3.73 (d, *J* = 6.7 Hz, 3H), 3.61 (dq, *J* = 12.3, 6.0 Hz, 1H), 3.48 (td, *J* = 12.4, 5.9 Hz, 1H), 2.50 – 2.37 (m, 3H), 2.08 (mz, 1H), 1.06 (dd, *J* = 14.7, 6.8 Hz, 6H), 0.92 – 0.80 (m, 6H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 176.99, 172.38, 171.10, 170.87, 154.91, 137.65, 136.25, 129.99, 123.94, 110.11, 77.16, 76.98, 76.80, 63.72, 57.13, 52.17, 35.57, 35.53, 31.18, 30.91, 19.49, 18.86, 18.08, 17.77. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. For $C_{21}H_{31}N_3O_5$ 406.2336, found 406.2340.

methyl-methyl-2-(3-((-4-methyl-2-((7-oxocyclohepta-1,3,5-trien-1-yl)amino)pentanamido) propanamido) pentanoate ***(3d).*** *(tr-Leu-β-ala-Leu-OMe)* The Pure product was obtained as light red Viscous liquid (230 mg, 68% yield) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.10 (m, 5H), 6.74 (t, *J* = 9.4 Hz, 1H), 6.55 – 6.34 (m, 2H), 4.51 (s, 1H), 3.99 (d, *J* = 5.7 Hz, 1H), 3.73 (s, 3H), 3.52 (dddd, *J* = 35.2, 27.0, 13.2, 6.1 Hz, 2H), 2.43 (dt, *J* = 32.7, 11.3 Hz, 2H), 1.83 (dt, *J* = 11.5, 8.0 Hz, 3H), 1.61 (d, *J* = 6.2 Hz, 2H), 1.54 – 1.38 (m, 1H), 1.36 – 1.21 (m, 1H), 1.02 – 0.83 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.07, 173.57, 172.25, 171.06, 154.62,

137.61, 136.30, 136.27, 130.22, 123.91, 109.90, 57.02, 52.35, 50.86, 41.13, 35.75, 25.09, 23.01, 22.76, 21.84, 21.48. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd. For $C_{23}H_{35}N_3O_5$ 456.2469, found 456.2441.

methyl-methyl-2-(3-((-3-methyl-2-((7-oxocyclohepta-1,3,5-trien-1-yl)amino)pentanamido) propanamido)pentanoate ***(3e).*** *(tr-Ile-β-ala-Ile-OMe)* The Pure product was obtained as light red Viscous liquid (340 mg, 81% yield) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 6.5 Hz, 1H), 7.36 – 7.09 (m, 4H), 6.77 – 6.68 (m, 1H), 6.52 (dd, *J* = 20.0, 8.8 Hz, 2H), 4.54 – 4.45 (m, 1H), 3.85 (t, *J* = 6.0 Hz, 1H), 3.72 (s, 3H), 3.55 (dtd, *J* = 27.4, 13.3, 6.5 Hz, 2H), 2.55 – 2.38 (m, 2H), 2.10 (dd, *J* = 32.4, 6.0 Hz, 1H), 1.81 (s, 1H), 1.62 (d, *J* = 6.4 Hz, 1H), 1.47 – 1.07 (m, 3H), 1.06 – 0.79 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.95, 172.43, 171.05, 170.84, 154.93, 137.55, 136.27, 129.85, 123.68, 109.92, 62.96, 56.46, 52.12, 37.70, 37.60, 35.63, 25.26, 25.19, 15.87, 15.45, 11.55, 11.47. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd. For $C_{23}H_{35}N_3O_5$ 456.2469, found 456.2441.

methyl,2-dimethyl-4,7,11-trioxo-3-oxa-5,8,12-triazatetradecan-14-oate ***(4a).*** *(Boc-Gly-β-ala-Gly-OMe)* The pure product was obtained as white solid (300 mg, 91% yield) ^{1}H NMR (700 MHz, $CDCl_3$) δ 6.98 (d, *J* = 70.7 Hz, 2H), 5.45 (s, 1H), 4.00 (d, *J* = 5.8 Hz, 2H), 3.74 (d, *J* = 7.4 Hz, 5H), 3.56 (dd, *J* = 11.9, 6.1 Hz, 2H), 2.49 – 2.44 (m, 2H), 2.06 (s, 2H), 1.42 (s, 9H). 13C NMR (101 MHz, CDCl3) δ 170.95, 170.10, 156.19, 80.22, 77.35, 77.03, 76.71, 52.44, 44.39, 41.22, 35.97, 35.74 , 28.30. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd. For $C_{13}H_{23}N_3O_6$ 340.1479, found 340.1476.

methyl-tetramethyl-4,7,11-trioxo-3-oxa-5,8,12-triazatetradecan-14-oate ***(4b).*** *(Boc-Al-β-ala-Ala-OMe)* The pure product was obtained as white solid (140 mg, 52% yield) ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.20 (d, *J* = 44.7 Hz, 2H), 5.19 (s, 1H), 4.56 (m, 1H), 4.01 (t, *J* = 7.1 Hz, 1H), 3.85 (d, *J* = 5.3 Hz, 2H), 3.75 (s, 3H), 3.20 (s, 1H), 2.44 – 2.27 (m, 2H), 2.04 (d, *J* = 14.2 Hz,

1H), 1.41 (s, 2H), 1.41 (s, 9H), 1.33 (d, *J* = 7.0 Hz, 3H). 13C NMR (101 MHz, CDCl3) δ 174.81, 173.52, 172.38, 155.76, 80.12, 52.59, 50.89, 48.37, 36.73, 28.29, 17.88, 16.96. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd. For $C_{15}H_{27}N_3O_6$ 368.1792, found 368.1795.

methyl-diisopropyl-2,2-dimethyl-4,7,11-trioxo-3-oxa-5,8,12-triazatetradecan-14-oate ***(4c).*** *(Boc-Val-β-ala-Val-OMe)* The pure product was obtained as white solid (250 mg, 89% yield) ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.46 – 7.38 (m, 1H), 4.42 (d, *J* = 5.7 Hz, 1H), 3.84 (d, *J* = 5.5 Hz, 1H), 3.76 (d, *J* = 6.4 Hz, 3H), 3.72 – 3.65 (m, 1H), 3.36 (t, *J* = 18.2 Hz, 3H), 2.46-2.43 (m, 2H), 2.18 – 2.16 (m, 1H), 2.07-2.05 (m, 1H), 1.47 – 1.42 (m, 10H), 0.99 – 0.88 (m, 12H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 173.29, 172.78, 156.31, 150.68, 129.14, 120.55, 80.01, 60.26, 58.00, 52.24, 36.11, 30.31, 29.67, 28.28, 19.23, 19.04, 18.12, 17.89. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. For $C_{19}H_{35}N_3O_6$ 402.2599, found 402.2565.

*methyl-diisobutyl-2,2-dimethyl-4,7,11-trioxo-3-oxa-5,8,12-triazatetradecan-14-oate***(4d).** *(Boc-Leu-β-ala-Leu-OMe)* The pure product was obtained as white solid (150 mg, 65% yield) ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.50 (d, *J* = 6.5 Hz, 1H), 7.28 – 7.21 (m, 1H), 5.05 (d, *J* = 7.4 Hz, 1H), 4.60 (td, *J* = 10.8, 4.4 Hz, 1H), 4.02 – 3.91 (m, 2H), 3.73 (s, 3H), 3.09 (td, *J* = 11.4, 3.1 Hz, 1H), 2.36 – 2.24 (m, 2H), 1.70 – 1.57 (m, 4H), 1.40 (s, 10H), 0.98 – 0.88 (m, 12H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 175.38, 173.57, 173.25, 156.27, 139.28, 114.08, 77.24,54.05, 52.52, 51.39, 40.80, 39.51, 37.48, 36.84, 29.70, 28.29, 24.93, 24.70, 22.98, 22.57, 22.26, 21.13. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd. For $C_{21}H_{39}N_3O_6$ 452.2731, found 452.2686.

methyl-sec-butyl)-6-(sec-butyl)-2-methyl-4,7,11-trioxo-3-oxa-5,8,12-triazatetradecan-14-oate ***(4e).*** *(Boc-lle-β-ala-Ile-OMe)* The pure product was obtained as white solid (250 mg, 91% yield) ^{1}H NMR (700 MHz, $CDCl_3$) δ 6.59 (s, 1H), 5.11 (s, 1H), 3.94 – 3.88 (m, 1H), 3.70 (s, 3H), 3.60 – 3.46 (m, 2H), 2.56 (t, *J* = 6.1 Hz, 2H), 1.85 (s, 1H), 1.44 (s, 10H), 1.14 – 1.06 (m, 1H), 0.90 (t, *J* = 7.6 Hz, 6H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 173.52, 172.43, 172.11, 156.09,

79.84, 77.22, 77.04, 76.86, 59.82, 57.07, 52.26, 36.86, 36.62, 36.19, 28.30, 25.32, 25.01, 15.68, 15.61 (d, *J* = 21.6 Hz), 11.42, 11.27. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd. For $C_{21}H_{39}N_3O_6$ 452.2731, found 452.2781.

3. NMR ($^{1}H/^{13}C$) and HRMS spectra of Tr-Gly-Gly-OMe (**2a**)

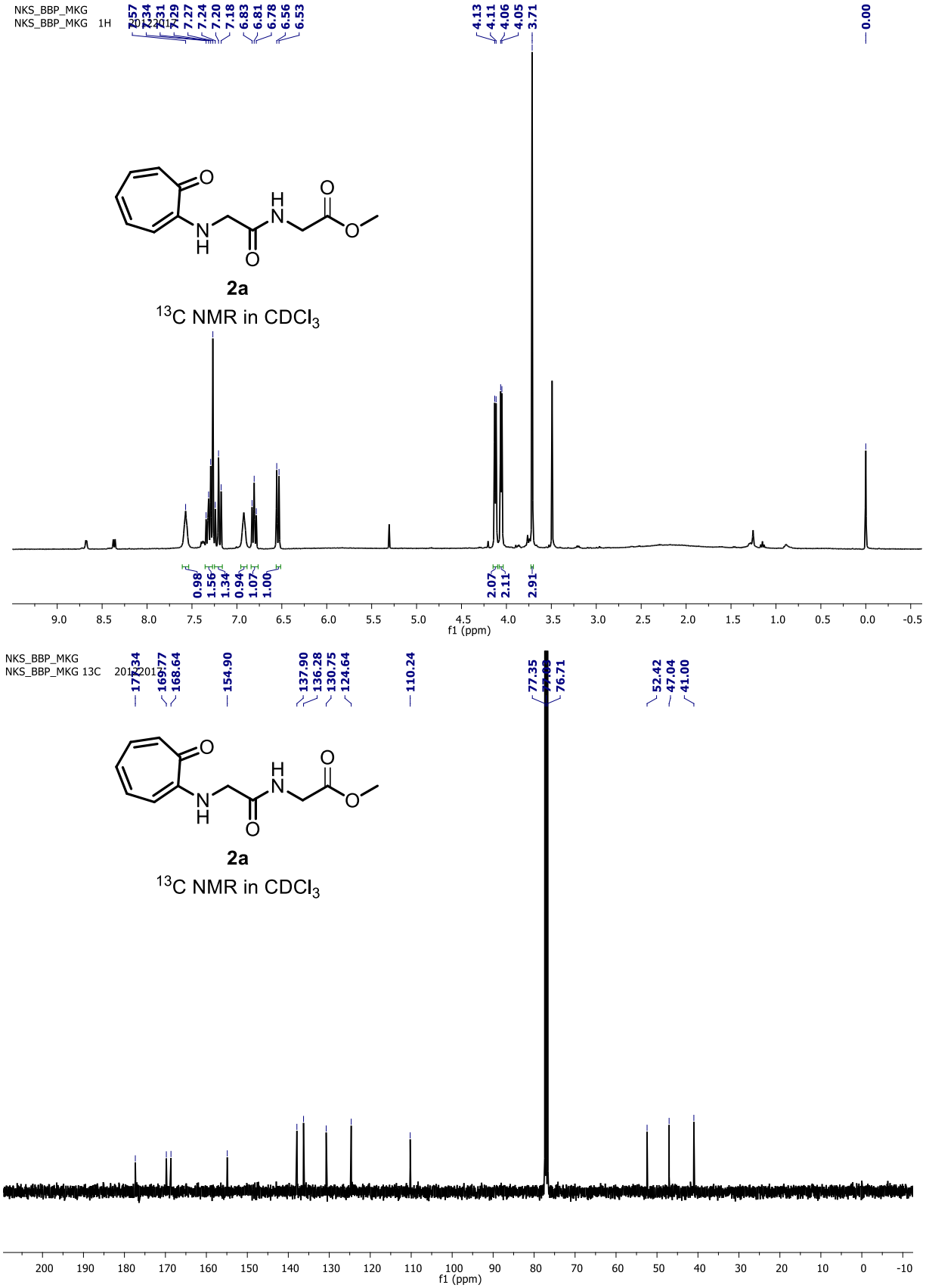


Fig. S1: $^{1}H,^{13}C$-NMR spectrum of Tr-Gly-Gly -OMe (**2a**) in $CDCl_3$

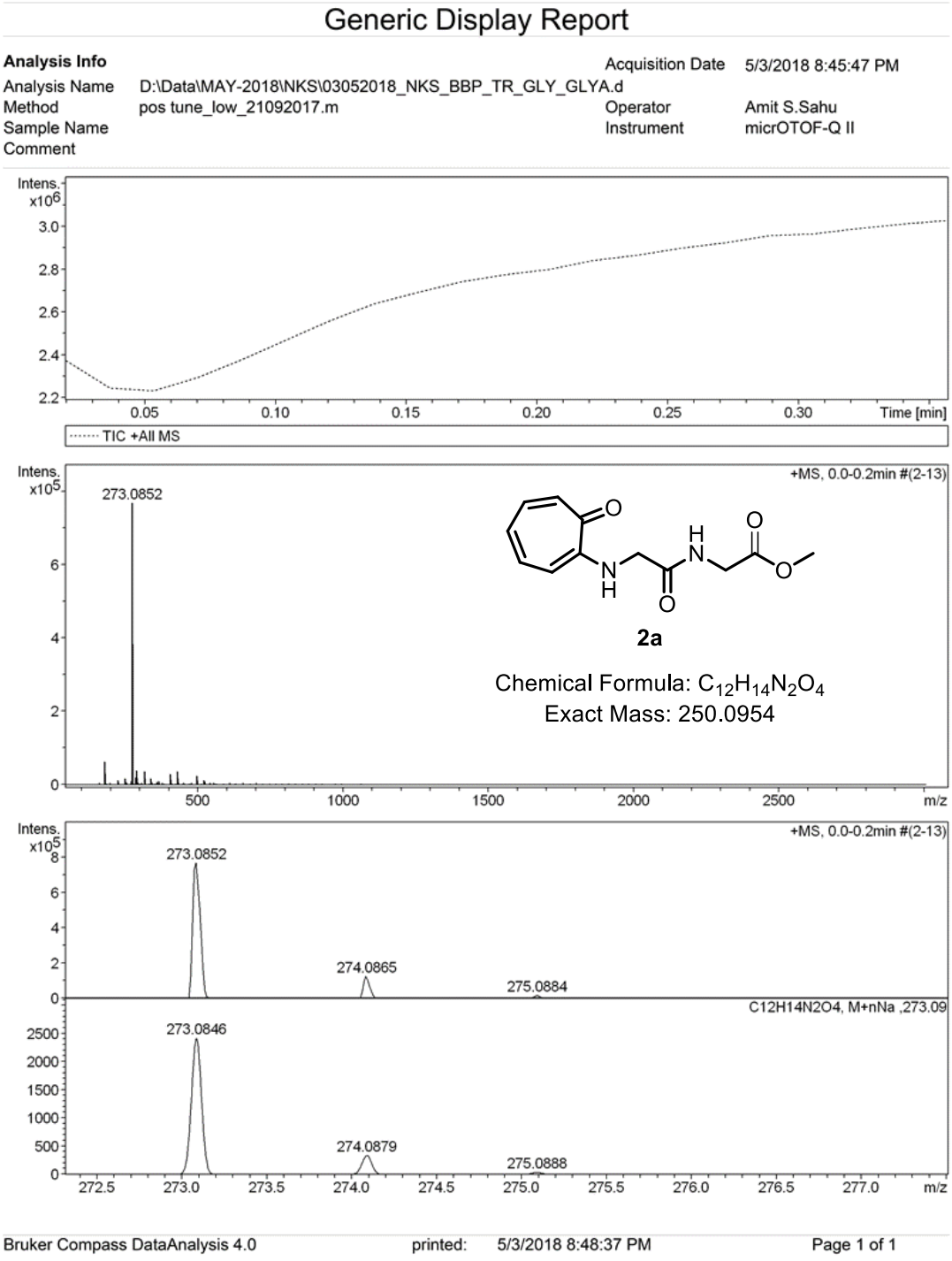


Fig. S2. ESI-MS/HRMS spectra of Tr-Gly-Gly -OMe (**2a**)

4. NMR ($^{1}H/^{13}C$) and HRMS spectra of Tr-Gly-Aal-OMe (**2b**)

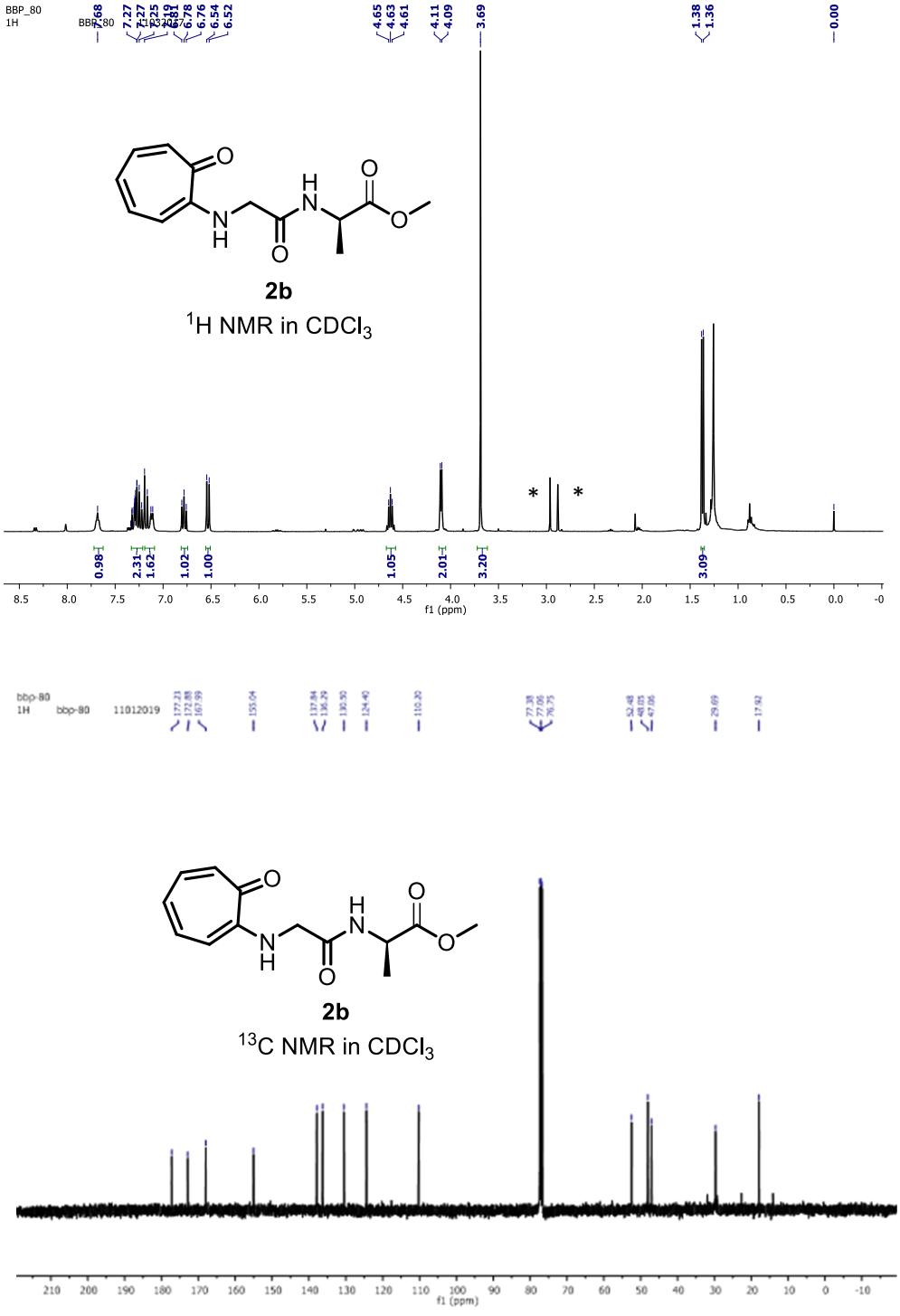


Fig. S3: $^{1}H,^{13}C$-NMR spectrum of Tr-Gly-Ala -OMe (**2b**) in $CDCl_3$ (*Impurites)

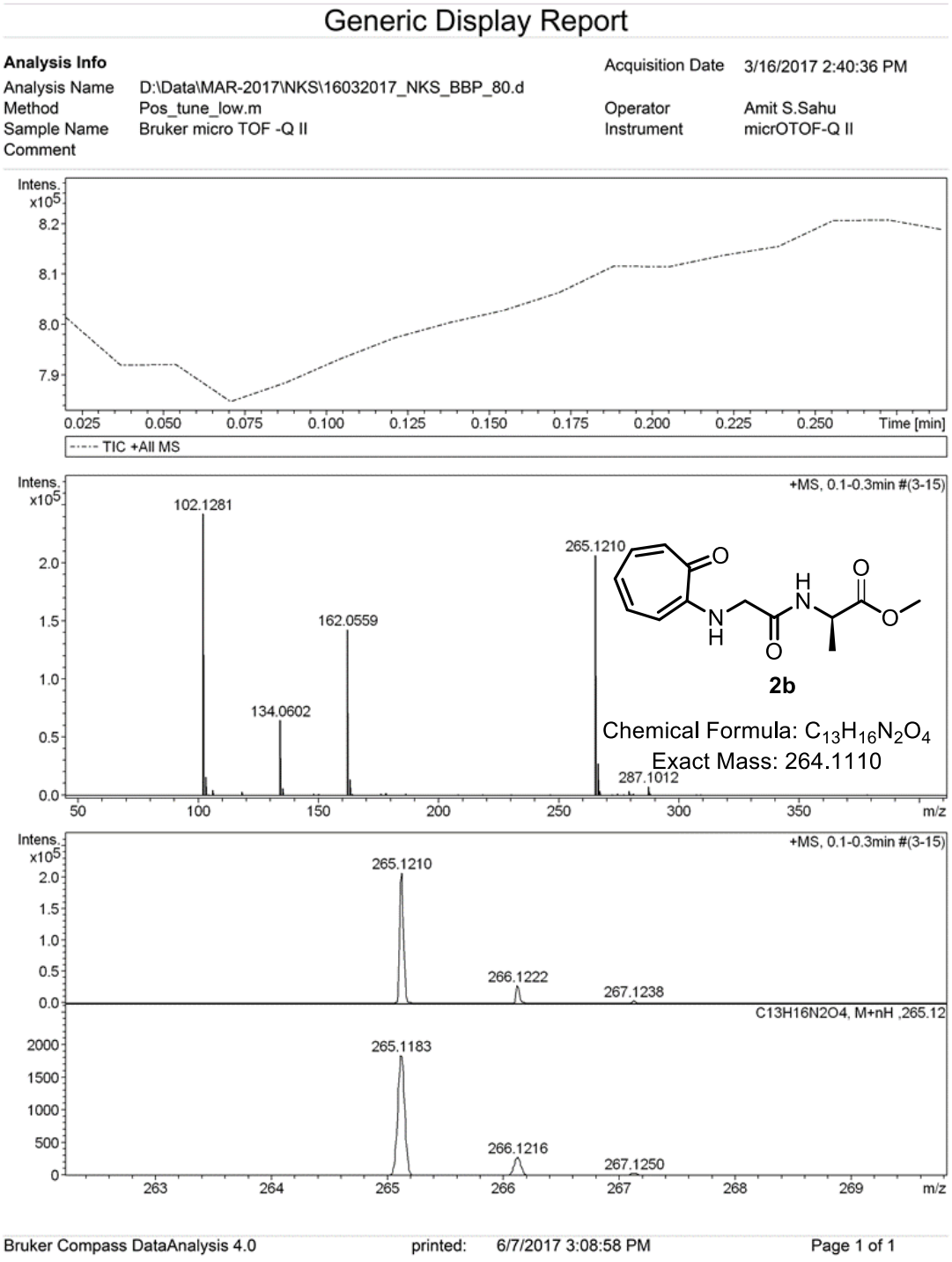


Fig. S4: ESI-MS/HRMS spectra of Tr-Gly-Ala -OMe (**2b**)

5. NMR ($^{1}H/^{13}C$) and HRMS spectra of Tr-Ala-Gly-OMe (**2c**)

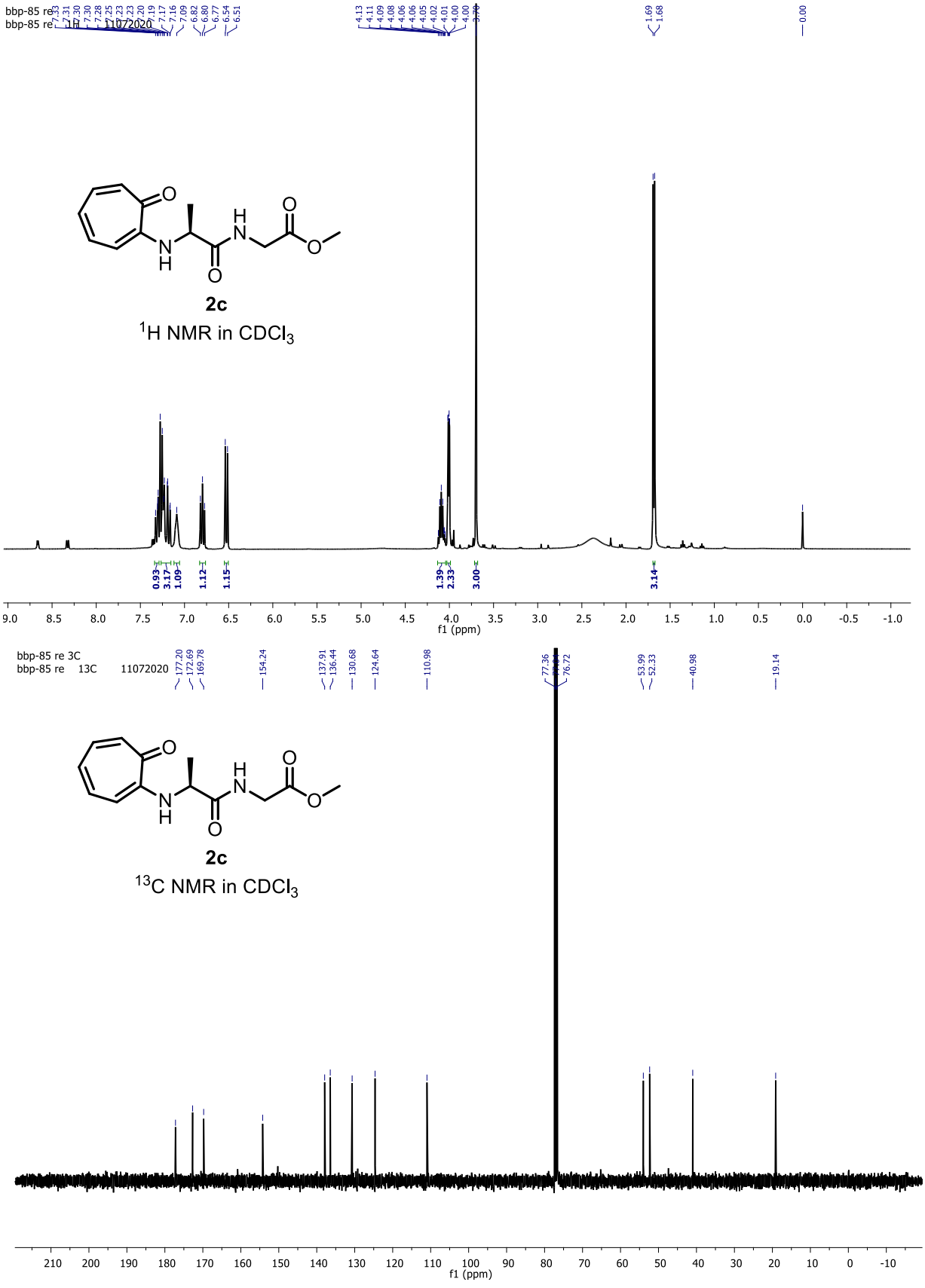


Fig. S5: Mass spectrum of Tr-Ala-Gly -OMe (**2c**) in $CDCl_3$

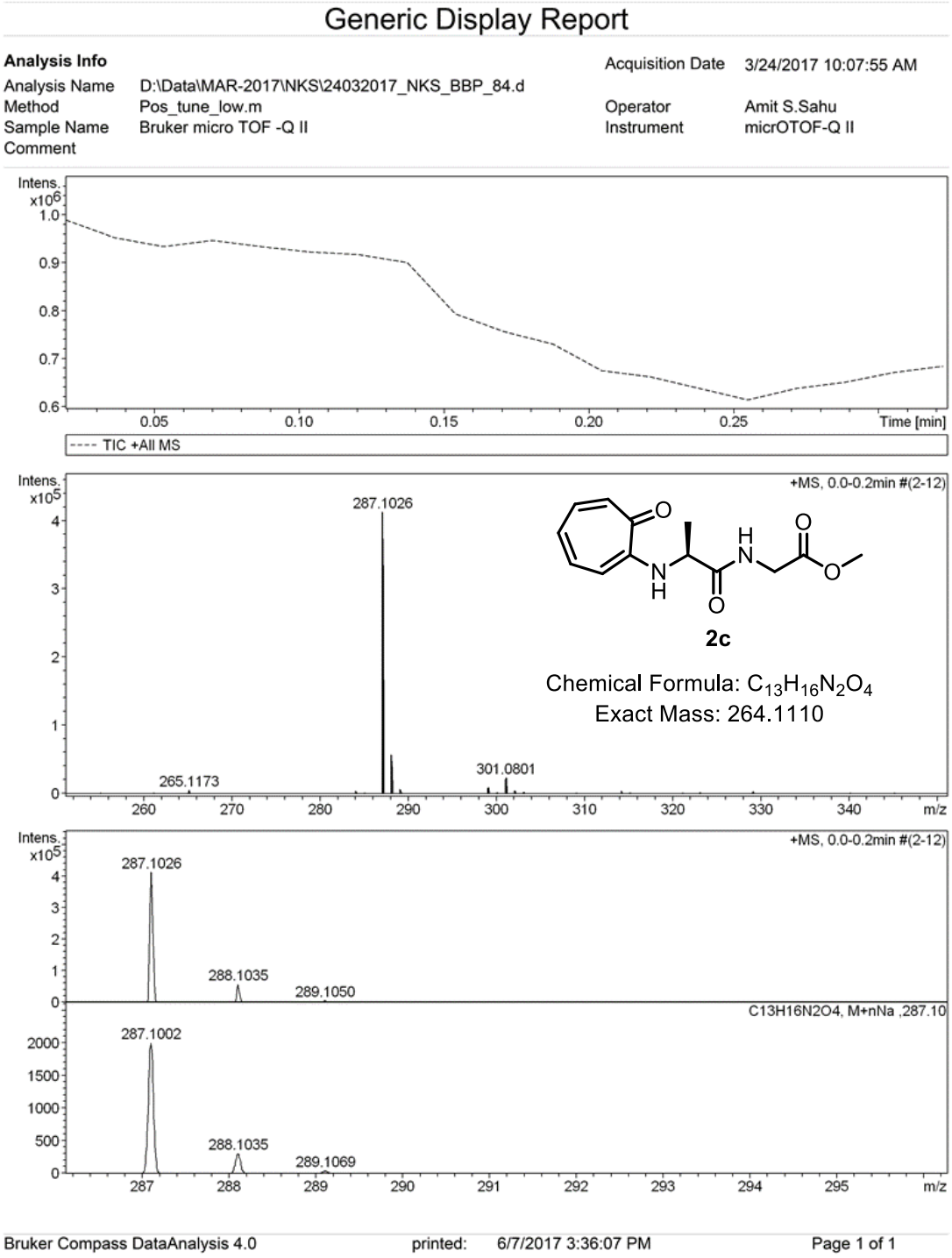


Fig. S6: ESI-MS/HRMS spectra of Tr-Ala-Gly -OMe (**2c**)

6. NMR ($^{1}H/^{13}C$) and HRMS spectra of Tr-val-Gly-OMe (**2d**)

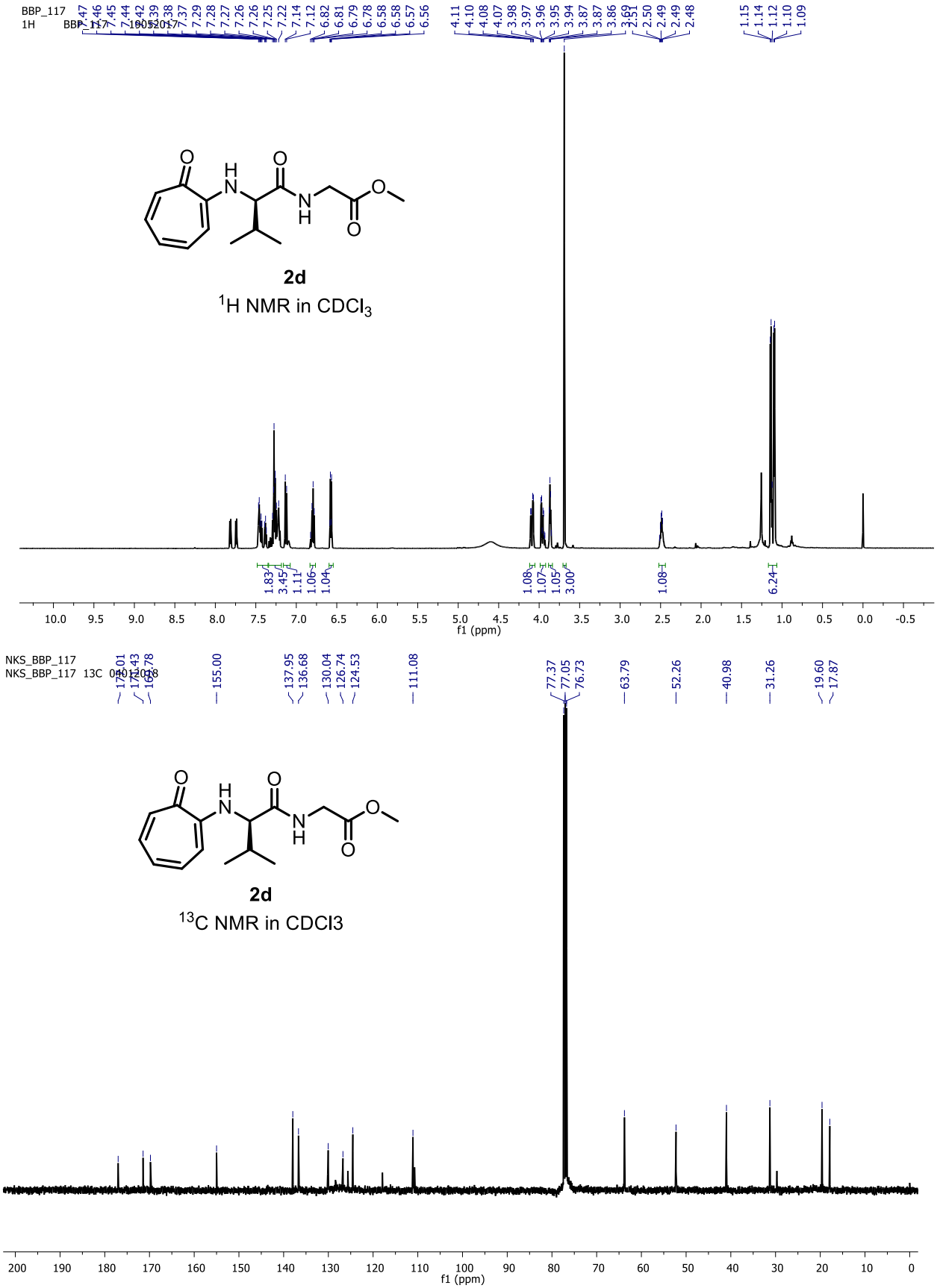


Fig. S7: Mass spectrum of Tr-Ala-Gly -OMe (**2d**) in $CDCl_3$

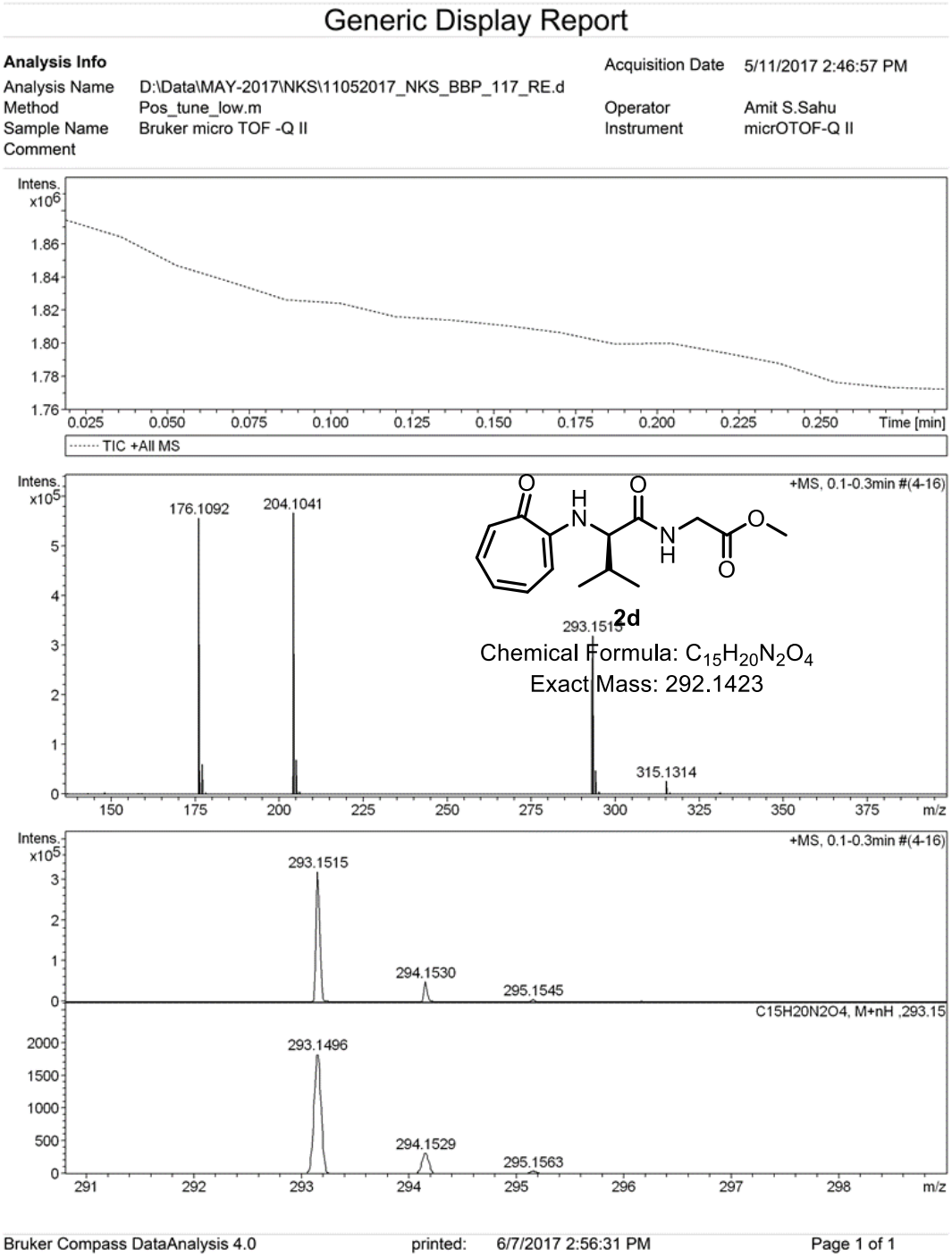


Fig. S8: ESI-MS/HRMS spectra of Tr-Val-Gly -OMe (**2d**)

7. NMR ($^{1}H/^{13}C$) and HRMS spectra of Tr-val-β-Ala-OMe (**2e**)

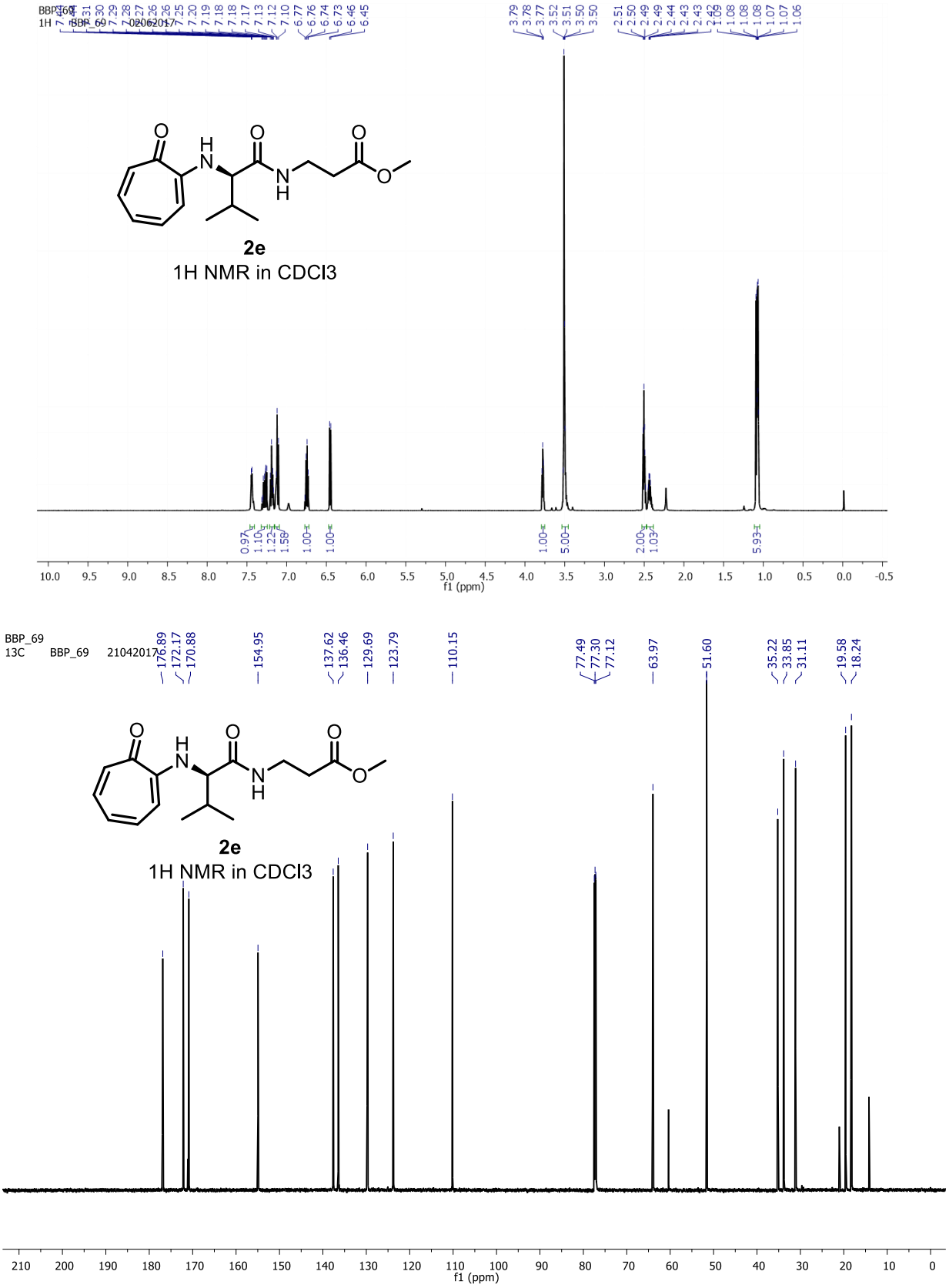


Fig. S9: $^{1}H,^{13}C$-NMR spectrum of Tr-val-β -OMe (**2e**) in $CDCl_3$

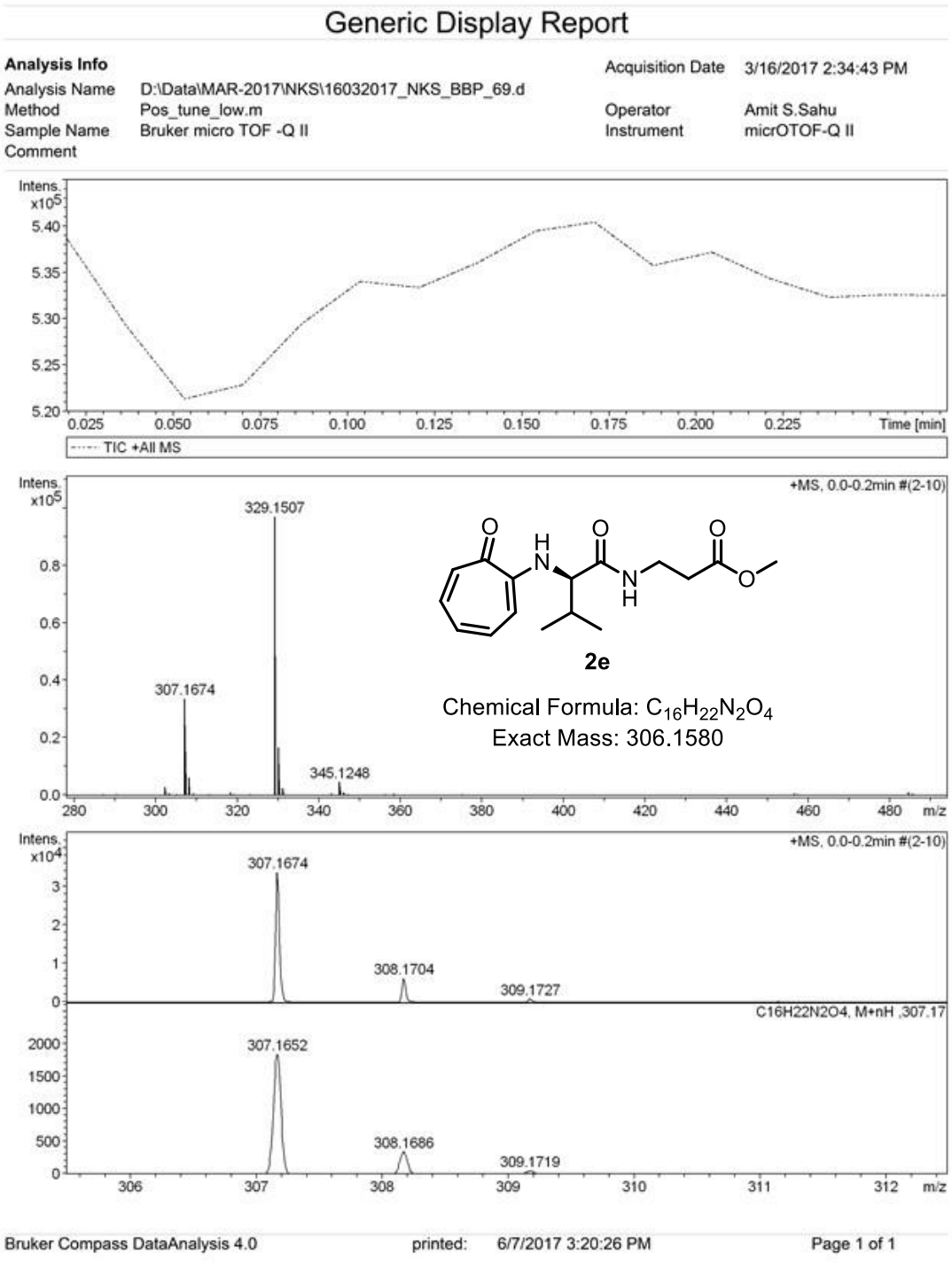


Fig. S10: ESI-MS/HRMS spectra of Tr-Val-*β*-Ala -OMe (**2d**)

8. NMR ($^{1}H/^{13}C$) and HRMS spectra of Tr-val-β-Ala-OMe (**2f**)

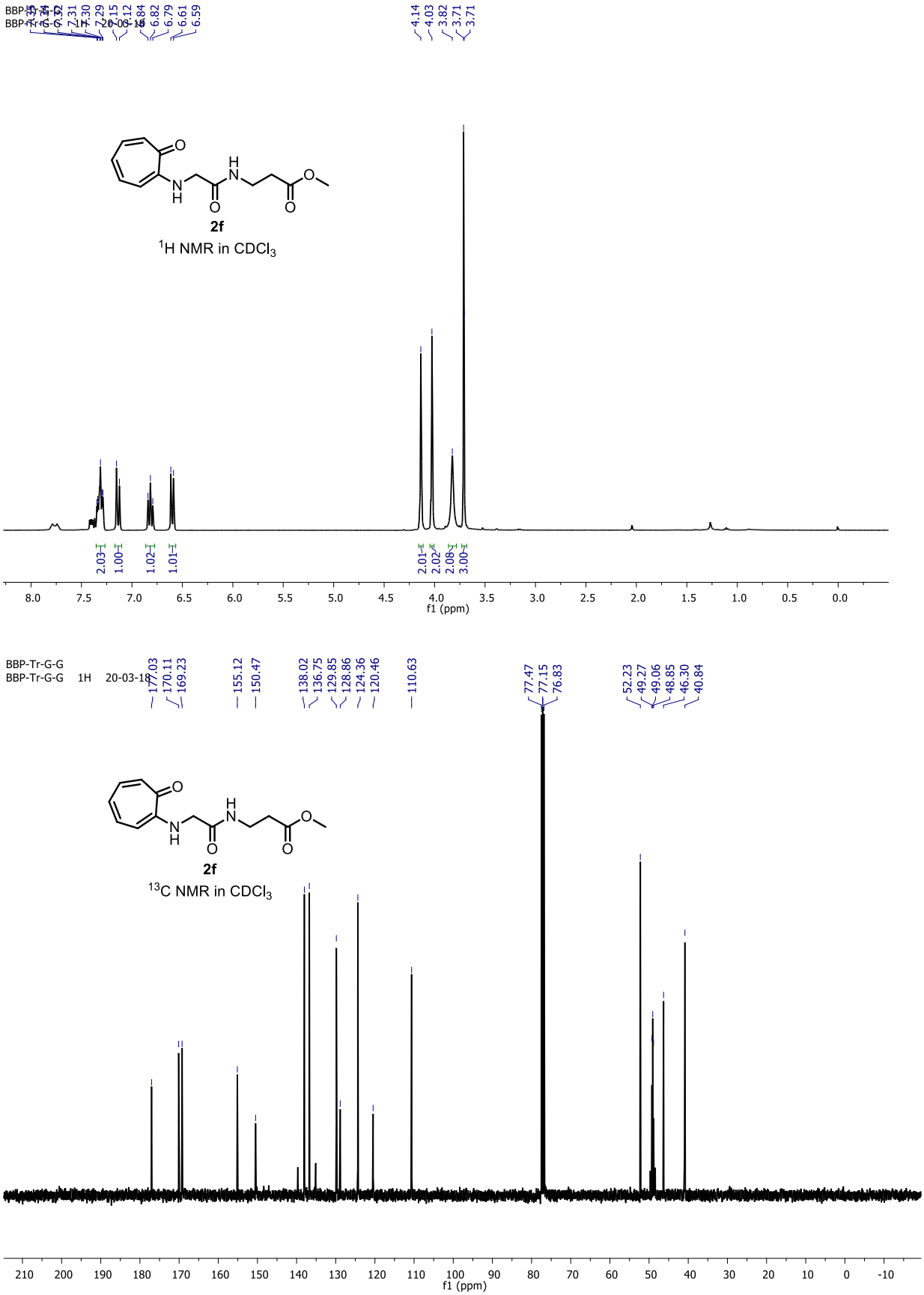


Fig. 11: $^{1}H,^{13}C$-NMR spectrum of Tr-Gly-β-Ala -OMe (**2f**) in $CDCl_3$

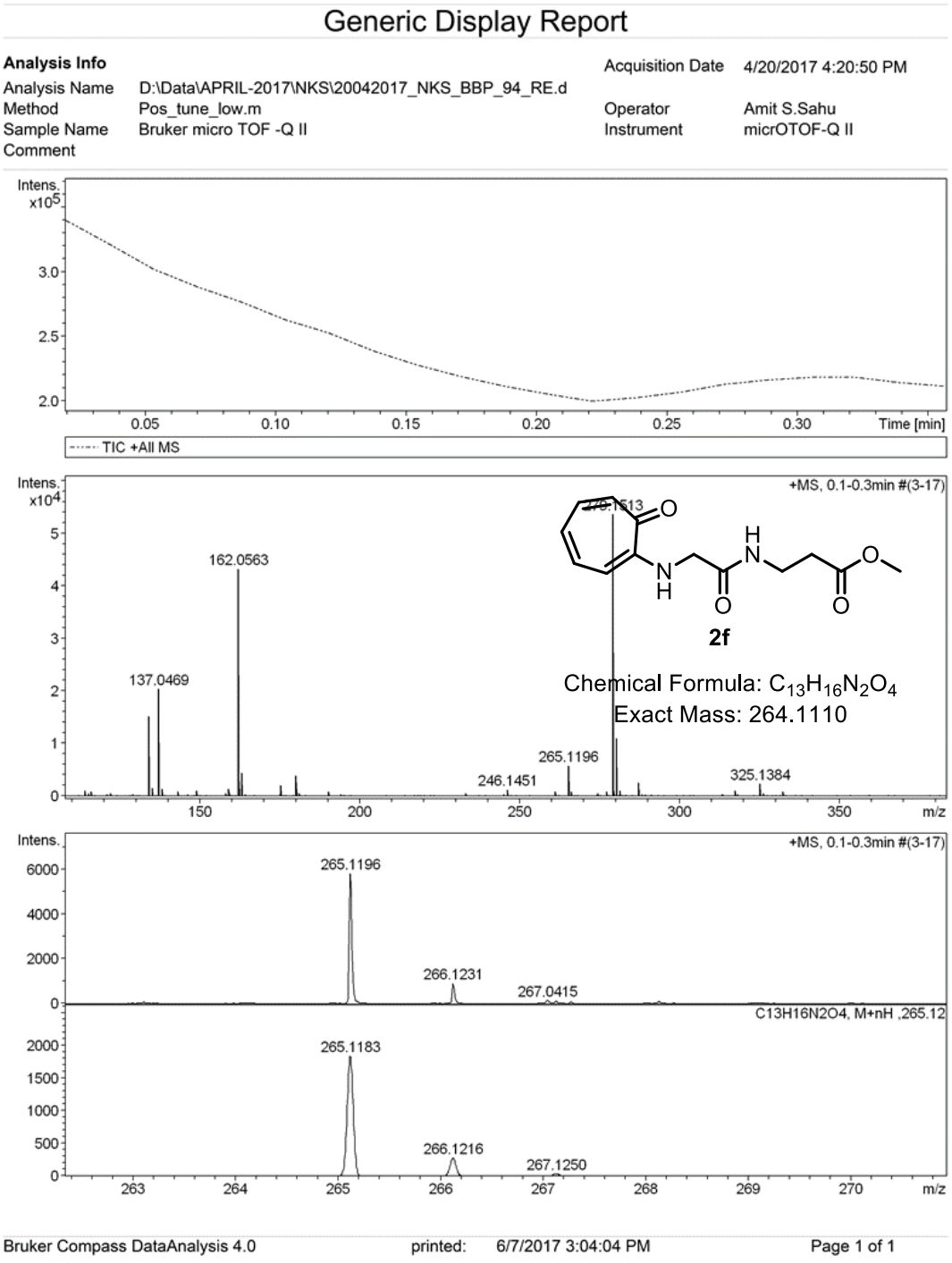


Fig. S12: ESI-MS/HRMS spectra of Tr-Gly-β-Ala -OMe (**2f**)

9. NMR ($^{1}H/^{13}C$) and HRMS spectra of Tr-Leu-β-Ala-OMe (**2g**)

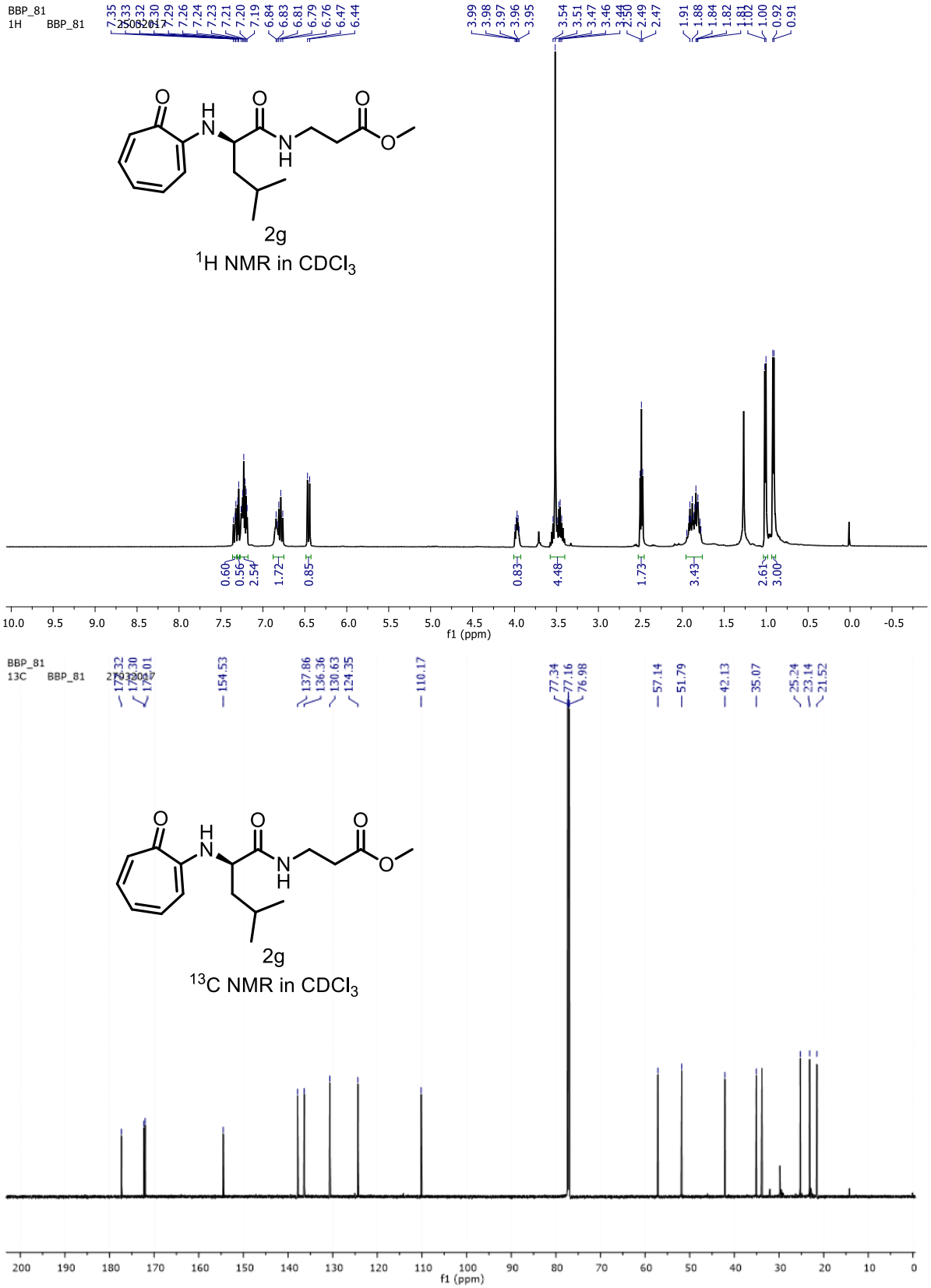


Fig. S13: $^{1}H,^{13}C$-NMR spectrum of Tr-Leu-β-Ala -OMe (**2g**) in $CDCl_3$

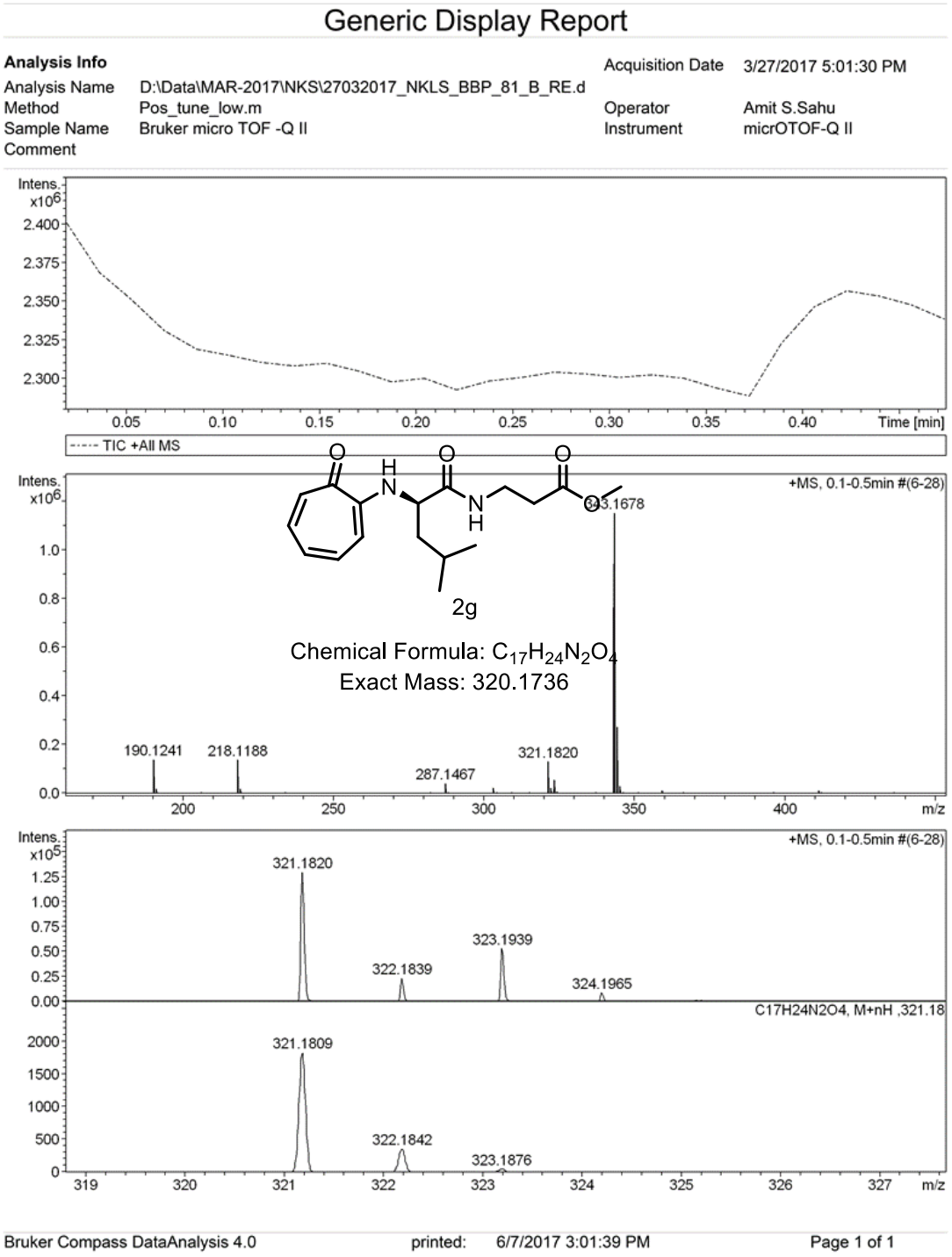


Fig. S14: ESI-MS/HRMS spectra of Tr-Leu-β-Ala -OMe (**2g**)

11. NMR ($^{1}H/^{13}C$) and HRMS spectra of Tr-Ala-β-Ala-OMe (**2h**)

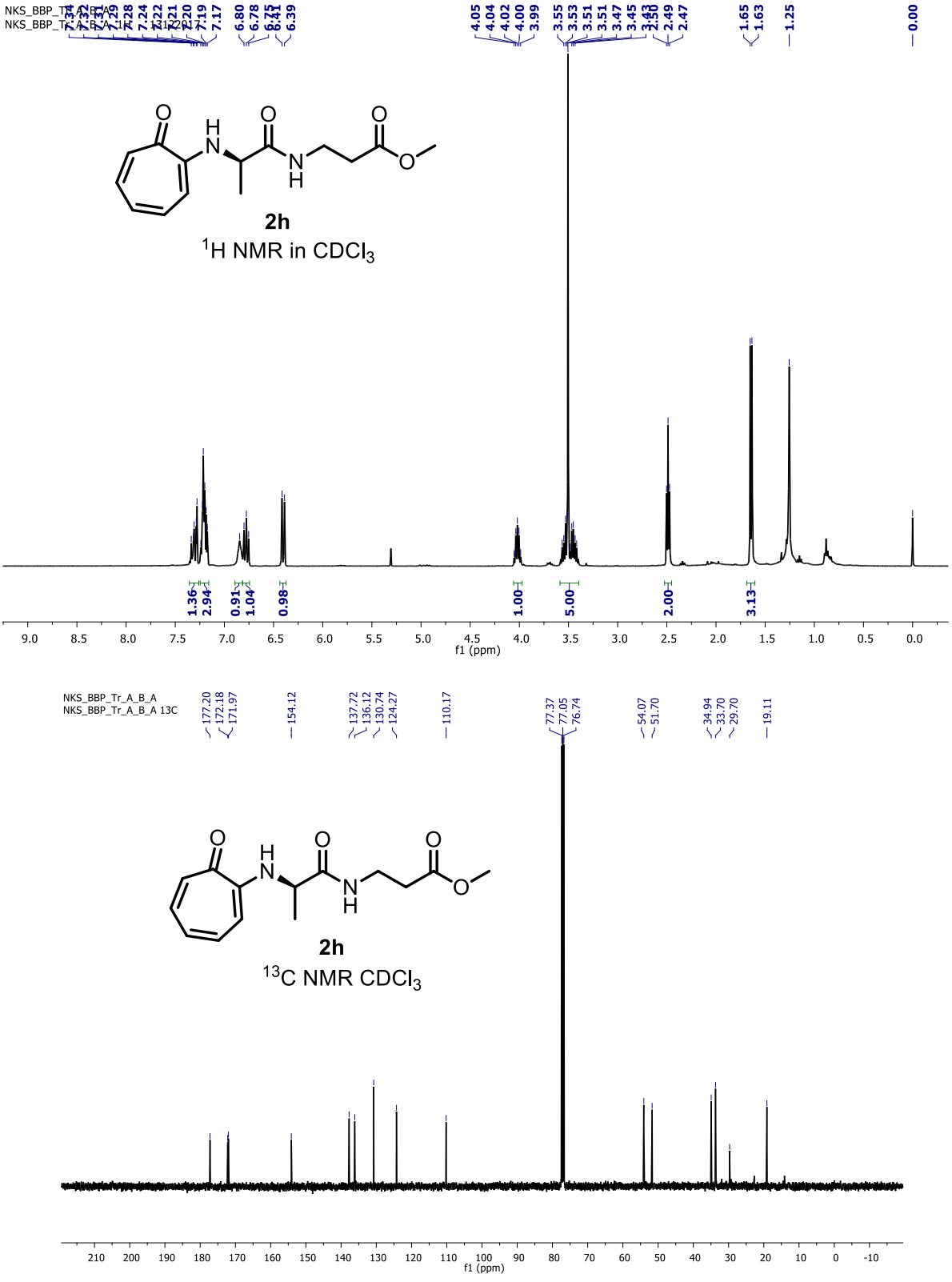


Fig. S15: $^{1}H,^{13}C$-NMR spectrum of Tr-Ala-β-Ala -OMe (**2h**) in $CDCl_3$

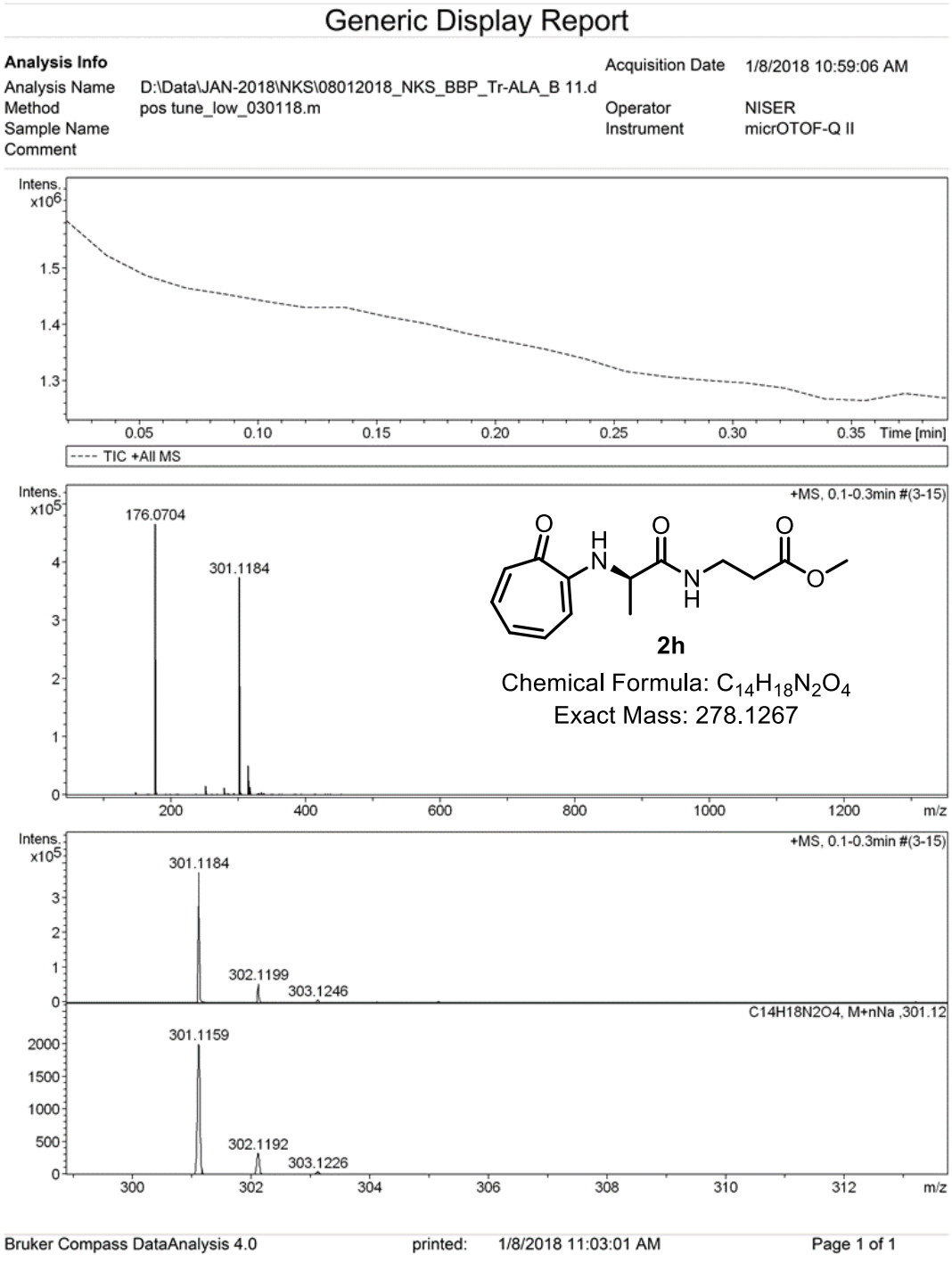


Fig. S16: ESI-MS/HRMS spectra of Tr-Gly-β-Ala -OMe (**2h**)

10. NMR ($^{1}H/^{13}C$) and HRMS spectra of Tr-Ile-*β*-Ala-OMe (**2i**)

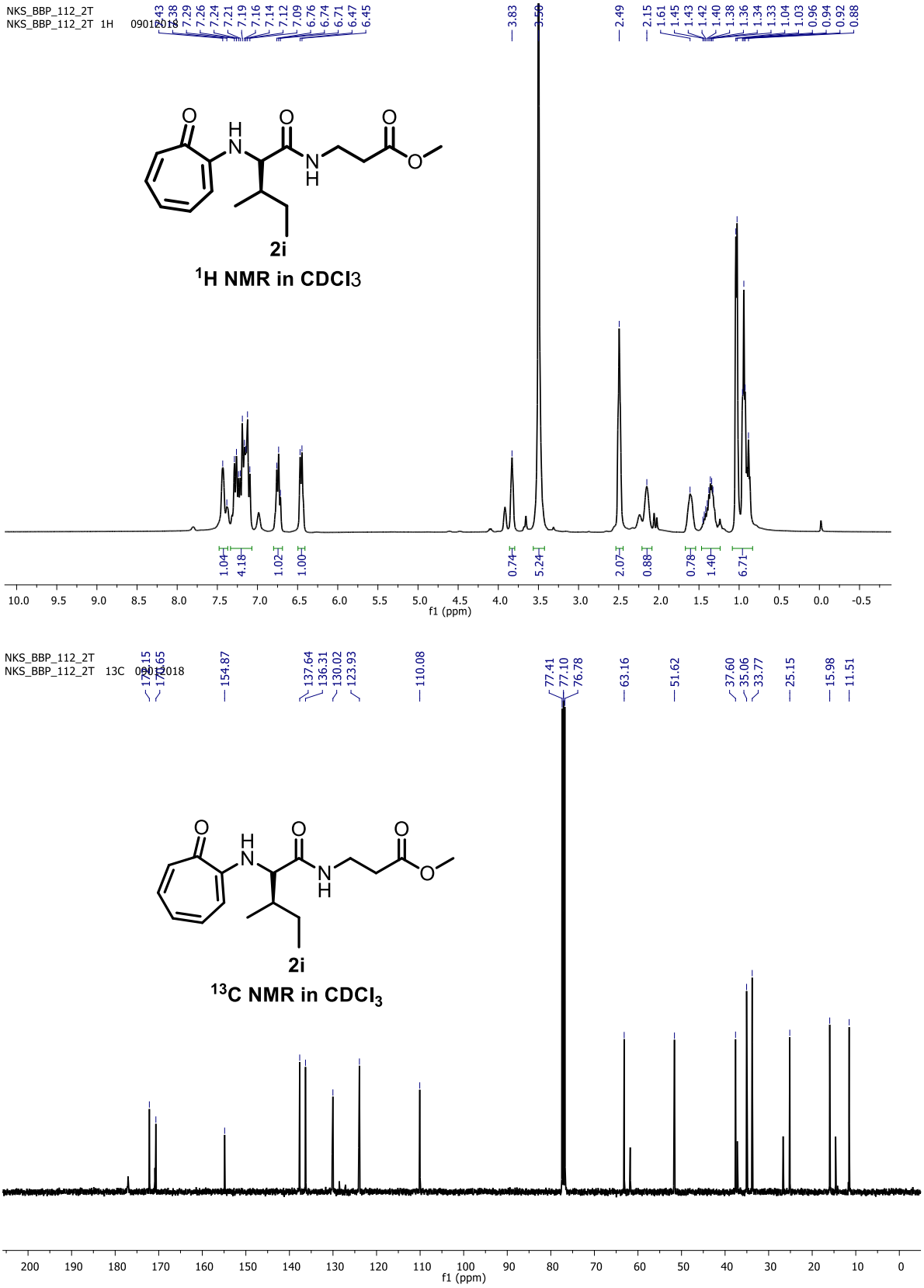


Fig. S17: $^{1}H,^{13}C$-NMR spectrum of Tr-Ile-*β*-Ala -OMe (**2i**) in $CDCl_3$

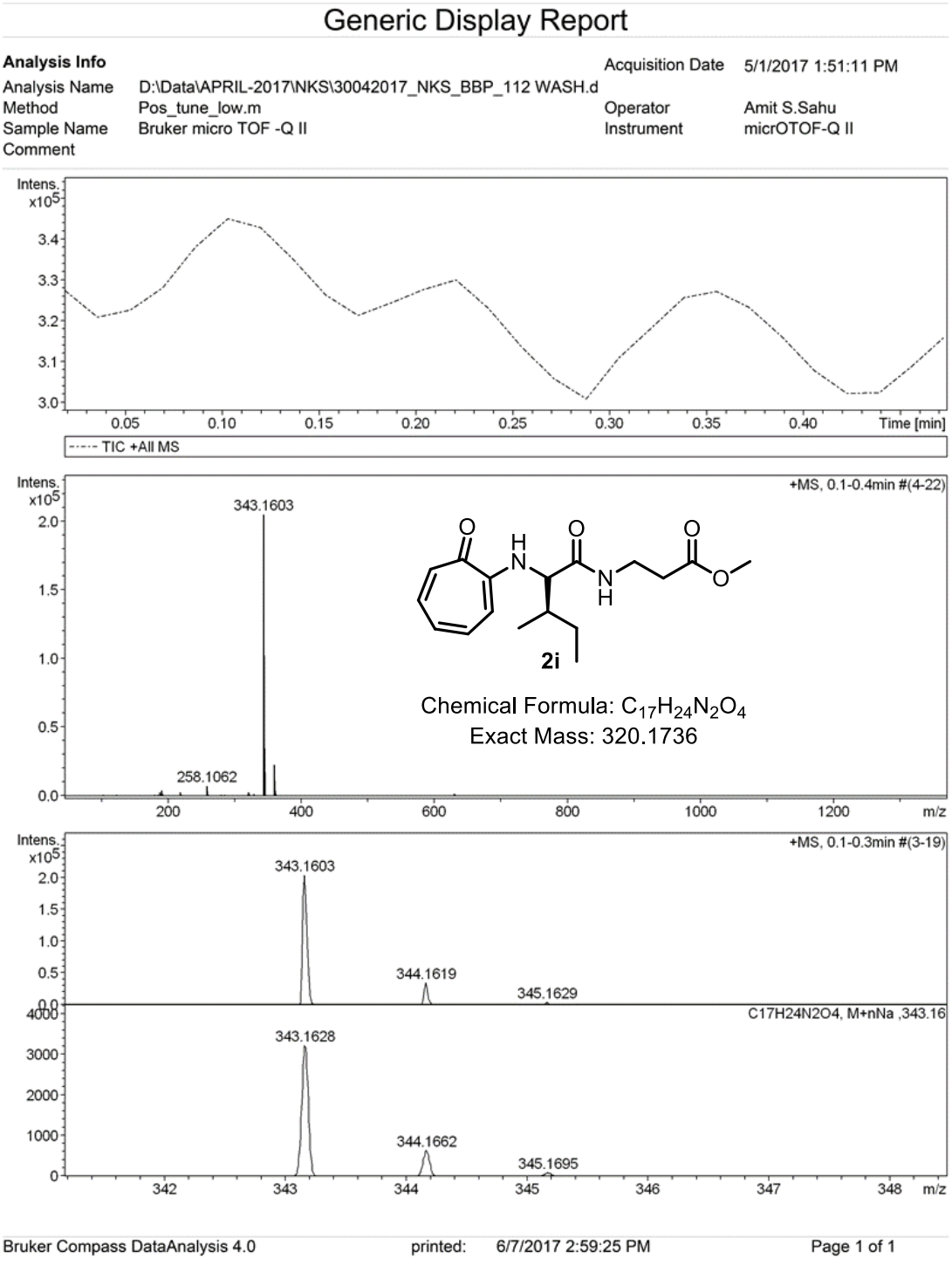


Fig. S18: ESI-MS/HRMS spectra of Tr-Ile-*β*-Ala -OMe (**2i**)

11. NMR ($^{1}H/^{13}C$) and HRMS spectra of Tr-Phe-Gly-OMe (**2j**)

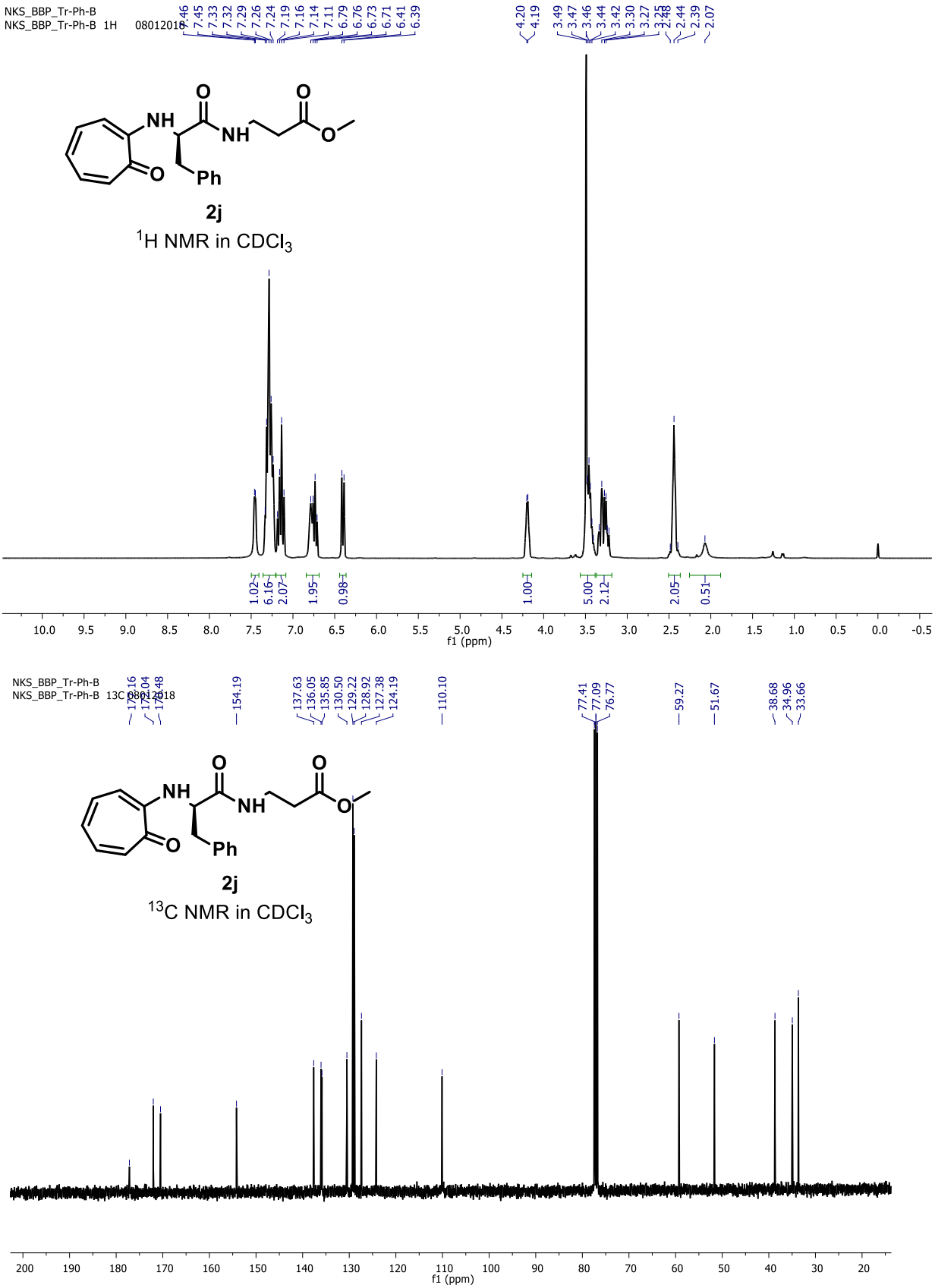


Fig. S19: $^{1}H,^{13}C$-NMR spectrum of Tr-Phe-β-Ala -OMe (**2j**) in $CDCl_3$

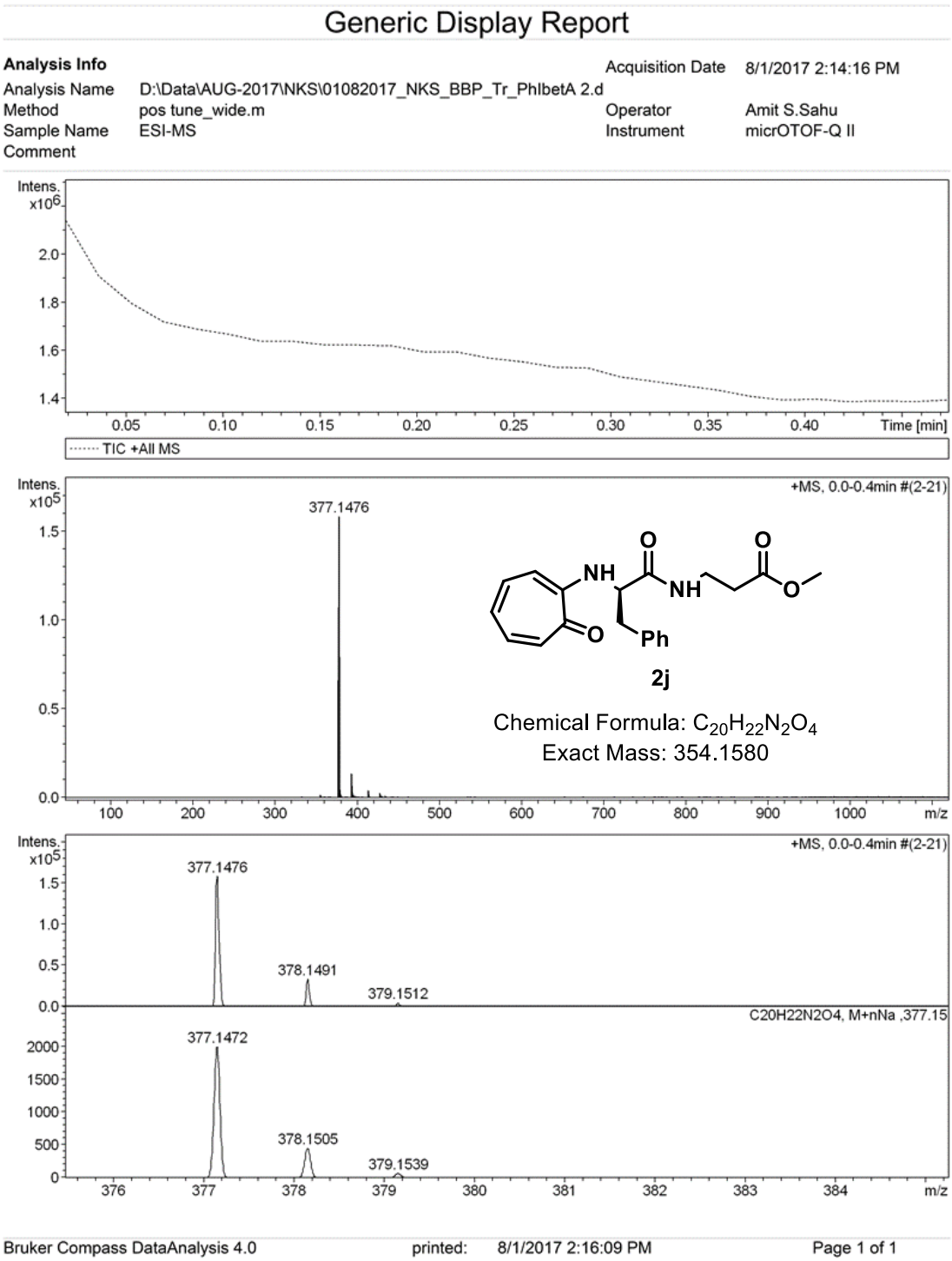


Fig. S20: ESI-MS/HRMS spectra of Tr-Phe-β-Ala -OMe (**2j**)

12. NMR ($^{1}H/^{13}C$) and HRMS spectra of Tr-Pro-Val-OMe (**2k**)

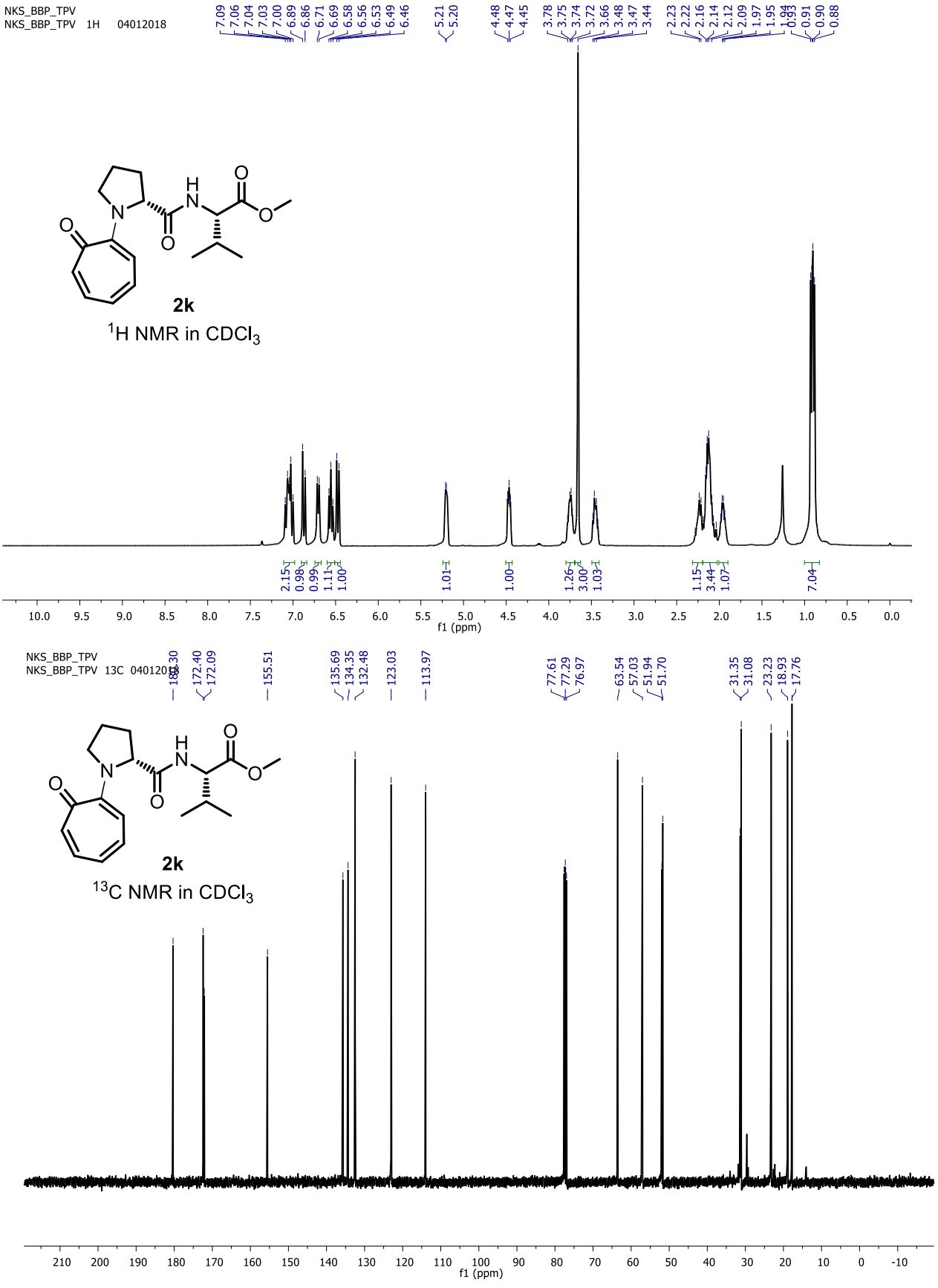


Fig. S21: $^{1}H,^{13}C$-NMR spectrum of Tr-Pro-Val -OMe (**2k**) in $CDCl_3$

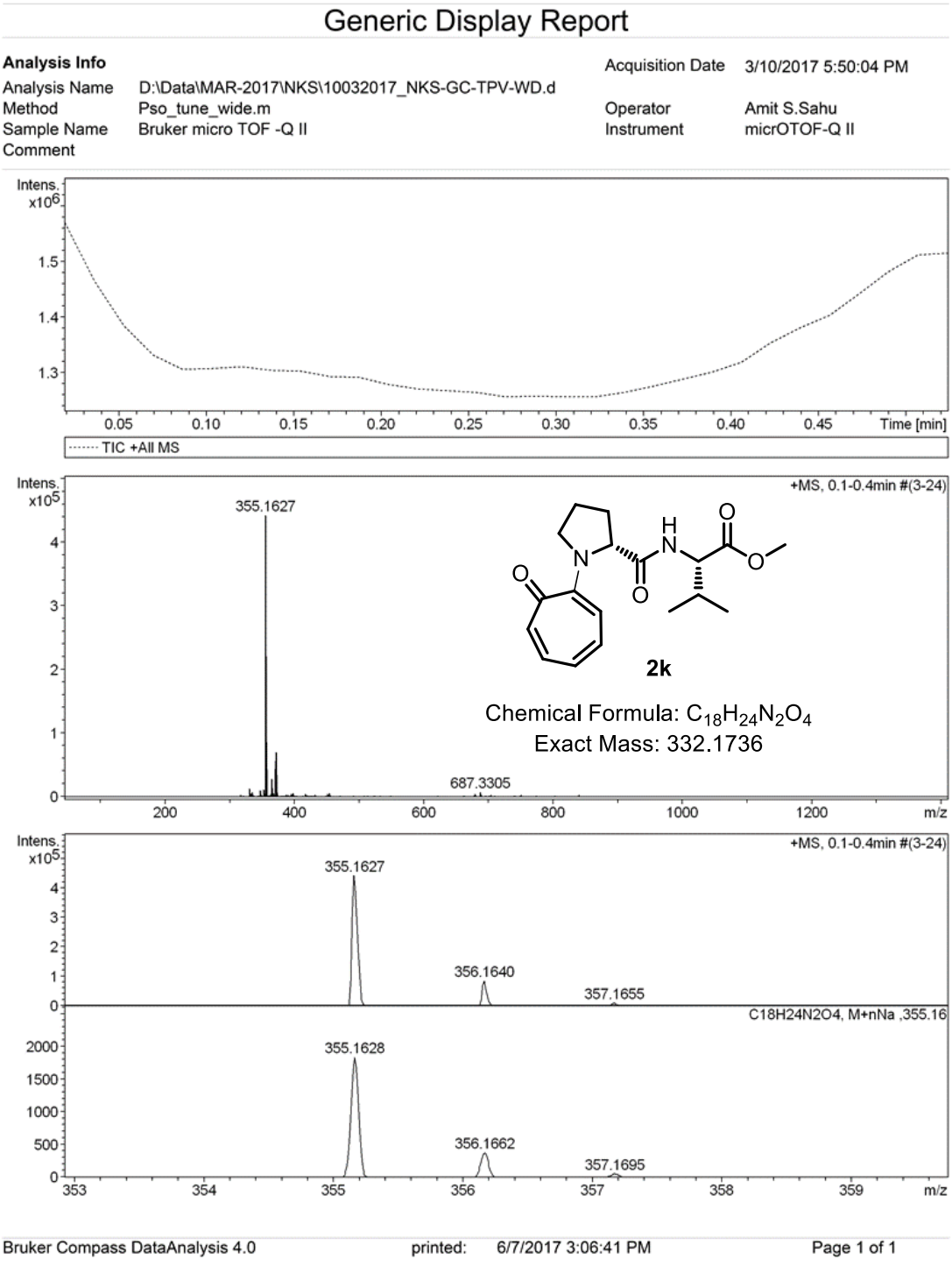


Fig. S22: ESI-MS/HRMS spectra of Tr-Pro-Val -OMe (**2k**)

13. NMR ($^{1}H/^{13}C$) and HRMS spectra of Tr-β-Ala-Pro-OMe **(2l)**

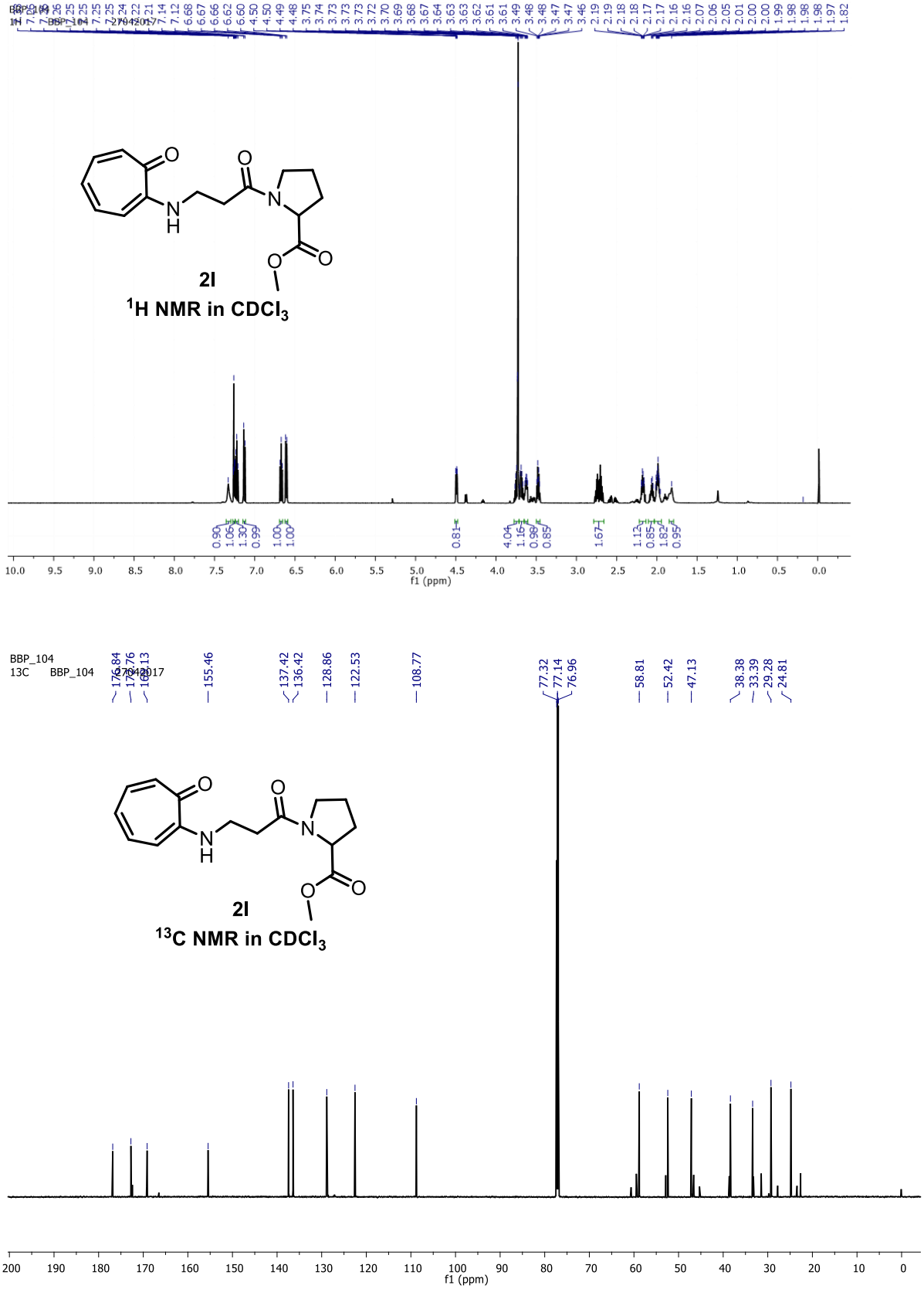


Fig. S23: $^{1}H,^{13}C$-NMR spectrum of Tr-β-Ala-Pro-OMe(**2l**) in $CDCl_3$

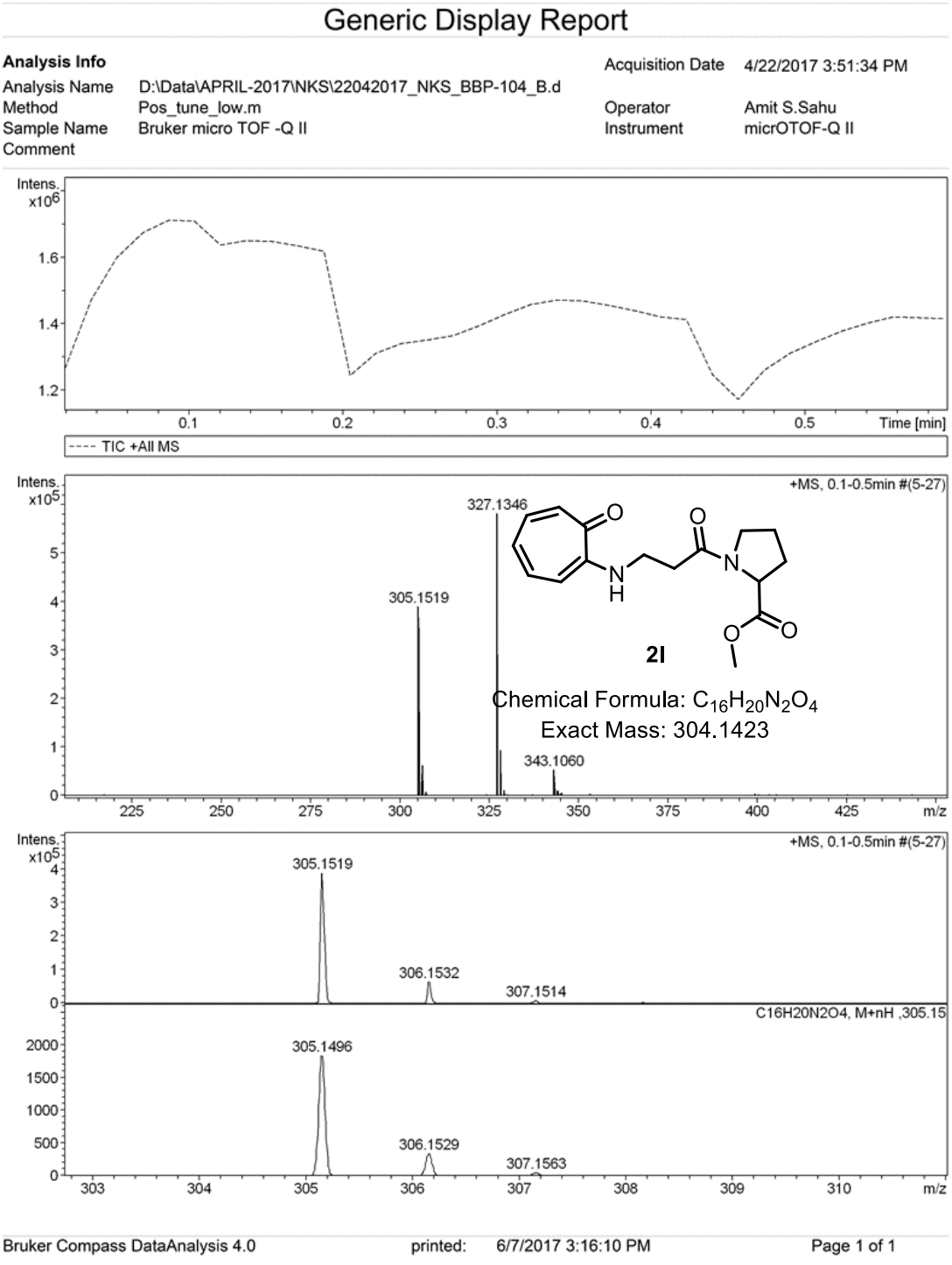


Fig. S24: ESI-MS/HRMS spectra of Tr-β-Ala-Pro-OMe(**2l**)

14. NMR ($^{1}H/^{13}C$) and HRMS spectra of Tr-Gly-β-Ala-Gly-OMe **(3a)**

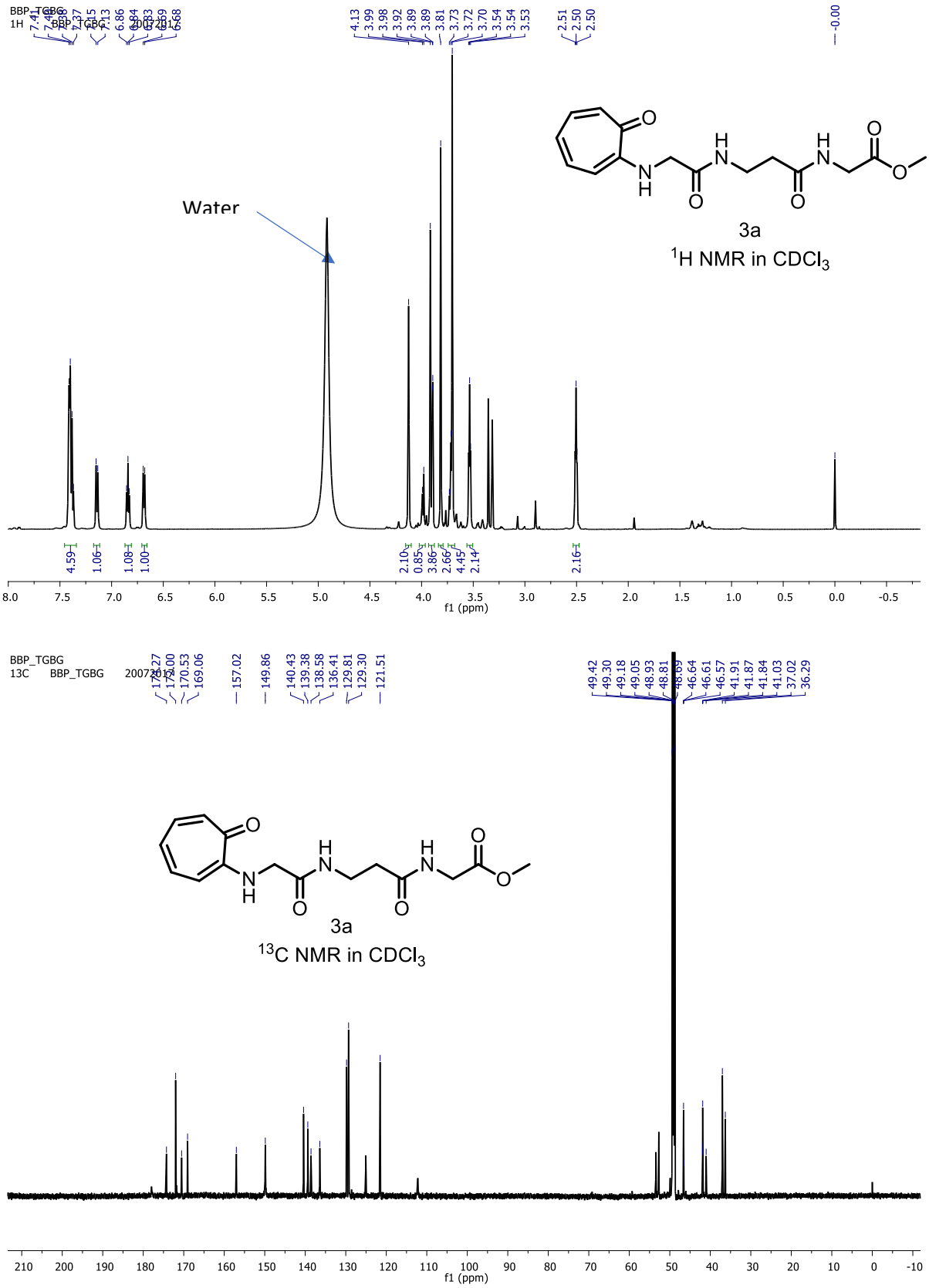


Fig. S25: $^{1}H,^{13}C$-NMR spectrum of Tr-Gly-β-Ala-Gly-OMe (**3a**) in $CDCl_3$

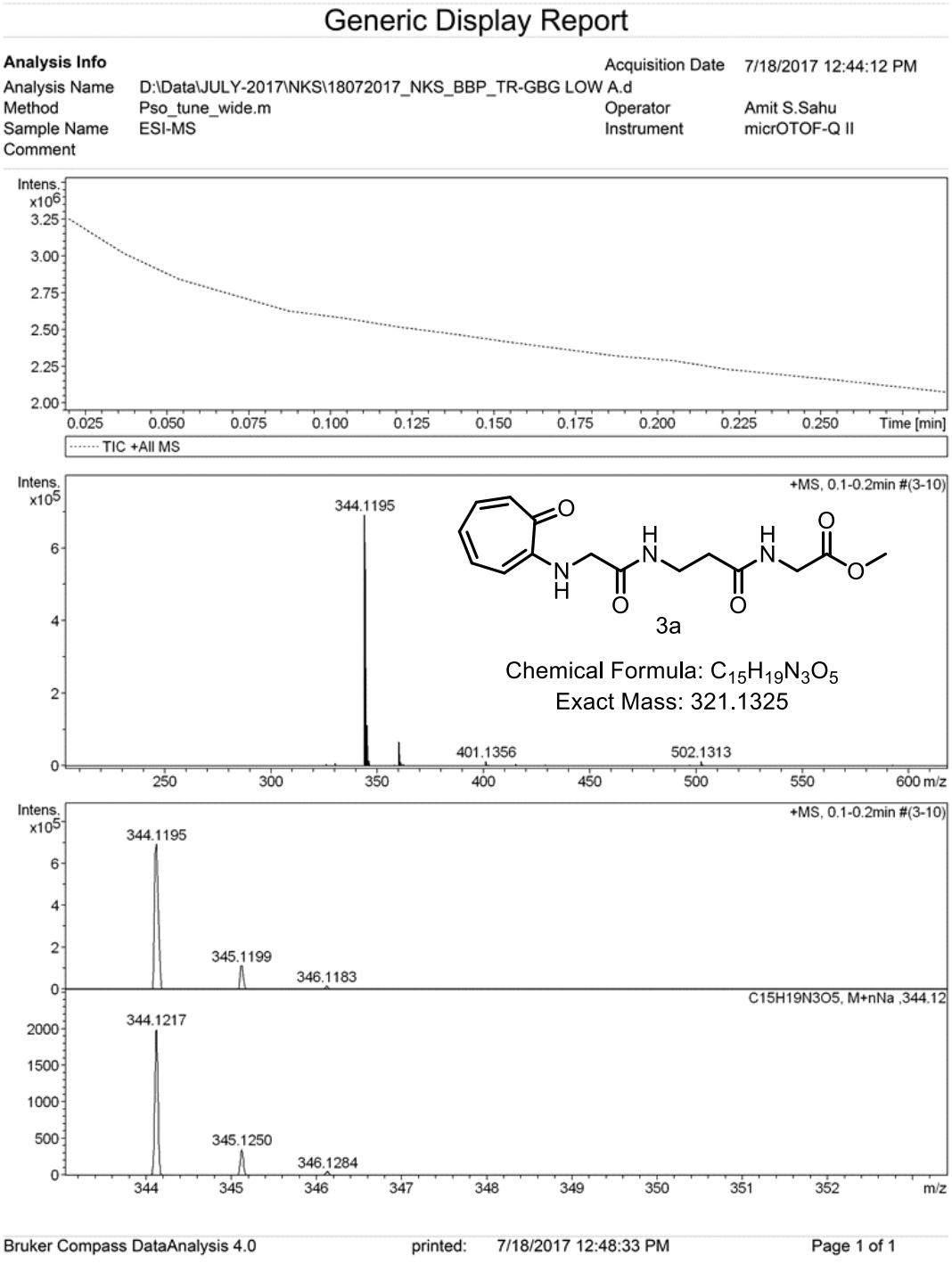


Fig. S26: ESI-MS/HRMS spectra of Tr-Gly-β-Ala-Gly-OMe (**3a**)

15. NMR (^{1}H/^{13}C) and HRMS spectra of Tr-Ala-*β*-Ala-OMe **(3b)**

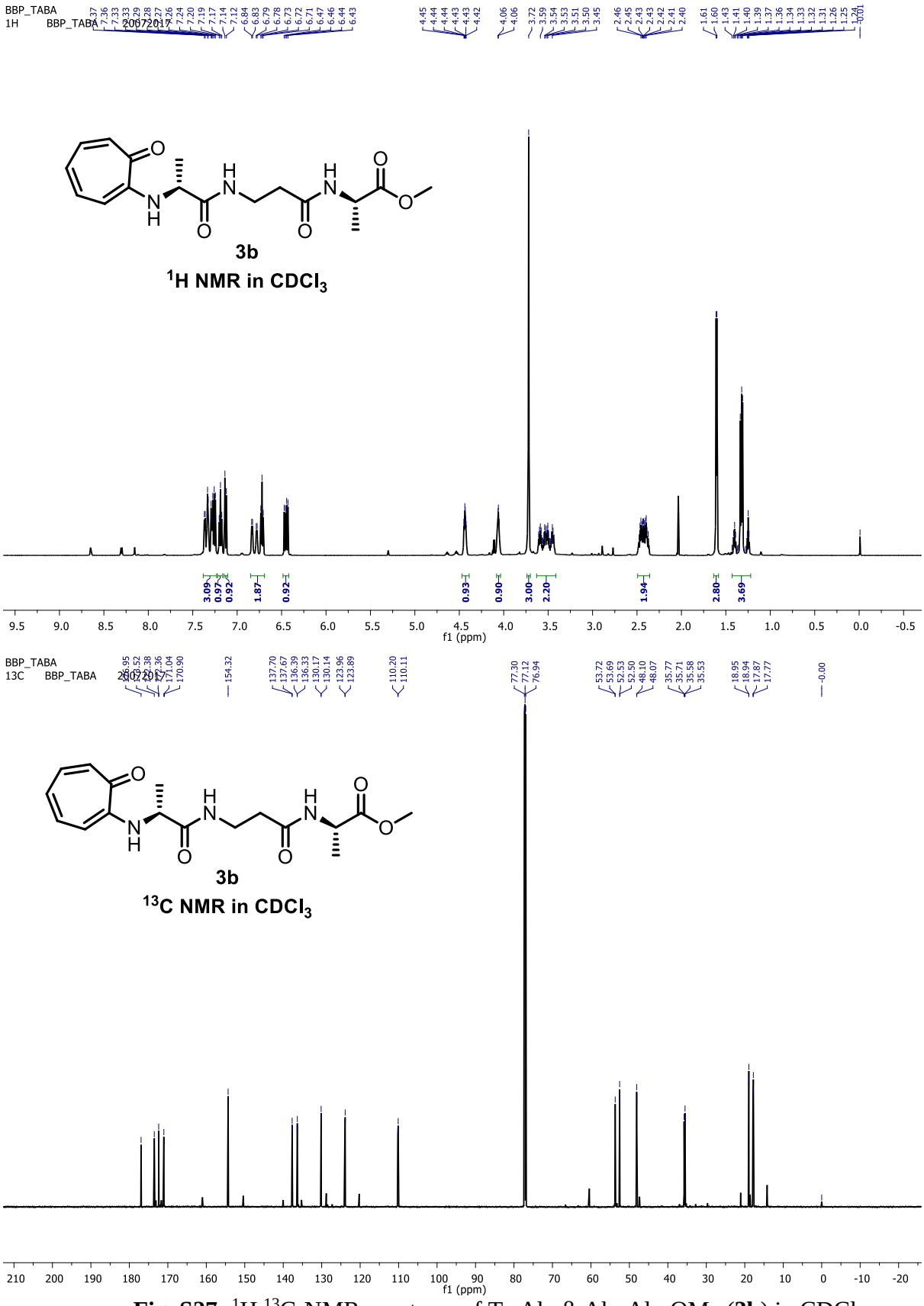


Fig. S27: ^{1}H,^{13}C-NMR spectrum of Tr-Ala-β-Ala-Ala-OMe (**3b**) in $CDCl_3$

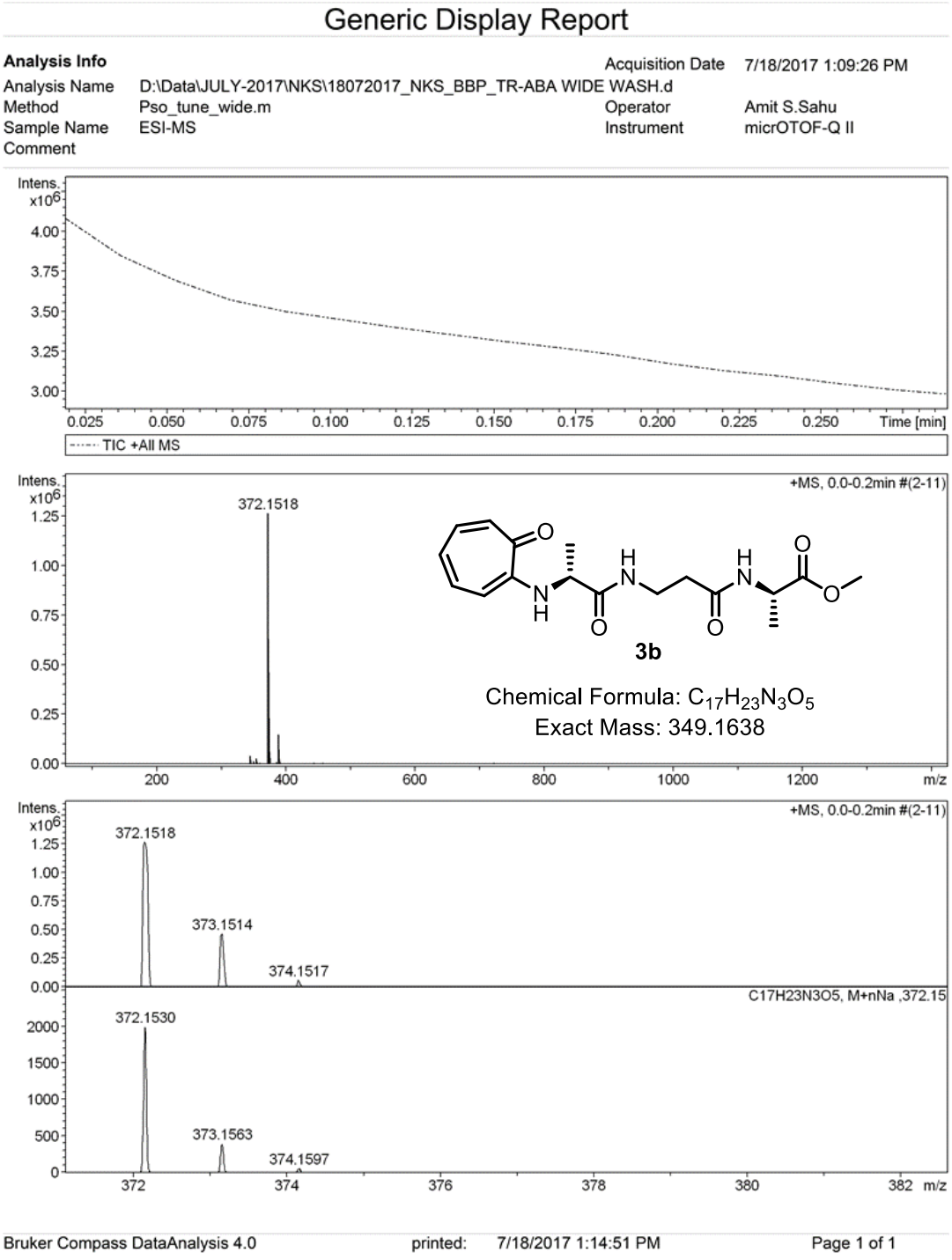
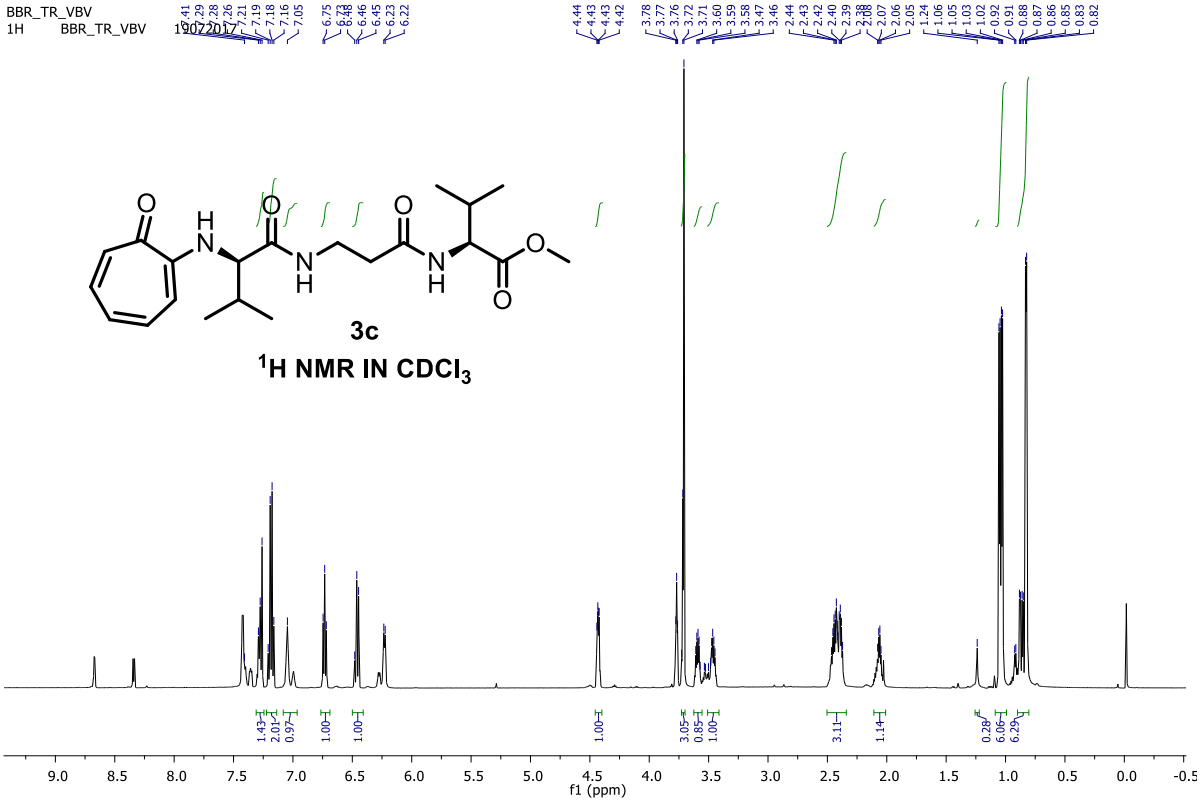


Fig. S28: ESI-MS/HRMS spectra of Tr-Ala-β-Ala-Ala-OMe (**3b**)

16. NMR ($^{1}H/^{13}C$) and HRMS spectra of Tr-Val-*β*-Ala-Val-OMe **(3c)**



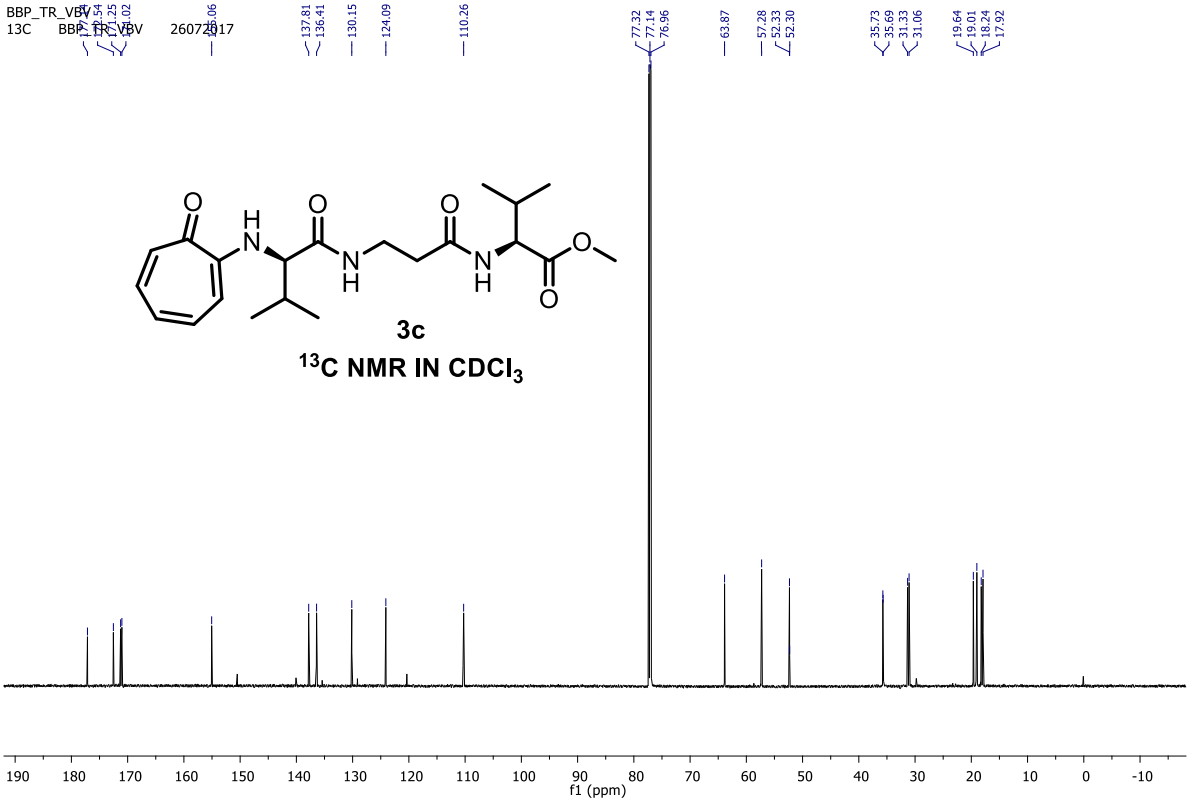


Fig. S29: $^{1}H,^{13}C$-NMR spectrum of Tr-Val-β-Ala-Val-OMe (**3c**) in $CDCl_3$

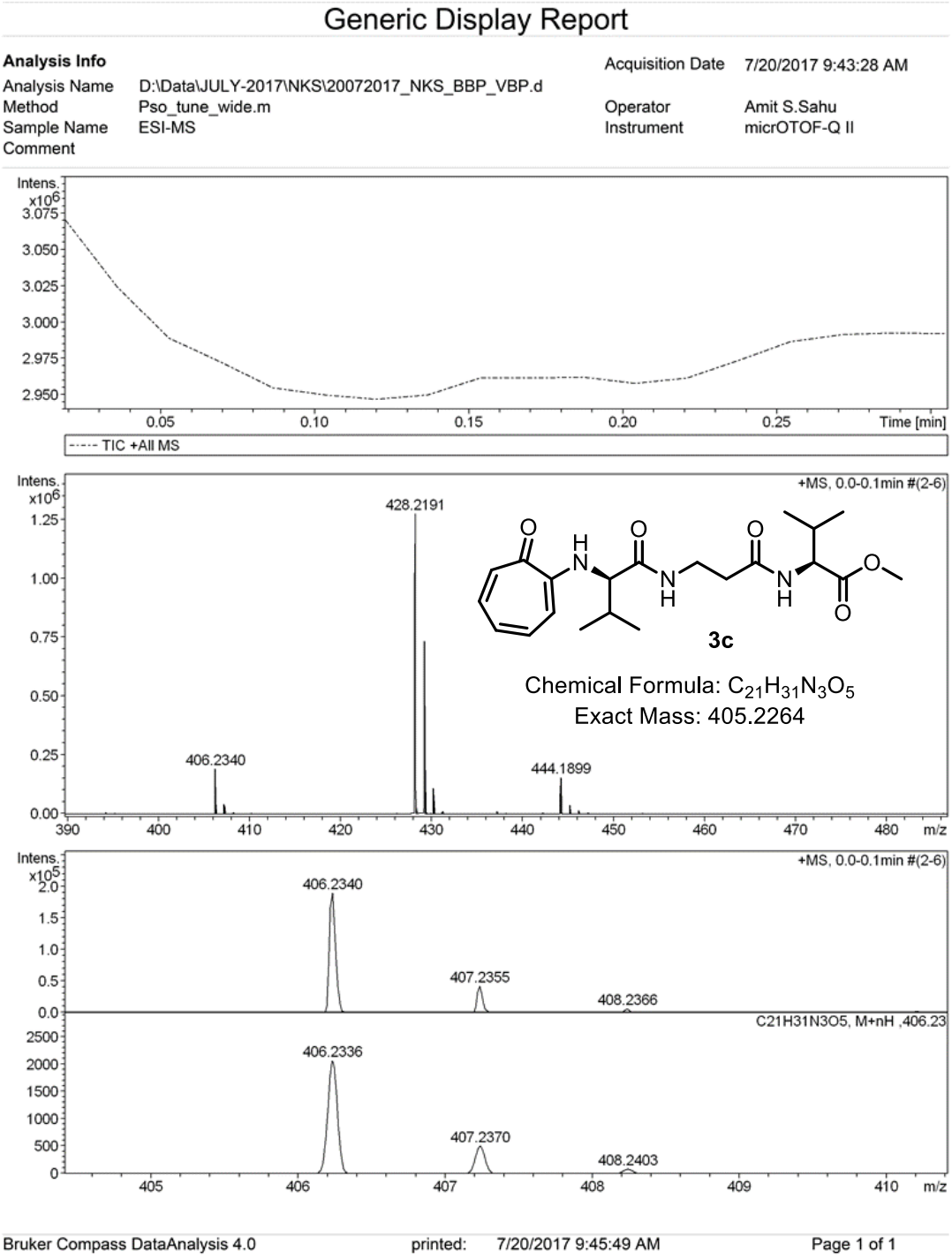


Fig. S30: ESI-MS/HRMS spectra of Tr-Val-*β*-Ala-Val-OMe (**3c**)

17. NMR (1H/13C) and HRMS spectra of Tr-Leu-β-Ala-Leu-OMe(**3d**)

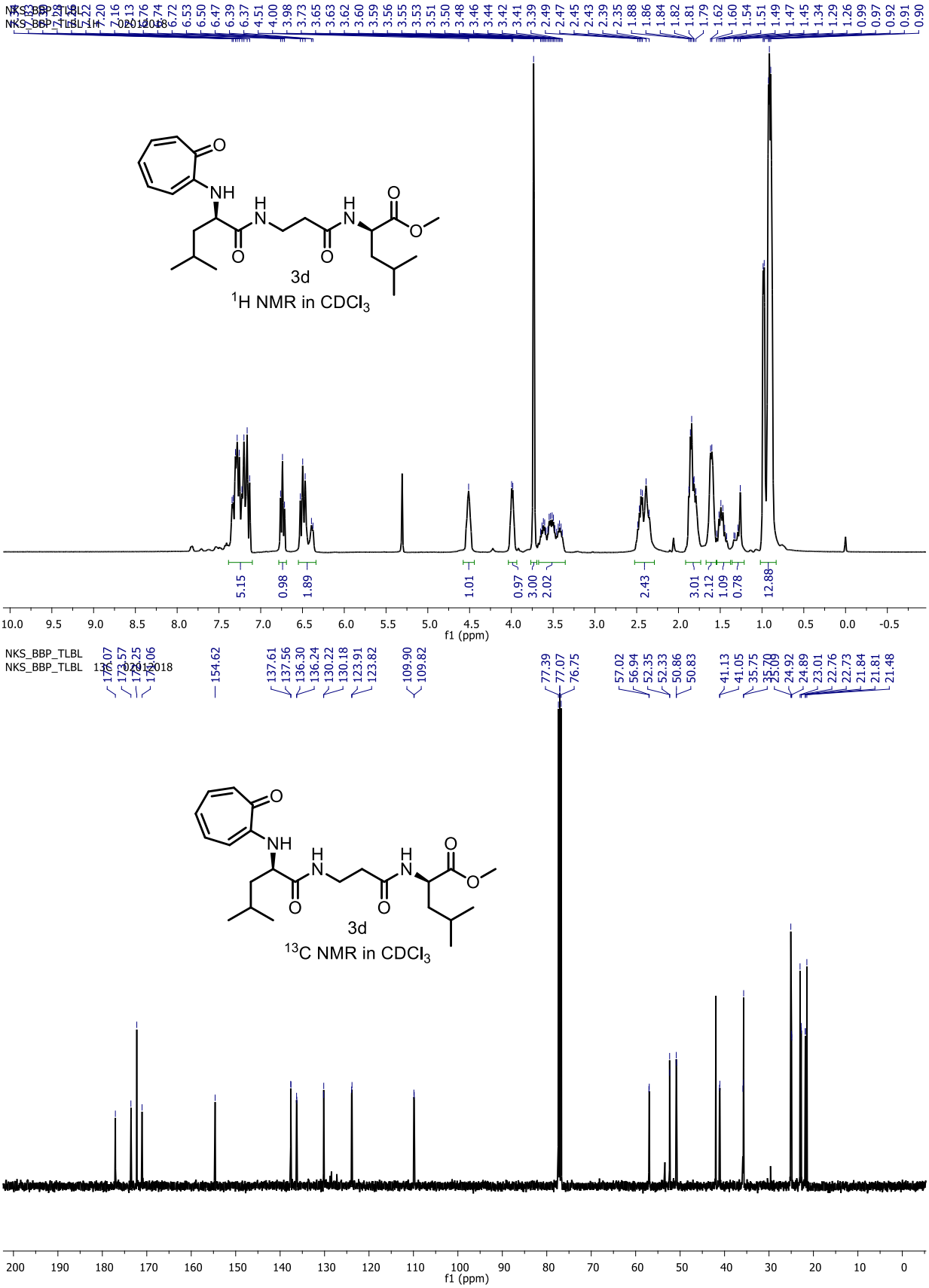


Fig. S31: $^{1}H,^{13}C$-NMR spectrum of Tr-Leu-*β*-Ala-Leu-OMe (**3d**) in $CDCl_3$

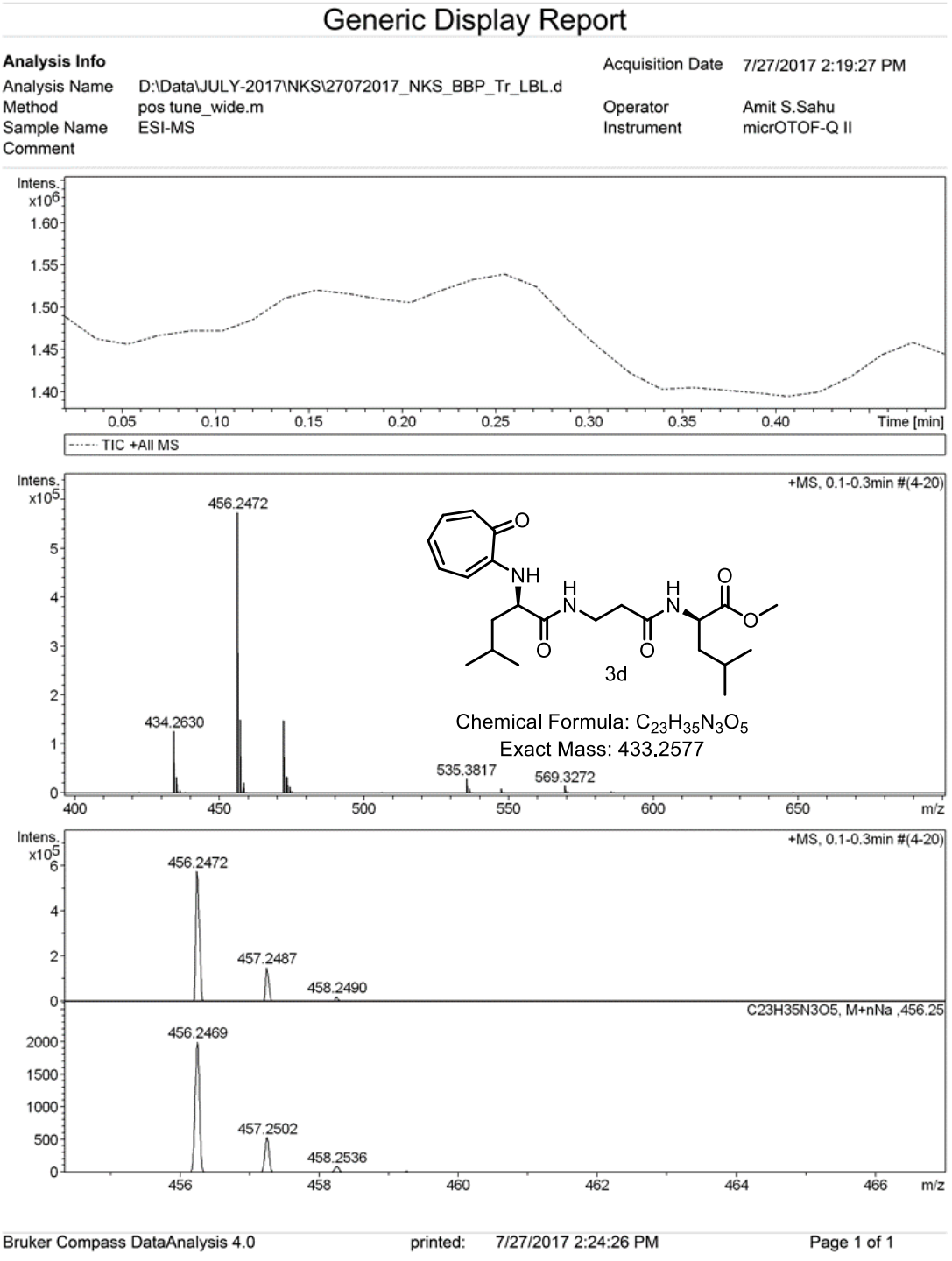


Fig. S32: ESI-MS/HRMS spectra of Tr-Leu-*β*-Ala-Leu-OMe (**3d**)

19. NMR ($^{1}H/^{13}C$) and HRMS spectra of Tr-Ilu-β-Ala-Ilu-OMe(**3e**)

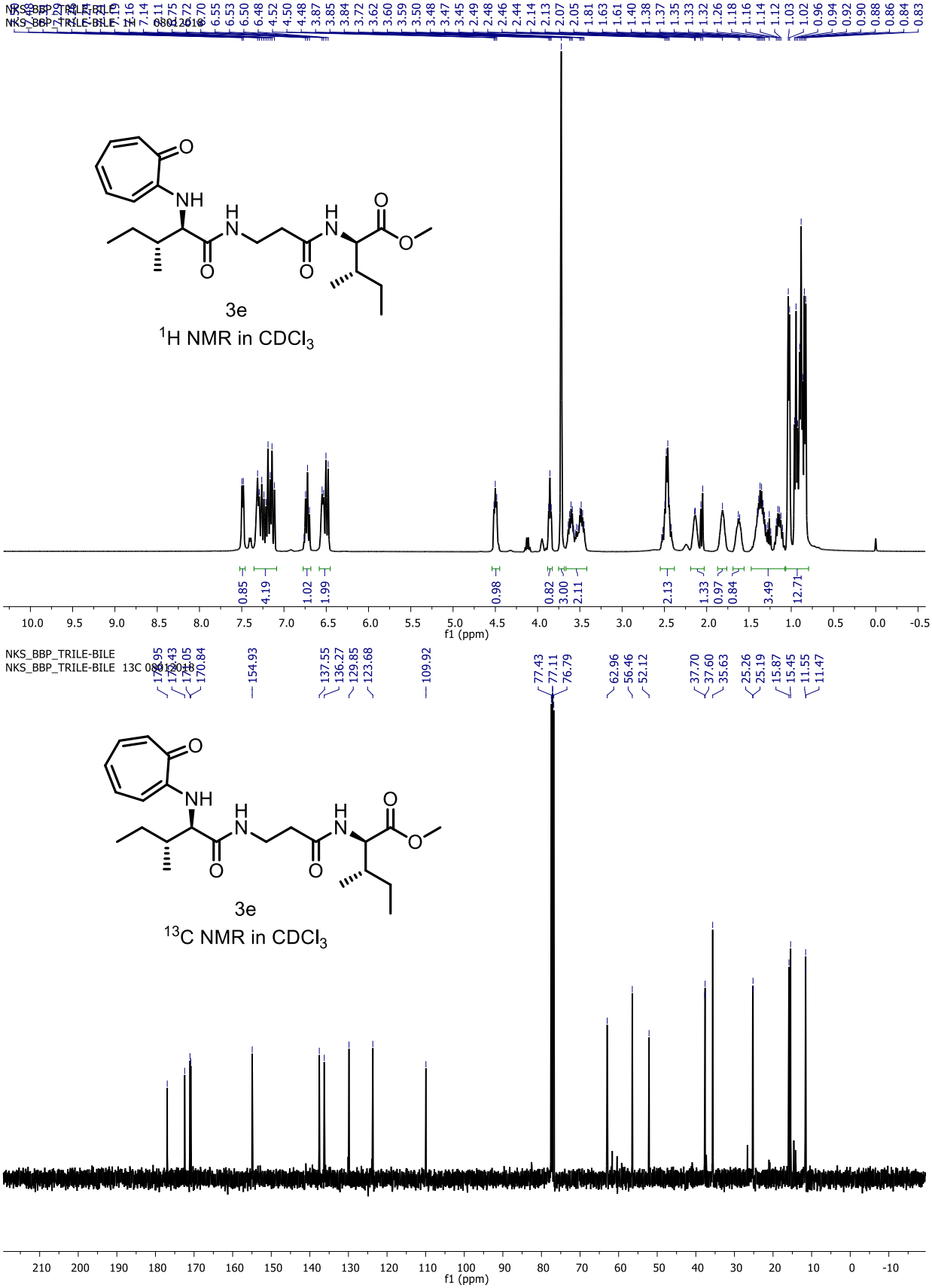


Fig. S33: $^{1}H,^{13}C$-NMR spectrum of Tr-Ile-β-Ala-Ile-OMe (**3e**) in $CDCl_3$

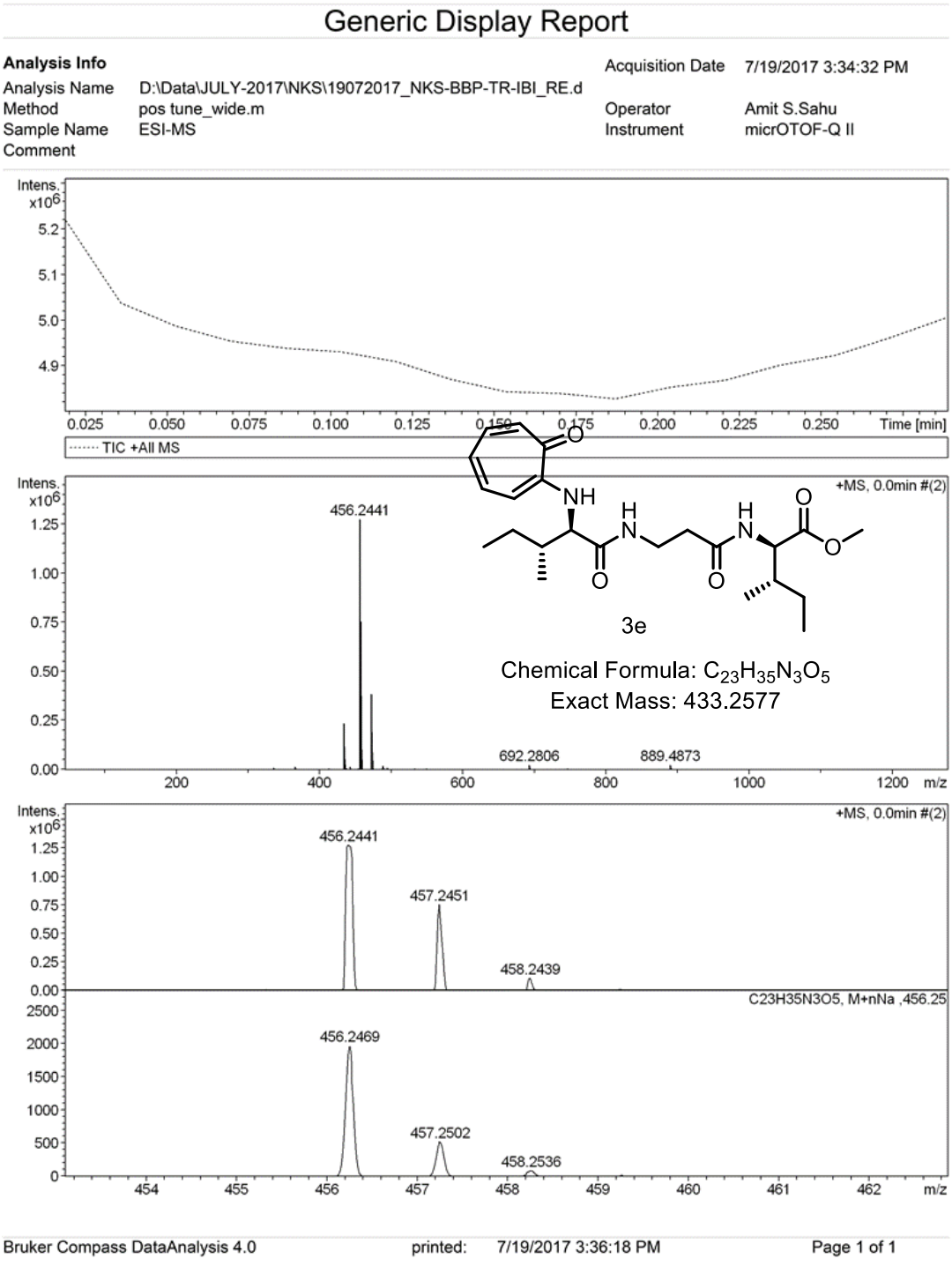


Fig. S34: ESI-MS/HRMS spectra of Tr-Ile-*β*-Ala-Ile-OMe (**3e**)

20. NMR ($^{1}H/^{13}C$) and HRMS spectra of Boc-Gly-*β*-Ala-Gly-OMe (**4a**)

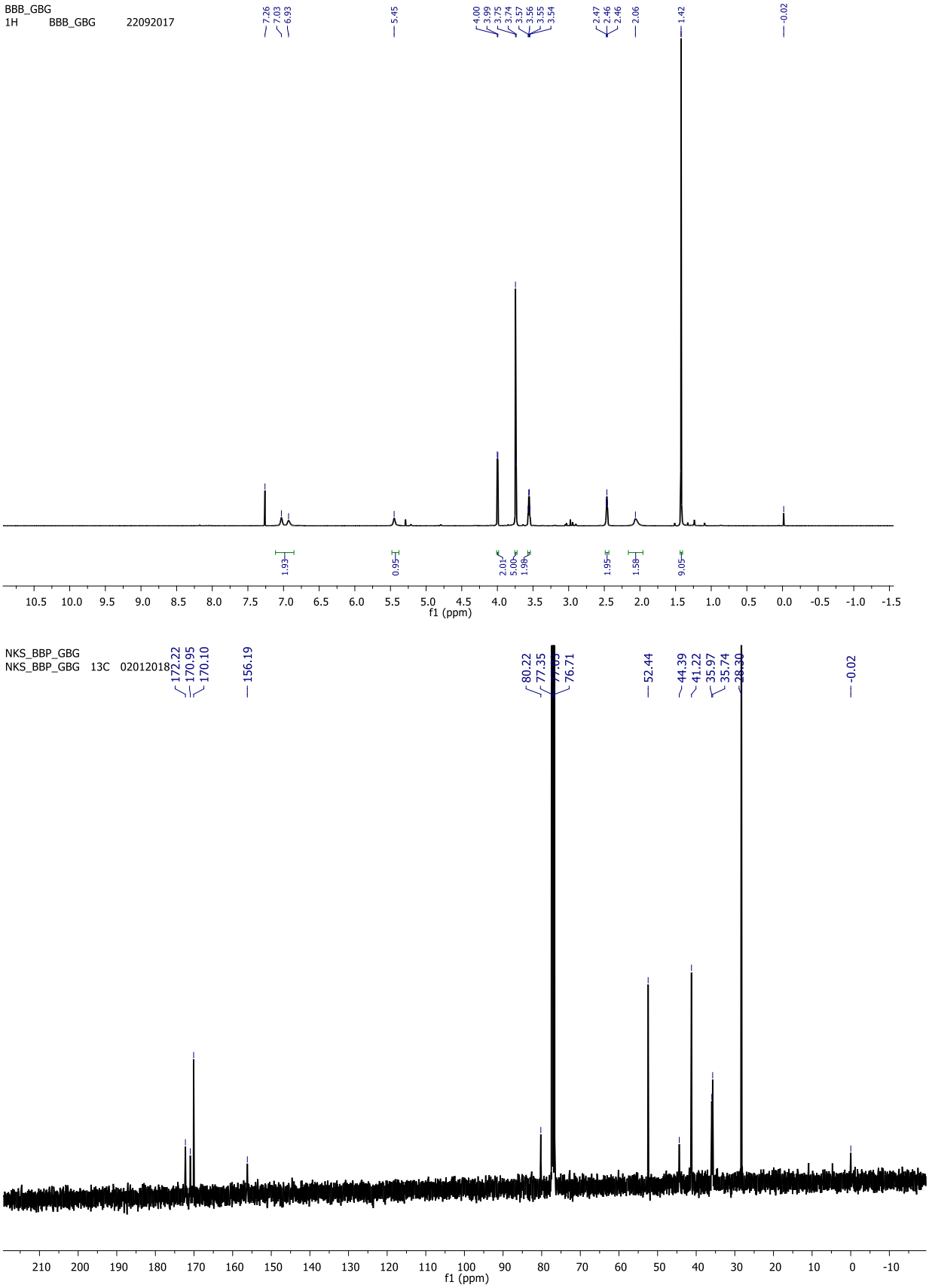


Fig. S35: $^{1}H,^{13}C$-NMR spectrum of Boc-Gly-β-Ala-Gly-OMe (**4**a) in $CDCl_3$

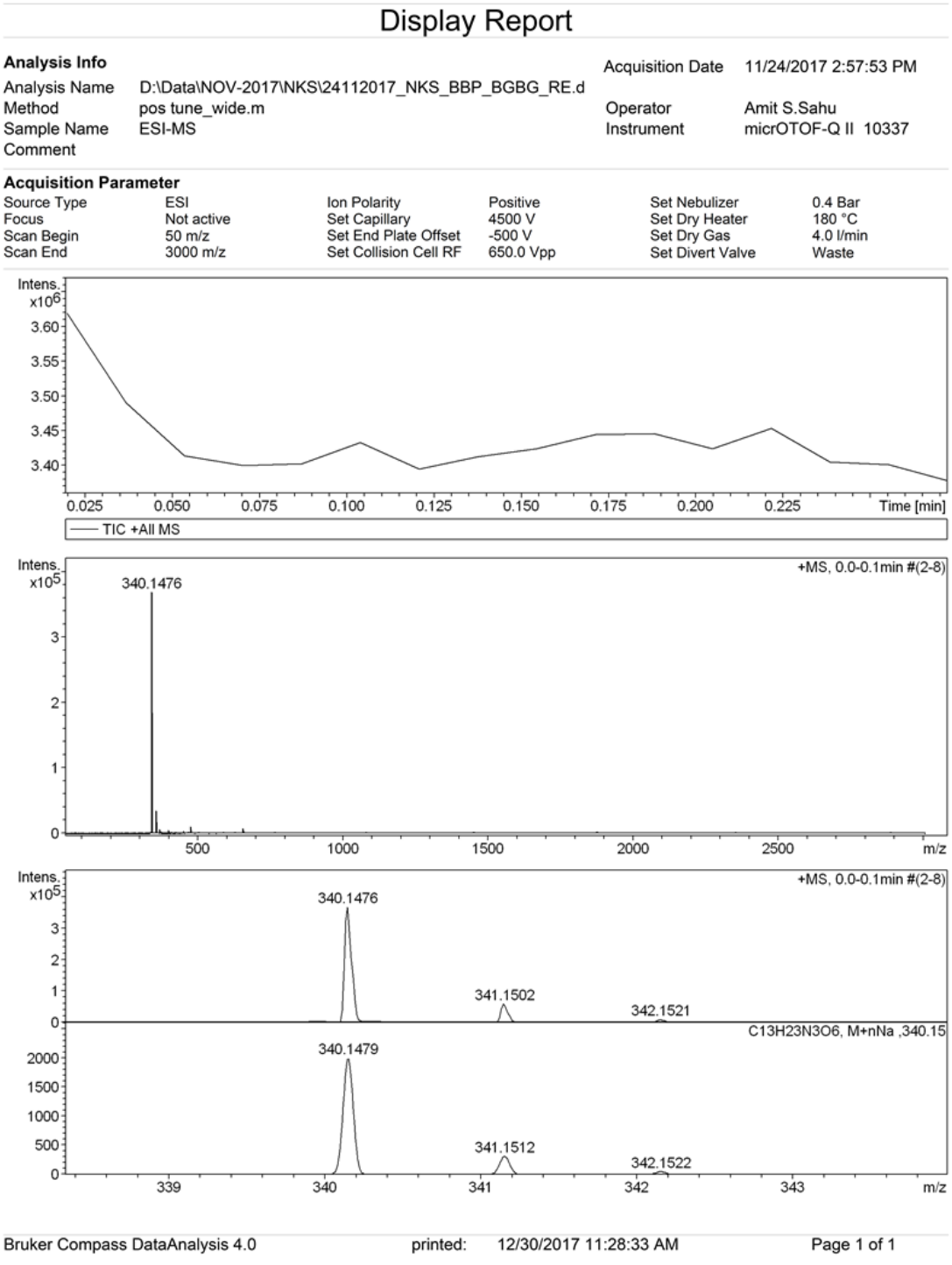


Fig. S36: ESI-MS/HRMS spectra of Boc-Gly-β-Ala-Gly-OMe(**4a**)

21. NMR ($^{1}H/^{13}C$) and HRMS spectra of Boc-Ala-*β*-Ala-Ala-OMe(**4b**)

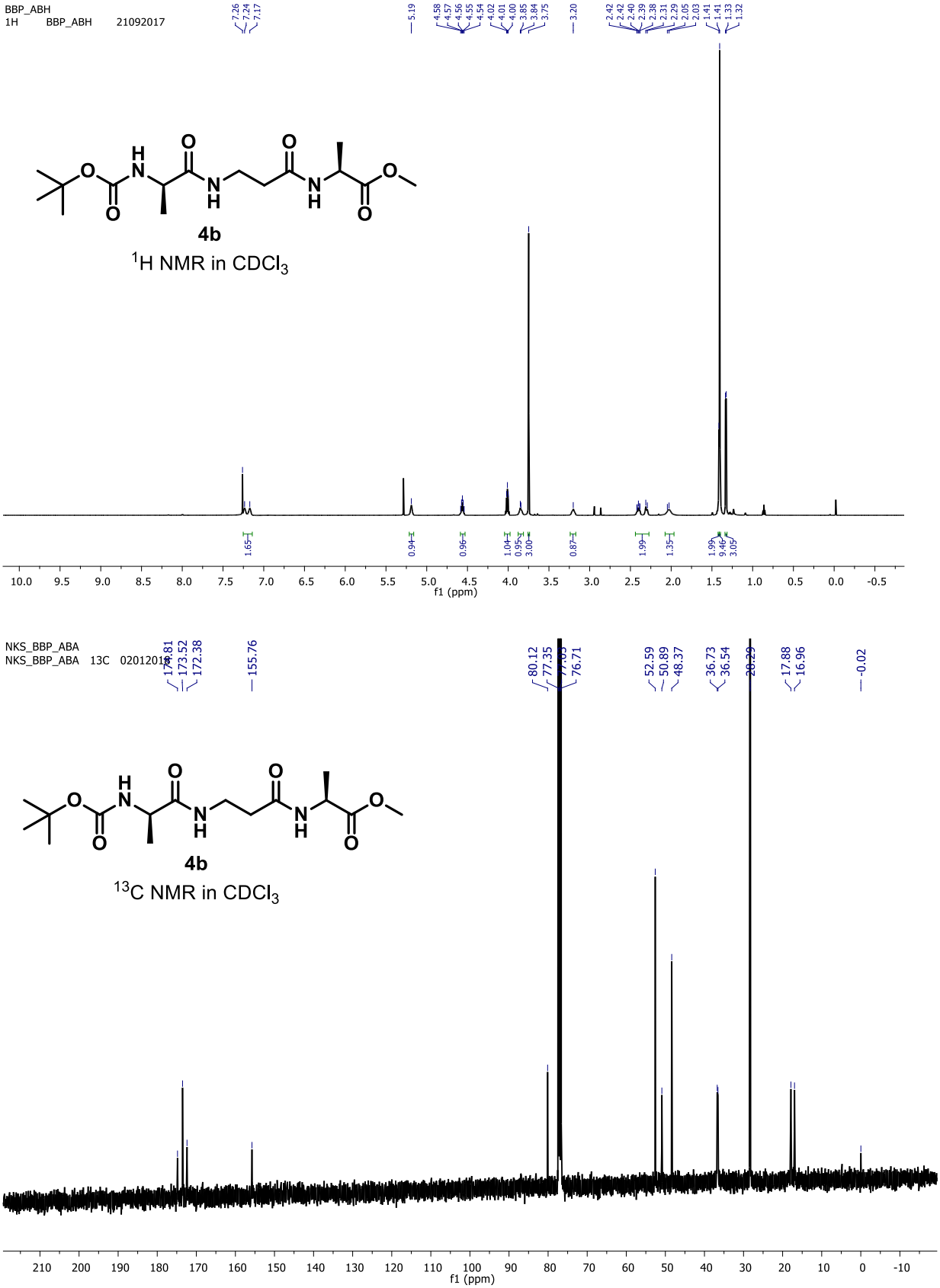


Fig. S37: $^{1}H,^{13}C$-NMR spectrum of Boc-Gly-*β*-Ala-Gly-OMe(**4b**) in CDCl3

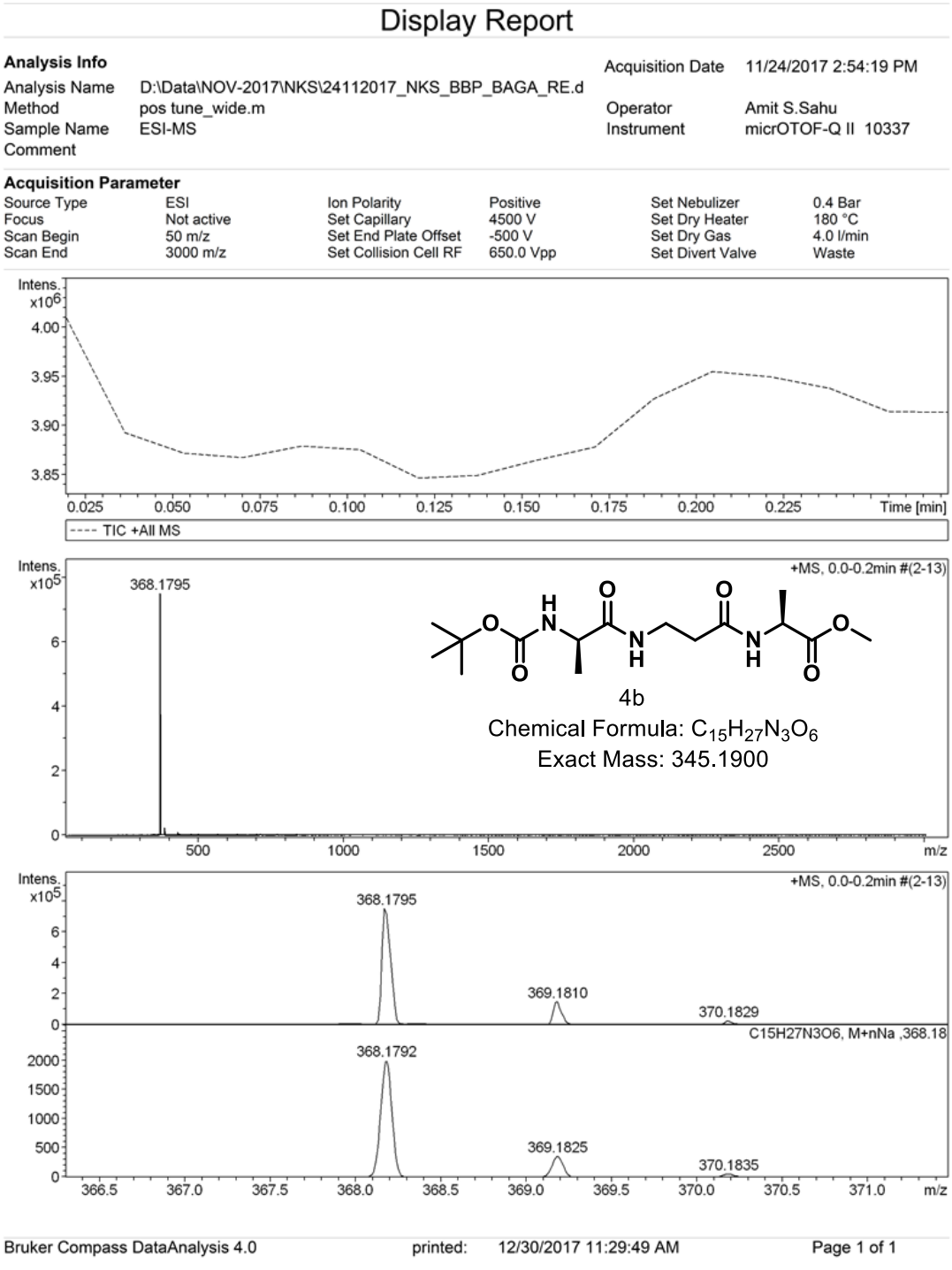


Fig. S38: ESI-MS/HRMS spectra of Boc-Ala-*β*-Ala-Ala-OMe(**4b**)

22. NMR ($^{1}H/^{13}C$) and HRMS spectra of Boc-Val-*β*-Ala-Val-OMe (**4c**)

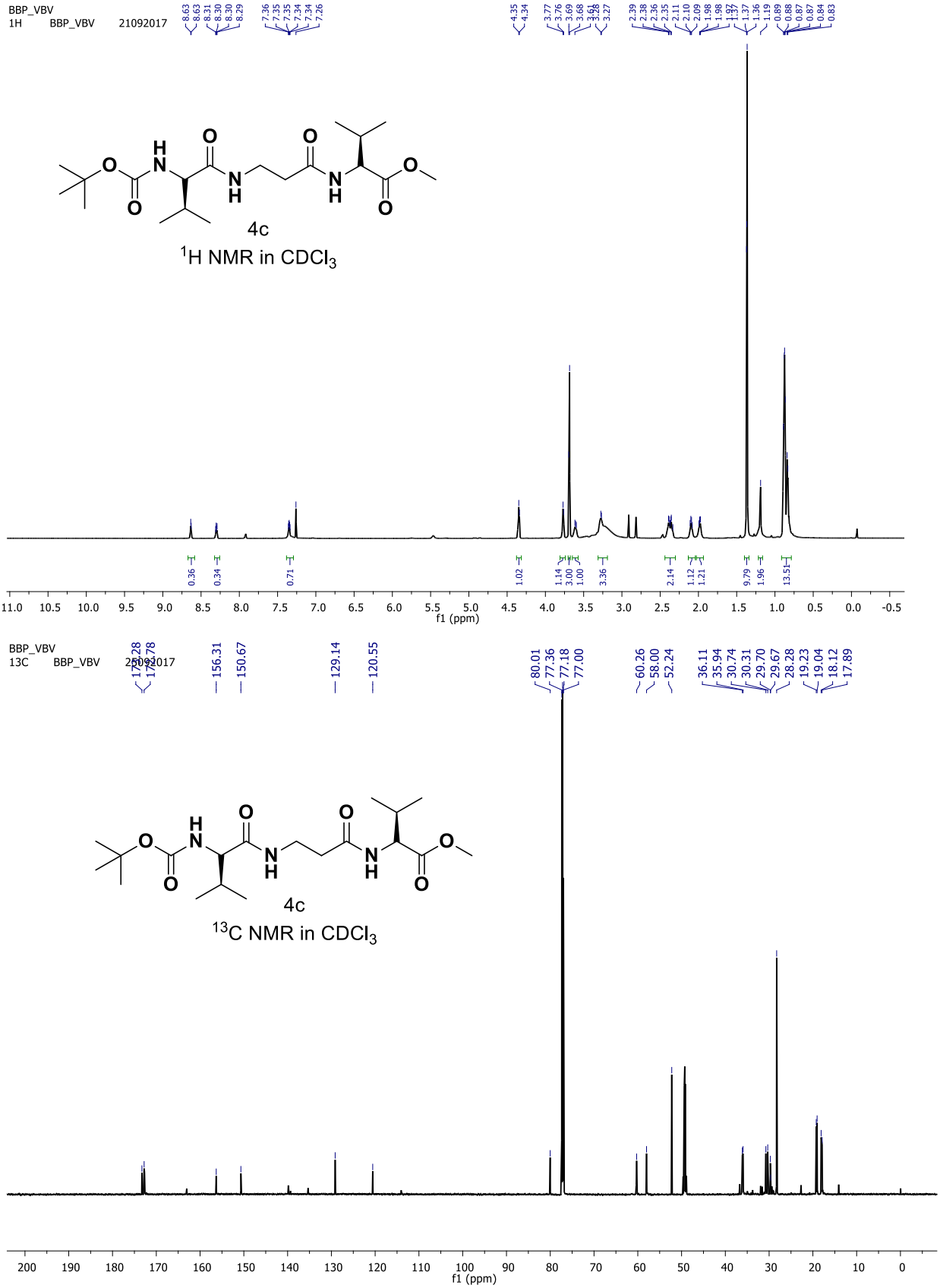


Fig. S39: 1H,13C-NMR spectrum of Boc-Gly-β-Ala-Gly-OMe(**4c**) in CDCl3

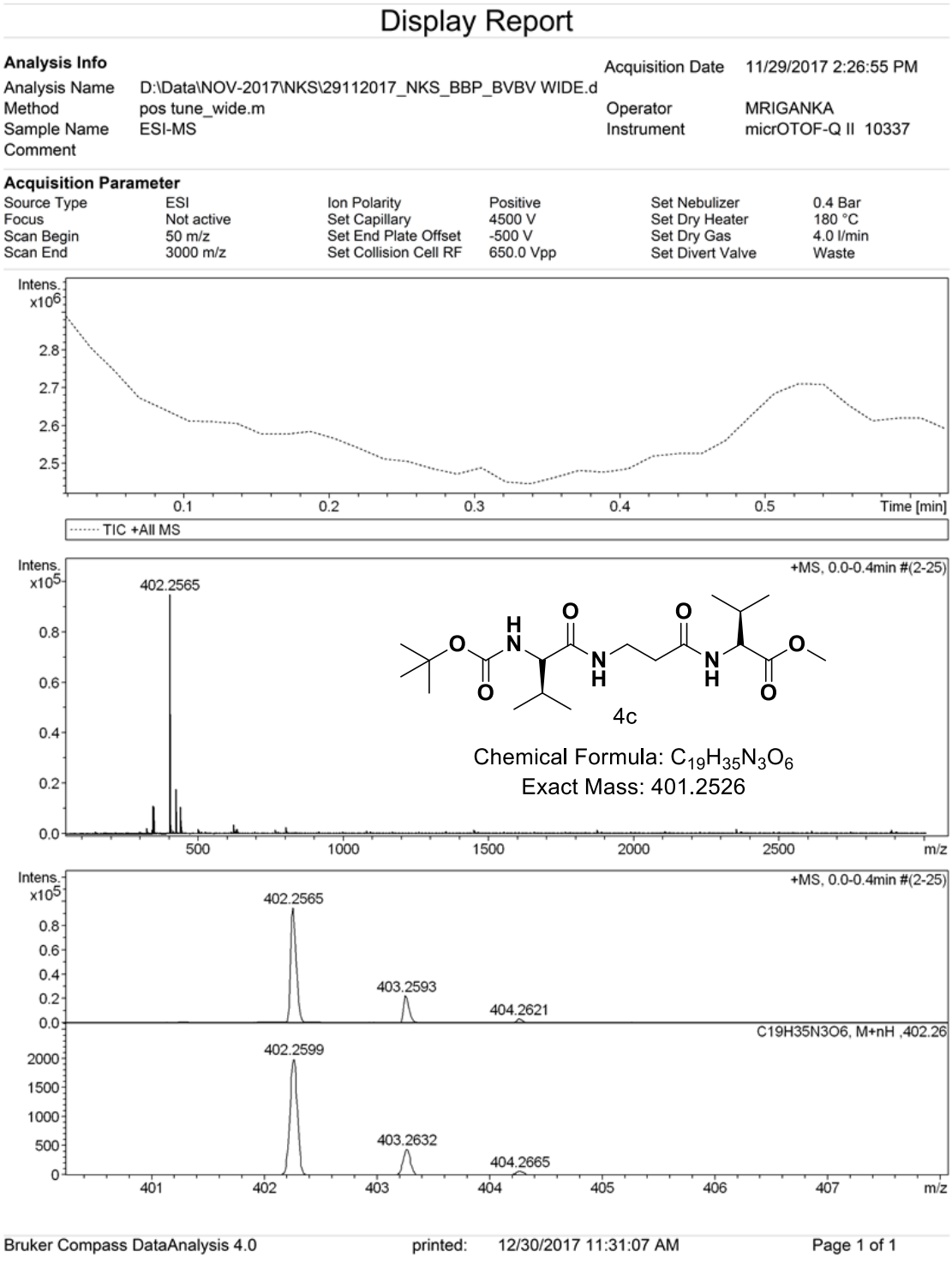


Fig. S40: ESI-MS/HRMS spectra of Boc-Ala-β-Ala-Ala-OMe (**4c**)

23. NMR ($^{1}H/^{13}C$) and HRMS spectra of Boc-Leu-*β*-Ala-Leu-OMe (**4d**)

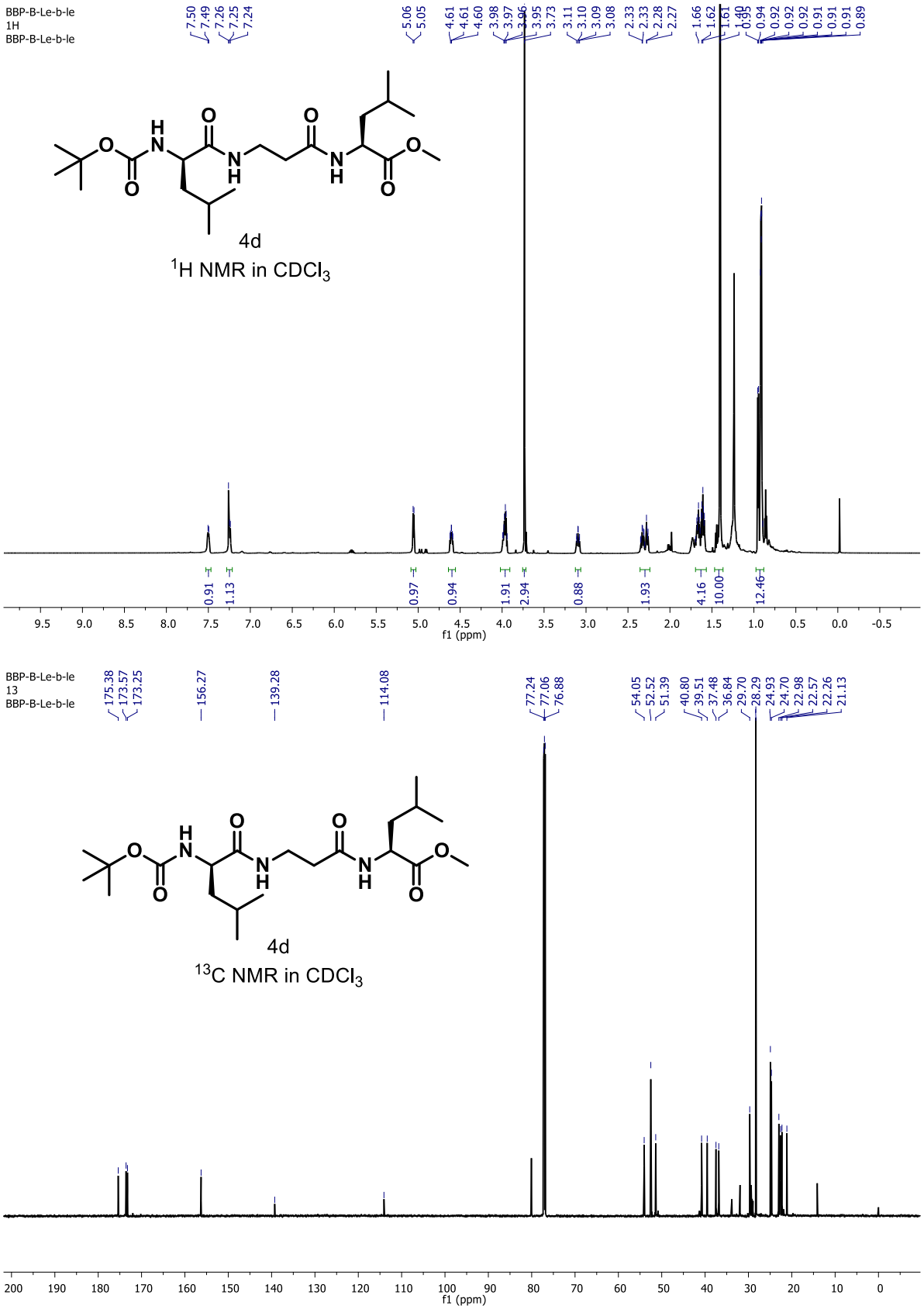


Fig. S41: $^{1}H,^{13}C$-NMR spectrum of Boc-Leu-β-Ala-Leu-OMe(**4d**) in $CDCl_3$

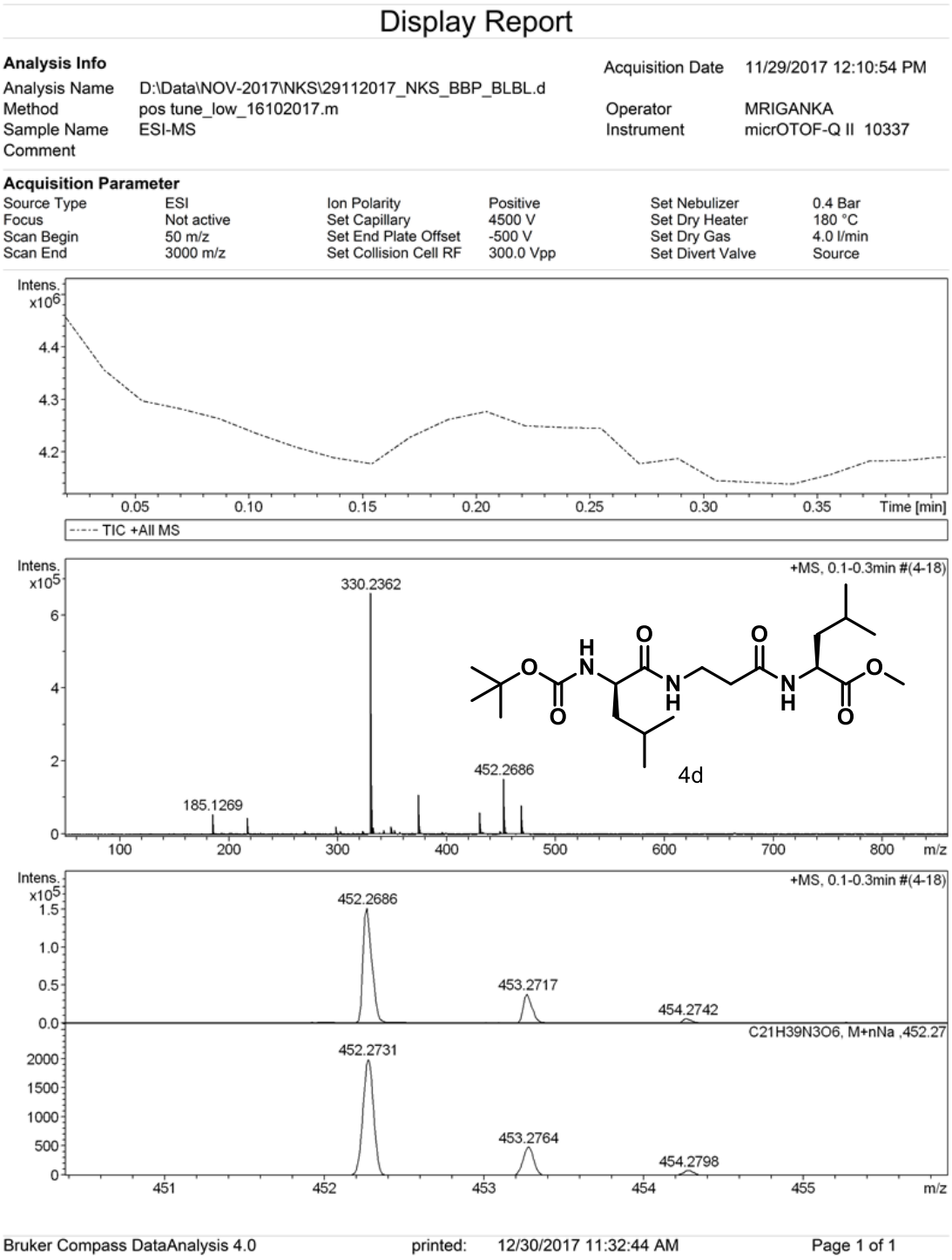


Fig. S42: ESI-MS/HRMS spectra of Boc-Ala-β-Ala-Ala-OMe(**4d**)

24. NMR ($^{1}H/^{13}C$) and HRMS spectra of Boc-Ile-β-Ala-Ile-OMe (**4e**)

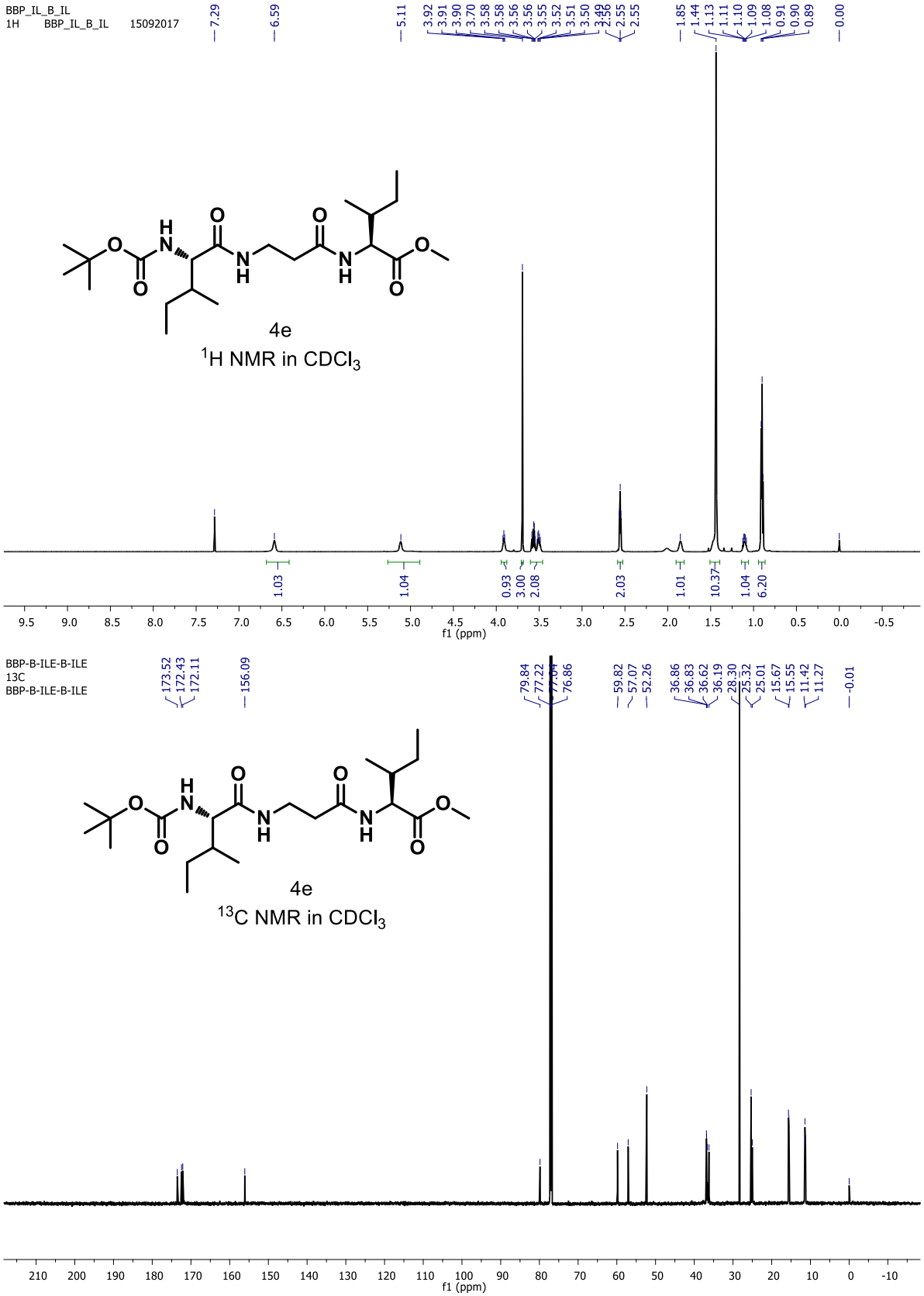


Fig. S43: $^{1}H,^{13}C$-NMR spectrum of Boc-Ile-β-Ala-Ile-OMe(**4e**) in $CDCl_3$

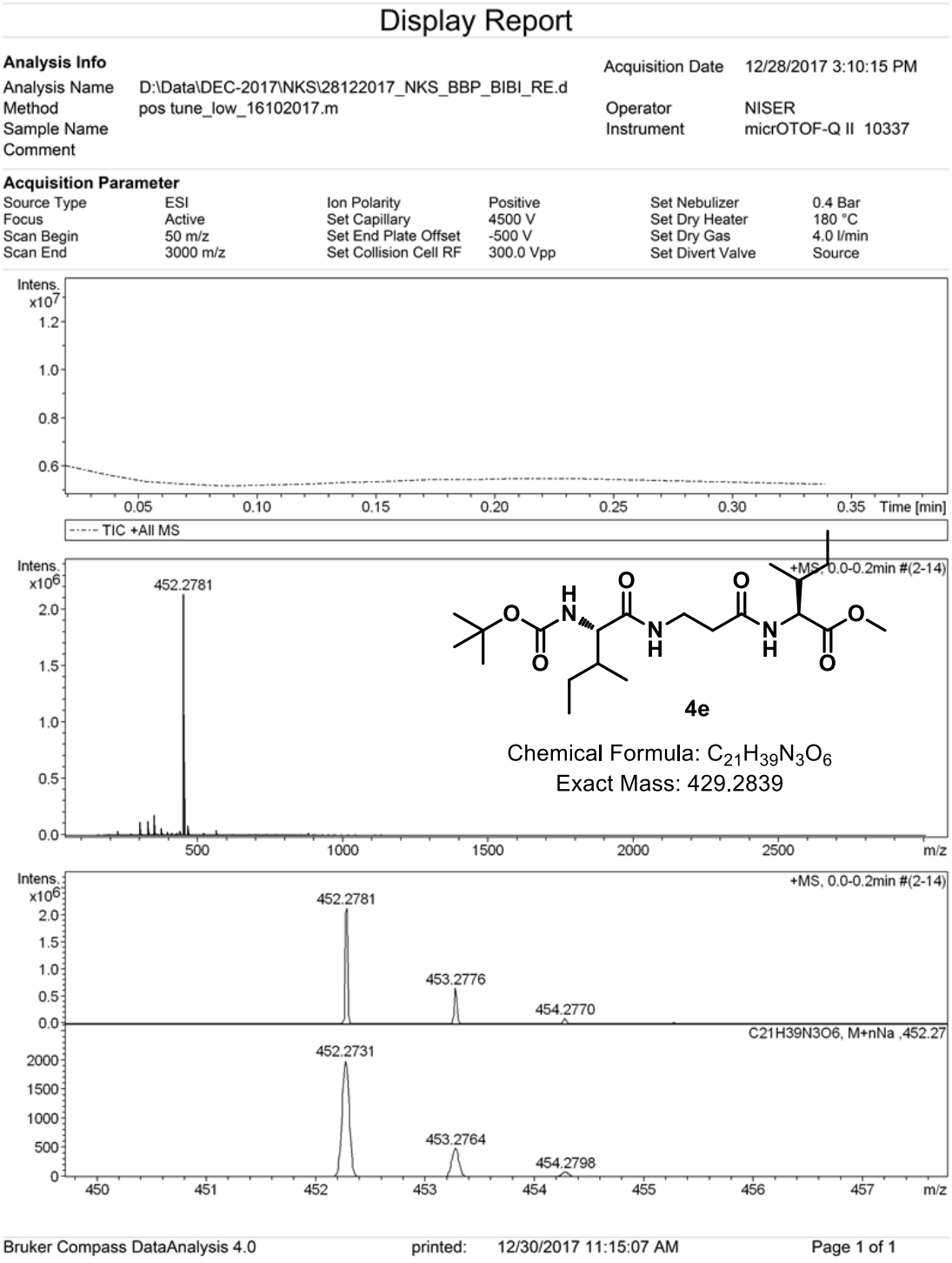


Fig. S44: ESI-MS/HRMS spectra of Boc-Ala-β-Ala-Ala-OMe(**4e**)

25. ^{1}H-^{1}H COSY and NOESY 2D NMR spectrum of dipeptide (**2a**)

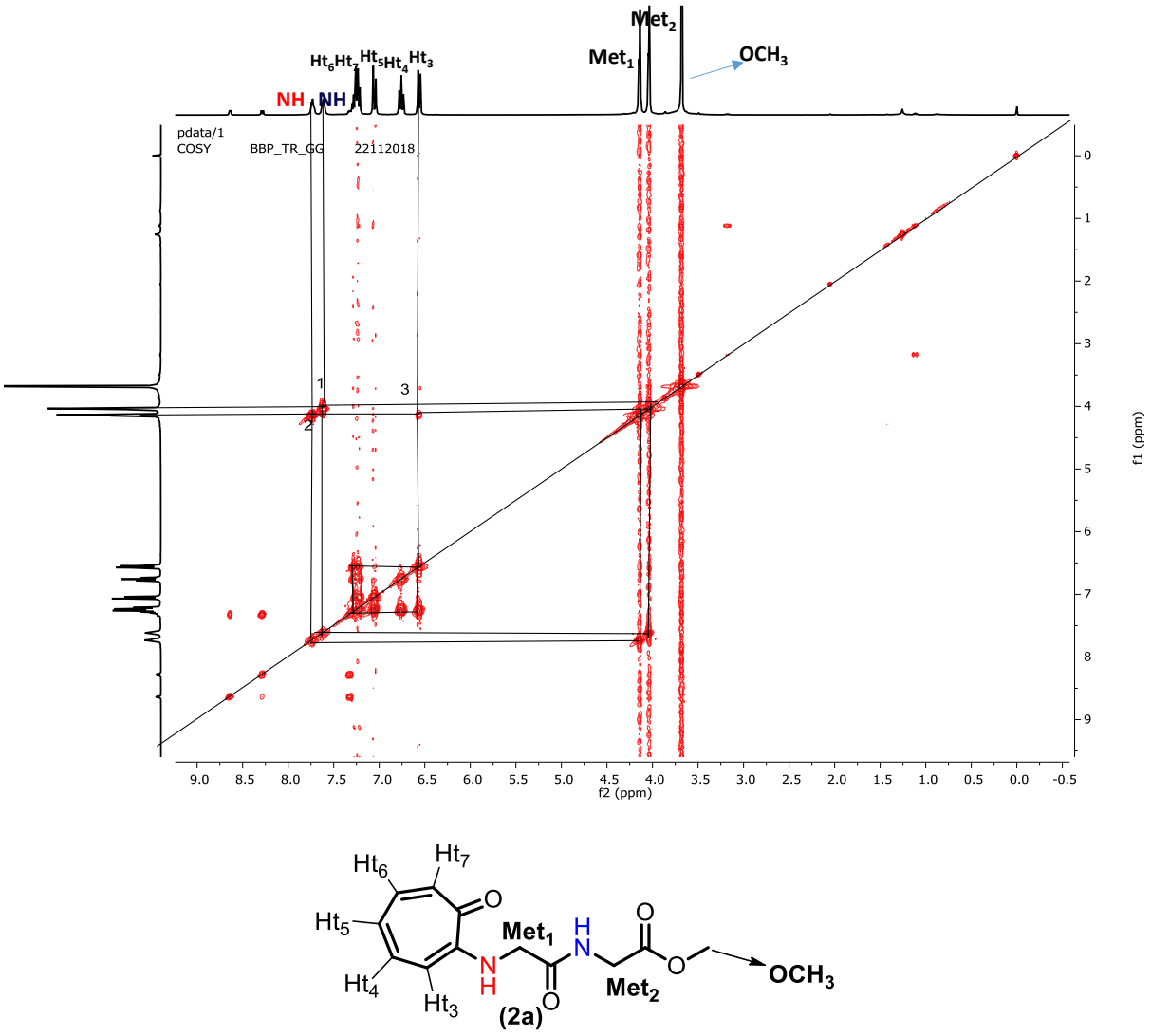
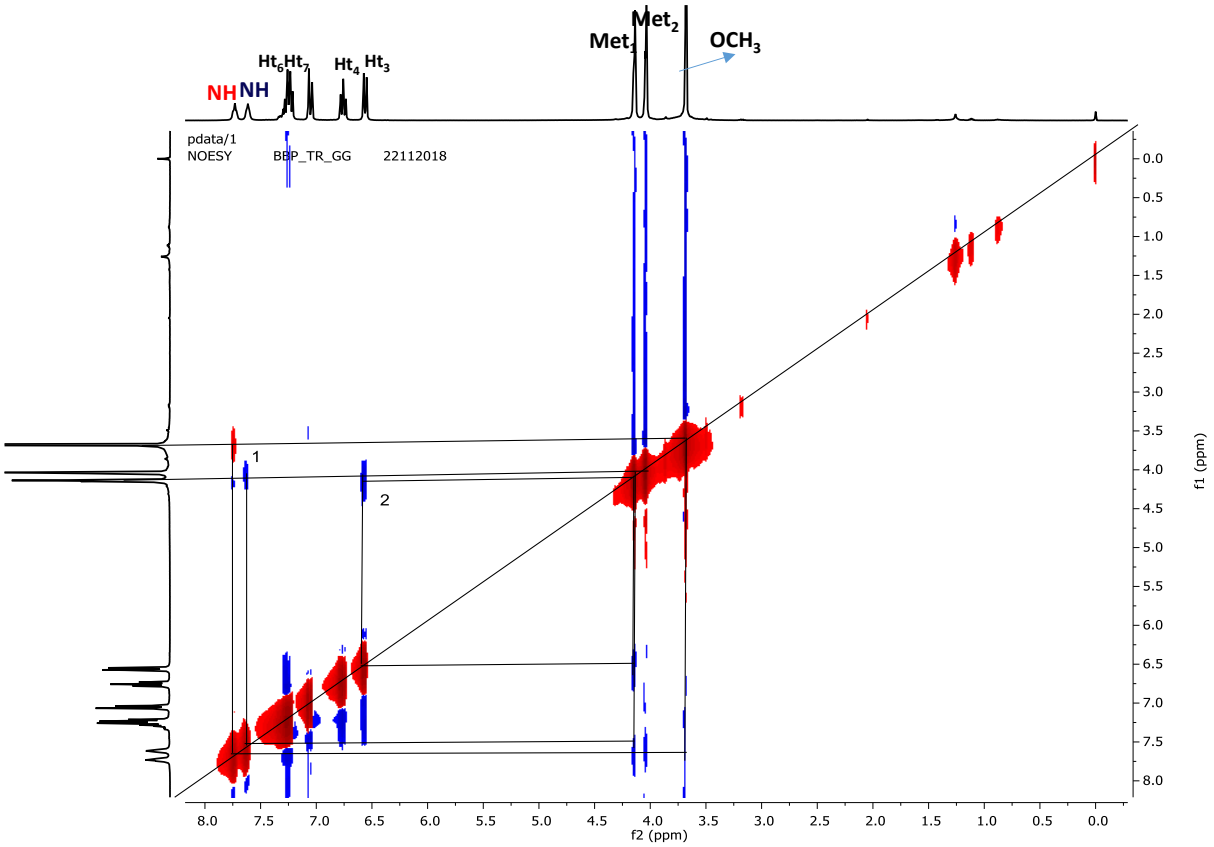
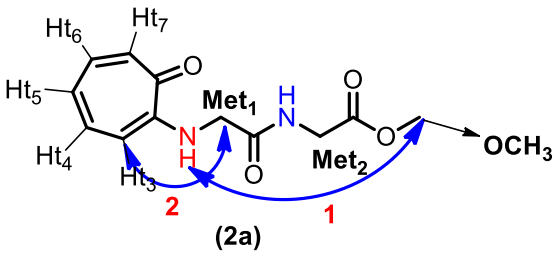
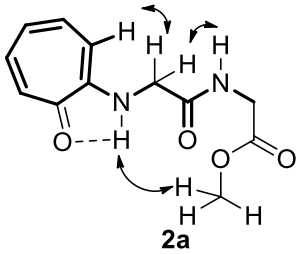


Fig. S45:^{1}H-^{1}H COSY spectra of (**2a**) in $CDCl_3$





(2a)



2a

Fig. S46:^{1}H-^{1}H NOESY spectra of (**2a**) in $CDCl_3$

26. ^{1}H-^{1}H COSY and NOESY 2D NMR spectrum of dipeptide (**2b**)

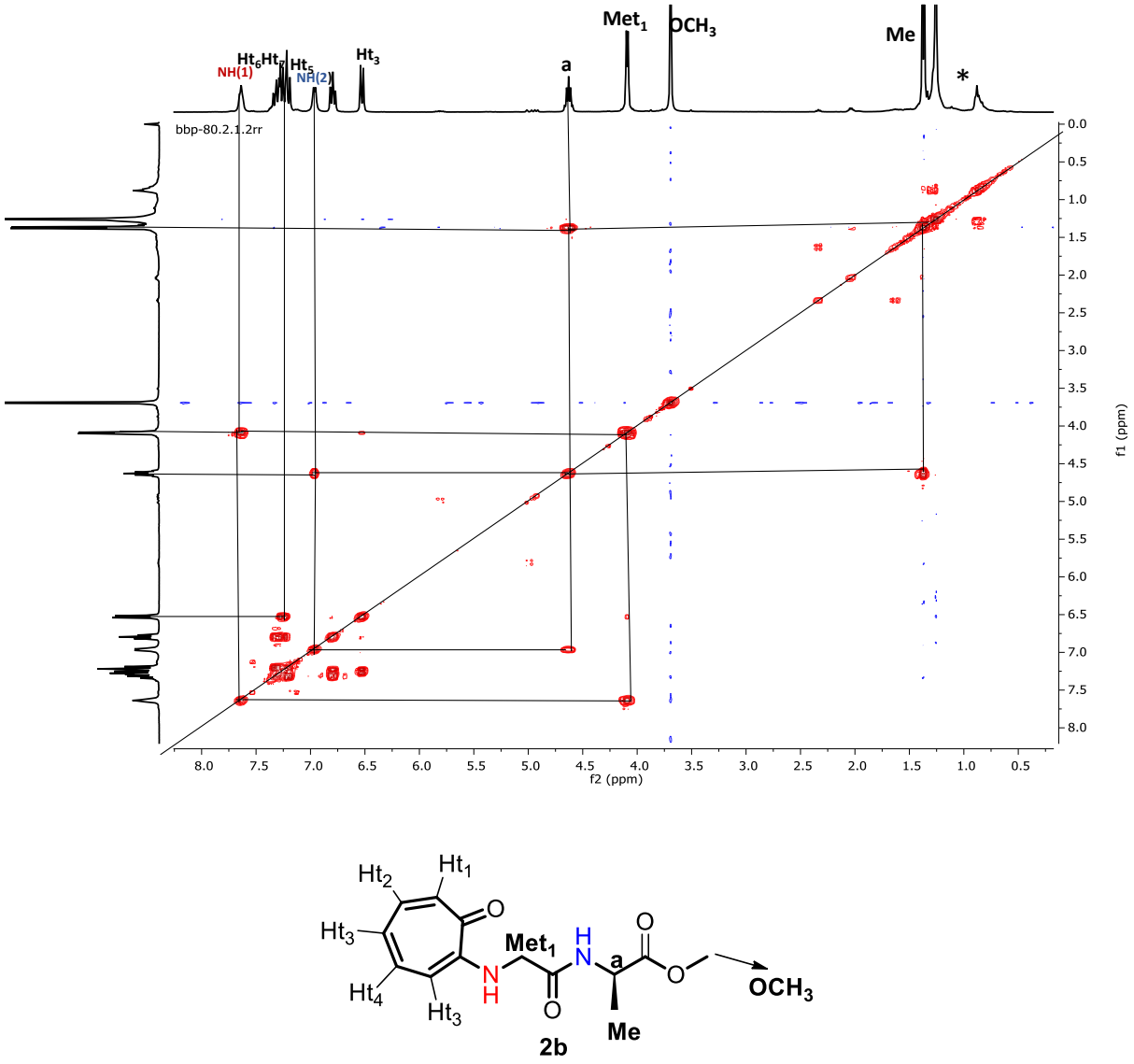


Fig. S47:^{1}H-^{1}H COSY spectra of (**2b**) in $CDCl_3$

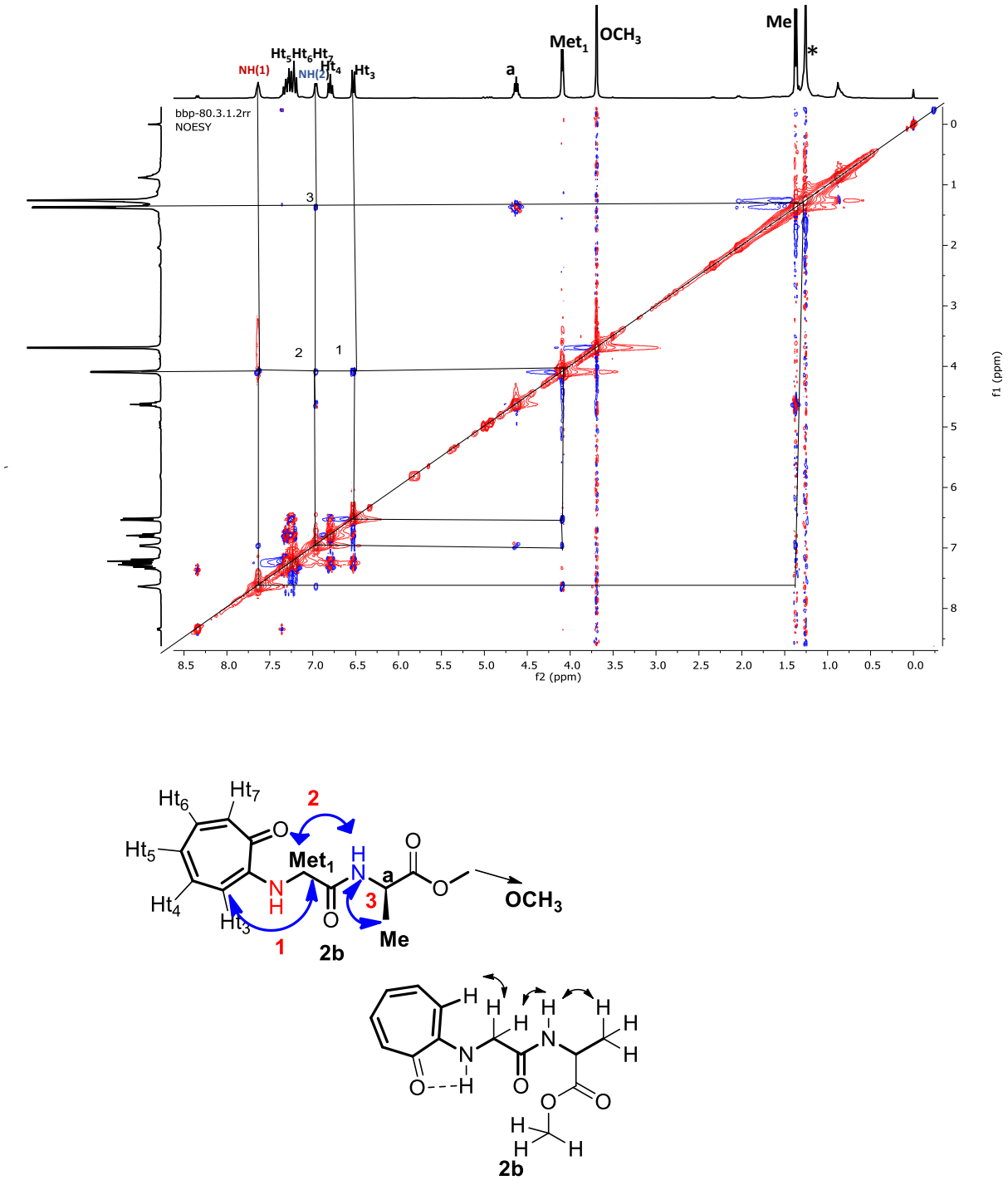
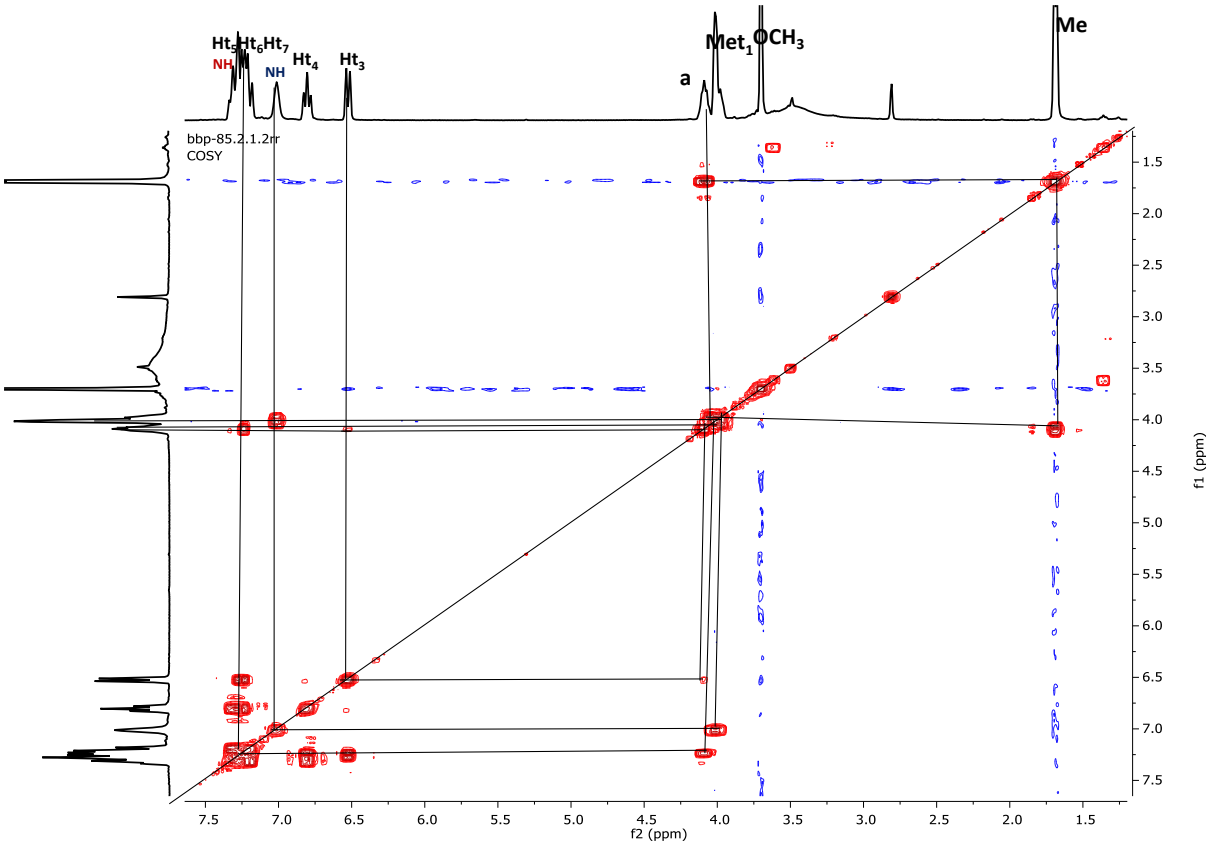
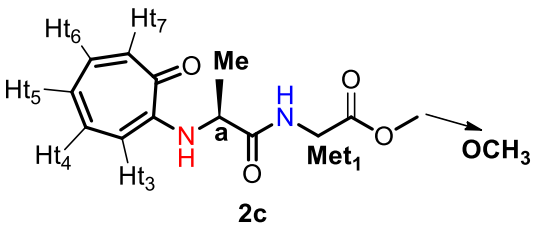


Fig. S48:^{1}H-^{1}H NOESY spectra of (**2b**) in $CDCl_3$

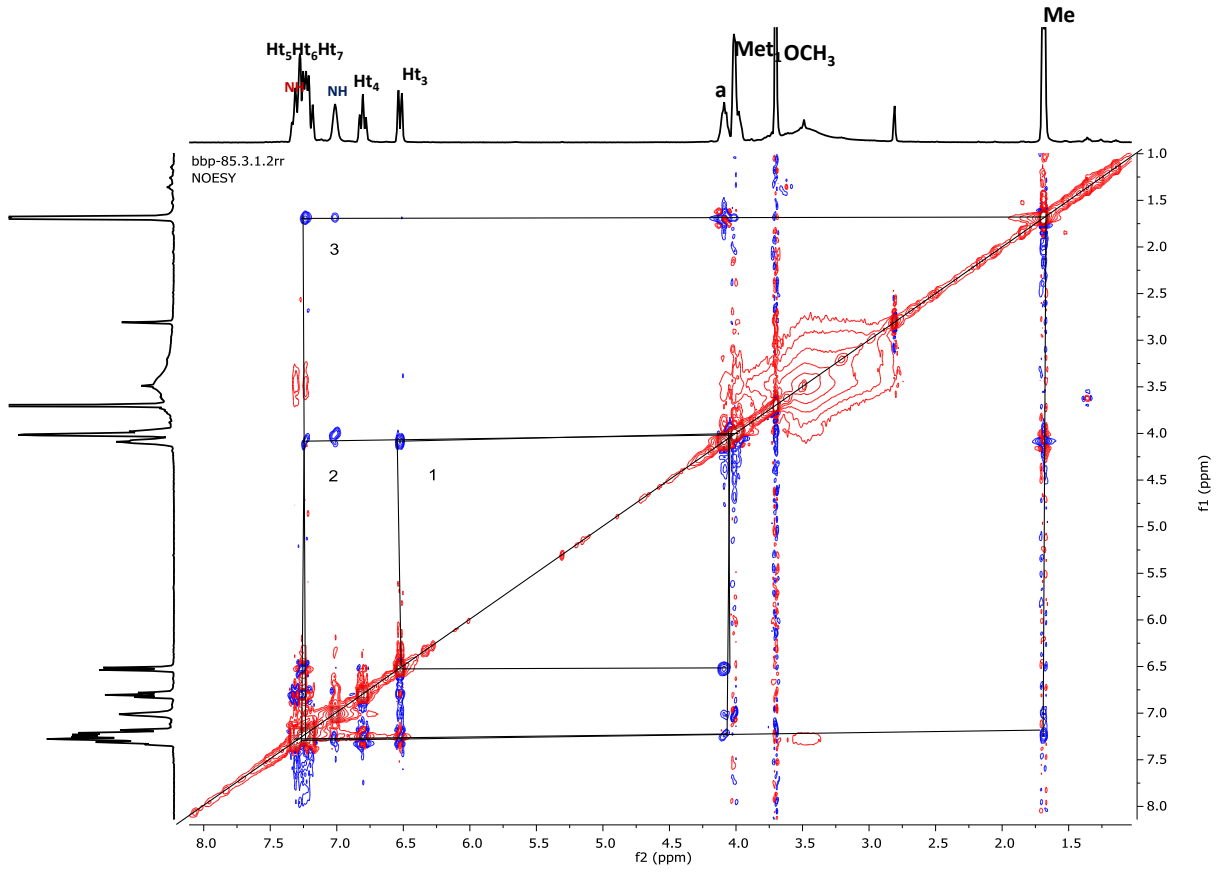
27. ^{1}H-^{1}H COSY and NOESY 2D NMR spectrum of dipeptide (**2c**)

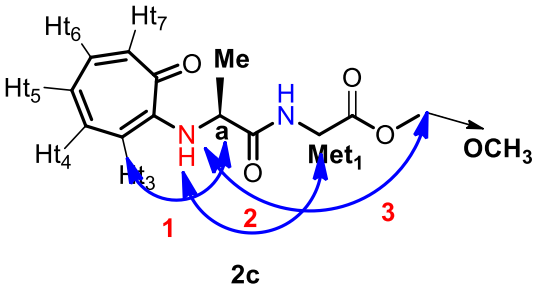




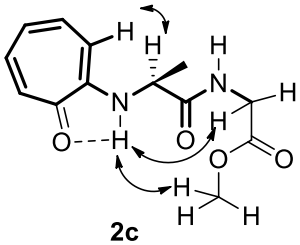
2c

Fig. 49:^{1}H-^{1}H COSY spectra of (**2c**) in $CDCl_3$





2c



2c

Fig. S50:^{1}H-^{1}H NOESY spectra of (**2c**) in $CDCl_3$

28. ^{1}H-^{1}H COSY and NOESY 2D NMR spectrum of dipeptide (**2e**)

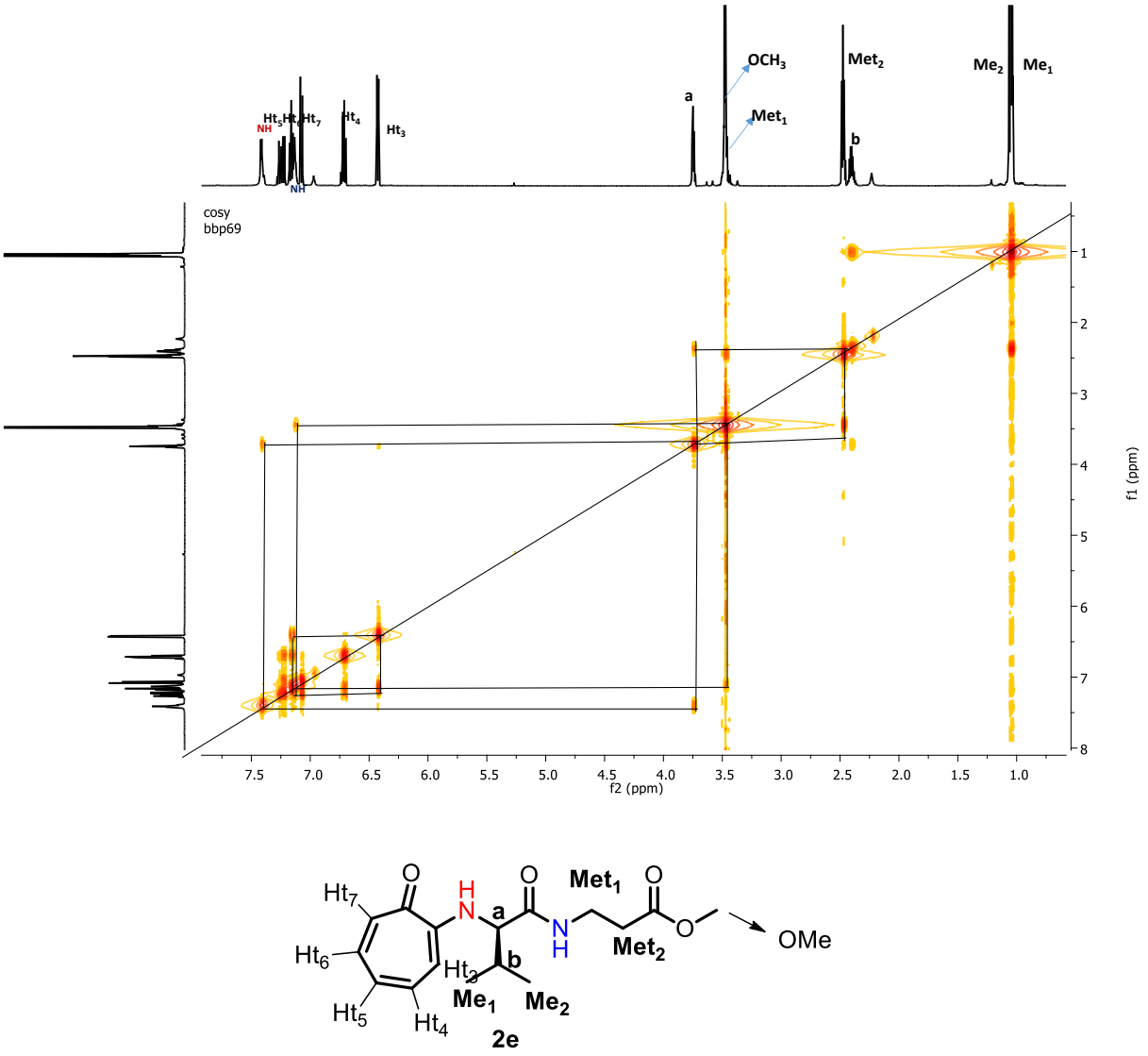


Fig. S51:^{1}H-^{1}H COSY spectra of (**2e**) in $CDCl_3$

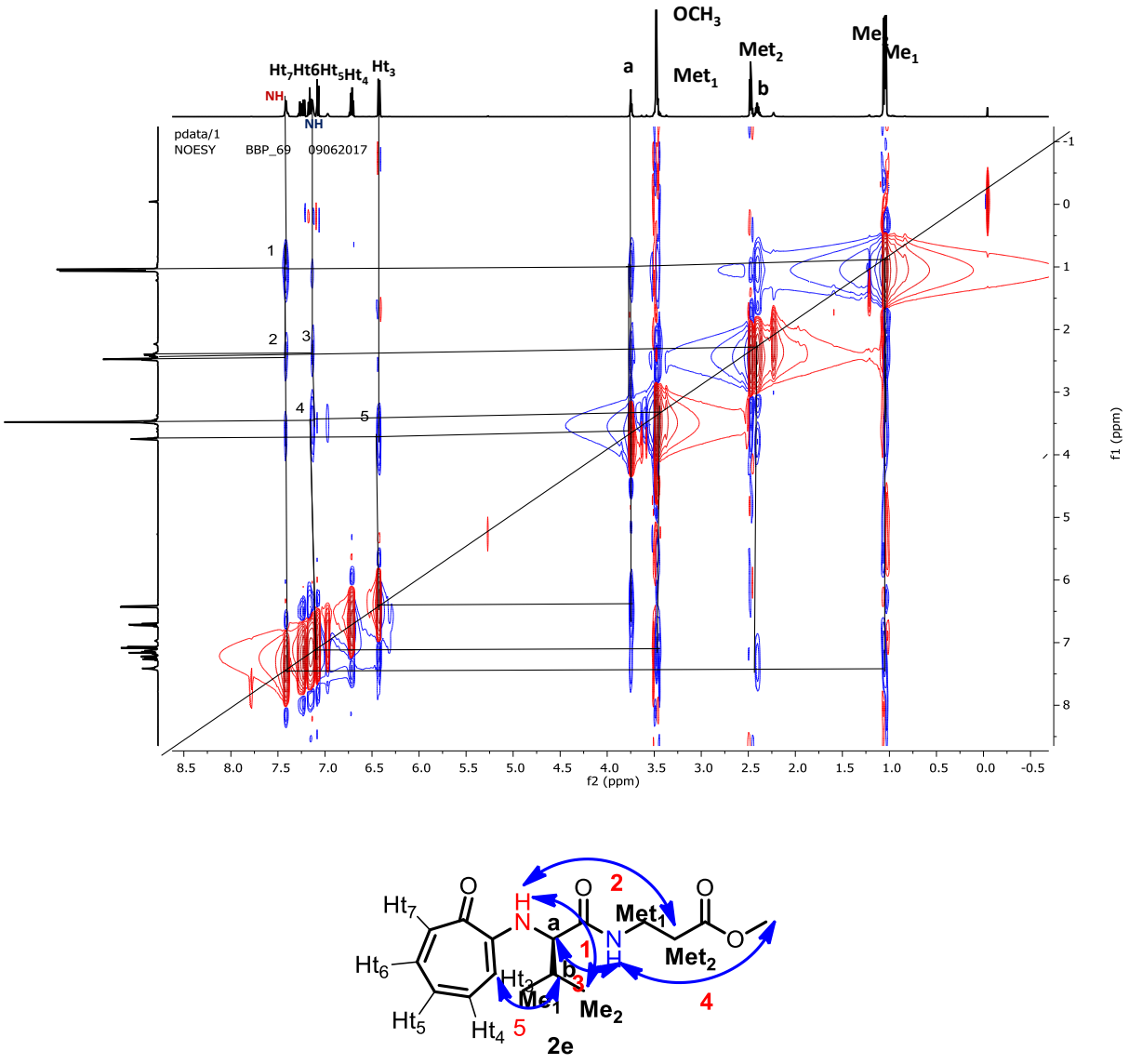


Fig. S52:^{1}H-^{1}H NOESY spectra of (**2e**) in $CDCl_3$

29. ^{1}H-^{1}H COSY and NOESY 2D NMR spectrum of dipeptide (**2j**)

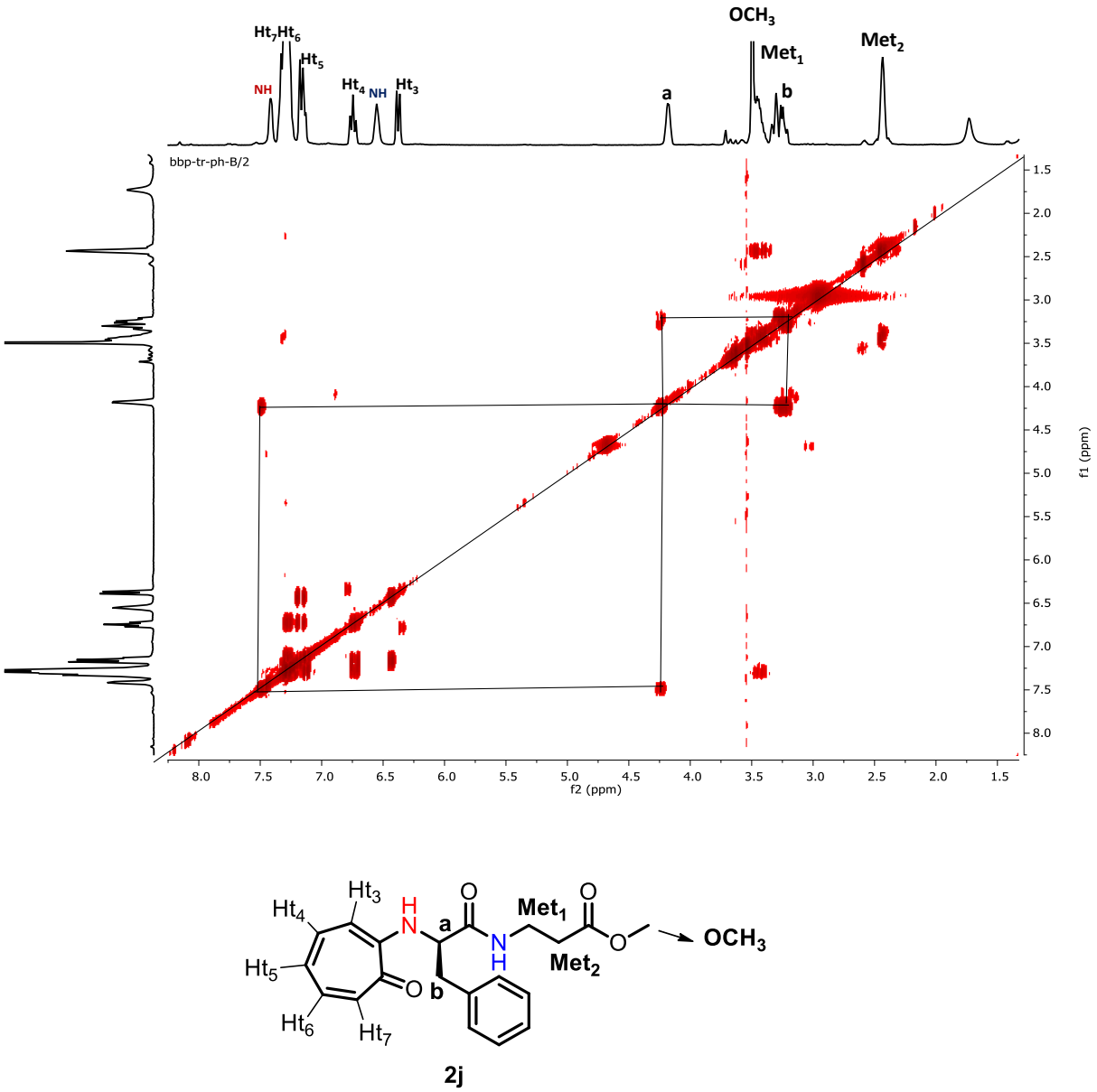
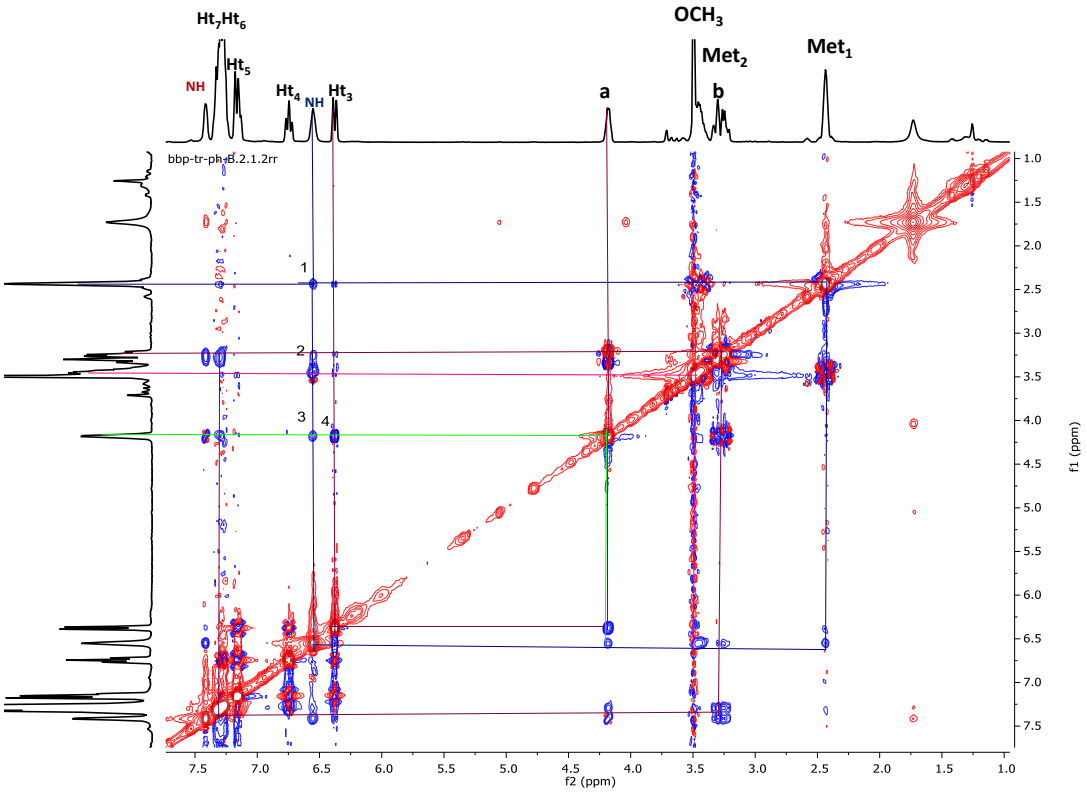


Fig. S53:^{1}H-^{1}H COSY spectra of (**2j**) in $CDCl_3$



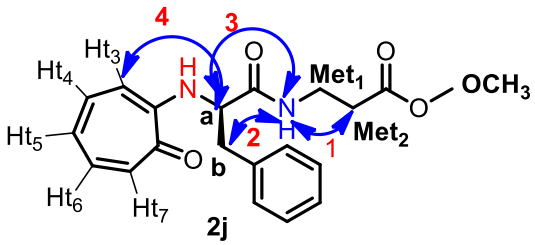


Fig. S54:^{1}H-^{1}H NOESY spectra of (**2j**) in $CDCl_3$

19. ^{1}H-^{1}H COSY and NOESY 2D NMR spectrum of tripeptide (**3d**)

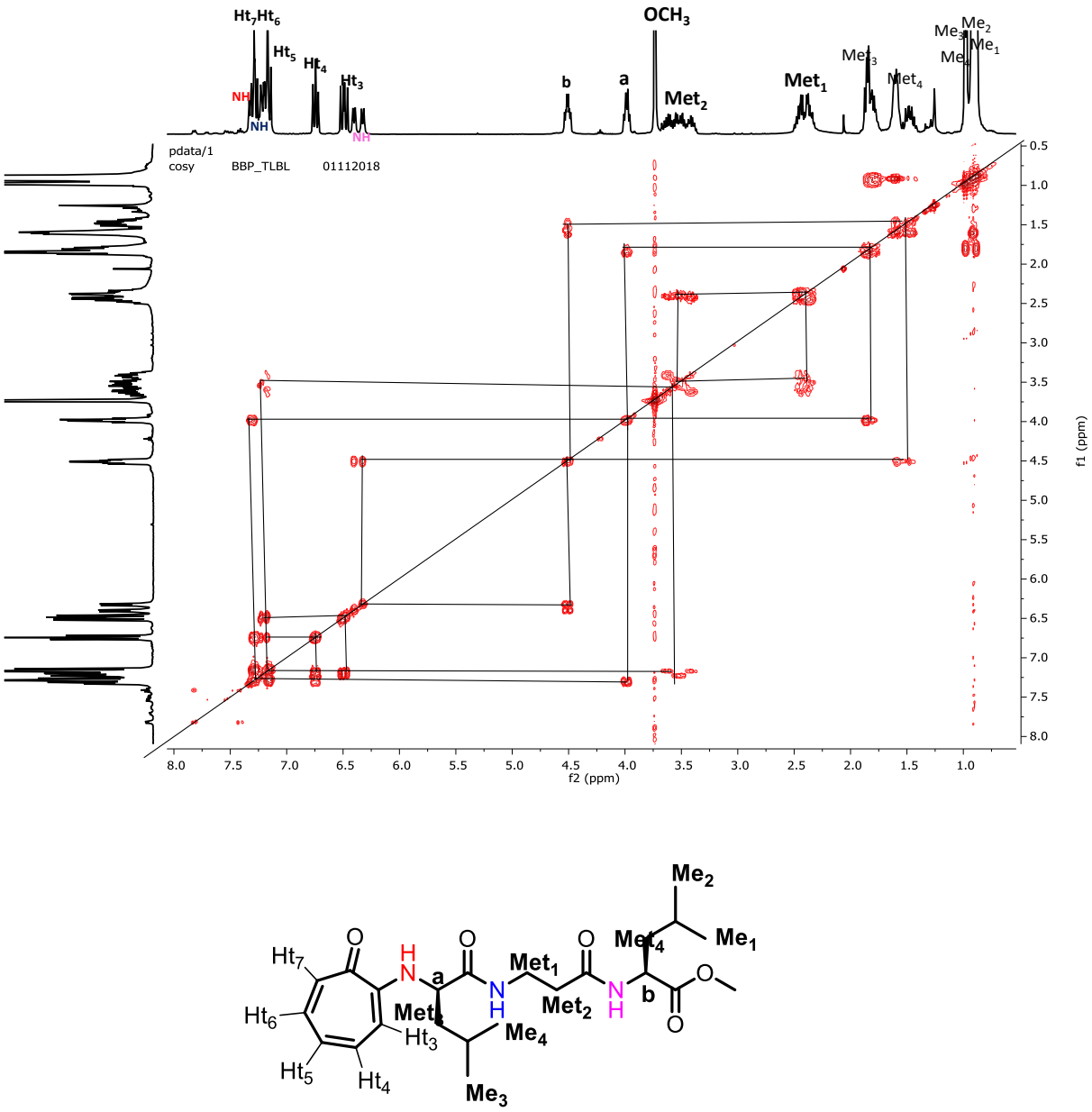


Fig. S55:^{1}H-^{1}H COSY spectra of (**3d**) in $CDCl_3$

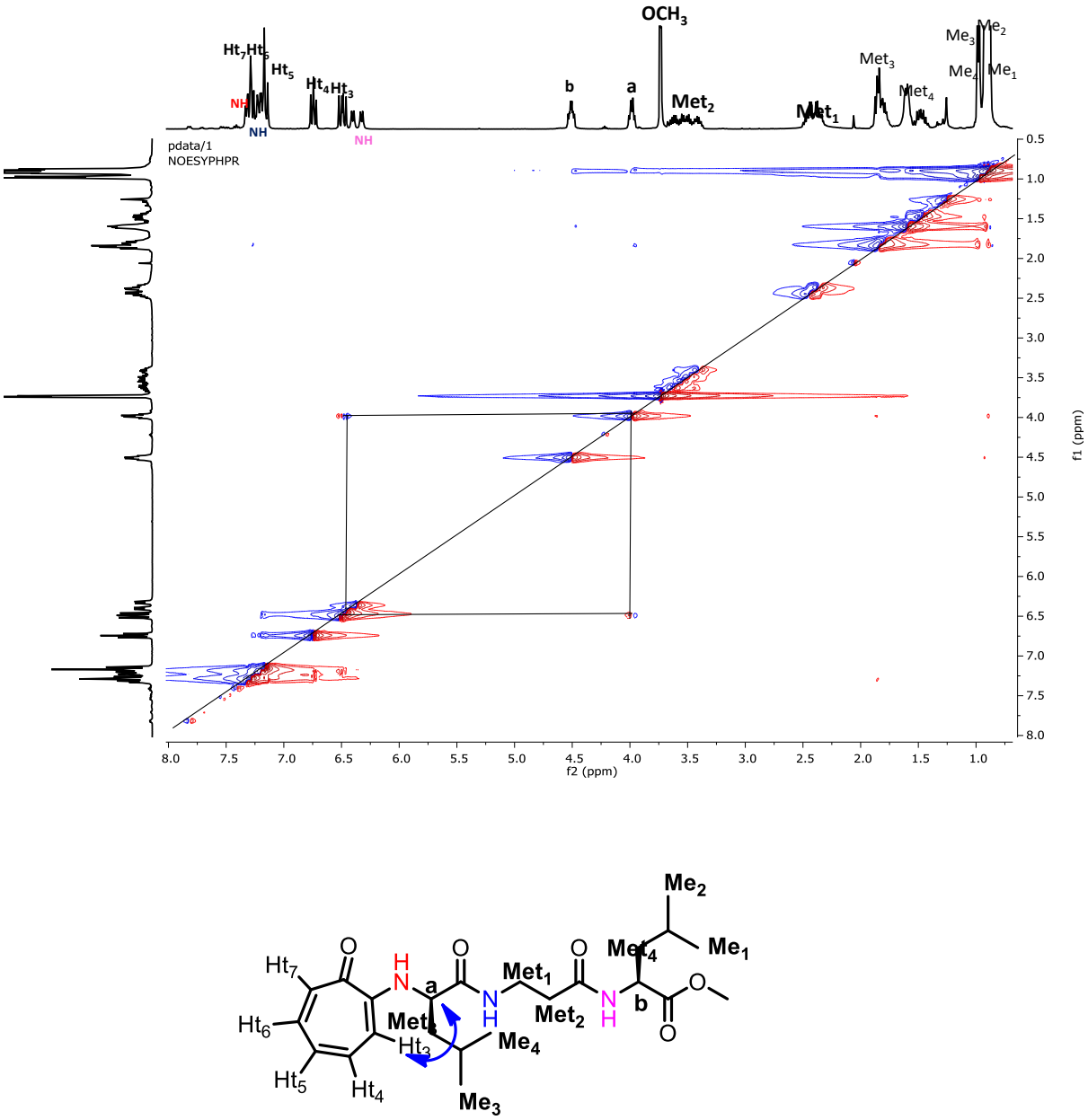
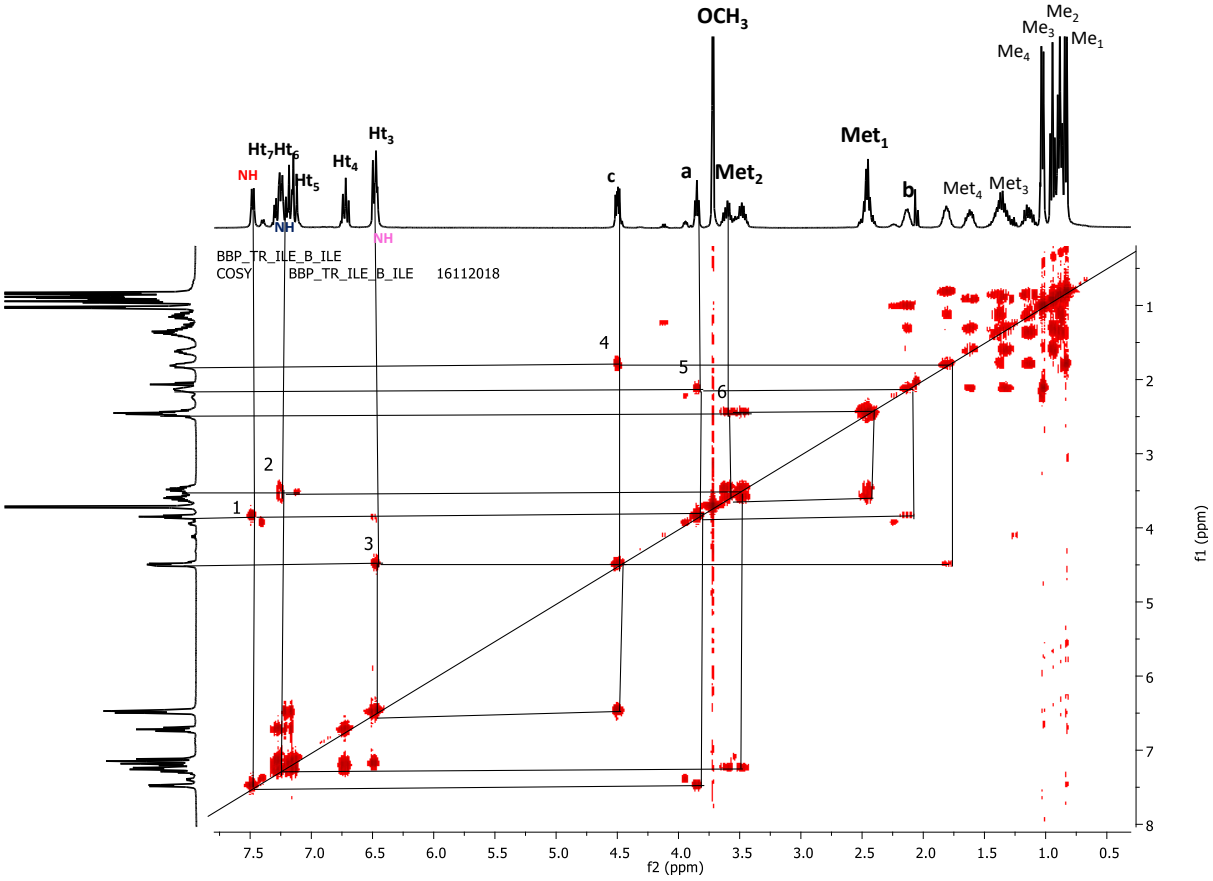


Fig. S56:^{1}H-^{1}H NOESY spectra of (**3d**) in $CDCl_3$

20. ^{1}H-^{1}H COSY and NOESY 2D NMR spectrum of tripeptide (**3e**)



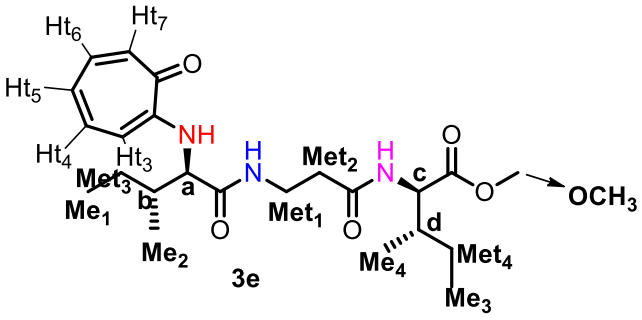


Fig. S57:^{1}H-^{1}H COSY spectra of (**3e**) in $CDCl_3$

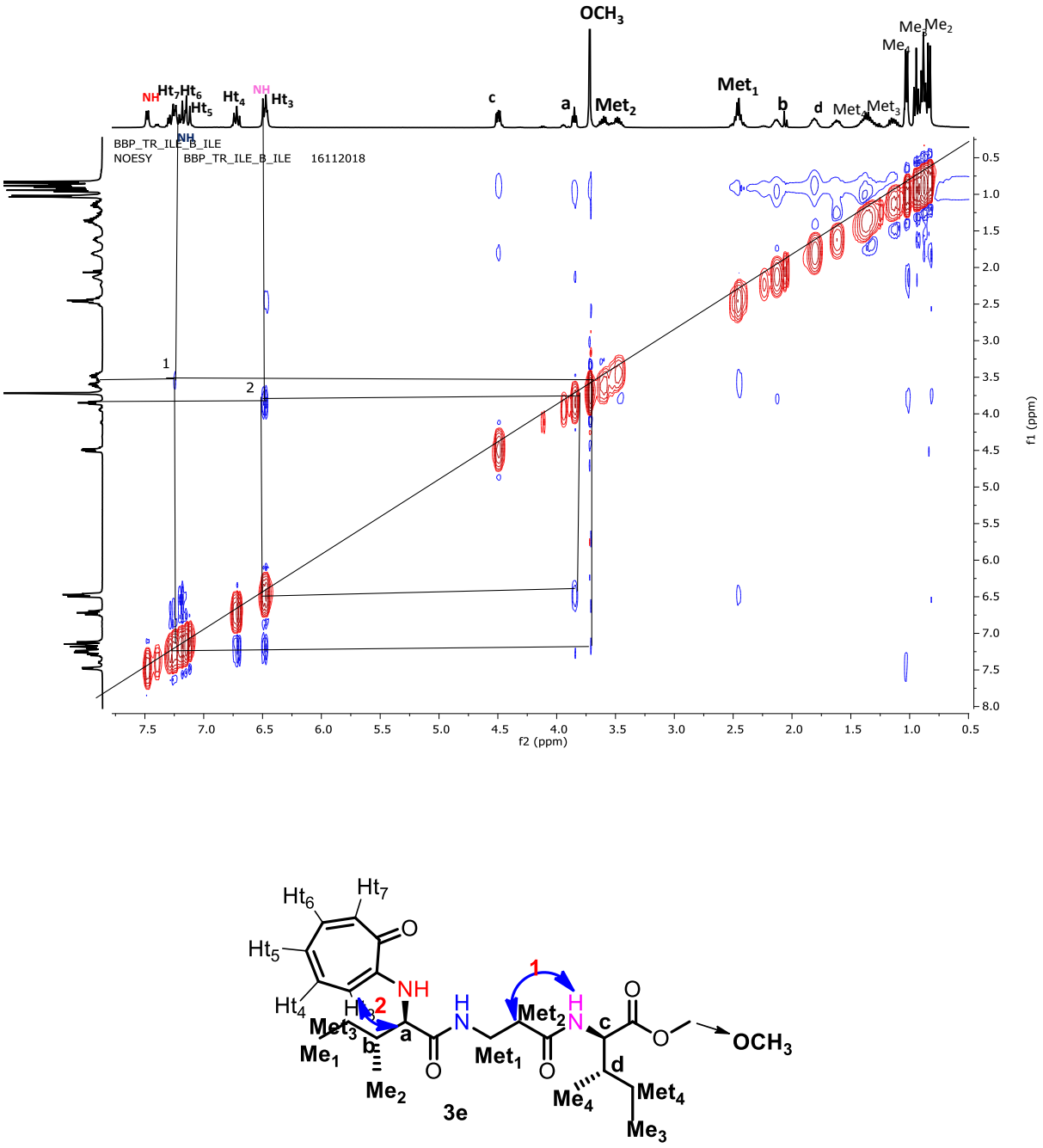


Fig. S58:^{1}H-^{1}H NOESY spectra of (**3e**) in $CDCl_3$

21. DMSO-d6 titration experiments by ^{1}H-NMR of peptides in $CDCl_3$

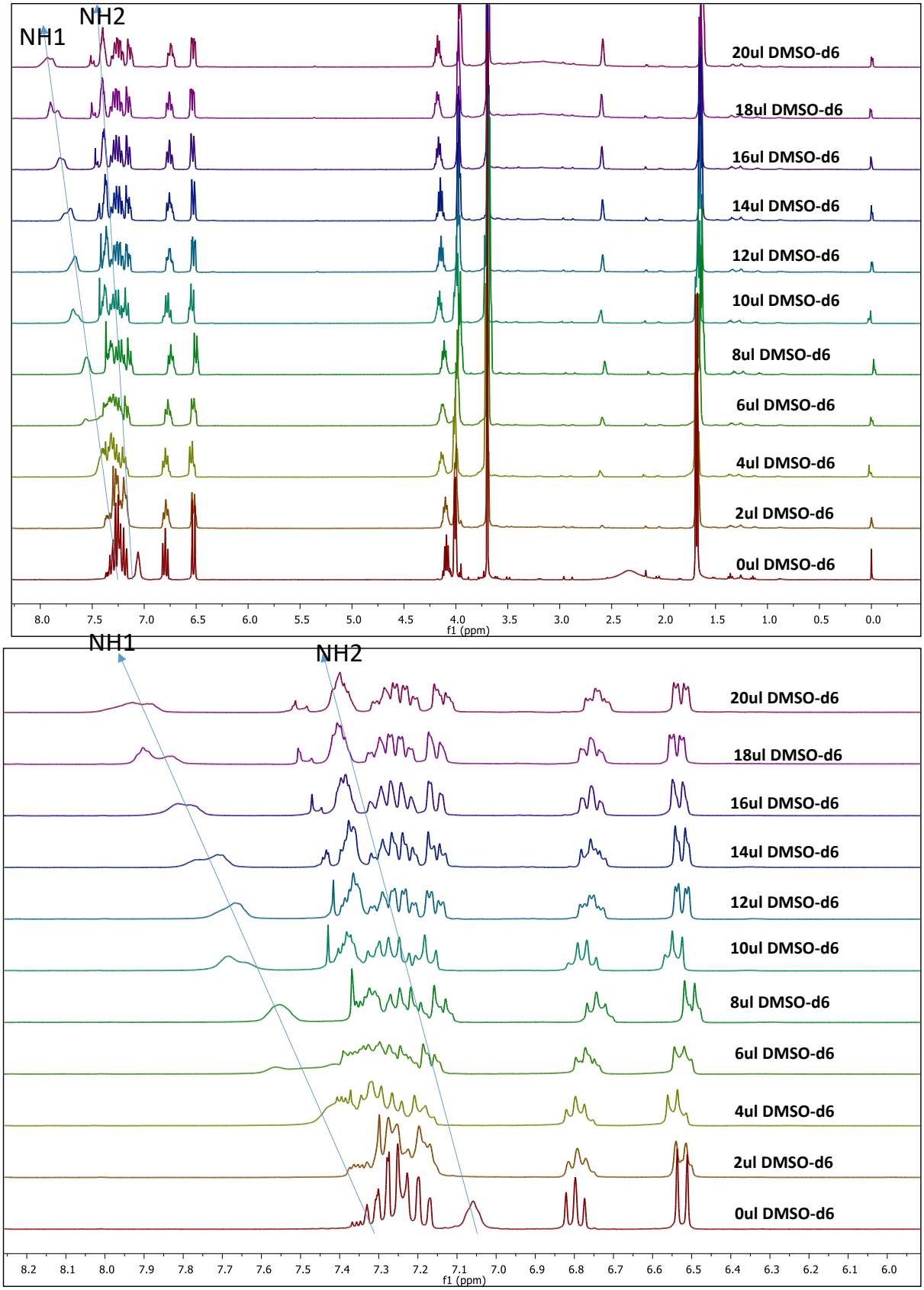
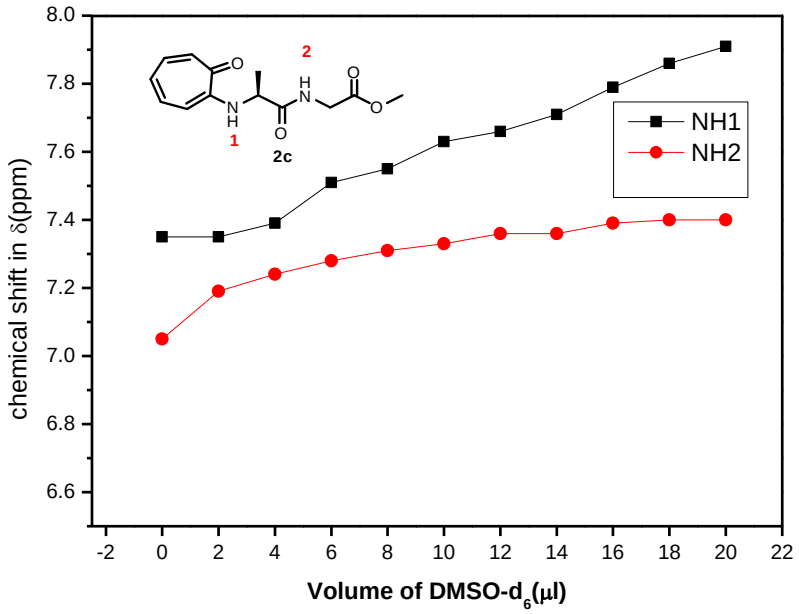
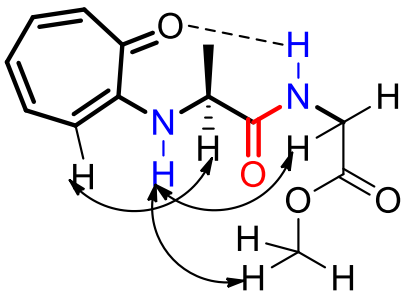


Fig. S59: Experiments by ^{1}H-NMR of DMSO-d6 titration of (**2c**) $CDCl_3$ & its expanded spectral region.



uL	0	2	4	6	8	10	12	14	16	18	20
NH_1	7.33	7.35	7.39	7.51	7.55	7.63	7.66	7.71	7.79	7.86	7.91
NH_2	7.05	7.19	7.24	7.28	7.31	7.33	7.36	7.36	7.39	7.40	7.40



(NOE and weak intramolecular Hydrogen bonding)

Fig. S60: DMSO-d6 titration profile of (**2c**) in $CDCl_3$

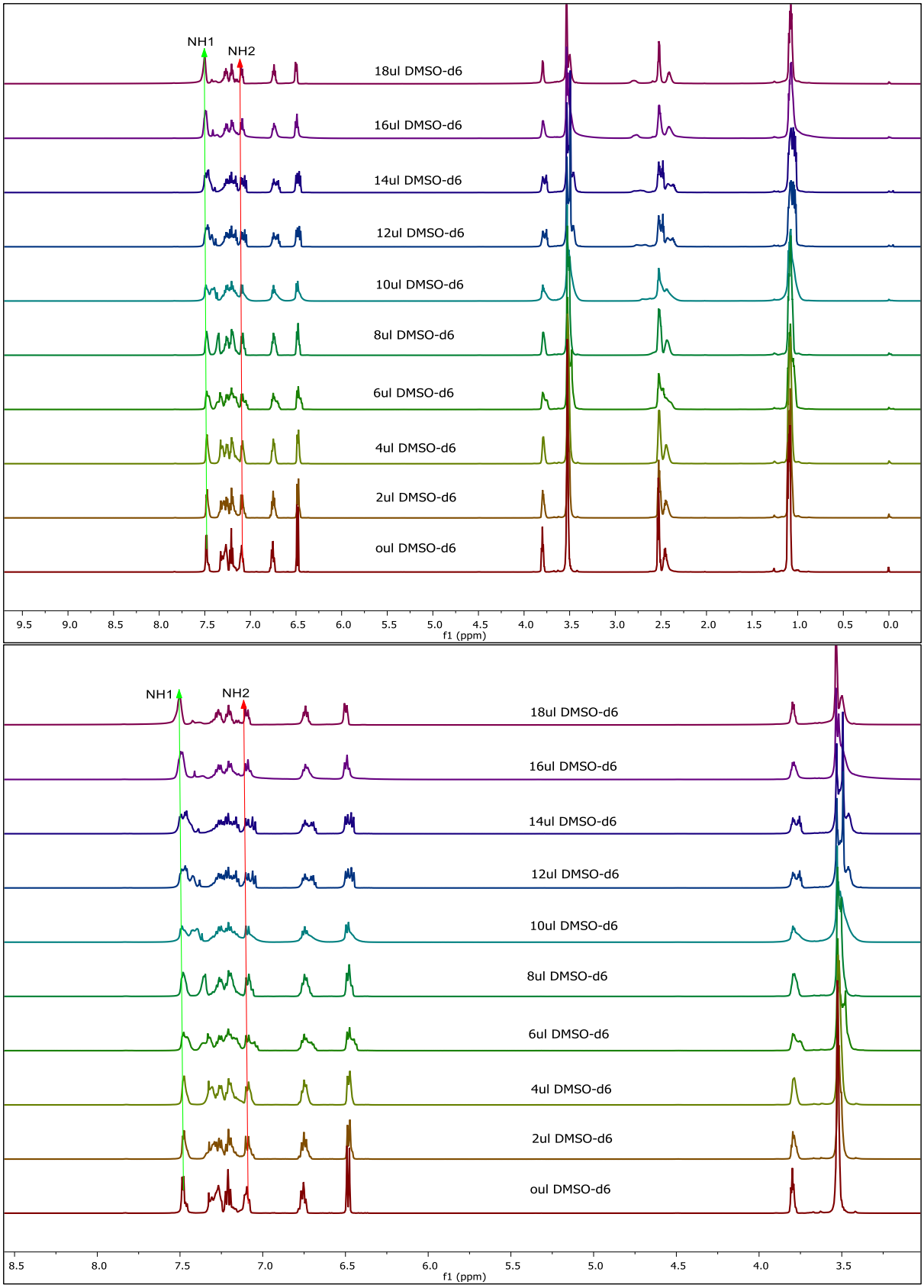
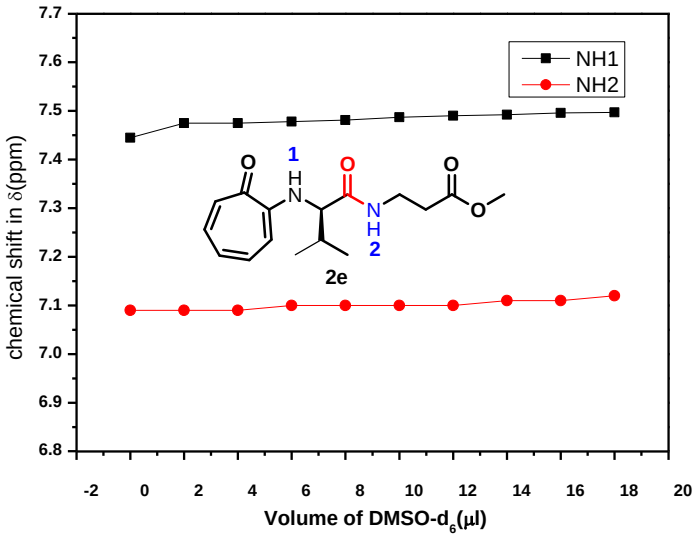
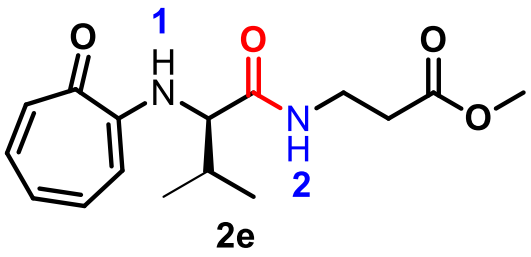
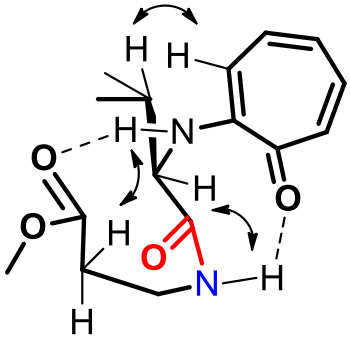


Fig. S61: Experiments by ^{1}H-NMR of DMSO-d6 titration of (**2e**) $CDCl_3$ & its expanded spectral region.







(NOE and possible Intramolecular Hydrogen bonding in tr-di-peptide (**2e**)

uL	0	2	4	6	8	10	12	14	16	18
NH_1	7.44	7.47	7.47	7.47	7.48	7.48	7.98	7.49	7.49	7.49
NH_2	7.09	7.09	7.09	7.10	7.10	7.10	7.10	7.11	7.11	7.12

Fig. S62: DMSO-d6 titration profile of (**2e**) in $CDCl_3$

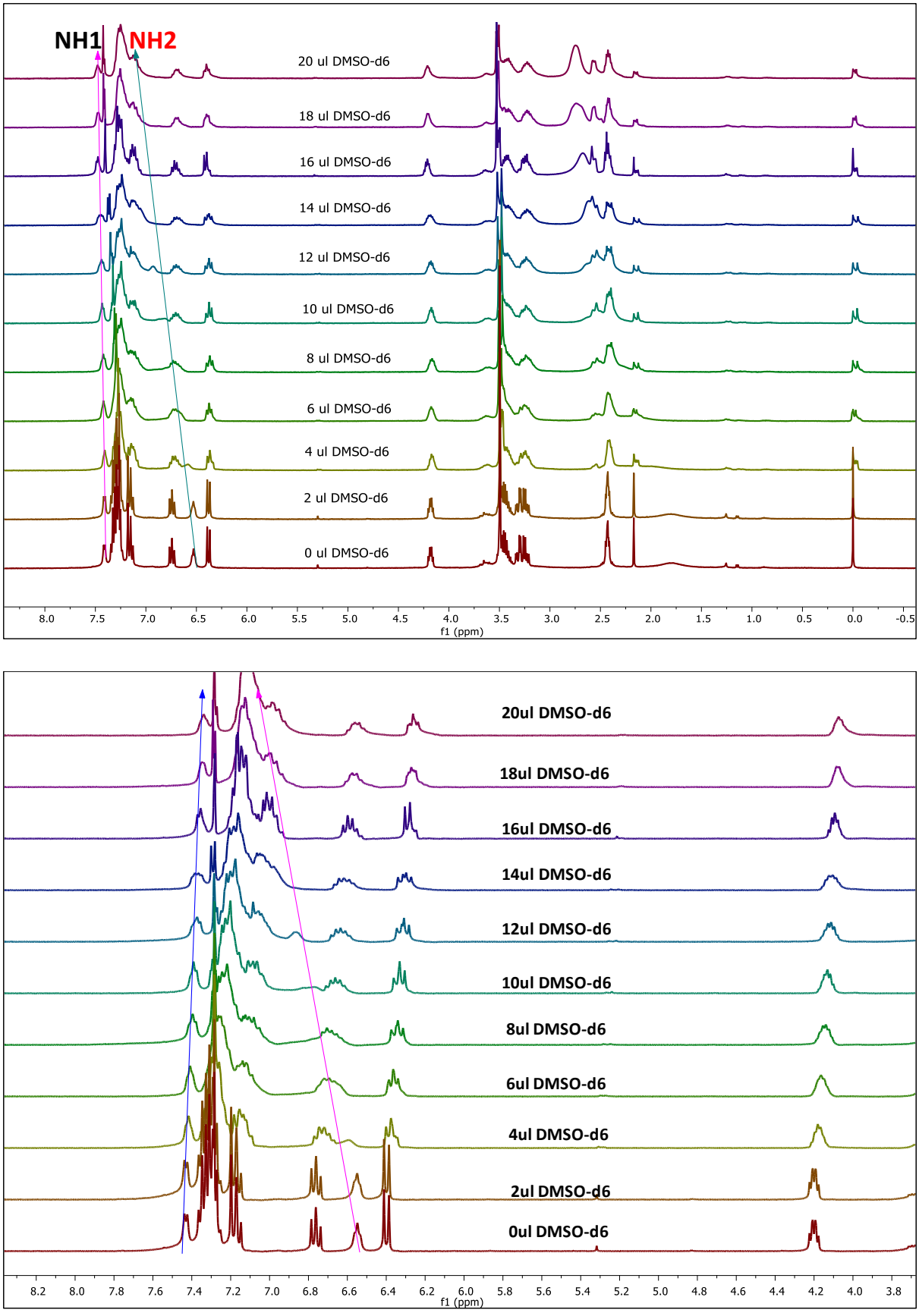
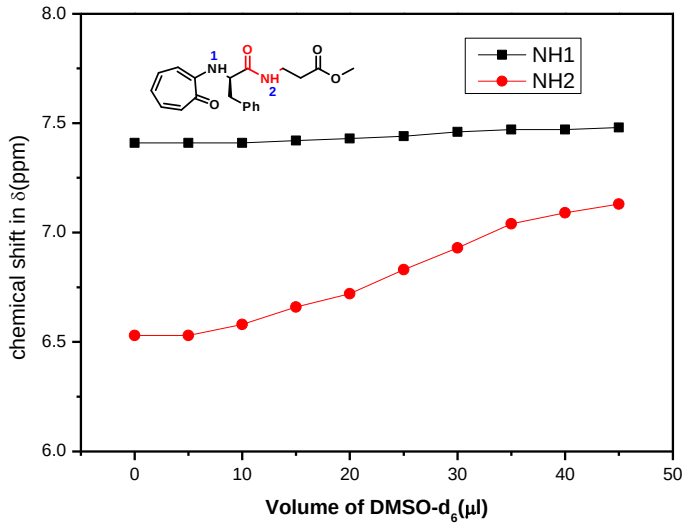
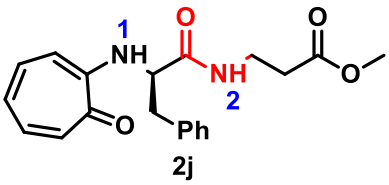
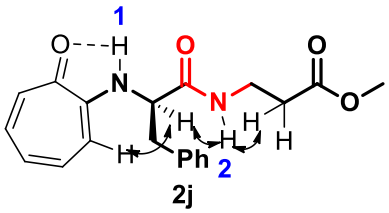


Fig. S63: Experiments by ^{1}H-NMR of DMSO-d6 titration of (**2j**) $CDCl_3$ & its expanded spectral region.





uL	0	2	4	6	8	10	12	14	16	18	20
NH_1	7.41	7.41	7.41	7.42	7.43	7.44	7.46	7.47	7.47	7.47	7.48
NH_2	6.53	6.53	6.58	6.66	6.72	6.83	6.83	6.93	7.04	7.09	7.13



(NOE and possible Intramolecular Hydrogen bonding in tr-di-peptide (**2j**)

Fig. S64: DMSO-d6 titration profile of (**2j**) in $CDCl_3$

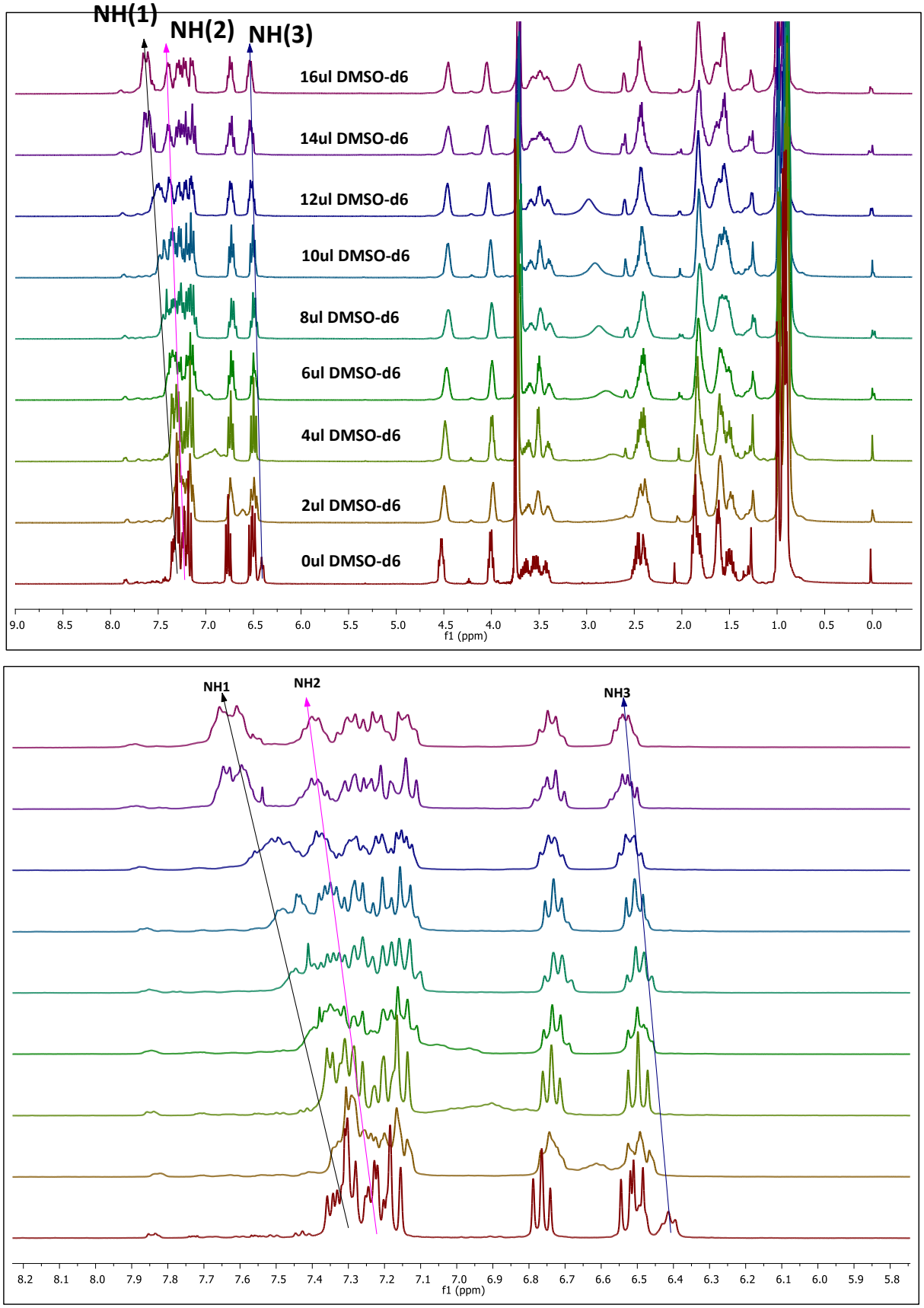
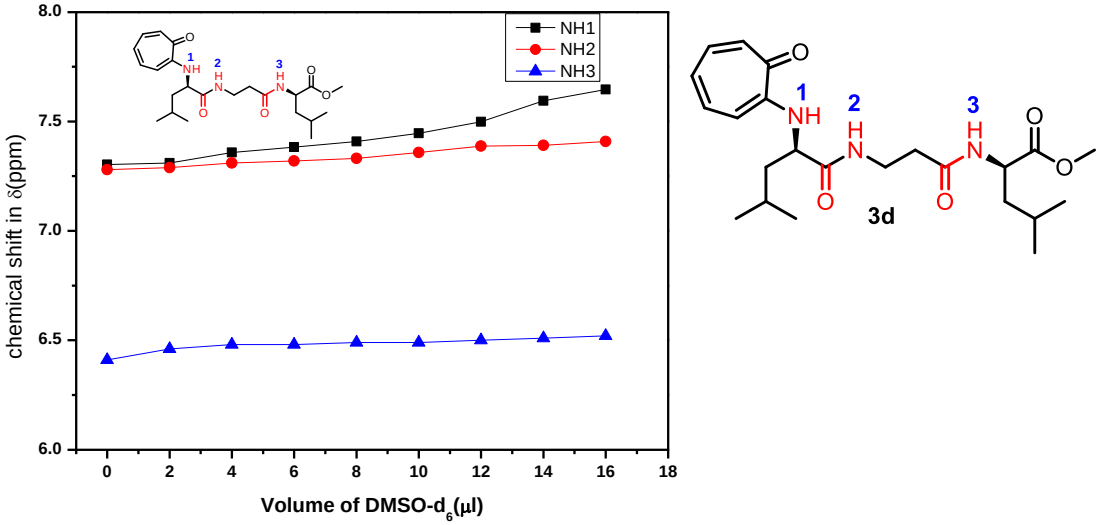
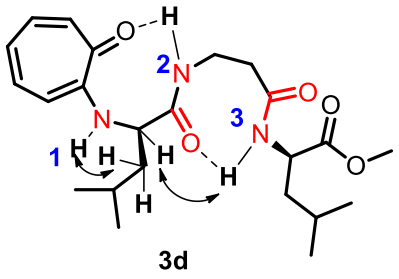


Fig. S65: Experiments by ^{1}H-NMR of DMSO-d6 titration of (**3d**) $CDCl_3$ & its expanded spectral region.



uL	0	2	4	6	8	10	12	14	16
NH_1	7.30	7.31	7.35	7.38	7.40	7.44	7.49	7.59	7.64
NH_2	7.28	7.28	7.31	7.31	7.33	7.35	7.38	7.39	7.40
NH3	6.41	6.46	6.48	6.48	6.49	6.49	6.50	6.51	6.52



NOE and Possible Intramolecular Hydrogen Bonding NH-2/NH-3 1ith troponyl carbonyl in **3d**

Fig. S66: DMSO-d6 titration profile of (**3d**) in $CDCl_3$

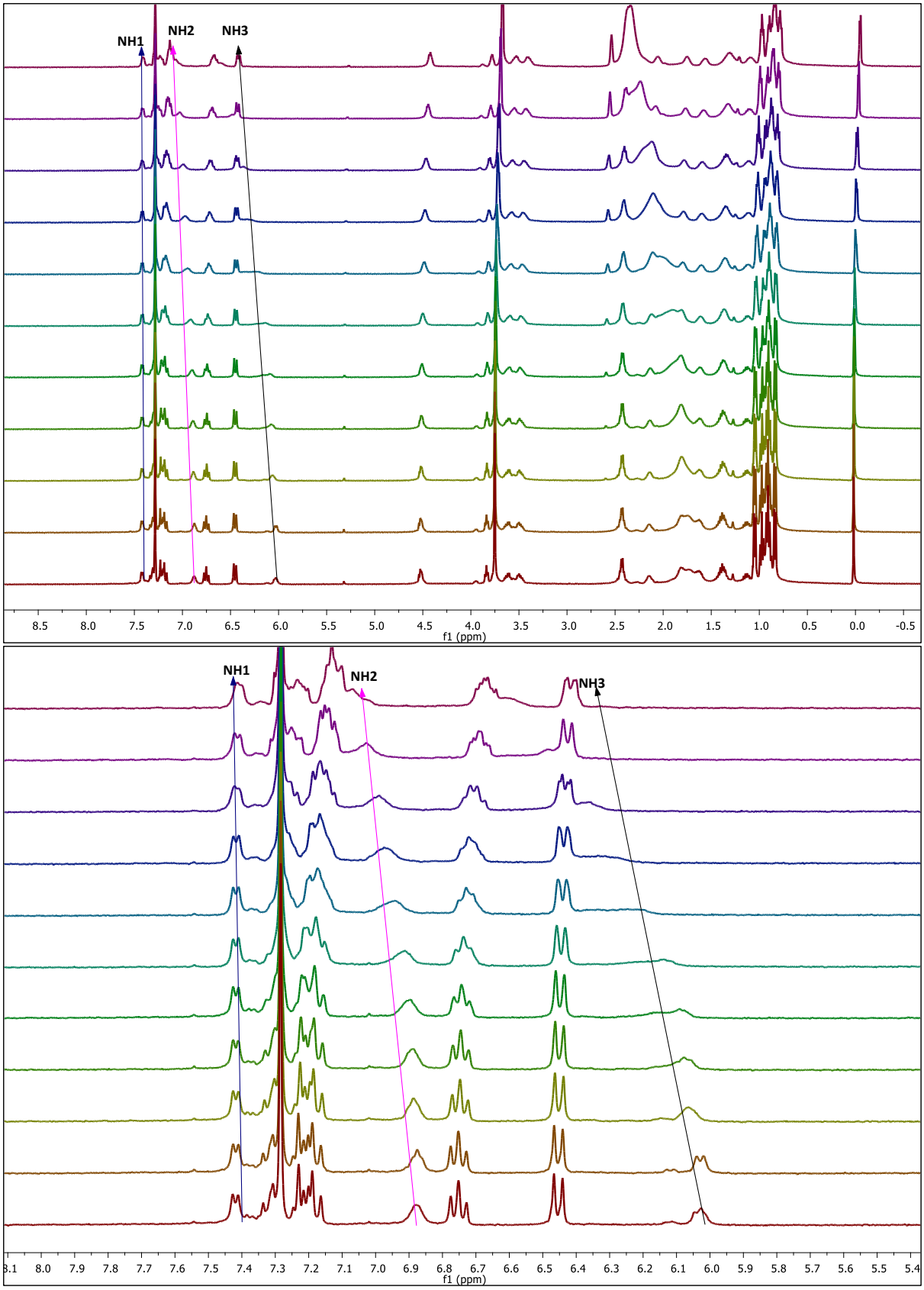
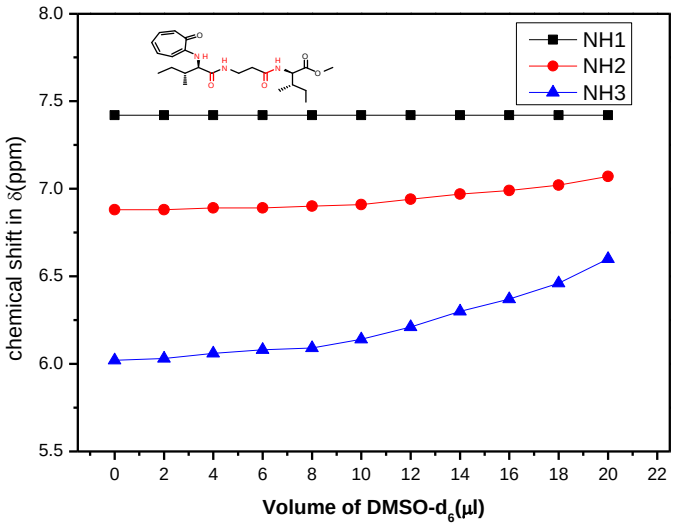
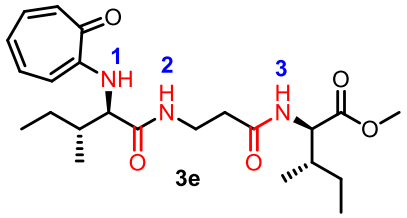
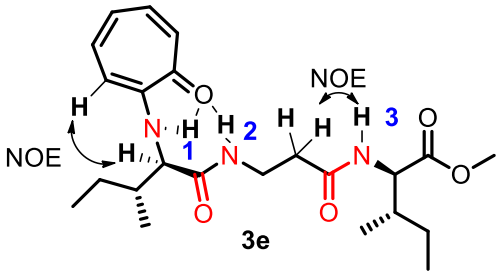


Fig. S67: Experiments by ^{1}H-NMR of DMSO-d6 titration of (**3e**) $CDCl_3$ & its expanded spectral region.





uL	0	2	4	6	8	10	12	14	16	18	20
NH_1	7.42	4.42	7.42	7.42	7.42	7.42	7.42	7.42	7.42	7.42	7.42
NH_2	6.88	6.88	6.89	6.89	6.90	6.91	6.94	6.97	6.99	7.02	7.02
NH3	6.02	6.03	6.06	6.08	6.09	6.14	6.21	6.30	6.37	6.46	6.66



(NOE and Possible Intramolecular Hydrogen Bonding NH-1/NH-2 1ith troponyl carbonyl in **3e**)

Fig. S68: DMSO-d6 titration profile of (**3e**) in $CDCl_3$

22. Crystal Structure determination:

Single crystal of (**2a/2b/2d/2e/2f/j**) were grown by slow diffusion of solution in Dichloromethane into hexane, followed by evaporation under atmospheric condition. The crystal data of all peptide were collected on a Bruker Kappa APEX II CCD diffractometer at 293 K and a Rigaku Oxford diffractometer at 293 K respectively. Selected data collection parameters and other crystallographic results are summarized in SI. The program package SHELXTL[1] and Olex2 was used for structure solution and packing diagram carried out by DIAMOND-3.2 software.

CCDC 1889029-1889034 contain the supplementary crystallographic data for **2a/2b/2d/2e/2f/2j**. These data can be obtained free of charge via https://www.ccdc.cam.ac.uk/data

Table S1: Crystallographic table

compounds	(**2a**)	(**2b**)	(**2d**)	(**2e**)	(**2f**)	(**2j**)
Identification code	CCDC 1889029	CCDC 1889030	CCDC 1889031	CCDC 1889033	CCDC 1889034	CCDC1889032
Empirical formula	$C_{12}H_{14}N_2O_4$	$C_{13}H_{16}N_2O_4$	$C_{15}H_{20}N_2O_4$	$C_{16}H_{22}N_2O_4$	$C_{13}H_{16}N_2O_4$	$C_{21}H_{27}N_5O_4$
Formula weight	250.25	264.28	292.33	306.35	264.28	357.48
Temperature/k	293(2)	296(2)	296(2)	296(2)	293(2)	293(2)
Crystal system	monoclinic	orthorhombic	triclinic	triclinic	monoclinic	triclinic
Space group	$P2_1/n$	$P2_12_12_1$	P-1	P-1	$P2_1/c$	P-1
A/å	13.8569(3)	6.8111(3)	7.8029(5)	8.2453(2)	13.8433(12)	9.5702(7)
B/å	4.87510(10)	7.3881(3)	10.6573(5)	9.1188(3)	11.6707(8)	9.7242(7)
C/å	18.1860(4)	27.5932(10)	10.8703(5)	11.2435(4)	8.3343(7)	11.5579(6)
α/°	90.00	90	115.740(4)	77.692(2)	90.00	72.878(6)
β/°	98.164(2)	90	99.231(3)	86.278(2)	100.376(7)	79.720(6)
γ/°	90.00	90	103.722(4)	86.449(2)	90.00	68.987(7)
Volume/å^3	1216.08(5)	1388.52(10)	754.32(7)	823.19(5)	1324.48(18)	956.37(11)
Z	4	4	2	2	4	2
ρ_{calc}g/cm^3	1.367	1.264	1.287	1.236	1.325	1.241
M/mm^{-1}	0.872	0.095	0.094	0.089	0.828	0.611
F(000)	528.0	560.0	312.0	328.0	560.0	384.0
Crystal size/mm^3	0.29 × 0.28 × 0.24	0.27 × 0.25 × 0.22	0.27 × 0.24 × 0.20	0.27 × 0.24 × 0.23	0.3 × 0.27 × 0.08	0.29 × 0.25 × 0.21
Radiation	CuKα (λ = 1.54184)	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)	CuKα (λ = 1.54184)	CuKα (λ = 1.54184)
2θ range for data collection/°	7.52 to 154.58	2.952 to 50.9	4.362 to 51.998	3.712 to 56.702	9.98 to 154.12	8.04 to 99.96
Index ranges	-14 ≤ h ≤ 17, -5 ≤ k ≤ 5, -22 ≤ l ≤ 23	-8 ≤ h ≤ 8, -7 ≤ k ≤ 8, -33 ≤ l ≤ 33	-9 ≤ h ≤ 9, -13 ≤ k ≤ 12, -13 ≤ l ≤ 13	-10 ≤ h ≤ 11, -12 ≤ k ≤ 12, -15 ≤ l ≤ 14	-15 ≤ h ≤ 17, -13 ≤ k ≤ 14, -10 ≤ l ≤ 10	-9 ≤ h ≤ 9, -9 ≤ k ≤ 9, -11 ≤ l ≤ 11
Reflections collected	9626	17437	10451	13278	9030	8659

Independent reflections	2482 [R_{int} = 0.0522, R_{sigma} = 0.0409]	2559 [R_{int} = 0.0561, R_{sigma} = 0.0396]	2967 [R_{int} = 0.0686, R_{sigma} = 0.0723]	4075 [R_{int} = 0.0203, R_{sigma} = 0.0198]	2695 [R_{int} = 0.0705, R_{sigma} = 0.0726]	1971 [R_{int} = 0.0847, R_{sigma} = 0.0770]
Data/restraints/ parameters	2482/0/164	2559/0/173	2967/0/190	4075/0/202	2695/0/173	1971/0/237
Goodness-of-fit on f^2	1.067	1.015	0.969	1.040	1.067	1.188
Final r indexes [i>=2σ (i)]	R_1 = 0.0420, wR_2 = 0.1202	R_1 = 0.0420, wR_2 = 0.0923	R_1 = 0.0505, wR_2 = 0.1080	R_1 = 0.0437, wR_2 = 0.1170	R_1 = 0.0767, wR_2 = 0.2220	R_1 = 0.0747, wR_2 = 0.2141
Final r indexes [all data]	R_1 = 0.0480, wR_2 = 0.1240	R_1 = 0.0808, wR_2 = 0.1083	R_1 = 0.0993, wR_2 = 0.1226	R_1 = 0.0580, wR_2 = 0.1289	R_1 = 0.1142, wR_2 = 0.2996	R_1 = 0.0928, wR_2 = 0.2237
Largest diff. Peak/hole / e $å^{-3}$	0.17/-0.18	0.17/-0.14	0.18/-0.22	0.20/-0.16	0.24/-0.41	0.33/-0.22

23. Circular Dichroism (CD) Spectra.

CD experiment were recorded in degassed HPLC grade solvent CH_3OH And CH_3CN at 20 ^{0}C. CD spectra recorded from 310-190 nm with peptide concentrations of 0.1 mM.CD data is collected with following parameters, Data pitch 2 nm, DIT 2 sec, Bandwidth 2nm, Scanning speed 100 nm/min.

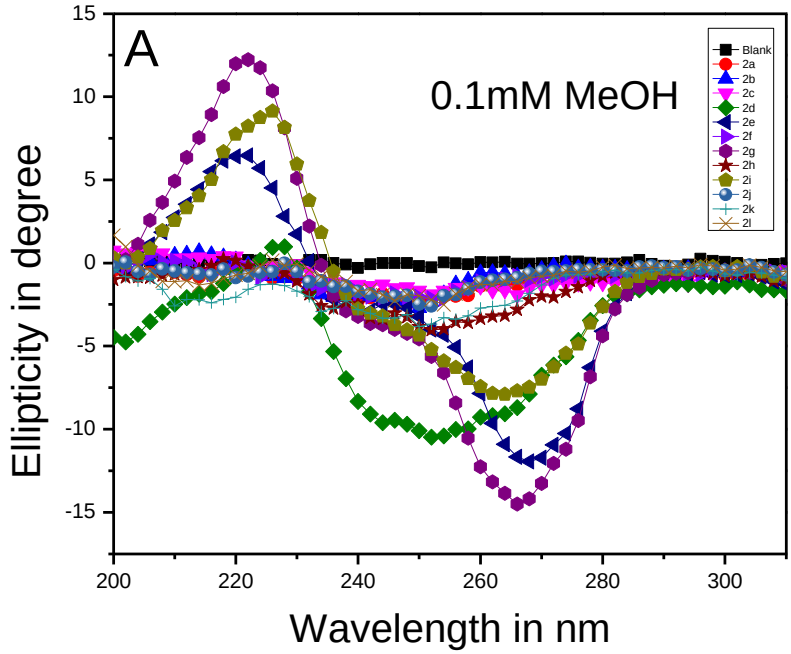


Fig. S69: CD spectra of peptide (**2a-2l**) in Methanol (MeOH)

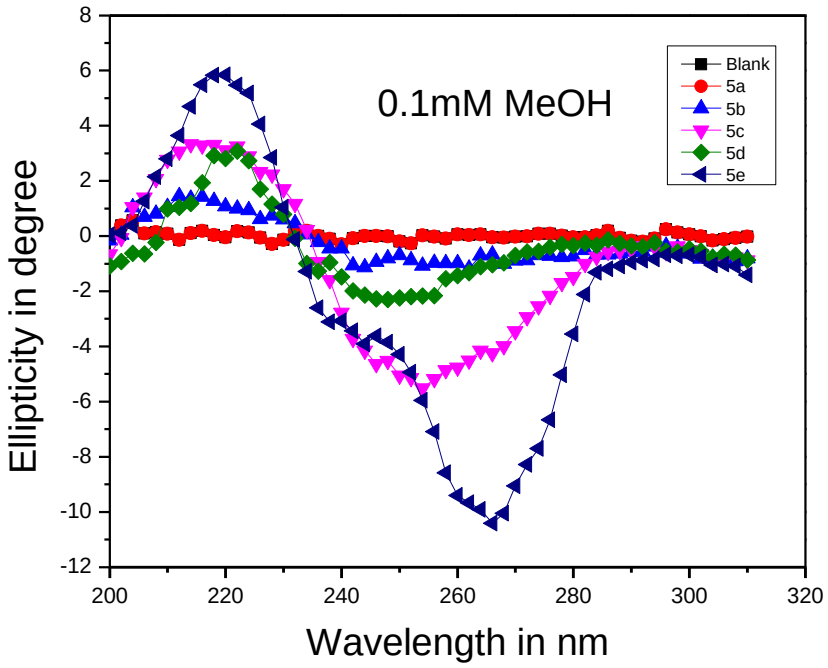


Fig. S70: CD spectra of *tri*-peptide (**3a-3e**) in Acetonitrile (MeOH)

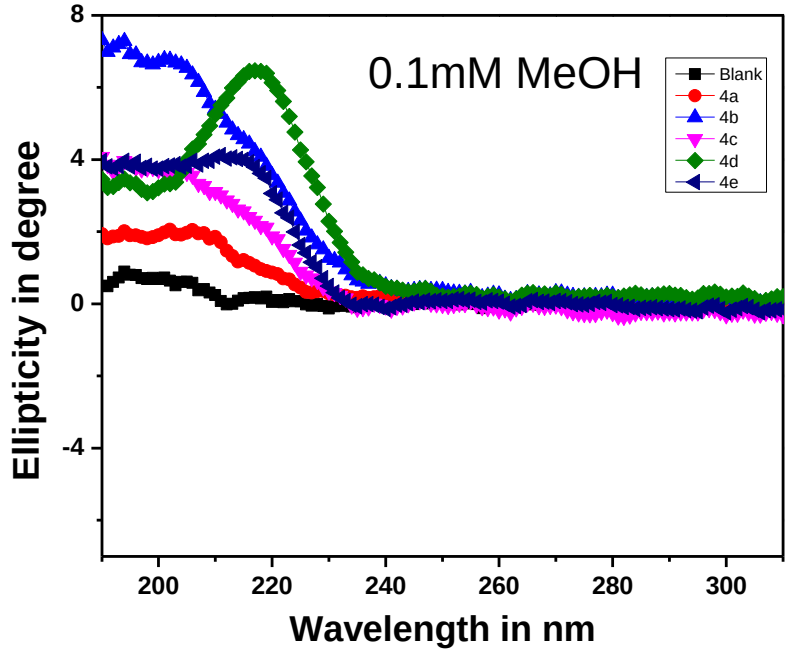


Fig. S71: CD spectra of peptide (**4a-4e**) in Methanol (MeOH)

24. References

1. synthesis and photophysical studies of difluoro boron complexes from 2-aminotropone scaffolds through N, O-chelation. *Org. Biomol. Chem.* **2019,** *17* (26), 6497-6505.
2. Instability of Amide Bond Comprising the 2-Aminotropone Moiety: Cleavable under Mild Acidic Conditions. *Org. Lett.* **2015,** *17* (16), 3948-3951